Stereoselective Radical Transformations with In Situ-Generated Aryl and Alkyl Diazomethanes via Co(II)-Based Metalloradical Catalysis

by

Yong Wang

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Advisor: Professor X. Peter Zhang

Among recent advances in devising different strategies for stereoselective homolytic reactions, metalloradical catalysis (MRC) has emerged as a conceptually new approach for controlling stereoselectivity of radical reactions. As stable metalloradicals, cobalt(II) complexes of D_2-symmetric chiral amidoporphyrins [Co(D_2-Por)] have proven to be effective catalysts for homolytically activating a series of diazo compounds to generate α-Co(III)-alkyl radicals for various C-centered radical transformations with well-confined reactivity and selectivity. Nevertheless, the applications of donor-, donor/donor- and alkyl diazo compounds have been largely underdeveloped. This dissertation mainly focuses on how the chemistry of these types of diazo compounds was initiated by using commonly available aldehyde-derived sulfonylhydrazones as diazo surrogates. In the context of Co(II)-MRC, in situ-generated diazo compounds can be effectively activated for various asymmetric radical transformations, including intermolecular radical cyclopropanation of alkenes and intramolecular radical alkylation of C–H bonds.

First, as a proof of concept, we have demonstrated the feasibility of using aryl aldehyde-derived sulfonylhydrazones as new radical precursors for diastereo- and enantioselective radical cyclopropanation of alkenes, and proven that the diazo in situ-generation protocol is well compatible with the catalytic radical process. Second, we have expanded the application of Co(II)-based MRC to a new territory by employing aliphatic diazo compounds for asymmetric cyclopropanation. The system is highlighted by the excellent enantioselectivity together with remarkable *cis*-selectivity. Finally, with the utilization of linear aliphatic aldehyde sulfonylhydrazones as diazo precursors, we have presented a new radical cyclization mode, involving hydrogen atom abstraction and radical substitution, for enantioselective synthesis of common five-membered rings via radical C–H alkylation. The system would offer a new retrosynthetic paradigm for construction of ring structures, where C–C bond can be disconnected as common C=O and C–H units of linear aldehydes.

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DEDICATED TO:

I dedicate this dissertation to my dearest wife, Xin Wen, who has accompanied me with full support and went through all the difficulties and challenges together with me during the past years. I am truly thankful for having you in my life. Thank you for making me feel that I am the luckiest man in the world every single day! Also, thank you for giving birth to our most beautiful and lovely daughter, Siyue Wang, who is also the greatest inspiration that I am fighting for our life and whom I can't force myself to stop loving. Dad is so proud of you growing and learning so fast in the past 5 years.

This work is also dedicated to my parents, Qilai Wang and Zhigen Zheng (who have always loved me unconditionally and whose good examples have taught me to work hard for the things that I aspire to achieve; I am born lucky to have you as my parents), my mother-in-law, Aiwen Guo (who has given me her unconditional love as her own son), my father-in-law in heaven, Xiuchun Wen (who treated me exactly like his boy and passed off their daughter to me with full trust), my sister, Weiwei Wang (who loves me so much and always supports me without a hesitation). Thank you all for taking care of Siyue with your unconditional love along her growing.

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Last but not least, thank all my friends at Boston College and University of South Florida for being so helpful and making my journey to become a scientist more joyful.

TABLE OF ABBREVIATIONS

Por: porphyrin

DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzo quinone

Xanthphos: 4,5-Bis(diphenylphosphino)-9, 9-dimethylxanthene

THF: tetrahydrofuran

DMAP: 4-dimethylaminopyridine

MeO: methoxy

Me: methyl

^{t}Bu: tert-butyl

Et: ethyl

Ar: aryl

Ph: phenyl

TPP: tetraphenyl porphyrin

TEMPO: 2,2,6,6-Tetramethyl-1-piperidinyloxy

Su: succinimidyl

Gly: glycine

Ala: alanine

PhMe: toluene

EtOAc: ethyl acetate

Ts: 4-methylphenyl sulfonyl

NDA: α-nitrodiazoacetate

ENDA: ethyl α-nitrodiazoacetate

CDA: α-cyanodiazoacetate

^{t}BCDA: *tert*-butyl α-cyanodiazoacetate

KDA: α-ketodiazoacetate

FDA: α-formyldiazoacetate

Tris: 2,4,6-triisopropyl phenylsulfonyl

PhH: benzene

Å: angstrom

MRC: metalloradical catalysis

ee: enantiomeric excess

er: enantiomeric ratio

de: diastereomeric excess

dr: diastereomeric ratio

equiv.: equivalent(s)

eq: equation

RT: room temperature

HPLC: high performance liquid chromatography

HRMS: high resolution mass spectrometry

y: yield

IR: infrared spectroscopy

TOF: time of flight

L: ligand

LG: leaving group

ESI: electrospray ionization

EPR: electron paramagnetic resonance

M: molar or metal

NMR: nuclear magnetic resonance

DART: direct analysis in real time

RA: radical addition

HAA: hydrogen atom abstraction

RS: radical substitution

FG: functional group

KIE: kinetic isotope effect

M.S.: molecular sieves

PhCl: chlorobenzene

DCM: dichloromethane

Ar: aryl

PPh_3: triphenyl phosphine

PPY: 4-pyrrolidinopyridine

PhthN: phthalimide

MeOH: methanol

EtOH: ethanol

SiO_2: silica gel

TBME: *tert*-butyl methyl ether

TFA: trifluoroacetic acid

Ac: acetate

Bn: benzyl

het: hetero

PBN: *N*-*tert*-butylnitrone

THF: tetrahydrofuran

^{i}Pr: *iso*-propyl

DMF: dimethylformamide

Et_2O: diethyl ether

DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene

Boc: *tert*-butoxycarbonyl

Boc_2O: di-*tert*-butyldicarbonate

DMSO: dimethyl sulfoxide

Et_3N: triethyl amine

aq: aqueous

CHAPTER 1

STEREOSELECTIVE RADICAL CYCLOPROPANATION REACTIONS OF ALKENES VIA COBALT(II)-BASED METALLORADICAL CATALYSIS

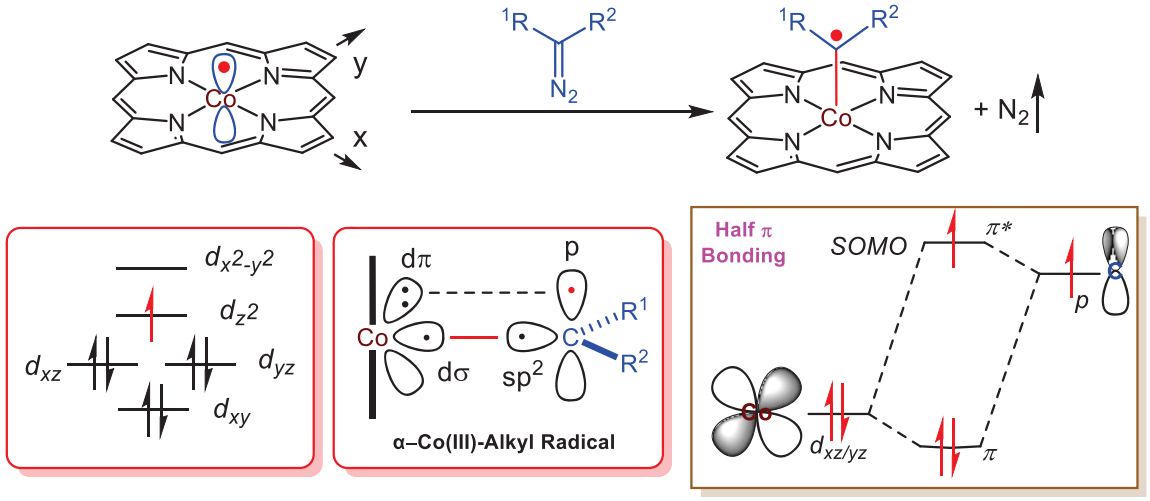
1.1 INTRODUCTION

Carbon-centered radicals, specifically alkyl radicals, have been extensively explored as versatile intermediates for chemical synthesis because of their potent reactivity and diverse pathways.[1] Among their important synthetic applications, alkyl radicals are well demonstrated to undergo radical additions, atom abstraction reactions, and varied fragmentation reactions, for construction of diversified organic molecules. Despite the rich reaction profiles of alkyl radicals, their reactivity and selectivity in the context of free radical reactions are, in general, difficult to control largely due to their free nature.

To harness the vast potential of homolytic radical reactions for stereoselective organic synthesis,[2] metalloradical catalysis (MRC) has recently been introduced as a conceptually new approach for addressing some enduring challenges in the field.[3,4] With cobalt(II) complexes of D_2-symmetric amidoporphyrins [Co(Por)], known to adopt a low-spin ground state with $(d_{xy})^2(d_{xz,yz})^4(d_z^2)^1$ electron configuration, as well-defined metalloradical catalysts, they are highly capable of activating various diazo compounds to generate [Co(Por)]-supported carbon-centered radicals (α-Co(III)-alkyl radicals) and release nitrogen gas as the only byproduct (Scheme 1.1).[5] The bonding interaction is thus dominated by the formation of a covalent Co–C bond between Co-dz^2 orbital and the carbon's sp^2 orbital. Additional bond interaction between Co-*dxz/yz* and carbon's *p*

orbitals, a common feature in classic metallocarbene complexes, is only fractional in part due to the fully-filled *dxz/yz* and singly-filled *p* orbitals. These metal-supported alkyl radicals have been shown to subsequently undergo a variety of typical radical reactions, especially radical addition reactions to alkenes for asymmetric cyclopropanation reactions with effective control of reactivity and stereoselectivity.

Scheme 1.2|| Molecular Orbital Diagram, the Bonding Interactions of Metalloradical Catalysts and Their Related Metalloalkyl Radicals

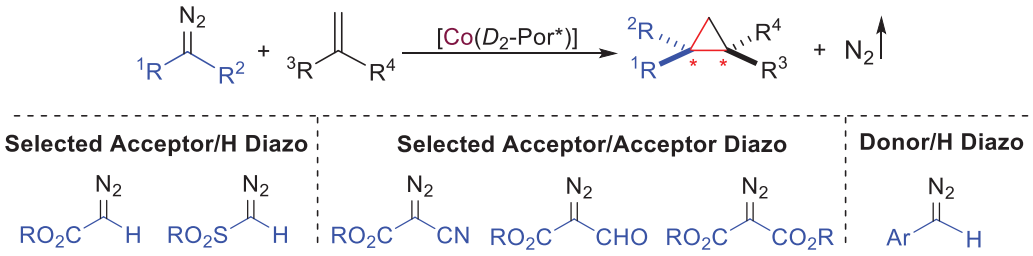


Optically active cyclopropanes are widely used as versatile synthetic building blocks in organic chemistry. They are also commonly found as basic structural elements in a wide range of naturally occurring compounds and pharmaceuticals. As a robust strategy, transition metal-catalyzed asymmetric cyclopropanation of olefins with diazo compounds has emerged as one of the most extensively studied reactions to construct optically active three-membered carbocycles.[6] The catalytic pathways are generally recognized through an electrophilic addition of the Fischer-type metallocarbene intermediates to olefin

compounds, termed as an electrophilic [1+2] addition. In the past years, various diazo compounds have been continuously applied for stereoselective cyclopropanation of alkenes through the development of a variety of metal complexes as the catalysts. For example, Rh_2(II)- and Cu(I)-based complexes have been shown to be effective for a wide range of asymmetric cyclopropanation reactions, producing chiral cyclopropane derivatives with high level of optical purity.[6] While many systems have been elegantly developed, there are still several remaining major challenges associated with metallocarbene cyclopropanation. On one hand, existing catalytic systems generally work well with styrene derivatives as well as some electron-rich olefins. Nevertheless, asymmetric cyclopropanation of electron-deficient olefins have been troublesome presumably due to the electrophilic nature of the formed metal-carbene intermediates in the catalytic cycles. On the other hand, the applications of utilizing acceptor/acceptor-substituted diazo compounds and donor-substituted diazo compounds for asymmetric olefin cyclopropanation are rarely reported. For instance, with diazo compounds containing two adjacent electron-withdrawing groups, they have inherently low reactivity with Lewis acidic metal catalysts for the formation of corresponding metallocarbene intermediates. Even if generated under forcing conditions, their subsequent reactions towards olefins are often difficult to control in terms of enantioselectivity due to the high electrophilicity of the acceptor/acceptor-substituted metallocarbenes.[6-7] It is noteworthy to mention that the dimerization of diazo compounds is a common side reaction in cyclopropanation systems, which usually require the use of excess olefins and slow addition of the diazo compounds to minimize this side reaction although they are not ideally practical.[8]

Fundamentally different from the previous electrophilic catalytic systems, asymmetric radical cyclopropanation reactions via Co(II)-based metalloradical catalysis have been shown to be highly capable of constructing a wide array of enantioenriched cyclopropane derivatives. The successful development of these radical cyclopropanation systems provides a complementary synthetic strategy to solve the aforementioned major challenges that associate with the previous 2e systems in the area of olefin cyclopropanation. In this review, we will provide an overview the recent progress in [Co(Por)]-catalyzed stereoselective radical cyclopropanation reactions with various diazo compounds as radical precursors, including acceptor/H-, acceptor/acceptor-, donor/H-substituted diazo compounds as shown in Scheme 1.2.

Scheme 1.2|| Asymmetric Radical Olefin Cyclopropanation with Different Diazo Compounds via Co(II)-Based Metalloradical Catalysis (MRC)

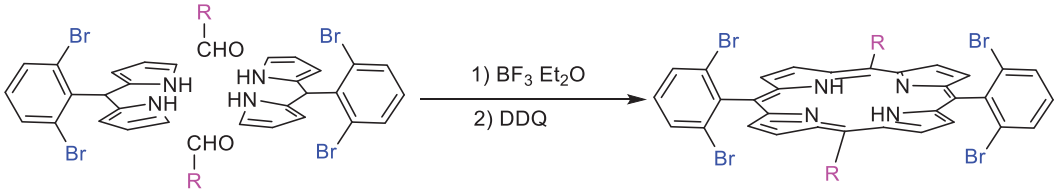


1.2 SYNTHESIS OF COBALT(II) COMPLEXES OF D_2-SYMMETRIC CHIRAL PORPHYRINS

As stable 15e metalloradicals, Co(II) complexes of porphyrins embrace excellent thermal stability and metal coordination stability due to the macrocyclic chelation effect

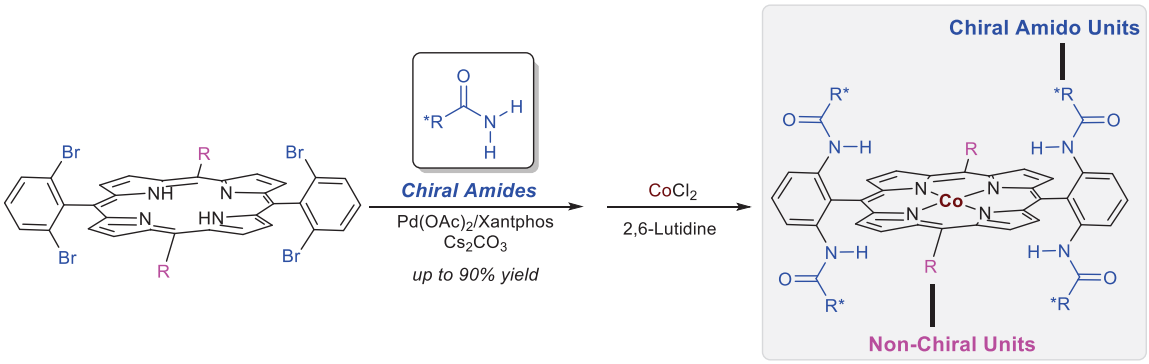
via the well-defined tetra-coordination. Based on the planar porphyrin backbone, the physical and chemical properties of the corresponding [Co(Por)] catalysts, in principle, can be systematically decorated through the installation of different substituents onto the aromatic ring structure of porphyrin ligands. Despite these unique features, one major issue that might impede the potential applicability of Co(II)-porphyrins for asymmetric catalysis is searching for facile and robust synthetic methods to access a range of chiral porphyrins with varied electronic, steric, and chiral environments. In this regard, our group have developed a general and durable synthetic protocol for the rapid construction of D_2-symmetric chiral porphyrins via palladium-catalyzed quadruple cross-coupling reactions by using 5,15-bis(2',6'-dibromophenyl)porphyrins as synthons.[9] As depicted in Scheme 1.3, the tetrabromoporphyrin synthon could be constructed from 2,2'-((2,6-dibromophenyl)methylene)bis(1*H*-pyrrole) and commercially available aldehydes via MacDonald [2+2] porphyrin synthesis by using Lindsey's condition.[10] The resulting core structures feature two *meso*-R groups at the 10- and 20-positions to modulate the electronic and steric properties.

Scheme 1.3|| General Synthetic Route for Synthesis of 5,15-Bis(2',6'-dibromophenyl)porphyrins Synthons



Upon the formation of tetrabromoporphyrin synthons, the combination of $Pd(OAc)_2$ and XantPhos could effectively catalyze the quadruple amidation reactions of the tetrabromoporphyrin synthons with optically pure amides to afford a series of chiral porphyrin ligands in up to 90% yield (Scheme 1.4).[11] With the subsequent cobalt metalation step, D_2-symmetric Co(II) complexes of chiral porphyrins could usually be synthesized as stable purple solids in high yields.

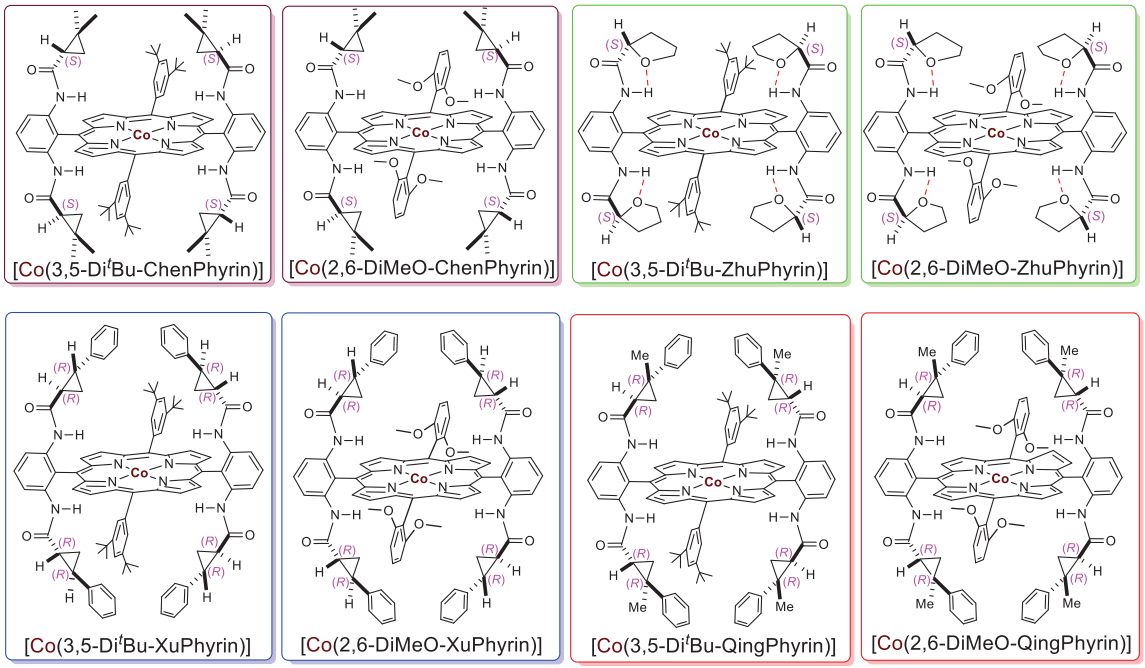
Scheme 1.4|| General Synthetic Route for Cobalt(II) Complexes of D_2-Symmetric Chiral Porphyrins [Co(D_2-Por*)]



The representative structures of the Co(II)-based amidoporphyrin catalysts are displayed in Scheme 1.5. These D_2-symmetric catalysts commonly embrace the following features: First, to minimize the steric repulsion, four substituted phenyl groups usually adopt a conformation that is almost perpendicular to the porphyrin plane. This unique geometry also enables the chiral amido groups as well as the nonchiral substituents on 10- and 20-position of the porphyrin to frame a cavity-like environment for asymmetric catalytic reactions. Second, with the partial double bond character of the four amido C–N bonds, the chiral units would have a good sense of rigidity for asymmetric induction, while

maintain a certain degree of flexibility to accommodate different substrates during catalytic reactions. Finally, the nonchiral substituents are also essential for the catalyst environment, because they would allow the facile modulation of cavity size, as well as the orientation of four chiral units.

Scheme 1.5|| Selected Examples of Cobalt(II) Complexes of *D*$_2$-Symmetric Chiral Porphyrins [Co(*D*$_2$-Por*)]

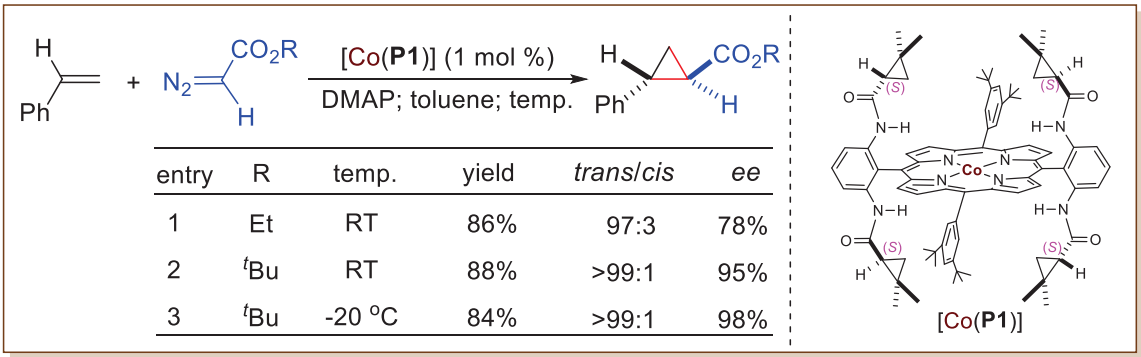


1.3 COBALT(II) PORPHYRIN-CATALYZED ASYMMETRIC RADICAL CYCLOPROPANATION WITH ACCEPTOR/H-SUBSTITUTED DIAZO

1.3.1 Asymmetric Radical Cyclopropanation with Alkyl Diazoacetates

As the benchmark reaction, alkyl diazoacetates were first employed successfully as radical precursors for asymmetric cyclopropanation of styrene by using the first generation catalyst: cobalt(II) complex of a D_2-symmetric chiral porphyrin 3,5-Di^{t}Bu-ChenPhyrin, [Co(**P1**)] (Scheme 1.6).[11] The desired cyclopropanes were obtained in up to 88% yield with >99:1 *dr* and 98% *ee*. It is noteworthy to mention that the [Co(**P1**)]-based metalloradical cyclopropanation system could be effectively operated in an one-time fashion with alkenes as limiting reagents. In addition, the dimerization of diazo compounds, a common side reaction in metal-carbene transfer processes, is significantly minimized, obviating the

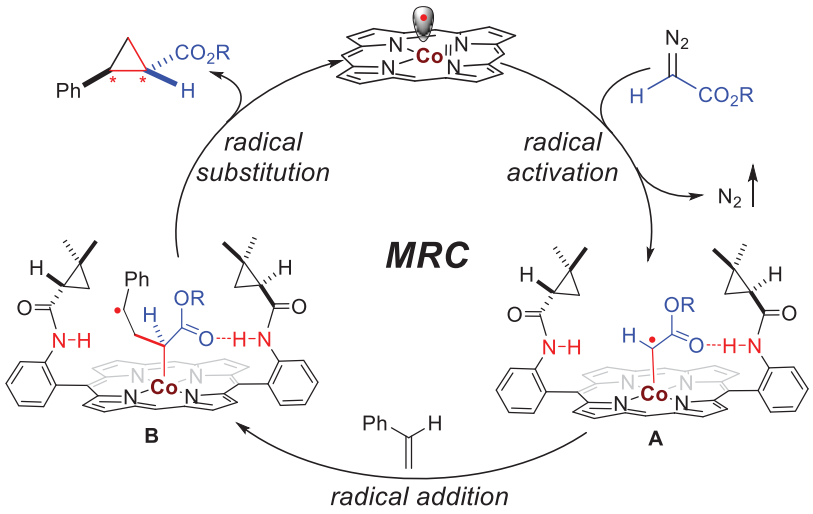
Scheme 1.6|| [Co(P1)]-Catalyzed Asymmetric Radical Cyclopropanation of Styrene with Diazoacetate



entry	R	temp.	yield	*trans*/*cis*	*ee*
1	Et	RT	86%	97:3	78%
2	^{t}Bu	RT	88%	>99:1	95%
3	^{t}Bu	-20 ^{o}C	84%	>99:1	98%

slow addition of diazo compounds. No significant formation of dimerization side products also suggests that Co-supported alkyl radical species distinctively favor addition to olefins rather than dimerization with another molecule of diazo compound. These complementary attributes are found to be quite general and suitable for all the radical cyclopropanation systems we developed later on.

Scheme 1.7|| Postulated Mechanism for [Co(P1)]-Catalyzed Asymmetric Radical Cyclopropanation of Styrene with Diazoacetates



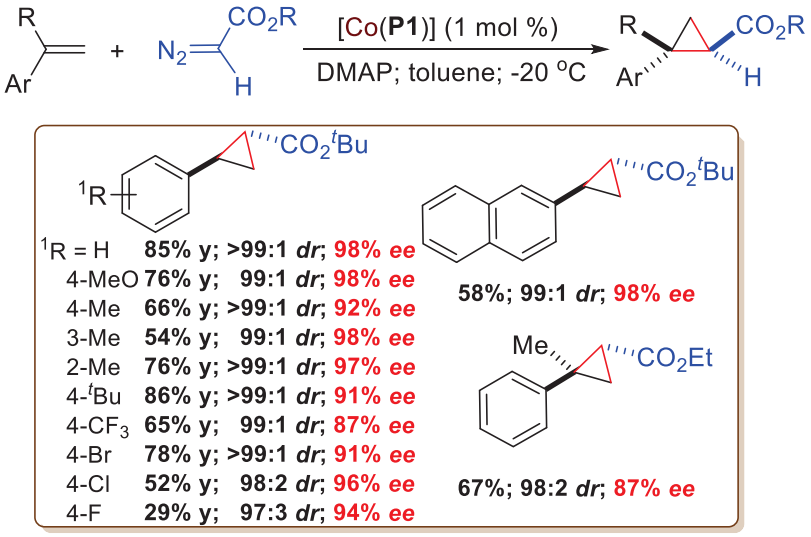
** For clarity, some chiral or achiral units of the ligands are omitted.*

The plausible reaction mechanism of this radical cyclopropanation system was proposed in Scheme 1.7. In addition to the rigidity and the cavity-like conformation of the catalyst, we rationalized that the key to achieve the well-controlled reactivity and selectivity of this radical process might be also due to the hydrogen bonding interaction between the chiral amide N–H unit on the ligand and the carbonyl unit of the carbene moiety, which plays an important role to further rigidify the radical intermediates **A** (*α*-

Co(III)-alkyl radicals) for enantioselective radical olefin addition to generate intermediates **B** (*γ*-Co(III)-alkyl radicals), and also presumably accelerate the reaction rate by lowering their energy in the transition state (Scheme 1.7). During the investigation, we found that the use of DMAP as the additive could significantly enhance the overall diastereo- and enantioselectivity of the radical cyclopropanation process albeit with slightly decreased yield.[11,12]

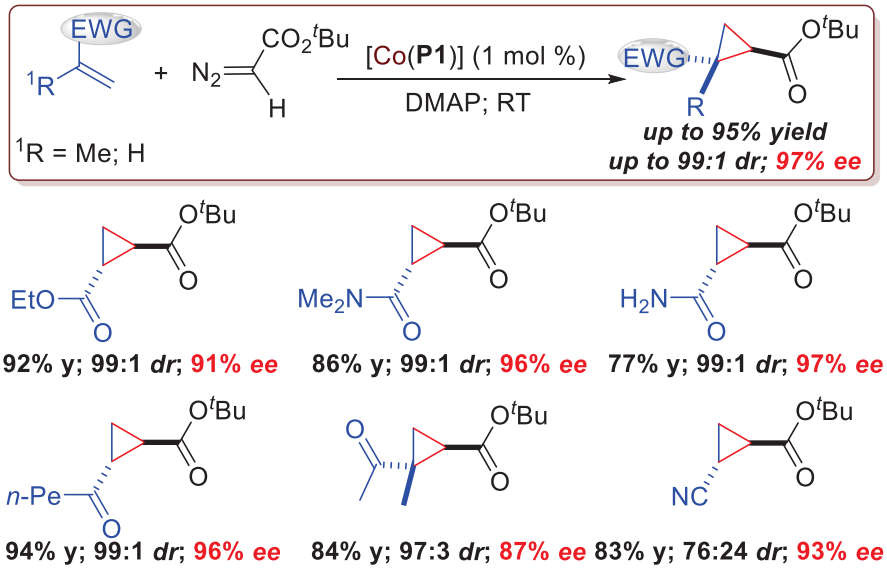
Further investigation showed that styrene and its derivatives bearing varied electronic and steric properties can be cyclopropanated with *tert*-butyl diazoacetate in high yields with excellent control of *trans*-selectivity and enantioselectivity (Scheme 1.8).[11,13] Notably, this asymmetric radical system remains its high *trans*-selectivity when other diazoacetates, such as less sterically hindered ethyl diazoacetate were used.

Scheme 1.8|| Asymmetric Radical Cyclopropanation of Different Styrene Derivatives with Diazoacetates Catalyzed by [Co(P1)]



After the initial results, we have further expanded the potential of this radical cyclopropanation system to tackle some of the long-standing challenges in metal-mediated carbene cyclopropanation (Scheme 1.9). As discussed, Fischer-type carbene species generally favor reactions with electron-rich olefins. The metal-carbene radical intermediates may be less sensitive to the electronic property of the alkenes used, enabling a broader spectrum of olefin scope, especially the electron-deficient ones. Such a hypothesis has led us to the discovery of stereoselective radical cyclopropanation of electron-deficient olefins by Co(II)-based MRC. By using [Co(**P1**)] as the catalyst, we reported the first transition metal-catalyzed asymmetric cyclopropanation of electron-deficient olefins, including unsaturated esters, amides, ketones, and nitriles (Scheme 1.9).[14]

Scheme 1.9|| [Co(P1)]-Catalyzed Asymmetric Radical Cyclopropanation of Electron-Deficient Olefins with *tert*-Butyl Diazoacetate



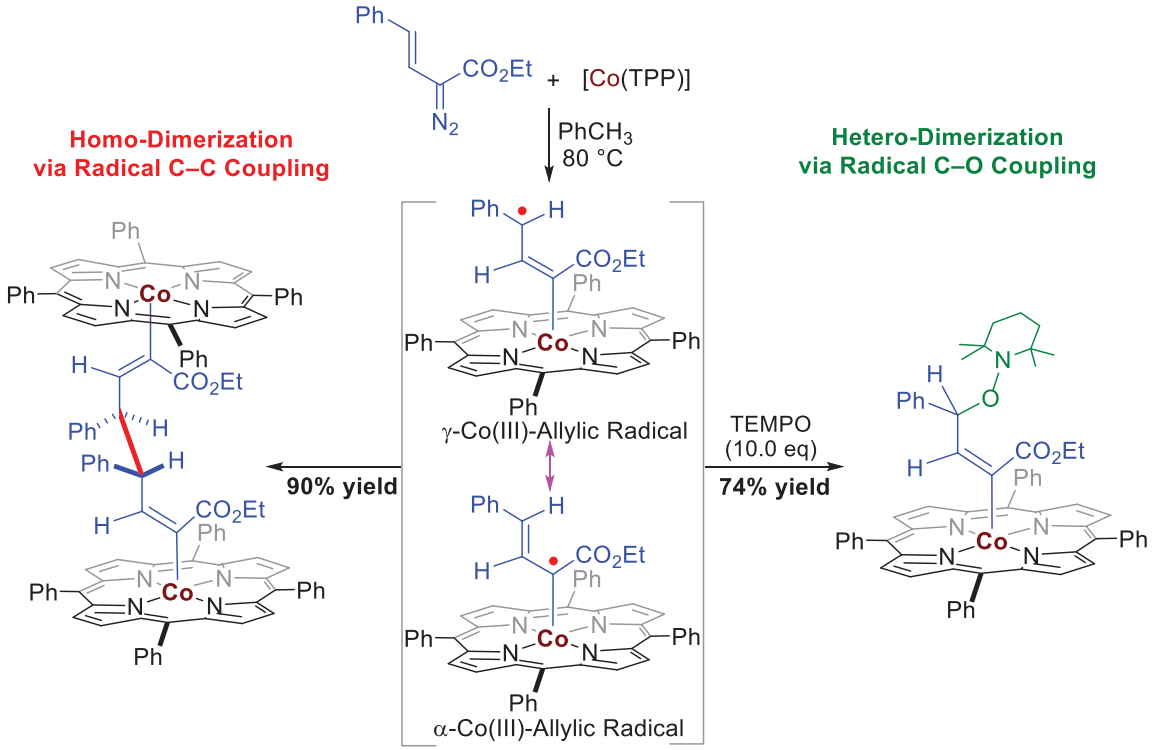
With the absence of dimerization of diazo compounds, the catalytic reactions were performed under mild conditions in a one-pot protocol using olefins as the limiting reagents, forming the desired electrophilic cyclopropane derivatives in high yields. In most cases, both excellent diastereo- and enantioselectivities were achieved.

The exceptional reactivity of Co(II)-based MRC towards electron-deficient olefins implies some nucleophilic character of the formed α-Co(III)-alkyl radical (vide supra, Scheme 1.7), which further differentiate [Co(Por)]-based radical cyclopropanation systems from typical electrophilic (Fischer-type) transition-metal carbene-mediated cyclopropanation systems. In collaboration with Prof. de Bruin, we carried out a comprehensive study on the mechanism of [Co(Por)]-catalyzed cyclopropanation of olefins with diazoacetates.[5a] EPR and HRMS experiments in combination with DFT calculations supported an unprecedented stepwise radical reaction mechanism of the Co(II)-catalyzed cyclopropanation (vide supra, Scheme 1.7). DFT calculations suggested the Co(II)-based metalloradical is able to decompose diazo compounds to generate an unusual α-Co(III)-alkyl radical (**A**) as the key intermediate of the catalytic cycle. The net process may be considered as a radical transfer in which the radical character is transferred from the cobalt-center to the α-carbon atom of the diazo moiety. The α-Co(III)-alkyl radical (**A**), which was detected experimentally using EPR and HRMS techniques, is capable of undergoing common radical reactions such as radical addition and substitution.[5] Consequently, radical addition of the radical intermediate **A** to the C=C bond of olefin substrates results in further radical transfer to form the γ-Co(III)-alkyl radical (**B**), which subsequently undergoes ring-closure reaction via intramolecular radical substitution by breaking the relatively weak Co–C bond and regenerates the metalloradical catalyst. Both

the α-Co(III)-alkyl radical and γ-Co(III)-alkyl radical are essentially carbon-based radicals, however, they are not "free" any more as their reactivity and selectivity are well regulated by the electronic, steric, and chiral environments of the covalently-attached [Co(Por)] moiety. Further computational study suggests that the carbon radical center in the intermediate **A** bears certain nucleophilicity, which makes its exceptional reactivity toward electron-deficient olefin understandable.[5b] Moreover, it is suggested that the charge of the alkyl radical could be deliberately tuned through the introduction of different α-carbon substituents of the original diazo compounds. Accordingly, the substituents of diazo compounds may be used as tools for tuning the electronic properties of the metal-supported alkyl radicals in order to match varied substrates in different carbene transformations.

Encouragingly, experimental observations also allowed us to shed more light on the possible existence of the cobalt(III)-alkyl radicals.[15] The stoichiometric reaction of [Co(TPP)] with ethyl styryldiazoacetate was found to produce a symmetric dinuclear cobalt(III) porphyrin complex in 90% yield (Scheme 1.10, left side). The dimeric complex was believed to form from radical dimerization of γ-Co(III)-allylic radical resonated from the initially generated α-cobalt(III)-allylic radical. In addition to the radical C–C coupling-based homo-dimerization, the γ-Co(III)-allylic radical intermediate was also effectively trapped by the radical scavenger TEMPO, resulting in the hetero-dimerization product via a radical C–O coupling reaction in 74% yield (Scheme 1.10, right side). Consistent with the computational studies, these experimental results further confirmed the existence of the cobalt(III)-alkyl radicals that were proposed as key intermediates in the radical-type mechanism of [Co(Por)]-catalyzed cyclopropanation (vide supra, Scheme 1.7).

Scheme 1.10|| Experimental Evidence for *α*-Cobalt(III)-Alkyl Radicals: Homo- and Hetero-Dimerizations



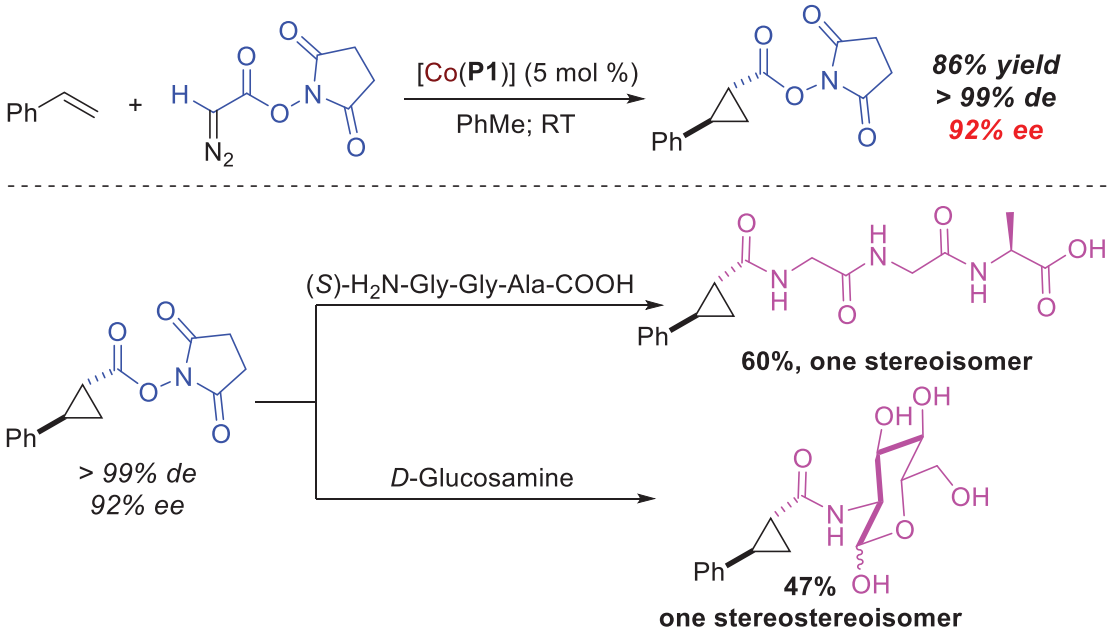
1.3.2 Asymmetric Radical Cyclopropanation with Succinimidyl Diazoacetates

In addition to alkyl diazoacetates, succinimidyl diazoacetates were also successfully applied to Co(II)-catalyzed asymmetric radical cyclopropanation of alkenes as shown in Scheme 1.11. For example, cyclopropane succinimidyl ester could be prepared in 86% yield with >99% *de* and 92% *ee* through [Co(**P1**)]-catalyzed asymmetric cyclopropanation of styrene with succinimidyl diazoacetate (N_2CHCO_2Su).[16]

To demonstrate the synthetic utility, the resulting cyclopropyl chiral synthons permitted the enantioselective synthesis of cyclopropyl carboxamides upon reacting with

various amines (Scheme 1.11). The hydroxylsuccinimide ester functionality in the enantioenriched chiral synthon was ready to react with a broad range of different amines such as the unprotected tripeptide (*S*)-H_2N-Gly-Ala-COOH and D-glucosamine under mild conditions to deliver the corresponding cyclopropyl tripeptide and cyclopropyl carboxamido sugar, respectively.

Scheme 1.11|| Co(II)-Catalyzed Asymmetric Radical Cyclopropanation with Succinimidyl Diazoacetates and its Synthetic Applications



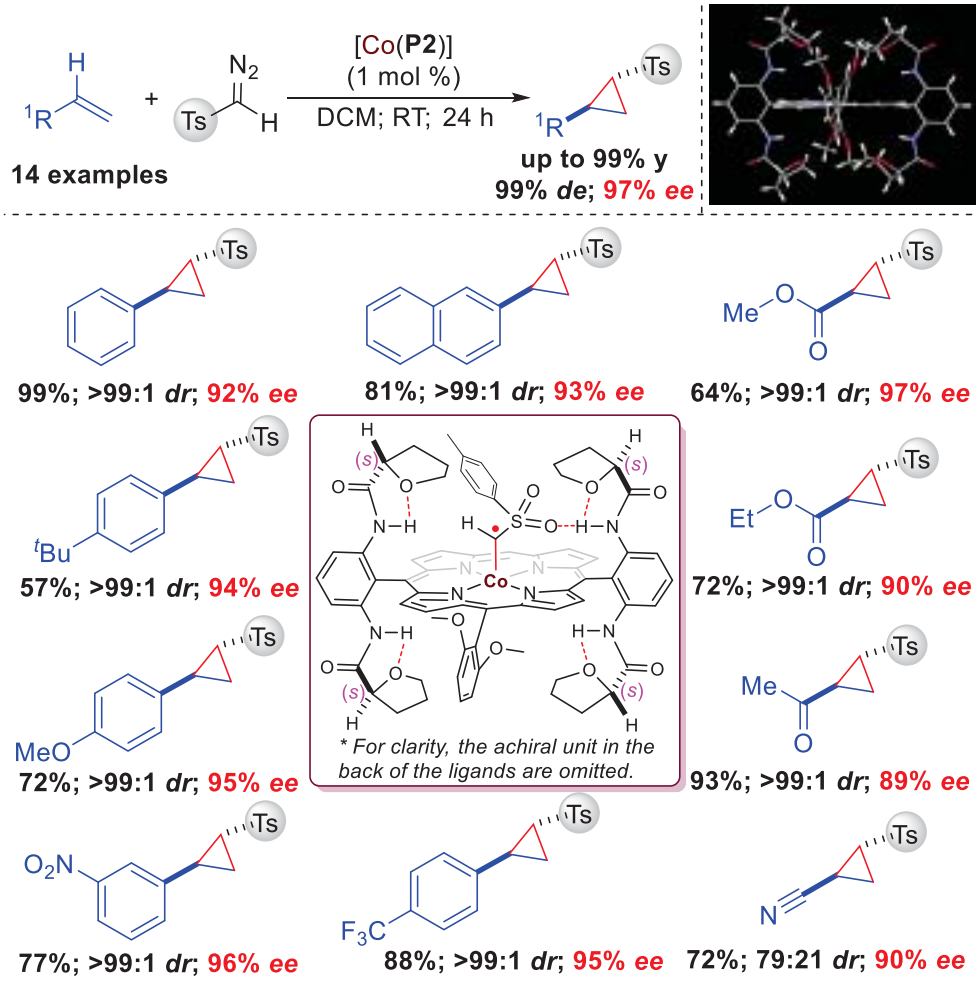
1.3.3 Asymmetric Radical Cyclopropanation with Diazosulfones

So far, most catalytic cyclopropanation systems typically employ diazocarbonyl compounds as carbene sources, the utilization of other acceptor/H-substituted diazo compounds in the context of metal-catalyzed asymmetric cyclopropanation has been less

developed. To showcase the effectiveness of [Co(Por)]-based catalytic systems, we have employed diazosulfones as diazo source, for the first time, for asymmetric radical cyclopropanation, leading to the streamlined synthesis of corresponding cyclopropyl sulfones in high yields with excellent stereocontrol (Scheme 1.12).[17] During the course of study, we designed and synthesized a new D_2-symmetric chiral porphyrin 2,6-DiMeO-ZhuPhyrin (**P2**) as supporting ligand, which features higher rigidity and polarity of the chiral environment due to intramolecular hydrogen bonding interactions and the use of the cyclic structure of (*S*)-2-tetrahydofurnancarboxamide as demonstrated by single crystal structures. The Co(II) complex of this chiral ligand [Co(**P2**)] was shown to effectively catalyze asymmetric olefin cyclopropanation with diazosulfones. The catalytic system can be generally applied to various aromatic olefins as well as electron-deficient olefins, leading to the high-yielding formation of the corresponding cyclopropyl sulfones with up to 99% *de* and 97% *ee*.

The model of hydrogen bonding interactions (Scheme 1.12, in the middle) also well explains the high reactivity and selectivity for this Co(II)-based MRC system. In addition to the ligand–diazo interaction, the hydrogen bonding in [Co(**P2**)] itself tends to prevent the chiral units from free rotation through a rigid bicyclic-like conformation. In this way, the chiral units of the catalyst is not only further rigidified, but also forced closer to the metal center to better transfer the chiral information.[17-18]

Scheme 1.12|| [Co(P2)]-Catalyzed Diastereo- and Enantioselective Cyclopropanation of Different Alkenes with Diazosulfones



1.4 COBALT(II) PORPHYRIN-CATALYZED ASYMMETRIC RADICAL CYCLOPROPANATION WITH ACCEPTOR/ACCEPTOR DIAZO

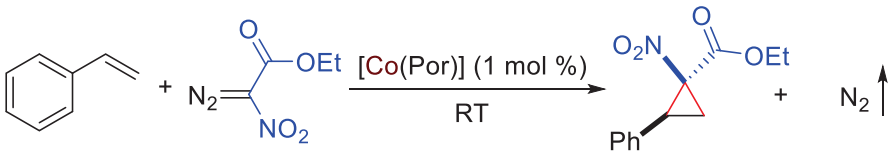
Diazo compounds bearing two electron-withdrawing groups, namely acceptor/acceptor-substituted diazo compounds, typically suffer low reactivity and poor

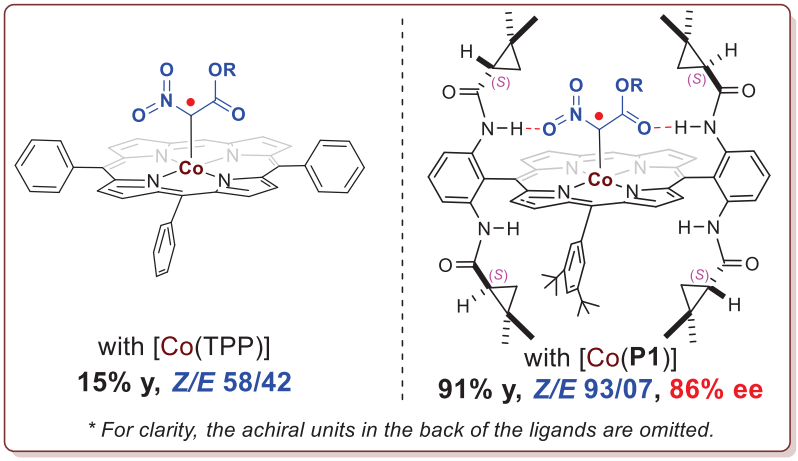
enantioselectivity in transition metal-catalyzed carbene transfer cyclopropanation reactions, presumably due to the electrophilic nature of formed Fischer-type metallocarbene intermediates.[6,7] In contrast to the 2e catalytic systems, Co(II)-based 1e cyclopropanation mode has emerged as a possible solution to this challenge partially because radical pathways are in general less influenced by electronic properties.

1.4.1 Asymmetric Radical Cyclopropanation with Alkyl α-Nitrodiazoacetates

Initial efforts were focused on the evaluation of *α*-nitrodiazoacetate (NDAs) as potential radical precursors for the cyclopropanation of styrene by different [Co(Por)] catalysts (Scheme 1.13).[19] By using ethyl *α*-nitrodiazoacetate (ENDA) as radical precursor, it was found that Co(TPP) displayed very low reactivity and diastereoselectivity. Considering the two electron-withdrawing *α*-substituents of ENDA are usually suitable hydrogen bonding acceptors, it is anticipated that the D_2-symmetric chiral amidoporphyrins might possibly facilitate the catalytic reactivity and selectivity by enabling double hydrogen bonding interactions between two of the chiral amide N–H moieties on the ligand and both electron-withdrawing groups of the carbene moiety. Indeed, with [Co(**P1**)] as the metalloradical catalyst, the experimental results confirmed our hypothesis by affording a dramatically accelerated cyclopropanation process.[19] In addition to the evidently promoted reactivity towards these less reactive diazo compounds, the potential double hydrogen bonding interactions also rigidify the *α*-cobalt(III)-alkyl radical intermediate towards its subsequent radical addition to the olefin substrates, which lead to a high level of stereocontrol.

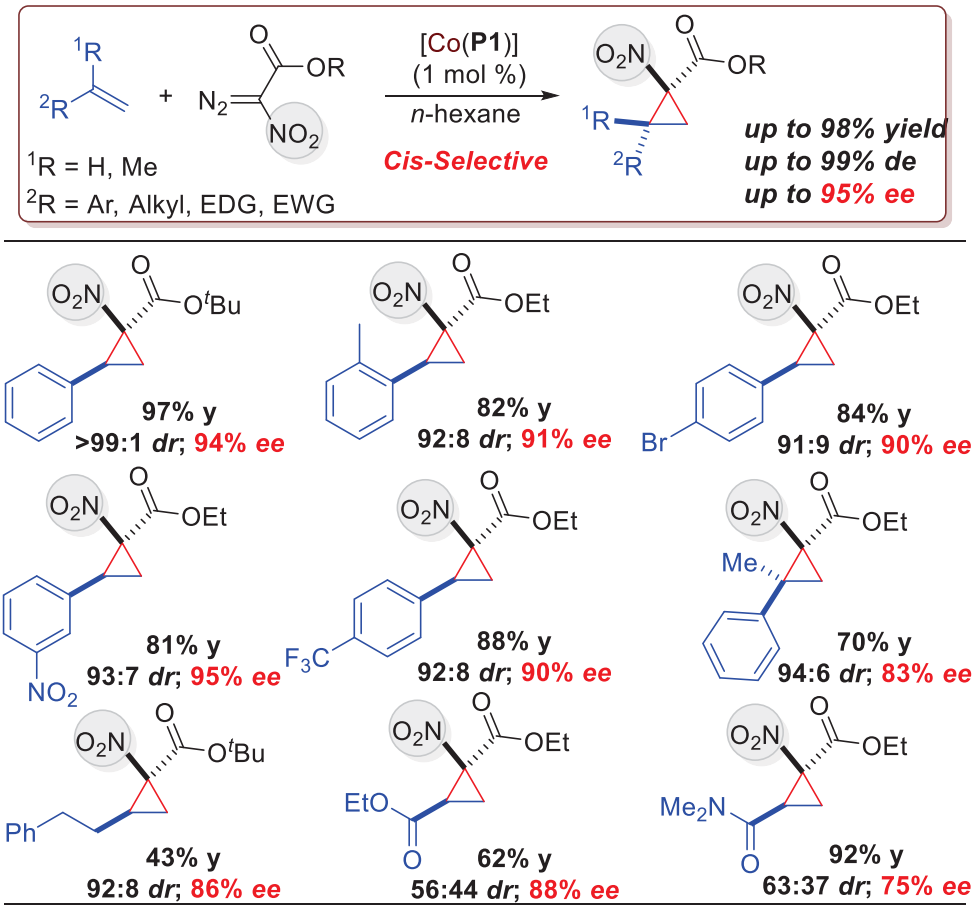
Scheme 1.13|| Enantioselective *Z*-Cyclopropanation of Styrene with Ethyl *α*-Nitro Diazoacetate: [Co(TPP)] Versus [Co(P1)]





The unique reactivity of [Co(**P1**)]-based catalytic radical system toward this challenging diazo compounds is general and suitable for a wide spectrum of alkenes, like electron-sufficient, electron-neutral, and electron-deficient ones, forming the corresponding optically active cyclopropyl nitroester compounds in up to 98% yield (Scheme 1.14). In addition to high diastereo- and enantioselectivity, the catalytic process exhibits the atypical *Z*-selectivity. The system also represents the first highly effective and selective catalytic system for asymmetric cyclopropanation with acceptor/acceptor-substituted diazo compounds as the radical source.[20]

Scheme 1.14|| [Co(P1)]-Catalyzed Asymmetric *Z*-Cyclopropanation Reactions of Different Alkenes with Alkyl *α*-NitroDiazoacetates

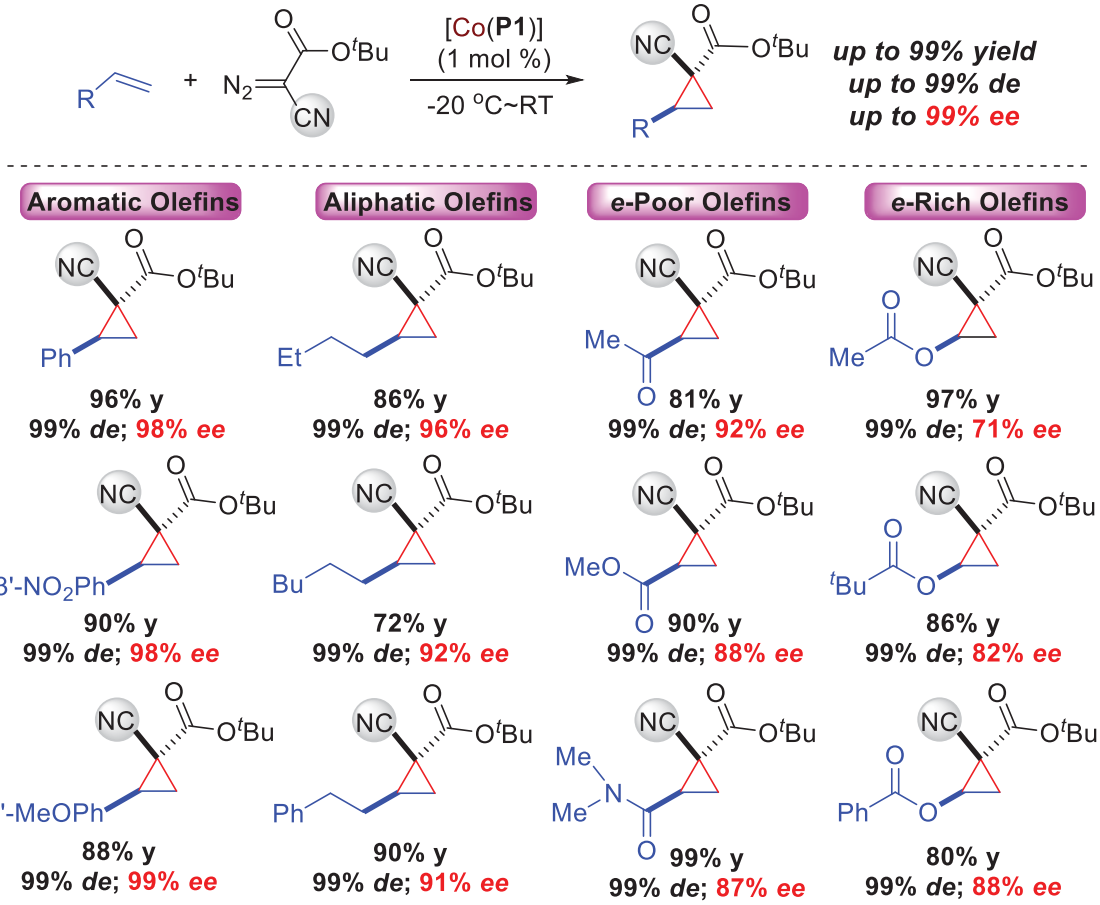


1.4.2 Asymmetric Radical Cyclopropanation with *α*-Cyanodiazoacetates

By adopting the aforementioned double H-bonding hypothesis, another type of acceptor/acceptor-substituted diazo compounds, *α*-cyanodiazoacetates (CDAs), were also attempted, where cyano group is normally considered as a stronger hydrogen bond acceptor than a nitro group. The results showed that [Co(**P1**)] is also an effective catalyst for olefin cyclopropanation with *tert*-butyl *α*-cyanodiazoacetate (*t*-BCDA) with even higher

stereoselectivity (Scheme 1.15).[21] Substrate evaluation revealed that the Co(II)-based catalytic system is suitable for both aromatic and aliphatic olefins with varied electronic properties, affording densely functionalized cyclopropane products with high optical purity.

Scheme 1.15|| [Co(P1)]-Catalyzed Asymmetric Radical Cyclopropanation of Alkenes with *α*-Cyanodiazoacetate



The resulting enantiomerically enriched 1,1-cyclopropanenitrile esters (Scheme 1.15), together with previous 1,1-cyclopropanenitro esters (Scheme 1.14), serve as versatile building blocks for a number of densely functionalized chiral cyclopropane

molecules. For instance, the facile reduction of the cyano, nitro, and ester groups would directly lead to the production of enantioenriched cyclopropyl amino acid derivatives and amino alcohols, which are of great interest for synthetic and biological applications.

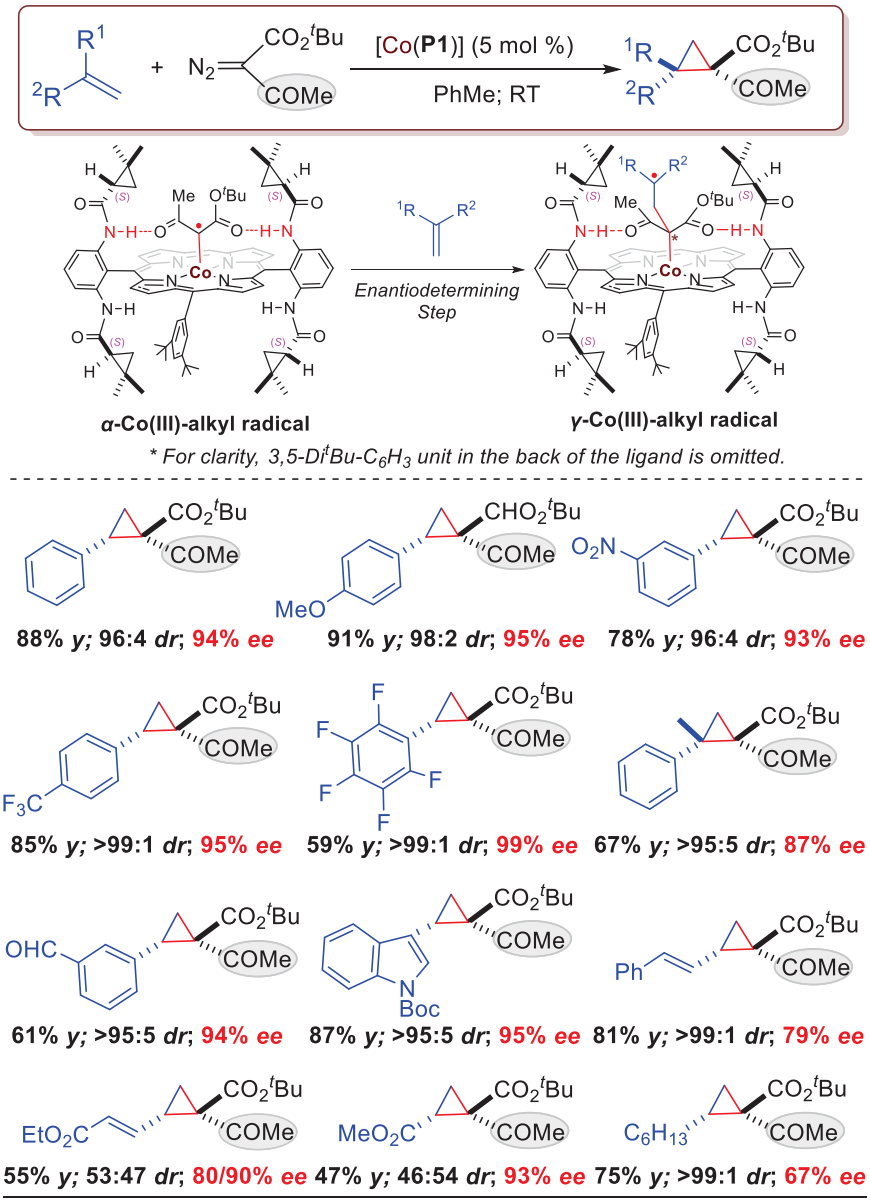
1.4.3 Asymmetric Radical Cyclopropanation with *α*-Ketodiazoacetates

The dicarbonyl diazo compounds such as *α*-ketodiazoacetates (KDAs) represent one class of important acceptor/acceptor-substituted diazo compounds (Scheme 1.16).[22] The development of asymmetric cyclopropanation reactions with KDAs would be highly attractive since the resulting chiral 1,1-cyclopropyl ketoesters serve as versatile synthons, which can not only be converted into chiral cyclopropane derivatives with different geminal functionalities, but also facilely be transformed into other valuable chiral molecules through various ring-opening and ring-expanding reactions in the presence of two electron-withdrawing groups at the geminal position.

Nevertheless, the high enantiocontrol of such a process is mechanistically challenging. As illustrated in Scheme 1.16, the postulated *α*-Co(III)-alkyl radical intermediate has to enable effective differentiation between two similar carbonyl groups from a common KDA in order to allow the selective radical olefin addition, which is rationalized as the enantiodetermining step. Moreover, the *3-exo-tet* cyclization of *γ*-Co(III)-alkyl radical intermediate is similarly challenging for obtaining high diastereoselectivity due to the same issue caused by the two analogous carbonyl-based substituents.

By evaluating different metalloradical catalysts and optimizing reaction conditions, we found that [Co(**P1**)] is a suitable catalyst to effectively activate KDAs and remarkably

Scheme 1.16|| [Co(P1)]-Catalyzed Asymmetric Radical Cyclopropanation of Alkenes with *α*-Ketodiazoacetates



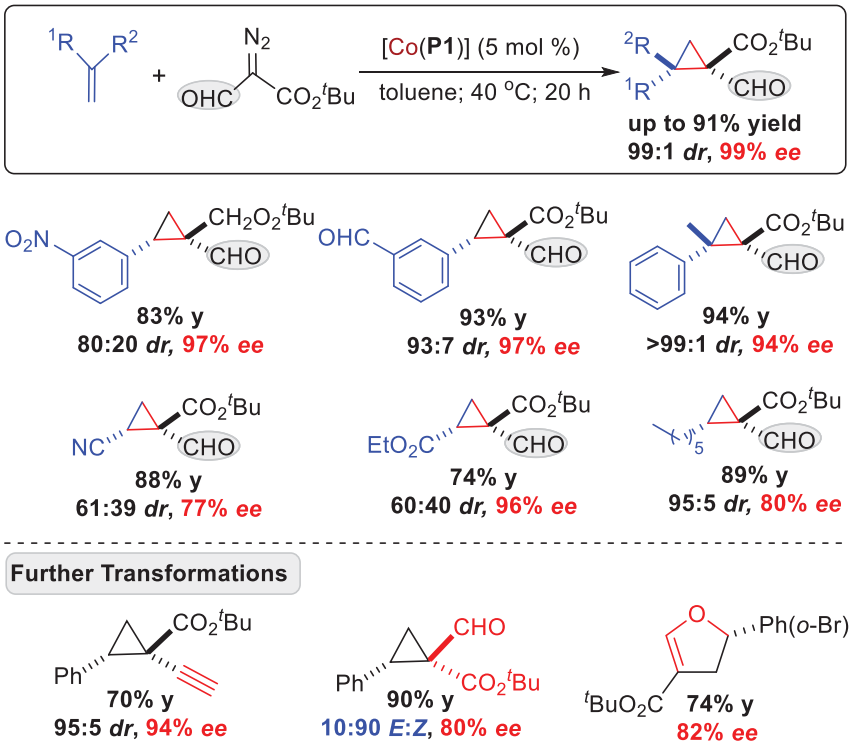
differentiate the two different acceptor-substituents for the high degree of enantioinduction.[22] Metalloradical catalyst [Co(**P1**)] has again been demonstrated to be the catalyst of choice for highly asymmetric olefin cyclopropanation with *α*-ketodiazoacetates (KDA) (Scheme 1.16).[22] With simple *α*-acetodiazoacetate, radical cyclopropanation

reactions of different kinds of olefins appeared to be highly yielding and selective, leading to effective synthesis of 1,1-cyclopropaneketoesters as *E* diastereoisomers with up to 99% *ee*.

1.4.4 Asymmetric Radical Cyclopropanation with Alkyl *α*-Formyldiazoacetates

To further challenge the capability of Co(II)-based MRC, we have explored the feasibility of accessing *α*-formyldiazoacetates (FDA) as radical precursors for asymmetric cyclopropanation reactions.[23] From the results shown in Scheme 1.17, upon diazo activation by [Co(**P1**)], the cobalt-supported alkyl radical smoothly underwent a highly

Scheme 1.17|| [Co(P1)]-Catalyzed Asymmetric Radical Cyclopropanation of Alkenes with *α*-Formyldiazoacetates.



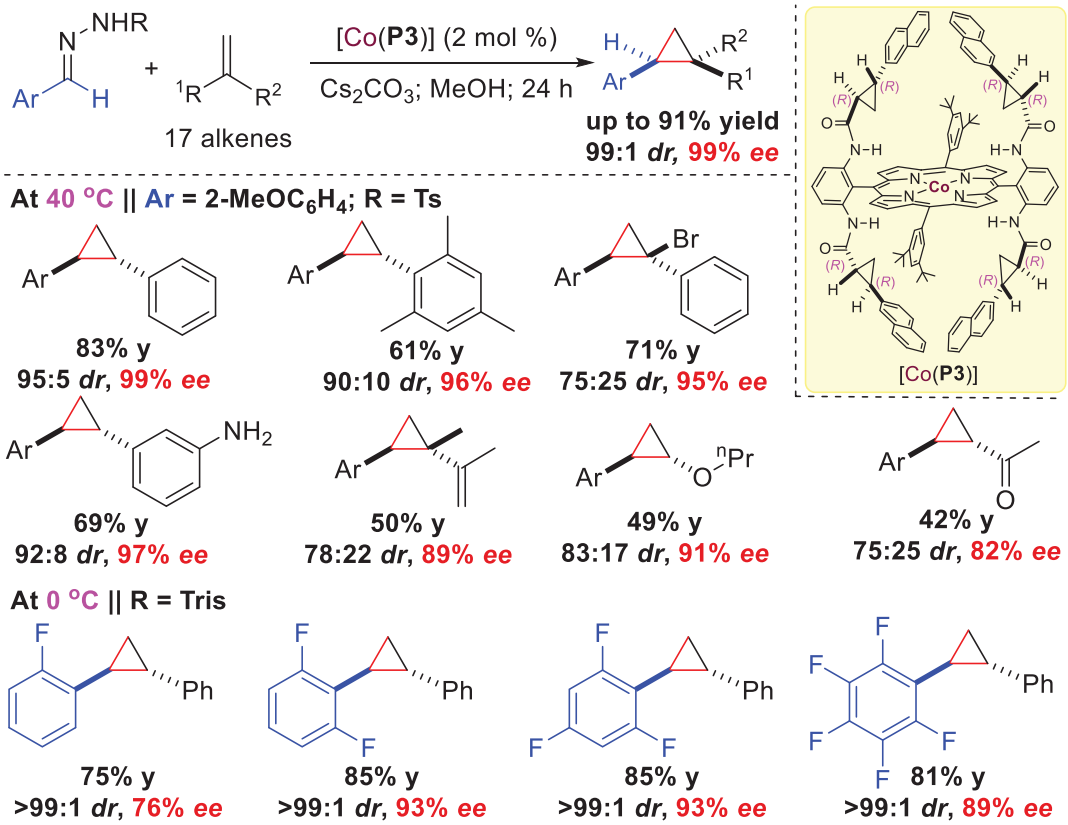
asymmetric olefin cyclopropanation, without affecting the otherwise reactive aldehyde functionality. This asymmetric radical process is generally applicable for a broad scope of alkenes, offering a direct method for the high-yielding synthesis of 1,1-cyclopropaneformylesters with excellent control of diastereo- and enantioselectivity. The great tolerance of functional groups that are otherwise reactive toward ionic reactions is believed to have close relevance to the radical pathway of Co(II)-based metalloradical catalysis. Notably, the resulting products were readily transformed into other chiral 1,1-bifunctionalized cyclopropanes and chiral dihydrofurans.

1.5 COBALT(II) PORPHYRIN-CATALYZED ASYMMETRIC RADICAL CYCLOPROPANATION WITH DONOR/H DIAZO

While tremendous progress has been made with the use of various diazo compounds, including aforementioned acceptor/H, acceptor/donor, acceptor/acceptor diazo compounds,[6] metal-catalyzed asymmetric carbene transfer cyclopropanation with donor-substituted diazo compounds has been rarely reported.[24] Along with their instability and short half-life of the diazo compounds, the underlying challenge might be also ascribed to the diminished electrophilicity of the corresponding donor-substituted metallocarbene intermediates, which would decrease the reactivity toward olefins for productive cyclopropanation. To this end, we developed a fundamentally new approach based on the concept of metalloradical catalysis (MRC) to address this long-standing challenge in the field via stereoselective radical chemistry (Scheme 1.18).[25]

With cobalt(II) complex of D_2-symmetric chiral porphyrin 3,5-Di^{t}Bu-Xu(2′-Naph)Phyrin, [Co(**P3**)], as the identified optimal catalyst, it can effectively catalyze asymmetric cyclopropanation of alkenes with donor-substituted diazo compounds, generated in situ from *N*-arylsulfonyl hydrazones in the presence of base.[25] The Co(II)-catalyzed radical cyclopropanation can be operated under mild conditions and is applicable to a broad spectrum of alkenes, affording the 1,2-bisaryl and related cyclopropane compounds in high yields with effective control of both diastereoselectivity and enantioselectivity. Among other additional attributes, the Co(II)-based cyclopropanation is

Scheme 1.18|| [Co(P3)]-Catalyzed Radical Cyclopropanation of Alkenes with In Situ-Generated Aryl Diazomethanes

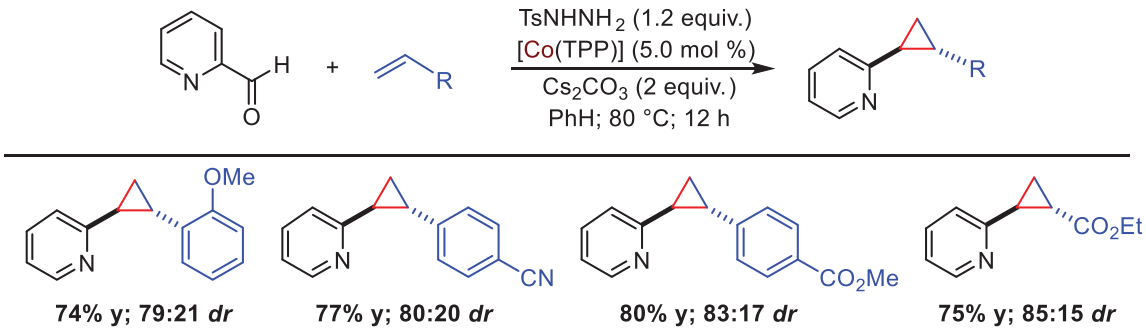


highlighted by its high degree of functional group tolerance, a feature that is closely related to its underlying radical mechanism. This system also signifies the compatibility of the Co(II)-based metalloradical system with the use of both bases and polar solvents.

Notably, by simply modulating the sulfonyl source from 4-methyl phenylsulfonyl (Ts) to 2,4,6-triisopropylphenylsulfonyl (Tris) as shown in Scheme 1.18, it allows the facile generation of donor-substituted diazo compounds from sulfonylhydrazones even at 0 °C for highly enantioselective radical cyclopropanation reactions.

Recently, Chattopadhyay and coworkers also demonstrated the possibility of using in situ-generated heteroaryl-substituted diazomethanes as radical precursors for olefin cyclopropanation reactions (Scheme 1.19).[26] In the presence of Co(TPP), the desired compounds could be obtained in good yields.

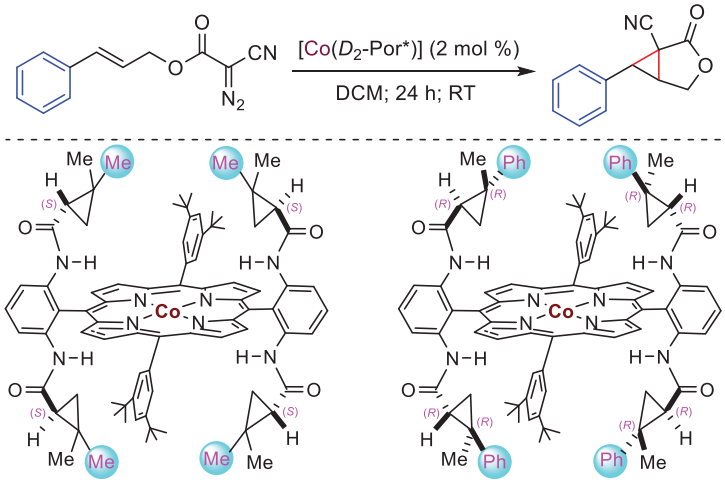
Scheme 1.19|| [Co(TPP)]-Catalyzed Radical Cyclopropanation of Alkenes with In Situ-Generated Heteroaryl Diazomethanes



1.6 COBALT(II) PORPHYRIN-CATALYZED ASYMMETRIC INTRAMOLECULAR RADICAL CYCLOPROPANATION WITH ACCEPTOR/ACCEPTOR DIAZO

In addition to the intermolecular version, asymmetric intramolecular cyclopropanation reactions via MRC has also been shown to be highly durable processes. At the beginning, these intramolecular cyclopropanation reactions catalyzed by [Co(**P1**)] was not optimal as shown in Scheme 1.20. The desired 3-oxabicyclo[3.1.0]hexan-2-one derivative was obtained in 99% yield and 99% *de*, yet with moderate 55% *ee*.[27]

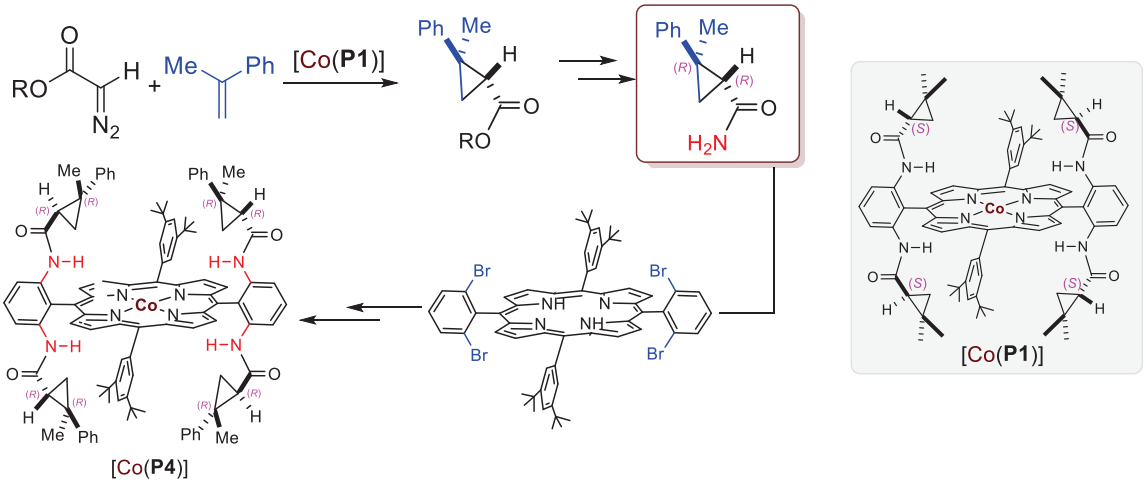
Scheme 1.20|| [Co(P4)]-Catalyzed Asymmetric Intramolecular Radical Cyclopropanation with *α*-Cyanodiazoacetate: [Co(P1)] Vs [Co(P4)]



During the course of catalyst development, the design of new Co(II) complex of 3,5-Di^{t}Bu-QingPhyrin ([Co(**P4**)]) via an iterative approach led to a perfect solution, and the enantioselectivity of the catalytic reaction was significantly improved to 96% *ee*. The

key for the catalyst innovation is to prepare the cyclopropanecarboxamide with two contiguous stereogenic centers (**P4**), which was synthesized iteratively via [Co(**P1**)]-catalyzed asymmetric intermolecular cyclopropanation of *α*-methylstyrene with diazoacetates (vide infra, Scheme 1.8).[11] This iterative approach has a great impact on the development of a new generation of [Co(D_2-Por*)] catalysts, which allows the chiral catalysts bearing two consecutive stereogenic centers on each chiral arm with more diverse asymmetric environments.

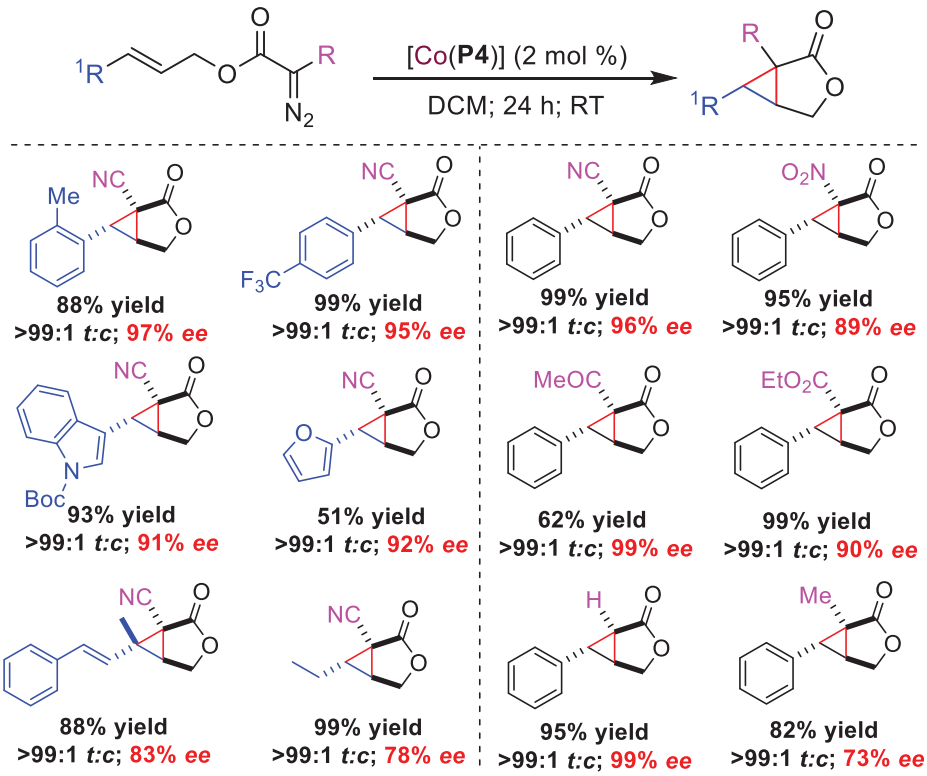
Scheme 1.21|| Iterative Approach for the Development of New Generation of Cobalt(II)-Based D_2-Symmetric Chiral Porphyrin [Co(P4)]



Systematically experimental studies disclosed that [Co(**P4**)] is capable of providing excellent asymmetric induction for intramolecular cyclopropanation of various allylic *α*-cyanodiazoacetates (Scheme 1.22, left side).[27] The formation of corresponding 3-oxabicyclo[3.1.0]hexan-2-one derivatives from the radical cyclopropanation were exclusively diastereoselective and highly enantioselective. The remarkable

diastereocontrol suggests that the final ring-closure step (intramolecular radical substitution) in the stepwise radical addition-substitution pathway for this intramolecular radical cyclopropanation is a low-barrier or barrierless process, which is the same as shown in the intermolecular cyclopropanation (vide supra, Scheme 1.7).[5a]

Scheme 1.22|| [Co(P4)]-Catalyzed Asymmetric Intramolecular Radical Cyclopropanation with Various Acceptor/Acceptor Diazo Compounds



The [Co(**P4**)]-catalyzed asymmetric intramolecular radical cyclopropanation was then successfully extended to a wide spectrum of other acceptor/acceptor-substituted diazo compounds, such as α-nitrodiazoacetates, α-ketodiazoacetates, and α-esterdiazoacetates (Scheme 1.22, right side).[27] Moreover, non-acceptor α-substituents, including hydrogen,

and electron-donating methyl group, were also shown to be suitable to afford the corresponding 3-oxabicyclo[3.1.0]hexan-2-one derivatives in high yields with excellent diastereoselectivities and enantioselectivities. The effectiveness of [Co(**P4**)] is believed to largely result from the multiple stereogenic centers of the new porphyrin ligands, which offer sufficient asymmetric induction, together with either double hydrogen-bonding interactions or mono hydrogen-bonding interaction in cases of acceptor/acceptor-substituted and monoacceptor-substituted diazo compounds, respectively.

1.7 SUMMARY AND OUTLOOK

Guided by the concept of metalloradical catalysis (MRC), the development of cobalt(II) complexes of D_2-symmetric chiral amidoporphyrin [Co(Por)] as stable metalloradical catalysts enables a fundamentally new approach for controlling stereoselectivity in asymmetric radical cyclopropanation reactions of alkenes. The Co(II)-based metalloradical catalysts have been shown to effectively activate a broad spectrum of diazo compounds, including acceptor/H, acceptor/acceptor and donor/H ones, to generate various α-Co(III)-alkyl radicals in a controlled and catalytic manner. The formed metal-supported alkyl radicals have further been demonstrated to be capable of undergoing radical additions to alkenes for asymmetric cyclopropanation reactions with effective control of reactivity and stereoselectivity by the modular porphyrin ligands. Attributed to the radical reaction profile, the radical olefin cyclopropanation reactions via Co(II)-based MRC are usually least affected by the electronic properties of substrates and reagents. Moreover, the mild reaction condition and high degree of functional group tolerance are

also important features that are likely related to the proposed radical mechanism. The establishment of Co(II)-catalyzed radical cyclopropanation reactions provides a solution for several major challenges in the corresponding $2e^-$ ionic cyclopropanation systems, including the successful employment of electron-deficient olefins, acceptor/acceptor-substituted and donor/H-substituted diazo compounds. The demonstrated general substrate scope and functional group tolerance encourage further applications of the Co(II)-based radical processes for new cyclopropane products with diverse substituents, especially active functionalities without the need of protection and deprotection.

Beyond radical addition reactions to double bond systems, α-Co(III)-alkyl radicals have also been demonstrated to undergo other radical reactions in a controlled manner, such as addition to alkynes[28] and C–H abstraction reactions.[29] The catalytic cycles based on these radical reactions allow for development of varied new asymmetric transformations. As one of the most attractive features of radical processes, radical cascades initiated by α-Co(III)-alkyl radical species would provide more opportunities for the construction of complicated organic molecules in a rapid fashion and with possible stereocontrol.[30]

1.8 REFRENCES

(1) (a) Chatgilialoglu, C.; Studer, A. *Encyclopedia of radicals in chemistry, biology, and materials*; John Wiley & Sons: Chichester, West Sussex ; Hoboken, N.J., 2012; (b) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of radical reactions: concepts, guidelines, and synthetic applications*; John Wiley & Sons, 2008; (c) Zard, S. Z. *Radical reactions in*

organic synthesis; Oxford University Press: Oxford, 2003; (d) Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. *J. Org. Chem.* **2016**, *81*, 6898; (e) Yan, M.; Lo, J. C.; Edwards, J. T.; Baran, P. S. *J. Am. Chem. Soc.* **2016**, *138*, 12692.

(2) (a) Sibi, M. P.; Manyem, S.; Zimmerman, J. *Chem. Rev.* **2003**, *103*, 3263; (b) Brimioulle, R.; Lenhart, D.; Maturi, M. M.; Bach, T. *Angew. Chem., Int. Ed.* **2015**, *54*, 3872; (c) Blum, T. R.; Miller, Z. D.; Bates, D. M.; Guzei, I. A.; Yoon, T. P. *Science* **2016**, *354*, 1391; (d) Kainz, Q. M.; Matier, C. D.; Bartoszewicz, A.; Zultanski, S. L.; Peters, J. C.; Fu, G. C. *Science* **2016**, *351*, 681; (e) Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Rose, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100; (f) Lin, J.-S.; Dong, X.-Y.; Li, T.-T.; Jiang, N.-C.; Tan, B.; Liu, X.-Y. *J. Am. Chem. Soc.* **2016**, *138*, 9357.

(3) Reviews and highlights on Co(II)-MRC, see: (a) Miyabe, H.; Kawashima, A.; Yoshioka, E.; Kohtani, S. *Chem. Eur. J.* **2017**, *23*, 6225; (b) Studer, A.; Curran, D. P. *Angew. Chem., Int. Ed.* **2016**, *55*, 58; (c) Pellissier, H.; Clavier, H. *Chem. Rev.* **2014**, *114*, 2775; (d) Lu, H. J.; Zhang, X. P. *Chem. Soc. Rev.* **2011**, *40*, 1899.

(4) Select examples on Ti(III)-MRC, see: (a) Gansauer, A.; Hildebrandt, S.; Vogelsang, E.; Flowers Ii, R. A. *Dalton Trans.* **2016**, *45*, 448; (b) Gansäuer, A.; Fleckhaus, A.; Lafont, M. A.; Okkel, A.; Kotsis, K.; Anoop, A.; Neese, F. *J. Am. Chem. Soc.* **2009**, *131*, 16989.

(5) For experimental and theoretical studies on the radical mechanism involving *α*-Co(III)-alkyl radical (also known as Co(III)-carbene radical) intermediates for olefin cyclopropanation, see: (a) Dzik, W. I.; Xu, X.; Zhang, X. P.; Reek, J. N. H.; de Bruin, B. *J. Am. Chem. Soc.* **2010**, *132*, 10891; (b) Belof, J. L.; Cioce, C. R.; Xu, X.; Zhang, X. P.;

Space, B.; Woodcock, H. L. *Organometallics* **2011**, *30*, 2739; (c) Dzik, W. I.; Zhang, X. P.; de Bruin, B. *Inorg. Chem.* **2011**, *50*, 9896.

(6) (a) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. *Synthesis* **2014**, *46*, 979; (b) Intrieri, D.; Caselli, A.; Gallo, E. *Eur. J. Inorg. Chem.* **2011**, 5071; (c) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977; (d) Davies, H. M. L.; Antoulinakis, E. G. In *Organic Reactions*; John Wiley & Sons, Inc.: 2001; Vol. 57, p 1; (e) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911; (f) Intrieri, D.; Carminati, D. M.; Gallo, E. *Dalton Trans.* **2016**, *45*, 15746.

(7) (a) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. *Chem. Rev.* **2010**, *110*, 704; (b) Lebel, H.; Marcoux, J. F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977.

(8) (a) Caballero, A.; Prieto, A.; Diaz-Requejo, M. M.; Perez, P. J. *Eur. J. Inorg. Chem.* **2009**, 1137; (b) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.

(9) (a) Chen, Y.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 4432; (b) Gao, G. Y.; Colvin, A. J.; Chen, Y.; Zhang, X. P. *Org. Lett.* **2003**, *5*, 3261; (c) Gao, G. Y. Y.; Chen, Y.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 6215; (d) Gao, G. Y.; Chen, Y.; Zhang, X. P. *Org. Lett.* **2004**, *6*, 1837; (e) Gao, G. Y.; Colvin, A. J.; Chen, Y.; Zhang, X. P. *J. Org. Chem.* **2004**, *69*, 8886; (f) Chen, Y.; Gao, G. Y.; Zhang, X. P. *Tetrahedron Lett.* **2005**, *46*, 4965; (g) Gao, G. Y.; Ruppel, J. V.; Allen, D. B.; Chen, Y.; Zhang, X. P. *J. Org. Chem.* **2007**, *72*, 9060; (h) Gao, G. Y.; Ruppel, J. V.; Fields, K. B.; Xu, X.; Chen, Y.; Zhang, X. P. *J. Org. Chem.* **2008**, *73*, 4855.

(10) Lindsey, J. S. In *The porphyrin handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 1, pp 45-118.

(11) Chen, Y.; Fields, K. B.; Zhang, X. P. *J. Am. Chem. Soc.* **2004**, *126*, 14718.

(12) Chen, Y.; Zhang, X. P. *Synthesis* **2006**, 1697.

(13) Chen, Y.; Zhang, X. P. *J. Org. Chem.* **2007**, *72*, 5931.

(14) Chen, Y.; Ruppel, J. V.; Zhang, X. P. *J. Am. Chem. Soc.* **2007**, *129*, 12074.

(15) Lu, H. J.; Dzik, W. I.; Xu, X.; Wojtas, L.; de Bruin, B.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 8518.

(16) Ruppel, J. V.; Gauthier, T. J.; Snyder, N. L.; Perman, J. A.; Zhang, X. P. *Org. Lett.* **2009**, *11*, 2273.

(17) Zhu, S. F.; Ruppel, J. V.; Lu, H. J.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2008**, *130*, 5042.

(18) Zhu, S. F.; Cui, X.; Zhang, X. P. *Eur. J. Inorg. Chem.* **2012**, 430.

(19) Zhu, S. F.; Perman, J. A.; Zhang, X. P. *Angew. Chem., Int. Ed.* **2008**, *47*, 8460.

(20) Doyle, M. P. *Angew. Chem., Int. Ed.* **2009**, *48*, 850.

(21) Zhu, S. F.; Xu, X.; Perman, J. A.; Zhang, X. P. *J. Am. Chem. Soc.* **2010**, *132*, 12796.

(22) Xu, X.; Zhu, S. F.; Cui, X.; Wojtas, L.; Zhang, X. P. *Angew. Chem., Int. Ed.* **2013**, *52*, 11857.

(23) Xu, X.; Wang, Y.; Cui, X.; Wojtas, L.; Zhang, X. P. *Chem. Sci.* **2017**, *8*, 4347.

(24) (a) Goudreau, S. R.; Charette, A. B. *J. Am. Chem. Soc.* **2009**, *131*, 15633; (b) Berkessel, A.; Kaiser, P.; Lex, J. *Chem. Eur. J.* **2003**, *9*, 4746; (c) Aggarwal, V. K.; Alonso, E.; Fang, G.; Ferrara, M.; Hynd, G.; Porcelloni, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1433; (d) Aggarwal, V. K.; Smith, H. W.; Jones, R. V. H.; Fieldhouse, R. *Chem. Commun.* **1997**, 1785; (e) Verdecchia, M.; Tubaro, C.; Biffis, A. *Tetrahedron Lett.* **2011**, *52*, 1136; (f) Dai, X.; Warren, T. H. *J. Am. Chem. Soc.* **2004**, *126*, 10085; (g) Maas, G.; Seitz, J. *Tetrahedron Lett.* **2001**, *42*, 6137; (h) Li, Y.; Huang, J.-S.; Zhou, Z.-Y.; Che, C.-M. *J. Am. Chem. Soc.*

2001, *123*, 4843; (i) Hamaker, C. G.; Djukic, J.-P.; Smith, D. A.; Woo, L. K. *Organometallics* **2001**, *20*, 5189.

(25) Wang, Y.; Wen, X.; Cui, X.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2017**, *139*, 1049.

(26) Roy, S.; Das, S. K.; Chattopadhyay, B. *Angew. Chem., Int. Ed.* **2018**, *57*, 2238.

(27) Xu, X.; Lu, H. J.; Ruppel, J. V.; Cui, X.; de Mesa, S. L.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 15292.

(28) Cui, X.; Xu, X.; Lu, H. J.; Zhu, S. F.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 3304.

(29) (a) Cui, X.; Xu, X.; Jin, L. M.; Wojtas, L.; Zhang, X. P. *Chem. Sci.* **2015**, *6*, 1219; (b) Wang, Y.; Wen, X.; Cui, X.; Zhang, X. P. *J. Am. Chem. Soc.* **2018**, *140*, 4792; (c) Wen, X.; Wang, Y.; Zhang, X. P. *Chem. Sci.* **2018**, *9*, 508.

(30) (a) Cui, X.; Xu, X.; Wojtas, L.; Kim, M. M.; Zhang, X. P. *J. Am. Chem. Soc.* **2012**, *134*, 19981; (b) Paul, N. D.; Mandal, S.; Otte, M.; Cui, X.; Zhang, X. P.; de Bruin, B. *J. Am. Chem. Soc.* **2014**, *136*, 1090.

CHAPTER 2

ASYMMETRIC RADICAL CYCLOPROPANATION OF ALKENES WITH IN SITU-GENERATED DONOR-SUBSTITUTED DIAZO REAGENTS VIA COBALT(II)-BASED METALLORADICAL CATALYSIS

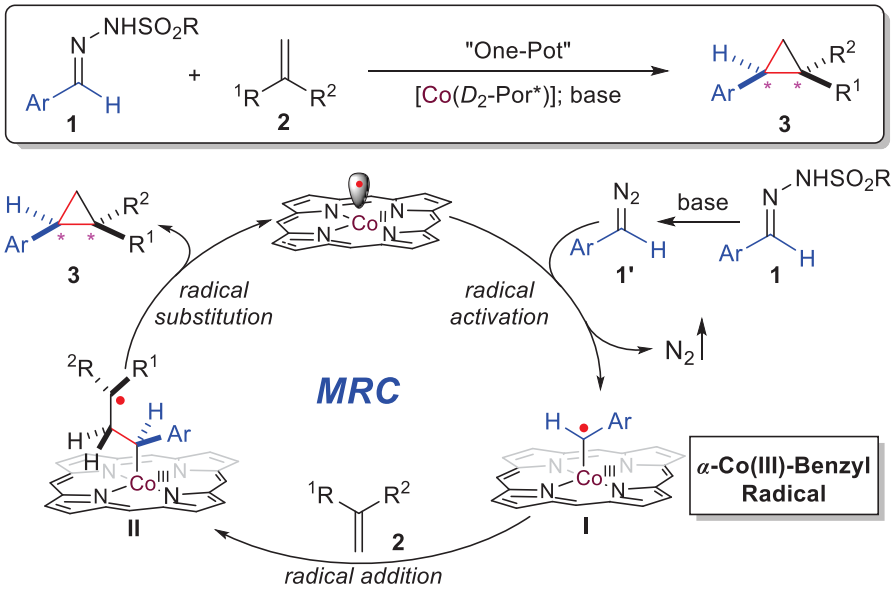
2.1 INTRODUCTION

There has been lasting interest in devising strategies to control stereoselectivities, especially enantioselectivities, of radical reactions for applications in organic synthesis.[1] Among recent advances,[1,2] metalloradical catalysis (MRC), which aims at the development of metalloradical-based systems for both catalytic initiation and selective control of radical processes, has led to the discovery of new catalytic pathways for stereoselective radical reactions.[3,4] As stable metalloradicals with well-defined open-shell d^7 electronic structures, cobalt(II) complexes of D_2-symmetric chiral porphyrins [Co(D_2-Por*)] have emerged as a new class of effective catalysts for asymmetric radical transformations through catalytic generation of metal-stabilized organic radicals, such as the fundamentally new α-metalloalkyl radicals and α-metalloaminyl radicals, as the key intermediates.[5] To date, Co(II)-based metalloradical catalysis (Co(II)-MRC) has exhibited capability of activating both acceptor- and acceptor/acceptor-substituted diazo reagents to generate corresponding α-Co(III)-alkyl radicals (also known as Co(III)-carbene radicals) as key intermediates for various C-centered radical processes, including radical cyclopropanation of alkenes.[6,7] Studies suggest that potential hydrogen-bonding interactions between carbonyl groups of these types of diazo reagents and the amide units of the porphyrin ligands in the resulting

α-Co(III)-alkyl radicals play an important role in enhancing reactivity and controlling stereoselectivity.

It was unclear if Co(II)-MRC could also be applicable to other types of diazo reagents that lack a carbonyl group, such as donor-substituted diazo reagents. Specifically, we wondered whether [Co(D_2-Por*)] metalloradical catalysts were able to activate aryldiazomethanes to generate the corresponding α-Co(III)-benzyl radical intermediate **I** (Scheme 2.1).

Scheme 2.1|| Proposed Catalytic Pathway for Asymmetric Radical Cyclopropanation with In Situ-Generated Donor-Substituted Diazo Reagents

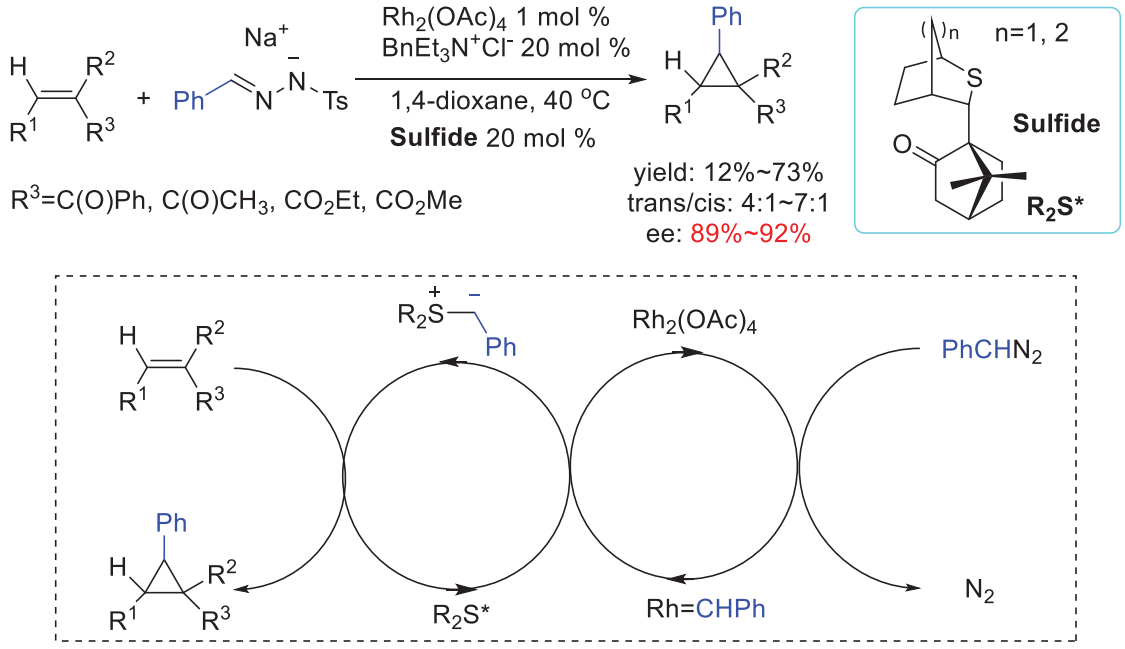


In the absence of carbonyl functionalities, what element of interaction could be explored for the effective control of enantioselectivity in the subsequent radical addition of the α-Co(III)-benzyl radical **I** to the olefin substrate? Furthermore, would the final step, *3-exo-tet* radical cyclization of the resulting γ-Co(III)-alkyl radicals **II**, be diastereoselective? Additional questions arose from the intrinsic instability of donor-substituted

diazomethanes, which are typically generated in situ from stable sulfonyl hydrazone precursors.[8] Would Co(II)-MRC system be compatible with the basic conditions required for the in-situ generation protocol? If these questions could be answered positively, it would further expand the application of Co(II)-based radical cyclopropanation for the catalytic synthesis of enantioenriched 1,2-bisaryl and related cyclopropane compounds **3**. Asymmetric olefin cyclopropanation with diazo reagents represents one of the most general methods for the construction of optically active three-membered carbocycles.[9] While tremendous progress has been made with the use of several types of diazo reagents, asymmetric cyclopropanation with donor-substituted diazo reagents has been much less developed.[10] The underlying challenge may be ascribed to the diminished electrophilicity of the corresponding donor-substituted metallocarbene intermediates associated with most catalytic systems, which would decrease the reactivity toward olefins for cyclopropanation.

As a novel alternative involving the further transfer of the initially formed electrophilic Rh_2-carbenes into nucleophilic chiral sulfur ylides (Scheme 2.2), Aggarwal and coworkers developed an indirect approach for asymmetric cyclopropanation with sulfonyl hydrazones as diazo precursors using the combination of dirhodium carboxylates and chiral sulfides as the catalyst that works specifically for electron-deficient olefins.[8c,10c] Nevertheless, it would be desirable to develop new catalytic systems that are capable of direct asymmetric cyclopropanation of diverse alkenes with donor-substituted diazo reagents.[11]

Scheme 2.2|| Asymmetric Radical Cyclopropanation with In Situ-Generated Donor-Substituted Diazo with Dirhodium Carboxylates and Chiral Sulfides as Catalysts



In view of the radical pathway of MRC (Scheme 2.1), we hypothesized that the radical cyclopropanation approach could potentially address the aforementioned issues with donor-substituted diazo reagents because a neutral radical process is generally less sensitive to electronic effects. In this project, we have developed the first asymmetric catalytic system that is highly effective for direct cyclopropanation of alkenes with α-aryl diazomethanes. Under mild conditions, the Co(II)-based metalloradical system is suitable for various alkenes, allowing for the efficient construction of the corresponding cyclopropane rings with excellent control of both diastereoselectivity and enantioselectivity. The Co(II)-catalyzed cyclopropanation is further highlighted by its

functional group tolerance, a feature that is in accordance with the underlying radical mechanism.

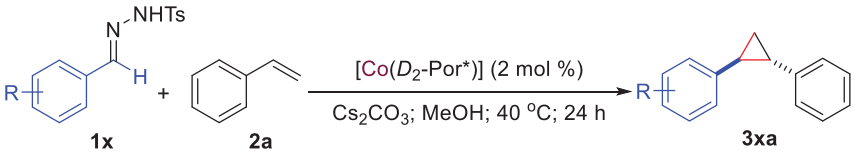
2.2 RESULTS AND DISCUSSION

2.2.1 Condition Optimization for Asymmetric Cyclopropanation of Styrene with Tosylhydrazone 1a

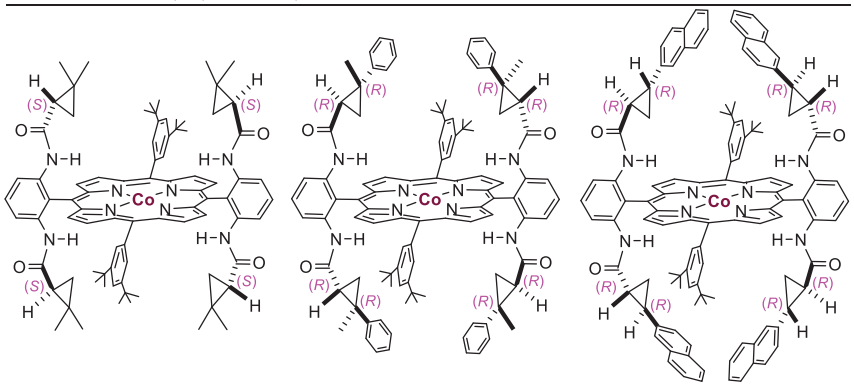
Our study began with the investigation of catalytic cyclopropanation of styrene (**2a**) with benzaldehyde tosylhydrazone (**1a**), which is known to generate α-phenyldiazomethane under basic conditions (Table 2.1). To our delight, even simple metalloradical catalyst [Co(TPP)] (TPP = 5,10,15,20-tetraphenylporphyrin) could catalyze the reaction in the presence of Cs_2CO_3 in methanol, forming the desired 1,2-diphenyl cyclopropane **3aa** in 46% yield (entry 1). This result signifies the compatibility of Co(II)-based metalloradical system with both bases and polar solvents that are required for in-situ generation of donor-substituted diazomethanes from the corresponding hydrazone precursors.

We then evaluated the possibility of stereoselective control of the catalytic reaction through the use of Co(II) complexes of D_2-symmetric chiral amidoporphyrins [Co(D_2-Por*)]. When the first-generation catalyst [Co(**P1**)] (**P1** = 3,5-Di^{t}Bu-ChenPhyrin) was used,[6i] cyclopropane **3aa** could form in higher yield with significant level of both enantioselectivity and diastereoselectivity (entry 2). To further improve the stereoselectivity of the catalytic reaction, we then turned our attention to the second-

Table 2.1|| Asymmetric Cyclopropanation of Styrene with Tosylhydrazones by Metalloradical Catalysts [Co(D_2-Por*)][a]



entry	R	catalyst	product	yield (%)[b]	dr[c]	ee (%)[d]
1	H (**1a**)	[Co(TPP)]	**3aa**	46	88:12	-
2	H (**1a**)	[Co(**P1**)]	**3aa**	64	89:11	-42
3	H (**1a**)	[Co(**P2**)]	**3aa**	65	78:22	<5
4	H (**1a**)	[Co(**P3**)]	**3aa**	67	95:5	26
5	2-MeO (**1b**)	[Co(**P3**)]	**3ba**	78	95:5	99
6	2-Et (**1c**)	[Co(**P3**)]	**3ca**	87	85:15	33
7	4-MeO (**1d**)	[Co(**P3**)]	**3da**	23	93:7	23
8	3-MeO (**1e**)	[Co(**P3**)]	**3ea**	69	95:5	23

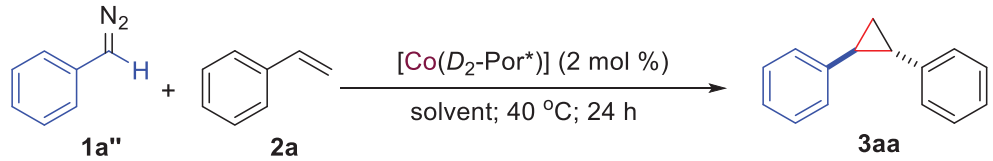


[a] Reactions were carried out with **1x** (0.1 mmol) and **2a** (1.5 equiv.) in the presence of Cs_2CO_3 (2 equiv.) by [Co(D_2-Por*)] (2 mol %) in methanol (0.6 mL) at 40 °C for 24 h. [b] Isolated yields. [c] The diastereomeric ratio (*dr*) was determined by ^{1}H NMR. [d] Enantiomeric excess of the major *trans* diastereomer was determined by chiral HPLC.

generation Co(II)-based metalloradical catalysts.[6b] While the phenyl-substituted [Co(**P2**)] (**P2** = 3,5-Di^{t}Bu-QingPhyrin) was found to be less selective, the naphthyl-substituted [Co(**P3**)] (**P3** = 3,5-Di^{t}Bu-Xu(2'-Naph)Phyrin)) could effectively catalyze the formation of cyclopropane **3aa** with excellent diastereoselectivity but lower enantioselectivity (entry

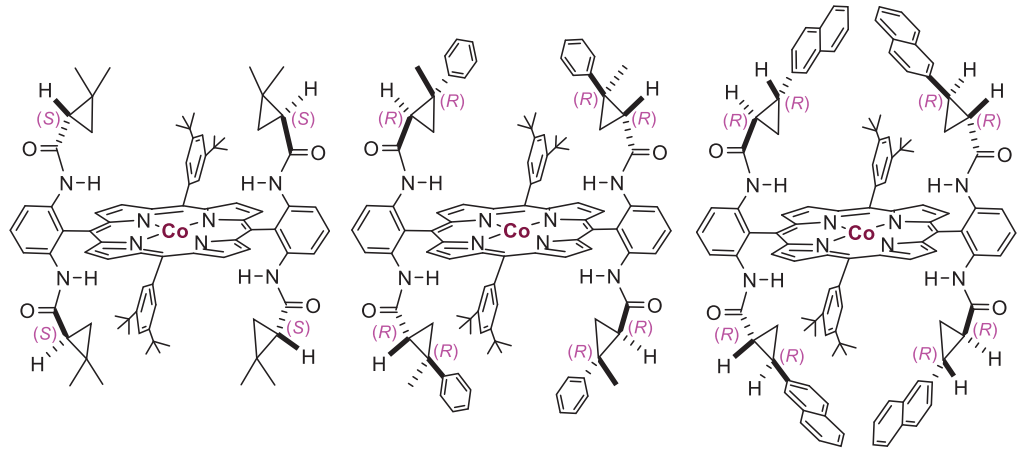
4). It should be noted that comparable reactivity was observed with the use of preformed *α*-phenyldiazomethane (Table 2.2).

Table 2.2|| Asymmetric Cyclopropanation of Styrene Directly with Phenyldiazomethane [a]



1a'' **2a** **3aa**

entry	Catalyst	solvent	yield (%)[b]	dr[d]	ee (%)[e]
1	[Co(**P1**)]	MeOH	36	89:11	-46
2	[Co(**P2**)]	MeOH	35	82:18	<5
3	[Co(**P3**)]	MeOH	72 (63)[c]	95:5	18
4	[Co(**P3**)]	n-hexane	42	95:5	45
5	[Co(**P3**)]	DCM	<10	-	-
6	[Co(**P3**)]	$PhCH_3$	<10	-	-



[Co(**P1**)] [Co(**P2**)] [Co(**P3**)]

[a] Carried out with **1a''** (0.1 mmol) and **2a** (1.5 equiv.) in solvent (0.6 mL). [b] NMR yields. [c] In the parenthesis, isolated yield. [d] Determined by ^{1}H NMR. [e] Determined by chiral HPLC for the major *trans* diastereomer.

The ineffective asymmetric induction is likely attributed to the low-barrier rotation of the *α*-benzyl radical unit around the Co(III)–C σ bond in intermediate **I** (vide supra, Scheme 2.1) that diminishes its approaching preference to the prochiral styrene substrate between the *re* and *si* faces. To restrict the rotation within the chiral pocket of the porphyrin ligand, we decided to use benzaldehyde tosylhydrazone derivative that contains an *ortho*-methoxy group (**1b**) as the radical precursor for the catalytic process (vide supra, Table 2.1, entry 5). Considering methoxy groups are known to serve as good hydrogen bond acceptors,[12] we postulated that the potential formation of N–H···O hydrogen bond between the amido group of the chiral ligand and the methoxy group of tosylhydrazone **1b** (Figure 2.1) might rigidify the resulting *α*-Co(III)-alkyl radical intermediate **I**, leading to an improved stereoselective outcome. We were excited that the corresponding cyclopropane **3ba** was indeed obtained in good yield (78%) with high diastereoselectivity (95:5 dr) as well as excellent enantioselectivity (99% ee) (Table 2.1, entry 5).

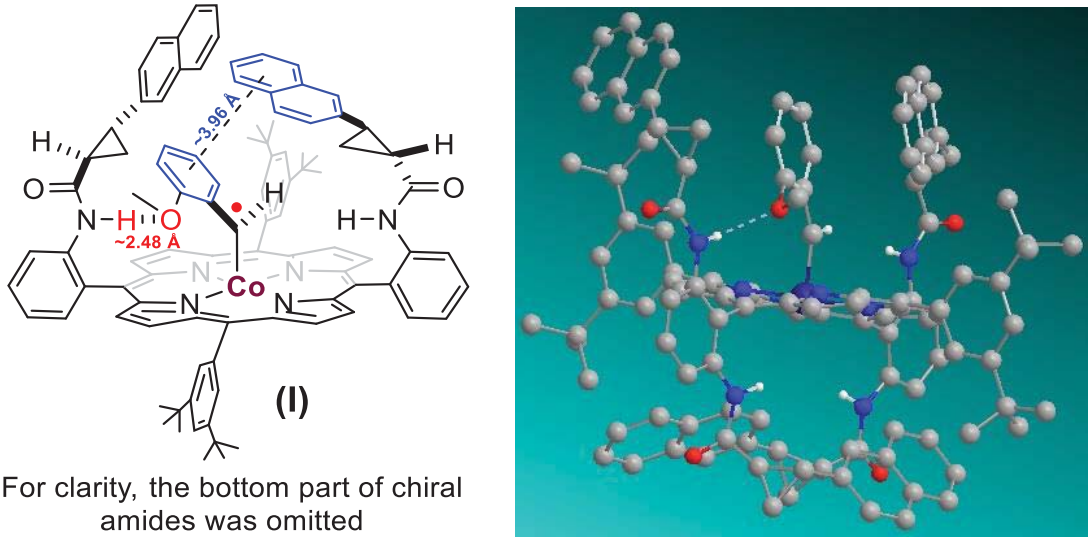
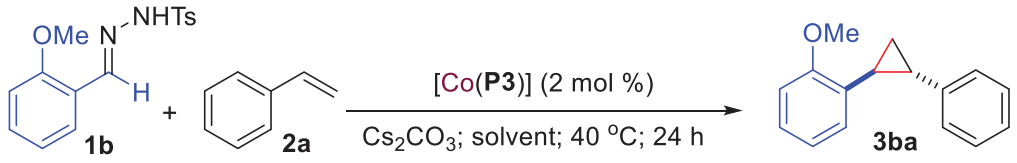


Figure 2.1|| Spartan Modeling of Proposed *α*-Co(III)-Alkyl Radical Intermediate I

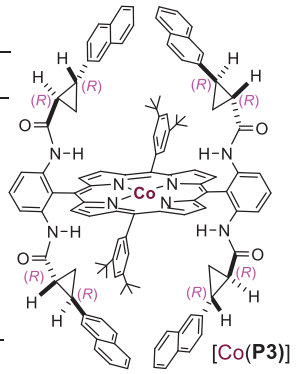
Accordingly, asymmetric induction of the cyclopropanation process was significantly reduced when the methoxy group in **1b** was replaced by a sterically comparable ethyl group despite the high reactivity (entry 6, Table 2.1). Moreover, low enantioselectivity was observed when the methoxy group in the tosylhydrazone **1b** was moved from *ortho*- to either *meta*- or *para*- positions of the phenyl ring although with similarly high diastereoselectivity (entries 7 and 8, Table 2.1). These results are in agreement with the hypothesized hydrogen-bonding interaction.

Further investigation of solvent effect on the developed radical cyclopropanation revealed that both polar and non-polar solvents were suitable albeit with varied yields and selectivities, and the solvent of choice was still methanol (Table 2.3).

Table 2.3|| Solvent Effect on Asymmetric Cyclopropanation of Styrene 2a with Tosylhydrazones 1b by [Co(P3)][a]



entry	solvent	yield (%)[b]	dr[c]	ee (%)[d]
1	MeOH	78	95:5	99
2	THF	25	88:12	83
3	DCM	65	82:18	93
4	PhCl	32	67:33	92
5	PhH	35	83:17	94



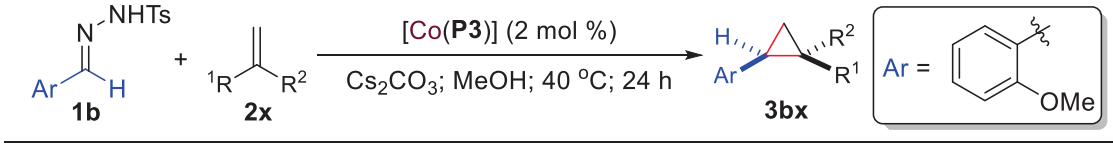
[a] Carried out with **1b** (0.1 mmol) and **2a** (1.5 equiv.) in the presence of Cs_2CO_3 (2 equiv.) in solvent (0.6 mL). [b] Isolated yields. [c] Determined by ^1H NMR. [d] Determined by chiral HPLC for the major *trans* diastereomer.

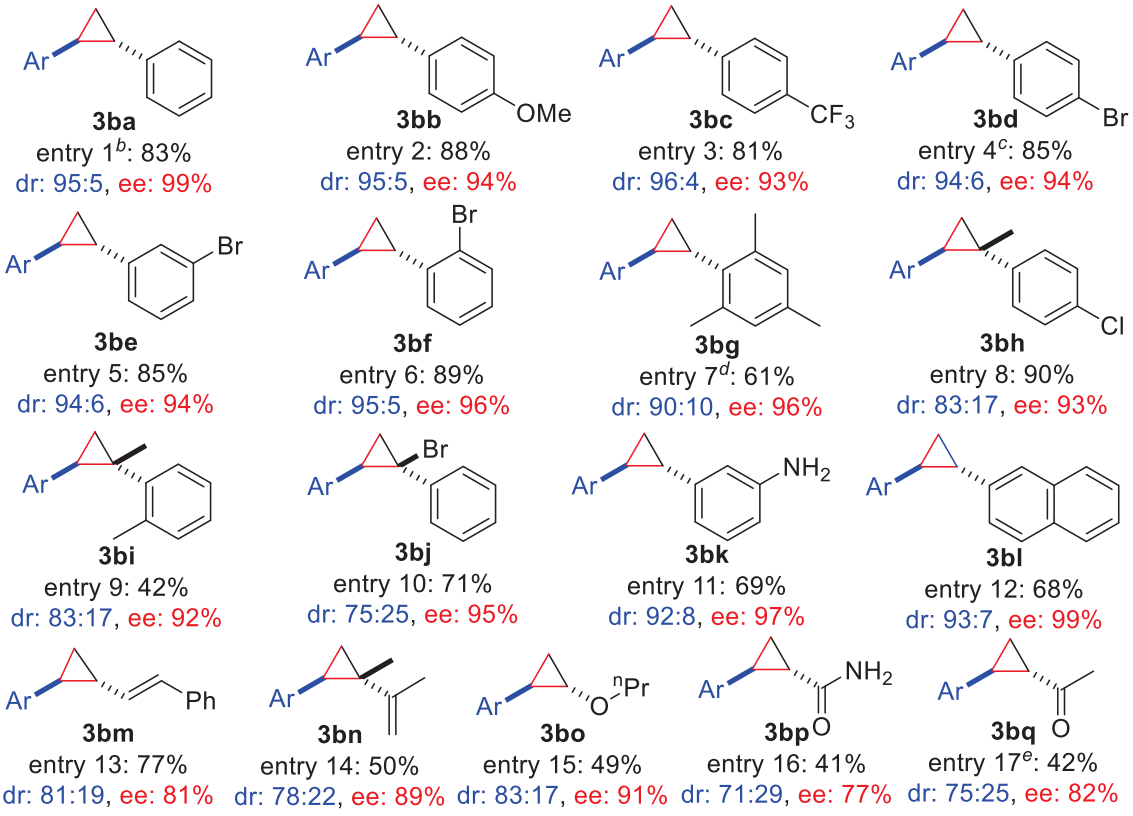
2.2.2 Asymmetric Radical Cyclopropanation of Different Alkenes

Under the optimized conditions, the scope of [Co(**P3**)]/**1b**-based catalytic system was then evaluated by employing different alkenes with varied steric and electronic properties as substrates for asymmetric radical cyclopropanation (Table 2.4). Like styrene, its derivatives bearing substituents with different electronic properties, including electron-donating MeO and electron-withdrawing CF_3 groups, could be radically cyclopropanated with **1b**, generating the corresponding 1,2-bisaryl cyclopropanes in high yields with excellent control of both diastereoselectivity and enantioselectivity (entries 1–3). Halogenated styrenes such as those with a Br atom at various positions were also shown to be suitable substrates for the catalytic process, providing the desired cyclopropanes in similarly high yields and stereoselectivities (entries 4–6). The relative and absolute configurations of cyclopropane **3bd** (entry 4) were established as *trans* and (1*S*,2*S*), respectively, by anomalous-dispersion effects in X-ray diffraction of its single crystal.

As demonstrated for 2-bromostyrene (**2f**) together with 2,4,6-trimethylstyrene (**2g**), sterically hindered styrene derivatives could also undergo productive cyclopropanation reactions with **1b** by [Co(**P3**)] (entries 6 and 7). Furthermore, this metalloradical system was also applicable for 1,1-disubstituted olefins as demonstrated with the reactions of α-substituted styrene derivatives **2h**, **2i** and **2j**, affording the desired cyclopropanes with enantioselective control of the newly-formed quaternary stereogenic centers (entries 8–10). Distinctly, the Co(II)-based radical process could tolerate functional groups as exemplified by the highly enantioselective cyclopropanation of 3-aminostyrene (entry 11). In addition to the expanded aromatic olefins such as 2-vinylnaphthalene (entry 12), conjugated dienes, including both aromatic diene **2m** and aliphatic diene **2n**, could also be employed as

Table 2.4|| Asymmetric Cyclopropanation of Different Olefins with Tosylhydrazone 1b Catalyzed by [Co(P3)][a]





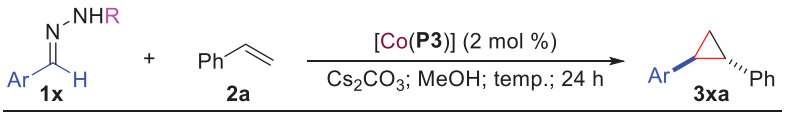
[a] Reactions were carried out with **1b** (0.1 mmol) and **2x** (1.5 equiv.) in the presence of Cs_2CO_3 (2 equiv.) by [Co(**P3**)] (2 mol %) in methanol (0.6 mL) at 40 °C for 24 h; Isolated yields; The diastereomeric ratio (dr) was determined by ^{1}H NMR; Enantiomeric excess of the major *trans* diastereomer was determined by chiral HPLC. [b] The reaction was performed on 1.0 mmol scale. [c] (1*S*,2*S*) Absolute configuration was determined in X-ray diffraction measurements on crystal. [d] 5 mol % [Co(**P3**)] was used. [e] 5.0 equiv. **2q**.

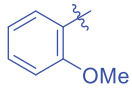
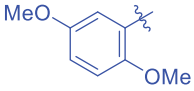
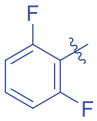
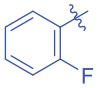
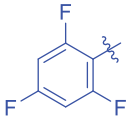
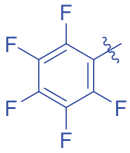
substrates for the Co(II)-based cyclopropanation but with relatively lower stereoselectivities (entries 13 and 14). It was notable that both electron-rich and -deficient non-aromatic olefins, such as vinyl ether **2o**, acrylamide **2p** and vinyl ketone **2q** could be enantioselectively cyclopropanated as well (entries 15–17) with moderate control of stereoselectivities. The observed substrate scope and reactivity profile of [Co(**P3**)]-catalyzed cyclopropanation is in agreement with the underlying radical mechanism via Co(II)-based metalloradical catalysis (vide supra, Scheme 2.1). It was also noteworthy to mention that the one-pot protocol of the Co(II)-catalyzed radical cyclopropanation could be scaled up ten-fold as demonstrated with the high-yielding synthesis of cyclopropane **3ba** on 1.0 mmol scale without affecting the excellent stereoselectivity (entry 1).

2.2.3 Asymmetric Cyclopropanation of Styrene with Various Benzaldehyde Sulfonylhydrazone Derivatives

Guided by the postulated importance of hydrogen-bonding interaction in the key *α*-Co(III)-benzyl radical intermediates **I**, we then sought to identify other benzaldehyde sulfonylhydrazone derivatives as effective radical precursors for asymmetric cyclopropanation (Table 2.5). Like arylhydrazone **1b** (entry 1), 2,5-dimethoxybenzaldehyde-derived tosylhydrazone (**1f**) could be also effectively activated by the metalloradical catalyst [Co(**P3**)] for radical cyclopropanation of styrene, affording the corresponding cyclopropane **3fa** in 91% yield with 90% de and 94% ee (entry 2). Considering that fluorine atoms in organic fluorides have been demonstrated as a potential hydrogen bond acceptor in application for asymmetric catalysis,[13] we explored the use of fluorine-containing arylhydrazones as diazo precursors for asymmetric radical styrene

Table 2.5|| Asymmetric Cyclopropanation of Styrene with Various Sulfonyl Hydrazones Catalyzed by [Co(P3)][a]



entry	Ar	R[b]	product	temp. (°C)	yield (%)[c]	dr[d]	ee (%)[e]
1		Ts (**1b**)	**3ba**	40	78	95:5	99
2		Ts (**1f**)	**3fa**	40	91	95:5	94
3		Ts (**1g**)	**3ga**	RT	90	94:6	86
4		Ts (**1g**)	**3ga**	0	<10	-	-
5		Tris (**1g'**)	**3g'a**	0	83	>99:1	93
6		Ts (**1h**)	**3ha**	RT	58	96:4	71
7		Tris (**1h'**)	**3h'a**	0	75	>99:1	76
8		Ts (**1i**)	**3ia**	RT	85	96:4	88
9		Tris (**1i'**)	**3i'a**	0	85	>99:1	93
10		Ts (**1j**)	**3ja**	RT	82	95:5	68
11		Tris (**1j'**)	**3j'a**	0	81	>99:1	89

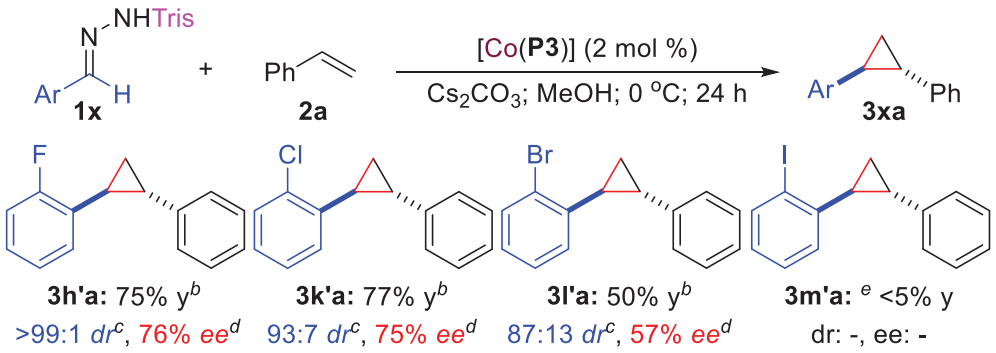
[a] Reactions were carried out with **1x** (0.1 mmol) and **2a** (1.5 equiv.) in the presence of Cs_2CO_3 (2 equiv.) by [Co(**P3**)] (2 mol %) in methanol (0.6 mL) for 24 h. [b] Ts = 4-toluenesulfonyl; Tris = (2,4,6-triisopropyl)phenyl sulfonyl. [c] Isolated yields. [d] The diastereomeric ratio (dr) was determined by ^{1}H NMR. [e] Enantiomeric excess of the major *trans* diastereomer was determined by chiral HPLC.

cyclopropanation. Remarkably, fluoroarene-based tosylhydrazones such as **1g**–**1j** were found to be even more active than **1b** as radical precursors for Co(II)-based

cyclopropanation, enabling the operation of the catalytic process even at room temperature (entries 3, 6, 8 and 10). The desired fluorine-containing bisaryl cyclopropane products **3ga**–**3ja** were obtained in up to 90% yield with 88–92% de and 68–88% ee. Attempts to further improve enantioselectivity of the cyclopropanation of styrene with 2,6-difluorobenzaldehyde-derived tosylhydrazone **1g** at lower temperature were unsuccessful due to ineffective generation of 2,6-difluorophenyl diazomethane at 0 °C (entry 4). Since the decomposition of the sterically bulky (2,4,6-triisopropylphenyl)sulfonyl hydrazone salt was shown to be considerably faster than tosylhydrazone salt,[14] the low temperature asymmetric cyclopropanation was reexamined with the use of 2,6-difluorobenzaldehyde-derived (2,4,6-triisopropylphenyl)sulfonyl hydrazone **1g'**. As expected, the catalytic cyclopropanation reaction could proceed effectively at 0 °C, affording the desired cyclopropane **3ga** in 83% yield with considerably enhanced stereoselectivities (entry 5). Likewise, the radical cyclopropanation reactions with related (2,4,6-triisopropylphenyl)sulfonyl hydrazones **1h'**–**1j'** could also be productively conducted at 0 °C, affording the cyclopropane derivatives **3ha**–**3ja** with significantly improved diastereoselectivity and enantioselectivity (entries 7, 9 and 11). Considering unique bioactivities of organofluorine compounds,[15] these enantioenriched fluorine-containing bisaryl cyclopropanes should find useful synthetic applications for chiral organic fluorides.

Under the same conditions, *o*-chlorobenzaldehyde-derived sulfonylhydrazone also gave a similar result compared to the result from *o*-fluorobenzaldehyde-derived sulfonylhydrazone (Scheme 2.3). Nevertheless, *o*-bromo- and *o*-iodobenzaldehyde-derived sulfonylhydrazones proved to be less effective radical precursors for the catalytic process.

Scheme 2.3|| Asymmetric Cyclopropanation of Styrene with Various *o*-Halogenated Benzaldehyde Sulfonyl Hydrazones 1x Catalyzed by [Co(P3)][a]

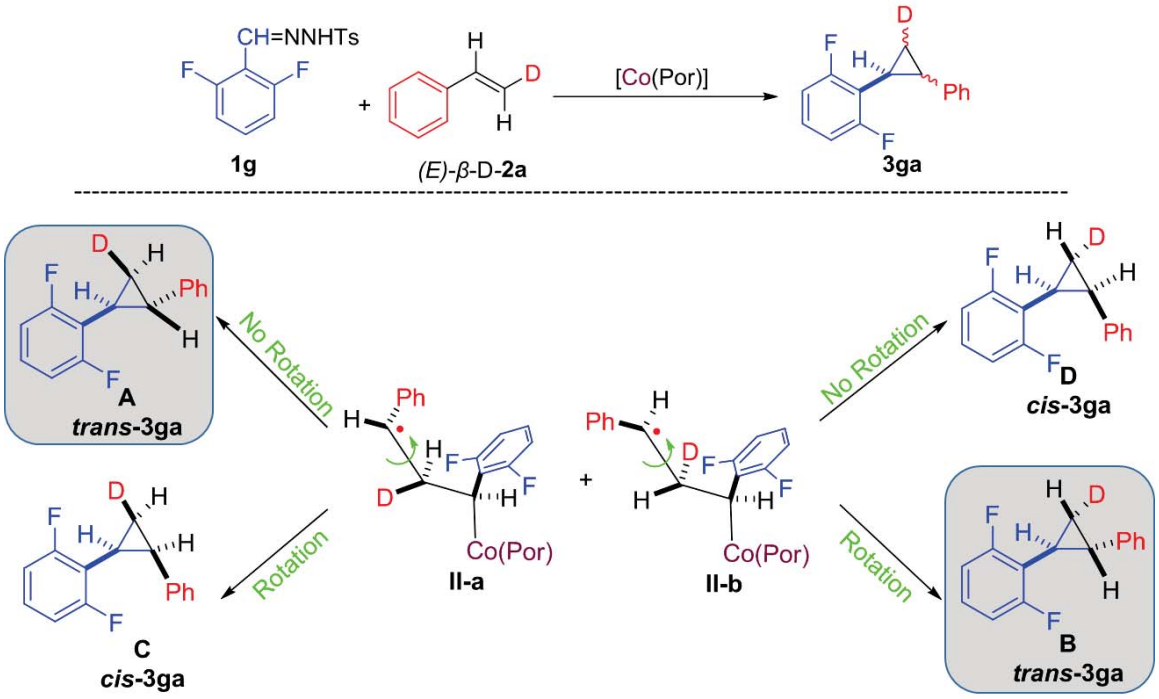


[a] Carried out with **1x** (0.1 mmol) and **2a** (1.5 equiv.) in the presence of Cs_2CO_3 (2 equiv.) in methanol (0.6 mL); Tris = (2,4,6-triisopropyl)phenyl sulfonyl. [b] Isolated yields. [c] Determined by ^{1}H NMR. [d] Determined by chiral HPLC for the major *trans* diastereomer. [e] 1,2-bis(2-iodophenyl)ethene and 2-iodobenzaldehyde were formed as major side products.

2.2.4 Mechanistic Insights by Using *(E)*- and *(Z)*-*β*-Deuterostyrenes as Radical Probe for Cyclopropanation

To probe the underlying stepwise radical mechanism of the Co(II)-catalyzed cyclopropanation process, both *(E)*- and *(Z)*-*β*-deuterostyrenes were employed as substrates for evaluation of product distribution. While a concerted mechanism is usually stereospecific, a stepwise radical mechanism (Scheme 2.1) would result in the formation of four possible diastereomers from either *(E)*- or *(Z)*-*β*-deuterostyrene: two *trans*-isotopomers **A** & **B** and two *cis*-isotopomers **C** & **D** due to the rotation of *β*-C–C bond in the *γ*-Co(III)-alkyl radical intermediate **II** before facile ring closure (Scheme 2.4).

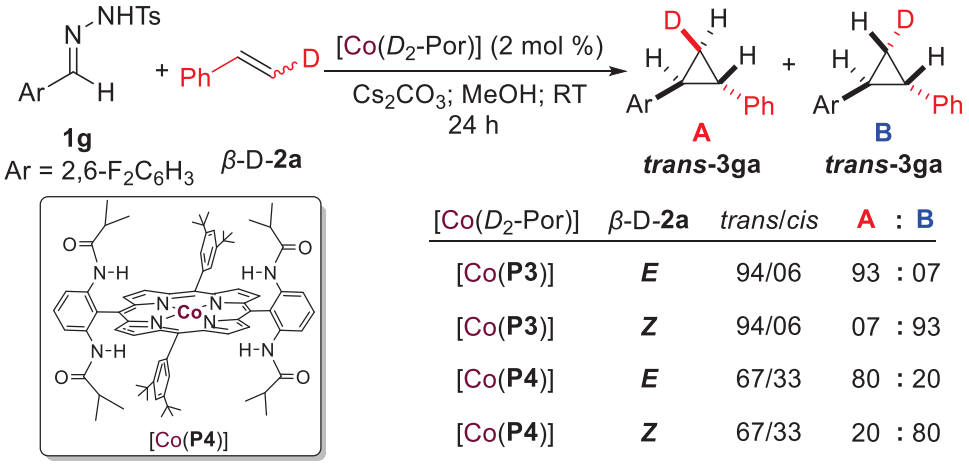
Scheme 2.4|| The Rationale of both Isotopomers A and B Formation in the Major *trans*-Cyclopropanes 3ga from Cyclopropanation of *(E)-β*-Deuterostyrene



Using [Co(**P3**)] as the catalyst, cyclopropanation of *(E)-β*-deuterostyrene with tosylhydrazone **1g** led to the formation of *trans*-**3ga** as the dominant product with a 93:7 ratio of isotopomers **A** and **B** (Scheme 2.4). Under the same conditions, the reaction of *(Z)-β*-deuterostyrene resulted in the identical 93:7 ratio of isotopomeric distribution but in favoring **B** over **A**. The observation of *trans*-isotopomer **B** from *(E)-β*-deuterostyrene as well as *trans*-isotopomer **A** from *(Z)-β*-deuterostyrene is evidently a result of the rotation of *β*-C–C bond in intermediate **II**. When sterically less-hindered [Co(**P4**)] (**P4** = 3,5-Di^{t}Bu-IbuPhyrin) was used as the catalyst,[16] a significantly different isotopomeric ratio of *trans*-isotopomers **A** & **B** (from 93:7 to 80:20) was observed, suggesting easier rotation of the *β*-C–C bond in a less-crowded ligand environment (Schemes 2.4). Together, these

observations convincingly support the proposed stepwise radical mechanism of the Co(II)-catalyzed cyclopropanation with *N*-arylsulfonyl hydrazones.

Scheme 2.4|| Cyclopropanation of *(E)*- and *(Z)*-*β*-Deuterostyrenes to Probe Radical Reaction Mechanism.



[Co(D_2-Por)]	*β*-D-**2a**	*trans*/*cis*	**A** : **B**
[Co(**P3**)]	***E***	94/06	93 : 07
[Co(**P3**)]	***Z***	94/06	07 : 93
[Co(**P4**)]	***E***	67/33	80 : 20
[Co(**P4**)]	***Z***	67/33	20 : 80

Furthermore, experiments were carried out for direct detection of the *α*-Co(III)-benzyl radical species **I** (Scheme 2.1) by high-resolution mass spectrometry (HRMS).[17] The exposure of [Co(**P4**)] to 10 equiv. of **1g** with base in methanol resulted in a mixture that was filtered and analyzed by HRMS in the absence of any additives such as formic acid that commonly acts as electron carriers for ESI ionization. As shown in Figure 2.2, the obtained spectrum clearly revealed a signal corresponding to [Co(**P4**)(2,6-$F_2C_6H_3CH$)]$^+$ (m/z = 1361.6515), which resulted from the neutral *α*-Co(III)-benzyl radical **I** by the loss of one electron. The success in direct detection of the [Co(**P4**)(2,6-$F_2C_6H_3CH$)]$^+$ by HRMS indicates possible stabilization of the *α*-Co(III)-benzyl radical by hydrogen-bonding interaction.

Qualitative Compound Report

Data File	YW-1-150.d	Sample Name	YW-I-150
Sample Type	Sample	Position	P1-C5
Instrument Name	Instrument 1	User Name	
Acq Method	direct_injection-Manetsch.m	Acquired Time	6/2/2014 11:35:24 AM
IRM Calibration Status	Success	DA Method	12.m
Comment			

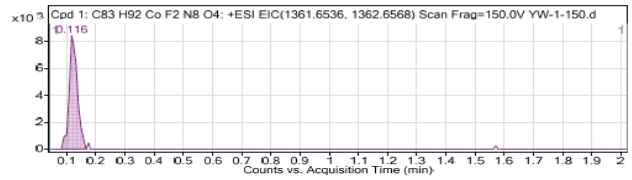
Sample Group — Info.

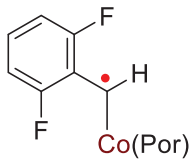
Acquisition SW Version: 6200 series TOF/6500 series Q-TOF B.05.01 (B5125)

Compound Table

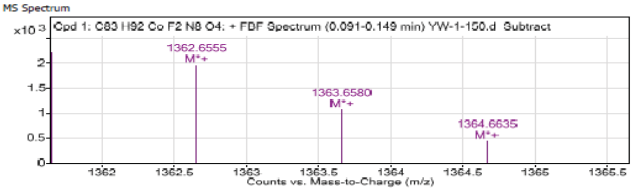
Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C83 H92 Co F2 N8 O4	0.116	1361.6521	2214	C83 H92 Co F2 N8 O4	1361.6542	-1.54	C83 H92 Co F2 N8 O4	C83 H92 Co F2 N8 O4

Compound Label	m/z	RT	Algorithm	Mass
Cpd 1: C83 H92 Co F2 N8 O4	1361.6515	0.116	Find By Formula	1361.6521

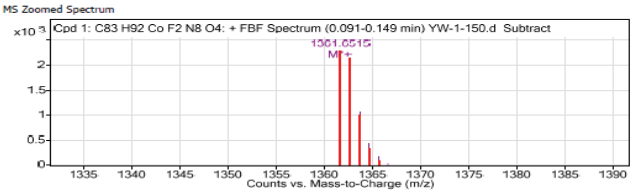




MS Spectrum



MS Zoomed Spectrum



MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
1361.6515	1	2214.14	C83H92CoF2N8O4	M*+
1362.6555	1	1956.79	C83H92CoF2N8O4	M*+
1363.658	1	1060.05	C83H92CoF2N8O4	M*+
1364.6635	1	432.52	C83H92CoF2N8O4	M*+
1365.6459	1	163.56	C83H92CoF2N8O4	M*+

--- End Of Report ---

Figure 2.2|| The Signal of Neutral *α*-Co(III)-Benzyl Radicals I from Electrospray Ionization Mass Spectrometry (ESI-MS)

2.3 CONCLUSIONS

In summary, Co(II)-based metalloradical catalysis (MRC) has, for the first time, been successfully applied to donor-substituted diazo reagents, generated from *N*-arylsulfonyl hydrazones in the presence of base, for cyclopropanation of alkenes. Chiral metalloradical complex [Co(**P3**)] has been shown to be an effective catalyst for asymmetric radical cyclopropanation with *α*-aryldiazomethane precursors. The Co(II)-based cyclopropanation system is applicable to a broad combination of *N*-arylsulfonyl hydrazones and alkenes, affording the corresponding cyclopropane derivatives in high yields with excellent control of both diastereoselectivity and enantioselectivity. In view of the underdevelopment of donor-substituted diazo reagents in asymmetric cyclopropanation, the successful development of this new catalytic radical process will encourage further research efforts in applying sulfonyl hydrazones as stable precursors for various asymmetric catalytic processes.

2.4 EXPERIMENTAL SECTION

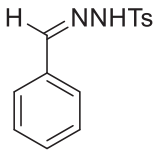
2.4.1 General Considerations

All cyclopropanation reactions were carried out under a nitrogen atmosphere in an oven-dried glassware following standard Schlenk techniques. Anhydrous methanol and other reagents were directly used as purchased. Thin layer chromatography was performed on Merck TLC plates (silica gel 60 F254). Flash column chromatography was performed with ICN silica gel (60 Å, 230-400 mesh, 32-63 μm).

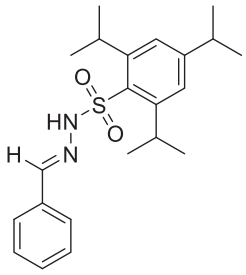
Proton and carbon nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on Varian Inova 400 MHz, Bruke 500 MHz and Varian 600 MHz instruments with chemical shifts reported relative to residual solvent. ^{19}F NMR spectra were recorded on a Varian Inova 400 spectrometer (376 MHz), using $CFCl_3$ ($\delta = 0$) as internal standard. Infrared spectra were measured with a Nicolet Avatar 320 spectrometer with a Smart Miracle accessory. Optical rotations were measured on a Rudolph Research Analytical AUTOPOL® IV digital polarimeter. HPLC measurements were carried out on a Shimadzu HPLC system with Chiralcel OD-H, OJ-H, AD-H and IC columns. HRMS data was obtained on an Agilent 6200 LC/MS ESI/TOF mass spectrometer with electrospray ionization and Agilent 7890 GC-7200 EI/QTOF MS. The X-ray diffraction data were collected using Bruker-AXS SMART-APEXII CCD diffractometer (CuKα, λ = 1.54178 Å). Spartan modelling was performed using Spartan14V118 software.

2.4.2 Typical Procedure for the Preparation of Tosylhydrazones[18]

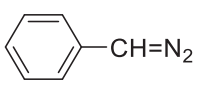
To a stirred solution of pure sulfonyl hydrizide (5.0 mmol) in methanol (12.0 mL), aldehyde (5.0 mmol) was added dropwise (or portionwise if solid) at room temperature. After approximately 3 h, the reaction mixture was cooled to 0 ºC and the product was removed by filtration, washed with a small quantity of cold methanol. The crude solid was further purified by recrystallization in hot methanol.



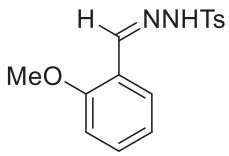
benzaldehyde tosylhydrazone 1a,[18] 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (b, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.78 (s, 1H), 7.63 – 7.50 (m, 2H), 7.40 – 7.33 (m, 3H), 7.30 (d, *J* = 8.4 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.86, 144.25, 135.24, 133.15, 130.39, 129.68, 128.60, 127.92, 127.34, 21.57.



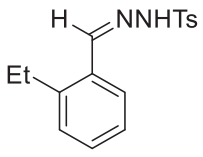
benzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone 1a',[19] 96% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.76 (s, 1H), 7.56 – 7.54 (m, 2H), 7.35 – 7.31 (m, 3H), 7.18 (s, 2H), 4.28 (hept, *J* = 6.8 Hz, 2H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.32 (d, *J* = 6.8 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.14, 154.03, 148.96, 135.98, 133.89, 132.89, 131.23, 129.93, 126.54, 36.84, 32.73, 27.52, 26.17.



Phenyl Diazomethane 1a'', Synthesized from benzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1a'** according to the known literature.[2] red liquid, 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.5 Hz, 2H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 2H), 4.92 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 132.41, 131.72, 126.52, 123.96 (As known in literature, diazo carbon is missing). IR (neat, cm^{-1}): 2962.03, 2062.25 ($C=N_2$), 1596.89, 1412.18, 1262.56, 1101.59, 1031.40, 819.76, 736.79, 690.89.

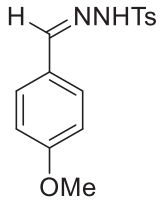


2-methoxybenzaldehyde tosylhydrazone 1b, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.83 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.70 (s, 1H), 7.36 – 7.32 (m, 1H), 7.30 (d, *J* = 8.3 Hz, 2H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 3.81 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.83, 144.10, 143.83, 135.39, 131.72, 129.61, 127.95, 126.57, 121.61, 120.79, 110.90, 55.48, 21.57. IR (neat, cm^{-1}): 3186.49, 1596.14, 1487.96, 1434.28, 1329.63, 1160.67, 1046.43, 811.98, 666.65. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{15}H_{17}N_2O_3S^+$: 305.0954, found 305.0942.

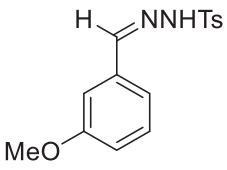


2-ethylbenzaldehyde tosylhydrazone 1c, 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.89 (d, *J* = 8.3 Hz, 2H), 7.69 (dd, *J* = 7.8 Hz, 1.3 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.22 – 7.11 (m, 2H), 2.71 (q, *J* = 7.6 Hz, 2H), 2.41 (s, 3H), 1.13 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.78, 144.24, 143.31, 135.29, 130.48, 130.34, 129.66, 129.27,

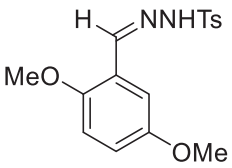
127.98, 127.38, 126.13, 26.00, 21.58, 15.85. IR (neat, cm^{-1}): 3143.63, 1597.23, 1442.73, 1324.67, 1161.54, 1042.62, 945.01, 811.89, 700.38. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{16}H_{19}N_2O_2S^+$: 303.1162, found 303.1169.



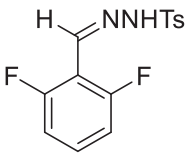
4-methoxybenzaldehyde tosylhydrazone 1d, 92% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 2H), 7.73 (s, 1H), 7.51 (d, J = 8.8 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.47, 148.25, 144.15, 135.31, 129.63, 128.98, 127.93, 125.88, 114.08, 55.34, 21.57. IR (neat, cm^{-1}): 3220.26, 1608.73, 1424.64, 1299.55, 1158.69, 951.07, 826.22, 702.14. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{15}H_{17}N_2O_3S^+$: 305.0954, found 305.0977.



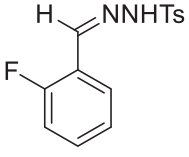
3-methoxybenzaldehyde tosylhydrazone 1e, 90% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.1 Hz, 2H), 7.74 (s, 1H), 7.31 (d, J = 8.1 Hz, 2H), 7.26 (t, J = 8.1 Hz, 2H), 7.15 (s, 1H), 7.11 (d, J = 7.5 Hz, 1H), 6.92 (d, J = 8.3 Hz, 1H), 3.82 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.74, 147.73, 144.30, 135.21, 134.49, 129.68, 129.62, 127.92, 120.48, 116.72, 111.48, 55.33, 21.58. IR (neat, cm^{-1}): 3154.89, 1596.61, 1493.57, 1167.37, 1033.35, 893.12, 793.05, 688.55. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{15}H_{17}N_2O_3S^+$: 305.0954, found 305.0961.



2,5-methoxybenzaldehyde tosylhydrazone 1f, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 3.2 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.88 (dd, *J* = 9.0, 3.2 Hz, 1H), 6.77 (d, *J* = 9.0 Hz, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.60, 152.47, 144.12, 143.65, 135.37, 129.60, 127.94, 122.15, 118.15, 112.45, 110.28, 56.12, 55.82, 21.57. IR (neat, cm^{-1}): 3169.09, 1577.57, 1494.71, 1452.99, 1329.08, 1159.86, 1050.23, 908.61, 799.06, 716.49. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{16}H_{19}N_2O_4S^+$: 335.1060, found 335.1083.

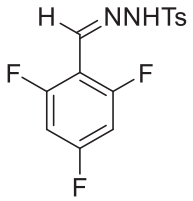


2,6-difluorobenzaldehyde tosylhydrazone 1g, 92% yield.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.90 (d, *J* = 8.1 Hz, 2H), 7.89 (s, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.29 (ddd, *J* = 8.5, 6.2, 2.3 Hz, 1H), 6.90 (t, *J* = 8.5 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.99 (dd, *J* = 257.6, 6.2 Hz), 144.34 (s), 137.59 (s), 135.02 (s), 131.31 (t, *J* = 10.5 Hz), 129.65 (s), 128.10 (s), 111.86 (d, *J* = 24.4 Hz), 111.03 (t, *J* = 13.6 Hz), 21.61 (s). ^{19}F NMR (376 MHz, $CFCl_3$, $CDCl_3$) δ -112.60 (m, 2F). IR (neat, cm^{-1}): 3141.82, 1624.52, 1465.42, 1324.20, 1159.43, 1059.69, 1002.66, 949.96, 806.85, 712.76. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{14}H_{13}F_2N_2O_2S^+$: 311.0660, found 311.0676.

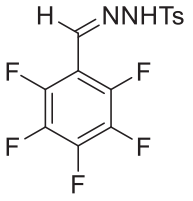


2-fluorobenzaldehyde tosylhydrazone 1h, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.01 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.87 – 7.81 (m, 1H), 7.37 – 7.33 (m, 1H), 7.32 (d, *J* = 8.5 Hz, 2H), 7.16 – 7.09 (m, 1H), 7.02 (ddd, *J* = 10.4, 8.4, 1.0 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$)

δ 161.18 (d, *J* = 252.5 Hz), 144.36 (s), 140.57 (d, *J* = 5.1 Hz), 135.19 (s), 131.92 (d, *J* = 8.5 Hz), 129.71 (s), 127.94 (s), 126.87 (d, *J* = 2.5 Hz), 124.37 (d, *J* = 3.5 Hz), 121.01 (d, *J* = 9.9 Hz), 115.69 (d, *J* = 20.9 Hz), 21.59 (s). ^{19}F NMR (376 MHz, $CFCl_3$, $CDCl_3$) δ -121.40 (m, 1F). IR (neat, cm^{-1}): 3189.09, 1595.87, 1487.95, 1457.44, 1329.97, 1166.68, 1059.66, 957.74, 757.20. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{14}H_{14}FN_2O_2S^+$: 293.0755, found 293.0749.



2,4,6-trifluorobenzaldehyde tosylhydrazone 1i, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.89 (d, *J* = 8.1 Hz, 2H), 7.82 (s, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 6.68 (t, *J* = 8.5 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.21 (dm, *J* = 254.3 Hz), 161.49 (dm, *J* = 259.3 Hz), 144.46 (s), 136.65 (s), 134.95 (s), 129.62 (s), 128.10 (s), 107.84(m), 100.99 (td, *J* = 26.0, 2.7 Hz), 21.63 (s). ^{19}F NMR (376 MHz, $CFCl_3$, $CDCl_3$) δ -104.23 (p, *J* = 8.4 Hz, 1F), -108.55 (t, *J* = 8.2 Hz, 2F). IR (neat, cm^{-1}): 3158.70, 1618.23, 1459.17, 1151.30, 931.13, 826.01, 720.28. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{14}H_{12}F_3N_2O_2S^+$: 329.0572, found 329.0570.

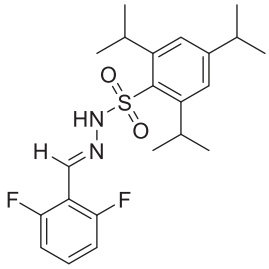


pentafluorobenzaldehyde tosylhydrazone 1j, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.80 (s, 1H), 7.34 (d, *J* = 8.4 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.05 (dm, *J* = 253.4 Hz), 144.78 (s), 141.73 (dm, *J* = 258.4 Hz), 137.70 (dm, *J* = 254.3 Hz), 134.58 (s), 129.73 (s), 128.04 (s), 108.77 (td, *J* = 12.0, 3.8 Hz), 21.62 (d, *J* = 335.3 Hz). ^{19}F NMR (376 MHz, $CFCl_3$, $CDCl_3$) δ -141.45 (d, *J* = 14.8 Hz, 2F), -151.57 (t, *J* = 20.8 Hz, 1F), -161.97 – -162.09 (m, 2F). IR (neat, cm^{-1}): 3176.38, 1652.07, 1595.97, 1493.99,

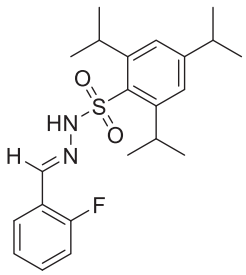
1324.16, 1160.50, 970.95, 906.78, 792.94. HRMS (ESI) ([M+H]$^+$) Calcd. For $C_{14}H_{10}F_5N_2O_2S^+$: 365.0383, found 365.0380.

2.4.3 Typical Procedure for the Preparation of 2,4,6-Triisopropyl Phenylsulfonyl Hydrazones[18]

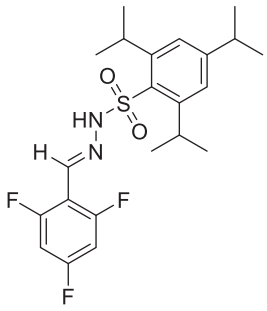
To a stirred solution of pure 2,4,6-triisopropylbenzenesulfonyl hydrazide (5.0 mmol) in THF (12.0 mL) at 0 ºC, aldehyde (5.0 mmol) was added dropwise (or portionwise if solid). After approximately 3 h, the solvent was removed directly under reduced pressure, and the crude solid was further purified by recrystallization in hot methanol.



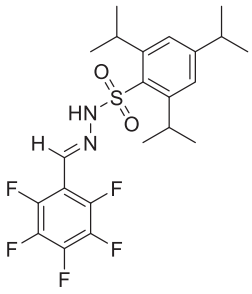
2,6-difluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone 1g', 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.92 (s, 1H), 7.30 – 7.20 (m, 1H), 7.19 (s, 2H), 6.86 (t, *J* = 8.5 Hz, 2H), 4.24 (hept, *J* = 6.7 Hz, 2H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.30 (d, *J* = 6.7 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.93 (dd, *J* = 257.9, 6.1 Hz), 153.50 (s), 151.54 (s), 136.09 (s), 131.06 (d, *J* = 7.6 Hz), 130.92 (s), 123.83 (s), 111.78 (d, *J* = 24.4 Hz), 111.14 (t, *J* = 13.4 Hz), 34.17 (s), 30.08 (s), 24.81 (s), 23.50 (s). ^{19}F NMR (376 MHz, $CFCl_3$, $CDCl_3$) -111.75 (dd, *J* = 8.2, 6.3 Hz, 2F). IR (neat, cm^{-1}): 3158.70, 1618.23, 1459.17, 1151.30, 931.13, 826.01, 789.01, 720.28. HRMS (ESI) ([M+H]$^+$) Calcd. For $C_{22}H_{29}F_2N_2O_2S^+$: 423.1918, found 423.1939.



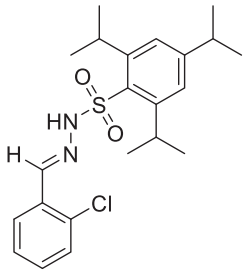
2-fluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone 1h', 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 8.01 (s, 1H), 7.80 (td, *J* = 7.6, 1.5 Hz, 1H), 7.36 – 7.28 (m, 1H), 7.19 (s, 2H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.06 – 6.98 (m, 1H), 4.27 (hept, *J* = 6.8 Hz, 2H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.31 (d, *J* = 6.8 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.15 (d, *J* = 252.0 Hz), 153.57 (s), 151.39 (s), 139.17 (d, *J* = 5.0 Hz), 131.73 (d, *J* = 8.4 Hz), 131.16 (s), 126.76 (s), 124.27 (s), 123.91 (s), 121.18 (d, *J* = 9.8 Hz), 115.68 (d, *J* = 21.0 Hz), 34.18 (s), 30.08 (s), 24.86 (s), 23.51 (s). ^{19}F NMR (376 MHz, $CFCl_3$, $CDCl_3$) δ -121.68 (m, 1F). IR (neat, cm^{-1}): 3179.06, 1601.47, 1441.29, 1167.20, 949.74, 839.60, 755.30. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{22}H_{30}FN_2O_2S^+$: 405.2012, found 405.1995.



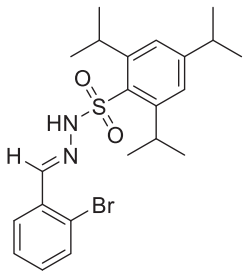
2,4,6-trifluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone 1i', 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.82 (s, 1H), 7.19 (s, 2H), 6.66 (t, *J* = 8.5 Hz, 2H), 4.20 (hept, *J* = 6.8 Hz, 2H), 2.89 (hept, *J* = 6.9 Hz, 1H), 1.29 (d, *J* = 6.7 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.03 (dm, *J* = 254.1 Hz), 161.29 (dm, *J* = 259.0 Hz), 153.58 (s), 151.55 (s), 135.21 (s), 131.00 (s), 123.86 (s), 108.01(m), 100.87 (td, *J* = 26.1, 2.4 Hz), 34.19 (s), 30.08 (s), 24.81 (s), 23.51 (s). ^{19}F NMR (376 MHz, $CFCl_3$, $CDCl_3$) δ -104.70 (p, *J* = 8.0 Hz, 1F), -108.30 (t, *J* = 8.4 Hz, 2F). IR (neat, cm^{-1}): 3185.54, 1615.83, 1435.14, 1166.49, 1027.07, 930.77, 837.06, 652.16. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{22}H_{28}F_3N_2O_2S^+$: 441.1824, found 441.1814.



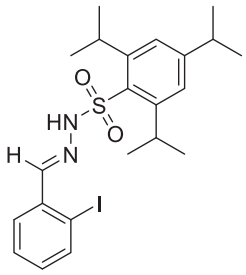
pentafluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone 1j', 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.80 (s, 1H), 7.20 (s, 2H), 4.19 (hept, *J* = 6.7 Hz, 2H), 2.92 (hept, *J* = 6.9 Hz, 1H), 1.29 (d, *J* = 6.7 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.90 (s), 151.61 (s), 144.97 (dm, *J* = 258.1 Hz), 141.59 (dm, *J* = 246.1, 13.3 Hz), 137.71 (dm, *J* = 249.4 Hz), 132.89 (s), 130.64 (s), 123.95 (s), 108.70(m), 34.21 (s), 30.11 (s), 24.78 (s), 23.49 (s). ^{19}F NMR (376 MHz, $CFCl_3$, $CDCl_3$) δ -141.37 (m, 2F), -152.04 (m, 1F), -162.33 (m, 2F). IR (neat, cm^{-1}): 3197.45, 1601.27, 1494.88, 1163.62, 968.82, 901.81, 794.34, 680.74. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{22}H_{26}F_5N_2O_2S^+$: 477.1635, found 477.1634.



2-Chlorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone 1k', 57% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.91 (s, 1H), 7.85 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.18 (s, 2H), 4.25 (hept, *J* = 6.9 Hz, 2H), 2.90 (hept, *J* = 6.4 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.24, 154.07, 145.13, 136.64, 133.86, 133.67, 133.55, 132.36, 130.01, 129.48, 126.57, 36.85, 32.77, 27.53, 26.17. IR (neat, cm^{-1}):3192.25, 1599.04, 1426.73, 1192.76, 945.51, 933.50, 845.51, 658.20. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{22}H_{30}ClN_2O_2S^+$: 421.1711, found 421.1717.



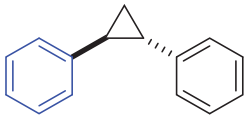
2-bromobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone 1l', 58% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.15 (s, 1H), 7.83 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.26 – 7.16 (m, 4H), 4.28 (hept, *J* = 6.7 Hz, 2H), 2.92 – 2.88 (m, 1H), 1.31 (d, *J* = 6.8 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.24, 154.05, 147.47, 135.62, 134.97, 133.95, 133.85, 130.42, 130.08, 126.57, 36.85, 32.76, 27.53, 26.17. IR (neat, cm^{-1}):3183.84, 1598.65, 1427.03, 1192.47, 1060.66, 932.10, 845.40, 653.77. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{22}H_{30}BrN_2O_2S^+$: 465.1206, found 465.1211.



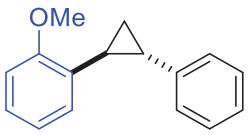
2-iodobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone 1m', 88% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.98 (s, 1H), 7.79 (ddd, *J* = 7.9, 3.2, 1.3 Hz, 2H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.18 (s, 2H), 7.03 (td, *J* = 7.7, 1.7 Hz, 1H), 4.25 (hept, *J* = 6.7 Hz, 2H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.23, 154.03, 151.87, 142.23, 137.65, 134.15, 133.85, 130.89, 130.41, 126.57, 101.70, 36.84, 32.76, 27.54, 26.18. IR (neat, cm^{-1}):3215.97, 1597.80, 1131.96, 1191.82, 1058.66, 940.40, 844.68, 754.49, 672.63. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{22}H_{30}IN_2O_2S^+$: 513.1067, found 513.1073.

2.4.4 General Procedure for [Co(Por)]-Catalyzed Cyclopropanation

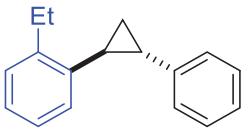
An oven-dried Schlenk tube was charged with 1.0 equivalent of sulfonyl hydrazone (0.1 mmol), [Co(Por)] (2 mol %) and 2.0 equivalent of Cs_2CO_3 (0.2 mmol). The Schlenk tube was then evacuated and back filled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, and olefin (0.15 mmol, 1.5 eq) and methanol (0.6 mL) were added. The Schlenk tube was then purged with nitrogen for 30 s and the rubber septum was replaced with a Teflon screw cap. The mixture was then stirred at 40 °C. After 24 h, the reaction mixture was concentrated and purified by flash chromatography. The fractions containing product were collected and concentrated by rotary evaporation to afford the compound as a mixture of *trans*/*cis* diastereomers. (In most cases, the cyclopropanated product was visualized on TLC using the cerium ammonium molybdate (CAM) stain)



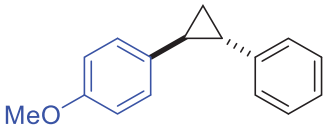
1,2-diphenylcyclopropane (3aa)[20]. Yield: 64%. R_f = 0.50 (ethyl acetate / hexanes = 1:50), isolated as a mixture of *trans/cis* diastereomers trans/cis: 89/11. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 5H), 7.24 – 7.13 (m, 5H), 2.18 (d, J = 7.2 Hz, 2H), 1.46 (dd, J = 7.2, 6.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.50, 128.36, 125.75, 125.72, 28.00, 18.18. HPLC analysis: *ee* (*trans*)-isomer = -42%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 10.12 min, t_{minor} = 8.37 min.



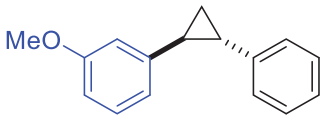
1-methoxy-2-(2-phenylcyclopropyl)benzene (3ba). Yield: 78%. R_f = 0.43 (ethyl acetate / hexanes = 1:20), isolated as a mixture of *trans/cis* diastereomers trans/cis: 95/5. $[\alpha]^{20}{}_D$ = +198.0 (*c* = 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.29 (m, 2H), 7.29 – 7.18 (m, 4H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 3.88 (s, 3H), 2.59 – 2.46 (m, 1H), 2.27 – 2.12 (m, 1H), 1.51 – 1.38 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.13, 142.97, 130.81, 128.25, 126.60, 126.10, 125.55, 125.05, 120.47, 110.26, 55.48, 26.52, 21.62, 17.03. IR (neat, cm^{-1}): 3061.93, 2965.26, 1602.47, 1489.30, 910.57, 835.92, 750.46. HPLC analysis: *ee* (*trans*)-isomer = 99%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 14.52 min, t_{minor} =13.78 min. HRMS (EI) ([M]+) Calcd. for $C_{16}H_{16}O^+$: 224.1195, Found 224.1196.



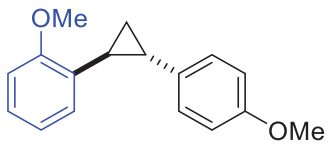
1-ethyl-2-(2-phenylcyclopropyl)benzene (3ca). Yield: 87%. R_f = 0.50 (ethyl acetate / hexanes = 1:50), isolated as a mixture of *trans/cis* diastereomers *trans/cis*: 85/15. ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.6 Hz, 2H), 7.23 – 7.16 (m, 5H), 7.12 – 7.08 (m, 1H), 7.03 – 6.99 (m, 1H), 2.74 (q, *J* = 7.6 Hz, 2H), 2.27 – 2.25 (m, 1H), 2.09 – 2.06 (m, 1H), 1.51 – 1.48 (m, 1H), 1.43 – 1.36 (m, 1H), 1.19 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.57, 142.81, 139.45, 128.38, 127.96, 127.38, 126.19, 125.84, 125.62, 125.34, 26.31, 25.98, 25.42, 16.60, 14.80. IR (neat, cm^{-1}): 3061.86, 2964.52, 1602.23, 1489.47, 929.09, 750.23, 695.26. HPLC analysis: *ee* (*trans*)-isomer = 33%. ODH (99.9% hexanes : 0.1% isopropanol, 0.8 mL/min) (*trans*)-isomer: t_{major} = 12.43 min, t_{minor} = 17.09 min. HRMS (EI) Calcd. for $C17H18^+$: 222.1403, Found 222.1402.



1-methoxy-4-(2-phenylcyclopropyl)benzene (3da)[21]. Yield: 23%. R_f = 0.43 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 93/7. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.19 (d, *J* = 6.8 Hz, 1H), 7.14 (d, *J* = 7.9 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 6.85 (d, *J* = 7.7 Hz, 2H), 3.80 (s, 3H), 2.16 – 2.07 (m, 2H), 1.41 – 1.38 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.84, 142.72, 134.51, 128.35, 126.90, 125.69, 125.61, 113.85, 55.33, 27.49, 27.31, 17.79. HPLC analysis: *ee* (*trans*)-isomer = 23%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 24.46 min, t_{minor} = 29.20 min.

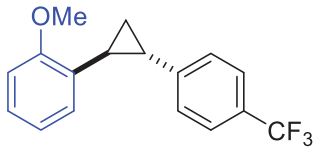


1-methoxy-3-(2-phenylcyclopropyl)benzene (3ea). Yield: 69%. R_f = 0.43 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 95/5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.17 (m, 6H), 6.86 – 6.73 (m, 3H), 3.84 (s, 3H), 2.22 – 2.18 (m, 2H), 1.50 – 1.47 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.71, 144.25, 142.42, 129.34, 128.37, 127.68, 125.74, 118.13, 111.64, 110.99, 55.17, 28.08, 28.03, 18.20. IR (neat, cm^{-1}): 3026.87, 2833.70, 1601.77, 1582.13, 1042.45, 993.87, 717.74, 692.66. HPLC analysis: *ee* (*trans*)-isomer = 23%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 28.00 min, t_{minor} = 32.64 min. HRMS (EI) (M^+) Calcd. for $C_{16}H_{16}O^+$: 224.1196, Found 224.1191.

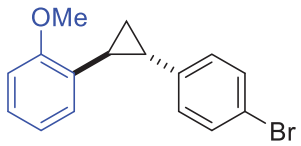


1-methoxy-2-(2-(4-methoxyphenyl)cyclopropyl)benzene (3bb). Yield: 88%. R_f = 0.29 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 95/5. $[\alpha]^{20}_D$ = +254.7 (*c* = 0.5, $CHCl_3$). ^{1}H

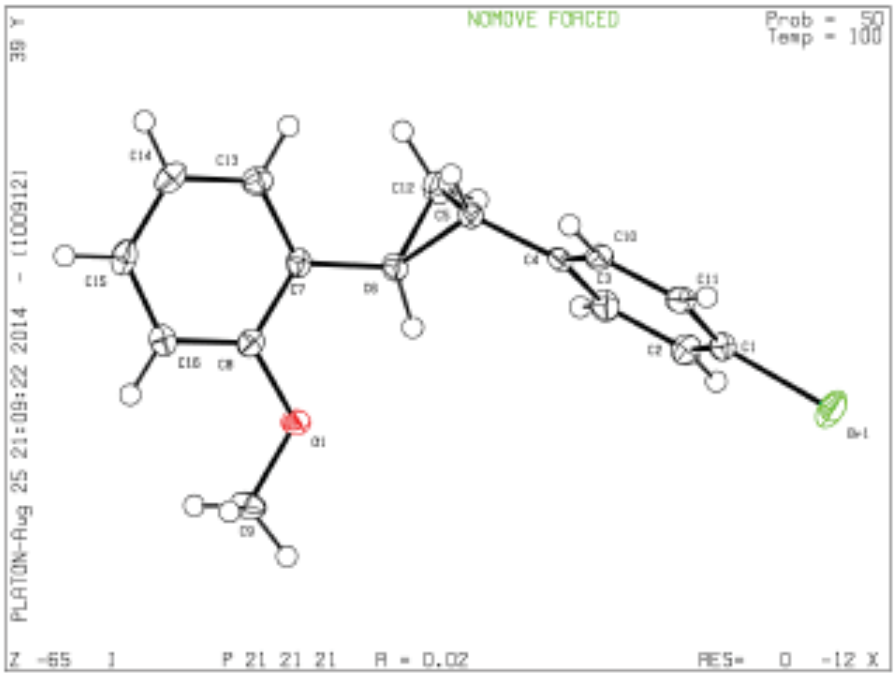
NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.14 (m, 3H), 6.97 (dd, J = 7.6, 1.7 Hz, 1H), 6.94 – 6.89 (m, 1H), 6.89 – 6.82 (m, 3H), 3.84 (s, 3H), 3.80 (s, 3H), 2.40 (dt, J = 8.5, 5.4 Hz, 1H), 2.09 (dt, J = 8.7, 5.4 Hz, 1H), 1.37 – 1.30 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.13, 157.71, 134.99, 131.00, 127.29, 126.50, 125.02, 120.46, 113.72, 110.24, 55.50, 55.30, 25.80, 21.07, 16.49. IR (neat, cm^{-1}): 2995.01, 1598.05, 1494.37, 1242.45, 1029.50, 903.31, 804.44, 697.03. HPLC analysis: *ee* (*trans*)-isomer = 94%. ODH (99.5% hexanes:0.5% isopropanol, 0.8 mL/min) (*trans*)-isomer: t_{major} = 12.52 min, t_{minor} = 19.06 min. HRMS (EI) (M^+) Calcd. for $C_{17}H_{18}O_2^+$: 254.1301, Found 254.1303.



1-methoxy-2-(2-(4-(trifluoromethyl)phenyl) cyclopropyl)benzene (3bc). Yield: 81%. R_f = 0.46 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 96/4. $[\alpha]^{20}_D$ = +203.8 (*c* = 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J = 8.4 Hz, 2H), 7.31 – 7.26 (m, 2H), 7.23 – 7.17 (m, 1H), 6.99 (dd, J = 7.6, 1.7 Hz, 1H), 6.96 – 6.91 (m, 1H), 6.88 (d, J = 8.2 Hz, 1H), 3.84 (s, 3H), 2.50 (ddd, J = 9.0, 6.2, 5.0 Hz, 1H), 2.15 (dt, J = 8.8, 5.3 Hz, 1H), 1.52 – 1.48 (m, 1H), 1.43 (dt, J = 9.0, 5.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.17, 147.33, 130.02, 127.74 (q, J = 32.2 Hz), 126.99, 126.18, 125.25 – 125.09 (m), 124.41 (q, J = 271.7 Hz), 120.49, 110.26, 55.45, 26.33, 22.55, 17.15. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.72 (s, 3F). IR (neat, cm^{-1}): 3002.00, 1614.91, 1496.23, 1323.24, 1117.08, 929.99, 818.51, 751.26. HPLC analysis: *ee* (*trans*)-isomer = 95%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 19.12 min, t_{minor} = 16.06 min. HRMS (EI) (M^+) Calcd. for $C_{17}H_{15}F_3O^+$: 292.1070, Found 292.1075.



1-(2-(4-bromophenyl)cyclopropyl)-2-methoxybenzene (3bd). Yield:85%. R_f = 0.42 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 94/6. $[\alpha]^{20}_D$ = +135.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.21 – 7.16 (m, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.96 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.92 (td, *J* = 7.5, 0.8 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 2.43 – 2.40 (m, 1H), 2.07 – 2.05 (m, 1H), 1.46 – 1.39 (m, 1H), 1.36 – 1.32 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.14, 142.09, 131.24, 130.32, 127.87, 126.82, 125.12, 120.47, 119.09, 110.25, 55.47, 25.99, 21.92, 16.73. IR (neat, cm^{-1}): 3000.63, 1599.82, 1488.71, 1244.12, 1028.76, 899.24, 814.98, 747.52. HPLC analysis: *ee* (*trans*)-isomer = 94%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 30.20 min, t_{minor} = 24.69 min. HRMS (EI) (M^+) Calcd. for $C_{16}H_{15}BrO^+$: 302.0301, Found 302.0308.

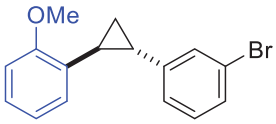


The X-ray diffraction data were measured on a Bruker D8 Venture PHOTON 100 CMOS diffractometer equipped with a Cu K_α INCOATEC Imus micro-focus source (λ =

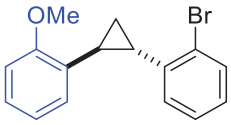
1.54178 Å). Indexing was performed using *APEX2* (Difference Vectors method). Data integration and reduction were performed using SaintPlus 6.01. Absorption correction was performed by multi-scan method implemented in SADABS. Space groups were determined using XPREP implemented in APEX2. The structure was solved using SHELXS-97 (direct methods) and refined using SHELXL-2013 (full-matrix least-squares on F^2) contained in APEX2, WinGX v1.70.01 and OLEX2. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were placed in geometrically calculated positions and included in the refinement process using riding model with isotropic thermal parameters with Uiso(H) = 1.2Ueq(-CH,-CH_2), Uiso(H) = 1.5Ueq(-CH_3). Crystal data and refinement conditions are shown in the following Table.

Crystal data and structure refinement for compound **3bd**	
Identification code	**3bd**
Empirical formula	$C_{16}H_{15}BrO$
Formula weight	303.19
Temperature/K	100.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	5.2682(2)
b/Å	13.5894(4)
c/Å	18.7378(5)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1341.47(7)
Z	4
ρ_{calc}g/cm^3	1.501
μ/mm^{-1}	4.041
F(000)	616.0
Crystal size/mm^3	0.09 × 0.06 × 0.03
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.036 to 137.574
Index ranges	$-6 \le h \le 6$, $-16 \le k \le 16$, $-22 \le l \le 22$
Reflections collected	17008

Independent reflections	2481 [R_{int} = 0.0490, R_{sigma} = 0.0262]
Data/restraints/parameters	2481/0/164
Goodness-of-fit on F^2	1.106
Final R indexes [I>=2σ (I)]	R_1 = 0.0228, wR_2 = 0.0597
Final R indexes [all data]	R_1 = 0.0229, wR_2 = 0.0598
Largest diff. peak/hole / e $Å^{-3}$	0.73/-0.34
Flack parameter	-0.022(7)

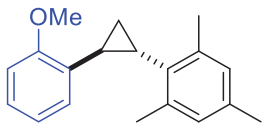


1-(2-(3-bromophenyl)cyclopropyl)-2-methoxybenzene (3be). Yield: 85%. R_f = 0.46 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 94/6. $[\alpha]^{20}_D$ = +400.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33– 7.32 (m, 1H), 7.31 – 7.26 (m, 1H), 7.20 – 7.09 (m, 3H), 6.97 – 6.82 (m, 3H), 3.82 (s, 3H), 2.42 – 2.40 (m, 1H), 2.08 – 2.04 (m, 1H), 1.43 – 1.32 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.16, 145.51, 130.19, 129.75, 129.21, 128.62, 126.88, 125.21, 124.90, 122.43, 120.46, 110.23, 55.46, 26.03, 22.05, 16.76. IR (neat, cm^{-1}): 3001.29, 1595.81, 1461.71, 1244.64, 926.25, 776.21, 687.69. HPLC analysis: *ee* (*trans*)-isomer = 94%. OJH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 40.36 min, t_{minor} = 34.22 min. HRMS (EI) (M^+) Calcd. for $C_{16}H_{15}BrO^+$: 302.0301, Found 302.0306.

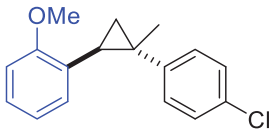


1-bromo-2-(2-(2-methoxyphenyl)cyclopropyl)benzene (3bf). Yield: 89%. R_f = 0.40 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 95/5. $[\alpha]^{20}_D$ = +116.1 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.9 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.24 – 7.16 (m, 2H), 7.13 – 7.03 (m, 2H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 1H), 3.87 (s, 3H), 2.54 – 2.38

(m, 2H), 1.45 – 1.39 (m, 1H), 1.38 – 1.32 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.22, 141.77, 132.36, 130.33, 127.28, 127.16, 127.00, 126.76, 125.94, 125.39, 120.48, 110.21, 55.51, 26.22, 20.79, 16.53. IR (neat, cm^{-1}): 3001.06, 1600.19, 1475.28, 1244.35, 1023.19, 905.39, 800.98, 659.99. HPLC analysis: *ee* (*trans*)-isomer = 96%. OJH (99.5% hexanes: 0.5% isopropanol, 0.8 mL/min) (*trans*)-isomer: t_{major} = 14.42 min, t_{minor} = 12.80 min. HRMS (EI) (M^+) Calcd. for $C_{16}H_{15}BrO^+$: 302.0301, Found 302.0307.

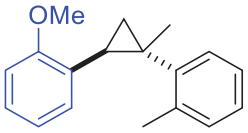


2-(2-(2-methoxyphenyl)cyclopropyl)-1,3,5-trimethylbenzene (3bg). Yield: 61%. R_f = 0.65 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*:90/10. $[\alpha]^{20}_D$ = +152.4 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 – 7.16 (m, 1H), 6.95 (d, *J* = 4.3 Hz, 2H), 6.91 (d, *J* = 8.2 Hz, 1H), 6.85 (s, 2H), 3.87 (s, 3H), 2.45 (dt, *J* = 9.1, 5.6 Hz, 1H), 2.37 (s, 6H), 2.28 (s, 3H), 2.10 – 2.06 (m, 1H), 1.36 – 1.33 (m, 1H), 1.28 – 1.24 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.79, 138.74, 135.62, 135.50, 131.66, 128.63, 126.13, 123.89, 120.62, 110.36, 55.51, 23.11, 20.81, 20.56, 19.55, 19.07. IR (neat, cm^{-1}): 2998.48, 1600.07, 1496.07, 1243.08, 1028.70, 921.04, 849.68, 747.06. HPLC analysis: *ee* (*trans*)-isomer = 96%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 8.87 min, t_{minor} = 10.71 min. HRMS (EI) (M^+) Calcd. for $C_{19}H_{22}O^+$: 266.1665, Found 266.1671.

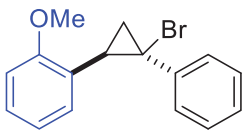


1-(2-(4-chlorophenyl)-2-methylcyclopropyl)-2-methoxybenzene (3bh) Yield: 90%. R_f = 0.65 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*:

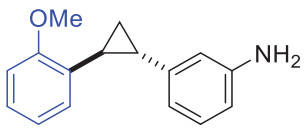
83/17. $[\alpha]^{20}_{D}$ = +121.3 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.24 (d, J = 8.1 Hz, 1H), 7.12 (d, *J* = 7.4 Hz, 1H), 6.96 – 6.87 (m, 2H), 3.91 (s, 3H), 2.31 (dd, *J* = 8.1, 7.1 Hz, 1H), 1.31 (dd, *J* = 8.7, 5.0 Hz, 1H), 1.17 – 1.13 (m, 1H), 0.99 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.53, 147.03, 130.33, 129.39, 129.34, 128.26, 127.70, 127.37, 120.15, 109.75, 55.26, 28.63, 26.36, 21.25, 17.38. IR (neat, cm^{-1}): 3064.36, 2998.26, 1599.36, 1492.02, 1240.29, 1027.87, 829.62, 732.31. HPLC analysis: *ee* (*trans*)-isomer = 93%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 10.09 min, t_{minor} = 11.99 min. HRMS (EI) (M^+) Calcd. for $C_{17}H_{17}ClO^+$: 272.0962, Found 272.0968.



1-methoxy-2-(2-methyl-2-(o-tolyl)cyclopropyl)benzene (3bi). Yield: 42%. R_f = 0.60 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*:83/17. $[\alpha]^{20}_{D}$ = +88.5 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.3 Hz, 1H), 7.30 – 7.11 (m, 5H), 6.99 – 6.93 (m, 2H), 3.97 (s, 3H), 2.55 – 2.52 (m, 1H), 2.49 (s, 3H), 1.25 (dd, *J* = 6.2, 4.8 Hz, 1H), 1.18 (dd, *J* = 8.7, 4.8 Hz, 1H), 0.98 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.48, 146.30, 137.48, 130.07, 129.91, 129.27, 128.13, 127.12, 126.16, 125.86, 120.06, 109.77, 55.15, 26.69, 25.07, 20.26, 19.13, 18.13. IR (neat, cm^{-1}): 2996.17, 1600.36, 1493.39, 1240.27, 1028.20, 927.08, 748.58, 696.80. HPLC analysis: *ee* (*trans*)-isomer = 92%. ODH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 13.30 min, t_{minor} =17.60 min. HRMS (EI) (M^+) Calcd. for $C_{18}H_{20}O^+$: 252.1509, Found 252.1501.

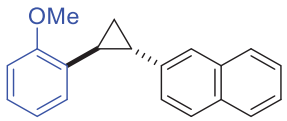


1-(2-bromo-2-phenylcyclopropyl)-2-methoxybenzene (3bj). Yield: 71%. R_f = 0.49 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*:75/25. $[\alpha]^{20}{}_D$ = +11.9 (*c* = 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.37 (dd, *J* = 10.6, 4.5 Hz, 2H), 7.35 – 7.24 (m, 2H), 7.18 – 7.14 (m, 1H), 6.98 (d, *J* = 7.7 Hz, 2H), 4.00 (s, 3H), 2.54 (t, *J* = 8.8 Hz, 1H), 1.83 (dd, *J* = 8.7, 1.2 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.19, 144.75, 129.62, 129.28, 128.99, 128.47, 128.33, 127.94, 120.11, 110.04, 55.47, 41.23, 26.65, 20.26. IR (neat, cm^{-1}): 3001.36, 1600.62, 1494.35, 1245.70, 1027.47, 893.04, 748.56, 695.89. HPLC analysis: *ee* (*trans*)-isomer = 95%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 13.62 min, t_{minor} = 17.70 min. HRMS (EI) (M^+) Calcd. for $C_{16}H_{15}BrO^+$: 302.0301, Found 302.0306.

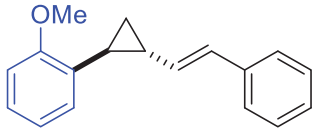


3-(2-(2-methoxyphenyl)cyclopropyl)aniline (3bk). Yield: 69%. R_f = 0.40 (ethyl acetate / hexanes = 1:3), isolated as a mixture of diastereomers *trans/cis*: 92/8. $[\alpha]^{20}{}_D$ = +267.9 (*c* = 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.14 (m, 1H), 7.09 (dd, *J* = 12.0, 4.7 Hz, 1H), 6.99 – 6.90 (m, 2H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.64 (d, *J* = 7.7 Hz, 1H), 6.53 (d, *J* = 6.4 Hz, 2H), 3.84 (s, 3H), 3.45 (br, 2H), 2.49 – 2.46 (m, 1H), 2.09 – 2.06 (m, 1H), 1.36 (td, *J* = 7.5, 1.1 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.12, 146.17, 144.33, 130.93, 129.20, 126.56, 124.98, 120.50, 116.74, 112.91, 112.72, 110.31, 55.54, 26.61, 21.42, 17.14. IR (neat, cm^{-1}): 3370.24, 3005.29, 1602.52, 1494.08, 1243,93, 1028.03, 865.37, 693.25. HPLC analysis: *ee* (*trans*)-isomer = 97%. ADH (97% hexanes : 3% isopropanol, 0.8 mL/min) (*trans*)-

isomer: t_{major} = 33.44 min, t_{minor} =41.82 min. HRMS (ESI) ([M+H]$^+$) Calcd. For $C_{16}H_{18}NO^+$: 240.1383, Found 240.1375.

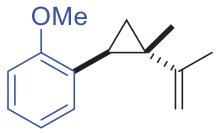


2-(2-(2-methoxyphenyl)cyclopropyl)naphthalene (3bl). Yield: 68%. R_f = 0.34 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 93/7. $[\alpha]^{20}_D$ = +112.1 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 11.6, 8.4 Hz, 3H), 7.65 (s, 1H), 7.43 (dt, *J* = 14.8, 6.9 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.20 (dd, *J* = 8.0, 7.5 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 3.84 (s, 3H), 2.60 – 2.56 (m, 1H), 2.32 – 2.28 (m, 1H), 1.55 – 1.47 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.19, 140.52, 133.54, 131.97, 130.74, 127.80, 127.57, 127.33, 126.68, 125.94, 125.16, 125.10, 124.93, 124.01, 120.50, 110.29, 55.49, 26.80, 21.93, 16.87. IR (neat, cm^{-1}): 3050.85, 2934.61, 1630.05, 1598.67, 1494.91, 1025.18, 911.19, 742.18. HPLC analysis: *ee* (*trans*)-isomer = 99%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 31.76 min, t_{minor} = 30.74 min. HRMS (EI) (M$^+$) Calcd. for $C_{20}H_{18}O^+$: 274.1353, Found 274.1350.

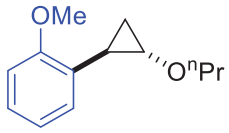


1-methoxy-2-(2-((*trans*)-styryl)cyclopropyl)benzene (3bm). Yield: 77%. R_f = 0.46 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 81/19. $[\alpha]^{20}_D$ = +193.1 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.3 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.21 – 7.12 (m, 2H), 6.95 – 6.81 (m, 3H), 6.50 (d, *J* = 15.8 Hz, 1H), 5.98 (dd, *J* = 15.8, 8.7 Hz, 1H), 3.85 (s, 3H), 2.39 – 2.35 (m, 1H), 1.81 – 1.80 (m, 1H), 1.31 – 1.27 (m,

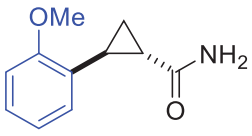
1H), 1.20 – 1.15 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.03, 137.69, 133.49, 130.38, 128.46, 127.89, 126.62, 126.52, 125.66, 124.76, 120.52, 110.33, 55.58, 26.03, 19.65, 16.05. IR (neat, cm^{-1}): 3023.96, 2931.60, 1645.79, 1494.54, 1242.80, 1027.44, 956.56, 692.08. HPLC analysis: *ee* (*trans*)-isomer = 81%. ODH (98% hexanes : 2% isopropanol, 0.8 mL/min) (*trans*)-isomer: t_{major} = 8.21 min, t_{minor} = 8.83 min. HRMS (EI) (M^+) Calcd. for $C_{18}H_{18}O^+$: 250.1352, Found 250.1336.



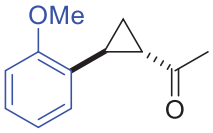
1-methoxy-2-(2-methyl-2-(prop-1-en-2-yl)cyclopropyl)benzene (3bn). Yield: 50%. R_f = 0.54 (ethyl acetate / hexanes = 1:50), isolated as a mixture of diastereomers *trans/cis*:78/22. $[\alpha]^{20}_D$ = -37.7 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 – 7.18 (m, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.90 (td, *J* = 7.5, 0.8 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 4.93 (s, 1H), 4.78 (s, 1H), 3.84 (s, 3H), 2.12 (dd, *J* = 8.4, 6.7 Hz, 1H), 1.88 (s, 3H), 1.18 (dd, *J* = 8.6, 4.8 Hz, 1H), 0.89 (dd, *J* = 6.3, 4.9 Hz, 1H), 0.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.48, 151.01, 129.15, 126.96, 119.93, 111.79, 109.70, 109.04, 55.13, 28.09, 25.39, 20.31, 18.04, 16.23. IR (neat, cm^{-1}): 3073.35, 2953.85, 1644.08, 1494.53, 1240.35, 1023.19, 890.13, 748.15. HPLC analysis: *ee* (*trans*)-isomer = 89%. ODH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 8.38 min, t_{minor} = 9.42 min. HRMS (EI) (M^+) Calcd. for $C_{14}H_{18}O^+$: 202.1352, Found 202.1347.



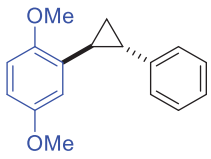
1-methoxy-2-(2-propoxycyclopropyl)benzene (3bo). Yield: 49%. R_f = 0.48 (ethyl acetate / hexanes = 1:10), isolated as a mixture of diastereomers *trans/cis*: 83/17. $[\alpha]^{20}_D$ = +89.7 (*c* = 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.15 (t, *J* = 7.8, 1.7 Hz, 1H), 6.85 (dd, *J* = 7.8, 1.8 Hz, 2H), 6.77 (dd, *J* = 7.4, 1.5 Hz, 1H), 3.86 (s, 3H), 3.63 – 3.57 (m, 1H), 3.57 – 3.50 (m, 1H), 3.30 – 3.27 (m, 1H), 2.34 – 2.30 (m, 1H), 1.64 – 1.60 (m, 2H), 1.24 – 1.19 (m, 1H), 1.03 (dd, *J* = 12.7, 6.5 Hz, 1H), 0.94 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.06, 129.39, 126.58, 125.53, 120.30, 110.07, 72.42, 61.12, 55.35, 22.80, 18.20, 14.26, 10.64. IR (neat, cm^{-1}): 2960.57, 1600.77, 1496.03, 1242.96, 1027.65, 938.07, 794.54, 747.61. HPLC analysis: *ee* (*trans*)-isomer = 91%. ODH (99% hexanes : 1% isopropanol, 0.8 mL/min) (*trans*)-isomer: t_{major} = 24.16 min, t_{minor} = 12.72 min. HRMS (EI) (M^+) Calcd. for $C_{13}H_{18}O_2^+$: 206.1301, Found 206.1298.



2-(2-methoxyphenyl)cyclopropane-1-carboxamide (3bp). Yield: 41%. R_f = 0.40 (ethyl acetate / hexanes = 3:1), isolated as a mixture of diastereomers *trans/cis*: 71/29. $[\alpha]^{20}_D$ = +33.2 (*c* = 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.17 (m, 1H), 6.92 – 6.84 (m, 3H), 5.63 (s, 1H), 5.51 (s, 1H), 3.84 (s, 3H), 2.72 – 2.68 (m, 1H), 1.60 – 1.55 (m, 1H), 1.32 – 1.27 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.91, 158.33, 128.66, 127.41, 125.96, 120.34, 110.32, 55.43, 24.30, 20.69, 14.53. IR (neat, cm^{-1}): 3399.91, 3199.69, 3007.49, 1638.45, 1434.96, 1243.99, 1020.30, 951.64, 799.30, 743.55. HPLC analysis: *ee* (*trans*)-isomer = 77%. OJH (90% hexanes : 10% isopropanol, 0.8 mL/min) (*trans*)-isomer: t_{major} = 18.18 min, t_{minor} = 25.97 min. HRMS (ESI) ($[M+Na]^+$) Calcd. For $C_{11}H_{13}NNaO_2^+$: 214.0838, found 214.0842.

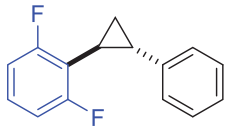


2-(2-methoxyphenyl)cyclopropyl)ethan-1-one (3bq). Yield: 42%. R_f = 0.35 (ethyl acetate / hexanes = 1:6). $[\alpha]^{20}{}_D$ = +50.8 (*c* = 0.5, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$) δ 7.21 – 7.19 (m, 1H), 6.94 – 6.84 (m, 3H), 3.84 (s, 3H), 2.68 (ddd, *J* = 9.1, 6.9, 4.2 Hz, 1H), 2.30 (s, 3H), 2.12 – 2.09 (m, 1H)), 1.64 (ddd, *J* = 9.2, 5.1, 4.3 Hz, 1H), 1.40 – 1.36 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.09, 160.98, 131.18, 130.23, 128.62, 122.99, 112.91, 58.03, 34.12, 33.17, 26.89, 19.59. IR (neat, cm^{-1}): 2919.91, 1695.98, 1463.35, 1354.29, 1246.84, 1048.27, 965.23, 753.26. HPLC analysis: *ee* (*trans*)-isomer = 82%. IC (99.5% hexanes : 0.5% isopropanol, 1.0 mL/min) (*trans*)-isomer: t_{major} = 34.73 min, t_{minor} = 51.20 min. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{12}H_{15}O_2^+$: 191.1067, found 191.1072.

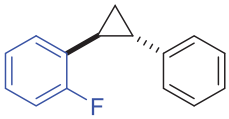


1,4-dimethoxy-2-(2-phenylcyclopropyl)benzene (3fa). Yield: 91%. R_f = 0.29 (ethyl acetate / hexanes = 1:20), isolated as a mixture of diastereomers *trans/cis*: 95/5. $[\alpha]^{20}{}_D$ = +366.8 (*c* = 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.29 (m, 2H), 7.23 – 7.16 (m, 3H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.70 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.56 (d, *J* = 3.0 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 2.51 – 2.47 (m, 1H), 2.19 – 2.12 (m, 1H), 1.43 – 1.38 (m, 2H).^{13}C NMR (125 MHz, $CDCl_3$) δ 153.80, 152.48, 142.76, 132.36, 128.26, 126.07, 125.62, 111.79, 111.51, 110.18, 56.32, 55.70, 26.84, 21.67, 17.34. IR (neat, cm^{-1}): 3024.22, 2998.62, 1603.03, 1496.39, 1157.29, 1048.03, 931.01, 797.21, 696.10. HPLC analysis: *ee* (*trans*)-isomer = 94%. ODH (99%

hexanes : 1% isopropanol, 0.8 mL/min) (*trans*)-isomer: t_{major} = 9.43 min, t_{minor} = 11.10 min. HRMS (EI) (M^+) Calcd. for $C_{17}H_{18}O_2^+$: 254.1301, Found 254.1303.

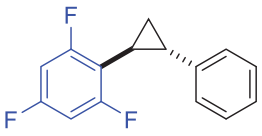


1,3-difluoro-2-(2-phenylcyclopropyl)benzene (3g'a). Yield: 83%. R_f = 0.54 (ethyl acetate / hexanes = 1:50). $[\alpha]^{20}{}_D$ = +131.4 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.18 (m, 5H), 7.11 (td, *J* = 7.9, 3.9 Hz, 1H), 6.84 (t, *J* = 7.9 Hz, 2H), 2.51 (dt, *J* = 8.8, 5.5 Hz, 1H), 2.12 (dt, *J* = 9.2, 5.6 Hz, 1H), 1.67 (dt, *J* = 8.7, 5.6 Hz, 1H), 1.49 – 1.40 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.12 (dd, *J* = 247.5, 8.3 Hz), 142.12 (s), 128.38 (s), 127.03 (t, *J* = 10.5 Hz), 126.17 (s), 125.94 (s), 117.69 (t, *J* = 16.6 Hz), 111.27 (dd, *J* = 19.2, 7.4 Hz), 24.07 (s), 17.17 (s), 15.58 (s). ^{19}F NMR (376 MHz , $CFCl_3$, $CDCl_3$) δ -115.47 (t, *J* = 6.9 Hz, 2F). IR (neat, cm^{-1}): 3029.23, 2926.13, 1604.44, 1482.60, 1267.08, 965.77, 714.05, 695.62. HPLC analysis: *ee* (*trans*)-isomer = 93%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 7.74 min, t_{minor} = 9.61 min. HRMS (EI) (M^+) Calcd. for $C_{15}H_{12}F_2^+$: 230.0902, Found 230.0894.

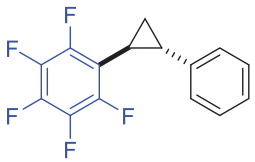


1-fluoro-2-(2-phenylcyclopropyl)benzene (3h'a). Yield: 75%. R_f = 0.49 (ethyl acetate / hexanes = 1:50). $[\alpha]^{20}{}_D$ = +131.4 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.19 (m, 2H), 7.24 – 7.18 (m, 3H), 7.18 – 7.13 (m, 1H), 7.12 – 6.99 (m, 3H), 2.41 – 2.36 (m, 1H), 2.24 – 2.20 (m, 1H), 1.50 – 1.43 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.68 (d, *J* = 245.4 Hz), 142.10 (s), 129.39 (d, *J* = 14.7 Hz), 128.47 (s), 127.60 (s), 127.08 (t, *J* = 16.8 Hz), 126.08 (dd, *J* = 21.5, 9.5 Hz), 123.97 (d, *J* = 3.1 Hz), 115.10 (d, *J* = 22.0 Hz), 26.53 (s), 20.73 (d, *J* = 4.5 Hz), 16.83 (s). ^{19}F

NMR (376 MHz, $CFCl_3$, $CDCl_3$) δ -119.99 – -120.20 (m, 1F). IR (neat, cm^{-1}): 3029.40, 2926.12, 1603.76, 1454.12, 1238.82, 907.78, 819.87, 749.91, 695.13. HPLC analysis: *ee* (*trans*)-isomer = 76%. ODH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 16.36 min, t_{minor} = 18.53 min. HRMS (EI) (M^+) Calcd. for $C_{15}H_{13}F^+$: 211.0996, Found 211.0991.

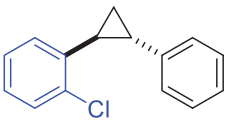


1,3,5-trifluoro-2-(2-phenylcyclopropyl)benzene (3i'a). Yield: 85%. R_f = 0.60 (ethyl acetate / hexanes = 1:50). $[\alpha]^{20}{}_D$ = +173.2 (*c* = 0.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.20 (m, 5H), 6.65 – 6.61 (m, 2H), 2.41 (dt, *J* = 8.8, 5.5 Hz, 1H), 2.01 (dt, *J* = 9.2, 5.6 Hz, 1H), 1.57 (dt, *J* = 8.8, 5.6 Hz, 1H), 1.44 (dt, *J* = 9.1, 5.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.15 (d, *J* = 246.5 Hz), 160.73 (d, *J* = 247.9 Hz), 141.85 (s), 128.41 (s), 126.18 (s), 126.03 (s), 113.85 (m), 99.84 (m), 23.90 (s), 16.41 (s), 15.29 (s). ^{19}F NMR (376 MHz, $CFCl_3$, $CDCl_3$) δ -111.91 (m, 3F). IR (neat, cm^{-1}): 3029.60, 2925.93, 1634.92, 1496.27, 1116.25, 999.09, 768.84, 695.10. HPLC analysis: *ee* (*trans*)-isomer = 93%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 7.27 min, t_{minor} =9.66 min. HRMS (EI) (M^+) Calcd. for $C_{15}H_{11}F_3^+$: 248.0808, Found 248.0802.

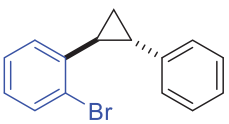


1,2,3,4,5-pentafluoro-6-(2-phenylcyclopropyl)benzene (3j'a). Yield: 81%. R_f = 0.63 (ethyl acetate / hexanes = 1:50). $[\alpha]^{20}{}_D$ = +156.8 (*c* = 0.5, $CHCl_3$).^1H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 2H), 7.26 – 7.19 (m, 3H), 2.51 – 2.46 (m, 1H), 2.07 – 2.05 (m, 1H), 1.65 – 1.60 (m, 1H), 1.56 – 1.51 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.89 – 144.13 (m), 140.85,

139.17 – 135.26 (m), 128.53, 126.41, 126.22, 115.72 – 114.99 (m), 24.18, 16.41, 15.23. ^{19}F NMR (376 MHz , $CFCl_3$, $CDCl_3$) δ -144.31 (dd, J = 21.9, 7.6 Hz, 2F), -158.40 (t, J = 21.0 Hz, 1F), -163.67 – -163.80 (m, 2F). IR (neat, cm^{-1}): 3030.43, 1605.60, 1492.93, 1463.70, 949.51, 843.57, 696.05. HPLC analysis: *ee* (*trans*)-isomer = 89%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} =9.08 min, t_{minor} =17.80 min. HRMS (EI) (M^+) Calcd. for $C_{15}H_9F_5^+$: 284.0619, Found 284.0619.



1-chloro-2-(2-phenylcyclopropyl)benzene (3k'a). Yield: 77%. R_f = 0.52 (ethyl acetate / hexanes = 1:50). $[\alpha]^{20}{}_D$ = +111.6 (c = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, J = 7.9 Hz, 1H), 7.32 (t, J = 7.6 Hz, 2H), 7.24 – 7.21 (m, 4H), 7.16 – 7.13 (m, 1H), 7.09 (d, J = 7.7 Hz, 1H), 2.52 – 2.49 (m, 1H), 2.16 – 2.13 (m, 1H), 1.47 – 1.44 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.81, 142.39, 138.03, 131.89, 131.02, 129.70, 129.39, 129.16, 128.76, 128.54, 29.38, 27.78, 19.46. IR (neat, cm^{-1}): 2956.97, 1604.00, 1498.45, 1479.85, 1259.88, 1072.94, 800.72, 696.31. HPLC analysis: *ee* (*trans*)-isomer = 75%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 8.95 min, t_{minor} = 8.33 min. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{14}Cl^+$: 229.0779, Found 229.0784.



1-bromo-2-(2-phenylcyclopropyl)benzene (3l'a). Yield: 50%. R_f = 0.57 (ethyl acetate / hexanes = 1:50). $[\alpha]^{20}{}_D$ = +82.1 (c = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, J = 7.8 Hz, 1H), 7.32 (t, J = 7.6 Hz, 2H), 7.28 – 7.20 (m, 4H), 7.10 – 7.06 (m, 2H), 2.50 – 2.46 (m, 1H), 2.15 – 2.12 (m, 1H), 1.46 – 1.44

(m, 2H).^{13}C NMR (150 MHz, $CDCl_3$) δ 144.81, 144.01, 135.18, 131.00, 130.07, 130.01, 129.55, 128.73, 128.52, 30.56, 29.53, 19.76. IR (neat, cm^{-1}):3026.08, 1063.59, 1497.80, 1268.18, 1100.36, 1022.23, 930.21, 775.09, 715.70. HPLC analysis: *ee* (*trans*)-isomer = 57%. ADH (100% hexanes, 0.8 mL/min) (*trans*)-isomer: t_{major} = 9.90 min, t_{minor} = 8.96 min. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{14}Br^+$: 273.0273, Found 273.0279.

2.5 REFERENCES

(1) For reviews on stereoselectivity of free radical transformations, see: (a) Yang, Y.-H.; Sibi, M. P. In *Encyclopedia of Radicals in Chemistry, Biology and Materials*; Chatgilialoglu, C., Studer, A., Eds.; Wiley: Weinheim, 2012, p 655; (b) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of radical reactions: concepts, guidelines, and synthetic applications*; John Wiley & Sons, 2008; (c) Zimmerman, J.; Sibi, M. P. *Top. Curr. Chem.* **2006**, *263*, 107; (d) Bar, G.; Parsons, A. F. *Chem. Soc. Rev.* **2003**, *32*, 251; (e) Zard, S. Z. *Radical reactions in organic synthesis*; Oxford University Press: Oxford, 2003; (f) Porter, N. A.; Giese, B.; Curran, D. P. *Acc. Chem. Res.* **1991**, *24*, 296; (g) Giese, B. *Angew. Chem., Int. Ed.* **1989**, *28*, 969.

(2) For select examples of stereoselective radical processes via photoredox catalysis, see: (a) Kainz, Q. M.; Matier, C. D.; Bartoszewicz, A.; Zultanski, S. L.; Peters, J. C.; Fu, G. C. *Science* **2016**, *351*, 681; (b) Brimioulle, R.; Lenhart, D.; Maturi, M. M.; Bach, T. *Angew. Chem., Int. Ed.* **2015**, *54*, 3872; (c) Huo, H. H.; Shen, X. D.; Wang, C. Y.; Zhang,

L. L.; Rose, P.; Chen, L. A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100; (d) Du, J. N.; Skubi, K. L.; Schultz, D. M.; Yoon, T. P. *Science* **2014**, *344*, 392.

(3) For reviews and highlights on Co(II)-MRC: (a) Studer, A.; Curran, D. P. *Angew. Chem., Int. Ed.* **2016**, *55*, 58; (b) Pellissier, H.; Clavier, H. *Chem. Rev.* **2014**, *114*, 2775; (c) Degennaro, L.; Trinchera, P.; Luisi, R. *Chem. Rev.* **2014**, *114*, 7881; (d) Olivos Suarez, A. I.; Lyaskovskyy, V.; Reek, J. N.; van der Vlugt, J. I.; de Bruin, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 12510; (e) Lu, H.; Zhang, X. P. *Chem. Soc. Rev.* **2011**, *40*, 1899; (f) Doyle, M. P. *Angew. Chem., Int. Ed.* **2009**, *48*, 850.

(4) For a recent review on Ti(III)-based MRC, see: (a) Gansäuer, A.; Hildebrandt, S.; Vogelsang, E.; Flowers Ii, R. A. *Dalton Trans.* **2016**, *45*, 448. For the first demonstration of Ti(III)-based metalloradical non-catalytic process, see: (b) RajanBabu, T. V.; Nugent, W. A. *J. Am. Chem. Soc.* **1994**, *116*, 986. For select examples of catalytic processes via Ti(III)-based MRC, see: (c) Gansäuer, A.; Hildebrandt, S.; Michelmann, A.; Dahmen, T.; von Laufenberg, D.; Kube, C.; Fianu, G. D.; Flowers, R. A. *Angew. Chem., Int. Ed.* **2015**, *54*, 7003; (d) Gansäuer, A.; Fleckhaus, A.; Lafont, M. A.; Okkel, A.; Kotsis, K.; Anoop, A.; Neese, F. *J. Am. Chem. Soc.* **2009**, *131*, 16989; (e) Gansäuer, A.; Fan, C.-A.; Keller, F.; Keil, J. *J. Am. Chem. Soc.* **2007**, *129*, 3484; (f) Gansäuer, A.; Rinker, B.; Pierobon, M.; Grimme, S.; Gerenkamp, M.; Mück-Lichtenfeld, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 3687.

(5) For detailed experimental and theoretical studies on the radical mechanism involving *α*-Co(III)-alkyl radical (also known as Co(III)-carbene radical) intermediates for olefin cyclopropanation and C–H alkylation, see: (a) Dzik, W. I.; Xu, X.; Zhang, X. P.; Reek, J. N. H.; de Bruin, B. *J. Am. Chem. Soc.* **2010**, *132*, 10891; (b) Belof, J. L.; Cioce, C. R.; Xu, X.; Zhang, X. P.; Space, B.; Woodcock, H. L. *Organometallics* **2011**, *30*, 2739; (c) Lu, H.

J.; Dzik, W. I.; Xu, X.; Wojtas, L.; de Bruin, B.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 8518; (d) Cui, X.; Xu, X.; Jin, L.-M.; Wojtas, L.; Zhang, X. P. *Chem. Sci.* **2015**, *6*, 1219. For studies on the similar radical mechanism involving α-Co(III)-aminyl radical (also known as Co(III)-nitrene radical) intermediates for olefin aziridination and C–H amination, see: (e) Suarez, A. I. O.; Jiang, H. L.; Zhang, X. P.; de Bruin, B. *Dalton Trans.* **2011**, *40*, 5697; (f) Hopmann, K. H.; Ghosh, A. *ACS Catal.* **2011**, *1*, 597; (g) Lyaskovskyy, V.; Suarez, A. I. O.; Lu, H. J.; Jiang, H. L.; Zhang, X. P.; de Bruin, B. *J. Am. Chem. Soc.* **2011**, *133*, 12264; (h) Goswami, M.; Lyaskovskyy, V.; Domingos, S. R.; Buma, W. J.; Woutersen, S.; Troeppner, O.; Ivanović-Burmazović, I.; Lu, H.; Cui, X.; Zhang, X. P.; Reijerse, E. J.; DeBeer, S.; van Schooneveld, M. M.; Pfaff, F. F.; Ray, K.; de Bruin, B. *J. Am. Chem. Soc.* **2015**, *137*, 5468.

(6) (a) Xu, X.; Zhu, S. F.; Cui, X.; Wojtas, L.; Zhang, X. P. *Angew. Chem., Int. Ed.* **2013**, *52*, 11857; (b) Xu, X.; Lu, H. J.; Ruppel, J. V.; Cui, X.; de Mesa, S. L.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 15292; (c) Cui, X.; Xu, X.; Lu, H. J.; Zhu, S. F.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 3304; (d) Zhu, S. F.; Xu, X.; Perman, J. A.; Zhang, X. P. *J. Am. Chem. Soc.* **2010**, *132*, 12796; (e) Ruppel, J. V.; Gauthier, T. J.; Snyder, N. L.; Perman, J. A.; Zhang, X. P. *Org. Lett.* **2009**, *11*, 2273; (f) Zhu, S. F.; Ruppel, J. V.; Lu, H. J.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2008**, *130*, 5042; (g) Zhu, S. F.; Perman, J. A.; Zhang, X. P. *Angew. Chem., Int. Ed.* **2008**, *47*, 8460; (h) Chen, Y.; Ruppel, J. V.; Zhang, X. P. *J. Am. Chem. Soc.* **2007**, *129*, 12074; (i) Chen, Y.; Fields, K. B.; Zhang, X. P. *J. Am. Chem. Soc.* **2004**, *126*, 14718; (j) Huang, L. Y.; Chen, Y.; Gao, G. Y.; Zhang, X. P. *J. Org. Chem*. **2003**, *68*, 8179; (k) Reddy, A. R.; Hao, F.; Wu, K.; Zhou, C.-Y.; Che,

C.-M. *Angew. Chem., Int. Ed.* **2016**, *55*, 1810; (l) Fantauzzi, S.; Gallo, E.; Rose, E.; Raoul, N.; Caselli, A.; Issa, S.; Ragaini, F.; Cenini, S. *Organometallics* **2008**, *27*, 6143.

(7) For other catalytic processes involving α-Co(III)-alkyl radicals as intermediates, see: (a) Das, B. G.; Chirila, A.; Tromp, M.; Reek, J. N. H.; Bruin, B. d. *J. Am. Chem. Soc.* **2016**, *138*, 8968; (b) Zhang, J.; Jiang, J.; Xu, D.; Luo, Q.; Wang, H.; Chen, J.; Li, H.; Wang, Y.; Wan, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 1231.

(8) (a) Xiao, Q.; Zhang, Y.; Wang, J. *Acc. Chem. Res.* **2013**, *46*, 236; (b) Barluenga, J.; Valdés, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 7486; (c) Fulton, J. R.; Aggarwal, V. K.; de Vicente, J. *Eur. J. Org. Chem.* **2005**, 1479.

(9) (a) Intrieri, D.; Carminati, D. M.; Gallo, E. *Dalton Trans.* **2016**, *45*, 15746; (b) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. *Synthesis* **2014**, *46*, 979; (c) Zhu, S. F.; Cui, X.; Zhang, X. P. *Eur. J. Inorg. Chem.* **2012**, 430; (d) Intrieri, D.; Caselli, A.; Gallo, E. *Eur. J. Inorg. Chem.* **2011**, 5071; (e) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977; (f) Davies, H. M. L.; Antoulinakis, E. G. *Org. React.* **2001**, *57*, 1; (g) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911.

(10) For asymmetric cyclopropanation reactions with donor-type diazo reagents, see: (a) Goudreau, S. R.; Charette, A. B. *J. Am. Chem. Soc.* **2009**, *131*, 15633; (b) Berkessel, A.; Kaiser, P.; Lex, J. *Chem. Eur. J.* **2003**, *9*, 4746; (c) Aggarwal, V. K.; Alonso, E.; Fang, G.; Ferrara, M.; Hynd, G.; Porcelloni, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1433; (d) Aggarwal, V. K.; Smith, H. W.; Jones, R. V. H.; Fieldhouse, R. *Chem. Commun.* **1997**, 1785. For non-asymmetric cyclopropanation reactions with donor-type diazo reagents, see: (e) Verdecchia, M.; Tubaro, C.; Biffis, A. *Tetrahedron Lett.* **2011**, *52*, 1136; (f) Dai, X.; Warren, T. H. *J. Am. Chem. Soc.* **2004**, *126*, 10085; (g) Maas, G.; Seitz, J. *Tetrahedron Lett.*

2001, *42*, 6137; (h) Li, Y.; Huang, J.-S.; Zhou, Z.-Y.; Che, C.-M. *J. Am. Chem. Soc.* **2001**, *123*, 4843; (i) Hamaker, C. G.; Djukic, J.-P.; Smith, D. A.; Woo, L. K. *Organometallics* **2001**, *20*, 5189.

(11) For non-asymmetric cyclopropanation using tosylhydrazones as donor-type diazo precursors, see: (a) Cyr, P.; Cote-Raiche, A.; Bronner, S. M. *Org. Lett.* **2016**, *18*, 6448; (b) Reddy, A. R.; Hao, F.; Wu, K.; Zhou, C.-Y.; Che, C.-M. *Angew. Chem., Int. Ed.* **2016**, *55*, 1810; (c) Barluenga, J.; Quiñones, N.; Tomás-Gamasa, M.; Cabal, M.-P. *Eur. J. Org. Chem.* **2012**, 2312; (d) Zhang, J.-L.; Hong Chan, P. W.; Che, C.-M. *Tetrahedron Lett.* **2003**, *44*, 8733; (e) Adams, L. A.; Aggarwal, V. K.; Bonnert, R. V.; Bressel, B.; Cox, R. J.; Shepherd, J.; de Vicente, J.; Walter, M.; Whittingham, W. G.; Winn, C. L. *J. Org. Chem.* **2003**, *68*, 9433; (f) Aggarwal, V. K.; de Vicente, J.; Bonnert, R. V. *Org. Lett.* **2001**, *3*, 2785. For intramolecular C–H alkylation using hydrazones as donor-type diazo precursors, see: (g) Soldi, C.; Lamb, K. N.; Squitieri, R. A.; Gonzalez-Lopez, M.; Di Maso, M. J.; Shaw, J. T. *J. Am. Chem. Soc.* **2014**, *136*, 15142; (h) Reddy, A. R.; Zhou, C. Y.; Guo, Z.; Wei, J.; Che, C. M. *Angew. Chem., Int. Ed.* **2014**, *53*, 14175.

(12) (a) Palusiak, M.; Grabowski, S. J. *J. Mol. Struct.* **2002**, *642*, 97; (b) Grabowski, S. J. *J. Phys. Org. Chem.* **2004**, *17*, 18.

(13) (a) Champagne, P. A.; Desroches, J.; Paquin, J. F. *Synthesis* **2015**, *47*, 306; (b) Jin, L. M.; Xu, X.; Lu, H. J.; Cui, X.; Wojtas, L.; Zhang, X. P. *Angew. Chem., Int. Ed.* **2013**, *52*, 5309.

(14) (a) Chamberlin, A. R.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 154; (b) Cusack, N. J.; Reese, C. B.; Risius, A. C.; Roozepeikar, B. *Tetrahedron* **1976**, *32*, 2157.

(15) (a) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; del Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. *Chem. Rev.* **2013**, *114*, 2432; (b) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320; (c) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881.

(16) Ruppel, J. V.; Jones, J. E.; Huff, C. A.; Kamble, R. M.; Chen, Y.; Zhang, X. P. *Org. Lett.* **2008**, *10*, 1995.

(17) Schäfer, M.; Drayß, M.; Springer, A.; Zacharias, P.; Meerholz, K. *Eur. J. Org. Chem.* **2007**, 5162.

(18) Aggarwal, V. K.; Alonso, E.; Bae, I.; Hynd, G.; Lydon, K. M.; Palmer, M. J.; Patel, M.; Porcelloni, M.; Richardson, J.; Stenson, R. A.; Studley, J. R.; Vasse, J.-L.; Winn, C. L. *J. Am. Chem. Soc.* **2003**, *125*, 10926.

(19) Zhu, S.; Xing, C.; Pang, W.; Zhu, S. *Tetrahedron Lett*. **2006**, *47*, 5897.

(20) Berkessel, A.; Kaiser, P.; Lex, J. *Chem. Eur. J.* **2003**, *9*, 4746.

(21) Yasuda, M.; Kojima, R.; Tsutsui, H.; Utsunomiya, D.; Ishii, K.; Jinnouchi, K.; Shiragami, T.; Yamashita, T. *J. Org. Chem.* **2003**, *68*, 7618.

CHAPTER 3

ENANTIOSELECTIVE RADICAL *CIS*-CYCLOPROPANATION OF ALKENES WITH IN SITU-GENERATED ALIPHATIC DIAZO COMPOUNDS

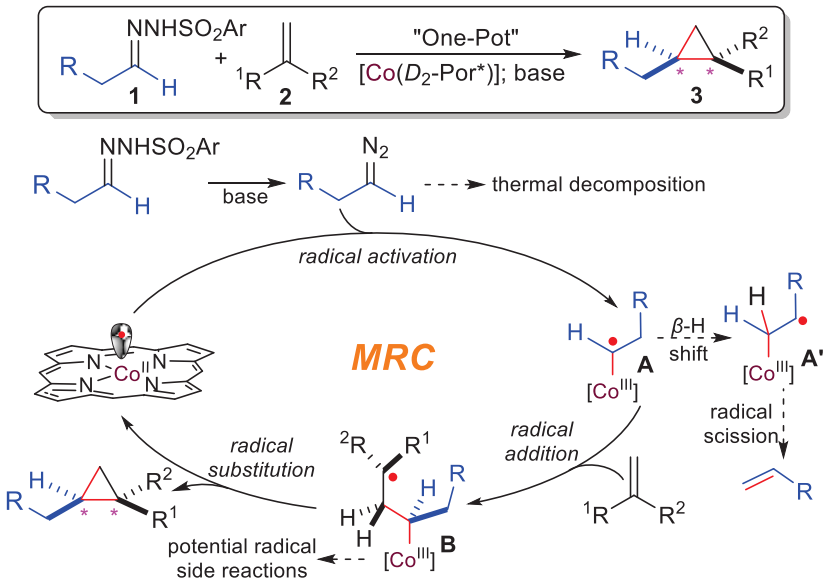
3.1 INTRODUCTION

The past decade has witnessed the renaissance of radical chemistry in organic synthesis. To address existing challenges associated with radical reactions,[1] the newly-emerged metalloradical catalysis (MRC) offers a conceptually new approach for the catalytic generation of metal-supported organic radicals and for commanding both reactivity and selectivity of their subsequent homolytic reactions.[2,3] As stable open-shell metalloradical complexes, Co(II) complexes of D_2-symmetric chiral amidoporphyrins [Co(D_2-Por*)] exhibit the unusual capability of activating various diazo compounds to generate α-Co(III)-alkyl radicals for catalytic radical transformations,[4,5] including olefin cyclopropanation and C–H alkylation, with effective control of diastereoselectivity and enantioselectivity. Their exceptional level of stereocontrol in these radical processes is in part attributed to the modular chiral porphyrin ligands that have pocket-like environment with tunable electronic, steric, as well as chiral properties.

Nevertheless, asymmetric radical alkene cyclopropanation with aliphatic diazo compounds,[5a] which would provide a streamlined synthetic route for optically active alkyl-substituted cyclopropane analogs, has remained as an unsolved challenge. As depicted in Scheme 3.1, it is envisaged that the ineffective metalloradical activation of diazo would otherwise lead to thermal decomposition of these less stabilized aliphatic diazo compounds

upon their accumulation. Also, we questioned that the presence of β-hydrogens in α-Co(III)-alkyl radicals **A** might potentially undergo undesired β-H-atom shift to form β-Co(III)-alkyl radicals **A'**, which would result in the formation of side olefinic product via radical β-scission. Moreover, with the postulated generation of intermediate **B**, it is unclear whether it will selectively lead to the desired cyclopropanation and minimize the occurrence of other possible radical side reactions. Mechanistically, it is critical to seek a suitable catalytic system to effectively induce the enantioselectivity in the subsequent radical addition of α-Co(III)-alkyl radical **A** to olefin substrate. Finally, by taking advantage of the stepwise radical mechanism, it would be highly compelling if a *cis*-selective radical substitution could be achieved during the final *3-exo-tet* radical cyclization of the resulting γ-Co(III)-alkyl radicals **B**. If the above concerns could be

Scheme 3.1|| Proposed Pathway for Radical Cyclopropanation of Alkenes with Aliphatic Diazo Compounds via Co-MRC



resolved, it would provide an enantioselective catalytic system for the access of optically active alkyl-substituted cyclopropanes. Moreover, the development of a *cis*-selective cyclopropanation protocol would also be of importance in expanding the current repertoire, which is still rather limited.[6]

In addition to serving as versatile synthetic building blocks for stereoselective organic synthesis, chiral cyclopropanes exist as common structural elements in a wide range of naturally occurring compounds and man-made pharmaceuticals.[7] Among various synthetic methods,[8,9] transition metal-catalyzed asymmetric olefin cyclopropanation with diazo compounds stands for one of the most general methods for stereoselective construction of the smallest three-membered carbocycles in optically active form.[9,10] While tremendous progress has been made, the general methods for approaching enantioenriched alkyl-substituted cyclopropanes are rather lacking. In particular, the development of asymmetric cyclopropanation with aliphatic diazo compounds, which would give rise to a highly attractive pathway for the enantioselective formation of alkyl-substituted three-membered rings, is largely undocumented.[11,12] Aside from the instability of aliphatic diazo compounds, the sluggish advancement might be largely due to the decreased electrophilicity of formed Fischer carbene intermediates towards olefins. While in the context of asymmetric catalysis, the absence of chelating groups at the neighboring site of diazo substrates might also pose inherent challenges for the effective stereoinduction. In view of the radical pathway of MRC (Scheme 3.1), we envisioned that the asymmetric radical cyclopropanation approach might potentially address the aforementioned issues because a neutral radical process is generally less sensitive to electronic effects of the substrates. Moreover, with the modular design of cavity-like porphyrin catalysts, an

enantioselective process might also be highly feasible. As a new synthetic application of MRC, we herein wish to report the development of the first asymmetric catalytic system that is highly effective for *cis*-selective cyclopropanation of alkenes with in situ-generated aliphatic diazo compounds. The Co(II)-based metalloradical system, which can be operated at room temperature, is suitable for various alkenes, allowing for the efficient construction of *cis*-selective cyclopropane rings with excellent control of enantioselectivity. The Co(II)-catalyzed cyclopropanation is further highlighted by its functional group tolerance and heteroarene compatibility.

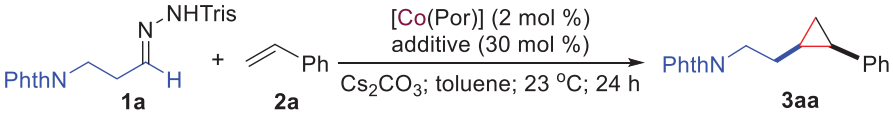
3.2 RESULTS AND DISCUSSION

3.2.1 Condition Optimization for Asymmetric Radical *Cis*-Cyclopropanation of Styrene with Aliphatic Diazo Precursors

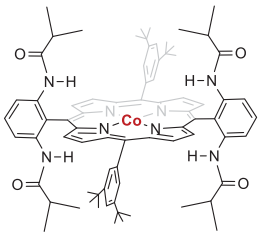
Our efforts towards developing enantioselective radical *cis*-selective cyclopropanation began with the use of a phthalimide-tethered propanal sulfonylhydrazone **1a** as radical precursors, since the resulting cyclopropanes feature an amino functionality that would be highly attractive. Gratifyingly, it was found that even the simple Co(II) complex of tetraphenylporphyrin [Co(TPP)] could be used as an effective metalloradical catalyst, delivering the masked aminoethyl cyclopropane **3aa** in 94% yield at room temperature (Table 3.1, entry 1). The high yield implies that the in situ-generation of the corresponding alkyl diazomethane from **1a** was facile at ambient conditions and properly matched with the rate of its activation by the catalyst toward productive radical

cyclopropanation of styrene (**2a**). However, the reaction predominantly favors the formation of thermodynamically more stable *trans*-cyclopropane as the major isomer with a *cis/trans* ratio of 19/81. Interestingly, when Co(II) complex of D_{2h}-symmetric achiral amidoporphyrin [Co(**P1**)] (**P1** = 3,5-Di^{t}Bu-IbuPhyrin) was used, the catalytic reaction led

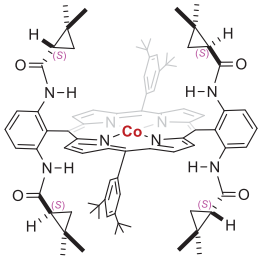
Table 3.1|| Asymmetric Cyclopropanation of Styrene with Sulfonylhydrazone 1a by Metalloradical Catalysts [Co(Por)][a]



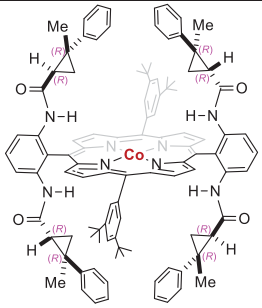
entry	catalyst	additive	yield (%)[b]	*cis/trans*[c]	ee (%)[d]
1	[Co(**TPP**)]	-	94	19:81	n/a
2	[Co(**P1**)]	-	89	52:48	n/a
3	[Co(**P2**)]	-	96	64:36	47
4	[Co(**P3**)]	-	95	61:39	94
5	[Co(**P3**)]	PPh_3	96	67:33	94
6	**[Co(P3)]**	**DMAP**	**92**	**83:17**	**99**
7	[Co(**P3**)]	PPY	93	80:20	99



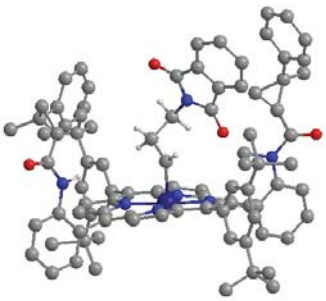
[Co(**P1**)]
(**P1** = 3,5-Di^{t}Bu-IbuPhyrin)



[Co(**P2**)]
(**P2** = 3,5-Di^{t}Bu-ChenPhyrin)



[Co(**P3**)]
(**P3** = 3,5-Di^{t}Bu-QingPhyrin)



Intermediate **A**
of entry 4

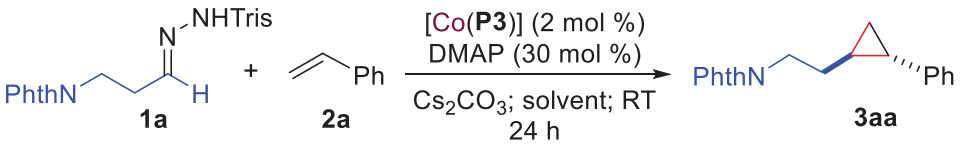
[a] Carried out with **1a** (0.1 mmol) and **2a** (2.0 equiv.) in the presence of Cs_2CO_3 (1.5 equiv.) in toluene (1.0 mL); Tris: 2,4,6-triisopropyl phenylsulfonyl group; PhthN: Phthalimide;

DMAP: 4-dimethylaminopyridine; PPY: 4-pyrrolidinopyridine. [b] Isolated yields. [c] Determined by ^{1}H NMR. [d] Determined by chiral HPLC for the major diastereomer.

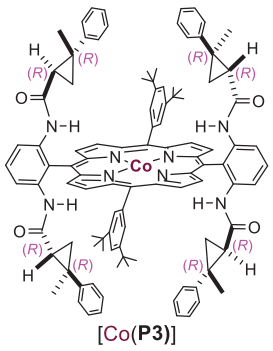
to the formation of **3aa** in 89% yield and, remarkably, with almost equal *cis*- and *trans*-isomeric distribution (entry 2). Aimed to devise a enantioselective *cis*-cyclopropanation system by using different chiral amidoporphyrin catalysts, we examined the first generation catalyst [Co(**P2**)] (**P2** = 3,5-Di^{t}Bu-ChenPhyrin) (entry 3). Gratifyingly, a slight improvement of diastereoselectivity favoring *cis*-cyclopropane was observed together with a significant level of enantioselectivity. Further ligand evaluation revealed that with sterically more encumbered [Co(**P3**)] (**P3** = 3,5-Di^{t}Bu-QingPhyrin) as the catalyst, the enantioinduction of the major isomer was substantially enhanced from 47% to 94%, albeit with a similar level of reactivity and diastereoselectivity (entry 4). The stereochemical model of intermediate **A** upon radical activation of diazo was constructed via Spartan software and shown in Table 3.1. To further improve both diastereoselectivity and enantioselectivity, we hypothesized that the involvement of potential coordinating additives[13] might have buttressing ligand effect to positively influence the outcome of stereoselectivity. Indeed, among different additives evaluated (entries 5-7), a substoichiometric amount of 4-dimethylaminopyridine (DMAP) led to the high-yielding formation of cyclopropane **3aa** with 83/17 *cis*/*trans* ratio and 99% *ee* (entry 6).

Further investigation on solvent effect (Table 3.2) revealed that aromatic solvents are relative better reaction medium than polar solvents for this radical cyclopropanation system, providing the desired compound **3aa** in high yields with varied *cis*-selectivity and enantioselectivity. Overall, the choice of solvent is still toluene.

Table 3.2|| Solvent Effect on Asymmetric Cyclopropanation of Styrene with Sulfonylhydrazone 1a by [Co(P3)][a]



entry	solvent	yield (%)[b]	*cis/trans*[c]	*ee* (%)[d]
1	PhMe	**92**	**83:17**	**99**
2	$PhCF_3$	87	76:24	99
3	PhH	98	77:23	99
4	TBME	76	80:20	99
5	EtOAc	18	73:27	98
6	dioxane	63	72:28	98
7	MeOH	25	56:46	92

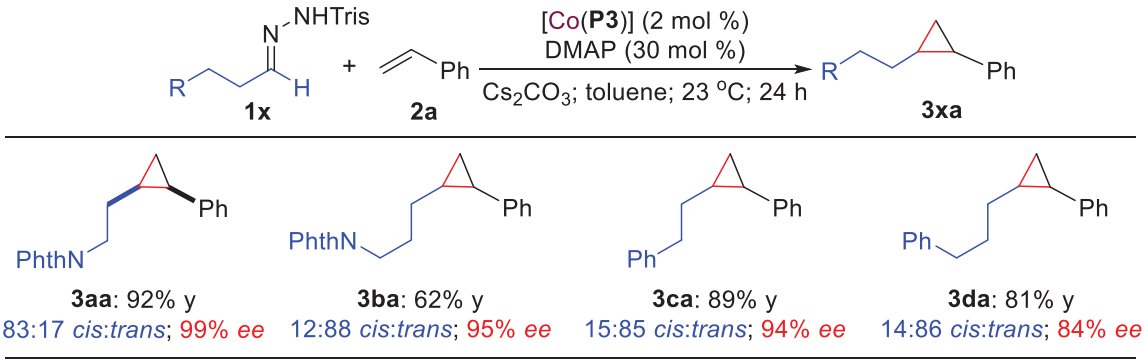


[a] Carried out with **1a** (0.1 mmol) and **2a** (2.0 equiv.) in the presence of Cs_2CO_3 (1.5 equiv.) in solvent (1.0 mL); Tris: 2,4,6-triisopropyl phenylsulfonyl group; PhthN: Phthalimide; DMAP: 4-dimethylaminopyridine. [b] Isolated yields. [c] Determined by ^1H NMR. [d] Determined by chiral HPLC for the major *cis* diastereomer.

Preliminary results showcased that the system is also applicable to other aliphatic diazo precursors under the optimized reaction conditions, yet with remarkable *trans*-selectivity. For example, when sulfonylhydrazone **1b**, with an elongated carbon chain by one more methylene from **1a**, was used, a *trans*-cyclopropanation reaction was observed and the desired cyclopropane **3ba** was delivered in 62% yield with 88/12 *trans*/*cis* and 95% *ee*. Moreover, by switching phthalimide-tethered propanal sulfonylhydrazone **1a** to its phenyl analogue **1c**, the all-carbon cyclopropane product **3ca** was also obtained predominately as *trans*-isomer in 89% yield with 94% *ee*. Finally, with the use of hydrazone **1d**, the cyclopropanation reaction was also shown to be *trans*-selective, by

affording cyclopropane **3da** in 81% yield with 86/14 *trans*/*cis* and 84% *ee*. The selective access of both diastereomers signifies the unique stepwise mechanism of Co(II)-based MRC and the detailed study of stereochemistry models is still ongoing.

Scheme 3.2|| Asymmetric Cyclopropanation of Styrene with Sulfonylhydrazones by [Co(P3)][a]



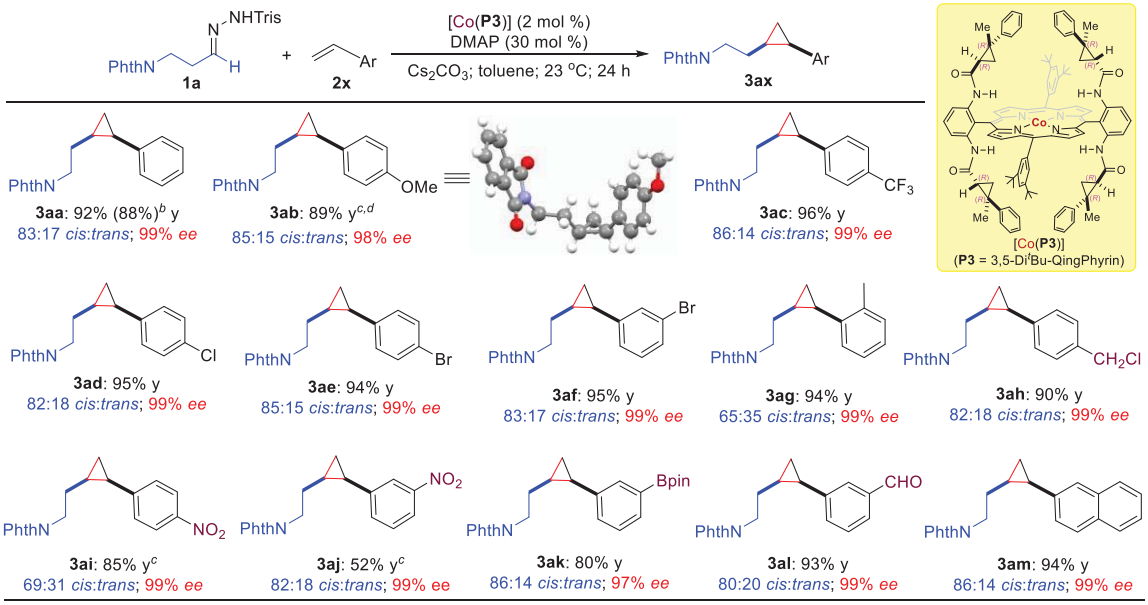
[a] Carried out with **1x** (0.1 mmol) and **2a** (2.0 equiv.) in the presence of Cs_2CO_3 (1.5 equiv.) in toluene (1.0 mL); Tris: 2,4,6-triisopropyl phenylsulfonyl group; PhthN: Phthalimide; DMAP: 4-dimethylaminopyridine; Isolated yields; *dr* was determined by ^{1}H NMR; *ee* was determined by chiral HPLC for the major diastereomer.

3.2.2 Asymmetric Radical Cyclopropanation of Different Alkenes with Aliphatic Diazo Precursor 1a

Inspired by the atypical [Co(**P3**)]/**1a**-based enantioselective *cis*-cyclopropanation reaction, we further investigated its generality by employing different alkenes. Like styrene, its derivatives bearing varied electronic and steric properties (**2a**–**2l**) could be cyclopropanated with in situ-generated aliphatic diazomethane by [Co(**P3**)], affording the corresponding aminoethyl-substituted cyclopropanes **3aa**–**3al** as *cis*-predominant

stereoisomers in high yields with excellent enantioselectivities (Scheme 3.3). Among them, halogenated styrenes such as those substituted with a Cl- or Br-atom at various positions (**2d**–**2f**) were all shown to be suitable alkene sources for highly enantioselective radical process and the resulting compounds containing aryl halide moieties would allow for further transformations such as transition metal-catalyzed cross-coupling reactions. As a demonstration of functional group tolerance, styrene derivatives bearing *p*-CH_2Cl, *p*-NO_2,

Scheme 3.3|| Enantioselective *Cis*-Cyclopropanation of Styrene Derivatives with In Situ-Generated Alkyl Diazo Compound 1a Catalyzed by [Co(P3)][a]

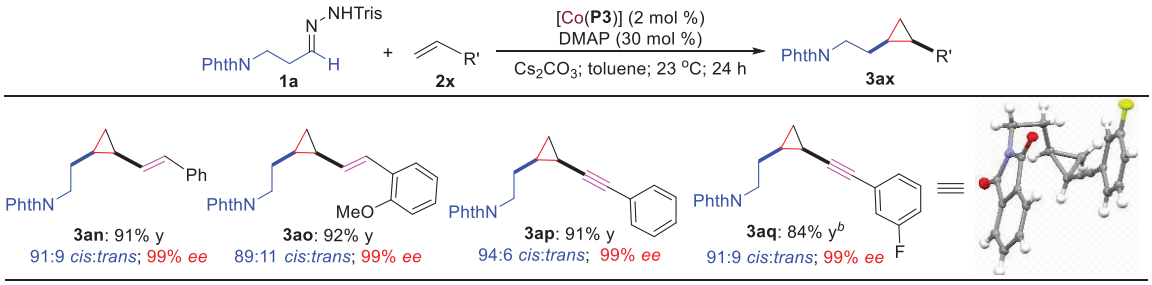


[a] Carried out with **1a** (0.1 mmol) and **2x** (2.0 equiv.) in the presence of Cs_2CO_3 (1.5 equiv.) in toluene (1.0 mL); isolated yields; *dr* was determined by ^1H NMR of crude material; *ee* of the major *cis* diastereomer was determined by chiral HPLC; Tris: 2,4,6-triisopropyl phenylsulfonyl group; PhthN: Phthalimide; DMAP: 4-dimethylaminopyridine. [b] Performed on 1.0 mmol scale. [c] 3 mol % [Co(**P3**)] was used. [d] Absolute configuration was determined by X-ray as (1*R*, 2*R*).

m-NO_2, *m*-Bpin, *m*-CHO groups could all be productively cyclopropanated to form *cis*-selective cyclopropanes **3ah**–**3al** with excellent enantioselectivities. Other aromatic olefins were also competent in this system, as exemplified by 2-vinyl naphthalene with the high-yielding formation of cyclopropane **3am** with 86/14 *cis/trans* and 99% *ee*. It was also noteworthy to mention that the one-pot protocol could be scaled up ten-fold, as demonstrated with the high-yielding synthesis of cyclopropane **3aa** on 1.0 mmol scale in 88% yield without affecting the excellent stereoselectivity.

In addition to the aromatic olefins, conjugated dienes (**2n**–**2o**) and enynes (**2p**–**2q**) could also be employed as suitable substrates for productive cyclopropanation reactions with relatively higher diastereoselectivities and excellent enantioselectivities (Scheme 3.4). The relative and absolute configurations of cyclopropanes **3ab** and **3aq** were both established as *cis* and (1*R*,2*R*), respectively.

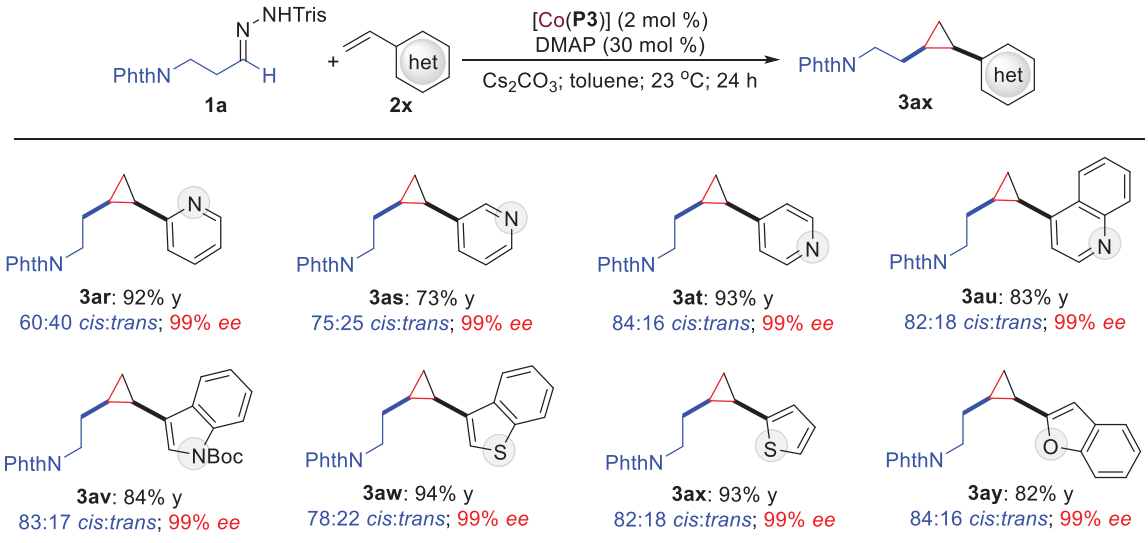
Scheme 3.4|| Enantioselective *Cis*-Cyclopropanation of Dienes and Enynes with In Situ-Generated Alkyl Diazo Compound 1a Catalyzed by [Co(P3)][a]



[a] Carried out with **1a** (0.1 mmol) and **2x** (2.0 equiv.) in the presence of Cs_2CO_3 (1.5 equiv.) in toluene (1.0 mL); isolated yields; *dr* was determined by ^{1}H NMR of crude material; *ee* of the major *cis* diastereomer was determined by chiral HPLC; Tris: 2,4,6-triisopropyl phenylsulfonyl group; PhthN: Phthalimide; DMAP: 4-dimethylaminopyridine. [b] Absolute configuration was determined by X-ray as (1*R*,2*R*).

Notably, this system was equally effective for enantioselective cyclopropanation of heteroaromatic olefins (Scheme 3.5), such as vinylpyridine analogs with different substitution patterns (**2r**–**2t**), 4-vinylquinoline (**2u**), 3-vinylindole (**2v**), 3-vinyl benzothiophene (**2w**), 2-vinylthiophene (**2x**), and 2-vinylbenzofuran (**2y**), providing heteroaryl-tethered cyclopropane derivatives **3ar**–**3ay** in high yields with equally excellent enantioselectivities (all 99% *ee*). Given that heteroarenes and amine functionality are prevalent structural elements in natural and synthetic bioactive compounds, the access of this family of three-membered carbocycles in high enantiopurity might find valuable applications in pharmaceutical research and development.

Scheme 3.5|| Enantioselective *Cis*-Cyclopropanation of Heteroaromatic Olefins with In Situ-Generated Alkyl Diazo Compound 1a Catalyzed by [Co(P3)][a]

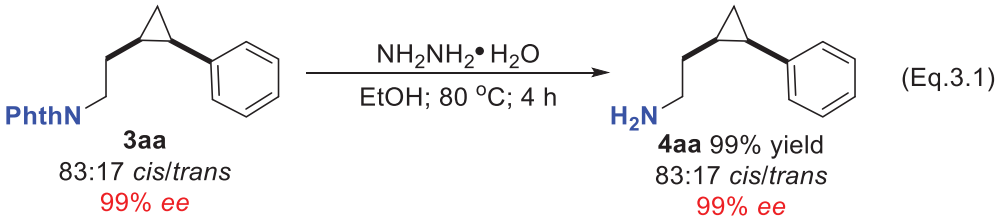


[a] Carried out with **1a** (0.1 mmol) and **2x** (2.0 equiv.) in the presence of Cs_2CO_3 (1.5 equiv.) in toluene (1.0 mL); isolated yields; *dr* was determined by ^1H NMR of crude material; *ee*

of the major *cis* diastereomer was determined by chiral HPLC; Tris: 2,4,6-triisopropyl phenylsulfonyl group; PhthN: Phthalimide; DMAP: 4-dimethylaminopyridine.

3.2.3 Deprotection of Phthalimide Unit in Resulting Optically Active Alkyl-Substituted Cyclopropane 3aa

As an initial exploration of synthetic applications, the phthalimide unit of the resulting chiral aminoethyl cyclopropane **3aa** could be readily deprotected to form the corresponding compound **4aa** with a primary amine group in 99% yield while retaining the original high enantiopurity (Eq. 3.1).

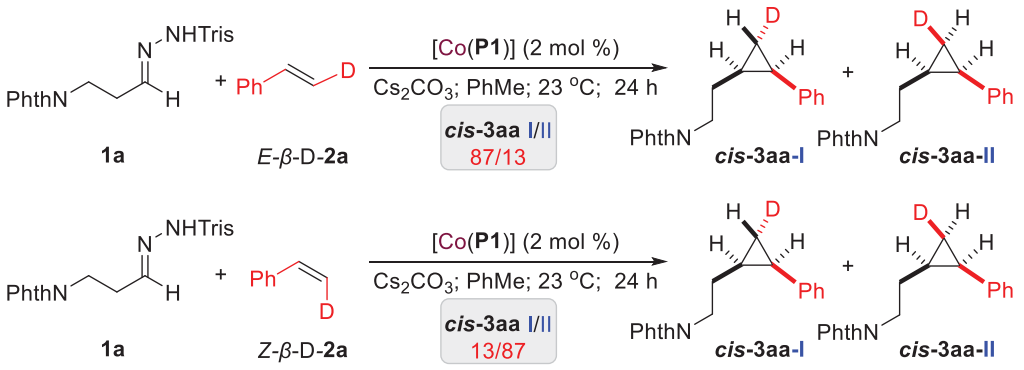


(Eq.3.1)

3.2.4 Mechanistic Investigation on Asymmetric Radical Cyclopropanation of In Situ-Generated Aliphatic Diazo Compounds

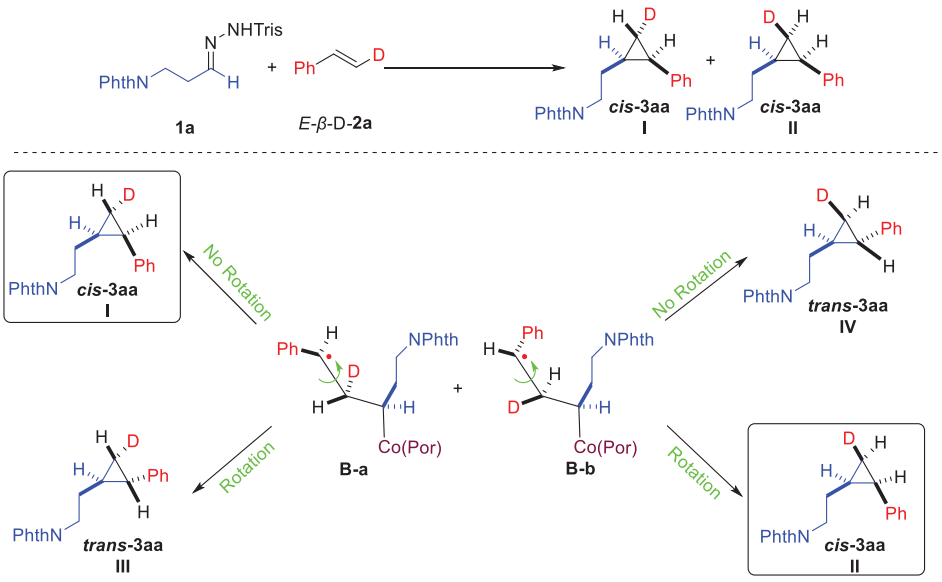
To gain insight into the underlying mechanism of this Co(II)-catalyzed asymmetric cyclopropanation, a set of mechanistic experiments were conducted. First, both (*E*)- and (*Z*)-*β*-deuterostyrenes were employed as substrates to study the stereospecificity of the catalytic process by analysis of in the resulting cyclopropane products (Scheme 3.6).[5c]

Scheme 3.6|| Cyclopropanation of *(E)*- and *(Z)*-*β*-Deuterostyrenes to Probe Radical Reaction Mechanism



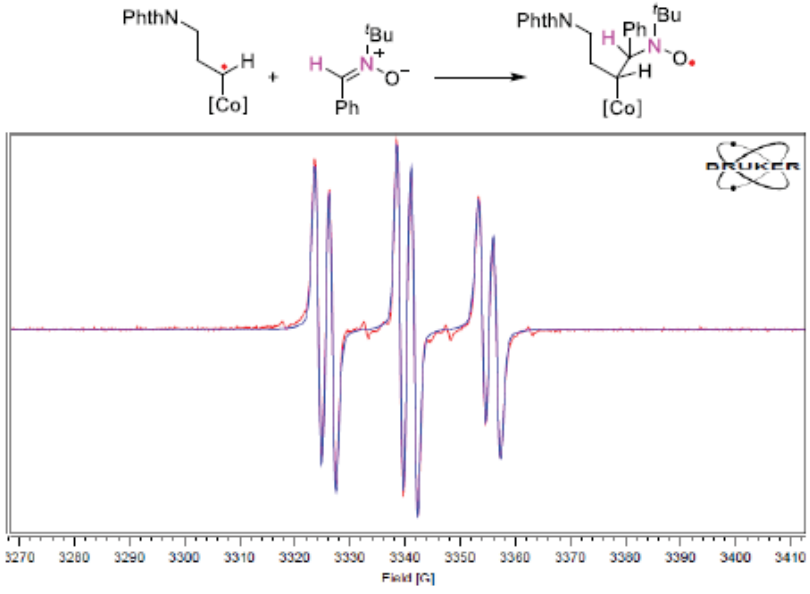
Using achiral catalyst [Co(**P1**)], cyclopropanation of *(E)*-*β*-deuterostyrene with diazo precursor **1a** indeed gave a 87:13 ratio of isotopomers **I** and **II** in the *cis*-cyclopropane products (Scheme 3.6), which might result from the rotation of *β*-C–C bond in the *γ*-Co(III)-alkyl radical intermediate **B** before ring closure (Scheme 3.7). Under the same conditions, the reaction of *(Z)*-*β*-deuterostyrene resulted in almost identical 13:87 ratio of isotopomeric distribution but in favoring **II** over **I**.

Scheme 3.7|| The Rationale of both Isotopomers A and B Formation in the Major *Cis*-Cyclopropanes 3aa from Cyclopropanation of *(E)*-*β*-Deuterostyrene ((*E*)-*β*-D-2a)



Furthermore, the α-Co(III)-benzyl radical species **A** (vide supra, Scheme 3.1) from the reaction of **1a** by [Co(**P1**)] could be directly detected with the loss of 1*e* from HRMS ($C_{87}H_{97}CoN_9O_6^+$, *m*/*z*: 1422.6879). In addition, the corresponding intermediate **A** was also trapped by spin trapping reagent phenyl *N*-*tert*-butylnitrone (PBN) to give the characteristic EPR signal. As shown in Scheme 3.8, the resulting EPR spectrum (in red), which is assigned to PBN-trapped Co(III)-supported alkyl radical intermediates, displays the characteristic triplet of doublet signal for alkyl radicals that are trapped by phenyl *N*-tert-butylnitrone (PBN). The spectrum has been simulated (in blue) with $g = 2.0061$, $A_N = 14.89$ G, $A_H = 2.52$ G, which is consistent with the resulting O-centered radical with the hyperfine splitting by the neighboring N and H atoms. The values are consistent with those for similar species reported in literature.[14]

Scheme 3.8|| Isotropic X-band EPR Spectrum of Phenyl *N*-*tert*-Butylnitrone (PBN)-Trapped Co(III)-Supported Alkyl Radical Intermediate



Collectively, these experimental observations convincingly support the proposed stepwise radical mechanism of the Co(II)-based cyclopropanation with aliphatic aldehyde-derived *N*-arylsulfonyl hydrazones.

3.3 CONCLUSIONS

In summary, aliphatic diazo compounds, generated in situ from aliphatic aldehyde-derived *N*-arylsulfonyl hydrazones, have for the first time been applied successfully for asymmetric olefin cyclopropanation via Co(II)-based metalloradical catalysis (MRC). Co(II) complex of D_2-symmetric chiral amidoporphyrin 3,5-Di^{t}Bu-QingPhyrin [Co(**P3**)] has been identified as an effective metalloradical catalyst for asymmetric *cis*-selective radical cyclopropanation with aliphatic diazo precursors. The Co(II)-based cyclopropanation is applicable to a broad range of alkenes at room temperature, affording the alkyl-substituted cyclopropane derivatives in high yields with *cis*-selectivity and excellent enantioselectivity. In view of the underdevelopment of aliphatic diazo compounds in asymmetric cyclopropanation, the successful development of this catalytic radical process will encourage further efforts in applying sulfonylhydrazones as aliphatic diazo surrogates for various asymmetric catalytic processes, including cyclopropanation and C–H alkylation reactions.

3.4 EXPERIMENTAL SECTION

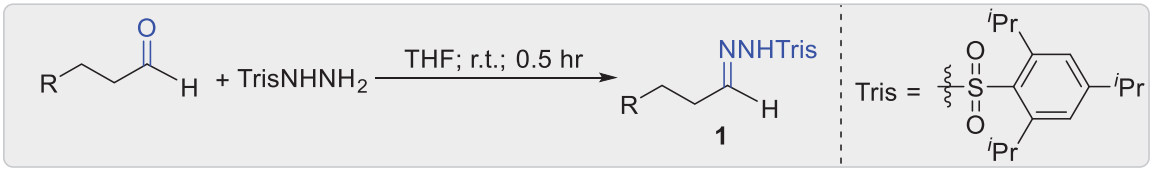
3.4.1 General Considerations

^{1}H NMR spectra were recorded on a Varian INOVA 400 (400 MHz), 500 (500 MHz) or 600 (600 MHz) spectrometer. Chemical shifts are internally referenced to residual $CHCl_3$ signal (δ 7.26 ppm). Data are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian INOVA 400 (100 MHz), 500 (125 MHz), or 600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with residual $CHCl_3$ as the internal standard (δ 77.0 ppm). High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS and JEOL Accu TOF Dart at the Mass Spectrometry Facility, Boston College. Infrared spectra were measured with a Nicolet Avatar 320 spectrometer with a Smart Miracle accessory. The X-ray diffraction data were collected using Bruker Kappa APEX DUO diffractometer and a Rigaku HighFlux Homelab diffractometer. Optical rotations were measured on a Rudolph Research Analytical AUTOPOL® IV digital polarimeter. HPLC measurements were carried out on a Shimadzu HPLC system with Chiralcel OJ-H, IA, IB, ID, IE, IF. X-band EPR spectra were recorded on a Bruker EMX-Plus spectrometer (Bruker BioSpin).

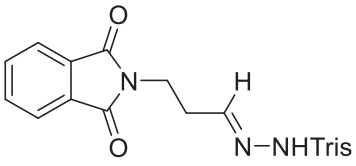
Unless otherwise noted, all cyclopropanation reactions were performed under an atmosphere of dry N_2, in oven-dried glassware with standard vacuum line techniques. Gas

tight syringes were used to transfer liquid reagents and solvents in catalytic reactions. Anhydrous solvents, as well as other commercial reagents were purchased from Sigma-Aldrich, Acros, Alfa Aesar, Strem, Oakwood Products Inc., TCI, or Matrix Scientific and used as received unless otherwise stated. Thin layer chromatography was performed on Merck TLC plates (silica gel 60 F254). Flash column chromatography was performed with ICN silica gel (60 Å, 230-400 mesh, 32-63 μm).

3.4.2 General Procedure for Preparation of 2,4,6-Triisopropyl Sulfonylhydrazones

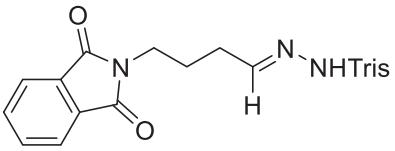


To a stirred solution of 2,4,6-triisopropyl sulfonylhydrazide (2 mmol) in THF (8 mL) at room temperature, aldehyde (1 equiv.) was added dropwise (or portionwise if solid). The reaction was completed within 0.5 h. After that, the solvent was removed directly under reduced pressure, and the crude mixture was further purified by flash chromatography.

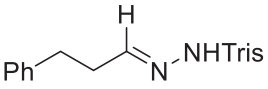


***N*'-(3-(1,3-dioxoisoindolin-2-yl)propylidene)-2,4,6-triisopropyl benzenesulfonohydrazide 1a**. Yield: 92%. R_f = 0.40 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of hydrazone *E*/*Z* isomers. δ 7.80 (dd, *J* = 5.4, 3.1 Hz, 1H), 7.70 – 7.69 (m, 3H), 7.20 (t, *J* = 5.2 Hz, 1H), 7.11 (s, 2H), 4.12 – 4.04 (m,

2H), 3.84 (t, J = 6.9 Hz, 2H), 2.91 – 2.83 (m, 1H), 2.58 – 2.54 (m, 2H), 1.23 and 1.19 (d, J = 6.9 Hz, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer. δ 168.12, 153.22, 151.38, 146.68, 133.98, 131.92, 130.96, 123.73, 123.31, 34.60, 34.08, 31.86, 29.87, 24.75, 23.49. IR (neat, cm^{-1}): 3134.5, 2957.0, 2359.1, 1776.2, 1699.0, 1397.7, 1313.9, 1152.8, 1041.0, 881.6, 720.8. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{26}H_{34}N_3O_4S$: 484.2265, Found 484.2252.

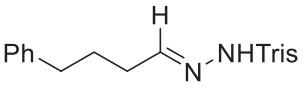


N'-(4-(1,3-dioxoisoindolin-2-yl)butylidene)-2,4,6-triisopropyl benzenesulfonohydrazide **1b.** Yield: 89%. R_f = 0.40 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of hydrazone *E*/*Z* isomers. δ 7.83 – 7.80 (m, 2H), 7.72 – 7.68 (m, 2H), 7.22 – 7.19 (m, 2H), 7.15 (s, 2H), 4.18 – 4.14 (m, 2H), 3.59 (t, J = 7.1 Hz, 2H), 2.90 – 2.85 (m, 1H), 2.25 – 2.17 (m, 2H), 1.84 – 1.78 (m, 2H), 1.25 – 1.22 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer. δ 168.22, 153.19, 151.21, 148.99, 133.96, 131.93, 131.13, 123.74, 123.19, 37.01, 34.09, 29.85, 29.68, 25.03, 24.76, 23.47. IR (neat, cm^{-1}): 3147.8, 2957.7, 2359.4, 1698.3, 1398.0, 1312.6, 1162.4, 898.3, 751.2. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{27}H_{36}N_3O_4S$: 498.2421, Found 498.2414.



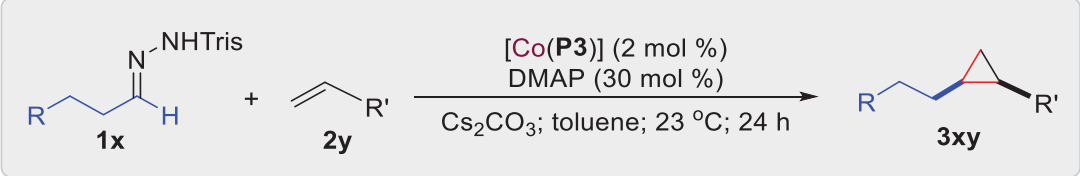
2,4,6-triisopropyl-N'-(3-phenylpropylidene) benzenesulfonohydrazide **1c.** Yield: 75%. R_f = 0.30 (ethyl acetate/hexanes: 1/8). ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of hydrazone *E*/*Z* isomers. δ 7.53 (br, 1H), 7.22 – 7.13 (m, 6H), 7.07 – 7.05 (m, 2H), 4.23 – 4.16 (m, 2H), 2.96 – 2.89 (m, 1H), 2.76 (t, J = 7.7 Hz, 2H), 2.54 – 2.49 (m, 2H), 1.28 – 1.25 (m, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): major

isomer. δ 153.29, 151.32, 149.81, 148.96, 140.48, 128.43, 128.28, 126.11, 123.81, 34.17, 33.83, 32.13, 29.93, 24.82, 23.55. IR (neat, cm^{-1}): 3189.2, 2954.9, 2359.5, 1600.6, 1453.6, 1275.3, 1154.5, 1036.8, 897.7, 749.57. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{24}H_{35}N_2O_2S$: 415.2414, Found 415.2414.

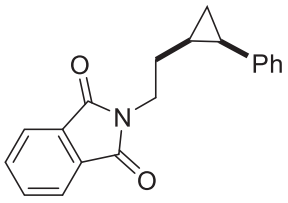


2,4,6-triisopropyl-N'-(4-phenylbutylidene) benzenesulfonohydrazide **1d.** Yield: 82%. R_f = 0.25 (ethyl acetate/hexanes: 1/10). ^1H NMR (500 MHz, $CDCl_3$): a mixture of hydrazone *E*/*Z* isomers. δ 7.52 (br, 1H), 7.29 – 7.20 (m, 2H), 7.17 (s, 2H), 7.16 – 7.04 (m, 3H), 4.22 – 4.15 (m, 2H), 2.93 – 2.84 (m, 1H), 2.52 – 2.49 (m, 2H), 2.22 – 2.18 (m, 2H), 1.79 – 1.73 (m, 2H), 1.27 – 1.22 (m, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer. δ 153.30, 151.25, 150.57, 149.05, 141.41, 128.41, 128.30, 125.88, 123.79, 34.85, 34.15, 31.57, 29.90, 27.57, 24.81, 23.50. IR (neat, cm^{-1}): 3223.0, 2955.8, 2359.4, 1599.4, 1461.7, 1259.8, 1166.6, 1035.4, 885.6, 763.9, 665.7. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{25}H_{37}N_2O_2S$: 429.2570, Found 429.2555.

3.4.3 General Procedure for [Co(P3)]-Catalyzed Asymmetric Radical Cyclopropanation with In Situ Generated Aliphatic Diazo Compounds



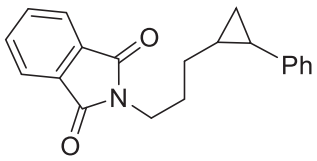
An oven-dried Schlenk tube was charged with 1.0 equivalent of sulfonyl hydrazone **1x** (0.1 mmol), [Co(**P3**)] (2 mol %), 4-dimethylaminopyridine (30 mol %) and 1.5 equivalent of Cs_2CO_3 (0.15 mmol). The Schlenk tube was then evacuated and back filled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, and olefin **2y** (0.2 mmol, 2.0 eq) and toluene (1.0 mL) were added. The Schlenk tube was then purged with nitrogen for 30 s and the rubber septum was replaced with a Teflon screw cap. The mixture was then stirred at room temperature. After 24 h, the reaction mixture was concentrated and purified by flash chromatography. The fractions containing product **3xy** were collected and concentrated by rotary evaporation to afford the compound as a mixture of *trans*/*cis* diastereomers.



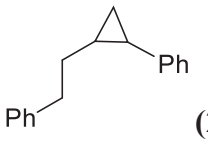
2-(2-(2-phenylcyclopropyl)ethyl)isoindoline-1,3-dione 3aa.

Following the general procedure with hydrazone **1a** and styrene **2a** as starting material. Yield: 92%. *Cis*/*trans*: 83/17. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.50. $[\alpha]^{20}{}_D$ = 28.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 – 7.78 (m, 2H), 7.68 – 7.67 (m, 2H), 7.17 – 7.14 (m, 2H), 7.11 – 7.08 (m, 3H), 3.71 – 3.62 (m, 2H), 2.12 (td, *J* = 8.7, 6.2 Hz, 1H), 1.63 – 1.56 (m, 1H), 1.33 (td, *J* = 14.2, 7.1 Hz, 1H), 1.15 – 1.13 (m, 1H), 0.99 (td, *J* = 8.4, 5.2 Hz, 1H), 0.69 (q, *J* = 5.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.25, 138.75, 133.66, 132.16, 128.69, 127.87, 125.67, 123.01, 37.75, 27.43, 20.65, 16.86, 9.49. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 19.15 min, t_{minor} = 17.57 min. IR (neat, cm^{-1}): 3061.3, 2999.4, 1771.02, 1710.5, 1466.8,

1396.7, 1363.3, 1187.0, 1029.3, 721.5. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{19}H_{18}NO_2$: 292.1332, Found 292.1319.

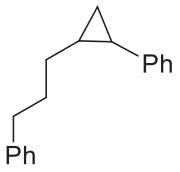


2-(3-(2-phenylcyclopropyl)propyl)isoindoline-1,3-dione 3ba. Following the general procedure with hydrazone **1b** and styrene **2a** as starting material. Yield: 62%. *Cis*/*trans*: 12/88. *ee*: 95%. Hexanes/ethyl acetate = 6/1, R_f = 0.40. $[\alpha]^{20}{}_D$ = -32.0 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.14 – 7.09 (m, 1H), 7.03 (d, *J* = 7.2 Hz, 2H), 3.72 (t, *J* = 7.3 Hz, 2H), 1.84 (p, *J* = 7.6 Hz, 2H), 1.65 – 1.62 (m, 1H), 1.48 – 1.41 (m, 2H), 1.10 – 1.04 (m, 1H), 0.89 (dt, *J* = 8.5, 5.0 Hz, 1H), 0.76 (dt, *J* = 8.6, 5.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.42, 143.49, 133.84, 132.12, 128.19, 125.63, 125.23, 123.14, 37.84, 31.58, 28.38, 23.13, 22.94, 16.03. HPLC analysis: *ee* = 95%. IB (95% hexanes : 5% isopropanol, 0.8 mL/min) : t_{major} = 17.49 min, t_{minor} = 16.78 min. IR (neat, cm^{-1}): 2927.4, 1770.8, 1714.9, 1466.9, 1396.9, 1370.7, 1035.1, 755.2, 721.9. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{20}H_{20}NO_2$: 306.1489, Found 306.1483.

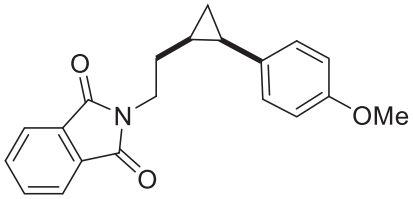


(2-phenethylcyclopropyl)benzene 3ca. Following the general procedure with hydrazone **1c** and styrene **2a** as starting material. Yield: 89%. *Cis*/*trans*: 15/85. *ee*: 94%. Hexanes/ethyl acetate = 20/1, R_f = 0.75. $[\alpha]^{20}{}_D$ = -69.4 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.18 (m, 8H), 7.03 – 7.00 (m, 2H), 2.81 – 2.71 (m, 2H), 1.72

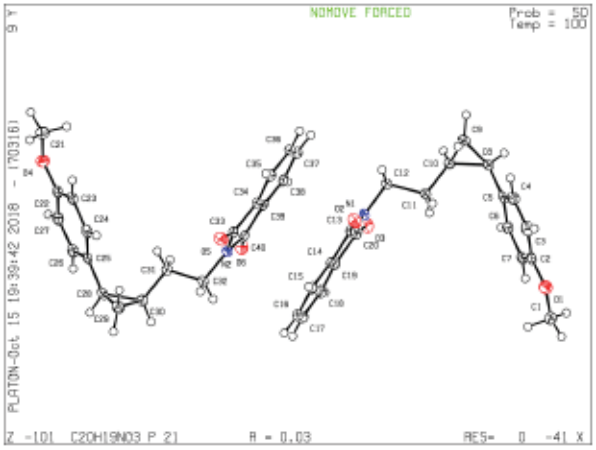
(dd, J = 14.8, 7.5 Hz, 2H), 1.65 – 1.62 (m, 1H), 1.11 – 1.06 (m, 1H), 0.91 (dt, J = 8.5, 4.9 Hz, 1H), 0.79 (dt, J = 8.7, 5.3 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.72, 142.26, 128.44, 128.26, 128.17, 125.67, 125.60, 125.19, 36.40, 35.75, 23.39, 23.34, 16.14. HPLC analysis: *ee* = 94%. IA (100% hexanes, 0.6 mL/min) : t_{major} = 11.21 min, t_{minor} = 10.38 min. IR (neat, cm^{-1}): 3025.3, 2921.2, 1603.7, 1495.3, 1453.4, 1218.8, 1089.1, 1030.0, 747.9, 694.7. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{17}H_{19}$: 223.1481, Found 223.1472.

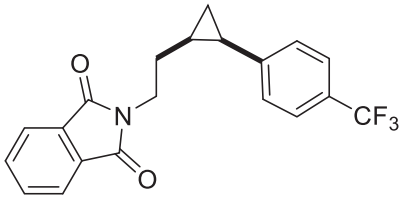


(3-(2-phenylcyclopropyl)propyl)benzene 3da. Following the general procedure with hydrazone **1d** and styrene **2a** as starting material. Yield: 81%. *Cis*/*trans*: 14/86. *ee*: 84%. Hexanes/ethyl acetate = 20/1, R_f = 0.75. $[\alpha]^{20}_D$ = -29.4 (c = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 4H), 7.20 (d, J = 7.2 Hz, 3H), 7.15 – 7.12 (m, 1H), 7.08 – 7.05 (m, 2H), 2.69 – 2.65 (m, 2H), 1.83 – 1.77 (m, 2H), 1.64 – 1.61 (m, 1H), 1.45 (dd, J = 14.9, 7.0 Hz, 2H), 1.07 – 1.01 (m, 1H), 0.90 (dt, J = 8.5, 4.9 Hz, 1H), 0.79 – 0.75 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.89, 142.60, 128.37, 128.25, 128.20, 125.63, 125.60, 125.17, 35.70, 33.99, 31.14, 23.59, 23.24, 16.09. HPLC analysis: *ee* = 84%. IE (100% hexanes, 1.2 mL/min) : t_{major} = 9.85 min, t_{minor} = 10.49 min. IR (neat, cm^{-1}): 3025.1, 2925.2, 2853.4, 1603.6, 1495.6, 1452.6, 1217.8, 1076.8, 1028.8, 874.7, 746.3. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{18}H_{21}$: 237.1638, Found 237.1628.

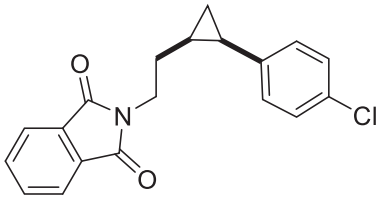


2-(2-(2-(4-methoxyphenyl)cyclopropyl)ethyl) isoindoline-1,3-dione 3ab. Following the general procedure with hydrazone **1a** and 4-methoxyl styrene **2b** as starting material in the presence of 3 mol % [Co(**P3**)]. Yield: 89%. *Cis*/*trans*: 85/15. *ee*: 98%. Hexanes/ethyl acetate = 5/1, R_f = 0.45. $[\alpha]^{20}_{D}$ = 3.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.68 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.70 (d, *J* = 8.6 Hz, 2H), 3.74 (s, 3H), 3.71 – 3.64 (m, 2H), 2.05 (td, *J* = 8.6, 6.1 Hz, 1H), 1.62 – 1.57 (m, 1H), 1.31 – 1.25 (m, 1H), 1.11 – 1.04 (m, 1H), 0.96 (td, *J* = 8.4, 5.1 Hz, 1H), 0.60 (q, *J* = 5.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.93, 160.35, 136.31, 134.85, 132.33, 129.28, 125.64, 116.03, 57.80, 40.49, 30.23, 22.47, 19.13, 12.22. HPLC analysis: *ee* = 98%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 25.57 min, t_{minor} = 22.40 min. IR (neat, cm^{-1}): 2996.9, 2933.8, 1770.4, 1708.9, 1513.7, 1393.0, 1247.4, 1034.4, 830.7, 720.8. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{20}H_{20}NO_3$: 322.1438, Found 322.1434.



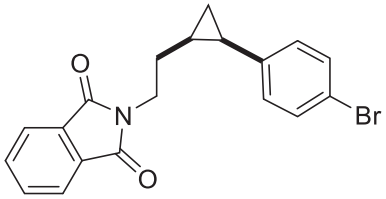


2-(2-(2-(4-trifluoromethylphenyl)cyclopropyl)ethyl) isoindoline-1,3-dione 3ac. Following the general procedure with hydrazone **1a** and 4-trifluoromethyl styrene **2c** as starting material. Yield: 96%. *Cis*/*trans*: 86/14. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.50. $[\alpha]^{20}{}_D$ = 11.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.68 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 3.67 (t, *J* = 6.7 Hz, 2H), 2.16 – 2.12 (m, 1H), 1.61 – 1.55 (m, 1H), 1.44 – 1.39 (m, 1H), 1.27 – 1.21 (m, 1H), 1.08 (td, *J* = 8.4, 5.4 Hz, 1H), 0.74 (d, *J* = 5.7 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.20, 143.31, 133.78, 132.08, 128.71, 127.89 (q, *J* = 32.3 Hz), 125.54, 124.76 (q, *J* = 3.6 Hz), 123.05, 37.68, 27.14, 20.75, 17.87, 10.22. HPLC analysis: *ee* = 99%. ID (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 15.01 min, t_{minor} = 14.19 min. IR (neat, cm^{-1}): 3067.2, 2939.3, 1771.8, 1713.9, 1394.5, 1327.9, 1164.6, 1122.4, 1070.3, 721.3. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{20}H_{17}F_3NO_2$: 360.1206, Found 360.1192.

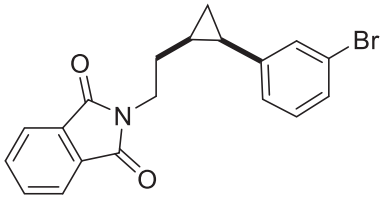


2-(2-(2-(4-chlorophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione 3ad. Following the general procedure with hydrazone **1a** and 4-chlorostyrene **2d** as starting material. Yield: 95%. *Cis*/*trans*: 82/18. *ee*: 99%. Hexanes/ethyl acetate = 5/1, R_f = 0.50. $[\alpha]^{20}{}_D$ = 19.1 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.68 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.06 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 8.2 Hz,

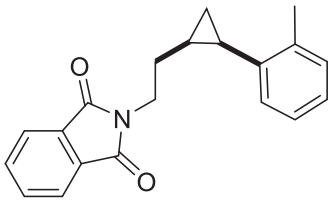
2H), 3.65 (d, J = 6.8 Hz, 2H), 2.06 (td, J = 8.6, 6.2 Hz, 1H), 1.60 – 1.53 (m, 1H), 1.39 – 1.32 (m, 1H), 1.19 – 1.11 (m, 1H), 1.01 (td, J = 8.4, 5.3 Hz, 1H), 0.65 – 0.62 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.22, 137.43, 133.73, 132.07, 129.83, 127.95, 126.78, 123.01, 37.69, 27.26, 20.19, 17.20, 9.92. HPLC analysis: *ee* = 99%. IE (95% hexanes : 5% isopropanol, 0.8 mL/min) : t_{major} = 36.30 min, t_{minor} = 24.84 min. IR (neat, cm^{-1}): 2999.4, 1935.9, 1770.1, 1707.2, 1493.5, 1391.6, 1089.4, 1012.8, 826.9, 720.8. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{19}H_{17}ClNO_2$: 326.0942, Found 326.0937.



2-(2-(2-(4-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione 3ae. Following the general procedure with hydrazone **1a** and 4-bromostyrene **2d** as starting material. Yield: 94%. *Cis*/*trans*: 85/15. *ee*: 99%. Hexanes/ethyl acetate = 5/1, R_f = 0.50. $[\alpha]^{20}_D$ = 4.0 (c = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, J = 5.4, 3.0 Hz, 2H), 7.69 (dd, J = 5.4, 3.0 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 8.3 Hz, 2H), 3.66 (t, J = 6.7 Hz, 2H), 2.04 (td, J = 8.6, 6.2 Hz, 1H), 1.59 – 1.52 (m, 1H), 1.40 – 1.33 (m, 1H), 1.19 – 1.12 (m, 1H), 1.04 – 0.99 (m, 1H), 0.63 (q, J = 5.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.23, 137.99, 133.74, 132.07, 130.89, 130.21, 123.03, 119.43, 37.70, 27.24, 20.28, 17.27, 9.94. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 27.09 min, t_{minor} = 20.85 min. IR (neat, cm^{-1}): 3000.7, 2936.6, 1705.5, 1489.1, 1434.9, 1390.3, 1360.9, 1177.7, 1073.3, 1008.5, 822.3, 718.8. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{19}H_{17}BrNO2$: 370.0437, Found 370.0428.

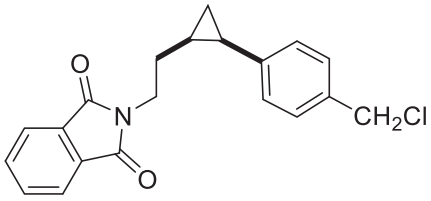


2-(2-(2-(3-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione 3af. Following the general procedure with hydrazone **1a** and 3-bromostyrene **2f** as starting material. Yield: 95%. *Cis*/*trans*: 83/17. *ee*: 99%. Hexanes/ethyl acetate = 7/1, R_f = 0.40. $[\alpha]^{20}_D$ = 19.5 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.68 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.26 (s, 1H), 7.23 – 7.21 (m, 1H), 7.03 – 7.02 (m, 2H), 3.71 – 3.63 (m, 2H), 2.08 (td, *J* = 8.6, 6.1 Hz, 1H), 1.63 – 1.56 (m, 1H), 1.32 (td, *J* = 14.3, 7.0 Hz, 1H), 1.19 – 1.13 (m, 1H), 1.02 (td, *J* = 8.4, 5.3 Hz, 1H), 0.66 (q, *J* = 5.8 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.23, 141.47, 133.77, 132.07, 131.83, 129.40, 128.86, 127.27, 123.06, 122.16, 37.65, 27.46, 20.46, 17.13, 9.95. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 22.37 min, t_{minor} = 21.43 min. IR (neat, cm^{-1}): 3063.3, 3001.8, 2936.6, 1770.3, 1708.7, 1435.4, 1393.7, 1041.7, 755.1, 720.9. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{19}H_{17}BrNO_2$: 370.0437, Found 370.0422.

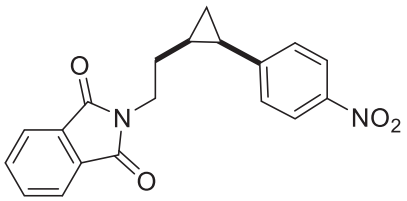


2-(2-(2-(2-methylphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione 3ag. Following the general procedure with hydrazone **1a** and 2-methyl styrene **2g** as starting material. Yield: 94%. *Cis*/*trans*: 65/35. *ee*: 99%. Hexanes/ethyl acetate = 6/1, R_f = 0.45. $[\alpha]^{20}_D$ = 105.0 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.68 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.11 – 7.05 (m, 3H), 7.03 – 7.02 (m, 1H), 3.72 – 3.64 (m, 2H), 2.36 (s, 3H), 2.05 – 2.00 (m, 1H), 1.70 – 1.62 (m, 1H), 1.25 – 1.19 (m, 1H),

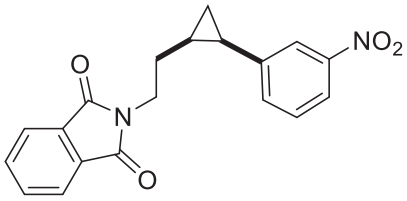
1.03 – 0.99 (m, 1H), 0.91 – 0.83 (m, 1H), 0.77 – 0.73 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.91, 141.02, 139.66, 136.39, 134.79, 132.15, 130.58, 128.62, 128.12, 125.71, 40.51, 30.41, 22.25, 21.86, 18.30, 11.84. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 18.06 min, t_{minor} = 16.79 min. IR (neat, cm^{-1}): 2990.4, 2858.0, 1704.9, 1432.4, 1396.1, 1361.9, 1178.9, 1030.5, 945.6, 864.3, 768.0, 717.3. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{20}H_{20}NO_2$: 306.1489, Found 306.1485.



2-(2-(2-(2-methylchrolophenyl)cyclopropyl)ethyl) isoindoline-1,3-dione 3ah. Following the general procedure with hydrazone **1a** and 4-methylchloro styrene **2h** as starting material. Yield: 90%. *Cis*/*trans*: 82/18. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.50. $[\alpha]^{20}_D$ = 8.2 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.68 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 4.50 (s, 2H), 3.67 (td, *J* = 6.8, 2.7 Hz, 2H), 2.10 (dd, *J* = 14.8, 8.6 Hz, 1H), 1.61 – 1.57 (m, 1H), 1.37 – 1.31 (m, 1H), 1.19 – 1.15 (m, 1H), 1.01 (td, *J* = 8.4, 5.3 Hz, 1H), 0.69 (q, *J* = 5.7 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.24, 139.35, 134.73, 133.70, 132.13, 128.91, 128.13, 123.04, 46.14, 37.75, 27.35, 20.47, 17.20, 9.82. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 27.11 min, t_{minor} = 22.97 min. IR (neat, cm^{-1}): 3002.7, 2926.4, 1770.5, 1712.5, 1435.7, 1397.2, 1363.0, 1266.0, 1186.9, 1045.3, 756.9, 721.2. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{20}H_{19}ClNO_2$: 340.1099, Found 340.1105.

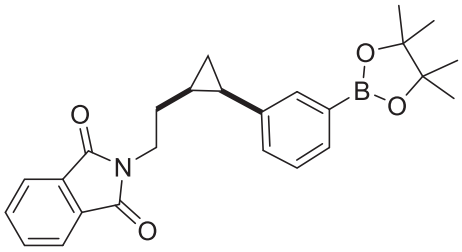


2-(2-(2-(4-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione 3ai. Following the general procedure with hydrazone **1a** and 4-nitrostyrene **2i** as starting material in the presence of 3 mol % [Co(**P3**)]. Yield: 85%. *Cis*/*trans*: 69/31. *ee*: 99%. Hexanes/ethyl acetate = 3/1, R_f = 0.35. $[\alpha]^{20}_D$ = 48.0 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.8 Hz, 2H), 7.74 – 7.67 (m, 4H), 7.17 (d, *J* = 8.7 Hz, 2H), 3.69 – 3.60 (m, 2H), 2.18 (td, *J* = 8.6, 6.3 Hz, 1H), 1.57 – 1.50 (m, 2H), 1.37 – 1.29 (m, 1H), 1.20 – 1.15 (m, 1H), 0.81 (q, *J* = 6.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.11, 147.53, 133.89, 131.97, 128.86, 125.74, 123.10, 122.99, 37.52, 26.93, 21.18, 19.01, 11.12. HPLC analysis: *ee* = 99%. ID (85% hexanes : 15% isopropanol, 0.8 mL/min) : t_{major} = 62.39 min, t_{minor} = 39.21 min. IR (neat, cm^{-1}): 3003.7, 2939.2, 1739.3, 1706.0, 1507.5, 1335.6, 1184.8, 1039.4, 853.2, 716.9. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{19}H_{17}N_2O_4$: 337.1183, Found 337.1181.



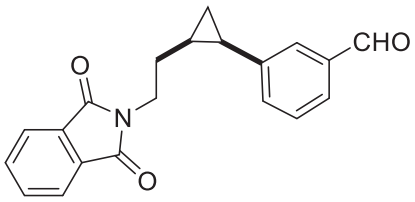
2-(2-(2-(3-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione 3aj. Following the general procedure with hydrazone **1a** and 3-nitrostyrene **2j** as starting material in the presence of 3 mol % [Co(**P3**)]. Yield: 52%. *Cis*/*trans*: 82/18. *ee*: 99%. Hexanes/ethyl acetate = 3/1, R_f = 0.45. $[\alpha]^{20}_D$ = 20.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 – 7.93 (m, 2H), 7.75 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.67 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.35 – 7.30 (m, 1H), 3.69 – 3.61 (m, 2H), 2.20 (td, *J* =

8.6, 6.2 Hz, 1H), 1.59 – 1.53 (m, 1H), 1.47 – 1.41 (m, 1H), 1.28 – 1.25 (m, 1H), 1.16 – 1.12 (m, 1H), 0.78 (q, J = 5.8 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.77, 150.60, 144.01, 137.08, 136.51, 134.60, 131.43, 126.20, 125.70, 123.52, 40.16, 29.84, 23.29, 20.44, 13.05. HPLC analysis: *ee* = 99%. ID (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 48.12 min, t_{minor} = 40.84 min. IR (neat, cm^{-1}): 3071.1, 2922.1, 1770.3, 1707.1, 1527.0, 1393.6, 1349.2, 1040.9, 806.4, 721.6. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{19}H_{17}N_2O_4$: 337.1183, Found 337.1181.

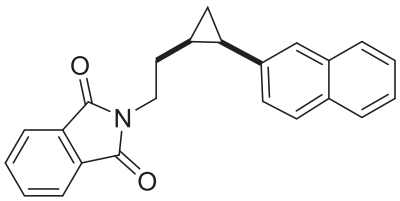


2-(2-(2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) phenyl)cyclopropyl)ethyl)isoindoline-1,3-dione 3ak. Following the general procedure with hydrazone **1a** and 4,4,5,5-tetramethyl-2-(3-vinylphenyl)-1,3,2-dioxaborolane **2k** as starting material. Yield: 80%. *Cis*/*trans*: 86/14. *ee*: 97%. Hexanes/ethyl acetate = 5/1, R_f = 0.40. $[\alpha]^{20}{}_D$ = 10.2 (c = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (dd, J = 5.4, 3.1 Hz, 2H), 7.67 (dd, J = 5.4, 3.0 Hz, 2H), 7.60 (s, 1H), 7.56 (d, J = 7.1 Hz, 1H), 7.23 (d, J = 7.7 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 3.72 – 3.64 (m, 2H), 2.16 – 2.11 (m, 1H), 1.69 – 1.63 (m, 1H), 1.34 (s, 12H), 1.19 – 1.09 (m, 2H), 0.98 (td, J = 8.2, 5.3 Hz, 1H), 0.74 (q, J = 5.5 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.27, 138.08, 135.35, 133.68, 132.28, 132.17, 131.69, 128.44, 127.32, 123.03, 83.67, 37.84, 27.83, 24.88, 20.49, 16.49, 9.60. HPLC analysis: *ee* = 97% (estimated). OJH (99.5% hexanes : 0.5% isopropanol, 1.0 mL/min) : t_{major} = 45.62 min, t_{minor} = 50.73 min. IR (neat, cm^{-1}):

2977.9, 2931.0, 2359.8, 1771.5, 1713.2, 1390.5, 1362.3, 1145.2, 965.3, 739.8, 720.9. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{25}H_{29}BNO_4$: 418.2184, Found 418.2175.

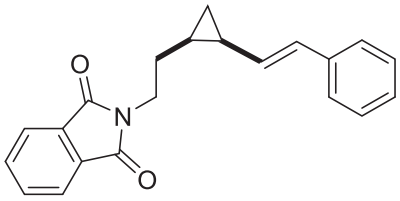


3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl) benzaldehyde 3al. Following the general procedure with hydrazone **1a** and 3-vinyl benzaldehyde **2l** as starting material. Yield: 93%. *Cis*/*trans*: 80/20. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.55. $[\alpha]^{20}{}_D$ = 29.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.66 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.60 – 7.58 (m, 2H), 7.37 – 7.30 (m, 2H), 3.69 – 3.60 (m, 2H), 2.17 (td, *J* = 8.6, 6.2 Hz, 1H), 1.59 – 1.52 (m, 1H), 1.43 – 1.36 (m, 1H), 1.26 – 1.19 (m, 1H), 1.08 (td, *J* = 8.4, 5.4 Hz, 1H), 0.76 (q, *J* = 5.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.31, 168.14, 140.22, 136.13, 134.59, 133.78, 132.02, 129.88, 128.59, 127.19, 123.03, 37.61, 27.26, 20.50, 17.36, 9.98. HPLC analysis: *ee* = 99%. IE (85% hexanes : 5% isopropanol, 0.8 mL/min) : t_{major} = 55.31 min, t_{minor} = 48.89 min. IR (neat, cm^{-1}): 3005.0, 2940.1, 1770.0, 1702.9, 1435.8, 1392.2, 1173.3, 1036.9, 751.4, 718.1. HRMS (ESI) ([M+H]$^+$) Calcd. For $C_{20}H_{18}NO_3$: 320.1281, Found 320.12.70.



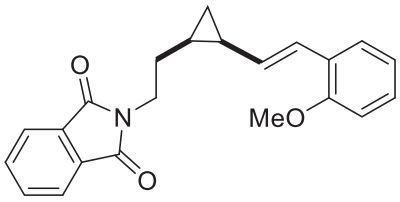
2-(2-(2-(naphthalen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione 3am. Following the general procedure with hydrazone **1a** and 2-vinyl

naphthelene **2m** as starting material. Yield: 94%. *Cis*/*trans*: 86/14. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.50. $[\alpha]^{20}_D$ = 31.2 (*c* = 1.0, $CHCl_3$).^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 – 7.59 (m, 7H), 7.49 (s, 1H), 7.41 – 7.35 (m, 2H), 7.32 – 7.29 (m, 1H), 3.71 – 3.64 (m, 2H), 2.29 – 2.25 (m, 1H), 1.70 – 1.64 (m, 1H), 1.40 – 1.34 (m, 1H), 1.25 – 1.20 (m, 1H), 1.11 – 1.07 (m, 1H), 0.84 (q, *J* = 5.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.23, 136.63, 133.59, 133.22, 131.99, 131.90, 127.66, 127.46, 127.44, 127.39, 126.63, 125.76, 124.99, 122.87, 37.82, 27.48, 20.99, 17.26, 9.89. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 25.17 min, t_{minor} = 22.45 min. IR (neat, cm^{-1}): 3057.4, 3000.7, 2934.2, 1769.7, 1705.7, 1391.5, 1360.6, 1039.3, 819.0, 750.6, 718.3. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{23}H_{20}NO_2$: 342.1489, Found 342.1498.

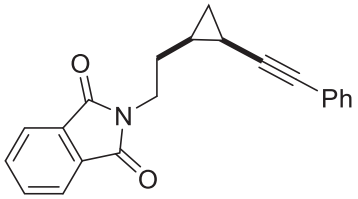


(*E*)-2-(2-(2-styrylcyclopropyl)ethyl)isoindoline-1,3-dione 3an. Following the general procedure with hydrazone **1a** and (*E*)-buta-1,3-dien-1-ylbenzene **2n** as starting material. Yield: 91%. *Cis*/*trans*: 91/9. *ee*: 99%. Hexanes/ethyl acetate = 6/1, R_f = 0.35. $[\alpha]^{20}_D$ = -66.4 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 5.3, 3.0 Hz, 2H), 7.49 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 2H), 7.13 – 7.07 (m, 3H), 6.13 (d, *J* = 15.7 Hz, 1H), 5.80 (dd, *J* = 15.7, 9.5 Hz, 1H), 3.84 – 3.77 (m, 2H), 1.94 (dq, *J* = 16.2, 5.4 Hz, 1H), 1.77 – 1.71 (m, 1H), 1.60 – 1.55 (m, 1H), 1.16 – 1.10 (m, 1H), 1.00 – 0.97 (m, 1H), 0.31 (dd, *J* = 10.9, 5.4 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.49, 137.23, 133.37, 132.04, 129.68, 129.53, 128.20, 126.46, 125.52, 122.84, 37.97, 28.22, 19.53, 17.52, 12.75. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol,

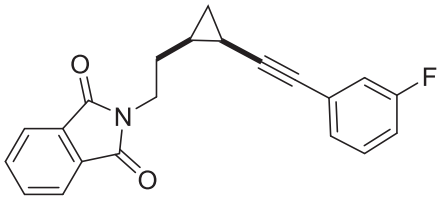
0.8 mL/min) : t_{major} = 23.31 min, t_{minor} = 18.79 min. IR (neat, cm^{-1}): 3023.3, 2937.6, 1770.9, 1703.6, 1435.5, 1392.6, 1174.1, 1068.5, 953.8, 748.2, 691.1. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{21}H_{20}NO_2$: 318.1489, Found 318.1500.



(*E*)-2-(2-(2-(2-methoxystyryl)cyclopropyl)ethyl) isoindoline-1,3-dione 3ao. Following the general procedure with hydrazone **1a** and (*E*)-1-(buta-1,3-dien-1-yl)-2-methoxybenzene **2o** as starting material. Yield: 92%. *Cis*/*trans*: 89/11. *ee*: 99%. Hexanes/ethyl acetate = 5/1, R_f = 0.40. $[\alpha]^{20}{}_D$ = -29.6 (*c* = 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.49 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 1H), 7.10 (t, *J* = 8.5 Hz, 1H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.50 (d, *J* = 15.9 Hz, 1H), 5.84 (dd, *J* = 15.9, 9.5 Hz, 1H), 3.82 – 3.75 (m, 2H), 3.75 (s, 3H), 1.93 – 1.88 (m, 1H), 1.75 (td, *J* = 15.1, 8.2 Hz, 1H), 1.65 – 1.58 (m, 1H), 1.15 – 1.08 (m, 1H), 0.97 (td, *J* = 8.3, 4.8 Hz, 1H), 0.31 (dd, *J* = 10.8, 5.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.51, 155.85, 133.69, 133.24, 132.08, 130.41, 127.35, 126.10, 124.14, 122.77, 120.43, 110.50, 55.21, 38.02, 28.30, 20.02, 17.52, 12.87. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 29.91 min, t_{minor} = 26.81 min. IR (neat, cm^{-1}): 2995.9, 2935.8, 1770.5, 1704.8, 1488.8, 1435.2, 1392.6, 1241.2, 1027.9, 970.8, 750.0. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{22}H_{22}NO_3$: 348.1594, Found 348.1585.

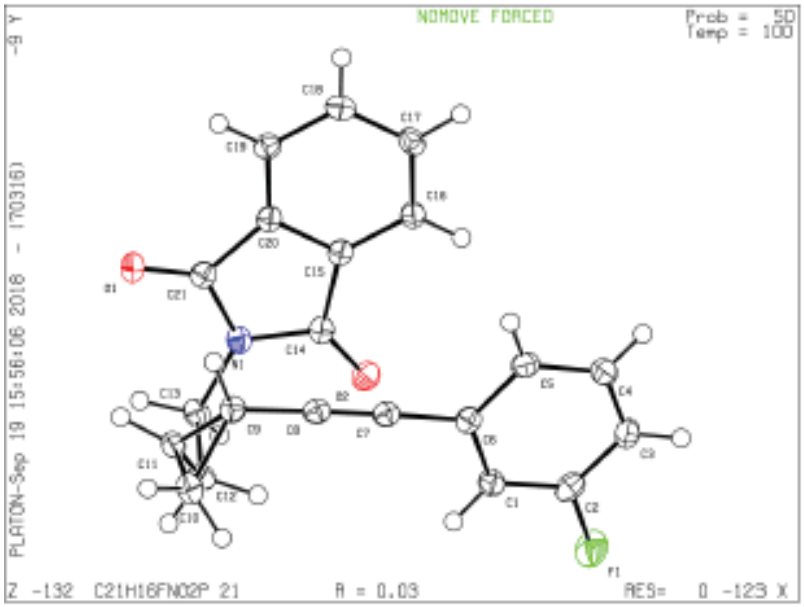


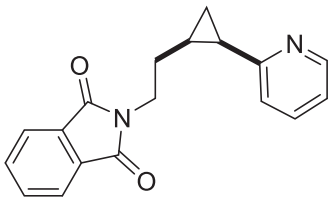
2-(2-(2-(phenylethynyl)cyclopropyl)ethyl)isoindoline-1,3-dione 3ap. Following the general procedure with hydrazone **1a** and but-3-en-1-yn-1-ylbenzene **2p** as starting material. Yield: 91%. *Cis*/*trans*: 94/6. *ee*: 99%. Hexanes/ethyl acetate = 8/1, R_f = 0.35. $[\alpha]^{20}{}_D$ = -79.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.60 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.27 – 7.24 (m, 2H), 7.24 – 7.21 (m, 3H), 3.91 – 3.88 (m, 2H), 1.98 (dq, *J* = 14.2, 5.8 Hz, 1H), 1.94 – 1.87 (m, 1H), 1.55 (td, *J* = 8.3, 5.4 Hz, 1H), 1.18 – 1.11 (m, 1H), 1.05 – 1.01 (m, 1H), 0.49 – 0.46 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.47, 133.53, 132.21, 131.52, 127.95, 127.28, 123.72, 123.00, 90.16, 78.75, 37.64, 29.22, 17.25, 14.40, 6.07. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 23.56 min, t_{minor} = 19.83 min. IR (neat, cm^{-1}): 2921.6, 2849.3, 1771.2, 1712.0, 1467.1, 1398.5, 1365.2, 1188.0, 1065.5, 758.1. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{21}H_{18}NO_2$: 316.1332, Found 316.1330.



2-(2-(2-((3-fluorophenyl)ethynyl)cyclopropyl)ethyl) isoindoline-1,3-dione 3aq. Following the general procedure with hydrazone **1b** and 1-(but-3-en-1-yn-1-yl)-3-fluorobenzene **2q** as starting material. Yield: 84%. *Cis*/*trans*: 91/9. *ee*: 99%. Hexanes/ethyl acetate = 8/1, R_f = 0.35. $[\alpha]^{20}{}_D$ = -48.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.62 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.20 – 7.15 (m, 1H), 7.04 (d, *J* = 7.7 Hz, 1H), 6.94 – 6.90 (m, 2H), 3.91 – 3.87 (m, 2H), 2.04 –

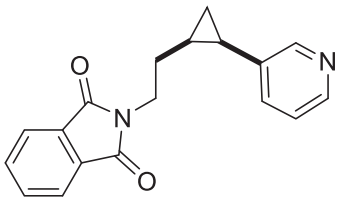
1.97 (m, 1H), 1.90 – 1.83 (m, 1H), 1.54 (td, J = 8.3, 5.4 Hz, 1H), 1.20 – 1.14 (m, 1H), 1.07 – 1.02 (m, 1H), 0.48 (dd, J = 10.9, 5.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.45, 162.19 (d, J = 245.6 Hz), 133.57, 132.21, 129.45 (d, J = 8.7 Hz), 127.39 (d, J = 2.8 Hz), 125.58 (d, J = 9.6 Hz), 123.01, 118.27 (d, J = 22.6 Hz), 114.61 (d, J = 21.2 Hz), 91.42, 77.65, 37.60, 29.24, 17.47, 14.44, 6.03. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 20.92 min, t_{minor} = 17.59 min. IR (neat, cm^{-1}): 2924.8, 2854.1, 1709.6, 1608.1, 1571.0, 1392.9, 1263.7, 1153.7, 1059.9, 862.5, 734.6. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{21}H_{17}FNO_2$: 334.1238, Found 334.1240.





2-(2-(2-(pyridin-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione 3ar. Following the general procedure with hydrazone **1a** and 2-vinyl pyridine **2r** as starting material. Yield: 92%. *Cis*/*trans*: 60/40. *ee*: 99%. Hexanes/ethyl acetate = 2/1, R_f =

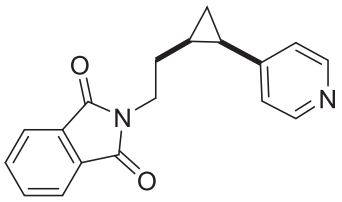
0.35. $[\alpha]^{20}_{D}$ value was not stable for some unknown reason. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 – 8.36 (m, 1H), 7.73 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.64 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.29 (td, *J* = 7.7, 1.8 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 6.94 – 6.92 (m, 1H), 3.63 – 3.55 (m, 2H), 2.17 (td, *J* = 8.5, 5.9 Hz, 1H), 1.78 – 1.72 (m, 2H), 1.30 – 1.25 (m, 1H), 1.04 (td, *J* = 8.4, 4.7 Hz, 1H), 0.82 (ddd, *J* = 8.5, 5.7, 4.5 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.12, 159.38, 148.65, 135.31, 133.56, 132.19, 123.49, 122.92, 120.30, 37.83, 25.92, 22.31, 19.31, 10.75. HPLC analysis: *ee* = 99%. IE (75% hexanes : 25% isopropanol, 1.0 mL/min) : t_{major} = 34.33 min, t_{minor} = 17.60 min. IR (neat, cm^{-1}): 3010.5, 2938.3, 1770.5, 1704.8, 1434.6, 1392.1, 1361.1, 1187.0, 1011.8, 900.5, 749.3. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{18}H_{17}N_2O_2$: 293.1285, Found: 293.1290.



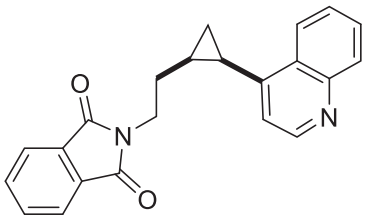
2-(3-(2-phenylcyclopropyl)propyl)isoindoline-1,3-dione 3as.

Following the general procedure with hydrazone **1a** and 3-vinyl pyridine **2s** as starting material. Yield: 73%. *Cis*/*trans*: 75/25. *ee*: 99%. Hexanes/ethyl acetate = 2/1, R_f = 0.35. $[\alpha]^{20}_{D}$ = 25.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 – 8.37 (m, 2H), 7.78 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.68 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.15 – 7.12 (m, 1H), 3.70 – 3.61 (m, 2H), 2.09 (dd, *J* = 14.7, 8.5 Hz, 1H), 1.60 – 1.54 (m, 1H), 1.29 (td, *J* = 14.4, 7.2 Hz, 1H), 1.24 – 1.17 (m, 1H), 1.11 – 1.05 (m, 1H), 0.71 (q, *J* = 5.7 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.84, 153.26, 149.81, 138.39, 136.58, 136.48, 134.68, 125.74, 125.48, 40.17, 30.20, 20.78, 19.43, 12.18. HPLC analysis: *ee* = 99%. IE (75% hexanes : 25% isopropanol, 0.8 mL/min) : t_{major} = 42.84 min, t_{minor} = 44.89 min. IR

(neat, cm^{-1}): 3002.3, 2936.9, 2359.8, 1769.8, 1702.1, 1435.0, 1390.2, 1360.9, 1175.7, 1034.7, 751.0. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{18}H_{17}N_2O_2$: 293.1285, Found: 293.1276.

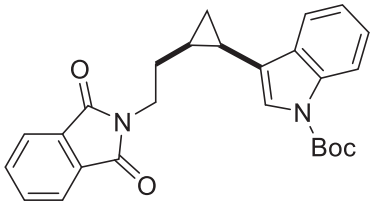


2-(2-(2-(pyridin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione 3at. Following the general procedure with hydrazone **1a** and 4-vinyl pyridine **2t** as starting material. Yield: 93%. *Cis*/*trans*: 84/16. *ee*: 99%. Hexanes/ethyl acetate = 2/1, R_f = 0.35. $[\alpha]^{20}_D$ = 29.0 (*c* = 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 2H), 7.76 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.68 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.97 (d, *J* = 4.9 Hz, 2H), 3.70 – 3.60 (m, 2H), 2.06 (dt, *J* = 8.6, 6.4 Hz, 1H), 1.57 – 1.45 (m, 2H), 1.29 – 1.23 (m, 1H), 1.09 (td, *J* = 8.4, 5.4 Hz, 1H), 0.77 (q, *J* = 5.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.15, 148.96, 148.63, 133.82, 132.00, 123.73, 123.07, 37.48, 26.81, 20.29, 18.39, 10.25. HPLC analysis: *ee* = 99%. IE (75% hexanes : 25% isopropanol, 0.8 mL/min) : t_{major} = 40.14 min, t_{minor} = 33.22 min. IR (neat, cm^{-1}): 3004.6, 2937.3, 2359.7, 1769.5, 1703.0, 1598.5, 1391.6, 1186.3, 1039.1, 898.4, 751.1. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{18}H_{17}N_2O_2$: 293.1285, Found: 293.1292.



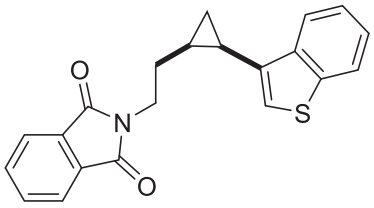
2-(2-(2-(quinolin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione 3au. Following the general procedure with hydrazone **1a** and 4-vinyl quinoline **2u** as starting material. Yield: 83%. *Cis*/*trans*: 82/18. *ee*: 99%. Hexanes/ethyl acetate = 1/1, R_f

= 0.45. $[\alpha]^{20}_{D}$ = 66.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.80 (d, *J* = 4.4 Hz, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 7.73 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.68 – 7.64 (m, 3H), 7.56 – 7.53 (m, 1H), 7.12 (d, *J* = 4.3 Hz, 1H), 3.66 – 3.57 (m, 2H), 2.56 – 2.53 (m, 1H), 1.61 – 1.49 (m, 2H), 1.25 – 1.22 (m, 1H), 0.97 – 0.90 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.19, 150.07, 147.91, 145.45, 133.79, 131.94, 129.89, 129.12, 126.44, 124.18, 123.07, 120.43, 116.48, 37.63, 27.78, 17.87, 17.10, 9.48. HPLC analysis: *ee* = 99%. IE (75% hexanes : 25% isopropanol, 1.0 mL/min) : t_{major} = 39.47 min, t_{minor} = 36.90 min. IR (neat, cm^{-1}): 3057.4, 2926.7, 2358.7, 1770.3, 1707.8, 1591.0, 1396.9, 1362.7, 1264.9, 1032.4, 792.2, 737.3. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{22}H_{19}N_2O_2$: 343.1441, Found: 343.1440.

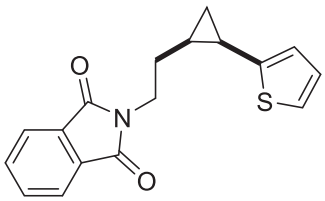


***tert*-butyl 3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl)-1H-indole-1-carboxylate 3av**. Following the general procedure with hydrazone **1a** and tert-butyl 3-vinyl-1*H*-indole-1-carboxylate **2v** as starting material. Yield: 84%. *Cis*/*trans*: 83/17. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.25. $[\alpha]^{20}_{D}$ value was not stable for some unknow reason. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.73 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.66 – 7.63 (m, 3H), 7.23 – 7.16 (m, 3H), 3.70 – 3.60 (m, 2H), 2.05 – 2.00 (m, 1H), 1.67 (s, 9H), 1.34 – 1.18 (m, 3H), 1.07 (td, *J* = 8.2, 4.9 Hz, 1H), 0.59 (dd, *J* = 10.7, 5.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.29, 149.70, 133.68, 132.01, 131.54, 124.32, 123.19, 122.95, 122.37, 121.02, 119.39, 119.31, 115.06, 83.35, 37.92, 28.22, 27.75, 15.57, 10.87, 9.66. HPLC analysis: *ee* = 99%. IF (90% hexanes : 10%

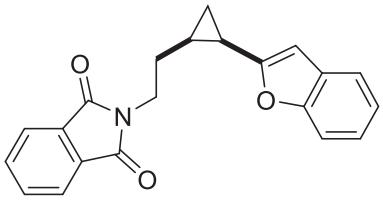
isopropanol, 0.8 mL/min) : t_{major} = 34.41 min, t_{minor} = 20.41 min. IR (neat, cm^{-1}): 2978.2, 2933.2, 1771.0, 1705.9, 1450.3, 1367.3, 1253.0, 1367.3, 1253.0, 1154.1, 1082.2, 1021.3, 856.4, 716.4. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{26}H_{27}N_2O_4$: 431.1965, Found 431.1978.



2-(2-(2-(benzo[*b*]thiophen-3-yl)cyclopropyl)ethyl) isoindoline-1,3-dione 3aw. Following the general procedure with hydrazone **1a** and 3-vinylbenzo[*b*]thiophene **2w** as starting material. Yield: 94%. *Cis*/*trans*: 78/22. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.30. $[\alpha]^{20}{}_D$ = 141.2 (*c* = 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.9 Hz, 1H), 7.79 – 7.77 (m, 1H), 7.73 (dd, *J* = 5.3, 3.2 Hz, 2H), 7.63 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.35 – 7.27 (m, 2H), 6.96 (s, 1H), 3.68 – 3.57 (m, 2H), 2.20 (dd, *J* = 14.8, 8.0 Hz, 1H), 1.69 – 1.62 (m, 1H), 1.32 – 1.26 (m, 1H), 1.24 – 1.17 (m, 1H), 1.13 (td, *J* = 8.3, 4.9 Hz, 1H), 0.72 (q, *J* = 5.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.24, 140.35, 139.95, 137.70, 133.67, 132.00, 124.27, 123.88, 122.97, 122.65, 122.08, 122.00, 37.86, 27.58, 15.90, 14.44, 9.66. HPLC analysis: *ee* = 99%. ID (95% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 31.98 min, t_{minor} = 33.42 min. IR (neat, cm^{-1}): 3061.3, 2934.5, 1769.7, 1704.2, 1431.8, 1392.7, 1359.7, 1174.6, 1080.1, 1030.9, 896.7, 763.0, 717.6. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{21}H_{18}NO_2S$: 348.1053, Found 348.1040.



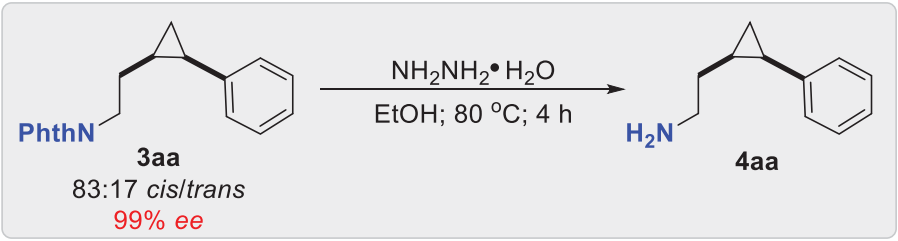
2-(2-(2-(thiophen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione 3ax. Following the general procedure with hydrazone **1a** and 3-vinylthiophene **2x** as starting material. Yield: 93%. *Cis*/*trans*: 82/18. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.50. $[\alpha]^{20}{}_D$ = 61.1 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, cdcl$_3$) δ 7.79 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.67 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.02 (dd, *J* = 5.2, 1.1 Hz, 1H), 6.82 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.68 – 6.67 (m, 1H), 3.78 – 3.63 (m, 2H), 2.21 – 2.17 (m, 1H), 1.74 – 1.67 (m, 1H), 1.44 – 1.38 (m, 1H), 1.15 – 1.10 (m, 2H), 0.66 – 0.61 (m, 1H). ^{13}C NMR (150 MHz, cdcl$_3$) δ 168.27, 143.23, 133.72, 132.17, 126.61, 125.09, 123.13, 123.05, 37.62, 27.64, 17.41, 15.46, 12.46. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 22.80 min, t_{minor} = 20.50 min. IR (neat, cm^{-1}): 2998.7, 2920.0, 1772.1, 1702.4, 1397.3, 1364.5, 1341.3, 1177.8, 1086.4, 1041.2, 1024.8, 852.7, 717.6. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{17}H_{16}NO_2S$: 298.0896, Found 298.0898.



2-(2-(2-(benzofuran-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione 3ay. Following the general procedure with hydrazone **1a** and 2-vinylbenzofuran **2y** as starting material. Yield: 82%, *Cis*/*trans*: 84/16. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.35. $[\alpha]^{20}{}_D$ = 1.2 (*c* = 1.0, $CHCl_3$).^{1}H NMR (500 MHz, cdcl$_3$) δ 7.68 – 7.65 (m, 2H), 7.63 – 7.60 (m, 2H), 7.30 – 7.28 (m, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 7.14 – 7.06 (m, 2H), 6.21 (s, 1H), 3.74 (t, *J* = 6.6 Hz, 2H), 2.11 (td, *J* = 8.5, 6.1 Hz, 1H), 1.85 – 1.79 (m, 1H),

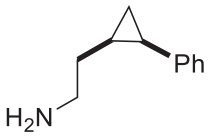
1.74 – 1.68 (m, 1H), 1.34 – 1.28 (m, 1H), 1.17 (dt, J = 8.5, 4.3 Hz, 1H), 0.83 – 0.79 (m, 1H). ^{13}C NMR (125 MHz, cdcl$_3$) δ 168.23, 157.55, 154.42, 133.58, 132.02, 128.62, 122.96, 122.85, 122.29, 119.88, 110.59, 103.04, 37.72, 27.64, 18.09, 14.29, 10.90. HPLC analysis: *ee* = 99%. IE (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 27.76 min, t_{minor} = 23.07 min. IR (neat, cm^{-1}): 2935.3, 2856.0, 1770.1, 1706.7, 1600.0, 1454.6, 1392.7, 1363.2, 1254.9, 1185.4, 1036.5, 954.5, 794.2, 751.2. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{21}H_{18}NO_3$: 332.1281, Found 332.1282.

3.4.4 Deprotection of Phthalimide Unit in Cyclopropane 3aa

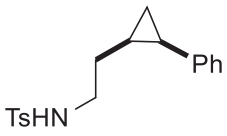


To a 10 mL round-bottom flask, optically active cyclopropane **3aa** (0.5 mmol) was dissolved in ethanol (2 mL), then 3.0 equivalent of hydrazine monohydrate (1.5 mmol) was added. The resulting mixture was heat at 80 °C for 4 hrs with the disappearance of starting material from TLC. During the reaction, white solid was precipitated. The reaction mixture was then filtrated and the residue was washed with ethanol (2 x 2 mL). The filtrate was then concentrated and purified by flash chromatography. The fractions containing product

4aa were collected and concentrated by rotary evaporation to afford the compound as a mixture of *trans*/*cis* diastereomers.

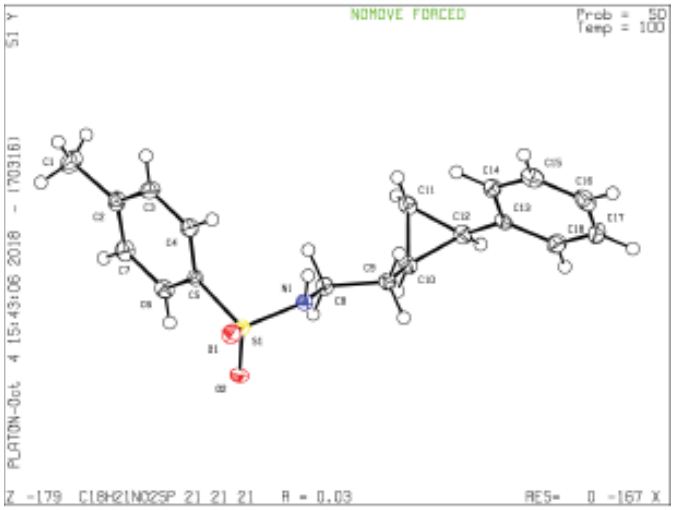


2-(2-phenylcyclopropyl)ethan-1-amine 4aa. Yield: 99%. *Cis*/*trans*: 83/17. *ee*: 99%. DCM/MeOH = 4/1, R_f = 0.20. $[\alpha]^{20}{}_D$ = 22.2 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.23 (m, 2H), 7.19 – 7.14 (m, 3H), 2.69 – 2.60 (m, 2H), 2.14 (dt, *J* = 14.5, 7.3 Hz, 1H), 1.56 – 1.52 (m, 3H), 1.33 – 1.28 (m, 1H), 1.07 – 0.98 (m, 2H), 0.70 (dd, *J* = 10.9, 5.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.29, 128.94, 127.88, 125.67, 42.03, 32.60, 20.54, 16.66, 9.35. IR (neat, cm^{-1}): 3061.3, 1924.3, 2359.4, 1496.4, 1312.0, 1027.3, 768.3, 726.2. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{11}H_{16}N$: 162.1277, Found 162.1274.



4-methyl-*N*-(2-(2-phenylcyclopropyl)ethyl)benzenesulfonamide 4aa'. In 10 mL tube, Et_3N (1.5 equiv.) was added into the solution of **4aa** (0.1 mmol) in DCM (0.6 mL). followed by tosyl chloride (0.15 mmol, 1.5 equiv.). The reaction was monitored by TLC. Upon the completion, the solution was concentrated and purified by flash chromatography to deliver the desired compound **4aa'**. Yield: 92%. *Cis*/*trans*: 83/17. *ee*: 99%. Hexanes/ethyl acetate = 4/1, R_f = 0.30. $[\alpha]^{20}{}_D$ = 13.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.29 – 7.22 (m, 5H), 7.09 (d, *J* = 7.3 Hz, 2H), 4.26 (t, *J* = 5.9 Hz, 1H), 2.88 (dd, *J* = 13.2, 6.8 Hz, 1H), 2.43 (s, 3H), 2.12 (td, *J* = 8.6, 6.3 Hz, 1H), 1.59 – 1.54 (m, 1H), 1.30 – 1.23 (m, 1H), 1.15 – 1.09 (m, 1H), 1.01 – 0.93 (m, 1H), 0.66 – 0.63 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.20, 138.50, 136.96,

129.59, 128.78, 128.06, 127.04, 125.94, 43.00, 28.48, 21.50, 20.53, 16.18, 9.18. HPLC analysis: *ee* = 99%. OJH (90% hexanes : 10% isopropanol, 0.8 mL/min) : t_{major} = 42.16 min, t_{minor} = 39.78 min. IR (neat, cm^{-1}): 3271.6, 3004.6, 2918.2, 2359.7, 1597.3, 1320.5, 1160.4, 1090.5, 812.1, 764.6, 701.4. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{18}H_{22}NO_2S$: 316.1366, Found 316.1368.



3.4.5 Procedure for HRMS Experiment

To an over-dried Schlenk tube, hydrazone **1a** (0.05 mmol) and Cs_2CO_3 (1.5 equiv.) were added. The Schlenk tube was then evacuated and backfilled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, CH_3CN (0.5 mL) was added via a gas-tight syringe. The mixture was then stirred at 40 °C for 0.5 h. The resulting light yellow solution was then passed through a short pad of Celite (to get rid of base and salt) under the flow of nitrogen and the filtrate was collected in a HPLC vial (vial A, degassed and backfilled with argon). During the time, [Co(**P1**)] (2 mol %) was charged into another HPLC vial (vial B, degassed and backfilled with argon) and dissolved in CH_3CN (0.5 mL). After mixing equal amount of solutions from vial A (0.1 mL) and vial B (0.1 mL), the

sample was further diluted with CH_3CN and immediately injected into HRMS instrument. The HRMS experiment was carried out in the absence of any additives such as formic acid, commonly act as electron carriers for ionization, allowing the detection of the molecular ion signals corresponding to Co(III)-alkyl radical ($C_{87}H_{97}CoN_9O_6$·) by the loss of one electron.

3.4.6 Procedure for EPR Experiment

To an oven-dried Schlenk tube A, sulfonylhydrazone **1a** (0.05 mmol), and Cs_2CO_3 (1.5 equiv.) were added. The Schlenk tube was then evacuated and backfilled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, benzene (0.5 mL) was added via a gas-tight syringe. The mixture was then stirred at 40 ^oC for 0.5 h. During the time, [Co(**P1**)] (2 mol %) was charged into another oven-dried Schlenk tube B. The Schlenk tube B was then evacuated and backfilled with nitrogen for 3 times. After 0.5 h, the resulting light yellow solution from tube A was passed through a short pad of Celite (to get rid of base and salt) under the flow of nitrogen and transferred to Schlenk tube B. The mixture was stirred for 1 min, followed by the addition of phenyl *N*-*tert*-butylnitrone (PBN, 0.05 mmol). The reaction mixture was stirred for 2 min and transferred into a degassed EPR tube (filled with argon) through a gas tight syringe. The sample was then carried out for EPR experiment at room temperature (EPR settings: T = 298 K; microwave frequency: 9.37762 GHz; power: 20 mW; modulation amplitude: 1.0 G).

3.5 REFERENCES

(1) (a) Sibi, M. P.; Manyem, S.; Zimmerman, J. *Chem. Rev.* **2003**, *103*, 3263; (b) Brimioulle, R.; Lenhart, D.; Maturi, M. M.; Bach, T. *Angew. Chem., Int. Ed.* **2015**, *54*, 3872; (c) Blum, T. R.; Miller, Z. D.; Bates, D. M.; Guzei, I. A.; Yoon, T. P. *Science* **2016**, *354*, 1391; (d) Kainz, Q. M.; Matier, C. D.; Bartoszewicz, A.; Zultanski, S. L.; Peters, J. C.; Fu, G. C. *Science* **2016**, *351*, 681; (e) Lin, J.-S.; Dong, X.-Y.; Li, T.-T.; Jiang, N.-C.; Tan, B.; Liu, X.-Y. *J. Am. Chem. Soc.* **2016**, *138*, 9357; (f) Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Rose, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100.

(2) For reviews and highlights on Co(II)-MRC, see: (a) Miyabe, H.; Kawashima, A.; Yoshioka, E.; Kohtani, S. *Chem. Eur. J.* **2017**, *23*, 6225; (b) Studer, A.; Curran, D. P. *Angew. Chem., Int. Ed.* **2016**, *55*, 58; (c) Pellissier, H.; Clavier, H. *Chem. Rev.* **2014**, *114*, 2775; (d) Lu, H. J.; Zhang, X. P. *Chem. Soc. Rev.* **2011**, *40*, 1899; (e) Doyle, M. P. *Angew. Chem., Int. Ed.* **2009**, *48*, 850.

(3) For select examples on Ti(III)-MRC, see: (a) Zhang, Y.-Q.; Vogelsang, E.; Qu, Z.-W.; Grimme, S.; Gansäuer, A. *Angew. Chem., Int. Ed.* **2017**, *56*, 12654; (b) Hao, W.; Wu, X.; Sun, J. Z.; Siu, J. C.; MacMillan, S. N.; Lin, S. *J. Am. Chem. Soc.* **2017**, *139*, 12141; (c) Gansäuer, A.; Hildebrandt, S.; Vogelsang, E.; Flowers II, R. A. *Dalton Trans.* **2016**, *45*, 448; (d) Gansäuer, A.; Fleckhaus, A.; Lafont, M. A.; Okkel, A.; Kotsis, K.; Anoop, A.; Neese, F. *J. Am. Chem. Soc.* **2009**, *131*, 16989.

(4) For detailed experimental and theoretical studies on the radical mechanism of Co(II)-MRC: (a) Lu, H. J.; Dzik, W. I.; Xu, X.; Wojtas, L.; de Bruin, B.; Zhang, X. P. *J. Am. Chem.*

Soc. **2011**, *133*, 8518; (b) Belof, J. L.; Cioce, C. R.; Xu, X.; Zhang, X. P.; Space, B.; Woodcock, H. L. *Organometallics* **2011**, *30*, 2739; (c) Dzik, W. I.; Xu, X.; Zhang, X. P.; Reek, J. N. H.; de Bruin, B. *J. Am. Chem. Soc.* **2010**, *132*, 10891.

(5) For select examples on asymmetric Co(II)-MRC, see: (a) Wang, Y.; Wen, X.; Cui, X.; Zhang, X. P. *J. Am. Chem. Soc.* **2018**, *140*, 4792; (b) Wen, X.; Wang, Y.; Zhang, X. P. *Chem. Sci.* **2018**, *9*, 5082; (c) Wang, Y.; Wen, X.; Cui, X.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2017**, *139*, 1049; (d) Cui, X.; Xu, X.; Jin, L.-M.; Wojtas, L.; Zhang, X. P. *Chem. Sci.* **2015**, *6*, 1219 (e) Xu, X.; Lu, H. J.; Ruppel, J. V.; Cui, X.; de Mesa, S. L.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 15292; (f) Cui, X.; Xu, X.; Lu, H. J.; Zhu, S. F.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 3304; (g) Zhu, S. F.; Ruppel, J. V.; Lu, H. J.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2008**, *130*, 5042; (h) Fantauzzi, S.; Gallo, E.; Rose, E.; Raoul, N.; Caselli, A.; Issa, S.; Ragaini, F.; Cenini, S. *Organometallics* **2008**, *27*, 6143; (i) Chen, Y.; Fields, K. B.; Zhang, X. P. *J. Am. Chem. Soc.* **2004**, *126*, 14718; For select examples on nonasymmetric Co(II)-MRC, see:(j) Roy, S.; Das, S. K.; Chattopadhyay, B. *Angew. Chem., Int. Ed.* **2018**, *57*, 2238; (k) te Grotenhuis, C.; van den Heuvel, N.; van der Vlugt, J. I.; de Bruin, B. *Angew. Chem., Int. Ed.* **2018**, *57*, 140; (l) Reddy, A. R.; Hao, F.; Wu, K.; Zhou, C.-Y.; Che, C. M. *Angew. Chem., Int. Ed.* **2016**, *55*, 1810; (m) Zhang, J.; Jiang, J.; Xu, D.; Luo, Q.; Wang, H.; Chen, J.; Li, H.; Wang, Y.; Wan, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 1231.

(6) For select examples on *cis*-selective cyclopropanation reactions, see: (a) Piou, T.; Romanov-Michailidis, F.; Ashley, M. A.; Romanova-Michaelides, M.; Rovis, T. *J. Am. Chem. Soc.* **2018**, *140*, 9587; (b) Brandenberg, O. F.; Prier, C. K.; Chen, K.; Knight, A. M.; Wu, Z.; Arnold, F. H. *ACS Catal.* **2018**, *8*, 2629; (c) Rosenberg, M. L.; Krivokapic, A.;

Tilset, M. *Org. Lett.* **2009**, *11*, 547; (d) Suematsu, H.; Kanchiku, S.; Uchida, T.; Katsuki, T. *J. Am. Chem. Soc.* **2008**, *130*, 10327; (e) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002; (f) Hu, W.; Timmons, D. J.; Doyle, M. P. *Org. Lett.* **2002**, *4*, 901; (g) Bachmann, S.; Furler, M.; Mezzetti, A. *Organometallics* **2001**, *20*, 2102.

(7) (a) Ebner, C.; Carreira, E. M. *Chem. Rev.* **2017**, *117*, 11651; (b) Chen, D. Y. K.; Pouwer, R. H.; Richard, J.-A. *Chem. Soc. Rev.* **2012**, *41*, 4631.

(8) (a) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256; (b) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323.

(9) For select reviews on asymmeric Simmons-Smith cyclopropanation reactions, see: (a) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. *Synthesis* **2014**, *46*, 979; (b) Pellissier, H. *Tetrahedron* **2008**, *64*, 7041; (c) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977.

(10) For select reviews on metal-catalyzed asymmeric olefin cyclopropanation with diazo compounds, see: (a) Intrieri, D.; Carminati, D. M.; Gallo, E. *Dalton Trans.* **2016**, *45*, 15746; (b) Intrieri, D.; Caselli, A.; Gallo, E. *Eur. J. Inorg. Chem.* **2011**, 5071; (c) Davies, H. M. L.; Antoulinakis, E. G. *Org. React.* **2001**, *57*, 1; (d) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911.

(11) For select examples on non-asymmetric olefin cyclopropanation with aliphatic diazo compounds, see: (a) Goulioukina, N. S.; Makukhin, N. N.; Beletskaya, I. P. *Tetrahedron* **2011**, *67*, 9535; (b) Berthon-Gelloz, G.; Marchant, M.; Straub, B. F.; Marko, I. E. *Chem. Eur. J.* **2009**, *15*, 2923; (c) Markó, I. E.; Kumamoto, T.; Giard, T. *Adv. Synth. Catal.* **2002**, *344*, 1063; (d) Cativiela, C.; D. Díaz-de-Villegas, M.; I. Jiménez, A. *Tetrahedron* **1994**, *50*,

9157; (e) Zhu, Y. F.; Yamazaki, T.; Tsang, J. W.; Lok, S.; Goodman, M. *J. Org. Chem.* **1992**, *57*, 1074; (f) Schneider, M.; Rau, A. *Angew. Chem.* **1979**, *91*, 239.

(12) For asymmetric olefin cyclopropanation with in situ-generated trifluoromethyl diazomethane, see: (a) Morandi, B.; Carreira, E. M. *Science* **2012**, *335*, 1471; (b) Morandi, B.; Mariampillai, B.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 1101.

(13) Chen, Y.; Zhang, X. P. *Synthesis* **2006**, 1697.

(14) Das, B. G.; Chirila, A.; Tromp, M.; Reek, J. N. H.; Bruin, B. d. *J. Am. Chem. Soc.* **2016**, *138*, 8968.

CHAPTER 4

ENANTIOSELECTIVE RADICAL CYCLIZATION FOR CONSTRUCTION OF 5-MEMBERED RING STRUCTURES BY METALLORADICAL C–H ALKYLATION

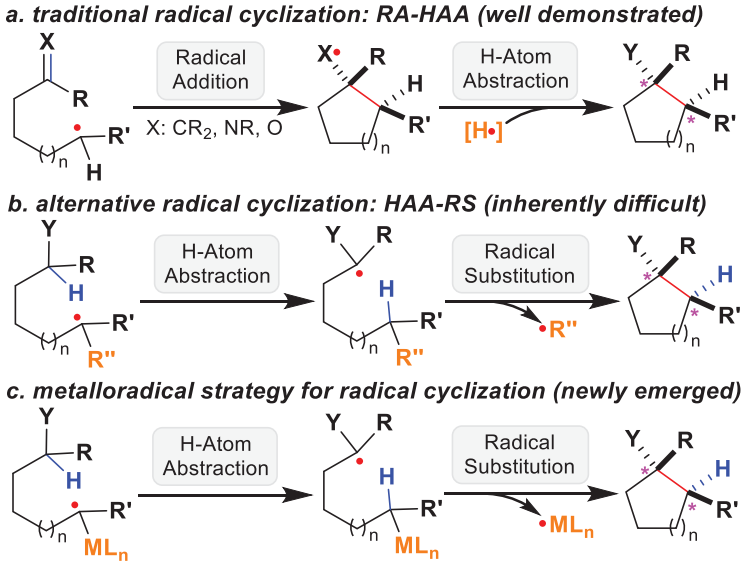
4.1 INTRODUCTION

Carbon-centered radicals, specifically alkyl radicals, have been extensively explored as versatile intermediates for chemical synthesis because of their potent reactivity and diverse pathway.[1] Among important synthetic applications, alkyl radicals have been well demonstrated to undergo radical cyclization for construction of various ring structures via C–C bond formation.[1] While numerous radical cyclization reactions have been elegantly implemented with alkyl radicals,[2] they are predominantly based on the utilization of radical addition as the key cyclization step, followed by further radical transformations such as H-atom abstraction to deliver cyclic products (Scheme 4.1a). Consequently, traditional radical cyclization reactions necessarily involve the use of substrates containing unsaturated bonds, such as alkenes, imines, and carbonyls.

In addition to the well-established cyclization sequence of radical addition and H-atom abstraction (RA-HAA) for unsaturated substrates, it is conceivable that the combination of H-atom abstraction and radical substitution (HAA-RS) could give rise to an alternative C–C bond forming pathway for radical cyclization that could employ saturated C–H substrates (Scheme 4.1b). While intramolecular H-atom abstraction is normally facile, the subsequent key cyclization step of intramolecular radical substitution

at the carbon center has been recognized as an inherently challenging pathway due to the requirement of a highly organized linear transition state involving three multi-substituted sp^3-carbon centers.[1a,3] For this reason, this alternative radical cyclization, although seemingly tenable, is largely undocumented for typical alkyl radicals.

Scheme 4.1|| Different Radical Cyclization Pathways for the Formation of Ring Structures via C–C Bond Formation

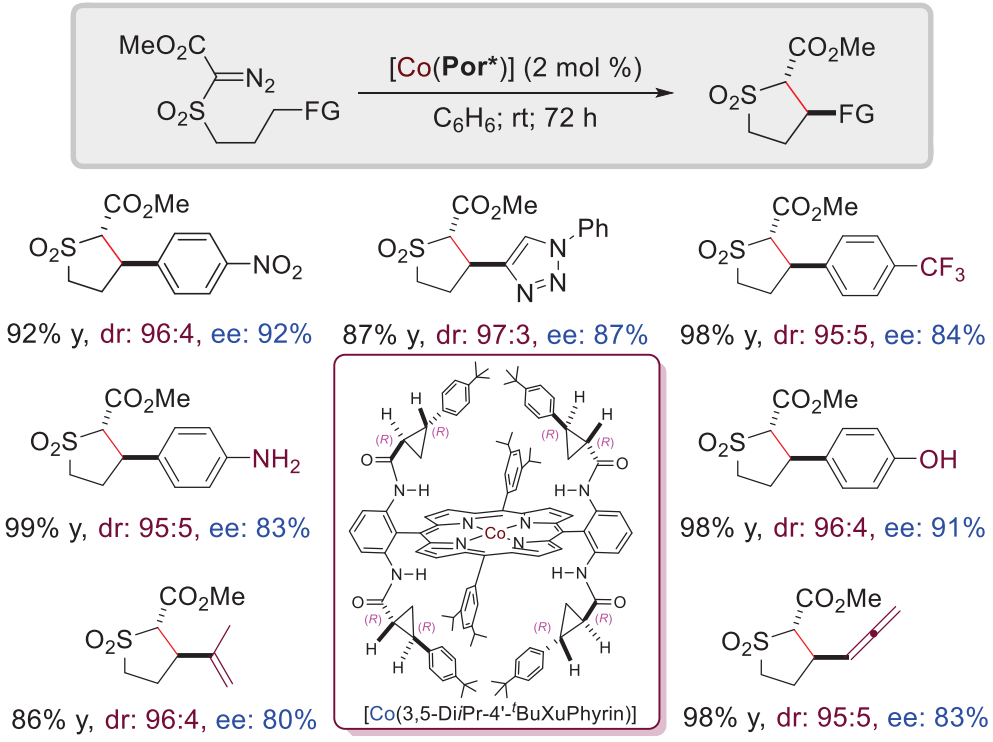


One potential solution to address the problem would be the introduction of *α*-metalloalkyl radicals $R_2(L_nM)C•$, where one of the substituents of common alkyl radicals is replaced by a metal complex unit (ML_n) (Scheme 4.1c). Since M–C bonds are typically more polar and weaker than C–C bonds, the radical substitution pathway would become both thermodynamically possible and kinetically feasible, especially with stable metalloradicals $L_nM•$ as outgoing radicals.[4] Furthermore, this metalloradical-based new mode of radical cyclization could be potentially rendered as a catalytic process while

offering the possibility of controlling enantioselectivity, allowing for stereoselective construction of cyclic compounds from linear C–H substrates.

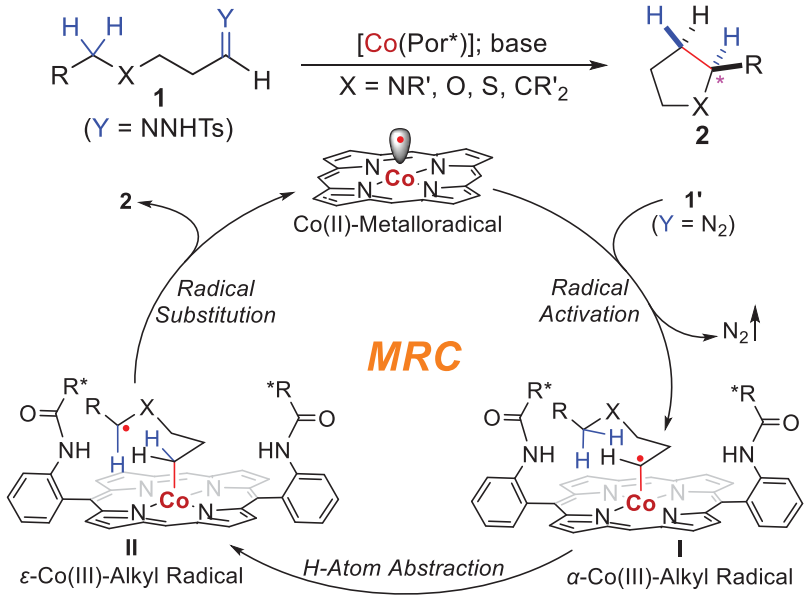
To harness the vast potential of homolytic radical reactions for stereoselective organic synthesis,[5] metalloradical catalysis (MRC) has recently been introduced as a conceptually new approach for addressing some enduring challenges in the field.[6,7] MRC aims at the development of metalloradical complexes as open-shell catalysts for generation of metal-supported organic radicals as key intermediates and for control of their subsequent homolytic reactions.

Scheme 4.2|| Asymmetric C–H Alkylation with Acceptor/Acceptor-Type Diazo Compounds via Co(II)-Based MRC



As stable metalloradicals, Co(II) complexes of D_2-symmetric chiral amidoporphyrins [Co(D_2-Por*)] exhibit the unusual capability of activating diazo compounds to generate α-Co(III)-alkyl radicals.[8] The α-metalloalkyl radicals can undergo radical addition and H-atom abstraction as well as subsequent radical substitution, leading to the invention of new catalytic systems for various stereoselective radical transformations.[9] Among them, we recently illustrated the aforementioned radical cyclization strategy with stereoselective formation of sulfolanes from α-methoxycarbonyl-α-diazosulfones (Scheme 4.2).[9b] To demonstrate the generality of this new mode of radical cyclization and broaden its synthetic utility, we were intrigued if Co(II)-based MRC could be applied for the asymmetric synthesis of more common ring structures, such as pyrrolidines, tetrahydrofurans, and other important 5-membered cyclic compounds, from linear aliphatic diazo compounds (Scheme 4.3), which are typically generated in situ from sulfonyl hydrazones of the corresponding carbonyl precursors due to their instability.

Scheme 4.3|| Proposed Radical Cyclization Mechanism via Metalloradical C–H Alkylation



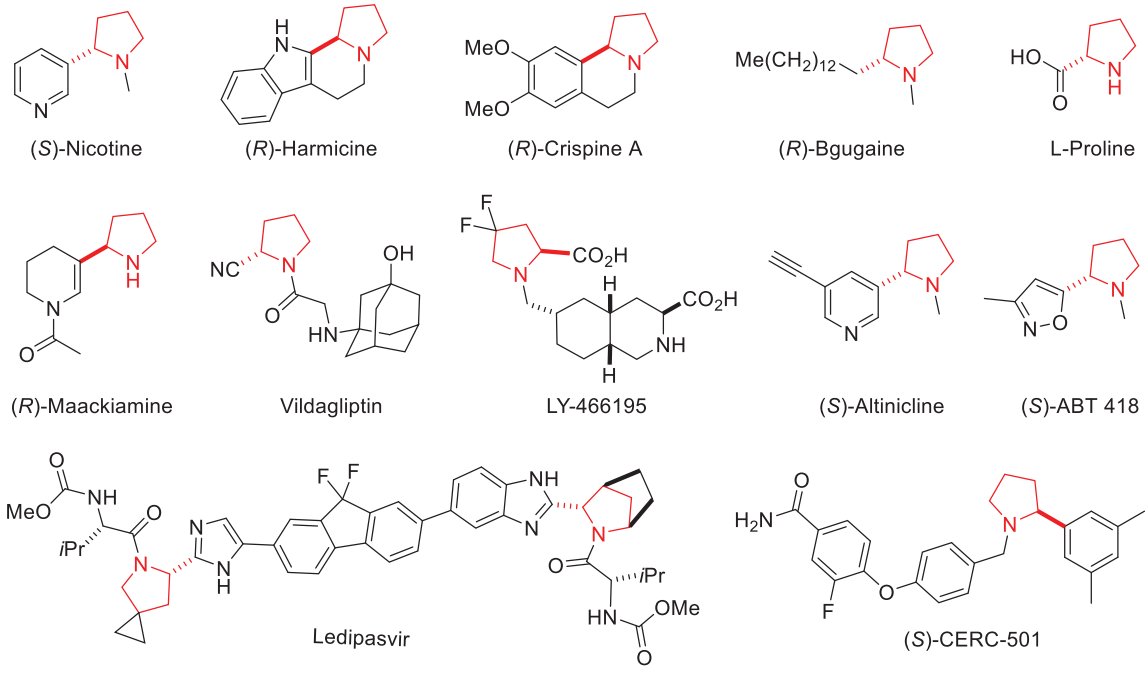
Mechanistically, it was unclear if aliphatic diazo compounds could be activated by metalloradical [Co(D_2-Por*)] to form the corresponding α-Co(III)-alkyl radicals **I** (Scheme 4.3). If so, could the rate of metalloradical activation of aliphatic diazo compounds be effectively matched with their in situ-generation to avoid unwanted thermal decomposition? Furthermore, it was uncertain whether α-Co(III)-alkyl radicals **I**, which possess accessible β-H atoms, could proceed subsequent 1,5-H atom abstraction for generation of ε-Co(III)-alkyl radicals **II** competitively over the potential β-H-atom shift, which would lead to olefin side products. Additional questions arose from the flexible nature of the linear alkyl chain that could pose extra challenges in achieving the intramolecular radical substitution of ε-Co(III)-alkyl radicals **II** for stereoselective construction of the 5-membered structures. Without conformational rigidity, would the intermediate **II** be capable of undergoing effective 5-*exo*-*tet* radical cyclization? What determinant factors could be explored for controlling the enantioselectivity of C–C bond forming process? We reasoned that the key to address these and related challenges is to develop suitable D_2-symmetric chiral amidoporphyrin ligands that direct the Co(II)-based catalysis for productive cyclization. If realized, it would provide a general catalytic strategy for stereoselective radical synthesis of five-membered cyclic molecules from aliphatic aldehyde-derived tosylhydrazones.

