The Utilization of Sulfonylhydrazones as New Radical Precursors for Asymmetric Radical C–H Alkylation via Co(II)-Based Metalloradical Catalysis

by

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Asymmetric C–H functionalization represents one of the central topics in modern organic chemistry, which allows for the direct installation of functional groups onto ubiquitous C–H bonds in organic molecules. Among numerous elegant strategies, transition metal-catalyzed C–H alkylation with diazo compounds represents one of the most powerful methods for C–C bond formation. Different from Fischer metallocarbene-based C–H insertion reactions, cobalt(II)-based metalloradical catalysis (MRC) is recently proven to be capable of activating acceptor/acceptor diazo compounds for radical C–H alkylation reactions via H-atom abstraction. In this dissertation, we have developed several systems by utilizing less-explored aryl and alkyl diazomethanes as new radical precursors for highly enantioselective radical C–H alkylation reactions, which permit the efficient synthesis of different optically active heterocyclic compounds.

First, we have demonstrated the feasibility of using aryl aldehyde-derived sulfonylhydrazones as new radical precursors for enantioselective radical C–H alkylation for the synthesis of enantioenriched 2,3-dihydrobenzofuran derivatives. Notably, a general and mild way for in situ generation of diazo compounds have been identified by using 2,4,6-triisopropyl sulfonyl hydrazone as diazo precursor, which allow us to regulate the reaction temperature to achieve the high enantioselectivity for the desired radical reactions. Second, the utility of Co(II)-based MRC has been further highlighted by enantioselective indoline synthesis. Through the design and synthesis of new catalysts, the system is shown to have a broad spectrum of substrate scope, forming various 2-substituted indolines with up to 98% yield and 96% *ee*. A series of mechanistic studies further support the underlying stepwise radical alkylation pathway. Finally, we further expand the applicability of MRC to even more challenging diazo compounds, aliphatic diazomethanes. Starting from alkyl aldehyde-derived sulfonylhydrazones as diazo precursors, the Co(II)-based radical alkylation reactions allow for the enantioselective synthesis for common 2-substituted tetrahydrofuran structures with high yields and excellent enantioselectivities.

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DEDICATED TO:

I dedicate this dissertation to my parents, my parents-in-law, my husband and our lovely daughter for their unconditional love and support.

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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
PhMe: toluene
EtOAc: ethyl acetate
Ts: 4-methylphenyl sulfonyl
Tris: 2,4,6-triisopropyl phenylsulfonyl
PhH: benzene
PhCl: chlorobenzene
DCM: dichloromethane
Ar: aryl
MeOH: methanol
EtOH: ethanol
SiO_2: silica gel
TBME: *tert*-butyl methyl ether
DME: Dimethoxyethane
TFA: trifluoroacetic acid
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
FG: functional group
KIE: kinetic isotope effect
M.S.: molecular sieves
het: hetero

Ac: acetate
Bn: benzyl
PBN: *N*-*tert*-butylnitrone
^{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

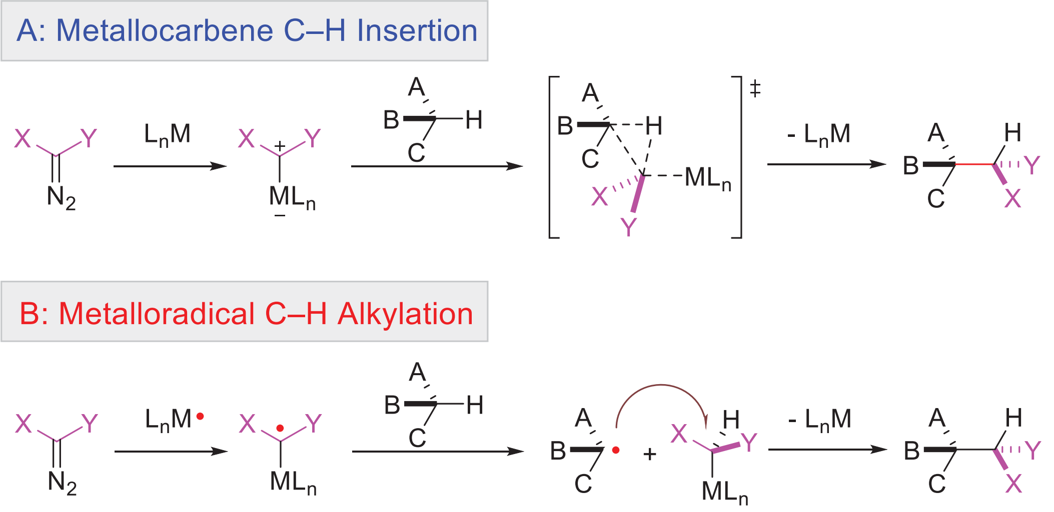
RECENT DEVELOPMENTS IN TRANSITION METAL-CATALYZED C–H ALKYLATION REACTIONS WITH DONOR- AND ALKYL-SUBSTITUTED DIAZO COMPOUNDS

1.1 INTRODUCTION

C–H functionalization, as one of the most central topics in modern organic chemistry for directly constructing C–C bonds, has attracted increasing attention by the community for synthetic applications.[1] The successful development of these attractive transformations also leads to the rapid synthesis of target molecules from ubiquitous C–H bonds. However, such appealing processes are inherently challenging in part due to the inertness of unactivated C–H bonds, which require the design of robust and efficient systems to catalytically activate inert C–H bonds with good control of chemo-, regio- and stereoselectivity. Among recent advances,[1] transition metal-catalyzed C–H alkylation reactions with diazo compounds represent one of the most effective methods for C–C bond formation,[2] which typically undergo two different pathways as displayed in Scheme 1.1: A) concerted electrophilic C–H alkylation via metal-catalyzed carbene insertion, including Rh_2, Cu, Ru, Ir, and Fe complexes; B) C–H alkylation via metalloradical catalysis, including Co(II)-Porphyrins [Co^{II}(**Por**)]. So far, these existing metal catalysts are shown to be highly effective for C–H alkylation reactions with a wide range of diazo compounds, including acceptor-, donor/acceptor-, and acceptor/acceptor-substituted diazo compounds.

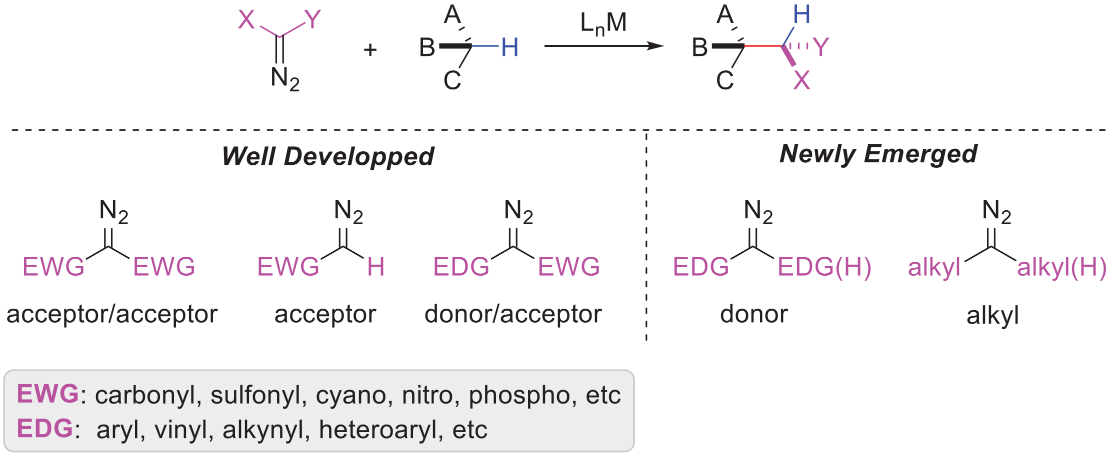
The methodology has been widely applied as a key strategy for the facile synthesis of various natural products and molecules with pharmaceutical interest.

Scheme 1.1| Transition Metal-Catalyzed C–H Functionalization with Diazo Compounds



Despite numerous catalytic systems are elegantly engineered, C–H alkylation reactions utilizing donor- or alkyl-substituted diazo compounds are still underdeveloped (Scheme 1.2).[3] One of the major challenges lies in the low stability of these aryl or alkyl diazomethanes. Since the strong electron-donating substituents would result in the electron-rich character of the α-carbon of diazo species, the isolation and utilization of those less stabilized diazo compounds are thus difficult to handle. To address this practical issue, *N*-sulfonylhydrazones have been reported as user-friendly surrogates for the in situ-generation of the reactive alkyl and aryl diazomethanes.[4] This in situ-generation protocol has recently triggered a significant progress in the area of C–H alkylation reactions by utilizing the aforementioned less stabilized diazo compounds. Notably, as the aryl or alkyl groups of diazomethanes are electronically and structurally different from unsaturated acceptor groups, some new reactivity and selectivity are also revealed. In this tutorial review, we will mainly overview the recent progress in transition metal-catalyzed C–H alkylation reactions by utilizing donor-, alkyl-substituted diazo compounds, which are generated in situ from the corresponding aldehyde or ketone-derived sulfonylhydrazones.

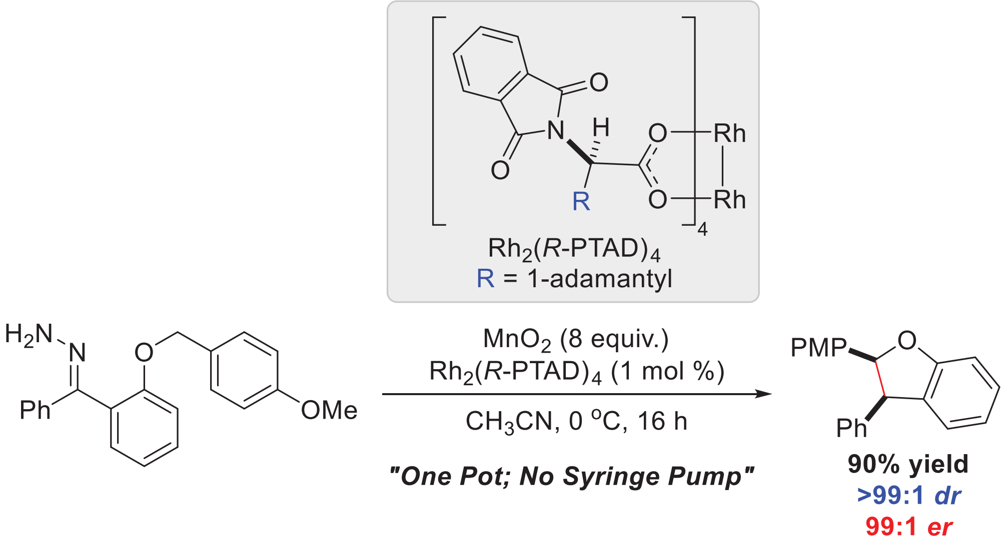
Scheme 1.2| Perspectives on Various Diazo Compounds Used for Metal-Catalyzed C–H Alkylation Reactions



1.2 C–H ALKYLATION REACTIONS WITH IN SITU-GENERATED DIARYL DIAZO COMPOUNDS

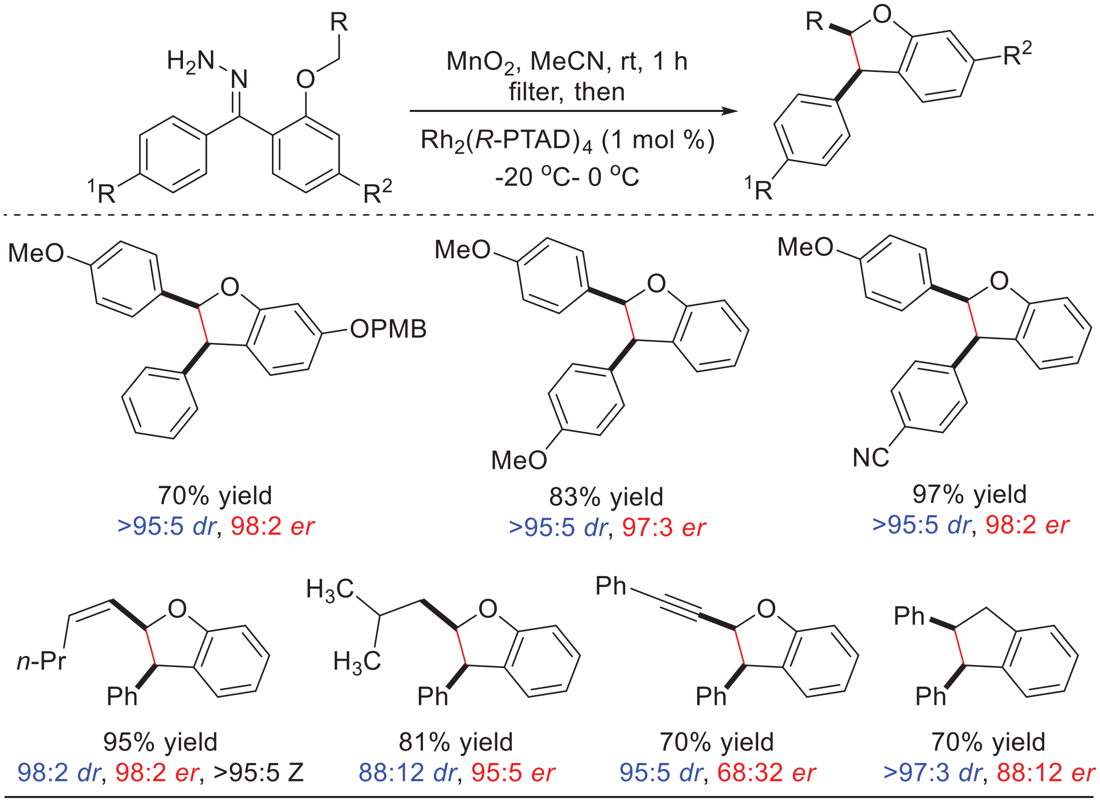
Different from acceptor-, acceptor/acceptor- or donor/acceptor-substituted diazo compounds, which are typically synthesized from diazo-transfer reagents such as 4-acetamidobenzenesulfonyl azide (*P*-ABSA), diaryl-substituted diazomethanes could be accessed through the oxidation of the corresponding ketone-derived hydrazone compounds. In 2013, Shaw and coworkers have, for the first time, developed a Rh_2-catalyzed asymmetric C–H insertion system by using donor/donor-substituted diazo compounds,[5] where these diazo compounds could be accessed in situ through the oxidation of the corresponding diaryl ketone-based hydrazones (Scheme 1.3).

Scheme 1.3| The Identification of $Rh_2(PTDA)_4$ for Asymmetric C–H Insertion Reaction with in Situ-Generated Diaryl Diazomethane



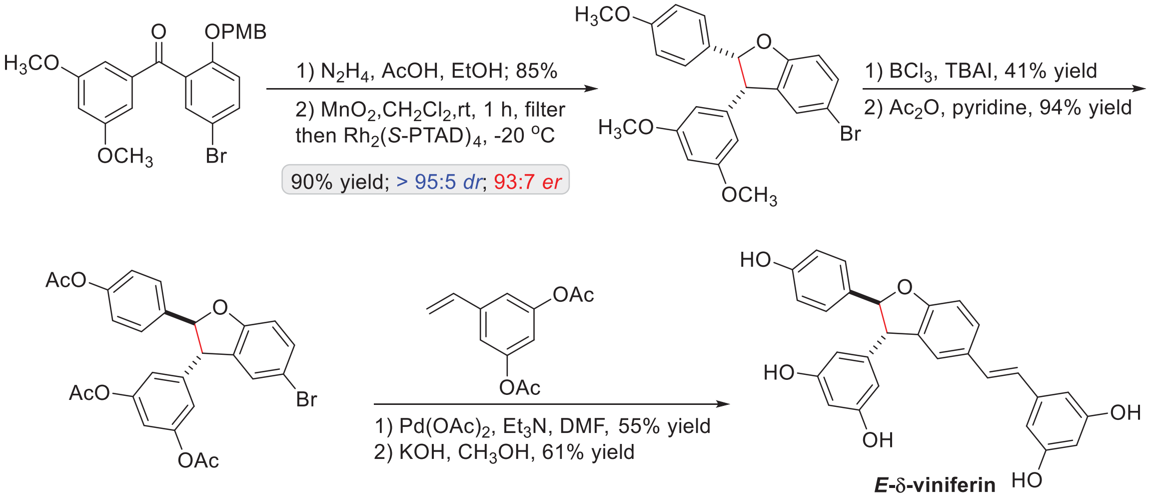
They found that the newly-designed catalyst $Rh_2(PTDA)_4$ could enable the effective activation of in situ-generated diaryl diazomethane and undergo C–H insertion reaction in CH_3CN at 0 °C, affording the desired 2,3-disubstituted dihydrobenzofuran compound in up to 90% yield with >99:1 *dr* and 99:1 *er*. The success of this reaction indicates that the metallocarbene system could be well incorporated with the in situ-generation protocol of diazos. Partially benefit from the in situ generation protocol, this catalytic system could be achieved without the need of syringe pump for slow addition. Moreover, the system was also amenable to a gram-scale C–H insertion reaction.

Scheme 1.4| $Rh_2(PTDA)_4$-Catalyzed Asymmetric C–H Insertion Reaction with in Situ-Generated Diaryl Diazomethanes



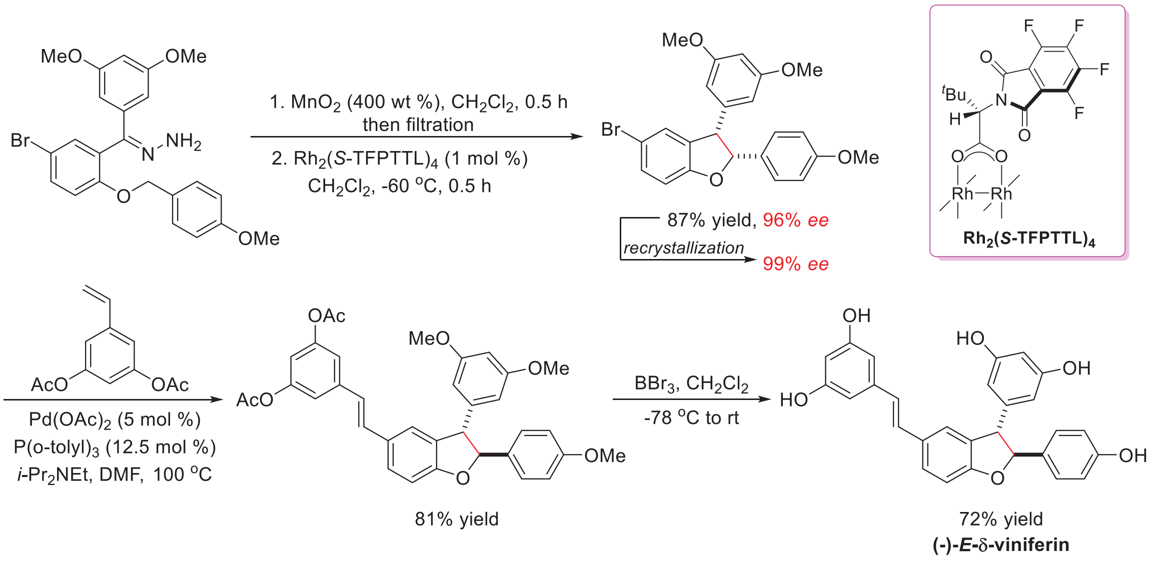
In their report, the Rh_2-catalyzed C−H insertion reactions of donor-donor diazomethanes could streamline the synthesis of densely substituted benzodihydrofurans with high levels of both enantio- and diastereoselectivity, by activating various C−H bonds including benzylic, allylic, propargylic and alkyl C−H bonds (Scheme 1.4). In particular, with allylic C−H substrates, only C−H insertion reaction was observed without detection of cyclopropanation products. Also, substituted allylic substrates with either *E*- or *Z*-configured alkene motifs only provided dihydrobenzofuran products with complete stereoretention. This work features the first example in metallocarbene-catalyzed alkylation reactions of diazo compounds with no pendant electron-withdrawing groups.

Scheme 1.5| Shaw's Method for Enantioselective Synthesis of *E*-δ-Viniferin



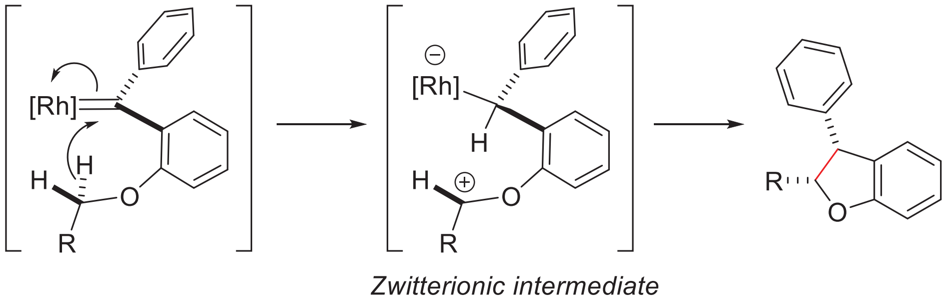
The utility of this new methodology has been further applied to the first enantioselective synthesis of an oligoresveratrol natural product (*E*-δ-viniferin), which is a resveratrol dimer containing a 2,3-diaryl-2,3-dihydrobenzofuran ring isolated from grapes in response to fungal infection.[6] This novel 6-step synthetic route is highly efficient for the enantioselective synthesis of the oligoresveratrol family of natural products (Scheme 1.5).[7]

Scheme 1.6| Hashimoto's Method for Enantioselective Synthesis of *E*-δ-Viniferin



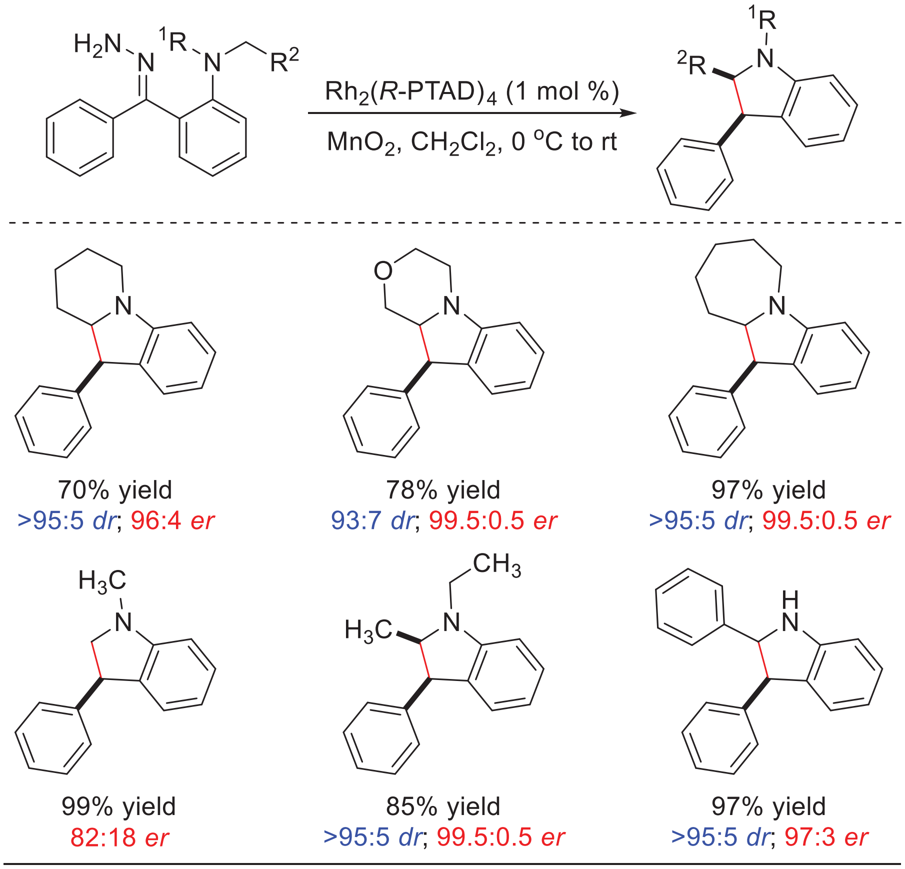
In 2015, Hashimoto and coworkers have further improved the synthetic route by improving the enantioselectivity of the C–H insertion step from 86% to 96% *ee*, and shortening the synthesis from 6 steps to 4 steps (Scheme 1.6).[8] By identifying a different Rh_2 complexes: dirhodium(II) tetrakis [*N*-tetrafluorophthaloyl-(*S*)-*tert*-leucinate] (Rh_2(*S*-TFPTTL)$_4$), it was found that the intramolecular C–H insertion reaction of the diaryldiazomethane derivative could afford the 2,3-diaryl-2,3-dihydrobenzofuran core structure with perfect *cis* diastereoselectivity and 96% *ee*.

Scheme 1.7| Proposed Mechanism for C–H Insertion Involving the Ylide Intermediate that Proceeds to Dihydrobenzofuran Product with a very Low Barrier



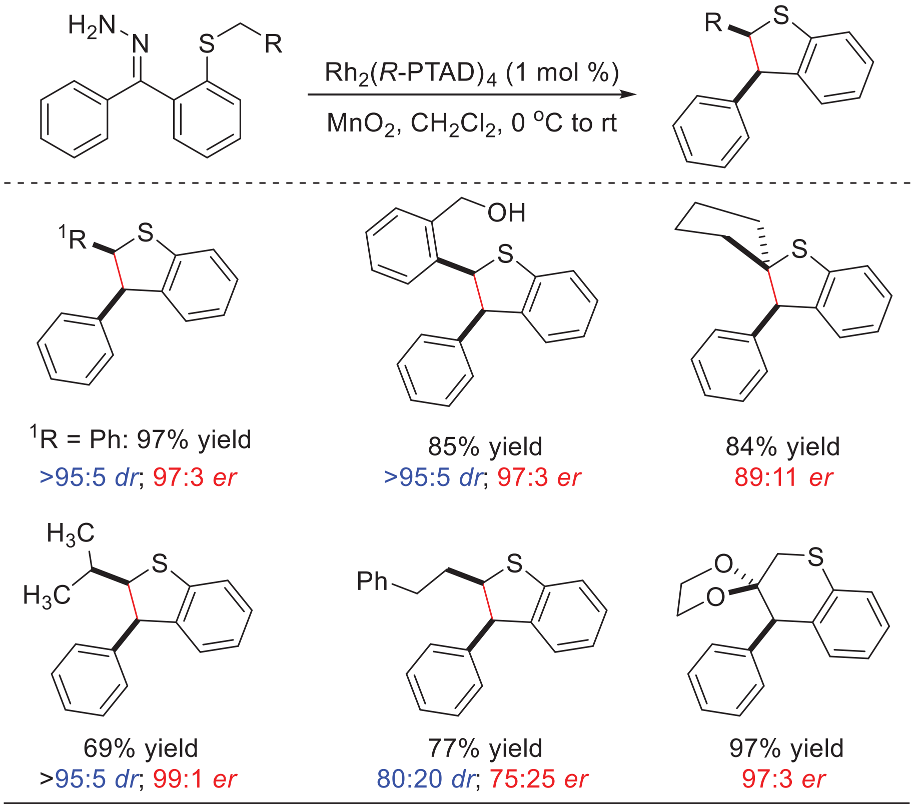
After the demonstration of their first Rh_2-catalyzed C–H insertion reactions with diaryl diazomethanes, Shaw and his coworkers have subsequently studied the detailed mechanism through computational study and proposed the following pathway as shown in Scheme 1.7.[9] Upon the formation of the metallocarbene intermediate, it most likely undergoes a subsequent hydride transfer step to deliver the ylide intermediate. Then, the ylide species converts into the desired C–H insertion product in a highly exothermic fashion, which might indicate that this step is a stereospecific process and the diastereoselectivity is mainly governed by the transition state for ylide formation. The rationale is in accord with many previous C–H insertion examples.

Scheme 1.8| Asymmetric Synthesis of 2,3-Disubstituted Indolines via $Rh_2(PTDA)_4$-Catalyzed C–H Insertion Reactions



Very recently, Shaw's group has further expanded the C–H insertion chemistry for the synthesis of other important core structures in addition to the aforementioned 2,3-disubstituted dihydrobenzofuran compounds. For example, indolines represent a common core structure among natural products and drug discovery candidates. In this work,[10] they have documented the first enantioselective synthesis of 2,3-disubstituted indoline derivatives from donor/donor-substituted diazo compounds (Scheme 1.8). A variety of indolines, including fused indolines derived from cyclic anilines and indoline derived from a free amine, could be approached in high yields with high levels of diastereo- and enantioselectivity.

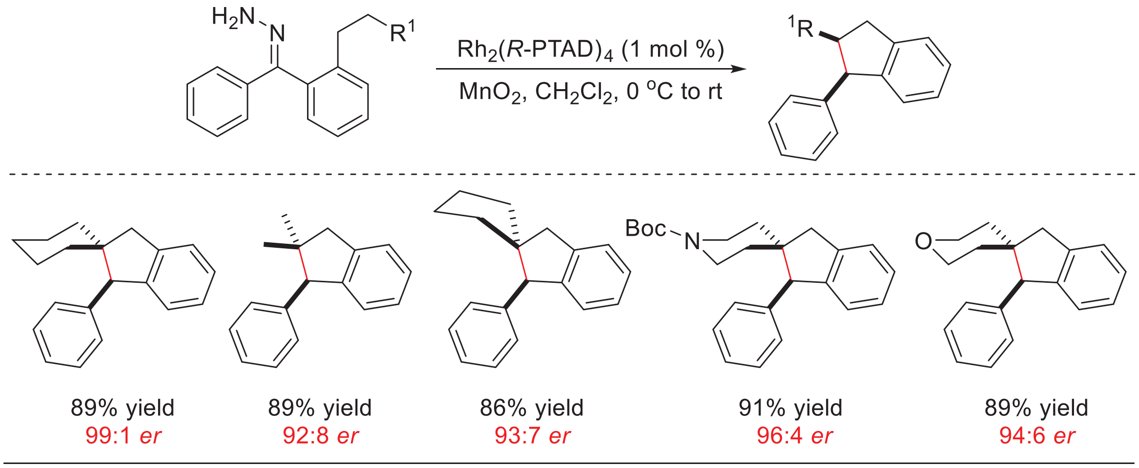
Scheme 1.9| Asymmetric Synthesis of 2,3-Disubstituted Dihydrobenzothiophenes via $Rh_2(PTDA)_4$-Catalyzed C–H Insertion Reactions



Dihydrobenzothiophenes are another interesting family of heterocycles, yet very few stereoselective synthetic methods have been reported so far.[11] In the context of metallocarbene-based C–H insertion, only a single report of a dihydrobenzothiophene synthesis carbenes with acceptor-substituted diazo compounds was disclosed.[12] Shaw and his team hypothesized that the sluggish development is largely due to the propensity of the highly nucleophilic sulfur atom that would attack the carbene directly to form an ylide.

However, in the case of donor/donor carbenes, attributed to the reduced electrophilicity of the formed Fischer carbene intermediates, it can permit the smooth synthesis of a wide array of dihydrobenzothiophenes in high yields with excellent stereocontrol (Scheme 1.9).[10] Among the broad range of substrate scope, it is highlighted that the free alcohol motif could be well tolerated, which would create a useful chemical handle for further modification without lengthy protection/deprotection steps.

Scheme 1.10| Asymmetric Synthesis of 2,3-Disubstituted Indanes via $Rh_2(PTDA)_4$-Catalyzed C–H Insertion Reactions



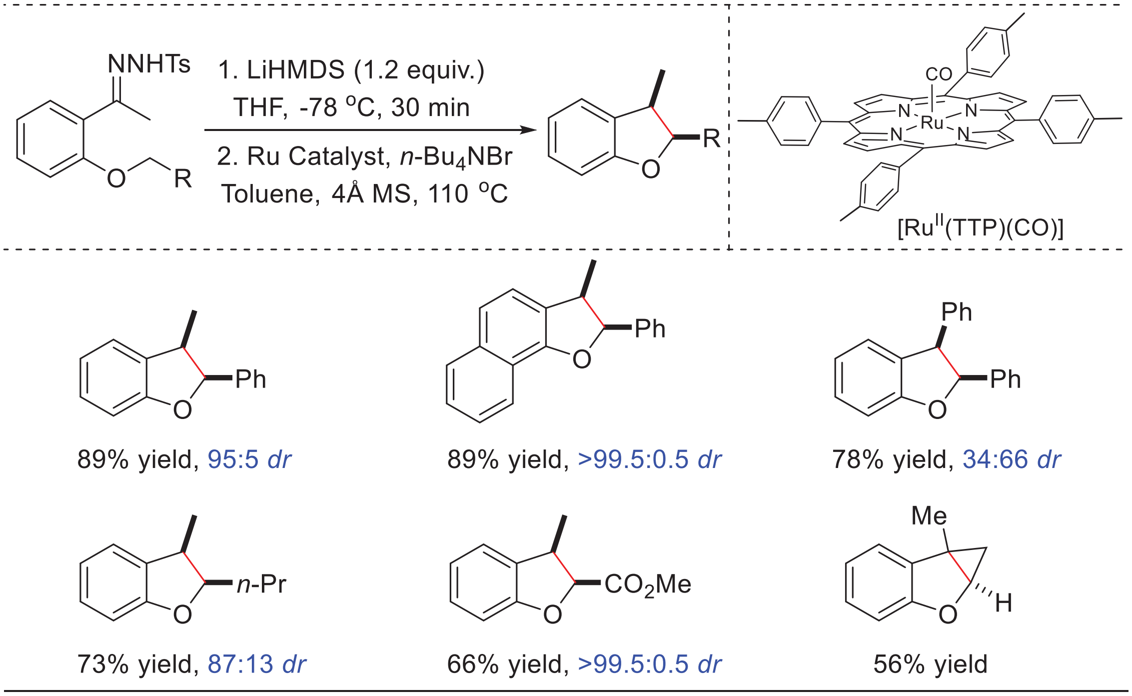
They have further expanded the scope of this chemistry to the asymmetric synthesis of a variety of carbocycle indanes (Scheme 1.10),[10] which prevail in both natural products and drug candidates presumably due to the less easily oxidized electron-neutral benzene and benzylic carbon by enzymes responsible for drug clearance. Under the optimized conditions, the desired indane derivatives could be obtained in high yields (up to 91% yield) with excellent control of both diastereoselectivity and enantioselectivity.

1.3 C–H ALKYLATION REACTIONS WITH IN SITU-GENERATED ARYL/ALKYL DIAZO COMPOUNDS

1.3.1 Intramolecular Alkylation of C(sp^3)–H with in Situ-Generated Aryl/Alkyl Diazo Compounds

In 2003, Che and his team reported a ruthenium porphyrin-catalyzed system for stereoselective intramolecular C–H insertion reactions (Scheme 1.11).[13] In this work, they can employ aryl ketone-derived tosylhydrazones as precursors for the in situ-generation of aryl/alkyl-substituted diazo compounds, where handling or accumulation of these unstable diazos could be avoided.

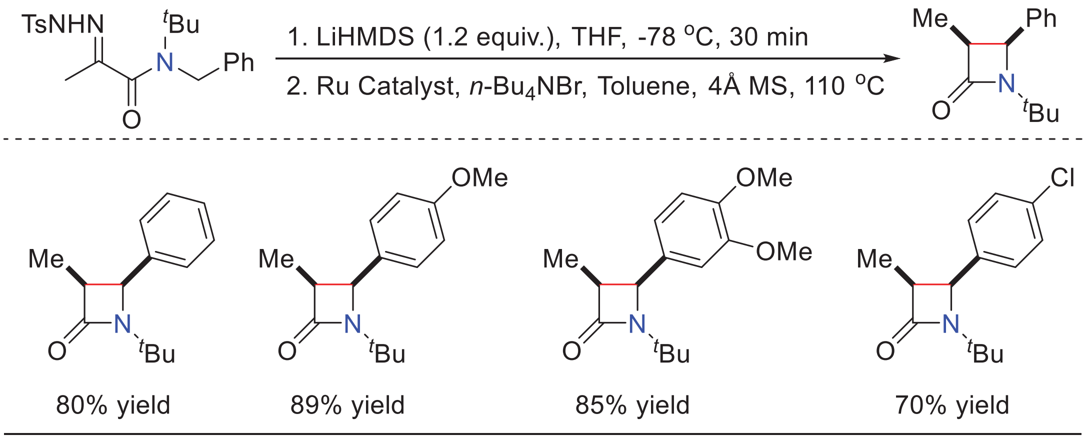
Scheme 1.11| Ru-Catalyzed C–H Insertion Reactions with in Situ-Generated Aryl/Alkyl Diazo Compounds for the Synthesis of *cis*-2,3-Disubstituted Dihydrobenzofurans



With the employment of [Ru^{II}(TTP)(CO)] as catalyst, they found that the in situ-formed diazo compounds could smoothly undergo intramolecular C–H insertion reactions in good yields with remarkable *cis* selectivity. Specifically, the treatment of the hydrazone salt with 1 mol % [Ru^{II}(TTP)(CO)] in toluene at 110 °C, the reaction could afford 2,3-disubstituted dihydrobenzofuran derivatives in moderate to high yields.

Notably, for substrates containing electron-withdrawing ester substituents that are generally not reactive for the electrophilic Rh-catalyzed carbenoid C–H insertion reactions, they were still able to undergo facile C–H insertion with the formation of the desired product in 66% yield with >99% *cis* selectivity. However, allylic C–H substrate preferentially underwent intramolecular cyclopropanation to afford the corresponding cyclopropane in 56% yield without detectable C–H insertion product (Scheme 1.11).

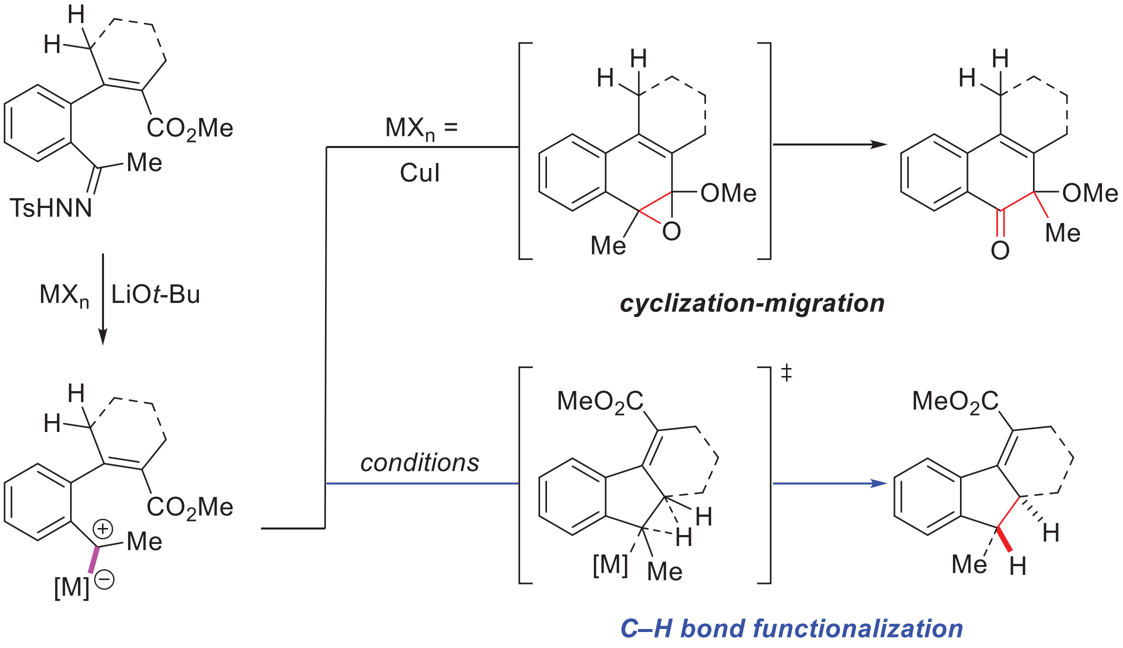
Scheme 1.12| Ru-Catalyzed C–H Insertion Reactions with in Situ-Generated Aryl/Alkyl Diazo Compounds for the Synthesis of *cis*-β-Lactams



Furthermore, the Che group have explored this Ru-catalyzed intramolecular C–H insertion protocol for synthesis of β-lactam ring structures (Scheme 1.12). Under the standard conditions, reactions of the *N*-benzyl-*N*-*tert*-butylacetamide tosylhydrazones could deliver β-lactam compounds in 70%-89% isolated yields with exclusive *cis*-selectivity. It is noteworthy to mention that the bulky *tert*-butyl protecting group is essential for the success of this transformation.

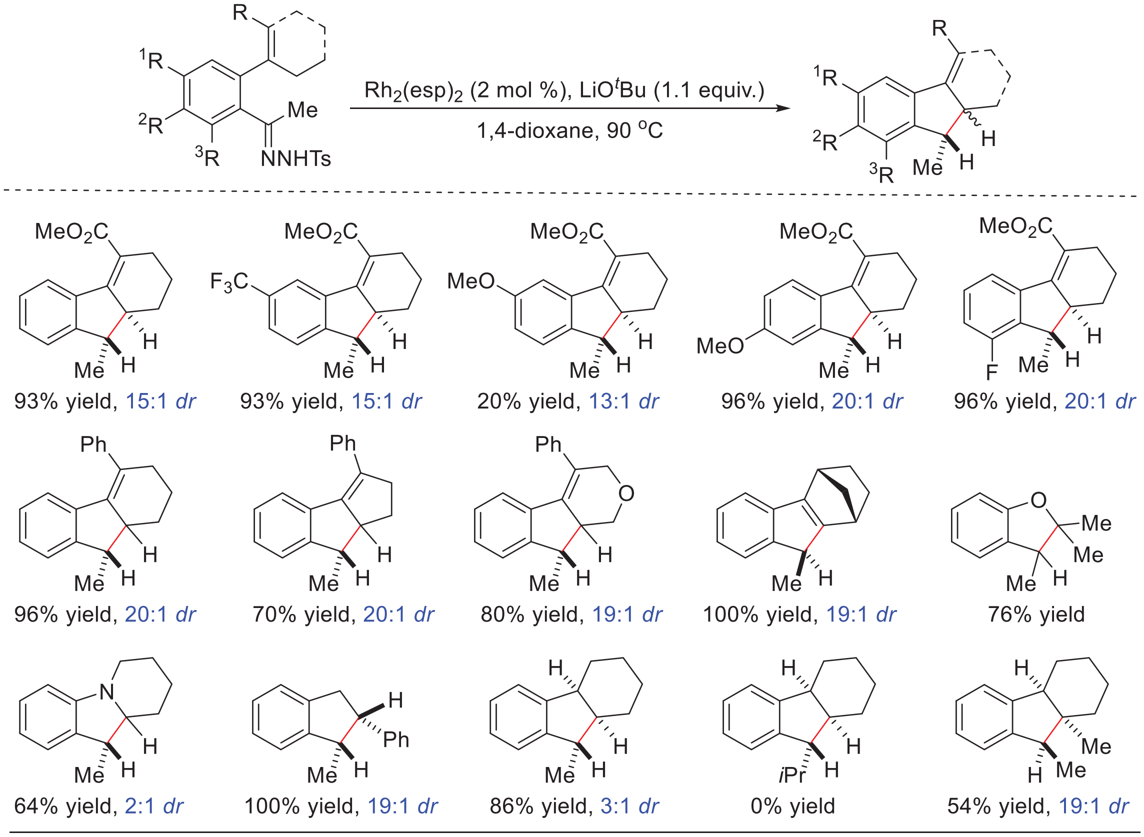
In 2017, the Driver research group discovered a catalyst-controlled site-selective C–H insertion system by using in situ-generated aryl/alkyl diazo compounds.[14] As drawn in Scheme 1.13, while copper-based aryl/alkyl carbenes typically react with the *o*-alkenyl substituent through a cyclization-migration pathway to afford α-alkoxy 2*H*-naphthalenones, rhodium(II) carboxylate catalyst instead triggers interestingly stereoselective allylic C−H alkylation reactions to produce 1*H*-indenes.

Scheme 1.13| Divergent Reactivity of Electron-Rich Metallocarbene Intermediates from Alkyl/Aryl Diazo Compounds



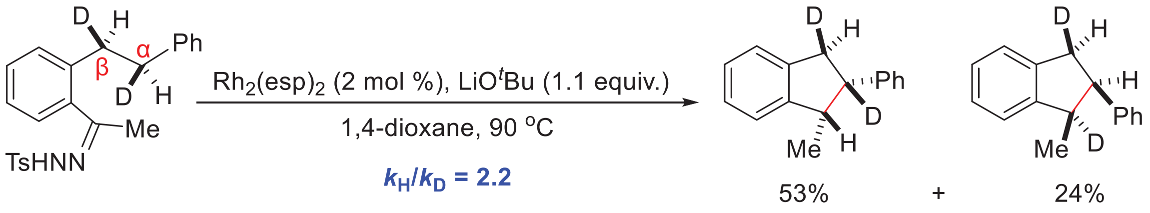
With Rh2(esp)2 as catalyst and by using *N*-tosylhydrazones derived from *ortho*-substituted aryl ketones as substrates, the C−H alkylation reactions allowed the formation of indane derivatives in high yields with good to excellent diastereoselectivities (Scheme 1.14). They were also able to vary the identity of the *ortho* substituent, such as changing from a carboxylate to a phenyl group, to undergo the C−H alkylation reactions with the formation of other multi-substituted indane derivatives. Moreover, the system was also found to effectively functionalize other activated C−H bonds. For example, substrates bearing ethereal, aminomethylene, or benzylic C−H bonds were all smoothly transformed into corresponding indane analogs.

Scheme 1.14| Rh$_2$(esp)$_2$-Catalyzed C–H Insertion Reactions with in Situ-Generated Aryl/Alkyl Diazo Compounds for the Formation of Disubstituted Indane Derivatives



To support a concerted insertion process of electron-rich metal carbenes into C−H bonds, they subjected the deuterated compound into the reaction conditions and only observed indanes without the scrambling of the stereogenic centers (Scheme 1.15). This result indicated that the C−H functionalization should go through the concerted mechanism. Moreover, an intramolecular KIE value of 2.2 is also similar to the k_H/k_D values reported for the intermolecular insertion reactions of electron-poor carboxylic ester- and imine-substituted rhodium(II) carbenes.

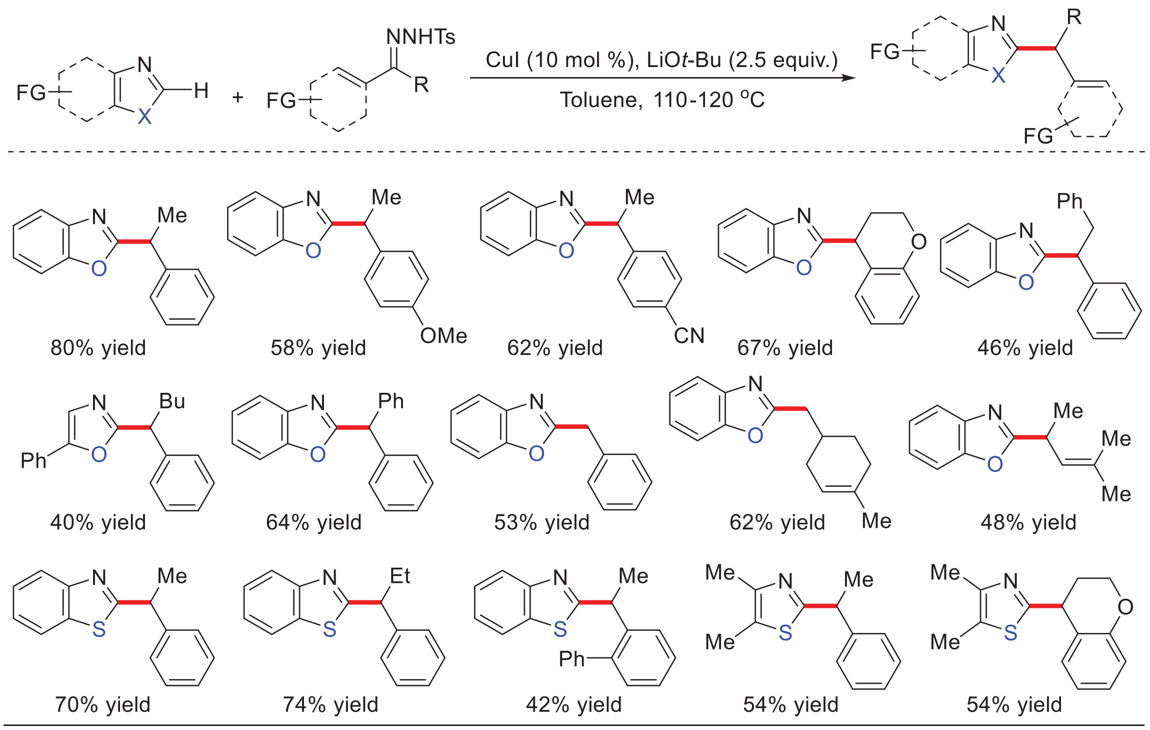
Scheme 1.15| Intramolecular Kinetic Isotope Effect for $Rh_2(esp)_2$-Catalyzed C–H Insertion Reactions with in Situ-Generated Aryl/Alkyl Diazo Compounds



1.3.2 Intermolecular Alkylation of C(sp^2)–H with in Situ-Generated Aryl/Alkyl Diazo Compounds

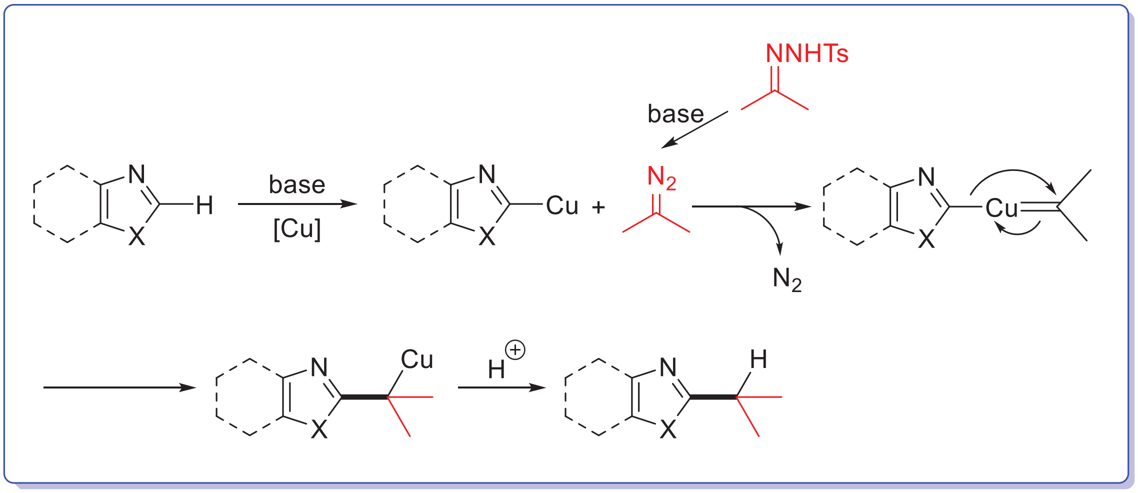
In addition to the aforementioned alkylation reactions of C(sp^3)–H bonds, in 2011, Wang and coworkers also reported a highly efficient Cu(I)-catalyzed system for direct benzylation or allylation of heteroaromatic C(sp^2)–H compounds with *N*-tosylhydrazones (Scheme 1.16).[15] By using CuI as the catalyst in the presence of LiO^{t}Bu in toluene at 110 ºC, the system was applicable to different benzo[d]oxazoles or thiazoles, which could be facilely coupled with various tosylhydrazones to provide the corresponding benzylated aromatic heterocycles in moderate to good yields. It is noteworthy to mention that other diazomethanes were also employed for this transformation, including aryl/alkyl, aryl/H, aryl/aryl, allyl/alkyl diazo compounds.

Scheme 1.16| Cu-Catalyzed Benzylation of Benzoxazoles or Thiazoles with in Situ-Generated Diazomethanes



A plausible mechanism was also proposed, where the authors postulated that the reaction most likely is initialized by the deprotonation of the relatively acidic heteroaromatic C–H bonds (Scheme 1.17). Subsequent transmetalation and dediazotization of the in situ-generated diazo substrates lead to the formation of a copper carbene species, which then undergoes a migratory insertion process and finally delivers the desired coupling product.

Scheme 1.17| Proposed Mechanism for Cu-Catalyzed Reaction of 1,3-Azole with *N*-Tosylhydrazone



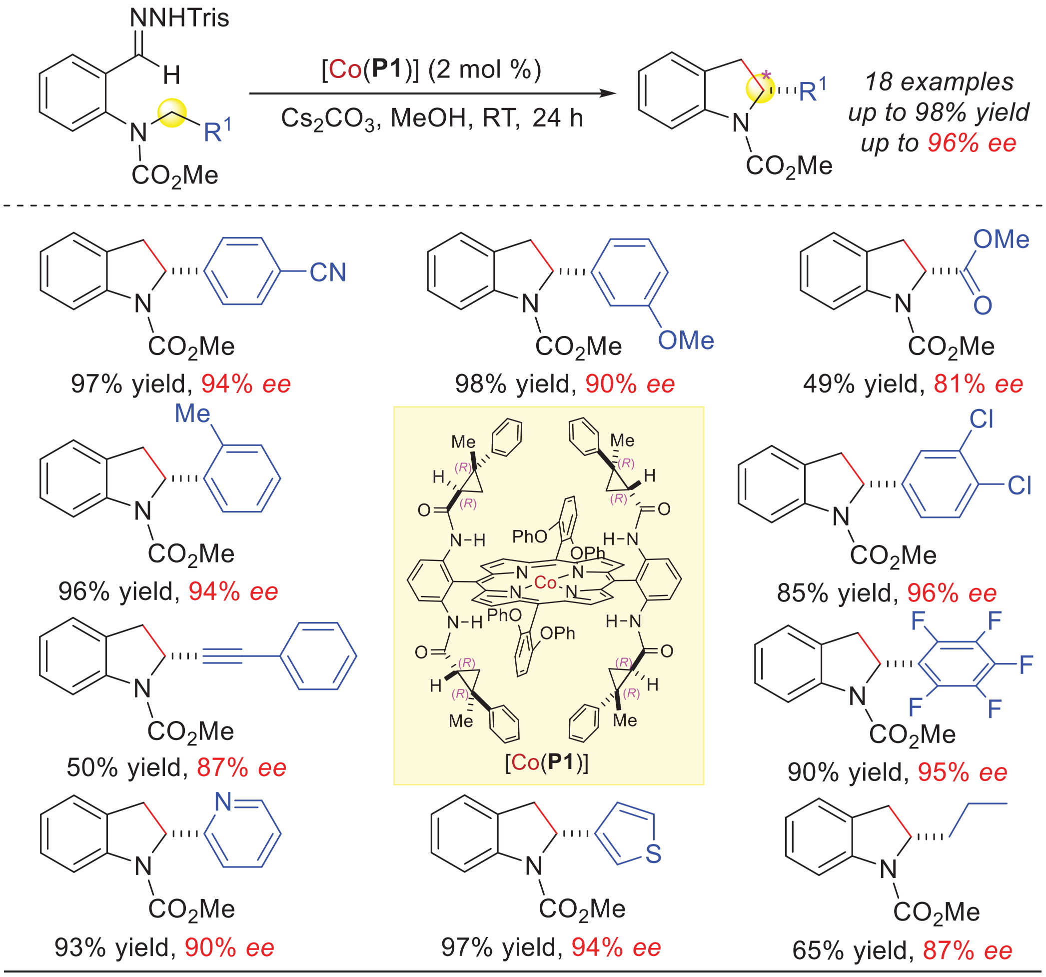
1.4 C–H ALKYLATION REACTIONS WITH IN SITU-GENERATED ARYL/H DIAZO COMPOUNDS

In addition to intramolecular C–H alkylation with in situ-generated aryl/aryl, aryl/alkyl diazo compounds, C–H alkylation reactions with aryl/H diazomethanes, formed through thermal decomposition of aryl aldehyde-derived sulfonylhydrazones, also allow the efficient construction of important organic molecules.

1.4.1 Intramolecular Alkylation of C(sp^3)–H with in Situ-Generated Aryl/H Diazo Compounds

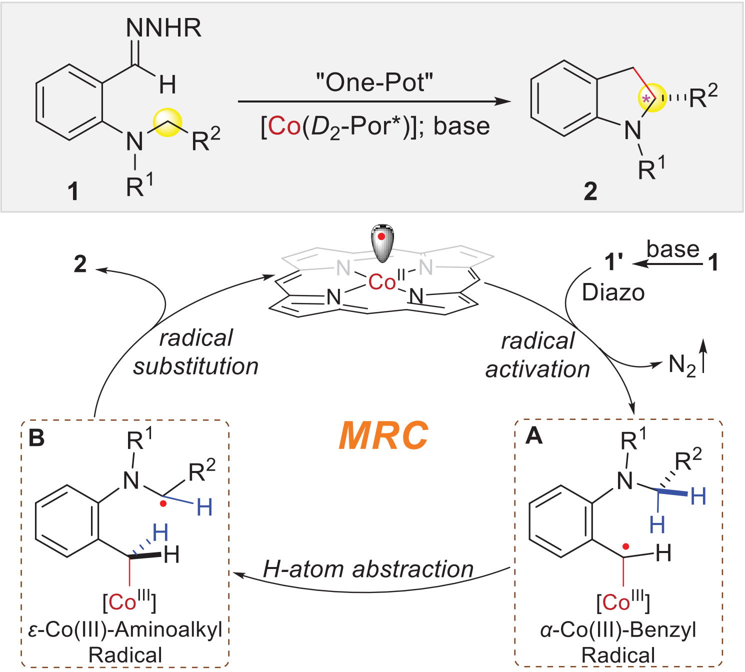
As mentioned earlier, chiral 2-substituted indolines exist ubiquitously in both natural and synthetic compounds with important biological properties. While tremendous efforts have been made towards their asymmetric synthesis, including catalytic hydrogenation, metal-catalyzed intramolecular coupling and kinetic resolution, the construction of chiral 2-substituted indolines based on direct C2–C3 bond formation via asymmetric C–H alkylation has been much less developed. The underdevelopment may be attributed to the inherent challenge for enantioselective formation of C–C bonds between two sp^3-carbon centers.

Scheme 1.18| [Co(P1)]-Catalyzed Enantioselective Radical C–H Alkylation for Construction of Chiral 2-Substituted Indolines



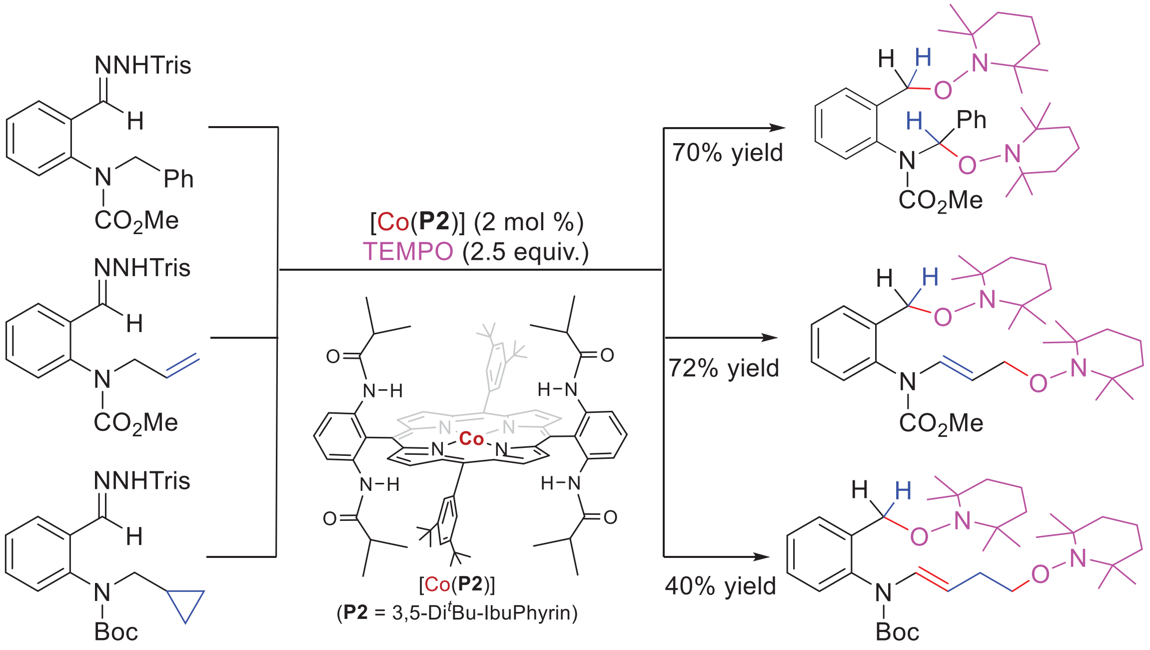
Very recently, Zhang and coworkers have presented a new C–C bond formation strategy based on the concept of metalloradical catalysis (MRC) for asymmetric construction of 2-substituted indolines via direct C–H alkylation using donor/H-type diazo compounds (Scheme 1.18).[16] With the design of a new chiral ligand, 2,6-DiPhO-QingPhyrin, the [Co(**P1**)]-based metalloradical system enables the efficient activation of in situ generated aryldiazomethane with *ortho*-amino functionality at room temperature for enantioselective intramolecular radical alkylation of a broad range of C(sp^3)–H bonds, including benzylic, heteroaromatic-adjacent, propargylic, alkyl substrates. A wide array of chiral 2-substituted indolines were obtained in high yields with excellent enantioselectivities. Among other attributes, this catalytic system features a remarkable level of functional group tolerance as well as excellent compatibility with heteroaryl units.

Scheme 1.19| Proposed Mechanism for Construction of 2-Substituted Indolines by Radical C–H Alkylation via Co(II)-MRC



The proposed mechanism is shown in Scheme 1.19. It was reasoned that, upon metalloradical activation, the resulting α-Co(III)-benzyl radical intermediates undergo intramolecular hydrogen atom abstraction (HAA) from the C–H bonds at the distal 5-position to form ε-Co(III)-aminoalkyl radical, where the C-centered radical is considerably stabilized by the lone pair of the adjacent nitrogen. Subsequently, the pendant α-aminoalkyl radical likely proceeds through a *5-exo-tet* radical cyclization at the α-carbon center to form C–C bond in an asymmetric fashion.

Scheme 1.20| Mechanistic Study with TEMPO-Trapping Experiments

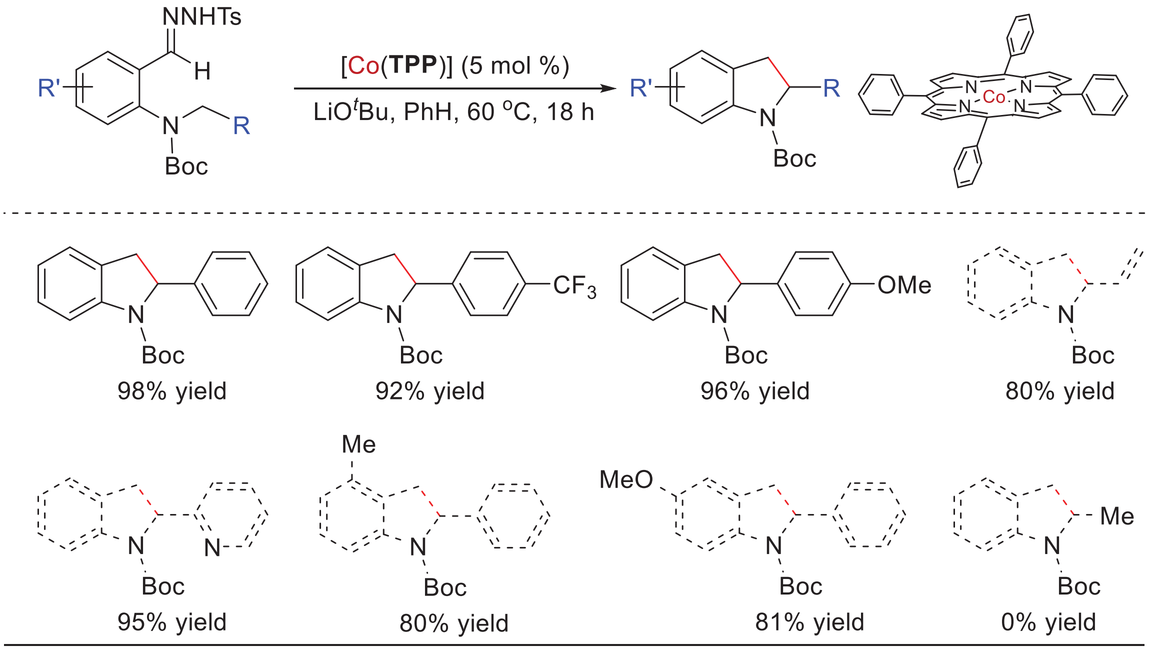


To further support the details of the underlying stepwise radical pathway, a series of mechanistic studies including TEMPO-trapping experiments of benzylic, allylic as well as cyclopropyl-tethered C–H substrates, were conducted by the group (Scheme 1.20). Addition of TEMPO (2.5 equiv.) to the reaction of benzylic and allylic C–H substrates by achiral catalyst [Co(**P2**)] resulted in complete inhibition of the C–H alkylation process.

Instead, the bis-TEMPO trapped products were isolated contained two TEMPO units at different positions. Collectively, all these experimental observations strongly support the proposed stepwise radical mechanism of the Co(II)-based C–H alkylation reaction.

At the same time, de Bruin and his team also disclosed a non-asymmetric method for the synthesis of 2-substituted indolines from *o*-aminobenzylidine *N*-tosylhydrazones with [Co^{II}(TPP)] as catalyst. The desired indoline derivatives bearing different substituents were obtained in 80%-98% yields (Scheme 1.21).[17] Computational investigations using density functional theory further supported the stepwise radical mechanism.

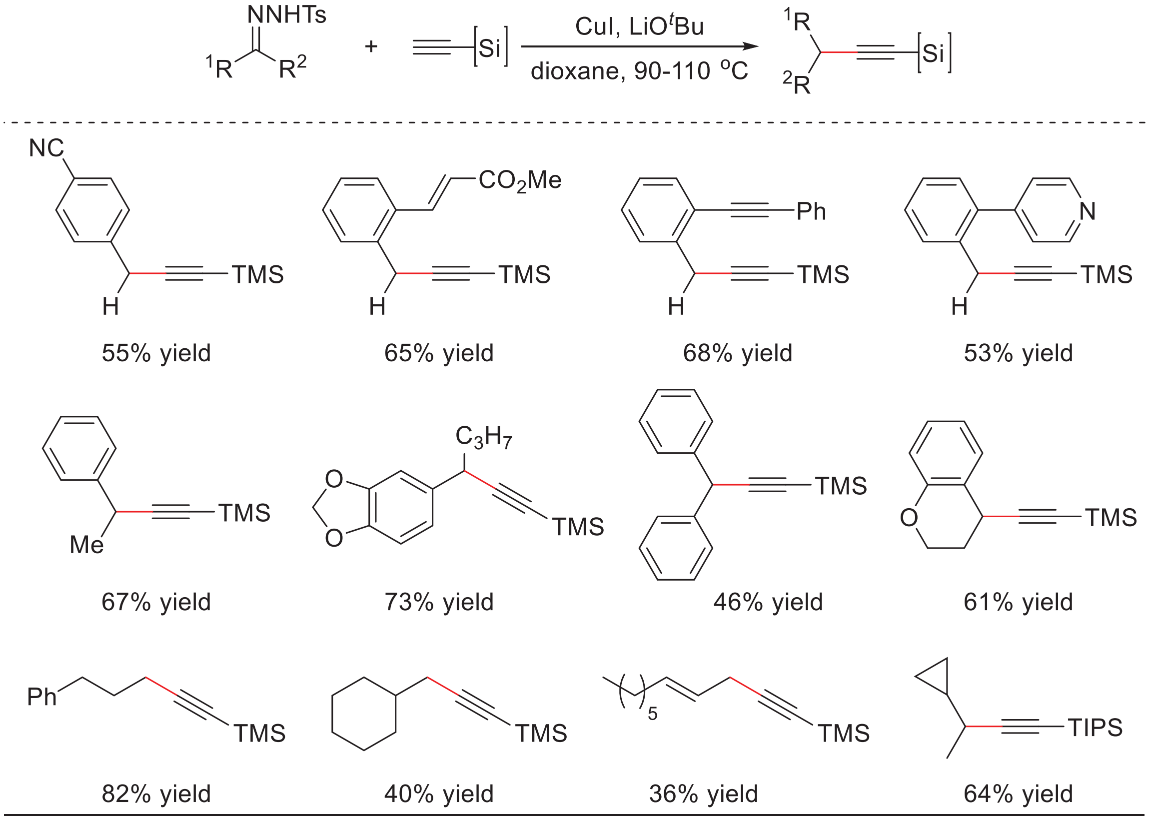
Scheme 1.21| [Co(TPP)]-Catalyzed Non-Asymmetric C–H Alkylation for Construction of 2-Substituted Indolines



1.4.2 Intermolecular Alkylation of C(sp)–H with in Situ-Generated Aryl/H Diazo Compounds

Following up their aforementioned work on Cu(I)-catalyzed direct C−H bond benzylation or allylation of 1,3-azoles with in situ-generated aryl/alkyl diazos, in 2012, the Wang group has developed another novel strategy for constructing C(sp)−C(sp^3) bonds starting from *N*-tosylhydrazones and trialkylsilylethynes in the presence of copper catalyst (Scheme 1.22).[18]

Scheme 1.22| Cu(I)-Catalyzed Cross-Coupling Reactions of Tosylhydrazones and Trimethylsilylethyne

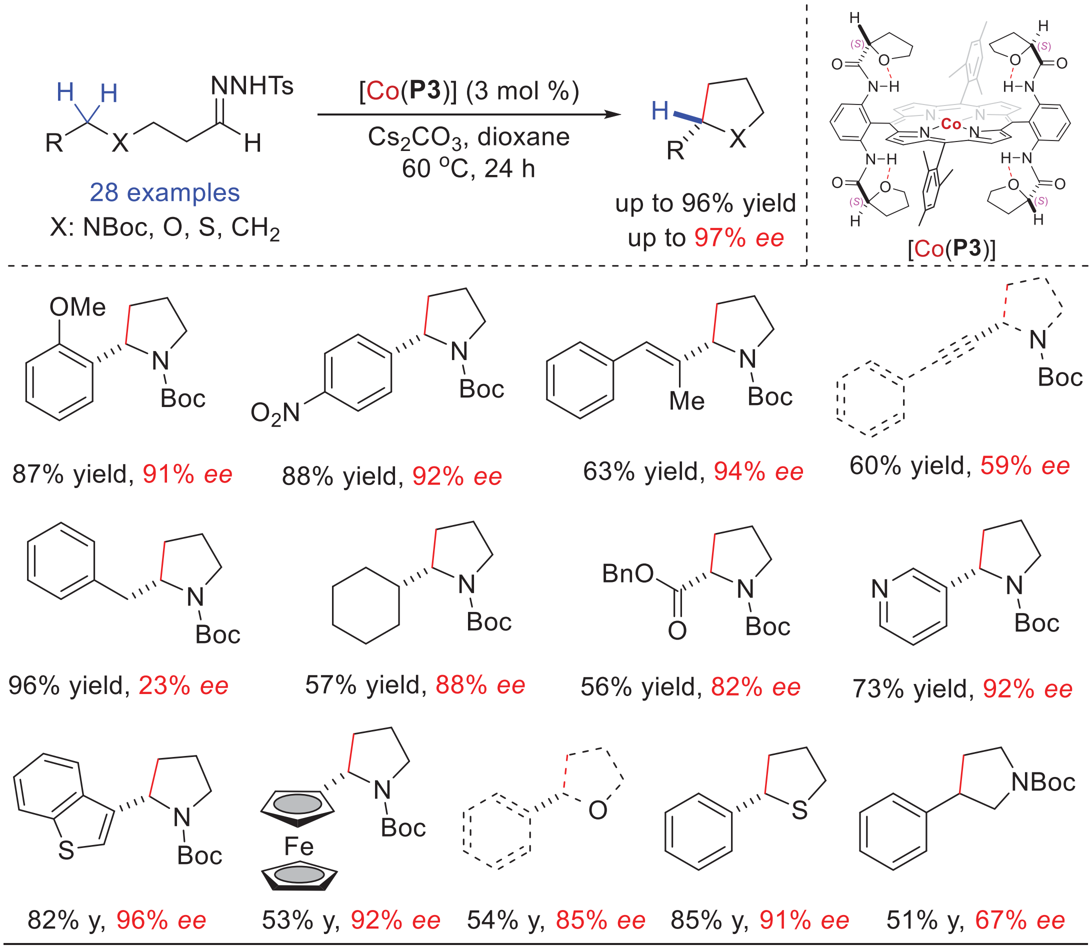


It was found that by using aryl aldehyde-derived tosylhydrazones and trimethylsilylethynes as substrates in the presence of CuI and LiO^{t}Bu in dioxane, the corresponding alkyne products were isolated in moderate to high yields. Further investigation revealed that *N*-tosylhydrazones derived from other carbonyl sources, such as aryl ketones, aliphatic aldehydes and ketones, were all suitable carbene candidates, affording the target products in varied yields. The authors claimed that the reaction undergoes a similar reaction mechanism as shown in Scheme 1.17, which is mechanistically different from other transition metal-catalyzed cross-coupling reactions with terminal alkynes.