(Eq. 4.1)

This new mode of radical cyclization based on metalloradical C–H alkylation would offer a new retrosynthetic paradigm for construction of ring structures where C–C bond can be disconnected as common C=O and C–H units of linear aldehydes (Equation 4.1).

Chiral pyrrolidines containing *α*-substituent are recurring core structures in a wide range of natural products and bioactive compounds (Scheme 4.4). Accordingly, considerable efforts have been devoted to devise effective strategies for their asymmetric synthesis. While most of the existing catalytic systems involve C–H functionalization of preformed pyrrolidine ring structures,[10] there has been no previous report on asymmetric construction of *α*-substituted chiral pyrrolidines via catalytic C–H alkylation with acyclic aliphatic diazo compounds.[11]

Scheme 4.4|| Selected Biologically Active Compounds Containing *α*-Substituted Pyrrolidine Moiety



As a demonstration of the aforementioned mode of radical cyclization (HAA-RS) for construction of common 5-membered ring structures, we have demonstrated a new Co(II)-based catalytic system that is highly efficient for stereoselective synthesis of α-substituted pyrrolidines. Supported by a new D_2-symmetric chiral amidoporphyrin, the Co(II) metalloradical catalyst is able to activate aliphatic diazo compounds for enantioselective intramolecular radical alkylation of a broad range of C(sp^3)–H bonds, constructing α-substituted chiral pyrrolidines in high yields with excellent enantioselectivities. In addition to chemoselective alkylation of allylic and propargylic C–H bonds and regioselective 1,5-alkylation, the new catalytic radical cyclization is highlighted by its tolerance of various functionalities, including compatibility with a variety of heteroaryl groups.

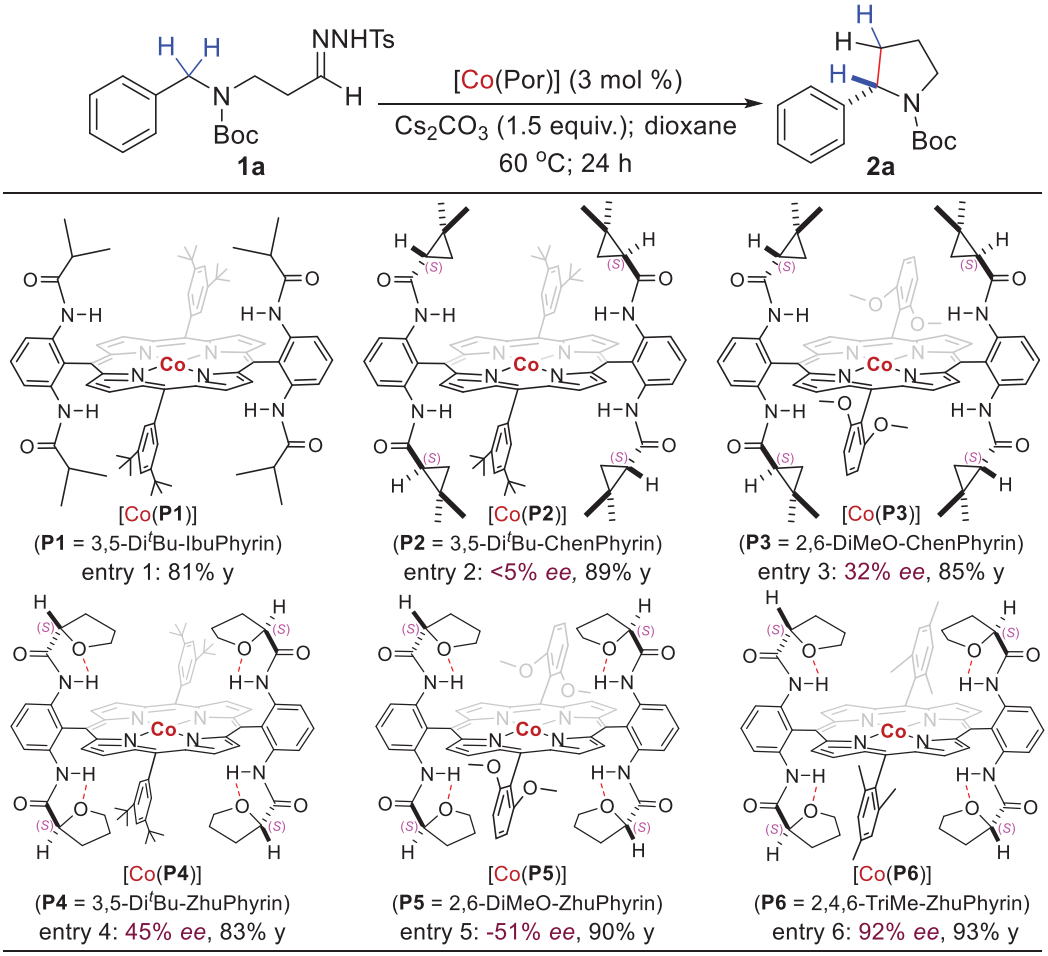
4.2 RESULTS AND DISCUSSIONS

4.2.1 Condition Optimization for Enantioselective Radical Cyclization of Aliphatic Diazo Precursor

At the outset of our effort, we chose aliphatic aldehyde-derived tosylhydrazone **1a** as the model substrate for proof-of-concept experiments to test the proposed radical cyclization via Co(II)-MRC (Table 4.1). Using the Co(II) complex of achiral amidoporphyrin 3,5-Di^{t}Bu-IbuPhyrin [Co(**P1**)][12] as the metalloradical catalyst, we were gratified to observe that the catalytic reaction could afford 2-phenylpyrrolidine (**2a**) in 81% yield (entry 1), demonstrating the feasibility of the HAA-RS pathway for productive radical

cyclization without complication from competitive olefin formation. The high yield of the radical cyclization also indicated that the aliphatic diazo compound generated in situ could be effectively incorporated into the catalytic cycle without accumulation to cause side reactions.

Table 4.1|| Ligand Effect on Co(II)-Catalyzed Enantioselective Radical Cyclization of Aliphatic Diazo Precursor[a]



[a] Reactions were carried out with **1a** (0.1 mmol) in the presence of Cs_2CO_3 (1.5 equiv.) by [Co(Por)] (3 mol %) in dioxane (0.6 mL) at 60 °C for 24 h; Yields refer to isolated yields

of purified products; Enantiomeric excess (*ee*) was determined by chiral HPLC analysis. Ts: 4-toluenesulfonyl; Boc: *tert*-butyloxycarbonyl.

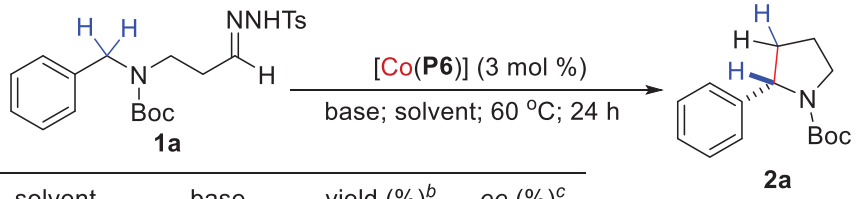
When the first-generation chiral metalloradical catalyst [Co(**P2**)] (**P2** = 3,5-Di^{t}Bu-ChenPhyrin) was employed,[9g] which has been shown to be effective for asymmetric radical cyclopropanation, it was found that the catalytic radical cyclization exhibited almost no asymmetric induction despite the high-yielding formation of desired **2a** (Table 4.1, entry 2). Considering the flexible nature of the linear alkyl chain, we were disappointed but not completely surprised by this negative result.

Without the hydrogen-bonding interaction at disposal to rigidify the Co(III)-alkyl radical intermediates, we decided to crowd the steric environment of the ligand pocket. Indeed, the employment of [Co(**P3**)] (**P3** = 2,6-DiMeO-ChenPhyrin) bearing more sterically hindered achiral *meso*-aryl groups resulted in observation of significant asymmetric induction without affecting the reactivity (entry 3).

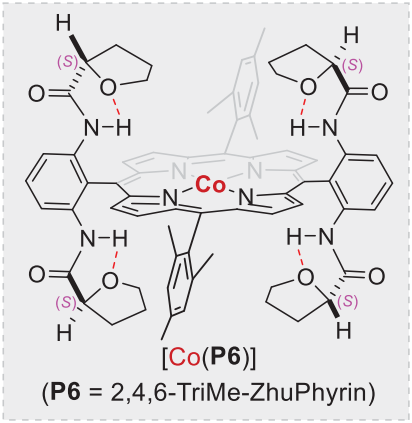
To further augment this positive buttressing effect, we then turned our attention to D_2-symmetric chiral amidoporphyrin 3,5-Di^{t}Bu-ZhuPhyrin (**P4**), which was previously shown to have a more rigid conformation and polar chiral environment because of the intramolecular O···H–N hydrogen-bonding interactions in the (*S*)-(-)-2-tetrahydrofurancarboxamide units,[9e] As expected, [Co(**P4**)] could catalyze the radical cyclization reaction to form **2a** in similarly high yield with substantially improved enantioselectivity (entry 4). Subsequent use of [Co(**P5**)] (**P5** = 2,6-DiMeO-ZhuPhyrin) as the catalyst resulted in further increase in both yield and enantioselectivity (entry 5).

Encouraged by the positive direction of ligand buttressing effect, we synthesized 2,4,6-TriMe-ZhuPhyrin ligand (**P6**), a new derivative of ZhuPhyrin series, where even more sterically demanding mesityl groups are attached at the two achiral *meso*-positions. We were exhilarated to find that [Co(**P6**)] could effectively catalyze the enantioselective radical C–H alkylation reaction, affording the desired cyclization product **2a** in 93% yield with 92% *ee* (entry 6). Also, the detailed study of solvent and base effects disclosed that dioxane and cesium carbonate are the optimal choice, respectively (Table 4.2).

Table 4.2|| Solvent and Base Effects on Co(II)-Catalyzed Enantioselective Radical Cyclization of Aliphatic Diazo Precursor 1a[a]



entry	solvent	base	yield (%)[b]	*ee* (%)[c]
1	Dioxane	Cs_2CO_3	95 (93)[d]	92
2	THF	Cs_2CO_3	71	92
3	CH_3CN	Cs_2CO_3	65	92
4	DCM	Cs_2CO_3	<10	92
5	PhMe	Cs_2CO_3	31	92
6	Dioxane	K_2CO_3	38	91
7	Dioxane	KO^tBu	27	89
8	Dioxane	DBU	47	93
9	Dioxane	—	n/d	n/a



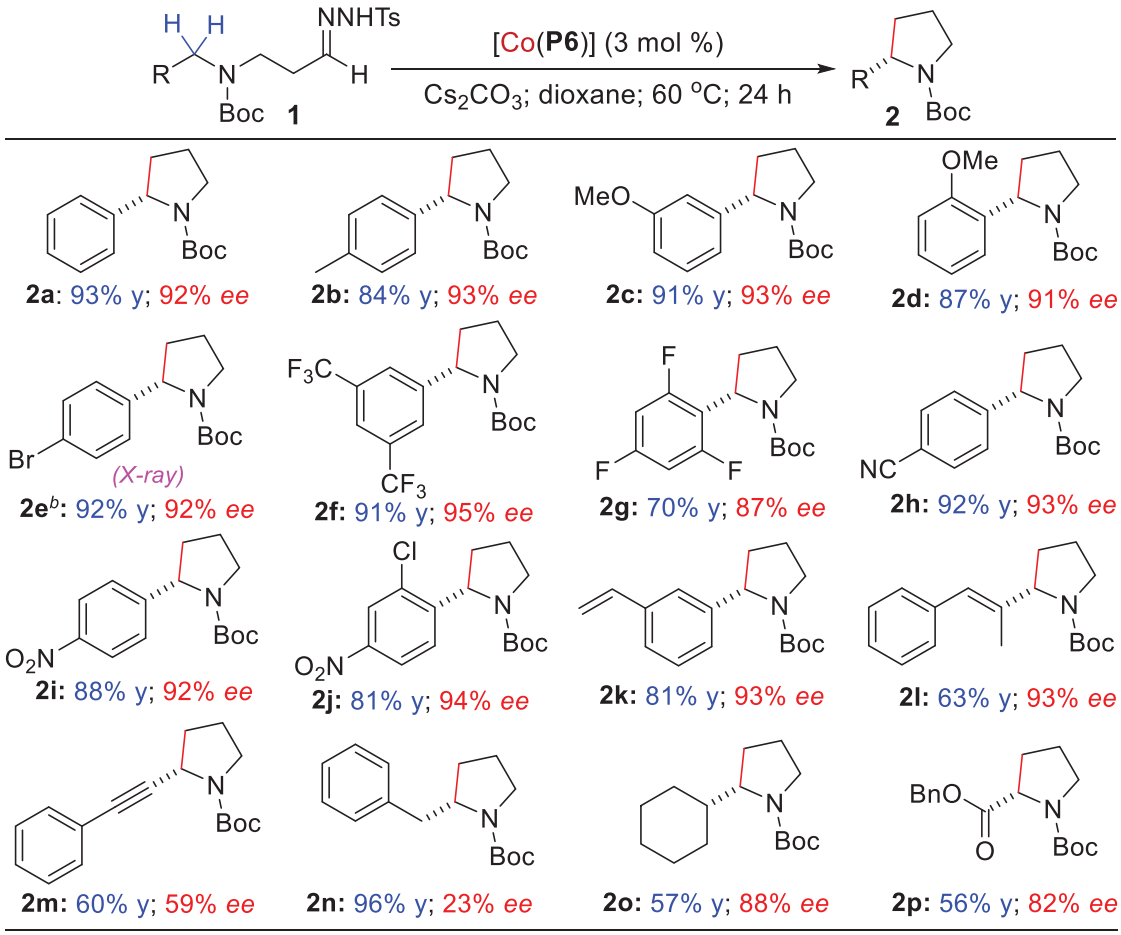
[a] Carried out with **1a** (0.1 mmol) in the presence of base (1.5 equiv.) by [Co(**P6**)] (3 mol %) in solvent (0.6 mL) at 60 °C for 24 h. [b] NMR yields with $(CHCl_2)_2$ as internal standard. [c] *ee* was determined by chiral HPLC analysis. [d] Isolated yield in the parenthesis. n/d: not detected. n/a: not applicable.

4.2.2 Enantioselective Radical Alkylation of Various C–H Bonds

Under the optimized conditions, the substrate scope of [Co(**P6**)]-catalyzed radical cyclization was then evaluated by employing aliphatic aldehyde-derived tosylhydrazone substrates **1** containing different types of C–H bonds (Table 4.3). As demonstrated by substrates **1a**–**1j**, benzylic C–H bonds with varied electronic and steric properties could all be intramolecularly alkylated, affording corresponding 2-arylpyrrolidines **2a**–**2j** in high yields with excellent enantioselectivities. The absolute configuration of the major enantiomer of **2f** was established by X-ray as (*S*). In addition to CN, NO_2, and halogen functionalities, it is noteworthy to mention that the metalloradical C–H alkylation system could tolerate vinyl groups without complication from the competitive cyclopropanation of the C=C bonds as exemplified with the reaction of substrate **1k**, forming the desired pyrrolidine **2k** in 81% yield with 93% *ee*. In a similar way, the Co(II)-based enantioselective radical system could undergo allylic C–H alkylation with high chemoselectivity, as demonstrated by the reaction of substrate **1l** to form 2-vinylpyrrolidine (**2l**) in good yield and excellent enantioselectivity. Likewise, propargylic C–H substrate **1m** also underwent the radical alkylation chemoselectively, giving 2-(phenylethynyl)pyrrolidine (**2m**) in a good yield with promising enantioselectivity. Furthermore, this metalloradical system was shown applicable for substrates even with non-activated C–H bonds. For example, when tosylhydrazone **1n**, which possesses accessible hydrogens at both benzylic and homobenzylic positions, was used as the substrate, [Co(**P6**)] could regioselectively alkylate the stronger homobenzylic over the

weaker benzylic C–H bonds, resulting in exclusive formation of five-membered pyrrolidine **2n** in 96% yield albeit with moderate enantioselectivity. This remarkable

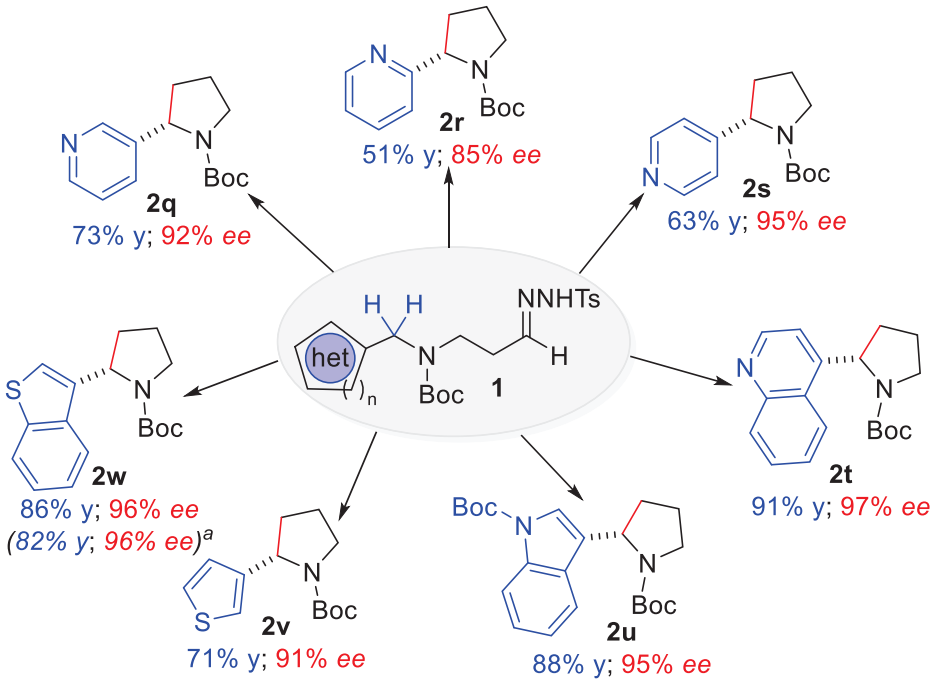
Table 4.3|| Enantioselective Radical Cyclization for Synthesis of *α*-Substituted Pyrrolidines via [Co(P6)]-Catalyzed C–H Alkylation[a]



[a] Carried out with **1** (0.1 mmol) in the presence of Cs_2CO_3 (1.5 equiv.) by [Co(**P6**)] (3 mol %) in dioxane (0.6 mL) at 60 °C for 24 h; isolated yields; *ee* was determined by chiral HPLC analysis. [b] Absolute configuration was determined by X-ray as (*S*).

regioselectivity indicated that the corresponding α-Co(III)-alkyl radicals **I** (Scheme 4.3) within the ligand pocket highly favors 1,5- over 1,6-H abstraction under the influence of the steric environment. In a similar fashion, the Co(II)-based catalytic system could undergo regioselective 1,5-alkylation of stronger secondary C–H bonds in the presence of weaker tertiary C–H bond as illustrated with the reaction of substrate **1o**, forming 2-cyclohexylpyrrolidine (**2o**) in good yield with high enantioselectivity. Notably, this radical cyclization strategy was even applicable for electron-deficient C–H substrates, as demonstrated by the productive formation of the benzyl ester of naturally occurring L-proline (**2p**) from diazo precursor **1p** in 56% yield with 82% *ee*. This result clearly manifested that the Co(II)-catalyzed alkylation is less sensitive to electronic property of C–H bonds, which is in good agreement with the underlying radical mechanism.

Scheme 4.5|| Enantioselective Radical Cyclization for Synthesis of α-Heteroarylpyrrolidines via [Co(P6)]-Catalyzed C–H Alkylation

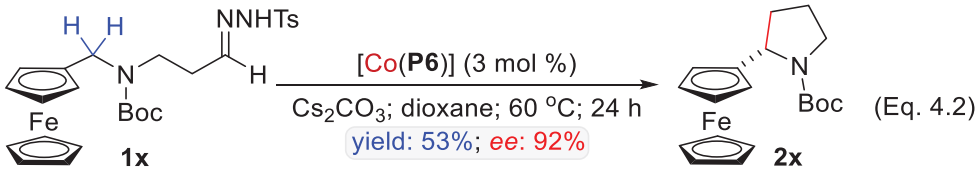


[a] Performed in 2.0 mmol scale with 2 mol % of [Co(**P6**)]

In addition to the tolerance for common functionalities, the Co(II)-based enantioselective radical cyclization was found to be compatible with substrates containing various heteroarenes, allowing for stereoselective construction of α-heteroarylpyrrolidines, which are prevalent structure motifs in natural products and synthetic compounds with wide biological activities (Scheme 4.5).[10] For example, 3-pyridine-based diazo precursor **1q** could be effectively activated by [Co(**P6**)] under the same condition to construct the nicotine derivative **2q** in 73% yield with 92% *ee*. The major enantiomer of **2q** was confirmed to have the same (*S*) absolute configuration as naturally occurring nicotine.[10c] By simply using 2- and 4-pyridine-tethered hydrazones **1r** and **1s**, the Co(II)-based radical cyclization permitted the streamlined synthesis of α- and γ-nicotine derivatives **2r** and **2s**, respectively, in high optical purity.

Likewise, this catalytic protocol could also be successfully applied for both quinoline- and indole-based C–H substrates **1t** and **1u** to form the corresponding optically active α-heteroarylpyrrolidines in high yields with excellent enantioselectivities. Furthermore, chiral pyrrolidine derivatives containing α-thiophene (**2v**) and α-benzothiophene (**2w**) groups were efficiently constructed in high optical purity from the corresponding hydrazone precursors **1v** and **1w**. Notably, the reaction could be scaled up 20-fold as demonstrated with the high-yielding synthesis of **2w** on 2.0 mmol scale without affecting the excellent enantioselectivity. It was evident that the Co(II)-based catalytic system could be well suited to substrates containing potentially coordinating heteroaryl groups without poisoning the catalytic activity or diminishing the high enantioselectivity, a common challenge that plagues many transition metal-catalyzed reactions.

The broad substrate scope and high functionality tolerance observed for the Co(II)-catalyzed radical alkylation prompted us to evaluate its potential applicability to C–H substrates beyond organic molecules, such as organometallic compounds. Considering the resulting product has potential applications as a chiral ligand in asymmetric catalysis,[13] we were specifically intrigued to find out whether this radical cyclization system would allow for construction of a chiral pyrrolidine ring structure directly onto ferrocene, the representative member of metallocene family of organometallic compounds. Accordingly, ferrocene-based C–H substrate **1x** was prepared and tested under the standard conditions. It was found that the C–H bond adjacent to one of the two cyclopentadienyl rings was selectively alkylated by catalyst [Co(**P6**)] for radical cyclization to form the chiral *α*-ferrocenylpyrrolidine **2x** in 53% yield with 92% *ee* (Equation 4.2), indicating the cavity-like environment of the ligand could accommodate relatively large substrates.

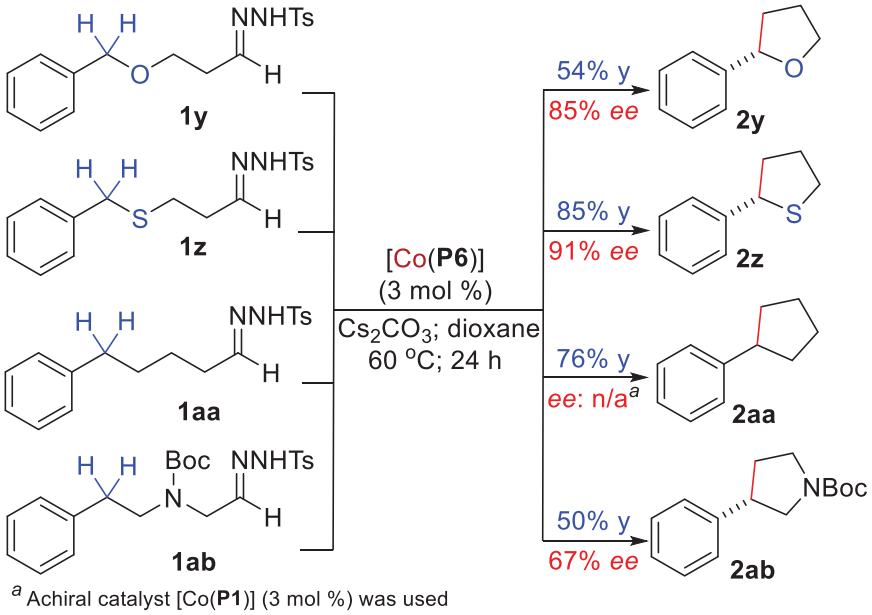


(Eq. 4.2)

While our initial effort was focused on stereoselective formation of chiral pyrrolidine structures, preliminary results showed this radical cyclization strategy could also be applied for construction of other common five-membered ring structures (Scheme 4.6). For example, [Co(**P6**)] could successfully catalyze intramolecular C–H alkylation of both ether- and thioether-linked diazo precursors **1y** and **1z** for enantioselective radical cyclization, forming *α*-phenyltetrahydrofuran (**2y**) and *α*-phenyltetrahydrothiophene (**2z**),

respectively, in good yields with high enantioselectivities. Furthermore, the Co(II)-based radical cyclization protocol even allowed for direct formation of cycloalkanes from diazo precursors with highly flexible all-methylene linkers, as exemplified by the high-yielding synthesis of phenylcyclopentane (**2aa**) from easily accessible 5-phenylpentanal tosylhydrazone (**1aa**). In fact, 5-membered cyclic compounds with varied substitution patterns could be accessed in a similar fashion from diazo precursors derived from aliphatic aldehydes with different linear linkers, as demonstrated in the catalytic reaction of substrate **1ab** by [Co(**P6**)], forming *β*-substituted pyrrolidine **2ab** in 50% yield with 67% *ee* under the same conditions.

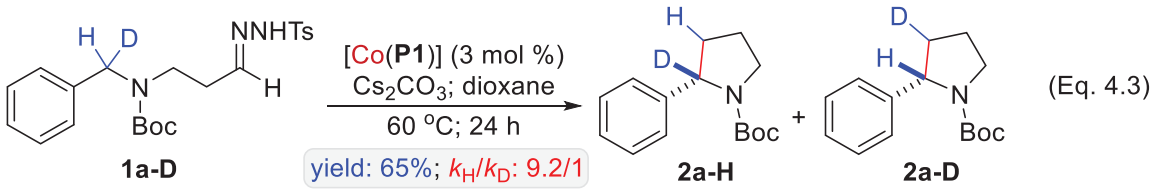
Scheme 4.6|| Enantioselective Construction of Different Five-Membered Cyclic Compounds via [Co(P6)]-Catalyzed C–H Alkylation



[a] Achiral catalyst [Co(**P1**)] (3 mol %) was used

4.2.3 Mechanistic Evidences for the Proposed Stepwise Radical Pathway

To shed light on the underlying stepwise radical mechanism of the Co(II)-catalyzed intramolecular C–H alkylation, several mechanistic experiments were performed. First, mono-deuterated tosylhydrazone **1a-D** was synthesized to measure the intramolecular kinetic isotope effect (KIE) of the C–H alkylation process (Equation 4.3). Under the standard conditions by the achiral catalyst [Co(**P1**)], both C–H (**2a-H**) and C–D (**2a-D**) alkylation products were formed in a combined yield of 65%. ^{1}H-NMR analysis of the product mixture revealed an intramolecular KIE ratio of k_H/k_D = 9.2/1. This high level of primary KIE was in well accordance with the proposed direct C–H bond breaking via H-atom abstraction by α-Co(III)-alkyl radical intermediate **I** (Scheme 4.3).

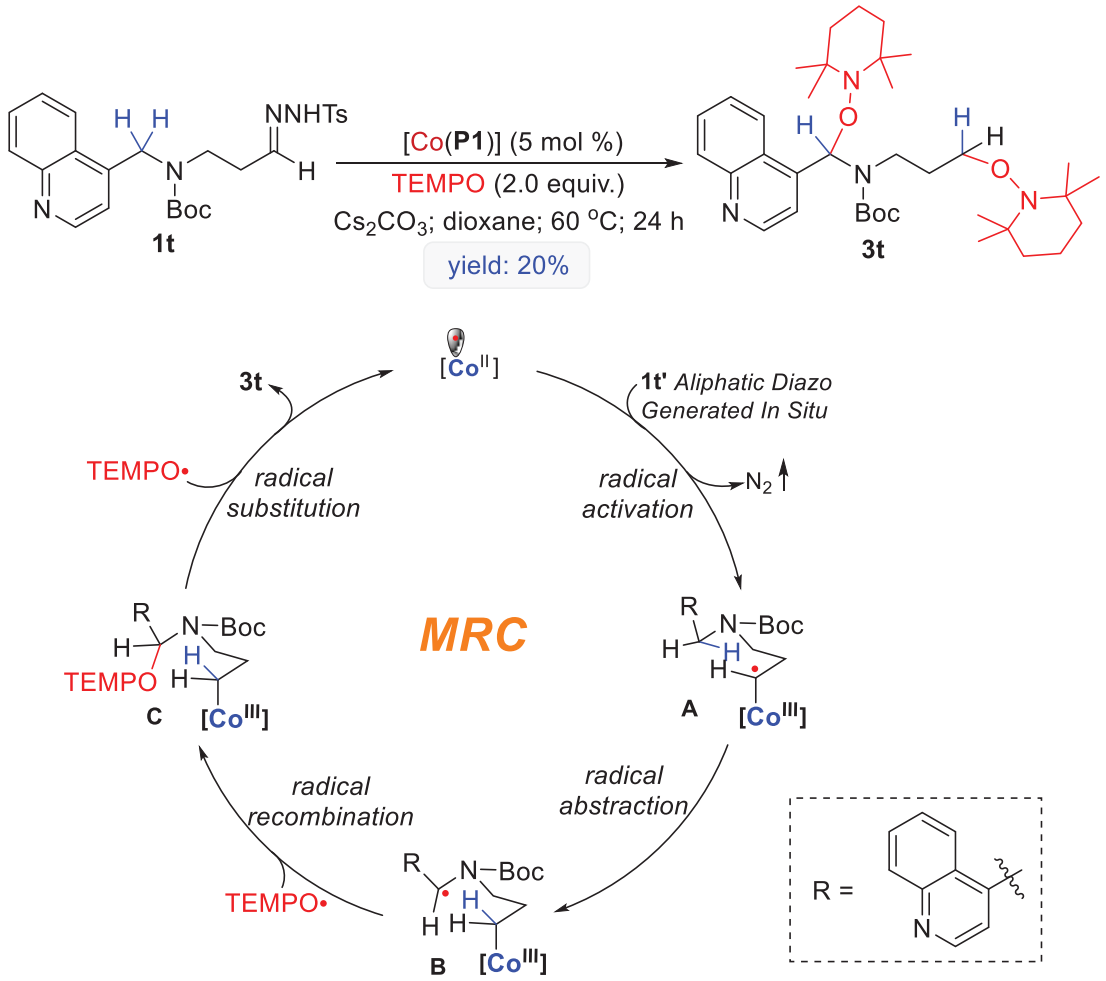


(Eq. 4.3)

Second, the effect of radical scavenger TEMPO on the Co(II)-catalyzed C–H alkylation was examined with the use of substrate **1t** (Scheme 4.7). In the presence of 2.0 equivalent of TEMPO, the catalytic reaction by [Co(**P1**)] resulted in no formation of the alkylation product **2t**. Instead, the TEMPO-trapped compound **3t** was isolated in 20% yield, which was characterized to contain two TEMPO units at the 1- and 5-positions via C–O bonds. The observation of **3t** supports the existence of ε-Co(III)-alkyl radical intermediate **II**, which was apparently trapped by one molecule of TEMPO at the pendant ε-carbon

radical center via radical hetero-dimerization and then reacted with the second molecule of TEMPO at the α-carbon center via radical substitution to cleave the Co(III)–C bond.

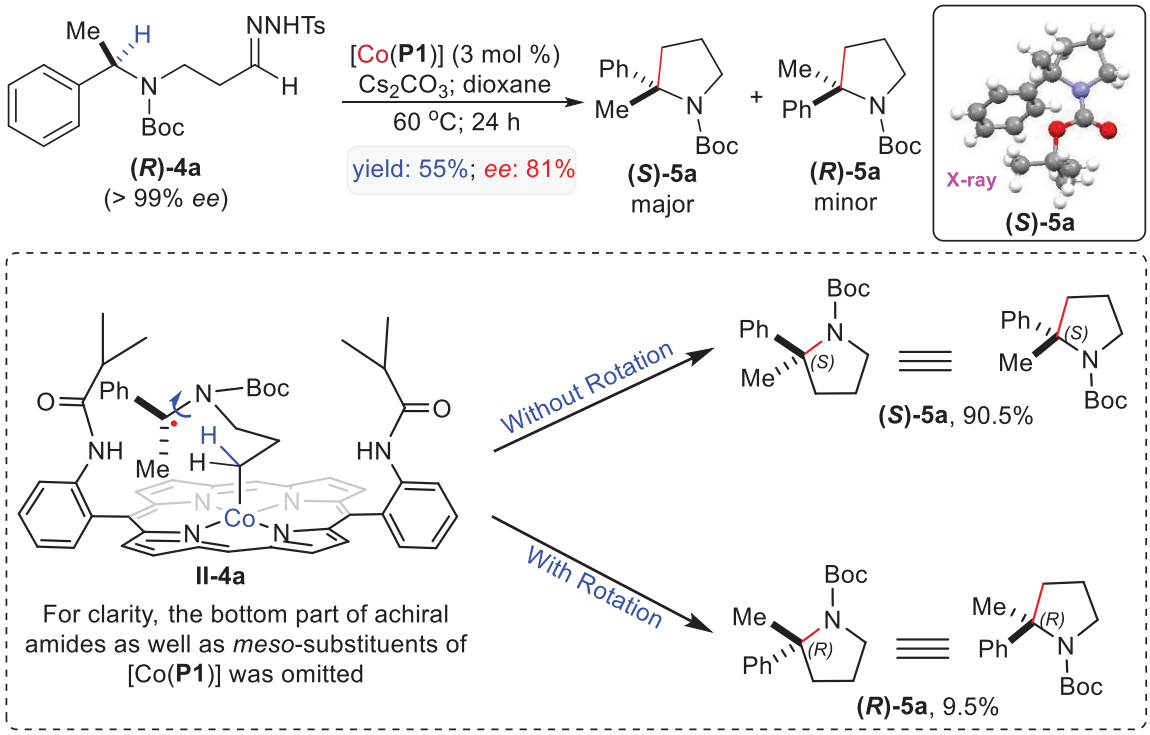
Scheme 4.7|| The Rationale for the Formation of Di-TEMPO Trapped Intermediate 3t



Third, the enantiopure substrate **4a** containing (*R*)-tertiary stereogenic carbon center was prepared to evaluate the stereochemistry outcome of the Co(II)-catalyzed radical C–H alkylation (Scheme 4.8). Under the standard conditions, it was shown that

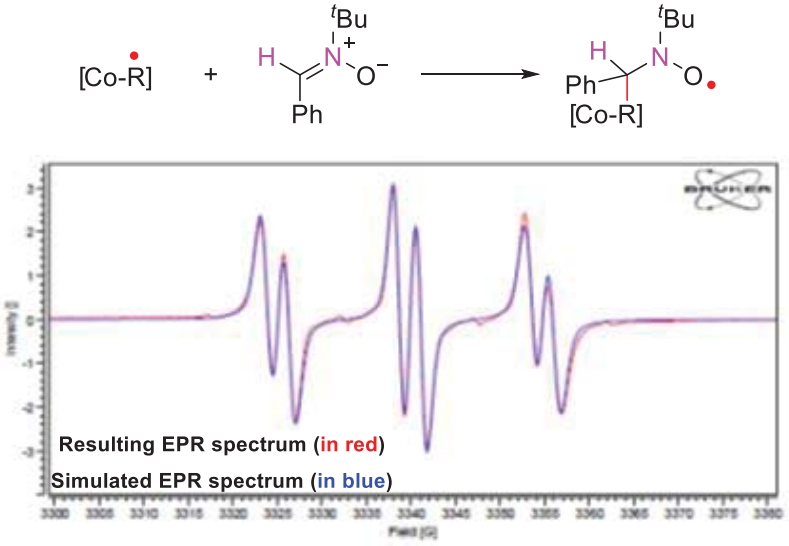
even the tertiary C–H bond in (*R*)-**4a** could be productively alkylated by the achiral catalyst [Co(**P1**)] to form the corresponding *α*,*α*-disubstituted pyrrolidine **5a** in 55% yield as a mixture of enantiomers (*S*)-**5a** and (*R*)-**5a**. Chiral HPLC analysis showed that the enantiopurity of the chiral product **5a** was 81% *ee* with (*S*)-**5a** as the major enantiomer, which was established by X-ray crystallographic analysis. The results indicated that the resulting pro-(*R*) *ε*-Co(III)-alkyl radical intermediate **II** from 1,5-H atom abstraction of the enantiopure (*R*)-tertiary C–H bond by radical intermediate **I** underwent subsequent radical substitution stereospecifically at a much faster rate than its racemization.

Scheme 4.8|| The Rationale for the *ee* Erosion via [Co(P1)]-Catalyzed Radical C–H Alkylation with Optically Active Tertiary C–H Substrate 4a



Last, the Co(III)-supported alkyl radical intermediates from the cyclization reaction of substrate **1a** by [Co(**P1**)] could be directly detected by HRMS and trapped by phenyl *N*-*tert*-butylnitrone (PBN) to give the characteristic EPR signal (Scheme 4.9).

Scheme 4.9|| Isotropic X-band EPR Spectrum of Phenyl *N*-*tert*-Butylnitrone (PBN)-Trapped Co(III)-Supported Alkyl Radical Intermediate



Together, these experimental results established the detailed mechanism for radical cyclization through Co(II)-based metalloradical C–H alkylation (vide supra, Scheme 4.3).

4.3 CONCLUSIONS

In summary, we have demonstrated the broad applicability of the newly emerged radical cyclization mode, which involves sequential radical H-atom abstraction and radical substitution (HAA-RS) via metalloradical catalysis (MRC), as a catalytic C–C bond forming strategy for stereoselective construction of common cyclic compounds from C–H substrates. This alternative strategy of radical cyclization, which is fundamentally different from the traditional radical cyclization of unsaturated substrates involving sequential radical addition and H-atom abstraction (RA-HAA), will provide a new retrosynthetic paradigm to synthesize five-membered chiral cyclic molecules from readily available linear aldehydes via enantioselective C–C bond formation through the union of C–H and C=O units.

4.4 EXPERIMENTAL SECTION

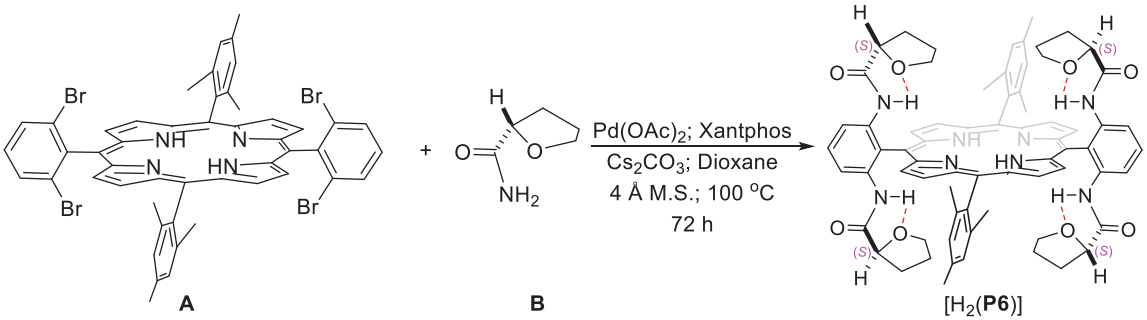
4.4.1 General Considerations

^{1}H NMR spectra were recorded on a Varian INOVA 400 (400 MHz), 500 (500 MHz) or 600 (600 MHz) spectrometer. Chemical shifts are internally referenced to residual $CHCl_3$ signal (δ 7.26 ppm). Data are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian INOVA 400 (100 MHz), 500 (125 MHz), or 600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with residual $CHCl_3$ as the internal standard (δ 77.0 ppm). High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS and JEOL Accu TOF Dart at the Mass Spectrometry Facility, Boston College. Infrared spectra were measured with a Nicolet Avatar 320 spectrometer with a Smart Miracle accessory. Optical rotations were measured on a Rudolph Research Analytical AUTOPOL® IV digital polarimeter. HPLC measurements were carried out on a Shimadzu HPLC system with Chiralcel AD-H, OD-H and OJ-H. The UV-Vis absorption spectra in the range 200 – 700 nm were measured with an Evolution 300 UV-VIS spectrophotometer using quartz cuvettes with 1.0 cm optical path length. X-band EPR spectra were recorded on a Bruker EMX-Plus spectrometer (Bruker BioSpin).

Unless otherwise noted, all C–H alkylation reactions were performed under an atmosphere of dry N_2, in oven-dried glassware with standard vacuum line techniques. Gas tight syringes were used to transfer liquid reagents and solvents in catalytic reactions.

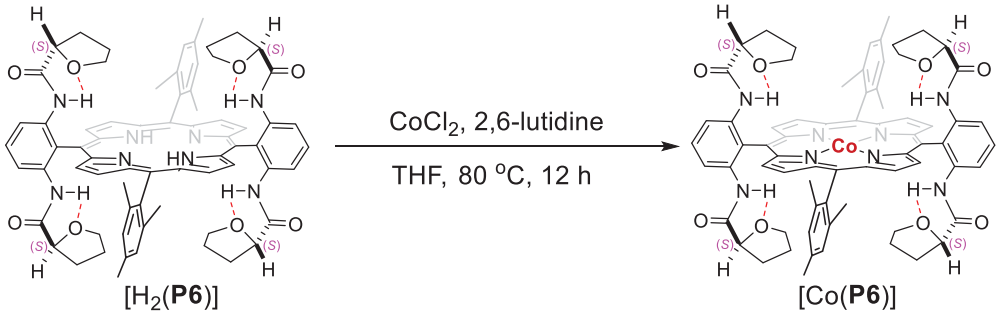
Anhydrous solvents as well as other commercial reagents were purchased from Sigma-Aldrich, Acros, Alfa Aesar, Strem, Oakwood Products Inc., TCI, or Matrix Scientific and used as received unless otherwise stated. Thin layer chromatography was performed on Merck TLC plates (silica gel 60 F254). Flash column chromatography was performed with ICN silica gel (60 Å, 230-400 mesh, 32-63 μm)

4.4.2 Synthesis of Catalyst [Co(P6)]



[H_2(**P6**)] was synthesized according to our previous reported procedure[9g] with 78% yield. The 5,15-bis(2,6-dibromophenyl)-10,20-bis(2,4,6-trimethyl-phenyl)-porphyrin **A**[9g] (0.2 mmol), (*S*)-tetrahydrofuran-2-carboxamide **B** (3.2 mmol), 4 Å molecular sieves, $Pd(OAc)_2$ (0.08 mmol), Xantphos (0.16 mmol), and Cs_2CO_3 (3.2 mmol) were placed in an oven-dried, resealable Schlenk tube. The tube was capped with a Teflon screwcap, evacuated, and backfilled with nitrogen for three times. After that, the screwcap was replaced with a rubber septum, and dioxane (10 mL) was added via gas-tight syringe. The tube was purged with nitrogen for 2 minutes, and then the septum was replaced with the Teflon screwcap. The tube was sealed and stirred at 100 °C for 72 hrs. The resulting mixture was cooled to room temperature, diluted in ethyl acetate, filtrated through a silica pad and

concentrated *in vacuo*. The pure compound was obtained as a purple solid after purification by flash column chromatography (ethyl acetate/hexanes 1/1 to 2/1). ^{1}H NMR (600 MHz, $CDC1_3$): δ 8.71 (br, 8H), 8.58 (d, J = 8.5 Hz, 4H), 7.91 (s, 4H), 7.86 (t, J = 8.5 Hz, 2H), 7.29 (s, 4H), 3.70 (dd, J = 7.7, 5.0 Hz, 4H), 2.63 (s, 6H), 1.83 (s, 12H), 1.62 – 1.57 (m, 12H), 0.74 (m, br, 4H), 0.43 (m, br, 8H), -2.38 (s, 2H). ^{13}C NMR (125 MHz, $CDC1_3$): δ 171.23, 138.85, 138.40, 137.00, 130.71, 128.05, 121.48, 119.64, 116.43, 109.99, 107.82, 77.77, 67.41, 29.54, 24.19, 21.69, 21.42. IR (neat, cm^{-1}): 3348.56, 2973.34, 1693.80, 1585.76, 1495.59, 1343.31, 1062.41, 965.80, 802.86. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{70}H_{71}N_8O_8$: 1151.5389, found 1151.5378. UV–vis (CH_2Cl_2), λ_{max} nm (log ε): 419(5.52), 514(4.27), 546(3.70), 590(3.74), 645(3.48).

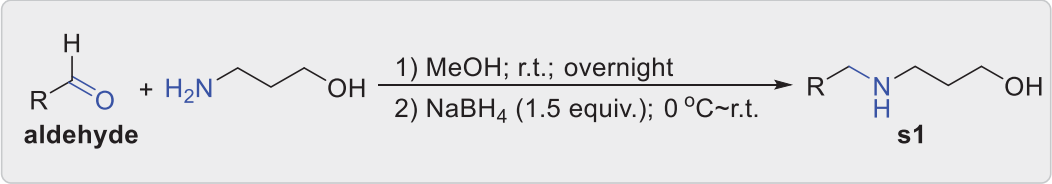


[H_2(**P6**)] [Co(**P6**)]

[Co(**P6**)] was synthesized according to our previous reported procedure[9g] with 90% yield. Free base porphyrin [H_2(**P6**)] and anhydrous $CoCl_2$ (8 equiv.) were placed in an oven-dried, resealable Schlenk tube. The tube was capped with a Teflon screwcap, evacuated, and backfilled with nitrogen. The screwcap was then replaced with a rubber septum, 2,6-lutidine (4 equiv.) and anhydrous THF were added via gas-tight syringe. The tube was purged with nitrogen for 2 minutes, and then the septum was replaced with the

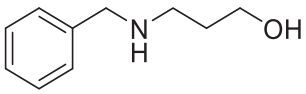
Teflon screwcap. The reaction was conducted at 80 ºC for 12 hrs. The resulting mixture was cooled to room temperature, diluted with ethyl acetate, and transferred to a separatory funnel. The reaction mixture was washed with water for 2 times and concentrated *in vacuo*. The target compound [Co(**P6**)] was isolated as a purple solid after purification by flash column chromatography (ethyl acetate/hexanes 1/1 to 2/1). IR (neat, cm^{-1}): 3345.37, 2975.30, 1691.41, 1584.59, 1496.60, 1343.08, 1291.12, 1163.92, 1062.85, 995.07, 796.97. HRMS (ESI) (M^{*+}) Calcd. for $C_{70}H_{68}CoN_8O_8$:1207.4492, found 1207.4480. UV–vis (CH_2Cl_2), λ_{max} nm (log ε): 412(5.40), 529(4.18).

4.4.3 General Procedure for Preparation of 3-Aminopropan-1-ol Derivative s1

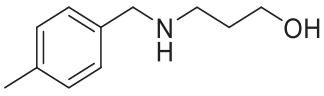


To a solution of aldehyde (10 mmol) in anhydrous methanol (20.0 mL) was added 3-amino-1-propanol (10 mmol) dropwise at room temperature. The reaction was stirred for overnight. After that, the reaction mixture was cooled down to 0 °C in an ice bath. Sodium borohydride (15 mmol) was added portionwise. After the bubbling stopped, the solvent was then evaporated. The resulting residue was then partitioned between H_2O (30 mL) and EtOAc (30 mL). The aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic extracts were then dried and concentrated under vacuum. The desired product **s1**

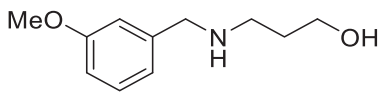
was then purified by flash chromatography (unless otherwise noted, the column conditions are: ethyl acetate, then dichloromethane/methanol 10/1 to 5/1).



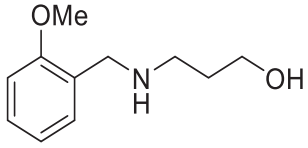
3-(benzylamino)propan-1-ol s1-a, known compound.[14] Following the general procedure with benzaldehyde as starting material. Yield: 75%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 5H), 3.82 – 3.80 (m, 4H), 3.13 (br, 2H), 2.90 (t, J = 5.6 Hz, 2H), 1.73 (p, J = 5.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.06, 128.45, 128.16, 127.18, 63.87, 53.76, 49.01, 30.66. IR (neat, cm^{-1}): 3292.27, 2928.78, 1453.11, 1068.01, 1026.71, 733.97, 697.39. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{16}NO$: 166.1226, found 166.1233.



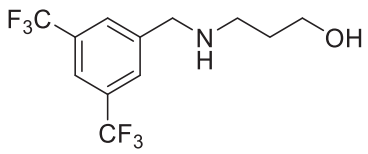
3-((4-methylbenzyl)amino)propan-1-ol s1-b. Following the general procedure with 4-methyl benzaldehyde as starting material. Yield: 76%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 7.9 Hz, 2H), 3.76 (t, J = 5.3 Hz, 2H), 3.71 (s, 2H), 3.23 (br, 2H), 2.84 (t, J = 5.8 Hz, 2H), 2.31 (s, 3H), 1.71 – 1.66 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.62, 136.28, 129.03, 128.00, 63.67, 53.47, 48.80, 30.75, 20.96. IR (neat, cm^{-1}): 3260.20, 2920.68, 1515.68, 1455.33, 1182.33, 1067.94, 879.23, 803.45. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{11}H_{18}NO$: 180.1383, found 180.1390.



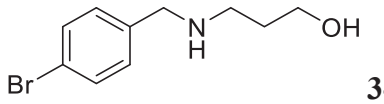
3-((3-methoxybenzyl)amino)propan-1-ol s1-c. Following the general procedure with 3-methoxy benzaldehyde as starting material. Yield: 70%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (t, *J* = 7.9 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.83 (s, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 3.79 –3.76 (m, br, 7H), 3.43 (br, 2H), 2.87 (t, *J* = 5.7 Hz, 2H), 1.72 (p, *J* = 5.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.71, 140.78, 129.44, 120.39, 113.56, 112.68, 63.84, 55.12, 53.72, 48.95, 30.70. IR (neat, cm^{-1}): 3294.57, 2934.71, 1589.83, 1585.04, 1454.58, 1262.23, 1154.06, 1040.91, 855.67, 778.62, 693.43. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{11}H_{18}NO_2$: 196.1332, found 196.1338.



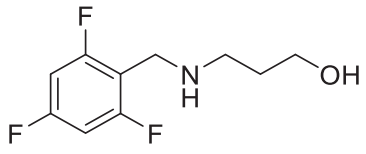
3-((2-methoxybenzyl)amino)propan-1-ol s1-d. Following the general procedure with 2-methoxy benzaldehyde as starting material.Yield: 73%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 6.94 – 6.86 (m, 2H), 4.93 (br, 2H), 3.88 – 3.83 (m, 5H), 3.78 (t, *J* = 5.4 Hz, 2H), 2.90 (t, *J* = 5.4 Hz, 2H), 1.76 (p, *J* = 5.4 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.66, 130.02, 128.44, 127.57, 120.34, 110.21, 64.66, 55.18, 49.31, 49.25, 30.48. IR (neat, cm^{-1}): 3306.05, 2936.56, 1601.41, 1493.10, 1463.17, 1241.02, 1026.73, 855.05. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{11}H_{18}NO_2$: 196.1332, found 196.1339.



3-((3,5-bis(trifluoromethyl)benzyl)amino)propan-1-ol s1-e, Following the general procedure with 3,5-bis(trifluoromethyl) benzaldehyde as starting material. Yield: 63%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (s, 2H), 7.78 (s, 1H), 3.93 (s, 2H), 3.80 (t, J = 5.3 Hz, 2H), 2.88 (t, J = 5.8 Hz, 2H), 2.77 (br, 2H), 1.77 (p, J = 5.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.12, 131.75 (q, J = 33.1 Hz), 128.19, 123.29 (q, J = 272.4 Hz), 121.21, 63.35, 53.05, 48.78, 31.18. IR (neat, cm^{-1}): 3262.88, 2943.83, 1622.66, 1467.68, 1372.90, 1276.12, 1155.57, 1061.61, 903.41, 842.38, 730.76. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{12}H_{14}F_6NO$: 302.0974, found 302.0985.

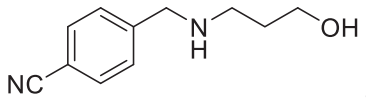


3-((4-bromobenzyl)amino)propan-1-ol s1-f. Following the general procedure with 4-bromobenzaldehyde as starting material. Yield: 77%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, J = 8.3 Hz, 2H), 7.18 (d, J = 8.3 Hz, 2H), 3.81 (t, J = 5.4 Hz, 2H), 3.75 (s, 2H), 2.88 (t, J = 5.7 Hz, 2H), 2.76 (br, 2H), 1.73 (p, J = 5.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.32, 131.52, 129.82, 120.95, 63.92, 53.19, 49.04, 30.79. IR (neat, cm^{-1}): 3294.51, 3084.01, 2909.99, 1590.67, 1444.98, 1189.24, 1065.62, 1002.84, 846.05, 799.05. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{15}BrNO$: 244.0332, found 244.0341.

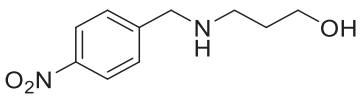


3-((2,4,6-trifluorobenzyl)amino)propan-1-ol s1-g.

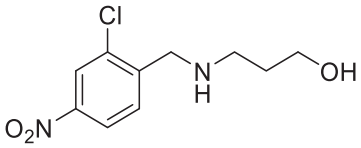
Following the general procedure with 2,4,6-trifluorobenzaldehyde as starting material. Yield: 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (t, *J* = 7.8 Hz, 2H), 3.83 (s, 2H), 3.75 (t, *J* = 5.0 Hz, 2H), 2.95 (br, 2H), 2.79 (t, *J* = 5.7 Hz, 2H), 1.68 (p, *J* = 5.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.04 (d, *J* = 15.2 Hz), 160.57 (d, *J* = 15.0 Hz), 111.43 (t, *J* = 20.4 Hz), 100.07 (t, *J* = 27.3 Hz), 63.59, 48.27, 39.99, 30.80. IR (neat, cm^{-1}): 3301.00, 2937.96, 1625.85, 1439.90, 1169.08, 1114.84, 997.09, 839.38, 736.80. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{13}F_3NO$: 220.0944, found 220.0951.



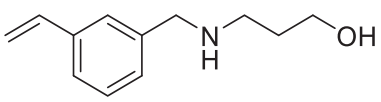
3-((4-nitrilebenzyl)amino)propan-1-ol s1-h. Following the general procedure with 4-nitrilebenzaldehyde as starting material. Yield: 89%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 8.1 Hz, 2H), 3.82 (s, 2H), 3.75 (t, *J* = 5.5 Hz, 2H), 2.94 (br, 2H), 2.83 (t, *J* = 5.9 Hz, 2H), 1.70 (p, *J* = 5.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.69, 131.84, 128.27, 118.38, 110.48, 63.08, 53.02, 48.48, 30.65. IR (neat, cm^{-1}): 3244.62, 2808.20, 2228.96, 1607.81, 1460.45, 1357.12, 1064.78, 982.87, 835.02. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{11}H_{15}N_2O$: 191.1179, found 191.1186.



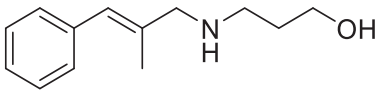
3-((4-nitrobenzyl)amino)propan-1-ol s1-i. Following the general procedure with 4-nitrobenzaldehyde as starting material. Yield: 86%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 8.5 Hz, 2H), 3.88 (s, 2H), 3.77 (t, J = 5.4 Hz, 2H), 2.87 – 2.84 (m, 4H), 1.73 (p, J = 5.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.23, 147.08, 128.65, 123.67, 63.69, 53.21, 49.07, 31.07. IR (neat, cm^{-1}): 3262.72, 3110.15, 2941.77, 1607.40, 1517.26, 1343.05, 1095.26, 966.70, 851.28. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{15}N_2O_3$: 211.1077, found 211.1086.



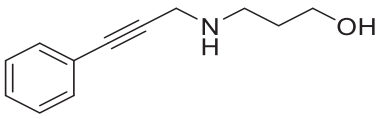
3-((2-chloro-4-nitrobenzyl)amino)propan-1-ol s1-j. Following the general procedure with 2-chloro-4-nitrobenzaldehyde as starting material. Yield: 66%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, J = 2.5 Hz, 1H), 8.00 (dd, J = 8.7, 2.7 Hz, 1H), 7.47 (d, J = 8.7 Hz, 1H), 3.90 (s, 2H), 3.73 (t, J = 5.6 Hz, 2H), 2.82 (t, br, J = 6.1 Hz, 4H), 1.72 (p, J = 5.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 146.45, 140.35, 139.23, 130.21, 124.33, 122.99, 62.68, 50.63, 48.17, 31.29. IR (neat, cm^{-1}): 3270.58, 2946.16, 1608.98, 1519.29, 1341.61, 1181.61, 1075.65, 830.25, 739.10. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{14}ClN_2O_3$: 245.0693, found 245.0703.



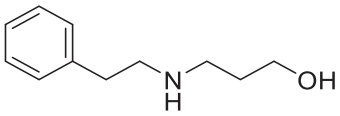
3-((3-vinylbenzyl)amino)propan-1-ol s1-k. Following the general procedure with 3-vinylbenzaldehyde as starting material. Yield: 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 3H), 7.17 (d, *J* = 6.9 Hz, 1H), 6.68 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.73 (d, *J* = 17.6 Hz, 1H), 5.25 (d, *J* = 10.9 Hz, 1H), 3.79 – 3.77 (m, 4H), 3.21 (br, 2H), 2.88 (t, *J* = 5.6 Hz, 2H), 1.71 (p, *J* = 5.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.43, 137.80, 136.64, 128.72, 127.69, 126.08, 125.13, 114.10, 63.93, 53.78, 49.09, 30.75. IR (neat, cm^{-1}): 3293.63, 2930.19, 1629.77, 1441.56, 1066.59, 990.42, 906.35, 796.77, 713.63. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{12}H_{18}NO$: 192.1383, found 192.1389.



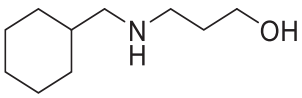
(*E*)-3-((2-methyl-3-phenylallyl)amino)propan-1-ol s1-l. Following the general procedure with *α*-methyl-*trans*-cinnamaldehyde as starting material. Yield: 73%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 7.1 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 6.43 (s, 1H), 3.83 (t, *J* = 5.3 Hz, 2H), 3.57 (br, 2H), 3.34 (s, 2H), 2.91 (t, *J* = 5.8 Hz, 2H), 1.91 (s, 3H), 1.75 (p, *J* = 5.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.57, 135.69, 128.80, 128.06, 126.91, 126.35, 64.07, 58.16, 48.95, 30.58, 16.52. IR (neat, cm^{-1}): 3289.52, 2932.76, 1489.80, 1442.46, 1070.76, 916.93, 743.02. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{13}H_{20}NO$: 206.1544, found 206.1545.



3-((3-phenylprop-2-yn-1-yl)amino)propan-1-ol s1-m. Following the general procedure with 3-phenylpropiolaldehyde as starting material. Yield: 70%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.40 (m, 2H), 7.30 – 7.28 (m, 3H), 3.81 (t, *J* = 5.3 Hz, 2H), 3.66 (s, 2H), 3.14 (br, 2H), 3.00 (t, *J* = 6.0 Hz, 2H), 1.75 (p, *J* = 5.7 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 131.62, 128.27, 128.15, 122.94, 86.65, 83.98, 63.54, 48.08, 38.68, 30.77. IR (neat, cm^{-1}): 3300.49, 2932.66, 1597.88, 1489.63, 1331.61, 1070.10, 758.97. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{12}H_{16}NO$: 190.1238, found 190.1232.

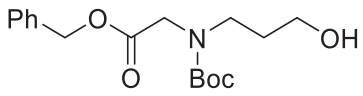


3-(phenethylamino)propan-1-ol s1-n. Following the general procedure with 2-phenylacetaldehyde as starting material. Yield: 93%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.18 (m, 5H), 3.79 (t, *J* = 5.1 Hz, 2H), 3.54 (br, 2H), 2.91 – 2.87 (m, 4H), 2.80 (t, *J* = 6.9 Hz, 2H), 1.69 (p, *J* = 5.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.39, 128.61, 128.48, 126.25, 63.83, 50.70, 49.44, 35.90, 30.45. IR (neat, cm^{-1}): 3290.02, 3026.79, 2931.95, 1602.66, 1453.40, 1110.09, 1067.97, 735.08, 698.60. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{11}H_{18}NO$: 180.1383, found 180.1388.

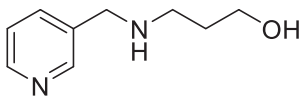


3-((cyclohexylmethyl)amino)propan-1-ol s1-o. Following the general procedure with cyclohexanecarbaldehyde as starting material. Yield: 59%. ^{1}H

NMR (600 MHz, $CDCl_3$) δ 3.80 (t, *J* = 5.2 Hz, 2H), 3.49 (br, 2H), 2.87 (t, *J* = 5.6 Hz, 2H), 2.44 (d, *J* = 6.6 Hz, 2H), 1.72 – 1.63 (m, 7H), 1.44 – 1.39 (m, 1H), 1.25 – 1.10 (m, 3H), 0.93 – 0.87 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 64.54, 56.53, 50.38, 37.72, 31.31, 30.30, 26.55, 25.97. IR (neat, cm^{-1}): 3255.27, 2920.26, 1447.79, 1264.73, 1068.06, 890.14, 733.69. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{22}NO$: 172.1696, found 172.1703.

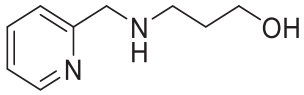


benzyl *N*-(*tert*-butoxycarbonyl)-*N*-(3-hydroxypropyl) glycinate s1-p. Prepared according to the literature[15] from benzyl 2-bromoacetate (6.0 mmol) and 3-aminopropan-1-ol (7.2 mmol) in two steps. R_f = 0.32 (ethyl acetate/hexanes: 1/2). Yield: 71%. ^1H NMR (500 MHz, $CDCl_3$) a mixture of amide rotamers. δ 7.35 – 7.33 (m, br, 5H), 5.17 and 5.14 (s, 2H), 4.01 and 3.89 (s, 2H), 3.66 – 3.58 (m, 2H), 3.47 – 3.37 (m, 3H), 1.65 – 1.63 (m, 2H), 1.48 and 1.36 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) major amide rotamer. δ 172.43, 159.13, 137.99, 131.28, 131.19, 131.16, 83.62, 69.54, 61.00, 52.57, 47.32, 33.28, 30.73. IR (neat, cm^{-1}): 3465.51, 2976.12, 1753.43, 1693.74, 1404.40, 1251.90, 1171.16, 756.23. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{17}H_{26}NO_5$: 324.1811, found 324.1821.

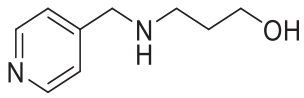


3-((pyridin-3-ylmethyl)amino)propan-1-ol s1-q. Following the general procedure with nicotinaldehyde as starting material. Yield: 85%. ^1H NMR (500 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.48 (d, *J* = 4.7 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.32 – 7.16

(m, 1H), 3.78 (s, 2H), 3.76 (t, J = 5.5 Hz, 2H), 2.96 (br, 2H), 2.85 (t, J = 5.9 Hz, 2H), 1.72 (p, J = 5.4 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.54, 148.62, 135.77, 134.91, 123.46, 63.65, 51.24, 48.99, 31.03. IR (neat, cm^{-1}): 3262.41, 2933.04, 1577.84, 1425.22, 1288.33, 1060.69, 791.05, 710.90. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_9H_{15}N_2O$: 167.1179, found 167.1186.

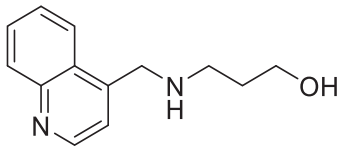


3-((pyridin-2-ylmethyl)amino)propan-1-ol s1-r. Following the general procedure with picolinaldehyde as starting material. Yield: 82%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J = 4.7 Hz, 1H), 7.61 (td, J = 7.7, 1.7 Hz, 1H), 7.24 (d, J = 7.8 Hz, 1H), 7.13 (dd, J = 7.1, 5.3 Hz, 1H), 3.87 (s, 2H), 3.77 (t, J = 5.4 Hz, 2H), 3.52 (br, 2H), 2.86 (t, J = 5.9 Hz, 2H), 1.71 (p, J = 5.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.91, 149.18, 136.51, 122.30, 122.03, 63.44, 54.77, 48.85, 30.94. IR (neat, cm^{-1}): 3375.78, 2952.78, 1595.26, 1437.42, 1219.35, 1153.47, 1066.09, 999.69, 767.24. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_9H_{15}N_2O$: 167.1179, found 167.1182.

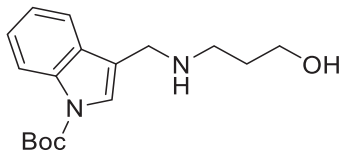


3-((pyridin-4-ylmethyl)amino)propan-1-ol s1-s. Following the general procedure with isonicotinaldehyde as starting material. Yield: 65%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (d, J = 5.8 Hz, 2H), 7.22 (d, J = 5.6 Hz, 2H), 3.80 – 3.78 (m, 4H), 3.03 (br, 2H), 2.86 (t, J = 5.9 Hz, 2H), 1.74 (p, J = 5.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.80, 148.59, 122.89, 63.52, 52.68, 48.95, 31.11. IR (neat, cm^{-1}): 3270.90,

2928.93, 1602.93, 1415.46, 1220.16, 1063.87, 1001.81, 796.89. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_9H_{15}N_2O$: 167.1179, found 167.1186.

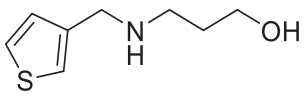


3-((quinolin-4-ylmethyl)amino)propan-1-ol s1-t. Following the general procedure with quinoline-4-carbaldehyde as starting material. Yield: 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.4 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 4.3 Hz, 1H), 4.15 (s, 2H), 3.73 (t, *J* = 5.5 Hz, 2H), 3.09 (br, 2H), 2.88 (t, *J* = 6.0 Hz, 2H), 1.72 (p, *J* = 5.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.03, 147.93, 144.95, 129.91, 129.08, 126.67, 126.53, 122.89, 119.61, 62.87, 49.92, 49.00, 31.34. IR (neat, cm^{-1}): 3271.45, 2929.27, 1592.97, 1424.22, 1239.68, 1067.21, 842.69, 752.92. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{13}H_{17}N_2O$: 217.1335, found 217.1346.

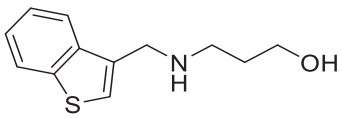


***tert*-butyl 3-(((3-hydroxypropyl)amino)methyl)-1*H*-indole-1-carboxylate s1-u.** Following the general procedure with *tert*-butyl 3-formyl-1*H*-indole-1-carboxylate as starting material. Yield: 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.5 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.50 (s, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.4 Hz, 1H), 3.91 (s, 2H), 3.81 (t, *J* = 5.3 Hz, 2H), 3.00 – 2.93 (m, 4H), 1.76 – 1.66 (m, 11H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.66, 135.64, 129.74, 124.49, 123.61, 122.59, 118.92, 118.76, 115.29, 83.60, 64.06, 49.45, 44.51, 30.84, 28.17. IR (neat, cm^{-1}): 3301.59, 2977.45, 1727.67, 1475.02, 1450.57, 1368.04, 1253.96, 1154.95, 1076.59, 855.37, 744.24. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{17}H_{25}N_2O_3$: 305.1860, found 305.1875.

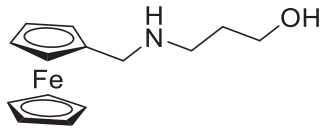


3-((thiophen-3-ylmethyl)amino)propan-1-ol s1-v. Following the general procedure with thiophene-3-carbaldehyde as starting material. Yield: 72%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.11 (d, *J* = 2.2 Hz, 1H), 7.03 (d, *J* = 4.9 Hz, 1H), 3.81 – 3.79 (m, 4H), 3.14 (br, 2H), 2.88 (t, *J* = 5.8 Hz, 2H), 1.71 (p, *J* = 5.5 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.57, 127.44, 125.89, 121.73, 64.18, 49.25, 48.73, 30.76. IR (neat, cm^{-1}): 3276.04, 3101.66, 2932.17, 1440.79, 1235.84, 1064.68, 913.06, 855.68, 771.00. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_8H_{14}NOS$: 172.0791, found 172.0794.

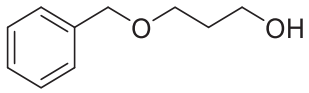


3-((benzo[*b*]thiophen-3-ylmethyl)amino)propan-1-ol s1-w. Following the general procedure with benzo[*b*]thiophene-3-carbaldehyde as starting material. Yield: 99%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.41 – 7.29 (m, 2H), 7.29 (s, 1H), 4.02 (s, 2H), 3.80 (t, *J* = 5.3 Hz, 2H), 3.14 (br, 2H), 2.95 (t, *J* = 5.8 Hz, 2H), 1.74 (p, *J* = 5.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.56, 138.09, 134.23, 124.36, 124.06, 123.26, 122.84, 121.46, 63.89, 49.41, 47.43,

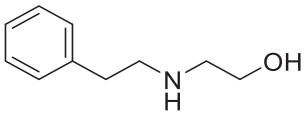
30.84. IR (neat, cm^{-1}): 3292.69, 2925.84, 1495.15, 1426.29, 1255.62, 1067.71, 836.00, 752.78. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{12}H_{16}NOS$: 222.0947, found 222.0958.



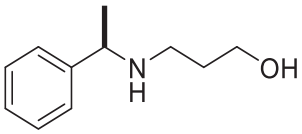
3-((ferrocenyl)amino)propan-1-ol s1-x. Following the general procedure with ferrocenecarboxaldehyde as starting material. Yield: 45%. ^1H NMR (500 MHz, $CDCl_3$) δ 4.15 – 4.09 (m, 9H), 3.79 (t, J = 5.2 Hz, 2H), 3.50 (s, 2H), 3.22 (br, 2H), 2.88 (t, J = 5.6 Hz, 2H), 1.69 (p, J = 5.4 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 86.16, 68.33, 68.19, 67.74, 64.22, 49.44, 48.67, 30.59. IR (neat, cm^{-1}): 3274.40, 2942.31, 2360.19, 1450.25, 1341.97, 1272.79, 1162.09, 1041.03, 913.33, 801.98. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{14}H_{20}FeNO$: 274.0889, found 274.0891.



3-(benzyloxy)propan-1-ol s1-y, known compound.[16] Prepared from benzyl bromide (10 mmol) and propane 1,3-diol (10 mmol) according to the literature.[16] R_f = 0.35 (ethyl acetate/hexanes: 1/3).Yield: 71%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H), 4.53 (s, 2H), 3.78 (s, 2H), 3.78 – 3.65 (m, 2H), 2.33 (s, 1H), 1.87 (p, J = 5.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.04, 128.41, 127.67, 127.61, 73.24, 69.34, 61.85, 32.09.

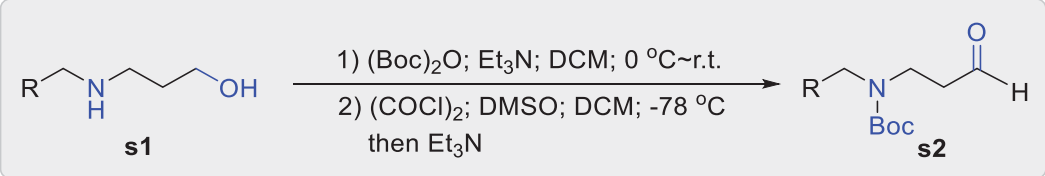


2-(phenethylamino)ethan-1-ol s1-z. Following the general procedure with 2-phenylacetaldehyde and 2-aminoethan-1-ol as starting material. Yield: 45%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.6 Hz, 2H), 7.22 – 7.20 (m, 3H), 3.63 (t, *J* = 5.2 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.81 (t, *J* = 7.1 Hz, 2H), 2.78 (t, *J* = 5.2 Hz, 2H), 2.51 (br, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.72, 128.66, 128.47, 126.20, 60.67, 50.87, 50.56, 36.28. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{16}NO$: 166.1232, found 166.1231.



(*R*)-3-((1-phenylethyl)amino)propan-1-ol s1-aa, known compound.[17] Prepared according to the literature[17] from optically pure (*R*)-(+)-1-phenylethylamine. Yield: 78%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.23 (m, 5H), 3.80 – 3.72 (m, 3H), 3.18 (br, 2H), 2.79 – 2.74 (m, 1H), 2.67 – 2.63 (m, 1H), 1.75 – 1.67 (m, 1H), 1.64 – 1.57 (m, 1H), 1.36 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.76, 128.54, 127.08, 126.44, 64.34, 58.61, 47.78, 31.18, 24.17.

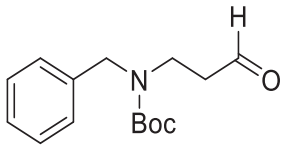
4.4.4 General Procedure for Preparation of *tert*-Butyl (3-Oxopropyl)carbamate Derivative s2



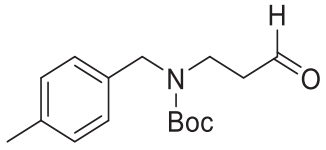
Step 1: To a solution of **s1** (5 mmol) and triethylamine (1.5 equiv.) in DCM (30.0 mL), di-*tert*-butyl dicarbonate (1.1 equiv.) was added portionwise at 0 °C. The reaction was then stirred at room temperature and monitored by TLC. After the reaction was completed, the mixture was filtrated through a short pad of silica and eluted with ethyl acetate. The filtrate was then evaporated and concentrated under vacuum. The obtained raw compound was directly used without further purification.

Step 2 (Swern oxidation via the standard procedure[18]): To a solution of oxalyl chloride (1.5 equiv.) in DCM (30 mL) at -78 °C was added dimethyl sulfoxide (3.0 equiv.) dropwise via syringe. After stirring for 20 min at -78 °C, a solution of *N*-Boc protected **s1** (crude product from previous amine protecting step) in DCM (5.0 mL) was added dropwise via syringe pump at a rate of 10 mL/hr. The solution was then stirred for 30 min at -78 °C, followed by the dropwise addition of triethylamine (4.5 equiv.). After 10 min, the reaction mixture was warmed up to room temperature, poured into brine (30 mL) and stirred for another 10 min. The layers were then separated and the aqueous layer was extracted with DCM (3 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4,

filtered and concentrated under vacuum. The oxidized product **s2** was further purified by flash chromatography.

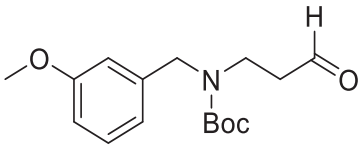


***tert*-butyl benzyl(3-oxopropyl)carbamate s2-a**. Following the general procedure with **s1-a** as starting material. Yield: 77%. R_f = 0.38 (ethyl acetate/hexanes: 1/5). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.73 (br, 1H), 7.34 – 7.22 (m, 5H), 4.44 (s, 2H), 3.52 – 3.47 (m, br, 2H), 2.65 – 2.59 (m, br, 2H), 1.45 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 201.01, 155.53, 138.19, 128.58, 127.77, 127.34, 80.27, 51.35, 43.05, 40.82, 28.38. IR (neat, cm^{-1}): 2976.59, 1722.96, 1686.92, 1454.19, 1413.06, 1365.85, 1244.53, 1162.92, 1126.53, 874.73, 734.29, 699.92. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{22}NO_3$: 264.1594, found 264.1598.

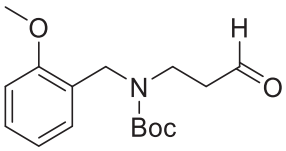


***tert*-butyl (4-methylbenzyl)(3-oxopropyl)carbamate s2-b**. Following the general procedure with **s1-b** as starting material. Yield: 83%. R_f = 0.52 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.71 (br, 1H), 7.11 (m, 4H), 4.39 (s, 2H), 3.48 (m, br, 2H), 2.62 (m, br, 2H), 2.32 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): major isomer δ 201.02, 155.51, 136.99, 135.00, 129.23, 127.23, 80.19, 50.97, 43.02, 40.63, 28.37, 21.04. IR (neat, cm^{-1}): 2975.20, 1722.62,

1687.11, 1463.61, 1407.44, 1365.32, 1243.63, 1162.95, 1126.59, 877.69, 772.39. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{24}NO_3$: 278.1751, found 278.1751.

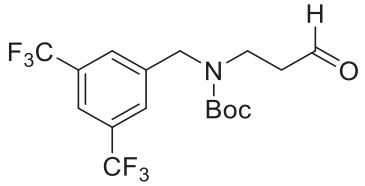


***tert*-butyl (3-methoxybenzyl)(3-oxopropyl)carbamate s2-c**. Following the general procedure with **s1-c** as starting material. Yield: 71%. R_f = 0.24 (ethyl acetate/hexanes: 1/5). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.73 (br, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 6.82 – 6.80 (m, 3H), 4.42 (s, 2H), 3.79 (s, 3H), 3.52 – 3.47 (m, br, 2H), 2.66 – 2.59 (m, br, 2H), 1.46 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 201.01, 159.85, 155.50, 139.86, 129.58, 119.50, 112.82, 112.70, 80.27, 55.16, 51.30, 43.04, 41.03, 28.38. IR (neat, cm^{-1}): 2974.55, 1721.94, 1686.89, 1463.46, 1410.88, 1365.52, 1245.63, 1161.91, 1048.31, 860.09, 773.10. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{24}NO_4$: 294.1700, found 294.1702.

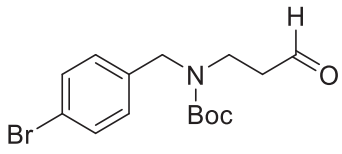


***tert*-butyl (2-methoxybenzyl)(3-oxopropyl)carbamate s2-d**. Following the general procedure with **s1-d** as starting material. Yield: 81%. R_f = 0.35 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.75 (br, 1H), 7.26 – 7.14 (m, 2H), 6.94 – 6.83 (m, 2H), 4.43 (s, 2H), 3.81 (s, 3H), 3.57 – 3.29 (m, 2H), 2.65 – 2.49 and 1.84 – 1.81 (m, 2H), 1.43 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$):

major isomer δ 201.29, 157.11, 155.81, 129.09, 128.37, 126.11, 120.42, 110.18, 80.00, 55.20, 45.98, 43.04, 41.17, 28.38. IR (neat, cm^{-1}): 2974.99, 1726.38, 1687.07, 1462.64, 1412.92, 1365.61, 1239.92, 1159.50, 1028.62, 877.77, 751.50. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{16}H_{24}NO_4$: 294.1700, found 294.1703.

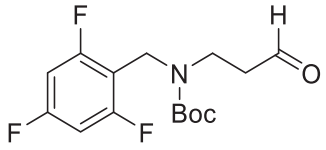


***tert*-butyl (3,5-bis(trifluoromethyl)benzyl)(3-oxopropyl) carbamate s2-e**. Following the general procedure with **s1-e** as starting material. Yield: 80%. R_f = 0.54 (ethyl acetate/hexanes: 1/3). ^1H NMR (400 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.77 (br, 1H), 7.77 – 7.66 (m, 3H), 4.54 (s, 2H), 3.70 – 3.52 (m, br, 2H), 2.75 – 2.63 (m, br, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): major isomer δ 200.57, 155.38, 141.27, 133.88 (q, J = 33.2 Hz), 127.25, 123.18 (q, J = 272.6 Hz), 121.27, 81.11, 51.08, 43.29, 41.44, 28.17. IR (neat, cm^{-1}): 2979.02, 1692.92, 1469.97, 1368.25, 1276.14, 1165.47, 1126.56, 901.45, 705.93, 681.71. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{17}H_{20}F_6NO_3$: 400.1342, found 400.1351.

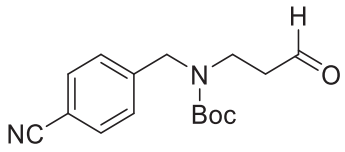


***tert*-butyl (4-bromobenzyl)(3-oxopropyl)carbamate s2-f**. Following the general procedure with **s1-f** as starting material. Yield: 79%. R_f = 0.36 (ethyl acetate/hexanes: 1/5). ^1H NMR (400 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.73

(br, 1H), 7.43 (d, J = 8.3 Hz, 2H), 7.09 (d, br, 2H), 4.38 (s, 2H), 3.47 and 3.25 (br, 2H), 2.66 and 2.49 (br, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): major isomer δ 200.78, 155.42, 137.26, 131.68, 128.79, 121.16, 80.49, 50.92, 43.17, 40.91, 28.35. IR (neat, cm^{-1}): 2974.88, 1723.02, 1686.67, 1487.44, 1401.05, 1365.44, 1244.47, 1161.47, 1127.02, 1010.80, 877.52, 771.38. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{21}BrNO_3$: 342.0699, found 342.0698.

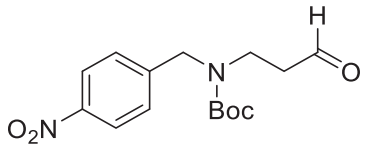


***tert*-butyl (2,4,6-trifluorobenzyl)(3-oxopropyl)carbamate s2-g**. Following the general procedure with **s1-g** as starting material. Yield: 63%. R_f = 0.35 (ethyl acetate/hexanes: 1/5). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.74 (br, 1H), 6.65 (t, J = 8.2 Hz, 2H), 4.49 (s, 2H), 3.52 (br, 2H), 2.65 (br, 2H), 1.42 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 200.86, 175.22, 161.86 (d, J = 248.9 Hz), 154.85, 110.20, 100.27 (t, J = 27.4 Hz), 80.57, 42.90, 40.89, 39.22, 28.21. IR (neat, cm^{-1}): 2978.33, 1690.07, 1495.83, 1414.50, 1366.58, 1247.18, 1164.64, 1118.48, 1046.76, 998.68, 840.75, 737.30. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{19}F_3NO_3$: 318.1312, found 318.1311.



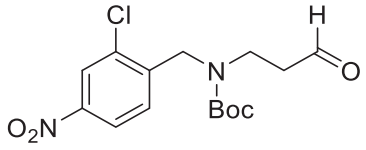
***tert*-butyl (4-nitrilebenzyl)(3-oxopropyl)carbamate s2-h**.

Following the general procedure with **s1-h** as starting material. Yield: 82%. R_f = 0.28 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.65 (br, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.32 (br, 2H), 4.49 (s, 2H), 3.52 and 3.47 (br, 2H), 2.70 (br, 2H), 1.48 and 1.39 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 200.70, 155.23, 144.13, 132.40, 127.51, 118.68, 111.13, 80.76, 51.39, 43.19, 41.34, 28.28. IR (neat, cm^{-1}): 2976.97, 2228.94, 1721.65, 1687.14, 1464.06, 1407.89, 1366.59, 1246.91, 1162.56, 911.52, 729.82. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{16}H_{20}NaN_2O_3$: 311.1366, found 311.1365.

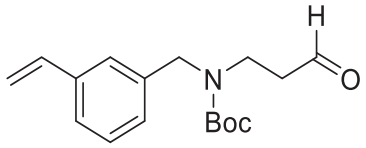


***tert*-butyl (4-nitrobenzyl)(3-oxopropyl)carbamate s2-i**.

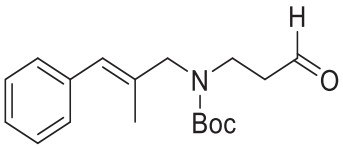
Following the general procedure with **s1-i** as starting material. Yield: 75%. R_f = 0.17 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.77 (br, 1H), 8.18 (d, *J* = 8.4 Hz, 2H), 7.37 (br, 2H), 4.54 (s, 2H), 3.54 and 3.49 (br, 2H), 2.75 and 2.69 (br, 2H), 1.49 and 1.39 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 200.66, 155.19, 147.24, 145.88, 127.50, 123.85, 80.88, 51.27, 43.24, 41.42, 28.30. IR (neat, cm^{-1}): 2976.04, 1687.82, 1519.17, 1407.08, 1343.25, 1245.80, 1161.45, 1129.70, 857.77, 736.67. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{21}N_2O_5$: 309.1445, found 309.1442.



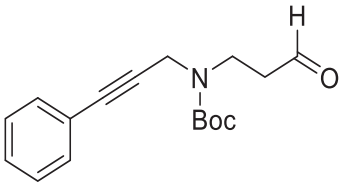
***tert*-butyl (2-chloro-4-nitrobenzyl)(3-oxopropyl) carbamate s2-j**. Following the general procedure with **s1-j** as starting material. Yield: 63%. R_f = 0.28 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.80 (br, 1H), 8.08 – 8.07 (m, br, 2H), 7.53 (d, *J* = 8.3 Hz, 1H), 4.60 (s, 2H), 3.60 (br, 2H), 2.79 (br, 2H), 1.52 and 1.39 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 200.01, 155.06, 146.88, 139.53, 137.63, 130.52, 123.19, 122.72, 81.12, 48.74, 43.16, 41.64, 28.26. IR (neat, cm^{-1}): 2974.99, 2358.32, 1721.79, 1690.64, 1524.76, 1345.34, 1165.17, 1050.10, 925.45, 742.97. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{20}ClN_2O_5$: 343.1060, found 343.1061.



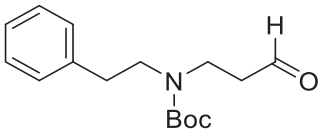
***tert*-butyl (3-vinylbenzyl)(3-oxopropyl)carbamate s2-k**. Following the general procedure with **s1-k** as starting material.Yield: 75%. R_f = 0.33 (ethyl acetate/hexanes: 1/5). ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.72 (br, 1H), 7.29 – 7.10 (m, 4H), 6.68 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.72 (d, *J* = 17.6 Hz, 1H), 5.23 (d, *J* = 10.9 Hz, 1H), 4.42 (s, 2H), 3.50 (br, 2H), 2.64 (br, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): major isomer δ 200.94, 155.51, 138.46, 137.87, 136.58, 128.76, 126.61, 125.58, 125.22, 114.13, 80.29, 51.24, 43.08, 40.84, 28.36. IR (neat, cm^{-1}): 2975.95, 1721.79, 1686.69, 1464.52, 1411.79, 1365.50, 1245.58, 1162.14, 1125.68, 990.63, 713.79. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{17}H_{24}NO_3$: 290.1751, found 290.1754.



***tert*-butyl (*E*)-(2-methyl-3-phenylallyl)(3-oxopropyl) carbamate s2-l**. Following the general procedure with **s1-l** as starting material. Yield: 76%. R_f = 0.43 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.80 (br, 1H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.21 (m, 3H), 6.32 (s, 1H), 3.98 and 3.93 (br, 2H), 3.56 (br, 2H), 2.72 (br, 2H), 1.82 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 201.07, 155.52, 137.35, 134.47, 128.82, 128.15, 126.94, 126.50, 80.09, 55.66, 43.09, 40.49, 28.38, 15.57. IR (neat, cm^{-1}): 2974.97, 2361.33, 1721.79, 1687.60, 1415.91, 1365.91, 1248.45, 1163.36, 1021.08, 746.89. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{18}H_{26}NO_3$: 304.1926, found 304.1913.

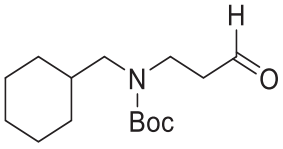


***tert*-butyl (3-oxopropyl)(3-phenylprop-2-yn-1-yl)carbamate s2-m**. Following the general procedure with **s1-m** as starting material.Yield: 57%. R_f = 0.48 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.82 (br, 1H), 7.41 – 7.29 (m, 5H), 4.32 and 4.25 (br, 2H), 3.70 (t, *J* = 6.7 Hz, 2H), 2.82 – 2.80 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 200.73, 154.80, 131.63, 130.08, 128.34, 122.65, 84.82, 83.41, 80.71, 43.14, 40.89, 38.27, 28.35. IR (neat, cm^{-1}): 2976.09, 1721.79, 1689.02, 1409.36, 1366.66, 1248.77, 1160.17, 862.86, 758.50. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{17}H_{22}NO_3$: 288.1611, found 288.1600.



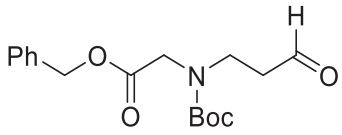
***tert*-butyl (3-oxopropyl)(phenethyl)carbamate s2-n**.

Following the general procedure with **s1-n** as starting material. Yield: 58%. R_f = 0.48 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.73 (br, 1H), 7.29 – 7.16 (m, 5H), 3.40 (br, 4H), 2.80 (br, 2H), 2.63 and 2.57 (br, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): major isomer δ 201.03, 155.33, 139.04, 128.85, 128.49, 126.32, 79.82, 49.94, 43.33, 41.49, 35.28, 28.35. IR (neat, cm^{-1}): 2975.04, 1721.62, 1685.77, 1454.24, 1413.22, 1365.29, 1248.67, 1161.74, 1123.58, 880.75, 736.43, 700.08. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{16}H_{24}NO_3$: 278.1751, found 278.1753.

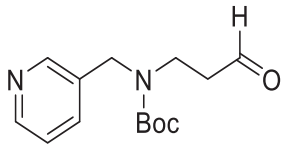


***tert*-butyl (cyclohexylmethyl)(3-oxopropyl)carbamate s2-o**.

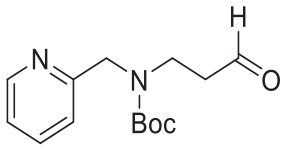
Following the general procedure with **s1-o** as starting material. Yield: 87%. R_f = 0.55 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.78 (t, *J* = 1.4 Hz, 1H), 3.49 (br, 2H), 3.01 (br, 2H), 2.69 (br, 2H), 1.72 – 1.62 (m, 6H), 1.43 (s, 9H), 1.24 – 1.12 (m, 3H), 0.89 (br, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 201.16, 155.75, 79.59, 53.97, 43.10, 41.52, 37.36, 30.81, 28.38, 26.44, 25.89. IR (neat, cm^{-1}): 2923.55, 1723.08, 1684.57, 1415.73, 1365.14, 1170.37, 1147.59, 961.17, 877.61, 771.73. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{28}NO_3$: 270.2064, found 270.2066.



benzyl *N*-(*tert*-butoxycarbonyl)-*N*-(3-oxopropyl)glycinate s2-p. Prepared from PCC (1.5 equiv.) oxidation of corresponding alcohol (2 mmol) in DCM (10 mL) at room temperature according to the literature.[19] R_f = 0.40 (ethyl acetate/hexanes: 1/3). Yield: 68%. ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.75 (br, 1H), 7.35 (m, br, 5H), 5.15 (s, 2H), 4.06 and 3.99 (s, 2H), 3.58 – 3.55 (m, 2H), 2.81 and 2.74 (t, *J* = 6.1 Hz, 2H), 1.47 and 1.34 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 201.22, 170.10, 155.06, 135.41, 128.58, 128.42, 128.24, 80.57, 66.79, 50.88, 43.41, 42.50, 28.09. IR (neat, cm^{-1}): 2926.99, 1750.26, 1700.34, 1457.77, 1367.63, 1173.24, 914.23, 736.59. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{17}H_{24}NO_5$: 322.1659, found 322.1654.

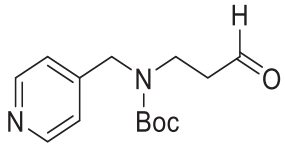


***tert*-butyl (3-oxopropyl)(pyridin-3-ylmethyl)carbamate s2-q**. Following the general procedure with **s1-q** as starting material. Yield: 71%. R_f = 0.20 (ethyl acetate/hexanes: 2/1). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.75 (br, 1H), 8.52 – 8.50 (m, br, 2H), 7.57 (br, 1H), 7.26 (dd, *J* = 7.4, 5.1 Hz, 1H), 4.45 (s, 2H), 3.51 (br, 2H), 2.71 and 2.66 (br, 2H), 1.44 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 200.70, 155.38, 148.84, 135.48, 134.83, 133.83, 123.52, 80.70, 49.19, 43.21, 41.07, 28.33. IR (neat, cm^{-1}): 2975.77, 1720.62, 1686.85, 1478.44, 1409.44, 1365.81, 1249.38, 1162.07, 1129.97, 875.86, 713.32. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{14}H_{21}N_2O_3$: 265.1547, found 265.1556.



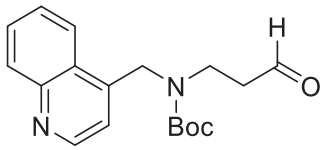
***tert*-butyl (3-oxopropyl)(pyridin-2-ylmethyl)carbamate s2-r**.

Following the general procedure with **s1-r** as starting material. Yield: 74%. R_f = 0.20 (ethyl acetate/hexanes: 2/1). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.75 (br, 1H), 8.50 (br, 1H), 7.64 (t, *J* = 7.7, 1H), 7.17 – 7.15 (m, 2H), 4.55 and 4.51 (s, 2H), 3.65 and 3.59 (br, 2H), 2.72 and 2.65 (br, 2H), 1.47 and 1.36 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 201.01, 158.37, 155.43, 149.18, 136.60, 122.13, 120.89, 80.28, 53.53, 43.05, 41.91, 28.28. IR (neat, cm^{-1}): 2975.74, 1687.60, 1591.29, 1475.96, 1408.49, 1365.67, 1246.26, 1163.19, 994.89, 878.62, 754.68. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{14}H_{21}N_2O_3$: 265.1547, found 265.1550.



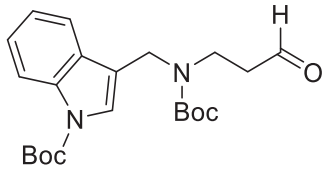
***tert*-butyl (3-oxopropyl)(pyridin-2-ylmethyl)carbamate s2-s**.

Following the general procedure with **s1-s** as starting material. Yield: 35%. R_f = 0.17 (ethyl acetate/hexanes: 2/1). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.76 (br, 1H), 8.55 – 8.53 (br, 2H), 7.11 (br, 2H), 4.44 (s, 2H), 3.54 and 3.48 (br, 2H), 2.74 and 2.67 (br, 2H), 1.48 and 1.37 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 200.66, 155.26, 149.70, 147.77, 121.70, 80.74, 50.85, 43.21, 41.52, 28.24. IR (neat, cm^{-1}): 2976.19, 1688.57, 1601.34, 1464.30, 1409.61, 1366.01, 1249.42, 1162.43, 1065.77, 879.94, 734.18. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{14}H_{21}N_2O_3$: 265.1547, found 265.1552.

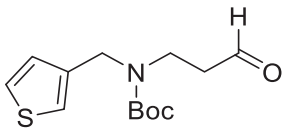


***tert*-butyl (3-oxopropyl)(quinolin-4-ylmethyl)carbamate s2-t**.

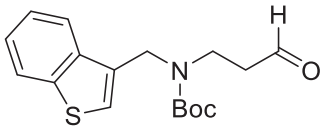
Following the general procedure with **s1-t** as starting material. Yield: 45%. R_f = 0.30 (ethyl acetate/hexanes: 2/1). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.76 (br, 1H), 8.87 (br, 1H), 8.14 (br, 1H), 8.01 (br, 1H), 7.72 (br, 1H), 7.57 (br, 1H), 7.20 (br, 1H), 4.96 (s, 2H), 3.60 and 3.50 (br, 2H), 2.76 and 2.63 (br, 2H), 1.51 and 1.37 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 200.21, 155.30, 150.18, 148.21, 143.20, 130.30, 129.39, 126.82, 126.35, 122.52, 118.08, 80.89, 48.51, 43.31, 41.42, 28.32. IR (neat, cm^{-1}): 2975.18, 1687.63, 1509.19, 1461.66, 1409.40, 1365.69, 1161.94, 1129.36, 840.48, 756.69. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{18}H_{23}N_2O_3$: 315.1703, found 315.1713.



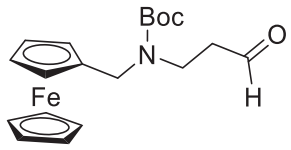
***tert*-butyl 3-(((*tert*-butoxycarbonyl)(3-oxopropyl)amino) methyl)-1*H*-indole-1-carboxylate s2-u.** Following the general procedure with **s1-u** as starting material. Yield: 60%. R_f = 0.41 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.72 (br, 1H), 8.13 (br, 1H), 7.64 (br, 1H), 7.52 (br, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.24 (t, J = 7.4 Hz, 1H), 4.59 (s, 2H), 3.52 and 3.46 (br, 2H), 2.64 and 2.58 (br, 2H), 1.68 (s, 9H), 1.52 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 200.70, 155.22, 149.54, 135.67, 129.39, 124.64, 122.70, 119.77, 119.06, 117.23, 115.23, 83.80, 80.35, 43.30, 41.64, 39.53, 28.43, 28.16. IR (neat, cm^{-1}): 2973.32, 1726.91, 1673.40, 1455.50, 1363.02, 1234.48, 1153.78, 1081.96, 874.61, 752.43. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{22}H_{31}N_2O_5$: 403.2227, found 403.2234.



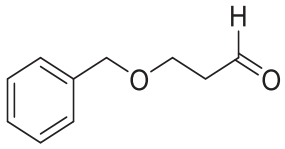
***tert*-butyl (3-oxopropyl)(thiophen-3-ylmethyl)carbamate s2-v.** Following the general procedure with **s1-v** as starting material. Yield: 88%. R_f = 0.40 (ethyl acetate/hexanes: 1/4). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.73 (br, 1H), 7.28 (d, br, 1H), 7.10 (br, 1H), 7.00 (br, 1H), 4.41 (s, 2H), 3.51 (br, 2H), 2.65 and 2.58 (br, 2H), 1.47 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 201.01, 155.27, 139.20, 127.09, 126.28, 121.98, 80.27, 46.76, 43.10, 40.86, 28.39. IR (neat, cm^{-1}): 2976.16, 1721.34, 1683.78, 1463.63, 1365.71, 1248.80, 1162.47, 1123.44, 854.76, 735.58. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{13}H_{20}NO_3S$: 270.1158, found 270.1162.



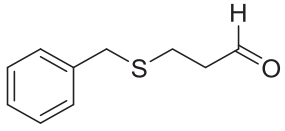
***tert*-butyl (benzo[*b*]thiophen-3-ylmethyl)(3-oxopropyl) carbamate s2-w.** Following the general procedure with **s1-w** as starting material. Yield: 89%. R_f = 0.29 (ethyl acetate/hexanes: 1/4). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.68 (br, 1H), 7.92 – 7.85 (m, br, 2H), 7.40 – 7.26 (m, 3H), 4.72 (s, 2H), 3.54 and 3.47 (br, 2H), 2.62 and 2.51 (br, 2H), 1.50 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 200.61, 155.24, 140.66, 137.92, 132.86, 124.91, 124.58, 124.26, 122.88, 122.29, 80.49, 44.46, 43.29, 39.67, 28.43. IR (neat, cm^{-1}): 2974.69, 1720.93, 1683.07, 1413.06, 1364.83, 1243.88, 1162.81, 862.20, 754.75. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{17}H_{22}NO_3S$: 320.1315, found 320.1312.



***tert*-butyl (ferrocenyl)(3-oxopropyl)carbamate s2-x.** Following the general procedure with **s1-x** as starting material. Yield: 89%. R_f = 0.32 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.70 (br, 1H), 4.20 – 4.11 (m, br, 11H), 3.42 (br, 2H), 2.61 and 2.51 (br, 2H), 1.49 and 1.45 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 200.90, 155.04, 84.18, 79.97, 69.40, 69.05, 68.59, 46.22, 43.54, 40.01, 28.45. IR (neat, cm^{-1}): 3049.39, 2937.10, 1720.99, 1684.63, 1414.52, 1365.01, 1249.79, 1159.30, 1105.13, 864.27, 819.97. HRMS (ESI) ($[M]^+$) Calcd. for $C_{19}H_{25}FeNO_3$: 371.1184, found 371.1180.

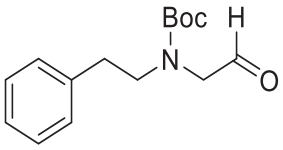


3-(benzyloxy)propanal s2-y, known compound.[20] Following the procedure of Swern oxidation with corresponding alcohol **s1-y** as starting material. Yield: 75%. R_f = 0.42 (ethyl acetate/hexanes: 1/10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.37 – 7.28 (m, 5H), 4.54 (s, 2H), 3.82 (t, J = 6.1 Hz, 2H), 2.70 (td, J = 6.1, 1.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.08, 137.82, 128.43, 127.76, 127.68, 73.25, 63.82, 43.86.

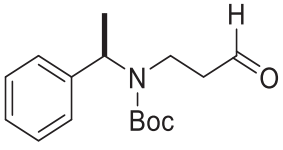


3-(benzylthio)propanal s2-z, known compound.[21] Prepared via Michael addition of benzenemethanethiol (10 mmol) and 2-propenal (12 mmol) according

to the literature.[21] Yield: 85%. R_f = 0.20 (ethyl acetate/hexanes: 1/10). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.34 – 7.24 (m, 5H), 3.74 (s, 2H), 2.71 – 2.69 (m, 2H), 2.67 – 2.64 (m, 2H).^{13}C NMR (150 MHz, $CDCl_3$) δ 200.43, 137.93, 128.80, 128.58, 127.16, 43.33, 36.54, 23.65.



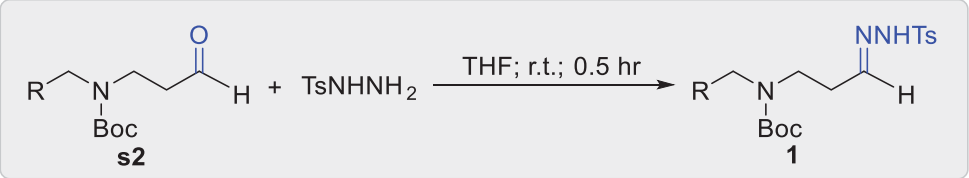
***tert*-butyl (2-oxoethyl)(phenethyl)carbamate s2-aa**. Following the general procedure with **s1-aa** as starting material. Yield: 62%. R_f = 0.40 (ethyl acetate/hexanes: 1/4). ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of amide rotamers. δ 9.46 and 9.36 (br, 1H), 7.29 – 7.13 (m, 5H), 3.81 and 3.66 (s, 2H), 3.51 and 3.47 (t, J = 7.3 Hz, 2H), 2.82 and 2.80 (t, J = 7.3 Hz, 2H), 1.44 and 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): major isomer δ 198.97, 155.68, 138.62, 128.79, 128.58, 126.49, 80.57, 57.68, 50.70, 35.26, 28.21. IR (neat, cm^{-1}): 2975.58, 1262.42, 1735.84, 1694.64, 1455.37, 1418.21, 1367.11, 1249.56, 1168.88, 890.59, 701.75. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{22}NO_3$: 264.1601, found 264.1600.



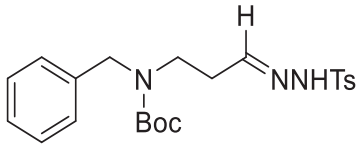
***tert*-butyl (*R*)-(3-oxopropyl)(1-phenylethyl)carbamate s2-ab**. Following the general procedure with **s1-ab** as starting material. Yield: 61%. R_f = 0.32 (ethyl acetate/hexanes: 1/4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (br, 1H), 7.32 (m, br, 5H),

5.47 and 5.37 (br, 1H), 3.32 (br, 2H), 2.51 and 2.37 (br, 2H), 1.53 and 1.48 (br, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): major isomer δ 200.95, 155.46, 141.24, 128.18, 127.40, 126.85, 80.20, 53.41, 44.50, 36.72, 28.33, 17.02. IR (neat, cm^{-1}): 2975.06, 2360.16, 1722.75, 1687.41, 1409.88, 1366.82, 1168.47, 1024.73, 863.41, 701.54. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{16}H_{23}NO_3Na$: 300.1570, found 300.1574.

4.4.5 General Procedure for Preparation of Tosylhydrazone Derivative 1

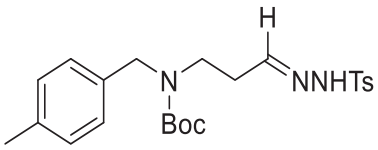


To a stirred solution of pure tosylhydrazide (1 mmol) in THF (2.0 mL) at room temperature, aldehyde **s2** (1 equiv.) was added dropwise (or portionwise if solid). The reaction was completed within 0.5 h. After that, the solvent was removed directly under reduced pressure, and the crude mixture was further purified by flash chromatography.

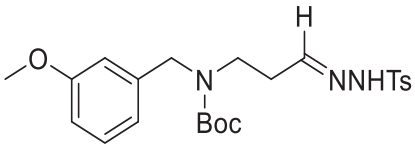


***tert*-butyl benzyl(3-(2-tosylhydrazono)propyl)carbamate 1a**. Following the general procedure with **s2-a** as starting material. Yield: 67%. R_f = 0.36 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 7.84 and 7.70 (d, J = 8.0 Hz, 2H), 7.71 – 7.63 (br, 1H), 7.30 –

7.26 (m, 5H), 7.17 – 7.15 (m, 2H), 7.08 and 6.68 (br, 1H), 4.37 and 4.32 (s, 2H), 3.33 – 3.17 (m, 2H), 2. 41 – 2.25 (m, br, 5H), 1.49 – 1.40 (br, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 155.58, 149.67, 144.10, 137.69, 129.57, 128.53, 127.85, 127.27, 126.68, 125.91, 80.09, 50.31, 43.61, 31.34, 28.37, 21.57. IR (neat, cm^{-1}): 2977.07, 1686.89, 1415.35, 1365.70, 1162.58, 873.32, 733.31, 700.98. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{22}H_{30}N_3O_4S$: 432.1952, found 432.1947.

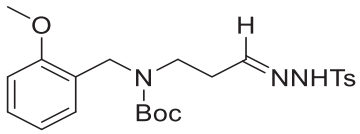


***tert*-butyl (4-methylbenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1b.** Following the general procedure with **s2-b** as starting material. Yield: 81%. R_f = 0.41 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 7.95 – 7.77 (m, 3H), 7.30 – 7.26 (m, 2H), 7.13 – 6.67 (m, 5H), 4.32 and 4.27 (s, 2H), 3.42 – 3.04 (m, 2H), 2.54 – 2.16 (m, 8H), 1.49 – 1.40 (br, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.59, 149.77, 143.95, 136.94, 135.45, 135.04, 129.57, 129.21, 127.84, 127.25, 80.04, 50.45, 43.41, 31.29, 28.39, 21.58, 21.08. IR (neat, cm^{-1}): 3122.77, 2973.91, 1665.43, 1430.9, 1365.17, 1166.33, 879.82, 732.50. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{23}H_{32}N_3O_4S$: 446.2108, found 446.2125.

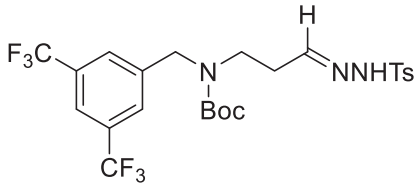


***tert*-butyl (3-methoxybenzyl)(3-(2-tosylhydrazono) propyl) carbamate 1c.** Following the general procedure with **s2-c** as starting material. Yield: 61%. R_f = 0.28 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture

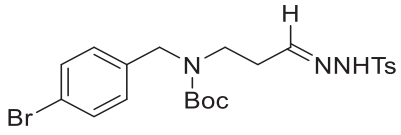
of amide rotamers and hydrazone E/Z isomers. δ 7.94 – 7.77 (m, 3H), 7.30 – 6.99 (m, 4H), 6.81 – 6.69 (m, 3H), 4.33 and 4.29 (s, 2H), 3.79 (s, 3H), 3.32 – 3.17 (m, 2H), 2.42 – 2.27 (m, 5H), 1.49 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 159.81, 155.57, 149.69, 143.98, 139.82, 135.43, 129.58, 129.54, 127.83, 119.52, 113.15, 112.55, 80.11, 55.18, 50.72, 43.54, 31.30, 28.38, 21.57. IR (neat, cm^{-1}): 2968.78, 2854.76, 1688.47, 1413.13, 1253.95, 1162.12, 1047.56, 872.20. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{23}H_{32}N_3O_5S$: 462.2057, found 462.2049.



***tert*-butyl (2-methoxybenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1d.** Following the general procedure with **s2-d** as starting material. Yield: 65%. R_f = 0.40 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 7.96 – 7.77 (m, 3H), 7.36 – 7.11 (m, 5H), 6.99 – 6.69 (m, 2H), 4.39 and 4.35 (s, 2H), 3.81 (s, 3H), 3.40 – 3.07 (m, 2H), 2.45 – 2.25 (m, 5H), 1.48 – 1.37 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 157.15, 155.88, 149.93, 146.65, 143.88, 135.49, 129.56, 128.79, 127.83, 126.09, 120.38, 110.16, 79.86, 55.05, 45.38, 43.76, 31.41, 28.40, 21.57. IR (neat, cm^{-1}): 2977.19, 1660.24, 1464.33, 1358.72, 1162.73, 1026.93, 885.05, 755.96. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{23}H_{32}N_3O_5S$: 462.2057, found 462.2048.

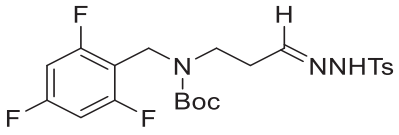


***tert*-butyl (3,5-bis(trifluoromethyl)benzyl)(3-(2-tosylhydrazono)propyl)carbamate 1e.** Following the general procedure with **s2-e** as starting material. Yield: 85%. R_f = 0.40 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.12 (br, 1H), 7.78 (d, *J* = 7.7 Hz, 3H), 7.63 (s, 2H), 7.31 – 7.20 (m, 3H), 4.45 and 4.42 (s, 2H), 3.41 – 3.30 (m, 2H), 2.48 – 2.40 (m, 5H), 1.44 and 1.36 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.18, 148.84, 144.24, 141.40, 135.27, 131.83 (q, *J* = 33.2 Hz), 129.63, 127.81, 127.15, 123.21 (q, *J* = 272.8 Hz), 121.21, 80.90, 50.48, 44.06, 31.44, 28.20, 21.51. IR (neat, cm^{-1}): 3194.52, 2978.63, 1694.05, 1668.00, 1367.42, 1276.06, 1161.98, 900.41, 680.93. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{24}H_{28}F_6N_3O_4S$: 568.1699, found 568.1710.

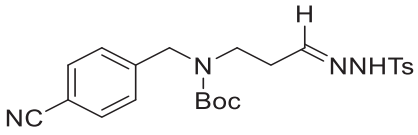


***tert*-butyl (4-bromobenzyl)(3-(2-tosylhydrazono) propyl) carbamate 1f.** Following the general procedure with **s2-f** as starting material. Yield: 75%. R_f = 0.37 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.09 (br, 1H), 7.86 – 7.76 (m, 2H), 7.43 (m, br, 2H), 7.31 – 7.26 (m, 2H), 7.14 – 7.04 (m, 3H), 4.30 (s, 2H), 3.33 and 3.24 (br, 2H), 2.43 – 2.31 (m, 5H), 1.44 (s, br, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.49, 149.34, 144.16, 137.31, 135.45, 131.62, 129.61, 128.83, 127.84, 121.03, 80.34, 50.34, 43.65, 31.47, 28.36, 21.60. IR (neat, cm^{-1}): 3130.31, 2975.16, 1666.19, 1427.70, 1339.69,

1166.46, 813.79, 723.12. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{22}H_{29}BrN_3O_4S$: 510.1057, found 510.1033.

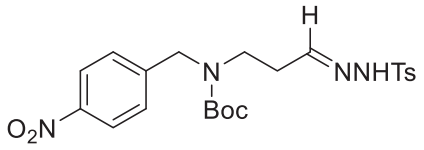


***tert*-butyl (2,4,6-trifluorobenzyl)(3-(2-tosylhydrazono) propyl) carbamate 1g.** Following the general procedure with **s2-g** as starting material. Yield: 67%. R_f = 0.45 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.02 (br, 1H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.15 (br, 1H), 6.71 – 6.62 (m, 2H), 4.42 and 4.34 (s, 2H), 3.35 – 3.18 (m, 2H), 2.40 – 2.26 (m, 5H), 1.47 – 1.37 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 162.80, 160.71, 155.01, 149.43, 143.99, 135.30, 129.55, 127.84, 109.98, 100.22, 80.39, 43.37, 38.59, 31.39, 28.22, 21.55. IR (neat, cm^{-1}): 3106.87, 2966.96, 1692.92, 1442.19, 1365.94, 1163.80, 1116.32, 1046.30, 872.38, 663.57. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{22}H_{27}F_3N_3O_4S$: 486.1669, found 486.1661.

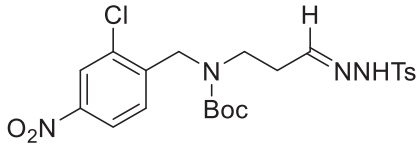


***tert*-butyl (4-nitrilebenzyl)(3-(2-tosylhydrazono) propyl) carbamate 1h.** Following the general procedure with **s2-h** as starting material. Yield: 57%. R_f = 0.21 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.20 (s, 1H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.59 (m, 2H), 7.31 – 7.25 (m, 4H), 7.17 (s, 1H), 4.41 and 4.38 (s, 2H), 3.38 – 3.28 (br, 2H),

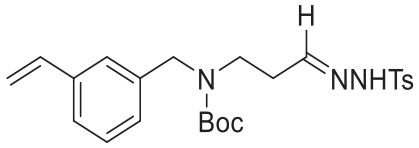
2.42 – 2.41 (m, 5H), 1.43 and 1.34 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.43, 149.01, 144.15, 135.41, 132.37, 129.63, 127.98, 127.80, 127.51, 118.76, 111.02, 80.63, 50.93, 44.11, 31.58, 28.28, 21.59. IR (neat, cm^{-1}): 3145.62, 2973.85, 2227.90, 1666.96, 1365.54, 1164.76, 1053.56, 812.85. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{23}H_{29}N_4O_4S$: 457.1904, found 457.1920.



***tert*-butyl (4-nitrobenzyl)(3-(2-tosylhydrazono) propyl) carbamate 1i.** Following the general procedure with **s2-i** as starting material. Yield: 59%. R_f = 0.26 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.15 (br, 2H), 7.90 (s, 1H), 7.83 – 7.75 (m, 2H), 7.39 – 7.07 (m, 5H), 4.44 and 4.42 (s, 2H), 3.40 and 3.29 (m, br, 2H), 2.40 – 2.39 (m, 5H), 1.42 and 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): major isomer δ 155.32, 148.92, 147.26, 145.96, 144.26, 135.37, 129.62, 128.02, 127.60, 123.78, 80.70, 50.80, 44.14, 31.64, 28.27, 21.56. IR (neat, cm^{-1}): 3198.38, 2976.31, 1667.31, 1342.94, 1160.54, 813.21, 664.41. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{22}H_{29}N_4O_6S$: 477.1802, found 477.1812.

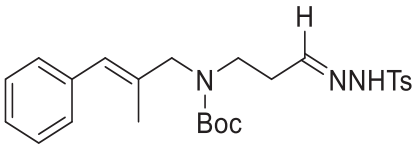


***tert*-butyl (2-chloro-4-nitrobenzyl)(3-(2-tosylhydrazono)propyl)carbamate 1j.** Following the general procedure with **s2-j** as starting material. Yield: 63%. R_f = 0.36 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.06 – 7.96 (m, 3H), 7.77 (d, *J* = 7.9 Hz, 2H), 7.52 (m, br, 1H), 7.31 – 7.28 (m, 2H), 7.20 (m, br, 1H), 4.50 and 4.45 (s, 2H), 3.45 – 3.31 (m, 2H), 2.49 – 2.40 (m, 5H), 1.46 and 1.36 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 157.86, 151.52, 149.50, 146.92, 142.35, 140.74, 137.99, 133.16, 132.30, 130.46, 125.84, 125.61, 83.72, 51.35, 47.20, 34.07, 30.90, 24.24. IR (neat, cm^{-1}): 3193.25, 2975.19, 1690.76, 1670.95, 1523.00, 1343.10, 1160.55, 1049.95, 812.31. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{22}H_{27}ClN_4NaO_6S$: 533.1232, found 533.1228.

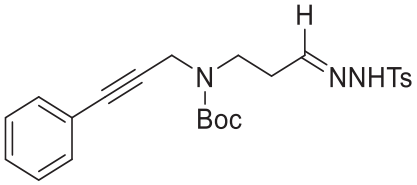


***tert*-butyl (3-vinylbenzyl)(3-(2-tosylhydrazono) propyl) carbamate 1k.** Following the general procedure with **s2-k** as starting material. Yield: 79%. R_f = 0.42 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.11 (br, 1H), 7.80 (d, *J* = 7.8 Hz, 2H), 7.26 – 7.25 (m, 5H), 7.20 (m, br, 2H), 6.72 – 6.66 (m, 1H), 5.73 (dd, *J* = 17.6, 3.4 Hz, 1H), 5.25 (d, *J* = 10.8 Hz, 1H), 4.35 and 4.31 (s, 2H), 3.33 – 3.19 (m, 2H), 2.40 – 2.29 (m, 5H), 1.48 – 1.39 (br, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.61, 149.57, 143.97, 138.48, 137.83, 136.59, 135.43, 129.57, 128.74, 127.82, 126.64, 125.43, 125.13, 114.19,

80.15, 50.66, 43.54, 31.32, 28.38, 21.57. IR (neat, cm^{-1}): 3192.54, 2976.69, 1688.26, 1414.31, 1365.24, 1160.59, 904.80, 663.86. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{24}H_{32}N_3O_4S$: 458.2108, found 458.2119.

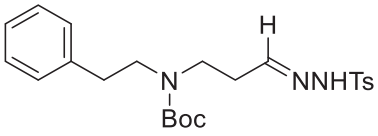


***tert*-butyl ((*E*)-2-methyl-3-phenylallyl)(3-(2-tosylhydrazono)propyl)carbamate 1l.** Following the general procedure with **s2-l** as starting material. Yield: 61%. R_f = 0.30 (ethyl acetate/hexanes: 1/2). ^1H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.20 (br, 1H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.33 – 7.21 (m, 8H), 6.25 (s, 1H), 3.86 (s, 2H), 3.36 – 3.20 (m, 2H), 2.44 – 2.37 (m, 5H), 1.76 (s, 3H), 1.48 – 1.41 (br, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 155.63, 149.72, 146.57, 143.87, 137.39, 134.46, 129.55, 128.82, 128.15, 127.82, 126.65, 126.49, 79.94, 55.13, 43.20, 31.46, 28.36, 21.53, 15.56. IR (neat, cm^{-1}): 2975.79, 1687.33, 1660.61, 1415.37, 1364.83, 1160.16, 1051.97, 699.62. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{25}H_{33}N_3NaO_4S$: 494.2084, found 494.2083.

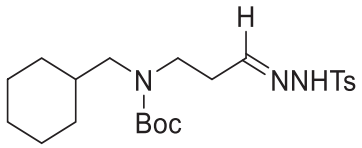


***tert*-butyl (3-phenylprop-2-yn-1-yl)(3-(2-tosylhydrazono)propyl)carbamate 1m.** Following the general procedure with **s2-m** as starting material. Yield: 88%. R_f = 0.43 (ethyl acetate/hexanes: 1/2). ^1H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 7.88 (br, 1H), 7.79 (d,

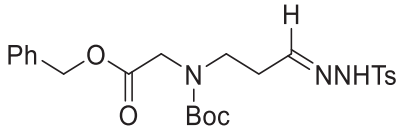
J = 8.0 Hz, 2H), 7.40 – 7.39 (m, 2H), 7.31 – 7.26 (m, 5H), 7.20 (t, *J* = 5.1 Hz, 1H), 4.20 and 4.14 (br, 2H), 3.51 – 3.39 (m, 2H), 2.56 – 2.49 (m, 2H), 2.39 (s, 3H), 1.49 and 1.43 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.84, 149.61, 144.07, 135.37, 131.64, 129.59, 128.36, 128.33, 127.86, 122.67, 84.82, 84.25, 80.50, 60.38, 43.43, 31.49, 28.35, 21.55. IR (neat, cm^{-1}): 3192.75, 2976.10, 1692.14, 1409.42, 1365.32, 1159.93, 1049.77, 756.86, 691.46. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{24}H_{29}N_3NaO_4S$: 478.1771, found 478.1774.



***tert*-butyl phenethyl(3-(2-tosylhydrazono) propyl)carbamate 1n**. Following the general procedure with **s2-n** as starting material. Yield: 58%. R_f = 0.40 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.46 (br, 1H), 7.76 (d, *J* = 7.8 Hz, 2H), 7.28 – 7.12 (m, 8H), 3.33 – 3.11 (m, 4H), 2.72 – 2.71 (m, 2H), 2.39 – 2.25 (m, 5H), 1.43 – 1.36 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.43, 149.48, 143.84, 139.06, 135.54, 129.55, 128.82, 128.49, 127.82, 126.30, 79.73, 49.43, 44.14, 35.26, 31.75, 28.34, 21.55. IR (neat, cm^{-1}): 3194.97, 2974.90, 1660.43, 1415.49, 1364.79, 1159.91, 813.28, 748.04, 700.45. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{23}H_{32}N_3O_4S$: 446.2108, found 446.2101.

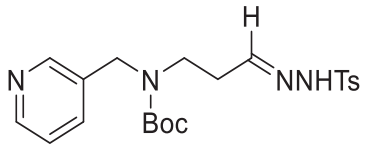


***tert*-butyl (cyclohexylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1o**. Following the general procedure with **s2-o** as starting material. Yield: 73%. R_f = 0.32 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.12 (br, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 2H), 7.17 (br, 1H), 3.29 – 3.11 (m, br, 2H), 2.96 – 2.90 (m, 2H), 2.41 – 2.38 (m, br, 5H), 1.69 – 1.59 (m, 5H), 1.46 – 1.38 (m, 10H), 1.22 – 1.12 (m, 3H), 0.88 – 0.84 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.84, 149.78, 146.13, 143.87, 129.55, 127.84, 79.47, 53.38, 44.18, 37.22, 31.38, 30.84, 28.37, 26.45, 25.90, 21.56. IR (neat, cm^{-1}): 3196.28, 2923.97, 1659.99, 1417.60, 1365.18, 1163.60, 1050.74, 812.99, 736.06. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{22}H_{36}N_3O_4S$: 438.2421, found 438.2427.

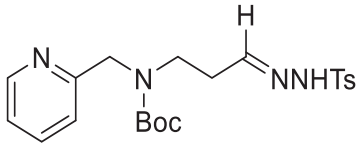


benzyl *N*-(*tert*-butoxycarbonyl)-*N*-(3-(2-tosylhydrazono)propyl)glycinate 1p. Following the general procedure with **s2-p** as starting material. Yield: 72%. R_f = 0.5 (ethyl acetate/hexanes: 1/1). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 7.94 (s, 1H), 7.85 – 7.75 (m, 2H), 7.38 – 7.25 (m, 7H), 7.14 – 7.13 and 6.80 - 6.76 (m, 1H), 5.21 and 5.12 (s, 2H), 3.94 and 3.80 (s, 2H), 3.44 – 3.30 (m, 2H), 2.46 – 2.37 (m, 5H), 1.41 and 1.25 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 169.92, 155.09, 149.57, 147.49, 144.03, 135.43, 129.61, 128.61, 128.46, 128.33, 127.84, 80.54, 66.81, 50.06, 45.80, 31.47, 28.08,

21.54. IR (neat, cm^{-1}): 3194.32, 2976.82, 1746.99, 1694.34, 1455.86, 1365.77, 1249.43, 1159.51, 888.95, 750.98. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{24}H_{32}N_3O_6S$: 490.2052, found 490.2065.

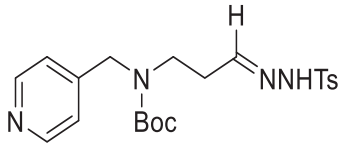


***tert*-butyl (pyridin-3-ylmethyl)(3-(2-tosylhydrazono) propyl) carbamate 1q**. Following the general procedure with **s2-q** as starting material. Yield: 56%. R_f = 0.40 (ethyl acetate/hexanes: 3/1). ^1H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.83 (br, 1H), 8.49 – 8.41 (m, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.54 (m, br, 1H), 7.34 – 7.12 (m, 4H), 4.36 and 4.32 (s, 2H), 3.36 – 3.27 (m, 2H), 2.43 – 2.39 (m, 5H), 1.45 – 1.36 (br, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.33, 148.91, 148.57, 143.95, 135.57, 135.04, 133.96, 129.91, 129.58, 127.77, 123.61, 80.52, 48.65, 43.87, 31.54, 28.32, 21.56. IR (neat, cm^{-1}): 2976.36, 1687.57, 1410.54, 1159.16, 1054.28, 813.41, 706.76. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{21}H_{29}N_4O_4S$: 433.1904, found 433.1917.

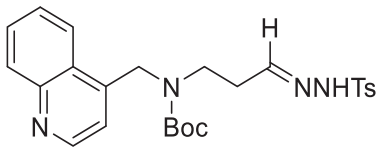


***tert*-butyl (pyridin-2-ylmethyl)(3-(2-tosylhydrazono) propyl) carbamate 1r.** Following the general procedure with **s2-r** as starting material. Yield: 61%. R_f = 0.43 (ethyl acetate/hexanes: 3/1). ^1H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.86 – 8.50 (m, br, 1H), 8.04 and 8.10 (s, 1H), 7.79 – 7.66 (m, 3H), 7.28 – 7.12 (m, 5H), 4.51 and 4.42 (s, 2H), 3.46 – 3.37 (m, 2H),

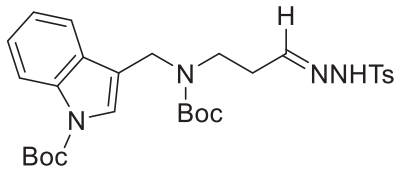
2.44 – 2.40 (m, 5H), 1.44 – 1.33 (br, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 160.99, 158.17, 152.21, 151.62, 146.23, 139.81, 138.77, 132.20, 130.50, 124.83, 123.67, 82.91, 56.81, 47.29, 34.31, 30.91, 24.22. IR (neat, cm^{-1}): 3128.02, 2973.70, 1656.61, 1464.10, 1408.22, 1319.68, 1163.60, 1059.44, 872.65. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{21}H_{29}N_4O_4S$: 433.1904, found 433.1910.



***tert*-butyl (pyridin-4-ylmethyl)(3-(2-tosylhydrazono) propyl) carbamate 1s**. Following the general procedure with **s2-s** as starting material. Yield: 49%. R_f = 0.23 (ethyl acetate/hexanes: 4/1). ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.51 – 8.50 (m, br, 3H), 7.76 (d, J = 8.0 Hz, 2H), 7.34 – 7.04 (m, 5H), 4.34 and 4.32 (s, 2H), 3.38 – 3.28 (m, br, 2H), 2.42 – 2.33 (m, 5H), 1.41 and 1.23 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.39, 149.75, 148.78, 147.95, 144.02, 135.62, 129.60, 127.79, 121.83, 80.62, 50.31, 44.24, 31.63, 28.27, 21.59. IR (neat, cm^{-1}): 2976.44, 1689.00, 1410.49, 1365.61, 1159.55, 885.60, 813.39, 752.47. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{21}H_{29}N_4O_4S$: 433.1904, found 433.1915.

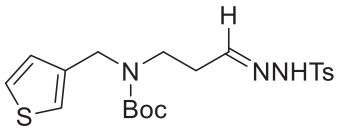


***tert*-butyl (quinolin-4-ylmethyl)(3-(2-tosylhydrazono) propyl) carbamate 1t**. Following the general procedure with **s2-t** as starting material. Yield: 79%. R_f = 0.30 (ethyl acetate/hexanes: 3/1). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.85 (m, br, 1H), 8.44 (m, br, 1H), 8.14 (m, br, 1H), 8.98 – 7.74 (m, 4H), 7.59 (m, br, 1H), 7.31 – 7.11 (m, 4H), 4.87 (br, 2H), 3.45 – 3.32 (m, 2H), 2.49 – 2.31 (m, 5H), 1.48 and 1.27 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.33, 150.06, 149.06, 147.86, 144.09, 143.67, 135.28, 130.08, 129.58, 127.77, 126.91, 126.32, 122.61, 119.27, 118.00, 80.72, 48.05, 44.15, 31.60, 28.28, 21.54. IR (neat, cm^{-1}): 2974.45, 1689.81, 1476.24, 1353.48, 1162.34, 1057.39, 894.38, 762.94, 680.14. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{25}H_{30}N_4NaO_4S$: 505.1880, found 505.1875.

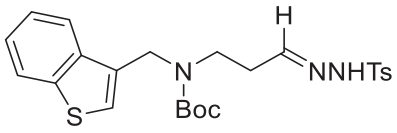


***tert*-butyl 3-(((*tert*-butoxycarbonyl)(3-(2-tosylhydrazono)propyl)amino)methyl)-1*H*-indole-1-carboxylate 1u**. Following the general procedure with **s2-u** as starting material. Yield: 88%. R_f = 0.35 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.13 (s, 1H), 7.81 and 7.76 (d, J = 8.0 Hz, 2H), 7.59 – 7.48 (m, 2H), 7.35 – 7.22 (m, 5H), 7.05 – 6.66 (m, 1H), 4.50 and 4.47 (s, 2H), 3.33 – 3.13 (m, 2H), 2.43 – 2.21 (m, 5H), 1.68 (s, 9H), 1.47 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 151.67, 149.77, 144.00, 142.47, 135.72, 131.75, 129.55, 127.98, 124.86, 123.72, 122.54,

119.13, 117.11, 115.73, 115.18, 82.56, 80.31, 61.51, 47.05, 41.31, 28.37, 28.19, 21.57. IR (neat, cm^{-1}): 2976.21, 1731.20, 1686.43, 1451.78, 1364.56, 1253.66, 1156.11, 1082.02, 855.63, 766.62, 663.65. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{29}H_{38}N_4NaO_6S$: 593.2404, found 593.2430.

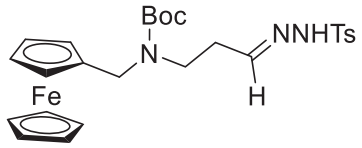


***tert*-butyl (thiophen-3-ylmethyl)(3-(2-tosylhydrazono) propyl) carbamate 1v**. Following the general procedure with **s2-v** as starting material. Yield: 87%. R_f = 0.34 (ethyl acetate/hexanes: 1/2). ^1H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.01 – 7.96 (m, 1H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.29 – 7.26 (m, 3H), 7.09 – 6.93 (m, 3H), 4.34 and 4.29 (s, 2H), 3.32 – 3.19 (m, 2H), 2.45 – 2.25 (m, 5H), 1.48 – 1.42 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.34, 149.67, 144.03, 139.15, 138.70, 135.45, 129.59, 127.85, 126.13, 122.46, 80.12, 46.29, 43.54, 31.41, 28.39, 21.59. IR (neat, cm^{-1}): 3107.86, 2977.68, 1659.83, 1366.08, 1250.89, 1162.09, 1053.71, 812.58, 734.14. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{20}H_{27}N_3NaO_4S_2$: 460.1335, found 460.1356.

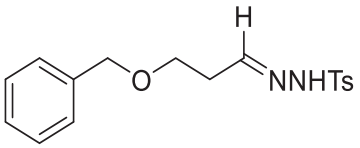


***tert*-butyl (benzo[*b*]thiophen-3-ylmethyl)(3-(2-tosylhydrazono)propyl)carbamate 1w**. Following the general procedure with **s2-w** (5 mmol) as starting material. Yield: 80%. R_f = 0.29 (ethyl acetate/hexanes: 1/2). ^1H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 7.87 – 7.76

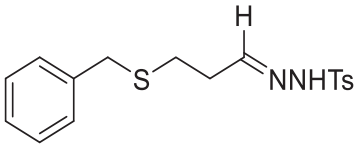
(m, 5H), 7.37 (m, 2H), 7.37 – 7.05 (m, 4H), 4.63 and 4.59 (s, 2H), 3.35 – 3.18 (m, 2H), 2.40 – 2.17 (m, 5H), 1.54-1.45 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.34, 149.65, 146.18, 144.12, 140.66, 137.95, 135.23, 132.87, 129.60, 127.85, 124.60, 124.34, 122.84, 121.61, 80.25, 44.33, 42.97, 31.50, 28.41, 21.58. IR (neat, cm^{-1}): 3191.11, 2975.32, 1661.25, 1414.33, 1364.38, 1160.79, 876.54, 767.28, 664.08. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{24}H_{29}N_3NaO_4S_2$: 510.1492, found 510.1512.



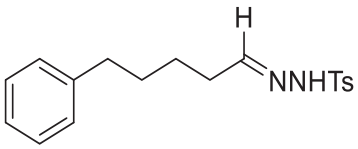
***tert*-butyl (ferrocenyl)(3-(2-tosylhydrazono)propyl) carbamate 1x.** Following the general procedure with **s2-x** as starting material. Yield: 50%. R_f = 0.17 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 7.81 – 7.68 (m, 3H), 7.30 (br, 2H), 6.67 – 6.65 (br, 1H), 4.33 – 3.86 (m, 11H), 3.22 –3.09 (m, br, 2H), 2.43 – 2.19 (br, 5H), 1.52 – 1.40 (br, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 157.77, 152.60, 146.59, 137.98, 132.21, 130.48, 82.46, 71.62 (br), 49.32, 46.11, 34.39, 31.11, 24.26. IR (neat, cm^{-1}): 3096.54, 2973.63, 1660.36, 1417.00, 1365.18, 1250.72, 1037.85, 812.76. HRMS (ESI) ($[M]^+$) Calcd. for $C_{26}H_{33}FeN_3O_4S$: 539.1541, found 539.1539.



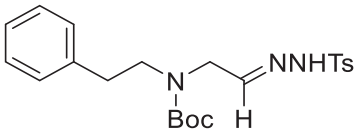
***N*'-(3-(benzyloxy)propylidene)-4-methylbenzene sulfonohydrazide 1y**. Following the general procedure with **s2-y** as starting material. Yield: 78%. R_f = 0.24 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of hydrazone E/Z isomers. δ 8.97 (s, 1H), 7.80 (d, *J* = 8.3 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.34 – 7.19 (m, 8H), 4.45 (s, 2H), 3.61 – 3.55 (m, 2H), 2.54 – 2.46 (m, 2H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.51, 143.67, 136.72, 135.54, 129.44, 128.63, 127.90, 127.80, 127.63, 73.59, 67.48, 28.86, 21.55. IR (neat, cm^{-1}): 3209.79, 2851.50, 1595.31, 1453.36, 1379.35, 1187.33, 1016.10, 892.07, 735.34, 666.22. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{17}H_{21}N_2O_3S$: 333.1267, found 333.1259.



***N*'-(3-(benzylthio)propylidene)-4-methylbenzene sulfonohydrazide 1z**. Following the general procedure with **s2-z** as starting material. Yield: 72%. R_f = 0.26 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of hydrazone E/Z isomers. δ 7.84 – 7.79 (m, 3H), 7.32 – 7.24 (m, 7H), 7.10 (t, *J* = 5.0 Hz, 1H), 3.66 and 3.63 (s, 2H), 2.52 (t, *J* = 7.2 Hz, 2H), 2.44 – 2.41 (m, 5H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 152.86, 146.82, 140.67, 137.84, 132.28, 131.46, 131.20, 130.58, 129.74, 38.84, 34.62, 30.36, 24.26. IR (neat, cm^{-1}): 3193.77, 2921.72, 1595.81, 1357.63, 1325.51, 1155.62, 1041.82, 1003.59, 924.56, 814.73. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{17}H_{21}N_2O_2S_2$: 349.1039, found 349.1042.

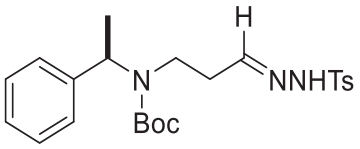


4-methyl-*N*′-(5-phenylpentylidene)benzenesulfonohydrazide 1aa. Following the general procedure with 5-phenylpentanal as starting material. Yield: 71%. R_f = 0.40 (ethyl acetate/hexanes: 1/3). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of hydrazone E/Z isomers. δ 8.01 and 7.92 (s, 1H), 7.83 and 7.80 (d, *J* = 8.3 Hz, 2H), 7.28 – 7.27 (m, 4H), 7.21 – 7.10 (m, 4H), 2.55 (t, *J* = 7.6 Hz, 2H), 2.42 and 2.39 (s, 3H), 2.21 (td, *J* = 7.3, 5.7 Hz, 1.5 H), 2.10 (td, *J* = 7.4, 5.5 Hz, 0.5H), 1.61 – 1.43 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 155.33, 146.72, 144.73, 137.91, 132.25, 131.00, 130.95, 130.54, 128.42, 38.16, 34.75, 33.21, 28.24, 24.24. IR (neat, cm^{-1}): 3205.50, 2939.40, 1437.91, 1354.08, 1317.49, 1160.42, 1039.46, 906.24, 815.23. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{18}H_{23}N_2O_2S$: 331.1475, found 331.1481.



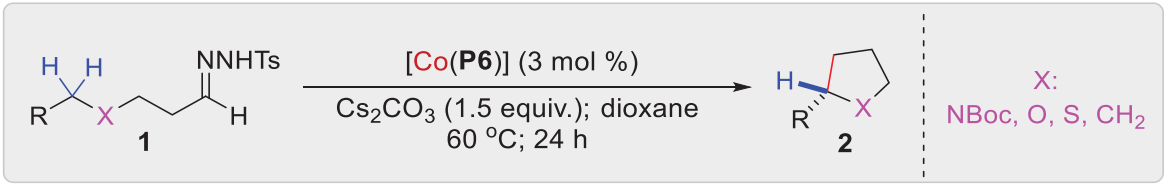
***tert*-butyl phenethyl(2-(2-tosylhydrazono)ethyl)carbamate 1ab**. Following the general procedure with **s2-aa** as starting material. Yield: 84%. R_f = 0.33 (ethyl acetate/hexanes: 1/2). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. δ 8.01 and 7.96 (s, 1H), 7.81 and 7.71 (d, *J* = 8.3 Hz, 2H), 7.27 – 7.24 (m, 5H), 7.08 – 7.03 (m, 2H), 6.86 – 6.65 (br, 1H), 3.84 and 3.68 (d, *J* = 6.2 Hz, 2H), 3.41 – 3.22 (m, 2H), 2.76 – 2.67 (m, 2H), 2.41-2.33 (br, 3H), 1.39 and 1.38 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 158.08, 149.66, 146.83, 141.45,

137.91, 132.27, 131.60, 131.15, 130.49, 129.02, 83.00, 51.76, 50.97, 37.57, 30.95, 24.16. IR (neat, cm^{-1}): 2975.01, 1662.62, 1454.17, 1365.19, 1339.53, 1157.90, 1094.23, 893.29, 700.35. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{22}H_{29}N_3NaO_4S$: 454.1771, found 454.1773.

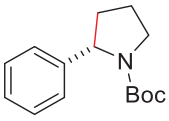


***tert*-butyl (*R*)-(1-phenylethyl)(3-(2-tosylhydrazono) propyl) carbamate 4a**. Following the general procedure with **s2-ab** as starting material. Yield: 83%. R_f = 0.27 (ethyl acetate/hexanes: 1/3). We are unable to get a consistent value for optical rotation, presumably due to the interconversion of amide rotamers in this linear molecule. ^1H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers and hydrazone E/Z isomers. 7.93 (s, 1H), 7.83 – 7.75 (m, 2H), 7.27 – 7.26 (m, 7H), 6.56 and 6.54 (br, 1H), 5.31 (br, 1H), 3.05 – 2.90 (m, br, 2H), 2.41 (br, 3H), 2.21 – 1.96 (br, 2H), 1.52 (s, 3H), 1.46 – 1.42 (br, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 155.49, 150.00, 143.81, 141.62, 135.69, 129.41, 128.31, 127.88, 127.19, 126.97, 79.92, 53.82, 32.84, 28.42, 28.39, 21.40, 17.20. HPLC analysis: *ee* = 99%. ADH (90% hexanes: 10% isopropanol, 1.0 mL/min) : t_{major} = 21.01 min, t_{minor} = 26.81 min. IR (neat, cm^{-1}): 3200.18, 2976.53, 1682.86, 1451.44, 1365.15, 1159.39, 1043.39, 813.42, 699.72. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{23}H_{31}N_3NaO_4S$: 468.1927, found 468.1921.

4.4.6 General Procedure for [Co(P6)]-Catalyzed Enantioselective Radical Cyclization

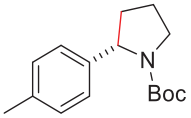


An oven-dried Schlenk tube was charged with sulfonyl hydrazone **1** (0.1 mmol), [Co(**P6**)] (3 mol %) and 1.5 equivalent of Cs_2CO_3 (0.15 mmol). The Schlenk tube was then evacuated and backfilled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, dioxane (0.6 mL) was added via a gas-tight syringe. The tube was then purged with nitrogen for 30 s and the rubber septum was replaced with a Teflon screw cap. The mixture was then stirred at 60 °C. After 24 h, the reaction mixture was concentrated and purified by flash chromatography. The fractions containing product were collected and concentrated by rotary evaporation to afford the desired compound **2**.

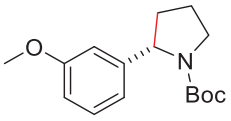


***tert*-butyl (*S*)-2-phenylpyrrolidine-1-carboxylate 2a**, known compound.[22] Following the general procedure with **1a** as starting material. Yield: 93%. *ee*: 92%. Hexanes/ethyl acetate = 8/1, R_f = 0.45. $[\alpha]^{20}_D$ = -55.6 (*c* = 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.30 – 7.15 (m, 5H), 4.96 and 4.76 (m, br, 1H), 3.62 and 3.52 (m, br, 2H), 2.31 (m, br, 1H), 1.90 – 1.83 (m, 3H), 1.45 (s, 3H), 1.17 (s,

6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.56, 145.13, 128.08, 126.44, 125.48, 79.15, 61.33, 47.08, 36.01, 28.12, 23.18. HPLC analysis: *ee* = 92%. OJH (99% hexanes : 1% isopropanol, 1.0 mL/min): t_{major} = 8.73 min, t_{minor} = 7.26 min. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{22}NO_2$: 248.1645, found 248.1654.

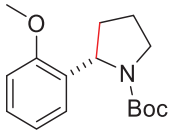


***tert*-butyl (*S*)-2-(*p*-tolyl)pyrrolidine-1-carboxylate 2b**, known compound.[22] Following the general procedure with **1b** as starting material. Yield: 84%. *ee*: 93%. Hexanes/ethyl acetate = 8/1, R_f = 0.45. $[\alpha]^{20}_D$ = -166.0 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.10 – 7.05 (m, 4H), 4.92 and 4.74 (m, br, 1H), 3.61 (m, br, 2H), 2.32 (m, br, 4H), 1.89 – 1.82 (m, 3H), 1.45 (s, 3H), 1.20 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.64, 142.05, 135.90, 128.72, 125.40, 79.09, 61.01, 46.99, 35.99, 28.18, 23.10, 21.02. HPLC analysis: *ee* = 93%. ADH (99.9% hexanes : 0.1% isopropanol, 1.0 mL/min): t_{major} = 19.55 min, t_{minor} = 18.40 min. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{16}H_{24}NO_2$: 262.1802, found 262.1804.

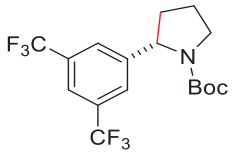


***tert*-butyl (*S*)-2-(3-methoxyphenyl)pyrrolidine-1-carboxylate 2c**, known compound.[22] Following the general procedure with **1c** as starting material. Yield: 91%. *ee*: 93%. Hexanes/ethyl acetate = 6/1, R_f = 0.40. $[\alpha]^{20}_D$ = -69.6 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.20 (t, *J* = 7.9 Hz, 1H), 6.76 –

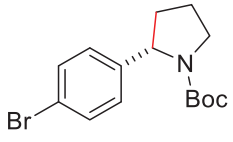
6.71 (m, 3H), 4.94 and 4.74 (m, br, 1H), 3.79 (s, 3H), 3.61 and 3.45 (m, br, 2H), 2.30 (m, br, 1H), 1.90 – 1.84 (m, 3H), 1.46 (s, 3H), 1.20 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 159.57, 154.57, 146.90, 129.11, 117.92, 111.66, 111.25, 79.18, 61.26, 55.17, 47.04, 35.91, 28.17, 23.18. HPLC analysis: *ee* = 93%. ADH (99% hexanes : 1% isopropanol, 1.0 mL/min): t_{major} = 16.75 min, t_{minor} = 14.06 min. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{16}H_{24}NO_3$: 278.1752, found 278.1756.



***tert*-butyl (*S*)-2-(2-methoxyphenyl)pyrrolidine-1-carboxylate 2d**, known compound.[22] Following the general procedure with **1d** as starting material. Yield: 87%. *ee*: 91%. Hexanes/ethyl acetate = 6/1, R_f = 0.40. $[\alpha]^{20}_D$ = -58.6 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.19 (t, *J* = 7.1 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 5.25 – 5.09 (m, br, 1H), 3.83 (s, 3H), 3.62 – 3.46 (m, br, 2H), 2.29 – 2.21 (m, br, 1H), 1.82 (m, br, 3H), 1.46 and 1.18 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 156.11, 154.57, 132.93, 127.32, 125.92, 120.12, 110.16, 78.84, 56.08, 55.34, 46.86, 33.88, 28.13, 23.09. HPLC analysis: *ee* = 91%. ADH (99% hexanes : 1% isopropanol, 1.0 mL/min): t_{major} = 9.57 min, t_{minor} = 11.71 min. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{16}H_{24}NO_3$: 278.1752, found 278.1758.

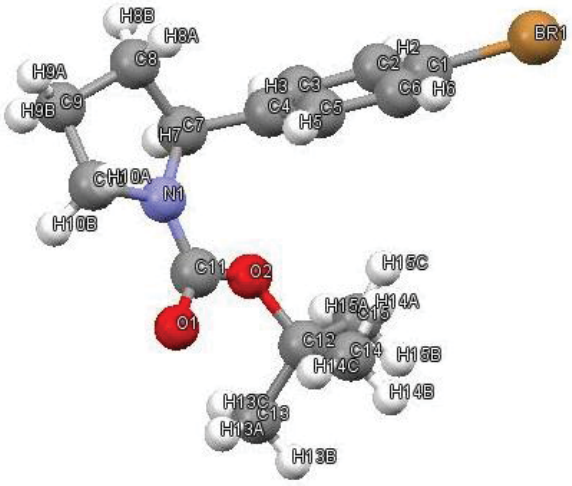


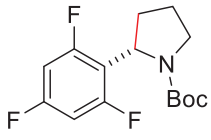
***tert*-butyl (*S*)-2-(3,5-bis(trifluoromethyl)phenyl)pyrrolidine-1-carboxylate 2e**, known compound.[23] Following the general procedure with **1e** as starting material. Yield: 91%. *ee*: 95%. Hexanes/ethyl acetate = 8/1, R_f = 0.43. $[\alpha]^{20}_D$ = -173.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.74 – 7.62 (m, 3H), 4.83 (m, br, 1H), 3.69 – 3.57 (m, 2H), 2.43 (m, br, 1H), 1.93 – 1.85 (m, 3H), 1.45 (s, 3H), 1.16 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.16, 147.91, 131.60 (q, *J* = 33.2 Hz), 125.83, 123.32 (q, *J* = 272.5 Hz), 120.55, 79.98, 60.92, 47.27, 36.07, 27.98, 23.47. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.37 (s, 6F). HPLC analysis: *ee* = 95%. ADH (99.8% hexanes : 0.2% isopropanol, 0.8 mL/min): t_{major} = 10.31 min, t_{minor} = 8.99 min. HRMS (ESI) ([M+Na]$^+$) Calcd. for $C_{17}H_{19}F_6NO_2Na$: 406.1212, found 406.1214.



***tert*-butyl (*S*)-2-(4-bromophenyl)pyrrolidine-1-carboxylate 2f**, known compound.[22] Following the general procedure with **1f** as starting material. Yield: 92%. *ee*: 92%. Hexanes/ethyl acetate = 8/1, R_f = 0.48. $[\alpha]^{20}_D$ = -90.6 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.41 (d, *J* = 6.7 Hz, 2H), 7.04 (d, *J* = 7.8 Hz, 2H), 4.88 and 4.71 (m, br, 1H), 3.60 (m, br, 2H), 2.30 (m, br, 1H), 1.88 – 1.85 (m, 2H), 1.84 – 1.82 (m, 1H), 1.44 (s, 3H), 1.20 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.43, 144.23, 131.18, 127.22, 120.06, 79.43, 60.79, 47.05, 35.92, 28.17, 23.12. HPLC analysis: *ee* = 92%. ADH (99% hexanes : 1% isopropanol, 1.0 mL/min):

t_{major} = 10.23 min, t_{minor} = 8.12 min. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{21}BrNO_2$: 326.0750, found 326.0735. The absolute stereochemistry of the major enantiomer was assigned by X-ray crystallography.

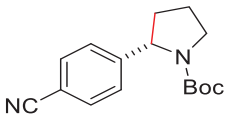




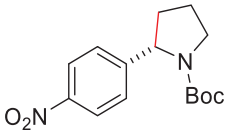
***tert*-butyl (*S*)-2-(2,4,6-trifluorophenyl)pyrrolidine-1-carboxylate 2g.**

Following the general procedure with **1g** as starting material. Yield: 70%. *ee*: 87%. Hexanes/ethyl acetate = 8/1, R_f = 0.45. $[\alpha]^{20}{}_D$ = -54.8 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 6.61 (t, *J* = 8.6 Hz, 2H), 5.02 – 4.99 (m, br, 1H), 3.72 – 3.46 (m, br, 2H), 2.35 – 2.32 (m, 1H), 2.01 – 1.83 (m, 3H), 1.41 (s, 3H), 1.21 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 161.26 (d, *J* = 248.2 Hz), 160.91 (d, J = 250.6 Hz), 153.82 (s), 116.45 (s), 100.06 (t, *J* = 27.5 Hz), 79.34, 51.24, 46.49, 33.44, 28.08, 24.62. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.93 – -111.25 (m, 1F), -112.76 – -113.03 (m, 2F). HPLC analysis: *ee* = 87%. ODH (99% hexanes : 1% isopropanol, 1.0 mL/min): t_{major} = 6.22 min, t_{minor} = 5.71 min. IR (neat, cm^{-1}): 2974.52, 1693.79, 1634.23, 1603.07,

1393.47, 1365.54, 1115.97, 999.07. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{19}F_3NO_2$: 302.1362, found 302.1377.

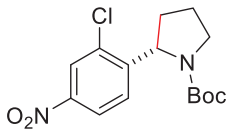


***tert*-butyl (*S*)-2-(4-cyanophenyl)pyrrolidine-1-carboxylate 2h**, known compound.[10c] Following the general procedure with **1h** as starting material. Yield: 92%. *ee*: 93%. Hexanes/ethyl acetate = 3/1, R_f = 0.35. $[\alpha]^{20}_D$ = -122.6 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.57 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 4.92 and 4.76 (m, br, 1H), 3.61 (m, br, 2H), 2.33 (m, br, 1H), 1.86 (m, br, 2H), 1.76 (m, br, 1H), 1.42 and 1.15 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.18, 150.80, 132.12, 126.21, 118.90, 110.41, 79.70, 61.15, 47.16, 35.89, 28.10, 23.26. HPLC analysis: *ee* = 93%. ADH (95% hexanes : 5% isopropanol, 1.0 mL/min): t_{major} = 12.38 min, t_{minor} = 9.09 min. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{21}N_2O_2$: 273.1604, found 273.1603.

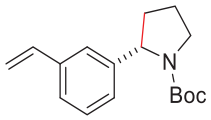


***tert*-butyl (*S*)-2-(4-nitrophenyl)pyrrolidine-1-carboxylate 2i.** Following the general procedure with **1i** as starting material. Yield: 88%. *ee*: 92%. Hexanes/ethyl acetate = 3/1, R_f = 0.35. $[\alpha]^{20}_D$ = -101.6 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 8.17 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.6 Hz, 2H), 4.98 and 4.84 (m, br, 1H), 3.66 – 3.65 (m, br, 2H), 2.39 (m, br, 1H), 1.91 – 1.90 (m, 2H), 1.80 (m, br, 1H), 1.45 and 1.18 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer

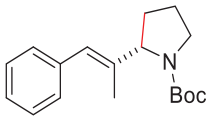
δ 154.22, 152.91, 146.83, 126.27, 123.65, 79.87, 61.03, 47.23, 35.98, 28.17, 23.34. HPLC analysis: *ee* = 92%. ADH (95% hexanes : 5% isopropanol, 1.0 mL/min): t_{major} = 15.08 min, t_{minor} = 7.75 min. IR (neat, cm^{-1}): 2974.37, 1690.31, 1517.18, 1388.56, 1156.40, 1111.56, 853.30. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{21}N_2O_4$: 293.1496, found 293.1501.



***tert*-butyl (*S*)-2-(2-chloro-4-nitrophenyl)pyrrolidine-1-carboxylate 2j.** Following the general procedure with **1j** as starting material. Yield: 81%. *ee*: 94%. Hexanes/ethyl acetate = 5/1, R_f = 0.41. $[\alpha]^{20}_D$ = -191.6 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 8.05 – 7.98 (m, 2H), 7.50 (t, *J* = 6.7 Hz, 1H), 5.25 – 5.15 (m, 1H), 3.74 – 3.55 (m, 2H), 2.46 – 2.42 (m, 1H), 1.92 – 1.79 (m, 3H), 1.46 and 1.17 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 154.42, 146.79, 143.31, 138.61, 130.37, 122.56, 121.53, 79.86, 58.66, 47.23, 33.82, 28.39, 23.23. HPLC analysis: *ee* = 94%. ODH (99.5% hexanes : 0.5% isopropanol, 1.0 mL/min): t_{major} = 16.61 min, t_{minor} = 15.79 min. IR (neat, cm^{-1}): 2974.26, 1693.57, 1523.64, 1390.46, 1347.37, 1251.32, 1159.81, 909.68, 757.43. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{20}ClN_2O_4$: 327.1106, found 327.1103.

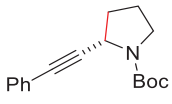


***tert*-butyl (*S*)-2-(3-vinylphenyl)pyrrolidine-1-carboxylate 2k.** Following the general procedure with **1k** as starting material. Yield: 81%. *ee*: 93%. Hexanes/ethyl acetate = 8/1, R_f = 0.46. $[\alpha]^{20}_D$ = -144.8 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.25 – 7.19 (m, 3H), 7.06 – 7.05 (m, 1H), 6.69 (dd, *J* = 17.6, 10.7 Hz, 1H), 5.73 (d, *J* = 17.6 Hz, 1H), 5.22 (d, *J* = 10.7 Hz, 1H), 4.95 and 4.75 (m, br, 1H), 3.63 and 3.52 (m, br, 2H), 2.32 (m, br, 1H), 1.91 – 1.84 (m, 3H), 1.46 (s, 3H), 1.18 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.57, 145.39, 137.39, 136.86, 128.32, 125.06, 124.35, 123.42, 113.71, 79.23, 61.26, 47.10, 35.97, 28.14, 23.25. HPLC analysis: *ee* = 93%. ADH (99.2% hexanes : 0.8% isopropanol, 1.0 mL/min): t_{major} = 9.25 min, t_{minor} = 10.36 min. IR (neat, cm^{-1}): 2976.26, 1684.19, 1478.10, 1392.01, 1265.11, 1161.51, 990.47, 874.91. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{17}H_{24}NO_2$: 274.1802, found 274.1808.

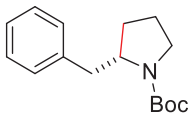


***tert*-butyl (*S*,*E*)-2-(1-phenylprop-1-en-2-yl)pyrrolidine-1-carboxylate 2l**. Following the general procedure with **1l** as starting material. Yield: 63%. *ee*: 94%. Hexanes/ethyl acetate = 8/1, R_f = 0.43. $[\alpha]^{20}_D$ = -124.4 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.24 – 7.12 (m, 5H), 6.19 (s, 1H), 4.18 (m, br, 1H), 3.50 and 3.39 (m, br, 2H), 2.03 (br, 1H), 1.85 – 1.70 (m, 6H), 1.34 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 154.72, 139.29, 138.03, 128.82, 128.05, 126.04, 123.53, 79.07, 64.38, 47.00, 31.82, 28.47, 23.21, 14.63. HPLC analysis: *ee* = 94%. ADH

(99% hexanes : 1% isopropanol, 0.8 mL/min): t_{major} = 11.19 min, t_{minor} = 9.94 min. IR (neat, cm^{-1}): 2972.67, 1679.83, 1394.69, 1362.69, 1246.31, 1157.14, 1115.51, 843.25, 752.51. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{18}H_{26}NO_2$: 288.1964, found 288.1966.

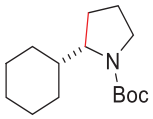


***tert*-butyl (*S*)-2-(phenylethynyl)pyrrolidine-1-carboxylate 2m.** Following the general procedure with **1m** as starting material. Yield: 60%. *ee*: 59%. Hexanes/ethyl acetate = 10/1, R_f = 0.46. $[\alpha]^{20}_D$ = -122.8 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.39 – 7.26 (m, 5H), 4.77 and 4.63 (m, br, 1H), 3.52 (m, br, 1H), 3.36 (m, br, 1H), 2.11 (m, br, 3H), 1.92 (m, br, 1H), 1.49 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 154.14, 131.52, 128.19, 127.93, 123.25, 89.94, 81.49, 79.60, 48.75, 45.59, 33.81, 28.52, 23.78. HPLC analysis: *ee* = 59%. ADH (95% hexanes : 5% isopropanol, 1.0 mL/min): t_{major} = 5.42 min, t_{minor} = 5.01 min. IR (neat, cm^{-1}): 2976.02, 2359.60, 1698.46, 1489.78, 1395.29, 1255.91, 1168.33, 1089.97, 758.74. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{17}H_{21}NNaO_2$: 294.1465, found 294.1464.

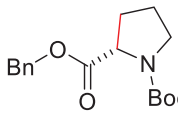


***tert*-butyl (*S*)-2-benzylpyrrolidine-1-carboxylate 2n**, known compound.[24] Following the general procedure with **1n** as starting material. Yield: 96%. *ee*: 23%. Hexanes/ethyl acetate = 6/1, R_f = 0.49. $[\alpha]^{20}_D$ = -3.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.29 – 7.18 (m, 5H), 4.05 and 3.96 (m, br, 1H), 3.38 and 3.29 (m, br, 2H), 3.18 and 3.07 (m, br, 1H), 2.55 (m, br, 1H), 1.76 (m, br, 4H), 1.51 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.53, 139.21, 129.37,

128.38, 126.19, 79.26, 58.87, 46.29, 40.59, 29.65, 28.61, 22.65. HPLC analysis: *ee* = 23%. ODH (99% hexanes : 1% isopropanol, 1.0 mL/min): t_{major} = 6.16 min, t_{minor} = 6.61 min.

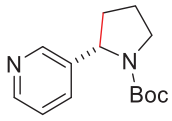


***tert*-butyl (*S*)-2-cyclohexylpyrrolidine-1-carboxylate 2o**, known compound.[10b] Following the general procedure with **1o** as starting material. Yield: 57%. *ee*: 88%. Hexanes/ethyl acetate = 10/1, R_f = 0.45. $[\alpha]^{20}_D$ = -61.6 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 3.70 and 3.61 (m, br, 1H), 3.50 and 3.40 (m, br, 1H), 3.22 – 3.16 (m, 1H), 1.81 – 1.59 (m, 10H), 1.45 (s, 9H), 1.25 – 0.90 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 155.04, 78.74, 61.80, 46.87, 40.77, 36.52, 30.12, 28.52, 27.93, 26.62, 24.32. HPLC analysis: *ee* = 88%. ADH (99.5% hexanes : 0.5% isopropanol, 1.0 mL/min): t_{major} = 5.91 min, t_{minor} = 6.35 min. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{15}H_{28}NO_2$: 254.2120, found 254.2128.

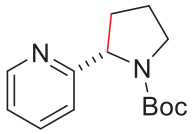


2-benzyl 1-(*tert*-butyl) (*S*)-pyrrolidine-1,2-dicarboxylate 2p, known compound.[25] Following the general procedure with **1p** as starting material. Yield: 56%. *ee*: 82%. Hexanes/ethyl acetate = 5/1, R_f = 0.50. $[\alpha]^{20}_D$ = -53.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.37 – 7.30 (m, 5H), 5.26 – 5.07 (m, 2H), 4.39 (dd, *J* = 8.6, 3.2 Hz, 0.4H) and 4.26 (dd, *J* = 8.6, 4.0 Hz, 0.6H), 3.58 – 3.34 (m, 2H), 2.26 – 2.15 (m, 1H), 1.99 – 1.83 (m, 3H), 1.46 and 1.34 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 173.02, 153.78, 135.65, 128.56, 128.27, 127.97, 79.87, 66.59,

59.17, 46.31, 30.87, 28.22, 23.59. HPLC analysis: *ee* = 82%. ADH (97% hexanes : 3% isopropanol, 0.8 mL/min): t_{major} = 21.68 min, t_{minor} = 14.26 min.

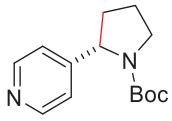


***tert*-butyl (*S*)-2-(pyridin-3-yl)pyrrolidine-1-carboxylate 2q**, known compound.[26] Following the general procedure with **1q** as starting material. Yield: 73%. *ee*: 92%. Hexanes/ethyl acetate = 2/1, R_f = 0.27. $[\alpha]^{20}_D$ = -48.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): a mixture of amide rotamers. δ 8.45 (br, 2H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.26 – 7.22 (m, 1H), 4.95 and 4.76 (br, 1H), 3.61 (br, 2H), 2.35 (br, 1H), 1.90 – 1.82 (m, 3H), 1.44 (s, 3H), 1.18 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.23, 148.07, 147.94, 140.32, 133.08, 123.30, 79.60, 59.24, 47.19, 35.96, 28.22, 23.27. HPLC analysis: *ee* = 92%. ADH (95% hexanes : 5% isopropanol, 1.0 mL/min): t_{major} = 19.47 min, t_{minor} = 25.97 min. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{14}H_{21}N_2O_2$: 249.1598, found 249.1610.

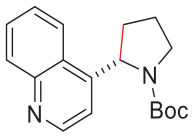


***tert*-butyl (*S*)-2-(pyridin-2-yl)pyrrolidine-1-carboxylate 2r**, known compound.[26] Following the general procedure with **1r** as starting material. Yield: 51%. *ee*: 85%. Hexanes/ethyl acetate = 2/1, R_f = 0.27. $[\alpha]^{20}_D$ = -72.4 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 8.53 (br, 1H), 7.62 (t, *J* = 7.1 Hz, 1H), 7.16 – 7.11 (m, 2H), 4.99 – 4.85 (m, br, 1H), 3.67 – 3.51 (m, 2H), 2.36 – 1.99 (m, br, 1H), 2.00 – 1.86 (m, 3H), 1.45 (s, 3H), 1.18 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 163.76, 154.49, 148.94, 136.22, 121.52, 119.62, 79.28, 62.83, 47.06, 34.27, 28.15, 23.21.

HPLC analysis: *ee* = 85%. ADH (90% hexanes : 10% isopropanol, 1.0 mL/min): t_{major} = 11.77 min, t_{minor} = 7.83 min. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{14}H_{21}N_2O_2$: 249.1598, found 249.1612.

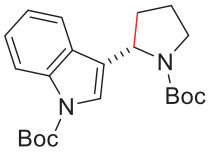


***tert*-butyl (*S*)-2-(pyridin-4-yl)pyrrolidine-1-carboxylate 2s**, known compound.[27] Following the general procedure with **1s** as starting material. Yield: 63%. *ee*: 95%. Hexanes/ethyl acetate = 2/1, R_f = 0.27. $[\alpha]^{20}_D$ = -58.0 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 8.52 (br, 2H), 7.10 – 7.10 (m, 2H), 4.90 and 4.73 (m, br, 1H), 3.63 (m, br, 2H), 2.35 (m, br, 1H), 1.88 – 1.80 (m, 3H), 1.45 (s, 3H), 1.19 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.17, 153.16, 149.67, 120.71, 79.77, 60.48, 47.10, 35.50, 28.11, 23.20. HPLC analysis: *ee* = 95%. OJH (98% hexanes : 2% isopropanol, 1.0 mL/min): t_{major} = 15.14 min, t_{minor} = 13.85 min. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{14}H_{21}N_2O_2$: 249.1598, found 249.1605.

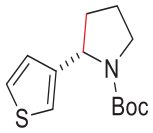


***tert*-butyl (*S*)-2-(quinolin-4-yl)pyrrolidine-1-carboxylate 2t.** Following the general procedure with **1t** as starting material. Yield: 91%. *ee*: 97%. Hexanes/ethyl acetate = 2/1, R_f = 0.26. $[\alpha]^{20}_D$ = -172.4 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 8.84 (d, *J* = 3.6 Hz, 1H), 8.15 – 8.11 (m, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.58 – 7.26 (m, 1H), 7.20 – 7.14 (m, 1H), 5.71 – 5.55 (m, br, 1H), 3.76 – 3.58 (m, 2H), 2.53 – 2.47 (m, br, 1H), 1.92 – 1.89 (m, 3H), 1.48 (s, 4H), 1.10

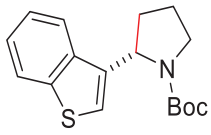
(s, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.24, 150.07, 148.87, 148.29, 130.33, 129.02, 126.45, 125.65, 122.77, 116.66, 79.68, 57.69, 46.93, 34.23, 28.05, 23.16. HPLC analysis: *ee* = 97%. ODH (95% hexanes : 5% isopropanol, 1.0 mL/min): t_{major} = 15.03 min, t_{minor} = 11.22 min. IR (neat, cm^{-1}): 2980.93, 1687.59, 1593.98, 1392.98, 1264.44, 1158.78, 896.45. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{18}H_{23}N_2O_3$: 315.1703, found 315.1715.



***tert*-butyl (*S*)-3-(1-(tert-butoxycarbonyl)pyrrolidin-2-yl)-1*H*-indole-1-carboxylate 2u**. Following the general procedure with **1u** as starting material. Yield: 88%. *ee*: 95%. Hexanes/ethyl acetate = 3/1, R_f = 0.35. $[\alpha]^{20}_D$ = -244.1 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 8.15 (br, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.31 – 7.21 (m, 3H), 5.20 and 5.06 (m, br, 1H), 3.62 and 3.50 (m, br, 2H), 2.25 (m, br, 1H), 2.04 – 1.87 (m, 3H), 1.65 (s, 9H), 1.47 (s, 4H), 1.23 (s, 5H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 154.63, 149.75, 135.91, 128.51, 124.22, 123.62, 122.32, 121.96, 119.11, 115.35, 83.50, 79.31, 54.17, 46.38, 33.29, 28.52, 28.21, 23.30. HPLC analysis: *ee* = 95%. ADH (99% hexanes : 1% isopropanol, 1.0 mL/min): t_{major} = 12.64 min, t_{minor} = 9.34 min. IR (neat, cm^{-1}): 2975.37, 1730.74, 1691.92, 1451.53, 1365.68, 1153.88, 1068.04, 855.98. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{22}H_{31}N_2O_4$: 387.2278, found 387.2287.

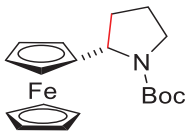


***tert*-butyl (*S*)-2-(thiophen-3-yl)pyrrolidine-1-carboxylate 2v**, known compound.[28] Following the general procedure with **1v** as starting material. Yield: 71%. *ee*: 91%. Hexanes/ethyl acetate = 6/1, R_f = 0.42. $[\alpha]^{20}_D$ = -78.4 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.27 – 7.23 (m, 1H), 6.97 and 6.93 (br, 2H), 5.05 and 4.89 (m, br, 1H), 3.54 and 3.49 (m, br, 2H), 2.22 (m, br, 1H), 2.18 – 1.87 (m, 3H), 1.46 (s, 3H), 1.27 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.57, 145.96, 125.84, 125.44, 119.56, 79.22, 57.20, 46.41, 34.72, 28.26, 23.22. HPLC analysis: *ee* = 91%. ADH (95% hexanes : 5% isopropanol, 0.8 mL/min): t_{major} = 6.50 min, t_{minor} = 6.07 min. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{13}H_{20}NO_2S$: 254.1209, found 254.1228.

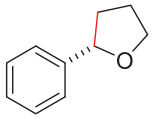


***tert*-butyl (*S*)-2-(benzo[*b*]thiophen-3-yl)pyrrolidine-1-carboxylate 2w**, known compound.[29] Following the general procedure with **1w** as starting material. Yield: 86%. *ee*: 96%. (For reaction with 2.0 mmol scale: yield: 82%. *ee*: 96%). Hexanes/ethyl acetate = 6/1, R_f = 0.38. $[\alpha]^{20}_D$ = -144.8 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.85 (br, 1H), 7.72 (d, *J* = 6.7 Hz, 1H), 7.35 (br, 2H), 7.06 (br, 1H), 5.37 – 5.20 (m, br, 1H), 3.71 – 3.50 (m, br, 2H), 2.31 (br, 1H), 1.98 and 1.92 (m, br, 3H), 1.48 (s, 3.5H), 1.16 (s, 5.5H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 154.55, 140.98, 139.07, 137.07, 124.15, 123.84, 122.96, 121.55, 120.55, 79.28, 56.70, 46.52, 33.23, 28.16, 23.17. HPLC analysis: *ee* = 96%. ADH (99% hexanes : 1% isopropanol, 1.0

mL/min): t_{major} = 14.66 min, t_{minor} = 11.01 min. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{17}H_{22}NO_2S$: 304.1366, found 304.1371.

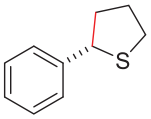


***tert*-butyl (*S*)-2-ferrocenylpyrrolidine-1-carboxylate 2x.** Following the general procedure with **1x** as starting material. Yield: 53%. *ee*: 92%. Hexanes/ethyl acetate = 5/1, R_f = 0.43. $[\alpha]^{20}_D$ = -26.0 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 4.88 and 4.72 (m, br, 1H), 4.52 and 4.36 (m, br, 1H), 4.15 and 4.10 (m, br, 8H), 3.50 and 3.31 (br, 2H), 2.24 – 2.14 (br, 2H), 2.04 – 1.91 (m, 2H), 1.45 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 154.61, 90.37, 79.41, 69.75, 68.55, 65.75, 55.72, 46.39, 32.72, 28.59, 24.71. HPLC analysis: *ee* = 92%. ODH (99% hexanes : 1% isopropanol, 1.0 mL/min): t_{major} = 9.85 min, t_{minor} = 13.10 min. IR (neat, cm^{-1}): 3092.07, 2972.86, 1690.94, 1390.64, 1248.38, 1165.54, 1106.86, 1000.94, 875.23, 819.20. HRMS (ESI) ([M]$^+$) Calcd. For $C_{19}H_{25}FeNO_2$: 355.1235, found 355.1244.

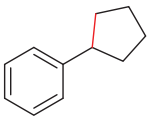


(*S*)-2-phenyltetrahydrofuran 2y, known compound.[30] Following the general procedure with **1y** as starting material. Yield: 54%. *ee*: 85%. Hexanes/ethyl acetate = 10/1; R_f = 0.35. $[\alpha]^{20}_D$ = -8.1 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 5H), 4.87 (t, *J* = 7.2 Hz, 1H), 4.08 (dd, *J* = 14.8, 7.0 Hz, 1H), 3.92 (dd, *J* = 14.8, 7.6 Hz, 1H), 2.30 (td, *J* = 12.5, 7.0 Hz, 1H), 2.03 – 1.95 (m, 2H), 1.79 (ddd, *J* = 16.0, 12.2, 7.6 Hz,

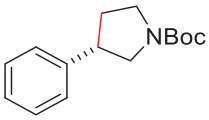
1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.41, 128.23, 127.06, 125.58, 80.63, 68.62, 34.57, 25.99. HPLC analysis: *ee* = 85%. ADH (100% hexanes, 0.8 mL/min): t_{major} = 19.89 min, t_{minor} = 24.78 min.



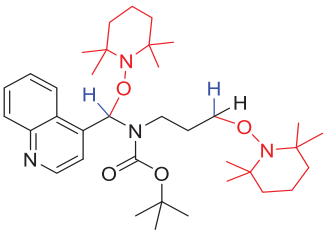
(*S*)-2-phenyltetrahydrothiophene 2z. Following the general procedure with **1z** as starting material. Yield: 85%. *ee*: 91%. Hexanes/ethyl acetate = 10/1; R_f = 0.70. $[\alpha]^{20}_D$ = -9.6 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 4.54 – 4.51 (m, 1H), 3.18 – 3.14 (m, 1H), 3.04 – 3.00 (m, 1H), 2.41 – 2.38 (m, 1H), 2.28 – 2.26 (m, 1H), 2.04 – 1.92 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 142.96, 128.35, 127.60, 126.95, 52.73, 40.50, 33.48, 31.04. HPLC analysis: *ee* = 91%. ODH (100% hexanes, 1.0 mL/min): t_{major} = 14.43 min, t_{minor} = 13.55 min. IR (neat, cm^{-1}): 2943.69, 1598.42, 1490.46, 1260.22, 1098.22, 1018.64, 758.87, 698.96. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{10}H_{13}S$: 165.0732, found 165.0741.



cyclopentylbenzene 2aa, known compound.[31] Following the general procedure with **1aa** as starting material and [Co(**P1**)] (3 mol %) as the catalyst. Yield: 76%. Pentane; R_f = 0.80. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 4H), 7.1 – 7.15 (m, 1H), 3.03 – 2.96 (m, 1H), 2.11 – 2.04 (m, 2H), 1.83 – 1.77 (m, 2H), 1.73 – 1.65 (m, 2H), 1.64 – 1.56 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.51, 128.19, 127.08, 125.63, 45.93, 34.59, 25.52.

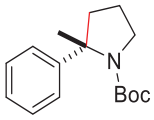


***tert*-butyl (*S*)-3-phenylpyrrolidine-1-carboxylate 2ab**. Following the general procedure with **1ab** as starting material. Yield: 50%. *ee*: 67%. Hexanes/ethyl acetate = 10/1; R_f = 0.50. $[\alpha]^{20}{}_D$ = -5.3 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 7.34 – 7.23 (m, 5H), 3.88 – 3.76 (m, 1H), 3.55 (t, *J* = 8.7 Hz, 1H), 3.44 – 3.27 (m, 3H), 2.26 – 2.25 (m, 1H), 2.02 – 1.97 (m, 1H), 1.47 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): major isomer δ 154.50, 141.46, 128.56, 127.04, 126.75, 79.18, 52.60, 45.62, 44.27, 32.44, 28.54. HPLC analysis: *ee* = 67%. OJH (99% hexanes : 1% isopropanol, 1.0 mL/min): t_{major} = 9.48 min, t_{minor} = 8.42 min. IR (neat, cm^{-1}): 2973.27, 1697.99, 1454.43, 1406.93, 1365.73, 1169.52, 1124.12, 880.73, 700.43. HRMS (ESI) ($[M+Na]^+$) Calcd. For $C_{15}H_{21}NNaO_2$: 270.1465, found 270.1466.



***tert*-butyl (quinolin-4-yl((2,2,6,6-tetramethylpiperidin-1-yl)oxy) methyl) (3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)carbamate 3t**. Reaction procedure: An oven-dried Schlenk tube was charged with 1.0 equivalent of sulfonyl hydrazone **1t** (0.1 mmol), [Co(**P1**)] (5 mol %) and 1.5 equivalent of Cs_2CO_3 (0.15 mmol). The Schlenk tube was then evacuated and backfilled with nitrogen for 3 times. Then TEMPO (2.0 equiv.) was added under nitrogen, followed by the injection of dioxane

(0.6 mL) via a gas-tight syringe. The Schlenk tube was then purged with nitrogen for 10 s and sealed with a Teflon screw cap. The mixture was then stirred at 60 ºC. After 24 h, the reaction mixture was concentrated and purified by flash chromatography. The fractions containing **3t** were collected and concentrated by rotary evaporation to afford the pure compound. Yield: 20%. Hexanes/ethyl acetate = 6/1, R_f = 0.50. ^{1}H NMR (600 MHz, $CDCl_3$): a mixture of amide rotamers. δ 8.96 and 8.94 (d, *J* = 4.3 Hz, 1H), 8.24 and 8.15 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.81 (br, 1H), 7.73 – 7.68 (m, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.40 and 7.30 (s, 1H), 3.34 – 3.17 (m, 4H), 1.67 (s, 3H), 1.58 – 1.43 (m, 12H), 1.40 – 1.36 (m, 6H), 1.29 – 1.11 (m, 10H), 1.03 – 0.98 (m, 9H), 0.89 (br, 3H), 0.83 (br, 3H), 0.17 – 0.07 (m, br, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 155.00, 154.02(minor), 150.15(minor), 149.89, 148.12(minor), 148.14, 145.87, 144.81(minor), 130.32(minor), 129.91, 129.18, 129.07(minor), 126.94, 126.62(minor), 125.97, 125.81(minor), 124.16, 123.29(minor), 119.10, 119.32(minor), 86.79, 86.44(minor), 80.61(minor), 80.04, 74.18, 74.11(minor), 60.95(minor), 60.88, 59.48, 59.39(minor), 40.53(minor), 40.45, 40.39(minor), 40.19, 39.82, 39.49, 33.30(minor), 33.00, 32.89(minor), 32.83(minor), 32.43, 28.69(minor), 28.31, 28.12, 27.17(minor), 20.48(minor), 20.46, 20.25(minor), 20.15(minor), 19.94, 17.14(minor), 17.07, 17.05. IR (neat, cm^{-1}): 2973.56, 2930.79, 1693.40, 1592.91, 1465.13, 1402.57, 1365.90, 1259.53, 1170.61, 1043.10, 910.39. HRMS (ESI) ($[M+H]^+$) Calcd. For $C_{36}H_{59}N_4O_4$: 611.4531, found 611.4530. The structure was further characterized and confirmed with H-H COSY, DEPT and HSQC.



***tert*-butyl (*S*)-2-methyl-2-phenylpyrrolidine-1-carboxylate 5a.** Following the general procedure with **4a** as starting material and with [Co(**P1**)] (3 mol %) as the catalyst. Yield: 55%. *ee*: 81%. Hexanes/ethyl acetate = 10/1, R_f = 0.40. $[\alpha]^{20}_D$ = -43.6 (*c* = 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): a mixture of amide rotamers δ 7.29 – 7.17 (m, 5H), 3.71 – 3.59 (m, 2H), 2.08 – 2.00 (m, 2H), 1.87 – 1.79 (m, 2H), 1.74 (s, 3H), 1.44 and 1.11 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): major isomer δ 154.28, 148.45, 127.84, 125.92, 125.01, 79.05, 64.87, 48.59, 45.80, 28.10, 25.43, 22.05. HPLC analysis: *ee* = 81%. ODH (99% hexanes : 1% isopropanol, 1.0 mL/min): t_{major} = 6.28 min, t_{minor} = 6.94 min. IR (neat, cm^{-1}): 2972.63, 1687.81, 1446.93, 1392.64, 1367.02, 1165.68, 1029.22, 761.48. HRMS (ESI) ($[M+Na]^+$) Calcd. for $C_{16}H_{23}NNaO_2$: 284.1621, found 284.1620. The absolute stereochemistry of the major enantiomer was assigned by X-ray crystallography.

4.4.7 Procedure for HRMS Experiment

To an over-dried Schlenk tube, tosylhydrazone **1a** (0.05 mmol) and Cs_2CO_3 (1.5 equiv.) were added. The Schlenk tube was then evacuated and backfilled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, CH_3CN (0.5 mL) was added via a gas-tight syringe. The mixture was then stirred at 60 °C for 1 h. The resulting light yellow solution was then passed through a short pad of Celite (to get rid of base and salt) under the flow of nitrogen and the filtrate was collected in a HPLC vial (vial A, degassed and backfilled with argon). During the time, [Co(**P1**)] (3 mol %) was charged into another HPLC vial (vial B, degassed and backfilled with argon) and dissolved in

CH_3CN (0.5 mL). After mixing equal amount of solutions from vial A (0.1 mL) and vial B (0.1 mL), the sample was further diluted with CH_3CN and immediately injected into HRMS instrument. The HRMS experiment was carried out in the absence of any additives such as formic acid, commonly act as electron carriers for ionization, allowing the detection of the molecular ion signals corresponding to Co(III)-alkyl radical ($C_{91}H_{109}CoN_9O_6^{\cdot}$) by the loss of one electron.

4.4.8 Procedure for EPR Experiment

To an oven-dried Schlenk tube A, tosylhydrazone **1a** (0.05 mmol), and Cs_2CO_3 (1.5 equiv.) were added. The Schlenk tube was then evacuated and backfilled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, benzene (0.5 mL) was added via a gas-tight syringe. The mixture was then stirred at 60 ^oC for 1 h. During the time, [Co(**P1**)] (3 mol %) was charged into another oven-dried Schlenk tube B. The Schlenk tube B was then evacuated and backfilled with nitrogen for 3 times. After 1 h, the resulting light yellow solution from tube A was passed through a short pad of Celite (to get rid of base and salt) under the flow of nitrogen and transferred to Schlenk tube B. The mixture was stirred for 1 min, followed by the addition of phenyl *N*-*tert*-butylnitrone (PBN, 0.05 mmol). The reaction mixture was stirred for 2 min and transferred into a degassed EPR tube (filled with argon) through a gas tight syringe. The sample was then carried out for EPR experiment at room temperature (EPR settings: T = 298 K; microwave frequency: 9.37762 GHz; power: 20 mW; modulation amplitude: 1.0 G)

4.5 REFERENCES

(1) (a) Chatgilialoglu, C.; Studer, A. *Encyclopedia of Radicals in Chemistry, Biology and Materials*; John Wiley & Sons: Chichester, U.K., 2012; (b) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions: Concepts, Guidelines, and Synthetic Applications*; Wiley-VCH: Weinheim, 2008; (c) Zard, S. Z. *Radical Reactions in Organic Synthesis*; Oxford University Press: Oxford, 2003; (d) Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. *J. Org. Chem.* **2016**, *81*, 6898; (e) Yan, M.; Lo, J. C.; Edwards, J. T.; Baran, P. S. *J. Am. Chem. Soc.* **2016**, *138*, 12692.

(2) For select recent examples, see: (a) Kern, N.; Plesniak, M. P.; McDouall, J. J. W.; Procter, D. J. *Nat. Chem.* **2017**, *9*, 1198; (b) Adams, K.; Ball, A. K.; Birkett, J.; Brown, L.; Chappell, B.; Gill, D. M.; Lo, P. K. T.; Patmore, N. J.; Rice, C. R.; Ryan, J.; Raubo, P.; Sweeney, J. B. *Nat. Chem.* **2017**, *9*, 396; (c) Brill, Z. G.; Grover, H. K.; Maimone, T. J. *Science* **2016**, *352*, 1078; (d) Logan, M. M.; Toma, T.; Thomas-Tran, R.; Du Bois, J. *Science* **2016**, *354*, 865; (e) Hashimoto, T.; Kawamata, Y.; Maruoka, K. *Nat. Chem.* **2014**, *6*, 702.

(3) Walton, J. C. *Acc. Chem. Res.* **1998**, *31*, 99.

(4) Bougeard, P.; Bury, A.; Cooksey, C. J.; Johnson, M. D.; Hungerford, J. M.; Lampman, G. M. *J. Am. Chem. Soc.* **1982**, *104*, 5230.

(5) For reviews and select examples, see: (a) Sibi, M. P.; Manyem, S.; Zimmerman, J. *Chem. Rev.* **2003**, *103*, 3263; (b) Brimioulle, R.; Lenhart, D.; Maturi, M. M.; Bach, T. *Angew. Chem., Int. Ed.* **2015**, *54*, 3872; (c) Blum, T. R.; Miller, Z. D.; Bates, D. M.; Guzei, I. A.; Yoon, T. P. *Science* **2016**, *354*, 1391; (d) Kainz, Q. M.; Matier, C. D.; Bartoszewicz,

A.; Zultanski, S. L.; Peters, J. C.; Fu, G. C. *Science* **2016**, *351*, 681; (e) Lin, J.-S.; Dong, X.-Y.; Li, T.-T.; Jiang, N.-C.; Tan, B.; Liu, X.-Y. *J. Am. Chem. Soc.* **2016**, *138*, 9357; (f) Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Rose, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100; (g) Nicewicz, D. A.; MacMillan, D. W. C. *Science* **2008**, *322*, 77.

(6) For reviews and highlights on Co(II)-based MRC, see: (a) Miyabe, H.; Kawashima, A.; Yoshioka, E.; Kohtani, S. *Chem. Eur. J.* **2017**, *23*, 6225; (b) Studer, A.; Curran, D. P. *Angew. Chem., Int. Ed.* **2016**, *55*, 58; (c) Pellissier, H.; Clavier, H. *Chem. Rev.* **2014**, *114*, 2775; (d) Lu, H. J.; Zhang, X. P. *Chem. Soc. Rev.* **2011**, *40*, 1899; (e) Doyle, M. P. *Angew. Chem., Int. Ed.* **2009**, *48*, 850.

(7) For select examples on Ti(III)-based MRC, see: (a) Zhang, Y.-Q.; Vogelsang, E.; Qu, Z.-W.; Grimme, S.; Gansäuer, A. *Angew. Chem., Int. Ed.* **2017**, *56*, 12654; (b) Hao, W.; Wu, X.; Sun, J. Z.; Siu, J. C.; MacMillan, S. N.; Lin, S. *J. Am. Chem. Soc.* **2017**, *139*, 12141; (c) Gansäuer, A.; Hildebrandt, S.; Vogelsang, E.; Flowers II, R. A. *Dalton Trans.* **2016**, *45*, 448; (d) Gansäuer, A.; Fleckhaus, A.; Lafont, M. A.; Okkel, A.; Kotsis, K.; Anoop, A.; Neese, F. *J. Am. Chem. Soc.* **2009**, *131*, 16989.

(8) For detailed experimental and theoretical studies on the radical mechanism involving *α*-Co(III)-alkyl radical (also known as Co(III)-carbene radical) intermediates for olefin cyclopropanation, see: (a) Lu, H. J.; Dzik, W. I.; Xu, X.; Wojtas, L.; de Bruin, B.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 8518; (b) Belof, J. L.; Cioce, C. R.; Xu, X.; Zhang, X. P.; Space, B.; Woodcock, H. L. *Organometallics* **2011**, *30*, 2739; (c) Dzik, W. I.; Xu, X.; Zhang, X. P.; Reek, J. N. H.; de Bruin, B. *J. Am. Chem. Soc.* **2010**, *132*, 10891.

(9) For select examples on asymmetric Co(II)-MRC, see: (a) Wang, Y.; Wen, X.; Cui, X.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2017**, *139*, 1049; (b) Cui, X.; Xu, X.; Jin, L.-M.; Wojtas, L.; Zhang, X. P. *Chem. Sci.* **2015**, *6*, 1219 (c) Xu, X.; Lu, H. J.; Ruppel, J. V.; Cui, X.; de Mesa, S. L.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 15292; (d) Cui, X.; Xu, X.; Lu, H. J.; Zhu, S. F.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2011**, *133*, 3304; (e) Zhu, S. F.; Ruppel, J. V.; Lu, H. J.; Wojtas, L.; Zhang, X. P. *J. Am. Chem. Soc.* **2008**, *130*, 5042; (f) Fantauzzi, S.; Gallo, E.; Rose, E.; Raoul, N.; Caselli, A.; Issa, S.; Ragaini, F.; Cenini, S. *Organometallics* **2008**, *27*, 6143; (g) Chen, Y.; Fields, K. B.; Zhang, X. P. *J. Am. Chem. Soc.* **2004**, *126*, 14718; For select examples on nonasymmetric Co(II)-MRC, see:(h) Roy, S.; Das, S. K.; Chattopadhyay, B. *Angew. Chem., Int. Ed.* **2018**, *57*, 2238; (i) te Grotenhuis, C.; van den Heuvel, N.; van der Vlugt, J. I.; de Bruin, B. *Angew. Chem., Int. Ed.* **2018**, *57*, 140; (j) Reddy, A. R.; Hao, F.; Wu, K.; Zhou, C.-Y.; Che, C. M. *Angew. Chem., Int. Ed.* **2016**, *55*, 1810; (k) Zhang, J.; Jiang, J.; Xu, D.; Luo, Q.; Wang, H.; Chen, J.; Li, H.; Wang, Y.; Wan, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 1231.

(10) For select examples on asymmetric synthesis of α-substituted pyrrolidine derivatives, see: (a) Jain, P.; Verma, P.; Xia, G.; Yu, J.-Q. *Nat. Chem.* **2017**, *9*, 140; (b) Cordier, C. J.; Lundgren, R. J.; Fu, G. C. *J. Am. Chem. Soc.* **2013**, *135*, 10946; (c) Campos, K. R.; Klapars, A.; Waldman, J. H.; Dormer, P. G.; Chen, C.-Y. *J. Am. Chem. Soc.* **2006**, *128*, 3538; (d) Shaw, M. H.; Shurtleff, V. W.; Terrett, J. A.; Cuthbertson, J. D.; MacMillan, D. W. C. *Science* **2016**, *352*, 1304.

(11) For select examples on C–H insertion with in situ-generated unstable diazo compounds, see: (a) Reddy, A. R.; Zhou, C. Y.; Guo, Z.; Wei, J.; Che, C. M. *Angew. Chem., Int. Ed.* **2014**, *53*, 14175; (b) Soldi, C.; Lamb, K. N.; Squitieri, R. A.; Gonzalez-Lopez, M.;

Di Maso, M. J.; Shaw, J. T. *J. Am. Chem. Soc.* **2014**, *136*, 15142; (c) Lindsay, V. N. G.; Viart, H. M. F.; Sarpong, R. *J. Am. Chem. Soc.* **2015**, *137*, 8368; (d) Su, N.; Deng, T.; Wink, D. J.; Driver, T. G. *Org. Lett.* **2017**, *19*, 3990.

(12) Ruppel, J. V.; Jones, J. E.; Huff, C. A.; Kamble, R. M.; Chen, Y.; Zhang, X. P. *Org. Lett.* **2008**, *10*, 1995.

(13) Dai, L.-X.; Hou, X.-L. In *Chiral Ferrocenes in Asymmetric Catalysis: Synthesis and Applications*; Wiley-VCH: Weinheim, 2010.

(14) Davies, S. G.; Figuccia, A. L. A.; Fletcher Paul, A. M.; Roberts, M.; Thomson, J. E. *J. Org. Chem.* **2016**, *81*, 6481.

(15) Blanco, J. B.; Dodero, V. I.; Vázquez, M. E.; Mosquera, M.; Castedo, L.; Mascareñas, J. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 8210.

(16) Brun, E.; Bellosta, V.; Cossy, J. *J. Org. Chem.* **2016**, *81*, 8206.

(17) Sheikh, N. S.; Leonori, D.; Barker, G.; Firth, J. D.; Campos, K. R.; Meijer, A. J. H. M.; O'Brien, P.; Coldham, I. *J. Am. Chem. Soc.* **2012**, *134*, 5300.

(18) Evans, D. A.; Fitch, D. M. *J. Org. Chem.* **1997**, *62*, 454.

(19) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, *16*, 2647.

(20) Anchoori, R. K.; Harikumar, K. B.; Batchu, V. R.; Aggarwal, B. B.; Khan, S. R. *Bioorg. Med. Chem.* **2010**, *18*, 229.

(21) Reddy, D. S.; Srinivas, P.; Balasubrahmanyam, D.; Iqbal, J. *Tetrahedron Lett.* **2007**, *48*, 4533.

(22) Chen, F.; Ding, Z.; Qin, J.; Wang, T.; He, Y.; Fan, Q.-H. *Org. Lett.* **2011**, *13*, 4348.

(23) Denmark, S. E.; Chang, W.-T. T.; Houk, K. N.; Liu, P. *J. Org. Chem.* **2015**, *80*, 313.

(24) Johnston, C. P.; Smith, R. T.; Allmendinger, S.; MacMillan, D. W. C. *Nature* **2016**, *536*, 322.

(25) Loughlin, W. A.; Schweiker, S. S.; Jenkins, I. D.; Henderson, L. C. *Tetrahedron* **2013**, *69*, 1576.

(26) Barker, G.; McGrath, J. L.; Klapars, A.; Stead, D.; Zhou, G.; Campos, K. R.; O'Brien, P. *J. Org. Chem.* **2011**, *76*, 5936.

(27) Zuo, Z.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2014**, *136*, 5257.

(28) Wu, S.; Lee, S.; Beak, P. *J. Am. Chem. Soc.* **1996**, *118*, 715.

(29) Oderinde, M. S.; Varela-Alvarez, A.; Aquila, B.; Robbins, D. W.; Johannes, J. W. *J. Org. Chem.* **2015**, *80*, 7642.

(30) Butova, E. D.; Barabash, A. V.; Petrova, A. A.; Kleiner, C. M.; Schreiner, P. R.; Fokin, A. A. *J. Org. Chem.* **2010**, *75*, 6229.

(31) Ghorai, S. K.; Jin, M.; Hatakeyama, T.; Nakamura, M. *Org. Lett.* **2012**, *14*, 1066.

Chapter 5

Spectral Data

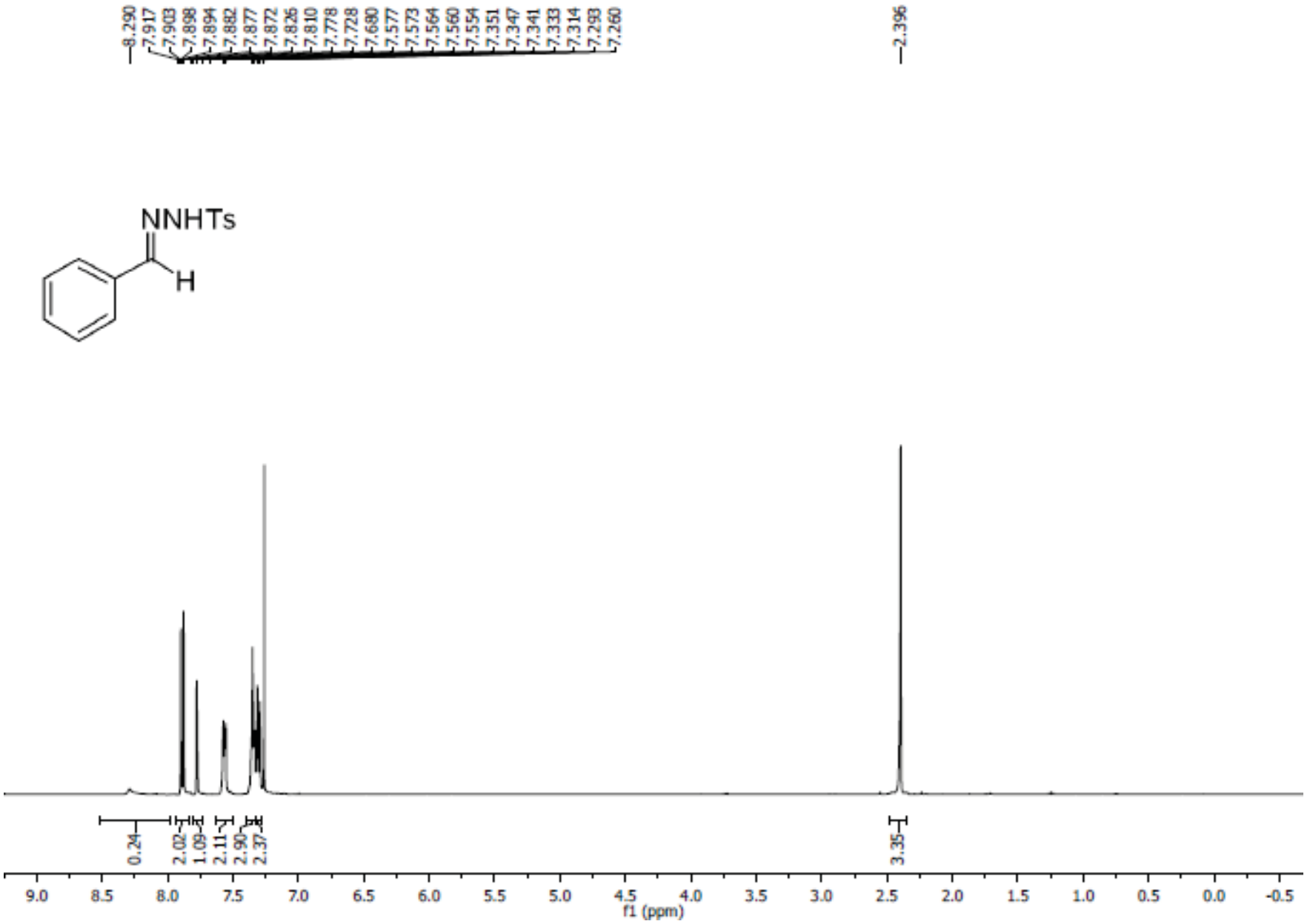
Spectral Data

for

Chapter 2

Asymmetric Radical Cyclopropanation of Alkenes with In Situ-Generated Donor-Substituted Diazo Reagents via Co(II)-Based Metalloradical Catalysis

benzaldehyde tosylhydrazone **1a**



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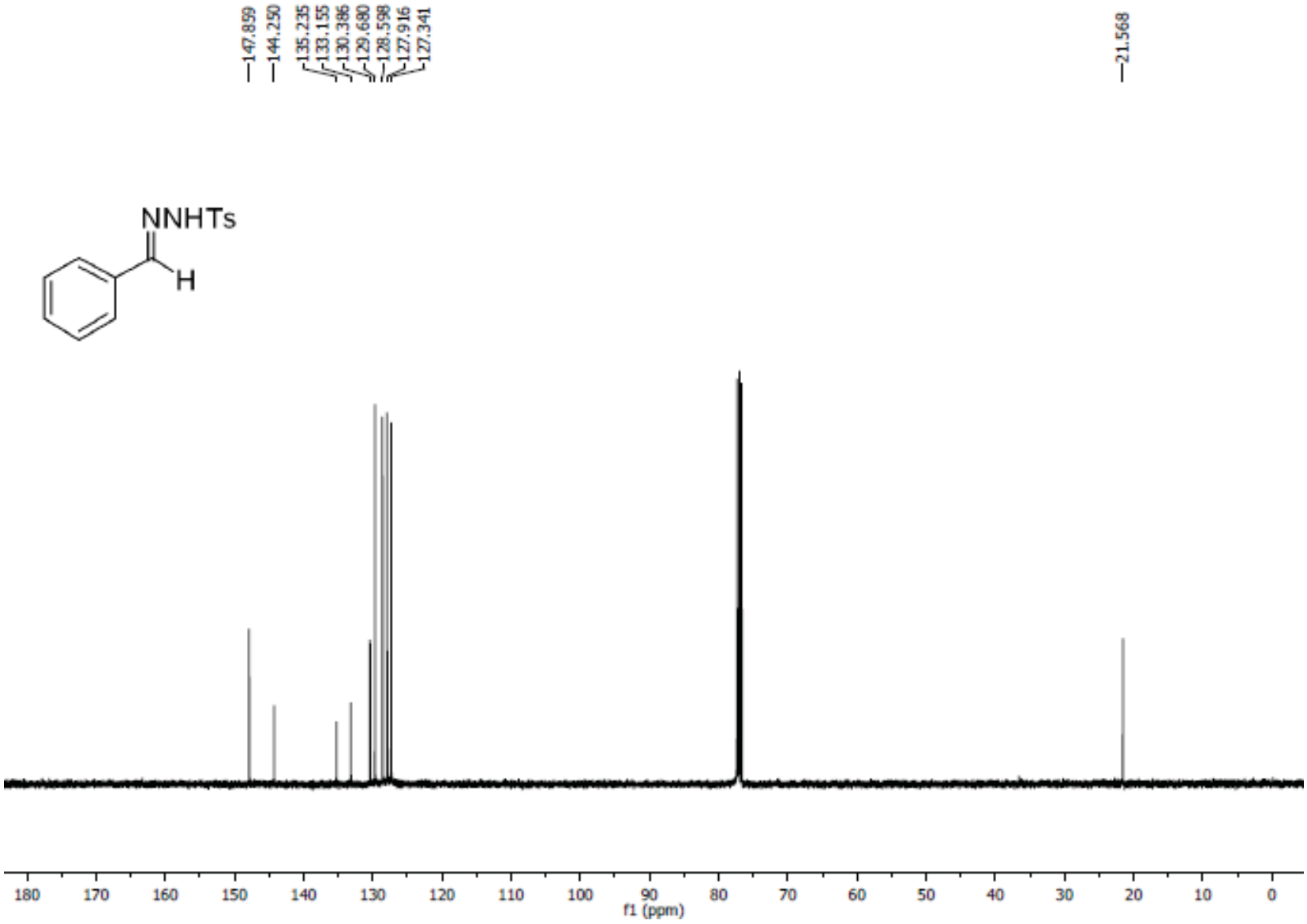

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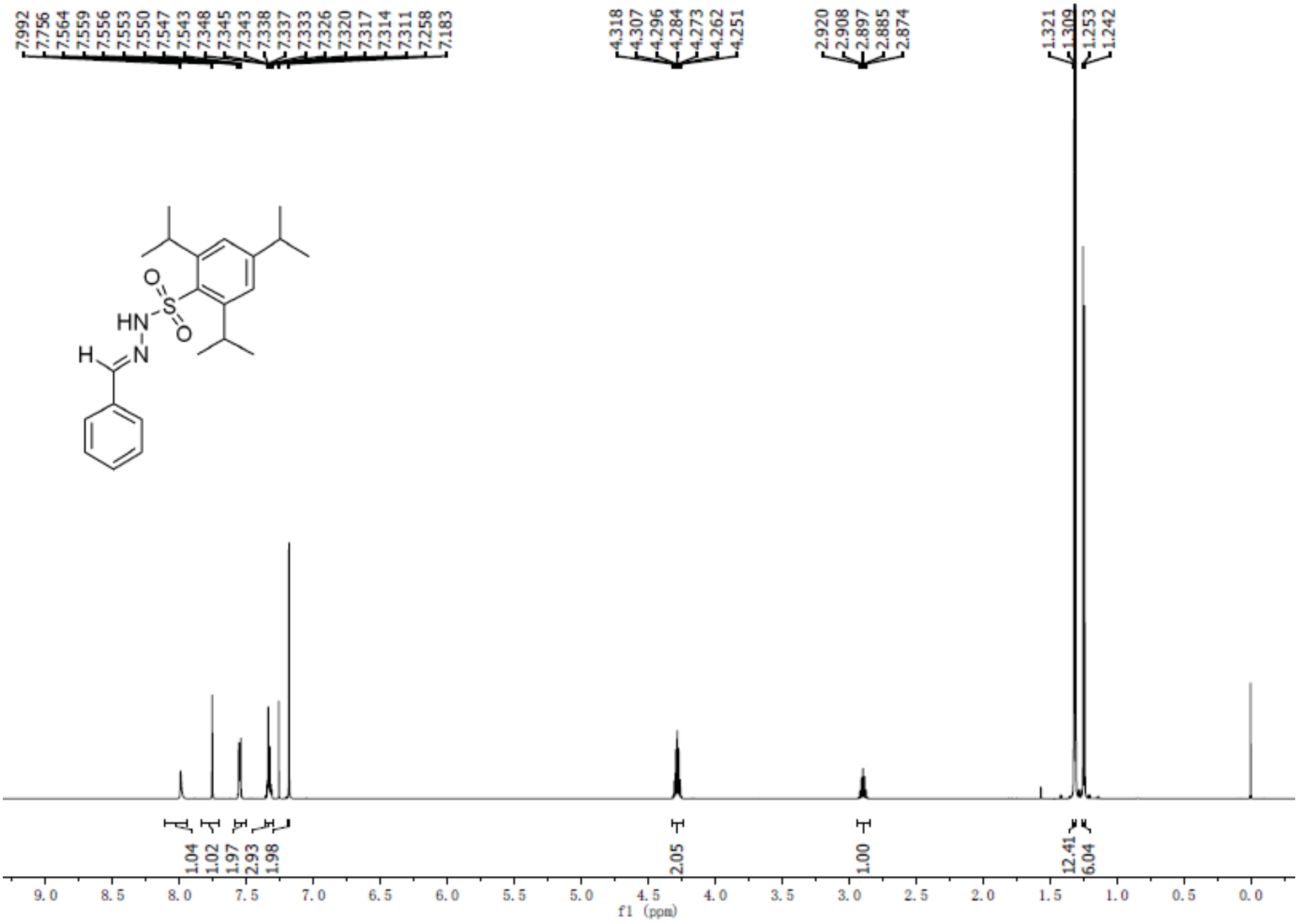
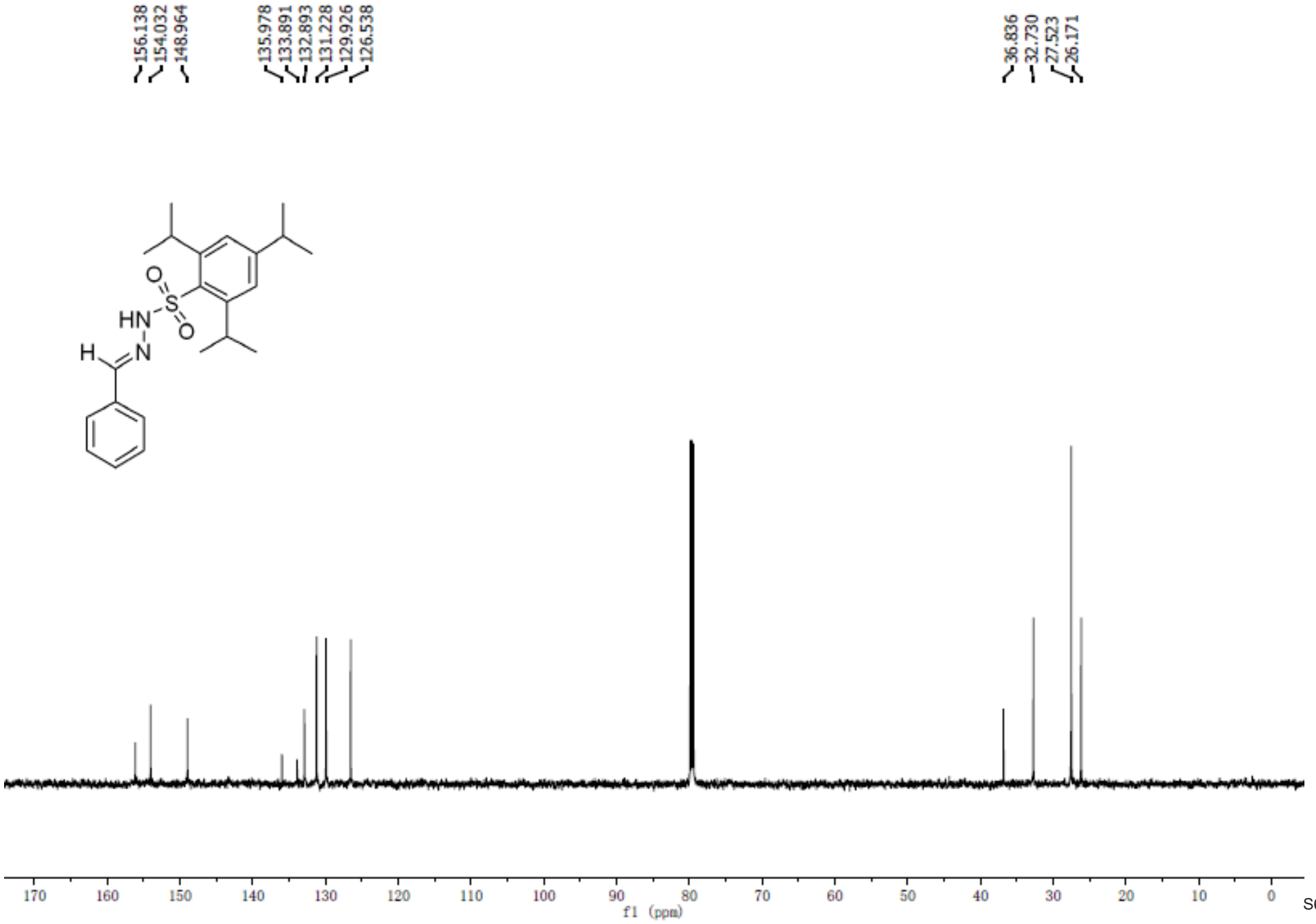


benzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1a'**



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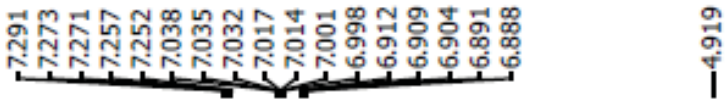
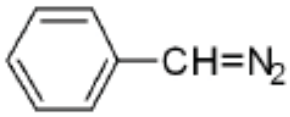
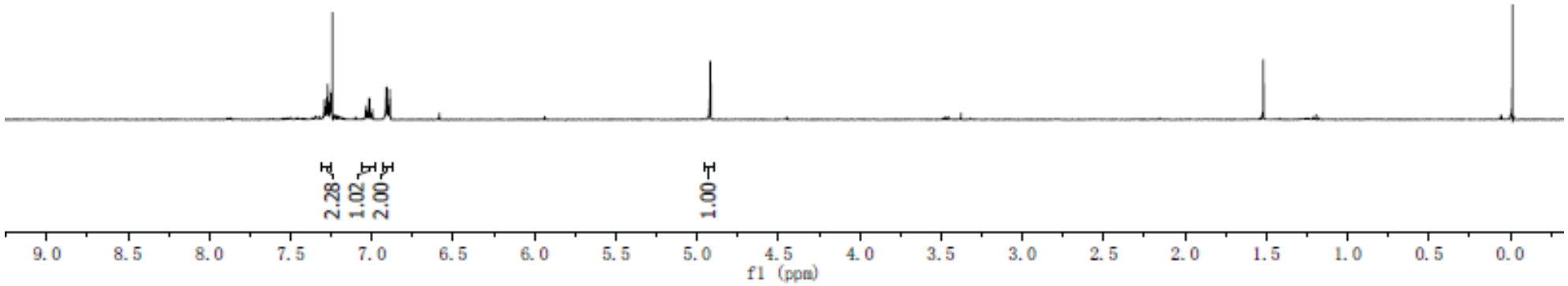
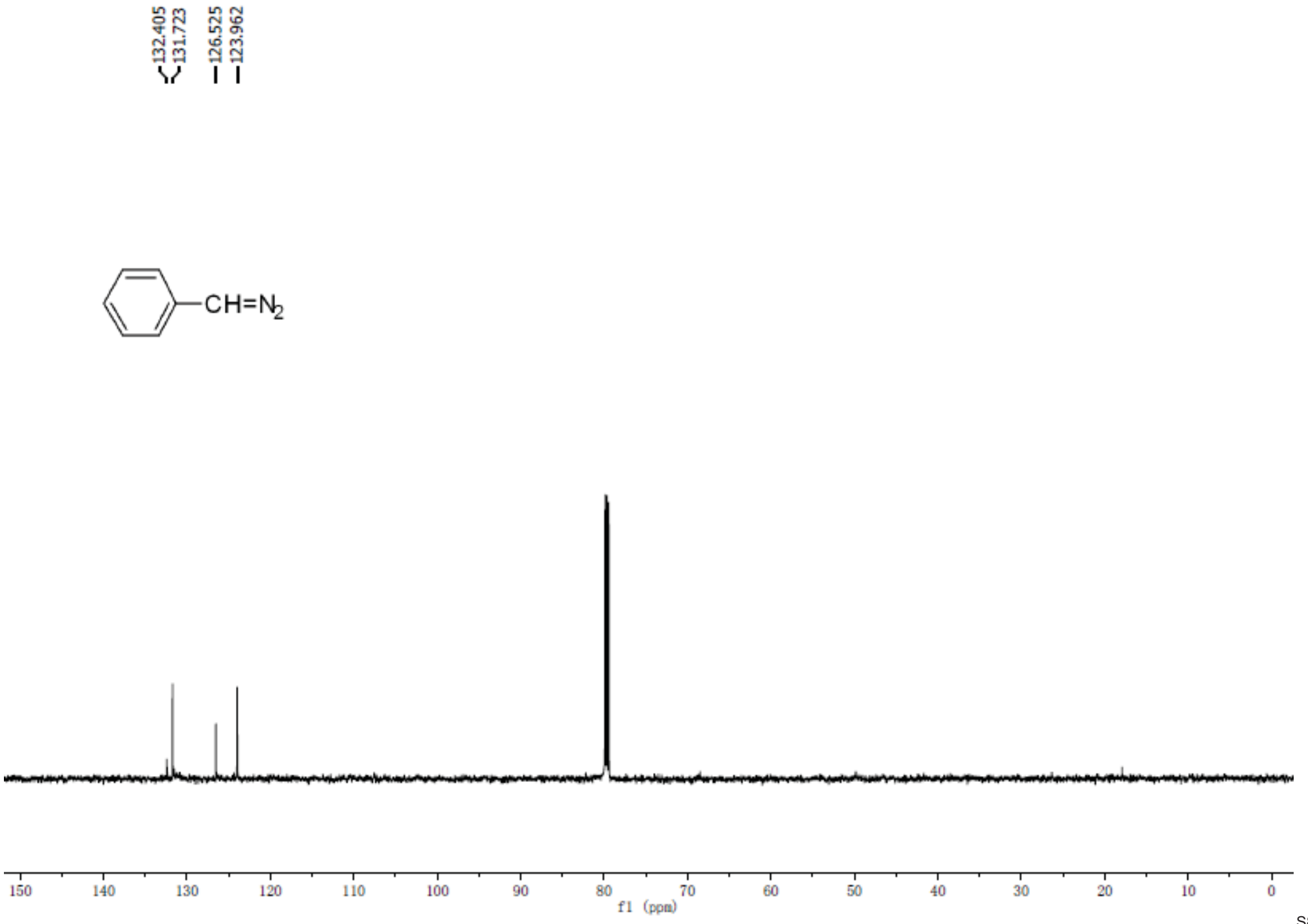


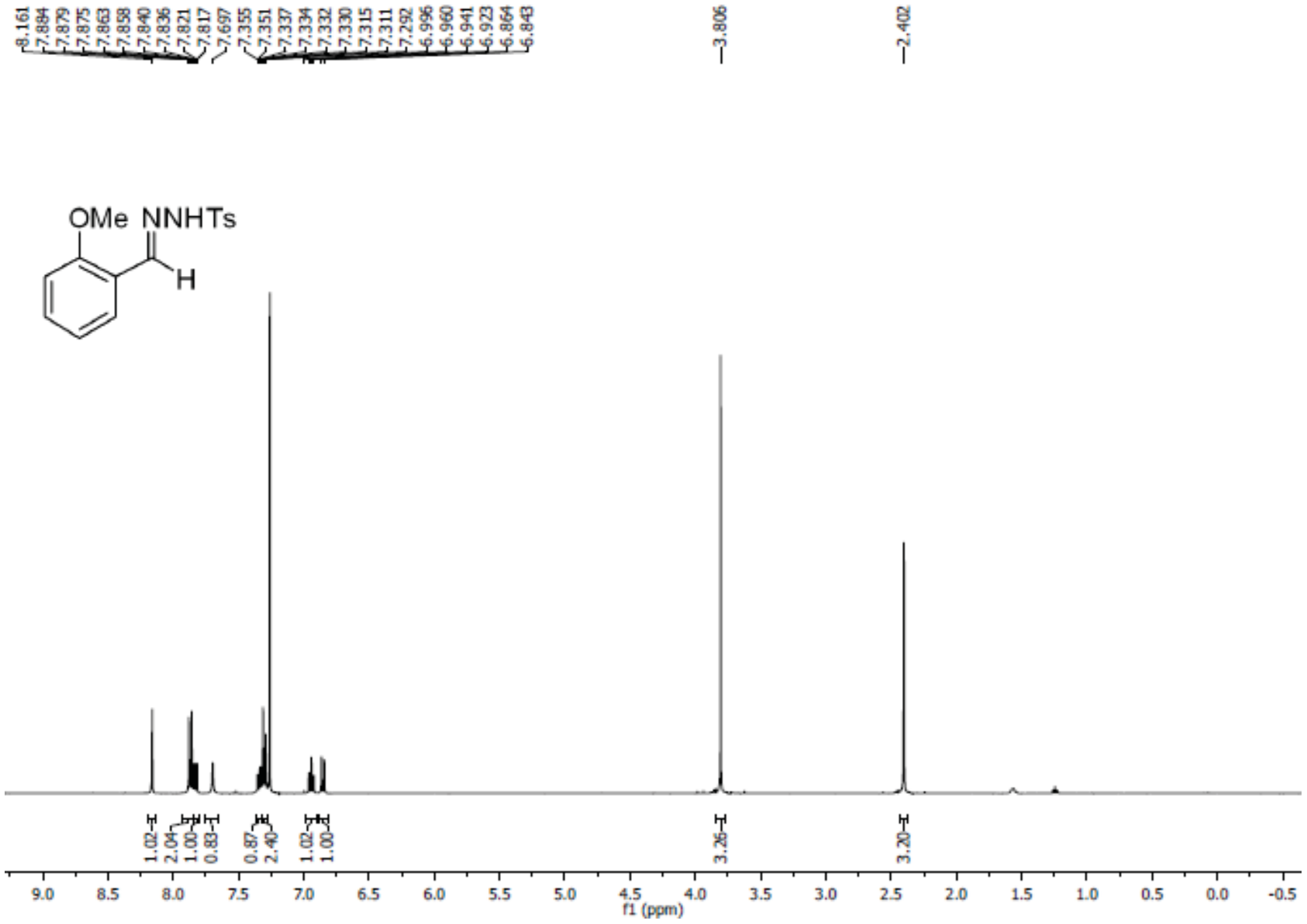




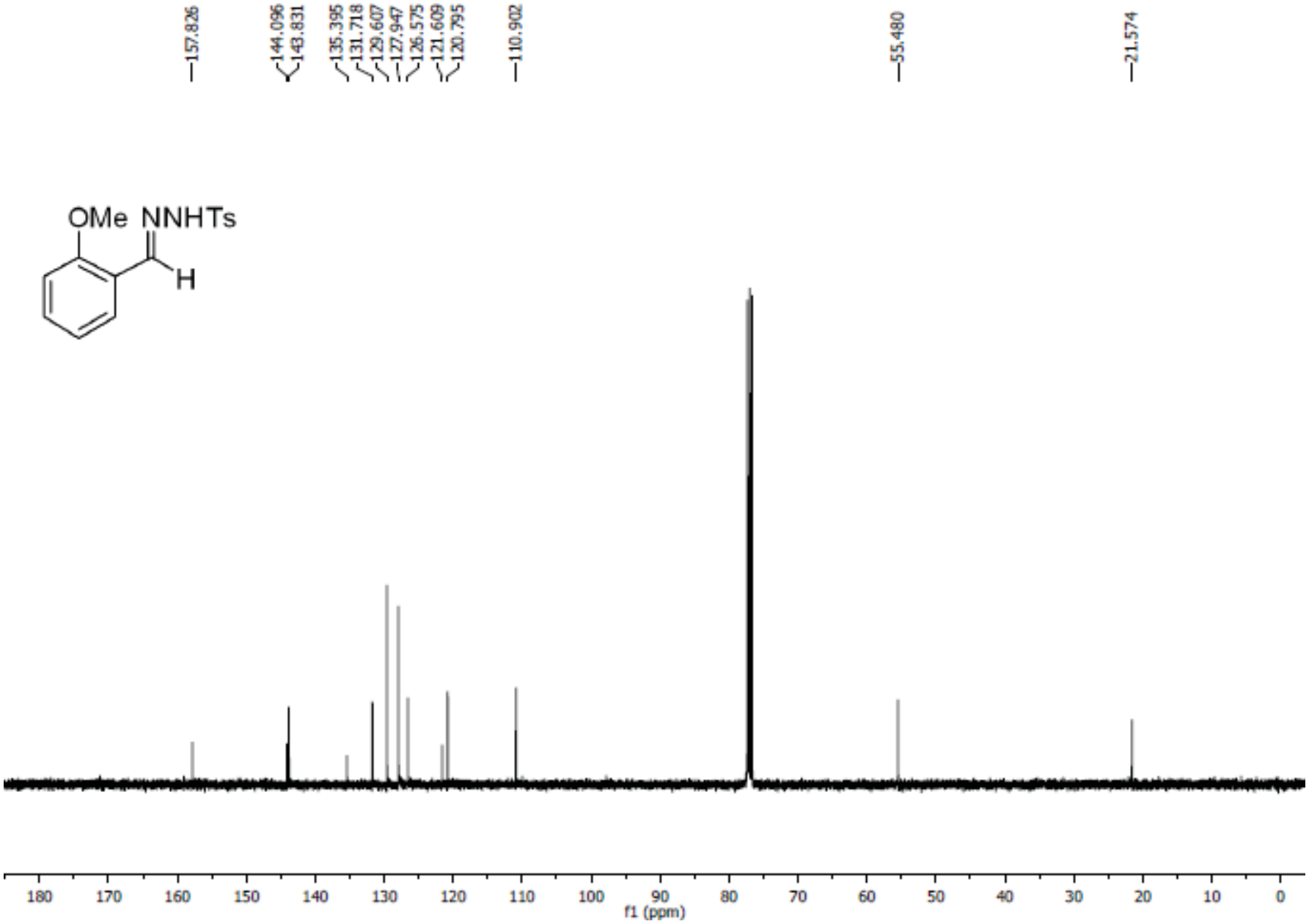
Phenyl Diazomethane **1a''**



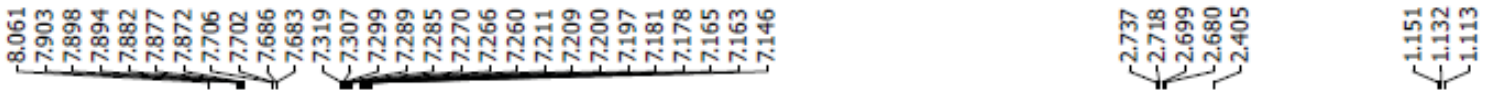
2-methoxybenzaldehyde tosylhydrazone **1b**

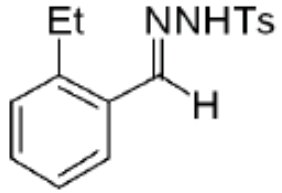


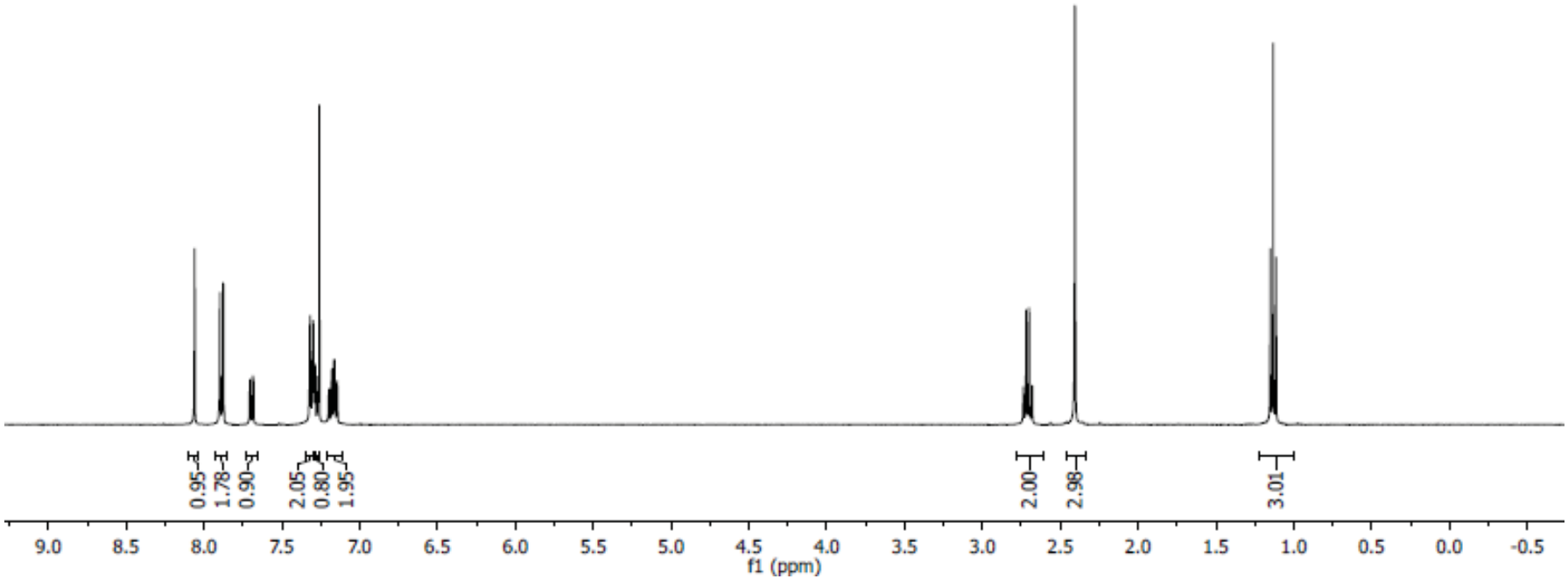
2-methoxybenzaldehyde tosylhydrazone **1b**



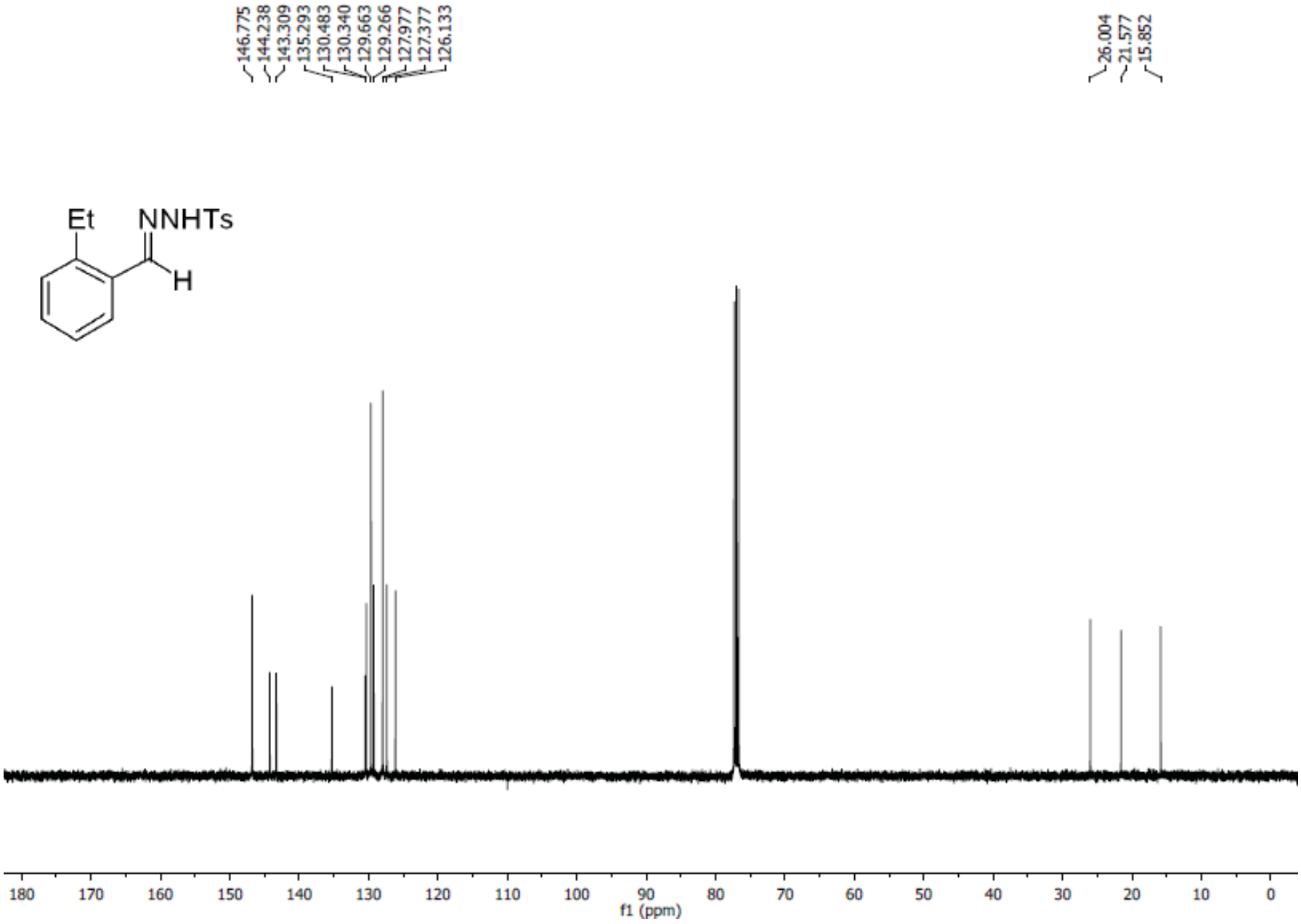
2-ethylbenzaldehyde tosylhydrazone **1c**



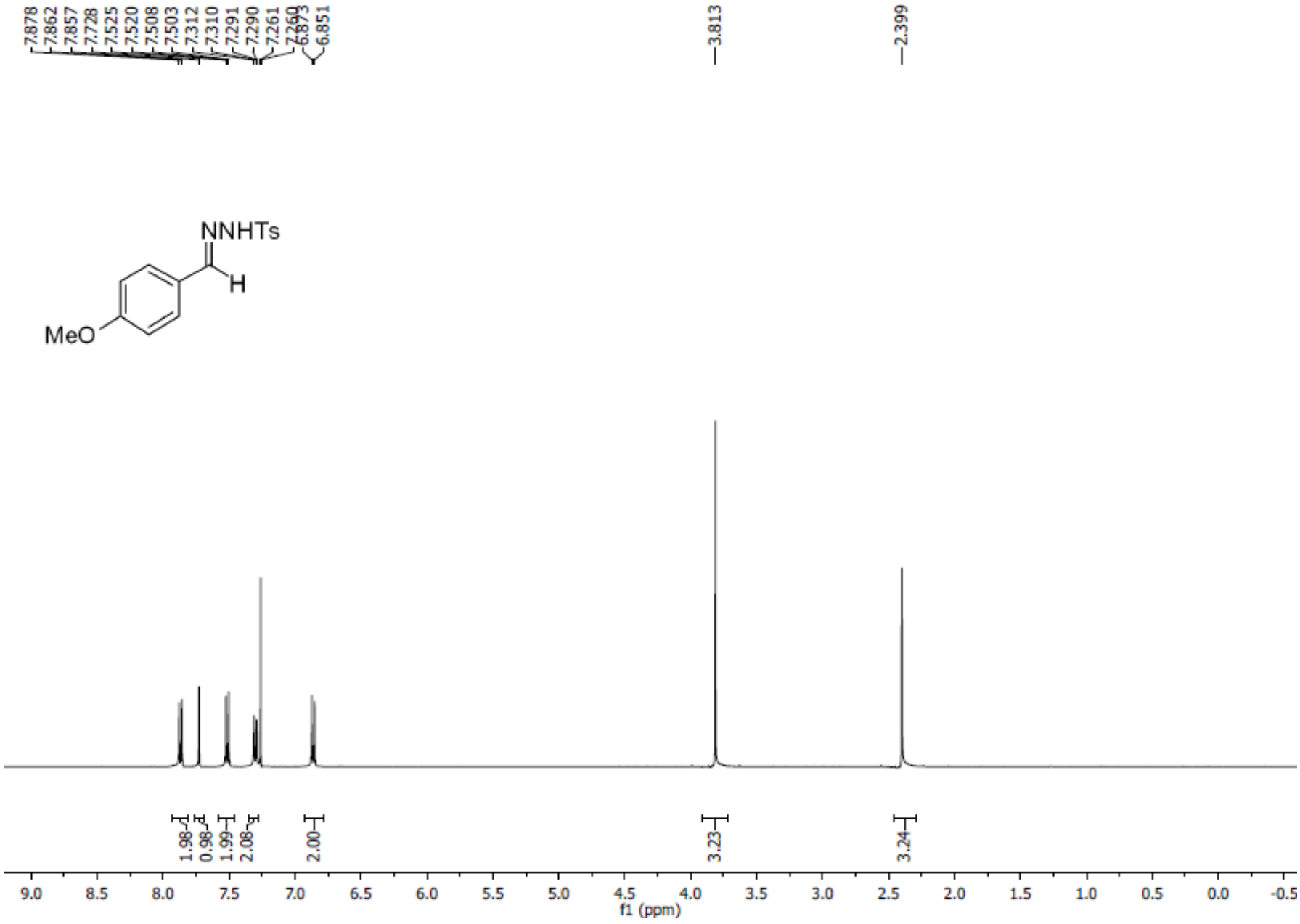




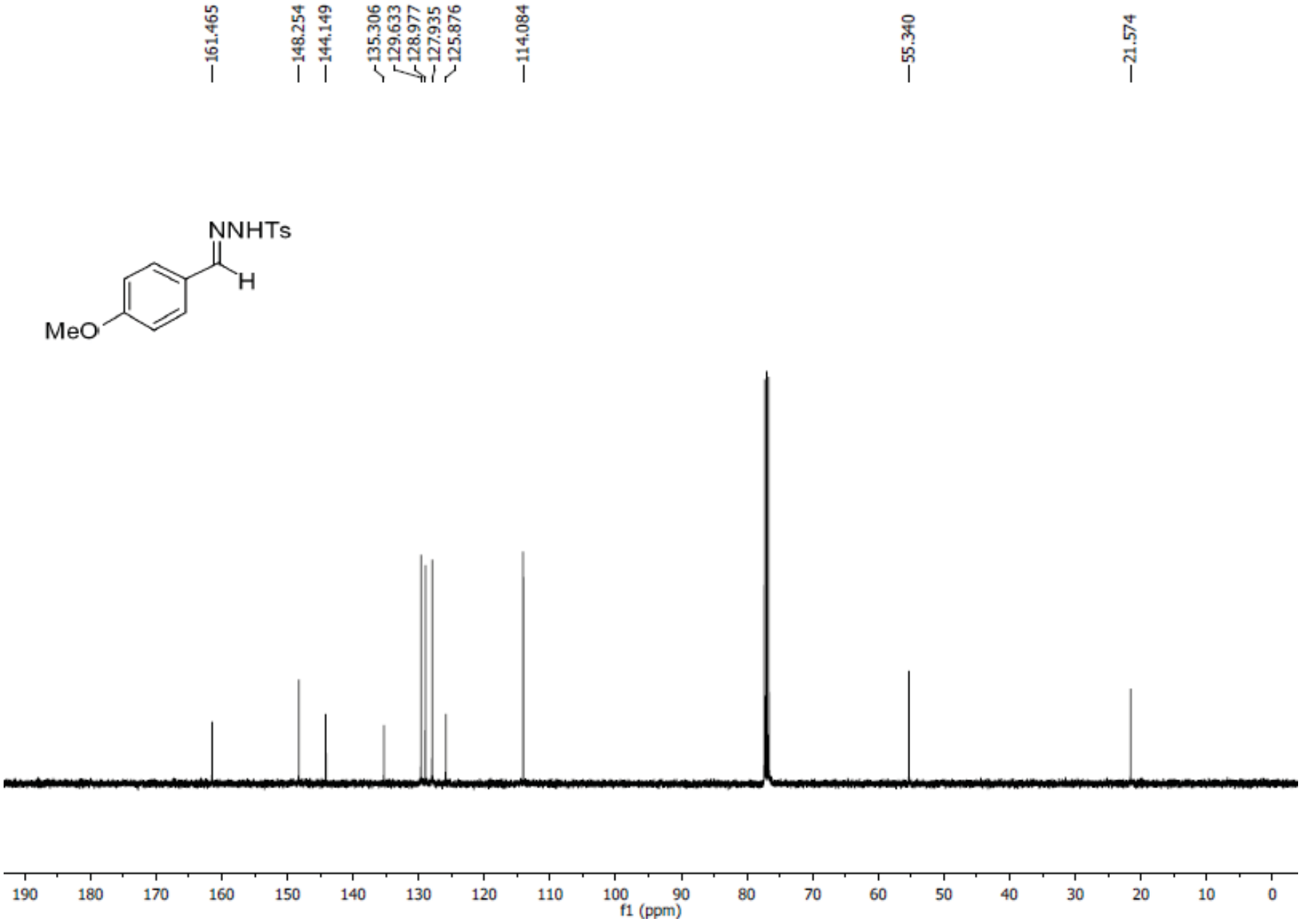
2-ethylbenzaldehyde tosylhydrazone **1c**



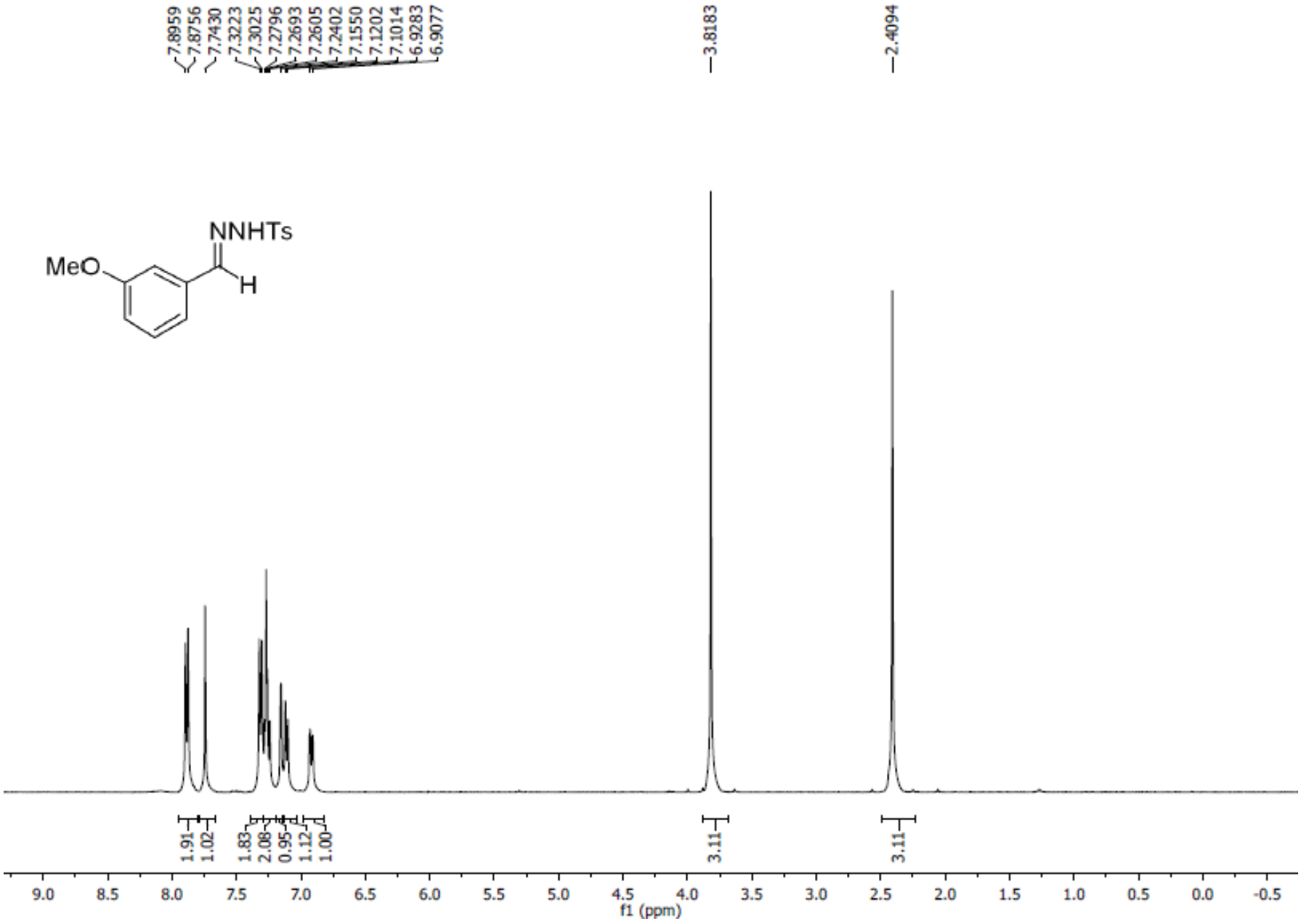
4-methoxybenzaldehyde tosylhydrazone **1d**



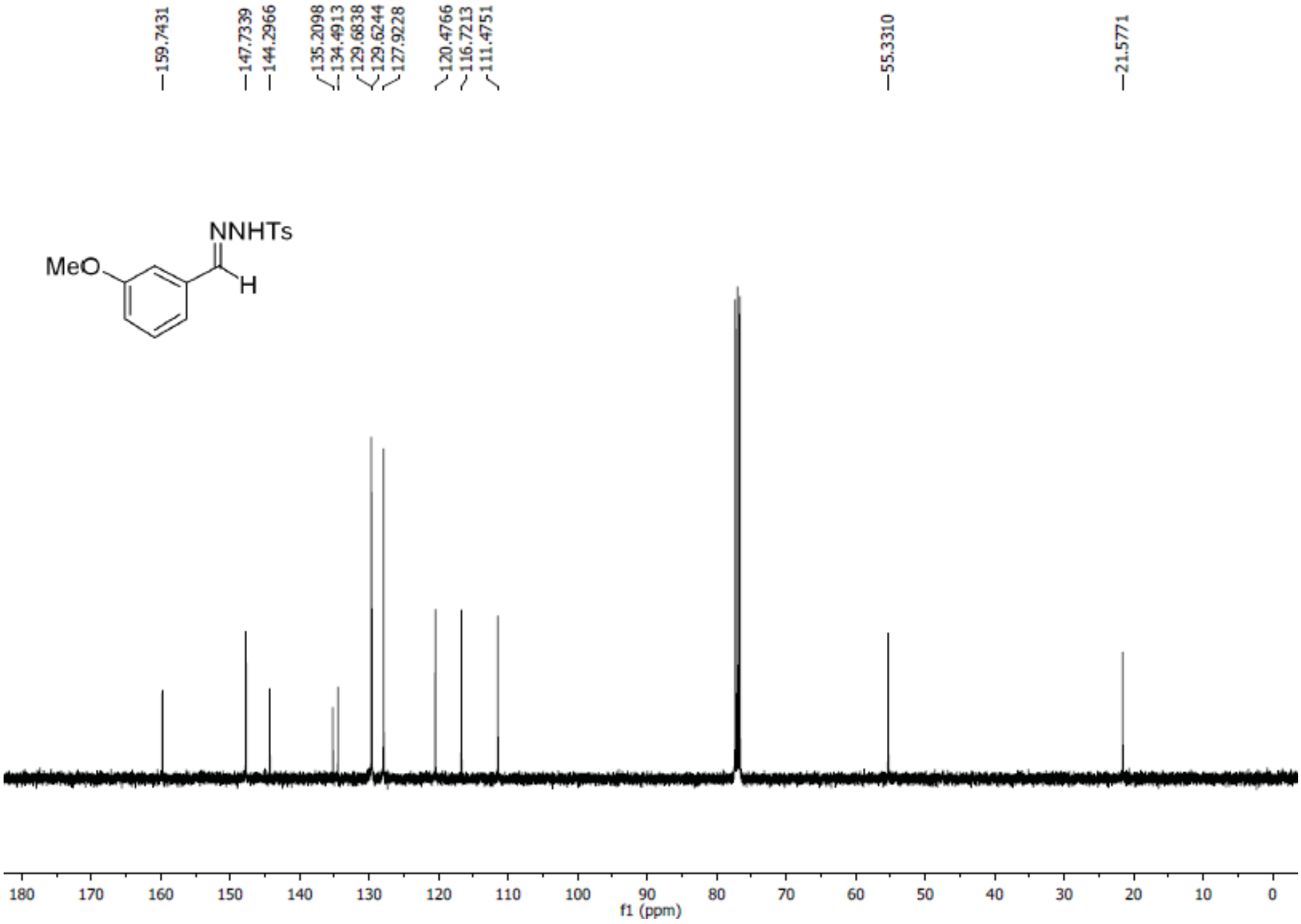
4-methoxybenzaldehyde tosylhydrazone **1d**



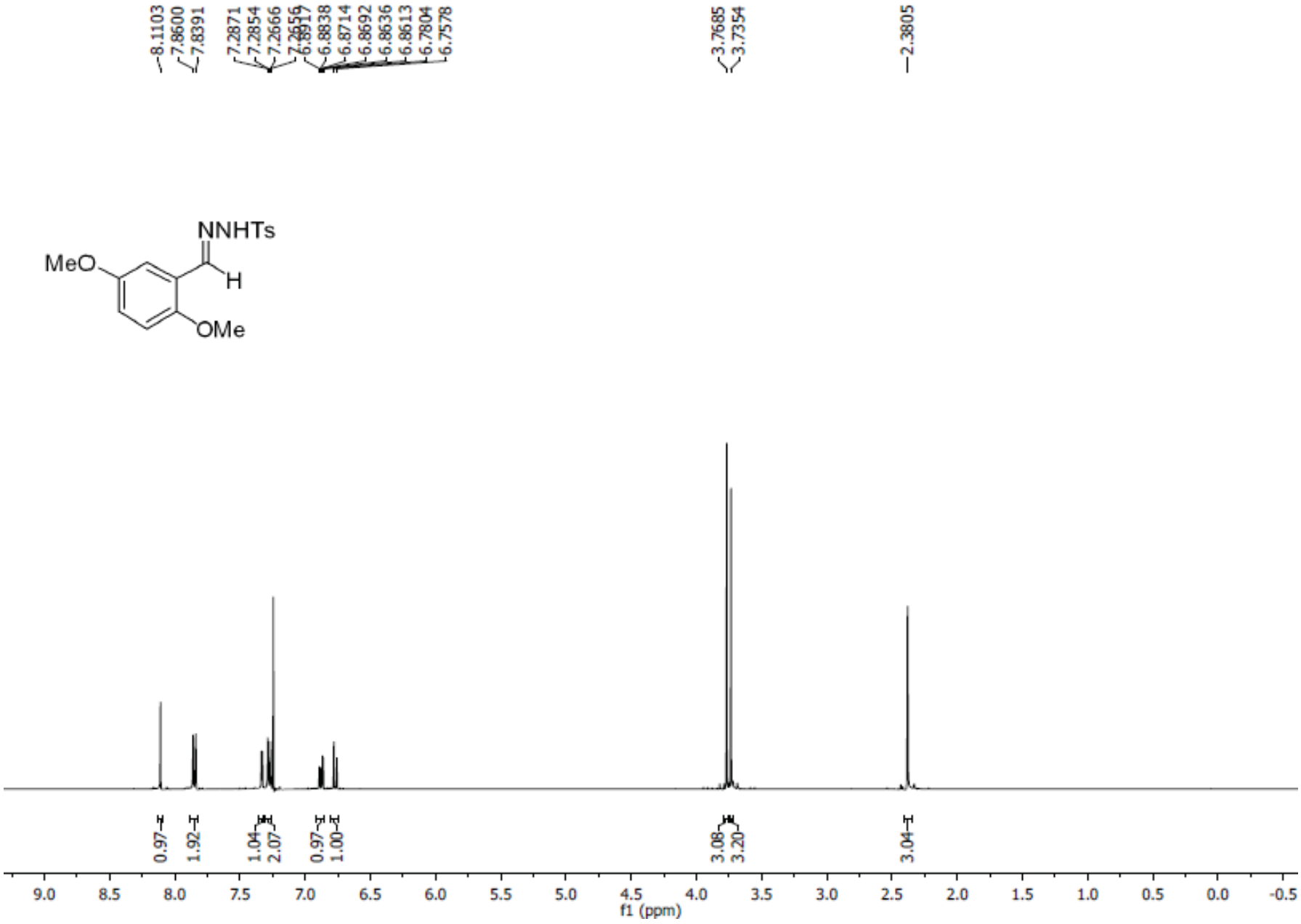
3-methoxybenzaldehyde tosylhydrazone **1e**



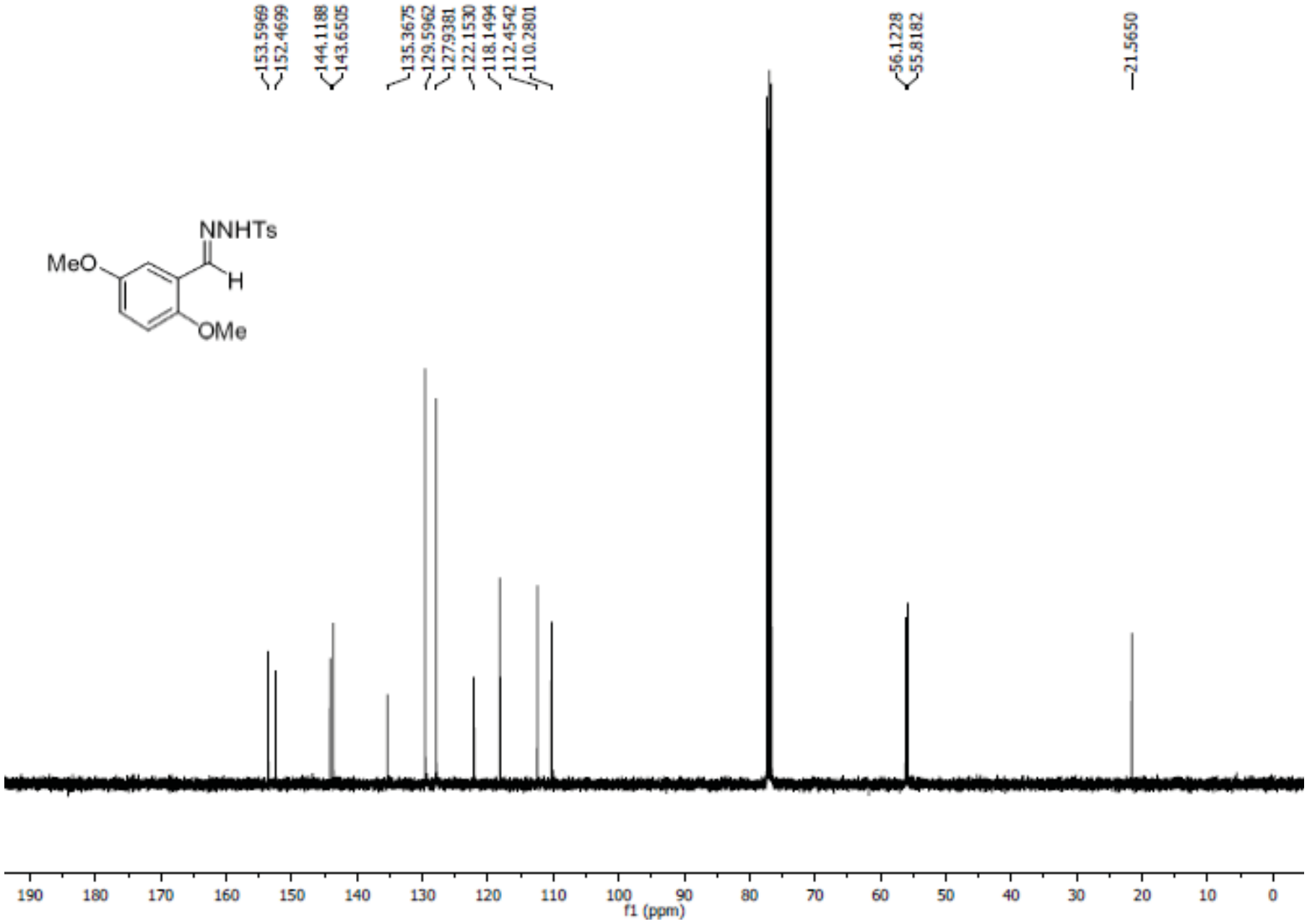
3-methoxybenzaldehyde tosylhydrazone **1e**



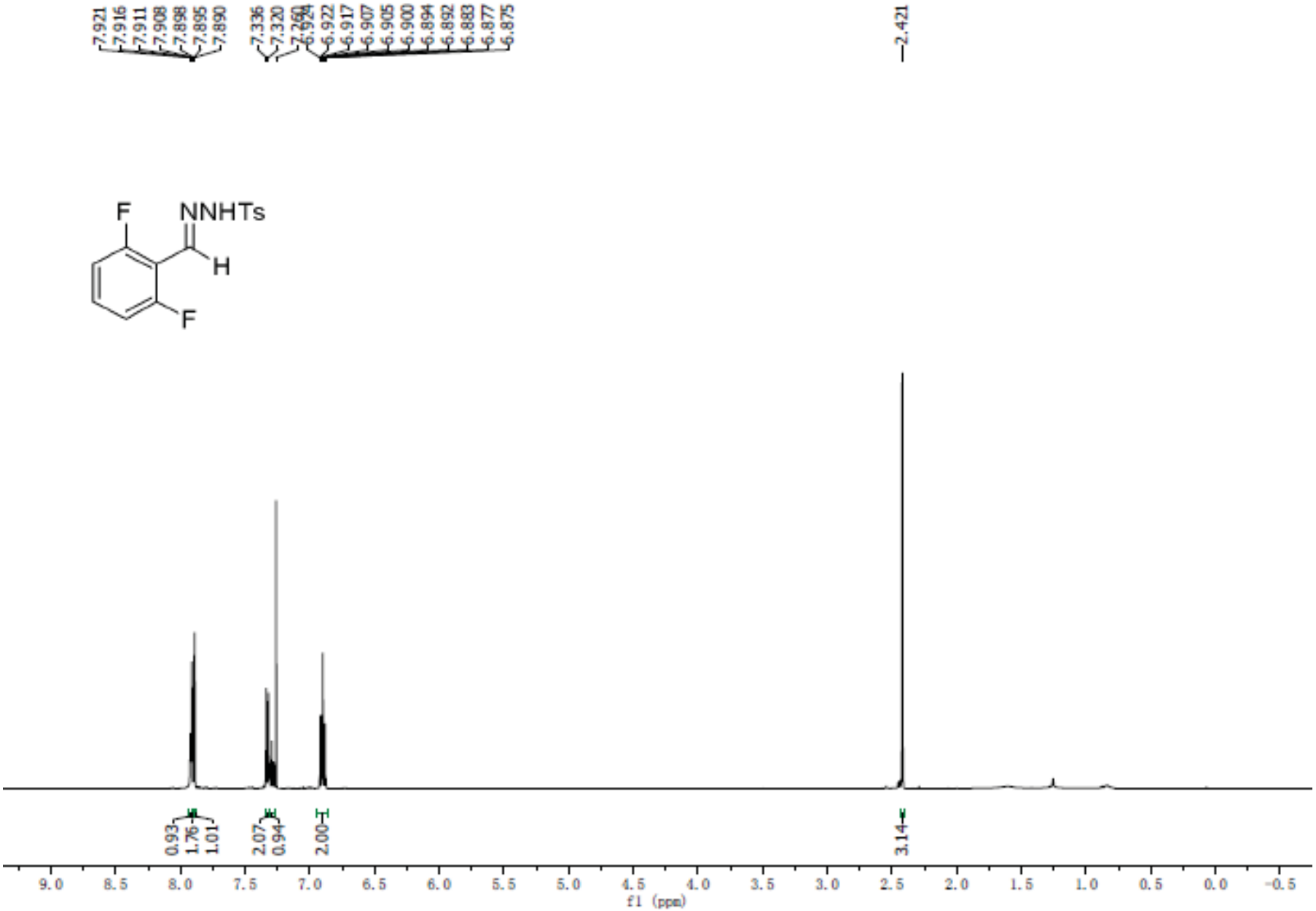
2,5-dimethoxybenzaldehyde tosylhydrazone **1f**



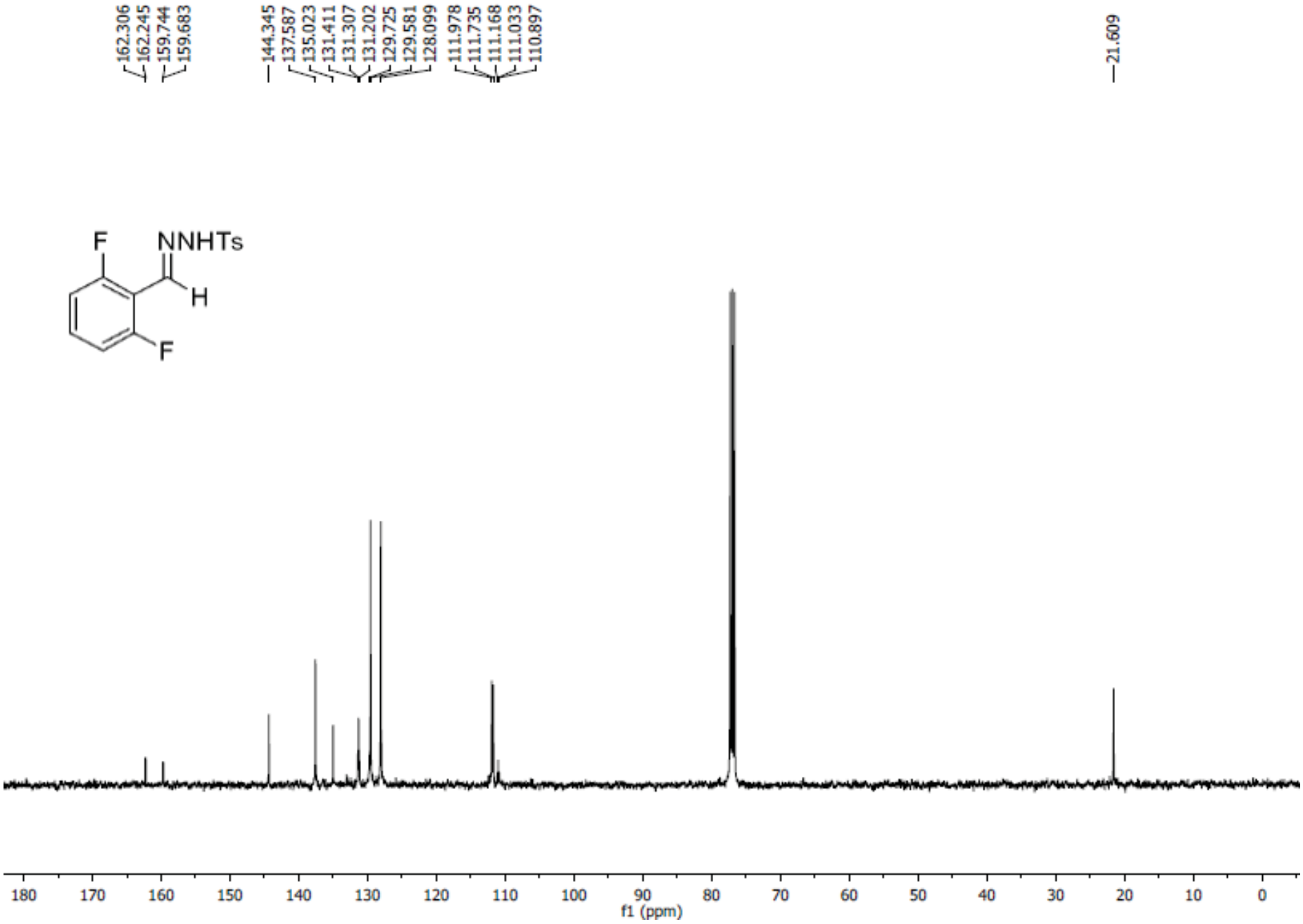
2,5-dimethoxybenzaldehyde tosylhydrazone **1f**



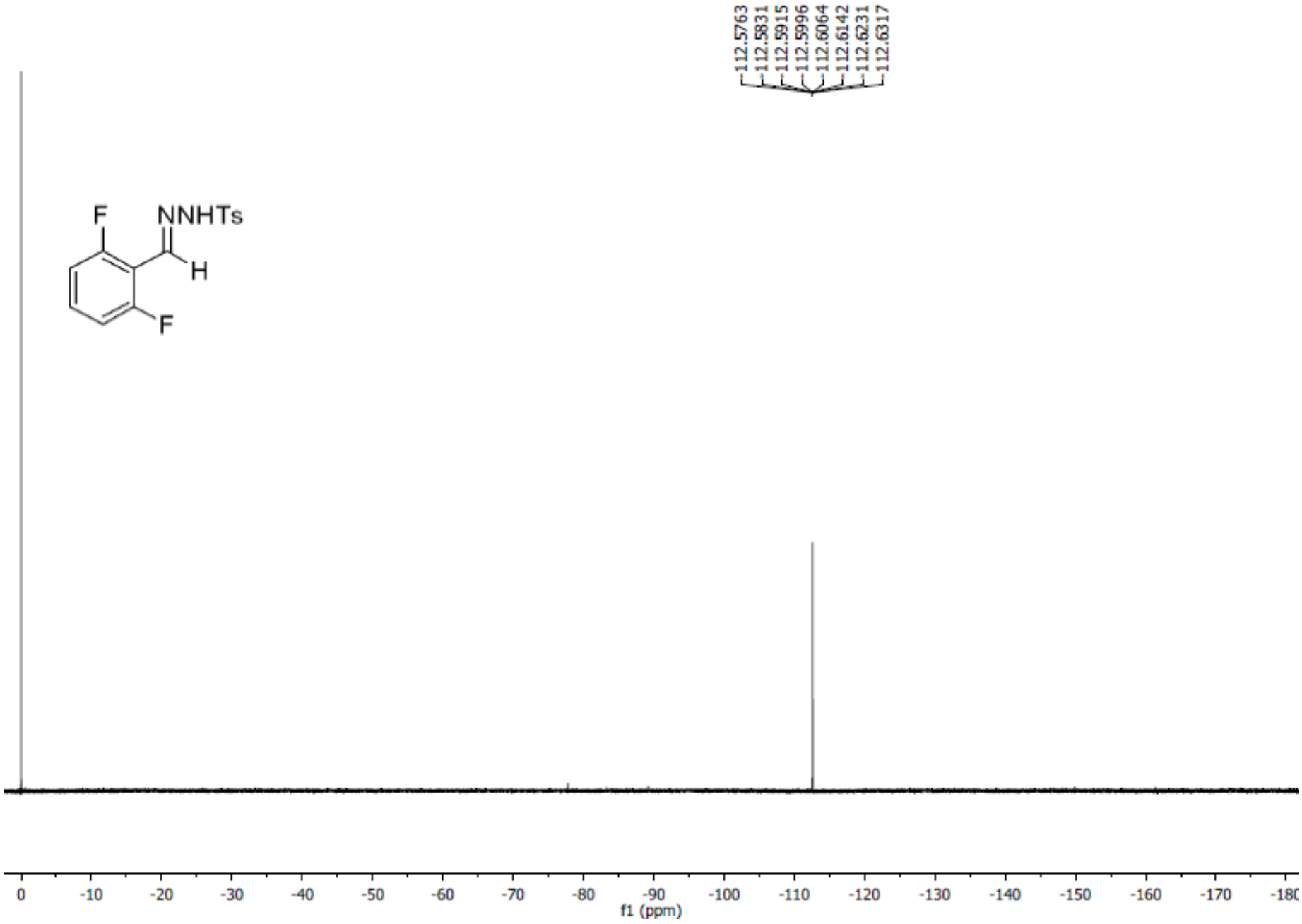
2,6-difluorobenzaldehyde tosylhydrazone **1g**



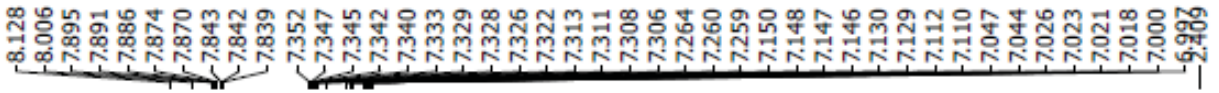
2,6-difluorobenzaldehyde tosylhydrazone **1g**

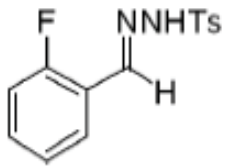


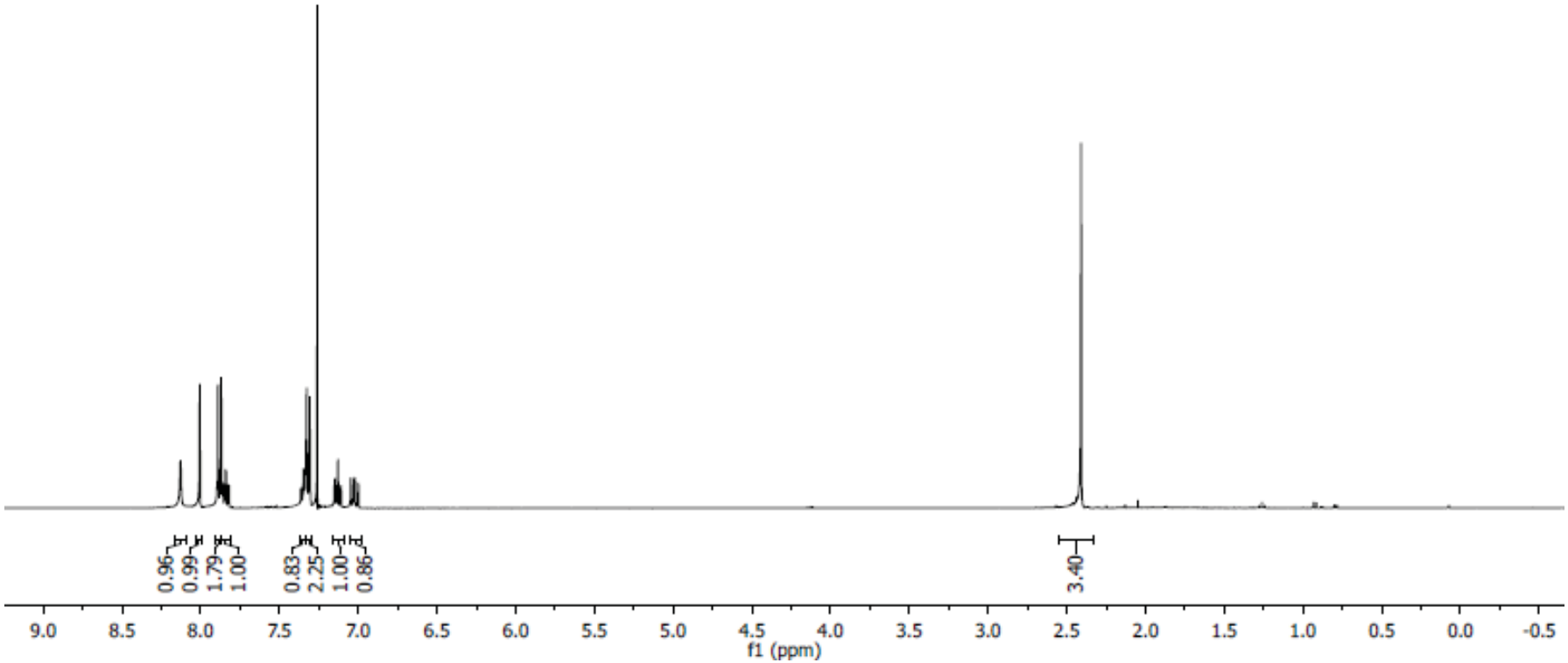
2,6-difluorobenzaldehyde tosylhydrazone **1g**



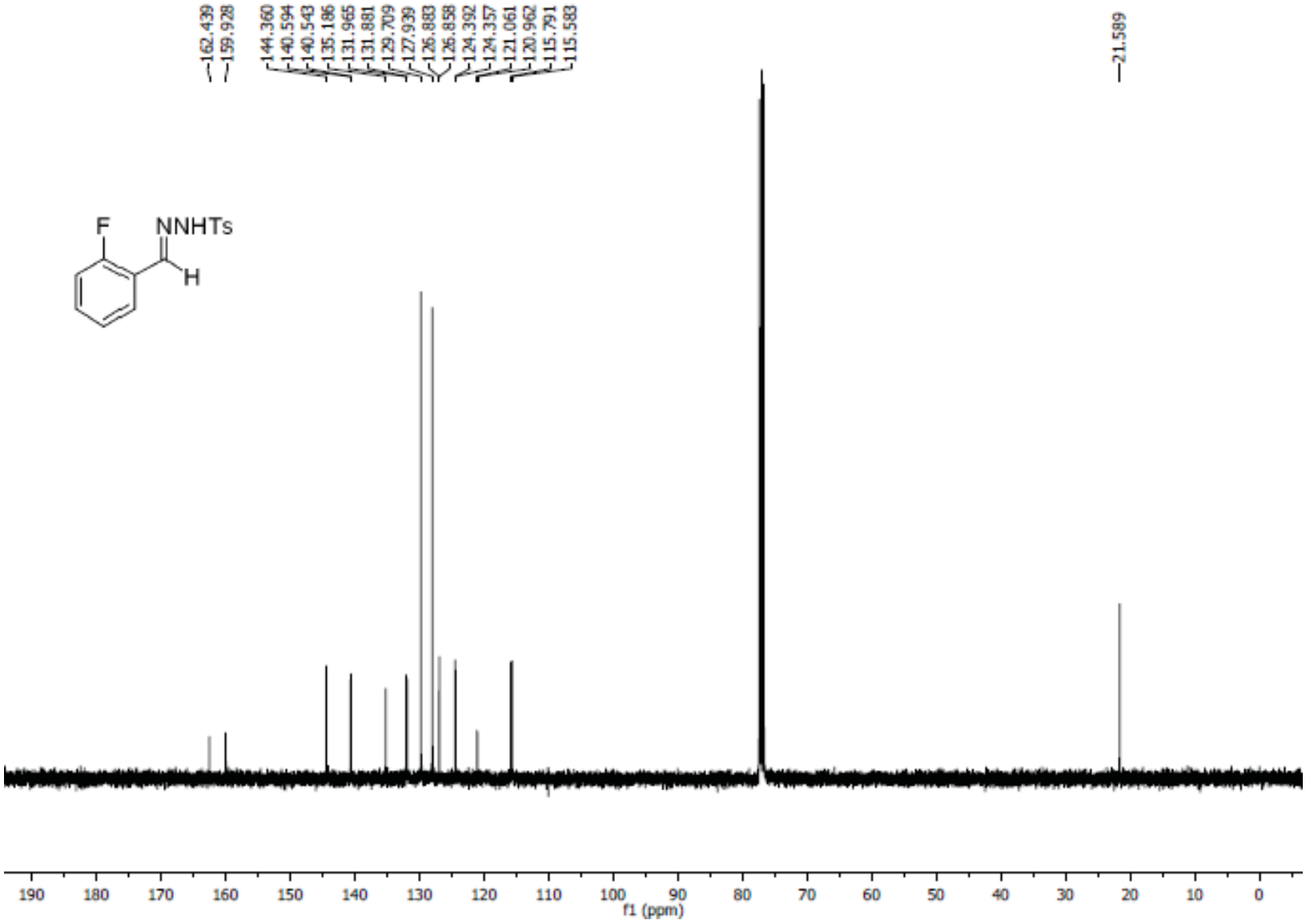
2-fluorobenzaldehyde tosylhydrazone **1h**



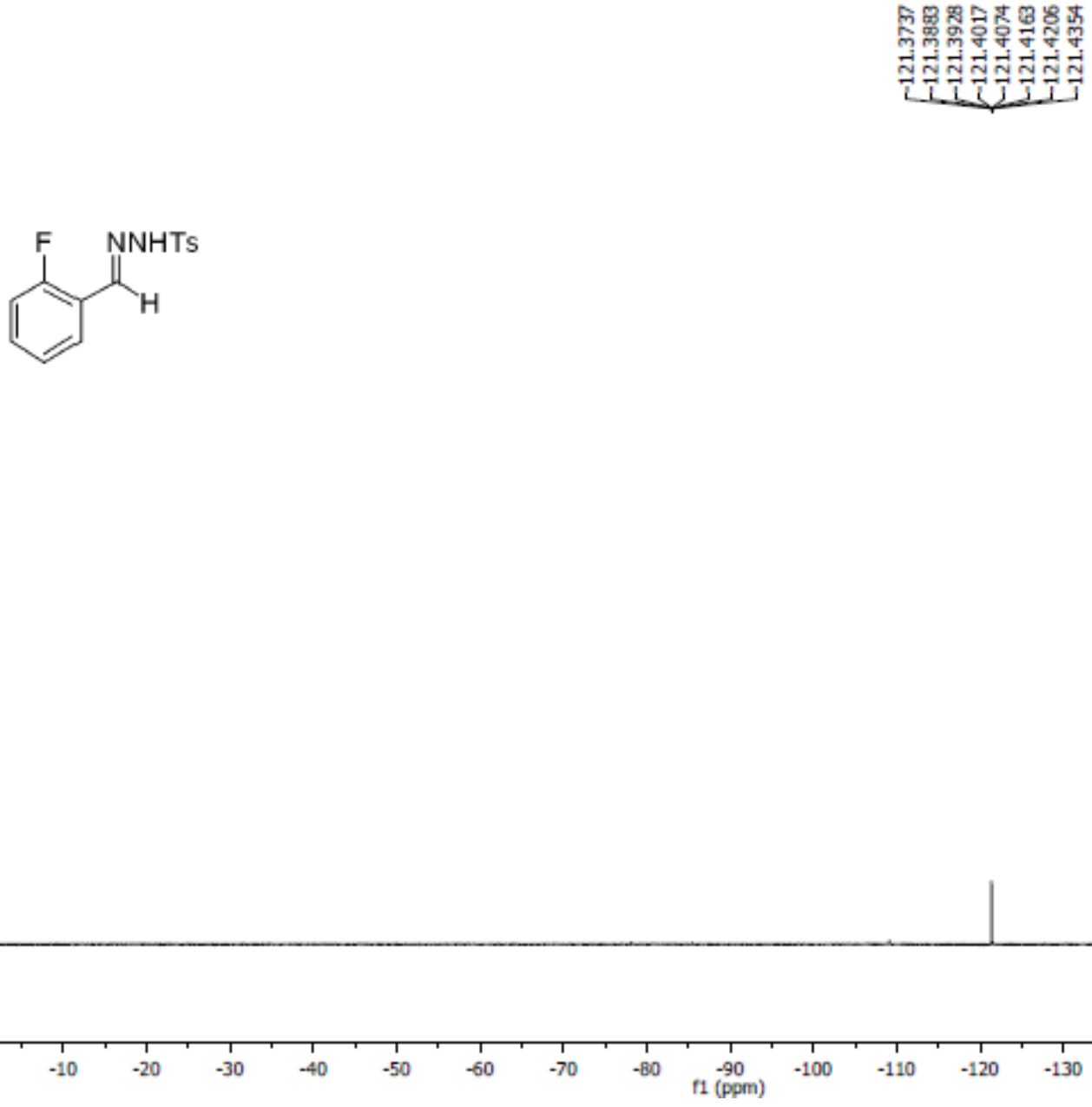




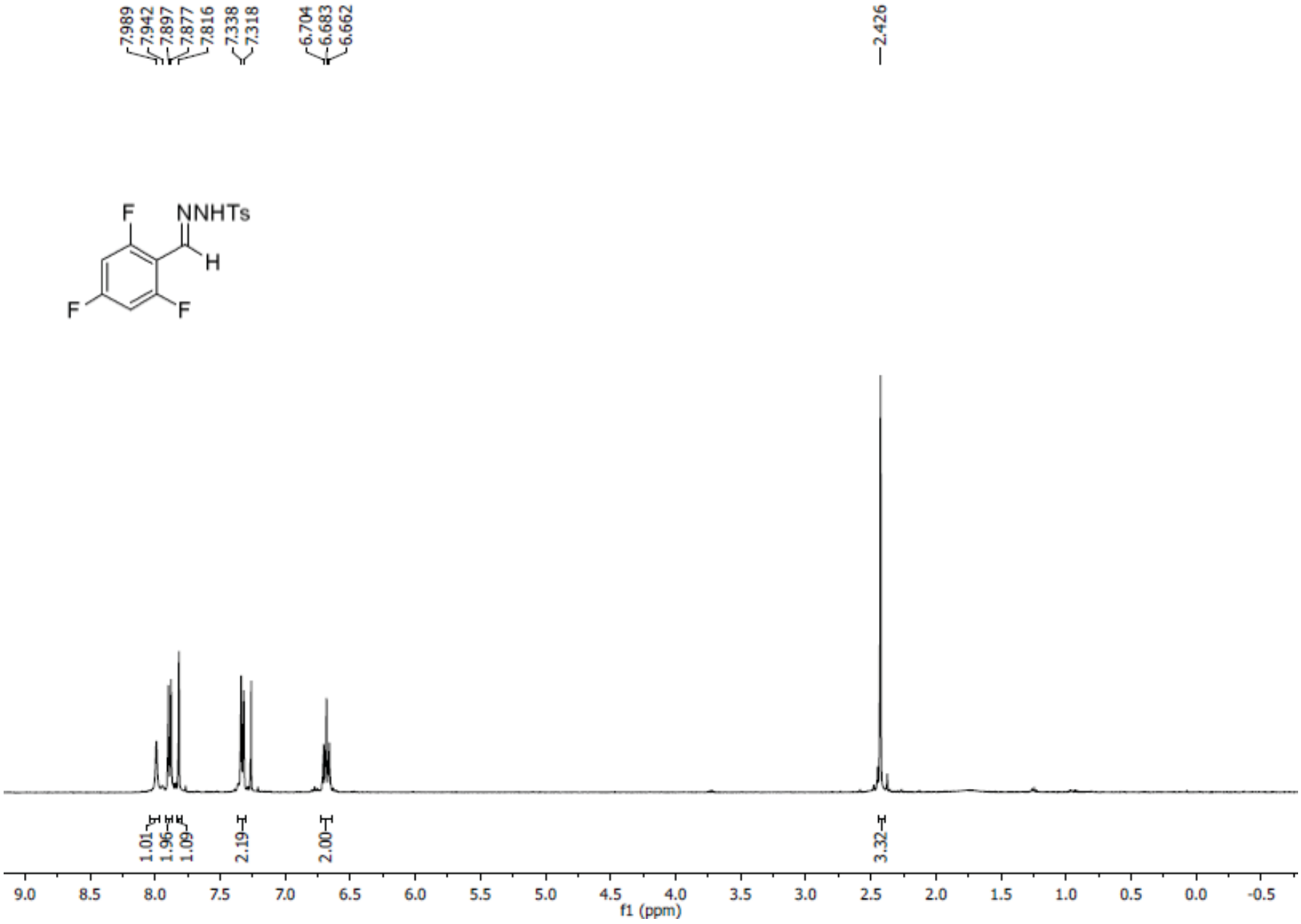
2-fluorobenzaldehyde tosylhydrazone **1h**



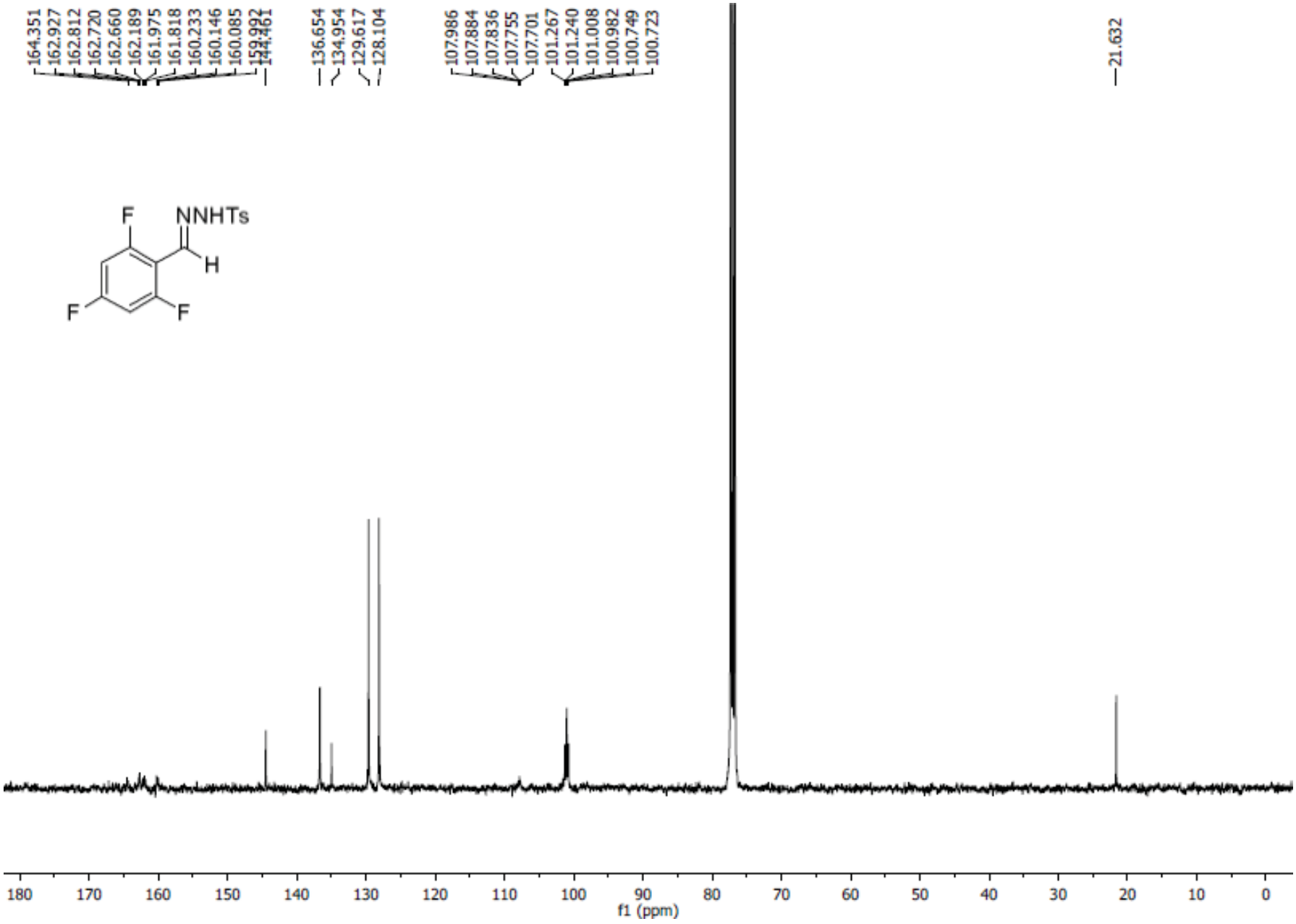
2-fluorobenzaldehyde tosylhydrazone **1h**



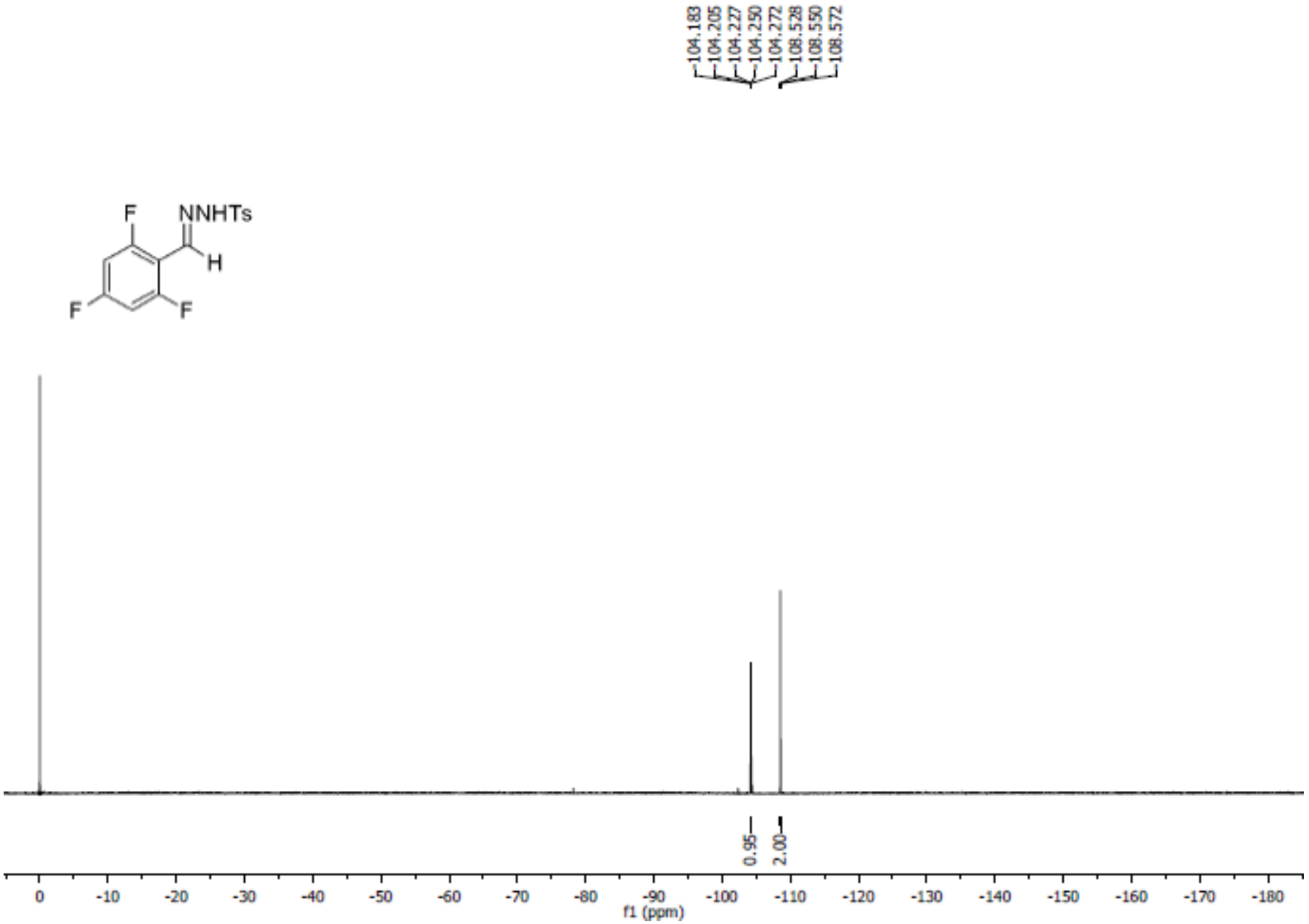
2,4,6-trifluorobenzaldehyde tosylhydrazone **1i**



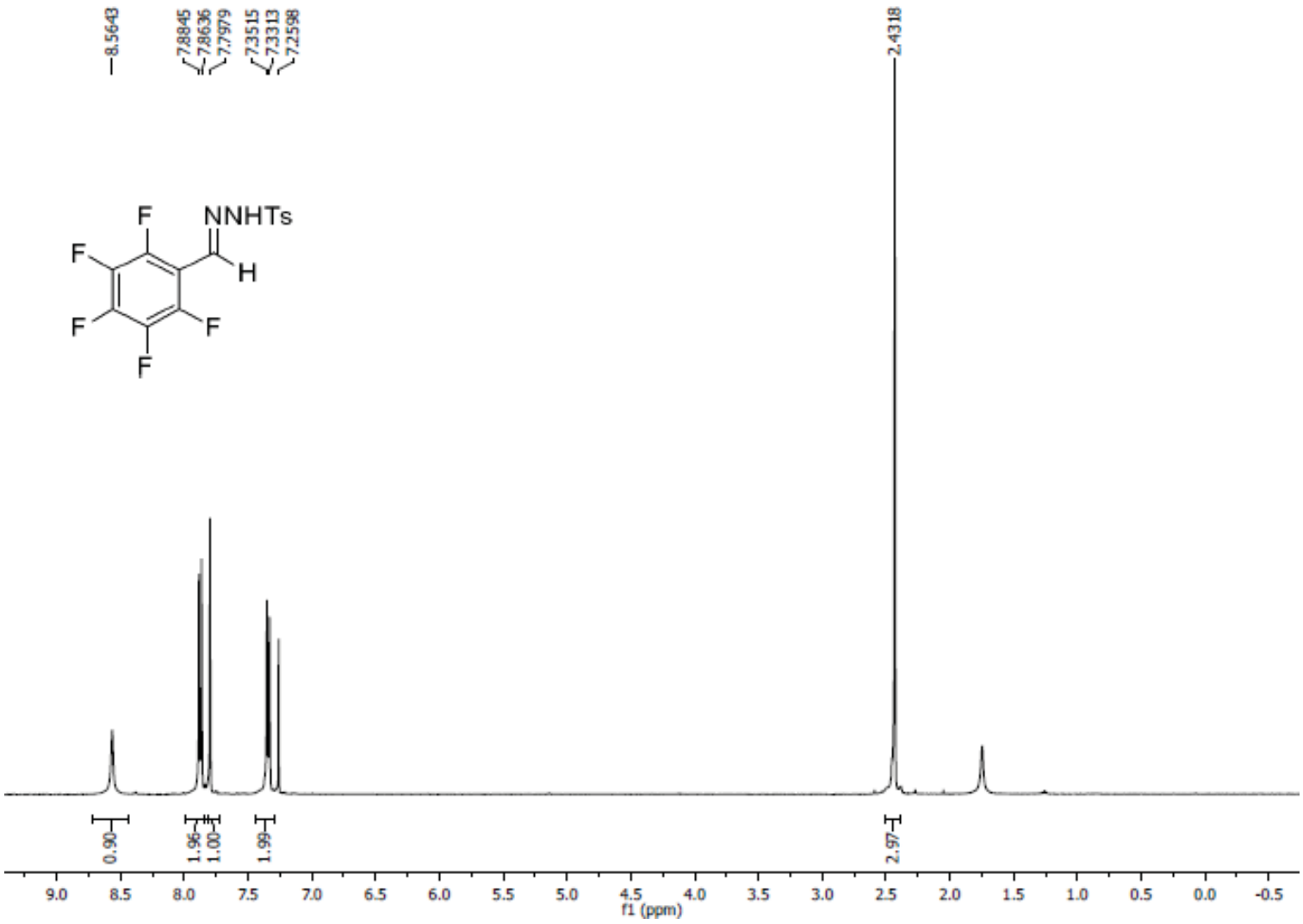
2,4,6-trifluorobenzaldehyde tosylhydrazone **1i**



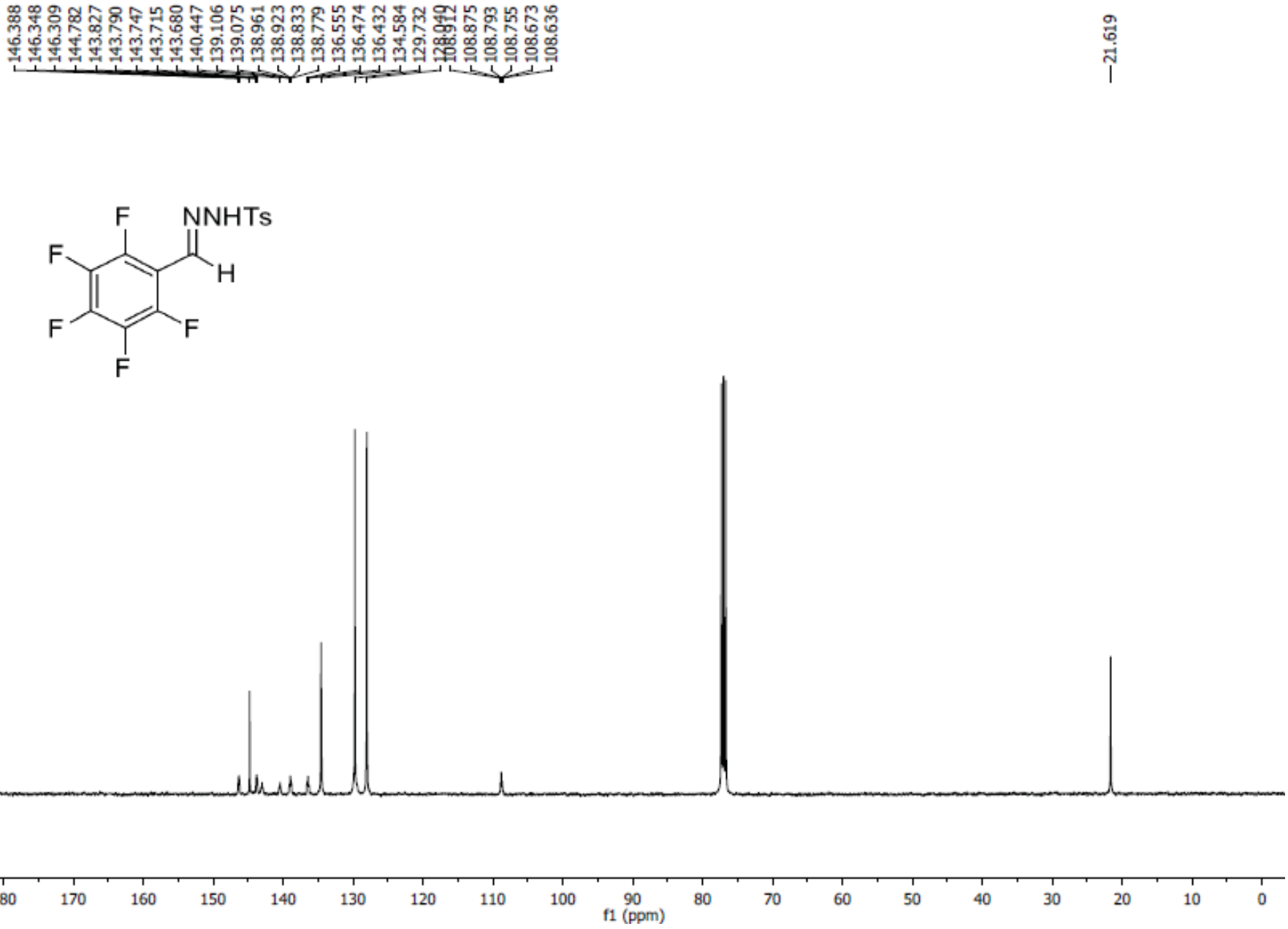
2,4,6-trifluorobenzaldehyde tosylhydrazone **1i**



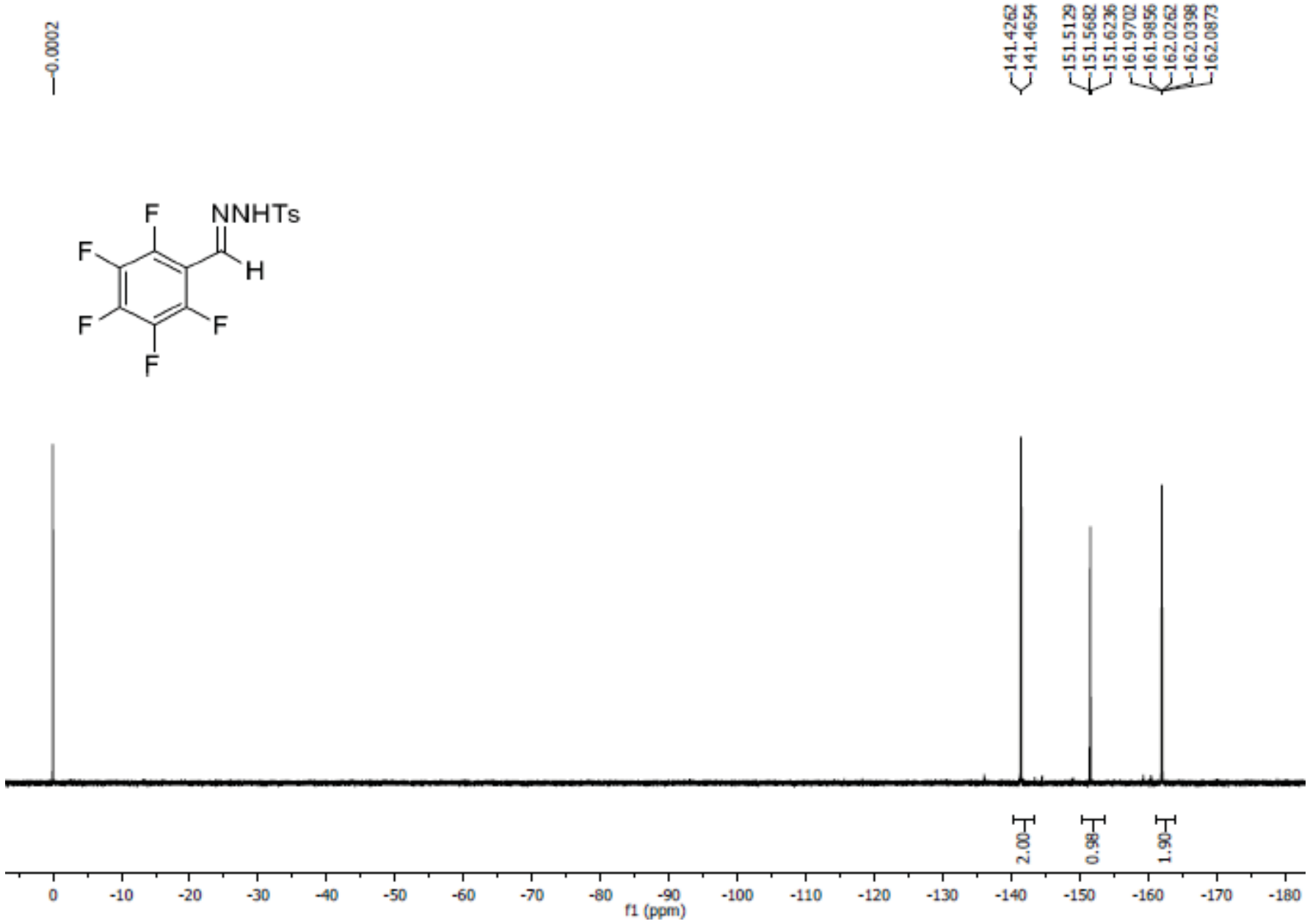
pentafluorobenzaldehyde tosylhydrazone **1j**



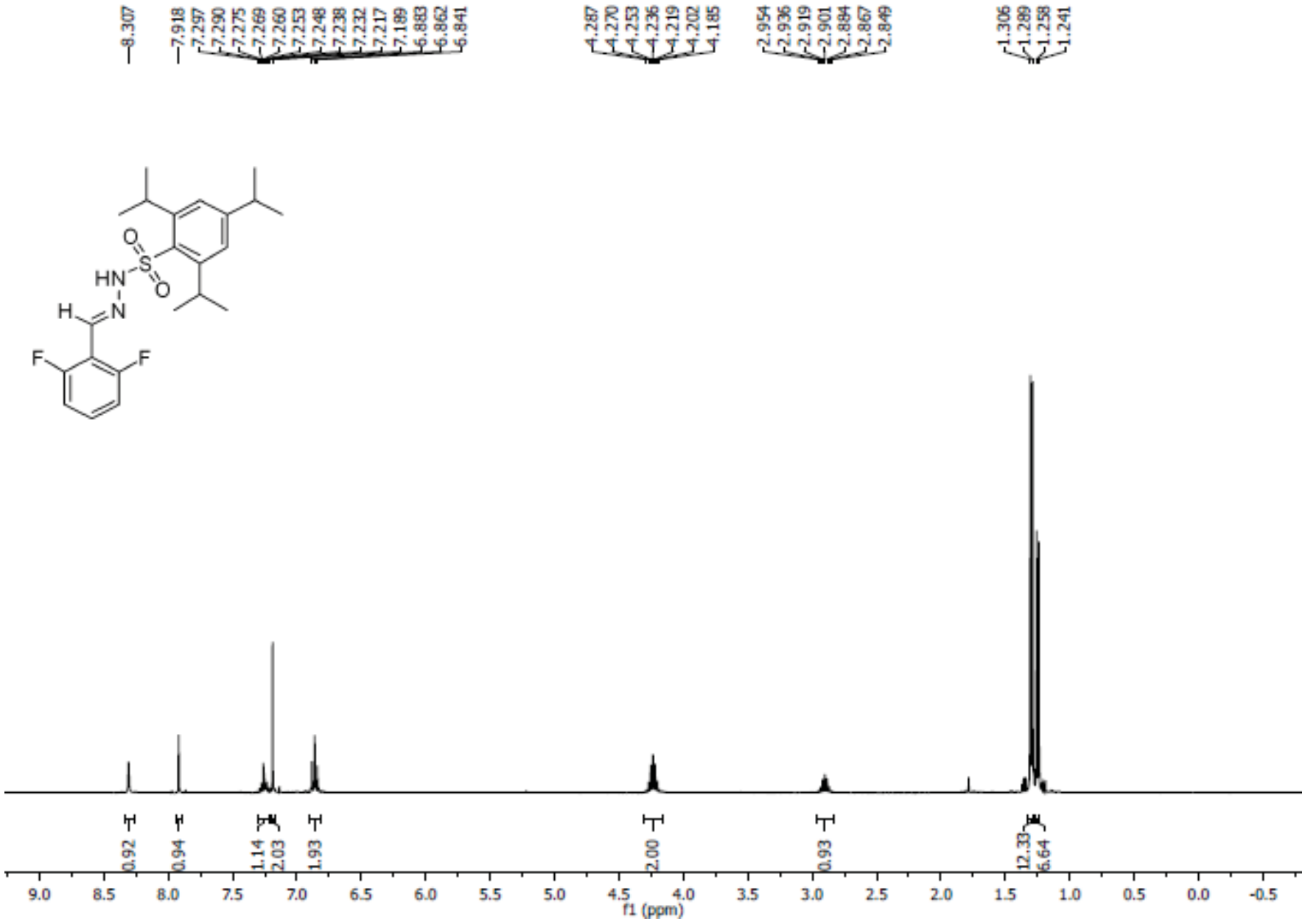
pentafluorobenzaldehyde tosylhydrazone **1j**



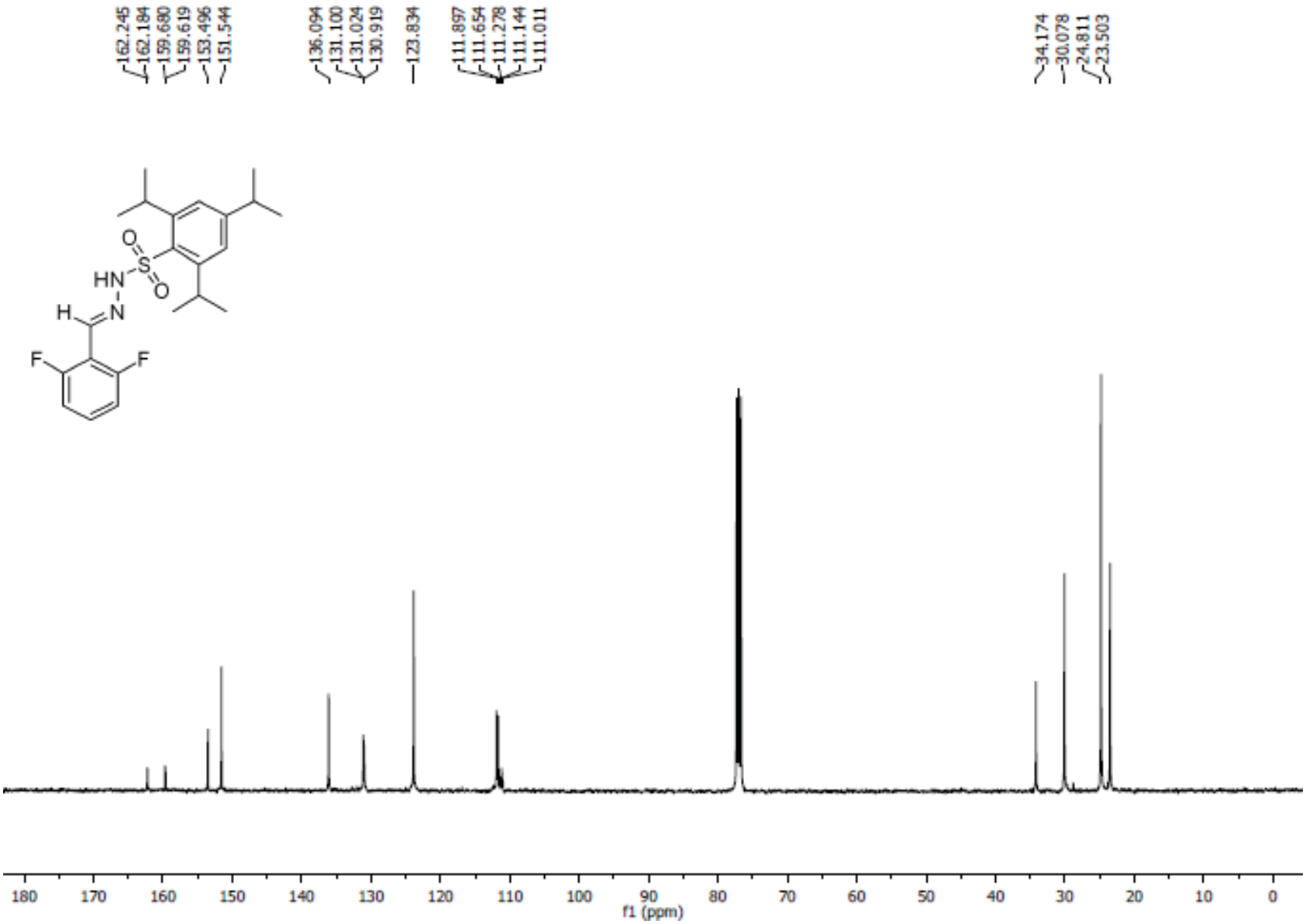
pentafluorobenzaldehyde tosylhydrazone **1j**



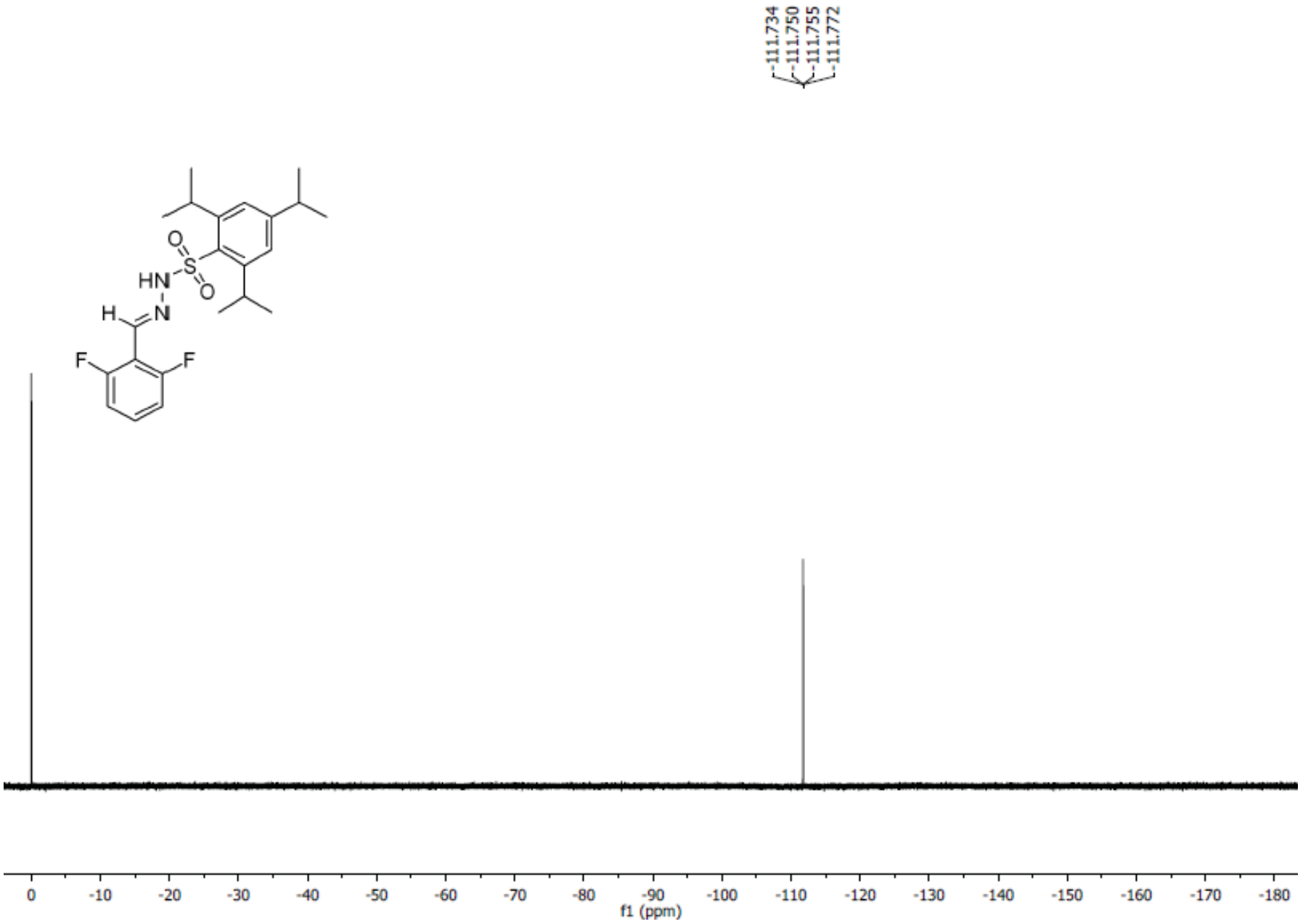
2,6-difluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1g'**



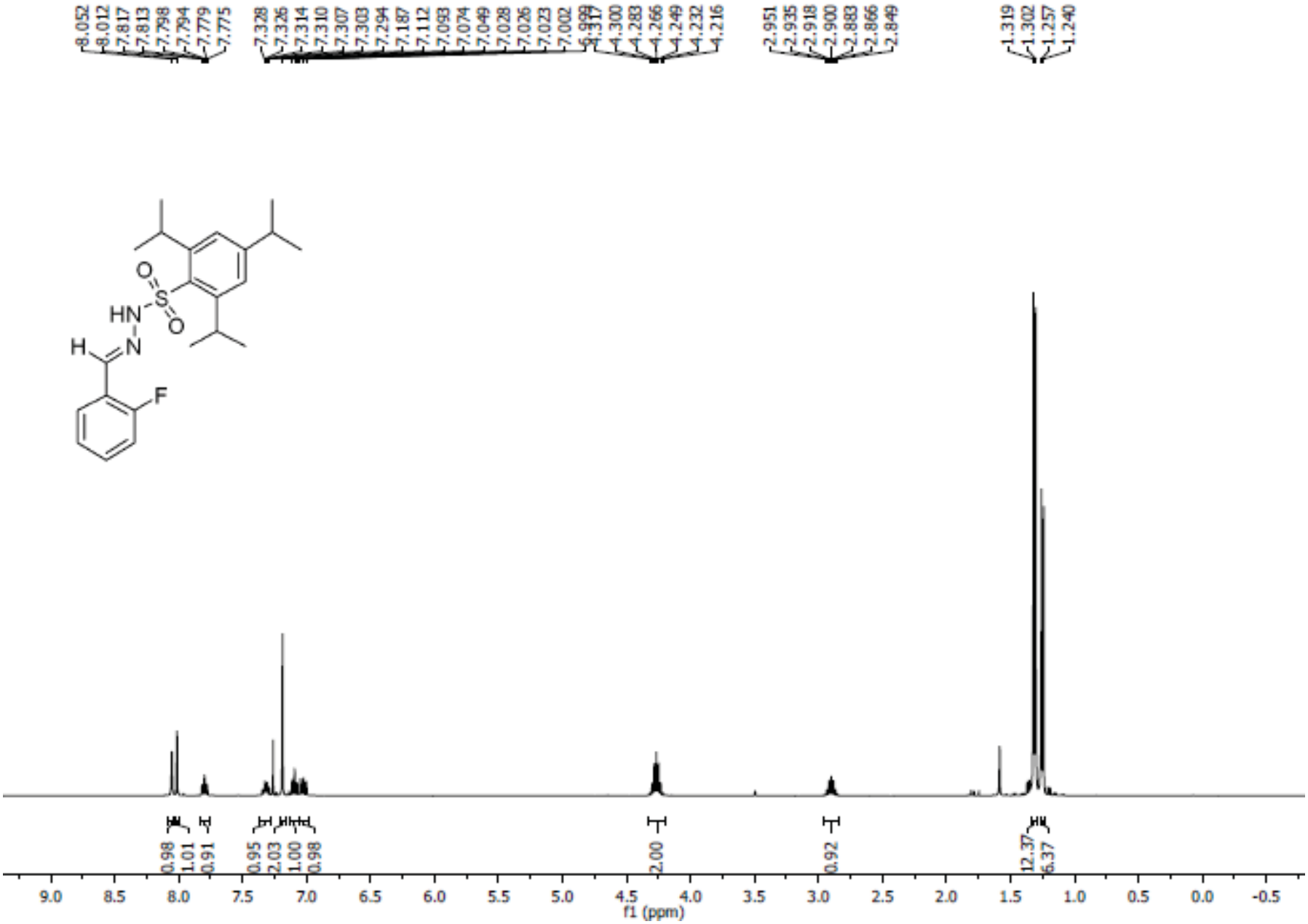
2,6-difluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1g'**



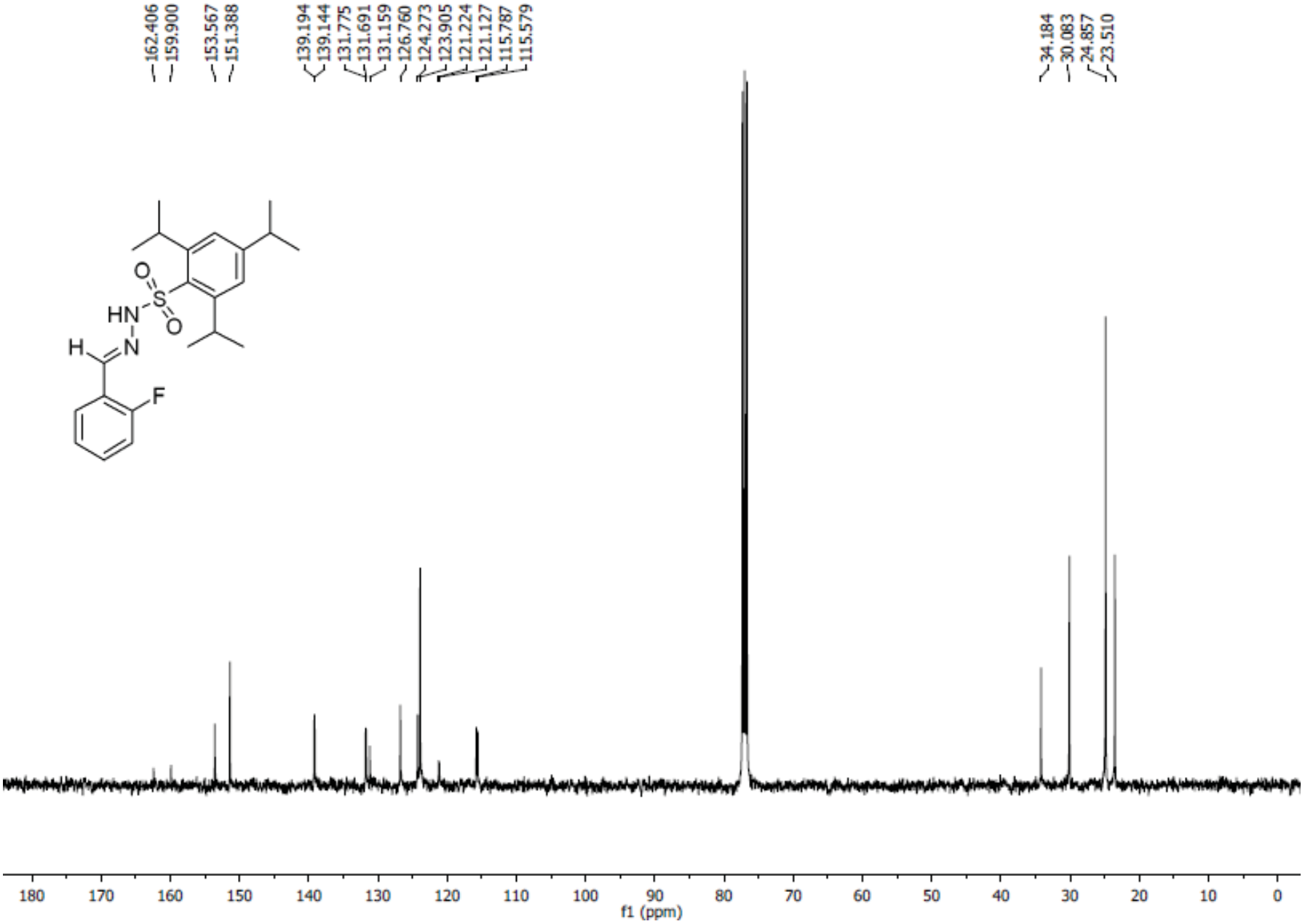
2,6-difluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1g'**



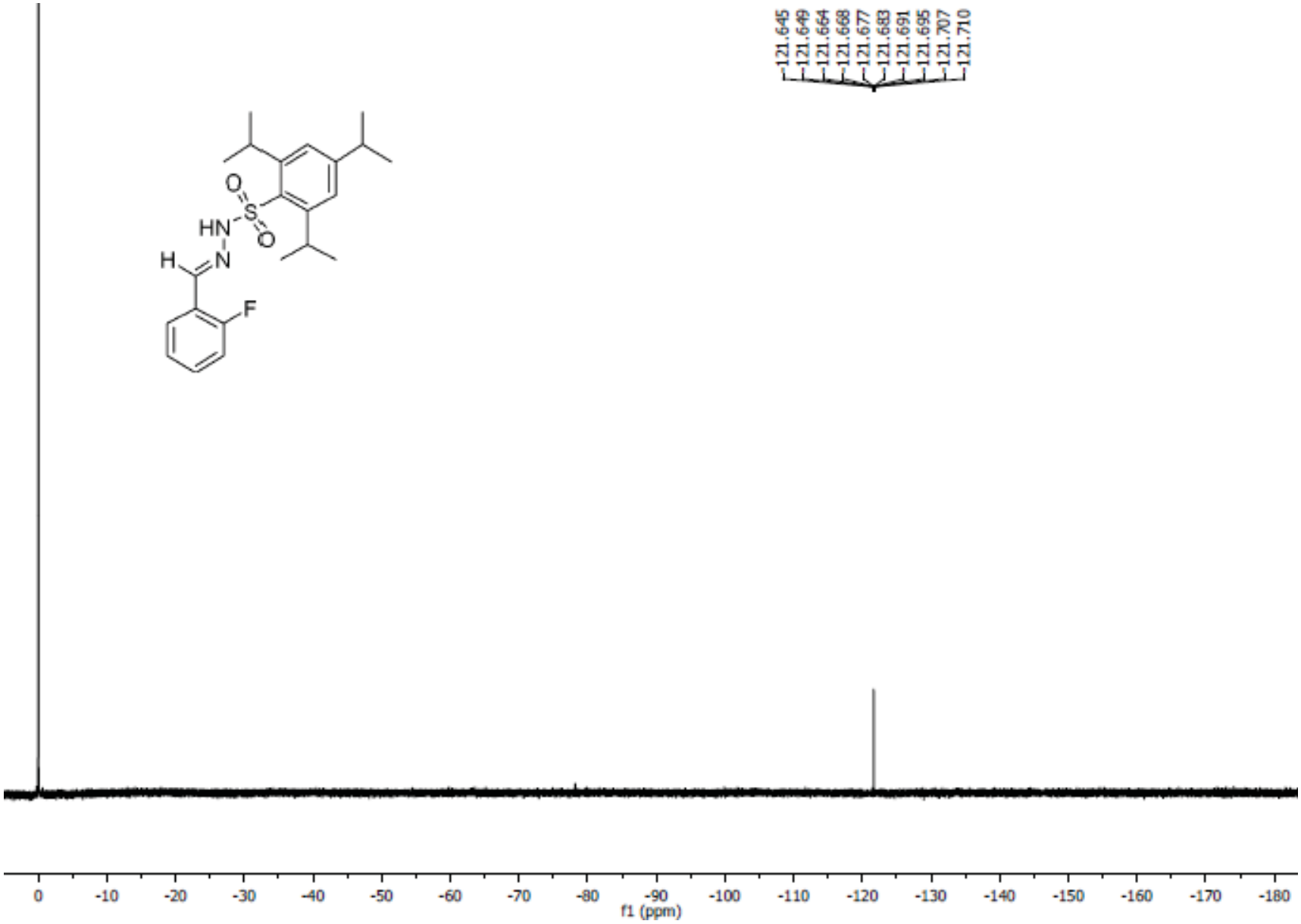
2-fluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1h'**



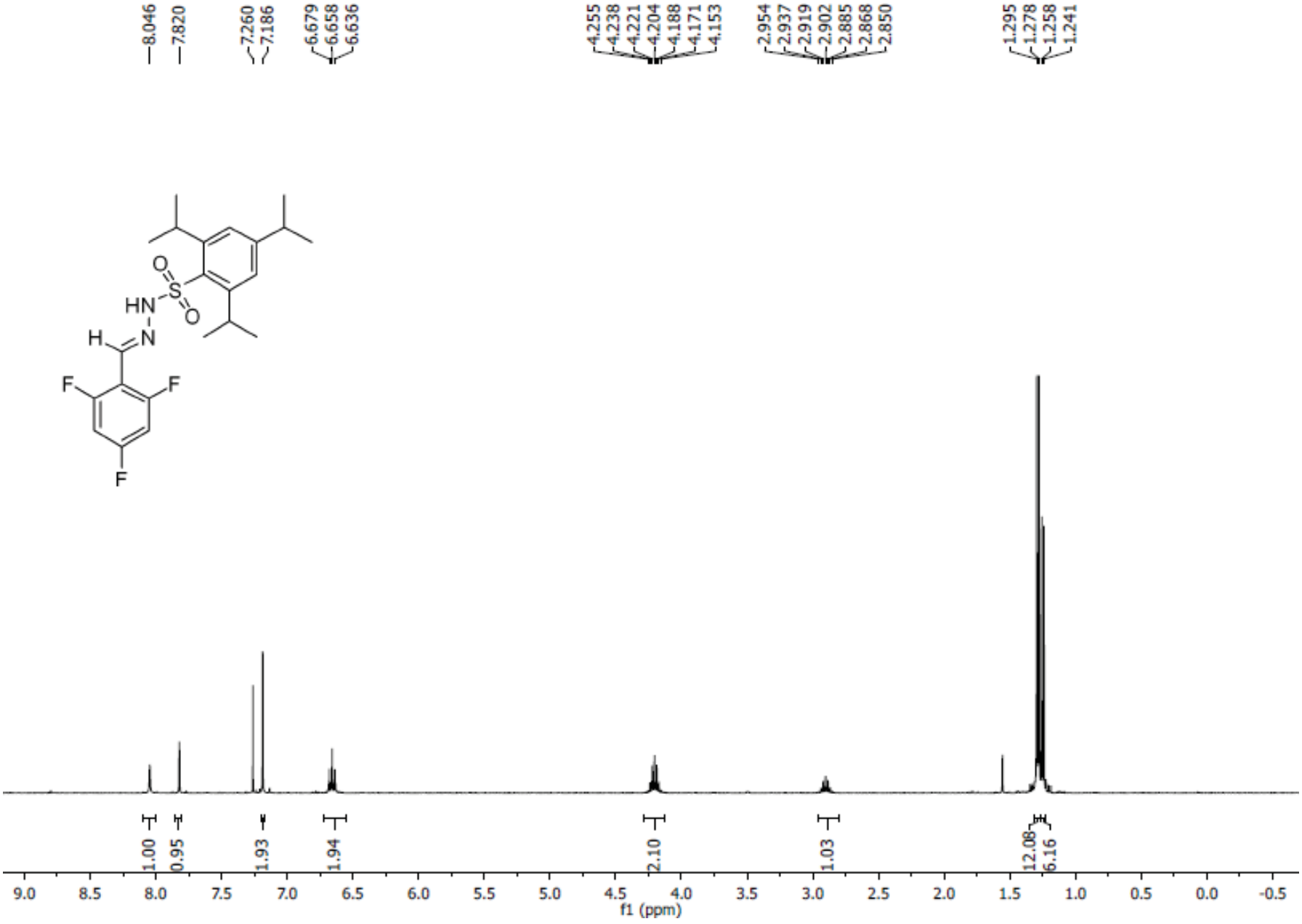
2-fluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1h'**



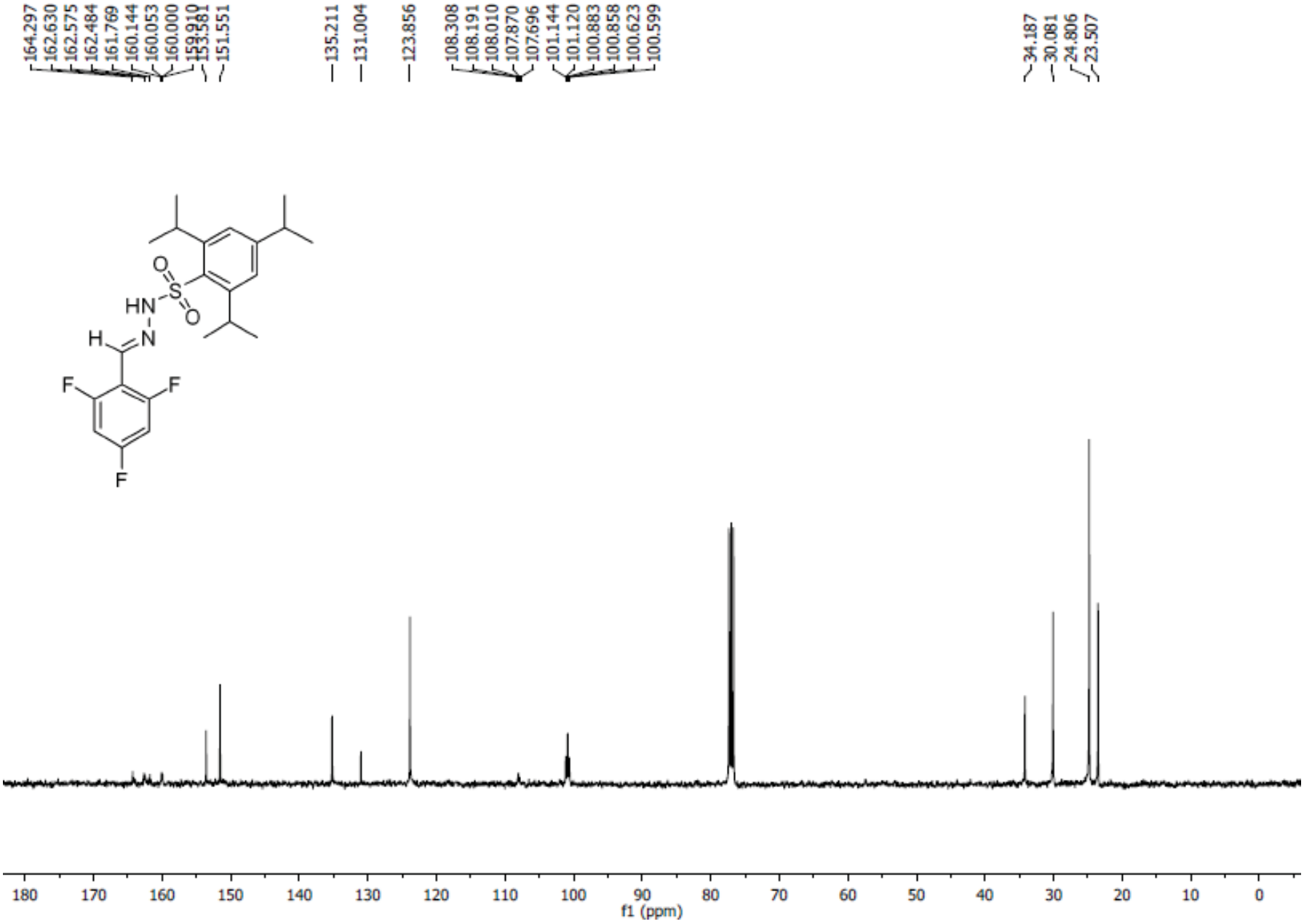
2-fluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1h'**



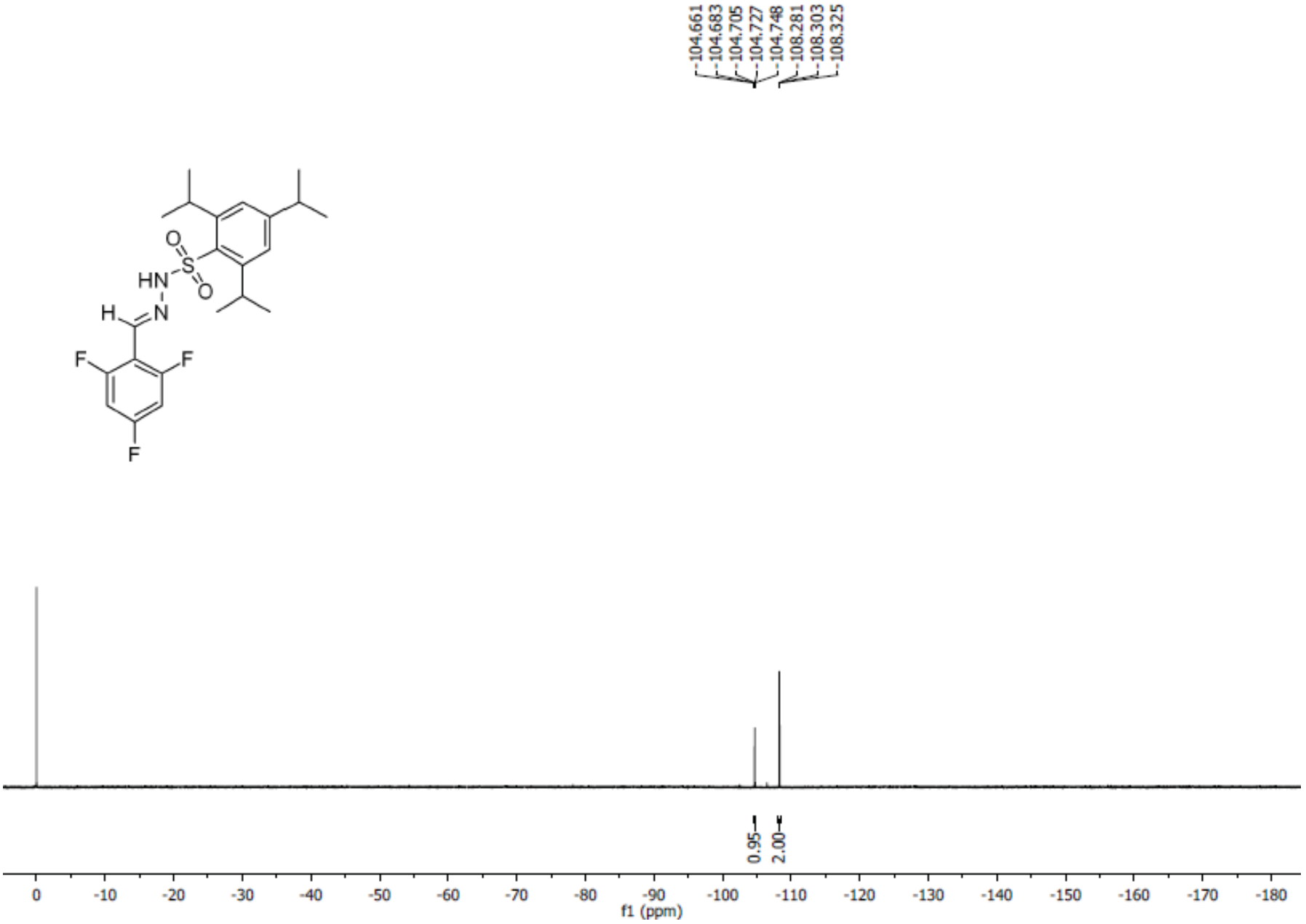
2,4,6-trifluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1i'**



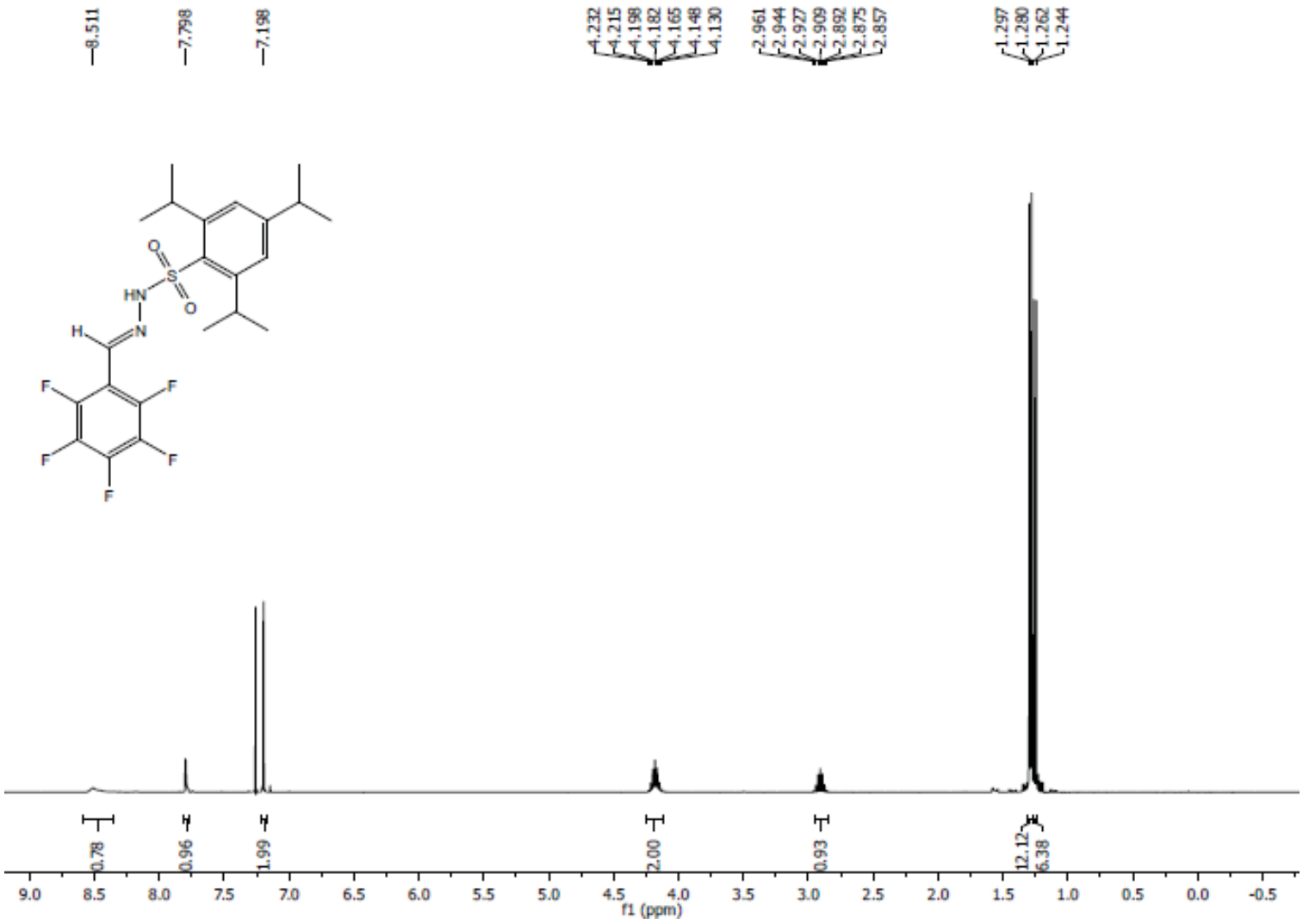
2,4,6-trifluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1i'**



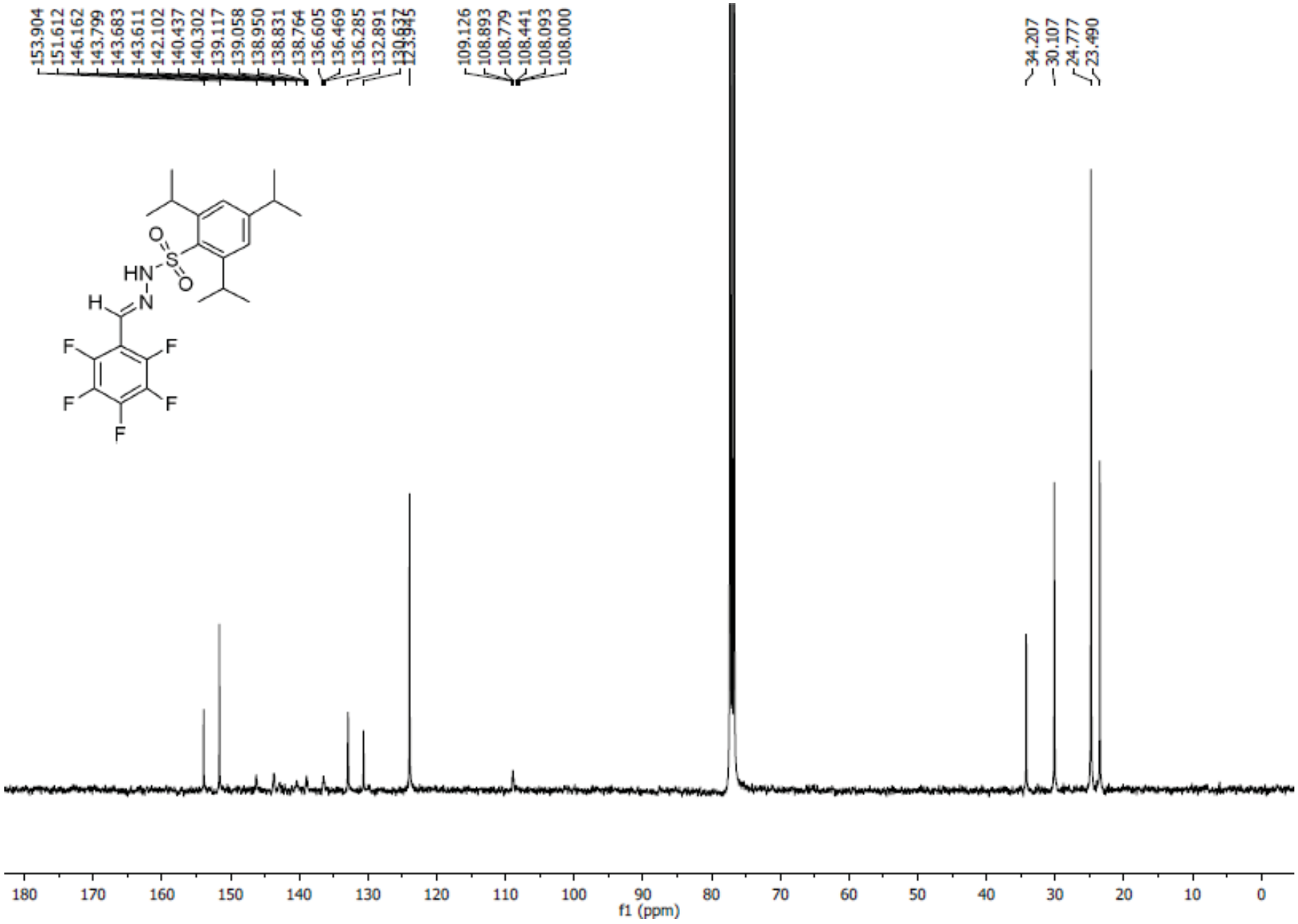
2,4,6-trifluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1i'**



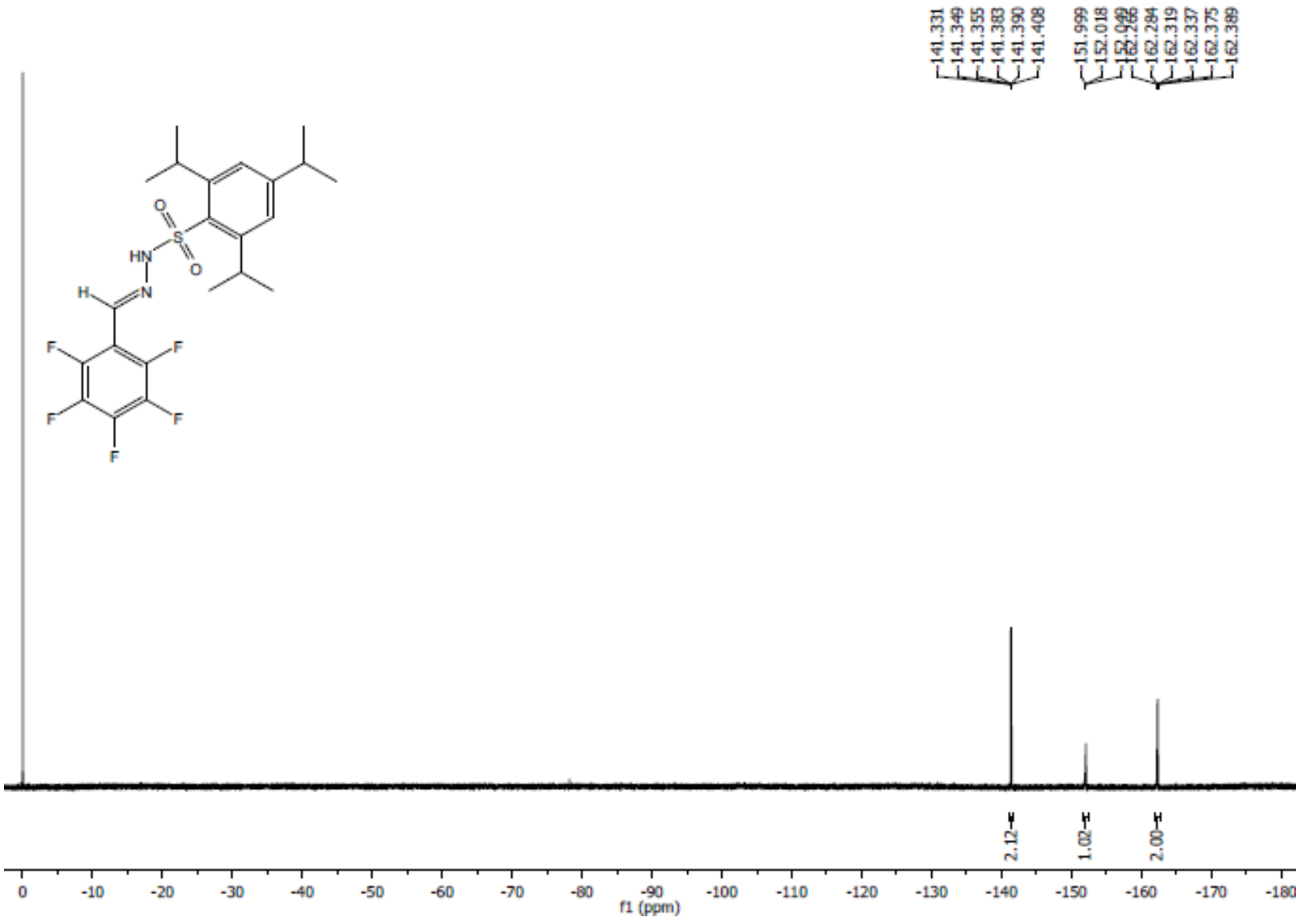
pentafluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1j'**



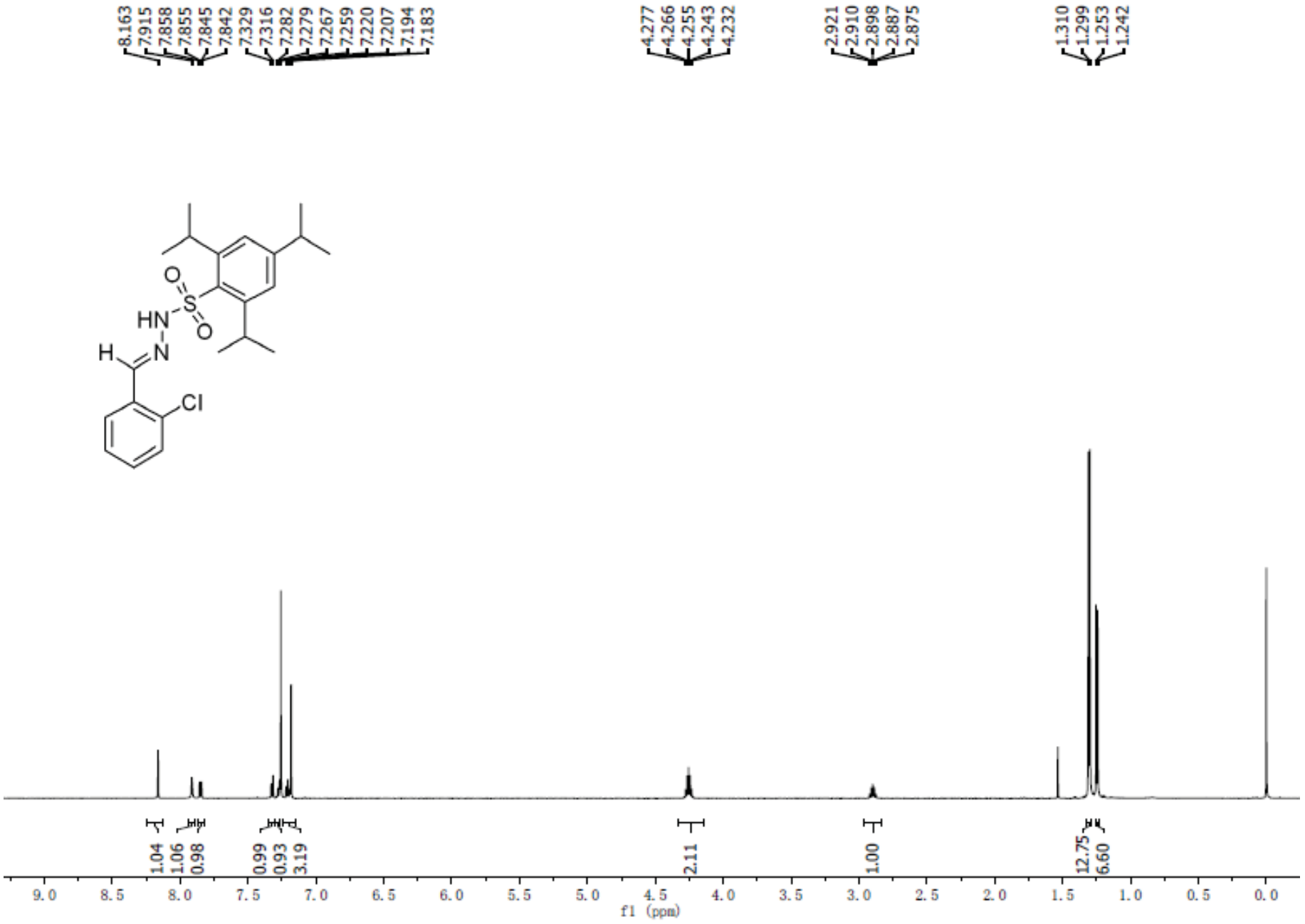
pentafluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1j'**



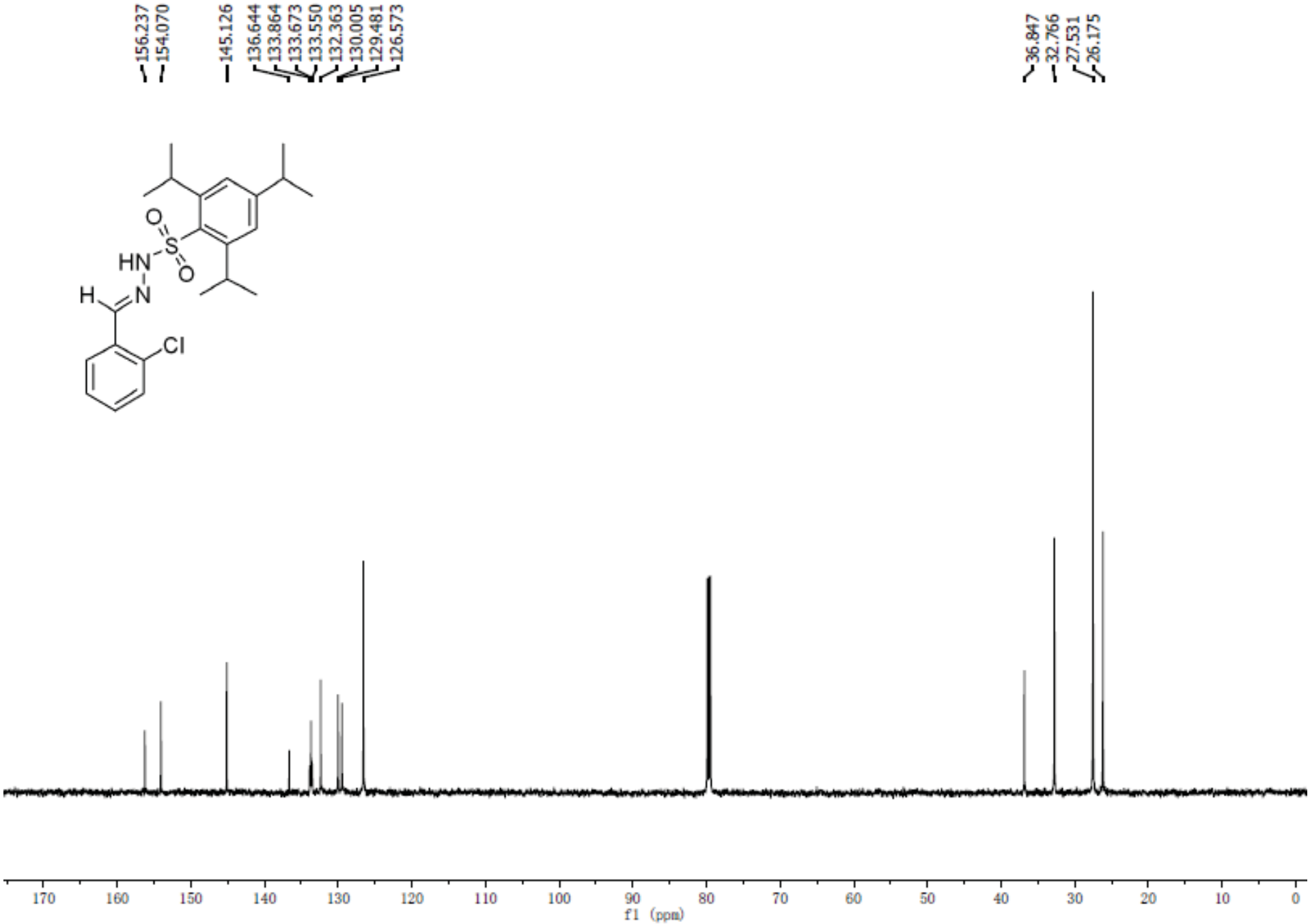
pentafluorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1j'**



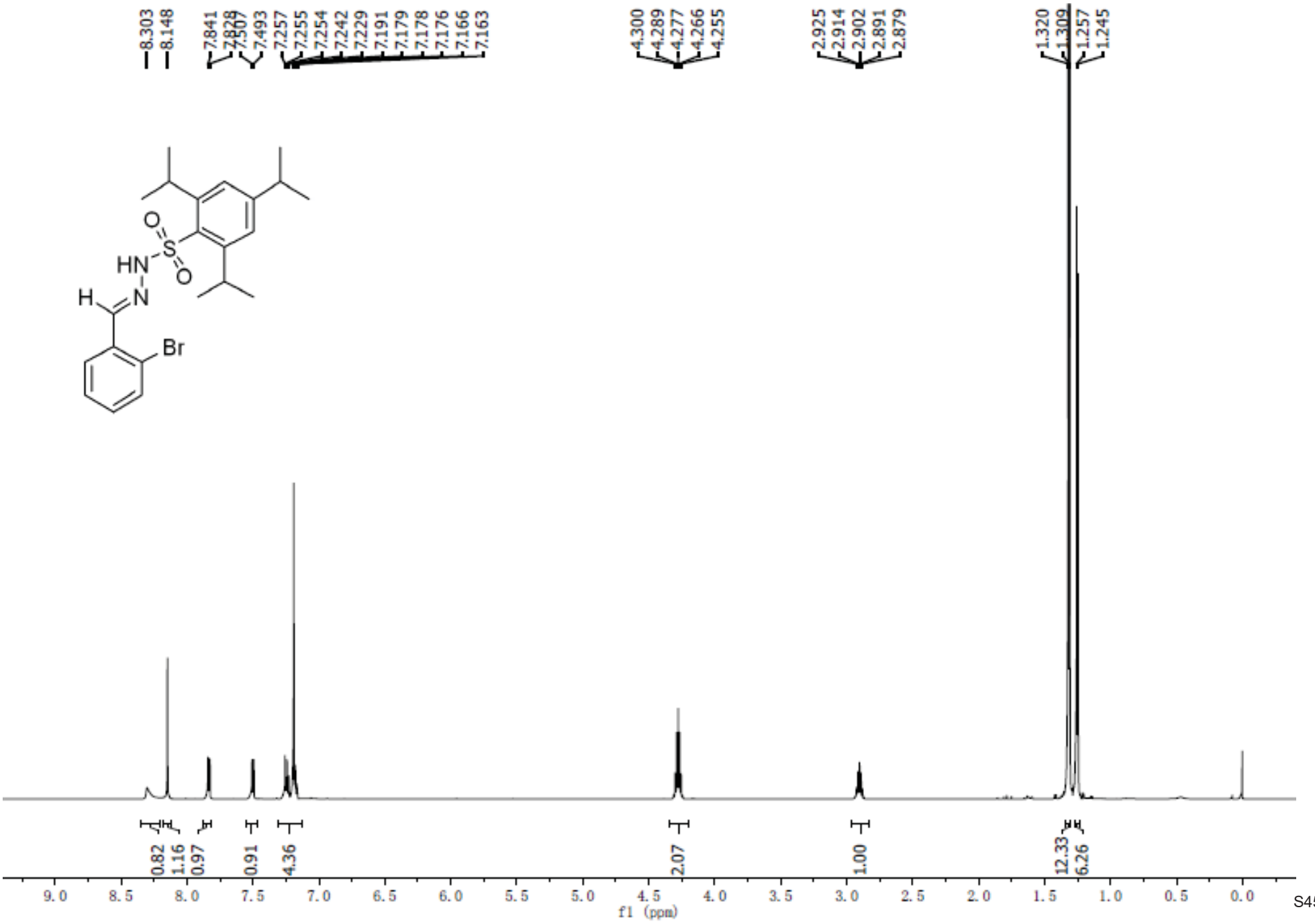
2-Chlorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1k'**



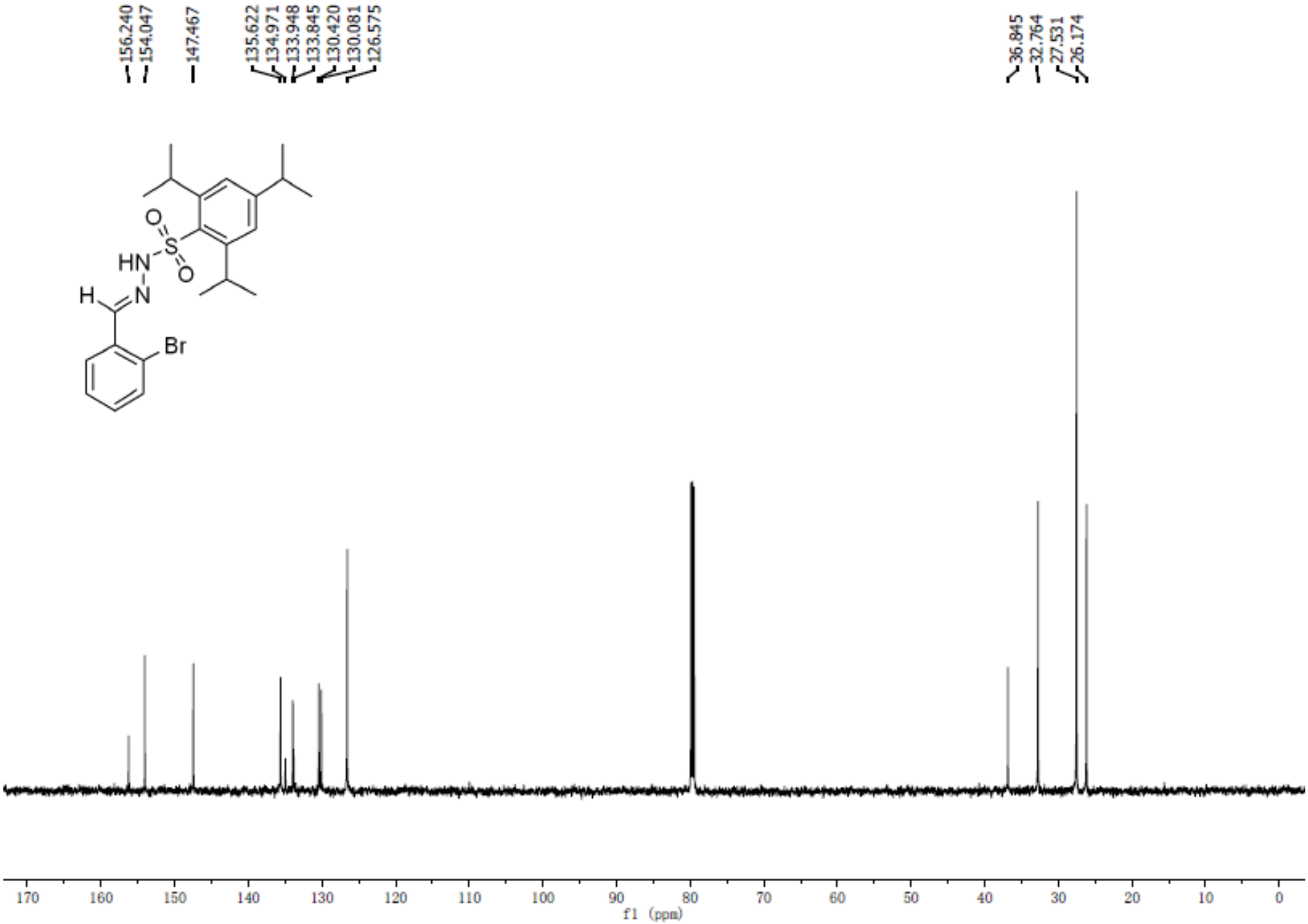
2-Chlorobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1k'**



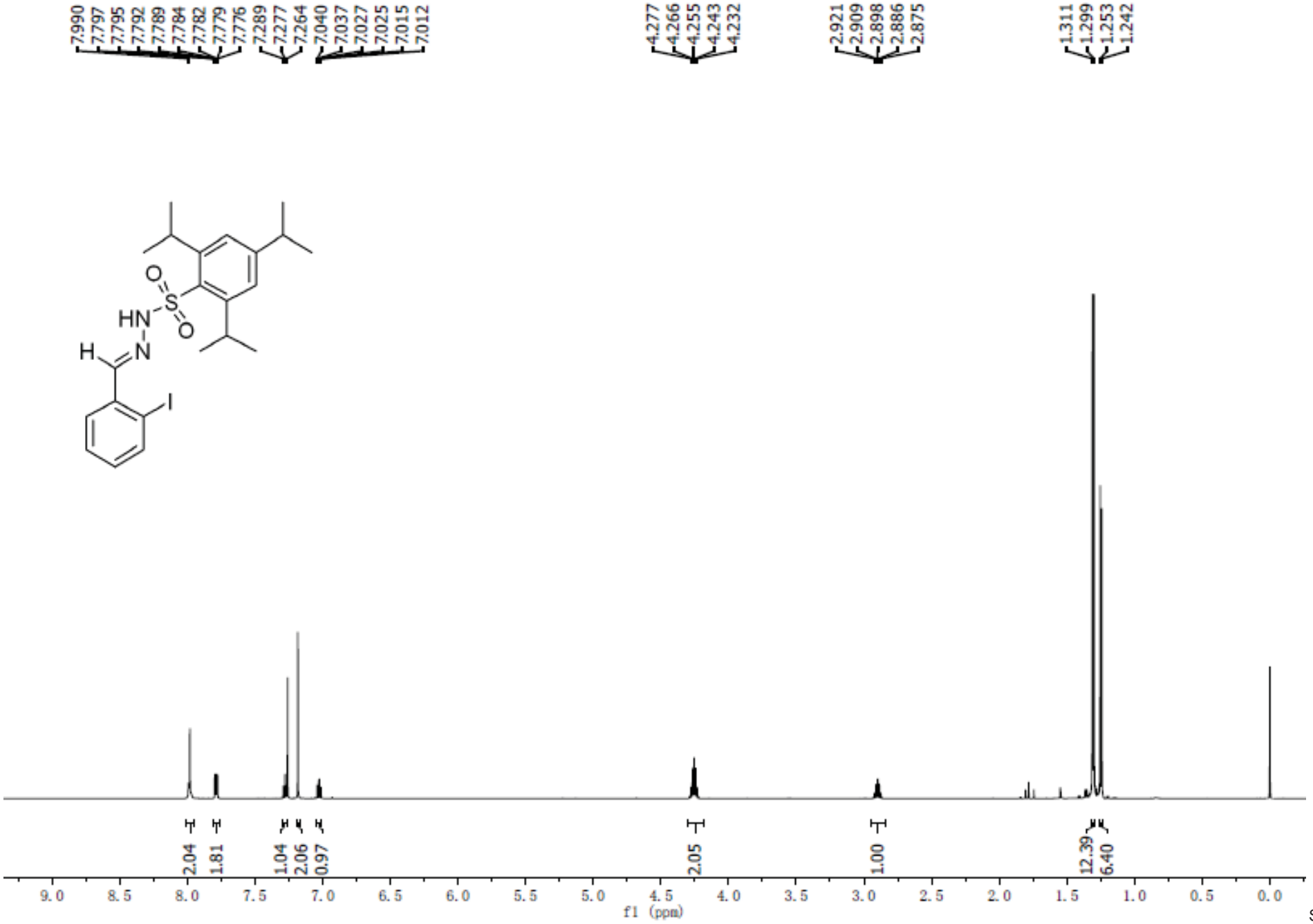
2-Bromobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1l'**



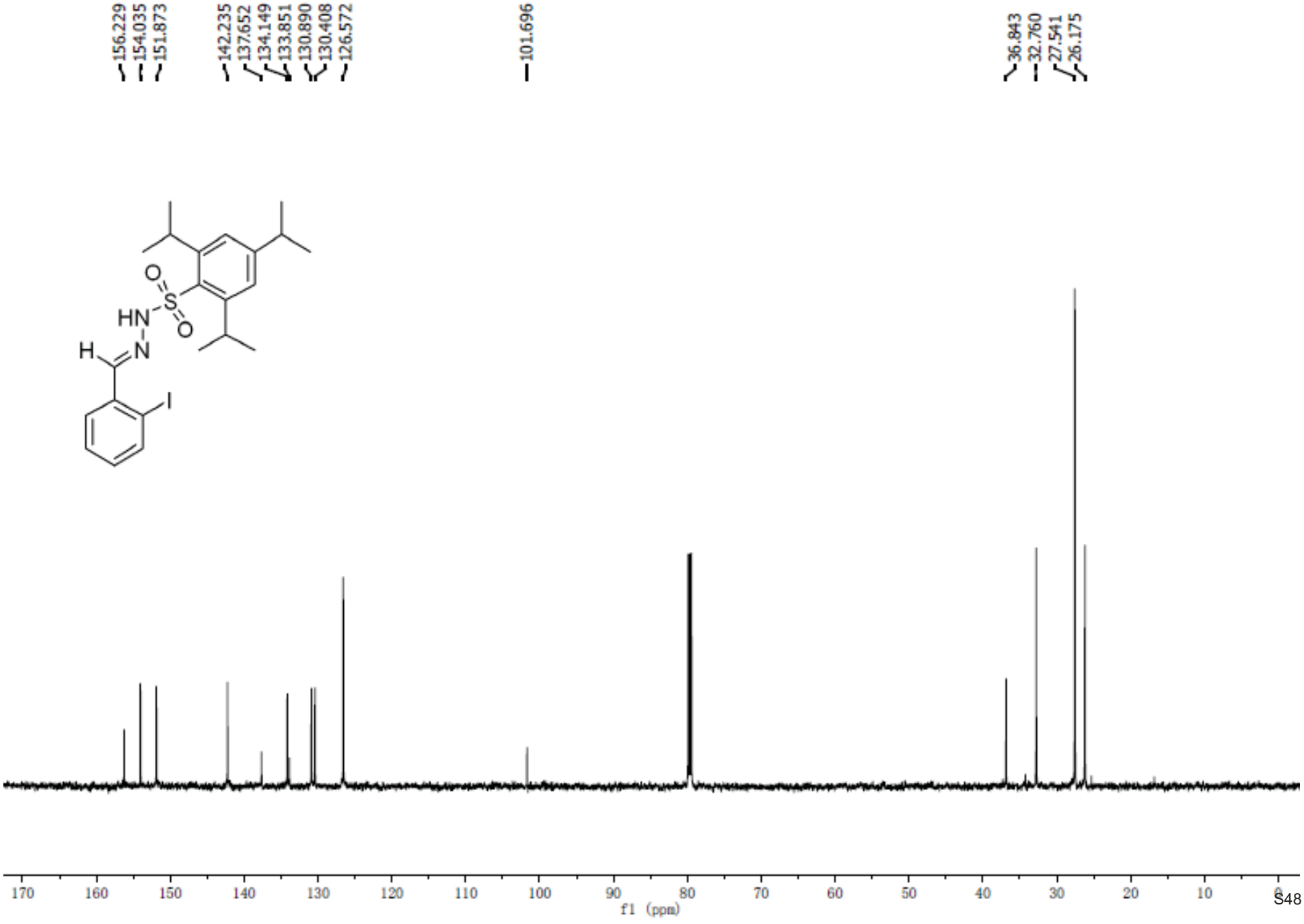
2-Bromobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1l'**



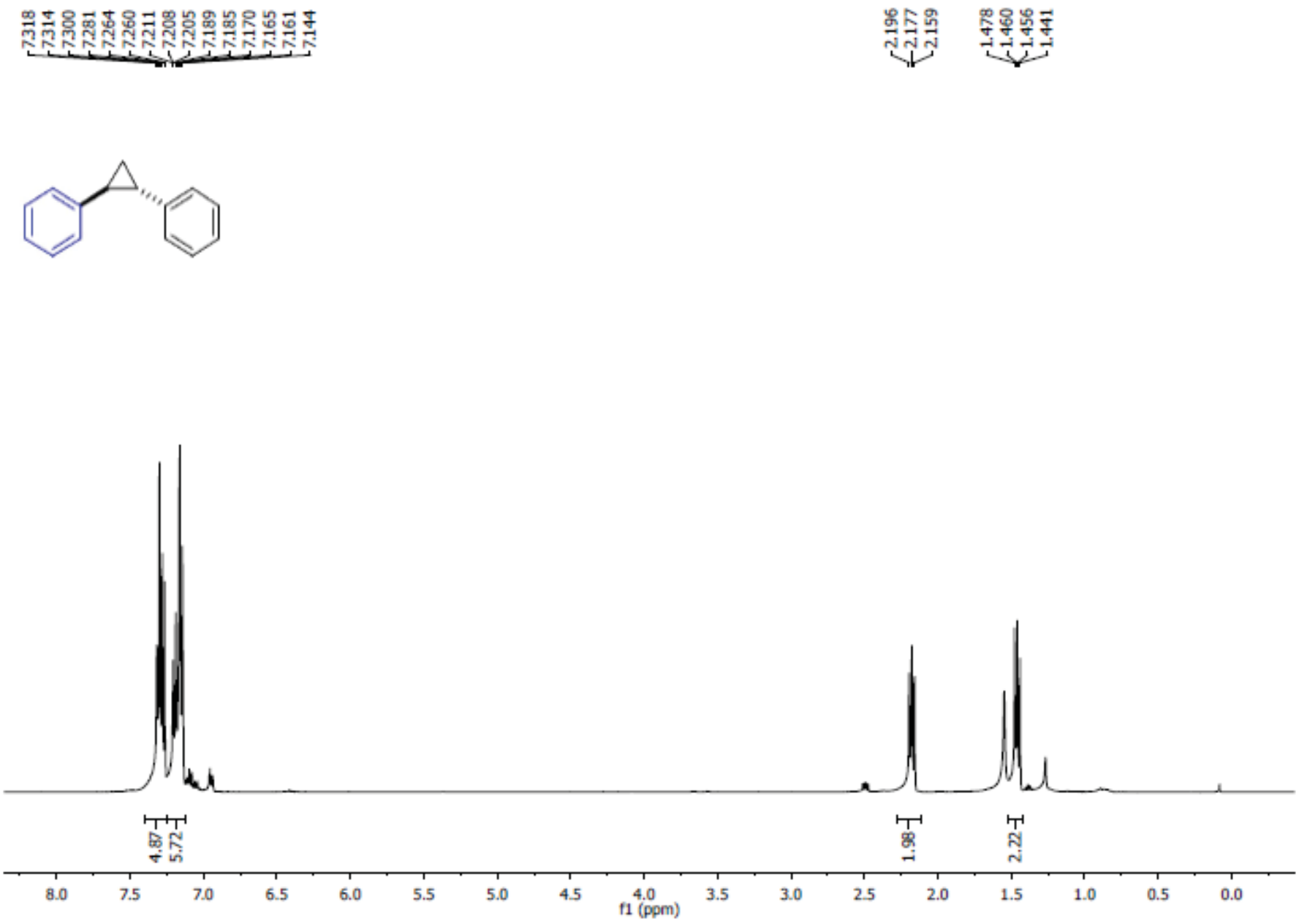
2-Iodobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1m'**



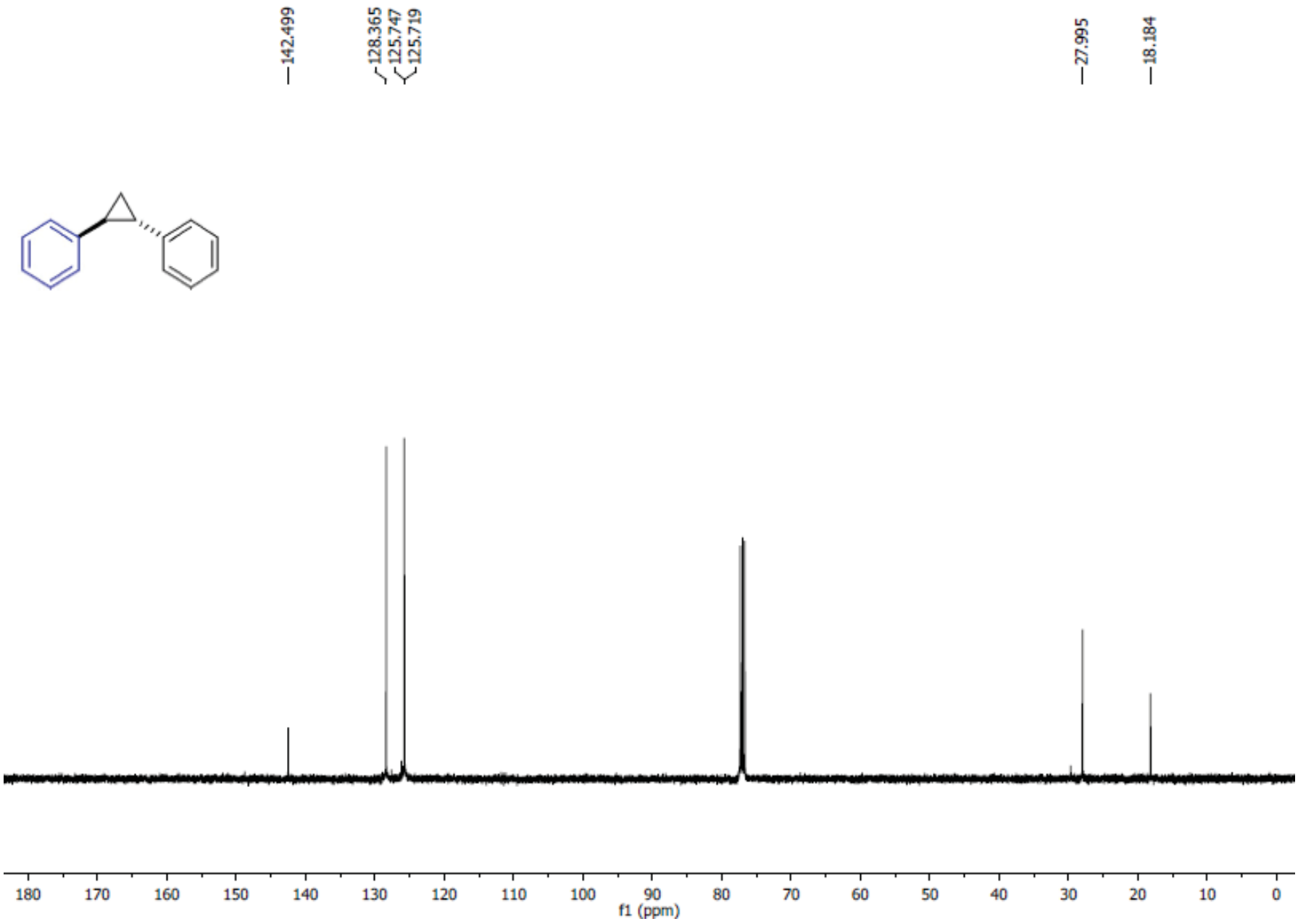
2-Iodobenzaldehyde 2,4,6-triisopropylbenzenesulfonyl hydrazone **1m'**



(1*S*,2*S*)-1,2-Diphenylcyclopropane **3aa**

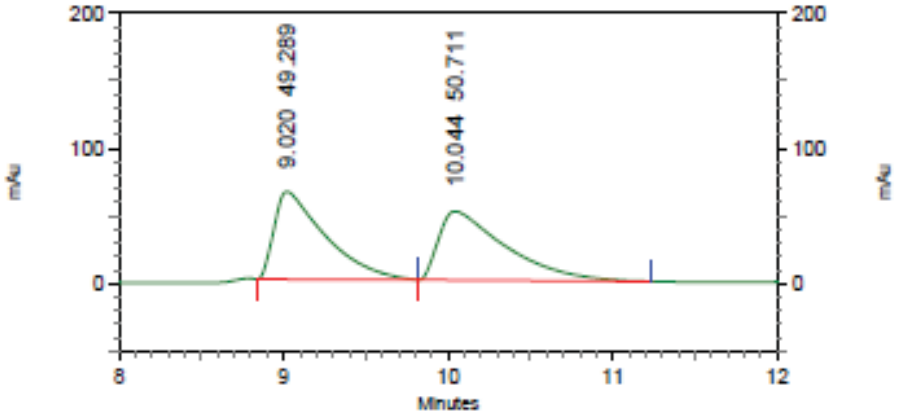


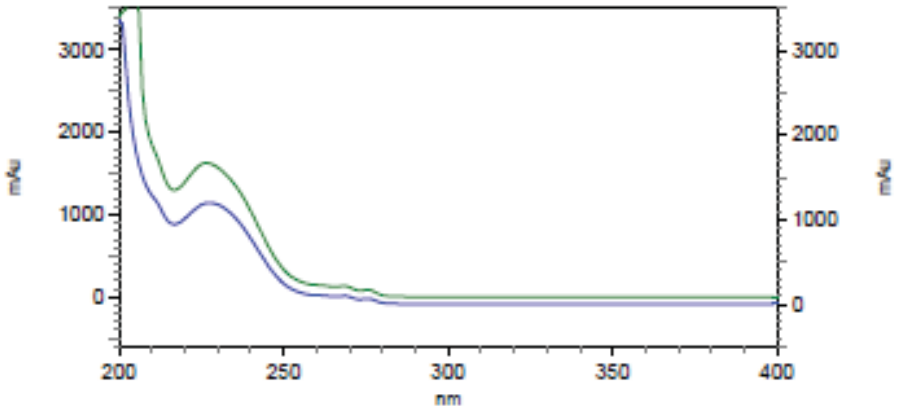
(1*S*,2*S*)-1,2-Diphenylcyclopropane **3aa**



(1*S*,2*S*)-1,2-Diphenylcyclopropane **3aa**

YW-II-34a ADH 0%0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-34a ADH 0%0.8 mL



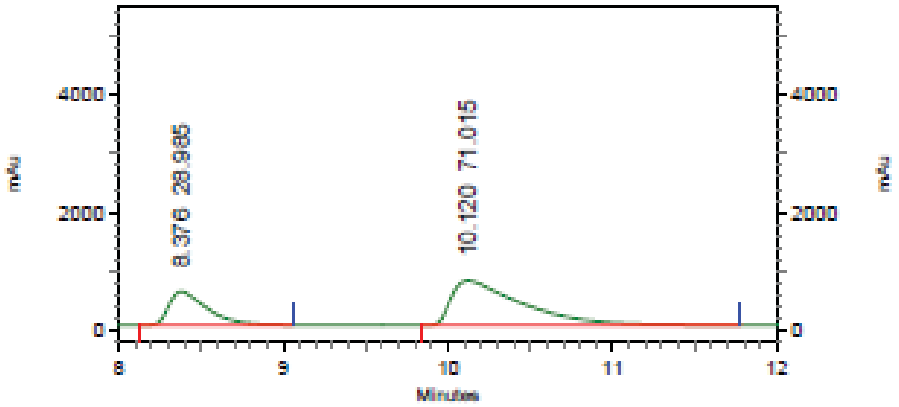


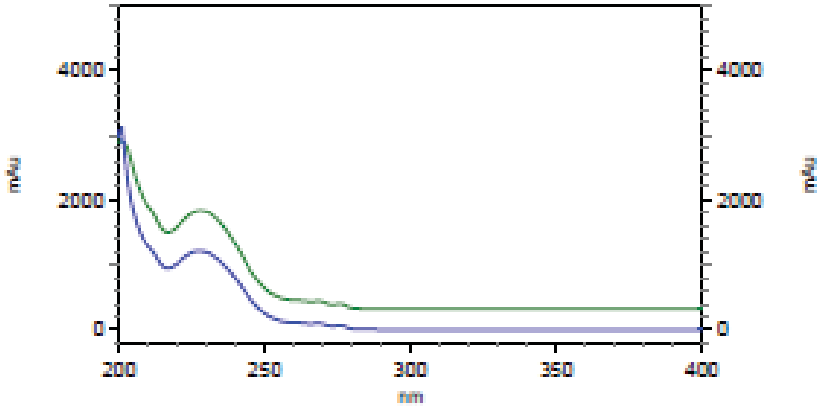
3: 277 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		9.020	49.289
2		10.044	50.711
Totals			100.000

(1*S*,2*S*)-1,2-Diphenylcyclopropane **3aa**

YW-II-53b ADH 0°0.8 mL
C:\EZStart\Projects\Default\Method\ywang1.met
C:\EZStart\Projects\Default\Data\YW-II-53b ADH 0°0.8 mL

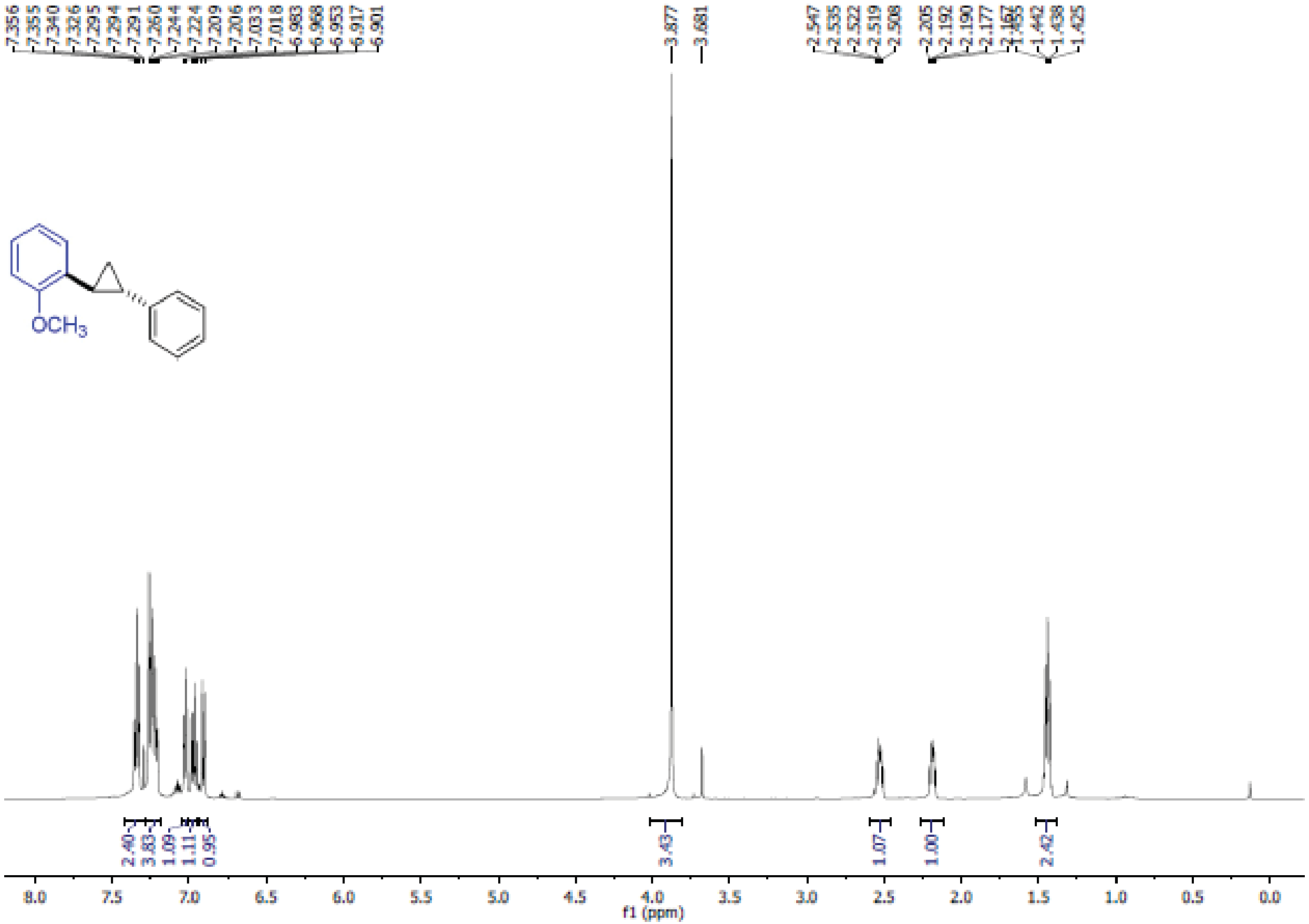




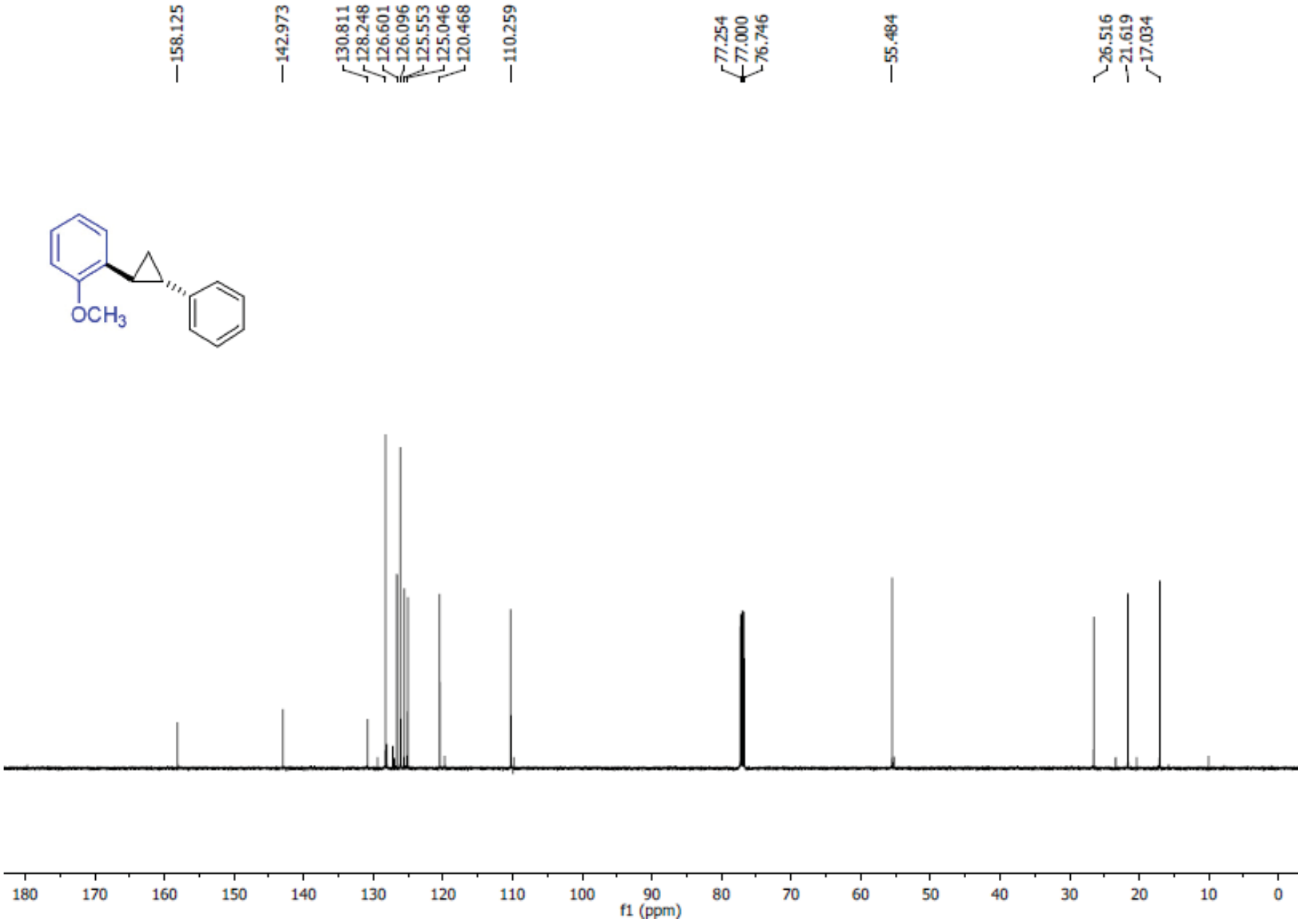
2: 277 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		8.376	28.985
2		10.120	71.015
Totals			100.000

1-methoxy-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3ba**)

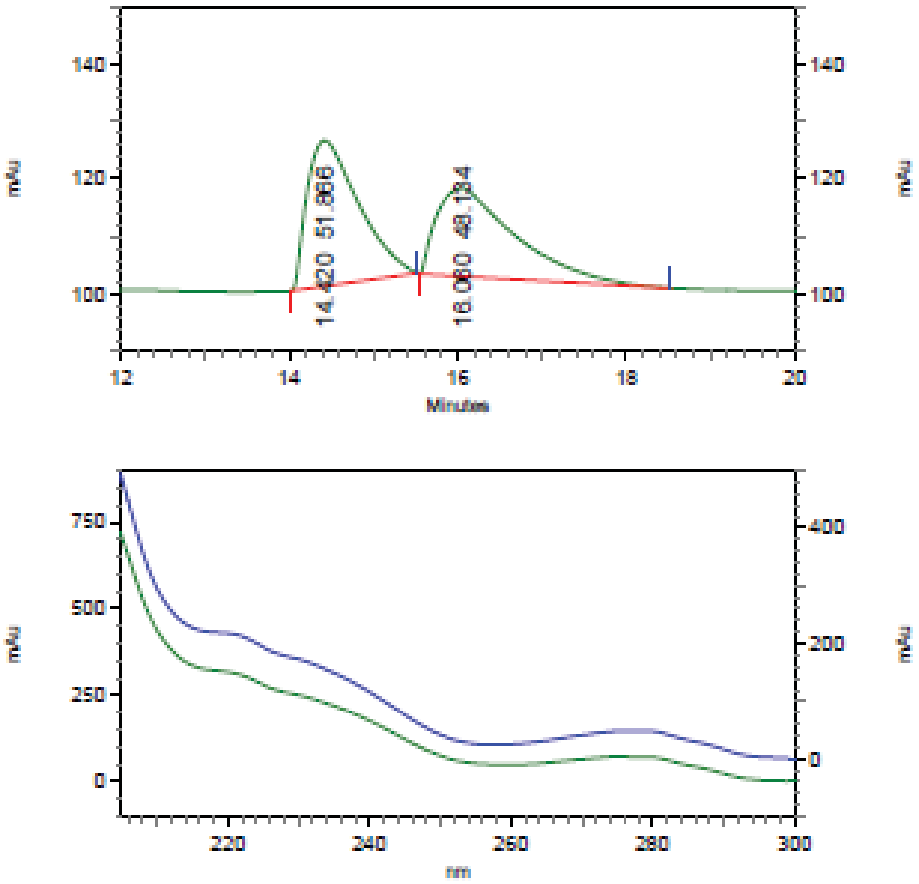


1-methoxy-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3ba**)



1-methoxy-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3ba**)

YW-I-138 ADH 0°0.8 mL
C:\EZStart\Projects\Default\Method\LSP-OD-H-1.0°-0.8ML.met
E:\HPLC-YW-I\YW-I-138 ADH 0°0.8 mL

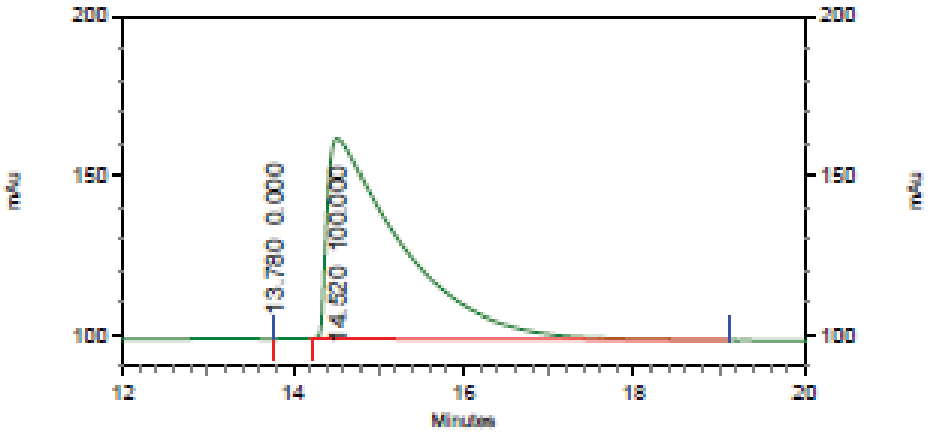


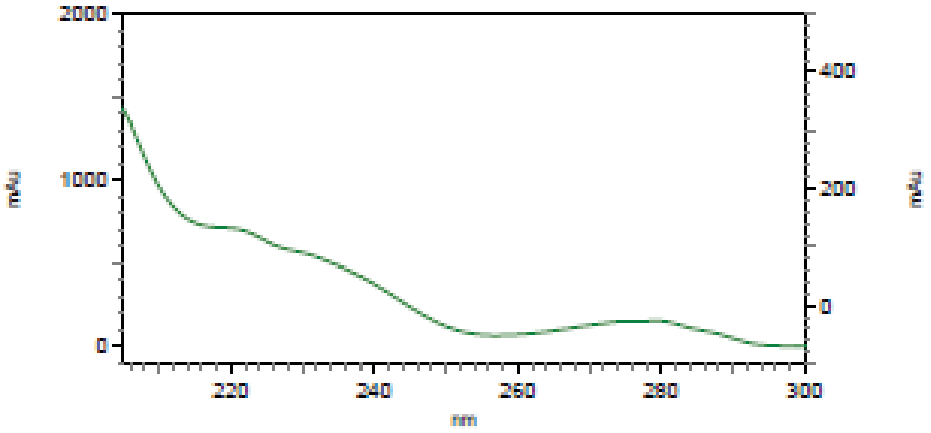
5: 227 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		14.420	51.866
2		16.060	48.134
Totals			100.000

1-methoxy-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3ba**)

YW-I-231a ADH 0@0.8 mL
C:\EZStart\Projects\Default\Method\LSP-OD-H-1.0@-0.8ML.met
E:\HPLC-YW-I\YW-I-231a ADH 0@0.8 mL

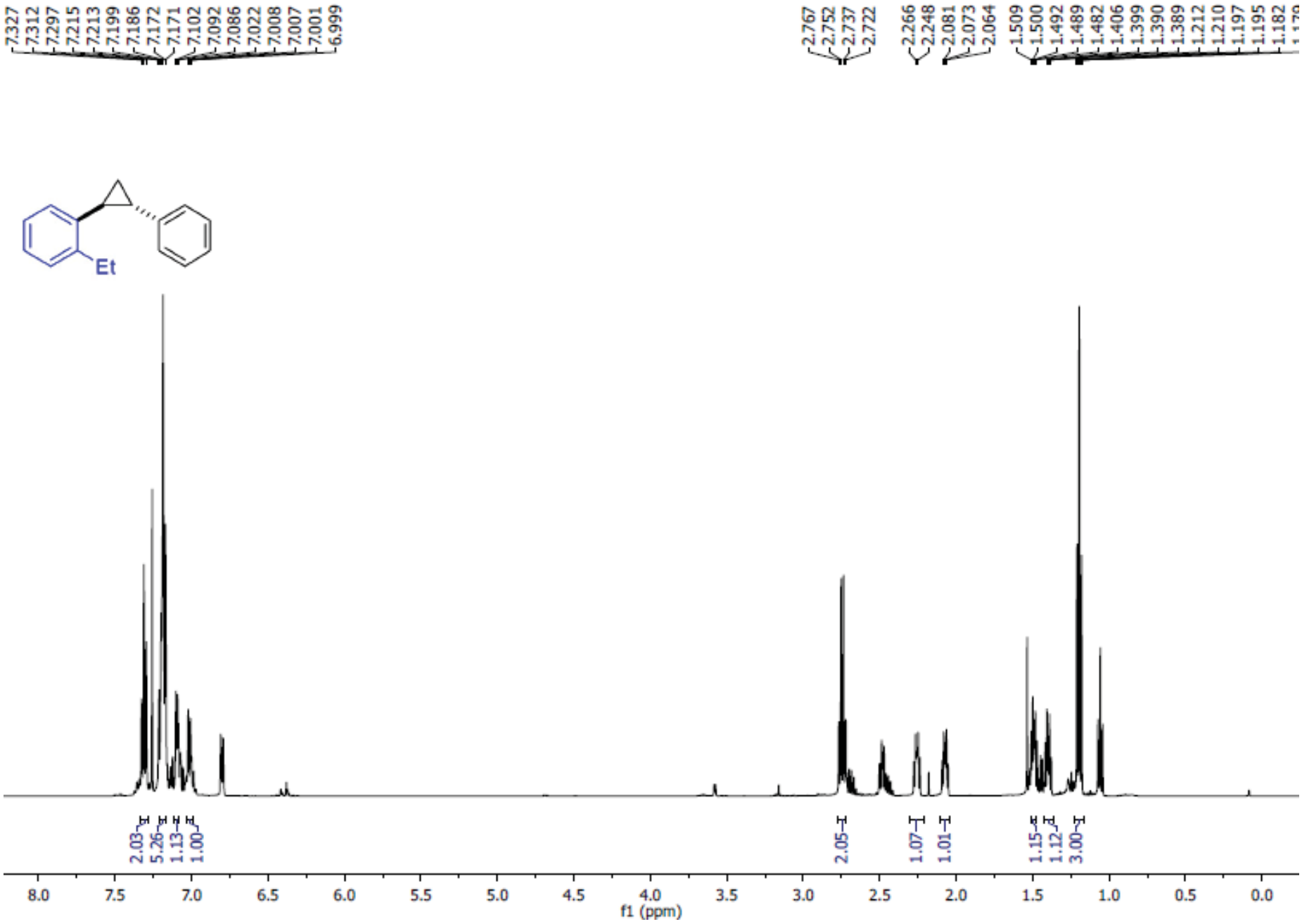




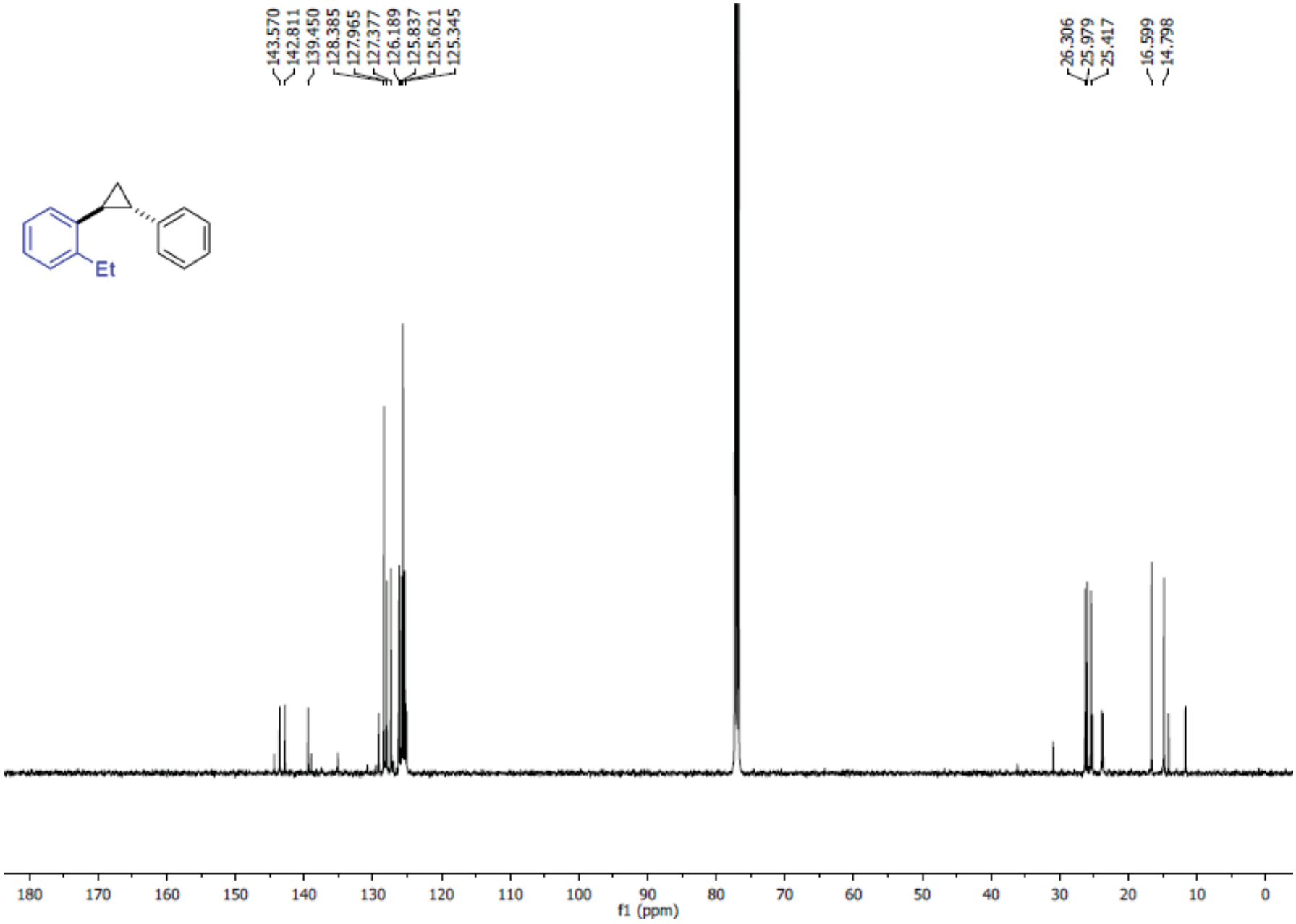
5: 226 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		13.780	0.000
2		14.520	100.000
Totals			100.000

1-ethyl-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3ca**

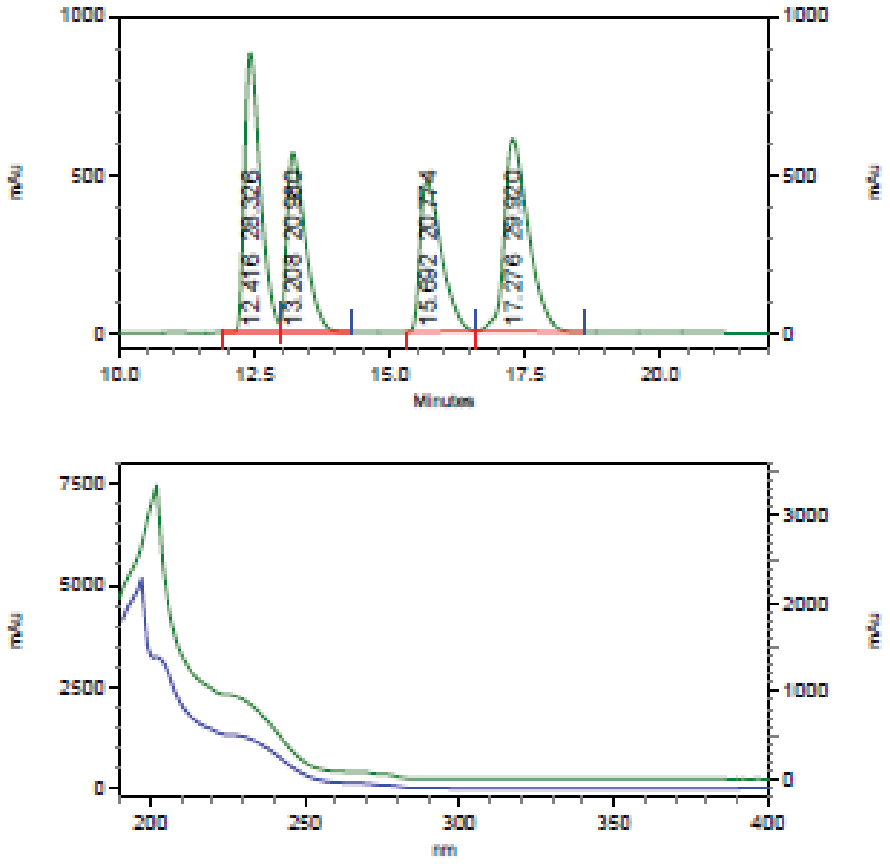


1-ethyl-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3ca**



1-ethyl-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3ca**

YW-II-43A ODH 0.1@0.8 mL
C:\EZStart\Projects\Default\Method\lk-5@0.8.met
C:\EZStart\Projects\Default\Data\YW-II-43A ODH 0.1@0.8 mL



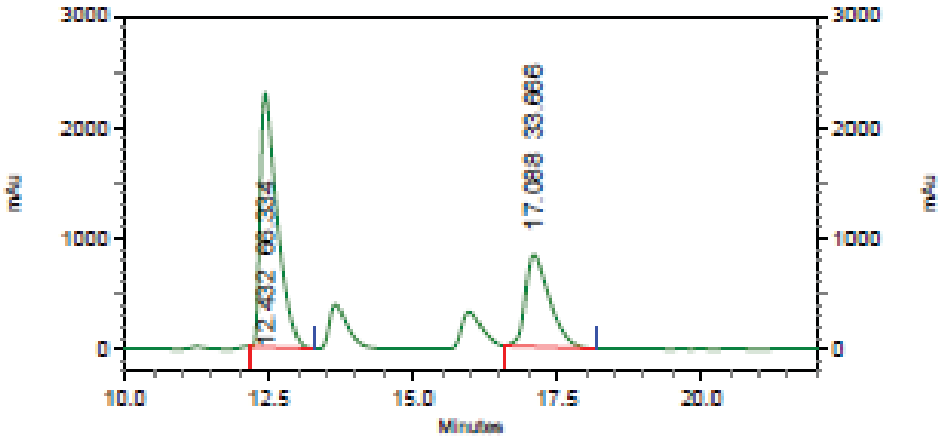
3: 231 nm, 4 nm
Results

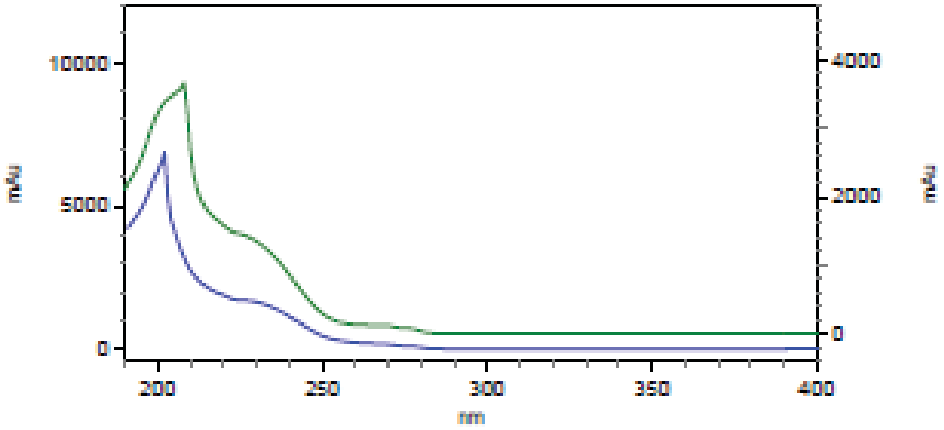
Name	Retention Time	Area Percent	Pk #
	12.416	28.326	1
	13.208	20.980	2
	15.692	20.774	3
	17.276	29.920	4

Totals	
	100.000

1-ethyl-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3ca**

YW-II-43B ODH 0.1@0.8 mL
C:\EZStart\Projects\Default\Method\lk-5@0.8.met
C:\EZStart\Projects\Default\Data\YW-II-43B ODH 0.1@0.8 mL



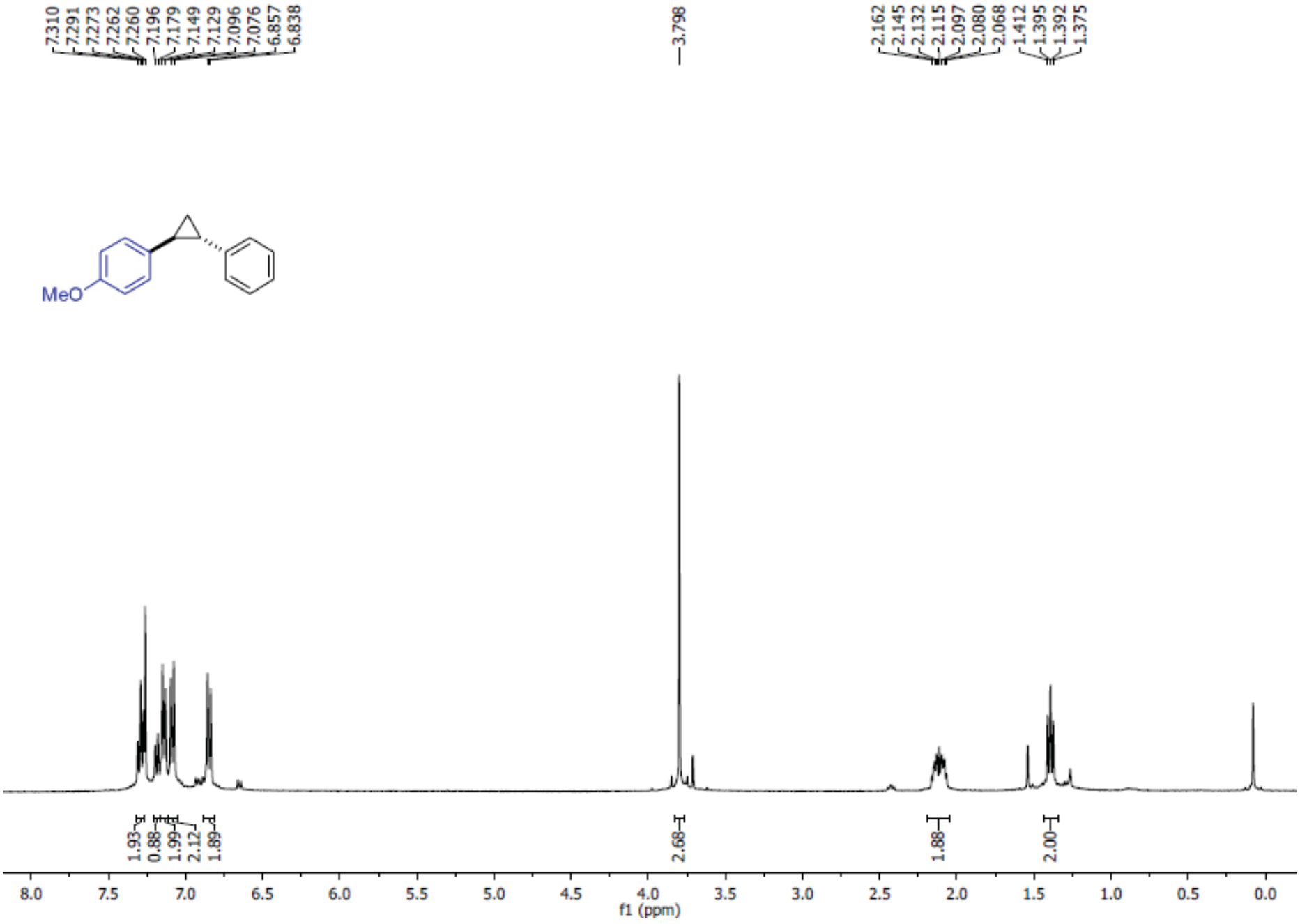


3: 226 nm, 4 nm
Results

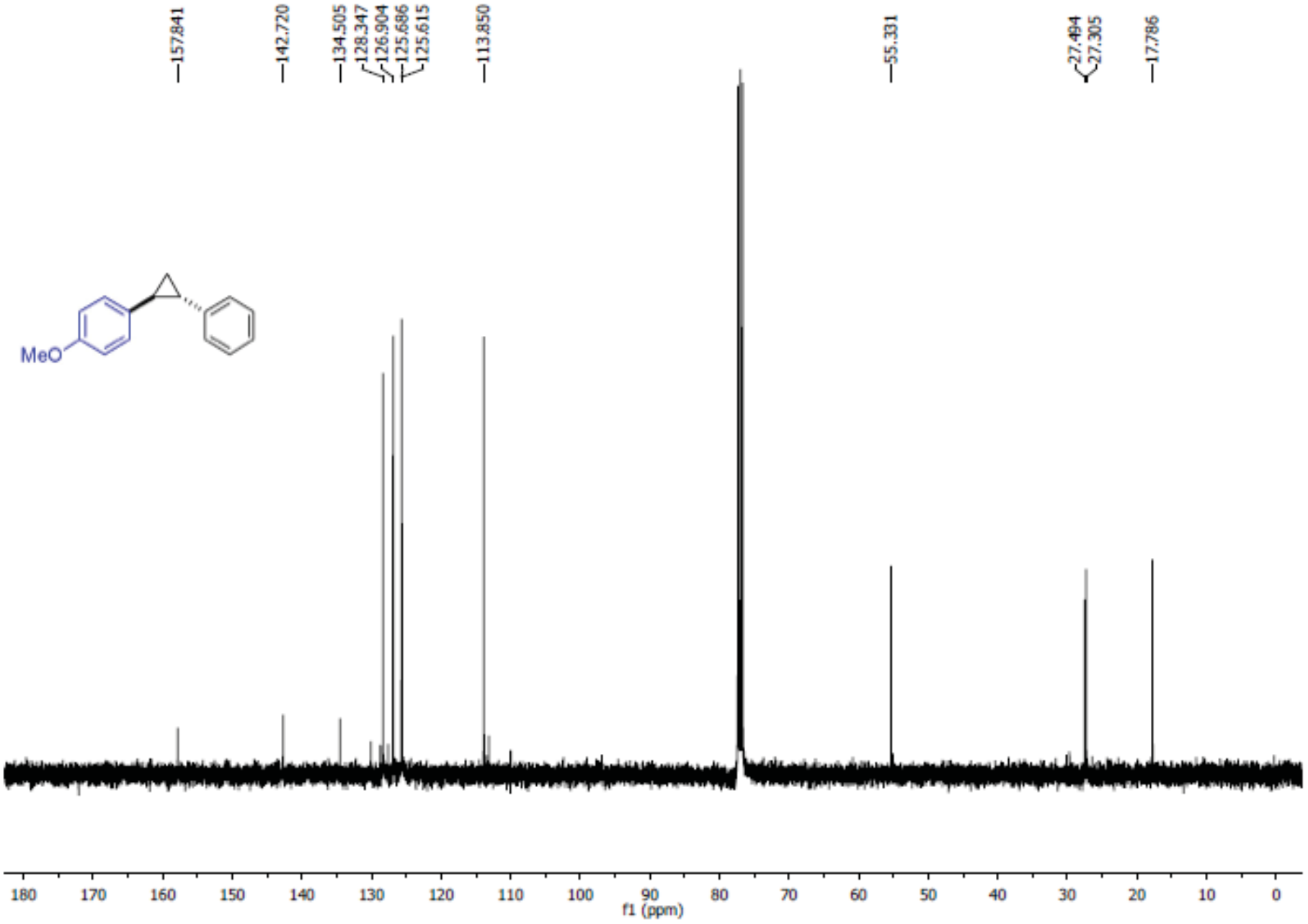
Name	Retention Time	Area Percent	Pk #
	12.432	66.334	1
	17.088	33.666	2

Totals	
	100.000

1-methoxy-4-((1S,2S)-2-phenylcyclopropyl)benzene **3da**

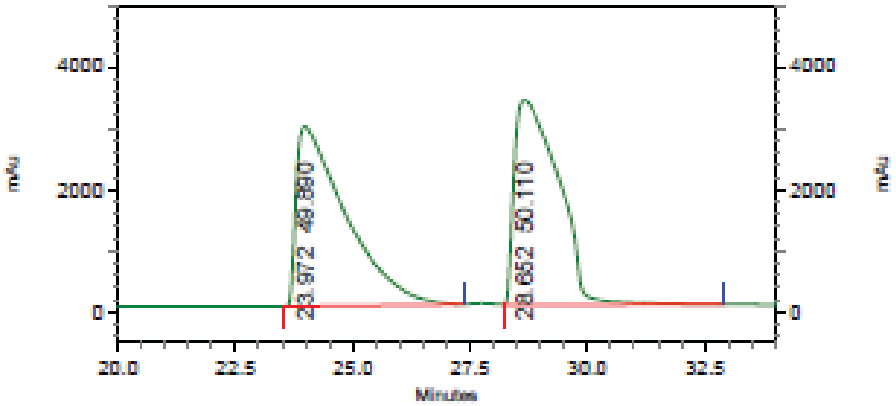


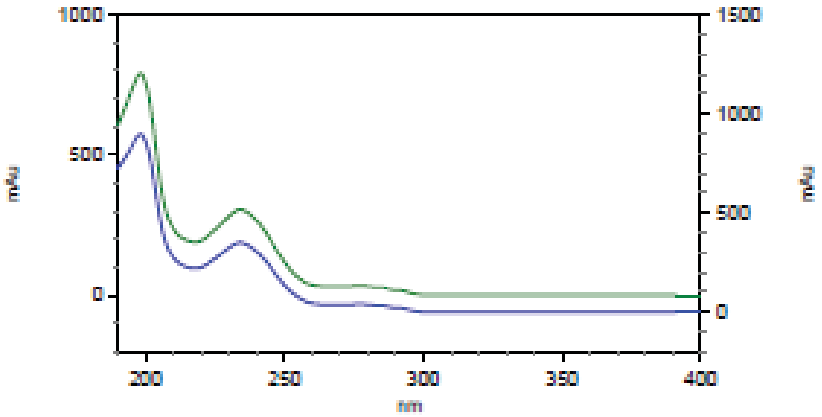
1-methoxy-4-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3da**



1-methoxy-4-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3da**

YW-II-45A NEW ADH 0# 0.8mL
C:\EZStart\Projects\Default\Method\ywang0.8.met
C:\EZStart\Projects\Default\Data\YW-II-45A NEW ADH 0# 0.8mL



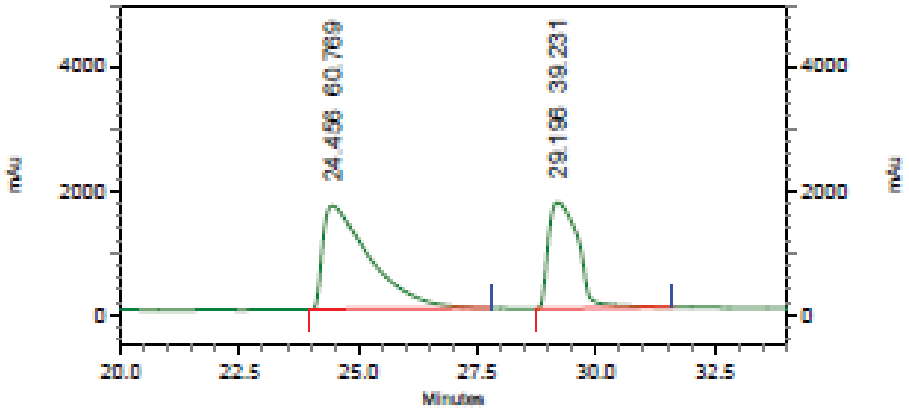


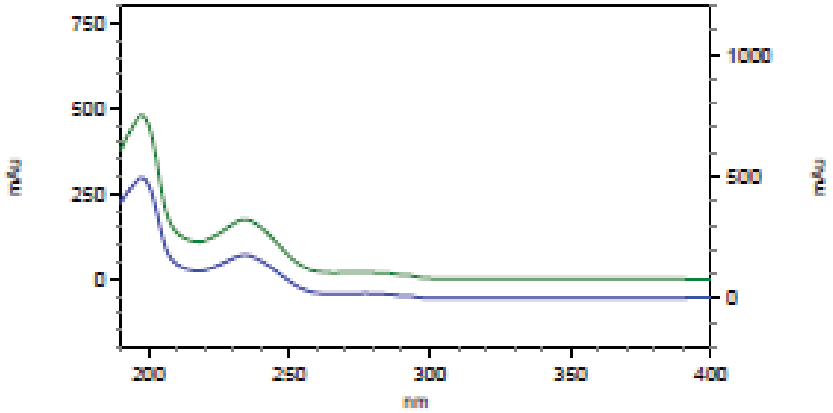
4: 245 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		23.972	49.890
2		28.652	50.110
Totals			100.000

1-methoxy-4-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3da**

YW-II-45B NEW ADH 0% 0.8mL
C:\EZStart\Projects\Default\Method\ywang0.8.met
C:\EZStart\Projects\Default\Data\YW-II-45B NEW ADH 0% 0.8mL

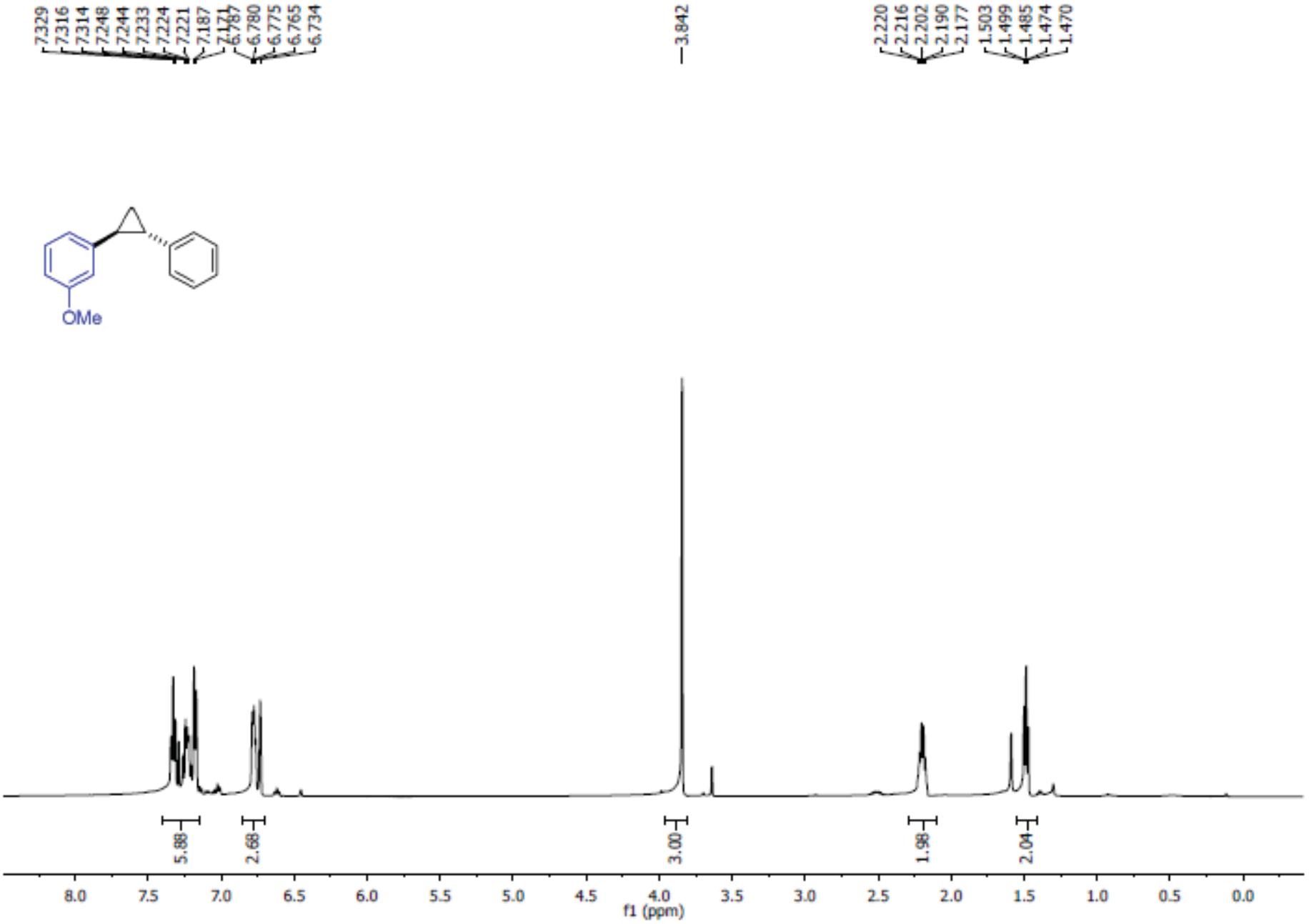




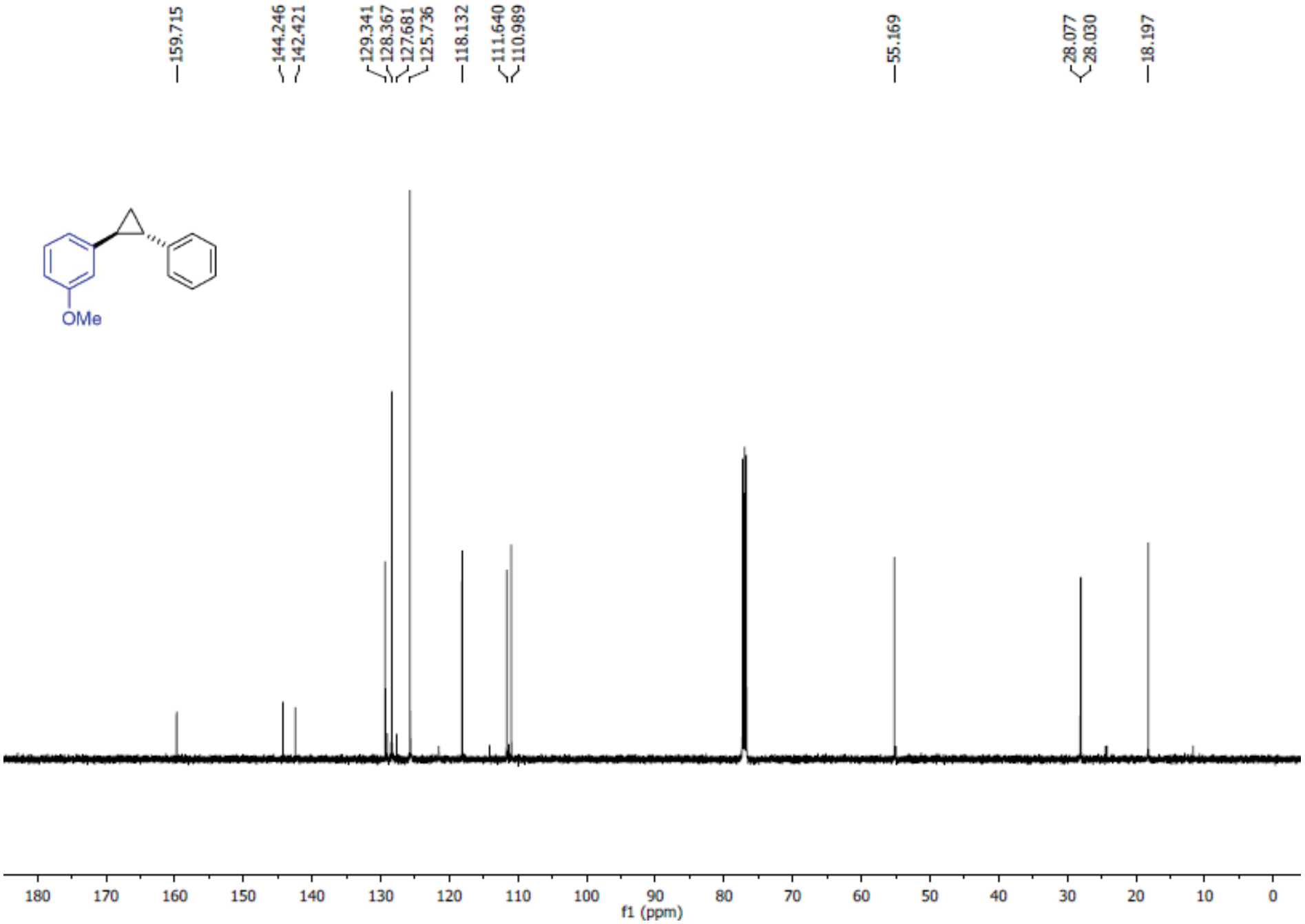
4: 245 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		24.456	60.769
2		29.196	39.231
Totals			100.000

1-methoxy-3-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3ea**

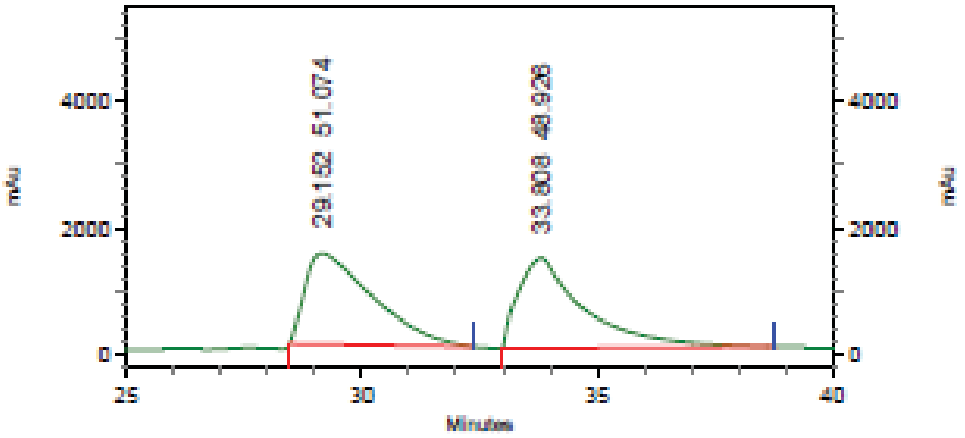


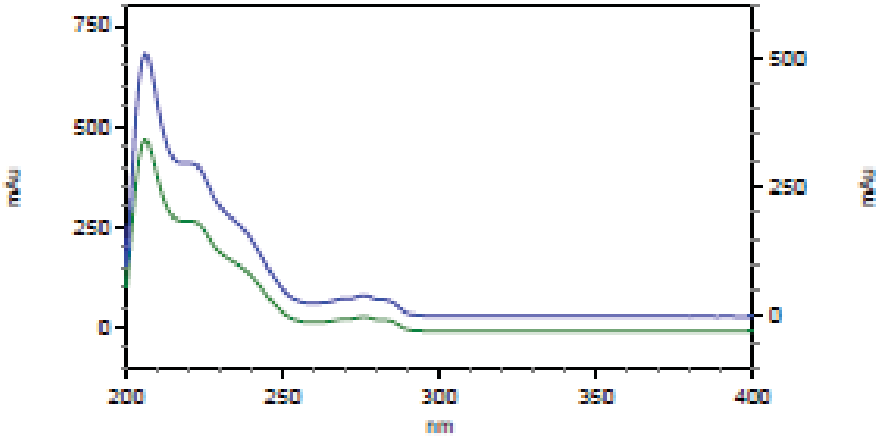
1-methoxy-3-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3ea**



1-methoxy-3-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3ea**

YW-II-85A-1 ADH 0%0.8 mL
C:\EZStart\Projects\Default\Method\ywang1.met
C:\EZStart\Projects\Default\Data\YW-II-85A-1 ADH 0%0.8 mL



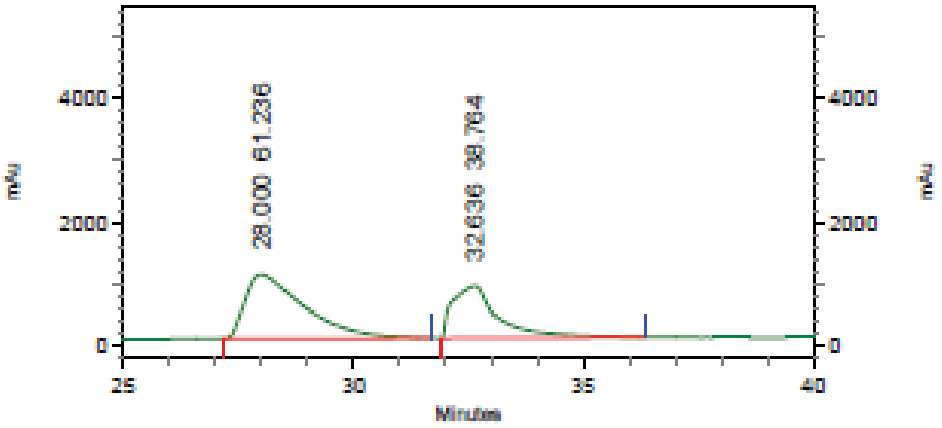


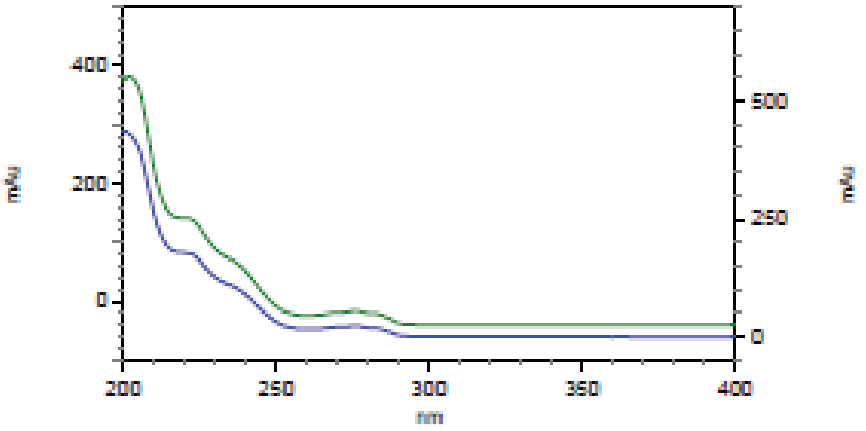
2: 245 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		29.152	51.074
2		33.808	48.926
Totals			100.000

1-methoxy-3-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3ea**

YW-II-85B ADH 0‡0.8 mL
C:\EZStart\Projects\Default\Method\ywang1.met
C:\EZStart\Projects\Default\Data\YW-II-85B ADH 0‡0.8 mL

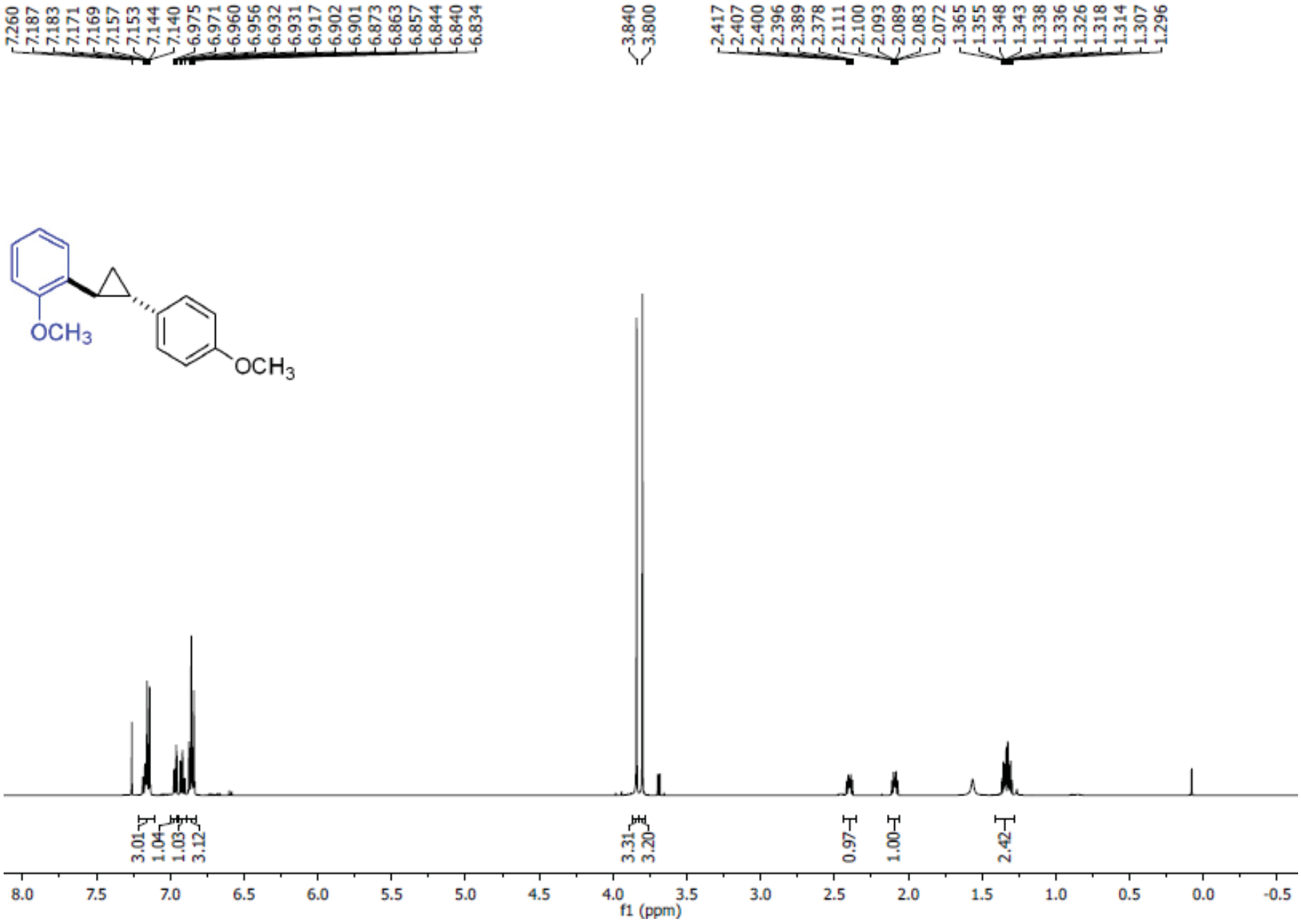




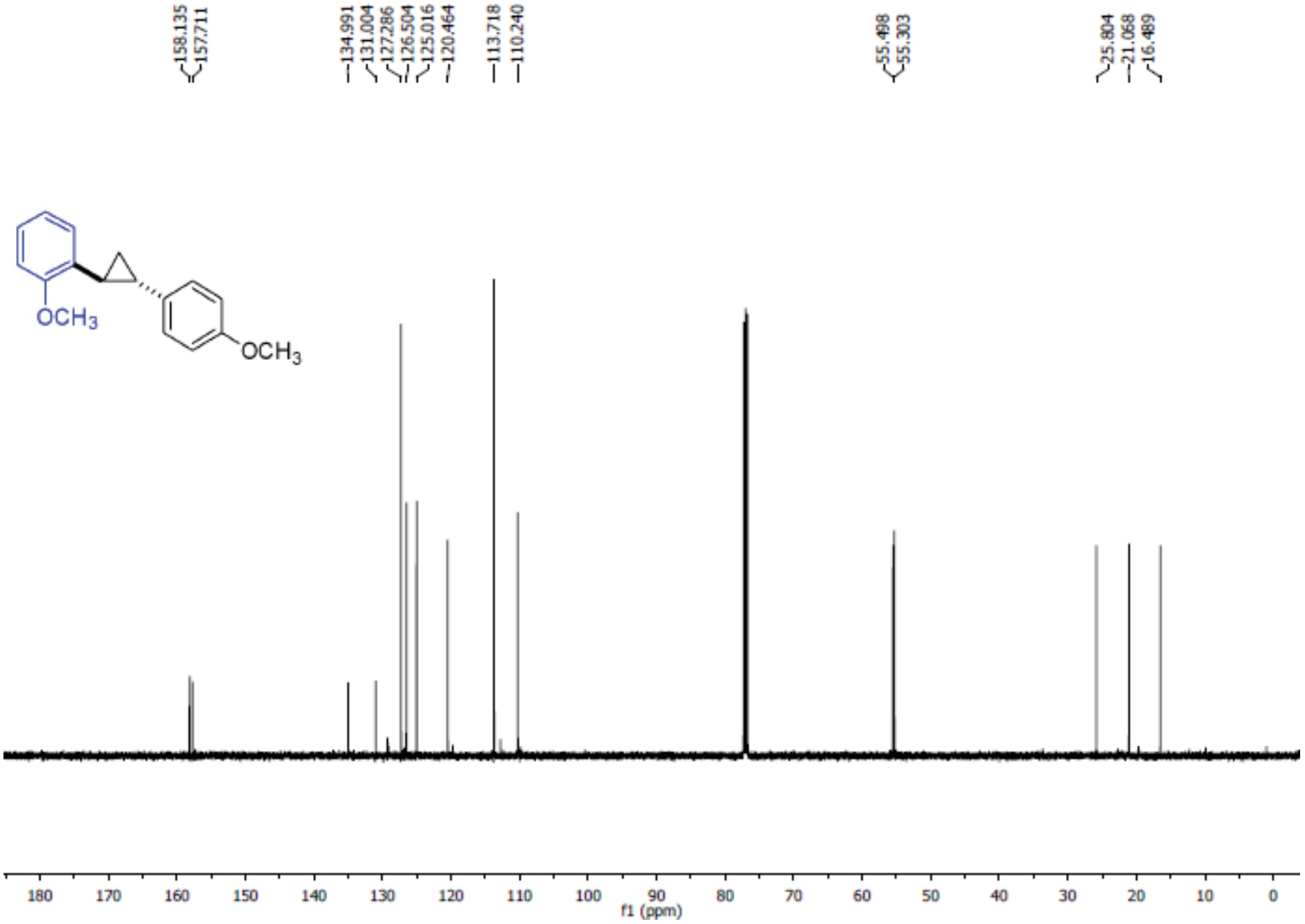
2: 245 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		28.000	61.236
2		32.636	38.764
Totals			100.000

1-methoxy-2-((1*S*,2*S*)-2-(4-methoxyphenyl)cyclopropyl)benzene **3bb**

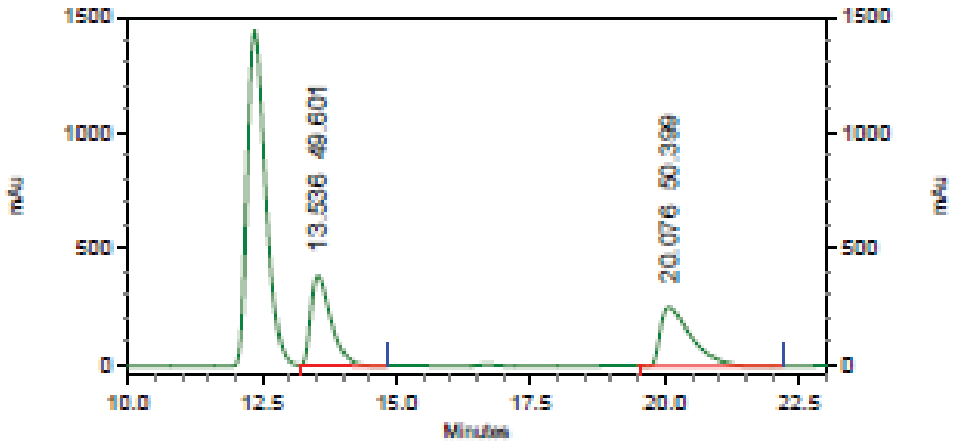


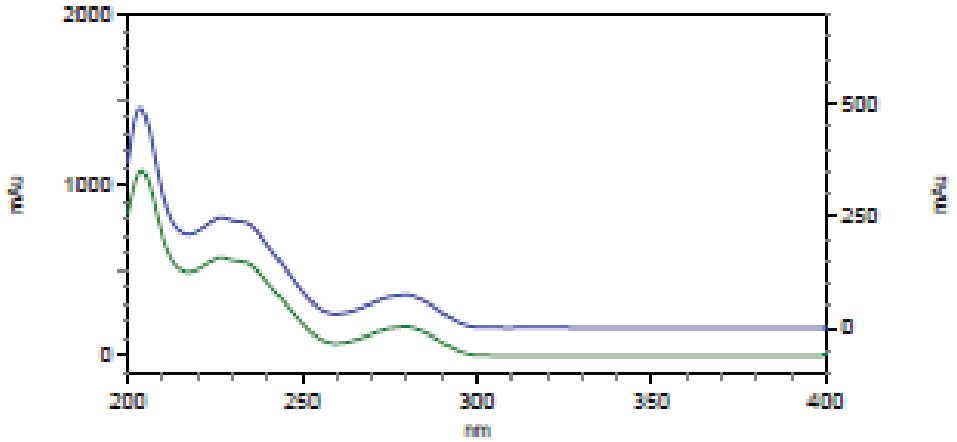
1-methoxy-2-((1*S*,2*S*)-2-(4-methoxyphenyl)cyclopropyl)benzene **3bb**



1-methoxy-2-((1*S*,2*S*)-2-(4-methoxyphenyl)cyclopropyl)benzene **3bb**

YW-I-247 ODH 0.5@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-I-247 ODH 0.5@0.8 mL



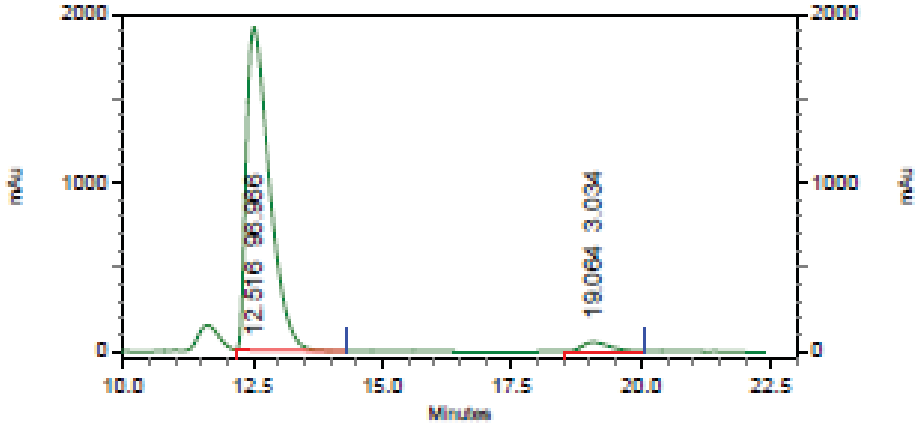


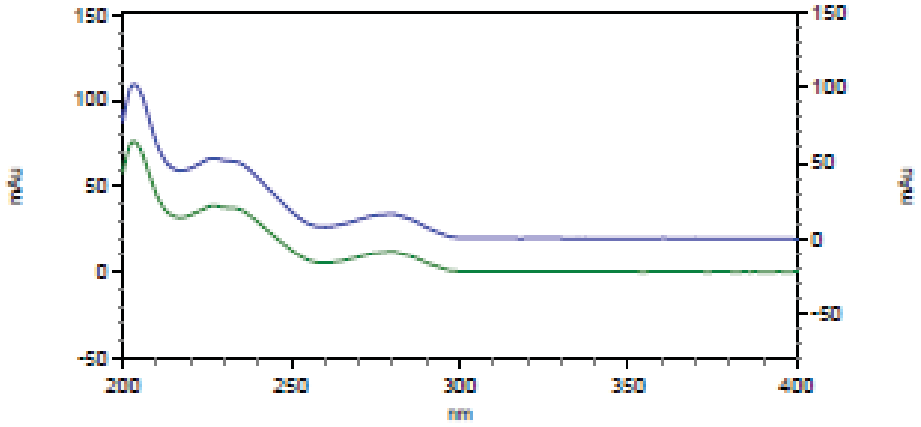
2: 227 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		13.536	49.601
2		20.076	50.399
Totals			100.000

1-methoxy-2-((1*S*,2*S*)-2-(4-methoxyphenyl)cyclopropyl)benzene **3bb**

YW-I-255-1 ODH 0.5@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
E:\HPLC-YW-I\YW-I-255-1 ODH 0.5@0.8 mL

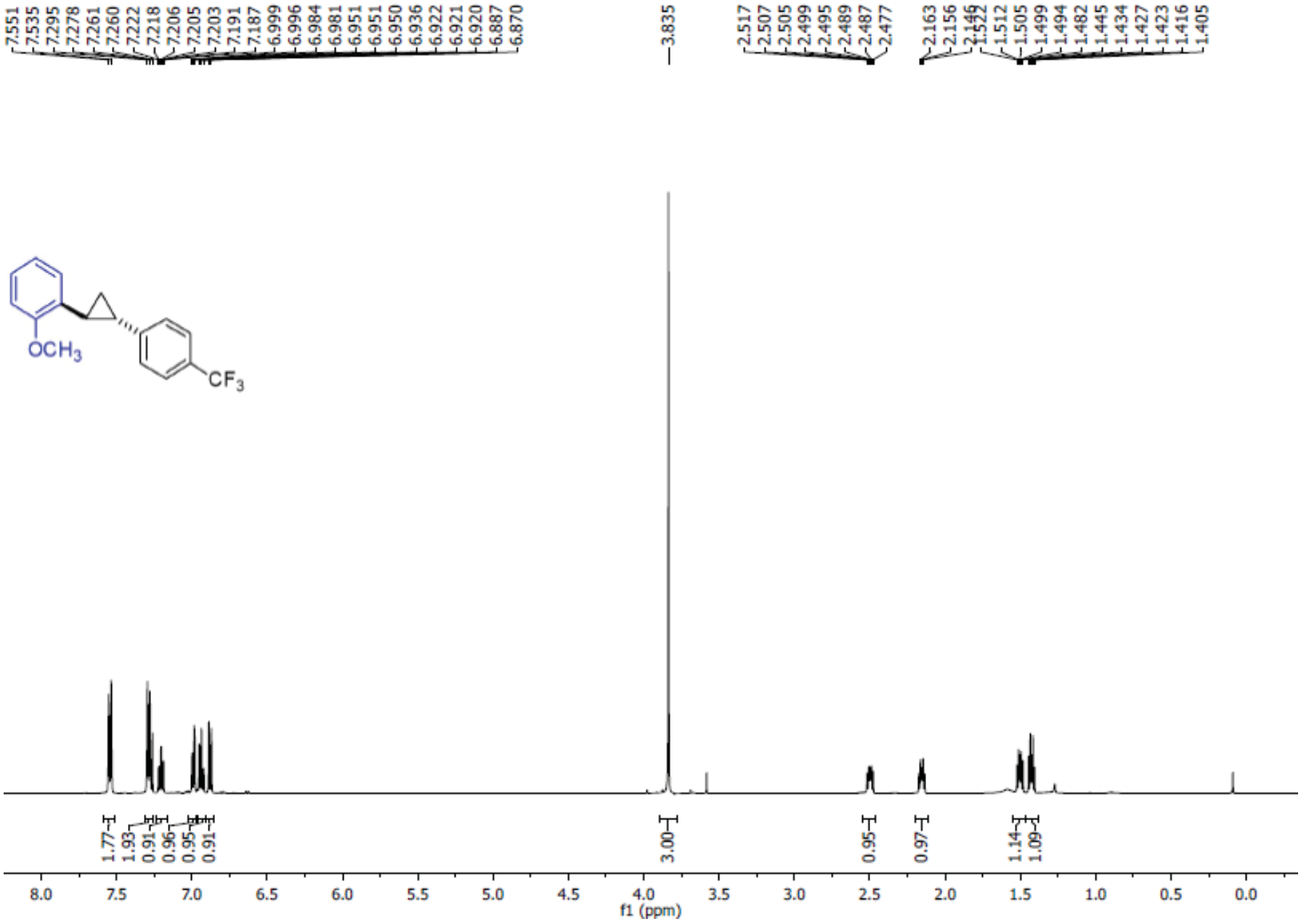




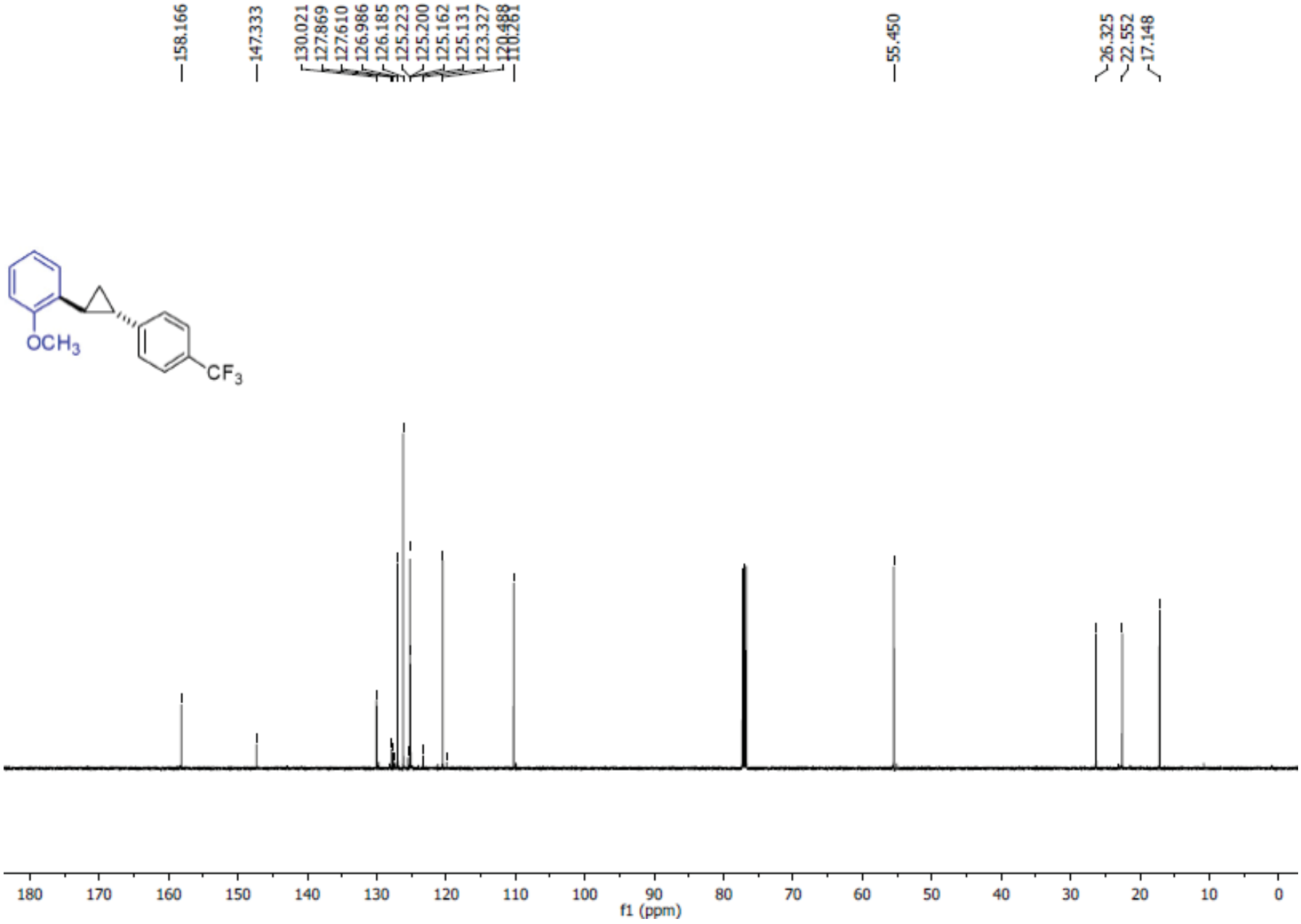
2: 227 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		12.516	96.966
2		19.064	3.034
Totals			100.000

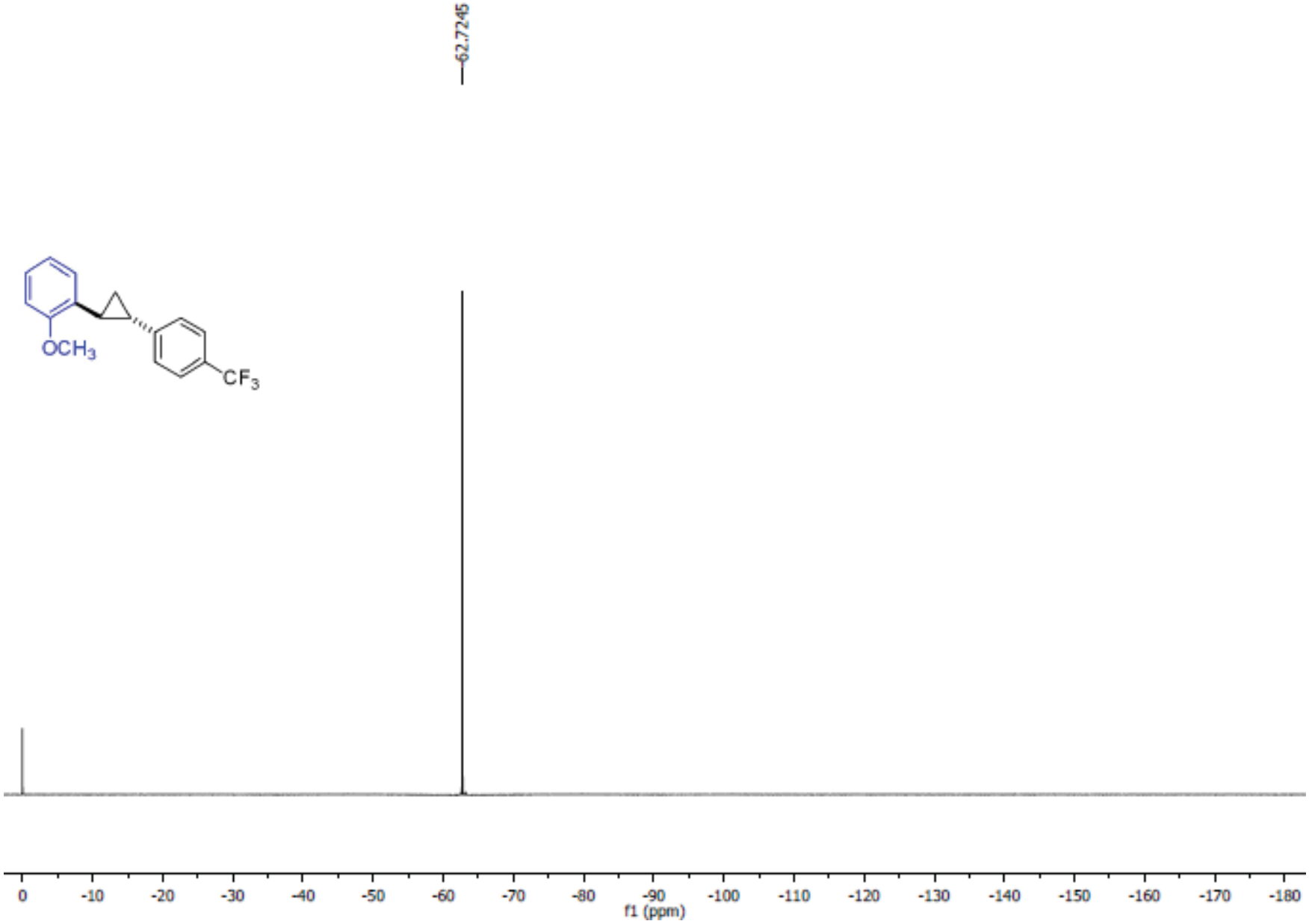
1-methoxy-2-((1*S*,2*S*)-2-(4-(trifluoromethyl)phenyl)cyclopropyl)benzene **3bc**



1-methoxy-2-((1*S*,2*S*)-2-(4-(trifluoromethyl)phenyl)cyclopropyl)benzene **3bc**

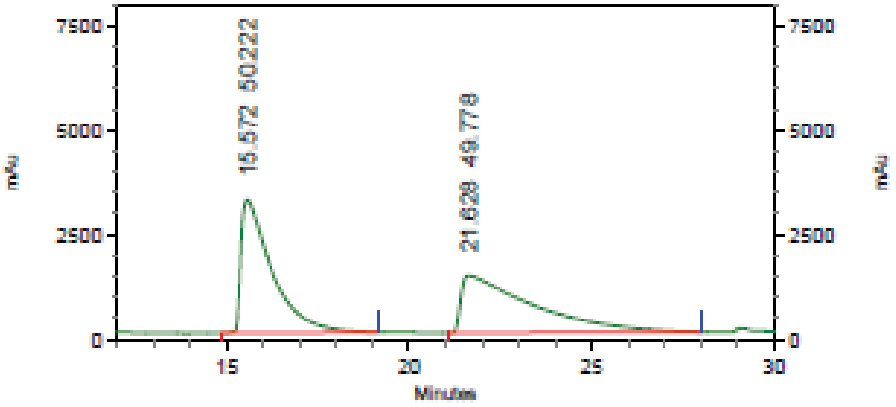


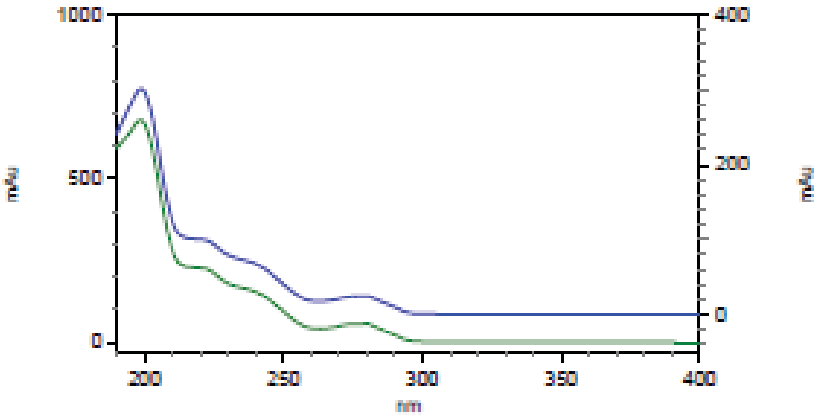
1-methoxy-2-((1*S*,2*S*)-2-(4-(trifluoromethyl)phenyl)cyclopropyl)benzene **3bc**



1-methoxy-2-((1*S*,2*S*)-2-(4-(trifluoromethyl)phenyl)cyclopropyl)benzene **3bc**

YW-I-238-ADH-new 0% 0.8mL
C:\EZStart\Projects\Default\Method\ywang0.8.met
C:\EZStart\Projects\Default\Data\YW-I-238-ADH-new 0% 0.8mL



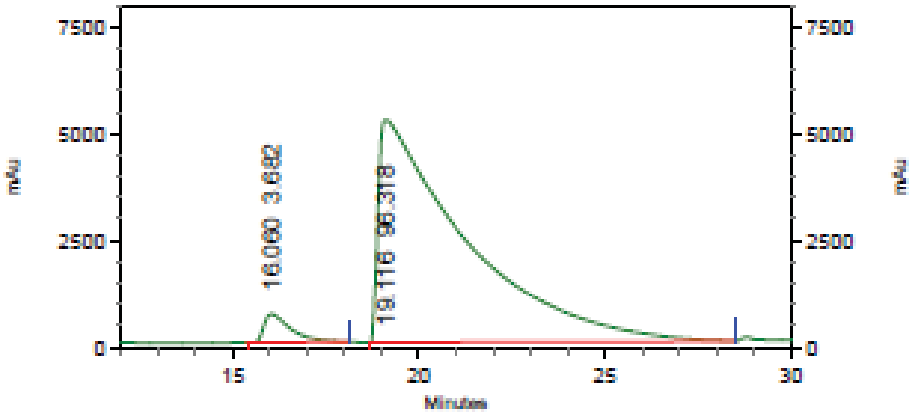


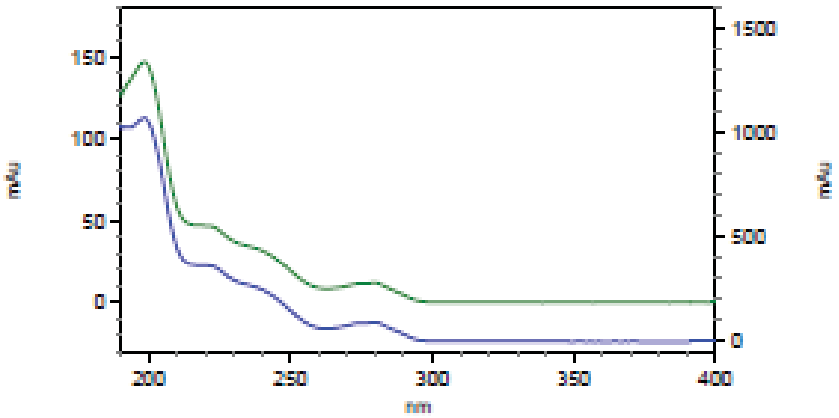
4: 224 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		15.572	50.222
2		21.628	49.778
Totals			100.000

1-methoxy-2-((1*S*,2*S*)-2-(4-(trifluoromethyl)phenyl)cyclopropyl)benzene **3bc**

YW-I-242-ADH-new 0# 0.6mL
C:\EZStart\Projects\Default\Method\ywang0.6.met
C:\EZStart\Projects\Default\Data\YW-I-242-ADH-new 0# 0.6mL

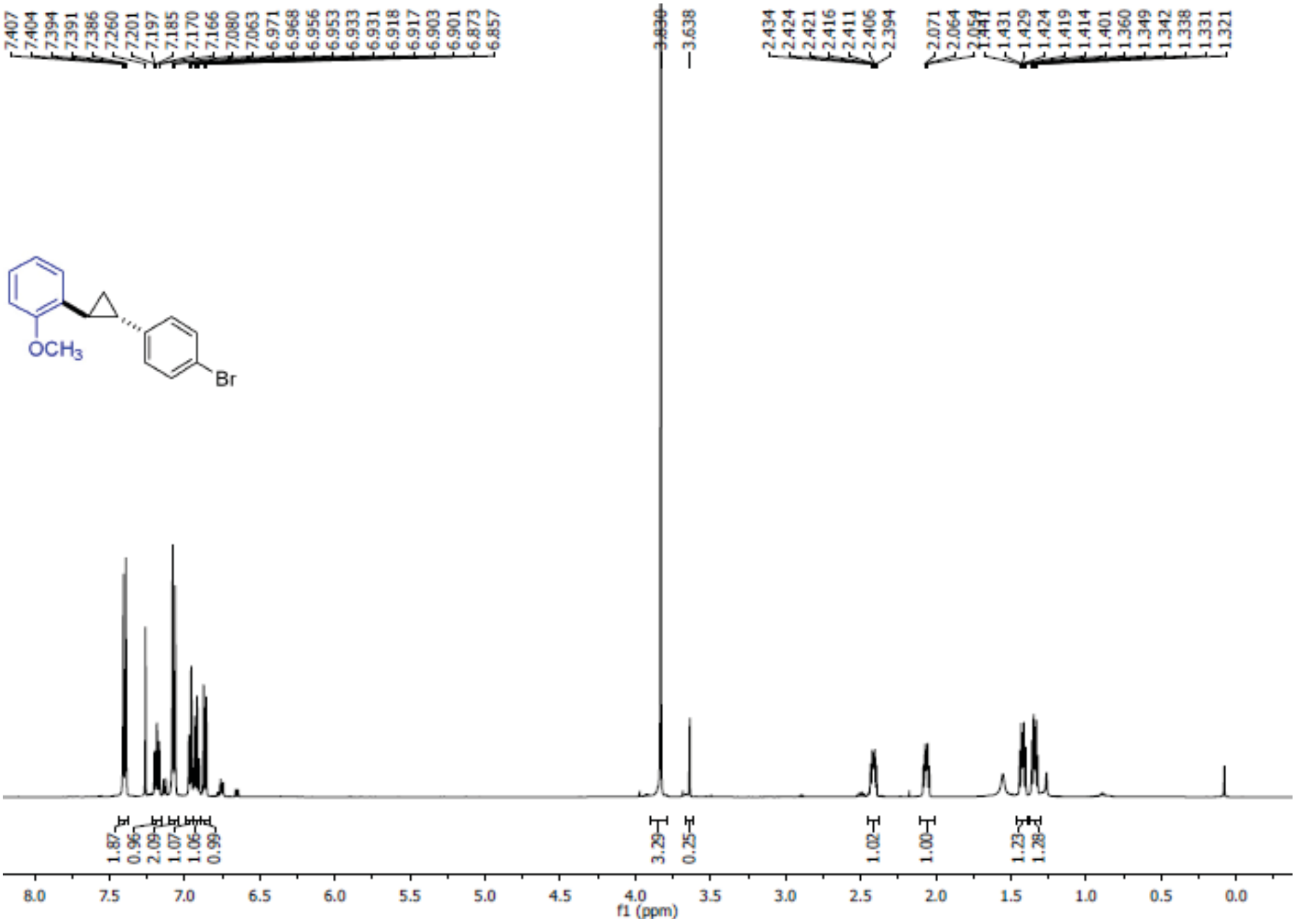




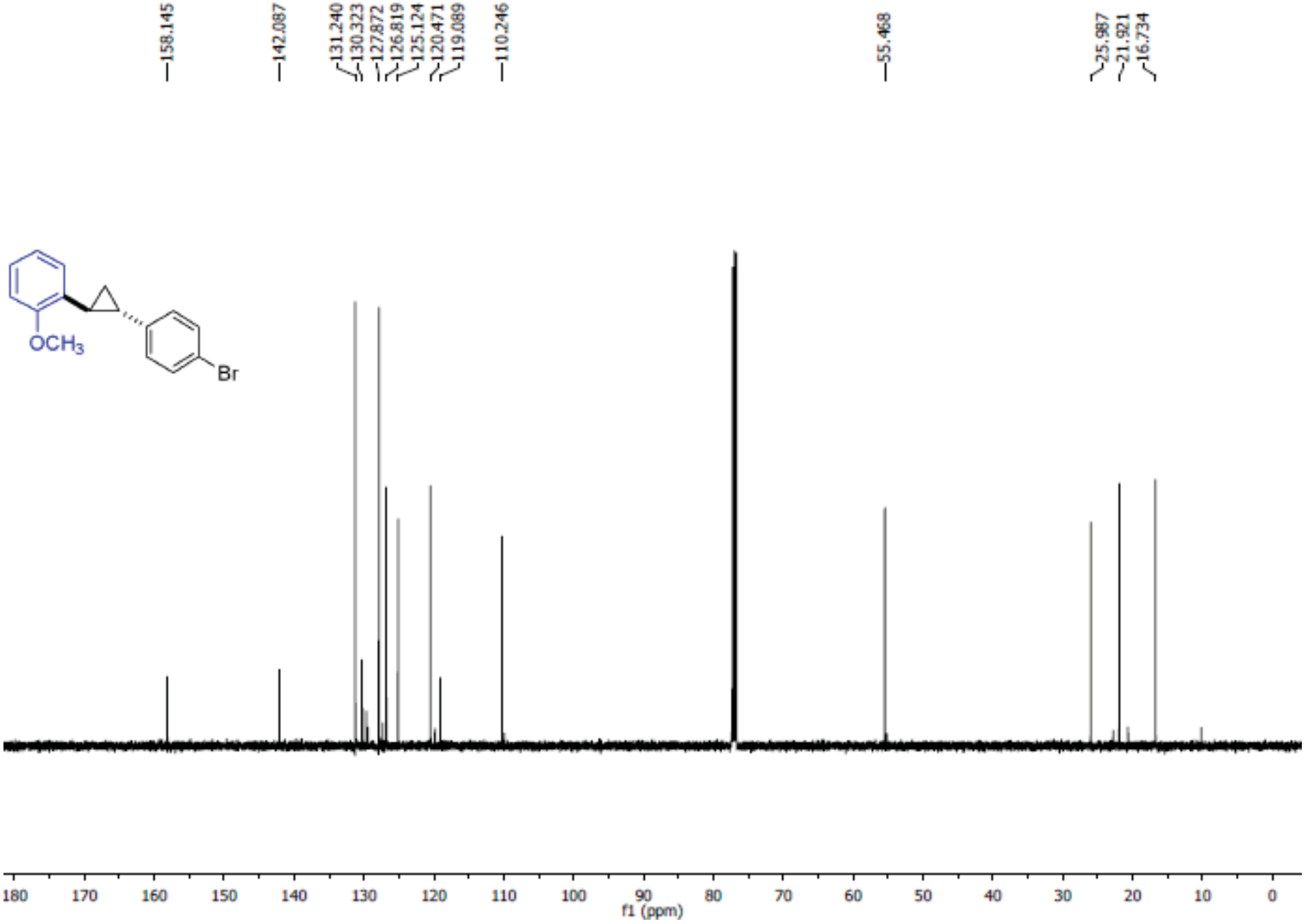
4: 224 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		16.060	3.682
2		19.116	96.318
Totals			100.000

1-((1*S*,2*S*)-2-(4-bromophenyl)cyclopropyl)-2-methoxybenzene **3bd**

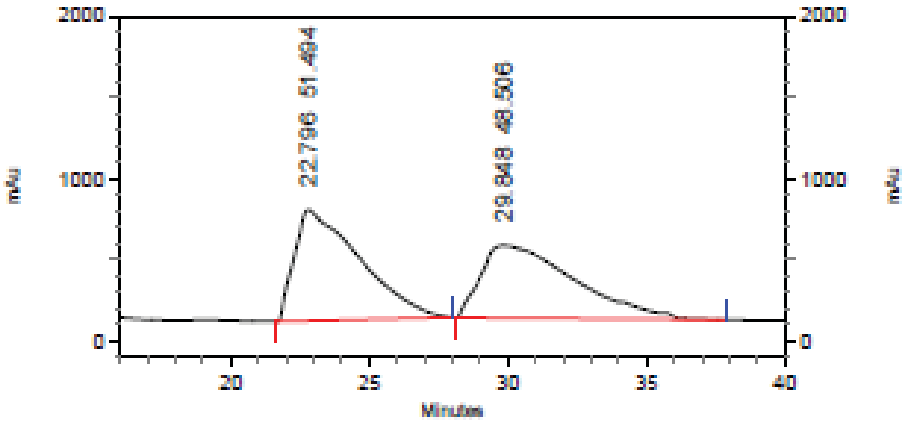


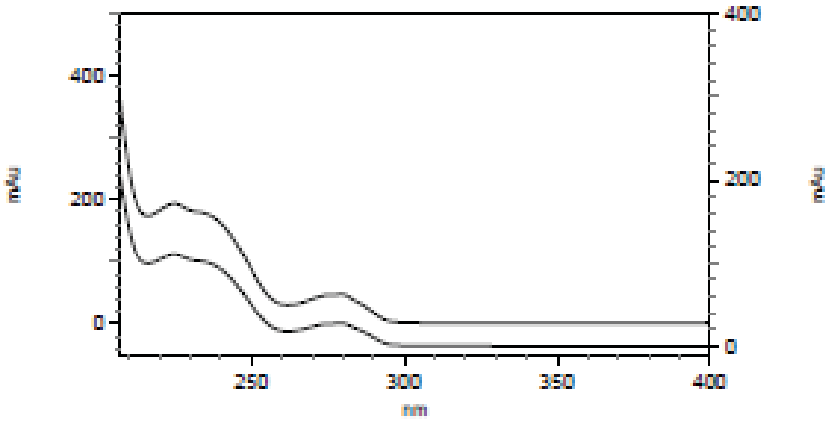
1-((1*S*,2*S*)-2-(4-bromophenyl)cyclopropyl)-2-methoxybenzene **3bd**



1-((1*S*,2*S*)-2-(4-bromophenyl)cyclopropyl)-2-methoxybenzene **3bd**

YW-I-232A-2 ADH 0% 0.8mL
C:\EZStart\Projects\Default\Method\ywangl.met
C:\EZStart\Projects\Default\Data\YW-I-232A-2 ADH 0% 0.8mL



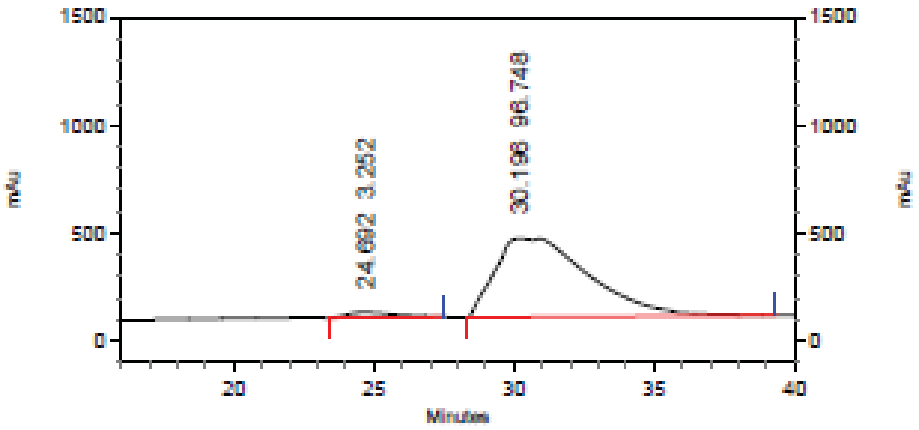


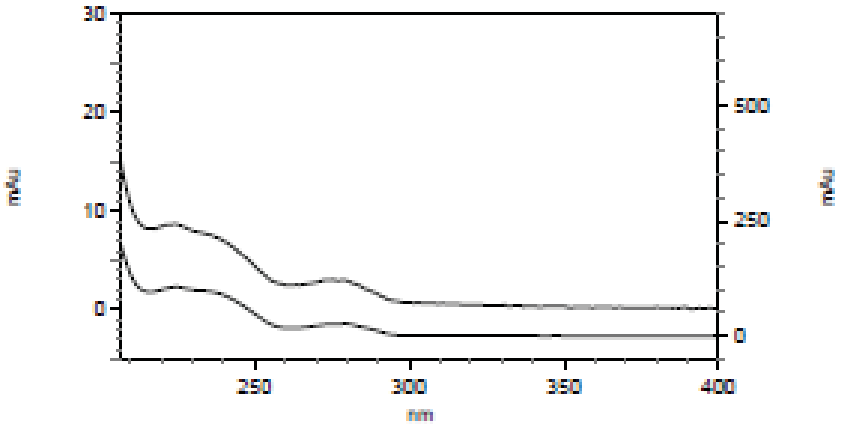
2: 254 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		22.796	51.494
2		29.848	48.506
Totals			100.000

1-((1*S*,2*S*)-2-(4-bromophenyl)cyclopropyl)-2-methoxybenzene **3bd**

YW-I-234 ADH 0% 0.8mL
C:\EZStart\Projects\Default\Method\ywangl.met
C:\EZStart\Projects\Default\Data\YW-I-234 ADH 0% 0.8mL

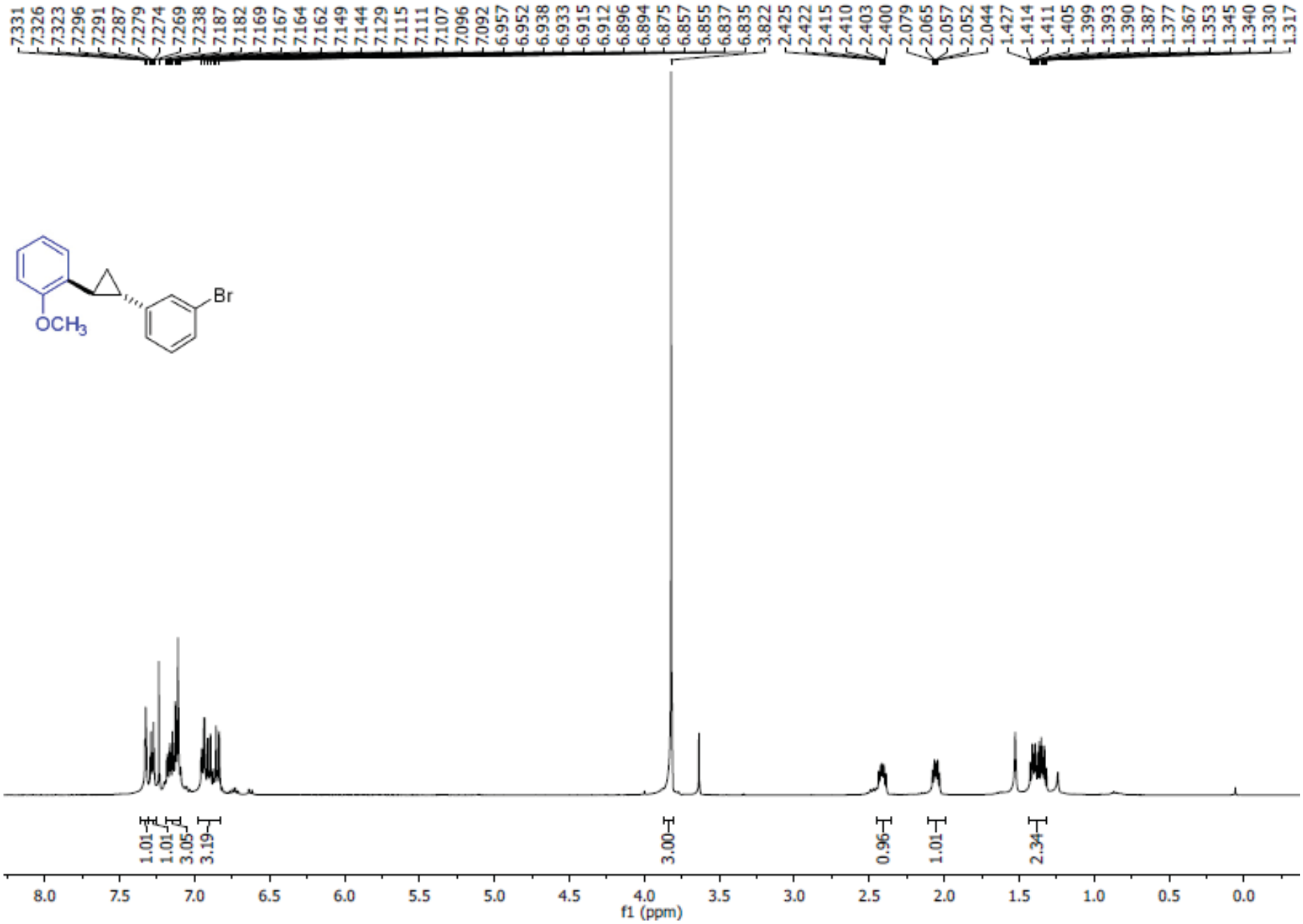




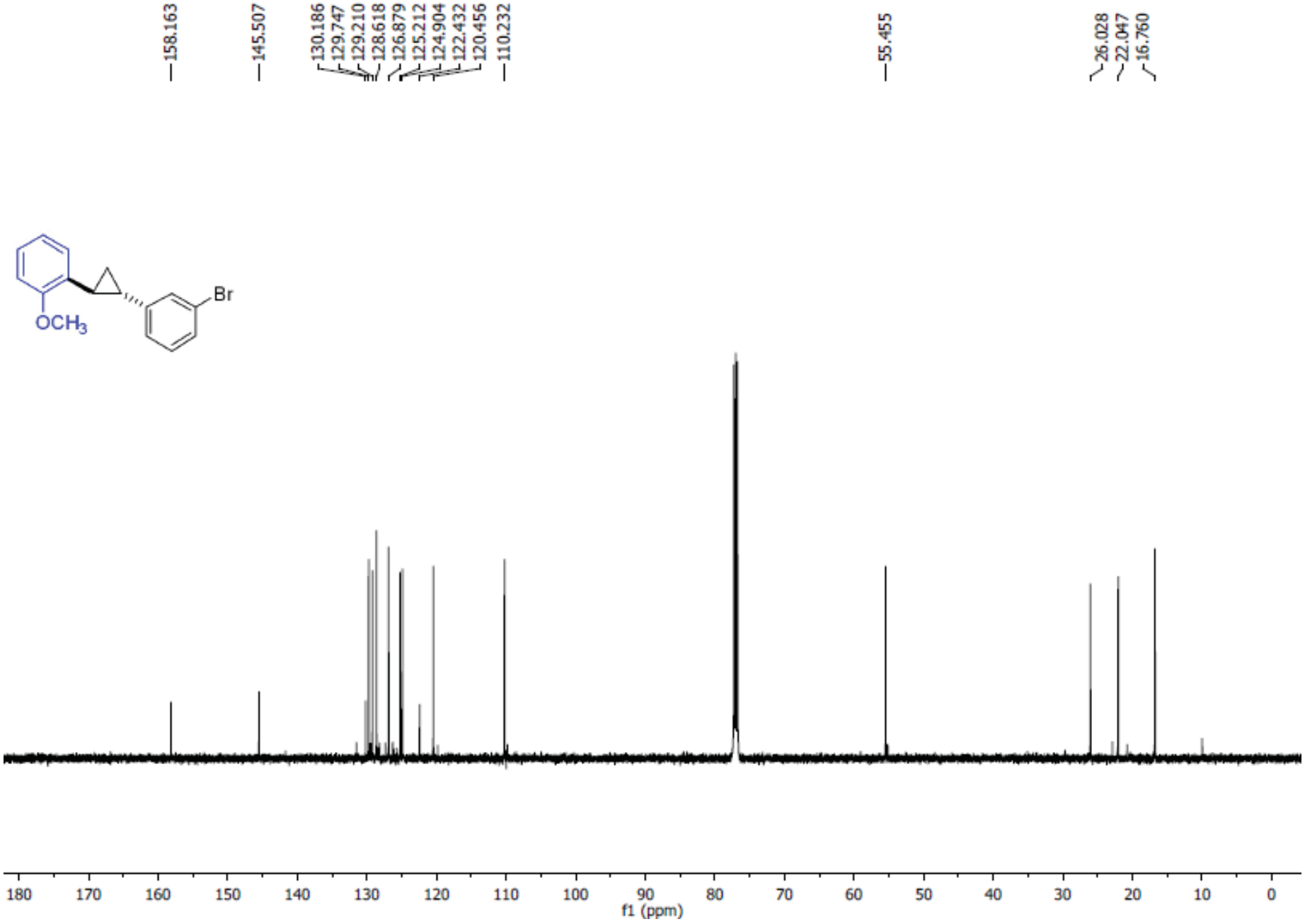
2: 274 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		24.692	3.252
2		30.196	96.748
Totals			100.000

1-((1*S*,2*S*)-2-(3-bromophenyl)cyclopropyl)-2-methoxybenzene **3be**

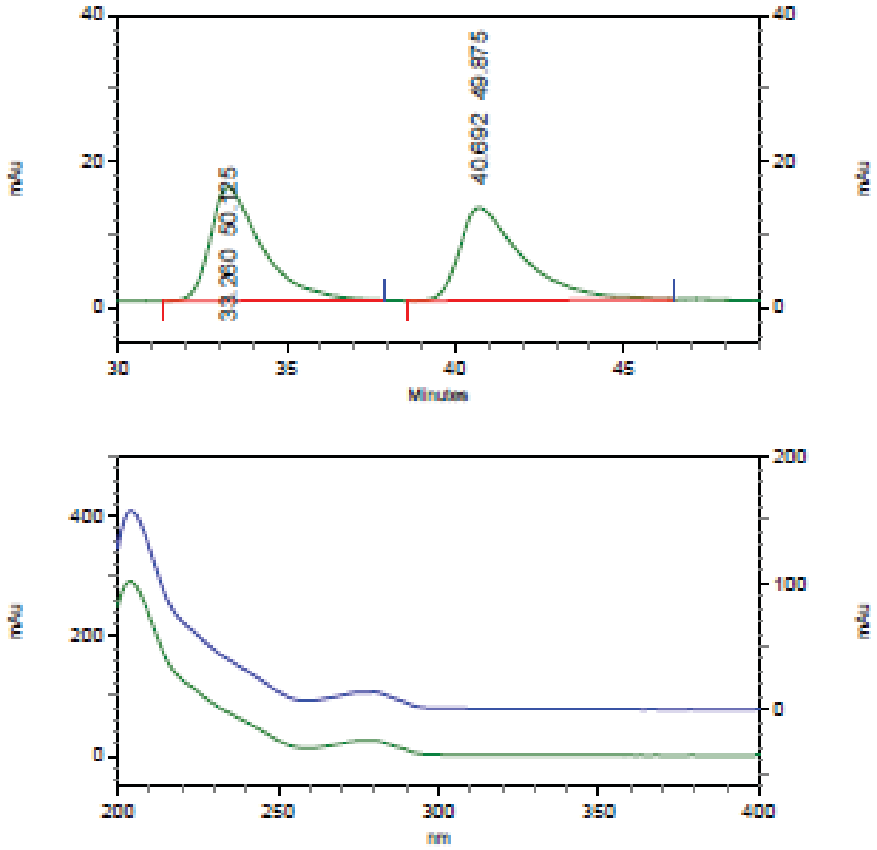


1-((1*S*,2*S*)-2-(3-bromophenyl)cyclopropyl)-2-methoxybenzene **3be**



1-((1*S*,2*S*)-2-(3-bromophenyl)cyclopropyl)-2-methoxybenzene **3be**

YW-II-93A OJH 0@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-93A OJH 0@0.8 mL

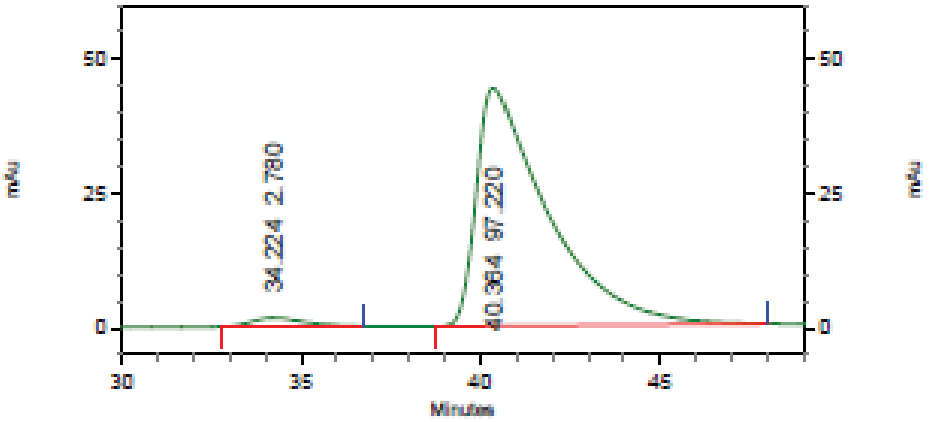


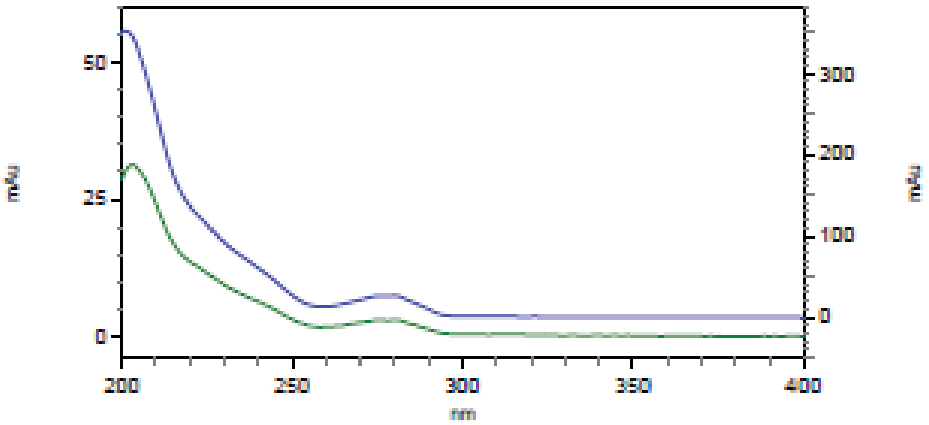
3: 279 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		33.260	50.125
2		40.692	49.875
Totals			100.000

1-((1*S*,2*S*)-2-(3-bromophenyl)cyclopropyl)-2-methoxybenzene **3be**

YW-II-93B OJH 0@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-93B OJH 0@0.8 mL

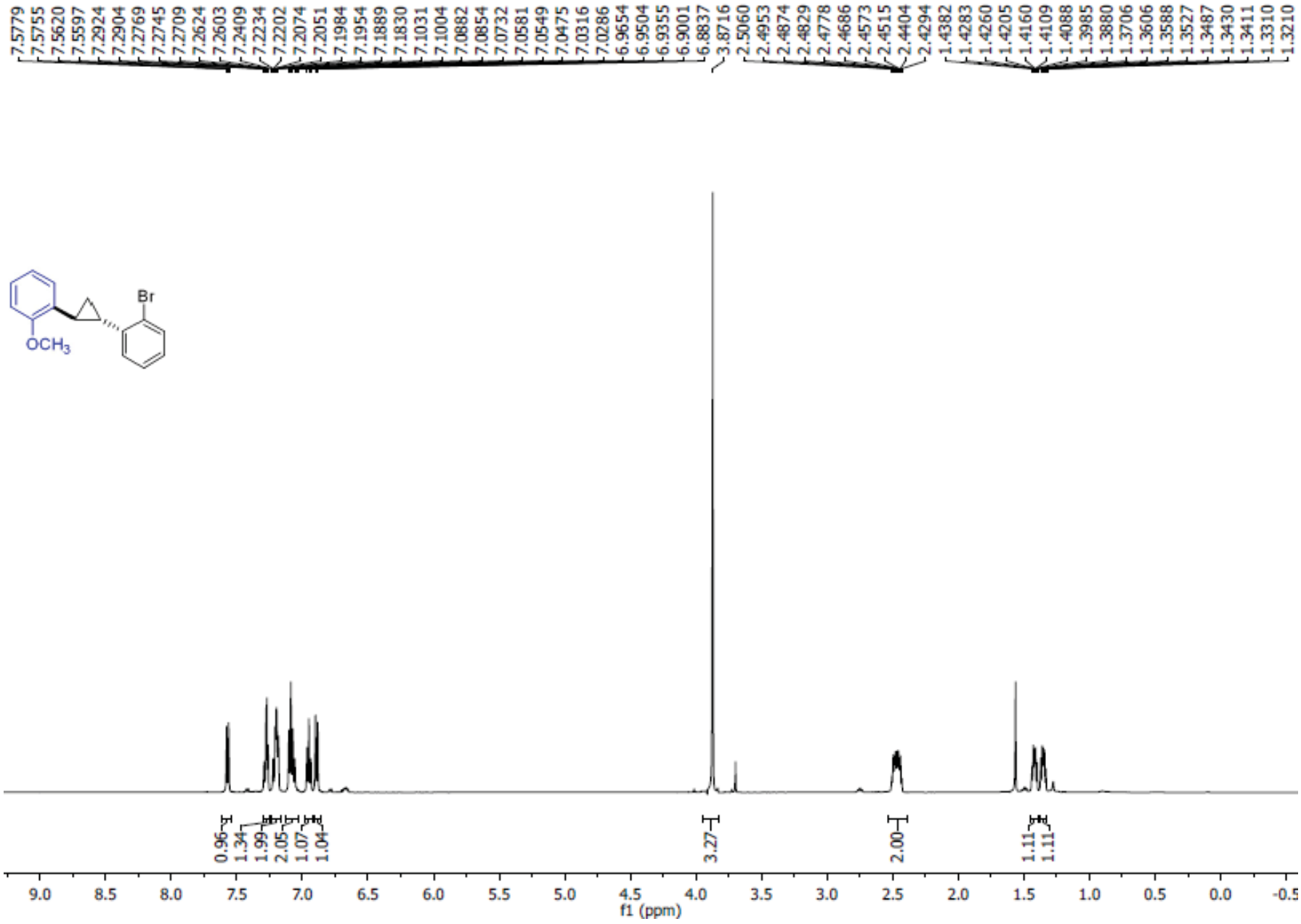




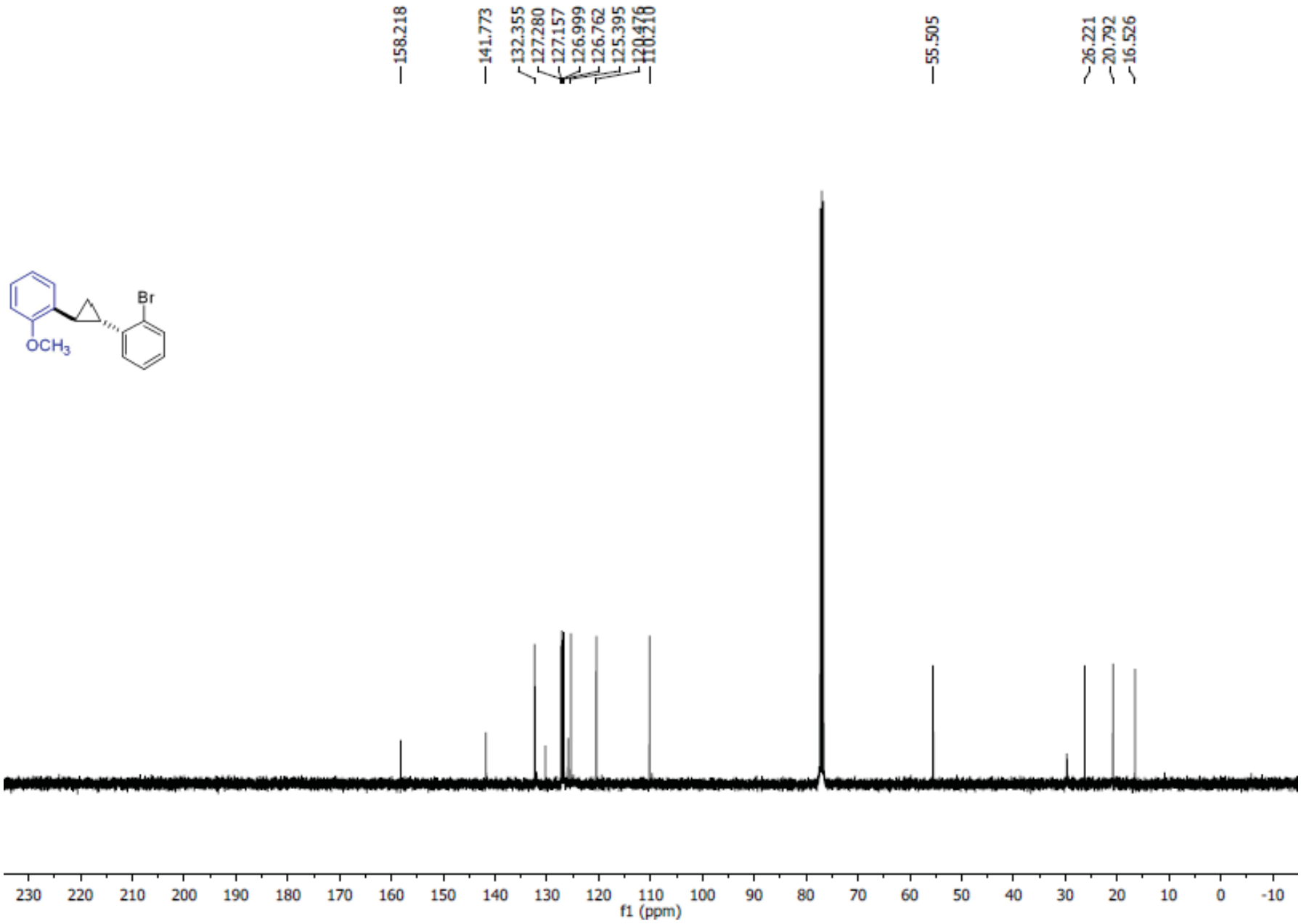
3: 279 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		34.224	2.780
2		40.364	97.220
Totals			100.000

1-bromo-2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)benzene **3bf**

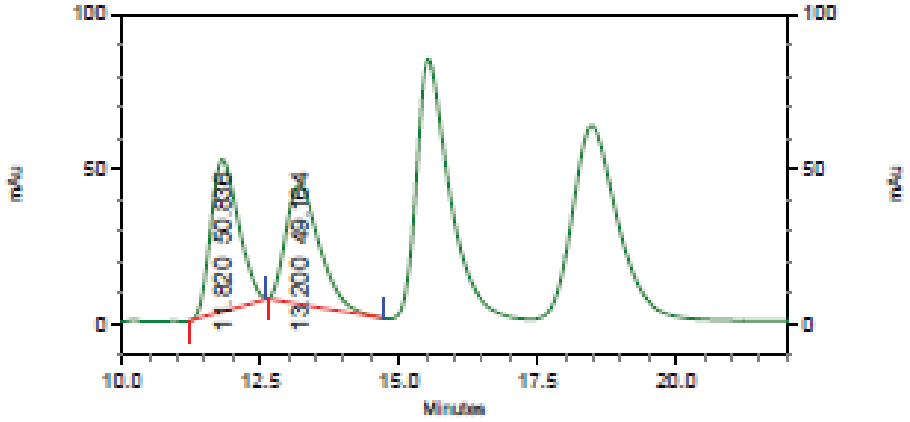


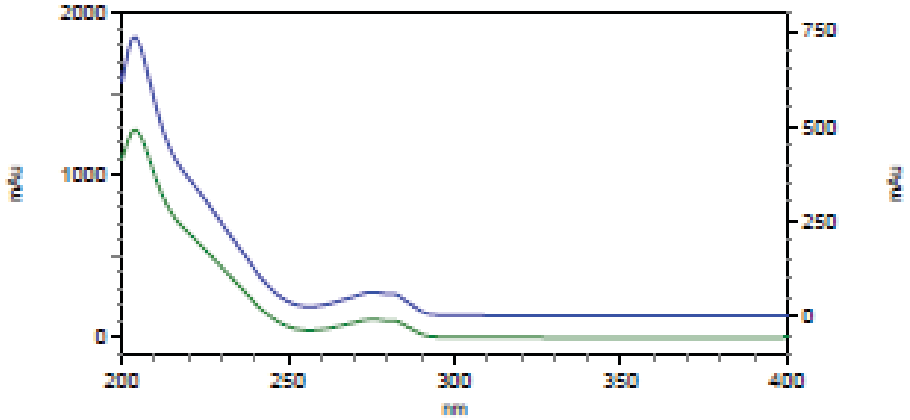
1-bromo-2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)benzene **3bf**



1-bromo-2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)benzene **3bf**

YW-I-249 OJH 0.5@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-I-249 OJH 0.5@0.8 mL



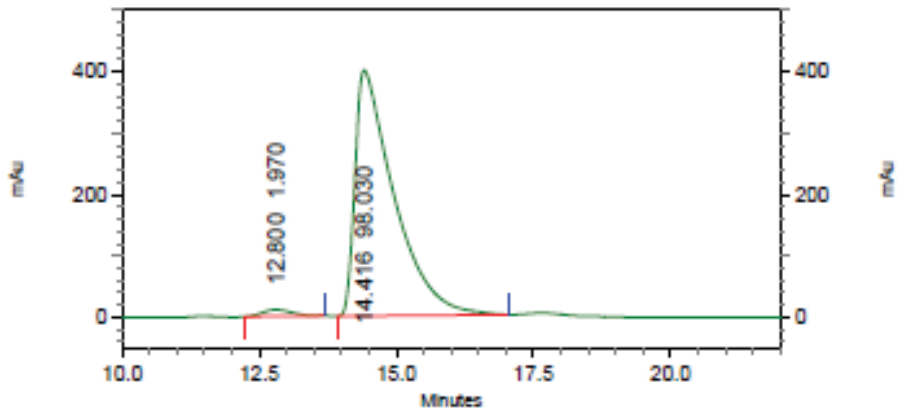


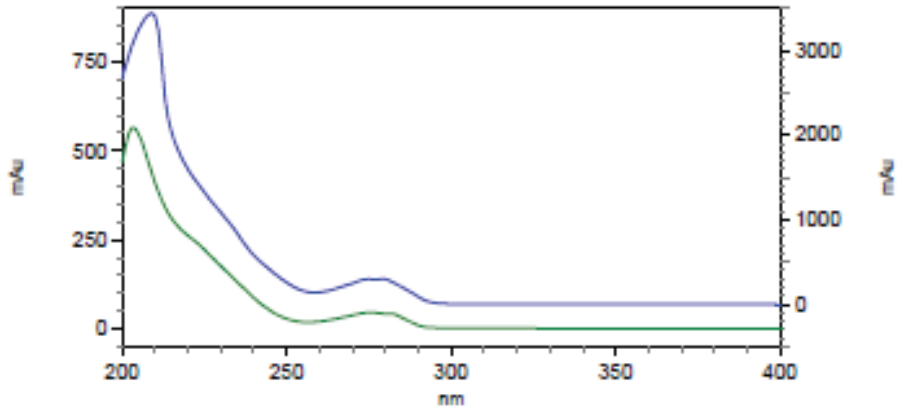
2: 249 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		11.820	50.836
2		13.200	49.164
Totals			100.000

1-bromo-2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)benzene **3bf**

YW-I-257 OJH 0.5%0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-I-257 OJH 0.5%0.8 mL

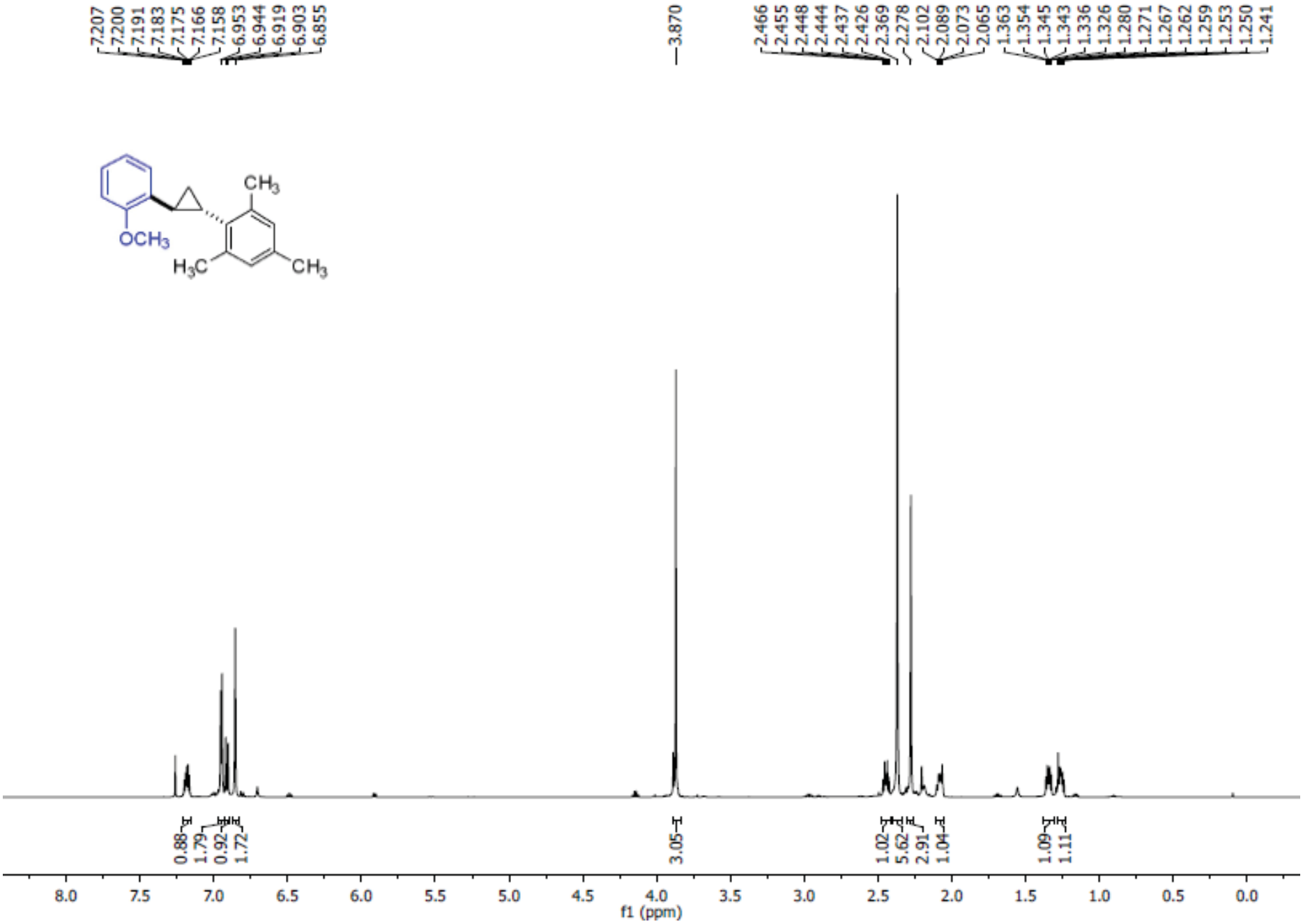




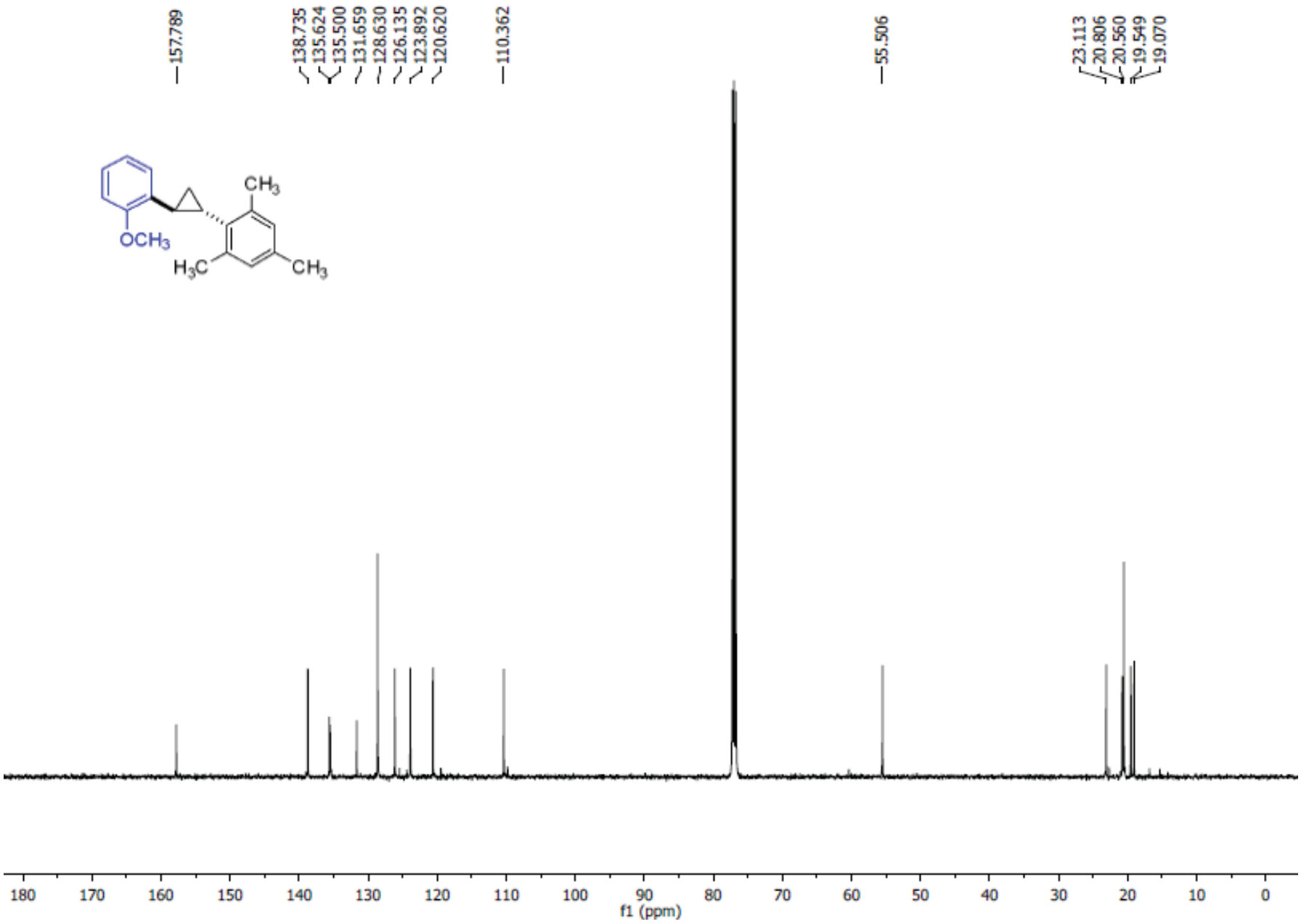
2: 256 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		12.800	1.970
2		14.416	98.030
Totals			100.000

2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)-1,3,5-trimethylbenzene **3bg**

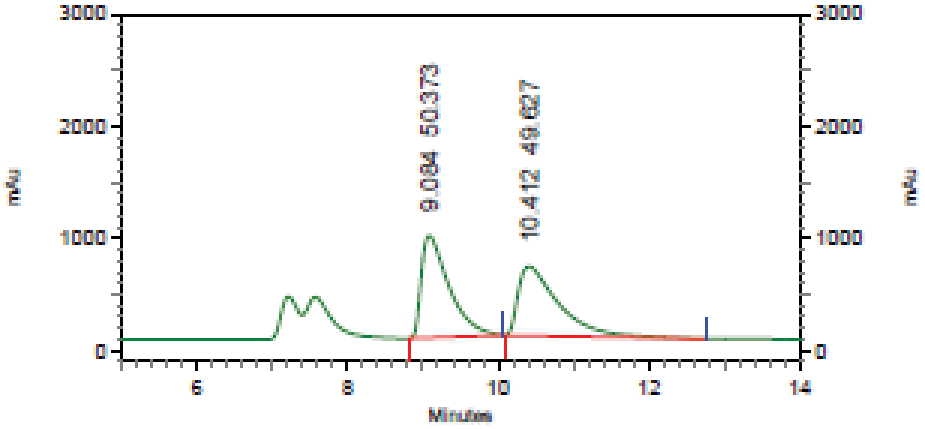


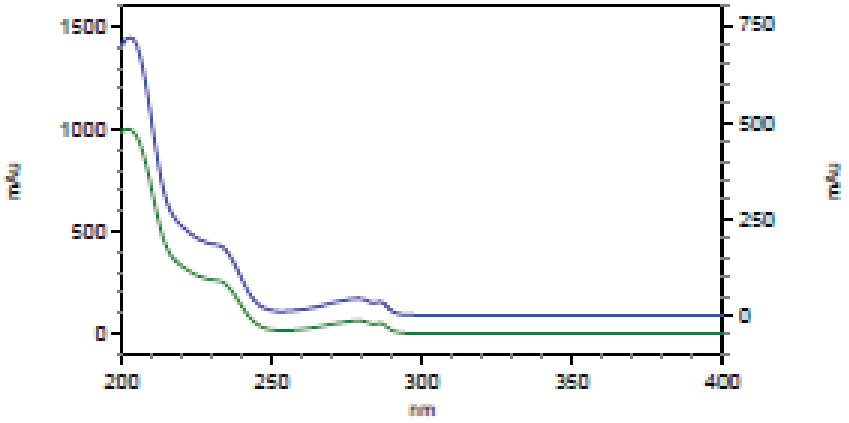
2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)-1,3,5-trimethylbenzene **3bg**



2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)-1,3,5-trimethylbenzene **3bg**

YW-I-237 NEW ADH 0% 0.8mL
C:\EZStart\Projects\Default\Method\ywang0.8.met
C:\EZStart\Projects\Default\Data\YW-I-237 NEW ADH 0% 0.8mL



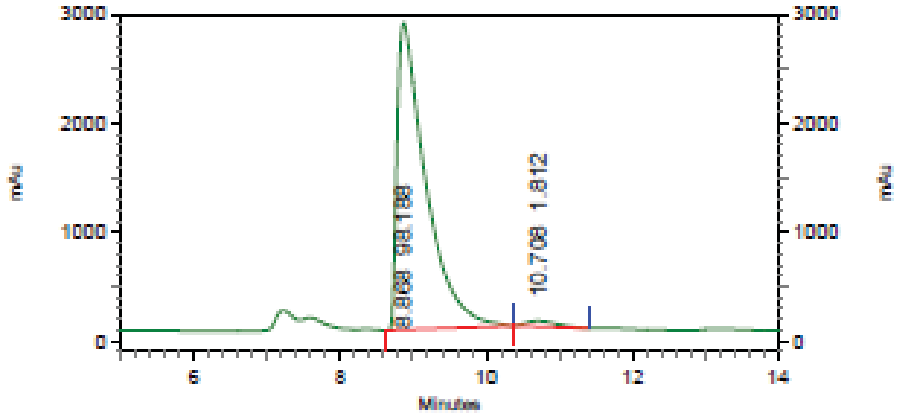


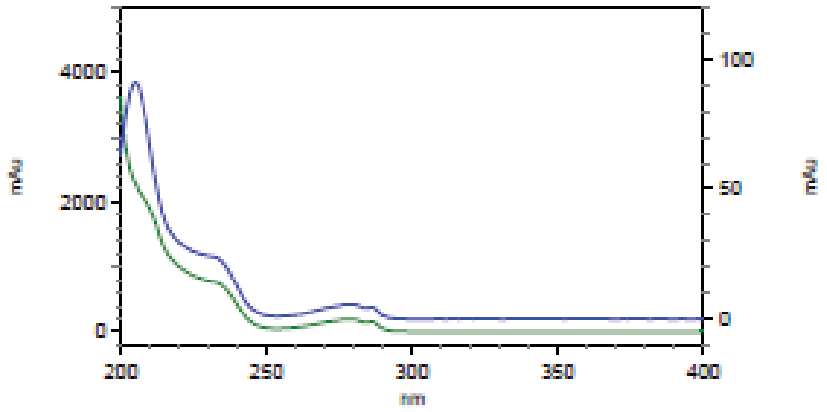
4: 279 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		9.084	50.373
2		10.412	49.627
Totals			100.000

2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)-1,3,5-trimethylbenzene **3bg**

YW-III-15 NEW ADH 0# 0.8mL
C:\EZStart\Projects\Default\Method\ywang0.8.met
C:\EZStart\Projects\Default\Data\YW-III-15 NEW ADH 0# 0.8mL

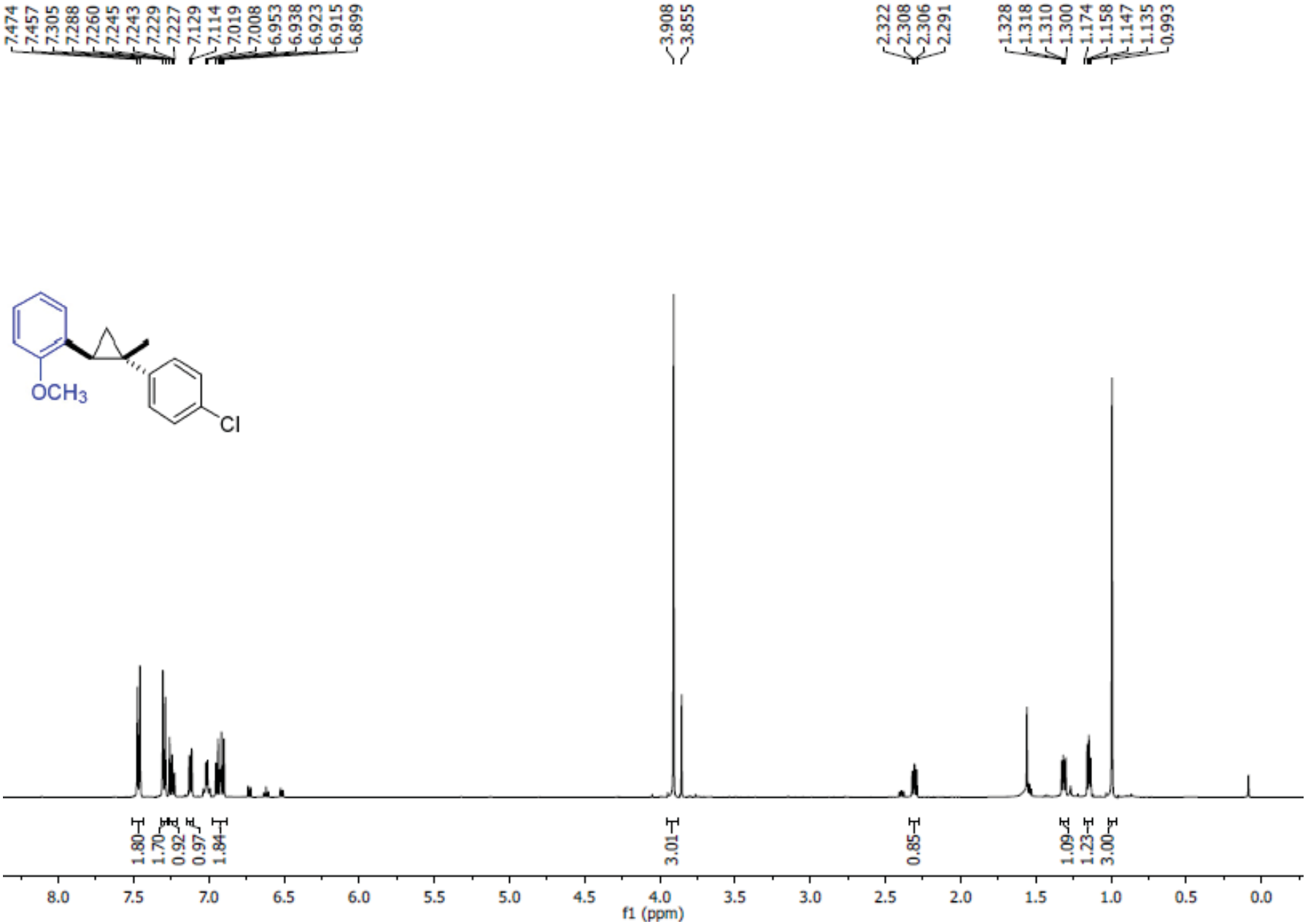




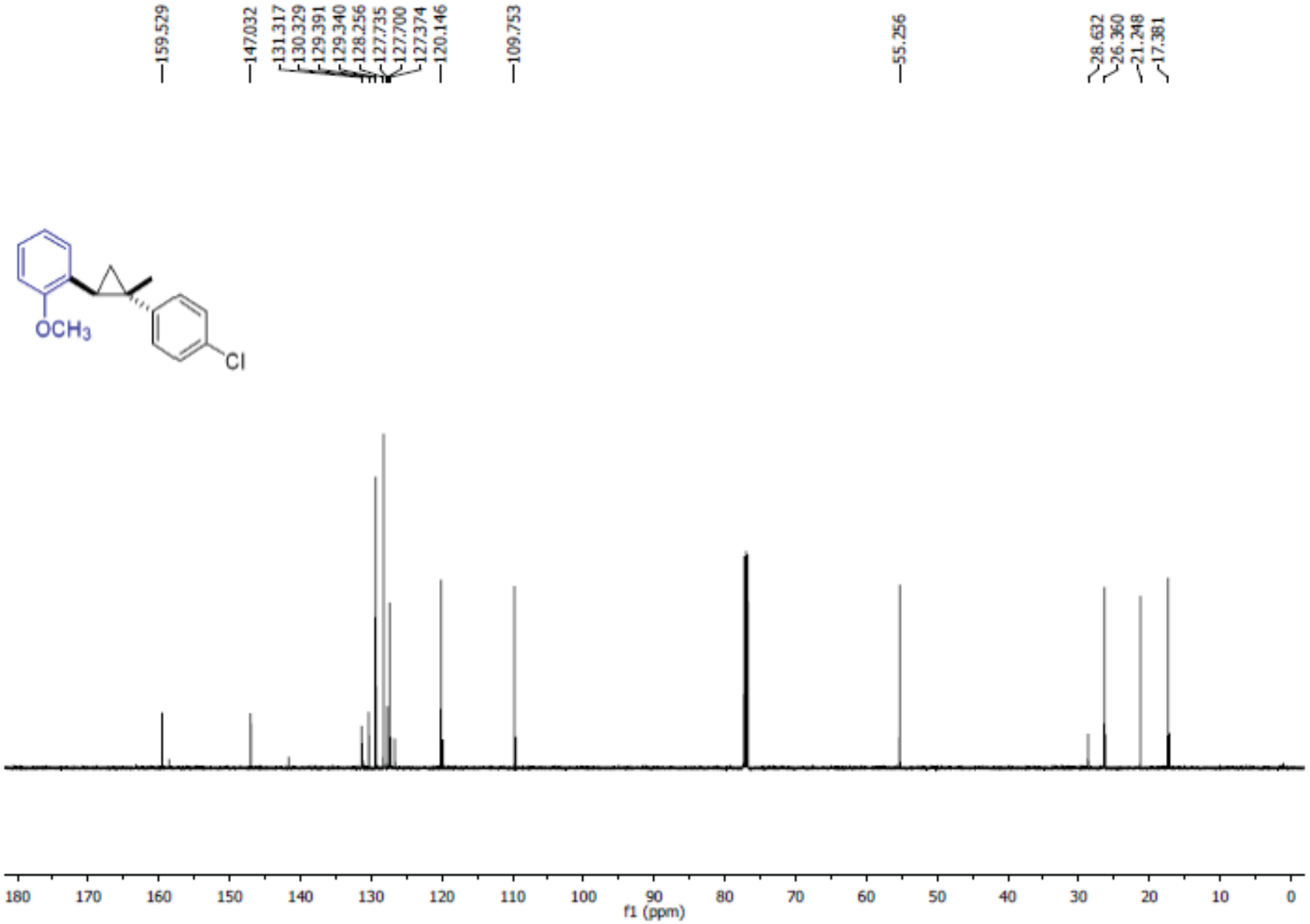
4: 279 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		8.868	98.188
2		10.708	1.812
Totals			100.000

1-((1*S*,2*S*)-2-(4-chlorophenyl)-2-methylcyclopropyl)-2-methoxybenzene **3bh**

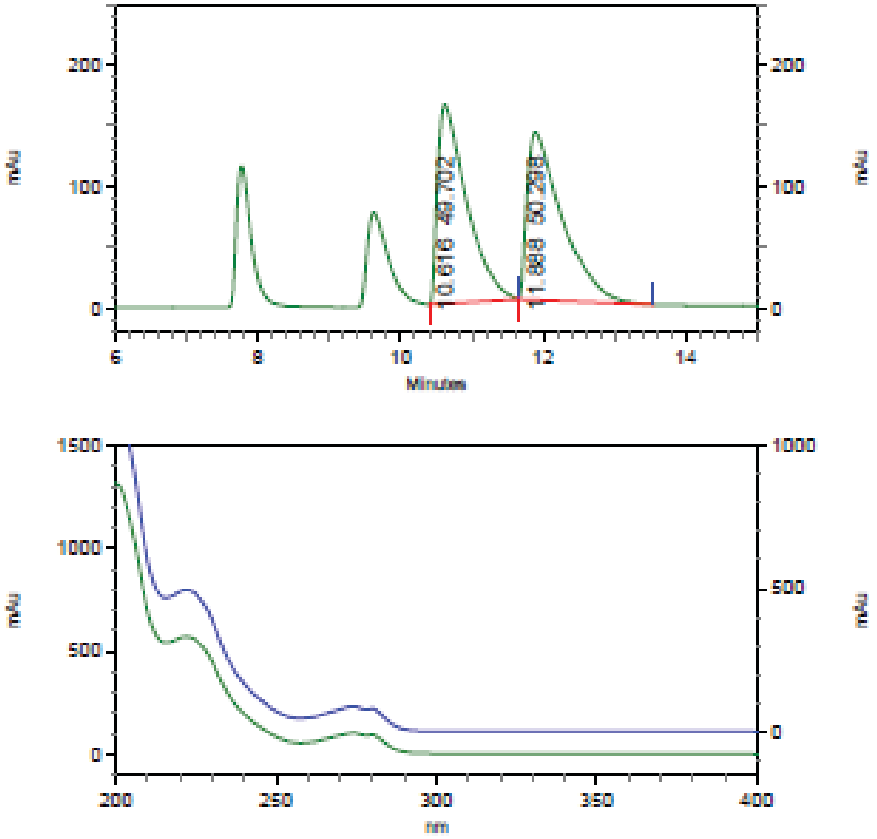


1-((1*S*,2*S*)-2-(4-chlorophenyl)-2-methylcyclopropyl)-2-methoxybenzene **3bh**



1-((1*S*,2*S*)-2-(4-chlorophenyl)-2-methylcyclopropyl)-2-methoxybenzene **3bh**

YW-I-246 ADH 0@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
E:\HPLC-YW-I\YW-I-246 ADH 0@0.8 mL

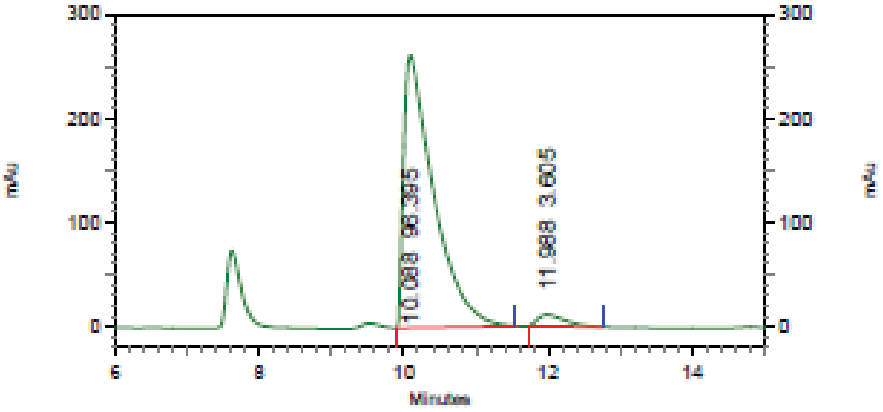


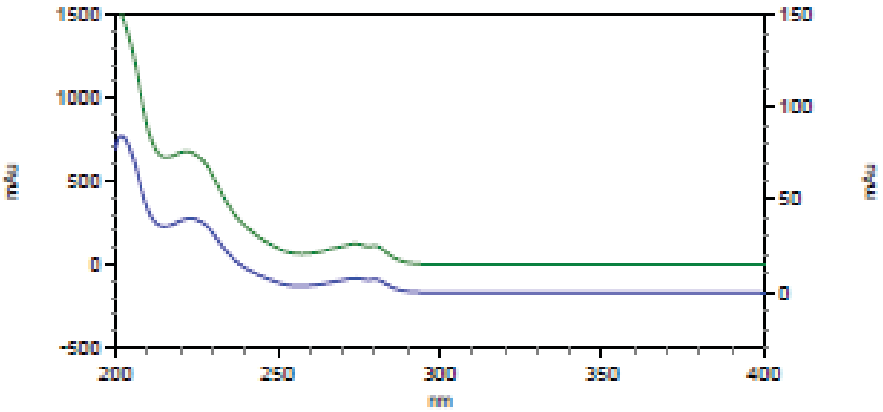
2: 242 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		10.616	49.702
2		11.868	50.298
Totals			100.000

1-((1*S*,2*S*)-2-(4-chlorophenyl)-2-methylcyclopropyl)-2-methoxybenzene **3bh**

YW-I-254 ADH 0#0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
E:\HPLC-YW-I\YW-I-254 ADH 0#0.8 mL

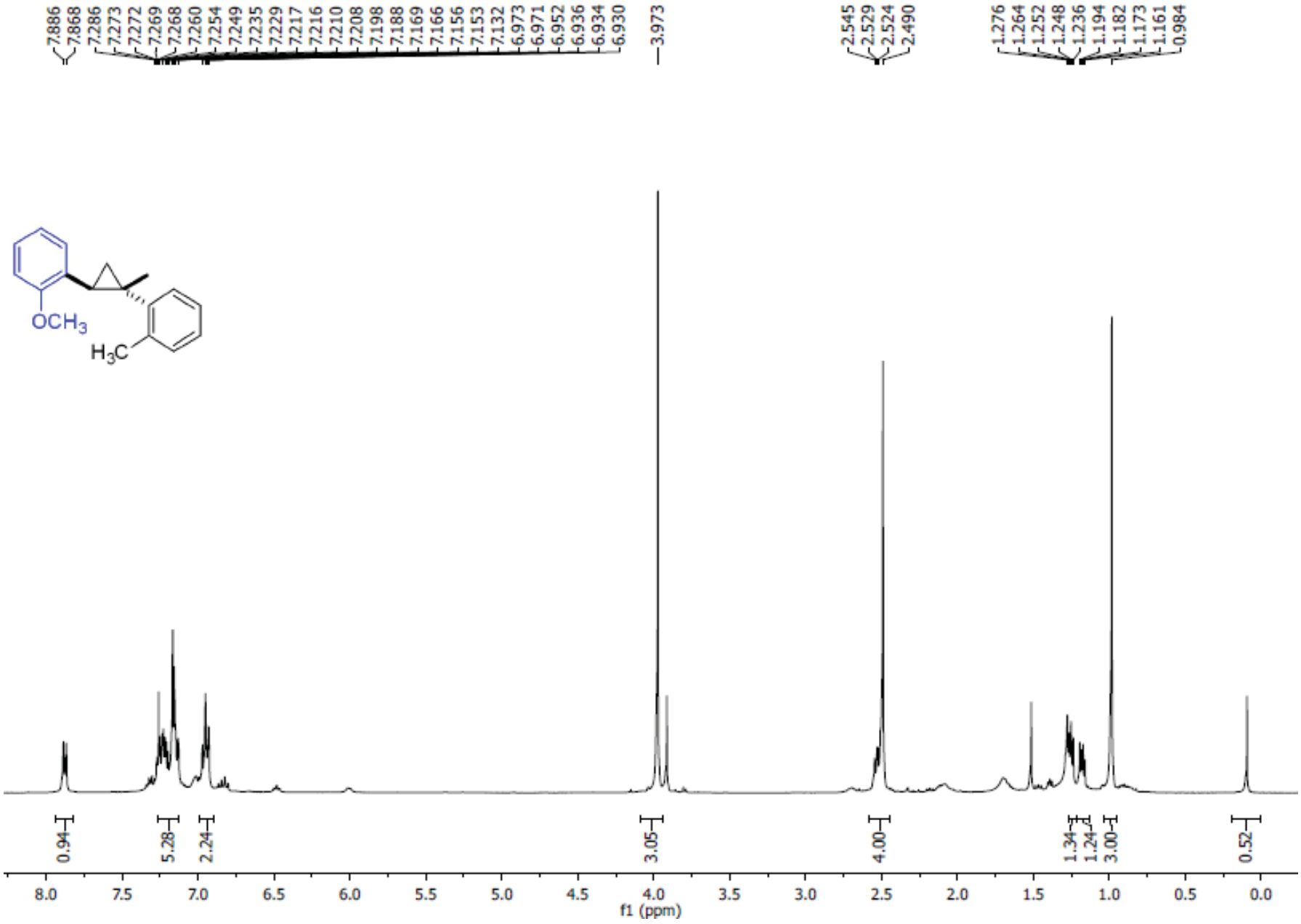




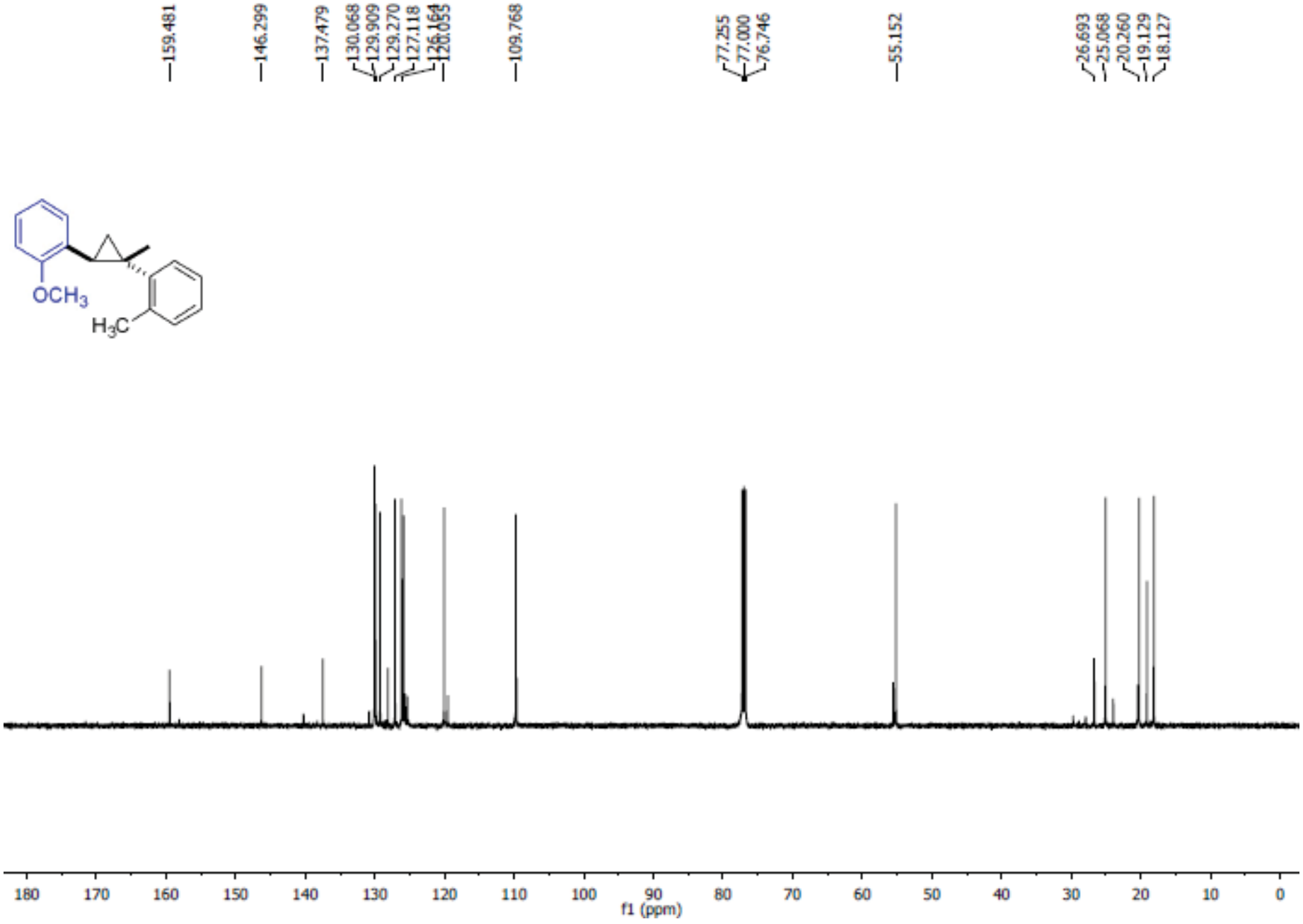
2: 242 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		10.088	96.395
2		11.988	3.605
Totals			100.000

1-methoxy-2-((1*S*,2*S*)-2-methyl-2-(o-tolyl)cyclopropyl)benzene **3bi**

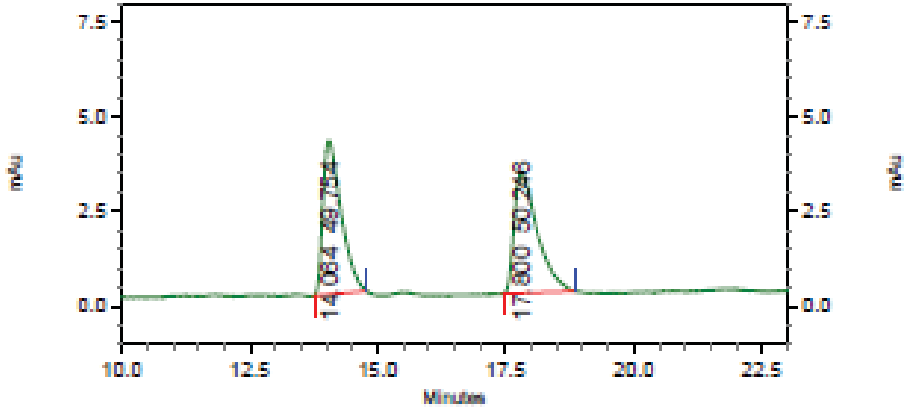


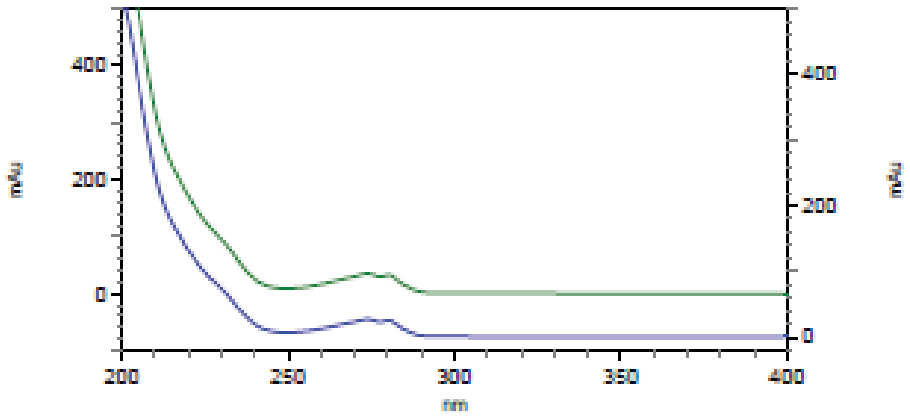
1-methoxy-2-((1*S*,2*S*)-2-methyl-2-(o-tolyl)cyclopropyl)benzene **3bi**



1-methoxy-2-((1*S*,2*S*)-2-methyl-2-(o-tolyl)cyclopropyl)benzene **3bi**

YW-II-20a-1 ODH 0@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-20a-1 ODH 0@0.8 mL



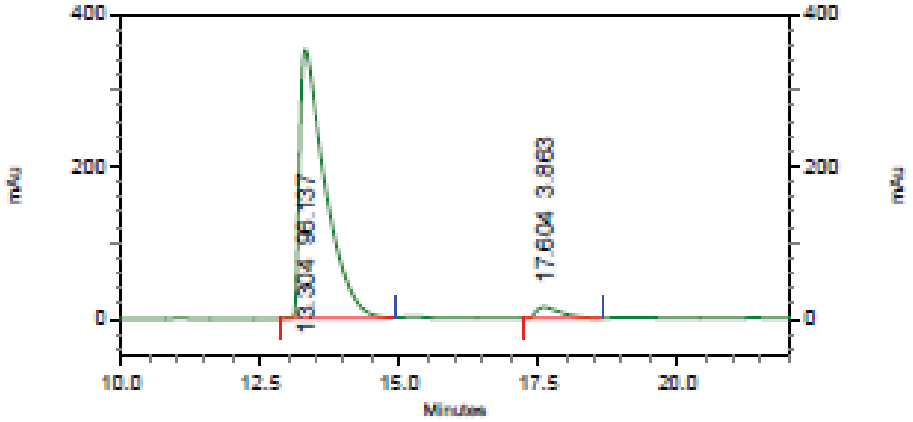


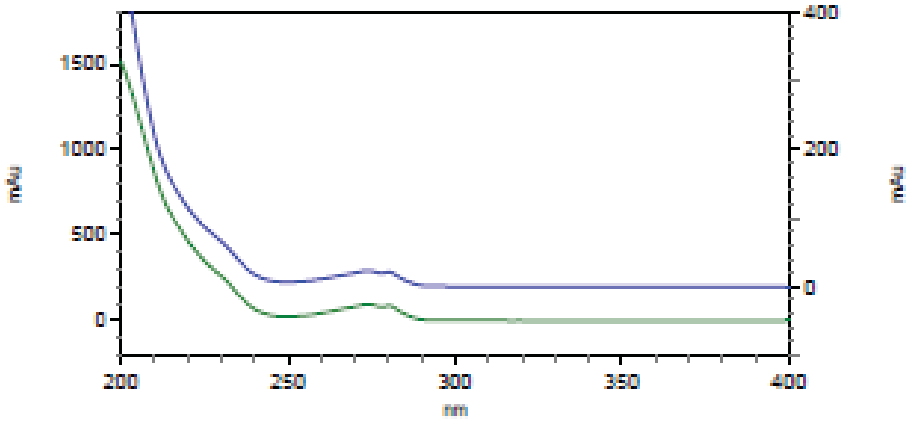
2: 289 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		14.064	49.754
2		17.800	50.246
Totals			100.000

1-methoxy-2-((1*S*,2*S*)-2-methyl-2-(o-tolyl)cyclopropyl)benzene **3bi**

YW-II-20b-1 ODH 0#0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-20b-1 ODH 0#0.8 mL

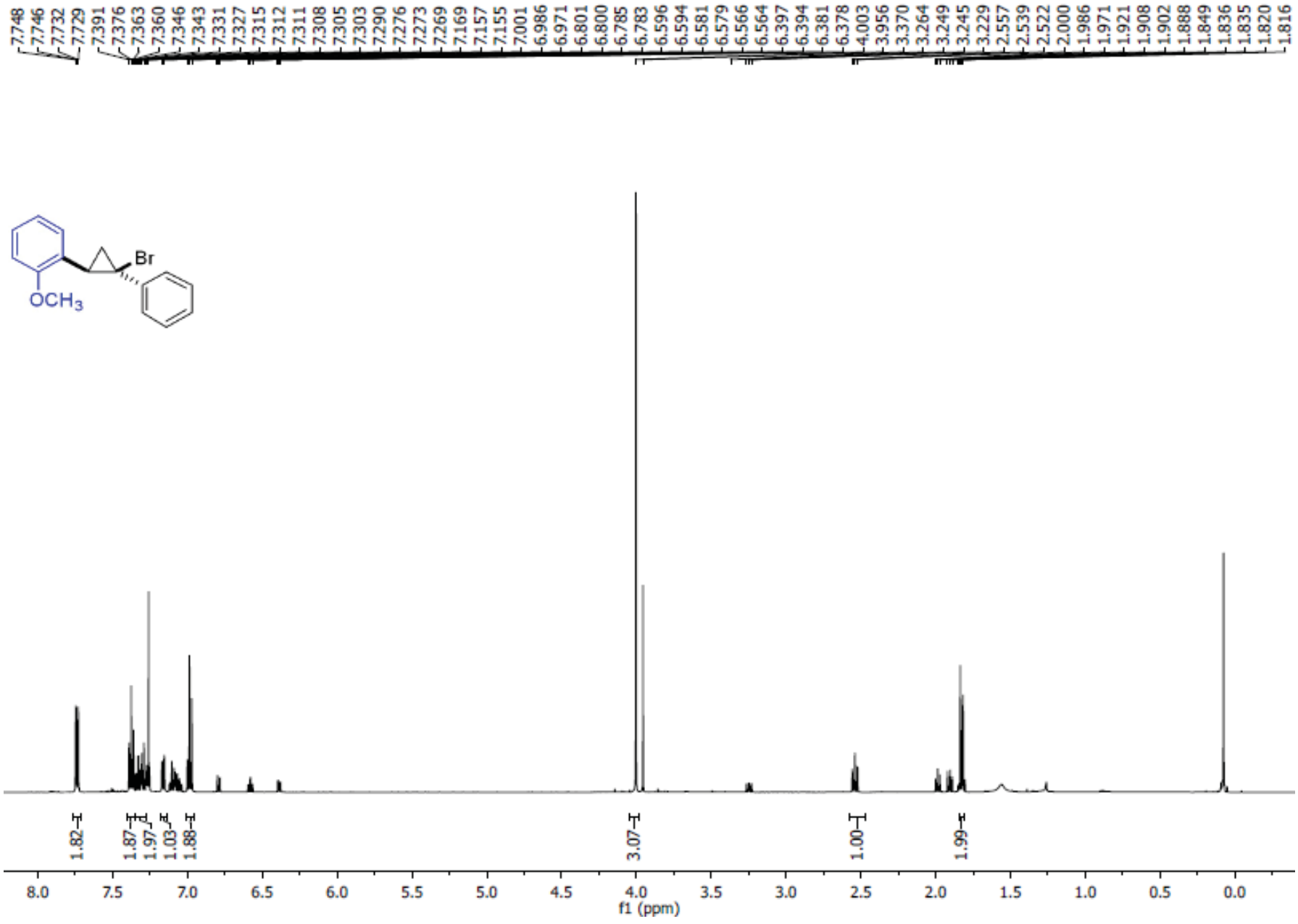




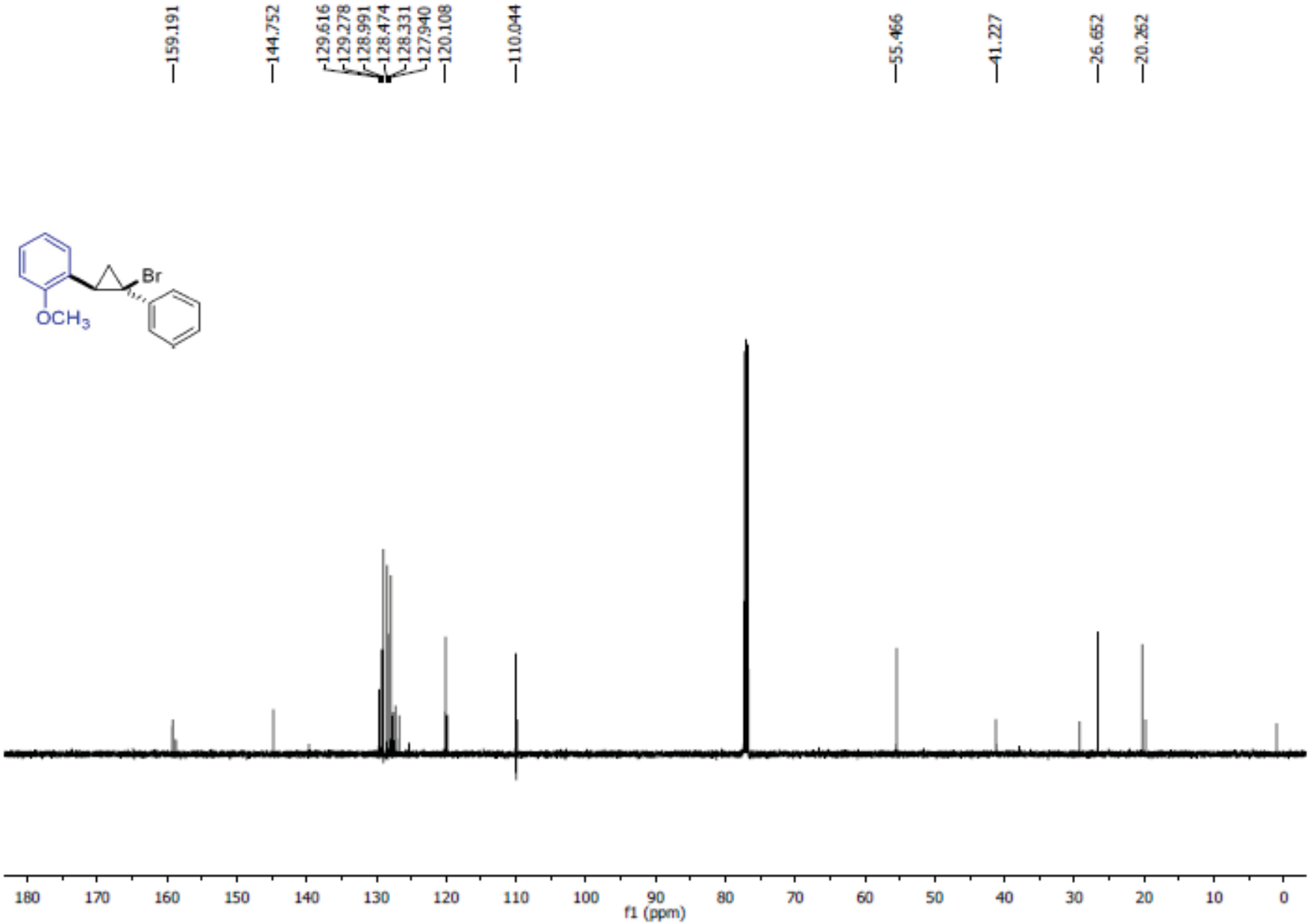
2: 263 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		13.304	96.137
2		17.604	3.863
Totals			100.000

1-((1*R*,2*R*)-2-bromo-2-phenylcyclopropyl)-2-methoxybenzene **3bj**

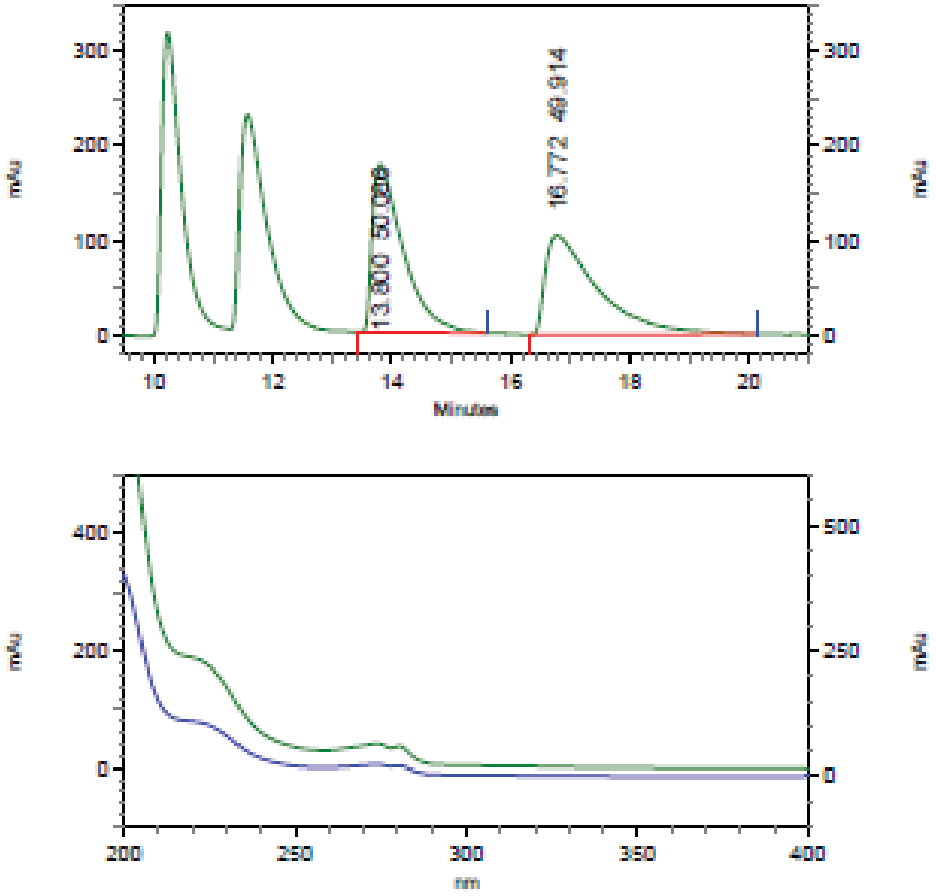


1-((1*R*,2*R*)-2-bromo-2-phenylcyclopropyl)-2-methoxybenzene **3bj**



1-((1*R*,2*R*)-2-bromo-2-phenylcyclopropyl)-2-methoxybenzene **3bj**

YW-I-260-2 ADH o@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
E:\HPLC-YW-I\YW-I-260-2 ADH o@0.8 mL

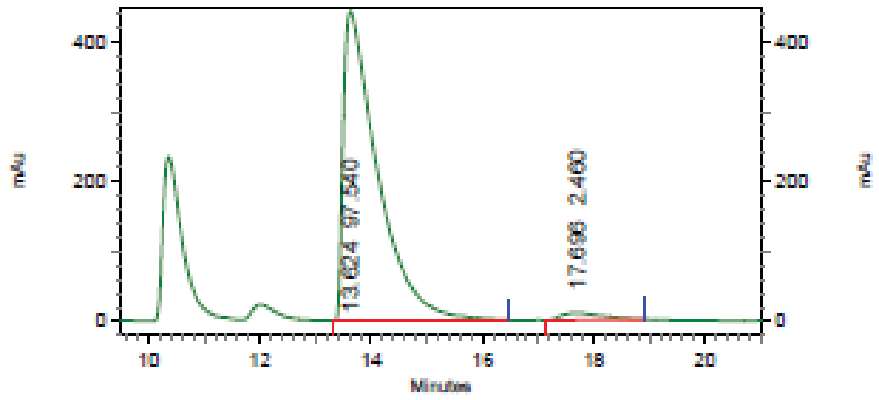


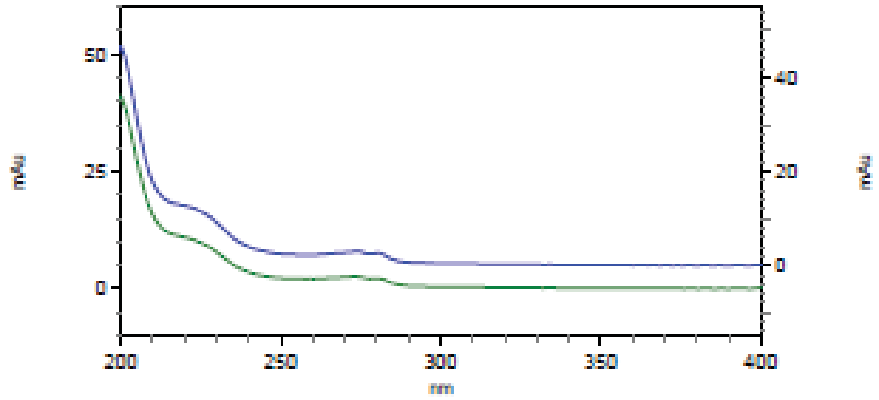
2: 223 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		13.800	50.086
2		16.772	49.914
Totals			100.000

1-((1*R*,2*R*)-2-bromo-2-phenylcyclopropyl)-2-methoxybenzene **3bj**

YW-I-266 ADH o@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
E:\HPLC-YW-I\YW-I-266 ADH o@0.8 mL

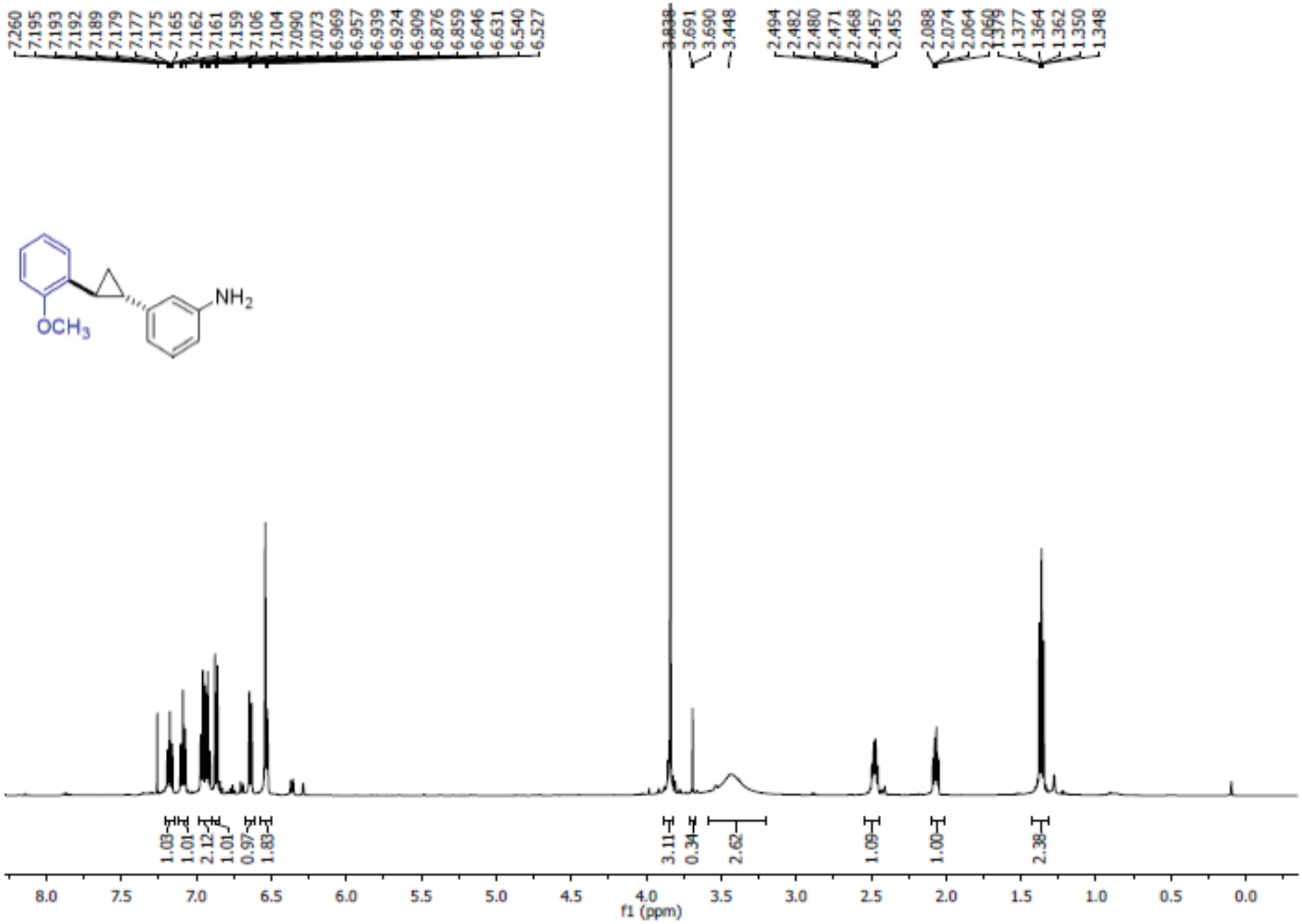




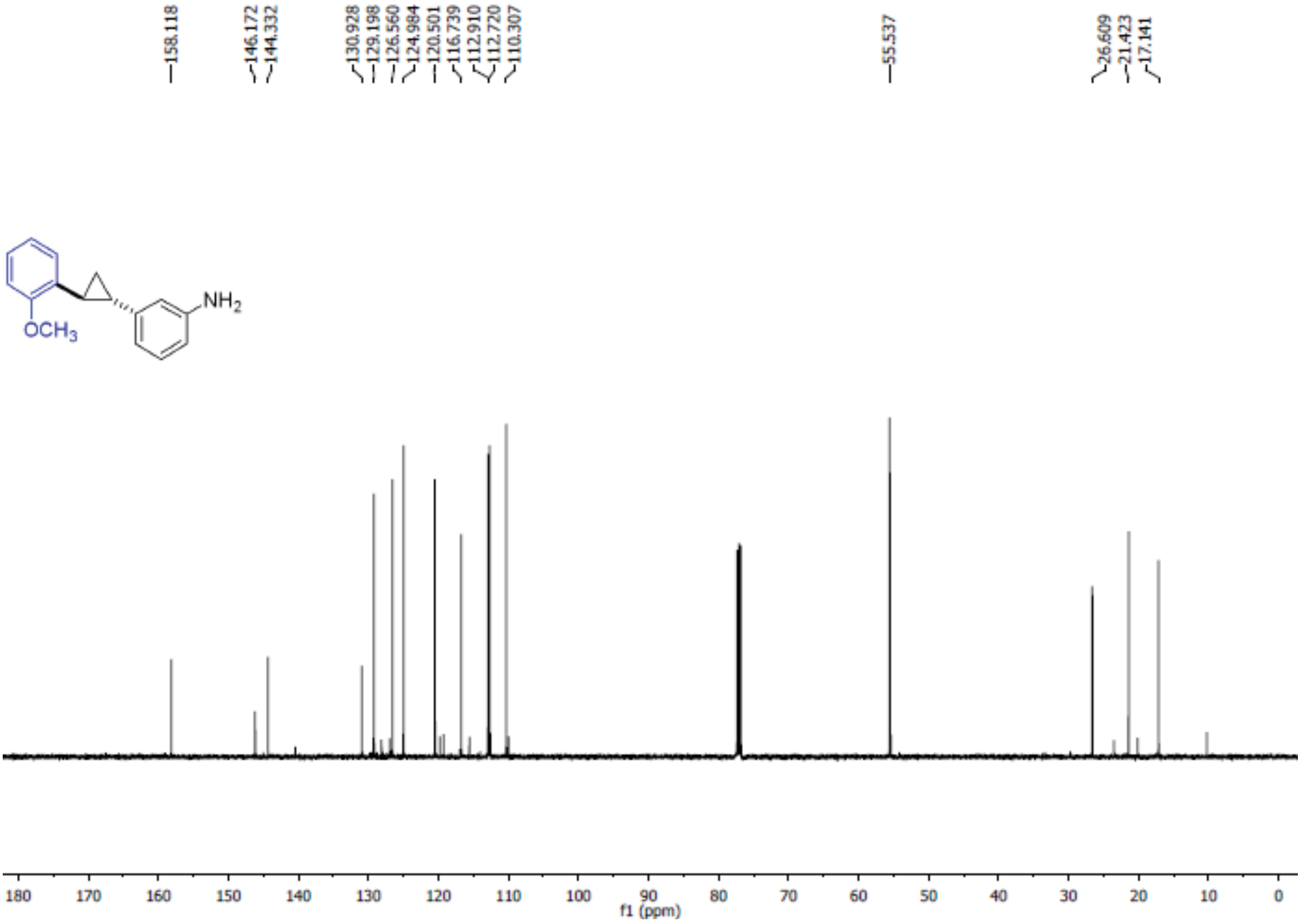
2: 223 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		13.624	97.540
2		17.696	2.460
Totals			100.000

3-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)aniline **3bk**

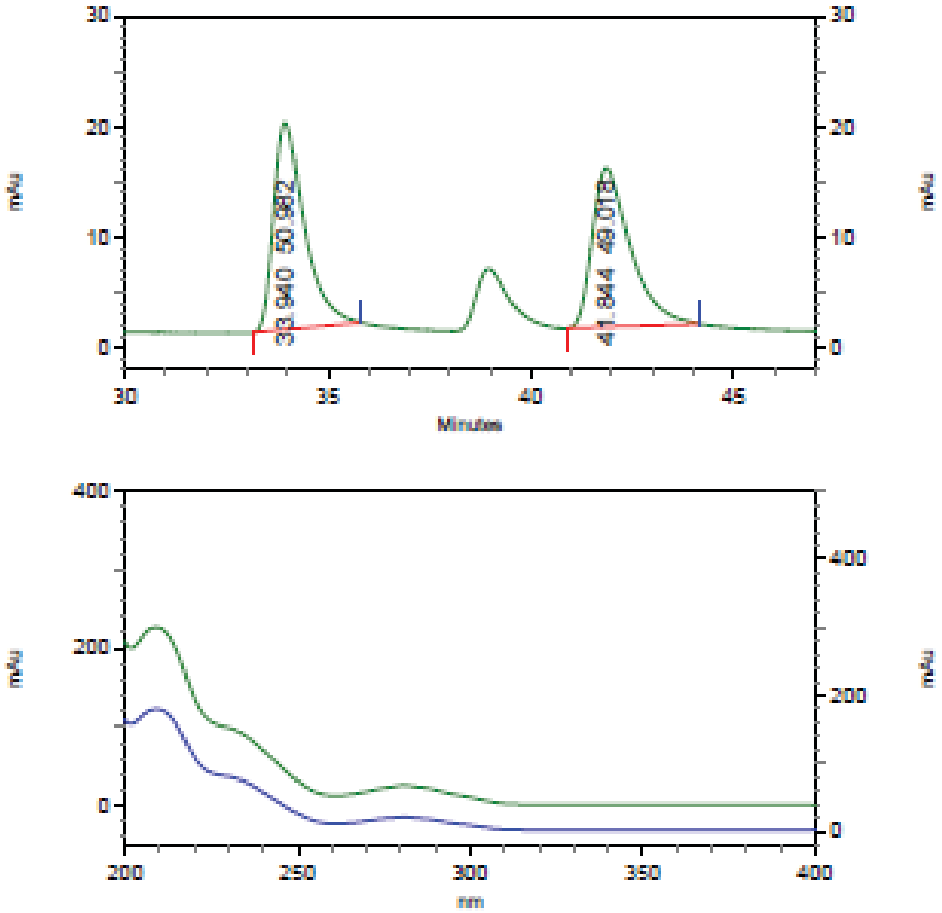


3-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)aniline **3bk**



3-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)aniline **3bk**

YW-I-235 ADH 3@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
E:\HPLC-YW-I\YW-I-235 ADH 3@0.8 mL

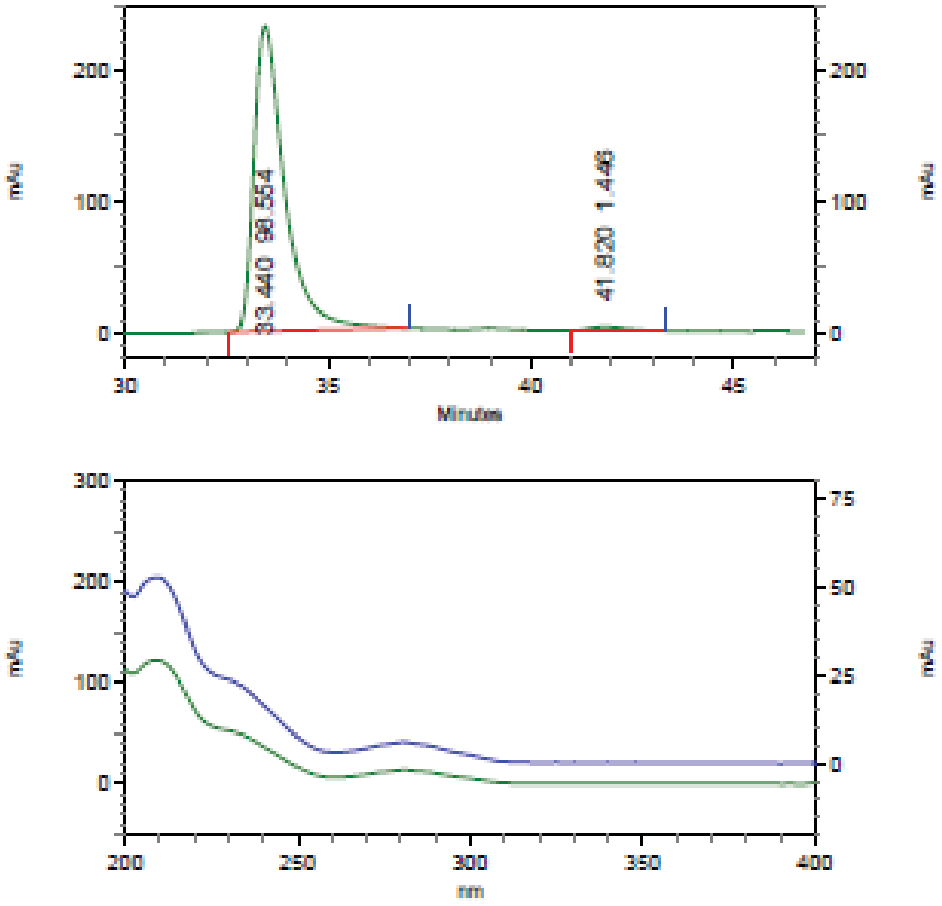


4: 290 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		33.940	50.982
2		41.844	49.018
Totals			100.000

3-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)aniline **3bk**

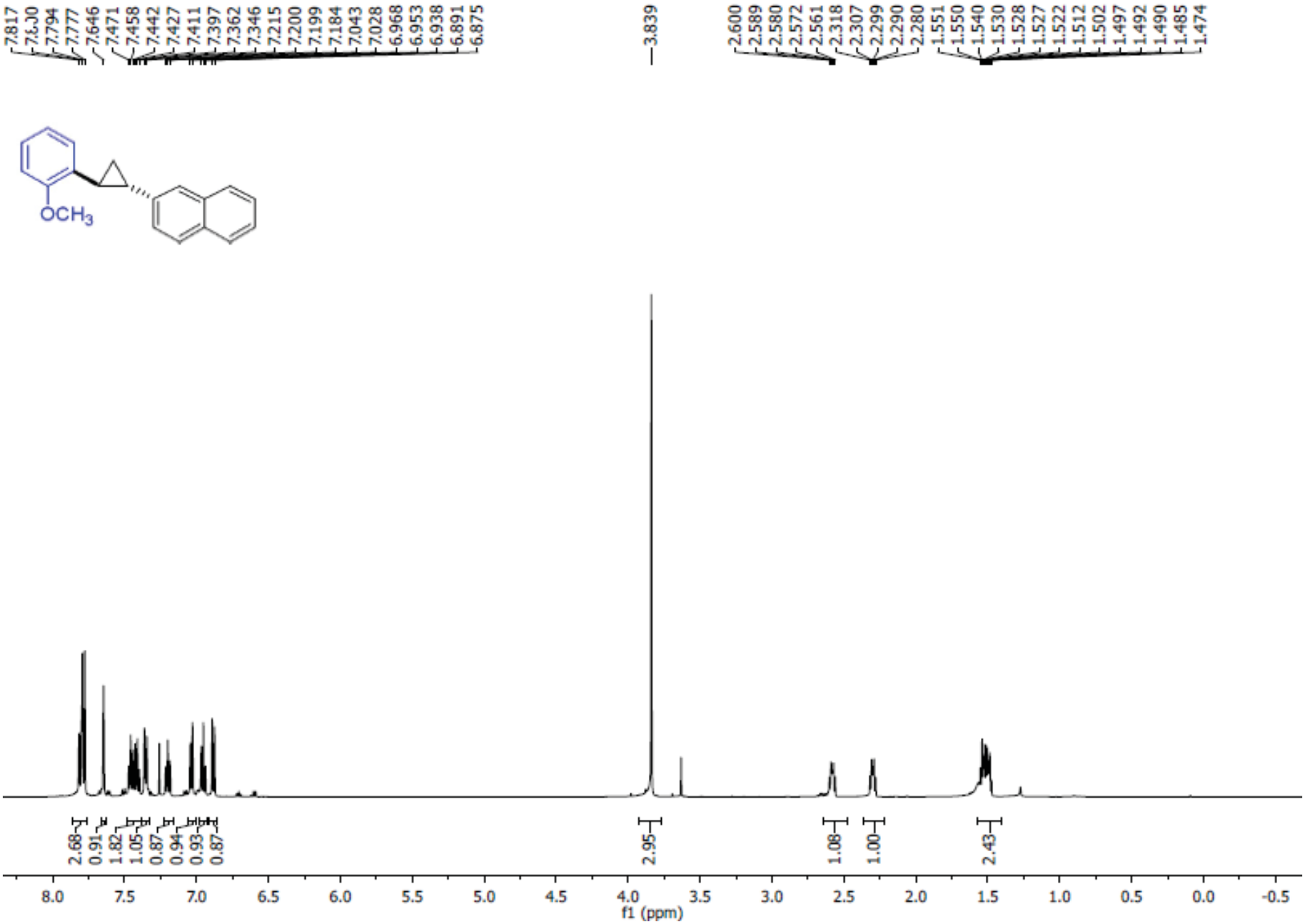
YW-I-239 ADH 3@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
E:\HPLC-YW-I\YW-I-239 ADH 3@0.8 mL



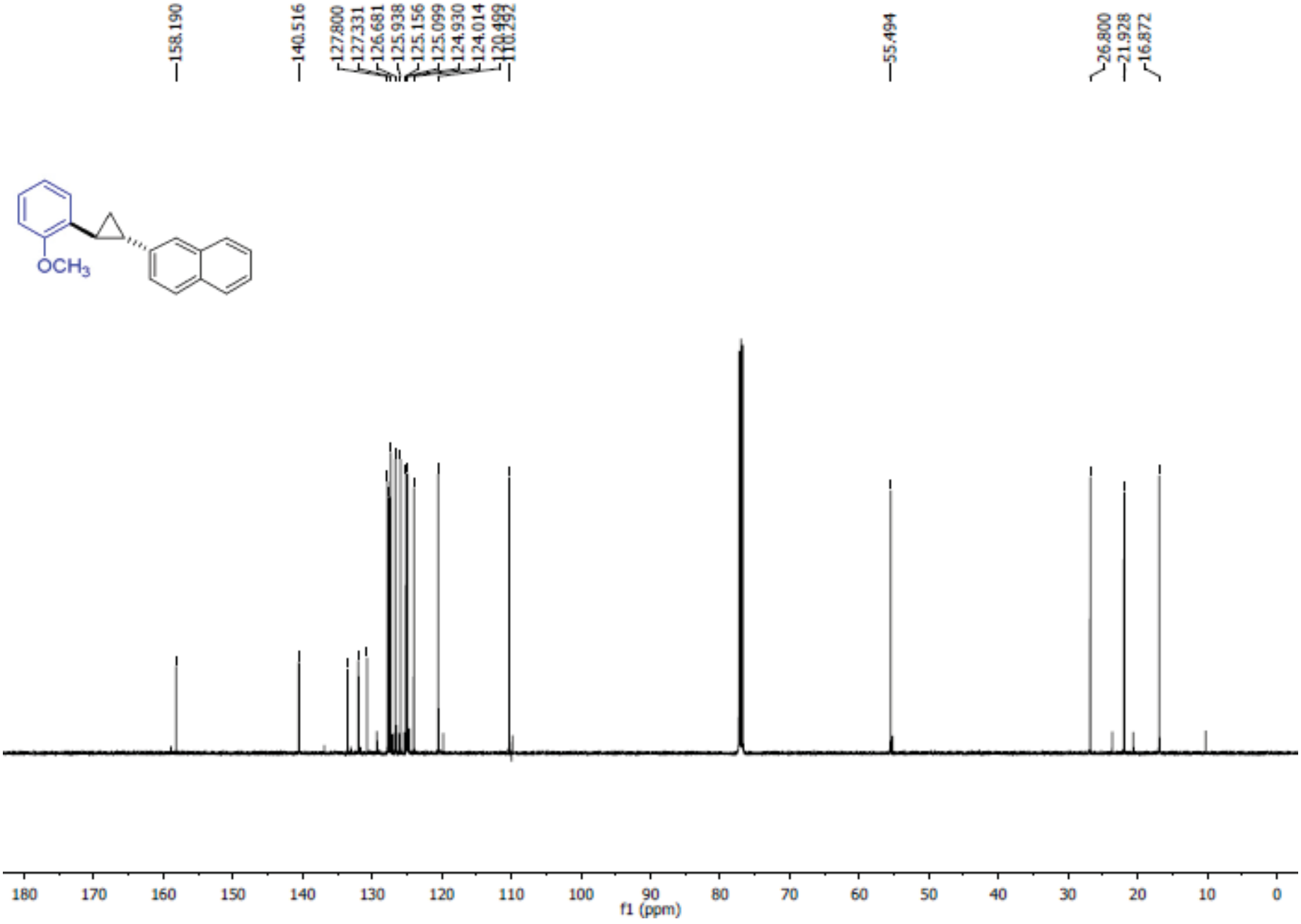
4: 290 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		33.440	98.554
2		41.820	1.446
Totals			100.000

2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)naphthalene **3bl**

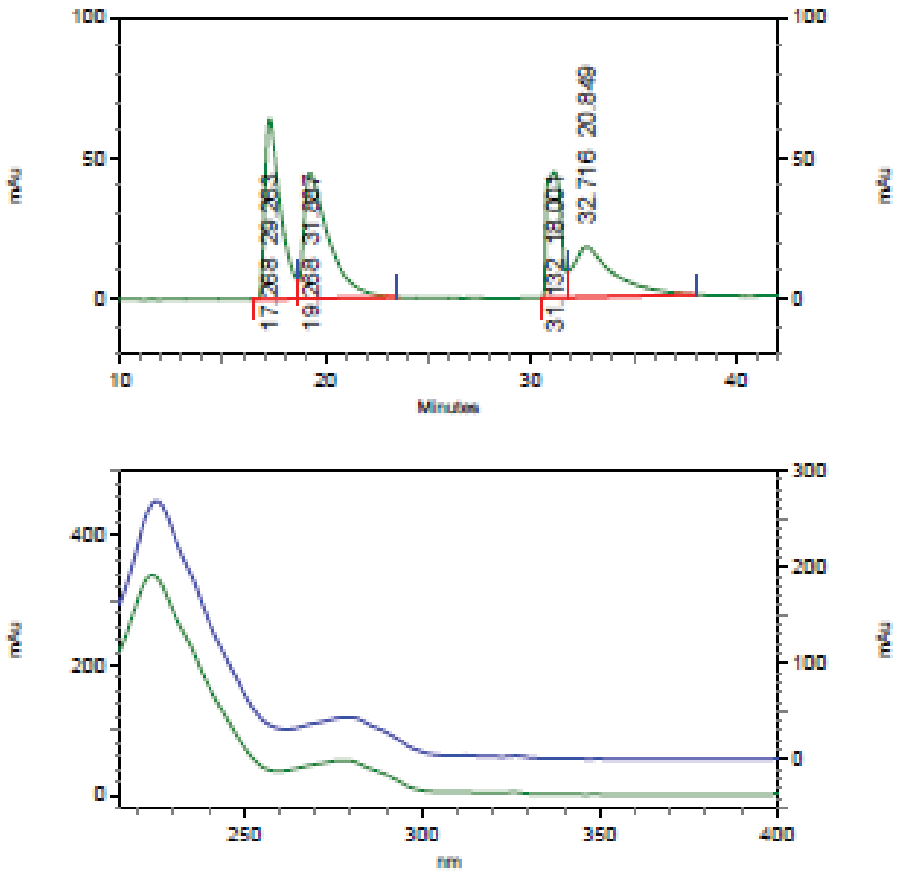


2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)naphthalene **3bl**



2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)naphthalene **3bl**

YW-II-22A-2 ADH 0@0.8 mL
C:\EZStart\Projects\Default\Method\lk-5@0.8.met
C:\EZStart\Projects\Default\Data\YW-II-22A-2 ADH 0@0.8 mL

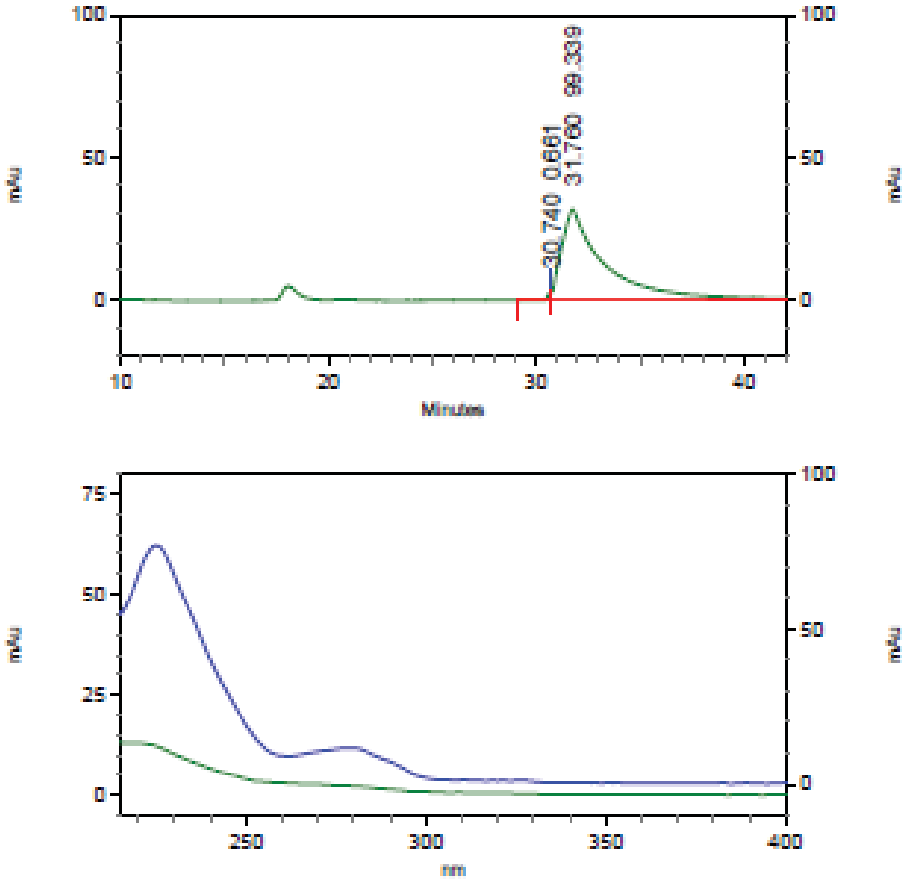


4: 268 nm, 4 nm
Results

Name	Retention Time	Area Percent	Pk #
	17.268	29.263	1
	19.268	31.887	2
	31.132	18.001	3
	32.716	20.849	4
Totals		100.000	

2-((1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropyl)naphthalene **3bl**

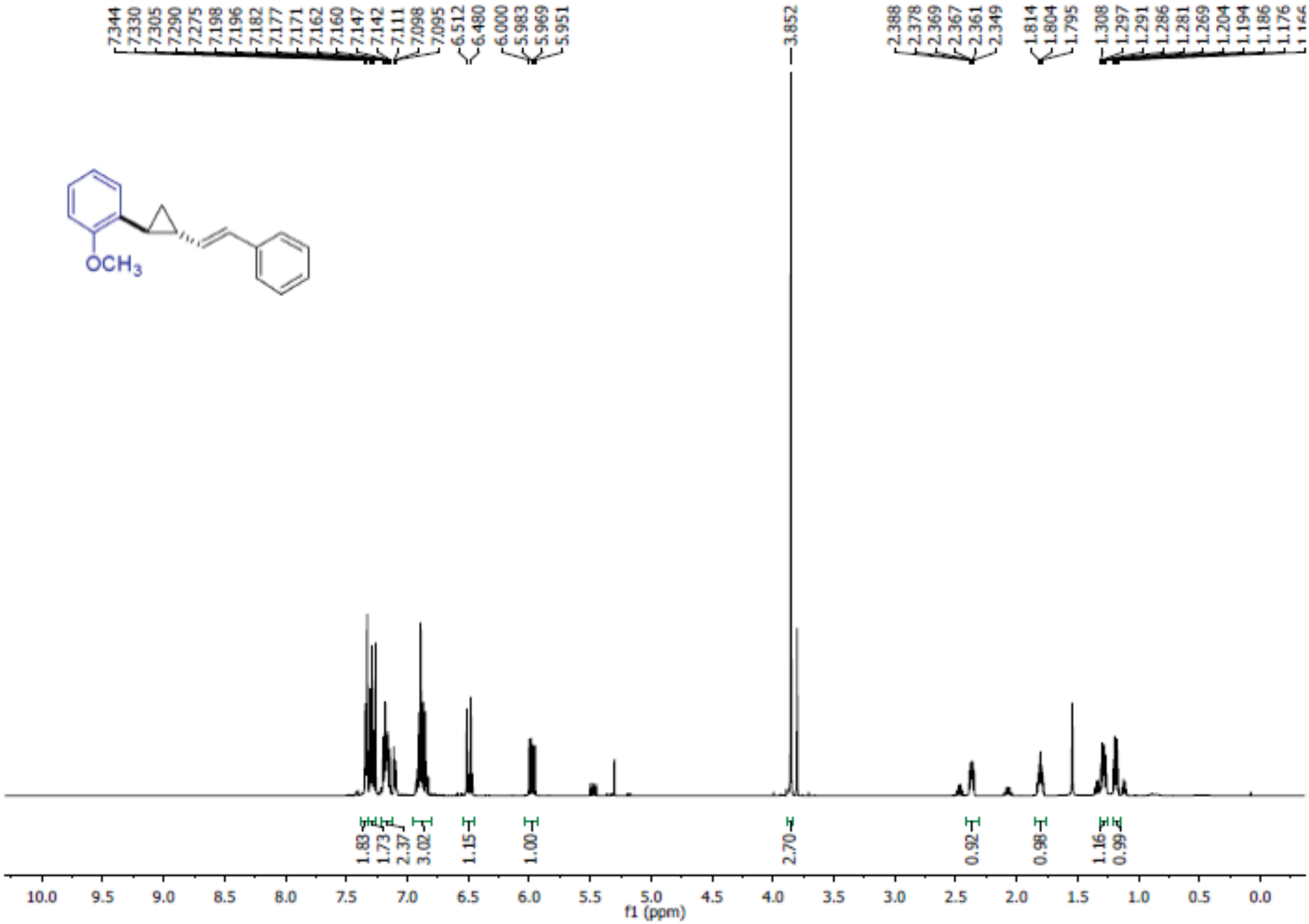
YW-II-22B-1 ADH 0%0.6 mL
C:\EZStart\Projects\Default\Method\lk-5%0.6.met
C:\EZStart\Projects\Default\Data\YW-II-22B-1 ADH 0%0.6 mL



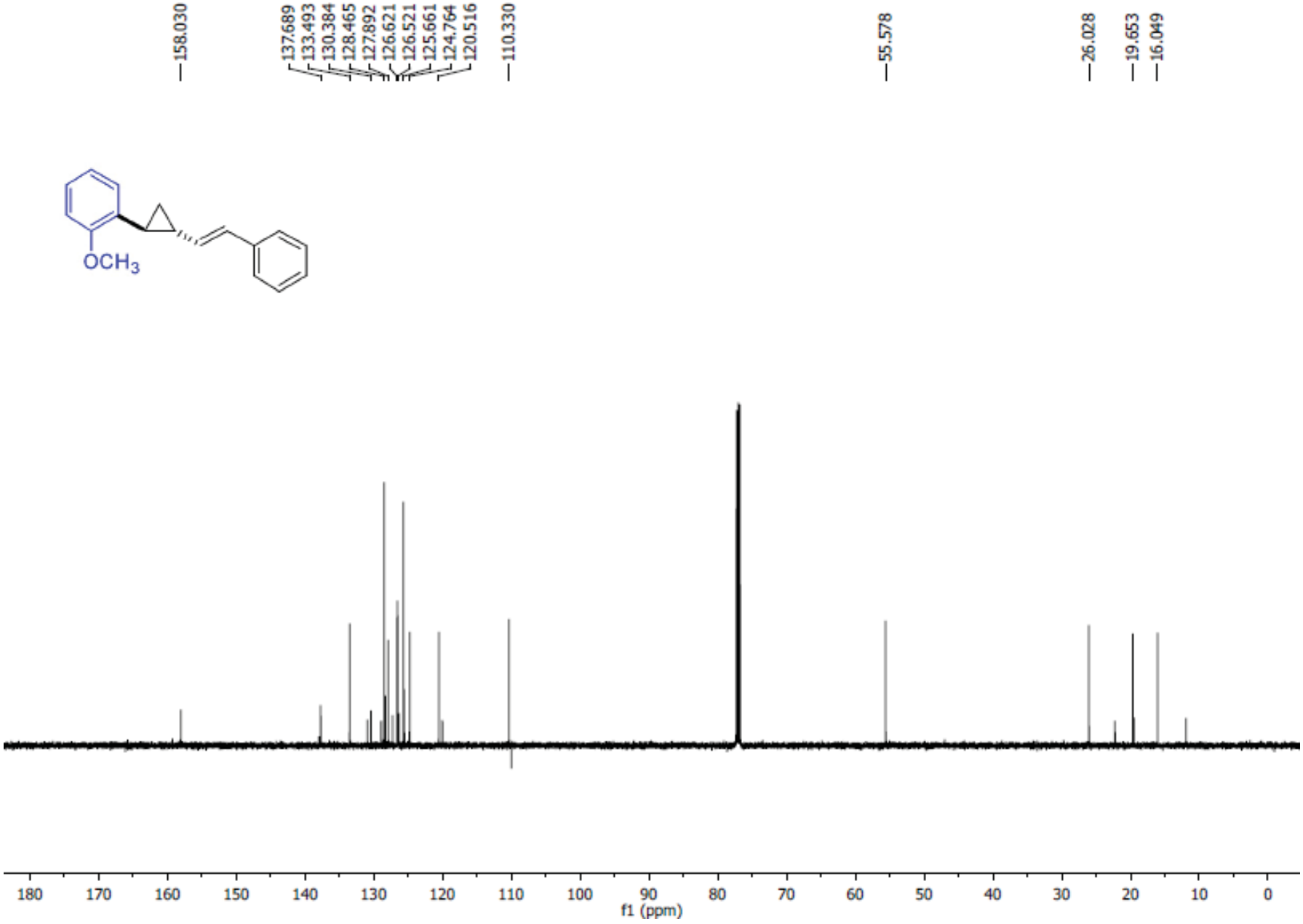
4: 267 nm, 4 nm
Results

Name	Retention Time	Area Percent	Pk #
	30.740	0.661	1
	31.760	99.339	2
Totals		100.000	

1-methoxy-2-((1*S*,2*R*)-2-((E)-styryl)cyclopropyl)benzene **3bm**

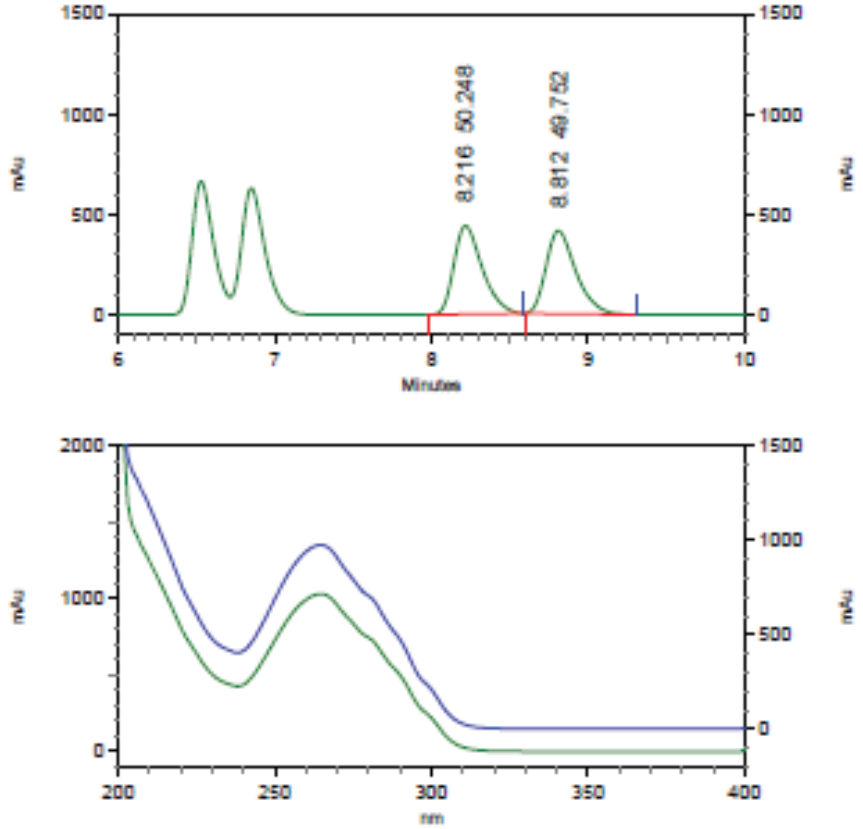


1-methoxy-2-((1*S*,2*R*)-2-((E)-styryl)cyclopropyl)benzene **3bm**



1-methoxy-2-((1*S*,2*R*)-2-((E)-styryl)cyclopropyl)benzene **3bm**

YW-II-56a-1 ODH 2@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-56a-1 ODH 2@0.8 mL

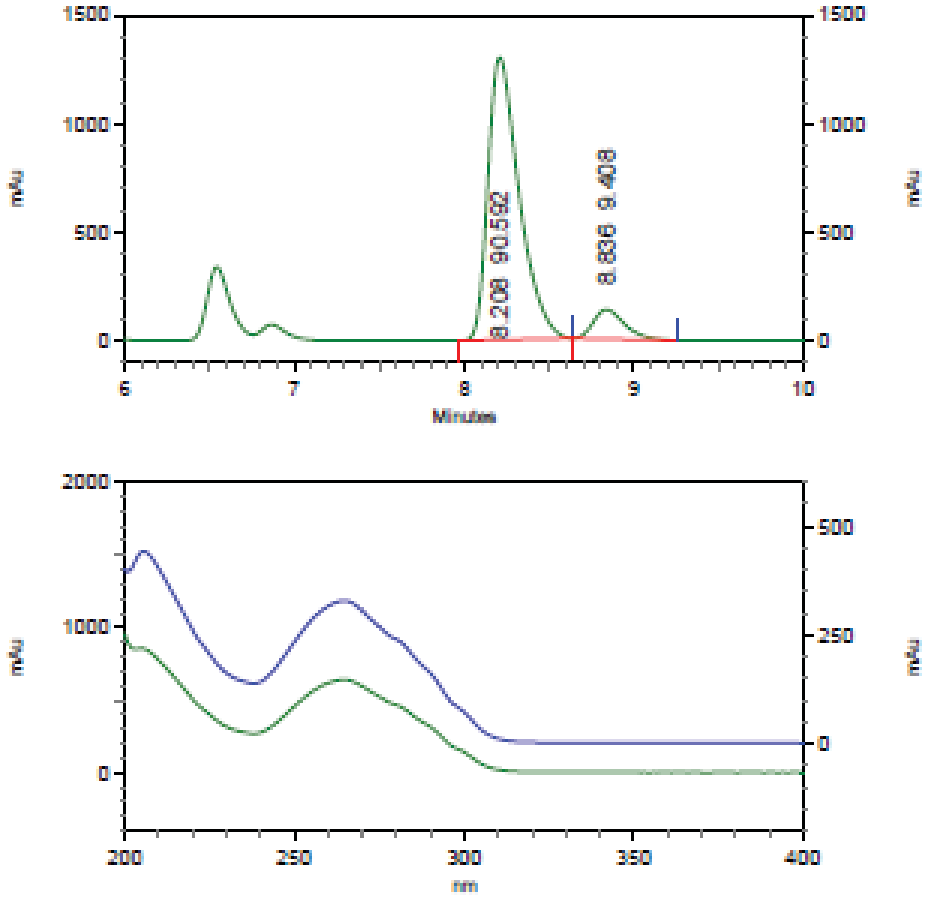


1: 240 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		8.216	50.248
2		8.812	49.752
Totals			100.000

1-methoxy-2-((1*S*,2*R*)-2-((E)-styryl)cyclopropyl)benzene **3bm**

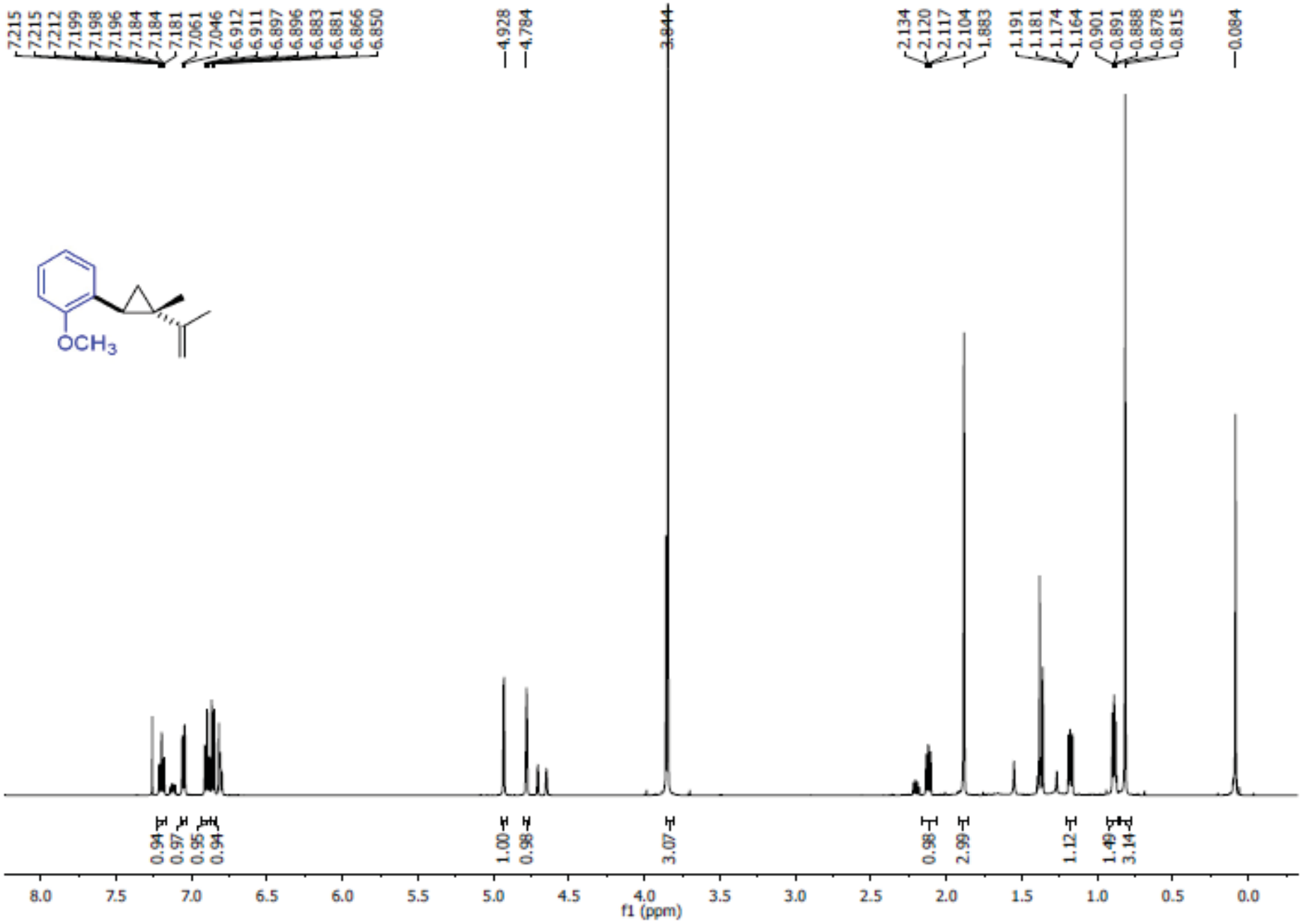
YW-II-56b2-1 ODH 2@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-56b2-1 ODH 2@0.8 mL



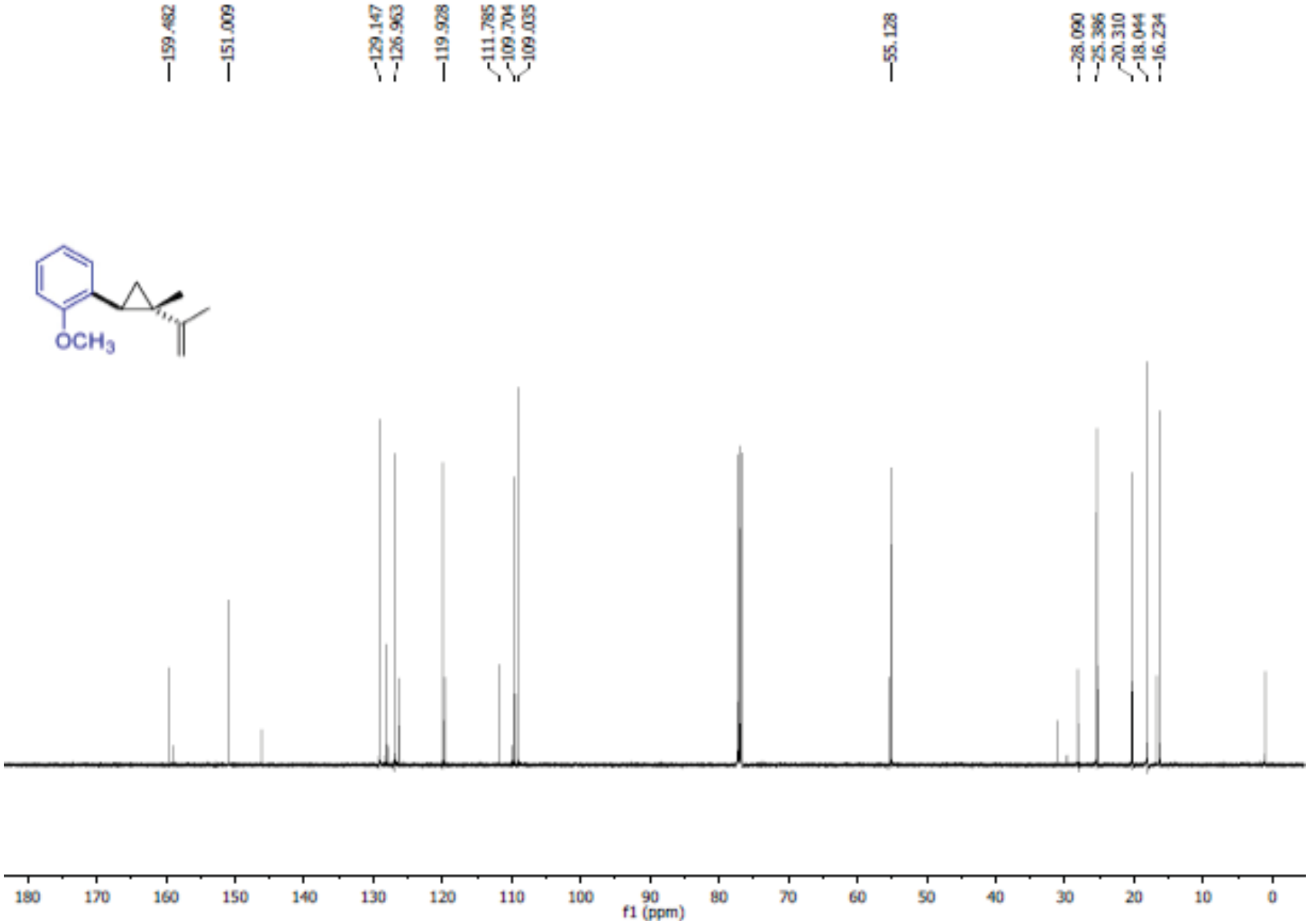
1: 240 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		8.208	90.592
2		8.836	9.408
Totals			100.000

1-methoxy-2-((1*S*,2*S*)-2-methyl-2-(prop-1-en-2-yl)cyclopropyl)benzene **3bn**

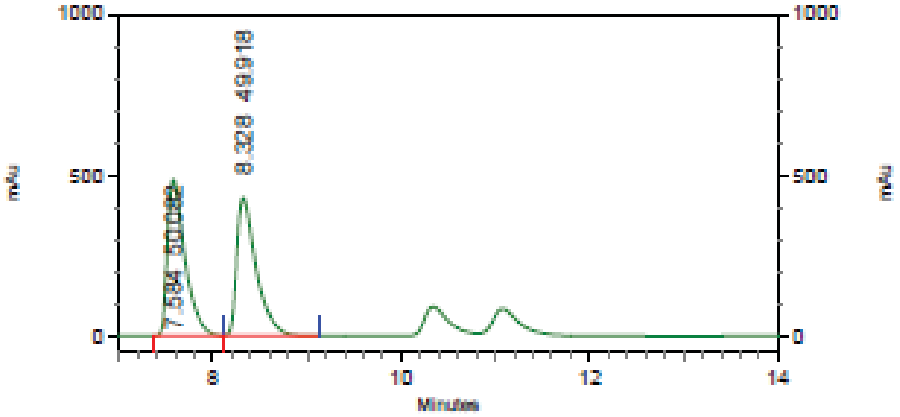


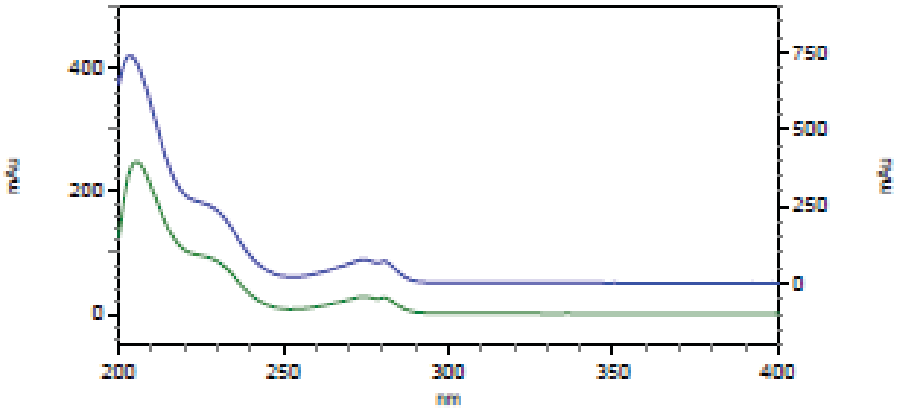
1-methoxy-2-((1*S*,2*S*)-2-methyl-2-(prop-1-en-2-yl)cyclopropyl)benzene **3bn**



1-methoxy-2-((1*S*,2*S*)-2-methyl-2-(prop-1-en-2-yl)cyclopropyl)benzene **3bn**

YW-I-298 ODH 0@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
E:\HPLC-YW-I\YW-I-298 ODH 0@0.8 mL



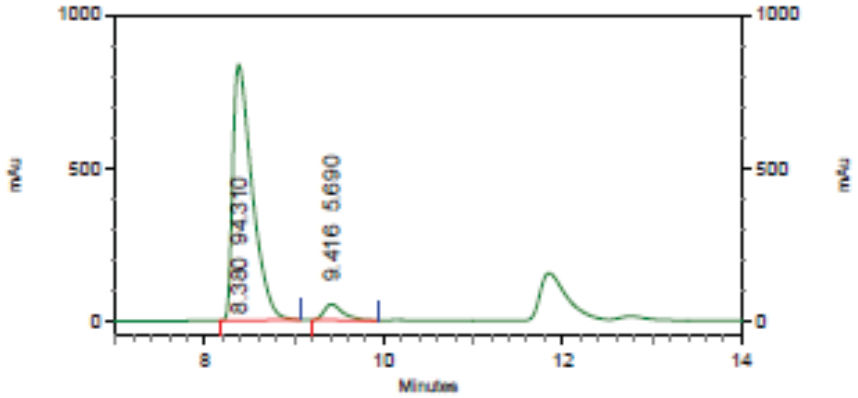


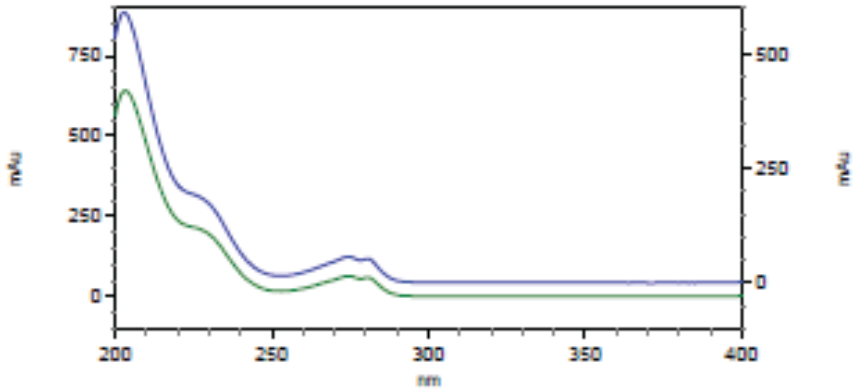
3: 273 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		7.584	50.082
2		8.328	49.918
Totals			100.000

1-methoxy-2-((1*S*,2*S*)-2-methyl-2-(prop-1-en-2-yl)cyclopropyl)benzene **3bn**

YW-II-3 ODH 0@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-3 ODH 0@0.8 mL

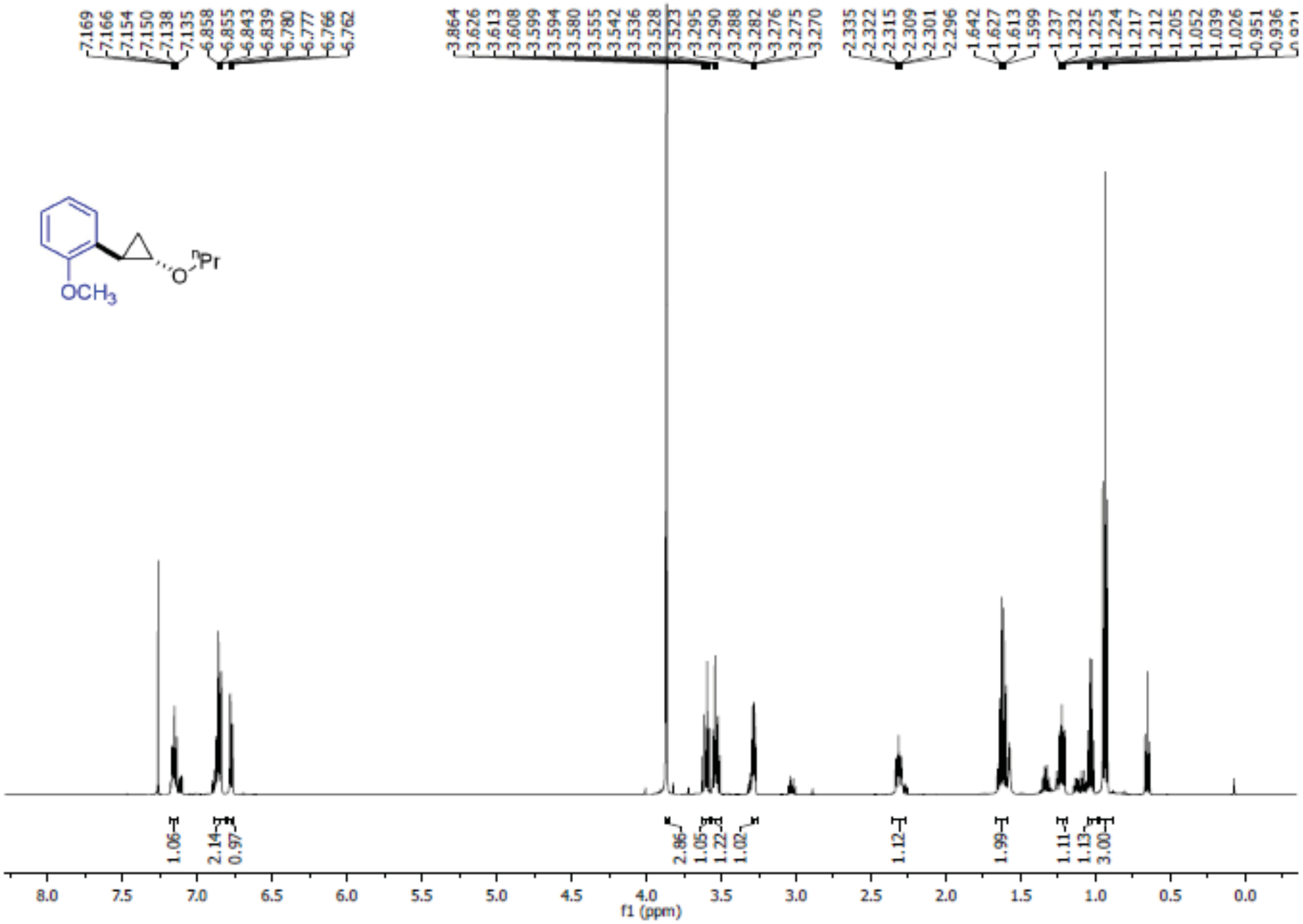




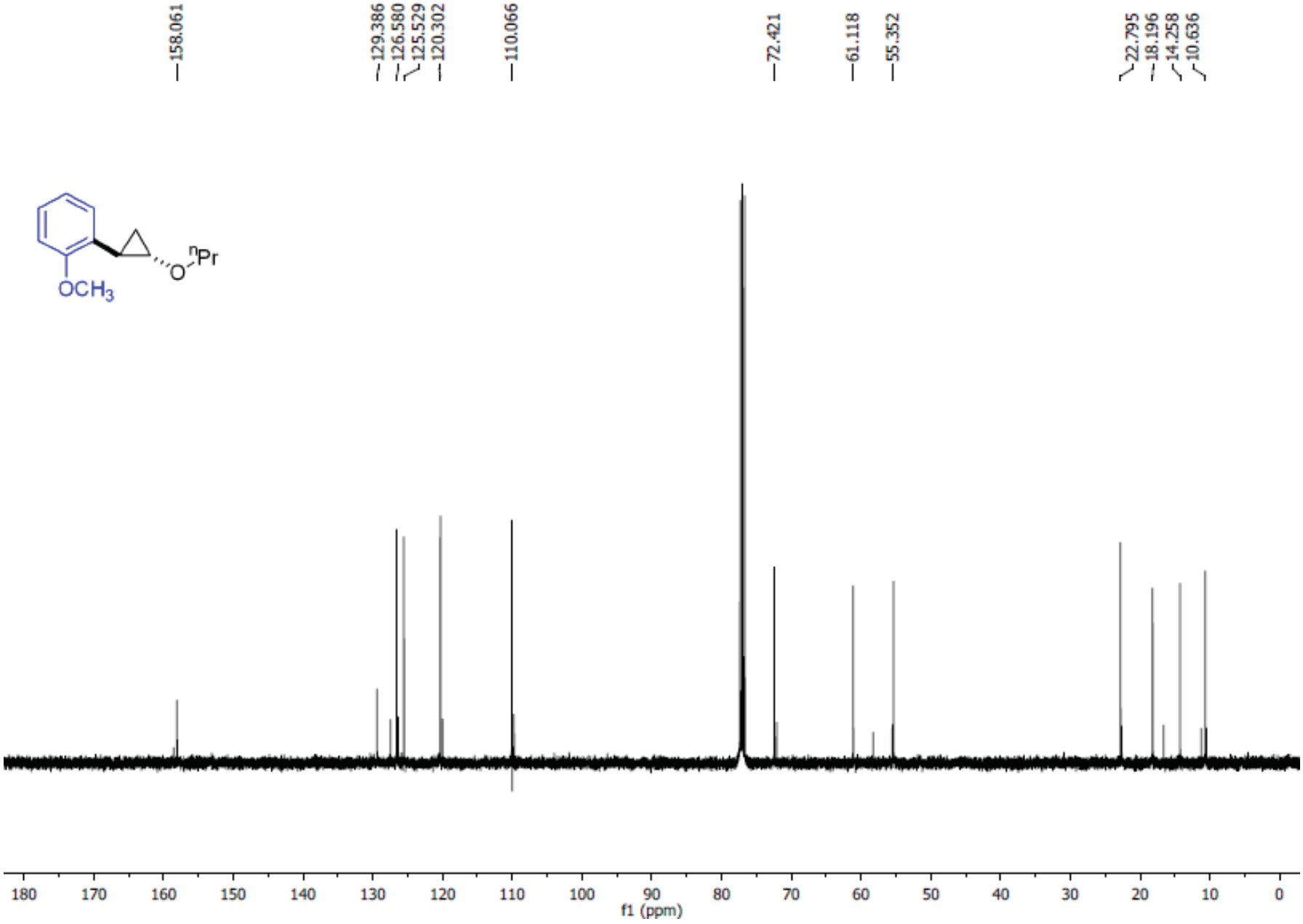
3: 273 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		8.380	94.310
2		9.416	5.690
Totals			100.000

1-methoxy-2-((1*R*,2*S*)-2-propoxycyclopropyl)benzene **3bo**

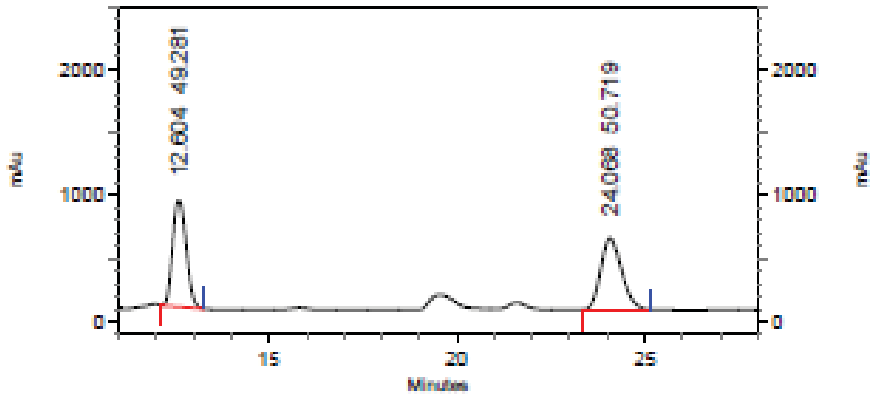


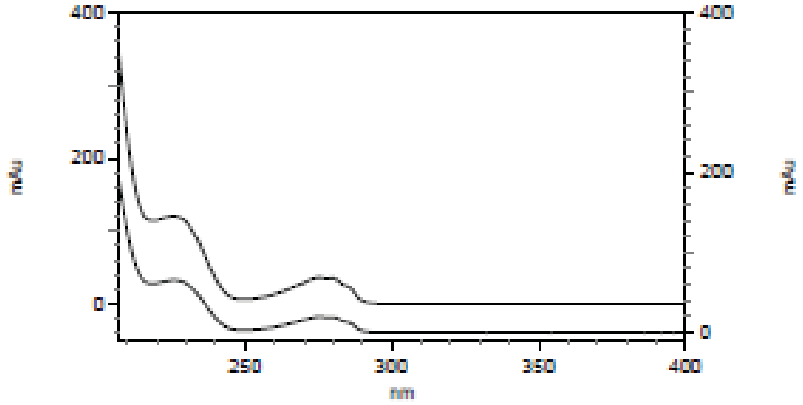
1-methoxy-2-((1*R*,2*S*)-2-propoxycyclopropyl)benzene **3bo**



1-methoxy-2-((1*R*,2*S*)-2-propoxycyclopropyl)benzene **3bo**

YW-II-243A ODH-3 1% 0.8mL
C:\EZStart\Projects\Default\Method\ywang1.met
C:\EZStart\Projects\Default\Data\YW-II-243A ODH-3 1% 0.8mL



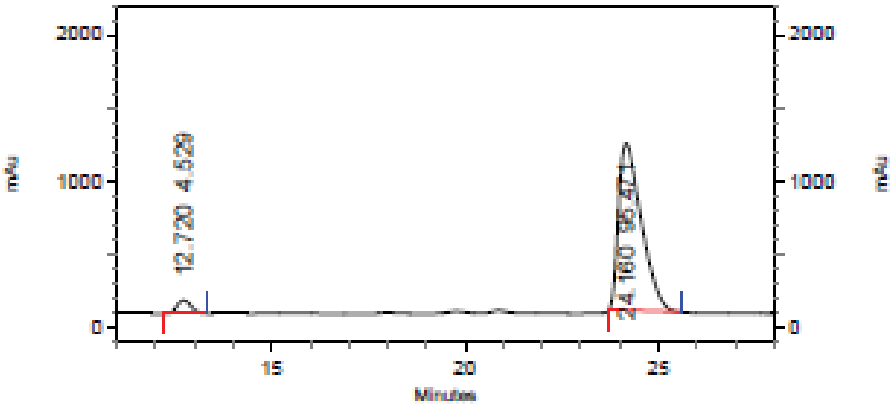


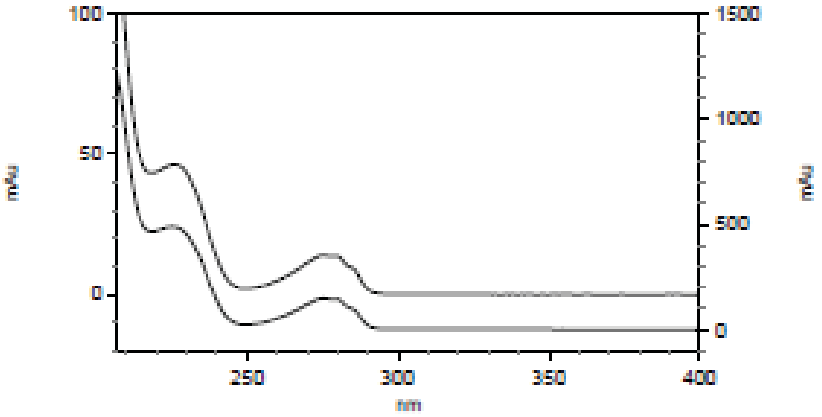
2: 236 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		12.604	49.281
2		24.068	50.719
Totals			100.000

1-methoxy-2-((1*R*,2*S*)-2-propoxycyclopropyl)benzene **3bo**

YW-I-287 ODH-4 1@ 0.8mL
C:\EZStart\Projects\Default\Method\ywangl.met
C:\EZStart\Projects\Default\Data\YW-I-287 ODH-4 1@ 0.8mL

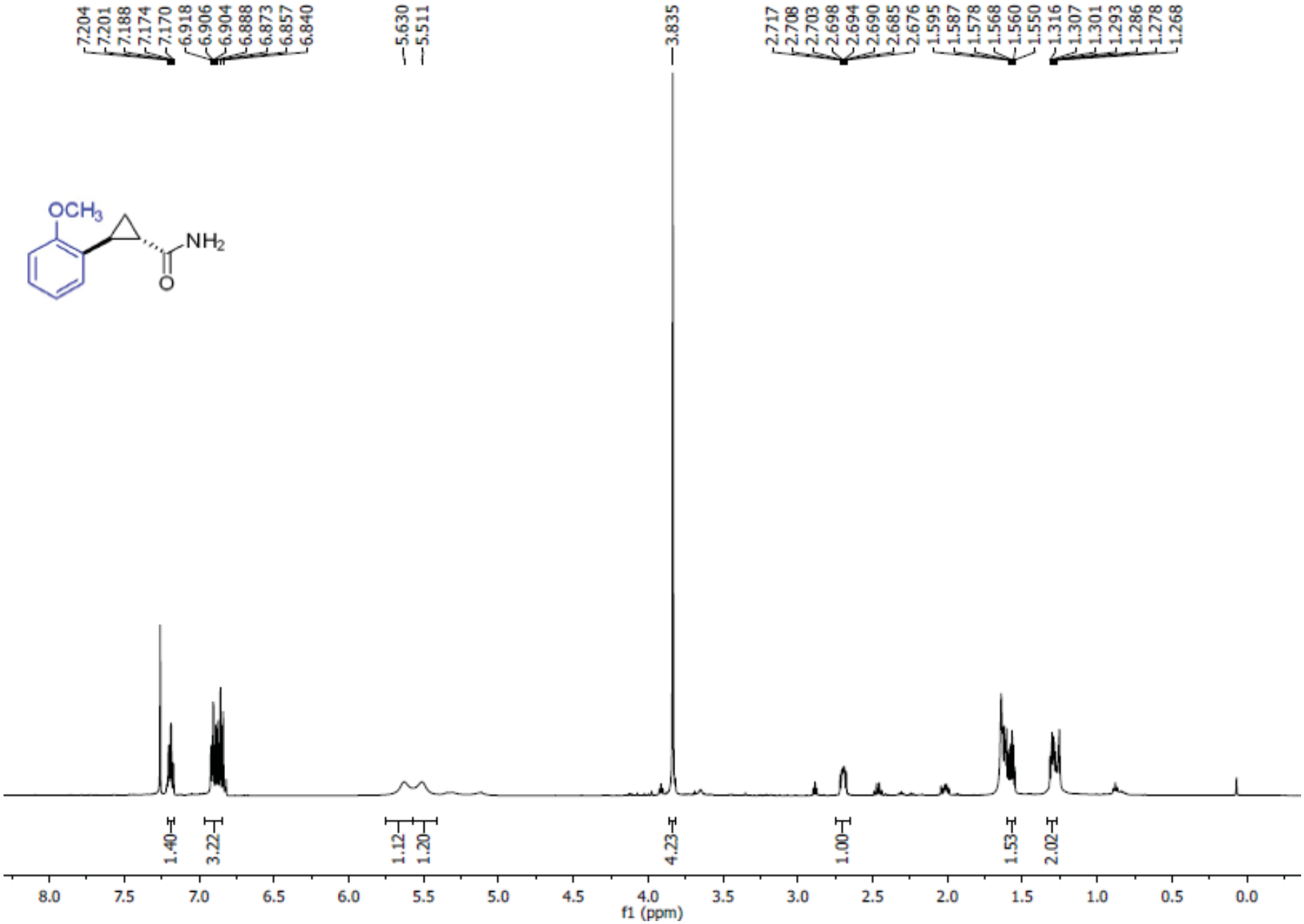




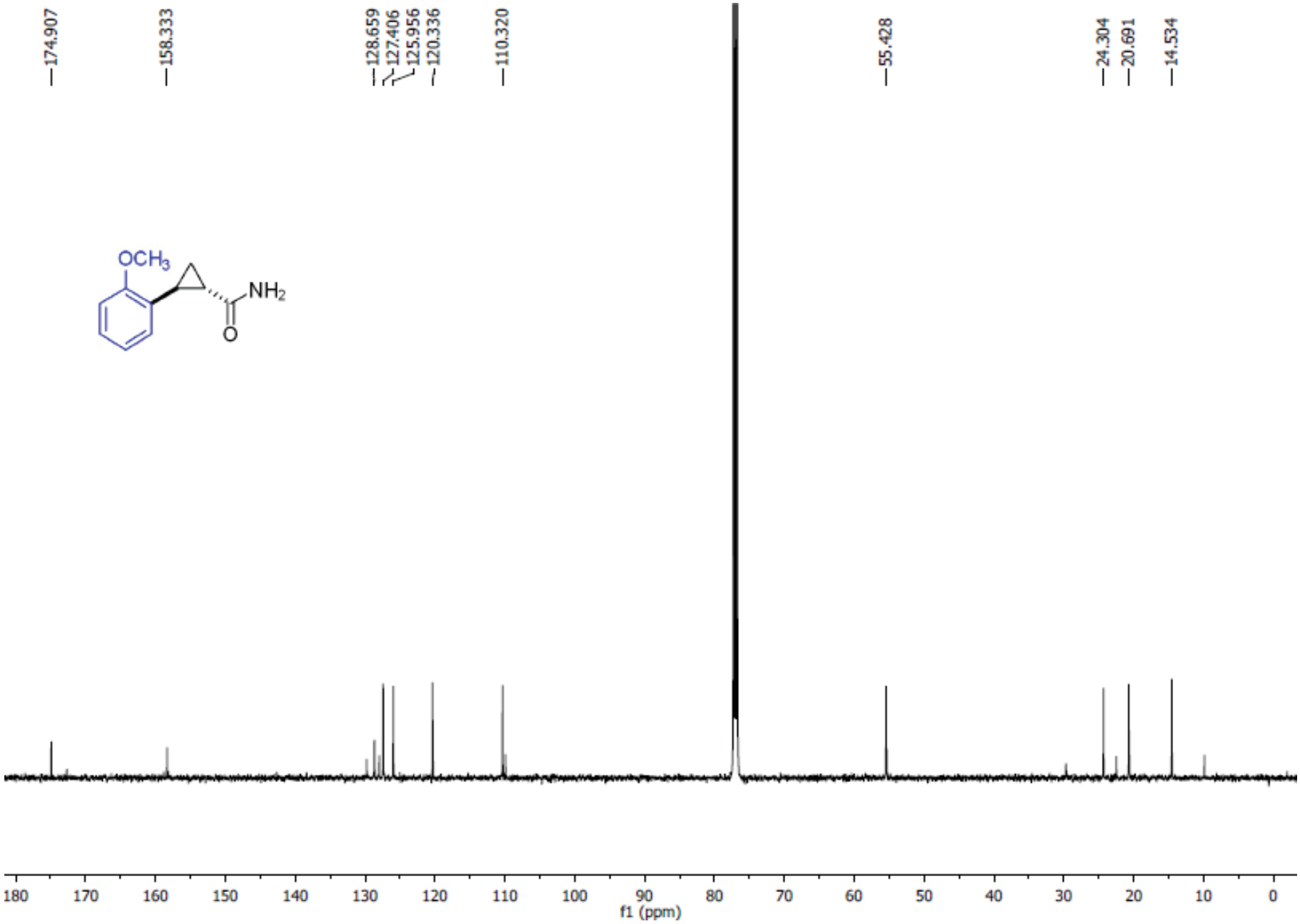
2: 264 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		12.720	4.529
2		24.160	95.471
Totals			100.000

(1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropane-1-carboxamide **3bp**

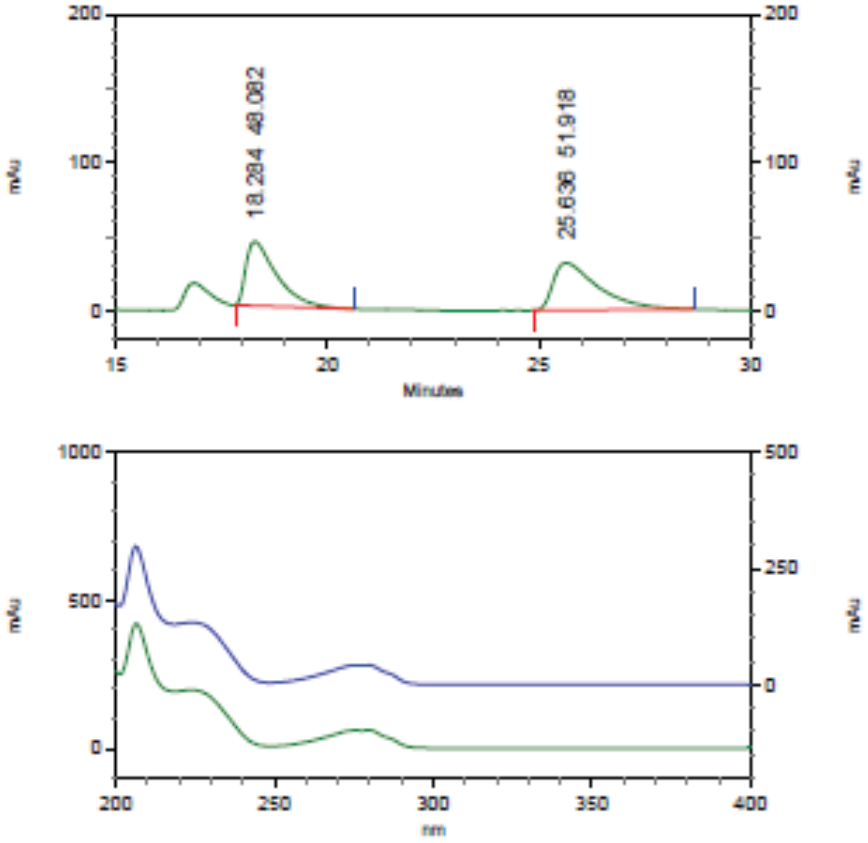


(1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropane-1-carboxamide **3bp**



(1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropane-1-carboxamide **3bp**

YW-II-38 OJH-1 10@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-38 OJH-1 10@0.8 mL

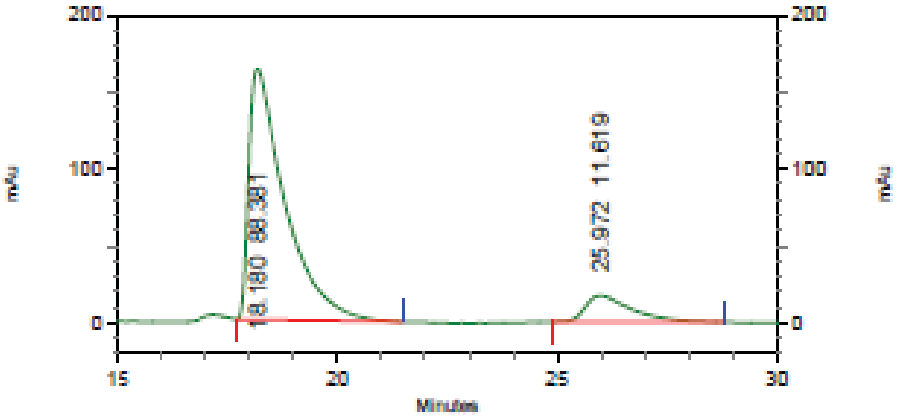


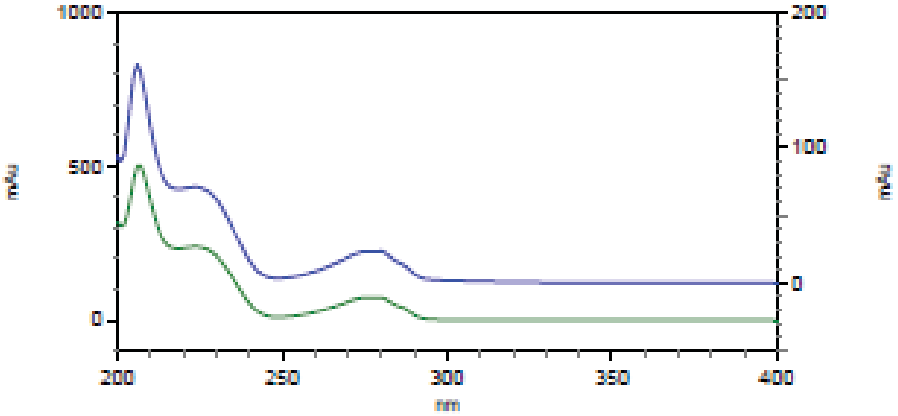
1: 240 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		18.284	48.082
2		25.636	51.918
Totals			100.000

(1*S*,2*S*)-2-(2-methoxyphenyl)cyclopropane-1-carboxamide **3bp**

YW-II-49 OJH 10@0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\YW-II-49 OJH 10@0.8 mL

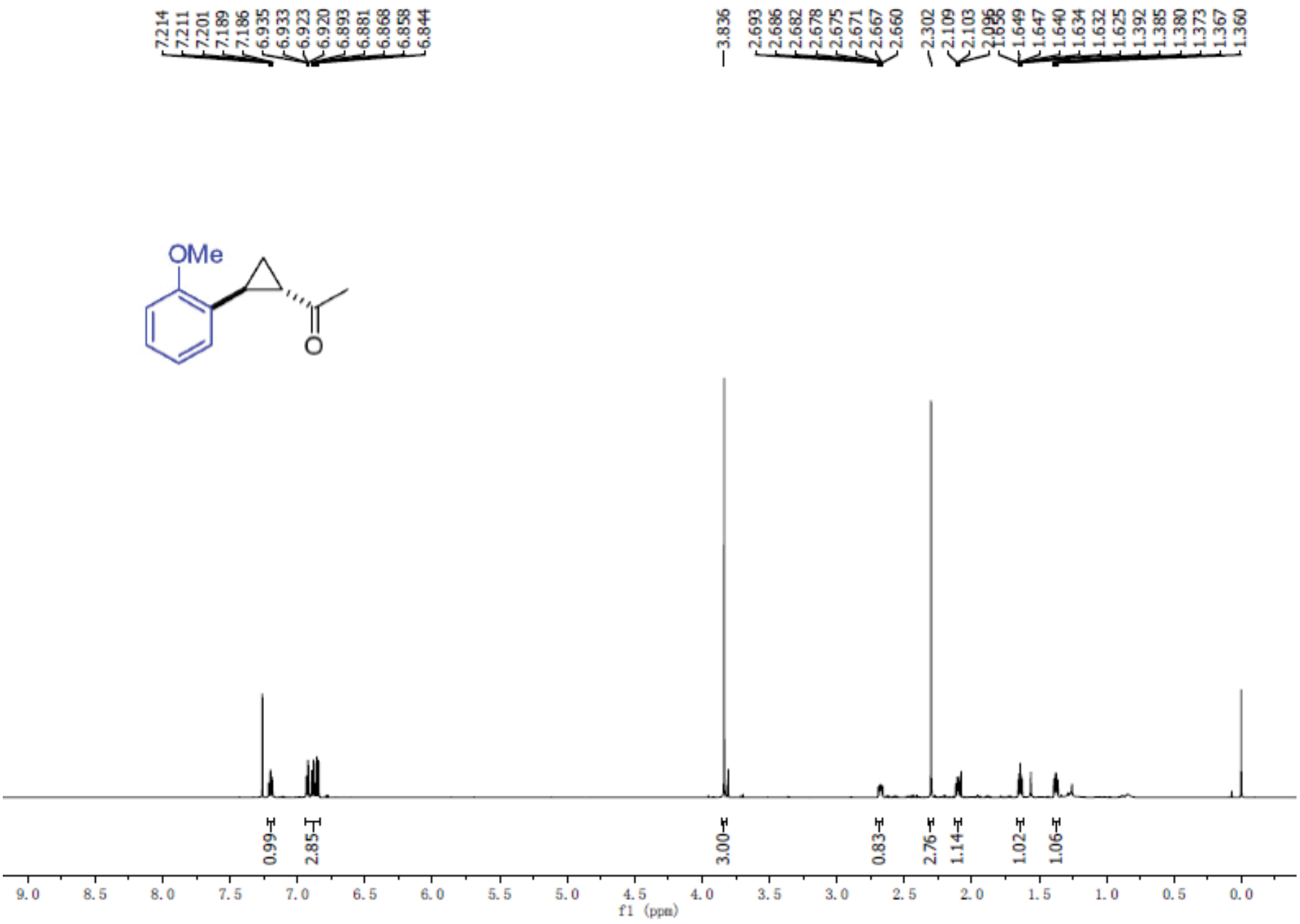




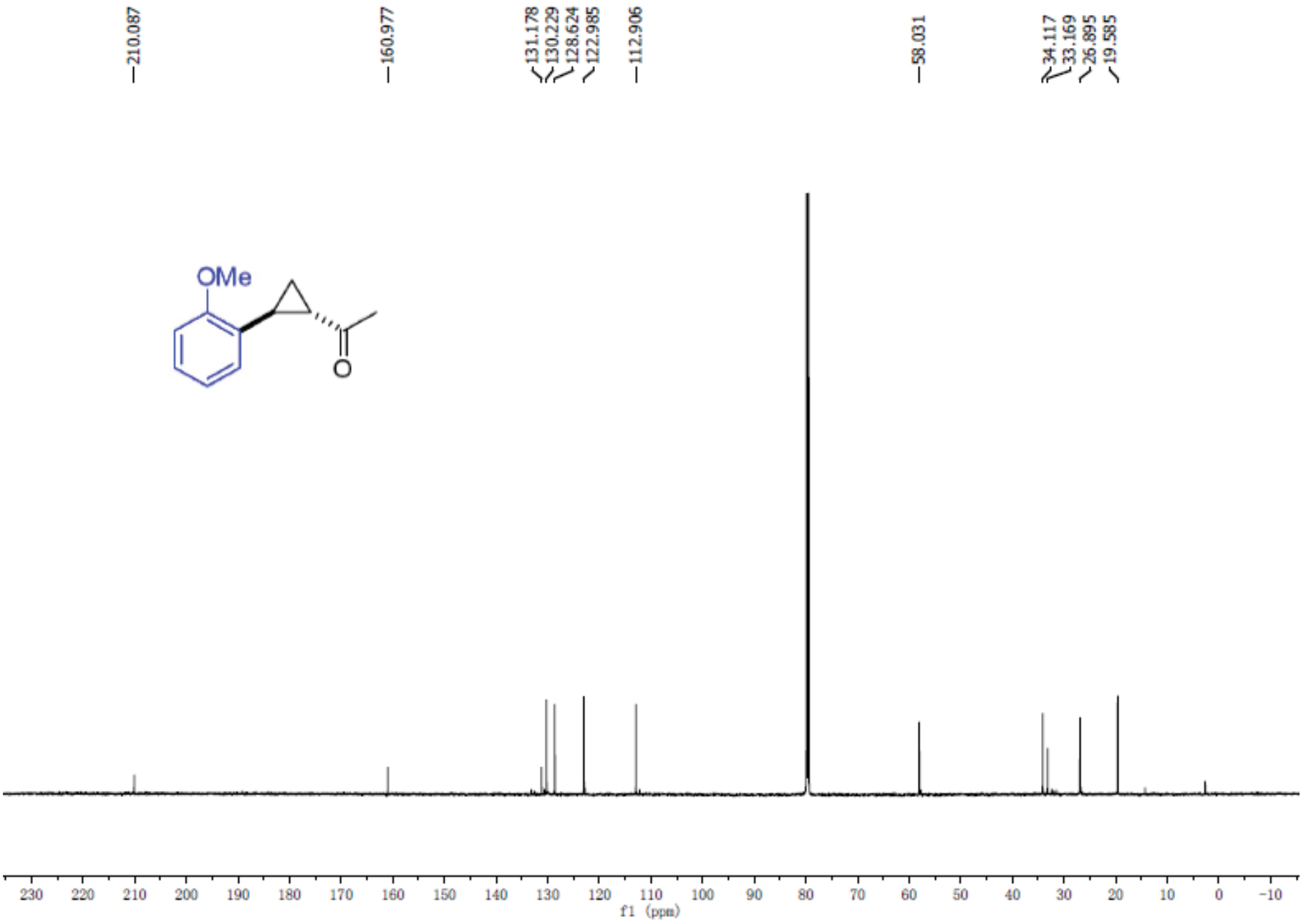
1: 240 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		18.180	88.381
2		25.972	11.619
Totals			100.000

(1S,2S)-2-(2-methoxyphenyl)cyclopropyl)ethan-1-one **3bq**



(1S,2S)-2-(2-methoxyphenyl)cyclopropyl)ethan-1-one **3bq**

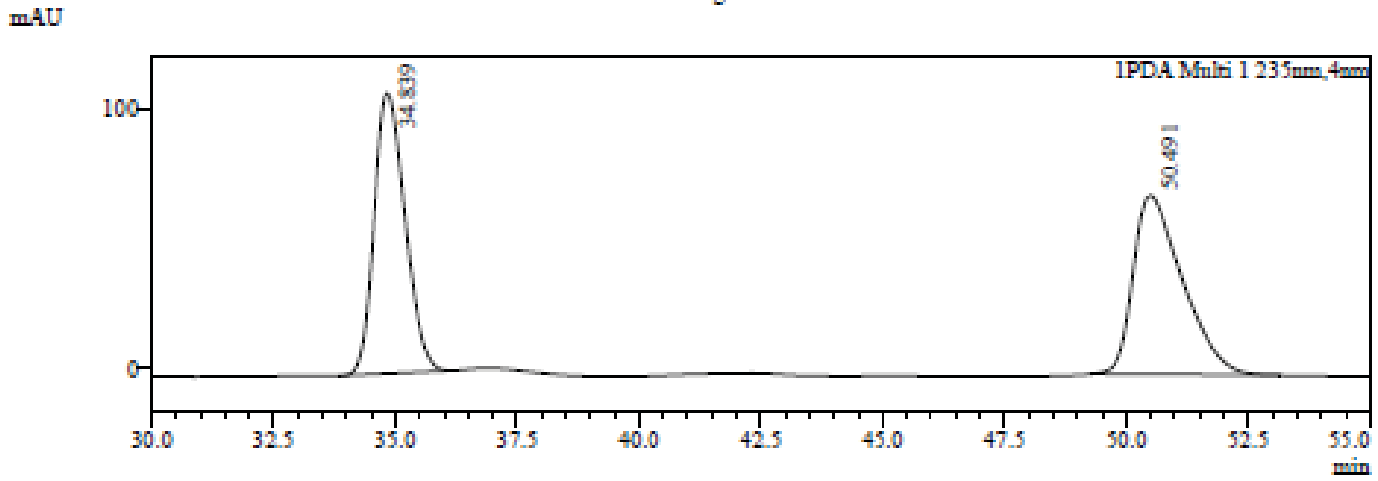


(1S,2S)-2-(2-methoxyphenyl)cyclopropyl)ethan-1-one **3bq**

Sample Information

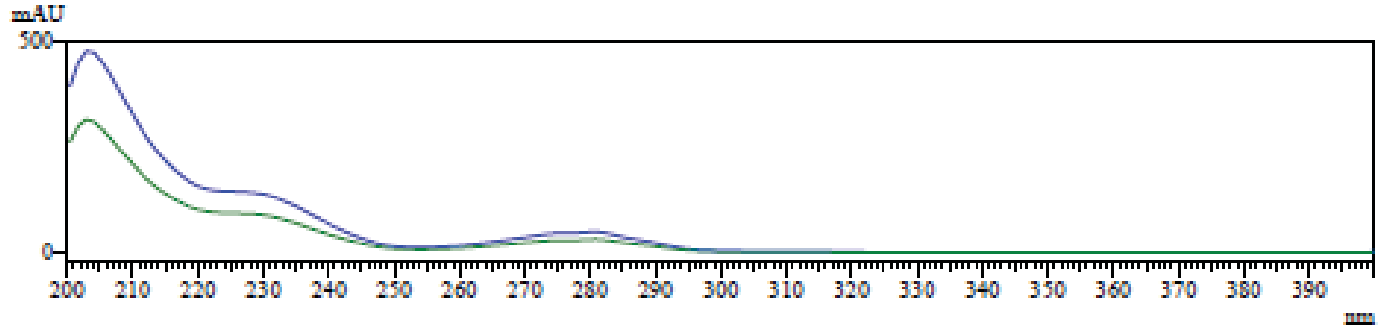
Sample Name	: Y0W-0125-IC-0.5%-1.0ML-isopropanol-solvent12172016
Sample ID	: Y0W-0125-IC-0.5%-1.0ML-isopropa
Data File	: Y0W-0125-IC-0.5%-1.0ML2.lcd
Method File	: YW-0.5%-1.0ml.lcm
Date Acquired	: 12/19/2016 11:51:56 PM

Chromatogram



UV Spectrum

Y0W-0125-IC-0.5%-1.0ML2.lcd



Peak Table

PDA Ch1 235nm

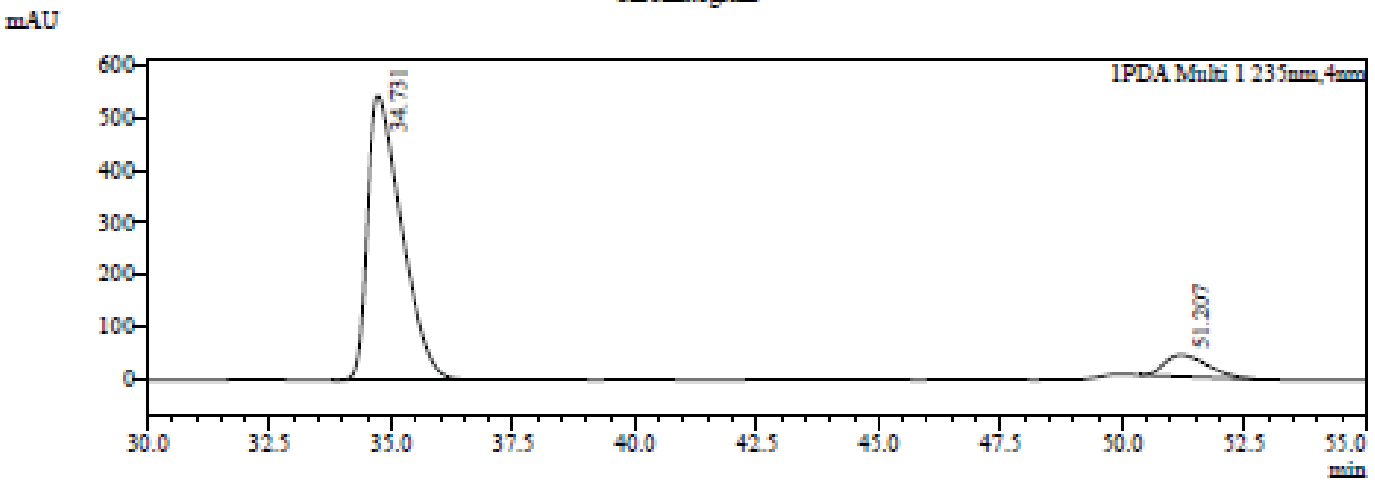
Peak#	Ret. Time	Area	Area%
1	34.839	4766800	49.659
2	50.491	4832228	50.341
Total		9599028	100.000

(1S,2S)-2-(2-methoxyphenyl)cyclopropyl)ethan-1-one **3bq**

Sample Information

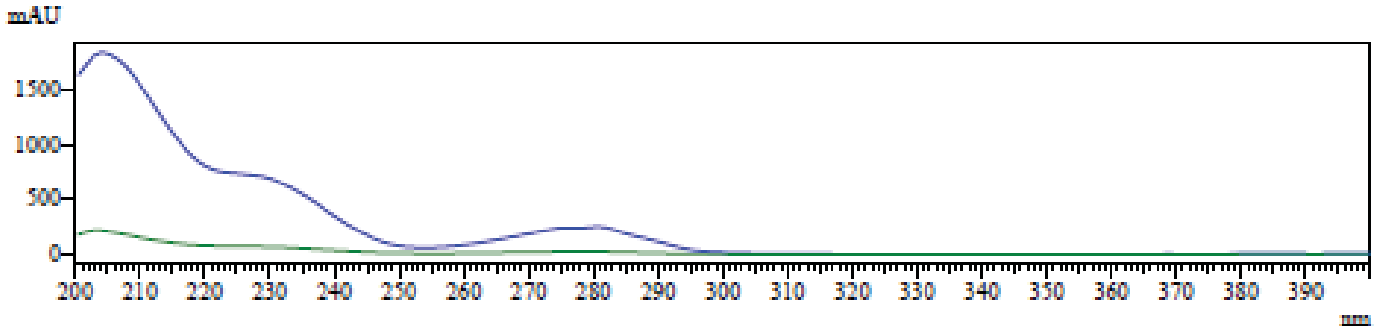
Sample Name	: Y0W-0126-IC-0.5%-1.0ML-isopropanol-solvent12172016
Sample ID	: Y0W-0126-IC-0.5%-1.0ML-isopropa
Data File	: Y0W-0126-IC-0.5%-1.0ML.lcd
Method File	: YW-0.5%-1.0ml.lcm
Date Acquired	: 12/19/2016 10:40:50 PM

Chromatogram



UV Spectrum

Y0W-0126-IC-0.5%-1.0ML.lcd

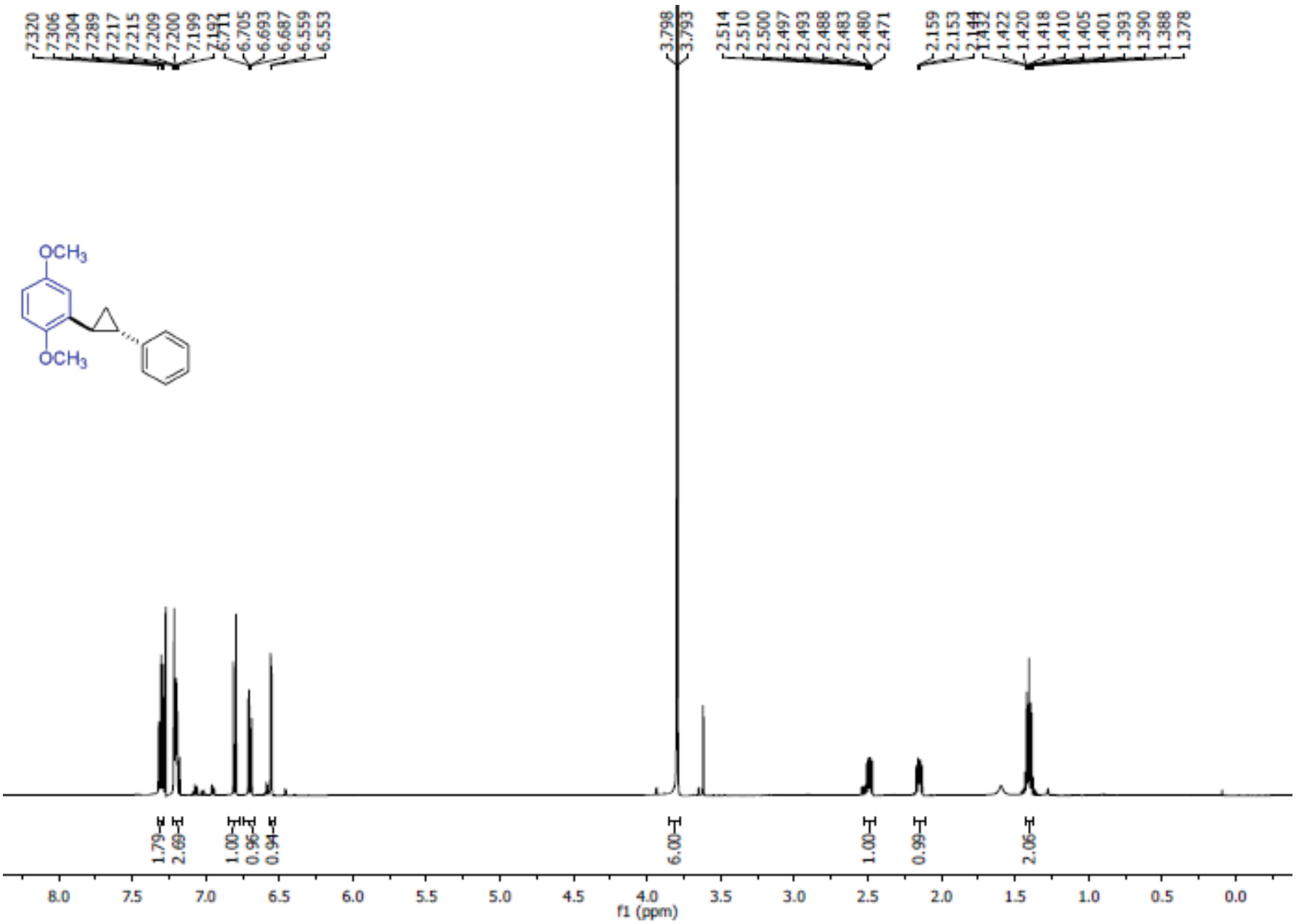


Peak Table

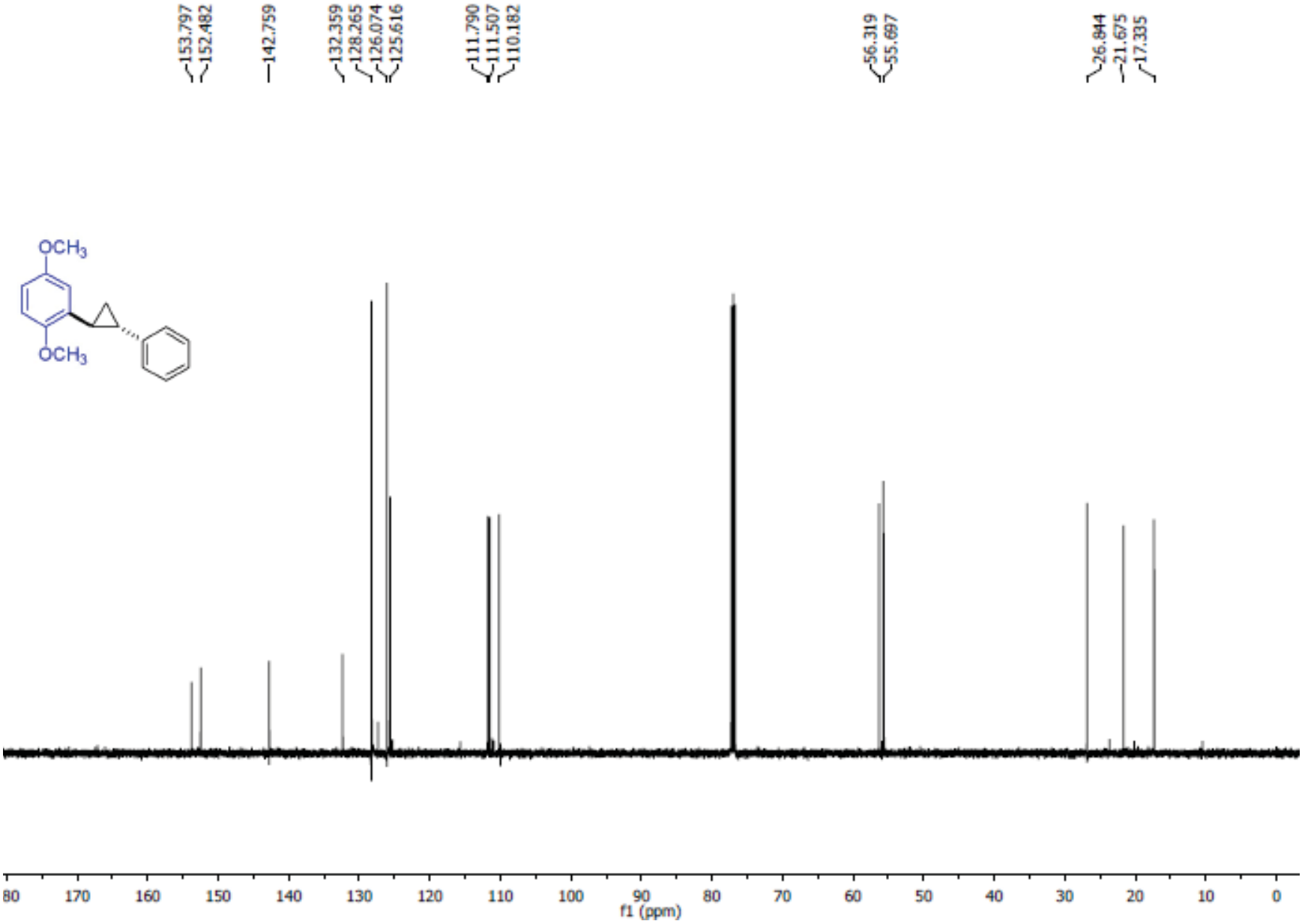
PDA Ch1 235nm

Peak#	Ret. Time	Area	Area%
1	34.731	26683140	91.077
2	51.207	2614272	8.923
Total		29297412	100.000

1,4-dimethoxy-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3fa**

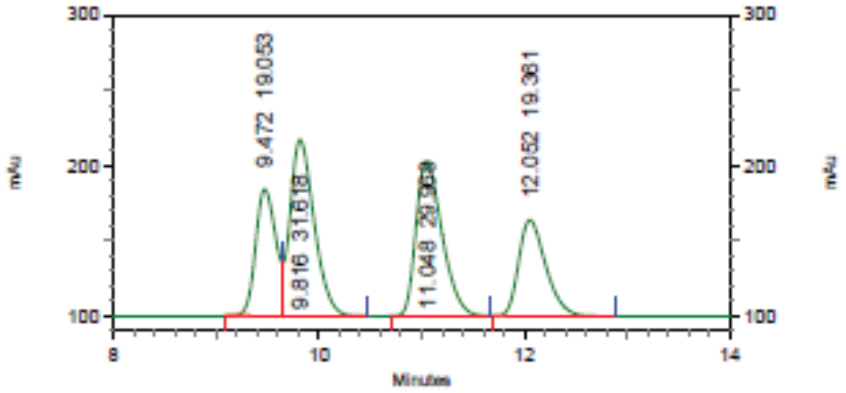


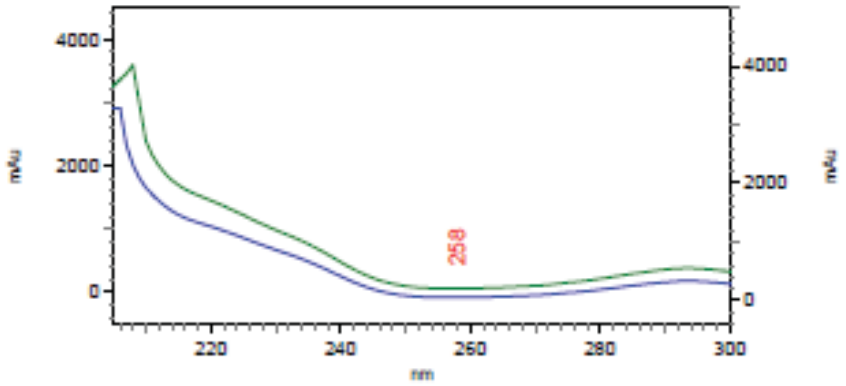
1,4-dimethoxy-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3fa**



1,4-dimethoxy-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3fa**

YW-I-213-2 ODH-2 1@0.8 mL
C:\EZStart\Projects\Default\Method\LSP-OD-H-1.0@-0.8ML.met
E:\HPLC-YW-I\YW-I-213-2 ODH-2 1@0.8 mL





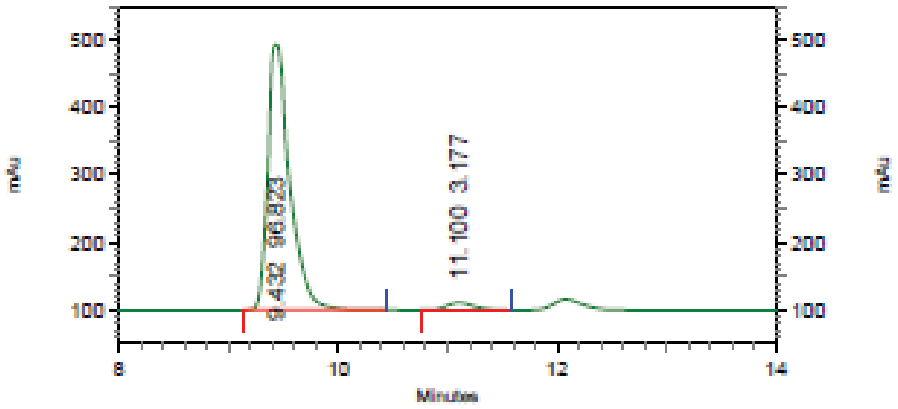
5: 226 nm, 4 nm
Results

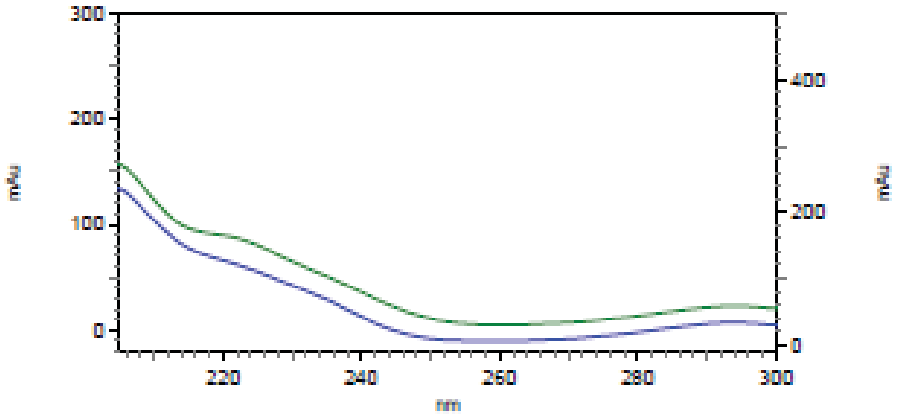
Pk #	Name	Retention Time	Area Percent
1		9.472	19.053
2		9.816	31.618
3		11.048	29.968
4		12.052	19.361
Totals			100.000

1,4-dimethoxy-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3fa**

estimated ee

YW-I-219-2 ODH 1@0.8 mL
C:\EZStart\Projects\Default\Method\LSP-OD-H-1.0@-0.8ML.met
E:\HPLC-YW-I\YW-I-219-2 ODH 1@0.8 mL

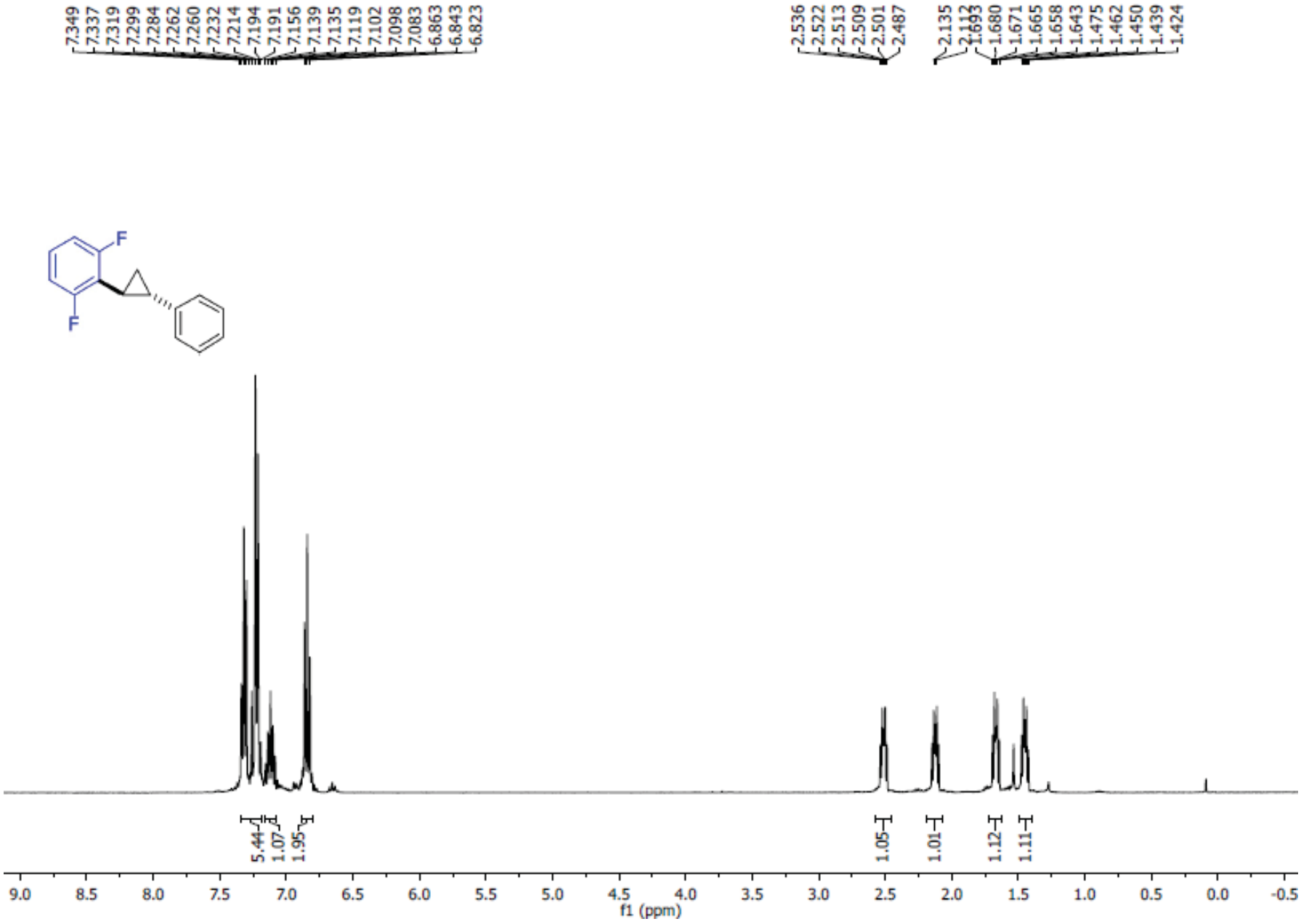




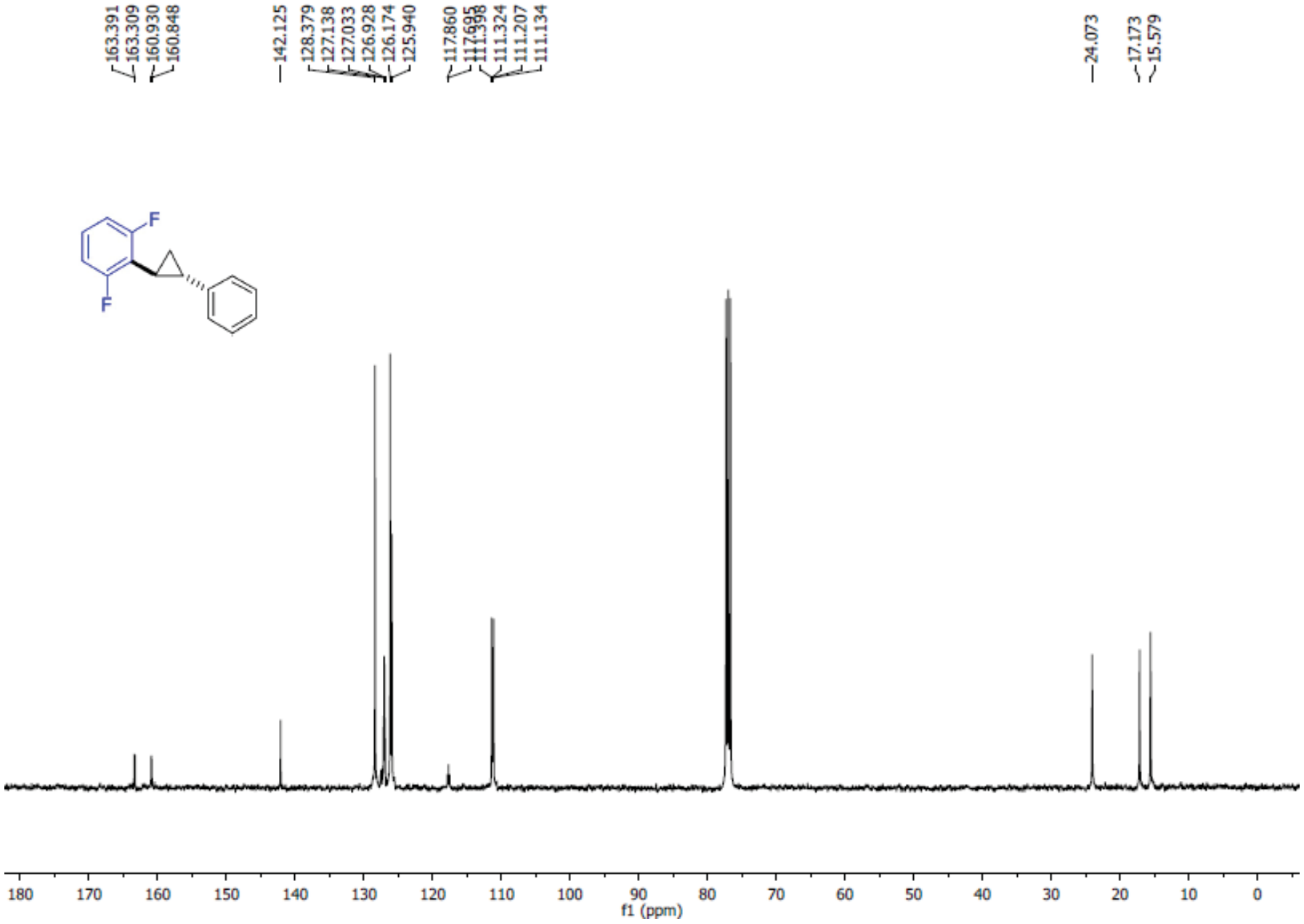
5: 225 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		9.432	96.823
2		11.100	3.177
Totals			100.000

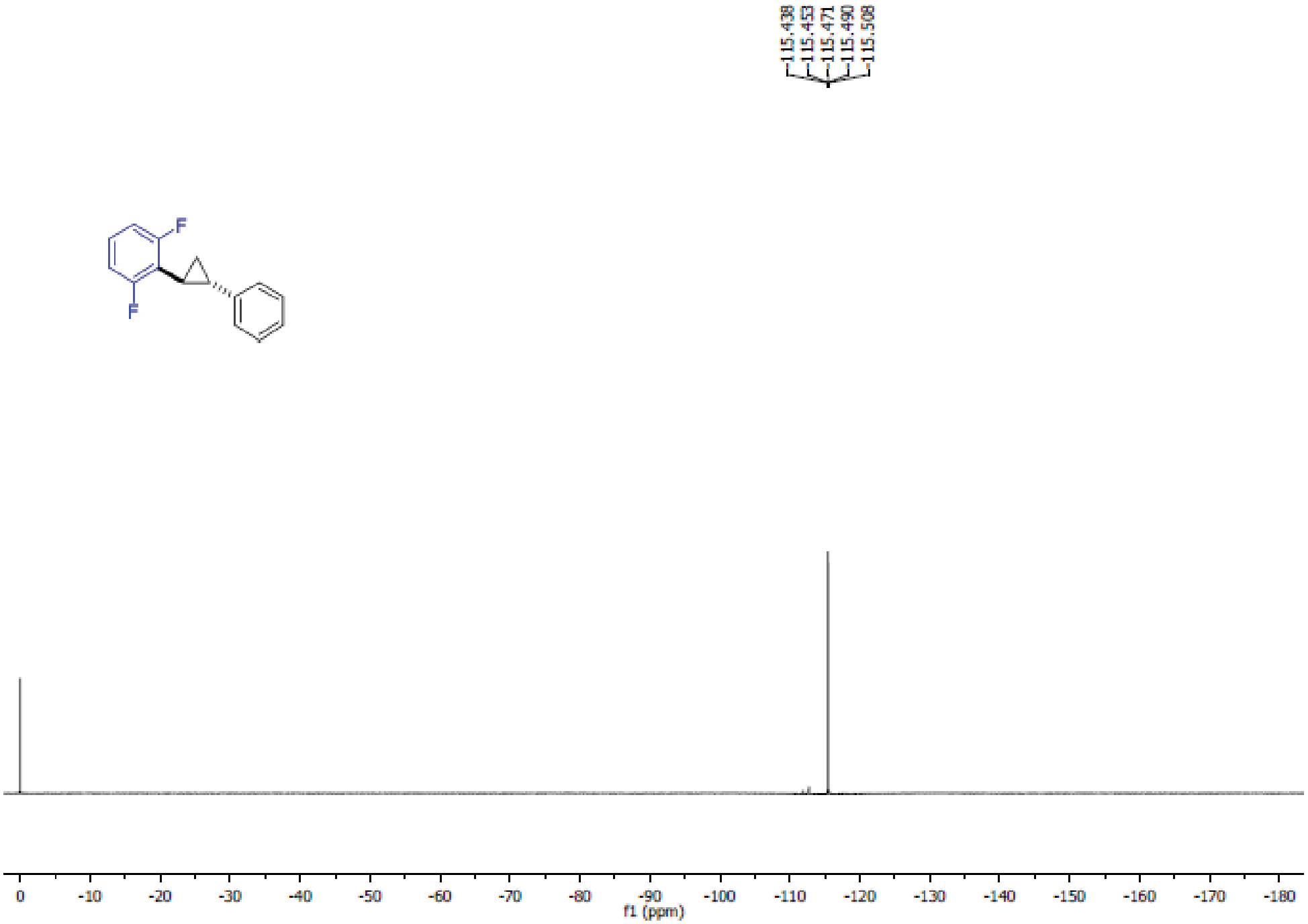
1,3-difluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3g'a**



1,3-difluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3g'a**

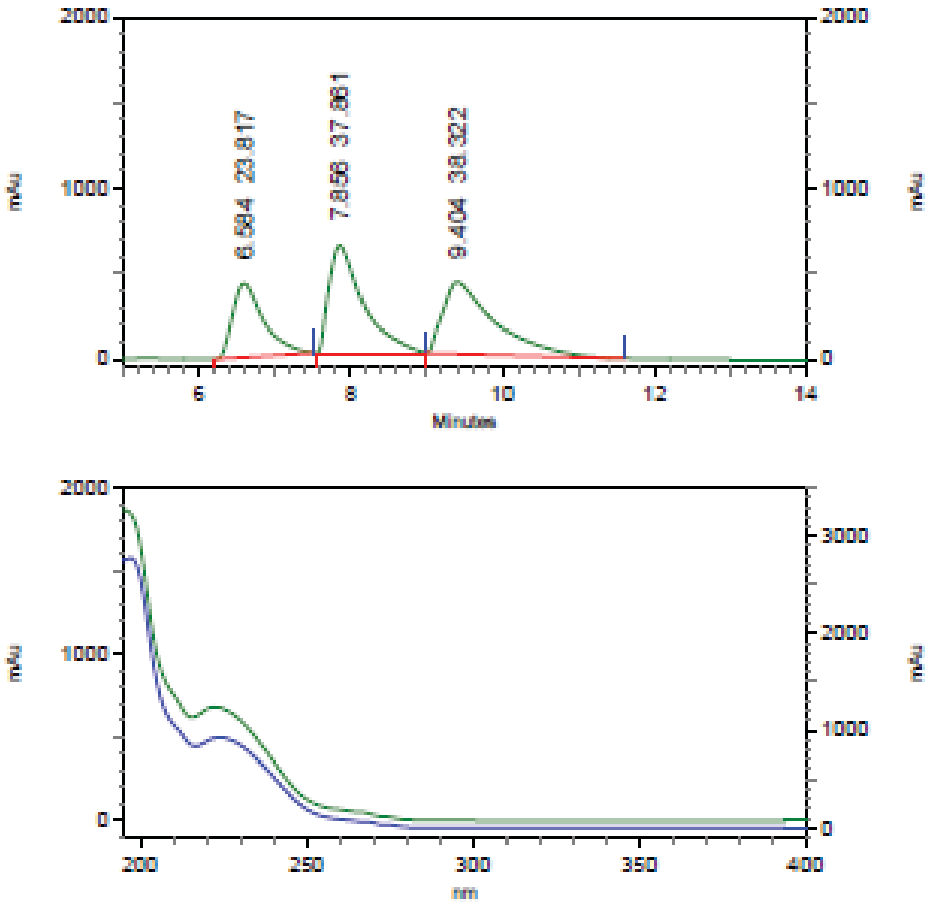


1,3-difluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3g'a**



1,3-difluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3g'a**

YW-II-270racemic ADH 0% 0.8mL
C:\EZStart\Projects\Default\Method\lk-5%0.8.met
C:\EZStart\Projects\Default\Data\YW-II-270racemic ADH 0% 0.8mL