1.5 C–H ALKYLATION REACTIONS WITH IN SITU-GENERATED ALKYL/H DIAZO COMPOUNDS

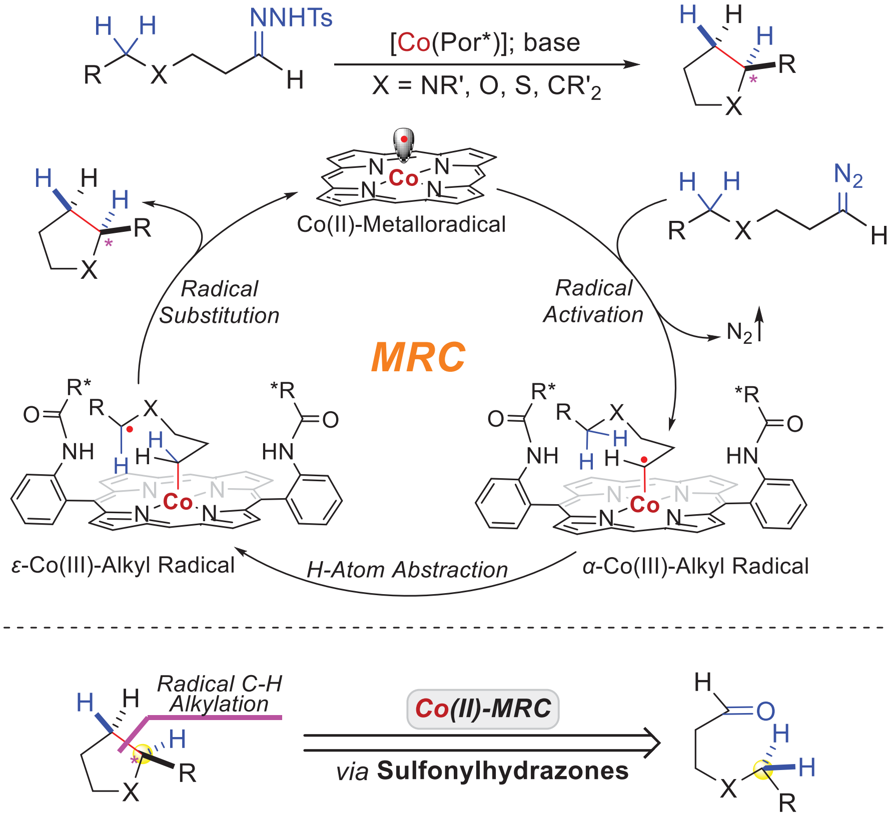
To further challenge the capability of Co(II)-based metalloradical catalysis for C−H alkylation, Zhang and coworkers have shown that linear aliphatic diazo compounds, which were generated in situ from alkyl aldehyde-derived sulfonylhydrazones, could also be utilized for enantioselective radical alkylation (Scheme 1.23).[19] With a new D_2-symmetric chiral porphyrin 2,4,6-TriMe-ZhuPhyrin as the supporting ligand, the Co(II)-based metalloradical catalyst is capable of activating different aliphatic diazo compounds to generate the corresponding α-Co(III)-alkyl radicals and undergo effective alkylation of both activated and nonactivated C–H bonds, streamlining the synthesis of chiral α-substituted pyrrolidines and other important 5-membered cyclic molecules in high yields with excellent enantioselectivities. In addition to remarkable chemoselectivity and regioselectivity, the metalloradical C–H alkylation system is highlighted by its tolerance to functional groups and compatibility with heteroaryl substrates, as showcased in the enantioselective synthesis of naturally occurring nicotine and L-proline derivatives from open-chain molecules.

Scheme 1.23| Enantioselective Radical Cyclization for Synthesis of α-Substituted Pyrrolidines via [Co(P3)]-Catalyzed C–H Alkylation



Distinct from conventional radical cyclization modes that predominantly rely on radical addition to unsaturated bonds as the key cyclization step, this system renders a novel cyclization pattern that involves radical H-atom abstraction and radical substitution (HAA-RS), a general strategy for enantioselective radical construction of common cyclic molecules from linear C–H substrates.

Scheme 1.24| Proposed Radical Cyclization Mechanism via Metalloradical C–H Alkylation

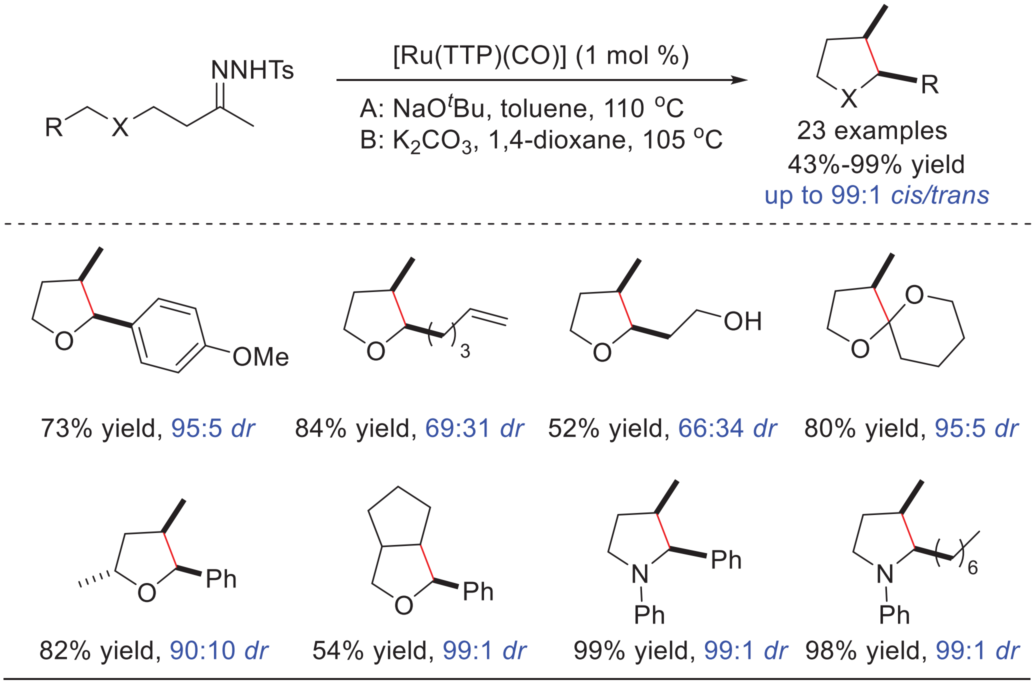


The detailed mechanism was proposed in Scheme 1.24 and backed up by a series of experiments including intramolecular kinetic isotope effect and TEMPO-trapping experiment, supporting the detailed stepwise radical mechanism. This radical cyclization system may provide a new retrosynthetic paradigm to prepare five-membered cyclic molecules from readily available linear aldehydes through the union of C–H and C=O elements for asymmetric C–C bond formation.

1.6 C–H ALKYLATION REACTIONS WITH IN SITU-GENERATED ALKYL/ALKYL DIAZO COMPOUNDS

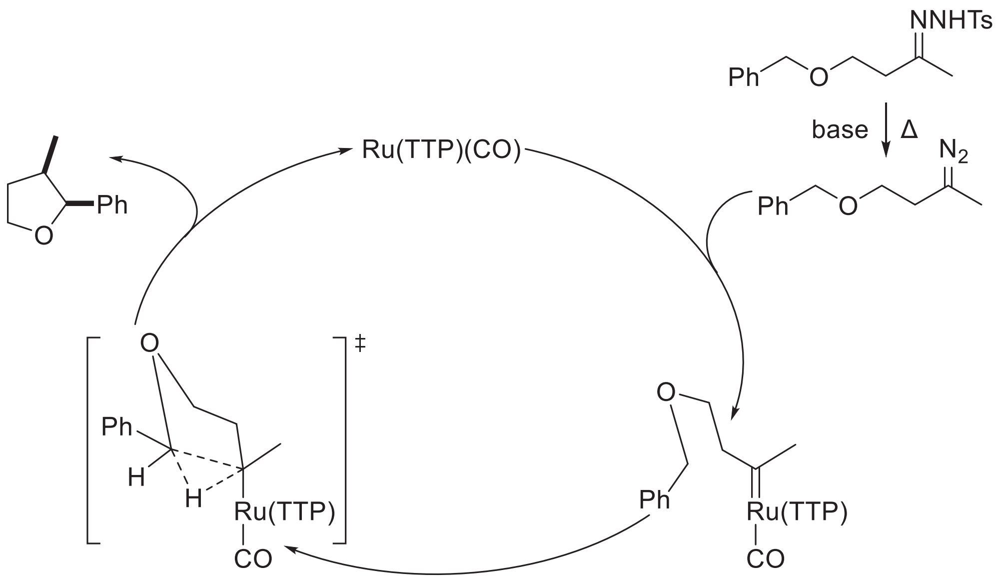
In 2014, Che and coworkers has, for the first time, shown that ruthenium-porphyrin catalyst could successfully activate in situ-generated alkyl/alkyl diazomethanes for intramolecular C(sp^3)–H insertion reactions (Scheme 1.25).[20]

Scheme 1.25| Ruthenium-Porphyrin-Catalyzed Cyclization of Tosylhydrazones to Construct Tetrahydrofurans and Pyrrolidines



With [Ru(TTP)(CO)] as the catalyst in the presence of NaO^{t}Bu in toluene at 110 ºC, aliphatic ketone-derived tosylhydrazones could be effectively converted into substituted tetrahydrofurans and pyrrolidines in up to 99% yield and with up to 99:1 *cis* selectivity. The reaction was highlighted by the good tolerance of many functionalities, and the procedure is simple without the need of a syringe pump for slow addition. Since alkyl *N*-tosylhydrazones can be obtained by the treatment of alkyl-substituted ketones with tosylhydrazine, they also turned the reactions into a one-pot manner for stereoselective intramolecular C–C bond formation directly from alkyl ketones. Later on, the group also successfully applied this methodology for the concise synthesis of (±)-pseudoheliotridane.

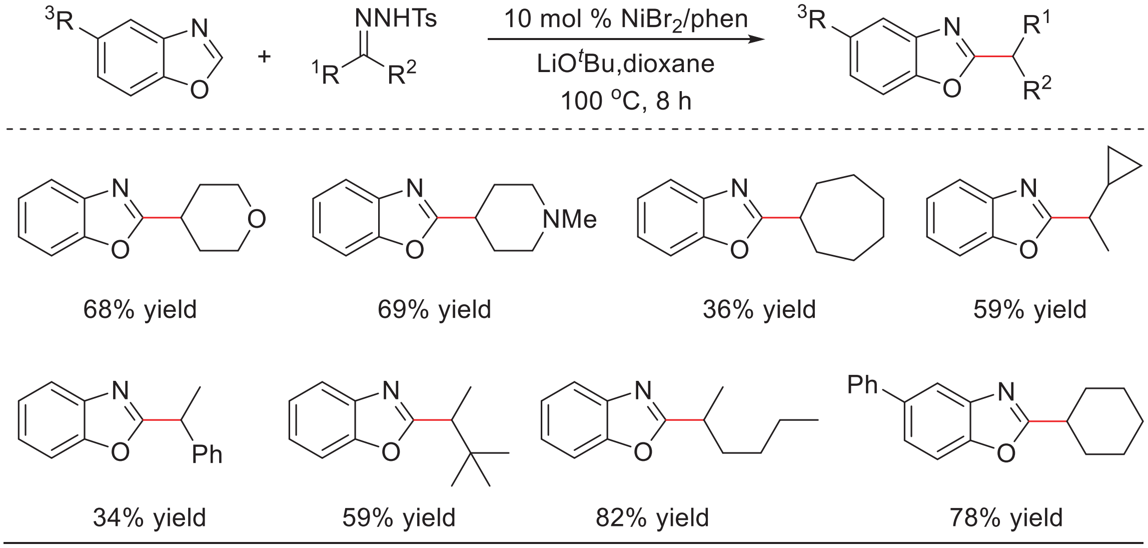
Scheme 1.26| Proposed Reaction Mechanism of the Alkyl Carbene C–H Insertion Catalyzed by [Ru(TTP)(CO)]



For the reaction mechanism, they proposed a plausible catalytic cycle involving electrophilic Fischer carbene intermediates (Scheme 1.26), which is fundamentally distinctive from [Co(**Por**)]-catalyzed stepwise radical pathway involving hydrogen atom abstraction of C–H bonds. Further mechanistic evidences such as KIE study using monodeuterated *N*-tosylhydrazone and DFT calculation were also provided.

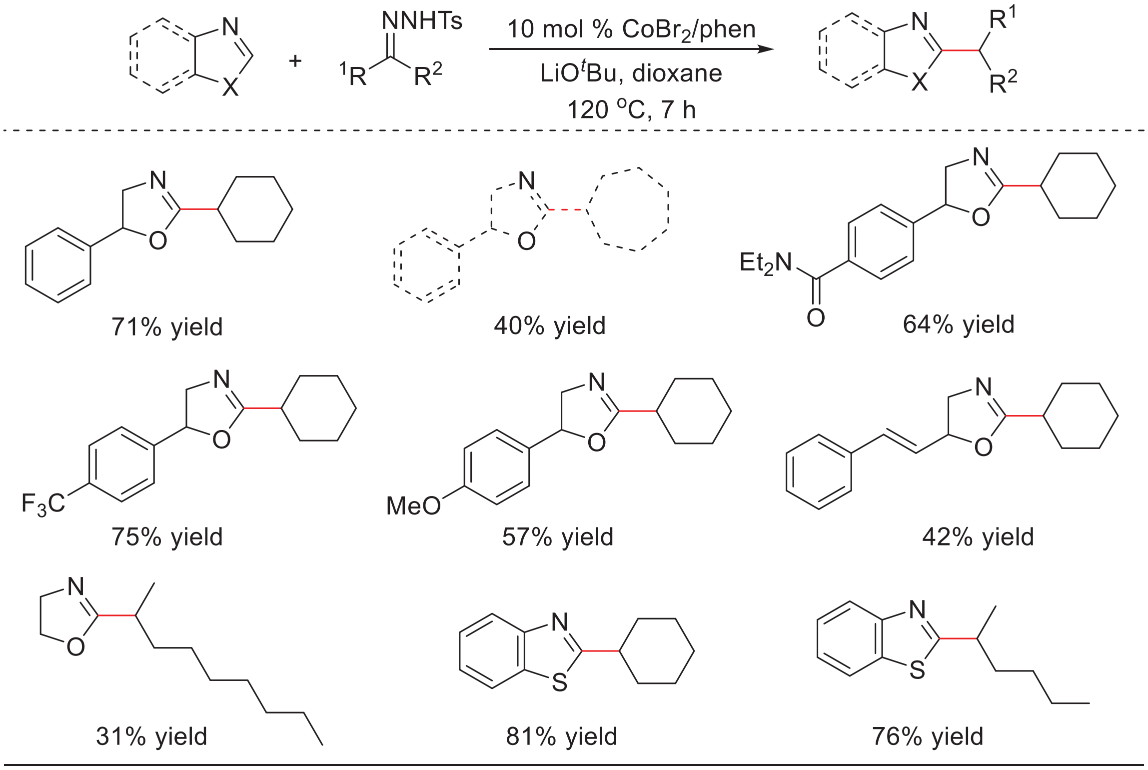
Based on Wang's work involving Cu(I)-catalyzed C−H benzylation or allylation of 1,3-azoles with in situ-generated aryl/alkyl diazo substrates, in 2012, Miura and coworkers further expanded the chemistry to more general substrates by using alkyl/alkyl diazo compounds, where nickel- and cobalt-based catalysts are applied for the direct alkylation of azoles with tosylhydrazones.[21]

Scheme 1.27| Nickel-Catalyzed Direct C−H Alkylation of Benzoxazoles with *N*-Tosylhydrazones



In particular, nickel catalysis enables the installation of unactivated secondary alkyl groups onto benzoxazole analogs in up to 82% yield (Scheme 1.27), whereas cobalt catalyst permits the possible alkylation of 5-aryloxazoles and benzothiazole in up to 81% yield (Scheme 1.28). 5-Aryloxazoles with electron- withdrawing group underwent the alkylation smoothly under standard conditions, while with the electron-donating methoxy substituent required the use of NaO^{t}Bu as the base. The catalytic systems are compatible with various unactivated secondary alkyl groups, including cyclic and even more challenging acyclic alkyl groups. This protocol might provide a concise access to azole cores tethering unactivated secondary alkyl side chains, which are difficult to prepare by using the precedent C–H alkylation methodologies.

Scheme 1.28| Cobalt-Catalyzed Direct C–H Alkylation of Azoles with *N*-Tosylhydrazones



1.7 SUMMARY AND OUTLOOK

C–H functionalization is a cutting-edge area of significant importance in modern organic chemistry. Transition metal-catalyzed C–H alkylation reactions with diazo compounds lie at the center of this field as a key technology for effectively constructing C–C bonds. In addition to the well demonstrated diazo compounds such as acceptor/acceptor-, acceptor-, donor/acceptor-substituted diazomethanes, the successful utilization of donor- and alkyl-substituted ones for C–H alkylation in the past decade not only significantly expands the scope of both substrates and products that are accessible by using this chemistry, but also offers possible solutions to some of the key hurdles in this area. Starting from the hydrazones to generate the diazo species in situ, previously unstable and inaccessible substrates are now approachable from a method that circumvents the practical problems. Even though the related methodology is still in its infancy, this tutorial review summarizing its recent impressive applications strongly indicates that utilizing less stabilized diazo compounds has great potentials for the future growth in this area, including asymmetric intermolecular C–H alkylation reactions.

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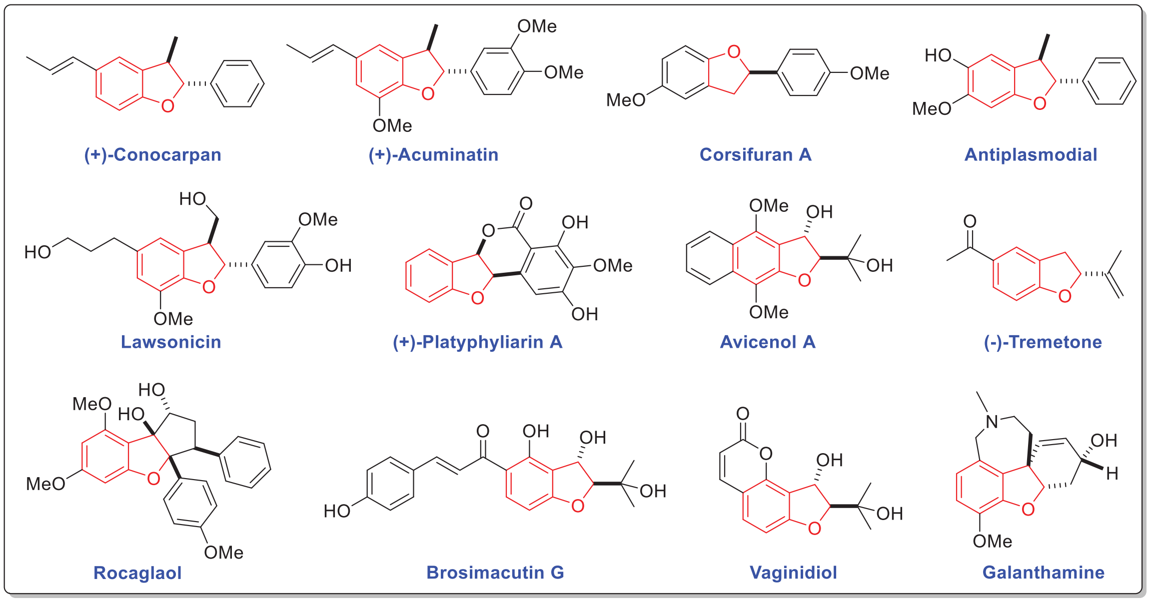
CHAPTER 2

ENANTIOSELECTIVE SYNTHESIS OF CHIRAL DIHYDROBENZOFURANS WITH IN SITU-GENERATED DONOR-SUBSTITUTED DIAZO REAGENTS VIA COBALT(II)-BASED METALLORADICAL C–H ALKYLATION

2.1 INTRODUCTION

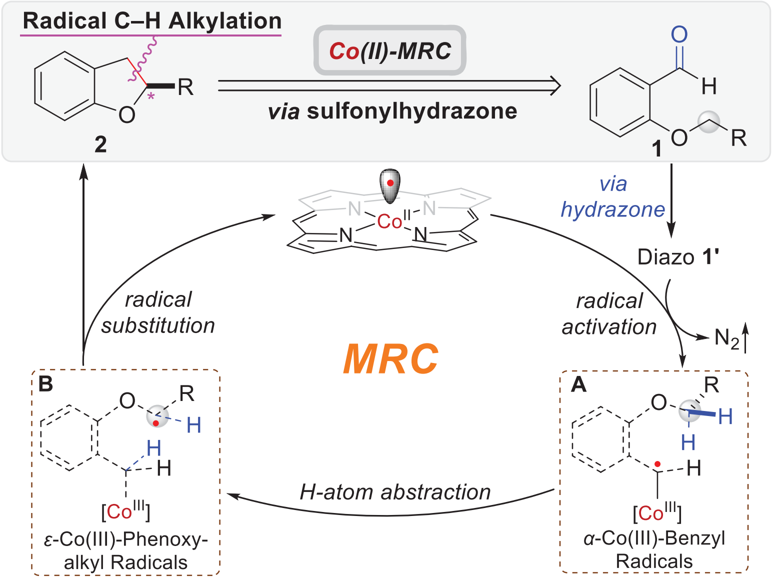
Radical cyclization has been extensively explored for construction of molecular structures of different ring sizes with diverse substitution patterns.[1] Despite its wide adoption, the control of stereochemistry, especially enantioselectivity, remains as one of the major hurdles that limits the applications of radical cyclization in stereoselective organic synthesis.[2] To address this and other long-standing challenges associated with the "free" nature of radicals, metalloradical catalysis (MRC), as a conceptually different approach, seeks the use of metal-centered radicals to homolytically activate substrates for catalytic generation of metal-stabilized organic radicals. As they are controlled by the supporting ligand environment, these metal-stabilized organic radicals are no longer “free” and function as effective intermediates for achieving stereoselective radical transformations.[3,4] As stable 15e metalloradicals with well-defined d^7 low-spin electron configuration, Co(II) complexes of D_2-symmetric chiral amidoporphyrins [Co(D_2-Por*)] have been demonstrated with unique capability of activating different diazo compounds as radical precursors for the generation of the fundamentally new α-Co(III)-alkyl radicals (also known as Co(III)-carbene radicals).[5] These Co-stabilized C-centered radicals, which are well confined within the pocket environment of the chiral porphyrin ligands, have been employed as catalytic intermediates for the development of a number of asymmetric radical processes.[6] Recently, the application of Co(II)-MRC has been further extended to the employment of donor-substituted diazo compounds such as α-aryldiazomethanes, generated *in situ* from sulfonylhydrazones, as new radical precursors for generation of the corresponding α-Co(III)-benzyl radicals that can serve as effective intermediates for different radical transformations,[7] including asymmetric radical cyclopropanation[7c] and enantioselective radical synthesis of indolines.[7a]

Figure 2.1| Selective Examples of Natural Products and Biologically Active Compounds Containing Dihydrobenzofuran Moiety



Given that optically active dihydrobenzofurans are important motifs in a wide range of natural products and biologically active compounds (Figure 2.1),[8] we were attracted to the possibility of constructing these core structures by enantioselective radical C–H alkylation of the corresponding α-aryldiazomethanes from the readily accessible 2-alkoxylbenzaldehyde-derived sulfonylhydrazones under Co(II)-MRC (Scheme 2.1). Upon metalloradical activation of α-aryldiazomethane by [Co(D_2-Por*)], the resulting α-Co(III)-benzyl radical **A** was expected to have the capability to undergo 1,5-H atom abstraction to form ε-Co(III)-phenoxyalkyl radical intermediate **B**. Considering the electronic and steric difference of α-alkoxyalkyl radicals in **B** from previously reported α-aminolkyl radicals,[7,9] it was unclear whether the C(sp^3)–C(sp^3) bond formation through subsequent intramolecular radical substitution (*5-exo-tet* radical cyclization) could be effectively facilitated and enantioselectively controlled by [Co(D_2-Por*)]. If achieved, it would offer a practical and appealing approach for enantioselective synthesis of chiral 2-substituted dihydrobenzofurans from readily available salicylaldehyde-derived sulfonylhydrazones via a fundamentally new radical C–H alkylation process.

Scheme 2.1| Proposed Pathway for Synthesis of Chiral Dihydrobenzofurans via Co(II)-Based Radical C–H Alkylation



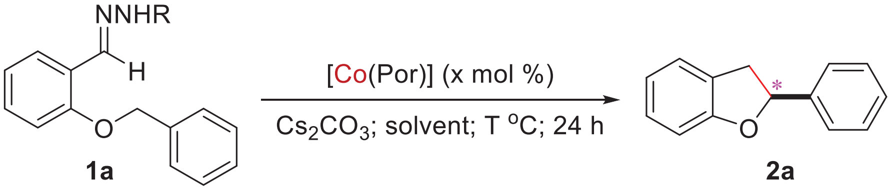
Asymmetric C−H alkylation with diazo compounds represents a powerful approach for stereoselective C(sp^3)−C(sp^3) bond formation directly from prevalent C(sp^3)–H bonds.[10] In the past decades, tremendous progress has been accomplished on asymmetric C−H functionalization via transition metal-catalyzed carbene insertion with different types of diazo compounds such as acceptor- and donor/acceptor-substituted diazo compounds.[11] Recently, Shaw and coworkers further extended the application to donor/donor-substituted diazo compounds, as demonstrated by their first example of Rh_2-catalyzed C−H insertion of *in situ*-generated diazo compounds for asymmetric synthesis of disubstituted benzodihydrofuran derivatives.[12] To the best of our knowledge, there has been no report on asymmetric catalytic system of C−H alkylation that employs donor-substituted diazo compounds for enantioselective synthesis of 2-substituted chiral dihydrobenzofurans.[13] As a new application of Co(II)-MRC, we developed an asymmetric metalloradical system that can utilize *in situ*-generated α-aryldiazomethanes as radical precursors for enantioselective C−H alkylation. At room temperature, the Co(II)-based metalloradical system is suitable for alkylation of various $C(sp^3)$–H bonds with varied electronic and steric properties, allowing for stereoselective construction of chiral dihydrobenzofuran derivatives in high yields with high enantioselectivities.

2.2 RESULTS AND DISCUSSION

2.2.1 Condition Optimization of Co(II)-Based Catalytic System for Enantioselective Radical C–H Alkylation

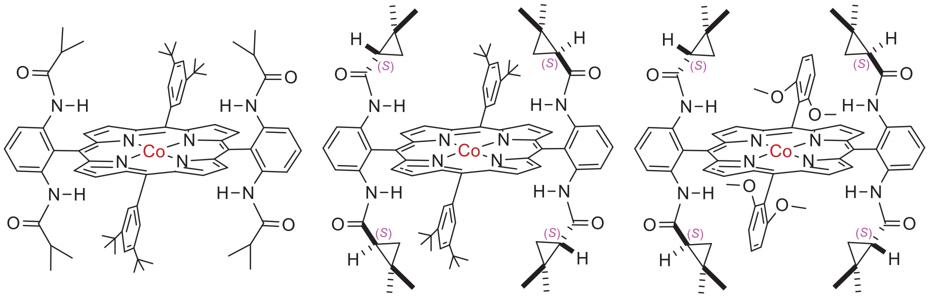
Initial experiments were carried out by using commercially available *O*-benzylsalicylaldehyde-derived *N*-tosylhydrazone (**1a**) as model substrate to examine the possibility of Co(II)-based metalloradical system for 2-phenyl dihydrobenzofuran synthesis by C–H alkylation (Table 1). Gratifyingly, with Co(II) complex of D_{2h}-symmetric achiral amidoporphyrin [Co(**P1**)] (**P1** = 3,5-Di^{t}Bu-IbuPhyrin)[14] as metalloradical catalyst (2 mol %), a productive reaction was achieved at 60 °C to deliver **2a** in 81% yield (entry 1). This result indicated that Co(II)-based metalloradical catalysis could well tolerate basic conditions as well as polar protic solvent for productive radical C–H alkylation. Aimed at developing an enantioselective radical process, we then turned our attention to chiral catalysts. When [Co(**P2**)] (**P2** = 3,5-Di^{t}Bu-ChenPhyrin)[6d] was employed under the same conditions, the desired C–H alkylation product **2a** was produced in 67% yield with a significant level of enantioselectivity (entry 2). Further investigation of the solvent effect revealed that the catalytic process could be carried out in a wide array of mediums to deliver **2a** in moderate yields with comparable enantiomeric ratios (entries 2–6). Among them, methanol was identified as the solvent of choice. To further enhance the asymmetric induction, the reaction was attempted at a lower temperature. However, the reaction with catalyst [Co(**P2**)] at 40 °C was less productive albeit with a slightly increased *er* (entry 7). Encouragingly, both the reactivity and selectivity were greatly enhanced when [Co(**P3**)] (**P3** = 2,6-DiMeO-ChenPhyrin)[6d] was used, where the ligand has sterically more demanding environment at the non-chiral *meso*-aryl substituents (entry 8). This observed buttressing ligand effect might facilitate the intramolecular 1,5-H abstraction process in a sterically more congested pocket. To further amplify the enantioinduction by lowering the reaction temperature to room temperature, it was found that the enantiomeric ratio was increased to 92:8 while the yield was relatively low (entry 9), which was mainly due to the slow generation of diazo compound from tosylsulfonyl hydrazone in the presence of base.

Table 2.1| Condition Optimization of Co(II)-Catalyzed Enantioselective Radical C–H Alkylation[a]



1a **2a**

entry	R[b]	catalyst (x mol %)	solvent	T (°C)	yield (%)[c]	*er*[d]
1	Ts	[Co(**P1**)] (2)	MeOH	60	81	--
2	Ts	[Co(**P2**)] (2)	MeOH	60	67	63:37
3	Ts	[Co(**P2**)] (2)	Dioxane	60	30	60:40
4	Ts	[Co(**P2**)] (2)	DCE	60	40	63:37
5	Ts	[Co(**P2**)] (2)	MTBE	60	41	64:36
6	Ts	[Co(**P2**)] (2)	DME	60	26	59:41
7	Ts	[Co(**P2**)] (4)	MeOH	40	32	65:35
8	Ts	[Co(**P3**)] (4)	MeOH	40	87	88:12
9	Ts	[Co(**P3**)] (4)	MeOH	RT	55	92:08



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

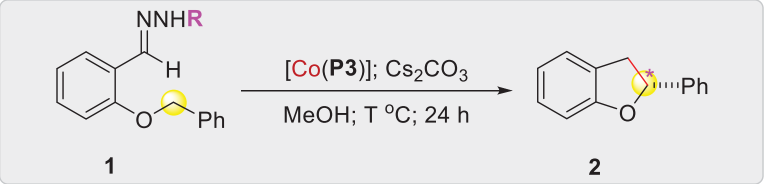
[Co(**P2**)]
(**P2** = 3,5-Di^{t}Bu-ChenPhyrin)

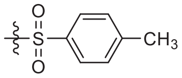
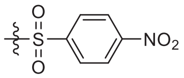
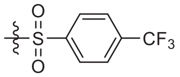
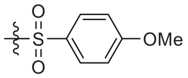
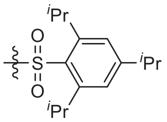
[Co(**P3**)]
(**P3** = 2,6-DiMeO-ChenPhyrin)

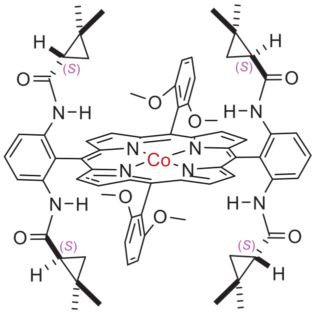
[a] Reactions were carried out with **1a** (0.1 mmol) in the presence of Cs_2CO_3 (2 equiv.) by [Co(Por)] in solvent (1.0 mL) for 24 h. [b] Ts = 4-toluenesulfonyl. [c] Isolated yields. [d] Enantiomeric ratio was determined by chiral HPLC. DCE = 1,2-dichloroethane; MTBE = methyl *tert*-butyl ether; DME = dimethoxyethane.

To accelerate the rate of diazo generation under ambient conditions, we then attempted to screen different hydrazone sources by tuning both electronics and steric hindrance (Table 2.2), which may affect the leaving speed of the aryl sulfonyl group, and thus facilitate the generation rate of diazo reagents. Different substituted sulfonyl hydrazones were then synthesized and tested at room temperature. Surprisingly, when we changed the $–CH_3$ group to $–NO_2$ group, almost no product was formed (entry 2), and other groups such as $–CF_3$ and $–OCH_3$ only gave moderate yield under the same conditions (entries 3-4). Intriguingly, when the highly sterically hindered triisopropyl sulfonyl hydrazone was subjected to the catalytic reactions, the desired product was formed in 77% yield with the same level of high enantiomeric ratio 92:8. It was worth mentioning that the same enantioselectivity was observed when different sulfonyl hydrazones were utilized as the starting materials, which may suggest that the chiral catalyst was not involved in the diazo generation step.

Table 2.2| The Reactivity of Different Sulfonyl Hydrazones on Stereoselective Radical C–H Alkylation[a]



entry	R	T (°C)	yield[b]	er[c]
1		RT	55%	92:8
2		RT	Trace	N.D.
3		RT	31%	92:8
4		RT	20%	92:8
5		**RT**	**77%**	92:8



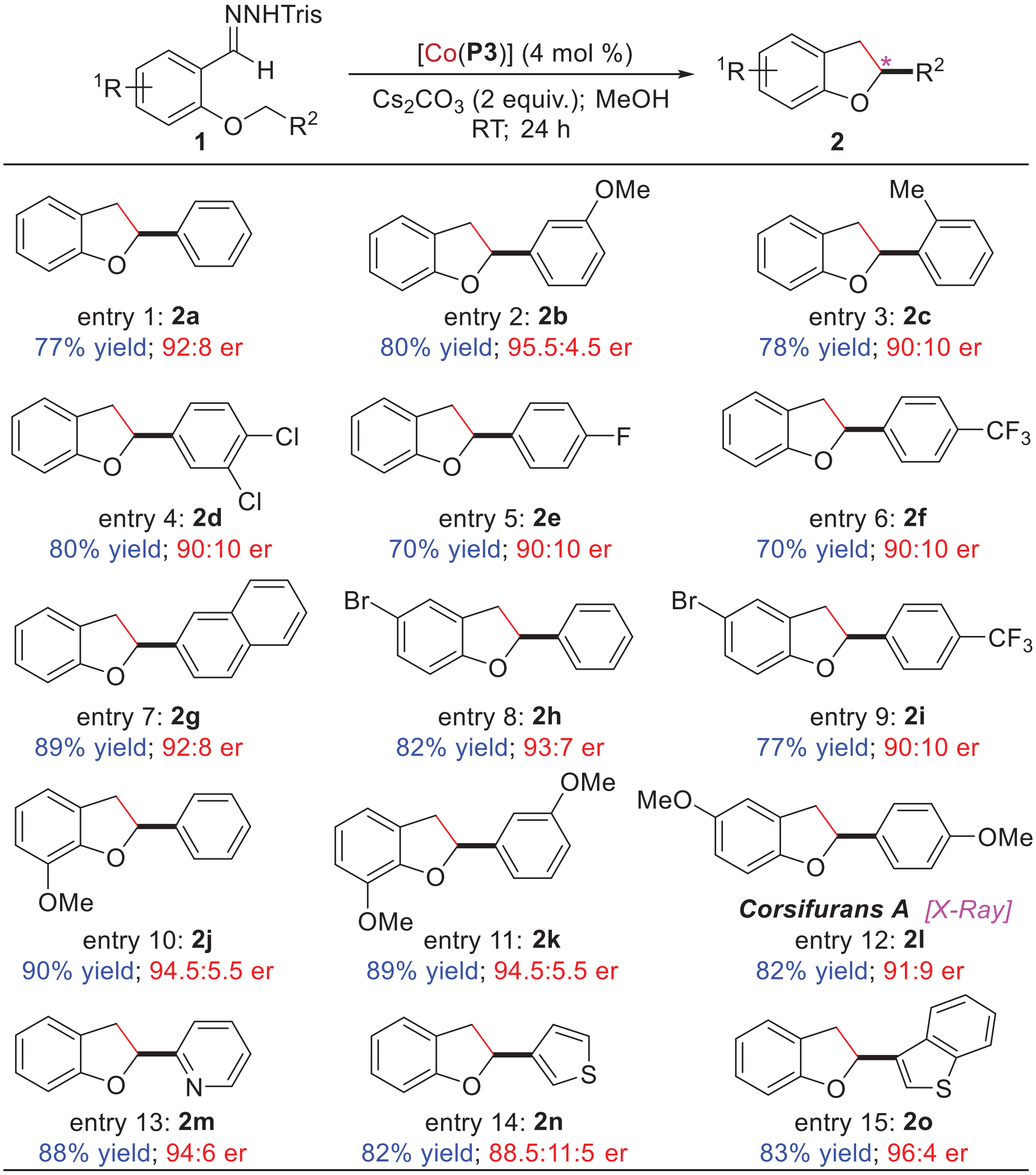
[Co(P3)]
(**P3** = 2,6-DiMeO-ChenPhyrin)

[a] Reactions were carried out with **1** (0.1 mmol) in the presence of Cs_2CO_3 (2 equiv.) by [Co(**P3**)] in MeOH (1.0 mL) for 24 h. [b] Isolated yields. [c] Enantiomeric ratio was determined by chiral HPLC.

2.2.2 Asymmetric Radical Alkylation of Different C–H Substrates for Chiral 2,3-dihydrobenzofuran Synthesis

Under the optimized conditions, the scope of this Co(II)-based radical alkylation system was evaluated by using different C–H substrates (Table 2.3). Like model substrate **1a**, other benzylic C–H substrates bearing either electron-donating or electron-withdrawing groups with different substitution patterns could readily undergo radical alkylation, generating 2-substituted dihydrobenzofurans **2b**–**2f** in high yields with high enantiomeric ratios (entries 2–6). The catalytic system could also efficiently alkylate C–H bonds adjacent to encumbered aryl groups as shown with the successful reaction of the 2-naphthyl-based substrate **1g** (entry 7). Attributed to the easy accessibility of salicylaldehyde derivatives, dihydrobenzofurans with substituents on both aryl groups could also be achieved through this enantioselective radical alkylation, as demonstrated by the high-yielding synthesis of optically active natural product *corsifurans A* (**2l**) and other alkylation products **2h**–**2k** (entries 8–12). The absolute configuration of **2l** was confirmed to be (*S*) by X-ray structural analysis. In particular, the productive formation of bromine-tethered products **2h**–**2i** would allow for the facile further transformations via metal-catalyzed coupling reactions (entries 8 and 9). It was noteworthy to mention that the metalloradical system could even tolerate heteroaryl functionalities, as exemplified by radical alkylation of C–H substrates bearing pyridine, thiophene and benzothiophene moieties, affording the linked biheterocyclic compounds **2m–2o** with good to excellent *er* (entries 13–15). Considering that both heteroarene and dihydrobenzofuran are prevalent as key structural elements in many bioactive natural and synthetic compounds, the readily access of these linked biheterocyclic compounds in high optically enriched form are appealing and may find applications in pharmaceutical research and development.

Table 2.3| Enantioselective Synthesis of Optically Active Dihydrobenzofurans via Radical C–H Alkylation by [Co(P3)]

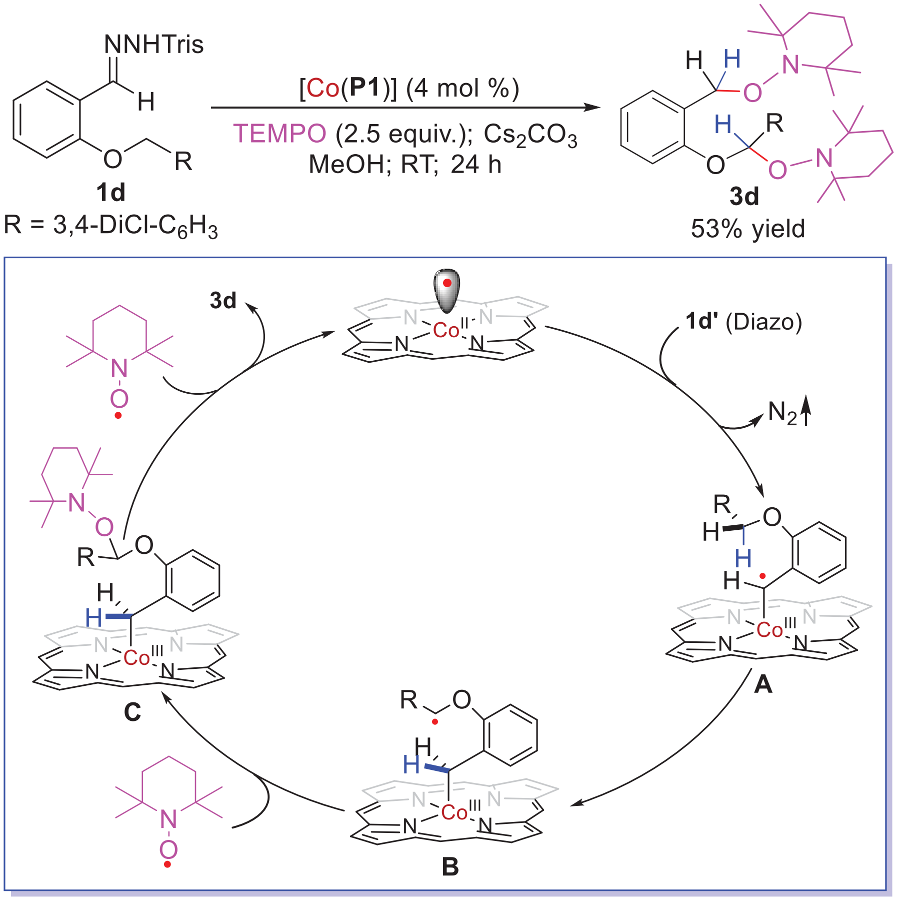


[a] Carried out with **1** (0.1 mmol) in the presence of Cs_2CO_3 (2 equiv.) by [Co(**P3**)] (4 mol %) in MeOH (1.0 mL) for 24 h; Yield refers to isolated yields; Enantiomeric excess was determined by chiral HPLC; Tris = (2,4,6-triisopropyl)phenylsulfonyl; MeOH = Methanol.

2.2.3 Mechanistic Insights for Radical C–H Alkylation

To shed light on the postulated stepwise radical pathway, several mechanistic experiments were performed. First, the effect of radical scavenger TEMPO on the catalytic C–H alkylation reaction was examined (Scheme 2.2).

Scheme 2.2| TEMPO Trapping Reaction as Supportive Evidence for the Proposed Radical Pathway



Under standard conditions, the addition of 2.5 equivalent of TEMPO to the catalytic reaction of benzyl C–H substrate **1d** by the achiral catalyst [Co(**P1**)] resulted in a complete inhibition of the C–H alkylation process. Instead, compound **3d** was isolated in 53% yield, the structure of which was confirmed to contain two TEMPO units at both 1- and 5-positions (Scheme 2.2).

The formation of **3d** is indicative of the presence of the initial α-Co(III)-benzyl radical **A** and the *ε*-Co(III)-alkyl radical **B** after 1,5-HAA, which might be subsequently capped by one molecule of TEMPO at the *ε*-position through radical recombination to generate intermediate **C**, then followed by radical substitution with a second molecule of TEMPO at the α-position to cleave the weak Co(III)–C bond and yield the formation of **3d**.

In addition to the TEMPO trapping experiment, the resulting Co(III)-supported alkyl radical intermediates **A** (Scheme 2.1) from the reaction of substrate **1a** by [Co(**P1**)] in the absence of TEMPO could be directly detected by HRMS ($C_{90}H_{100}CoN_8O_5^+$, *m*/*z*: calculated: 1431.7143, found: 1431.7125). The HRMS experiment was carried out in the absence of any additives such as formic acid, which commonly act as electron carriers for ionization, allowing for the detection of the molecular ion signals corresponding to Co(III)-alkyl radical ($C_{90}H_{100}CoN_8O_5\cdot$) by the loss of one electron.

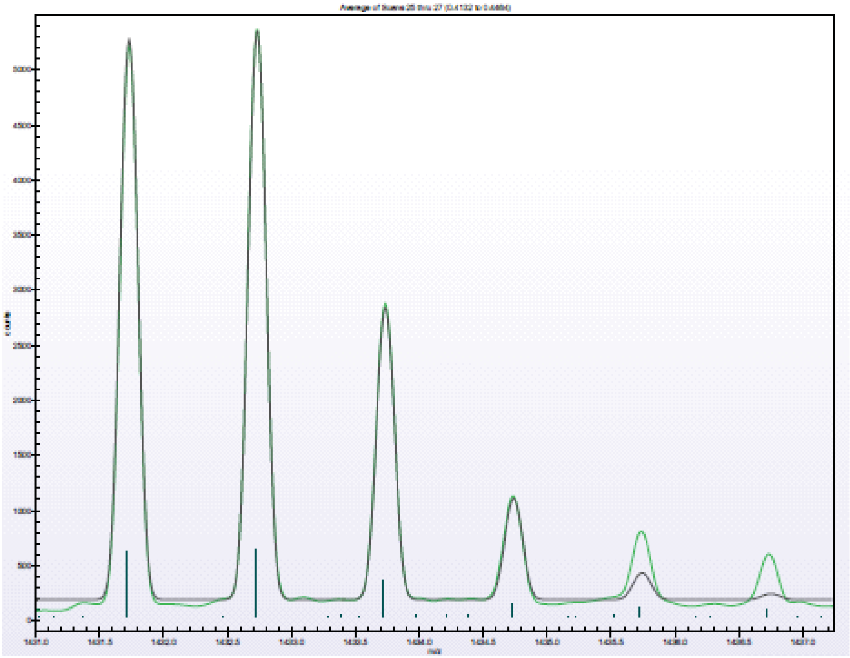
Scheme 2.3| High Resolution Mass Spectroscopy (HRMS) Spectrum for Co(III)-Supported Alkyl Radical Intermediate

```
sCLIPS Report  -  J:\0460.d\AcqData\MSProfile.bin

    Self-Calibration Mass Range (Da)
                        Start:      -0.41
                        End:        0.41

RT Windows
    Average of Scans 25 thru 27 (0.4132 to 0.4464)

sCLIPS Parameters
    Accurate Mass:                  1431.7125
    Charge:                         1
    Mass Tolerance (mDa):           10.00
    Electron State:                 Both

    Double Bond Equivalent Range
                        Minimum:    -1.00
                        Maximum:    50.00

    Profile Mass Range (Da)
                        Start:      -1.00
                        End:        5.50

    Empirical Rules:                Enabled
      Empirical Elemental Limits:   Wiley
      H/C Ratio:                    Extended
      Heteroatom Ratios:            Extended


    Element     Minimum     Maximum
       C           85          90
       H           95         101
       Co           0           1
       N            0          10
       O            0          10
```

Chemical Formula: $C_{90}H_{100}CoN_8O_5^+$
Calculated Mass: 1431.7143
Found Mass: 1431.7125

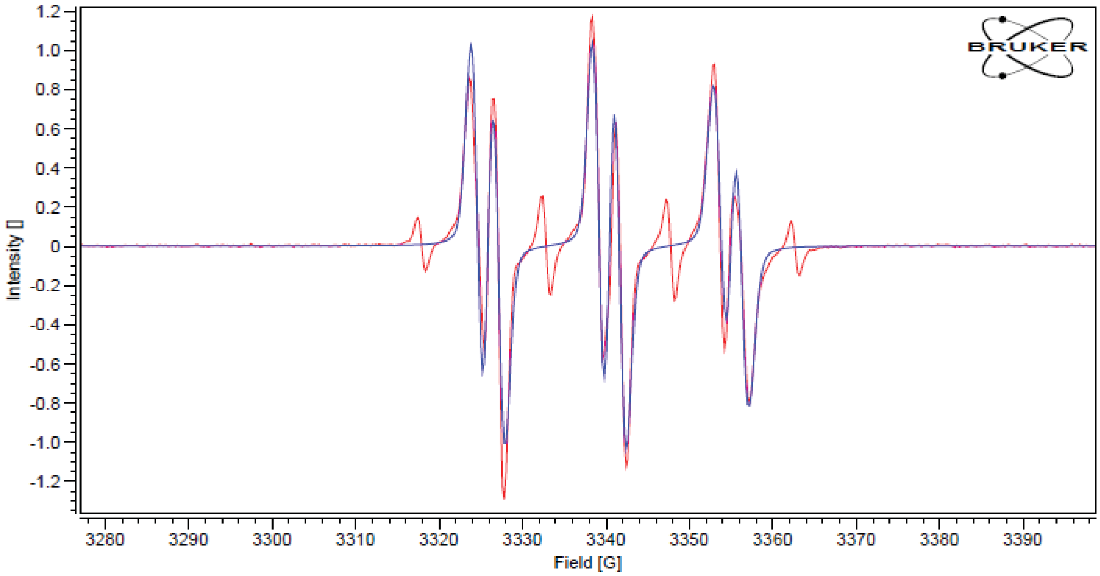
sCLIPS Search Results

	Formula	Mono Isotope	Mass Error (mDa)	Mass Error (PPM)	Spectral Accuracy	RMSE	DBE
1	C90H95N8O9	1,431.7217	-9.1531	-6.3931	92.8833	81	47.5
2	C90H100CoN8O5	1,431.7143	-1.8200	-1.2712	92.6295	84	45.0
3	85H100CoN10O7	1,431.7103	2.2028	1.5386	91.5792	96	41.0



Besides the HR-MS experiment, the corresponding intermediate **A** (Scheme 2.1) was also trapped by spin trapping reagent phenyl *N*-*tert*-butylnitrone (PBN) to give the characteristic EPR signal. As shown in Scheme 2.4, 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 with $g = 2.006$, $A_N = 14.6$ G, $A_H = 2.6$ 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 litrature.[7d]

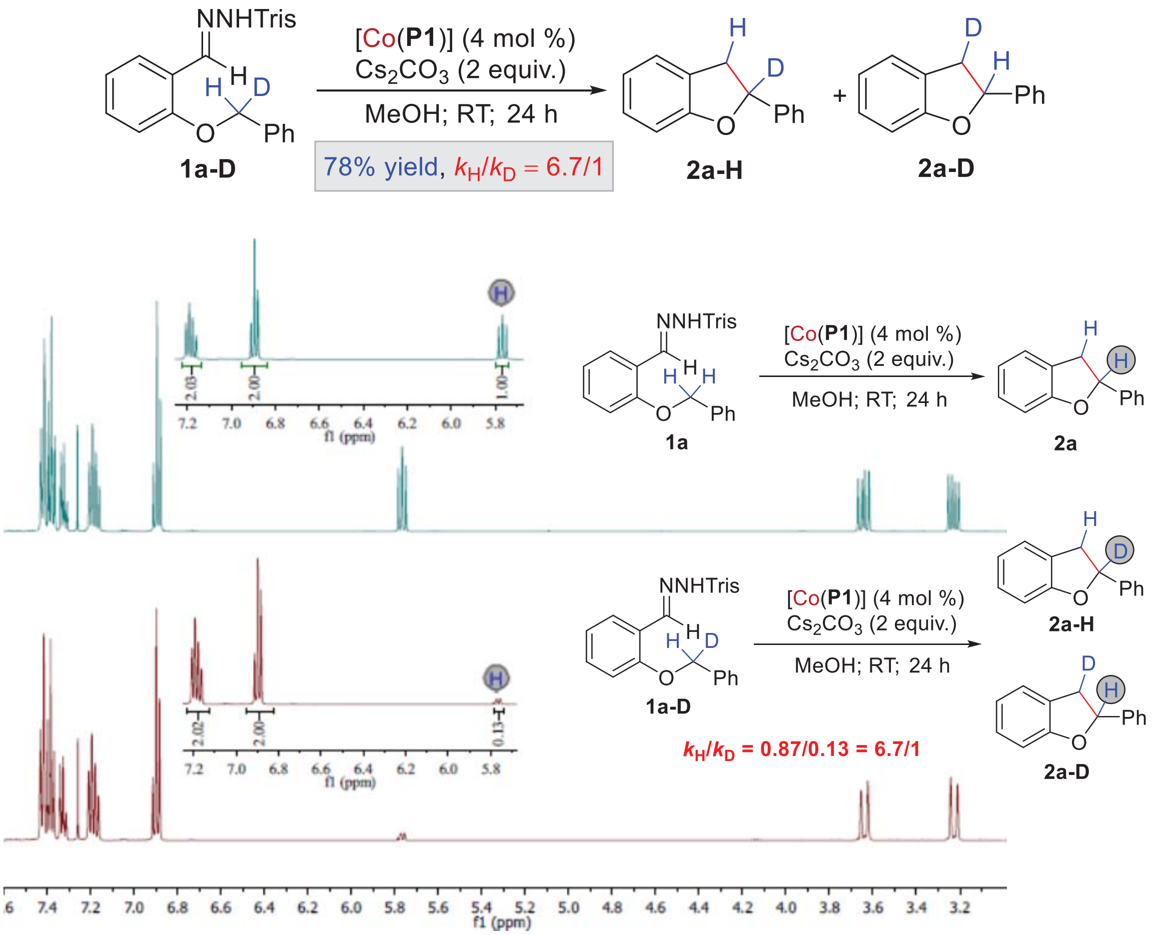
Scheme 2.4| Isotropic X-band EPR Spectrum of Phenyl *N*-*tert*-butylnitrone (PBN)-Trapped Co(III)-Supported Alkyl Radical Intermediate



Furthermore, mono-deuterated sulfonylhydrazone **1a-D** was synthesized to evaluate the intramolecular kinetic isotope effect (KIE) of the C–H activation process

(Scheme 2.5). 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 78%. ^{1}H-NMR analysis of the product mixture revealed an intramolecular KIE ratio of $k_H/k_D = 6.7/1$. This significantly 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)-benzyl radical intermediate **A** (Scheme 2.1). Together, these observed results including intramolecular KIE study and TEMPO-trapping experiment are well supportive for the postulated stepwise radical mechanism.

Scheme 2.5| Intramolecular Kinetic Isotope Effect for the Radical C–H Alkylation



2.3 CONCLUSIONS

In summary, an asymmetric radical pathway for the synthesis of enantioenriched 2-substituted dihydrobenzofuran derivatives is achieved via Co(II)-based enantioselective radical C–H alkylation. The Co(II) complex of D_2-symmetric chiral amidoporphyrin 2,6-DiMeO-ChenPhyrin, [Co(**P3**)], is identified as effective metalloradical catalyst to activate *in situ*-generated α-aryldiazomethanes for enantioselective intramolecular radical alkylation of C–H bonds that are adjacent to a variety of aromatic functional groups with varied electronic and steric properties. The corresponding 2-substituted dihydrobenzofurans are achieved in high yields with good enantioselectivities. This enantioselective radical process would offer a streamlined synthesis of chiral 2-substituted dihydrobenzofurans from readily available 2-alkoxylbenzaldehyde-derived sulfonylhydrazones.

2.4 EXPERIMENTAL SECTION

2.4.1 General Considerations

^{1}H NMR spectra were recorded on a Varian INOVA 400 (400 MHz), 500 (500 MHz) or a 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, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian INOVA 500 (125 MHz), or 600 (150 MHz) spectrometers 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. 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. HPLC measurements were carried out on a Shimadzu HPLC system with Chiralcel AD-H, ODH, OJH, and ChiralPak Immobilized columns: IA, and IB. Infrared (IR) spectra were recorded on a Termo Scientific Nicolet Is5 System. Frequencies are reported in wavenumbers (cm^{-1}). HRMS data was obtained on an Agilent 6210 Time-of-Flight LC/MS with ESI as the ion source. Optical rotations were measured on a Rudolph Research Analytical AUTOPOL® IV digital polarimeter. The X-ray diffraction data were collected using Bruker Kappa APEX DUO diffractometer and a Rigaku HighFlux Homelab diffractometer. X-band EPR spectra were recorded on a Bruker EMX-Plus spectrometer (Bruker BioSpin).

Unless otherwise noted, all C–H alkylation reactions were performed in oven-dried glassware under dry N_2 atmosphere with standard Schlenk vacuum line techniques. Gastight 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).

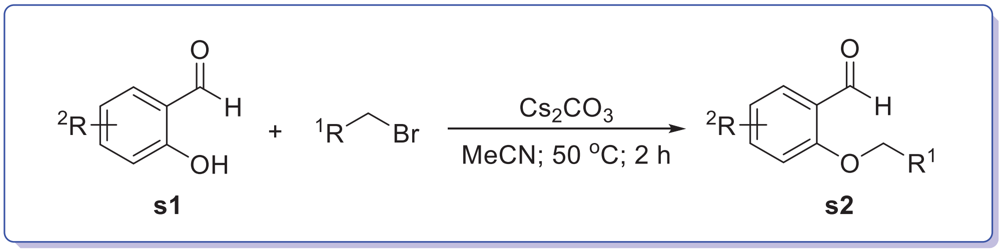
2.4.2 Procedure for HRMS Experiment

To an oven-dried Schlenk tube, sulfonylhydrazone **1a** (0.05 mmol) and Cs_2CO_3 (2.0 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, and CH_3CN (0.5 mL) was added via a gastight syringe. The mixture was then stirred at 60 °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**)] (4 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, which commonly act as electron carriers for ionization, allowing for the detection of the molecular ion signals corresponding to Co(III)-alkyl radical ($C_{90}H_{100}CoN_8O_5$•) by the loss of one electron.

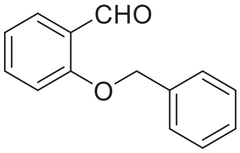
2.4.3 Procedure for EPR Experiment

To an oven-dried Schlenk tube A, sulfonylhydrazone **1a** (0.05 mmol) and Cs_2CO_3 (2.0 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, and benzene (0.5 mL) was added via a gastight syringe. The mixture was then stirred at 60 ºC for 0.5 h. During the time, [Co(**P1**)] (4 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 3 min and transferred into a degassed EPR tube (filled with argon) through a gastight syringe. The sample was then carried out for EPR experiment at room temperature (EPR settings: T = 298 K; microwave frequency: 9.37762 GHz; power: 6.325 mW; modulation amplitude: 1.0 G).

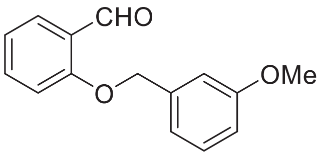
2.4.4 Synthetic Procedure for 2-(Benzyloxy)benzaldehyde Derivatives s2



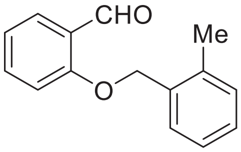
To a solution of **s1** (2 mmol) and Cs_2CO_3 (2.4 mmol) in MeCN (20 mL) was added alkyl bromide (2.4 mmol) at room temperature. The reaction was heated at 50 °C for 2 h. The resulting mixture was cooled down to room temperature and filtered through a short pad of silica. The combined organic mixture was concentrated under vacuum and purified by flash column chromatography.



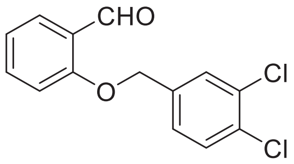
2-(benzyloxy)benzaldehyde s2-a Yield: 99%. Hexanes/ethyl acetate = 8/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.57 (s, 1H), 7.87 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.57 – 7.51 (m, 1H), 7.45 (d, *J* = 7.1 Hz, 2H), 7.41 (dd, *J* = 9.9, 4.8 Hz, 2H), 7.36 (t, *J* = 7.1 Hz, 1H), 7.05 (t, *J* = 8.0 Hz, 2H), 5.20 (s, 2H). ^{13}C NMR (100MHz, $CDCl_3$) δ 189.70, 161.02, 136.05, 135.86, 128.71, 128.44, 128.25, 127.26, 125.19, 120.99, 113.01,70.46. IR (neat, cm^{-1}): 2870.51, 1726.84, 1682.48, 1598.14, 1510.54, 1221.15, 1156.32, 1104.94, 1011.07, 823.10, 753.20, 649.21 601.86.



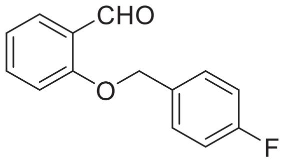
2-((3-methoxybenzyl)oxy)benzaldehyde s2-b Yield: 98%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.57 (s, 1H), 7.86 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.58 – 7.49 (m, 1H), 7.32 (t, *J* = 7.9 Hz, 1H), 7.09 – 6.97 (m, 4H), 6.89 (dd, *J* = 8.2, 2.4 Hz, 1H), 5.18 (s, 2H), 3.83 (s, 3H). ^{13}C NMR (125MHz, $CDCl_3$) δ 189.70, 160.97, 159.89, 137.65, 135.88, 129.79, 128.49, 125.15, 121.02, 119.36, 113.59, 113.01, 112.78, 70.30, 55.26. IR (neat, cm^{-1}): 2864.32, 2834.06, 1682.62, 1597.87, 1584.20, 1453.39, 1040.20, 846.51, 763.82, 687.94, 663.02,439.39. HRMS (EI) (M^+) Calcd. for $C_{15}H_{14}O_3^+$: 242.0937, found 242.0943.



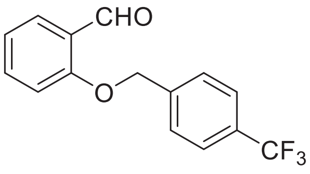
2-((2-methylbenzyl)oxy)benzaldehyde s2-c Yield: 98%. Hexanes/ethyl acetate = 7/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ ^{1}H NMR (600 MHz, $cdcl_3$) δ 10.52 (s, 1H), 7.86 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.57 – 7.54 (m, 1H), 7.41 (d, *J* = 7.3 Hz, 1H), 7.28 – 7.27 (m, 1H), 7.25 – 7.22 (m, 2H), 7.09 (d, *J* = 8.4 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 5.16 (s, 2H), 2.39 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.61, 161.16, 136.50, 135.84, 133.90, 130.53, 130.27, 128.55, 128.44, 126.12, 125.26, 120.98, 112.93, 69.12, 18.90. IR (neat, cm^{-1}): 3033.82, 2853.31, 2760.02, 1683.47, 1595.89, 1486.13, 1452.50, 1401.09, 1294.99, 1248.84, 1028.16, 739.78, 653.42. HRMS (EI) (M^+) Calcd. for $C_{15}H_{14}O_2^+$: 226.0988, found 226.0982.



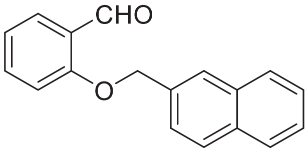
2-((3,4-dichlorobenzyl)oxy)benzaldehyde s2-d Yield: 98%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.57 (td, *J* = 7.7, 1.5 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 3H), 6.77 (d, *J* = 8.5 Hz, 2H), 4.89 and 4.75 (br, 2H), 3.76 (s, 3H), 3.63 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.57, 159.31, 156.07, 143.30, 134.75, 132.91, 130.34, 128.89, 128.60, 128.44, 127.89, 113.92, 55.18, 54.51, 53.29. IR (neat, cm^{-1}): 2955.10, 2837.50, 2758.23, 1711.53, 1611.89, 1598.52, 1514.07, 1459.69, 1251.04, 1034.18. HRMS (ESI) (M+H$^+$) Calcd. for $C_{17}H_{18}NO_4^+$: 300.1230, found 300.1232.



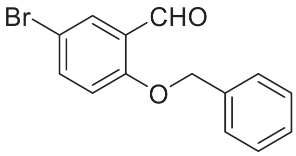
2-((4-fluorobenzyl)oxy)benzaldehyde s2-e Yield: 99%. Hexanes/ethyl acetate = 8/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.53 (s, 1H), 7.86 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.54 (ddd, *J* = 8.4, 7.4, 1.9 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.12 – 7.02 (m, 4H), 5.15 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.62, 162.62 (d, *J* = 247.0 Hz), 160.83, 135.91, 131.82 (d, *J* = 3.2 Hz), 129.21 (d, *J* = 8.2 Hz), 128.60, 125.17, 121.16, 115.69 (d, *J* = 21.5 Hz) 112.95, 69.83. IR (neat, cm^{-1}): 2870.51, 1682.48, 1598.14, 1483.85, 1456.88, 1221.15, 1156.32, 1104.94, 1011.77, 823.10, 753.2. HRMS (EI) (M$^+$) Calcd. for $C_{14}H_{11}FO_2^+$: 230.0738, found 230.0729.



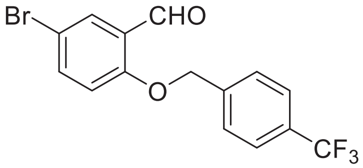
2-((4-(trifluoromethyl)benzyl)oxy)benzaldehyde s2-f Yield: 95%. Hexanes/ethyl acetate = 8/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.57 (s, 1H), 7.88 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.55 (t, *J* = 8.4 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 5.26 (s, 2H). ^{13}C NMR (100MHz, CDCl$_3$) δ 189.36, 160.49, 140.09, 135.91, 130.46 (q, *J* = 32.4 Hz, 1C), 128.84, 127.23, 125.69, 125.19, 123.95 (q, *J* = 270 Hz, 1C), 121.38, 112.79, 69.53. IR (neat, cm^{-1}): 2910.54, 2870.84, 1920.47, 1684.76, 1622.70, 1598.14, 1487.35, 1451.76, 1405.03, 1321.36, 1302.01, 1103.66, 1067.67, 822.69, 747.90. HRMS (EI) (M$^+$) Calcd. for $C_{15}H_{11}F_3O_2^+$: 280.0706, found 280.0702.



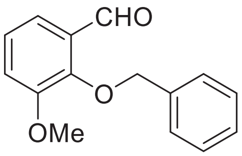
2-(naphthalen-2-ylmethoxy)benzaldehyde s2-g Yield: 99%. Hexanes/ethyl acetate = 7/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 10.63 (s, 1H), 7.90 – 7.85 (m, 5H), 7.56 – 7.50 (m, 4H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.08 – 7.03 (m, 1H), 5.36 (s, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.70, 161.04, 135.88, 133.51, 133.22, 133.13, 128.62, 128.49, 127.92, 127.77, 126.44, 126.30, 126.26, 125.23, 124.88, 121.05, 113.09, 70.62. IR (neat, cm^{-1}): 3078.80, 2852.31, 2761.05, 1684.99, 1595.92, 1482.09, 1456.78, 1303.00, 1240.17, 1014.26, 824.59. HRMS (ESI) (M+H$^+$) Calcd. for $C_{18}H_{15}O_2^+$: 263.1067, found 263.1069.



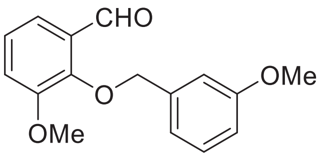
2-(benzyloxy)-5-bromobenzaldehyde s2-h Yield: 95%. Hexanes/ethyl acetate = 7/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.46 (s, 1H), 7.95 (d, *J* = 2.6 Hz, 1H), 7.61 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.46 – 7.33 (m, 5H), 6.95 (d, *J* = 8.9 Hz, 1H), 5.18 (s, 2H). ^{13}C NMR (125MHz, CDCl$_3$) δ 188.27, 159.87, 138.22, 135.50, 131.06, 128.81, 128.48, 127.31, 126.44, 115.11, 113.83, 70.85. IR (neat, cm^{-1}): 3074.35, 2922.97, 2865.62, 2760.99, 1676.62, 1588.92, 1474.82, 1448.97, 1395.10, 1382.03, 1273.55, 1236.59, 1183.89, 1123.23, 1022.57. HRMS (EI) (M$^+$) Calcd. for $C_{14}H_{11}BrO_2^+$: 289.9937, found 289.9925.



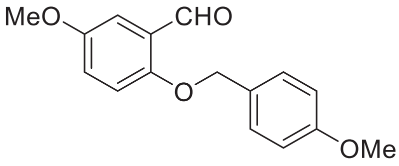
5-bromo-2-((4-(trifluoromethyl)benzyl)oxy)benzaldehyde s2-i Yield: 90%. Hexanes/ethyl acetate = 7/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.46 (s, 1H), 7.96 (d, *J* = 2.6 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.62 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 1H), 5.24 (s, 2H). ^{13}C NMR (100MHz, CDCl$_3$) δ 187.87, 159.36, 139.52, 138.27, 131.39, 130.68 (q, *J* = 32.5 Hz, 1C), 127.29, 126.44, 125.78, 123.88 (q, *J* = 270 Hz, 1C), 114.85, 114.22, 69.91. IR (neat, cm^{-1}): 2915.71, 2874.21, 1917.19, 1676.46, 1591.57, 1478.27, 1452.63, 1323.06, 1271.37, 1237.57, 1164.37, 1165.57, 1106.09. HRMS (EI) (M$^+$) Calcd. for $C_{15}H_{10}BrF_3O_2^+$: 357.9811, found 357.9790.



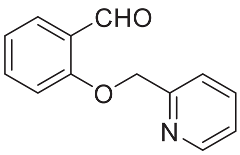
2-(benzyloxy)-3-methoxybenzaldehyde s2-j Yield: 98%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.23 (s, 1H), 7.41 – 7.31 (m, 6H), 7.20 – 7.12 (m, 2H), 5.18 (s, 2H), 3.95 (s, 3H). ^{13}C NMR (125MHz, $CDCl_3$) δ 190.23, 153.02, 151.02, 136.32, 130.30, 128.65, 128.58, 128.52, 124.24, 119.01, 117.96, 76.33, 56.08. IR (neat, cm^{-1}): 3008.09, 2967.36, 2877.99, 2840.97, 1688.13, 1594.12, 1583.01, 1478.28, 1454.55, 1438.21, 1365.78, 1060.52, 964.77, 750.64. HRMS (EI) (M^+) Calcd. for $C_{15}H_{14}O_3^+$: 242.0937, found 242.0923.



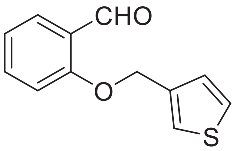
3-methoxy-2-((3-methoxybenzyl)oxy)benzaldehyde s2-k Yield: 97%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.26 (s, 1H), 7.39 (dd, J = 7.5, 1.7 Hz, 1H), 7.28 (t, J = 7.8 Hz, 1H), 7.20 – 7.12 (m, 2H), 6.98 – 6.93 (m, 2H), 6.88 (dd, J = 8.2, 2.4 Hz, 1H), 5.15 (s, 2H), 3.95 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (125MHz, $CDCl_3$) δ 190.38, 159.73, 152.99, 151.04, 137.86, 130.29, 129.63, 124.25, 120.77, 119.05, 117.97, 114.03, 113.99, 76.20, 56.09, 55.24. IR (neat, cm^{-1}): 2939.71, 2837.80, 1687.60, 1583.83, 1480.01, 1454.92, 1438.43, 1366.78, 1262.21, 1247.37, 781.63, 751.27. HRMS (EI) (M^+) Calcd. for $C_{16}H_{16}O_4^+$: 272.1043, found 272.1044.



5-methoxy-2-((4-methoxybenzyl)oxy)benzaldehyde s2-l[15] Yield: 96%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.46 (s, 1H), 7.35 – 7.33 (m, 3H), 7.11 (dd, *J* = 9.0, 3.2 Hz, 1H), 7.02 (d, *J* = 9.1 Hz, 1H), 6.92 (d, *J* = 8.6 Hz, 2H), 5.08 (s, 2H), 3.82 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.64, 155.93, 153.85, 129.16, 128.25, 125.62, 123.48, 115.36, 114.09, 110.16, 71.29, 55.80, 55.30. IR (neat, cm^{-1}): 2961.70, 2953.04, 2878.94, 1669.67, 1611.23, 1514.99, 1490.37, 1279.57, 1212.22, 1027.74, 993.12, 880.06, 704.72.

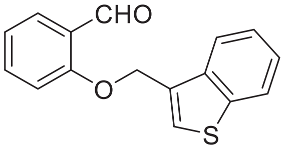


2-(pyridin-2-ylmethoxy)benzaldehyde s2-m Yield: 90%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.61 (d, *J* = 4.8 Hz, 1H), 7.86 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.75 (td, *J* = 7.7, 1.7 Hz, 1H), 7.62 – 7.43 (m, 2H), 7.26 (t, *J* = 7.3 Hz, 1H), 7.10 – 6.94 (m, 2H), 5.32 (s, 2H). ^{13}C NMR (125MHz, $CDCl_3$) δ 189.51, 160.53, 156.27, 149.33, 137.00, 135.97, 128.80, 125.07, 122.92, 121.21, 112.96, 71.02. IR (neat, cm^{-1}): 3073.94, 2865.91, 2761.70, 1683.67, 1583.43, 1600.44, 1486.54, 1434.36, 1282.46, 1194.79, 1171.88, 995.03, 850.81, 838.70, 750.54. HRMS (EI) (M$^+$) Calcd. for $C_{13}H_{11}NO_2^+$: 213.0784, found 213.0777.



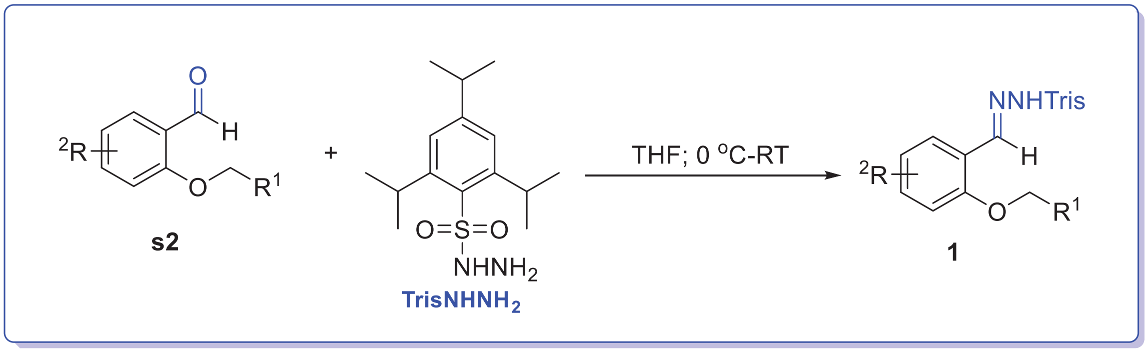
2-(thiophen-3-ylmethoxy)benzaldehyde s2-n Yield: 90%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.53 (s, 1H), 7.86 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.38 – 7.34 (m, 2H), 7.16 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.07 – 7.03 (m, 2H), 5.21 (s, 2H). ^{13}C NMR (125MHz, $CDCl_3$) δ 189.63, 160.91, 136.98, 135.82, 128.50, 126.69, 126.61, 125.25, 123.26, 121.08, 112.98, 66.29. IR (neat, cm^{-1}):

2918.48, 2849.49, 1686.70, 1598.53, 1482.60, 1457.32, 1286.20, 1239.14, 761.63. HRMS (EI) (M^+) Calcd. for $C_{12}H_{11}O_2S^+$: 219.0474, found 219.0477.