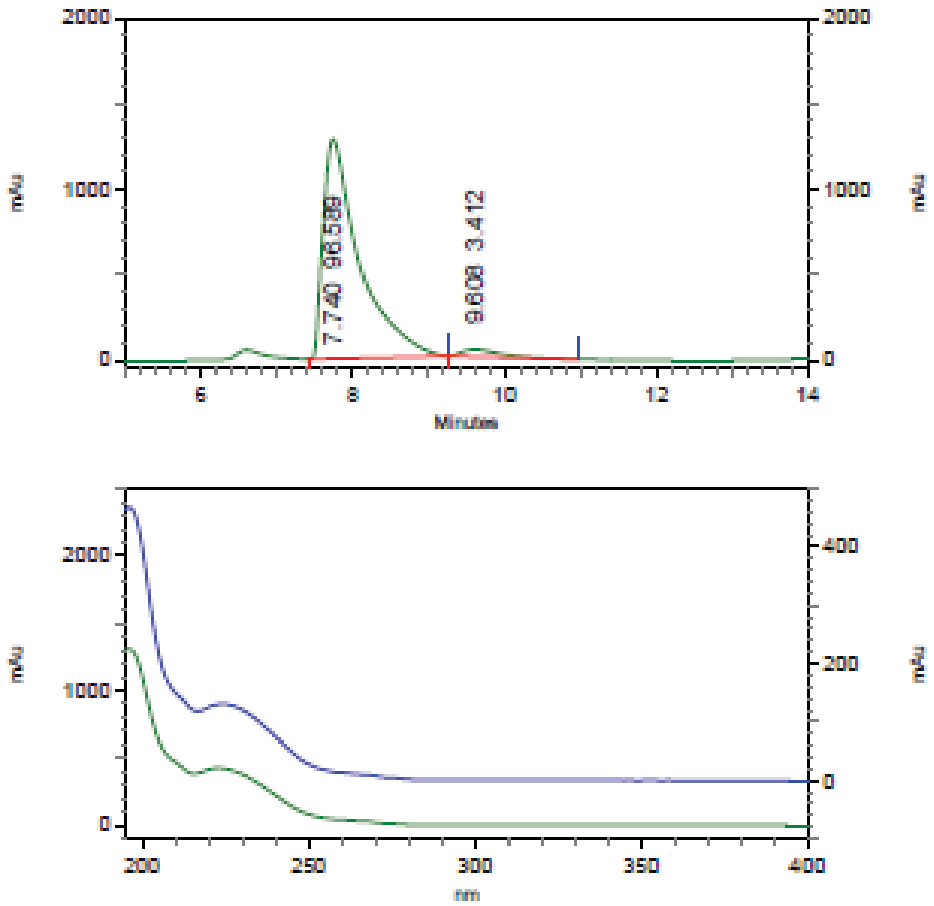


4: 220 nm, 4 nm
Results

Name	Retention Time	Area Percent	Pk #
	6.584	23.817	1
	7.856	37.861	2
	9.404	38.322	3
Totals		100.000	

1,3-difluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3g'a**

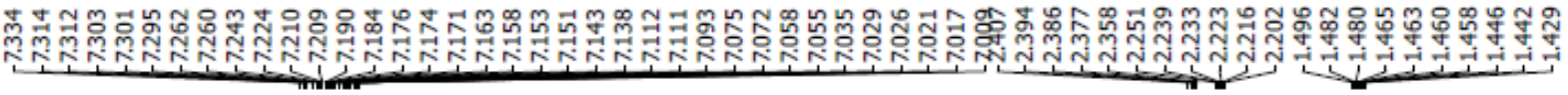
YW-II-270-1--ADH 0# 0.8mL
C:\EZStart\Projects\Default\Method\1k-5#0.8.met
C:\EZStart\Projects\Default\Data\YW-II-270-1--ADH 0# 0.8mL

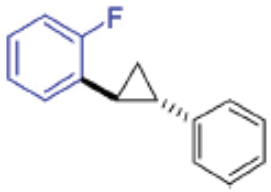


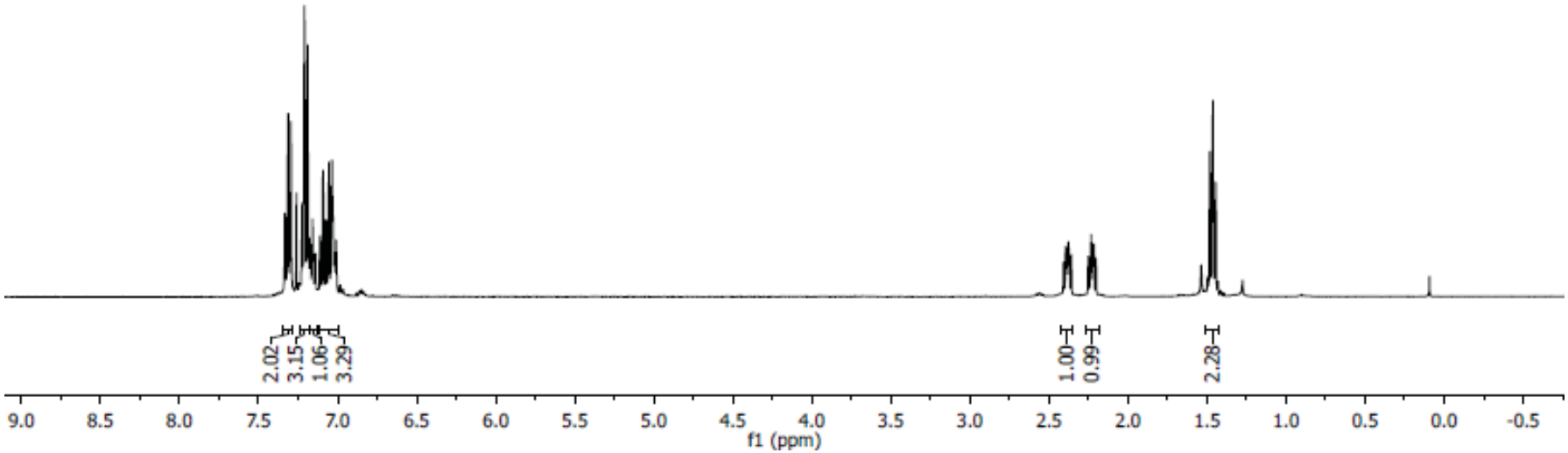
4: 220 nm, 4 nm
Results

Name	Retention Time	Area Percent	Pk #
	7.740	96.589	1
	9.608	3.412	2
Totals		100.000	

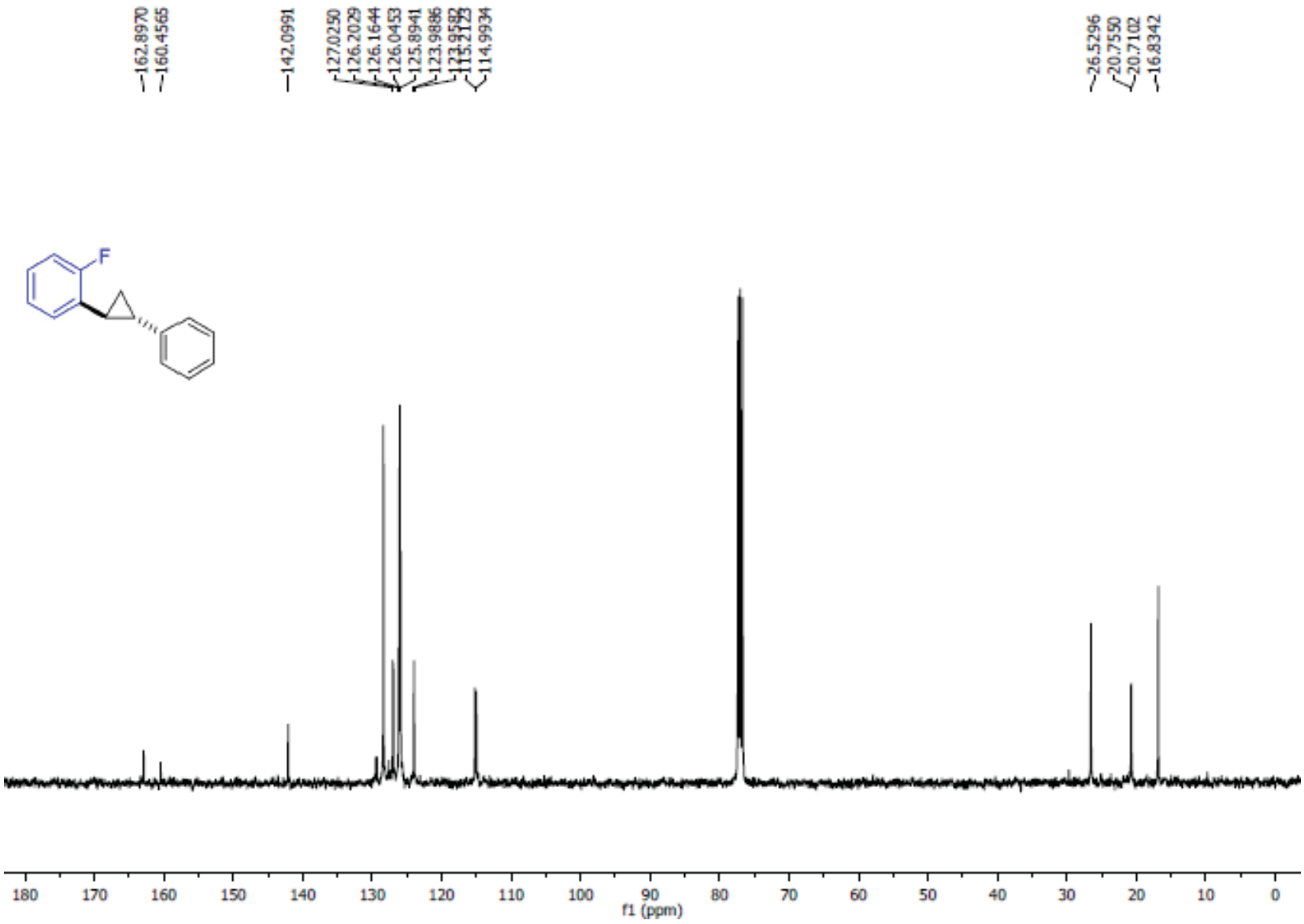
1-fluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3h'a**)



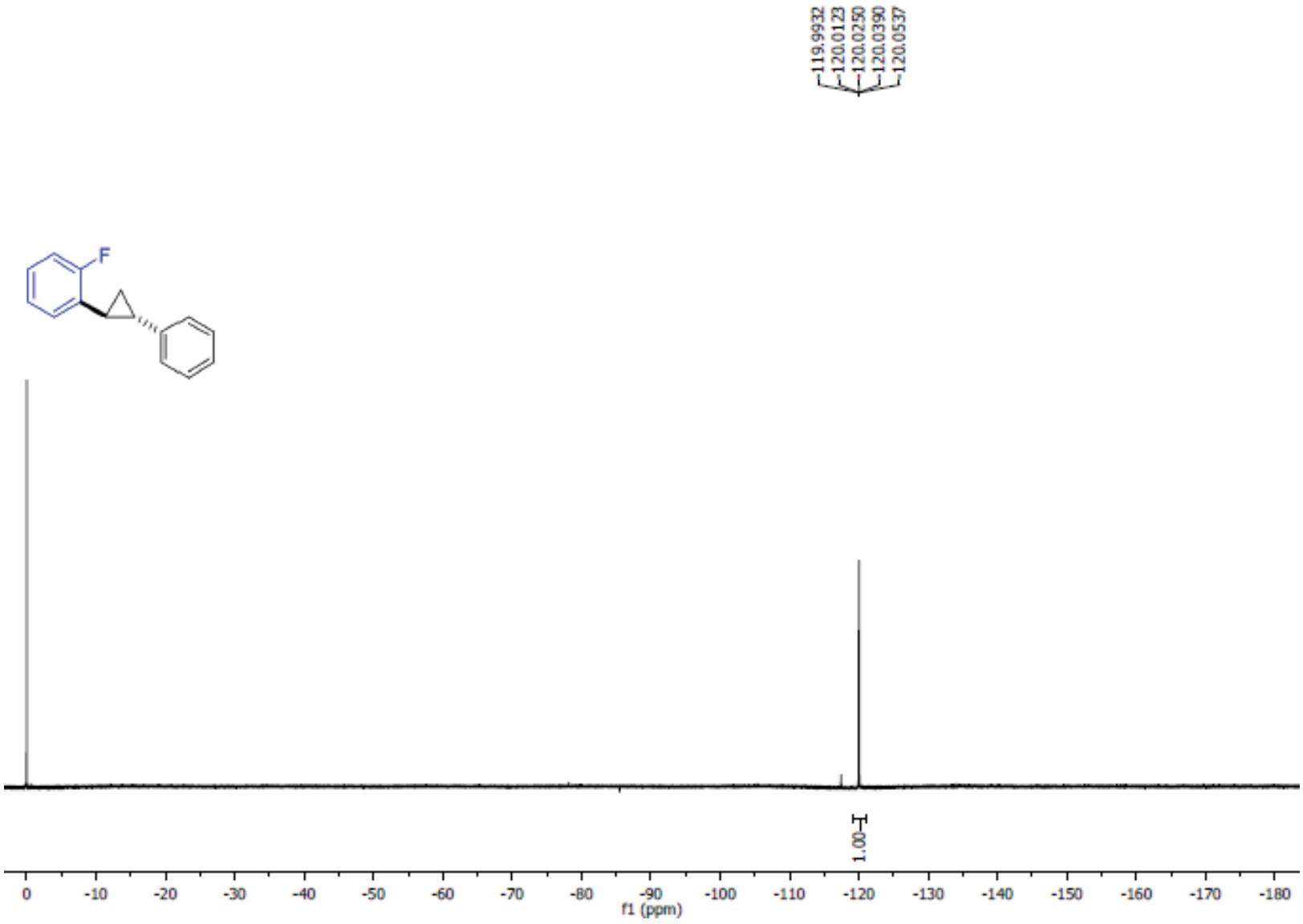




1-fluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3h'a**)

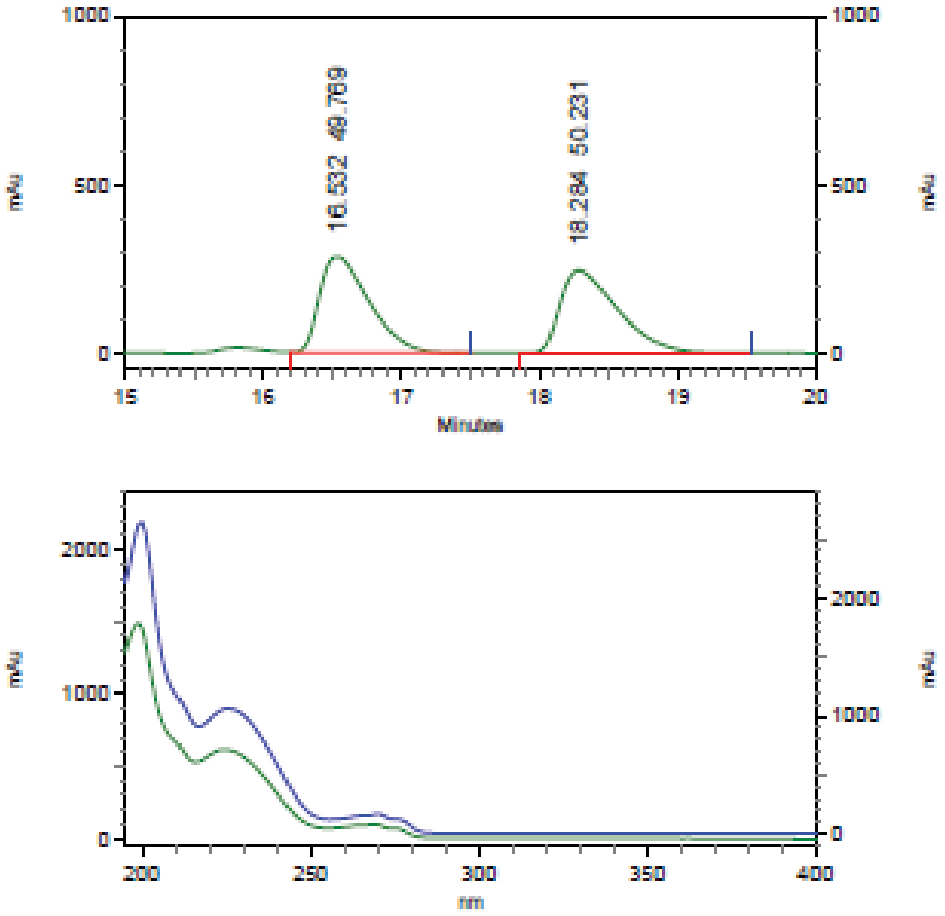


1-fluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3h'a**



1-fluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3h'a**

YW-II-10a ADH 0# 0.8mL
C:\EZStart\Projects\Default\Method\1k-5#0.8.met
C:\EZStart\Projects\Default\Data\YW-II-10a ODH 0# 0.8mL

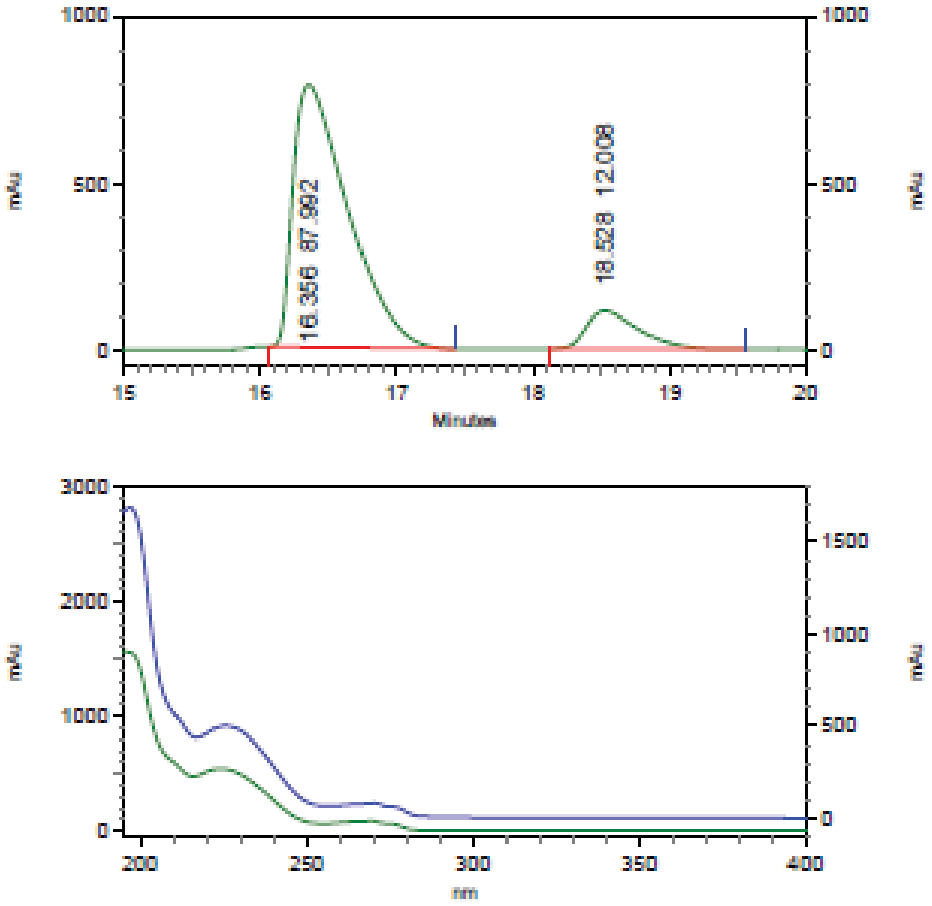


4: 241 nm, 4 nm
Results

Name	Retention Time	Area Percent	Pk #
	16.532	49.769	1
	18.284	50.231	2
Totals		100.000	

1-fluoro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3h'a**

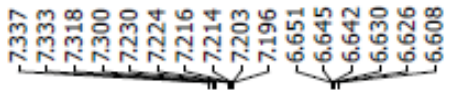
YW-II-277 ADH 0% 0.8mL
C:\EZStart\Projects\Default\Method\lk-5%0.8.met
C:\EZStart\Projects\Default\Data\YW-II-277 ODH 0% 0.8mL

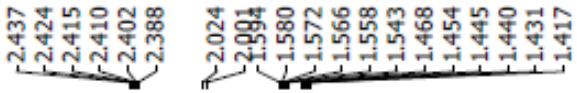


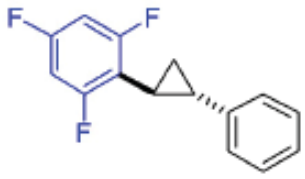
4: 241 nm, 4 nm
Results

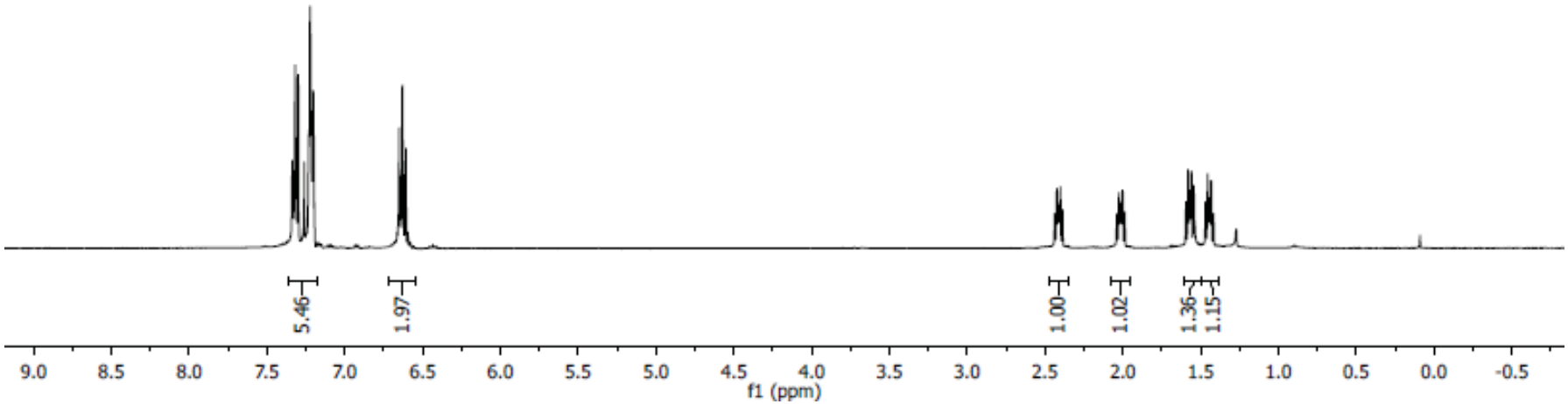
Name	Retention Time	Area Percent	Pk #
	16.356	87.992	1
	18.528	12.008	2
Totals		100.000	

1,3,5-trifluoro-2-((1S,2S)-2-phenylcyclopropyl)benzene **3i'a**

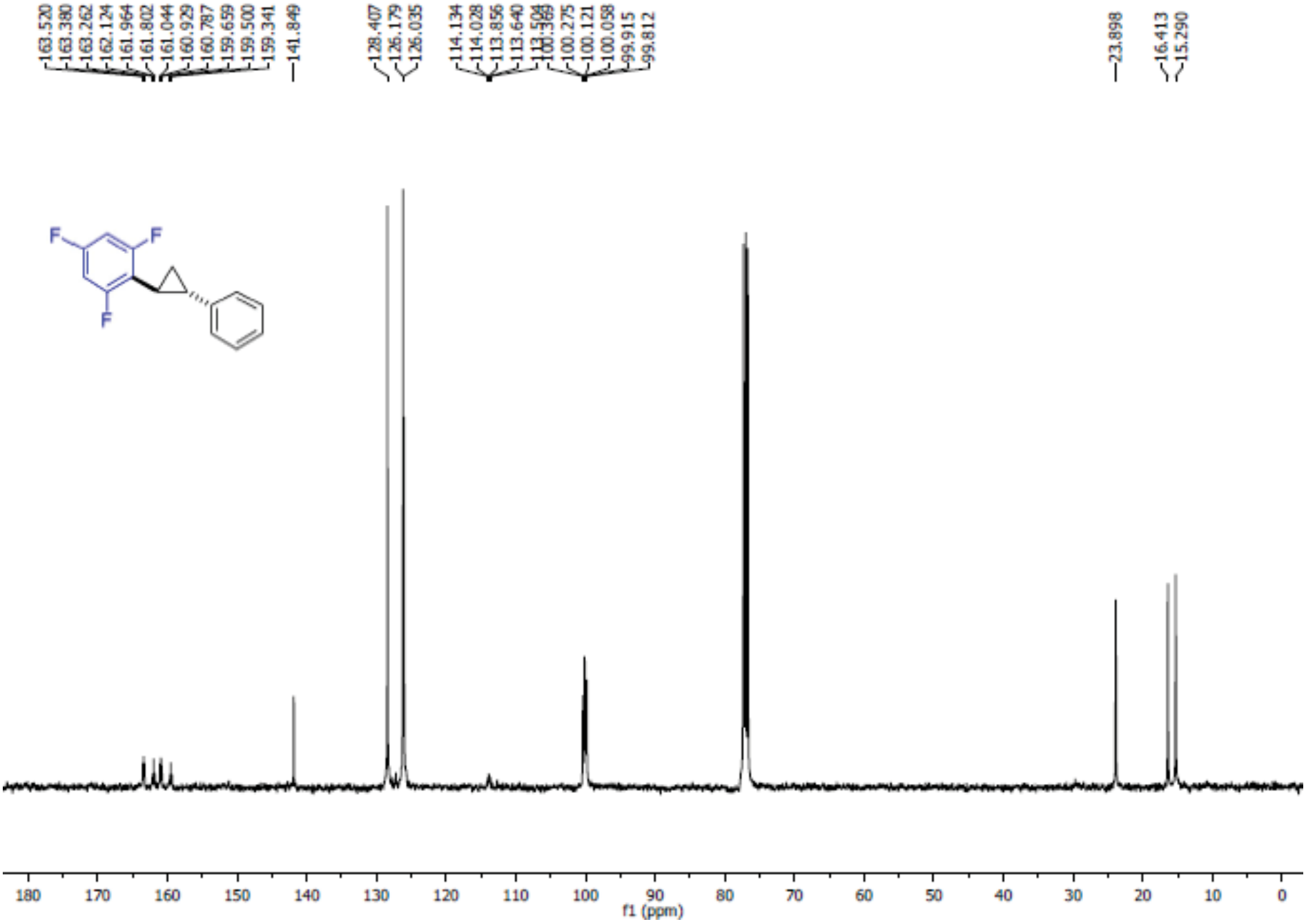




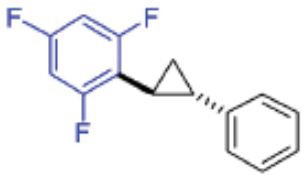


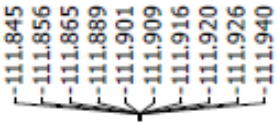


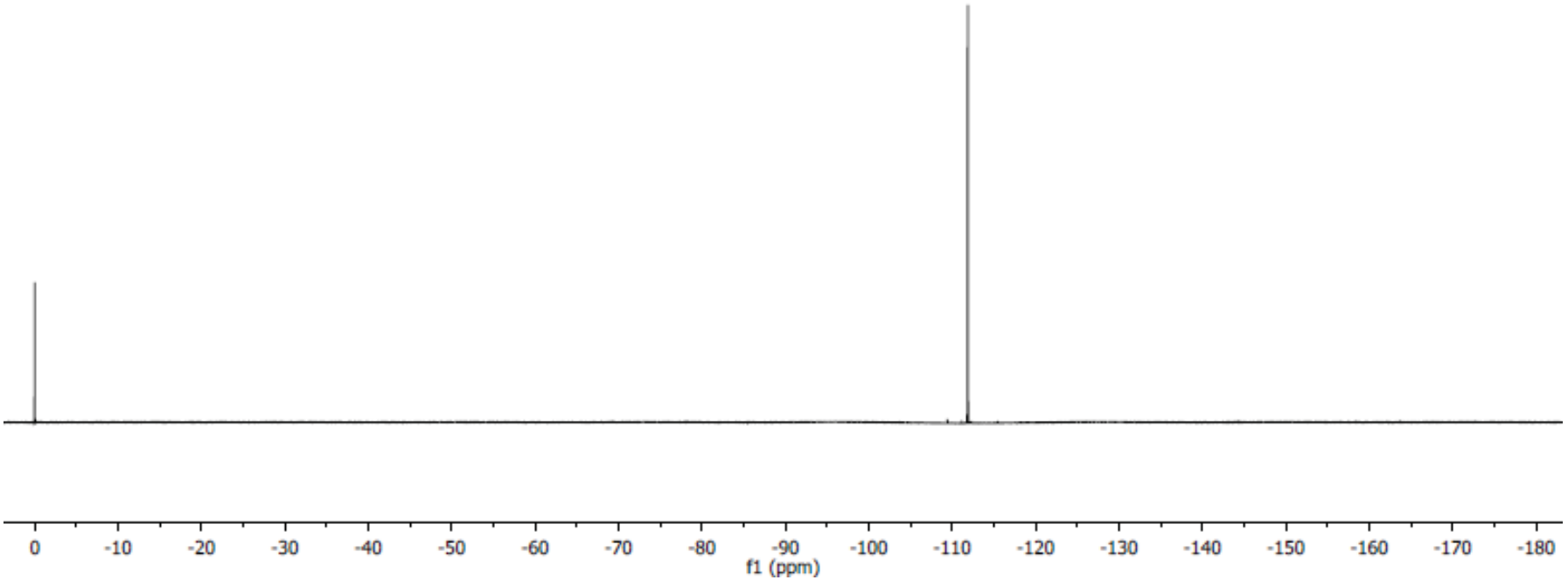
1,3,5-trifluoro-2-((1S,2S)-2-phenylcyclopropyl)benzene **3i'a**



1,3,5-trifluoro-2-((1S,2S)-2-phenylcyclopropyl)benzene **3i'a**

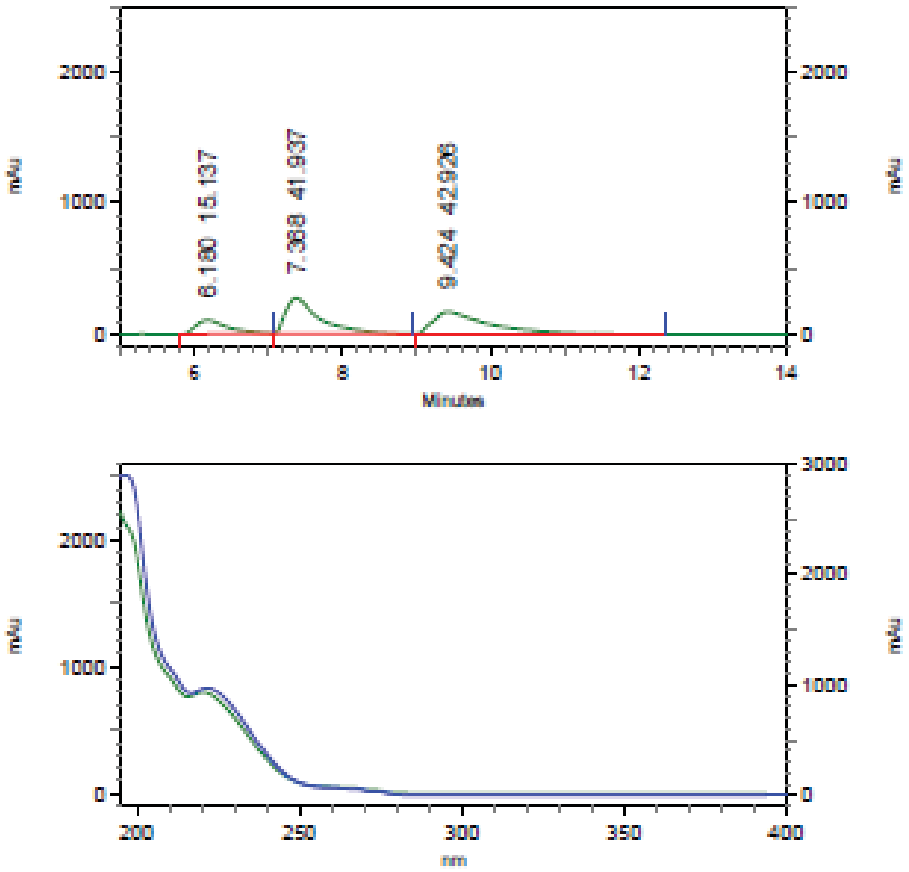






1,3,5-trifluoro-2-((1S,2S)-2-phenylcyclopropyl)benzene **3i'a**

YW-II-265 ADH 0# 0.8mL
C:\EZStart\Projects\Default\Method\lk-5#0.8.met
C:\EZStart\Projects\Default\Data\YW-II-265 ADH 0# 0.8mL

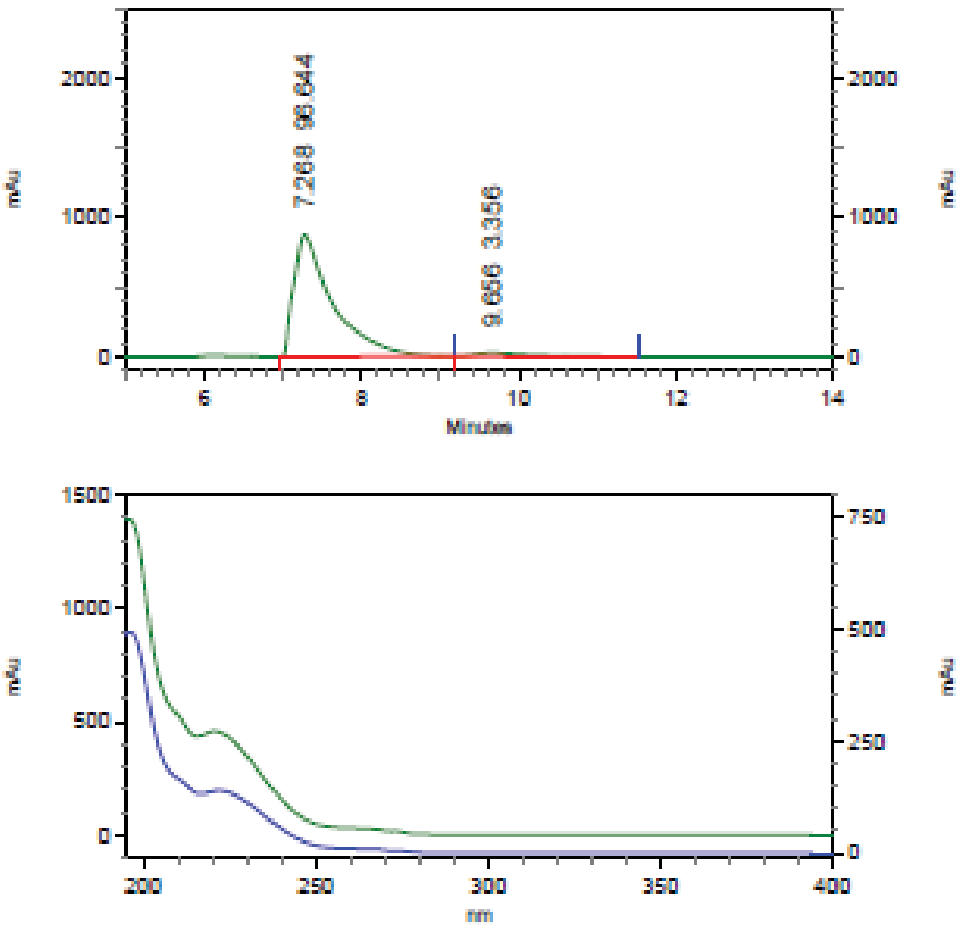


4: 240 nm, 4 nm
Results

Name	Retention Time	Area Percent	Pk #
	6.180	15.137	1
	7.368	41.937	2
	9.424	42.926	3
Totals		100.000	

1,3,5-trifluoro-2-((1S,2S)-2-phenylcyclopropyl)benzene **3i'a**

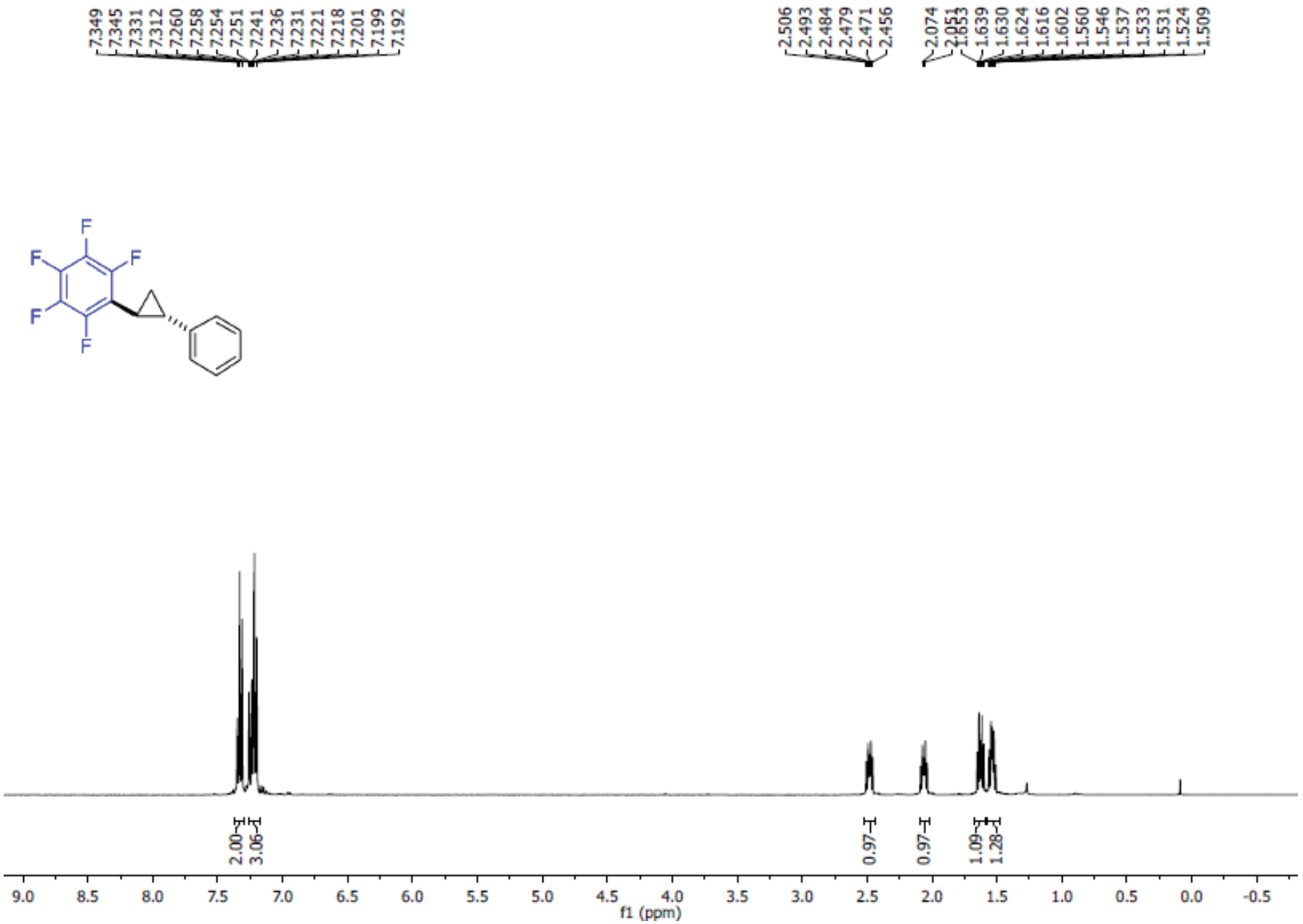
YW-II-278 ADH 0# 0.8mL
C:\EZStart\Projects\Default\Method\1k-5#0.8.met
C:\EZStart\Projects\Default\Data\YW-II-278 ADH 0# 0.8mL



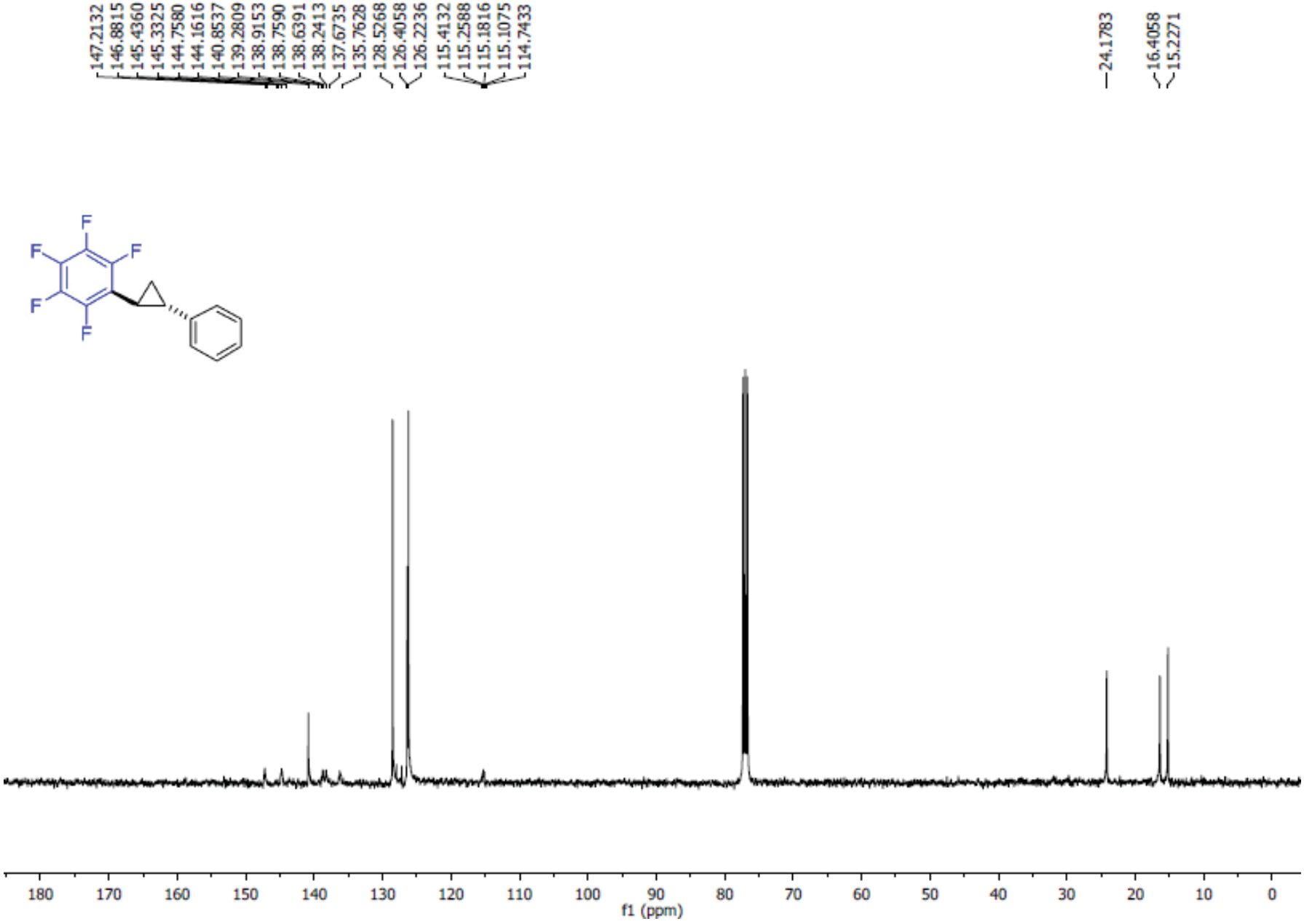
4: 240 nm, 4 nm
Results

Name	Retention Time	Area Percent	Pk #
	7.268	96.644	1
	9.656	3.356	2
Totals		100.000	

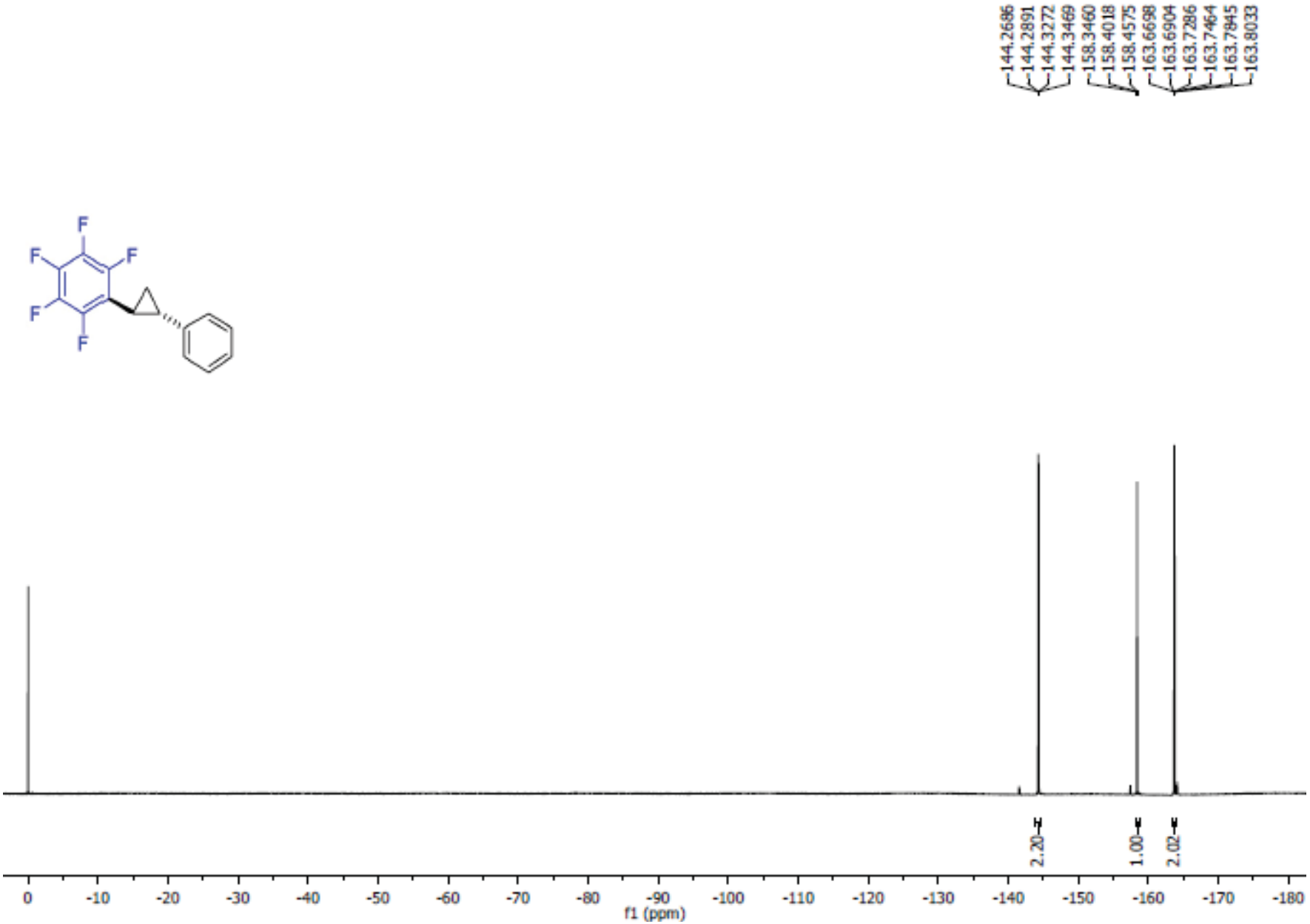
1,2,3,4,5-pentafluoro-6-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3j'a**



1,2,3,4,5-pentafluoro-6-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3j'a**

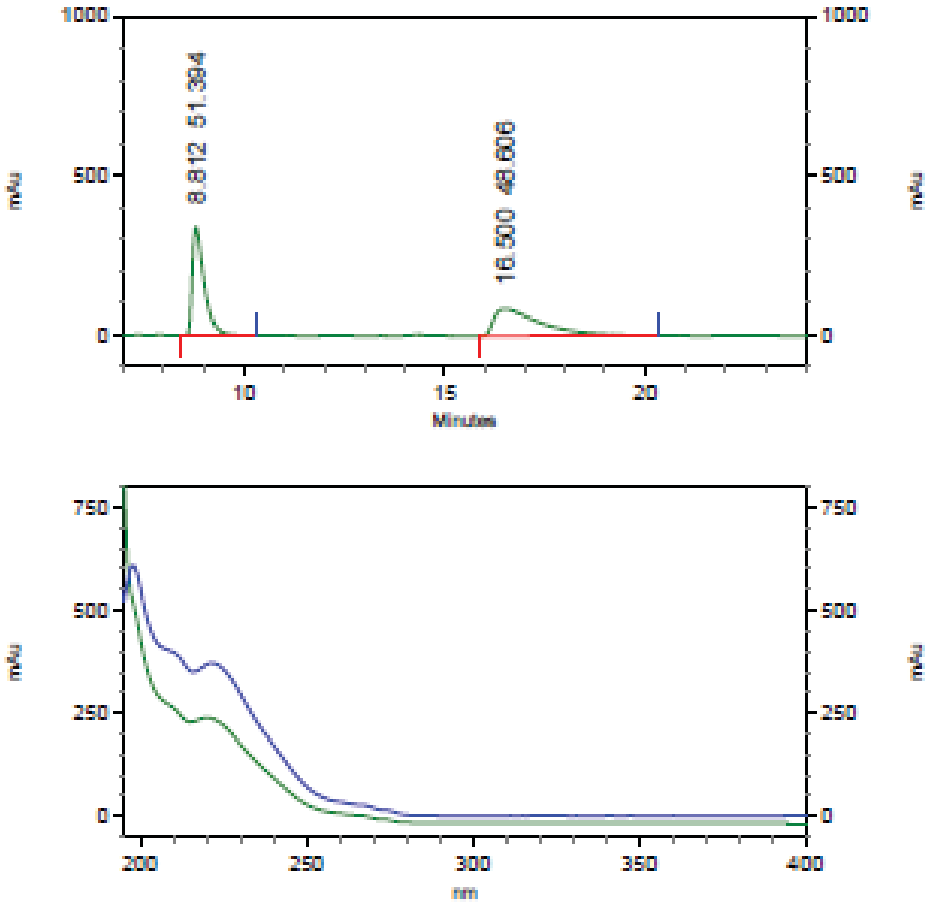


1,2,3,4,5-pentafluoro-6-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3j'a**



1,2,3,4,5-pentafluoro-6-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3j'a**

YW-I-71a-1 ADH 0@0.8 mL
C:\EZStart\Projects\Default\Method\lk-5@0.8.met
F:\HPLC\YongWang\HPLC-YW-I\YW-I-71a-1 ADH 0@0.8 mL

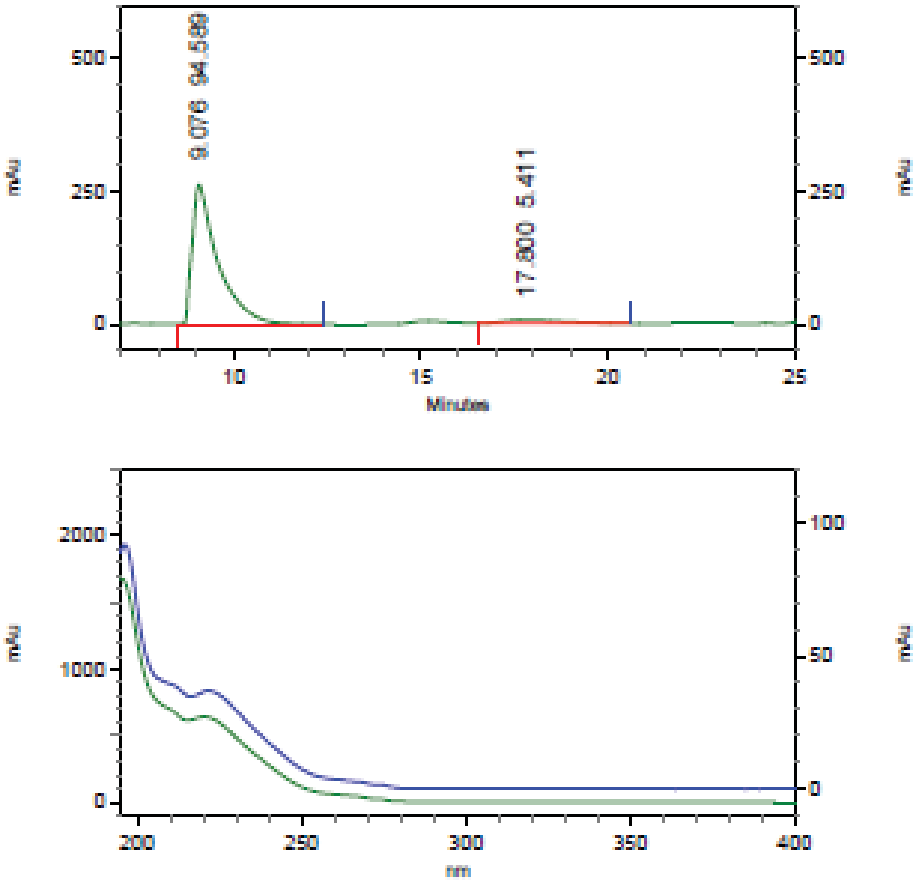


4: 240 nm, 4 nm
Results

Name	Retention Time	Area Percent	Pk #
	8.812	51.394	1
	16.500	48.606	2
Totals		100.000	

1,2,3,4,5-pentafluoro-6-((1*S*,2*S*)-2-phenylcyclopropyl)benzene **3j'a**

YW-II-280 ADH 0# 0.8mL
C:\EZStart\Projects\Default\Method\1k-5#0.8.met
C:\EZStart\Projects\Default\Data\YW-II-280 ADH 0# 0.8mL

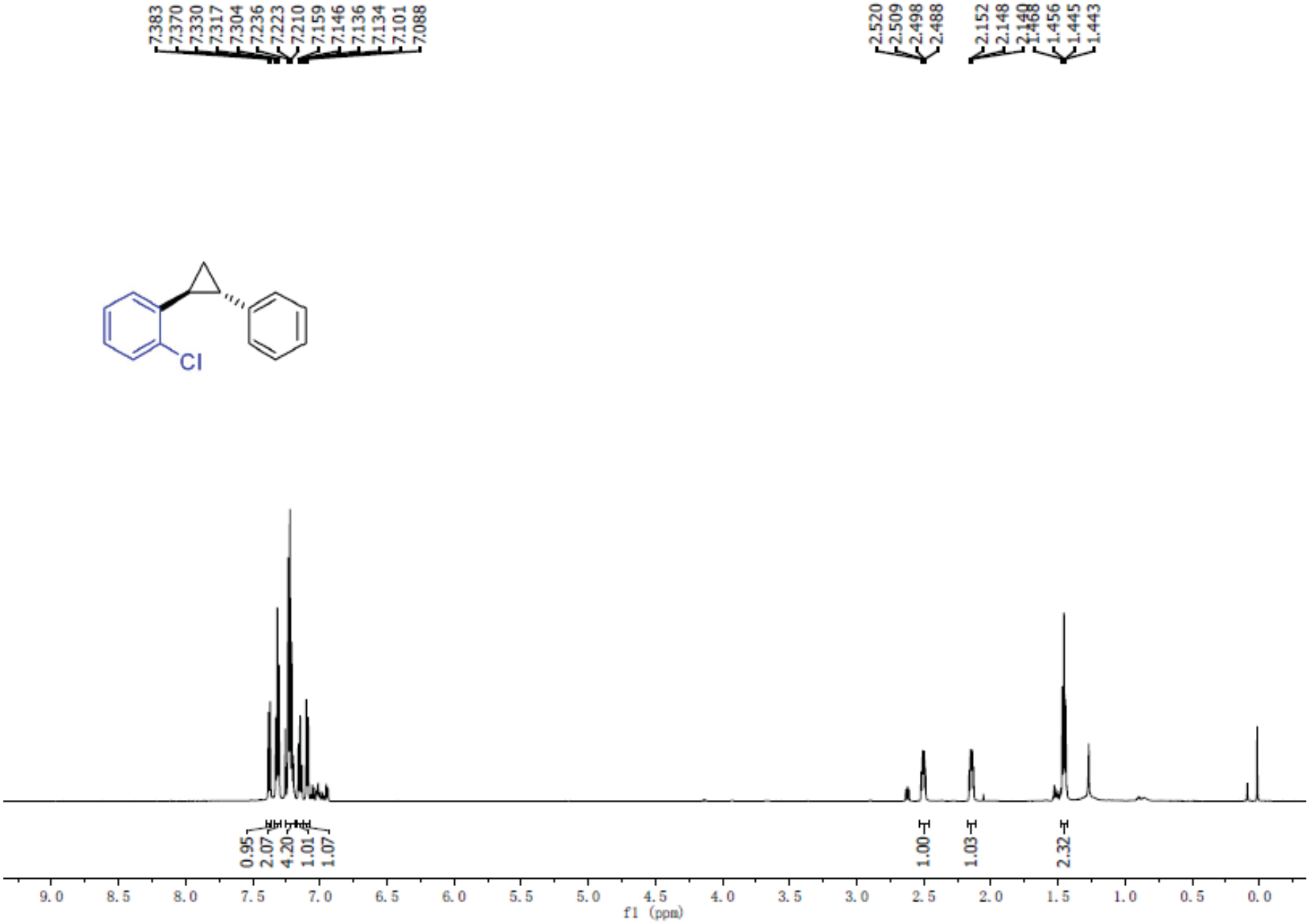


4: 241 nm, 4 nm
Results

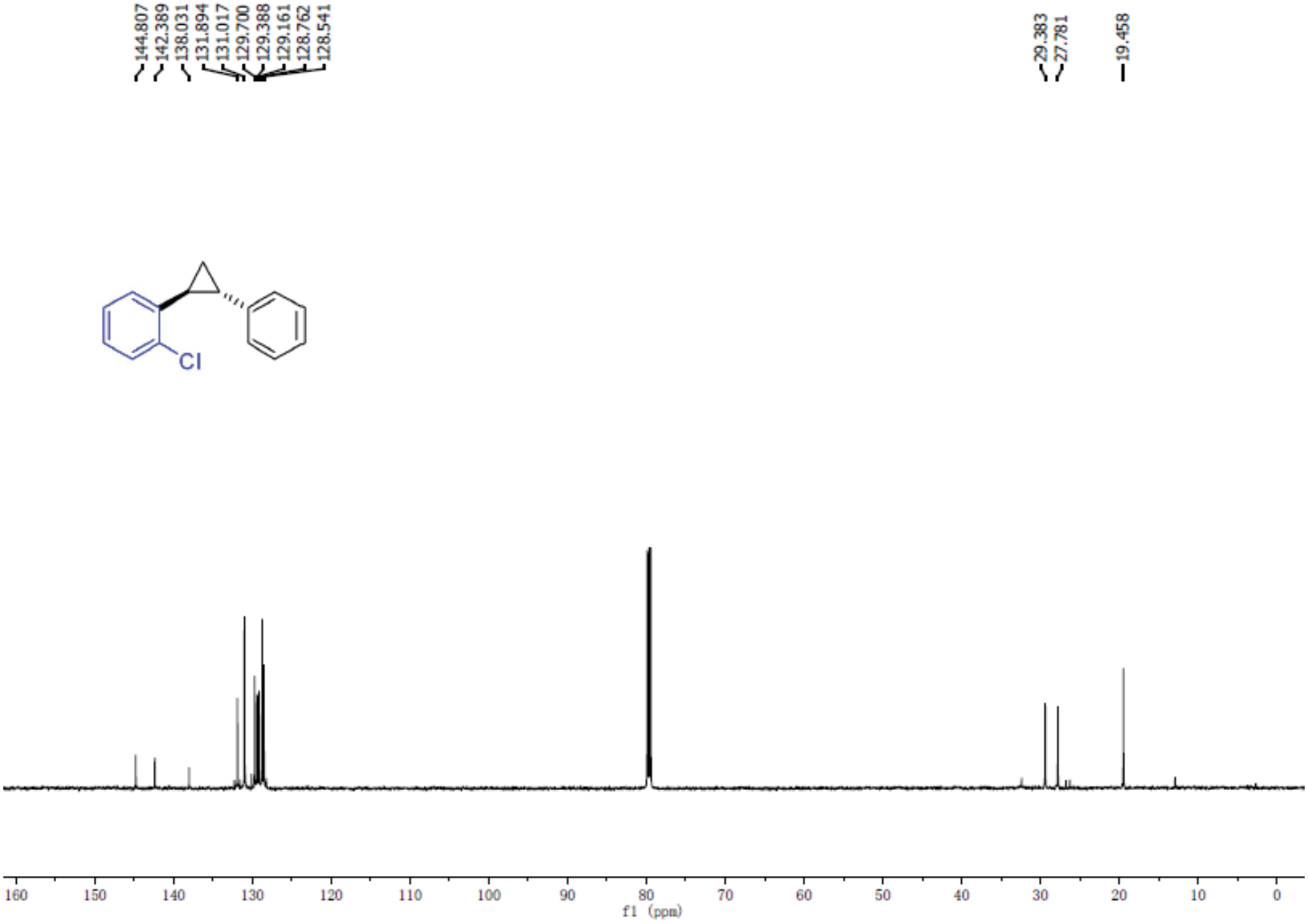
Name	Retention Time	Area Percent	Pk #
	9.076	94.589	1
	17.800	5.411	2

Totals	
	100.000

1-Chloro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3k'a**)



1-Chloro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3k'a**)

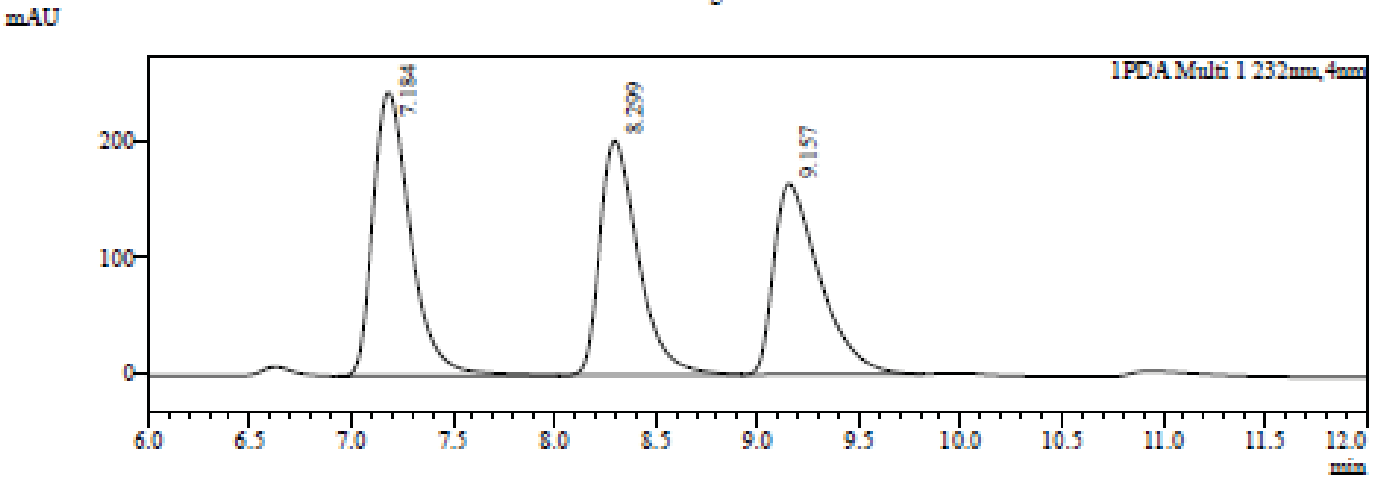


1-Chloro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3k'a**)

Sample Information

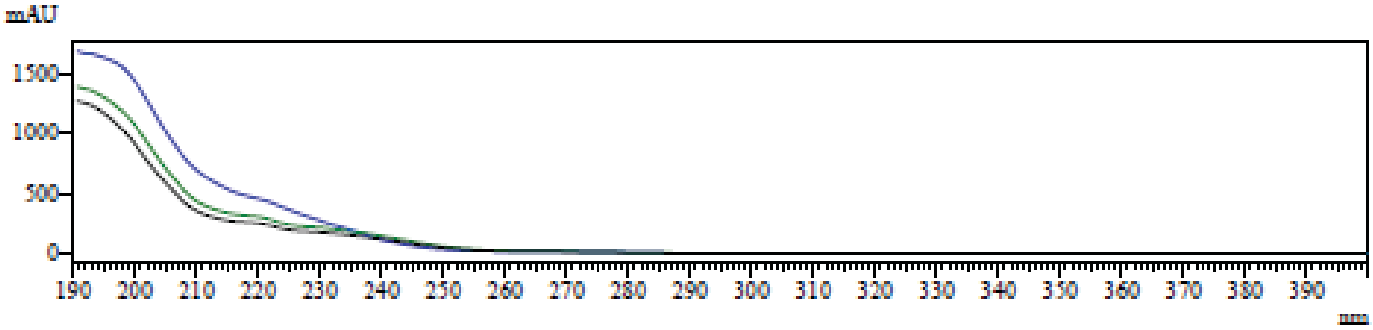
Sample Name	: X0W-0085-ADH-0%-0.8ML
Sample ID	: X0W-0085-ADH-0%-0.8ML
Data File	: X0W-0085-ADH-0%-0.8ML.lcd
Method File	: YW-0%-0.8ml.lcm
Date Acquired	: 12/21/2016 3:57:31 PM

Chromatogram



UV Spectrum

X0W-0085-ADH-0%-0.8ML.lcd



Peak Table

PDA Ch1 232nm

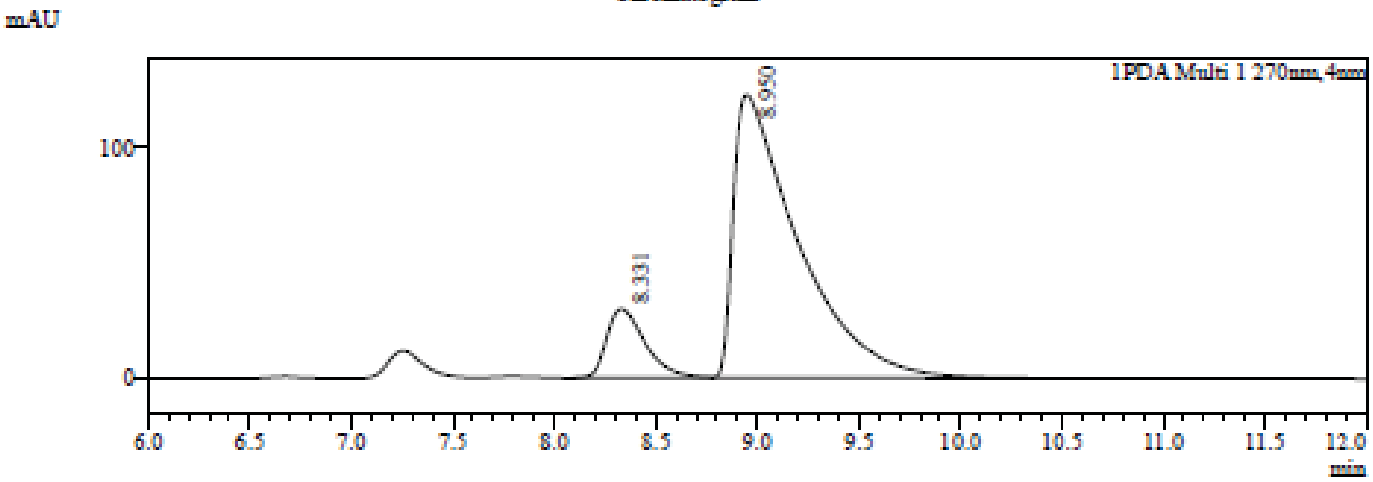
Peak#	Ret. Time	Area	Area%
1	7.184	3129173	37.276
2	8.299	2659077	31.676
3	9.157	2606300	31.048
Total		8394550	100.000

1-Chloro-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3k'a**)

Sample Information

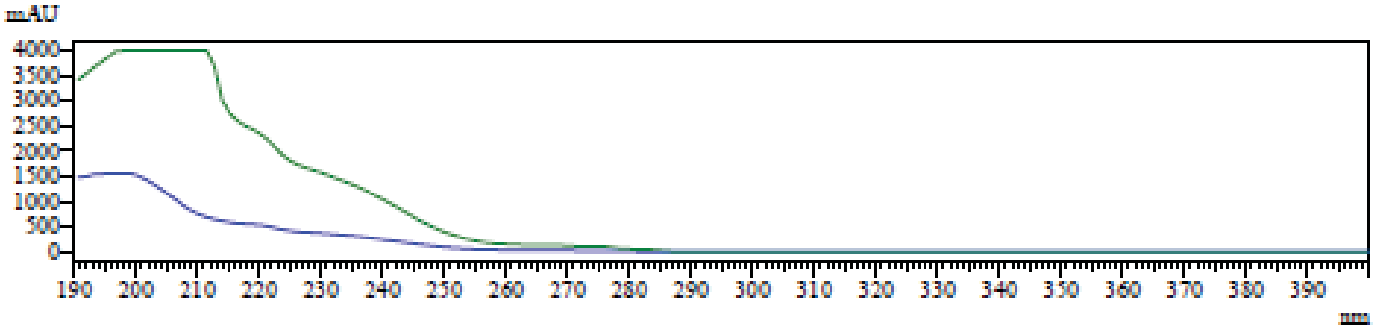
Sample Name	: X0W-0086-ADH-0%-0.8ML
Sample ID	: X0W-0086-ADH-0%-0.8ML
Data File	: X0W-0086-ADH-0%-0.8ML.lcd
Method File	: YW-0%-0.8ml.lcm
Date Acquired	: 12/21/2016 4:18:09 PM

Chromatogram



UV Spectrum

X0W-0086-ADH-0%-0.8ML.lcd

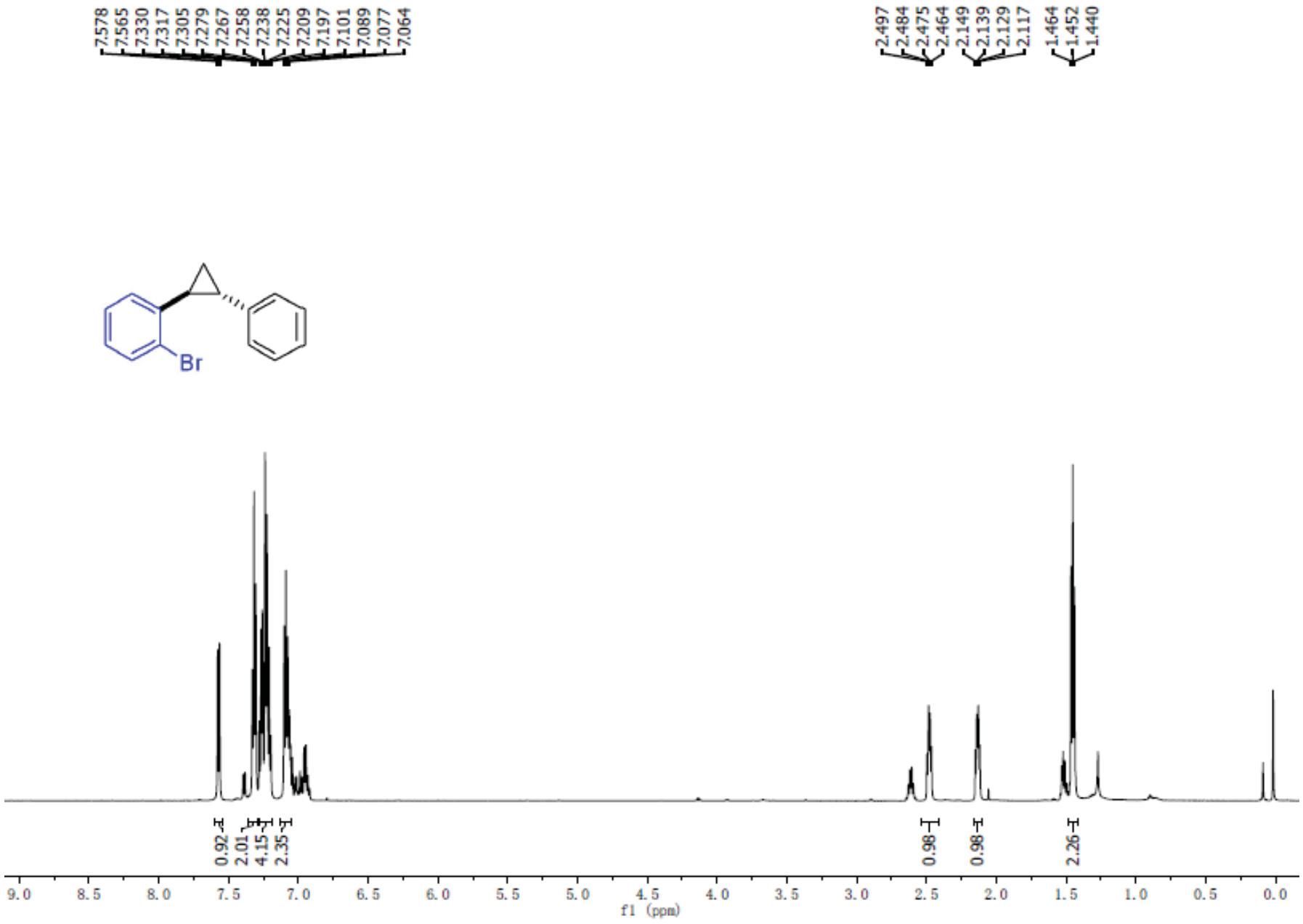


Peak Table

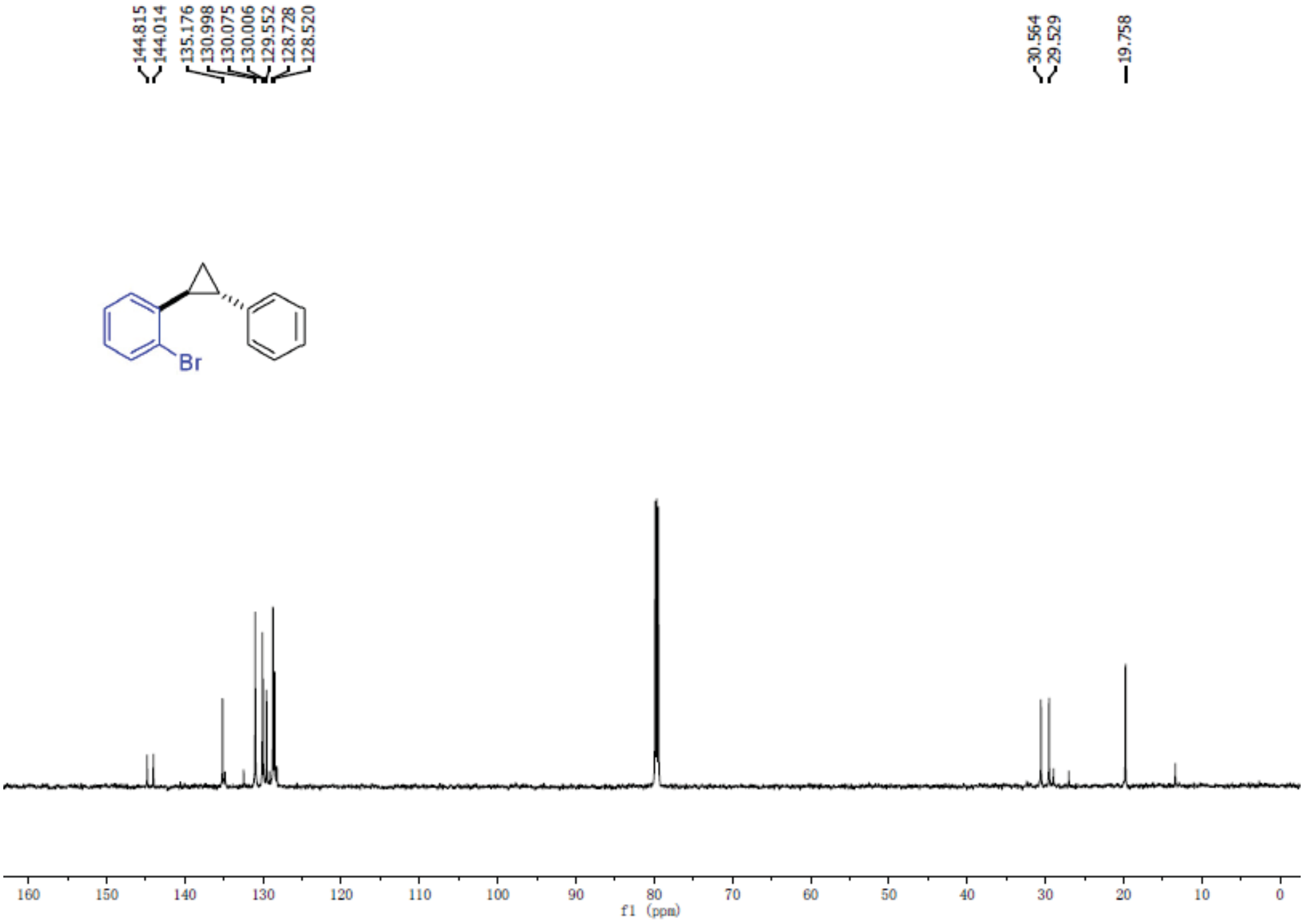
PDA Ch1 270nm

Peak#	Ret. Time	Area	Area%
1	8.331	386332	12.448
2	8.950	2717218	87.552
Total		3103550	100.000

1-Bromo-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3l'a**)



1-Bromo-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3l'a**)

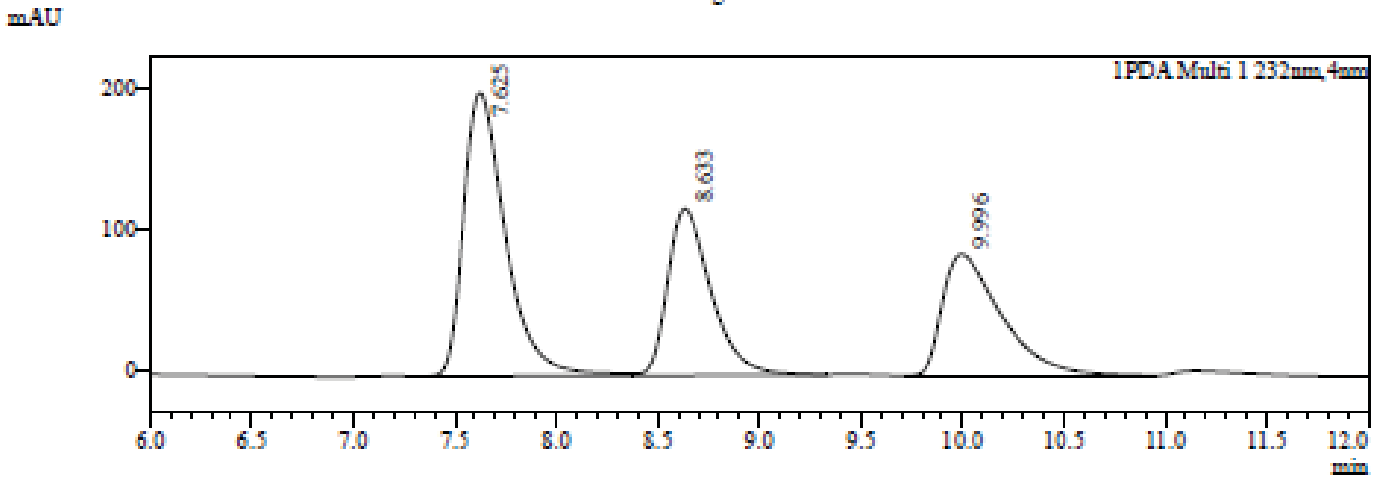


1-Bromo-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3l'a**)

Sample Information

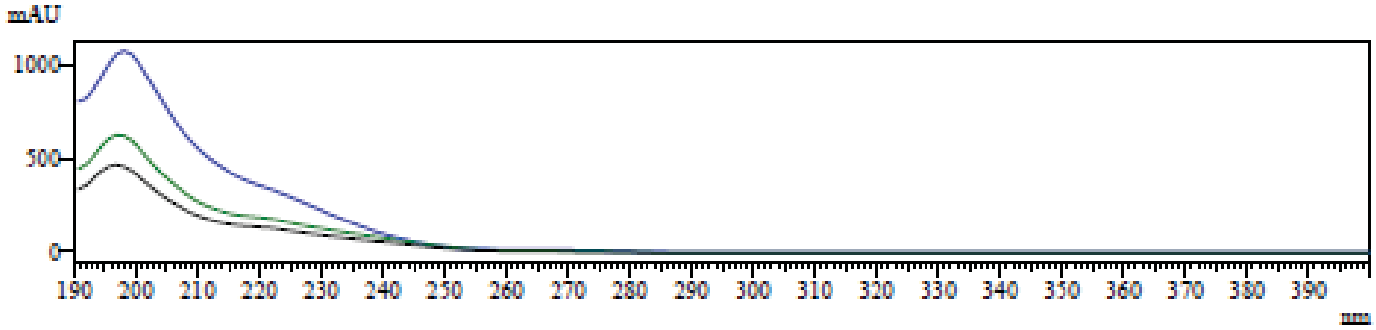
Sample Name	: X0W-0087-ADH-0%-0.8ML
Sample ID	: X0W-0087-ADH-0%-0.8ML
Data File	: X0W-0087-ADH-0%-0.8ML001.lcd
Method File	: YW-0%-0.8ml.lcm
Date Acquired	: 12/21/2016 4:50:43 PM

Chromatogram



UV Spectrum

X0W-0087-ADH-0%-0.8ML001.lcd



Peak Table

PDA Ch1 232nm

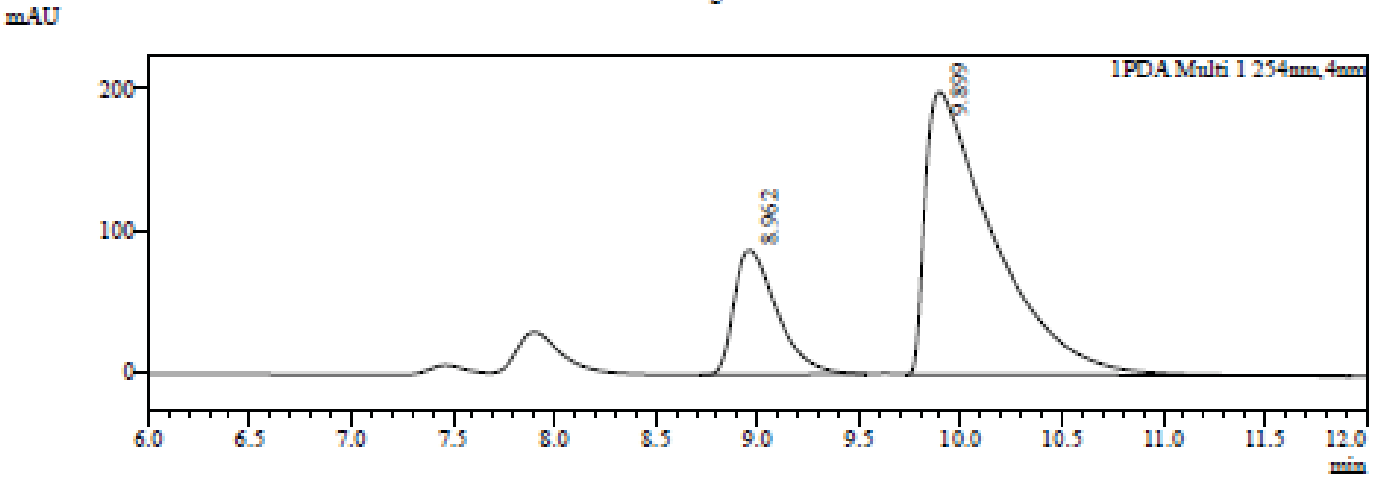
Peak#	Ret. Time	Area	Area%
1	7.625	2886907	45.245
2	8.633	1757918	27.551
3	9.996	1735749	27.204
Total		6380573	100.000

1-Bromo-2-((1*S*,2*S*)-2-phenylcyclopropyl)benzene (**3l'a**)

Sample Information

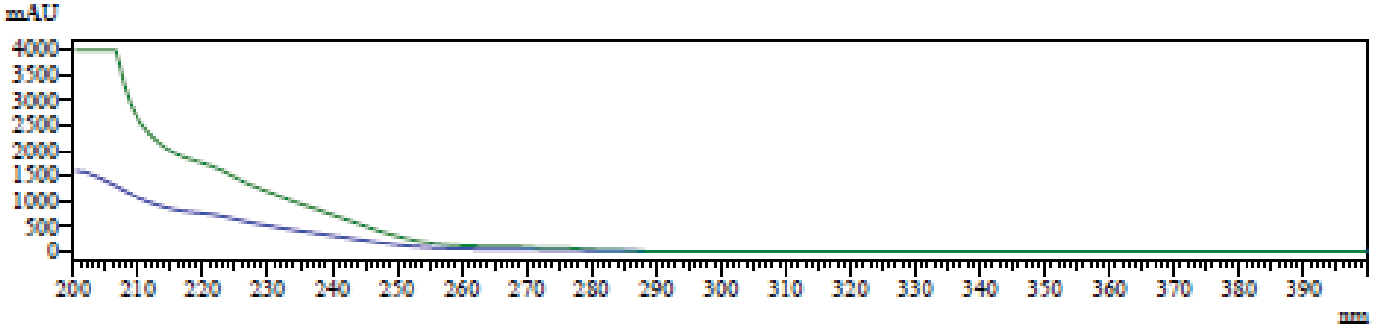
Sample Name	: X0W-0088-ADH-0%-0.8ML
Sample ID	: X0W-0088-ADH-0%-0.8ML
Data File	: X0W-0088-ADH-0%-0.8ML001. lcd
Method File	: YW-0%-0.8ml.lcm
Date Acquired	: 12/21/2016 3:37:28 PM

Chromatogram



UV Spectrum

X0W-0088-ADH-0%-0.8ML001.lcd



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	8.962	1293865	21.593
2	9.899	4698098	78.407
Total		5991963	100.000

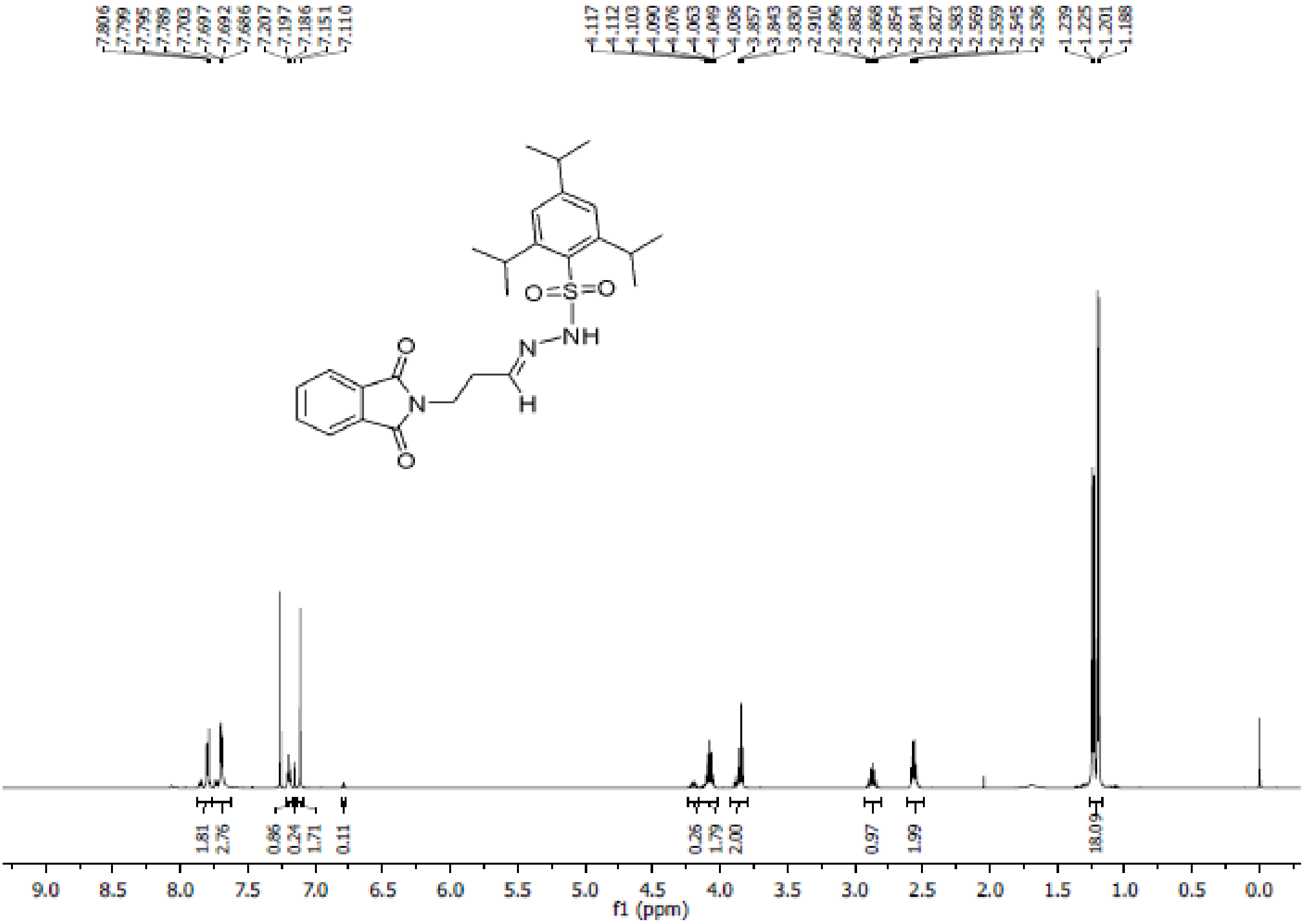
Spectral Data

for

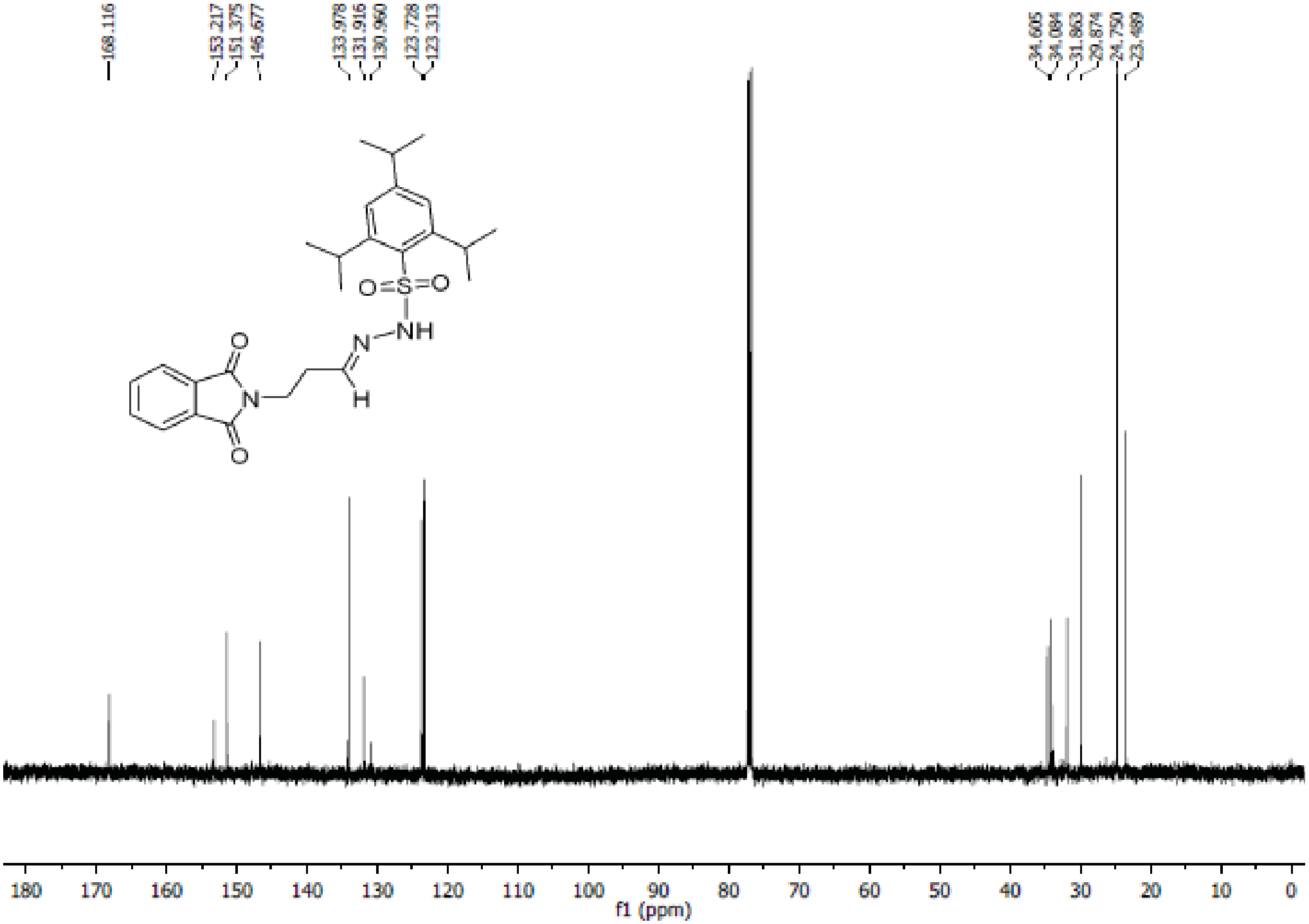
Chapter 3

Enantioselective Radical *Cis*-Cyclopropanation of Alkenes with In Situ-Generated Aliphatic Diazo Compound

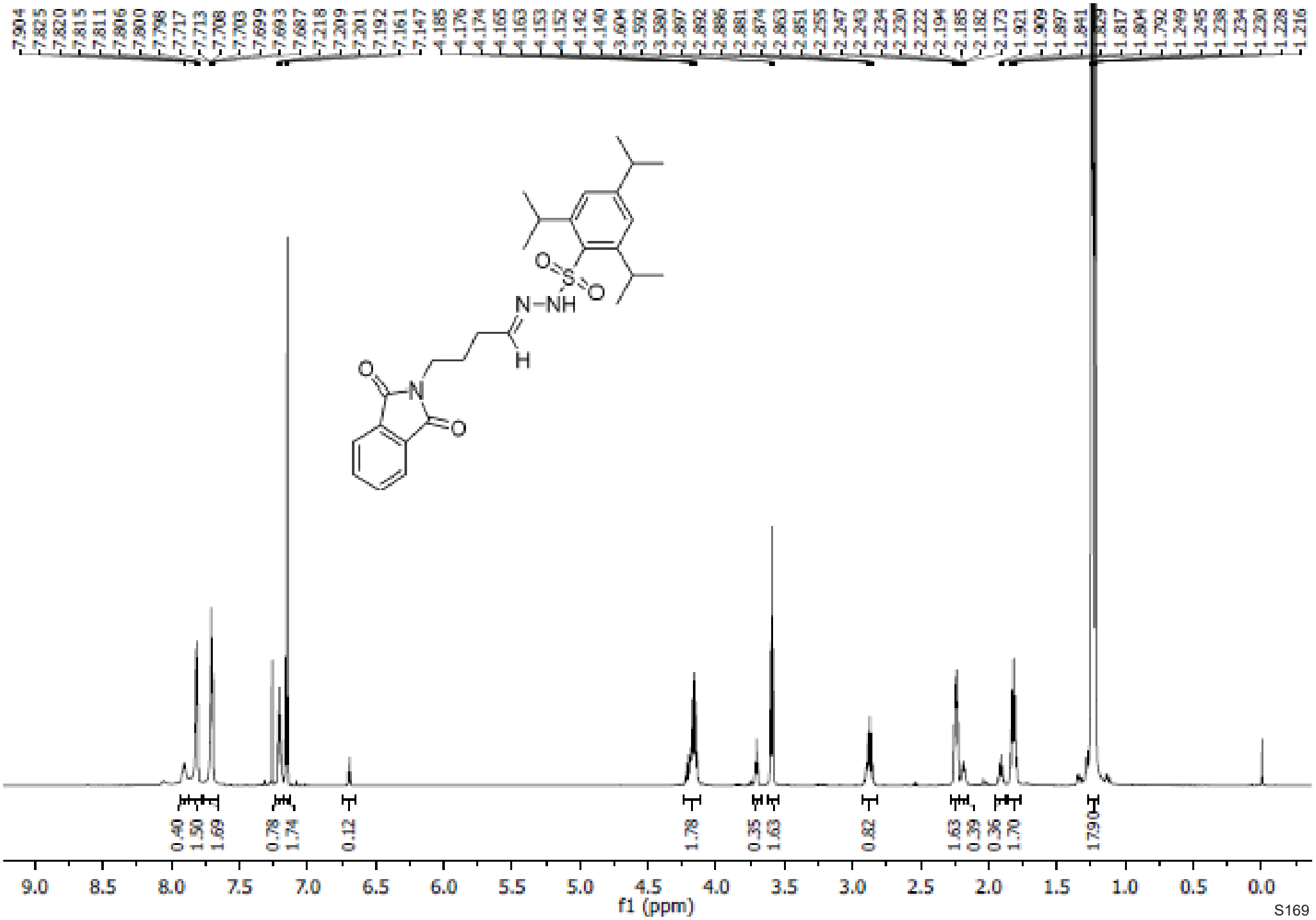
N'-(3-(1,3-dioxoisoindolin-2-yl)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



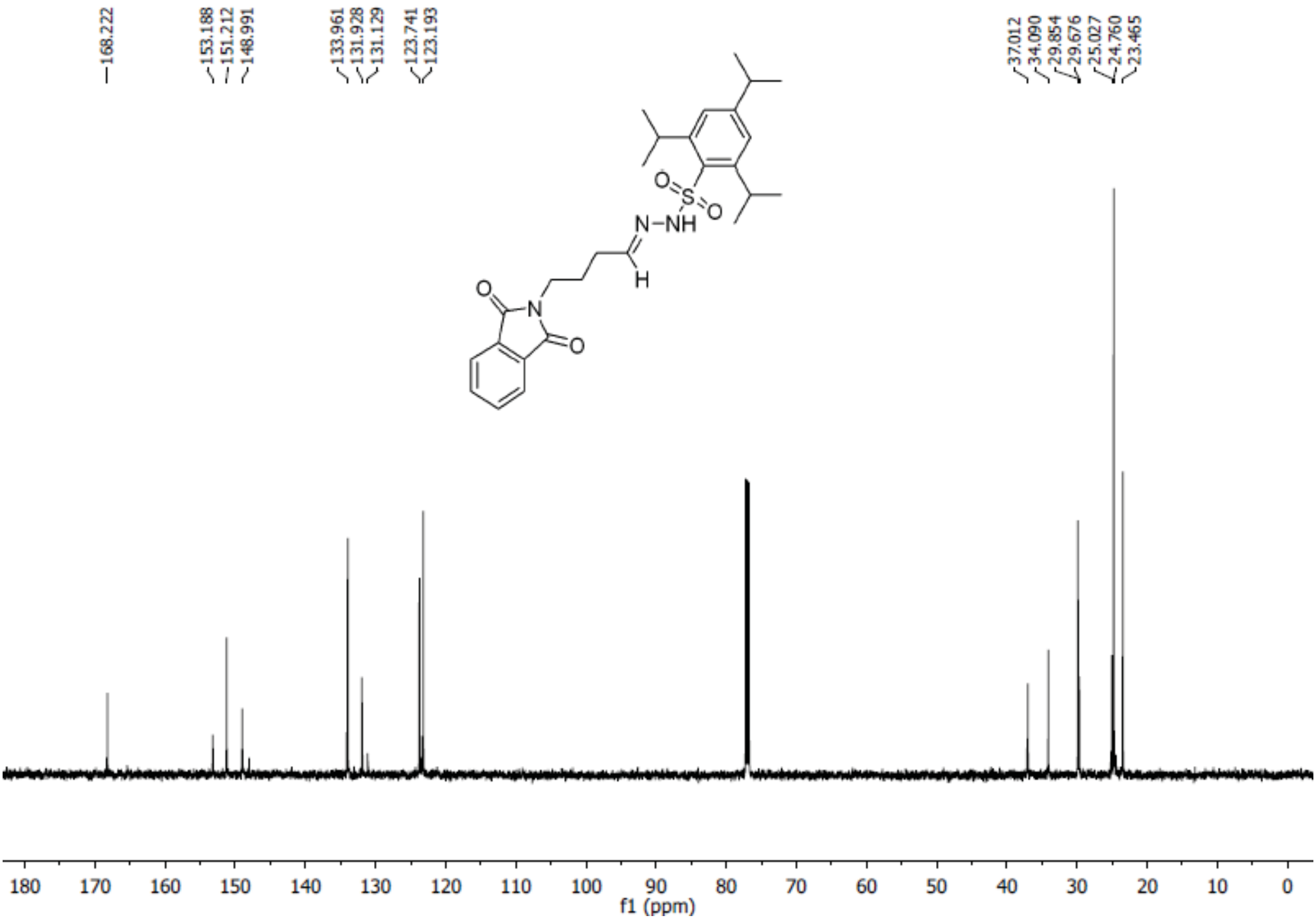
N'-(3-(1,3-dioxoisoindolin-2-yl)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



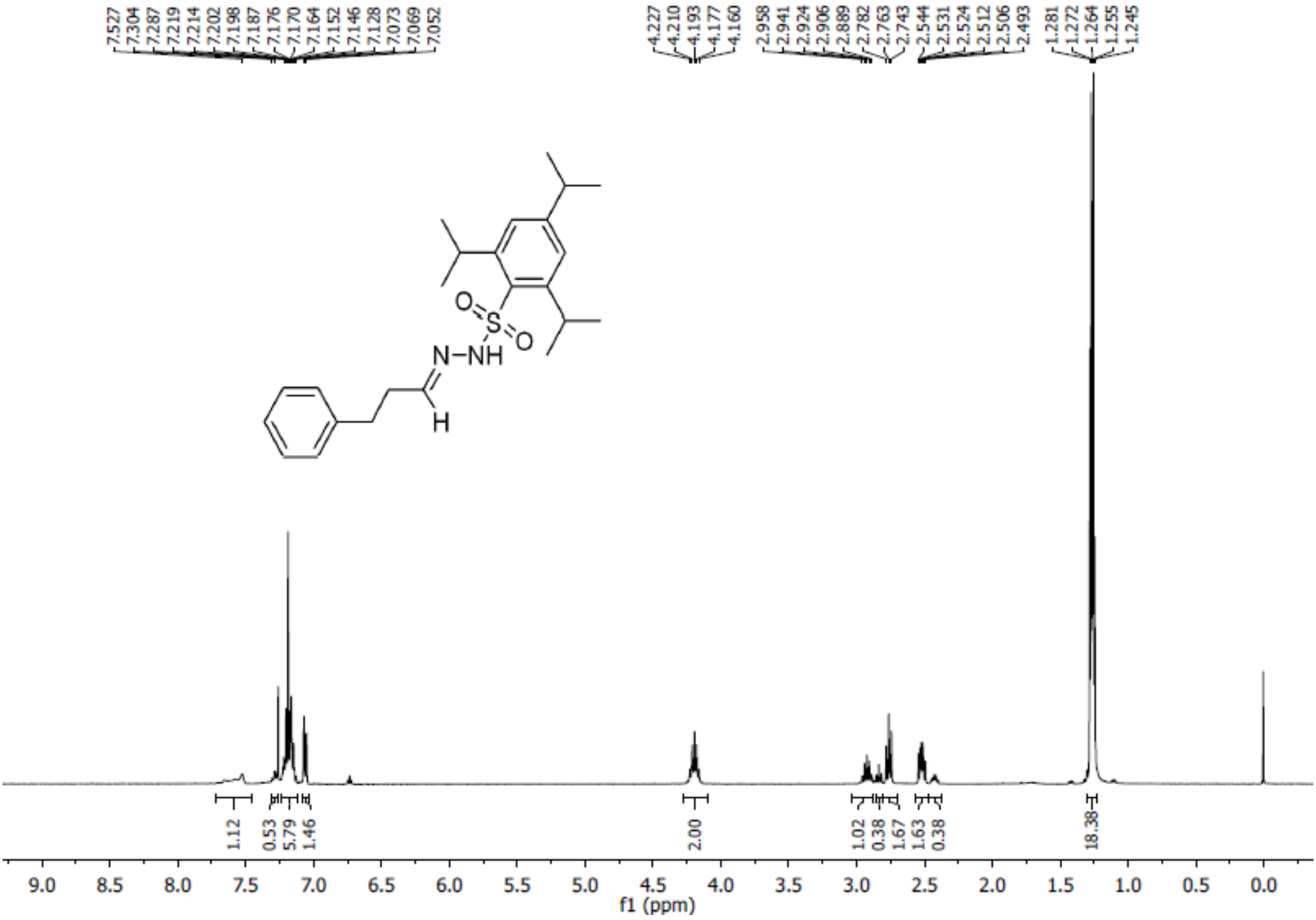
N'-(4-(1,3-dioxoisoindolin-2-yl)butylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



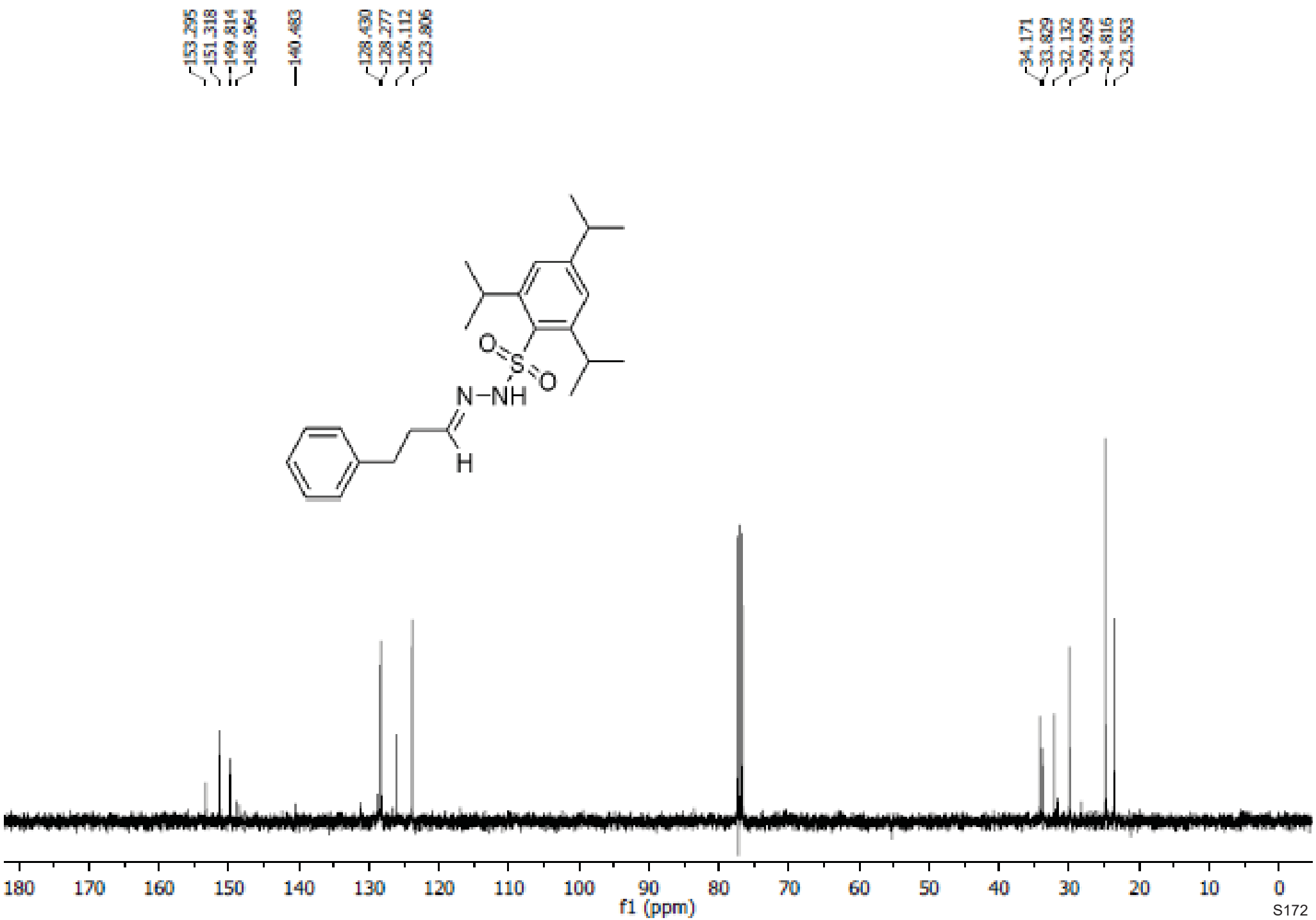
N'-(4-(1,3-dioxoisoindolin-2-yl)butylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



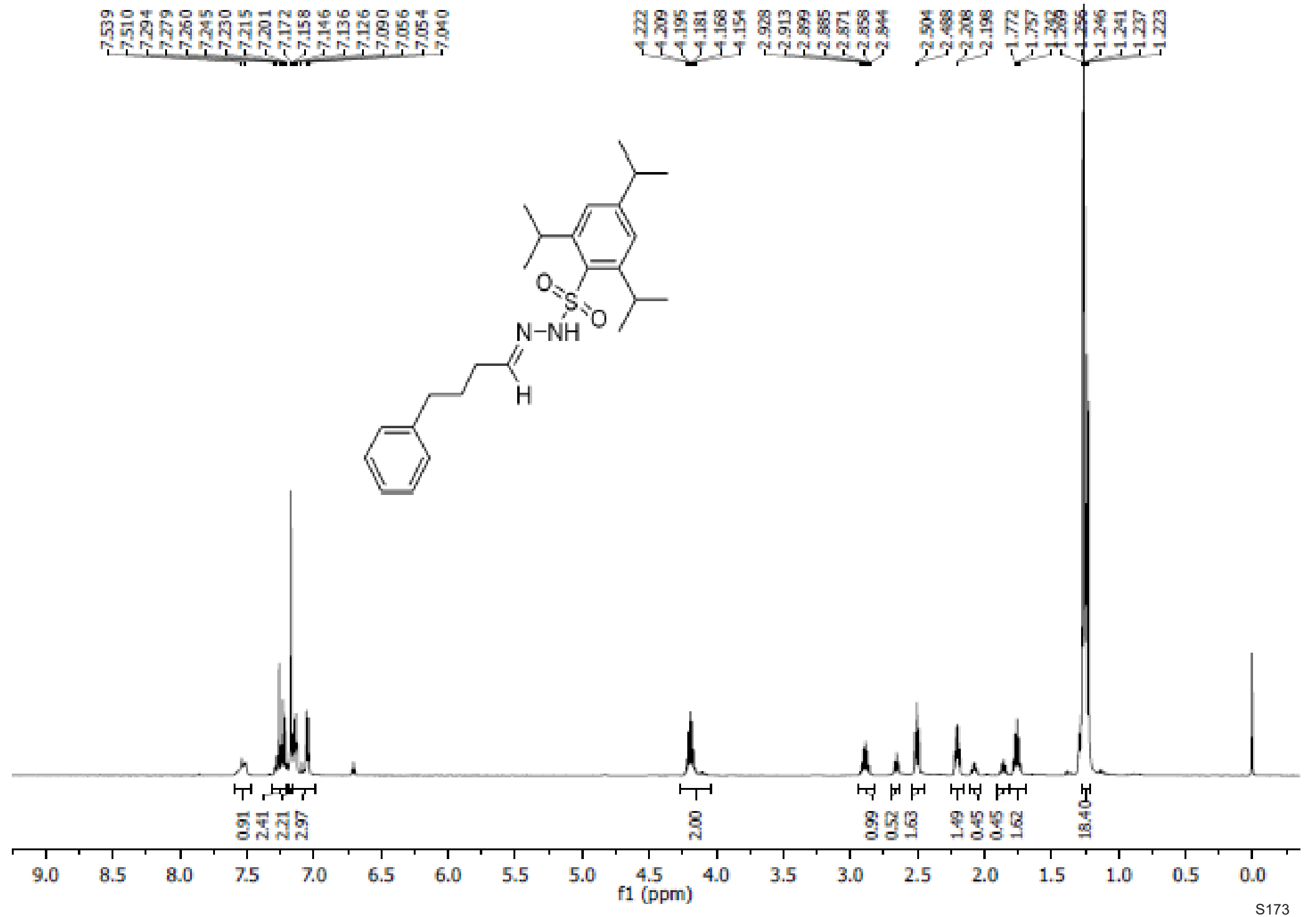
2,4,6-triisopropyl-N'-(3-phenylpropylidene)benzenesulfonohydrazide



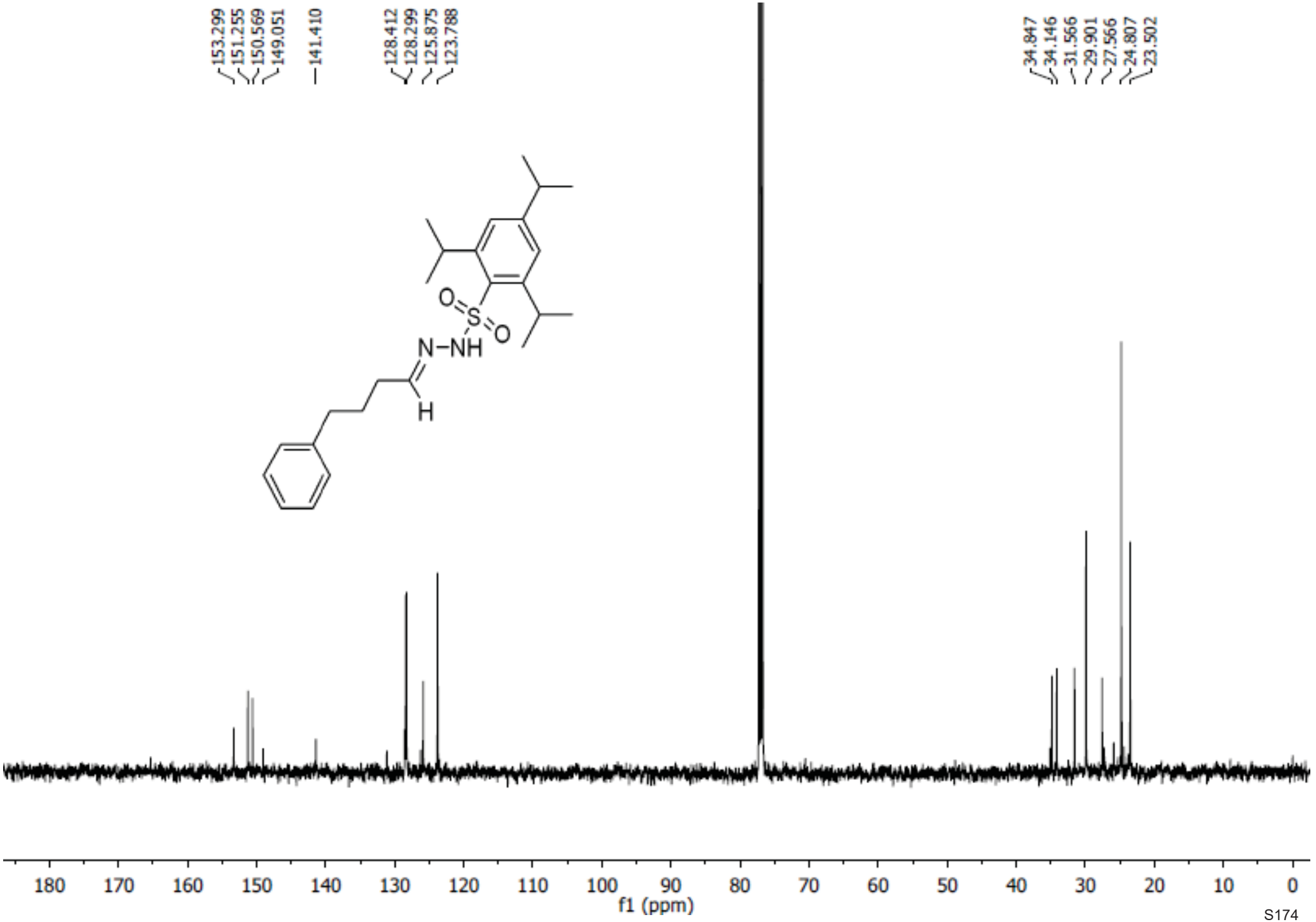
2,4,6-triisopropyl-N'-(3-phenylpropylidene)benzenesulfonohydrazide



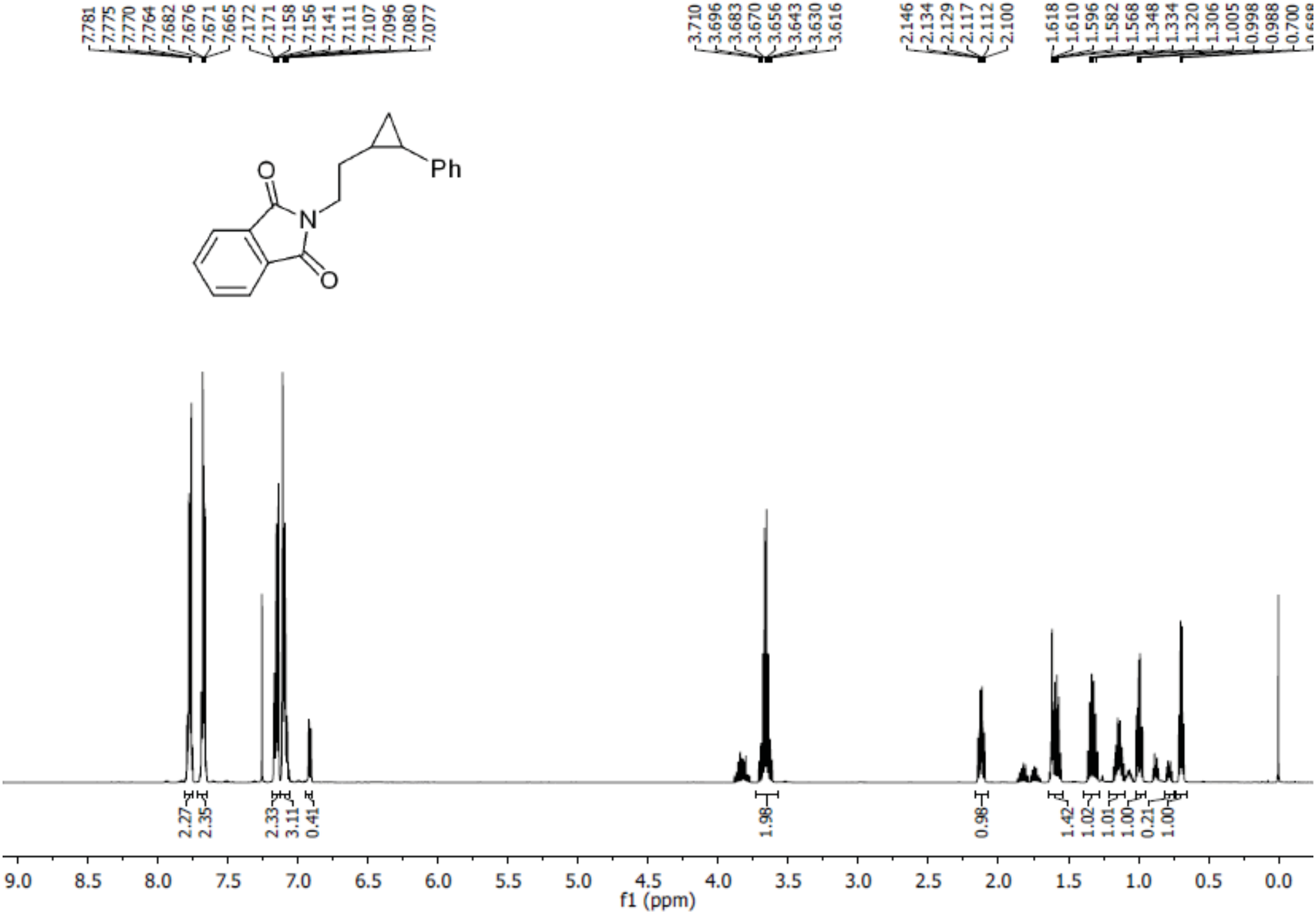
2,4,6-triisopropyl-N'-(4-phenylbutylidene)benzenesulfonohydrazide



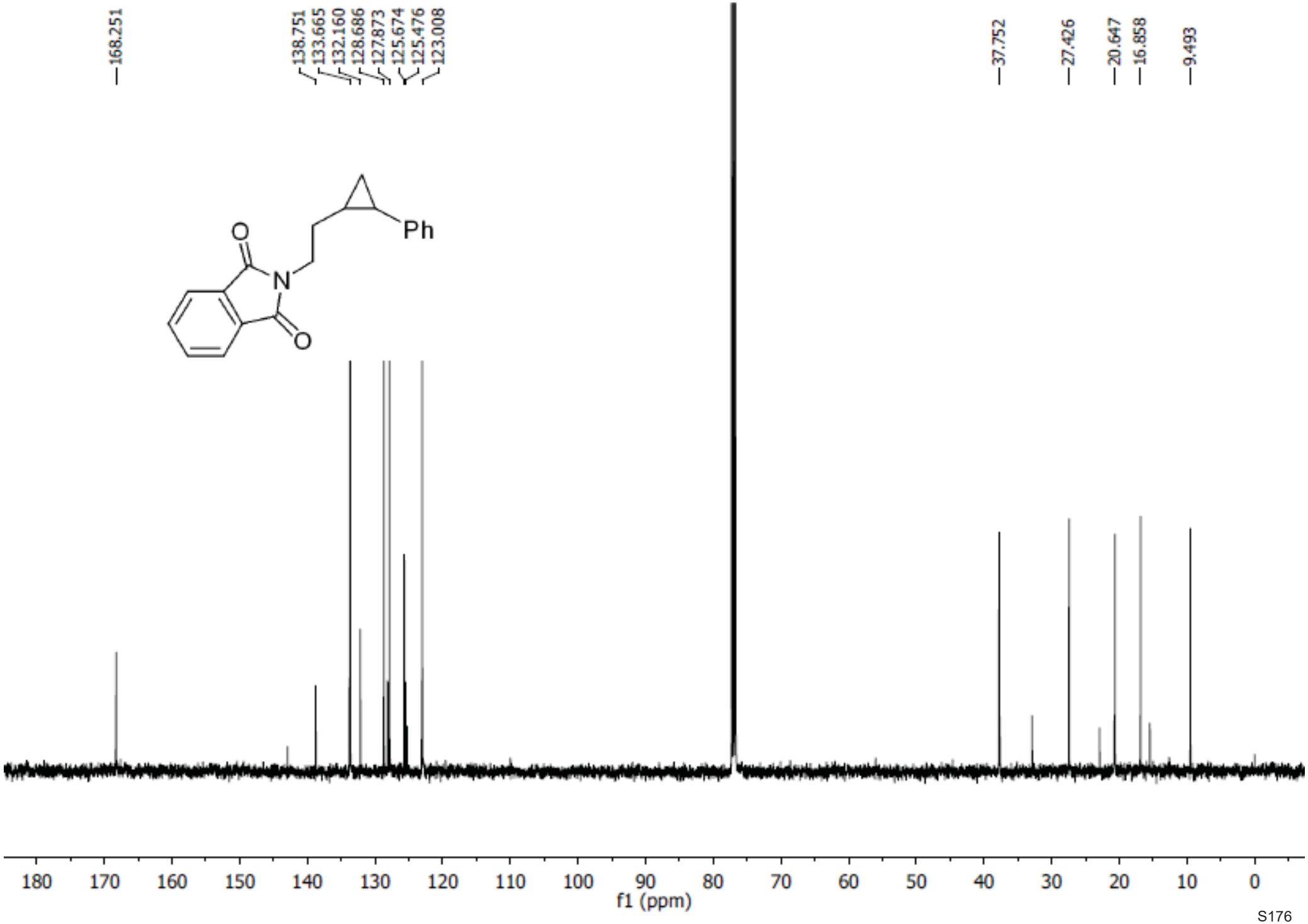
2,4,6-triisopropyl-N'-(4-phenylbutylidene)benzenesulfonohydrazide



2-(2-(2-phenylcyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-phenylcyclopropyl)ethyl)isoindoline-1,3-dione

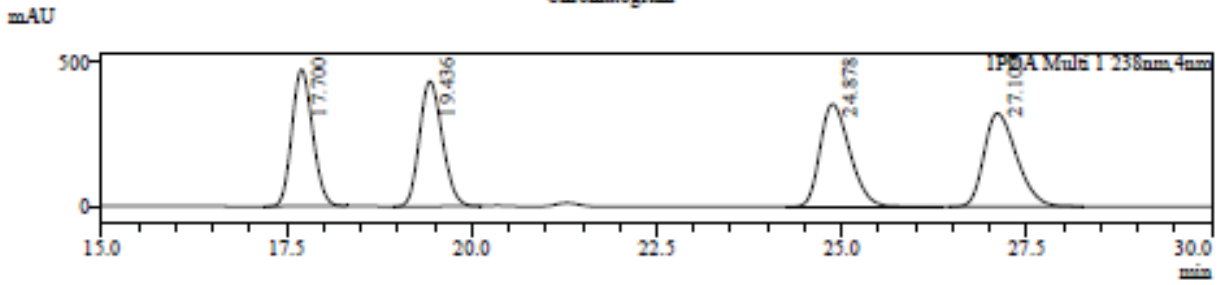


2-(2-(2-phenylcyclopropyl)ethyl)isoindoline-1,3-dione

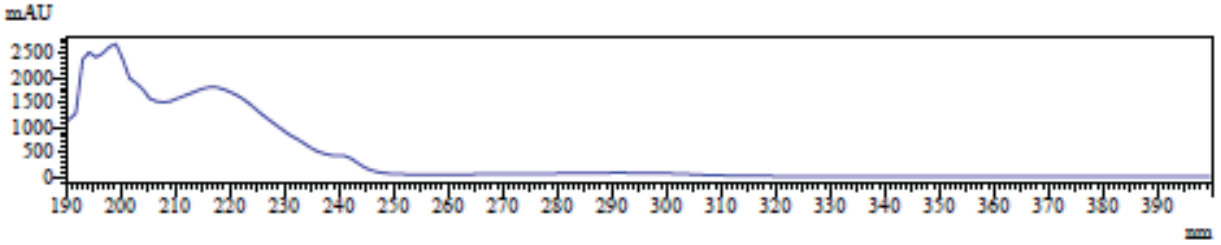
Sample Information

Data File	: Y0W-584-IE-10%0.8mL-iPrOH.lcd
Sample Name	: Y0W-584-IE-10%0.8mL-iPrOH
Sample ID	: Y0W-584-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

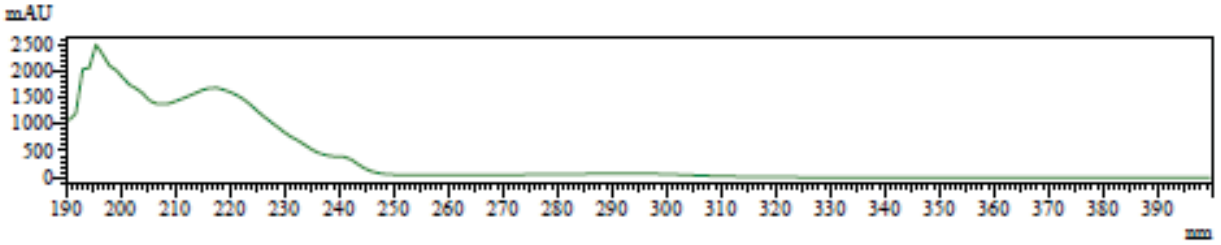
Chromatogram



UV Spectrum
Retention time = 17.700



UV Spectrum
Retention time = 19.436



Peak Table

PDA Ch1 238nm

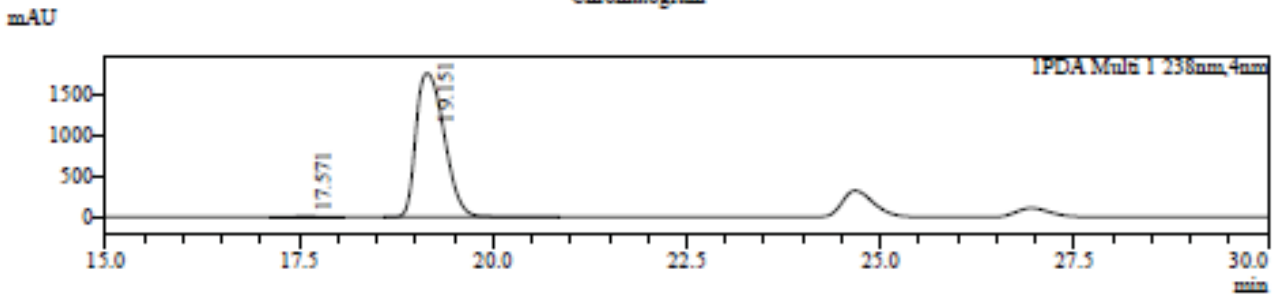
Peak#	Ret. Time	Area	Area%
1	17.700	9186978	24.068
2	19.436	9252327	24.239
3	24.878	9888392	25.905
4	27.109	9843491	25.788
Total		38171187	100.000

2-(2-(2-phenylcyclopropyl)ethyl)isoindoline-1,3-dione

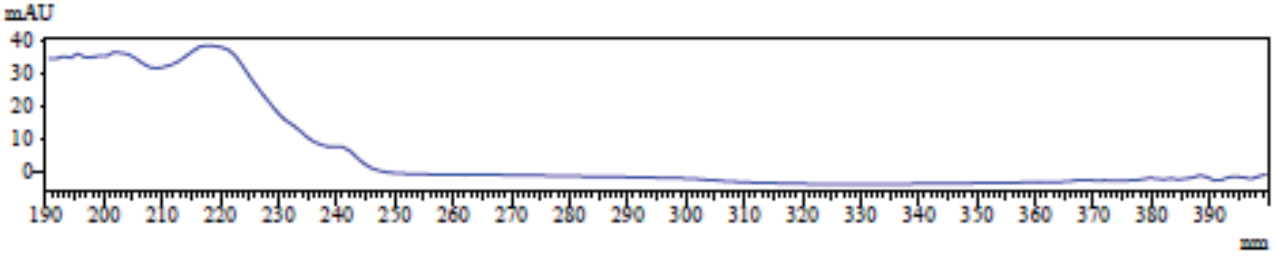
Sample Information

Data File	: Y0W-586-IE-10%0.8mL-iPrOH001.lcd
Sample Name	: Y0W-586-IE-10%0.8mL-iPrOH
Sample ID	: Y0W-586-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

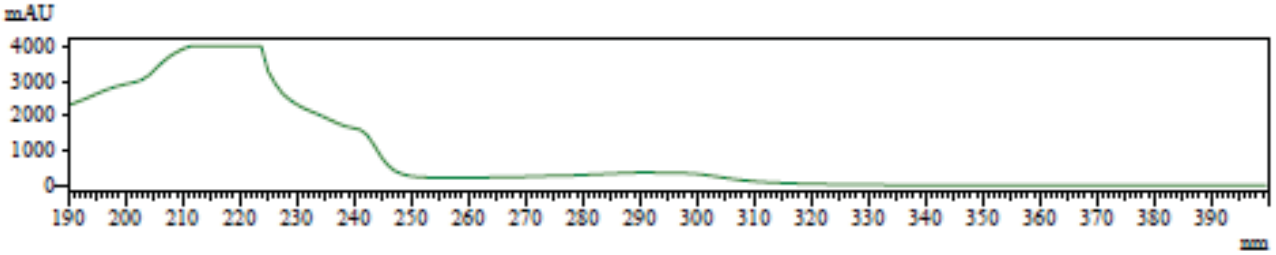
Chromatogram



UV Spectrum
Retention time = 17.571



UV Spectrum
Retention time = 19.151

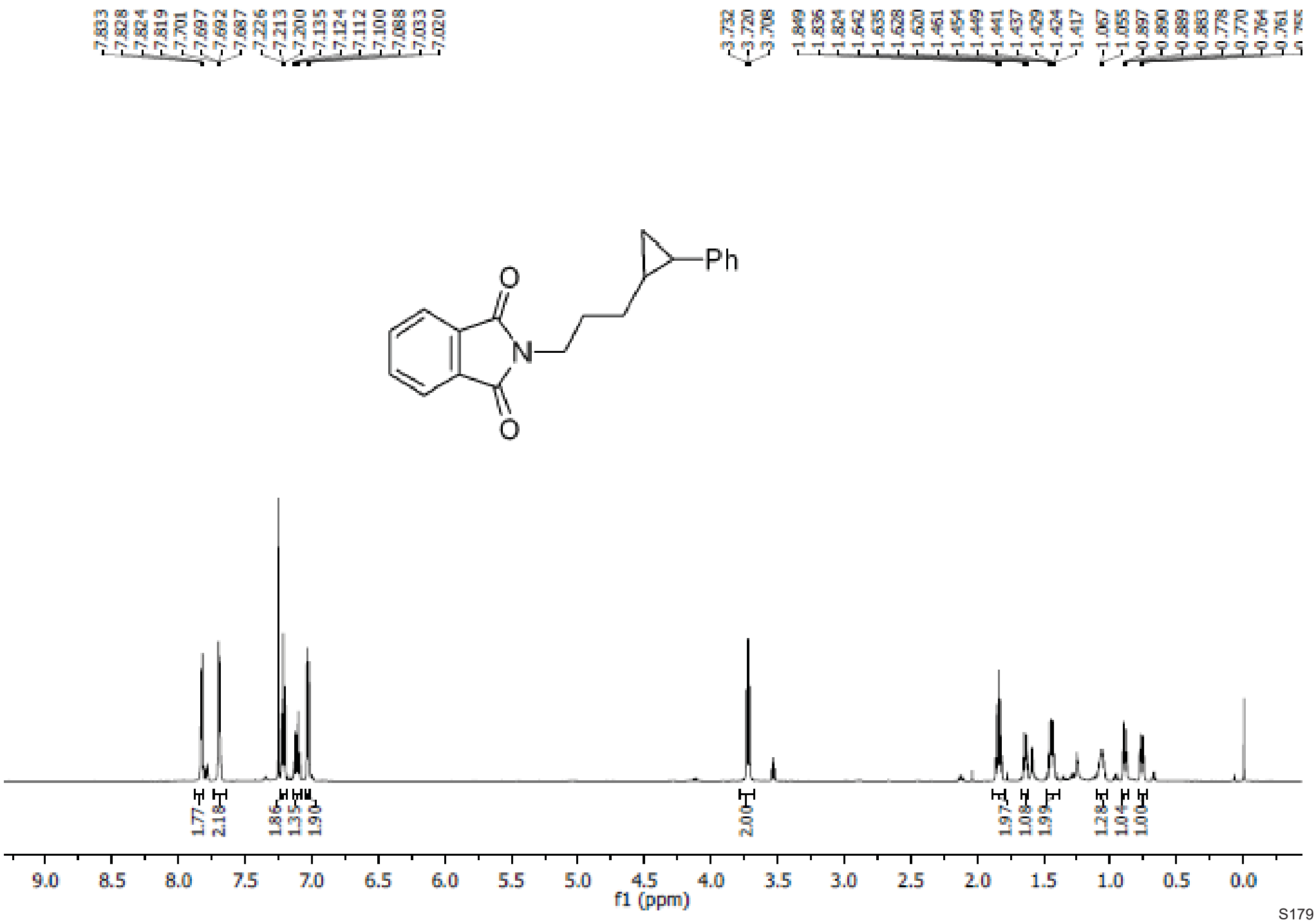


Peak Table

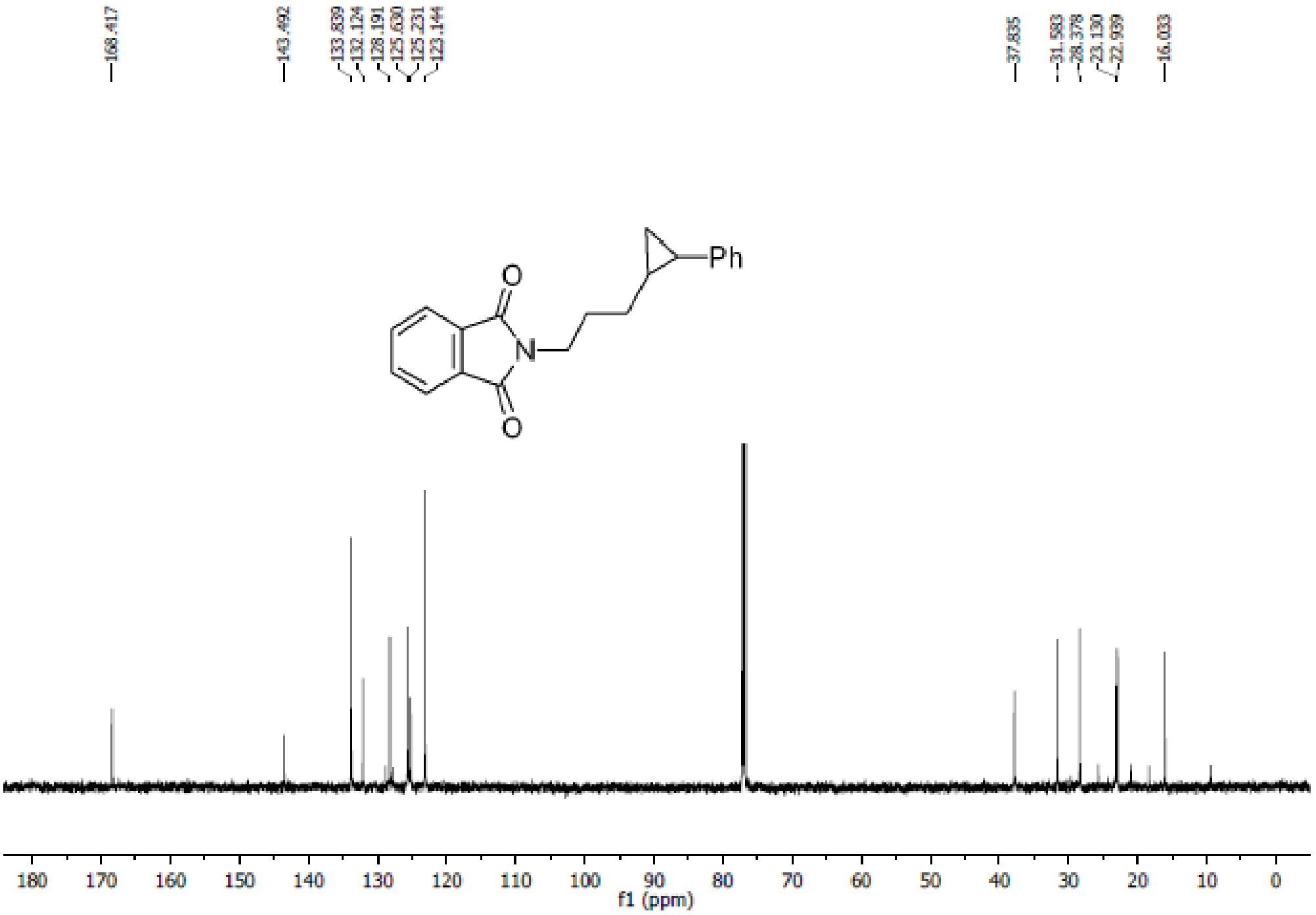
PDA Ch1 238nm

Peak#	Ret. Time	Area	Area%
1	17.571	183516	0.409
2	19.151	44674969	99.591
Total		44858485	100.000

2-(3-(2-phenylcyclopropyl)propyl)isoindoline-1,3-dione



2-(3-(2-phenylcyclopropyl)propyl)isoindoline-1,3-dione

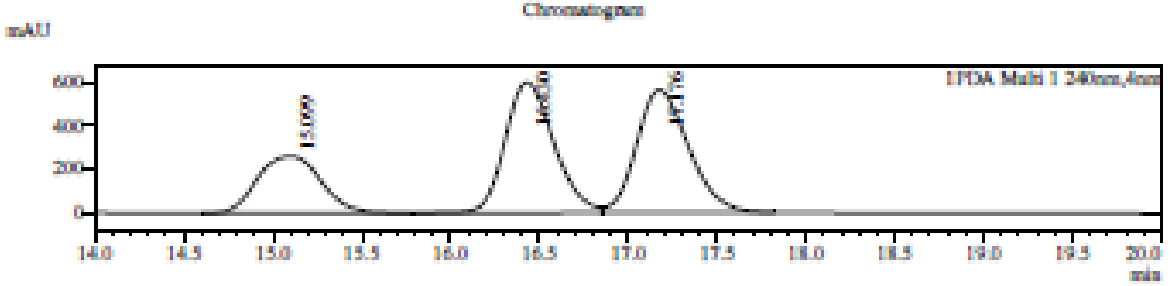


2-(3-(2-phenylcyclopropyl)propyl)isoindoline-1,3-dione

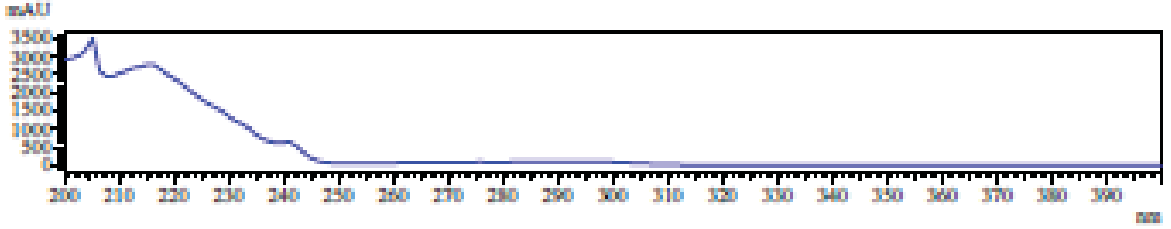
Sample Information

Data File	: Y0W-812-IB-5%0.8mL-iPrOH.lcd
Sample Name	: Y0W-812-IB-5%0.8mL-iPrOH
Sample ID	: Y0W-812-IB-5%0.8mL-iPrOH
Method File	: YW-5.0%-0.8ml.lcm

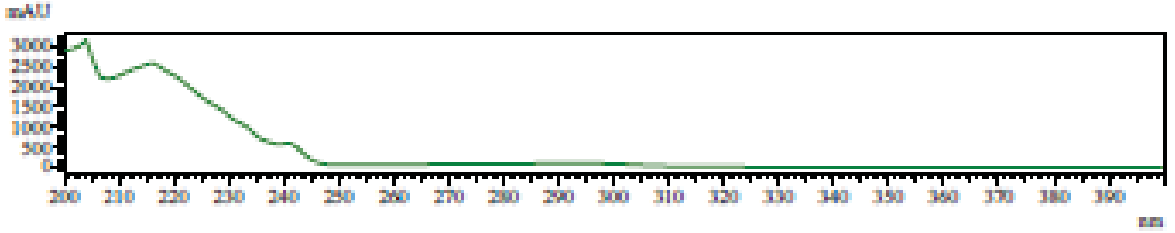
Chromatogram



UV Spectrum
Retention time = 16.430



UV Spectrum
Retention time = 17.176



Peak Table

PDA Ch1 240nm

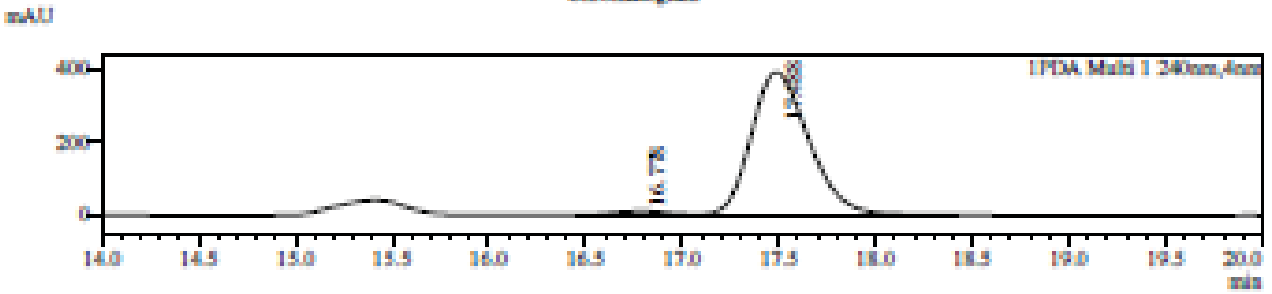
Peak#	Ret. Time	Area	Area%
1	15.099	6416012	21.989
2	16.430	11383375	39.014
3	17.176	11378344	38.997
Total		29177732	100.000

2-(3-(2-phenylcyclopropyl)propyl)isoindoline-1,3-dione

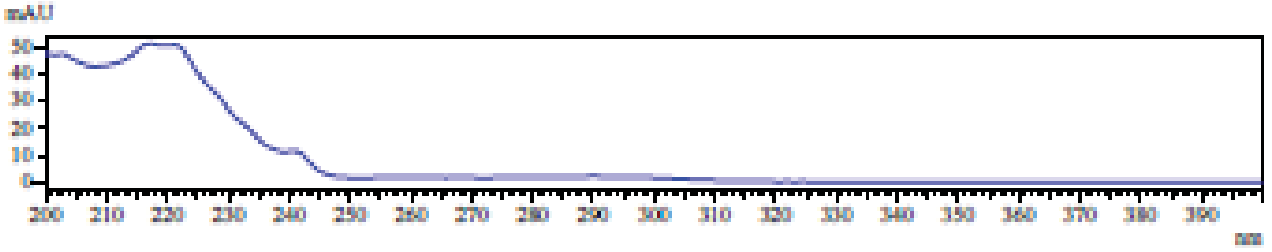
Sample Information

Data File	: Y0W-813-IB-5%0.8mL-iPrOH.lcd
Sample Name	: Y0W-813-IB-5%0.8mL-iPrOH
Sample ID	: Y0W-813-IB-5%0.8mL-iPrOH
Method File	: YW-5.0%-0.8ml.lcm

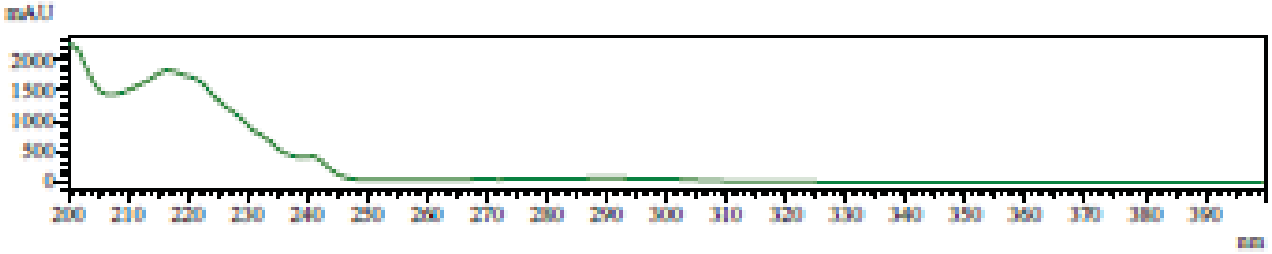
Chromatogram



UV Spectrum
Retention time = 16.778



UV Spectrum
Retention time = 17.488

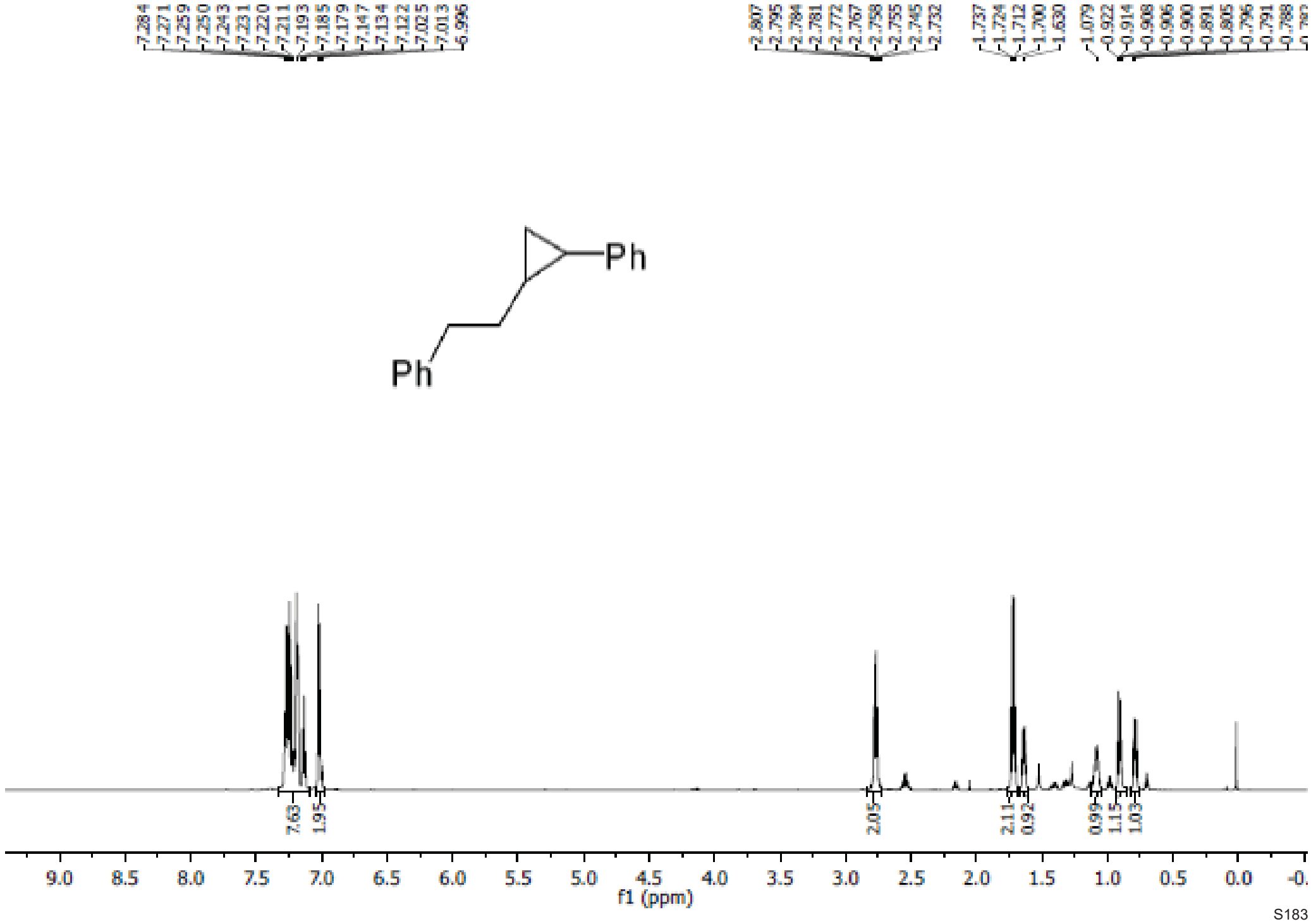


Peak Table

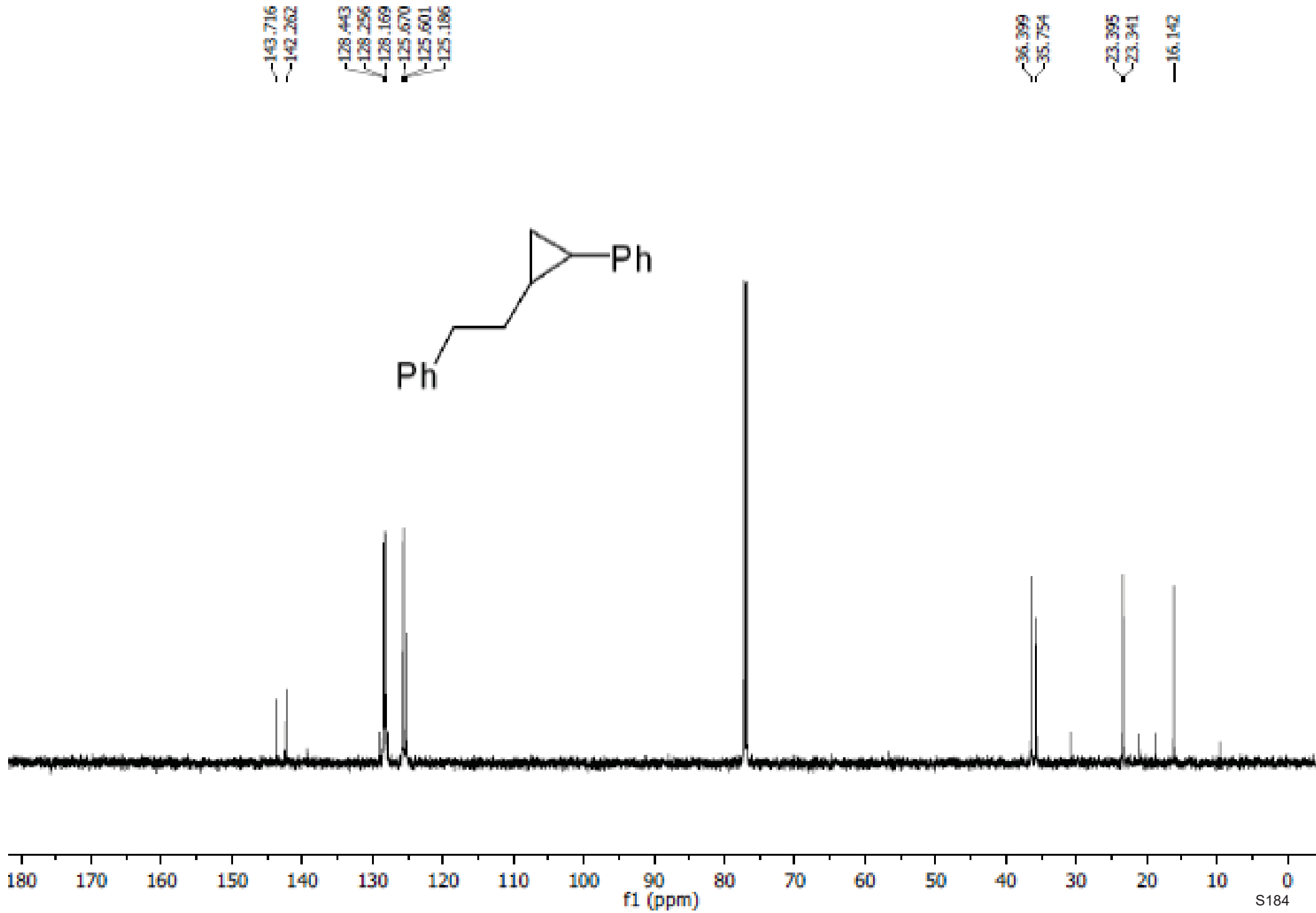
PDA Ch1 240nm

Peak#	Ret. Time	Area	Area%
1	16.778	194781	2.366
2	17.488	8036372	97.634
Total		8231153	100.000

(2-phenethylcyclopropyl)benzene



(2-phenethylcyclopropyl)benzene

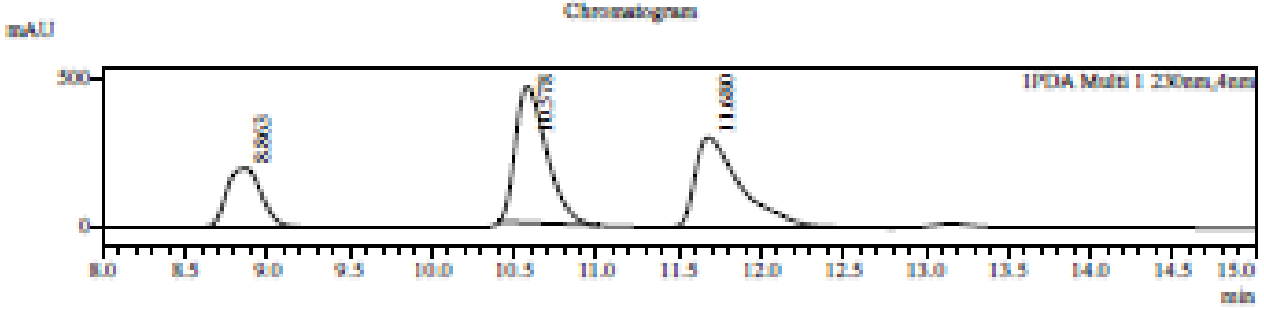


(2-phenethylcyclopropyl)benzene

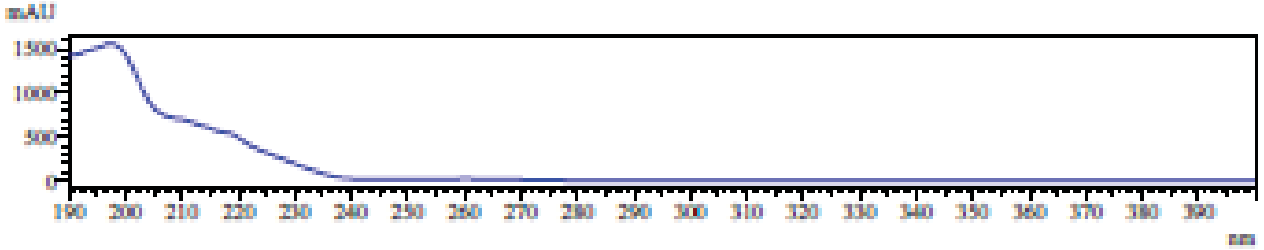
Sample Information

Data File	: SWE-0002-IA-0%-0.6mL-hexane.lcd
Sample Name	: SWE-0002-IA-0%-0.6mL-hexane
Sample ID	: SWE-0002-IA-0%-0.6mL-hexane
Method File	: SWE-0%-0.6ml.lcm

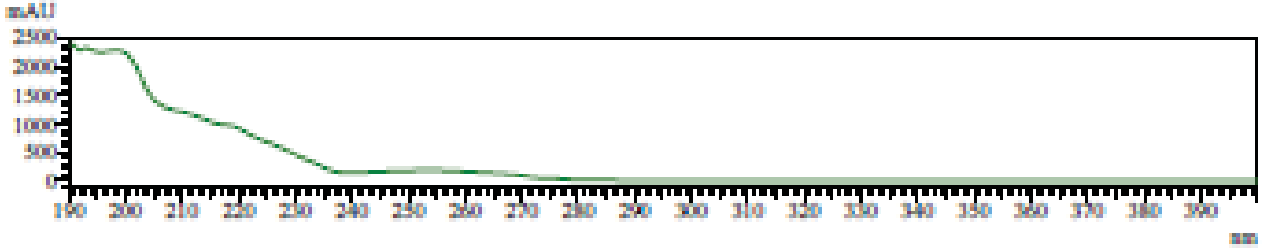
Chromatogram



UV Spectrum
Retention time = 8.863



UV Spectrum
Retention time = 10.578



Peak Table

PDA Ch1 230nm

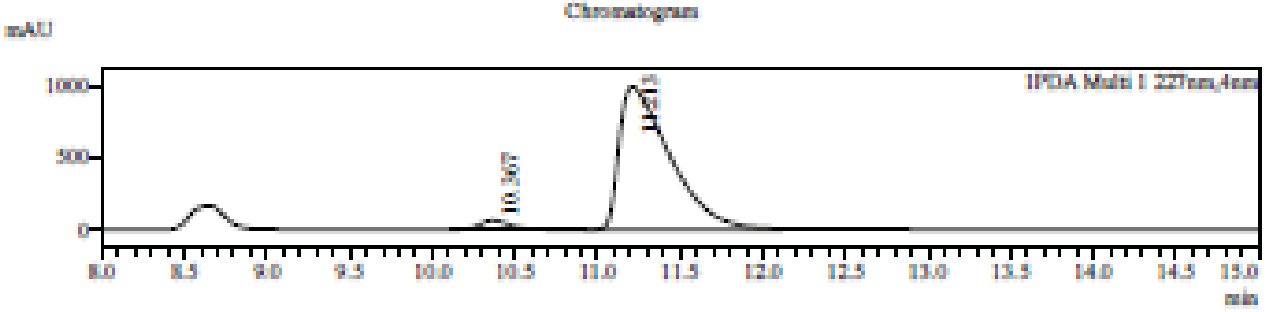
Peak#	Ret. Time	Area	Area%
1	8.863	2858436	19.566
2	10.578	5976276	40.908
3	11.680	5774528	39.527
Total		14609240	100.000

(2-phenethylcyclopropyl)benzene

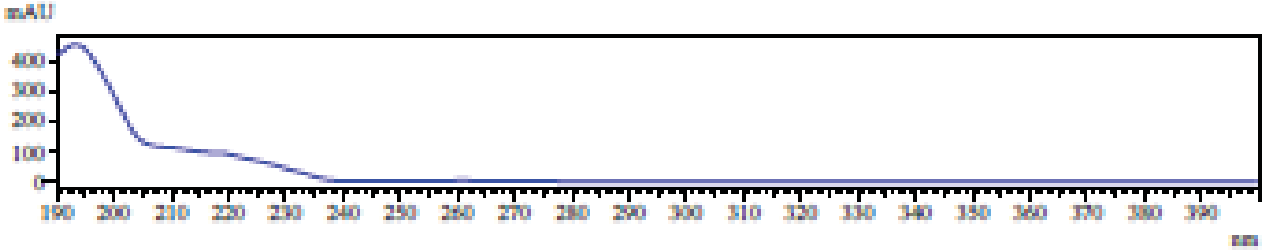
Sample Information

Data File	: SWE-0043-1A-0%-0.6mL-hexane001.lcd
Sample Name	: SWE-0043-1A-0%-0.6mL-hexane001
Sample ID	: SWE-0043-1A-0%-0.6mL-hexane001
Method File	: SWE-0%-0.6ml.lcm

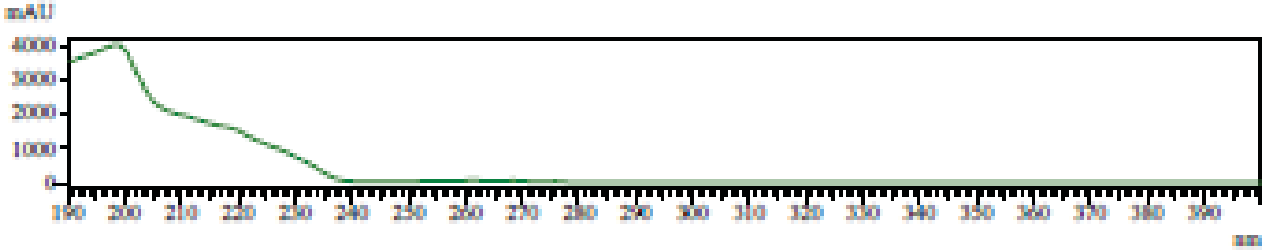
Chromatogram



UV Spectrum
Retention time = 10.367



UV Spectrum
Retention time = 11.213

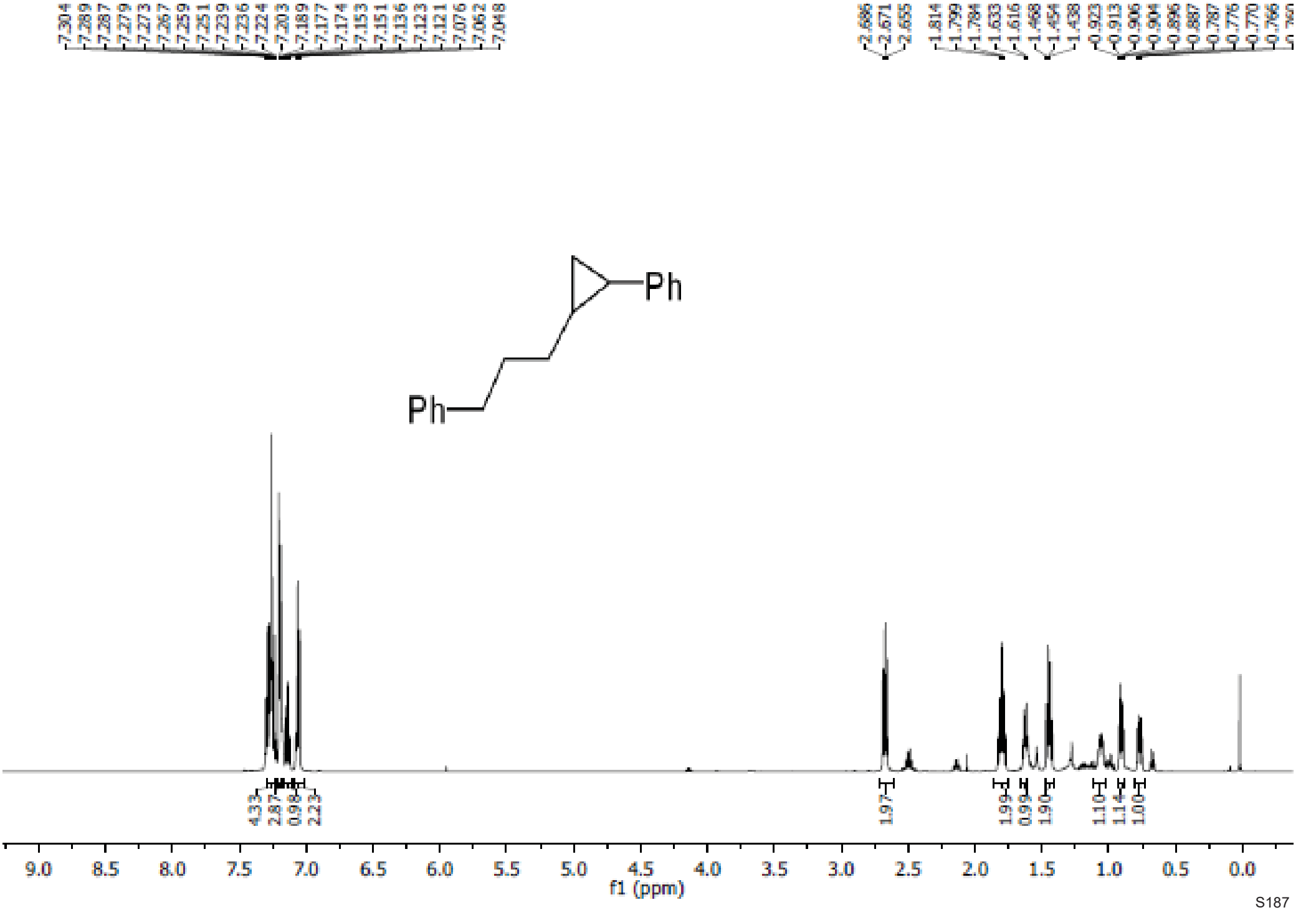


Peak Table

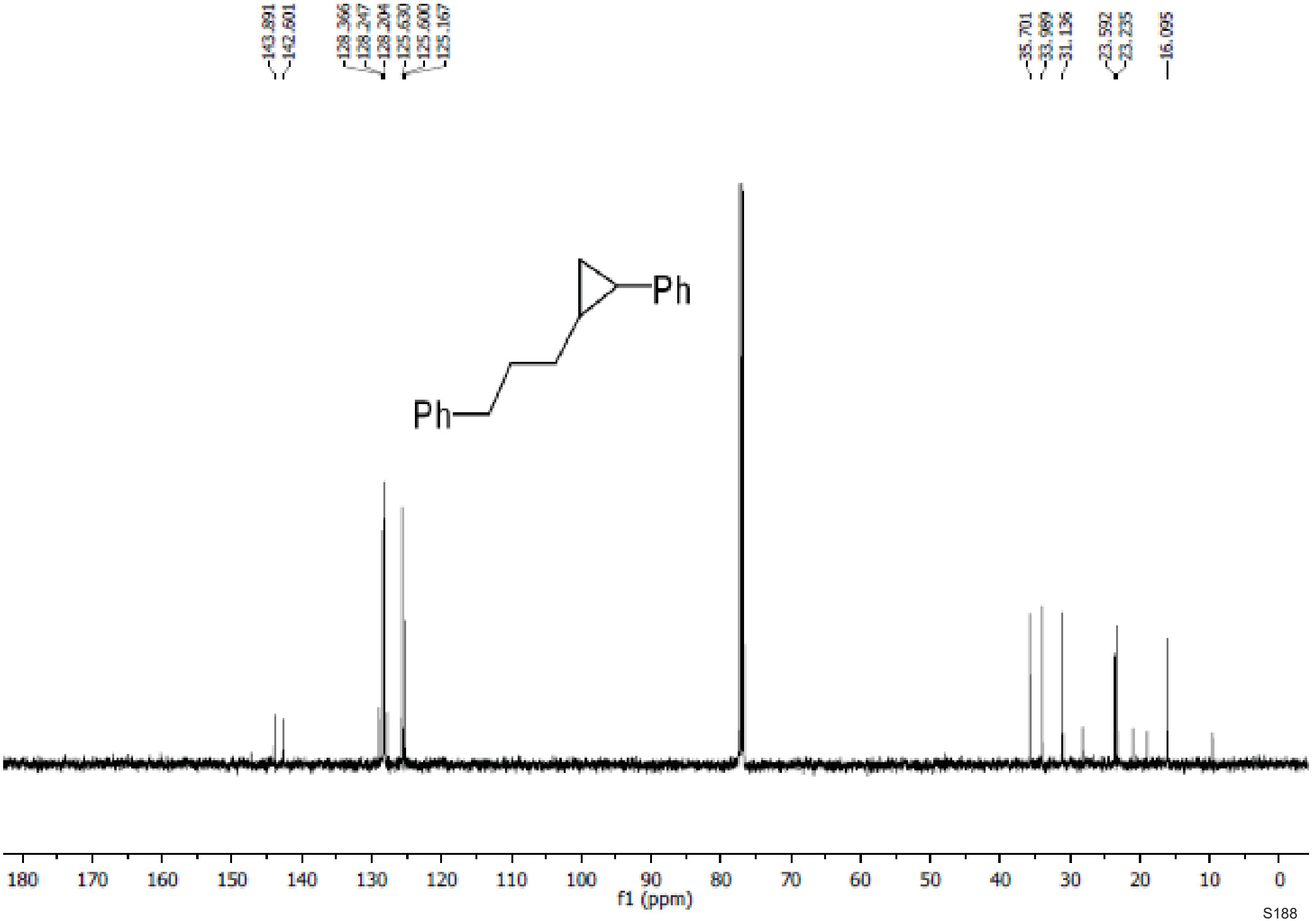
PDA Ch1 227nm

Peak#	Ret. Time	Area	Area%
1	10.367	723713	3.314
2	11.213	21113881	96.686
Total		21837593	100.000

(3-(2-phenylcyclopropyl)propyl)benzene



(3-(2-phenylcyclopropyl)propyl)benzene

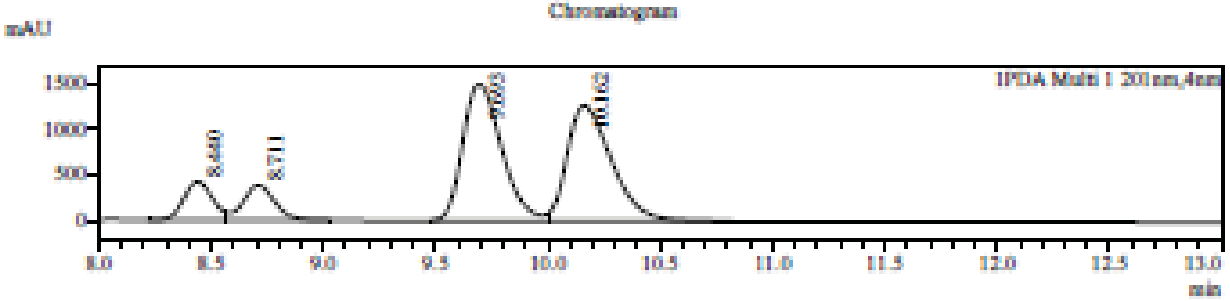


(3-(2-phenylcyclopropyl)propyl)benzene

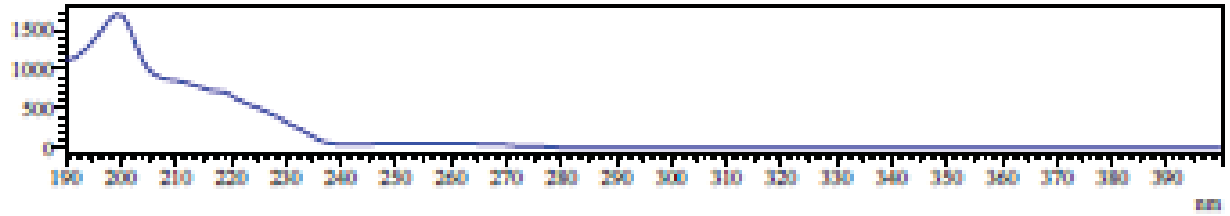
Sample Information

Data File	: Y0W-822-1A-0%1.2mL-hexane.lcd
Sample Name	: Y0W-822-1A-0%1.2mL-hexane
Sample ID	: Y0W-822-1A-0%1.2mL-hexane
Method File	: YW-0%-1.2ml.lcm

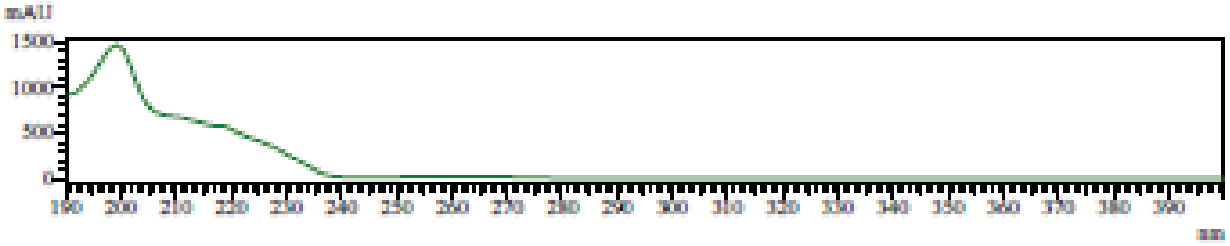
Chromatogram



UV Spectrum
Retention time = 9.693



UV Spectrum
Retention time = 10.162



Peak Table

PDA Ch1 201nm

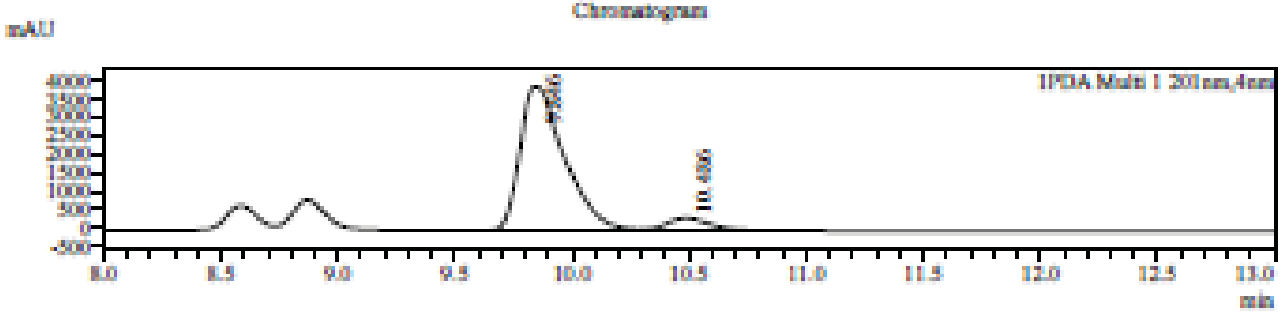
Peak#	Ret. Time	Area	Area%
1	8.440	3681723	8.685
2	8.711	3674083	8.667
3	9.693	17890264	42.205
4	10.162	17143353	40.443
Total		42389423	100.000

(3-(2-phenylcyclopropyl)propyl)benzene

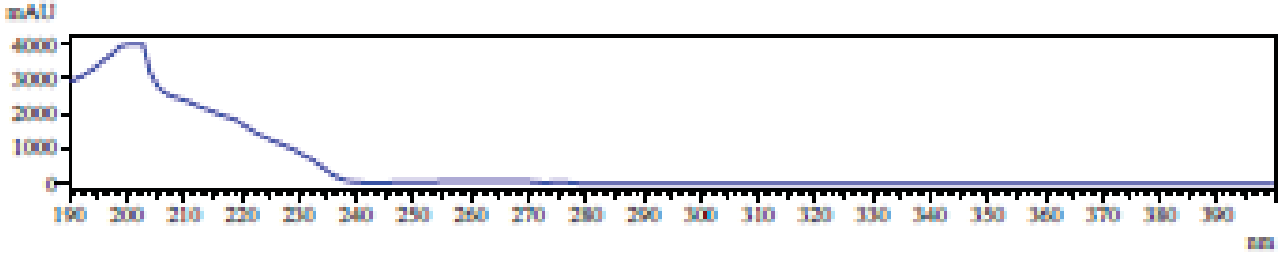
Sample Information

Data File	: Y0W-823-IA-0%1.2mL-hexane.lcd
Sample Name	: Y0W-823-IA-0%1.2mL-hexane
Sample ID	: Y0W-823-IA-0%1.2mL-hexane
Method File	: YW-0%-1.2ml.lcm

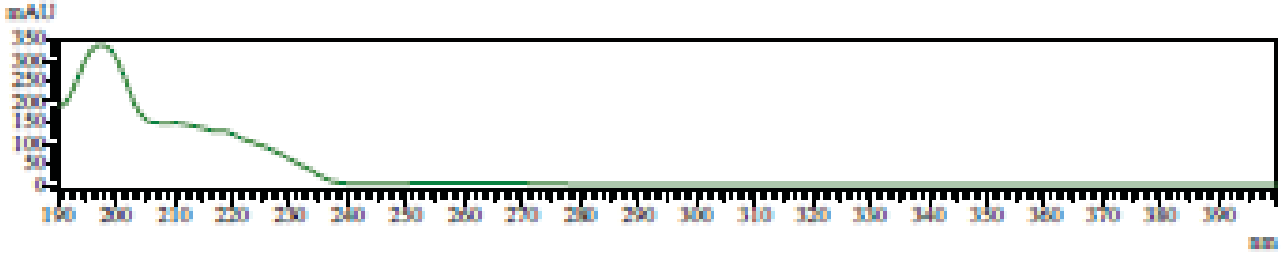
Chromatogram



UV Spectrum
Retention time = 9.846



UV Spectrum
Retention time = 10.486

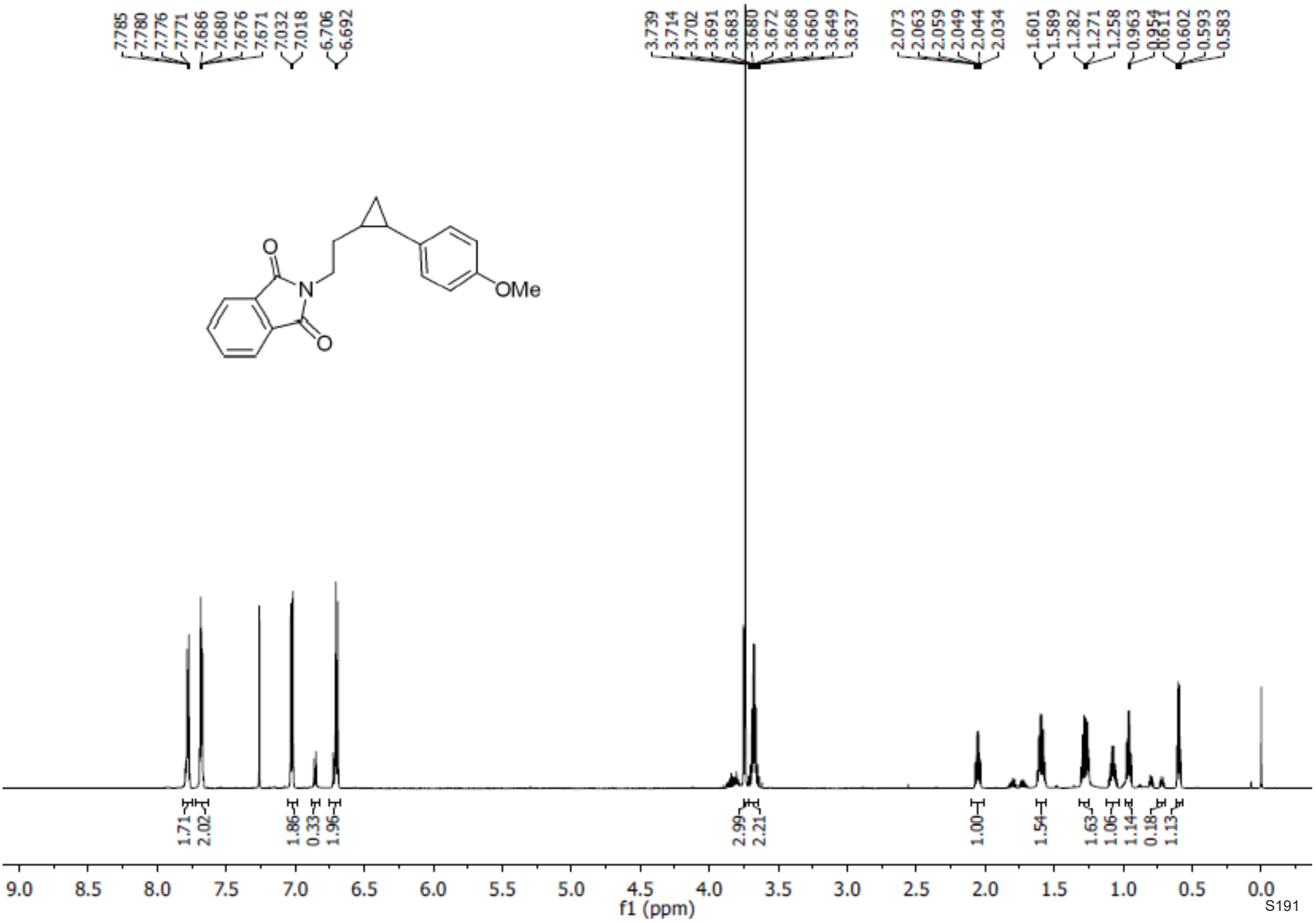


Peak Table

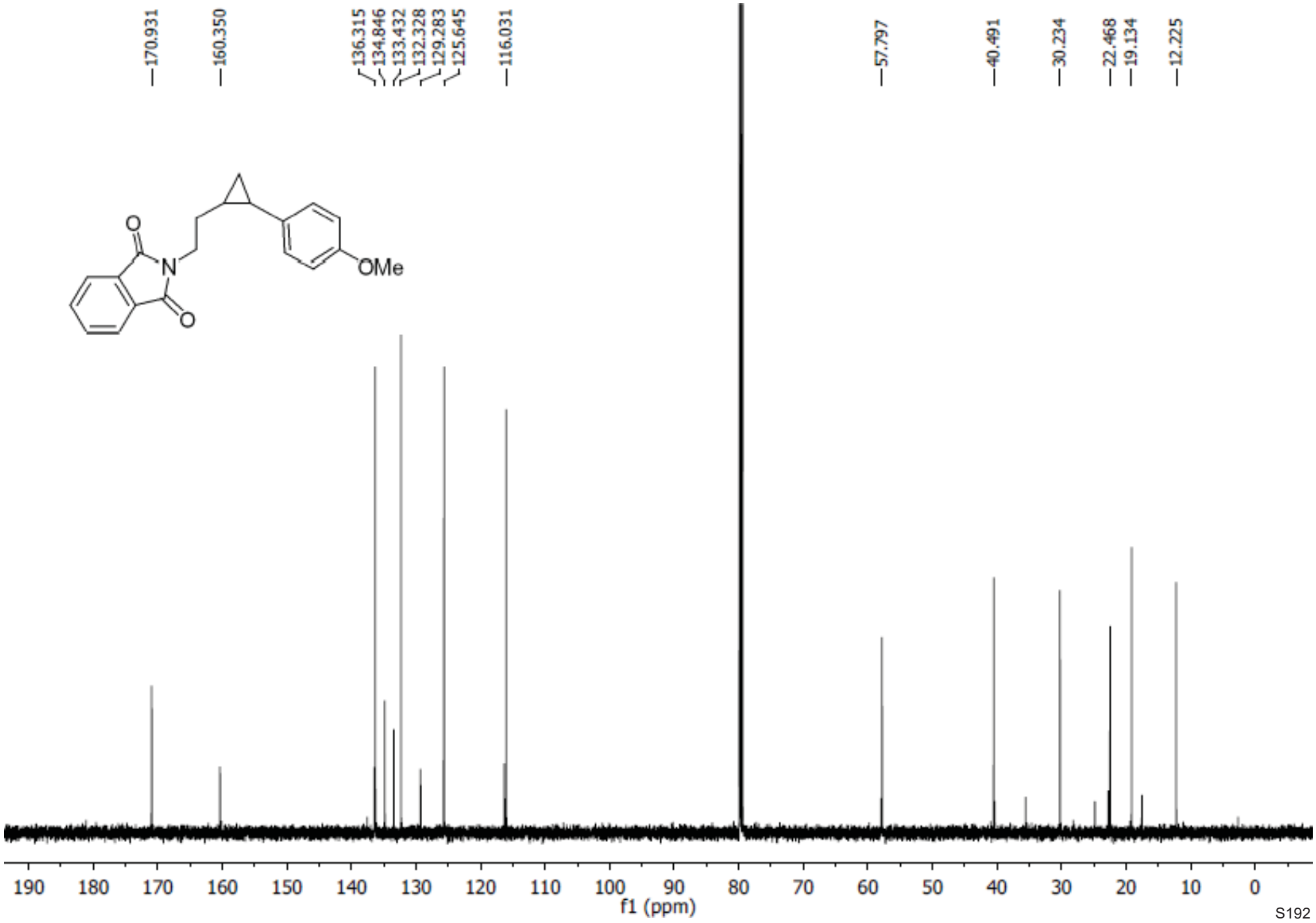
PDA Ch1 201nm

Peak#	Ret. Time	Area	Area%
1	9.846	51429985	92.069
2	10.486	4430289	7.931
Total		55860274	100.000

2-(2-(2-(4-methoxyphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(4-methoxyphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

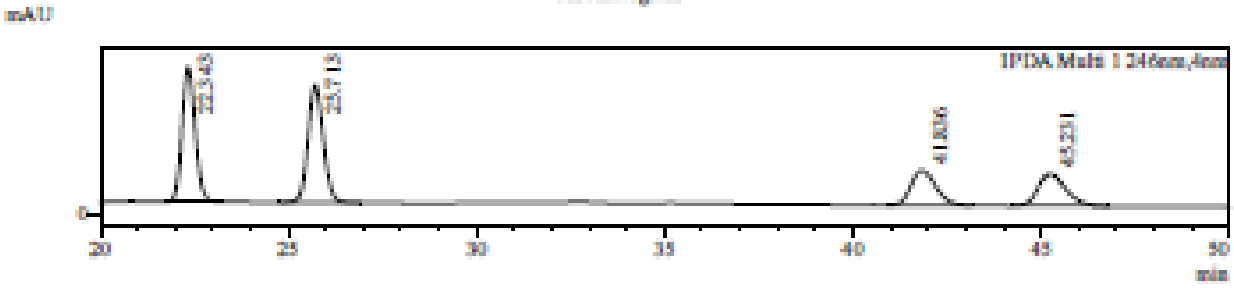


2-(2-(2-(4-methoxyphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

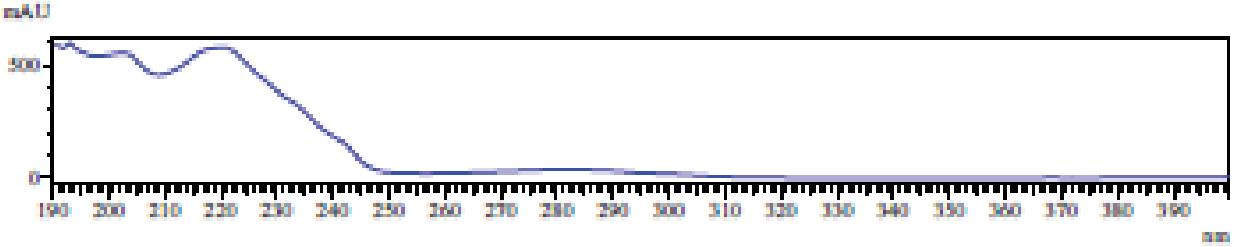
Sample Information

Data File	: YOW-610-IE-10%0.8mL-iPrOH001.lcd
Sample Name	: YOW-610-IE-10%0.8mL-iPrOH
Sample ID	: YOW-610-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

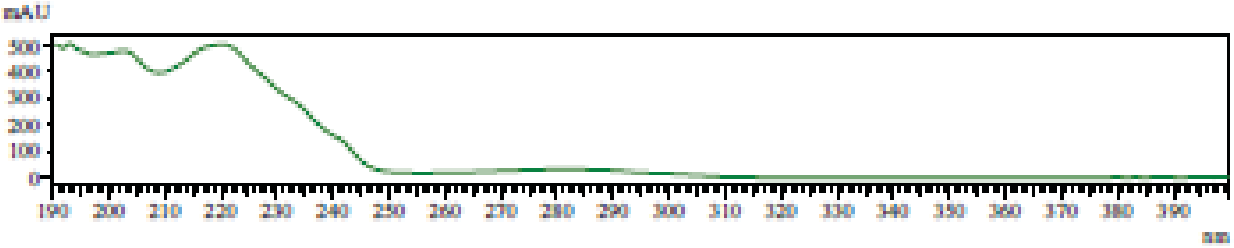
Chromatogram



UV Spectrum
Retention time = 22.343



UV Spectrum
Retention time = 25.713



Peak Table

PDA Ch1 246nm

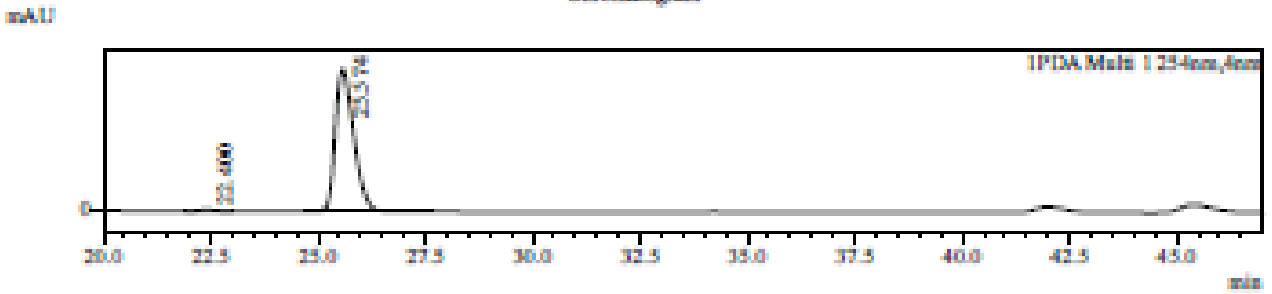
Peak#	Ret. Time	Area	Area%
1	22.343	1550995	33.528
2	25.713	1573812	34.021
3	41.836	737786	15.949
4	45.231	763434	16.503
Total		4626026	100.000

2-(2-(2-(4-methoxyphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

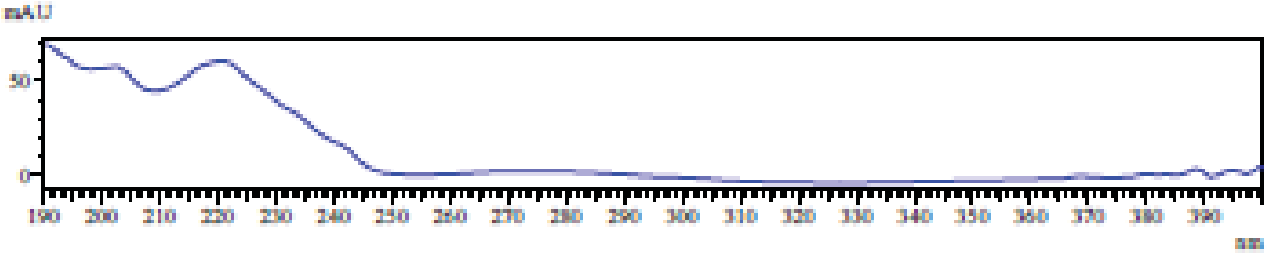
Sample Information

Data File	: YOW-611-IE-10%0.8mL-iPrOH001.lcd
Sample Name	: YOW-611-IE-10%0.8mL-iPrOH
Sample ID	: YOW-611-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.1cm

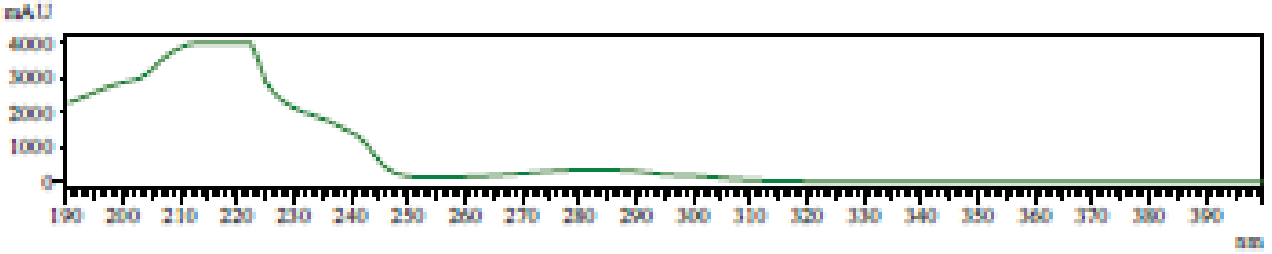
Chromatogram



UV Spectrum
Retention time = 22.400



UV Spectrum
Retention time = 25.574

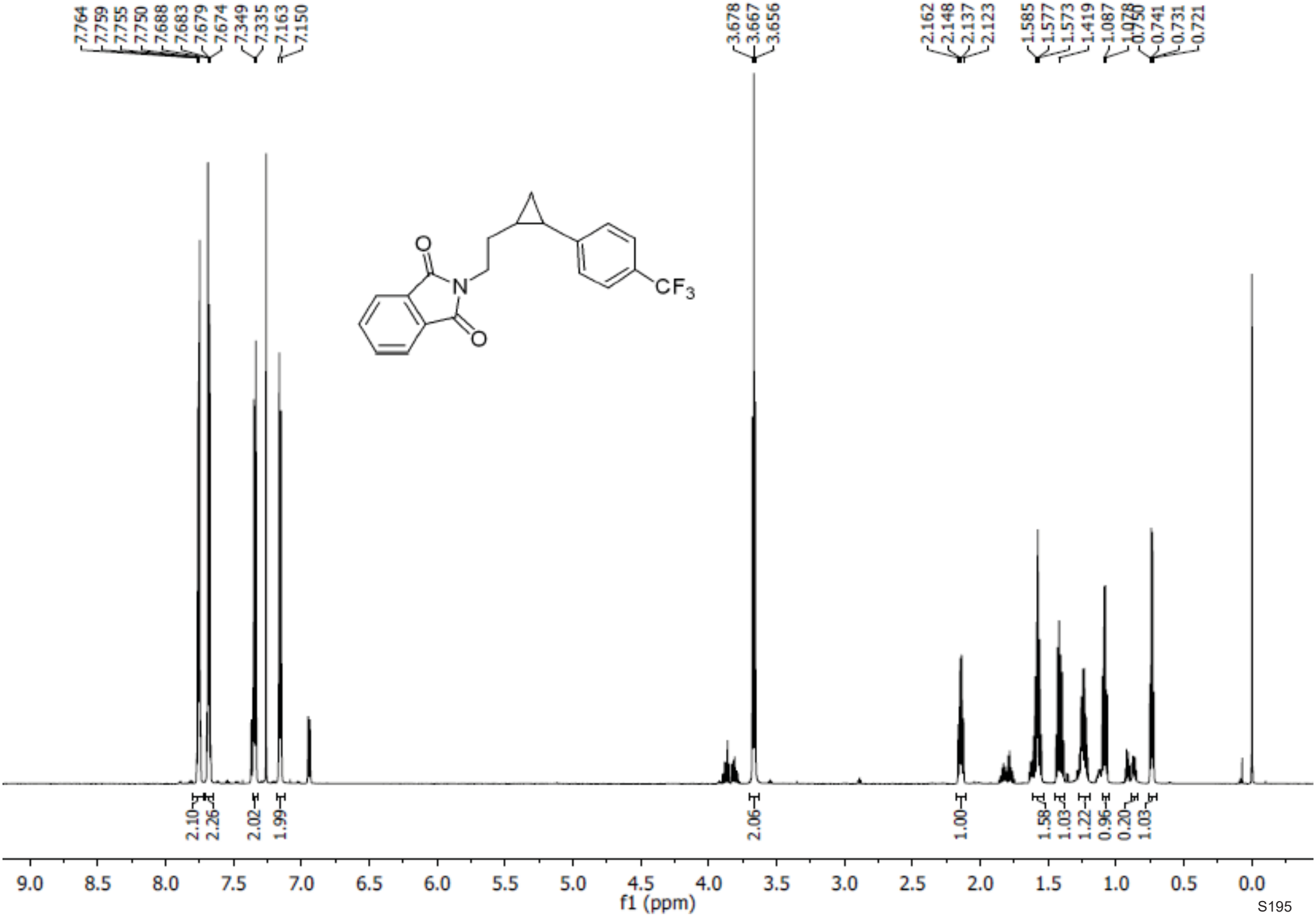


Peak Table

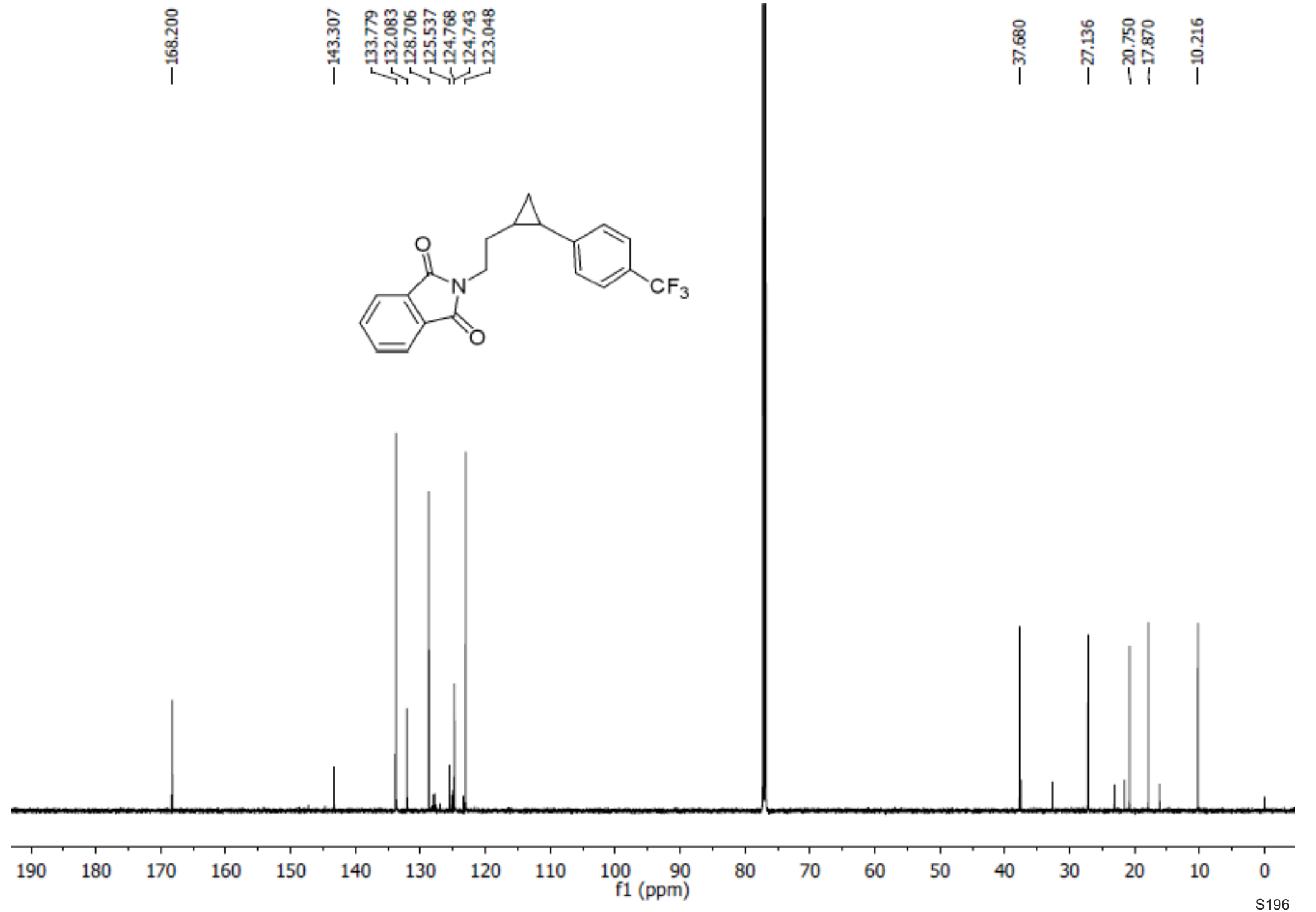
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	22.400	49022	1.134
2	25.574	4275156	98.866
Total		4324178	100.000

2-(2-(2-(4-trifluoromethylphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(4-trifluoromethylphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

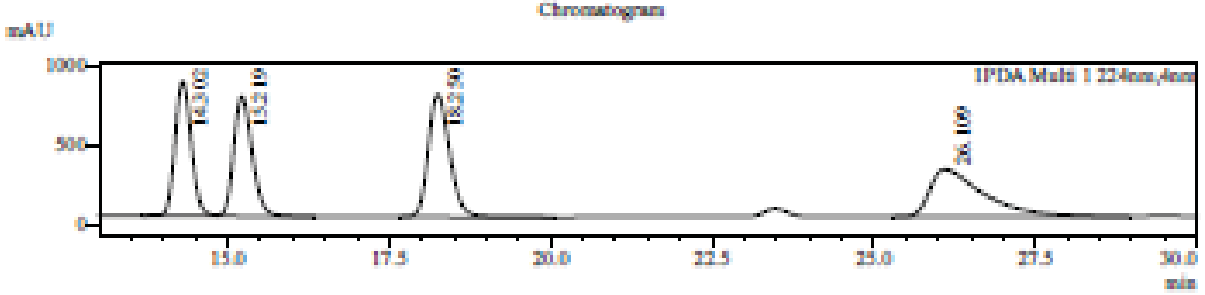


2-(2-(2-(4-trifluoromethylphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

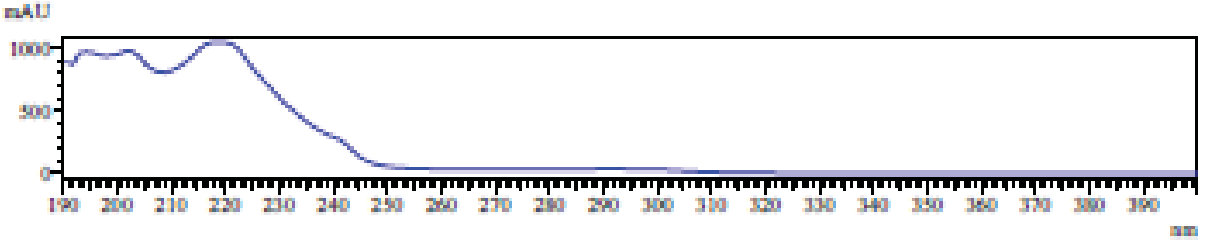
Sample Information

Data File	: YOW-625-ID-10%0.8mL-iPrOH1.lcd
Sample Name	: YOW-625-ID-10%0.8mL-iPrOH
Sample ID	: YOW-625-ID-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.1cm

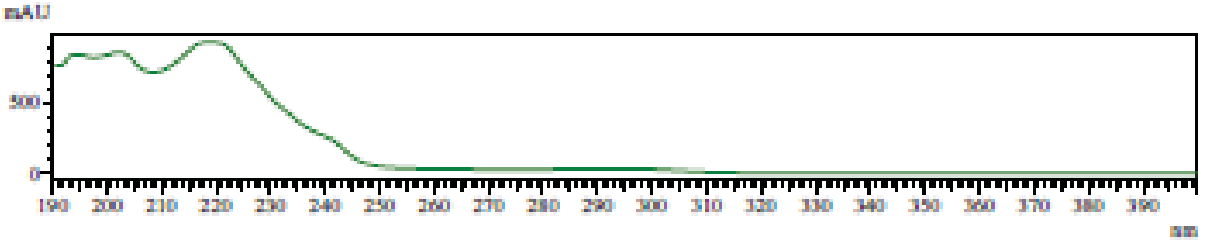
Chromatogram



UV Spectrum
Retention time = 14.302



UV Spectrum
Retention time = 15.219



Peak Table

PDA Ch1 224nm

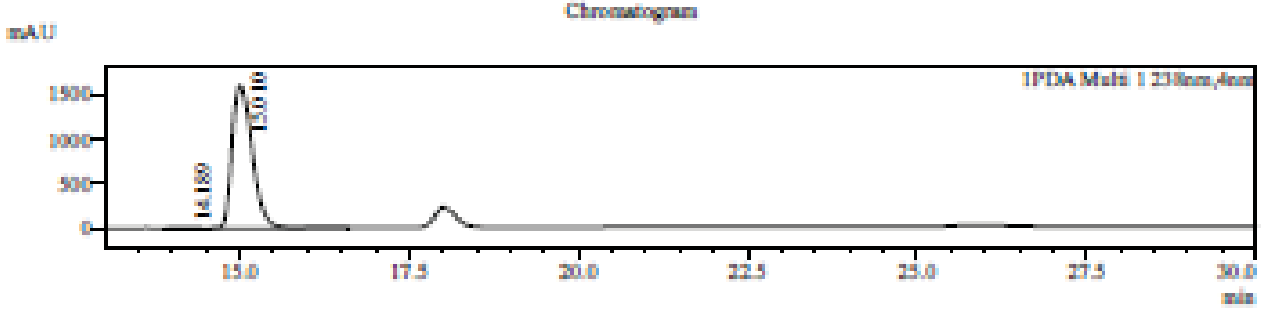
Peak#	Ret. Time	Area	Area%
1	14.302	14879233	22.794
2	15.219	14970210	22.934
3	18.250	17792355	27.257
4	26.109	17634549	27.015
Total		65276348	100.000

2-(2-(2-(4-trifluoromethylphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

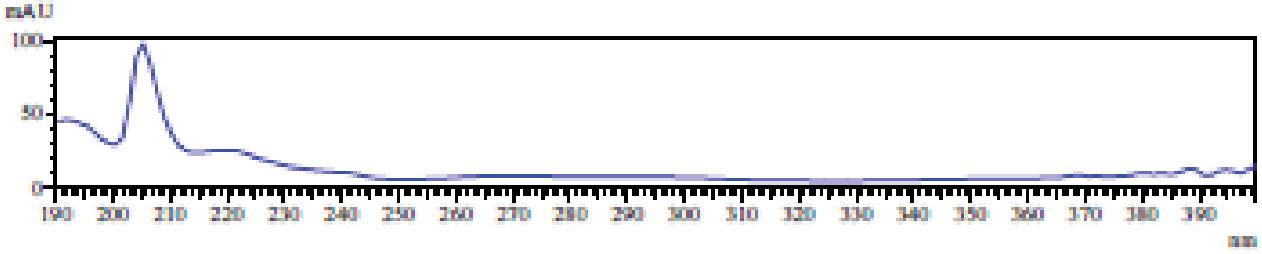
Sample Information

Data File	: YOW-626-ID-10%0.8mL-iPrOH.lcd
Sample Name	: YOW-626-ID-10%0.8mL-iPrOH
Sample ID	: YOW-626-ID-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

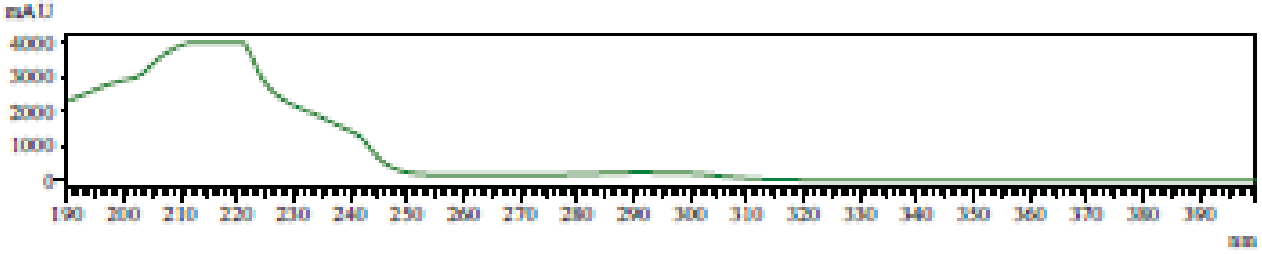
Chromatogram



UV Spectrum
Retention time = 14.189



UV Spectrum
Retention time = 15.010

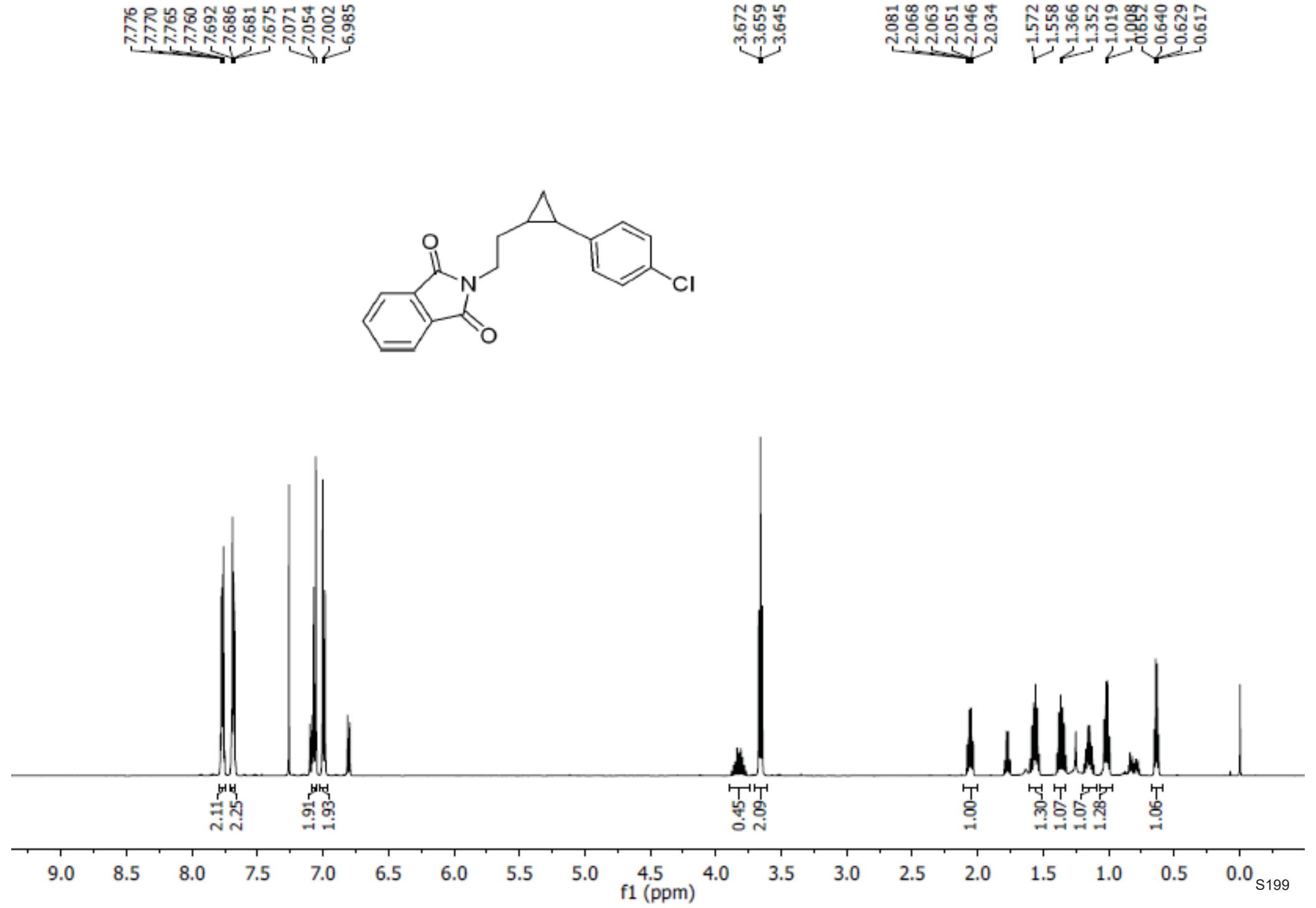


Peak Table

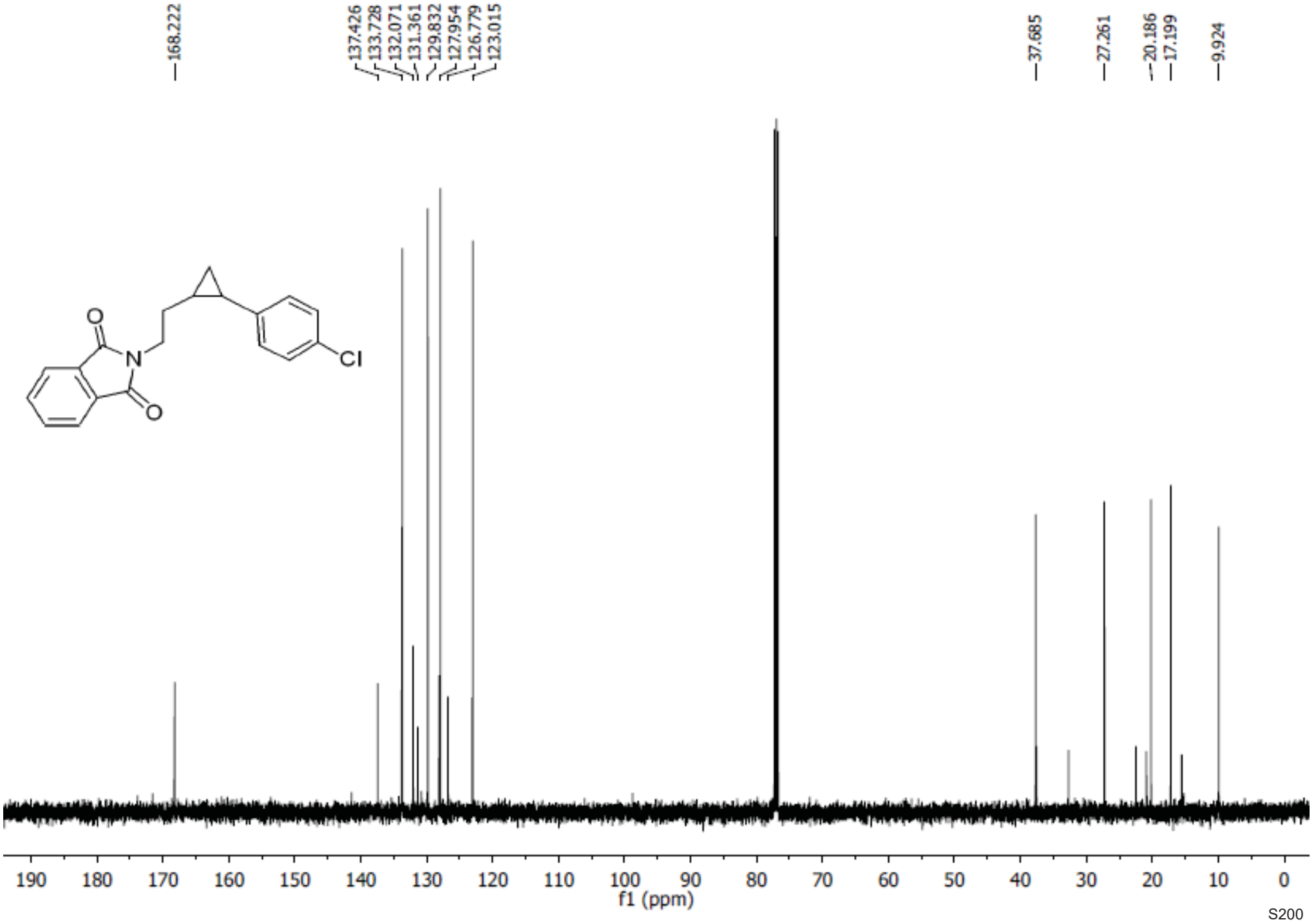
PDA Ch1 238nm

Peak#	Ret. Time	Area	Area%
1	14.189	130849	0.392
2	15.010	33230130	99.608
Total		33360979	100.000

2-(2-(2-(4-chlorophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(4-chlorophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

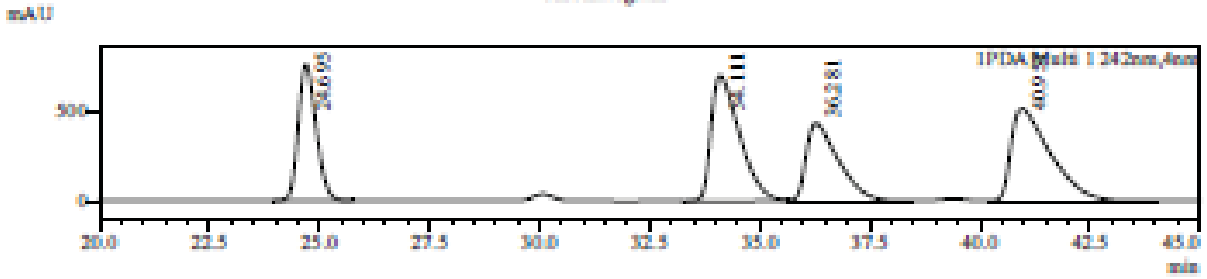


2-(2-(2-(4-chlorophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

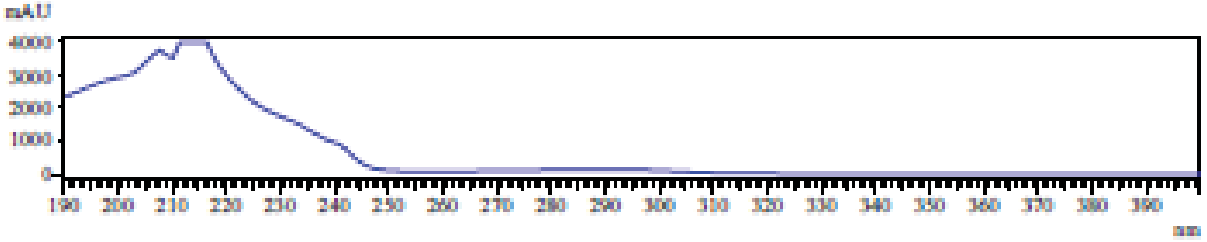
Sample Information

Data File	: YOW-638-IE-5%0.8mL-iPrOH001.lcd
Sample Name	: YOW-638-IE-5%0.8mL-iPrOH001
Sample ID	: YOW-638-IE-5%0.8mL-iPrOH001
Method File	: YW-5.0%-0.8ml.lcm

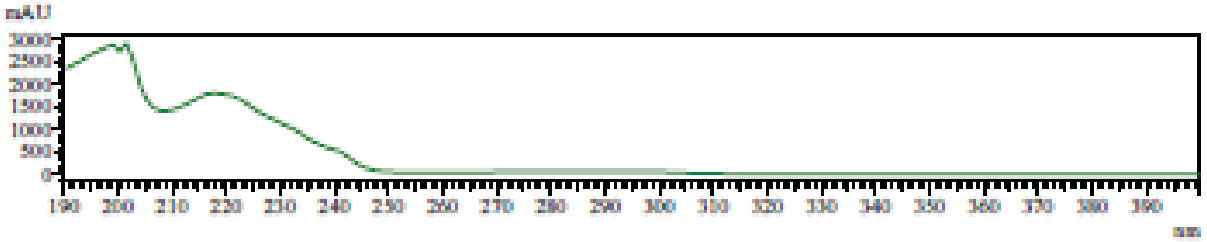
Chromatogram



UV Spectrum
Retention time = 24.695



UV Spectrum
Retention time = 36.281



Peak Table

PDA Ch1 242nm

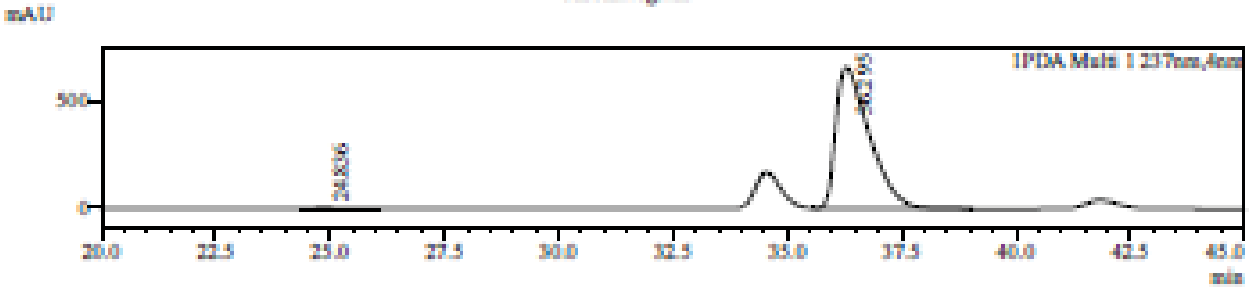
Peak#	Ret. Time	Area	Area%
1	24.695	21382282	20.155
2	34.111	31163721	29.375
3	36.281	22042877	20.778
4	40.957	31500444	29.692
Total		106089324	100.000

2-(2-(2-(4-chlorophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

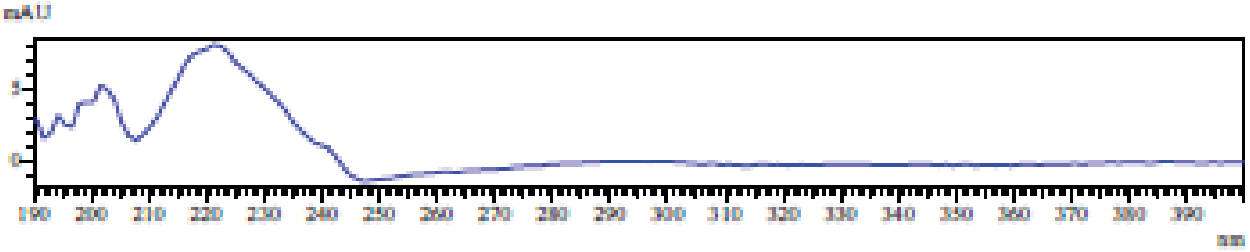
Sample Information

Data File	: YOW-639-IE-5%0.8mL-iPrOH003.lcd
Sample Name	: YOW-639-IE-5%0.8mL-iPrOH003
Sample ID	: YOW-639-IE-5%0.8mL-iPrOH003
Method File	: YW-5.0%-0.8ml.lcm

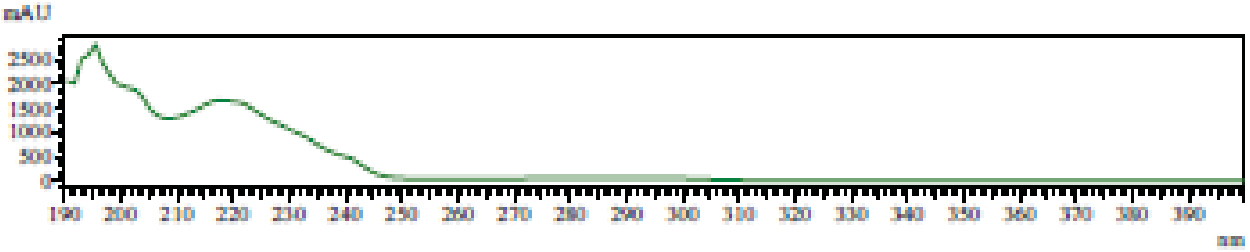
Chromatogram



UV Spectrum
Retention time = 24.836



UV Spectrum
Retention time = 36.295

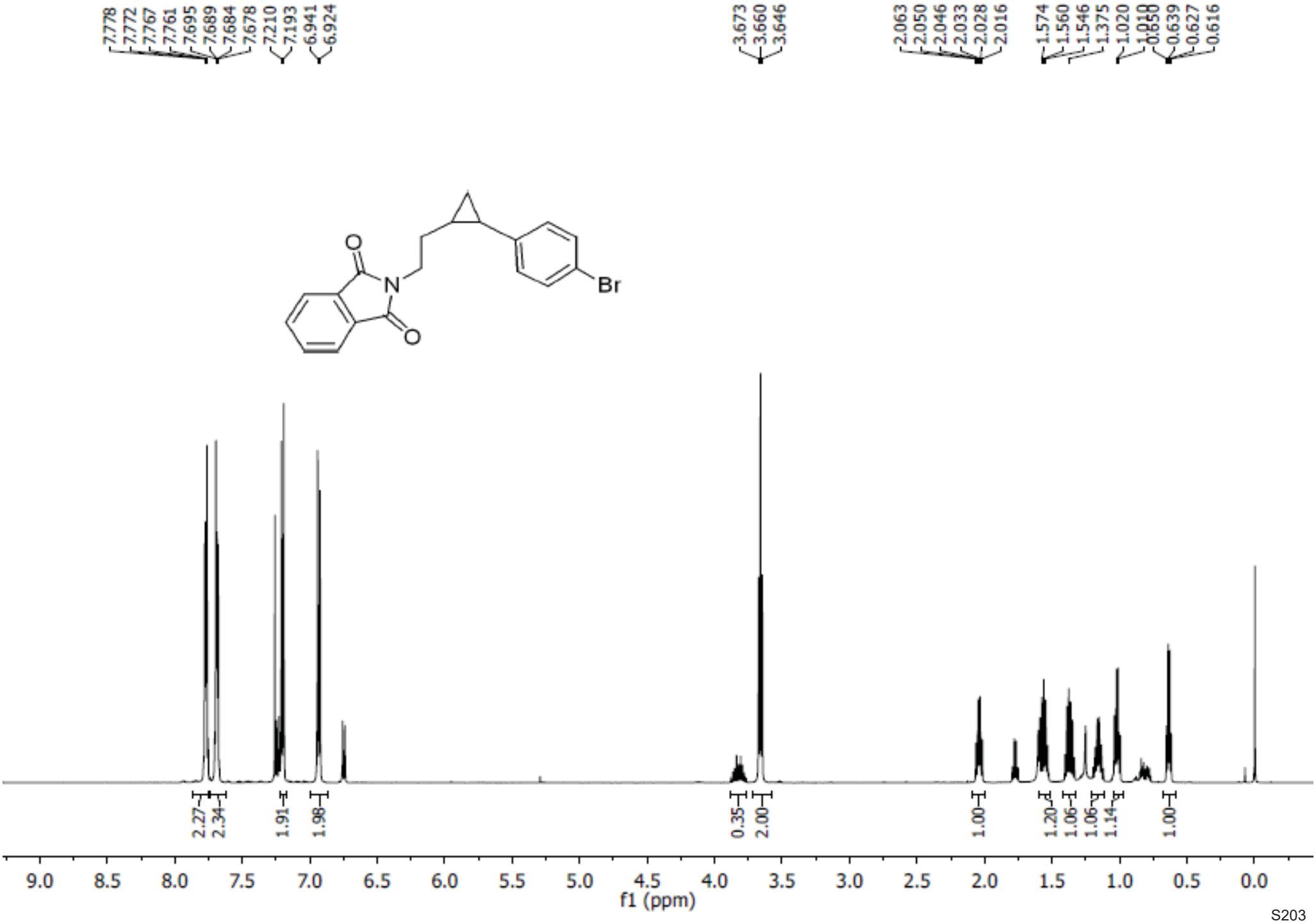


Peak Table

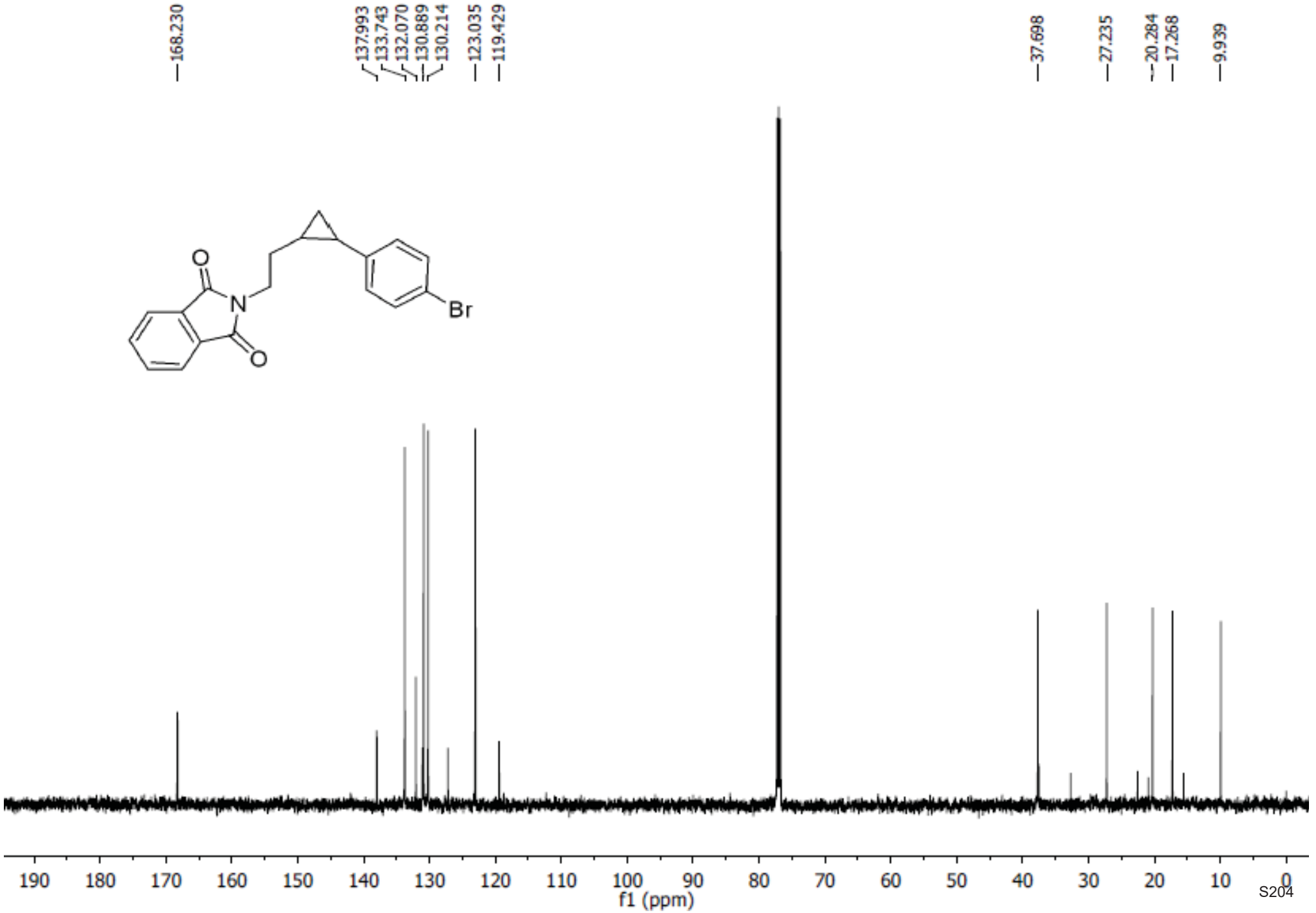
PDA Ch1 237nm

Peak#	Ret. Time	Area	Area%
1	24.836	135644	0.402
2	36.295	33572453	99.598
Total		33708098	100.000

2-(2-(2-(4-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(4-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

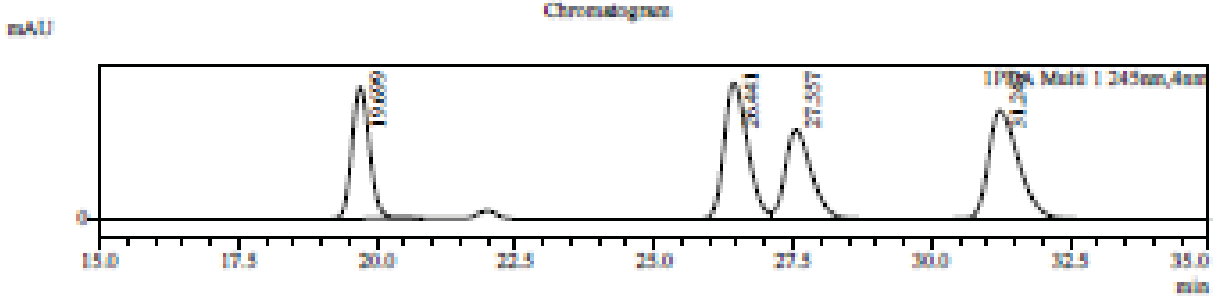


2-(2-(2-(4-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

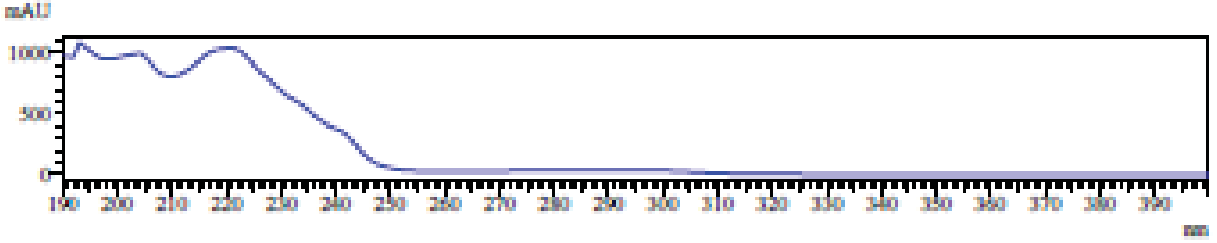
Sample Information

Data File	: Y0W-794-4Br-IE-10%0.8mL-iPrOH002.lcd
Sample Name	: Y0W-794-4Br-IE-10%0.8mL-iPrOH002
Sample ID	: Y0W-794-4Br-IE-10%0.8mL-iPrOH00
Method File	: YW-10%-0.8mL.lcm

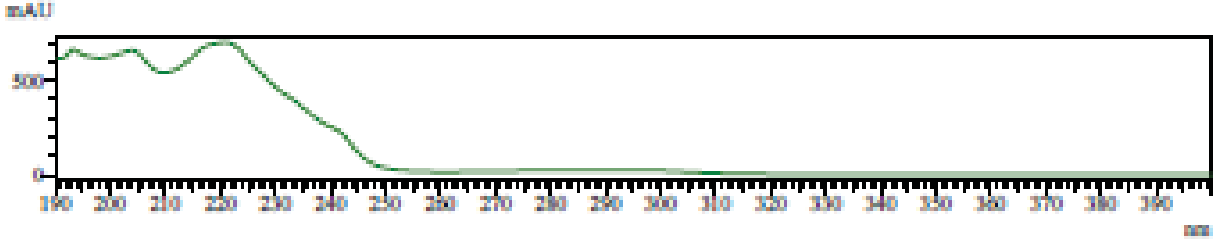
Chromatogram



UV Spectrum
Retention time = 19.699



UV Spectrum
Retention time = 27.557



Peak Table

PDA Ch1 245nm

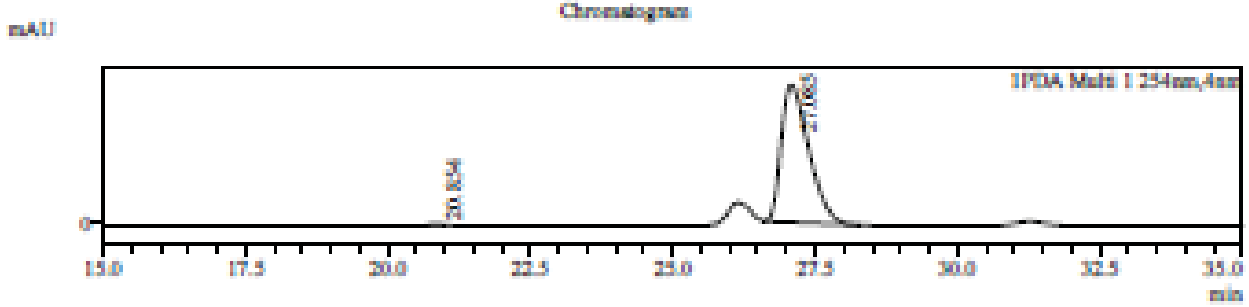
Peak#	Ret. Time	Area	Area%
1	19.699	4422102	20.588
2	26.441	6151748	28.640
3	27.557	4515610	21.023
4	31.247	6389924	29.749
Total		21479383	100.000

2-(2-(2-(4-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

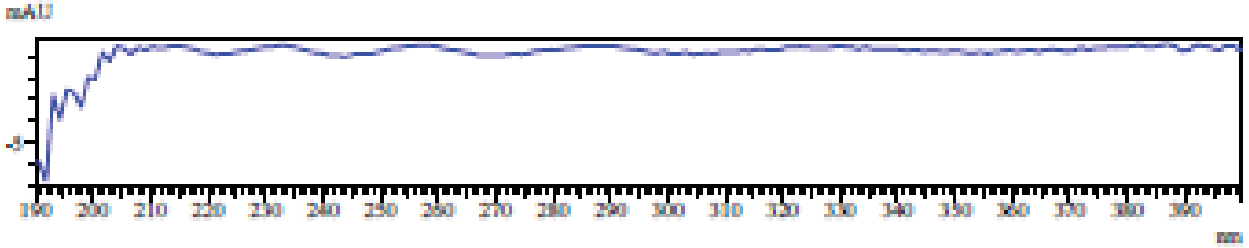
Sample Information

Data File	: Y0W-795-4Br-IE-10%0.8mL-iPrOH002.lcd
Sample Name	: Y0W-795-4Br-IE-10%0.8mL-iPrOH002
Sample ID	: Y0W-795-4Br-IE-10%0.8mL-iPrOH00
Method File	: YW-10%-0.8ml.lcm

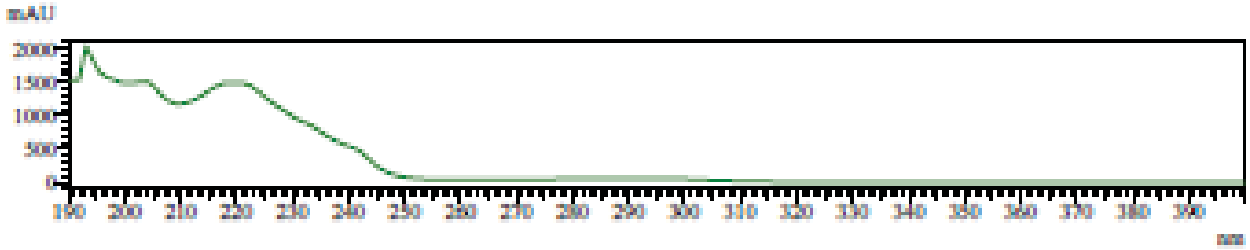
Chromatogram



UV Spectrum
Retention time = 20.854



UV Spectrum
Retention time = 27.085

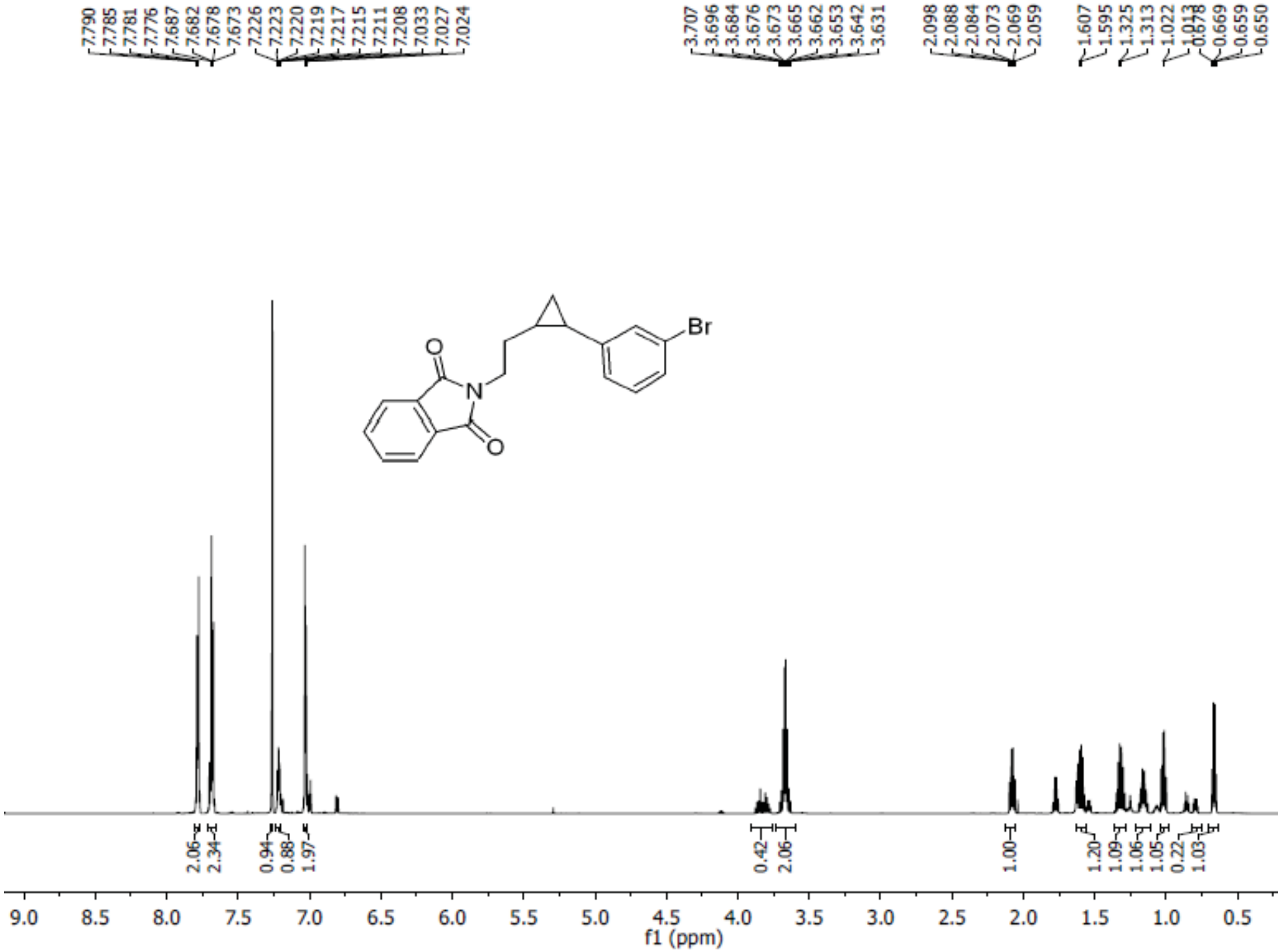


Peak Table

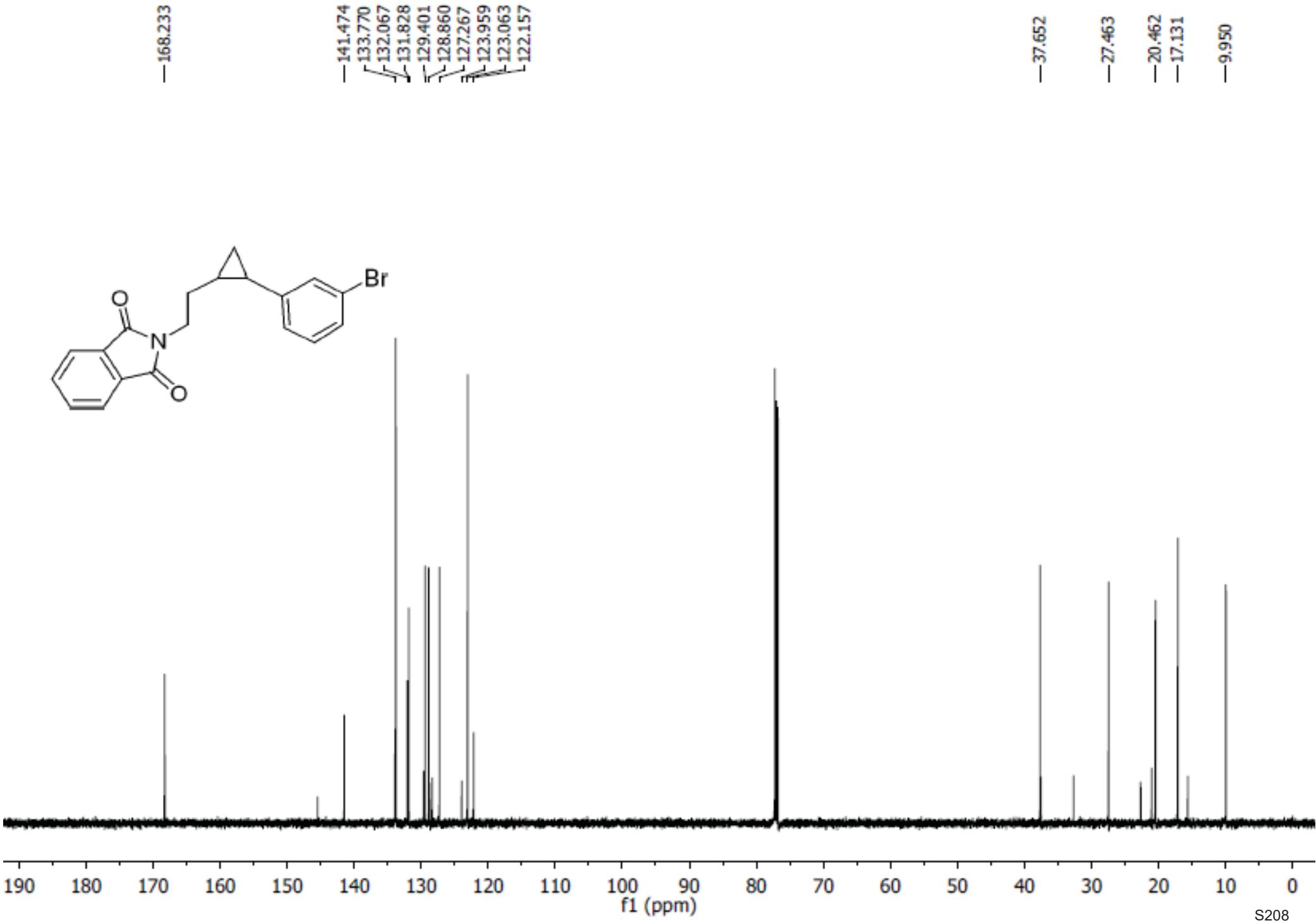
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	20.854	1106	0.066
2	27.085	1683736	99.934
Total		1684841	100.000

2-(2-(2-(3-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(3-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

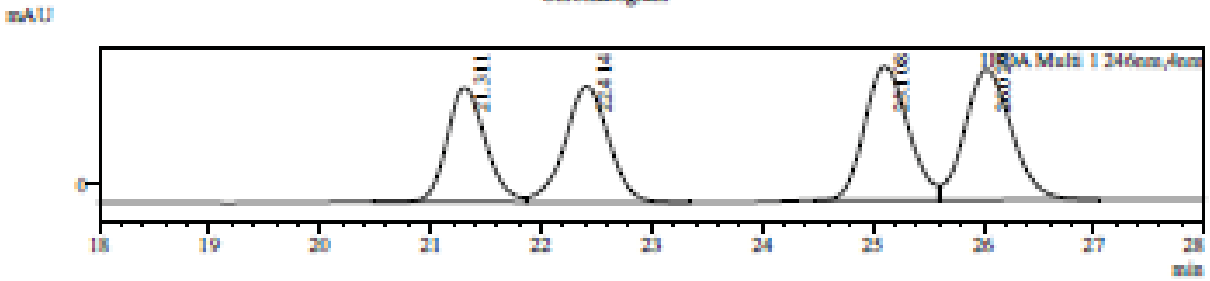


2-(2-(2-(3-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

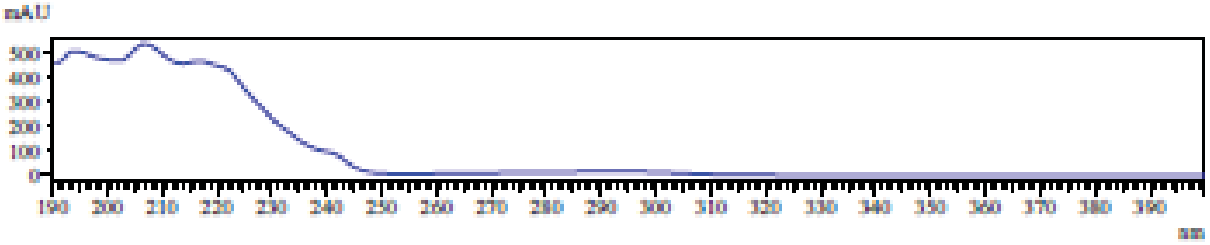
Sample Information

Data File	: YOW-615-IE-10%0.8mL-iPrOH.lcd
Sample Name	: YOW-615-IE-10%0.8mL-iPrOH
Sample ID	: YOW-615-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

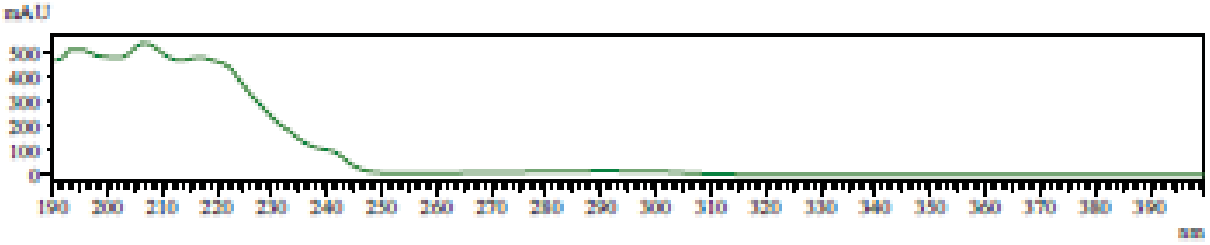
Chromatogram



UV Spectrum
Retention time = 21.311



UV Spectrum
Retention time = 22.414



Peak Table

PDA Ch1 246nm

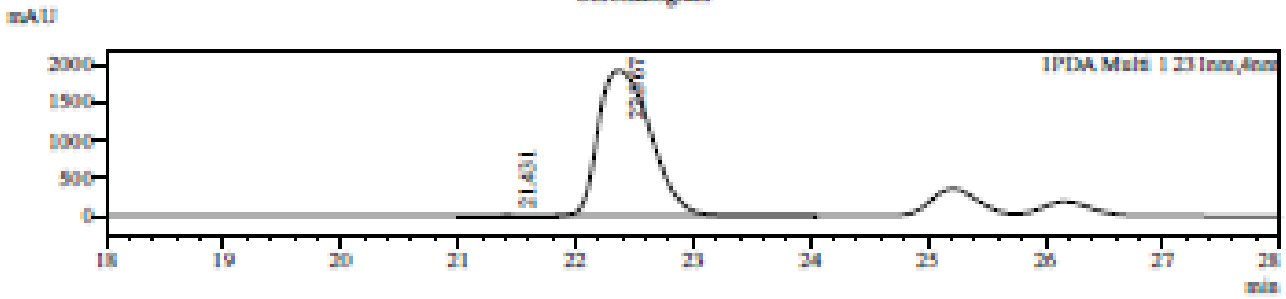
Peak#	Ret. Time	Area	Area%
1	21.311	986291	20.661
2	22.414	1134841	23.773
3	25.108	1301916	27.273
4	26.029	1350561	28.292
Total		4773609	100.000

2-(2-(2-(3-bromophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

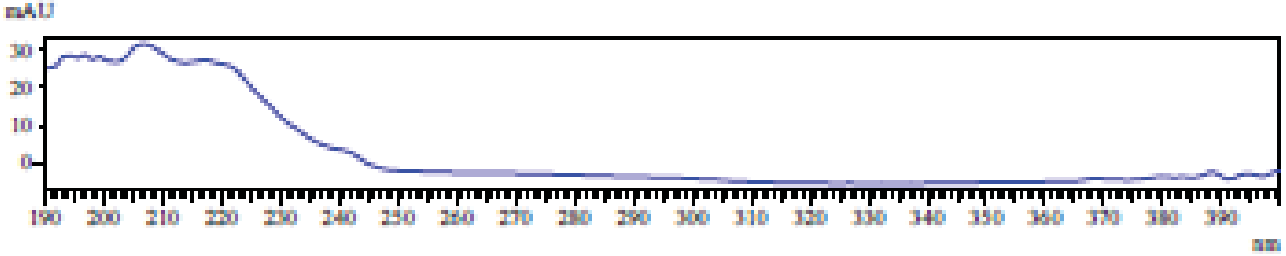
Sample Information

Data File	: YOW-616-IE-10%0.8mL-iPrOH.lcd
Sample Name	: YOW-616-IE-10%0.8mL-iPrOH
Sample ID	: YOW-616-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

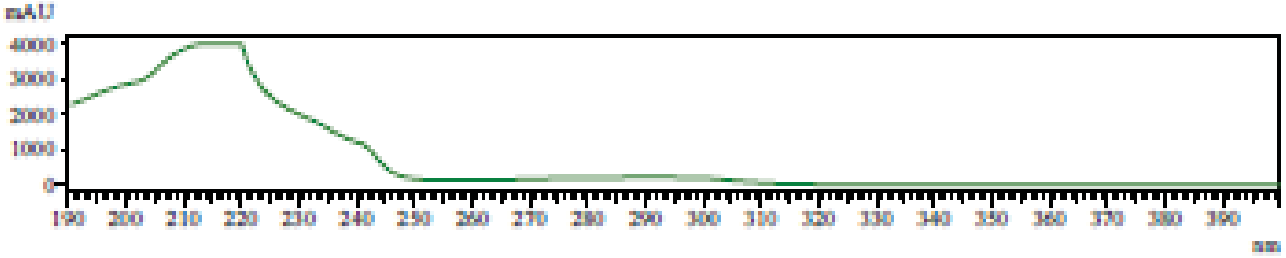
Chromatogram



UV Spectrum
Retention time = 21.431



UV Spectrum
Retention time = 22.367

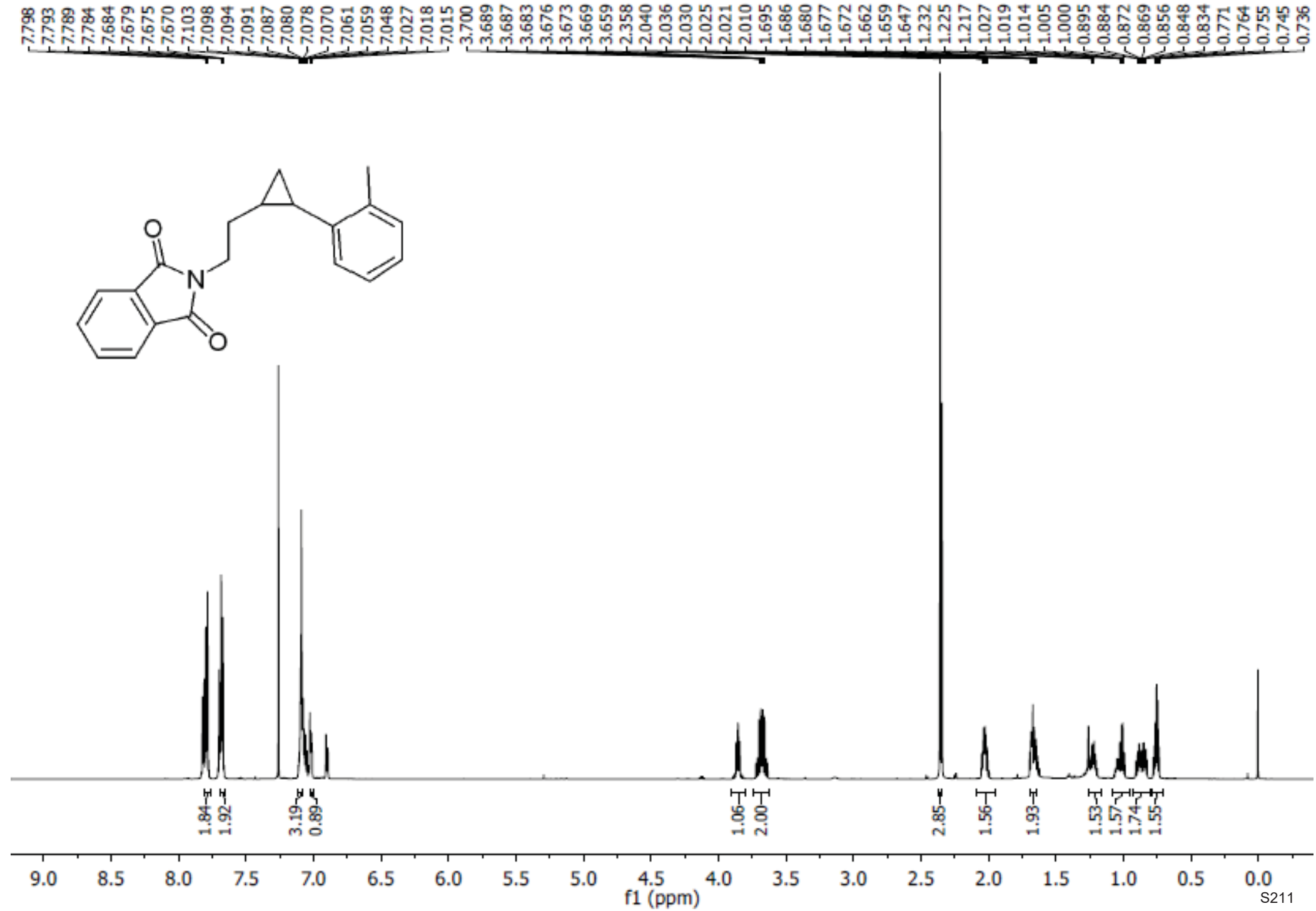


Peak Table

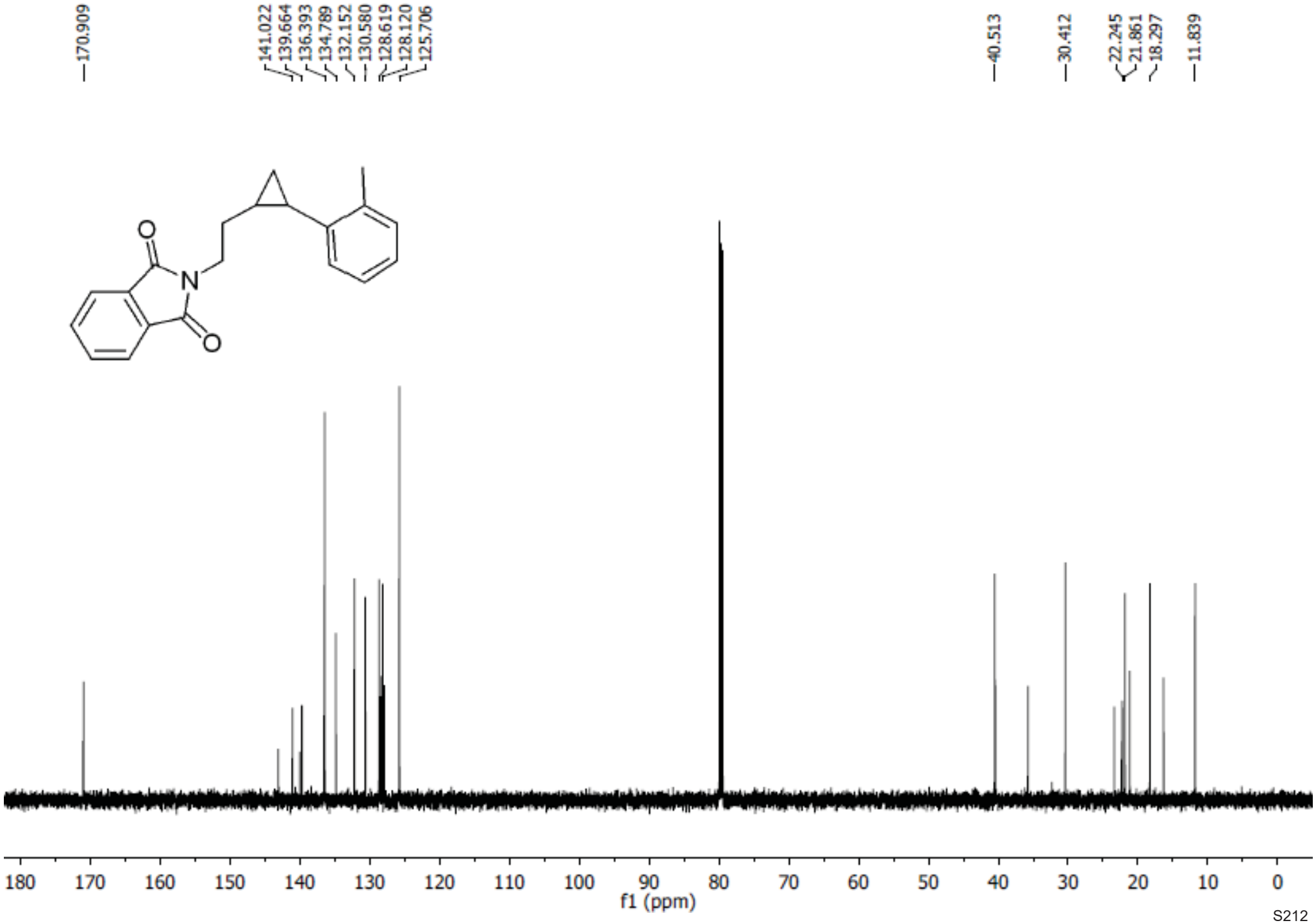
PDA Ch1 231nm

Peak#	Ret. Time	Area	Area%
1	21.431	241278	0.404
2	22.367	59422353	99.596
Total		59663632	100.000

2-(2-(2-(2-methylphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(2-methylphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

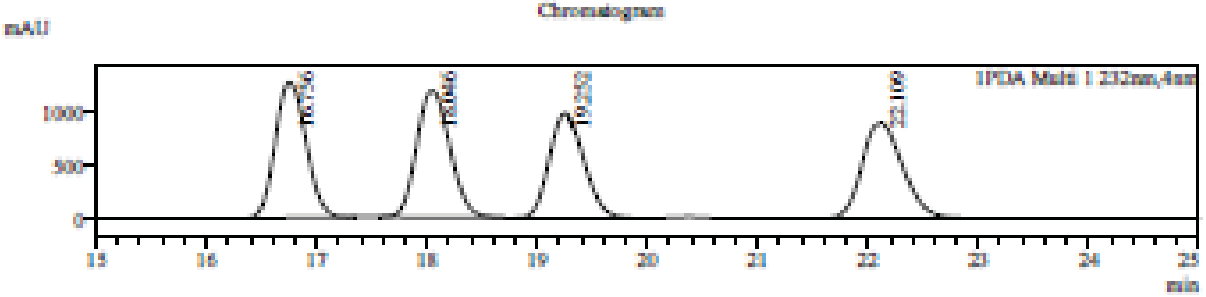


2-(2-(2-(2-methylphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

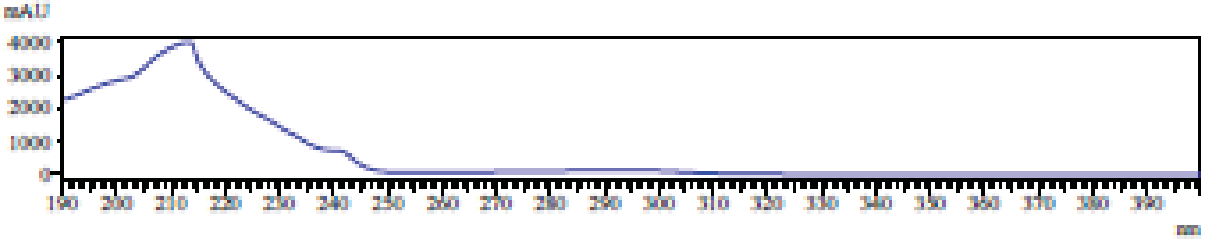
Sample Information

Data File : Y0W-636-IE-10%0.8mL-iPrOH003.lcd
Sample Name : Y0W-636-IE-10%0.8mL-iPrOH003
Sample ID : Y0W-636-IE-10%0.8mL-iPrOH003
Method File : YW-10%-0.8ml.lcm

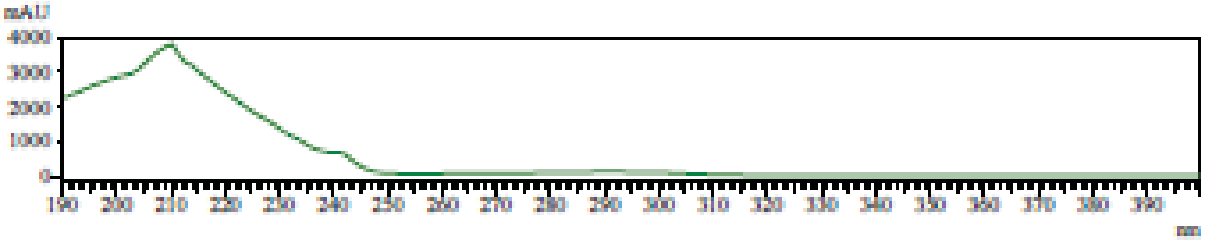
Chromatogram



UV Spectrum
Retention time = 16.756



UV Spectrum
Retention time = 18.046



Peak Table

PDA Ch1 232nm

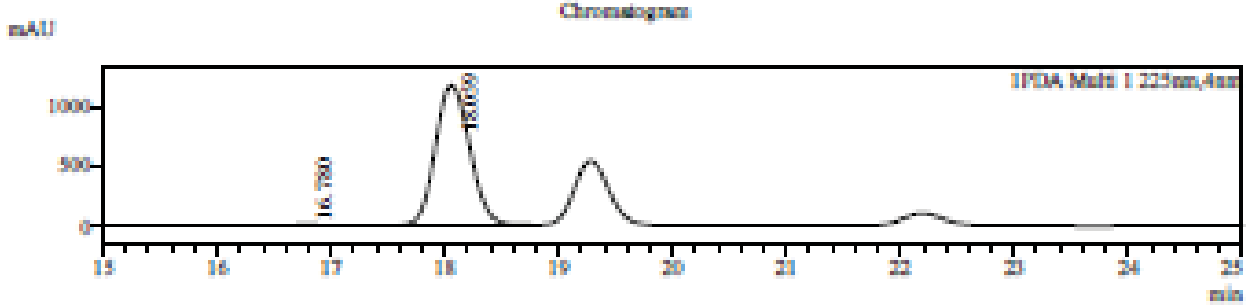
Peak#	Ret. Time	Area	Area%
1	16.756	24908240	26.162
2	18.046	25232764	26.503
3	19.252	21687794	22.780
4	22.109	23378035	24.555
Total		95206834	100.000

2-(2-(2-(2-methylphenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

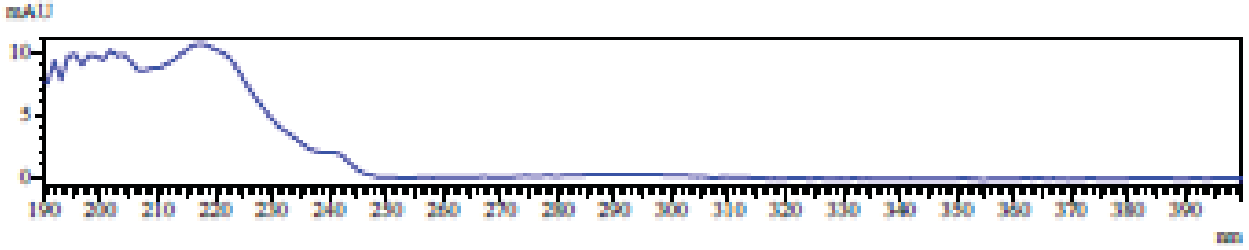
Sample Information

Data File	: Y0W-637-IE-10%0.8mL-iPrOH002.lcd
Sample Name	: Y0W-637-IE-10%0.8mL-iPrOH002
Sample ID	: Y0W-637-IE-10%0.8mL-iPrOH002
Method File	: YW-10%-0.8ml.lcm

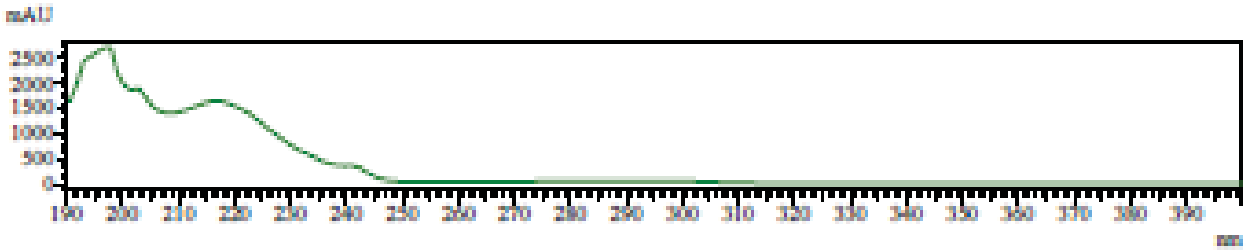
Chromatogram



UV Spectrum
Retention time = 16.780



UV Spectrum
Retention time = 18.059

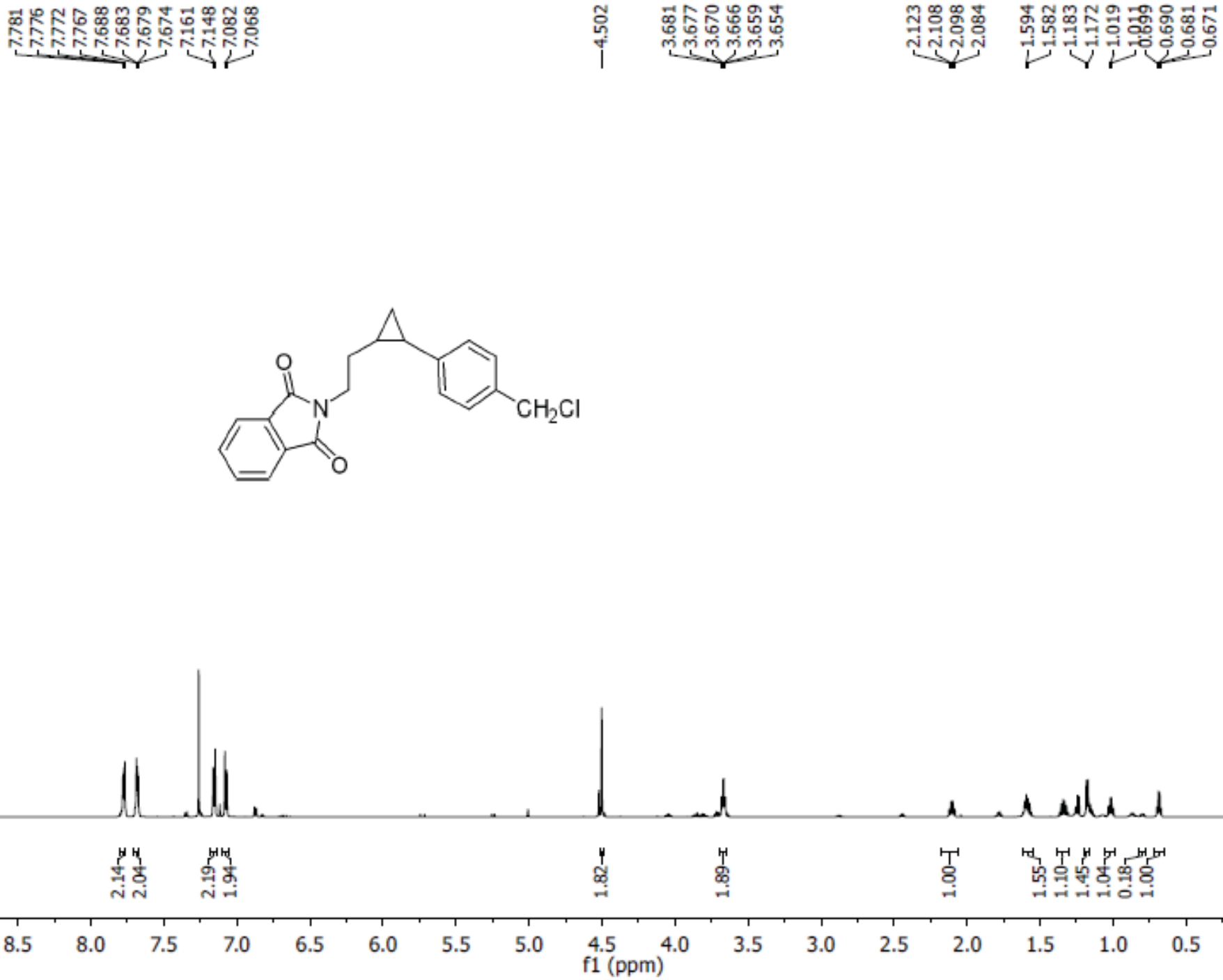


Peak Table

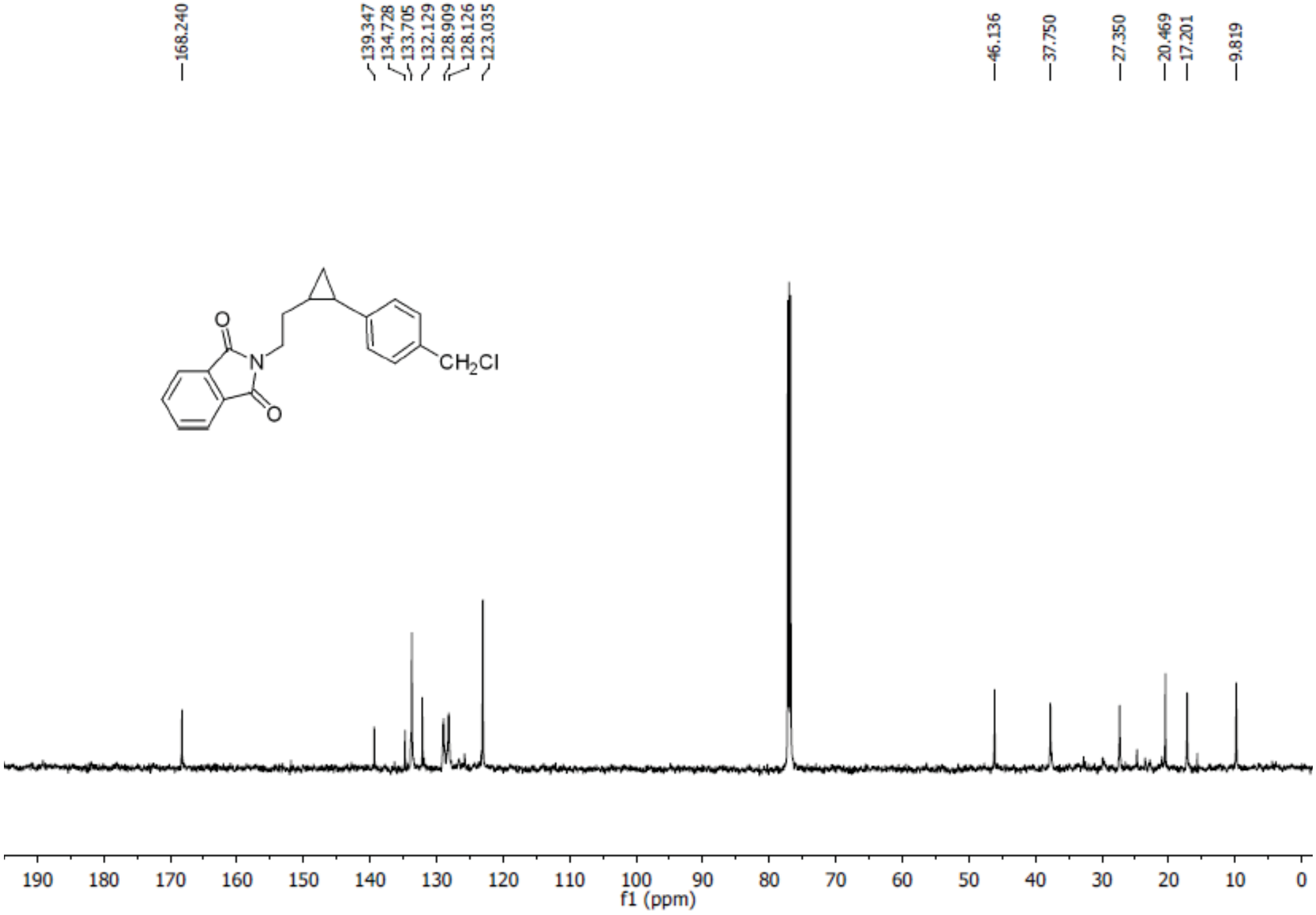
PDA Ch1 225nm

Peak#	Ret. Time	Area	Area%
1	16.780	123407	0.496
2	18.059	24734702	99.504
Total		24858109	100.000

2-(2-(2-(2-methylchrolophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(2-methylchrolophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

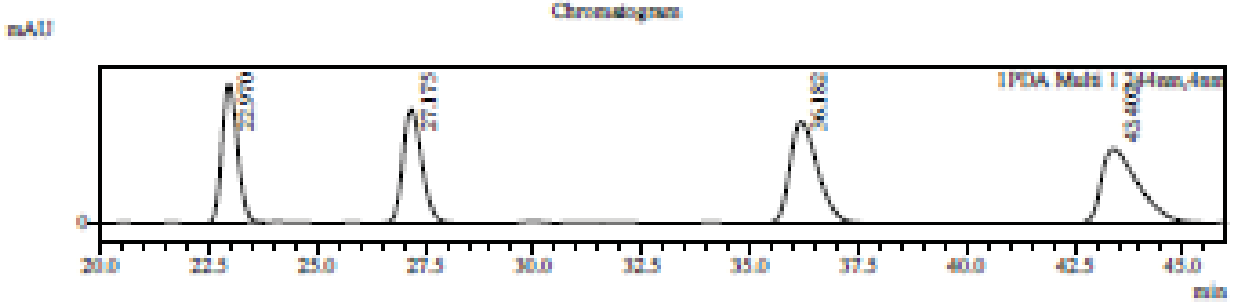


2-(2-(2-(2-methylchrolophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

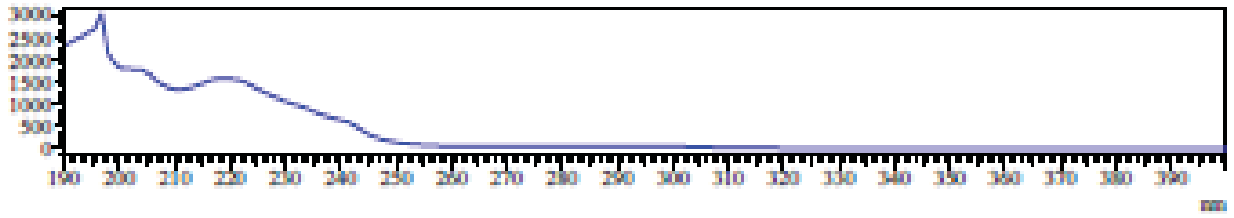
Sample Information

Data File	: Y0W-693-IE-10%0.8mL-iPrOH004.lcd
Sample Name	: Y0W-693-IE-10%0.8mL-iPrOH004
Sample ID	: Y0W-693-IE-10%0.8mL-iPrOH004
Method File	: YW-10%-0.8ml.lcm

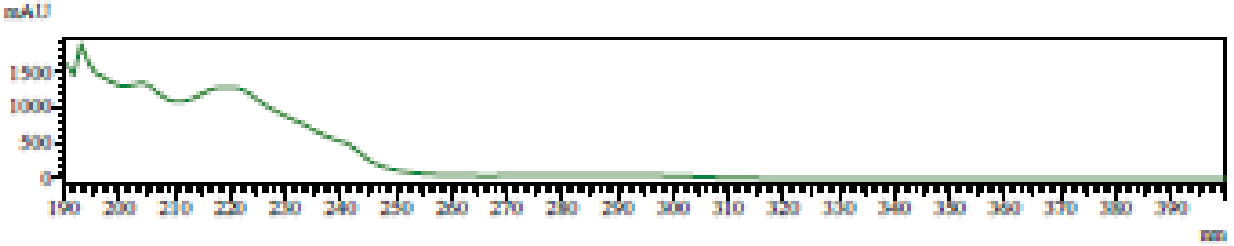
Chromatogram



UV Spectrum
Retention time = 22.970



UV Spectrum
Retention time = 27.175



Peak Table

PDA Ch1 244nm

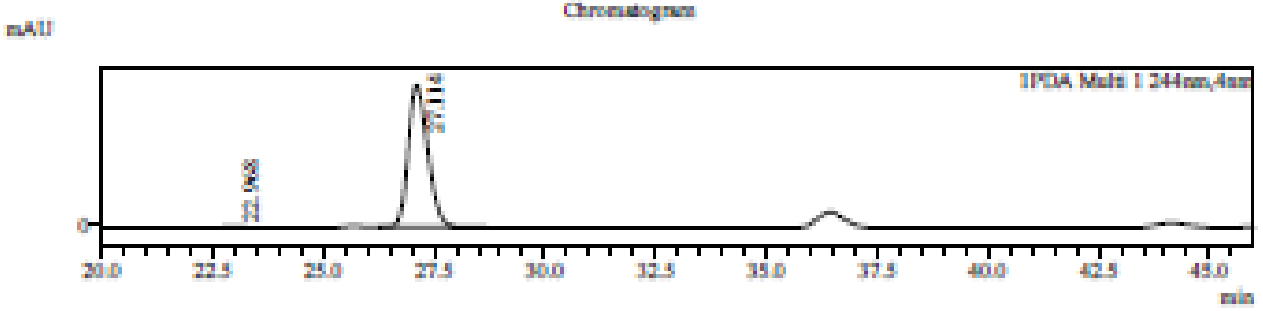
Peak#	Ret. Time	Area	Area%
1	22.970	10144357	21.850
2	27.175	10105883	21.767
3	36.182	13267294	28.577
4	43.402	12909273	27.806
Total		46426807	100.000

2-(2-(2-(2-methylchrolophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

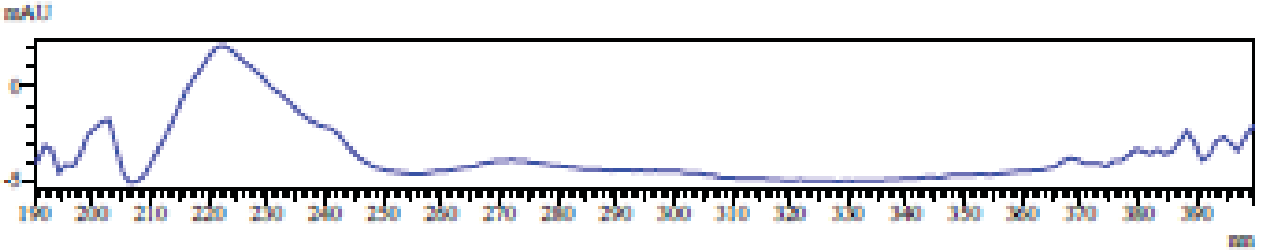
Sample Information

Data File	: Y0W-694-IE-10%0.8mL-iPrOH004.lcd
Sample Name	: Y0W-694-IE-10%0.8mL-iPrOH004
Sample ID	: Y0W-694-IE-10%0.8mL-iPrOH004
Method File	: YW-10%-0.8ml.lcm

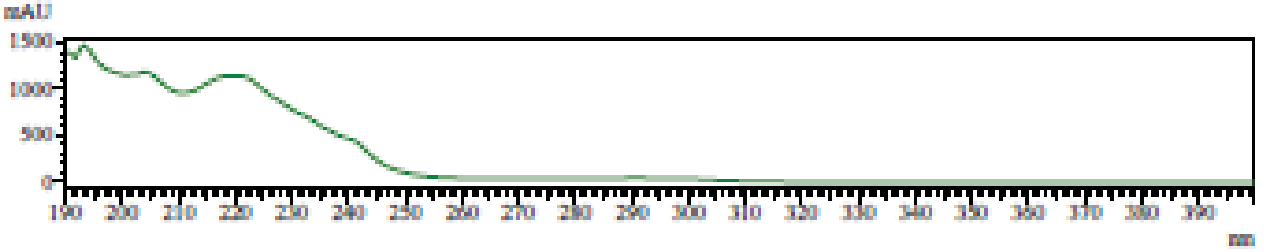
Chromatogram



UV Spectrum
Retention time = 22.968



UV Spectrum
Retention time = 27.114

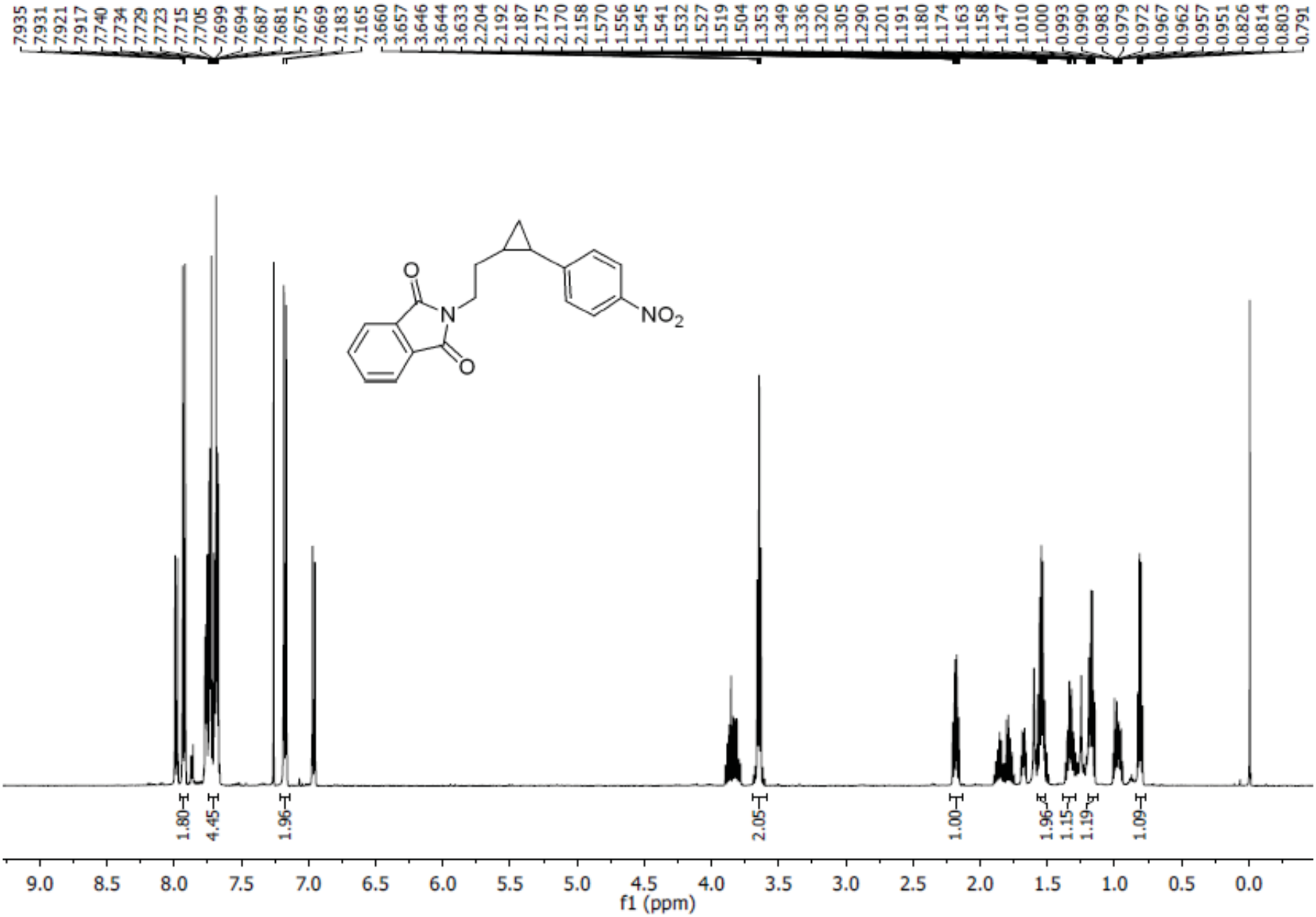


Peak Table

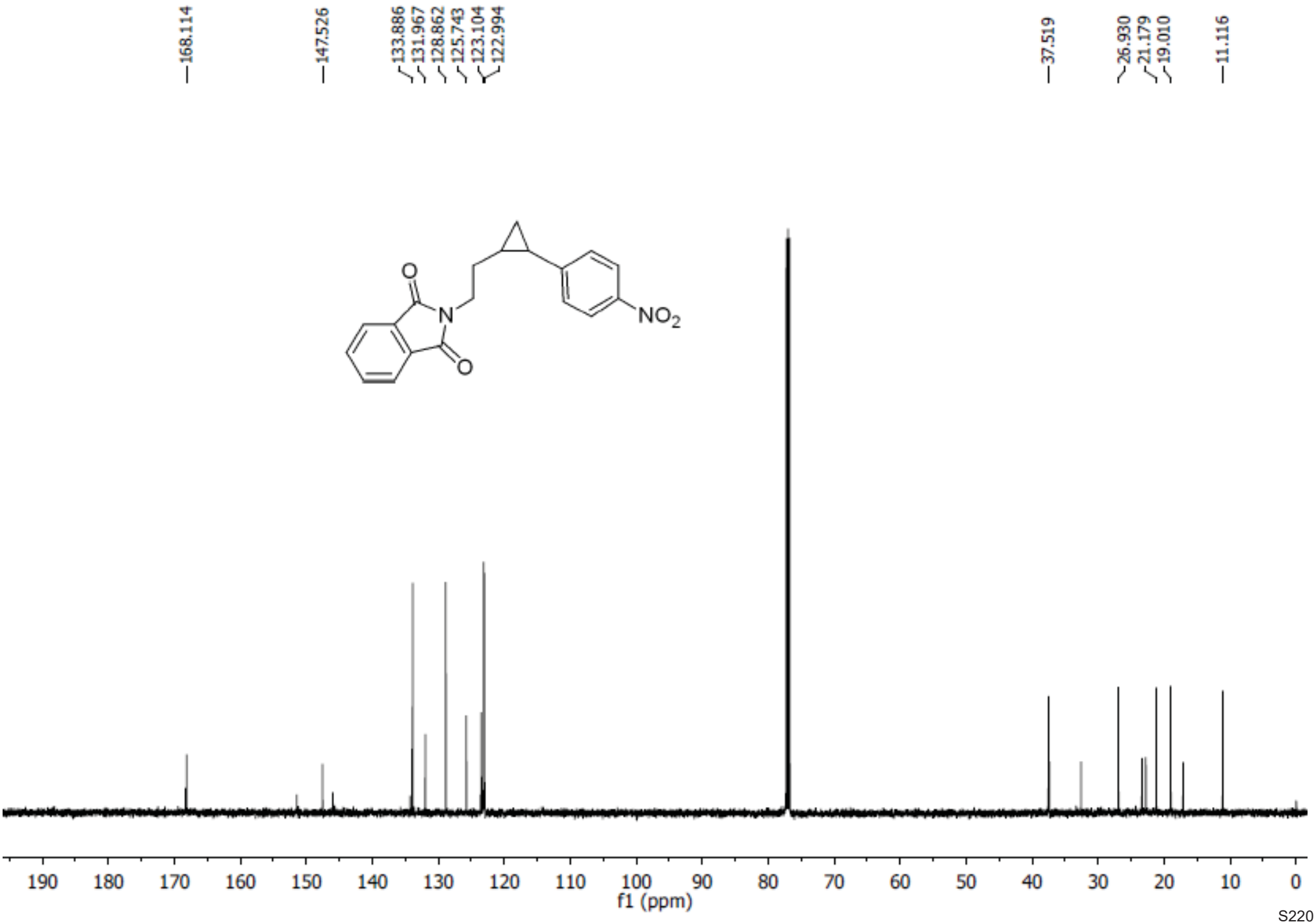
PDA Ch1 244nm

Peak#	Ret. Time	Area	Area%
1	22.968	45601	0.498
2	27.114	9109030	99.502
Total		9154631	100.000

2-(2-(2-(4-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(4-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

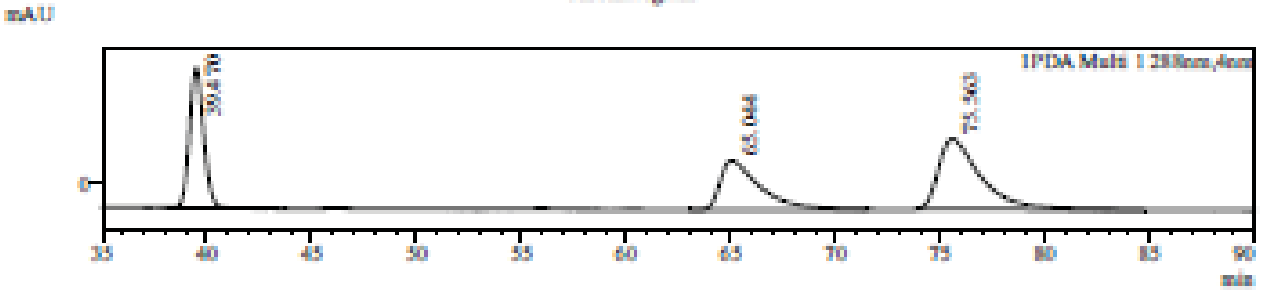


2-(2-(2-(4-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

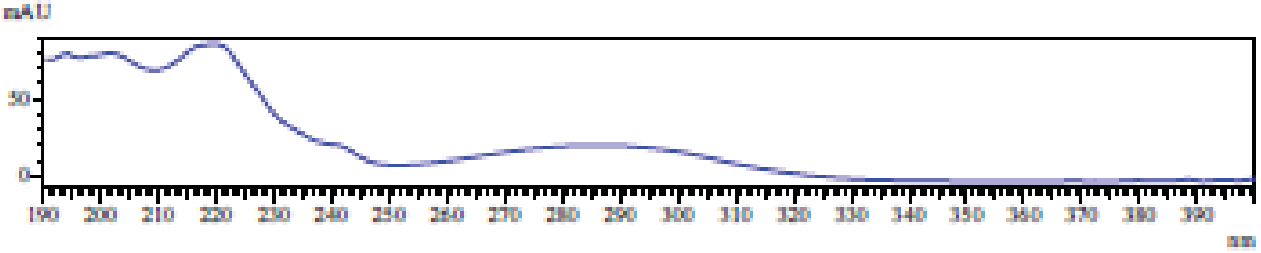
Sample Information

Data File	: YOW-652-ID-15%0.8mL-iPrOH003.lcd
Sample Name	: YOW-652-ID-15%0.8mL-iPrOH003
Sample ID	: YOW-652-ID-15%0.8mL-iPrOH003
Method File	: YW-15.0%-0.8ml.lcm

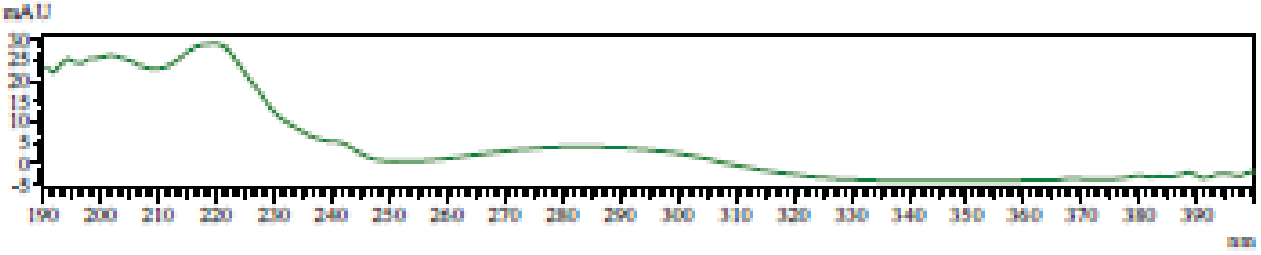
Chromatogram



UV Spectrum
Retention time = 39.470



UV Spectrum
Retention time = 65.044



Peak Table

PDA Ch1 288nm

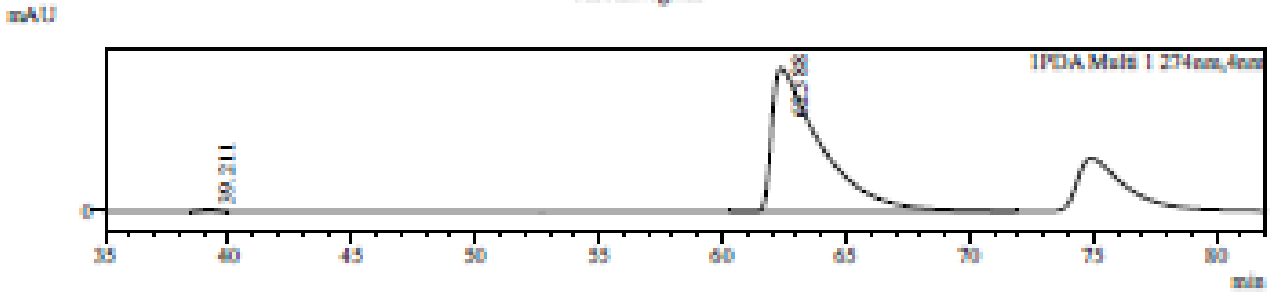
Peak#	Ret. Time	Area	Area%
1	39.470	1127820	28.892
2	65.044	1102109	28.234
3	75.563	1673606	42.874
Total		3903535	100.000

2-(2-(2-(4-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

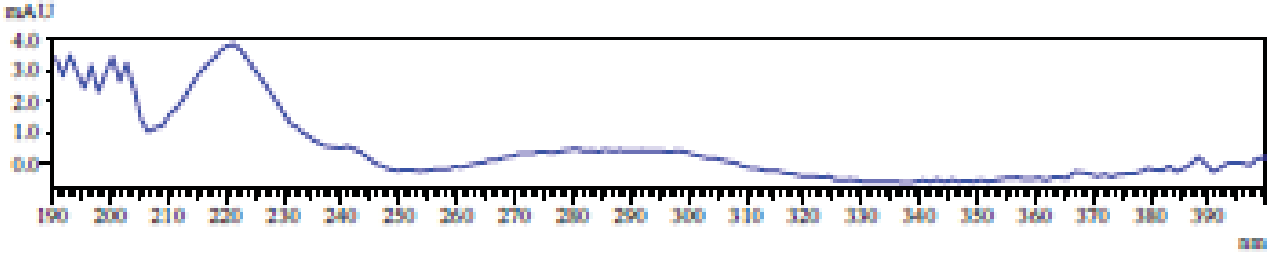
Sample Information

Data File	: YOW-653-ID-15%0.8mL-iPrOH005.lcd
Sample Name	: YOW-653-ID-15%0.8mL-iPrOH004
Sample ID	: YOW-653-ID-15%0.8mL-iPrOH004
Method File	: YW-15.0%-0.8ml.lcm

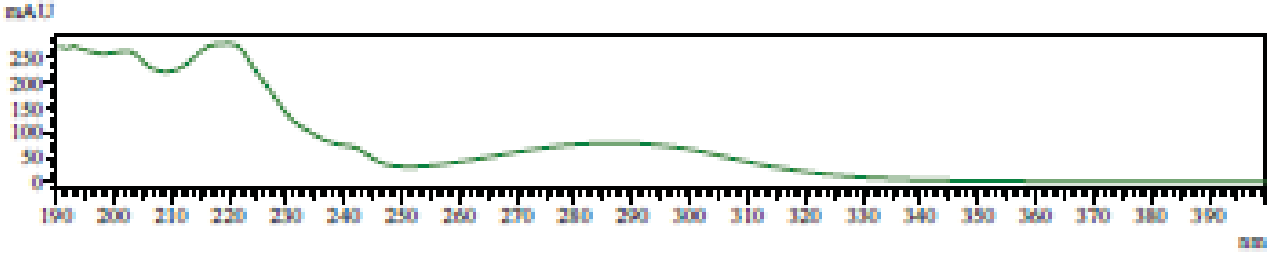
Chromatogram



UV Spectrum
Retention time = 39.211



UV Spectrum
Retention time = 62.388

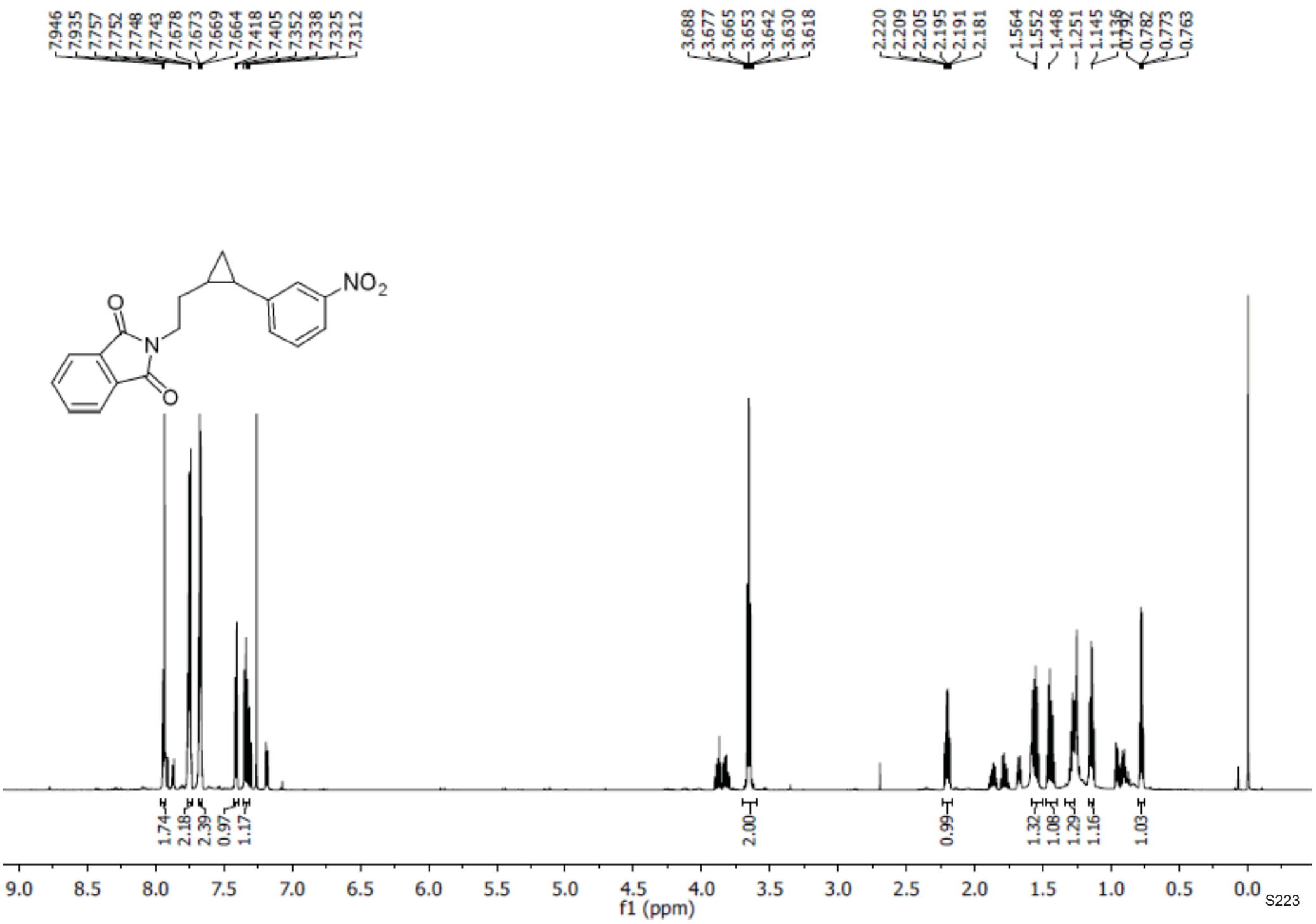


Peak Table

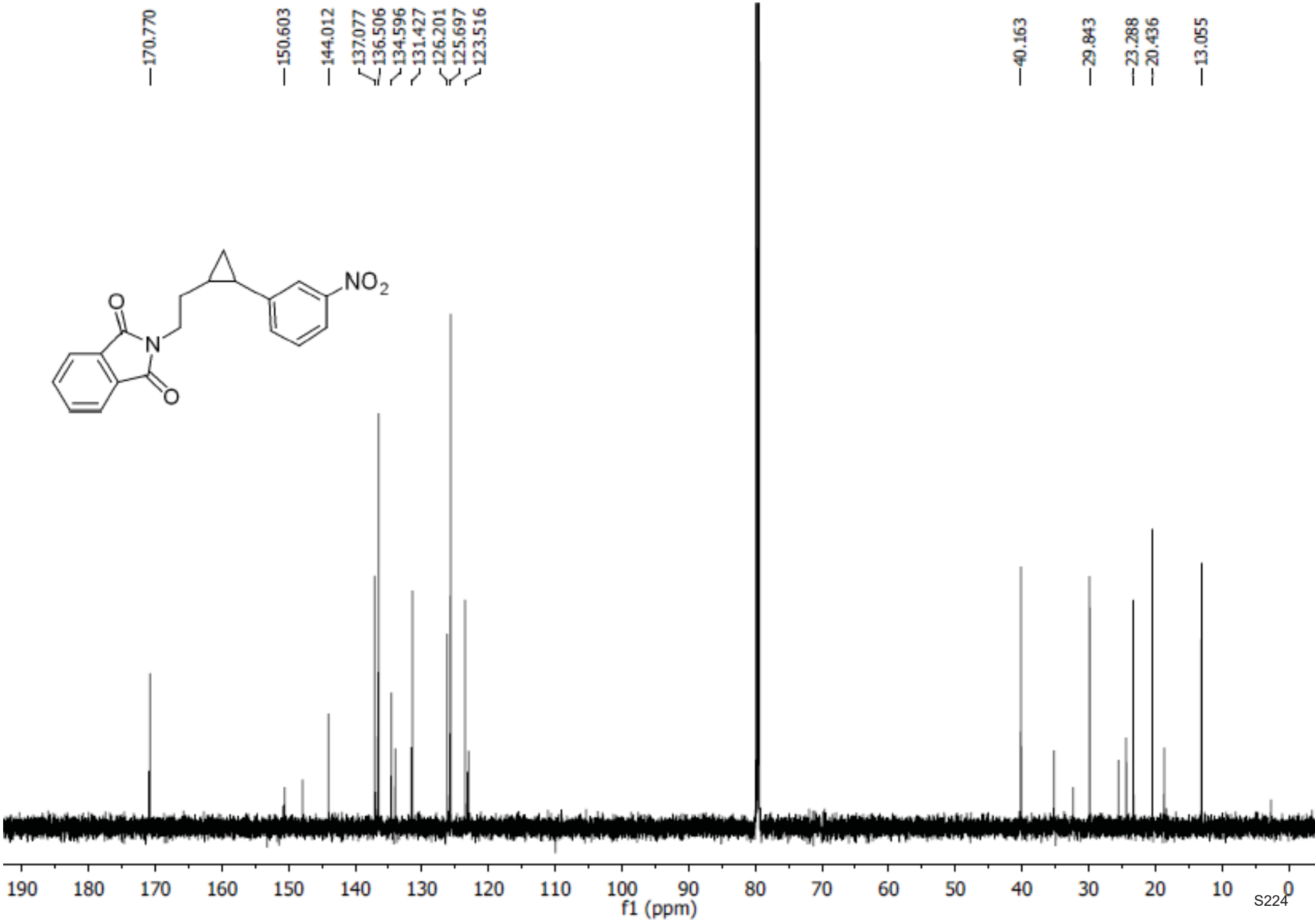
PDA Ch1 274nm

Peak#	Ret. Time	Area	Area%
1	39.211	49133	0.530
2	62.388	9220670	99.470
Total		9269802	100.000

2-(2-(2-(3-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(3-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

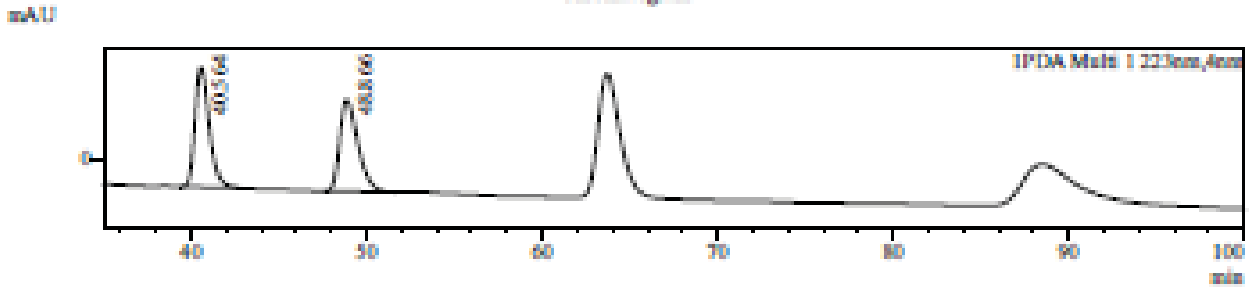


2-(2-(2-(3-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

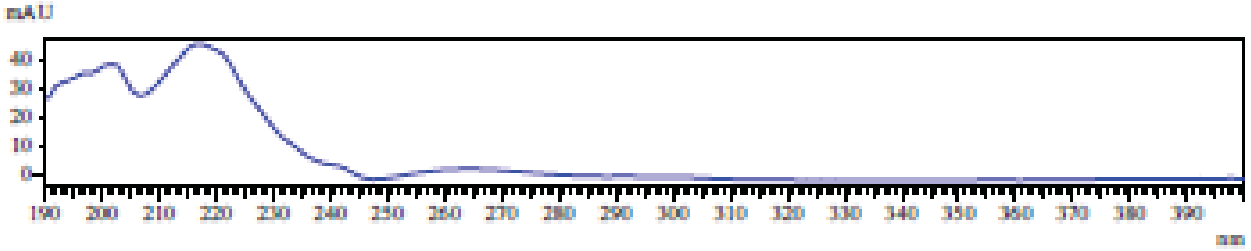
Sample Information

Data File	: YOW-632-ID-10%0.8mL-MeOH.lcd
Sample Name	: YOW-632-ID-10%0.8mL-MeOH
Sample ID	: YOW-632-ID-10%0.8mL-MeOH
Method File	: YW-10%-1.0ml.1cm

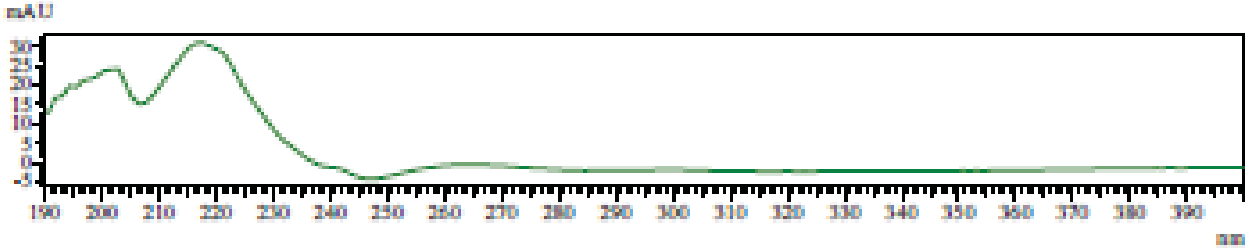
Chromatogram



UV Spectrum
Retention time = 40.564



UV Spectrum
Retention time = 48.866



Peak Table

PDA Ch1 223nm

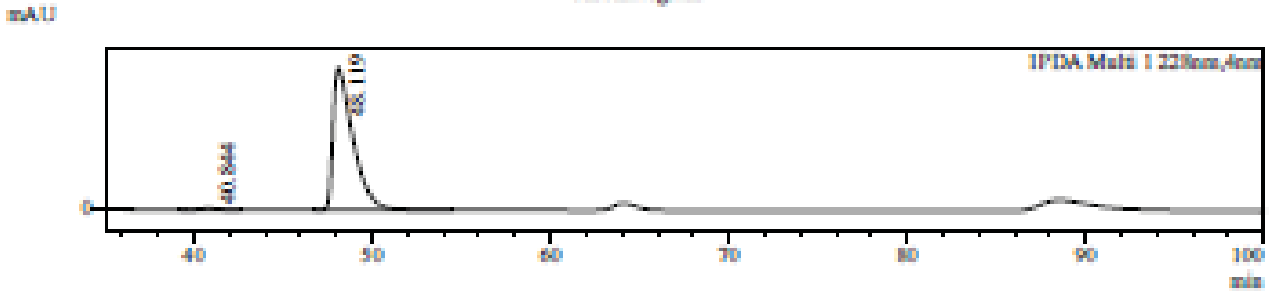
Peak#	Ret. Time	Area	Area%
1	40.564	2559560	50.231
2	48.866	2536022	49.769
Total		5095581	100.000

2-(2-(2-(3-nitrophenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

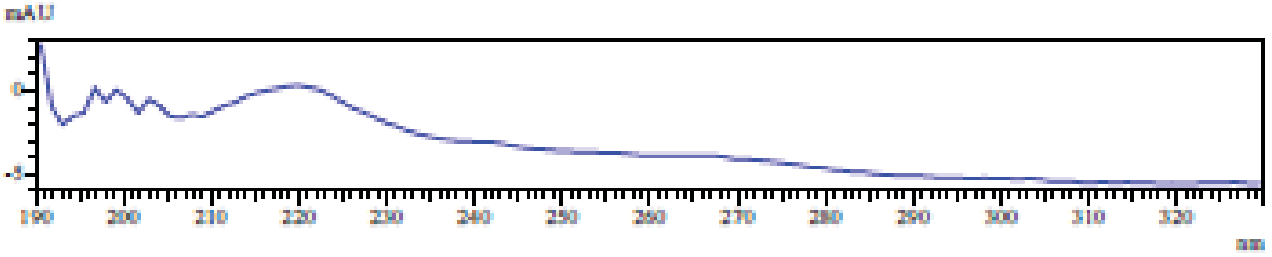
Sample Information

Data File	: YOW-633-ID-10%1.0mL-MeOH.lcd
Sample Name	: YOW-633-ID-10%1.0mL-MeOH
Sample ID	: YOW-633-ID-10%1.0mL-MeOH
Method File	: YW-10%-1.0ml.lcm

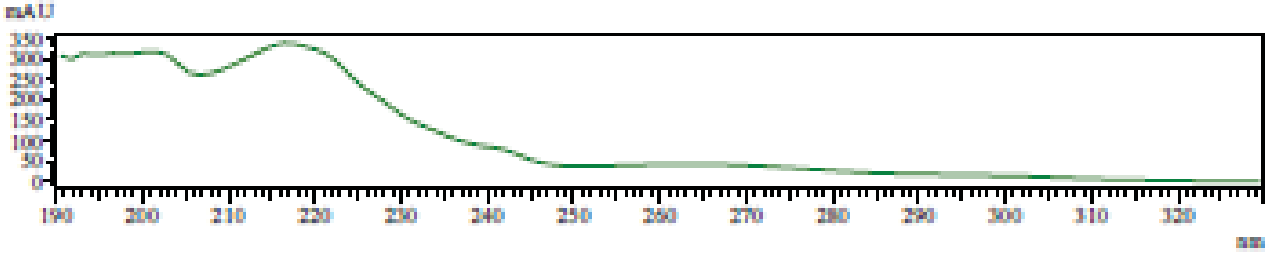
Chromatogram



UV Spectrum
Retention time = 40.844



UV Spectrum
Retention time = 48.119

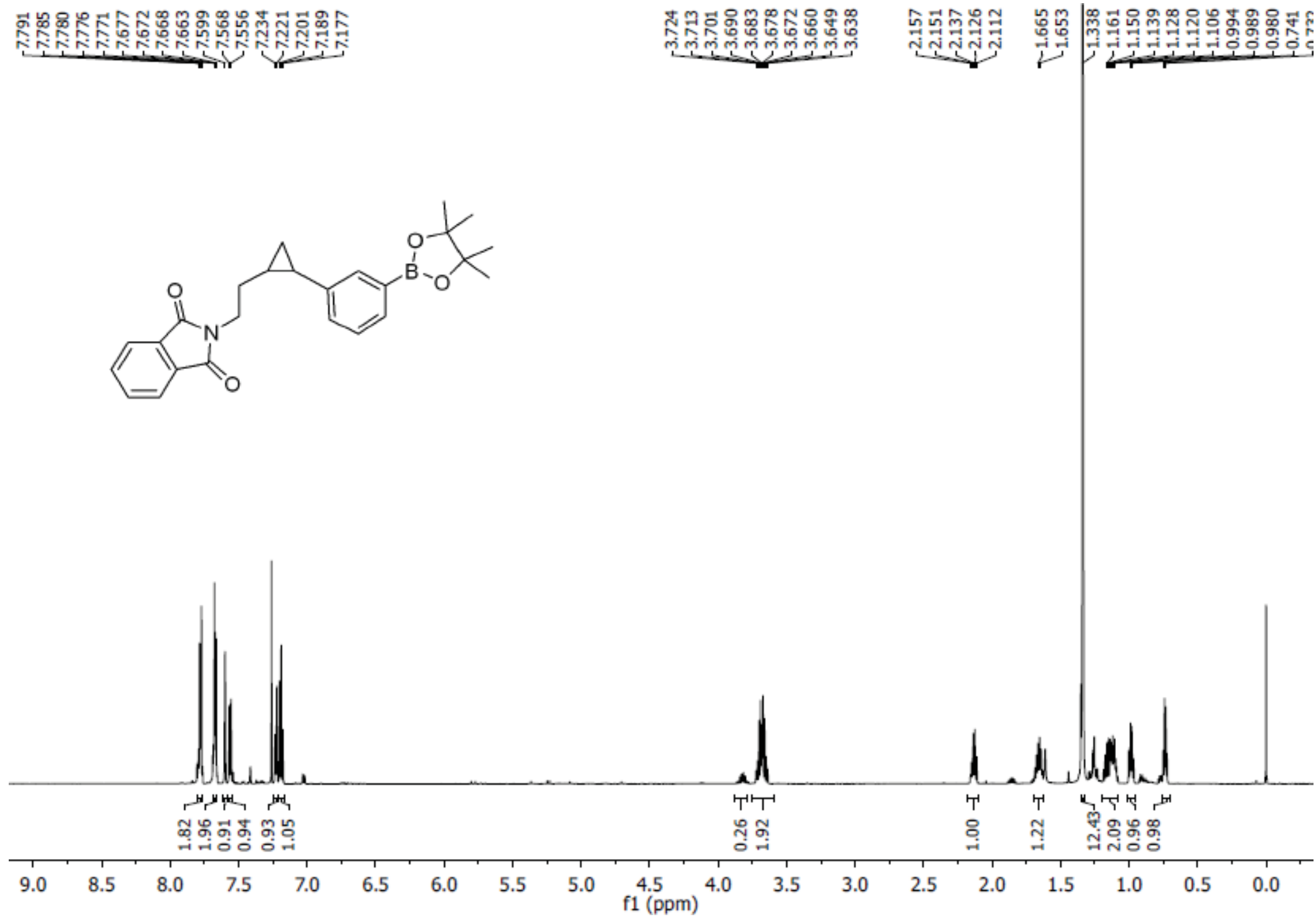


Peak Table

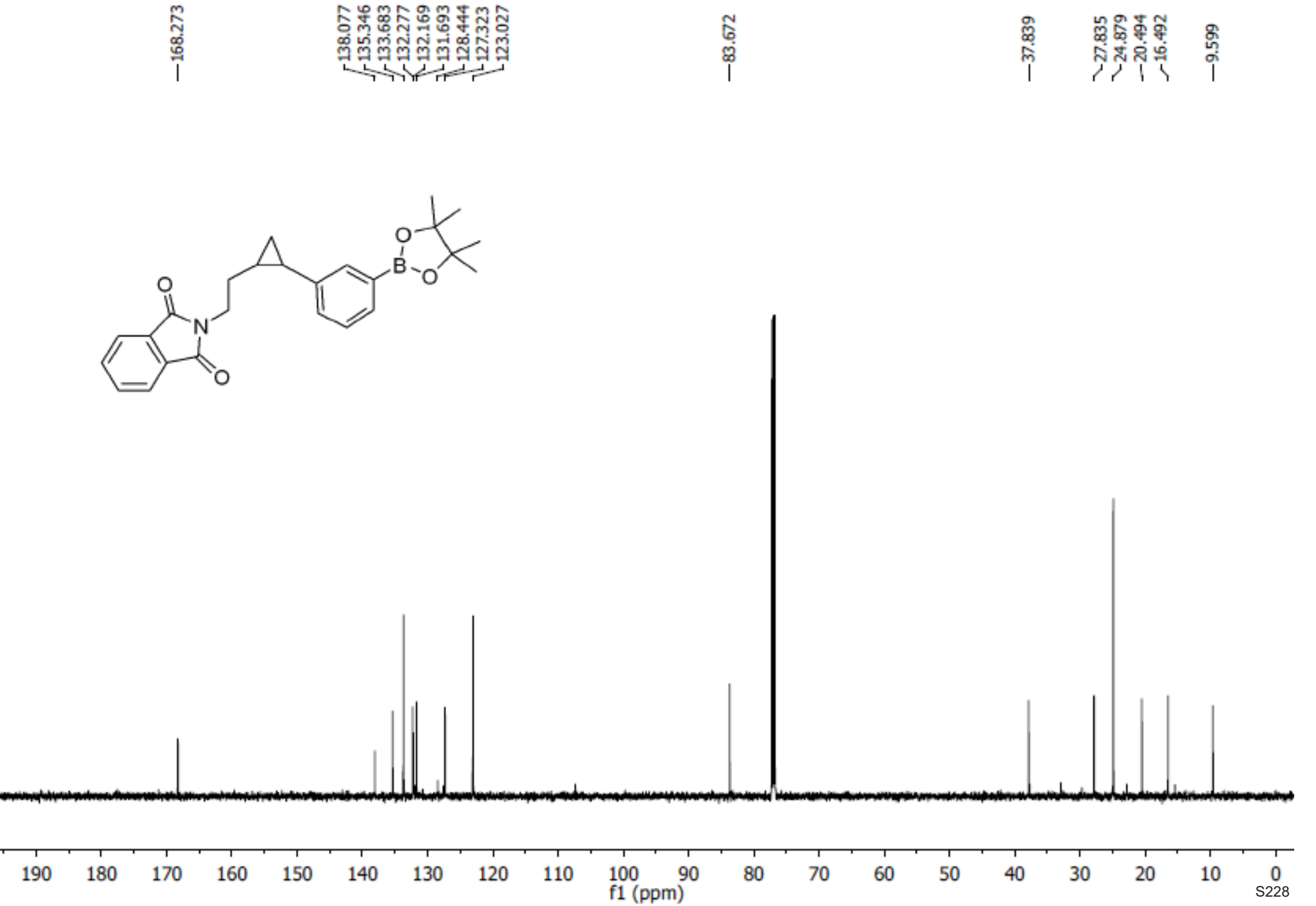
PDA Ch1 228nm

Peak#	Ret. Time	Area	Area%
1	40.844	109708	0.714
2	48.119	15250345	99.286
Total		15360053	100.000

2-(2-(2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

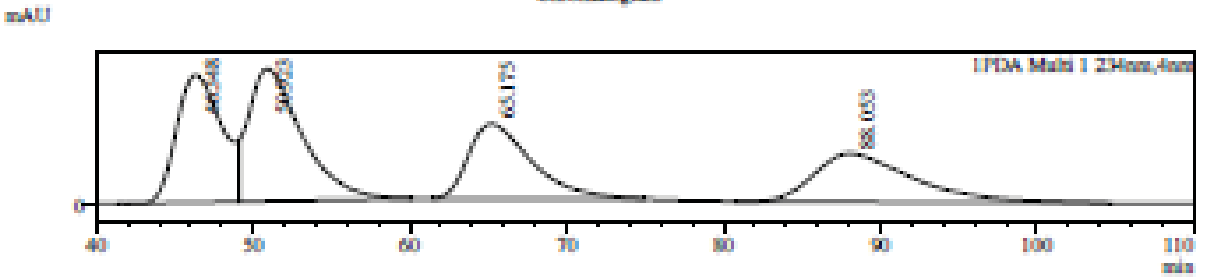


2-(2-(2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

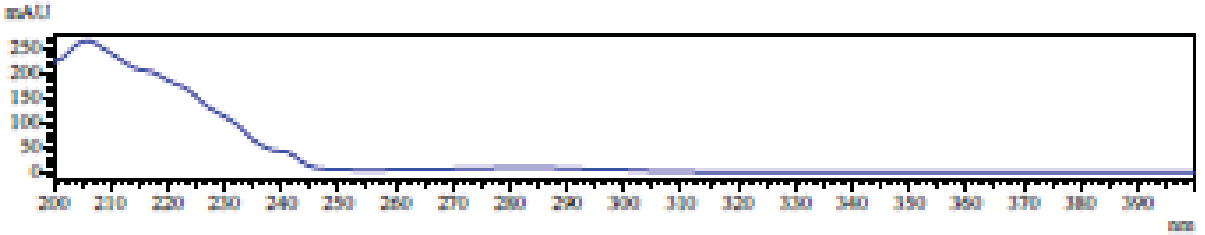
Sample Information

Data File	: Y0W-654-OJH-0.5%1.0mL-iPrOH004.lcd
Sample Name	: Y0W-654-OJH-0.5%1.0mL-iPrOH004
Sample ID	: Y0W-654-OJH-0.5%1.0mL-iPrOH004
Method File	: YW-0.5%-1.0ml.lcm

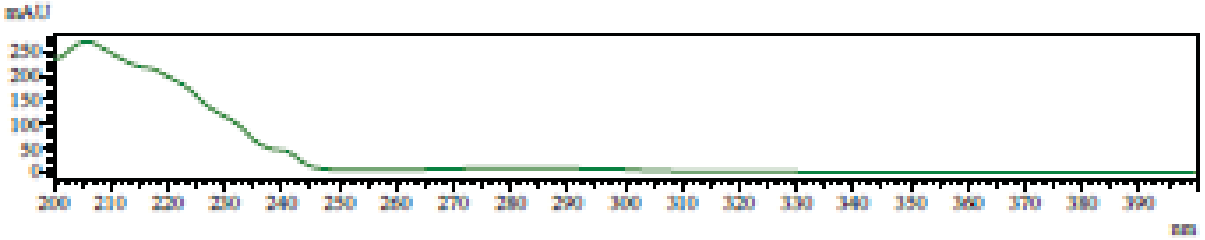
Chromatogram



UV Spectrum
Retention time = 46.348



UV Spectrum
Retention time = 50.923



Peak Table

PDA Ch1 234nm

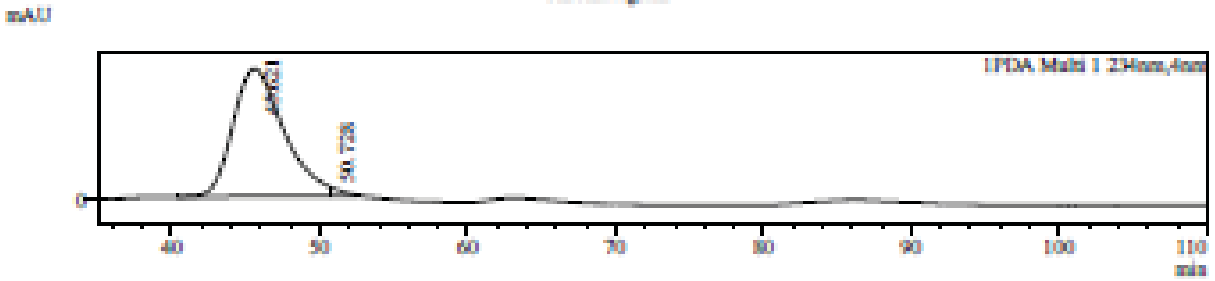
Peak#	Ret. Time	Area	Area%
1	46.348	14664632	25.906
2	50.923	17945792	31.703
3	65.175	11920137	21.058
4	88.053	12076201	21.333
Total		56606762	100.000

2-(2-(2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclopropyl)ethyl)isoindoline-1,3-dione

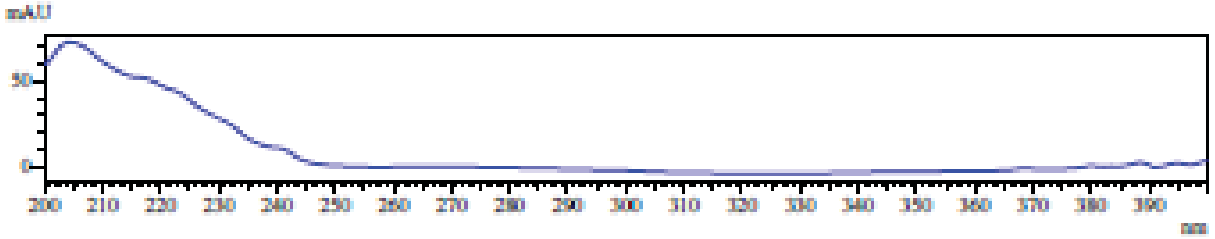
Sample Information

Data File	: Y0W-655-OJH-0.5%1.0mL-iPrOH004.lcd
Sample Name	: Y0W-655-OJH-0.5%1.0mL-iPrOH004
Sample ID	: Y0W-655-OJH-0.5%1.0mL-iPrOH004
Method File	: YW-0.5%-1.0ml.lcm

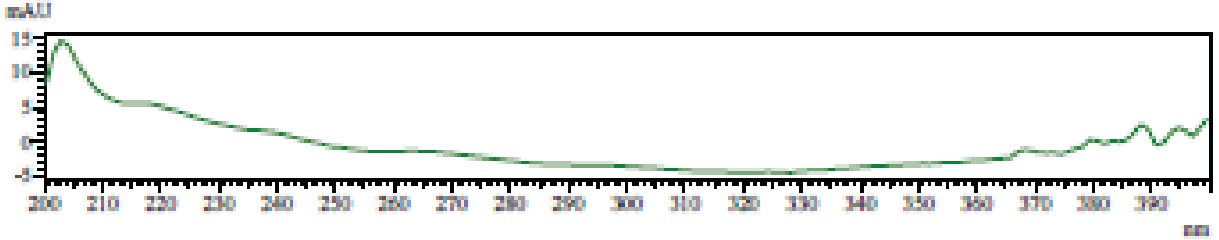
Chromatogram



UV Spectrum
Retention time = 45.621



UV Spectrum
Retention time = 50.728

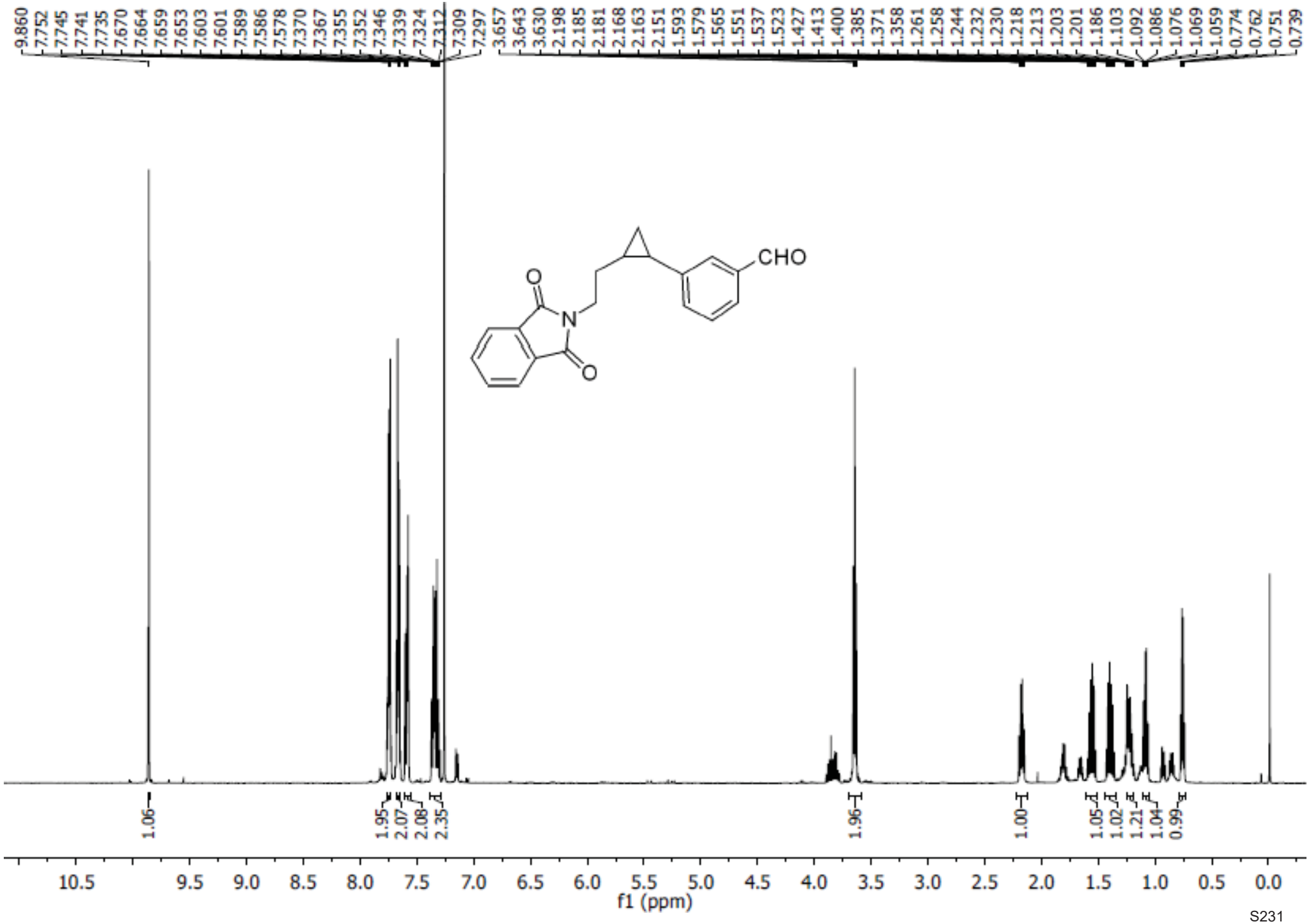


Peak Table

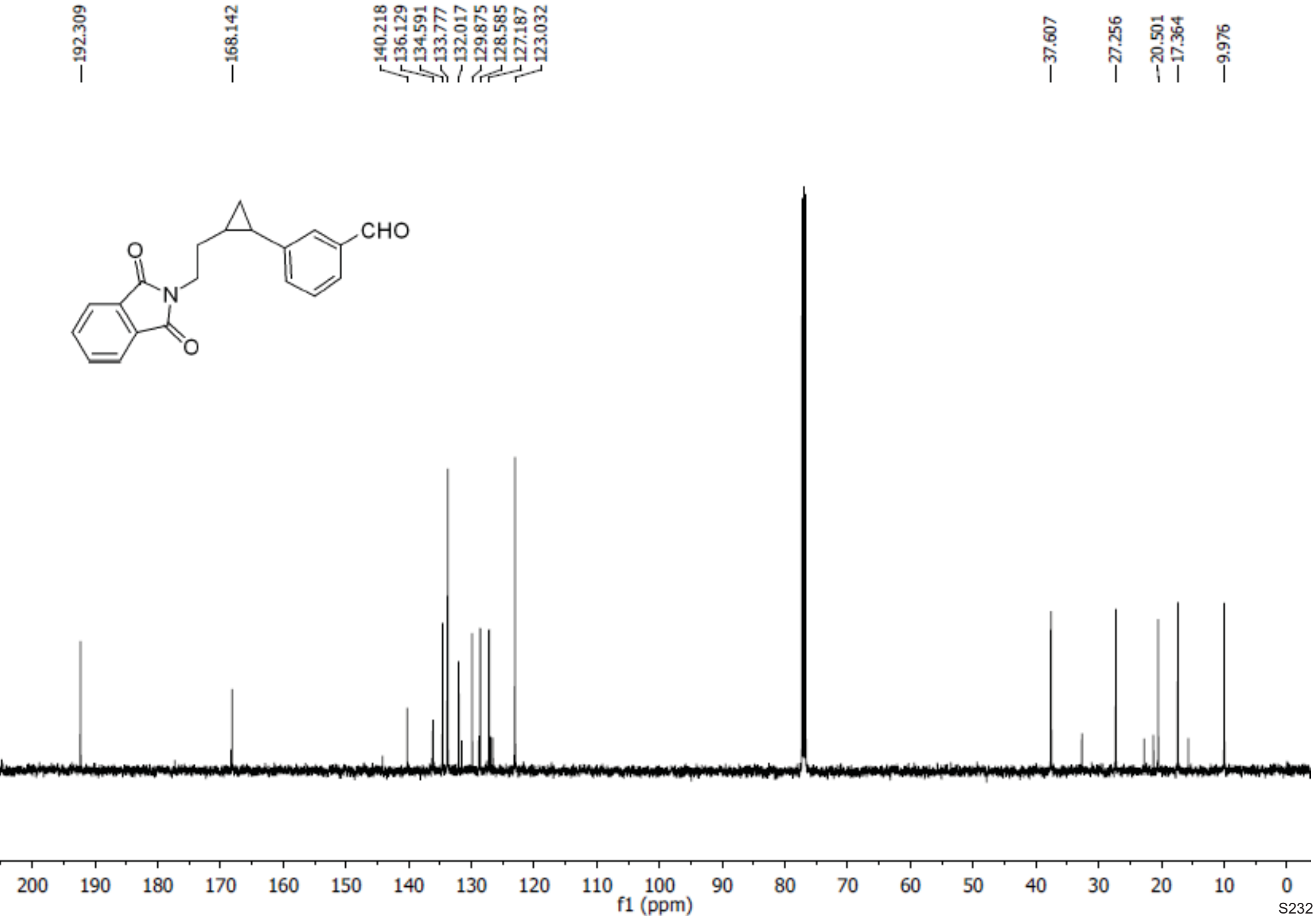
PDA Ch1 234nm

Peak#	Ret. Time	Area	Area%
1	45.621	4427681	98.654
2	50.728	60411	1.346
Total		4488091	100.000

3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl)benzaldehyde



3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl)benzaldehyde

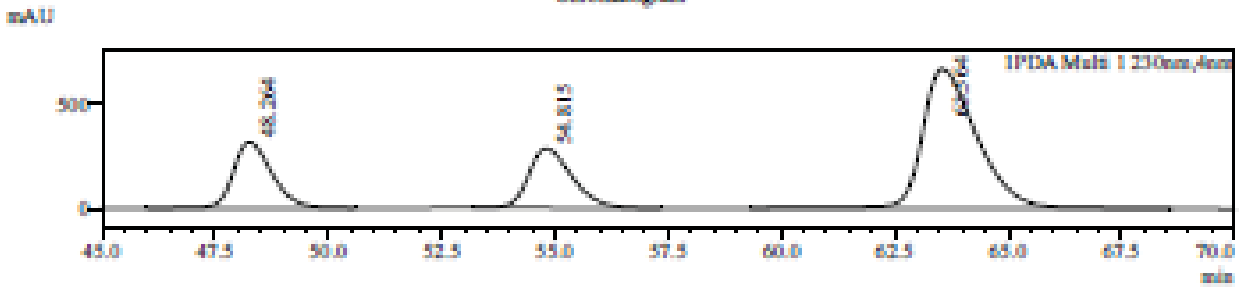


3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl)benzaldehyde

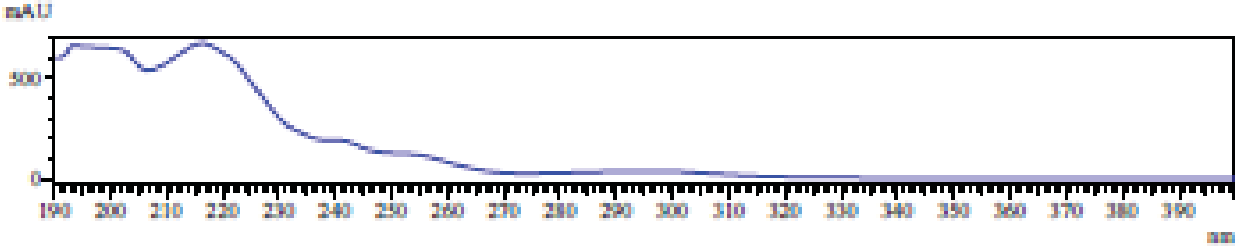
Sample Information

Data File	: YOW-656-IE-15%0.8mL-iPrOH004.lcd
Sample Name	: YOW-656-IE-15%0.8mL-iPrOH004
Sample ID	: YOW-656-IE-15%0.8mL-iPrOH004
Method File	: YW-15.0%-0.8ml.lcm

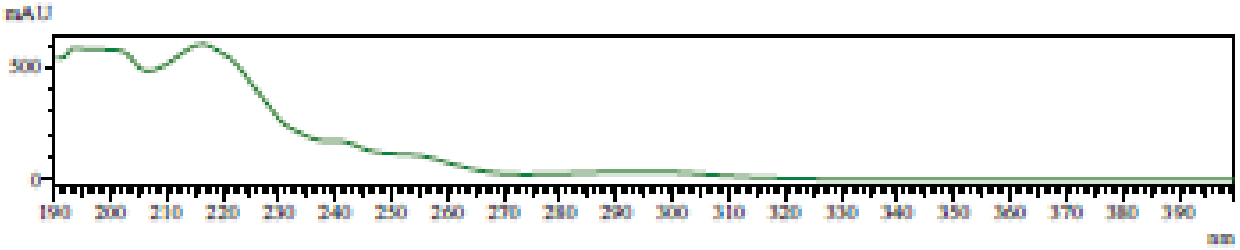
Chromatogram



UV Spectrum
Retention time = 48.264



UV Spectrum
Retention time = 54.815



Peak Table

PDA Ch1 230nm

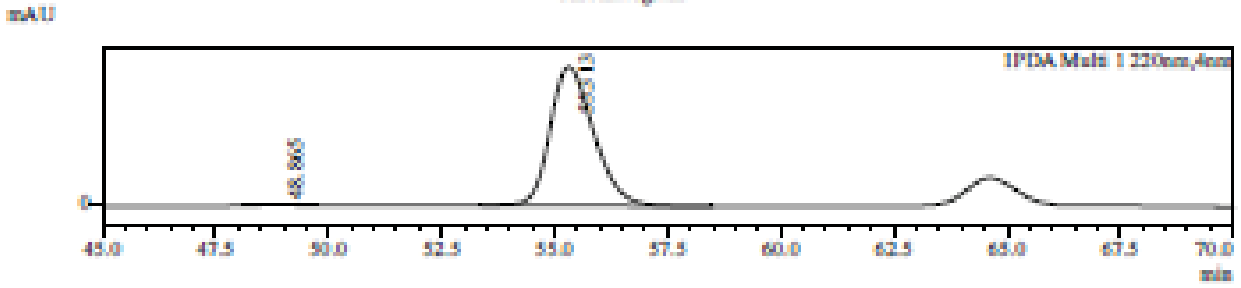
Peak#	Ret. Time	Area	Area%
1	48.264	18539342	19.988
2	54.815	18714306	20.154
3	63.564	55580583	59.858
Total		92854431	100.000

3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl)benzaldehyde

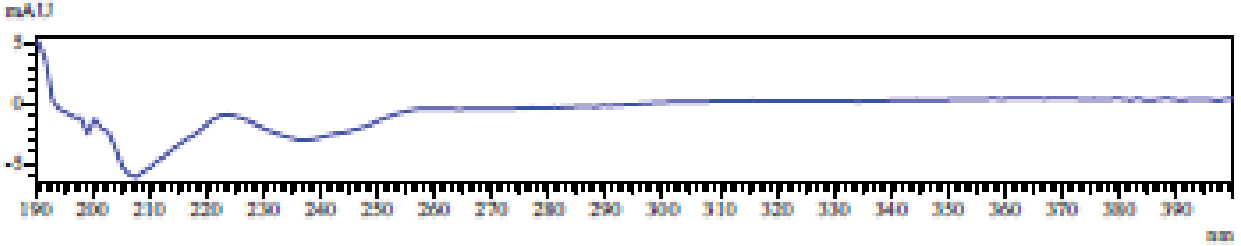
Sample Information

Data File	: YOW-657-IE-15%0.8mL-iPrOH005.lcd
Sample Name	: YOW-657-IE-15%0.8mL-iPrOH005
Sample ID	: YOW-657-IE-15%0.8mL-iPrOH005
Method File	: YW-15.0%-0.8ml.lcm

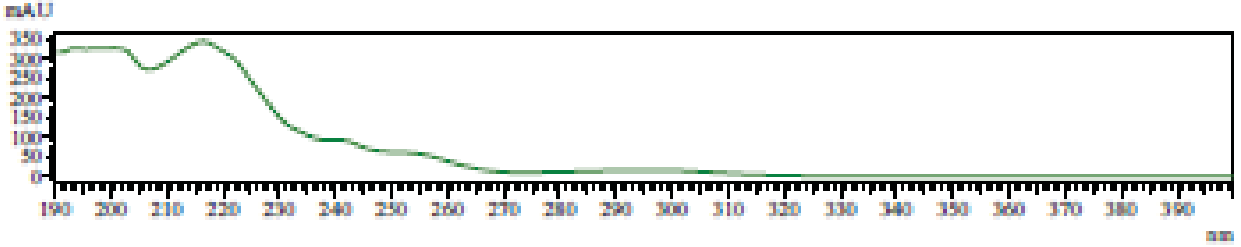
Chromatogram



UV Spectrum
Retention time = 48.865



UV Spectrum
Retention time = 55.313

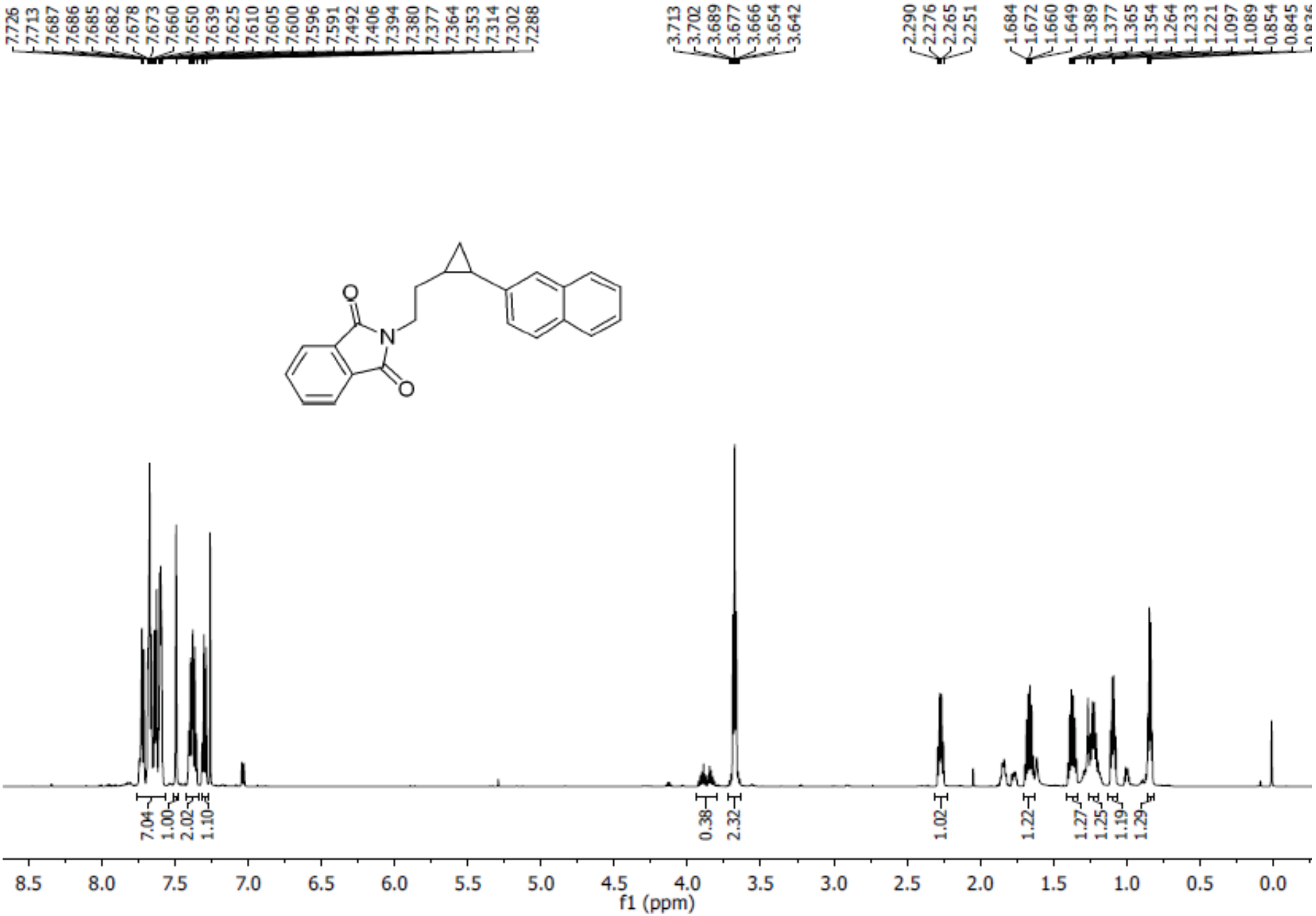


Peak Table

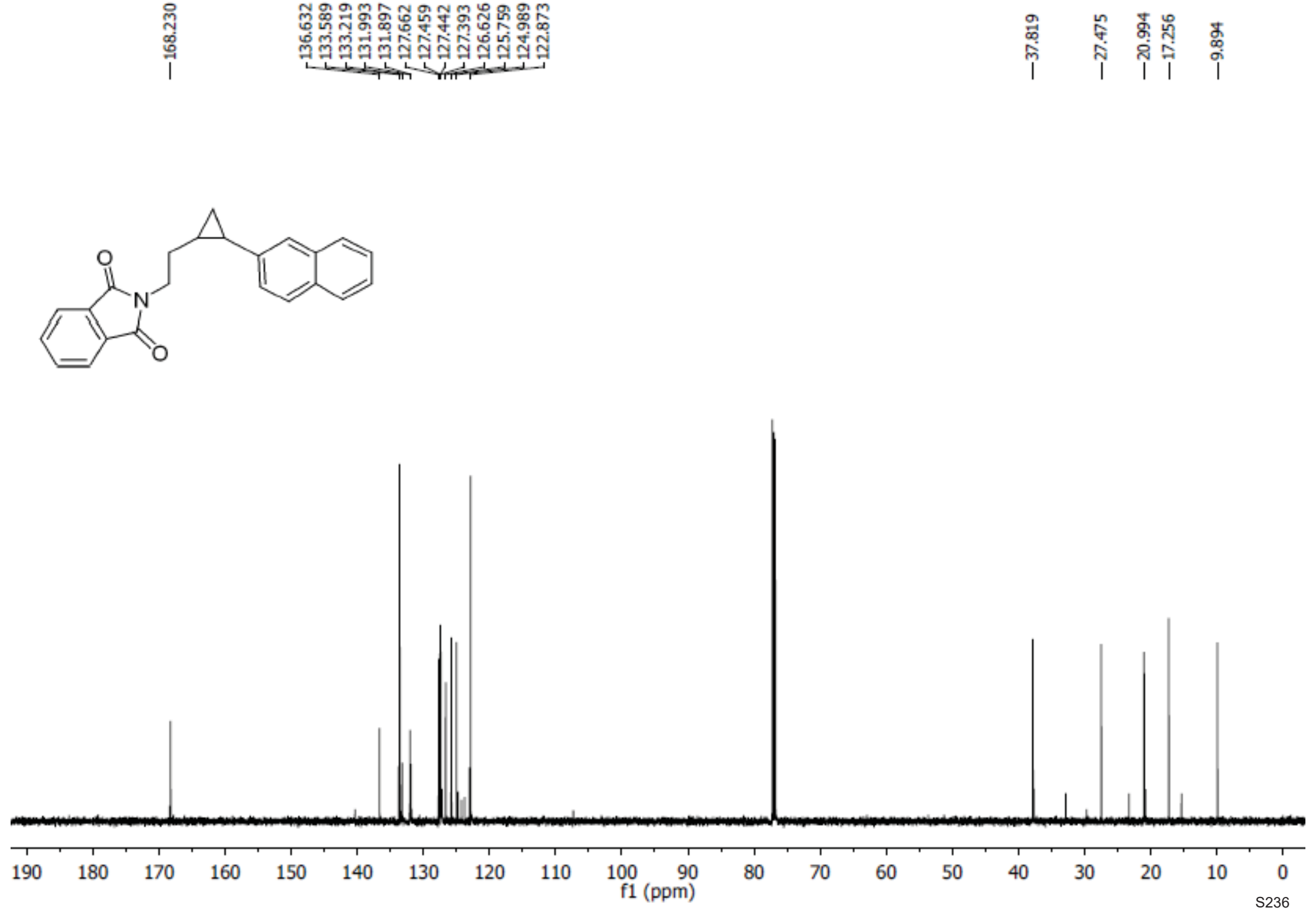
PDA Ch1 220nm

Peak#	Ret. Time	Area	Area%
1	48.865	137437	0.643
2	55.313	21231195	99.357
Total		21368632	100.000

2-(2-(2-(naphthalen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(naphthalen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

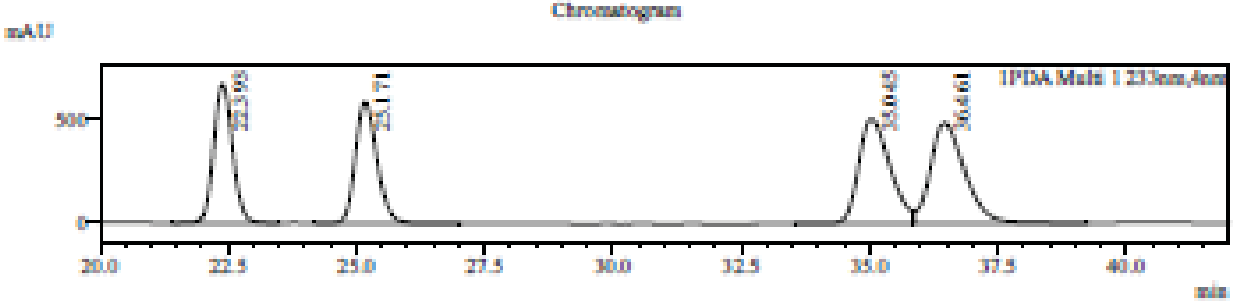


2-(2-(2-(naphthalen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

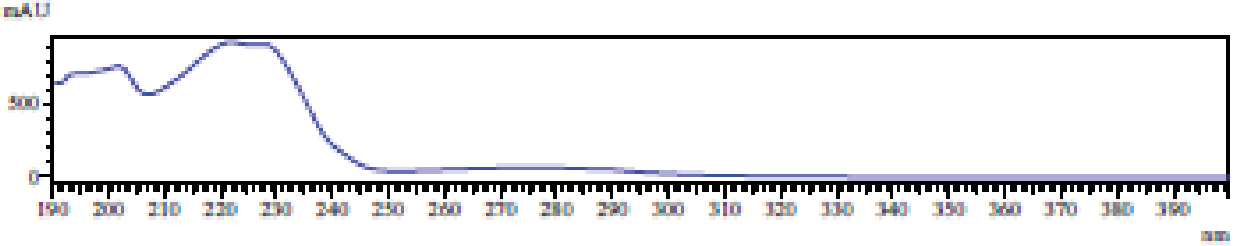
Sample Information

Data File	: Y0W-618-IE-10%0.8mL-iPrOH.lcd
Sample Name	: Y0W-618-IE-10%0.8mL-iPrOH
Sample ID	: Y0W-618-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

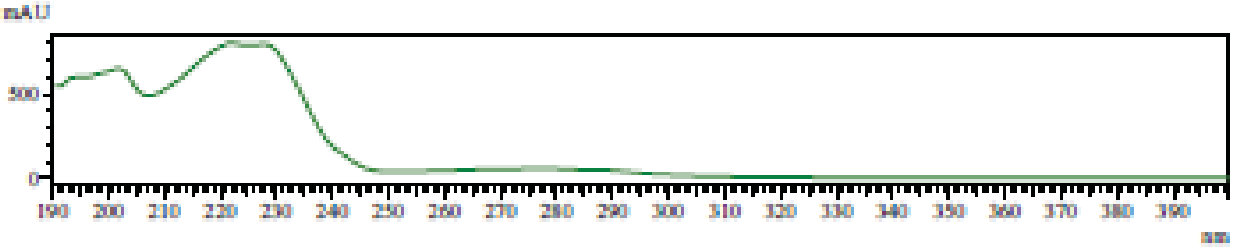
Chromatogram



UV Spectrum
Retention time = 22.393



UV Spectrum
Retention time = 25.171



Peak Table

PDA Ch1 233nm

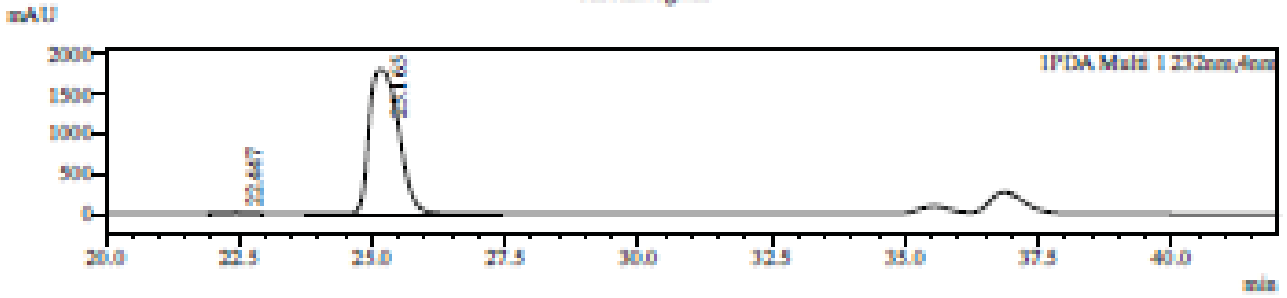
Peak#	Ret. Time	Area	Area%
1	22.393	17267306	21.801
2	25.171	17421317	21.996
3	35.045	21681988	27.375
4	36.461	22833170	28.828
Total		79203780	100.000

2-(2-(2-(naphthalen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

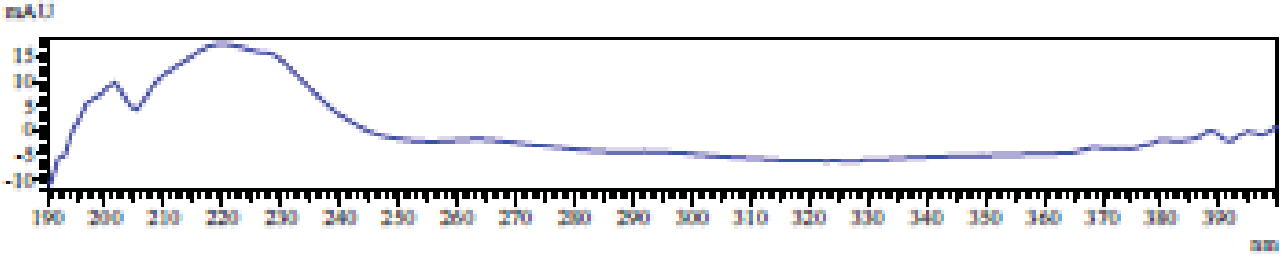
Sample Information

Data File	: Y0W-621-IE-10%0.8mL-iPrOH.lcd
Sample Name	: Y0W-621-IE-10%0.8mL-iPrOH
Sample ID	: Y0W-621-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

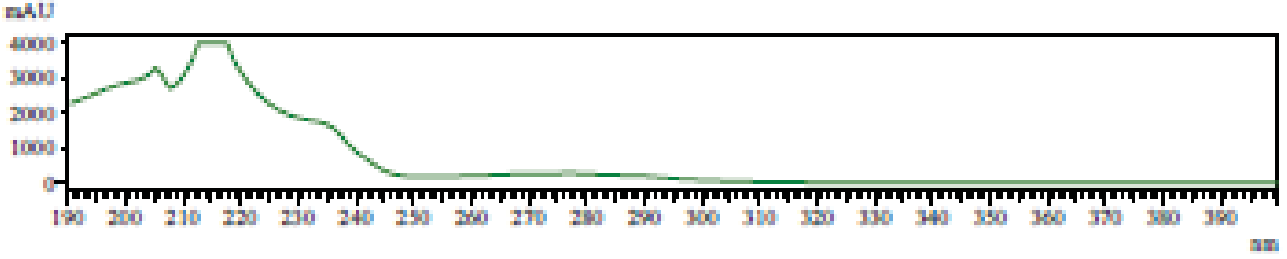
Chromatogram



UV Spectrum
Retention time = 22.447



UV Spectrum
Retention time = 25.165

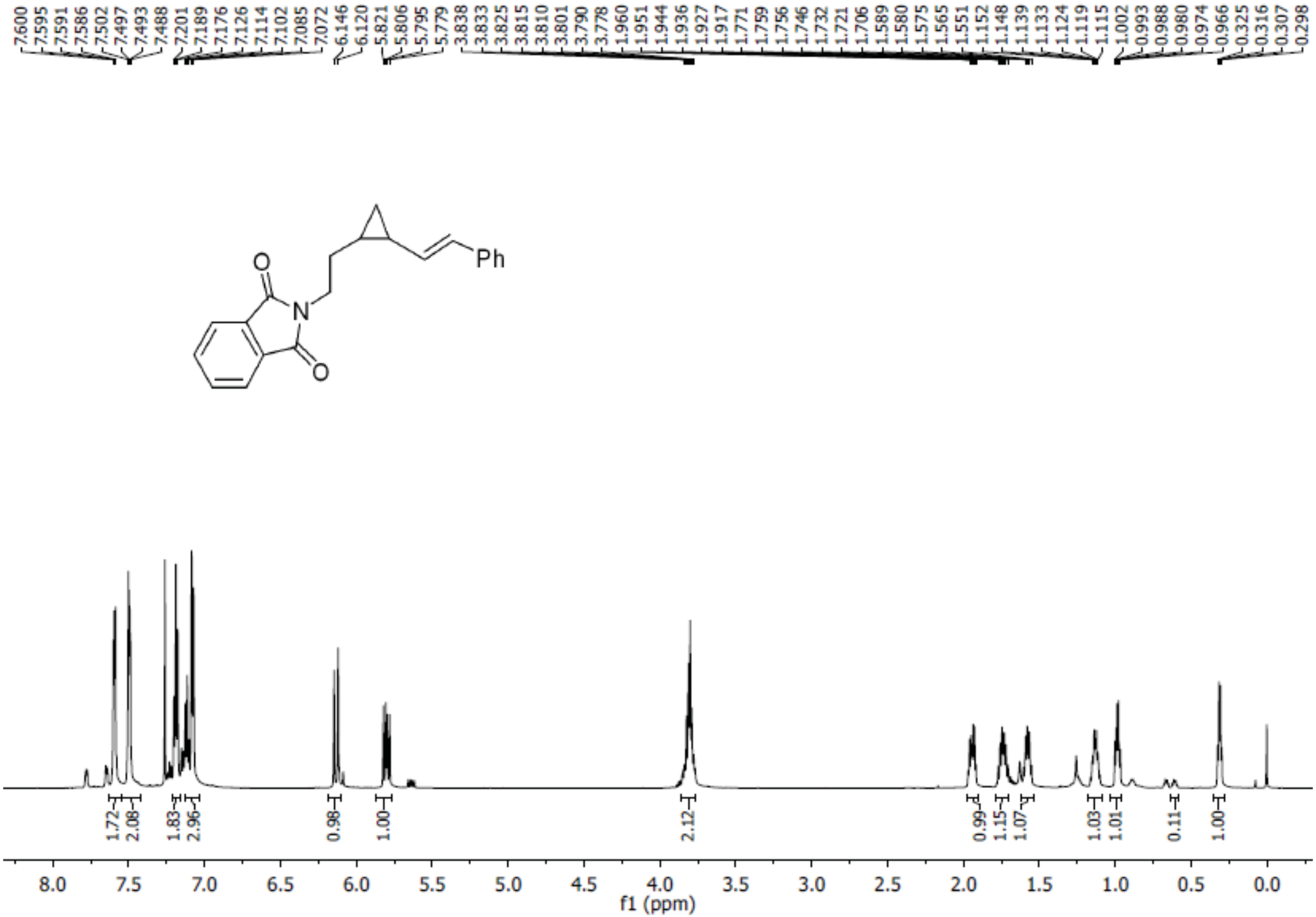


Peak Table

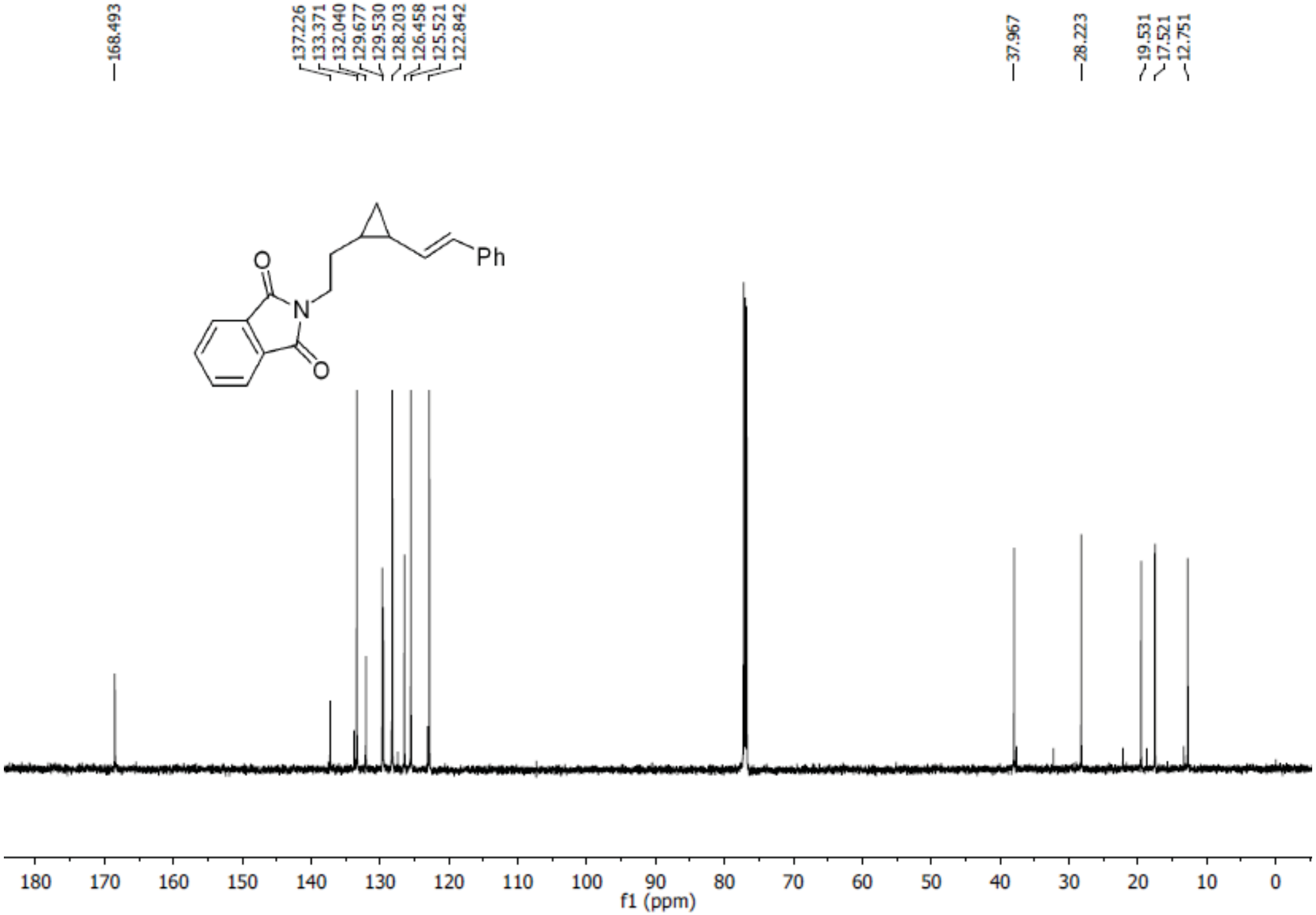
PDA Ch1 232nm

Peak#	Ret. Time	Area	Area%
1	22.447	226806	0.325
2	25.165	69577553	99.675
Total		69804358	100.000

(E)-2-(2-(2-styrylcyclopropyl)ethyl)isoindoline-1,3-dione



(E)-2-(2-(2-styrylcyclopropyl)ethyl)isoindoline-1,3-dione

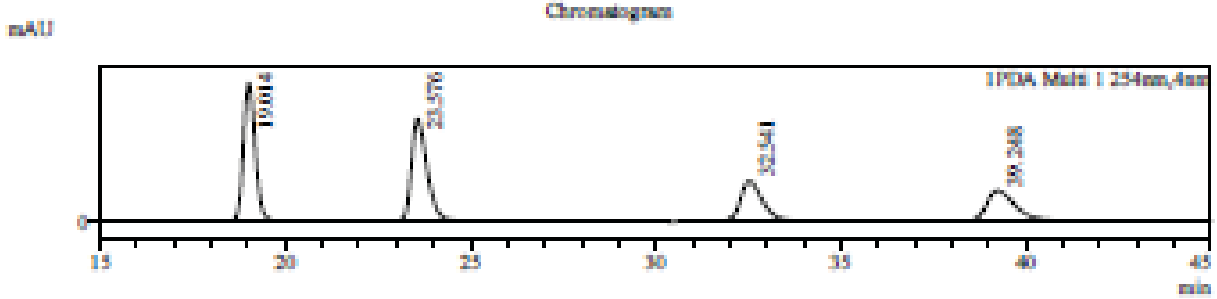


(E)-2-(2-(2-styrylcyclopropyl)ethyl)isoindoline-1,3-dione

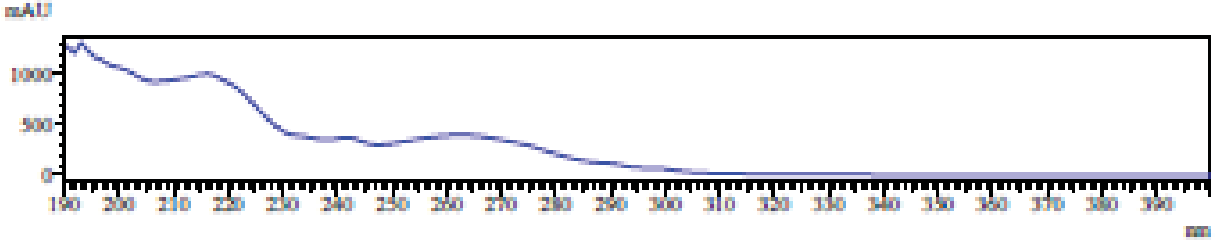
Sample Information

Data File	: PKL-016-IE-10%0.8mL.lcd
Sample Name	: PKL-016-IE-10%0.8mL
Sample ID	: PKL-016-IE-10%0.8mL
Method File	: PKL-10%-0.8ml.lcm

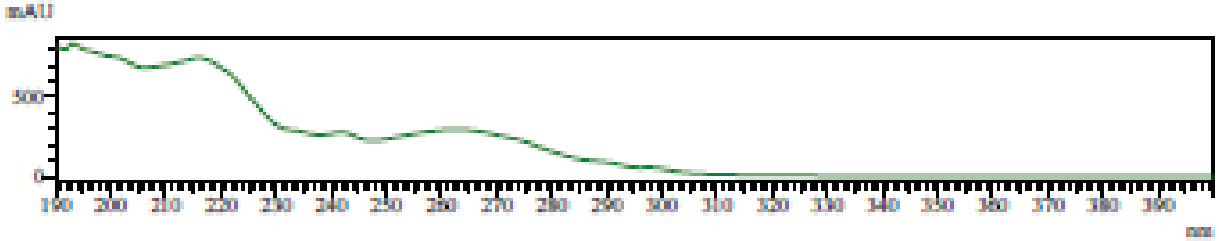
Chromatogram



UV Spectrum
Retention time = 19.014



UV Spectrum
Retention time = 23.576



Peak Table

PDA Ch1 254nm

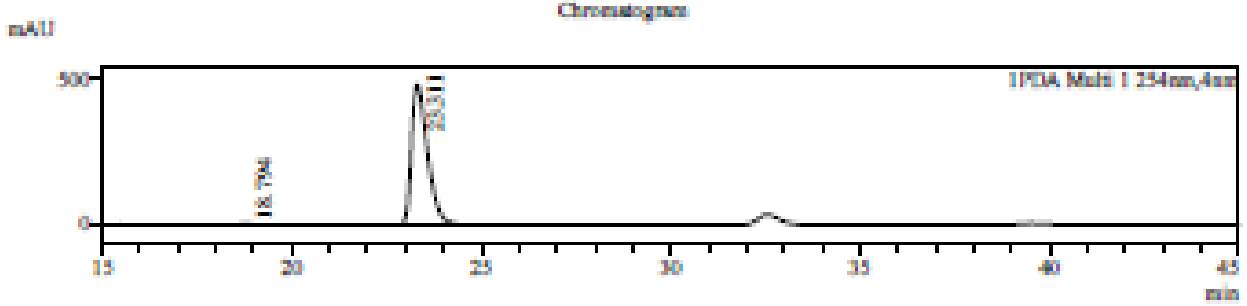
Peak#	Ret. Time	Area	Area%
1	19.014	7721576	32.681
2	23.576	7687028	32.535
3	32.541	4106985	17.382
4	39.248	4111549	17.402
Total		23627137	100.000

(E)-2-(2-(2-styrylcyclopropyl)ethyl)isoindoline-1,3-dione

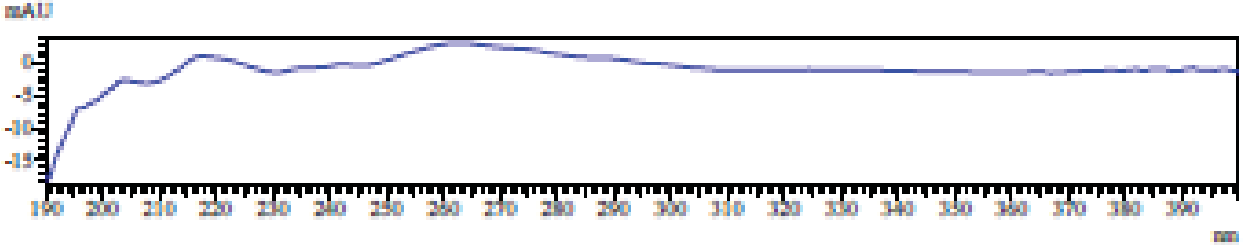
Sample Information

Data File	: Y0W-711-IE-10%0.8mL-iPrOH.lcd
Sample Name	: Y0W-711-IE-10%0.8mL-iPrOH
Sample ID	: Y0W-711-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

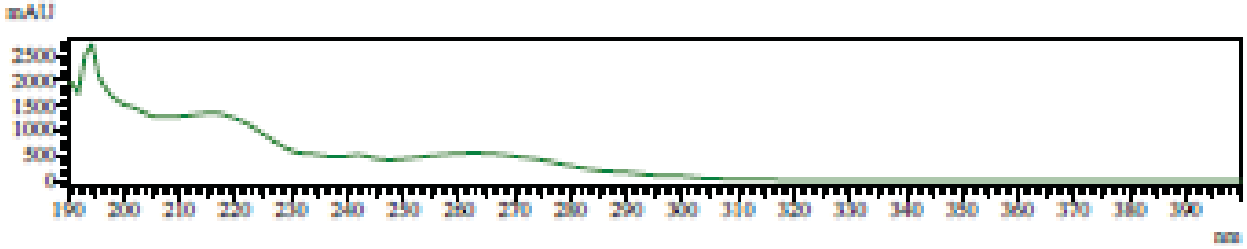
Chromatogram



UV Spectrum
Retention time = 18.794



UV Spectrum
Retention time = 23.311

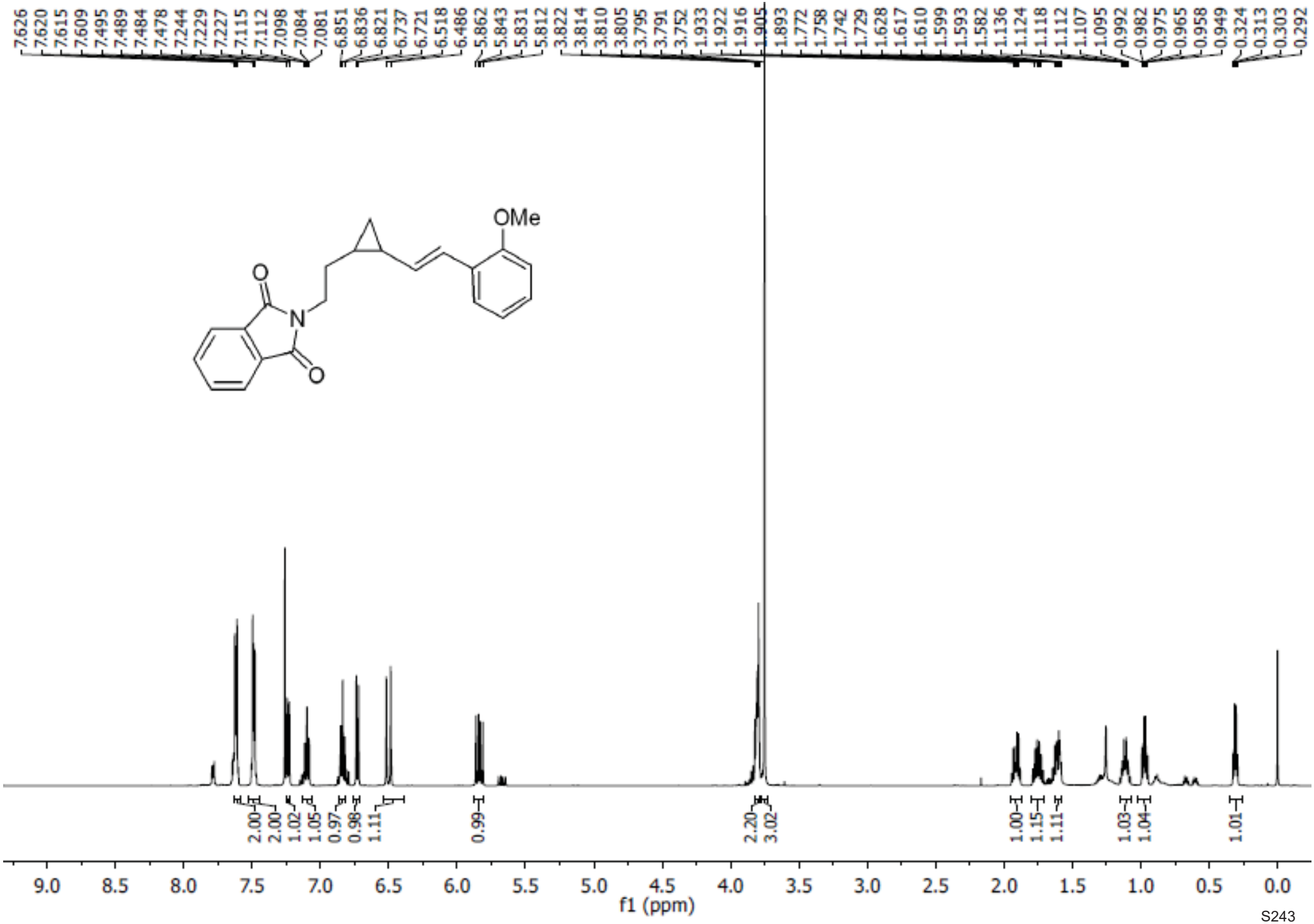


Peak Table

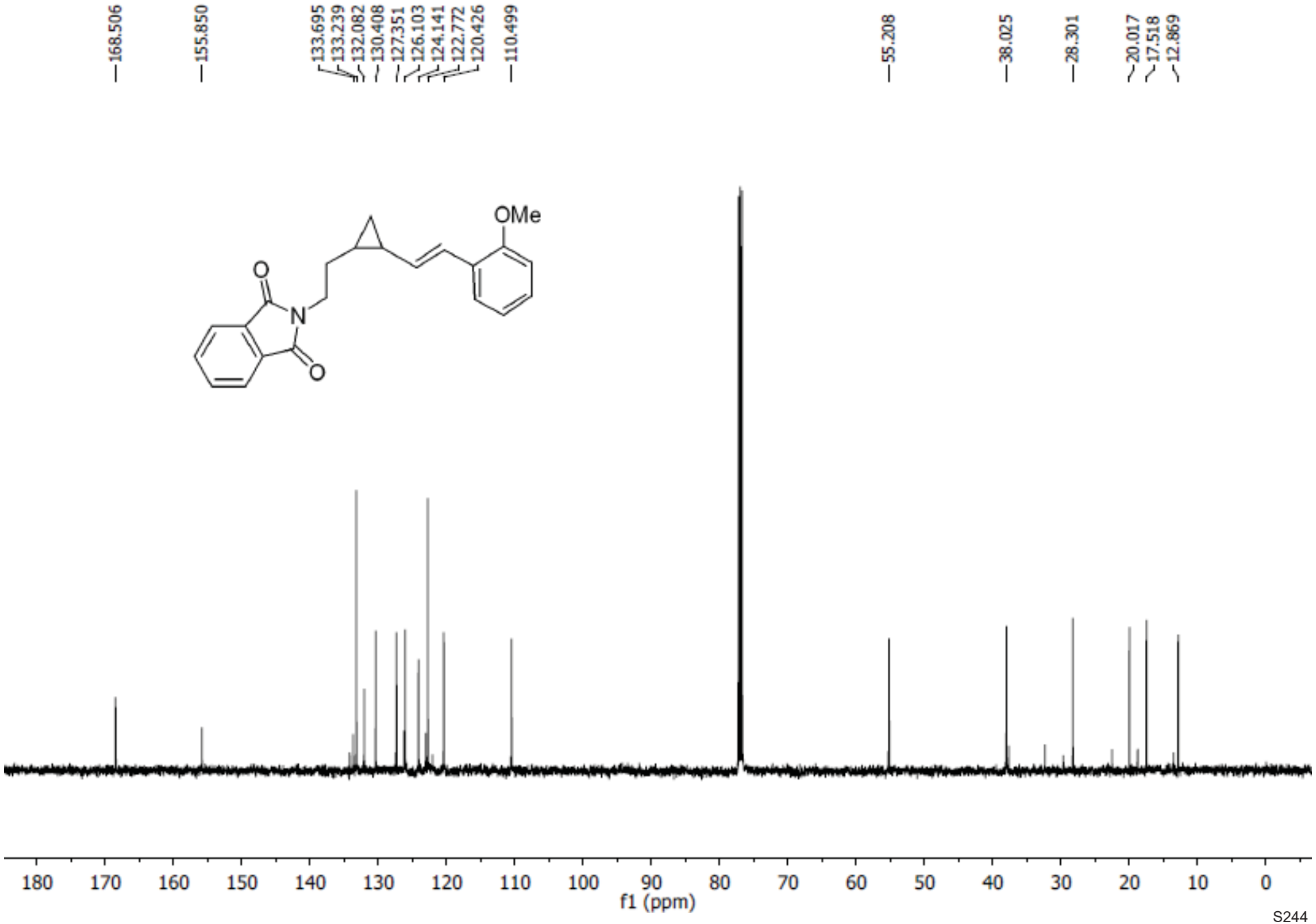
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	18.794	81556	0.568
2	23.311	14279534	99.432
Total		14361090	100.000

(E)-2-(2-(2-(2-methoxystyryl)cyclopropyl)ethyl)isoindoline-1,3-dione



(E)-2-(2-(2-(2-methoxystyryl)cyclopropyl)ethyl)isoindoline-1,3-dione

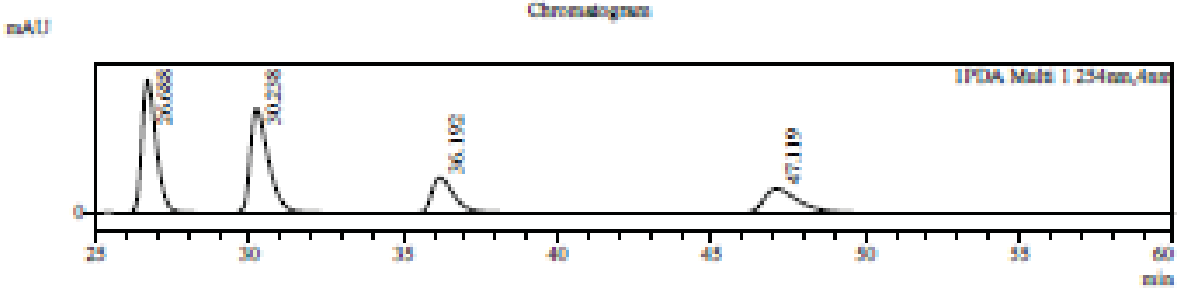


(E)-2-(2-(2-(2-methoxystyryl)cyclopropyl)ethyl)isoindoline-1,3-dione

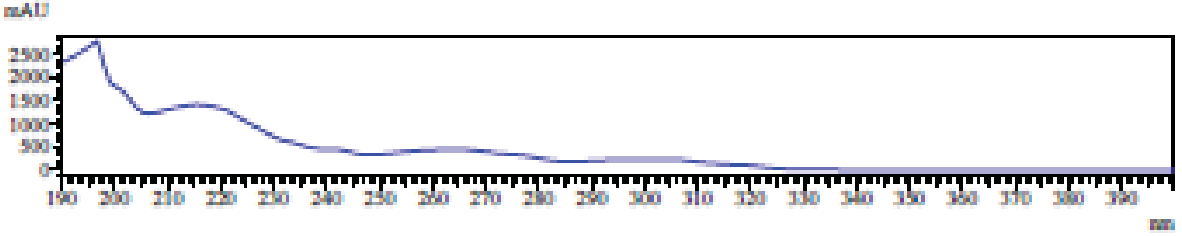
Sample Information

Data File	: Y0W-753-IE-10%0.8mL-iPrOH001.lcd
Sample Name	: Y0W-753-IE-10%0.8mL-iPrOH001
Sample ID	: Y0W-753-IE-10%0.8mL-iPrOH001
Method File	: YW-10%-0.8ml.lcm

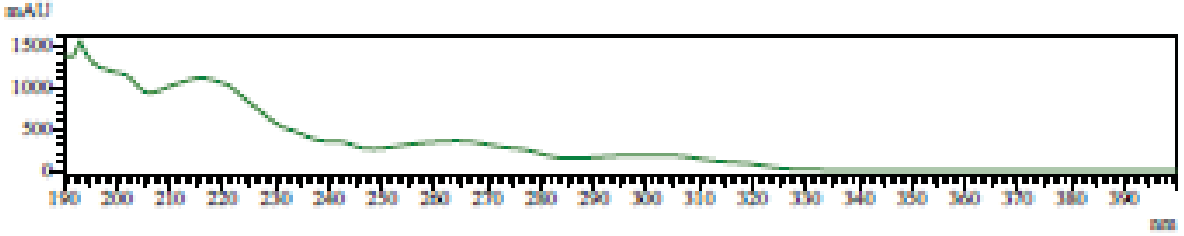
Chromatogram



UV Spectrum
Retention time = 26.688



UV Spectrum
Retention time = 30.238



Peak Table

PDA Ch1 254nm

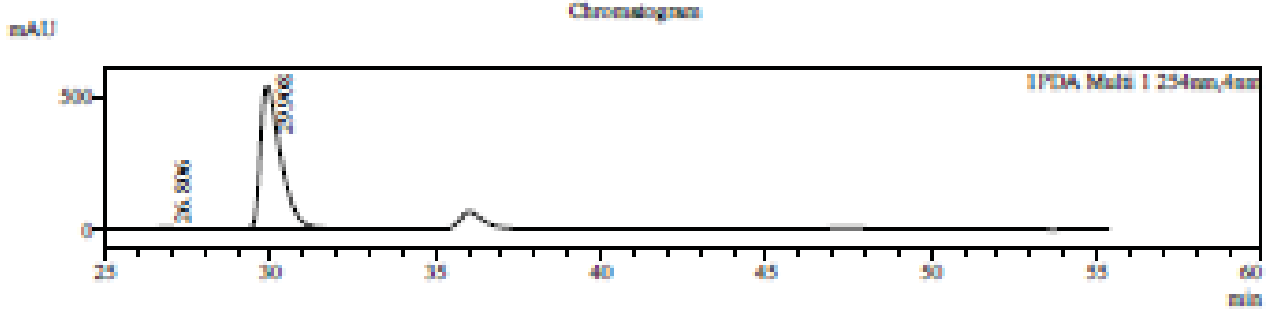
Peak#	Ret. Time	Area	Area%
1	26.688	12371416	35.065
2	30.238	12296334	34.852
3	36.192	5144588	14.582
4	47.119	5468907	15.501
Total		35281246	100.000

(E)-2-(2-(2-(2-methoxystyryl)cyclopropyl)ethyl)isoindoline-1,3-dione

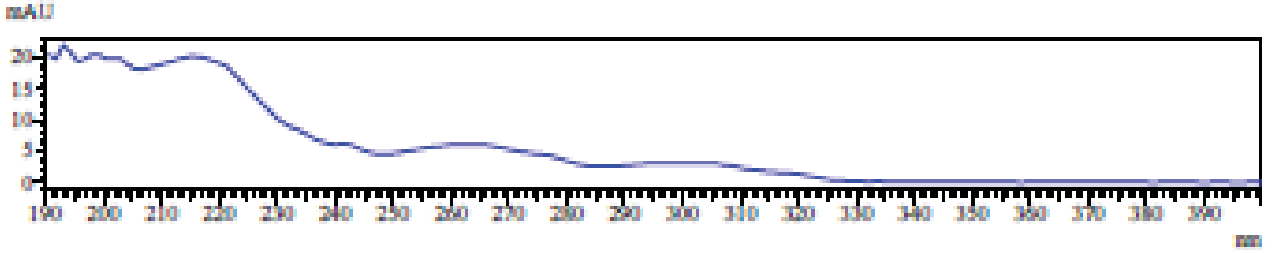
Sample Information

Data File	: Y0W-754-IE-10%0.8mL-iPrOH001.lcd
Sample Name	: Y0W-754-IE-10%0.8mL-iPrOH001
Sample ID	: Y0W-754-IE-10%0.8mL-iPrOH001
Method File	: YW-10%-0.8mL.lcm

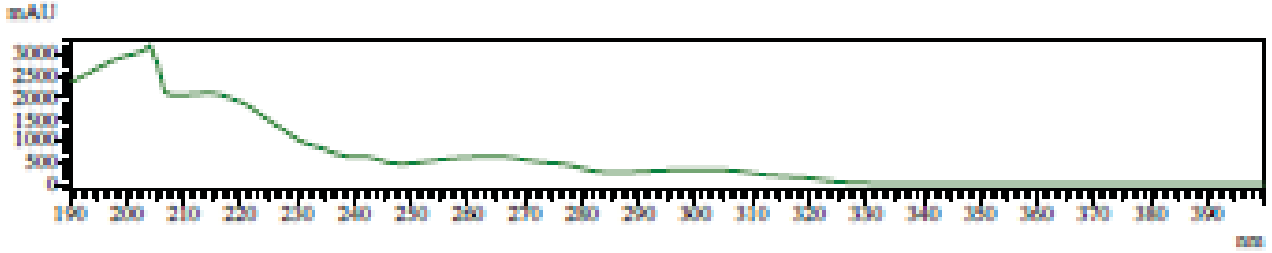
Chromatogram



UV Spectrum
Retention time = 26.806



UV Spectrum
Retention time = 29.908

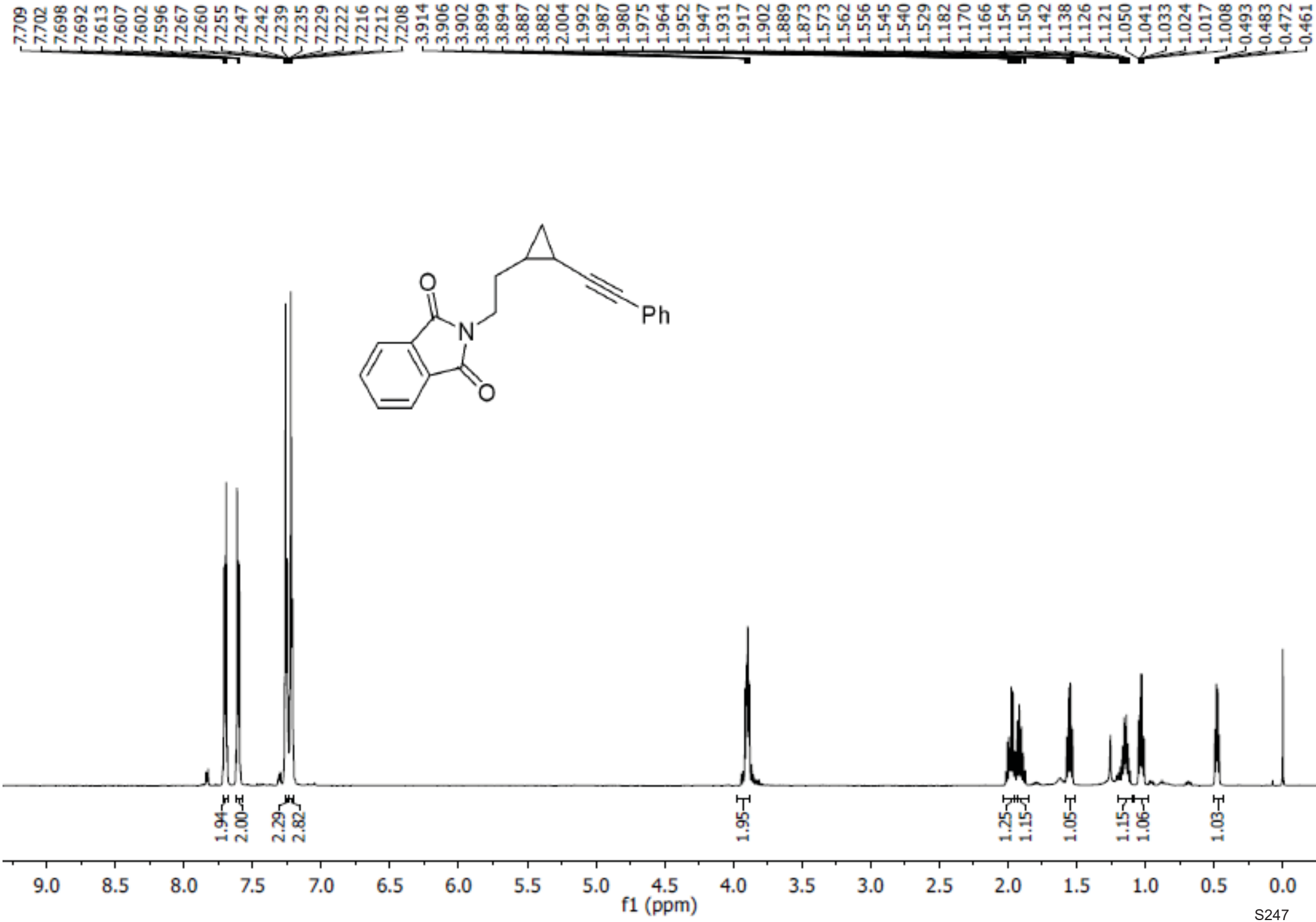


Peak Table

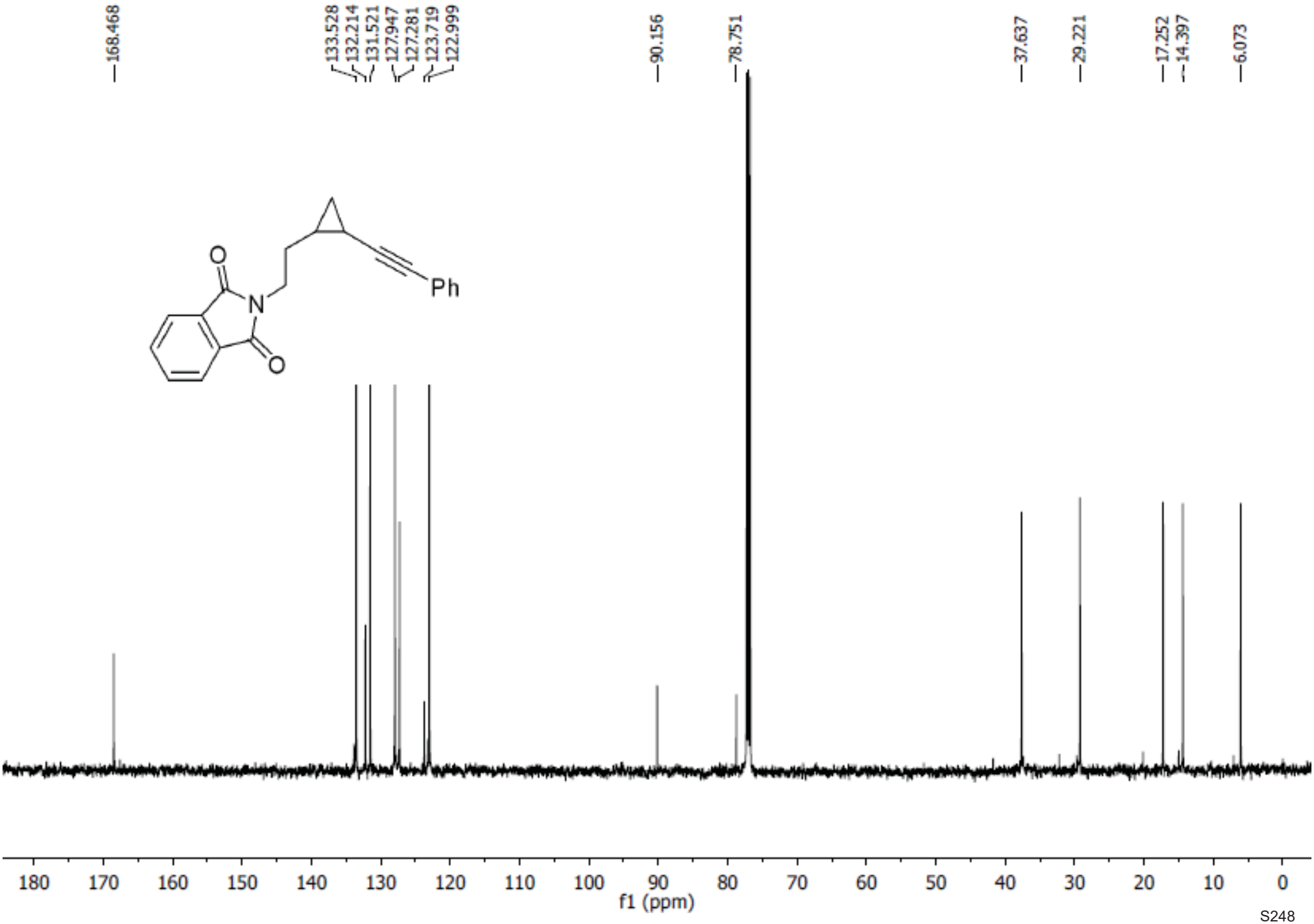
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	26.806	137968	0.598
2	29.908	22947637	99.402
Total		23085605	100.000

2-(2-(2-(phenylethynyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(phenylethynyl)cyclopropyl)ethyl)isoindoline-1,3-dione

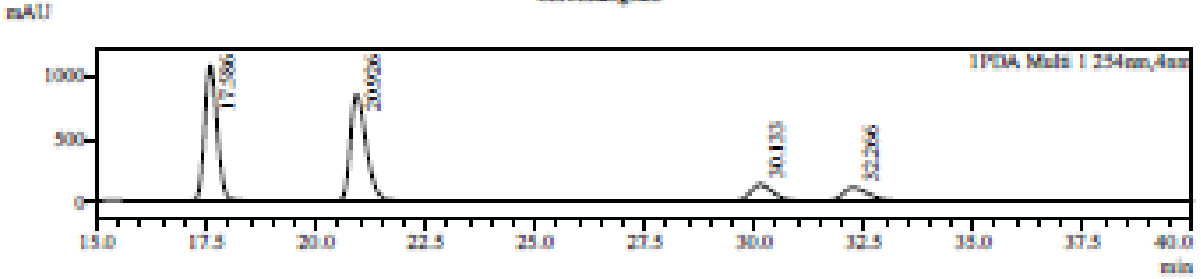


2-(2-(2-(phenylethynyl)cyclopropyl)ethyl)isoindoline-1,3-dione

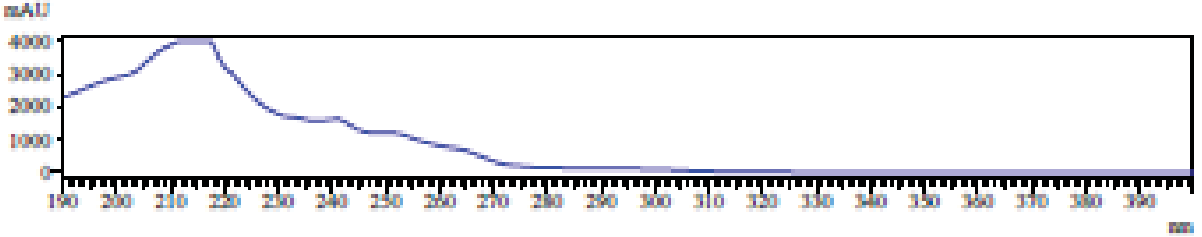
Sample Information

Data File	: PKL-020-ENYNE-IE-10%0.8mL.lcd
Sample Name	: PKL-020-ENYNE-IE-10%0.8mL
Sample ID	: PKL-020-ENYNE-IE-10%0.8mL
Method File	: PKL-10%-0.8ml.lcm

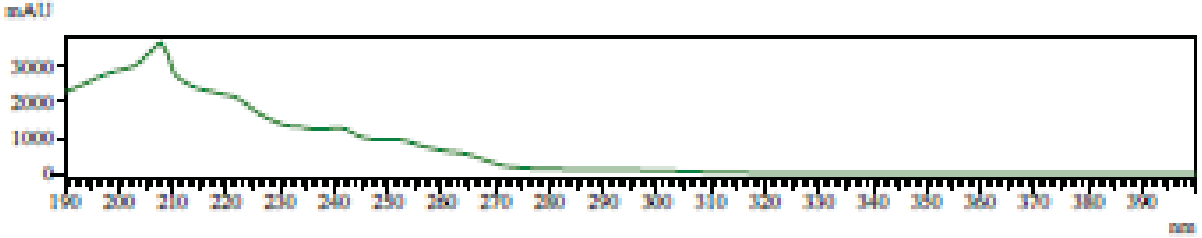
Chromatogram



UV Spectrum
Retention time = 17.586



UV Spectrum
Retention time = 20.926



Peak Table

PDA Ch1 254nm

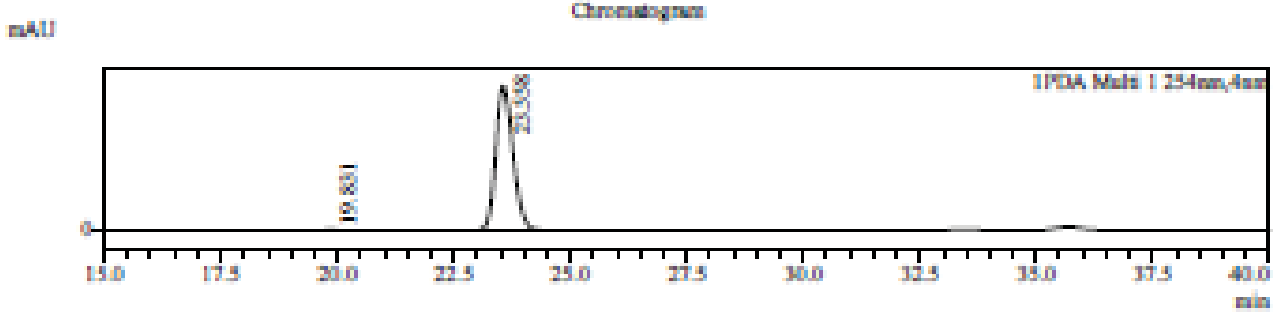
Peak#	Ret. Time	Area	Area%
1	17.586	21096706	40.441
2	20.926	21572858	41.353
3	30.133	4949887	9.489
4	32.266	4547672	8.718
Total		52167123	100.000

2-(2-(2-(phenylethynyl)cyclopropyl)ethyl)isoindoline-1,3-dione

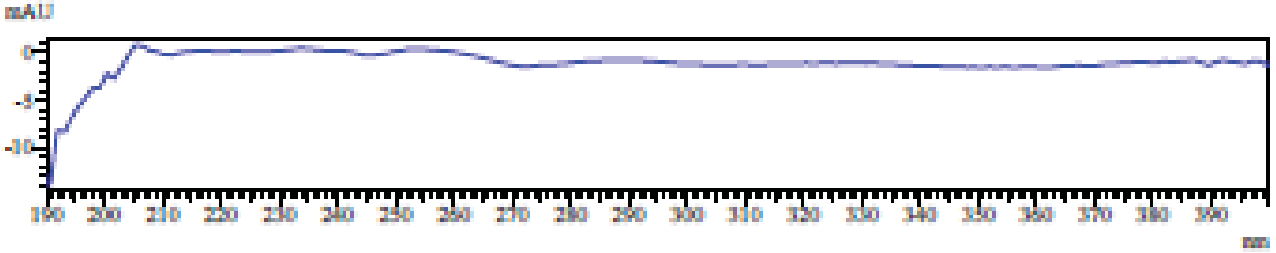
Sample Information

Data File	: Y0W-718-IE-10%0.8mL-iPrOH.lcd
Sample Name	: Y0W-718-IE-10%0.8mL-iPrOH
Sample ID	: Y0W-718-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

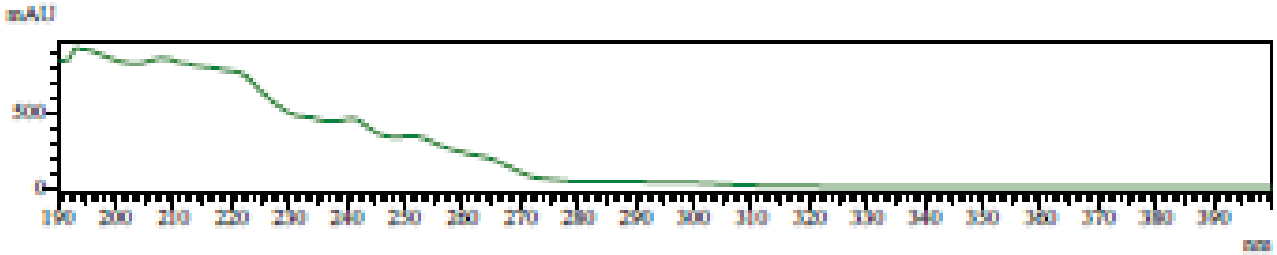
Chromatogram



UV Spectrum
Retention time = 19.831



UV Spectrum
Retention time = 23.558

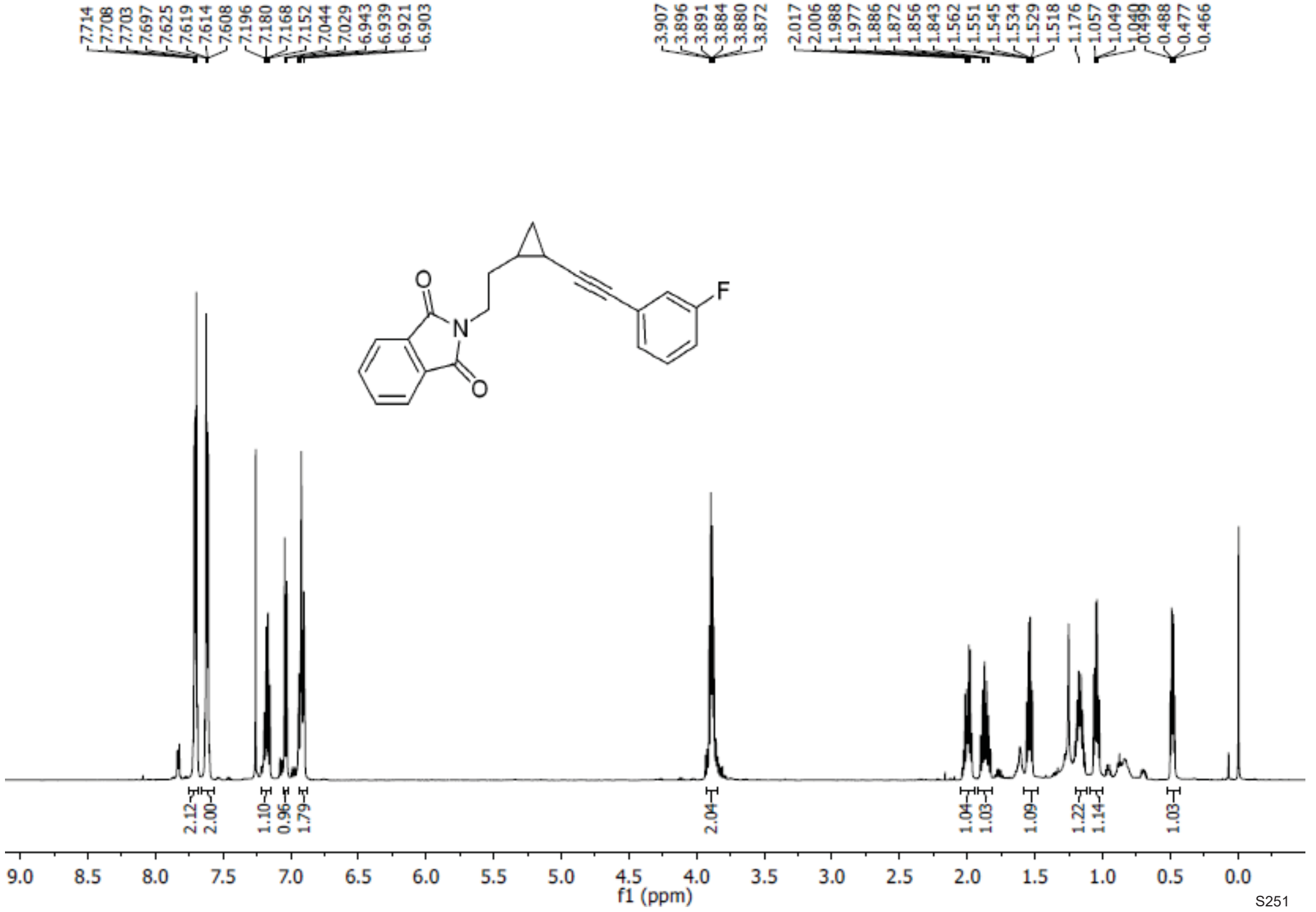


Peak Table

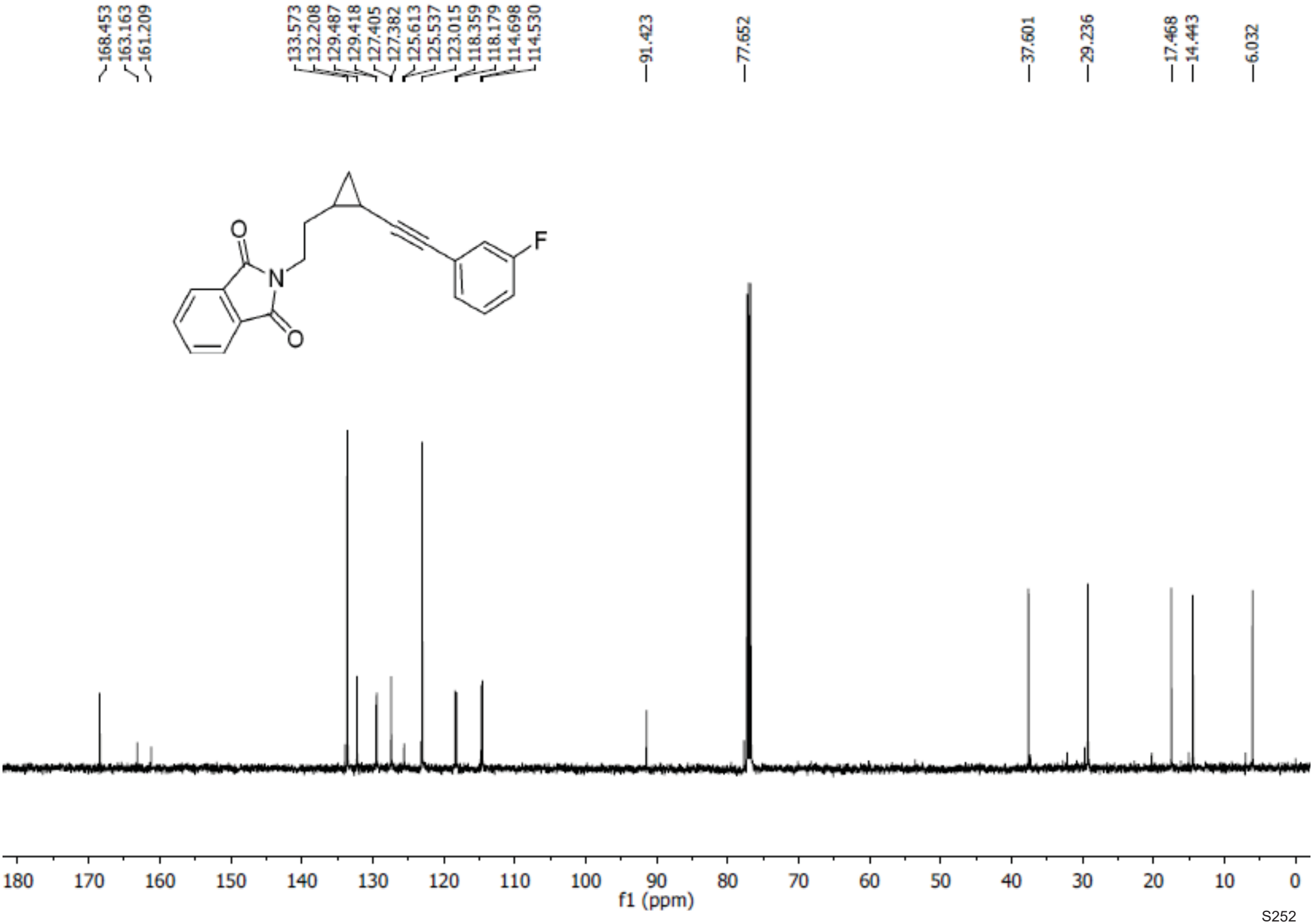
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	19.831	43853	0.538
2	23.558	8106384	99.462
Total		8150237	100.000

2-(2-(2-((3-fluorophenyl)ethynyl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-((3-fluorophenyl)ethynyl)cyclopropyl)ethyl)isoindoline-1,3-dione

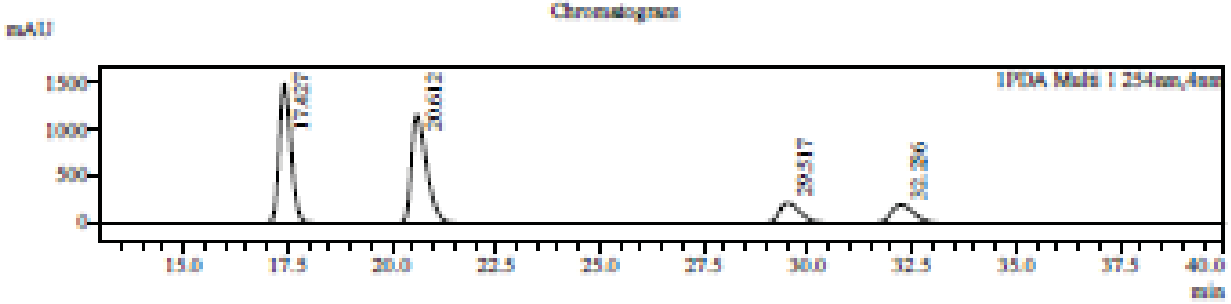


2-(2-(2-((3-fluorophenyl)ethynyl)cyclopropyl)ethyl)isoindoline-1,3-dione

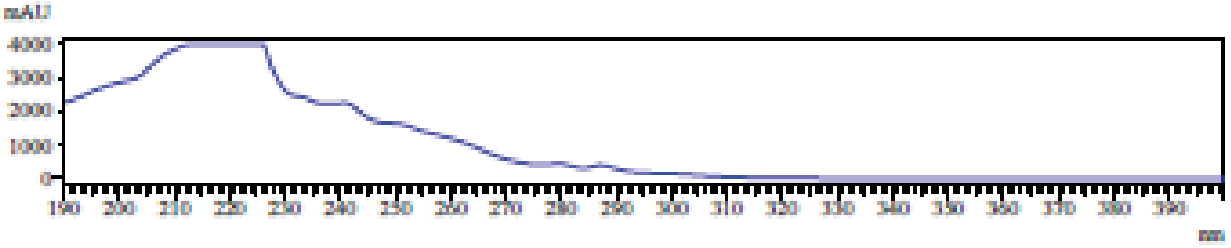
Sample Information

Data File	: Y0W-804-IE-10%0.8mL-iPrOH.lcd
Sample Name	: Y0W-804-IE-10%0.8mL-iPrOH
Sample ID	: Y0W-804-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8mL.lcm

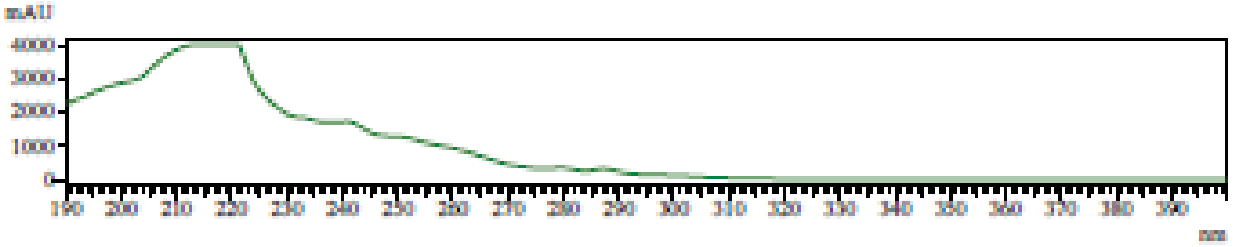
Chromatogram



UV Spectrum
Retention time = 17.427



UV Spectrum
Retention time = 20.612



Peak Table

PDA Ch1 254nm

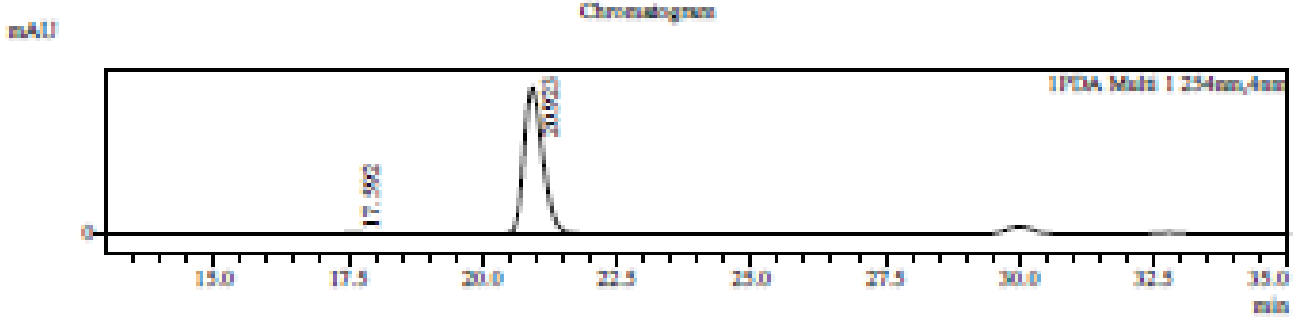
Peak#	Ret. Time	Area	Area%
1	17.427	29294732	39.222
2	20.612	29567248	39.587
3	29.517	7918621	10.602
4	32.236	7908200	10.588
Total		74688800	100.000

2-(2-(2-((3-fluorophenyl)ethynyl)cyclopropyl)ethyl)isoindoline-1,3-dione

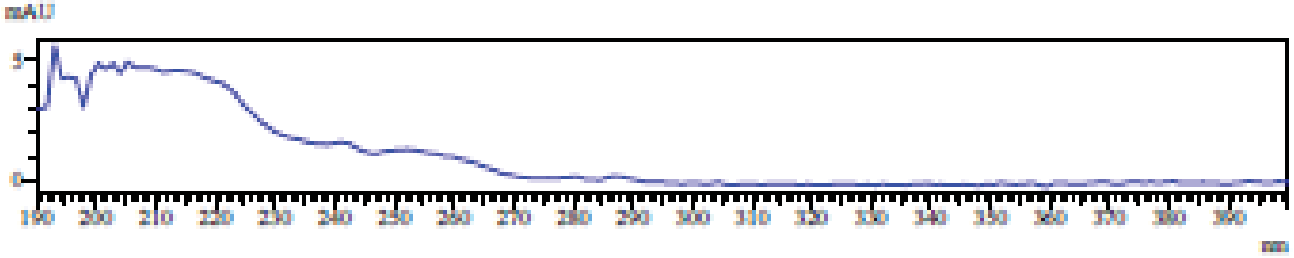
Sample Information

Data File	: Y0W-805-IE-10%0.8mL-iPrOH001.lcd
Sample Name	: Y0W-805-IE-10%0.8mL-iPrOH
Sample ID	: Y0W-805-IE-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

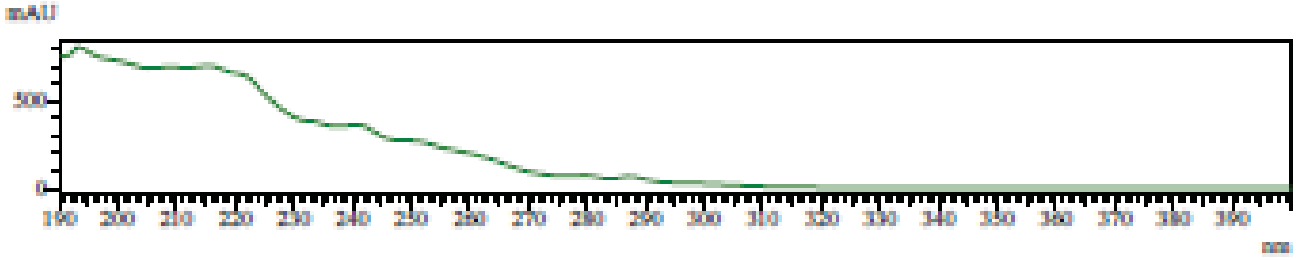
Chromatogram



UV Spectrum
Retention time = 17.592



UV Spectrum
Retention time = 20.923

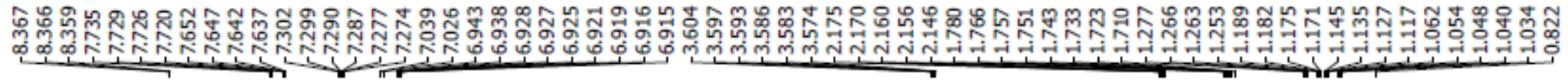


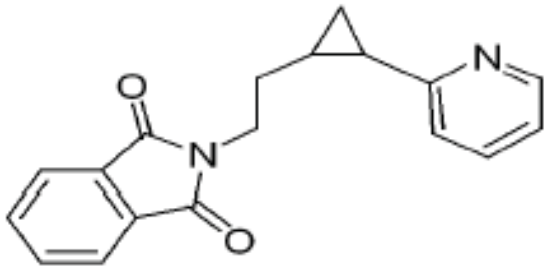
Peak Table

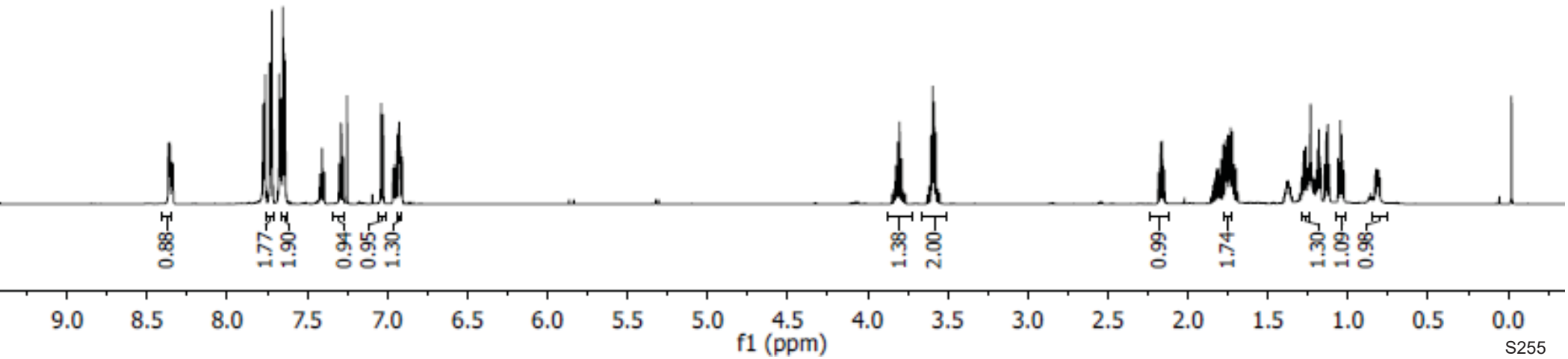
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.592	33729	0.552
2	20.923	6071686	99.448
Total		6105415	100.000

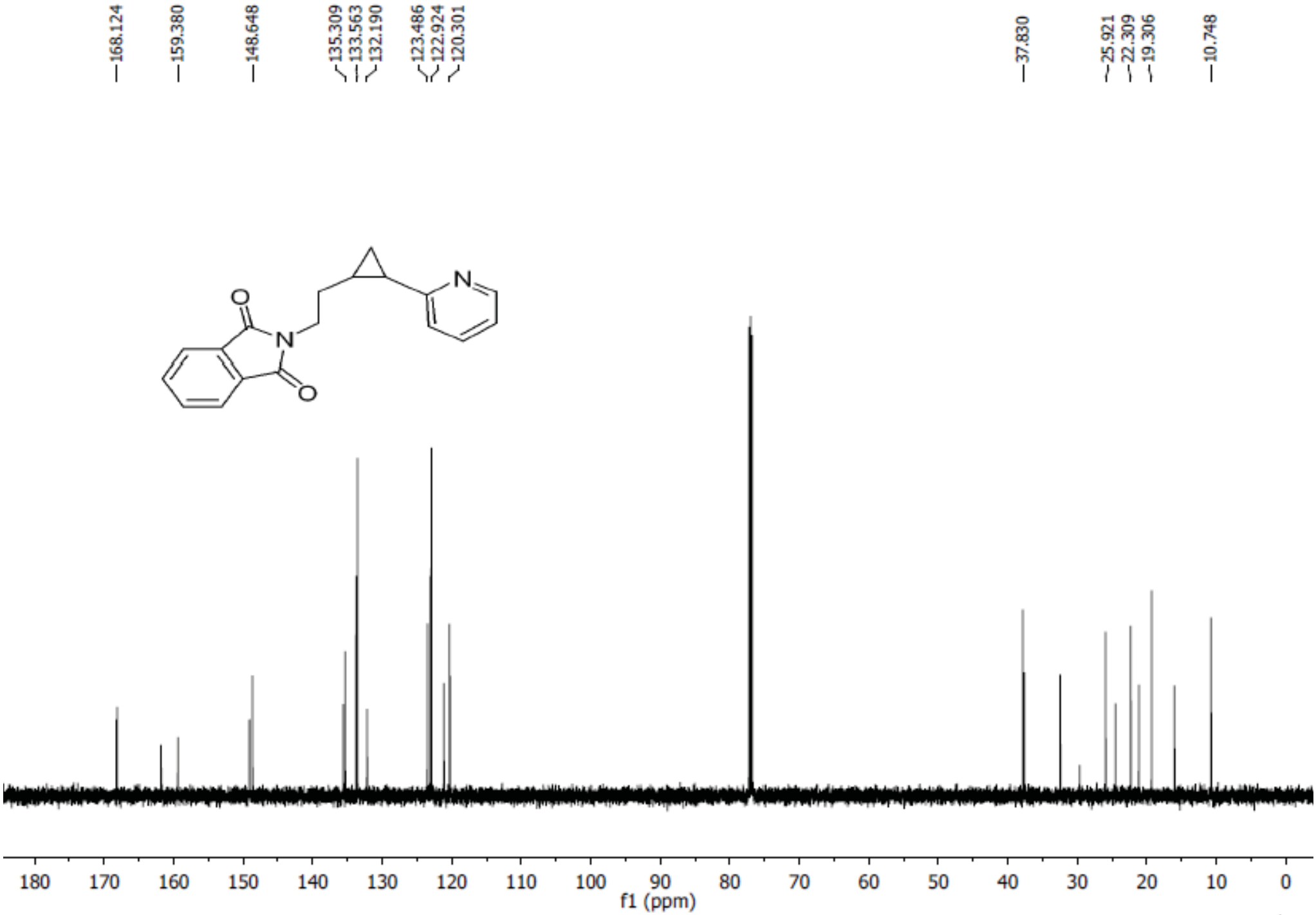
2-(2-(2-(pyridin-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione







2-(2-(2-(pyridin-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

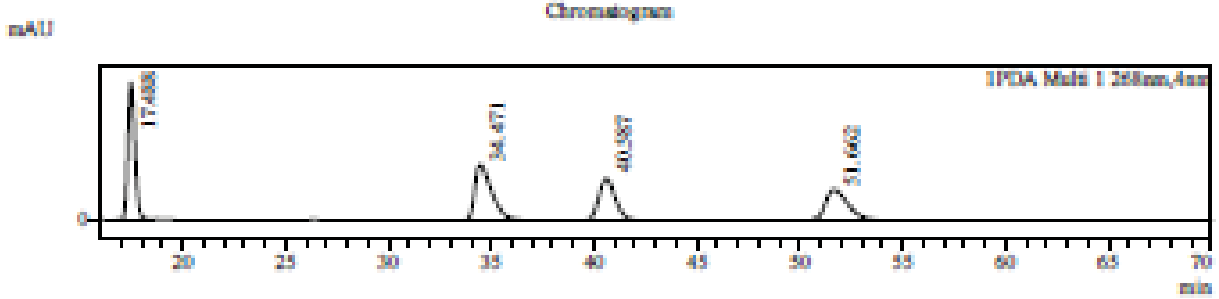


2-(2-(2-(pyridin-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

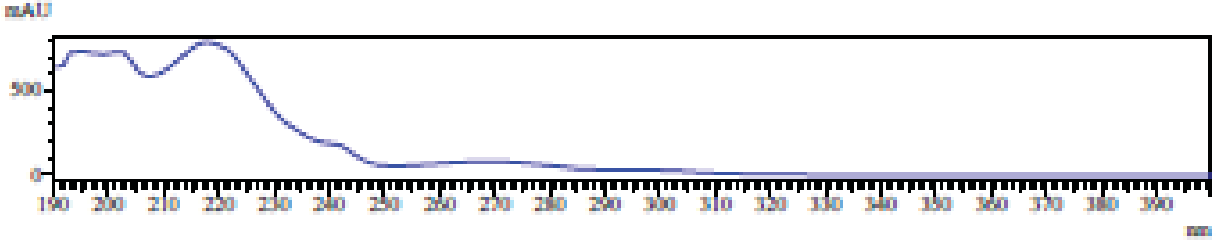
Sample Information

Data File	: Y0W-667-IE-25%1.0mL-iPrOH.lcd
Sample Name	: Y0W-667-IE-25%1.0mL-iPrOH
Sample ID	: Y0W-667-IE-25%1.0mL-iPrOH
Method File	: YW-25.0%-1.0ml.lcm

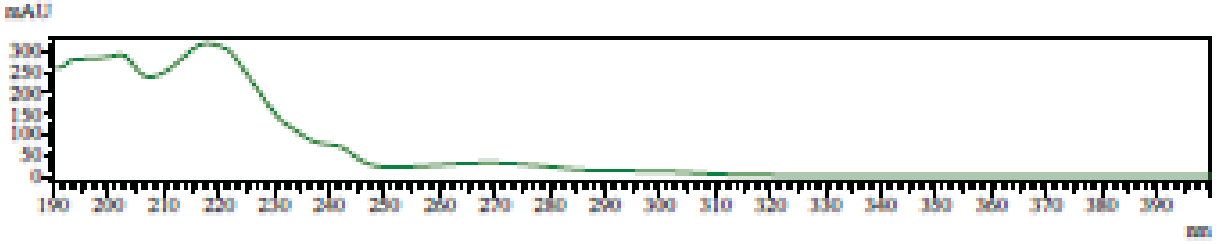
Chromatogram



UV Spectrum
Retention time = 17.488



UV Spectrum
Retention time = 34.471



Peak Table

PDA Ch1 268nm

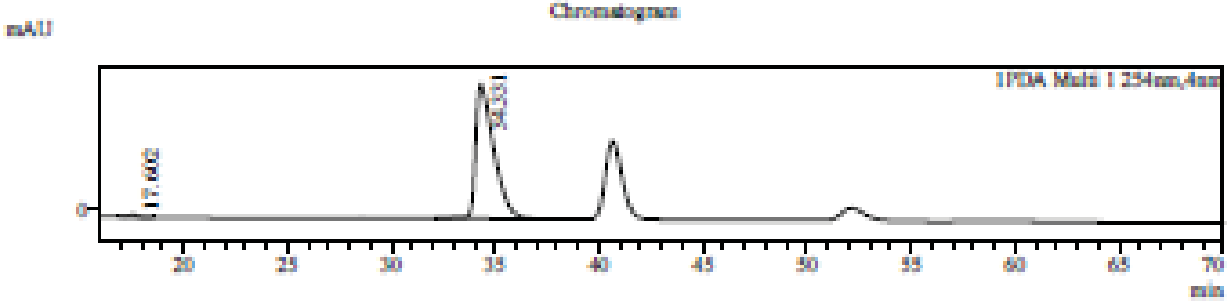
Peak#	Ret. Time	Area	Area%
1	17.488	1825832	28.950
2	34.471	1814147	28.765
3	40.587	1339092	21.233
4	51.662	1327678	21.052
Total		6306749	100.000

2-(2-(2-(pyridin-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

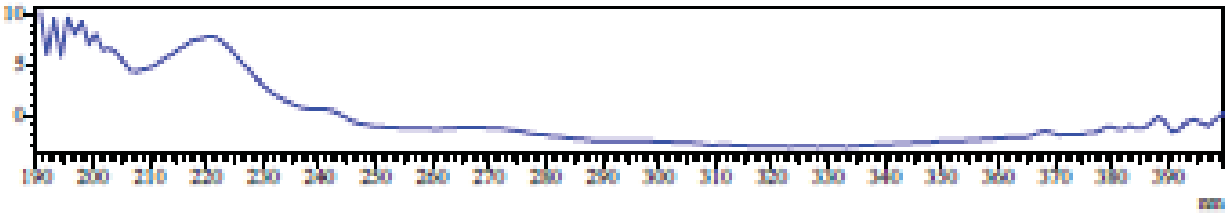
Sample Information

Data File	: Y0W-668-IE-25%1.0mL-iPrOH004.lcd
Sample Name	: Y0W-668-IE-25%1.0mL-iPrOH004
Sample ID	: Y0W-668-IE-25%1.0mL-iPrOH004
Method File	: YW-25.0%-1.0ml.lcm

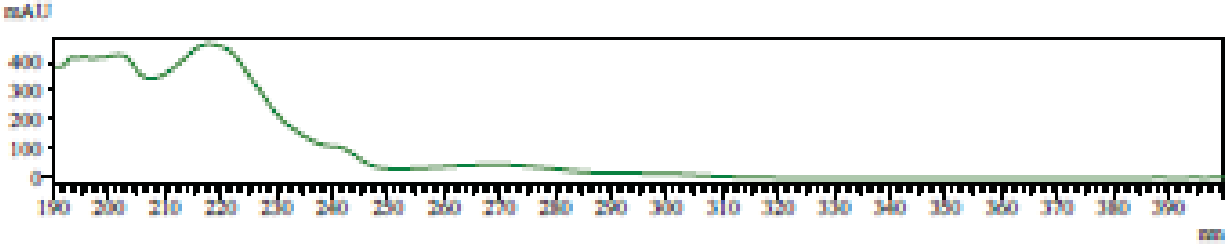
Chromatogram



UV Spectrum
Retention time = 17.602



UV Spectrum
Retention time = 34.331

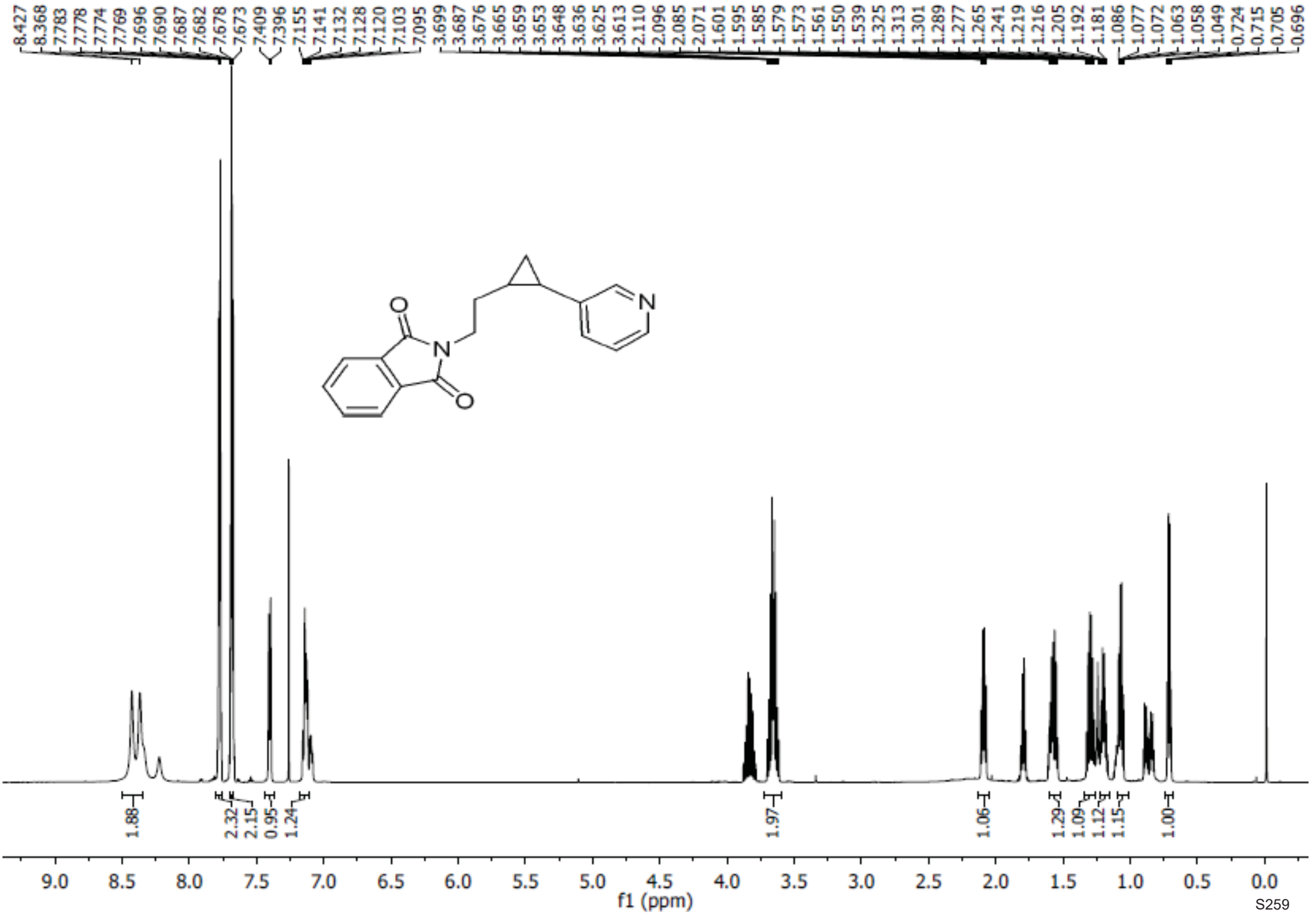


Peak Table

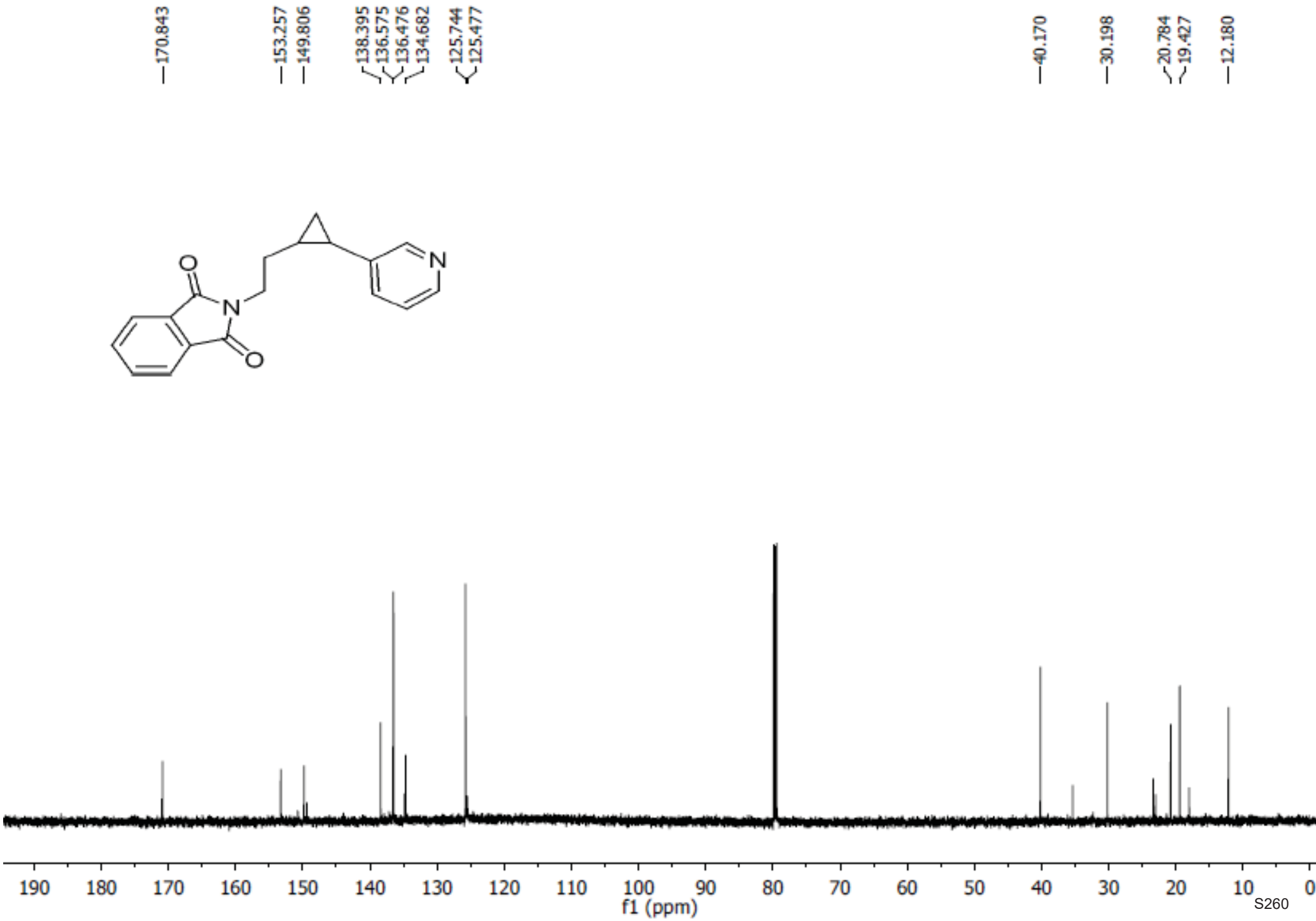
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.602	13833	0.668
2	34.331	2058541	99.332
Total		2072375	100.000

2-(2-(2-(pyridin-3-yl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(pyridin-3-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

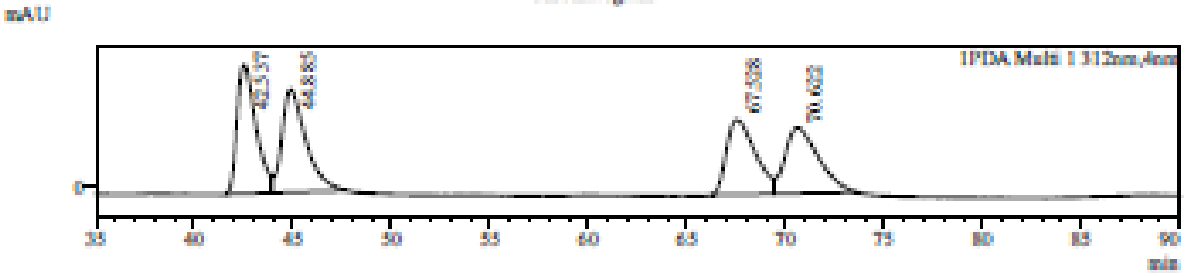


2-(2-(2-(pyridin-3-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

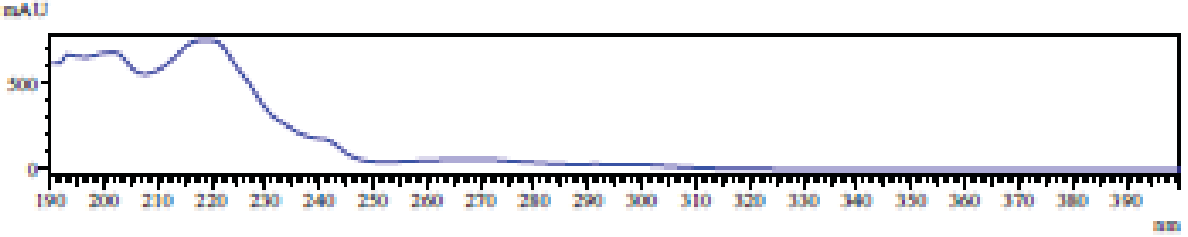
Sample Information

Data File	: YOW-683-IE-25%1.0mL-iPrOH004.lcd
Sample Name	: YOW-683-IE-25%1.0mL-iPrOH004
Sample ID	: YOW-683-IE-25%1.0mL-iPrOH004
Method File	: YW-25.0%-1.0ml.lcm

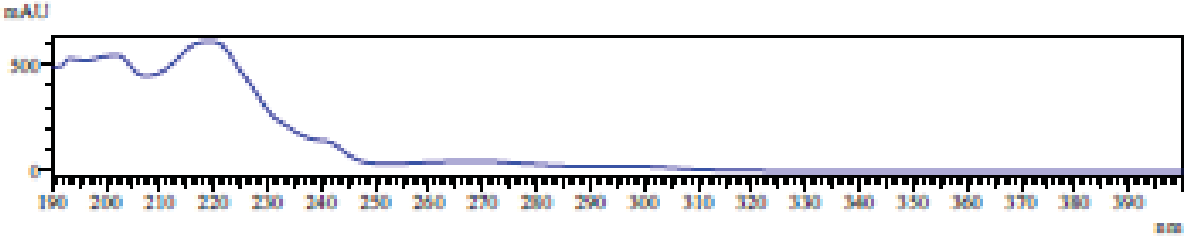
Chromatogram



UV Spectrum
Retention time = 42.537



UV Spectrum
Retention time = 44.885



Peak Table

PDA Ch1 312nm

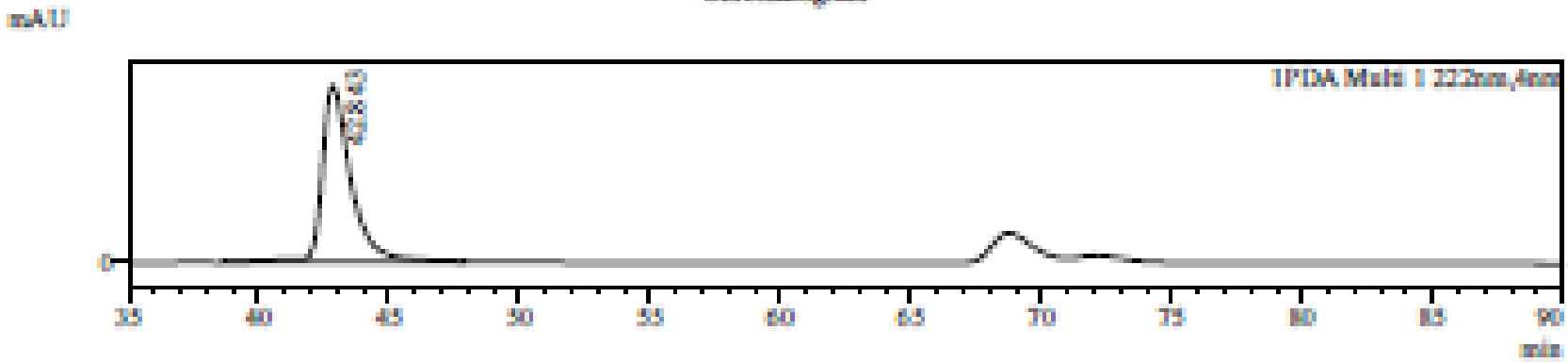
Peak#	Ret. Time	Area	Area%
1	42.537	593913	26.354
2	44.885	598934	26.577
3	67.528	525980	23.339
4	70.622	534794	23.730
Total		2253621	100.000

2-(2-(2-(pyridin-3-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

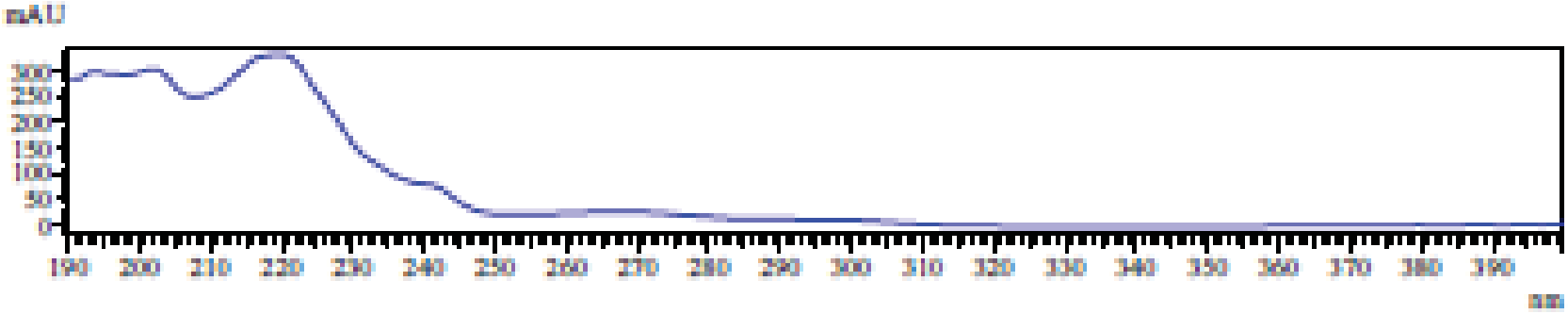
Sample Information

Data File	: Y0W-686-IE-25%1.0mL-iPrOH004.lcd
Sample Name	: Y0W-686-IE-25%1.0mL-iPrOH004
Sample ID	: Y0W-686-IE-25%1.0mL-iPrOH004
Method File	: YW-25.0%-1.0ml.lcm

Chromatogram



UV Spectrum
Retention time = 42.843

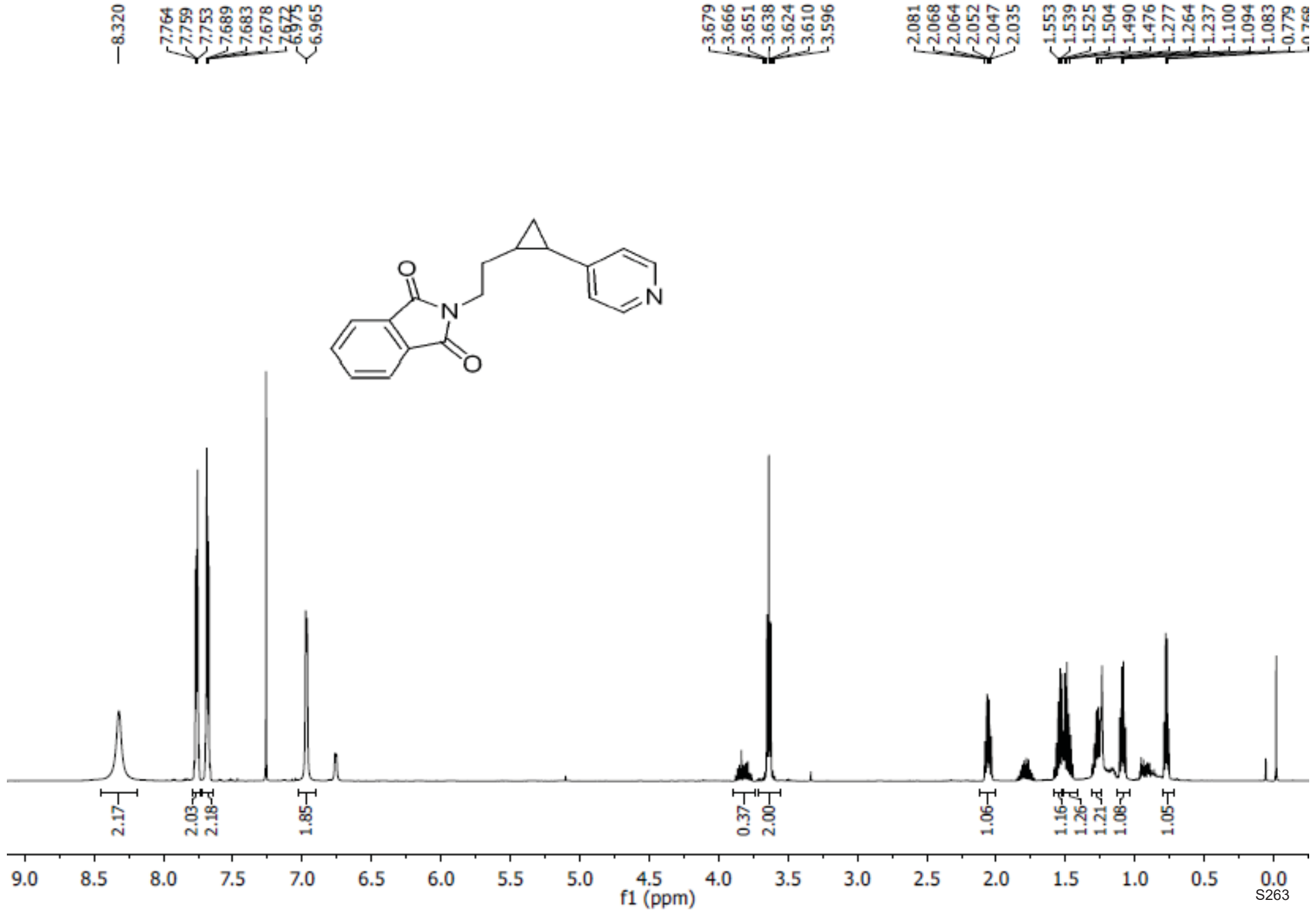


Peak Table

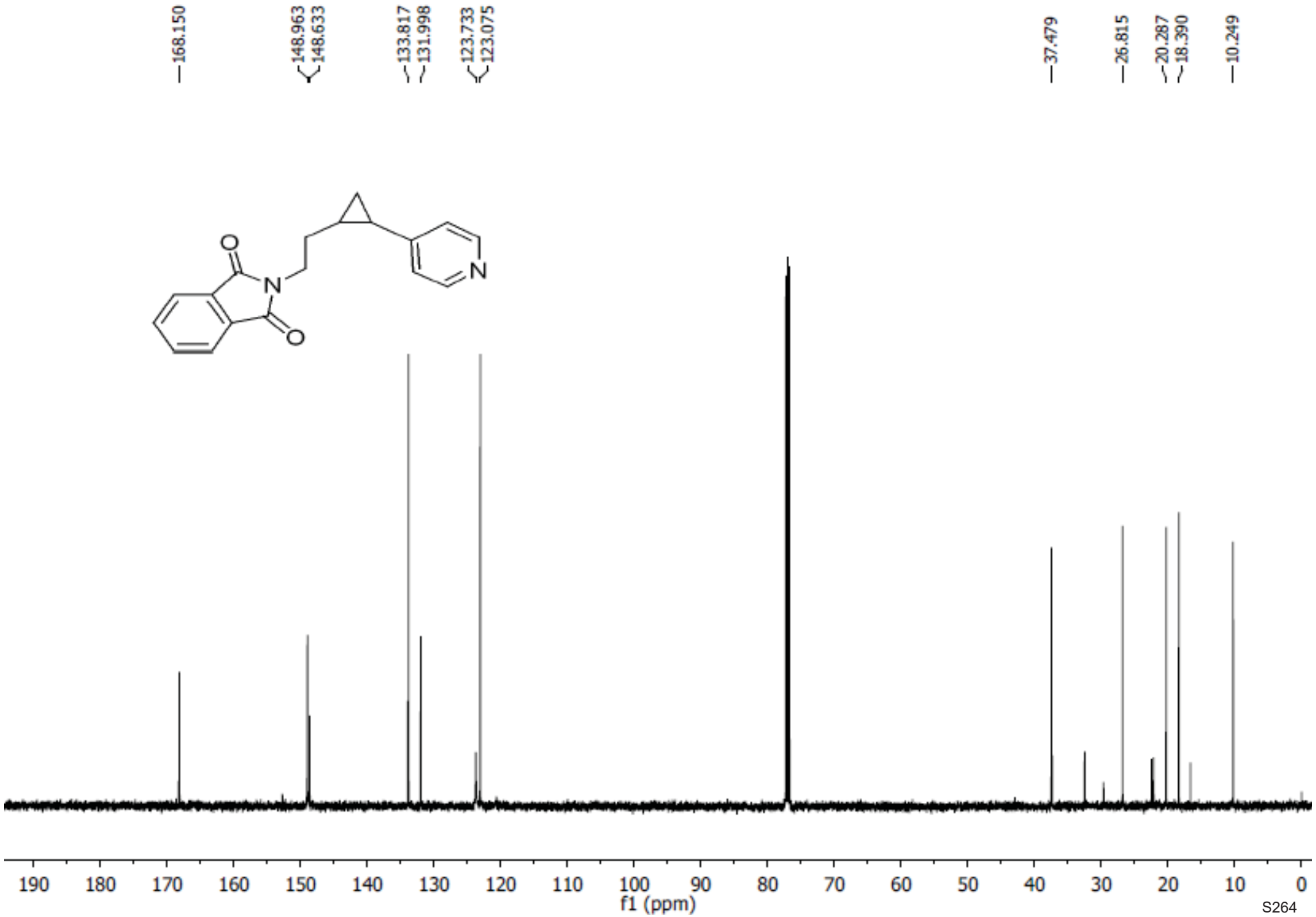
PDA Ch1 222nm

Peak#	Ret. Time	Area	Area%
1	42.843	23426656	100.000
Total		23426656	100.000

2-(2-(2-(pyridin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(pyridin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

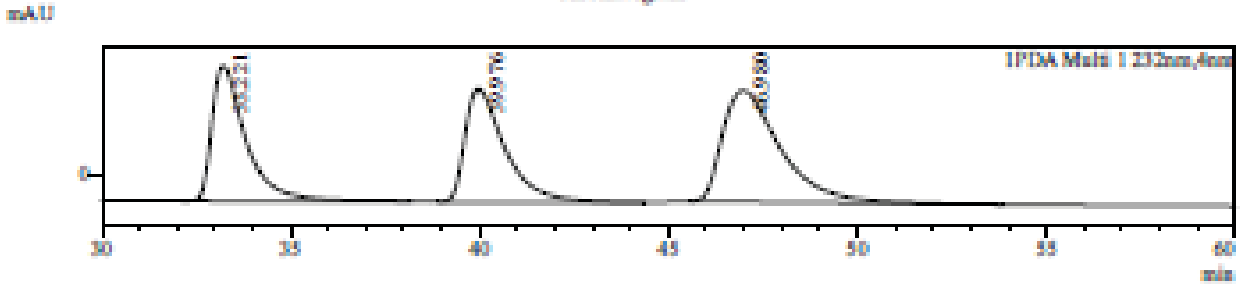


2-(2-(2-(pyridin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

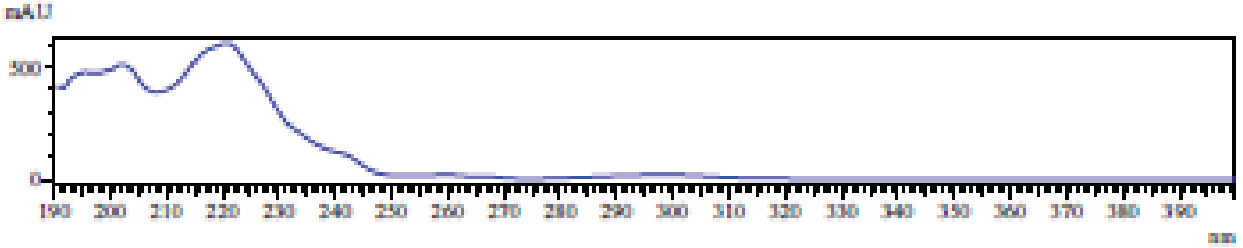
Sample Information

Data File	: YOW-642-IE-25%1.0mL-iPrOH003.lcd
Sample Name	: YOW-642-IE-25%1.0mL-iPrOH003
Sample ID	: YOW-642-IE-25%1.0mL-iPrOH003
Method File	: YW-25.0%-1.0ml.lcm

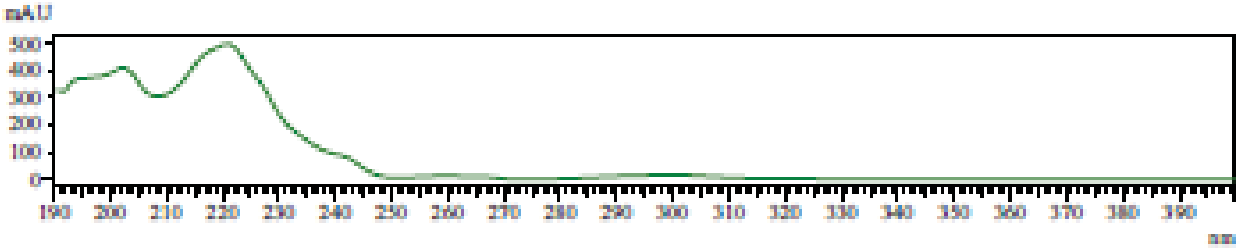
Chromatogram



UV Spectrum
Retention time = 33.221



UV Spectrum
Retention time = 39.976



Peak Table

PDA Ch1 232nm

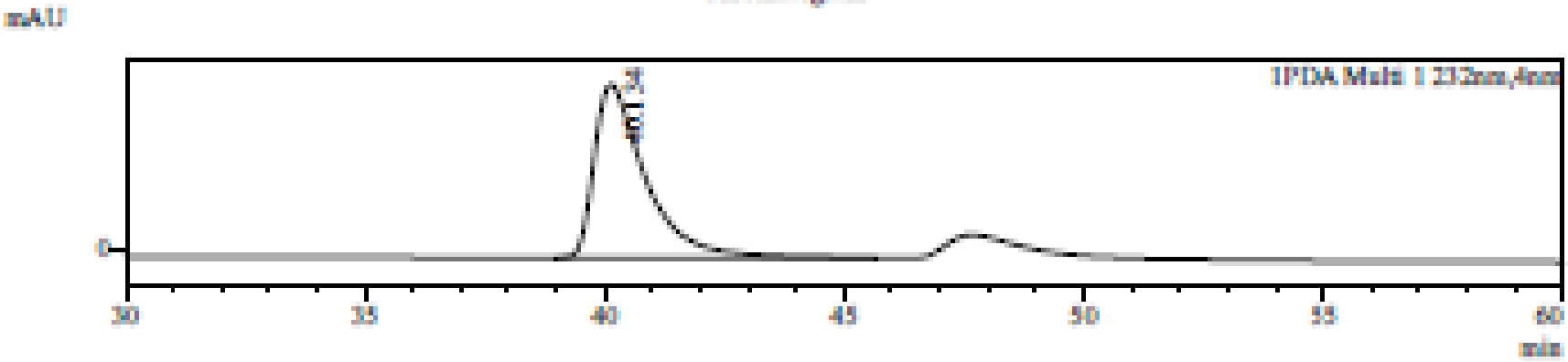
Peak#	Ret. Time	Area	Area%
1	33.221	19653692	29.397
2	39.976	19500943	29.168
3	46.980	27702475	41.435
Total		66857110	100.000

2-(2-(2-(pyridin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

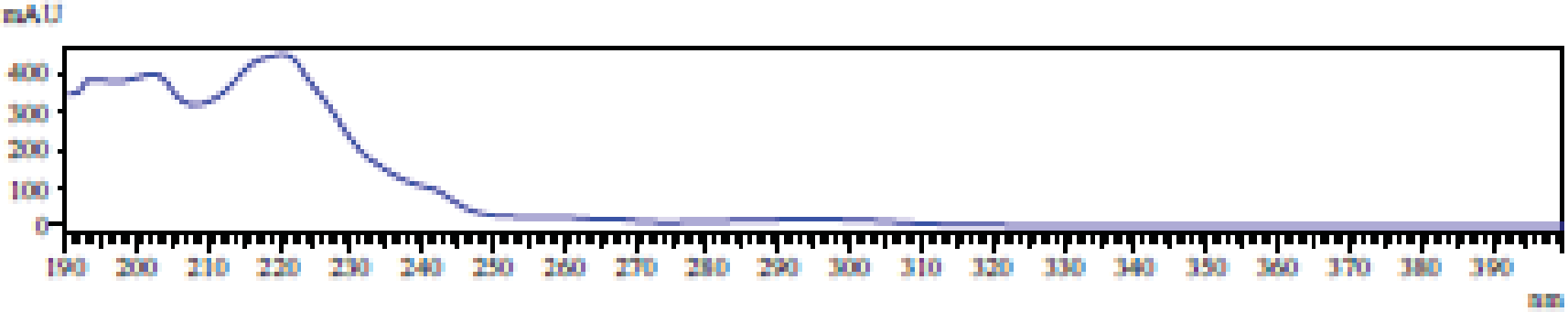
Sample Information

Data File	: YOW-643-IE-25%1.0mL-iPrOH004.lcd
Sample Name	: YOW-643-IE-25%1.0mL-iPrOH004
Sample ID	: YOW-643-IE-25%1.0mL-iPrOH004
Method File	: YW-25.0%-1.0ml.lcm

Chromatogram



UV Spectrum
Retention time = 40.134

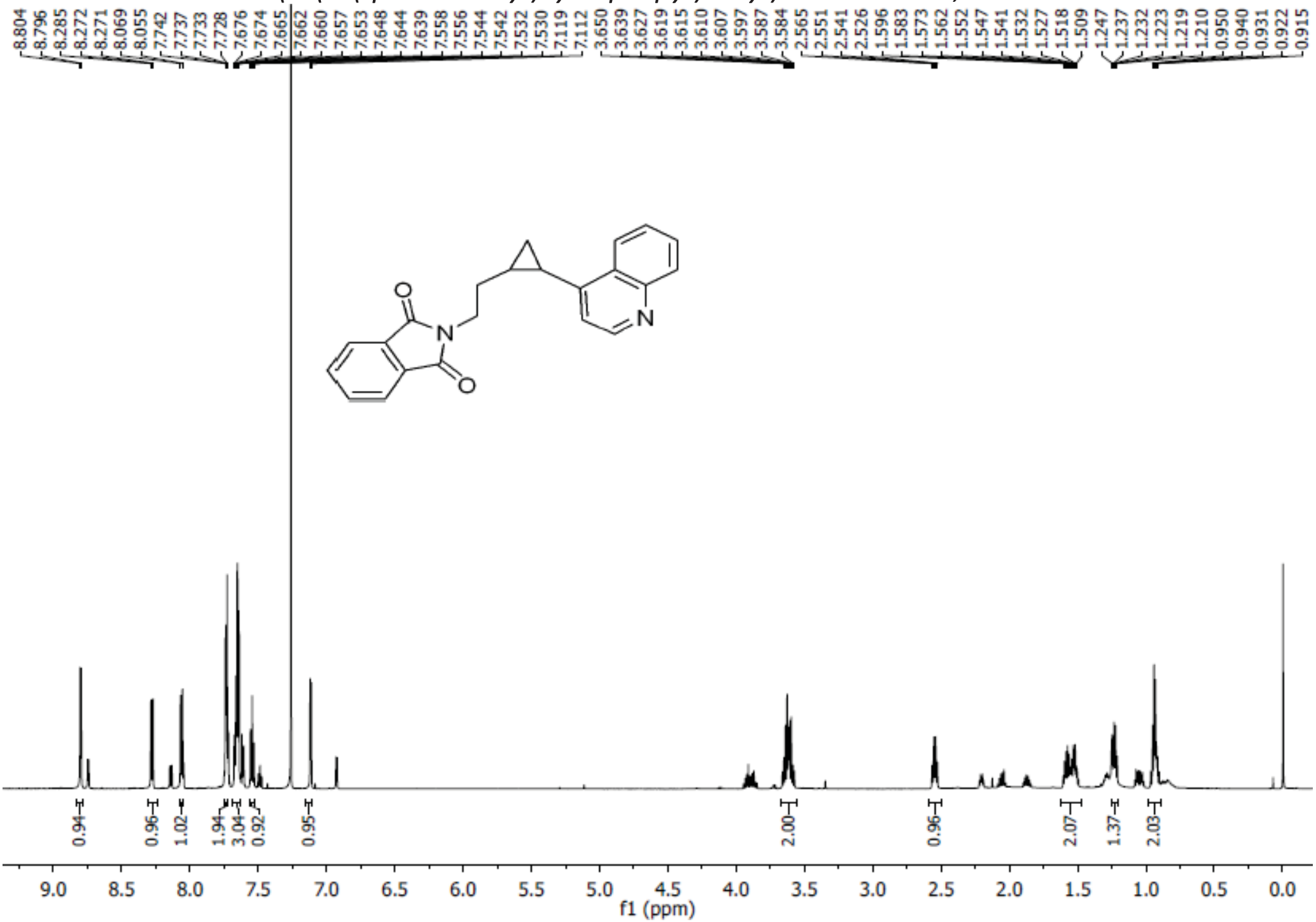


Peak Table

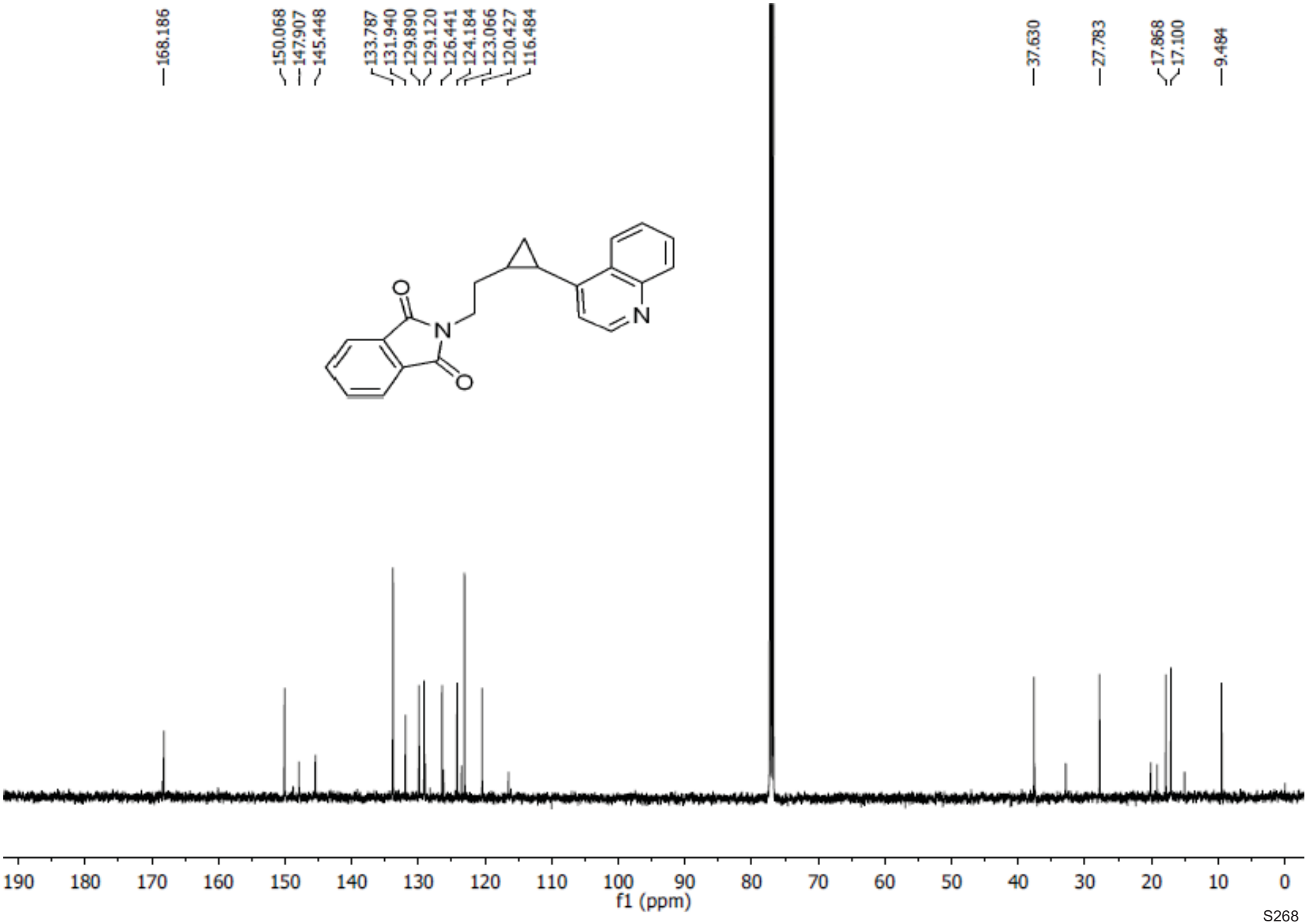
PDA Ch1 232nm

Peak#	Ret. Time	Area	Area%
1	40.134	15534192	100.000
Total		15534192	100.000

2-(2-(2-(quinolin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(quinolin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

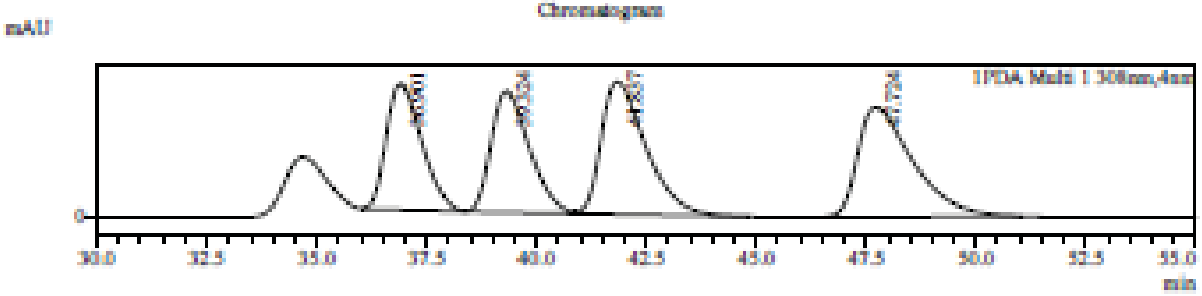


2-(2-(2-(quinolin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

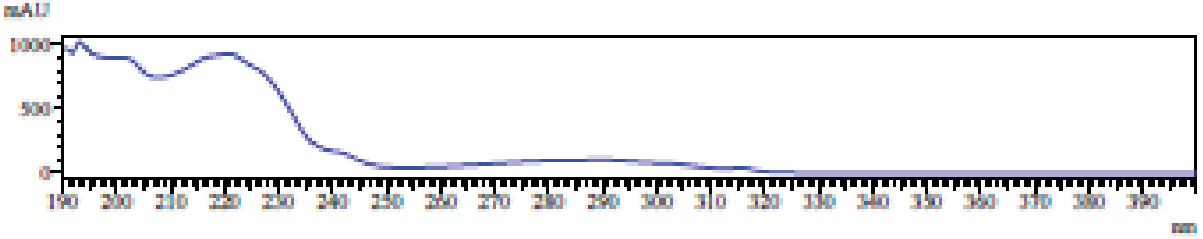
Sample Information

Data File	: Y0W-688-IE-25%1.0mL-iPrOH.lcd
Sample Name	: Y0W-668-IE-25%1.0mL-iPrOH
Sample ID	: Y0W-668-IE-25%1.0mL-iPrOH
Method File	: YW-25.0%-1.0ml.lcm

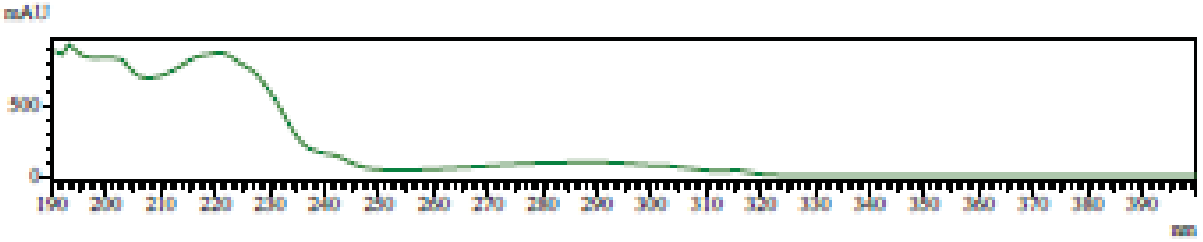
Chromatogram



UV Spectrum
Retention time = 36.901



UV Spectrum
Retention time = 39.324



Peak Table

PDA Ch1 308nm

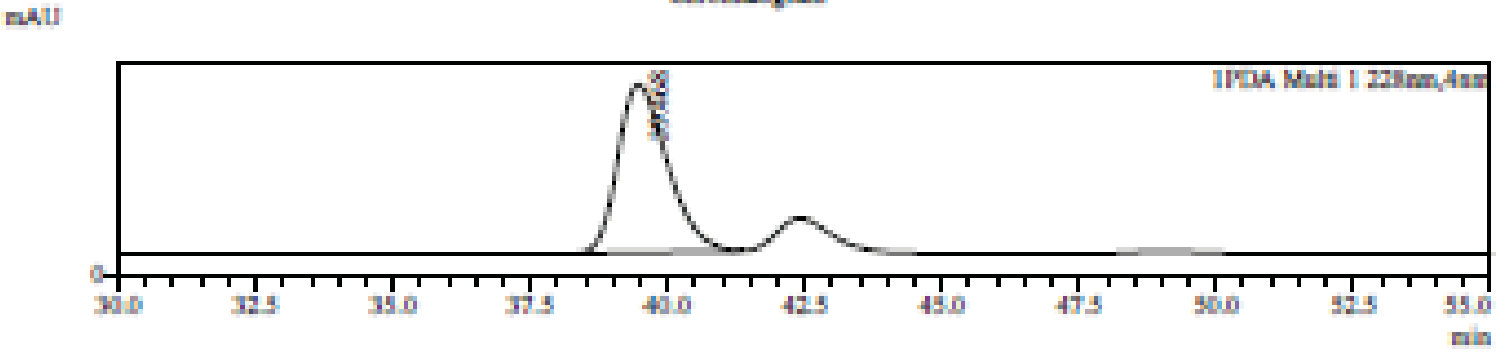
Peak#	Ret. Time	Area	Area%
1	36.901	2590406	21.182
2	39.324	2684587	21.952
3	41.837	3435340	28.091
4	47.724	3518840	28.774
Total		12229174	100.000

2-(2-(2-(quinolin-4-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

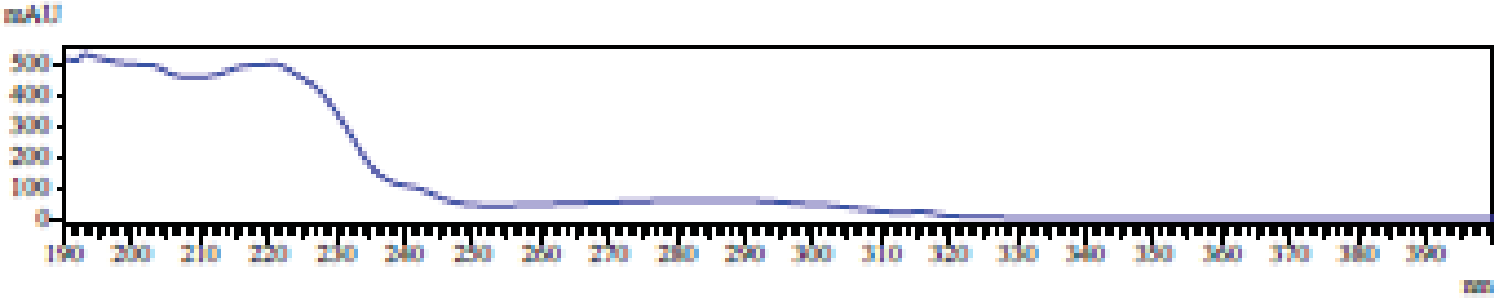
Sample Information

Data File	: Y0W-689-IE-25%1.0mL-iPrOH004.lcd
Sample Name	: Y0W-689-IE-25%1.0mL-iPrOH004
Sample ID	: Y0W-689-IE-25%1.0mL-iPrOH004
Method File	: YW-25.0%-1.0ml.lcm

Chromatogram



UV Spectrum
Retention time = 39.468

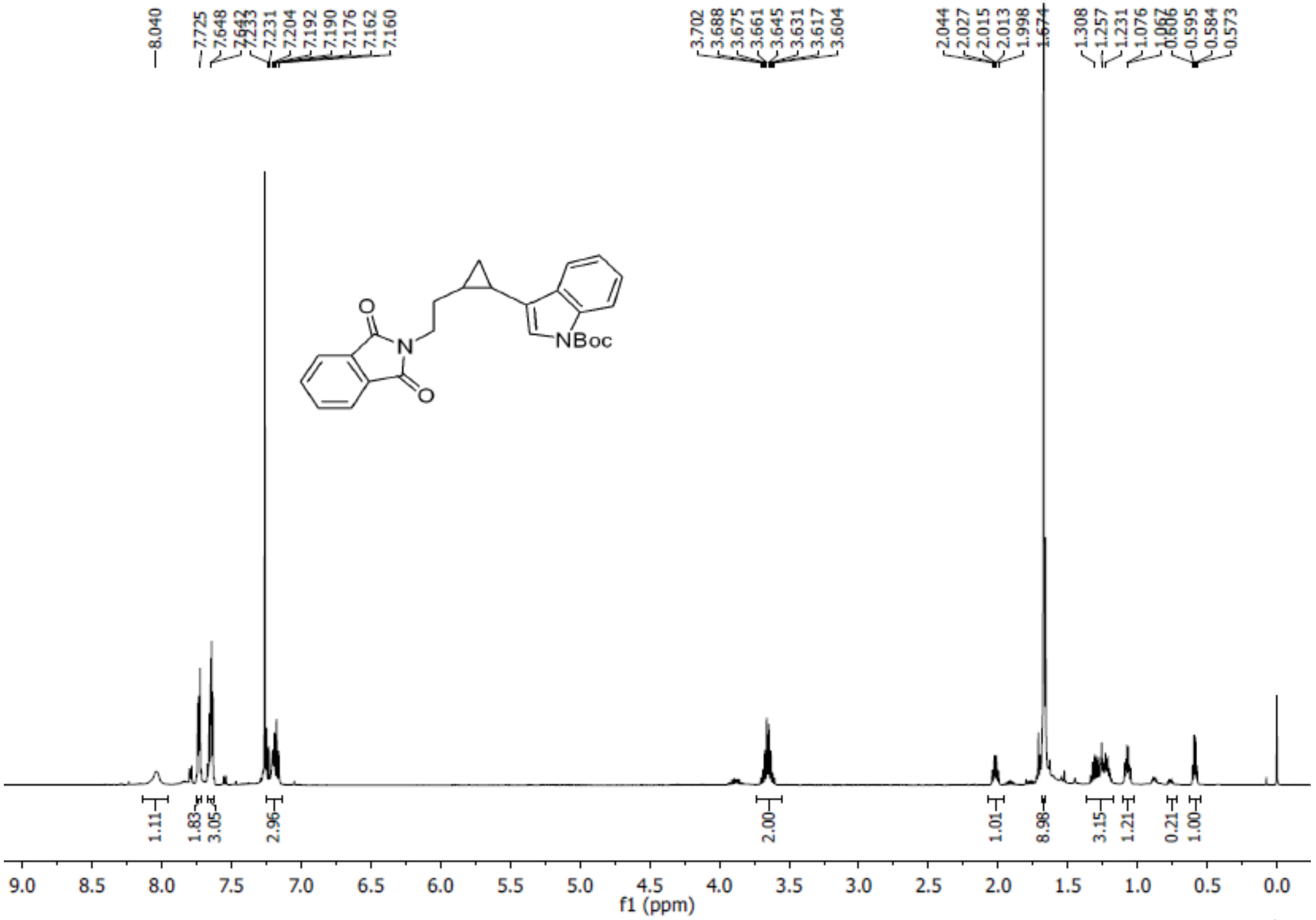


Peak Table

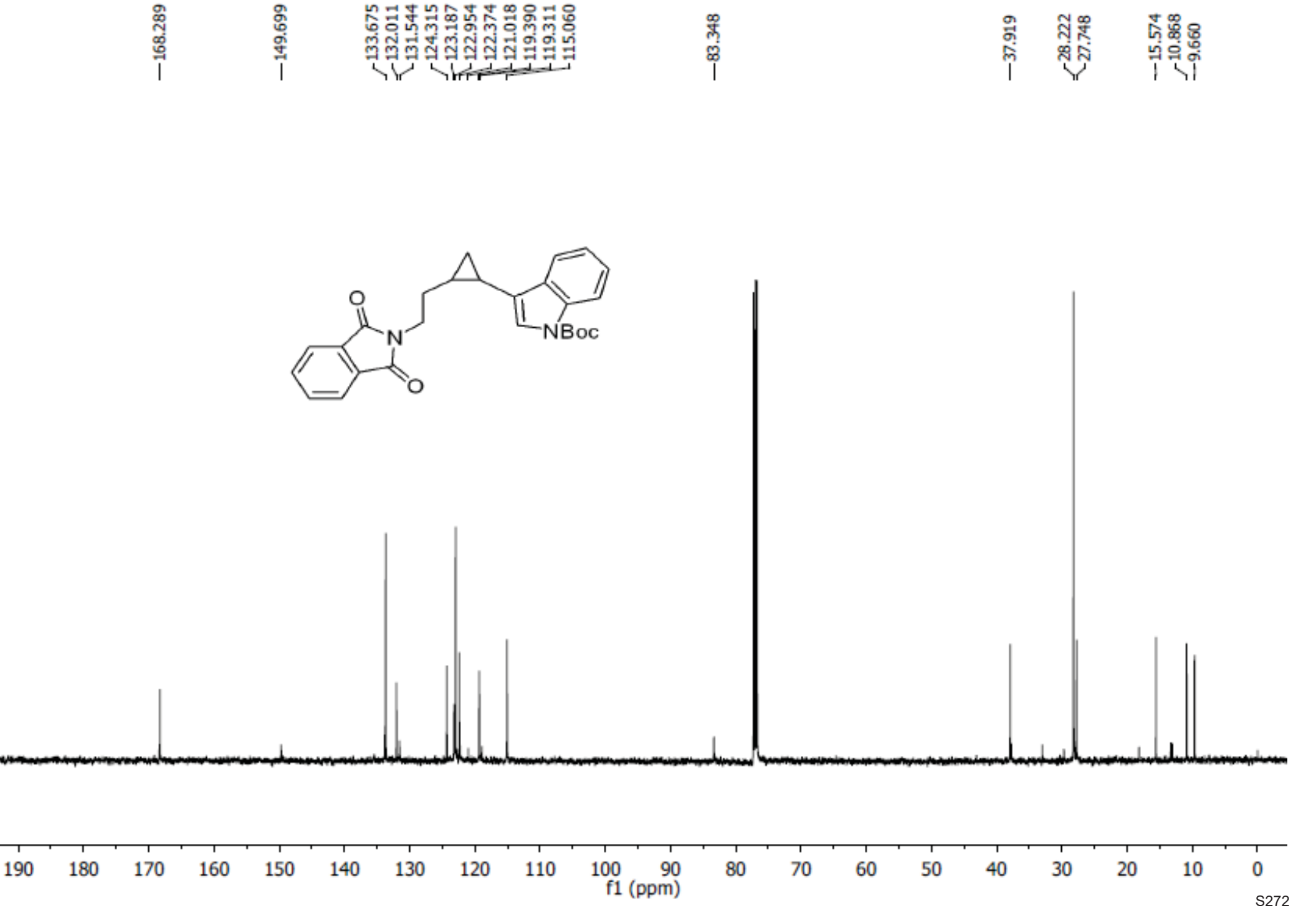
PDA Ch1 228nm

Peak#	Ret. Time	Area	Area%
1	39.468	21580313	100.000
Total		21580313	100.000

tert-butyl 3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl)-1H-indole-1-carboxylate



tert-butyl 3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl)-1H-indole-1-carboxylate

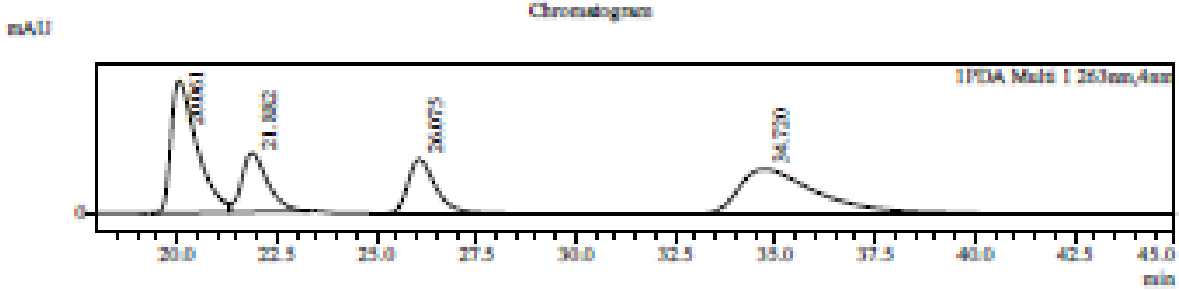


tert-butyl 3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl)-1H-indole-1-carboxylate

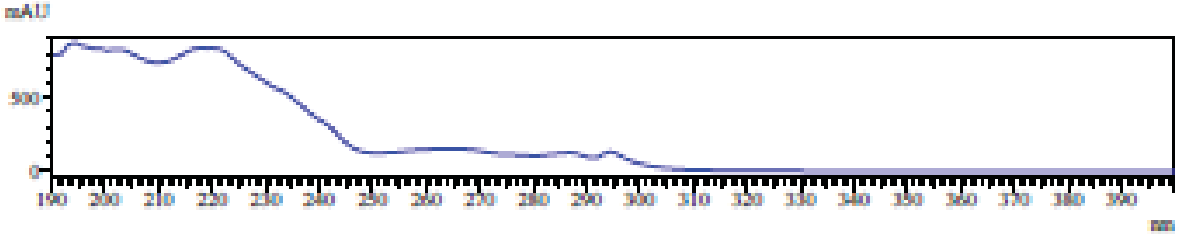
Sample Information

Data File	: PKL-015-IF-10%0.8mL.lcd
Sample Name	: PKL-015-IF-10%0.8mL
Sample ID	: PKL-015-IF-10%0.8mL
Method File	: PKL-10%-0.8ml.lcm

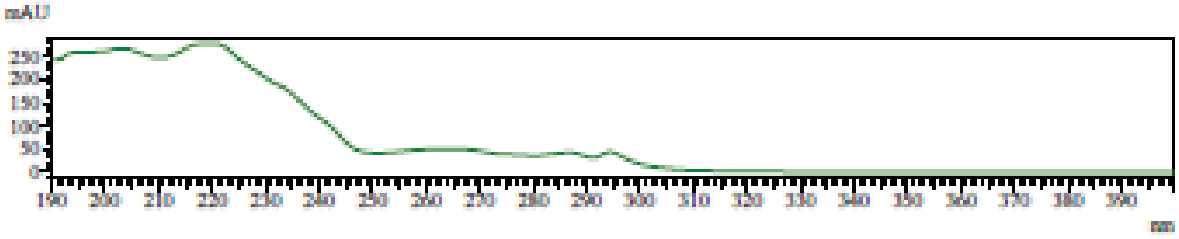
Chromatogram



UV Spectrum
Retention time = 20.061



UV Spectrum
Retention time = 34.720



Peak Table

PDA Ch1 263nm

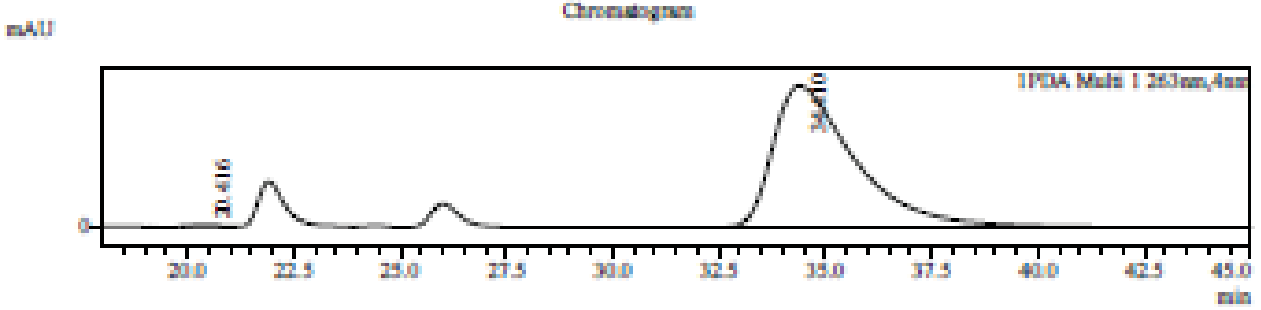
Peak#	Ret. Time	Area	Area%
1	20.061	6646309	34.356
2	21.882	2916879	15.078
3	26.075	2975619	15.382
4	34.720	6806349	35.184
Total		19345056	100.000

tert-butyl 3-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)cyclopropyl)-1H-indole-1-carboxylate

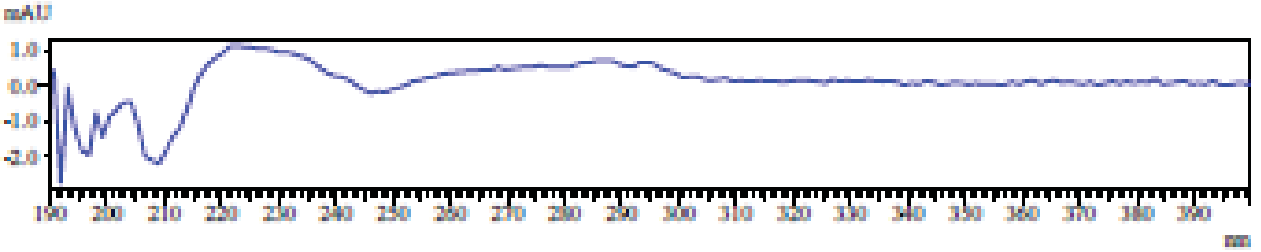
Sample Information

Data File	: Y0W-712-IF-10%0.8mL-iPrOH.lcd
Sample Name	: Y0W-712-IF-10%0.8mL-iPrOH
Sample ID	: Y0W-712-IF-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

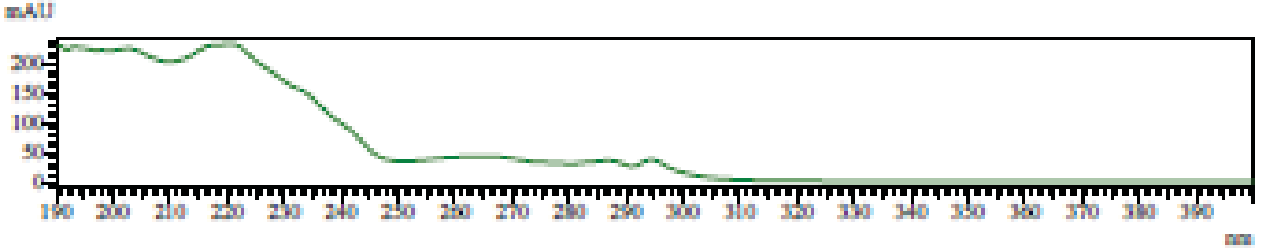
Chromatogram



UV Spectrum
Retention time = 20.416



UV Spectrum
Retention time = 34.410

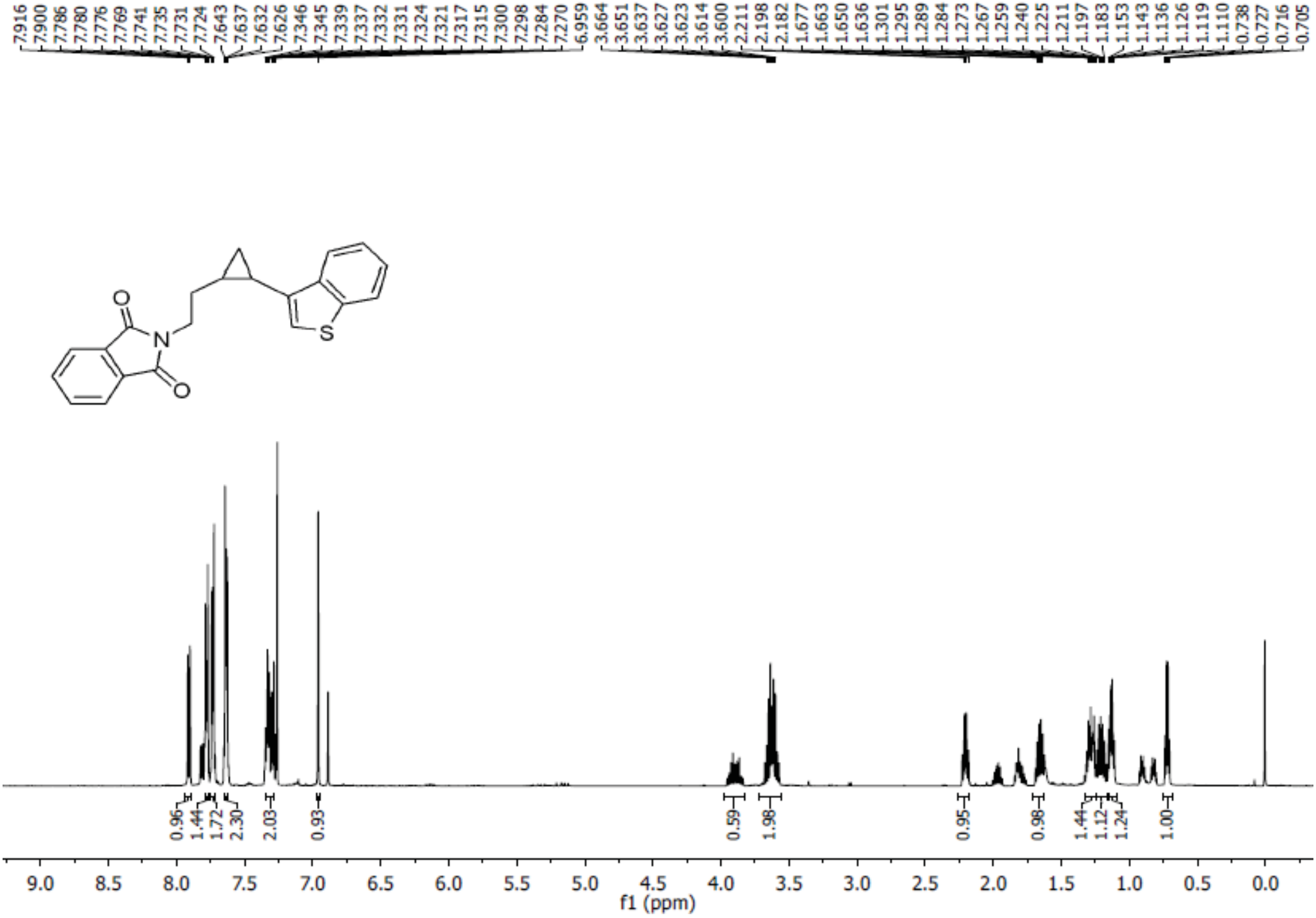


Peak Table

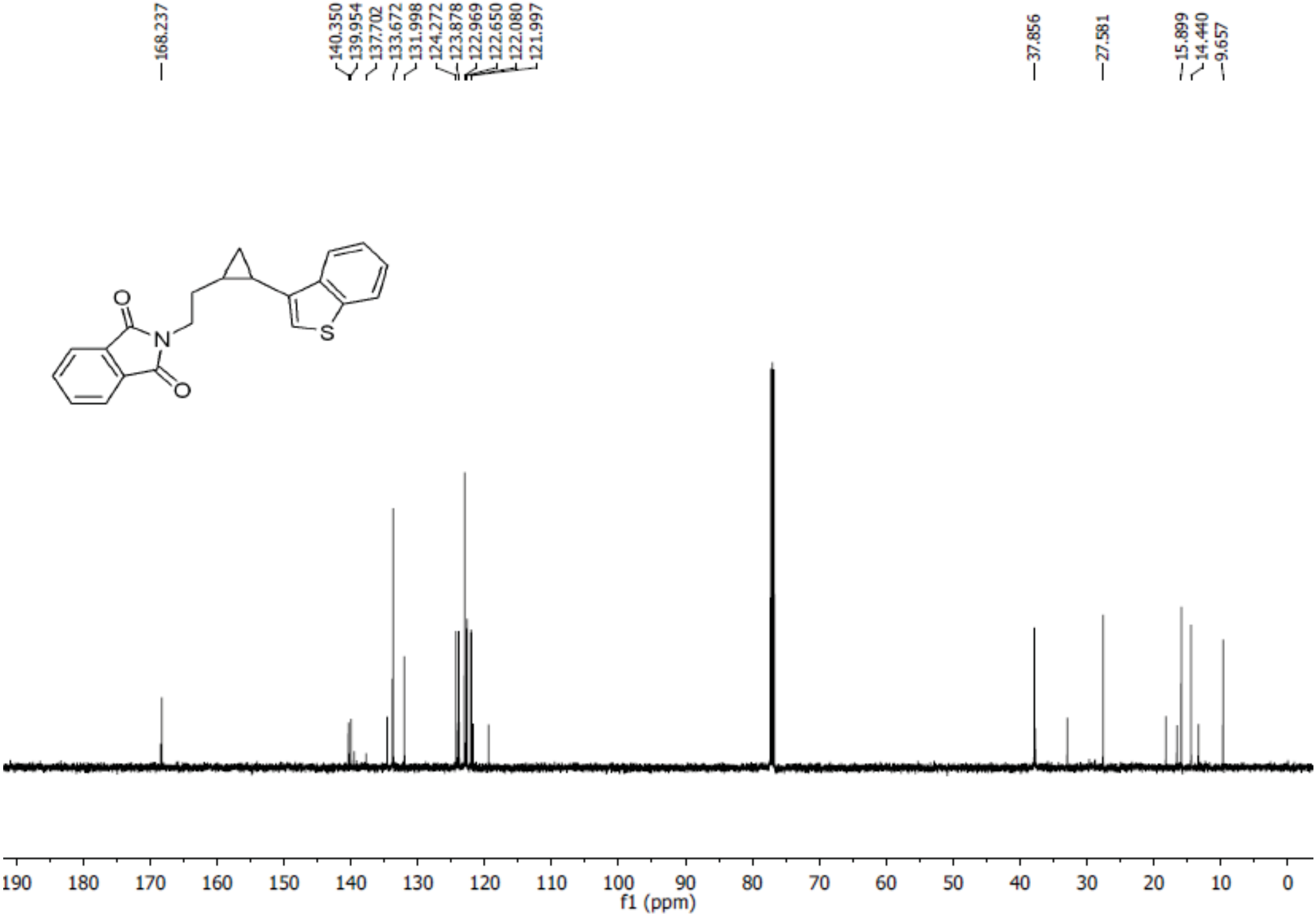
PDA Ch1 263nm

Peak#	Ret. Time	Area	Area%
1	20.416	20621	0.361
2	34.410	5697803	99.639
Total		5718424	100.000

2-(2-(2-(benzo[b]thiophen-3-yl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(benzo[b]thiophen-3-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

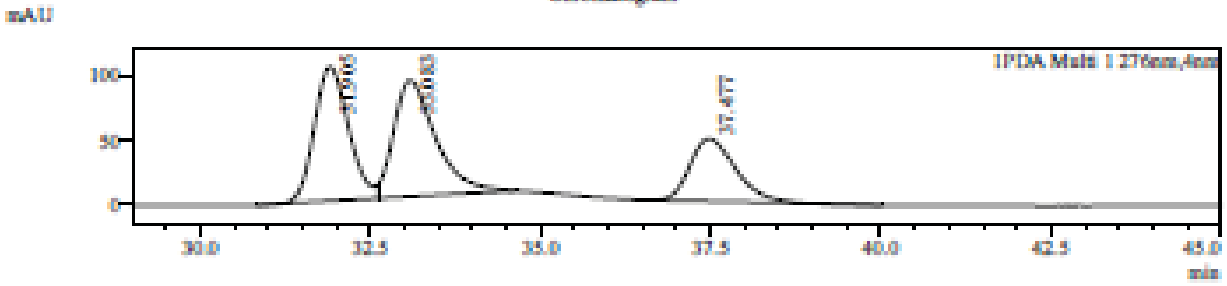


2-(2-(2-(benzo[b]thiophen-3-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

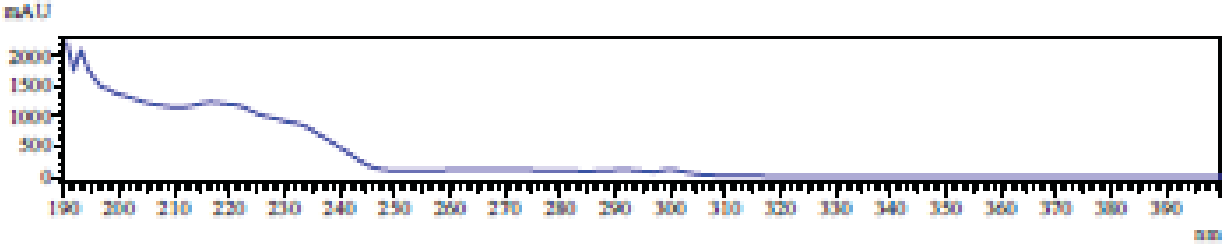
Sample Information

Data File	: YOW-683-ID-5%0.8mL-iPrOH004.lcd
Sample Name	: YOW-683-ID-5%0.8mL-iPrOH004
Sample ID	: YOW-683-ID-5%0.8mL-iPrOH004
Method File	: YW-5.0%-0.8ml.lcm

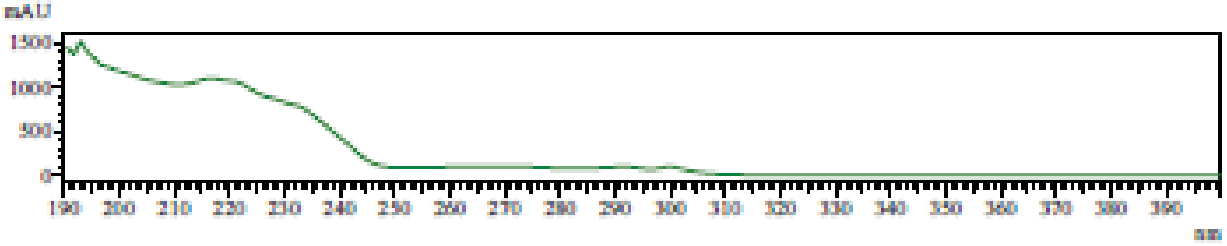
Chromatogram



UV Spectrum
Retention time = 31.905



UV Spectrum
Retention time = 33.083



Peak Table

PDA Ch1 276nm

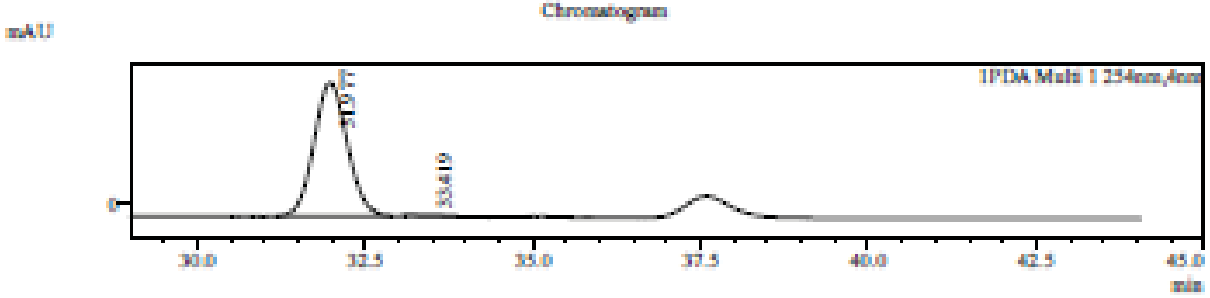
Peak#	Ret. Time	Area	Area%
1	31.905	3644911	37.490
2	33.083	3832142	39.415
3	37.477	2245408	23.095
Total		9722462	100.000

2-(2-(2-(benzo[b]thiophen-3-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

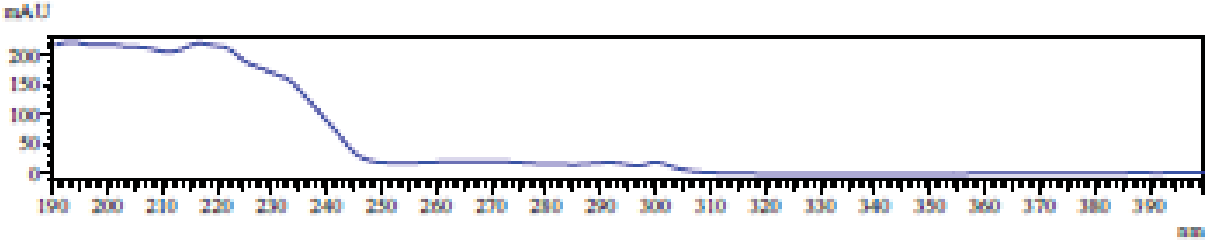
Sample Information

Data File	: Y0W-684-ID-3%0.8mL-iPrOH004.lcd
Sample Name	: Y0W-684-ID-3%0.8mL-iPrOH004
Sample ID	: Y0W-684-ID-3%0.8mL-iPrOH004
Method File	: YW-5.0%-0.8ml.lcm

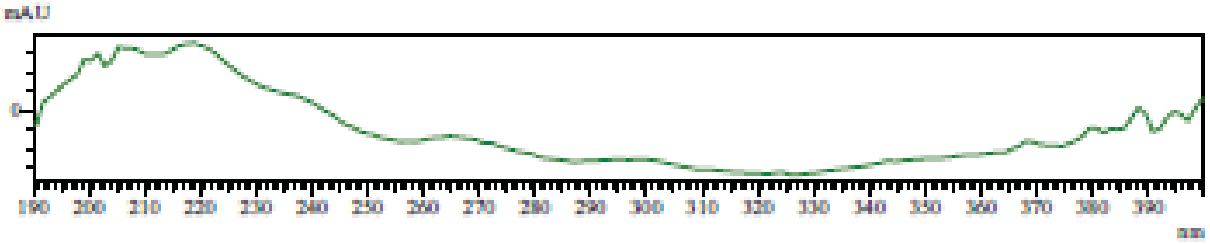
Chromatogram



UV Spectrum
Retention time = 31.977



UV Spectrum
Retention time = 33.419

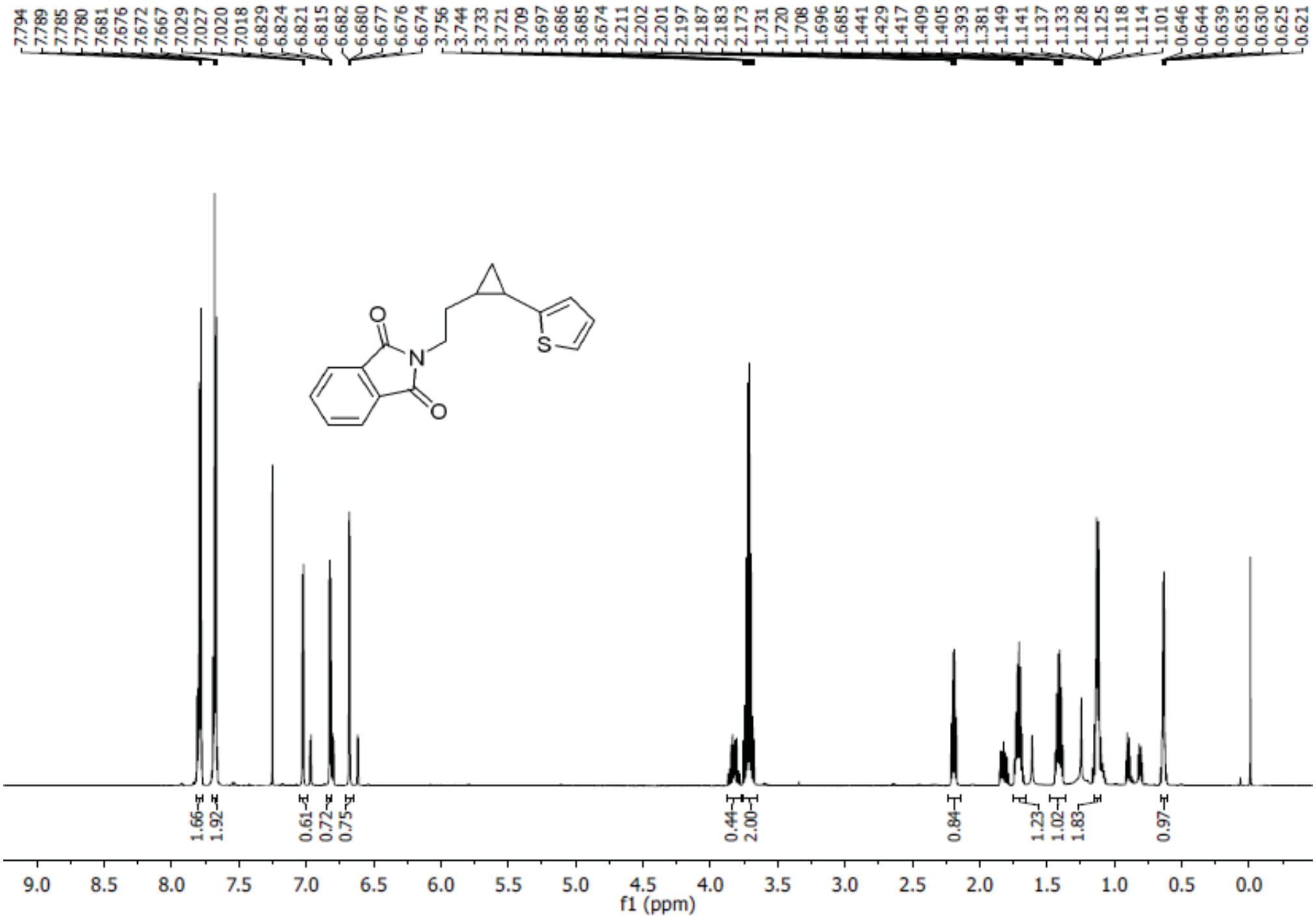


Peak Table

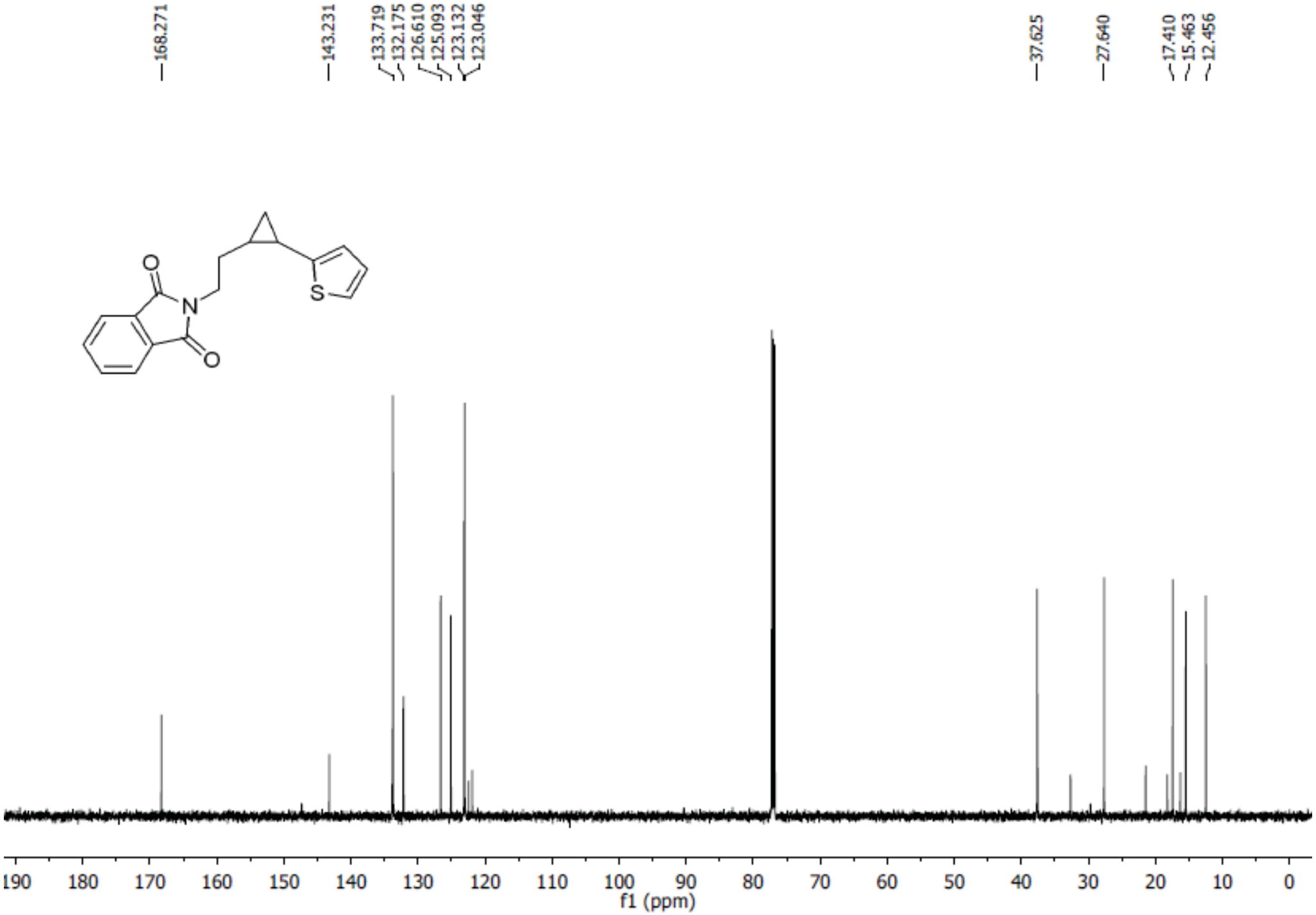
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	31.977	644275	99.509
2	33.419	3178	0.491
Total		647453	100.000

2-(2-(2-(thiophen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(thiophen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

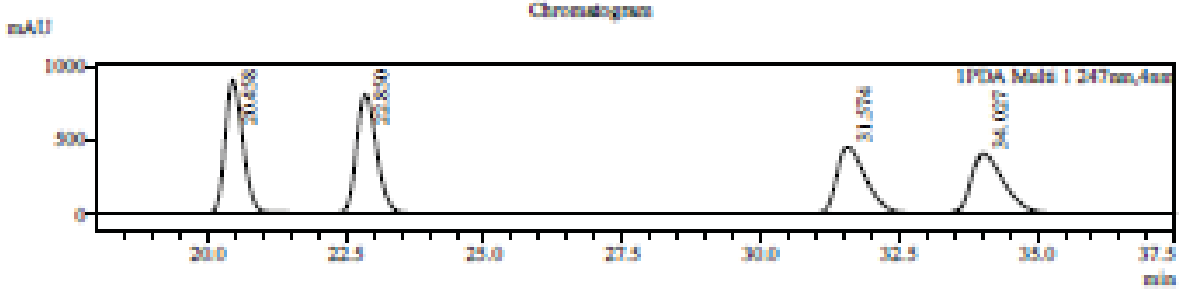


2-(2-(2-(thiophen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

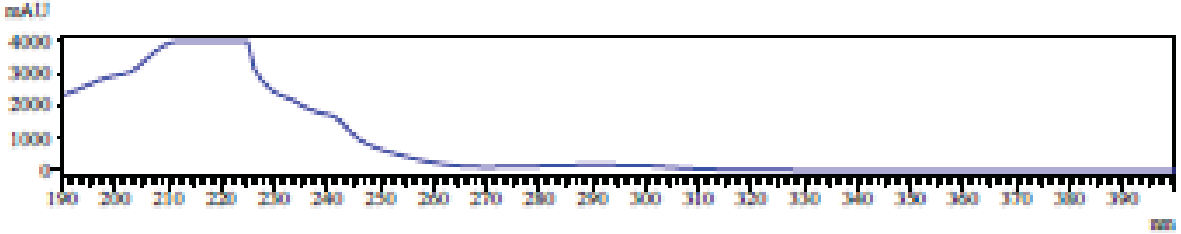
Sample Information

Data File	: Y0W-697-IE-10%0.8mL-iPrOH005.lcd
Sample Name	: Y0W-697-IE-10%0.8mL-iPrOH004
Sample ID	: Y0W-697-IE-10%0.8mL-iPrOH004
Method File	: YW-10%-0.8ml.lcm

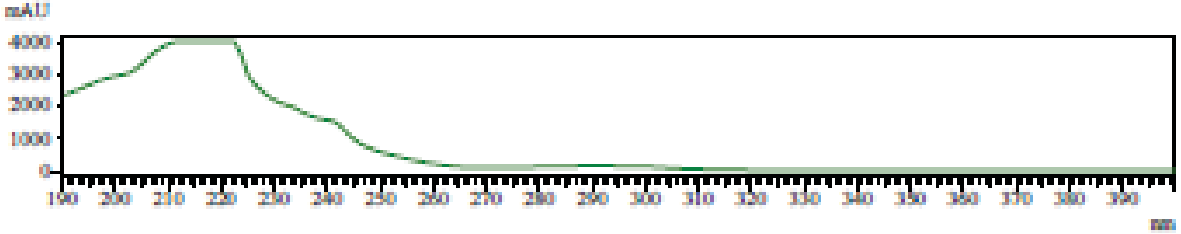
Chromatogram



UV Spectrum
Retention time = 20.458



UV Spectrum
Retention time = 22.850



Peak Table

PDA Ch1 247nm

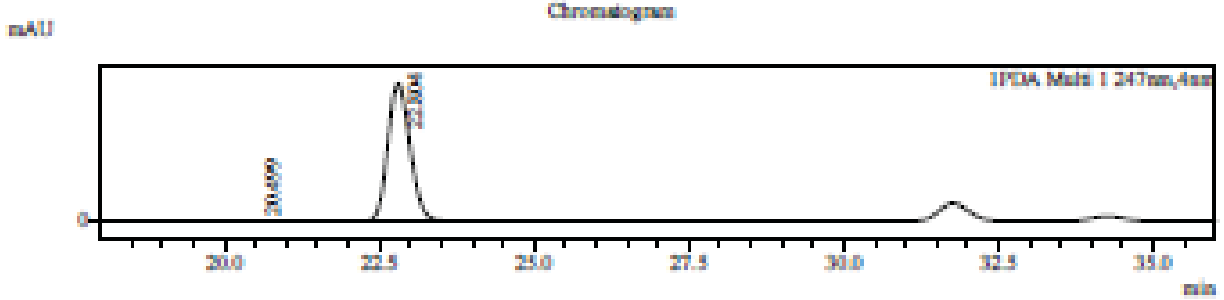
Peak#	Ret. Time	Area	Area%
1	20.458	20765129	27.654
2	22.850	20671376	27.529
3	31.574	16750895	22.308
4	34.027	16902906	22.510
Total		75090305	100.000

2-(2-(2-(thiophen-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

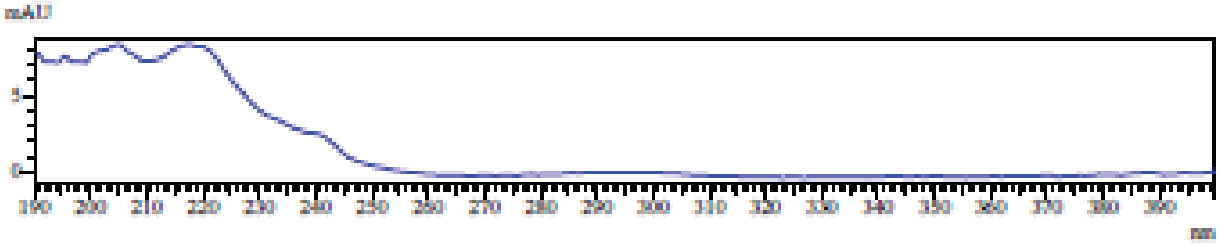
Sample Information

Data File	: Y0W-698-IE-10%0.8mL-iPrOH004.lcd
Sample Name	: Y0W-698-IE-10%0.8mL-iPrOH004
Sample ID	: Y0W-698-IE-10%0.8mL-iPrOH004
Method File	: YW-10%-0.8ml.lcm

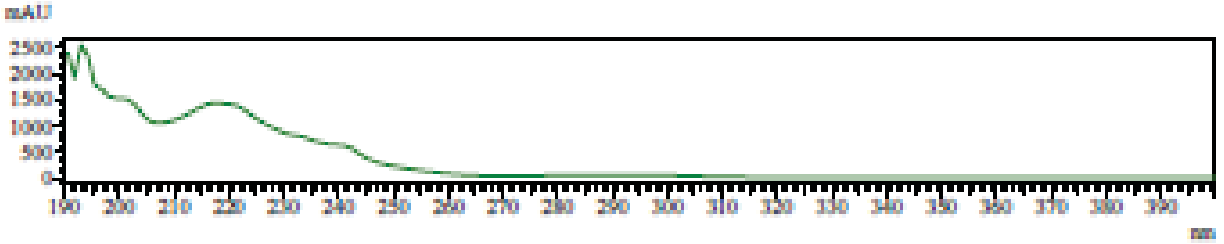
Chromatogram



UV Spectrum
Retention time = 20.499



UV Spectrum
Retention time = 22.804

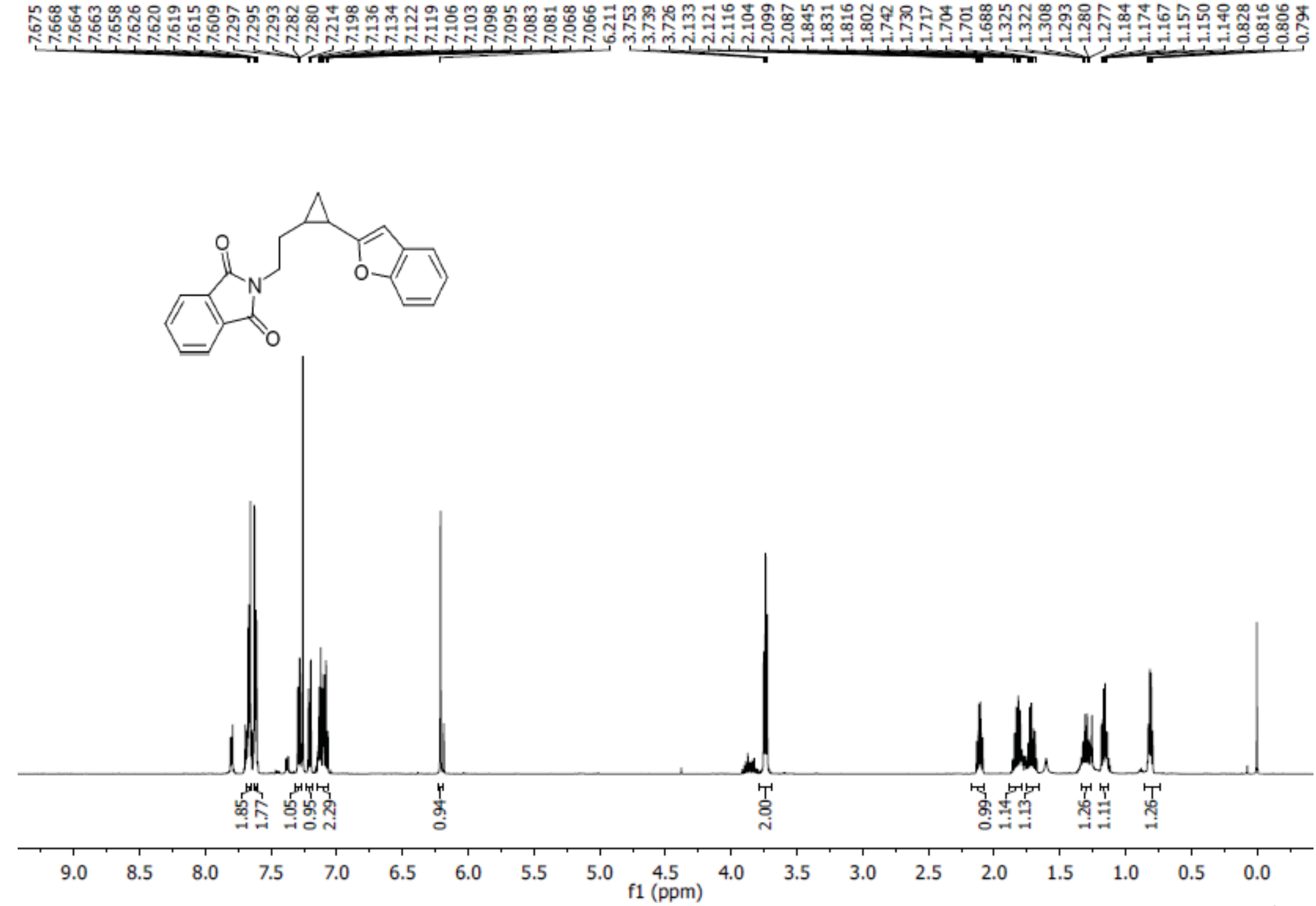


Peak Table

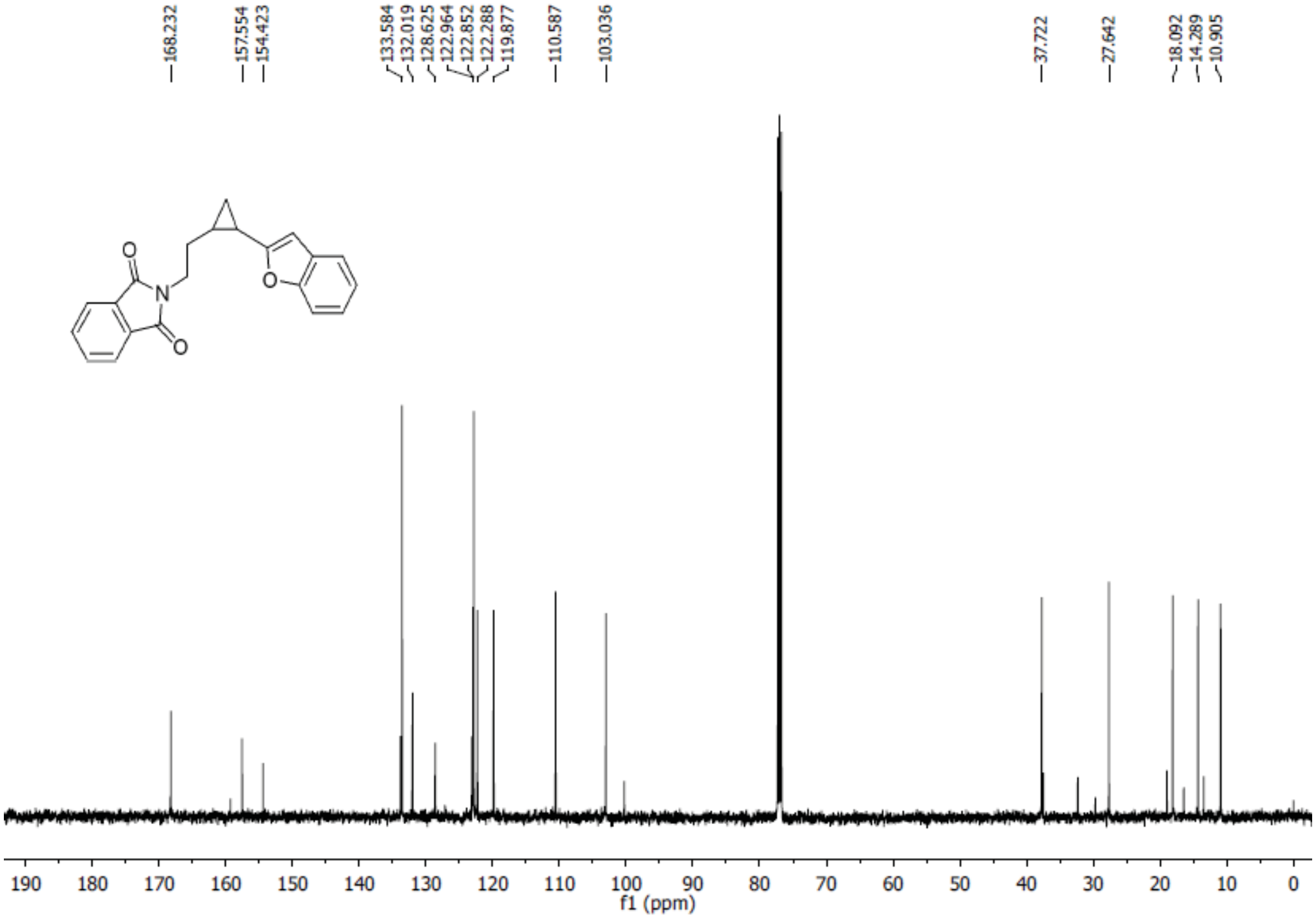
PDA Ch1 247nm

Peak#	Ret. Time	Area	Area%
1	20.499	29508	0.372
2	22.804	7906762	99.628
Total		7936271	100.000

2-(2-(2-(benzofuran-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione



2-(2-(2-(benzofuran-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

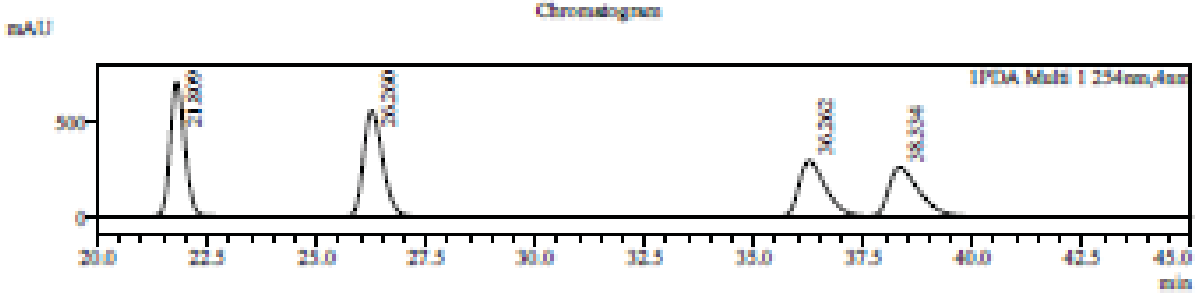


2-(2-(2-(benzofuran-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

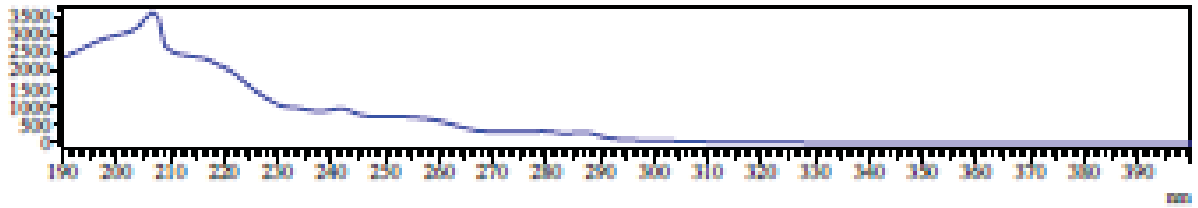
Sample Information

Data File	: Y0W-748-IE-10%0.8mL-iPrOH001.lcd
Sample Name	: Y0W-748-IE-10%0.8mL-iPrOH001
Sample ID	: Y0W-748-IE-10%0.8mL-iPrOH001
Method File	: YW-10%-0.8ml.lcm

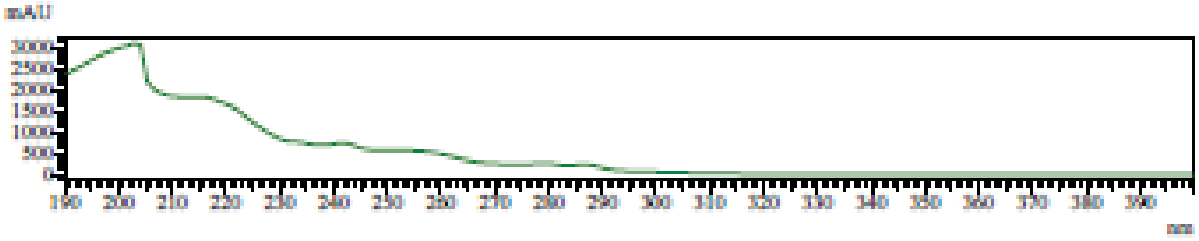
Chromatogram



UV Spectrum
Retention time = 21.809



UV Spectrum
Retention time = 26.260



Peak Table

PDA Ch1 254nm

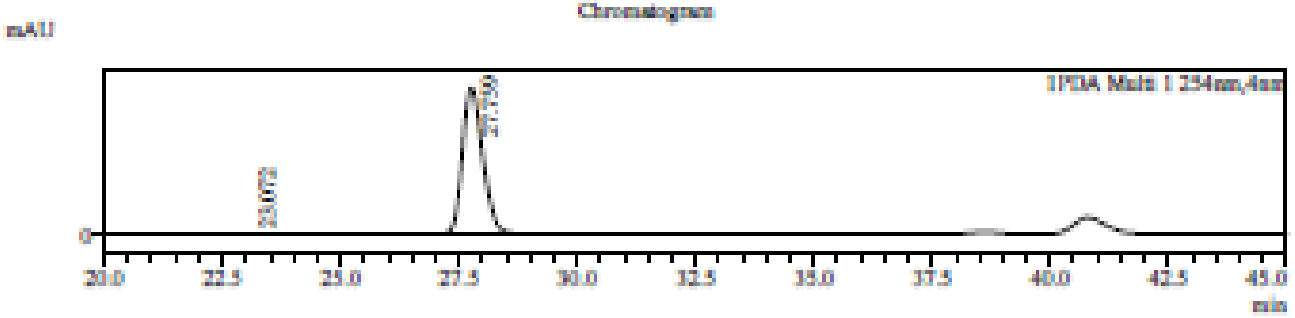
Peak#	Ret. Time	Area	Area%
1	21.809	16440122	27.793
2	26.260	17213113	29.099
3	36.262	12707775	21.483
4	38.334	12791647	21.625
Total		59152657	100.000

2-(2-(2-(benzofuran-2-yl)cyclopropyl)ethyl)isoindoline-1,3-dione

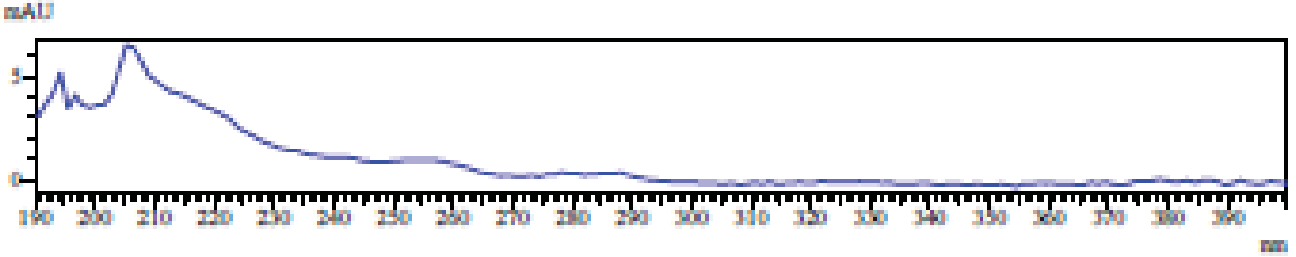
Sample Information

Data File	: Y0W-749-IE-10%0.8mL-iPrOH001.lcd
Sample Name	: Y0W-749-IE-10%0.8mL-iPrOH001
Sample ID	: Y0W-749-IE-10%0.8mL-iPrOH001
Method File	: YW-10%-0.8ml.lcm

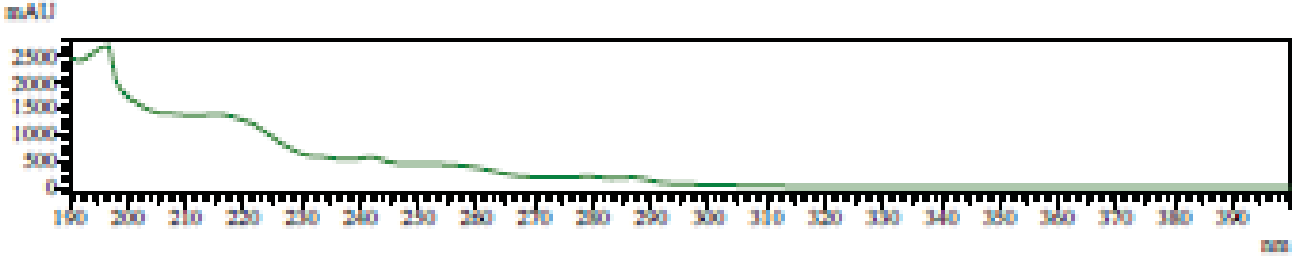
Chromatogram



UV Spectrum
Retention time = 23.072



UV Spectrum
Retention time = 27.759

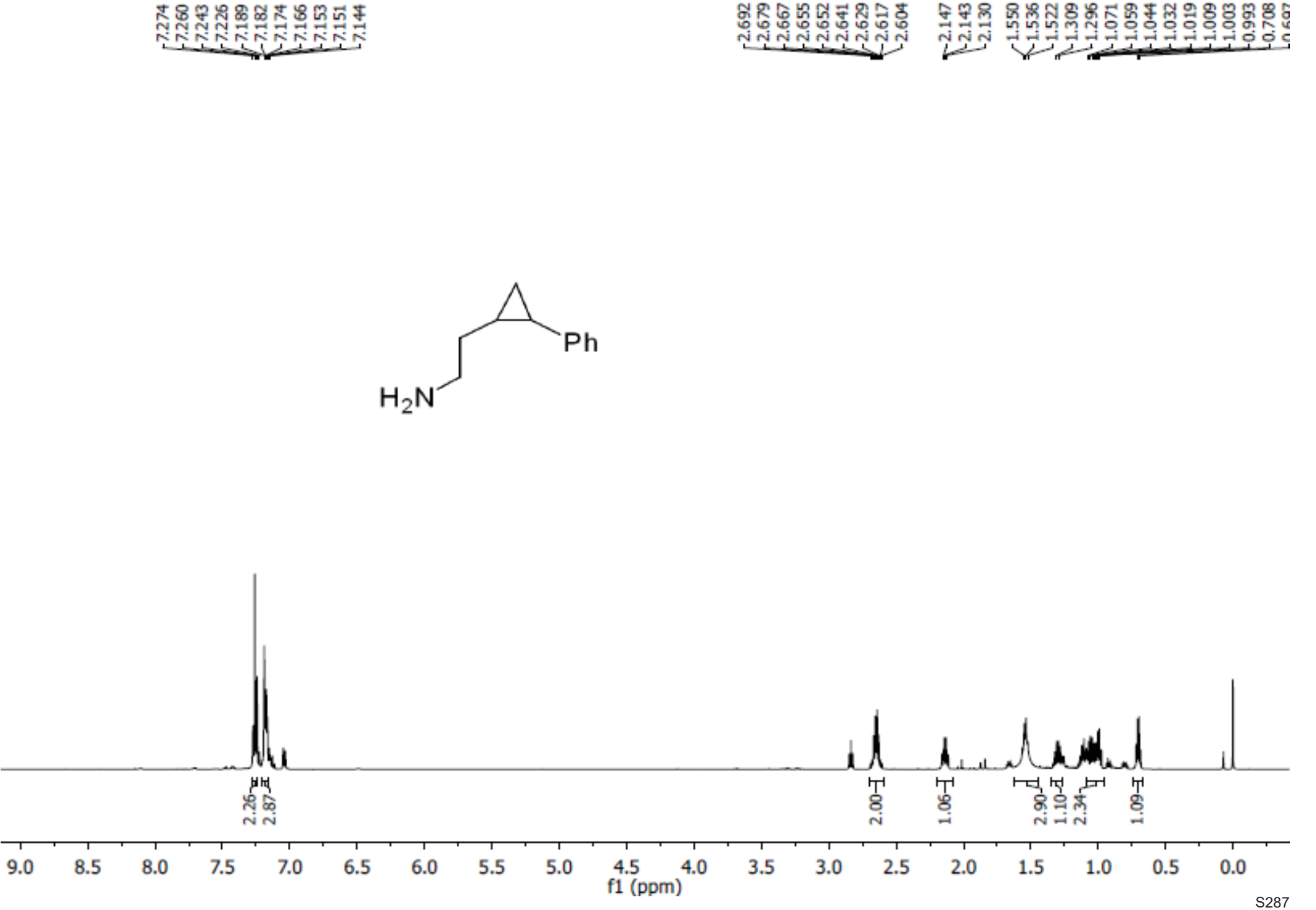


Peak Table

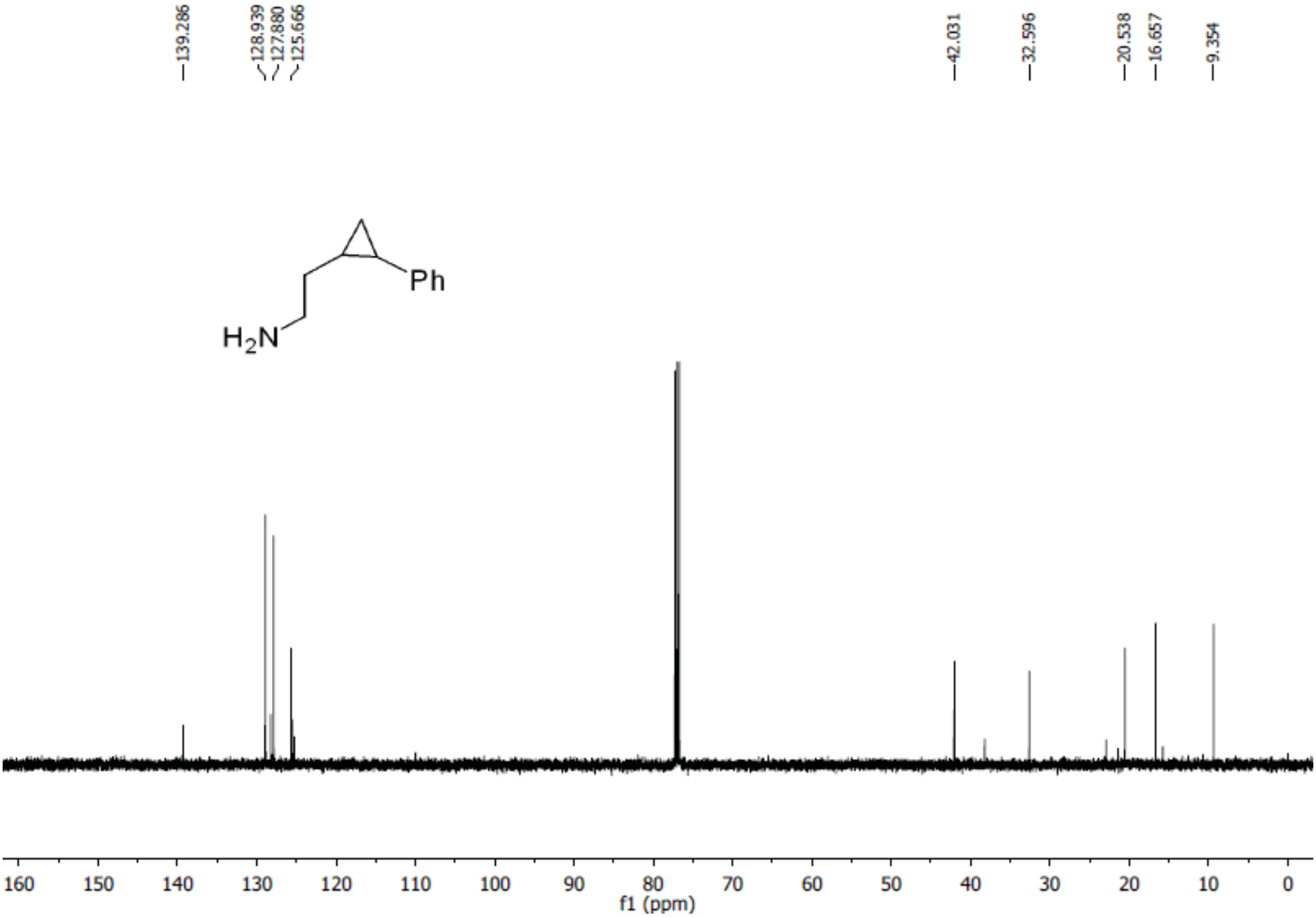
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	23.072	22588	0.174
2	27.759	12943894	99.826
Total		12966482	100.000

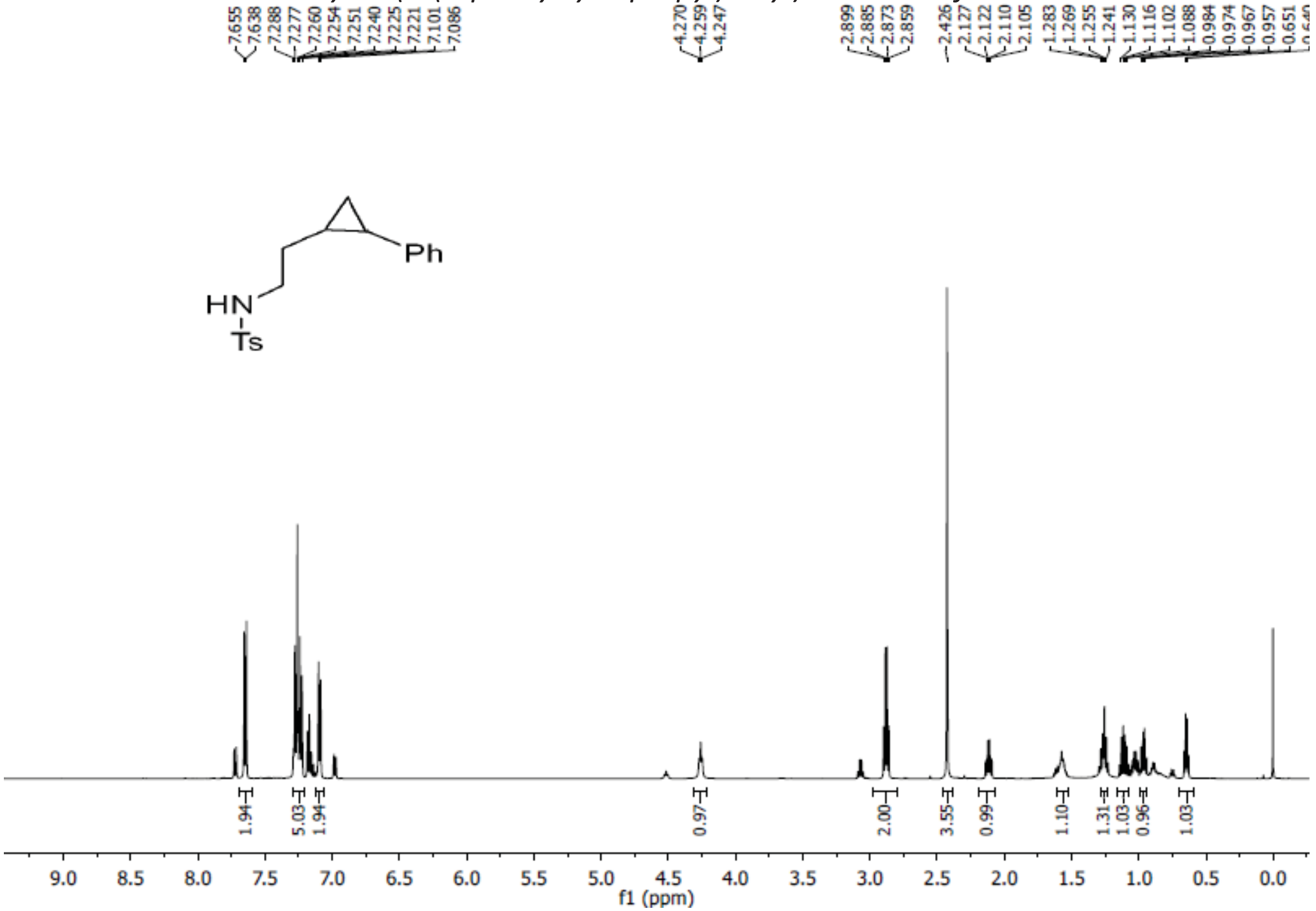
2-(2-phenylcyclopropyl)ethan-1-amine



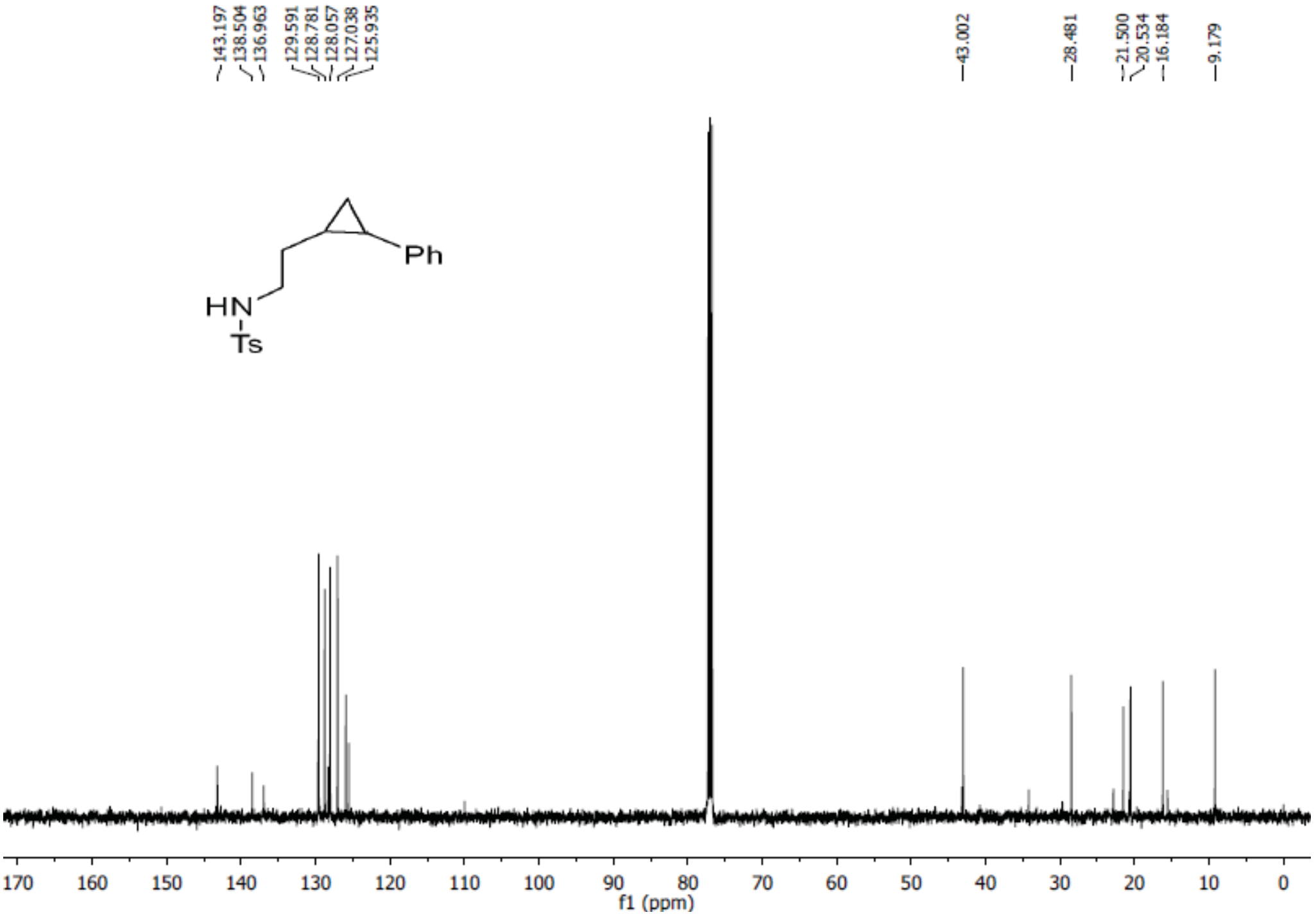
2-(2-phenylcyclopropyl)ethan-1-amine



4-methyl-N-(2-(2-phenylcyclopropyl)ethyl)benzenesulfonamide



4-methyl-N-(2-(2-phenylcyclopropyl)ethyl)benzenesulfonamide

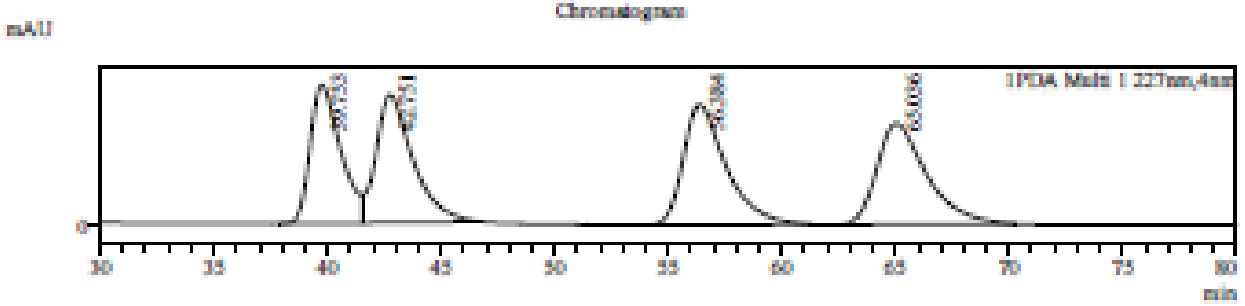


4-methyl-N-(2-(2-phenylcyclopropyl)ethyl)benzenesulfonamide

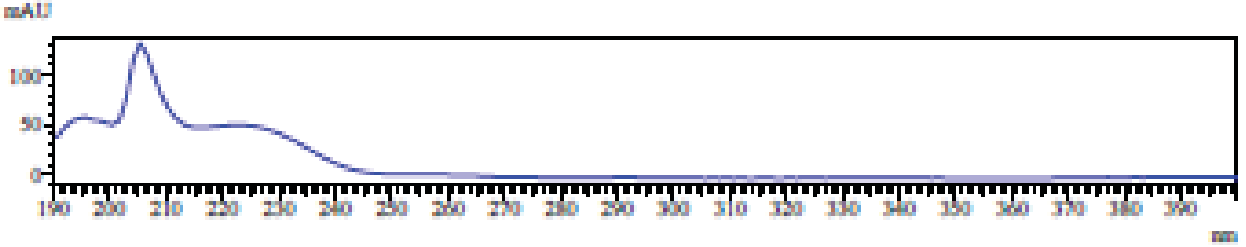
Sample Information

Data File	: Y0W-802-OJH-10%0.8mL-iPrOH.lcd
Sample Name	: Y0W-802-OJH-10%0.8mL-iPrOH
Sample ID	: Y0W-802-OJH-10%0.8mL-iPrOH
Method File	: YW-10%-0.8ml.lcm

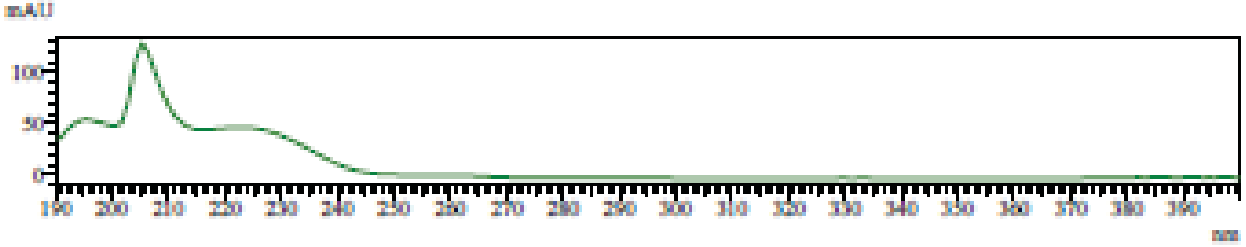
Chromatogram



UV Spectrum
Retention time = 39.753



UV Spectrum
Retention time = 42.751



Peak Table

PDA Ch1 227nm

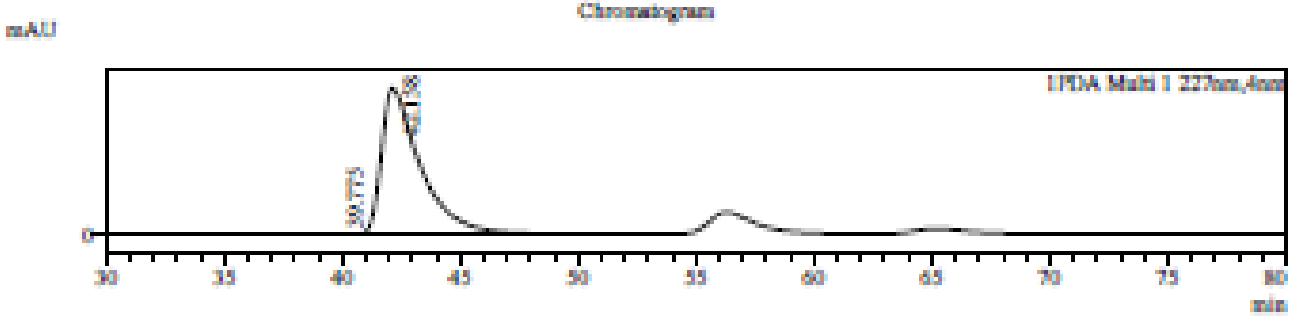
Peak#	Ret. Time	Area	Area%
1	39.753	4230278	21.990
2	42.751	4740021	24.640
3	56.384	5207747	27.071
4	65.036	5059064	26.298
Total		19237111	100.000

4-methyl-N-(2-(2-phenylcyclopropyl)ethyl)benzenesulfonamide

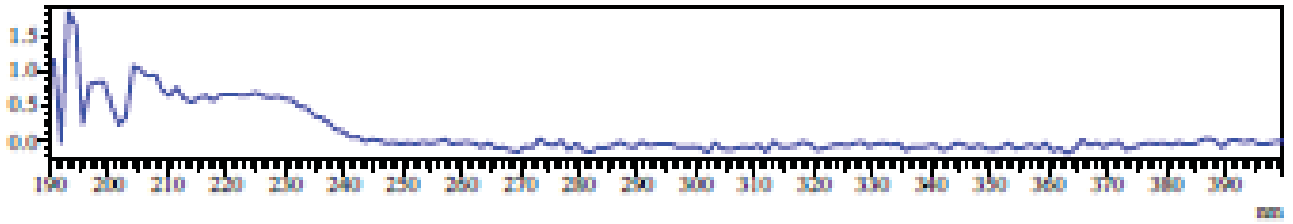
Sample Information

Data File	: Y0W-803-OJH-10%0.8mL-iPrOH001.lcd
Sample Name	: Y0W-803-OJH-10%0.8mL-iPrOH001
Sample ID	: Y0W-803-OJH-10%0.8mL-iPrOH001
Method File	: YW-10%-0.8ml.lcm

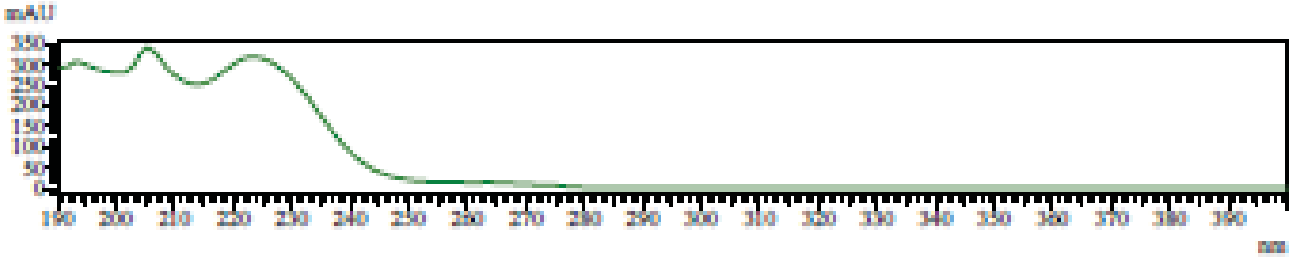
Chromatogram



UV Spectrum
Retention time = 39.775



UV Spectrum
Retention time = 42.158



Peak Table

PDA Ch1 227nm

Peak#	Ret. Time	Area	Area%
1	39.775	53977	0.159
2	42.158	33829531	99.841
Total		33883508	100.000

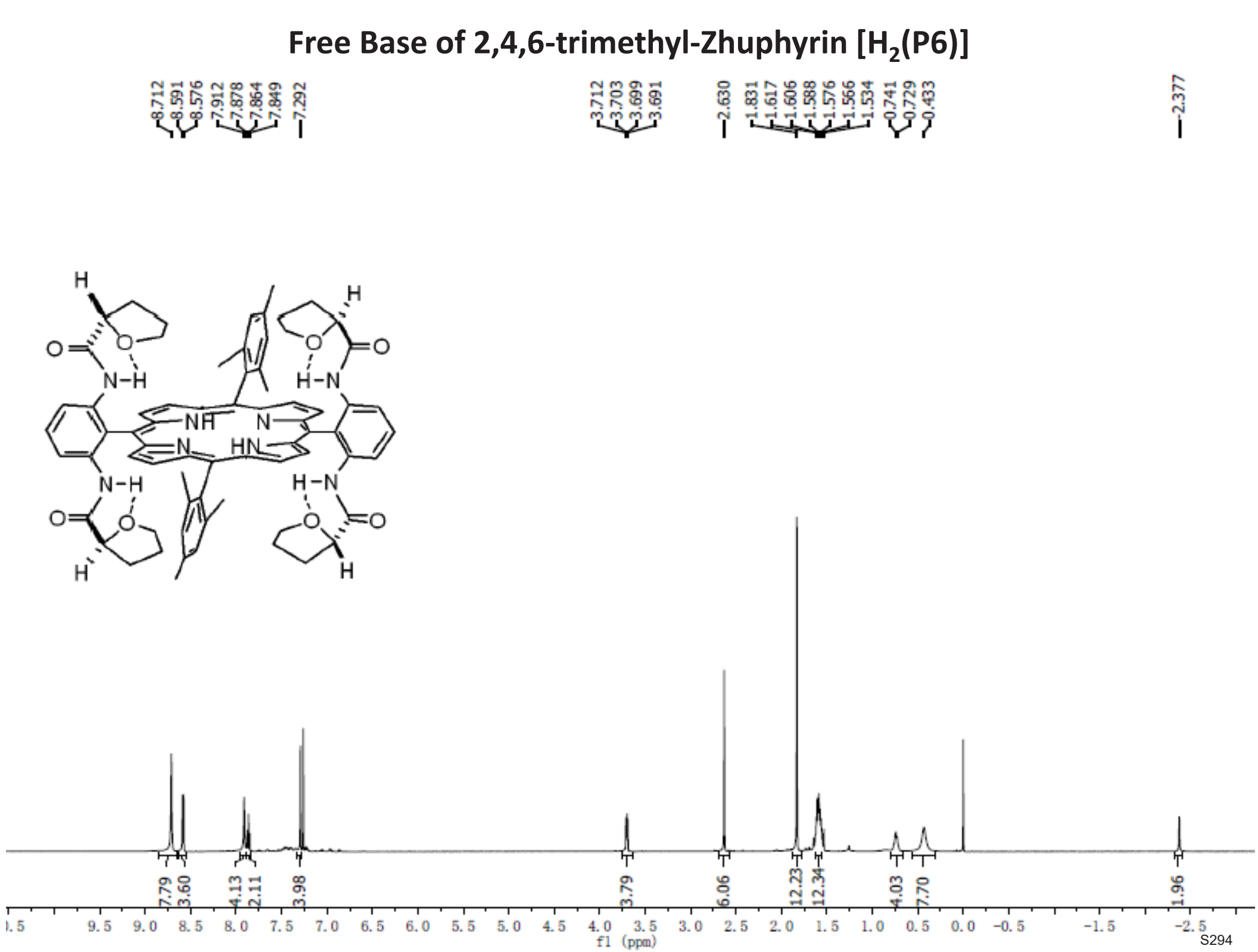
Spectral Data

for

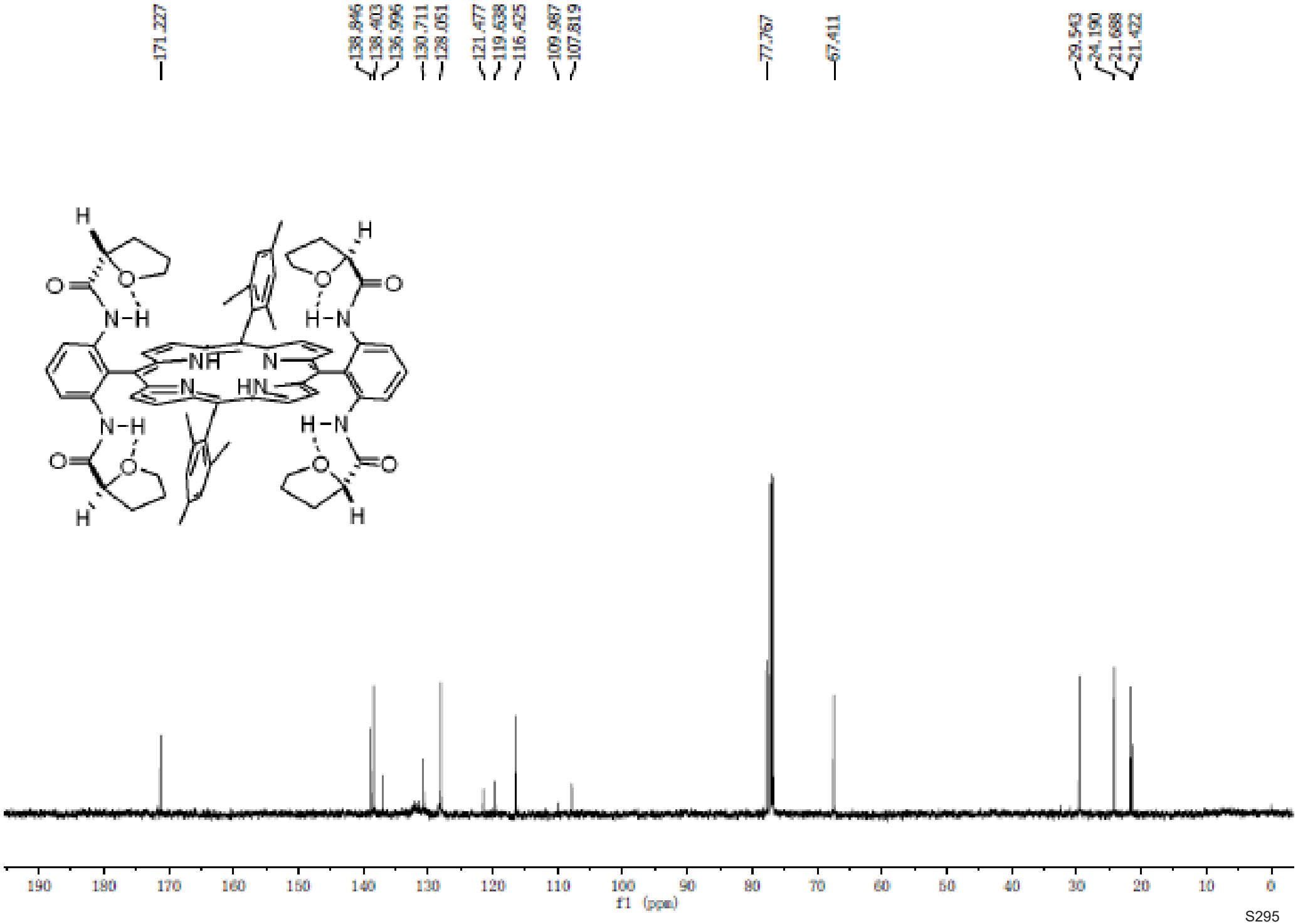
Chapter 4

Enantioselective Radical Cyclization for Construction of 5-Membered Ring Structures by Metalloradical C–H Alkylation

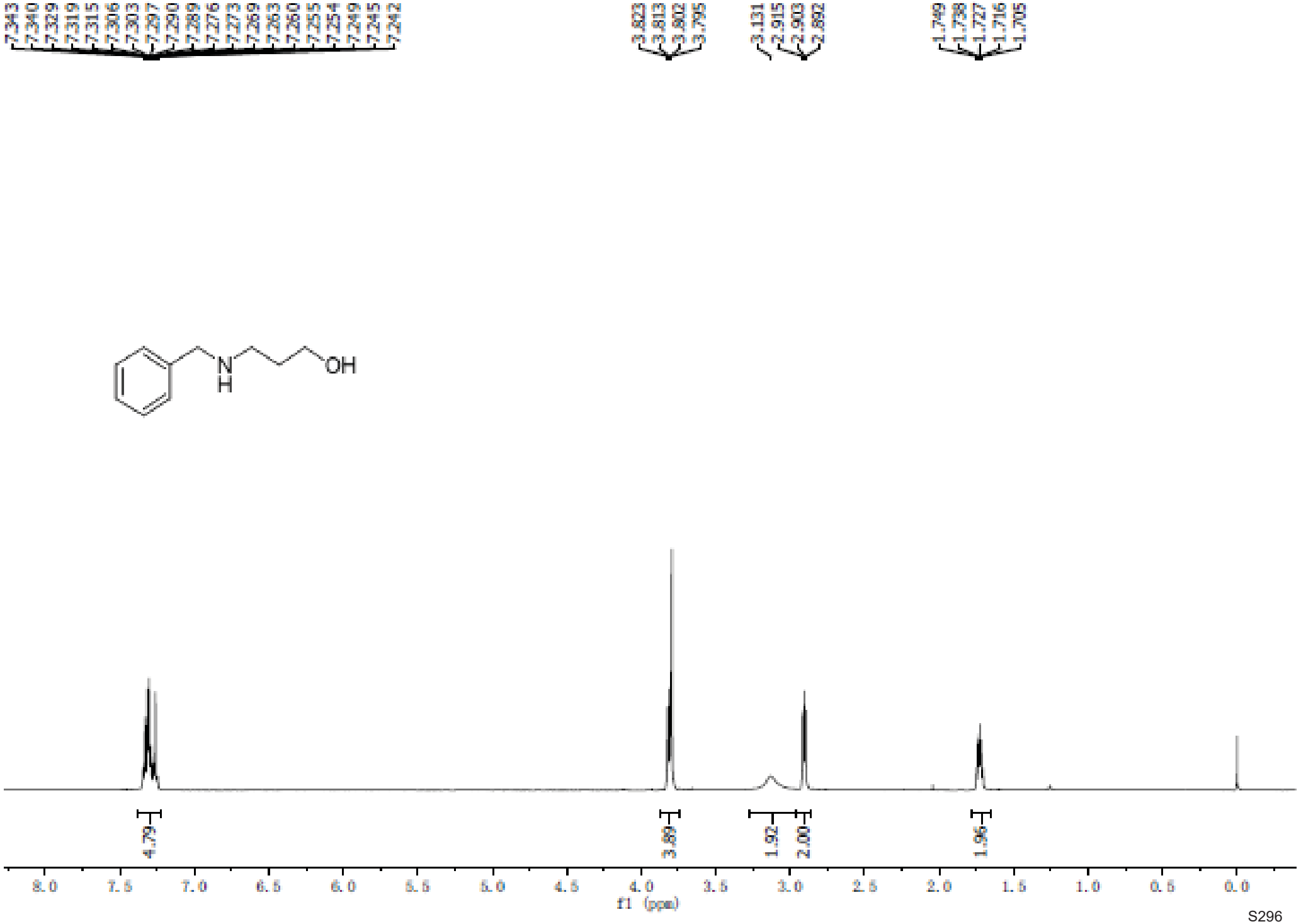
Free Base of 2,4,6-trimethyl-Zhuphyrin [H_2(P6)]



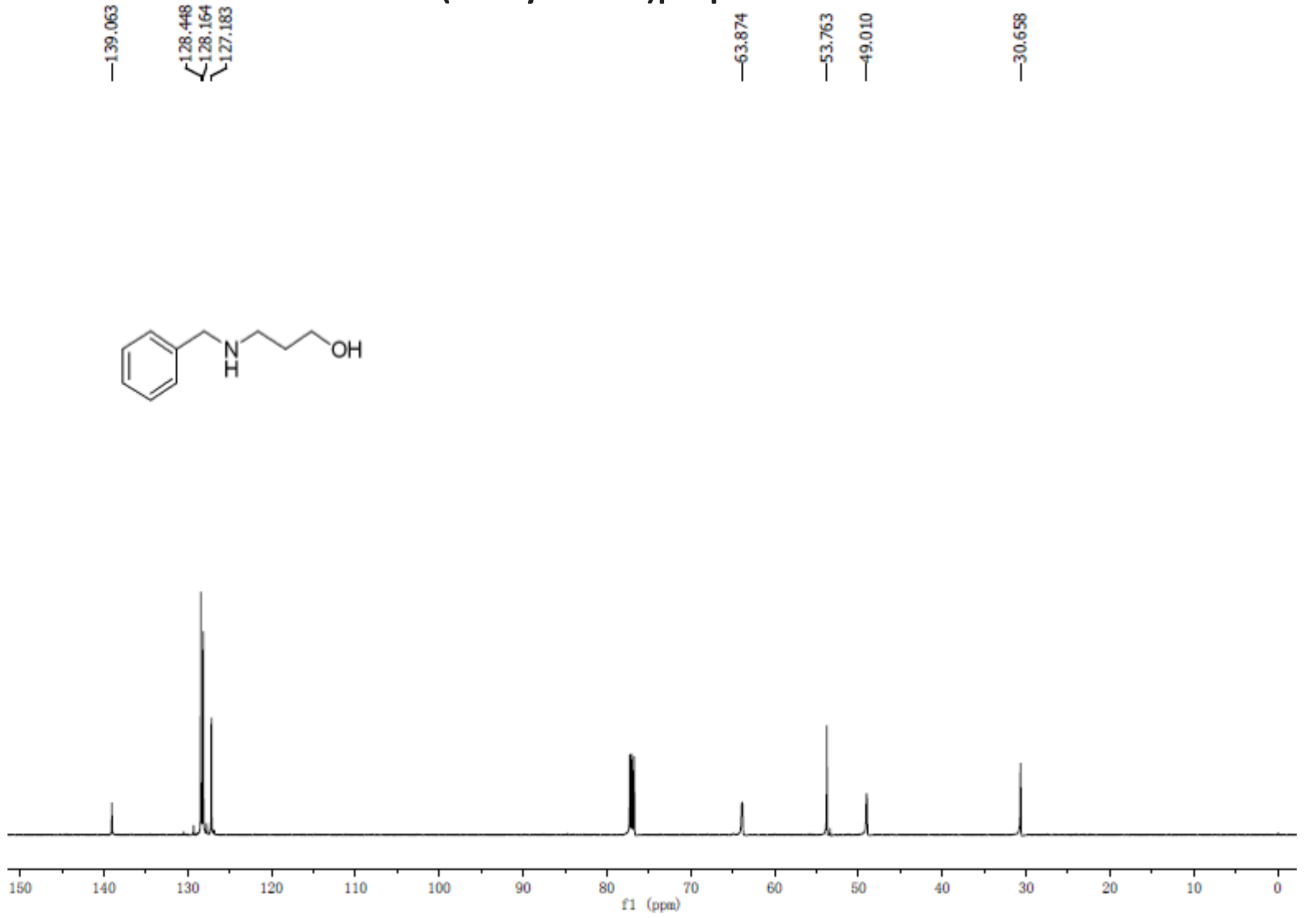
Free Base of 2,4,6-trimethyl-Zhuphyrin [H_2(P6)]



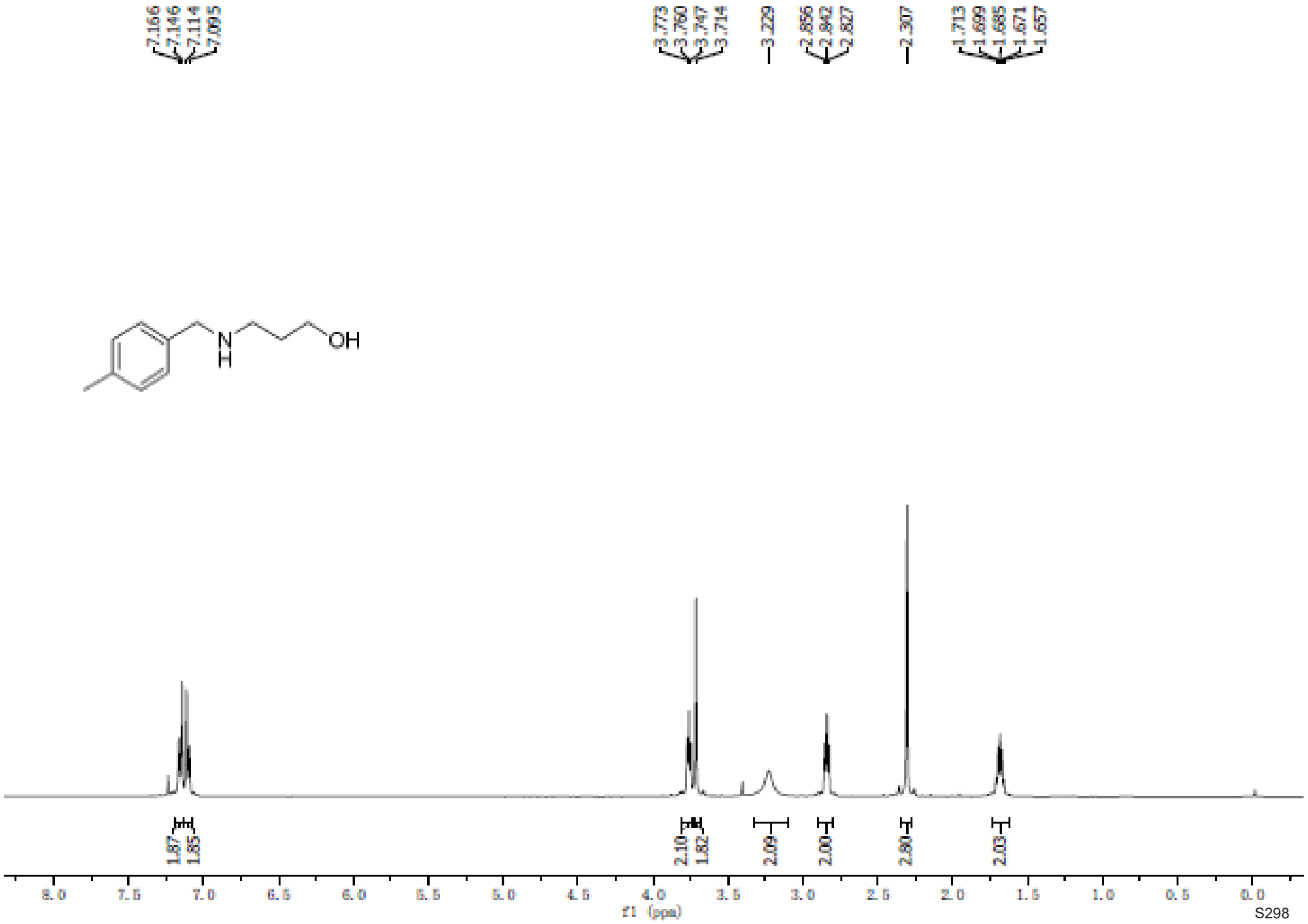
3-(benzylamino)propan-1-ol s1-a



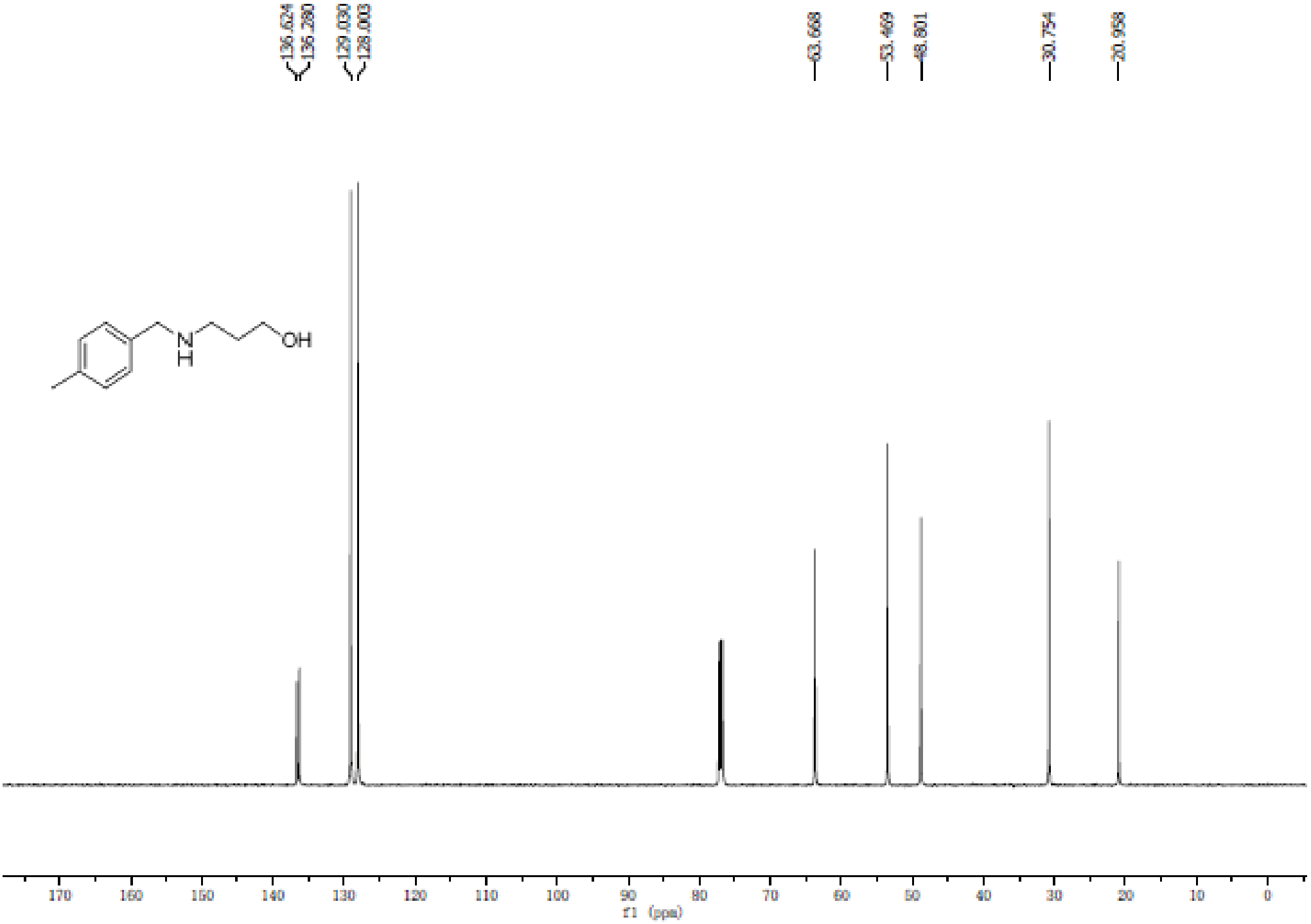
3-(benzylamino)propan-1-ol s1-a



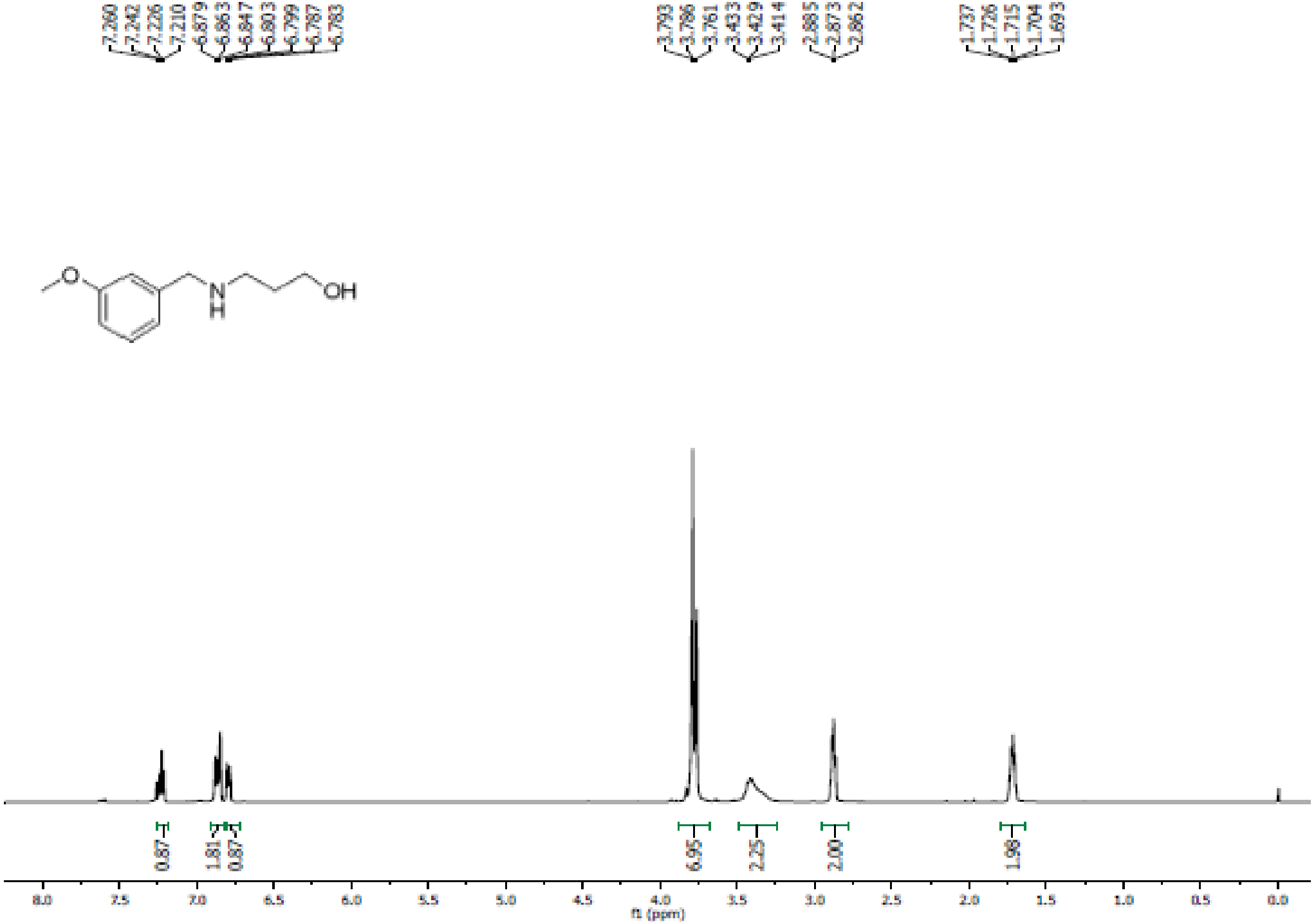
3-((4-methylbenzyl)amino)propan-1-ol s1-b



3-((4-methylbenzyl)amino)propan-1-ol s1-b

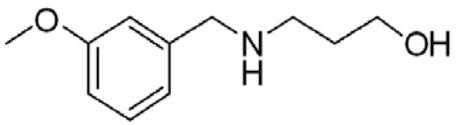


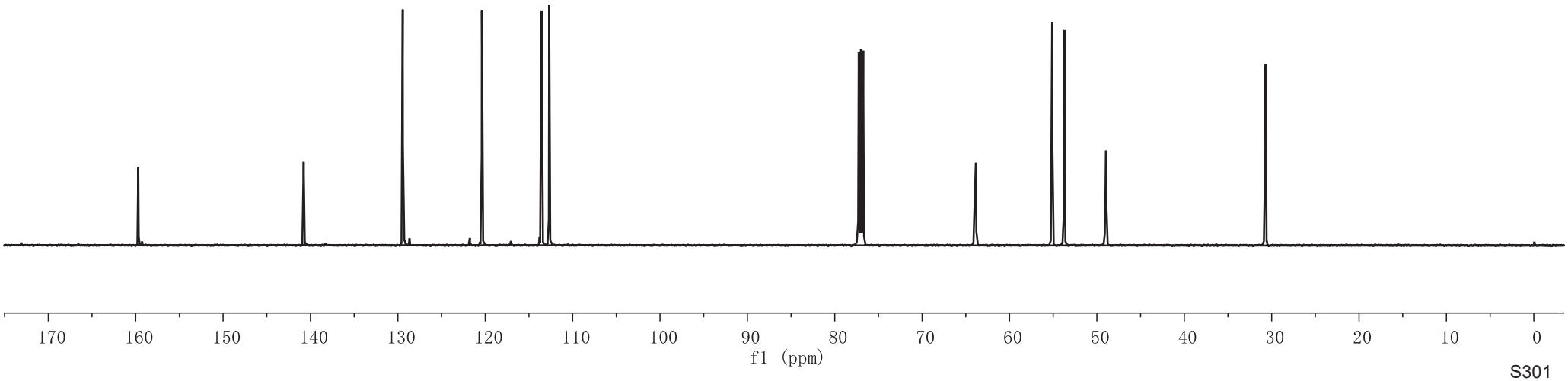
3-((3-methoxybenzyl)amino)propan-1-ol s1-c



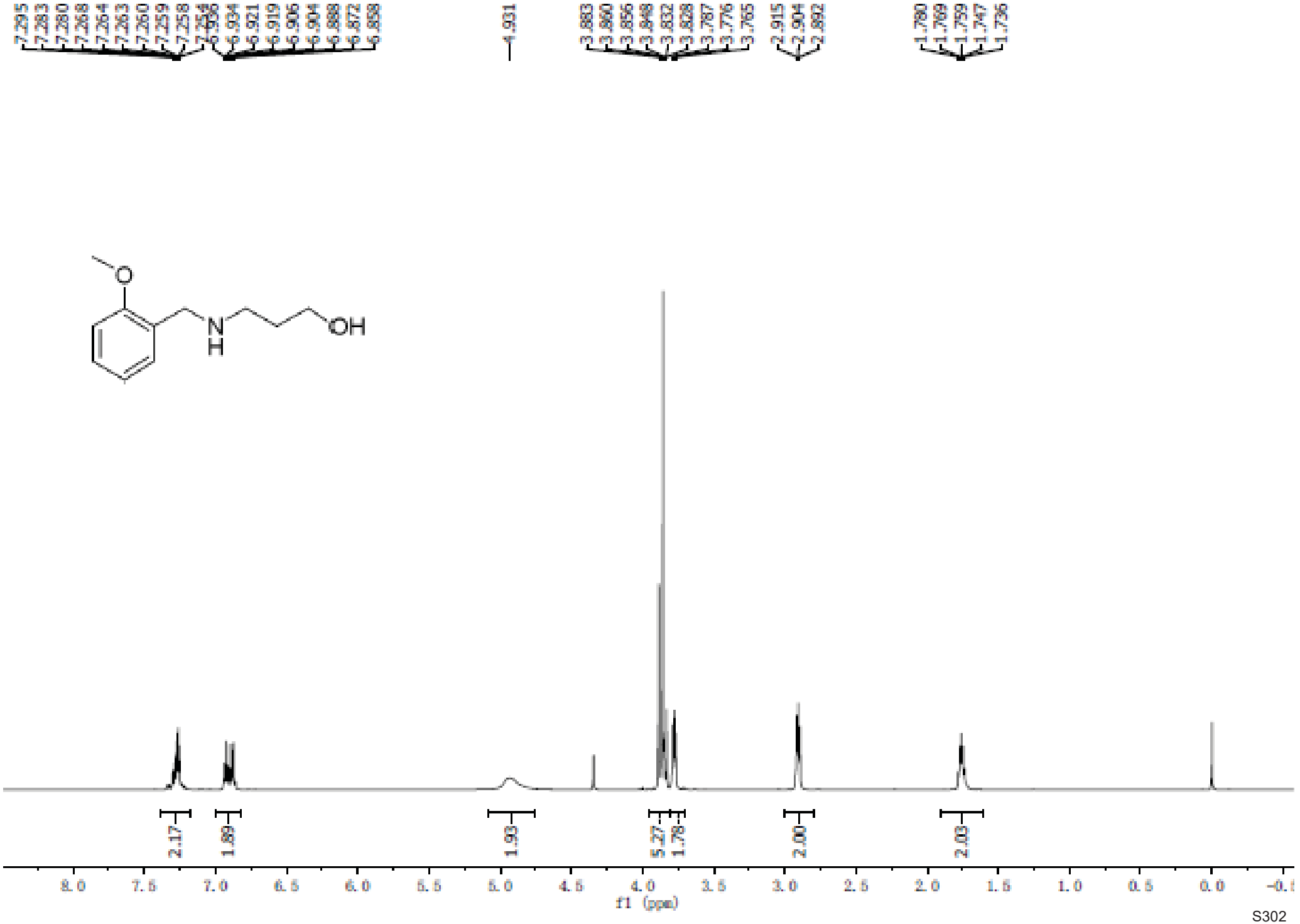
3-((3-methoxybenzyl)amino)propan-1-ol s1-c

159.706
140.781
129.445
120.389
113.561
112.682
63.844
55.122
53.724
48.953
30.699

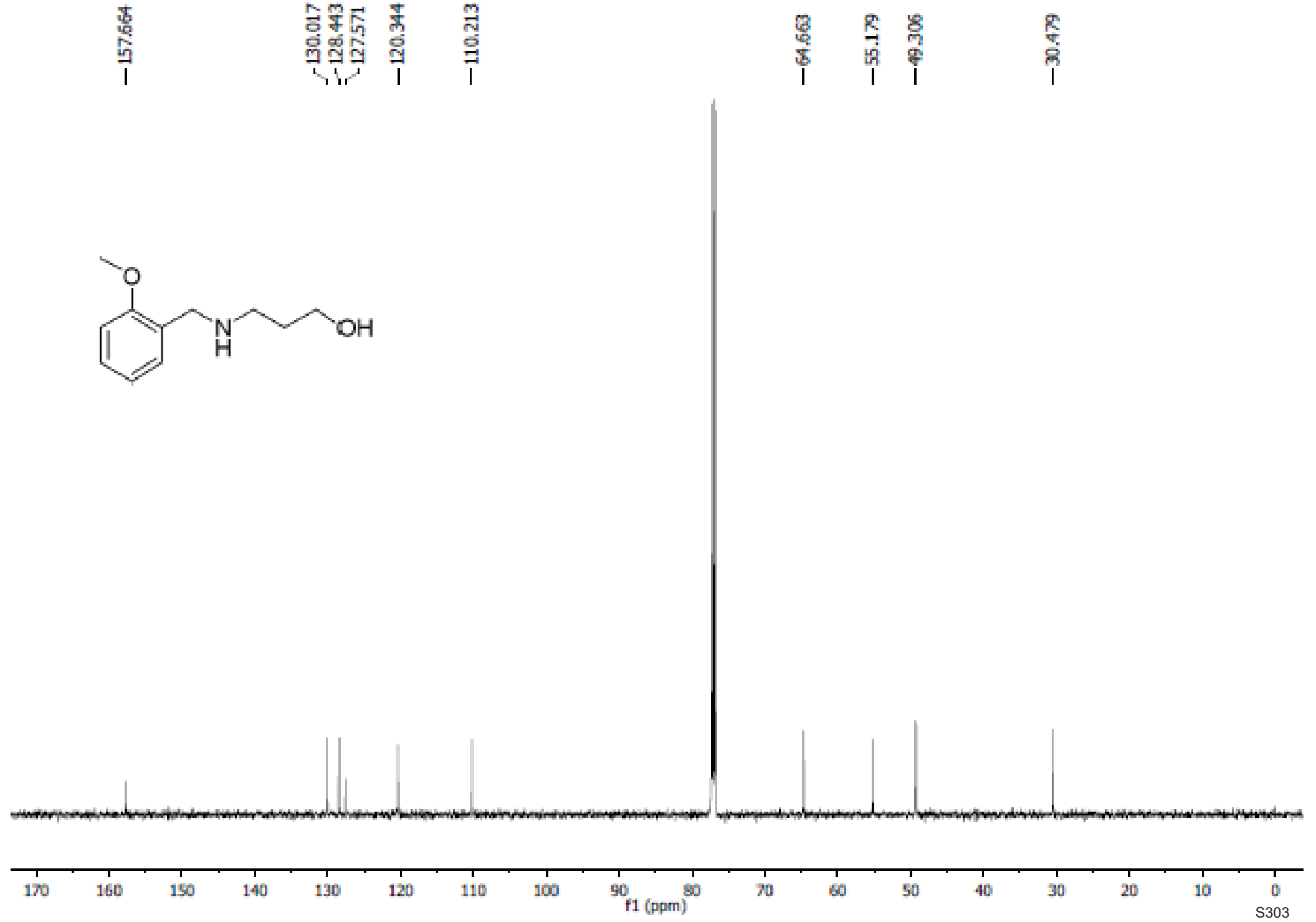




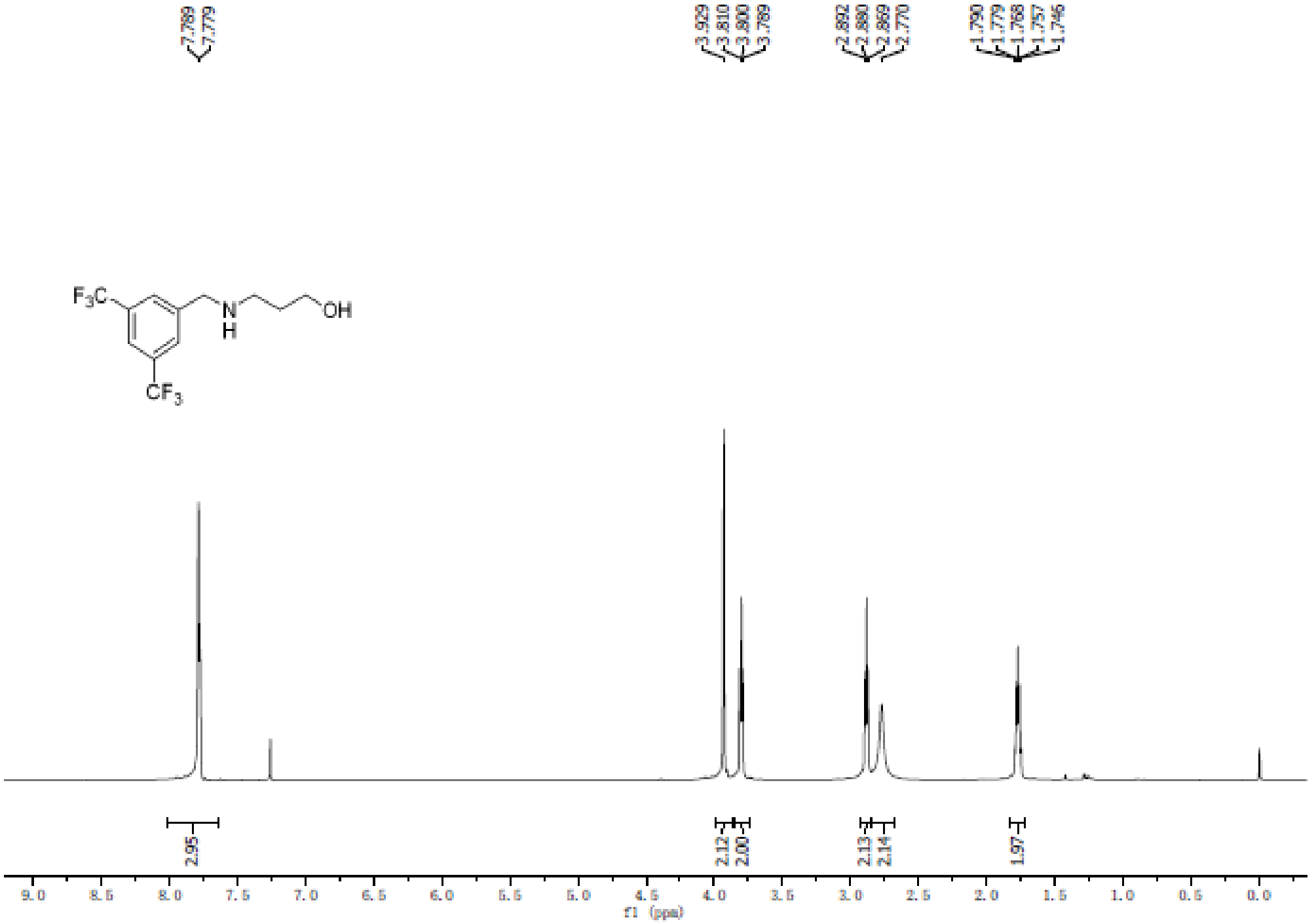
3-((2-methoxybenzyl)amino)propan-1-ol s1-d



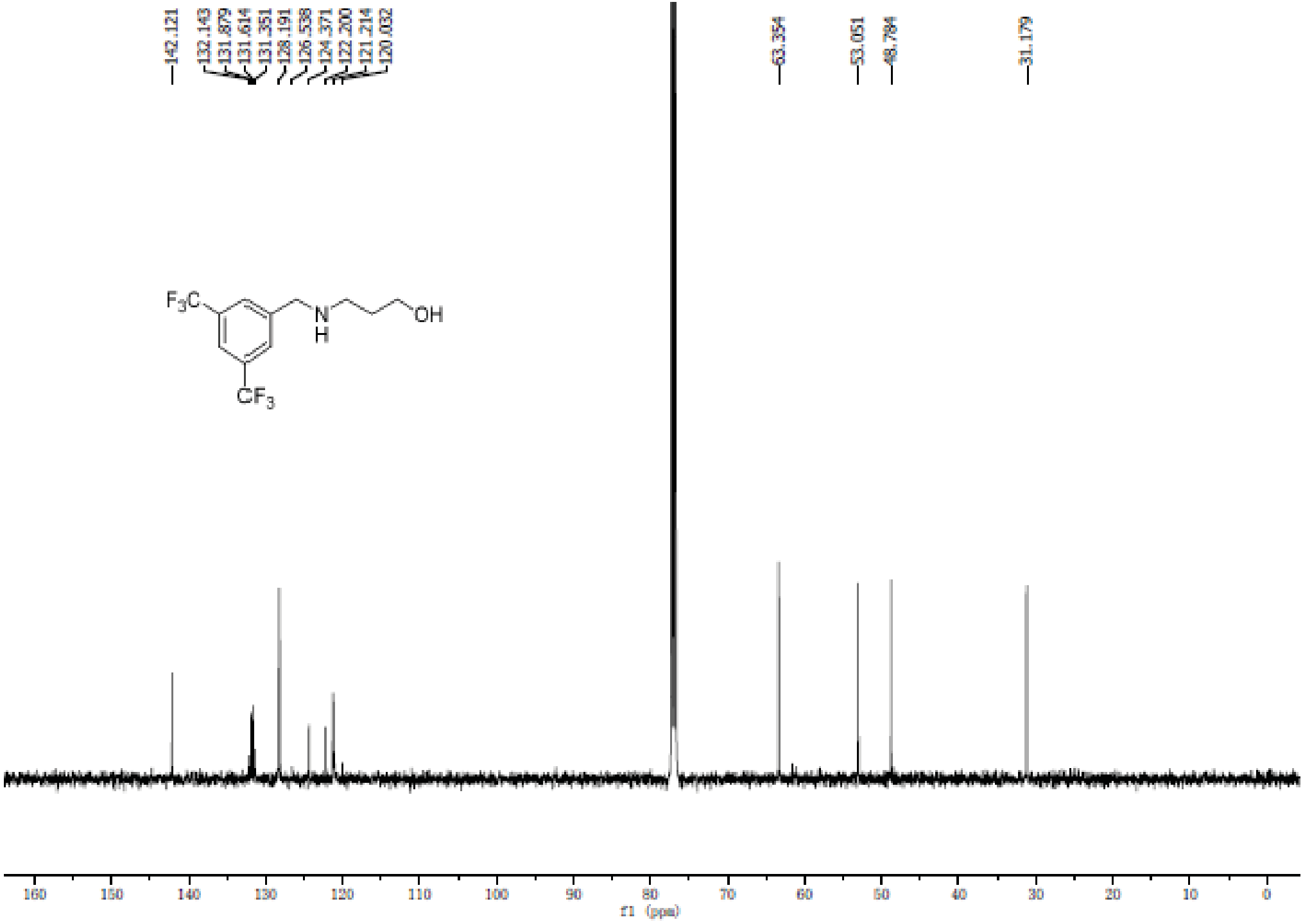
3-((2-methoxybenzyl)amino)propan-1-ol s1-d



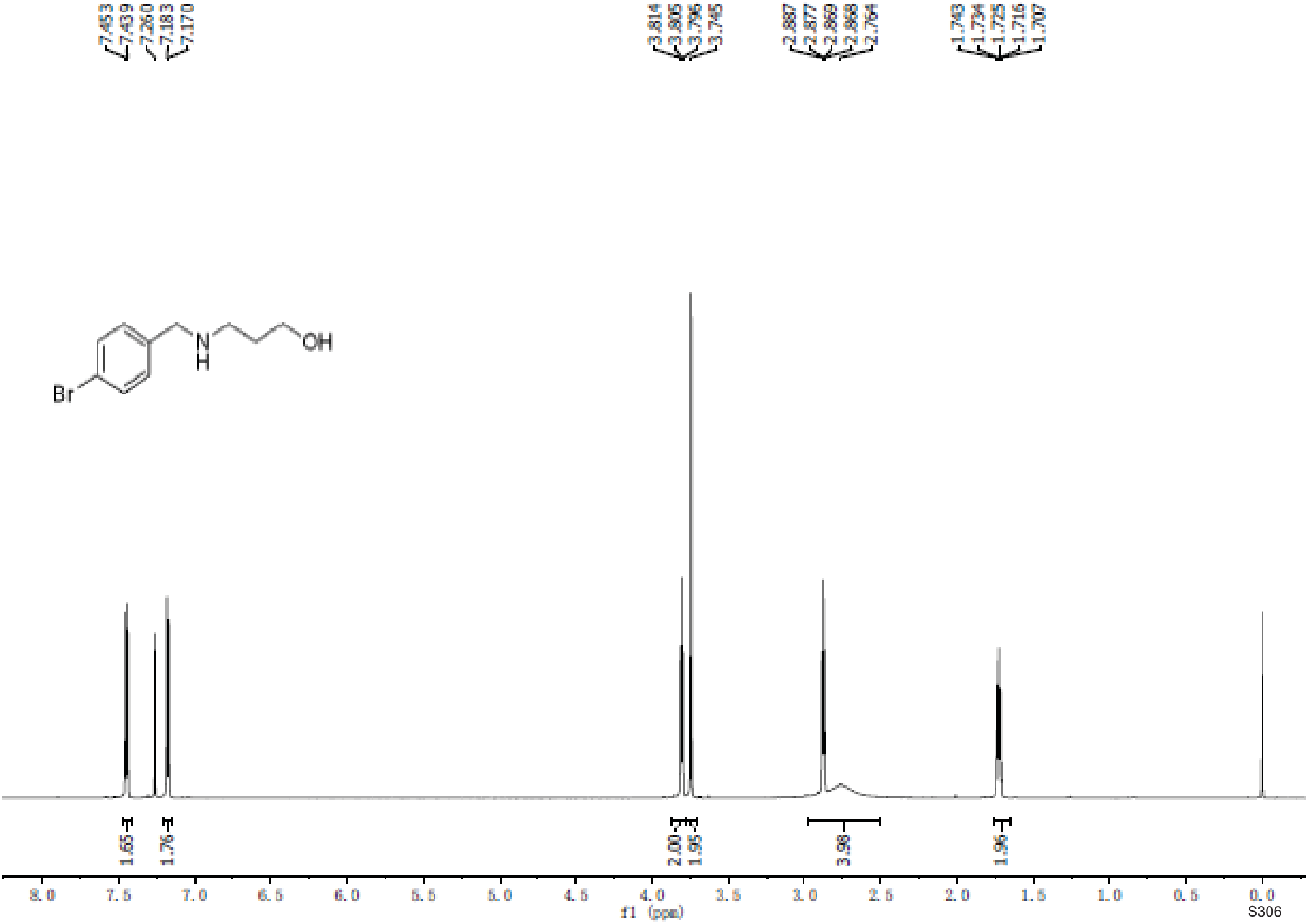
3-((3,5-bis(trifluoromethyl)benzyl)amino)propan-1-ol s1-e



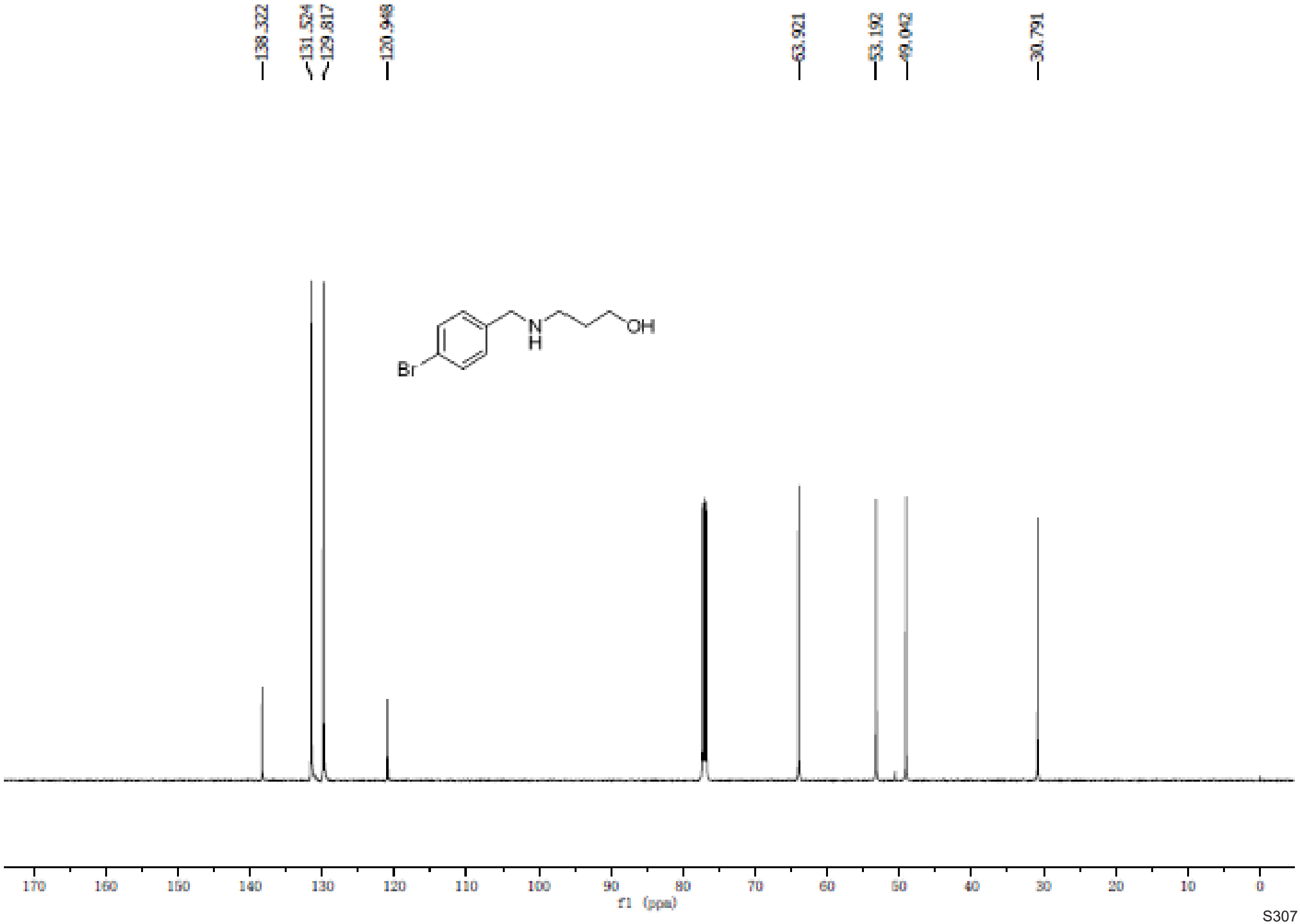
3-((3,5-bis(trifluoromethyl)benzyl)amino)propan-1-ol s1-e



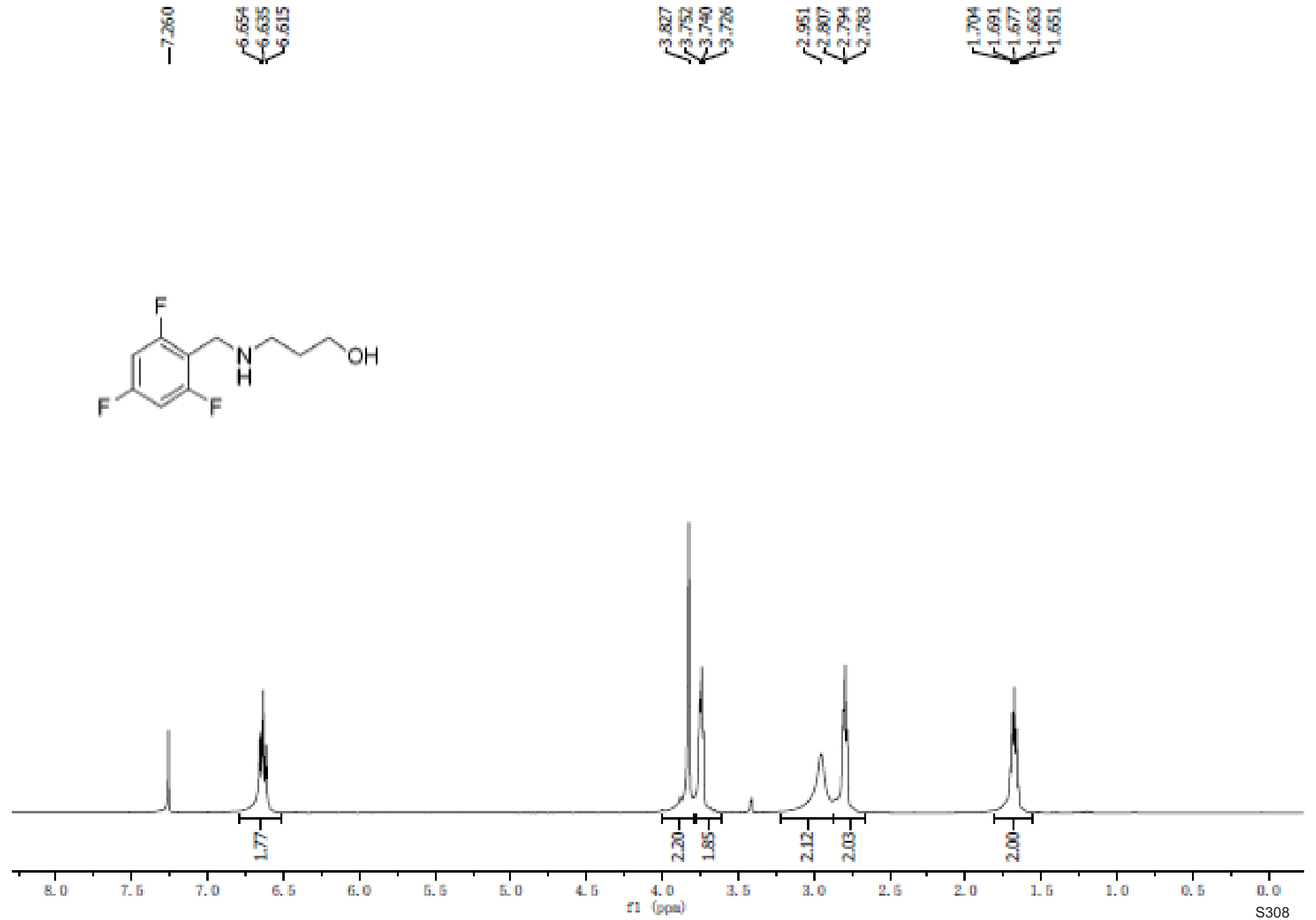
3-((4-bromobenzyl)amino)propan-1-ol s1-f



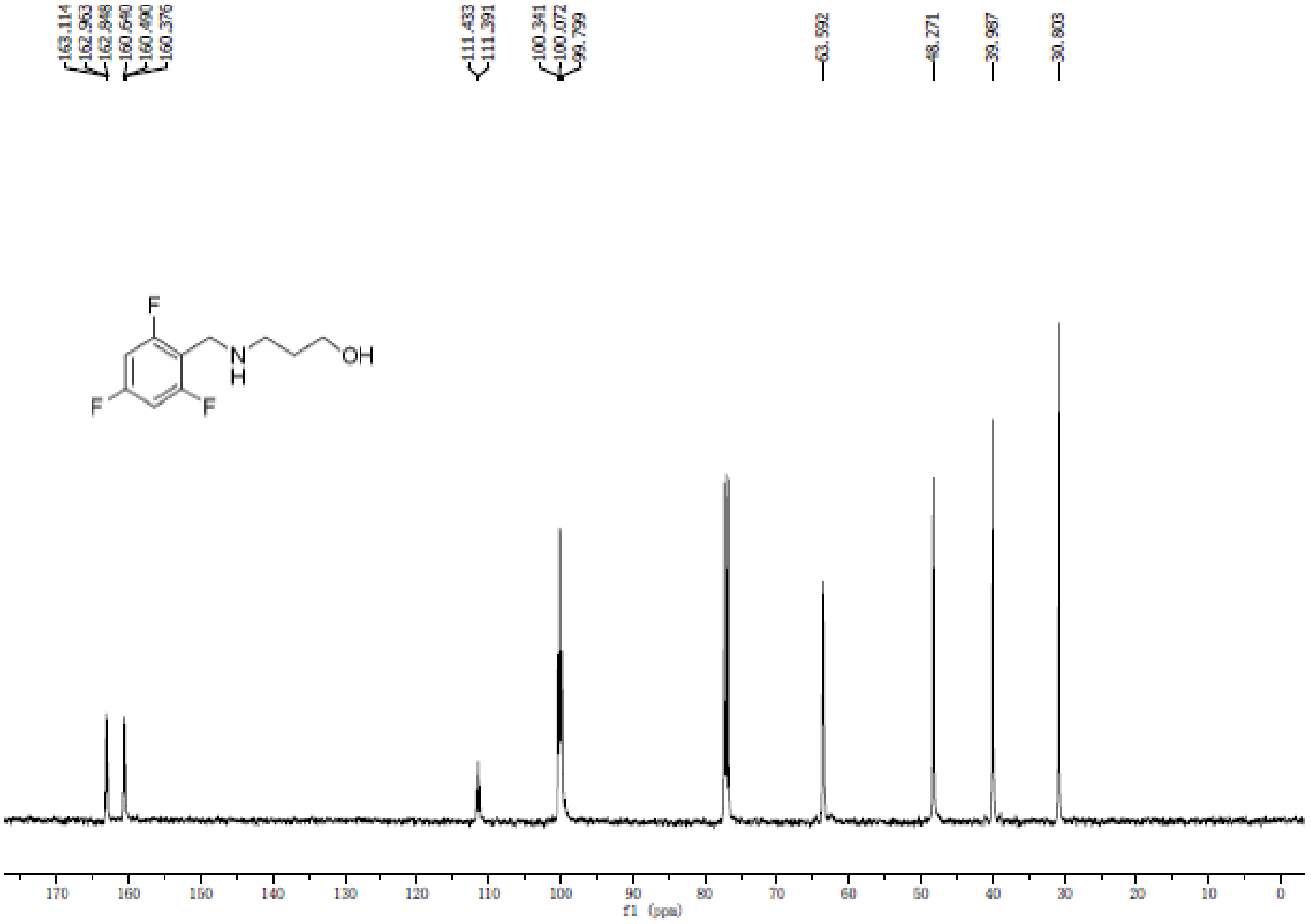
3-((4-bromobenzyl)amino)propan-1-ol s1-f



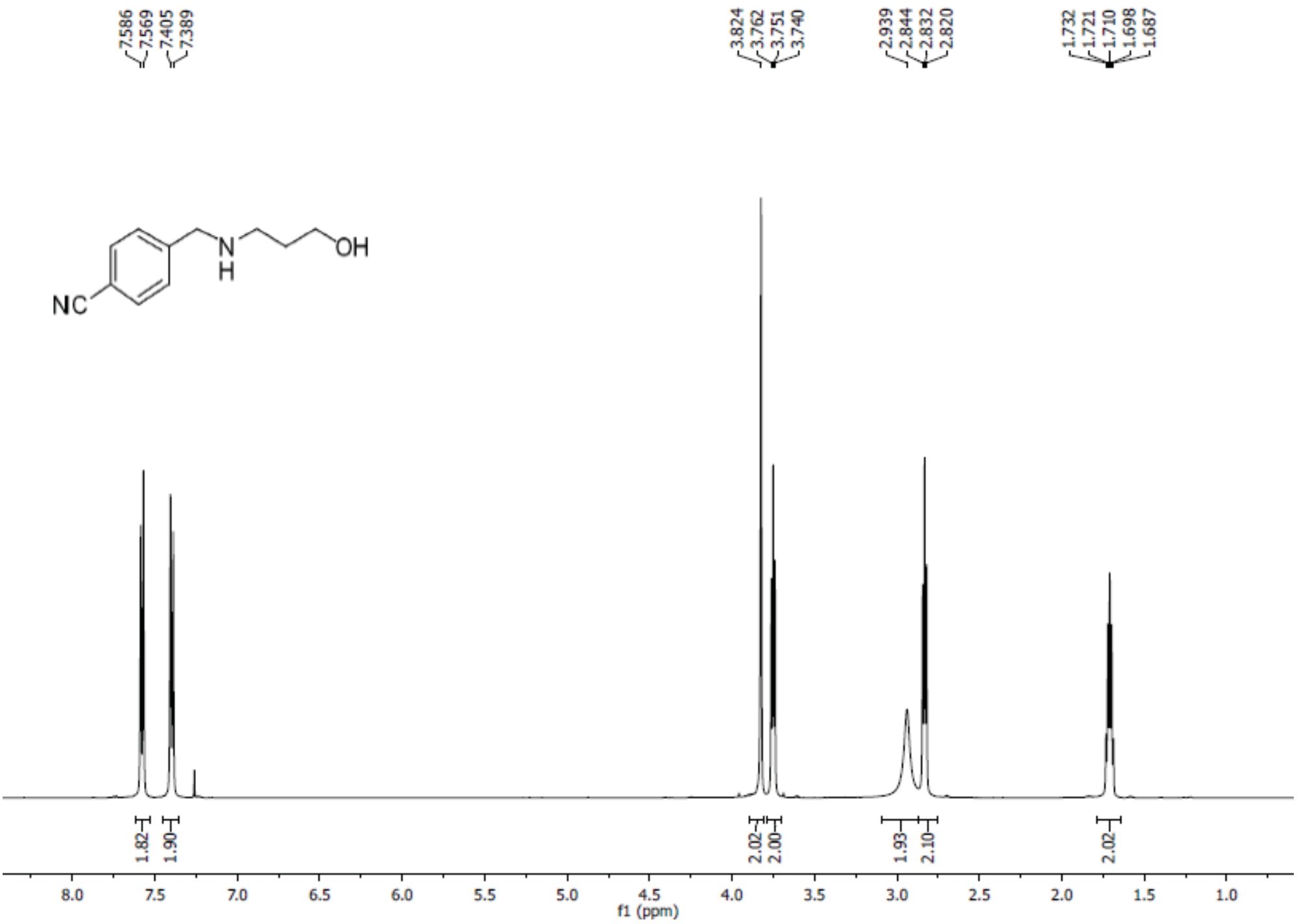
3-((2,4,6-trifluorobenzyl)amino)propan-1-ol s1-g



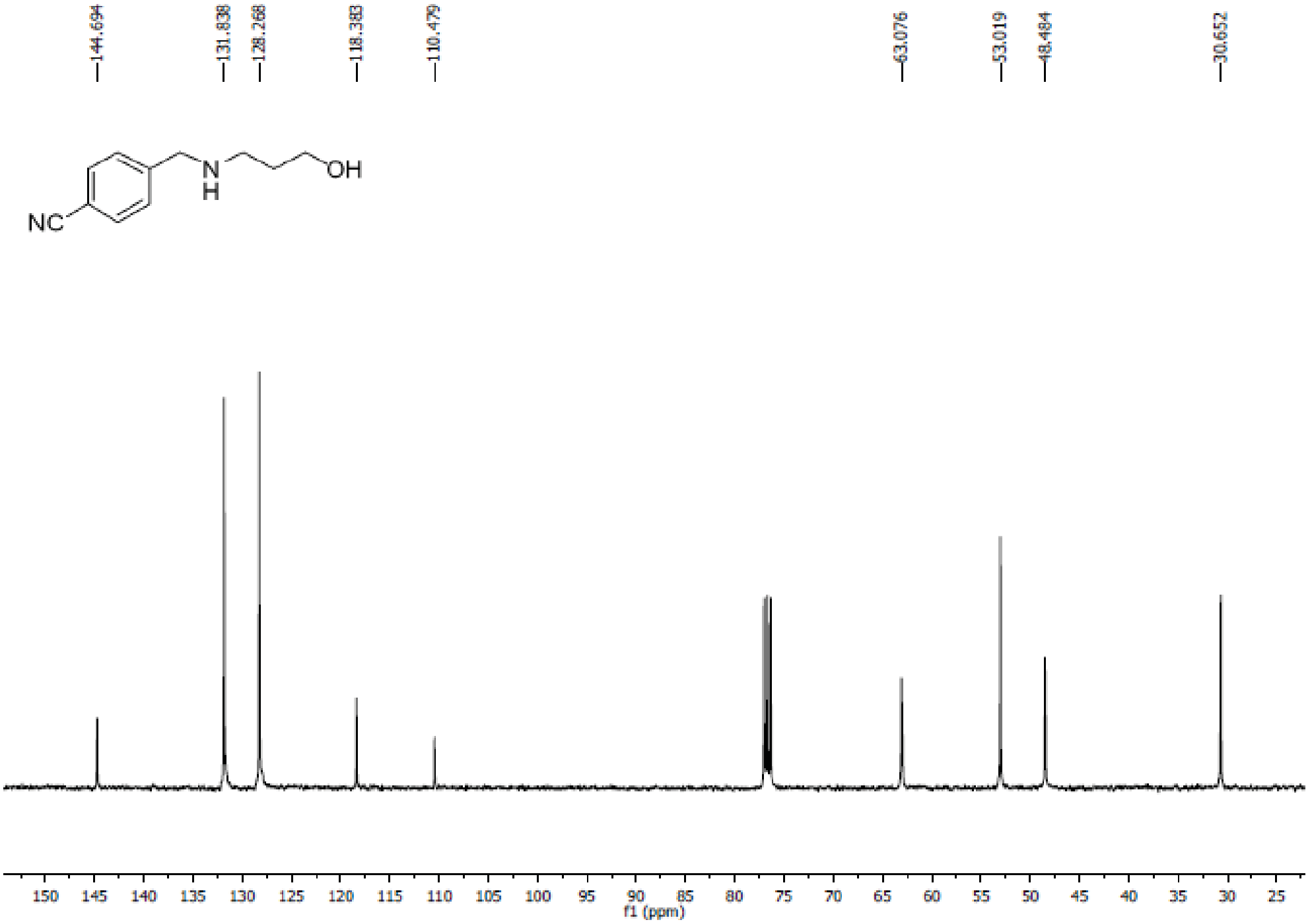
3-((2,4,6-trifluorobenzyl)amino)propan-1-ol s1-g



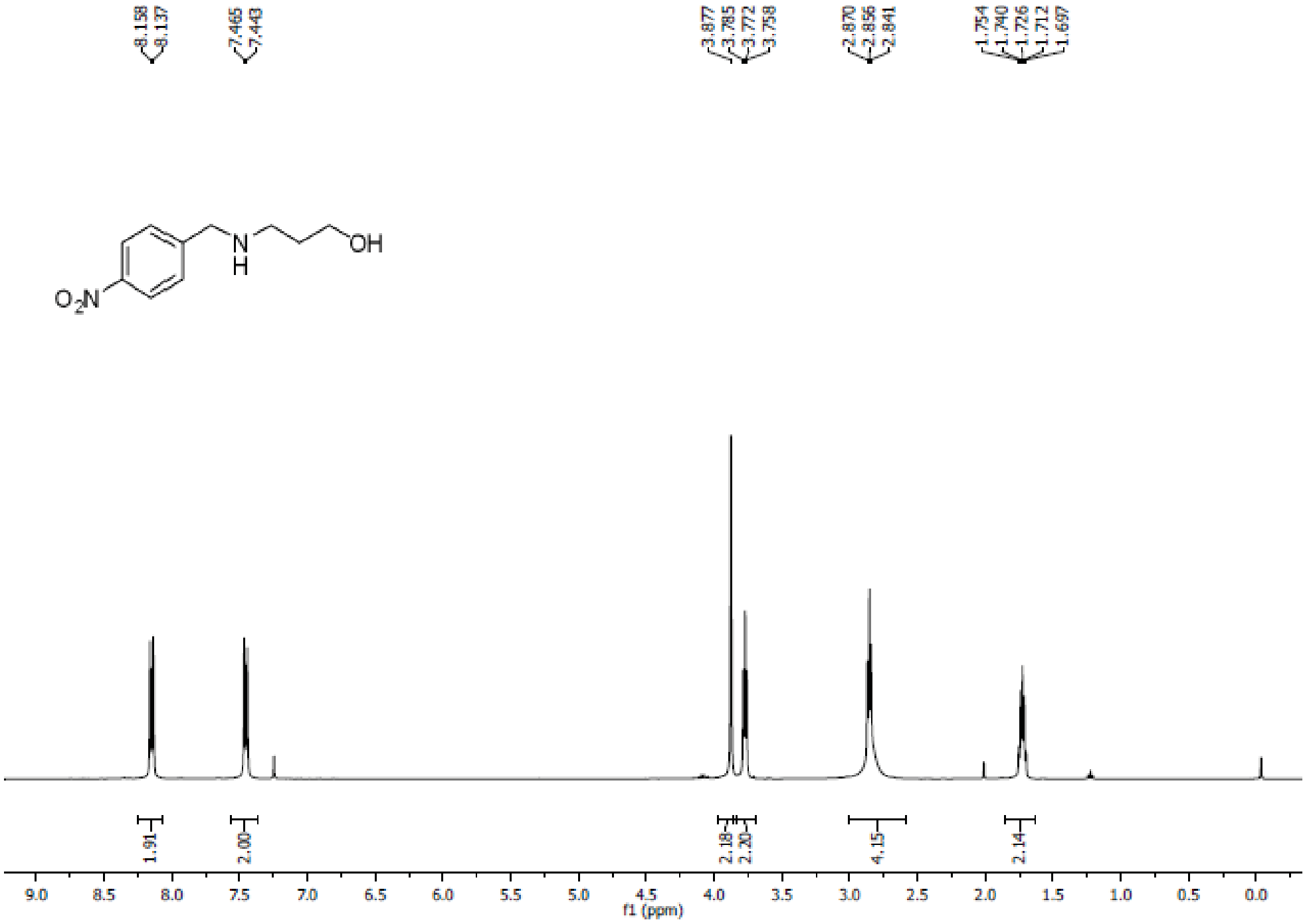
3-((4-nitrilebenzyl)amino)propan-1-ol s1-h



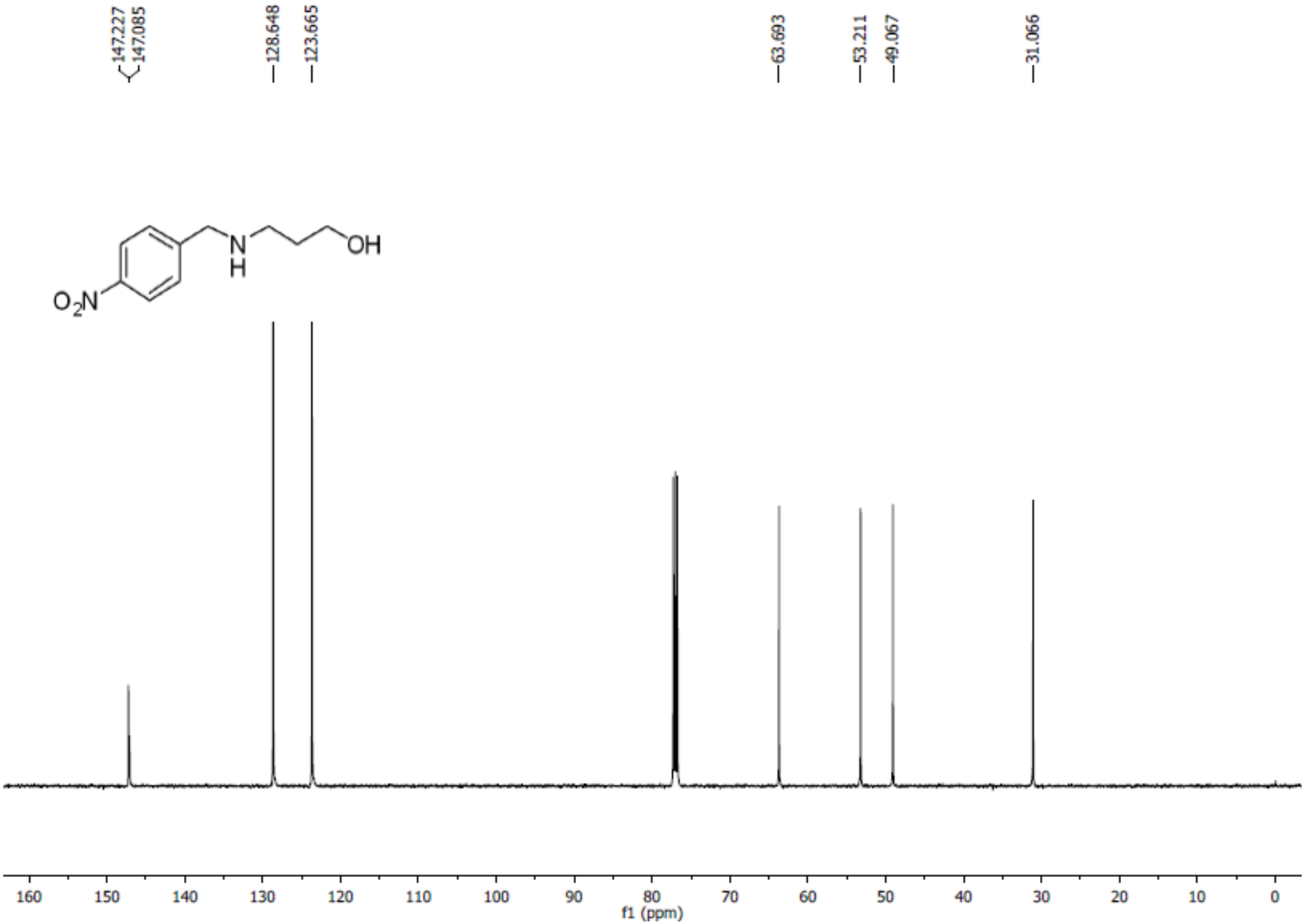
3-((4-nitrilebenzyl)amino)propan-1-ol s1-h



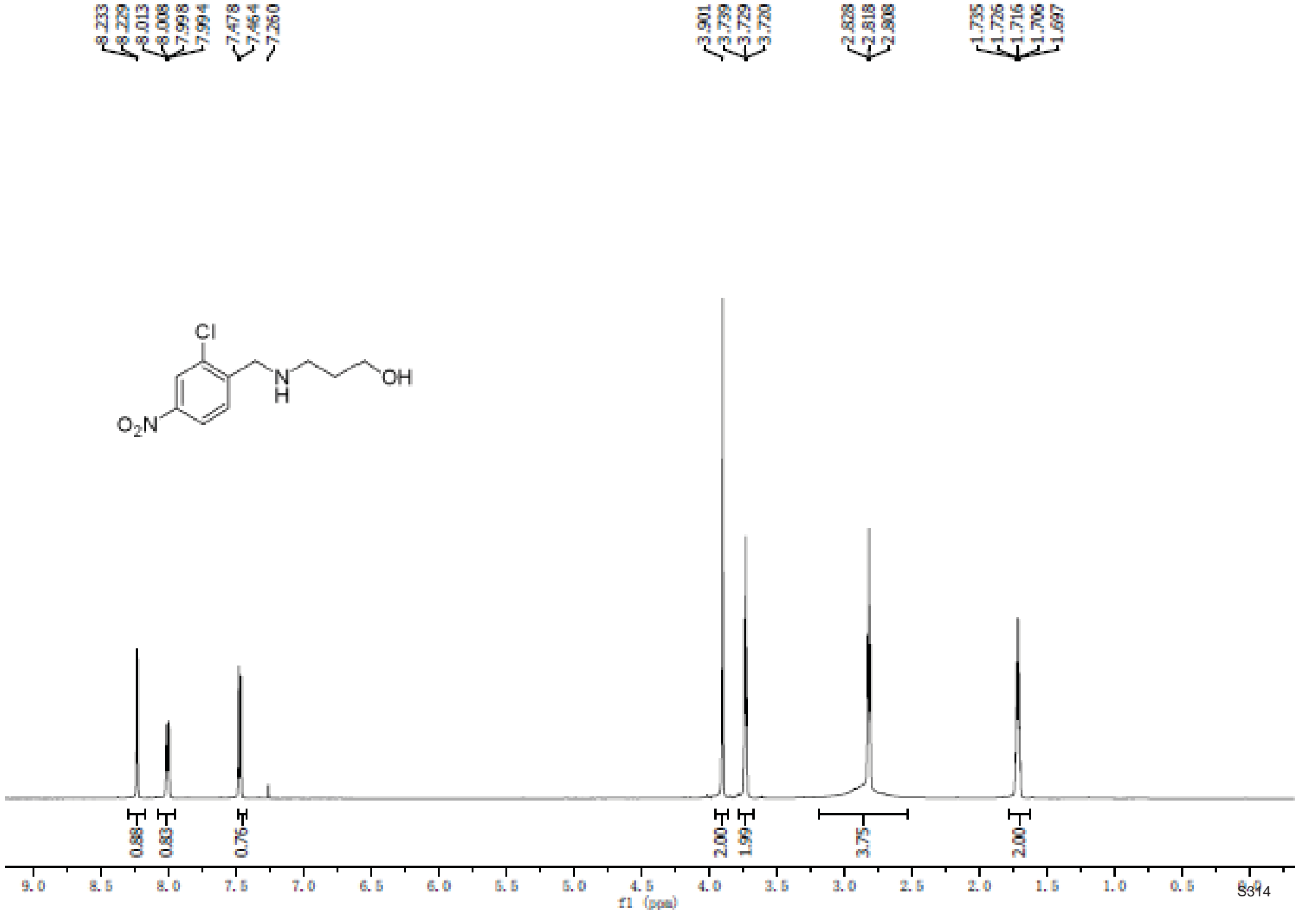
3-((4-nitrobenzyl)amino)propan-1-ol s1-i



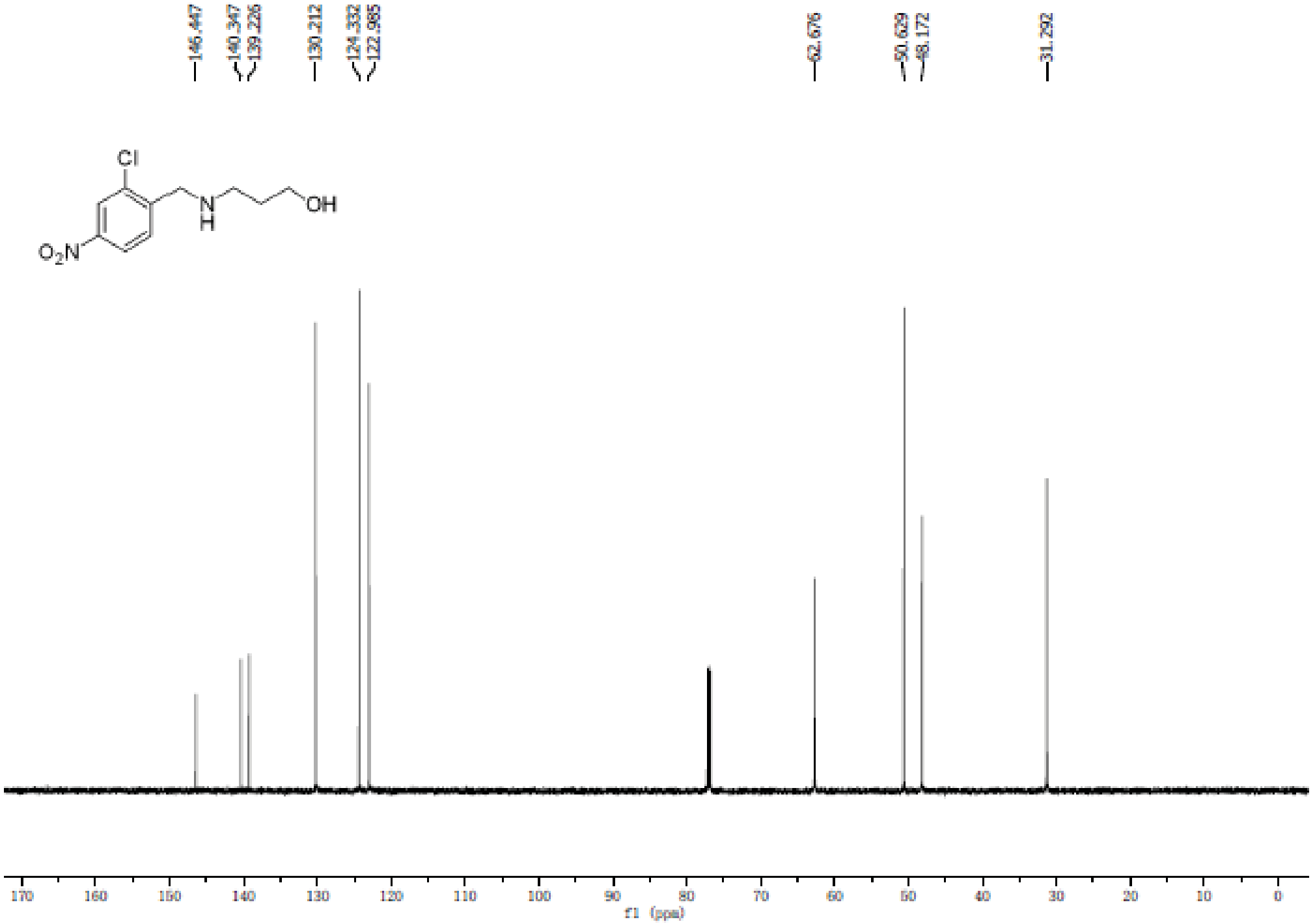
3-((4-nitrobenzyl)amino)propan-1-ol s1-i



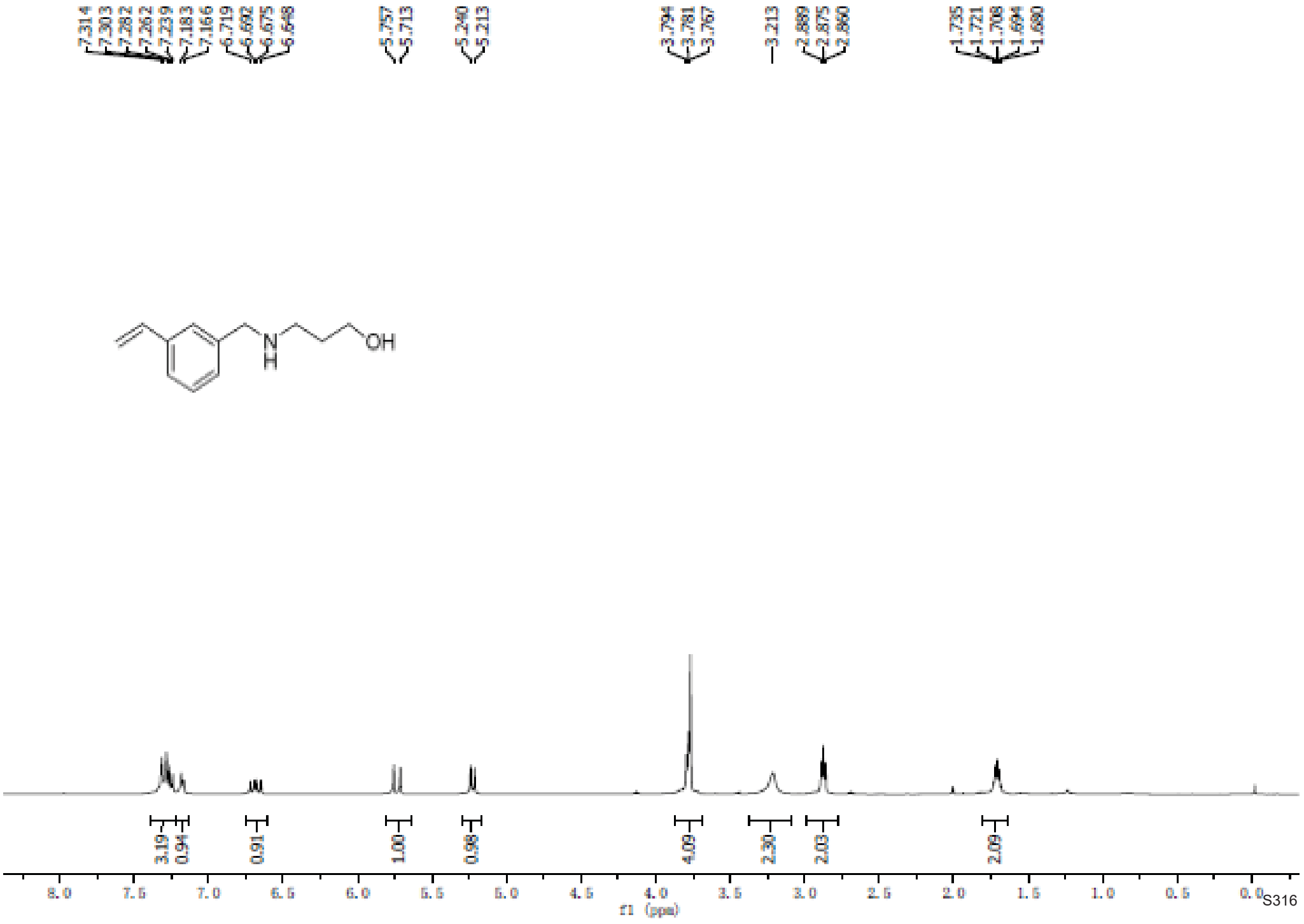
3-((2-chloro-4-nitrobenzyl)amino)propan-1-ol s1-j



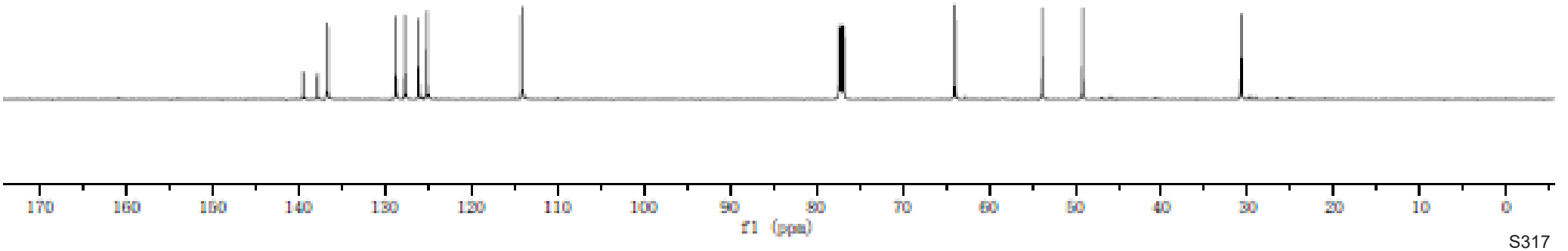
3-((2-chloro-4-nitrobenzyl)amino)propan-1-ol s1-j



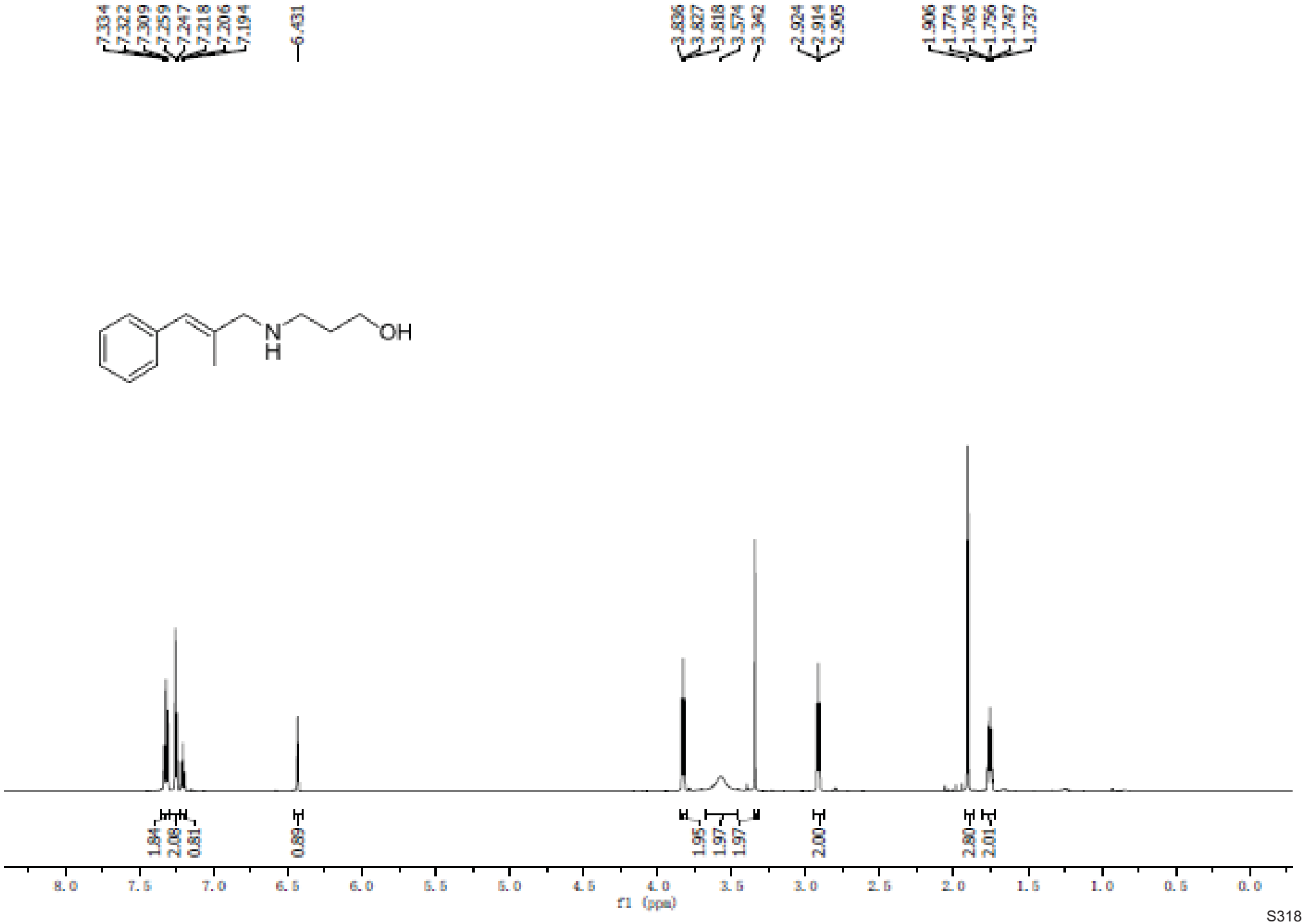
3-((3-vinylbenzyl)amino)propan-1-ol s1-k



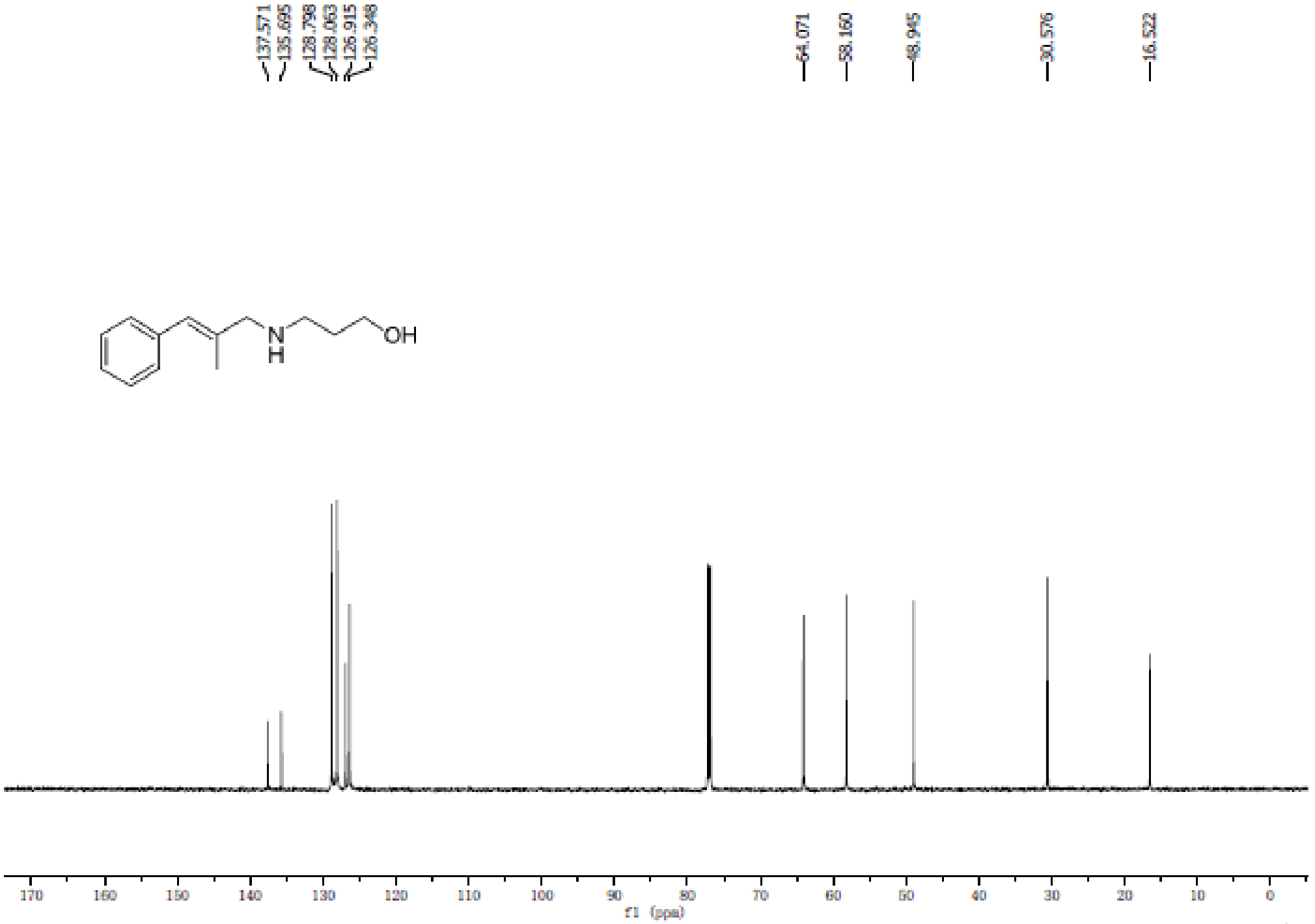
3-((3-vinylbenzyl)amino)propan-1-ol s1-k



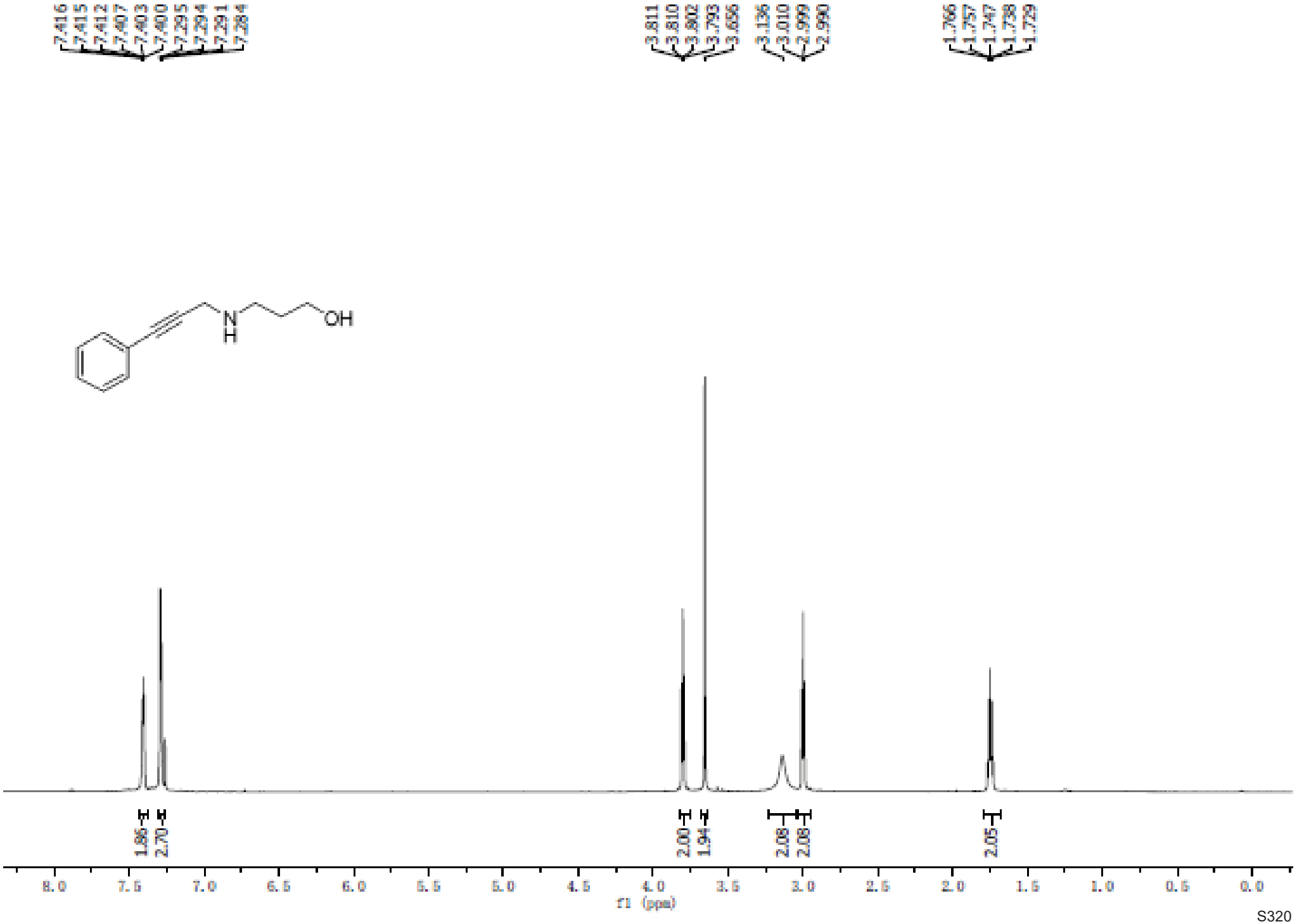
(*E*)-3-((2-methyl-3-phenylallyl)amino)propan-1-ol s1-l



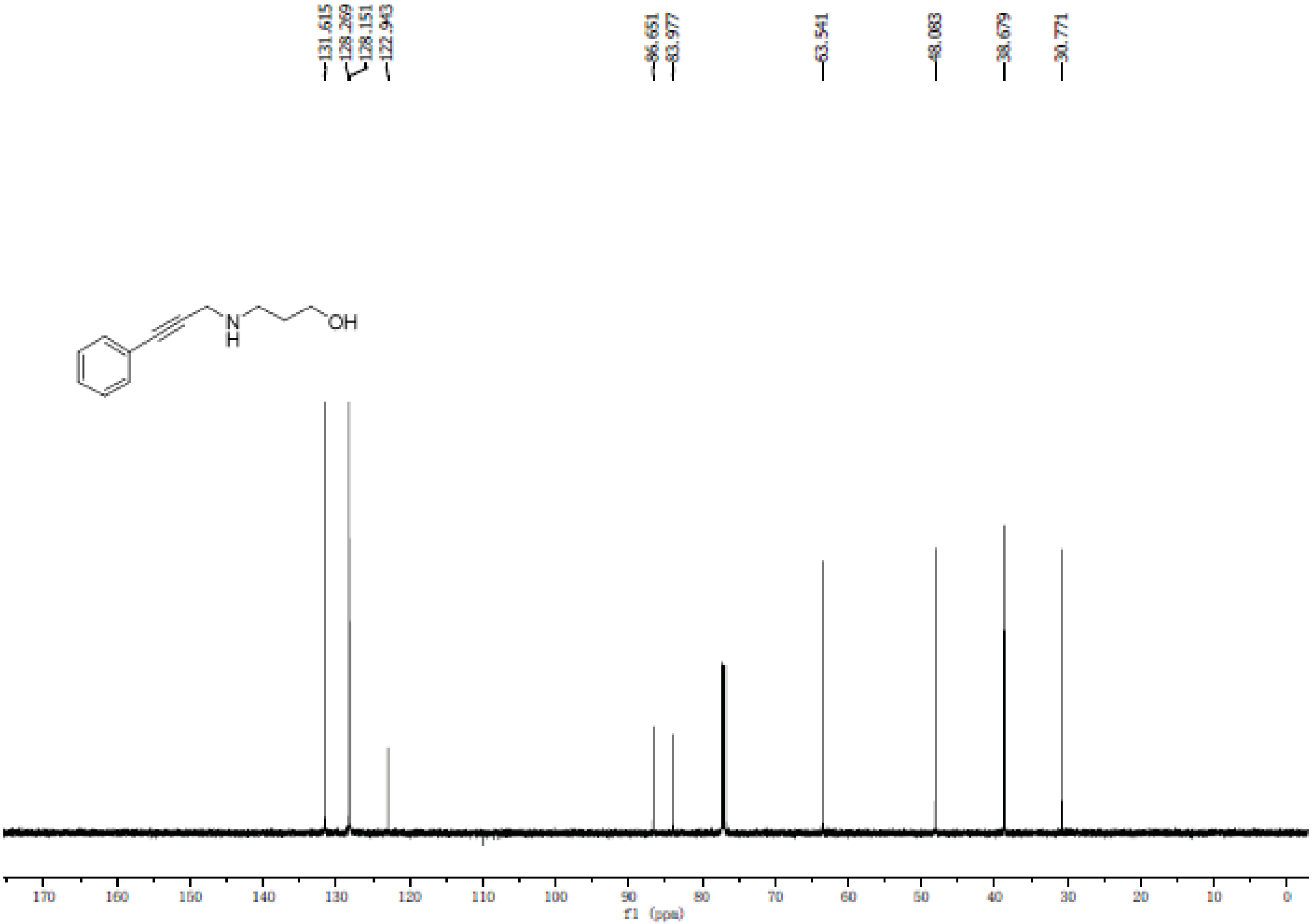
(*E*)-3-((2-methyl-3-phenylallyl)amino)propan-1-ol s1-l



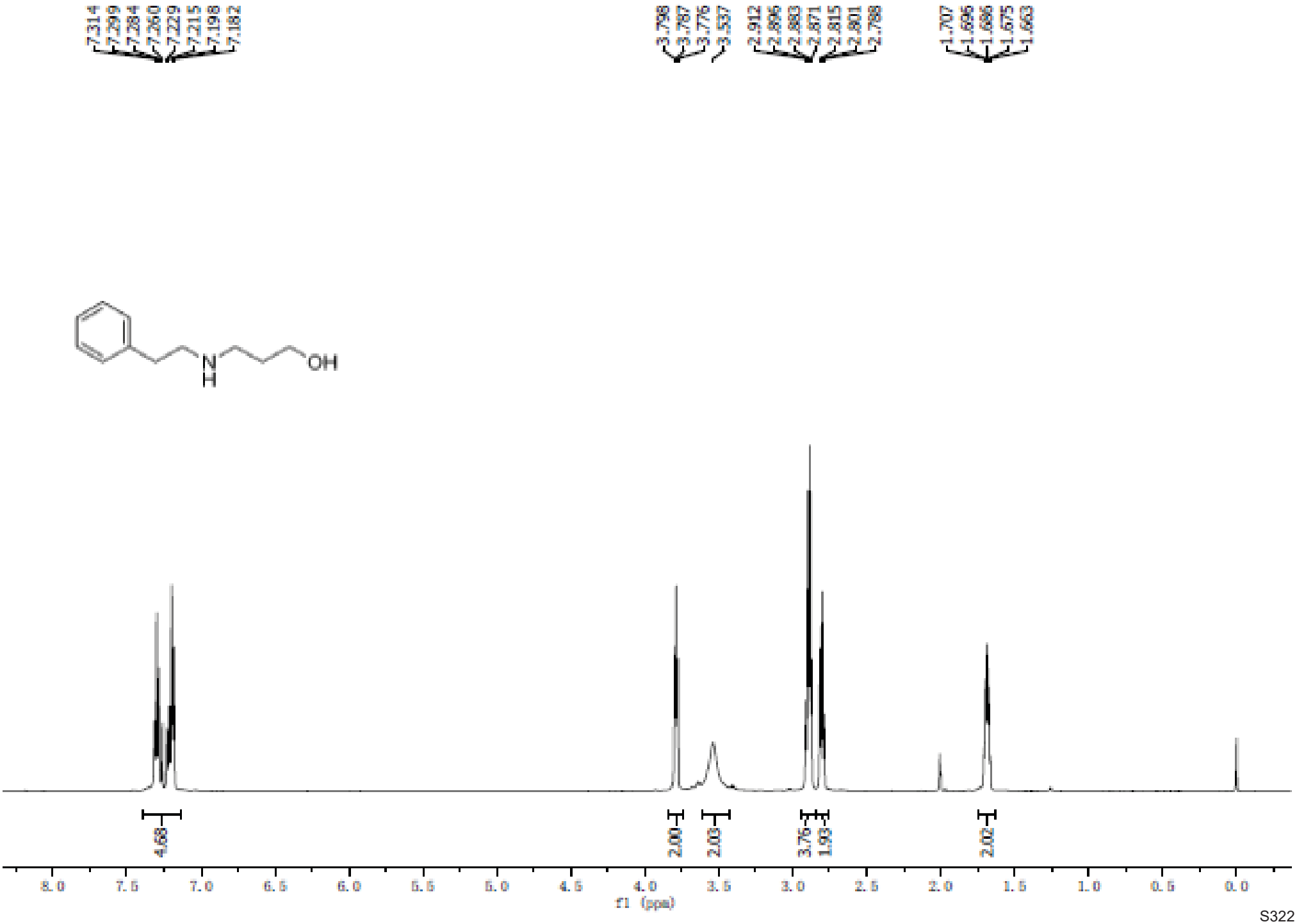
3-((3-phenylprop-2-yn-1-yl)amino)propan-1-ol s1-m



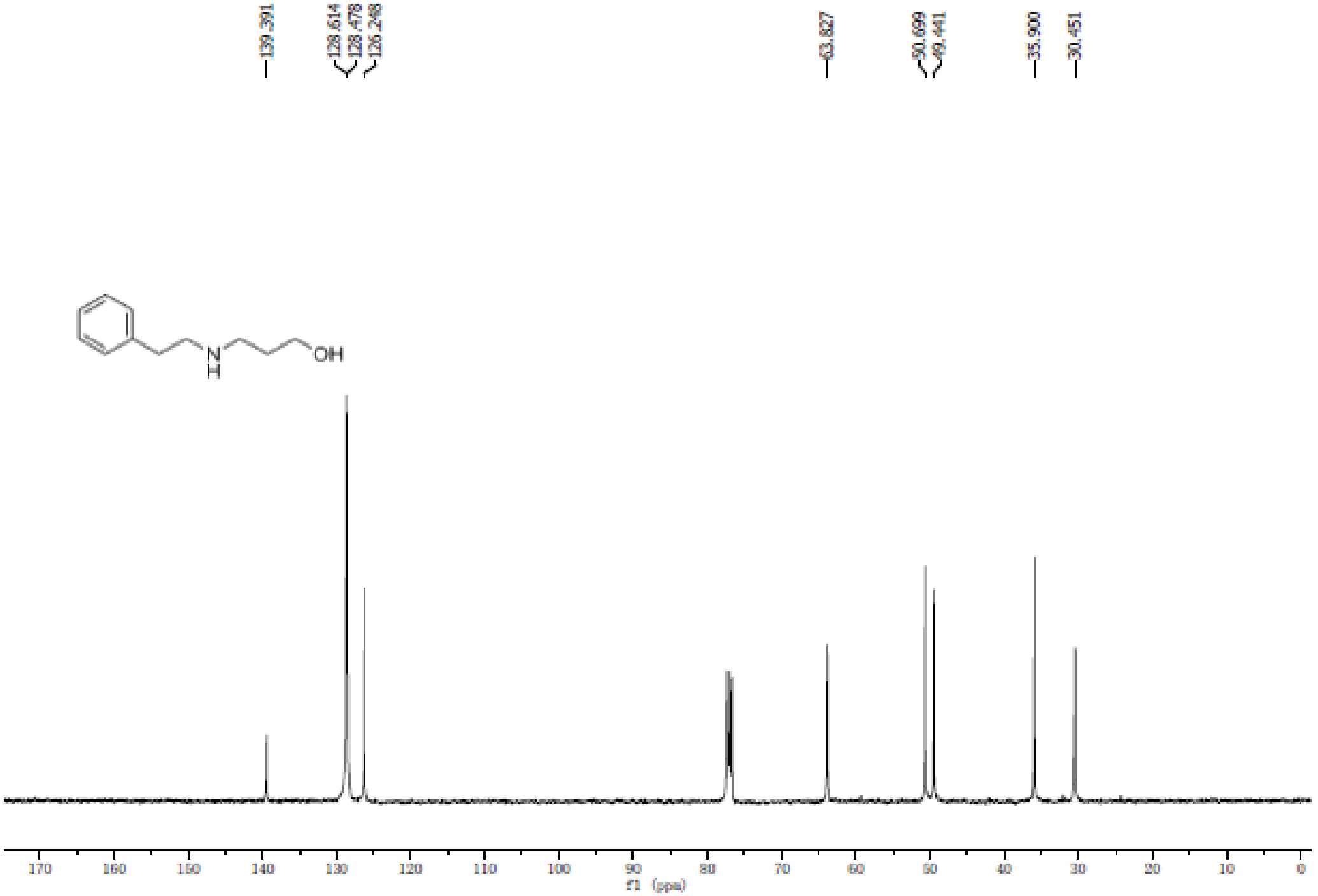
3-((3-phenylprop-2-yn-1-yl)amino)propan-1-ol s1-m