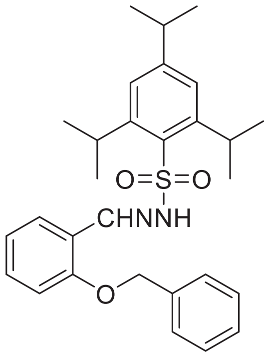


2-(benzo[b]thiophen-3-ylmethoxy)benzaldehyde s2-o Yield: 97%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.49 (s, 1H), 7.91 – 7.85 (m, 3H), 7.59 – 7.57 (m, 1H), 7.53 (s, 1H), 7.44 – 7.39 (m, 2H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 5.43 (s, 2H). ^{13}C NMR (150MHz, $CDCl_3$) δ 189.54, 160.84, 140.59, 137.56, 135.84, 130.84, 128.58, 125.59, 125.33, 124.80, 124.51, 122.97, 121.73, 121.22, 112.92, 65.36. IR (neat, cm^{-1}): 2842.73, 2754.12, 1676.36, 1598.85, 1307.10, 1244.51, 1053.45, 1010.87, 839.86, 779.96, 746.58. HRMS (EI) (M^+) Calcd. for $C_{16}H_{13}O_2S^+$: 269.0631, found 269.0629.

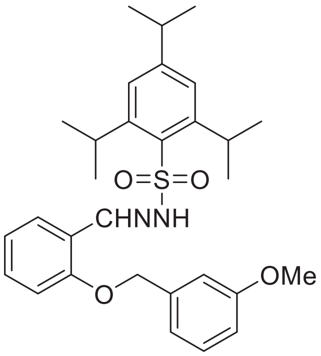
2.4.5 The Synthetic Procedure for Triisopropyl Sulfonylhydrazone Derivatives 1



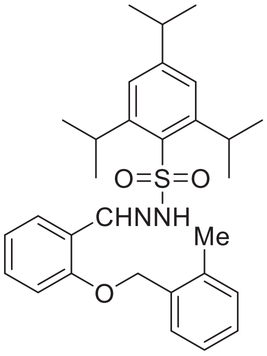
To a stirred solution of pure 2,4,6-triisopropylbenzenesulfonohydrazide ($TrisNHNH_2$, 2 mmol) in THF (10.0 mL) at 0 ºC, aldehyde **s2** (1 equiv.) was added dropwise (or portionwise if solid). The reaction was monitored by TLC. After the reaction was completed, the solvent was removed directly under reduced pressure, and the crude solid was further purified by flash column chromatography.



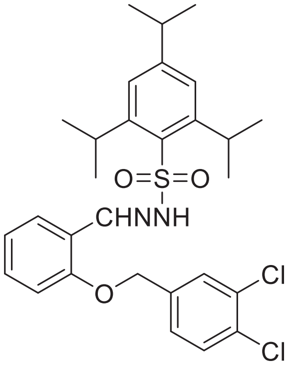
***N′*-(2-(benzyloxy)benzylidene)-2,4,6-triisopropylbenzene-sulfonohydrazide 1-a** Yield: 80%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.21 (s, 1H), 7.81 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.41 – 7.32 (m, 4H), 7.29 (td, *J* = 8.2, 1.7 Hz, 1H), 7.17 (s, 2H), 6.92 (dd, *J* = 7.7, 6.4 Hz, 2H), 5.06 (s, 2H), 4.27 (hept, *J* = 6.7 Hz, 2H), 2.90 (hept, *J* = 6.8 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (125MHz, CDCl$_3$) δ 156.95, 153.27, 151.31, 142.36, 136.38, 131.43, 131.40, 128.63, 128.15, 127.40, 126.57, 123.80, 122.17, 120.97, 112.44, 70.37, 34.15, 30.03, 24.85, 23.52. IR (neat, cm^{-1}): 3146.18, 2958.54, 1597.71, 1451. 12, 1425.95, 1293.54, 1259.37, 1153.52, 748.34, 544.27. HRMS (ESI) (M+H$^+$) Calcd. for $C_{29}H_{37}N_2O_3S^+$: 493.2519, found 493.2502.



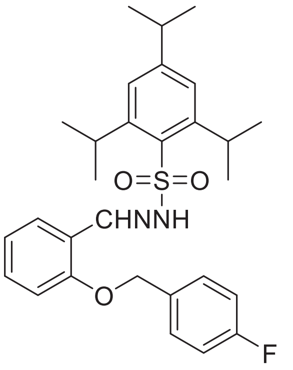
2,4,6-triisopropyl-*N'*-(2-((3-methoxybenzyl)oxy)benzylidene) benzenesulfonohydrazide 1-b Yield: 85%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (500 MHz, CDCl3) δ 8.21 (s, 1H), 7.80 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.78 (s, 1H), 7.33 – 7.26 (m, 2H), 7.17 (s, 2H), 6.97 – 6.86 (m, 5H), 5.03 (s, 2H), 4.26 (hept, *J* = 6.7 Hz, 2H), 3.81 (s, 3H), 2.89 (hept, *J* = 6.9 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 13H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (125MHz, CDCl3) δ 159.81, 156.91, 153.27, 151.32, 142.27, 137.97, 131.43, 131.41, 129.73, 126.57, 123.80, 122.15, 120.99, 119.58, 113.41, 113.09, 112.31, 70.28, 55.24, 34.15, 30.04, 24.86, 23.52. IR (neat, cm-1): 3192.99, 2958.12, 1598.12, 1450.63, 1427.93, 1316.48, 1247.70, 1147.74, 1036.04, 955.99, 848.71, 749.04, 669.94, 554.45. HRMS (ESI) (M+H+) Calcd. for $C_{30}H_{39}N_{2}O_{4}S^{+}$: 523.2625, found 523.2645.



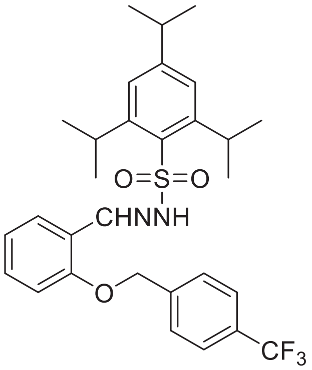
2,4,6-triisopropyl-*N'*-(2-((2-methylbenzyl)oxy)benzylidene)-benzenesulfonohydrazide 1-c Yield: 88%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.81 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.74 (s, 1H), 7.34 – 7.27 (m, 3H), 7.24 – 7.20 (m, 2H), 7.17 (s, 2H), 6.96 (d, *J* = 8.3 Hz, 1H), 6.93 (t, *J* = 7.5 Hz, 1H), 5.03 (s, 2H), 4.26 (hept, *J* = 6.7 Hz, 2H), 2.89 (hept, *J* = 6.9 Hz, 1H), 2.33 (s, 3H), 1.29 (d, *J* = 6.7 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.08, 153.28, 151.32, 142.24, 136.69, 134.25, 131.47, 131.41, 130.50, 128.69, 128.54, 126.63, 126.10, 123.80, 122.13, 120.99, 112.15, 68.98, 34.16, 30.03, 24.86, 23.52, 18.87. IR (neat, cm^{-1}): 3185.38, 2960.41, 2926.86, 1598.05, 1450.78, 1319.23, 1250.20, 1150.49, 751.55, 666.68. HRMS (ESI) (M+H$^+$) Calcd. for $C_{30}H_{39}N_2O_3S^+$: 507.2676, found 507.2664.



***N′*-(2-((3,4-dichlorobenzyl)oxy)benzylidene)-2,4,6-triisopropyl-benzenesulfonohydrazide 1-d** Yield: 82%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ δ 8.17 (s, 1H), 7.82 (br, 1H), 7.81 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.31 – 7.22 (m, 1H), 7.21 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.17 (s, 2H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 8.3 Hz, 1H), 5.01 (s, 2H), 4.26 (hept, *J* = 6.8 Hz, 2H), 2.89 (hept, *J* = 6.9 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 12H), 1.24 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.52, 153.39, 151.35, 142.05, 140.44, 131.47, 131.34, 130.50, 130.18, 127.30, 126.79, 125.62, 123.85, 122.27, 121.34, 112.15, 69.45, 34.16, 30.06, 24.84, 23.50. IR (neat, cm^{-1}): 3194.76, 2960.03, 1598.92, 1449.73, 1323.92, 1247.77, 1149.75, 1057.72, 957.72, 749.98, 657.53, 538.48. HRMS (ESI) (M+H$^+$) Calcd. for $C_{29}H_{35}Cl_2N_2O_3S^+$: 561.1740, found 561.1748.

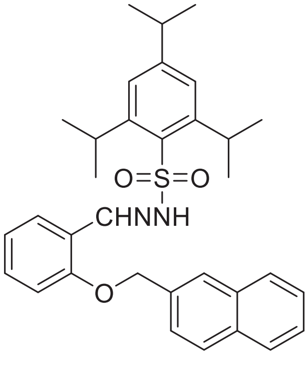


***N′*-(2-((4-fluorobenzyl)oxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide 1-e** Yield: 85%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.18 (s, 1H), 7.82 (s, 1H), 7.80 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.34 (dd, *J* = 8.5, 5.4 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.17 (s, 2H), 7.06 (t, *J* = 8.6 Hz, 2H), 6.94-6.89 (m, 1H), 5.02 (s, 1H), 4.26 (hept, *J* = 6.8 Hz, 2H), 2.89 (hept, *J* = 6.8 Hz, 1H), 1.29 (d, *J* = 6.8 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, cdcl$_3$) δ 162.55 (d, *J* = 246.9 Hz), 156.75, 153.30, 151.29, 142.21, 132.09 (d, *J* = 2.7 Hz), 131.43, 131.33, 129.28 (d, *J* = 8.2 Hz), 129.24, 126.66, 123.79, 122.14, 121.10, 115.58 (d, *J* = 21.6 Hz), 112.21, 77.27, 76.95, 76.63, 69.72, 34.13, 30.01, 24.81, 23.48. IR (neat, cm^{-1}): 3145.65, 2961.27, 1599.14, 1511.73, 1258.98, 1223.20, 1153.55, 1032.21, 927.12, 747.91, 532.61. HRMS (ESI) (M+H$^+$) Calcd. for $C_{29}H_{36}FN_2O_3S^+$: 511.2425, found 511.2428.

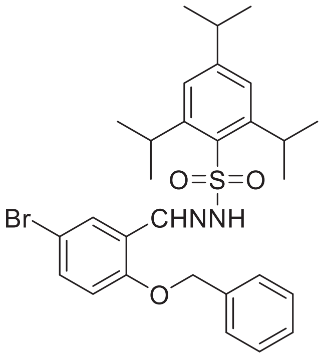


2,4,6-triisopropyl-*N′*-(2-((4-(trifluoromethyl)benzyl)oxy)-benzylidene)benzenesulfonohydrazide 1-f Yield: 85%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.25 (s, 1H), 8.07 (s, 1H), 7.82 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.63

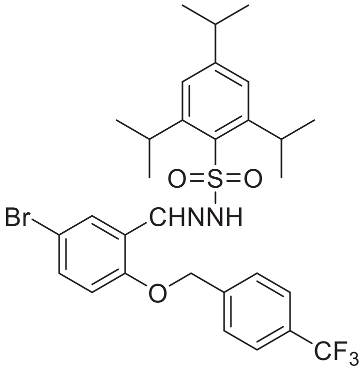
(d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.29 (ddd, *J* = 8.3, 7.4, 1.8 Hz, 1H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 5.13 (s, 2H), 4.29 (hept, *J* = 6.7 Hz, 2H), 2.93 (hept, *J* = 6.8 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100MHz, CDCl$_3$) δ 156.52, 153.39, 151.35, 142.05, 140.44, 131.47, 131.34, 130.50, 130.18, 127.30, 126.79, 125.62, 123.85, 122.27, 121.34, 112.15, 69.45, 34.16, 30.06, 24.84, 23.50. IR (neat, cm^{-1}): 3204.84, 2963.91, 1600.01, 1452.06, 1324.04, 1256.33, 1152.94, 1116.15, 1066.06, 822.65, 749.70, 651.71, 532.26. HRMS (ESI) (M+H$^+$) Calcd. for $C_{30}H_{35}F_3N_2O_3S^+$: 561.2393, found 561.2397.



2,4,6-triisopropyl-*N'*-(2-(naphthalen-2-ylmethoxy)benzylidene)benzenesulfonohydrazide 1-g Yield: 80%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.25 (s, 1H), 7.87 – 7.82 (m, 6H), 7.52 – 7.47 (m, 3H), 7.31 – 7.28 (m, 1H), 7.18 (s, 2H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.92 (t, *J* = 7.6 Hz, 1H), 5.22 (s, 2H), 4.27 (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 (150 MHz, CDCl$_3$) δ 157.02, 153.30, 151.34, 142.34, 133.83, 133.22, 133.12, 131.48, 131.43, 128.56, 127.92, 127.77, 126.64, 126.48, 126.42, 126.29, 125.16, 123.82, 122.21, 121.05, 112.39, 70.63, 34.17, 30.06, 24.87, 23.53. IR (neat, cm^{-1}): 3192.11, 2959.75, 2862.08, 1597.50, 1448.89, 1321.80, 1254.22, 1164.14, 1051.95, 943.36, 808.77, 737.37, 664.50. HRMS (ESI) (M+H$^+$) Calcd. for $C_{33}H_{39}N_2O_3S^+$: 543.2676, found 543.2673.

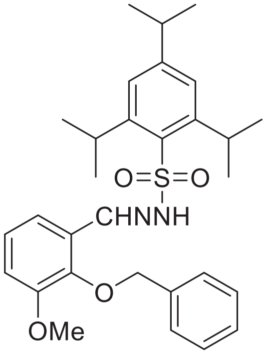


***N′*-(2-(benzyloxy)-5-bromobenzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide 1-h** Yield: 88%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.91 (d, *J* = 2.3 Hz, 1H), 7.84 (s, 1H), 7.47 – 7.34 (m, 6H), 7.19 (s, 2H), 6.79 (d, *J* = 8.8 Hz, 1H), 5.04 (s, 2H), 4.24 (hept, *J* = 6.5 Hz, 2H), 2.90 (hept, *J* = 6.8 Hz, 1H), 1.31 (d, *J* = 6.7 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (125MHz, $CDCl_3$) δ 155.78, 153.49, 151.48, 140.47, 135.88, 133.70, 131.21, 129.08, 128.70, 128.33, 127.40, 124.08, 123.89, 114.20, 113.70, 70.70, 34.17, 30.13, 24.89, 23.52. IR (neat, cm^{-1}): 3182.03, 2958.50, 1597.26, 1450.14, 1267.84, 1254.29, 1149.70, 750.46, 542.35. HRMS (ESI) (M+H$^+$) Calcd. for $C_{29}H_{36}BrN_2O_3S^+$: 571.1625, found 571.1623.

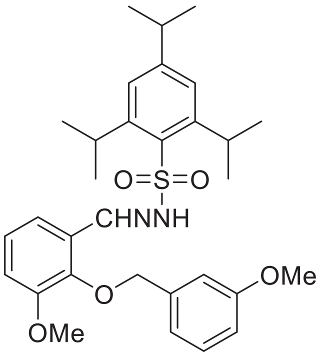


***N′*-(5-bromo-2-((4-(trifluoromethyl)benzyl)oxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide 1-i** Yield: 82%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.93 (d, *J* = 2.5 Hz, 1H), 7.88 (br, 1H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.37 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.19 (s, 2H), 6.75 (d, *J* = 8.9 Hz, 1H), 5.11 (s, 2H), 4.25 (hept, *J* = 6.8 Hz, 2H), 2.91 (hept,

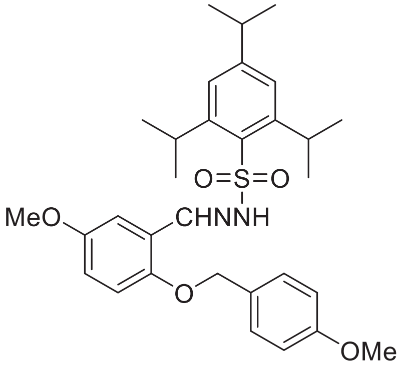
J = 6.9 Hz, 1H), 1.31 (d, J = 6.8 Hz, 12H), 1.26 (d, J = 6.9 Hz, 6H). ^{13}C NMR (100MHz, $CDCl_3$) δ 155.38, 153.60, 151.50, 140.09, 139.87, 133.81, 131.15, 129.37, 127.44, 125.74, 124.08, 123.94, 114.14, 113.95, 77.32, 77.00, 76.68, 69.83, 34.20, 30.16, 24.90, 23.53. IR (neat, cm^{-1}): 3137.24, 2969.07, 1596.83, 1425.26, 1325.83, 1255.19, 1154.23, 1121.32, 1067.12, 943.74, 537.75. HRMS (ESI) (M+H$^+$) Calcd. for $C_{30}H_{35}BrF_3N_2O_3S^+$: 639.1498, found 639.1495.



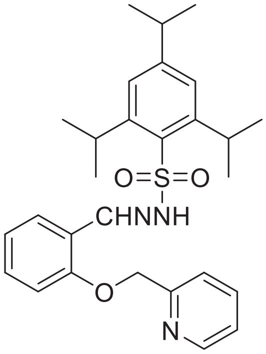
***N′*-(2-(benzyloxy)-3-methoxybenzylidene)-2,4,6-triisopropyl-benzenesulfonohydrazide 1-j** Yield: 80%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.65 (br, 1H), 7.36 – 7.33 (m, 6H), 7.16 (s, 2H), 7.00 (t, J = 8.0 Hz, 1H), 6.92 (dd, J = 8.2, 1.5 Hz, 1H), 4.99 (s, 2H), 4.28 – 4.17 (m, 2H), 3.88 (s, 3H), 2.95 – 2.83 (m, 1H), 1.28 (d, J = 6.8 Hz, 12H), 1.24 (d, J = 6.9 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.32, 152.65, 151.30, 146.93, 142.37, 136.84, 131.33, 128.51, 128.45, 128.35, 127.51, 124.09, 123.80, 117.92, 113.72, 75.83, 55.83, 34.16, 30.00, 24.85, 23.52. IR (neat, cm^{-1}): 3187.41, 2958.91, 1598.65, 1437.65, 1321.66, 1272.55, 1164.80, 1153.97, 729.03, 578.67. HRMS (ESI) (M+H$^+$) Calcd. for $C_{30}H_{39}N_2O_4S^+$: 523.2625, found 523.2615.



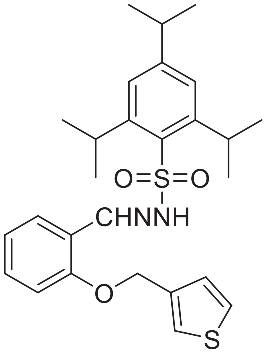
2,4,6-triisopropyl-*N′*-(3-methoxy-2-((3-methoxybenzyl)oxy)benzylidene)benzenesulfonohydrazide 1-k Yield: 85%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.91 (s, 1H), 7.64 (s, 1H), 7.35 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.16 (s, 2H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.97 – 6.90 (m, 3H), 6.87 (ddd, *J* = 8.3, 2.5, 1.0 Hz, 1H), 4.96 (s, 2H), 4.25 (hept, *J* = 6.8 Hz, 2H), 3.87 (s, 3H), 3.81 (s, 3H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.28 (d, *J* = 6.8 Hz, 12H), 1.24 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100MHz, CDCl$_3$) δ 159.88, 153.33, 152.64, 151.32, 147.00, 142.40, 138.44, 131.36, 129.58, 127.51, 124.29, 123.81, 120.52, 117.97, 113.98, 113.77, 113.71, 75.72, 55.86, 55.26, 34.17, 30.02, 24.86, 23.52. IR (neat, cm^{-1}): 3126.64, 2968.93, 1597.92, 1572.65, 1462.20, 1427.24, 1317.69, 1272.68, 1257.67, 1163.71, 1153.02, 1040.17, 1021.88, 895.79, 785.66, 544.47. HRMS (ESI) (M+H$^+$) Calcd. for $C_{31}H_{41}N_2O_5S^+$: 553.2731, found 553.2724.



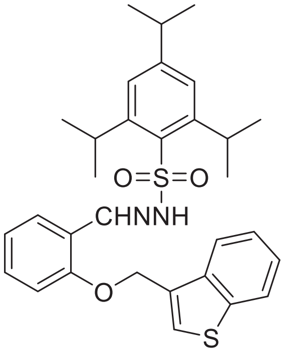
2,4,6-triisopropyl-*N′*-(5-methoxy-2-((4-methoxybenzyl)oxy)benzylidene)benzenesulfonohydrazide 1-l Yield: 87%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.84 (s, 1H), 7.30 – 7.26 (m, 3H), 7.18 (s, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 6.86 (s, 2H), 4.92 (s, 2H), 4.27 (hept, *J* = 6.7 Hz, 2H), 3.82 (s, 3H), 3.72 (s, 3H), 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 (150 MHz, $CDCl_3$) δ 159.57, 153.82, 153.33, 151.65, 151.24, 142.37, 131.32, 129.24, 128.60, 123.81, 122.85, 118.59, 114.52, 114.02, 109.51, 71.25, 55.68, 55.29, 34.16, 29.97, 24.87, 23.51. IR (neat, cm^{-1}): 3178.36, 2956.81, 1491.59, 1511.53, 1319.37, 1245.12, 1033.26, 910.09, 550.63. HRMS (ESI) (M+H^{+}) Calcd. for $C_{31}H_{41}N_2O_5S^{+}$: 553.2731, found 553.2731.



2,4,6-triisopropyl-N'-(2-(pyridin-2-ylmethoxy)benzylidene)-benzenesulfonohydrazide 1-m Yield: 80%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.69 (s, 1H), 8.58 (d, *J* = 4.7 Hz, 1H), 8.43 (s, 1H), 7.84 (t, *J* = 7.7 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.39 – 7.29 (m, 2H), 7.23 (s, 2H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 5.22 (s, 2H), 4.25 (hept, *J* = 6.7 Hz, 2H), 2.89 (hept, *J* = 6.8 Hz, 1H), 1.21 (d, *J* = 6.8 Hz, 12H), 1.18 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.86, 156.66, 153.10, 150.86, 149.58, 141.13, 137.46, 133.02, 131.80, 125.47, 124.05, 123.49, 122.71, 121.86, 121.46, 113.64, 70.99, 33.82, 29.67, 25.18, 23.85. IR (neat, cm^{-1}): 3024.22, 2998.62, 1603.03, 1496.39, 1157.29, 1048.03, 931.01, 797.21, 696.10. HRMS (ESI) (M+H^{+}) Calcd. for $C_{28}H_{36}N_3O_3S^{+}$: 494.2472, found 494.2462.

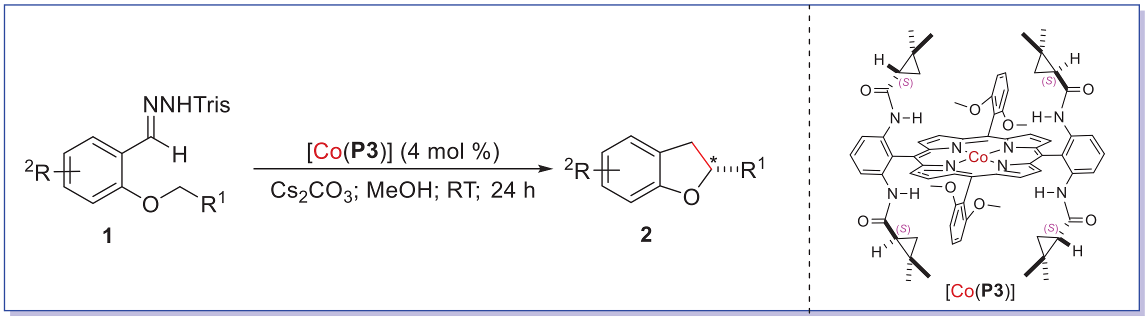


2,4,6-triisopropyl-N'-(2-(thiophen-3-ylmethoxy)benzylidene)-benzenesulfonohydrazide 1-n Yield: 90%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.18 (s, 1H), 7.88 (br, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.33 – 7.27 (m, 3H), 7.18 (s, 2H), 7.09 (d, *J* = 4.8 Hz, 1H), 6.93 – 6.91 (m, 2H), 5.07 (s, 2H), 4.29 – 4.25 (m, 2H), 2.93 – 2.86 (m, 1H), 1.30 (d, *J* = 6.7 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 156.87, 153.29, 151.34, 142.36, 137.33, 131.43, 126.88, 126.62, 126.48, 123.81, 123.26, 122.28, 121.09, 112.37, 66.10, 34.16, 30.05, 24.86, 23.52. IR (neat, cm^{-1}): 3145.26, 2958.52, 2865.78, 1598.66, 1458.52, 1426.76, 1258.19, 1153.46, 774.63. HRMS (ESI) (M+H$^+$) Calcd. for $C_{27}H_{35}N_2O_3S_2^+$: 499.2084, found 499.2072.

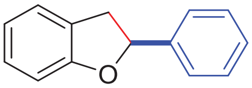


N'-(2-(benzo[b]thiophen-3-ylmethoxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide 1-o Yield: 93%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.11 (s, 1H), 7.90 – 7.77 (m, 4H), 7.45 (s, 1H), 7.40 – 7.37 (m, 2H), 7.35 – 7.32 (m, 1H), 7.17 (s, 2H), 7.03 (d, *J* = 8.3 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 5.29 (s, 2H), 4.24 (hept, *J* = 6.7 Hz, 2H), 2.90 (hept, *J* = 6.8 Hz, 1H), 1.28 (d, *J* = 6.8 Hz, 12H), 1.26 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.87, 153.29, 151.34, 142.36, 137.33, 131.43, 126.88, 126.62, 126.48, 123.81, 123.26, 122.28, 121.09, 112.37, 66.10, 34.16, 30.05, 24.86, 23.52. IR (neat, cm^{-1}): 3203.90, 3139.50, 2956.61, 2867.26, 1601.39, 1455.55, 1252.70, 1149.64, 786.69. HRMS (ESI) (M+H$^+$) Calcd. for $C_{31}H_{37}N_2O_3S_2^+$: 549.2240, found 549.2245.

2.4.6 General Procedure for [Co(P6)]-Catalyzed Enantioselective Radical C–H Alkylation

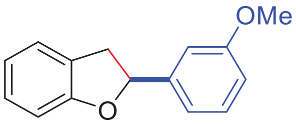


An oven-dried Schlenk tube was charged with sulfonyl hydrazone **1** (0.1 mmol), [Co(**P3**)] (2 mol %) and Cs_2CO_3 (0.2 mmol). The Schlenk tube was then evacuated and back filled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, methanol (1.0 mL) was added via a gastight syringe. 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 RT. After 24 h, the reaction mixture was filtrated through a short pad of silica gel, concentrated under vacuum and purified by flash column chromatography. The fractions containing product were collected and concentrated under vacuum to afford the desired compound **2**.

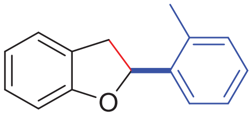


(S)-2-phenyl-2,3-dihydrobenzofuran 2a[16] Yield: 77%. 92:8 *er*. Hexanes/ethyl acetate = 10/1, $R_f = 0.70$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.40 (m, 2H), 7.40 – 7.35 (m, 2H), 7.35 – 7.29 (m, 1H), 7.23 – 7.13 (m, 2H), 6.95 – 6.82 (m, 2H), 5.77 (t, *J* = 8.9 Hz, 1H), 3.64 (dd, *J* = 15.6, 9.5 Hz, 1H), 3.23 (dd, *J* = 15.6, 8.2 Hz, 1H).

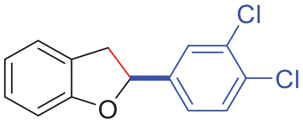
^{13}C NMR (125MHz, $CDCl_3$) δ 153.24, 142.38, 129.36, 128.55, 127.66, 127.56, 127.33, 123.97, 118.13, 107.19, 72.18, 39.47, 34.26. HPLC analysis: ADH (100% hexanes, 0.8 mL/min): t_{major} = 17.68 min, t_{minor} = 22.33 min. $[\alpha]^{20}{}_D$=-56.14 (*c*=0.5, $CHCl_3$).



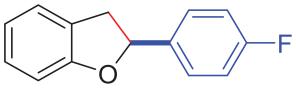
(S)-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran 2b Yield: 80%. 95.4:4.5 *er*. Hexanes/ethyl acetate = 8/1, R_f = 0.65. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.9 Hz, 1H), 7.24 – 7.10 (m, 2H), 7.01 – 6.93 (m, 2H), 6.93 – 6.79 (m, 3H), 5.74 (t, *J* = 8.8 Hz, 1H), 3.81 (s, 3H), 3.63 (dd, *J* = 15.6, 9.5 Hz, 1H), 3.22 (dd, *J* = 15.6, 8.2 Hz, 1H). ^{13}C NMR (125MHz, $CDCl_3$) δ 159.82, 159.56, 143.58, 129.71, 128.17, 126.42, 124.83, 120.65, 118.00, 113.44, 111.24, 109.37, 83.86, 55.25, 38.40. HPLC analysis: ADH (99% hexanes, 1.0 mL/min): t_{major} = 13.46 min, t_{minor} = 17.40 min. $[\alpha]^{20}{}_D$ =-59.02 (*c*=0.5, $CHCl_3$) HRMS (EI) (M^+) Calcd. for $C15H14O2^+$: 226.0988, found 226.0981.



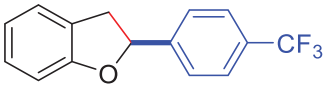
(S)-2-(*o*-tolyl)-2,3-dihydrobenzofuran 2c[16] Yield: 78%. 90:10 *er*. Hexanes/ethyl acetate = 10/1, R_f = 0.67. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 – 7.46 (m, 1H), 7.23 – 7.17 (m, 5H), 6.92 – 6.88 (m, 2H), 6.00 – 5.93 (m, 1H), 3.67 (dd, *J* = 15.5, 9.6 Hz, 1H), 3.10 (dd, *J* = 15.5, 8.2 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.69, 140.23, 134.18, 130.49, 128.19, 127.60, 126.31, 126.25, 124.95, 124.92, 120.62, 109.37, 81.52, 37.44, 19.22. HPLC analysis: IA (99.8% hexanes, 0.8 mL/min): t_{major} = 11.58 min, t_{minor} = 10.19 min. $[\alpha]^{20}{}_D$ = -56.14 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{15}H_{14}O^+$: 210.1039, found 210.1042.



(S)-2-(3,4-dichlorophenyl)-2,3-dihydrobenzofuran 2d Yield: 80%. 90:10 *er*. Hexanes/ethyl acetate = 9/1, $R_f = 0.68$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, $J = 2.0$ Hz, 1H), 7.44 (d, $J = 8.3$ Hz, 1H), 7.23 (dd, $J = 8.3, 1.9$ Hz, 1H), 7.18 (t, $J = 6.9$ Hz, 2H), 6.97 – 6.82 (m, 2H), 5.71 (dd, $J = 9.4, 8.1$ Hz, 1H), 3.65 (dd, $J = 15.6, 9.6$ Hz, 1H), 3.15 (dd, $J = 15.6, 7.9$ Hz, 1H). ^{13}C NMR (125MHz, $CDCl_3$) δ 159.20, 142.37, 132.74, 131.85, 130.63, 128.41, 127.71, 125.69, 124.99, 124.92, 121.05, 109.48, 82.38, 38.37. HPLC analysis: OJH (99% hexanes, 1.0 mL/min): $t_{major} = 24.31$ min, $t_{minor} = 22.28$ min. $[\alpha]^{20}{}_D = -71.66$ (c=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{14}H_{10}Cl_2O^+$: 264.0103, found 264.0094.

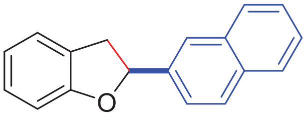


(S)-2-(4-fluorophenyl)-2,3-dihydrobenzofuran 2e[16] Yield: 70%. 90:10 *er*. Hexanes/ethyl acetate = 10/1, $R_f = 0.70$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 2H), 7.23 – 7.13 (m, 2H), 7.11 – 7.01 (m, 2H), 6.90 (td, $J = 7.5, 0.9$ Hz, 1H), 6.87 (d, $J = 8.0$ Hz, 1H), 5.77 – 5.70 (m, 1H), 3.63 (dd, $J = 15.6, 9.4$ Hz, 1H), 3.19 (dd, $J = 15.6, 8.2$ Hz, 1H). ^{13}C NMR (125MHz, $CDCl_3$) δ 163.43, 161.47, 159.40, 137.73, 137.71, 128.27, 127.58, 127.52, 126.24, 124.85, 120.77, 115.58, 115.41, 109.37, 83.37, 38.43. HPLC analysis: ODH (100% hexanes, 0.8 mL/min): $t_{major} = 29.86$ min, $t_{minor} = 34.90$ min. $[\alpha]^{20}{}_D = -41.40$ (c=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{14}H_{11}FO^+$: 214.0788, found 214.0776.

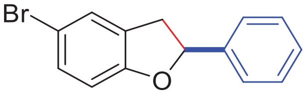


(S)-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran 2f[16] Yield: 70%. 90:10 *er*. Hexanes/ethyl acetate = 10/1, $R_f = 0.70$. ^{1}H NMR (500 MHz,

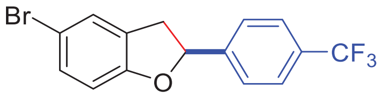
$CDCl_3$) δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.52 (d, *J* = 8.1 Hz, 2H), 7.25 – 7.13 (m, 2H), 7.00 – 6.84 (m, 2H), 5.81 (t, *J* = 8.8 Hz, 1H), 3.70 (dd, *J* = 15.6, 9.6 Hz, 1H), 3.17 (dd, *J* = 15.6, 7.9 Hz, 1H). ^{13}C NMR (125MHz, $CDCl_3$) δ 159.38, 146.14, 128.41, 125.92, 125.82, 125.68, 125.65, 125.62, 125.58, 124.95, 121.03, 109.48, 82.99, 38.48. HPLC analysis: ODH (99% hexanes, 1 mL/min): t_{major} = 21.09 min, t_{minor} = 11.82 min. $[\alpha]^{20}{}_{D}$ = -86.52 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{15}H_{11}F_3O^+$: 264.0757, found 264.0748.



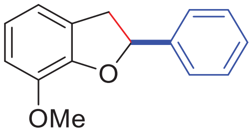
(S)-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran 2g Yield: 70%. 90:10 *er*. Hexanes/ethyl acetate = 10/1, R_f = 0.70. ^1H NMR (600 MHz, $CDCl_3$) δ 7.88 – 7.84 (m, 4H), 7.53 – 7.48 (m, 3H), 7.22 (dd, *J* = 13.2, 7.3 Hz, 2H), 6.93 (dd, *J* = 15.2, 7.7 Hz, 2H), 5.94 (t, *J* = 8.9 Hz, 1H), 3.71 (dd, *J* = 15.6, 9.5 Hz, 1H), 3.31 (dd, *J* = 15.6, 8.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.68, 139.22, 133.18, 133.10, 128.65, 128.24, 128.01, 127.69, 126.45, 126.27, 126.05, 124.89, 124.68, 123.57, 120.70, 109.42, 84.01, 38.41. HPLC analysis: IB (99.5% hexanes, 0.8 mL/min): t_{major} = 20.94 min, t_{minor} = 22.76 min. $[\alpha]^{20}{}_{D}$ = -56.82 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{18}H_{14}O^+$: 246.1039, found 246.1042.



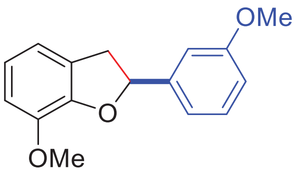
(S)-5-bromo-2-phenyl-2,3-dihydrobenzofuran 2h Yield: 82%. 93:7 *er*. Hexanes/ethyl acetate = 9/1, R_f = 0.70. ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 4.4 Hz, 4H), 7.36 – 7.31 (m, 1H), 7.31 – 7.24 (m, 2H), 6.75 (d, *J* = 8.4 Hz, 1H), 5.78 (dd, *J* = 9.3, 8.2 Hz, 1H), 3.63 (dd, *J* = 15.9, 9.5 Hz, 1H), 3.21 (dd, *J* = 15.9, 8.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.78, 141.33, 130.96, 128.97, 128.70, 128.22, 127.79, 125.68, 112.37, 110.86, 84.70, 38.15. HPLC analysis: ADH (99% hexanes, 1.0 mL/min): t_{major} = 13.78 min, t_{minor} = 10.80 min. $[\alpha]^{20}{}_{D}$ = 26.70 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{14}H_{11}BrO^+$: 273.9988, found 273.9978.



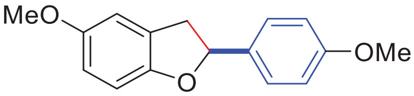
(S)-5-bromo-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzo- furan 2i Yield: 77%. 90:10 *er*. Hexanes/ethyl acetate = 9/1, R_f = 0.70. ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 4.4 Hz, 4H), 7.36 – 7.31 (m, 1H), 7.31 – 7.24 (m, 2H), 6.75 (d, *J* = 8.4 Hz, 1H), 5.78 (dd, *J* = 9.3, 8.2 Hz, 1H), 3.63 (dd, *J* = 15.9, 9.5 Hz, 1H), 3.21 (dd, *J* = 15.9, 8.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.57, 145.47, 131.20, 130.35 (q, *J* = 32.4 Hz, 1C), 128.33, 127.91, 125.84, 125.72, 125.69, 112.79, 110.98, 83.56, 38.21. HPLC analysis: OJH (99% hexanes, 1.0 mL/min): t_{major} = 65.36 min, t_{minor} = 44.72 min. $[\alpha]^{20}{}_{D}$ = 4.16 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{15}H_{10}BrF_3O^+$: 341.9862, found 341.9853.



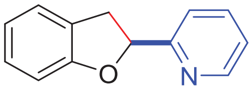
(S)-7-methoxy-2-phenyl-2,3-dihydrobenzofuran 2j Yield: 90%. 94.5:5.5 *er*. Hexanes/ethyl acetate = 7/1, R_f = 0.60. ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 2H), 7.40 – 7.33 (m, 2H), 7.33 – 7.27 (m, 1H), 6.89 – 6.78 (m, 3H), 5.81 (t, *J* = 9.0 Hz, 1H), 3.90 (s, 3H), 3.64 (dd, *J* = 15.5, 9.5 Hz, 1H), 3.26 (dd, *J* = 15.5, 8.5 Hz, 1H). ^{13}C NMR (125MHz, $CDCl_3$) δ 147.91, 144.39, 141.61, 128.51, 127.98, 127.64, 125.98, 121.21, 117.01, 111.38, 84.80, 77.25, 55.98, 38.83. HPLC analysis: ADH (99% hexanes, 1.0 mL/min): t_{major} = 20.64 min, t_{minor} = 16.26 min. $[\alpha]^{20}{}_{D}$ = -109.66 (*c*=0.5, $CHCl_3$) HRMS (EI) (M^+) Calcd. for $C_{15}H_{14}O_2{}^+$: 226.0988, found 226.0984.



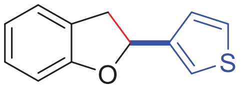
***(S)*-7-methoxy-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran 2k** Yield: 89%. 94.5:5.5 *er*. Hexanes/ethyl acetate = 7/1, R_f = 0.60. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (t, *J* = 7.5 Hz, 1H), 7.06 – 6.94 (m, 2H), 6.93 – 6.73 (m, 4H), 5.78 (t, *J* = 9.0 Hz, 1H), 3.90 (s, 3H), 3.80 (s, 3H), 3.63 (dd, *J* = 15.5, 9.5 Hz, 1H), 3.26 (dd, *J* = 15.5, 8.6 Hz, 1H). ^{13}C NMR (125MHz, $CDCl_3$) δ 159.73, 147.89, 144.40, 143.23, 129.58, 127.61, 121.23, 118.25, 117.00, 113.47, 111.46, 111.40, 84.66, 55.98, 55.24, 38.83. HPLC analysis: OJH (98% hexanes, 1.0 mL/min): t_{major} = 55.82 min, t_{minor} = 43.22 min. $[\alpha]^{20}{}_D$ = -108.36 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{16}H_{16}O_3^+$: 256.1094, found 256.1102.



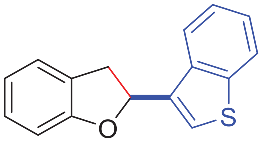
***(S)*-7-methoxy-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran 2l** Yield: 82%. 91:9 *er*. Hexanes/ethyl acetate = 6/1, R_f = 0.60. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.79 (br, 1H), 6.75 (d, *J* = 8.6 Hz, 1H), 6.70 (dd, *J* = 8.6, 2.4 Hz, 1H), 5.69 (t, *J* = 8.8 Hz, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.55 (dd, *J* = 15.7, 9.2 Hz, 1H), 3.20 (dd, *J* = 15.7, 8.4 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.43, 154.20, 153.70, 133.90, 127.68, 127.26, 113.97, 112.94, 111.16, 109.14, 84.15, 56.01, 55.29, 38.69. HPLC analysis: IB (99% hexanes, 0.8 mL/min): t_{major} = 26.98 min, t_{minor} = 30.61 min. $[\alpha]^{20}{}_D$ =-50.180 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{16}H_{16}O_3^+$: 256.1099, found 256.1102.



(S)-2-(2,3-dihydrobenzofuran-2-yl)pyridine 2m[16] Yield: 88%. 94:6 *er*. Hexanes/ethyl acetate = 5/1, $R_f = 0.56$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 4.8 Hz, 1H), 7.68 (td, *J* = 7.7, 1.7 Hz, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.25 – 7.12 (m, 3H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.89 (t, *J* = 7.4 Hz, 1H), 5.87 (dd, *J* = 9.9, 7.0 Hz, 1H), 3.74 (dd, *J* = 15.8, 9.9 Hz, 1H), 3.39 (dd, *J* = 15.8, 7.0 Hz, 1H). ^{13}C NMR (125MHz, $CDCl_3$) δ 161.25, 159.42, 149.31, 136.82, 128.10, 126.11, 125.03, 122.60, 120.89, 119.97, 109.42, 83.87, 36.74. HPLC analysis: OJH (97% hexanes, 1.0 mL/min): t_{major} = 12.17 min, t_{minor} = 22.97 min. $[\alpha]^{20}_{D}$ = 139.82 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{13}H_{11}NO^+$: 197.0841, found 197.0843.

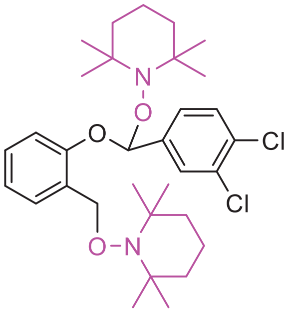


(S)-2-(thiophen-3-yl)-2,3-dihydrobenzofuran 2n Yield: 82%. 88.5:11.5 *er*. Hexanes/ethyl acetate = 6/1, $R_f = 0.60$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.32 (m, 1H), 7.32 (s, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.16 (t, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 4.8 Hz, 1H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.83 (t, *J* = 8.6 Hz, 1H), 3.59 (dd, *J* = 15.4, 9.3 Hz, 1H), 3.27 (dd, *J* = 15.4, 7.9 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.29, 142.75, 128.18, 126.63, 126.41, 125.51, 124.84, 121.83, 120.62, 109.46, 80.36, 37.45. HPLC analysis: ID (99.5% hexanes, 0.8 mL/min): t_{major} = 15.11 min, t_{minor} = 16.23 min. $[\alpha]^{20}_{D}$ = 59.18 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{12}H_{10}OS^+$: 202.0447, found 202.0448.


(S)-2-(benzo[b]thiophen-3-yl)-2,3-dihydrobenzofuran 2o Yield: 83%. 96:4 *er*. Hexanes/ethyl acetate = 7/1, R_f = 0.60. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 – 7.85 (m, 1H), 7.76 – 7.73 (m, 1H), 7.45 (s, 1H), 7.38 – 7.35 (m, 2H), 7.24 – 7.17 (m, 2H), 6.91 (t, *J* = 7.0 Hz, 2H), 6.09 (t, *J* = 8.9 Hz, 1H), 3.68 (dd, *J* = 15.5, 9.6 Hz, 1H), 3.40 (dd, *J* = 15.5, 8.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.39, 141.10, 136.82, 136.20, 128.30, 126.32, 124.98, 124.56, 124.24, 123.08, 123.06, 122.08, 120.78, 109.57, 80.00, 36.31. HPLC analysis: *ee* = 92%. ID (99.5% hexanes, 0.8 mL/min): t_{major} = 17.62 min, t_{minor} = 19.92 min. $[\alpha]^{20}{}_D$ = 69.90 (*c*=0.5, $CHCl_3$). HRMS (EI) (M^+) Calcd. for $C_{13}H_{11}NO^+$: 197.0841, found 197.0843.

2.4.7 General Procedure for TEMPO Trapping Reactions

An oven-dried Schlenk tube was charged with 1.0 equivalent of sulfonyl hydrazone **1d** (0.1 mmol), [Co(**P1**)] (4 mol %) and 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, TEMPO (2.5 equiv.) was added under nitrogen flow and methanol (1.0 mL) was added via a gastight syringe. The Schlenk tube was then purged with nitrogen for 10 s and the rubber septum was replaced with a Teflon screw cap. The mixture was then stirred at RT. After 24 h, the reaction mixture was filtrated through a short pad of silica, concentrated under vacuum and purified by flash column chromatography. The fractions containing product were collected and concentrated under vacuum to afford the desired compound.



2,2,6,6-tetramethyl-1-((2-(phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methoxy)benzyl)oxy)piperidine 3d Yield: 53%.^{1}H NMR (600 MHz, CDCl$_3$) δ 7.59 (d, *J* = 1.6 Hz, 1H), 7.44 (d, *J* = 7.3 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.31 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 1H), 7.17 (t, *J* = 7.3 Hz, 1H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.38 (s, 1H), 4.78 (d, *J* = 12.1 Hz, 1H), 4.71 (d, *J* = 12.1 Hz, 1H), 1.64 – 1.56 (m, 4H), 1.49 – 1.48 (m, 4H), 1.38 – 1.33 (m, 2H), 1.23 – 1.11 (m, 26H). 4.75 (dd, *J* = 41.1, 12.1 Hz, 2H), 1.64 – 1.56 (m, 4H), 1.49 – 1.48 (m, 4H), 1.38 – 1.33 (m, 2H), 1.23 – 1.11 (m, 26H).^{13}C NMR (150 MHz, CDCl$_3$) δ 153.47, 138.70, 132.28, 130.11, 128.66, 128.53, 128.29, 127.61, 125.96, 121.34, 115.72, 105.86, 73.53, 61.07, 59.82, 59.79, 59.76, 40.32, 39.97, 39.64, 39.62, 33.13, 32.96, 32.86, 32.77, 20.69, 20.47, 20.28, 20.19, 17.05, 17.03. HRMS (ESI) (M+H$^+$) Calcd. for $C_{32}H_{46}Cl_2N_2O_3^+$: 577.2958, found 577.2963.

2.5 REFERENCES

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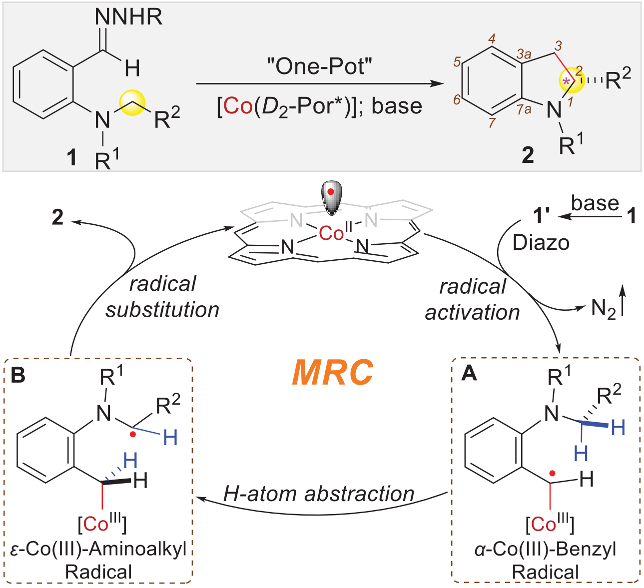
CHAPTER 3

ENANTIOSELECTIVE RADICAL PROCESS FOR SYNTHESIS OF CHIRAL INDOLINES BY CO(II)-BASED METALLORADICAL ALKYLATION OF DIVERSE C(SP^3)–H BONDS

3.1 INTRODUCTION

Recent years have witnessed intense research efforts in exploring the unique features of radical reactions for organic synthesis.[1] Among the diverse types of radical reactions, hydrogen atom abstraction (HAA) has been recognized as a general and straightforward pathway to activate C(sp^3)–H bonds, offering a potentially powerful approach for C–C bond formation via direct radical C–H alkylation.[2] In addition to the prerequisite for controlled generation of the incoming radicals, development of HAA-based radical C–H alkylation, however, faces formidable challenges associated with governing the reactivity and selectivity of the outgoing alkyl radicals for ensuing C–C bond formation. In particular, control of enantioselectivity of radical reactions is typically difficult, in part due to the lack of general strategies to exert adequate catalyst-substrate interaction that is essential for asymmetric induction.[1,2e] Among recent developments,[3] metalloradical catalysis (MRC), which involves the use of metal-centered radicals for catalytic generation of metal-stabilized organic radicals while controlling the subsequent radical reactions, has emerged as a conceptually new approach for the development of stereoselective radical processes.[4,5]

Scheme 3.1| Working Proposal for Construction of 2-Substituted Indolines by Radical C–H Alkylation via Co(II)-MRC

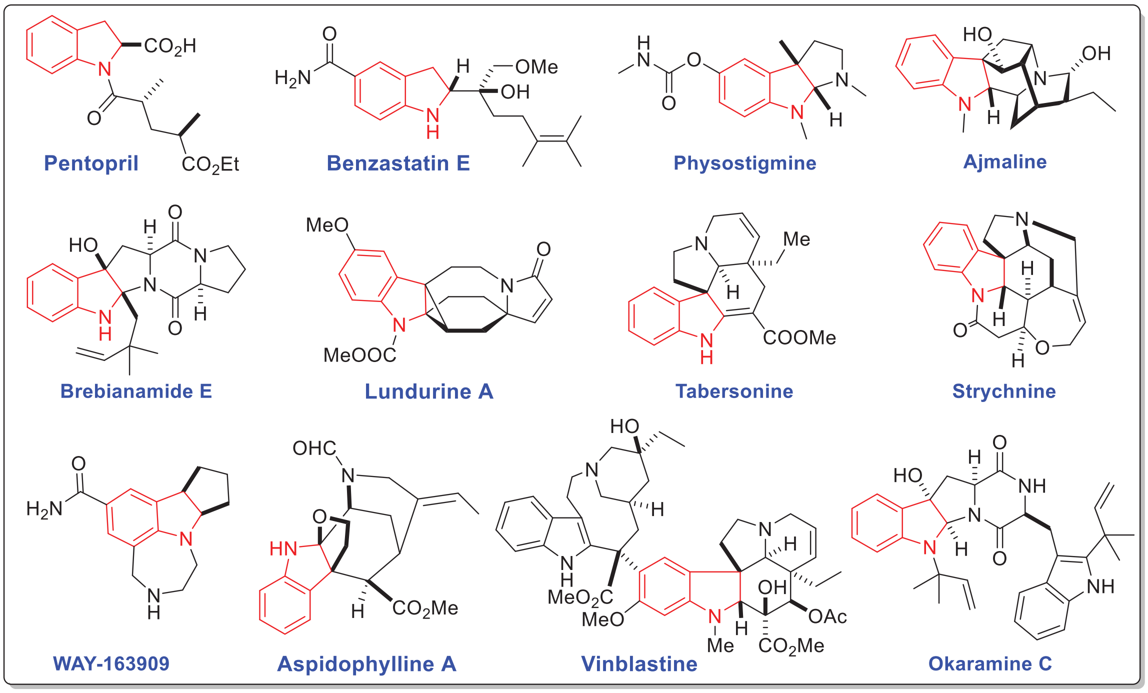


As stable metalloradicals, Co(II) complexes of D_2-symmetric chiral amidoporphyrins [Co(D_2-Por*)] exhibit the unusual capability of homolytically activating diazo compounds as radical precursors to generate α-Co(III)-alkyl radicals (also known as Co(III)-carbene radicals), a fundamentally new class of metal-supported organic radicals.[6] These Co-stabilized C-centered radicals, which are confined inside the pocket-like environment of the chiral porphyrin ligands, can serve as key catalytic intermediates for an array of asymmetric radical transformations.[7]

Recently, the applications of Co(II)-based MRC were further extended to the use of *in situ* generated donor-substituted diazo compounds such as aryldiazomethanes as radical precursors.[8] It was shown that, upon metalloradical activation, the resulting α-Co(III)-benzyl radical intermediates underwent radical addition to C=C bonds and succeeding radical substitution for stereoselective radical cyclopropanation.[8c]

Besides radical addition, we were interested in exploring the potential ability of these α-Co(III)-benzyl radicals for HAA that might lead to radical alkylation of C–H bonds. Particularly, we were attracted to the case of aryldiazomethane **1'** with *ortho*-amino functionality on the basis of the hypothesis that the corresponding α-Co(III)-benzyl radical intermediate **A** would favor intramolecular HAA from the C–H bonds at the distal 5-position to form ε-Co(III)-aminoalkyl radical **B**, where the C-centered radical would be considerably stabilized by the lone pair of the adjacent nitrogen (Scheme 3.1). If the pendant α-aminoalkyl radical in **B** could subsequently proceed *5-exo-tet* radical cyclization at the α-carbon center for C–C bond formation in an asymmetric fashion, it would lead to a new catalytic system for enantioselective radical C–H alkylation to construct optically active 2-substituted indolines, which exist ubiquitously in both natural and synthetic compounds with interesting biological properties (Figure 3.1).[9]

Figure 3.1| Examples of Natural Products and Biologically Active Compounds Containing Indoline Moiety



Tremendous efforts have been devoted to develop catalytic systems for asymmetric synthesis of 2-substituted indolines due to their biological importance.[10] Among others,[11] existing methods have explored strategies that are based on asymmetric hydrogenation of C2=C3 bond,[11a,11b] asymmetric alkylation at C2 position,[11c] asymmetric formation of C3–C3a bond,[11d,11e] as well as asymmetric formation of N1–C7a[11f-h] and N1-C2 bonds (Scheme 3.1).[11i] However, stereoselective construction of chiral 2-substituted indolines that is based on asymmetric formation of C2–C3 bond via C–H alkylation has been much less developed.[12] This underdevelopment may be attributed to the inherent challenge for enantioselective formation of C–C bonds between two sp^3-carbon centers. Recently, Wirth and coworkers reported asymmetric synthesis of 2,3-disubstituted indolines by Rh$_2$-catalyzed C–H insertion of donor/acceptor-type diazo compounds in 33%-94% *ee*.[12c] To the best of our knowledge, there is no previous report on asymmetric construction of 2-substituted indolines through C2(sp^3)–C3(sp^3) bond formation via stereoselective C(sp^3)–H alkylation using donor-type diazo compounds. As a new synthetic application of Co(II)-based MRC, we have developed the first catalytic system for asymmetric synthesis of 2-substituted indolines via enantioselective radical C–H alkylation of aryldiazomethanes, which can be generated *in situ* from readily accessible aryl aldehyde-derived hydrazone precursors. Through the design of a new D_2-symmetric chiral amidoporphyrin as the supporting ligand, the Co(II)-catalyzed radical process can effectively alkylate diverse types of C–H bonds at room temperature, offering a streamlined synthesis of optically active 2-substituted indoline derivatives. We also describe our detailed mechanistic studies that shed light on the stepwise radical pathway of this new catalytic C–H alkylation process.

3.2 RESULTS AND DISCUSSION

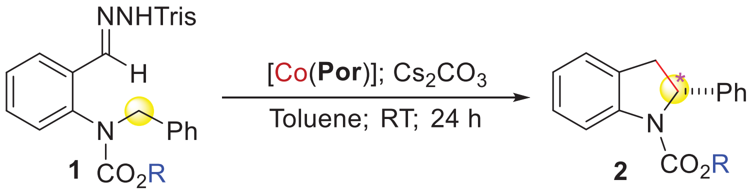
3.2.1 Condition Optimization of Co(II)-Based Catalytic System for Enantioselective Radical C–H Alkylation of Aryldiazomethanes

At the outset of this study, *o*-aminobenzaldehyde-derived hydrazone **1a** was selected as the model substrate to examine the feasibility of Co(II)-catalyzed radical C–H alkylation (Table 3.1). We were gratified to find that Co(II) complex of D_{2h}-symmetric achiral amidoporphyrin [Co(**P1**)] (**P1** = 3,5-Di^{t}Bu-IbuPhyrin)[13] was an effective metalloradical catalyst for the reaction, delivering the desired 2-phenylindoline **2a** in 81% yield using 2 mol % catalyst loading even at room temperature (entry 1). The high product yield implies that the *in situ* generation of the corresponding aryldiazomethane from hydrazone **1a** was facile and properly matched with the rate of its metalloradical activation by the catalyst toward the desired C–H alkylation without the accumulation of the unstable donor-substituted diazo compound.

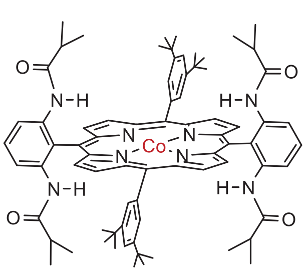
To achieve enantioselectivity, the initial use of the first-generation catalyst [Co(**P2**)] (**P2** = 3,5-Di^{t}Bu-ChenPhyrin),[7a] which is known for asymmetric radical cyclopropanation, resulted in the formation of **2a** in a similar yield with a low but significant enantioselectivity (entry 2). The asymmetric induction was improved without negatively affecting the product yield when [Co(**P3**)] (**P3** = 2,6-DiMeO-ChenPhyrin) was used as the catalyst where the ligand has a sterically more demanding environment as a result of the non-chiral *meso*-aryl substituents (entry 3). This positive ligand buttressing effect prompted us to evaluate the activity of the second-generation catalyst [Co(**P4**)] (**P4**

= 3,5-Di^{t}Bu-QingPhyrin),[7c] which consists of more sterically hindered chiral amides with two stereogenic centers.

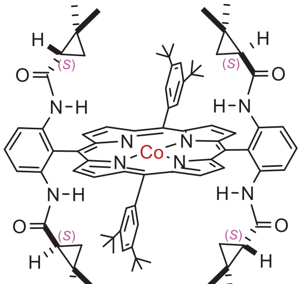
Table 3.1| Ligand Effect of Co(II)-Based Catalytic System for Enantioselective Radical C–H Alkylation of Aryldiazomethanes



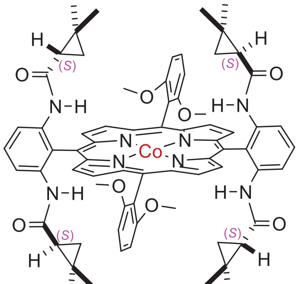
entry	R	catalyst	solvent	yield (%)^b	*ee* (%)^c
1	*t*-Bu (**1a**)	[Co(**P1**)]	toluene	81	--
2	*t*-Bu (**1a**)	[Co(**P2**)]	toluene	74	10
3	*t*-Bu (**1a**)	[Co(**P3**)]	toluene	75	19
4	*t*-Bu (**1a**)	[Co(**P4**)]	toluene	92	38
5	*t*-Bu (**1a**)	[Co(**P5**)]	toluene	90	42
6	*t*-Bu (**1a**)	[Co(**P6**)]	toluene	82	66



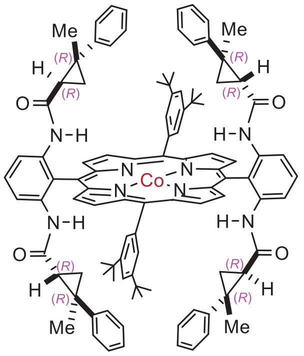
[Co(**P1**)]



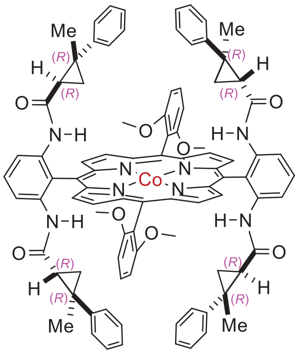
[Co(**P2**)]



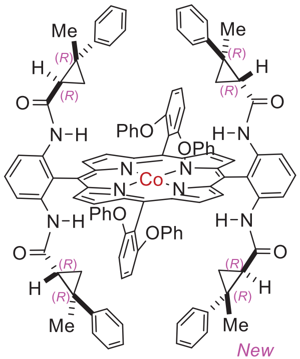
[Co(**P3**)]



[Co(**P4**)]



[Co(**P5**)]

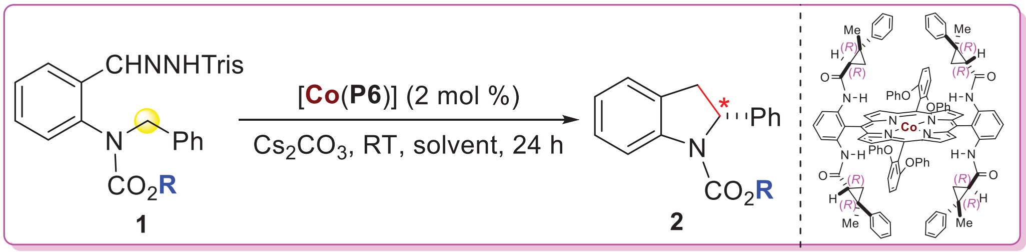


[Co(**P6**)] *New (X-ray)*

^{a} Carried out with **1** (0.1 mmol) in the presence of Cs_2CO_3 (2.0 equiv.) by [Co(Por)] (2 mol %) in Toluene (1.0 mL); Tris = 2,4,6-triisopropylphenyl sulfonyl; ^{b} Isolated yields; ^{c} Determined by chiral HPLC.

As expected, both the reactivity and enantioselectivity were significantly enhanced (Table 3.1, entry 4). In a similar trend, when sterically more encumbered [Co(**P5**)] (**P5** = 2,6-DiMeO-QingPhyrin) was used, improvement in asymmetric induction continued (entry 5). To amplify such effect, we synthesized the new catalyst [Co(**P6**)] (**P6** = 2,6-DiPhO-QingPhyrin) by replacing the methoxy groups at the 2,6-positions of the *meso*-aryl substituents in **P5** with phenoxy groups. It was satisfying to find that [Co(**P6**)] could catalyze the formation of **2a** in 82% yield with 66% *ee* (entry 6).

Table 3.2| Protecting Group and Solvent Effect of Co(II)-Based Catalytic System for Enantioselective Radical C–H Alkylation of Aryldiazomethanes

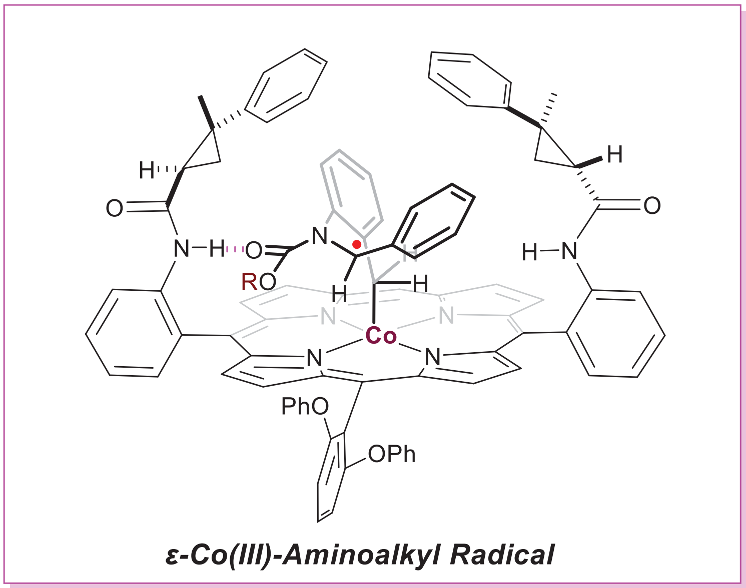


entry	R	solvent	yield (%)	*ee* (%)
1	*t*-Bu (**1a**)	$PhCH_3$	82	66
2	Et (**1b**)	$PhCH_3$	92	86
3	Me (**1c**)	$PhCH_3$	99	86
4	Me (**1c**)	PhH	99	86
5	Me (**1c**)	PhCl	99	86
6	Me (**1c**)	DCE	99	84
7	Me (**1c**)	DCM	99	82
8	Me (**1c**)	THF	78	86
9	Me (**1c**)	Dioxane	40	84
10	Me (**1c**)	TBME	99	86
11	Me (**1c**)	DME	95	88
12	**Me (1c)**	**MeOH**	**92**	**94**
13	Me (**1c**)	Et_2O	98	82
14	Me (**1c**)	DMF	trace	N.D.

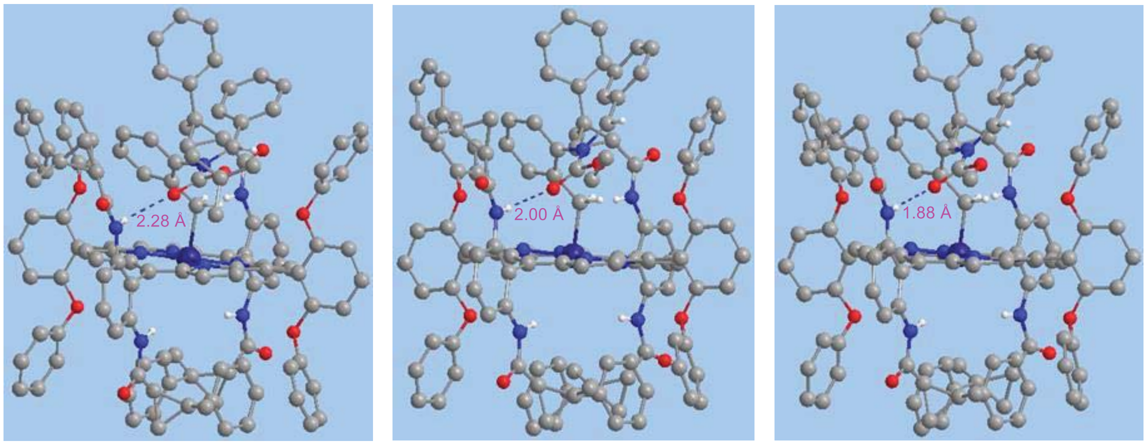
[a] Carried out with **1** (0.1 mmol) in the presence of Cs_2CO_3 (2.0 equiv.) by [Co(**P6**)] (2 mol %) in solvent (1.0 mL); Tris = 2,4,6-triisopropylphenyl sulfonyl; $PhCH_3$ = toluene; PhH =

benzene; PhCl = Chlorobenzene; DCE = 1,2-Dichloroethene; DCM = Dichloromethane; THF = Tetrahydrofuran; TBME = Methyl *tert*-butyl ether; DME = Dimethoxyethane; MeOH = Methanol; Et_2O = Diethyl ether; DMF = Dimethylformamide. [b] Isolated yields; [c] Determined by chiral HPLC.

Figure 3.2| Molecular Modeling of Proposed *ε*-Co(III)-Aminoalkyl Radical Intermediates Showing Potential Hydrogen-bonding Interactions



ε-Co(III)-Aminoalkyl Radical



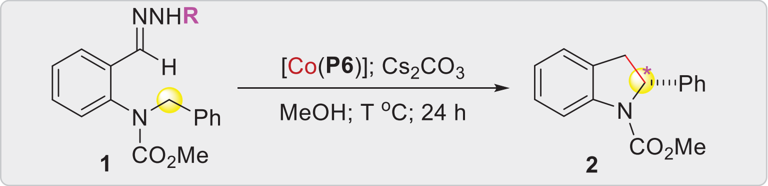
R = ^{t}Bu[b] **R = Et[c]** **R = Me[d]**

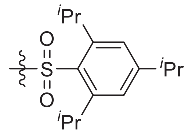
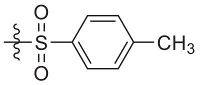
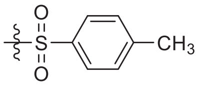
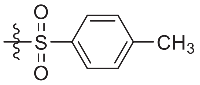
With [Co(**P6**)] in hand, we then examined the effect of different *N*-substituents of substrate **1** on the catalytic reaction (Table 3.2). It was shown that changes from *t*-butyl (**1a**) to ethyl (**1b**) to methyl (**1c**) carbamates led to a successive increase in both yield and enantioselectivity, achieving almost quantitative yield and 86% *ee* in the case of substrate **1c** (entries 1–3). This outcome is possibly attributed to the potential hydrogen-bonding interaction between the carbonyl group of the carbamate and the amido group of the chiral catalyst, which strengthens upon the decrease in steric hinderance as indicated in the Spartan model (Figure 3.2).

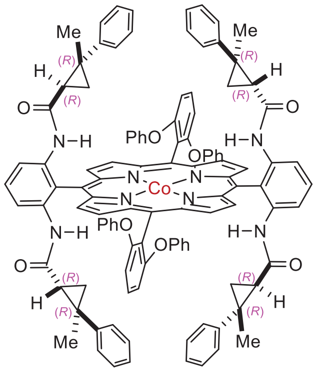
Further investigation of the different solvent effect revealed that except for DMF, both polar and non-polar solvents were suitable for this asymmetric radical process, delivering the desired product with different yields and enantioselectivities (Table 3.2, entries 3–14). Interestingly, when methanol was employed as the solvent, it afforded 2-phenylindoline **2c** at room temperature in 92% yield with 94% *ee* (entry 12).

Like Tris-protected hydrazones (Table 3.3, entry 1), catalytic reactions of Ts-protected hydrazones could also proceed at room temperature (entry 2), affording the desired indoline with the equally high enantioselectivity but in a much lower yield (47%). The same enantioselectivity observed is consistent with the proposed mechanism in Scheme 3.1 where the hydrazones are not directly involved in the catalytic cycle, and the lower yield is contributed to the slower generation of the corresponding diazo compounds from Ts-protected hydrazones at room temperature. At elevated temperatures such as 40 ºC and 60 ºC, the catalytic reactions of simple Ts-protected hydrazones could produce the desired indolines in the similarly high yields but with relatively lower enantioselectivities (Table 3.3, entries 3-4).

Table 3.3| The Effect of Different R Groups on Enantioselective Radical C–H Alkylation of Aryldiazomethanes[a]



entry	R	T (°C)	yield	*ee*
1	 (**Tris**)	RT	92%	94%
2	 (**Ts**)	RT	47%	93%
3	 (**Ts**)	40	92%	91%
4	 (**Ts**)	60	95%	89%



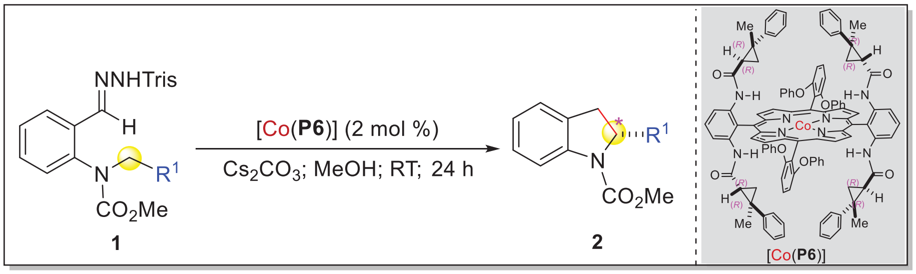
[Co(**P6**)]

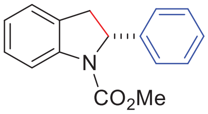
[a] Carried out with 1 (0.1 mmol) in the presence of Cs_2CO_3 (2.0 equiv.) by [Co(**P6**)] (2 mol %) in solvent (1.0 mL); Yield refers to isolated yield; *ee* was determined by chiral HPLC; Tris = 2,4,6-triisopropylphenyl sulfonyl.

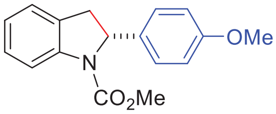
3.2.2 Enantioselective Radical C–H Alkylation for Construction of Chiral 2-Substituted Indolines with Various C(sp^3)–H Bonds

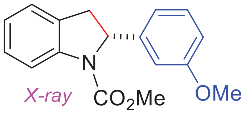
Under the optimized conditions, the scope of [Co(**P6**)]-catalyzed radical alkylation was evaluated by employing different C–H substrates, and the results were summarized in Table 3.4.

Table 3.4| [Co(P6)]-Catalyzed Enantioselective Radical C–H Alkylation for Construction of Chiral 2-Substituted Indolines[a]



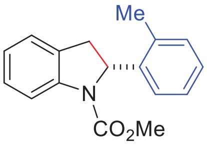

entry 1: **2c**
92% yield, 94% *ee*

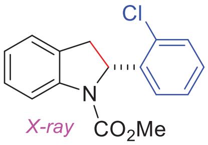

entry 2: **2d**
98% yield, 94% *ee*



entry 3: **2e**
98% yield, 90% *ee*

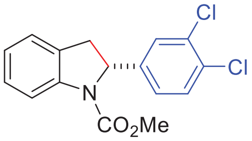

2e

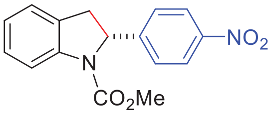

entry 4: **2f**
96% yield, 94% *ee*

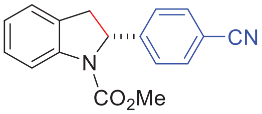


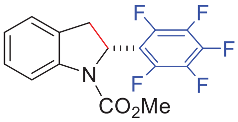
entry 5: **2g**
92% yield, 93% *ee*

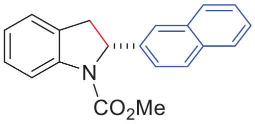

2g

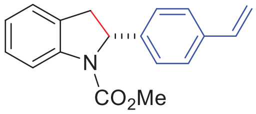

entry 6: **2h**
85% yield, 96% *ee*

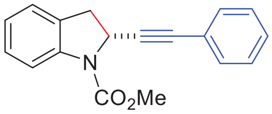

entry 7: **2i**
96% yield, 87% *ee*

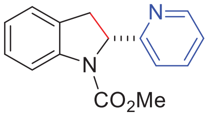

entry 8: **2j**
97% yield, 94% *ee*

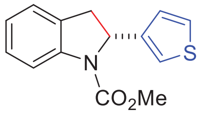

entry 9: **2k**
90% yield, 95% *ee*

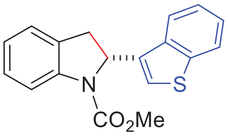

entry 10: **2l**
90% yield, 94% *ee*

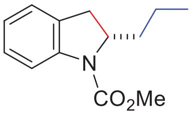

entry 11: **2m**
57% yield, 95% *ee*

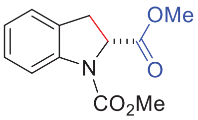

entry 12: **2n**
50% yield, 87% *ee*

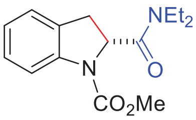

entry 13: **2o**
93% yield, 90% *ee*


entry 14: **2p**
97% yield, 94% *ee*


entry 15: **2q**
80% yield, 92% *ee*


entry 16[b]: **2r**
65% yield, 87% *ee*


entry 17[c]: **2s**
49% yield, 81% *ee*


entry 18[c]: **2t**
92% yield, 68% *ee*

[a] Carried out with **1** (0.1 mmol) in the presence of Cs_2CO_3 (2.0 equiv.) in MeOH (1.0 mL); Yields refer to isolated yields; *ee* was determined by chiral HPLC; [b] At 60 ºC; [c] At 40 ºC. Tris = 2,4,6-triisopropyl phenylsulfonyl.