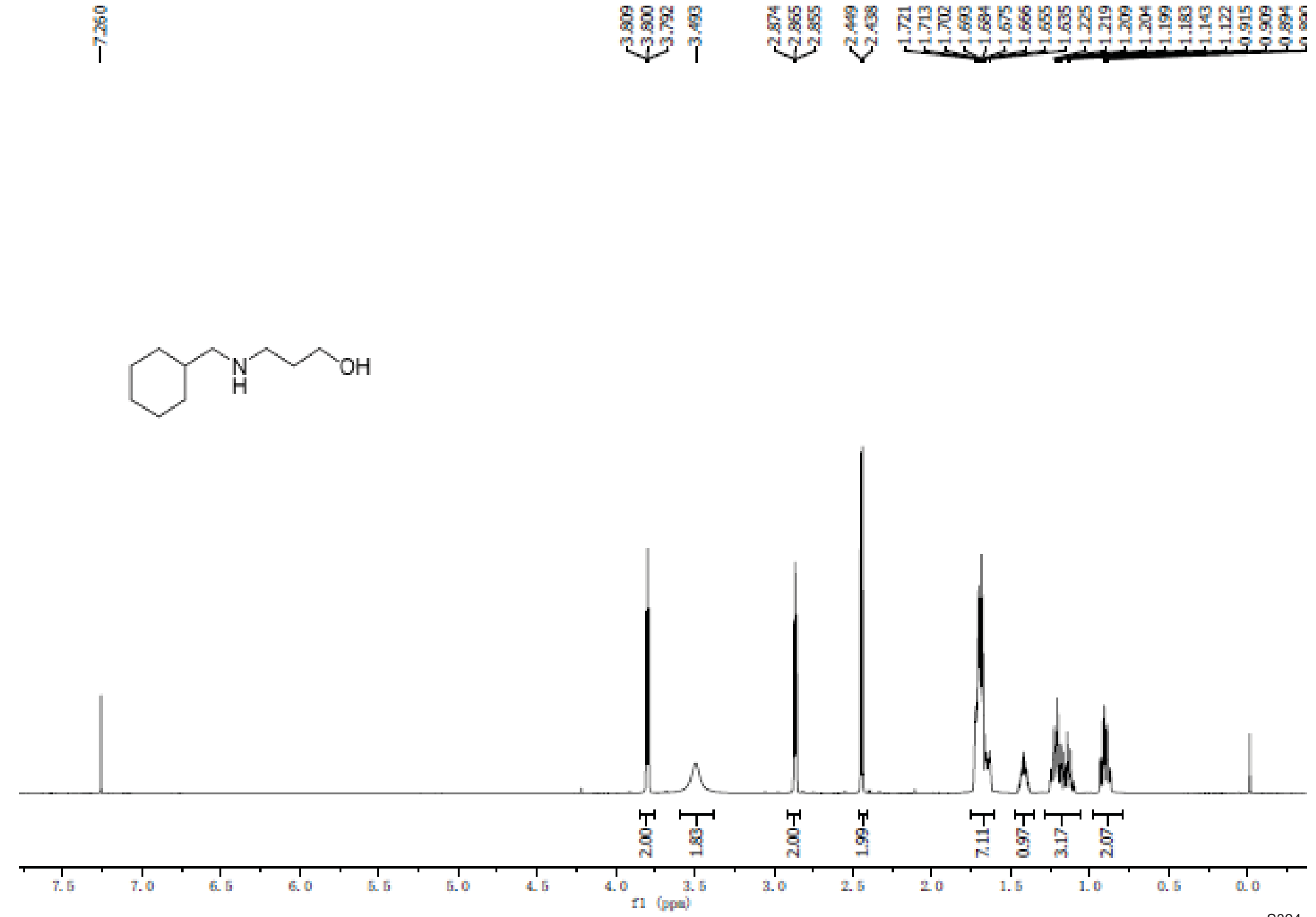
3-(phenethylamino)propan-1-ol s1-n



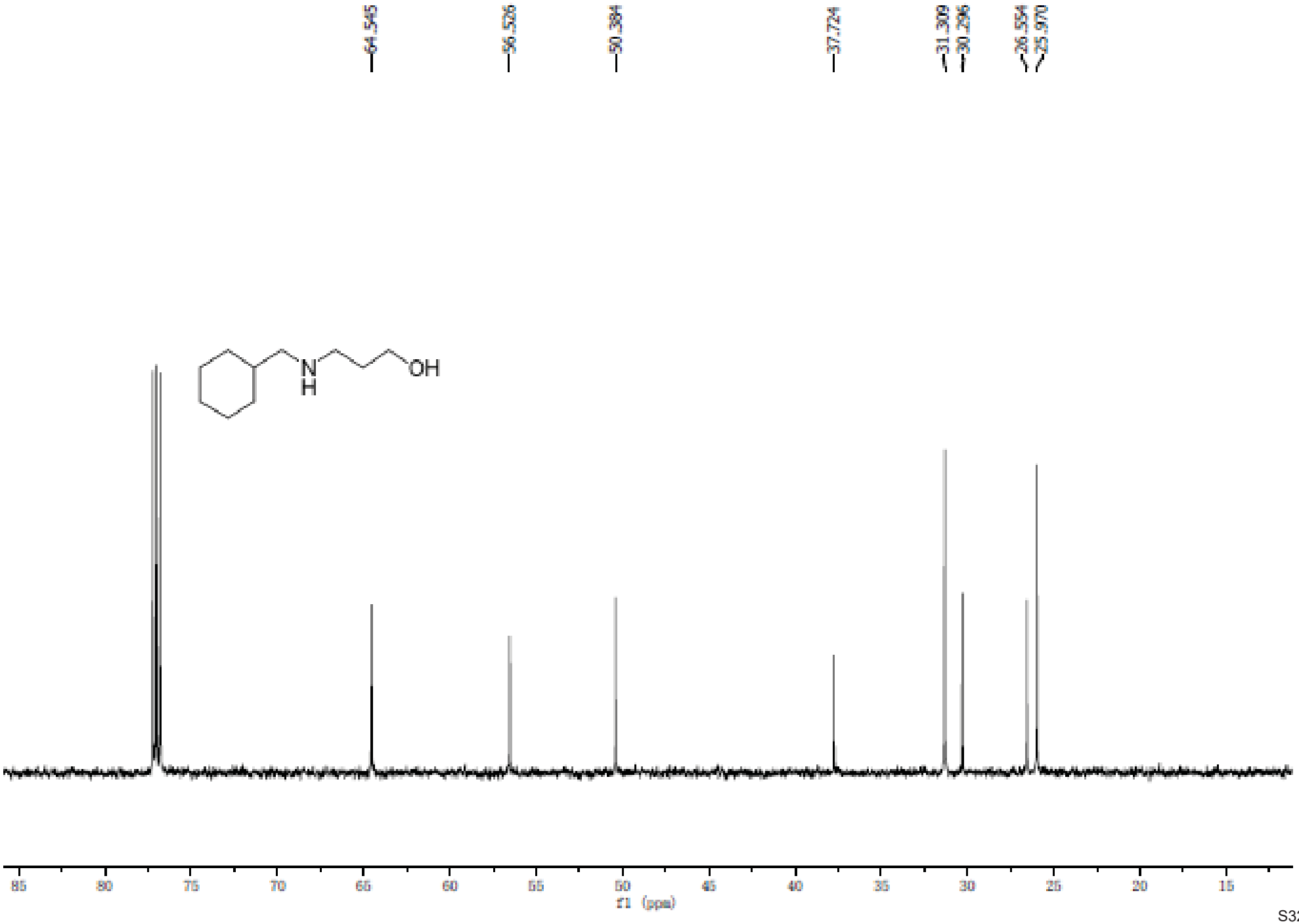
3-(phenethylamino)propan-1-ol s1-n



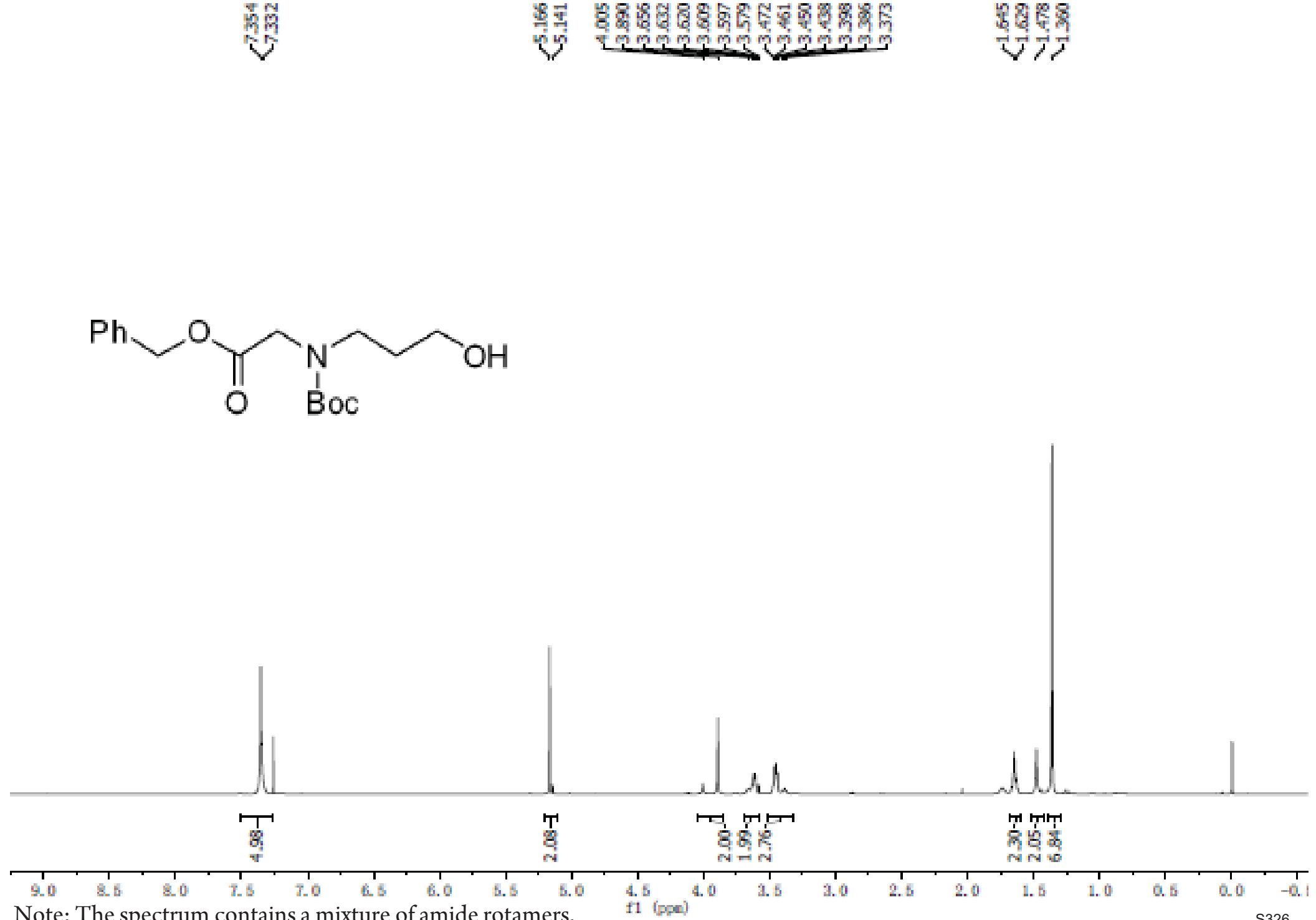
3-((cyclohexylmethyl)amino)propan-1-ol s1-o



3-((cyclohexylmethyl)amino)propan-1-ol s1-o

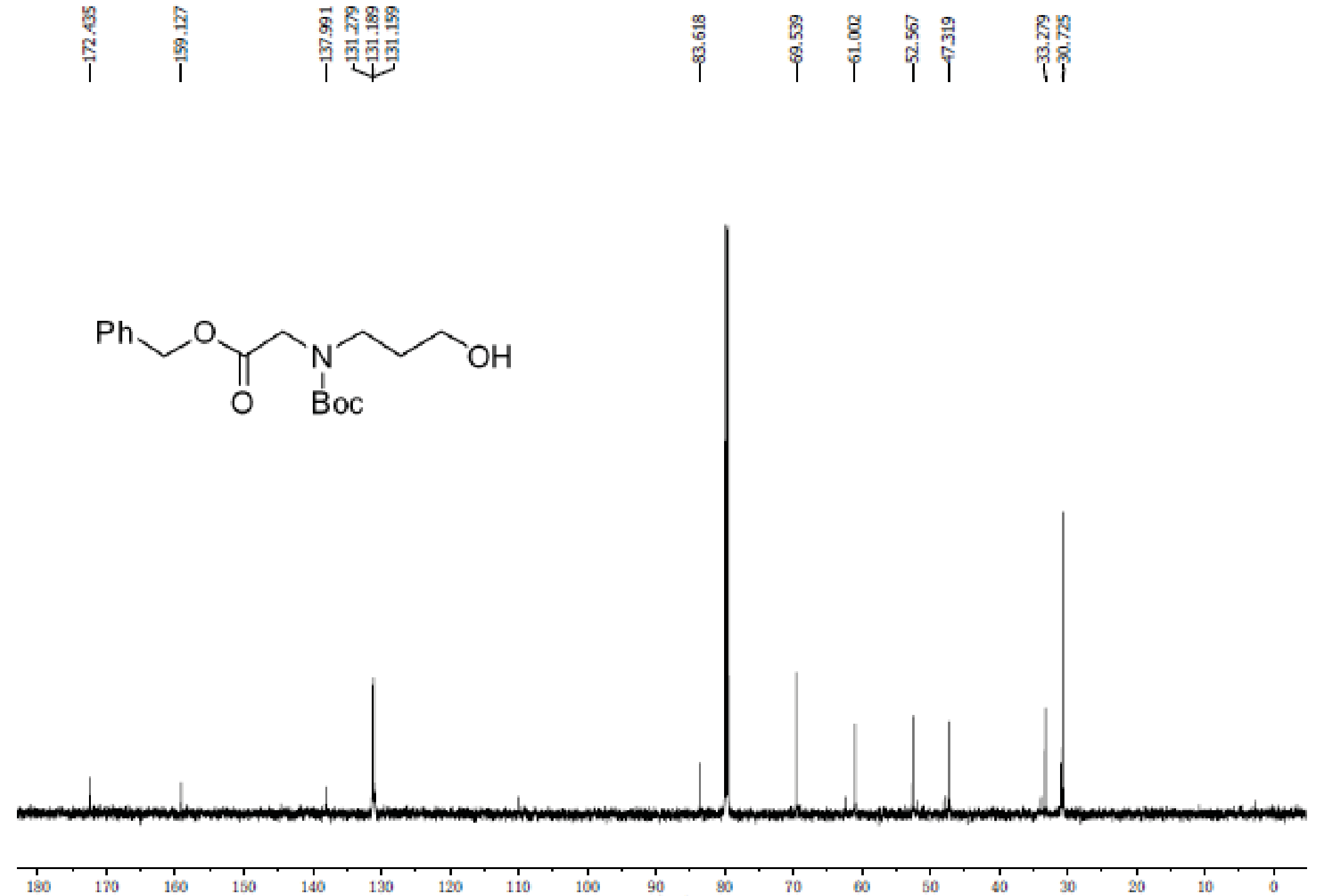


benzyl *N*-(*tert*-butoxycarbonyl)-*N*-(3-hydroxypropyl)glycinate s1-p



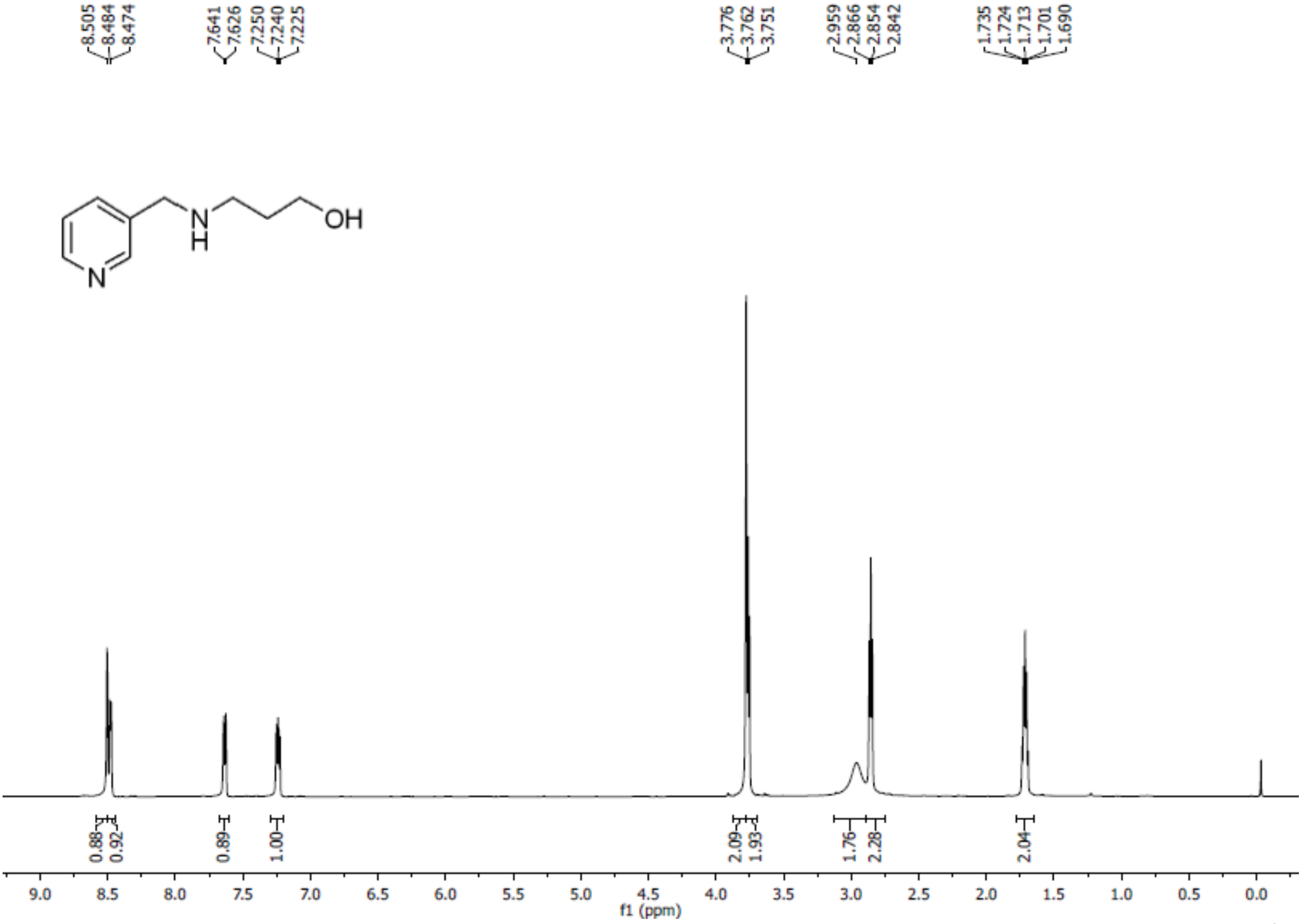
Note: The spectrum contains a mixture of amide rotamers.

benzyl *N*-(*tert*-butoxycarbonyl)-*N*-(3-hydroxypropyl)glycinate s1-p

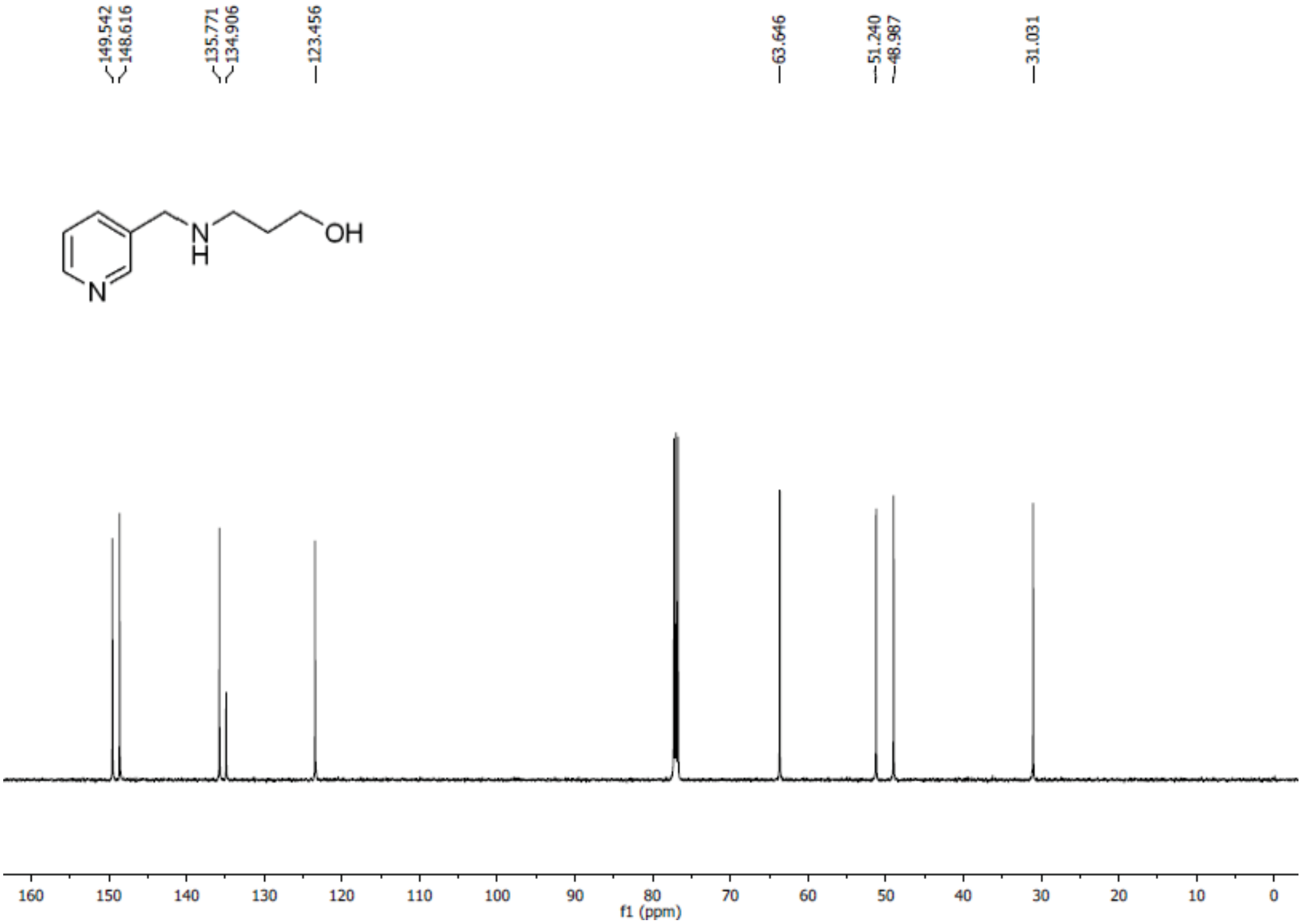


Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

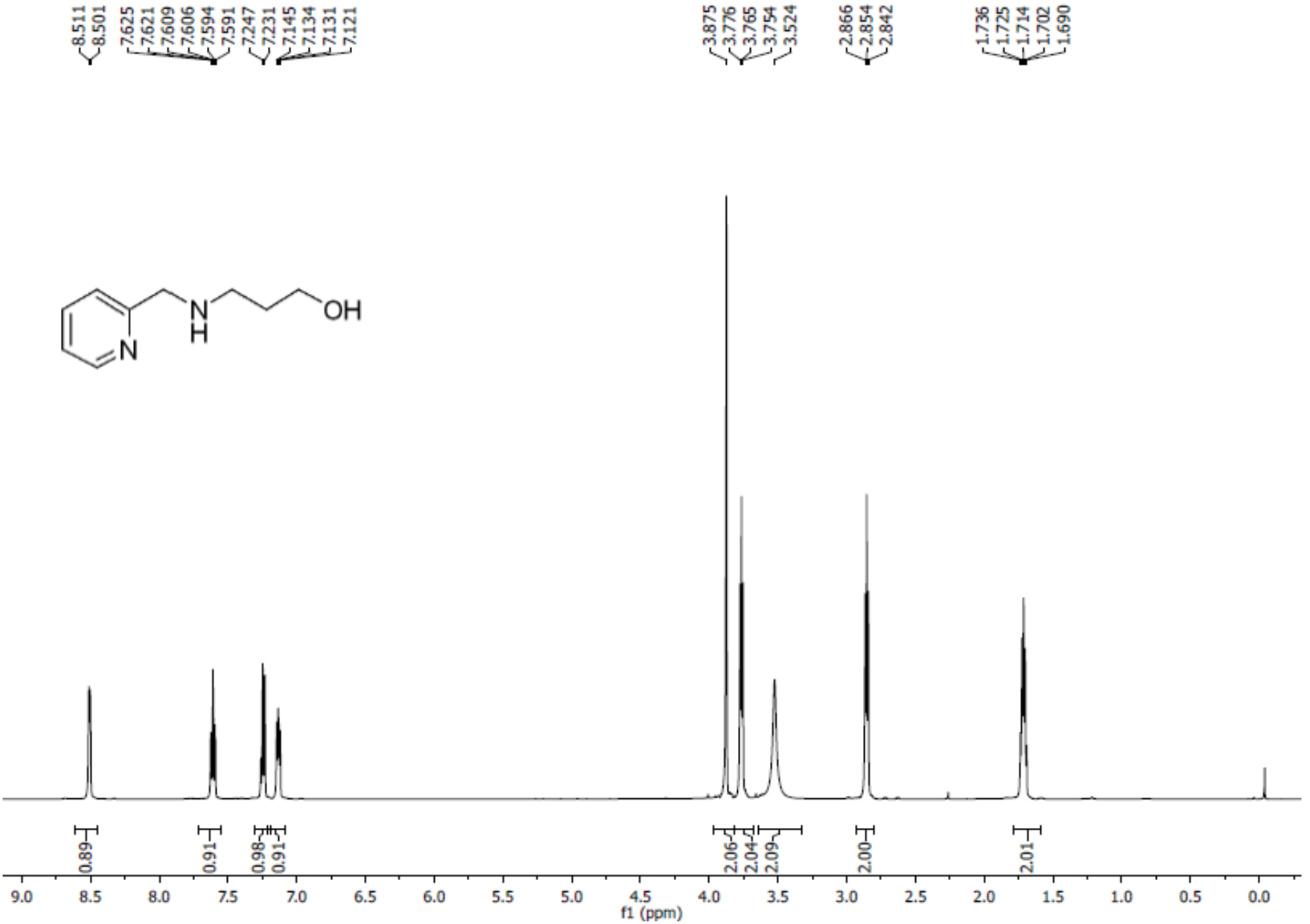
3-((pyridin-3-ylmethyl)amino)propan-1-ol s1-q



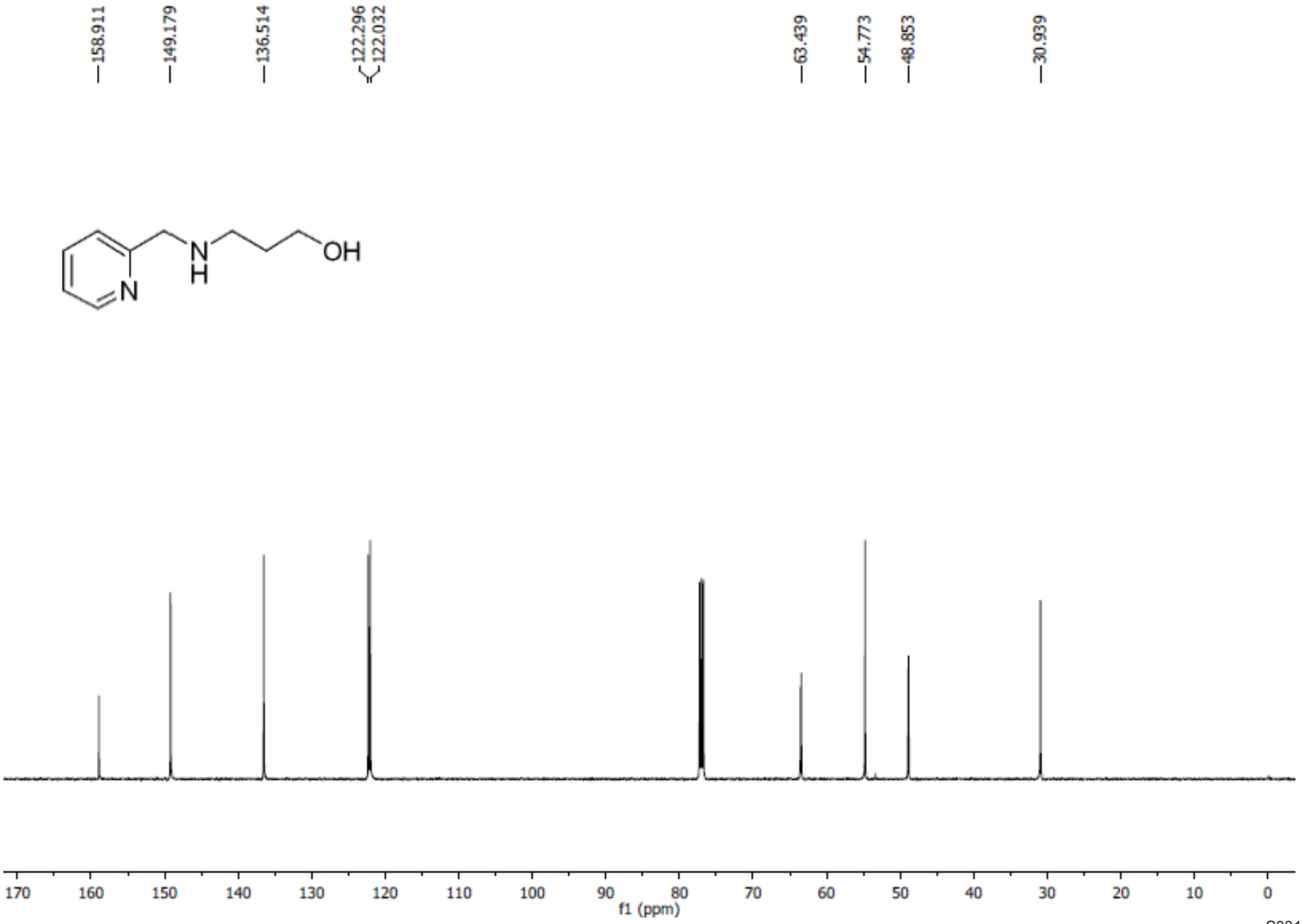
3-((pyridin-3-ylmethyl)amino)propan-1-ol s1-q



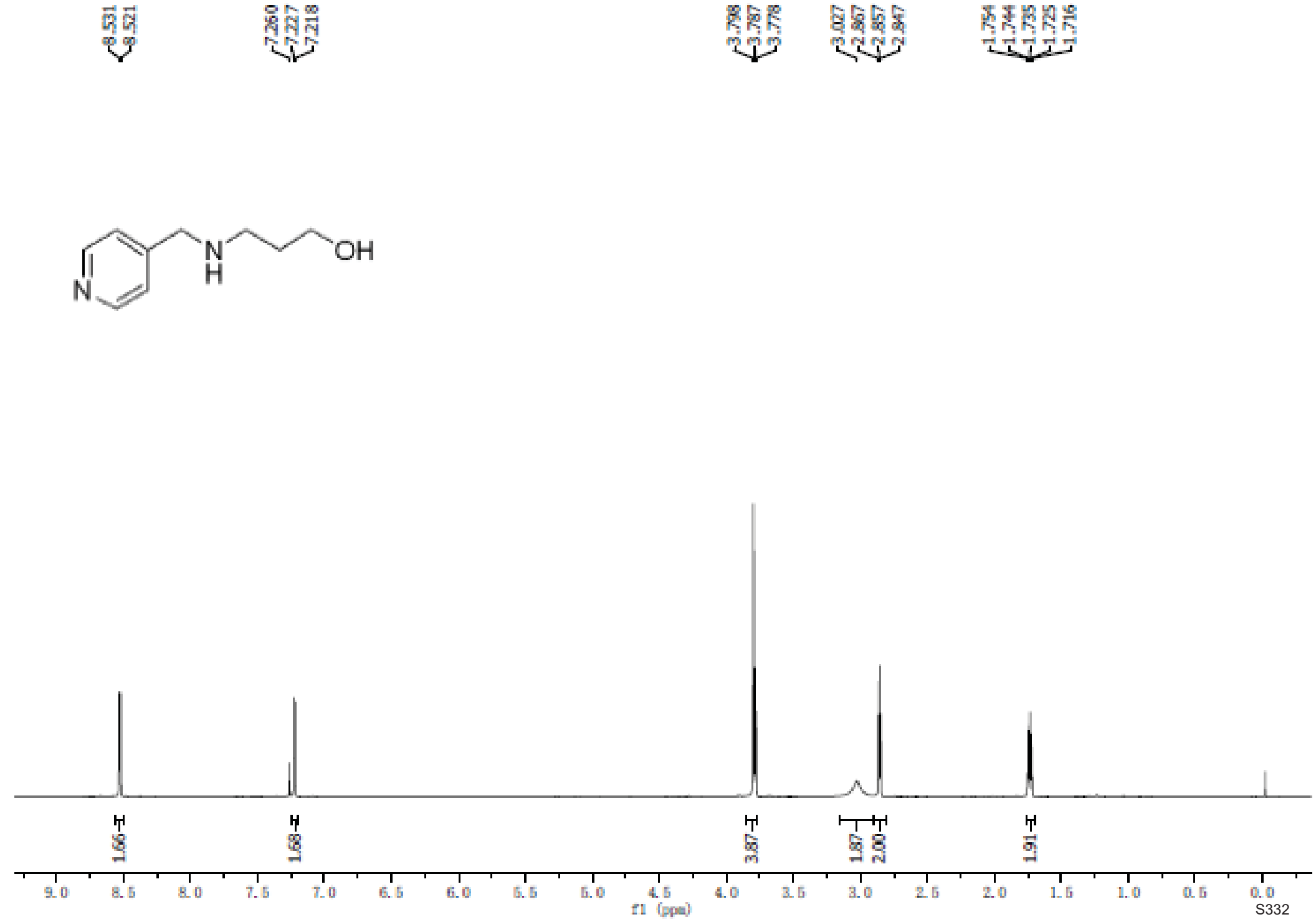
3-((pyridin-2-ylmethyl)amino)propan-1-ol s1-r



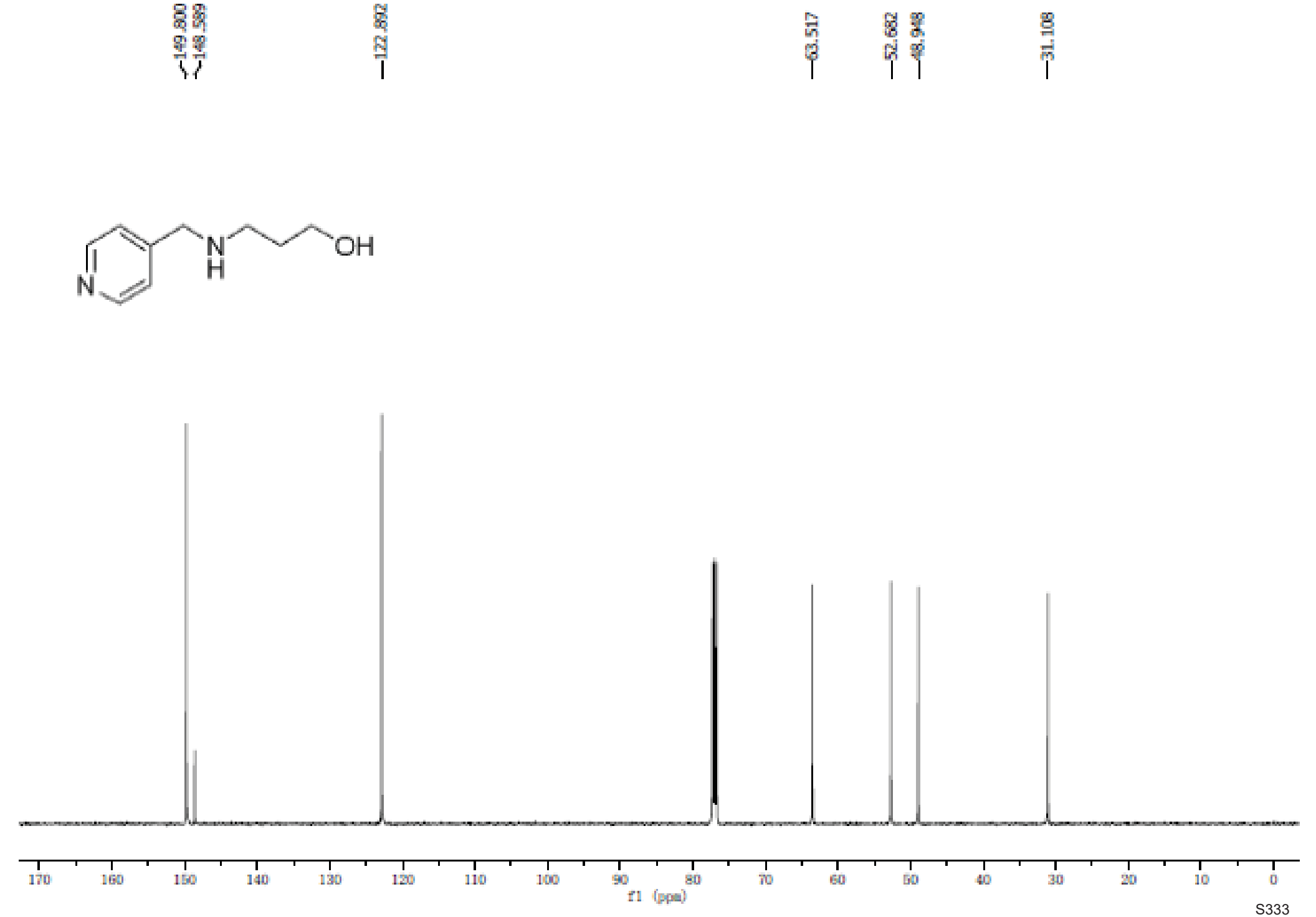
3-((pyridin-2-ylmethyl)amino)propan-1-ol s1-r



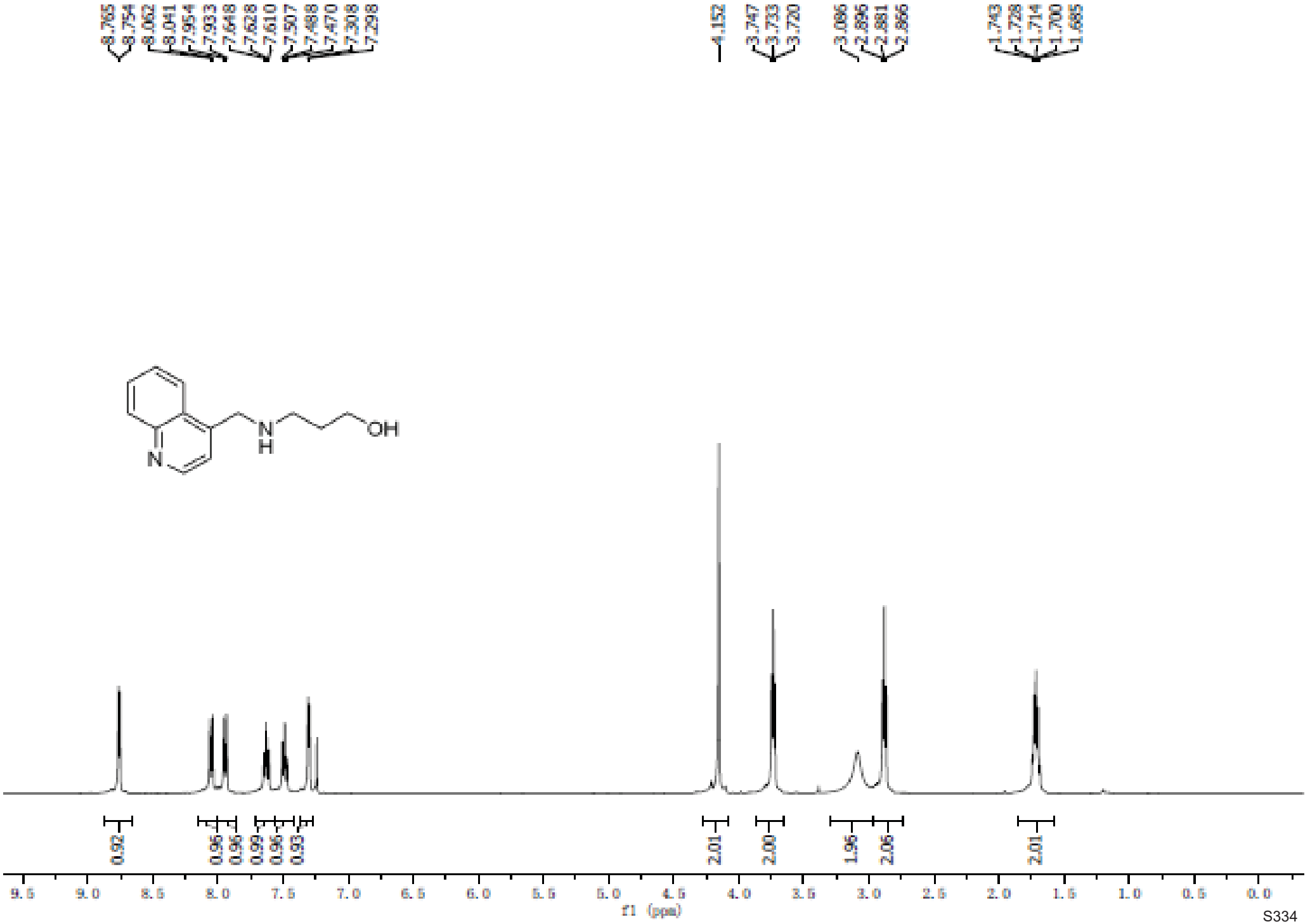
3-((pyridin-4-ylmethyl)amino)propan-1-ol s1-s



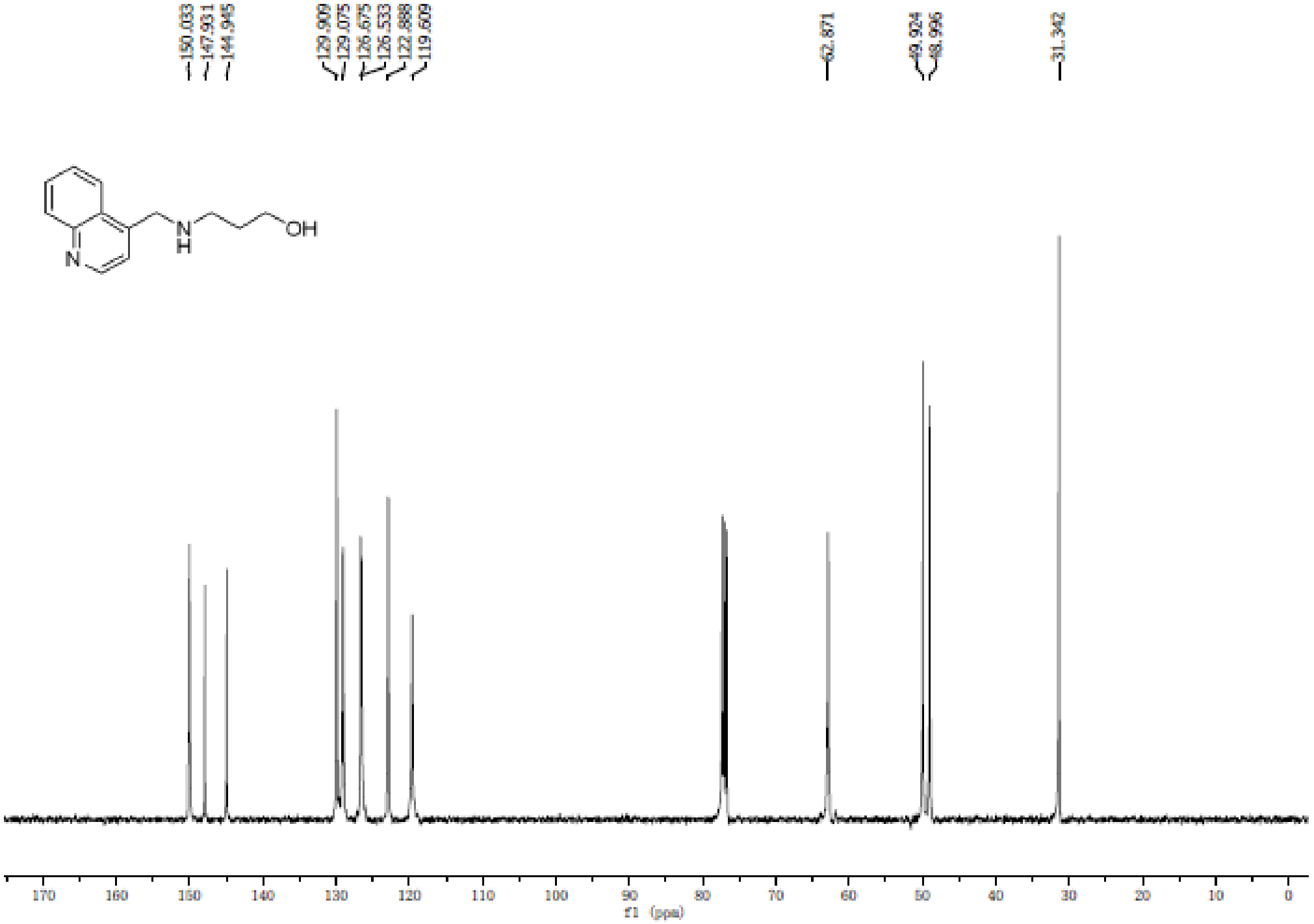
3-((pyridin-4-ylmethyl)amino)propan-1-ol s1-s



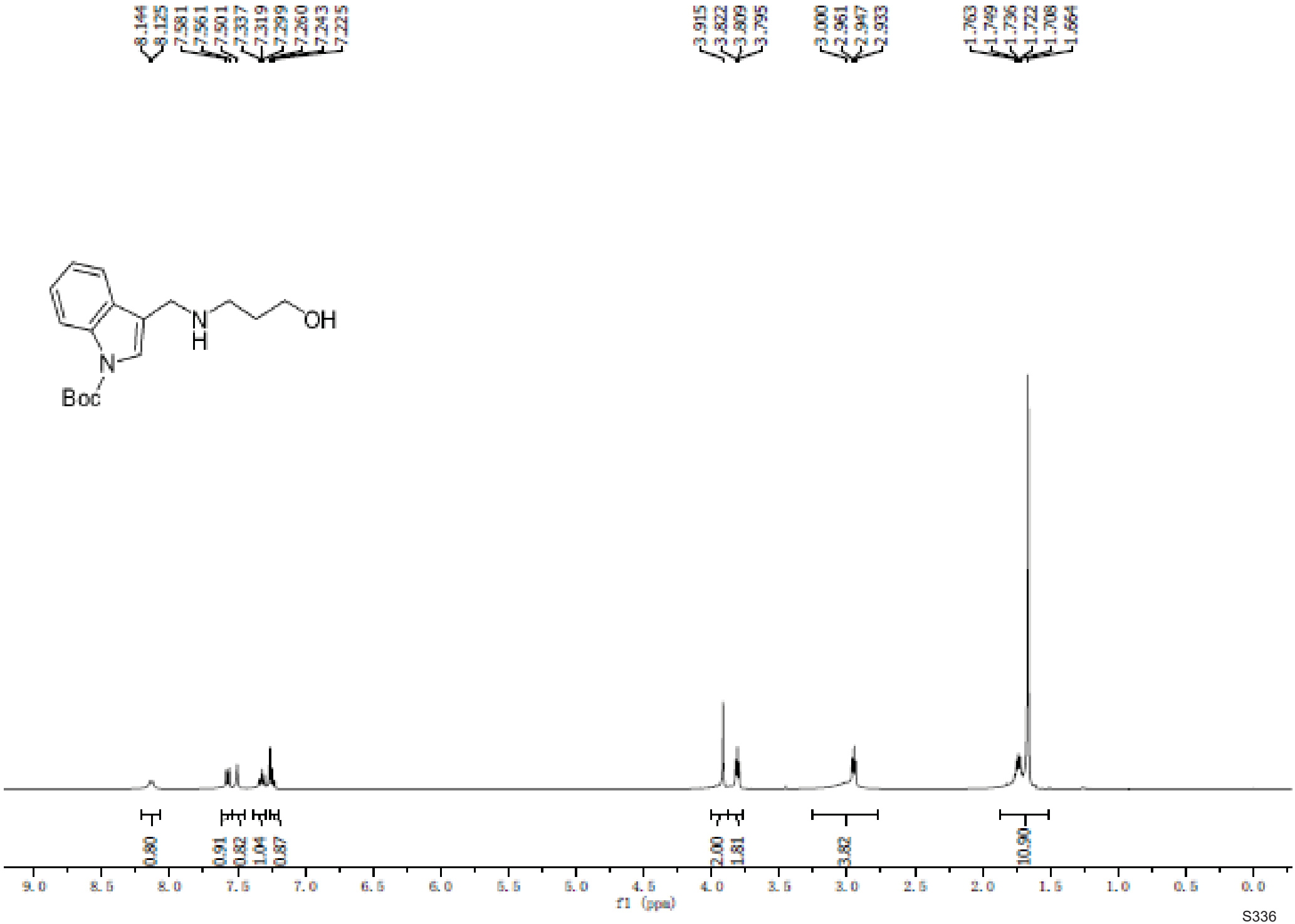
3-((quinolin-4-ylmethyl)amino)propan-1-ol s1-t



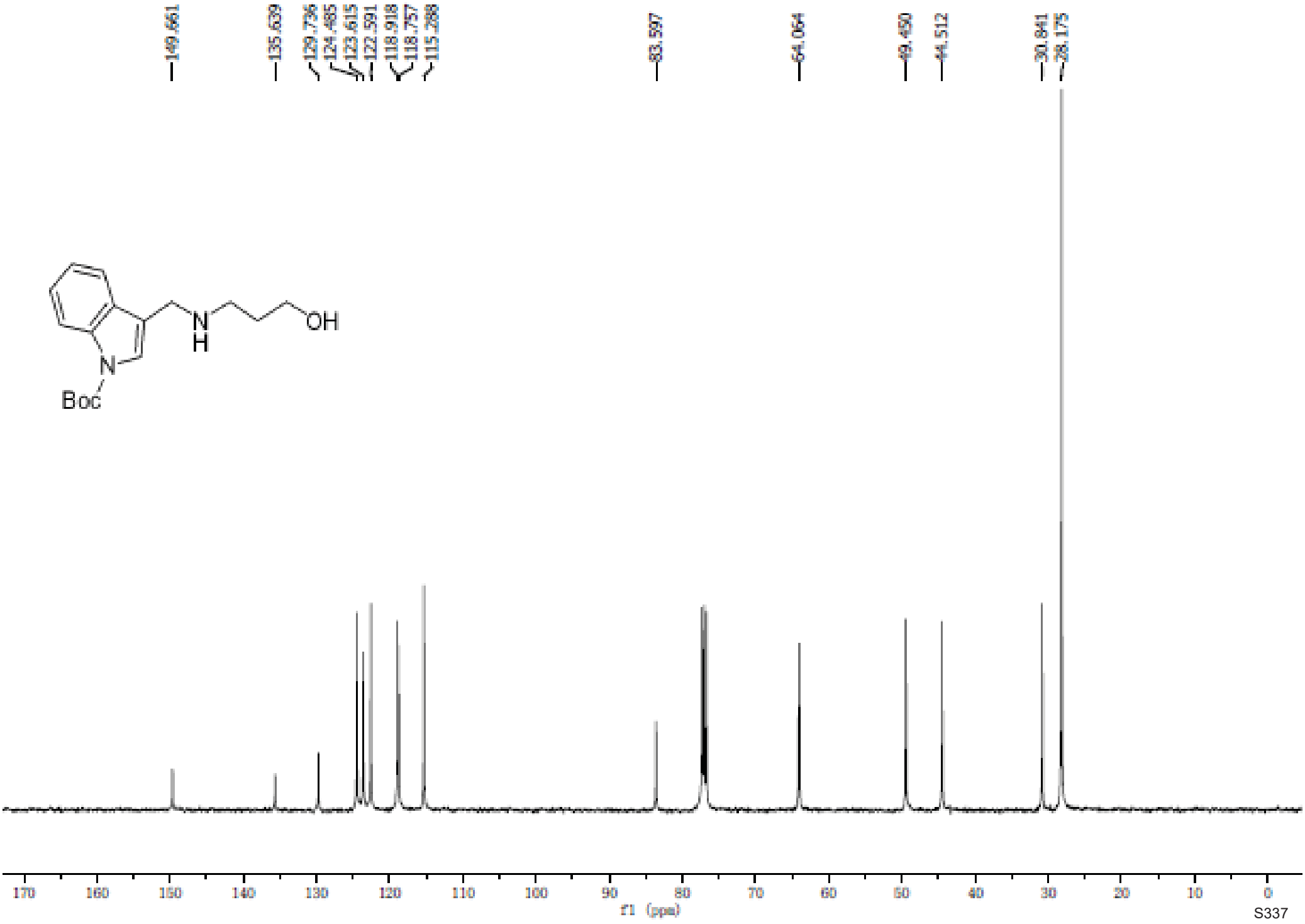
3-((quinolin-4-ylmethyl)amino)propan-1-ol s1-t



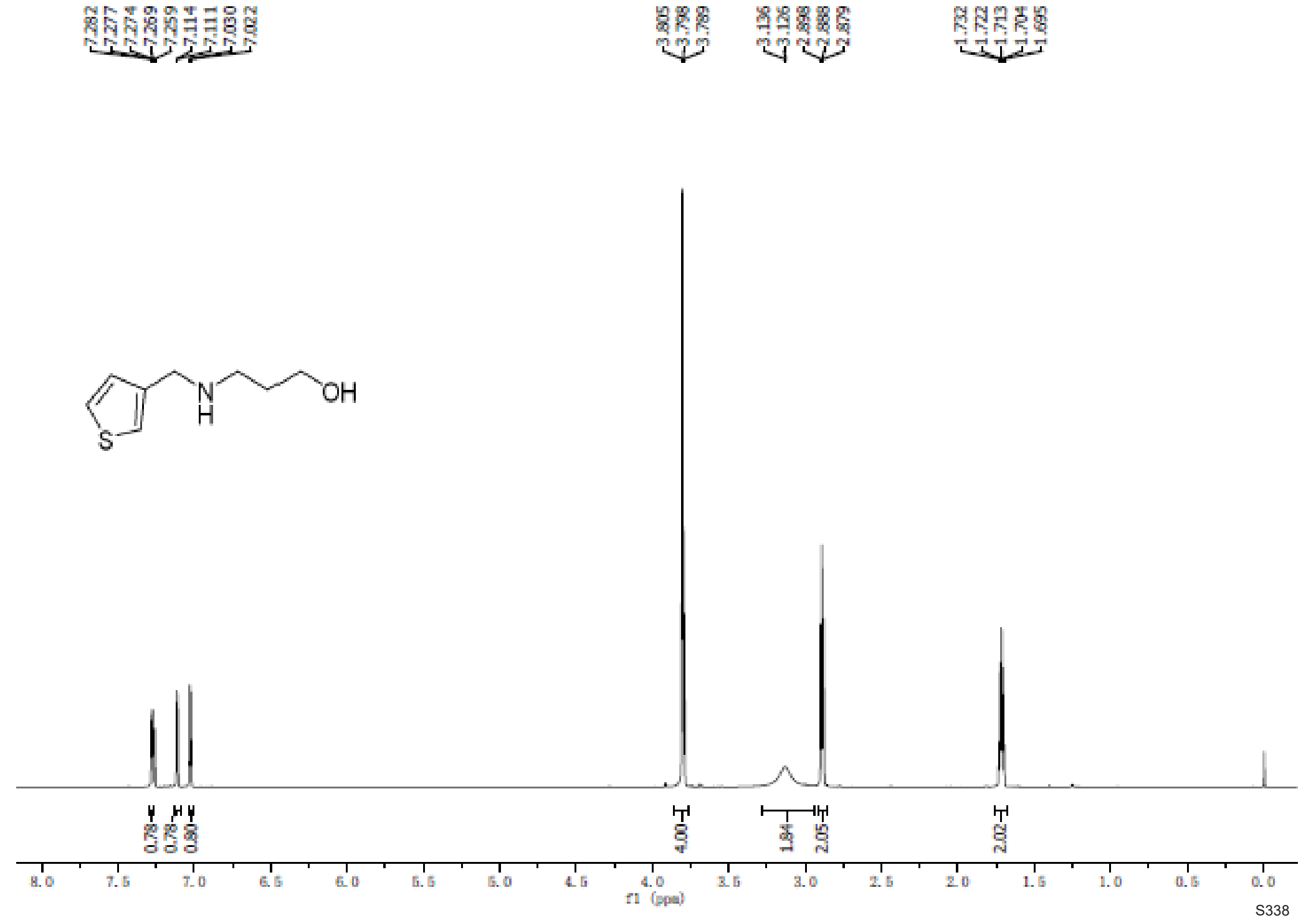
tert-butyl 3-(((3-hydroxypropyl)amino)methyl)-1H-indole-1-carboxylate s1-u



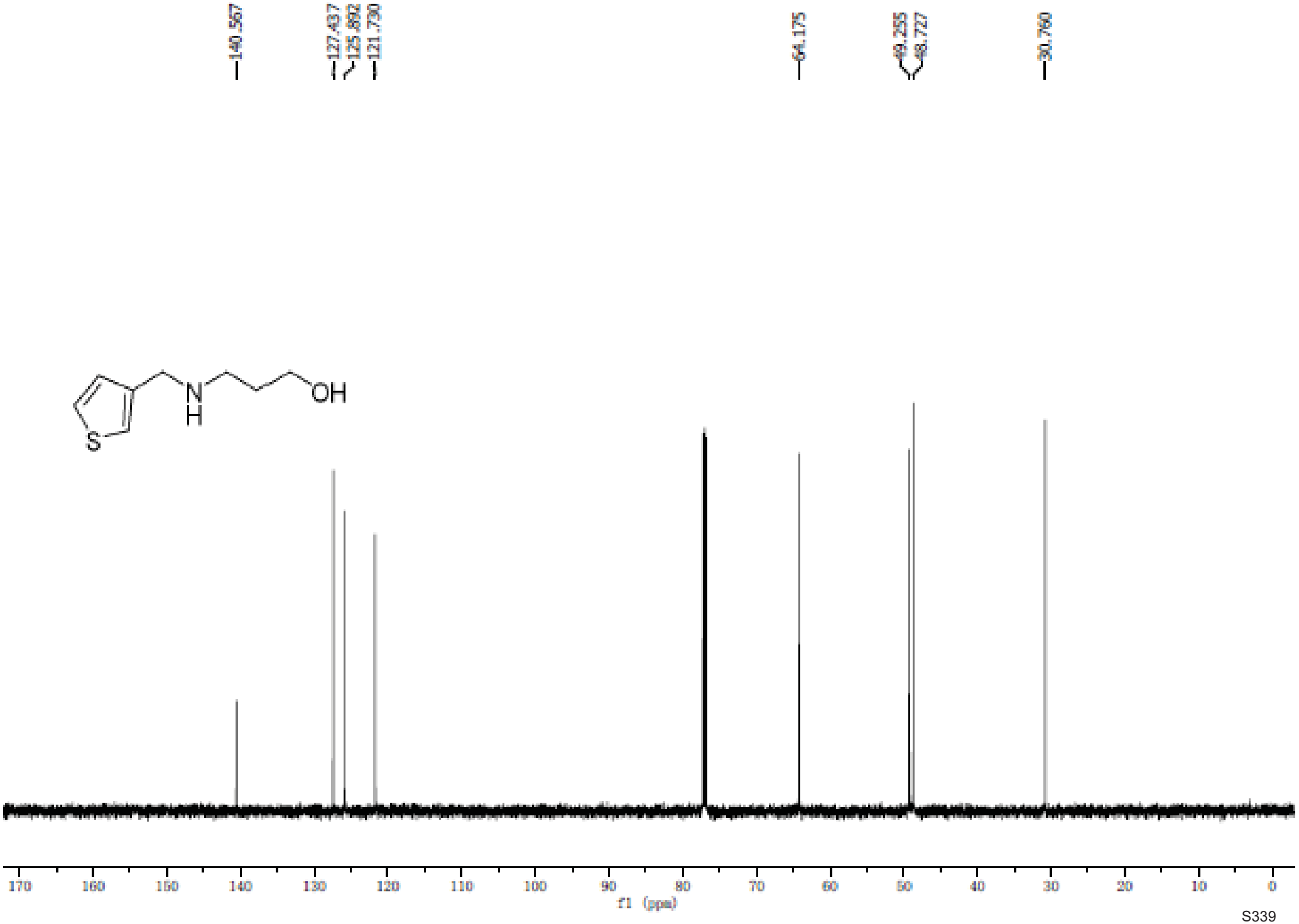
tert-butyl 3-(((3-hydroxypropyl)amino)methyl)-1H-indole-1-carboxylate s1-u



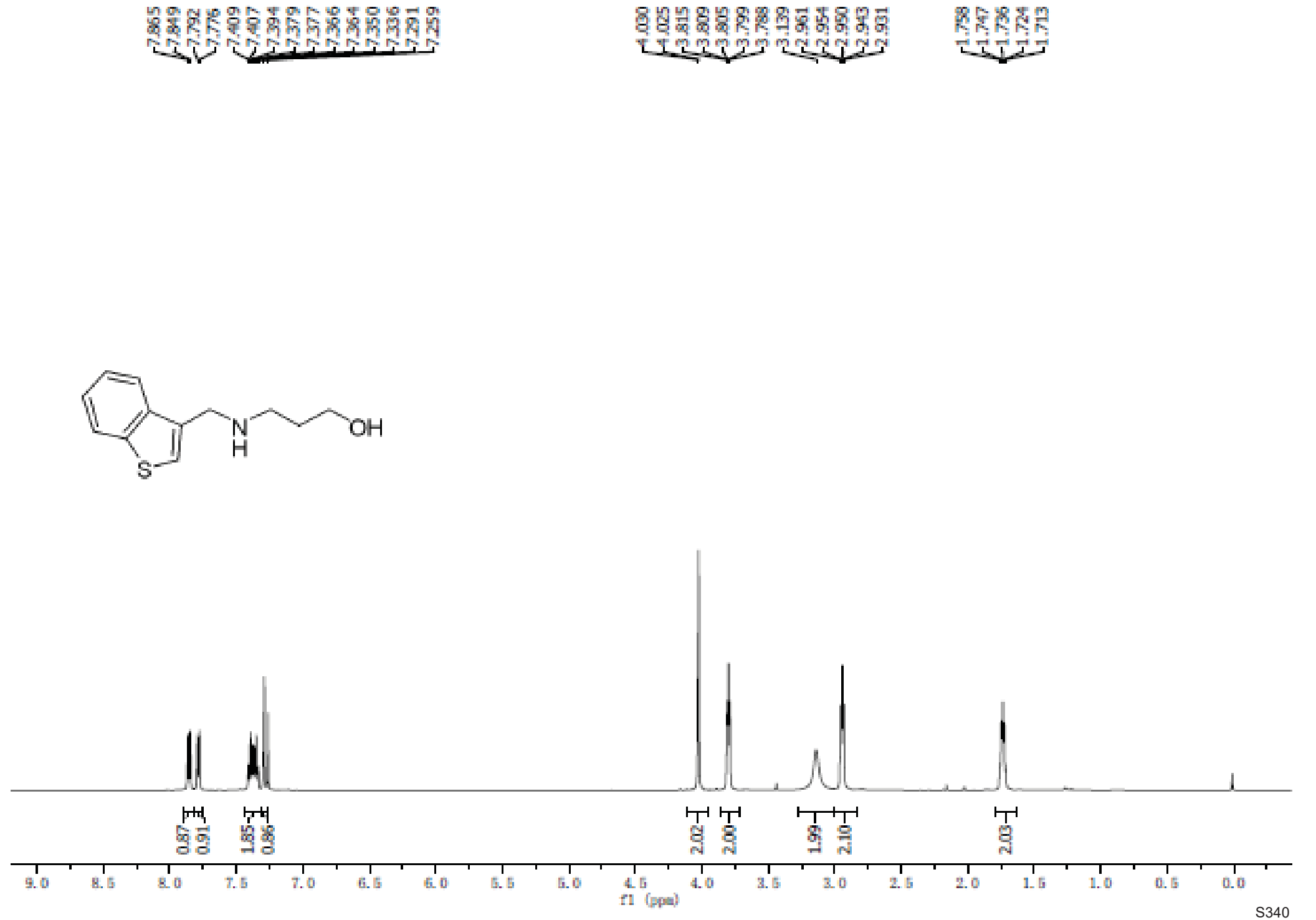
3-((thiophen-3-ylmethyl)amino)propan-1-ol s1-v



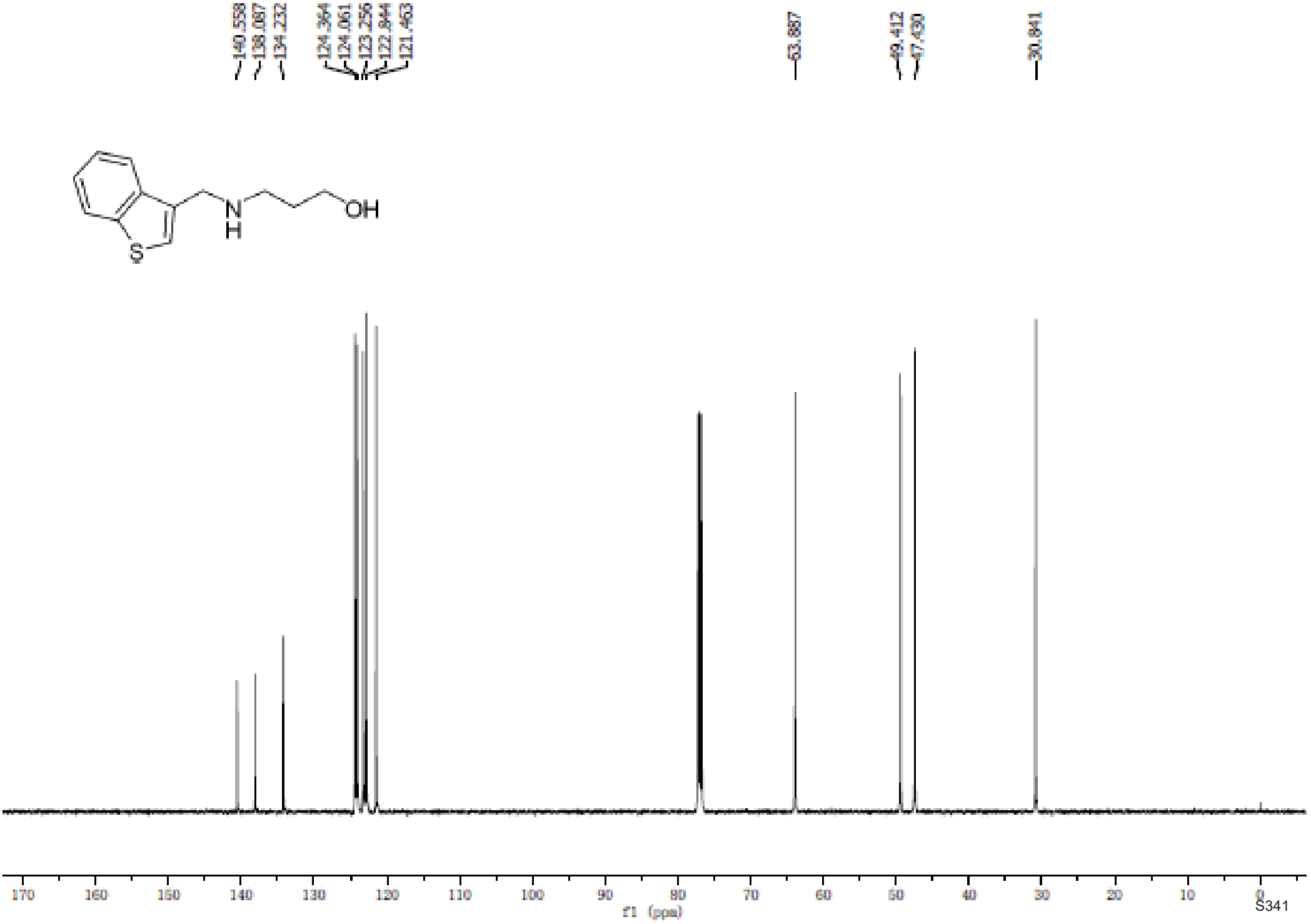
3-((thiophen-3-ylmethyl)amino)propan-1-ol s1-v



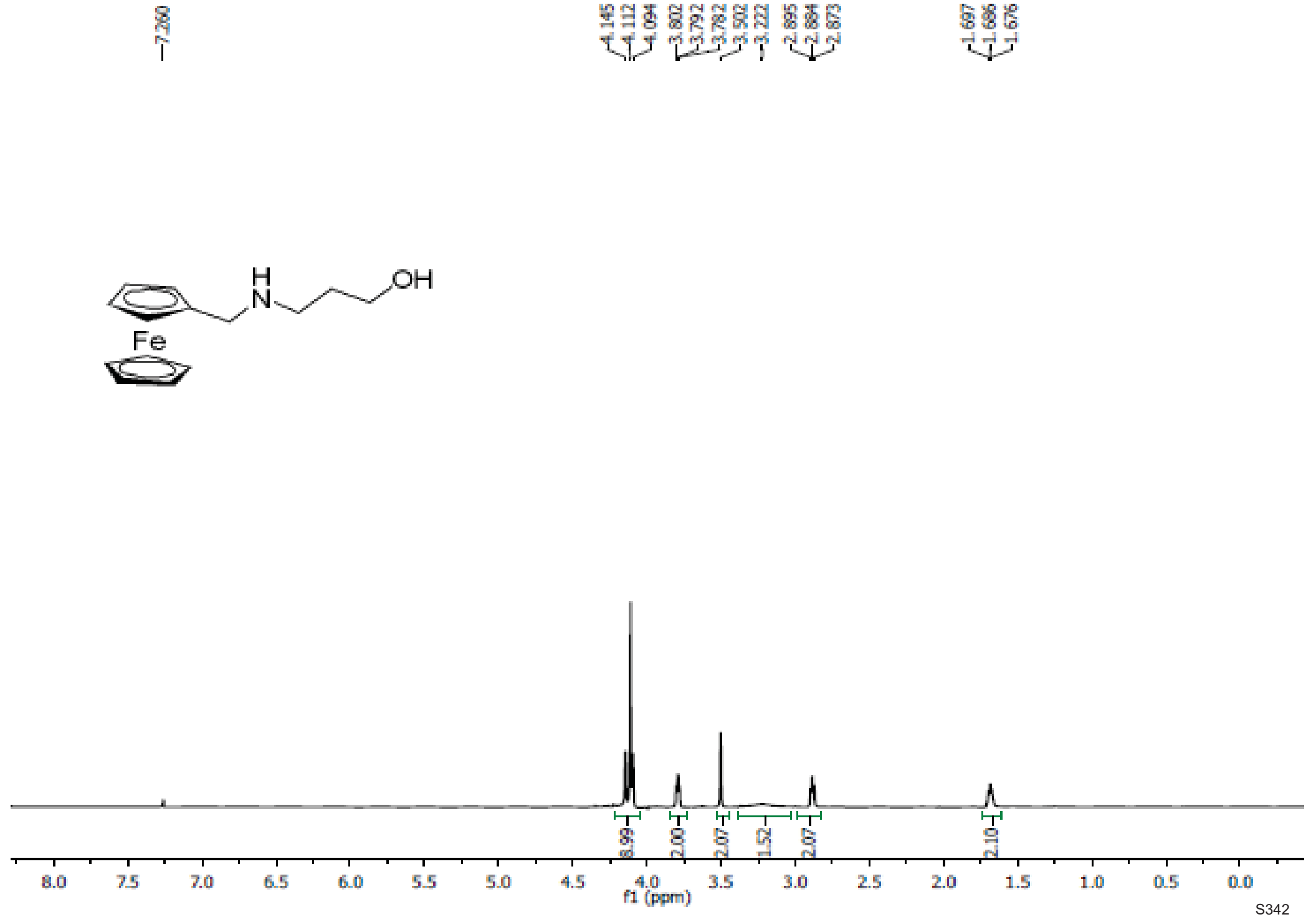
3-((benzo[b]thiophen-3-ylmethyl)amino)propan-1-ol s1-w



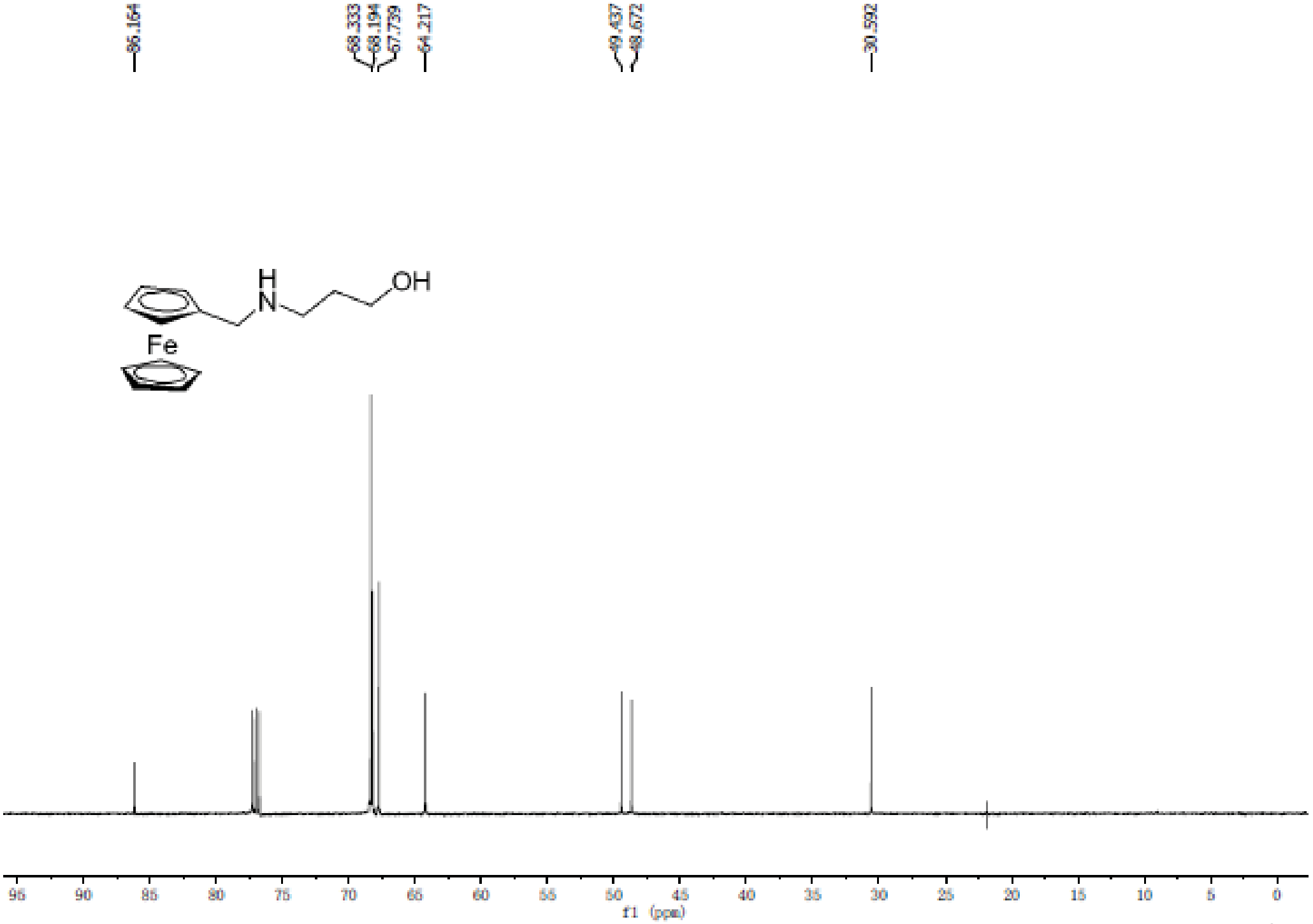
3-((benzo[b]thiophen-3-ylmethyl)amino)propan-1-ol s1-w



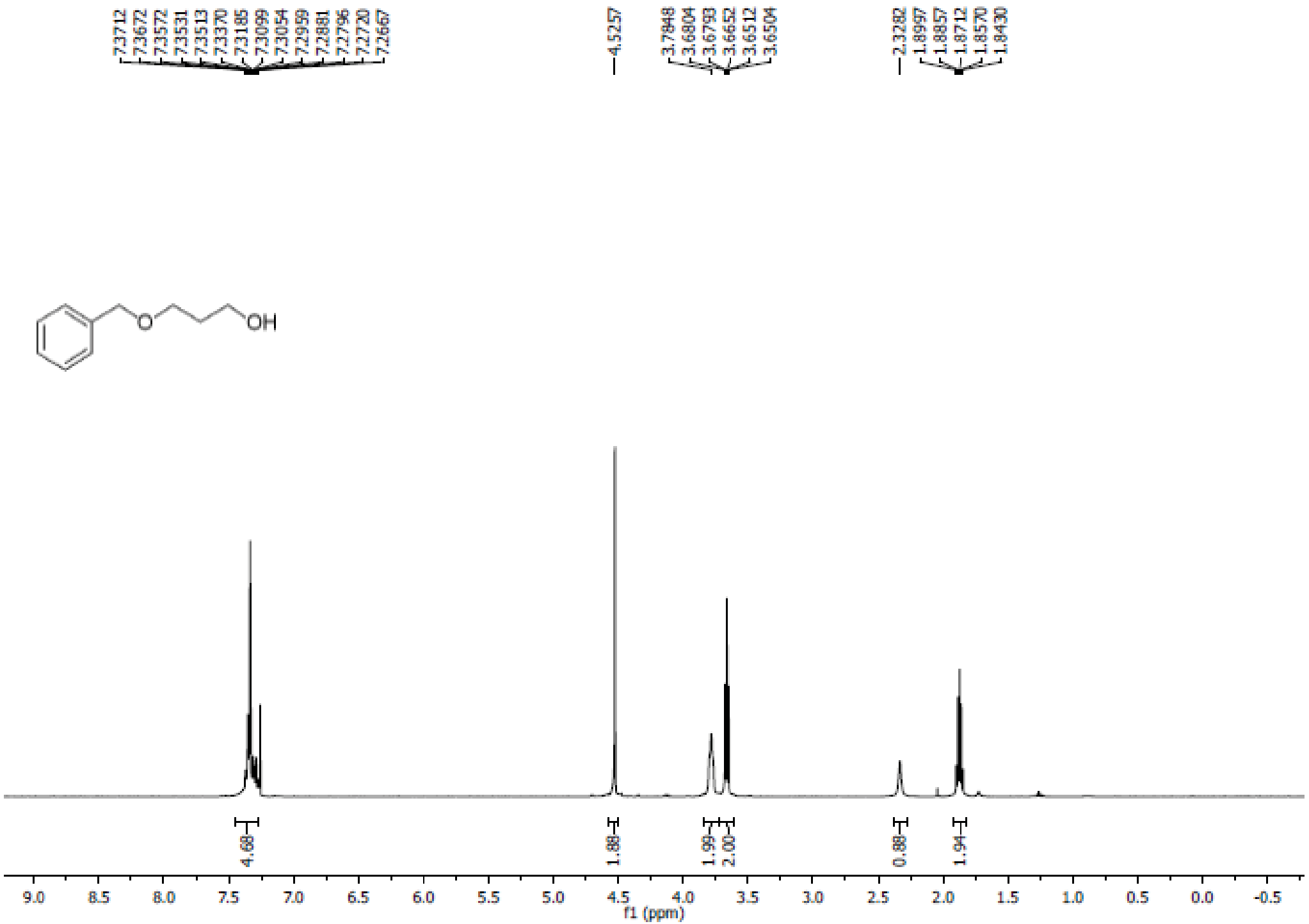
3-((ferrocenyl)amino)propan-1-ol s1-x



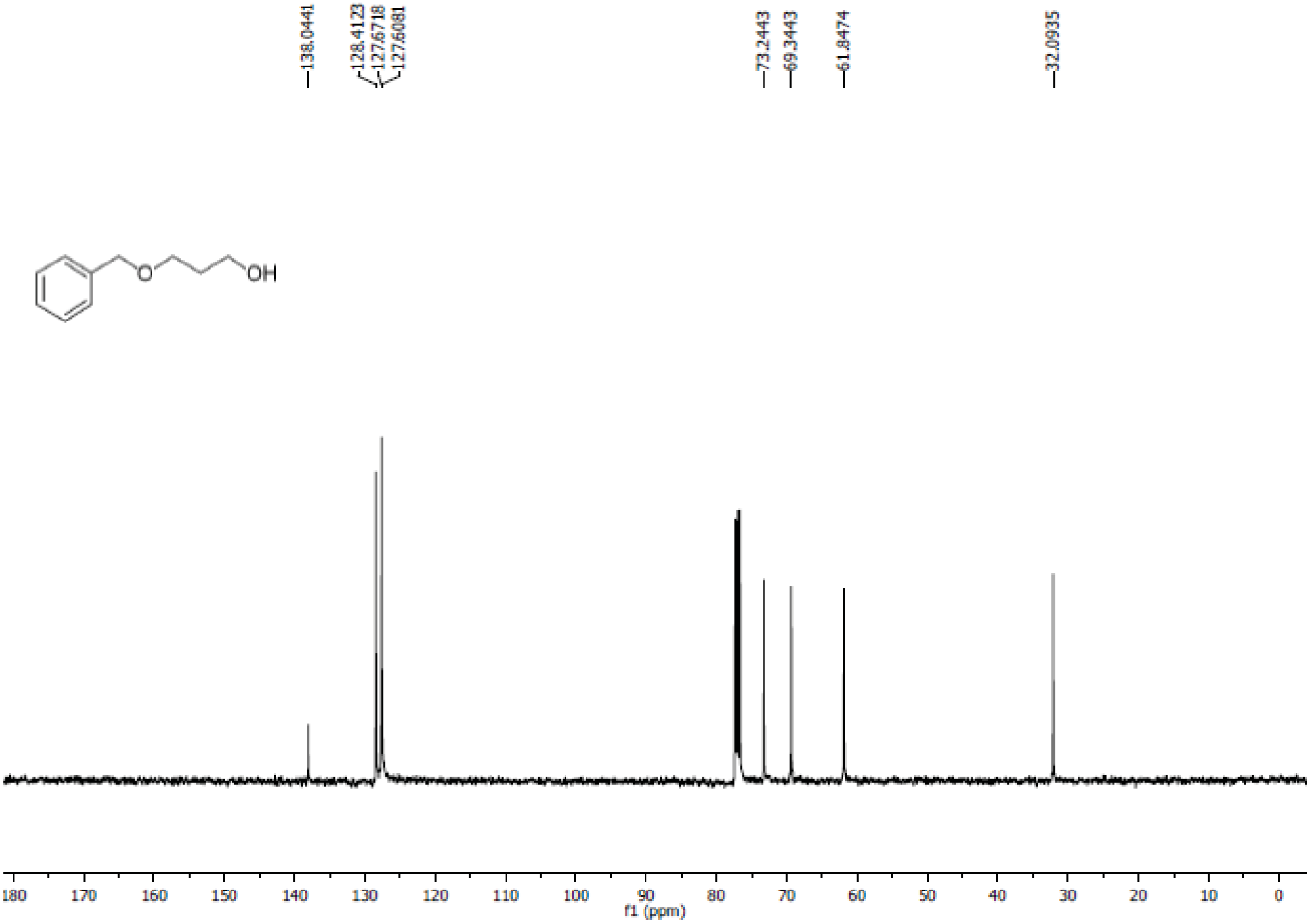
3-((ferrocenyl)amino)propan-1-ol s1-x



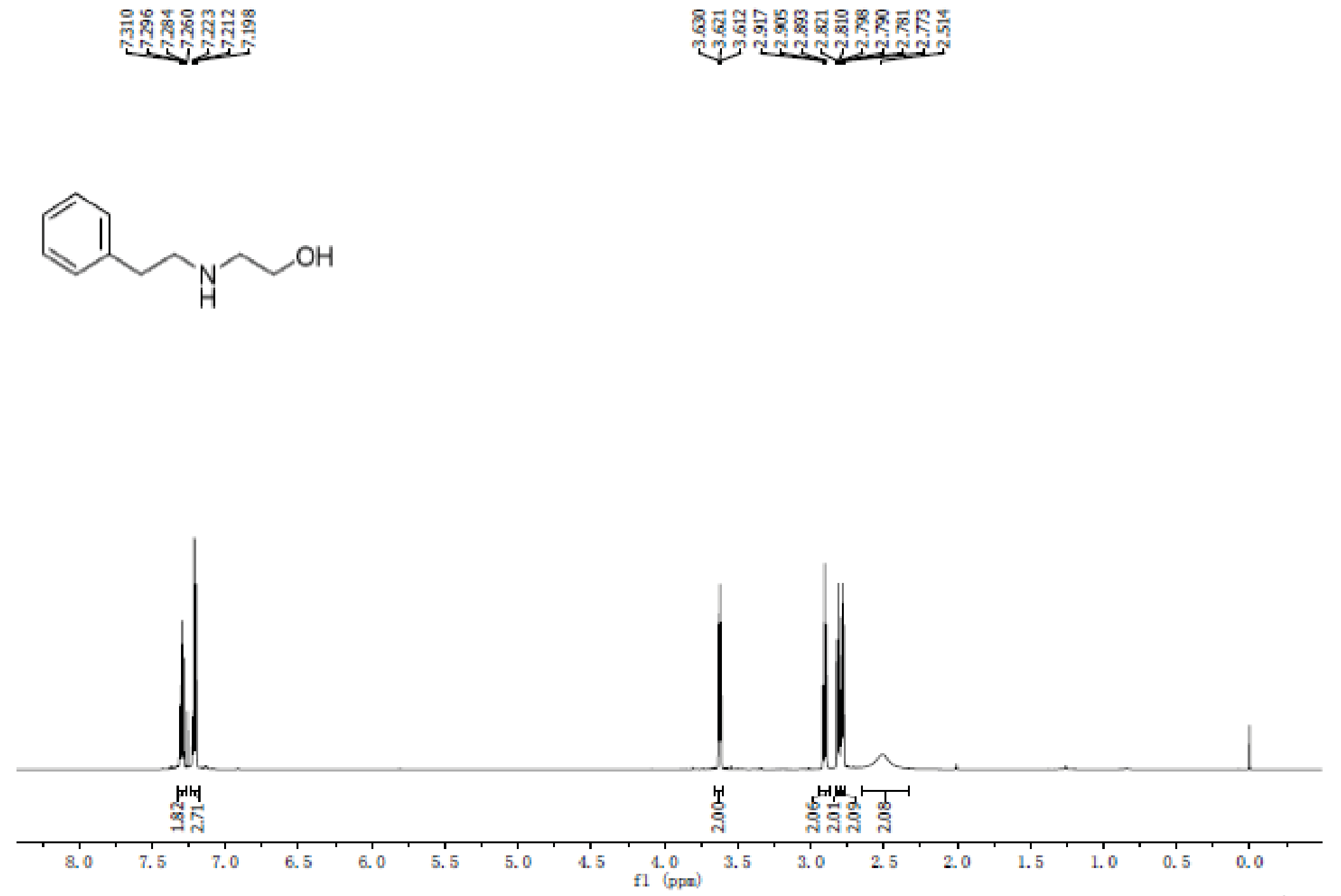
3-(benzyloxy)propan-1-ol s1-y



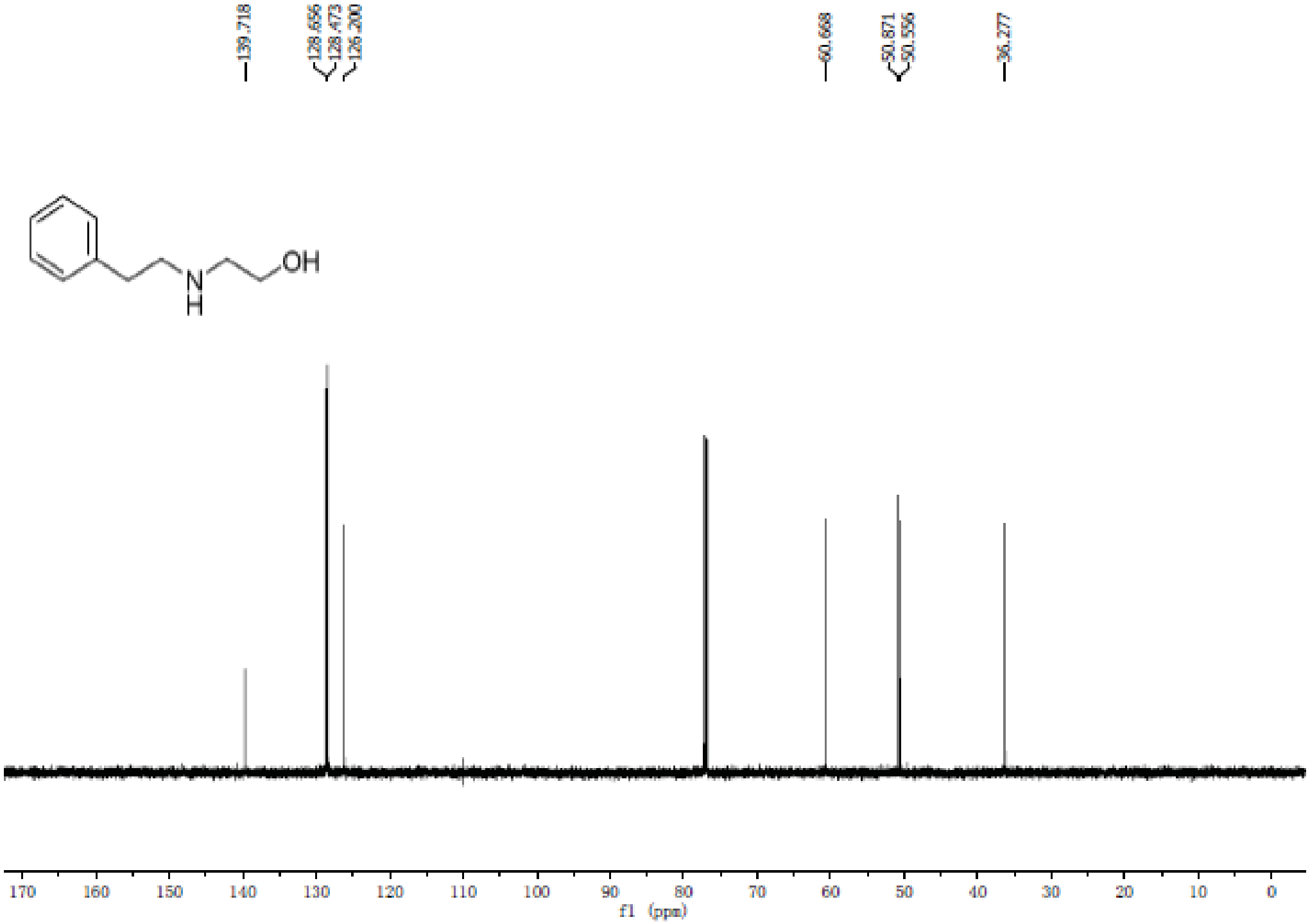
3-(benzyloxy)propan-1-ol s1-y



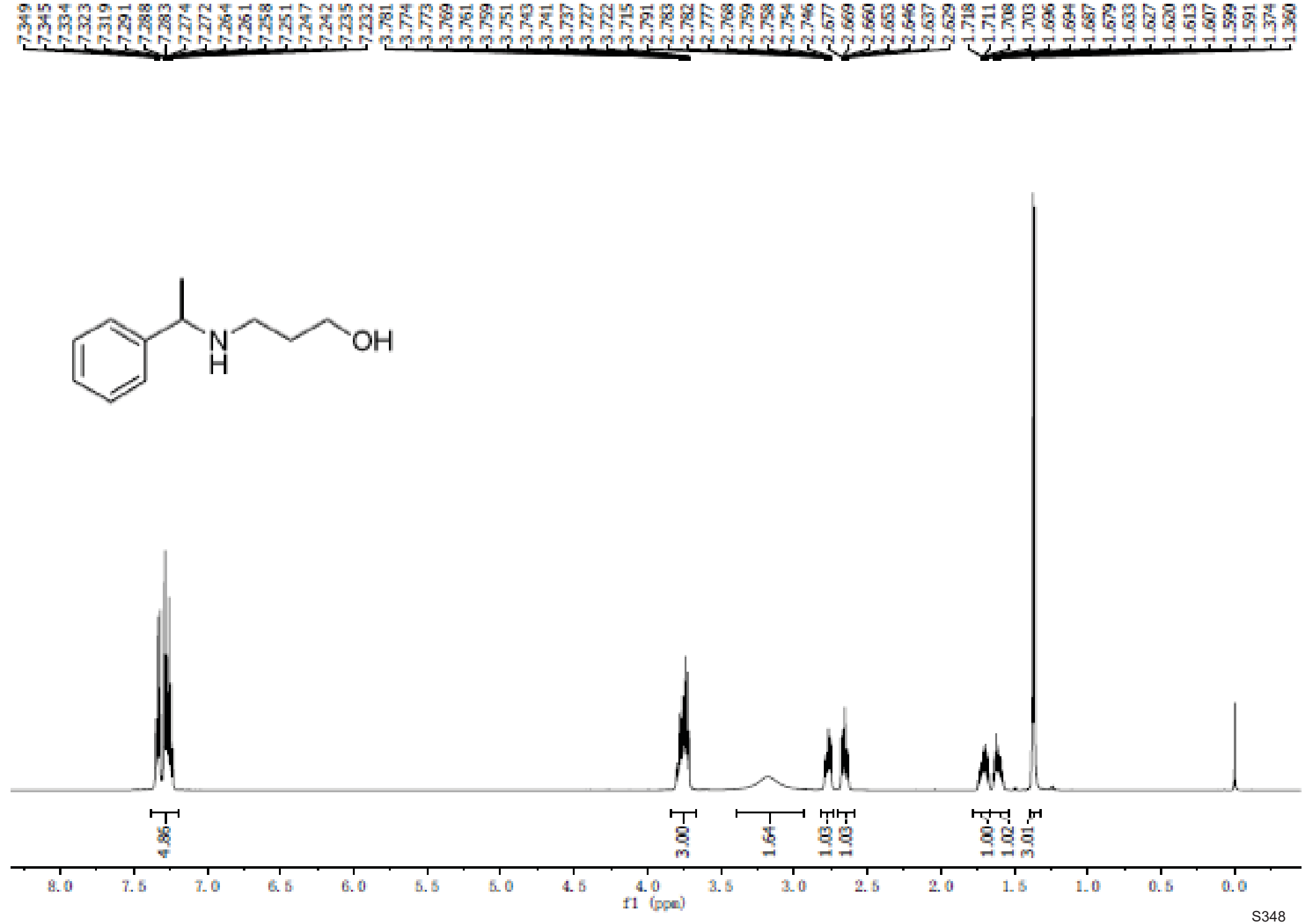
2-(phenethylamino)ethan-1-ol s1-z



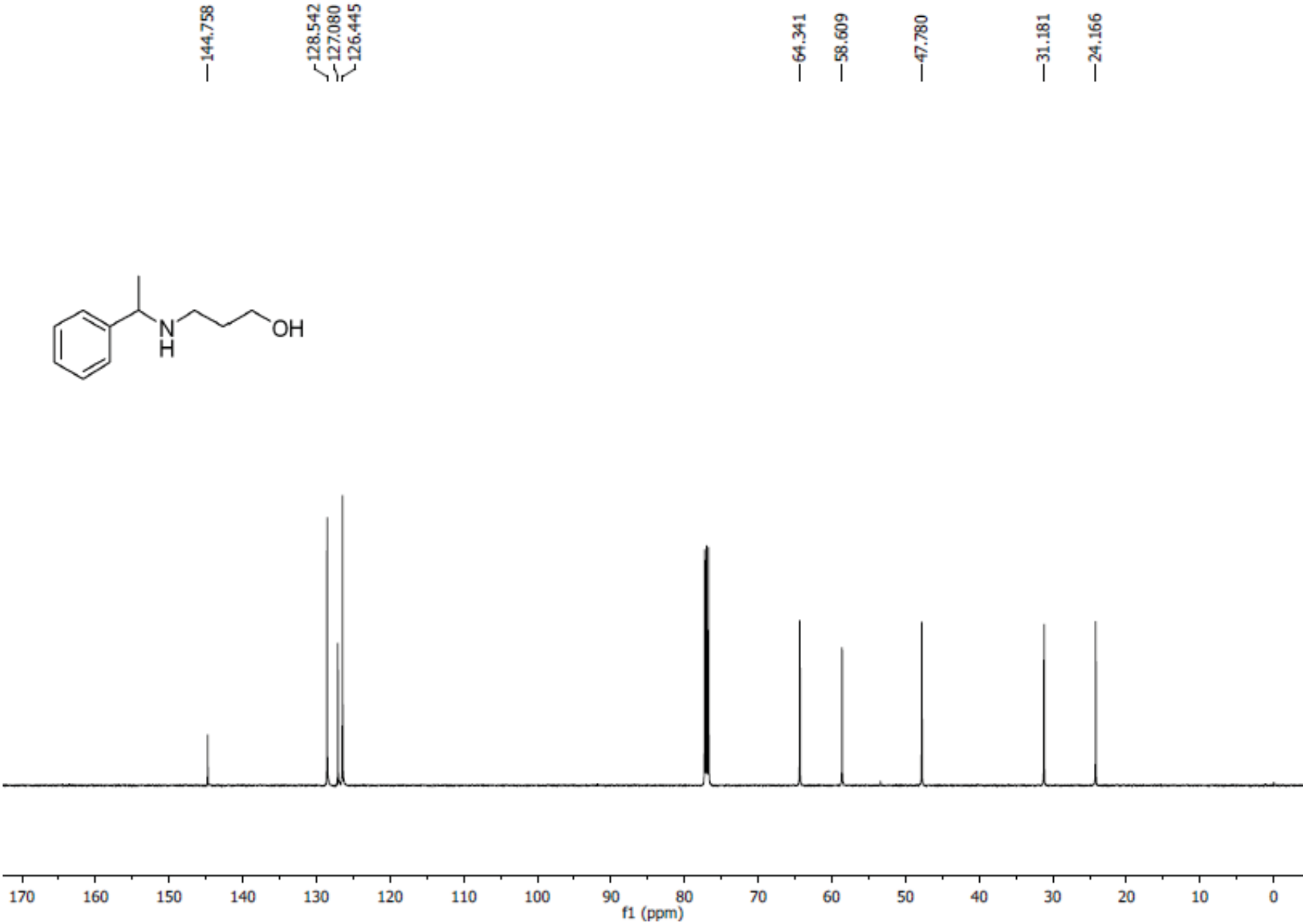
2-(phenethylamino)ethan-1-ol s1-z



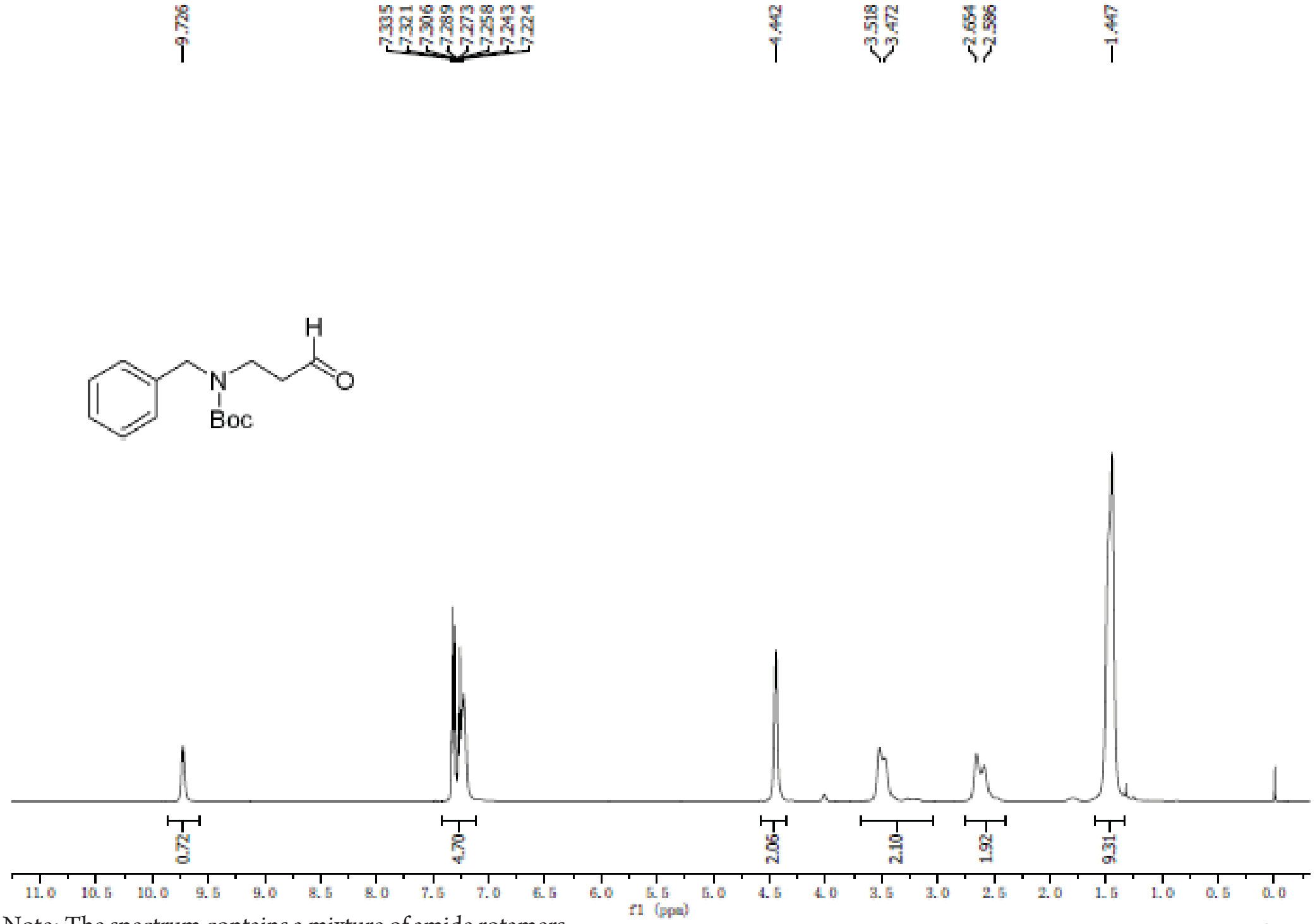
(*R*)-3-((1-phenylethyl)amino)propan-1-ol s1-aa



(*R*)-3-((1-phenylethyl)amino)propan-1-ol s1-aa

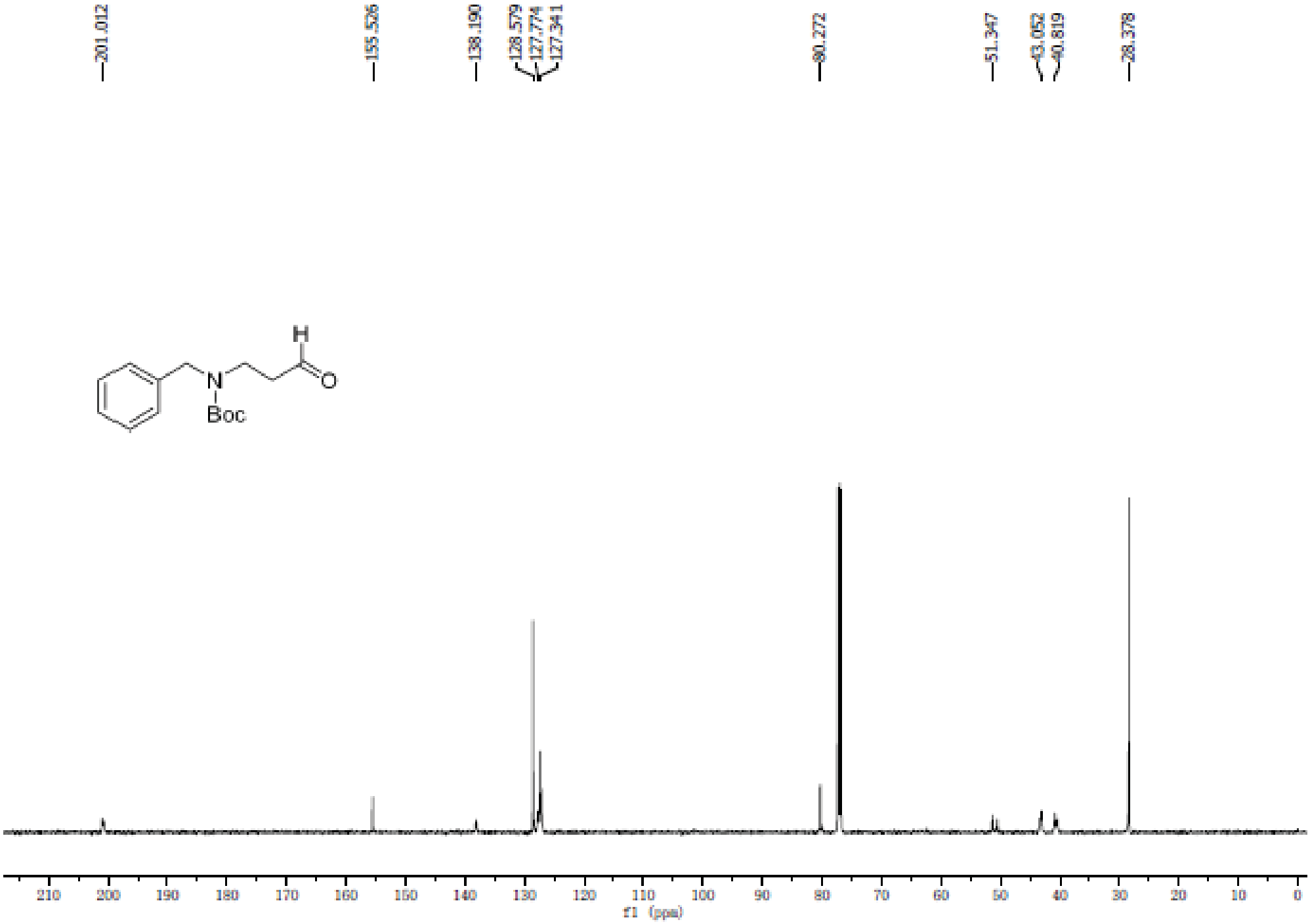


tert-butyl benzyl(3-oxopropyl)carbamate s2-a



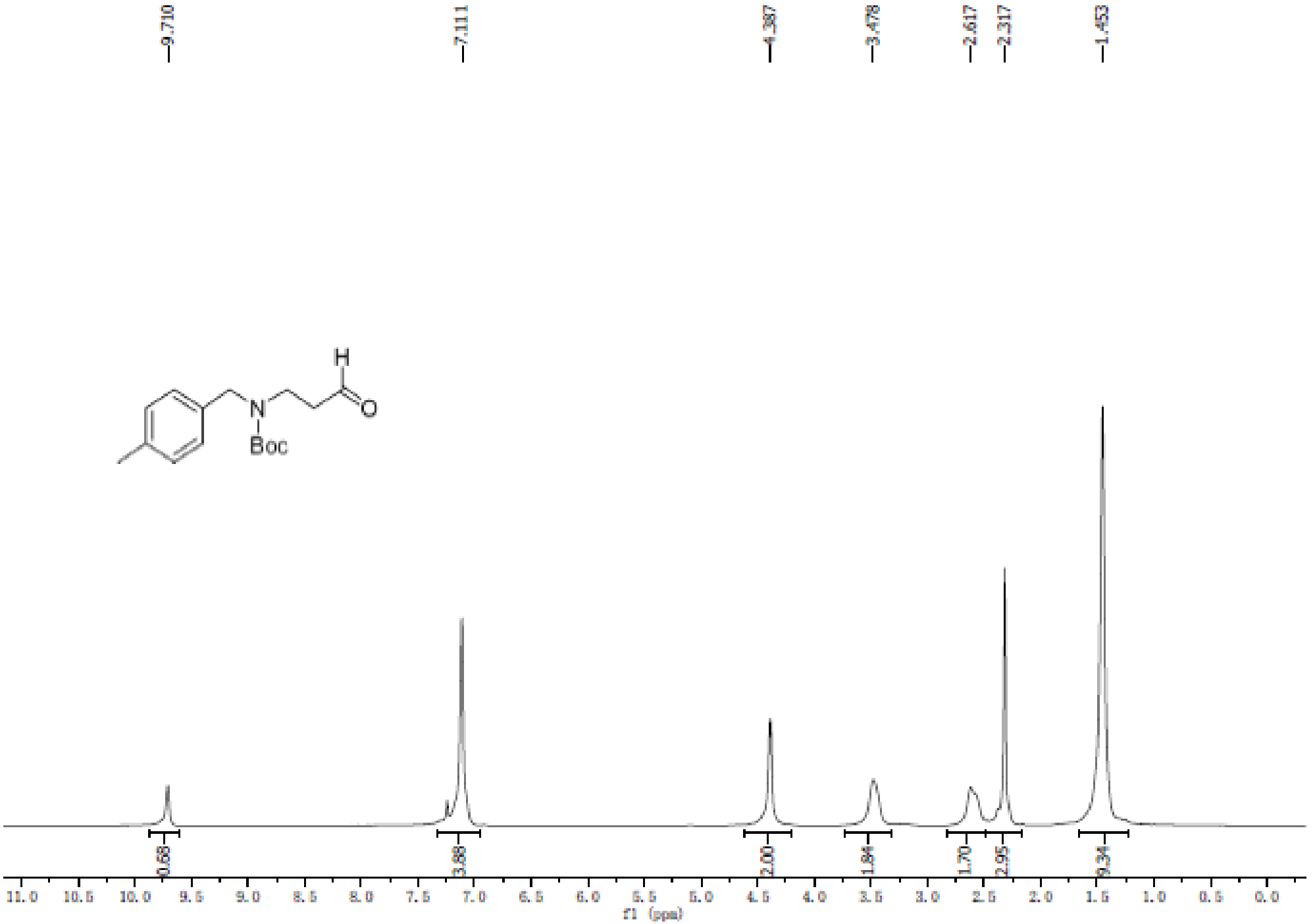
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl benzyl(3-oxopropyl)carbamate s2-a



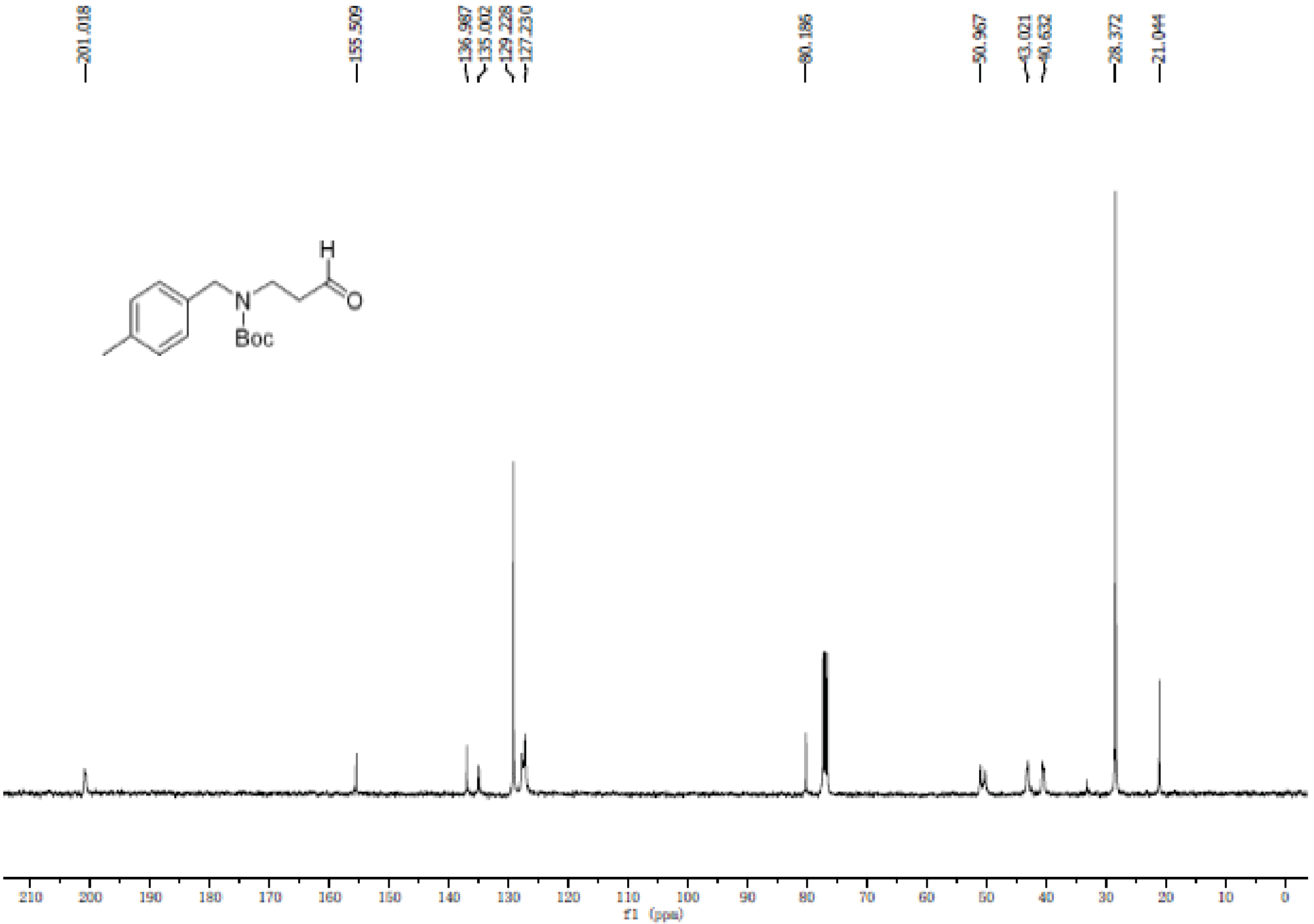
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (4-methylbenzyl)(3-oxopropyl)carbamate s2-b



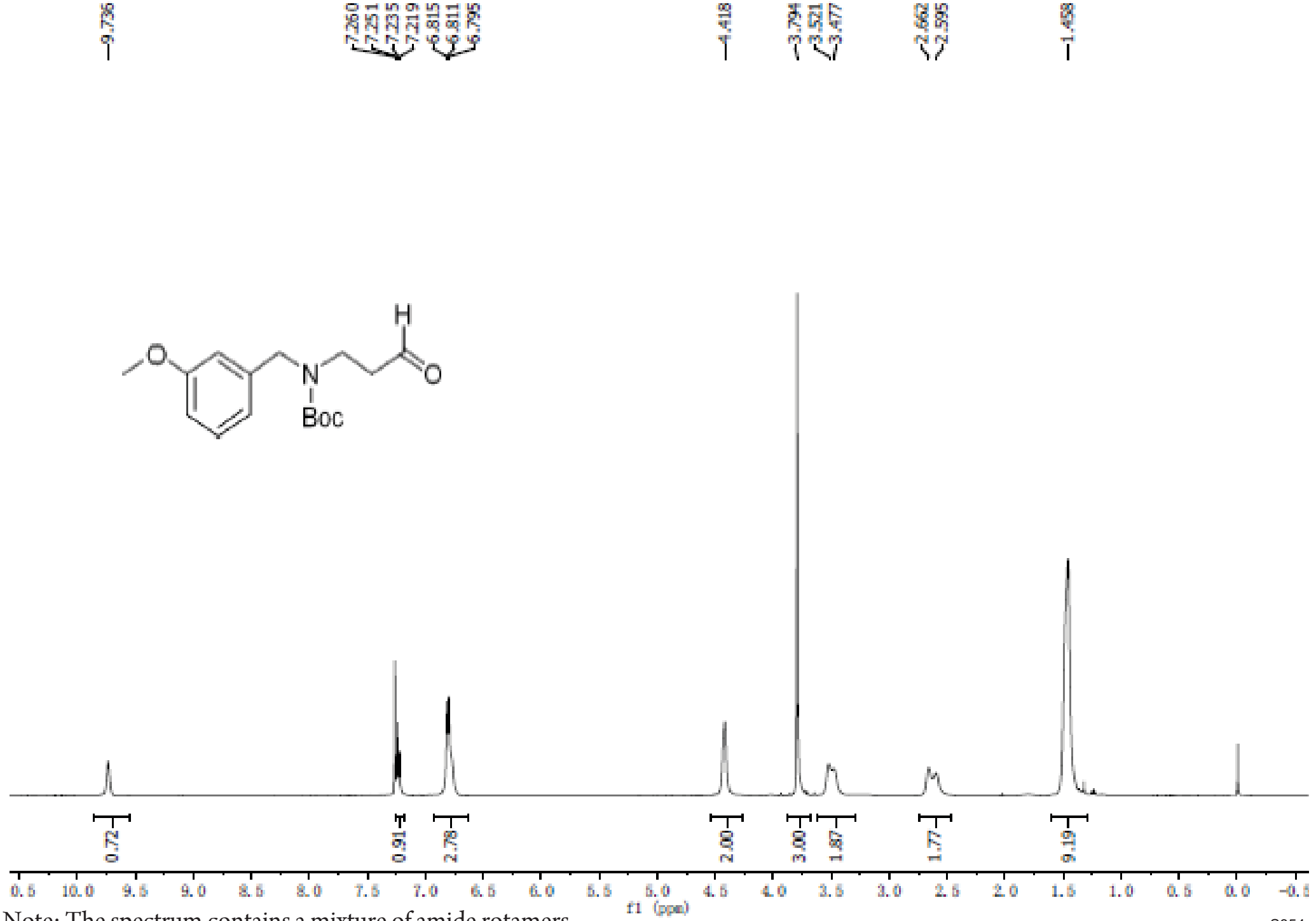
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (4-methylbenzyl)(3-oxopropyl)carbamate s2-b



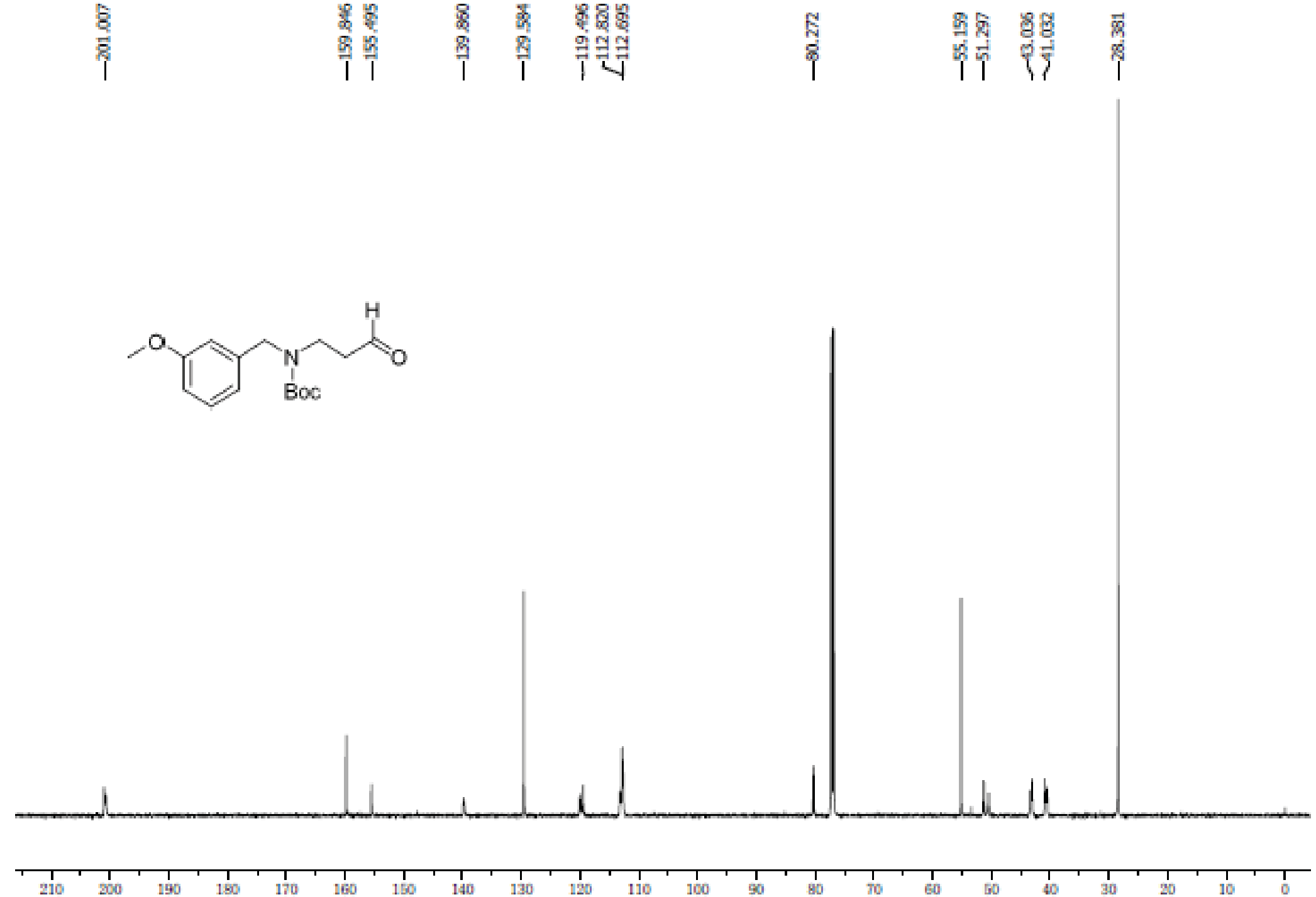
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3-methoxybenzyl)(3-oxopropyl)carbamate s2-c



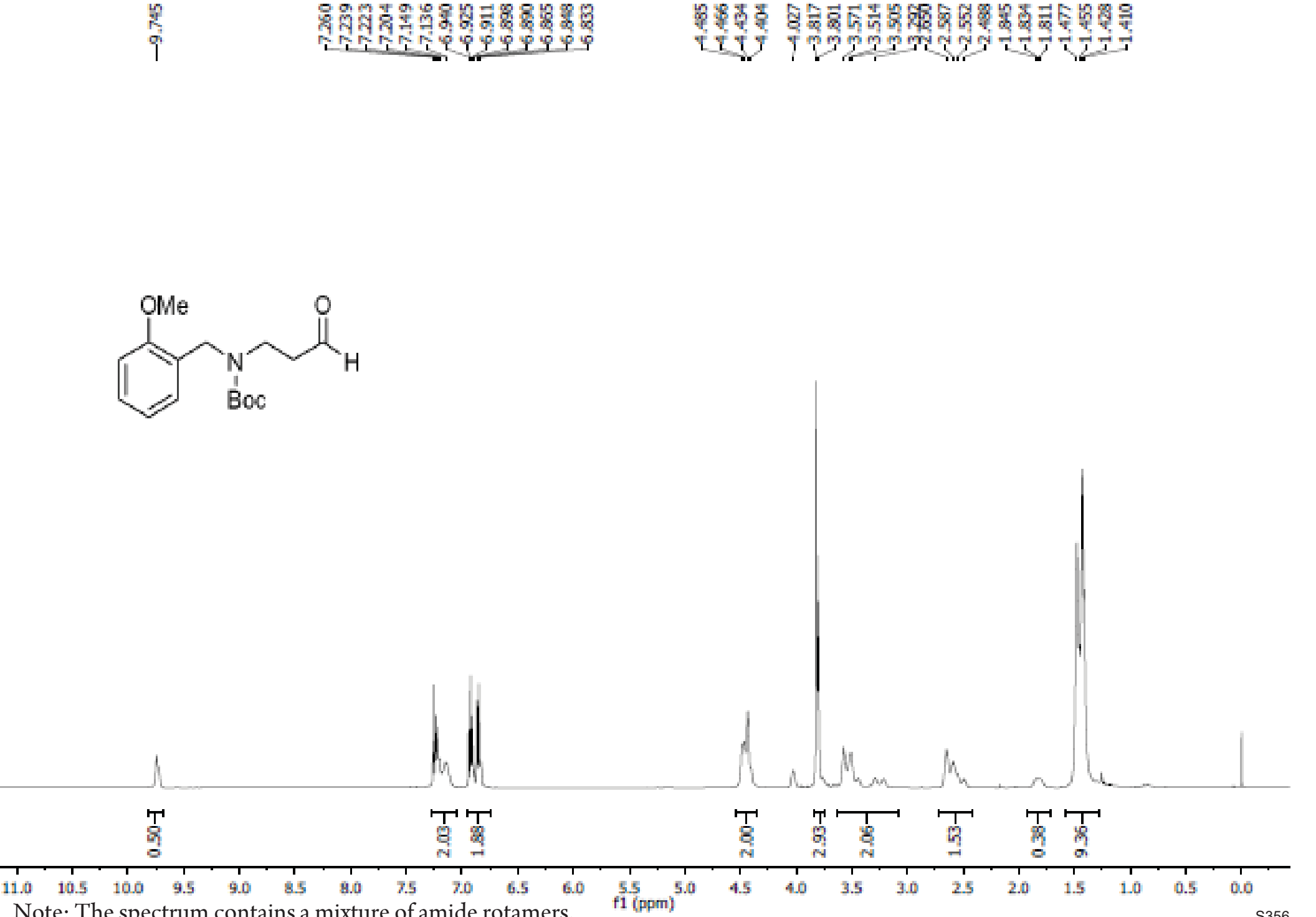
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3-methoxybenzyl)(3-oxopropyl)carbamate s2-c



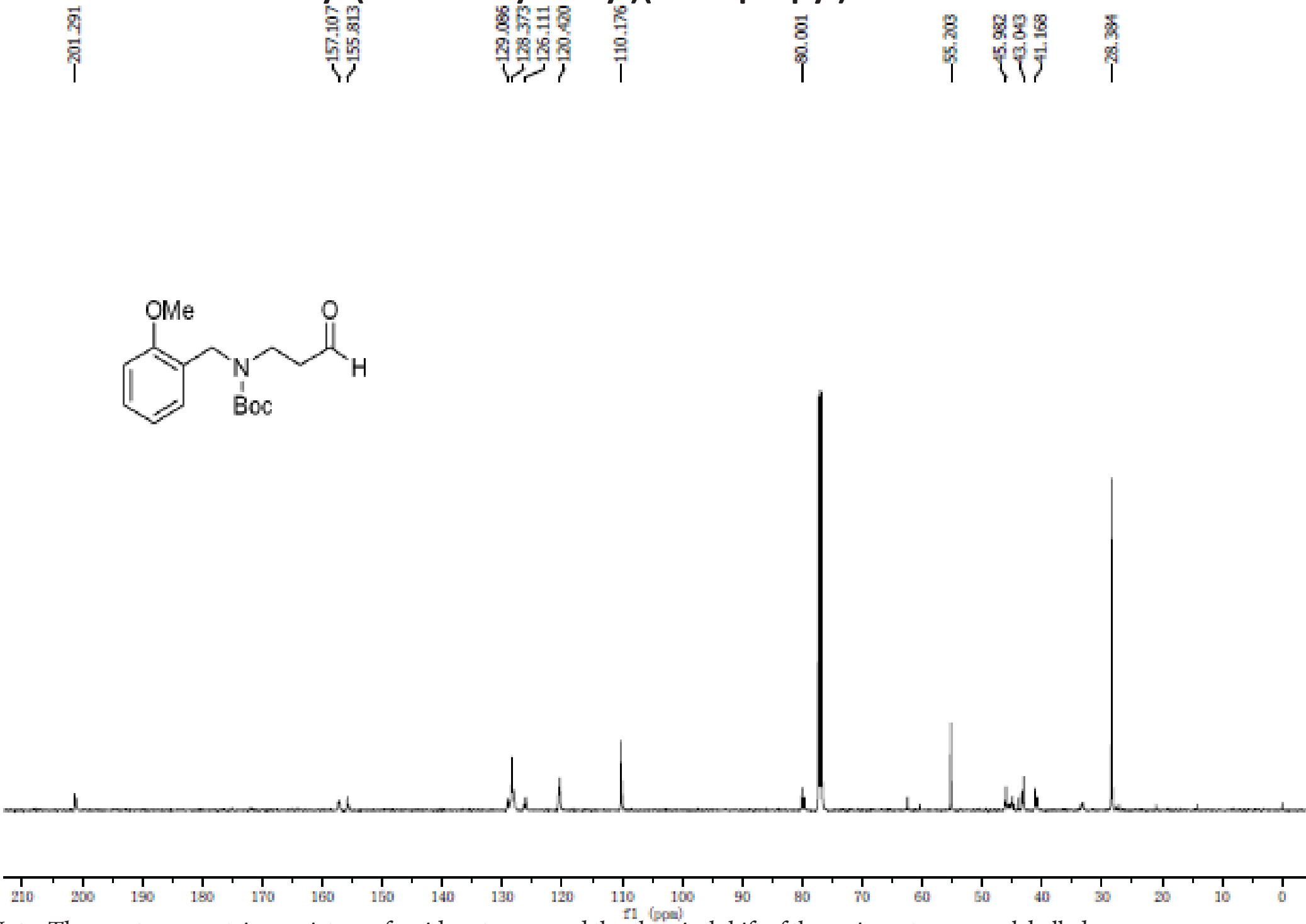
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (2-methoxybenzyl)(3-oxopropyl)carbamate s2-d



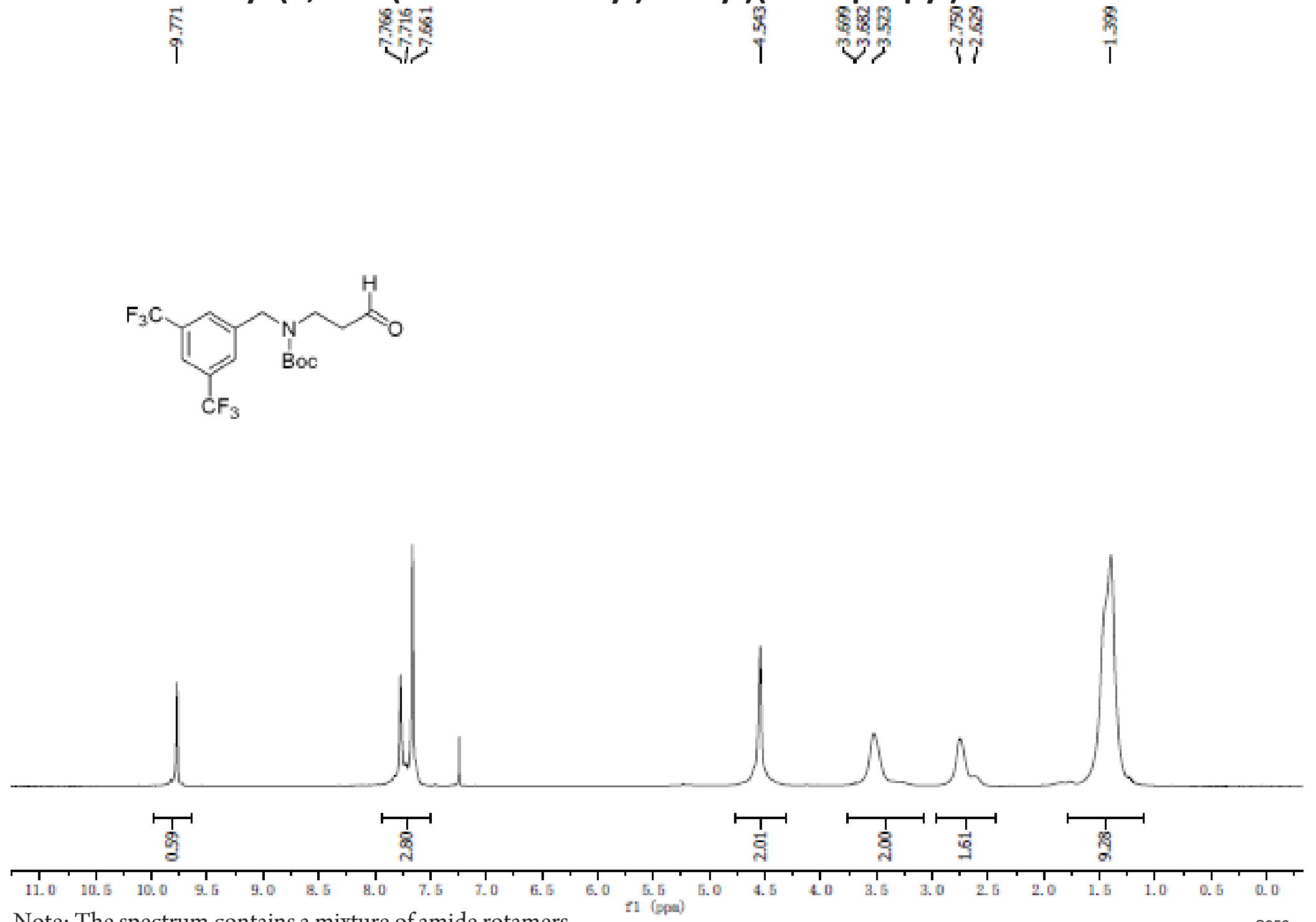
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (2-methoxybenzyl)(3-oxopropyl)carbamate s2-d



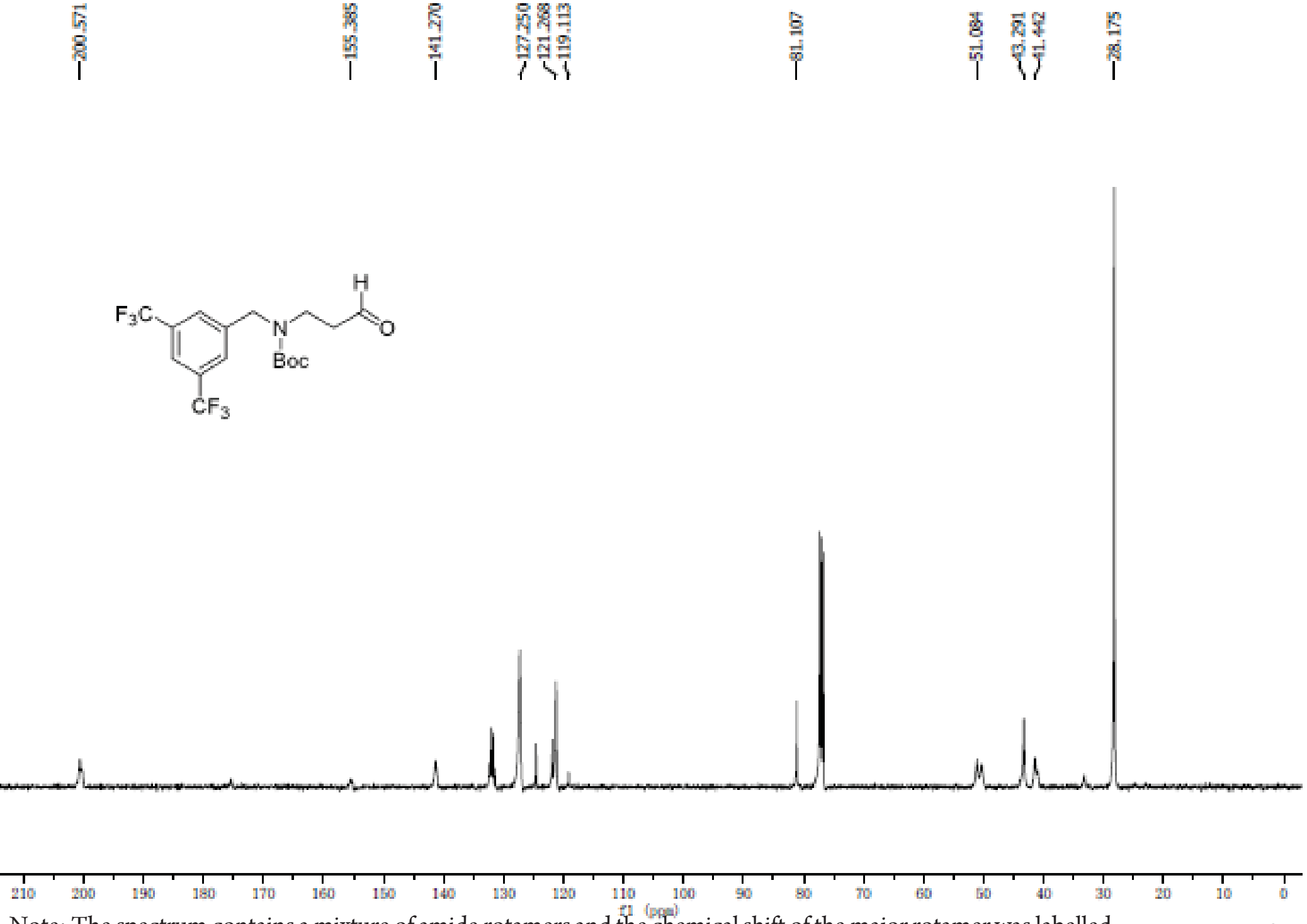
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3,5-bis(trifluoromethyl)benzyl)(3-oxopropyl)carbamate s2-e



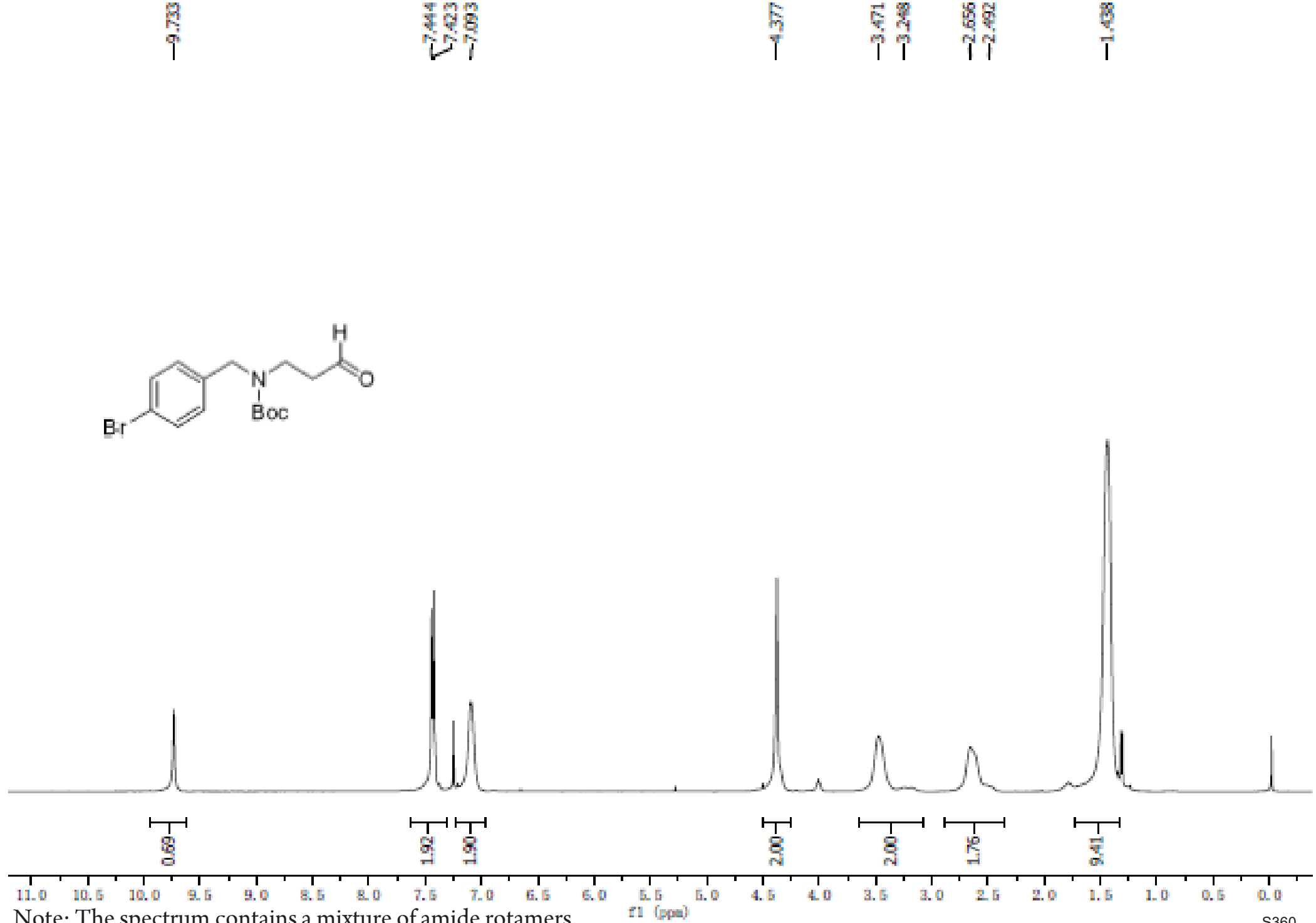
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3,5-bis(trifluoromethyl)benzyl)(3-oxopropyl)carbamate s2-e



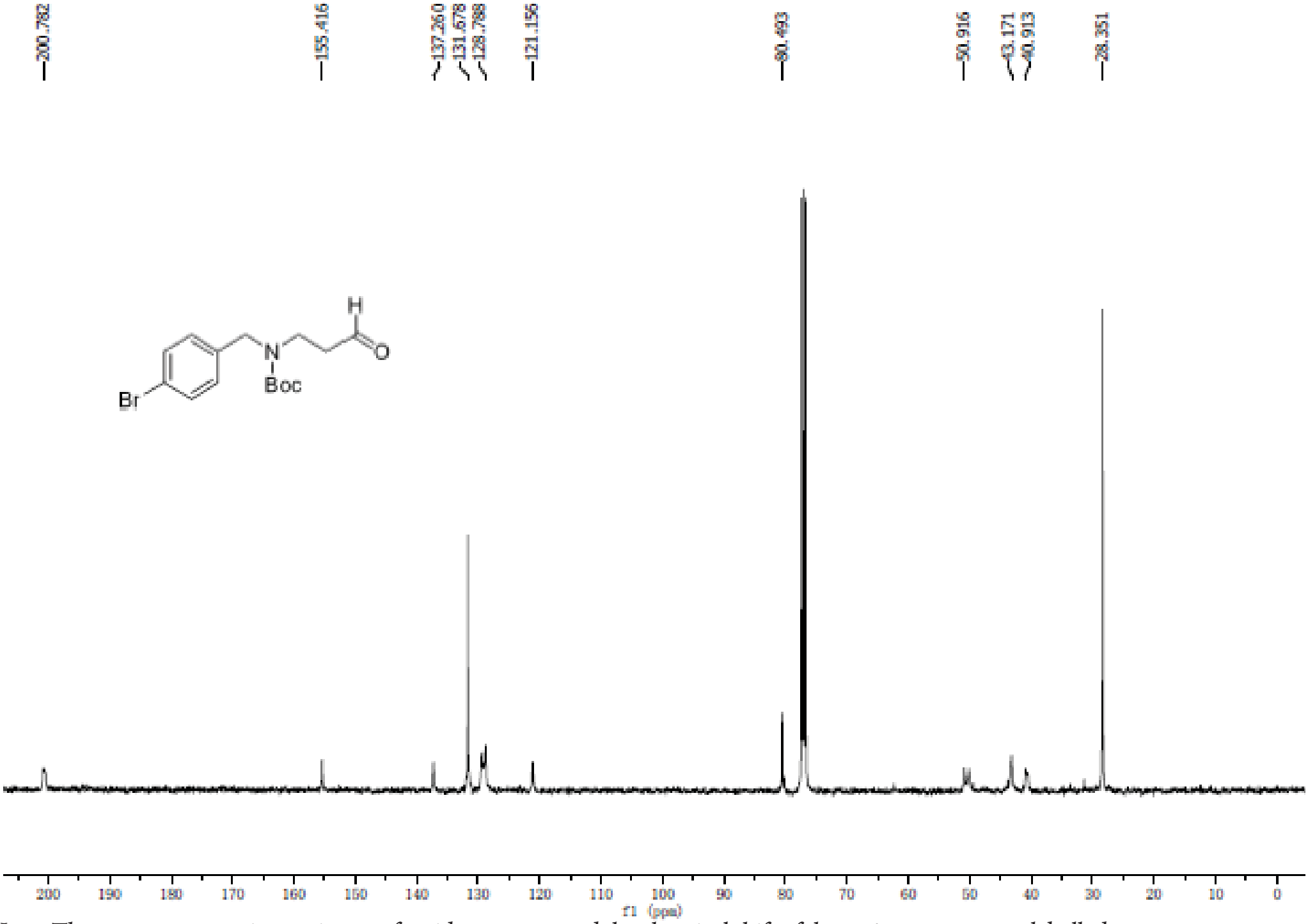
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (4-bromobenzyl)(3-oxopropyl)carbamate s2-f



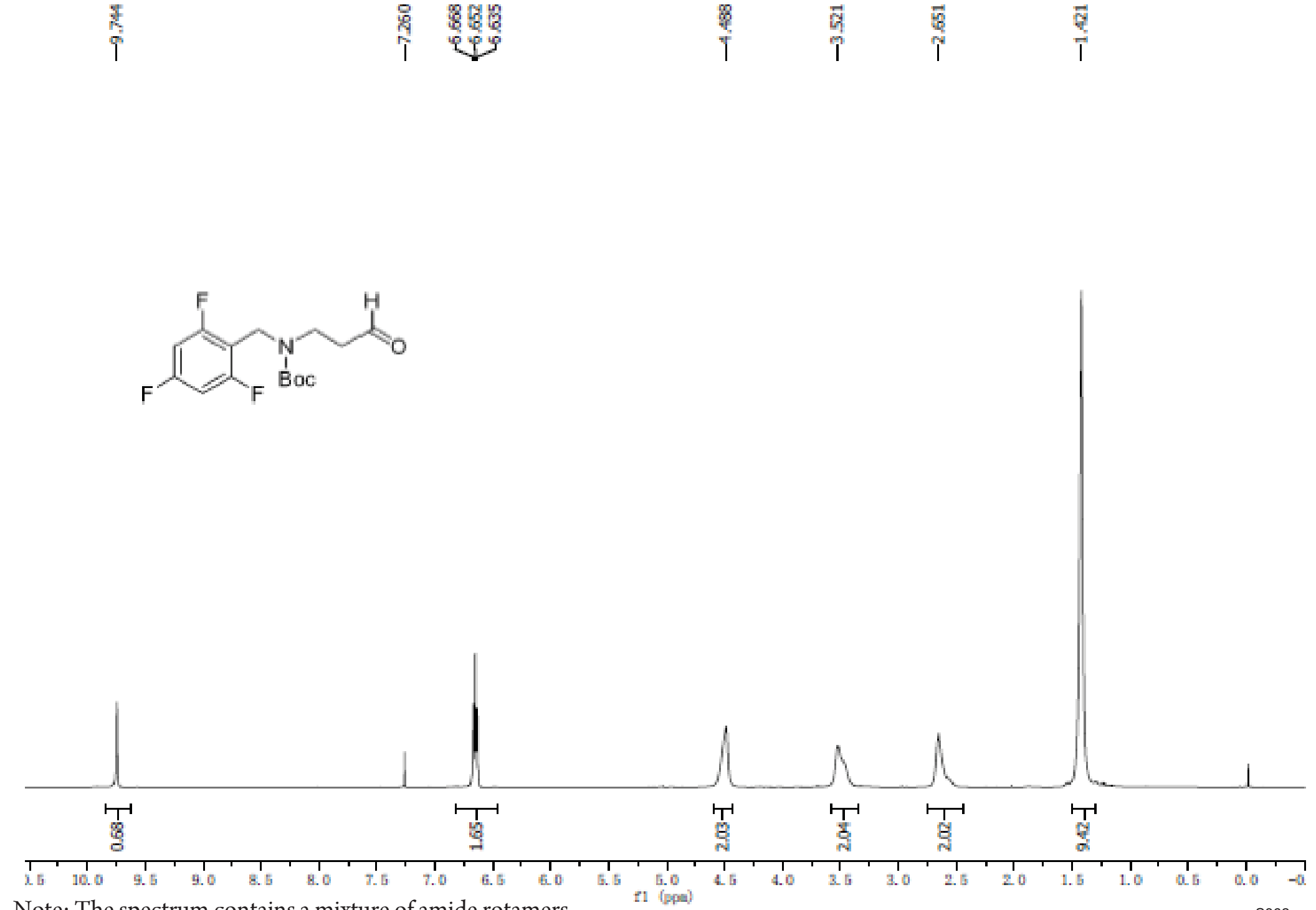
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (4-bromobenzyl)(3-oxopropyl)carbamate s2-f



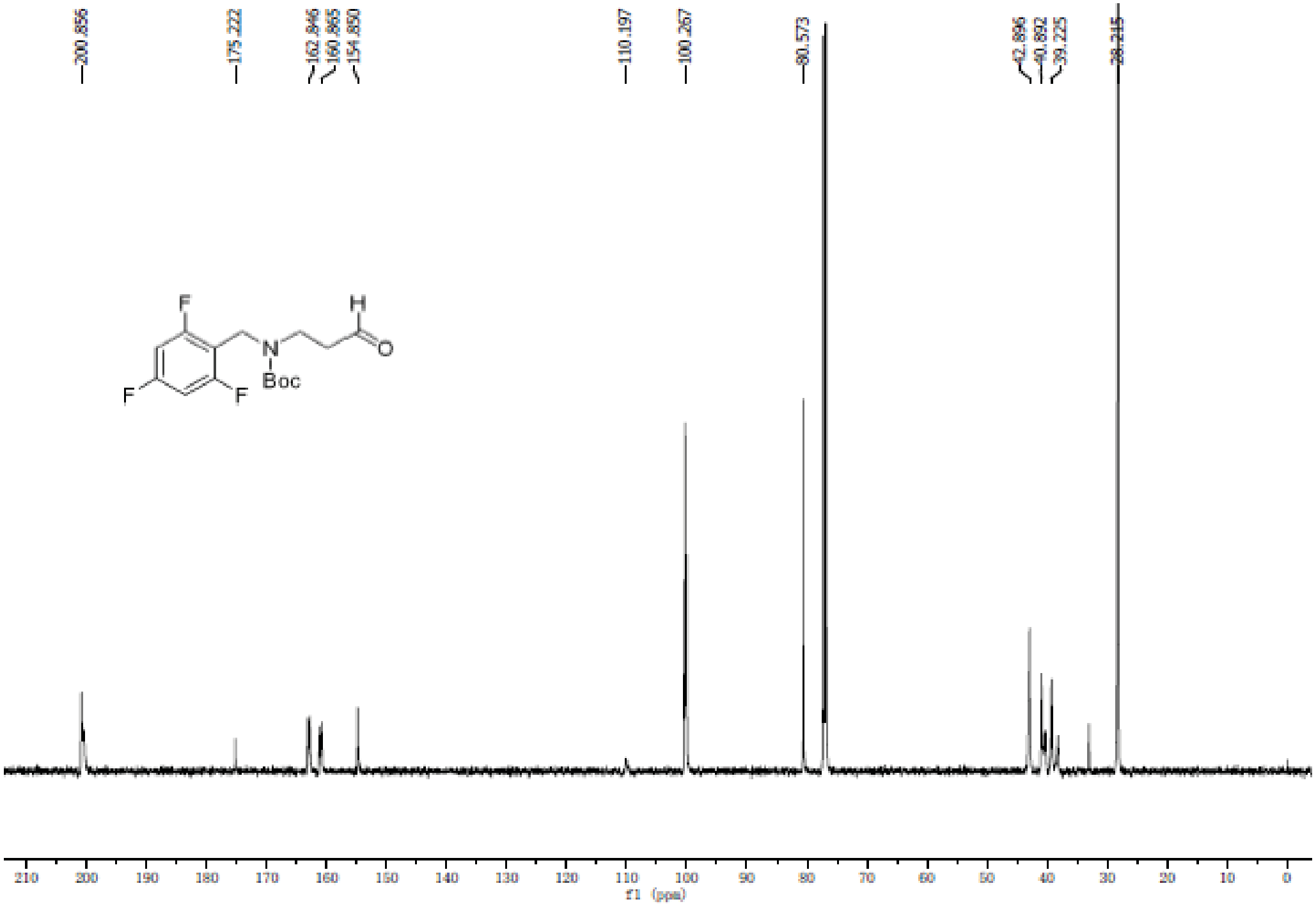
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (2,4,6-trifluorobenzyl)(3-oxopropyl)carbamate s2-g



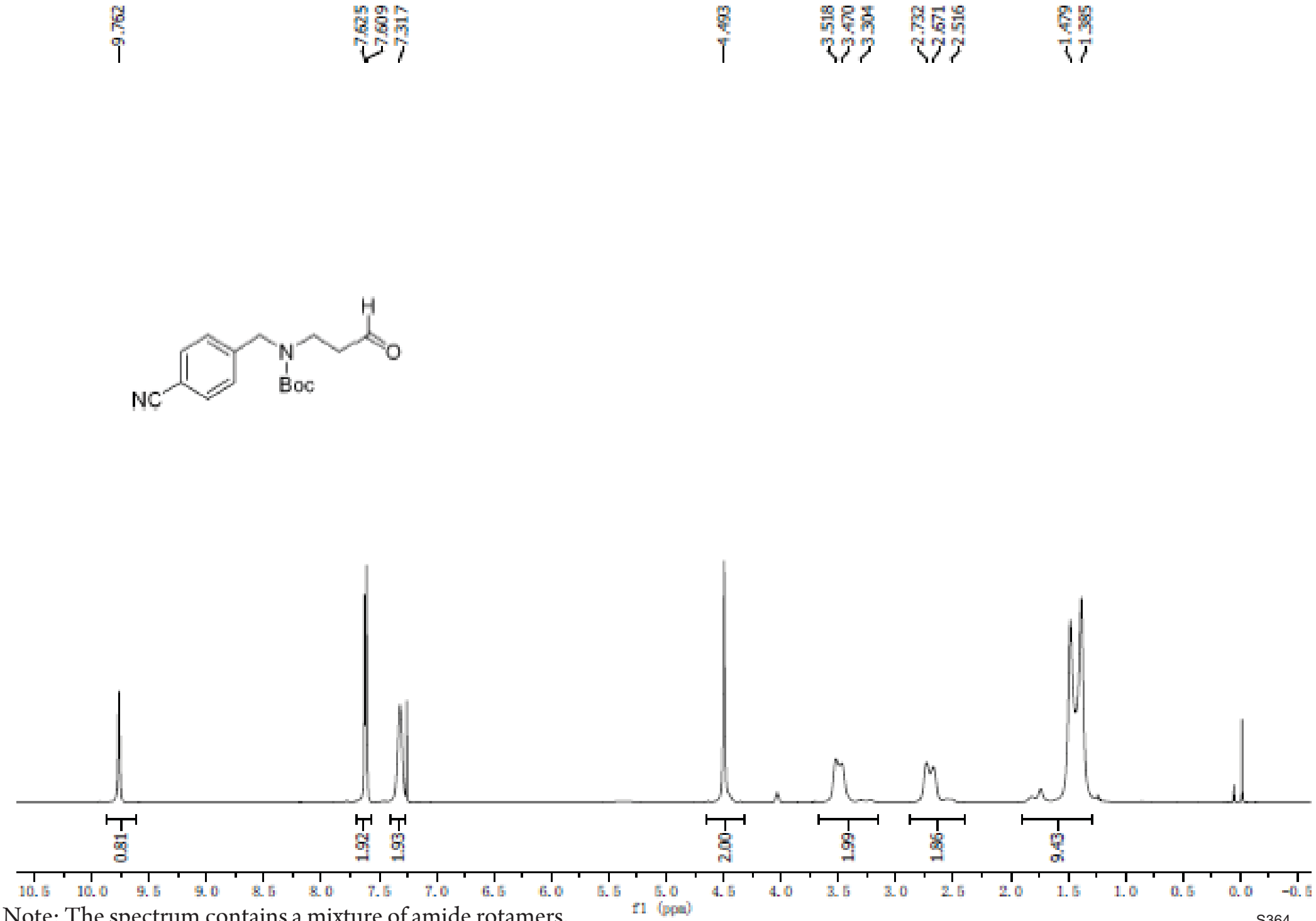
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (2,4,6-trifluorobenzyl)(3-oxopropyl)carbamate s2-g



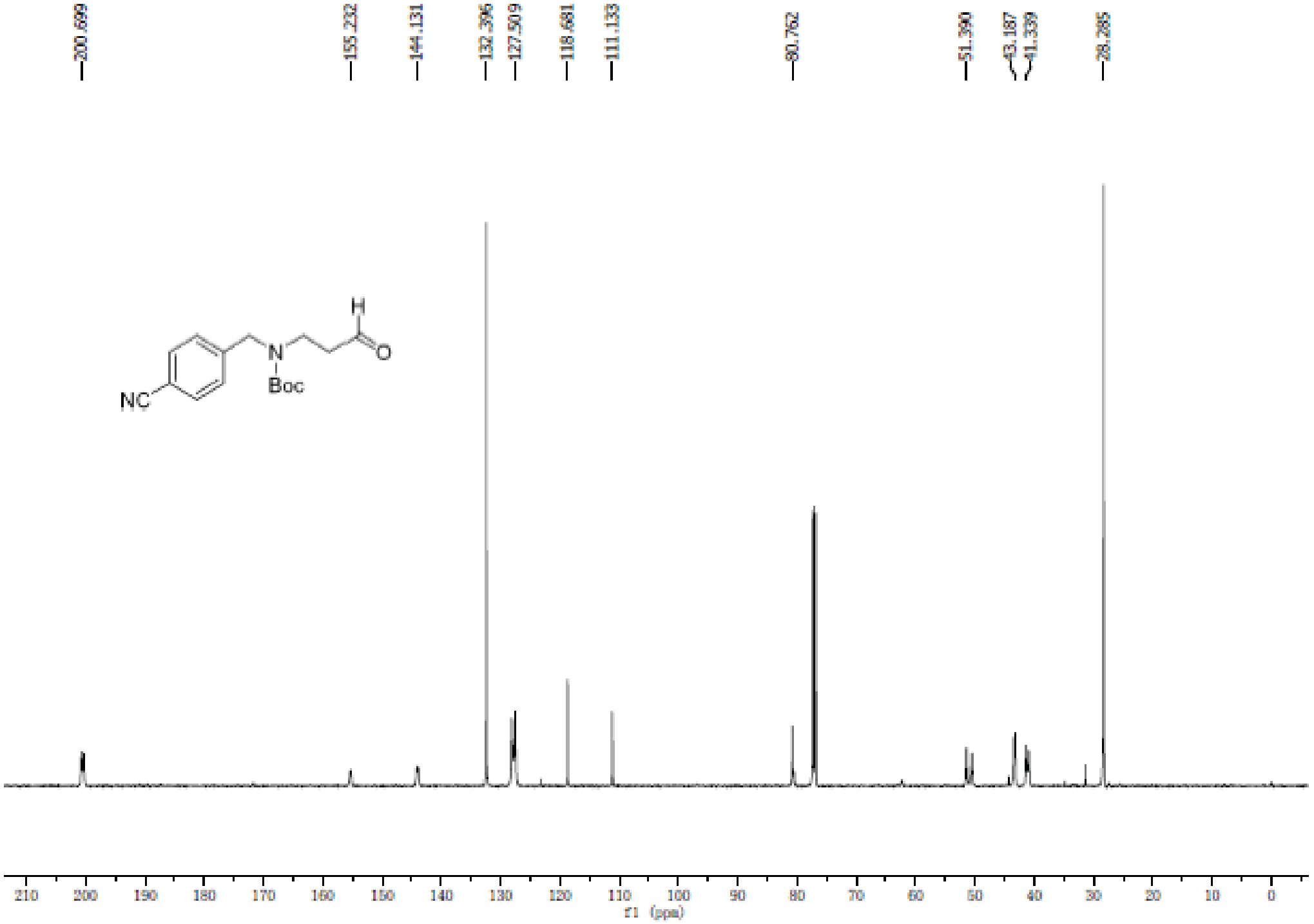
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (4-nitrilebenzyl)(3-oxopropyl)carbamate s2-h



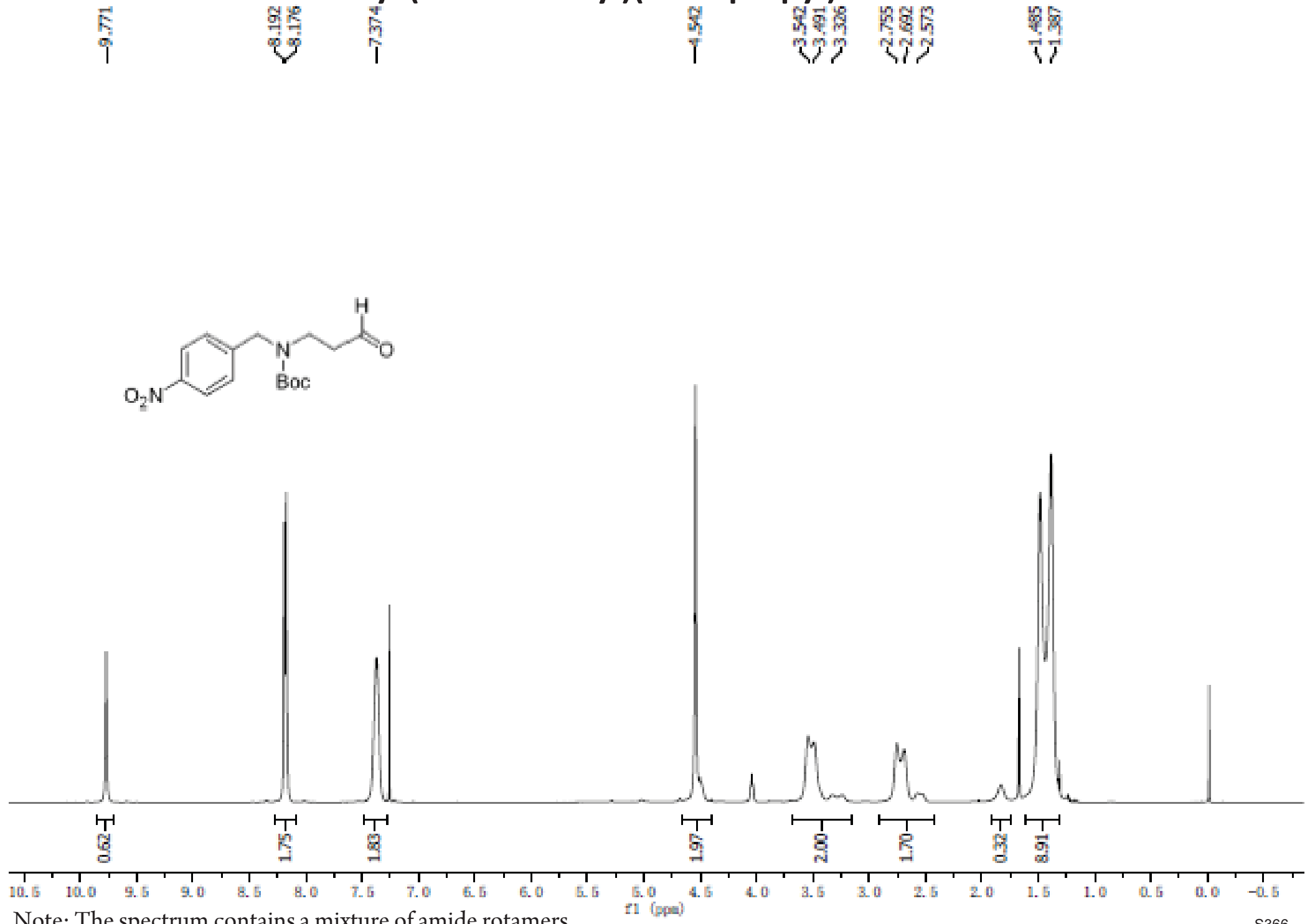
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (4-nitrilebenzyl)(3-oxopropyl)carbamate s2-h



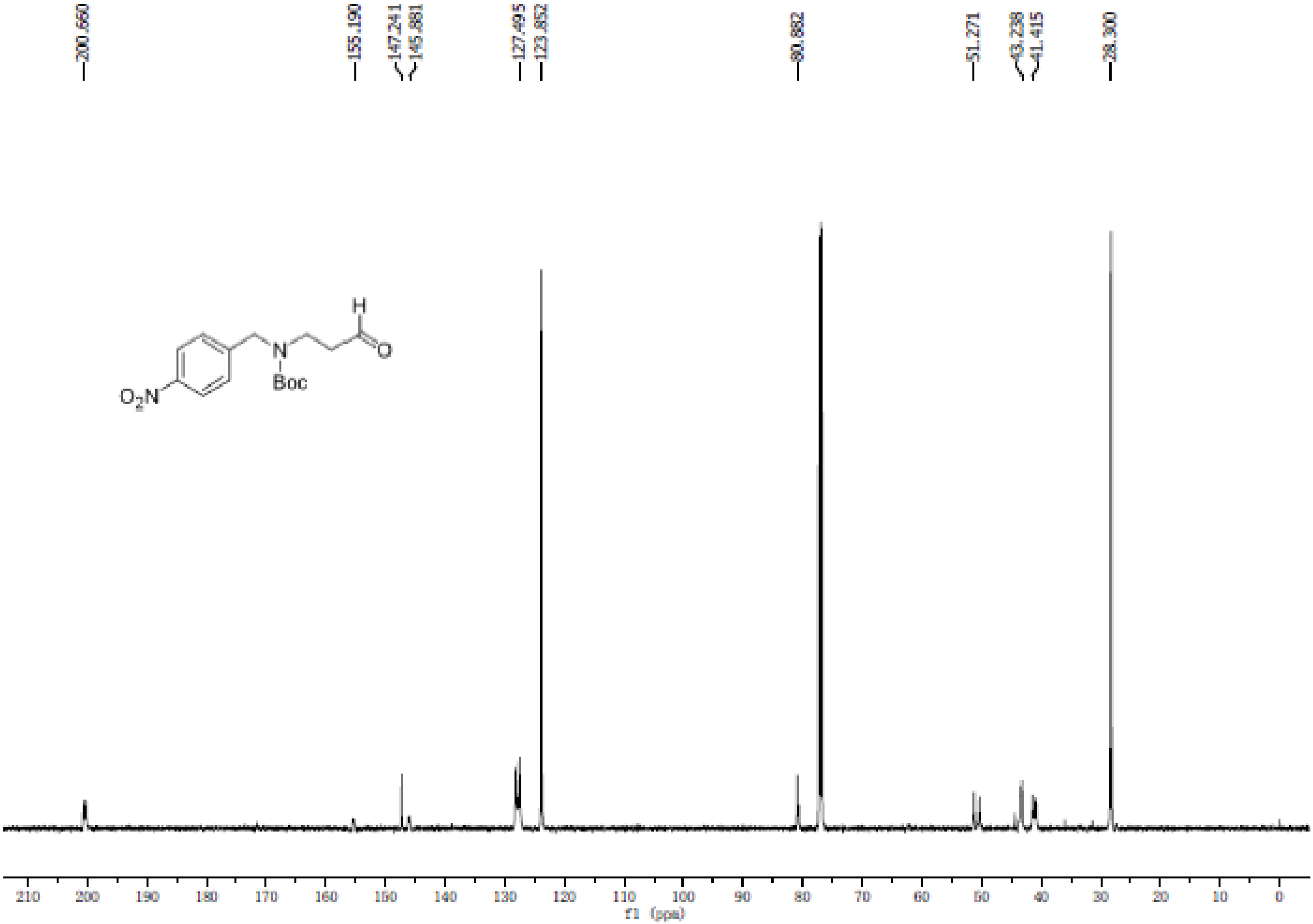
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (4-nitrobenzyl)(3-oxopropyl)carbamate s2-i



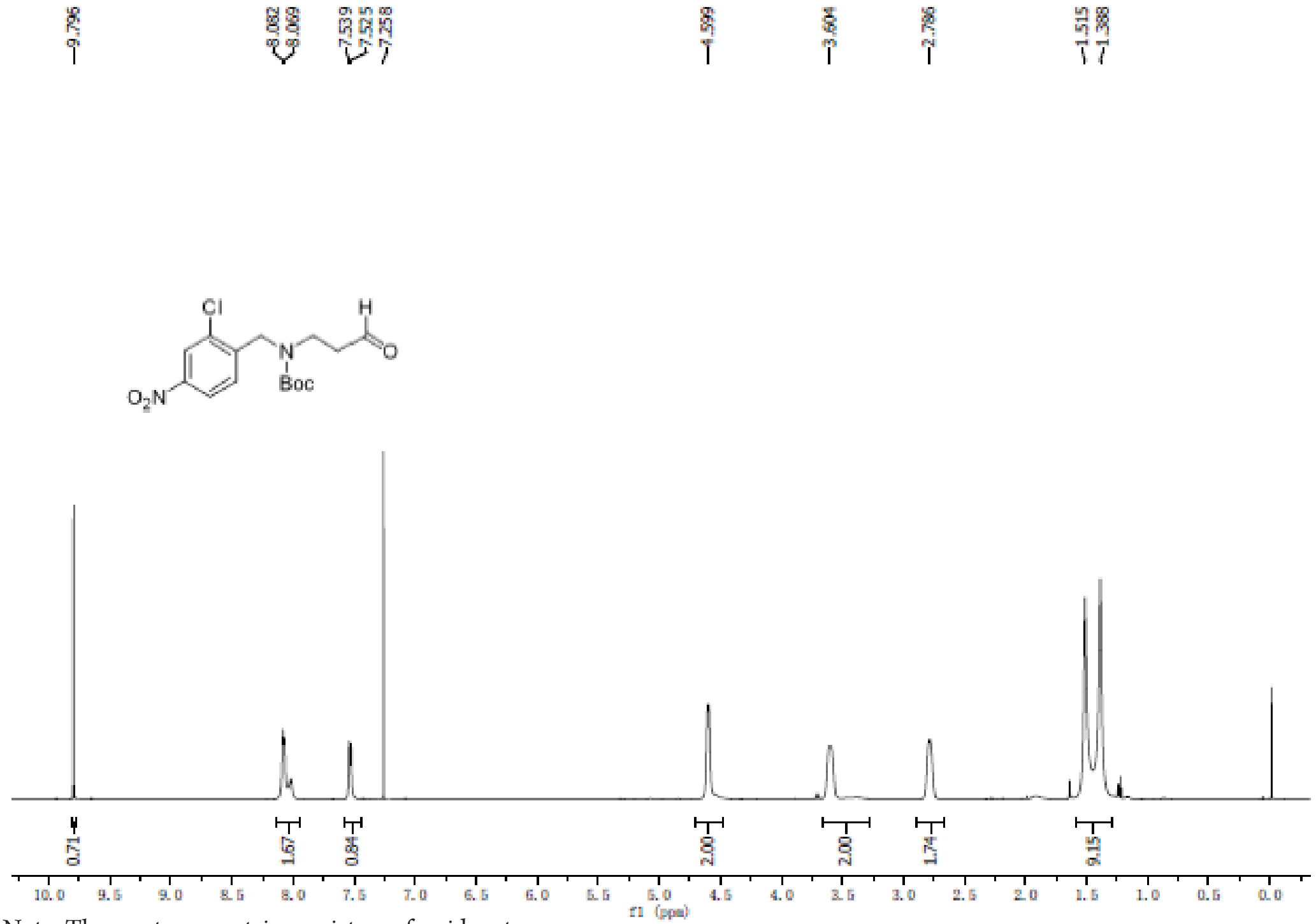
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (4-nitrobenzyl)(3-oxopropyl)carbamate s2-i



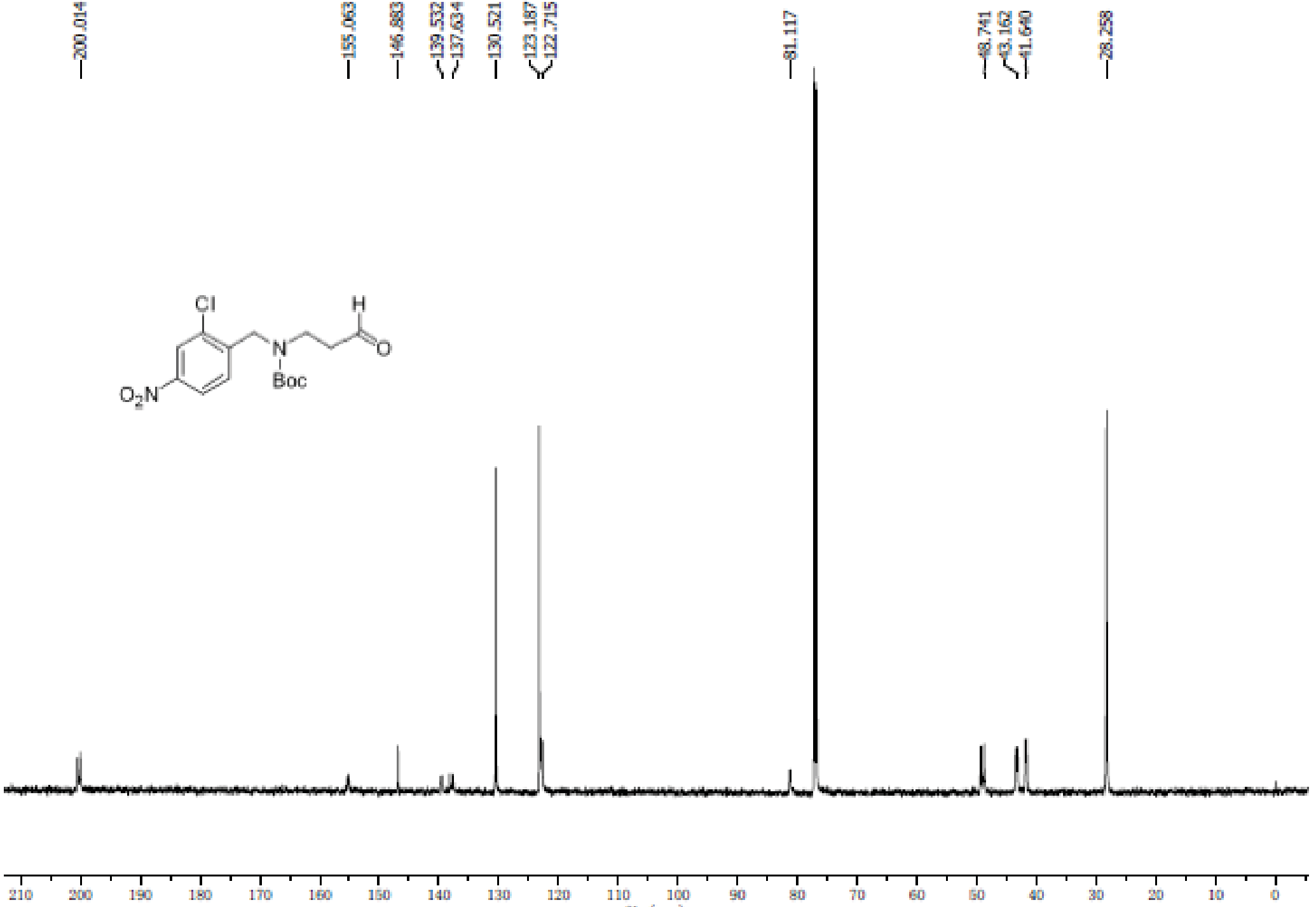
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (2-chloro-4-nitrobenzyl)(3-oxopropyl)carbamate s2-j



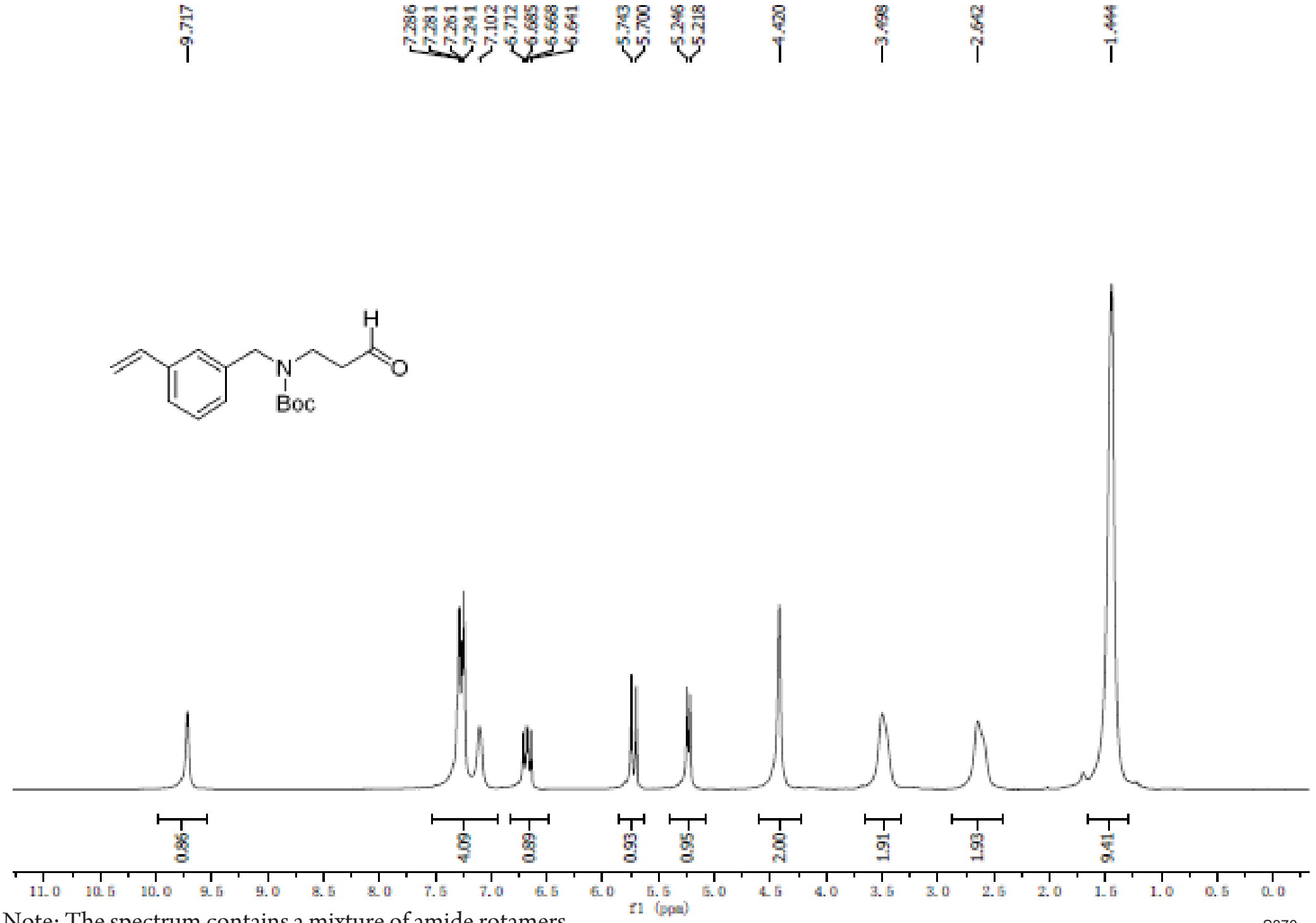
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (2-chloro-4-nitrobenzyl)(3-oxopropyl)carbamate s2-j



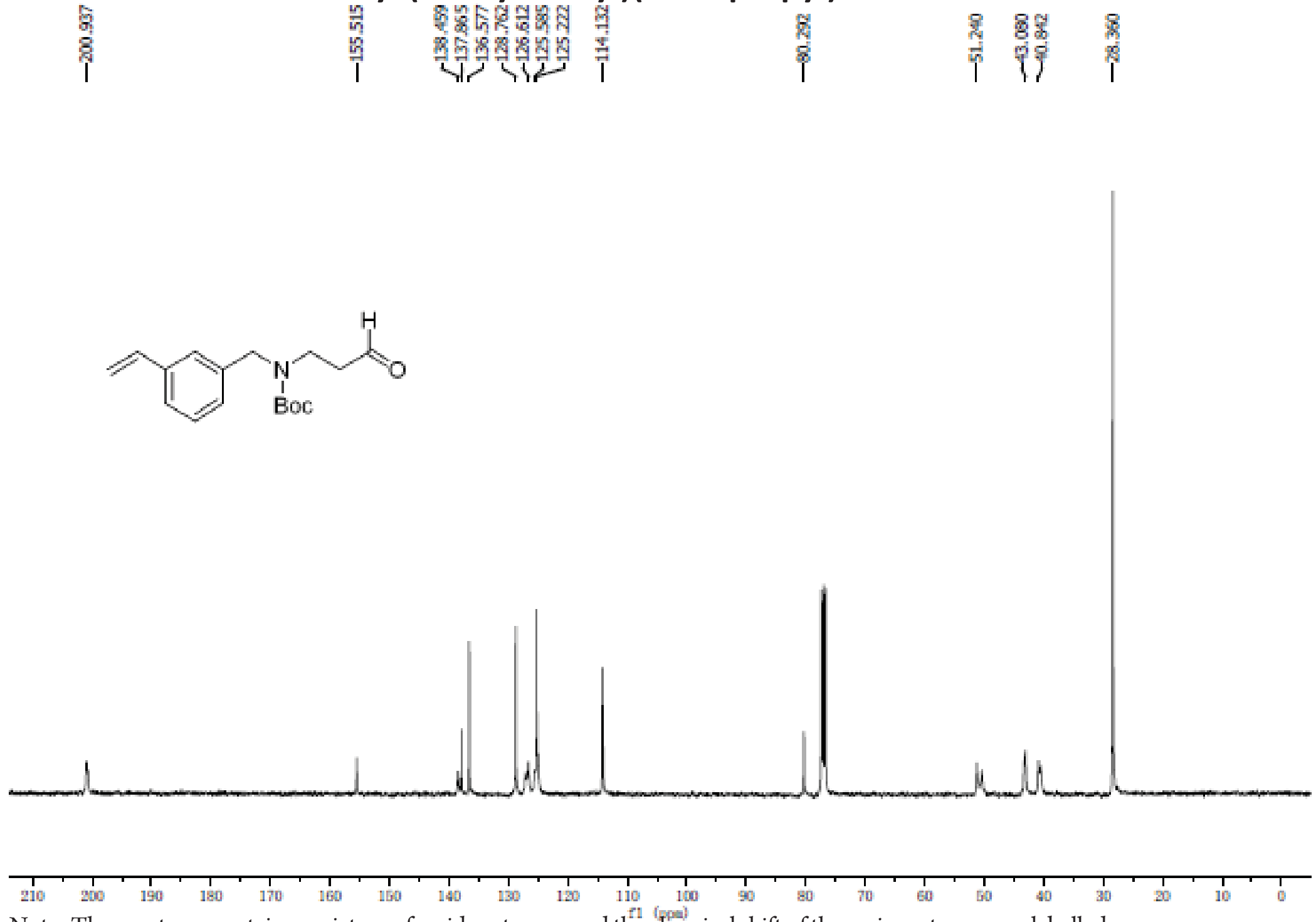
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3-vinylbenzyl)(3-oxopropyl)carbamate s2-k



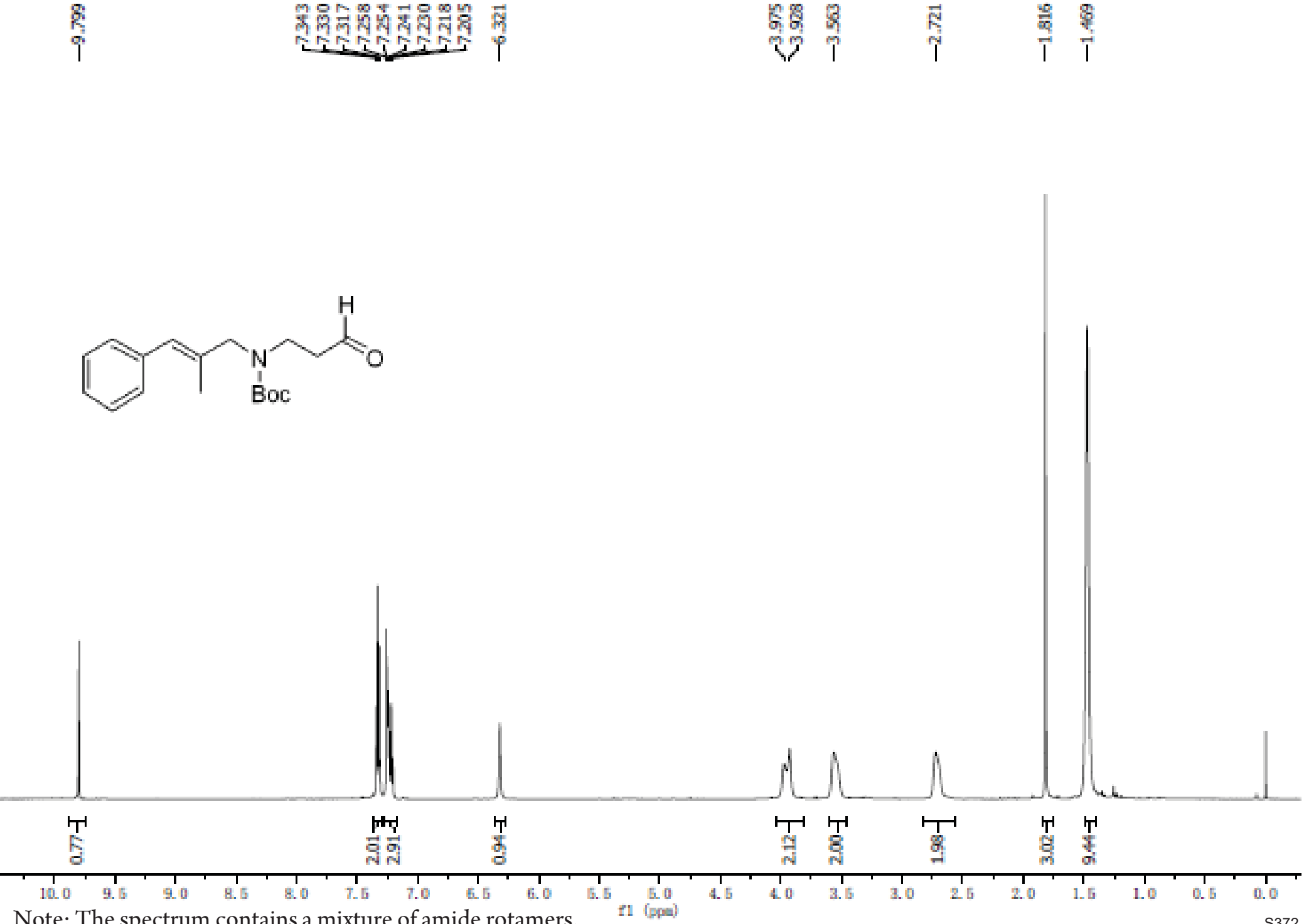
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3-vinylbenzyl)(3-oxopropyl)carbamate s2-k



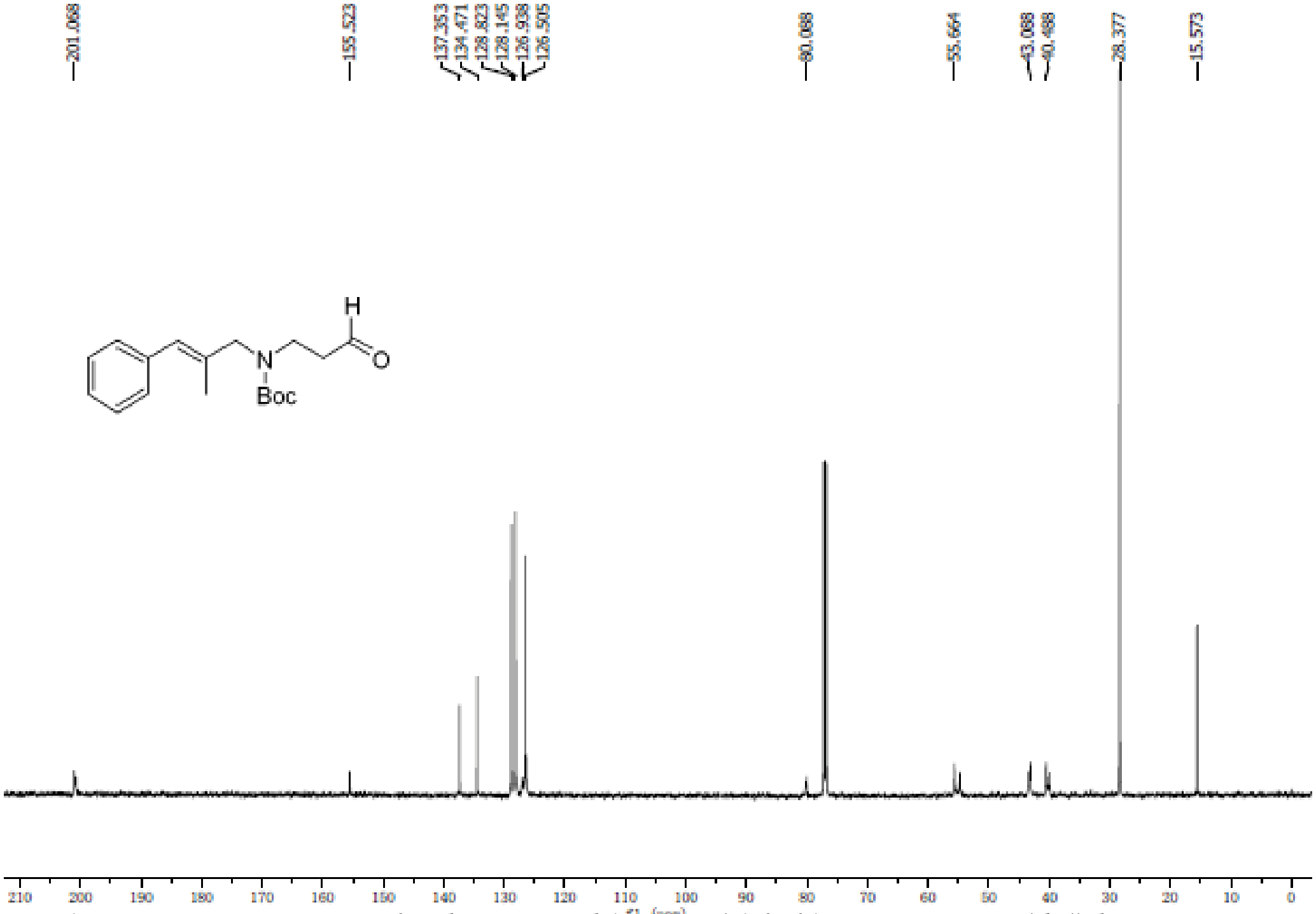
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (*E*)-(2-methyl-3-phenylallyl)(3-oxopropyl)carbamate s2-l



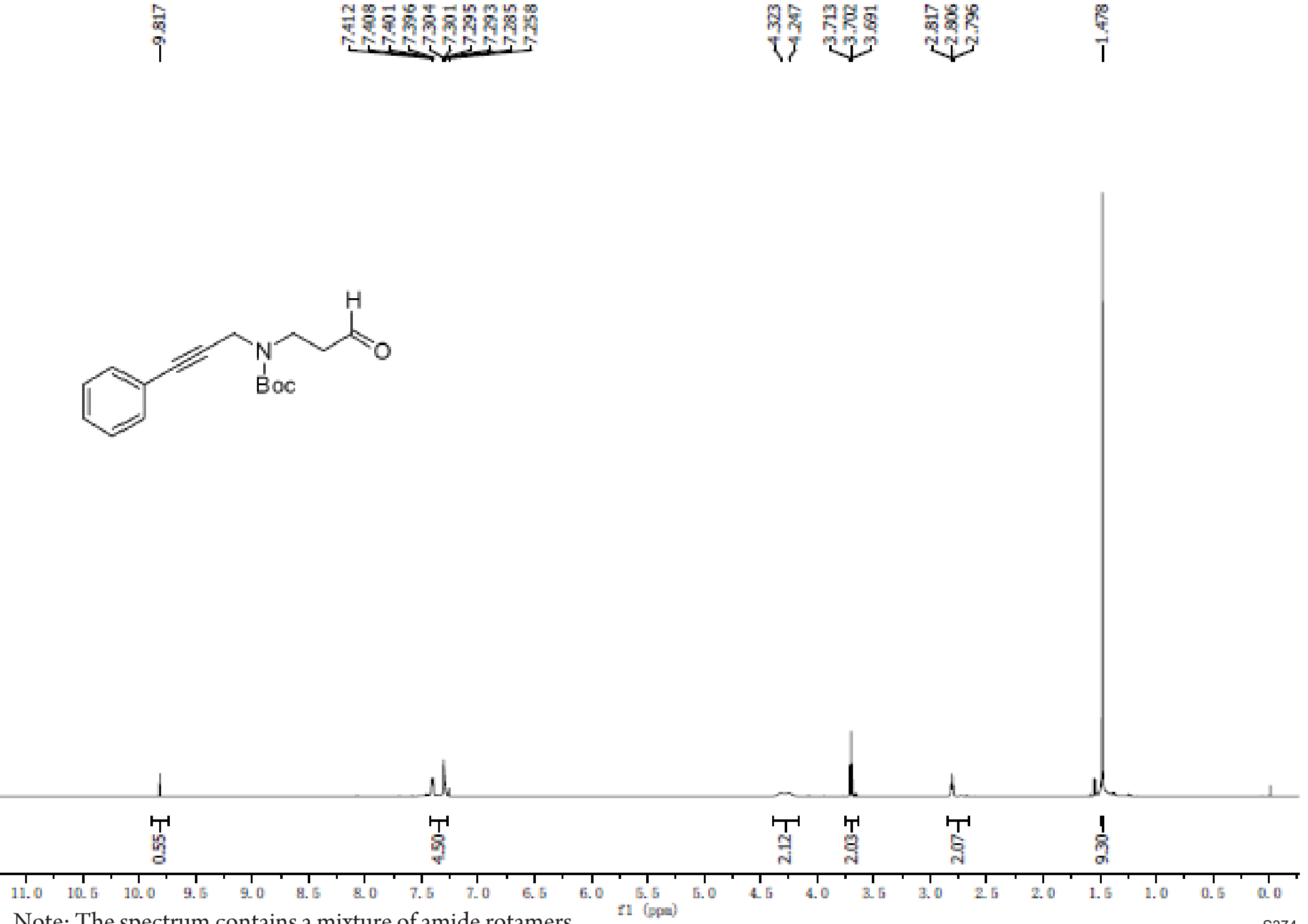
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*E*)-(2-methyl-3-phenylallyl)(3-oxopropyl)carbamate s2-l



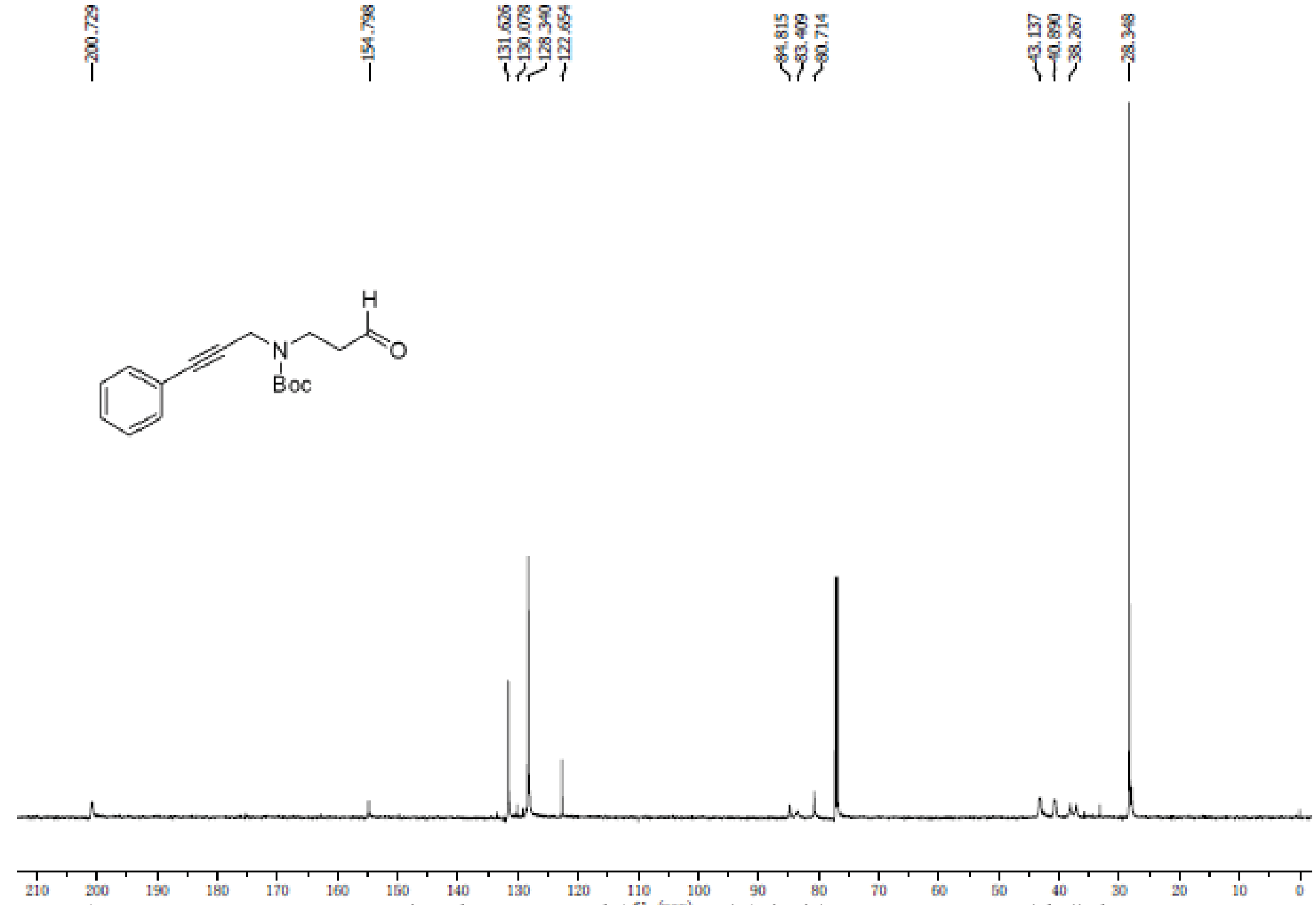
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3-oxopropyl)(3-phenylprop-2-yn-1-yl)carbamate s2-m



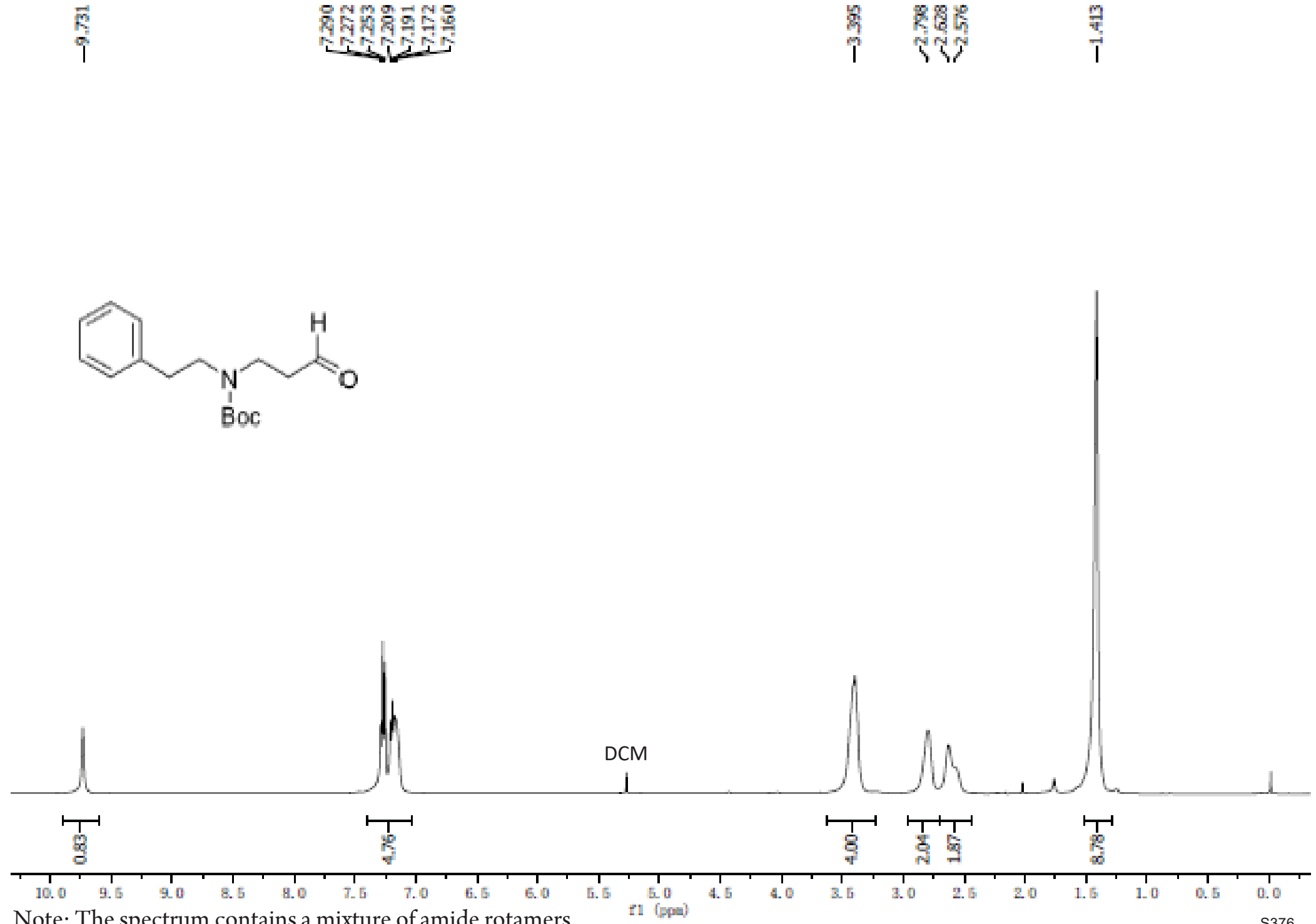
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3-oxopropyl)(3-phenylprop-2-yn-1-yl)carbamate s2-m



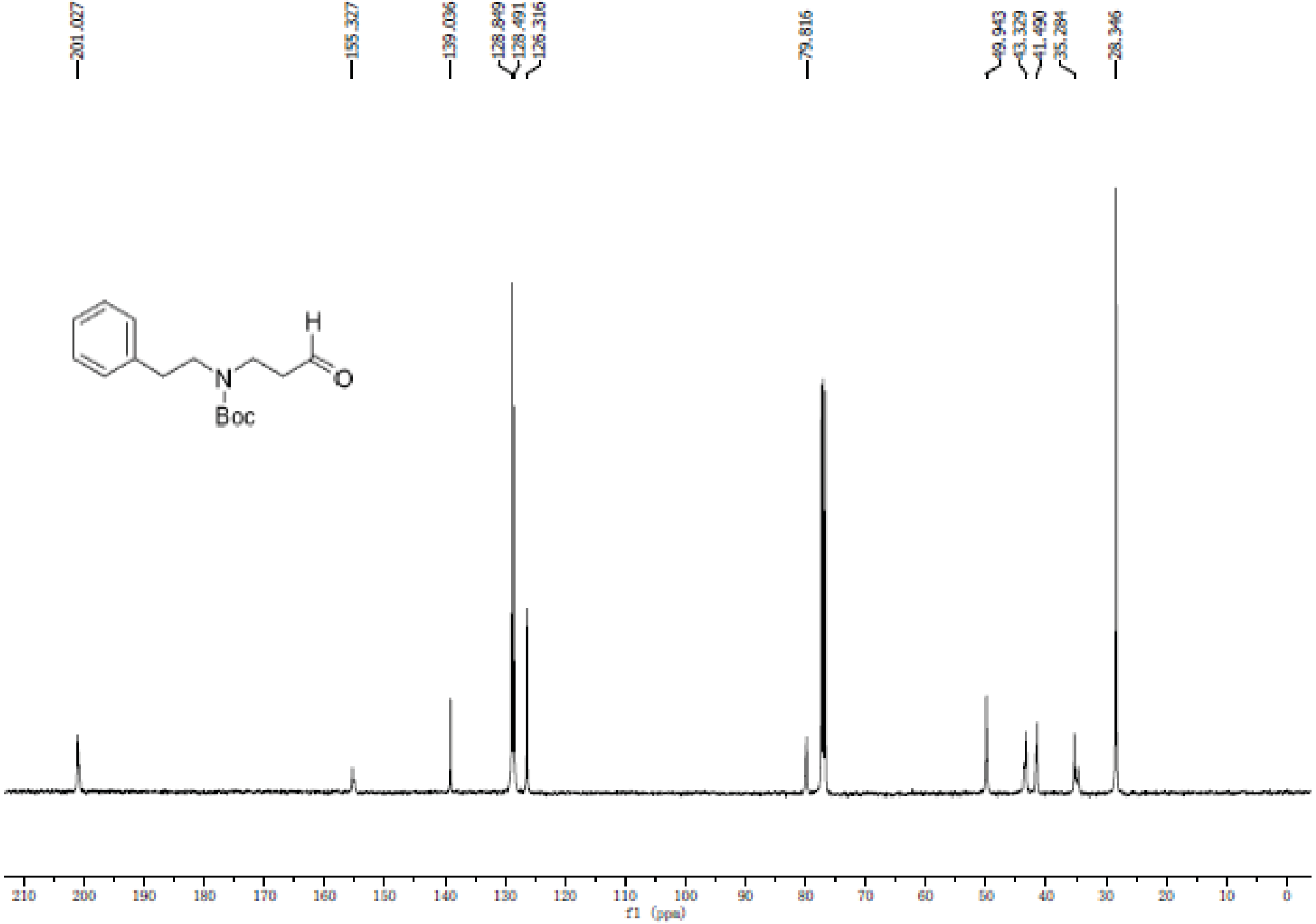
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3-oxopropyl)(phenethyl)carbamate s2-n



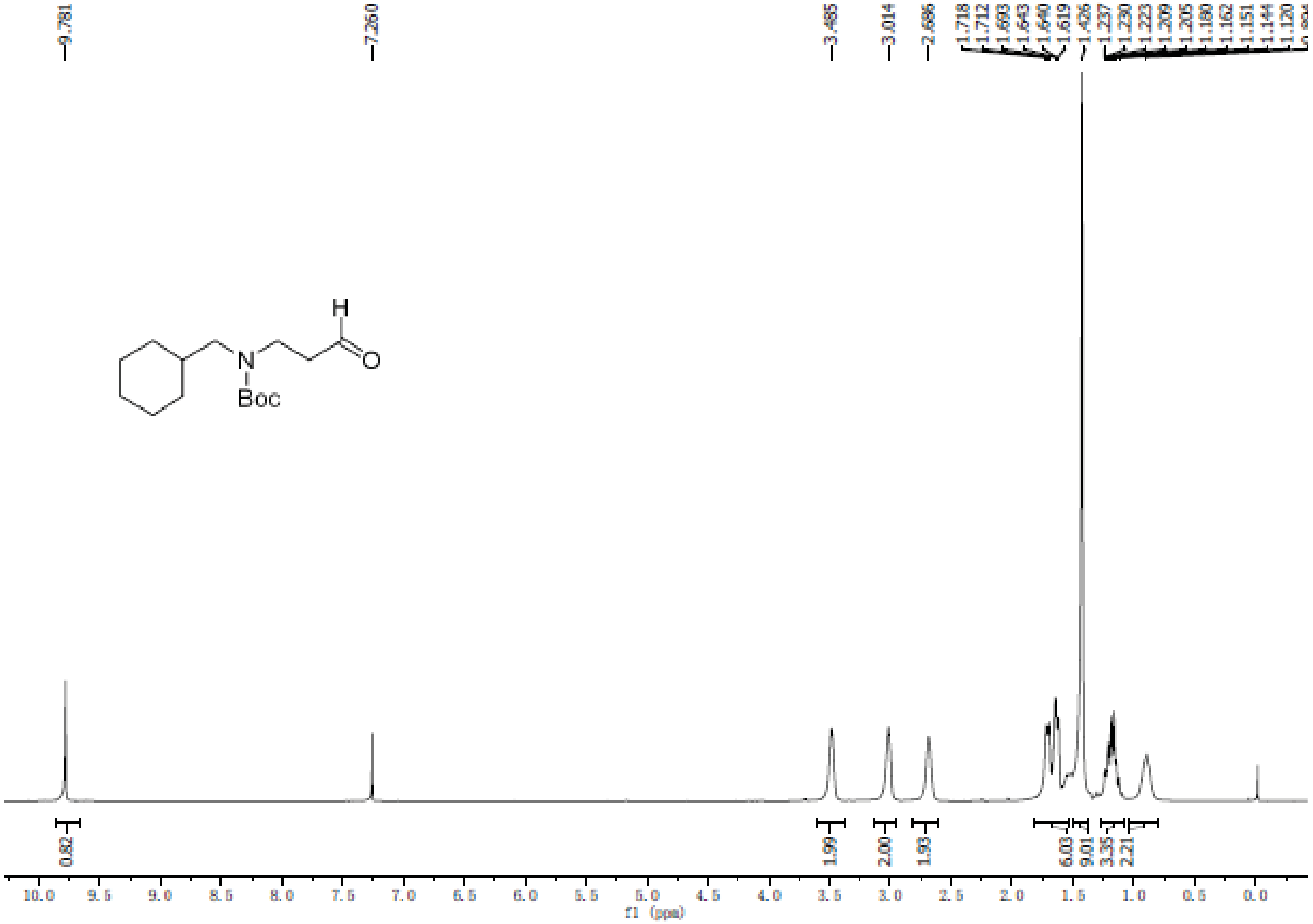
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3-oxopropyl)(phenethyl)carbamate s2-n



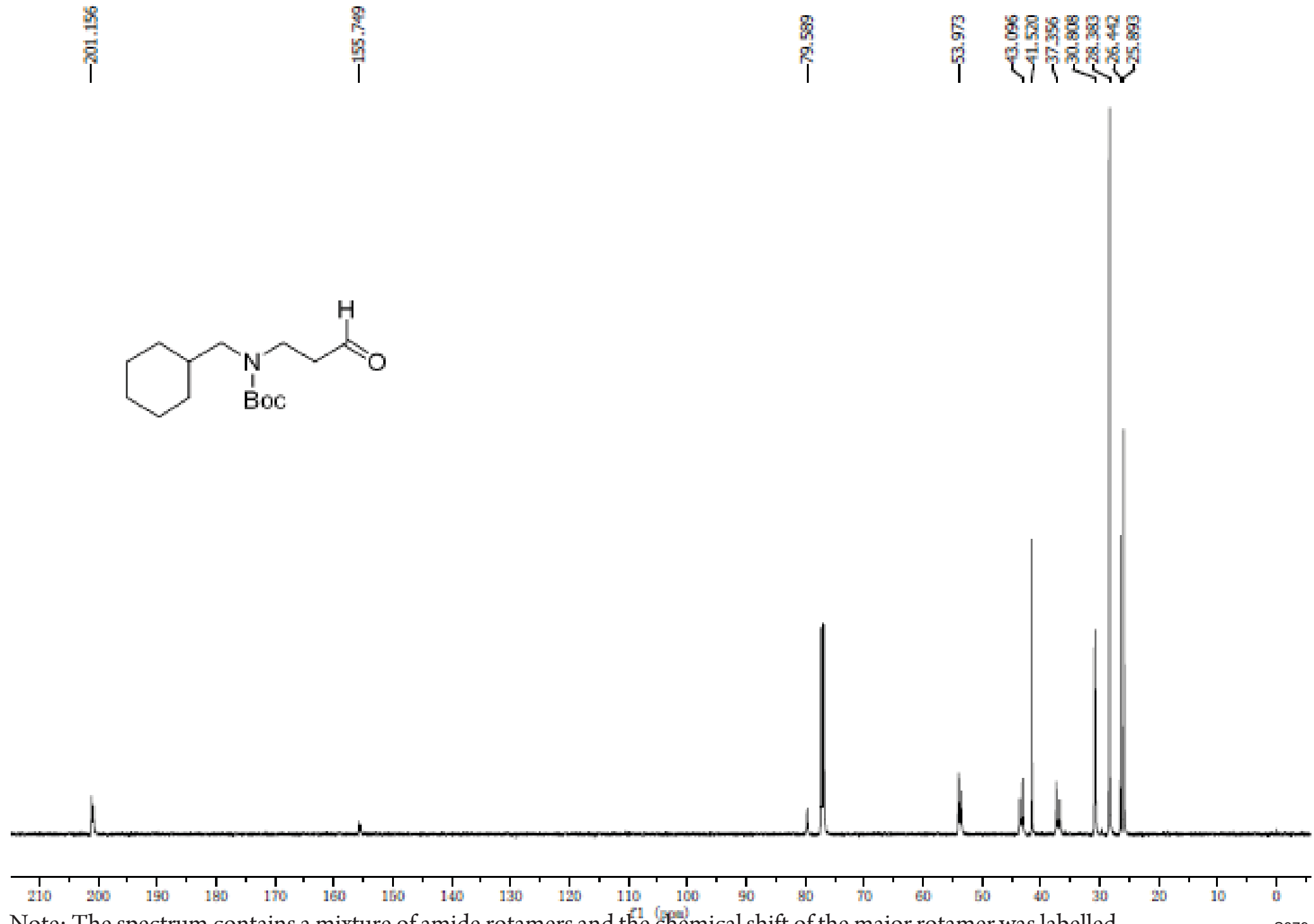
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (cyclohexylmethyl)(3-oxopropyl)carbamate s2-o



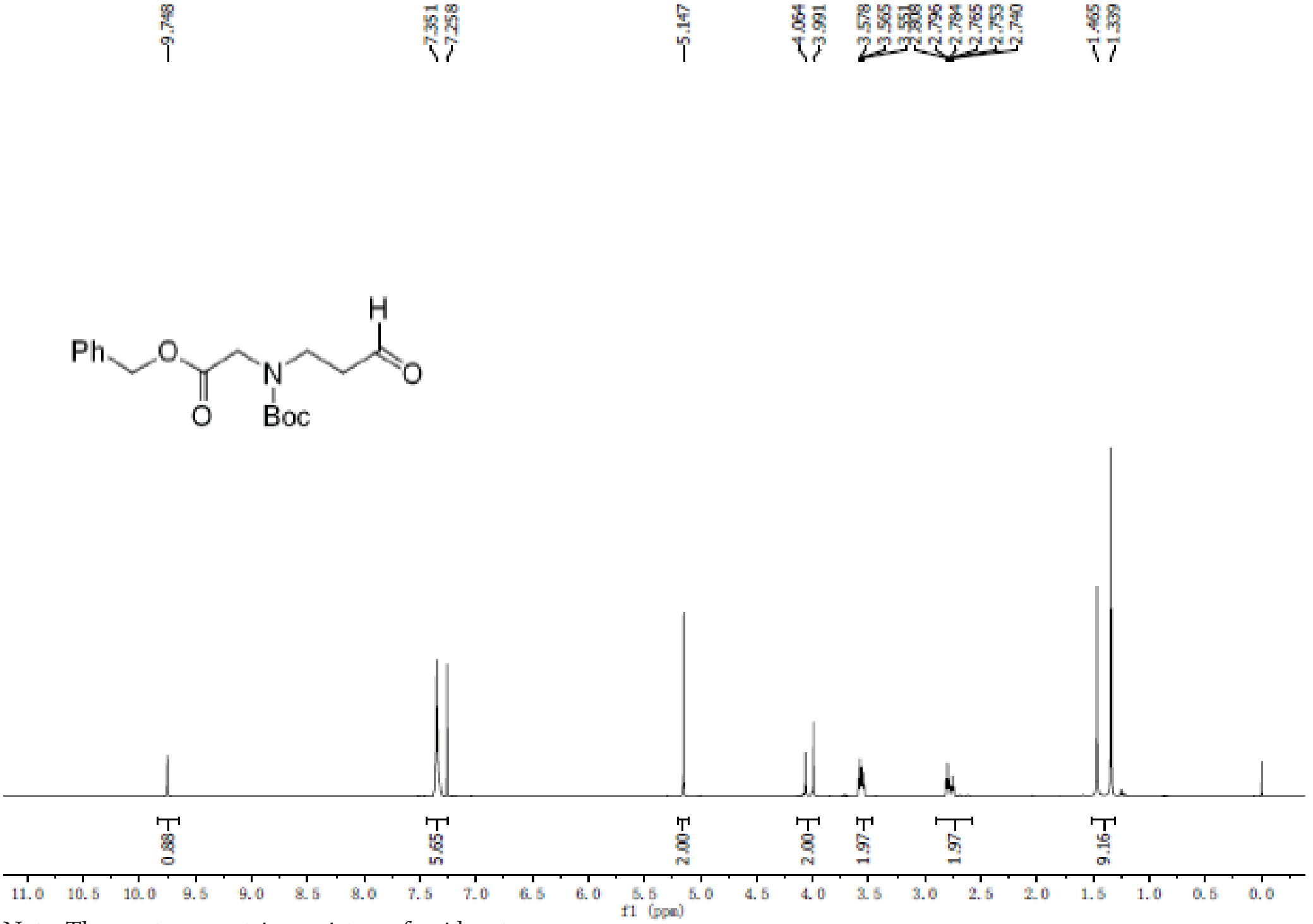
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (cyclohexylmethyl)(3-oxopropyl)carbamate s2-o



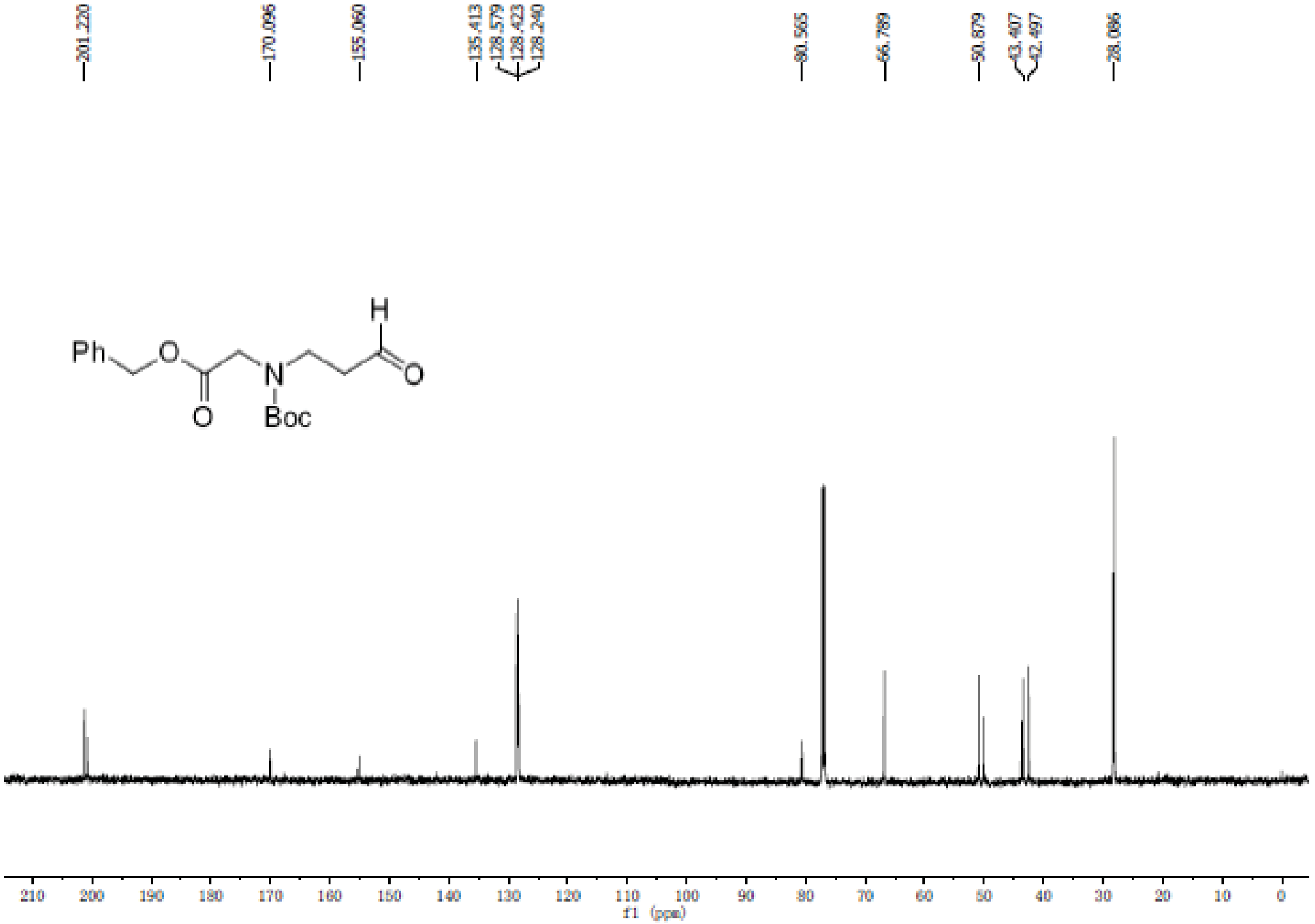
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

benzyl *N*-(*tert*-butoxycarbonyl)-*N*-(3-oxopropyl)glycinate s2-p



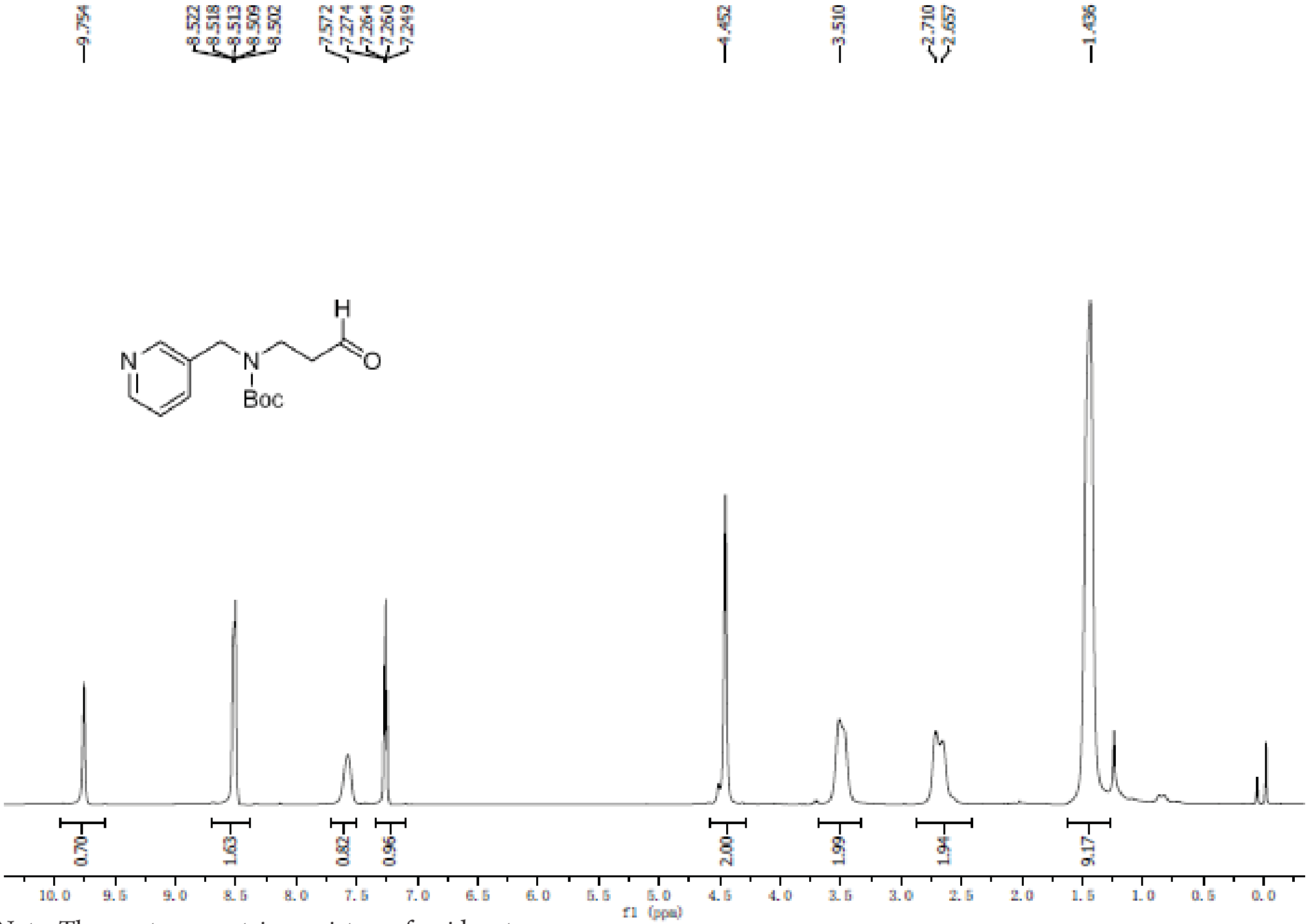
Note: The spectrum contains a mixture of amide rotamers.

benzyl *N*-(*tert*-butoxycarbonyl)-*N*-(3-oxopropyl)glycinate s2-p



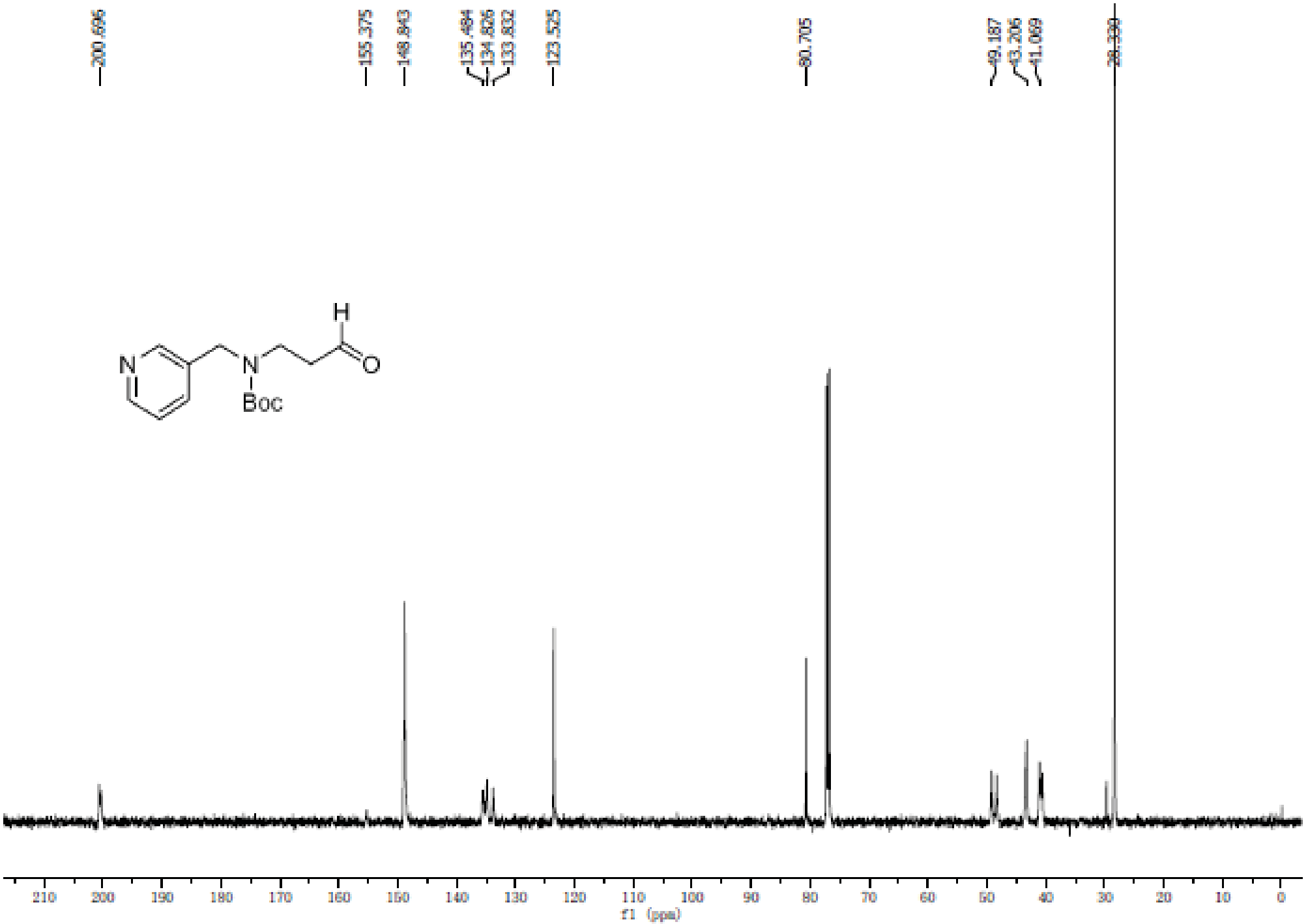
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3-oxopropyl)(pyridin-3-ylmethyl)carbamate s2-q



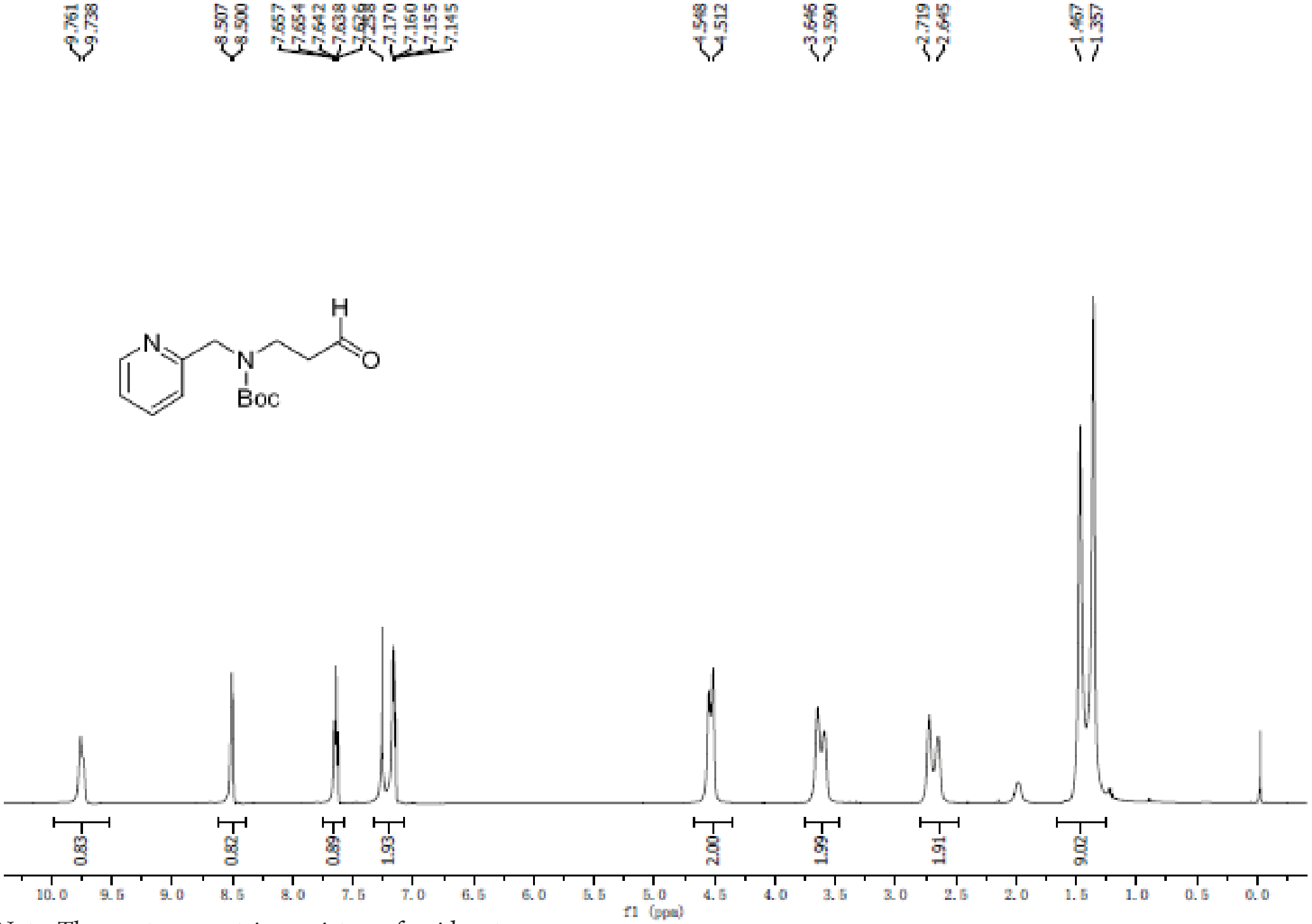
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3-oxopropyl)(pyridin-3-ylmethyl)carbamate s2-q



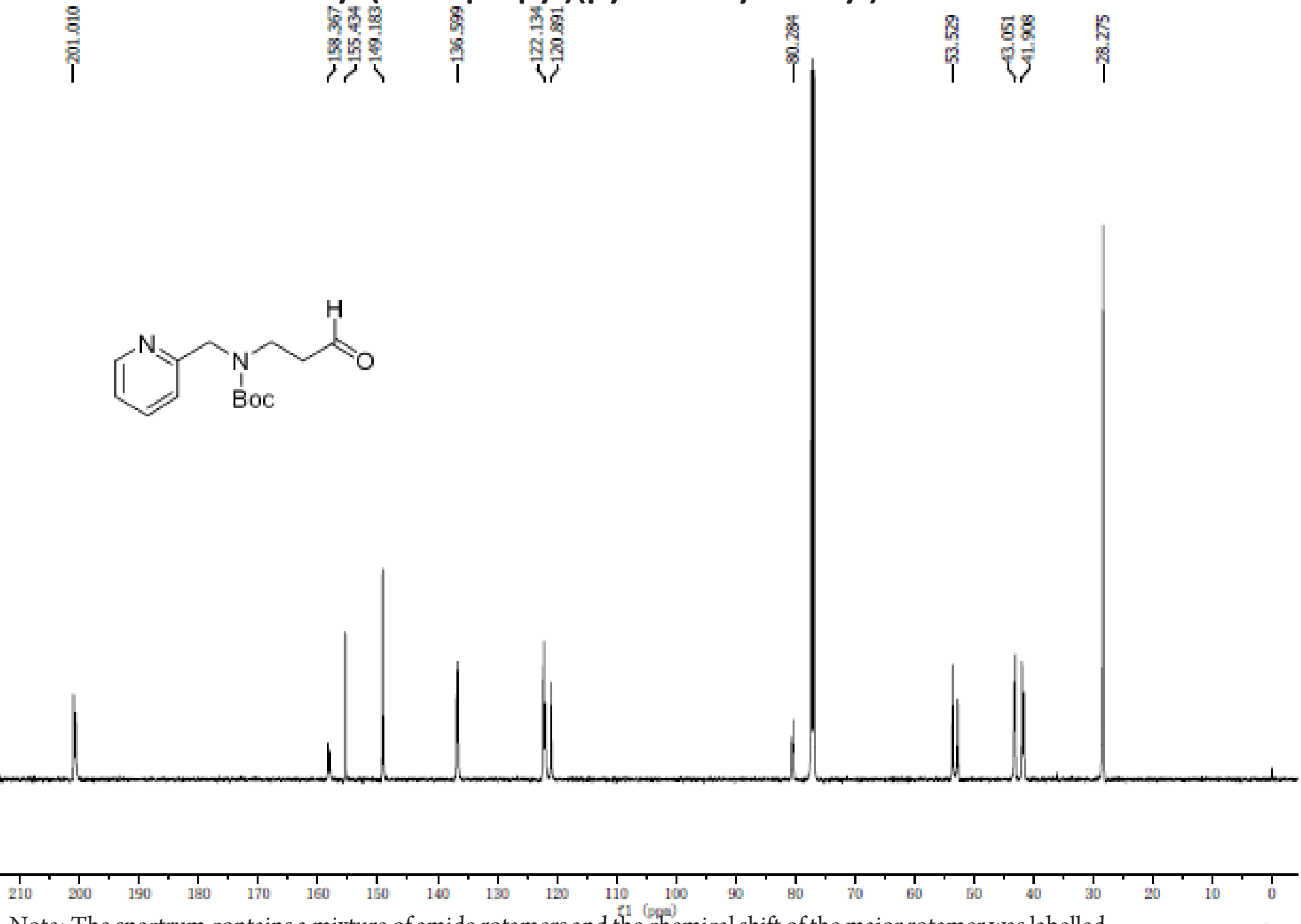
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3-oxopropyl)(pyridin-2-ylmethyl)carbamate s2-r



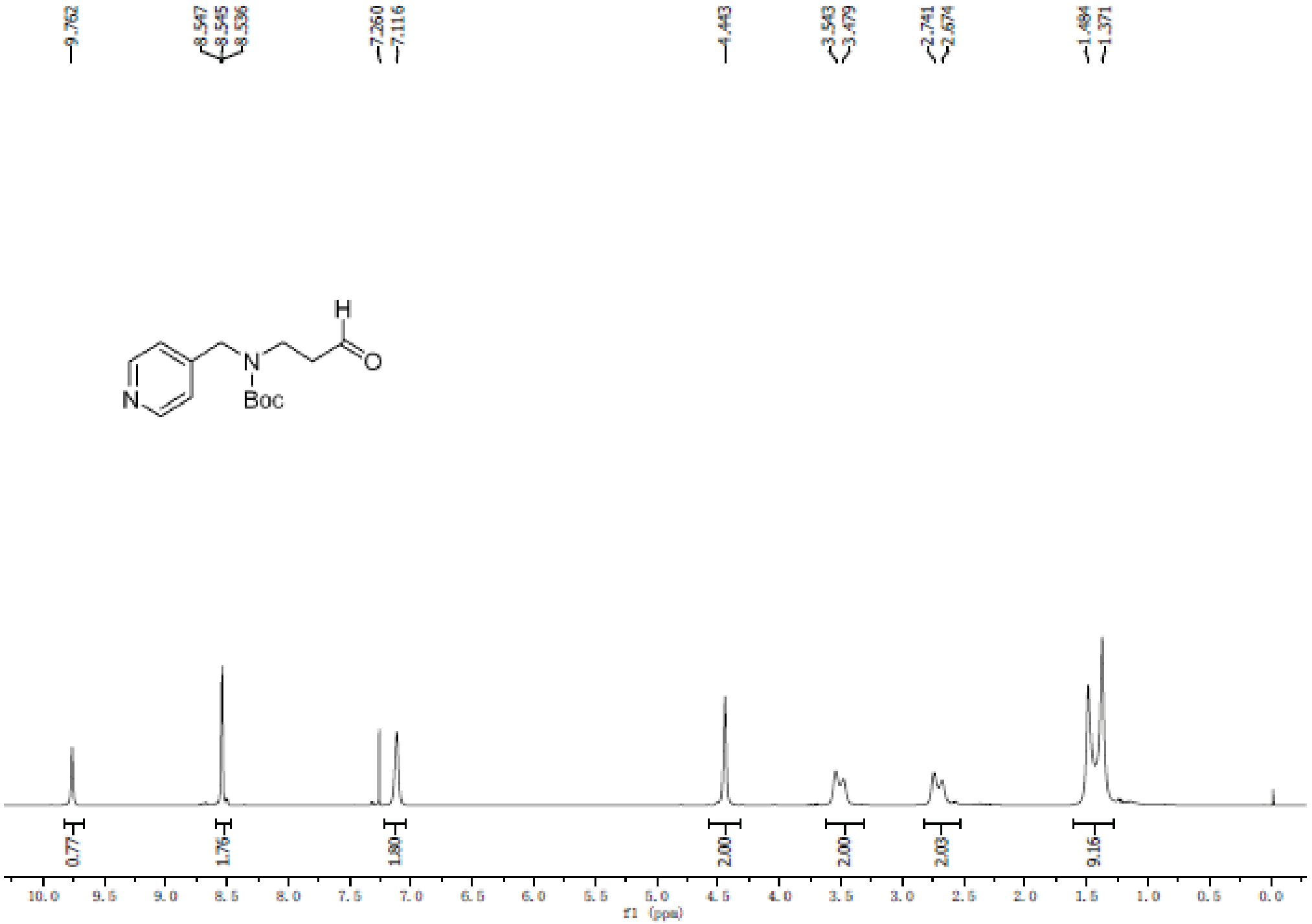
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3-oxopropyl)(pyridin-2-ylmethyl)carbamate s2-r



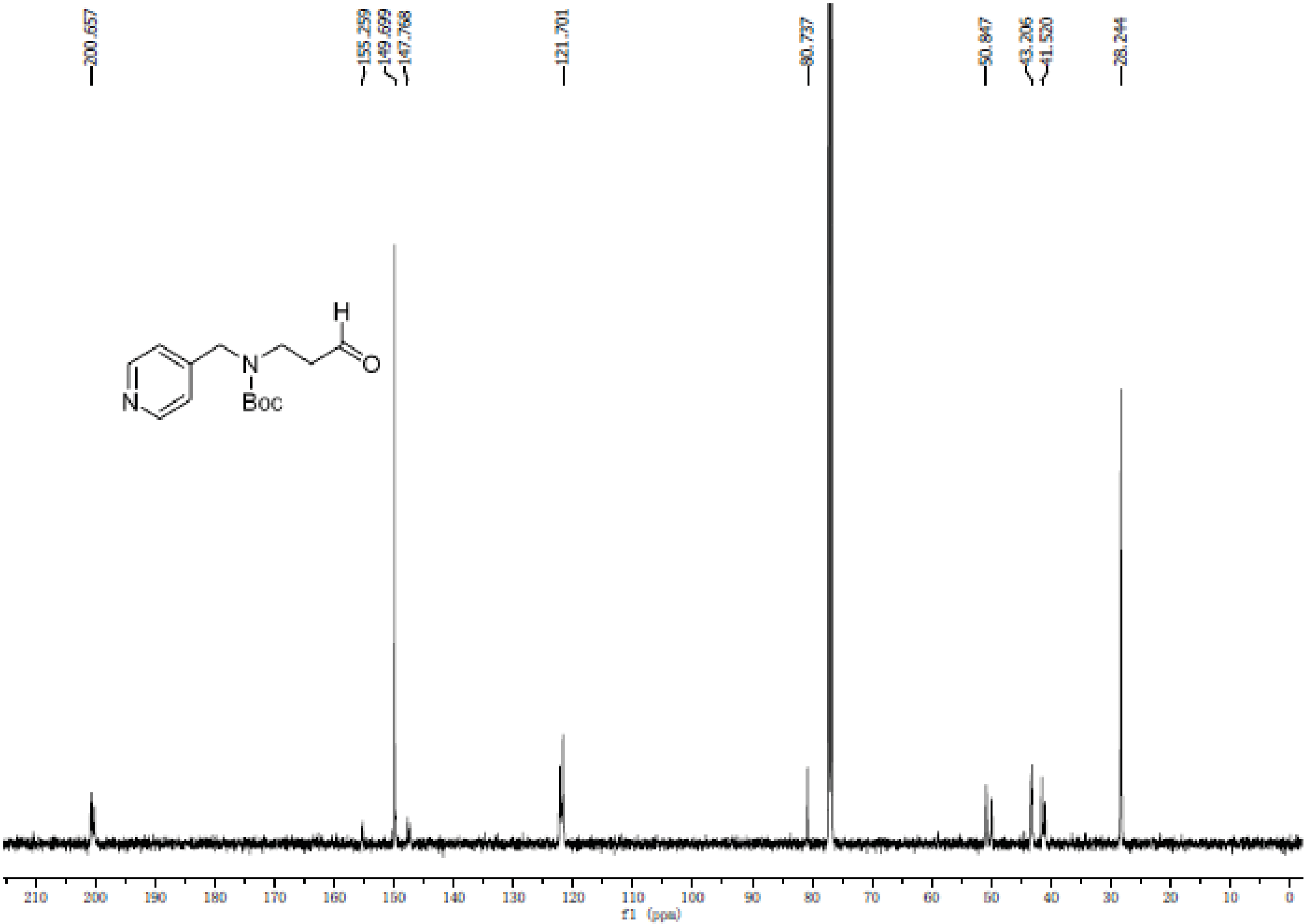
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3-oxopropyl)(pyridin-4-ylmethyl)carbamate s2-s



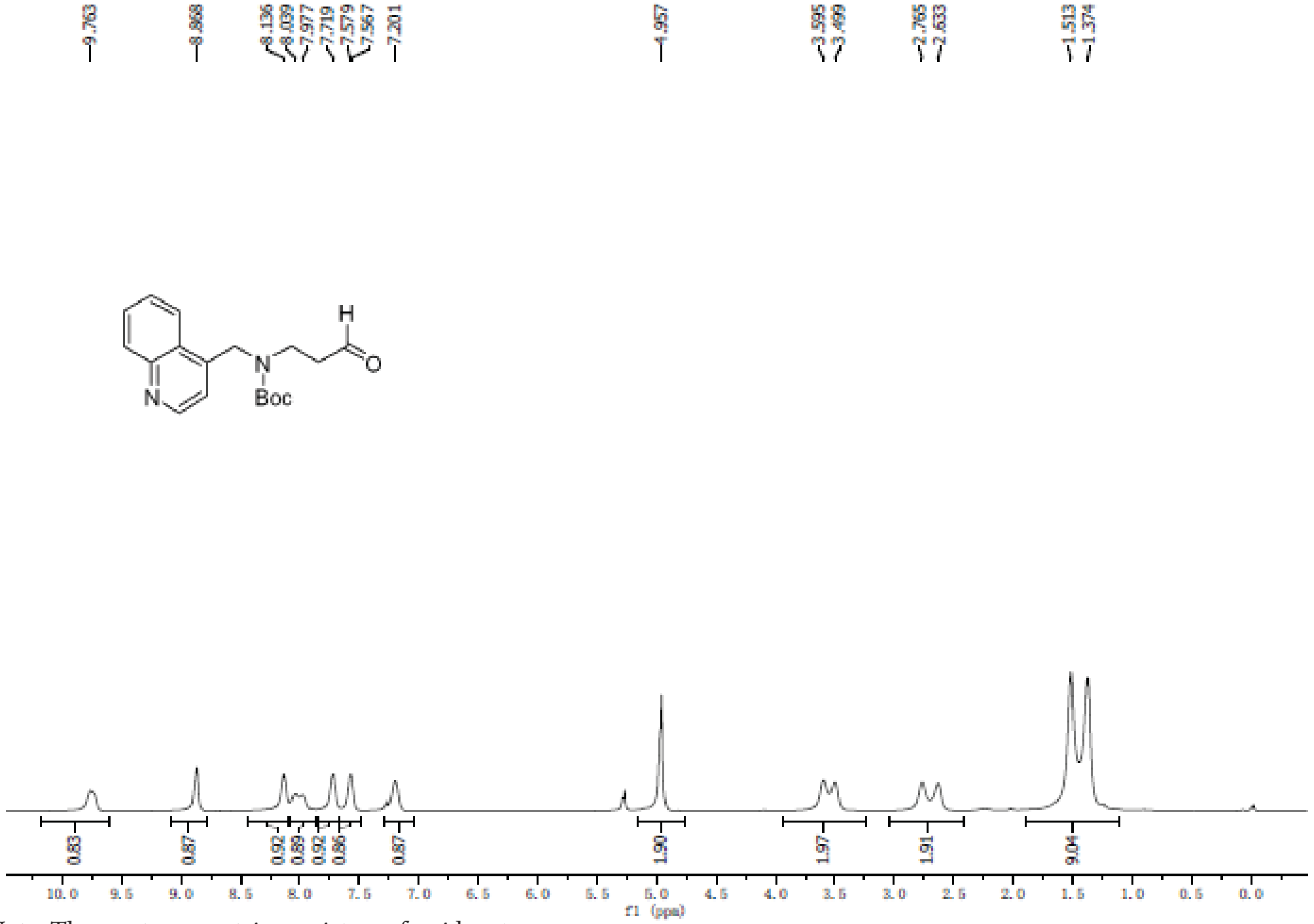
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3-oxopropyl)(pyridin-4-ylmethyl)carbamate s2-s



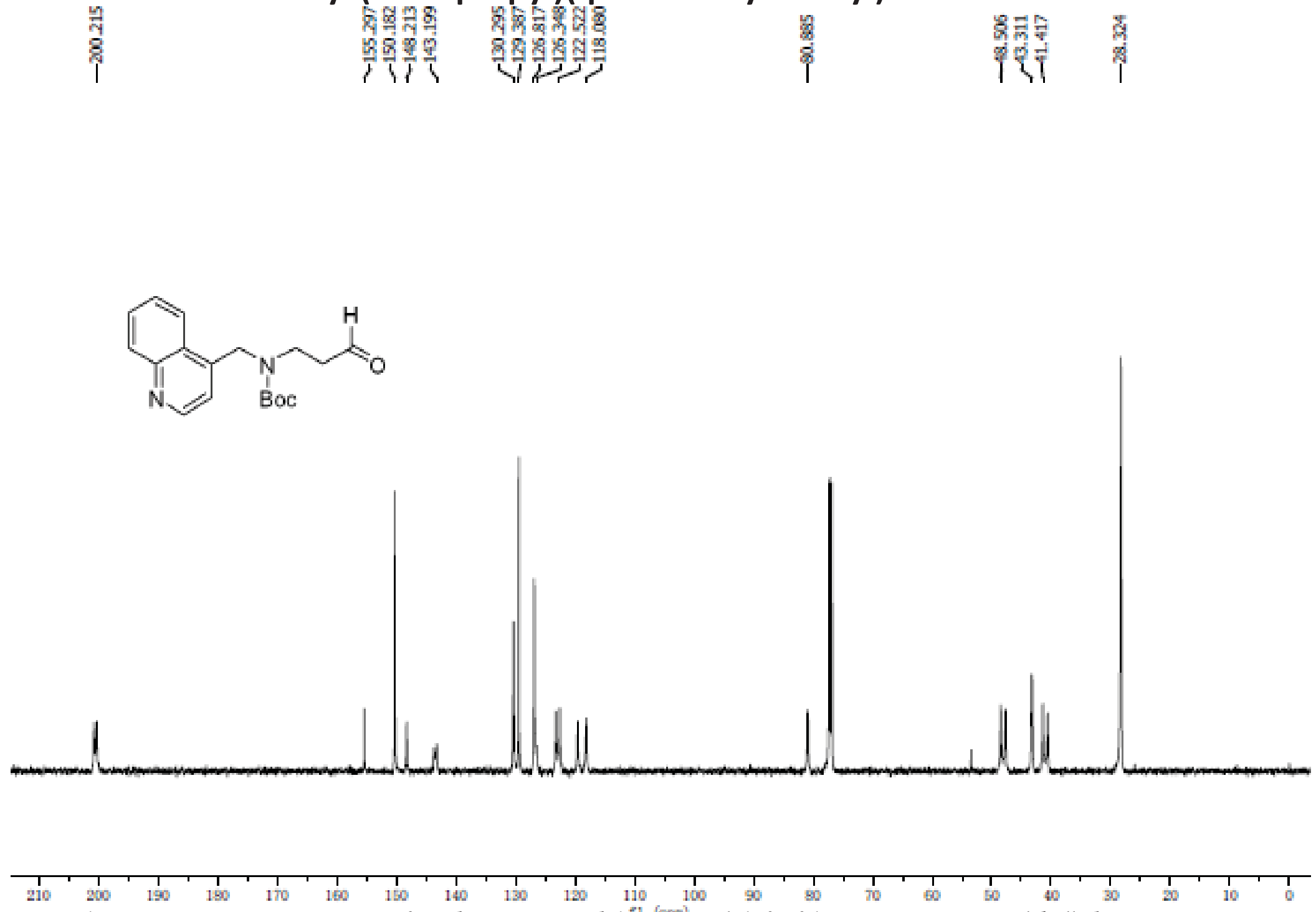
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3-oxopropyl)(quinolin-4-ylmethyl)carbamate s2-t



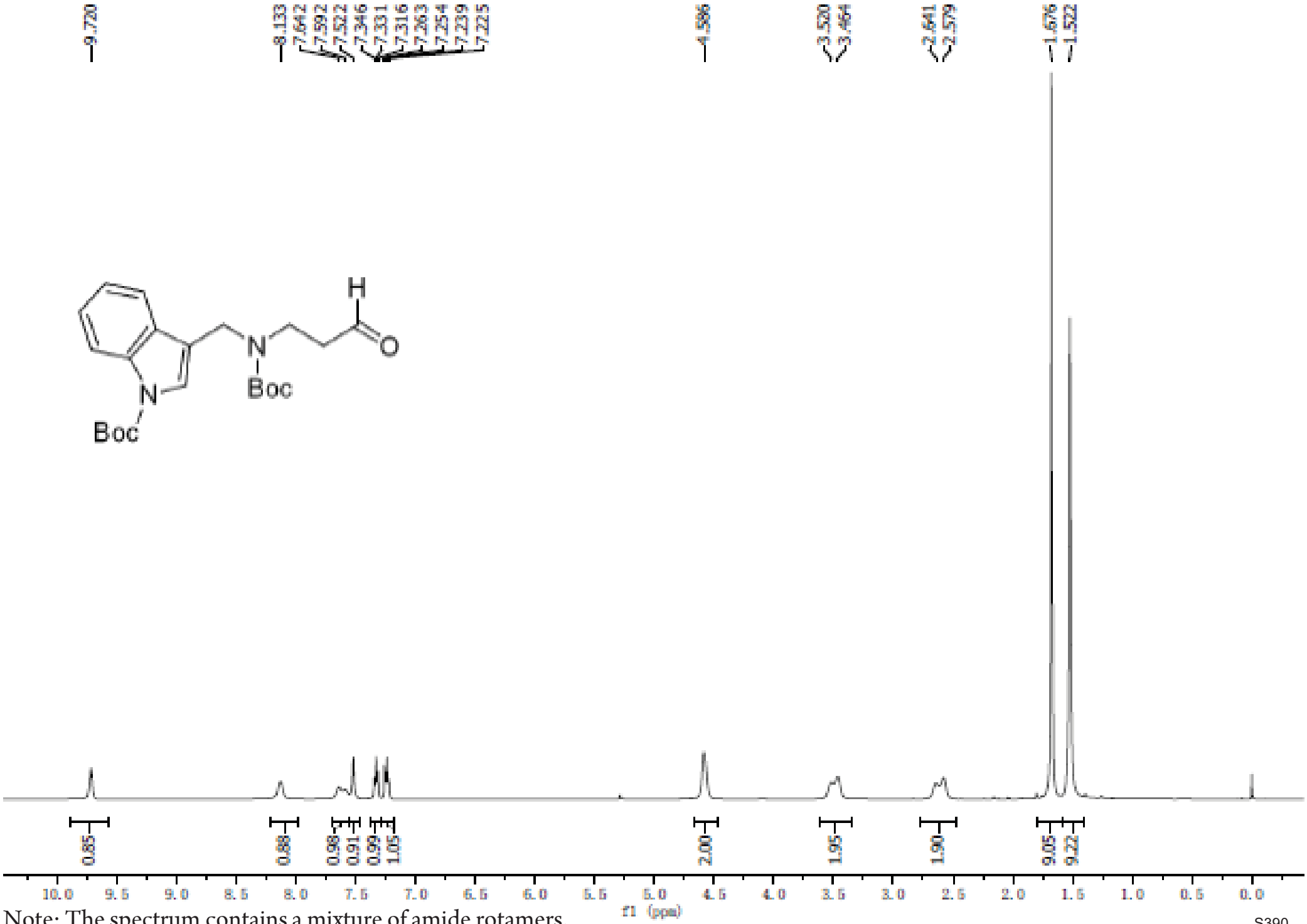
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3-oxopropyl)(quinolin-4-ylmethyl)carbamate s2-t



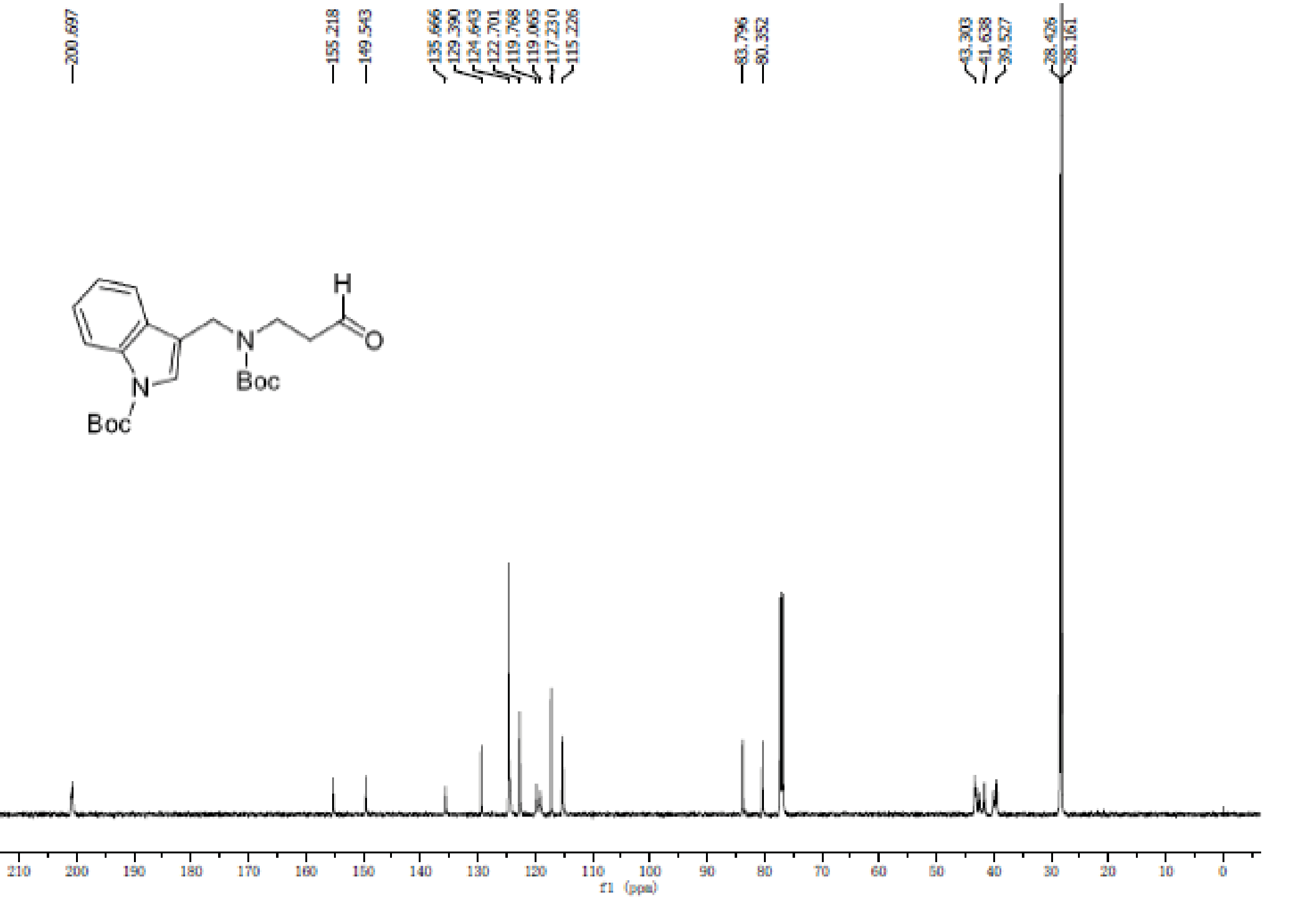
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl 3-(((*tert*-butoxycarbonyl)(3-oxopropyl)amino)methyl)-1H-indole-1-carboxylate s2-u



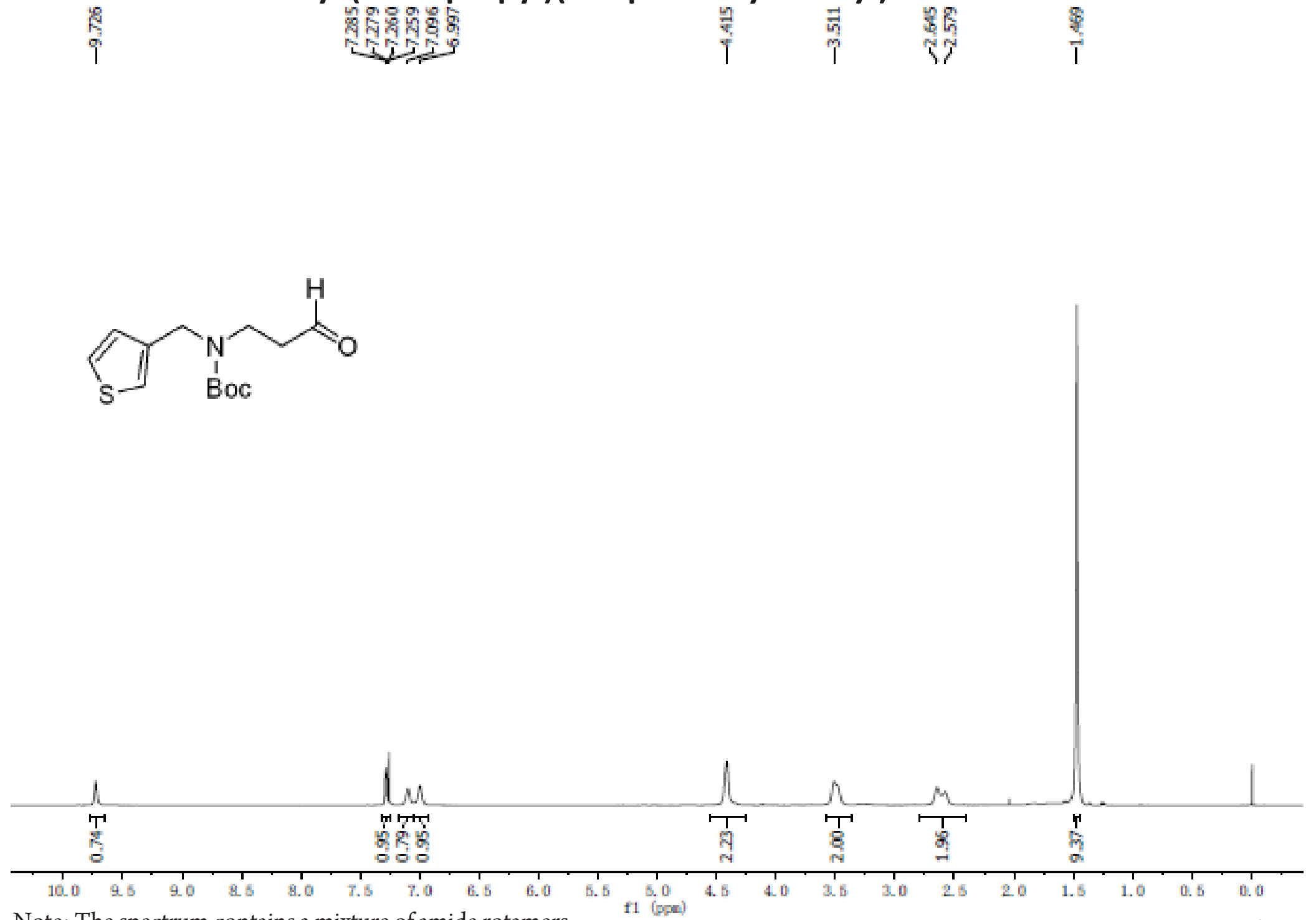
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl 3-(((*tert*-butoxycarbonyl)(3-oxopropyl)amino)methyl)-1H-indole-1-carboxylate s2-u



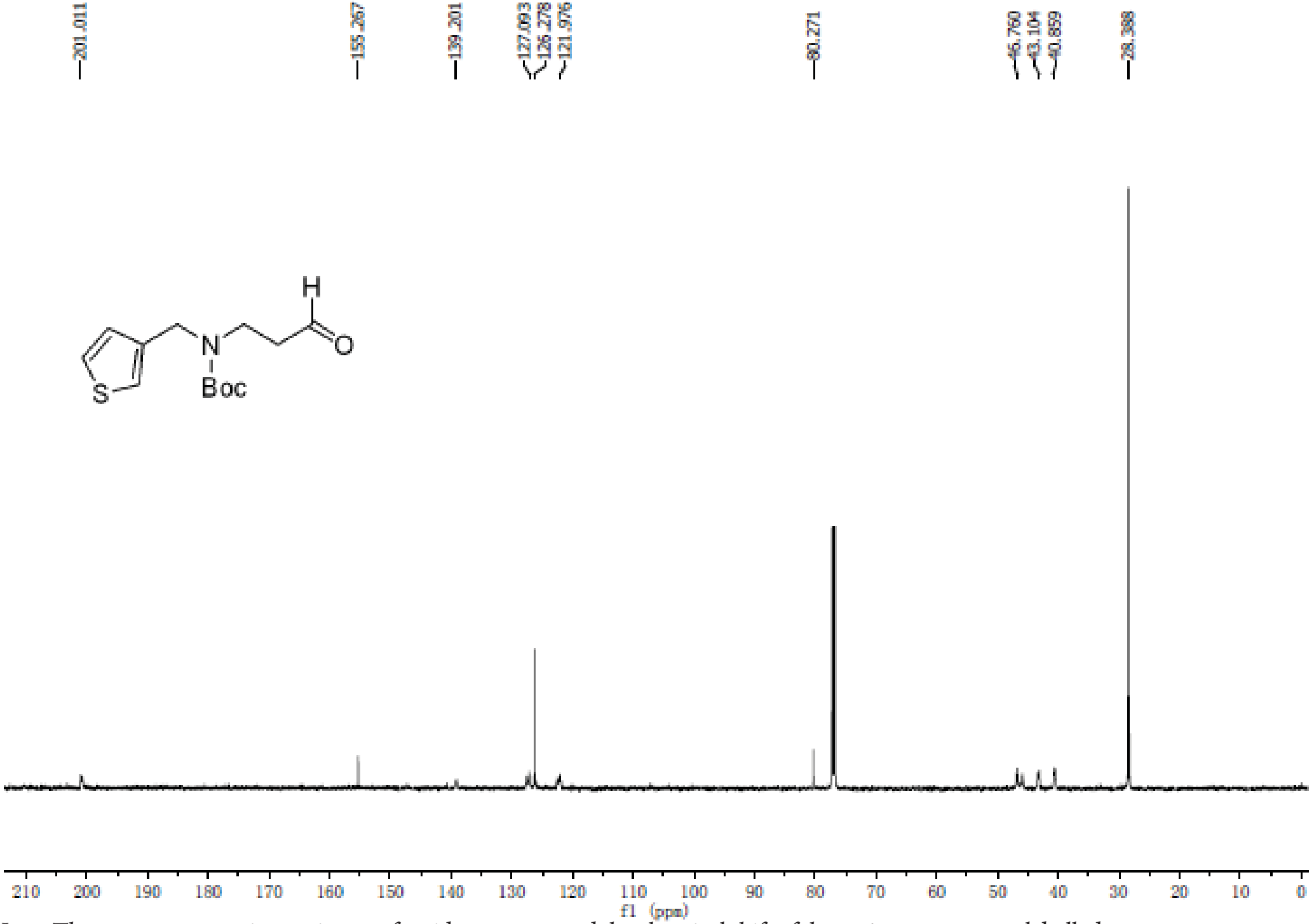
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (3-oxopropyl)(thiophen-3-ylmethyl)carbamate s2-v



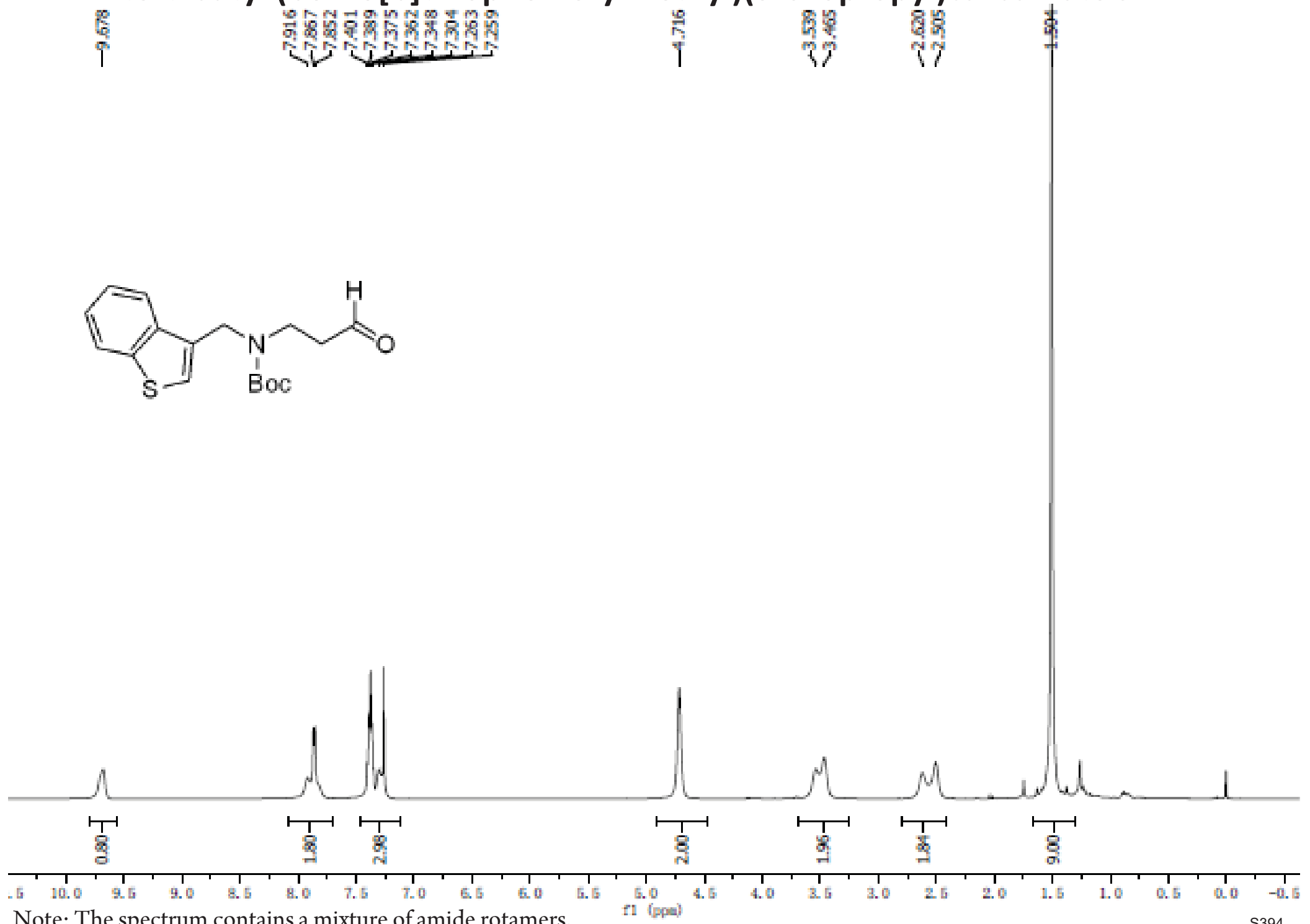
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (3-oxopropyl)(thiophen-3-ylmethyl)carbamate s2-v



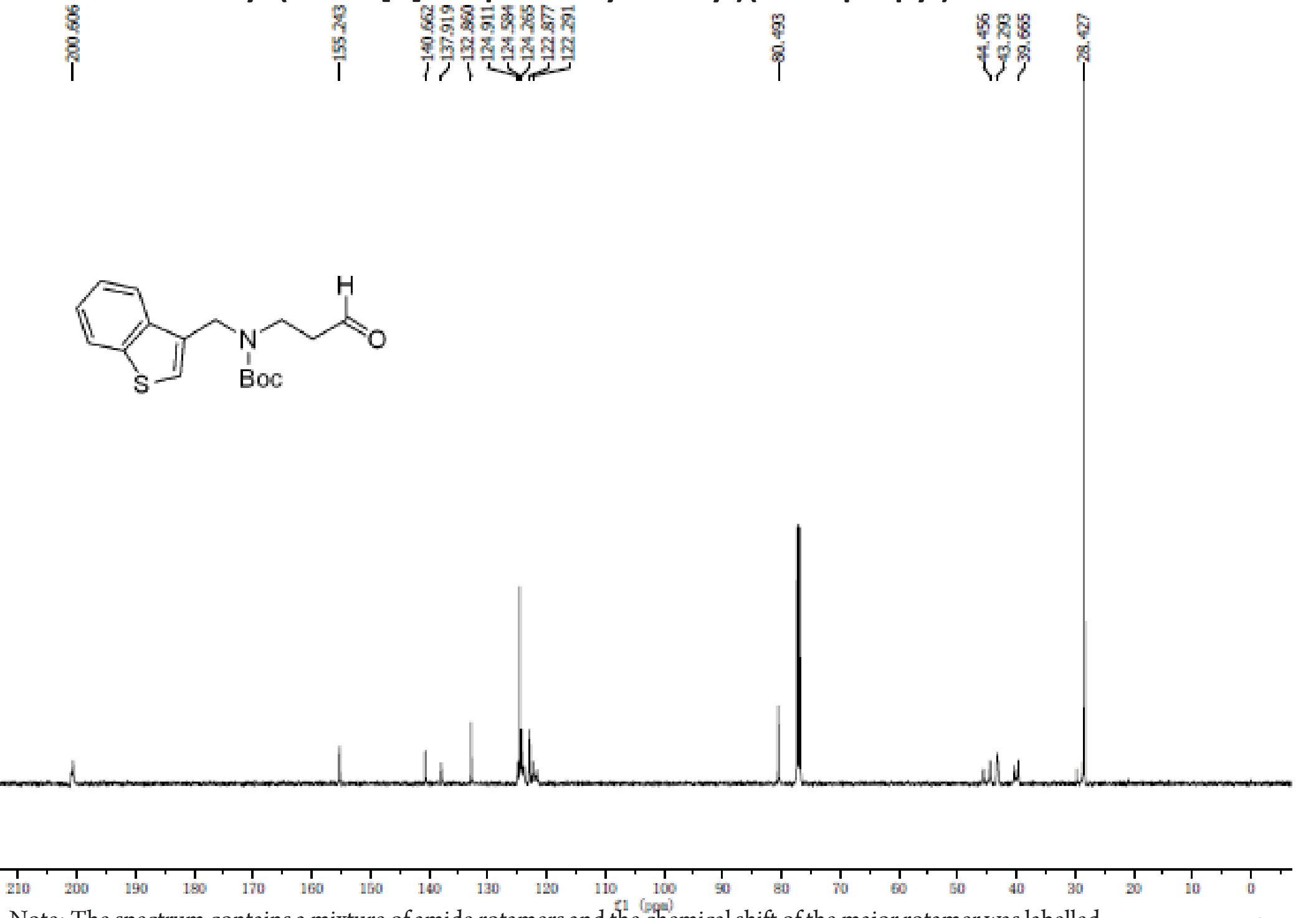
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (benzo[b]thiophen-3-ylmethyl)(3-oxopropyl)carbamate s2-w



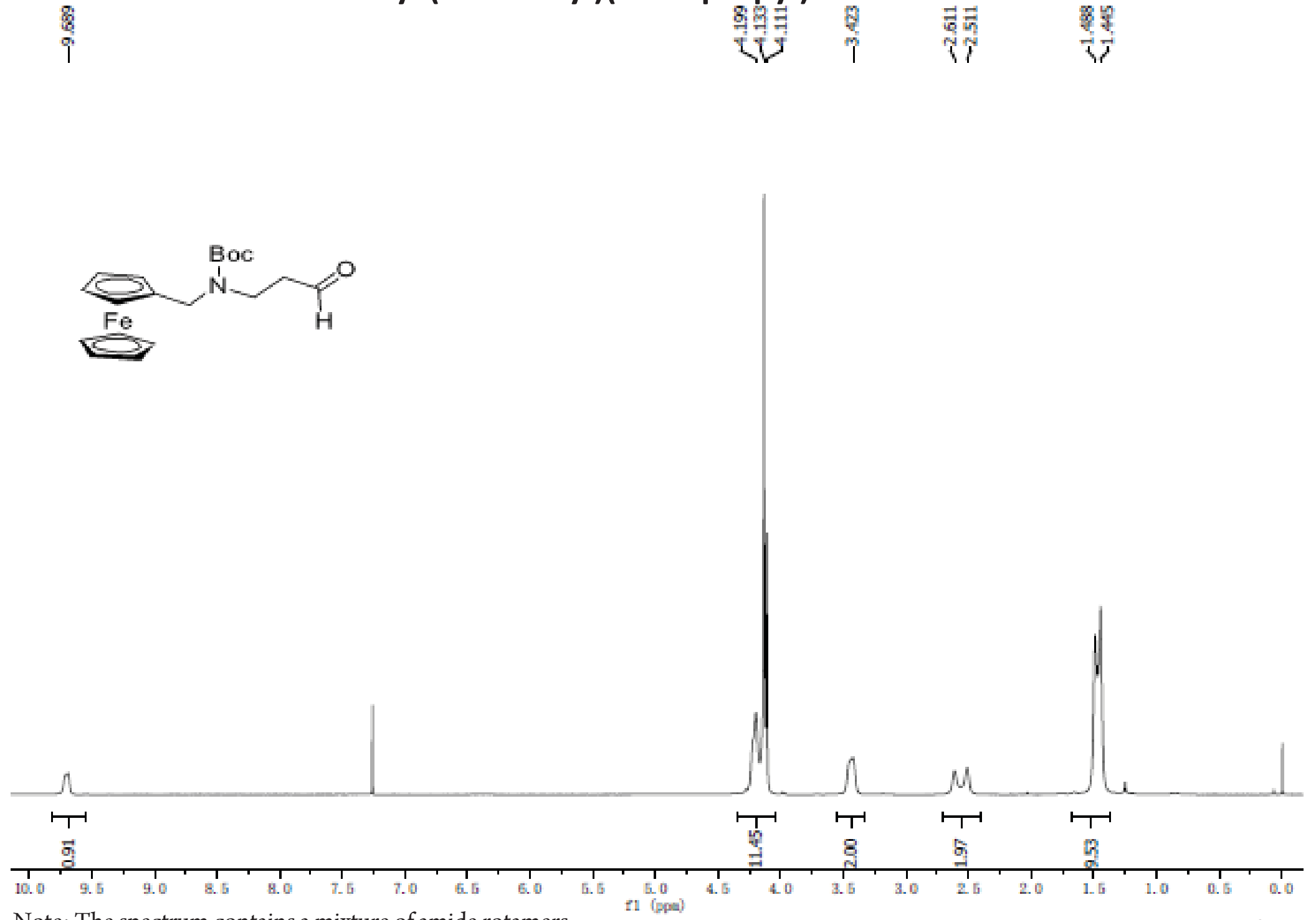
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (benzo[b]thiophen-3-ylmethyl)(3-oxopropyl)carbamate s2-w



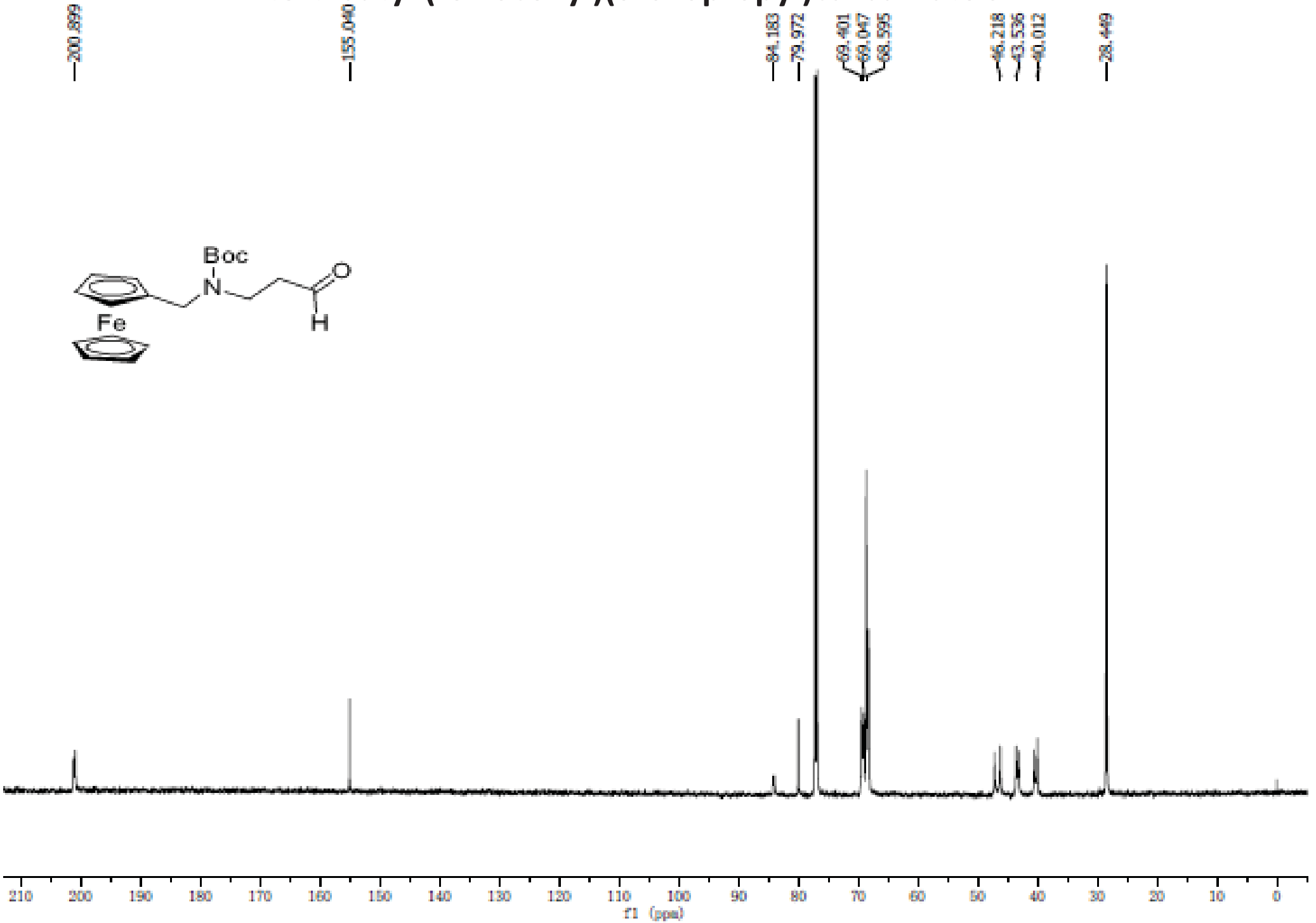
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (ferrocenyl)(3-oxopropyl)carbamate s2-x



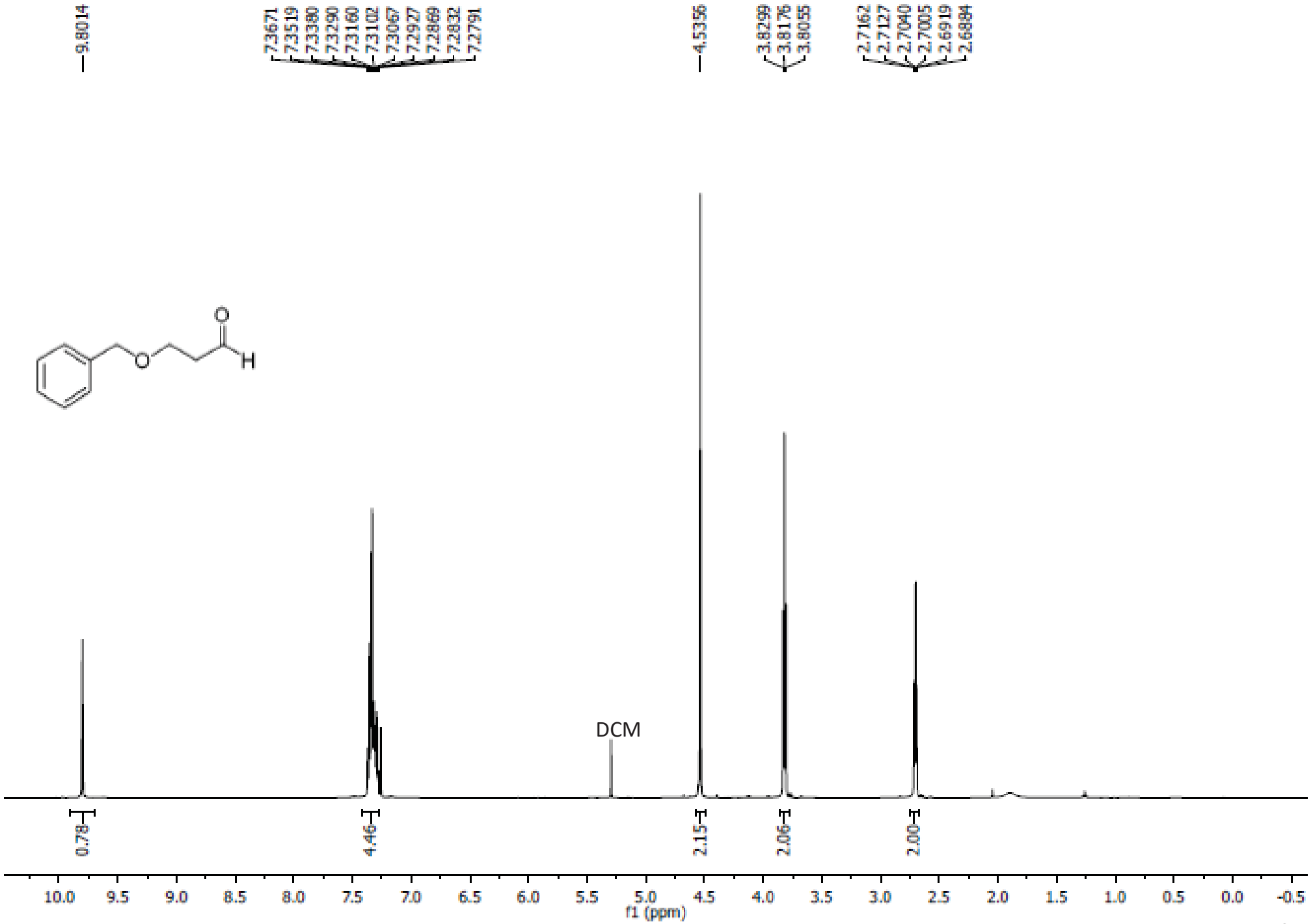
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (ferrocenyl)(3-oxopropyl)carbamate s2-x

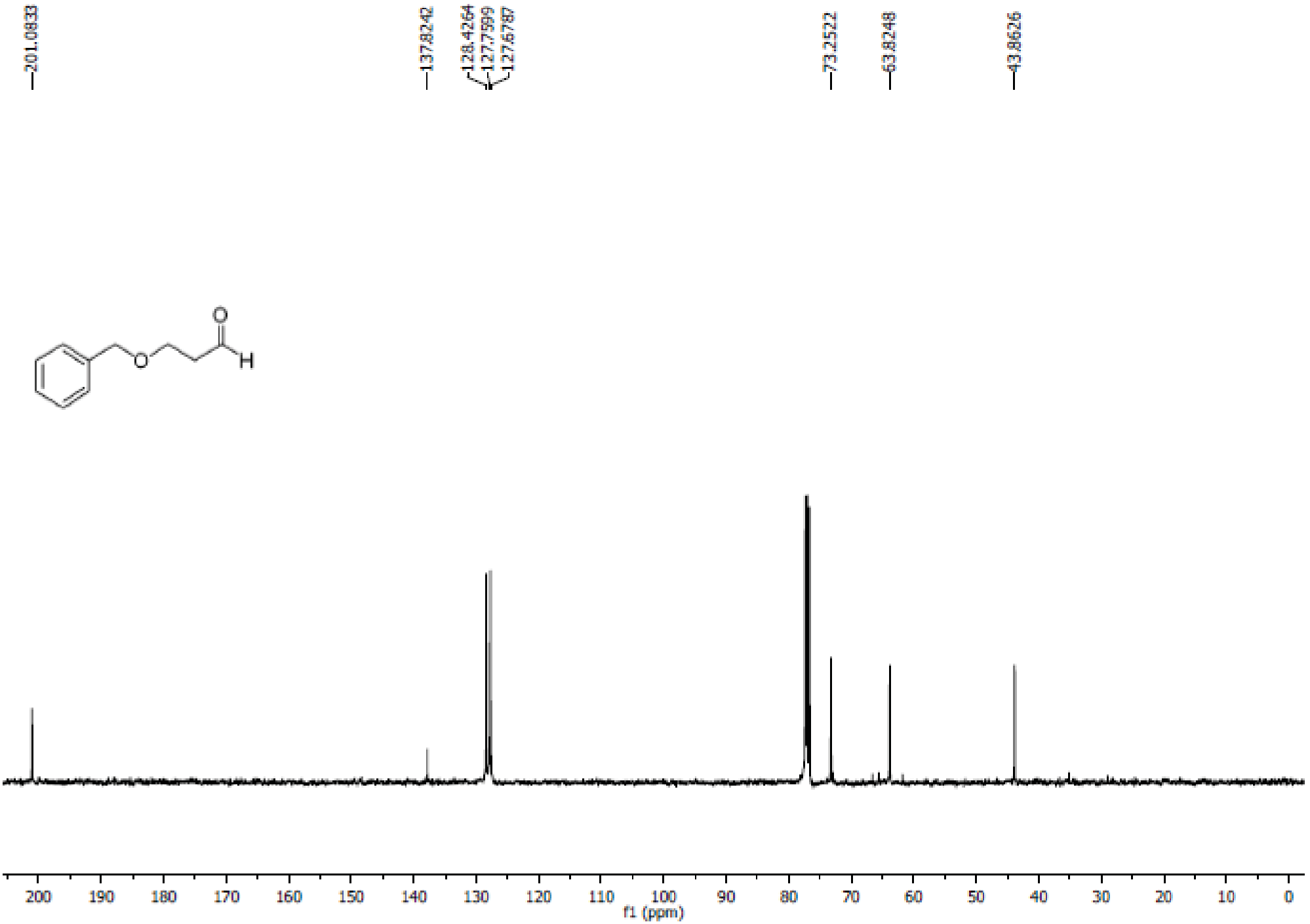


Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

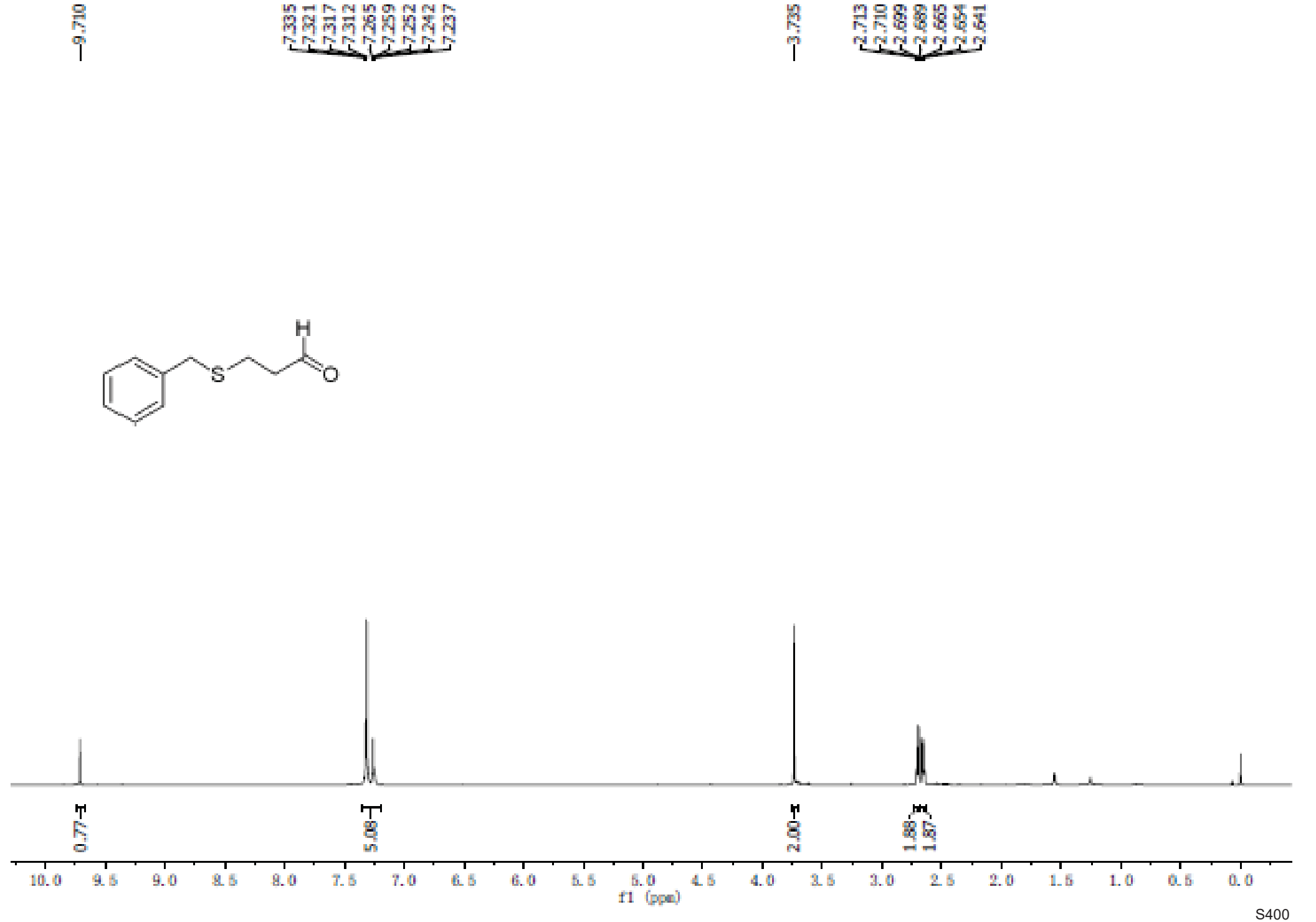
3-(benzyloxy)propanal s2-y



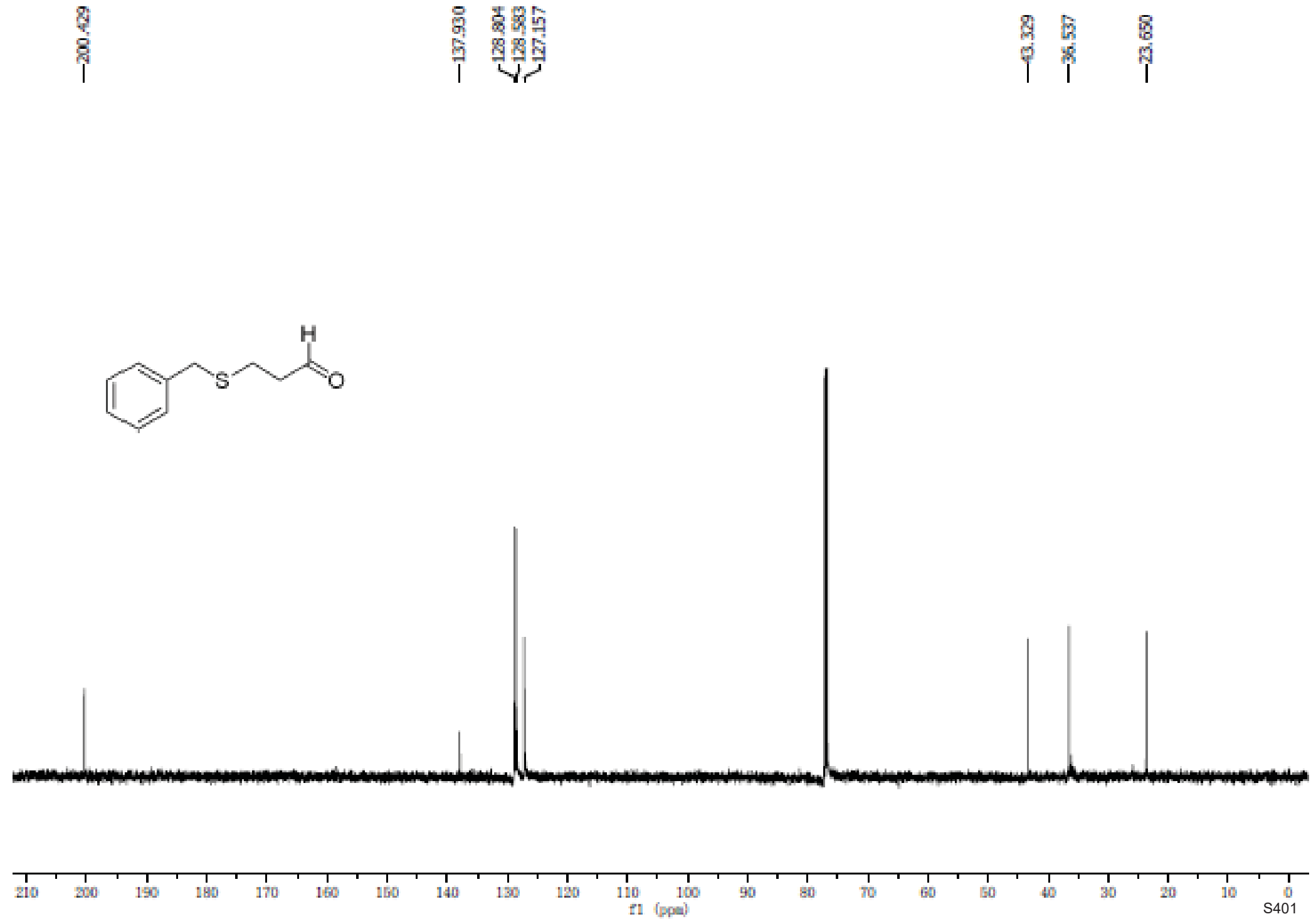
3-(benzyloxy)propanal s2-y



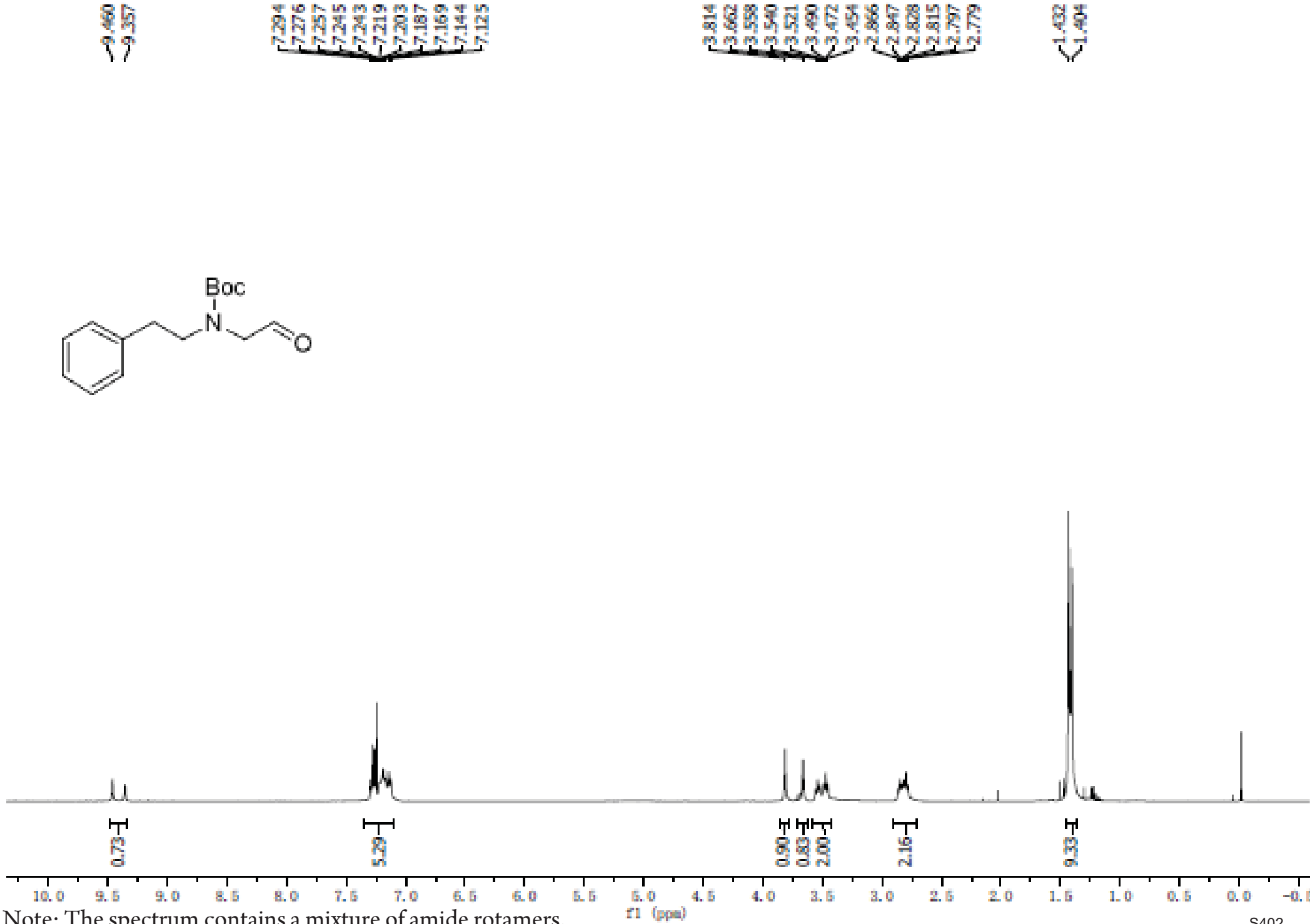
3-(benzylthio)propanal s2-z



3-(benzylthio)propanal s2-z

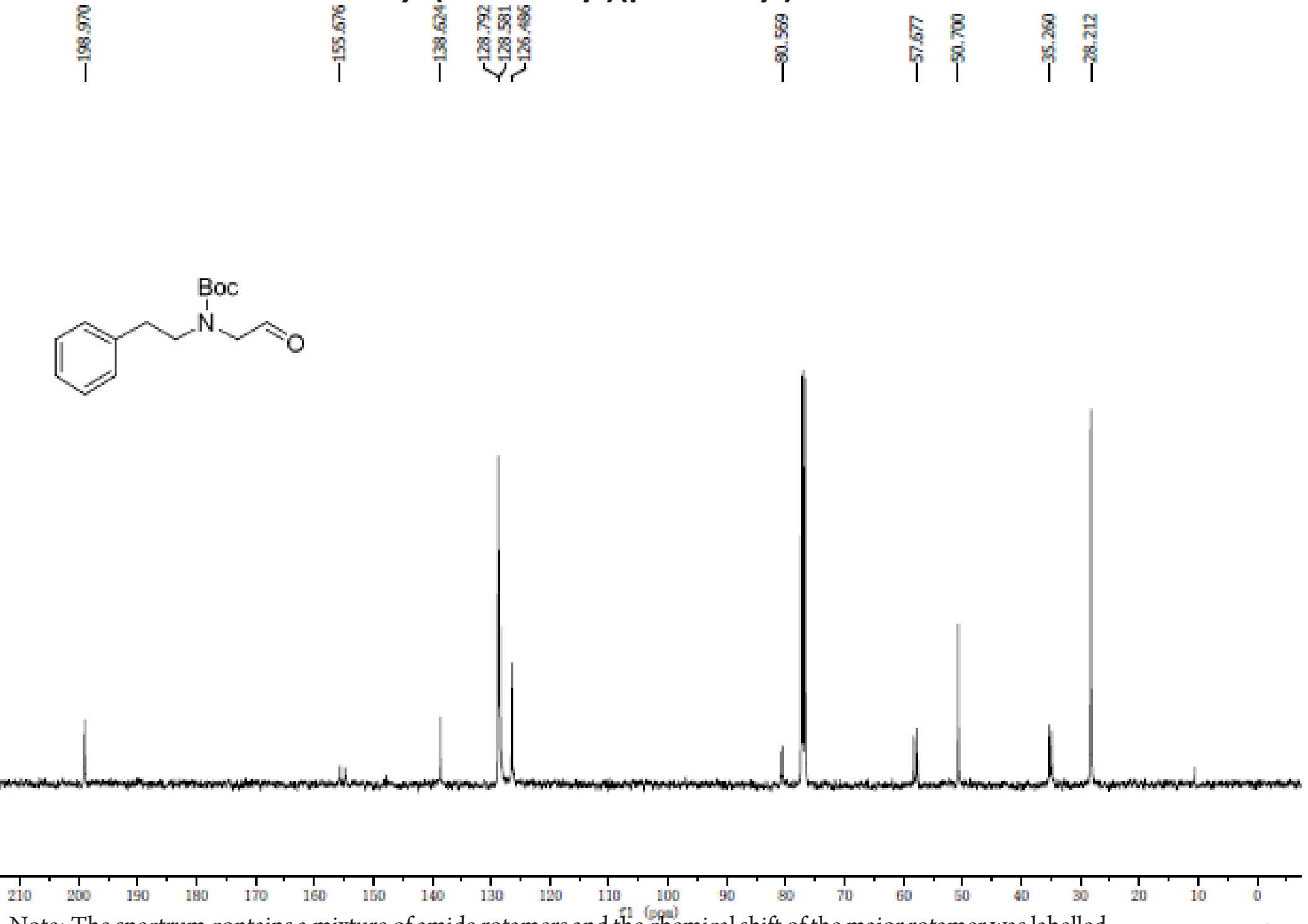


tert-butyl (2-oxoethyl)(phenethyl)carbamate s2-aa



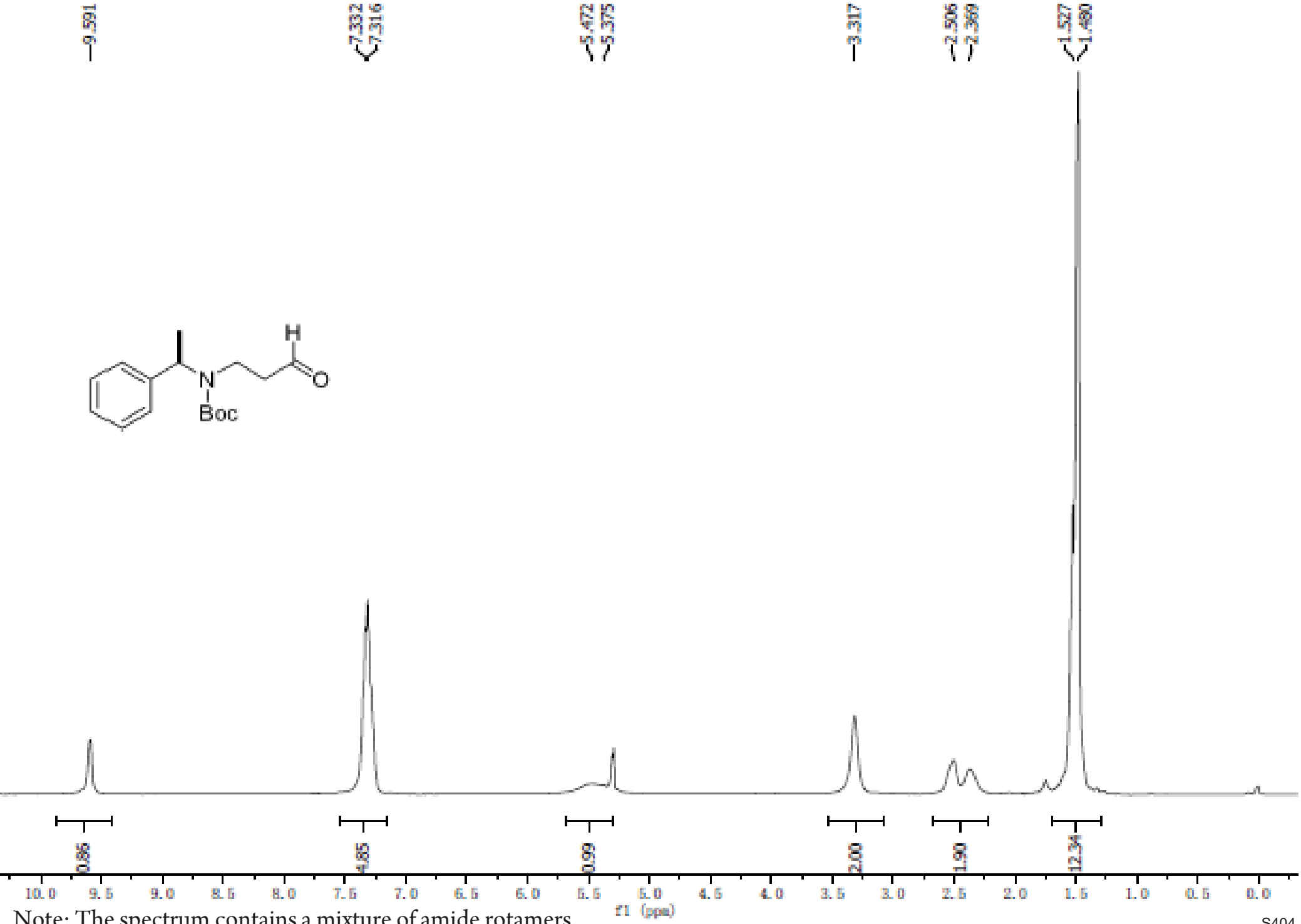
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (2-oxoethyl)(phenethyl)carbamate s2-aa



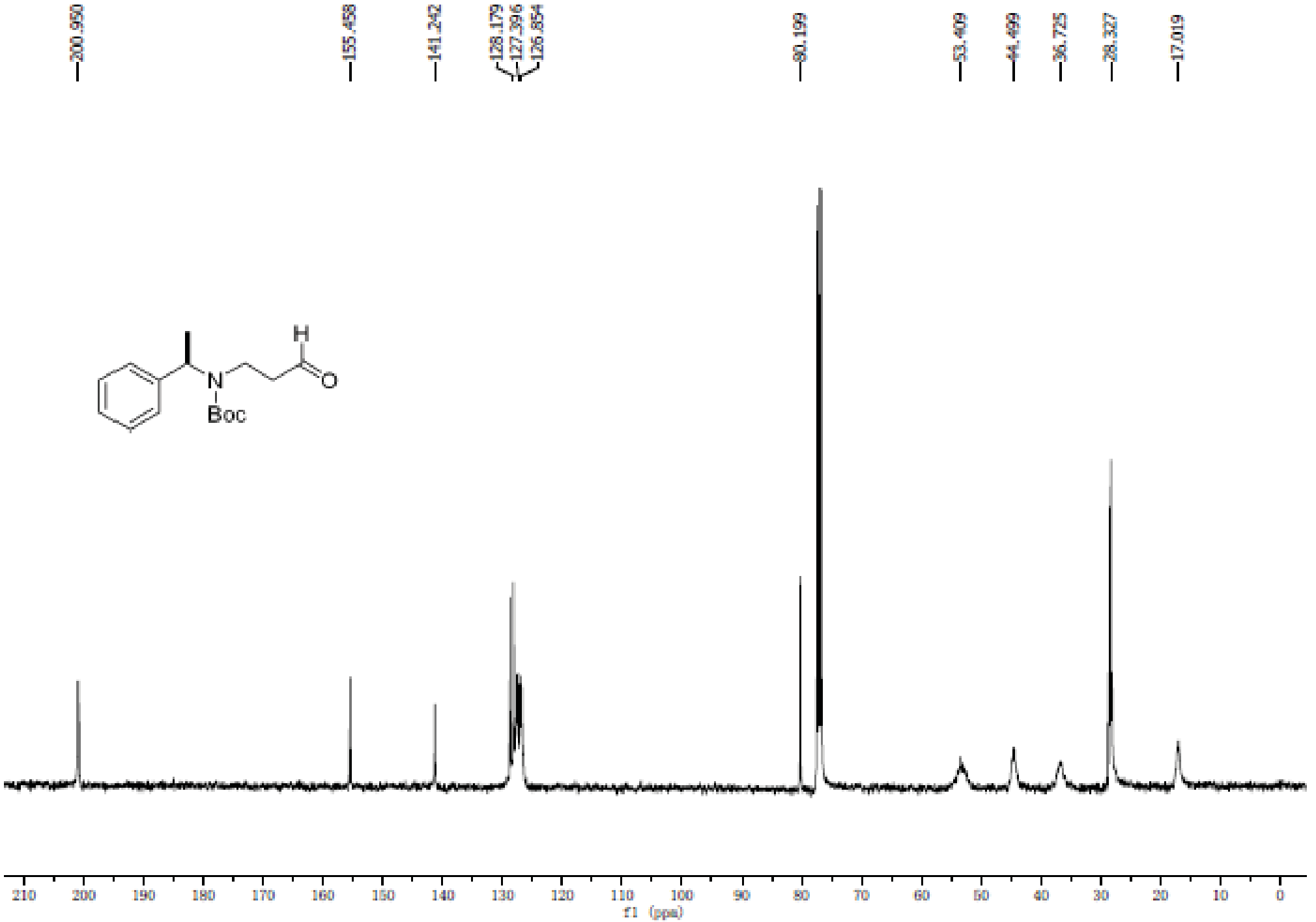
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl (*R*)-(3-oxopropyl)(1-phenylethyl)carbamate s2-ab



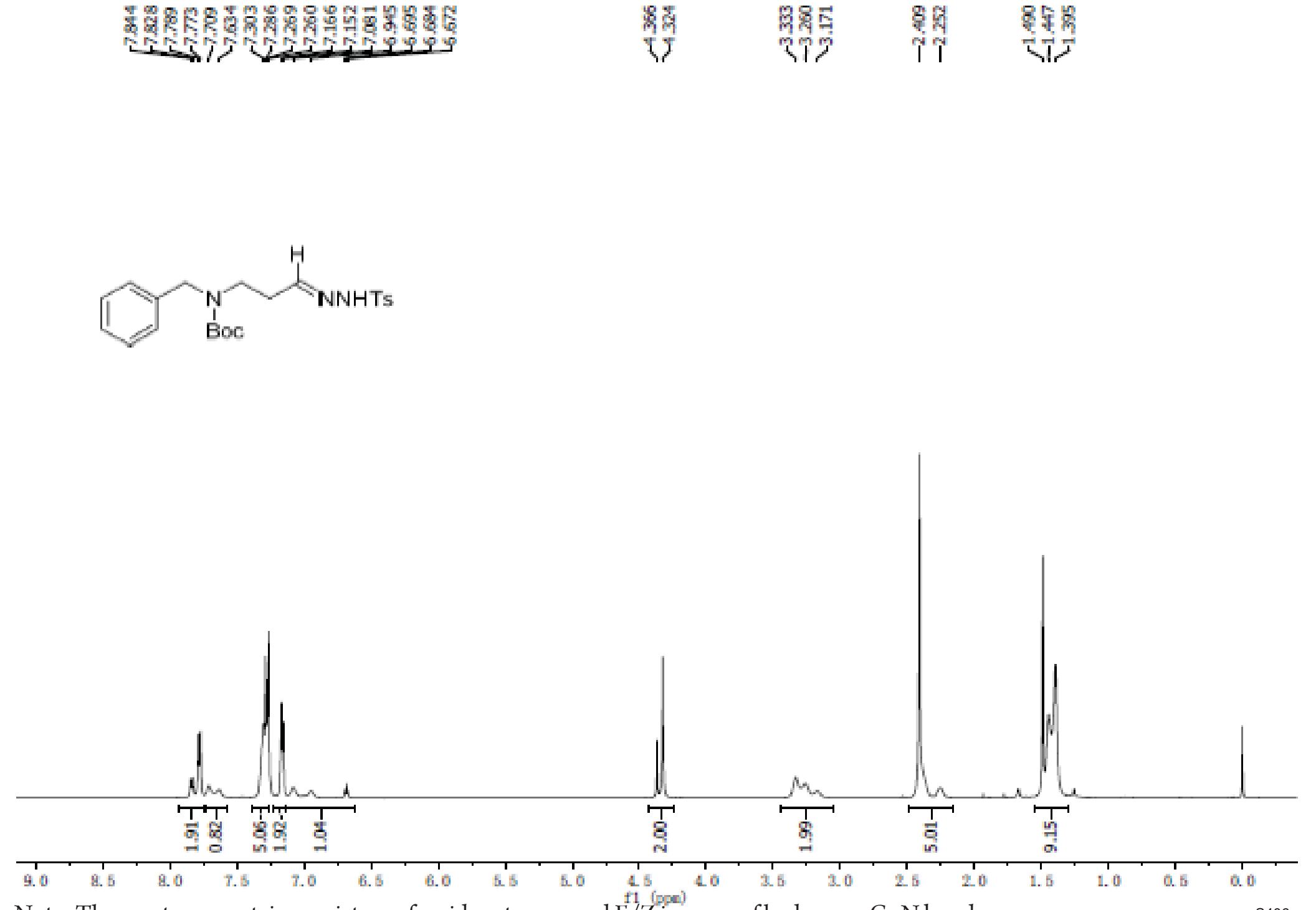
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*R*)-(3-oxopropyl)(1-phenylethyl)carbamate s2-ab



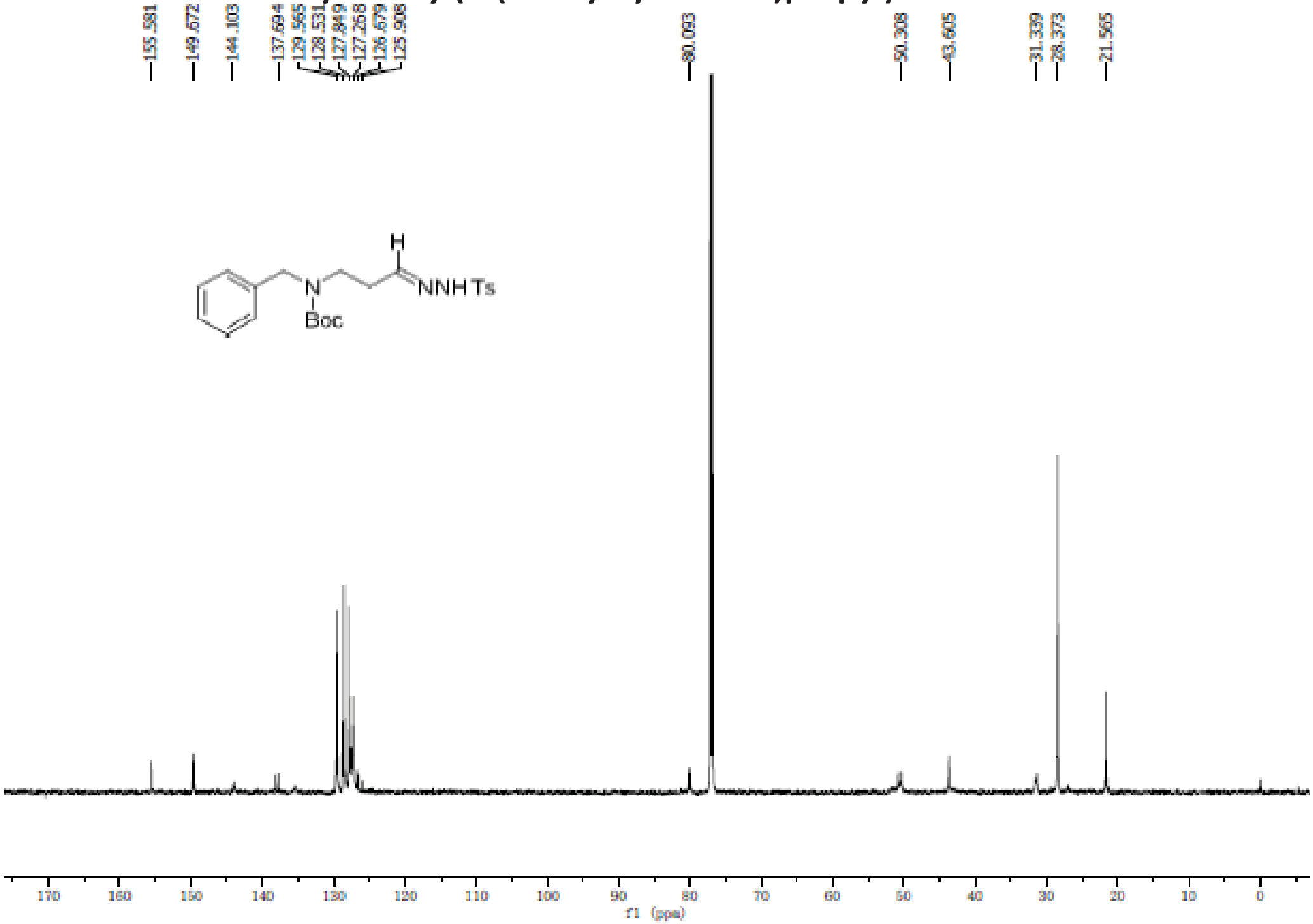
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major rotamer was labelled.

tert-butyl benzyl(3-(2-tosylhydrazono)propyl)carbamate 1a



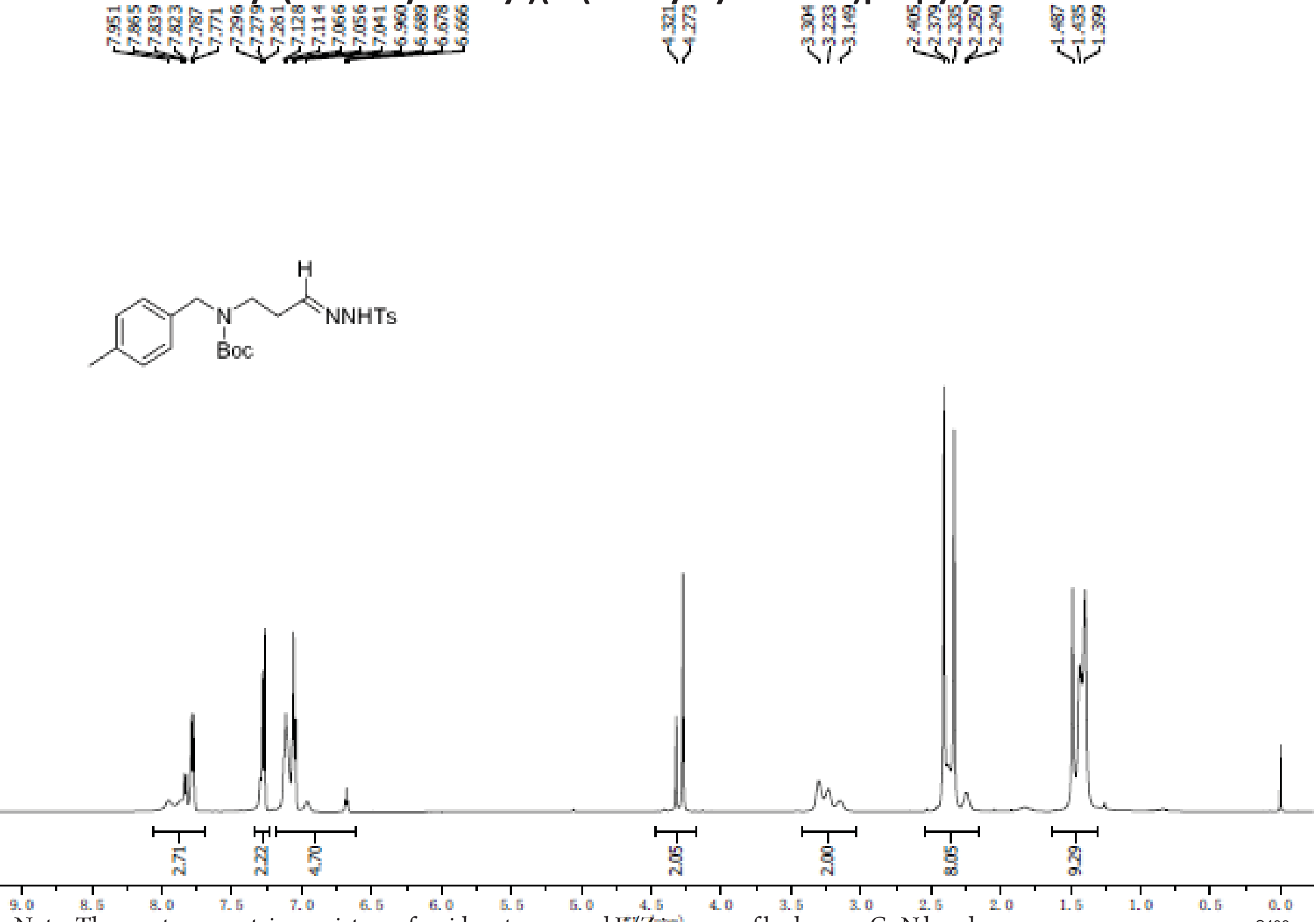
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl benzyl(3-(2-tosylhydrazono)propyl)carbamate 1a



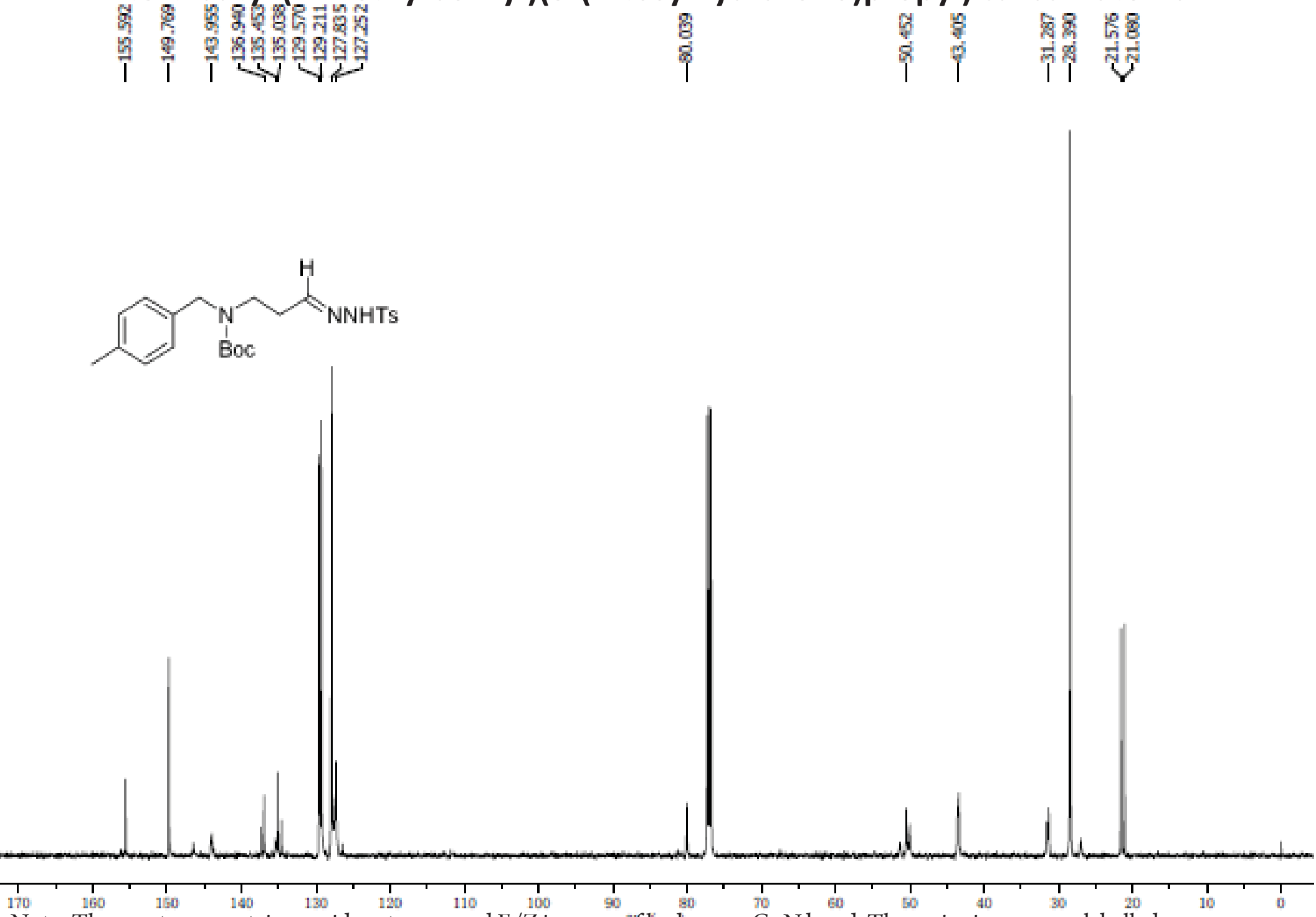
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (4-methylbenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1b



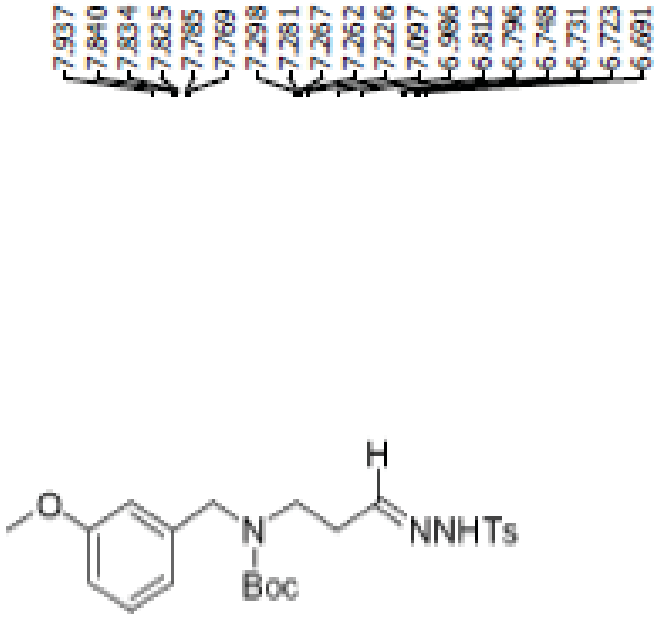
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (4-methylbenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1b



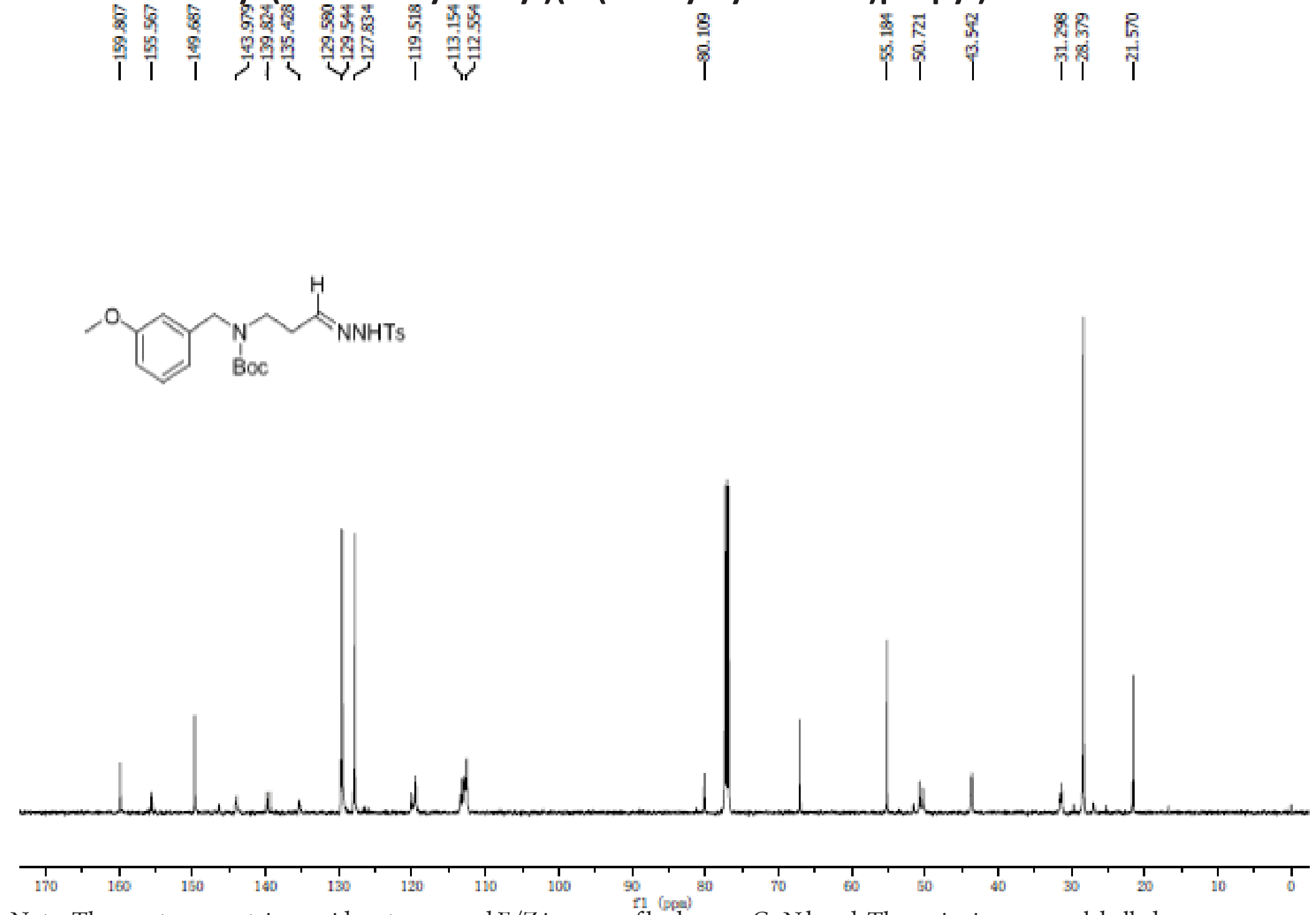
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (3-methoxybenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1c



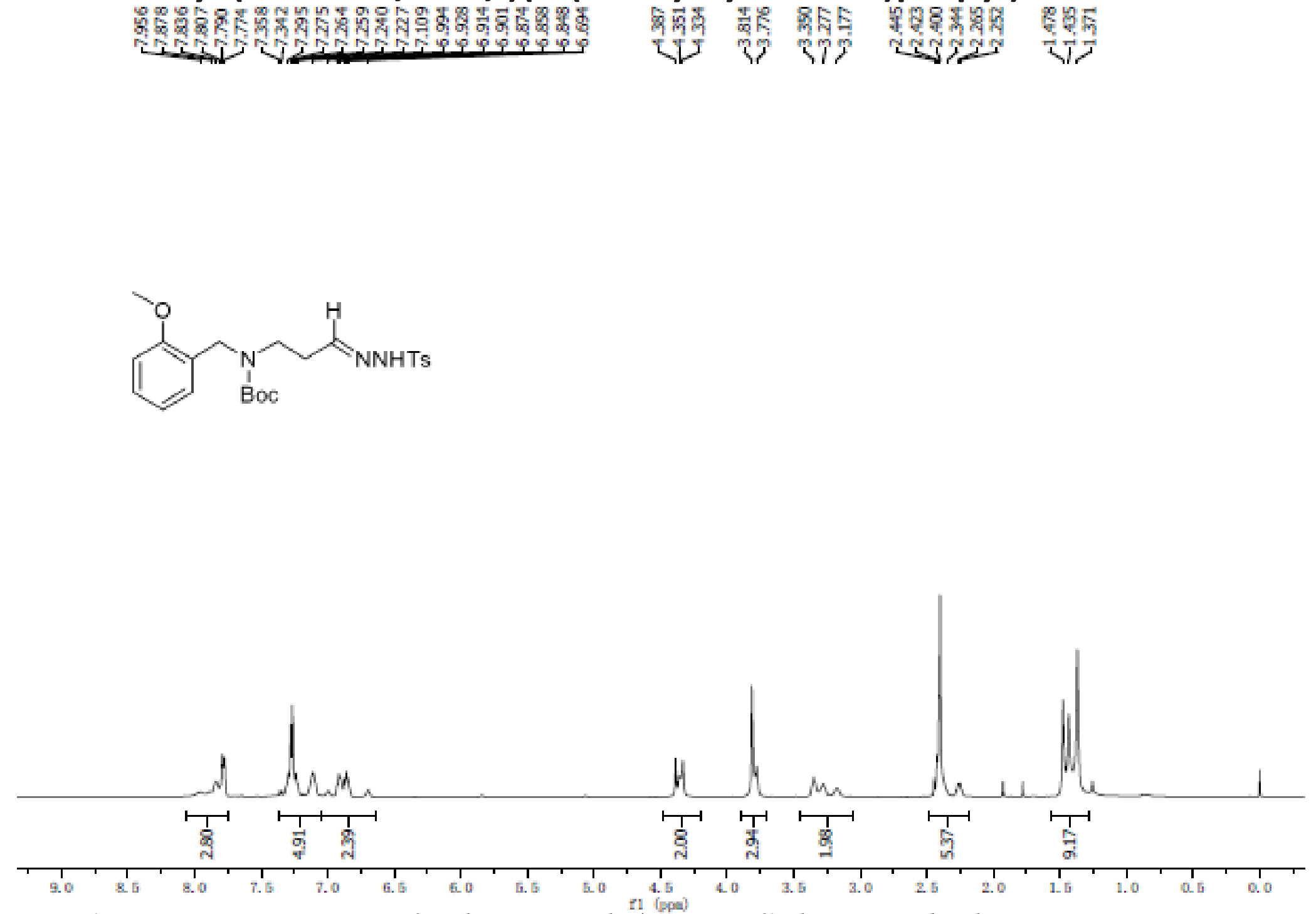
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (3-methoxybenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1c



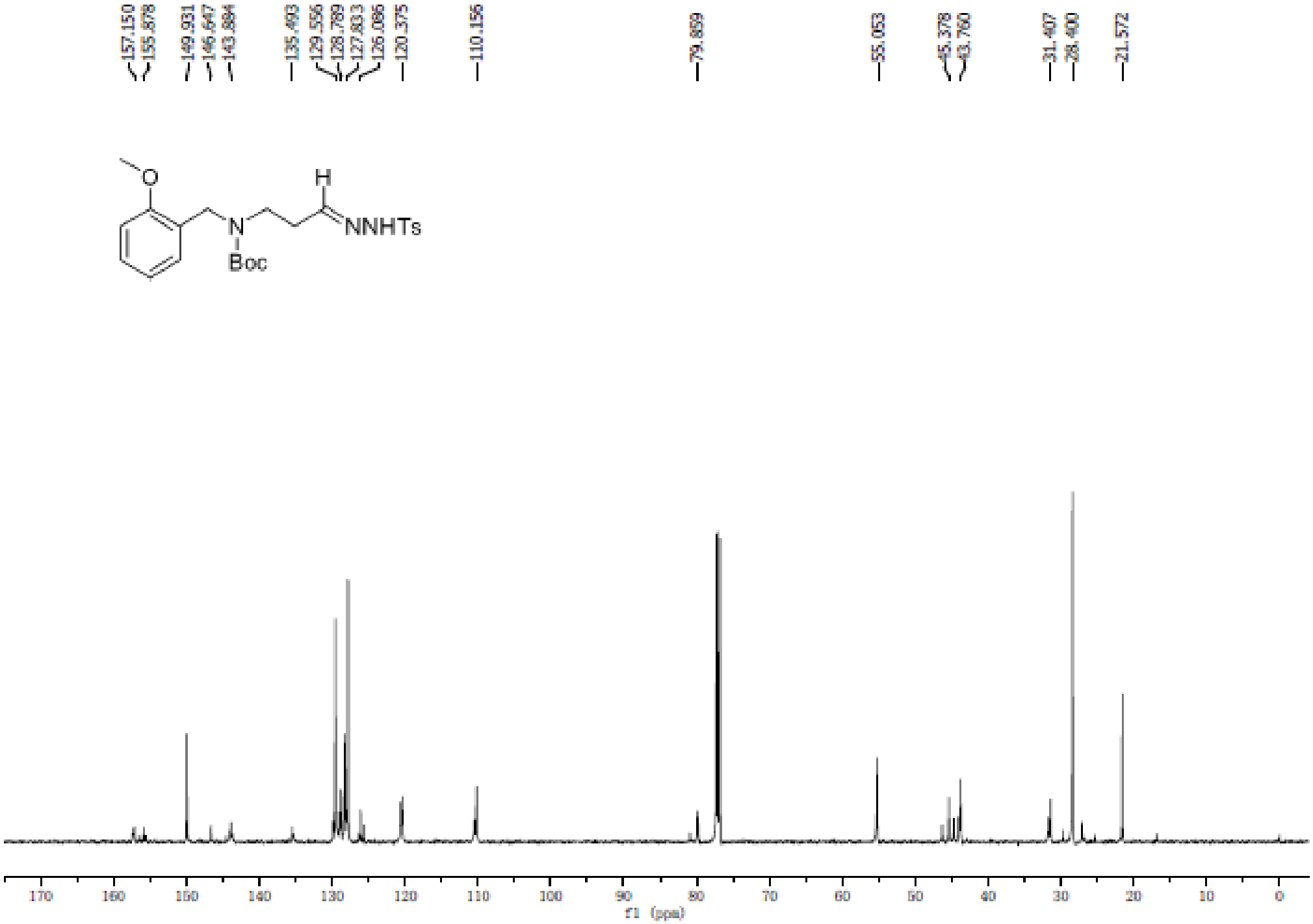
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (2-methoxybenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1d



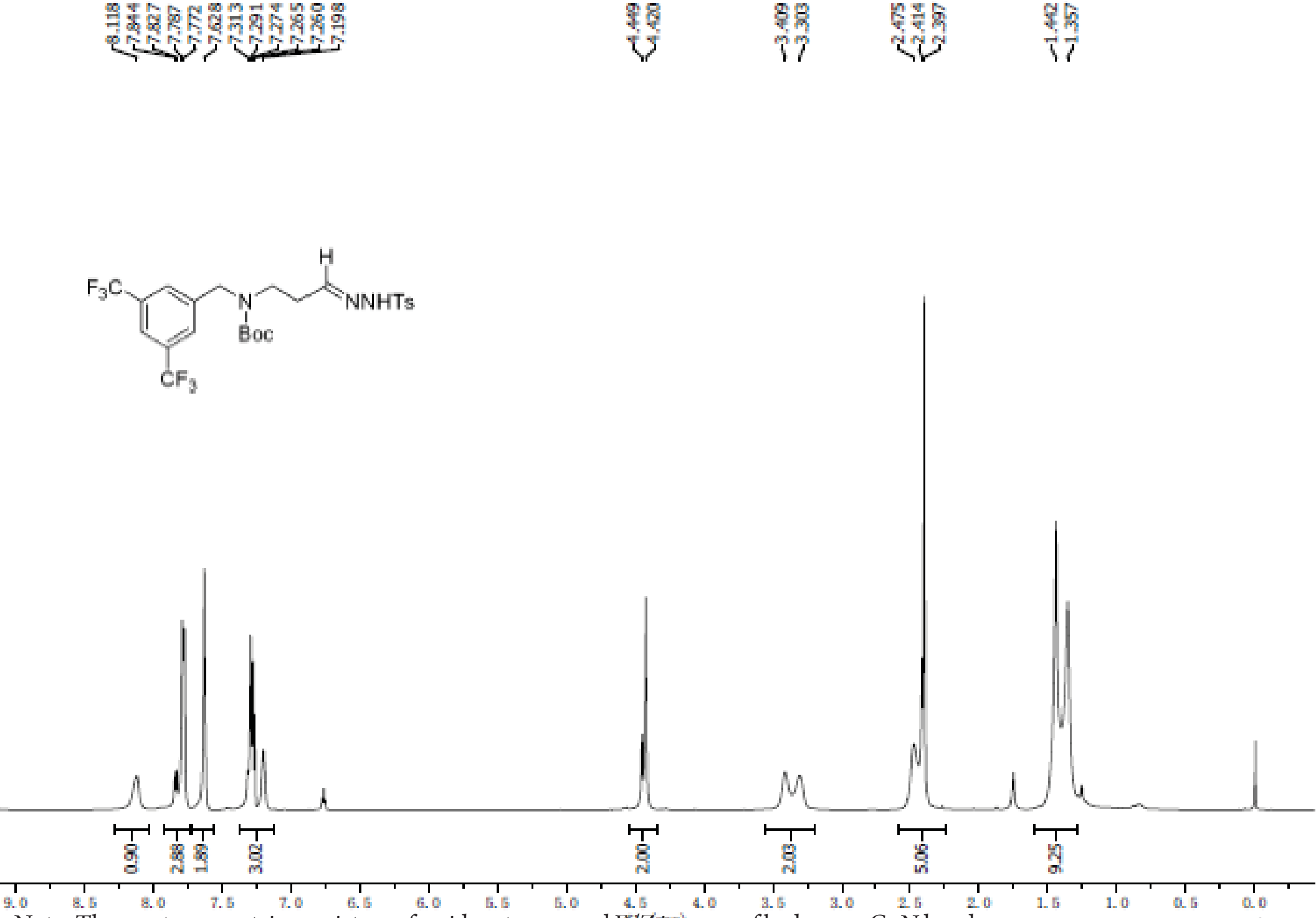
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (2-methoxybenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1d



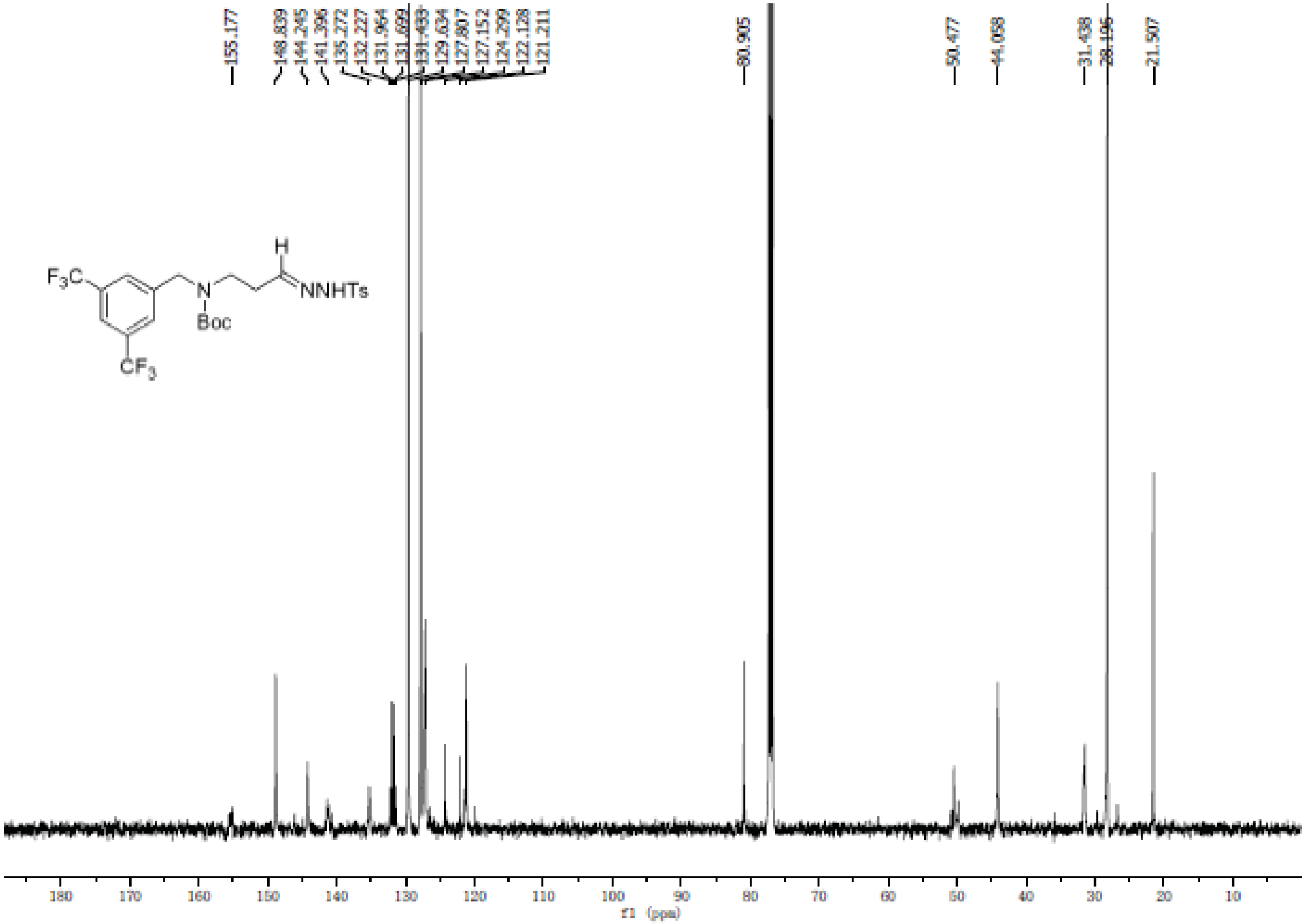
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (3,5-bis(trifluoromethyl)benzyl)(3-(2-tosylhydrazono)propyl)carbamate 1e



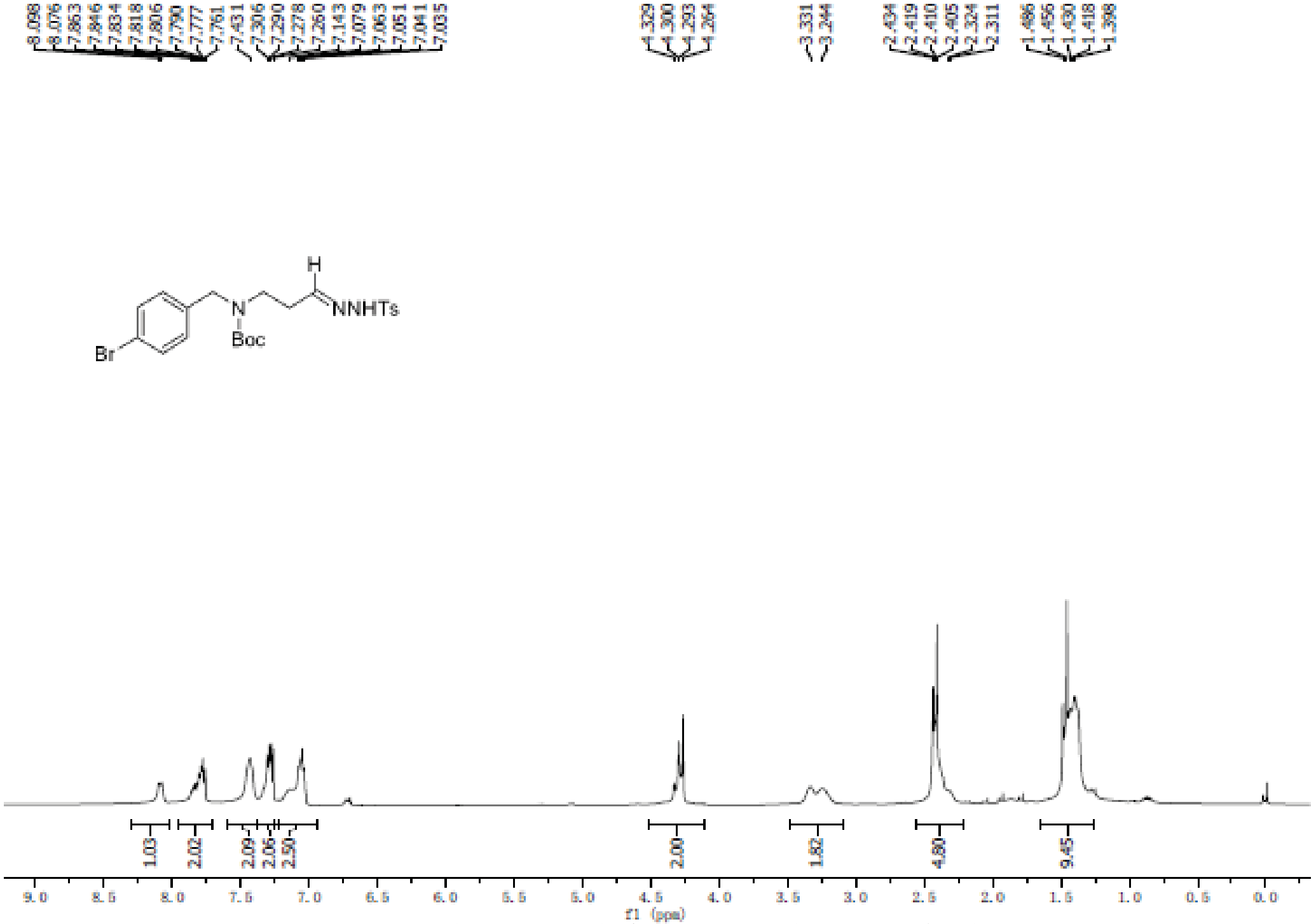
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (3,5-bis(trifluoromethyl)benzyl)(3-(2-tosylhydrazono)propyl)carbamate 1e



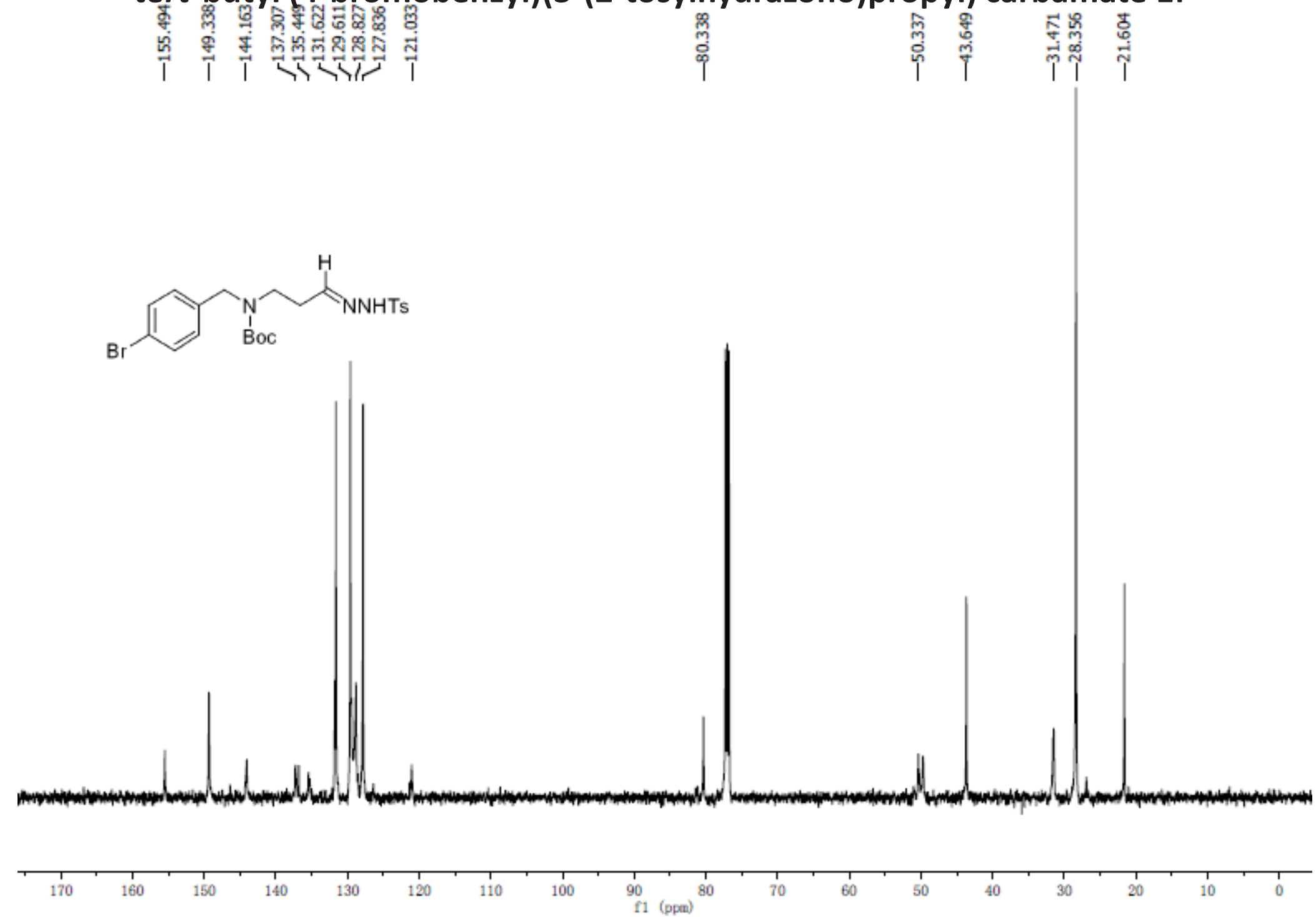
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (4-bromobenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1f



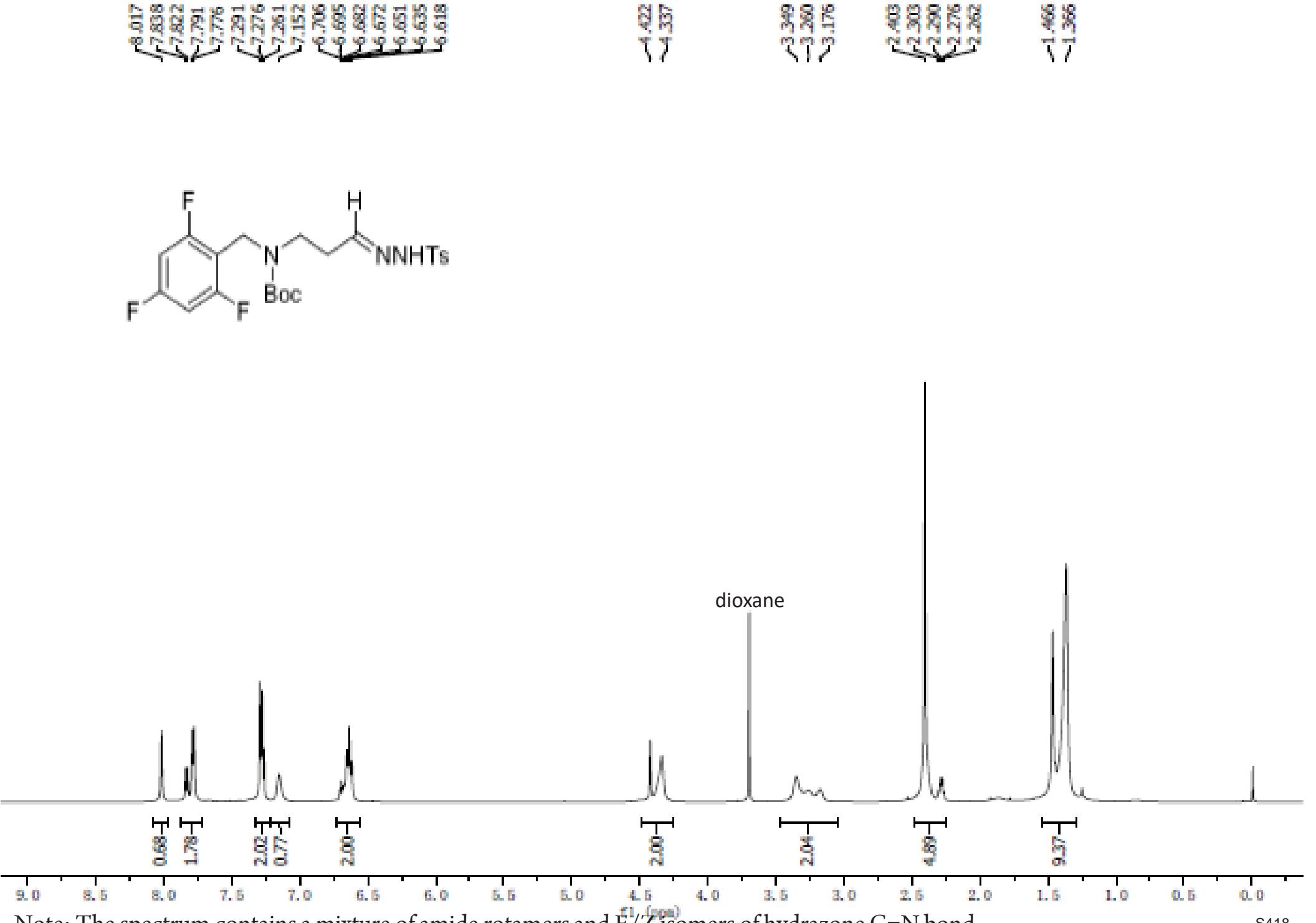
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (4-bromobenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1f



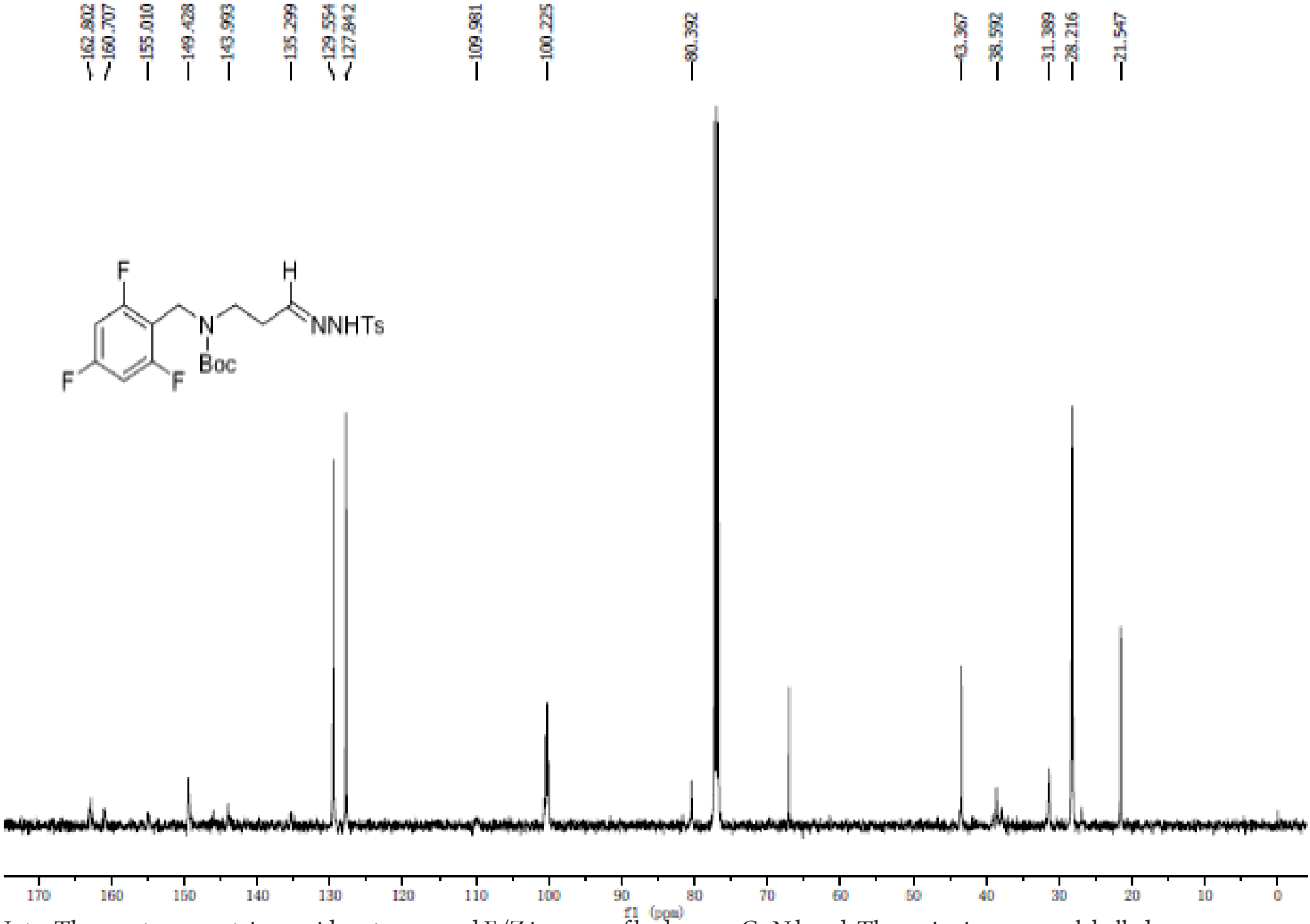
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (2,4,6-trifluorobenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1g



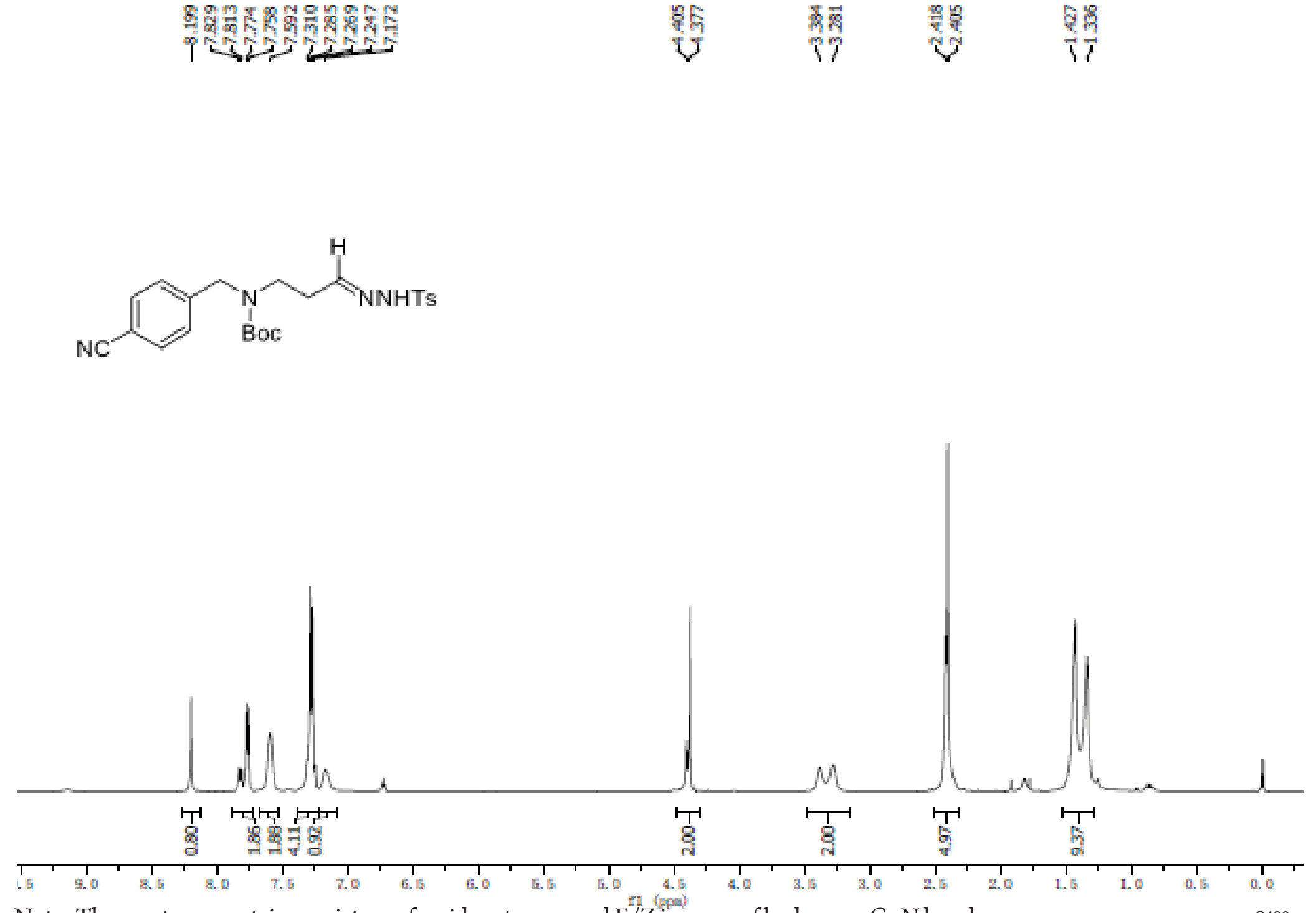
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (2,4,6-trifluorobenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1g



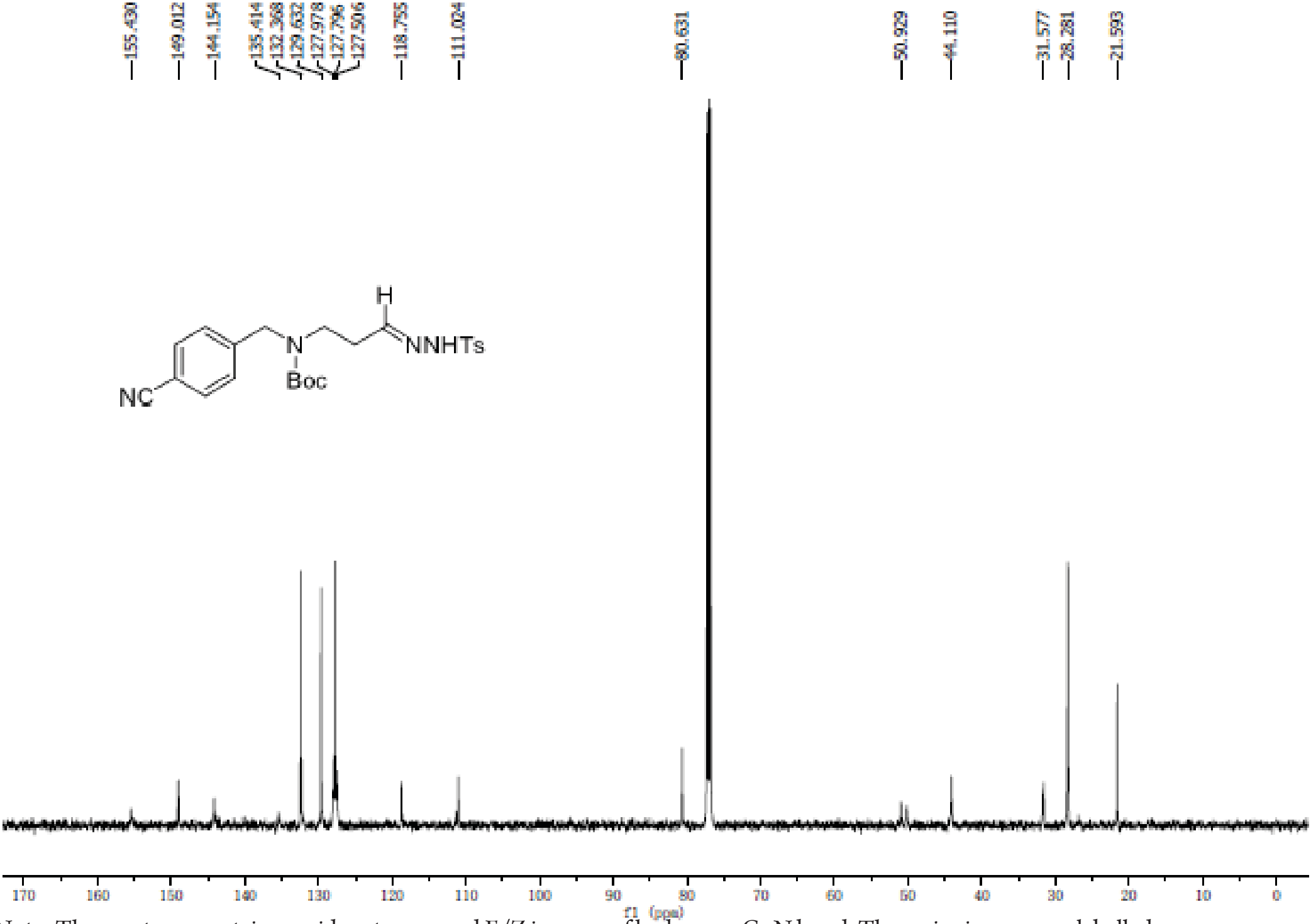
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (4-nitrilebenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1h



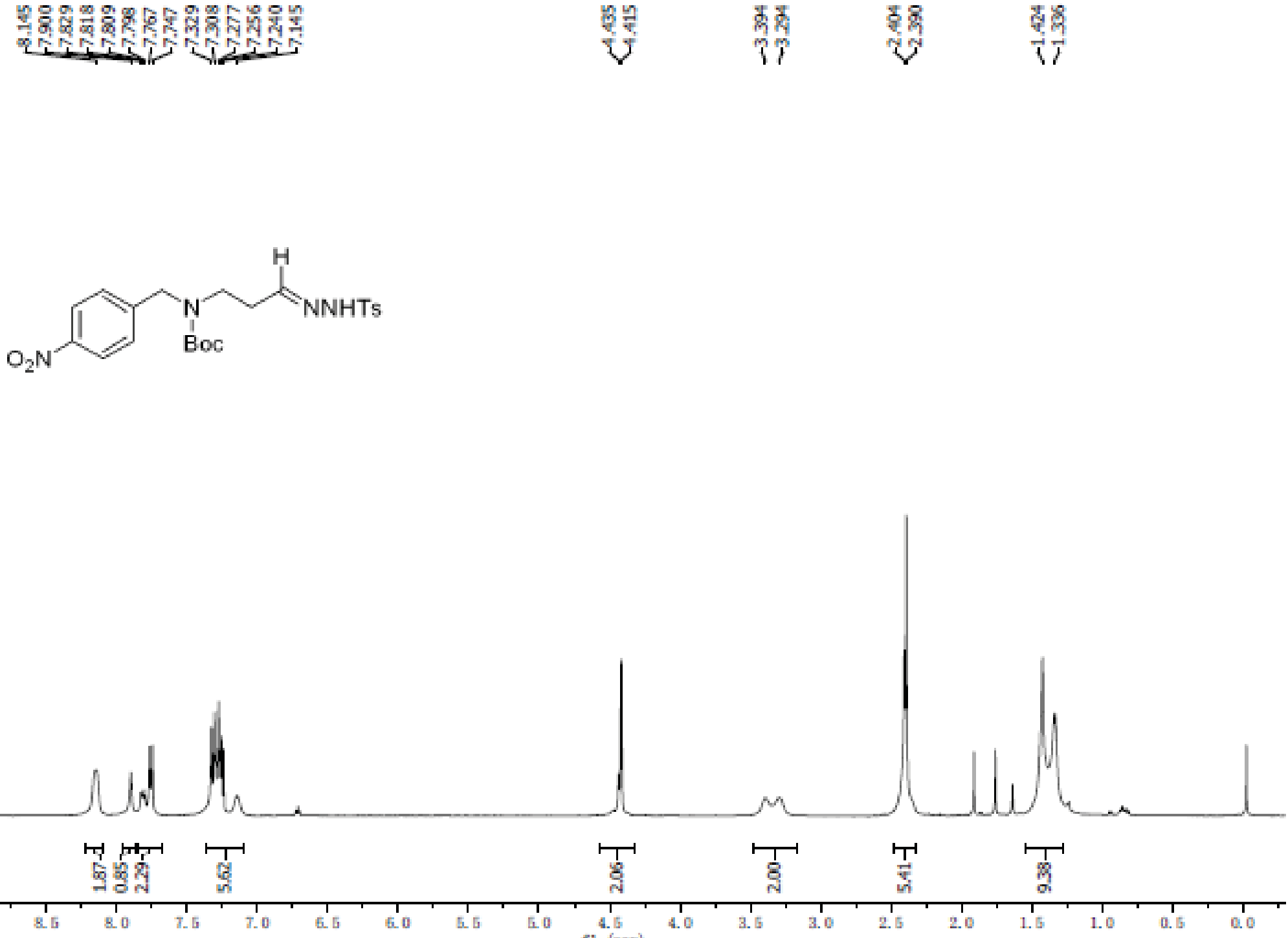
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (4-nitrilebenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1h



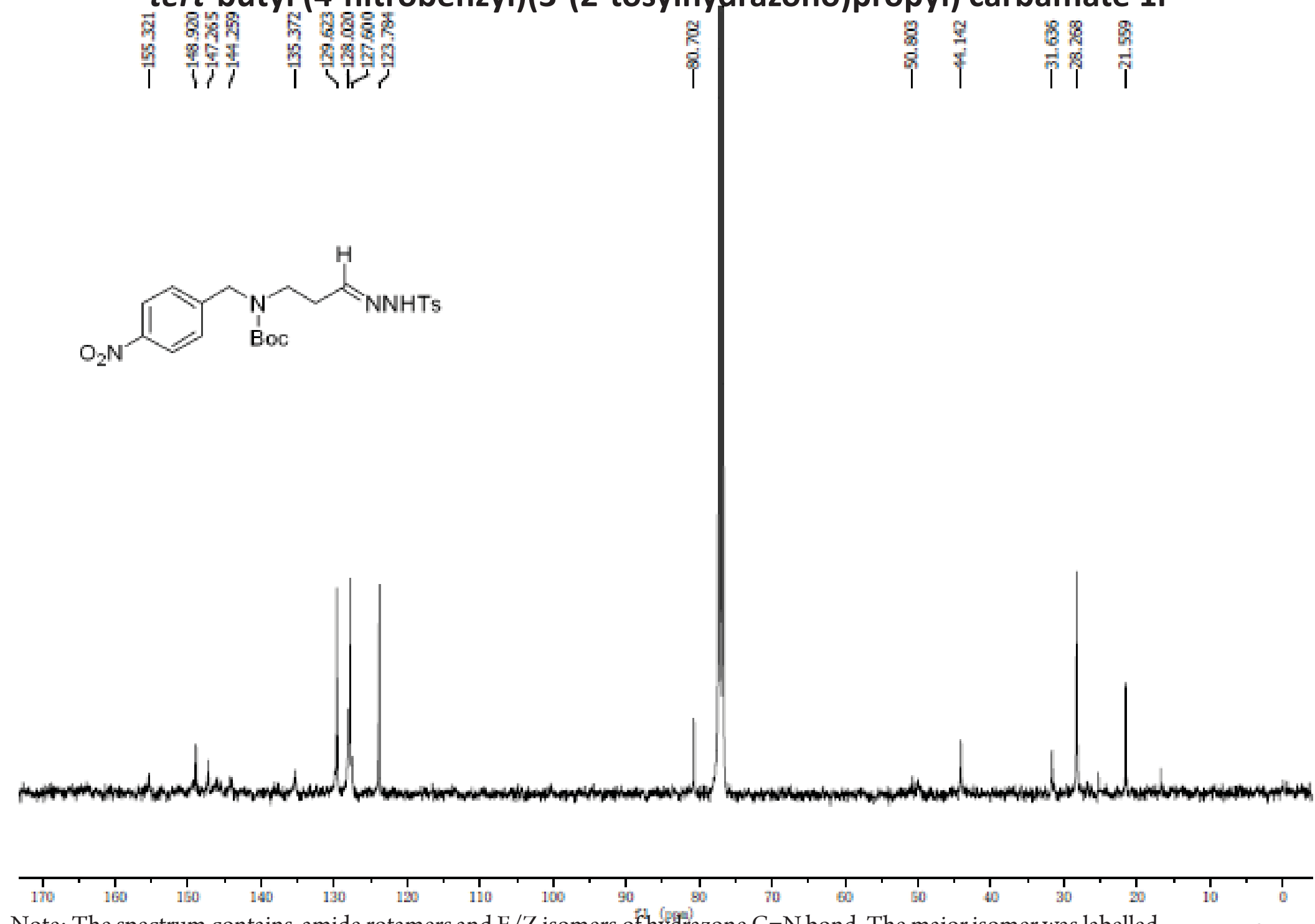
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (4-nitrobenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1i



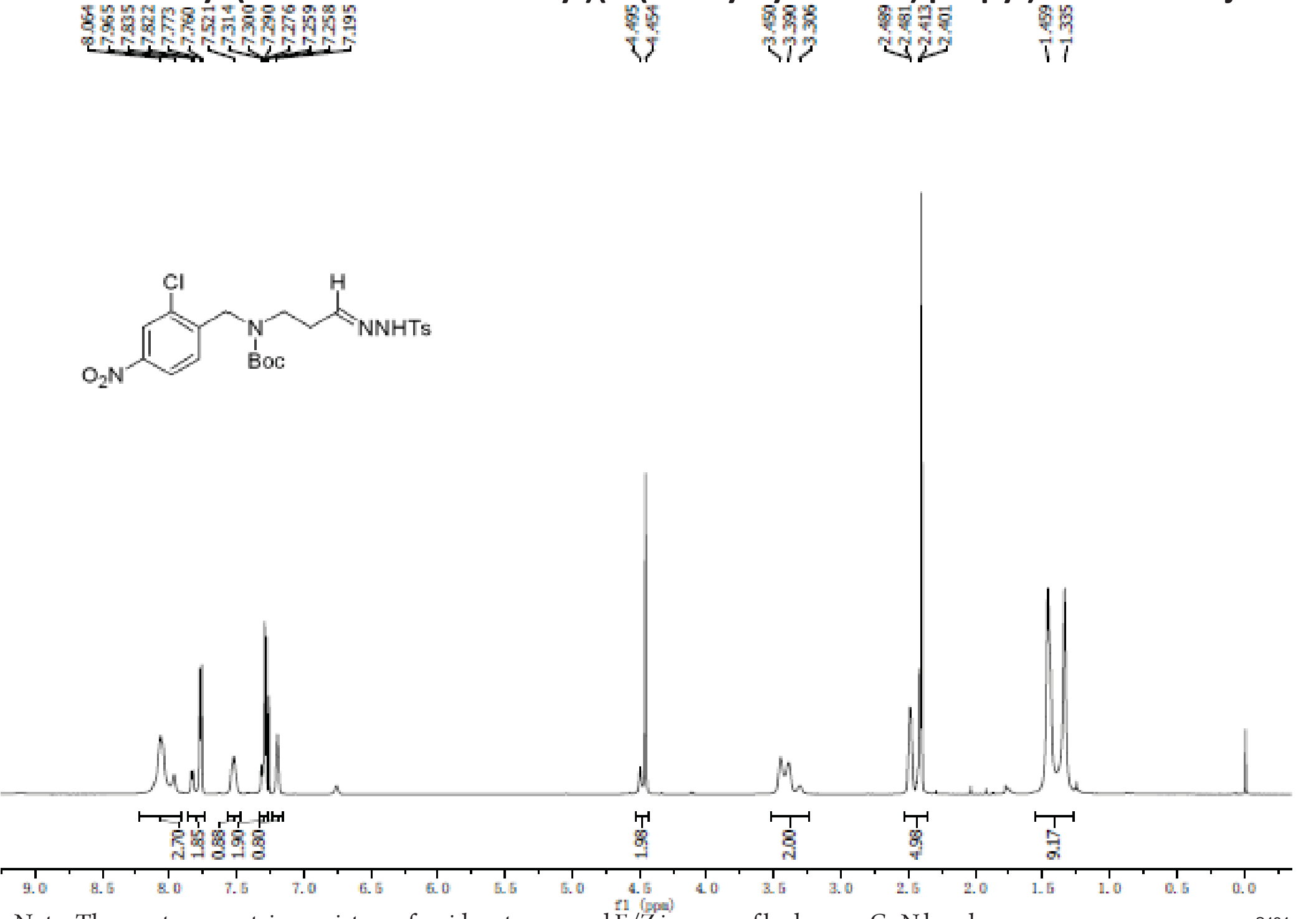
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (4-nitrobenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1i



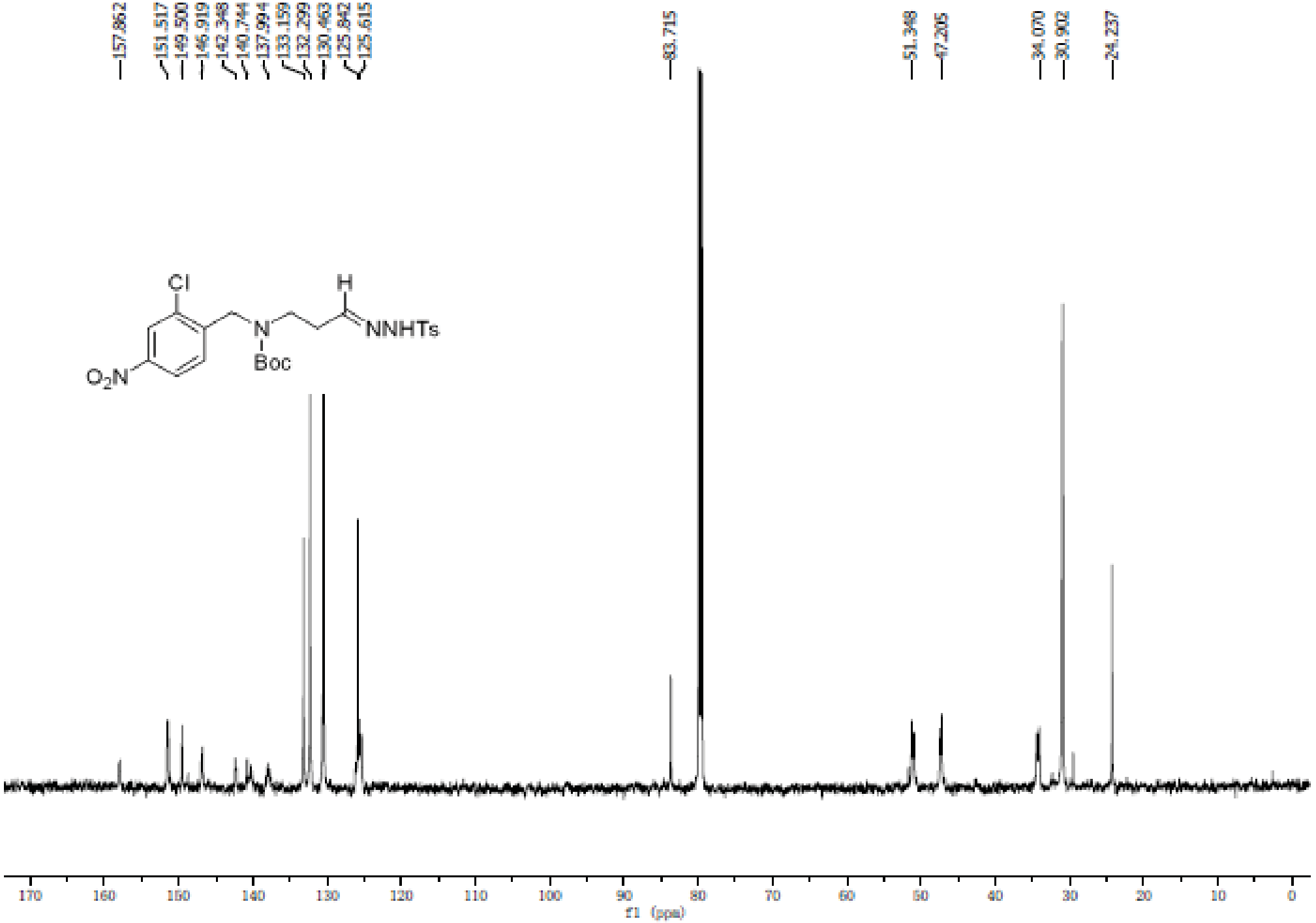
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (2-chloro-4-nitrobenzyl)(3-(2-tosylhydrazono) propyl)carbamate 1j



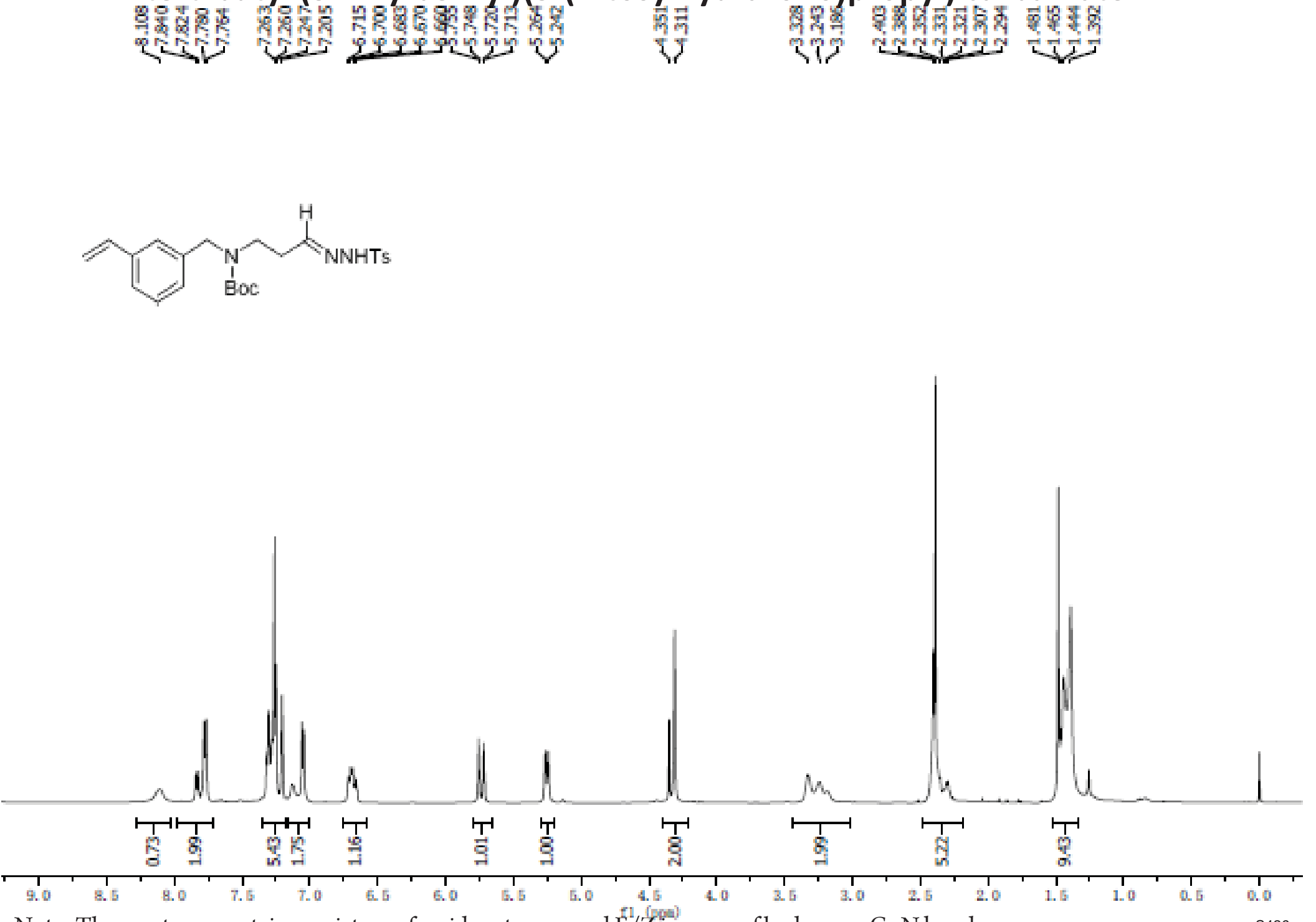
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (2-chloro-4-nitrobenzyl)(3-(2-tosylhydrazono) propyl)carbamate 1j



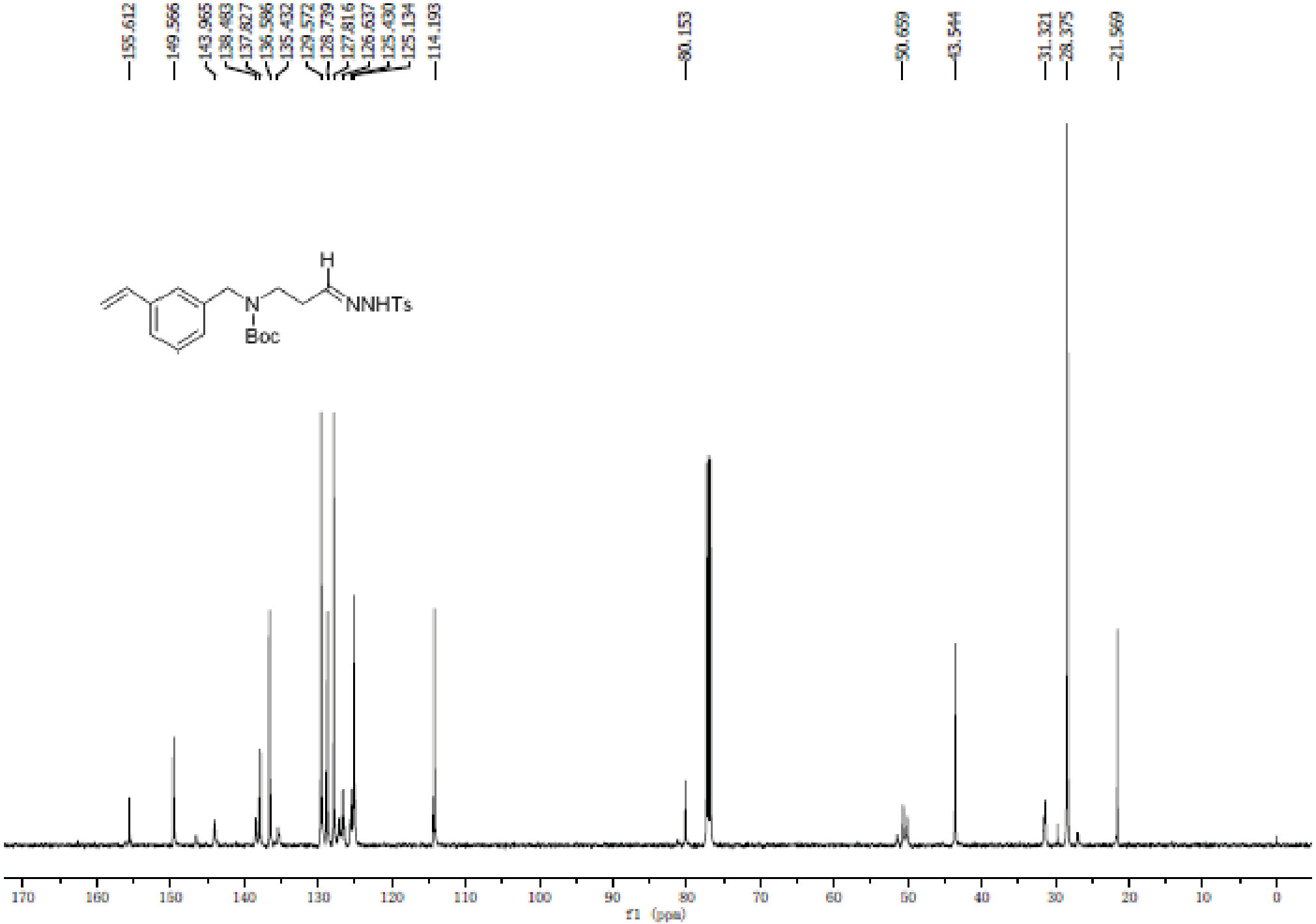
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (3-vinylbenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1k



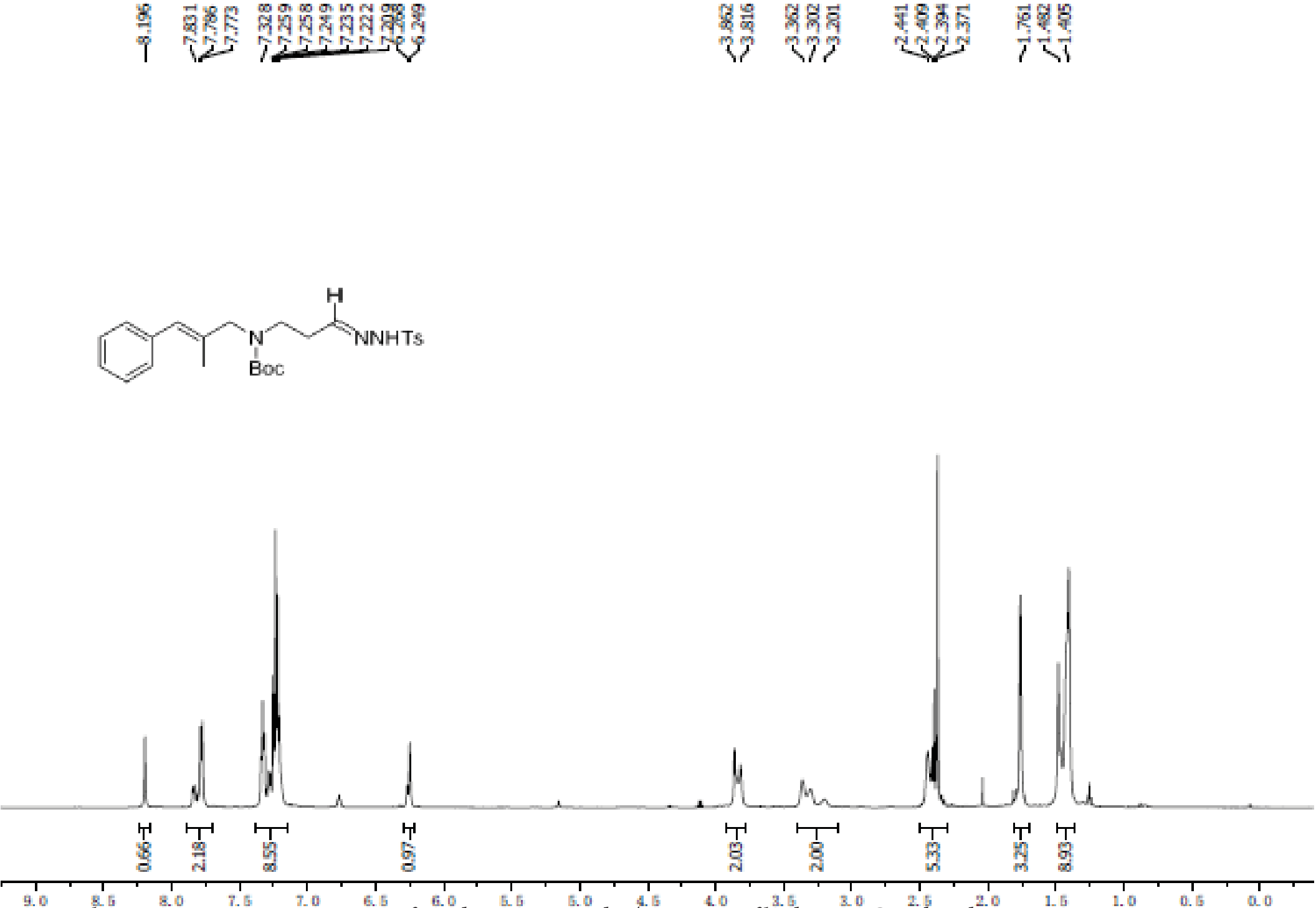
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (3-vinylbenzyl)(3-(2-tosylhydrazono)propyl) carbamate 1k



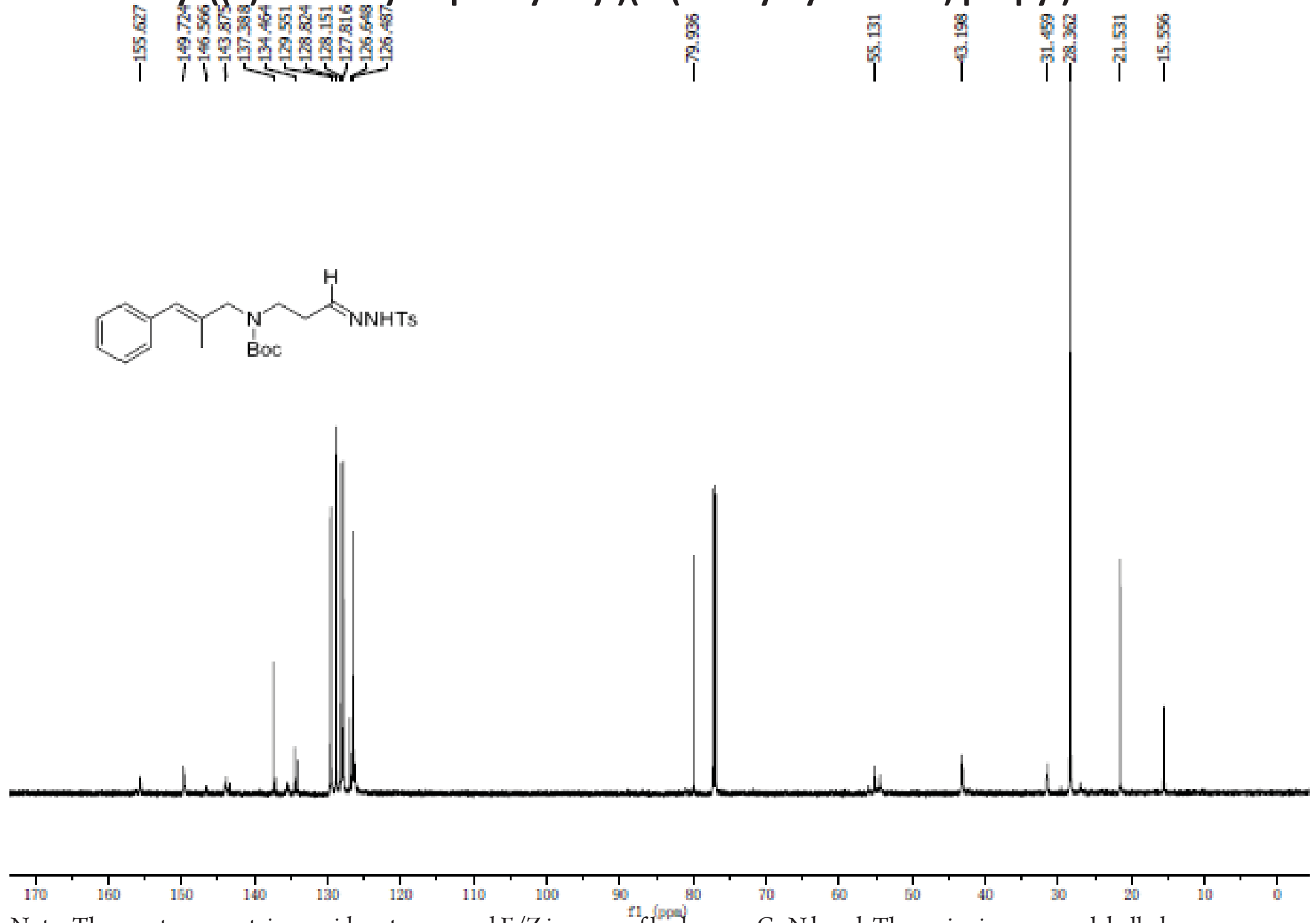
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl ((*E*)-2-methyl-3-phenylallyl)(3-(2-tosylhydrazono) propyl)carbamate 1l



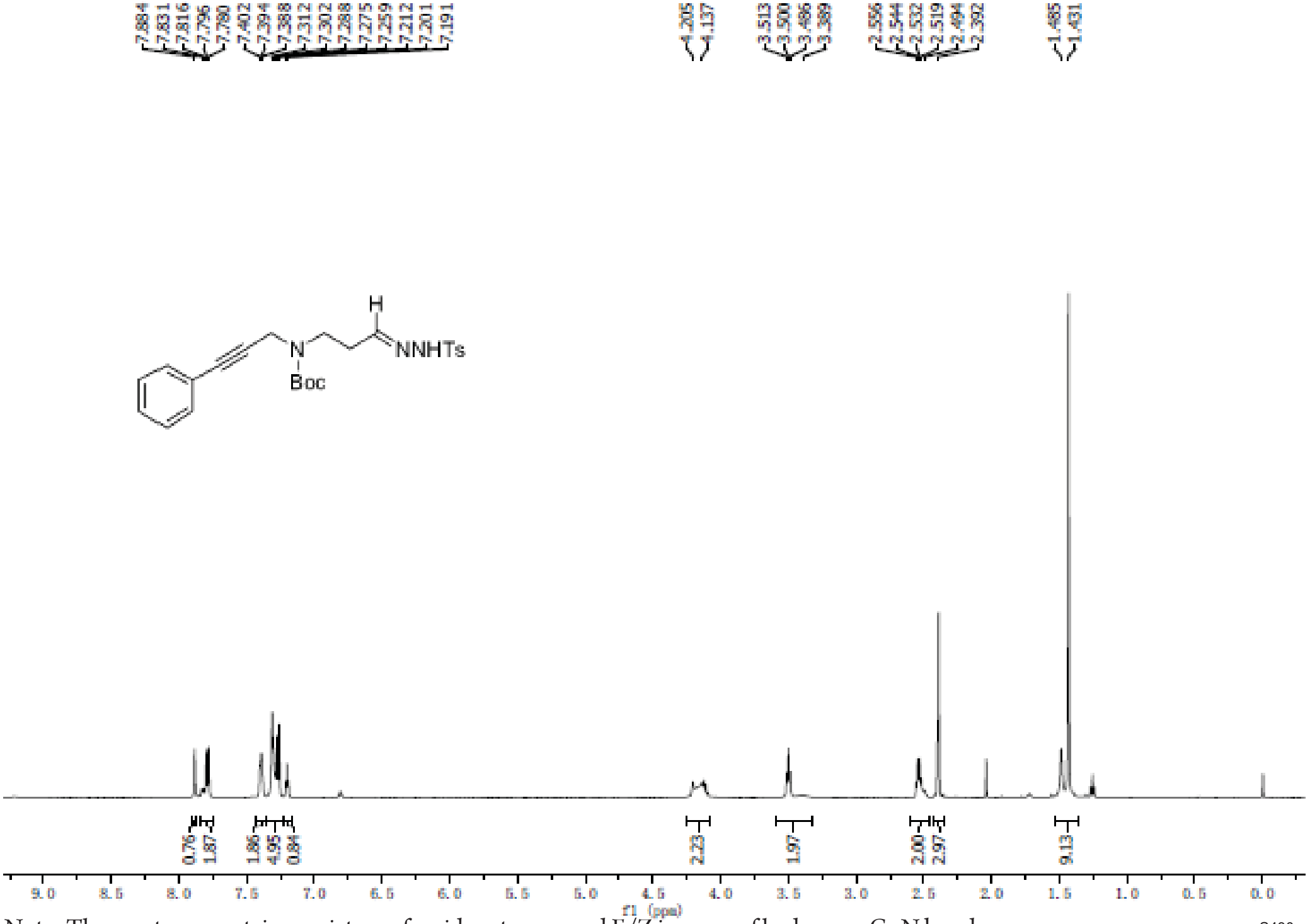
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl ((*E*)-2-methyl-3-phenylallyl)(3-(2-tosylhydrazono) propyl)carbamate 1l



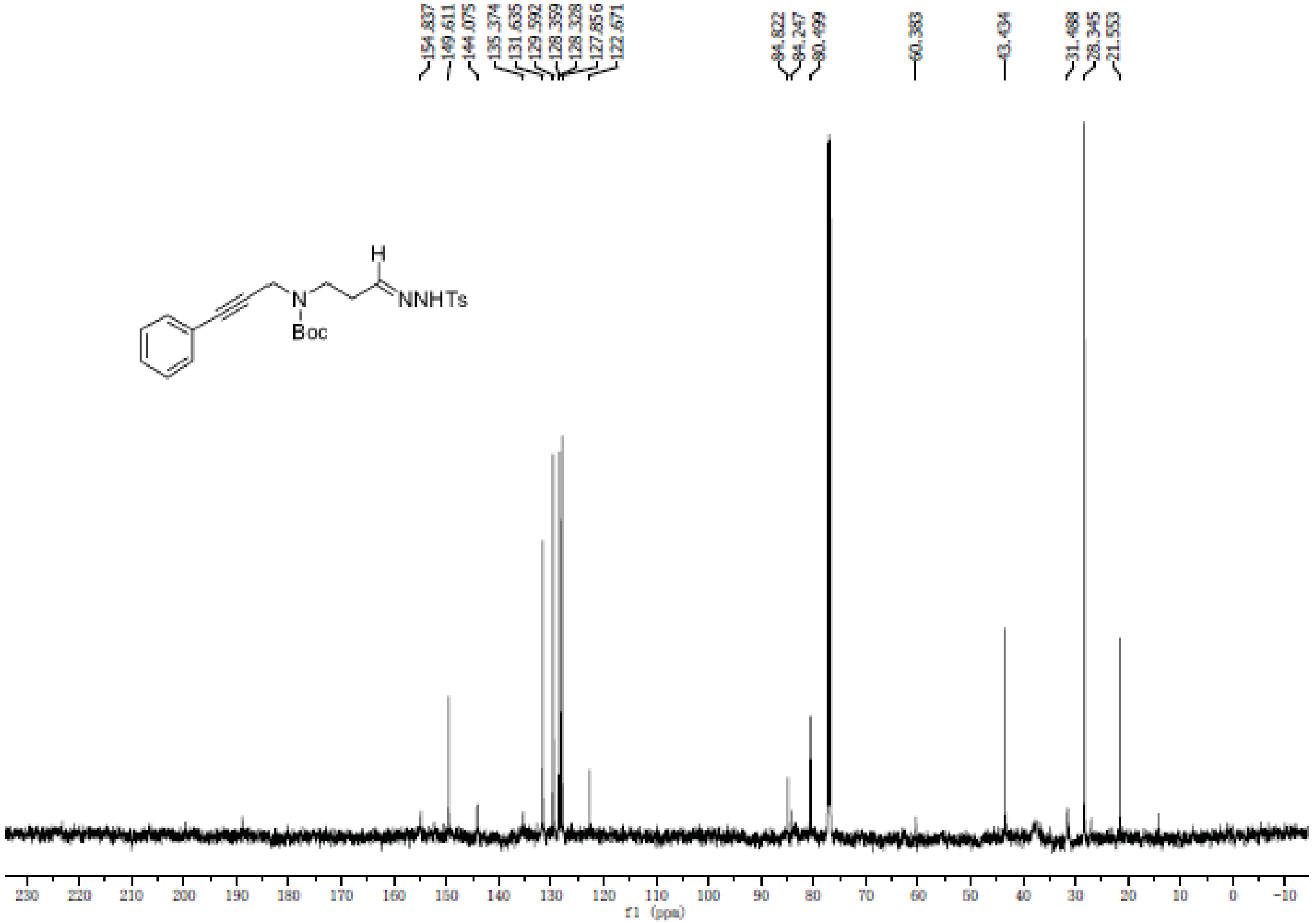
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (3-phenylprop-2-yn-1-yl)(3-(2-tosylhydrazono) propyl)carbamate 1m



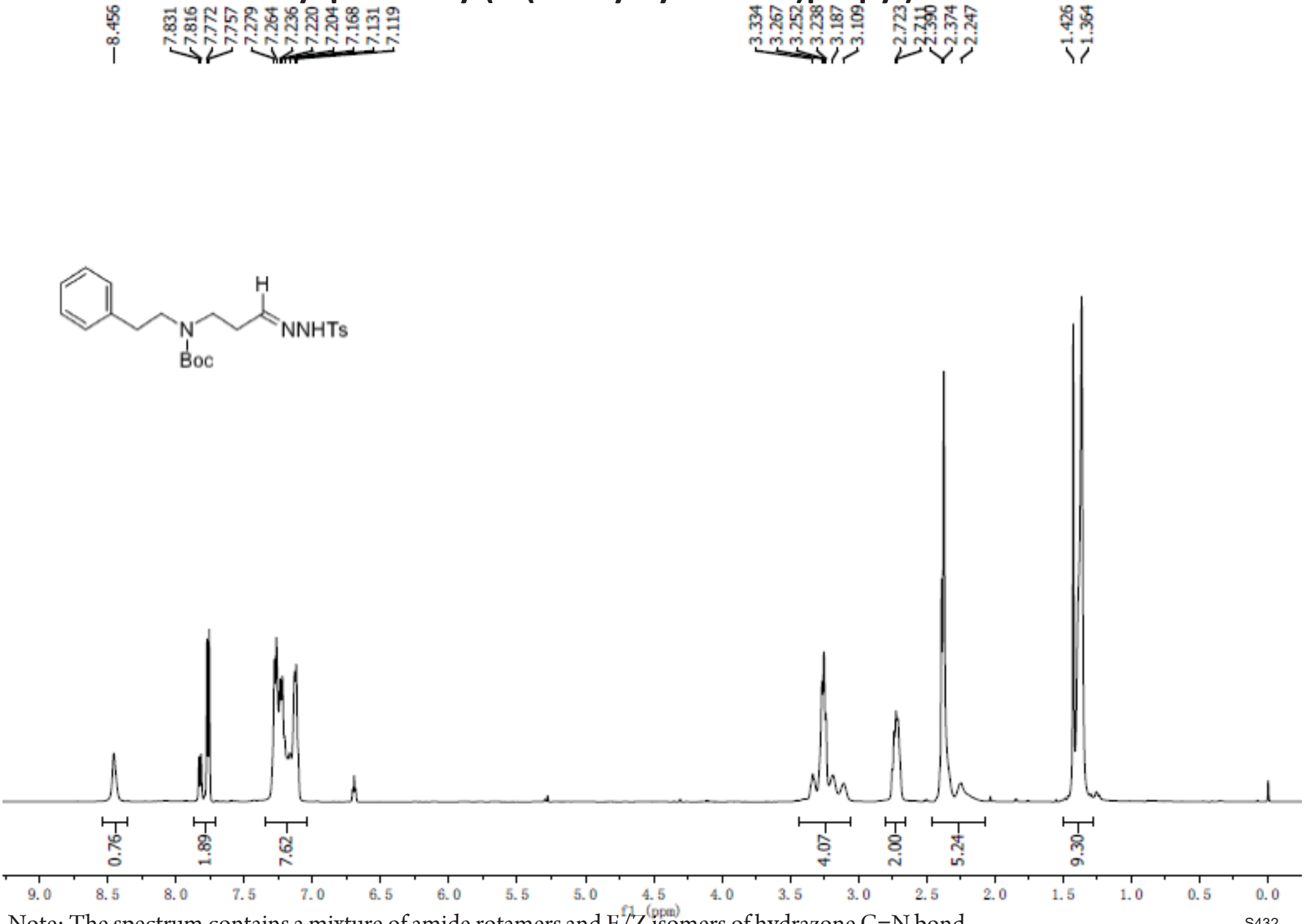
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (3-phenylprop-2-yn-1-yl)(3-(2-tosylhydrazono) propyl)carbamate 1m



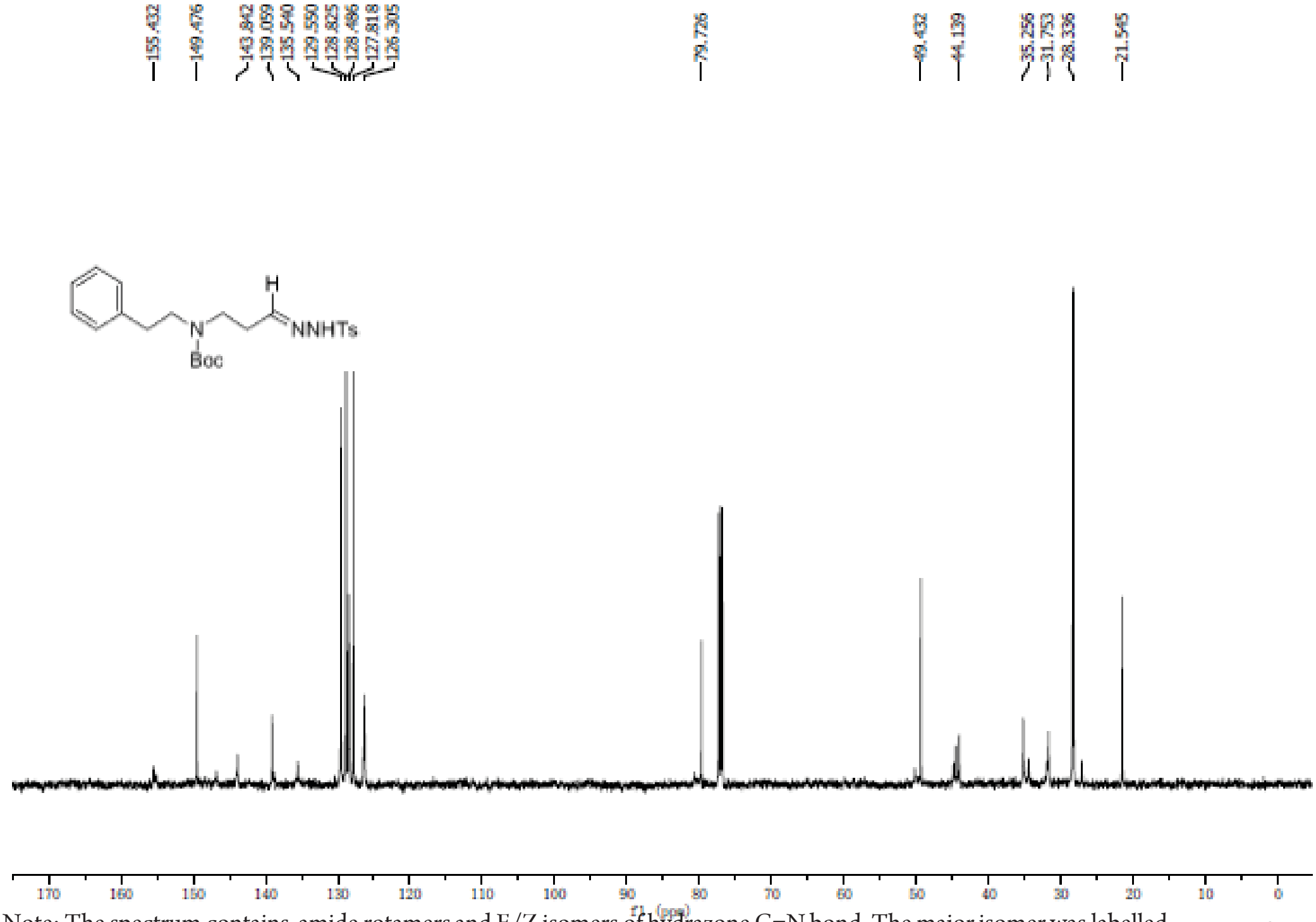
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl phenethyl(3-(2-tosylhydrazono)propyl)carbamate 1n



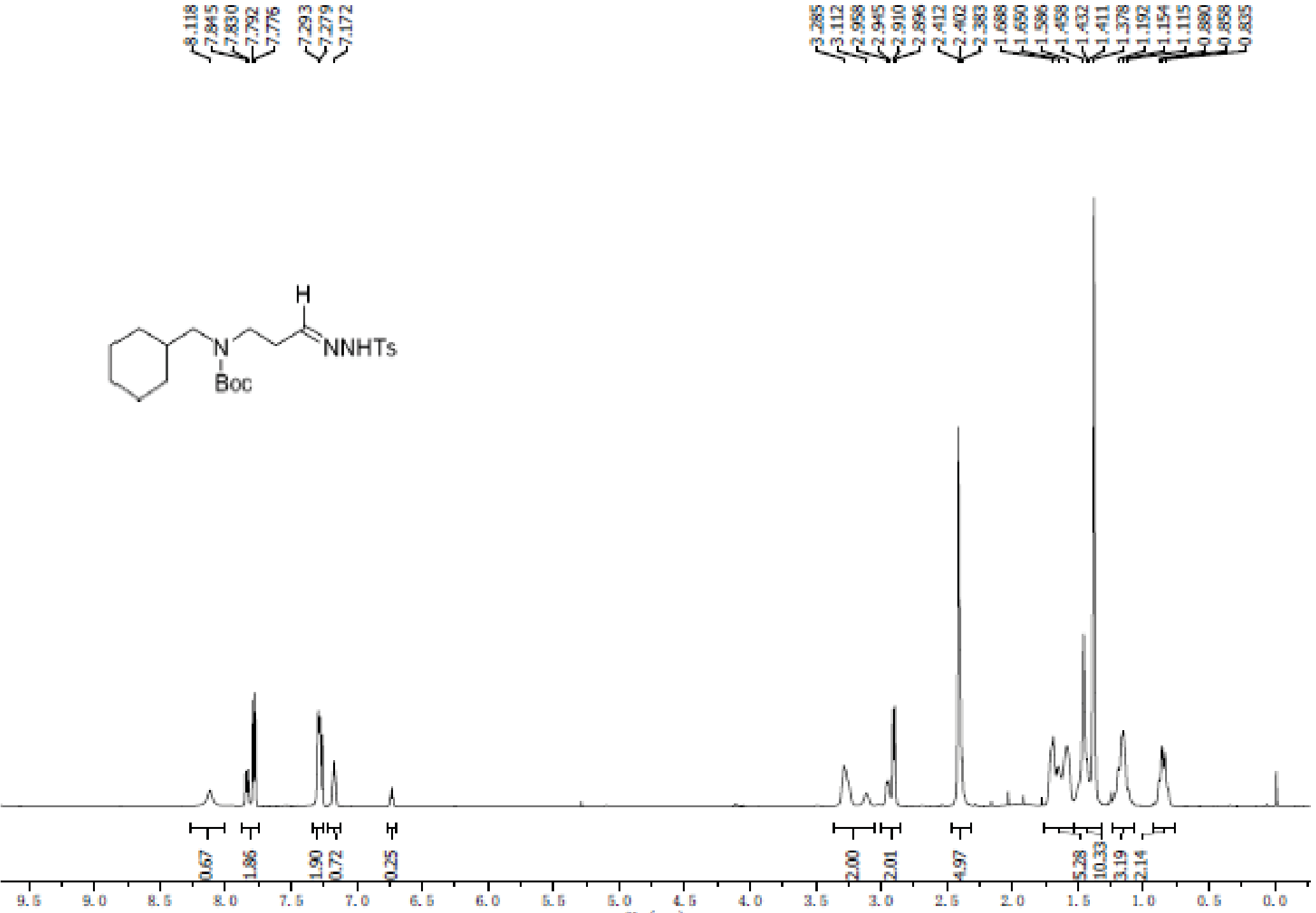
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl phenethyl(3-(2-tosylhydrazono)propyl)carbamate 1n



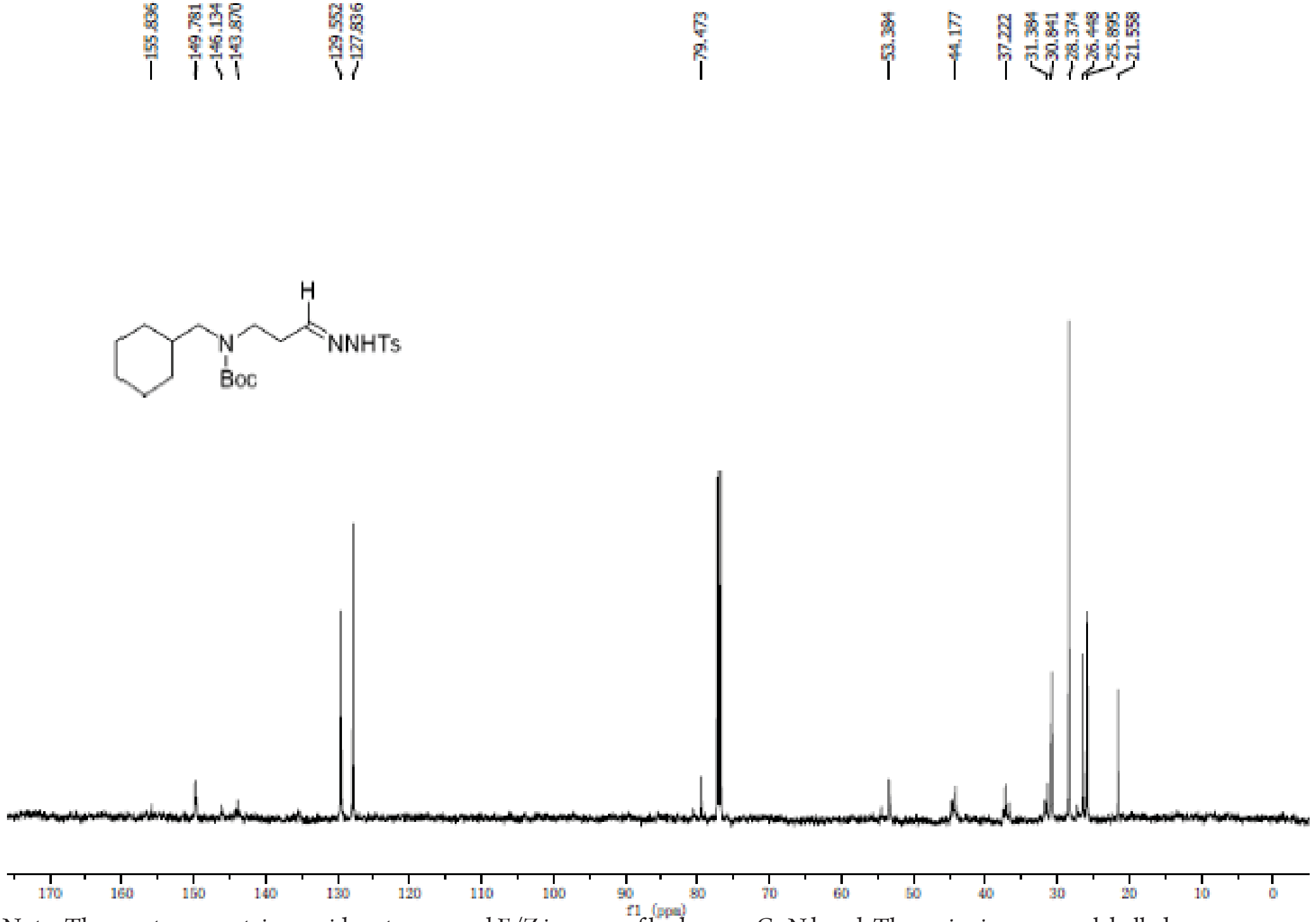
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (cyclohexylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1o



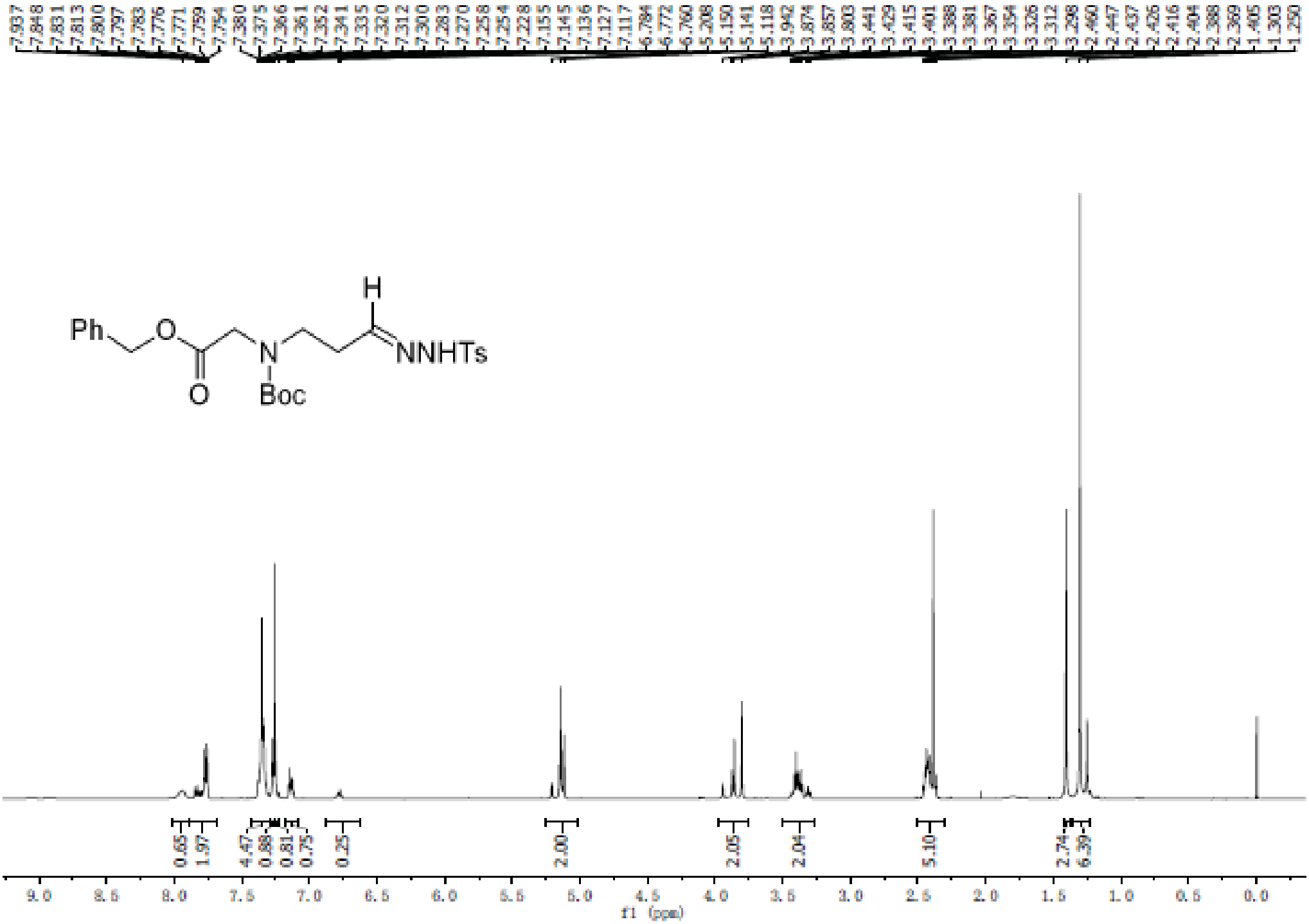
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (cyclohexylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1o



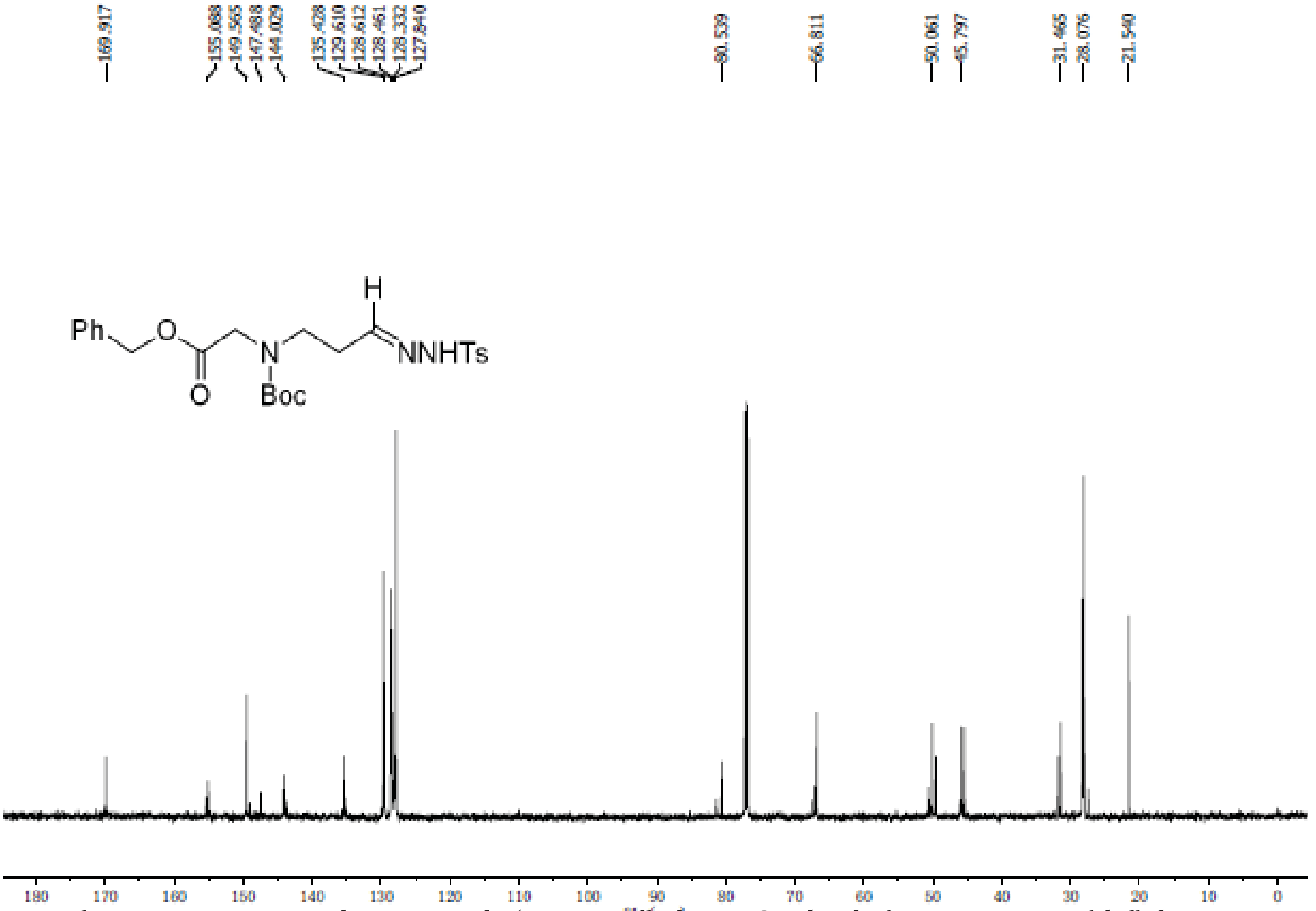
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

benzyl *N*-(*tert*-butoxycarbonyl)-*N*-(3-(2-tosylhydrazono) propyl)glycinate 1p



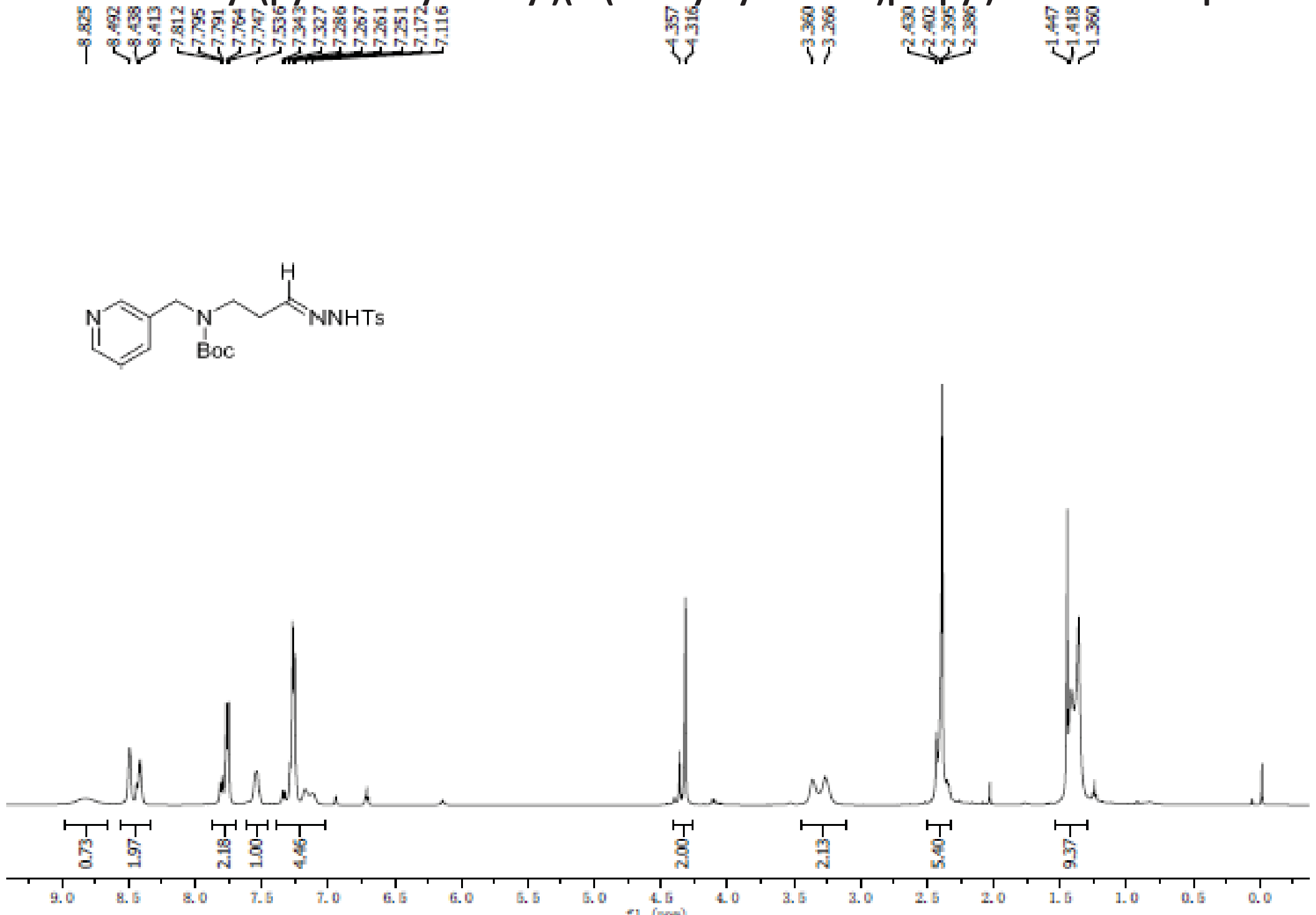
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

benzyl *N*-(*tert*-butoxycarbonyl)-*N*-(3-(2-tosylhydrazono) propyl)glycinate 1p



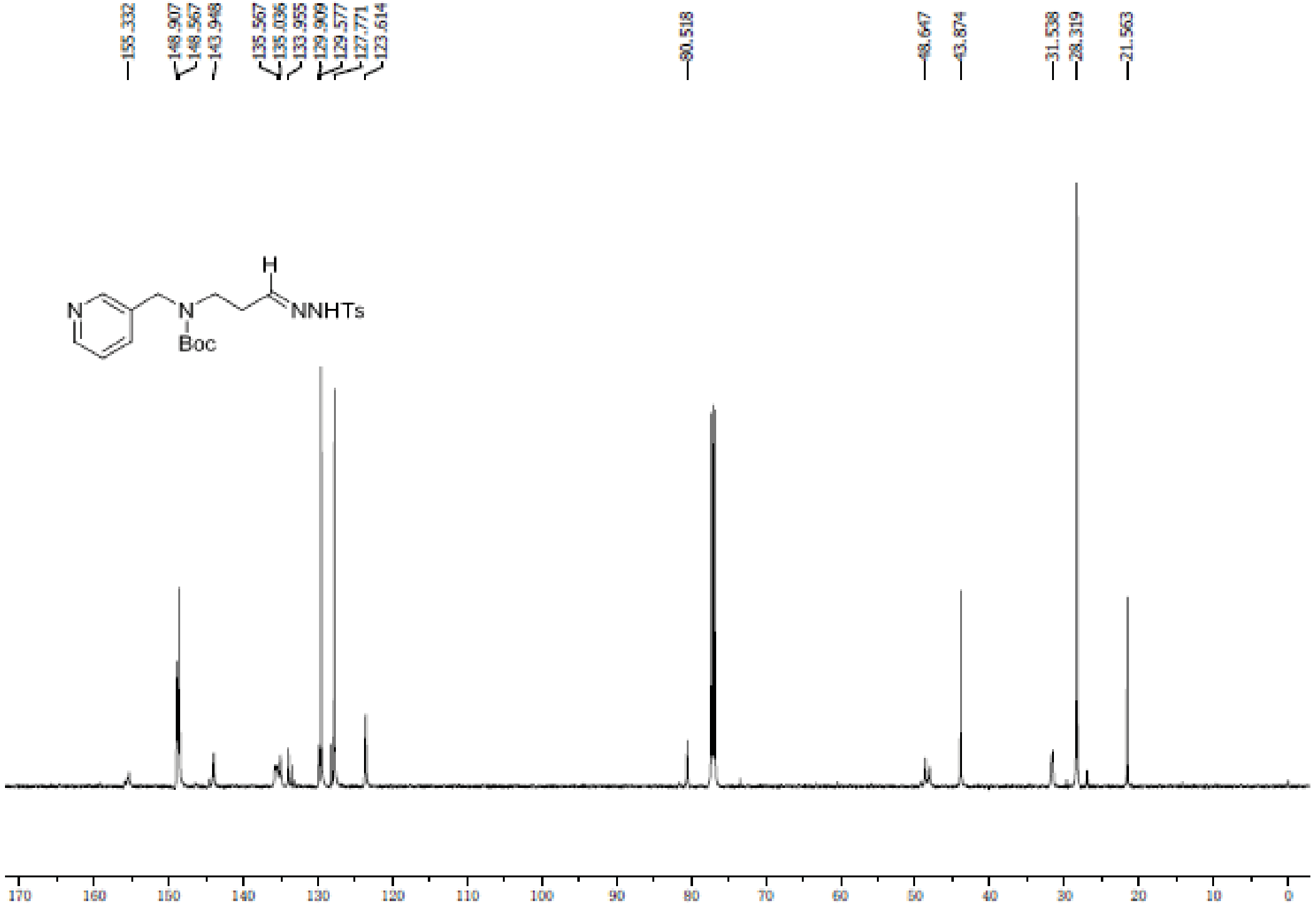
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (pyridin-3-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1q



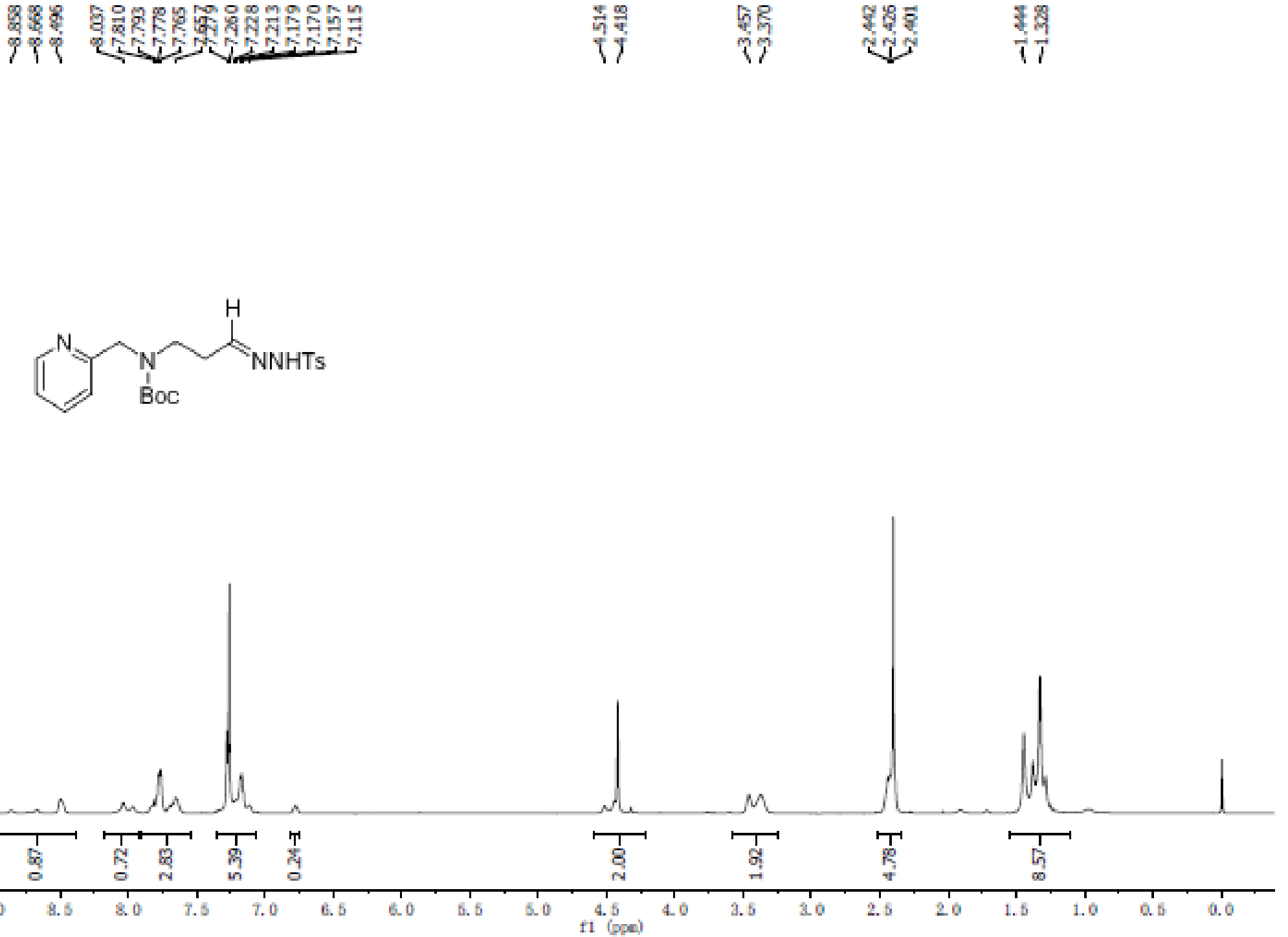
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (pyridin-3-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1q



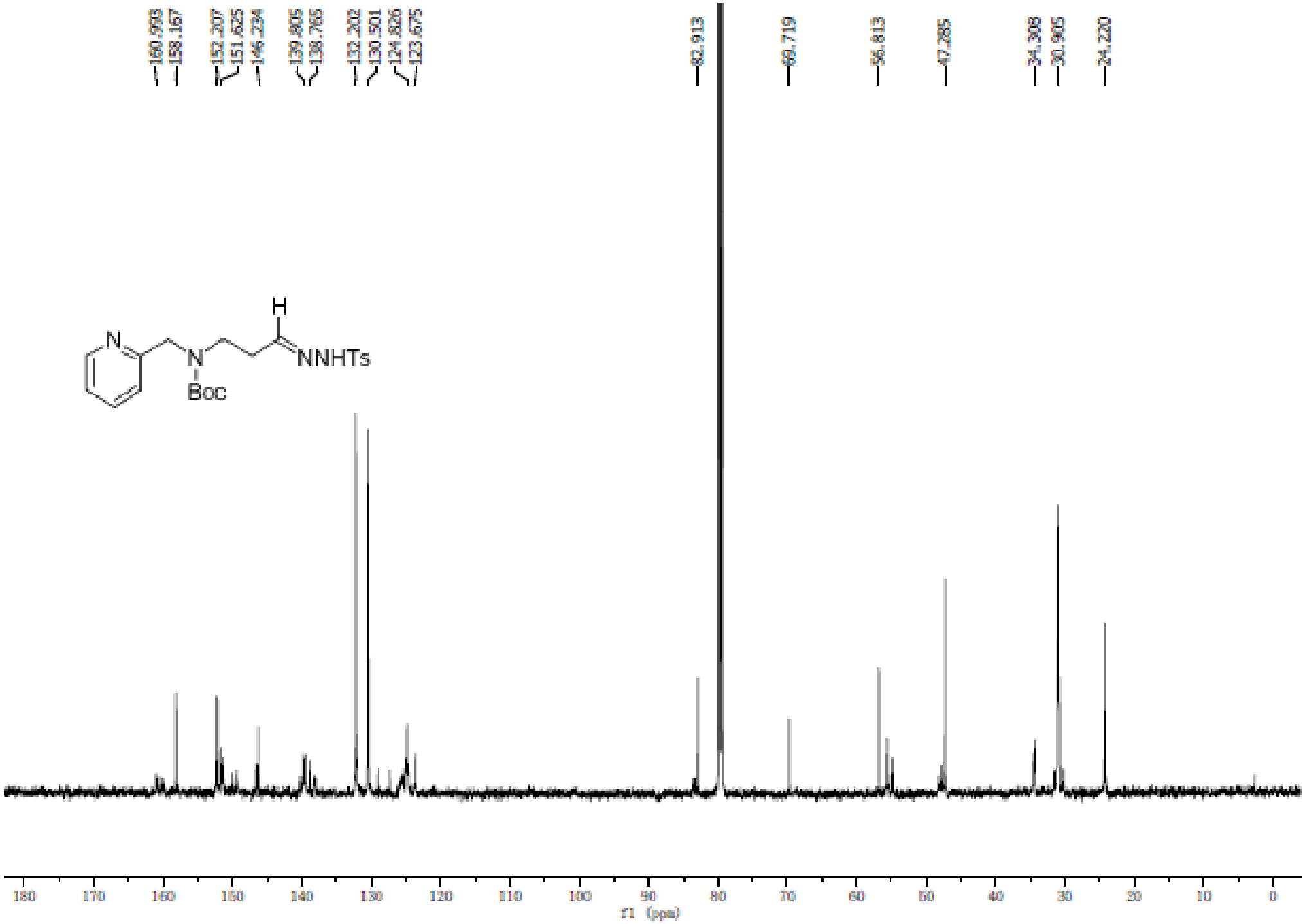
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (pyridin-2-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1r



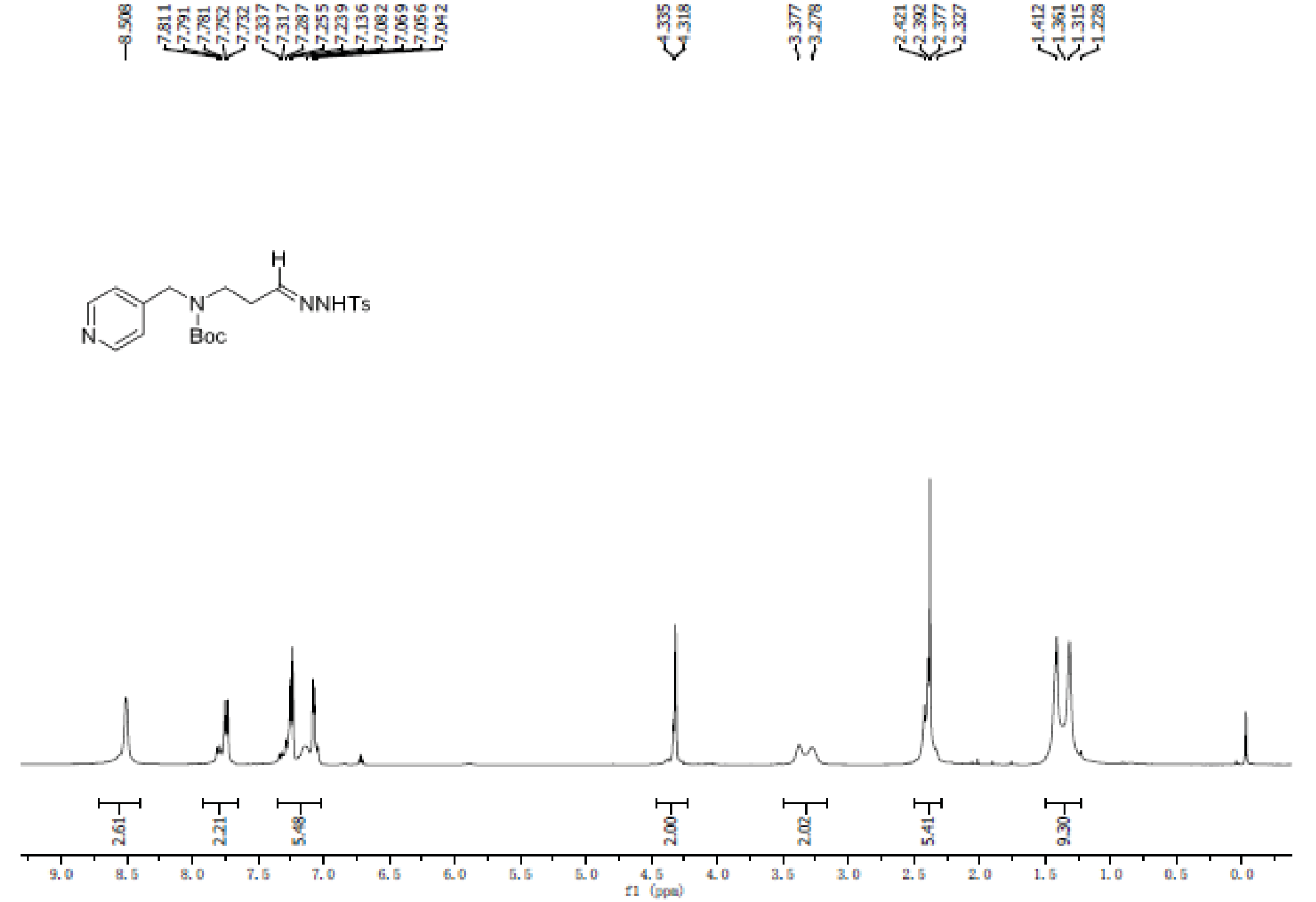
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (pyridin-2-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1r



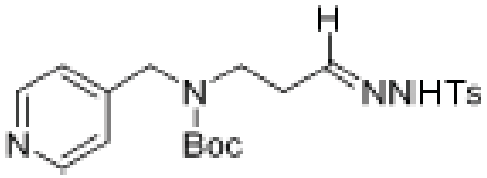
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

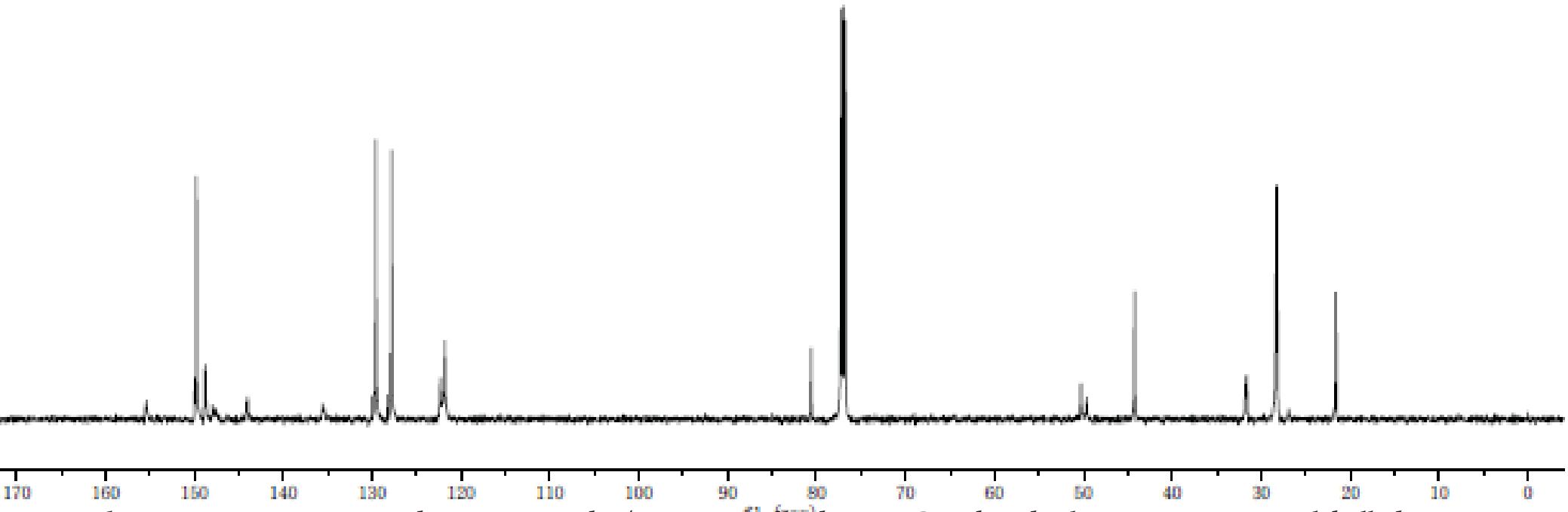
tert-butyl (pyridin-4-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1s



Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

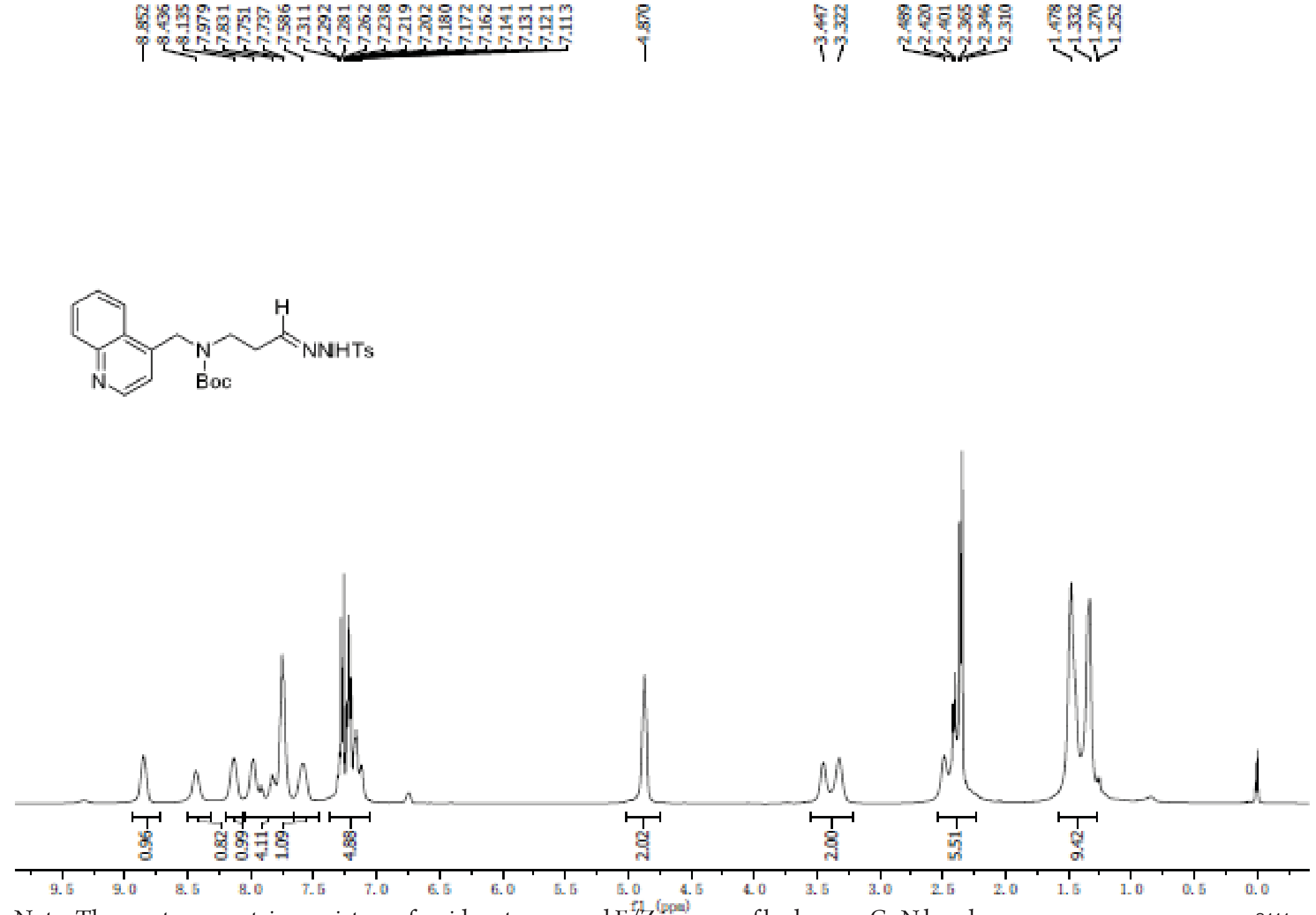
tert-butyl (pyridin-4-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1s





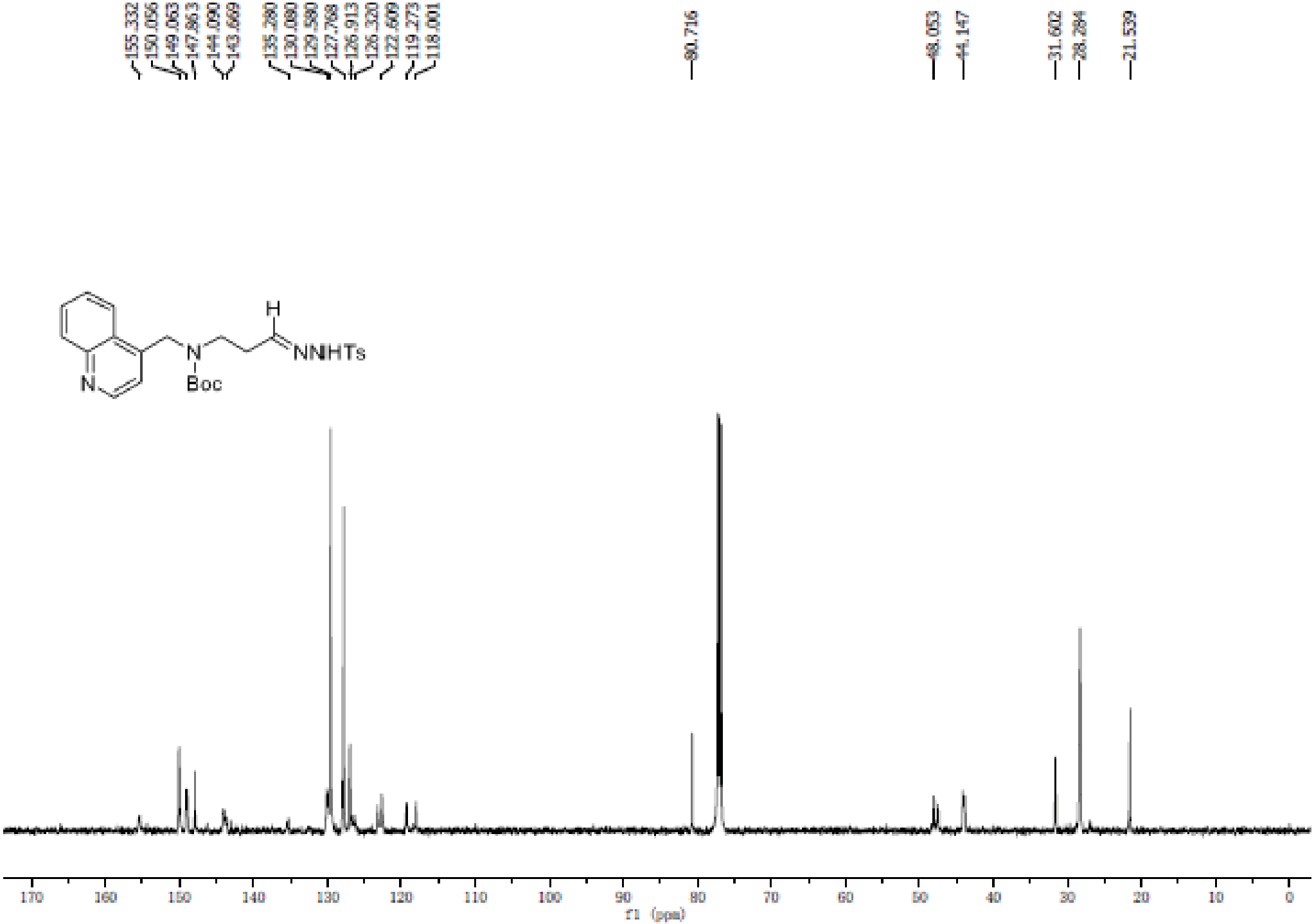
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (quinolin-4-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1t



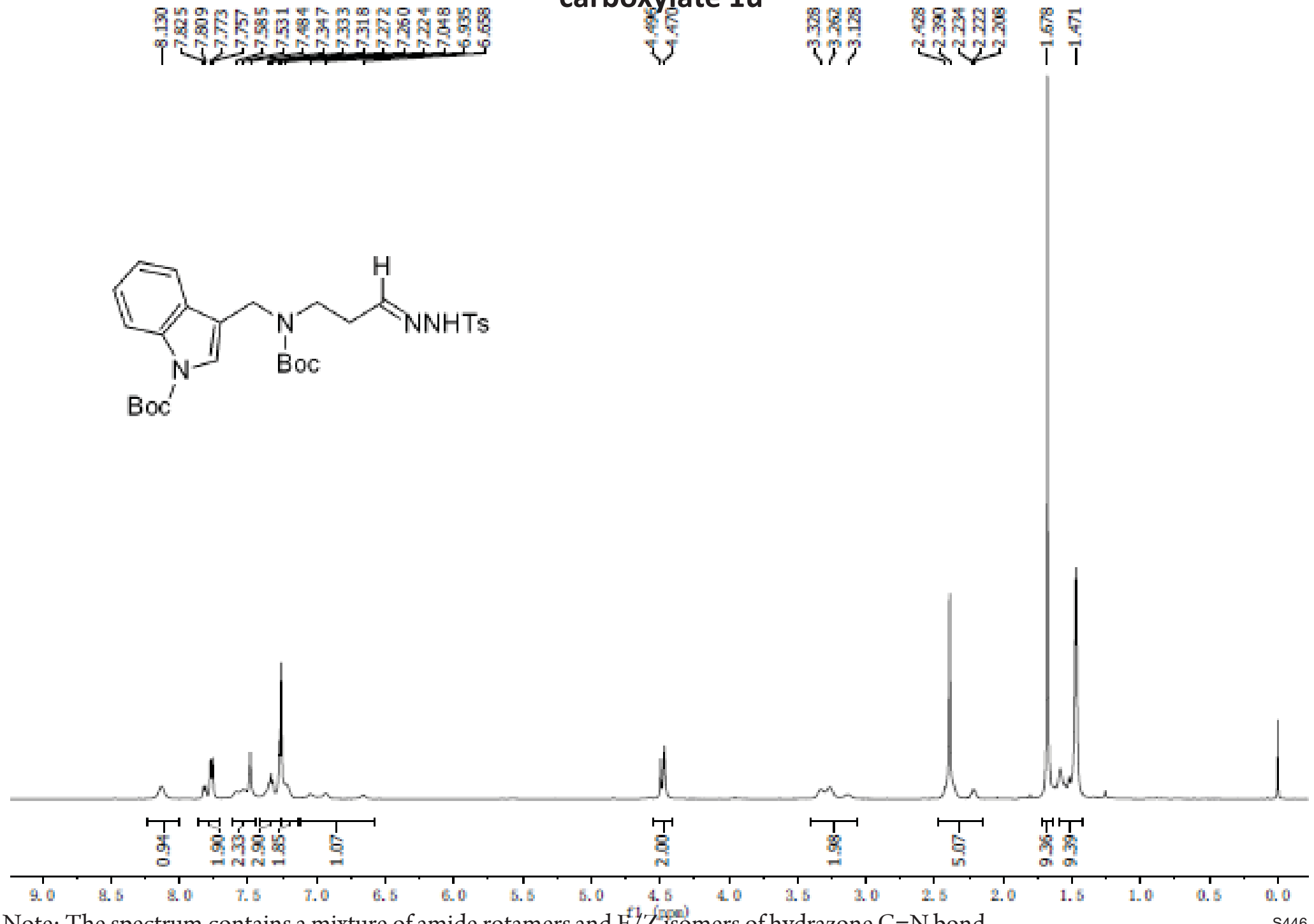
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (quinolin-4-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1t



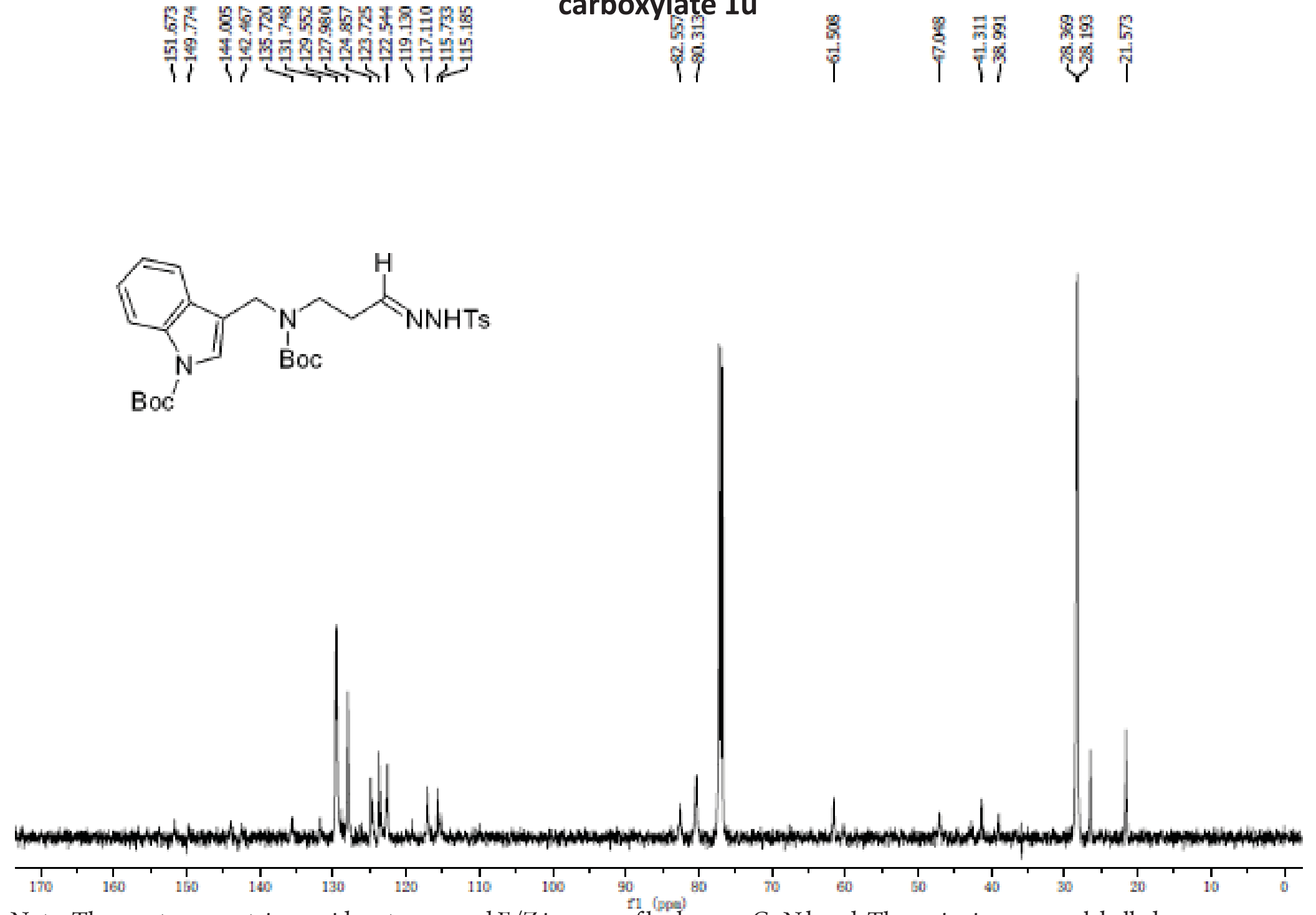
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl 3-(((_tert_-butoxycarbonyl)(3-(2-tosylhydrazono) propyl)amino)methyl)-1H-indole-1-carboxylate 1u



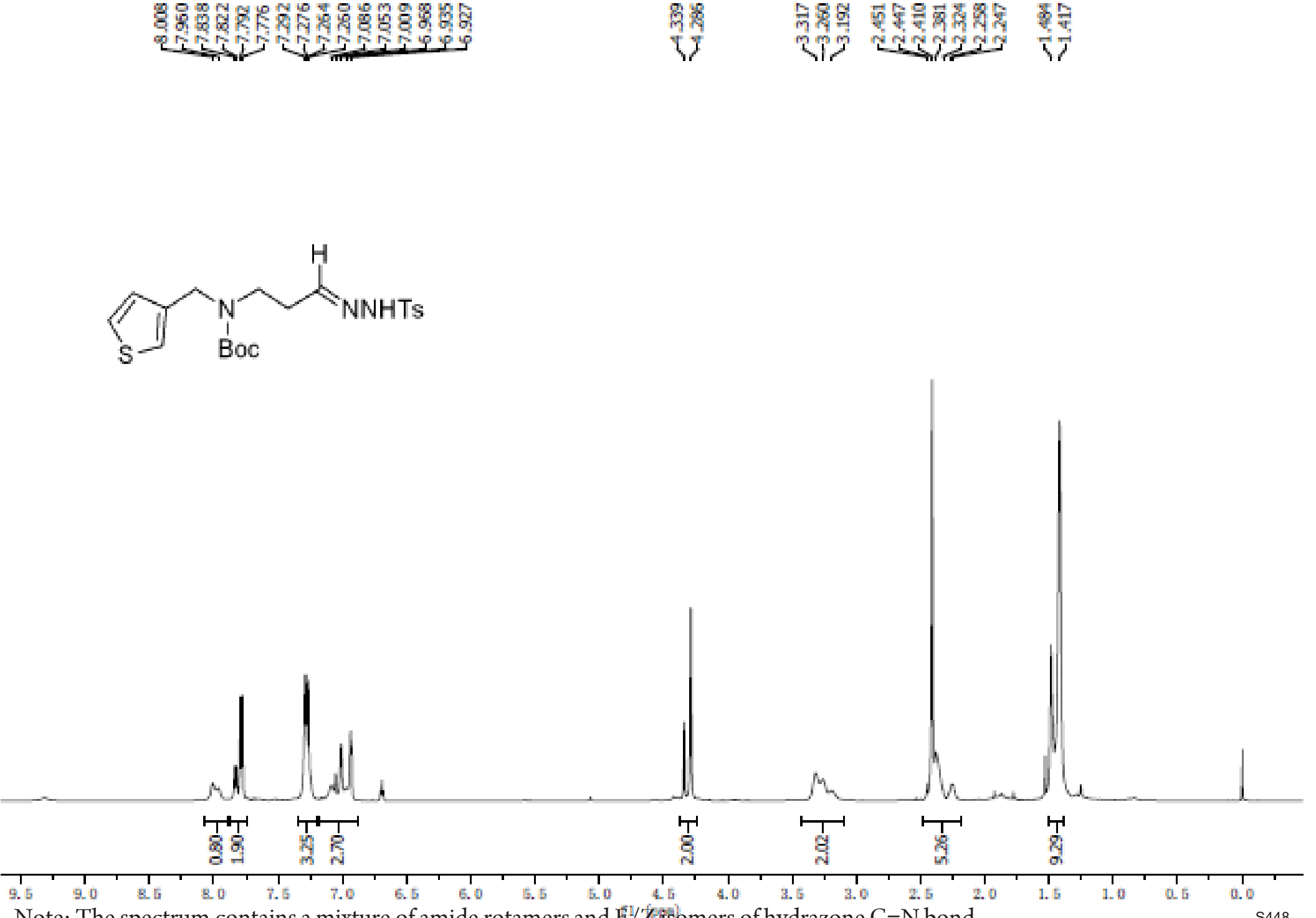
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl 3-(((*tert*-butoxycarbonyl)(3-(2-tosylhydrazono) propyl)amino)methyl)-1H-indole-1-carboxylate 1u



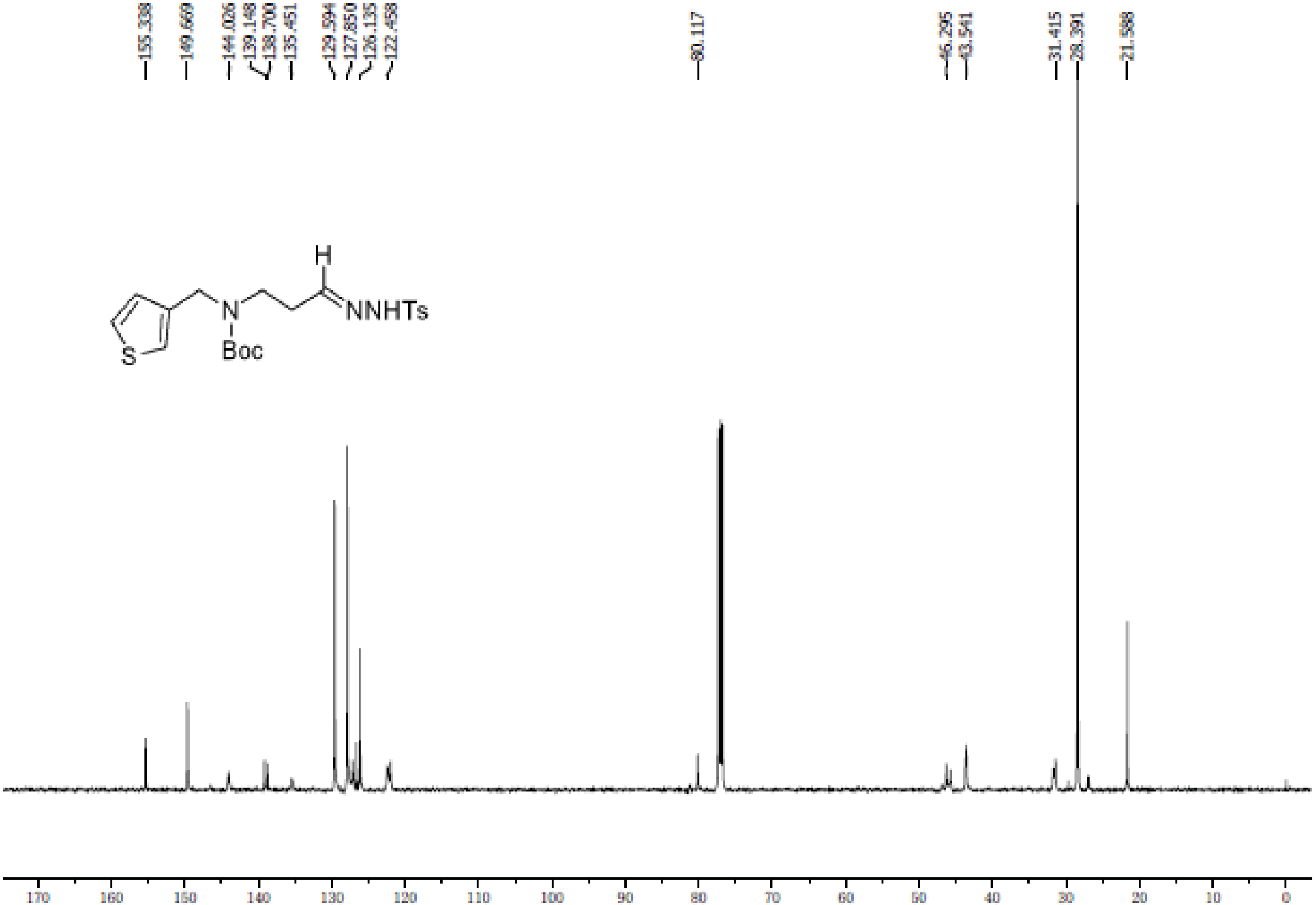
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (thiophen-3-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1v



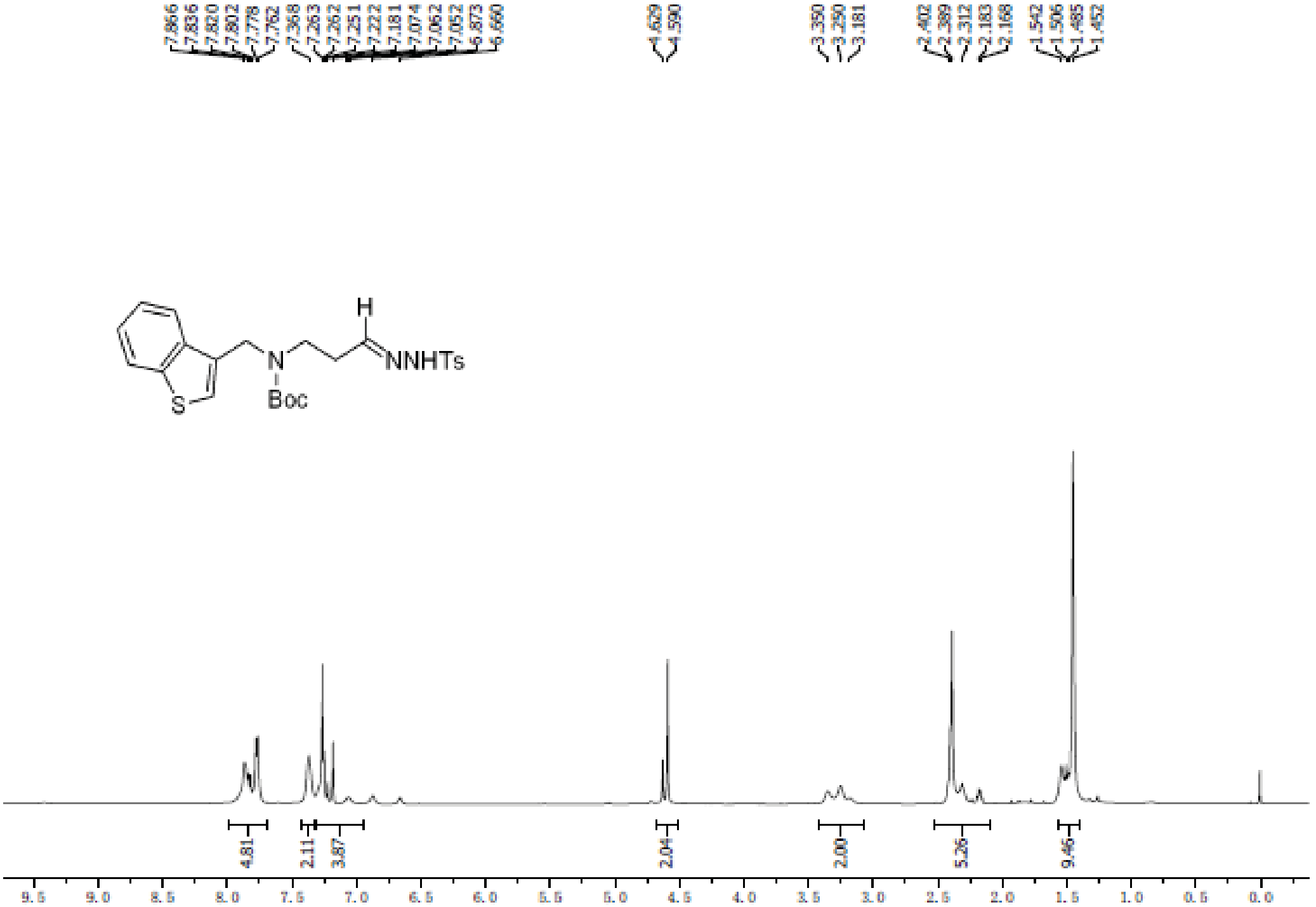
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (thiophen-3-ylmethyl)(3-(2-tosylhydrazono)propyl) carbamate 1v



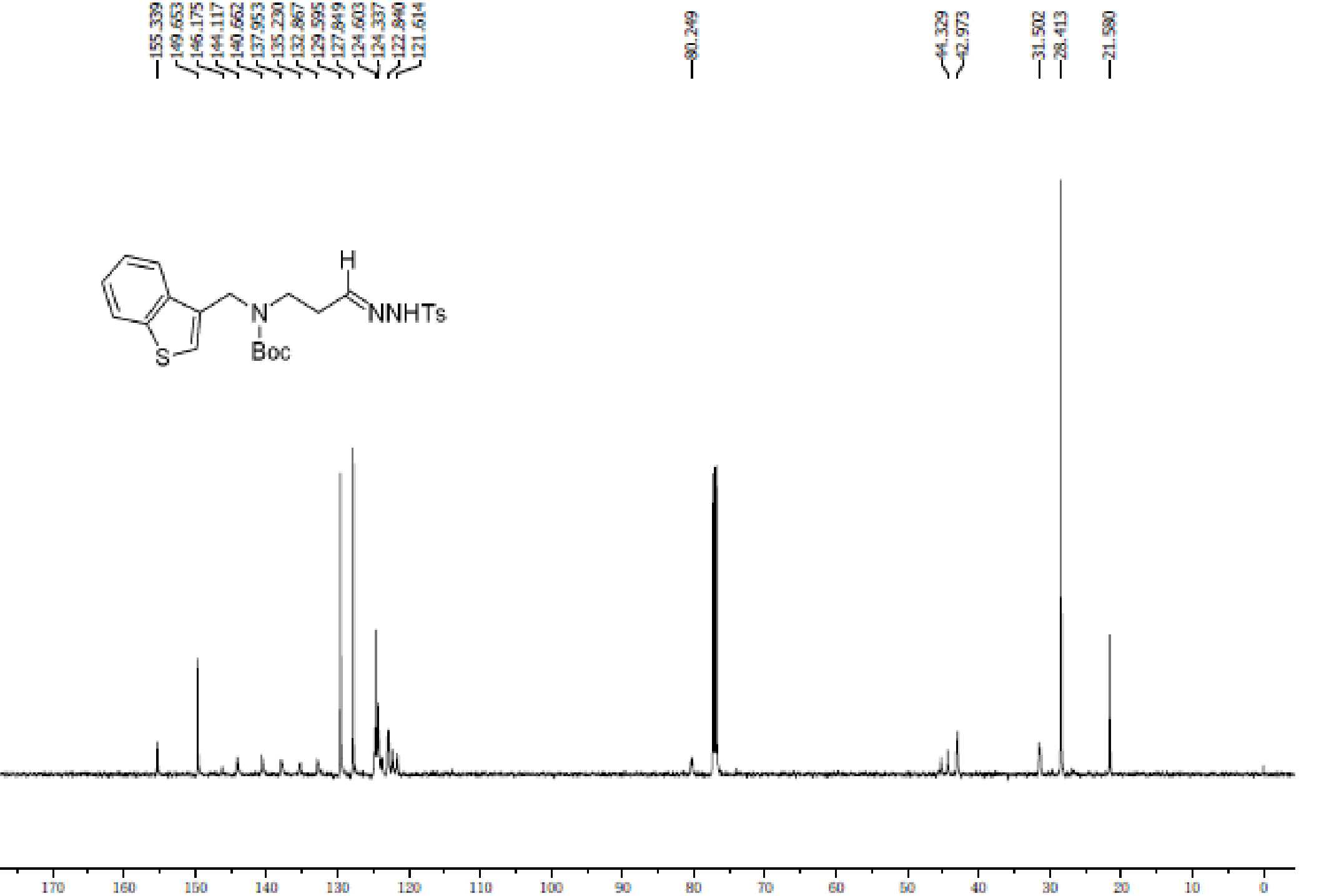
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (benzo[b]thiophen-3-ylmethyl)(3-(2-tosylhydrazono) propyl)carbamate 1w



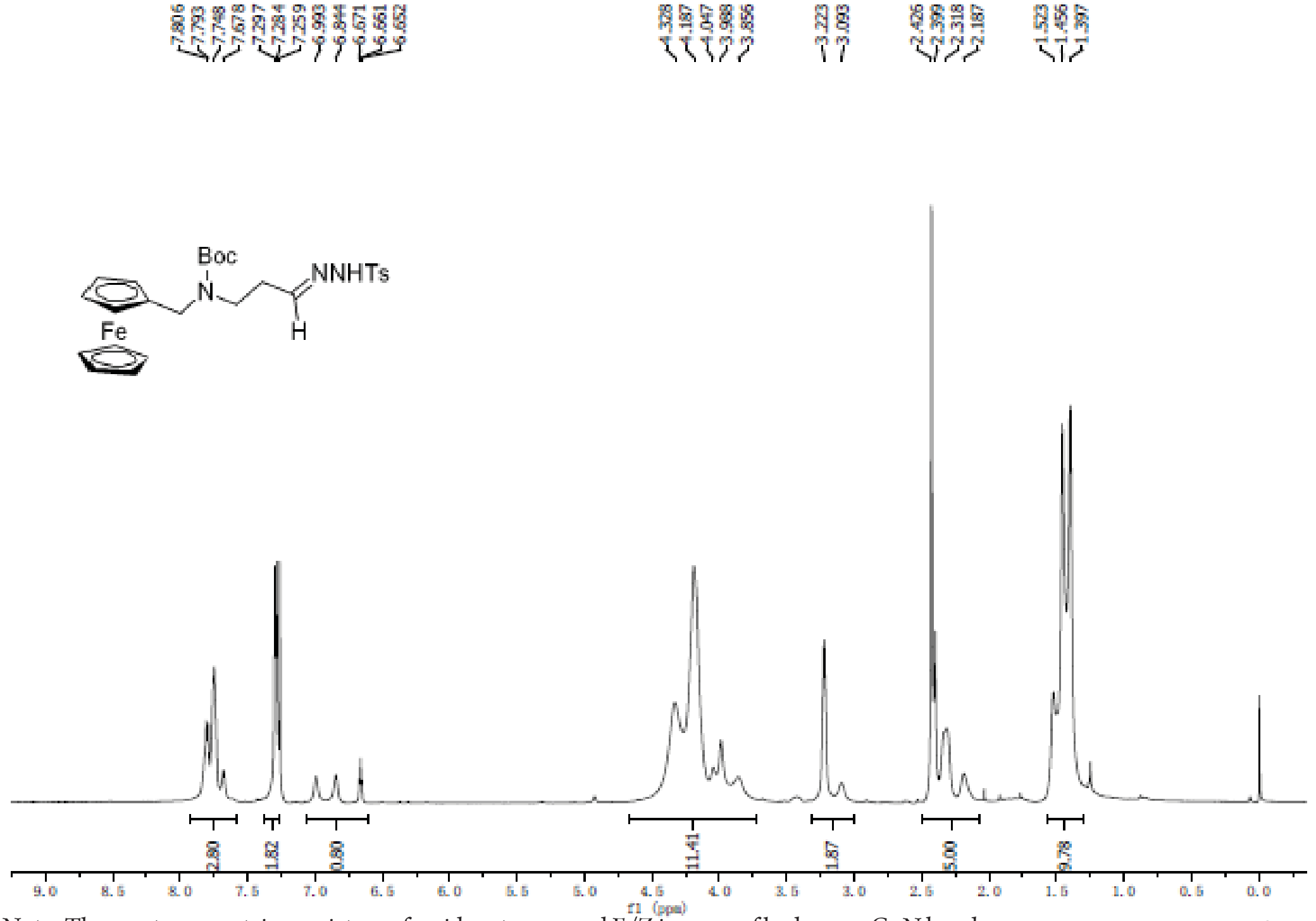
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (benzo[b]thiophen-3-ylmethyl)(3-(2-tosylhydrazono) propyl)carbamate 1w



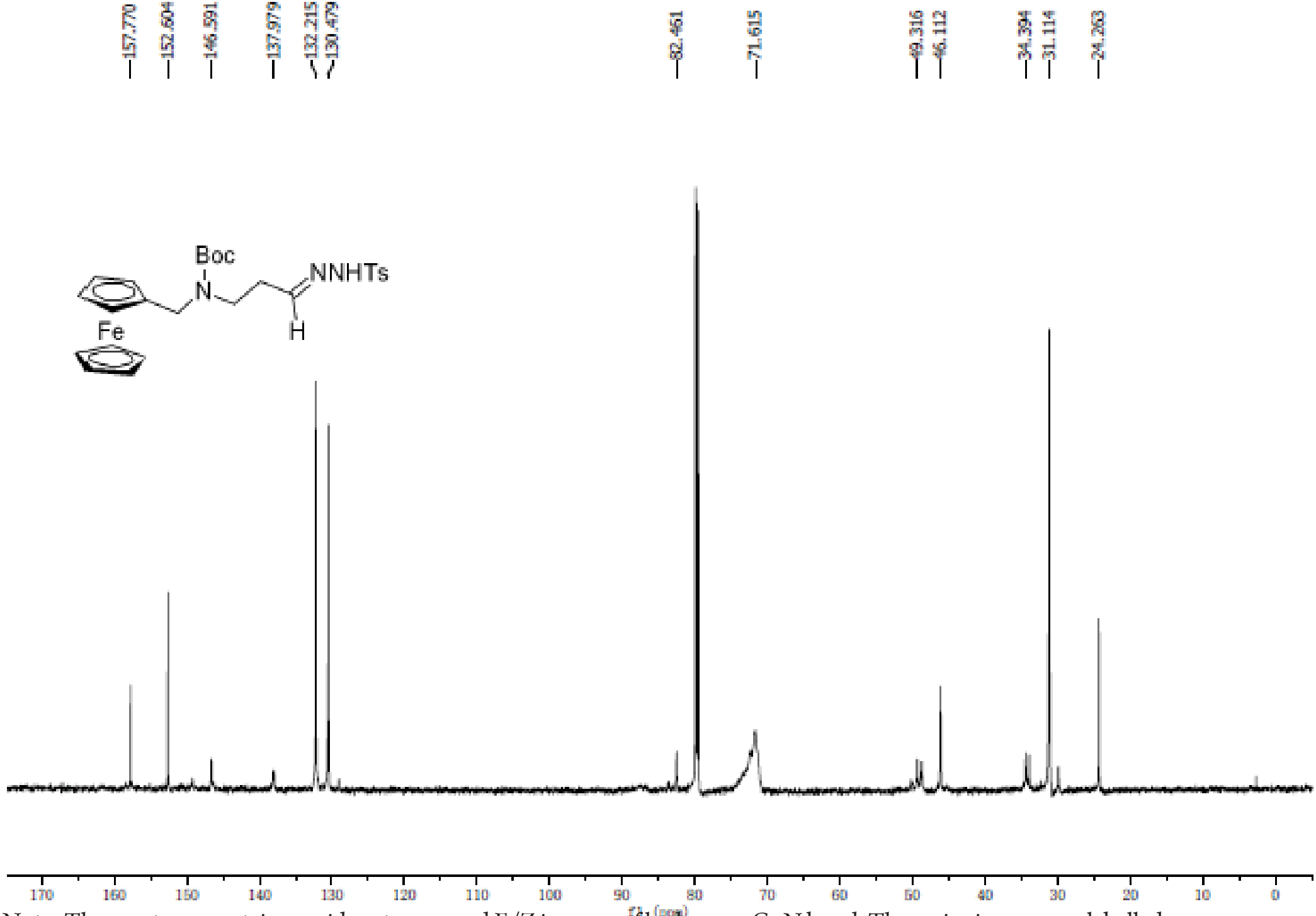
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl (ferrocenyl)(3-(2-tosylhydrazono)propyl) carbamate 1x



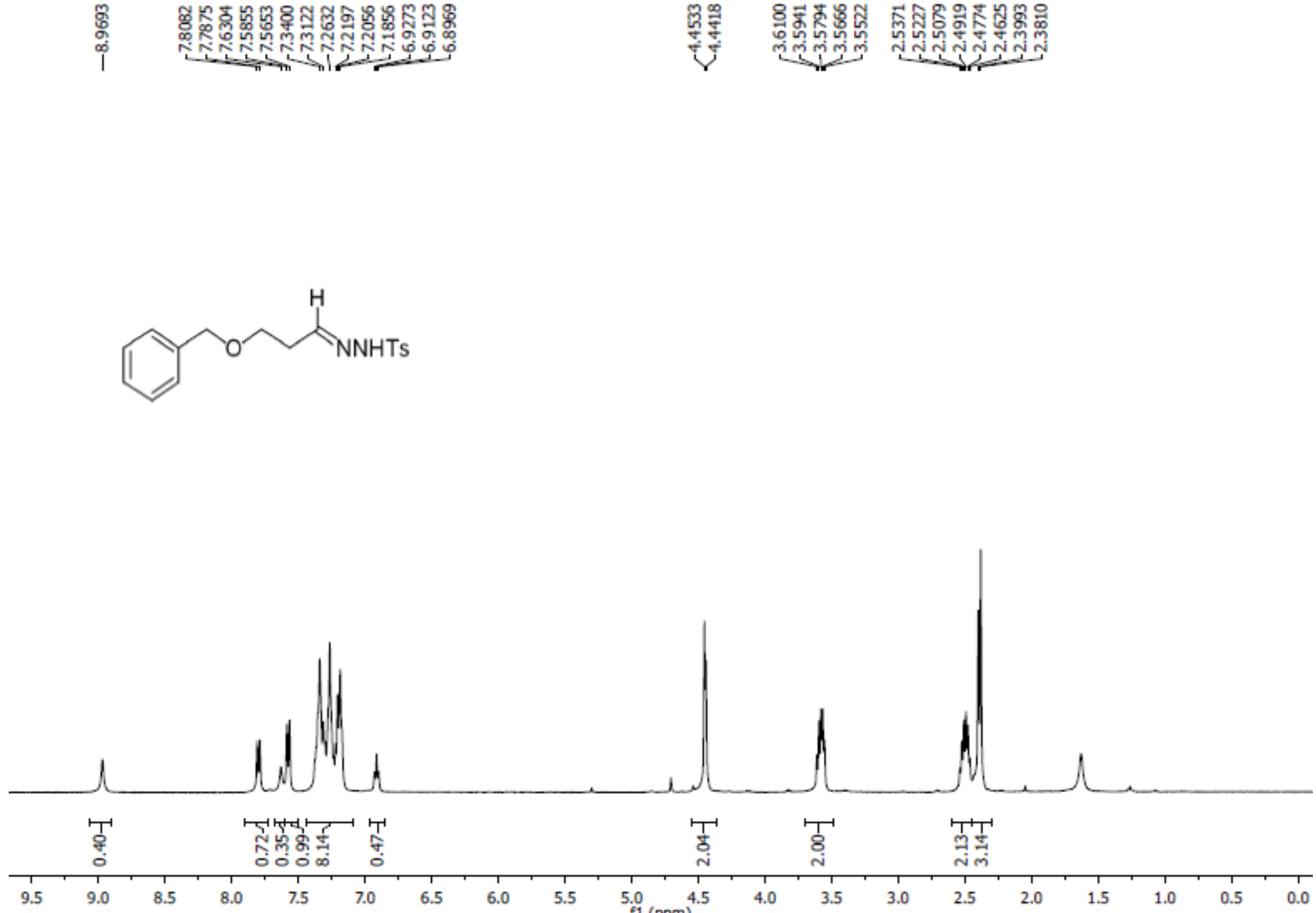
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl (ferrocenyl)(3-(2-tosylhydrazono)propyl) carbamate 1x



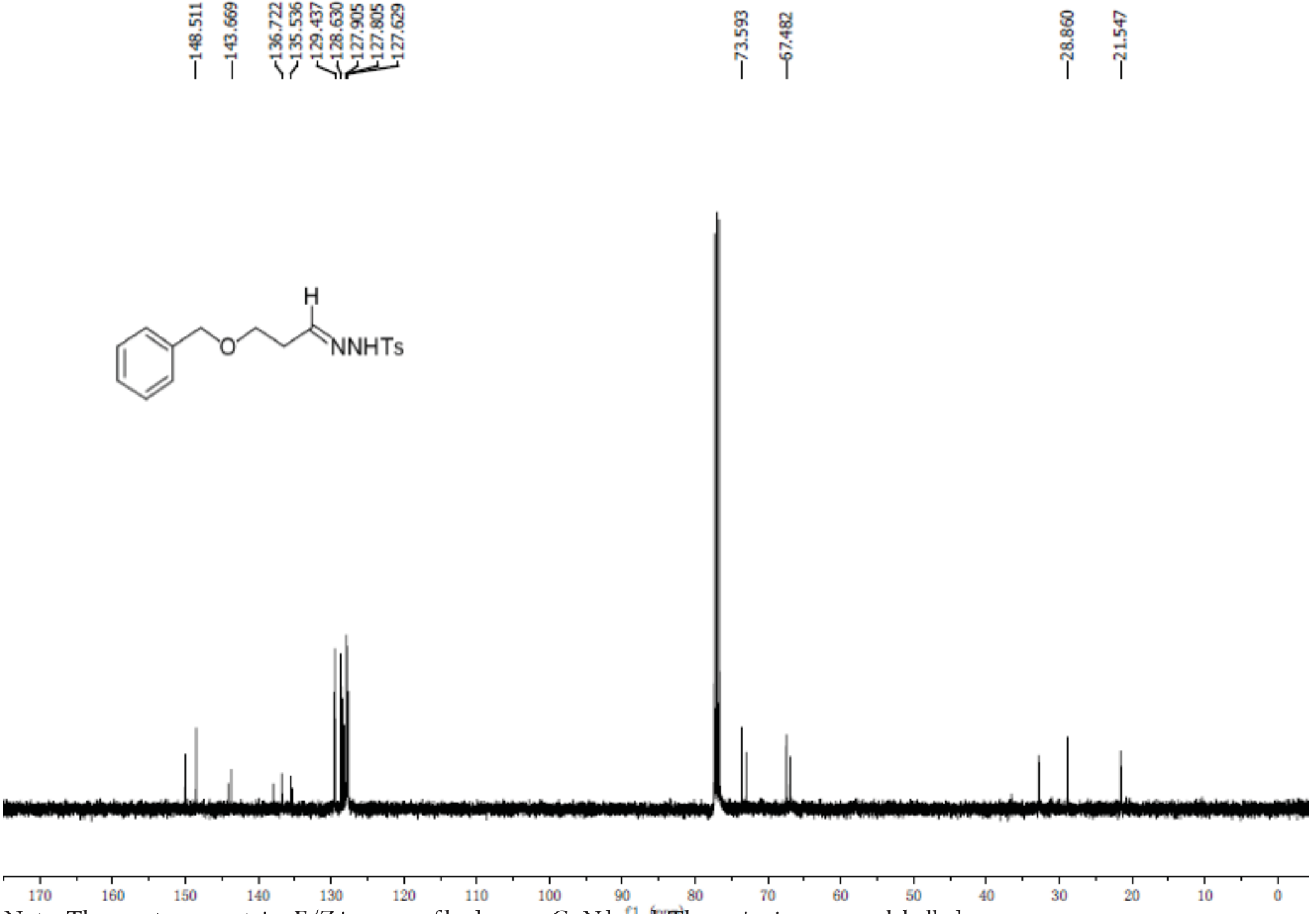
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

N'-(3-(benzyloxy)propylidene)-4-methylbenzenesulfonohydrazide 1y



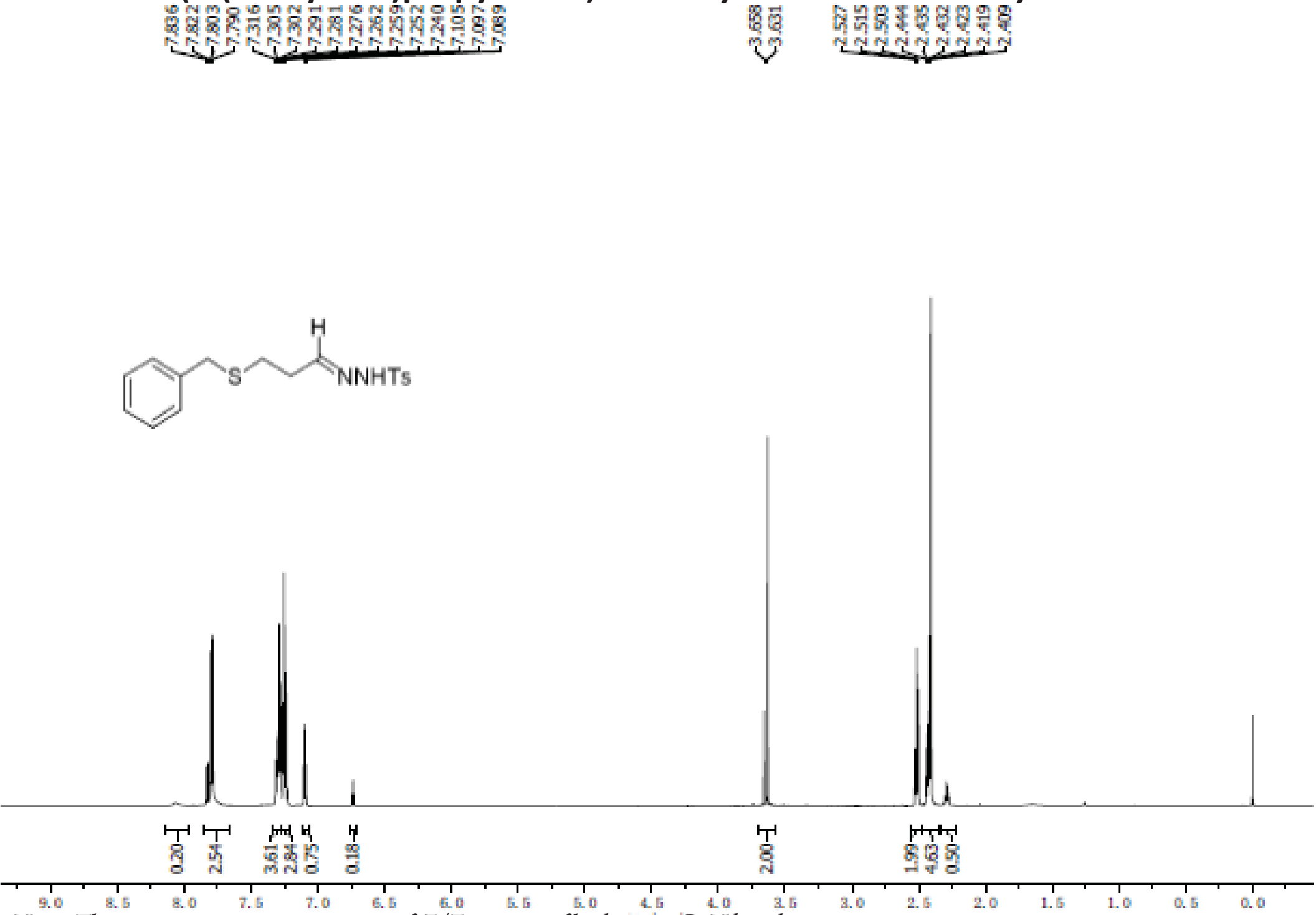
Note: The spectrum contains a mixture of E/Z isomers of hydrazone C=N bond.

N'-(3-(benzyloxy)propylidene)-4-methylbenzenesulfonohydrazide 1y



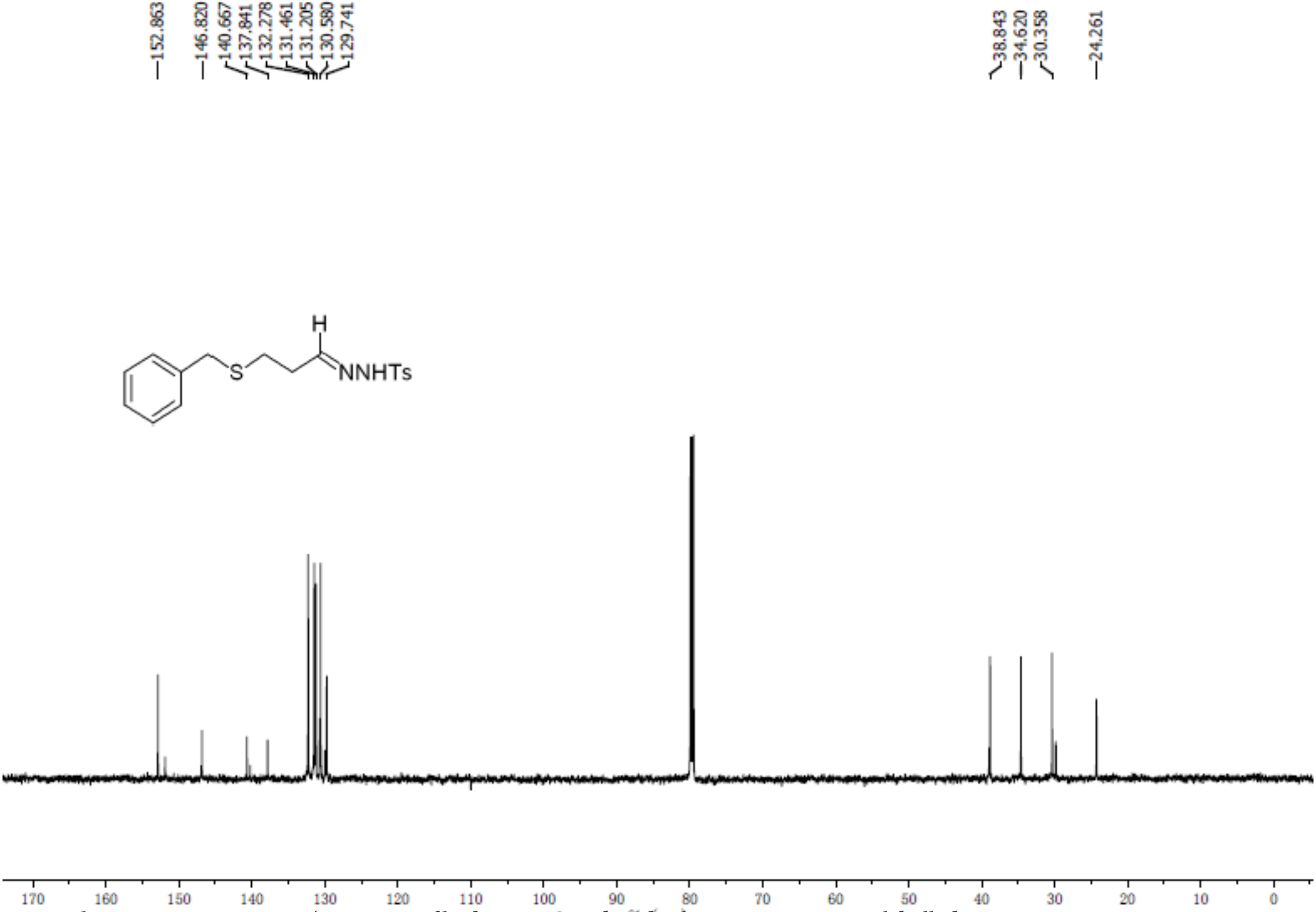
Note: The spectrum contains E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

N'-(3-(benzylthio)propylidene)-4-methylbenzene sulfonohydrazide 1z



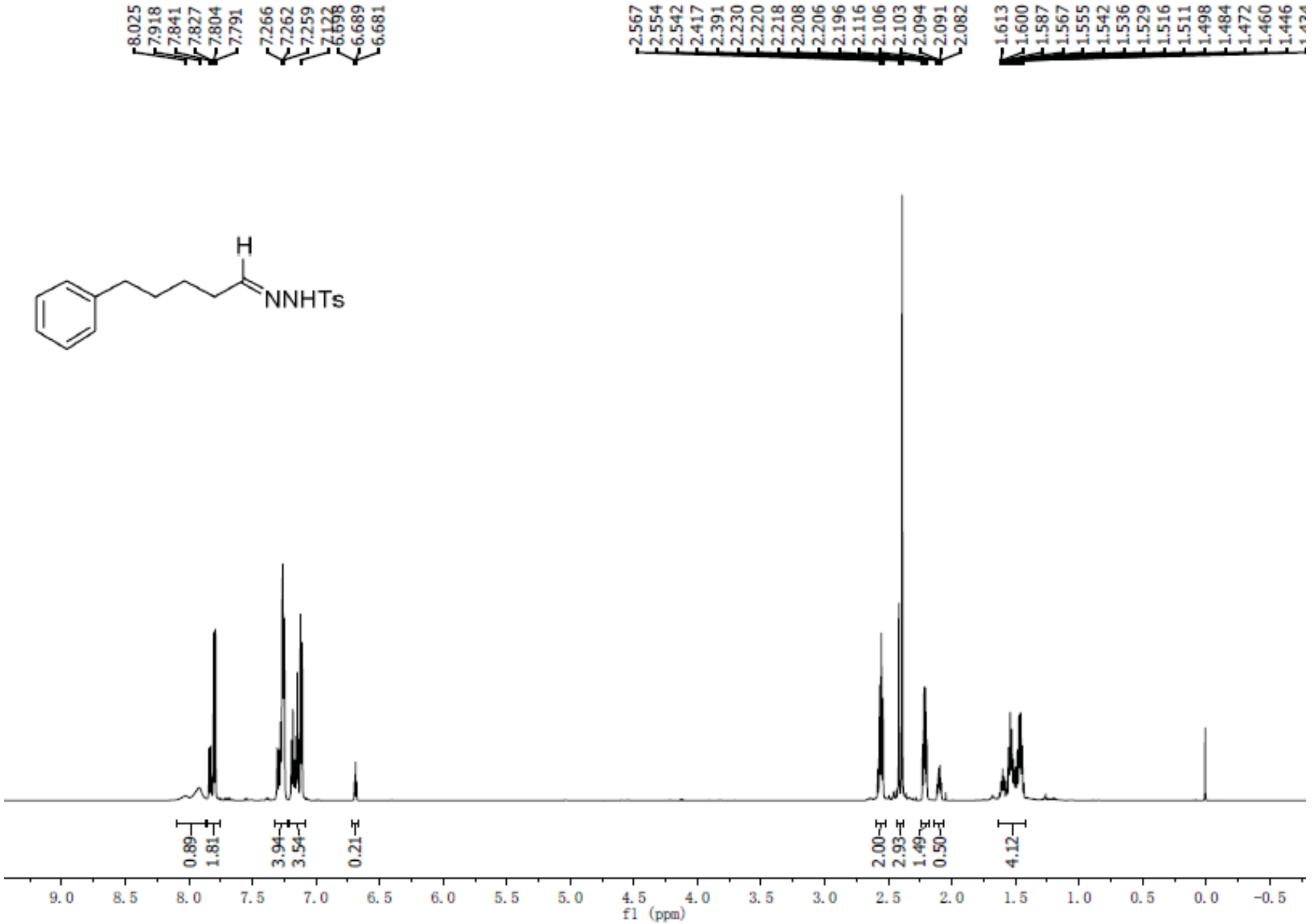
Note: The spectrum contains a mixture of E/Z isomers of hydrazone C=N bond.

N'-(3-(benzylthio)propylidene)-4-methylbenzene sulfonohydrazide 1z



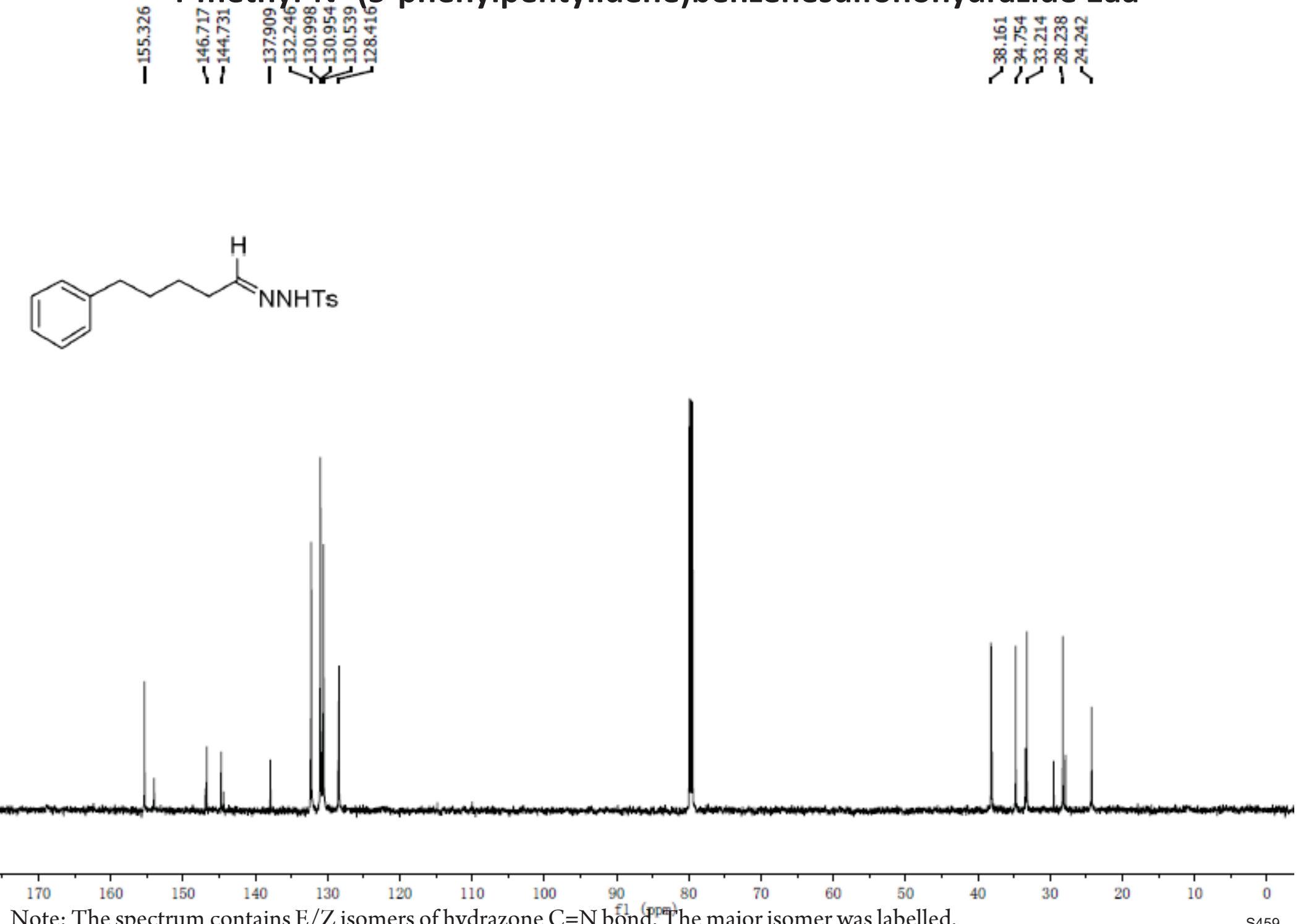
Note: The spectrum contains E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

4-methyl-N'-(5-phenylpentylidene)benzenesulfonohydrazide 1aa



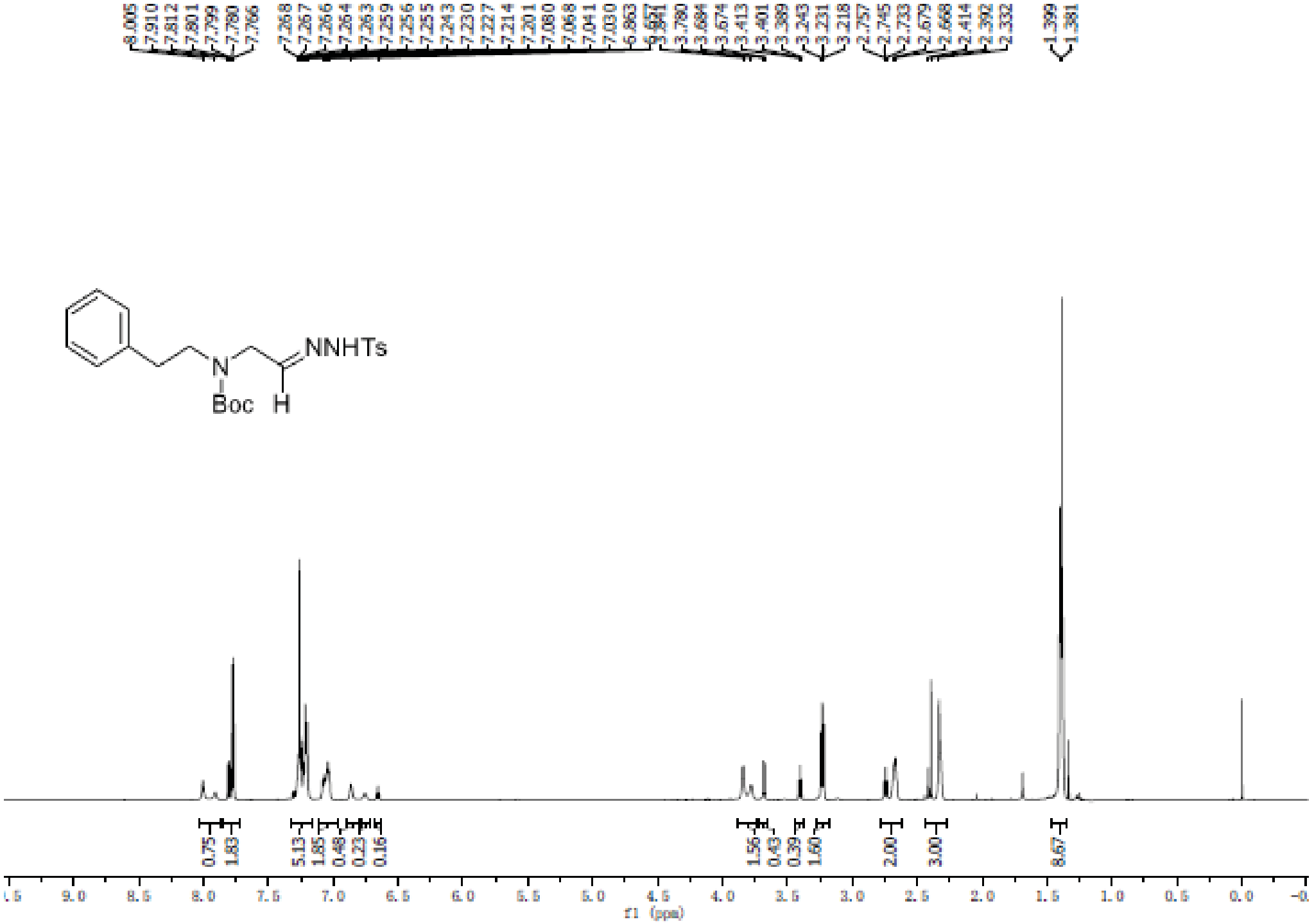
Note: The spectrum contains a mixture of E/Z isomers of hydrazone C=N bond.

4-methyl-N'-(5-phenylpentylidene)benzenesulfonohydrazide 1aa



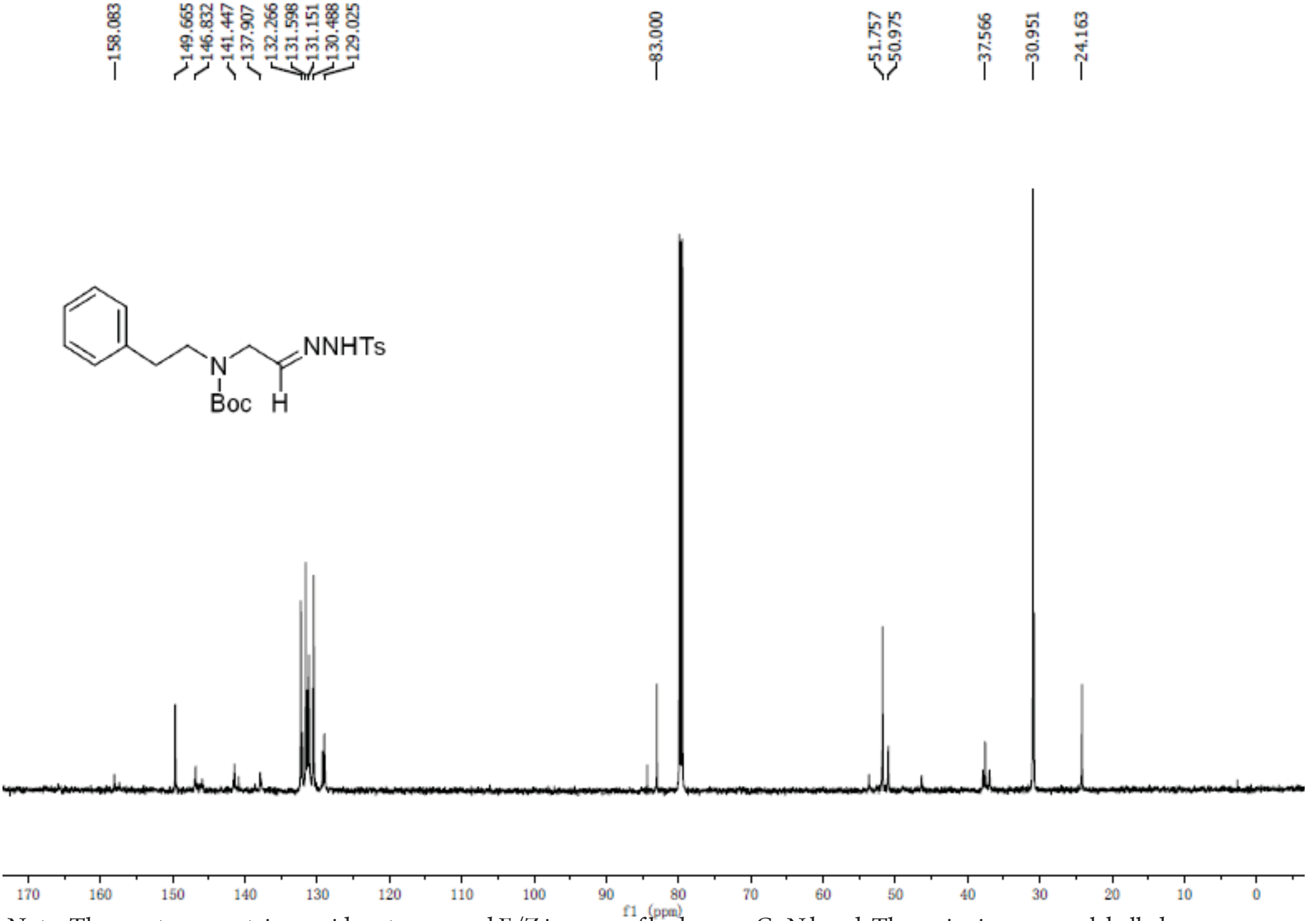
Note: The spectrum contains E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

4-methyl-N'-(5-phenylpentylidene)benzenesulfonohydrazide 1ab



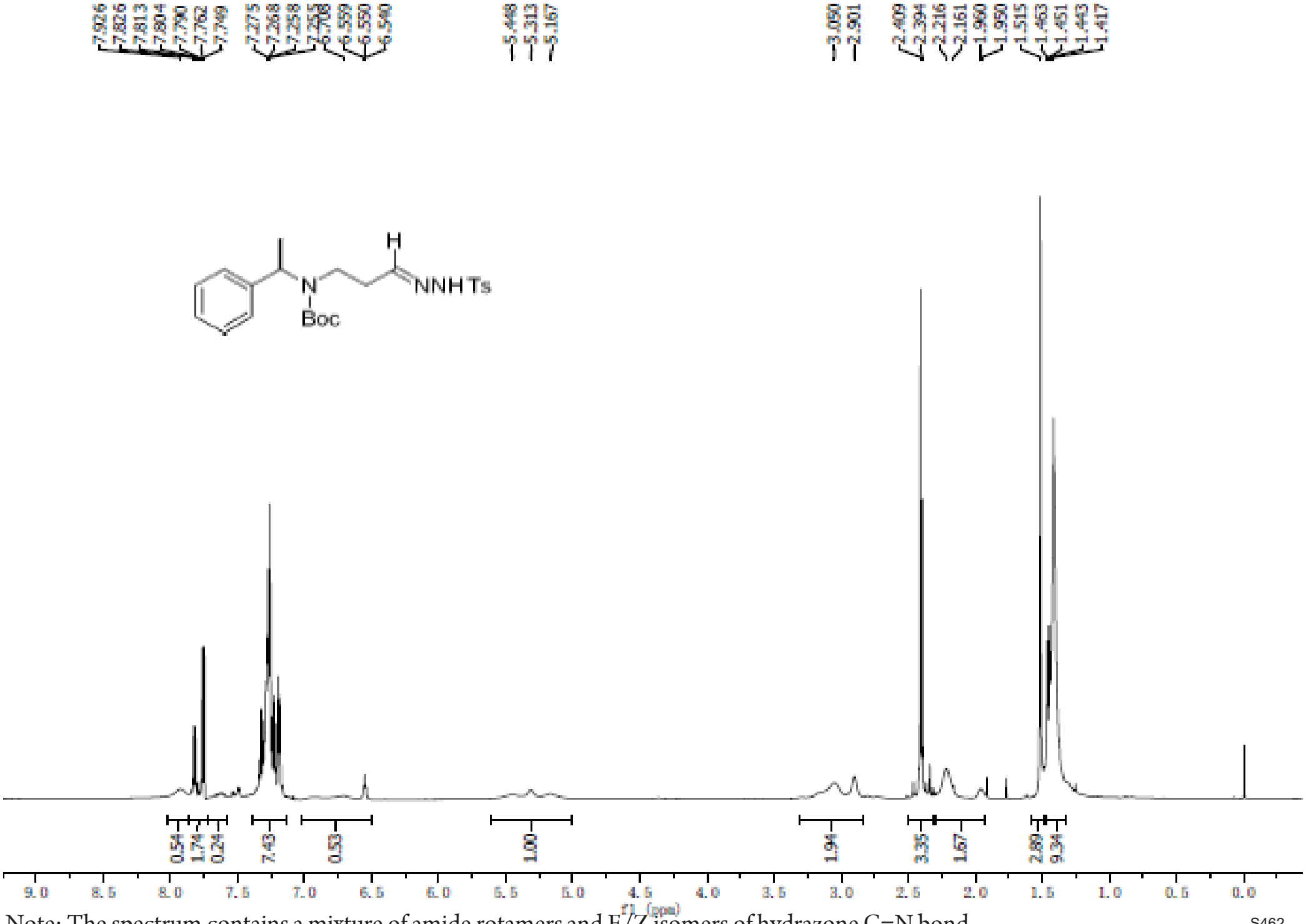
Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

4-methyl-N'-(5-phenylpentylidene)benzenesulfonohydrazide 1ab



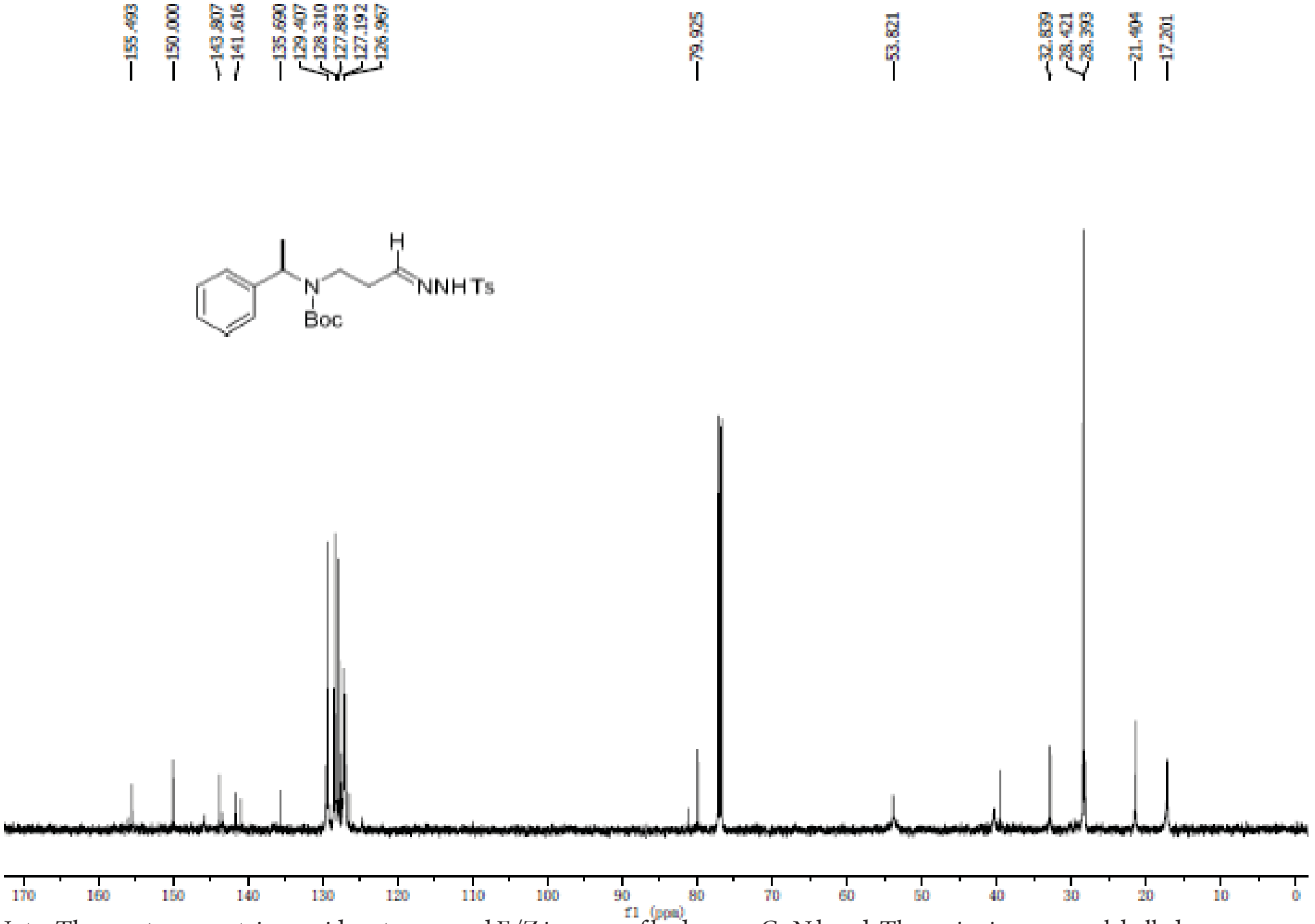
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl phenethyl(2-(2-tosylhydrazono)ethyl)carbamate 4a



Note: The spectrum contains a mixture of amide rotamers and E/Z isomers of hydrazone C=N bond.

tert-butyl phenethyl(2-(2-tosylhydrazono)ethyl)carbamate 4a



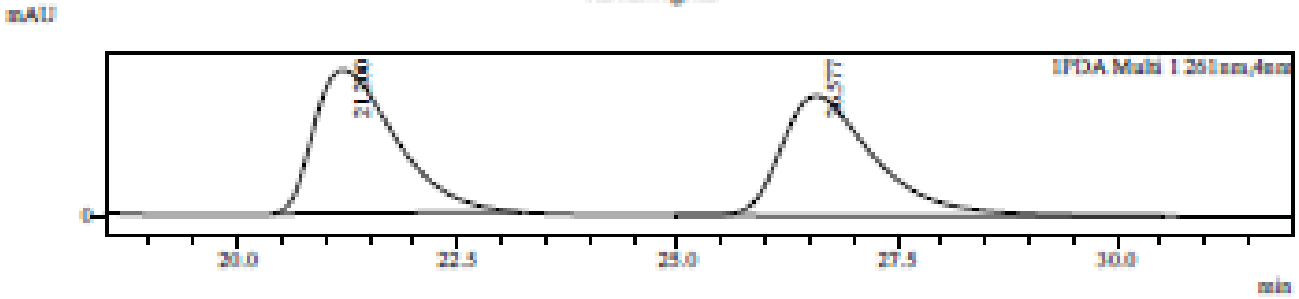
Note: The spectrum contains amide rotamers and E/Z isomers of hydrazone C=N bond. The major isomer was labelled.

tert-butyl phenethyl(2-(2-tosylhydrazono)ethyl)carbamate 4a

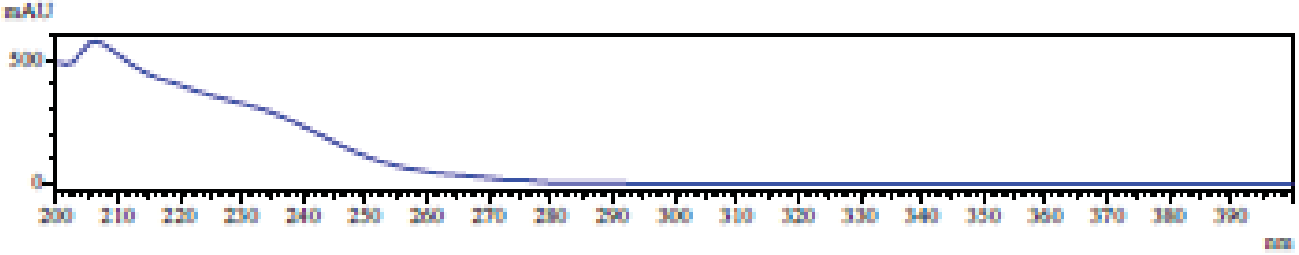
Sample Information

Data File	: YW-IV-13-ADH-10%-1ML001.lcd
Sample Name	: YW-IV-13-ADH-10%-1ML001
Sample ID	: YW-IV-13-ADH-10%-1ML001
Method File	: YW-10.0%-1.0ml.lcm

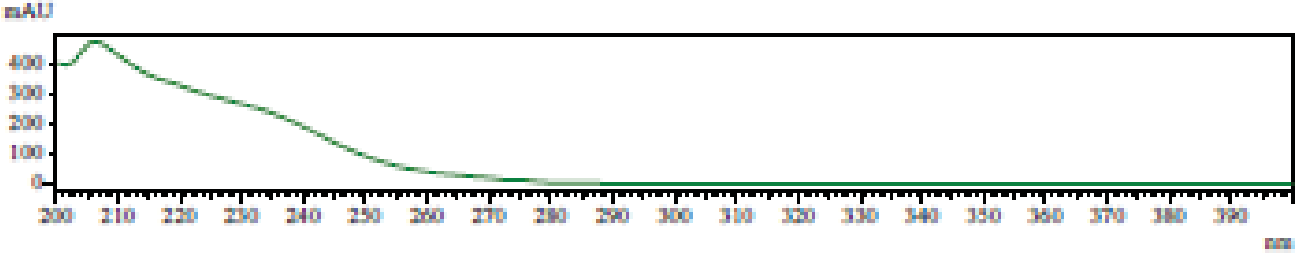
Chromatogram



UV Spectrum
Retention time = 21.200



UV Spectrum
Retention time = 26.577



Peak Table

PDA Ch1 261nm

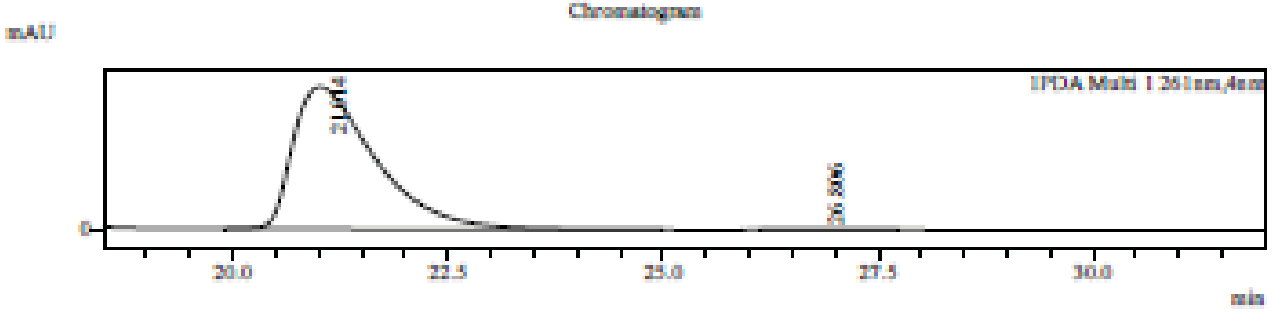
Peak#	Ret. Time	Area	Area%
1	21.200	2875208	51.234
2	26.577	2736751	48.766
Total		5611959	100.000

tert-butyl phenethyl(2-(2-tosylhydrazono)ethyl)carbamate 4a

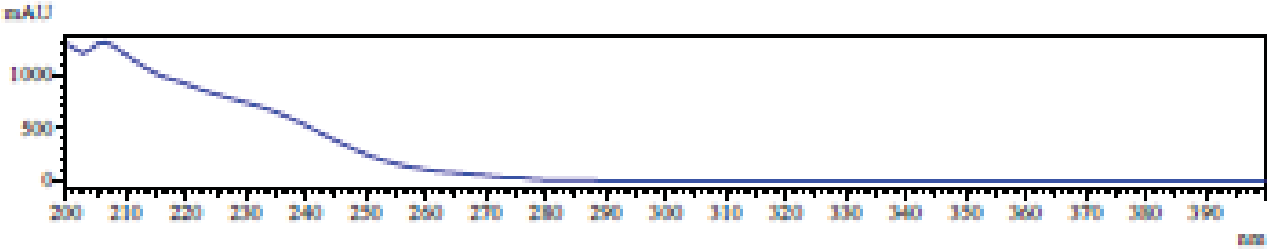
Sample Information

Data File	: YW-IV-250-ADH-10%-1ML002.lcd
Sample Name	: YW-IV-250-ADH-10%-1ML002
Sample ID	: YW-IV-250-ADH-10%-1ML002
Method File	: YW-10.0%-1.0ml.lcm

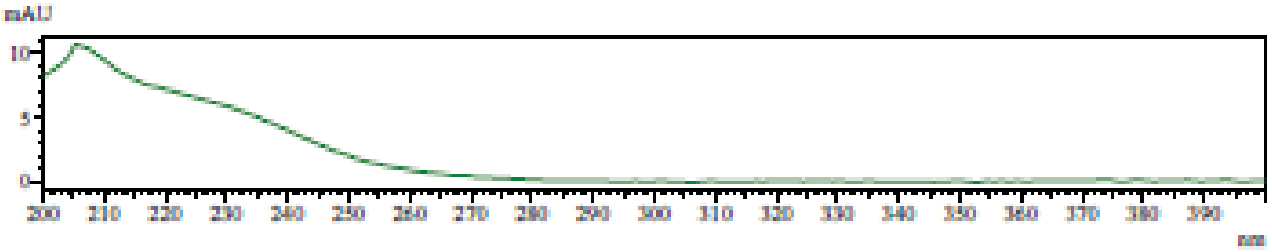
Chromatogram



UV Spectrum
Retention time = 21.014



UV Spectrum
Retention time = 26.806

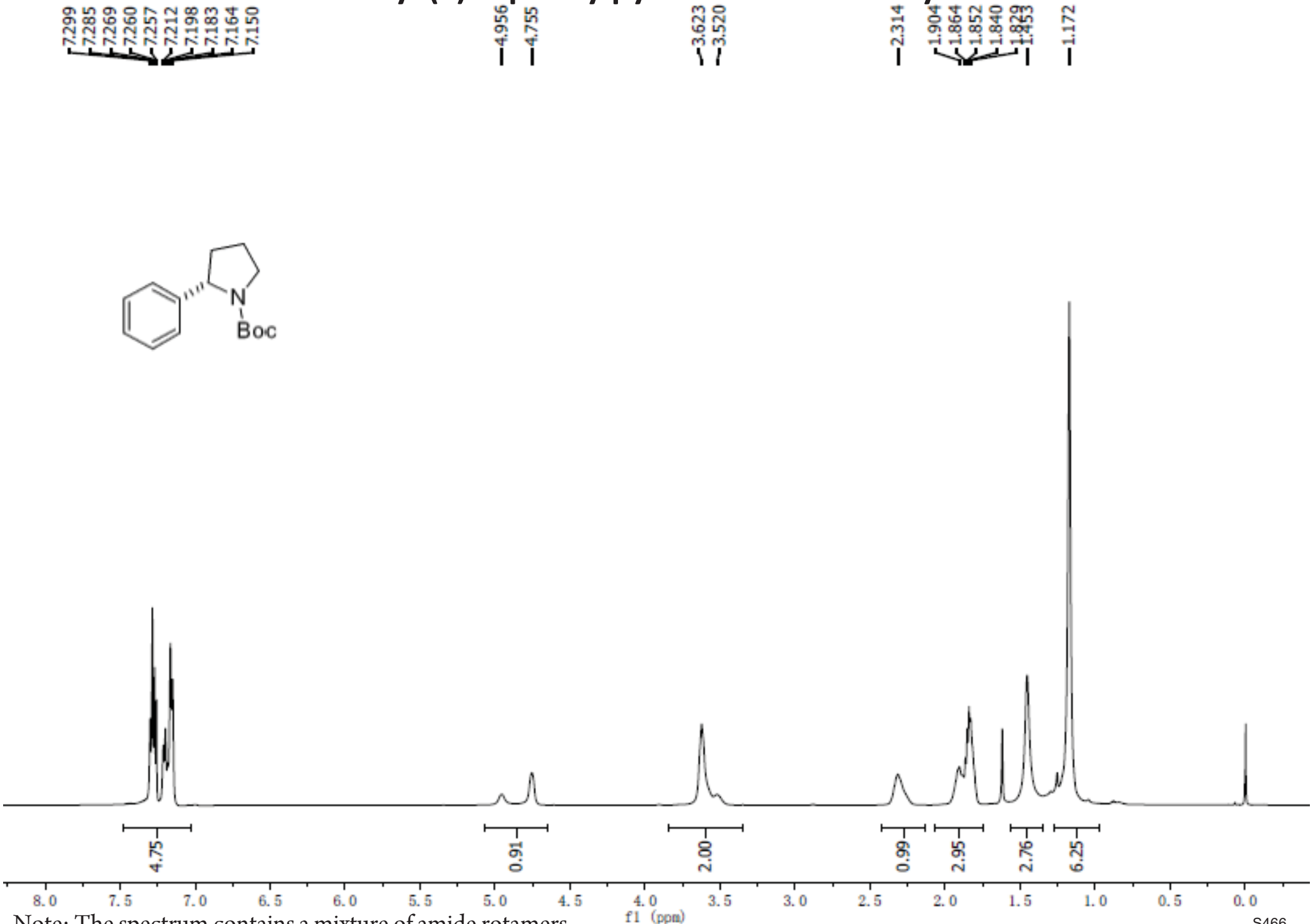


Peak Table

PDA Ch1 261nm

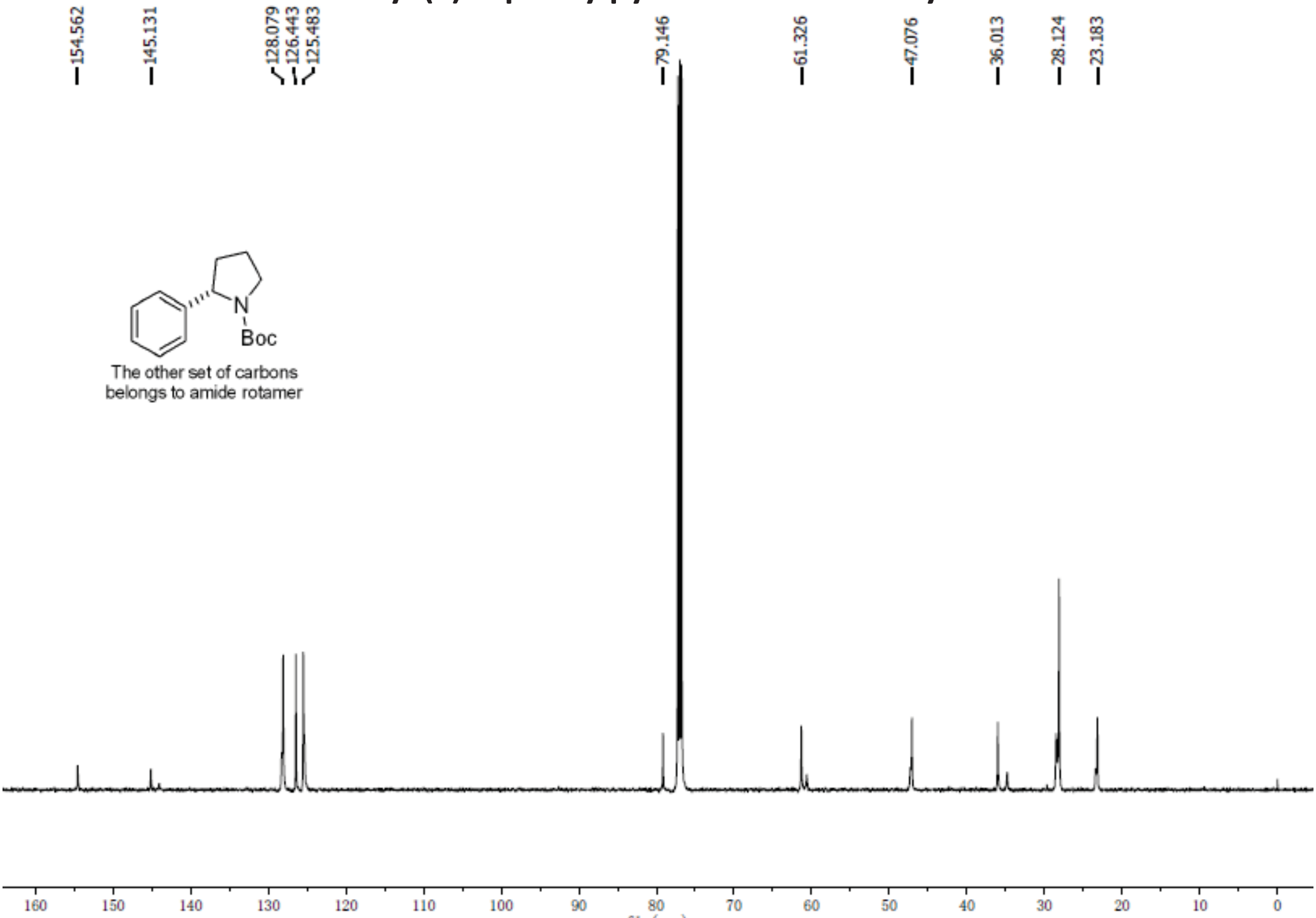
Peak#	Ret. Time	Area	Area%
1	21.014	6802850	99.578
2	26.806	28815	0.422
Total		6831665	100.000

tert-butyl (*S*)-2-phenylpyrrolidine-1-carboxylate 2a



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-phenylpyrrolidine-1-carboxylate 2a



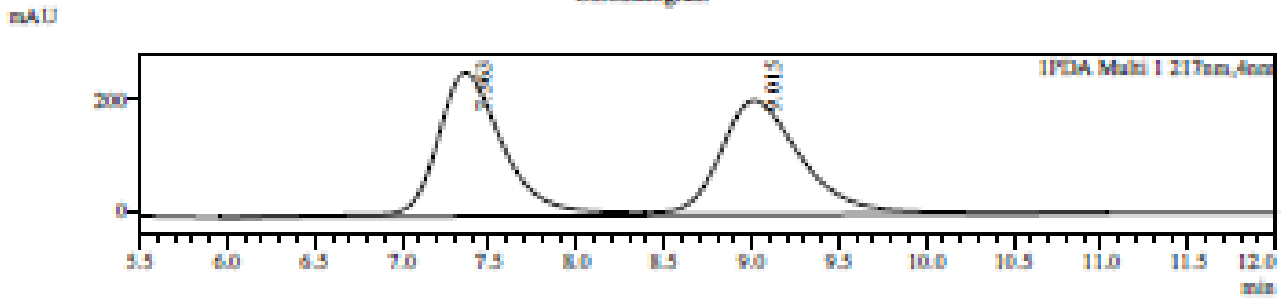
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-phenylpyrrolidine-1-carboxylate 2a

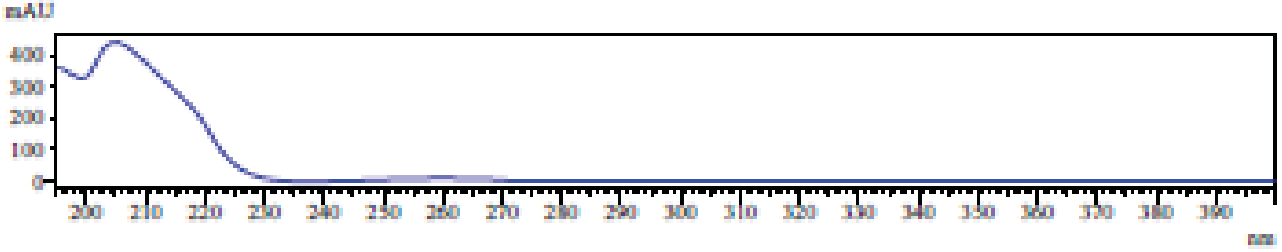
Sample Information

Sample Name	: YW-III-290a-OJH-1%-1ML003
Sample ID	: YW-III-290a-OJH-1%-1ML003
Data File	: YW-III-290a-OJH-1%-1ML003.lcd
Method File	: YW-1%-1.0ml.lcm

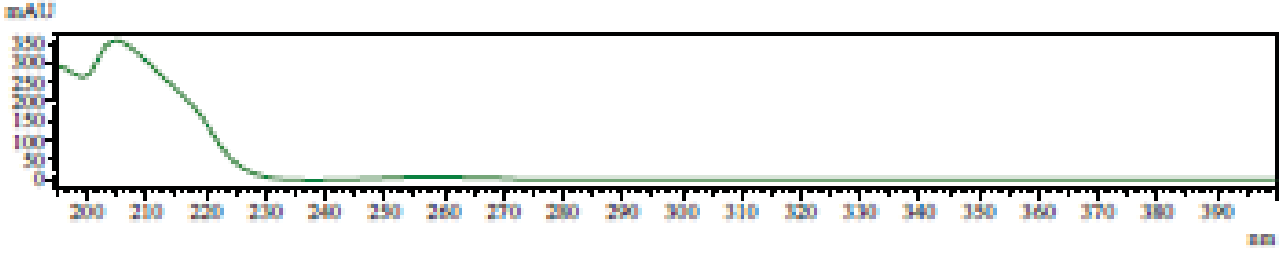
Chromatogram



UV Spectrum
Retention time = 7.363



UV Spectrum
Retention time = 9.015



Peak Table

PDA Ch1 217nm

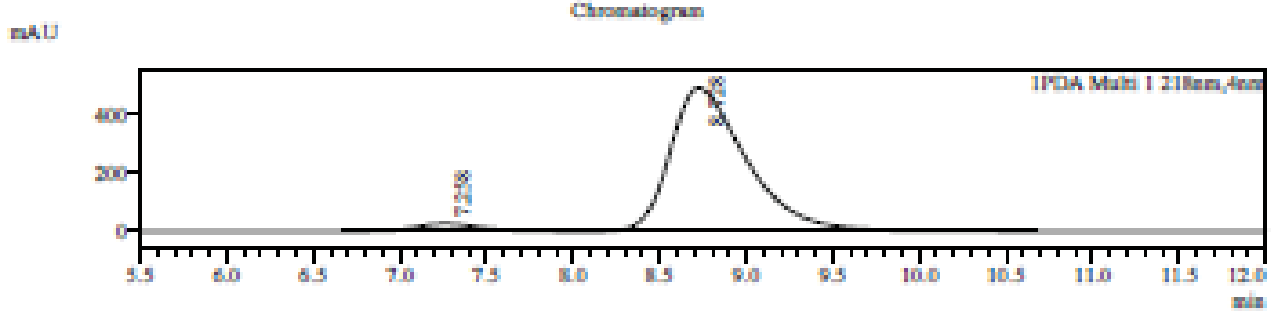
Peak#	Ret. Time	Area	Area%
1	7.363	6745283	50.340
2	9.015	6654094	49.660
Total		13399377	100.000

tert-butyl (*S*)-2-phenylpyrrolidine-1-carboxylate 2a

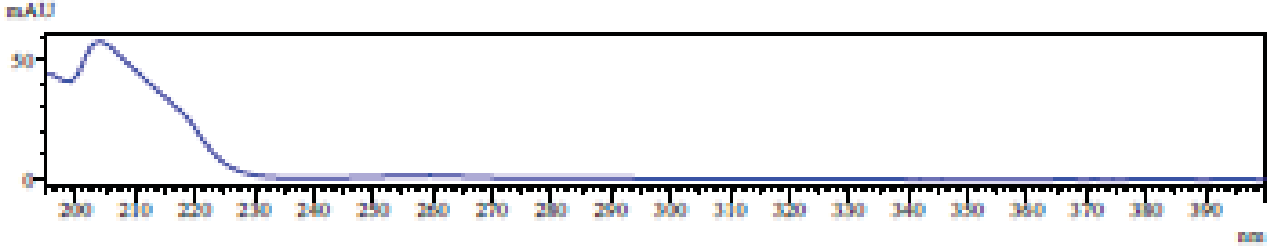
Sample Information

Sample Name	: YW-III-290b-OJH-1%-1ML003
Sample ID	: YW-III-290b-OJH-1%-1ML003
Data File	: YW-III-290b-OJH-1%-1ML003.lcd
Method File	: YW-1%-1.0ml.lcm

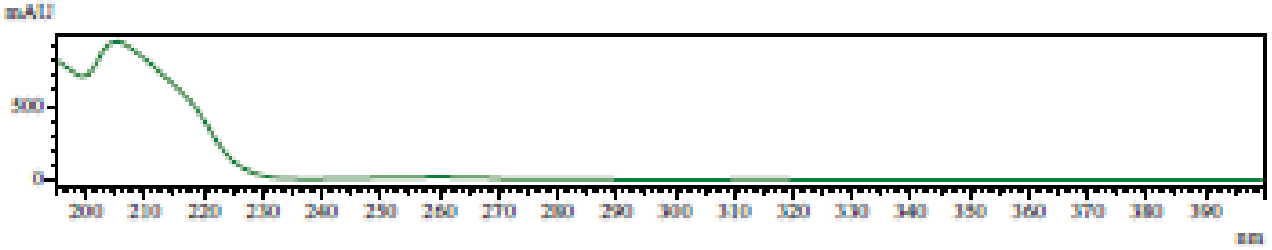
Chromatogram



UV Spectrum
Retention time = 7.258



UV Spectrum
Retention time = 8.728

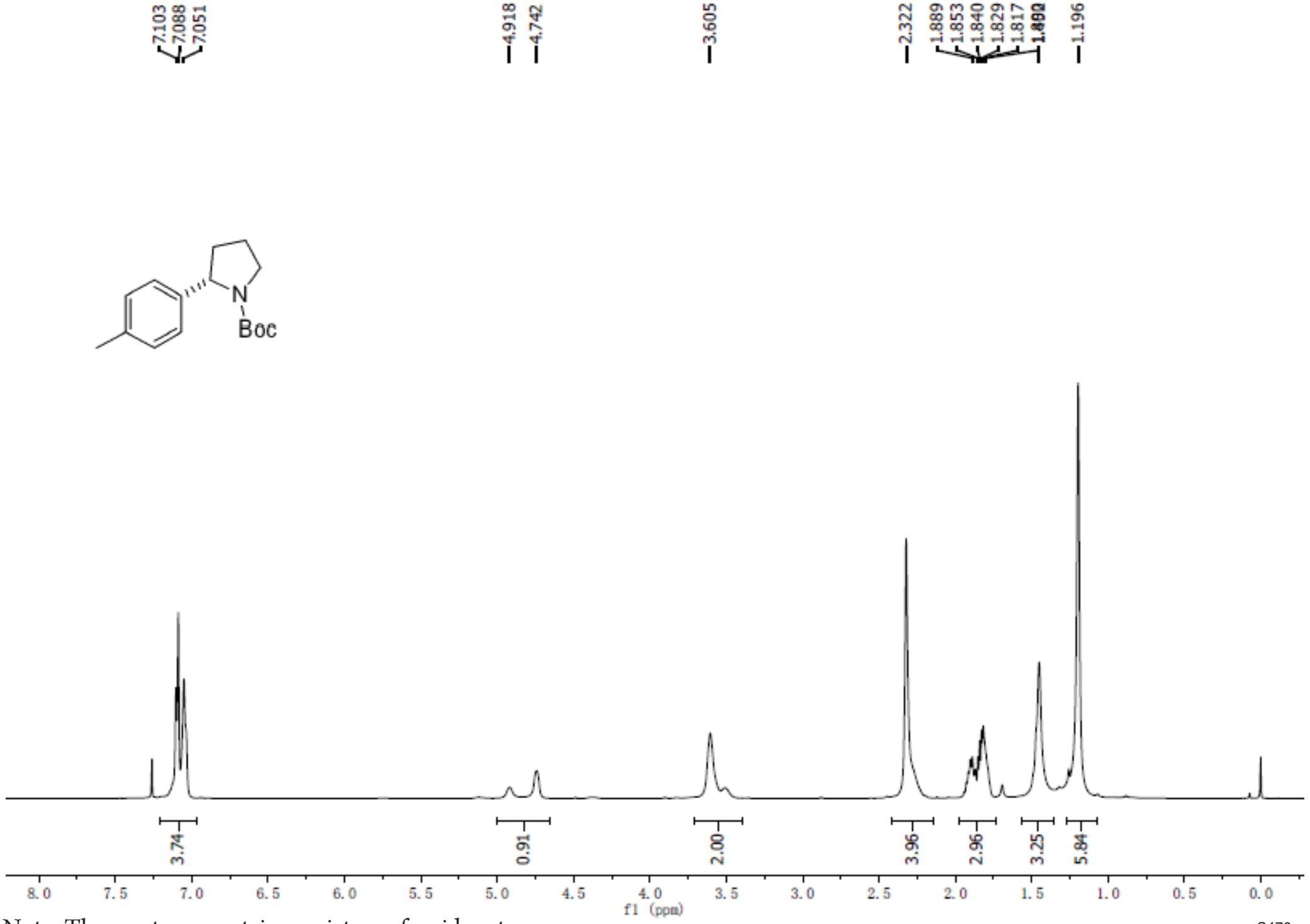


Peak Table

PDA Ch1 218nm

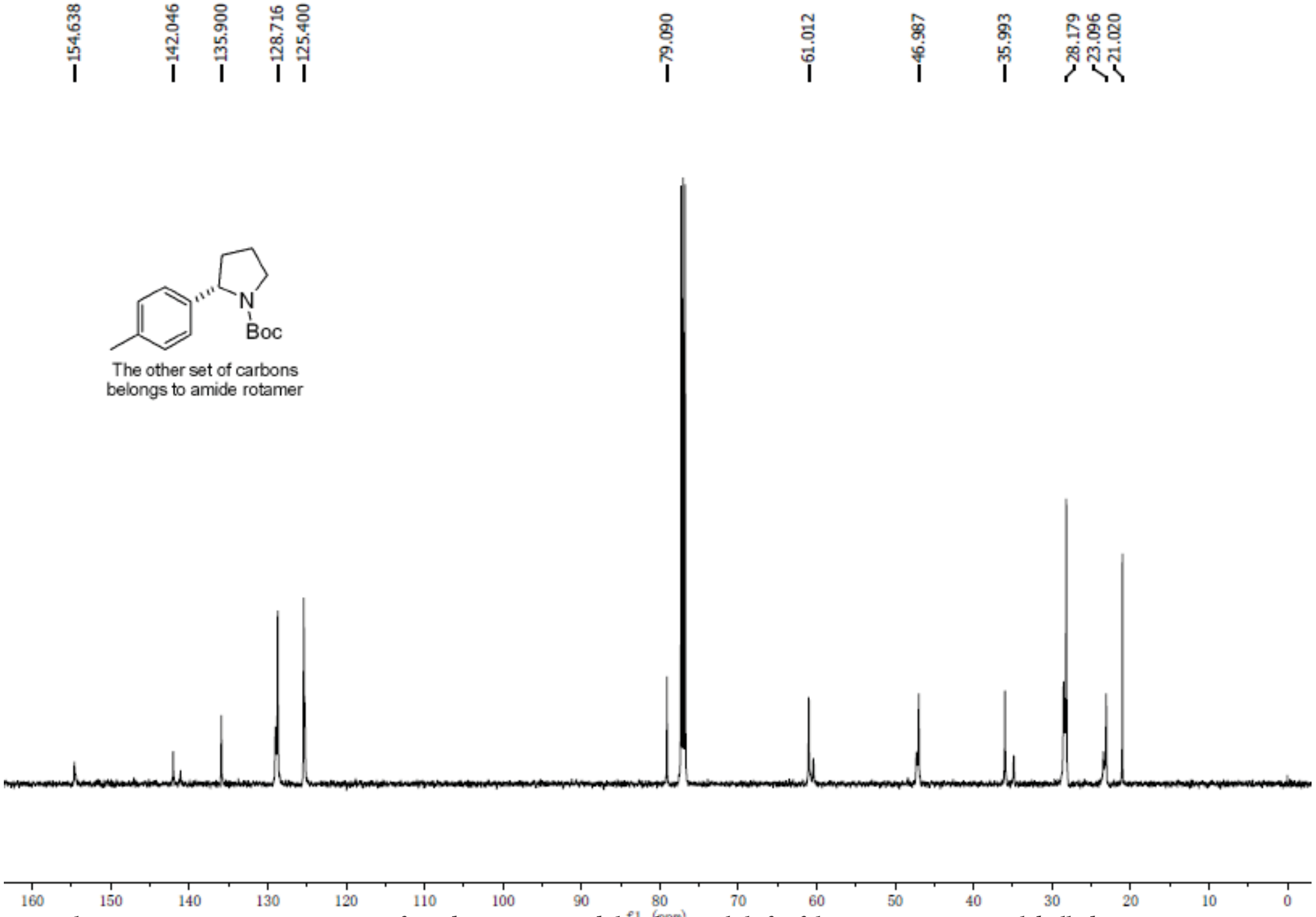
Peak#	Ret. Time	Area	Area%
1	7.258	624630	4.031
2	8.728	14872926	95.969
Total		15497556	100.000

tert-butyl (*S*)-2-(4-methylphenyl)pyrrolidine-1-carboxylate 2b



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(4-methylphenyl)pyrrolidine-1-carboxylate 2b



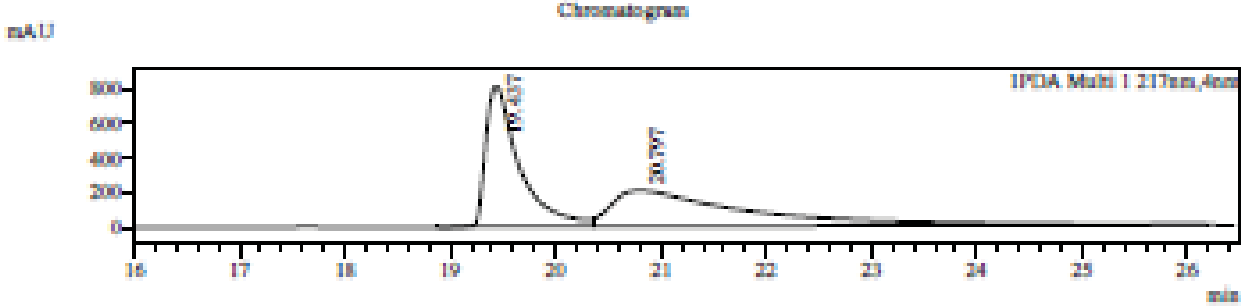
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(4-methylphenyl)pyrrolidine-1-carboxylate 2b

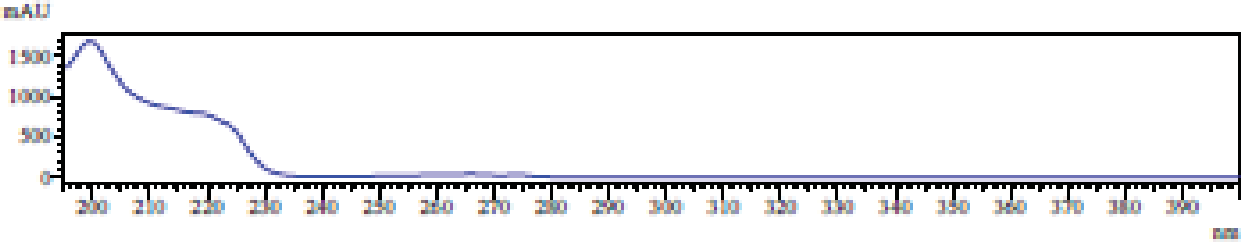
Sample Information

Sample Name : YW-IV-74A-ADH-0.1%-1.0ML
Sample ID : YW-IV-74A-ADH-0.1%-1.0ML
Data File : YW-IV-74A-ADH-0.1%-1.0ML.lcd
Method File : YW-0.1%-1.0ml.lcm

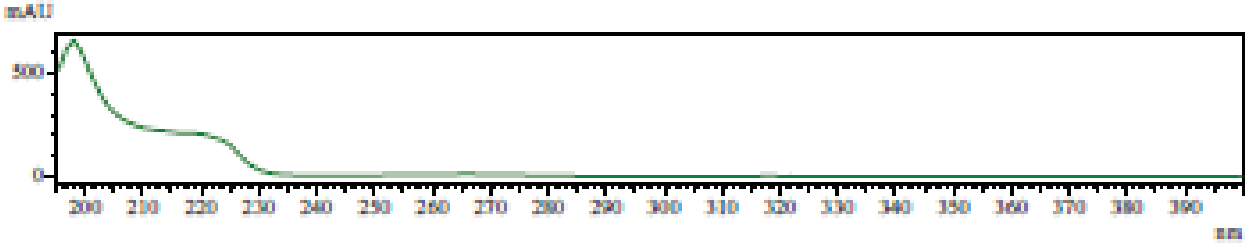
Chromatogram



UV Spectrum
Retention time = 19.437



UV Spectrum
Retention time = 20.797



Peak Table

PDA Ch1 217nm

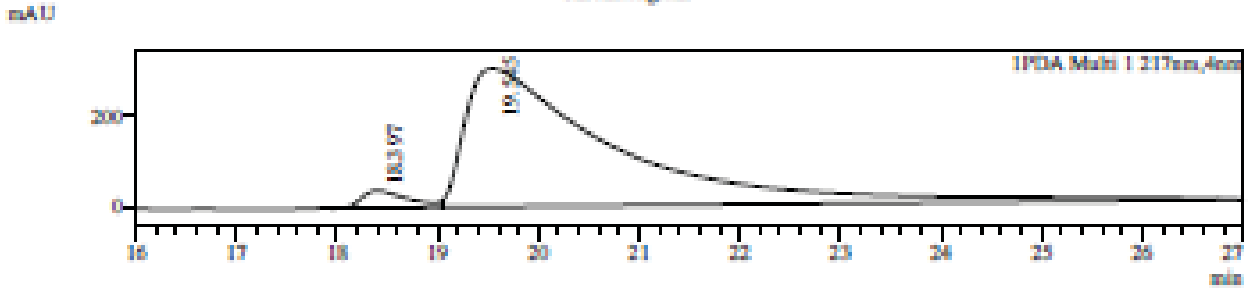
Peak#	Ret. Time	Area	Area%
1	19.437	17885081	49.332
2	20.797	18369380	50.668
Total		36254461	100.000

tert-butyl (*S*)-2-(4-methylphenyl)pyrrolidine-1-carboxylate 2b

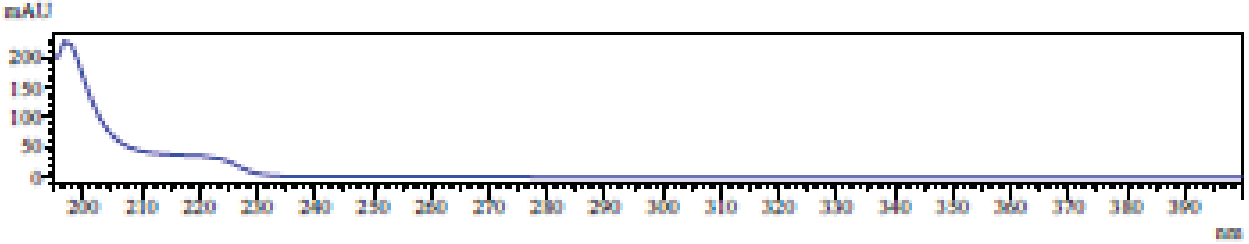
Sample Information

Sample Name	: YW-IV-74B-ADH-0.1%-1.0ML-1
Sample ID	: YW-IV-74B-ADH-0.1%-1.0ML-1
Data File	: YW-IV-74B-ADH-0.1%-1.0ML-1.lcd
Method File	: YW-0.1%-1.0ml.lcm

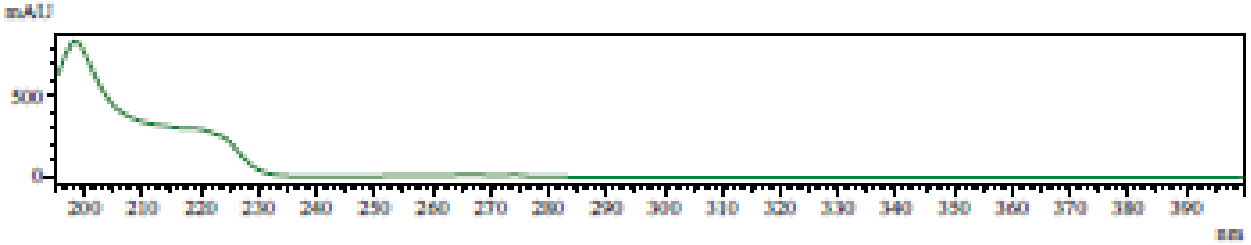
Chromatogram



UV Spectrum
Retention time = 18.397



UV Spectrum
Retention time = 19.545

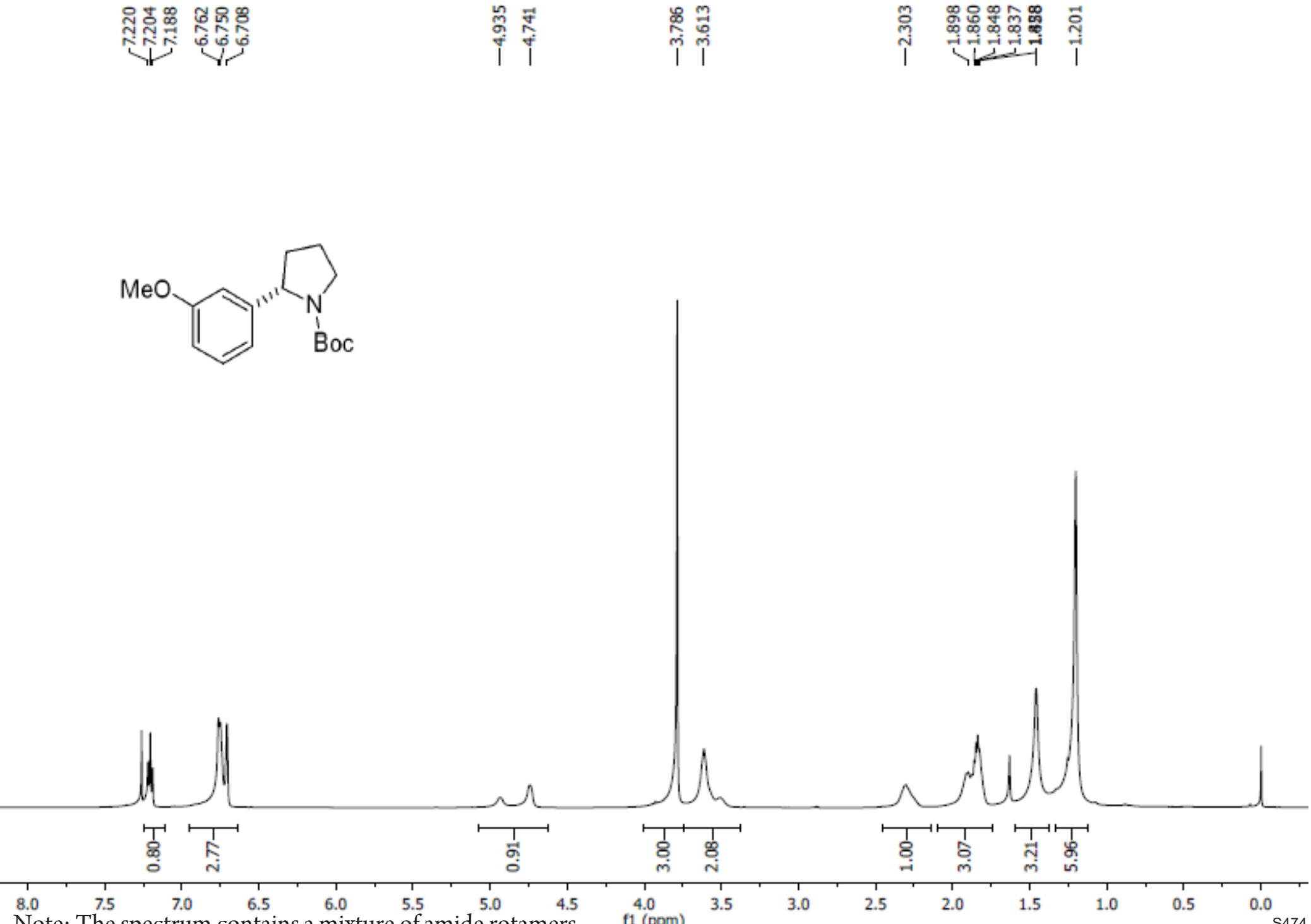


Peak Table

PDA Ch1 217nm

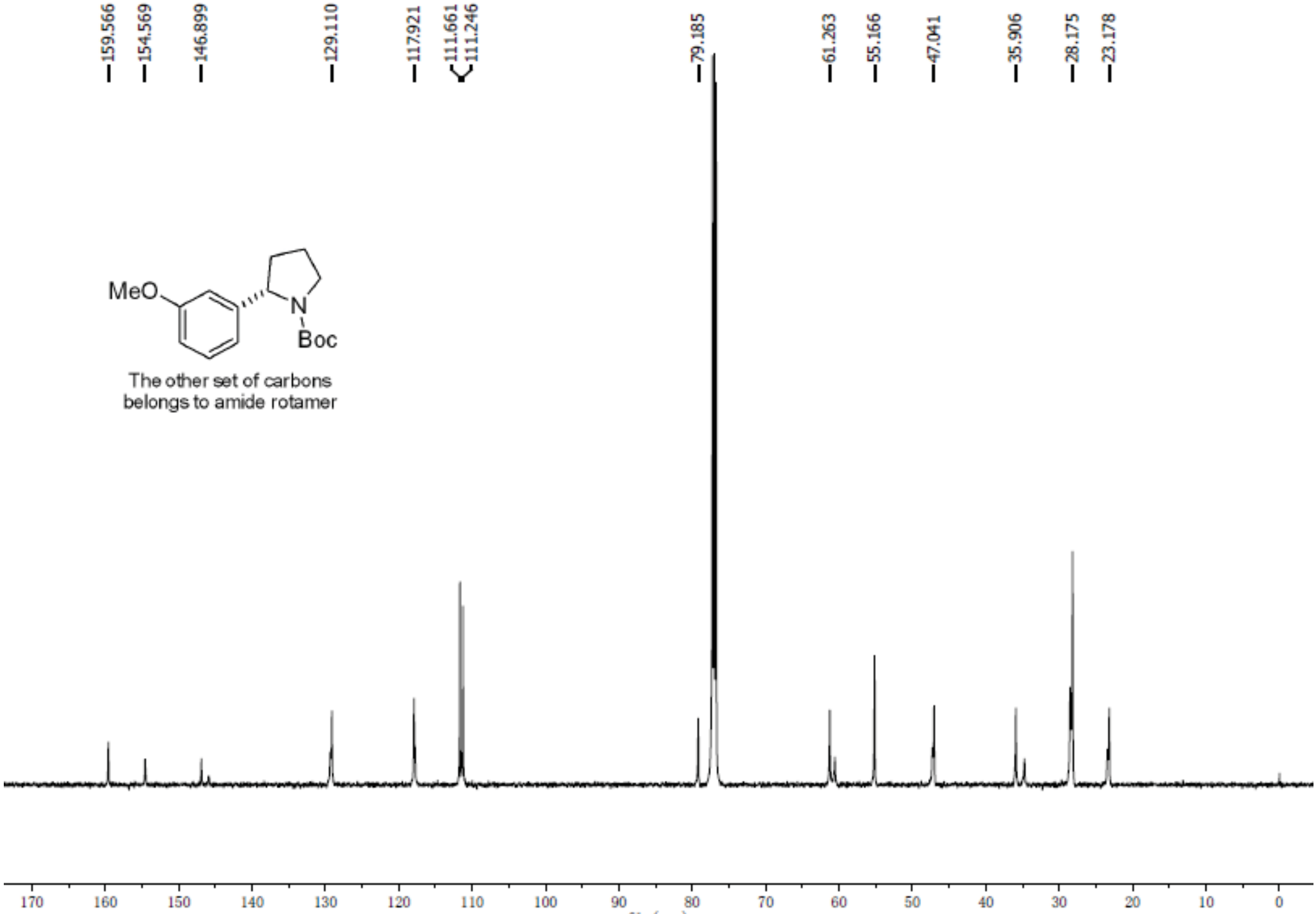
Peak#	Ret. Time	Area	Area%
1	18.397	1168290	3.566
2	19.545	31596299	96.434
Total		32764589	100.000

tert-butyl (*S*)-2-(3-methoxyphenyl)pyrrolidine-1-carboxylate 2c



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(3-methoxyphenyl)pyrrolidine-1-carboxylate 2c



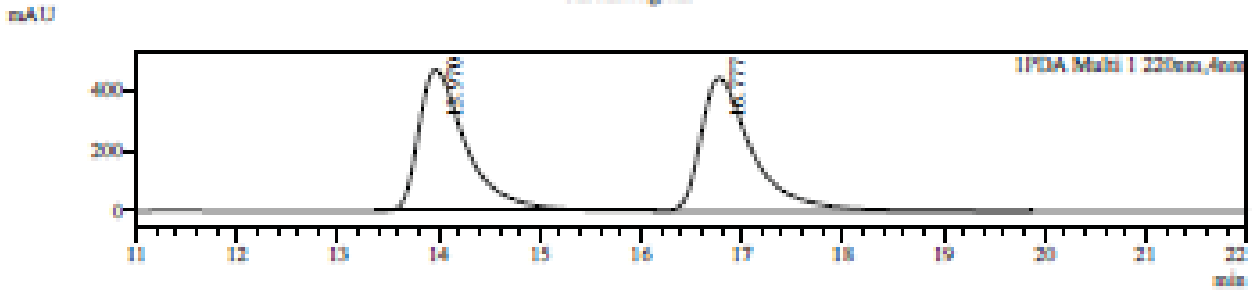
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (S)-2-(3-methoxyphenyl)pyrrolidine-1-carboxylate 2c

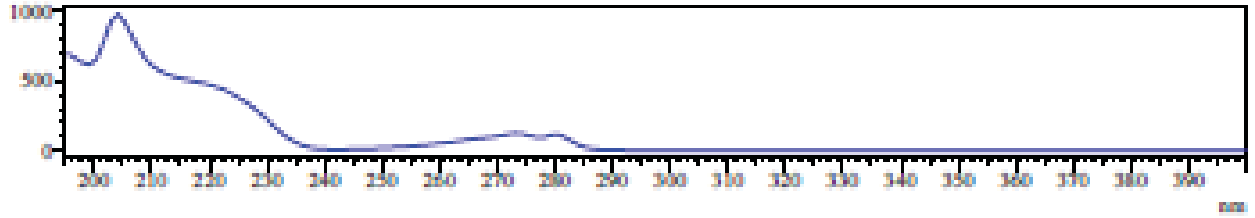
Sample Information

Sample Name	: YW-III-293A-ADH-1%-1ML
Sample ID	: YW-III-293A-ADH-1%-1ML
Data File	: YW-III-293A-ADH-1%-1ML.lcd
Method File	: YW-1%-1.0ml.lcm

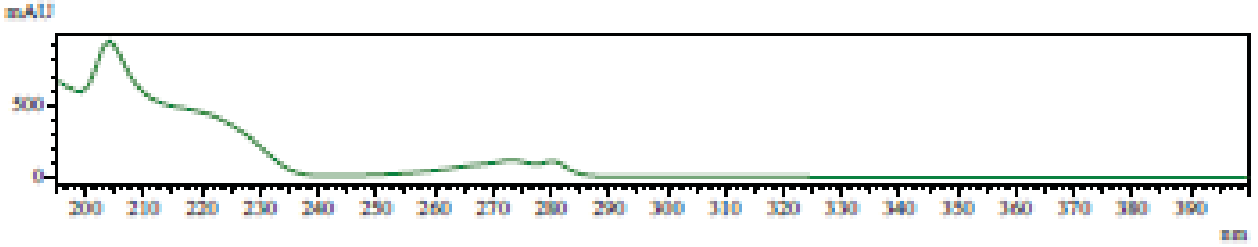
Chromatogram



UV Spectrum
Retention time = 13.970



UV Spectrum
Retention time = 16.777



Peak Table

PDA Ch1 220nm

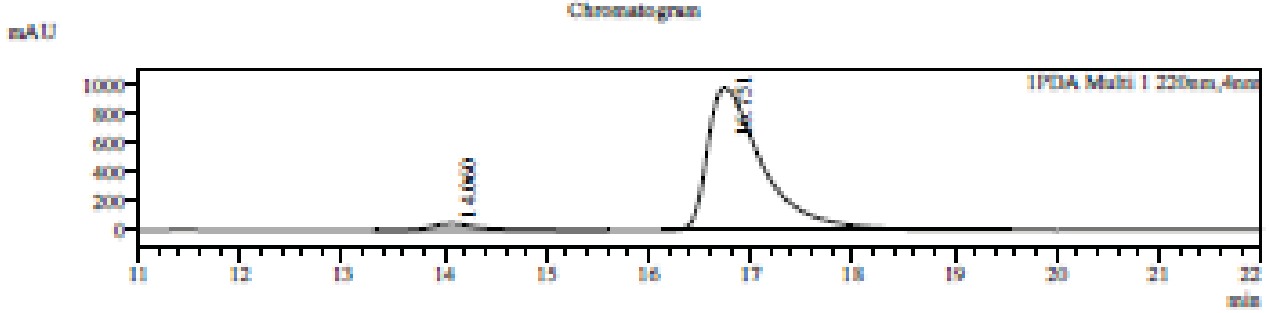
Peak#	Ret. Time	Area	Area%
1	13.970	15276980	49.674
2	16.777	15477404	50.326
Total		30754385	100.000

tert-butyl (*S*)-2-(3-methoxyphenyl)pyrrolidine-1-carboxylate 2c

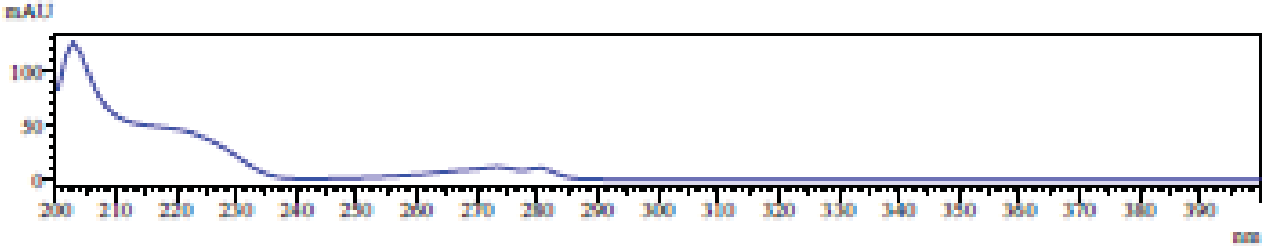
Sample Information

Sample Name	: YW-III-293B-ADH-1%-1ML
Sample ID	: YW-III-293B-ADH-1%-1ML
Data File	: YW-III-293B-ADH-1%-1ML.lcd
Method File	: YW-1%-1.0ml.lcm

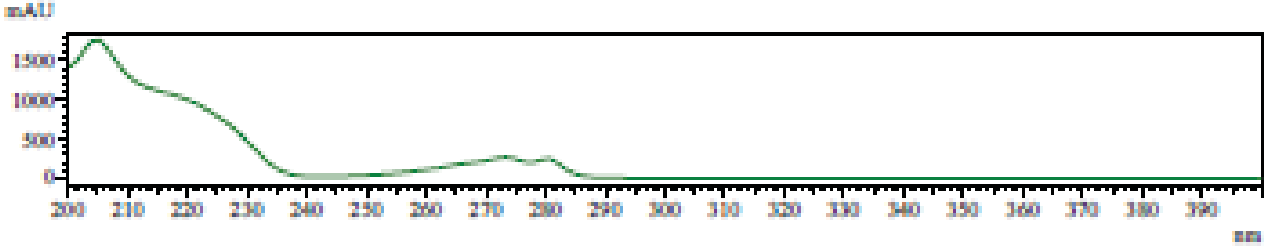
Chromatogram



UV Spectrum
Retention time = 14.060



UV Spectrum
Retention time = 16.751

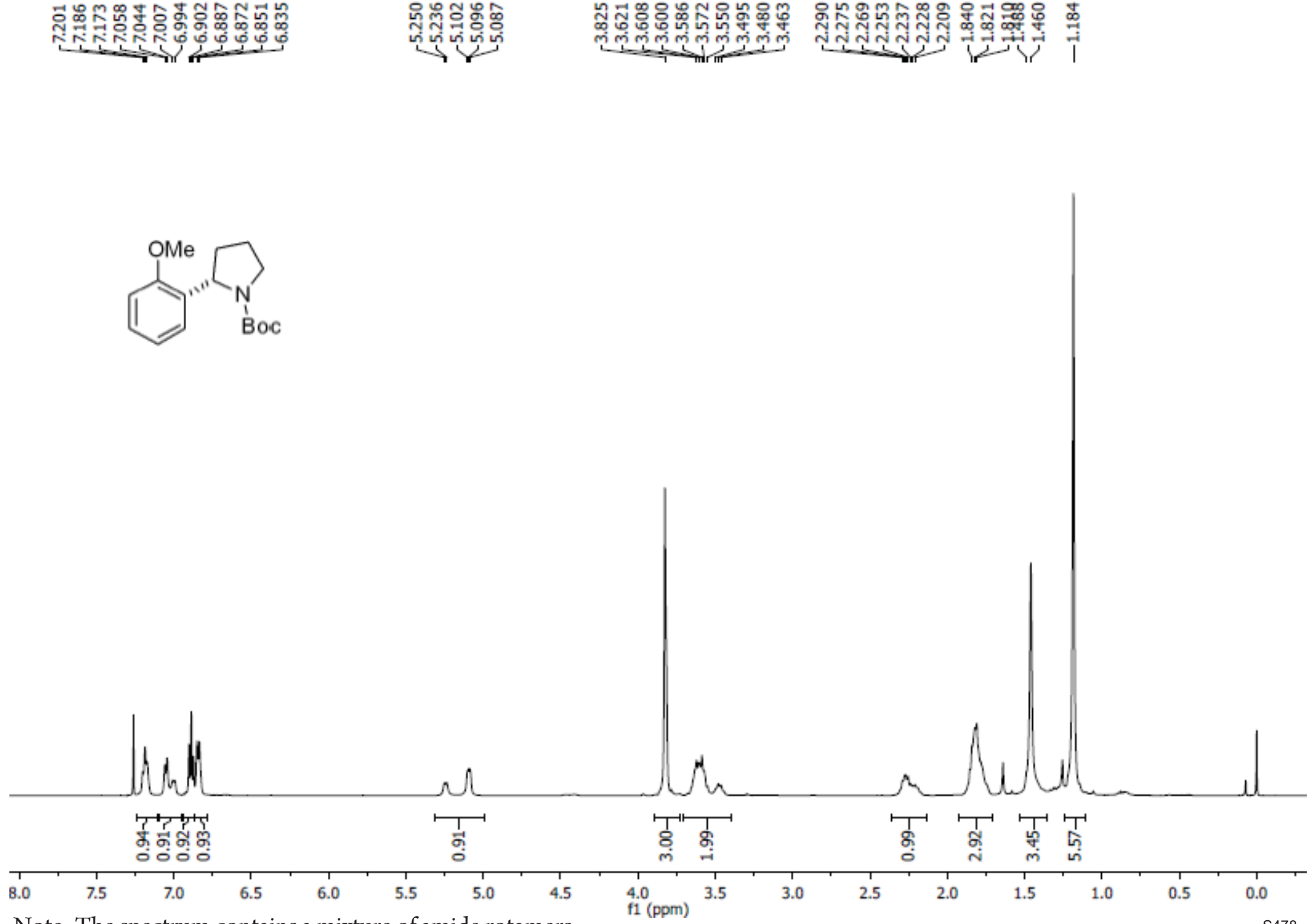


Peak Table

PDA Ch1 220nm

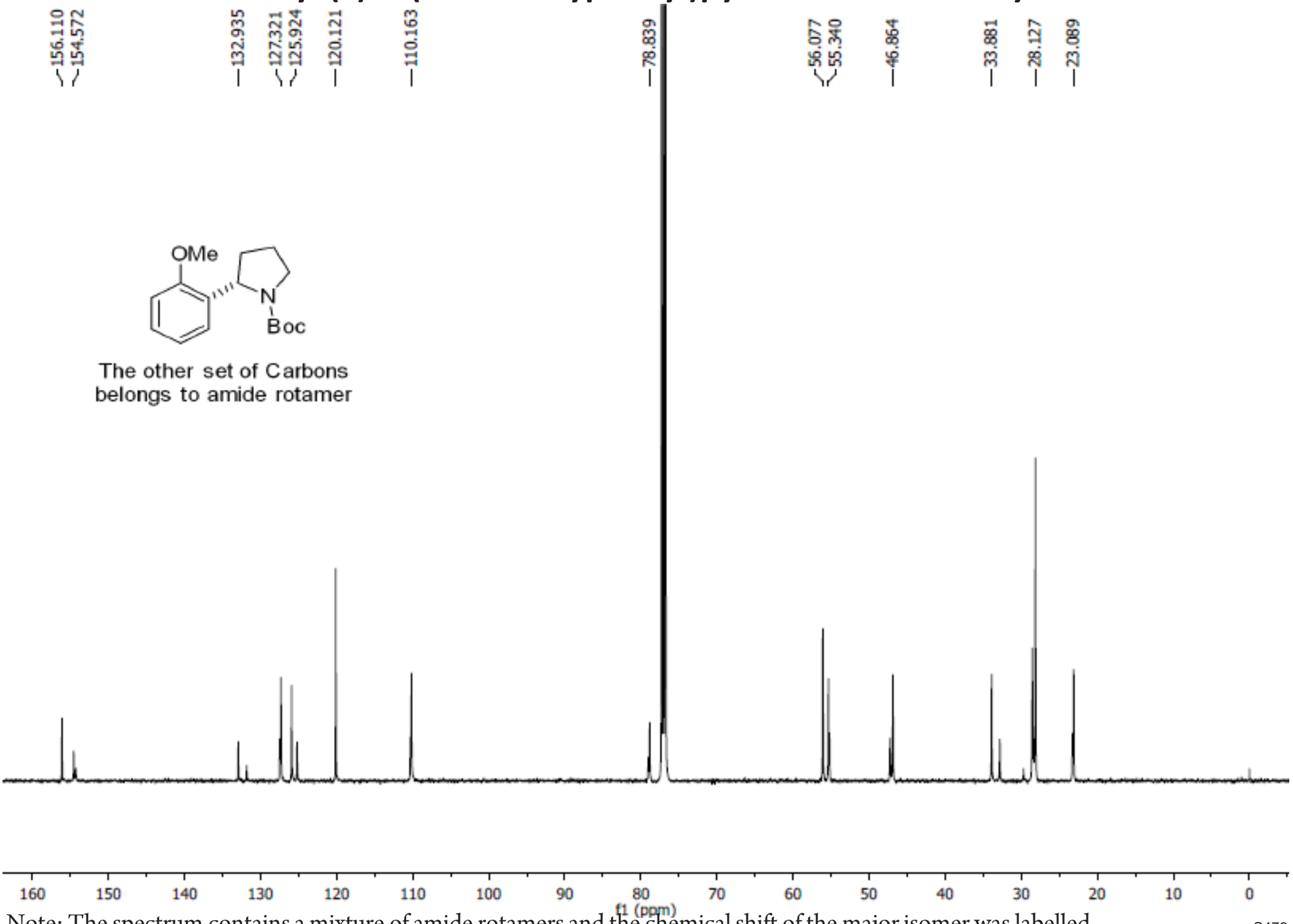
Peak#	Ret. Time	Area	Area%
1	14.060	1421822	3.738
2	16.751	36617980	96.262
Total		38039802	100.000

tert-butyl (*S*)-2-(2-methoxyphenyl)pyrrolidine-1-carboxylate 2d



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(2-methoxyphenyl)pyrrolidine-1-carboxylate 2d



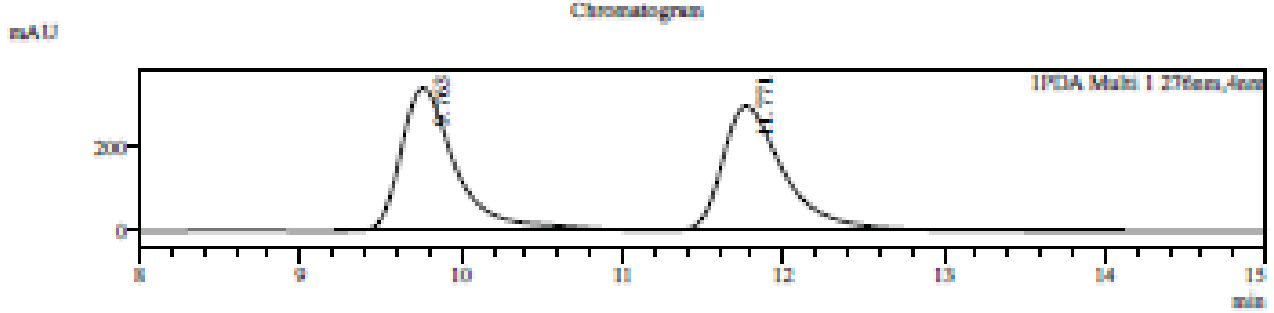
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(2-methoxyphenyl)pyrrolidine-1-carboxylate 2d

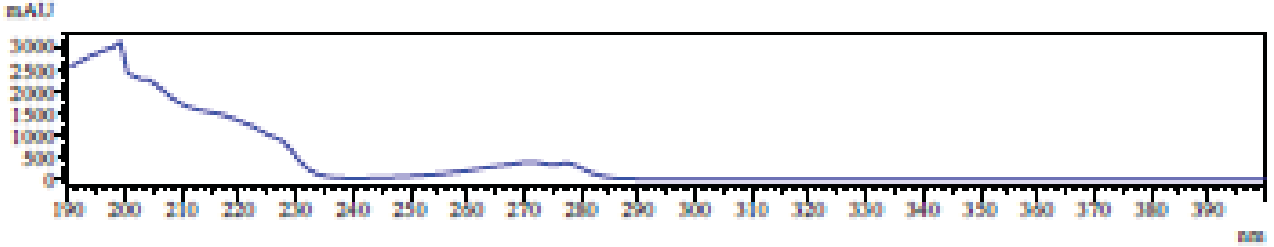
Sample Information

Sample Name	: YW-III-212a-ADH3-1%-IML
Sample ID	: YW-III-212a-ADH4-1%-IML
Data File	: YW-III-212a-ADH4-1%-IML.lcd
Method File	: YW-ADH-1.0%-1.0ml.lcm

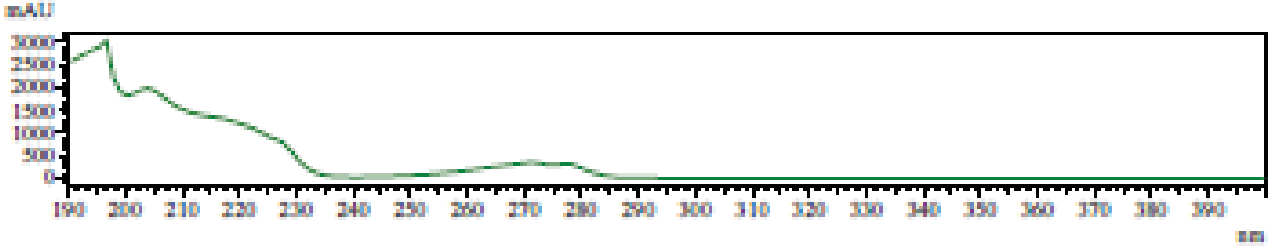
Chromatogram



UV Spectrum
Retention time = 9.763



UV Spectrum
Retention time = 11.771



Peak Table

PDA Ch1 276nm

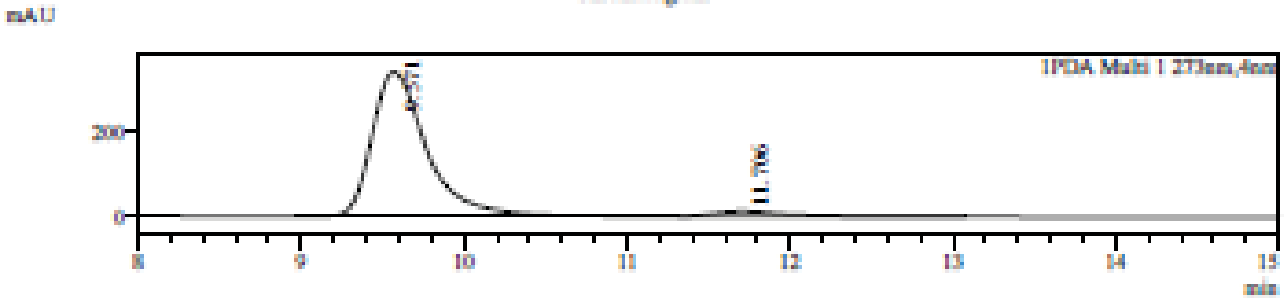
Peak#	Ret. Time	Area	Area%
1	9.763	8228725	50.659
2	11.771	8014681	49.341
Total		16243406	100.000

tert-butyl (*S*)-2-(2-methoxyphenyl)pyrrolidine-1-carboxylate 2d

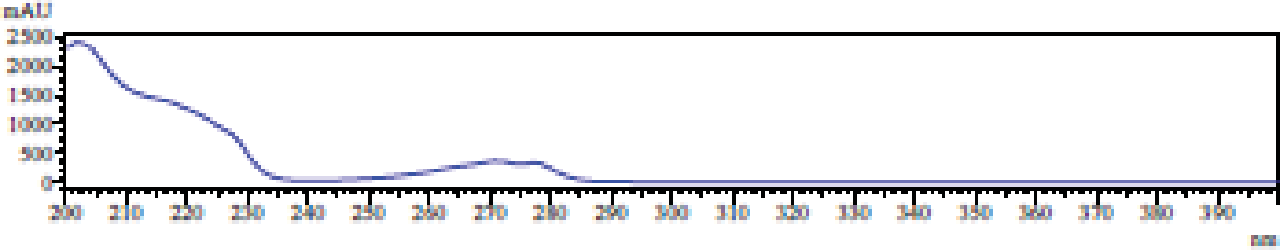
Sample Information

Sample Name	: YW-III-254a-ADH2-1%-1ML
Sample ID	: YW-III-254a-ADH2-1%-1ML
Data File	: YW-III-254a-ADH2-1%-1ML.lcd
Method File	: YW-ADH-1.0%-1.0ml.lcm

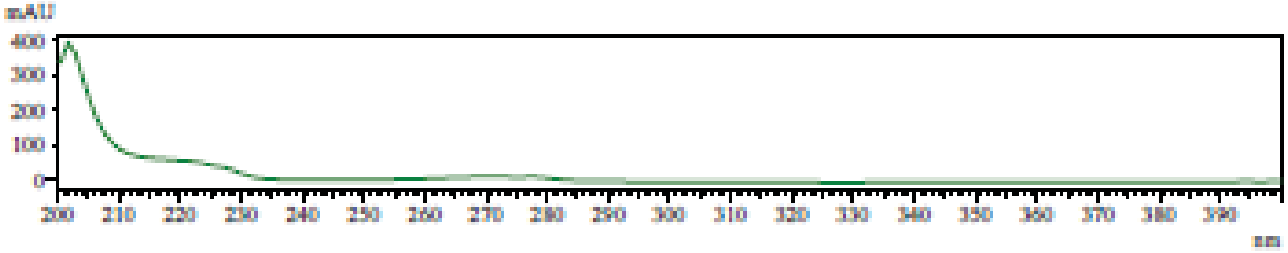
Chromatogram



UV Spectrum
Retention time = 9.571



UV Spectrum
Retention time = 11.706

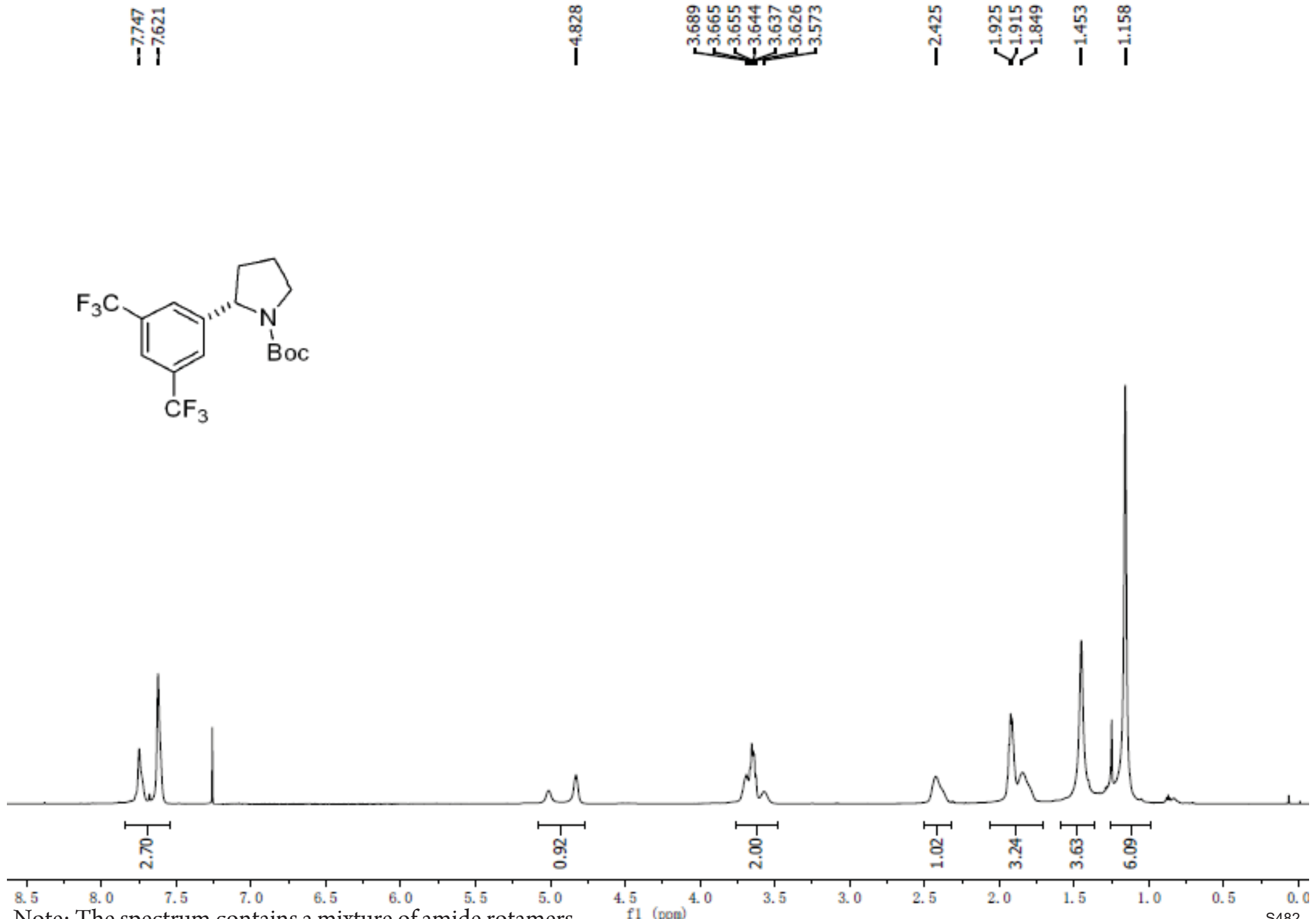


Peak Table

PDA Ch1 273nm

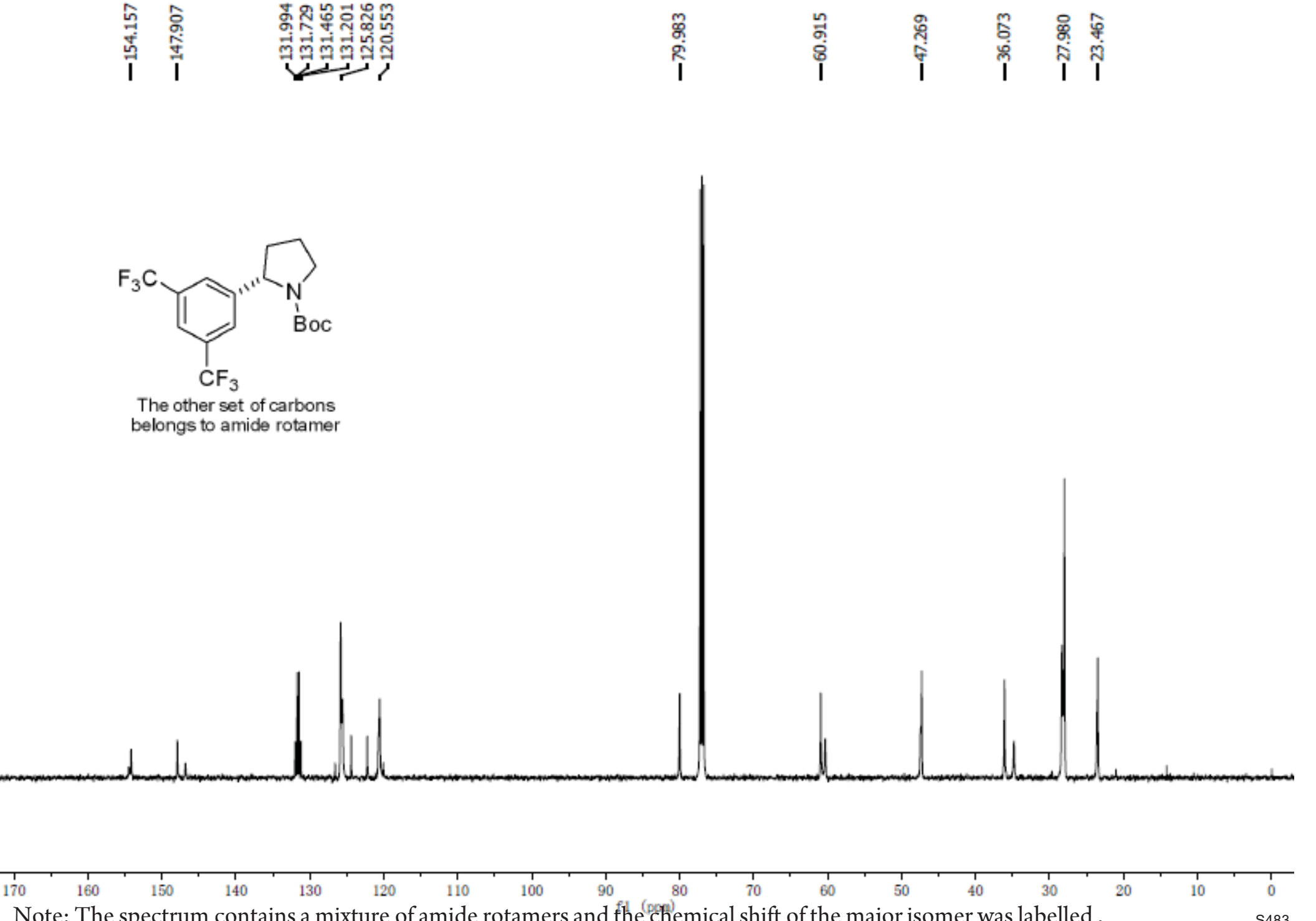
Peak#	Ret. Time	Area	Area%
1	9.571	7884496	95.676
2	11.706	356343	4.324
Total		8240839	100.000

tert-butyl (S)-2-(3,5-bis(trifluoromethyl)phenyl)pyrrolidine-1-carboxylate 2e



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (S)-2-(3,5-bis(trifluoromethyl)phenyl)pyrrolidine-1-carboxylate 2e



Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

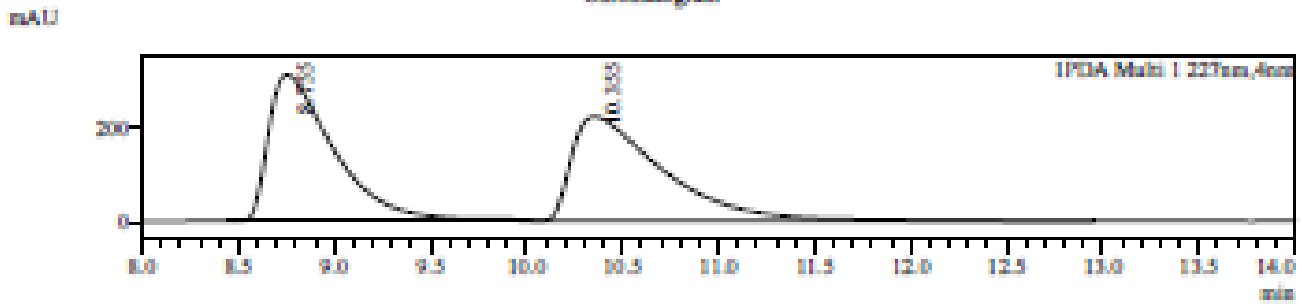
tert-butyl (S)-2-(3,5-bis(trifluoromethyl)phenyl)pyrrolidine-1-carboxylate 2e

tert-butyl (S)-2-(3,5-bis(trifluoromethyl)phenyl)pyrrolidine-1-carboxylate 2e

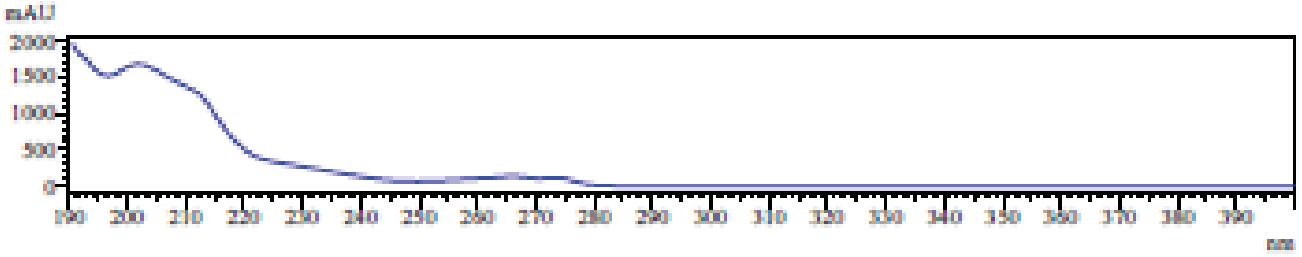
Sample Information

Sample Name	: YW-IV-75A-ADH-0.2%-0.8ML008
Sample ID	: YW-IV-75A-ADH-0.2%-0.8ML008
Data File	: YW-IV-75A-ADH-0.2%-0.8ML008.lcd
Method File	: YW-0.2%-0.8ml.lcm

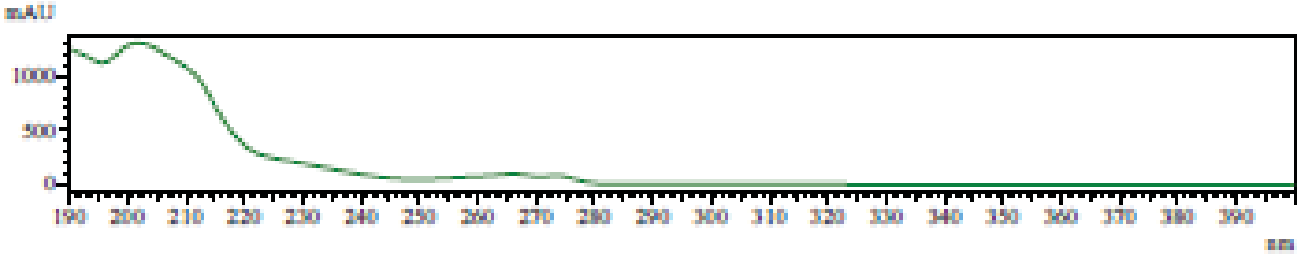
Chromatogram



UV Spectrum
Retention time = 8.755



UV Spectrum
Retention time = 10.355



Peak Table

PDA Ch1 227nm

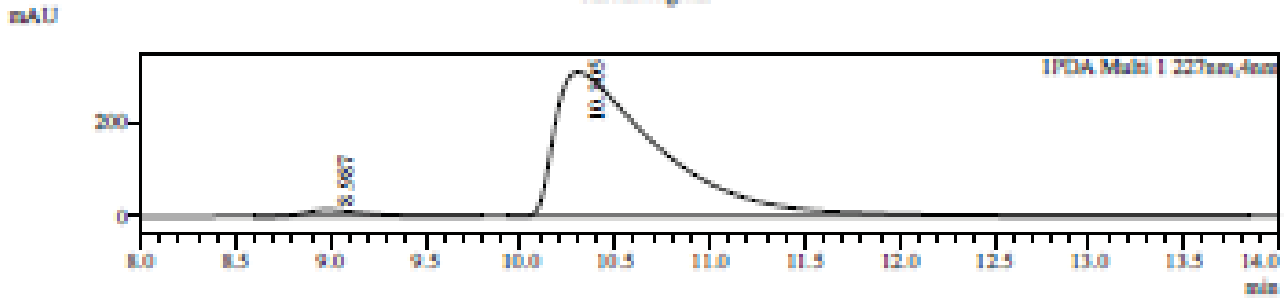
Peak#	Ret. Time	Area	Area%
1	8.755	7393606	49.914
2	10.355	7419192	50.086
Total		14812798	100.000

tert-butyl (S)-2-(3,5-bis(trifluoromethyl)phenyl)pyrrolidine-1-carboxylate 2e

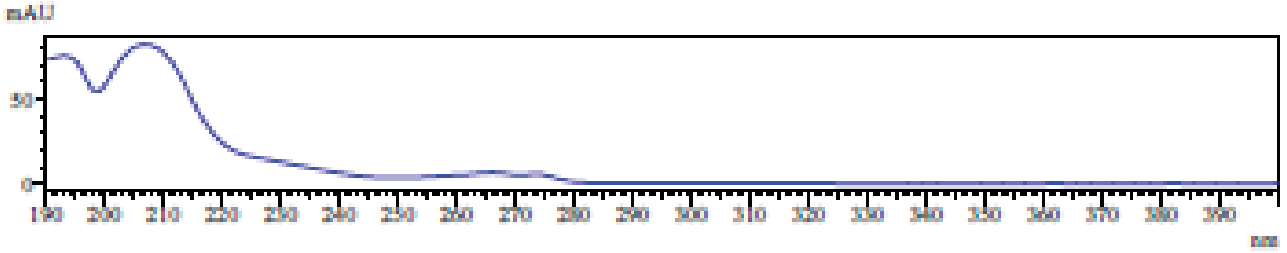
Sample Information

Sample Name	: YW-IV-75B-ADH-0.2%-0.8ML008
Sample ID	: YW-IV-75B-ADH-0.2%-0.8ML008
Data File	: YW-IV-75B-ADH-0.2%-0.8ML008.lcd
Method File	: YW-0.2%-0.8ml.lcm

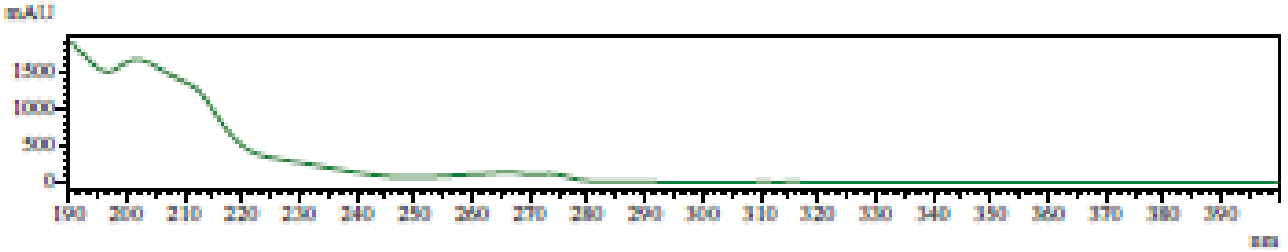
Chromatogram



UV Spectrum
Retention time = 8.987



UV Spectrum
Retention time = 10.305

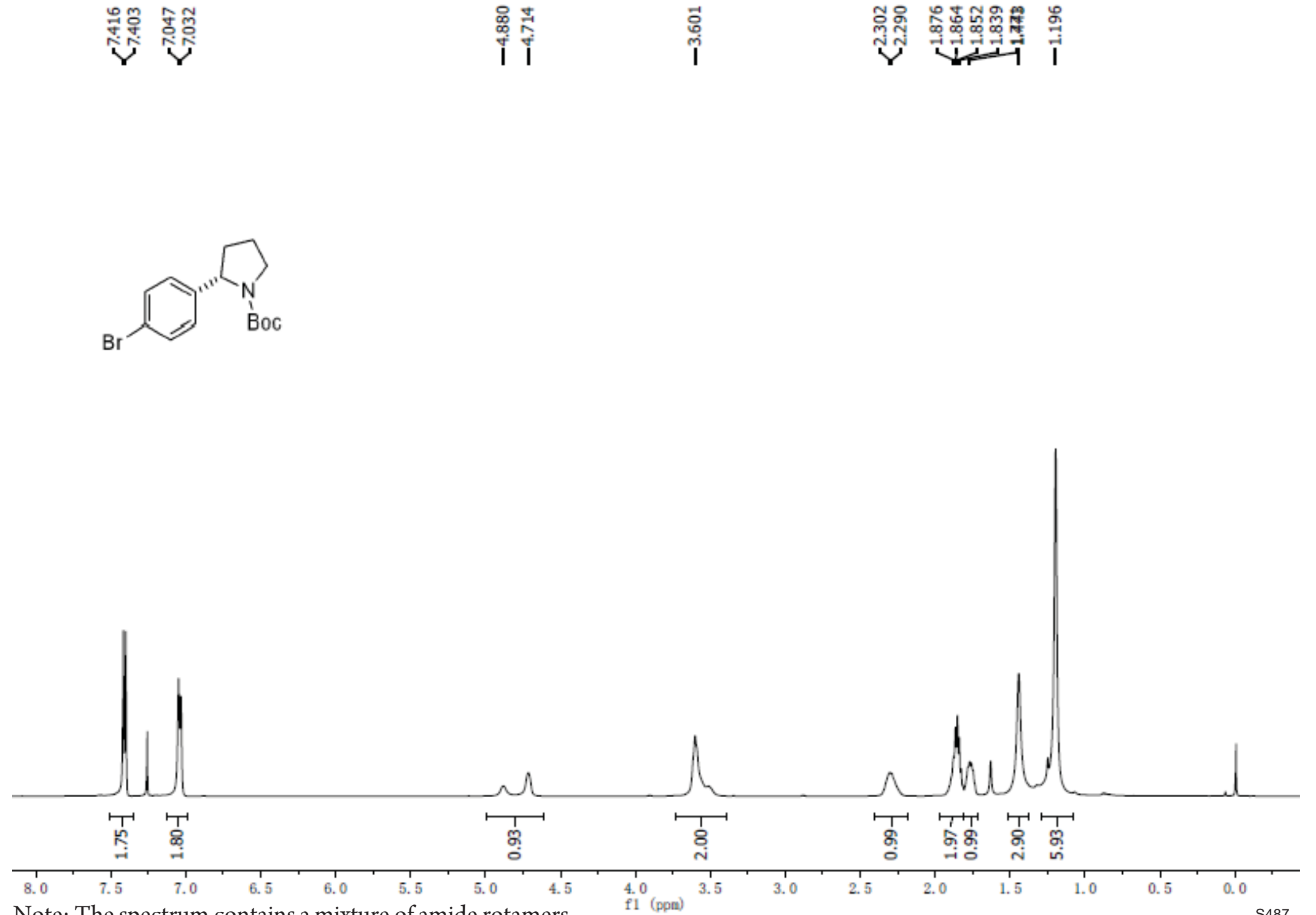


Peak Table

PDA Ch1 227nm

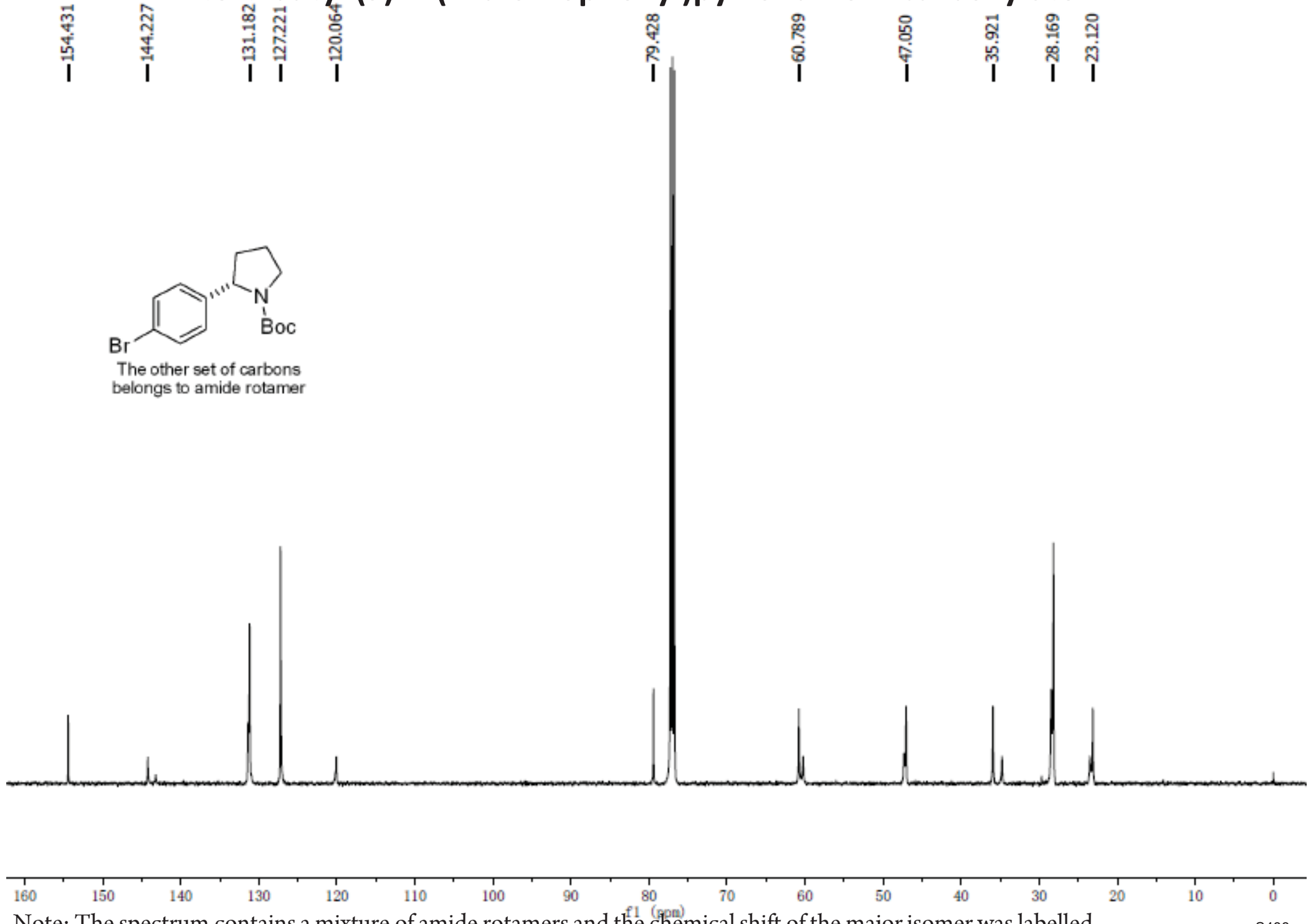
Peak#	Ret. Time	Area	Area%
1	8.987	278093	2.352
2	10.305	11545314	97.648
Total		11823407	100.000

tert-butyl (*S*)-2-(4-bromophenyl)pyrrolidine-1-carboxylate 2f



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(4-bromophenyl)pyrrolidine-1-carboxylate 2f



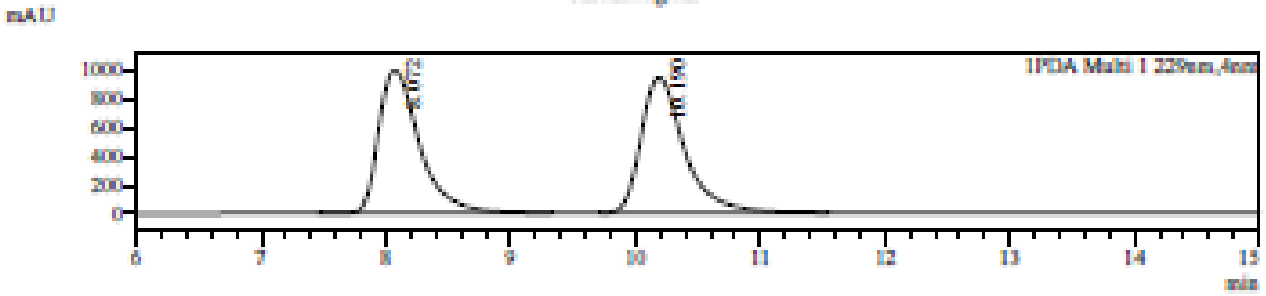
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(4-bromophenyl)pyrrolidine-1-carboxylate 2f

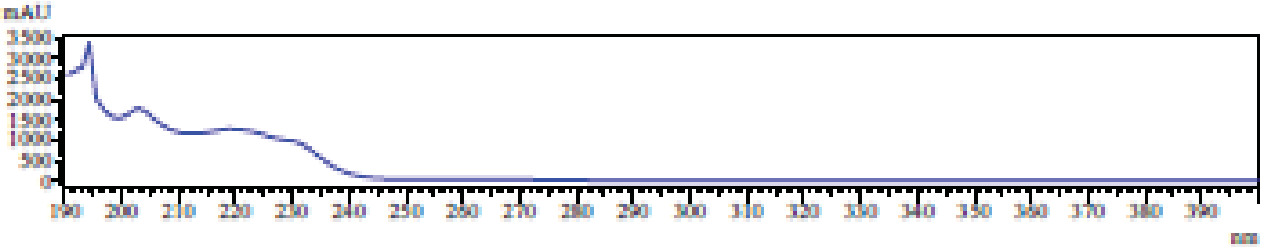
Sample Information

Sample Name	: YW-III-292A-ADH-1%-1ML
Sample ID	: YW-III-292A-ADH-1%-1ML
Data File	: YW-III-292A-ADH-1%-1ML.lcd
Method File	: YW-1%-1.0ml.lcm

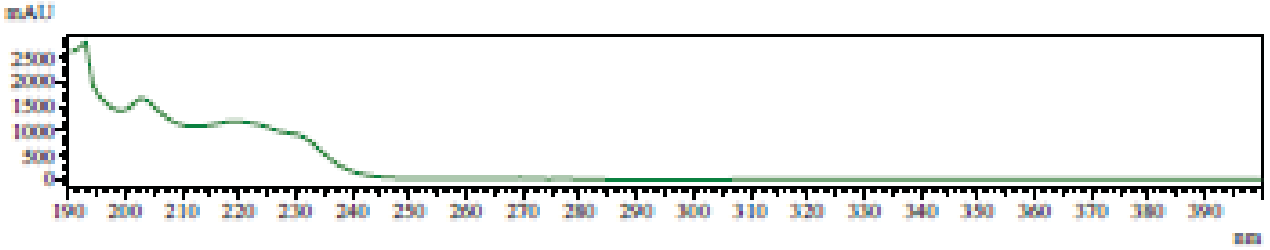
Chromatogram



UV Spectrum
Retention time = 8.072



UV Spectrum
Retention time = 10.190



Peak Table

PDA Ch1 229nm

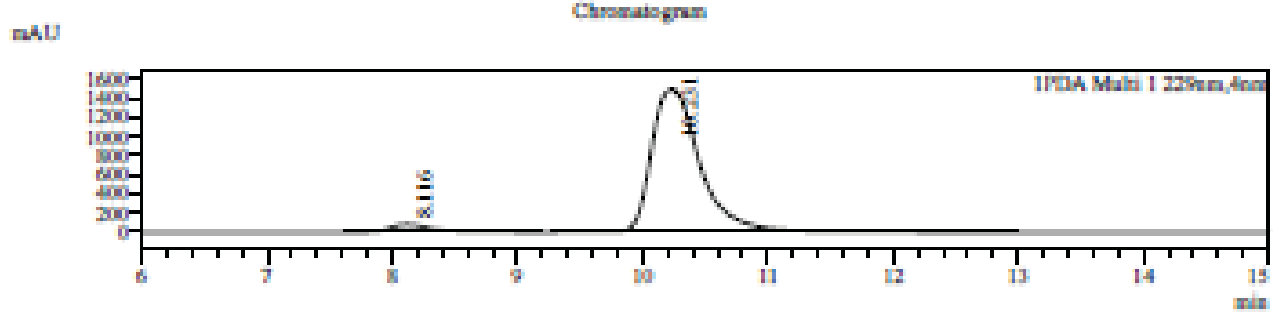
Peak#	Ret. Time	Area	Area%
1	8.072	22595043	49.762
2	10.190	22810923	50.238
Total		45405966	100.000

tert-butyl (*S*)-2-(4-bromophenyl)pyrrolidine-1-carboxylate 2f

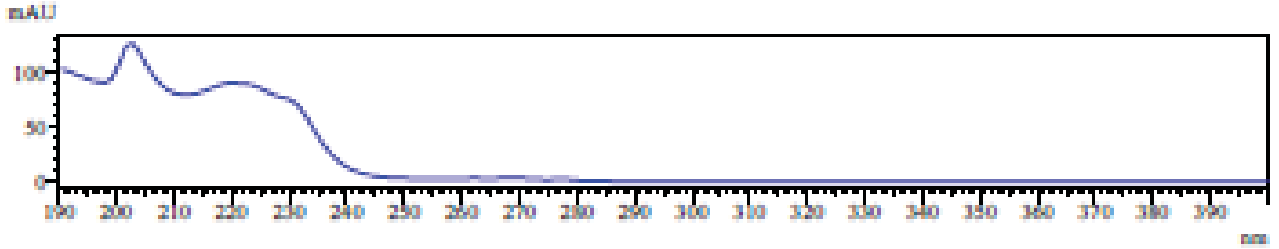
Sample Information

Sample Name	: YW-III-292B-ADH1-1%-1ML
Sample ID	: YW-III-292B-ADH1-1%-1ML
Data File	: YW-III-292B-ADH1-1%-1ML.lcd
Method File	: YW-1%-1.0ml.lcm

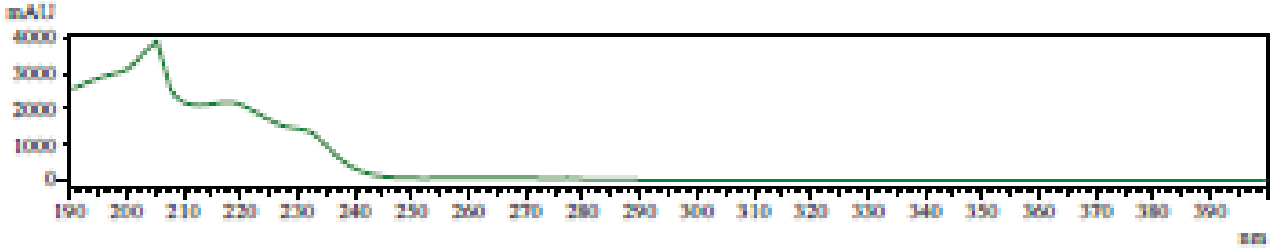
Chromatogram



UV Spectrum
Retention time = 8.116



UV Spectrum
Retention time = 10.231

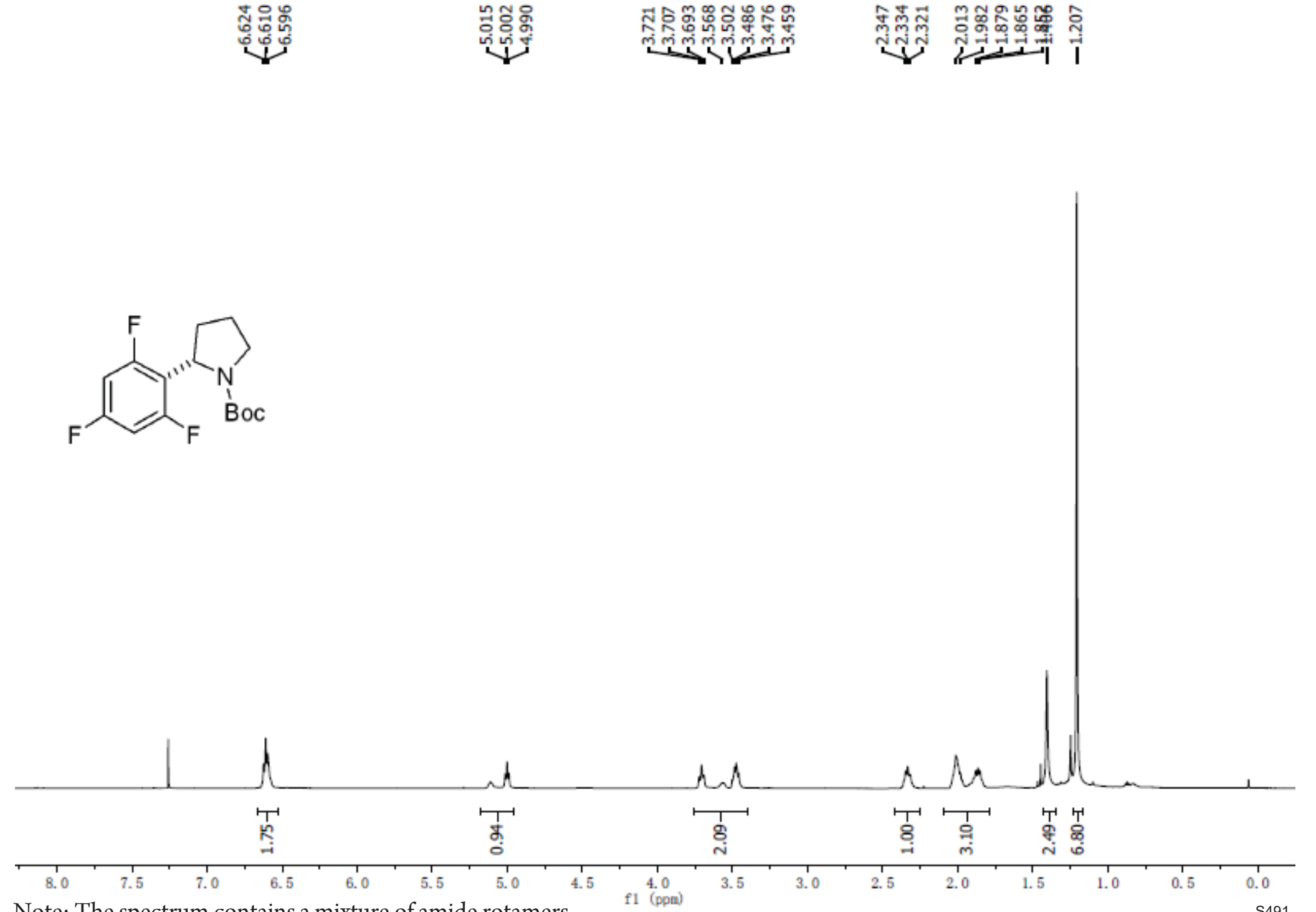


Peak Table

PDA Ch1 229nm

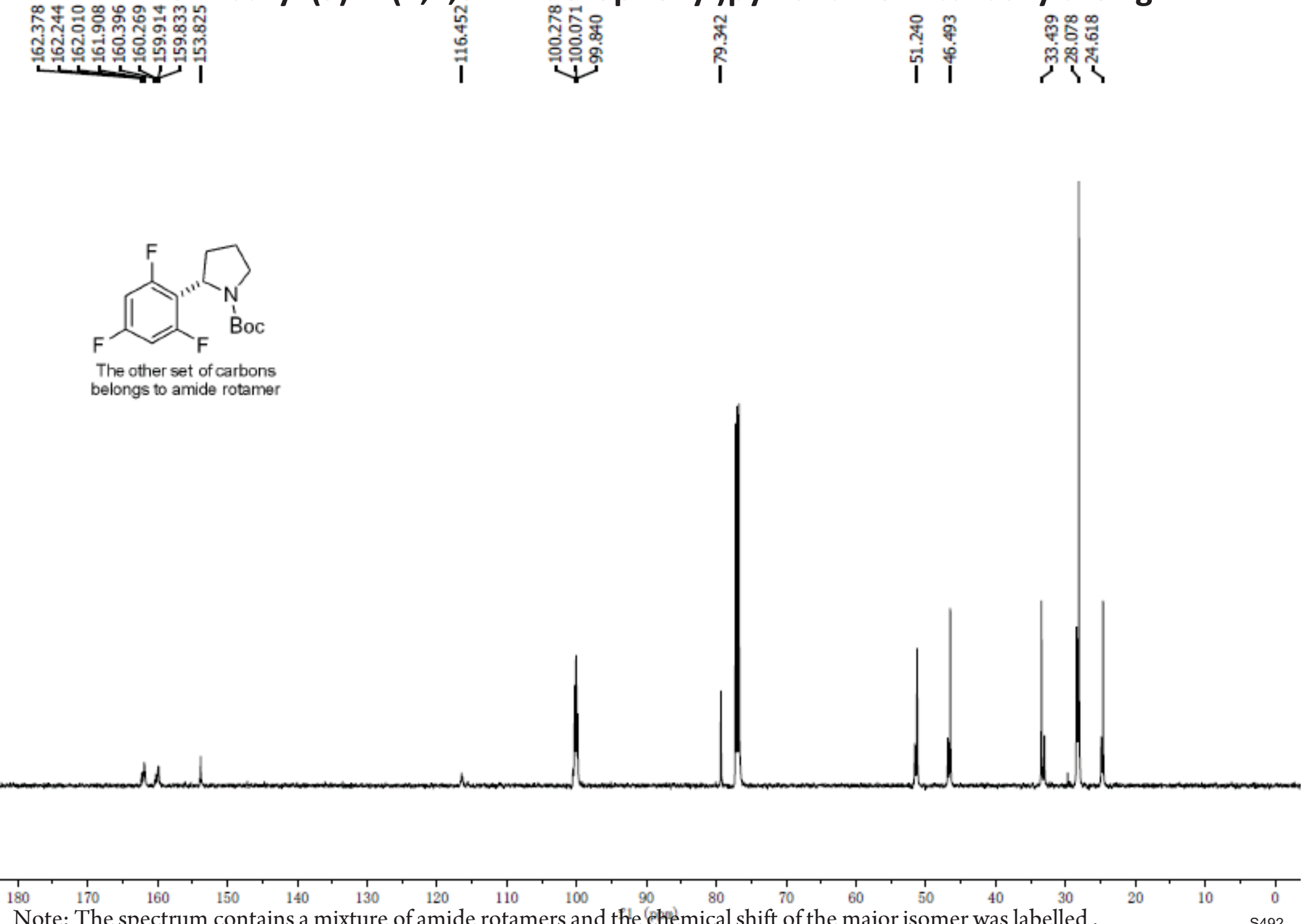
Peak#	Ret. Time	Area	Area%
1	8.116	1659147	4.007
2	10.231	39748284	95.993
Total		41407430	100.000

tert-butyl (*S*)-2-(2,4,6-trifluorophenyl)pyrrolidine-1-carboxylate 2g



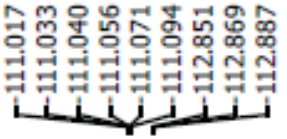
Note: The spectrum contains a mixture of amide rotamers.