As demonstrated with substrates **1c**–**1k**, benzylic C–H bonds having varied electronic and steric properties could be effectively alkylated at room temperature in a highly enantioselective fashion, affording chiral 2-arylindoline derivatives **2c**–**2k** in excellent yields (entries 1–9). The absolute configurations of both **2e** and **2g** were established by X-ray crystal structural analysis as *(R)*. The availability of halogenated products such as **2g** and **2h** in high enantiopurity may allow for further transformations via metal-catalyzed couplings and related reactions (entries 5 and 6).

It is noteworthy to mention that even the highly electron-deficient pentafluorobenzylic C–H bond in substrate **1k** could successfully undergo radical alkylation, forming 2-perfluorophenylindoline (**2k**) in 90% yield with 95% *ee* (entry 9). The catalytic system could also efficiently alkylate C–H bonds adjacent to other aryl groups as shown with the successful reaction of the 2-naphthyl-based substrate **1l** (entry 10). Besides -NO_2 and -CN functionalities (entries 7 and 8), the C–H alkylation was shown to tolerate both alkenyl and alkynyl groups, as demonstrated by the stereoselective formation of indolines **2m** and **2n** without complications from potential reactions with the C=C and C≡C bonds, respectively (entries 11 and 12).

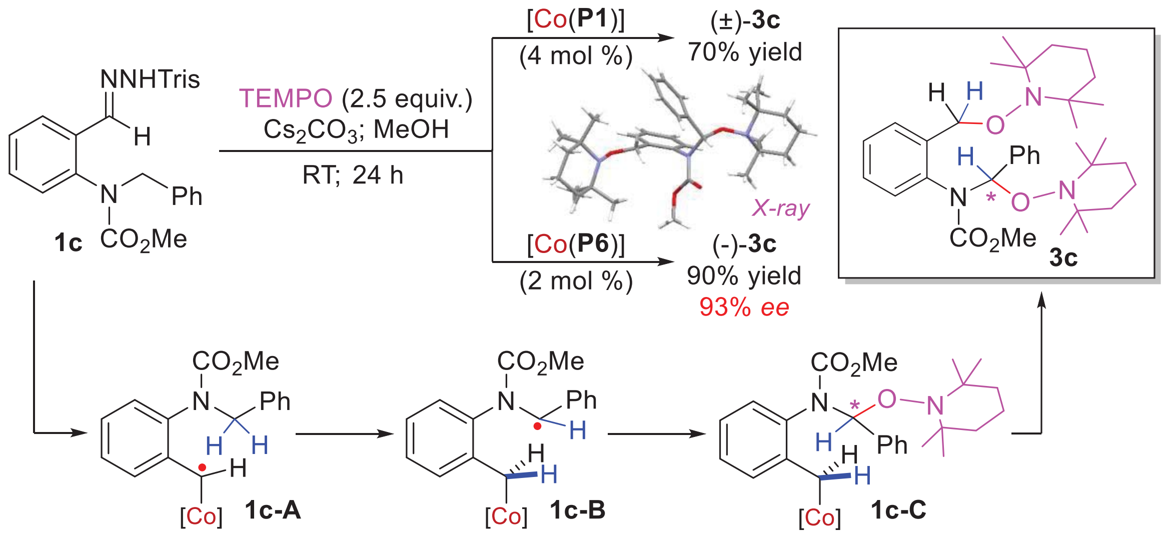
Notably, this system was equally effective for alkylation of C–H bonds next to heteroaryl groups, such as pyridine (**1o**), thiophene (**1p**), and benzothiophene (**1q**), providing 2-heteroarylindolines **2o**–**2q** in high yields with high enantioselectivities (entries 13–15). Given that both heteroarene and indoline are prevalent as key structural elements in many bioactive natural and synthetic compounds, the easy access of these linked biheterocyclic compounds in high enantiopurity may find applications in pharmaceutical research and development.

Furthermore, non-activated C–H bonds could also be alkylated by the system, as exemplified by the regioselective radical 1,5-alkylation of substrate **1r**, forming 2-propylindoline (**2r**) in 65% yield with 87% *ee* although 60 ºC was needed (entry 16). The alkylation was further highlighted by its applicability to even C–H bonds that are directly attached to electron-withdrawing groups. For example, electron-poor C–H bonds that are adjacent to ester (**1s**) and amide (**1t**) groups were smoothly alkylated at 40 ºC to furnish the 2-ester- (**2s**) and 2-amido- (**2t**) indolines in varied yields and enantioselectivities (entries 17 and 18). These results clearly manifested the low sensitivity of the Co(II)-based metalloradical alkylation to the electronic properties of C–H bonds, which are consistent with its underlying radical mechanism.

3.2.3 Mechanistic Studies on Co(II)-Catalyzed Intramolecular Radical C–H Alkylation of *o*-Aminoaryldiazomethanes

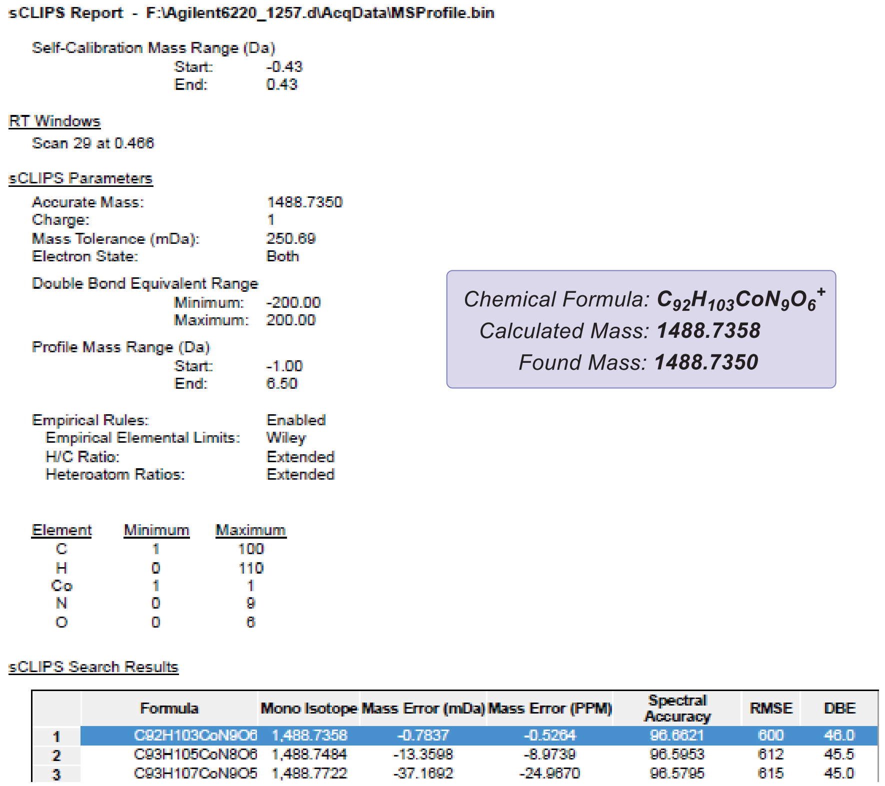
To gain insight into the underlying mechanism of this Co(II)-catalyzed C–H alkylation, a set of mechanistic experiments were conducted. We first examined the effect of the radical scavenger TEMPO on the process under the standard conditions (Scheme 3.2). Addition of TEMPO (2.5 equiv.) to the reaction of benzyl C–H substrate **1c** by achiral catalyst [Co(**P1**)] resulted in complete inhibition of the C–H alkylation without observation of **2c**. Instead, compound (±)-**3c** was isolated in 70% yield, whose structure was confirmed by X-ray analysis to contain two TEMPO units at the 1- and 5-positions, respectively. The formation of (±)-**3c** is indicative of the formation of the initial α-Co(III)-benzyl radical (**1c-A**) as well as the resulting ε-Co(III)-aminoalkyl radical (**1c-B**) from 1,5-HAA, which was presumably capped subsequently by one molecule of TEMPO at the ε-position through radical recombination to generate intermediate **1c-C** and then followed by radical substitution with the second molecule of TEMPO at the α-position to break the weak Co(III)–C bond for final production of (±)-**3c**.

Scheme 3.2| Mechanistic Studies on Co(II)-Catalyzed Intramolecular Radical C–H Alkylation of *o*-Aminoaryldiazomethanes: Effect of TEMPO on Benzylic C–H Reaction



To gain information on stereochemistry, the same reaction was performed with chiral catalyst [Co(**P6**)] (Scheme 3.2). The same bis-TEMPO-capped compound (-)-**3c** was also generated, but in a much higher yield of 90% and, remarkably, with 93% *ee*. The fact that the enantioselectivity for the C–O bond formation (93% *ee*) of the TEMPO-capped product (-)-**3c** was almost identical to the one observed for the C–C bond formation (94% *ee*) of the C–H alkylation product **2c** in the absence of TEMPO (Table 3.4, entry 1) implies that the prochiral α-aminoalkyl radical in **1c-B** was confined inside the chiral pocket of [Co(**P6**)] to adapt a stable, well-defined configuration.

Scheme 3.3| High Resolution Mass Spectroscopy (HRMS) Spectrum for Co(III)-Supported Alkyl Radical Intermediate

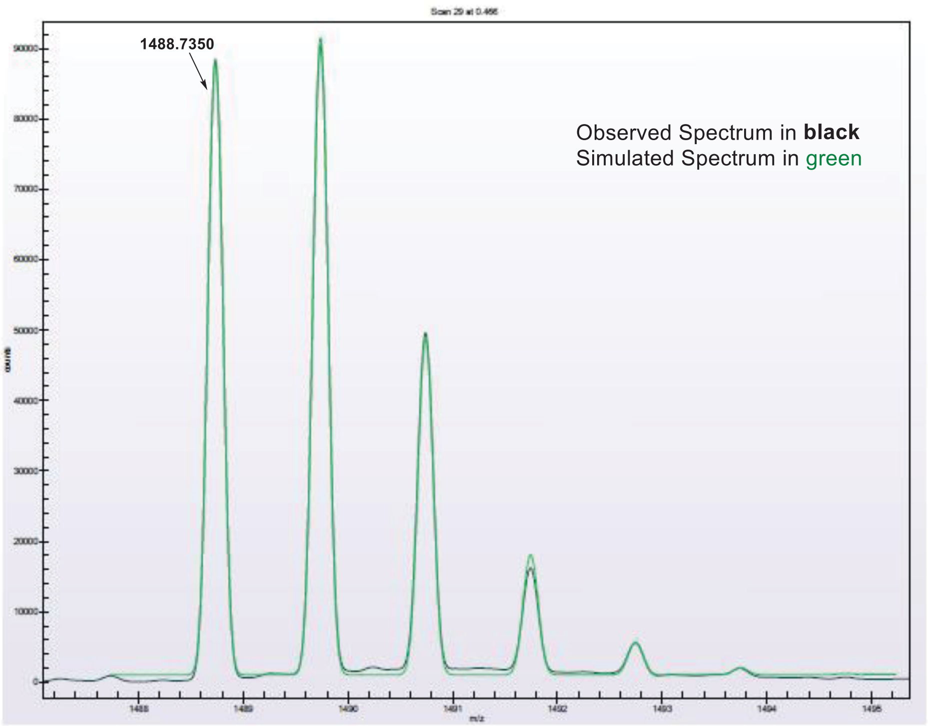


```
sCLIPS Report  -  F:\Agilent6220_1257.d\AcqData\MSProfile.bin

  Self-Calibration Mass Range (Da)
                 Start:       -0.43
                 End:          0.43

RT Windows
  Scan 29 at 0.466

sCLIPS Parameters
  Accurate Mass:               1488.7350
  Charge:                      1
  Mass Tolerance (mDa):        250.69
  Electron State:              Both
  Double Bond Equivalent Range
                 Minimum:     -200.00
                 Maximum:      200.00
  Profile Mass Range (Da)
                 Start:       -1.00
                 End:          6.50

  Empirical Rules:             Enabled
    Empirical Elemental Limits: Wiley
    H/C Ratio:                 Extended
    Heteroatom Ratios:         Extended

  Element   Minimum   Maximum
     C         1        100
     H         0        110
     Co        1          1
     N         0          9
     O         0          6
```

sCLIPS Search Results

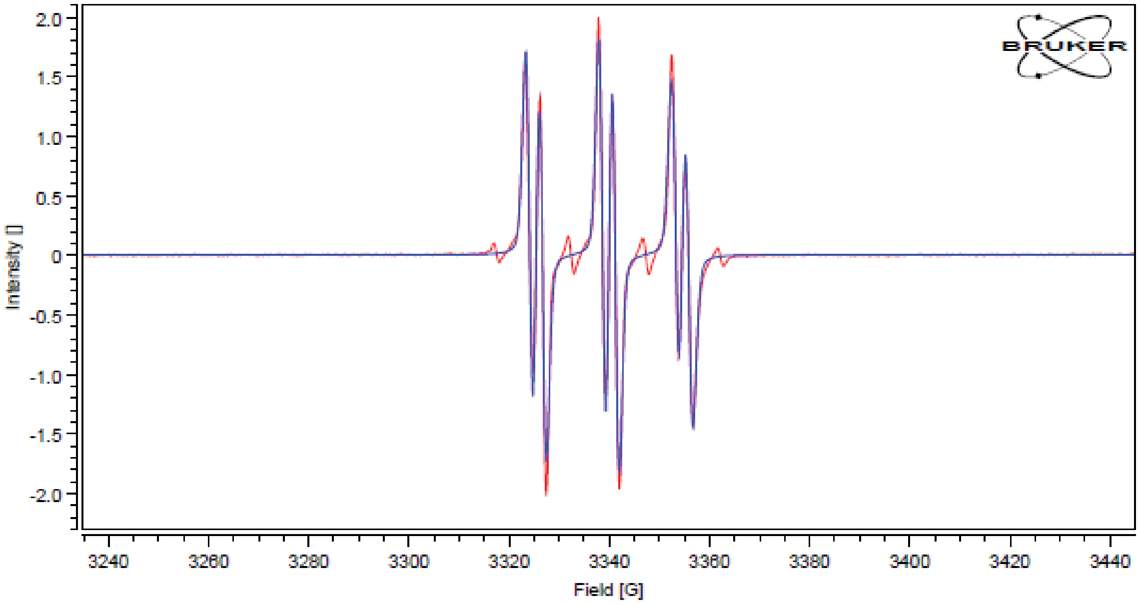
	Formula	Mono Isotope	Mass Error (mDa)	Mass Error (PPM)	Spectral Accuracy	RMSE	DBE
1	C92H103CoN9O6	1,488.7358	-0.7837	-0.5264	96.6621	600	46.0
2	C93H105CoN8O6	1,488.7484	-13.3598	-8.9739	96.5953	612	45.5
3	C93H107CoN9O5	1,488.7722	-37.1692	-24.9670	96.5795	615	45.0

Chemical Formula: $C_{92}H_{103}CoN_9O_6^+$
Calculated Mass: ***1488.7358***
Found Mass: ***1488.7350***



In addition, the resulting Co(III)-supported alkyl radical intermediates from the reaction of substrate **1c** by [Co(**P1**)] in the absence of TEMPO could be directly detected by HRMS ($C_{92}H_{103}CoN_9O_6^+$, *m*/*z*: calculated: 1488.7358, found: 1488.7350) (Scheme 3.3). The HRMS experiment was carried out in the absence of any additives such as formic acid, which commonly act as electron carriers for ionization, allowing for the detection of the molecular ion signals corresponding to Co(III)-alkyl radical ($C_{92}H_{103}CoN_9O_6\cdot$) by the loss of one electron.

Scheme 3.4| Isotropic X-band EPR Spectrum of Phenyl *N*-*tert*-butylnitrone (PBN)-Trapped Co(III)-Supported Alkyl Radical Intermediate

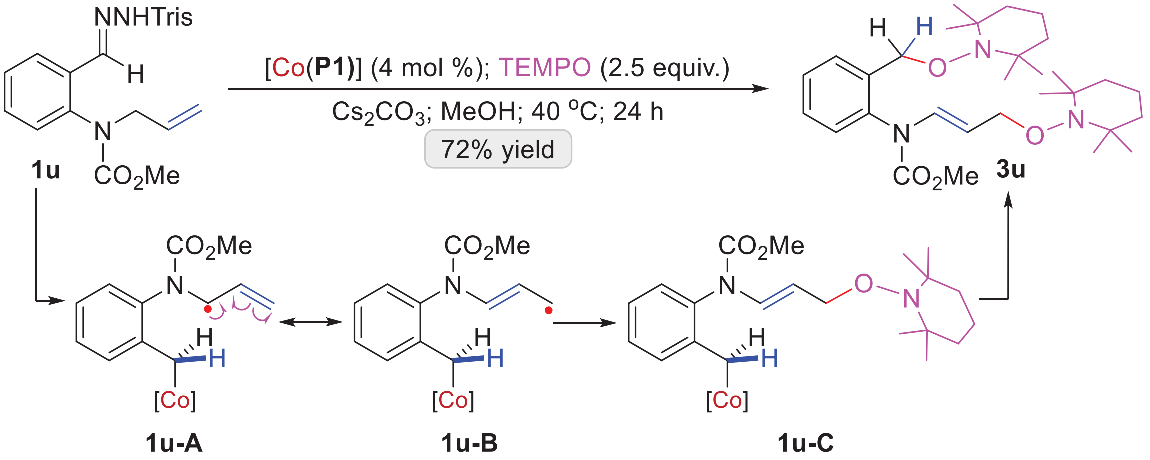


Besides the HRMS experiment, the corresponding alkyl radical intermediate was also trapped by spin trapping reagent phenyl *N*-*tert*-butylnitrone (PBN) to give the characteristic EPR signal. As shown in Scheme 3.4, the resulting EPR spectrum (in red), which is assigned to PBN-trapped Co(III)-supported 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 $g = 2.006$, $A_N = 14.6$ G, $A_H = 2.6$ 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 litrature.[8b]

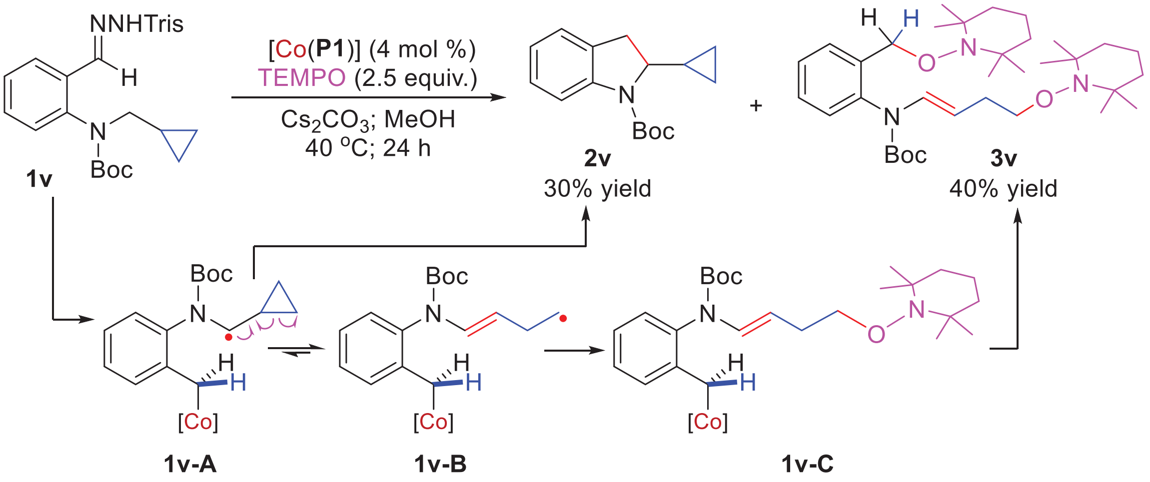
To gather further evidence to support the stepwise radical mechanism of the catalytic process, we also designed specific substrates as radical probes to shed more light on the nature of *ε*-Co(III)-aminoalkyl radical intermediates.

Scheme 3.5| Mechanistic Studies on Co(II)-Catalyzed Intramolecular Radical C–H Alkylation of *o*-Aminoaryldiazomethanes: Effect of TEMPO on Allylic C–H Reaction-Olefin Isomerization



First, allylic C–H substrate **1u** was prepared as a radical resonance probe to evaluate potential olefin isomerization via the resulting allylic radical intermediate after 1,5-HAA (Scheme 3.5). Under the standard conditions, the catalytic reaction of **1u** by [Co(**P1**)] was carried out in the presence of TEMPO (2.5 equiv.) at 40 ºC. As observed for the benzylic C–H substrate **1c** (Scheme 3.2), a similar type of bis-TEMPO-capped compound **3u** was isolated in 72% yield without formation of the corresponding C–H alkylation product (Scheme 3.5). Characterizations of **3u** revealed that the C=C double bond was isomerized from the terminal to internal position. Clearly, the resulting *ε*-Co(III)-aminoalkyl radical, which can be represented by its two resonance forms **1u-A** and **1u-B** as an allylic radical, was captured by TEMPO to give intermediate **1u-C** and then underwent further radical substitution with another molecule of TEMPO to deliver the final product **3u**. The predominant production of **3u** is presumably a result of the much faster capping rate of resonance form **1u-B** (a primary allylic radical) than resonance form **1u-A** (a secondary allylic radical) by the sterically demanding TEMPO radical.

Scheme 3.6| Mechanistic Studies on Co(II)-Catalyzed Intramolecular Radical C–H Alkylation of *o*-Aminoaryldiazomethanes: Effect of TEMPO on Cyclopropylmethyl C–H Reaction-Ring Opening



Second, substrate **1v** bearing a cyclopropyl ring was synthesized as a radical clock to examine possible ring-opening of the cyclopropylmethyl radical generated from 1,5-HAA (Scheme 3.6). Interestingly, the catalytic reaction of **1v** under similar conditions by

[Co(**P1**)] in the presence of TEMPO (2.5 equiv.) resulted in the formation of bis-TEMPO-capped compound **3v** in 40% yield as well as the C–H alkylation product **2v** in 30% yield. Obviously, the corresponding *ε*-Co(III)-aminoalkyl radical intermediate **1v-A** underwent two competitive pathways during the catalytic process. While its radical substitution resulted in the formation of the 2-cyclopropylindoline **2v**, the cyclopropylcarbinyl radical in **1v-A** also proceeded ring-opening competitively to generate homoallylic alkyl radical **1v-B**, which was transformed to the final enamine **3v** upon two sequential capture reactions by TEMPO *via* intermediate **1v-C**. The fact that **2v** and **3v** were produced in similar yields indicated that the forming rate of C2–C3 bond via radical substitution to construct the indoline ring was fast, considering that the rate constant of ring-opening of the parent cyclopropylmethyl radical is 8.6×10^{7} s^{-1}.[14]

Collectively, all these experimental observations strongly support the proposed stepwise radical mechanism of the Co(II)-based C–H alkylation with *N*-arylsulfonyl hydrazones.

3.3 CONCLUSIONS

In summary, we have developed the new Co(II)-based metalloradical system for asymmetric C–C bond formation via enantioselective radical alkylation of $C(sp^3)$–H bonds. The enantioselective radical process has been demonstrated for stereoselective synthesis of chiral indolines through asymmetric C2–C3 bond formation. With the design of the new chiral ligand 2,6-DiPhO-QingPhyrin, this Co(II)-catalyzed system can effectively activate *ortho*-aminoaryldiazomethanes at room temperature, which are readily generated *in situ* from hydrazone precursors, for highly stereoselective radical alkylation of different types of C(sp^3)–H bonds with varied electronic and steric properties. In addition to the attributes of chemoselectivity and regioselectivity, this catalytic radical system features a high level of functional group tolerance as well as good compatibility with heteroaryl units. Detailed mechanistic studies also provided insight into the underlying stepwise radical pathway. This enantioselective radical process represents a new synthetic application of Co(II)-based MRC and offers a streamlined construction of chiral 2-substituted indolines from readily available starting materials.

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 a 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, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian INOVA 500 (125 MHz), or 600 (150 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm with residual CHCl3 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. 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. HPLC measurements were carried out on a Shimadzu HPLC system with ChiralPak Immobilized columns: IA, IB and IC. Infrared (IR) spectra were recorded on a Termo Scientific Nicolet Is5 System. Frequencies are reported in wavenumbers (cm^{-1}). HRMS data was obtained on an Agilent 6210 Time-of-Flight LC/MS with ESI as the ion source. Optical rotations were measured on a Rudolph Research Analytical AUTOPOL® IV digital polarimeter. The X-ray diffraction data were collected using Bruker Kappa APEX DUO diffractometer and a Rigaku HighFlux Homelab diffractometer. X-band EPR spectra were recorded on a Bruker EMX-Plus spectrometer

(Bruker BioSpin). Spartan modelling was performed using Spartan'14 software from Wavefunction, Inc.

Unless otherwise noted, all C–H alkylation reactions were performed in oven-dried glassware under dry N_2 atmosphere with standard vacuum line techniques. Gastight 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).

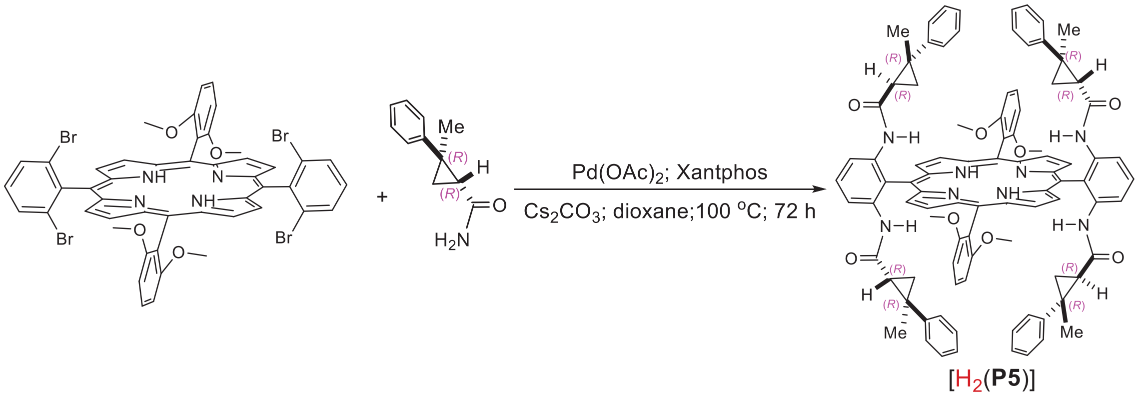
3.4.2 Procedure for HRMS Experiment

To an oven-dried Schlenk tube, sulfonylhydrazone **1c** (0.05 mmol) and Cs_2CO_3 (2.0 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, and CH_3CN (0.5 mL) was added via a gastight syringe. The mixture was then stirred at 60 ^{o}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, which commonly act as electron carriers for ionization, allowing for the detection of the molecular ion signals corresponding to Co(III)-alkyl radical ($C_{92}H_{103}CoN_9O_6\cdot$) by the loss of one electron.

3.4.3 Procedure for EPR Experiment

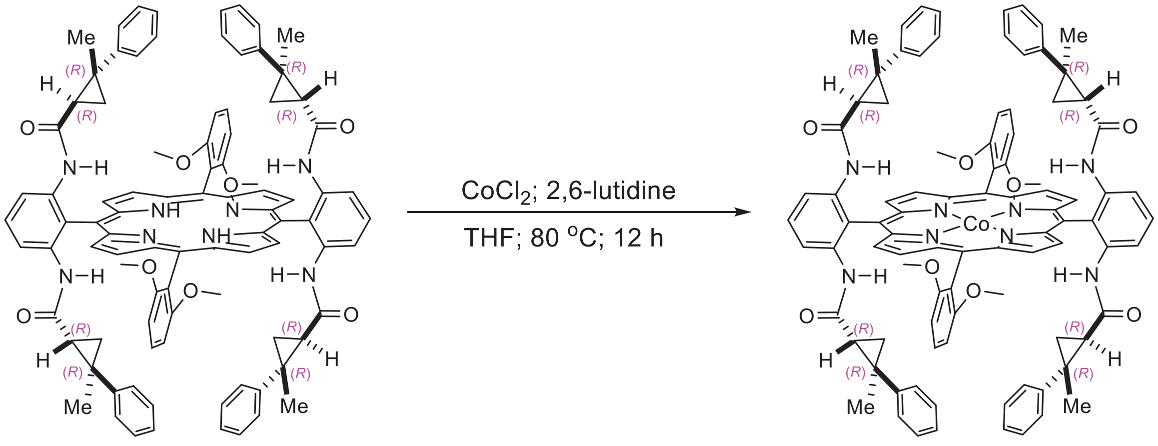
To an oven-dried Schlenk tube A, sulfonylhydrazone **1c** (0.05 mmol) and Cs_2CO_3 (2.0 equiv.) were added. The Schlenk tube was then evacuated and backfilled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, and benzene (0.5 mL) was added via a gastight syringe. The mixture was then stirred at 60 ºC for 0.5 h. During the time, [Co(**P1**)] (4 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 3 min and transferred into a degassed EPR tube (filled with argon) through a gastight syringe. The sample was then carried out for EPR experiment at room temperature (EPR settings: T = 298 K; microwave frequency: 9.37762 GHz; power: 6.325 mW; modulation amplitude: 1.0 G).

3.4.4 Procedure for Synthesis of Catalyst [Co(P5)]



[H$_2$(P5)] was synthesized according to our previous reported procedure[7a] with 58% yield. The 5,15-bis(2,6-dibromophenyl)-10,20-bis(2,6-dimethoxyphenyl)porphyrin (0.2 mmol), (1*R*, 2*R*)-2-methyl-2-phenylcyclopropane-1-carboxamide[7c] (3.2 mmol), Pd(OAc)$_2$ (0.08 mmol), Xantphos (0.16 mmol), and Cs$_2$CO$_3$ (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. The screwcap was replaced with a rubber septum, and dioxane (10 mL) was added via a gastight 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 h. The resulting mixture was cooled down to room temperature, diluted in ethyl acetate, filtrated through a silica pad and concentrated under vacuum. The pure compound was obtained as a purple solid after purification by flash column chromatography (hexanes/DCM/ethyl acetate: 10/10/2 to 10/10/3). ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.88 (s, 8H), 8.48 (d, J = 5.9 Hz, 4H), 7.89 (t, J = 8.3 Hz, 2H), 7.69 (t, J = 8.5 Hz, 2H), 6.90 (d, J = 8.6 Hz, 4H), 6.68 (s, 4H), 5.98 (s, 4H), 5.31 (br, 16H), 2.96 (s, 12H), 0.99 – 0.96 (m, 16H), 0.56 (br, 4H), 0.18 (br, 4H), -2.12 (s, 2H). ^{13}C NMR (125 MHz,

$CDCl_3$) δ 168.60, 160.36, 144.50, 139.05, 132.77, 130.79, 130.28, 130.01, 126.81, 125.94, 124.97, 121.46, 117.81, 117.15, 114.78, 106.81, 103.80, 55.07, 30.01, 29.92, 19.42, 17.71. IR (neat, cm^{-1}): 3409.14, 3313.83, 2928.10, 2836.12, 1690.30, 1586.35, 1464.60, 1249.90, 1108.38, 731.66. HRMS (ESI) (M+H$^+$) Calcd. for $C_{92}H_{83}N_8O_8^+$: 1427.6328, found 1427.6301. UV–vis (CH_2Cl_2), λ_{max} nm (log ε): 421(5.43), 514(4.23), 588(3.74), 643(3.34).

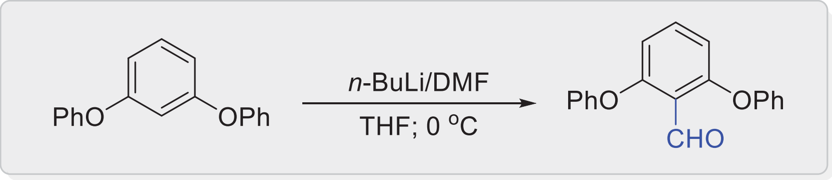


[H_2(**P5**)]

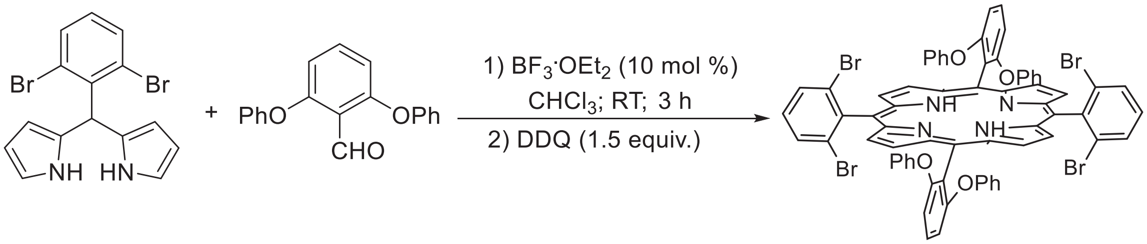
[Co(**P5**)]

[Co(P5)] was synthesized according to our previous reported procedure[7a] with 92% yield. Free base porphyrin [H_2(**P5**)] 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 a gastight 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 °C for 12 h. The resulting mixture was cooled down to room temperature, diluted with ethyl acetate, and transferred to a separatory funnel. The reaction mixture was washed with water 3 times and concentrated under vacuum. The target compound [Co(**P5**)] was isolated as a purple solid after purification by flash column chromatography with hexanes/ethyl acetate (2/1) as eluent. IR (neat, cm^{-1}): 3405.77, 2930.13, 1691.39, 1584.23, 1464.43, 1249.49, 1107.50, 997.65, 762.32. HRMS (ESI) (M*$^{+}$) Calcd. for $C_{92}H_{80}CoN_8O_8^+$: 1483.5426, found 1483.5488. UV–vis (CH_2Cl_2), λ_{max} nm (log ε): 413(4.90), 532(3.77).

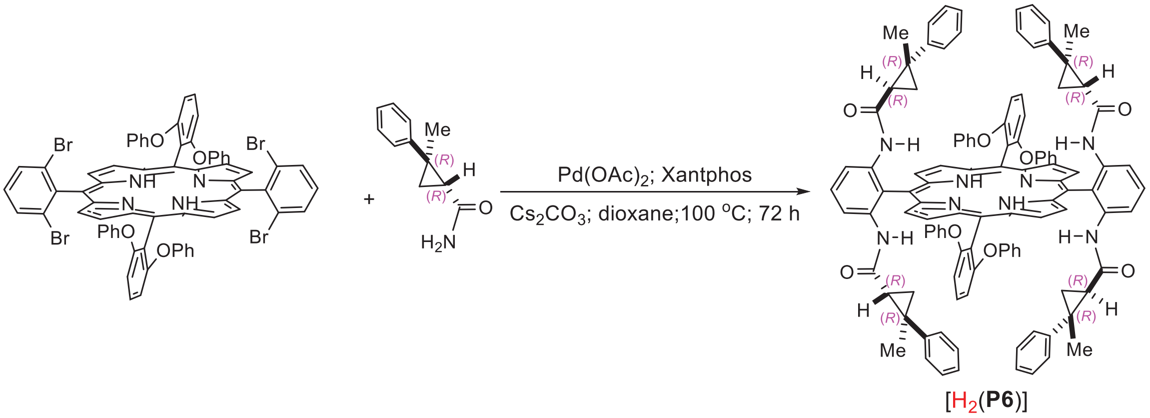
3.4.5 Procedure for Synthesis of Catalyst [Co(P6)]



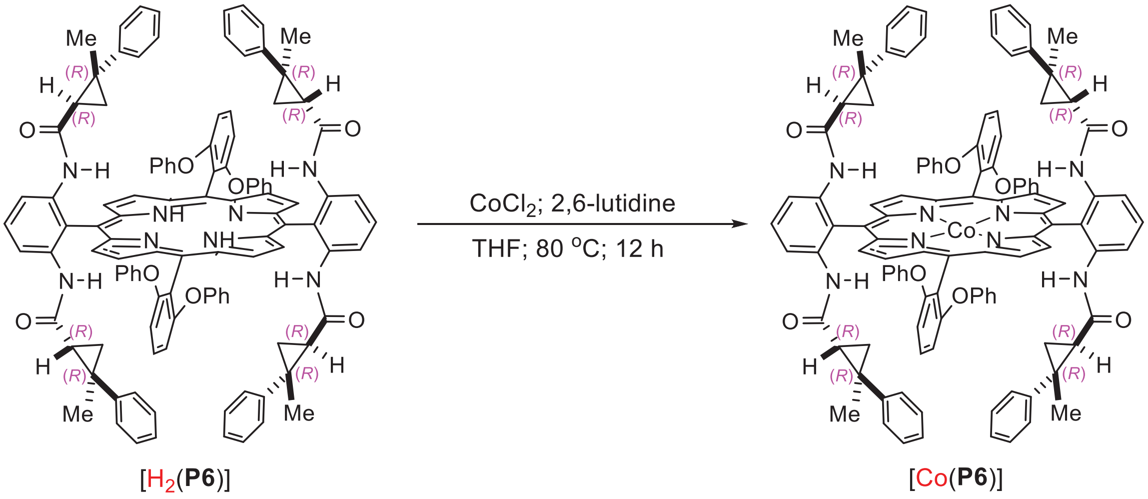
2, 6-diphenoxybenzaldehyde was synthesized according to previous reported procedure.[15] To a stirred solution of 1,3-diphenoxybenzene (10 mmol) in dry THF (60 mL) at 0 °C, *n*-BuLi (8 mL, 1.5 M in hexanes) was added dropwise for 1 h. Then the mixture was stirred at room temperature for 2 h and followed by the slow addition of DMF (1.83 g, 25 mmol). After 2 h, the mixture was poured into ice water. The organic phase was separated and the aqueous phase was extracted with ether (3×30 mL). The combined organic layer was dried over anhydrous Na_2SO_4. After the removal of solvent under vacuum, the product was purified by column chromatography with hexanes/ethyl acetate (9:1 to 6:1) as eluent to afford 2, 6-diphenoxybenzaldehyde as a white solid in 70% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.61 (s, 1H), 7.39 (t, J = 7.9 Hz, 4H), 7.32 (t, J = 8.4 Hz, 1H), 7.18 (t, J = 7.4 Hz, 2H), 7.10 – 7.08 (m, 4H), 6.58 (d, J = 8.4 Hz, 2H).^{13}C NMR (150 MHz, $CDCl_3$) δ 188.15, 159.85, 156.13, 135.09, 129.95, 124.31, 119.61, 118.47, 112.72. IR (neat, cm^{-1}): 2774.28, 1688.49, 1598.71, 1570.31, 1487.76, 1454.31, 1409.35, 1204.09, 1030.85, 772.93, 717.85, 685.53. HRMS (ESI) (M+H$^+$) Calcd. for $C_{19}H_{15}O_3^+$: 291.1021, found 291.1034.



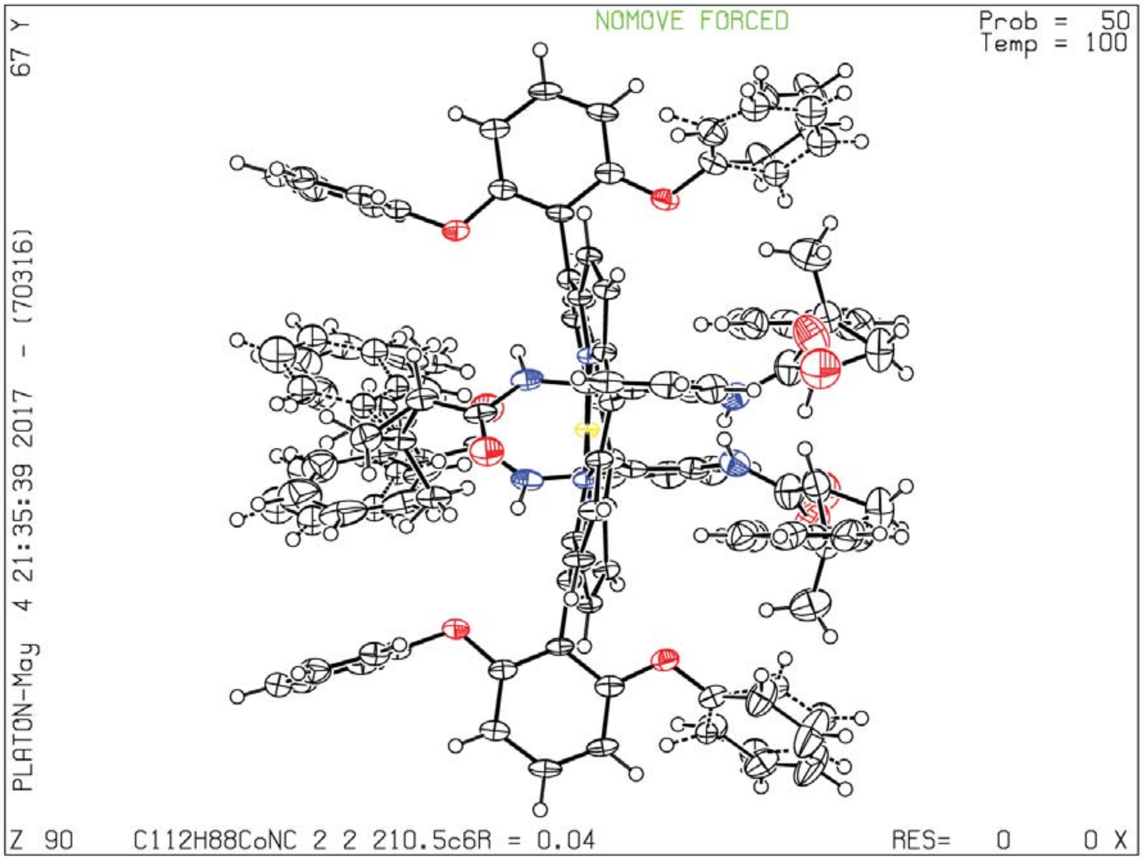
5,15-bis(2,6-dibromophenyl)-10,20-bis(2,6-diphenoxyphenyl)porphyrin was synthesized according to our previous reported procedure[7a] with 60% yield. A mixture of *meso*-(2,6-dibromophenyl)dipyrromethane (5 mmol), 2, 6-diphenoxybenzaldehyde (5 mmol) in chloroform (500 mL) was purged with nitrogen for 10 min. The flask was wrapped with aluminum foil to shield it from light. Then boron trifluoride diethyl etherate was added dropwise via a syringe. After the solution was stirred under the nitrogen atmosphere at room temperature for 3 h, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (7.5 mmol) was added at one time. After 1 h, triethylamine (10 mL) was added. The reaction solution was then directly poured into a silica gel column that was rinsed with dichloromethane. The column was eluted with dichloromethane. The fractions containing the product were collected and concentrated under vacuum. The residue was washed several times with methanol to afford the pure compound. ^{1}H NMR (600 MHz, CD_2Cl_2) δ 9.00 (s, 4H), 8.62 (s, 4H), 8.06 (d, *J* = 7.7 Hz, 4H), 7.68 (t, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 4H), 6.89 (d, *J* = 5.8 Hz, 8H), 6.70 (d, *J* = 6.5 Hz, 12H), -2.73 (s, 2H). ^{13}C NMR (150 MHz, CD_2Cl_2) δ 159.40, 156.70, 143.47, 131.93, 131.61, 130.68, 129.58, 128.78, 124.59, 123.70, 119.58, 118.31, 113.27, 111.14. IR (neat, cm^{-1}): 3311.65, 1570.06, 1487.58, 1449.43, 1230.13, 1209.38, 1023.02, 1012.10, 979.66, 796.47, 721.44. HRMS (ESI) (M+H$^+$) Calcd. for $C_{68}H_{43}Br_4N_4O_4^+$: 1295.0012, found 1295.0050. UV–vis (CH_2Cl_2), λ_{max} nm (log ε): 422(5.63), 516(4.37), 592(3.87), 646(3.11).



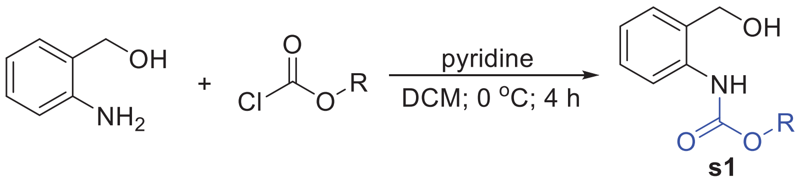
[H_2(P6)] was synthesized according to our previous reported procedure[7a] with 61% yield. The 5,15-bis(2,6-dibromophenyl)-10,20-bis(2,6-diphenoxyphenyl)porphyrin (0.2 mmol), (1*R*, 2*R*)-2-methyl-2-phenylcyclopropane-1-carboxamide[7c] (3.2 mmol), Pd(OAc)$_2$ (0.08 mmol), Xantphos (0.16 mmol), and Cs_2CO_3 (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. The screwcap was replaced with a rubber septum, and dioxane (10 mL) was added via a gastight 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 h. The resulting mixture was cooled down to room temperature, diluted in ethyl acetate, filtrated through a silica pad and concentrated under vacuum. The pure compound was obtained as a purple solid after purification by flash column chromatography (hexanes/ethyl acetate: 3/1 to 2/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.18 (d, *J* = 4.4 Hz, 4H), 8.92 (d, *J* = 4.4 Hz, 4H), 8.49 (br, 4H), 7.89 (t, *J* = 8.3 Hz, 2H), 7.52 (t, *J* = 8.6 Hz, 2H), 6.87 (t, *J* = 7.9 Hz, 8H), 6.82 (d, *J* = 8.5 Hz, 4H), 6.74 (t, *J* = 7.3 Hz, 4H), 6.58 (br, 4H), 6.52 (d, *J* = 7.9 Hz, 8H), 6.04 (br, 4H), 5.60 (br, 8H), 5.44 (br, 8H), 0.77 (s, 12H), 0.60 (br, 4H), 0.22 (br, 4H), 0.09 (br, 4H), -2.27(s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.77, 159.50, 155.55, 144.27, 139.06, 132.58, 130.48, 130.35, 129.21, 126.92, 125.71, 125.07, 123.63, 121.64, 121.44, 119.90, 117.38, 113.00, 110.70, 107.55, 30.13, 29.36, 19.10, 18.31. IR (neat, cm^{-1}): 3409.85, 3009.75, 1686.60, 1686.60, 1488.40, 1450.74, 1208.39, 1160.10, 978.20, 749.56, 692.35. HRMS (ESI) (M+H^{+}) Calcd. for $C_{112}H_{91}N_8O_8^{+}$: 1675.6954, found 1675.6960. UV–vis (CH_2Cl_2), λ_{max} nm (log ε): 422(5.46), 515(4.25), 591(3.75), 645(3.12).



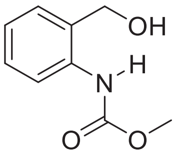
[Co(P6)] was synthesized according to our previous reported procedure[7a] with 92% yield. Free base porphyrin [H_2(**P6**)] and anhydrous $CoCl_2$ (8 equiv.) were placed in an oven-dried, resealable Schlenk tube. The tube was capped with a Teflon screwcap, evacuated, and backfilled with nitrogen. The screwcap was then replaced with a rubber septum, 2,6-lutidine (4 equiv.) and anhydrous THF were added via a gastight 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 h. The resulting mixture was cooled down to room temperature, diluted with ethyl acetate, and transferred to a separatory funnel. The reaction mixture was washed with water for 3 times and concentrated under vacuum. The target compound [Co(**P6**)] was isolated as a purple solid after purification by flash column chromatography with hexanes/ethyl acetate (2/1) as eluent. IR (neat, cm^{-1}): 3407.80, 1692.64, 1488.16, 1449.06, 1206.20, 1159.67, 998.09, 759.70, 690.98. HRMS (ESI) (M^{*+}) Calcd. for $C_{112}H_{88}CoN_8O_8^+$: 1731.6057, found 1731.6057. UV–vis (CH_2Cl_2), λ_{max} nm (log ε): 414(4.84), 534(3.67).



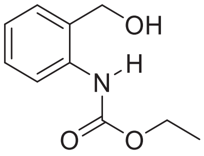
3.4.6 Synthetic Procedure for (2-(Hydroxymethyl)phenyl)carbamates s1



The compound **s1** was synthesized according to the previous reported procedure.[16] To a solution of 2-aminobenzyl alcohol (20 mmol) and pyridine (26 mmol) in DCM (80.0 mL) at 0 °C, methyl chloroformate (or ethyl chloroformate) (22 mmol) was added dropwise. The reaction was then stirred at 0 °C for 4 h. After that, the reaction was quenched by the addition of 0.1 M HCl and extracted with DCM (80 mL) for 3 times. The combined organic layers were then dried over anhydrous Na_2SO_4 and concentrated under vacuum. The mixture was then purified by flash column chromatography.

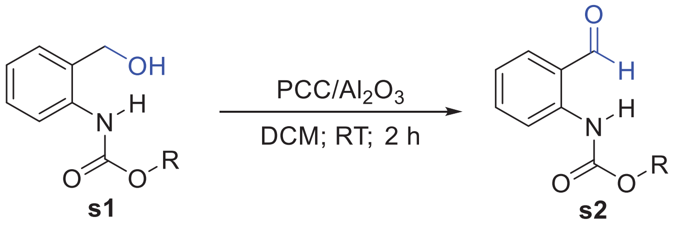


methyl (2-(hydroxymethyl)phenyl)carbamate s1-a White solid. Yield: 81%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.6 Hz, 1H), 7.90 (s, 1H), 7.34 (td, J = 8.0, 1.6 Hz, 1H), 7.17 (dd, J = 7.5, 1.6 Hz, 1H), 7.04 (td, J = 7.5, 1.1 Hz, 1H), 4.72 (d, J = 5.8 Hz, 2H), 3.78 (s, 3H), 1.96 (t, J = 5.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.57, 137.61, 129.17, 128.89, 128.78, 123.42, 120.98, 64.22, 52.29. IR (neat, cm^{-1}): 3288.39, 1697.47, 1528.92, 1455.34, 1294.08, 1247.81, 1024.00, 664.01. HRMS (ESI) (M+H$^+$) Calcd. for $C_9H_{12}NO_3^+$: 182.0812, found 182.0810.

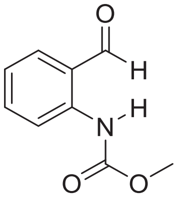


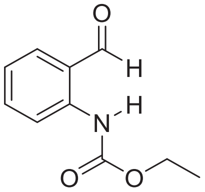
ethyl (2-(hydroxymethyl)phenyl)carbamate s1-b, known compound.[17] White solid. Yield: 77%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 – 7.86 (m, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.16 (d, *J* = 7.1 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 4.69 (d, *J* = 5.7 Hz, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.25 (t, *J* = 5.7 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.16, 137.74, 129.21, 128.83, 123.31, 120.98, 64.29, 61.21, 14.52.

3.4.7 Synthetic Procedure for (2-Formylphenyl)carbamates s2

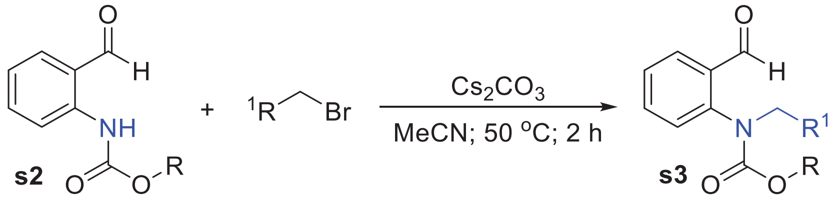


The compound **s2** was synthesized according to the previous reported procedure.[18] To a solution of carbamate **s1** (15 mmol) in 150 mL of DCM was added pyridinium chlorochromate (PCC, 30 mmol) and Al_2O_3 (use same amount as PCC in order to ease the separation of the desired product from the PCC residue). The reaction mixture was stirred at room temperature for 2 h and then filtered through a pad of silica. The filtrate was concentrated under reduced pressure and purified by flash column chromatography with hexanes/ethyl acetate (4/1) as eluent.

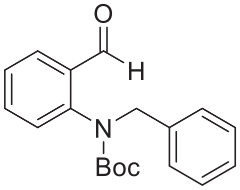

methyl (2-formylphenyl)carbamate s2-a White solid. Yield: 90%. ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.61 (s, 1H), 9.90 (s, 1H), 8.45 (d, *J* = 8.5 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 3.80 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 195.03, 154.09, 141.22, 135.99, 135.97, 121.92, 121.31, 118.24, 52.39. IR (neat, cm^{-1}): 3277.15, 3023.56, 2957.46, 2843.22, 2764.22, 1731.62, 1522.48, 1455.43, 1214.36, 1058.89, 1044.52, 769.03, 695.17. HRMS (ESI) (M+H^{+}) Calcd. for $C_9H_{10}NO_3^+$: 180.0661, found 180.0666.


ethyl (2-formylphenyl)carbamate s2-b White solid. Yield: 85%. ^{1}H NMR (600 MHz, CDCl$_3$) δ 10.56 (s, 1H), 9.91 (s, 1H), 8.46 (d, *J* = 8.5 Hz, 1H), 7.64 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.16 (td, *J* = 7.6, 0.9 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 195.03, 153.70, 141.37, 135.99, 121.80, 121.28, 118.27, 61.39, 14.46. IR (neat, cm^{-1}): 3278.69, 2985.48, 1729.45, 1654.96, 1585.28, 1522.65, 1451.42, 1242.86, 1191.63, 1058.03, 1042.13, 871.07, 764.43. HRMS (ESI) (M+H^{+}) Calcd. for $C_{10}H_{12}NO_3^+$: 194.0812, found 194.0809.

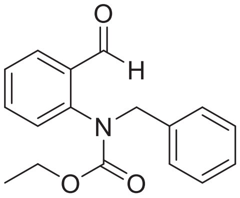
3.4.8 Synthetic Procedure for Benzyl(2-formylphenyl)carbamate Derivatives s3

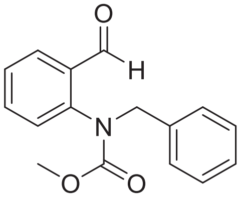


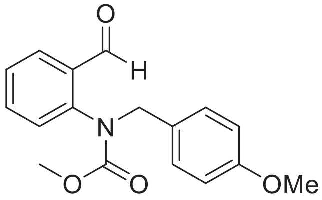
To a solution of **s2** (2 mmol) and Cs_2CO_3 (2.4 mmol) in MeCN (20 mL) was added alkyl bromide (2.4 mmol) at room temperature. The reaction was heated at 50 ºC for 2 h. The resulting mixture was cooled down to room temperature and filtered through a short pad of silica. The combined organic mixture was concentrated under vacuum and purified by flash column chromatography.



***tert*-butyl benzyl(2-formylphenyl)carbamate s3-a** Yield: 95%. Hexanes/ethyl acetate = 10/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.82 (d, *J* = 6.5 Hz, 1H), 7.57 – 7.54 (m, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.25 – 7.14 (m, 6H), 4.99 and 4.78 (br, 2H), 1.33 (br, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.80, 154.58, 144.27, 136.99, 134.59, 132.88, 128.73, 128.55, 128.37, 128.15, 127.76, 127.36, 81.36, 54.29, 28.12. IR (neat, cm^{-1}): 2978.49, 2873.61, 1682.42, 1595.02, 1484.35, 1445.89, 1367.81, 1152.81, 1016.51, 861.22, 740.86. HRMS (ESI) (M+H$^+$) Calcd. for $C_{19}H_{22}NO_3^+$: 312.1594, found 312.1596.

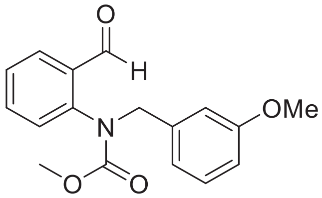

ethyl benzyl(2-formylphenyl)carbamate s3-b Yield: 94%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.72 (br, 1H), 7.84 (d, J = 7.2 Hz, 1H), 7.56 (td, J = 7.7, 1.6 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.26 – 7.25 (m, 3H), 7.18 – 7.13 (m, 3H), 4.96 and 4.82 (br, 2H), 4.18 and 4.07 (br, 2H), 1.09 (br, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.58, 155.64, 143.50, 136.48, 134.71, 132.87, 128.91, 128.59, 127.93, 127.77, 62.28, 54.92, 14.45. IR (neat, cm^{-1}): 2917.25, 2848.98, 1709.73, 1598.20, 1455.24, 1378.29, 1216.68, 1019.37, 701.86. HRMS (ESI) (M+H$^+$) Calcd. for $C_{17}H_{18}NO_3{}^+$: 284.1289, found 284.1287.


methyl benzyl(2-formylphenyl)carbamate s3-c Yield: 99%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.58 – 7.55 (m, 1H), 7.43 – 7.39 (m, 1H), 7.28 – 7.23 (m, 3H), 7.17 (d, J = 3.3 Hz, 2H), 7.12 (d, J = 7.8 Hz, 1H), 4.92 and 4.84 (br, 2H), 3.65 (br, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.55, 156.13, 143.26, 134.78, 132.85, 129.16, 129.00, 128.80, 128.62, 128.00, 127.95, 127.76, 55.12, 53.38. IR (neat, cm^{-1}): 3030.97, 2954.16, 2855.87, 1713.47, 1598.69, 1454.69, 1382.03, 1270.69, 734.74. HRMS (ESI) (M+H$^+$) Calcd. for $C_{16}H_{16}NO_3{}^+$: 270.1125, found 270.1126.



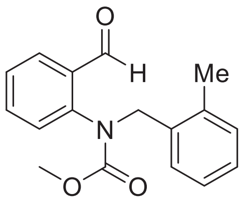
methyl (2-formylphenyl)(4-methoxybenzyl)carbamate s3-d

Yield: 98%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.71 (s, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.57 (td, *J* = 7.7, 1.5 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 3H), 6.77 (d, *J* = 8.5 Hz, 2H), 4.89 and 4.75 (br, 2H), 3.76 (s, 3H), 3.63 (s, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.57, 159.31, 156.07, 143.30, 134.75, 132.91, 130.34, 128.89, 128.60, 128.44, 127.89, 113.92, 55.18, 54.51, 53.29. IR (neat, cm^{-1}): 2955.10, 2837.50, 2758.23, 1711.53, 1611.89, 1598.52, 1514.07, 1459.69, 1251.04, 1034.18. HRMS (ESI) (M+H$^+$) Calcd. for $C_{17}H_{18}NO_4^+$: 300.1230, found 300.1232.

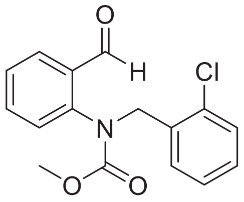


methyl (2-formylphenyl)(3-methoxybenzyl)carbamate s3-e

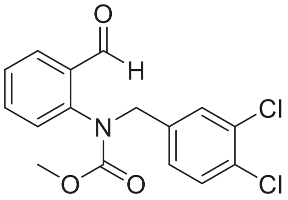
Yield: 99%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.76 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.59 – 7.54 (m, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 6.80 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.73 (s, 1H), 4.88 and 4.82 (br, 2H), 3.73 (s, 3H), 3.83 and 3.64 (br, 3H).^{13}C NMR (150 MHz, CDCl$_3$) δ 189.59, 159.70, 156.11, 143.25, 137.85, 134.75, 132.85, 129.63, 129.20, 128.72, 127.92, 121.20, 114.43, 113.50, 55.17, 55.02, 53.37. IR (neat, cm^{-1}): 3002.67, 2953.35, 2836.31, 1692.94, 1597.51, 1488.11, 1445.75, 1377.15, 1299.06, 1264.77, 1192.76, 1051.67, 769.19, 740.54. HRMS (ESI) (M+H$^+$) Calcd. for $C_{17}H_{18}NO_4^+$: 300.1230, found 300.1236.



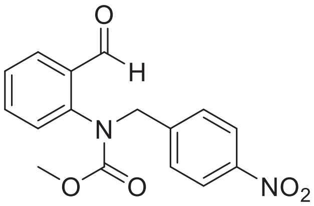
methyl (2-formylphenyl)(2-methylbenzyl)carbamate s3-f Yield: 99%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.74 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.55 – 7.53 (m, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.16 – 7.15 (m, 1H), 7.10 (t, *J* = 8.0 Hz, 2H), 7.05 (br, 2H), 4.98 and 4.90 (br, 2H), 3.66 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.42, 156.06, 143.11, 136.59, 134.70, 134.24, 133.06, 130.54, 130.12, 129.23, 128.89, 128.06, 127.98, 126.07, 53.39, 52.16, 19.02. IR (neat, cm^{-1}): 3022.23, 2953.91, 2860.00, 1711.08, 1598.43, 1486.9, 1457.43, 1377.82, 1304.30, 1272.43, 1194.06, 743.36. HRMS (ESI) (M+H$^+$) Calcd. for $C_{17}H_{18}NO_3^+$: 284.1281, found 284.1284.



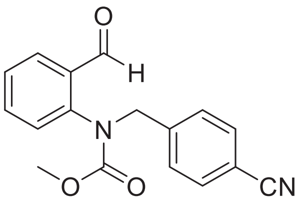
methyl (2-chlorobenzyl)(2-formylphenyl)carbamate s3-g Yield: 99%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.88 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.55 (td, *J* = 7.8, 1.4 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.29 – 7.27 (m, 1H), 7.21 – 7.18 (m, 2H), 7.16 (d, *J* = 7.8 Hz, 1H), 5.05 (br, 2H), 3.79 and 3.67 (s, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.61, 156.12, 143.00, 134.68, 134.04, 132.89, 131.34, 129.63, 129.31, 128.55, 127.96, 127.56, 127.02, 126.85, 53.47, 51.90. IR (neat, cm^{-1}): 3004.63, 2953.62, 2360.00, 1712.93, 1598.56, 1444.12, 1379.73, 1302.25, 1277.42, 765.24, 742.13. HRMS (ESI) (M+H$^+$) Calcd. for $C_{16}H_{15}ClNO_3^+$: 304.0735, found 304.0739.

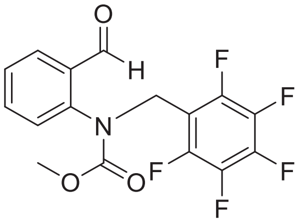


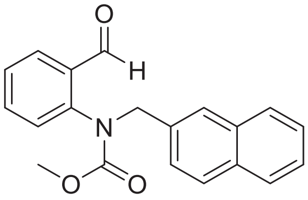
methyl (3,4-dichlorobenzyl)(2-formylphenyl)carbamate s3-h Yield: 98%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.87 (s, 1H), 7.88 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.59 (td, *J* = 7.7, 1.7 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.32 (s, 1H), 7.06 (t, *J* = 8.3 Hz, 2H), 4.91 and 4.70 (br, 2H), 3.66 (s, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.46, 156.08, 142.69, 142.52, 136.88, 134.87, 134.69, 132.63, 132.46, 132.08, 130.75, 130.57, 128.82, 128.24, 53.94, 53.51. IR (neat, cm^{-1}): 3002.67, 2953.42, 2860.35, 2746.50, 1712.18, 1598.16, 1447.29, 1374.56, 1297.34, 1216.67, 1032.47, 738.51. HRMS (ESI) (M+H$^+$) Calcd. for $C_{16}H_{14}Cl_2NO_3^+$: 338.0345, found 338.0347.

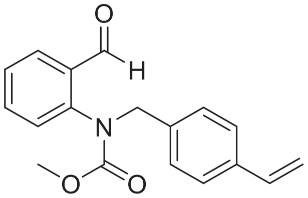


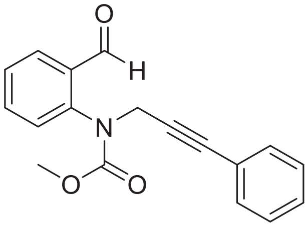
methyl (2-formylphenyl)(4-nitrobenzyl)carbamate s3-i Yield: 80%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.87 (s, 1H), 8.14 (d, *J* = 8.2 Hz, 2H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 5.9 Hz, 1H), 5.05 and 4.83 (br, 2H), 3.66 (s, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.44, 156.12, 147.57, 143.97, 142.31, 134.91, 132.37, 131.10, 129.60, 128.72, 128.33, 123.83, 54.33, 53.58. IR (neat, cm^{-1}): 3077.25, 2955.54, 2857.16, 2756.27, 1691.77, 1597.46, 1518.47, 1445.74, 1344.17, 1307.21, 1267.61, 1192.18, 732.85. HRMS (ESI) (M+H$^+$) Calcd. for $C_{16}H_{15}N_2O_5^+$: 315.0975, found 315.0977.


methyl (4-cyanobenzyl)(2-formylphenyl)carbamate s3-j Yield: 98%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.85 (s, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.56 (m, 3H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.4 Hz, 1H), 4.99 and 4.80 (br, 2H), 3.65 (br, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 189.40, 156.10, 142.41, 141.95, 134.88, 134.72, 132.39, 130.85, 129.44, 128.68, 128.27, 118.45, 111.86, 54.62, 53.53. IR (neat, cm^{-1}): 2954.98, 2851.81, 2751.36, 2228.37, 1708.46, 1598.31, 1456.80, 1379.91, 1316.36, 1269.35, 1193.78, 778.53, 735.44, HRMS (ESI) (M+H$^+$) Calcd. for $C_{17}H_{15}N_2O_3^+$: 295.1077, found 295.1079.

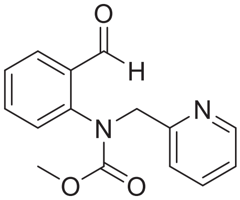

methyl (2-formylphenyl)((perfluorophenyl)methyl)carbamate s3-k Yield: 97%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.94 (s, 1H), 7.87 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.61 (td, *J* = 7.7, 1.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 5.02 (br, 2H), 3.64 (br, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.48, 155.50, 145.45 (md, *J* = 250.0 Hz), 141.50, 141.12 (md, *J* = 255.3 Hz), 137.31 (md, *J* = 252.6 Hz), 134.82, 132.69, 131.10, 129.04, 128.53, 109.95, 53.58, 41.88. IR (neat, cm^{-1}): 2957.90, 2838.25, 2751.54, 1706.21, 1526.90, 1503.64, 1456.77, 1439.58, 1383.57, 1278.56, 966.81, 945.34, 760.50. HRMS (ESI) (M+H$^+$) Calcd. for $C_{16}H_{11}F_5NO_3^+$: 360.0654, found 360.0657.


methyl (2-formylphenyl)(naphthalen-2-ylmethyl)carbamate s3-l Yield: 99%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.83 (s, 1H), 7.84 – 7.70 (m, 3H), 7.73 – 7.72 (m, 1H), 7.57 (s, 1H), 7.53 (td, *J* = 7.7, 1.5 Hz, 1H), 7.47 – 7.44 (m, 2H), 7.41-7.38 (m, 2H), 7.11 (br, 1H), 5.08 and 5.02 (br, 2H), 3.67 (br, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.58, 156.26, 143.16, 134.73, 133.93, 133.15, 132.87, 132.72, 129.46, 129.42, 128.81, 128.52, 127.94, 127.81, 127.67, 126.63, 126.22, 126.11, 55.20, 53.42. IR (neat, cm^{-1}): 3015.95, 2952.55, 2856.83, 2752.36, 1708.72, 1597.93, 1446.53, 1365.74, 755.23. HRMS (ESI) (M+H$^+$) Calcd. for $C_{20}H_{18}NO_3^+$: 320.1281, found 320.1282.

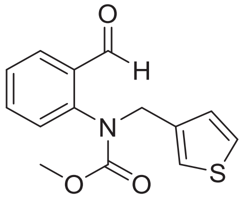

methyl (2-formylphenyl)(4-vinylbenzyl)carbamate s3-m Yield: 80%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.78 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.56 (td, *J* = 7.6, 1.6 Hz, 1H), 7.40 – 7.43 (m, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.17 – 7.07 (m, 3H), 6.66 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.71 (d, *J* = 17.6 Hz, 1H), 5.23 (d, *J* = 10.9 Hz, 1H), 4.86 (s, 2H), 3.65 (br, 3H).^{13}C NMR (150 MHz, CDCl$_3$) δ 189.56, 156.13, 137.26, 136.26, 135.90, 134.75, 132.78, 129.33, 129.14, 128.79, 127.93, 126.42, 114.17, 54.80, 53.36. IR (neat, cm^{-1}): 2953.28, 2855.09, 2754.32, 1707.44, 1597.93, 1446.39, 1379.05, 1269.78, 1193.14, 990.30, 910.56, 779.90. HRMS (ESI) (M+H$^+$) Calcd. for $C_{18}H_{18}NO_3^+$: 296.1281, found 296.1282.



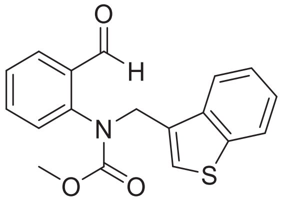
methyl (2-formylphenyl)(3-phenylprop-2-yn-1-yl)carbamate s3-n Yield: 95%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.21 (s, 1H), 7.97 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.70 – 7.66 (m, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.31 – 7.27 (m, 5H), 4.85 and 4.67 (br, 2H), 3.67 (br, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.77, 155.48, 142.56, 134.87, 133.24, 131.45, 129.18, 128.84, 128.44, 128.38, 128.19, 122.12, 85.46, 83.36, 53.51, 41.33. IR (neat, cm^{-1}): 2955.69, 2861.87, 1698.24, 1597.94, 1489.13, 1375.69, 1443.87, 1271.73, 758.84. HRMS (ESI) (M+H^{+}) Calcd. for $C_{18}H_{16}NO_3^{+}$: 294.1125, found 294.1126.



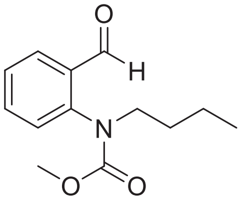
methyl (2-formylphenyl)(pyridin-2-ylmethyl)carbamate s3-o Yield: 50%. Hexanes/ethyl acetate = 1/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 10.03 (s, 1H), 8.49 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.63 (td, *J* = 7.7, 1.7 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.17 – 7.15 (m, 1H), 5.03 and 5.00 (br, 2H), 3.65 (br, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 190.08, 156.50, 156.12, 149.36, 143.70, 136.64, 134.73, 132.67, 129.34, 128.23, 127.77, 122.95, 122.57, 56.45, 53.40. IR (neat, cm^{-1}): 2955.07, 2854.05, 2359.77, 2343.66, 1711.48, 1598.24, 1486.57, 1459.02, 1310.65, 1271.14, 1193.08, 779.37. HRMS (ESI) (M+H^{+}) Calcd. for $C_{15}H_{15}N_2O_3^{+}$: 271.1077, found 271.1081.



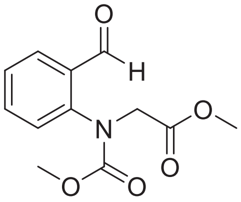
methyl (2-formylphenyl)(thiophen-3-ylmethyl)carbamate s3-p Yield: 99%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.69 (s, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.59 (td, *J* = 7.7, 1.4 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.24 (m, 1H), 7.13 (d, *J* = 7.7 Hz, 1H), 7.00 (d, *J* = 1.5 Hz, 1H), 6.97 (d, *J* = 2.2 Hz, 1H), 4.94 and 4.79 (br, 2H), 3.63 (br, 3H).^{13}C NMR (150 MHz, CDCl$_3$) δ 189.41, 155.90, 143.20, 136.85, 134.81, 132.96, 129.05, 128.82, 128.02, 126.42, 124.39, 53.32, 49.64. IR (neat, cm^{-1}): 2953.44, 2852.10, 2360.47, 2339.74, 1713.03, 1598.52, 1458.39, 1374.07, 1270.54, 1193.41, 738.61. HRMS (ESI) (M+H$^+$) Calcd. for $C_{14}H_{14}NO_3S^+$: 276.0689, found 276.0691.



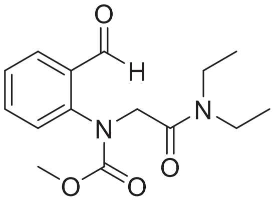
methyl (benzo[*b*]thiophen-3-ylmethyl)(2-formylphenyl)-carbamate s3-q Yield: 80%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.63 (s, 1H), 7.83 – 7.80 (m, 3H), 7.53 (td, *J* = 7.5, 1.3 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.37 – 7.33 (m, 2H), 7.05 (s, 2H), 5.19 and 5.11 (br, 2H), 3.67 (s, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.30, 156.02, 142.75, 140.34, 137.86, 134.70, 133.09, 131.19, 129.39, 129.01, 128.12, 126.74, 124.62, 124.45, 122.87, 122.04, 53.48, 48.07. IR (neat, cm^{-1}): 2952.77, 2852.10, 1692.59, 1597.84, 1446.29, 1268.88, 1193.07, 768.87, 734.65. HRMS (ESI) (M+Na$^+$) Calcd. for $C_{18}H_{15}NNaO_3S^+$: 348.0665, found 348.0666.



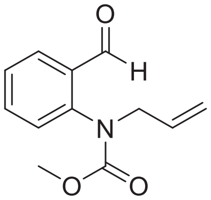
methyl butyl(2-formylphenyl)carbamate s3-r Yield: 50%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.10 (s, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.25 (s, 1H), 3.70 and 3.61 (br, 5H), 1.55 – 1.52 (m, 2H), 1.34 – 1.27 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.82, 155.81, 143.92, 134.83, 132.79, 129.22, 128.63, 127.72, 53.12, 51.21, 30.13, 19.98, 13.70. IR (neat, cm^{-1}): 2958.28, 2934.23, 2863.57, 1715.49, 1599.16, 1459.51, 1388.38, 1305.41, 1193.94, 772.69, 739.25. HRMS (ESI) (M+H$^+$) Calcd. for $C_{13}H_{18}NO_3^+$: 236.1281, found 236.1283.