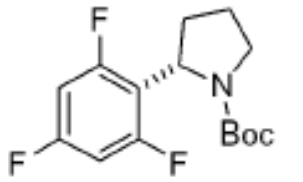
tert-butyl (*S*)-2-(2,4,6-trifluorophenyl)pyrrolidine-1-carboxylate 2g



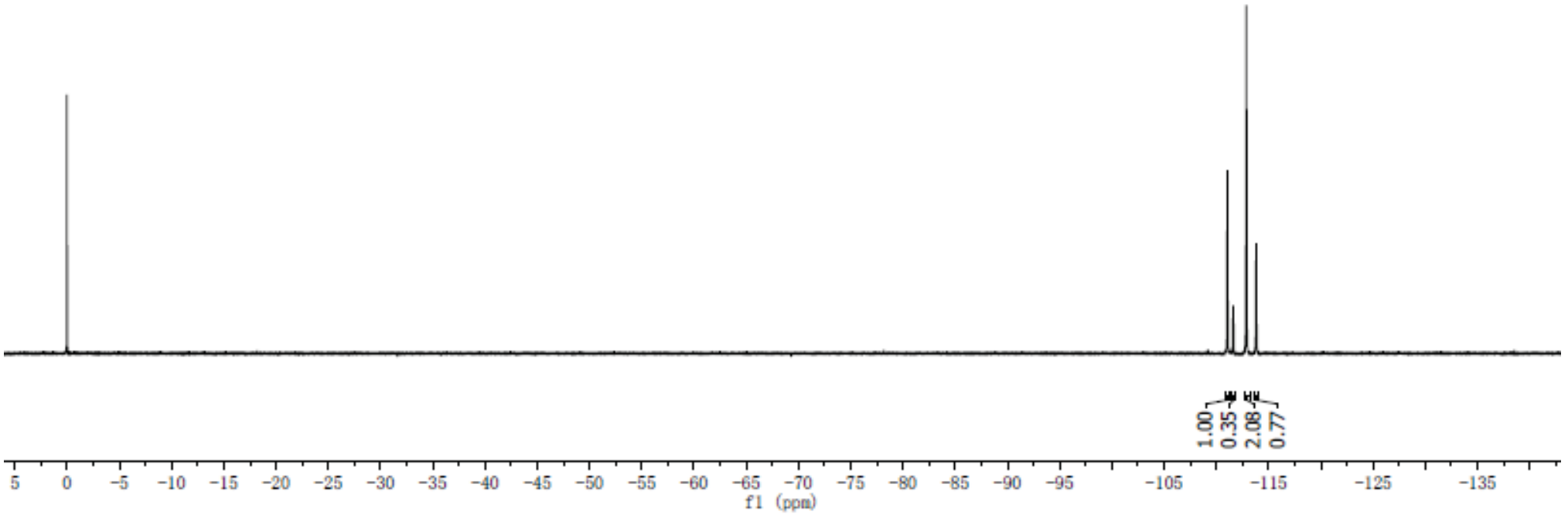
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(2,4,6-trifluorophenyl)pyrrolidine-1-carboxylate 2g





The other set of carbons belongs to amide rotamer

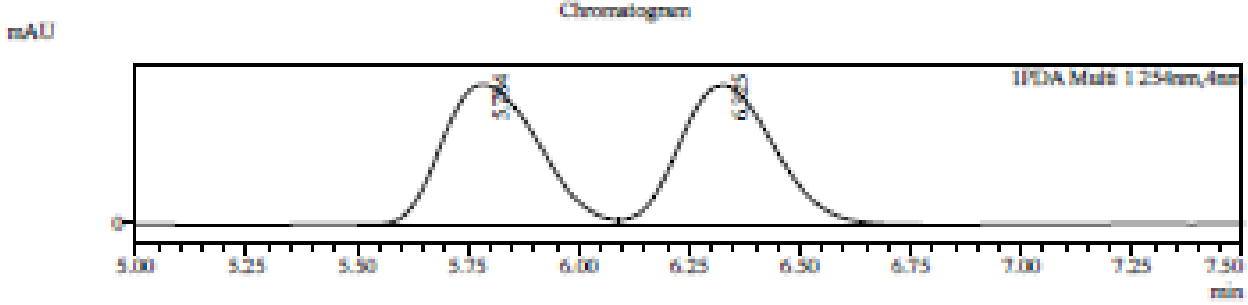


tert-butyl (*S*)-2-(2,4,6-trifluorophenyl)pyrrolidine-1-carboxylate 2g

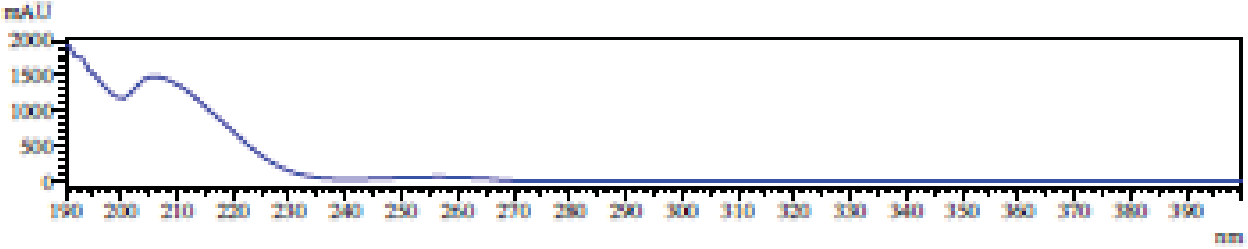
Sample Information

Sample Name	: YW-IV-27aODH-1%-1ML003
Sample ID	: YW-IV-27aODH-1%-1ML003
Data File	: YW-IV-27aODH-1%-1ML003.lcd
Method File	: YW-1%-1.0ml.lcm

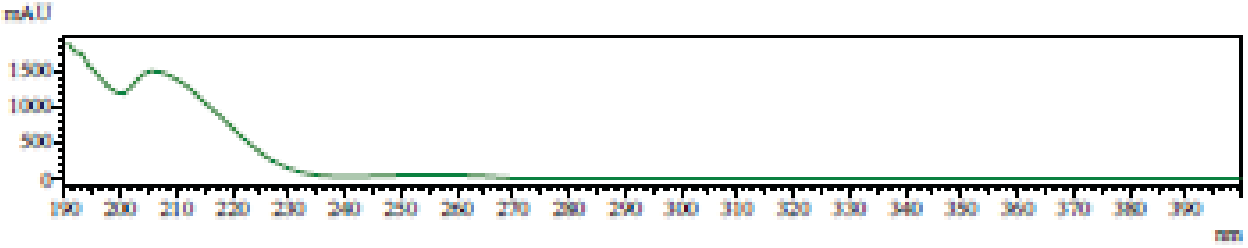
Chromatogram



UV Spectrum
Retention time = 5.784



UV Spectrum
Retention time = 6.325



Peak Table

PDA Ch1 254nm

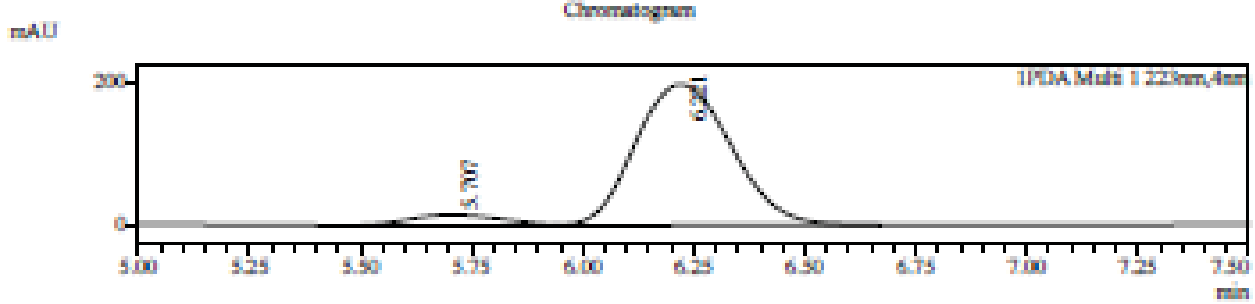
Peak#	Ret. Time	Area	Area%
1	5.784	851042	50.365
2	6.325	838702	49.635
Total		1689744	100.000

tert-butyl (*S*)-2-(2,4,6-trifluorophenyl)pyrrolidine-1-carboxylate 2g

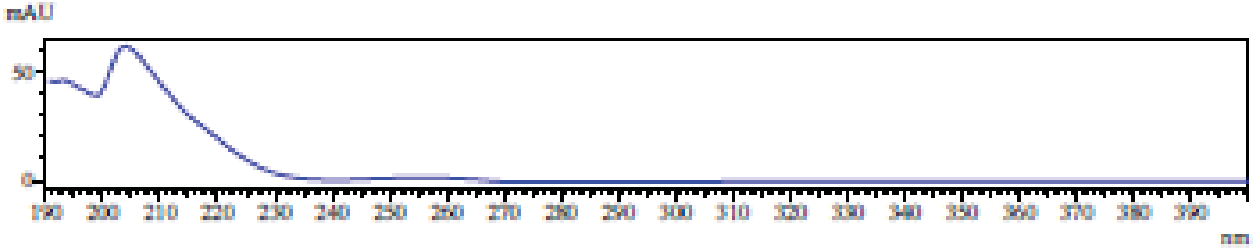
Sample Information

Sample Name	: YW-IV-276-ODH-1%-1ML003
Sample ID	: YW-IV-276-ODH-1%-1ML003
Data File	: YW-IV-276-ODH-1%-1ML003.lcd
Method File	: YW-1%-1.0ml.lcm

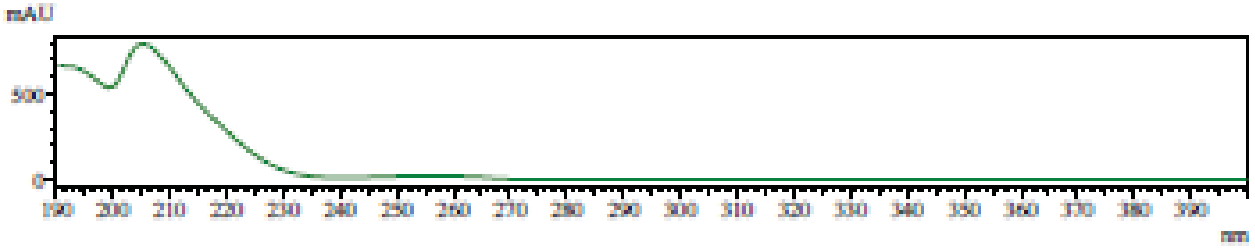
Chromatogram



UV Spectrum
Retention time = 5.707



UV Spectrum
Retention time = 6.221

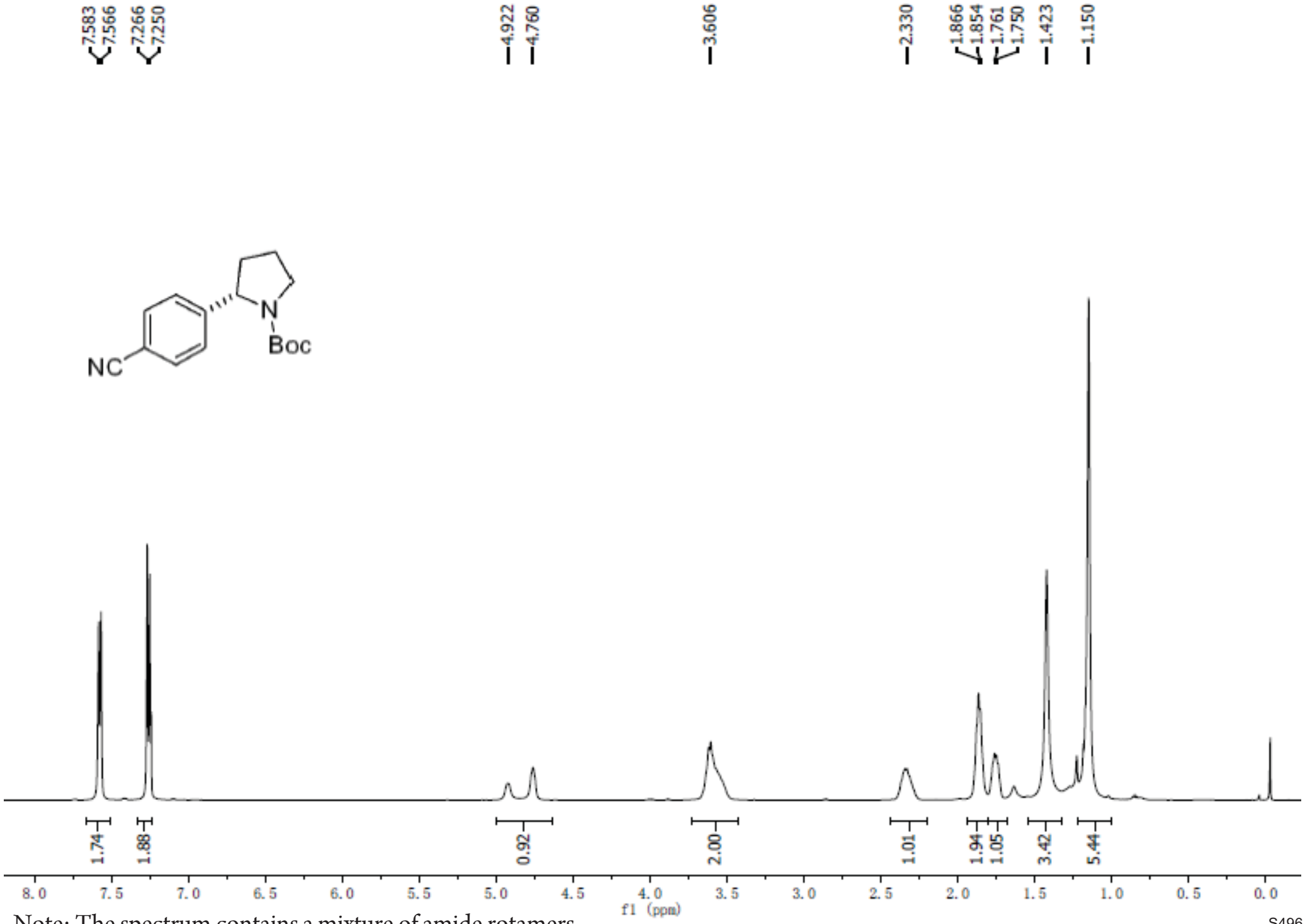


Peak Table

PDA Ch1 223nm

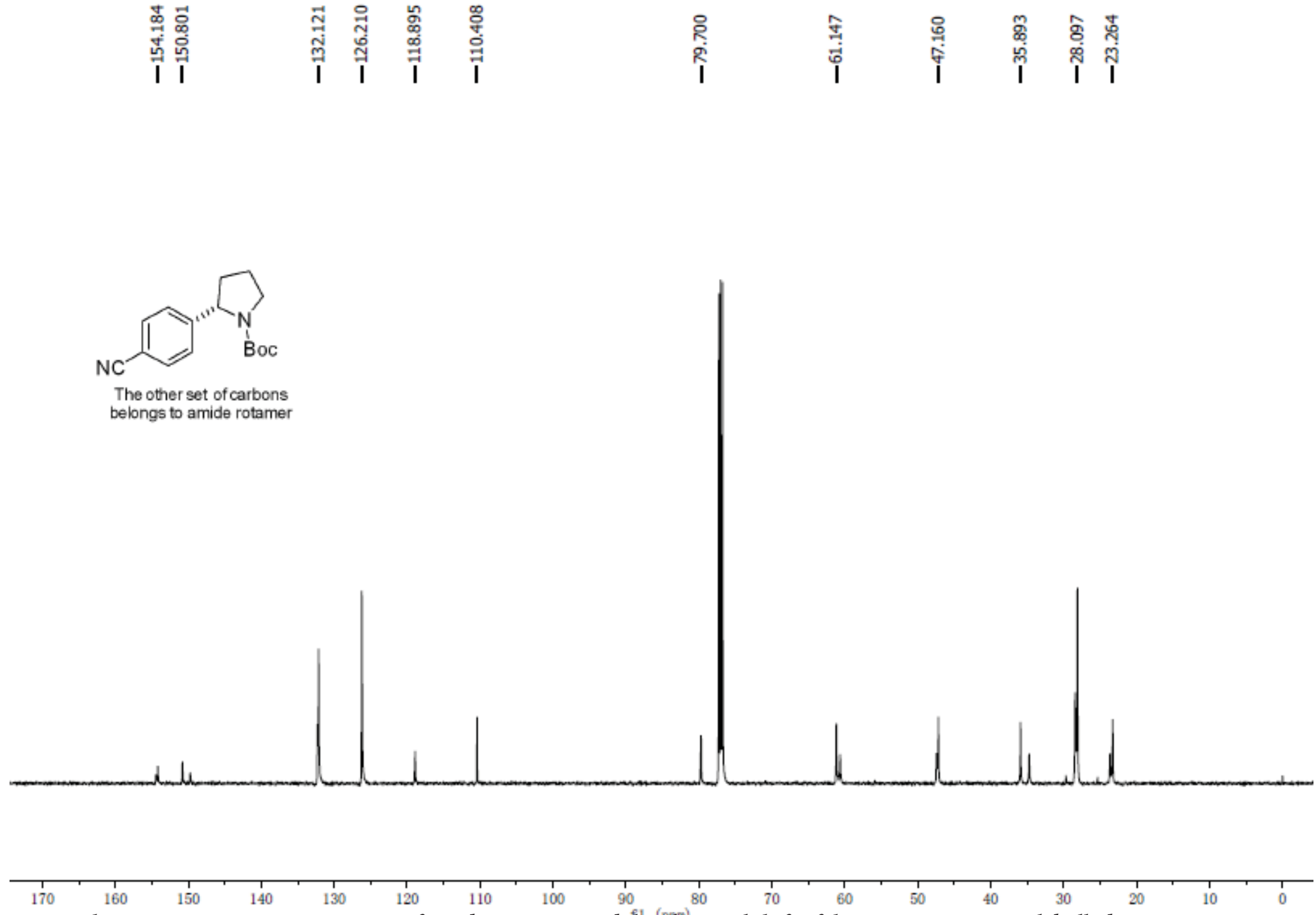
Peak#	Ret. Time	Area	Area%
1	5.707	207393	6.522
2	6.221	2972746	93.478
Total		3180139	100.000

tert-butyl (*S*)-2-(4-cyanophenyl)pyrrolidine-1-carboxylate 2h



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(4-cyanophenyl)pyrrolidine-1-carboxylate 2h



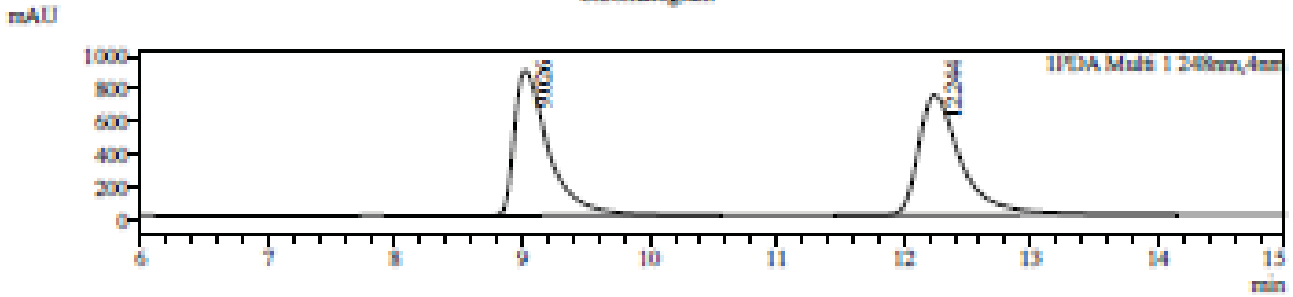
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(4-cyanophenyl)pyrrolidine-1-carboxylate 2h

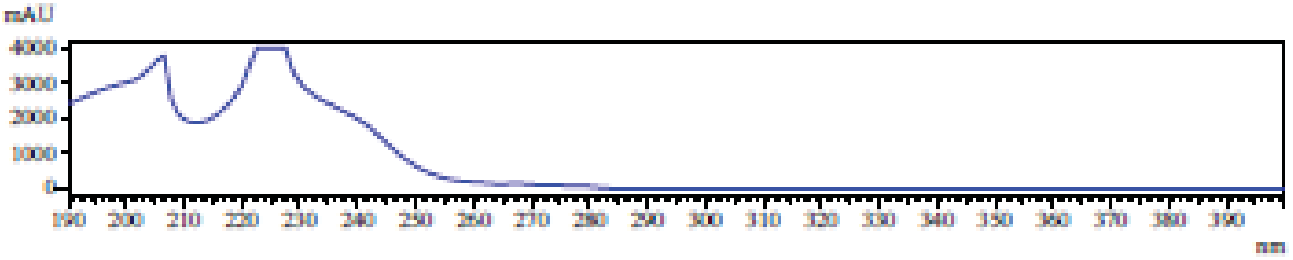
Sample Information

Sample Name	: YW-III-272A-ADH-5%-1ML
Sample ID	: YW-III-272A-ADH-5%-1ML
Data File	: YW-III-272A-ADH-5%-1ML.lcd
Method File	: YW-ADH-5.0%-1.0ml.lcm

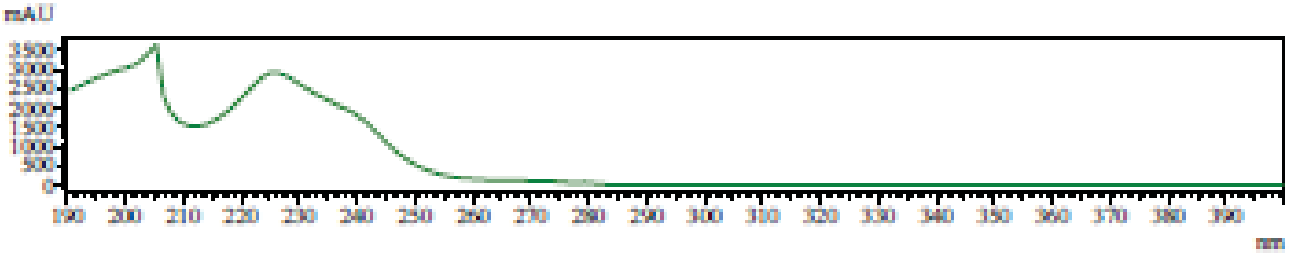
Chromatogram



UV Spectrum
Retention time = 9.026



UV Spectrum
Retention time = 12.244



Peak Table

PDA Ch1 248nm

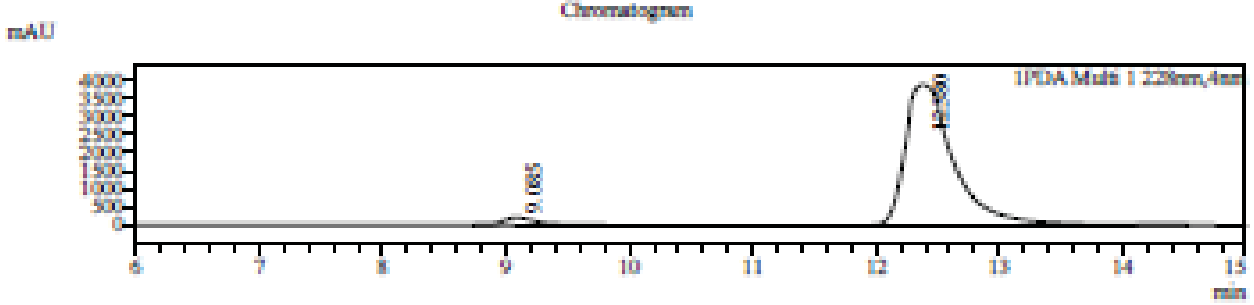
Peak#	Ret. Time	Area	Area%
1	9.026	16676449	49.534
2	12.244	16989933	50.466
Total		33666382	100.000

tert-butyl (*S*)-2-(4-cyanophenyl)pyrrolidine-1-carboxylate 2h

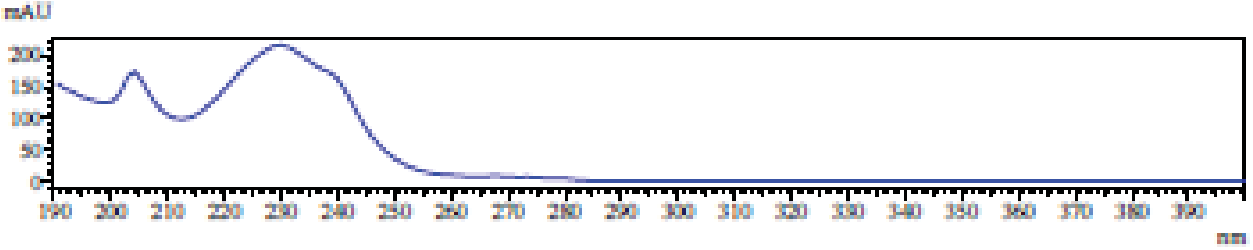
Sample Information

Sample Name	: YW-III-272B-ADH-5%-1ML
Sample ID	: YW-III-272B-ADH-5%-1ML
Data File	: YW-III-272B-ADH-5%-1ML.lcd
Method File	: YW-ADH-5.0%-1.0ml.lcm

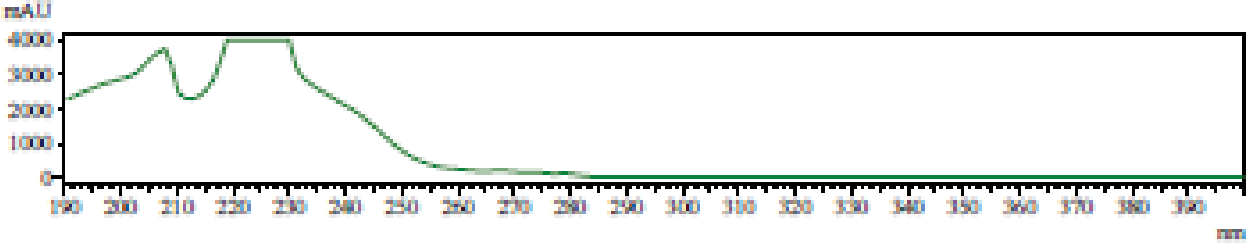
Chromatogram



UV Spectrum
Retention time = 9.085



UV Spectrum
Retention time = 12.380

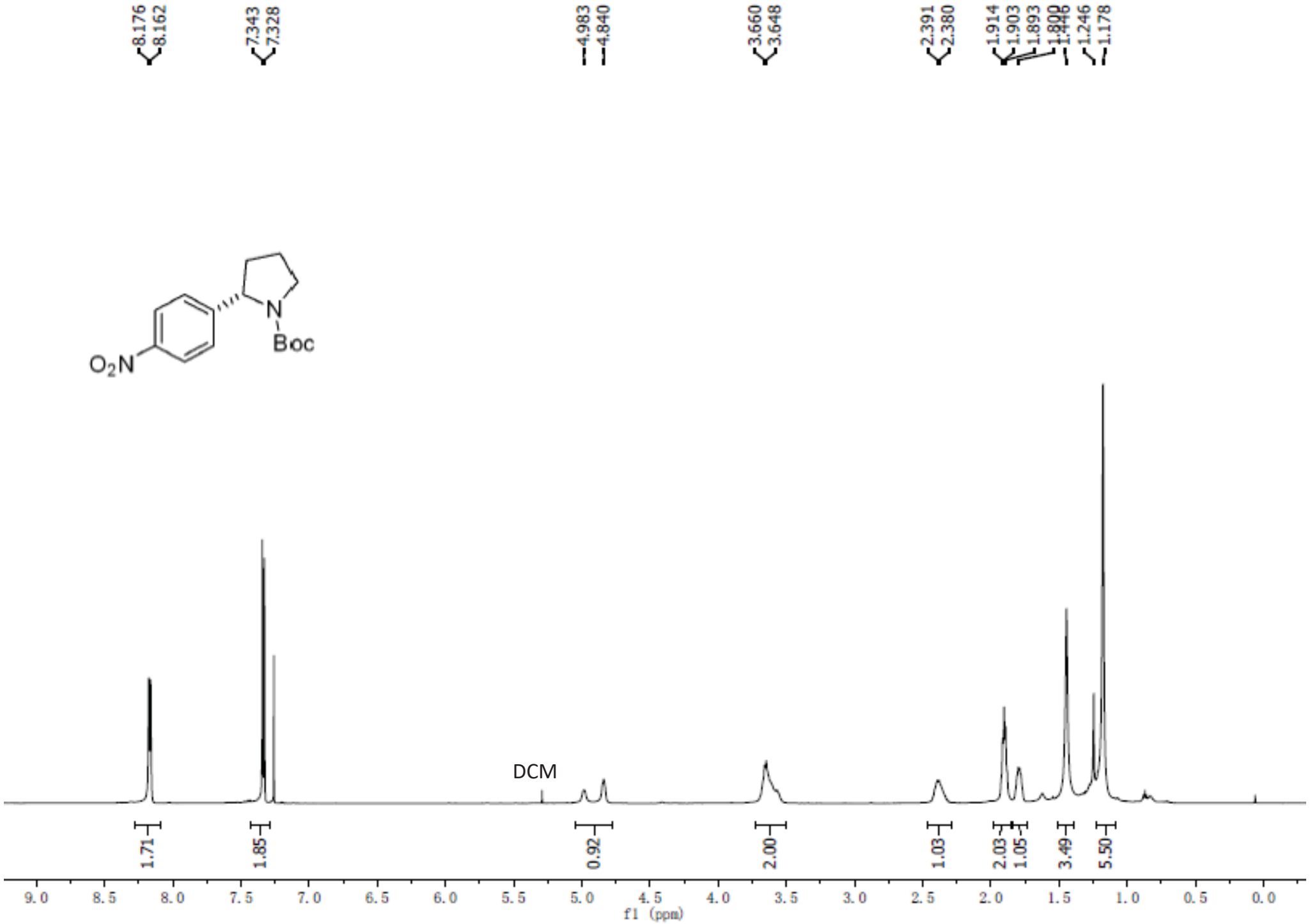


Peak Table

PDA Ch1 228nm

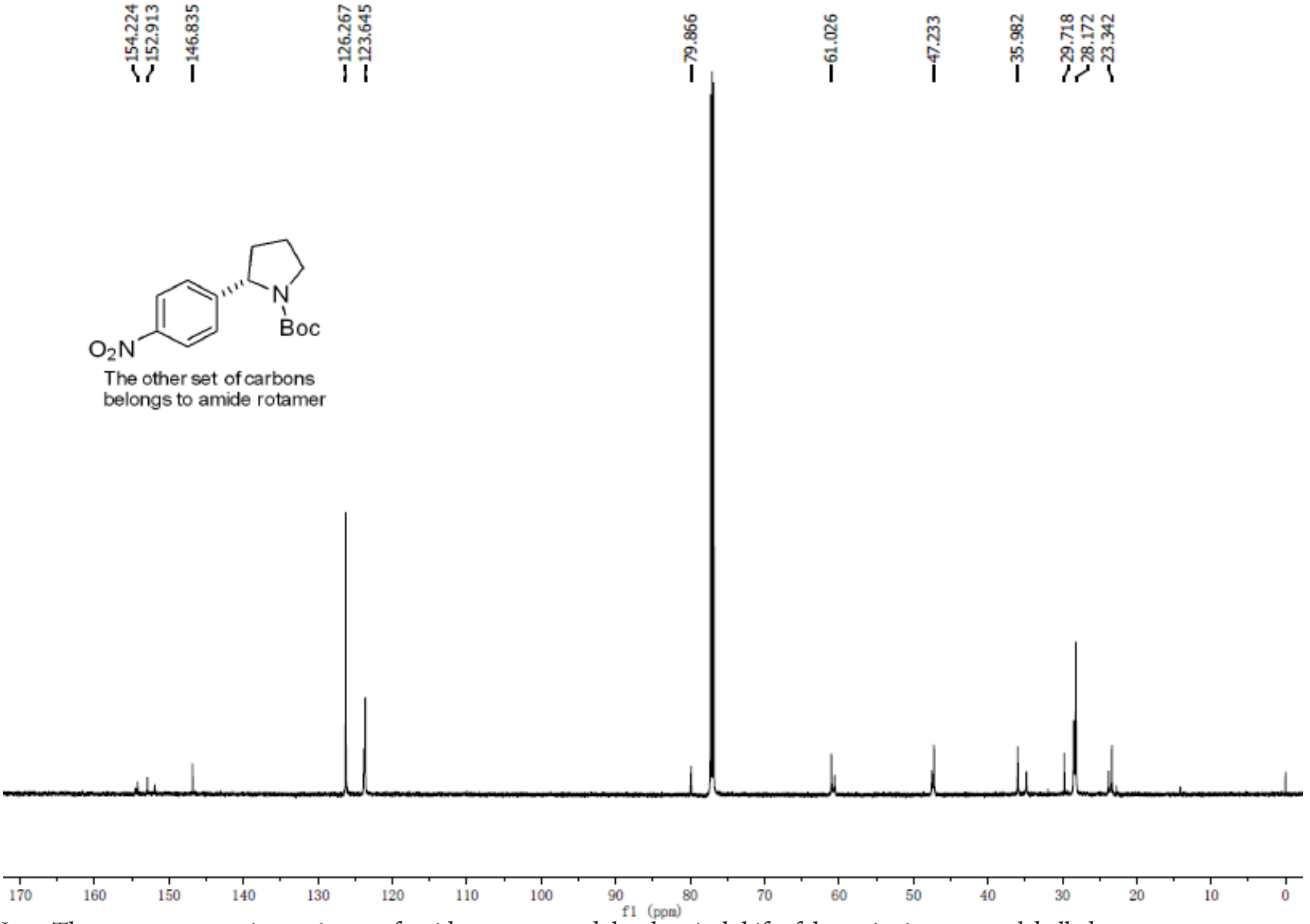
Peak#	Ret. Time	Area	Area%
1	9.085	3805213	3.452
2	12.380	106441374	96.548
Total		110246588	100.000

tert-butyl (S)-2-(4-nitrophenyl)pyrrolidine-1-carboxylate 2i



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (S)-2-(4-nitrophenyl)pyrrolidine-1-carboxylate 2i



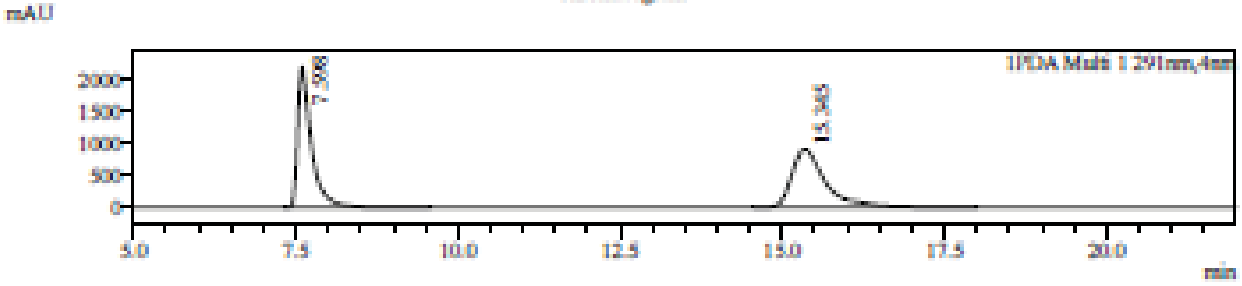
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (S)-2-(4-nitrophenyl)pyrrolidine-1-carboxylate 2i

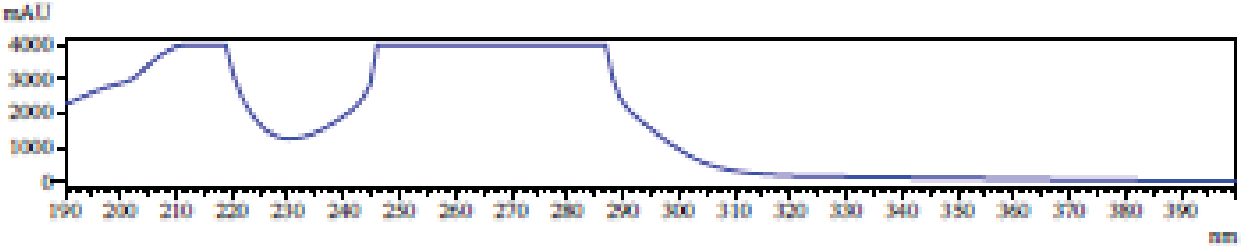
Sample Information

Sample Name	: YW-III-273A-ADH-5%-1ML
Sample ID	: YW-III-273A-ADH-5%-1ML
Data File	: YW-III-273A-ADH-5%-1ML.lcd
Method File	: YW-ADH-5.0%-1.0ml.lcm

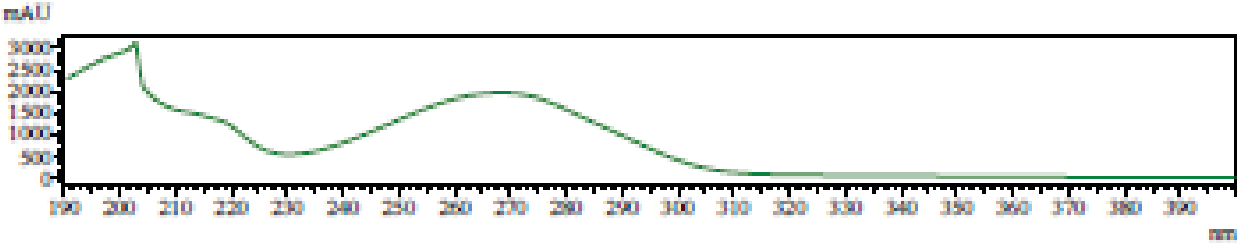
Chromatogram



UV Spectrum
Retention time = 7.598



UV Spectrum
Retention time = 15.345



Peak Table

PDA Ch1 291nm

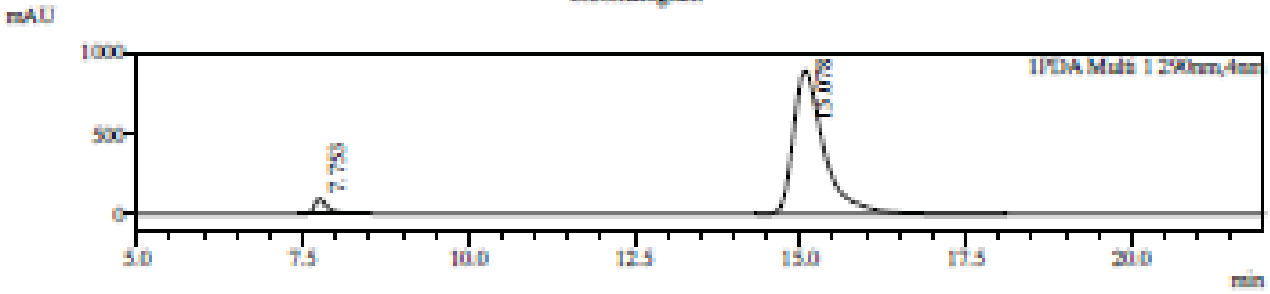
Peak#	Ret. Time	Area	Area%
1	7.598	31615217	49.618
2	15.345	32102576	50.382
Total		63717793	100.000

tert-butyl (S)-2-(4-nitrophenyl)pyrrolidine-1-carboxylate 2i

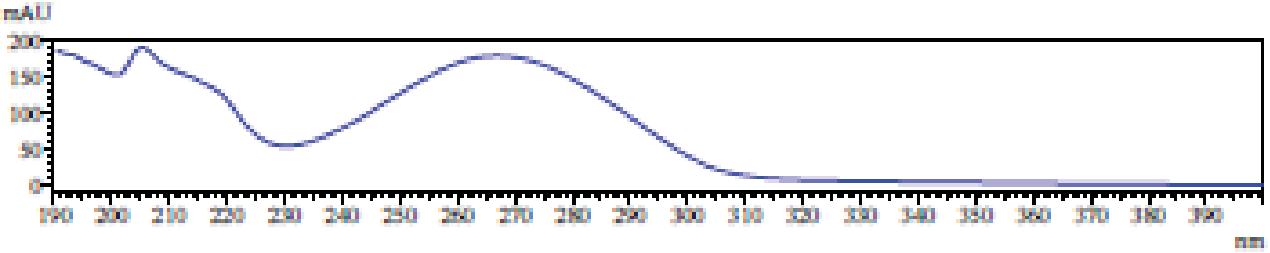
Sample Information

Sample Name	: YW-III-273B-ADH1-5%-1ML
Sample ID	: YW-III-273B-ADH1-5%-1ML
Data File	: YW-III-273B-ADH1-5%-1ML.lcd
Method File	: YW-ADH-5.0%-1.0ml.lcm

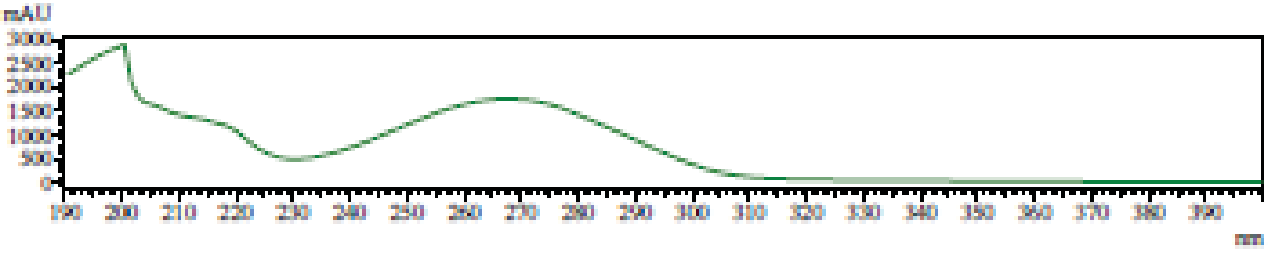
Chromatogram



UV Spectrum
Retention time = 7.753



UV Spectrum
Retention time = 15.078

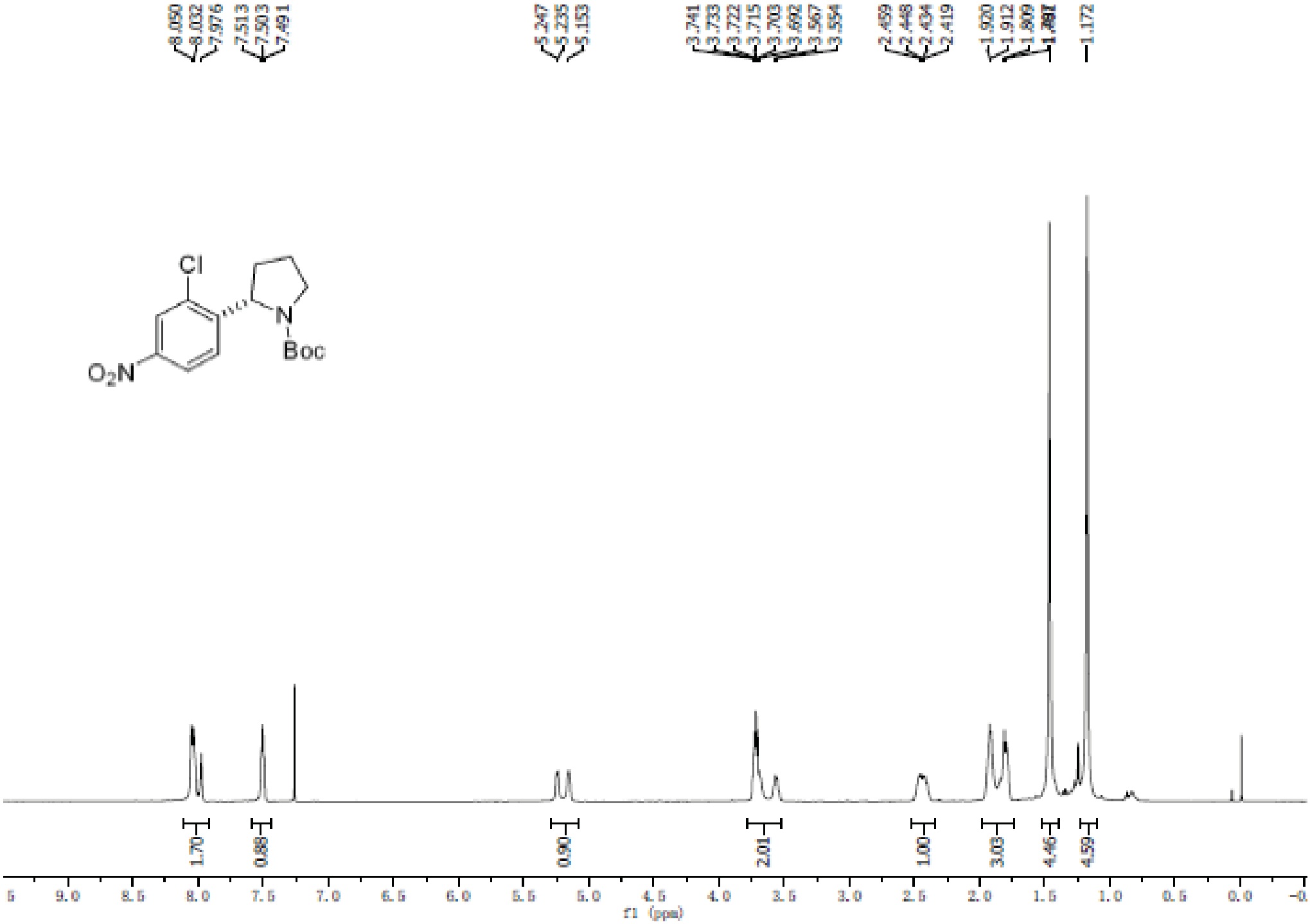


Peak Table

PDA Ch1 290nm

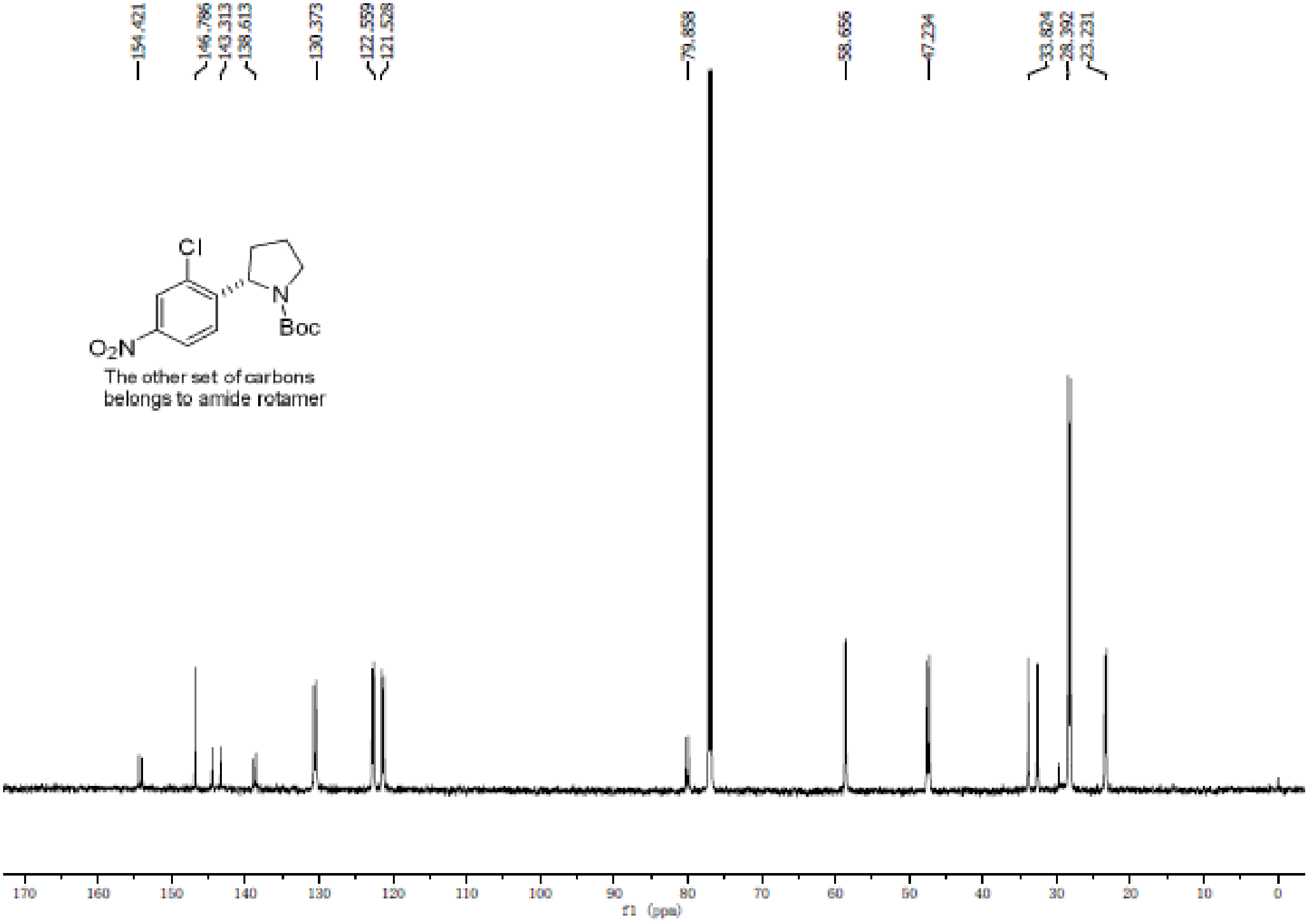
Peak#	Ret. Time	Area	Area%
1	7.753	1272172	4.224
2	15.078	28843392	95.776
Total		30115564	100.000

tert-butyl (*S*)-2-(2-chloro-4-nitrophenyl)pyrrolidine-1-carboxylate 2j



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(2-chloro-4-nitrophenyl)pyrrolidine-1-carboxylate 2j



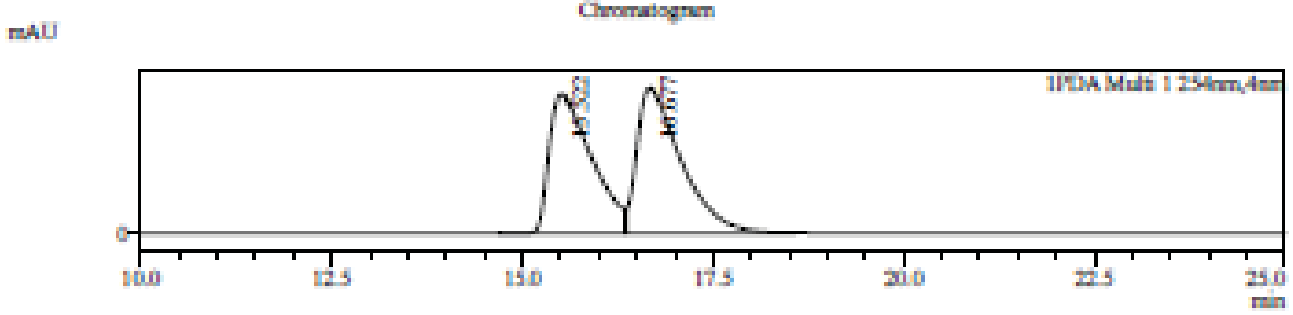
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(2-chloro-4-nitrophenyl)pyrrolidine-1-carboxylate 2j

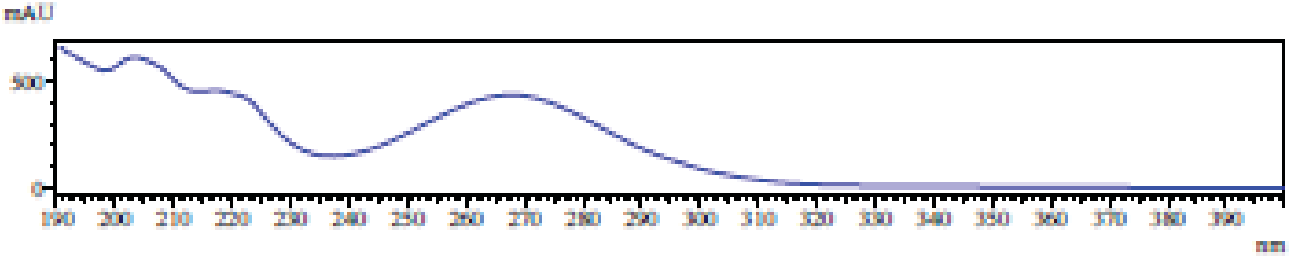
Sample Information

Sample Name : YW-IV-136a-ODH-0.5%-1ML
Sample ID : YW-IV-136a-ODH-0.5%-1ML
Data File : YW-IV-136a-ODH-0.5%-1ML001.lcd
Method File : YW-0.5%-1.0ml.lcm

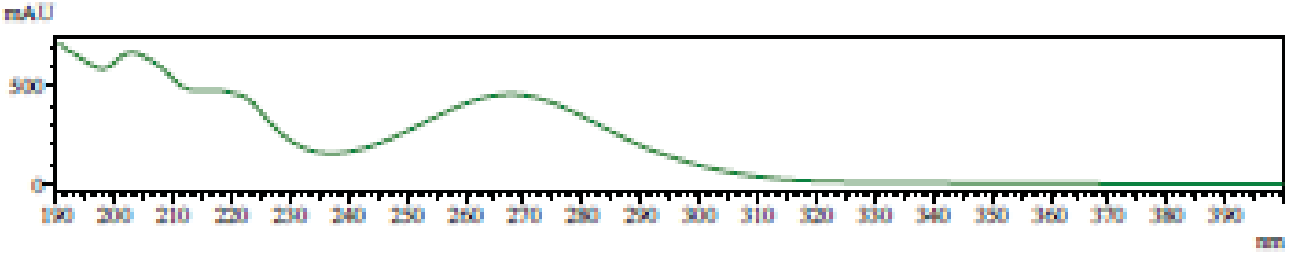
Chromatogram



UV Spectrum
Retention time = 15.522



UV Spectrum
Retention time = 16.677



Peak Table

PDA Ch1 254nm

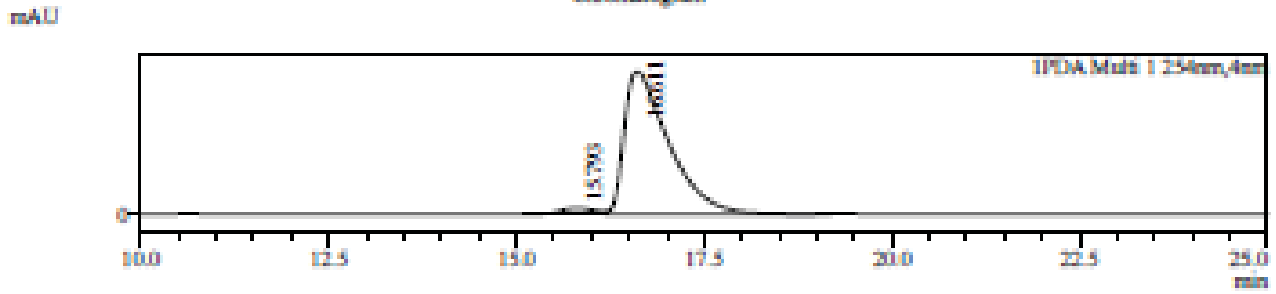
Peak#	Ret. Time	Area	Area%
1	15.522	12157594	48.008
2	16.677	13166744	51.992
Total		25324338	100.000

tert-butyl (*S*)-2-(2-chloro-4-nitrophenyl)pyrrolidine-1-carboxylate 2j

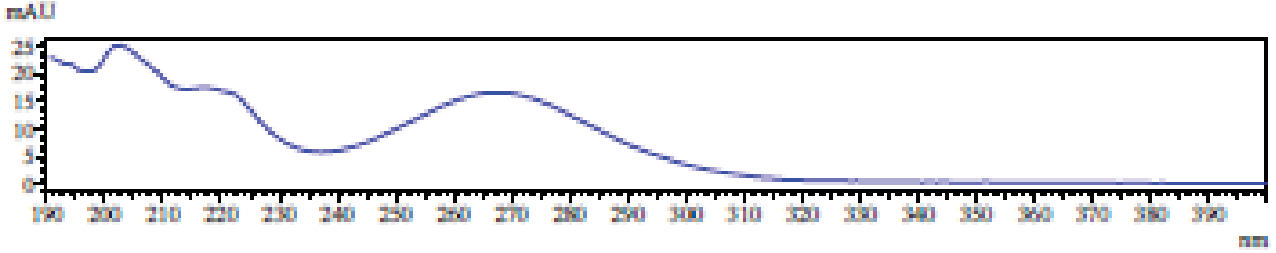
Sample Information

Sample Name	: YW-IV-136B-ODH-0.5%-1ML
Sample ID	: YW-IV-136B-ODH-0.5%-1ML
Data File	: YW-IV-136B-ODH-0.5%-1ML.lcd
Method File	: YW-0.5%-1.0ml.lcm

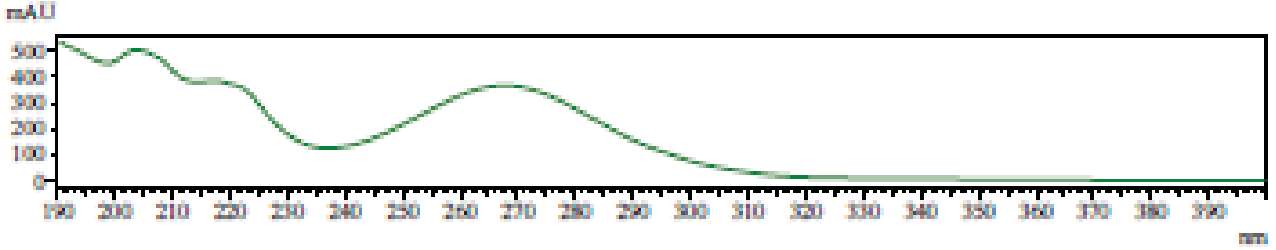
Chromatogram



UV Spectrum
Retention time = 15.793



UV Spectrum
Retention time = 16.611

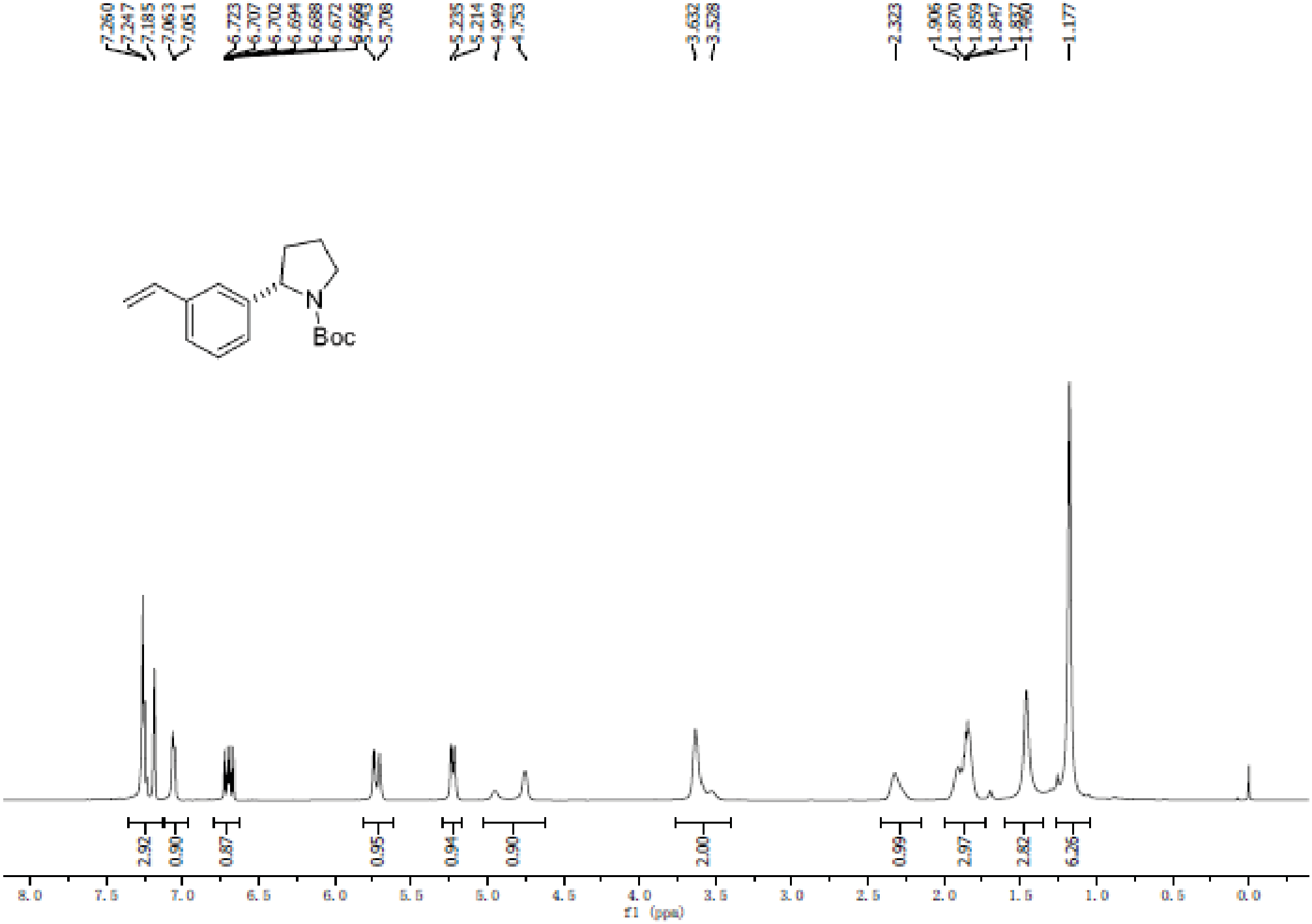


Peak Table

PDA Ch1 254nm

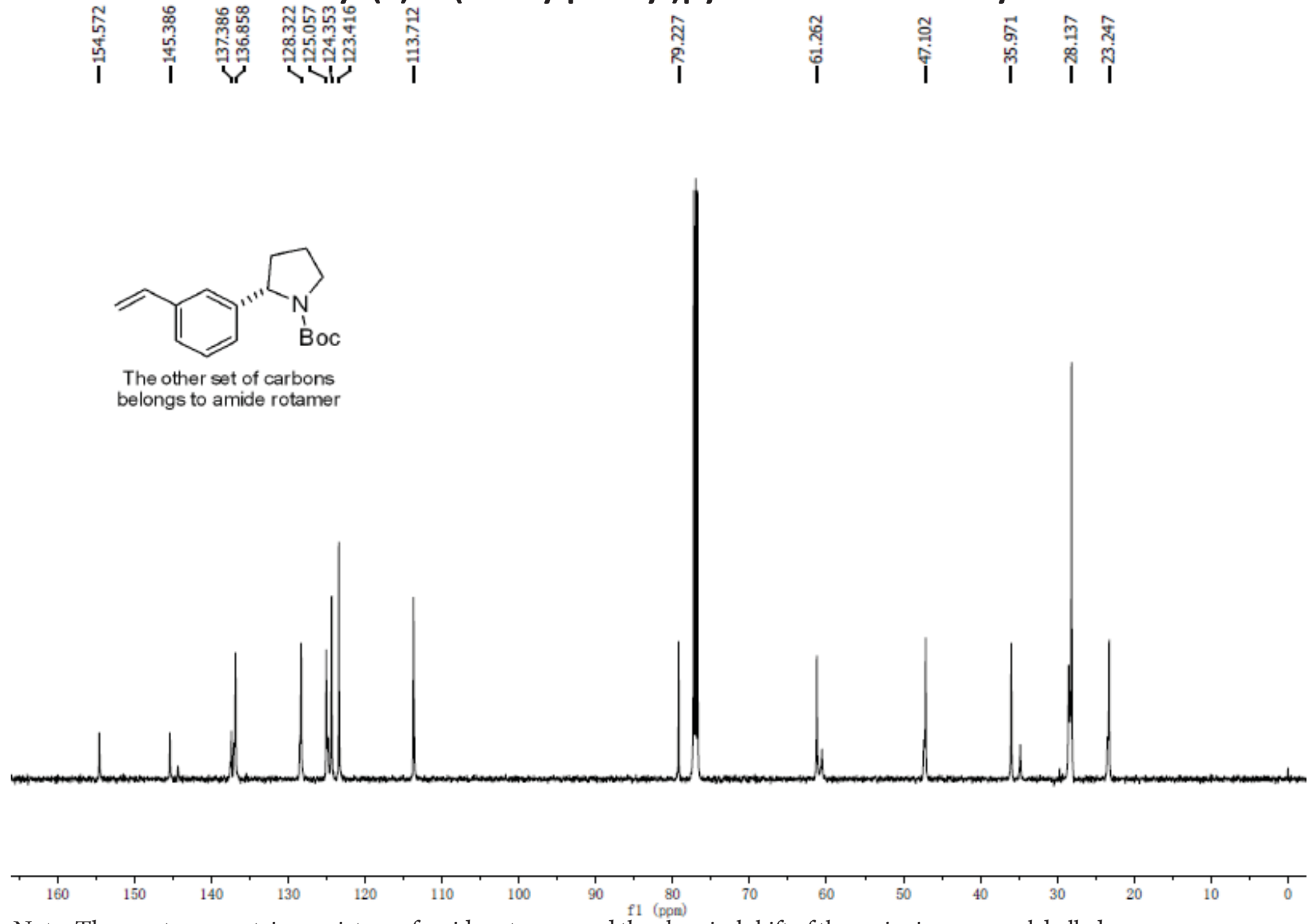
Peak#	Ret. Time	Area	Area%
1	15.793	370042	3.278
2	16.611	10917000	96.722
Total		11287042	100.000

tert-butyl (*S*)-2-(3-vinylphenyl)pyrrolidine-1-carboxylate 2k



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(3-vinylphenyl)pyrrolidine-1-carboxylate 2k



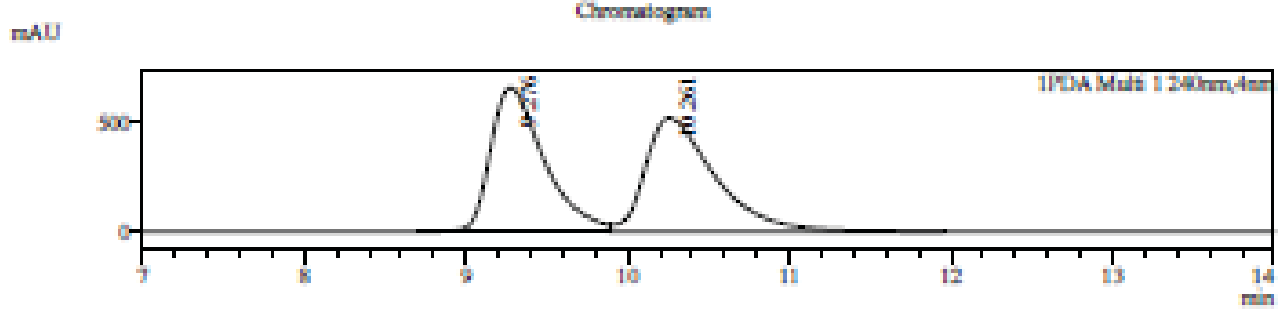
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(3-vinylphenyl)pyrrolidine-1-carboxylate 2k

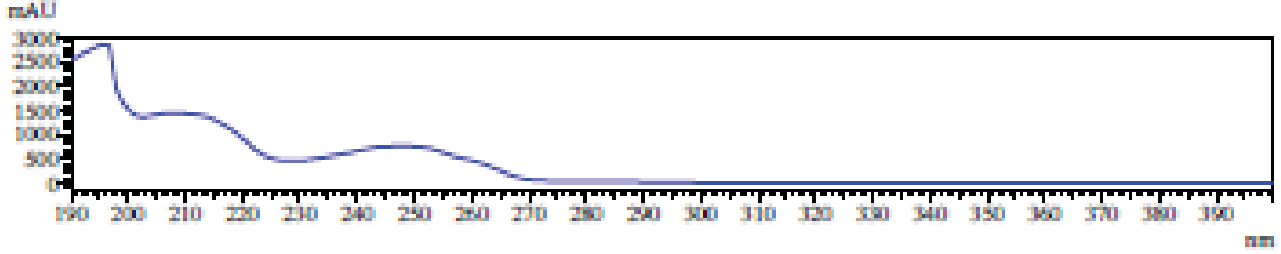
Sample Information

Sample Name	: YW-IV-77A-ADH-0.8%-1.0ML
Sample ID	: YW-IV-77A-ADH-0.8%-1.0ML
Data File	: YW-IV-77A-ADH-0.8%-1.0ML.lcd
Method File	: YW-0.8%-1.0ml.lcm

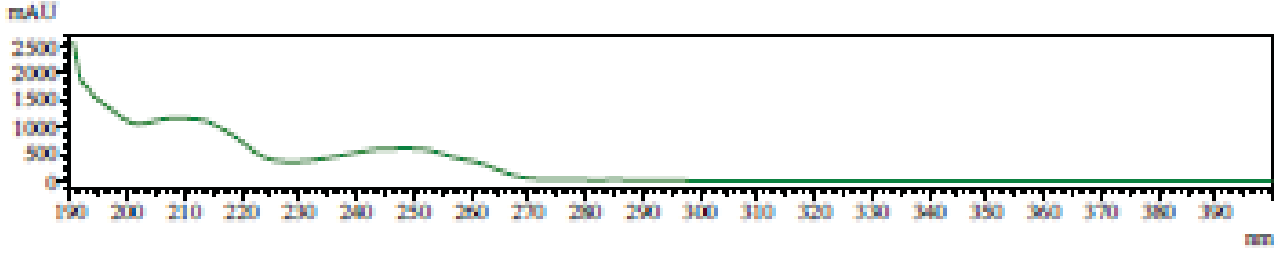
Chromatogram



UV Spectrum
Retention time = 9.276



UV Spectrum
Retention time = 10.261



Peak Table

PDA Ch1 240nm

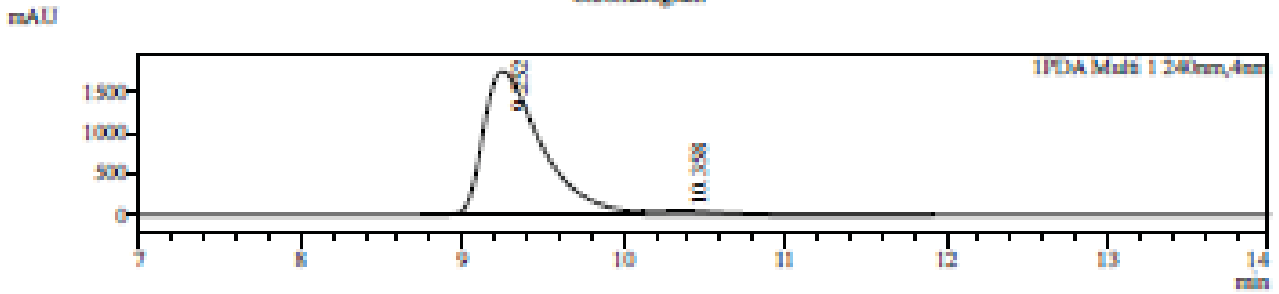
Peak#	Ret. Time	Area	Area%
1	9.276	15232694	49.401
2	10.261	15602009	50.599
Total		30834703	100.000

tert-butyl (*S*)-2-(3-vinylphenyl)pyrrolidine-1-carboxylate 2k

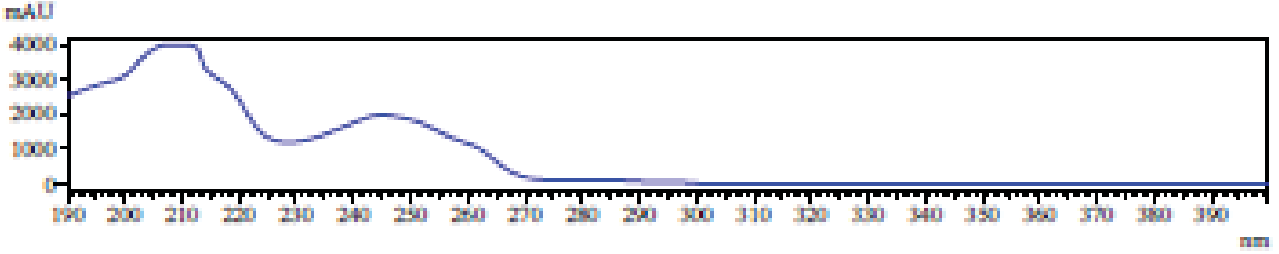
Sample Information

Sample Name	: YW-IV-77B-ADH-0.8%-1.0ML
Sample ID	: YW-IV-77B-ADH-0.8%-1.0ML
Data File	: YW-IV-77B-ADH-0.8%-1.0ML.lcd
Method File	: YW-0.8%-1.0ml.1cm

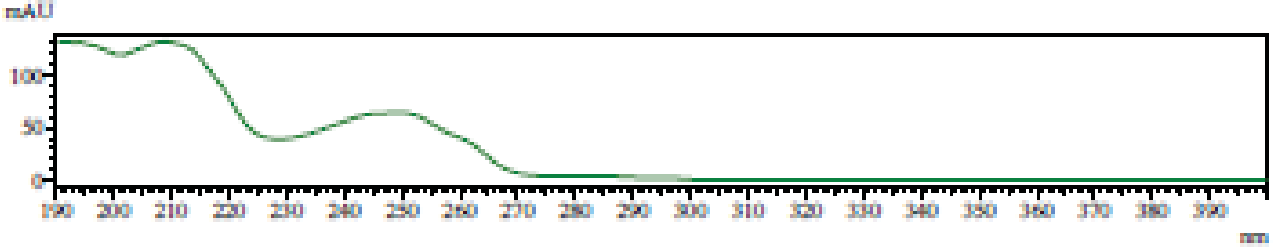
Chromatogram



UV Spectrum
Retention time = 9.252



UV Spectrum
Retention time = 10.358

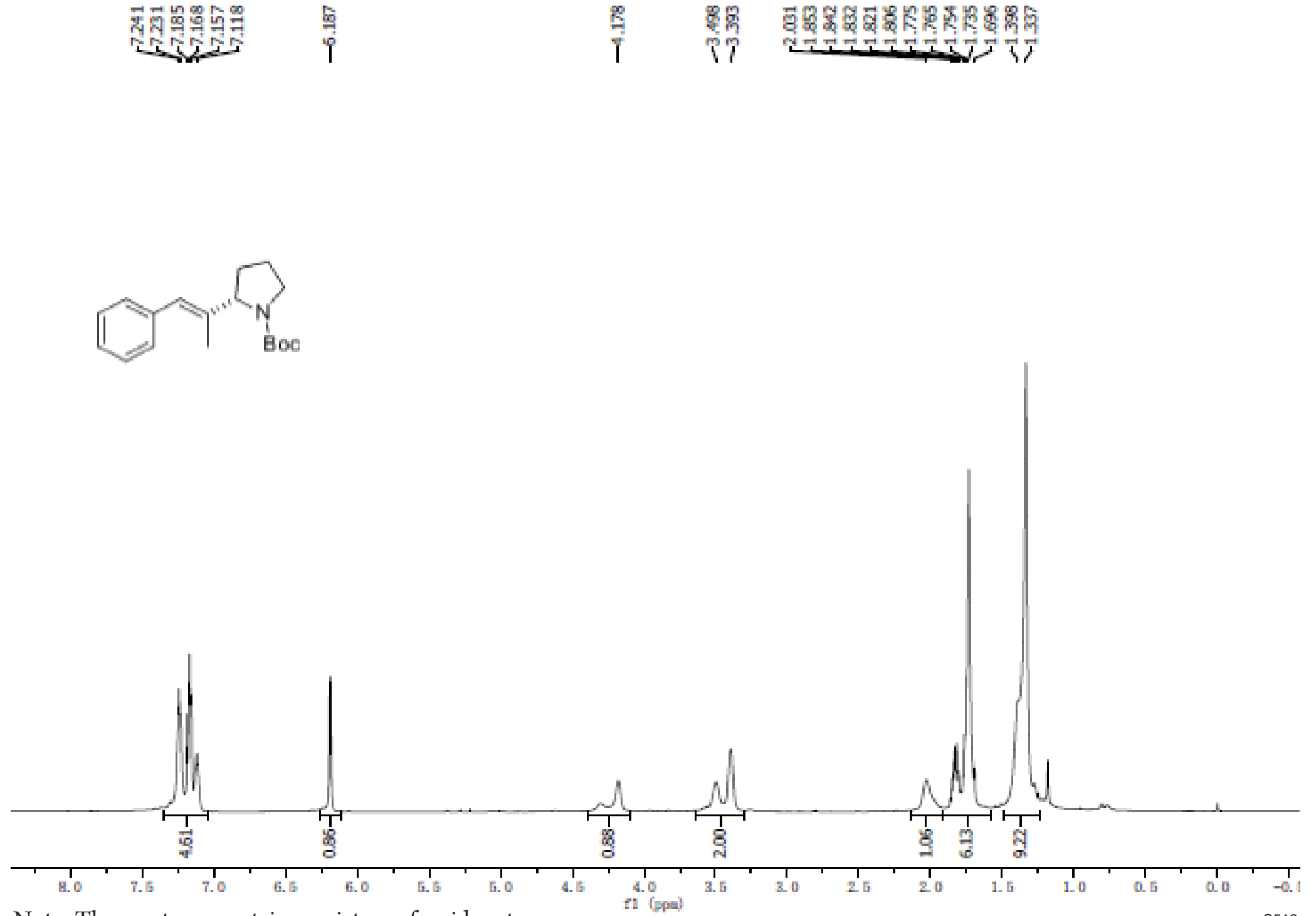


Peak Table

PDA Ch1 240nm

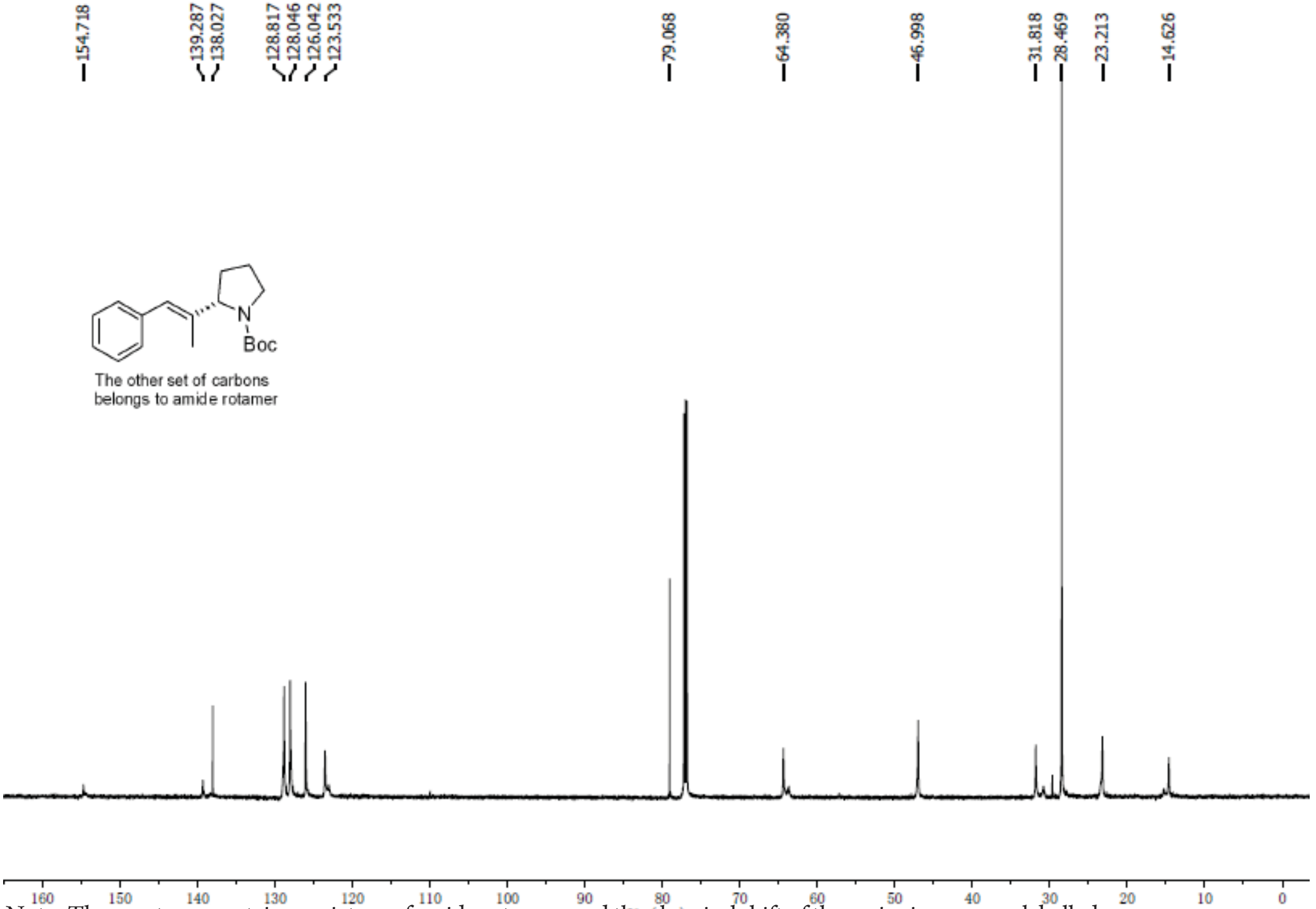
Peak#	Ret. Time	Area	Area%
1	9.252	43687490	96.398
2	10.358	1632597	3.602
Total		45320087	100.000

tert-butyl (*S*,*E*)-2-(1-phenylprop-1-en-2-yl)pyrrolidine-1-carboxylate 2l



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*,*E*)-2-(1-phenylprop-1-en-2-yl)pyrrolidine-1-carboxylate 2l



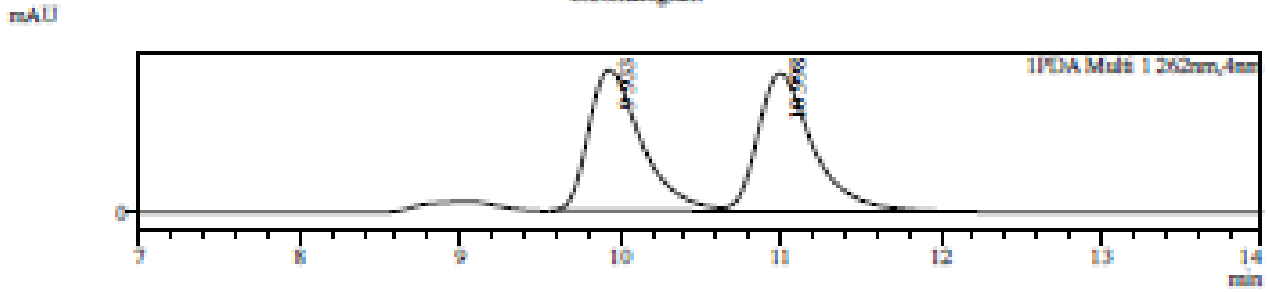
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*,*E*)-2-(1-phenylprop-1-en-2-yl)pyrrolidine-1-carboxylate 2l

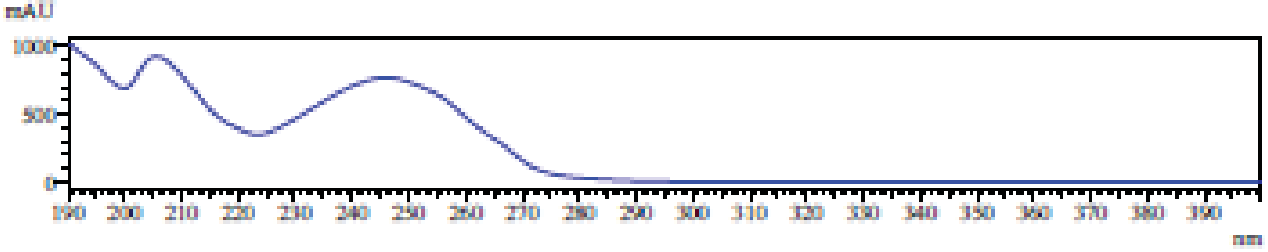
Sample Information

Sample Name	: YW-IV-122a-ADH-1%-0.8ML
Sample ID	: YW-IV-122a-ADH-1%-0.8ML
Data File	: YW-IV-122a-ADH-1%-0.8ML.lcd
Method File	: YW-1%-0.8ml.lcm

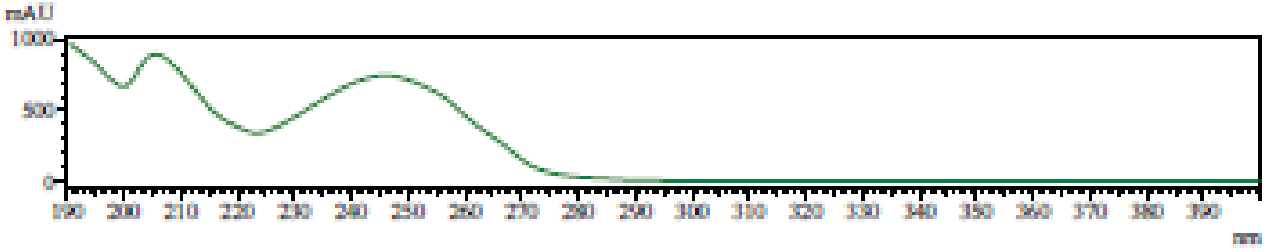
Chromatogram



UV Spectrum
Retention time = 9.933



UV Spectrum
Retention time = 10.998



Peak Table

PDA Ch1 262nm

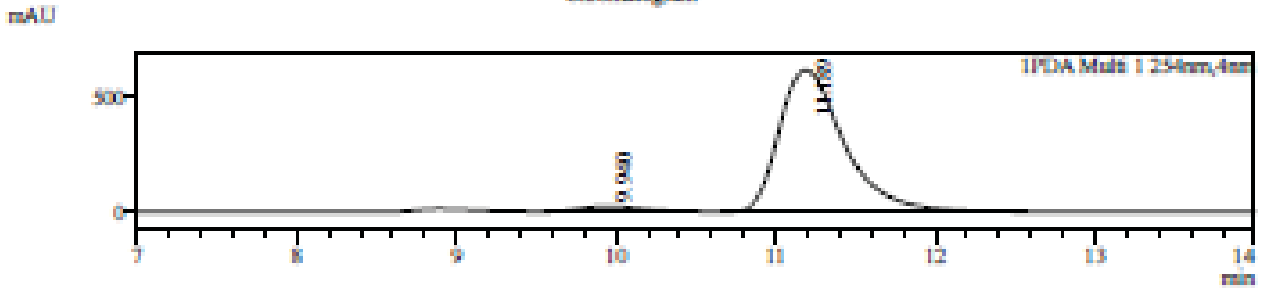
Peak#	Ret. Time	Area	Area%
1	9.933	9286580	49.505
2	10.998	9472139	50.495
Total		18758720	100.000

tert-butyl (*S*,*E*)-2-(1-phenylprop-1-en-2-yl)pyrrolidine-1-carboxylate 2l

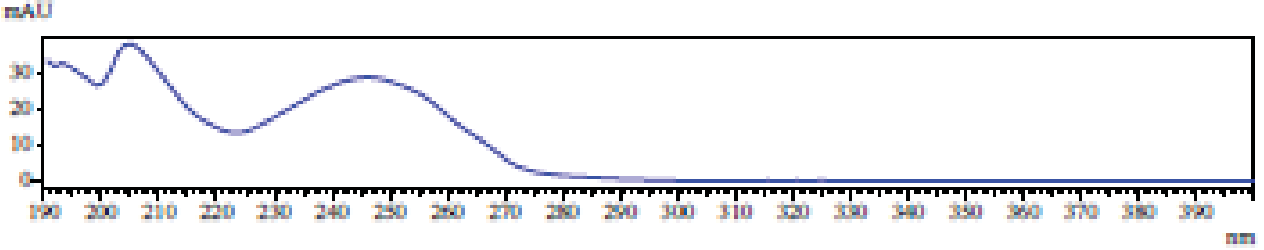
Sample Information

Sample Name	: YW-IV-122b-ADH-1%-0.8ML
Sample ID	: YW-IV-122b-ADH-1%-0.8ML
Data File	: YW-IV-122b-ADH-1%-0.8ML.lcd
Method File	: YW-1%-0.8ml.lcm

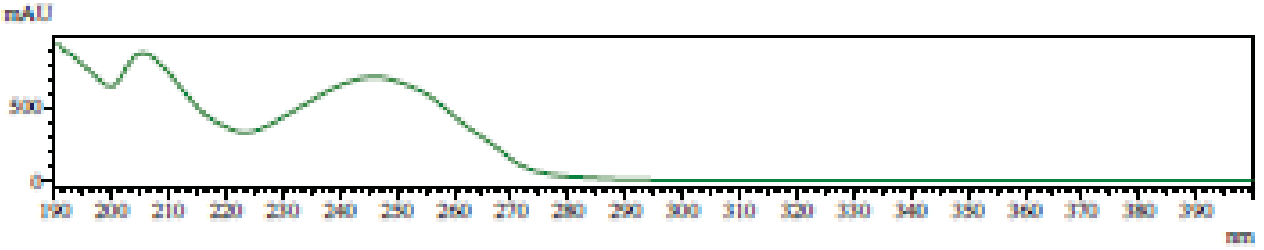
Chromatogram



UV Spectrum
Retention time = 9.940



UV Spectrum
Retention time = 11.189

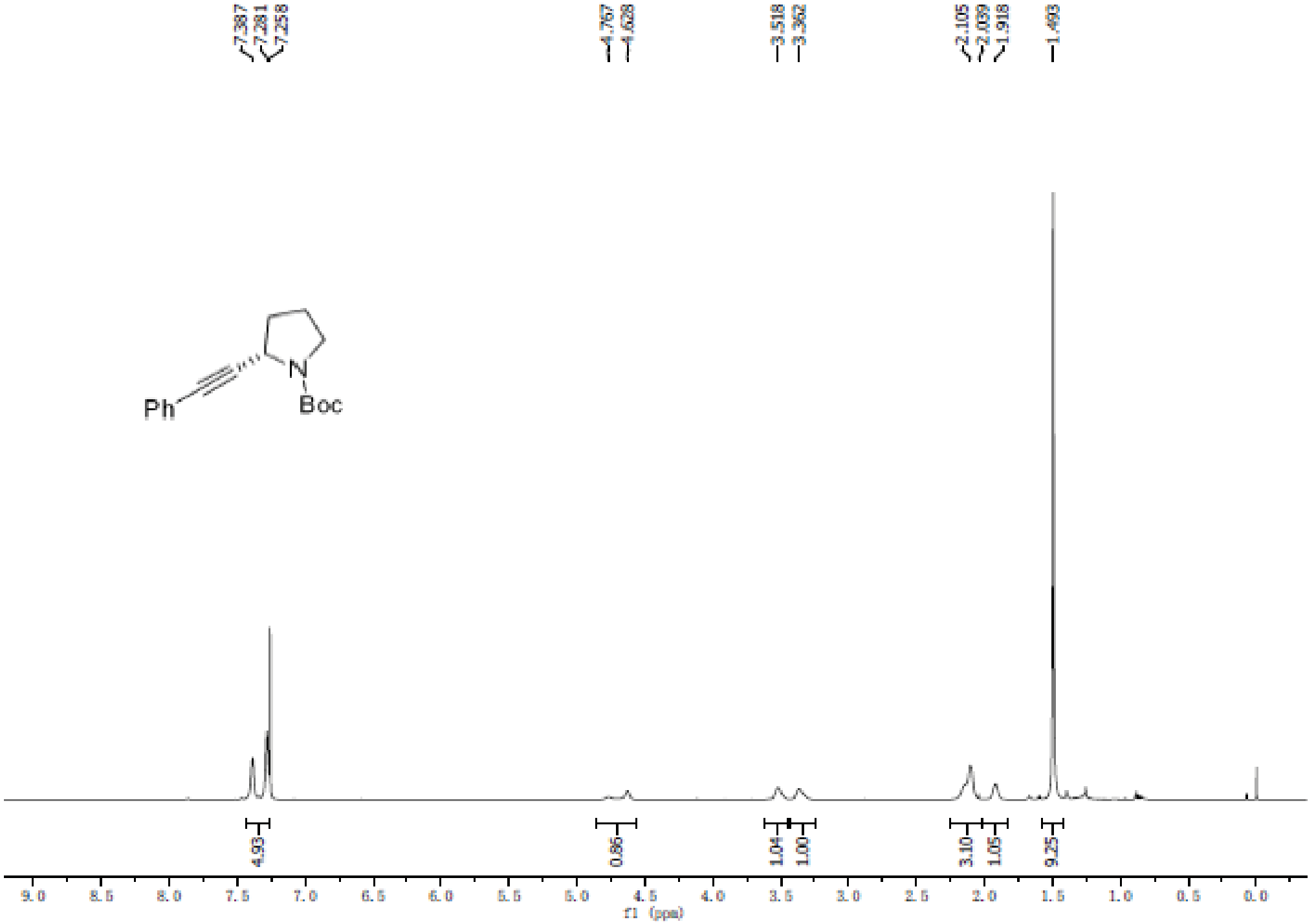


Peak Table

PDA Ch1 254nm

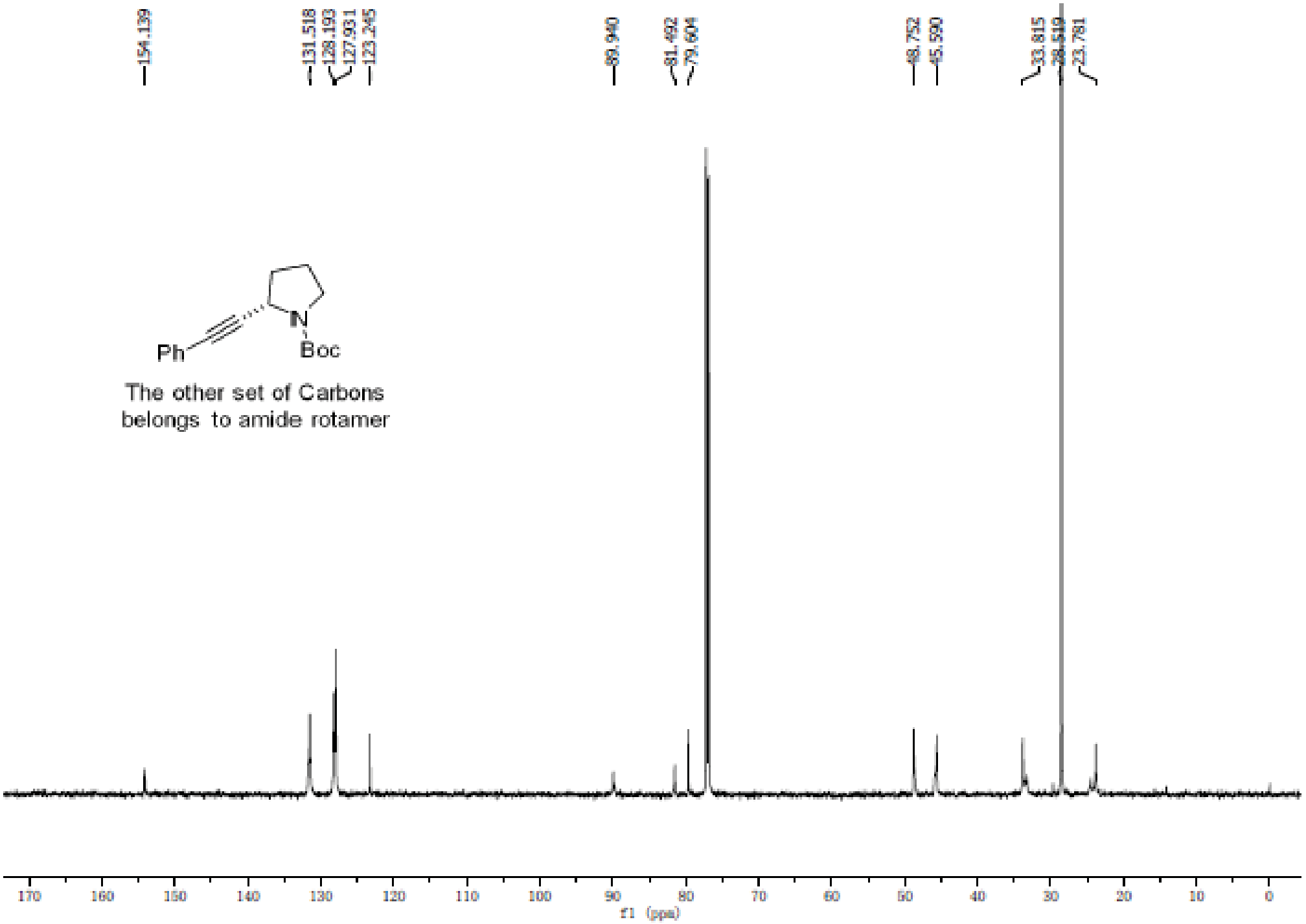
Peak#	Ret. Time	Area	Area%
1	9.940	550651	3.076
2	11.189	17352179	96.924
Total		17902831	100.000

tert-butyl (*S*)-2-phenethylpyrrolidine-1-carboxylate 2m



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-phenethylpyrrolidine-1-carboxylate 2m



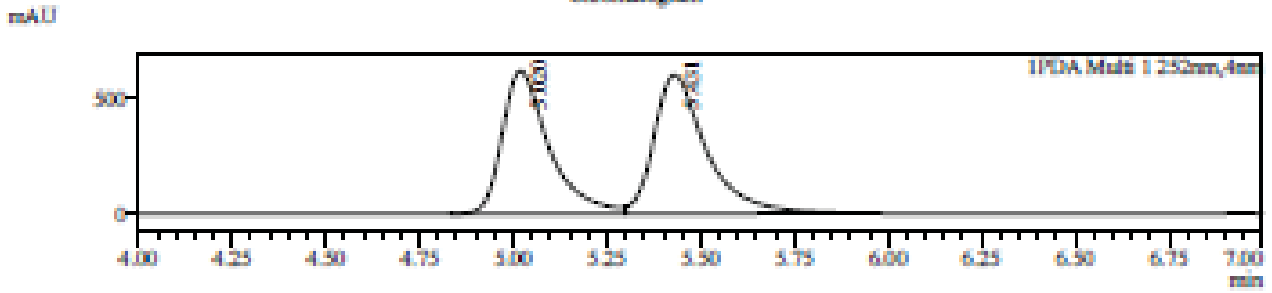
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-phenethylpyrrolidine-1-carboxylate 2m

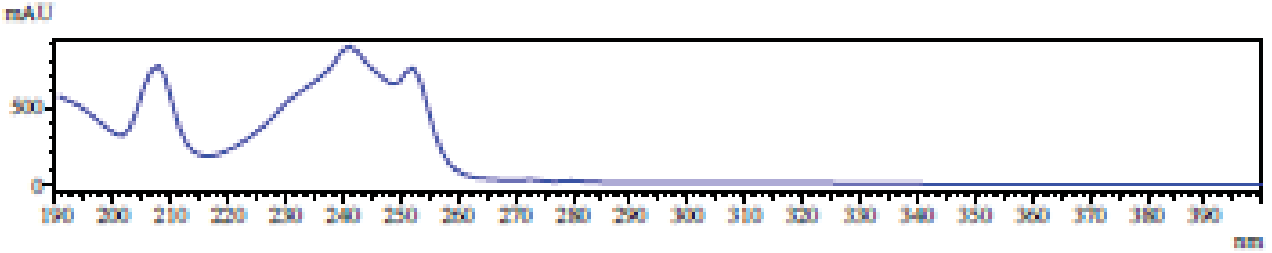
Sample Information

Sample Name	: YW-IV-137a-ADH-5%-1ML
Sample ID	: YW-IV-137a-ADH-5%-1ML
Data File	: YW-IV-137a-ADH-5%-1ML001.lcd
Method File	: YW-5.0%-1.0ml.lcm

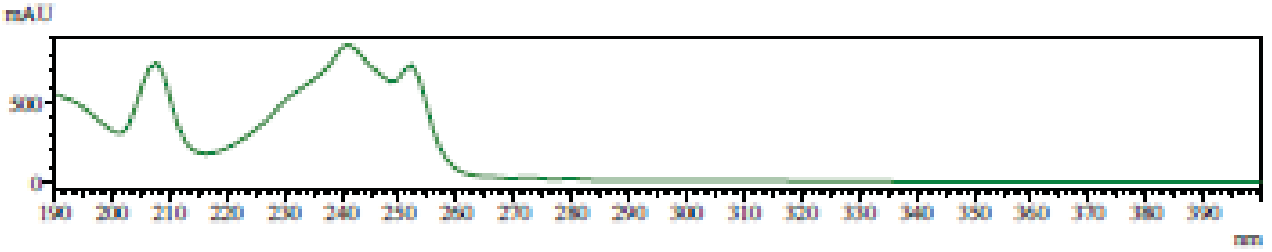
Chromatogram



UV Spectrum
Retention time = 5.020



UV Spectrum
Retention time = 5.431



Peak Table

PDA Ch1 252nm

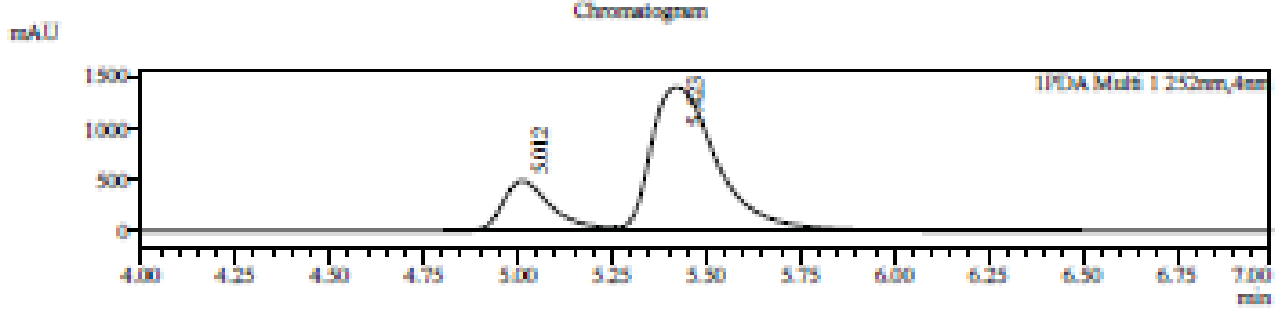
Peak#	Ret. Time	Area	Area%
1	5.020	5369381	48.095
2	5.431	5794662	51.905
Total		11164043	100.000

tert-butyl (*S*)-2-phenethylpyrrolidine-1-carboxylate 2m

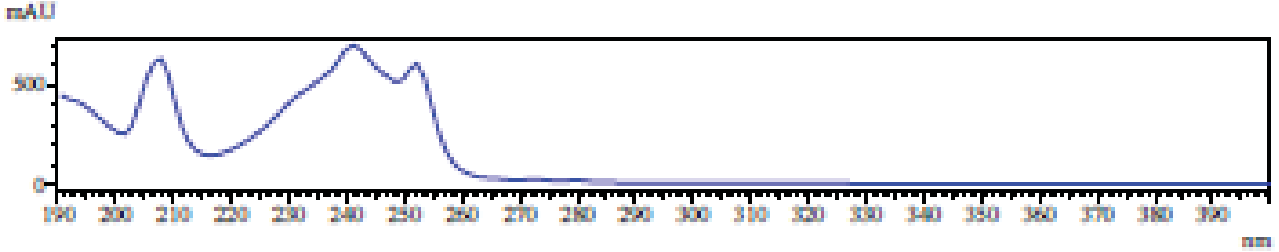
Sample Information

Sample Name	: YW-IV-137b-ADH-5%-1ML
Sample ID	: YW-IV-137b-ADH-5%-1ML
Data File	: YW-IV-137b-ADH-5%-1ML.lcd
Method File	: YW-5.0%-1.0ml.lcm

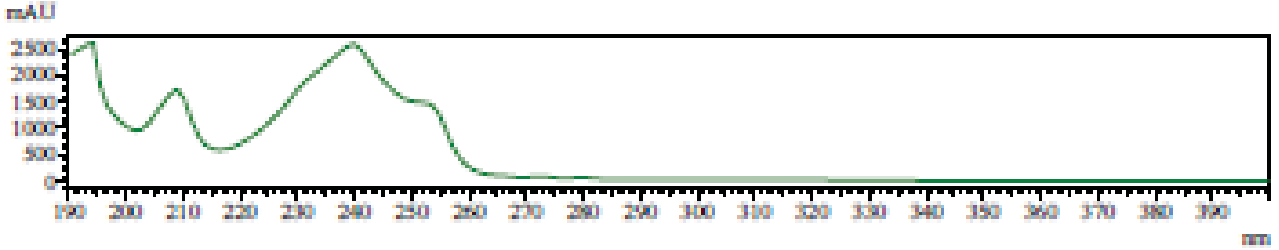
Chromatogram



UV Spectrum
Retention time = 5.012



UV Spectrum
Retention time = 5.423

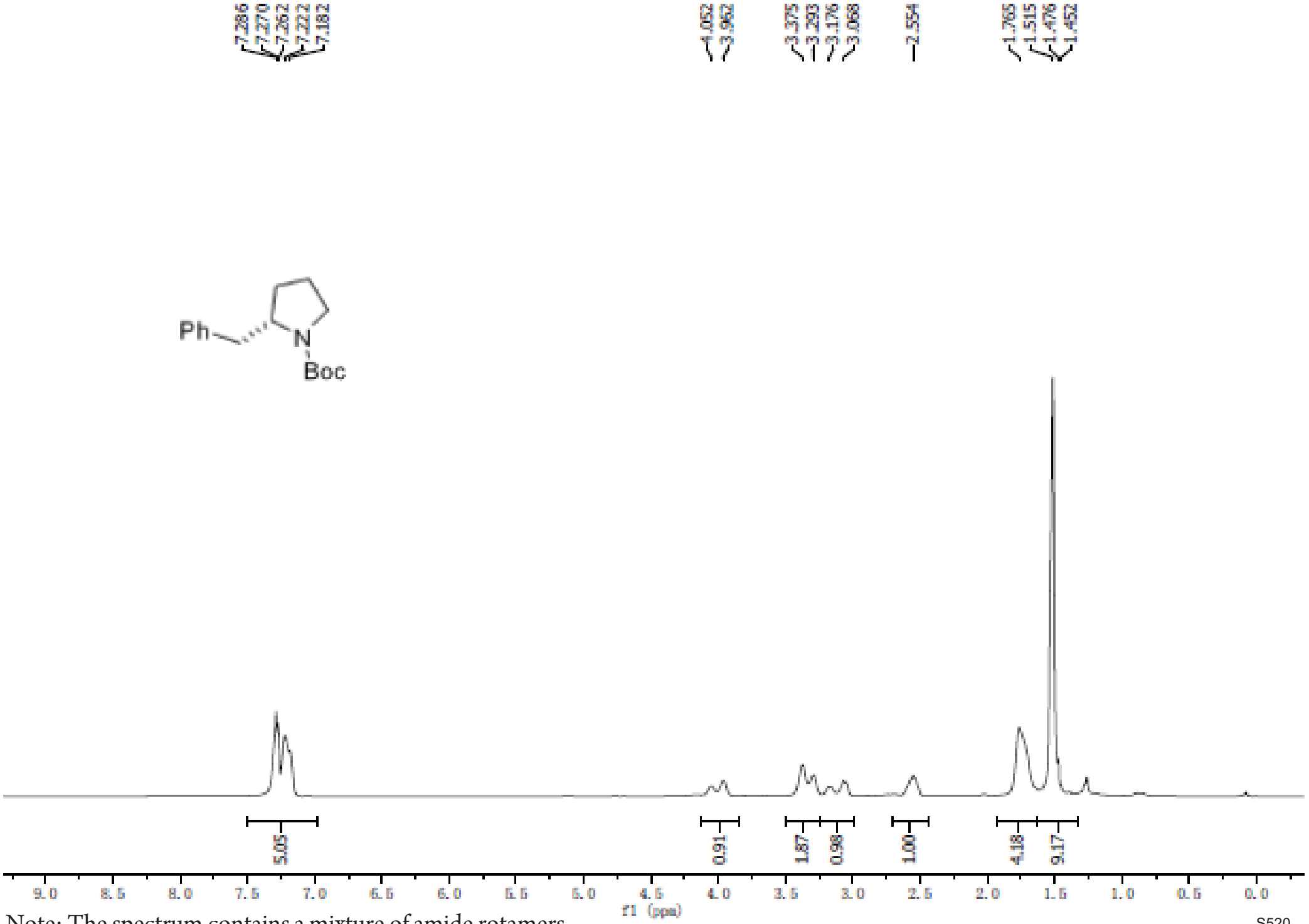


Peak Table

PDA Ch1 252nm

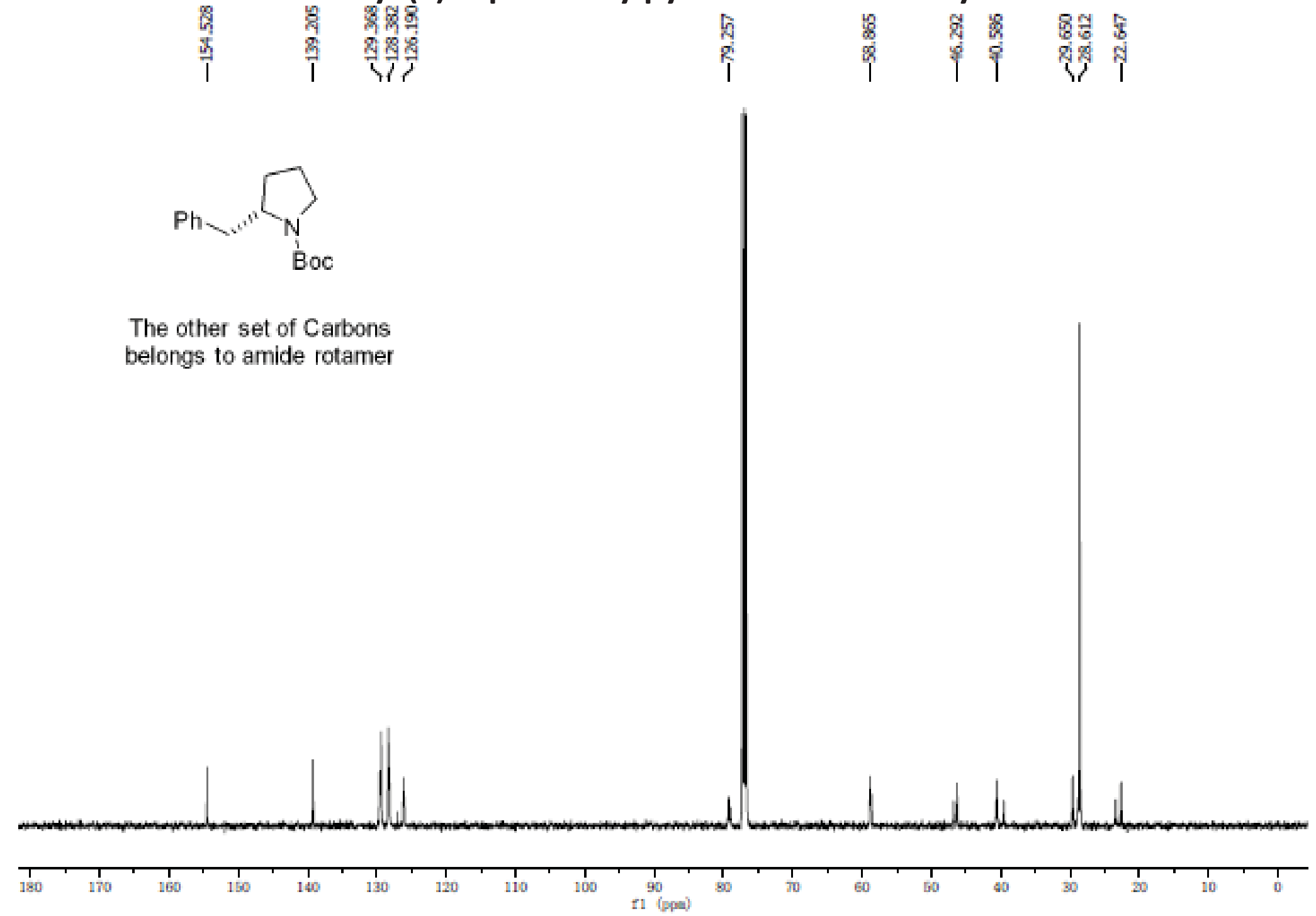
Peak#	Ret. Time	Area	Area%
1	5.012	4394186	20.526
2	5.423	17013445	79.474
Total		21407631	100.000

tert-butyl (*S*)-2-phenethylpyrrolidine-1-carboxylate 2n



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-phenethylpyrrolidine-1-carboxylate 2n



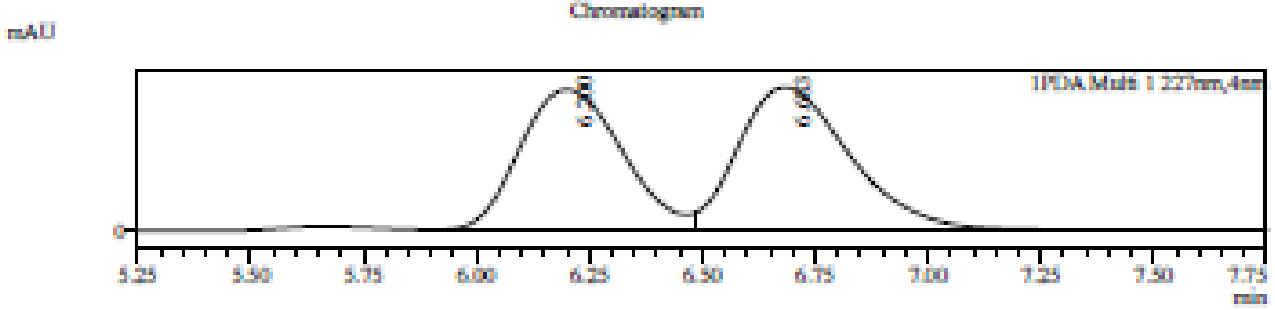
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-phenethylpyrrolidine-1-carboxylate 2n

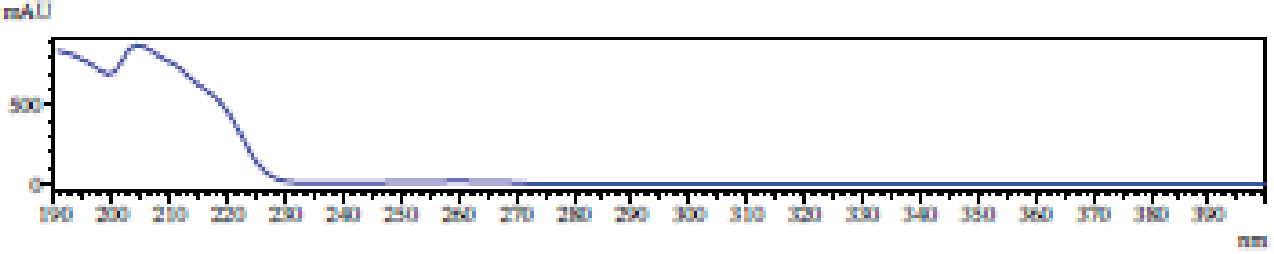
Sample Information

Sample Name	: YW-IV-16a-ODH1-1%-1ML003
Sample ID	: YW-IV-16a-ODH1-1%-1ML003
Data File	: YW-IV-16a-ODH1-1%-1ML003.lcd
Method File	: YW-1%-1.0ml.lcm

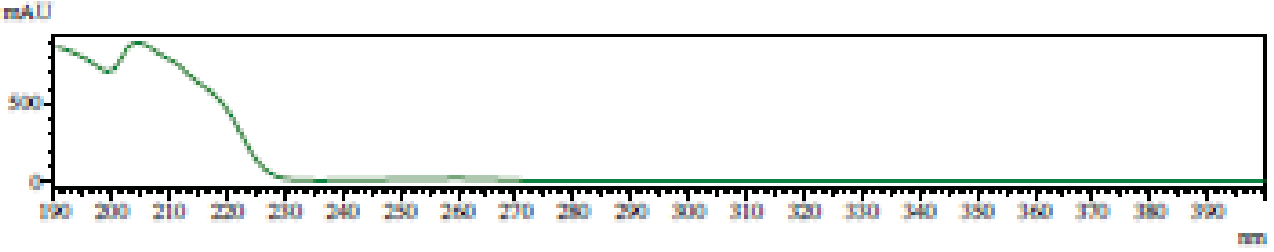
Chromatogram



UV Spectrum
Retention time = 6.200



UV Spectrum
Retention time = 6.683



Peak Table

PDA Ch1 227nm

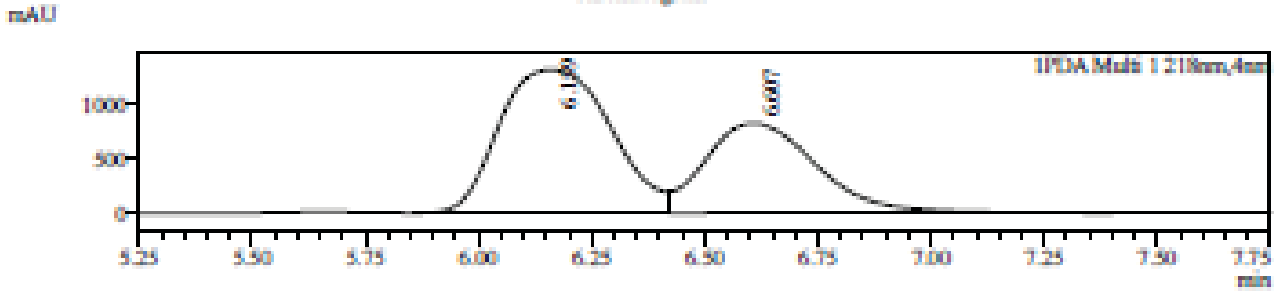
Peak#	Ret. Time	Area	Area%
1	6.200	1364023	47.554
2	6.683	1504344	52.446
Total		2868368	100.000

tert-butyl (*S*)-2-phenethylpyrrolidine-1-carboxylate 2n

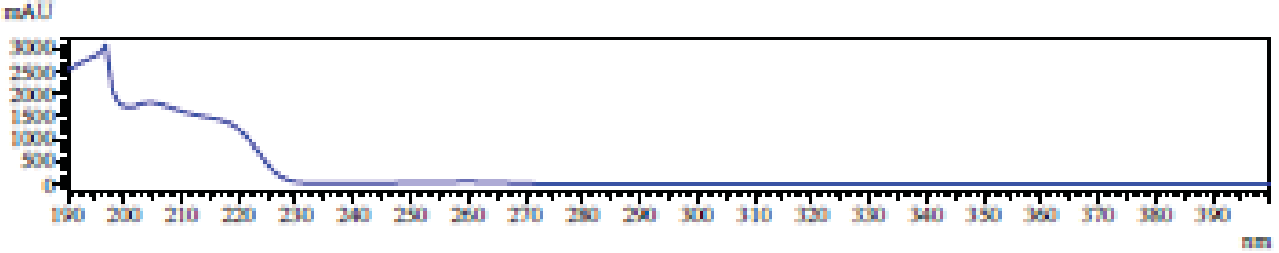
Sample Information

Sample Name	: YW-IV-16b-ODH-1%-1ML003
Sample ID	: YW-IV-16b-ODH-1%-1ML003
Data File	: YW-IV-16b-ODH-1%-1ML005.lcd
Method File	: YW-1%-1.0ml.lcm

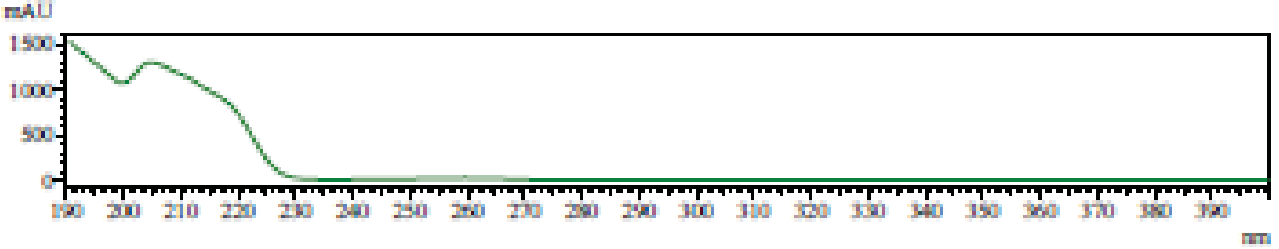
Chromatogram



UV Spectrum
Retention time = 6.159



UV Spectrum
Retention time = 6.607

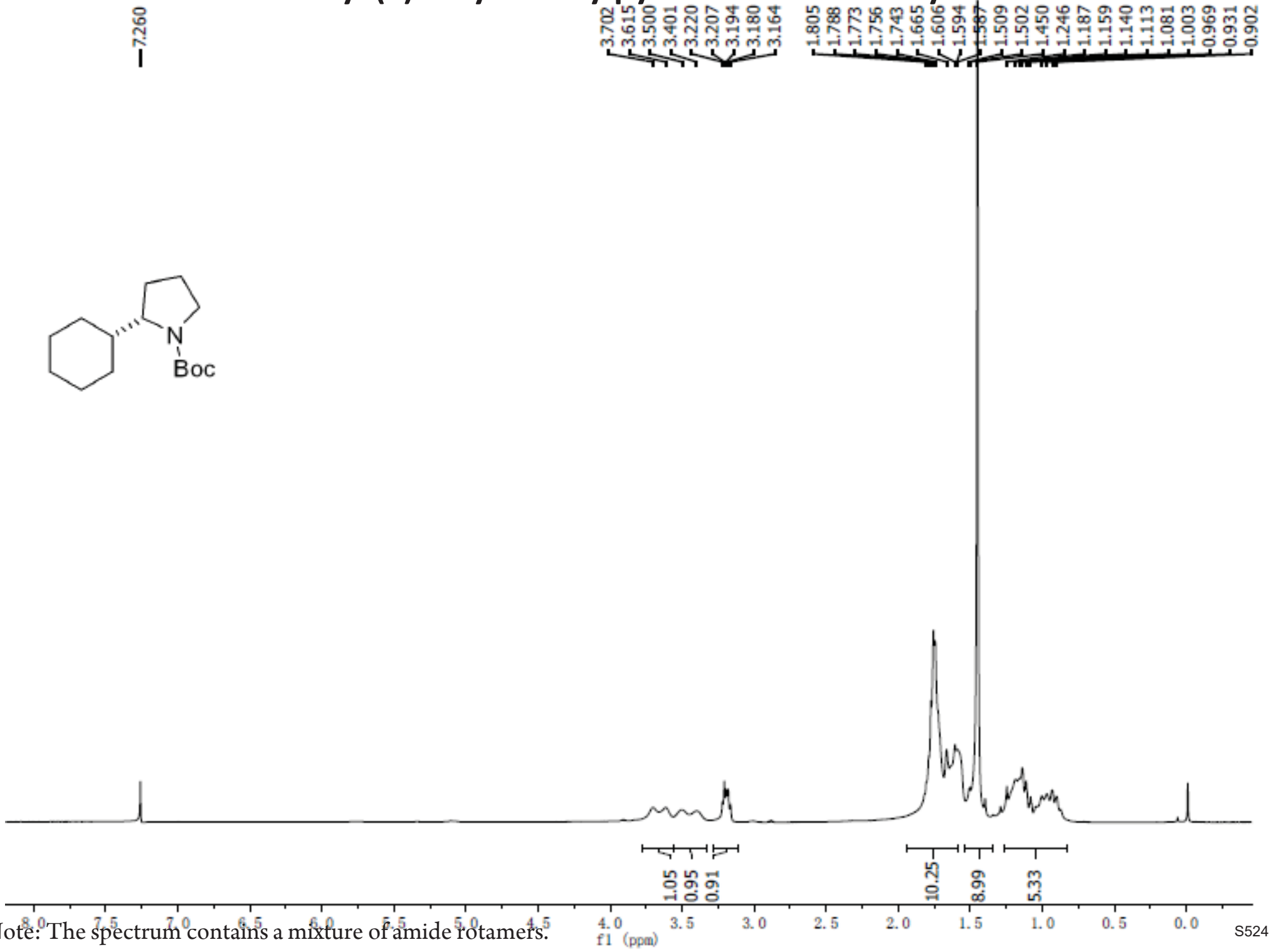


Peak Table

PDA Ch1 218nm

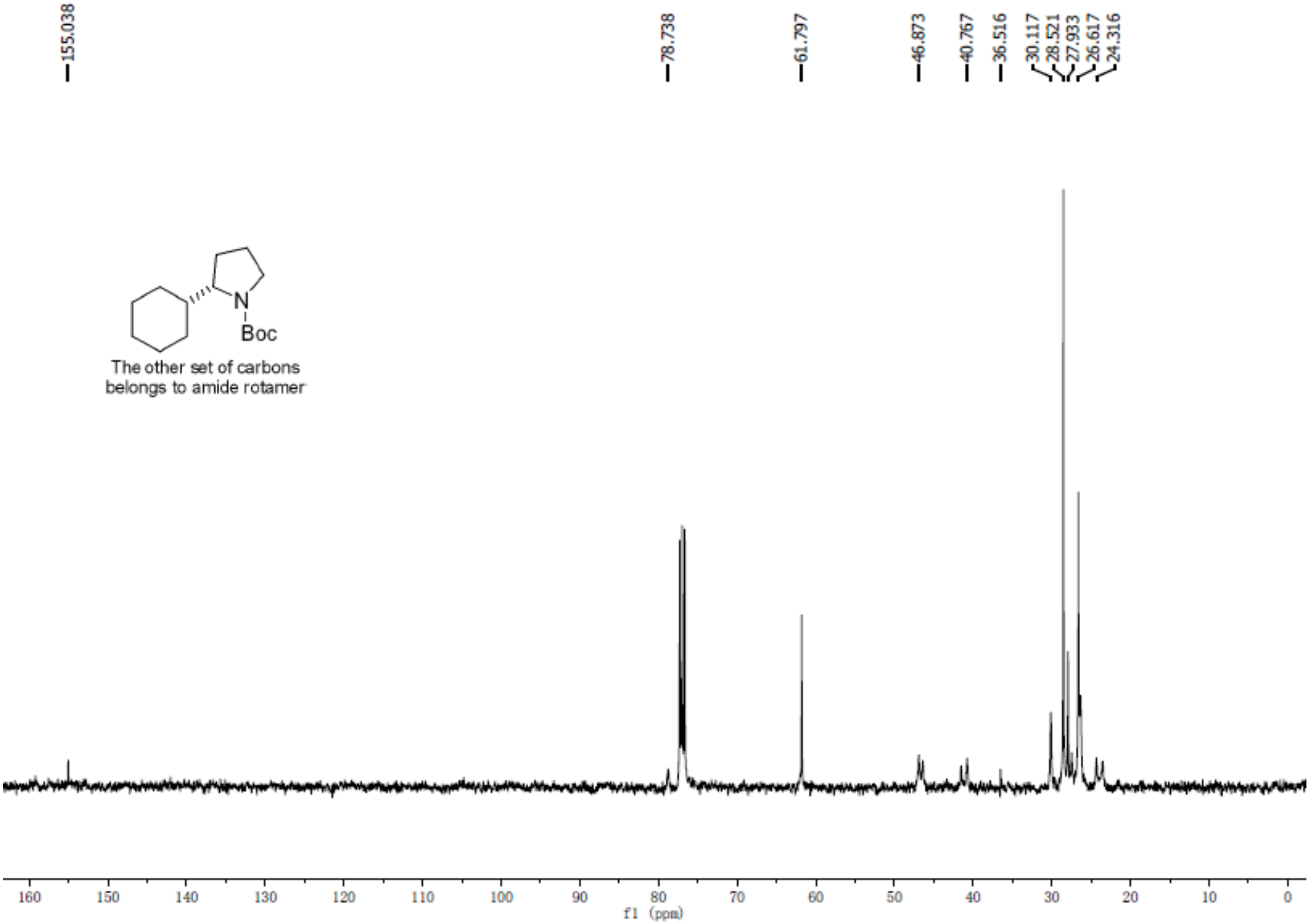
Peak#	Ret. Time	Area	Area%
1	6.159	22513129	61.646
2	6.607	14007089	38.354
Total		36520218	100.000

tert-butyl (S)-2-cyclohexylpyrrolidine-1-carboxylate 2o



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (S)-2-cyclohexylpyrrolidine-1-carboxylate 2o



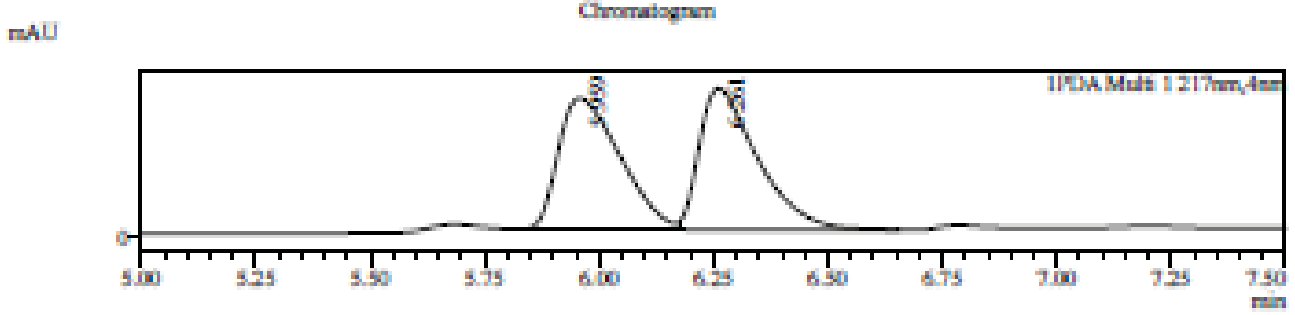
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (S)-2-cyclohexylpyrrolidine-1-carboxylate 2o

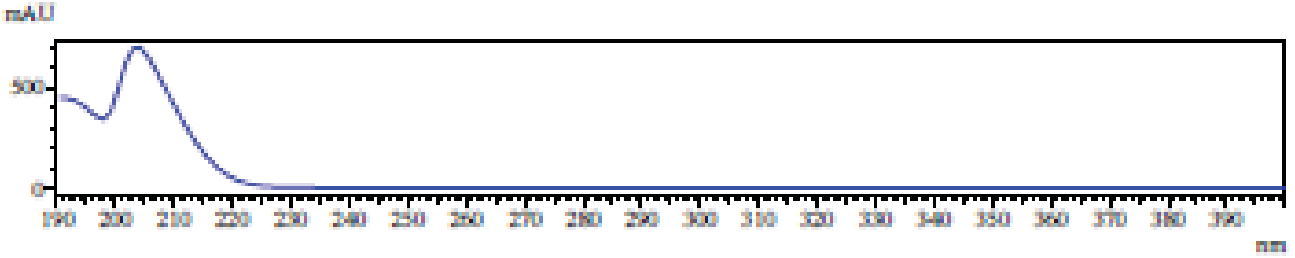
Sample Information

Sample Name	: YW-IV-112A-ADH-0.5%-1ML
Sample ID	: YW-IV-112A-ADH-0.5%-1ML
Data File	: YW-IV-112A-ADH-0.5%-1ML.lcd
Method File	: YW-0.5%-1.0ml.lcm

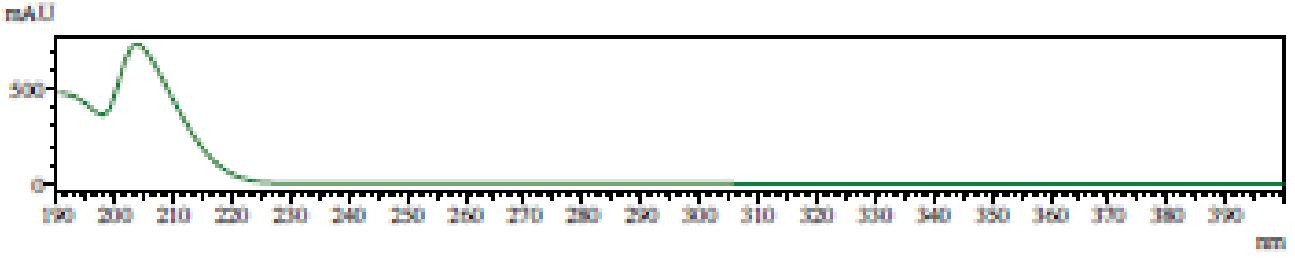
Chromatogram



UV Spectrum
Retention time = 5.959



UV Spectrum
Retention time = 6.261



Peak Table

PDA Ch1 217nm

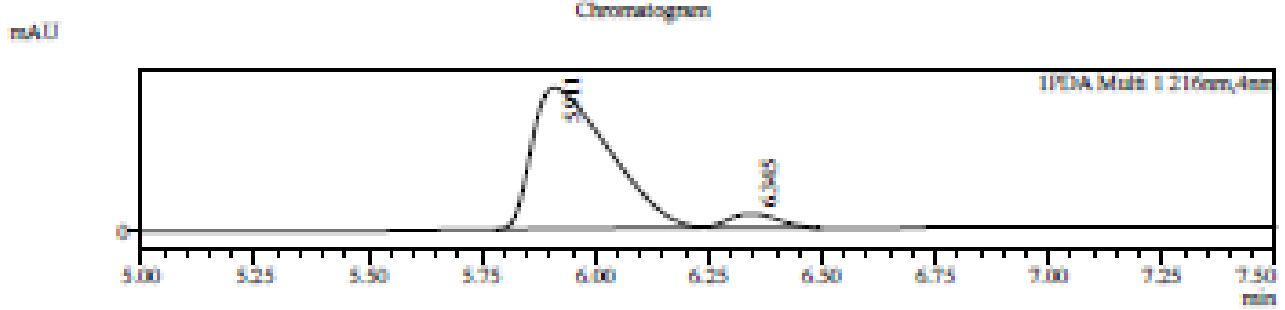
Peak#	Ret. Time	Area	Area%
1	5.959	1079166	49.544
2	6.261	1099033	50.456
Total		2178198	100.000

tert-butyl (S)-2-cyclohexylpyrrolidine-1-carboxylate 2o

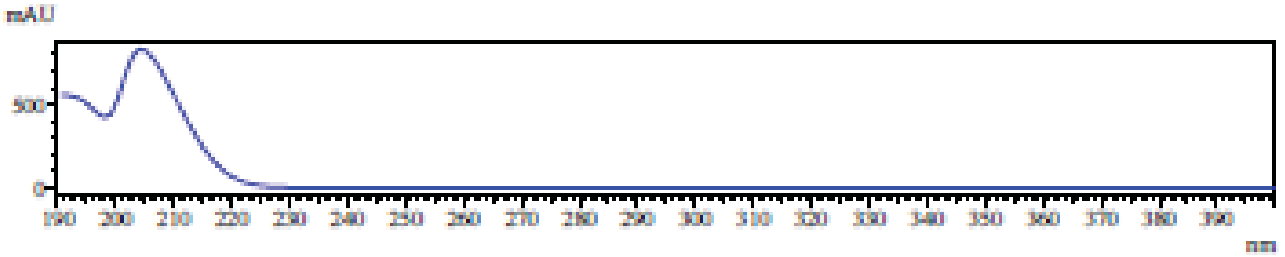
Sample Information

Sample Name	: YW-IV-112B-ADH-0.5%-1ML001
Sample ID	: YW-IV-112B-ADH-0.5%-1ML001
Data File	: YW-IV-112B-ADH-0.5%-1ML001.lcd
Method File	: YW-0.5%-1.0ml.lcm

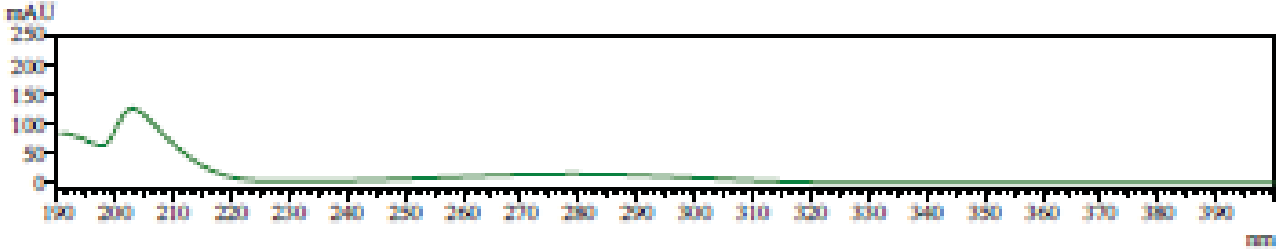
Chromatogram



UV Spectrum
Retention time = 5.911



UV Spectrum
Retention time = 6.345

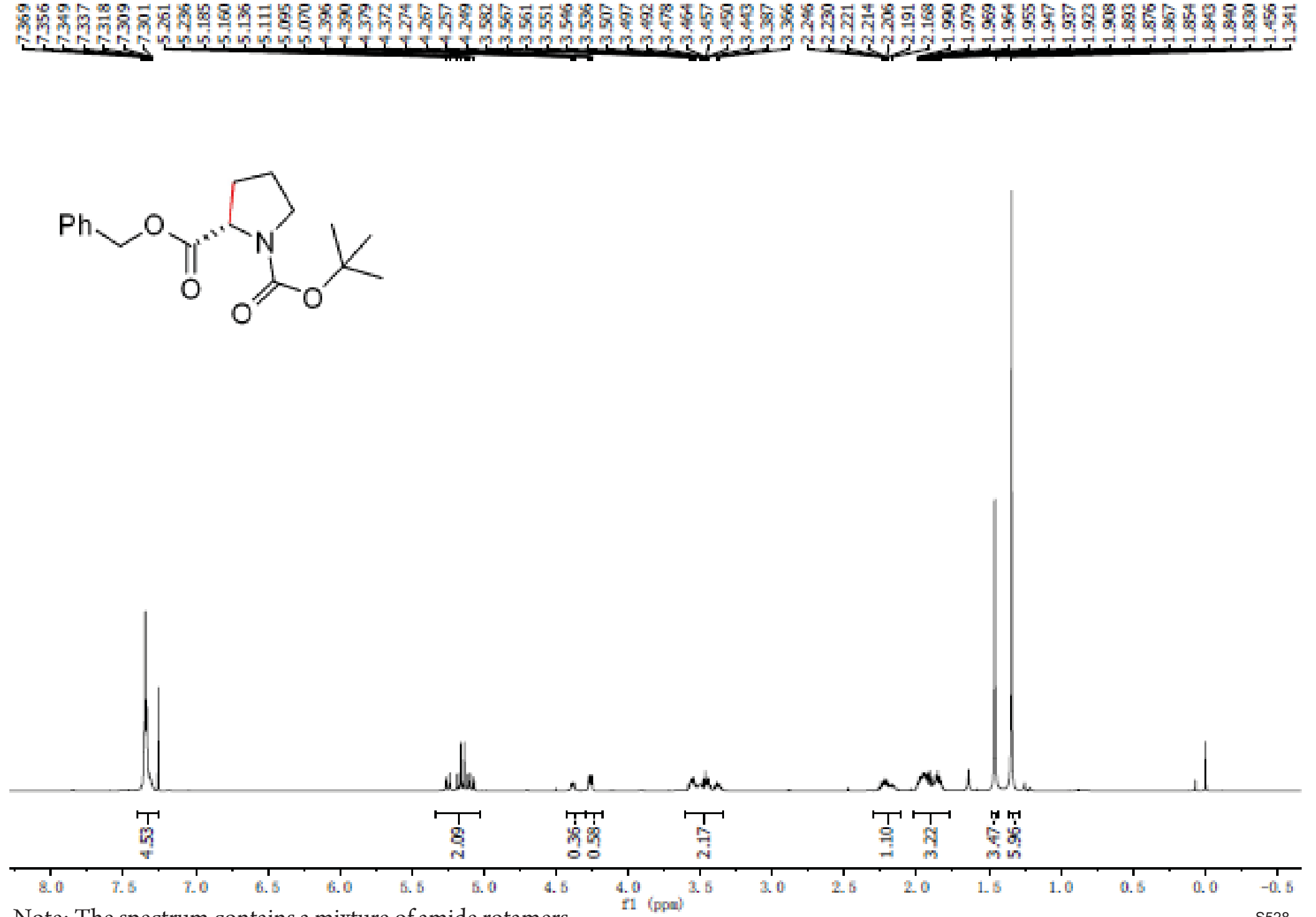


Peak Table

PDA Ch1 216nm

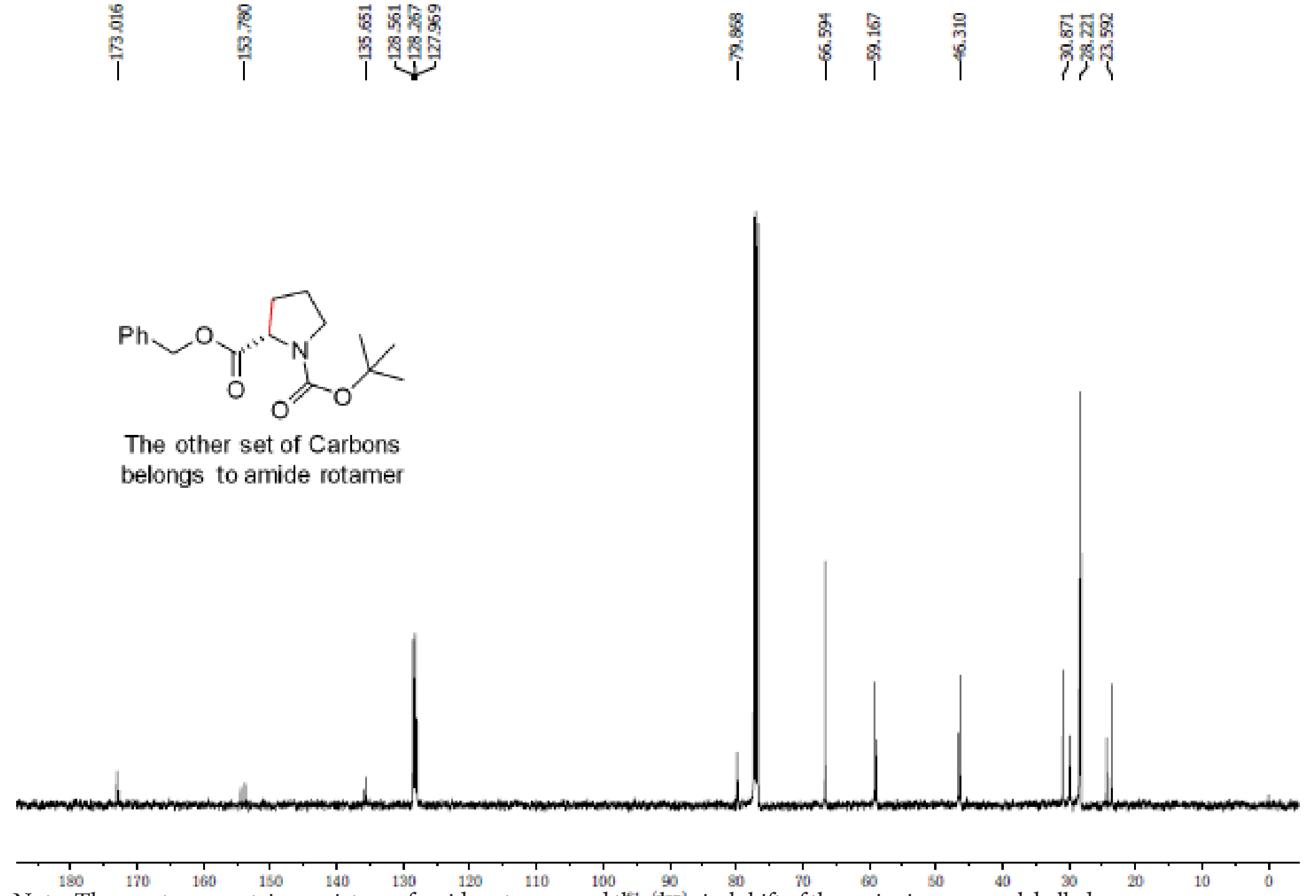
Peak#	Ret. Time	Area	Area%
1	5.911	2534681	94.126
2	6.345	158166	5.874
Total		2692847	100.000

2-benzyl 1-(*tert*-butyl) (*S*)-pyrrolidine-1,2-dicarboxylate 2p



Note: The spectrum contains a mixture of amide rotamers.

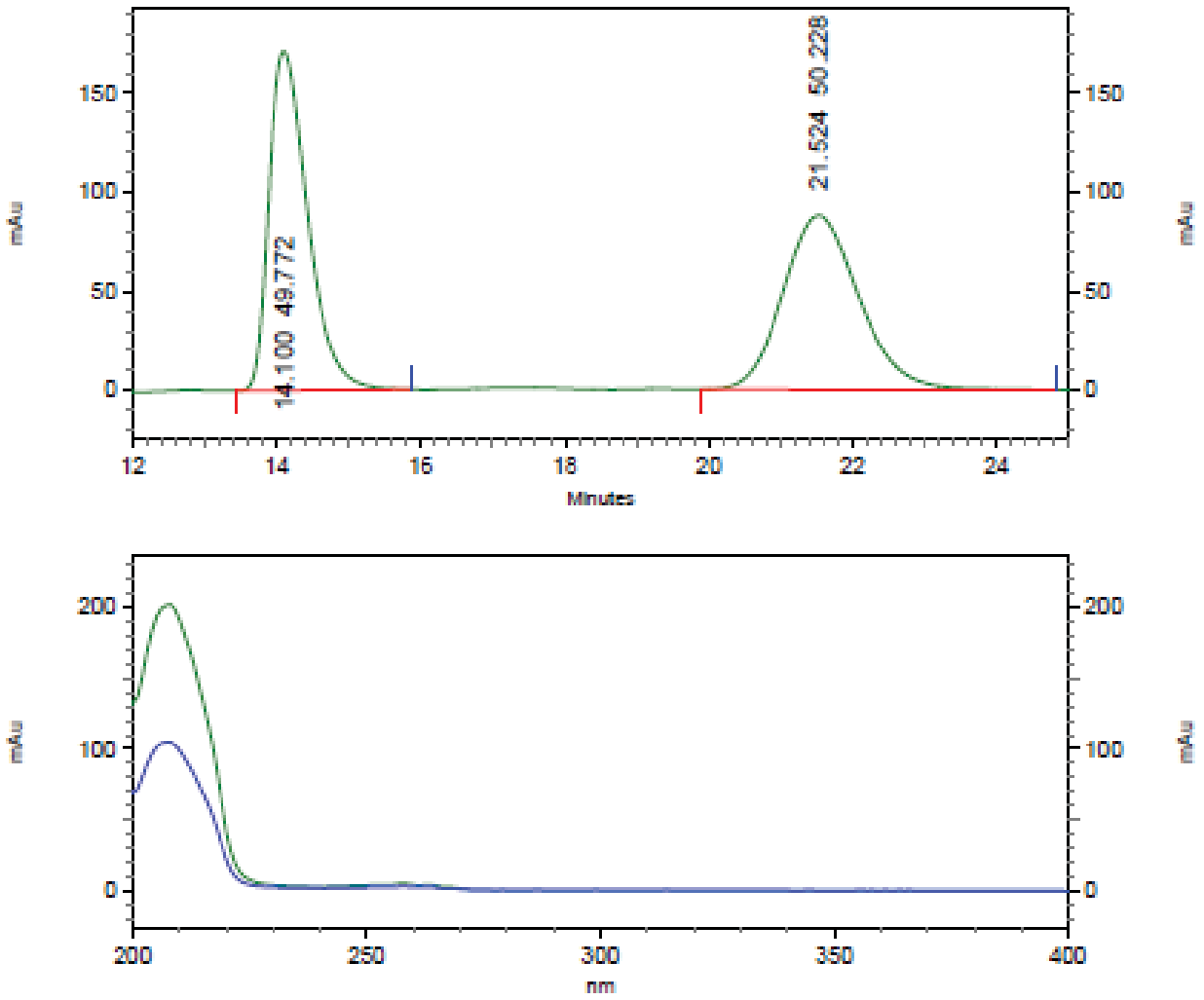
2-benzyl 1-(*tert*-butyl) (*S*)-pyrrolidine-1,2-dicarboxylate 2p



Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

2-benzyl 1-(*tert*-butyl) (*S*)-pyrrolidine-1,2-dicarboxylate 2p

C:\EZStart\Projects\Default\Data\YW-0480-ADH-3%-0.8mL-iPrOH-1
C:\Documents and Settings\zhang\Desktop\DSW\0404.met

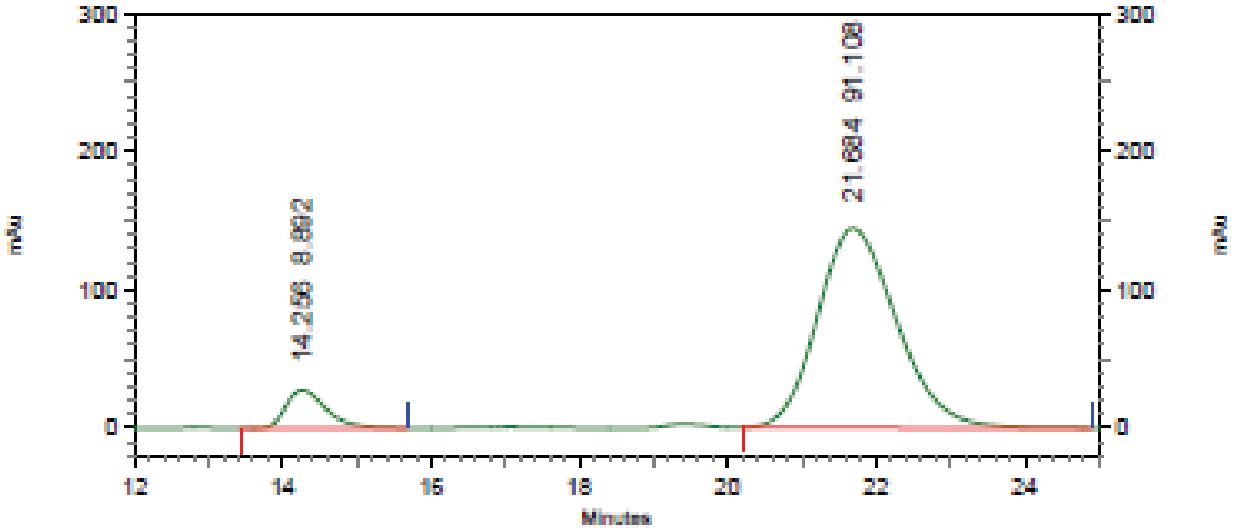


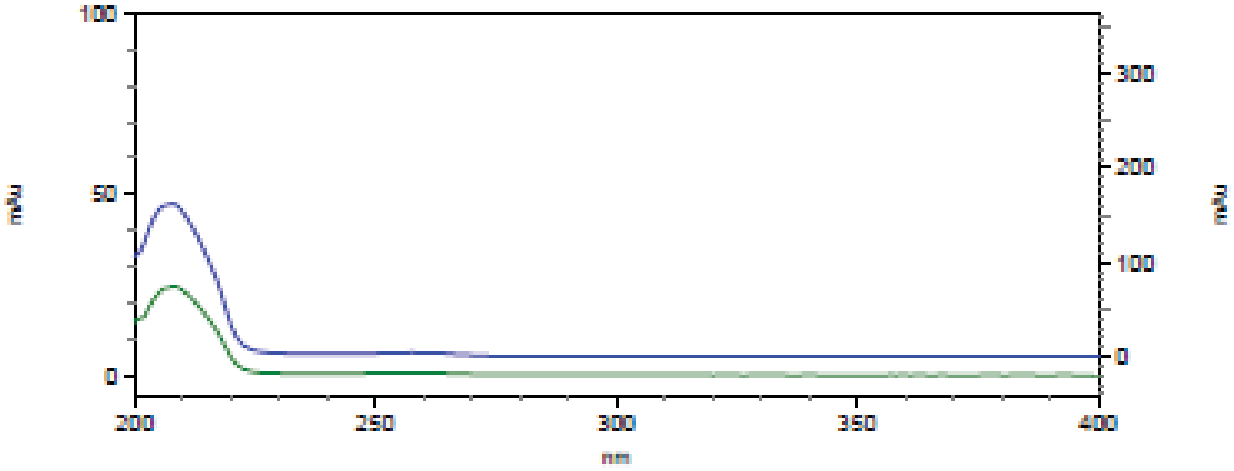
4: 212 nm, 4
nm Results

Pk #	Retention Time	Area Percent
1	14.100	49.772
2	21.524	50.228
Totals		100.000

2-benzyl 1-(*tert*-butyl) (*S*)-pyrrolidine-1,2-dicarboxylate 2p

C:\EZStart\Projects\Default\Data\YW-0481-ADH-3#-0.6mL-iPrOH
C:\Documents and Settings\zhang\Desktop\DSW\0404.met

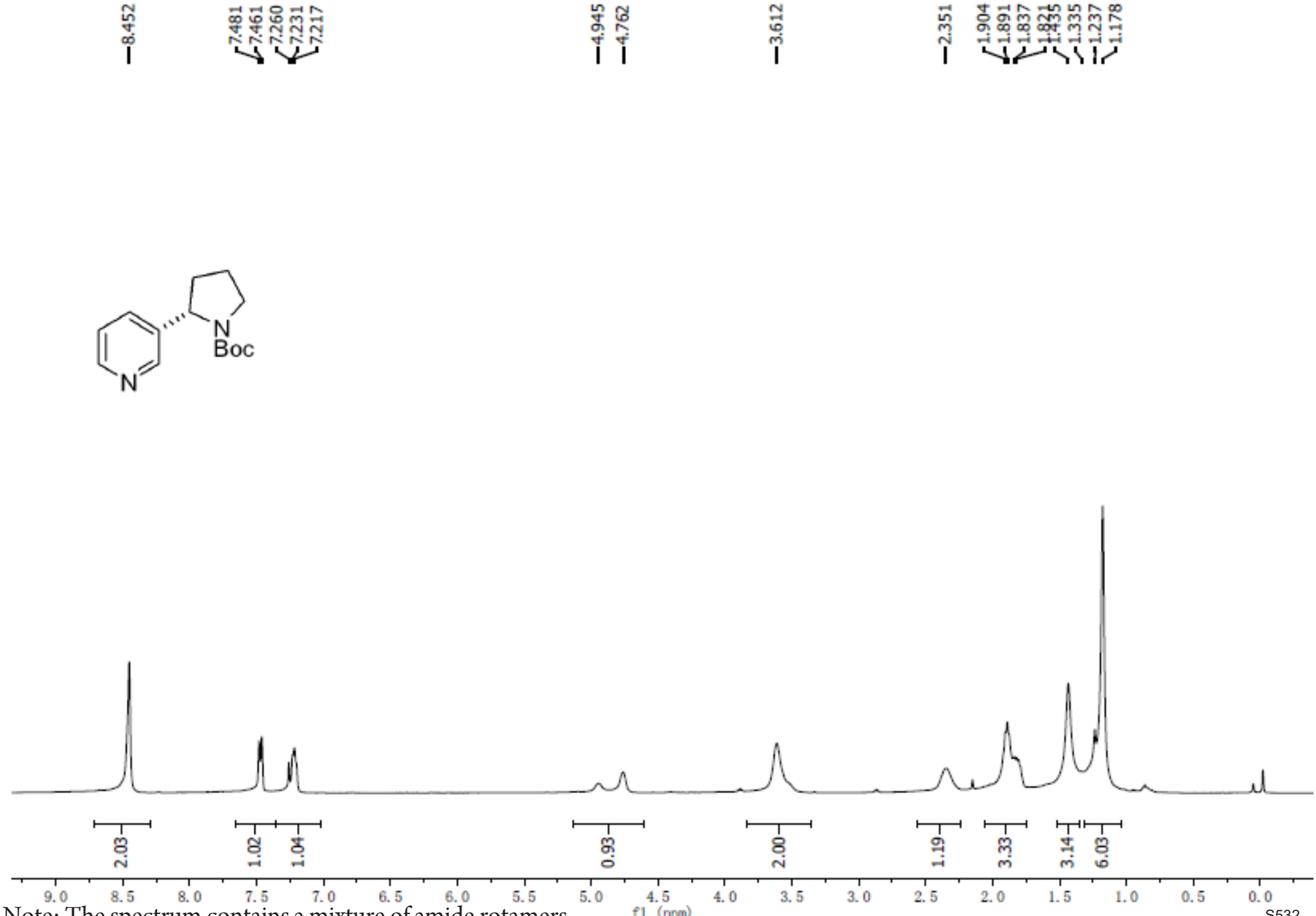




4: 212 nm, 4
nm Results

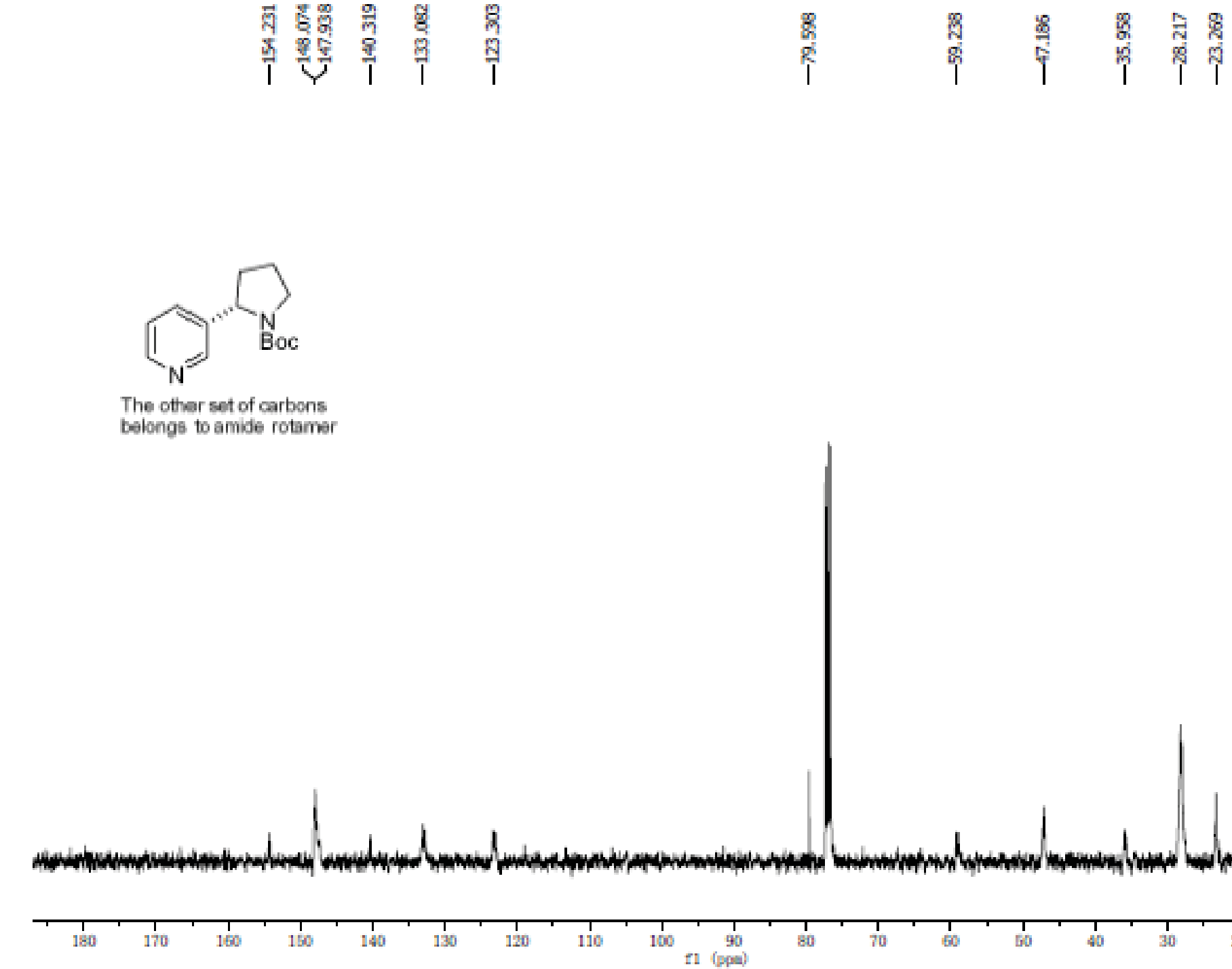
Pk #	Retention Time	Area Percent
1	14.256	8.892
2	21.684	91.108
Totals		100.000

tert-butyl (*S*)-2-(pyridin-3-yl)pyrrolidine-1-carboxylate 2q



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(pyridin-3-yl)pyrrolidine-1-carboxylate 2q



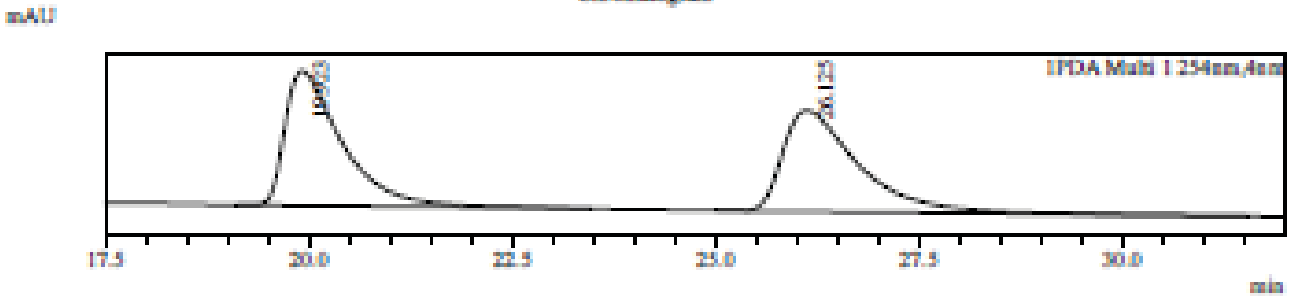
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(pyridin-3-yl)pyrrolidine-1-carboxylate 2q

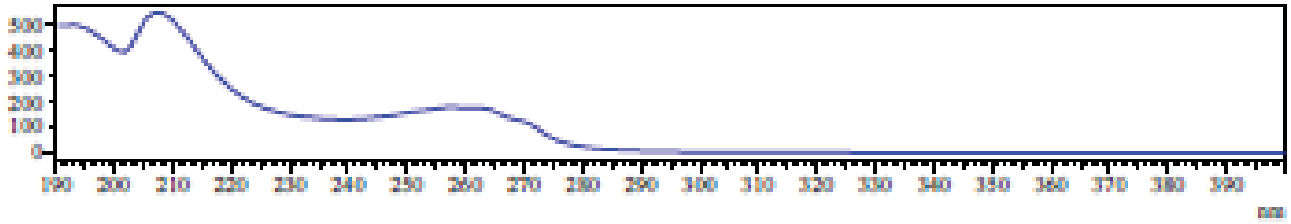
Sample Information

Data File	: YW-IV-111a-ADH-5%-1ML.lcd
Sample Name	: YW-IV-111a-ADH-5%-1ML
Sample ID	: YW-IV-111a-ADH-5%-1ML
Method File	: YW-5.0%-1.0ml.lcm

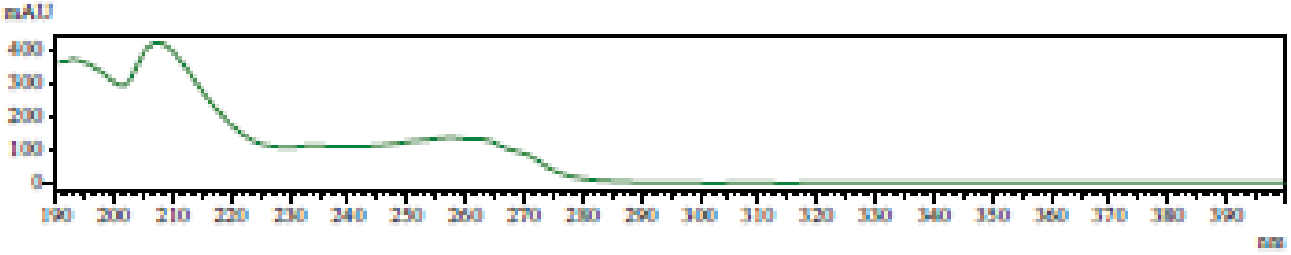
Chromatogram



UV Spectrum
Retention time = 19.923



UV Spectrum
Retention time = 26.125



Peak Table

PDA Ch1 254nm

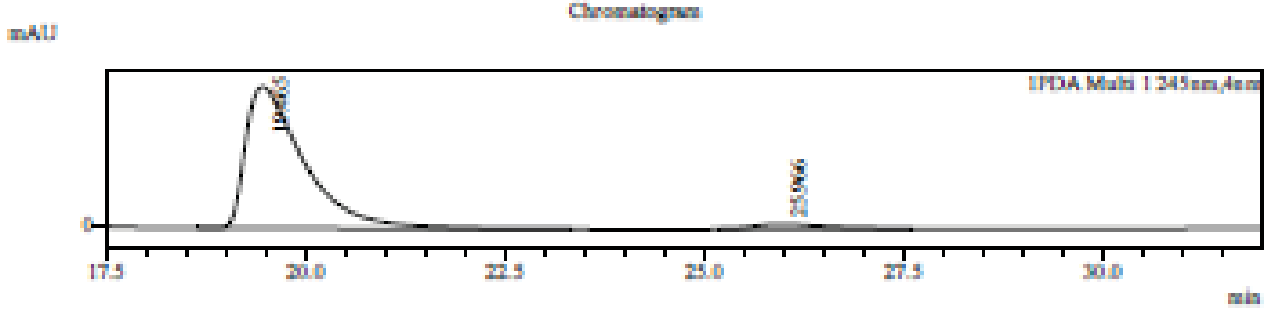
Peak#	Ret. Time	Area	Area%
1	19.923	6434525	50.006
2	26.125	6432964	49.994
Total		12867489	100.000

tert-butyl (*S*)-2-(pyridin-3-yl)pyrrolidine-1-carboxylate 2q

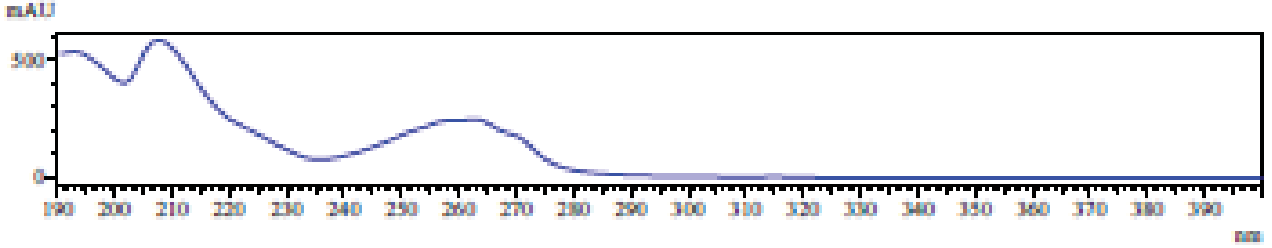
Sample Information

Data File	: YW-IV-111B-ADH-5%-1ML.lcd
Sample Name	: YW-IV-111B-ADH-5%-1ML
Sample ID	: YW-IV-111B-ADH-5%-1ML
Method File	: YW-5.0%-1.0ml.lcm

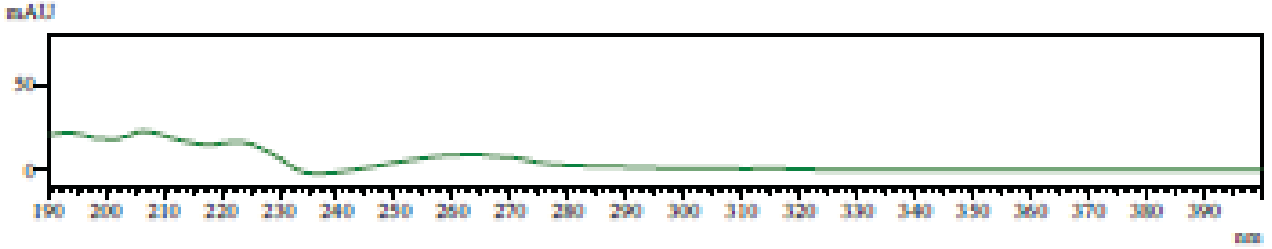
Chromatogram



UV Spectrum
Retention time = 19.465



UV Spectrum
Retention time = 25.966

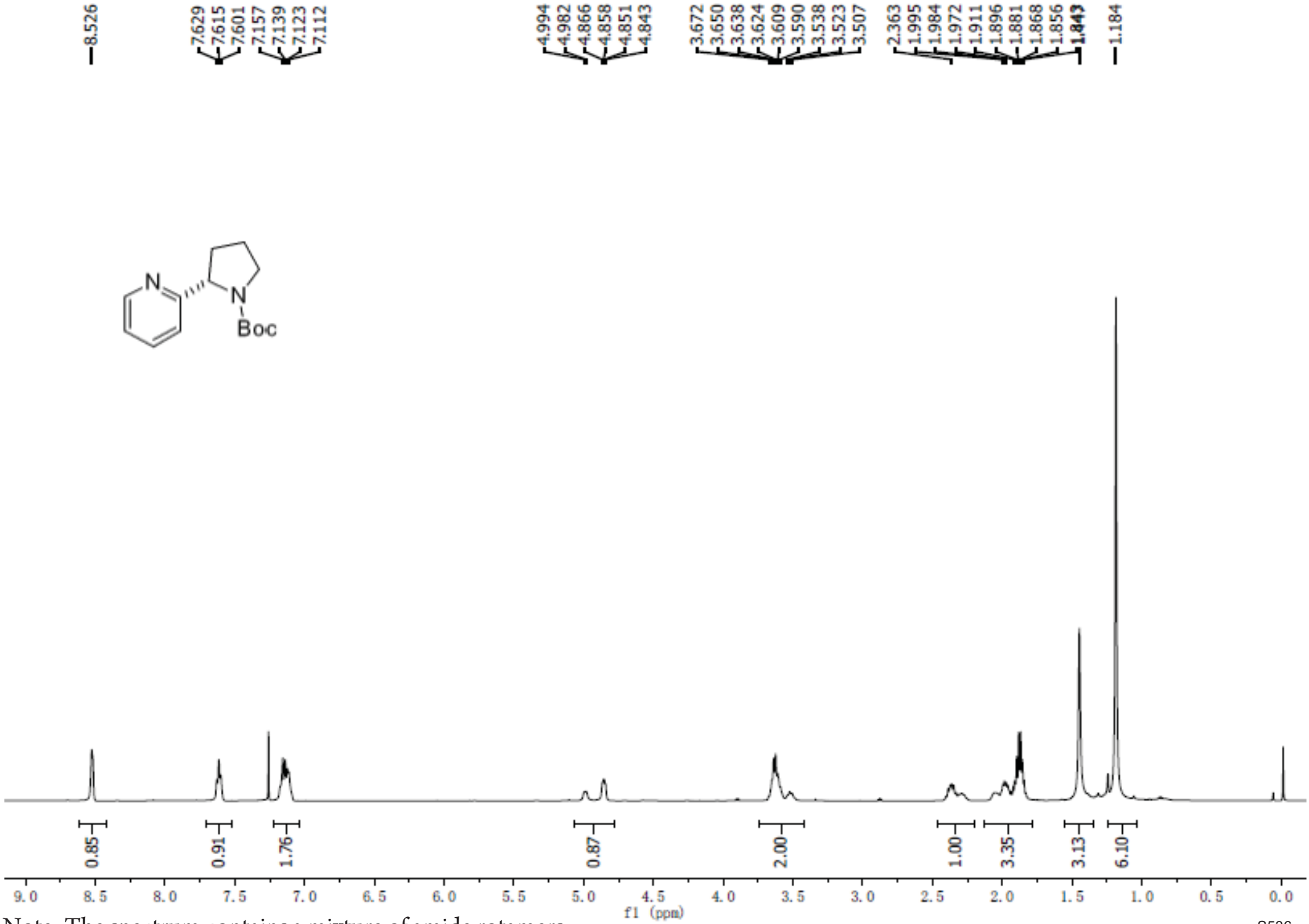


Peak Table

PDA Ch1 245nm

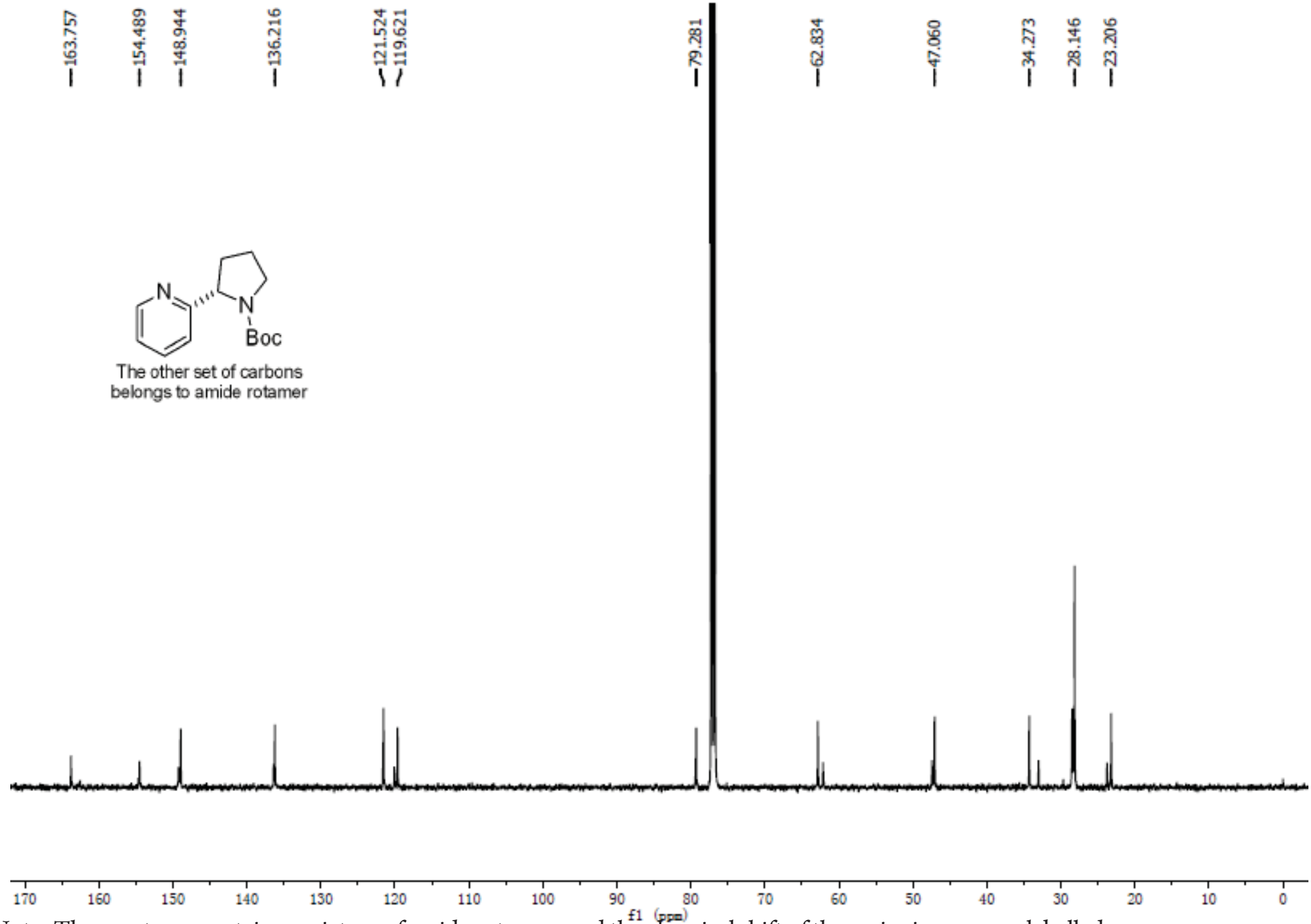
Peak#	Ret. Time	Area	Area%
1	19.465	6725777	96.117
2	25.966	271690	3.883
Total		6997467	100.000

tert-butyl (*S*)-2-(pyridin-2-yl)pyrrolidine-1-carboxylate 2r



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(pyridin-2-yl)pyrrolidine-1-carboxylate 2r



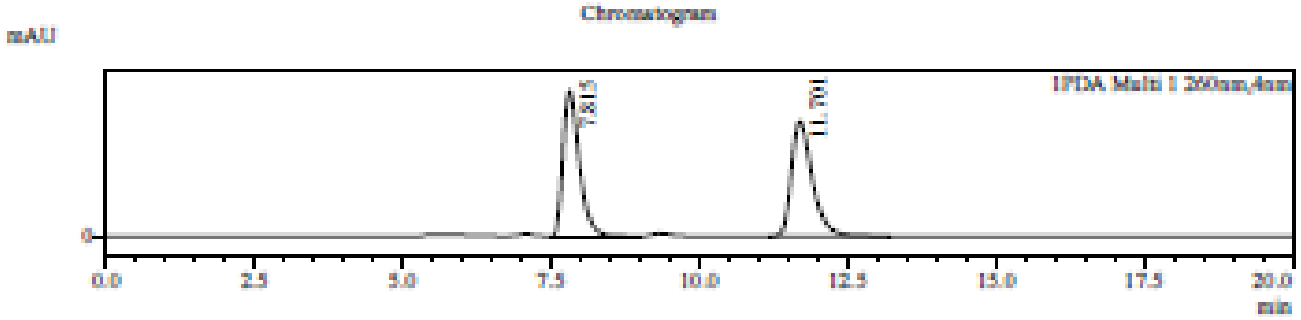
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(pyridin-2-yl)pyrrolidine-1-carboxylate 2r

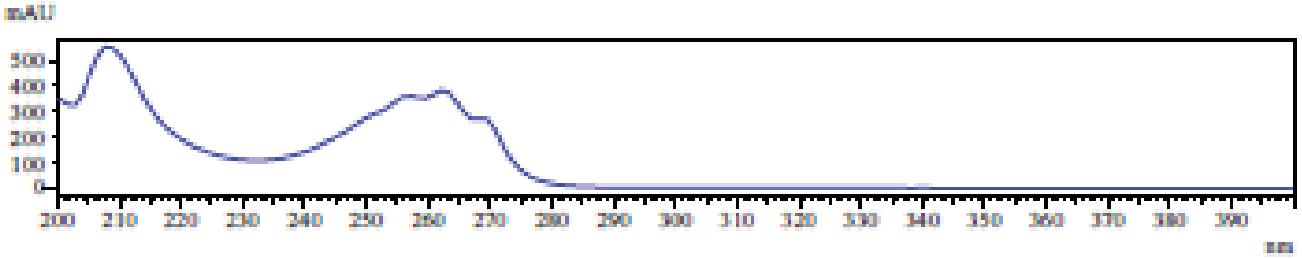
Sample Information

Data File : YW-IV-28A-ADH-10%-1mL-IPrOH001.lcd
Method File : YW-10%-1.0ml.lcm

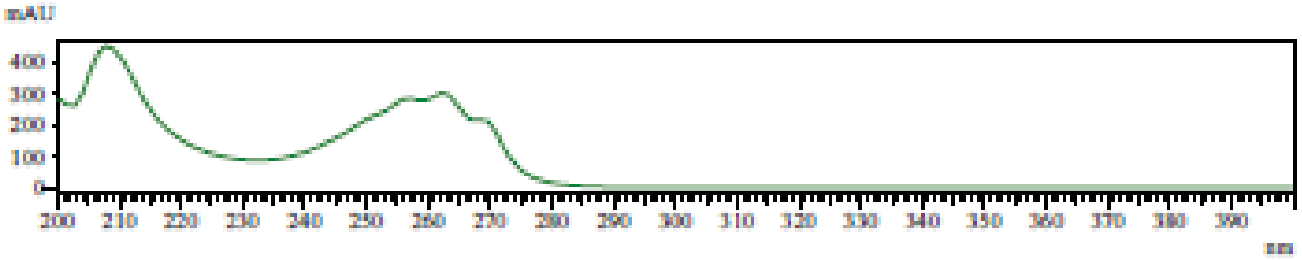
Chromatogram



UV Spectrum
Retention time = 7.815



UV Spectrum
Retention time = 11.701



Peak Table

PDA Ch1 260nm

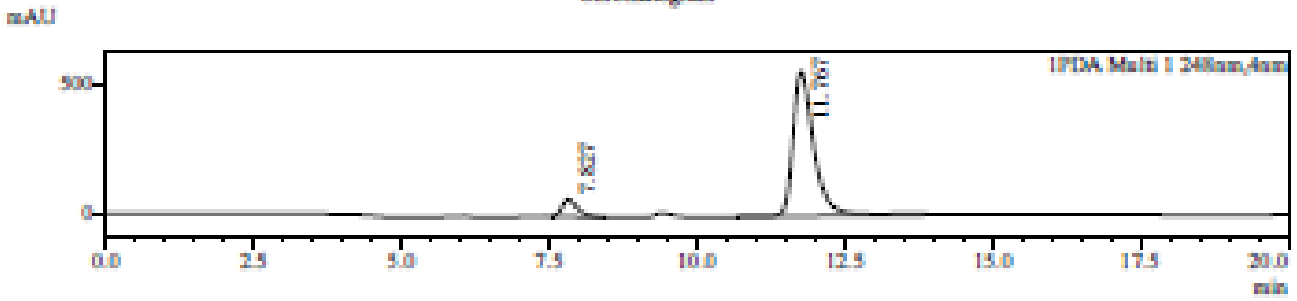
Peak#	Ret. Time	Area	Area%
1	7.815	7015012	49.882
2	11.701	7048075	50.118
Total		14063086	100.000

tert-butyl (*S*)-2-(pyridin-2-yl)pyrrolidine-1-carboxylate 2r

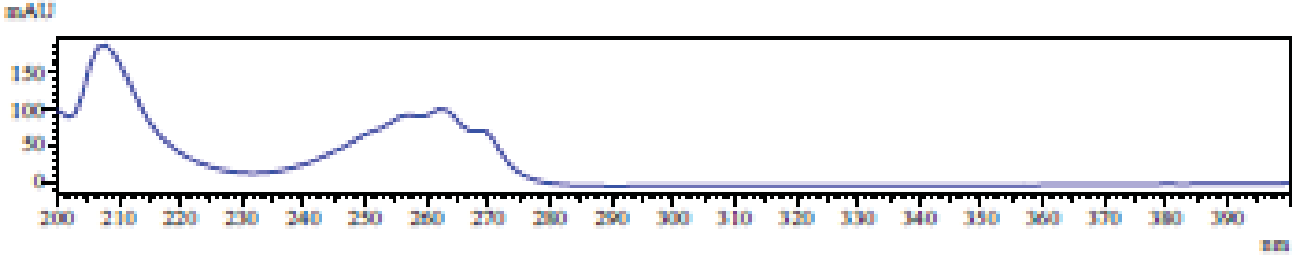
Sample Information

Data File : YW-IV-28b-ADH-10%-1mL-IPrOH.lcd
Method File : YW-10%-1.0ml.lcm

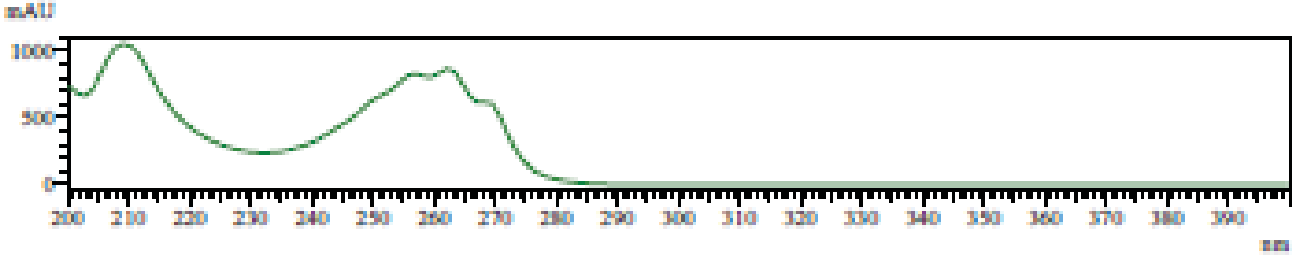
Chromatogram



UV Spectrum
Retention time = 7.827



UV Spectrum
Retention time = 11.767

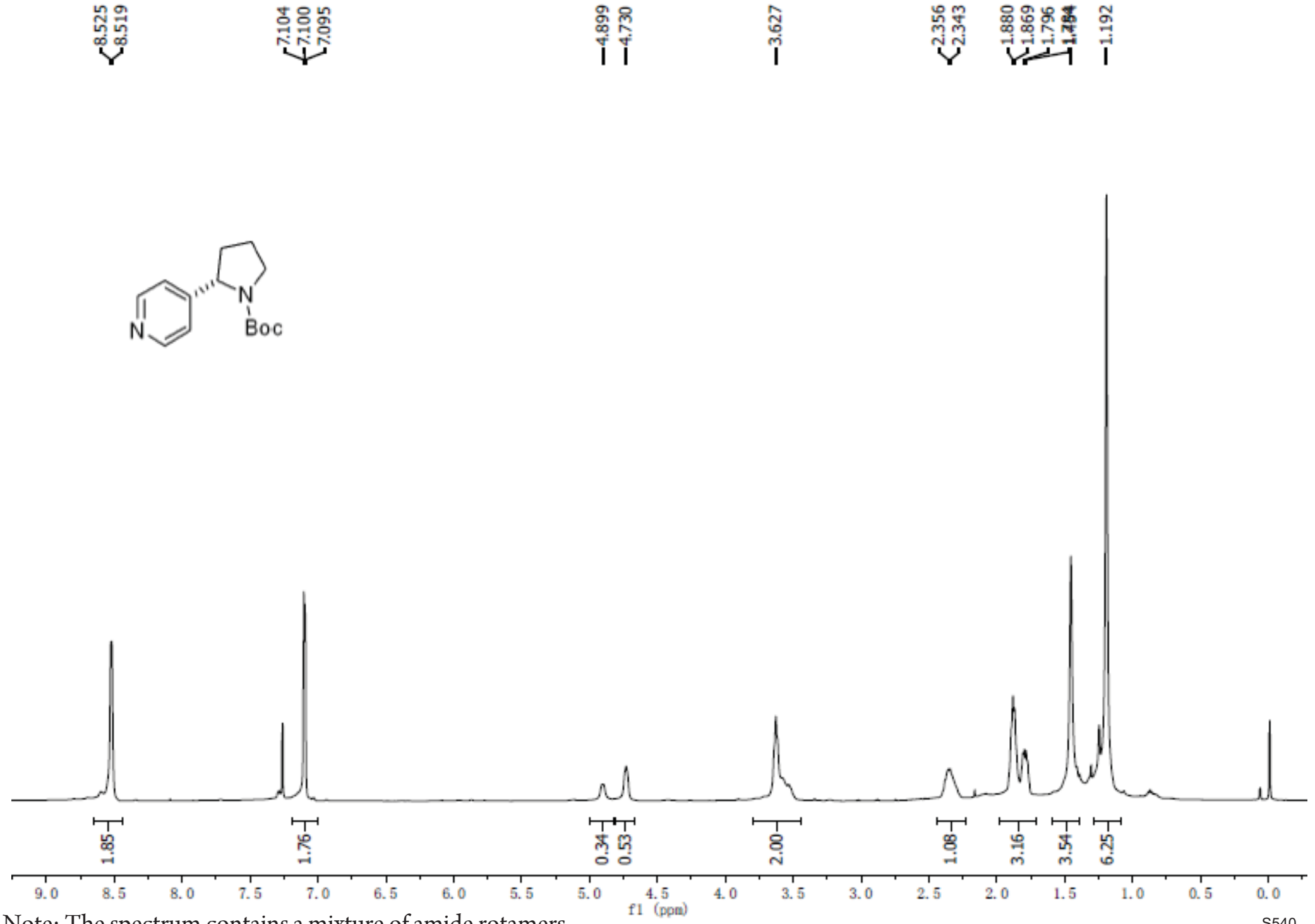


Peak Table

PDA Ch1 248nm

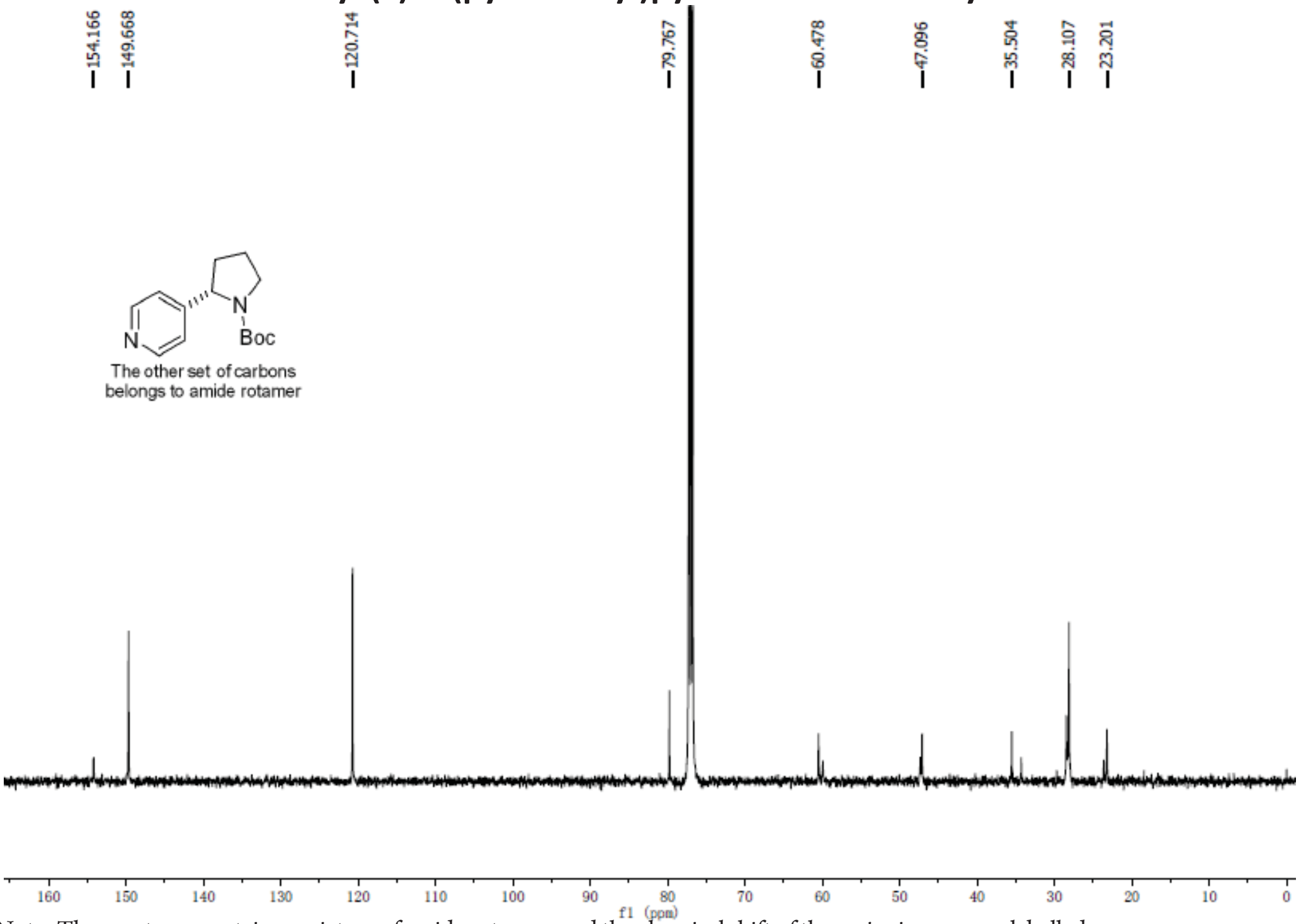
Peak#	Ret. Time	Area	Area%
1	7.827	1183408	7.695
2	11.767	14195583	92.305
Total		15378991	100.000

tert-butyl (*S*)-2-(pyridin-4-yl)pyrrolidine-1-carboxylate 2s



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(pyridin-4-yl)pyrrolidine-1-carboxylate 2s



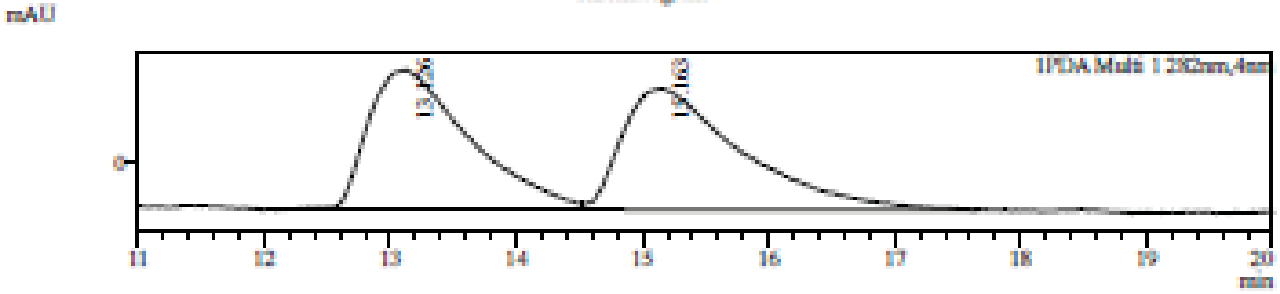
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(pyridin-4-yl)pyrrolidine-1-carboxylate 2s

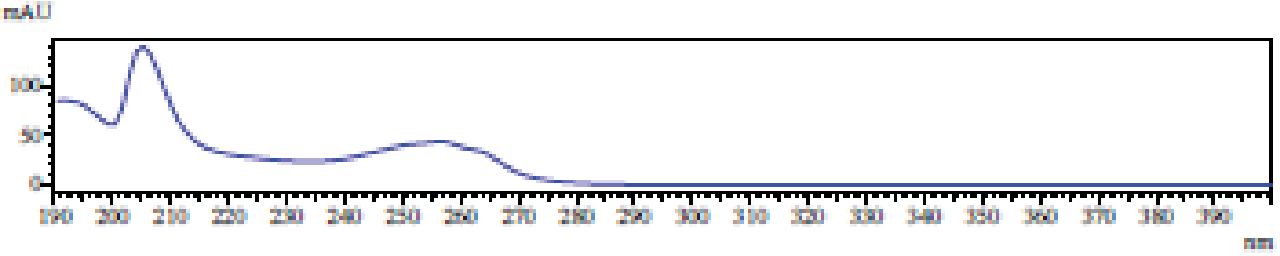
Sample Information

Sample Name	: YW-IV-39a-OJH-2%-1.0ML003
Sample ID	: YW-IV-39a-OJH-2%-1.0ML003
Data File	: YW-IV-39a-OJH-2%-1.0ML003.lcd
Method File	: YW-2%-1.0ml.lcm

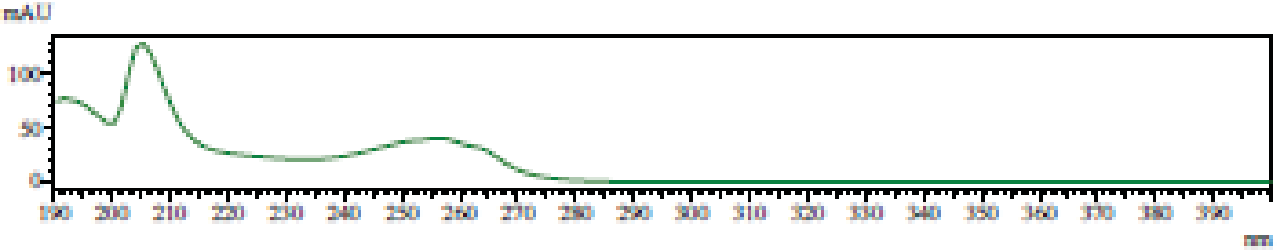
Chromatogram



UV Spectrum
Retention time = 13.126



UV Spectrum
Retention time = 15.163



Peak Table

PDA Ch1 282nm

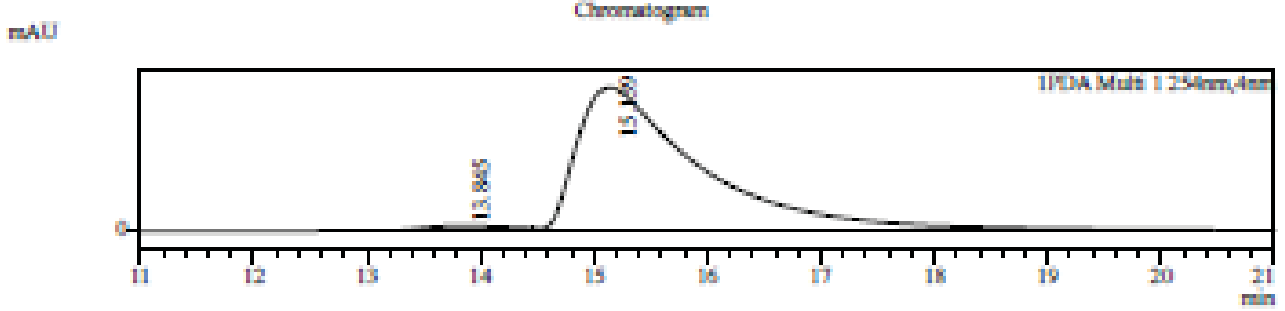
Peak#	Ret. Time	Area	Area%
1	13.126	94072	49.600
2	15.163	95589	50.400
Total		189661	100.000

tert-butyl (*S*)-2-(pyridin-4-yl)pyrrolidine-1-carboxylate 2s

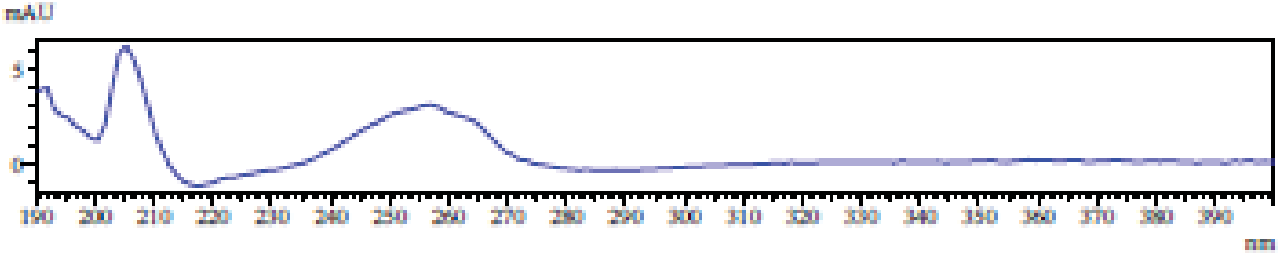
Sample Information

Sample Name	: YW-IV-39B-OJH-2%-1.0ML003
Sample ID	: YW-IV-39B-OJH-2%-1.0ML003
Data File	: YW-IV-39B-OJH-2%-1.0ML003.lcd
Method File	: YW-2%-1.0ml.lcm

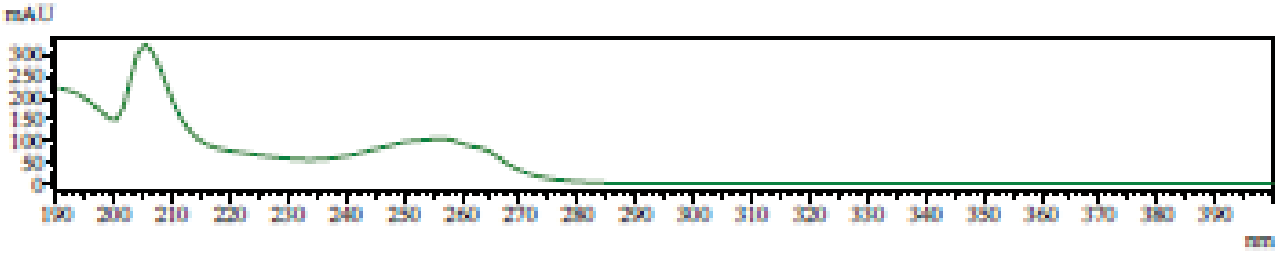
Chromatogram



UV Spectrum
Retention time = 13.845



UV Spectrum
Retention time = 15.139

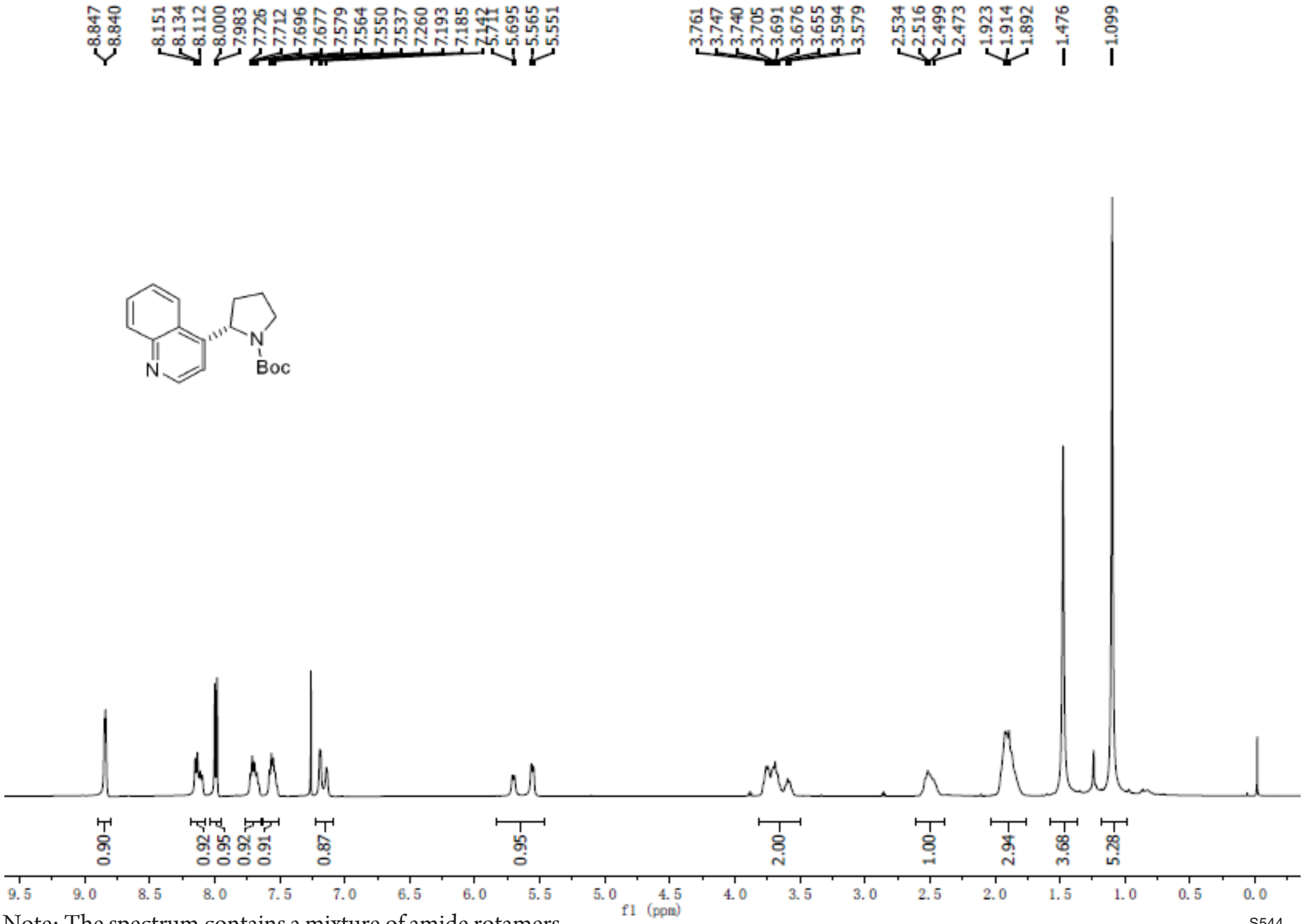


Peak Table

PDA Ch1 254nm

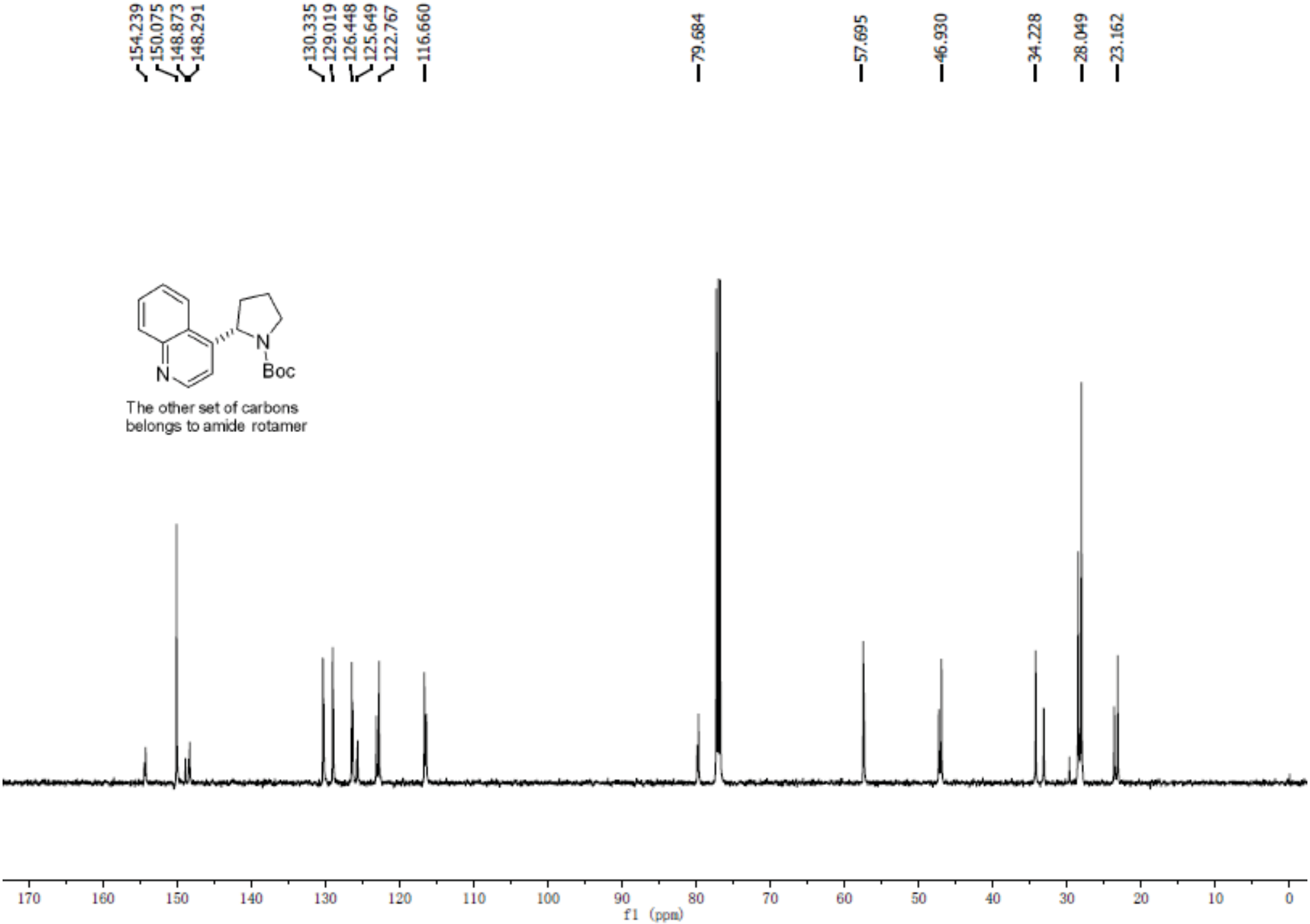
Peak#	Ret. Time	Area	Area%
1	13.845	179792	2.254
2	15.139	7796365	97.746
Total		7976157	100.000

tert-butyl (*S*)-2-(quinolin-4-yl)pyrrolidine-1-carboxylate 2t



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(quinolin-4-yl)pyrrolidine-1-carboxylate 2t



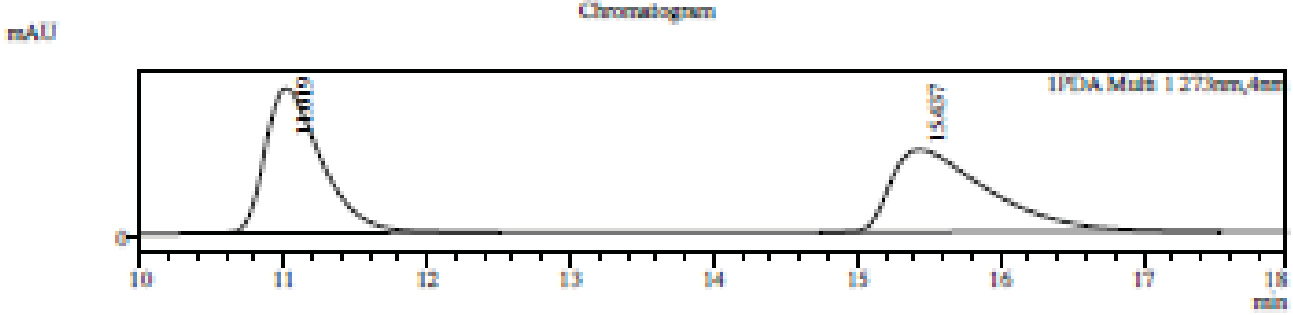
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(quinolin-4-yl)pyrrolidine-1-carboxylate 2t

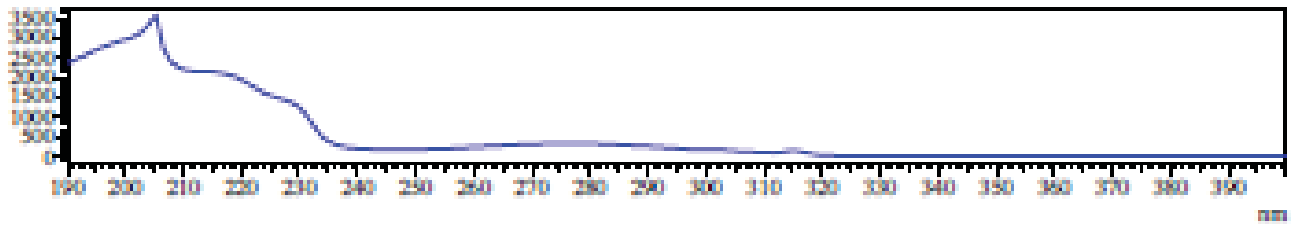
Sample Information

Sample Name	: YW-IV-107a-ODH-5%-1.0ML
Sample ID	: YW-IV-107a-ODH-5%-1.0ML
Data File	: YW-IV-107a-ODH-5%-1.0ML.lcd
Method File	: YW-5.0%-1.0ml.lcm

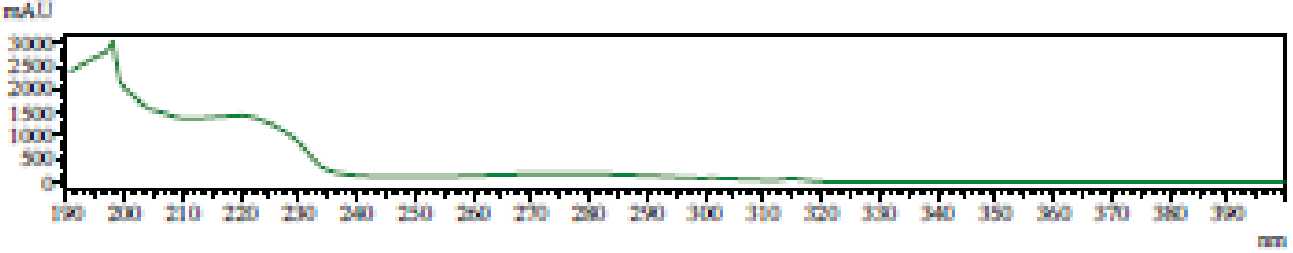
Chromatogram



UV Spectrum
Retention time = 11.019



UV Spectrum
Retention time = 15.437



Peak Table

PDA Ch1 273nm

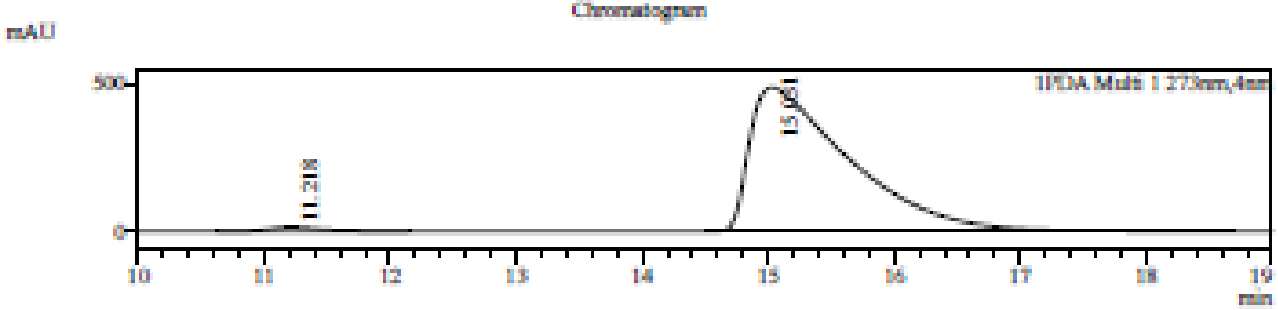
Peak#	Ret. Time	Area	Area%
1	11.019	8445144	50.362
2	15.437	8323572	49.638
Total		16768716	100.000

tert-butyl (*S*)-2-(quinolin-4-yl)pyrrolidine-1-carboxylate 2t

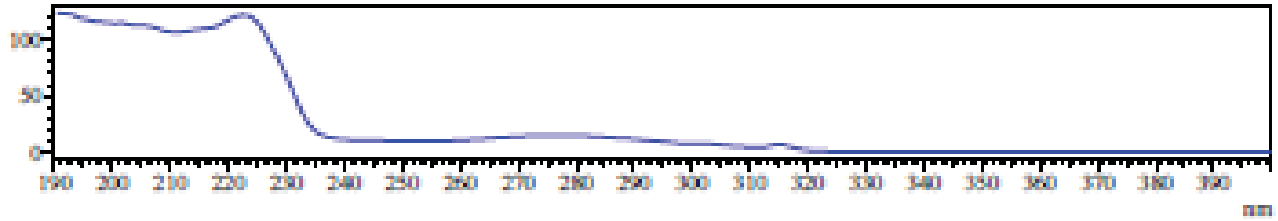
Sample Information

Sample Name	: YW-IV-107b-ODH-3%-1.0ML
Sample ID	: YW-IV-107b-ODH-3%-1.0ML
Data File	: YW-IV-107b-ODH-3%-1.0ML.lcd
Method File	: YW-3.0%-1.0ml.lcm

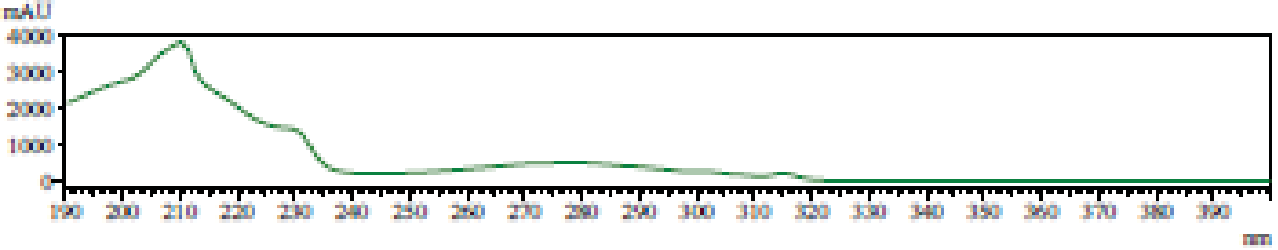
Chromatogram



UV Spectrum
Retention time = 11.218



UV Spectrum
Retention time = 15.031

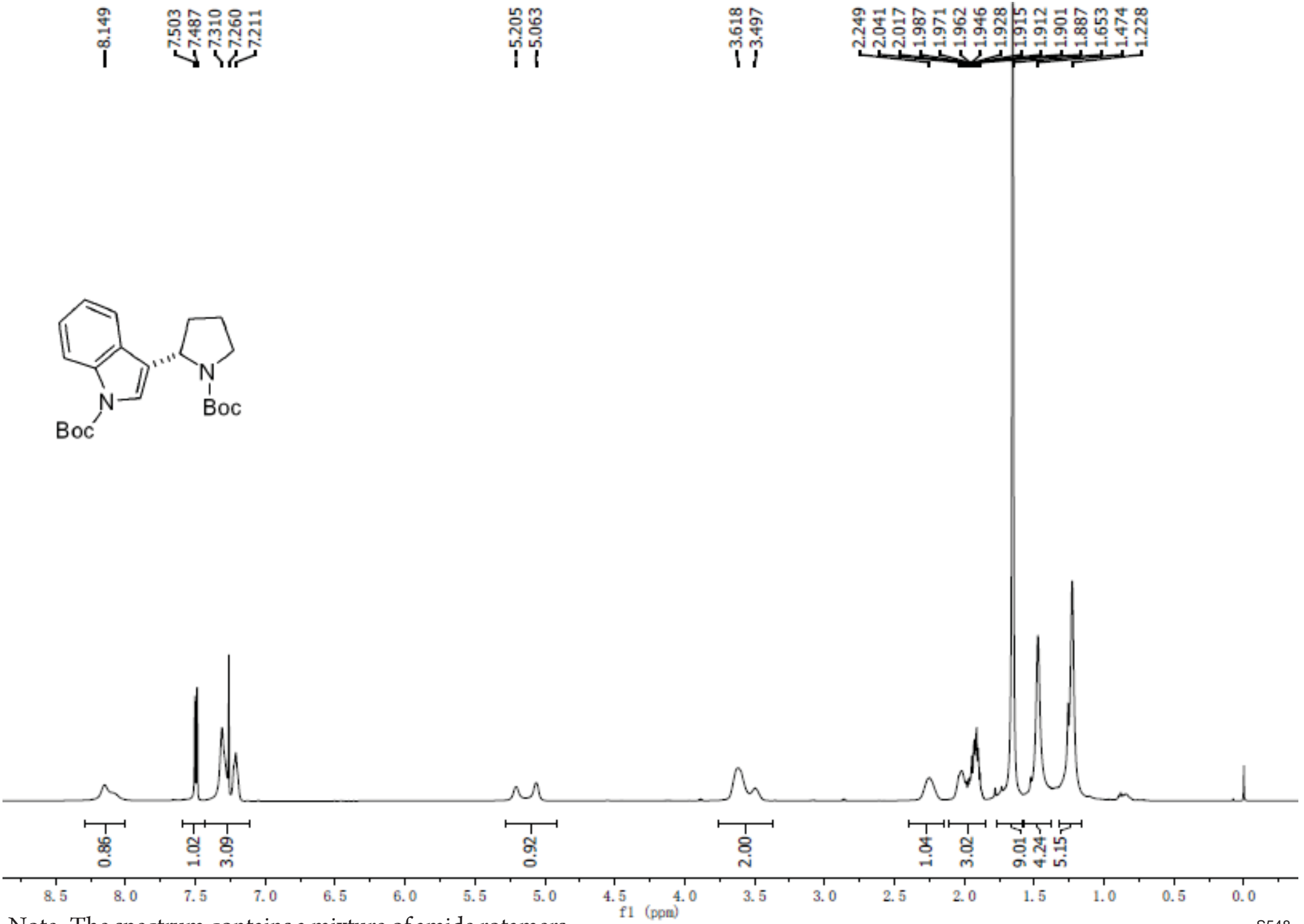


Peak Table

PDA Ch1 273nm

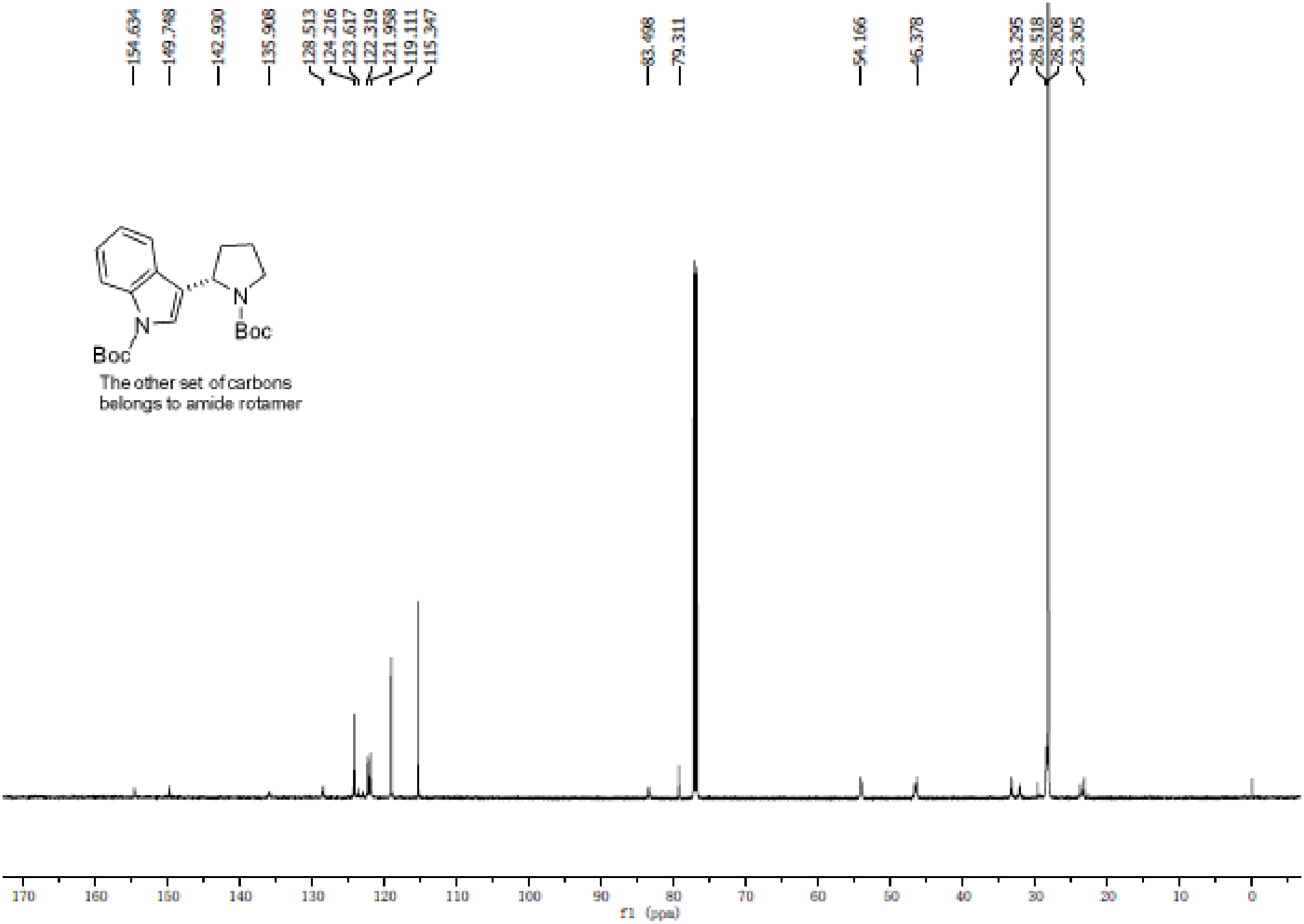
Peak#	Ret. Time	Area	Area%
1	11.218	378521	1.413
2	15.031	26417113	98.587
Total		26795634	100.000

tert-butyl (*S*)-3-(1-(tert-butoxycarbonyl)pyrrolidin-2-yl)-1H-indole-1-carboxylate 2u



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-3-(1-(tert-butoxycarbonyl)pyrrolidin-2-yl)-1H-indole-1-carboxylate 2u



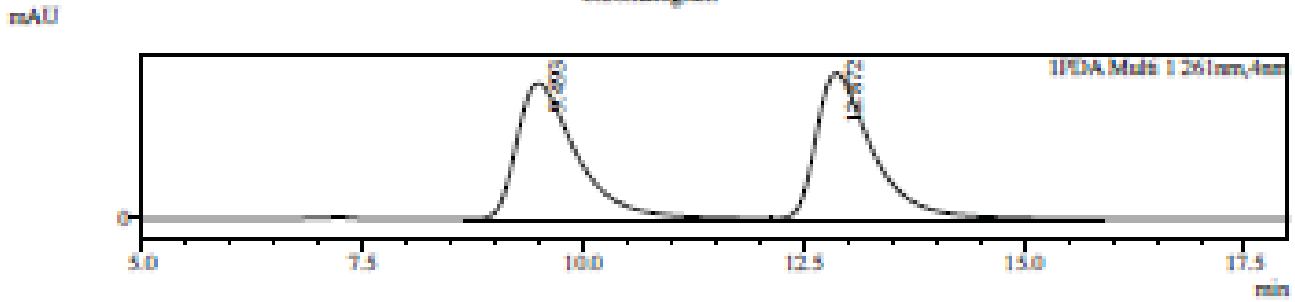
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-3-(1-(tert-butoxycarbonyl)pyrrolidin-2-yl)-1H-indole-1-carboxylate 2u

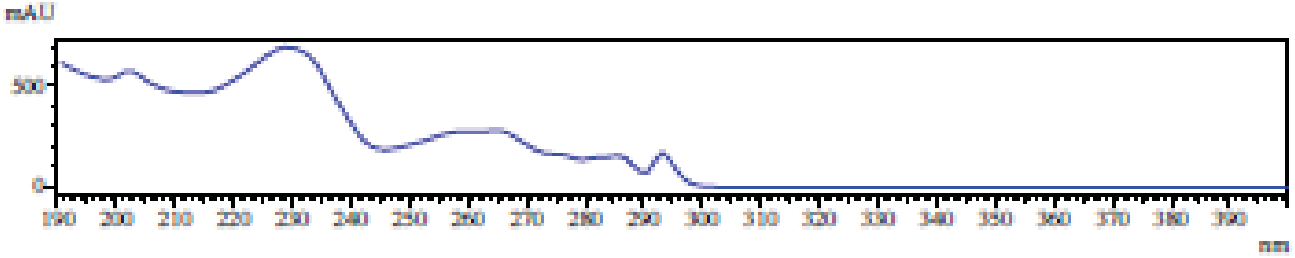
Sample Information

Sample Name	: YW-IV-108a-ADH-1%-1.0ML
Sample ID	: YW-IV-108a-ADH-1%-1.0ML
Data File	: YW-IV-108a-ADH-1%-1.0ML.lcd
Method File	: YW-1%-1.0ml.lcm

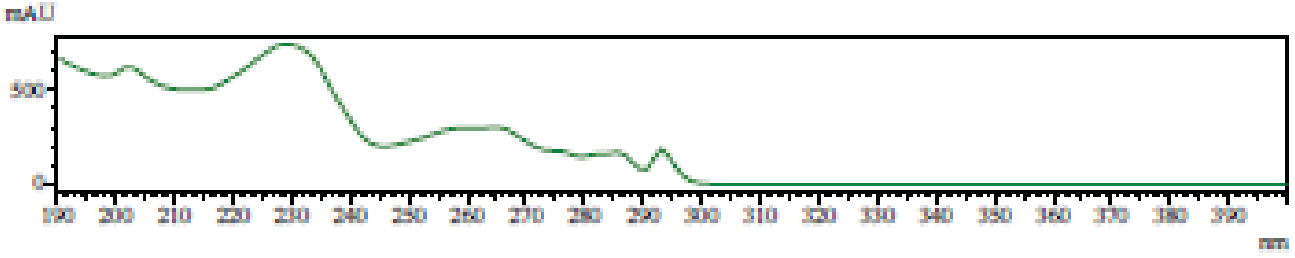
Chromatogram



UV Spectrum
Retention time = 9.493



UV Spectrum
Retention time = 12.872



Peak Table

PDA Ch1 261nm

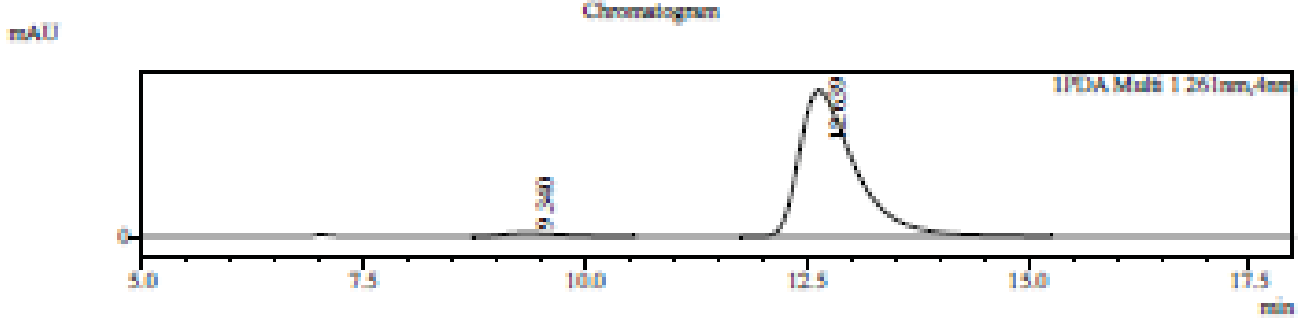
Peak#	Ret. Time	Area	Area%
1	9.493	13103308	49.837
2	12.872	13189163	50.163
Total		26292472	100.000

tert-butyl (*S*)-3-(1-(tert-butoxycarbonyl)pyrrolidin-2-yl)-1H-indole-1-carboxylate 2u

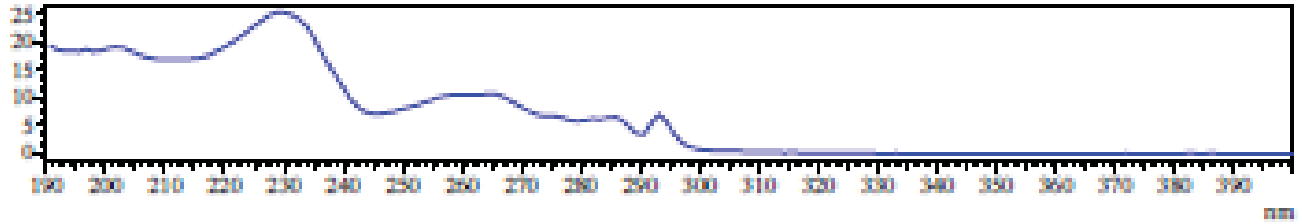
Sample Information

Sample Name : YW-IV-108b-ADH-1%-1.0ML
Sample ID : YW-IV-108b-ADH-1%-1.0ML
Data File : YW-IV-108b-ADH-1%-1.0ML.lcd
Method File : YW-1%-1.0ml.lcm

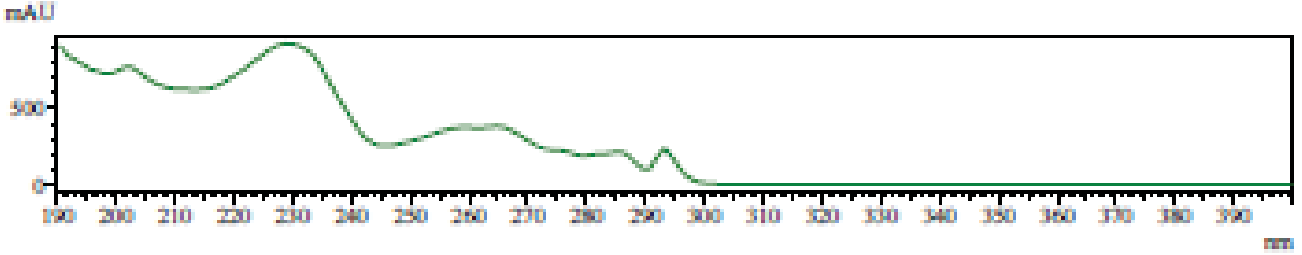
Chromatogram



UV Spectrum
Retention time = 9.340



UV Spectrum
Retention time = 12.639

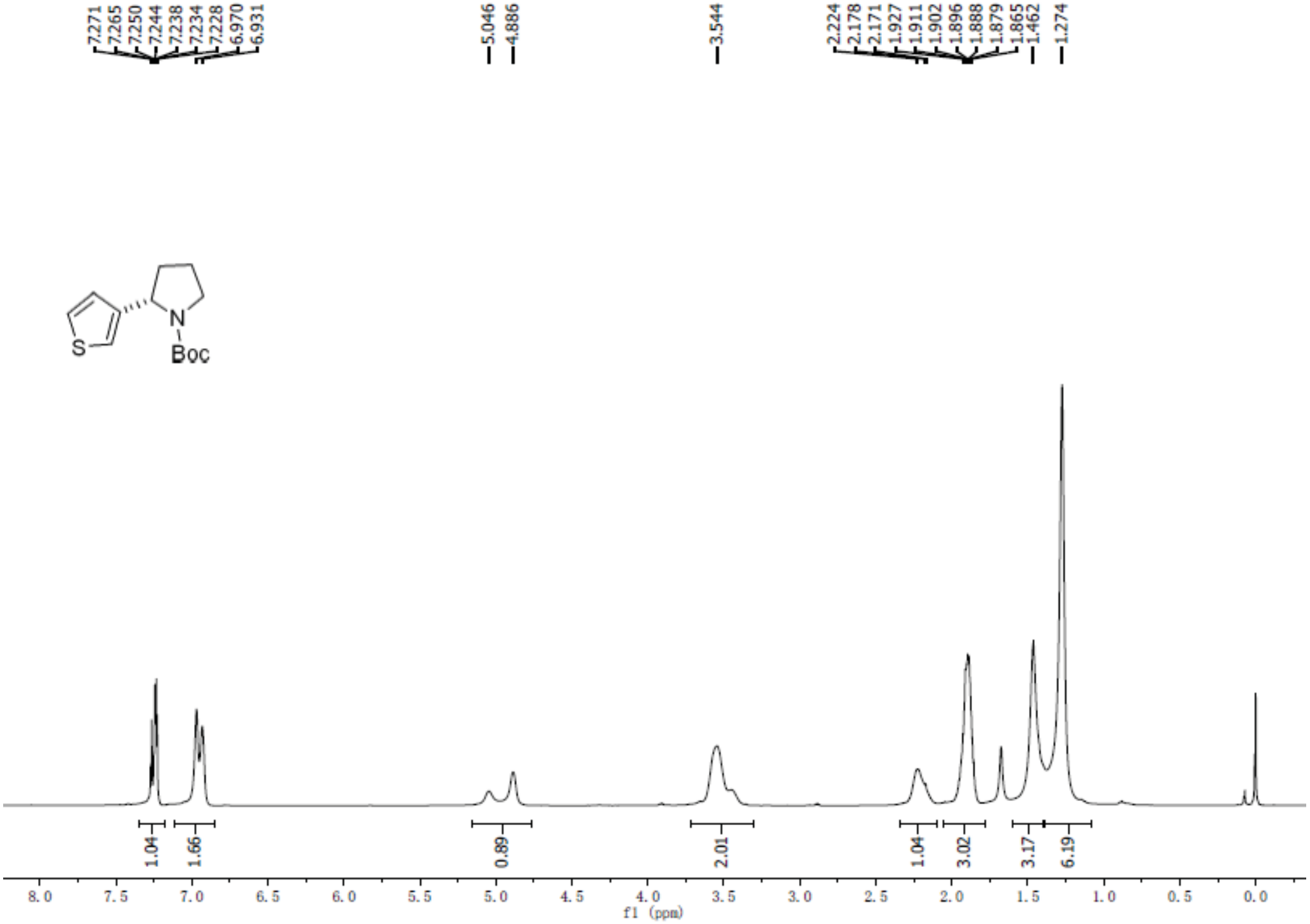


Peak Table

PDA Ch1 261nm

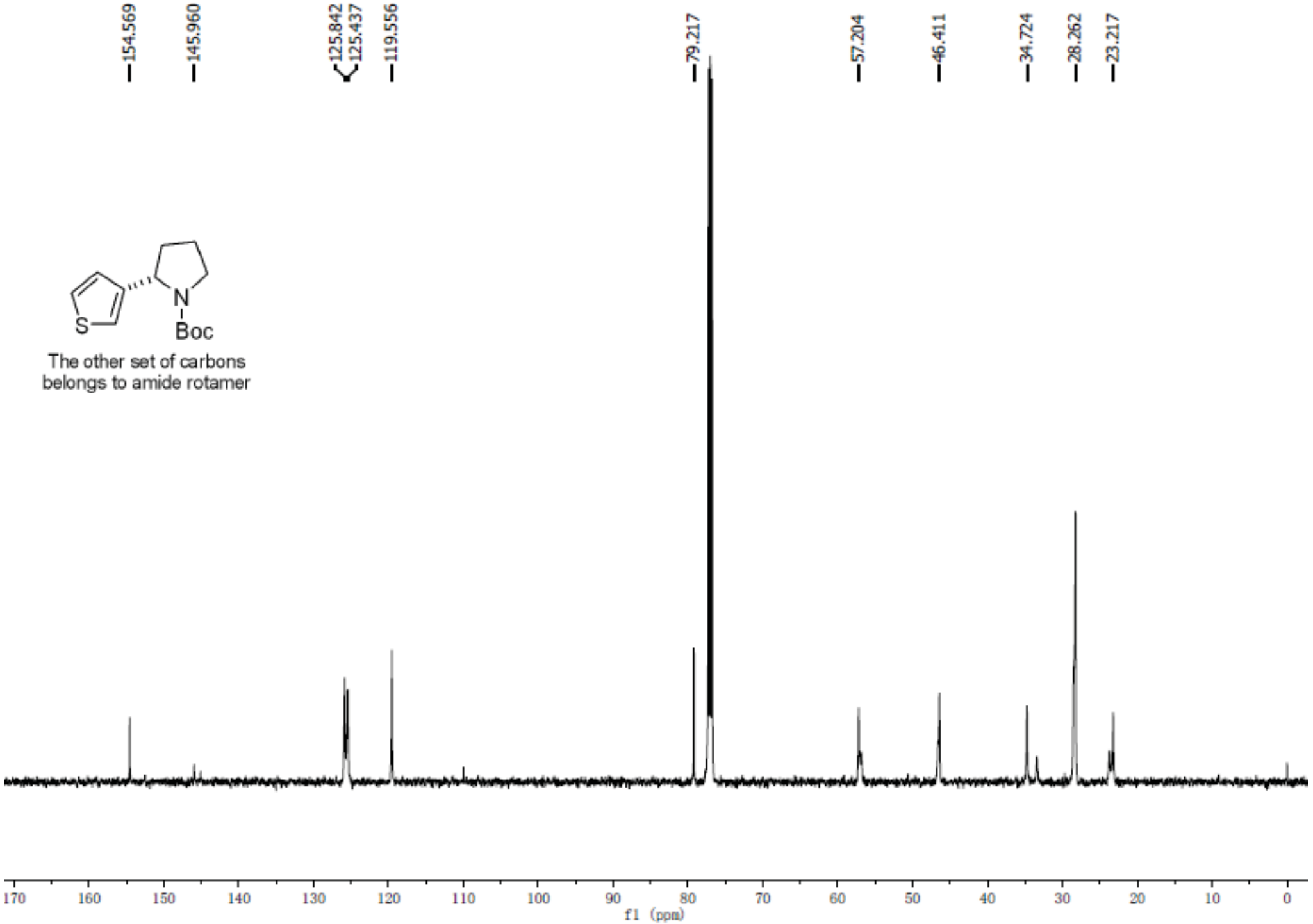
Peak#	Ret. Time	Area	Area%
1	9.340	412776	2.471
2	12.639	16292498	97.529
Total		16705273	100.000

tert-butyl (*S*)-2-(thiophen-3-yl)pyrrolidine-1-carboxylate 2v



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(thiophen-3-yl)pyrrolidine-1-carboxylate 2v



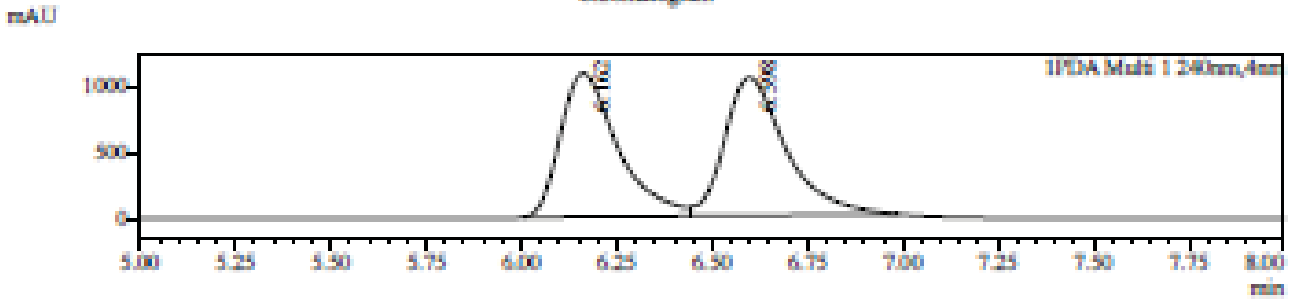
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(thiophen-3-yl)pyrrolidine-1-carboxylate 2v

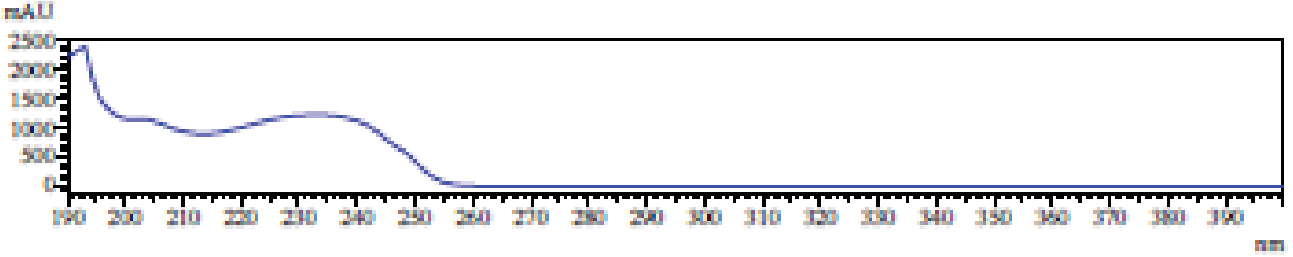
Sample Information

Sample Name	: YW-IV-42a-ADH-5%-0.8ML003
Sample ID	: YW-IV-42a-ADH-5%-0.8ML003
Data File	: YW-IV-42a-ADH-5%-0.8ML003.lcd
Method File	: YW-5.0%-0.8ml.lcm

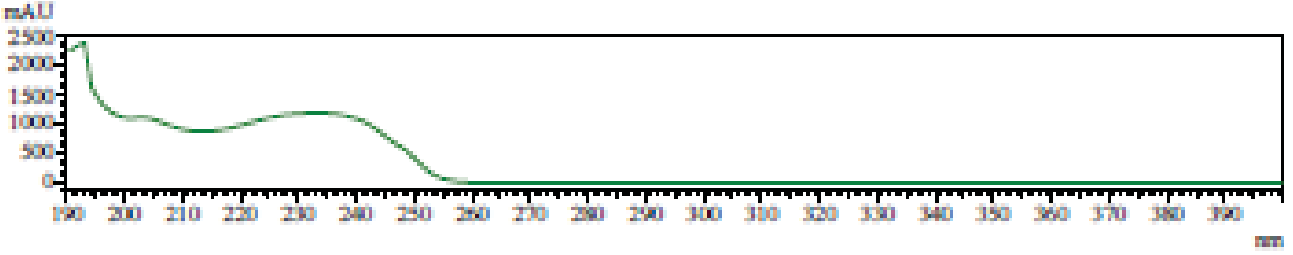
Chromatogram



UV Spectrum
Retention time = 6.162



UV Spectrum
Retention time = 6.598



Peak Table

PDA Ch1 240nm

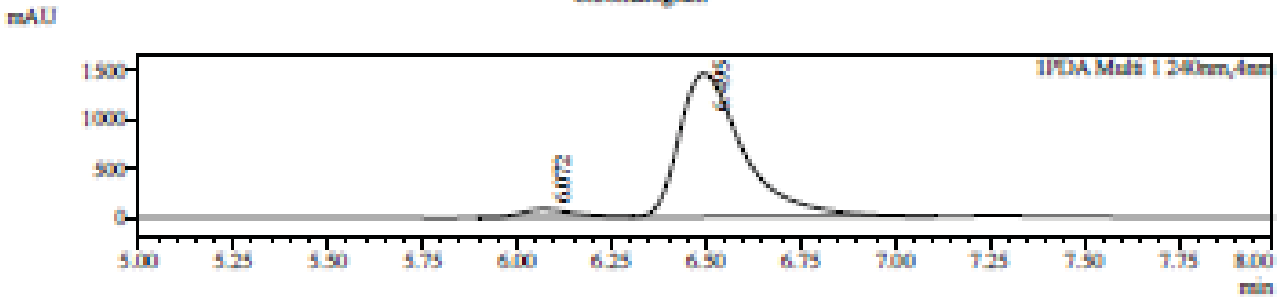
Peak#	Ret. Time	Area	Area%
1	6.162	11440723	49.505
2	6.598	11669290	50.495
Total		23110013	100.000

tert-butyl (*S*)-2-(thiophen-3-yl)pyrrolidine-1-carboxylate 2v

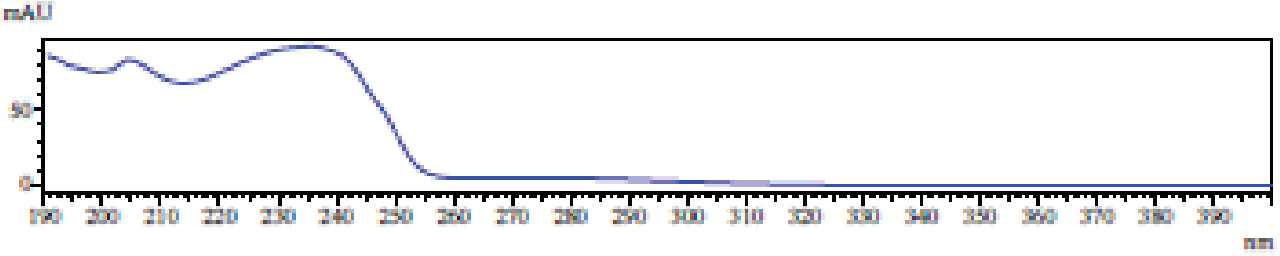
Sample Information

Sample Name	: YW-IV-42B-ADH-5%-0.8ML003
Sample ID	: YW-IV-42B-ADH-5%-0.8ML003
Data File	: YW-IV-42B-ADH-5%-0.8ML003.lcd
Method File	: YW-5.0%-0.8ml.lcm

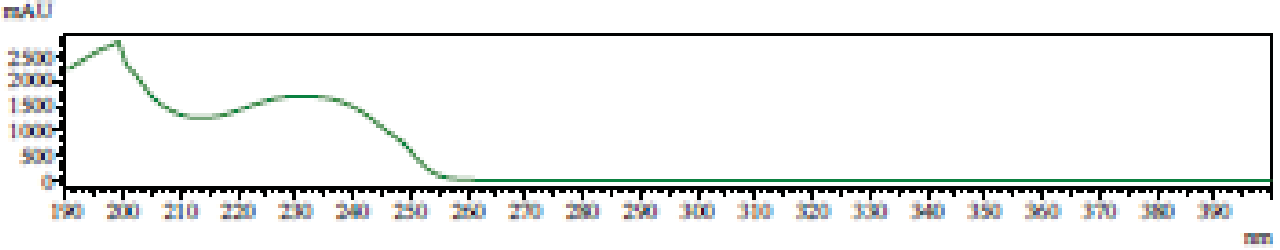
Chromatogram



UV Spectrum
Retention time = 6.072



UV Spectrum
Retention time = 6.495

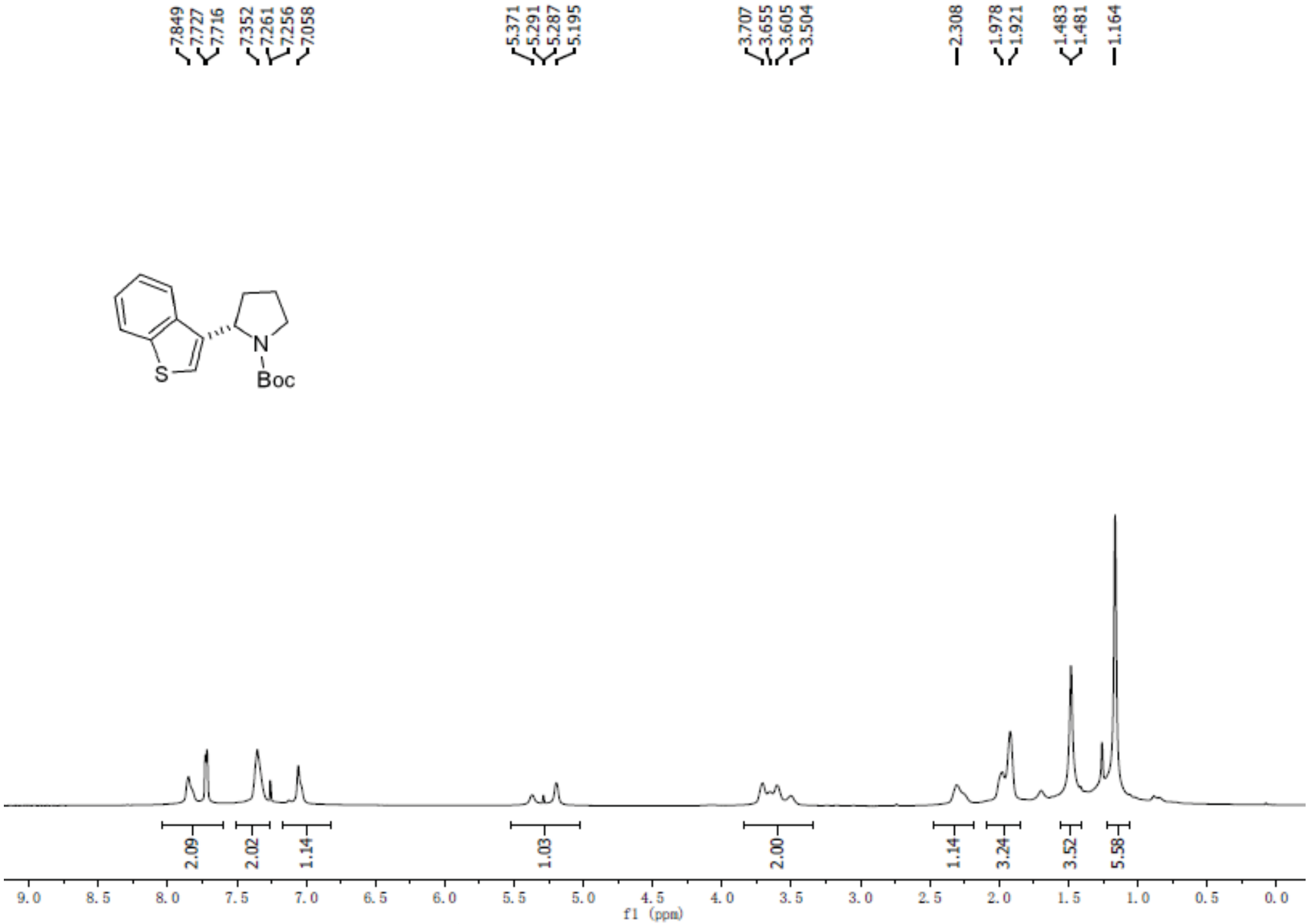


Peak Table

PDA Ch1 240nm

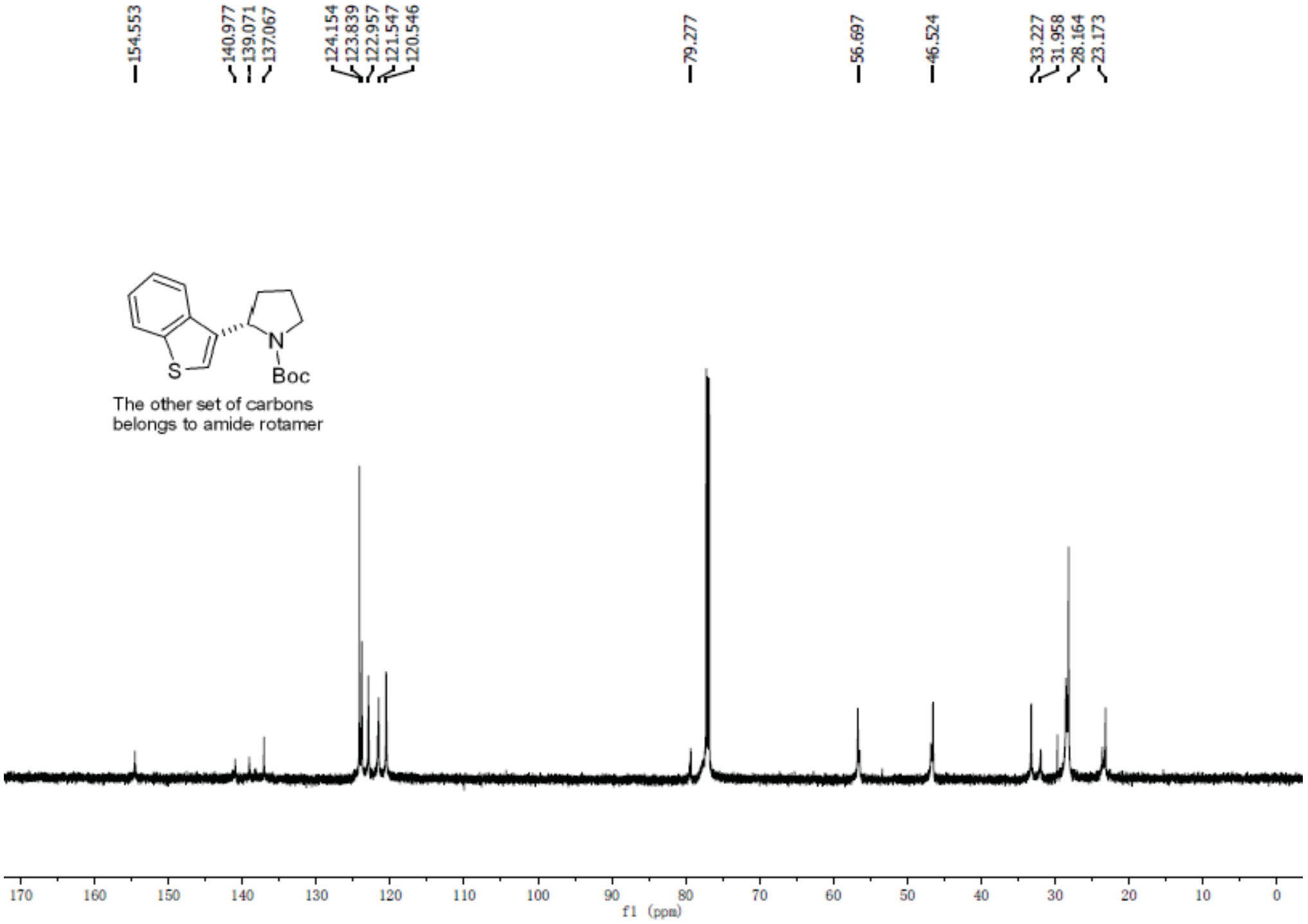
Peak#	Ret. Time	Area	Area%
1	6.072	788163	4.402
2	6.495	17117570	95.598
Total		17905733	100.000

tert-butyl (*S*)-2-(benzo[b]thiophen-3-yl)pyrrolidine-1-carboxylate 2w



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(benzo[b]thiophen-3-yl)pyrrolidine-1-carboxylate 2w



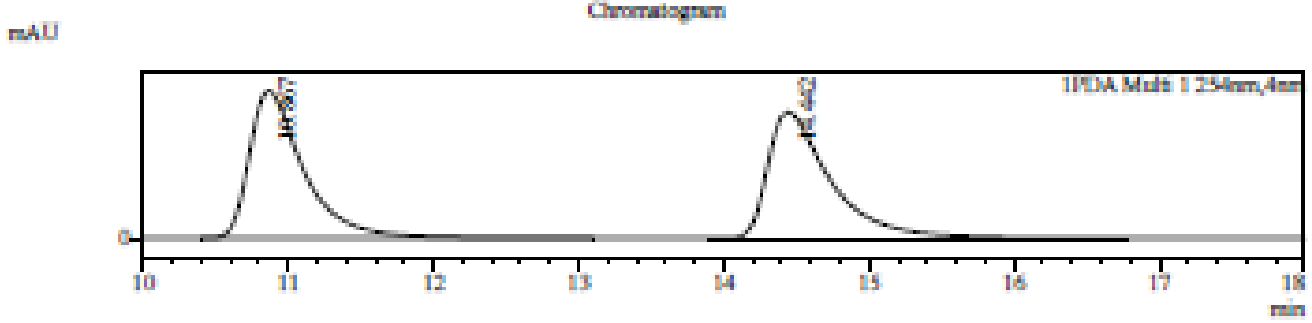
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(benzo[b]thiophen-3-yl)pyrrolidine-1-carboxylate 2w

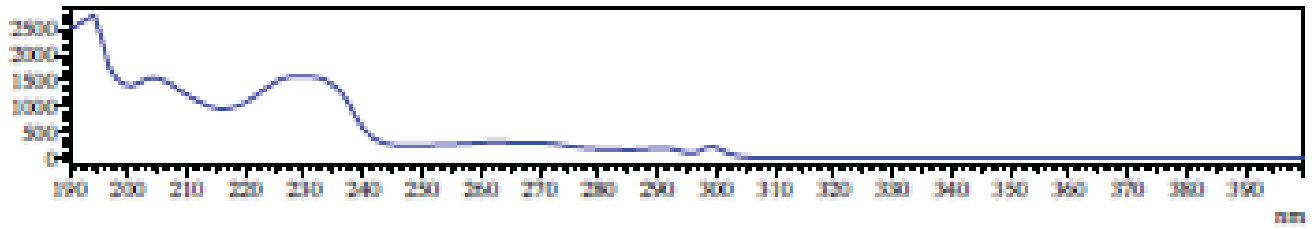
Sample Information

Sample Name	: YW-IV-103a-ADH-1%-1.0ML
Sample ID	: YW-IV-103a-ADH-1%-1.0ML
Data File	: YW-IV-103a-ADH-1%-1.0ML001.lcd
Method File	: YW-1%-1.0ml.lcm

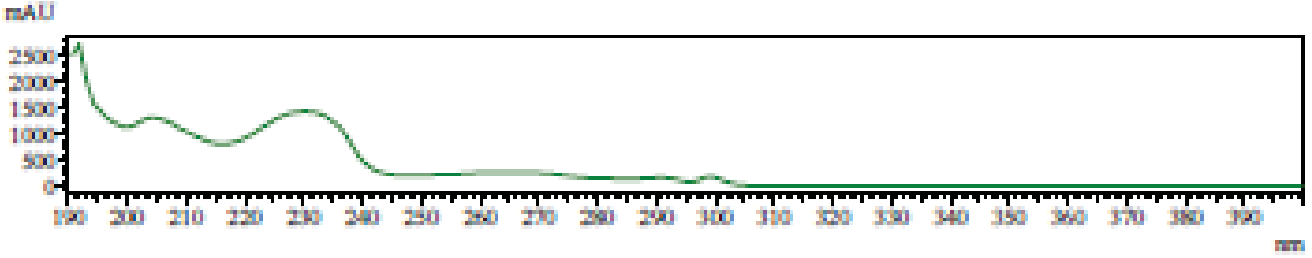
Chromatogram



UV Spectrum
Retention time = 10.867



UV Spectrum
Retention time = 14.442



Peak Table

PDA Ch1 254nm

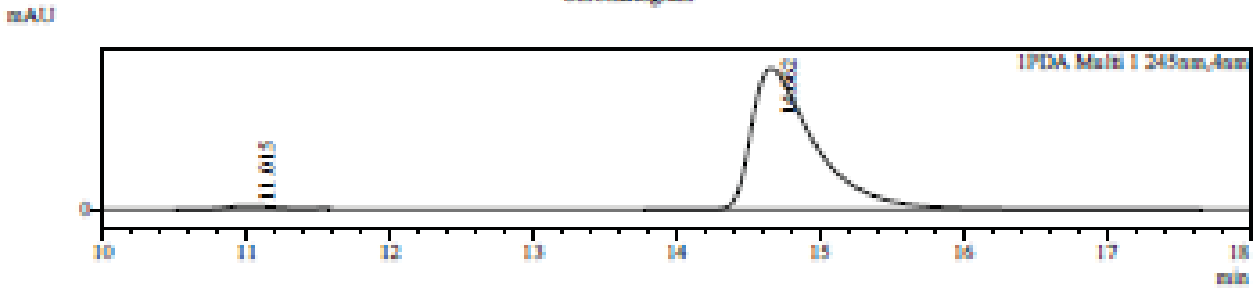
Peak#	Ret. Time	Area	Area%
1	10.867	6709263	50.330
2	14.442	6621274	49.670
Total		13330538	100.000

tert-butyl (*S*)-2-(benzo[b]thiophen-3-yl)pyrrolidine-1-carboxylate 2w

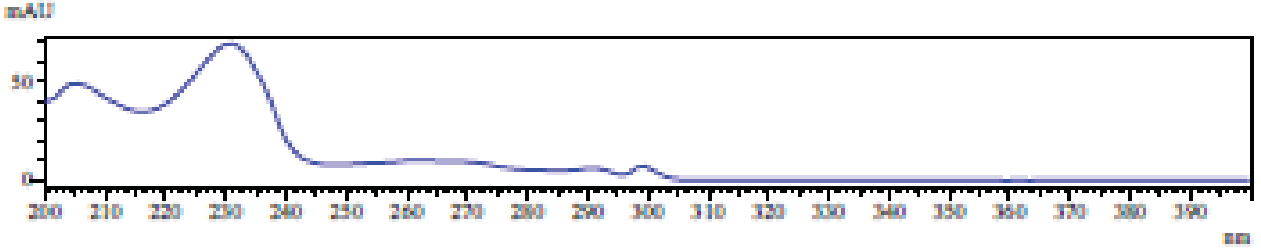
Sample Information

Sample Name	: YW-IV-103b-ADH-1%-1.0ML
Sample ID	: YW-IV-103b-ADH-1%-1.0ML
Data File	: YW-IV-103b-ADH-1%-1.0ML.lcd
Method File	: YW-1%-1.0ml.lcm

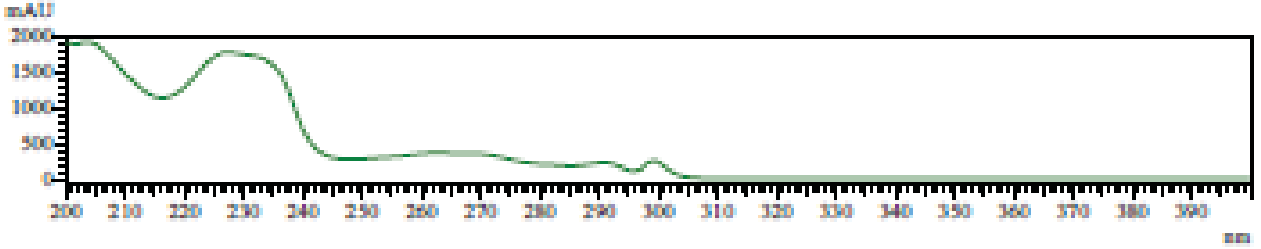
Chromatogram



UV Spectrum
Retention time = 11.015



UV Spectrum
Retention time = 14.662

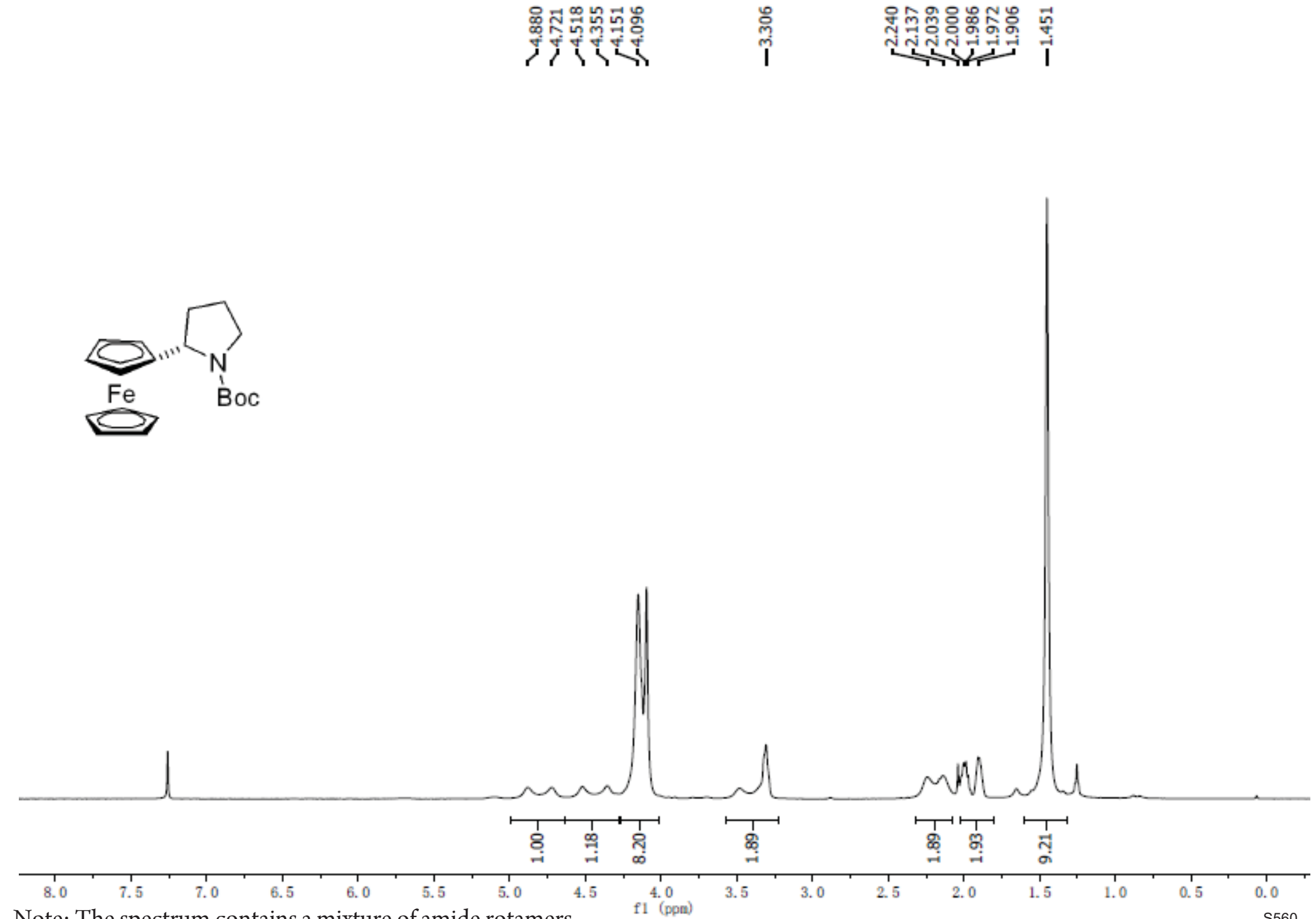


Peak Table

PDA Ch1 245nm

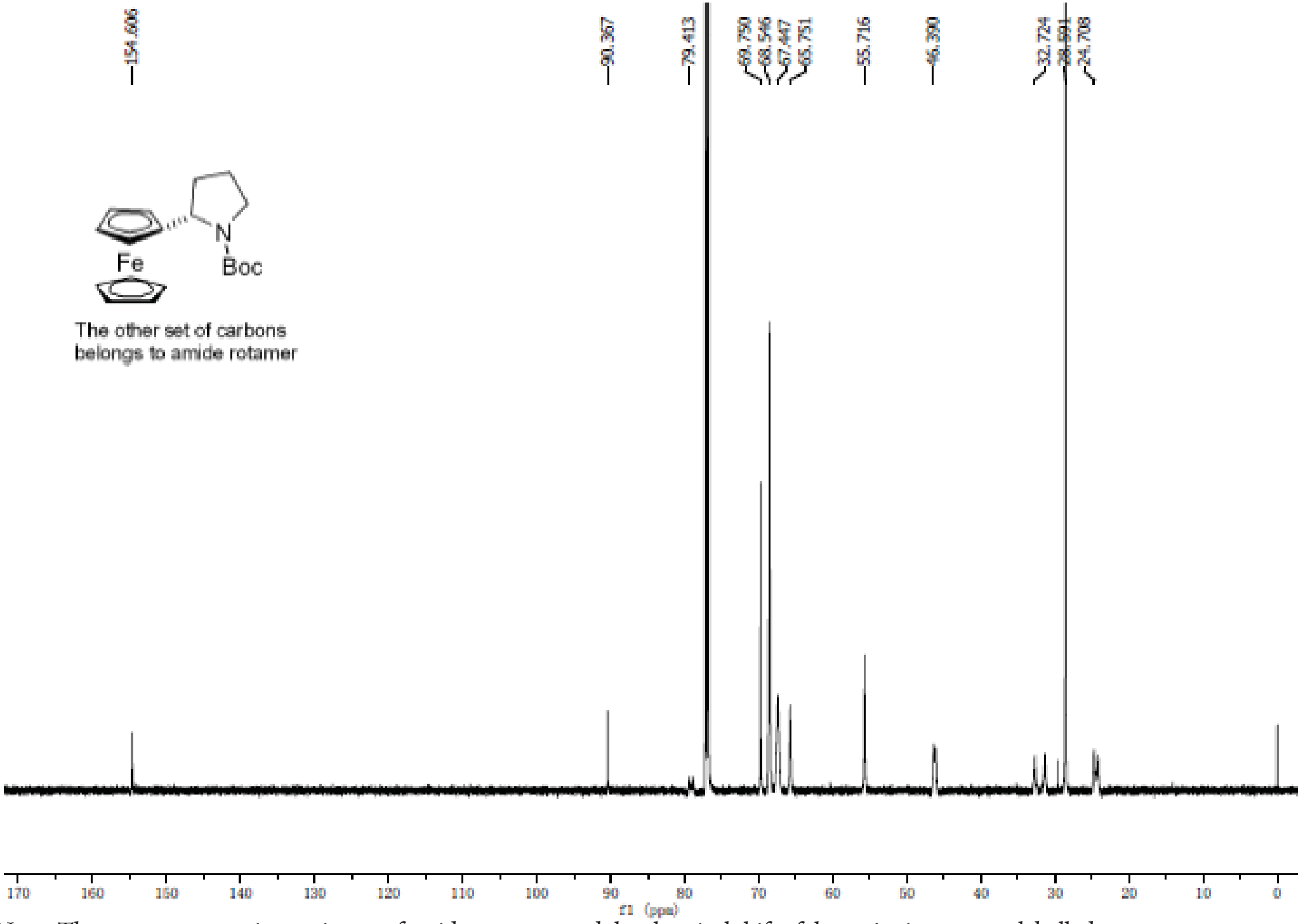
Peak#	Ret. Time	Area	Area%
1	11.015	209356	1.927
2	14.662	10653571	98.073
Total		10862927	100.000

tert-butyl (*S*)-2-(2-ferrocenyl)pyrrolidine-1-carboxylate 2x



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-(2-ferrocenyl)pyrrolidine-1-carboxylate 2x



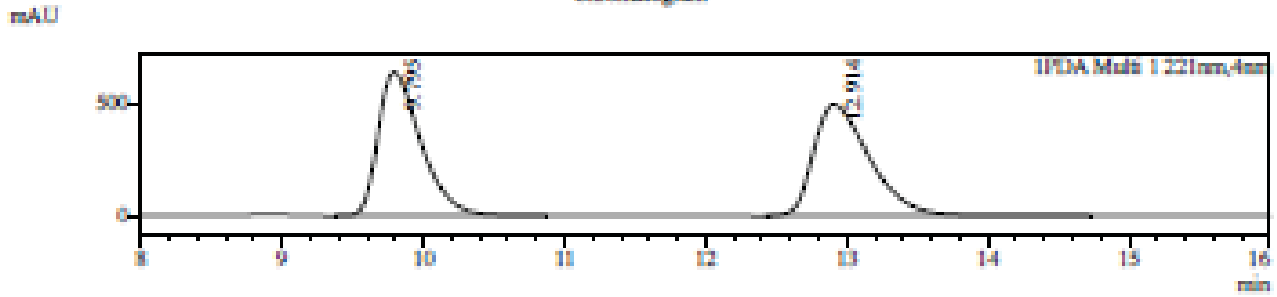
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-(2-ferrocenyl)pyrrolidine-1-carboxylate 2x

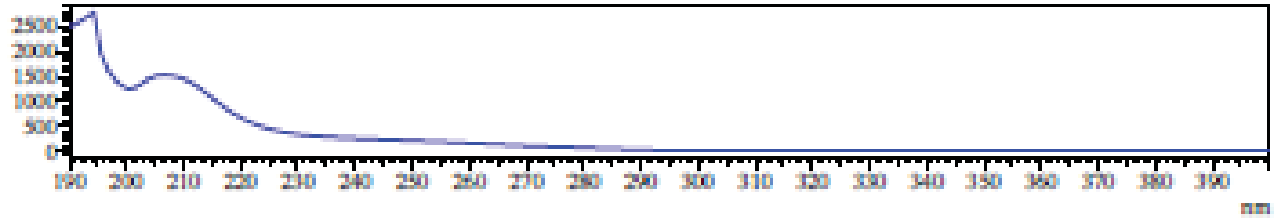
Sample Information

Sample Name	: YW-IV-121a-ODH-1%-1.0ML
Sample ID	: YW-IV-121a-ODH-1%-1.0ML
Data File	: YW-IV-121a-ODH-1%-1.0ML.lcd
Method File	: YW-1%-1.0ml.lcm

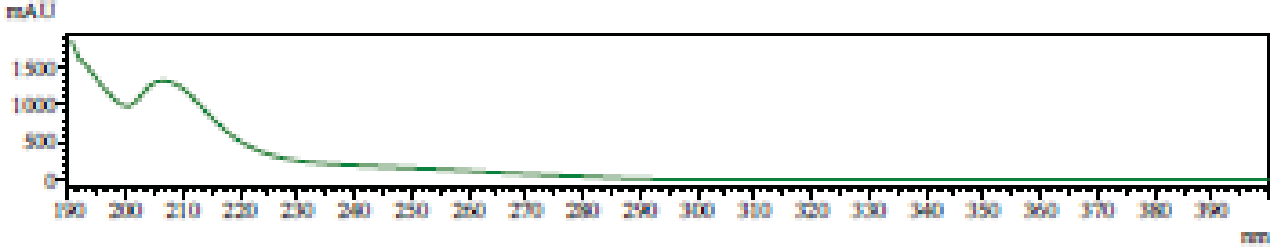
Chromatogram



UV Spectrum
Retention time = 9.795



UV Spectrum
Retention time = 12.914



Peak Table

PDA Ch1 221nm

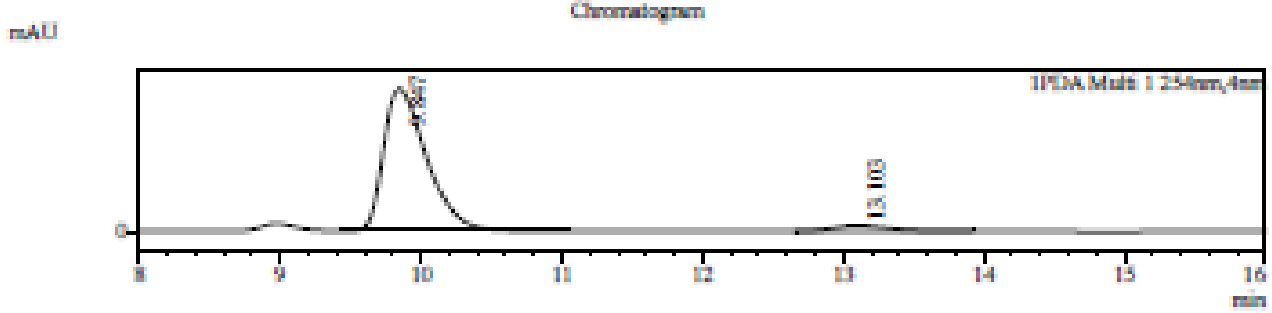
Peak#	Ret. Time	Area	Area%
1	9.795	13424308	49.729
2	12.914	13570388	50.271
Total		26994695	100.000

tert-butyl (*S*)-2-(2-ferrocenyl)pyrrolidine-1-carboxylate 2x

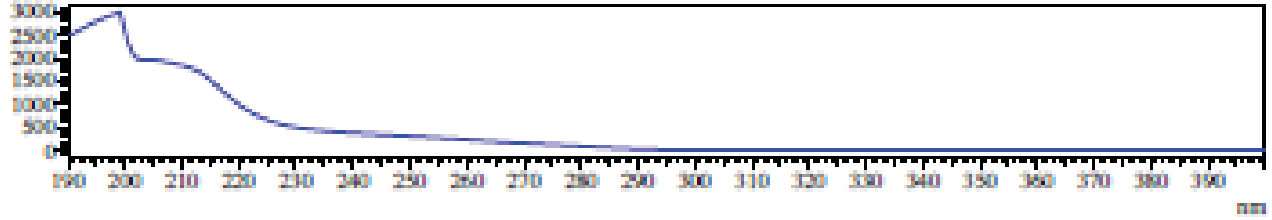
Sample Information

Sample Name	: YW-IV-121b-ODH-1%-1.0ML
Sample ID	: YW-IV-121b-ODH-1%-1.0ML
Data File	: YW-IV-121b-ODH-1%-1.0ML.lcd
Method File	: YW-1%-1.0ml.lcm

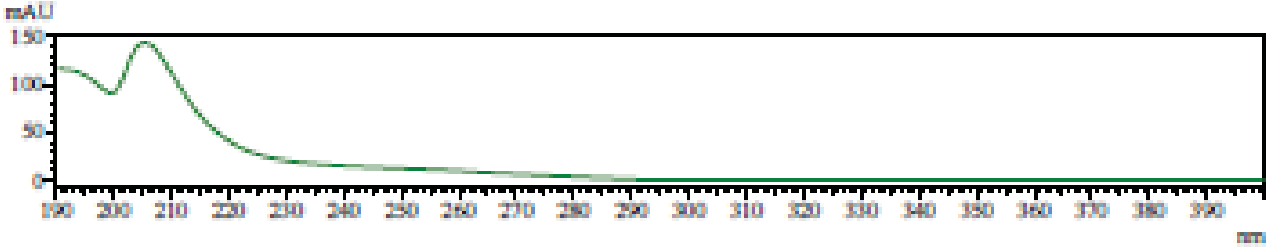
Chromatogram



UV Spectrum
Retention time = 9.847



UV Spectrum
Retention time = 13.103

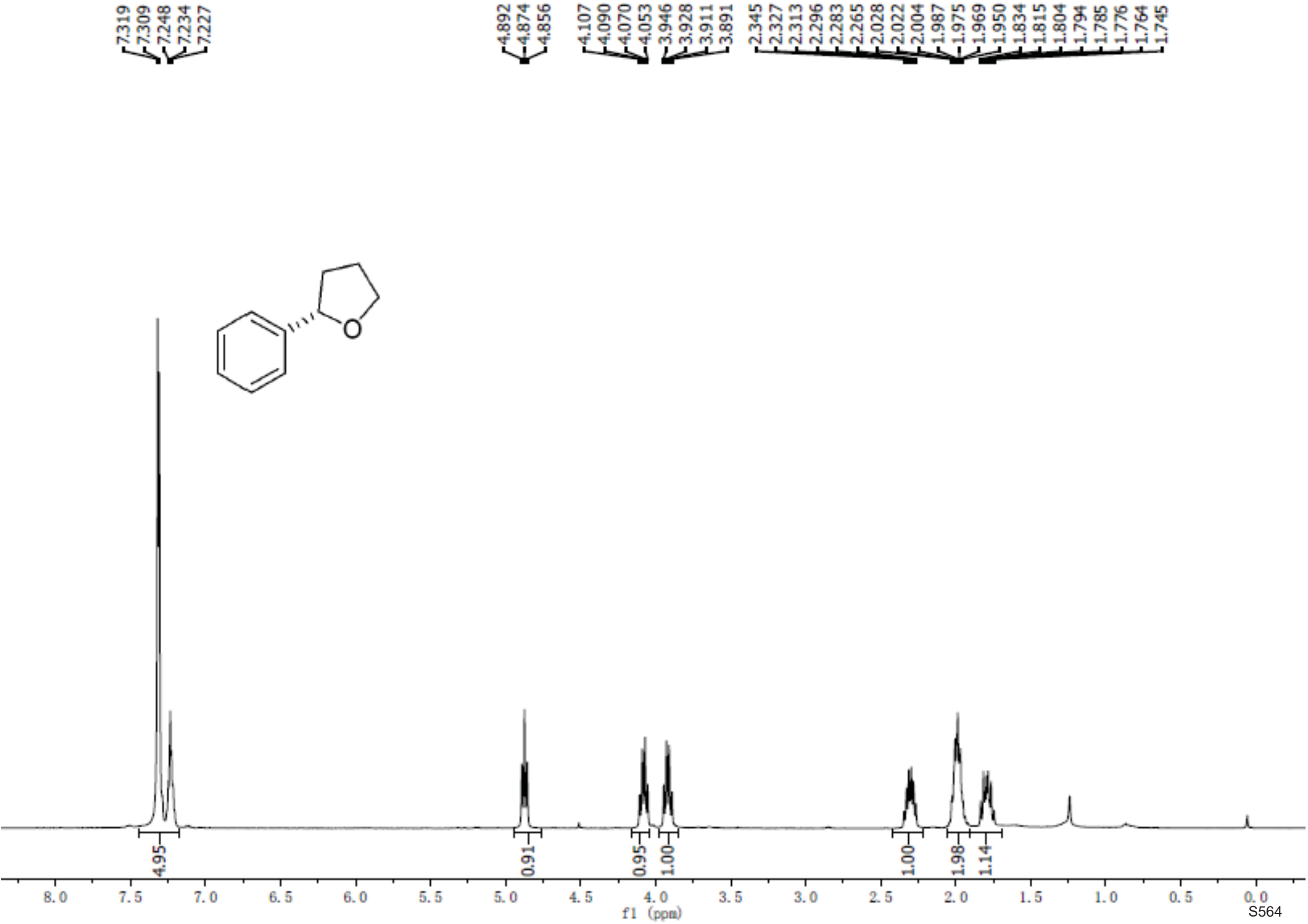


Peak Table

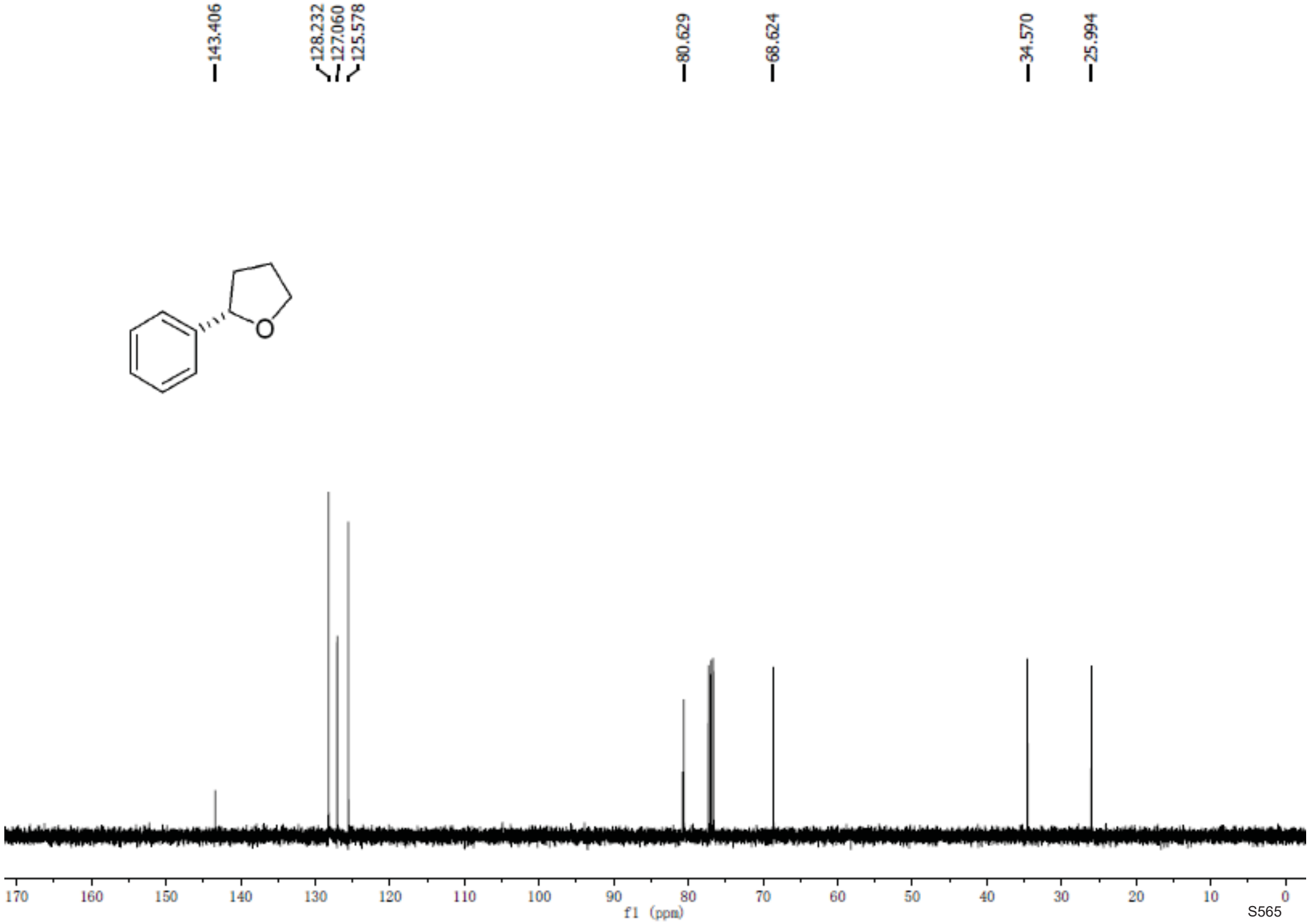
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	9.847	5956130	95.725
2	13.103	265997	4.275
Total		6222127	100.000

(*S*)-2-phenyltetrahydrofuran 2y



(*S*)-2-phenyltetrahydrofuran 2y

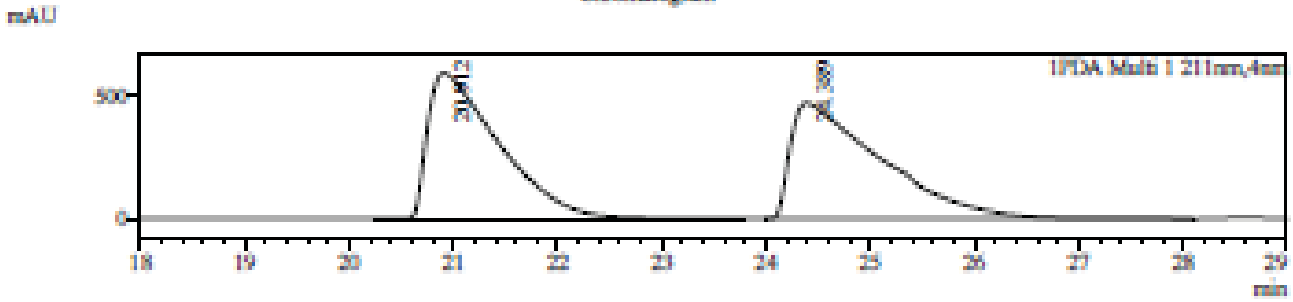


(*S*)-2-phenyltetrahydrofuran 2y

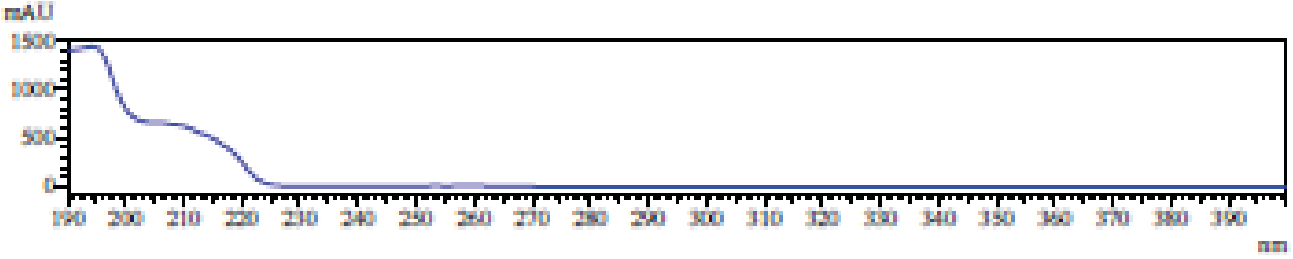
Sample Information

Sample Name	: YW-IV-89B-Ibu-ADH-0%-0.8ML
Sample ID	: YW-IV-89B-Ibu-ADH-0%-0.8ML
Data File	: YW-IV-89B-Ibu-ADH-0%-0.8ML.lcd
Method File	: YW-0%-0.8ml.lcm

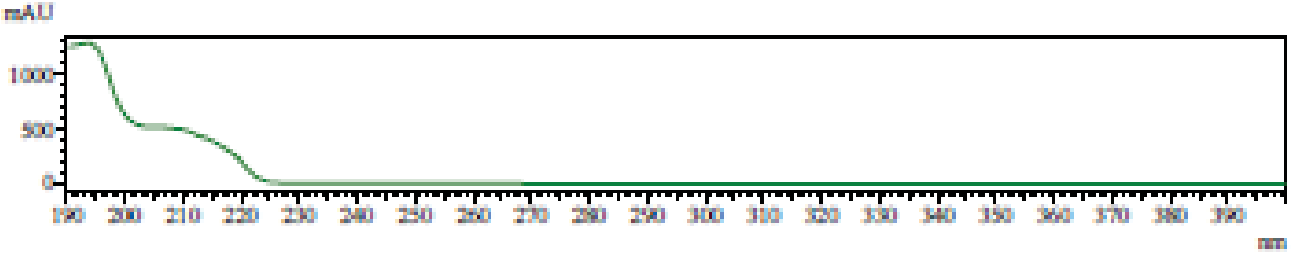
Chromatogram



UV Spectrum
Retention time = 20.912



UV Spectrum
Retention time = 24.389



Peak Table

PDA Ch1 211nm

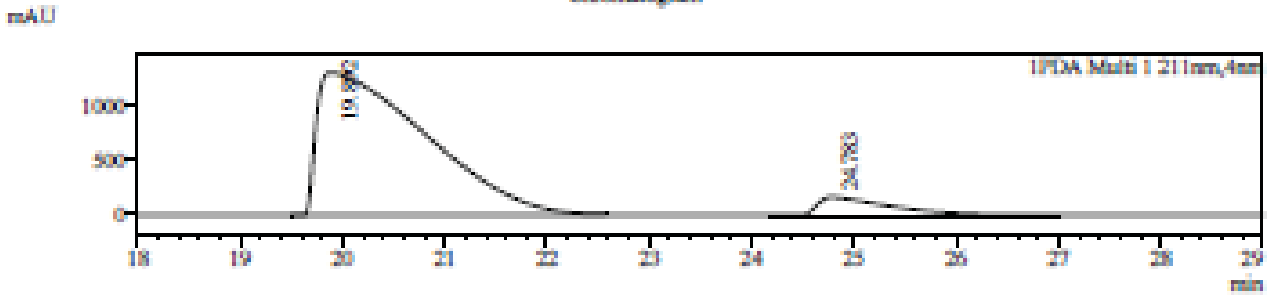
Peak#	Ret. Time	Area	Area%
1	20.912	27749386	49.717
2	24.389	28065521	50.283
Total		55814907	100.000

(*S*)-2-phenyltetrahydrofuran 2y

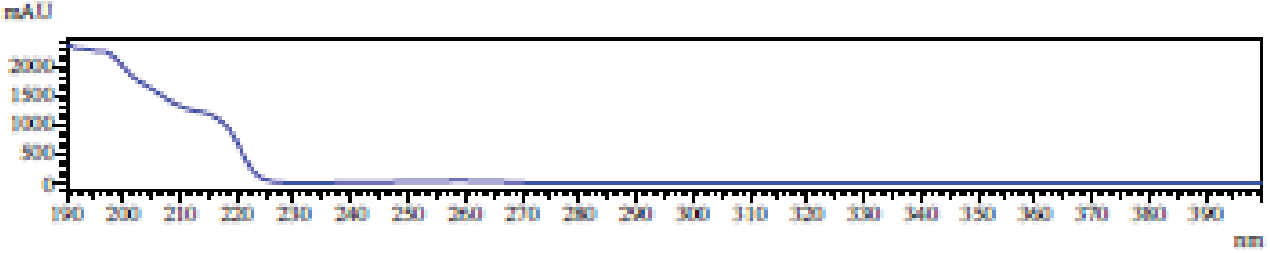
Sample Information

Sample Name	: YW-IV-89-ADH-0%-0.8ML
Sample ID	: YW-IV-89-ADH-0%-0.8ML
Data File	: YW-IV-89-ADH-0%-0.8ML001.lcd
Method File	: YW-0%-0.8ml.lcm

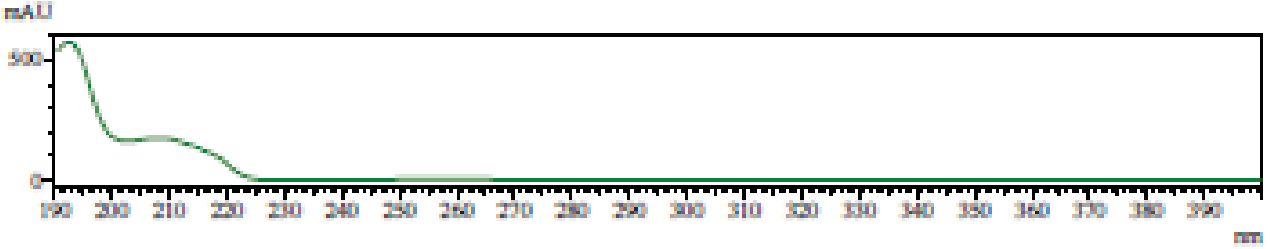
Chromatogram



UV Spectrum
Retention time = 19.892



UV Spectrum
Retention time = 24.783

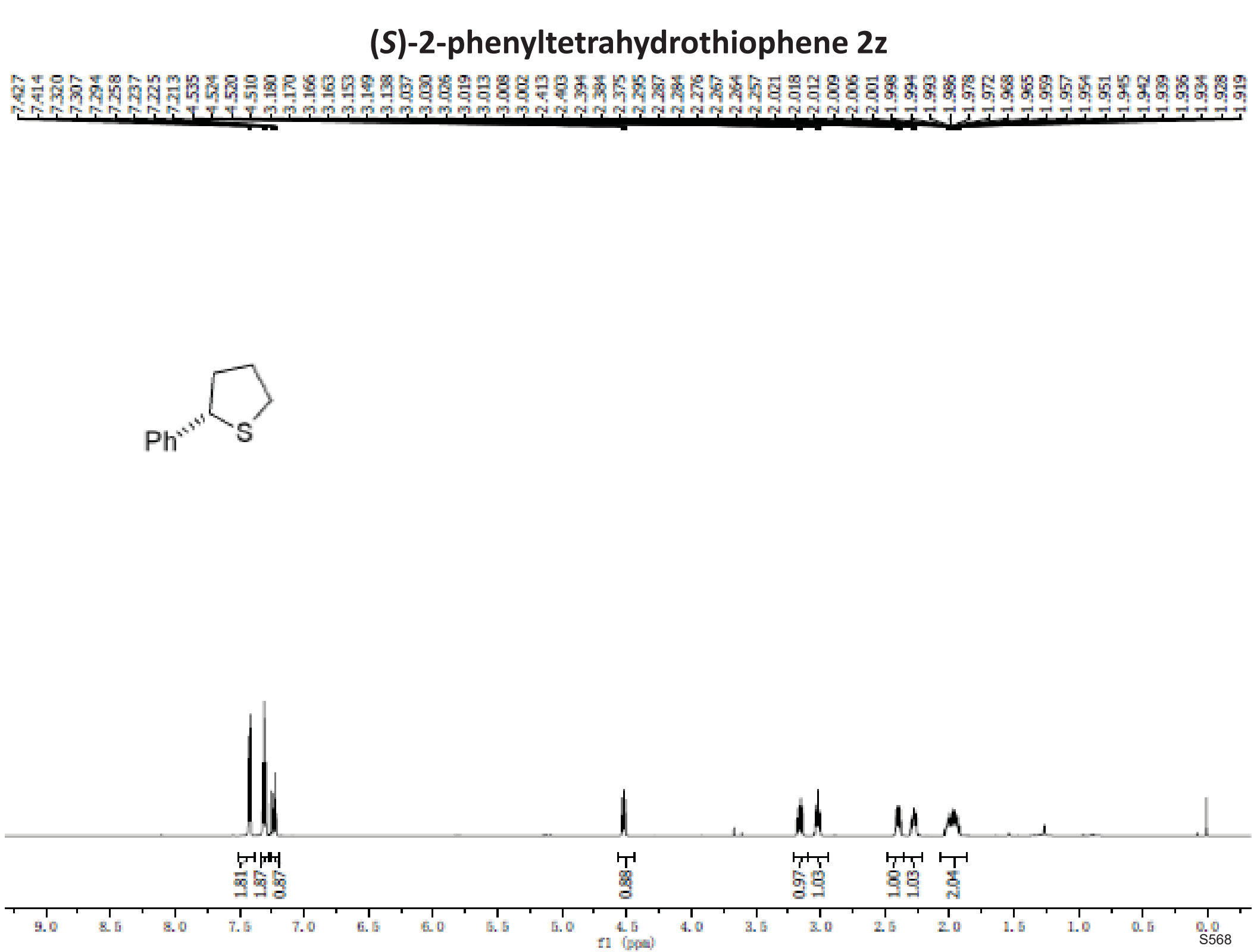


Peak Table

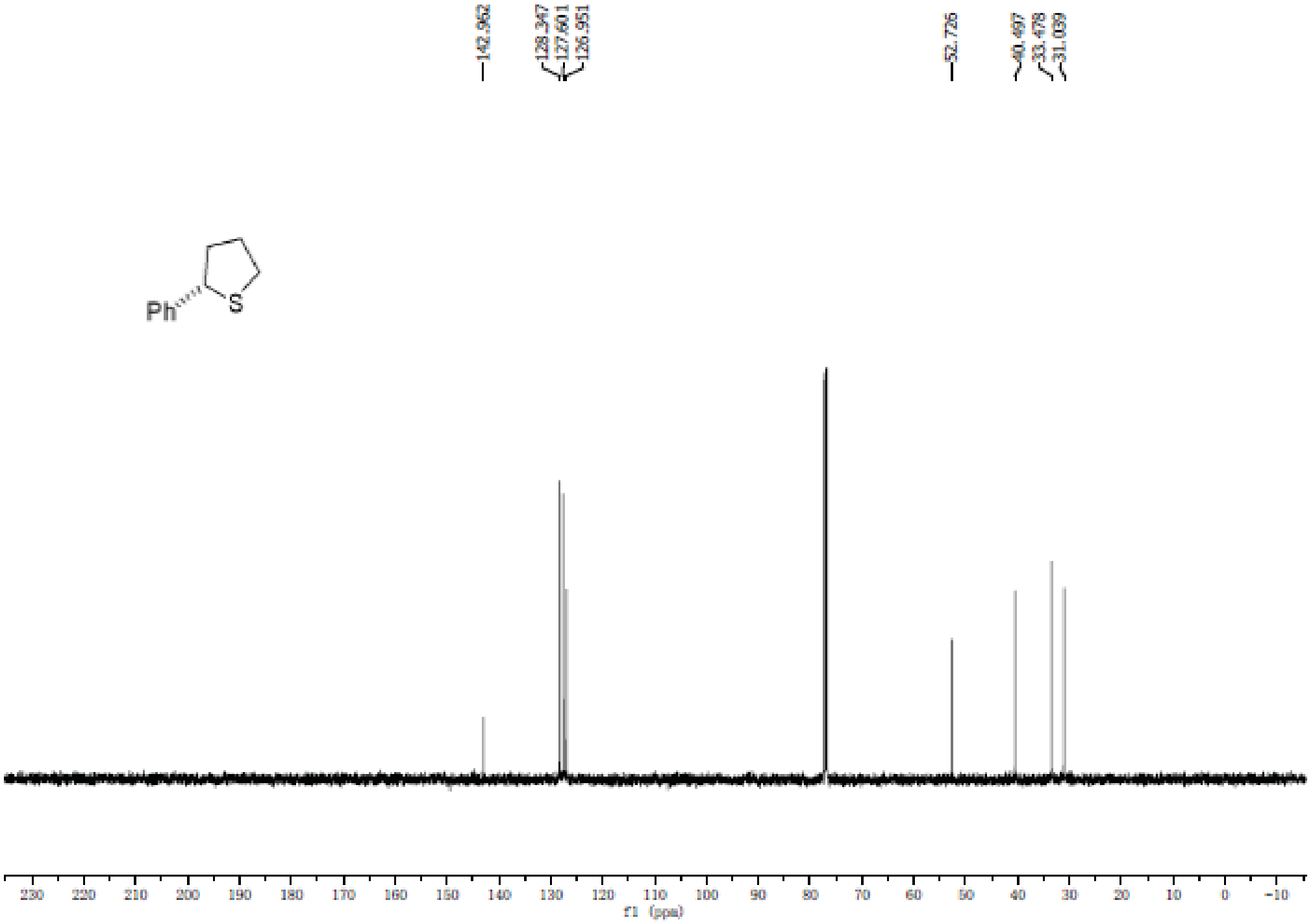
PDA Ch1 211nm

Peak#	Ret. Time	Area	Area%
1	19.892	97025230	92.413
2	24.783	7966048	7.587
Total		104991278	100.000

(*S*)-2-phenyltetrahydrothiophene 2z



(*S*)-2-phenyltetrahydrothiophene 2z

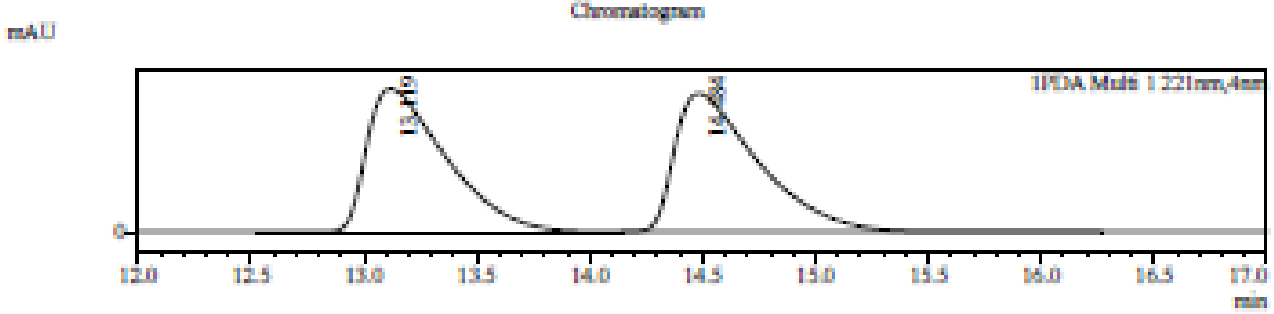


(*S*)-2-phenyltetrahydrothiophene 2z

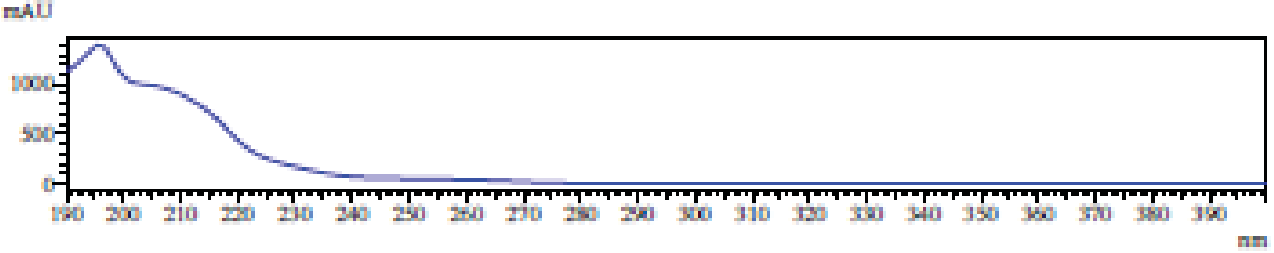
Sample Information

Sample Name : YW-IV-152a-ODH-0%-1.0ML
Sample ID : YW-IV-152a-ODH-0%-1.0ML
Data File : YW-IV-152a-ODH-0%-1.0ML001.lcd
Method File : YW-0%-1.0ml.lcm

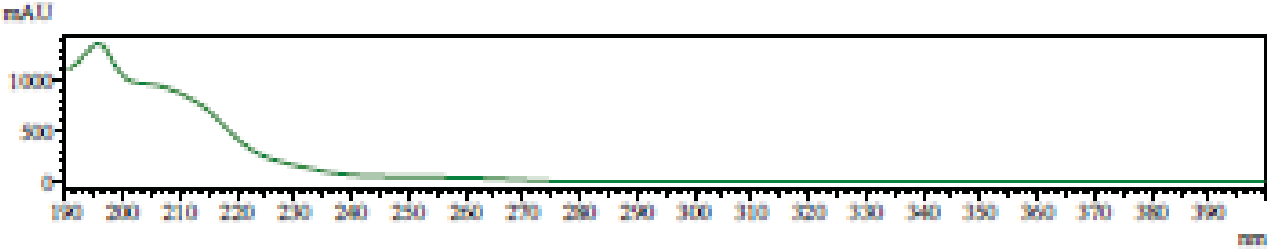
Chromatogram



UV Spectrum
Retention time = 13.119



UV Spectrum
Retention time = 14.484



Peak Table

PDA Ch1 221nm

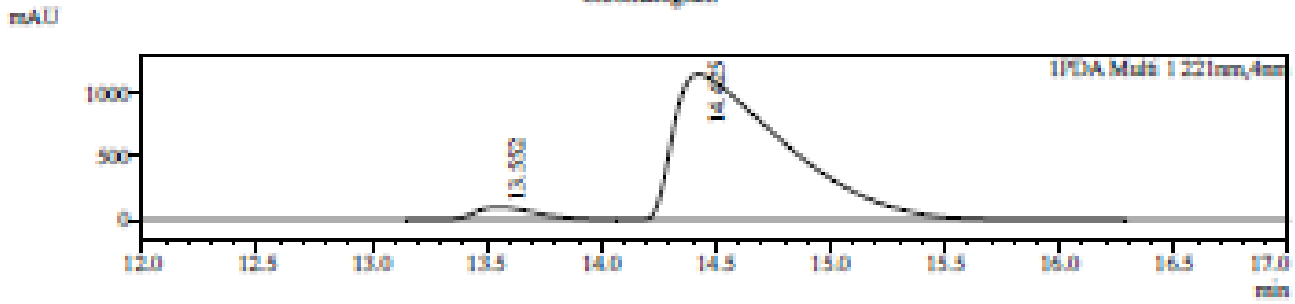
Peak#	Ret. Time	Area	Area%
1	13.119	10121942	49.525
2	14.484	10316236	50.475
Total		20438178	100.000

(*S*)-2-phenyltetrahydrothiophene 2z

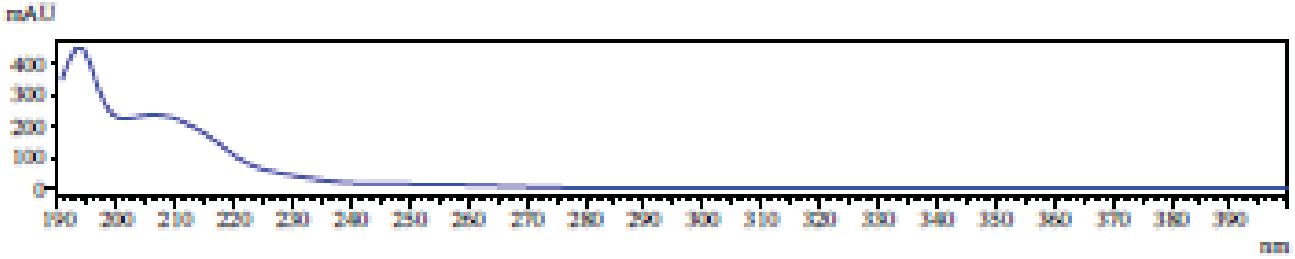
Sample Information

Sample Name	: YW-IV-152B-ODH-0%-1.0ML
Sample ID	: YW-IV-152B-ODH-0%-1.0ML
Data File	: YW-IV-152B-ODH-0%-1.0ML001.lcd
Method File	: YW-0%-1.0ml.lcm

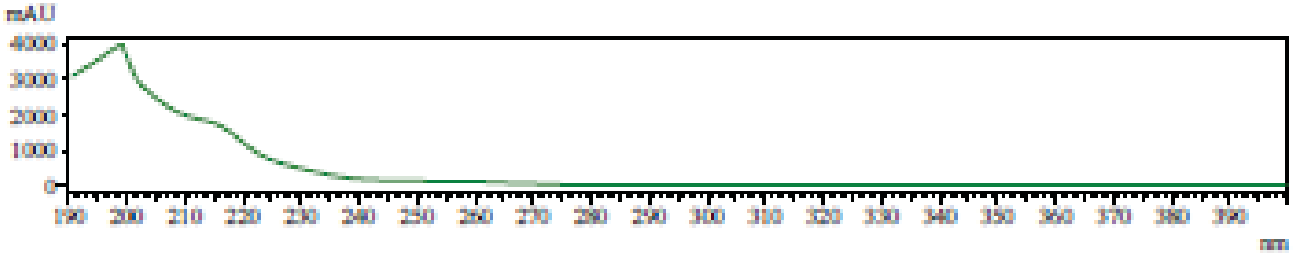
Chromatogram



UV Spectrum
Retention time = 13.552



UV Spectrum
Retention time = 14.425

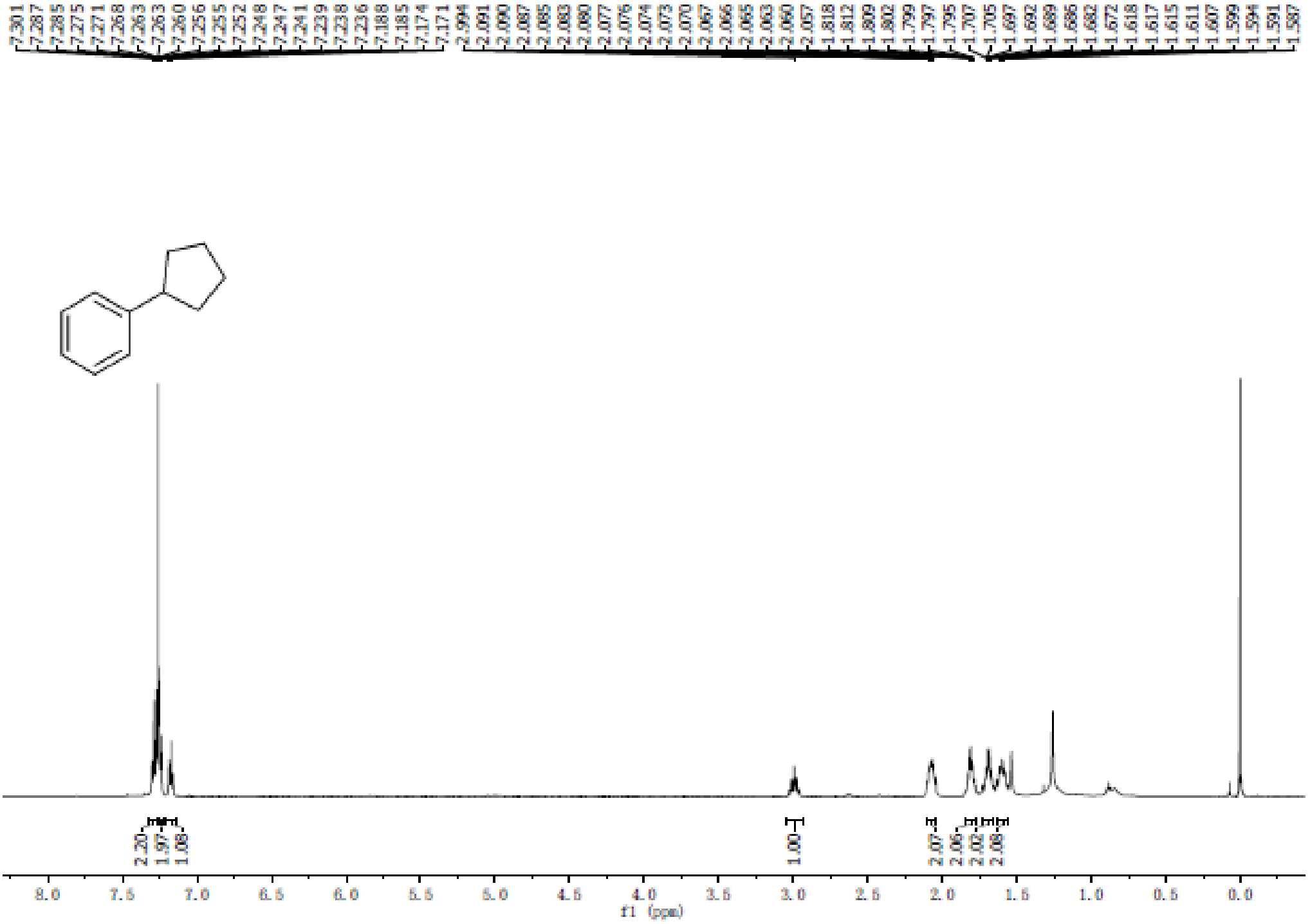


Peak Table

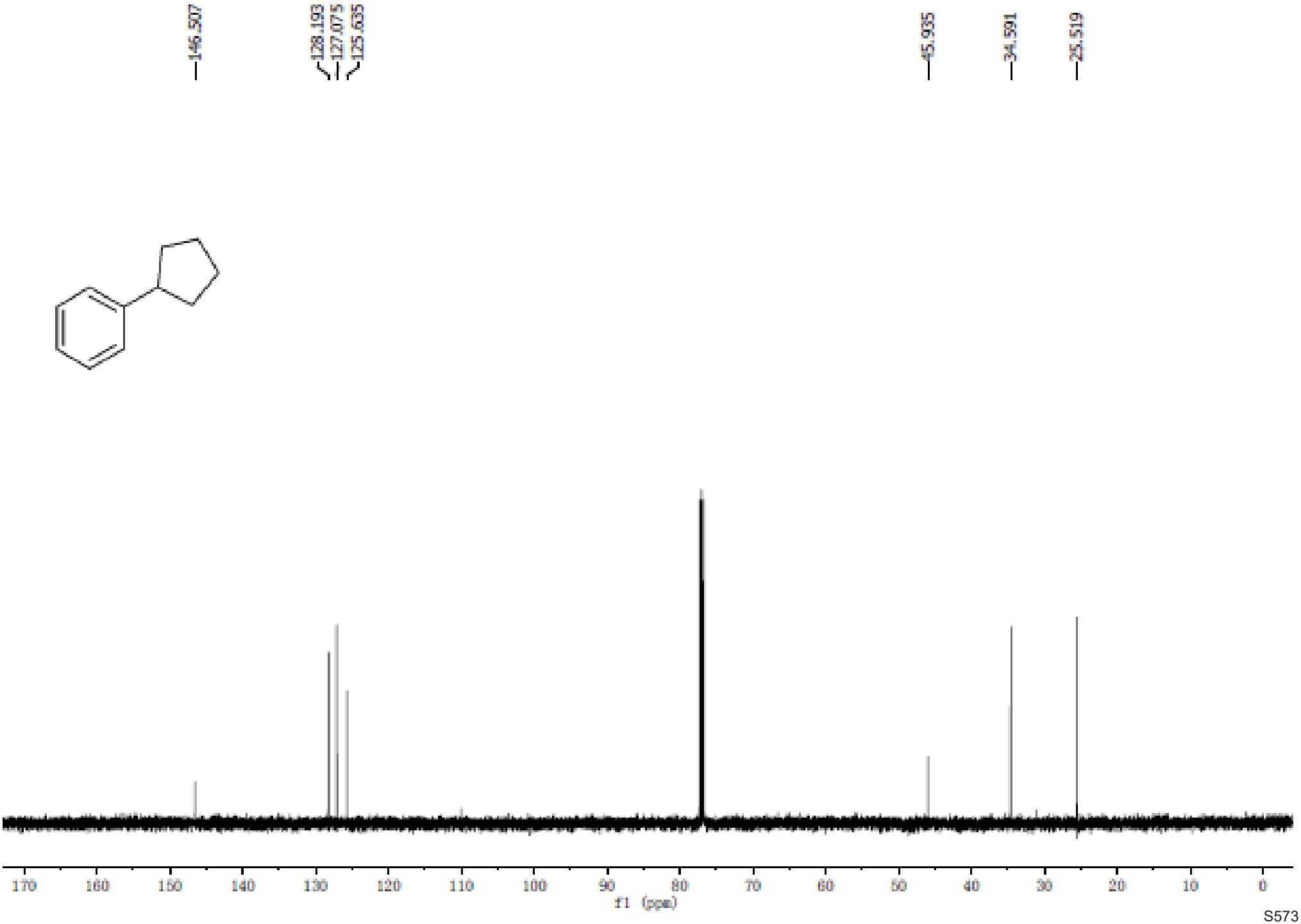
PDA Ch1 221nm

Peak#	Ret. Time	Area	Area%
1	13.552	1826329	4.544
2	14.425	38369817	95.456
Total		40196145	100.000

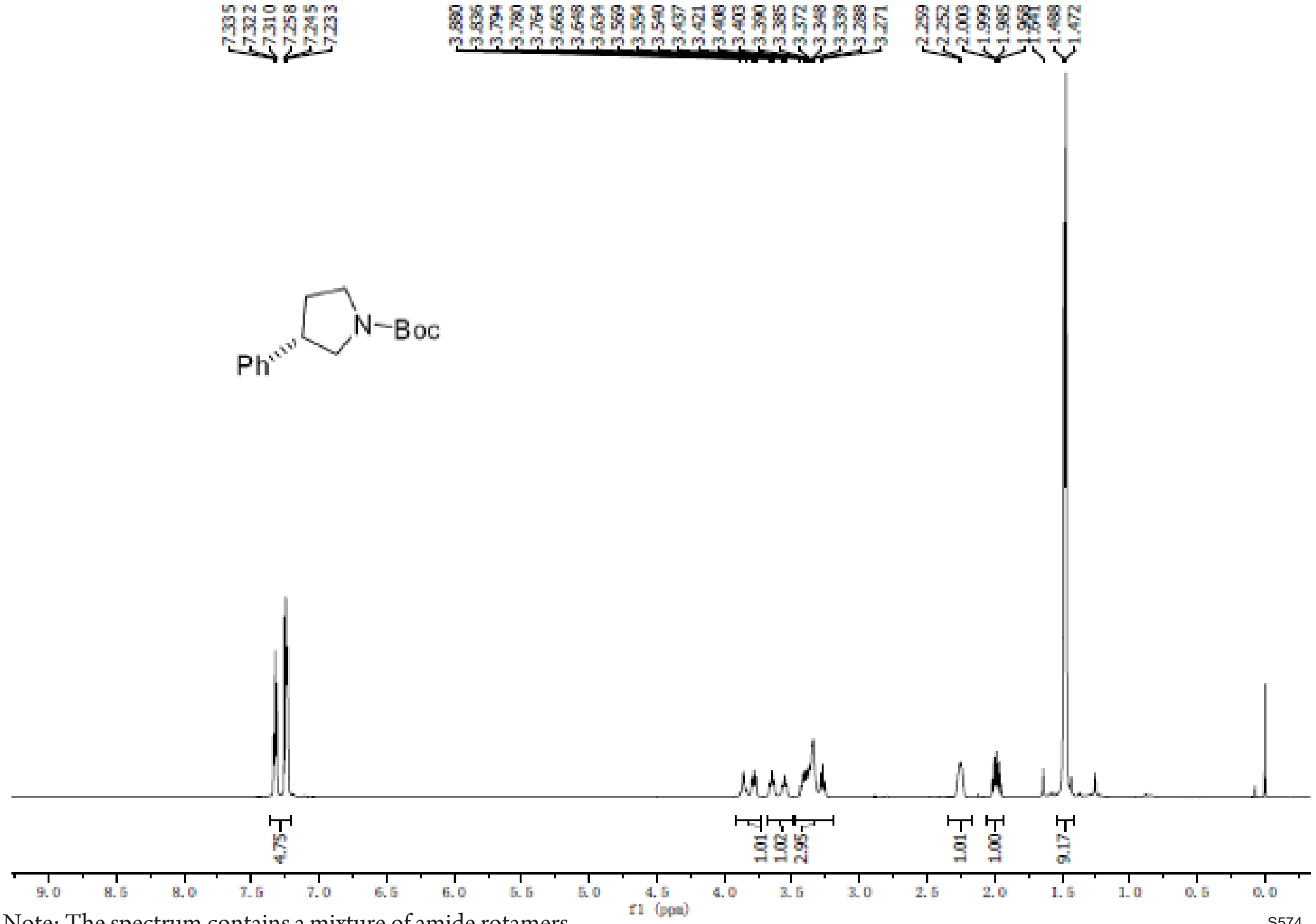
cyclopentylbenzene 2aa



cyclopentylbenzene 2aa

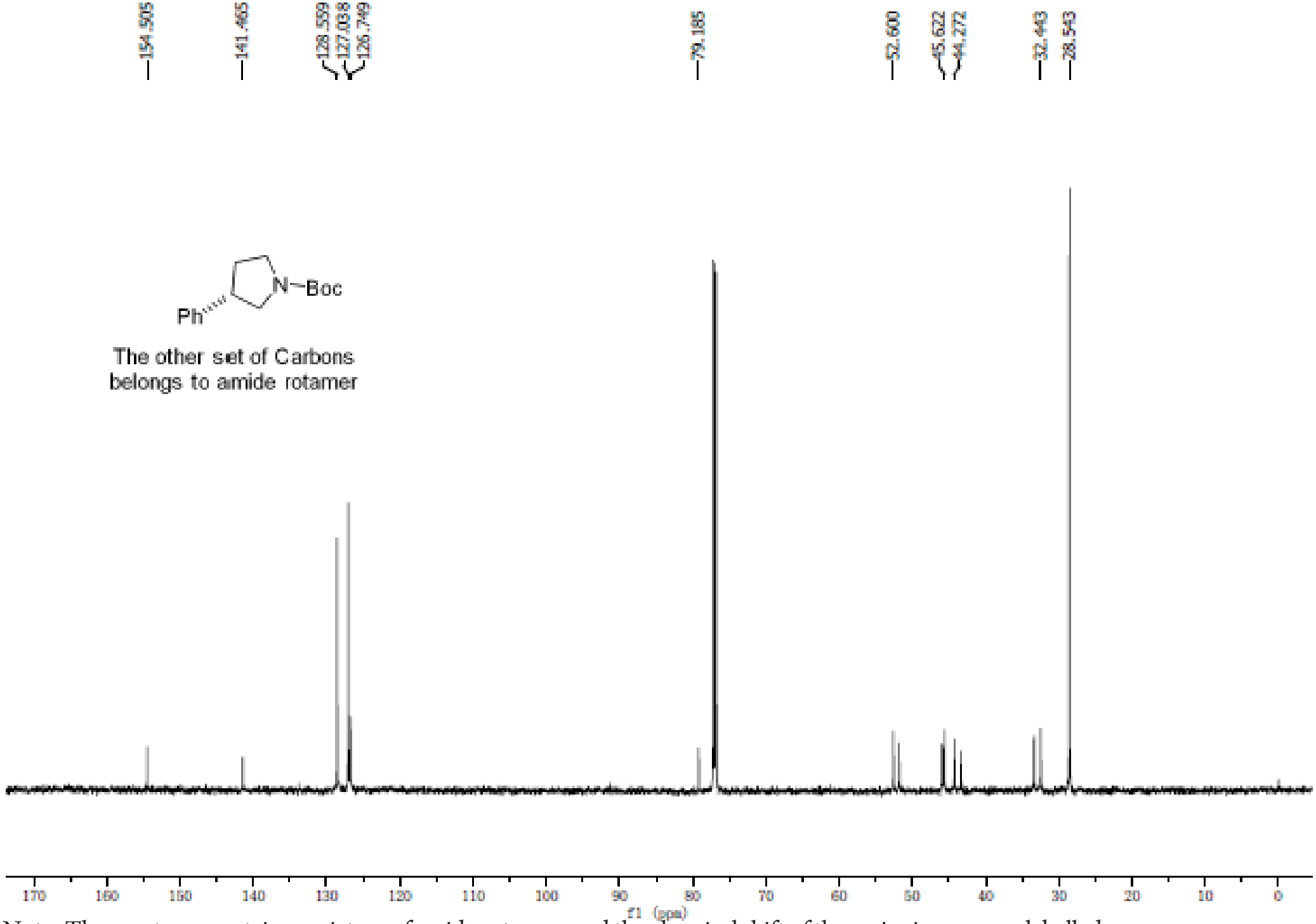


tert-butyl (*S*)-3-phenylpyrrolidine-1-carboxylate 2ab



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-3-phenylpyrrolidine-1-carboxylate 2ab



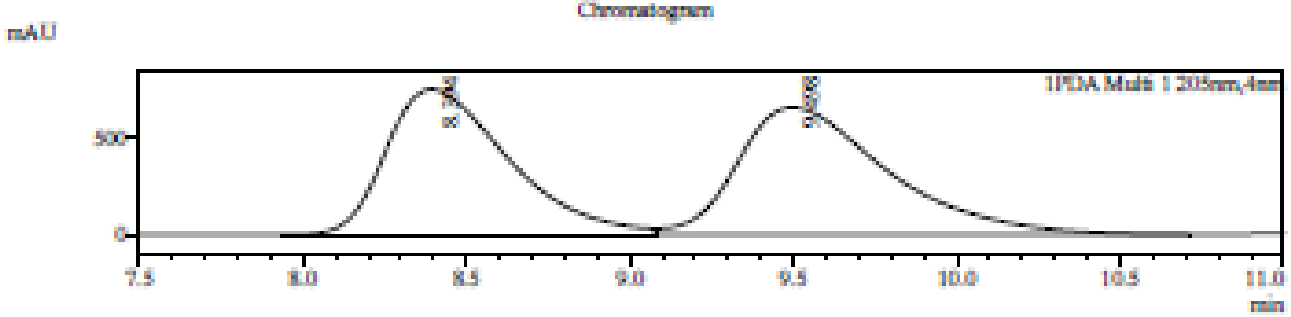
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-3-phenylpyrrolidine-1-carboxylate 2ab

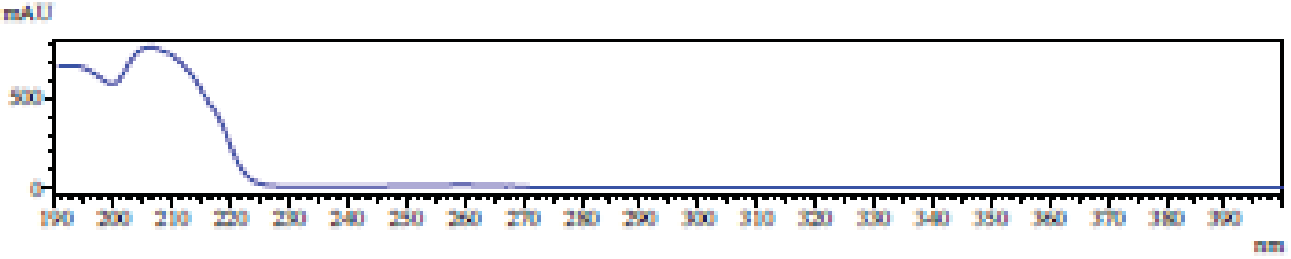
Sample Information

Sample Name	: YW-IV-211a-OJH-1%-1.0ML
Sample ID	: YW-IV-211a-OJH-1%-1.0ML
Data File	: YW-IV-211a-OJH-1%-1.0ML001.lcd
Method File	: YW-1%-1.0ml.lcm

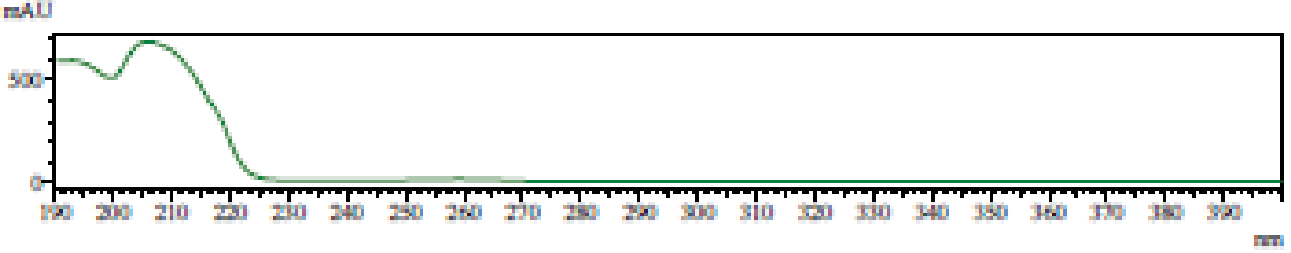
Chromatogram



UV Spectrum
Retention time = 8.394



UV Spectrum
Retention time = 9.498



Peak Table

PDA Ch1 205nm

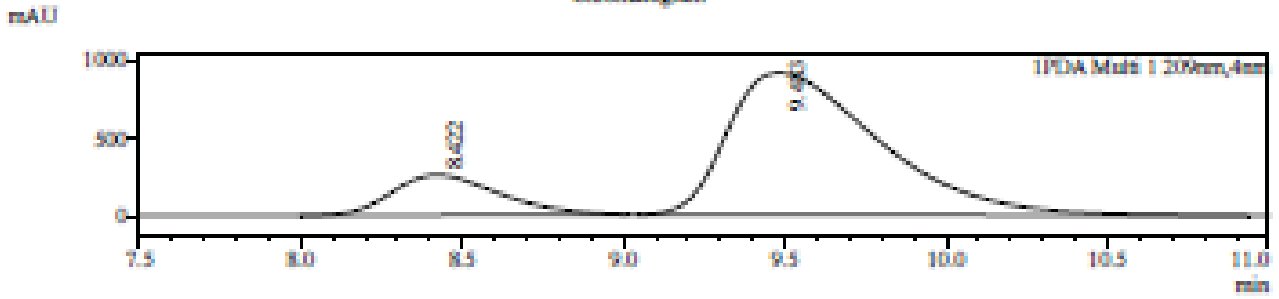
Peak#	Ret. Time	Area	Area%
1	8.394	19289115	48.266
2	9.498	20674898	51.734
Total		39964013	100.000

tert-butyl (*S*)-3-phenylpyrrolidine-1-carboxylate 2ab

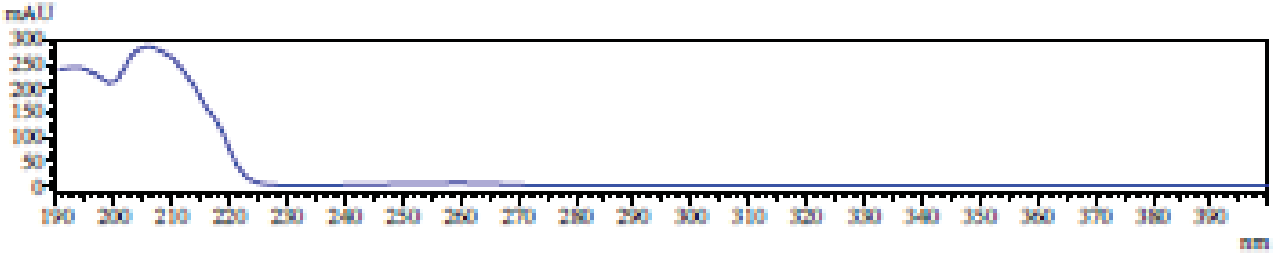
Sample Information

Sample Name	: YW-IV-211B-OJH-1%-1.0ML001
Sample ID	: YW-IV-211B-OJH-1%-1.0ML001
Data File	: YW-IV-211B-OJH-1%-1.0ML001.lcd
Method File	: YW-1%-1.0ml.lcm

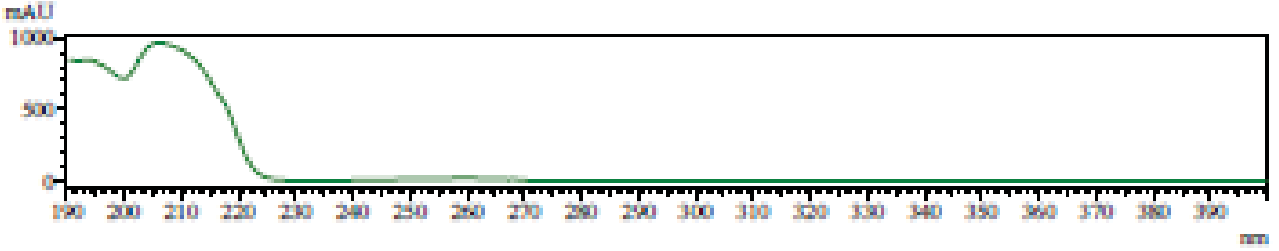
Chromatogram



UV Spectrum
Retention time = 8.422



UV Spectrum
Retention time = 9.483

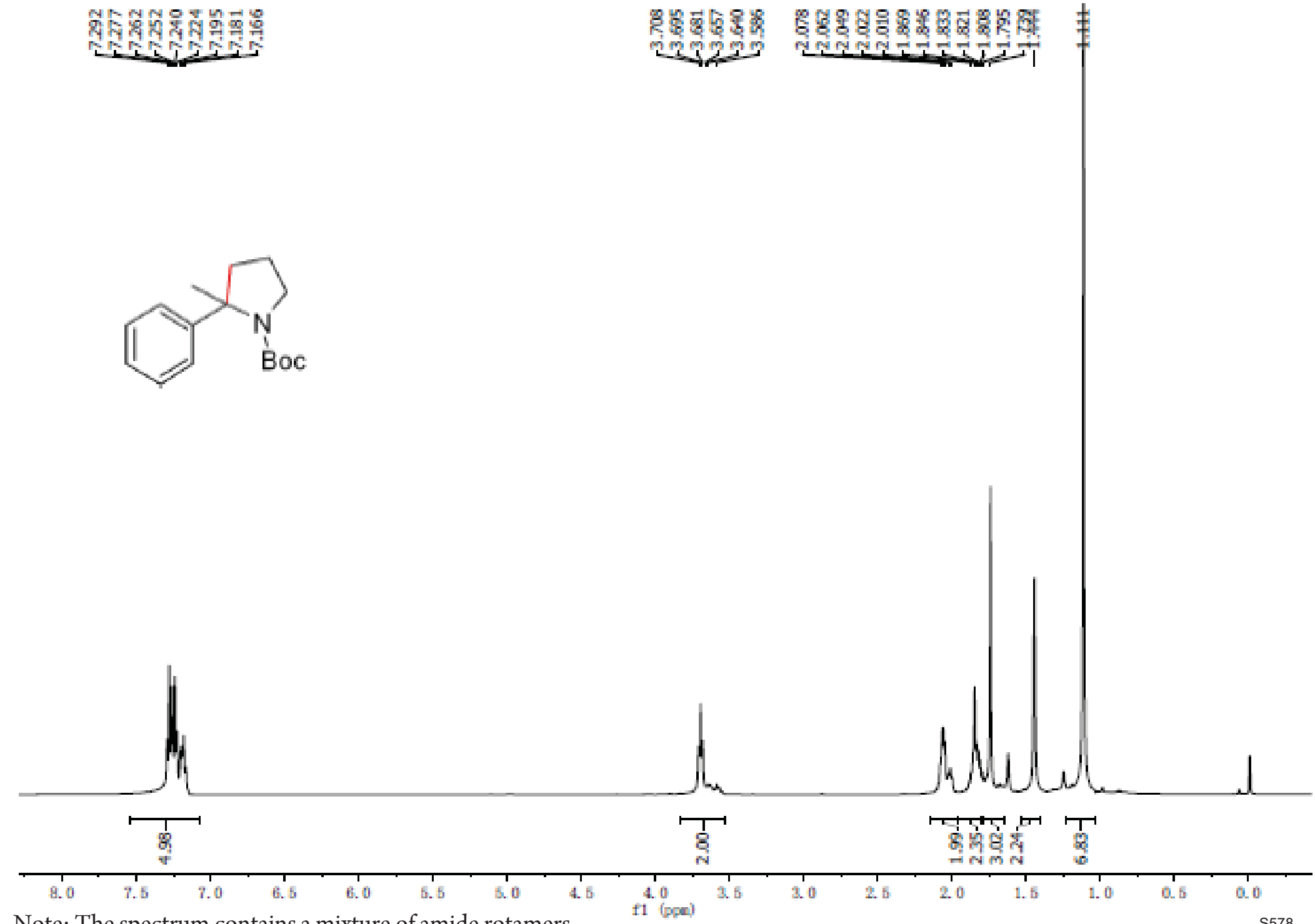


Peak Table

PDA Ch1 209nm

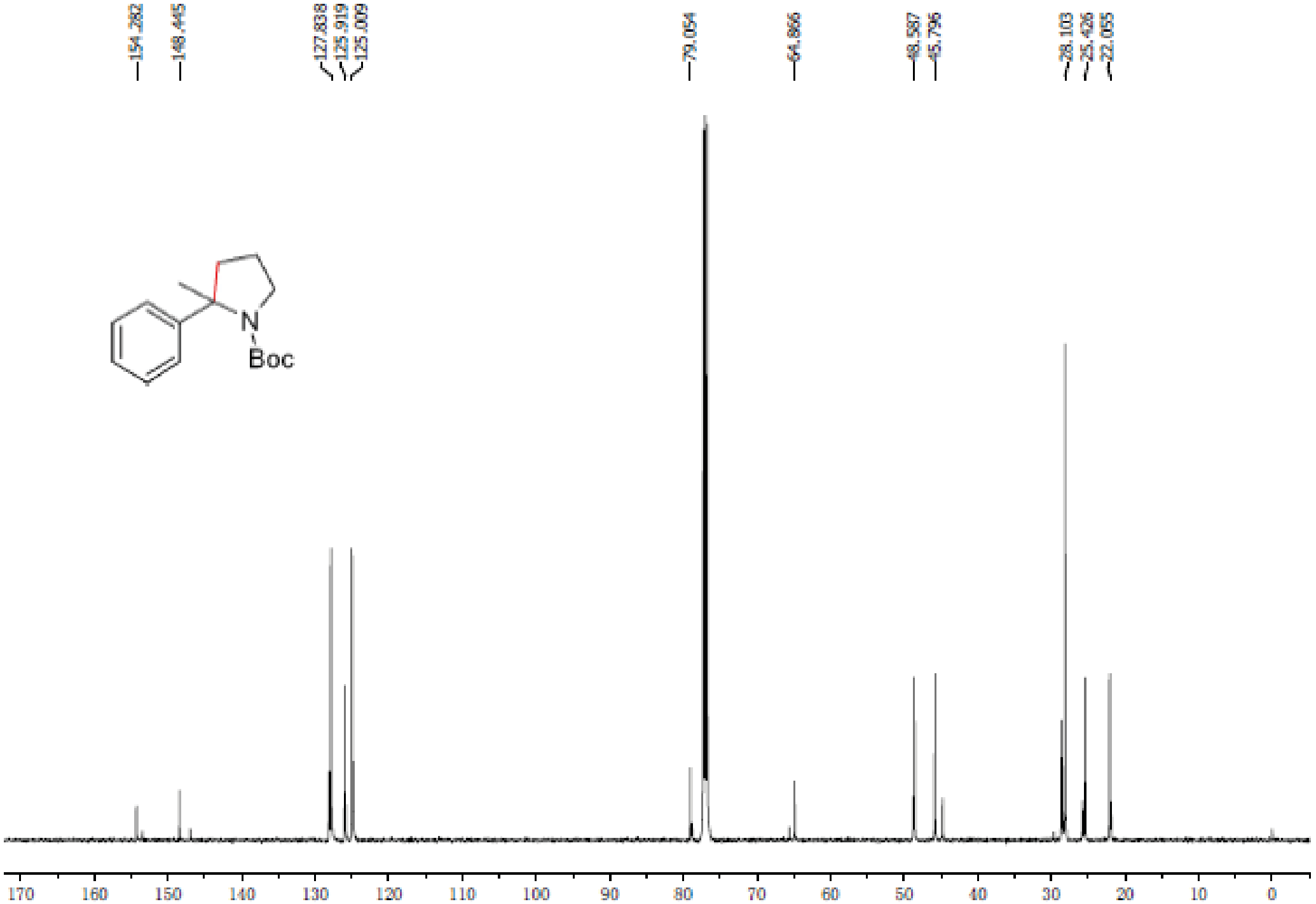
Peak#	Ret. Time	Area	Area%
1	8.422	5999661	16.798
2	9.483	29716364	83.202
Total		35716024	100.000

tert-butyl (*S*)-2-methyl-2-phenylpyrrolidine-1-carboxylate 5a



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (*S*)-2-methyl-2-phenylpyrrolidine-1-carboxylate 5a



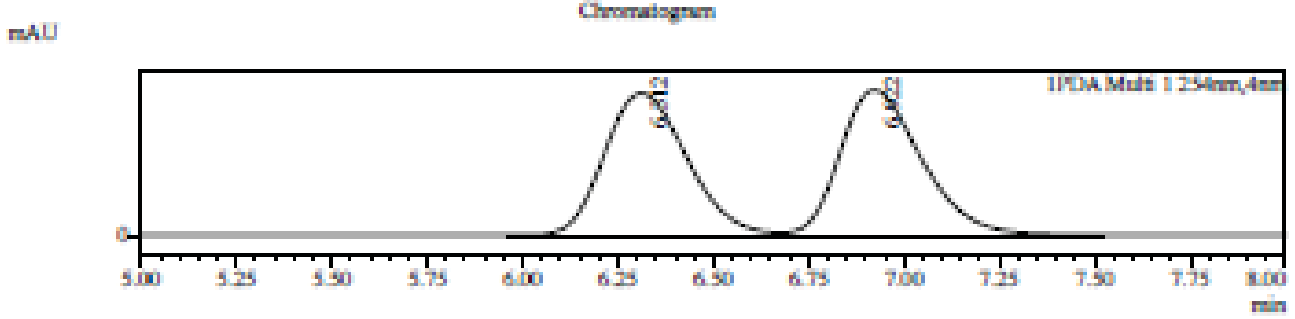
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (*S*)-2-methyl-2-phenylpyrrolidine-1-carboxylate 5a

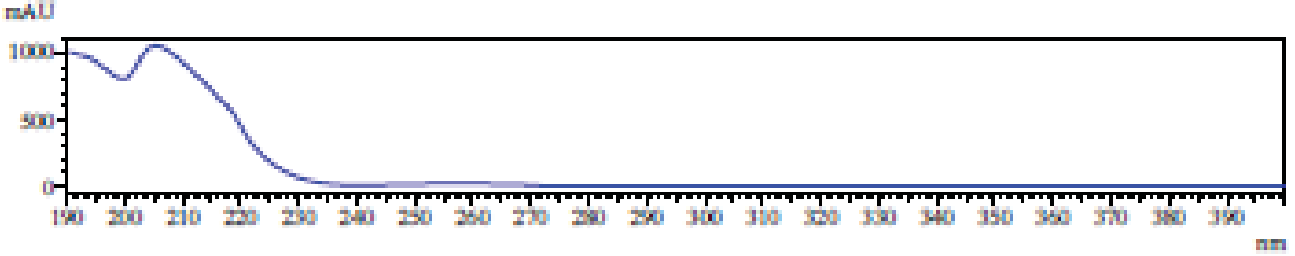
Sample Information

Sample Name	: YW-IV-1A-ODH-1%-1ML001
Sample ID	: YW-IV-1A-ODH-1%-1ML001
Data File	: YW-IV-1A-ODH-1%-1ML001.lcd
Method File	: YW-1%-1.0ml.lcm

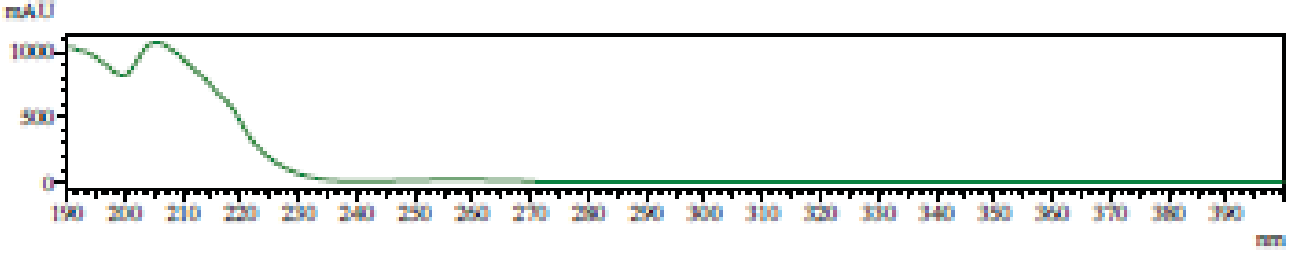
Chromatogram



UV Spectrum
Retention time = 6.312



UV Spectrum
Retention time = 6.922



Peak Table

PDA Ch1 254nm

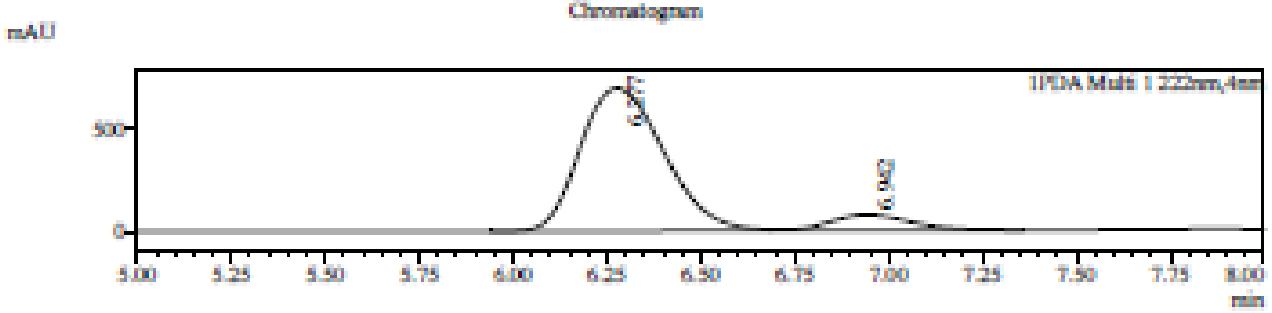
Peak#	Ret. Time	Area	Area%
1	6.312	294717	49.692
2	6.922	298369	50.308
Total		593085	100.000

tert-butyl (*S*)-2-methyl-2-phenylpyrrolidine-1-carboxylate 5a

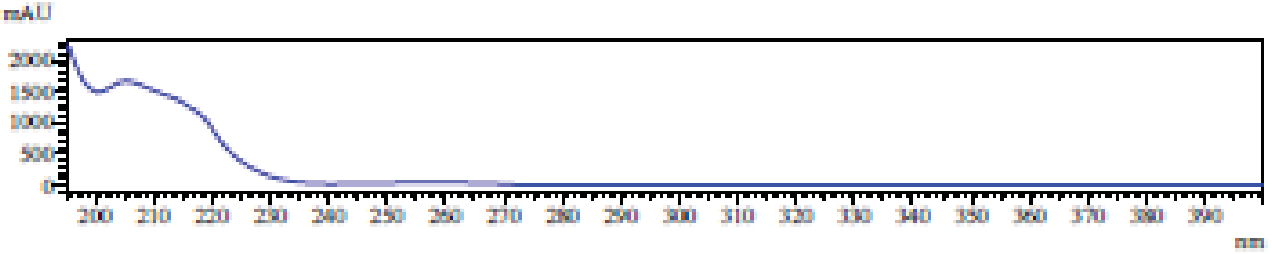
Sample Information

Sample Name	: YW-IV-251-ODH-1%-1ML001
Sample ID	: YW-IV-251-ODH-1%-1ML001
Data File	: YW-IV-251-ODH-1%-1ML001.lcd
Method File	: YW-1%-1.0ml.lcm

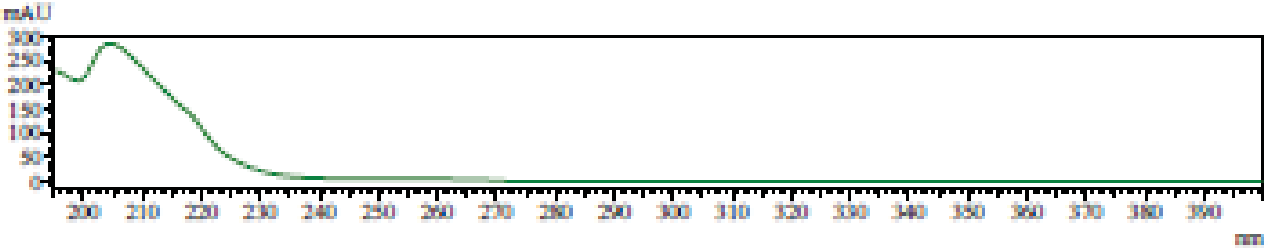
Chromatogram



UV Spectrum
Retention time = 6.277



UV Spectrum
Retention time = 6.942

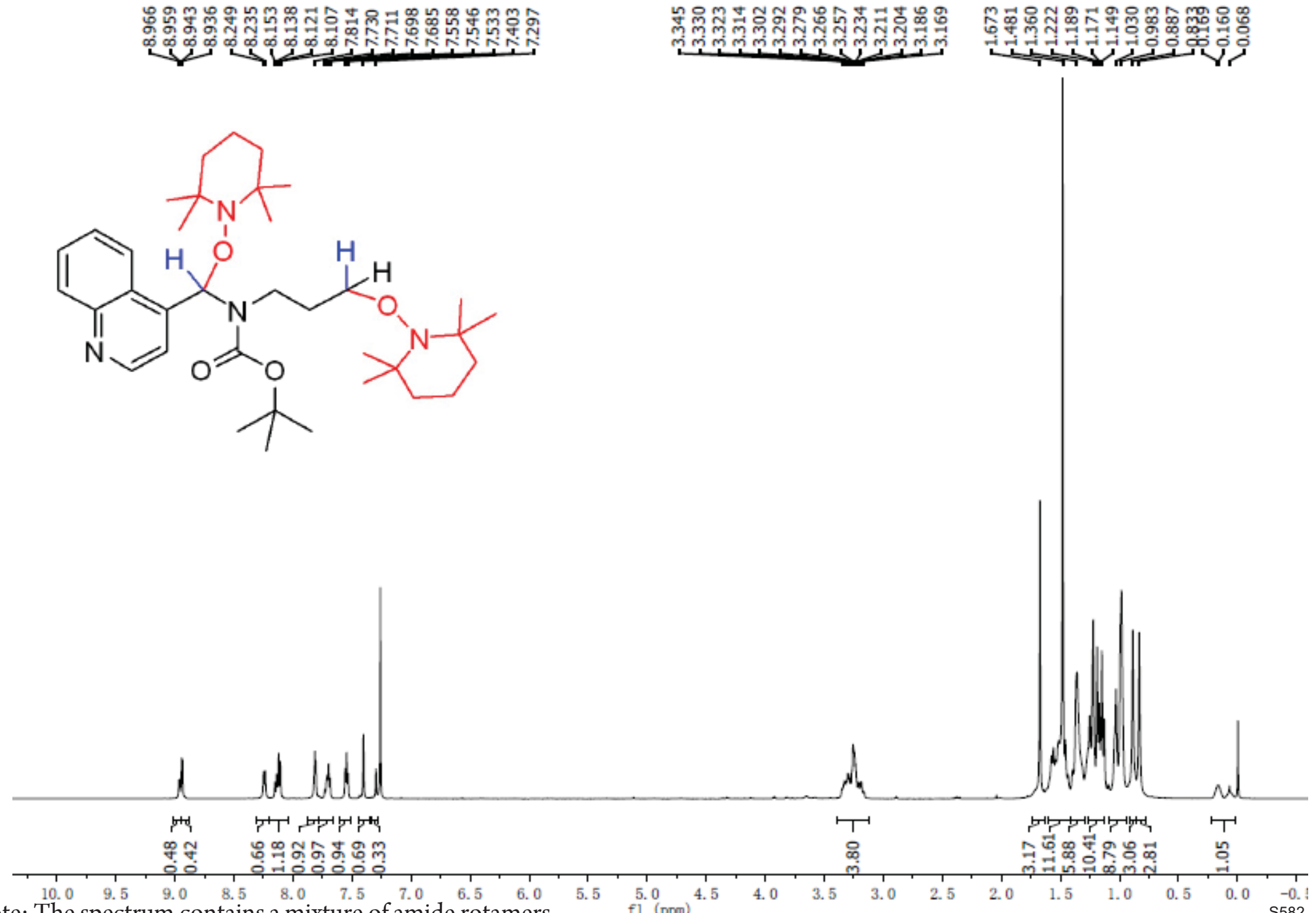


Peak Table

PDA Ch1 222nm

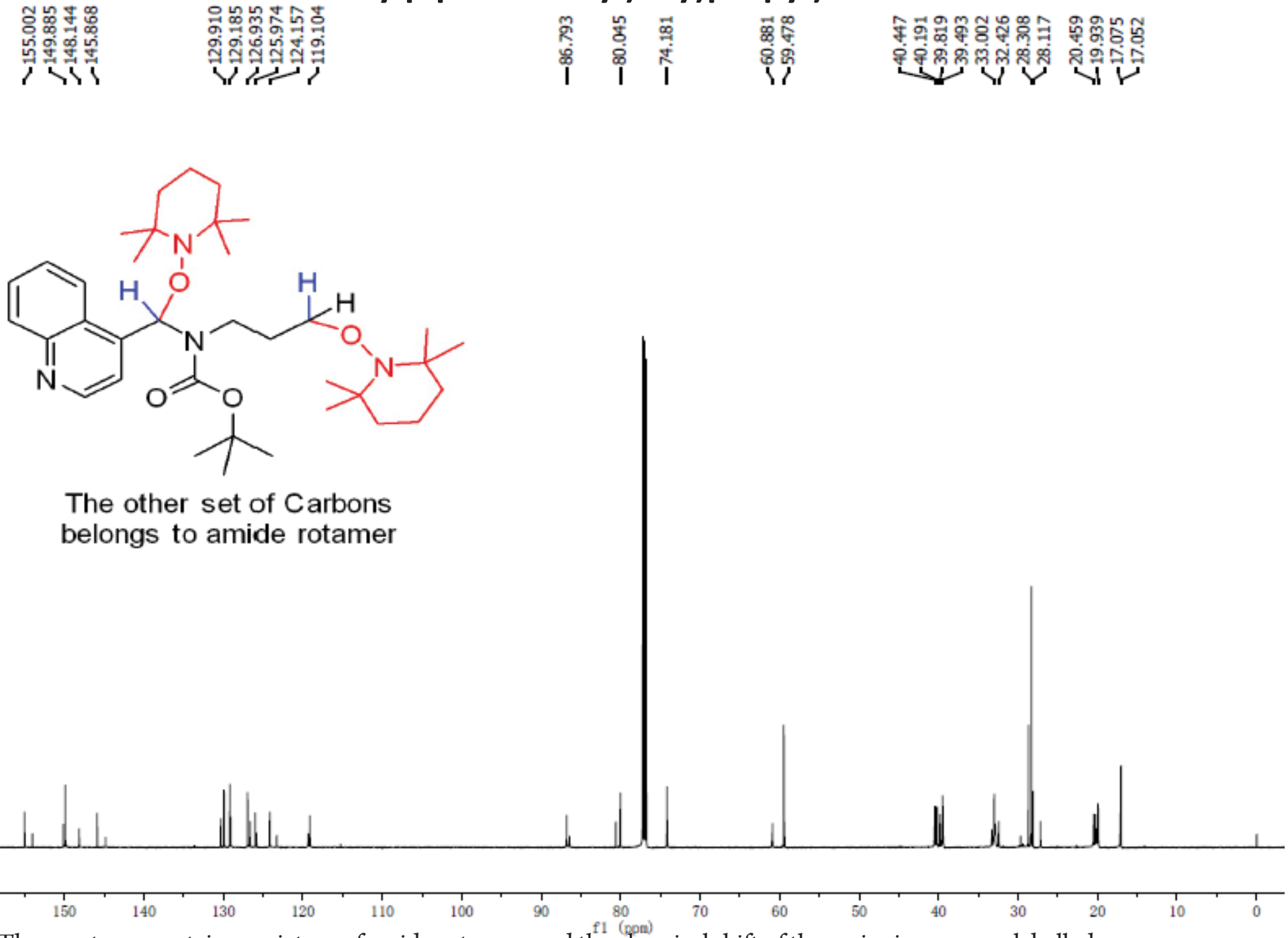
Peak#	Ret. Time	Area	Area%
1	6.277	10586236	90.549
2	6.942	1104905	9.451
Total		11691141	100.000

tert-butyl (quinolin-4-yl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)carbamate 3t



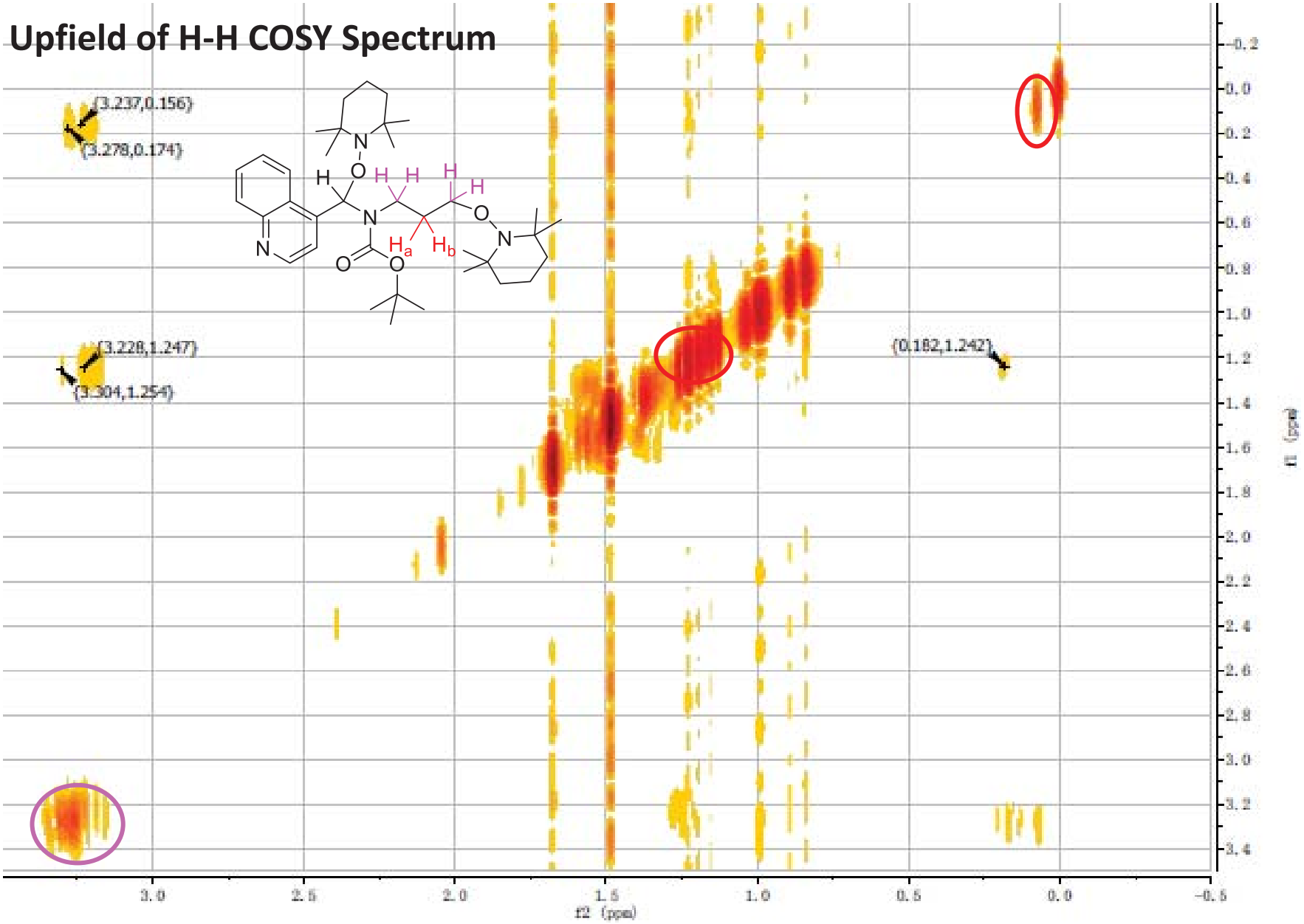
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (quinolin-4-yl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)carbamate 3t



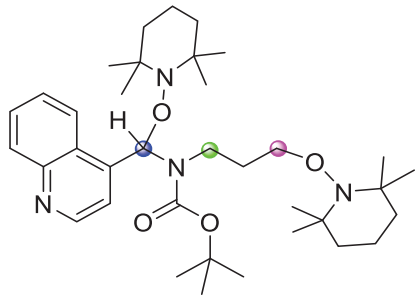
Note: The spectrum contains a mixture of amide rotamers and the chemical shift of the major isomer was labelled .

tert-butyl (quinolin-4-yl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)carbamate 3t



Note: The hydrogens in pink are correlated with the ones in red, indicating either H_a or H_b has a chemical shift around 0.16 ppm while the other (in red) is around 1.24 ppm.

tert-butyl (quinolin-4-yl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)carbamate 3t

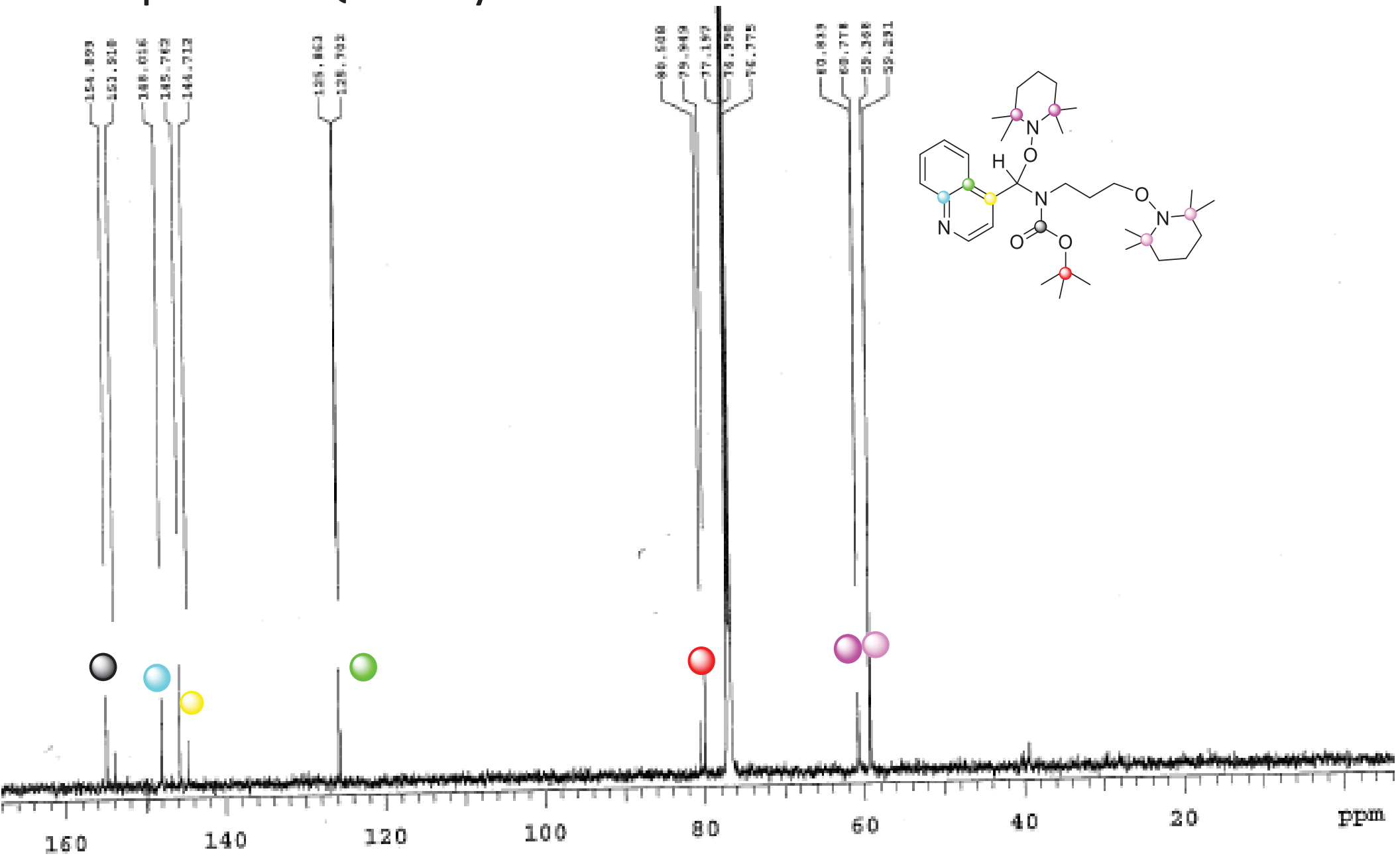


2D HSQC Experiment

Note: From HSQC, it is confirmed that the protons with chemical shift around 3.17 – 3.35 ppm are attached to two different carbons, as highlighted in green and pink balls. Moreover, the proton with chemical shift around 7.40 ppm is highly deshielded by two heteroatom and sp^2 carbon, and it is confirmed from HSQC that the proton is from the benzylic methine group.

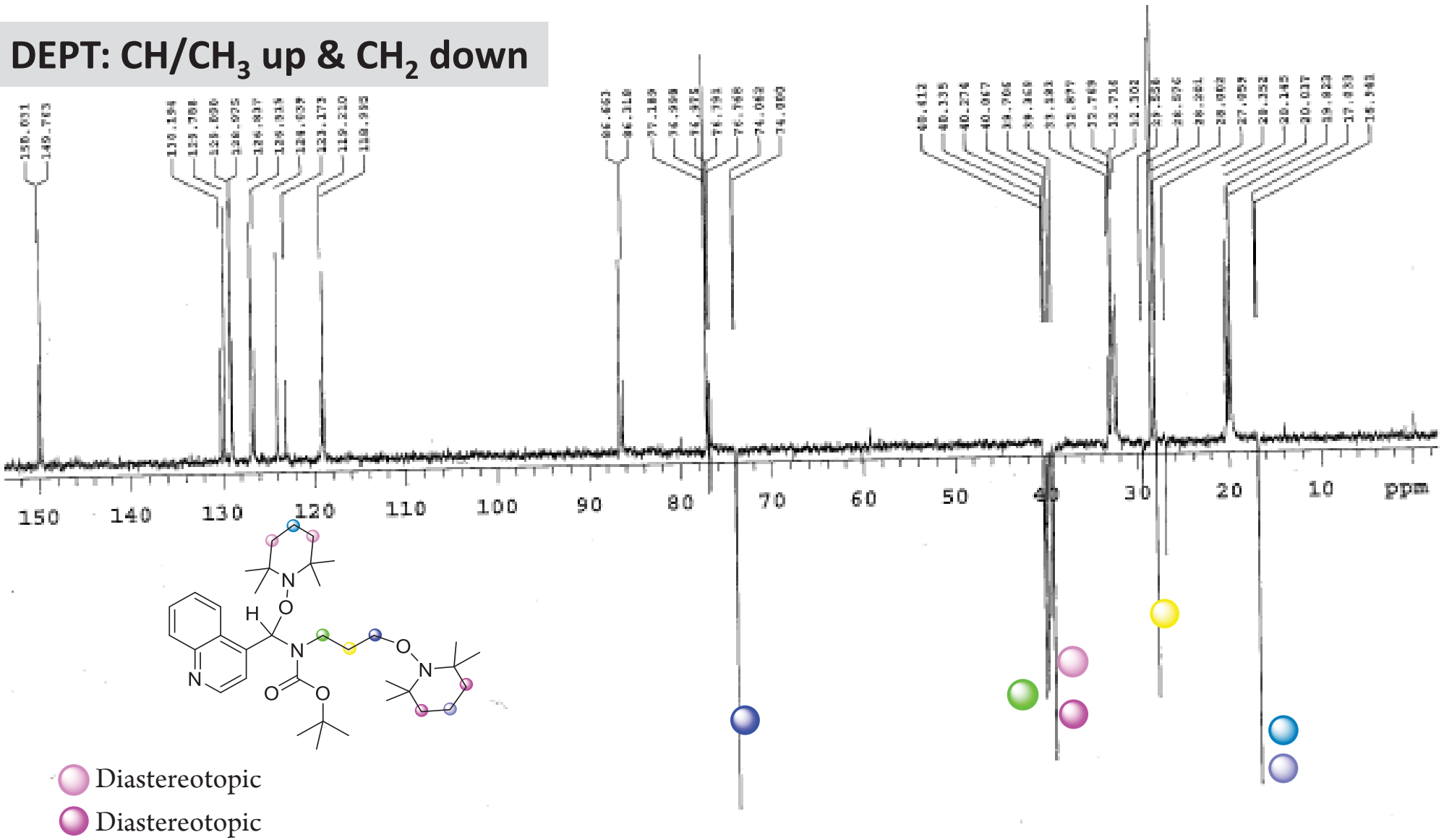
tert-butyl (quinolin-4-yl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)carbamate 3t

DEPT Experiment of Quaternary Carbons



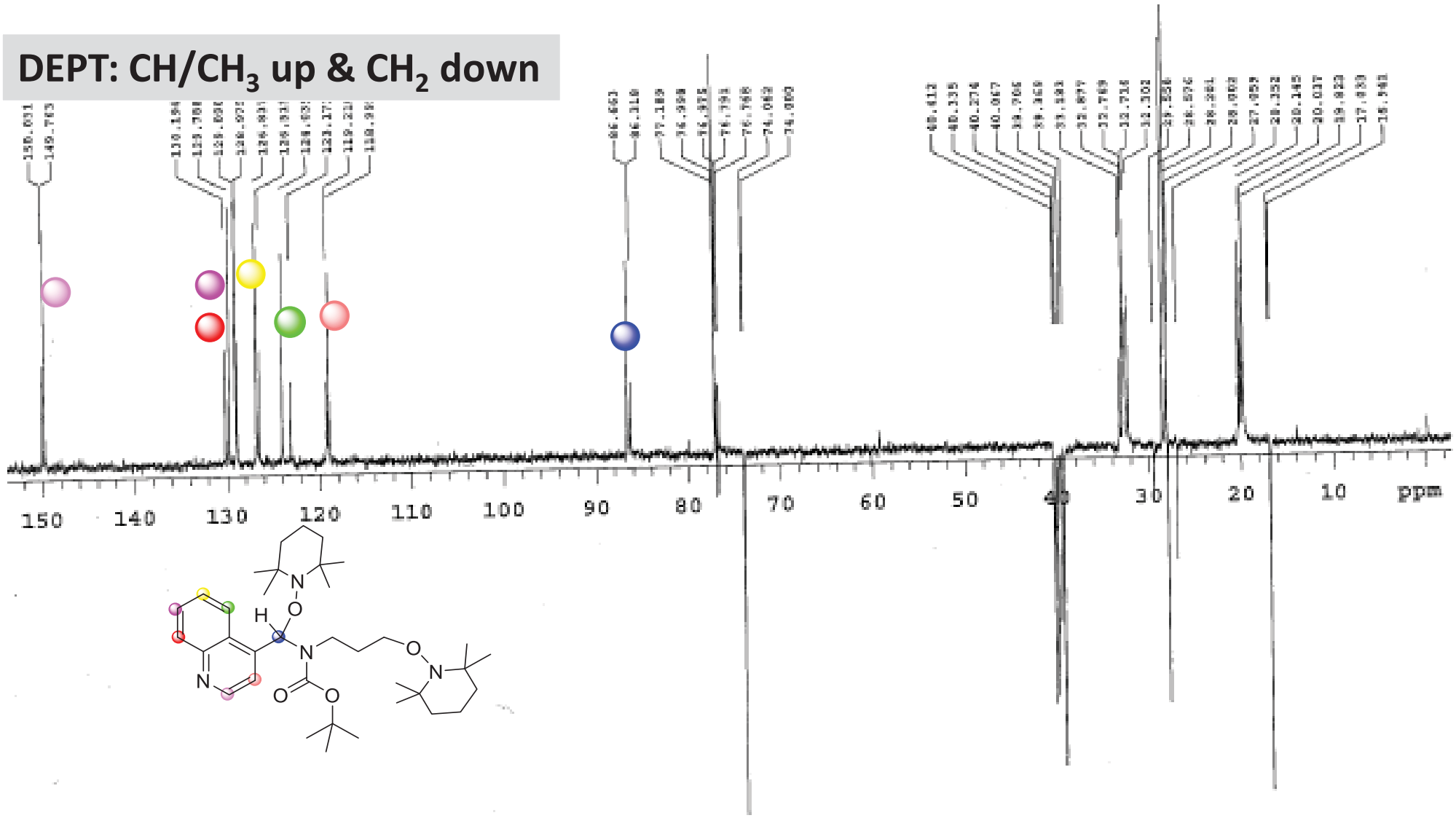
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (quinolin-4-yl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)carbamate 3t



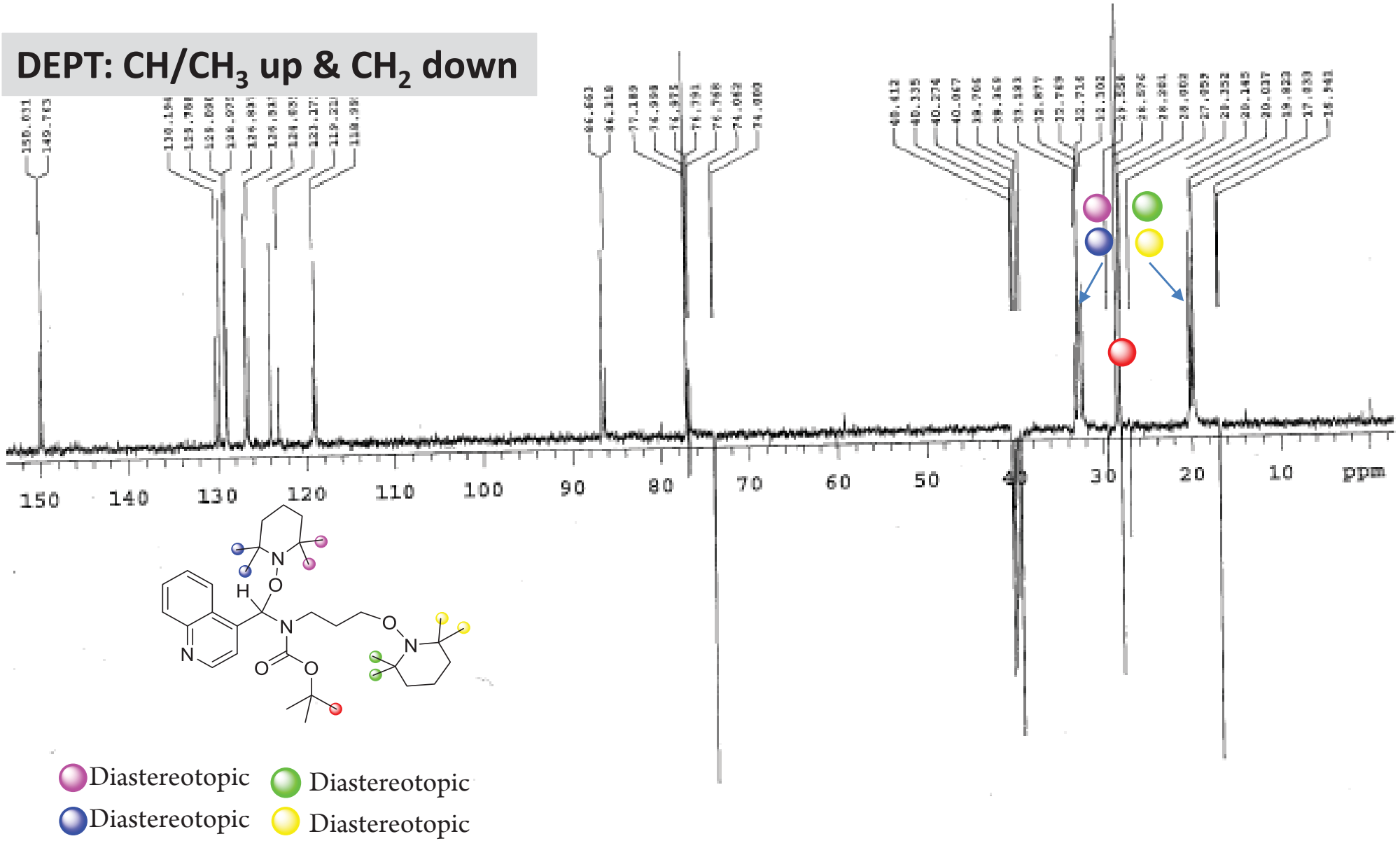
Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (quinolin-4-yl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)carbamate 3t



Note: The spectrum contains a mixture of amide rotamers.

tert-butyl (quinolin-4-yl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)carbamate 3t



Note: The spectrum contains a mixture of amide rotamers.