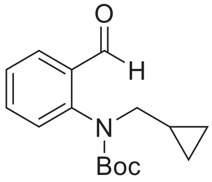
methyl *N*-(2-formylphenyl)-*N*-(methoxycarbonyl)glycinate s3-s Yield: 63%. Hexanes/ethyl acetate = 2/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.27 (s, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.62 (t, J = 7.7, 1H), 7.47 – 7.43 (m, 2H), 4.53 (d, J = 17.6 Hz, 1H), 4.32 (d, J = 17.6 Hz, 1H), 3.75 (s, 3H), 3.81 and 3.67 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.20, 169.60, 155.86, 143.16, 134.86, 132.55, 130.12, 129.51, 128.18, 53.65, 52.32, 52.22. IR (neat, cm^{-1}): 2955.86, 2854.05, 1749.40, 1714.17, 1694.29, 1599.00, 1486.45, 1447.36, 1375.33, 1271.26, 1214.81, 776.76. HRMS (ESI) (M+H$^+$) Calcd. for $C_{12}H_{14}NO_5^+$: 252.0866, found 252.0868.



methyl (2-(diethylamino)-2-oxoethyl)(2-formylphenyl)-carbamate s3-t Yield: 78%. Hexanes/ethyl acetate = 2/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.30 (s, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.60 – 7.59 (m, 2H), 7.42 – 7.39 (m, 1H), 4.67 (d, *J* = 16.2 Hz, 1H), 4.21 (d, *J* = 16.2 Hz, 1H), 3.63 (s, 3H), 3.43 – 3.33 (br, m, 2H), 3.32 – 3.24 (br, m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 190.61, 166.65, 155.98, 143.86, 134.67, 132.48, 129.23, 128.56, 127.70, 53.39, 52.20, 41.18, 40.63, 14.14, 12.97. IR (neat, cm^{-1}): 2975.98, 2934.23, 1712.52, 1693.54, 1654.68, 1485.49, 1459.82, 1379.82, 1265.69, 1195.86, 760.72. HRMS (ESI) (M+H$^+$) Calcd. for $C_{15}H_{21}N_2O_4^+$: 293.1496, found 293.1498.

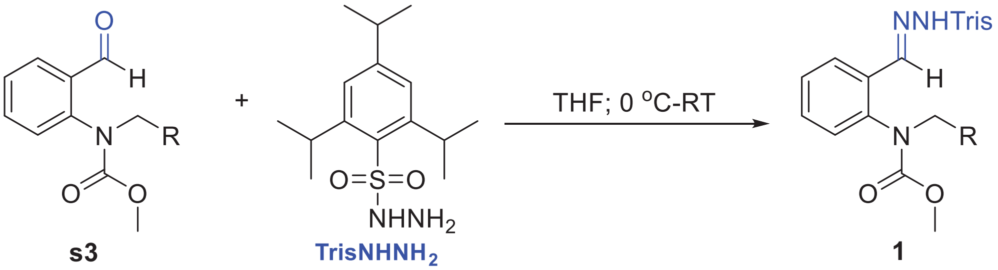


methyl allyl(2-formylphenyl)carbamate s3-u Yield: 99%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 10.06 (s, 1H), 7.88 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.60 (t, *J* = 7.7, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.26 – 7.24 (m, 1H), 5.89 (ddt, *J* = 16.8, 10.2, 6.6 Hz, 1H), 5.12 – 5.07 (m, 2H), 4.28 (br, 2H), 3.61 (br, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 189.84, 155.72, 143.38, 134.78, 132.67, 132.49, 129.44, 128.67, 127.86, 119.14, 54.01, 53.26. IR (neat, cm^{-1}): 2969.80, 1721.22, 1599.12, 1456.18, 1375.60, 1229.57. HRMS (ESI) (M+H$^+$) Calcd. for $C_{12}H_{14}NO_3^+$: 220.0968, found 220.0974.

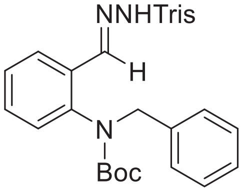


***tert*-butyl (cyclopropylmethyl)(2-formylphenyl)carbamate s3-v** Yield: 45%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.22 (s, 1H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.62 – 7.60 (m, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.26 (br, 1H), 3.81 (s, 1H), 3.38 (s, 1H), 1.59 – 1.31 (m, 9H), 0.97 (br, 1H), 0.43 (br, 2H), 0.15 (s, 1H), 0.03 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) major rotamer: δ 190.46, 154.43, 145.09, 134.70, 133.27, 129.82, 128.31, 127.31, 80.94, 54.87, 29.70, 28.15, 9.96, 3.73. IR (neat, cm^{-1}): 2979.07, 2929.87, 2855.13, 2760.04, 1684.56, 1596.35, 1429.78, 1369.43, 1291.66, 1149.82, 1129.13, 974.20, 760.89. HRMS (ESI) (M+Na$^+$) Calcd. for $C_{16}H_{21}NNaO_3^+$: 298.1414, found 298.1413.

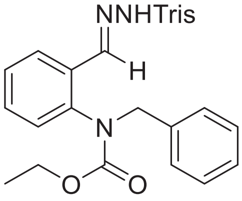
3.4.9 Synthetic Procedure for Triisopropyl Sulfonylhydrazone Derivatives 1



To a stirred solution of pure 2,4,6-triisopropylbenzenesulfonohydrazide ($TPSNHNH_2$, 2 mmol) in THF (10.0 mL) at 0 °C, aldehyde **s3** (1 equiv.) was added dropwise (or portionwise if solid). The reaction was monitored by TLC. After the reaction was completed, the solvent was removed directly under reduced pressure, and the crude solid was further purified by flash column chromatography.

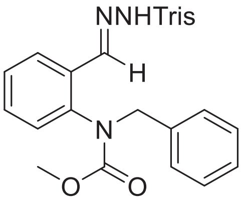


***tert*-butyl benzyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)-hydrazono)methyl)phenyl)carbamate 1-a** Yield: 70%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.98 (s, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.47 (s, 1H), 7.33 (br, 1H), 7.24 – 7.14 (m, 8H), 6.89 (s, 1H), 4.76 (d, *J* = 14.7 Hz, 1H), 4.57 (d, *J* = 14.7 Hz, 1H), 4.26 (hept, *J* = 6.7 Hz, 2H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.33 – 1.25 (m, 27H).^{13}C NMR (125 MHz, CDCl$_3$) δ 154.82, 153.38, 151.36, 142.47, 141.10, 137.24, 131.38, 131.01, 130.54, 128.84, 128.48, 127.75, 127.49, 127.27, 126.38, 123.82, 80.86, 54.10, 34.17, 30.01, 28.20, 24.89, 23.53. IR (neat, cm^{-1}): 3178.54, 2963.62, 1669.48, 1600.75, 1399.42, 1315.89, 1157.20, 1071.86, 855.44, 757.16, 731.40. HRMS (ESI) (M+H$^+$) Calcd. for $C_{34}H_{46}N_3O_4S^+$: 592.3249, found 592.3274.

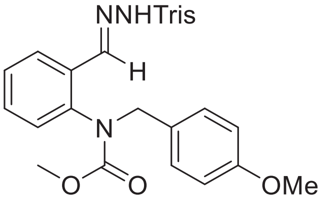


ethyl benzyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono) methyl) phenyl)carbamate 1-b Yield: 86%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.10 (s, 1H), 7.82 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.45 (s, 1H), 7.29 – 7.20 (m, 5H), 7.17 – 7.14 (m, 4H), 6.91 (s, 1H), 4.79 and 4.76 (br, 1H), 4.63 and 4.61 (br, 1H), 4.25 (hept, *J* = 6.7 Hz, 2H), 4.03 (br, 2H), 2.89 (hept, *J* = 6.9 Hz, 1H), 1.30 – 1.27 (m, 12H), 1.25 (d, *J* = 6.9 Hz, 6H), 0.99 (br, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 155.87, 153.38, 151.34, 141.87, 140.22, 136.72, 131.42, 131.14, 130.62, 129.05, 128.53, 127.94, 127.66, 126.52, 123.99, 123.81, 62.12, 54.74, 34.17, 30.00, 24.88, 23.52, 14.46. IR (neat, cm^{-1}):

2960.77, 2869.70, 1673.95, 1600.11, 1455.15, 1319.36, 1297.65, 1166.56, 1037.84, 942.18, 743.78, 657.99. HRMS (ESI) (M+H$^+$) Calcd. for $C_{32}H_{42}N_3O_4S^+$: 564.2891, found 564.2876.

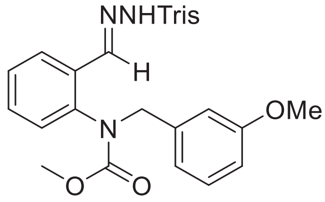


methyl benzyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)-hydrazono)methyl)phenyl) carbamate 1-c Yield: 90%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.13 (s, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.46 (s, 1H), 7.28 (td, *J* = 7.6, 1.4 Hz, 1H), 7.25 – 7.22 (m, 4H), 7.18 (s, 2H), 7.15 (br, 2H), 6.91 (d, *J* = 6.5 Hz, 1H), 4.75 (d, *J* = 14.5 Hz, 1H), 4.65 (d, *J* = 14.5 Hz, 1H), 4.24 (hept, *J* = 6.7 Hz, 2H), 3.54 (s, 3H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.30 – 1.28 (m, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 156.31, 153.41, 151.33, 141.80, 140.04, 136.54, 131.36, 131.18, 130.71, 129.12, 128.67, 128.56, 128.03, 127.83, 126.58, 123.82, 54.93, 53.26, 34.17, 30.00, 24.87, 23.52. IR (neat, cm^{-1}): 3213.94, 2958.2, 2869.64, 1696.82, 1601.14, 1321.40, 1166.54, 1152.04. HRMS (ESI) (M+H$^+$) Calcd. for $C_{31}H_{40}N_3O_4S^+$: 550.2734, found 550.2740.

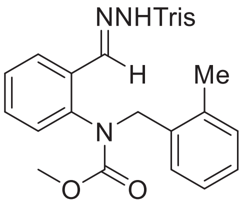


methyl (4-methoxybenzyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-d Yield: 87%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.24 (s, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.51 (s, 1H), 7.31 – 7.27 (m, 1H), 7.24 – 7.20 (m, 1H), 7.18 (s, 2H), 7.07 (d, *J* = 7.5 Hz, 2H), 6.90 – 6.86

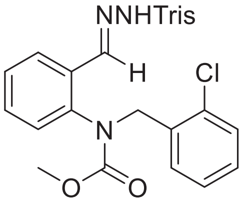
(m, 1H), 6.78 (d, *J* = 8.5 Hz, 2H), 4.75 (d, *J* = 14.3 Hz, 1H), 4.51 (d, *J* = 14.3 Hz, 1H), 4.25 (hept, *J* = 6.7 Hz, 2H), 3.77 (s, 3H), 3.52 (s, 3H), 2.89 (hept, *J* = 6.9 Hz, 1H), 1.29 (d, *J* = 6.7 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 159.30, 156.29, 153.38, 151.33, 141.79, 140.01, 131.38, 131.15, 130.61, 130.44, 128.82, 128.64, 127.77, 126.52, 123.80, 113.87, 55.19, 54.29, 53.20, 34.16, 29.99, 24.85, 23.52. IR (neat, cm^{-1}): 3161.77, 2957.90, 2868.98, 2359.85, 2342.17, 1704.86, 1681.69, 1456.72. HRMS (ESI) (M+H$^+$) Calcd. for $C_{32}H_{42}N_3O_5S^+$: 580.2840, found 580.2839.



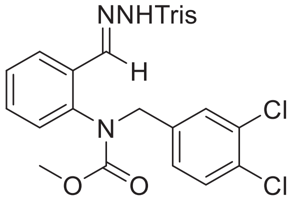
methyl (3-methoxybenzyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl) hydrazono)methyl)phenyl)carbamate 1-e Yield: 94%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.18 (s, 1H), 7.82 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.50 (s, 1H), 7.27 (ddd, *J* = 5.8, 4.9, 1.6 Hz, 1H), 7.23 (td, *J* = 7.6, 0.9 Hz, 1H), 7.18 – 7.15 (m, 3H), 6.91 (br, 1H), 6.79 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.73 (d, *J* = 7.0 Hz, 1H), 6.69 (s, 1H), 4.76 (d, *J* = 14.5 Hz, 1H), 4.56 (d, *J* = 14.5 Hz, 1H), 4.24 (hept, *J* = 6.7 Hz, 2H), 3.72 (s, 3H), 3.53 (s, 3H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.28 (d, *J* = 6.7 Hz, 12H), 1.24 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (125MHz, CDCl$_3$) δ 159.62, 156.32, 153.40, 151.33, 141.80, 140.03, 138.04, 131.40, 131.17, 130.67, 129.58, 128.68, 127.84, 126.56, 123.81, 121.30, 114.79, 113.31, 55.19, 54.85, 53.27, 34.17, 30.00, 24.86, 23.52. IR (neat, cm^{-1}): 3182.56, 2958.18, 2932.27, 2869.32, 2359.69, 2343.66, 1706.33, 1679.61, 1454.13, 1263.22, 1153.49, 735.74. HRMS (ESI) (M+H$^+$) Calcd. for $C_{32}H_{42}N_3O_5S^+$: 580.2840, found 580.2839.



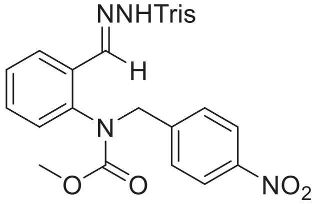
methyl (2-methylbenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-f Yield: 94%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.06 (br, 1H), 7.80 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.47 (s, 1H), 7.23 (td, *J* = 7.6, 1.5 Hz, 2H), 7.18 (s, 2H), 7.10 (t, *J* = 7.3 Hz, 2H), 7.04 (t, *J* = 7.6 Hz, 2H), 6.87 (br, 1H), 4.87 (d, *J* = 14.4 Hz, 1H), 4.69 (d, *J* = 14.4 Hz, 1H), 4.24 (hept, *J* = 6.7 Hz, 2H), 3.56 (br, 3H), 2.90 (hept, *J* = 6.9 Hz, 1H), 2.01 (s, 3H), 1.28 (br, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 158.95, 156.05, 153.99, 144.33, 142.49, 139.24, 137.15, 134.05, 133.29, 133.11, 132.80, 131.38, 130.74, 130.50, 129.21, 128.72, 126.66, 126.48, 55.95, 54.43, 36.83, 32.66, 27.53, 26.19, 21.59. IR (neat, cm^{-1}): 3184.54, 2957.29, 2868.69, 2360.21, 2342.60, 1706.76, 1676.98, 1456.36, 1152.06, 746.98, 658.54. HRMS (ESI) (M+H$^+$) Calcd. for $C_{32}H_{42}N_3O_4S^+$: 564.2891, found 564.2895.



methyl (2-chlorobenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-g Yield: 85%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.96 (s, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.60 (s, 1H), 7.28 – 7.25 (m, 1H), 7.21 (t, *J* = 6.9 Hz, 3H), 7.17 (s, 2H), 7.13 – 7.10 (m, 2H), 6.98 (br, 1H), 4.90 and 4.88 (br, 2H), 4.23 (hept, *J* = 6.6 Hz, 2H), 3.57 (s, 3H), 2.90 (hept, *J* = 6.7 Hz, 1H), 1.29 (br, 12H), 1.24 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 156.27, 153.36, 151.31, 141.58, 139.60, 133.99, 133.80, 131.44, 131.40, 131.24, 130.55, 129.54, 129.36, 128.31, 127.84, 126.88, 126.53, 123.82, 53.41, 51.72, 34.17, 30.00, 24.86, 23.52. IR (neat, cm^{-1}): 3162.51, 2958.56, 2929.17, 2868.95, 2360.16, 2342.85, 1684.03, 1599.56, 1456.61, 1383.67, 1166.61, 739.94. HRMS (ESI) ($M+H^+$) Calcd. for $C_{31}H_{39}ClN_3O_4S^+$: 584.2344, found 584.2347.

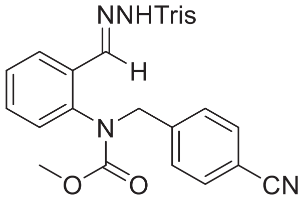


methyl (3,4-dichlorobenzyl)(2-((2-((2,4,6-triisopropylphenyl)-sulfonyl)hydrazono)methyl)phenyl)carbamate 1-h Yield: 85%. Hexanes/ethyl acetate = 4/1. ^1H NMR (600 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.83 (d, *J* = 7.0 Hz, 1H), 7.62 (s, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.30 – 7.27 (m, 3H), 7.19 (s, 2H), 6.98 (d, *J* = 7.0 Hz, 1H), 6.82 (br, 1H), 4.92 (d, *J* = 14.3 Hz, 1H), 4.38 – 4.22 (m, 3H), 3.56 (br, 3H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.29 (d, *J* = 6.5 Hz, 12H), 1.24 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (125MHz, $CDCl_3$) δ 156.38, 153.53, 151.35, 141.26, 139.61, 136.89, 132.58, 132.10, 131.28, 130.83, 130.69, 130.53, 128.72, 128.21, 128.12, 127.11, 123.87, 53.69, 53.45, 34.18, 30.03, 24.85, 23.51. IR (neat, cm^{-1}): 3182.21, 2959.02, 2869.36, 1708.61, 1680.94, 1455.62, 1374.93, 1151.17, 1033.78. HRMS (ESI) ($M+H^+$) Calcd. for $C_{31}H_{38}Cl_2N_3O_4S^+$: 618.1955, found 618.1960.

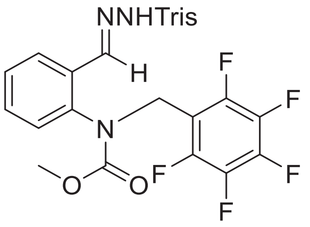


methyl (4-nitrobenzyl)(2-((2-((2,4,6-triisopropylphenyl)-sulfonyl)hydrazono)methyl)phenyl)carbamate 1-i Yield: 50%. Hexanes/ethyl acetate = 4/1. ^1H NMR (600 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.12 (d, *J* = 8.5 Hz, 2H), 7.83 (br, 1H), 7.72 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.27 – 7.25 (m, 2H), 7.19 (s, 2H), 6.80 (s, 1H), 5.10

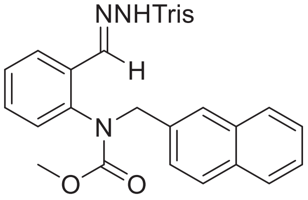
(d, *J* = 14.4 Hz, 1H), 4.39 (d, *J* = 14.4 Hz, 1H), 4.25 (hept, *J* = 6.7 Hz, 2H), 3.58 (br, 3H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.29 (d, *J* = 6.7 Hz, 12H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.38, 153.63, 151.34, 147.57, 143.91, 141.15, 139.57, 131.17, 130.77, 130.75, 129.68, 128.59, 128.21, 127.23, 123.89, 123.80, 54.07, 53.53, 34.18, 30.02, 24.83, 23.51. IR (neat, cm^{-1}): 3218.81, 2960.23, 2359.80, 1670.43, 1519.94, 1346.84, 738.21. HRMS (ESI) (M+H$^+$) Calcd. for $C_{31}H_{39}N_4O_6S^+$: 595.2585, found 595.2587.



methyl (4-cyanobenzyl)(2-((2-((2,4,6-triisopropylphenyl)-sulfonyl)hydrazono)methyl)phenyl)carbamate 1-j Yield: 80%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, CDCl3) 8.44 (br, 1H), 7.82 (br, 1H), 7.71 (s, 1H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.29 – 7.24 (m, 4H), 7.19 (s, 2H), 6.79 (br, 1H), 5.05 (d, *J* = 14.6 Hz, 1H), 4.35 (d, *J* = 14.6 Hz, 1H), 4.26 (hept, *J* = 6.7 Hz, 2H), 3.57 (br, 3H), 2.91 (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 (150 MHz, $CDCl_3$) δ 156.42, 153.60, 151.34, 141.92, 141.17, 139.60, 132.37, 131.23, 130.81, 130.68, 129.51, 128.56, 128.15, 127.17, 123.88, 118.44, 111.87, 54.37, 53.50, 34.17, 30.02, 24.85, 23.51. IR (neat, cm^{-1}): 3190.41, 2959.79, 2870.26, 2360.11, 2343.40, 1706.75, 1684.15, 1265.40, 742.06. HRMS (ESI) (M+H$^+$) Calcd. for $C_{32}H_{39}N_4O_4S^+$: 575.2687, found 575.2691.

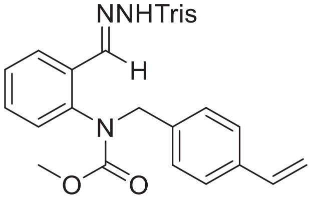


methyl ((perfluorophenyl)methyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-k Yield: 92%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.28 (s, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.71 (s, 1H), 7.31 (td, *J* = 7.6, 1.4 Hz, 1H), 7.27 – 7.25 (m, 1H), 7.18 (s, 2H), 6.98 (d, *J* = 7.8 Hz, 1H), 4.96 (d, *J* = 14.3 Hz, 1H), 4.84 (d, *J* = 14.3 Hz, 1H), 4.24 (hept, *J* = 6.7 Hz, 2H), 3.58 (br, 3H), 2.90 (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 (150 MHz, CDCl$_3$) δ 155.78, 153.51, 151.36, 145.39 (md, *J* = 253.0 Hz), 141.12 (md, *J* = 251.6 Hz), 140.78, 138.56, 137.31 (md, *J* = 253.7 Hz), 131.32, 131.22, 130.73, 128.35, 128.04, 127.05, 123.85, 109.61, 53.61, 41.62, 34.18, 30.02, 24.80, 23.50. IR (neat, cm^{-1}): 3170.74, 2959.60, 2869.98, 1714.25, 1687.55, 1504.90, 1036.45, 738.86. HRMS (ESI) (M+H$^+$) Calcd. for $C_{31}H_{35}F_5N_3O_4S^+$: 640.2263, found 640.2264.

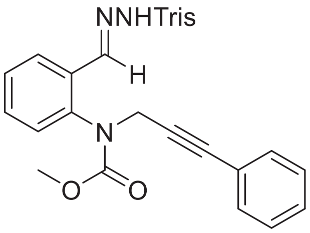


methyl (naphthalen-2-ylmethyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-l Yield: 96%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.04 (br, 1H), 7.83 – 7.82 (m, 1H), 7.80 – 7.79 (m, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.73 – 7.71 (m, 1H), 7.61 (s, 1H), 7.55 (s, 1H), 7.45 (p, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.24 – 7.20 (m, 2H), 7.17 (s, 2H), 6.84 (br, 1H), 5.09 (d, *J* = 14.6 Hz, 1H), 4.59 (d, *J* = 14.6 Hz, 1H), 4.23 (hept, *J* = 6.6 Hz, 2H), 3.55 (br, 3H), 2.89 (hept, *J* = 6.9 Hz, 1H), 1.27 (d, *J* = 6.6 Hz, 12H), 1.24 (d, *J* = 6.9 Hz, 6H).^{13}C

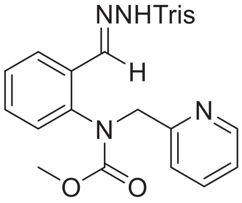
NMR (150 MHz, $CDCl_3$) δ 156.53, 153.38, 151.32, 141.58, 139.98, 134.01, 133.12, 132.83, 131.40, 131.00, 130.56, 128.77, 128.40, 128.03, 127.84, 127.66, 126.66, 126.25, 126.14, 123.81, 54.99, 53.34, 34.16, 29.99, 24.84, 23.52. IR (neat, cm^{-1}): 3169.11, 2956.97, 2867.76, 2359.96, 1679.88, 1600.27, 1152.06, 751.50. HRMS (ESI) ($M+H^+$) Calcd. for $C_{35}H_{42}N_3O_4S^+$: 600.2891, found 600.2891.



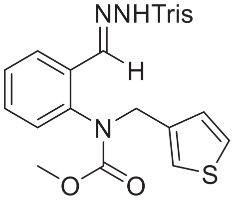
methyl (2-((2-((2,4,6-triisopropylphenyl)sulfonyl)-hydrazono)methyl)phenyl)(4-vinylbenzyl)carbamate 1-m Yield: 85%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.82 (dd, J = 7.7, 1.7 Hz, 1H), 7.50 (s, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.27 – 7.22 (m, 2H), 7.17 (s, 2H), 7.11 (d, J = 7.7 Hz, 2H), 6.88 (d, J = 7.5 Hz, 1H), 6.67 (dd, J = 17.6, 10.9 Hz, 1H), 5.72 (d, J = 17.6 Hz, 1H), 5.25 (d, J = 10.9 Hz, 1H), 4.82 (d, J = 14.5 Hz, 1H), 4.51 (d, J = 14.5 Hz, 1H), 4.23 (hept, J = 6.7 Hz, 2H), 3.53 (br, 3H), 2.89 (hept, J = 6.9 Hz, 1H), 1.28 (d, J = 6.7 Hz, 12H), 1.24 (d, J = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.37, 153.40, 151.79, 151.33, 141.65, 139.99, 137.26, 136.20, 131.37, 131.03, 130.60, 129.23, 128.73, 126.66, 126.37, 123.99, 123.81, 114.27, 54.58, 53.28, 34.16, 29.99, 24.85, 23.52. IR (neat, cm^{-1}): 3182.58, 2959.56, 2869.56, 1682.03, 1456.25, 1384.34, 1265.36, 742.69. HRMS (ESI) ($M+H^+$) Calcd. for $C_{33}H_{42}N_3O_4S^+$: 576.2891, found 576.2895.



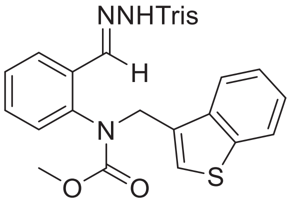
methyl (3-phenylprop-2-yn-1-yl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-n Yield: 76%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.50 (s, 1H), 7.99 (s, 1H), 7.94 (d, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.33 – 7.28 (m, 5H), 7.23 (d, *J* = 6.5 Hz, 2H), 7.18 (s, 2H), 4.60 (s, 2H), 4.27 (hept, *J* = 6.7 Hz, 2H), 3.56 (s, 3H), 2.91 (hept, *J* = 6.9 Hz, 1H), 1.29 (d, *J* = 6.7 Hz, 12H), 1.26 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 155.83, 153.36, 151.34, 141.74, 139.40, 131.70, 131.51, 130.78, 128.48, 128.39, 128.32, 128.27, 126.54, 123.83, 122.16, 85.33, 83.48, 53.52, 41.22, 34.18, 30.02, 24.82, 23.53. IR (neat, cm^{-1}): 3188.68, 2960.16, 2868.25, 1682.88, 1600.66, 1454.10, 1280.56, 1167.12, 755.85. HRMS (ESI) (M+H$^+$) Calcd. for $C_{33}H_{40}N_3O_4S^+$: 574.2734, found 574.2732.



methyl (pyridin-2-ylmethyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-o Yield: 76%. Hexanes/ethyl acetate = 2/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.48 (s, 1H), 8.33 (s, 1H), 7.89 (s, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.57 (td, *J* = 7.7, 1.4 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.17 (s, 2H), 7.13 – 7.08 (m, 2H), 4.86 (br, 2H), 4.27 (hept, *J* = 6.7 Hz, 2H), 3.55 (s, 3H), 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 (150 MHz, CDCl$_3$) δ 156.30, 153.31, 151.31, 149.35, 142.27, 140.43, 136.62, 131.53, 131.26, 130.63, 128.09, 127.73, 126.56, 123.80, 123.68, 122.98, 122.65, 56.27, 53.34, 34.17, 30.00, 24.88, 23.53. IR (neat, cm^{-1}): 3208.37, 2957.41, 2867.81, 2359.66, 2341.70, 1683.12, 1596.95, 1445.71, 1375.62, 1164.31, 737.28. HRMS (ESI) (M+H$^+$) Calcd. for $C_{30}H_{39}N_4O_4S^+$: 551.2687, found 551.2693.

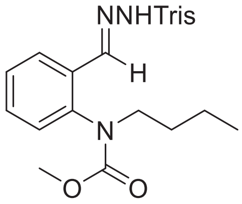


methyl (thiophen-3-ylmethyl)(2-((2-((2,4,6-triisopropylphenyl)-sulfonyl)hydrazono)methyl)phenyl)carbamate 1-p Yield: 85%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.04 (s, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.39 (s, 1H), 7.31 (td, *J* = 7.6, 1.3 Hz, 1H), 7.26 – 7.24 (m, 1H), 7.21 – 7.20 (m, 1H), 7.18 (s, 2H), 7.00 – 6.92 (m, 3H), 4.73 – 4.65 (m, 2H), 4.25 (hept, *J* = 6.7 Hz, 2H), 3.53 (s, 3H), 2.90 (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 (150 MHz, CDCl$_3$) δ 156.12, 153.42, 151.35, 141.73, 139.99, 137.08, 131.39, 131.30, 130.75, 128.60, 128.30, 127.90, 126.53, 126.25, 124.57, 123.83, 53.24, 49.37, 34.18, 30.02, 24.89, 23.53. IR (neat, cm^{-1}): 3196.36, 2957.33, 2868.55, 1681.89, 1454.44, 1374.11, 1153.88, 768.53, 588.75. HRMS (ESI) (M+H$^+$) Calcd. for $C_{29}H_{38}N_3O_4S_2^+$: 556.2298, found 556.2301.

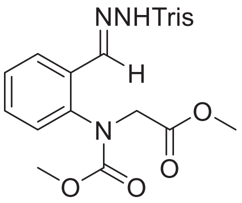


methyl (benzo[*b*]thiophen-3-ylmethyl)(2-((2-((2,4,6-triisopropyl phenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-q Yield: 80%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.91 (br, 1H), 7.87 – 7.86 (m, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.40 (p, *J* = 6.5 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.15 (s, 2H), 7.08 (br, 2H), 6.94 (s, 1H), 6.91 (d, *J* = 7.3 Hz, 1H), 5.21 (d, *J* =

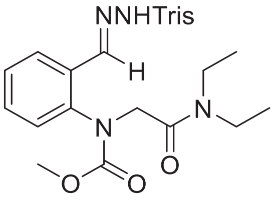
14.7Hz, 1H), 4.82 (d, *J* = 14.7 Hz, 1H), 4.14 (hept, *J* = 6.7 Hz, 2H), 3.54 (br, 3H), 2.88 (hept, *J* = 6.9 Hz, 1H), 1.28 – 1.23 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.25, 153.32, 151.27, 141.60, 140.33, 139.41, 138.01, 131.55, 131.36, 131.01, 130.62, 128.67, 127.94, 127.09, 126.35, 124.58, 124.41, 123.75, 123.11, 122.07, 53.35, 47.86, 34.13, 29.93, 24.85, 23.50. IR (neat, cm^{-1}): 3170.74, 2959.60, 2869.98, 1714.25, 1687.55, 1521.47, 1504.90, 1122.65, 944.15, 738.86. HRMS (ESI) (M+H$^+$) Calcd. for $C_{33}H_{40}N_3O_4S_2^+$: 606.2455, found 606.2456.



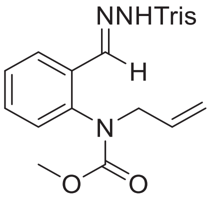
methyl butyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)-hydrazono)methyl)phenyl)carbamate 1-r Yield: 67%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.88 (s, 1H), 7.37 – 7.35 (m, 1H), 7.28 – 7.26 (m, 1H), 7.18 (s, 2H), 7.10 (d, *J* = 7.8 Hz, 1H), 4.30 (hept, *J* = 6.7 Hz, 2H), 3.67 (br, 1H), 3.54 (s, 3H), 3.41 (br, 1H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.48 – 1.43 (m, 2H), 1.30 (d, *J* = 6.7 Hz, 12H), 1.29 – 1.27 (m, 2H), 1.25 (d, *J* = 6.9 Hz, 6H), 0.84 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.18, 153.30, 151.27, 141.28, 140.26, 131.56, 131.18, 130.61, 128.50, 127.69, 126.48, 123.79, 53.14, 51.01, 34.17, 29.98, 29.78, 24.87, 23.52, 19.92, 13.68. IR (neat, cm^{-1}): 3155.25, 2956.43, 2868.74, 2359.98, 2342.85, 1682.72, 1601.37, 1456.82, 1315.52, 1152.59, 555.64. HRMS (ESI) (M+H$^+$) Calcd. for $C_{28}H_{42}N_3O_4S^+$: 516.2891, found 516.2898.



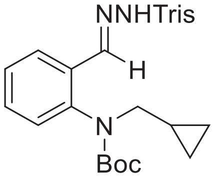
methyl *N*-(methoxycarbonyl)-*N*-(2-((2-((2,4,6-triisopropylphenyl) sulfonyl) hydrazono)methyl)phenyl)glycinate 1-s Yield: 90%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.34(s, 1H), 8.17 (s, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.35 (td, *J* = 7.5, 1.1 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.18 (s, 2H), 4.31 – 4.18 (m, 3H), 3.78 (d, *J* = 11.2 Hz, 1H), 3.70 (s, 3H), 3.56 (s, 3H), 2.89 (hept, *J* = 6.9 Hz, 1H), 1.30 (d, *J* = 6.7 Hz, 12H), 1.24 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 169.56, 156.15, 153.32, 151.30, 142.46, 140.38, 131.52, 131.32, 130.83, 128.07, 127.84, 126.70, 123.80, 53.57, 52.28, 52.24, 34.16, 30.00, 24.85, 23.52. IR (neat, cm^{-1}): 3176.72, 3057.43, 2958.72, 1752.67, 1692.37, 1599.82, 1264.81, 1165.49, 734.33, 703.22. HRMS (ESI) (M+H$^+$) Calcd. for $C_{27}H_{38}N_3O_6S^+$: 532.2476, found 532.2479.



methyl (2-(diethylamino)-2-oxoethyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-t Yield: 78%. Hexanes/ethyl acetate = 1/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.46 (s, 1H), 8.38 (s, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.24 – 7.23 (m, 1H), 7.17 (s, 2H), 4.36 – 4.28 (m, 4H), 3.52 (s, 3H), 3.38 – 3.30 (m, 2H), 3.26 – 3.18 (m, 2H), 2.89 (hept, *J* = 6.9 Hz, 1H), 1.30 (t, *J* = 6.7 Hz, 12H), 1.24 (d, *J* = 6.9 Hz, 6H), 1.16 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 166.43, 156.25, 153.19, 151.29, 143.43, 141.16, 131.68, 131.51, 130.64, 128.11, 127.67, 126.48, 123.76, 53.40, 52.33, 41.12, 40.67, 34.15, 29.98, 24.88, 23.52, 14.10, 12.99. IR (neat, cm^{-1}): 3159.61, 2958.54, 2869.40, 1694.41, 1651.06, 1455.46, 1153.45, 1036.92, 944.22, 757.98. HRMS (ESI) (M+H$^+$) Calcd. for $C_{30}H_{45}N_4O_5S^+$: 573.3105, found 573.3108.

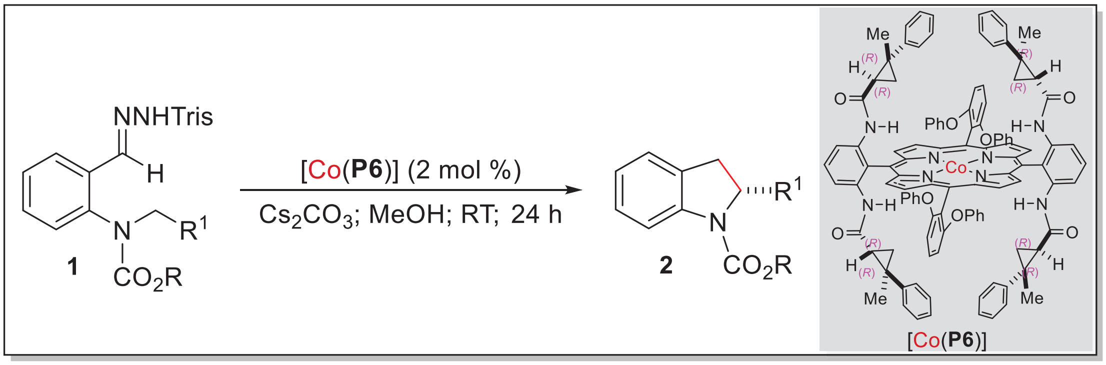


methyl allyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)-methyl)phenyl)carbamate 1-u Yield: 90%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.07 (br, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.76 (s, 1H), 7.35 (td, *J* = 7.7, 1.6 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.18 (s, 2H), 7.09 (d, *J* = 7.9 Hz, 1H), 5.80 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.08 – 5.02 (m, 2H), 4.30 – 4.21 (m, 3H), 4.02 (br, 1H), 3.54 (br, 3H), 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 (125 MHz, CDCl$_3$) δ 156.04, 153.37, 151.31, 141.63, 132.18, 131.48, 131.17, 130.64, 128.51, 127.82, 126.60, 124.00, 123.81, 119.20, 53.83, 53.23, 34.18, 30.00, 24.86, 23.52. IR (neat, cm^{-1}): 3146.27, 2959.08, 2869.15, 1675.25, 1601.09, 1455.41, 1376.42, 1278.58, 1058.74, 1038.32, 937.35, 751.55. HRMS (ESI) (M+H$^+$) Calcd. for $C_{27}H_{38}N_3O_4S^+$: 500.2578, found 500.2583.

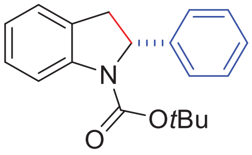


***tert*-butyl (cyclopropylmethyl)(2-((2-((2,4,6-triisopropylphenyl)-sulfonyl)hydrazono)methyl)phenyl)carbamate 1-v** Yield: 83%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.01 (s, 1H), 7.88 (s, 1H), 7.86 (d, J = 7.9 Hz, 1H), 7.34 (t, J = 7.3 Hz, 1H), 7.22 (t, J = 7.6 Hz, 1H), 7.17 (s, 2H), 7.12 (s, 1H), 4.31 – 4.25 (m, 2H), 3.37 – 3.34 (m, 2H), 2.93 – 2.86 (m, 1H), 1.48 (br, 2H), 1.30 – 1.24 (m, 25H), 0.86 (s, 1H), 0.35 and 0.29 (br, 2H), 0.10 – 0.03 (m, 1H), 0.01 – -0.05 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.74, 153.32, 151.34, 142.51, 141.47, 131.43, 131.29, 130.41, 128.46, 127.12, 126.18, 123.78, 80.47, 54.69, 34.16, 29.99, 28.20, 24.87, 23.52, 9.90, 3.76, 3.44. IR (neat, cm^{-1}): 3163.62, 2961.96, 2867.56, 2359.83, 1670.21, 1601.26, 1154.31, 757.50, 590.96. HRMS (ESI) (M+Na$^+$) Calcd. for $C_{31}H_{45}N_3NaO_4S^+$: 578.3023, found 578.3021.

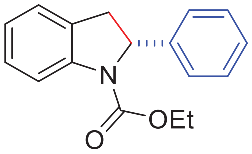
3.4.10 Procedure for [Co(P6)]-Catalyzed Enantioselective Radical C–H Alkylation



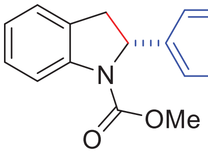
An oven-dried Schlenk tube was charged with sulfonyl hydrazone **1** (0.1 mmol), [Co(**P6**)] (2 mol %) and Cs_2CO_3 (0.2 mmol). The Schlenk tube was then evacuated and back filled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, methanol (1.0 mL) was added via a gastight syringe. 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 RT. After 24 h, the reaction mixture was filtrated through a short pad of silica gel, concentrated under vacuum and purified by flash column chromatography. The fractions containing product were collected and concentrated under vacuum to afford the desired compound **2.**



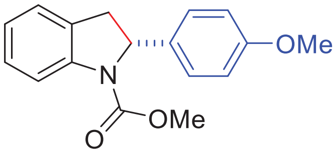
***tert*-butyl (*R*)-2-phenylindoline-1-carboxylate 2a** Yield: 82%. *ee*: 66%. Hexanes/ethyl acetate = 9/1, $R_f = 0.50$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.28 – 7.17 (m, 6H), 7.11 (d, *J* = 7.3 Hz, 1H), 6.97 (t, *J* = 7.4 Hz, 1H), 5.36 (br, 1H), 3.66 (dd, *J* = 16.2, 10.7 Hz, 1H), 2.95 (d, *J* = 16.2 Hz, 1H), 1.30 (br, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.34, 144.60, 143.00, 129.10, 128.47, 127.58, 127.10, 125.24, 124.75, 122.52, 114.62, 80.73, 62.58, 37.76, 28.13. IR (neat, cm^{-1}): 2977.25, 2929.13, 1693.35, 1482.59, 1387.15, 1139.31, 1015.13, 760.13, 701.62. HPLC analysis: *ee* = 66%. IA (99.7% hexanes: 0.3% isopropanol, 0.8 mL/min): t_{major} = 17.03 min, t_{minor} = 14.45 min. $[\alpha]^{20}{}_D = 29.6$ (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{19}H_{22}NO_2^+$: 296.1645, found 296.1648.



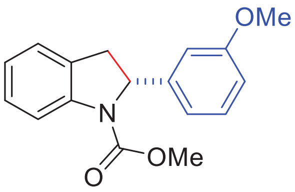
ethyl (*R*)-2-phenylindoline-1-carboxylate 2b Yield: 92%. *ee*: 86%. Hexanes/ethyl acetate = 8/1, $R_f = 0.55$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.28 – 7.18 (m, 6H), 7.14 (d, *J* = 7.3 Hz, 1H), 7.00 (t, *J* = 7.4 Hz, 1H), 5.43 (br, 1H), 4.13 (br, 2H), 3.70 (dd, *J* = 16.2, 10.6 Hz, 1H), 2.99 (d, *J* = 16.2 Hz, 1H), 1.08 (br, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.28, 143.98, 129.25, 128.54, 127.67, 127.27, 125.36, 124.82, 122.88, 114.85, 62.36, 61.36, 37.84, 14.32. IR (neat, cm^{-1}): 2979.21, 2928.36, 1709.64, 1486.22, 1407.35, 1382.31, 1274.04, 1055.34, 755.99. HPLC analysis: *ee* = 86%. IA (99% hexanes: 1% isopropanol, 0.8 mL/min): t_{major} = 17.07 min, t_{minor} = 12.02 min. $[\alpha]^{20}{}_D = 50.8$ (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{17}H_{18}NO_2^+$: 268.1338, found 268.1342.



methyl (*R*)-2-phenylindoline-1-carboxylate 2c Yield: 92%. *ee*: 94%. Hexanes/ethyl acetate = 8/1, $R_f = 0.50$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.29 – 7.18 (m, 6H), 7.14 (d, *J* = 7.3 Hz, 1H), 7.00 (t, *J* = 7.4 Hz, 1H), 5.46 and 5.44 (br, 1H), 3.71 (dd, *J* = 16.2, 10.5 Hz, 1H), 3.70 (br, 3H), 2.98 (dd, *J* = 16.2, 2.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.72, 143.74, 142.55, 129.42, 128.60, 127.42, 127.30, 125.23, 124.86, 123.00, 114.88, 62.30, 52.51, 37.92. IR (neat, cm^{-1}): 2952.64, 2920.54, 1705.53, 1483.87, 1440.85, 1386.08, 1274.07, 1055.93, 753.68. HPLC analysis: *ee* = 94%. IA (99.5% hexanes: 0.5% isopropanol, 0.8 mL/min): t_{major} = 26.13 min, t_{minor} = 19.12 min. $[\alpha]^{20}{}_D = 52.8$ (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{16}H_{16}NO_2^+$: 254.1176, found 254.1181.

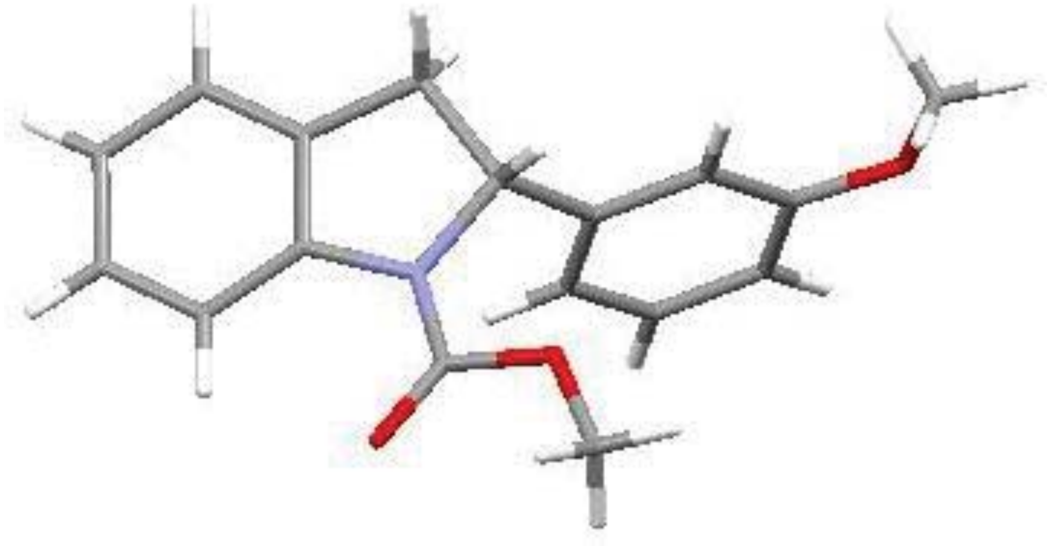


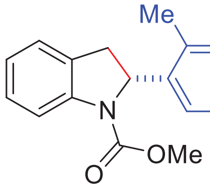
methyl (*R*)-2-(4-methoxyphenyl)indoline-1-carboxylate 2d Yield: 98%. *ee*: 94%. Hexanes/ethyl acetate = 5/1, $R_f = 0.48$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 7.16 – 7.12 (m, 3H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.42 and 5.40 (br, 1H), 3.77 (s, 3H), 3.71 (br, 3H), 3.69 (dd, *J* = 16.2, 10.4 Hz, 1H), 2.97 (dd, *J* = 16.2, 2.1 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.81, 153.76, 142.51, 135.98, 129.91, 127.64, 126.56, 124.85, 122.95, 114.92, 113.92, 61.84, 55.21, 52.52, 37.93. IR (neat, cm^{-1}): 2951.72, 1704.02, 1612.04, 1512.83, 1459.71, 1247.99, 1051.36, 1025.76, 846.10, 742.09. HPLC analysis: *ee* = 94%. IA (99% hexanes: 1% isopropanol, 1.0 mL/min): t_{major} = 24.97 min, t_{minor} = 19.37 min. $[\alpha]^{20}{}_D = 72.8$ (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{17}H_{18}NO_3^+$: 284.1281, found 284.1278.



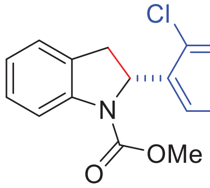
methyl (*R*)-2-(3-methoxyphenyl)indoline-1-carboxylate 2e

Yield: 98%. *ee*: 90%. Hexanes/ethyl acetate = 5/1, R_f = 0.45. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.26 – 7.23 (m, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 7.3 Hz, 1H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.78 – 6.76 (m, 2H), 6.73 (s, 1H), 5.43 and 5.42 (br, 1H), 3.75 – 3.68 (m, 7H), 2.97 (dd, *J* = 16.2, 2.7 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.77, 153.74, 145.48, 129.73, 127.69, 124.88, 123.03, 117.70, 117.48, 114.90, 113.20, 112.26, 111.26, 62.27, 55.14, 52.59, 37.93. IR (neat, cm^{-1}): 2955.13, 1701.26, 1599.57, 1483.93, 1440.81, 1385.47, 1264.11, 1134.70, 1056.34, 733.23. HPLC analysis: *ee* = 90%. IA (99% hexanes: 1% isopropanol, 1.0 mL/min): t_{major} = 24.61 min, t_{minor} = 15.78 min. $[\alpha]^{20}{}_D$ = 47.2 (*c* = 0.5, $CHCl_3$). HRMS (ESI) (M+H$^+$) Calcd. for $C_{17}H_{18}NO_3^+$: 284.1281, found 284.1282.



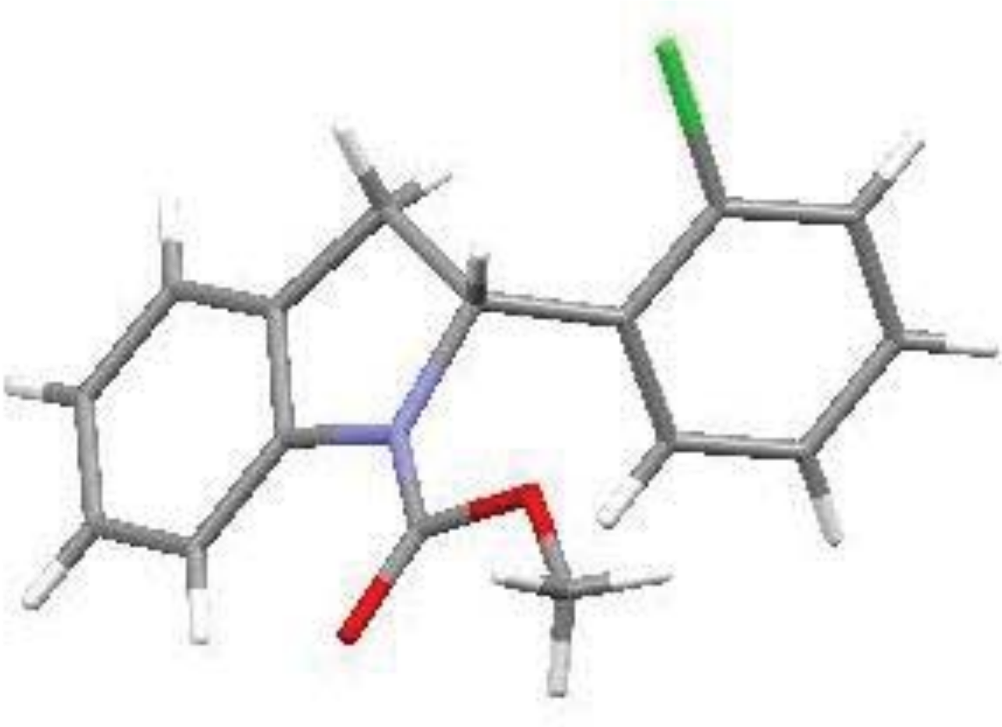


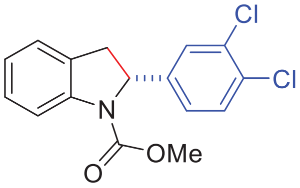
methyl (*R*)-2-(o-tolyl)indoline-1-carboxylate 2f Yield: 96%. *ee*: 94%. Hexanes/ethyl acetate = 6/1, $R_f = 0.5$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.27 – 7.25 (m, 1H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.14 – 7.10 (m, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 7.01 – 6.99 (m, 2H), 5.67 and 5.66 (br, 1H), 3.73 (dd, *J* = 16.0, 10.6 Hz, 1H), 3.67 (br, 3H), 2.84 (dd, *J* = 16.0, 3.0 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.74, 142.81, 141.90, 133.67, 130.50, 129.33, 127.71, 126.97, 126.38, 125.07, 123.53, 123.03, 114.87, 59.16, 52.63, 37.03, 19.28. IR (neat, cm^{-1}): 2954.05, 1702.15, 1599.16, 1485.45, 1440.67, 1265.75, 1191.94, 1054.33, 737.90. HPLC analysis: *ee* = 94%. IA (99.5% hexanes: 0.5% isopropanol, 0.8 mL/min): t_{major} = 25.25 min, t_{minor} = 18.29 min. $[\alpha]^{20}{}_D = 167.2$ (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{17}H_{18}NO_2^+$: 268.1332, found 268.1336.



methyl (*R*)-2-(2-chlorophenyl)indoline-1-carboxylate 2g Yield: 92%. *ee*: 93%. Hexanes/ethyl acetate = 6/1, $R_f = 0.55$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.15 – 7.11 (m, 2H), 7.06 (d, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 7.4 Hz, 1H), 5.86 and 5.84 (br, 1H), 3.79 (dd, *J* = 16.3, 10.5 Hz, 1H), 3.69 (s, 3H), 2.89 (dd, *J* = 16.3, 2.3 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.60, 142.64, 140.88, 131.50, 129.73, 129.00, 128.22, 127.75, 127.10, 125.29, 125.08, 123.23, 114.93, 59.53, 52.70, 36.92. IR (neat, cm^{-1}): 2954.71, 1701.97, 1601.19, 1484.01, 1439.31, 1385.42, 1056.01, 744.34, 628.11. HPLC analysis: *ee* = 93%. IA (99% hexanes: 1% isopropanol, 0.8 mL/min): t_{major} = 15.71 min, t_{minor} = 12.04 min. $[\alpha]^{20}{}_D = 77.6$

(*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{16}H_{15}ClNO_2^+$: 288.0786, found 288.0792.

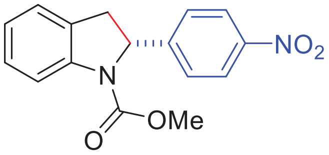




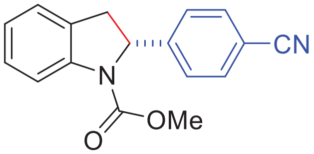
methyl (*R*)-2-(3,4-dichlorophenyl)indoline-1-carboxylate 2h

Yield: 85%. *ee*: 96%. Hexanes/ethyl acetate = 6/1, R_f = 0.55. ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.15 (d, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 2H), 5.40 and 5.38 (br, 1H), 3.73 (dd, *J* = 16.3, 10.6 Hz, 1H), 3.71 (br, 3H), 2.93 (dd, *J* = 16.3, 3.0 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.44, 143.98, 132.69, 131.36, 130.72, 127.98, 127.46, 124.98, 124.71, 123.36, 115.00, 61.38, 52.77, 37.73. IR (neat, cm^{-1}): 2953.91, 1705.31, 1601.07, 1484.60, 1441.48, 1383.34, 1274.30, 1057.23, 1030.58, 738.80. HPLC analysis: *ee* = 96%. IB (99.5% hexanes: 0.5% isopropanol, 0.8

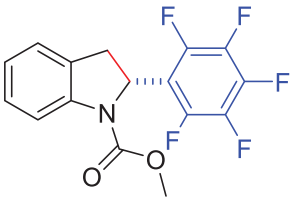
mL/min): t_{major} = 18.57 min, t_{minor} = 23.24 min. $[\alpha]^{20}{}_{D}$ = 58.0 (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{16}H_{14}Cl_2NO_2^+$: 322.0396, found 322.0393.



methyl (*R*)-2-(4-nitrophenyl)indoline-1-carboxylate 2i Yield: 96%. *ee*: 87%. Hexanes/ethyl acetate = 4/1, R_f = 0.38. ^1H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.6 Hz, 2H), 7.95 (br, 1H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.16 (d, *J* = 7.3 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 5.55 and 5.53 (br, 1H), 3.77 (dd, *J* = 16.3, 10.7 Hz, 1H), 3.71 (br, 3H), 2.95 (dd, *J* = 16.3, 3.0 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.86, 147.28, 128.10, 126.20, 125.03, 124.13, 123.49, 115.00, 61.78, 52.82, 37.60. IR (neat, cm^{-1}): 2961.51, 2940.10, 1714.04, 1595.41, 1509.88, 1483.70, 1382.51, 1141.76, 1055.66, 762.06. HPLC analysis: *ee* = 87%. IA (98% hexanes: 2% isopropanol, 1.0 mL/min): t_{major} = 27.95 min, t_{minor} = 34.67 min. $[\alpha]^{20}{}_{D}$ = 43.2 (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{16}H_{15}N_2O_4^+$: 299.1026, found 299.1026.

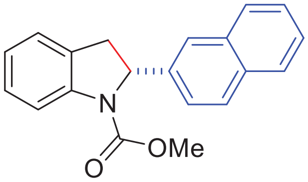


methyl (*R*)-2-(4-cyanophenyl)indoline-1-carboxylate 2j Yield: 97%. *ee*: 94%. Hexanes/ethyl acetate = 4/1, R_f = 0.40. ^1H NMR (600 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.31 – 7.25 (m, 3H), 7.15 (d, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 5.49 and 5.48 (br, 1H), 3.75 (dd, *J* = 16.3, 10.7 Hz, 1H), 3.71 (br, 3H), 2.93 (dd, *J* = 16.3, 3.0 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.47, 148.89, 132.64, 128.57, 128.03, 126.09, 125.00, 123.42, 118.63, 114.96, 111.34, 61.96, 52.77, 37.63. IR (neat, cm^{-1}): 2954.50, 2228.06, 1701.14, 1607.61, 1483.90, 1463.55, 1384.31, 1272.02, 1055.25, 749.31. HPLC analysis: *ee* = 94%. IA (98% hexanes: 2% isopropanol, 1.0 mL/min): t_{major} = 28.18 min, t_{minor} = 32.55 min. $[\alpha]^{20}{}_{D}$ = 114.4 (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{17}H_{15}N_2O_2^+$: 279.1128, found 279.1132.



methyl (*R*)-2-(perfluorophenyl)indoline-1-carboxylate 2k

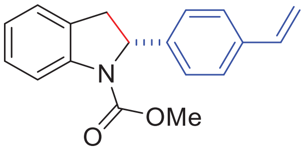
Yield: 90%. *ee*: 95%. Hexanes/ethyl acetate = 7/1, R_f = 0.6. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 and 7.51 (br, 1H), 7.26 – 7.24 (m, 1H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 5.81 (br, 1H), 3.85 (br, 3H), 3.76 (dd, *J* = 16.5, 11.4 Hz, 1H), 3.12 (dd, *J* = 16.5, 4.8 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.80, 144.97 (md, *J* = 253.6 Hz), 141.89, 140.94, 140.59 (md, *J* = 254.0 Hz), 137.51 (md, *J* = 251.4 Hz), 128.46, 127.92, 124.14, 123.26, 116.47, 52.84, 35.78, 35.20. IR (neat, cm^{-1}): 2961.76, 1713.96, 1503.70, 1484.98, 1602.15, 1442.06, 1387.29, 1282.30, 1193.43, 1123.53, 1011.90, 752.80. HPLC analysis: *ee* = 95%. IA (99.5% hexanes: 0.5% isopropanol, 0.8 mL/min): t_{major} = 33.47 min, t_{minor} = 14.21 min. $[\alpha]^{20}{}_{D}$ = -54.4 (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{16}H_{11}F_5NO_2^+$: 344.0704, found 344.0708.



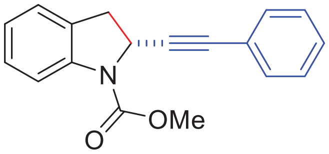
methyl (*R*)-2-(naphthalen-2-yl)indoline-1-carboxylate 2l

Yield: 90%. *ee*: 94%. Hexanes/ethyl acetate = 7/1, R_f = 0.58. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.80 – 7.77 (m, 3H), 7.64 (br, 1H), 7.46 – 7.43 (m, 2H), 7.31 – 7.28 (m, 2H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.03 (td, *J* = 7.5, 0.7 Hz, 1H), 5.63 and 5.62 (br, 1H), 3.78

(dd, *J* = 16.3, 10.6 Hz, 1H), 3.68 (s, 3H), 3.05 (dd, *J* = 16.3, 2.5 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.82, 141.06, 133.28, 132.79, 128.72, 127.92, 127.77, 127.61, 126.14, 125.74, 124.94, 123.77, 123.52, 123.10, 114.95, 62.48, 52.60, 37.99. IR (neat, cm^{-1}): 2917.63, 2849.15, 1701.58, 1598.18, 1485.44, 1440.01, 1274.59, 1152.34, 1054.00, 748.53. HPLC analysis: *ee* = 94%. IA (99% hexanes: 1% isopropanol, 0.8 mL/min): t_{major} = 27.96 min, t_{minor} = 20.63 min. $[\alpha]^{20}{}_{D}$ = 83.2 (*c* = 0.5, $CHCl_3$). HRMS (ESI) (M+H$^+$) Calcd. for $C_{20}H_{18}NO_2^+$: 304.1332, found 304.1337.

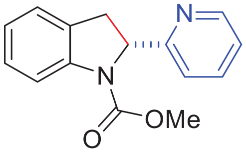


methyl (*R*)-2-(4-vinylphenyl)indoline-1-carboxylate 2m Yield: 57%. *ee*: 95%. Hexanes/ethyl acetate = 6/1, R_f = 0.50. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.26 – 7.24 (m, 1H), 7.15 – 7.10 (m, 3H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.67 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.70 (d, *J* = 17.6 Hz, 1H), 5.45 and 5.43 (br, 1H), 5.21 (d, *J* = 10.9 Hz, 1H), 3.72 (br, 3H), 3.71 (dd, *J* = 16.1, 10.4 Hz, 1H), 2.97 (dd, *J* = 16.2, 2.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.70, 145.14, 143.34, 136.76, 136.38, 128.06, 127.72, 126.50, 125.48, 124.89, 123.04, 114.91, 113.74, 62.12, 52.57, 37.94. IR (neat, cm^{-1}): 2952.07, 1705.42, 1483.20, 1439.26, 1382.70, 1271.60, 1136.01, 1053.63, 733.20. HPLC analysis: *ee* = 95%. IA (99.5% hexanes: 0.5% isopropanol, 0.8 mL/min): t_{major} = 30.74 min, t_{minor} = 22.49 min. $[\alpha]^{20}{}_{D}$ = 40.8 (*c* = 0.5, $CHCl_3$). HRMS (ESI) (M+H$^+$) Calcd. for $C_{18}H_{18}NO_2^+$: 280.1332, found 280.1336.

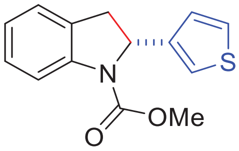


methyl (*R*)-2-(phenylethynyl)indoline-1-carboxylate 2n

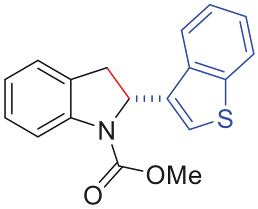
Yield: 50%. *ee*: 87%. Hexanes/ethyl acetate = 7/1, $R_f = 0.60$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.30 – 7.19 (m, 5H), 7.01 (t, *J* = 7.4 Hz, 1H), 5.35 and 5.33 (br, 1H), 3.91 (s, 3H), 3.58 (dd, *J* = 15.9, 10.2 Hz, 1H), 3.27 (dd, *J* = 15.9, 2.1 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.38, 141.12, 131.77, 129.13, 128.31, 128.15, 127.76, 124.78, 122.96, 122.56, 115.21, 88.74, 82.65, 52.83, 50.74, 36.47. IR (neat, cm^{-1}): 2916.84, 2848.92, 1708.75, 1598.12, 1485.02, 1441.52, 1385.53, 1269.92, 1192.02, 1130.13, 1056.18, 755.55, 691.55. HPLC analysis: *ee* = 87%. IC (99% hexanes: 1% isopropanol, 0.8 mL/min): t_{major} = 30.67 min, t_{minor} = 34.95 min. $[\alpha]^{20}{}_D = 18.0$ (*c* = 0.5, $CHCl_3$). HRMS (ESI) (M+H$^+$) Calcd. for $C_{18}H_{16}NO_2^+$: 278.1176, found 278.1180.



methyl (*R*)-2-(pyridin-2-yl)indoline-1-carboxylate 2o Yield: 93%. *ee*: 90%. Hexanes/ethyl acetate = 2/1, $R_f = 0.40$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.7 Hz, 1H), 7.97 (s, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.26 – 7.23 (m, 1H), 7.16 – 7.12 (m, 3H), 7.00 (t, *J* = 7.4 Hz, 1H), 5.60 and 5.58 (br, 1H), 3.74 (dd, *J* = 16.1, 10.9 Hz, 1H), 3.69 (s, 3H), 3.14 and 3.12 (br, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.18, 153.83, 149.53, 136.90, 129.08, 127.68, 124.93, 123.20, 122.21, 118.94, 118.83, 115.00, 63.64, 52.65, 36.55. IR (neat, cm^{-1}): 2922.76, 1709.13, 1591.33, 1484.77, 1465.88, 1265.66, 1058.53, 738.98. HPLC analysis: *ee* = 90%. IC (95% hexanes: 5% isopropanol, 1.0 mL/min): t_{major} = 36.35 min, t_{minor} = 29.75 min. $[\alpha]^{20}{}_D = 130.4$ (*c* = 0.5, $CHCl_3$). HRMS (ESI) (M+H$^+$) Calcd. for $C_{15}H_{15}N_2O_2^+$: 255.1128, found 255.1133.

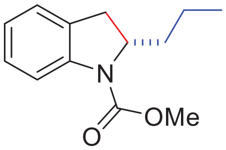


methyl (*R*)-2-(thiophen-3-yl)indoline-1-carboxylate 2p Yield: 97%. *ee*: 94%. Hexanes/ethyl acetate = 6/1, R_f = 0.60. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (br, 1H), 7.25 – 7.21 (m, 2H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.08 (br, 1H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 4.7 Hz, 1H), 5.58 and 5.57 (br, 1H), 3.77 (br, 3H), 3.64 (dd, *J* = 16.0, 10.1 Hz, 1H), 3.01 (dd, *J* = 16.0, 2.1 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.76, 144.00, 141.89, 129.65, 127.68, 126.15, 125.36, 124.85, 123.02, 120.64, 115.19, 58.36, 52.56, 36.96. IR (neat, cm^{-1}): 2952.85, 1700.19, 1601.40, 1482.94, 1440.10, 1382.32, 1273.15, 1054.83, 736.24. HPLC analysis: *ee* = 94%. IA (99.5% hexanes: 0.5% isopropanol, 0.8 mL/min): t_{major} = 34.25 min, t_{minor} = 23.41 min. $[\alpha]^{20}{}_D$ = 63.2 (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{14}H_{14}NO_2S^+$: 260.0740, found 260.0741.

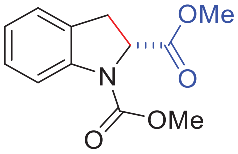


methyl (*R*)-2-(benzo[*b*]thiophen-3-yl)indoline-1-carboxylate 2q Yield: 97%. *ee*: 94%. Hexanes/ethyl acetate = 6/1, R_f = 0.40. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.86 (d, *J* = 6.9 Hz, 1H), 7.69 (d, *J* = 6.9 Hz, 1H), 7.38 – 7.36 (m, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 7.3 Hz, 1H), 7.10 (s, 1H), 7.02 (t, *J* = 7.4 Hz, 1H), 5.89 and 5.87 (br, 1H), 3.75 (dd, *J* = 16.0, 10.4 Hz, 1H), 3.73 (br, 3H), 3.07 (dd, *J* = 16.0, 2.4 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.73, 141.16, 137.54, 136.61, 127.81, 125.07, 124.41, 124.10, 123.21, 123.12, 121.53, 121.31, 115.21, 58.03, 52.70, 36.15. IR (neat, cm^{-1}): 2917.57, 2849.54, 1706.67, 1600.89, 1484.33, 1441.52, 1388.37, 1273.64, 761.73. HPLC analysis: *ee* = 92%. IA (99% hexanes: 1% isopropanol, 0.8 mL/min): t_{major} = 27.22

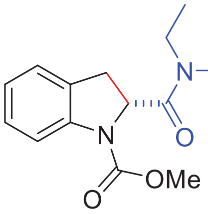
min, t_{minor} = 21.61 min. $[\alpha]^{20}{}_{D}$ = 127.2 (c = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{18}H_{16}NO_2S^+$: 310.0896, found 310.0896.



methyl (*S*)-2-propylindoline-1-carboxylate 2r Yield: 65%. *ee*: 87%. Hexanes/ethyl acetate = 6/1, R_f = 0.65. ^1H NMR (600 MHz, $CDCl_3$) δ 7.78 (br, 1H), 7.17 (t, J = 7.7 Hz, 1H), 7.14 (d, J = 7.4 Hz, 1H), 6.96 (t, J = 7.4 Hz, 1H), 4.45 (br, 1H), 3.84 (s, 3H), 3.29 (dd, J = 16.0, 9.5 Hz, 1H), 2.75 (d, J = 16.0 Hz, 1H), 1.71 (br, 1H), 1.54 – 1.52 (m, 1H), 1.35 – 1.31 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.77, 130.42, 127.33, 124.83, 124.66, 122.68, 115.34, 59.33, 52.42, 36.75, 33.42, 18.10, 13.98. IR (neat, cm^{-1}): 2956.18, 2871.65, 2359.34, 2341.70, 1711.07, 1602.79, 1487.15, 1443.56, 1393.64, 1291.74, 765.20. HPLC analysis: *ee* = 87%. IA (99.8% hexanes: 0.2% isopropanol, 0.8 mL/min): t_{major} = 25.18 min, t_{minor} = 18.77 min. $[\alpha]^{20}{}_{D}$ = 27.2 (c = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{13}H_{18}NO_2^+$: 220.1332, found 220.1332.



dimethyl (*R*)-indoline-1,2-dicarboxylate 2s Yield: 49%. *ee*: 81%. Hexanes/ethyl acetate = 5/1, R_f = 0.35. ^1H NMR (600 MHz, $CDCl_3$) δ 7.92 and 7.51 (s, br, 1H), 7.22 (br, 1H), 7.13 (d, J = 7.4 Hz, 1H), 6.98 (t, J = 7.4 Hz, 1H), 4.94 (br, 1H), 3.93 and 3.80 (br, 3H), 3.75 (s, 3H), 3.58 – 3.53 (m, 1H), 3.15 (d, J = 16.4 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.06, 152.93, 142.21, 127.98, 124.78, 124.36, 122.99, 114.79, 59.99, 52.76, 52.53, 32.96 and 32.11 (a pair of s). IR (neat, cm^{-1}): 2956.69, 1749.89, 1698.64, 1484.85, 1433.36, 1049.66, 1001.19, 751.73. HPLC analysis: *ee* = 81%. IA (95% hexanes: 5% isopropanol, 0.8 mL/min): t_{major} = 17.40 min, t_{minor} = 13.67 min. $[\alpha]^{20}{}_{D}$ = 20.0 (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{12}H_{14}NO_4^+$: 236.0917, found 236.0925.

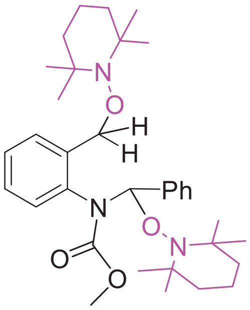


methyl (*R*)-2-(diethylcarbamoyl)indoline-1-carboxylate 2t Yield: 92%. *ee*: 68%. Hexanes/ethyl acetate = 1/1, R_f = 0.35. ^1H NMR (500 MHz, $CDCl_3$) δ 7.93 and 7.51 (d, *J* = 6.5 Hz, 1H), 7.20 – 7.16 (m, 1H), 7.09 (d, *J* = 7.1 Hz, 1H), 6.95 – 6.93 (m, 1H), 5.18 and 5.09 (d, *J* = 8.4 Hz, 1H), 3.90 (s, 1H), 3.75 – 3.34 (m, 7H), 3.01 (d, *J* = 11.4 Hz, 1H), 1.33 – 1.25 (m, 3H), 1.13 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) major rotamer: δ 170.42, 152.80, 143.04, 128.95, 127.89, 124.27, 122.60, 114.66, 57.94, 52.43, 41.58, 40.71, 33.43, 14.44, 12.91. IR (neat, cm^{-1}): 2976.38, 2936.18, 1715.66, 1652.06, 1488.71, 1445.25, 1392.19, 1266.04, 1138.22, 1063.88, 740.66. HPLC analysis: *ee* = 68%. IA (92% hexanes: 8% isopropanol, 0.8 mL/min): t_{major} = 38.78 min, t_{minor} = 36.22 min. $[\alpha]^{20}{}_{D}$ = 91.6 (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{15}H_{21}N_2O_3^+$: 277.1547, found 277.1550.

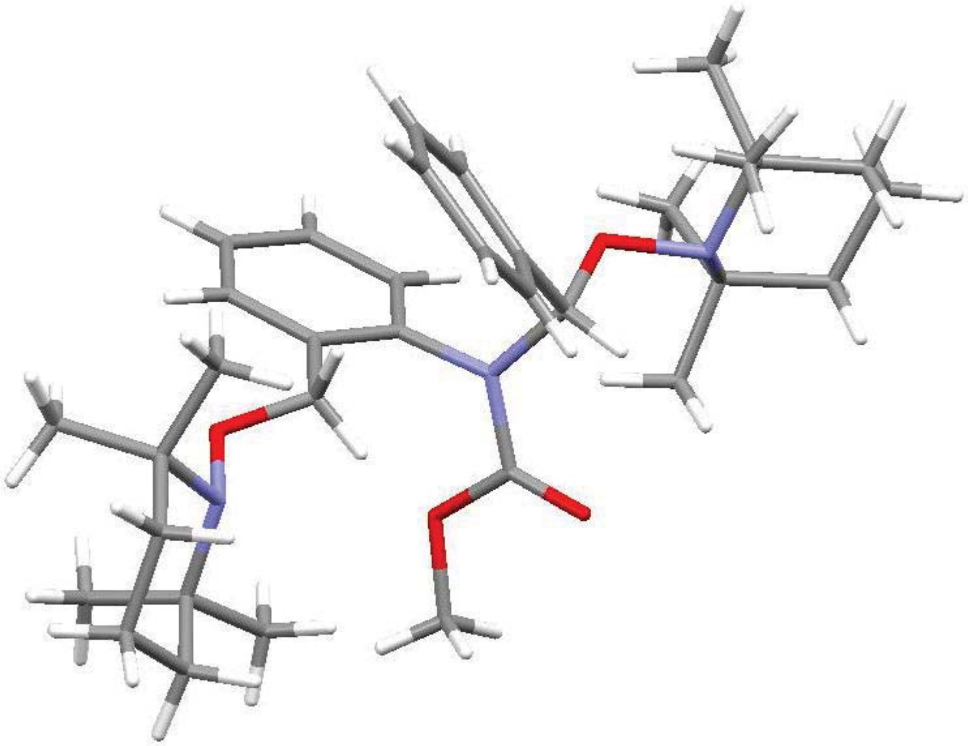
3.4.11 General Procedure for TEMPO Trapping Reactions

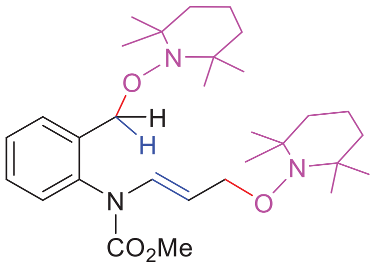
An oven-dried Schlenk tube was charged with 1.0 equivalent of sulfonyl hydrazone **1** (0.1 mmol), [Co(**Por**)] (2 mol %) and Cs_2CO_3 (0.2 mmol). The Schlenk tube was then evacuated and back filled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, TEMPO (2.5 equiv.) was added under nitrogen flow and methanol

(1.0 mL) was added via a gastight syringe. The Schlenk tube was then purged with nitrogen for 10 s and the rubber septum was replaced with a Teflon screw cap. The mixture was then stirred at RT or 40 ºC. After 24 h, the reaction mixture was filtrated through a short pad of silica, concentrated under vacuum and purified by flash column chromatography. The fractions containing product were collected and concentrated under vacuum to afford the desired compound.

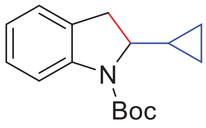


methyl (phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)carbamate 3c Yield: 90%. *ee*: 93%. Hexanes/ethyl acetate = 8/1, R_f = 0.70. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.3 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.17 (s, 1H), 7.08 – 7.05 (m, 5H), 4.30 (d, *J* = 13.7 Hz, 1H), 3.66 (d, *J* = 13.7 Hz, 1H), 3.87 and 3.64 (s, 3H), 1.65 – 1.34 (m, 18H), 1.12 – 1.01 (m, 12H), 0.89 – 0.77 (m, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.40, 138.01, 137.54, 133.91, 128.13, 127.83, 126.97, 126.81, 126.51, 125.80, 125.48, 93.20, 72.79, 60.11, 59.31, 59.13, 52.60, 39.91, 39.64, 39.05, 32.98, 32.63, 32.49, 31.87, 20.17, 19.85, 19.53, 16.49. IR (neat, cm^{-1}): 2974.31, 2932.90, 1711.46, 1439.23, 1301.16, 1026.18, 732.55, 700.86. HPLC analysis: *ee* = 93%. IA (99.7% hexanes: 0.3% isopropanol, 0.8 mL/min): t_{major} = 8.05 min, t_{minor} = 9.15 min. $[\alpha]^{20}{}_D$ = -116.4 (*c* = 0.5, $CHCl_3$). HRMS (ESI) ($M+H^+$) Calcd. for $C_{34}H_{52}N_3O_4^+$: 566.3952, found 566.3959.

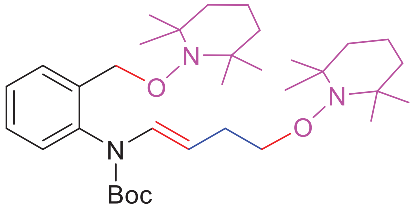




methyl (2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)prop-1-en-1-yl)carbamate **3u** Yield: 72%. Hexanes/ethyl acetate = 8/1, R_f = 0.70. ^{1}H NMR (600 MHz, $CDCl_3$) (Contains both E/Z isomers of enamine) δ 7.67 and 7.62 (d, *J* = 7.6 Hz, 1H), 7.44 – 7.29 (m, 2.5 H), 7.18 and 7.12 (d, *J* = 7.6 Hz, and d, *J* = 6.6 Hz, 1H), 6.75 (br, 0.5 H), 4.82 – 4.78 (m, 0.5 H), 4.79 – 4.68 (m, 2H), 4.41 – 4.37 (m, 0.5 H), 4.17 (br, 1H), 3.67 (br, 3H), 3.47 (br, 1H), 1.61 – 0.86 (m, 36H). ^{13}C NMR (150 MHz, $CDCl_3$) (Contains both E/Z isomers of enamine) δ 154.29, 136.83, 136.34, 136.12, 134.86, 131.00, 128.65, 128.48, 128.37, 128.20, 128.12, 128.02, 127.92, 127.65, 125.07, 109.41, 106.26, 75.54, 73.98, 73.94, 71.71, 59.69, 59.62, 59.26, 58.90, 53.11, 53.06, 39.37, 39.28, 39.16, 32.64, 32.56, 32.45, 29.37, 20.03, 19.82, 19.60, 16.81, 16.76. IR (neat, cm^{-1}): 2977.25, 2930.79, 1715.52, 1661.25, 1442.54, 1314.88, 1215.86, 766.94. HRMS (ESI) (M+H$^+$) Calcd. for $C_{30}H_{50}N_3O_4^+$: 516.3796, found 516.3807.



***tert*-butyl 2-cyclopropylindoline-1-carboxylate 2v** Yield: 50%. Hexanes/ethyl acetate = 8/1, R_f = 0.60. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.18 – 7.14 (m, 2H), 6.94 (t, *J* = 7.4 Hz, 1H), 4.00 (br, 1H), 3.29 (dd, *J* = 15.8, 9.4 Hz, 1H), 2.79 (d, *J* = 15.8 Hz, 1H), 1.57 (s, 9H), 1.10 – 1.04 (m, 1H), 0.65 – 0.60 (m, 1H), 0.53 – 0.48 (m, 1H), 0.44 – 0.38 (m, 1H), 0.23 – 0.18 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.78, 142.28, 130.63, 127.20, 124.67, 122.32, 115.62, 80.67, 62.93, 34.14, 28.49, 16.43, 4.22, 1.29. IR (neat, cm^{-1}): 2976.54, 1695.12, 1603.06, 1482.27, 1387.98, 1167.23, 1138.53, 1012.96, 740.25. HRMS (Dart$^+$) Calcd. for $C_{16}H_{22}NO_2^+$: 260.1645, found 260.1651.



***tert*-butyl (4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-but-1-en-1-yl)(2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)-carbamate 3v** Yield: 40%. Hexanes/ethyl acetate = 9/1, R_f = 0.70. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.10 (d, *J* = 13.3 Hz, 1H), 6.99 (d, *J* = 6.6 Hz, 1H), 4.72 – 4.67 (m, 2H), 4.25 (dt, *J* = 14.4, 7.3 Hz, 1H), 3.59 (t, *J* = 7.0 Hz, 2H), 2.13 (br, 2H), 1.48 – 1.00 (m, 45H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.41, 136.60, 135.91, 129.22, 128.69, 128.01, 127.73, 127.62, 107.54, 80.70, 74.11, 59.93, 59.57, 39.64, 39.59, 33.06, 32.89, 29.22, 28.08, 20.35, 20.00, 17.09. IR (neat, cm^{-1}): 2975.35, 2931.05, 1710.91, 1662.69, 1454.51, 1373.32, 1320.14, 1263.84, 1169.25, 1048.75, 741.49. HRMS (ESI) (M+H$^+$) Calcd. for $C_{34}H_{58}N_3O_4^+$: 572.4422, found 572.4424.

3.5 REFERENCES

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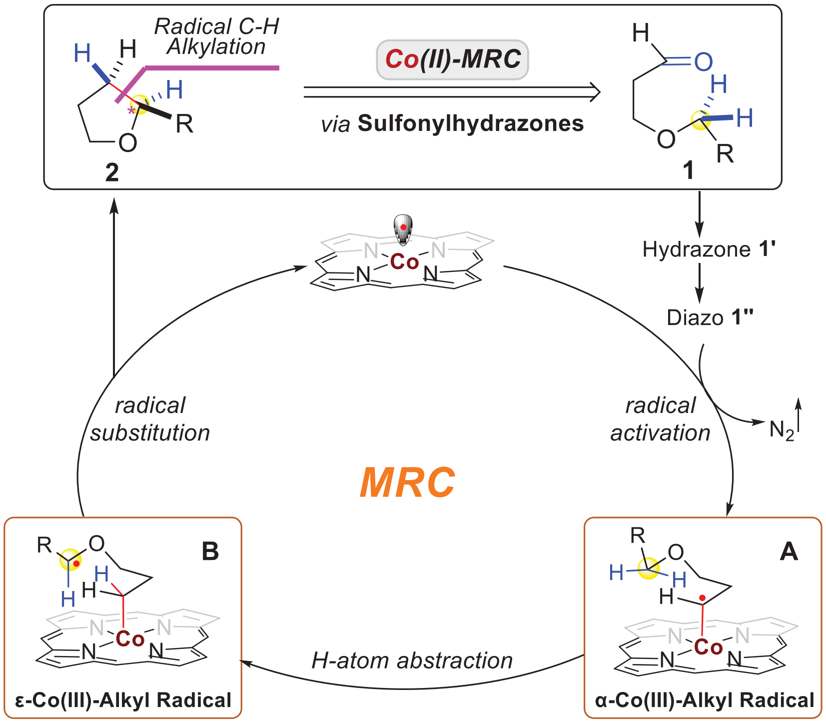
CHAPTER 4

ENANTIOSELECTIVE SYNTHESIS OF 2-SUBSTITUTED TETRAHYDROFURANS BY CO(II)-CATALYZED RADICAL C–H ALKYLATION

4.1 INTRODUCTION

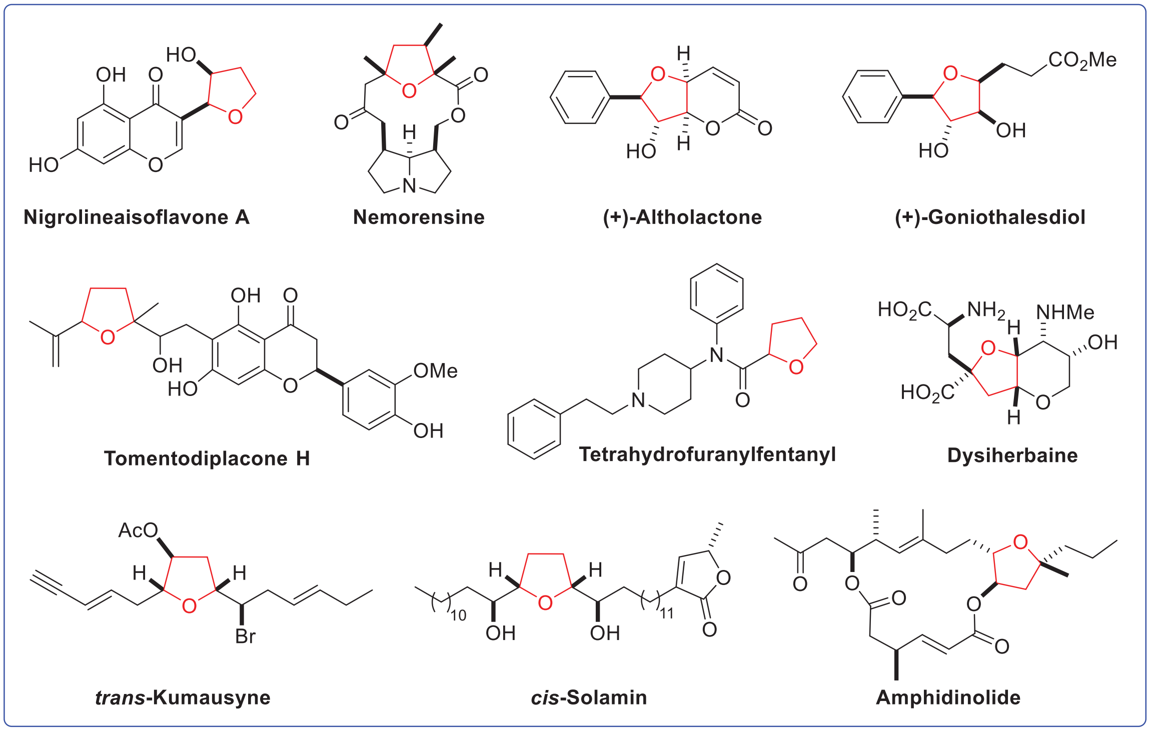
Due to their rich reaction profile, carbon-centered radicals, especially alkyl radicals, have been extensively explored as highly active intermediates for chemical synthesis.[1] Despite their great potential, the application of alkyl radicals for practical organic synthesis has faced several long-standing challenges that are inherently associated with the "free" nature of these radical species and proceed typically under substrate control. In this regard,[2] metalloradical catalysis (MRC) [3,4] has recently emerged as a conceptually new approach in addressing the aforementioned challenges through catalytic generation of metal-stabilized organic radicals to regulate both reactivity and selectivity of their subsequent homolytic reactions.[5] 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 such as donor-, acceptor-, and acceptor/acceptor-substituted diazo reagents to generate α-Co(III)-alkyl radicals for various catalytic radical transformations with excellent control of both reactivity and stereoselectivity.[6] Recently, we have further broadened the applications of Co(II)-based MRC by using in situ-generated aliphatic diazo compounds for asymmetric C–H alkylation, permitting the formation of a wide array of optically active α-substituted pyrrolidine derivatives.[7]

Scheme 4.1| Proposed Pathway for Synthesis of α-Substituted Tetrahydrofurans by Co(II)-Based Radical C–H Alkylation



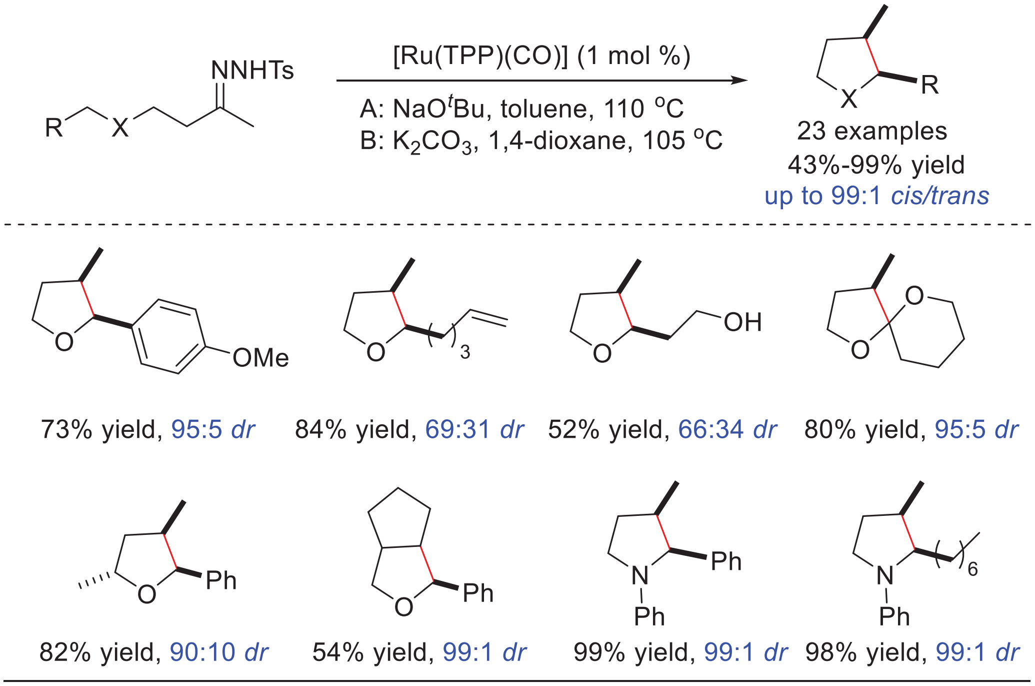
To this end, we are intrigued to see whether this radical alkylation pathway could also be applied to the enantioselective synthesis of α-substituted tetrahydrofurans. Starting from the readily available aldehyde-derived sulfonylhydrazone **1’** (Scheme 4.1), we questioned, in particular, whether the aliphatic diazo compound could be even generated under much milder conditions. If so, could the rate of metalloradical activation of aliphatic diazo compounds still be effectively matched with their in situ-generation to avoid their accumulation, leading to a series of decomposition reactions?[8] Moreover, upon the metalloradical activation to form α-Co(III)-alkyl radicals, it is equally critical to seek a suitable catalytic system to effectively induce the enantioselectivity in the subsequent radical hydrogen atom abstraction and radical substitution reaction. If the above concerns could be well positively addressed, it would provide a general catalytic strategy for stereoselective radical synthesis of α-substituted tetrahydrofurans from aliphatic aldehyde-derived tosylhydrazones, essentially via enantioselective C–C bond formation through the union of C–H and C=O units (Scheme 4.1).

Figure 4.1| Selected Biologically Active Compounds Containing Tetrahydrofuran Moiety



As recurring core structures, α-substituted tetrahydrofurans prevail in a wide range of natural products and bioactive compounds (Figure 4.1). As a result, considerable efforts have been devoted to devise effective strategies for their asymmetric synthesis,[9] nevertheless, few example has been reported for enantioselective construction of α-substituted tetrahydrofurans from linear substrates via metallocarbene-based intramolecular C–H alkylation of aliphatic diazo compounds.[10] In 2014, Che and coworkers developed a ruthenium porphyrin-catalyzed system for diastereoselective intramolecular C–H insertion reaction with in situ-generated alkyl diazomethanes, which permits the formation of substituted tetrahydrofurans in high yields with excellent diastereoselectivity (Scheme 4.2).[11] This offers a valuable synthetic pathway for the preparation of multisubstituted tetrahydrofurans from linear molecules, however, no asymmetric version has been demonstrated so far. The sluggish development might be in part due to the absence of chelating groups at the neighboring site of diazo carbon that poses inherent challenges for achieving positive stereoinduction.

Scheme 4.2| Ruthenium-Porphyrin-Catalyzed Cyclization of Tosylhydrazones to Construct Tetrahydrofurans and Pyrrolidines



As a new synthetic application, we have demonstrated a general synthetic strategy for the asymmetric formation of α-substituted tetrahydrofuran structures from flexible aliphatic diazo compounds, which could be ultimately derived from the readily accessible aldehydes (Scheme 4.1). Supported by a D_2-symmetric chiral amidoporphyrin, the Co(II)-based metalloradical catalyst is able to activate aliphatic diazo compounds even at room temperature for enantioselective intramolecular radical alkylation of a broad range of C(sp^3)–H bonds, affording a series of α-substituted chiral tetrahydrofuran compounds in high yields with excellent enantioselectivities. In addition to a good level of chemoselectivivity, the system also features tolerance of various functionalities as well as compatibility with a variety of heteroaryl groups.

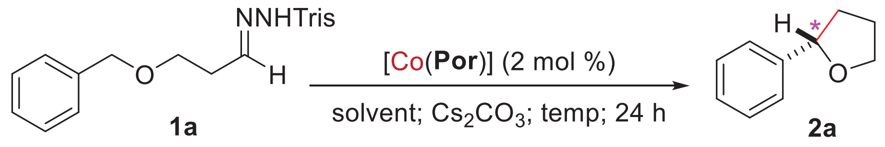
4.2 RESULTS AND DISCUSSIONS

4.2.1 Condition Optimization for Enantioselective Radical C–H Alkylation of Aliphatic Diazo Precursors

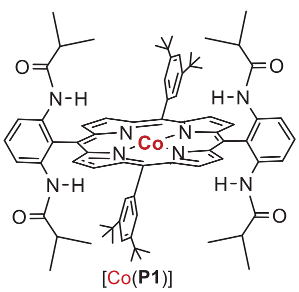
To begin with, we synthesized aliphatic aldehyde-derived triisopropylphenyl sulfonylhydrazone **1a** as the radical precursor, which is expected to generate the corresponding aliphatic diazo compound in situ under basic conditions (Table 4.1). Gratifyingly, even with achiral metalloradical catalyst [Co(**P1**)] (**P1** = 3,5-Di^{t}Bu-IbuPhyrin),[12] the desired C−H alkylation product 2-phenyl tetrahydrofuran (**2a**) was obtained in 55% yield in the presence of Cs_2CO_3 in methanol at 40 °C (entry 1), demonstrating the in situ-generation protocol could be well compatible with the radical catalytic cycle for productive radical alkylation.

To achieve the enantioselective radical process, the first-generation metalloradical catalyst [Co(**P2**)] (**P2** = 3,5-Di^{t}Bu-ChenPhyrin),[6h] which has proven to be efficient in radical olefin cyclopropanation, was employed in the catalytic system. The desired product **2a** could be obtained with promising enantioselectivity (15% ee) albeit in a relative low yield (entry 2). By simply switching catalyst [Co(**P2**)] to [Co(**P3**)] (**P3** = 2,6-DiMeO-ChenPhyrin) with sterically bulkier 2,6-diMeO groups at the *meso*-positions, we were gratified to observe a significant level of enantiomeric excess as well as improved reaction yield (entry 3). This ligand buttressing effect led us to the exploration of another unique family of D_2-symmetric chiral amidoporphyrins [Co(**P4**–**P6**)],[6f] which could be routinely synthesized from commercially available chiral amide (*S*)-(-)-2-tetrahydrofuran-carboxamide and have been recognized to possess much more rigid and polar chiral environment due to the intramolecular O···H–N hydrogen bonding interactions. Indeed, with the employment of [Co(**P4**)] (**P4** = 3,5-Di^{t}Bu-ZhuPhyrin), the enantioselectivity was further improved to 44% *ee* (entry 4). While the sterically more congested catalyst [Co(**P5**)] (**P5** = 2,6-DiMeO-ZhuPhyrin) could afford **2a** in excellent yield of 92%, only 20% *ee* was observed (entry 5). Remarkably, by using even bulkier [Co(**P6**)] (**P6** = 2,4,6-TriMe-ZhuPhyrin),[7] it could facilitate the enantioselective radical alkylation process, by affording **2a** in 44% yield with substantially improved enantioselectivity (entry 6). To further enhance the enantioselectivity, we attempted to lower the reaction temperature down to room temperature. However, only trace amount of the desired product **2a** was observed with remaining of starting material sulfonylhydrazone (entry 7). By replacing methanol with aprotic polar solvents or aromatic solvents, the desired product **2a** could be obtained in varied yields with globally enhanced enantioselectivity at room temperature (entries 8–14). Among them, tetrahydrofuran is the solvent of choice, where **2a** could be delivered in 90% yield with 92% *ee*. (entry 12).

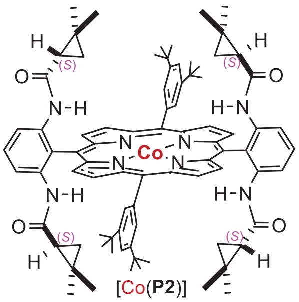
Table 4.1| Ligand and Solvent Effects on Formation of Tetrahydrofuran by Co(II)-Catalyzed Radical C–H Alkylation^{a}



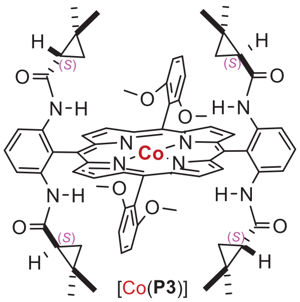
entry	catalyst	solvent	temp (°C)	yield (%)^{b}	*ee* (%)^{c}
1	[Co(**P1**)]	MeOH	40	55	--
2	[Co(**P2**)]	MeOH	40	40	15
3	[Co(**P3**)]	MeOH	40	60	30
4	[Co(**P4**)]	MeOH	40	56	44
5	[Co(**P5**)]	MeOH	40	92	20
6	[Co(**P6**)]	MeOH	40	44	80
7	[Co(**P6**)]	MeOH	23	trace	n.d.
8	[Co(**P6**)]	MTBE	23	36	93
9	[Co(**P6**)]	EtOAc	23	60	90
10	[Co(**P6**)]	Dioxane	23	65	92
11	[Co(**P6**)]	DME	23	78	91
12	[Co(**P6**)]	**THF**	**23**	**90**	**92**
13	[Co(**P6**)]	$PhCH_3$	23	47	93
14	[Co(**P6**)]	PhH	23	50	94



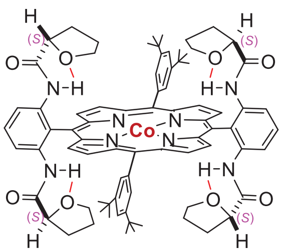
[Co(**P1**)]
(**P1** = 3,5-Di^{t}Bu-IbuPhyrin)



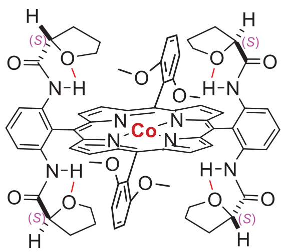
[Co(**P2**)]
(**P2** = 3,5-Di^{t}Bu-ChenPhyrin)



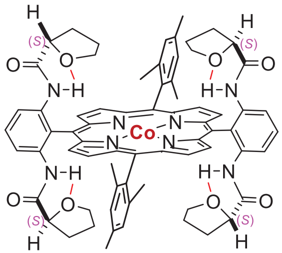
[Co(**P3**)]
(**P3** = 2,6-DiMeO-ChenPhyrin)



[Co(**P4**)]
(**P4** = 3,5-Di^{t}Bu-ZhuPhyrin)



[Co(**P5**)]
(**P5** = 2,6-DiMeO-ZhuPhyrin)



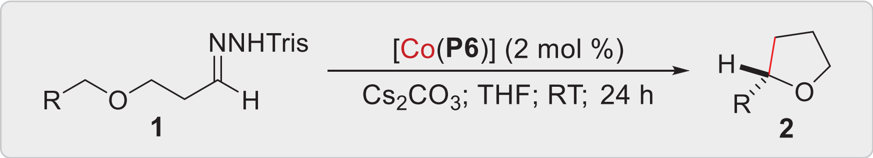
[Co(**P6**)]
(**P6** = 2,4,6-TriMe-ZhuPhyrin)

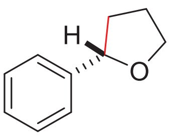
[a] Reactions were carried out with **1a** (0.1 mmol) in the presence of Cs_2CO_3 (2.0 equiv.) by [Co(**Por**)] (2.0 mol %) in solvent (0.8 mL) for 24 h. [b] Isolated yields. [c] Enantiomeric excess was determined by chiral HPLC. Tris = 2,4,6-triisopropylphenyl sulfonyl; MTBE = Methyl *tert*-butyl ether; DME = Dimethoxylethane; THF = Tetrahydrofuran; $PhCH_3$ = Toluene; PhH = Benzene.

4.2.2 Enantioselective Radical Alkylation of Various C–H Bonds

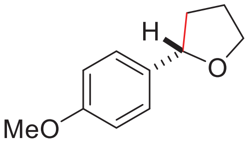
Under the optimized conditions, the applicability of this radical alkylation protocol was further evaluated by employing different substrates with various C–H bonds. As summarized in Table 4.2, tetrahydrofuran derivatives with various substituents at 2-position could be enantioselectively constructed from the aliphatic aldehyde-derived sulfonylhydrazones via the Co(II)-catalyzed radical C–H alkylation. First, benzylic C–H substrates with various electronic and steric properties were subjected under the standard conditions (entries 1–12). As exemplified by the radical precursors **1a**–**1l**, both electron-rich as well as electron-poor benzylic C–H bonds could be radically abstracted and alkylated, delivering the desired alkylated products in up to 93% yield with up to 96% *ee*. The lower sensitivity of this system towards electronic properties of differnet C–H bonds is in good agreement with the hypothesized radical mechanism. It is noteworthy to mention that C–H substrates with Cl- or Br-atoms substituted at various positions (**1c**, **1g**, **1i**–**1j**) were all shown to be suitable candidates for the 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. Moreover, the metalloradical alkylation system exhibited a high degree of tolerance toward functional groups, as exemplified by the high-yielding formation of **2d** and **2e** bearing -CN and -NO_2 groups. Like other benzylic C–H substrates, 2-naphthalenyl-contained C–H bond was also competent in this system, forming alkylated product **2l** in 82% yield with 92% *ee* (entry 12).

Table 4.2| Enantioselective Construction of α-Substituted Tetrahydrofurans by [Co(P6)]-Catalyzed Radical C−H Alkylation[a]

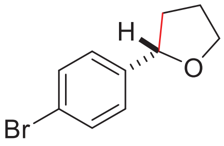




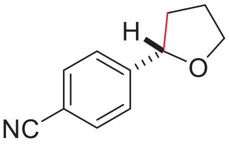
entry 1: **2a**
90% yield; 92% ee



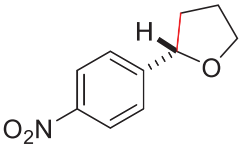
entry 2: **2b**
91% yield; 91% ee



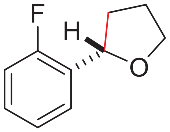
entry 3: **2c**
92% yield; 95% ee



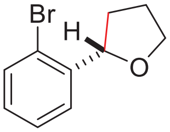
entry 4: **2d**
90% yield; 95% ee



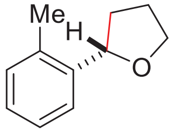
entry 5: **2e**
75% yield; 95% ee



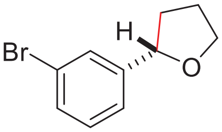
entry 6: **2f**
75% yield; 90% ee



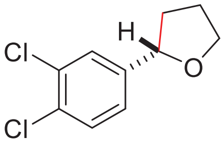
entry 7: **2g**
78% yield; 90% ee



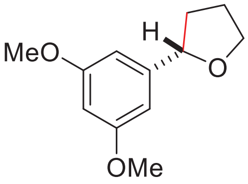
entry 8: **2h**
84% yield; 94% ee



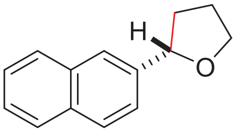
entry 9: **2i**
88% yield; 96% ee



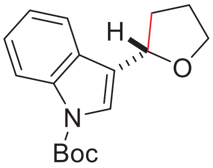
entry 10: **2j**
93% yield; 94% ee



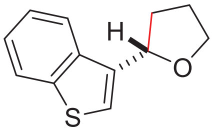
entry 11: **2k**
75% yield; 92% ee



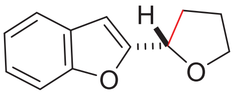
entry 12: **2l**
82% yield; 92% ee



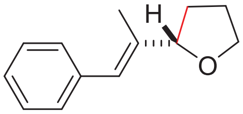
entry 13: **2m**
82% yield; 94% ee



entry 14: **2n**
86% yield; 95% ee



entry 15: **2o**
90% yield; 76% ee



entry 16: **2p**
92% yield; 92% ee

[a] Reactions were carried out with **1** (0.1 mmol) in the presence of Cs_2CO_3 (2.0 equiv.) by [Co(**P6**)] (2.0 mol %) in THF (0.8 mL) at RT for 24 h; Yields refers to isolated yields; Enantiomeric excess (*ee*) was determined by chiral HPLC; Tris = 2,4,6-triisopropylphenyl sulfonyl; THF = Tetrahydrofuran.

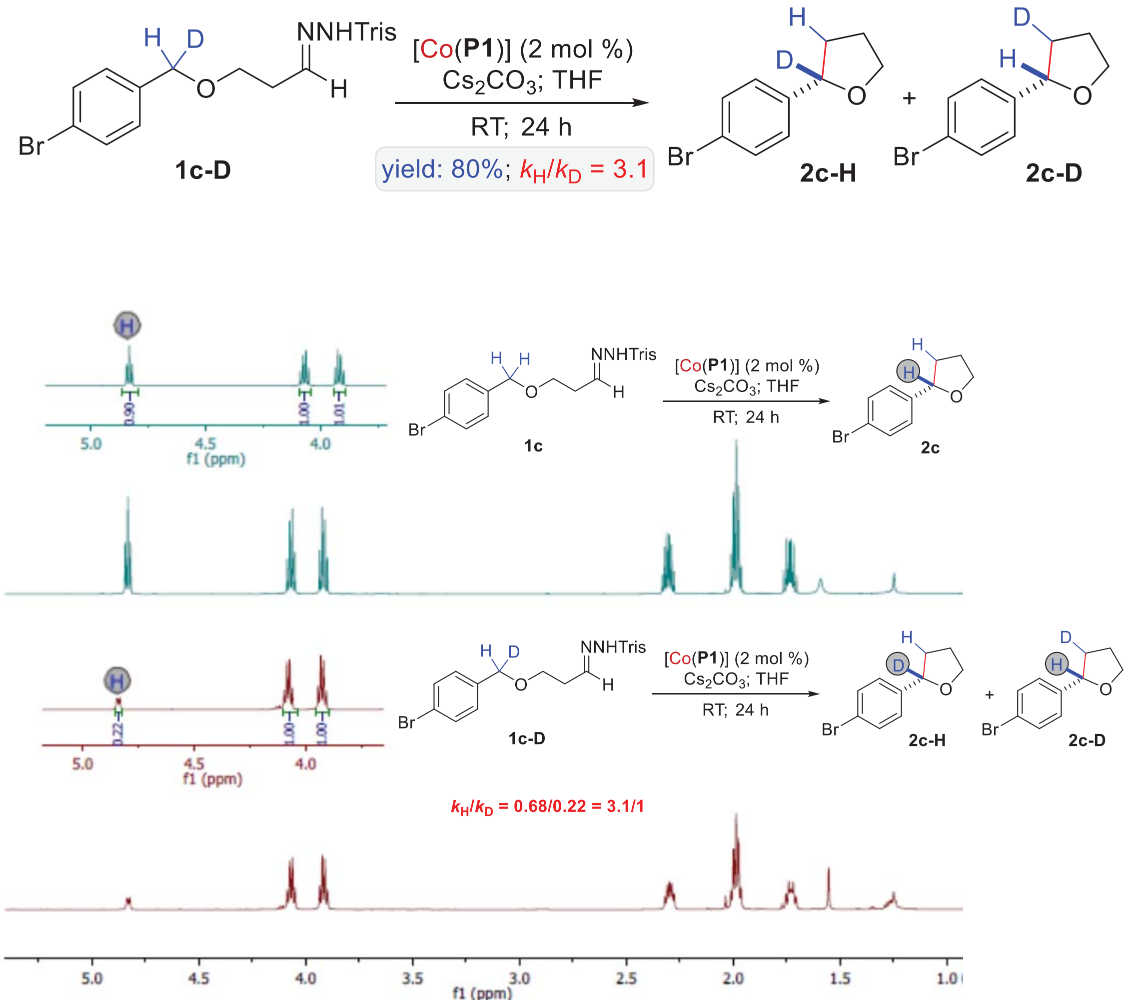
In addition, the Co(II)-based enantioselective radical alkylation reaction was further highlighted by its compatibility with substrates containing various heteroarenes, allowing for stereoselective construction of α-heteroaryl tetrahydrofurans. For example, 3-indole-based diazo precursor **1m** could be effectively activated by [Co(**P6**)] to construct **2m** in 82% yield with 94% *ee* at room temperature (entry 13). Likewise, this catalytic protocol could also be successfully applied for both benzothiophene- and benzofuran-based C–H substrates **1n** and **1o** to form the corresponding optically active α-heteroaryl tetrahydrofurans in high yields with varied enantioselectivities (entries 14-15). 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, a common challenge that plagues many transition metal-catalyzed reactions. The obtained compounds might also find valuable applications in pharmaceutical research and development, given that heteroarenes and tetrahydrofuran functionality are prevalent structural elements in natural and synthetic bioactive compounds.

Furthermore, less reactive allylic C–H bonds could also be homolytically activated. For example, allylic substrate **1p** could be chemoselectively alkylated to form tetrahydrofuran derivatives **2p** in 92% yield with 92% *ee*, without complication from the competitive cyclopropanation of the neighboring C=C bonds (entry 16).

4.2.3 Mechanistic Evidences for the Proposed Stepwise Radical Pathway

To shed light on the underlying stepwise radical mechanism for this Co(II)-catalyzed radical C–H alkylation, several mechanistic experiments were designed and conducted.

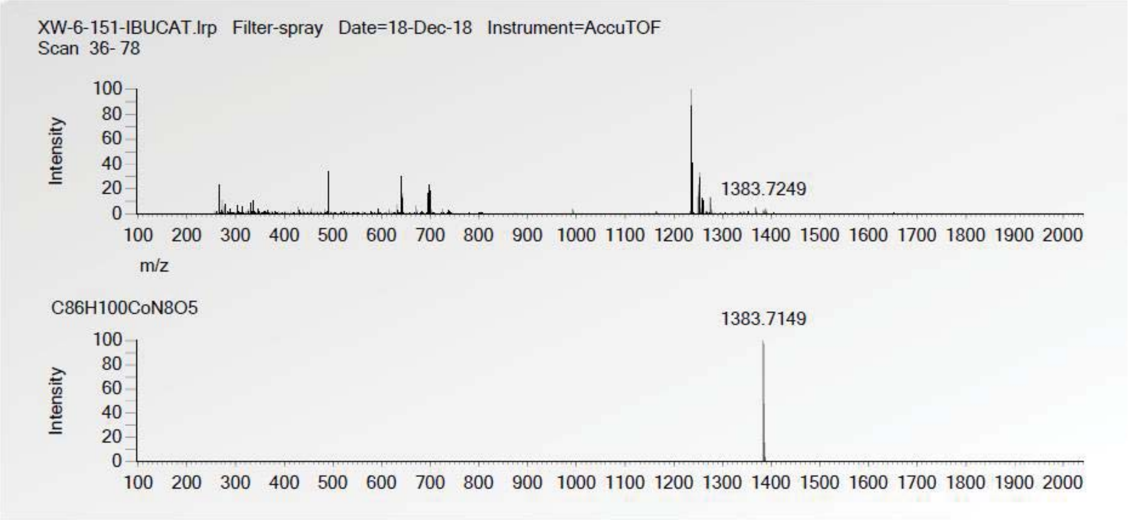
Scheme 4.3| Intramolecular Kinetic Isotope Effect of the C–H Activation Process

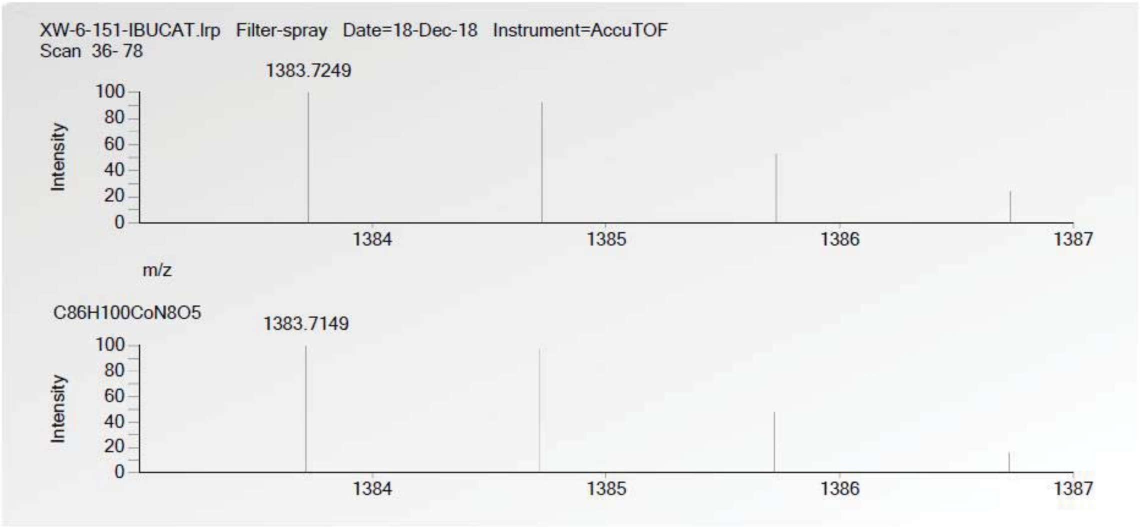


First, to examine the intramolecular kinetic isotope effect (KIE), mono-deuterated triisopropylphenyl sulfonylhydrazone **1c-D** was synthesized. Under the standard conditions, the use of [Co(**P1**)] as catalyst could catalyze the reaction effectively and generate both C–H and C–D alkylation products in 80% yield (Scheme 4.3). ^{1}H-NMR analysis of the product mixture revealed an intramolecular KIE ratio of $k_H/k_D = 3.1/1$. This KIE value agrees well with the proposed C–H bond cleavage by hydrogen-atom abstraction (Scheme 4.1).

In addition, the resulting Co(III)-supported alkyl radical intermediates **A** (Scheme 4.1) from the reaction of substrate **1a** by [Co(**P1**)] could be directly detected by HRMS ($C_{86}H_{100}CoN_8O_5^+$, *m*/*z*: calculated: 1383.7149, found: 1383.7249) (Scheme 4.4). The HRMS experiment was carried out in the absence of any additives such as formic acid, which commonly act as electron carriers for ionization, allowing for the detection of the molecular ion signals corresponding to Co(III)-alkyl radical ($C_{86}H_{100}CoN_8O_5\cdot$) by the loss of one electron.

Scheme 4.4| The High Resolution Mass Spectroscopy (HRMS) Spectrum for Co(III)-Supported Alkyl Radical Intermediate





Elemental Compositions

Data File: XW-6-151-IBUCAT.lrp Scan: 36- 78

Selected Isotopes : $C_{0-86}\ H_{95-100}\ Co_{1}\ N_{1-8}\ O_{1-5}$

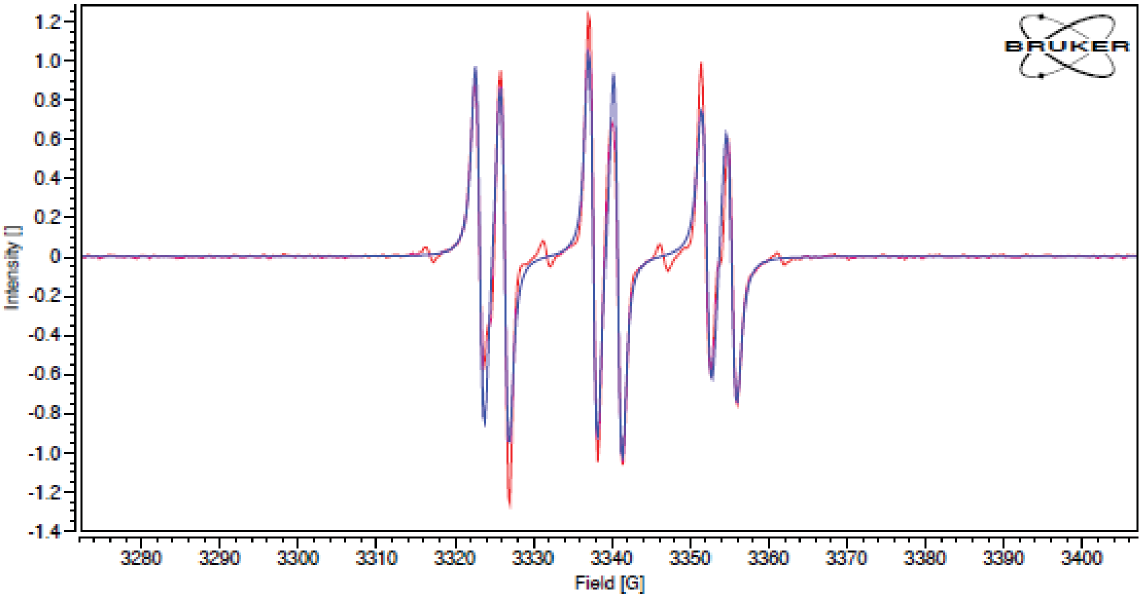
Error Limit : 50 ppm

Unsaturation Limits : -10 to 500

Measured Mass	Formula	Calculated Mass	Error (ppm)	r + db
1383.7249	$C_{86}H_{100}CoN_{8}O_{5}$	1383.7149	7.3	41.5

Lastly, the corresponding alkyl radical intermediate was also trapped by spin trapping reagent phenyl *N*-*tert*-butylnitrone (PBN) to give the characteristic EPR signal. As shown in Scheme 4.5, 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 $A_N = 14.5$, $A_H = 3.2$, $g = 2.006$, 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 litrature.[13]

Scheme 4.5| Isotropic X-band EPR Spectrum of Phenyl *N*-*tert*-butylnitrone (PBN)-trapped Co(III)-Supported Alkyl Radical Intermediate



Together, these experimental results provided strong evidence for the proposed radical mechanism through Co(II)-based metalloradical C–H alkylation (Scheme 4.1).

4.3 CONCLUSIONS

In summary, Co(II)-based metalloradical catalysis (MRC) has been successfully applied to aliphatic diazo compounds for enantioselective synthesis of α-substituted tetrahydrofuran analogs by radical C–H alkylation. Aliphatic alkoxylethyl diazomethanes were effectively generated in situ from corresponding sulfonylhydrazones and well served as radical precursors for Co(II)-based metalloradical catalysis (MRC) at room temperature. With the Co(II) complex of D_2-symmetric chiral porphyrin [Co(2,4,6-TriMe-ZhuPhyrin)] as the catalyst, it enables the activation of different aliphatic diazo compounds at milder reaction conditions and undergoes effective alkylation of a broad range of C–H bonds, including benzylic, allylic and heteroaryl-adjacent C(sp^3)–H bonds to afford the corresponding compounds in high yields with effective control of enantioselectivities. Remarkably, this Co(II)-based metalloradical system has demonstrated a series of attributes such as functional group tolerance, high chemoselectivity, as well as excellent compatibility with heteroaryl functionalities. This general radical C–H alkylation route via Co(II)-based metalloradical catalysis will hopefully provide a new retrosynthetic paradigm for approaching optically active α-substituted tetrahydrofuran derivatives by linking carbonyl groups (C=O) with various C–H bonds.

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 a 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, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian INOVA 500 (125 MHz), or 600 (150 MHz) spectrometers 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. 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. HPLC measurements were carried out on a Shimadzu HPLC system with Chiralcel AD-H, and ChiralPak Immobilized columns: IA, IB, IC, ID, IE, and IF. Infrared (IR) spectra were recorded on a Termo Scientific Nicolet Is5 System. Frequencies are reported in wavenumbers (cm^{-1}). Optical rotations were measured on a Rudolph Research Analytical AUTOPOL® IV digital polarimeter. The X-ray diffraction data were collected using Bruker Kappa APEX DUO diffractometer and a Rigaku HighFlux Homelab diffractometer. X-band EPR spectra were recorded on a Bruker EMX-Plus spectrometer (Bruker BioSpin).

Unless otherwise noted, all C–H alkylation reactions were performed in oven-dried glassware under dry N_2 atmosphere with standard schlenk vacuum line techniques. Gastight 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).

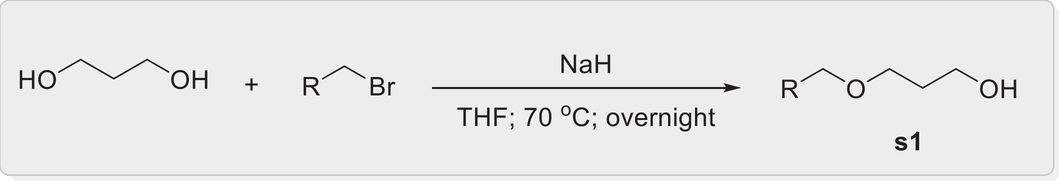
4.4.2 Procedure for HRMS Experiment

To an oven-dried Schlenk tube, sulfonylhydrazone **1a** (0.05 mmol) and Cs_2CO_3 (2.0 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, and CH_3CN (0.5 mL) was added via a gastight syringe. The mixture was then stirred at 60 ºC 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, which commonly act as electron carriers for ionization, allowing for the detection of the molecular ion signals corresponding to Co(III)-alkyl radical ($C_{86}H_{100}CoN_8O_5\cdot$) by the loss of one electron.

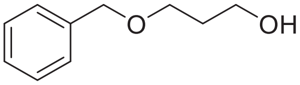
4.4.3 Procedure for EPR Experiment

To an oven-dried Schlenk tube A, sulfonylhydrazone **1a** (0.05 mmol) and Cs_2CO_3 (2.0 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, and benzene (0.5 mL) was added via a gastight syringe. The mixture was then stirred at 60 ºC for 0.5 h. During the time, [Co(**P1**)] (4 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 3 min and transferred into a degassed EPR tube (filled with argon) through a gastight syringe. The sample was then carried out for EPR experiment at room temperature (EPR settings: T = 298 K; microwave frequency: 9.37762 GHz; power: 6.325 mW; modulation amplitude: 1.0 G).

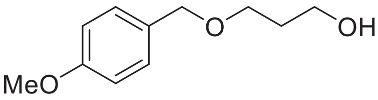
4.4.4 General Procedure for 3-(benzyloxy)propan-1-ol Derivatives s1



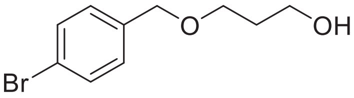
Prepared according to the literature.[14] To a suspension of sodium hydride (60% in oil, 12 mmol, 1 equiv.) in dry THF (50 mL) was added dropwise 1,3-propanediol (1 equiv.). The mixture was stirred at rt for 45 min. Bromide (1 equiv.) was added dropwise. The reaction mixture was stirred for 5 h to overnight using TLC to monitor the reaction. After completed, the reaction mixture was quenched by the addition of H_2O (50 mL). The phases were separated, and the aqueous layer was extracted three times with Et_2O (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The crude material was then purified by flash column chromatography.



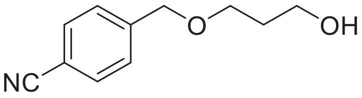
3-(benzyloxy)propan-1-ol s1-a Yield: 71%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H), 4.53 (s, 2H), 3.78 (s, 2H), 3.78 – 3.65 (m, 2H), 2.33 (s, 1H), 1.87 (p, J = 5.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.04, 128.41, 127.67, 127.61, 73.24, 69.34, 61.85, 32.09. IR (neat, cm^{-1}): 3315.61, 2945.96, 2863.78, 1351.59, 1282.54, 1174.29, 1074.84, 1004.21, 926.92, 866.58, 786.08, 750.21, 697.60. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{15}O_2^+$: 167.1067, found 167.1066.



3-((4-methoxybenzyl)oxy)propan-1-ol s1-b Yield: 68%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.45 (s, 2H), 3.80 (s, 3H), 3.77 (q, *J* = 5.5 Hz, 2H), 2.31 (t, *J* = 5.4 Hz, 1H), 1.90 – 1.81 (m, 2H).^{13}C NMR (150 MHz, CDCl$_3$) δ 159.23, 130.14, 129.26, 113.83, 72.92, 69.15, 62.02, 55.26, 32.06. IR (neat, cm^{-1}): 3410.13, 2917.34, 2849, 70, 1512.36, 1247.68, 1032.38, 819.75, 767.85. HRMS (ESI) ([M+H]$^{+}$) Calcd. for $C_{11}H_{17}O_3^{+}$: 197.1172, found 197.1175.

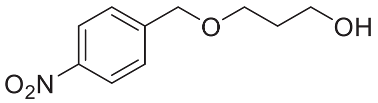


3-((4-bromobenzyl)oxy)propan-1-ol s1-c Yield: 74%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 4.47 (s, 2H), 3.78 (q, *J* = 5.5 Hz, 2H), 3.65 (t, *J* = 5.8 Hz, 2H), 2.13 (t, *J* = 5.3 Hz, 1H), 1.90 – 1.85 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 137.11, 131.55, 129.22, 121.55, 72.49, 69.28, 61.74, 32.13. IR (neat, cm^{-1}): 3324.30, 2918.83, 2859.51, 1486.87, 1092.23, 1070.60, 1012.20, 803.82. HRMS (ESI) ([M+H]$^{+}$) Calcd. for $C_{10}H_{14}BrO_2^{+}$: 245.0172, found 245.0175.

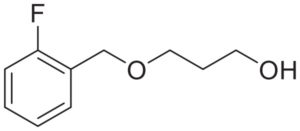


4-((3-hydroxypropoxy)methyl)benzonitrile s1-d Yield: 72%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 7.9 Hz, 2H), 4.58 (s, 2H), 3.80 (t, *J* = 5.8 Hz, 2H), 3.69 (t, *J* = 5.9 Hz, 2H), 2.02 (s, 1H), 1.94 – 1.86 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 143.71, 132.25, 127.65, 118.75, 111.46, 72.21, 69.52, 61.32, 32.18. IR (neat, cm^{-}

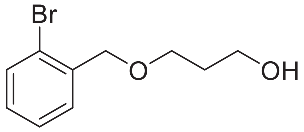
^{1}): 3325.29, 2921.54, 2865.45, 2228.14, 1610.15, 1413.84, 1364.84, 1096.48, 820.25. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{11}H_{14}NO_2^+$: 192.1019, found 192.1022.



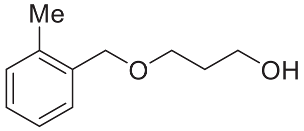
3-((4-nitrobenzyl)oxy)propan-1-ol s1-e Yield: 71%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 8.7 Hz, 2H), 4.62 (s, 1H), 3.82 (q, *J* = 5.5 Hz, 1H), 3.71 (t, *J* = 5.9 Hz, 1H), 1.95 – 1.89 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.41, 145.75, 127.66, 123.69, 71.96, 69.57, 61.30, 32.20. IR (neat, cm^{-1}): 3234.15, 2922.50, 2865.86, 1604.34, 1518.37, 1345.09, 1105.59, 859.44, 738.98. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{14}NO_4^+$: 212.0917, found 212.0915.



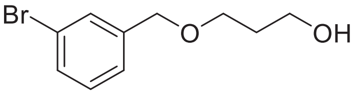
3-((2-fluorobenzyl)oxy)propan-1-ol s1-f Yield: 74%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (td, *J* = 7.5, 1.5 Hz, 1H), 7.27 (tdd, *J* = 7.4, 5.3, 2.0 Hz, 1H), 7.12 (td, *J* = 7.5, 0.8 Hz, 1H), 7.05 – 7.02 (m, 1H), 4.58 (s, 2H), 3.77 (dd, *J* = 10.1, 5.1 Hz, 2H), 3.68 (t, *J* = 5.8 Hz, 2H), 2.25 (s, 1H), 1.88 – 1.84 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.74 (d, *J* = 246.9 Hz), 129.92 (d, *J* = 4.3 Hz), 129.45 (d, *J* = 8.2 Hz), 125.10 (d, *J* = 14.7 Hz), 124.09 (d, *J* = 3.5 Hz), 115.26 (d, *J* = 21.5 Hz), 69.54, 66.73, 61.72, 32.09. IR (neat, cm^{-1}): 3315.41, 2921.45, 2868.07, 1586.89, 1490.66, 1455.32, 1229.03, 1181.81, 1086.94, 759.19. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{14}FO_2^+$: 185.0972, found 185.0973.



3-((2-bromobenzyl)oxy)propan-1-ol, s1-g Yield: 82%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.16 (t, *J* = 7.7 Hz, 1H), 4.59 (s, 2H), 3.81 (t, *J* = 5.6 Hz, 2H), 3.74 (t, *J* = 5.8 Hz, 2H), 2.20 (s, 1H), 1.91 (p, *J* = 5.8 Hz, 2H).^{13}C NMR (125 MHz, CDCl$_3$) δ 137.36, 132.61, 129.12, 129.05, 127.43, 122.84, 72.58, 69.73, 61.72, 32.17.IR (neat, cm^{-1}): 3279.51, 2917.31, 2850.57, 1469.05, 1439.20, 1361.97, 1101.40, 1027.54, 752.36. HRMS (ESI) ([M+H]$^{+}$) Calcd. for $C_{10}H_{14}BrO_2^{+}$: 245.0172, found 245.0175.

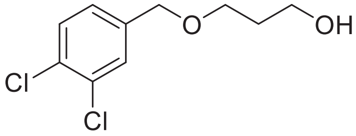


3-((2-methylbenzyl)oxy)propan-1-ol, s1-h Yield: 86%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.30 (d, *J* = 7.0 Hz, 1H), 7.23 – 7.17 (m, 3H), 4.52 (s, 2H), 3.79 (s, 2H), 3.68 (t, *J* = 5.8 Hz, 2H), 2.34 (s, 3H), 2.26 (s, 1H), 1.88 (p, *J* = 5.8 Hz, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 136.60, 135.89, 130.26, 128.51, 127.89, 125.78, 71.68, 69.43, 61.90, 32.15, 18.74. IR (neat, cm^{-1}): 3314.21, 2917.25, 2849.24, 1462.02, 1363.33, 1090.09, 746.14. HRMS (ESI) ([M+H]$^{+}$) Calcd. for $C_{11}H_{17}O_2^{+}$: 181.1223, found 181.1221.

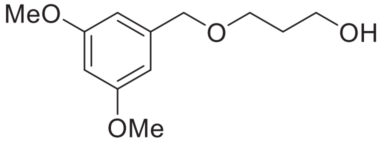


3-((3-bromobenzyl)oxy)propan-1-ol, s1-i Yield: 75%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.49 (d, *J* = 6.7 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.27 – 7.20 (m, 2H), 4.49 (s, 2H), 3.80 (dd, *J* = 12.3, 6.4 Hz, 2H), 3.66 (dd, *J* = 12.6, 6.6 Hz, 2H), 2.15 (s, 1H), 1.91 – 1.86 (m, 2H). ^{13}C NMR (150 MHz, CDCl$_3$)

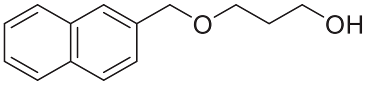
δ 140.43, 130.71, 130.49, 130.00, 125.99, 122.53, 77.21, 77.00, 76.79, 72.36, 69.33, 61.55, 32.13. IR (neat, cm^{-1}): 3313.35, 2920.71, 2862.46, 1570.41, 1472.79, 1427.58, 1360.07, 1199.88, 1085.60, 1069.55, 779.53, 670.74. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{14}BrO_2^+$: 245.0172, found 245.0172.



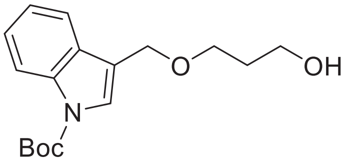
3-((3,4-dichlorobenzyl)oxy)propan-1-ol s1-j Yield: 85%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.42 – 7.40 (m, 2H), 7.15 (dd, *J* = 8.2, 1.6 Hz, 1H), 4.46 (s, 2H), 3.78 (t, *J* = 5.7 Hz, 2H), 3.64 (t, *J* = 5.9 Hz, 2H), 2.13 (s, 1H), 1.87 (p, *J* = 5.8 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 138.45, 132.53, 131.57, 130.42, 129.36, 126.67, 71.79, 69.32, 61.43, 32.14. IR (neat, cm^{-1}): 3324.08, 2918.97, 2862.04, 1471.41, 1389.13, 1349.79, 1204.22, 1103.57, 1031. 49, 818.39. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{13}Cl_2O_2^+$: 235.0287, found 235.0285.



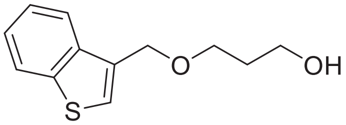
3-((3,5-dimethoxybenzyl)oxy)propan-1-ol s1-k Yield: 70%. Hexanes/ethyl acetate = 2/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 6.48 (d, *J* = 2.2 Hz, 2H), 6.38 (t, *J* = 2.2 Hz, 1H), 4.46 (s, 2H), 3.78 (s, 9H), 3.64 (t, *J* = 5.8 Hz, 2H), 2.31 (s, 1H), 1.87 (p, *J* = 5.7 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 160.87, 140.51, 105.26, 99.64, 73.13, 69.20, 61.74, 55.31, 32.16. IR (neat, cm^{-1}): 3386.49, 2917.81, 2849.08, 1735.10, 1596.52, 1461.60, 1203.86, 832.43. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{12}H_{19}O_4^+$: 227.1278, found 227.1282.



3-(naphthalen-2-ylmethoxy)propan-1-ol s1-l, Yield: 85%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.85 – 7.83 (m, 3H), 7.77 (s, 1H), 7.50 – 7.46 (m, 3H), 4.69 (s, 2H), 3.81 (t, *J* = 5.6 Hz, 2H), 3.71 (t, *J* = 5.8 Hz, 2H), 2.33 (s, 1H), 1.90 (p, *J* = 5.8 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 135.51, 133.22, 132.97, 128.25, 127.83, 127.67, 126.41, 126.12, 125.89, 125.60, 73.35, 69.35, 61.87, 32.13. IR (neat, cm^{-1}): 3280.02, 2924.42, 2869.46, 1365.11, 1344.90, 1079.21, 1021.38, 861.96, 767.02, 745.80. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{14}H_{17}O_2^+$: 217.1223, found 217.1226.

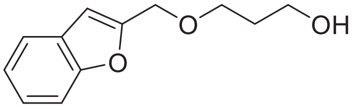


***tert*-butyl 3-((3-hydroxypropoxy)methyl)-1H-indole-1-carboxylate s1-m** Yield: 75%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.13 (s, 1H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.57 (s, 1H), 7.34 – 7.32 (m, 1H), 7.27 – 7.25 (m, 1H), 4.67 (s, 2H), 3.76 (t, *J* = 5.7 Hz, 2H), 3.68 (t, *J* = 5.8 Hz, 2H), 1.86 (p, *J* = 5.7 Hz, 2H), 1.67 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 149.64, 135.70, 129.59, 124.62, 122.76, 119.39, 117.44, 115.27, 83.75, 68.99, 64.92, 61.80, 32.11, 28.18. IR (neat, cm^{-1}): 3339.03, 2929.42, 2863.88, 1731.61, 1451.57, 1370.11, 1349.14, 1256.77, 1159.96, 1091.42, 768.36, 748.22. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{17}H_{24}NO_4^+$: 306.1700, found 306.1703.

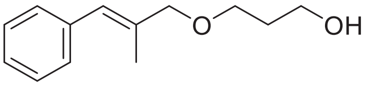


3-((3,4-dichlorobenzyl)oxy)propan-1-ol s1-n Yield: 58%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.87 – 7.85 (m, 2H), 7.41 –

7.35 (m, 3H), 4.77 (s, 2H), 3.77 (t, *J* = 5.7 Hz, 2H), 3.70 (t, *J* = 5.8 Hz, 2H), 2.16 (s, 1H), 1.87 (p, *J* = 5.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.61, 138.01, 133.10, 124.73, 124.52, 124.20, 122.78, 122.01, 69.11, 67.52, 61.63, 32.12. IR (neat, cm^{-1}): 3280.79, 2918.56, 2850.55, 1460.77, 1427.42, 1103.29, 1073.53, 758.60, 734.34. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{12}H_{15}O_2S^+$: 223.0787, found 223.0788.

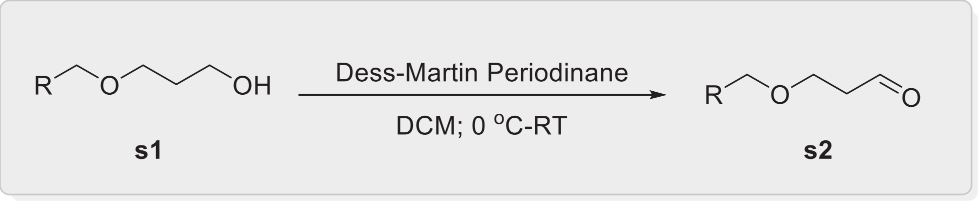


3-(benzofuran-2-ylmethoxy)propan-1-ol, Yield: 65%. Hexanes/ethyl acetate = 3/1. ^{1}H NMR (600 MHz, CDCl3) δ 7.55 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.23 – 7.21 (m, 1H), 7.23 – 7.21 (m, 1H), 6.69 (s, 1H), 4.62 (s, 2H), 3.78 (d, *J* = 2.8 Hz, 2H), 3.73 (t, *J* = 5.9 Hz, 2H), 2.17 (s, 1H), 1.88 (p, *J* = 5.8 Hz, 2H). ^{13}C NMR (150 MHz, CDCl3) δ 155.14, 154.09, 127.98, 124.40, 122.76, 121.05, 111.31, 105.65, 69.34, 65.59, 61.44, 32.09. IR (neat, cm^{-1}): 3276.90, 2918.19, 2867.39, 1453.47, 1364.64, 1254.86, 1087.03, 943.21, 754.04. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{12}H_{15}O_3^+$: 207.1016, found 207.1019.

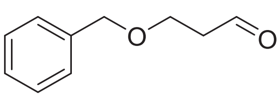


3-((2-methyl-3-phenylallyl)oxy)propan-1-ol, Yield: 54%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.49 (s, 1H), 4.04 (s, 2H), 3.81 (q, *J* = 5.5 Hz, 2H), 3.65 (t, *J* = 5.8 Hz, 2H), 2.36 (t, *J* = 5.3 Hz, 1H), 1.91 – 1.87 (m, 5H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.36, 134.88, 128.87, 128.09, 127.00, 126.49, 77.35, 69.18, 62.04, 32.10, 15.39. IR (neat, cm^{-1}): 3348.40, 2917.14, 2853.89, 1738.09, 1490.79, 1443.61, 1352.47, 1091.26, 747.50, 700.22. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{13}H_{19}O_2^+$: 207.1380, found 207.1382.

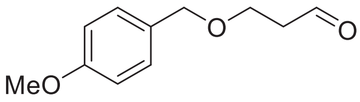
4.4.5 General Procedure for Preparation of 3-(benzyloxy)propanal Derivatives s2



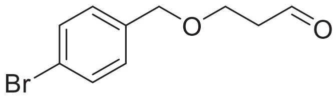
To a solution of **s1** (4 mmol, 1.0 equiv.) in DCM (30 mL) was added portion-wise Dess-Martin periodinane (6 mmol, 1.5 equiv.) reagent at 0 ºC. The mixture was stirred at rt and using TLC to monitor the reaction. After completed, the reaction mixture was diluted with 50 mL of diethyl ether, followed by slow addition of a 1:1:1 mixture of saturated aqueous sodium thiosulfate solution (15 mL), saturated aqueous sodium bicarbonate (15 mL), and water (15 mL, total volume 45 mL). The resulting biphasic mixture was stirred vigorously for 0.5 h resulting in two layers. The layers were separated and the aqueous layer was extracted three times with diethyl ether. The ethereal solution was then washed three times with water and once with brine; the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The crude material was then purified by flash column chromatography.



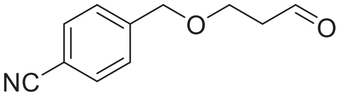
3-(benzyloxy)propanal s2-a, known compound.[2f] Yield: 80%. Hexanes/ethyl acetate = 10/1. ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.80 (s, 1H), 7.37 – 7.28 (m, 5H), 4.54 (s, 2H), 3.82 (t, *J* = 6.1 Hz, 2H), 2.70 (td, *J* = 6.1, 1.8 Hz, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 201.08, 137.82, 128.43, 127.76, 127.68, 73.25, 63.82, 43.86.



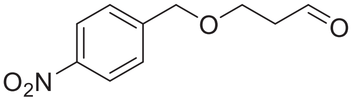
3-((4-methoxybenzyl)oxy)propanal s2-b Yield: 90%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.78 (s, 1H), 7.25 (d, *J* = 8.5 Hz, 2H), 6.89 – 6.87 (m, 2H), 4.46 (s, 2H), 3.80 (s, 3H), 3.78 (t, *J* = 6.1 Hz, 2H), 2.68 (td, *J* = 6.1, 1.8 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.19, 159.29, 129.91, 129.33, 113.78, 72.90, 63.50, 55.26, 43.86. IR (neat, cm^{-1}): 2918.19, 2852.81, 1723.15, 1612.21, 1513.55, 1248.97, 1095.84, 1034.43, 820.62. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{11}H_{15}O_3^+$: 195.1016, found 195.1018.



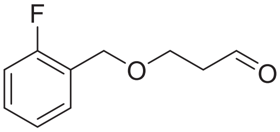
3-((4-bromobenzyl)oxy)propanal s2-c Yield: 80%. Hexanes/ethyl acetate = 8/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.80 (s, 1H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 4.48 (s, 2H), 3.80 (t, *J* = 6.0 Hz, 2H), 2.71 (t, *J* = 6.0 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.77, 136.88, 131.54, 129.25, 121.62, 72.48, 63.93, 43.82. IR (neat, cm^{-1}): 2918.58, 2849.34, 2358.68, 2340.54, 1723.00, 1487.79, 1394.23, 1094.26, 1012.14, 909.68, 759.81, 735.52. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{12}BrO_2^+$: 243.0015, found 243.0018.



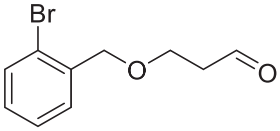
4-((3-oxopropoxy)methyl)benzonitrile s2-d Yield: 90%. Hexanes/ethyl acetate = 6/1.^{1}H NMR (600 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 2H), 4.57 (s, 2H), 3.84 (t, *J* = 6.0 Hz, 2H), 2.74 (td, *J* = 6.0, 1.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.40, 143.43, 132.25, 127.67, 118.74, 111.40, 72.24, 64.47, 43.79. IR (neat, cm^{-1}): 2864.34, 2359.09, 2228.99, 1723.52, 1265.37, 1094.89, 819.05, 735.18, 703.51. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{11}H_{12}NO_2^+$: 190.0863, found 190.0865.



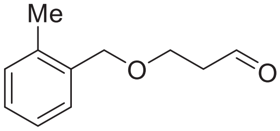
3-((4-nitrobenzyl)oxy)propanal s2-e Yield: 75%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.20 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 4.63 (s, 3H), 3.87 (t, *J* = 6.0 Hz, 2H), 2.76 (td, *J* = 6.0, 1.5 Hz, 2H).^{13}C NMR (150 MHz, $CDCl_3$) δ 200.43, 147.41, 145.46, 127.65, 123.64, 71.95, 64.40, 43.76. IR (neat, cm^{-1}): 2917.76, 2850.05, 1720.17, 1602.96, 1514.88, 1341.68, 1104.89, 849.98, 737.61, 693.68. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{12}NO_4^+$: 210.0761, found 210.0765.



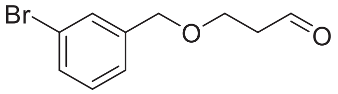
3-((2-fluorobenzyl)oxy)propanal s2-f Yield: 75%. Hexanes/ethyl acetate = 8/1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.39 (td, *J* = 7.4, 1.2 Hz, 1H), 7.29 – 7.26 (m, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.06 – 7.02 (m, 1H), 4.60 (s, 2H), 3.85 (t, *J* = 6.1 Hz, 2H), 2.71 (td, *J* = 6.1, 1.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.98, 160.70 (d, *J* = 246.7 Hz), 129.98 (d, *J* = 4.1 Hz), 129.51 (d, *J* = 8.2 Hz), 124.87 (d, *J* = 14.6 Hz), 124.11 (d, *J* = 3.4 Hz), 115.24 (d, *J* = 21.5 Hz), 66.62 (d, *J* = 3.7 Hz), 64.10, 43.77. IR (neat, cm^{-1}): 2915.91, 2849.02, 1722.13, 1491.74, 1455.84, 1093.29, 761.37. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{12}FO_2^+$: 183.0816, found 183.0818.



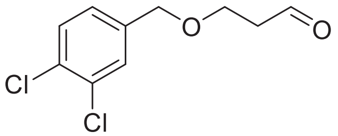
3-((2-bromobenzyl)oxy)propanal s2-g Yield: 85%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.83 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.43 (dd, *J* = 7.6, 0.4 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.15 (td, *J* = 7.9, 1.1 Hz, 1H), 4.60 (s, 2H), 3.90 (t, *J* = 6.0 Hz, 2H), 2.74 (td, *J* = 6.0, 1.7 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.96, 137.14, 132.53, 129.06, 127.42, 122.72, 72.46, 64.40, 43.79. IR (neat, cm^{-1}): 2917.57, 2848.19, 1723.23, 1469.56, 1439.25, 1105.20, 755.13. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{12}BrO_2^+$: 243.0015, found 243.0015.



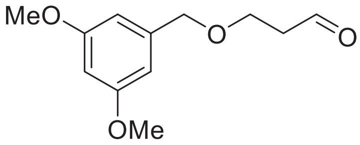
3-((2-methylbenzyl)oxy)propanal s2-h Yield: 88%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.80 (s, 1H), 7.29 (d, *J* = 6.7 Hz, 1H), 7.23 – 7.17 (m, 3H), 4.53 (s, 2H), 3.83 (t, *J* = 6.1 Hz, 2H), 2.70 (t, *J* = 6.0 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 201.08, 136.74, 135.65, 130.29, 128.63, 127.99, 125.77, 71.72, 63.90, 43.85, 18.73. IR (neat, cm^{-1}): 2916.69, 2848.97, 1723.53, 1462.16, 1360.93, 1259.04, 1093.09, 746.99. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{11}H_{15}O_2^+$: 179.1067, found 179.1068.



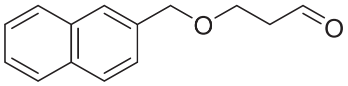
3-((3-bromobenzyl)oxy)propanal s2-i Yield: 82%. Hexanes /ethyl acetate = 6/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.47 (s, 1H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.25 – 7.19 (m, 2H), 4.49 (s, 2H), 3.81 (t, *J* = 6.1 Hz, 2H), 2.72 (t, *J* = 6.1 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.96, 137.14, 132.53, 129.06, 127.42, 122.72, 72.46, 64.40, 43.79. IR (neat, cm^{-1}): 2918.58, 2849.80, 1724.38, 1570.50, 1473.42, 1358.20, 1110.63, 781.22. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{12}BrO_2^+$: 243.0015, found 243.0013.



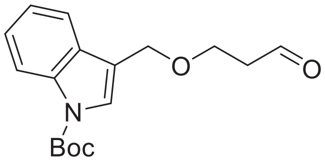
3-((3,4-dichlorobenzyl)oxy)propanal s2-j Yield: 85%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl3) δ 9.80 (s, 1H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.14 (dd, *J* = 8.2, 1.6 Hz, 1H), 4.47 (s, 2H), 3.81 (t, *J* = 6.0 Hz, 2H), 2.72 (td, *J* = 6.0, 1.6 Hz, 2H). 13C NMR (150 MHz, CDCl3) δ 200.56, 138.19, 132.50, 131.60, 130.38, 129.33, 126.67, 71.78, 64.07, 43.76. IR (neat, cm^{-1}): 2917.20, 2849.55, 1723.77, 1471.54, 1386.84, 1106.48, 1031.69, 819.23, 689.43. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{11}Cl_2O_2^+$: 233.0131, found 233.0135.



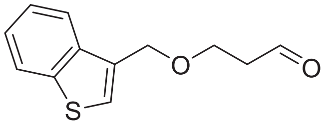
3-((3,5-dimethoxybenzyl)oxy)propanal s2-k Yield: 70%. Hexanes/ethyl acetate = 4/1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.80 (s, 1H), 6.48 (s, 2H), 6.39 (s, 1H), 4.47 (s, 2H), 3.80 (t, *J* = 6.4 Hz, 2H), 3.79 (s, 6H), 2.70 (t, *J* = 6.0 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 201.01, 160.90, 140.27, 105.33, 99.74, 73.16, 63.79, 55.31, 43.86. IR (neat, cm^{-1}): 2917.75, 2849.22, 1725.15, 1598.01, 1462.77, 1260.62, 1205.03, 1155.88, 1094.56, 805.93. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{12}H_{17}O_4^+$: 225.1121, found 225.1124.



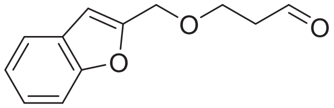
3-(naphthalen-2-ylmethoxy)propanal s2-l Yield: 80%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.82 (s, 1H), 7.84 (dd, *J* = 8.2, 3.2 Hz, 3H), 7.77 (s, 1H), 7.50 – 7.44 (m, 3H), 4.70 (s, 2H), 3.86 (t, *J* = 6.1 Hz, 2H), 2.72 (td, *J* = 6.1, 1.8 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.56, 138.19, 132.50, 131.60, 130.38, 129.33, 126.67, 71.78, 64.07, 43.76. IR (neat, cm^{-1}): 2920.54, 2850.47, 1723.46, 1368.19, 1096.92, 820.38, 754.45. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{14}H_{15}O_2^+$: 215.1067, found 215.1068.



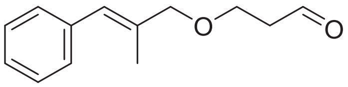
***tert*-butyl 3-((3-oxopropoxy)methyl)-1H-indole-1-carboxylate s2-m** Yield: 75%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.77 (s, 1H), 8.14 (s, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.57 (s, 1H), 7.35 – 7.32 (m, 1H), 7.27 – 7.24 (m, 1H), 4.69 (s, 2H), 3.83 (t, *J* = 6.1 Hz, 2H), 2.68 (td, *J* = 6.1, 1.7 Hz, 2H), 1.67 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 201.07, 149.61, 135.71, 129.53, 124.67, 124.64, 122.74, 119.51, 117.21, 115.24, 83.76, 64.95, 63.48, 43.83, 28.17. IR (neat, cm^{-1}): 2977.10, 2933.22, 2868.02, 1726.58, 1450.80, 1368.59, 1347.76, 1255.39, 1154.34, 1087.95, 1016.67, 855.00, 748.08. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{17}H_{22}NO_4^+$: 304.1543, found 304.1543.



3-(benzo[b]thiophen-3-ylmethoxy)propanal s2-n Yield: 85%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.77 (s, 1H), 7.86 (t, *J* = 8.9 Hz, 2H), 7.41 – 7.35 (m, 3H), 4.79 (s, 2H), 3.85 (t, *J* = 6.0 Hz, 2H), 2.70 (td, *J* = 6.0, 1.7 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.96, 140.63, 137.99, 132.88, 124.93, 124.55, 124.21, 122.76, 122.16, 67.57, 63.70, 43.80. IR (neat, cm^{-1}): 2917.78, 2849.70, 1722.24, 1460.76, 1427.55, 1104.62, 760.04, 735.84. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{12}H_{13}O_2S^+$: 221.0631, found 221.0632.



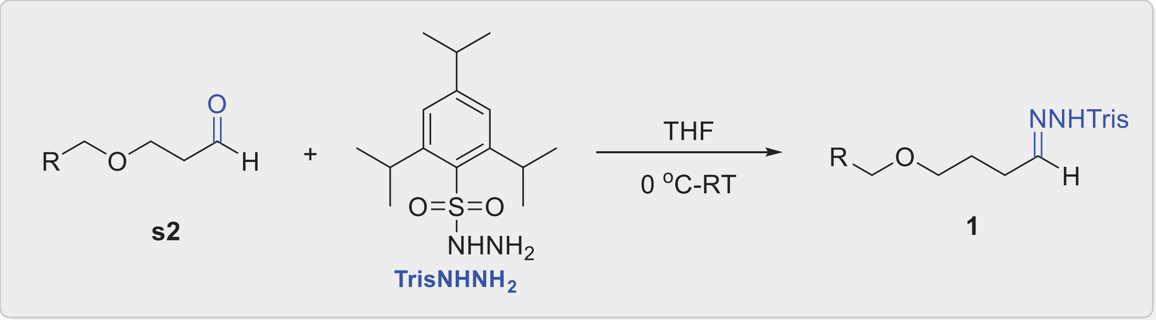
3-(benzofuran-2-ylmethoxy)propanal s2-o Yield: 88%. Hexanes/ethyl acetate = 5/1. ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.79 (s, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.30 – 7.27 (m, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 6.70 (s, 1H), 4.63 (s, 2H), 3.89 (t, *J* = 6.1 Hz, 2H), 2.72 (td, *J* = 6.1, 1.5 Hz, 2H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 200.72, 155.17, 153.84, 127.96, 124.48, 122.80, 121.10, 111.33, 105.90, 65.66, 64.05, 43.75. IR (neat, cm^{-1}): 2918.01, 2849.87, 1722.59, 1453.78, 1362.48, 1254.64, 1091.15, 942.89, 755.45. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{12}H_{13}O_3^+$: 205.0859, found 205.0861.



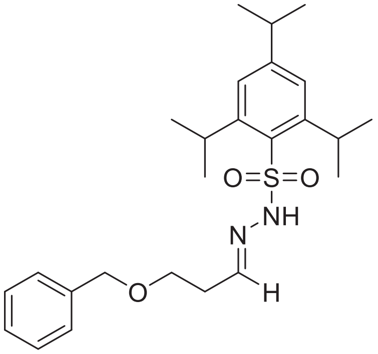
(*E*)-3-((2-methyl-3-phenylallyl)oxy)propanal, Yield: 90%. Hexanes/ethyl acetate = 6/1. ^{1}H NMR (600 MHz, CDCl$_3$) 9.83 (s, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 7.1 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.50 (s, 1H), 4.05 (s, 2H), 3.81 (t, *J* = 6.1 Hz, 2H), 2.71 (td, *J* = 6.1, 1.8 Hz, 2H), 1.89 (d, *J* = 1.1 Hz, 3H). ^{13}C NMR (150 MHz,

$CDCl_3$) δ 201.08, 137.30, 134.74, 128.85, 128.08, 127.16, 126.50, 76.79, 63.51, 43.86, 15.33. IR (neat, cm^{-1}): 2918.77, 2852.10, 1723.61, 1491.52, 1447.26, 1353.86, 1118.10, 751.06, 701.46. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{13}H_{17}O_2^+$: 205.1223, found 205.1226.

4.4.6 The Synthetic Procedure for Triisopropyl Sulfonylhydrazone Derivatives 1

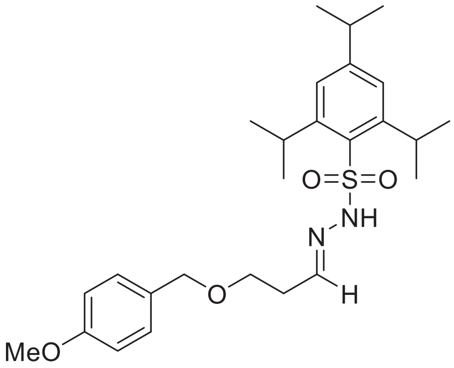


To a stirred solution of pure 2,4,6-triisopropylbenzenesulfonohydrazide ($TrisNHNH_2$, 2 mmol, 1 equiv.) in THF (10.0 mL) at 0 ºC, aldehyde **s2** (1 equiv.) was added dropwise (or portionwise if solid). The reaction was monitored by TLC. After the reaction was completed, the solvent was removed directly under reduced pressure, and the crude solid was further purified by flash column chromatography.

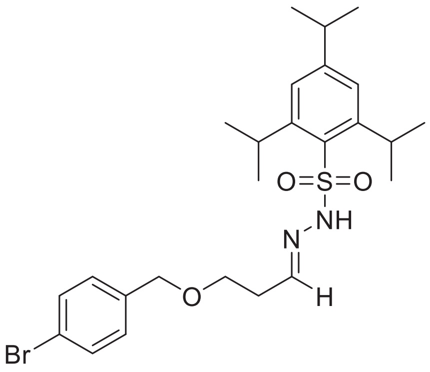


***N′*-(3-(benzyloxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide, 1-a** Yield: 85%. Hexanes/ethyl acetate = 5/1, R_f = 0.48. ^{1}H

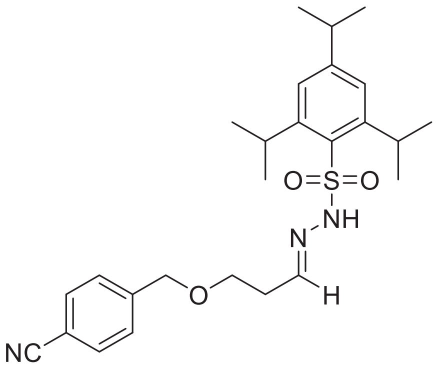
NMR (600 MHz, $CDCl_3$) δ 8.78 and 7.64 (s, 1H), 7.36 – 6.84 (m, 8H), 4.55 and 4.43 (s, 1H), 4.30 – 4.15 (m, 2H), 3.61 – 3.57 (m, 2H), 2.94 – 2.86 (m, 1H), 2.50 (dd, *J* = 11.7, 6.3 Hz, 1.25H) and 2.43 (q, *J* = 5.7 Hz, 0.75 H), 1.27 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.27 and 153.07, 151.30, 148.29 and 146.79, 137.90 and 136.96, 131.40 and 131.18, 128.55 and 128.39, 127.98 and 127.83, 127.68 and 127.63, 123.78 and 123.73, 73.44 and 72.98, 67.05 and 66.71, 34.14 and 32.83, 29.78, 28.63, 24.80, 23.52. IR (neat, cm^{-1}): 3224.85, 2961.17, 1599.51, 1395.35, 1155.78, 1119.83, 883.67, 657.75. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{25}H_{37}N_2O_3S^+$: 445.2519, found 445.2509.



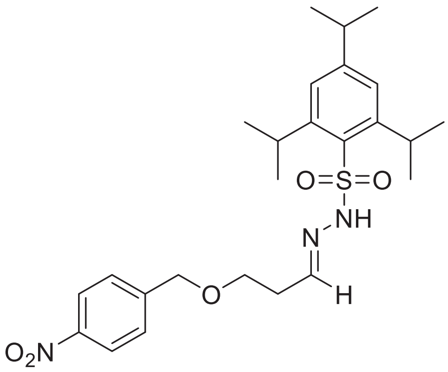
2,4,6-triisopropyl-*N'*-(3-((4-methoxybenzyl)oxy)-propylidene)benzenesulfonohydrazide, 1-b Yield: 88%. Hexanes/ethyl acetate = 4/1, R_f = 0.40. ^1H NMR (500 MHz, $CDCl_3$) δ 8.85 and 7.58 (s, 1H), 7.24 – 7.06 (m, 5H), 6.90 – 6.82 (m, 2H), 4.48 and 4.35 (s, 1H), 4.26 – 4.14 (m, 2H), 3.79 and 3.80 (s, 3H), 3.57 – 3.53 (m, 2H), 2.93 – 2.86 (m, 1H), 2.48 (dd, *J* = 11.7, 6.3 Hz, 1H), 2.40 (q, *J* = 5.7 Hz, 1H), 1.27 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.39 and 153.34, 151.32, 147.60 and 147.38, 146.21, 145.56, 144.45, 131.11, 127.94 and 127.62, 123.81 and 123.62, 72.25 and 71.67, 67.61, 34.14, 32.76, 29.91, 28.31, 24.79, 23.51.IR (neat, cm^{-1}): 3212.26, 2954.66, 1511.41, 1465.98, 1244.89, 1171.14, 1039.02, 662.77. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{26}H_{39}N_2O_4S^+$: 475.2625, found 475.2617.



***N′*-(3-((4-bromobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide, 1-c** Yield: 90%. Hexanes/ethyl acetate = 5/1, R_f = 0.43. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70 and 7.65 (s, 1H), 7.47 and 7.43 (d, *J* = 8.3 Hz, 2H), 7.21 (t, *J* = 5.1 Hz, 0.75H) and 6.84 (t, *J* = 5.7 Hz, 0.25H), 7.19 – 7.16 (m, 4H), 4.49 and 4.37 (s, 2H), 4.25 – 4.15 (m, 2H), 3.60 – 3.57 (m, 2H), 2.94 – 2.87 (m, 1H), 2.50 (dd, *J* = 11.6, 6.3 Hz, 1.5H) and 2.43 (q, *J* = 5.7 Hz, 0.5H), 1.26 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.33 and 153.17, 151.31, 148.01 and 146.55, 136.95 and 135.99, 131.69 and 131.49, 131.28 and 131.14, 129.42 and 129.20, 123.79 and 123.76, 121.93 and 121.53, 72.69 and 72.18, 67.13 and 66.91, 34.14 and 32.79, 29.90, 28.53, 24.79, 23.52. IR (neat, cm^{-1}): 3209.14, 2957.18, 2866.01, 1596.97, 1463.48, 1296.56, 1167.81, 1037.36, 844.29, 662.85. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{25}H_{36}BrN_2O_3S^+$: 523.1625, found 523.1606.

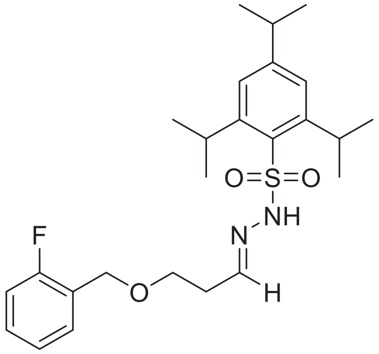


N′-(3-((4-cyanobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide, 1d Yield: 82%. Hexanes/ethyl acetate = 5/1, $R_f = 0.43$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 and 7.84 (s, 1H), 7.63 and 7.59 (d, *J* = 8.1 Hz, 2H), 7.42 and 7.36 (d, *J* = 8.0 Hz, 2H), 7.24 (t, *J* = 5.1 Hz, 0.75H) and 6.85 (t, *J* = 5.7 Hz, 0.25H), 7.17 and 7.17 (s, 2H), 4.59 and 4.47 (s, 1H), 4.24 – 4.15 (m, 2H), 3.66 (t, *J* = 5.7 Hz, 1H) and 3.63 (t, *J* = 6.4 Hz, 1H), 2.94 – 2.87 (m, 1H), 2.53 (dd, *J* = 11.7, 6.2 Hz, 1H) and 2.47 (q, *J* = 5.7 Hz, 1H), 1.26 – 1.23 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.3 and 153.30, 151.31, 147.63 and 146.31, 143.55 and 142.52, 132.38 and 132.19, 131.14 and 131.09, 127.86 and 127.62, 123.79, 118.75 and 118.65, 111.70 and 111.32, 72.46 and 71.91, 67.53 and 67.49, 34.13 and 32.75, 29.89, 28.36, 24.78 and 24.76, 23.51. IR (neat, cm^{-1}): 3211.76, 2958.73, 2929.21, 2866.98, 2227.58, 1597.12, 1167.10, 818.42, 662.14. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{26}H_{36}N_3O_3S^+$: 470.2472, found 470.2481.



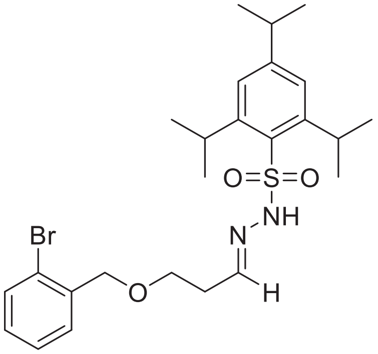
2,4,6-triisopropyl-N′-(3-((4-nitrobenzyl)oxy)propylidene)benzenesulfonohydrazide, 1e Yield: 80%. Hexanes/ethyl acetate = 5/1, $R_f =$

0.43. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.58 (s, 0.75H) and 7.81 (s, 0.25H), , 8.20 and 8.16 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 0.5H) and 7.41 (d, *J* = 8.3 Hz, 1.5H), 7.24 (t, *J* = 5.1 Hz, 0.75H) and 6.86 (t, *J* = 5.7 Hz, 0.25H), 7.17 (s, 2H), 4.64 and 4.52 (s, 2H), 4.26 – 4.16 (m, 2H), 3.68 (t, *J* = 5.7 Hz, 0.5H), 3.65 (t, *J* = 6.4 Hz, 1.5H), 2.94 – 2.87 (m, 1H), 2.54 (dd, *J* = 11.6, 6.2 Hz, 1.5H), 2.48 (q, *J* = 5.6 Hz, 0.5H), 1.26 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 153.39 and 153.33, 151.31, 147.59 and 147.33, 146.26, 145.58, 144.51, 131.11 and 131.04, 127.91 and 127.61, 123.80 and 123.60, 72.19 and 71.64, 67.60 and 67.57, 34.12 and 32.76, 29.90, 28.32, 24.78 and 24.76, 23.50. IR (neat, cm^{-1}): 3209.22, 2959.35, 2929.28, 2867.09, 1597.73, 1523.17, 1461.68, 1343.44, 1166.36, 883.46, 663.20, 564.39. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{25}H_{36}N_3O_5S^+$: 490.2370, found 490.2390.

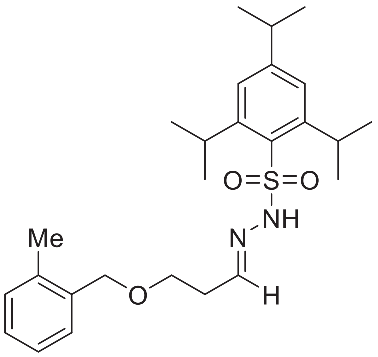


***N′*-(3-((2-fluorobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide, 1f** Yield: 88%. Hexanes/ethyl acetate = 5/1, R$_f$ = 0.45. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.65 and 7.64 (s, 1H), 7.44 – 7.28 (m, 1.5H) and 7.26 – 7.24 (m, 0.5H), 7.21 (t, *J* = 5.2 Hz, 0.75H) and 6.84 (t, *J* = 5.7 Hz, 0.25H), , 7.17 and 7.16 (s, 2H), 7.14 – 6.99 (m, 2H), 4.62 and 4.49 (s, 2H), 4.24 – 4.15 (m, 2H), 3.65 (t, *J* = 5.7 Hz, 0.5H) and 3.61 (t, *J* = 6.4 Hz, 1.5H), 2.92 – 2.87 (m, 1H), 2.50 (dd, *J* = 11.8, 6.3 Hz, 1.5H), 2.43 (q, *J* = 5.7 Hz, 0.5H), 1.26 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 161.48 and 159.87, 153.28 and 153.11, 151.30, 148.20 and 146.64, 131.35 and 131.16, 130.22 and

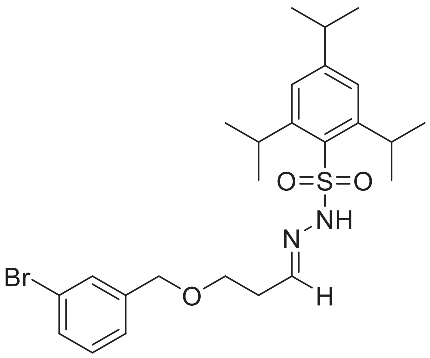
129.97, 129.81 and 129.48, 125.00 and 124.90, 124.39 and 124.09, 123.78 and 123.74, 115.29 and 115.15, 67.34 and 67.02, 66.70 and 66.42, 34.14 and 32.77, 29.90, 28.52, 24.78, 23.52. IR (neat, cm^{-1}): 2958.40, 2928.30, 2868.48, 1599.08, 1456.60, 1151.84, 881.86, 756.75, 660.84. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{25}H_{36}FN_2O_3S^+$: 463.2425, found 463.2420.



***N′*-(3-((2-bromobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide 1g** Yield: 85%. Hexanes/ethyl acetate = 5/1, R_f = 0.46. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.62 and 7.57 (s, 1H), 7.54 and 7.52 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.42 and 7.36 (dd, *J* = 7.6, 1.4 Hz, 2H), 7.32 (td, *J* = 7.5, 1.0 Hz, 1H), 7.24 (t, *J* = 5.3 Hz, 0.7H) and 6.89 (t, *J* = 5.6 Hz, 0.3H), 7.17 and 7.16 (s, 2H), 7.13 and 7.26 (td, *J* = 7.8, 1.6 Hz, 1H), 4.62 and 4.49 (s, 2H), 4.23 – 4.14 (m, 2H), 3.70 (t, *J* = 5.7 Hz, 0.65H), 3.66 (t, *J* = 6.4 Hz, 1.35H), 2.94 – 2.85 (m, 1H), 2.54 (dd, *J* = 11.6, 6.3 Hz, 1.35H) and 2.47 (dd, *J* = 11.4, 5.7 Hz, 0.65H), 1.27 – 1.23 (m, 18H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.29 and 153.11, 151.32, 148.21 and 146.69, 137.23, 132.62 and 132.53, 131.37 and 131.17, 129.35 and 129.33, 129.11 and 129.02, 127.66 and 127.40, 123.79 and 123.69, 122.82 and 122.76, 72.65 and 72.27, 67.62 and 67.30, 34.14 and 32.81, 29.92, 28.51, 24.80, 23.52. IR (neat, cm^{-1}): 3212.41, 2964.09, 2926.76, 2869.85, 1598.22, 1438.82, 1157.54, 1019.73, 878.43, 659.07. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{25}H_{36}BrN_2O_3S^+$: 523.1625, found 523.1627.

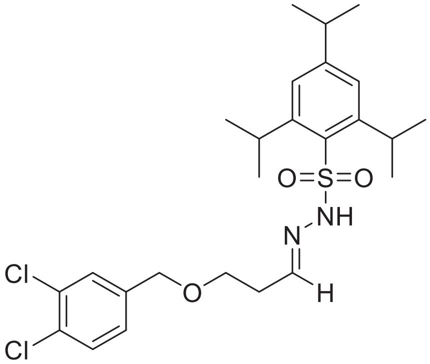


2,4,6-triisopropyl-*N′*-(3-((2-methylbenzyl)oxy)propylidene)benzenesulfonohydrazide, 1h Yield: 92%. Hexanes/ethyl acetate = 5/1, R_f = 0.47. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.70 and 7.59 (s, 1H), 7.28 – 7.25 (m, 0.75H) and 6.84 (t, *J* = 5.6 Hz, 0.25H), 7.23 – 7.06 (m, 6H), 4.57 and 4.43 (s, 2H), 4.24 – 4.15 (m, 2H), 3.60 (t, *J* = 6.3 Hz, 2H), 2.94 – 2.87 (m, 1H), 2.50 (dd, *J* = 11.8, 6.2 Hz, 1.5H), 2.42 (q, *J* = 5.7 Hz, 0.5H), 2.32 and 2.26 (s, 3H), 1.27 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 153.28 and 153.07, 151.31 and 151.26, 148.36 and 146.78, 136.76 and 136.64, 135.75 and 134.85, 131.41 and 131.18, 130.40 and 130.24, 128.79 and 128.49, 128.19 and 127.92, 125.86 and 125.77, 123.79 and 123.73, 71.76 and 71.45, 67.16 and 66.62, 34.15 and 32.87, 29.91, 28.59, 24.80, 23.53, 18.83 and 18.71. IR (neat, cm^{-1}): 3201.67, 2958.41, 2867.70, 1598.99, 1460.38, 1425.05, 1152.31, 1092.57, 882.48, 738.87, 661.45. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{26}H_{39}N_2O_3S^+$: 459.2676, found 459.2693.

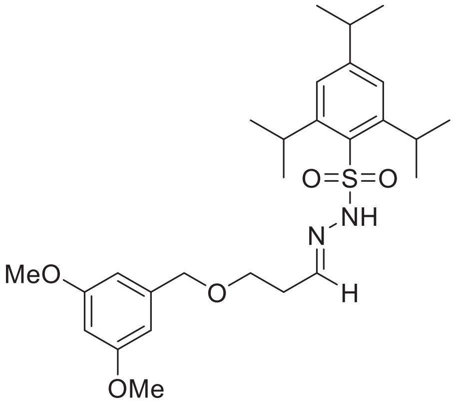


***N′*-(3-((3-bromobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide 1i** Yield: 91%. Hexanes/ethyl acetate = 5/1, R_f = 0.46.

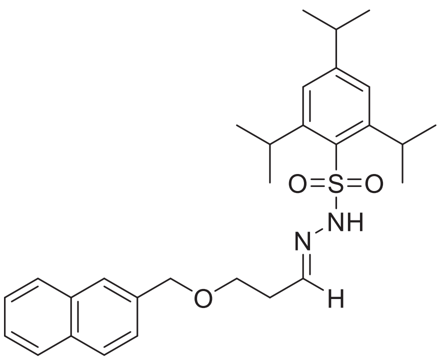
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.62 and 7.64 (s, 1H), 7.55 – 7.23 (m, 3H), 7.22 (t, J = 5.0 Hz, 0.75H) and 6.84 (t, J = 5.6 Hz, 0.25H), 7.18 – 7.17 (m, 3H), 4.51 and 4.38 (s, 2H), 4.24 – 4.15 (m, 2H), 3.61 – 3.57 (m, 2H), 2.94 – 2.87 (m, 1H), 2.51 (dd, J = 11.7, 6.3 Hz, 1.35H) and 2.43 (q, J = 5.7 Hz, 0.65H), 1.27 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 153.31 and 153.16, 151.30, 147.97 and 146.53, 140.31 and 139.37, 131.13 and 131.06, 130.72 and 130.62, 130.45 and 130.25, 129.99, 126.30 and 126.00, 123.79 and 123.76, 122.55 and 122.50, 72.57 and 72.12, 67.27 and 66.94, 34.04 and 32.77, 29.77, 28.44, 24.80, 23.52. IR (neat, cm^{-1}): 3212.46, 2956.46, 2865.72, 1597.14, 1462.40, 1165.77, 1104.87, 883.46, 778.18, 664.33. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{25}H_{36}BrN_2O_3S^+$: 523.1625, found 523.1625.



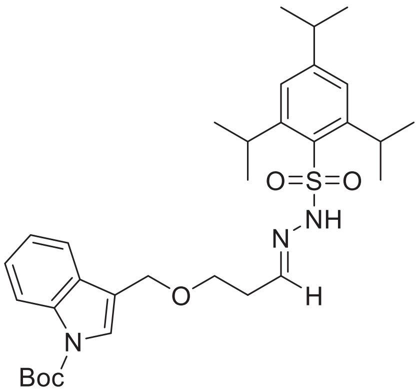
N'-(3-((3,4-dichlorobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide 1j Yield: 92%. Hexanes/ethyl acetate = 5/1, R_f = 0.45. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.60 and 7.73 (s, 1H), 7.42 – 7.34 (m, 2H), 7.22 (t, J = 5.1 Hz, 0.75H) and 6.84 (t, J = 5.6 Hz, 0.25H), , 7.17 (s, 2H), 7.08 (dd, J = 8.2, 1.9 Hz, 1H), 4.48 and 4.36 (s, 2H), 4.24 – 4.14 (m, 2H), 3.62 – 3.57 (m, 2H), 2.92 – 2.87 (m, 1H), 2.51 (dd, J = 11.6, 6.4 Hz, 1.3H) and 2.44 (q, J = 5.7 Hz, 0.7H), 1.26 – 1.24 (m, 18H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.35 and 153.24, 151.30, 147.76 and 146.38, 138.28 and 137.34, 132.59 and 132.45, 131.96 and 131.55, 131.16 and 131.12, 130.65 and 130.38, 129.50 and 129.29, 126.97 and 126.67, 123.79, 72.00 and 71.52, 67.31 and 67.06, 34.14 and 32.75, 29.90, 28.37, 24.79, 23.51. IR (neat, cm^{-1}): 3209.21, 2957.31, 2930.18, 2866.48, 1597.03, 1462.47, 1296.39, 1167.29, 1104.74, 883.98, 817.88, 664.11, 564.71. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{25}H_{35}Cl_2N_2O_3S^+$: 513.1740, found 513.1741.



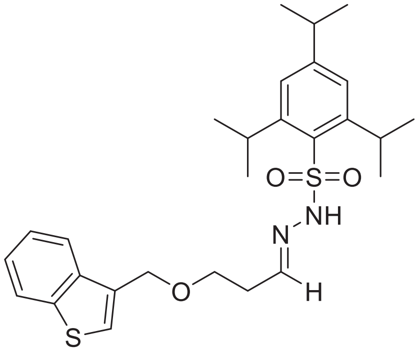
***N′*-(3-((3,5-Dimethoxybenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide 1k** Yield: 90%. Hexanes/ethyl acetate = 5/1, $R_f = 0.40$. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.82 and 7.58 (s, 1H), 7.21 (t, *J* = 5.1 Hz, 0.7H) and 6.85 (t, *J* = 5.7 Hz, 0.3H), 7.17 and 7.16 (s, 2H), 6.46 and 6.43 (s, 2H), 6.39 and 6.37 (s, 1H), 4.49 and 4.37 (s, 2H), 4.25 – 4.15 (m, 2H), 3.78 (s, 6H), 3.59 – 3.56 (m, 2H), 2.93 – 2.87 (m, 1H), 2.50 (dd, *J* = 12.1, 6.1 Hz, 1.3H) and 2.43 (q, *J* = 5.6 Hz, 0.7H), 1.26 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.98 and 160.87, 153.29 and 153.10, 151.34 and 151.29, 148.32 and 146.91, 140.33 and 139.33, 131.34 and 131.17, 123.79 and 123.73, 105.45 and 105.42, 100.24 and 99.62, 73.36 and 72.95, 67.05 and 66.67, 55.38 and 55.31, 34.14 and 32.84, 29.94 and 29.91, 28.65, 24.79, 23.52. IR (neat, cm^{-1}): 2957.32, 2867.92, 1597.55, 1460.34, 1428.19, 1203.65, 1152.06, 1059.12, 883.05, 661.95. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{27}H_{41}N_2O_5S^+$: 505.2731, found 505.2732.



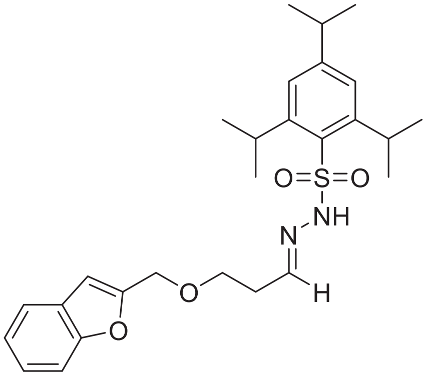
2,4,6-triisopropyl-*N′*-(3-(naphthalen-2-ylmethoxy)-propylidene)benzenesulfonohydrazide 1l Yield: 87%. Hexanes/ethyl acetate = 5/1, R_f = 0.44. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.83 (s, 1H) and 7.52 (s, 1H), 7.89 – 7.71 (m, 4H), 7.48 – 7.38 (m, 3H), 7.22 (t, *J* = 5.2 Hz, 0.65H) and 6.86 (t, *J* = 5.8 Hz, 0.35H), 7.16 (s, 2H), 4.72 and 4.59 (s, 2H), 4.26 – 4.16 (m, 2H), 3.64 – 3.61 (m, 2H), 2.92 – 2.85 (m, 1H), 2.52 (dd, *J* = 11.8, 6.1 Hz, 1.3H) and 2.44 (q, *J* = 5.7 Hz, 0.7H), 1.26 – 1.23 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.30 and 153.10, 151.34 and 151.31, 148.36 and 146.81, 135.37 and 134.38, 133.22, 128.47 and 128.23, 127.98 and 127.83, 127.67, 126.77, 126.46, 126.22, 126.14 and 126.07, 125.92, 125.63 and 125.58, 123.79 and 123.75, 73.60 and 73.13, 67.07 and 66.80, 34.15 and 32.87, 29.92, 28.69, 24.80, 23.52. IR (neat, cm^{-1}): 3207.88, 2958.29, 2867.50, 1599.43, 1461.03, 1319.48, 1152.48, 1124.57, 881.53, 815.88, 660.69. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{29}H_{39}N_2O_3S^+$: 495.2676, found 495.2662.



***tert*-butyl 3-((3-(2-((2,4,6-triisopropylphenyl)-sulfonyl)hydrazineylidene)propoxy)methyl)-1H-indole-1-carboxylate, 1m** Yield: 82%. Hexanes/ethyl acetate = 4/1, R_f = 0.46. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79 and 7.53 (s, 1H), 8.13 (s, 1H), 7.60 – 7.57 (m, 2H), 7.34 – 7.31 (m, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.17 (s, 2H), 7.15 (t, *J* = 5.1 Hz, 0.7H) and 6.81 (t, *J* = 5.7 Hz, 0.3H), 4.72 and 4.58 (s, 1H), 4.25 – 4.15 (m, 2H), 3.60 – 3.58 (m, 2H), 2.93 – 2.86 (m, 1H), 2.48 (dd, *J* = 11.8, 6.3 Hz, 1.25H) and 2.39 (q, *J* = 5.7 Hz, 0.75H), 1.67 (s, 9H), 1.26 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.25 and 153.06, 151.28, 149.60, 148.33 and 146.76, 135.68, 131.46 and 131.19, 129.54 and 129.35, 125.15, 124.70 and 124.63, 123.77 and 123.73, 122.89 and 122.70, 119.50 and 119.38, 117.28 and 116.36, 115.26 and 115.24, 83.88 and 83.77, 66.63 and 66.19, 64.88 and 64.58, 34.13 and 32.82, 29.93 and 29.89, 28.17, 24.79, 23.51. IR (neat, cm^{-1}): 2959.97, 2930.32, 2868.50, 1731.77, 1599.45, 1451.40, 1368.95, 1255.90, 1152.25, 1088.25, 746.22, 661.28. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{32}H_{46}N_3O_5S^+$: 584.3153, found 584.3143.

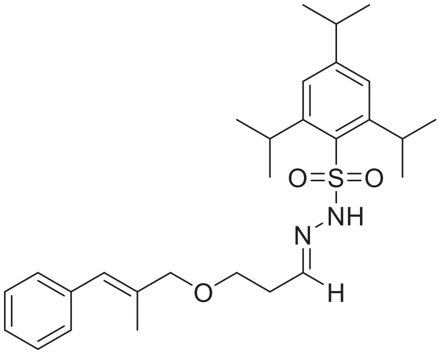


***N′*-(3-(benzo[b]thiophen-3-ylmethoxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide, 1n** Yield: 85%. Hexanes/ethyl acetate = 4/1, $R_f = 0.47$. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.76 and 7.71 (s, 1H), 7.88 – 7.79 (m, 2H), 7.39 – 7.29 (m, 3H), 7.18 (s, 2H), 7.16 (t, *J* = 5.2 Hz, 0.7H) and 6.82 (t, *J* = 5.6 Hz, 0.3H), 4.81 and 4.68 (s, 2H), 4.26 – 4.16 (m, 2H), 3.65 – 3.59 (m, 2H), 2.94 – 2.87 (m, 1H), 2.49 (dd, *J* = 11.7, 6.2 Hz, 1.3H) and 2.41 (q, *J* = 5.7 Hz, 0.7H), 1.27 – 1.25 (m, 18H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 153.27 and 153.13, 151.29, 148.18 and 146.72, 140.59, 137.97 and 137.79, 132.90 and 132.06, 131.36 and 131.19, 125.48 and 124.80, 124.60 and 124.51, 124.35 and 124.16, 123.78 and 123.75, 122.74, 122.10 and 122.04, 67.44 and 67.23, 66.89 and 66.49, 34.12 and 32.80, 29.89, 28.46, 24.79, 23.51. IR (neat, cm^{-1}): 3200.82, 2957.90, 2867.22, 1598.92, 1460.58, 1425.96, 1317.52, 1152.20, 1102.53, 1070.93, 881.20, 756.58, 660.44. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{27}H_{37}N_2O_3S_2^+$: 501.2240, found 501.2237.



***N′*-(3-(benzofuran-2-ylmethoxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide, 1o** Yield: 80%. Hexanes/ethyl acetate = 4/1, R_f =

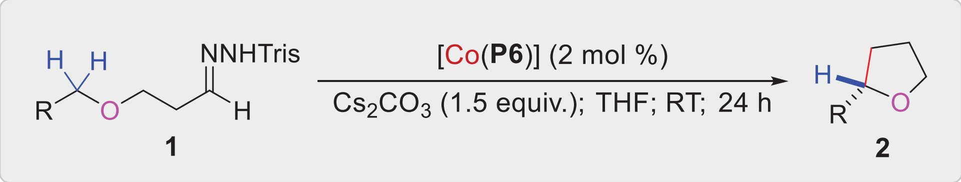
0.43. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 and 7.77 (s, 1H), 7.31 – 7.26 (m, 1H), 7.23 – 7.21 (m, 1H), 7.20 (t, *J* = 5.2 Hz, 0.7H) and 6.84 (t, *J* = 5.7 Hz, 0.3H), , 7.17 (s, 2H), 6.71 and 6.63 (s, 1H), 4.64 and 4.51 (s, 2H), 4.26 – 4.17 (m, 2H), 3.70 (t, *J* = 5.7 Hz, 0.7H) and 3.65 (t, *J* = 6.5 Hz, 1.3H), 2.90 (hept, *J* = 6.9 Hz, 1H), 2.50 (dd, *J* = 11.7, 6.4 Hz, 1.3H) and 2.43 (q, *J* = 5.7 Hz, 0.7H), 1.27 – 1.24 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.16 and 155.12, 153.89 and 153.27, 153.17 and 153.12, 151.31 and 151.27, 147.84 and 146.61, 131.32 and 131.16, 127.93 and 127.88, 124.58 and 124.42, 123.76 and 123.73, 122.84 and 122.77, 121.16 and 121.06, 111.40 and 111.28, 106.24 and 105.76, 67.28 and 67.02, 65.64 and 65.34, 34.12 and 32.71, 29.88, 28.42, 24.78, 23.50. IR (neat, cm^{-1}): 3208.79, 2959.39, 2929.46, 2867.69, 1595.86, 1454.43, 1165.50, 1101.37, 940.01, 885.26, 662.51. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{27}H_{37}N_2O_4S^+$: 485.2468, found 485.2463.



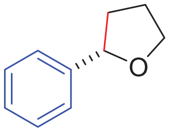
2,4,6-triisopropyl-*N′*-3-(((E)-2-methyl-3-phenylallyl)oxy)propylidene)benzenesulfonohydrazide, 1p Yield: 90%. Hexanes/ethyl acetate = 4/1, R_f = 0.47. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.89 and 7.76 (s, 1H), 7.34 – 7.31 (m, 2H), 7.29 (d, *J* = 7.0 Hz, 1H), 7.26 – 7.20 (m, 2.7H) and 6.89 (t, *J* = 5.7 Hz, 0.3H), 7.17 (s, 2H), 6.48 and 6.44 (s, 1H), 4.30 – 4.17 (m, 2H), 4.07 and 3.94 (s, 2H), 3.62 (t, *J* = 5.6 Hz, 0.75H) and 3.57 (t, *J* = 6.5 Hz, 1.25H), 2.93 – 2.86 (m, 1H), 2.51 (dd, *J* = 11.7, 6.4 Hz, 1.25H) and 2.46 (dd, *J* = 11.3, 5.7 Hz, 0.75H), 1.89 and 1.81 (s, 3H), 1.28 – 1.25 (m, 18H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 153.26 and 153.07, 151.30, 148.28, 146.88, 137.31 and 137.08, 134.84 and 134.00, 131.40 and 131.19, 128.88 and 128.09, 127.11, 126.48, 123.74, 77.70 and 77.06, 66.78 and 66.64, 34.14 and 32.87, 29.92 and 29.87, 28.67, 24.81 and 24.78, 23.52, 15.42. IR (neat, cm^{-1}): 2957.72, 2927.19, 2867.29, 1598.95, 1460.64, 1361.95, 1316.87, 1163.73, 1152.35, 881.15, 745.83, 661.15. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{27}H_{37}N_2O_4S^+$: 485.2832, found 485.44.

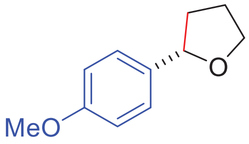
4.4.7 General Procedure for [Co(P6)]-Catalyzed Enantioselective Radical C–H Alkylation



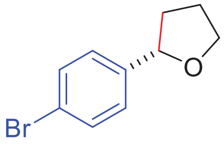
An oven-dried Schlenk tube was charged with sulfonyl hydrazone **1** (0.1 mmol), [Co(**P6**)] (2 mol %) and Cs_2CO_3 (0.2 mmol). The Schlenk tube was then evacuated and back filled with nitrogen for 3 times. The Teflon screw cap was replaced with a rubber septum, THF (0.8 mL) was added via a gastight syringe. 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 RT. After 24 h, the reaction mixture was filtrated through a short pad of silica gel, concentrated under vacuum and purified by flash column chromatography. The fractions containing product were collected and concentrated under vacuum to afford the desired compound **2**.



(*S*)-2-phenyltetrahydrofuran 2a Known compound.[2f] Yield: 90%. Hexanes/ethyl acetate = 10/1, R_f = 0.35. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.09 (m, 1H), 4.87 (t, *J* = 7.2 Hz, 1H), 4.08 (dd, *J* = 14.8, 7.0 Hz, 1H), 3.92 (dd, *J* = 14.5, 7.6 Hz, 1H), 2.30 (td, *J* = 12.5, 7.0 Hz, 1H), 2.05 – 1.90 (m, 1H), 1.79 (ddd, *J* = 16.0, 12.2, 7.7 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. IR (neat, cm^{-1}): 2970.44, 2866.20, 1737.63, 1492.89, 1451.35, 1060.06, 754.81. HPLC analysis: *ee* = 92%. ADH (100% hexanes, 0.8 mL/min): t_{major} = 41.49 min, t_{minor} = 50.92 min. $[\alpha]^{20}{}_D$ = -8.6 (*c* = 0.5, $CHCl_3$).

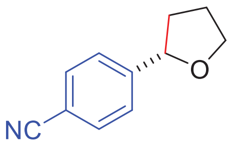


(*S*)-2-(4-methoxyphenyl)tetrahydrofuran 2b Known compound.[15] Yield: 91%. Hexanes/ethyl acetate = 6/1, R_f = 0.40. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.83 (t, *J* = 7.2 Hz, 1H), 4.08 (dd, *J* = 14.4, 7.5 Hz, 1H), 3.91 (td, *J* = 8.0, 6.3 Hz, 1H), 3.80 (s, 3H), 2.30 – 2.25 (m, 1H), 2.06 – 1.95 (m, 2H), 1.82 – 1.76 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.78, 135.31, 126.93, 113.67, 80.42, 68.46, 55.26, 34.44, 26.05. IR (neat, cm^{-1}): 2950.38, 2866.99, 1612.68, 1511.76, 1242.25, 1056.98, 1033.29, 827.29. HPLC analysis: *ee* = 91%. IF (99% hexanes, 0.8 mL/min): t_{major} = 26.04 min, t_{minor} = 28.58 min. $[\alpha]^{20}{}_D$ = -15.6 (*c* = 0.5, $CHCl_3$).

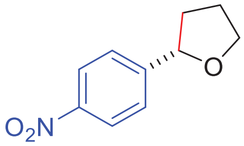


(*S*)-2-(4-bromophenyl)tetrahydrofuran 2c Yield: 92%. Hexanes/ethyl acetate = 8/1, R_f = 0.40 ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J*

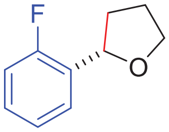
= 8.4 Hz, 2H), 4.84 (t, *J* = 7.2 Hz, 1H), 4.08 (dd, *J* = 15.0, 6.9 Hz, 1H), 3.93 (dd, *J* = 15.0, 7.2 Hz, 1H), 2.31 (td, *J* = 12.9, 6.8 Hz, 1H), 2.02 – 1.97 (m, 2H), 1.74 (dq, *J* = 12.3, 7.8 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.56, 131.31, 127.31, 120.77, 79.98, 68.70, 34.62, 25.93. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{12}BrO^+$: 227.0066, found 227.0060. IR (neat, cm^{-1}): 2943.11, 2864.95, 1485.52, 1068.49, 1023.69, 821.29. HPLC analysis: *ee* = 95%. IE (99.8% hexanes, 0.8 mL/min): t_{major} = 24.57 min, t_{minor} = 27.92 min. $[\alpha]^{20}{}_D$ = -51.6 (*c* = 0.5, $CHCl_3$).



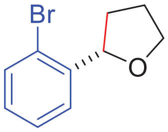
(*S*)-4-(tetrahydrofuran-2-yl)benzonitrile 2d Yield: 90%. Hexanes/ethyl acetate = 8/1, R_f = 0.30. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 4.93 (t, *J* = 7.2 Hz, 1H), 4.10 (dd, *J* = 15.0, 6.9 Hz, 1H), 3.96 (dd, *J* = 15.0, 7.5 Hz, 1H), 2.38 (td, *J* = 13.0, 7.1 Hz, 1H), 2.04 – 1.98 (m, 2H), 1.74 (dq, *J* = 12.3, 7.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.20, 132.15, 126.13, 118.93, 110.80, 79.81, 68.93, 34.68, 25.91. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{11}H_{11}NO^+$: 174.0913, found 174.0912. IR (neat, cm^{-1}): 2923.56, 2868.89, 2226.75, 1610.33, 1067.01, 841.80. HPLC analysis: *ee* = 95%. IF (99% hexanes, 0.8 mL/min): t_{major} = 37.09 min, t_{minor} = 39.60 min. $[\alpha]^{20}{}_D$ = -25.2 (*c* = 0.5, $CHCl_3$).



(*S*)-2-(4-nitrophenyl)tetrahydrofuran 2e Yield: 75%. Hexanes/ethyl acetate = 6/1, R_f = 0.40. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 8.8 Hz, 2H), 4.98 (t, *J* = 7.3 Hz, 1H), 4.12 (dd, *J* = 15.0, 7.0 Hz, 1H), 3.98 (dd, *J* = 14.5, 7.7 Hz, 1H), 2.41 (td, *J* = 12.8, 7.2 Hz, 1H), 2.07 – 1.98 (m, 2H), 1.76 (dq, *J* = 12.4, 7.8 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 151.29, 147.06, 126.16, 123.59, 79.66, 69.00, 34.78, 25.93. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{12}NO_3^+$: 194.0812, found 194.0802. IR (neat, cm^{-1}): 2940.96, 2878.74, 1603.94, 1513.34, 1339.90, 1064.01, 847.74, 746.99, 697.42. HPLC analysis: *ee* = 95%. IF (99% hexanes, 0.8 mL/min): t_{major} = 40.09 min, t_{minor} = 41.82 min. $[\alpha]^{20}{}_D$ = -21.2 (*c* = 0.5, $CHCl_3$).

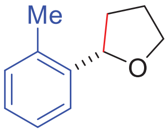


(*S*)-2-(2-fluorophenyl)tetrahydrofuran 2f Yield: 75%. Hexanes/ethyl acetate = 9/1, R_f = 0.45. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (t, *J* = 7.5 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.02 – 6.98 (m, 1H), 5.14 (t, *J* = 7.1 Hz, 1H), 4.10 (dd, *J* = 14.5, 7.1 Hz, 1H), 3.94 (dd, *J* = 14.7, 7.3 Hz, 1H), 2.40 (dq, *J* = 13.4, 6.8 Hz, 1H), 2.00 (p, *J* = 7.0 Hz, 2H), 1.79 (dq, *J* = 15.2, 7.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.78 (d, *J* = 245.6 Hz), 130.81 (d, *J* = 13.4 Hz), 128.37 (d, *J* = 8.1 Hz), 126.77 (d, *J* = 4.7 Hz), 123.95 (d, *J* = 3.3 Hz), 115.03 (d, *J* = 21.3 Hz), 75.05 (d, *J* = 2.4 Hz), 68.67, 33.48, 25.95. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{10}H_{12}FO^+$: 167.0867, found 167.0866. IR (neat, cm^{-1}): 2927.17, 2869.89, 1486.48, 1455.96, 1230.70, 1064.79, 760.04. HPLC analysis: *ee* = 90%. IA (100% hexanes, 0.8 mL/min): t_{major} = 32.01 min, t_{minor} = 34.76 min. $[\alpha]^{20}{}_D$ = -21.6 (*c* = 0.5, $CHCl_3$).

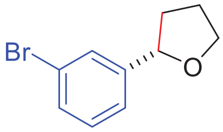


(*S*)-2-(2-bromophenyl)tetrahydrofuran 2g Yield: 78%. Hexanes/ethyl acetate = 8/1, R_f = 0.40. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 7.1, 4.3 Hz, 2H), 7.30

(t, J = 7.5 Hz, 1H), 7.10 (td, J = 7.8, 1.5 Hz, 1H), 5.16 (t, J = 7.0 Hz, 1H), 4.17 (dd, J = 13.6, 7.6 Hz, 1H), 3.96 (dd, J = 15.0, 7.3 Hz, 1H), 2.54 (dt, J = 14.0, 7.2 Hz, 1H), 2.02 – 1.93 (m, 2H), 1.69 (dt, J = 14.6, 7.1 Hz, 1H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 143.18, 132.48, 128.33, 127.39, 126.55, 121.31, 79.81, 69.12, 33.35, 25.76. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{12}BrO^+$: 227.0066, found 227.0067. IR (neat, cm^{-1}): 2945.59, 2866.07, 1466.24, 1439.40, 1069.77, 1022.85, 754.04. HPLC analysis: *ee* = 90%. IE (99.8% hexanes, 0.8 mL/min): t_{major} = 19.48 min, t_{minor} = 22.94 min. $[\alpha]^{20}{}_D$ = -44.8 (c = 0.5, CHCl$_3$).

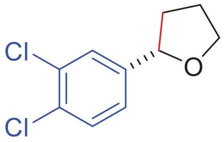


(*S*)-2-(o-tolyl)tetrahydrofuran 2h Yield: 84%. Hexanes/ethyl acetate = 8/1, R$_f$ = 0.40. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.45 (d, J = 7.6 Hz, 1H), 7.20 (t, J = 7.4 Hz, 1H), 7.17 – 7.12 (m, 2H), 5.07 (t, J = 7.2 Hz, 1H), 4.16 (dt, J = 13.5, 6.9 Hz, 1H), 3.94 (dd, J = 15.1, 7.2 Hz, 1H), 2.36 (dt, J = 12.8, 7.3 Hz, 1H), 2.32 (s, 3H), 2.05 – 1.97 (m, 2H), 1.69 (ddd, J = 15.5, 12.3, 7.4 Hz, 1H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 141.79, 134.15, 130.09, 126.73, 125.96, 124.51, 77.94, 68.61, 33.13, 26.01, 19.21. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{11}H_{15}O^+$: 163.1117, found 163.1124. IR (neat, cm^{-1}): 2947.16, 2864.46, 1485.17, 1460.71, 1064.47, 753.25. HPLC analysis: *ee* = 94%. IE (99.8% hexanes, 0.8 mL/min): t_{major} = 23.28 min, t_{minor} = 28.95 min. $[\alpha]^{20}{}_D$ = -69.6 (c = 0.5, CHCl$_3$).

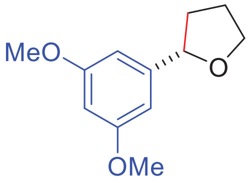


(*S*)-2-(3-bromophenyl)tetrahydrofuran 2i Yield: 88%. Hexanes/ethyl acetate = 8/1, R$_f$ = 0.40. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.49 (s, 1H), 7.37 (d, J = 7.7 Hz, 1H), 7.24 (d, J = 7.7 Hz, 1H), 7.19 (t, J = 7.7 Hz, 1H), 4.86 (t, J = 7.1 Hz, 1H), 4.09 (dd, J

= 14.8, 7.0 Hz, 1H), 3.93 (dd, *J* = 14.8, 7.4 Hz, 1H), 2.33 (td, *J* = 12.9, 6.9 Hz, 1H), 2.03 – 1.97 (m, 2H), 1.77 (dq, *J* = 12.4, 7.7 Hz, 1H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 146.00, 130.10, 129.84, 128.61, 124.18, 122.47, 79.85, 68.77, 34.64, 25.91. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{12}BrO^+$: 227.0066, found 227.0062. IR (neat, cm^{-1}): 2947.42, 2868.36, 1596.40, 1567.98, 1474.11, 1425.29, 1207.38, 1063.85, 781.60. 758.50. HPLC analysis: *ee* = 96%. IE (99.8% hexanes, 0.8 mL/min): t_{major} = 28.81 min, t_{minor} = 24.82 min. $[\alpha]^{20}{}_D$ = -18.8 (*c* = 0.5, CHCl$_3$).

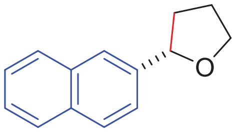


(*S*)-2-(3,4-dichlorophenyl)tetrahydrofuran 2j Yield: 93%. Hexanes/ethyl acetate = 8/1, R$_f$ = 0.45. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.43 (d, *J* = 1.9 Hz, 1H), 7.38 (d, *J* = 8.3 Hz, 1H), 7.15 (dd, *J* = 8.3, 1.9 Hz, 1H), 4.84 (t, *J* = 7.1 Hz, 1H), 4.08 (dd, *J* = 15.0, 6.9 Hz, 1H), 3.93 (dd, *J* = 15.2, 7.0 Hz, 1H), 2.33 (dq, *J* = 13.4, 6.7 Hz, 1H), 2.02 – 1.97 (m, 2H), 1.74 (dq, *J* = 12.3, 7.7 Hz, 1H). ^{13}C NMR (150 MHz, CDCl$_3$) 143.99, 132.35, 130.80, 130.22, 127.56, 124.93, 79.35, 68.81, 34.63, 25.87. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{10}H_{11}Cl_2O^+$: 217.0181, found 217.0177. IR (neat, cm^{-1}): 2948.17, 2868.14, 1737.97, 1468.76, 1068.35, 1029.96, 822.24. HPLC analysis: *ee* = 94%. IE (99.8% hexanes, 0.8 mL/min): t_{major} = 24.77 min, t_{minor} = 21.86 min. $[\alpha]^{20}{}_D$ = -51.2 (*c* = 0.5, CHCl$_3$).

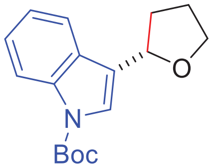


(*S*)-2-(3,5-dimethoxyphenyl)tetrahydrofuran 2k Yield: 84%. Hexanes/ethyl acetate = 7/1, R$_f$ = 0.36. ^{1}H NMR (600 MHz, CDCl$_3$) δ 6.50 (d, *J* = 2.3 Hz, 2H), 6.35 (t, *J* = 2.3 Hz, 1H), 4.85 (t, *J* = 7.1 Hz, 1H), 4.08 (dd, *J* = 14.7, 7.1 Hz, 1H), 3.93

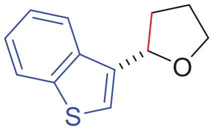
(dt, *J* = 14.4, 7.3 Hz, 1H), 3.79 (s, 6H), 2.33 – 2.28 (m, 1H), 2.02 – 1.95 (m, 2H), 1.80 (ddd, *J* = 15.8, 12.3, 7.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.78, 146.18, 103.43, 99.05, 80.51, 68.69, 55.31, 34.50, 25.89. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{12}H_{17}O_3^+$: 209.1172, found 209.1172. IR (neat, cm^{-1}): 2938.45, 2837.90, 1596.64, 1460.05, 1427.53, 1362.12, 1204.01, 1153.86, 1054.85, 837.18. HPLC analysis: *ee* = 92%. IF (99% hexanes, 0.8 mL/min): t_{major} = 45.28 min, t_{minor} = 54.63 min. $[\alpha]^{20}_{D}$ = -12.4 (*c* = 0.5, $CHCl_3$).



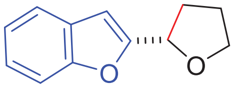
(*S*)-2-(naphthalen-2-yl)tetrahydrofuran 2l Yield: 82%. Hexanes/ethyl acetate = 8/1, R_f = 0.37. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 – 7.80 (m, 4H), 7.49 – 7.43 (m, 3H), 5.07 (t, *J* = 7.2 Hz, 1H), 4.18 (dd, *J* = 14.9, 7.0 Hz, 1H), 4.01 (dd, *J* = 14.4, 7.8 Hz, 1H), 2.44 – 2.37 (m, 1H), 2.09 – 2.04 (m, 2H), 1.93 – 1.87 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ140.87, 133.27, 132.76, 128.05, 127.86, 127.61, 125.98, 125.54, 124.00, 80.75, 68.80, 34.59, 26.05. HRMS (ESI) ($[M+H]^+$) Calcd. for $C_{14}H_{15}O^+$: 199.1117, found 199.1107. IR (neat, cm^{-1}): 2942.71, 2864.80, 1739.39, 1510.59, 1066.69, 820.29, 749.89. HPLC analysis: *ee* = 92%. IE (99% hexanes, 0.8 mL/min): t_{major} = 25.03 min, t_{minor} = 23.48 min. $[\alpha]^{20}_{D}$ = -13.2 (*c* = 0.5, $CHCl_3$).



***tert*-butyl (*S*)-3-(tetrahydrofuran-2-yl)-1H-indole-1-carboxylate 2m** Yield: 82%. Hexanes/ethyl acetate = 5/1, R_f = 0.35. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.52 (s, 1H), 7.33 – 7.30 (m, 1H), 7.25 – 7.22 (m, 1H), 5.14 (t, *J* = 6.6 Hz, 1H), 4.10 (dt, *J* = 13.7, 6.7 Hz, 1H), 3.95 – 3.92 (m, 1H), 2.38 – 2.33 (m, 1H), 2.11 – 2.01 (m, 3H), 1.67 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 149.76, 135.97, 128.85, 124.36, 122.50, 122.45, 122.07, 119.69, 115.31, 83.50, 74.59, 68.15, 32.03, 28.20, 25.94. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{17}H_{22}NO_3^+$: 288.1594, found 288.1587. IR (neat, cm^{-1}): 2934.05, 2864.11, 1732.09, 1452.86, 1373.60, 1256.91, 1160.14, 1060.23, 749.28. HPLC analysis: *ee* = 94%. IF (99% hexanes, 0.8 mL/min): t_{major} = 26.09 min, t_{minor} = 35.72 min. $[\alpha]^{20}{}_D$ = -7.6 (*c* = 0.5, CHCl$_3$).

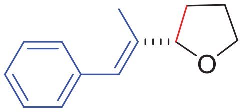


(S)-2-(benzo[b]thiophen-3-yl)tetrahydrofuran 2n Yield: 86%. Hexanes/ethyl acetate = 6/1, R$_f$ = 0.36. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.86 (dd, *J* = 7.1, 1.2 Hz, 1H), 7.80 (dd, *J* = 7.0, 1.2 Hz, 1H), 7.39 – 7.33 (m, 3H), 5.27 (dd, *J* = 10.3, 3.4 Hz, 1H), 4.16 – 4.12 (m, 1H), 3.99 – 3.95 (m, 1H), 2.45 – 2.39 (m, 1H), 2.10 – 1.99 (m, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 141.02, 138.15, 137.43, 124.23, 123.90, 122.87, 122.19, 121.23, 76.64, 68.32, 32.17, 25.85. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{12}H_{13}OS+$: 205.0682, found 205.0679. IR (neat, cm^{-1}): 2851.82, 2922.35, 1736.96, 1459.60, 1428.18, 1256.96, 1066.63, 760.04, 733.84. HPLC analysis: *ee* = 95%. IF (99.5% hexanes, 0.8 mL/min): t_{major} = 24.53 min, t_{minor} = 28.72 min. $[\alpha]^{20}{}_D$ = -37.2 (*c* = 0.5, CHCl$_3$).



(*S*)-2-(tetrahydrofuran-2-yl)benzofuran 2o Yield: 90%. Hexanes/ethyl acetate = 6/1, R$_f$ = 0.36. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.53 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.25 (dd, *J* = 11.3, 4.0 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 6.63 (s, 1H), 5.08 (t, *J* = 6.8 Hz, 1H), 4.08 (dd, *J* = 14.3, 7.5 Hz, 1H), 3.95 (dd, *J* = 14.1, 7.8 Hz, 1H), 2.33 – 2.27 (m, 1H), 2.21 (tt, *J* = 14.3, 6.4 Hz, 1H), 2.15 – 2.09 (m, 1H), 2.07 – 2.00

(m, 1H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 158.15, 155.01, 128.15, 123.95, 122.61, 120.86, 111.20, 102.98, 74.31, 68.65, 30.67, 25.87. IR (neat, cm^{-1}): 2920.16, 2849.85, 1737.73, 1454.23, 1254.54, 1055.47, 806.97, 753.20. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{12}H_{13}O_2^+$: 189.0910, found 189.0905. HPLC analysis: *ee* = 76%. IF (99.5% hexanes, 0.8 mL/min): t_{major} = 25.73 min, t_{minor} = 29.14 min. $[\alpha]^{20}{}_D$ = -3.6 (*c* = 0.5, CHCl$_3$).



(*S*, *E*)-2-(1-phenylprop-1-en-2-yl)tetrahydrofuran 2p Yield: 92%. Hexanes/ethyl acetate = 6/1, R_f = 0.36. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.32 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 6.55 (s, 1H), 4.39 (t, *J* = 7.3 Hz, 1H), 4.00 (dd, *J* = 14.8, 6.9 Hz, 1H), 3.88 (dd, *J* = 14.0, 7.7 Hz, 1H), 2.14 – 2.08 (m, 1H), 2.01 – 1.93 (m, 2H), 1.84 (d, *J* = 1.0 Hz, 3H), 1.80 – 1.74 (m, 1H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 138.55, 137.84, 128.91, 127.98, 126.22, 124.46, 83.94, 68.66, 30.93, 26.05, 13.92. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{13}H_{17}O^+$: 189.1274, found 189.1265. IR (neat, cm^{-1}): 2960.35, 2917.51, 2850.47, 1737.65, 1259.18, 1056.20, 806.54, 699.91. HPLC analysis: *ee* = 92%. ID (99.7% hexanes, 0.8 mL/min): t_{major} = 21.69 min, t_{minor} = 20.35 min. $[\alpha]^{20}{}_D$ = -13.2 (*c* = 0.5, CHCl$_3$).

4.5 REFERENCES

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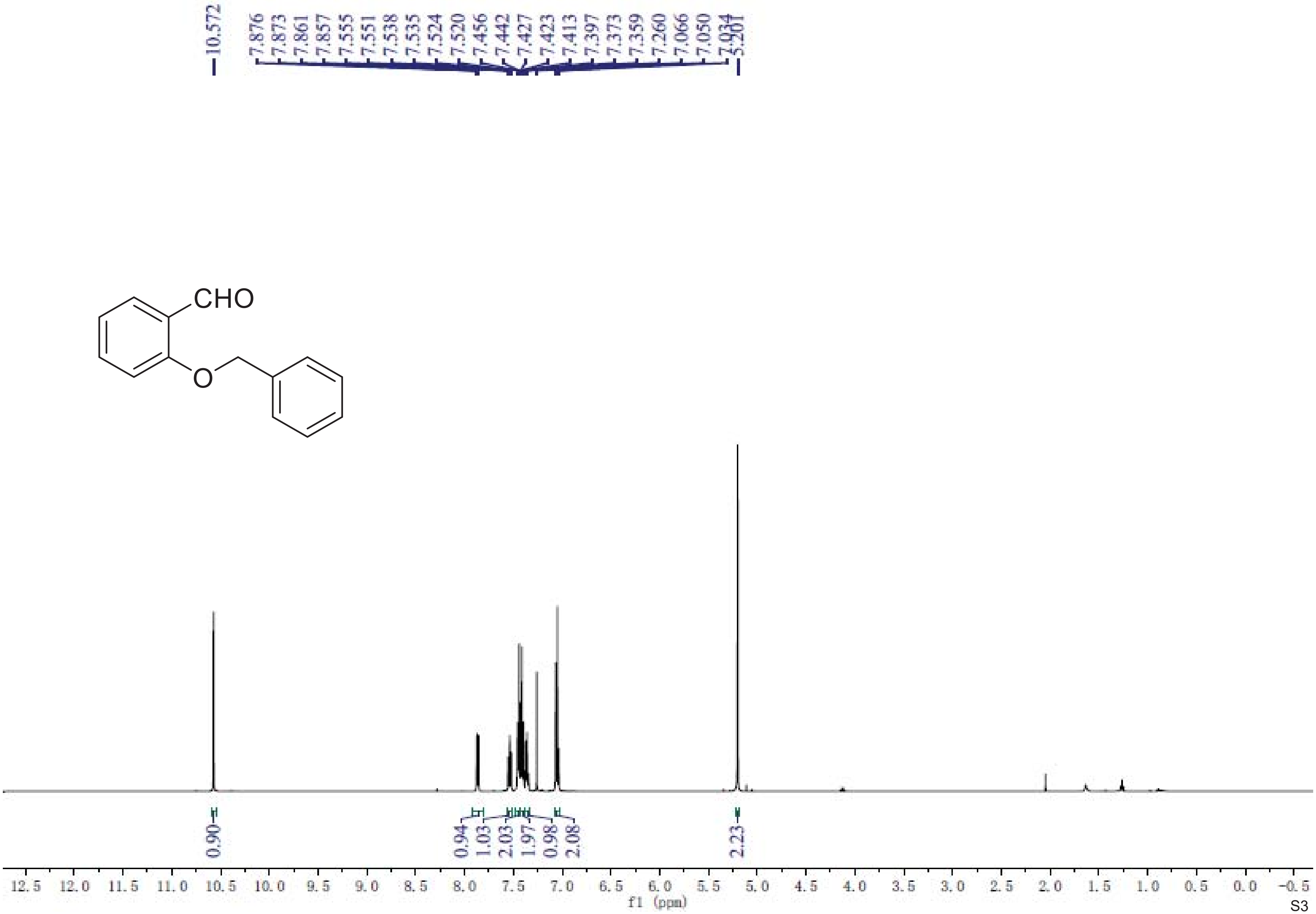
Chapter 5

Spectral Data

Spectral Data for Chapter 2

Enantioselective Synthesis of Chiral Dihydrobenzofurans with in Situ-generated Donor-Substituted Diazo Reagents via Cobalt(II)-based Metalloradical C–H Alkylation

2-(benzyloxy)benzaldehyde



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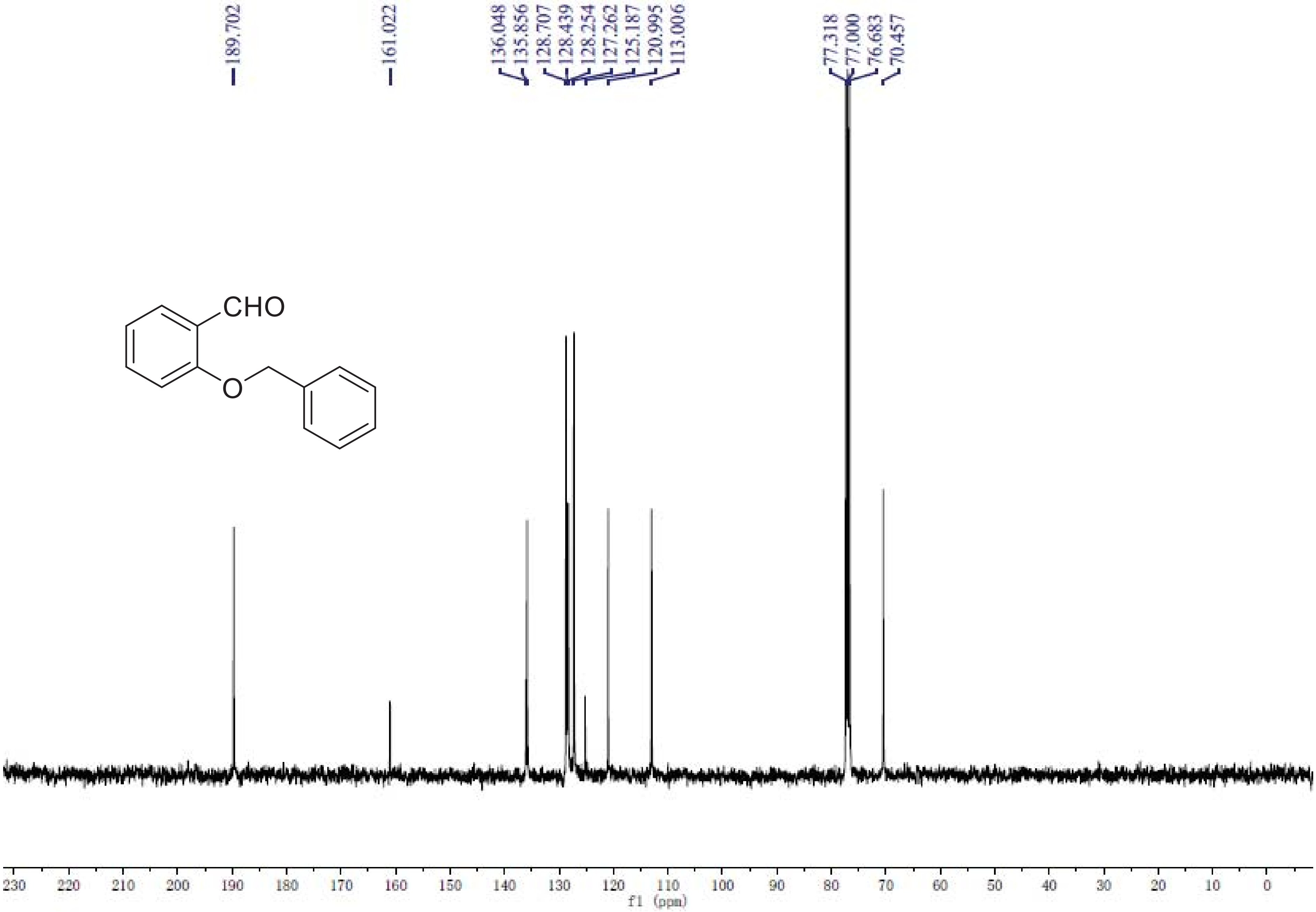

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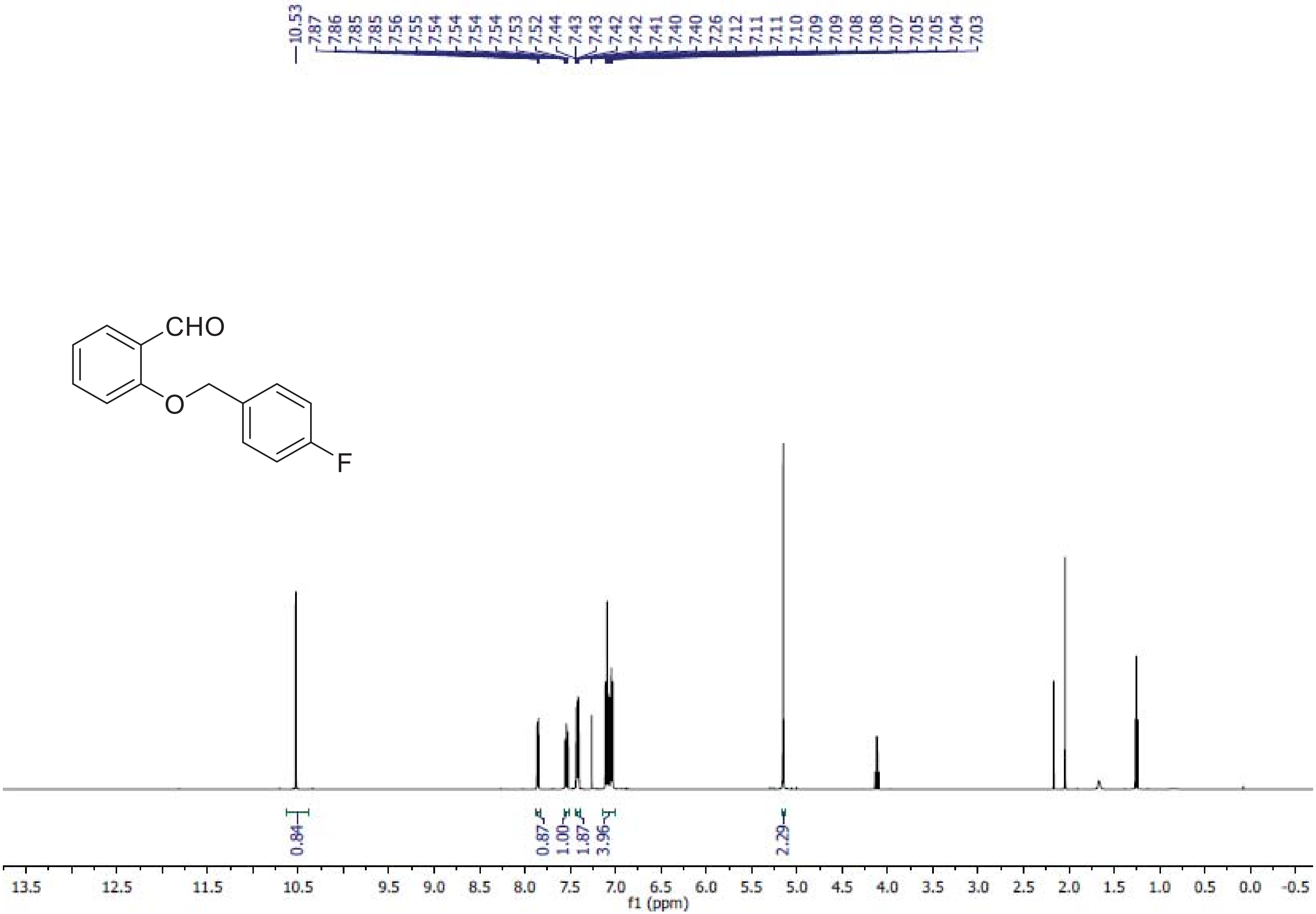

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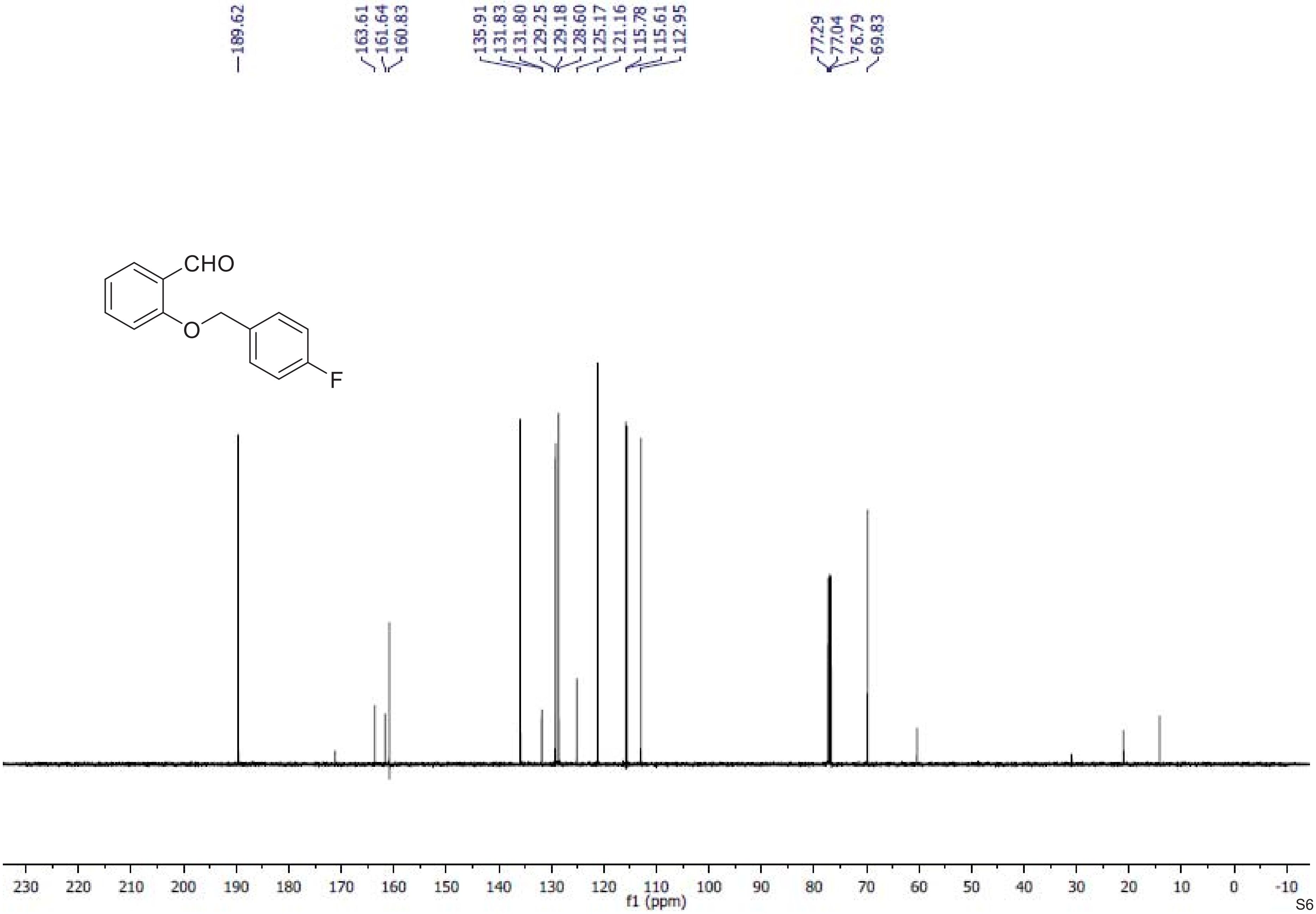

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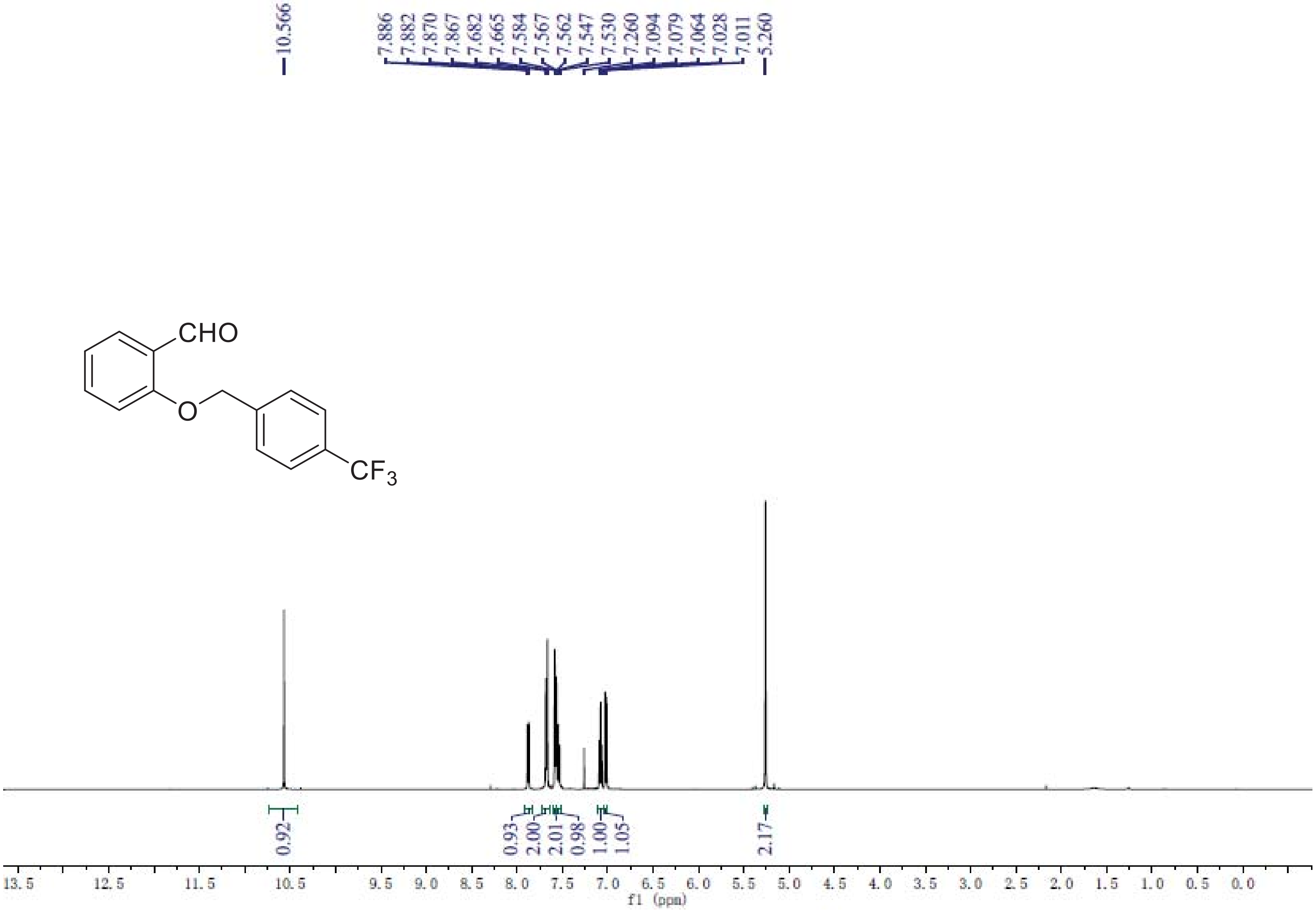

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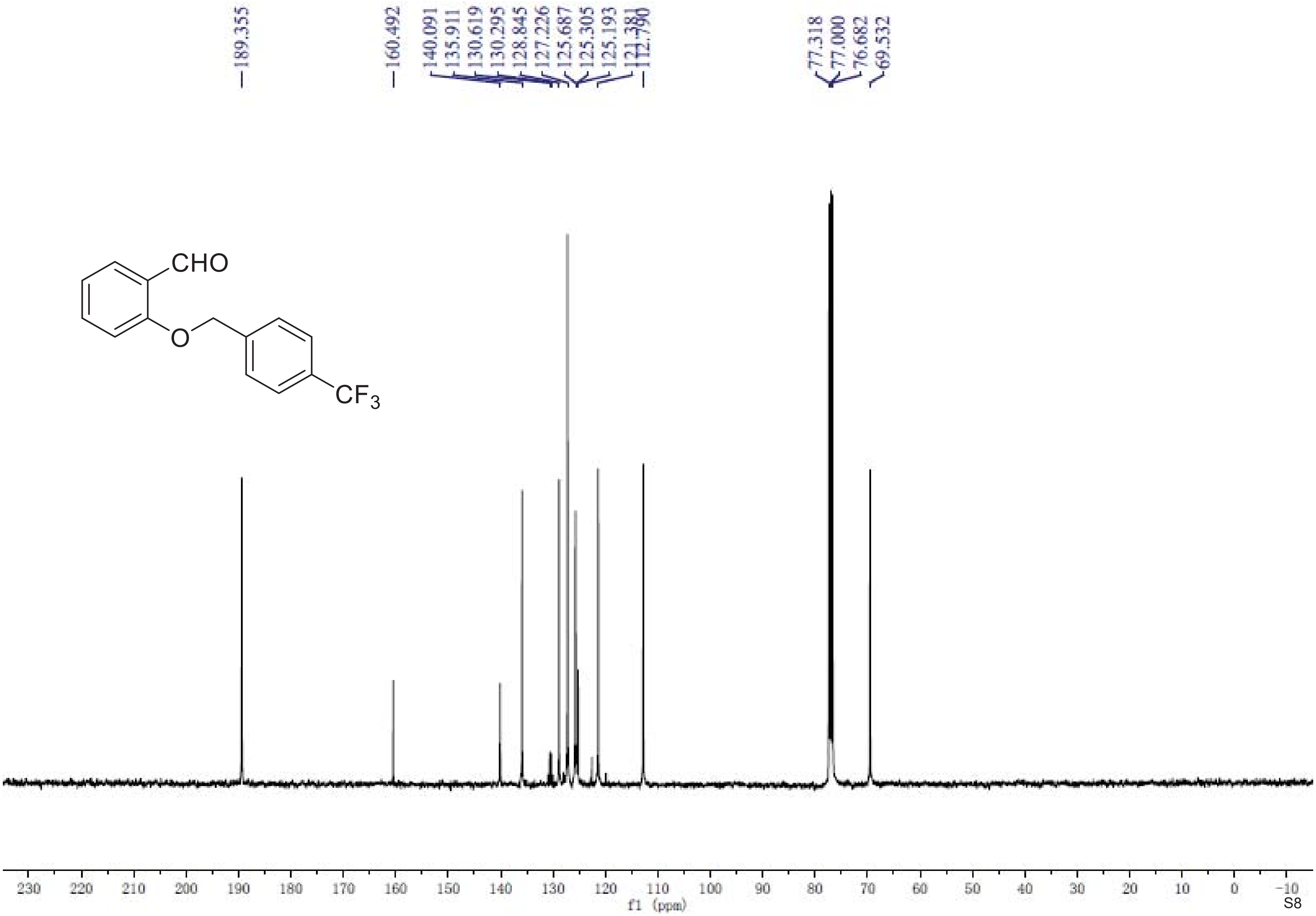

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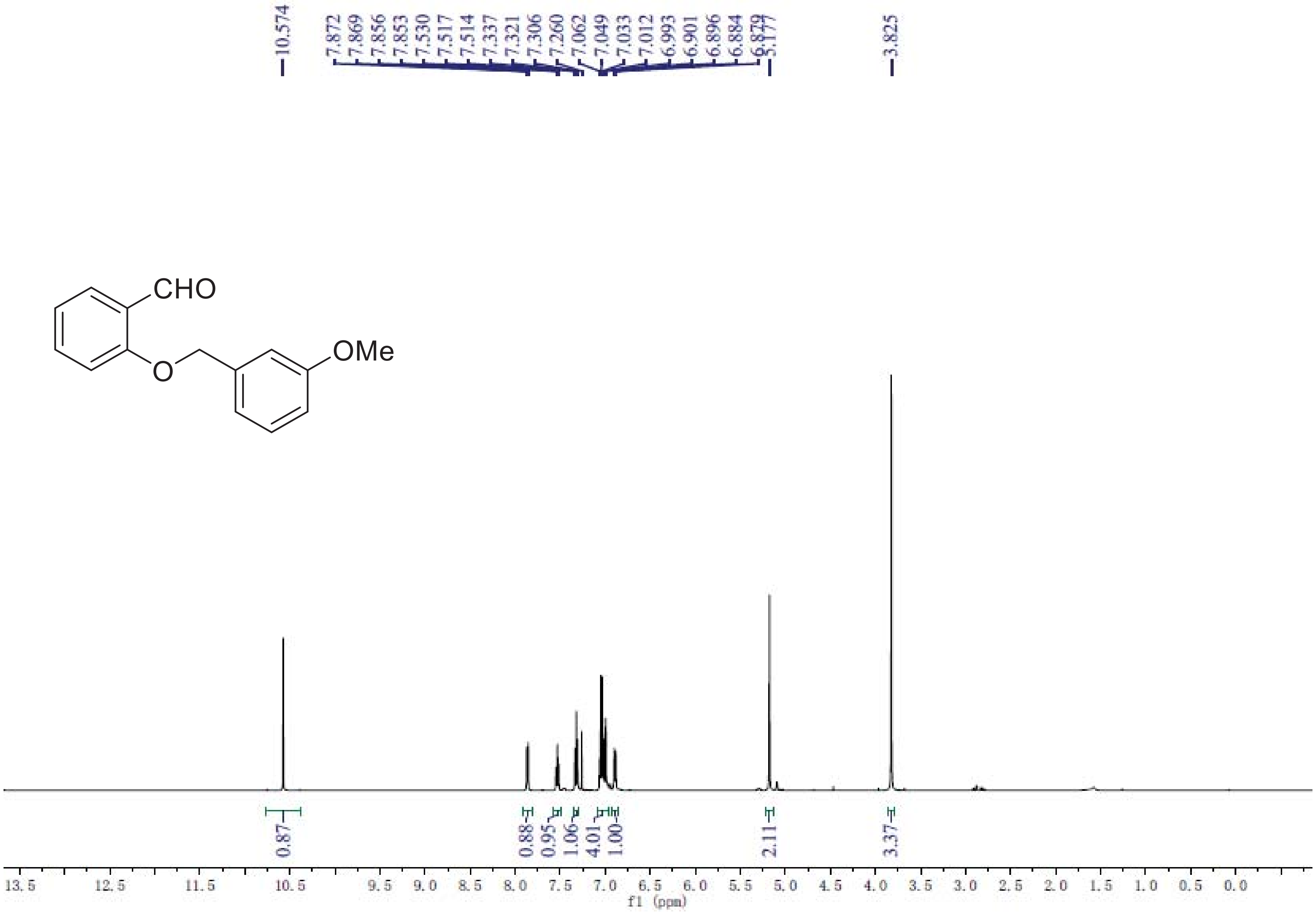

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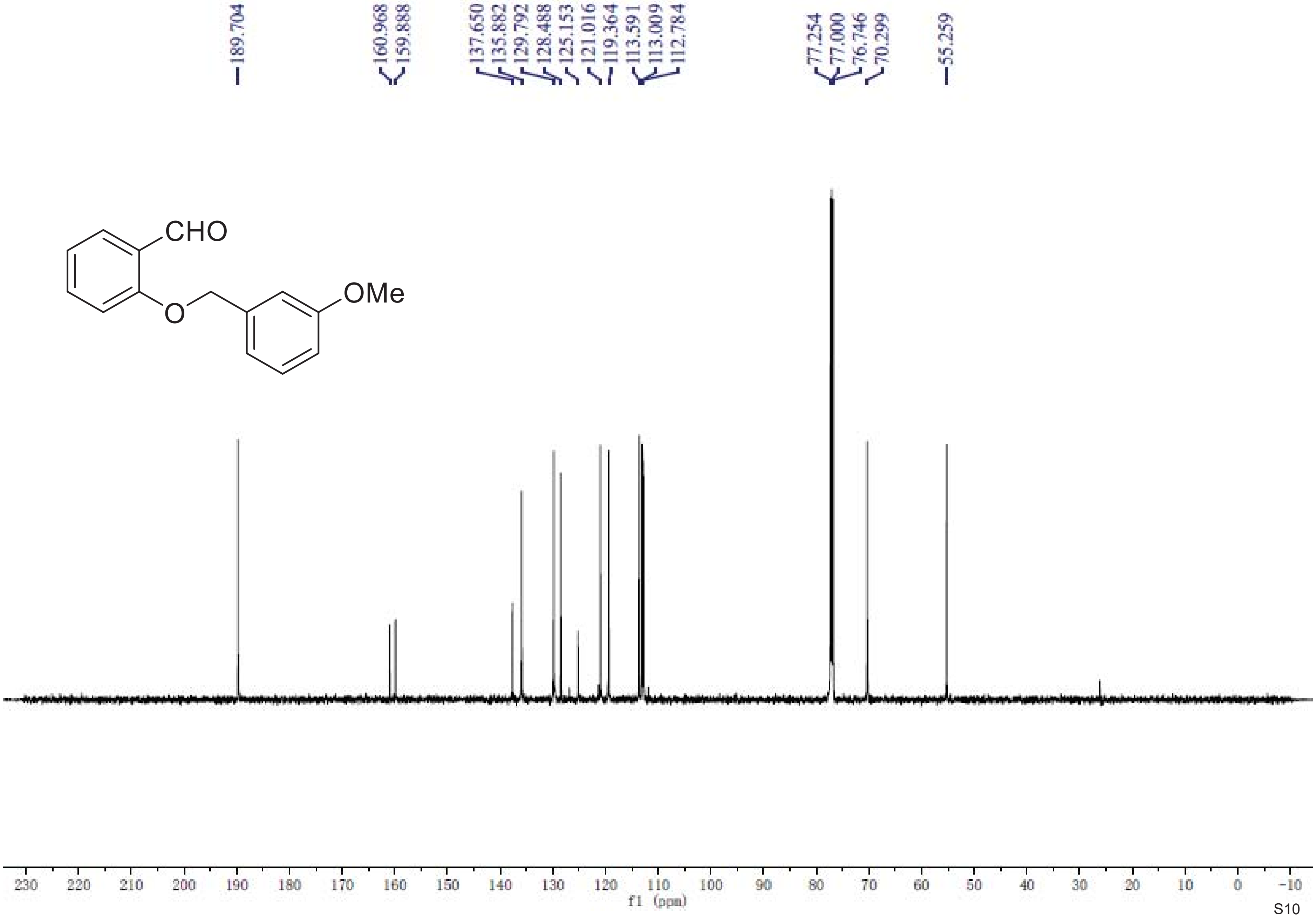

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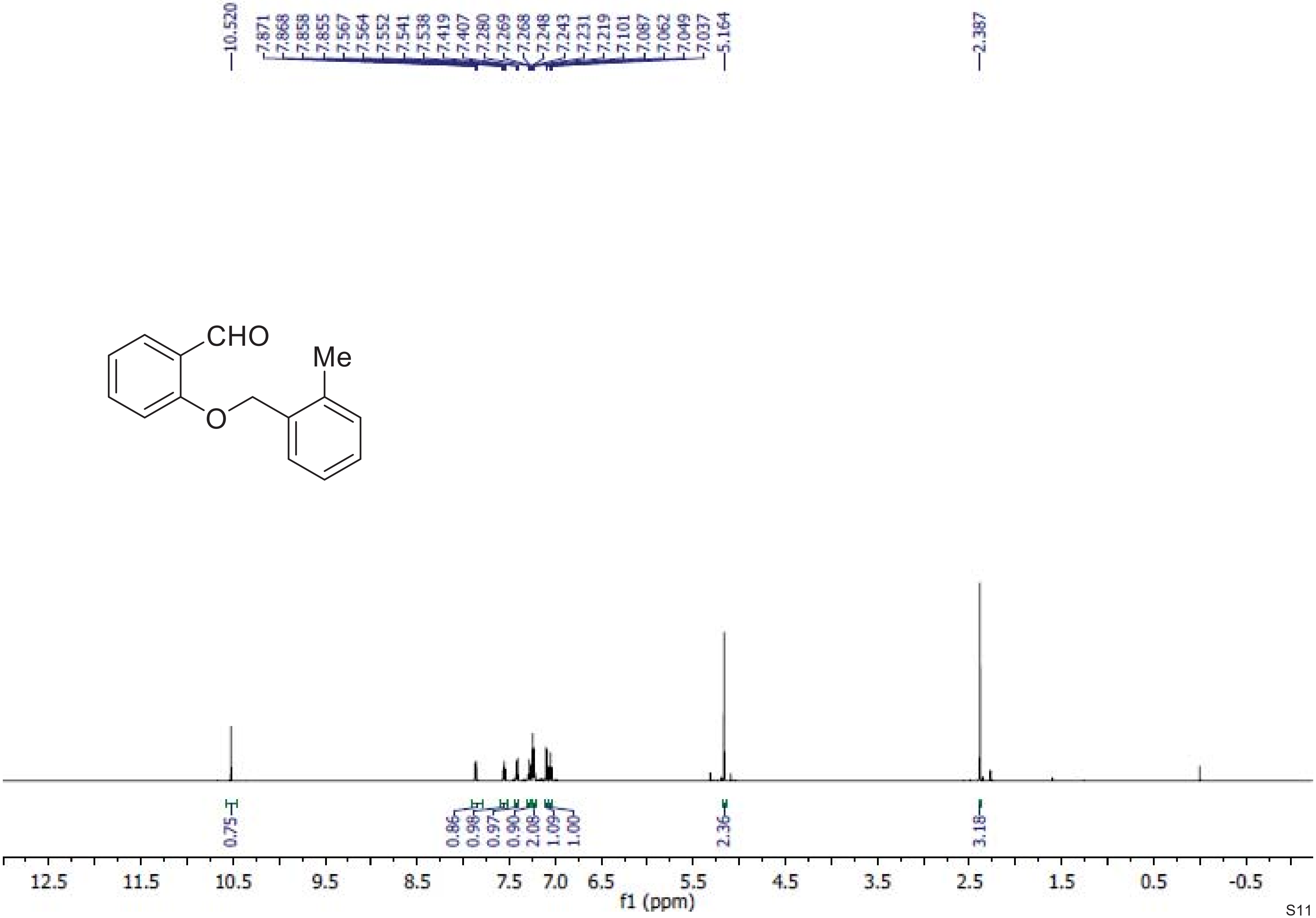

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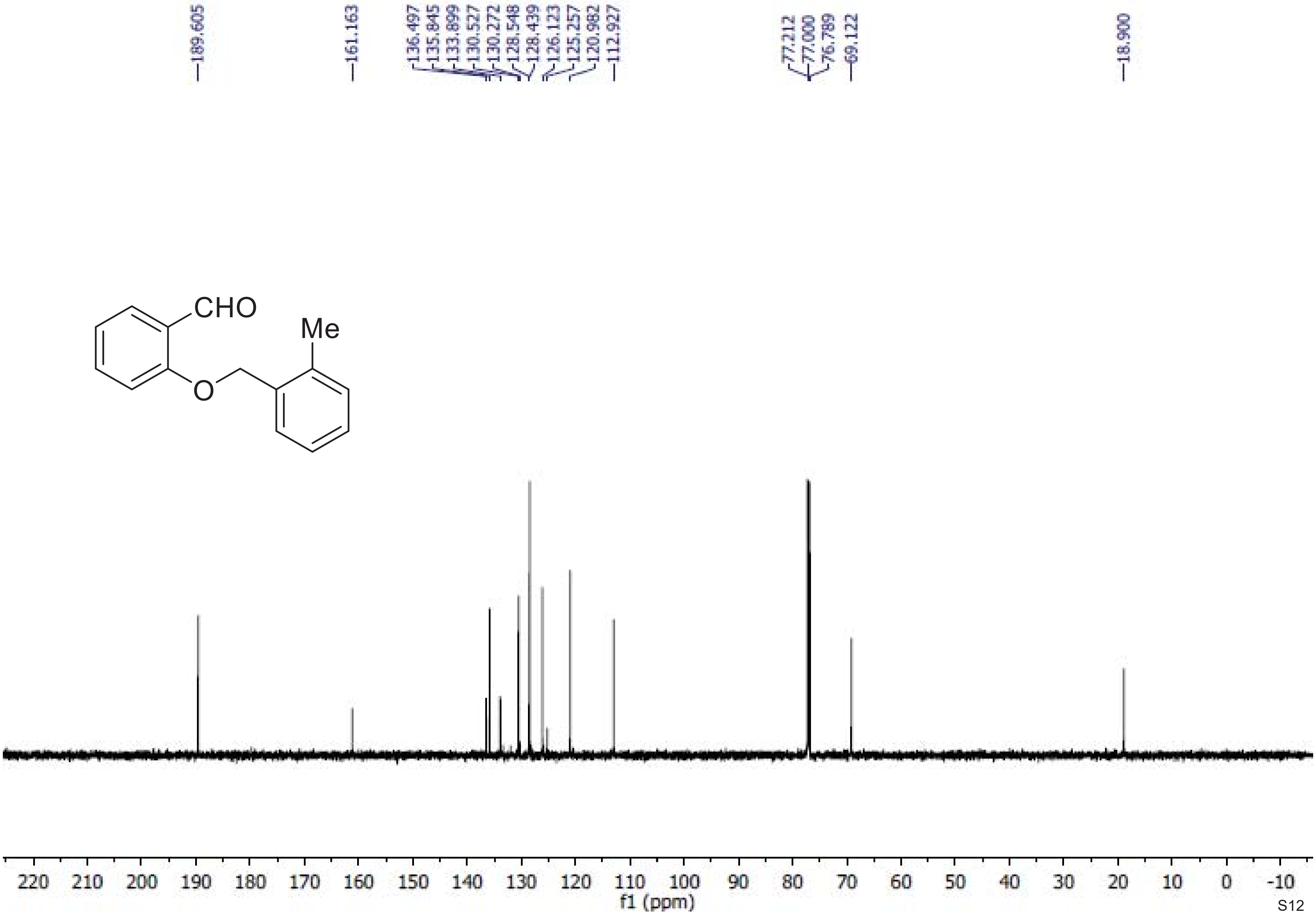

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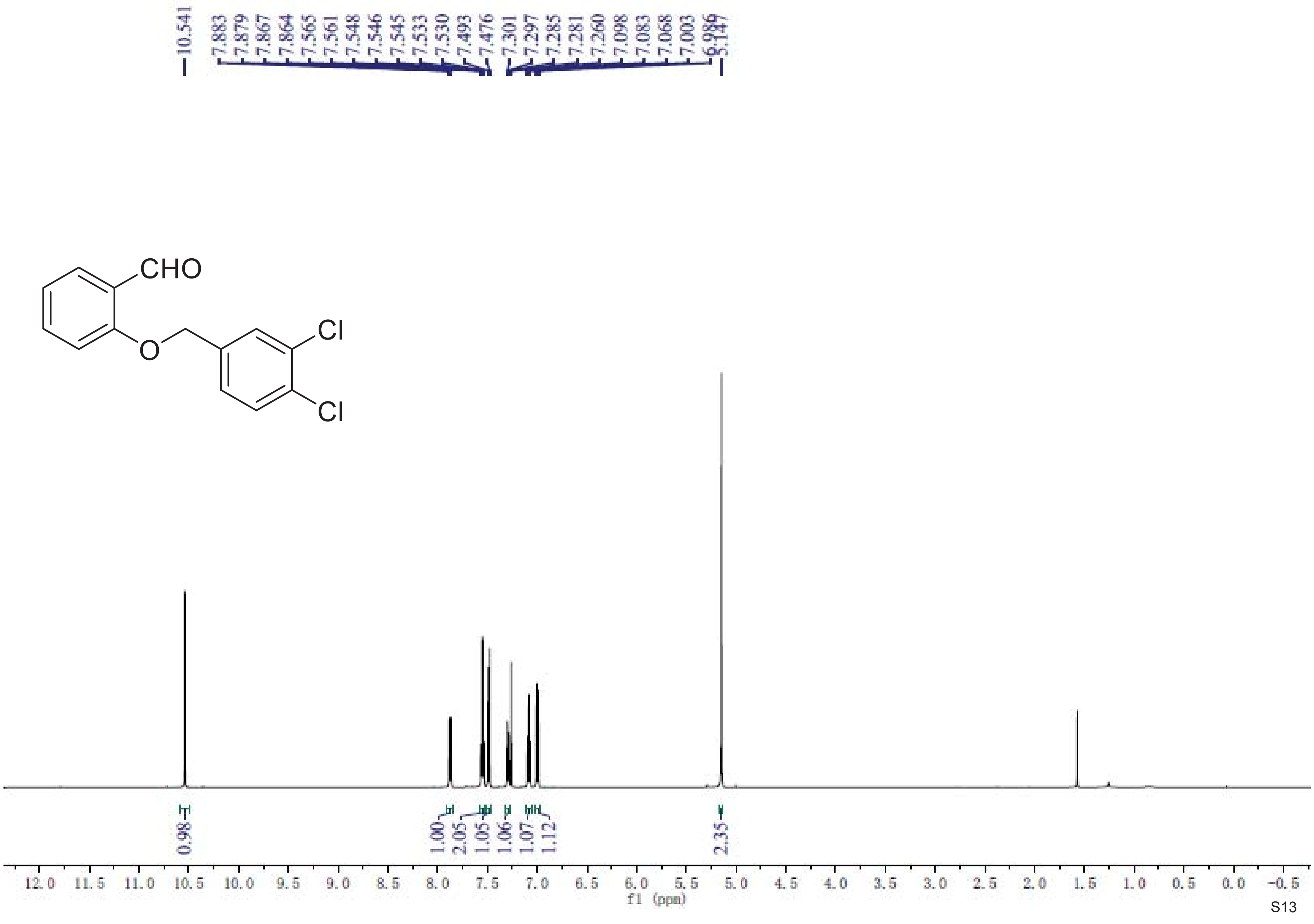

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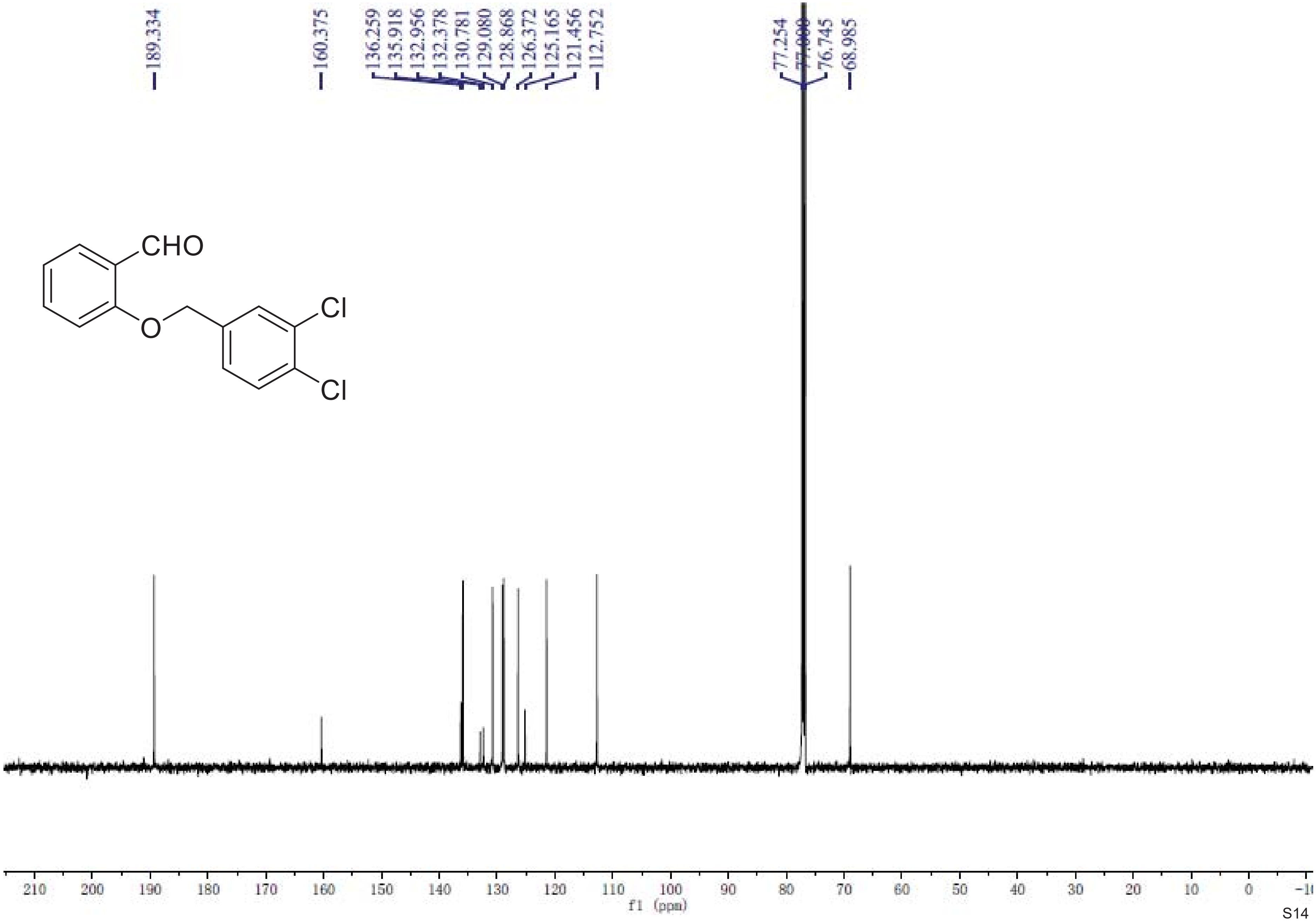

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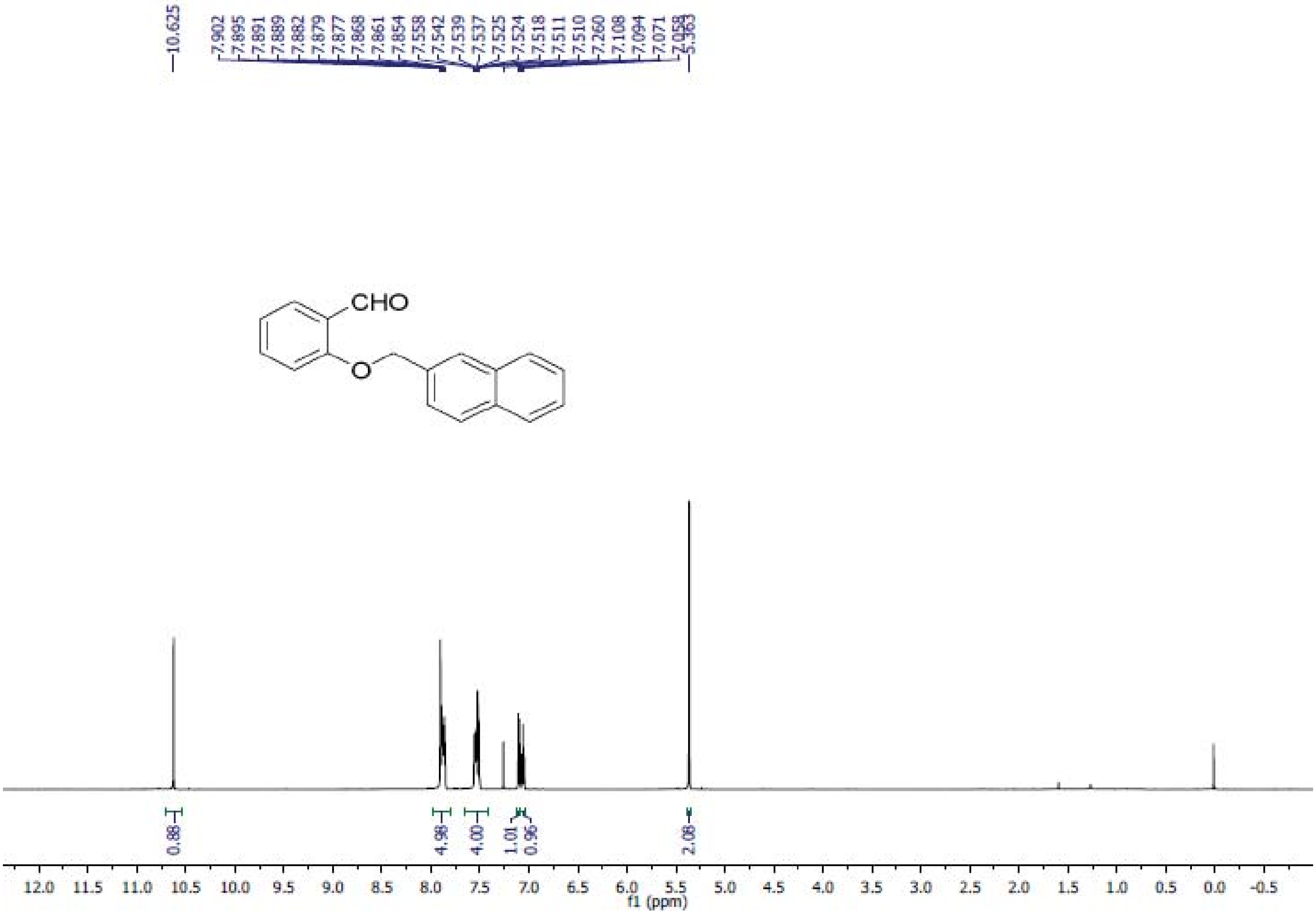

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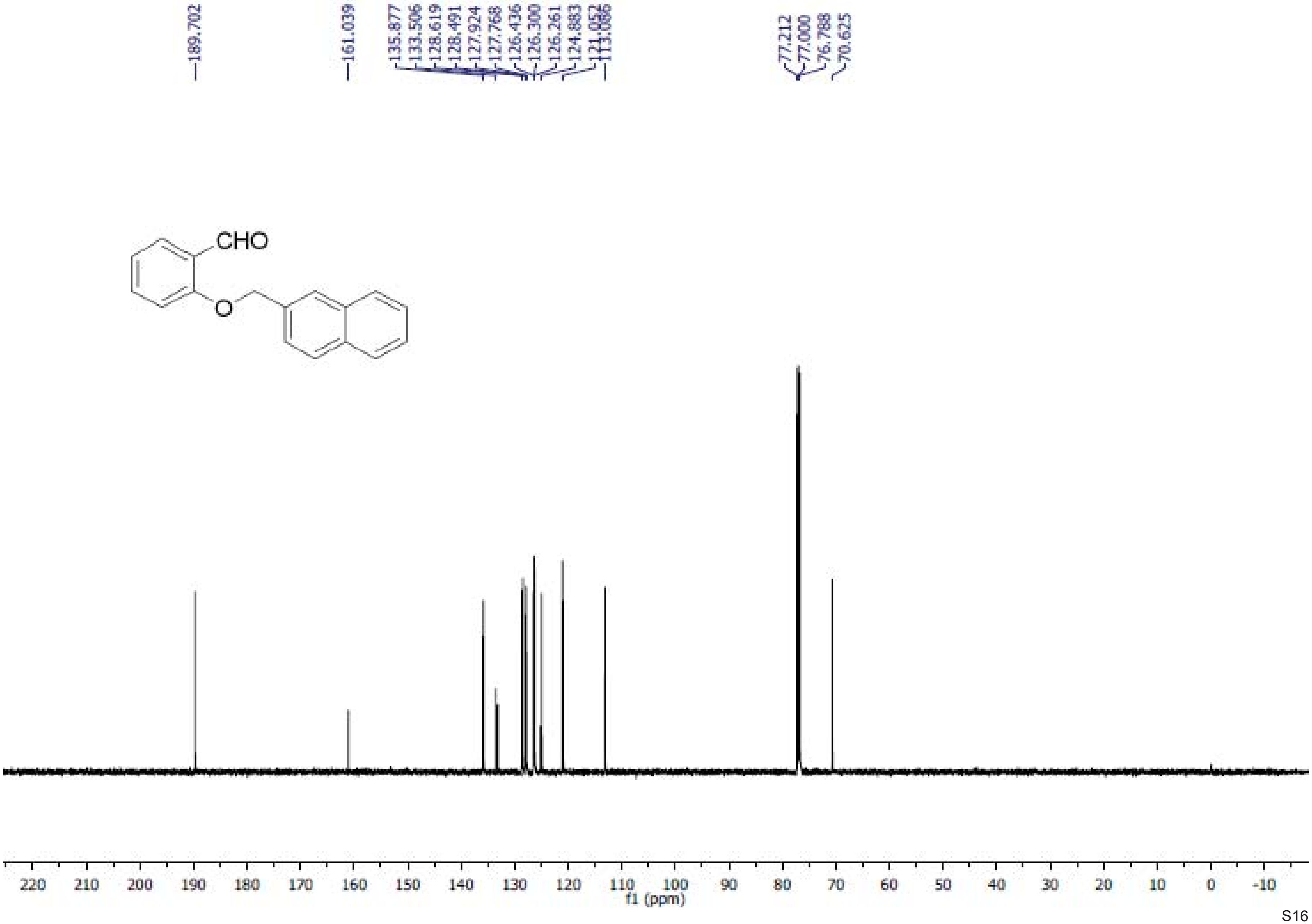

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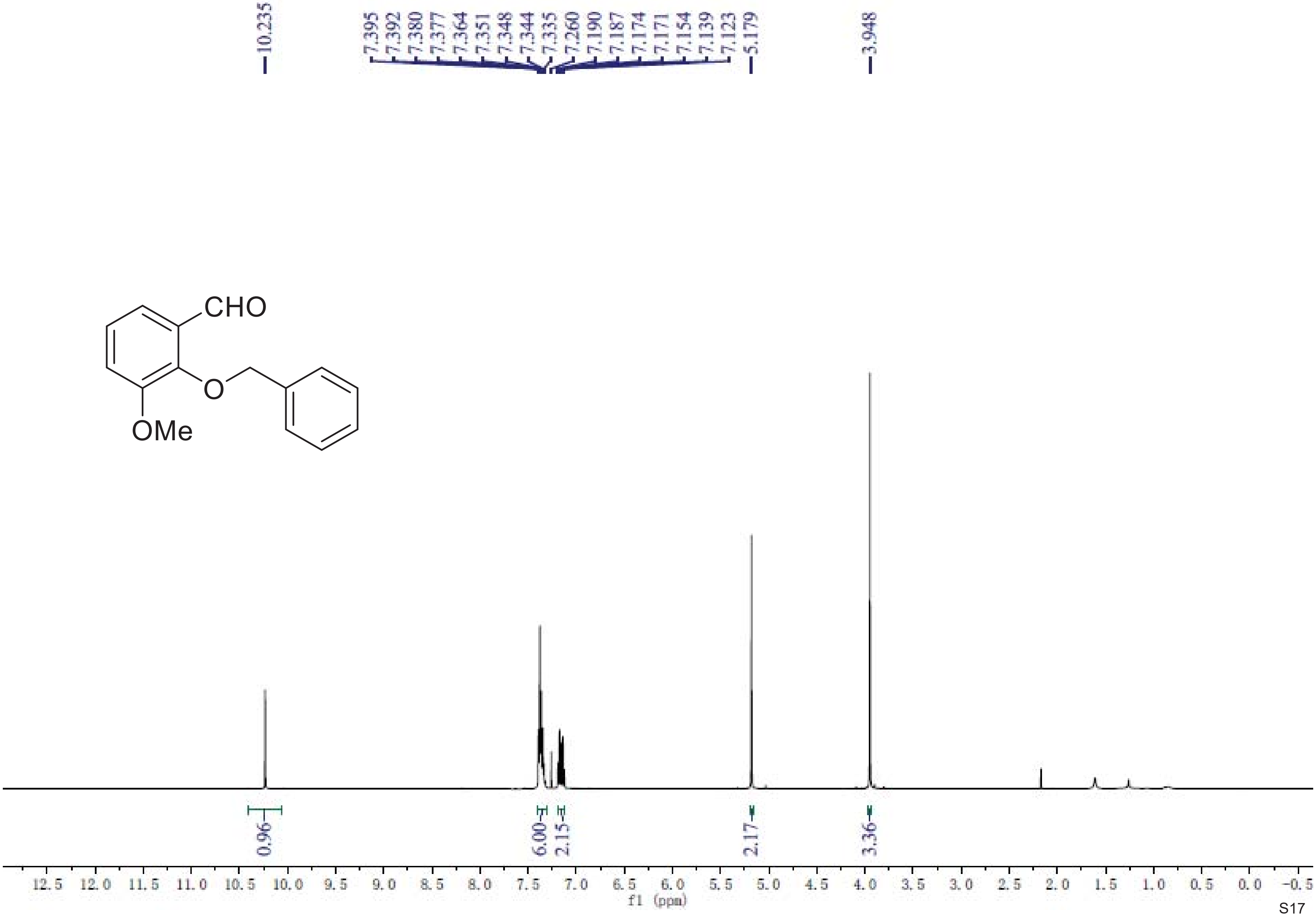

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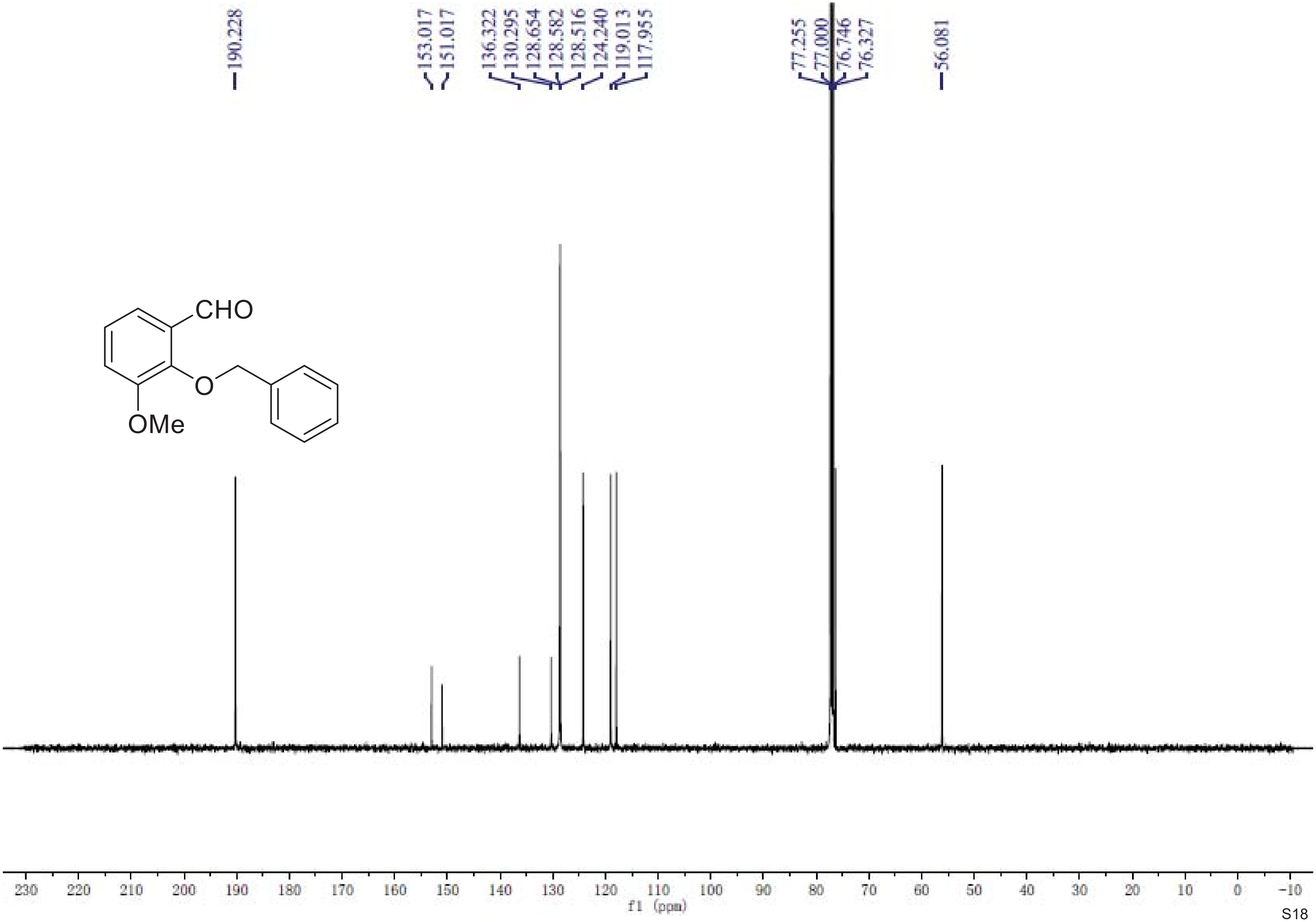

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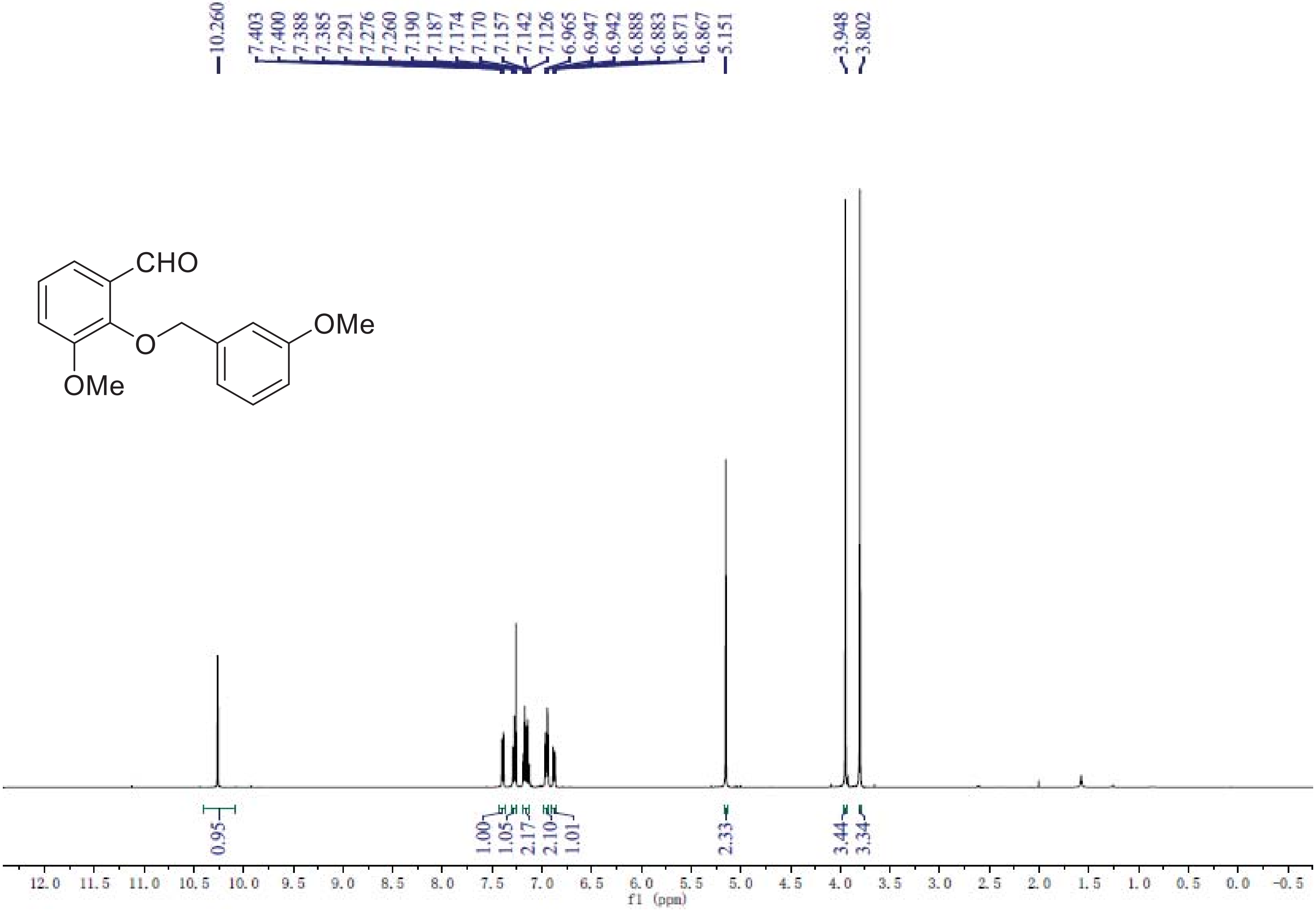

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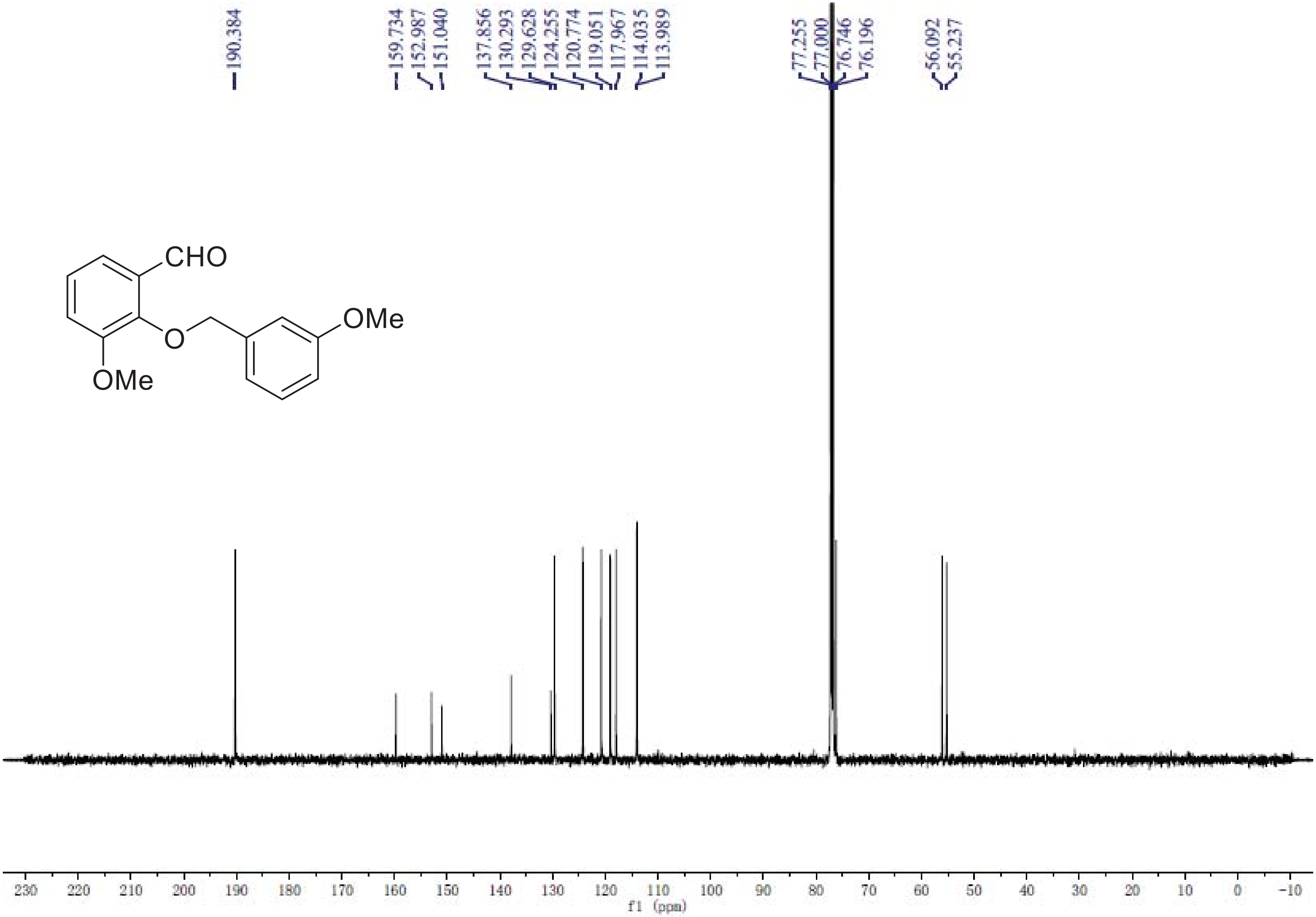

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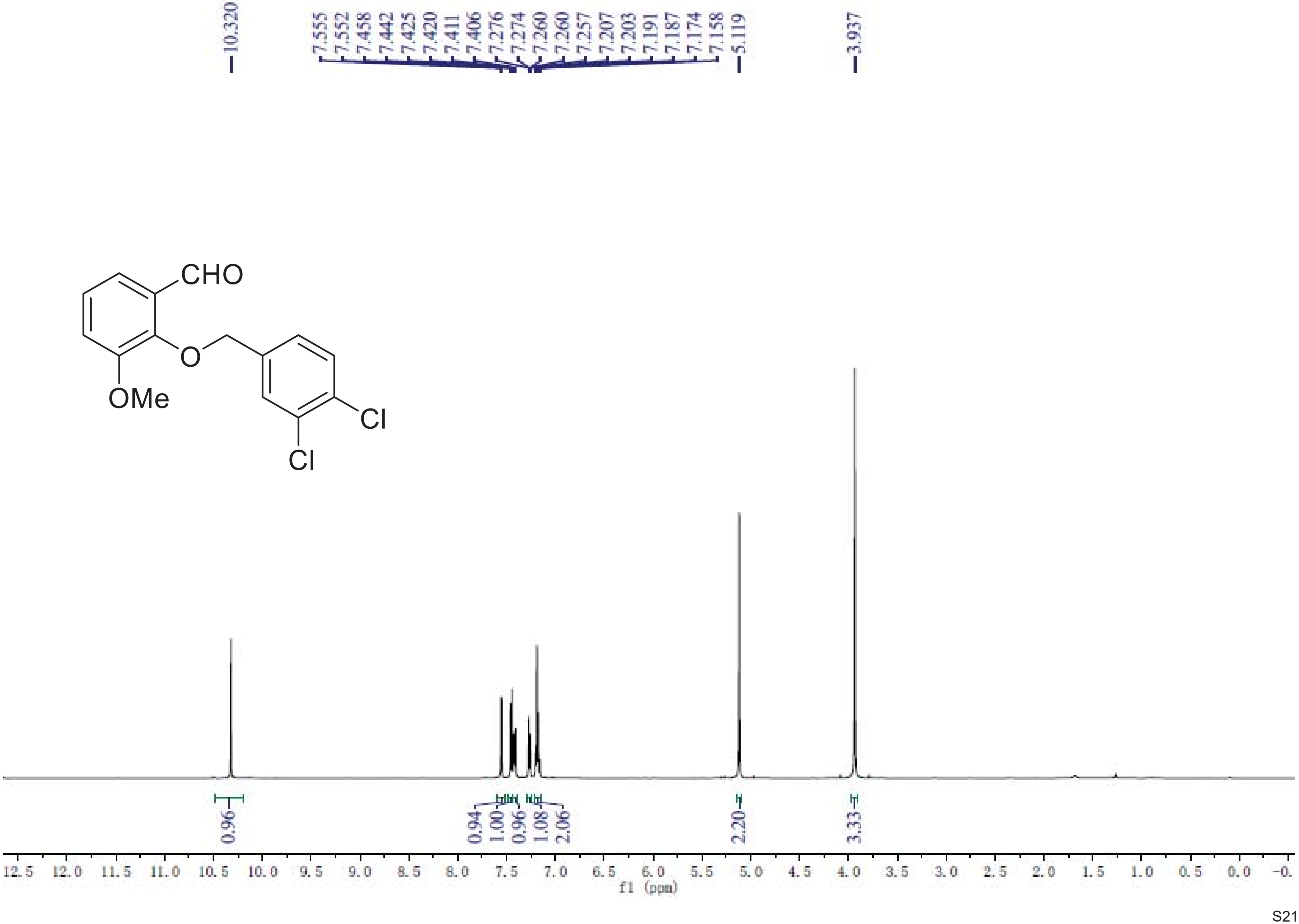

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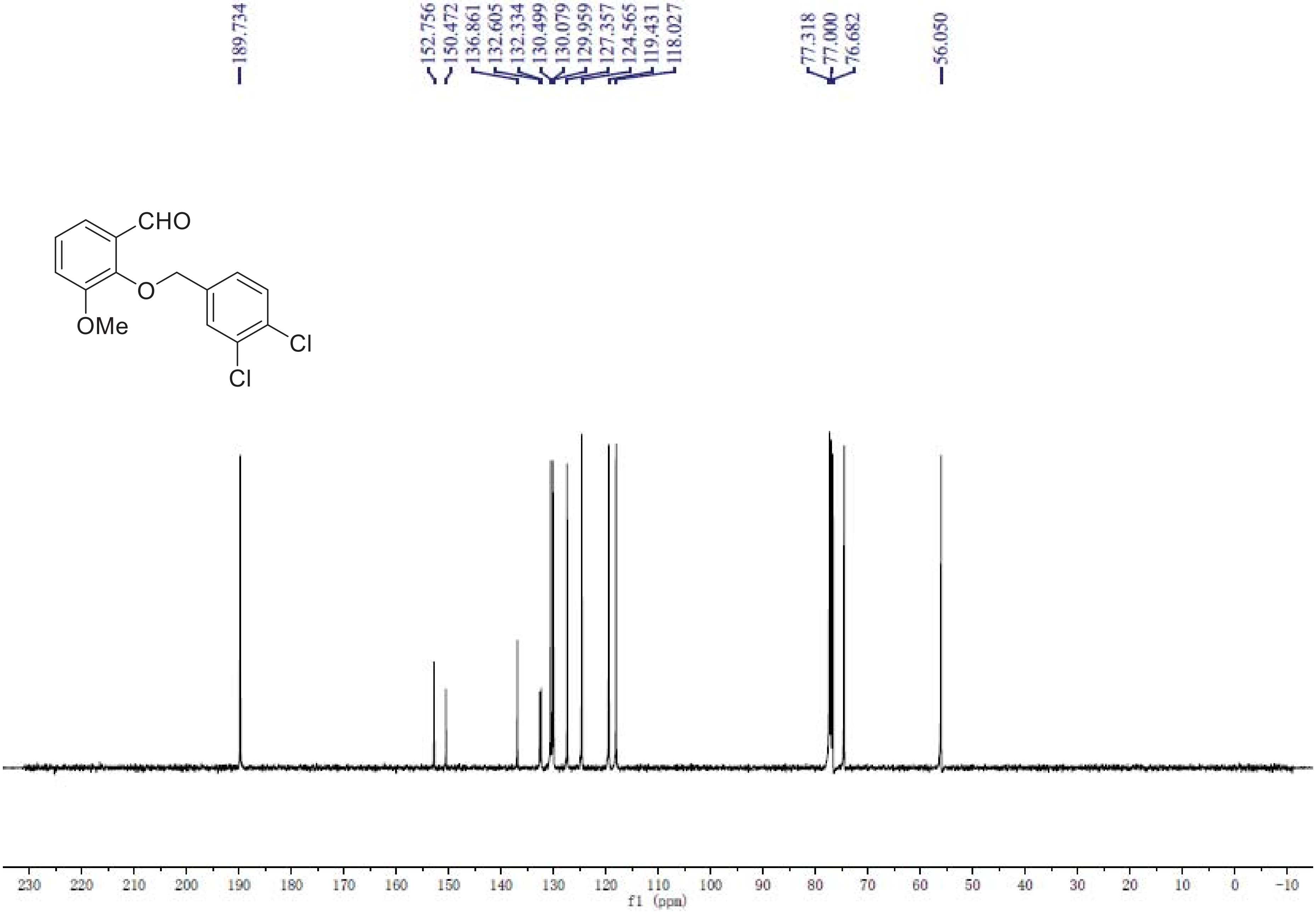

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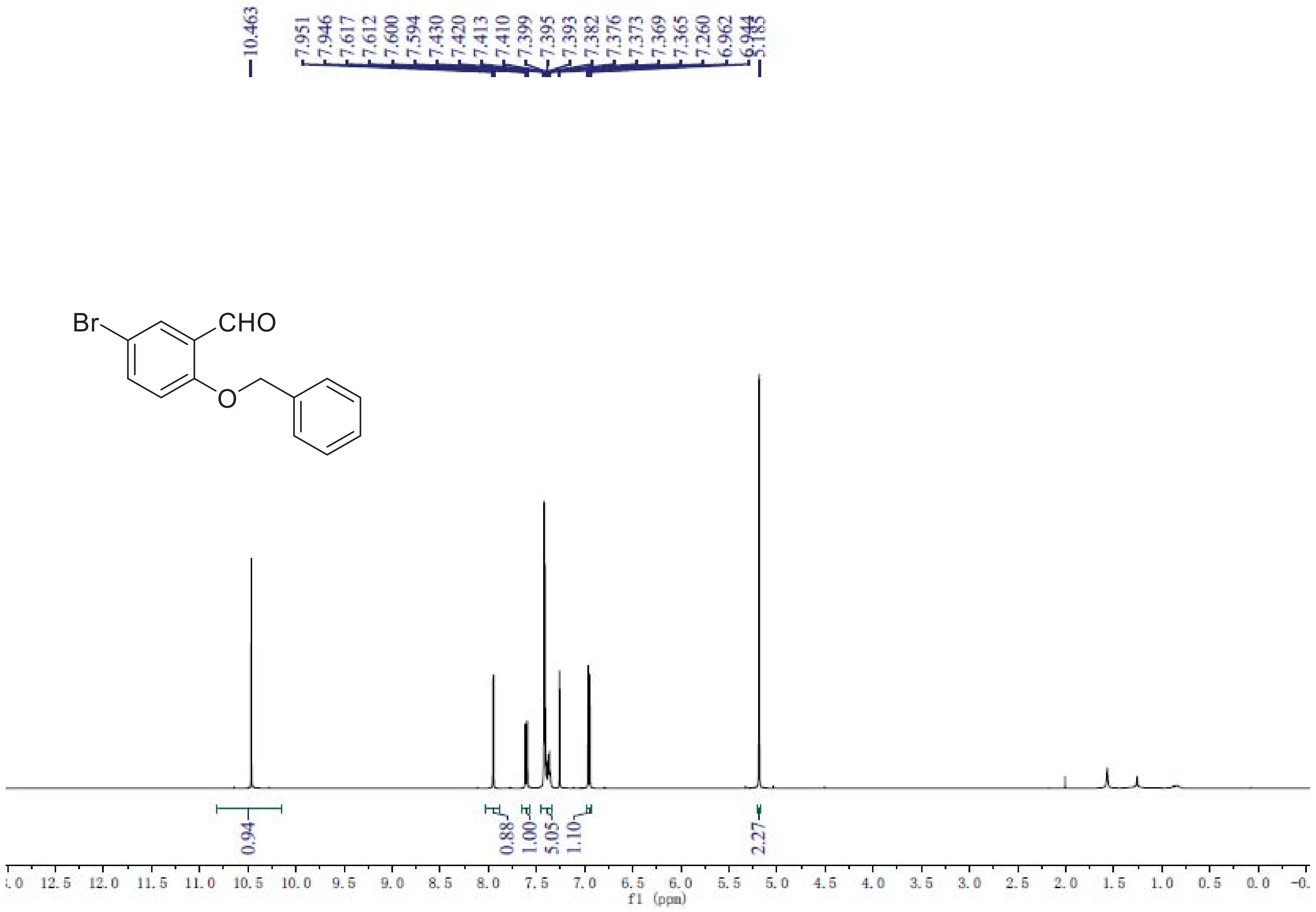

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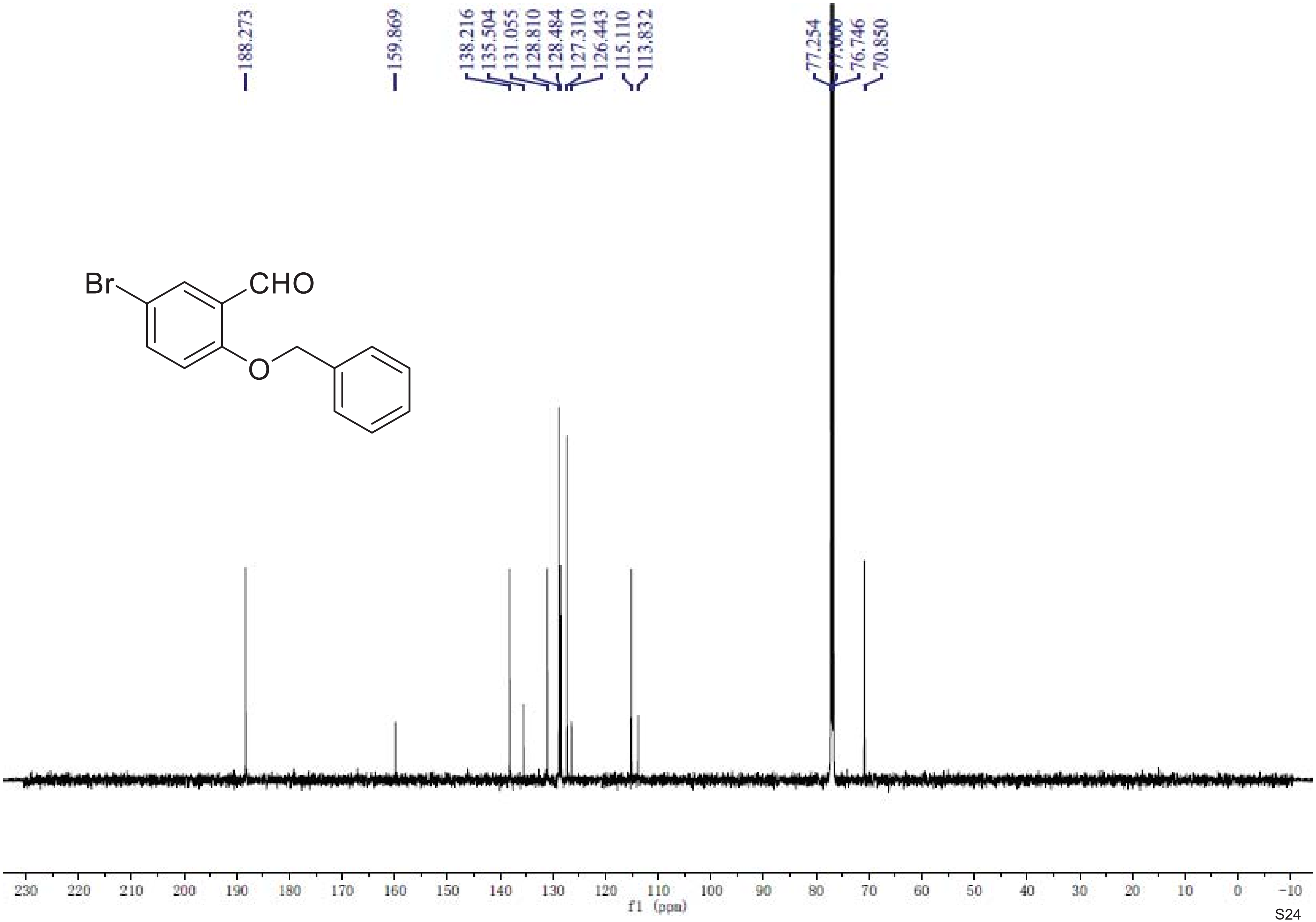

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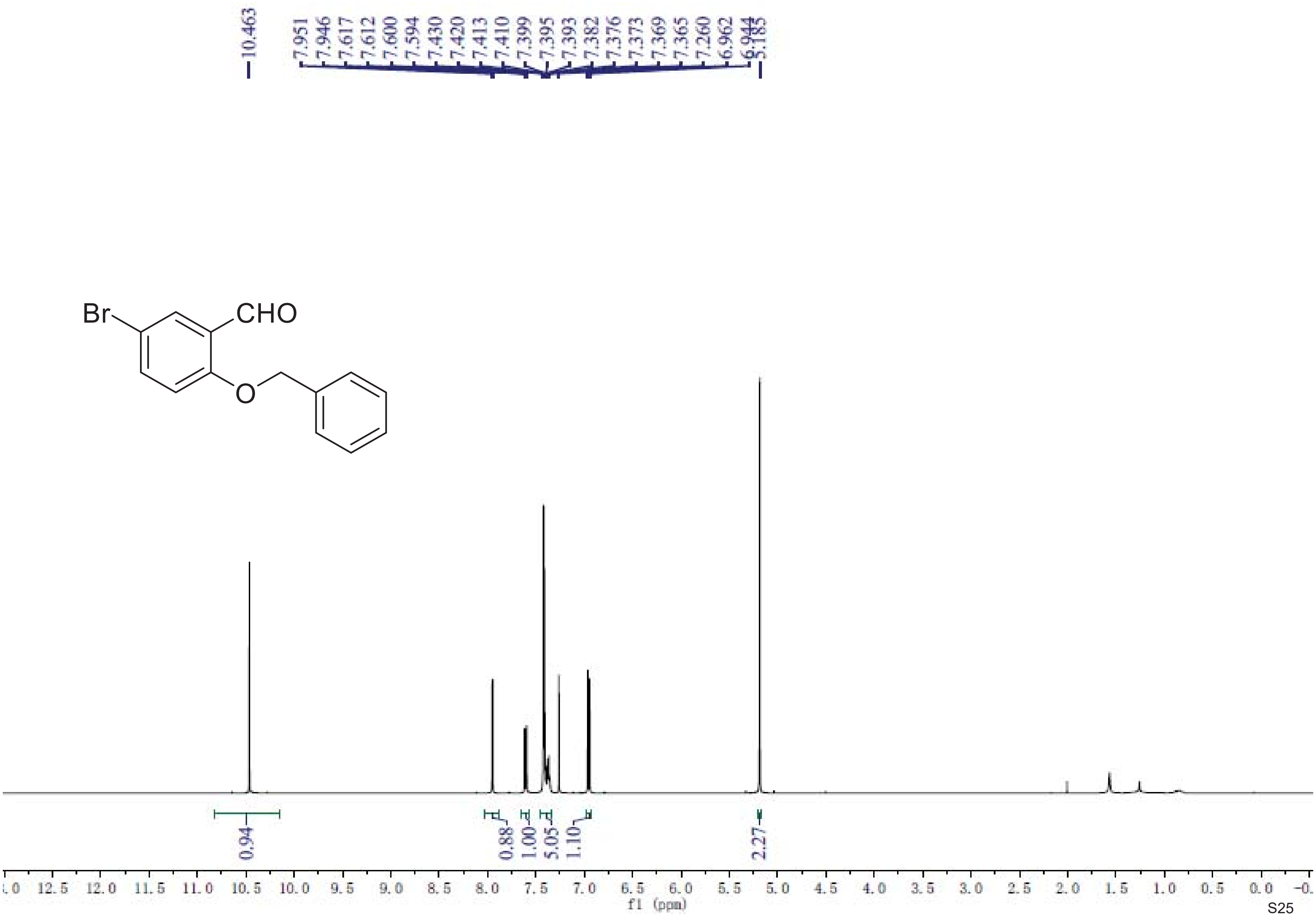
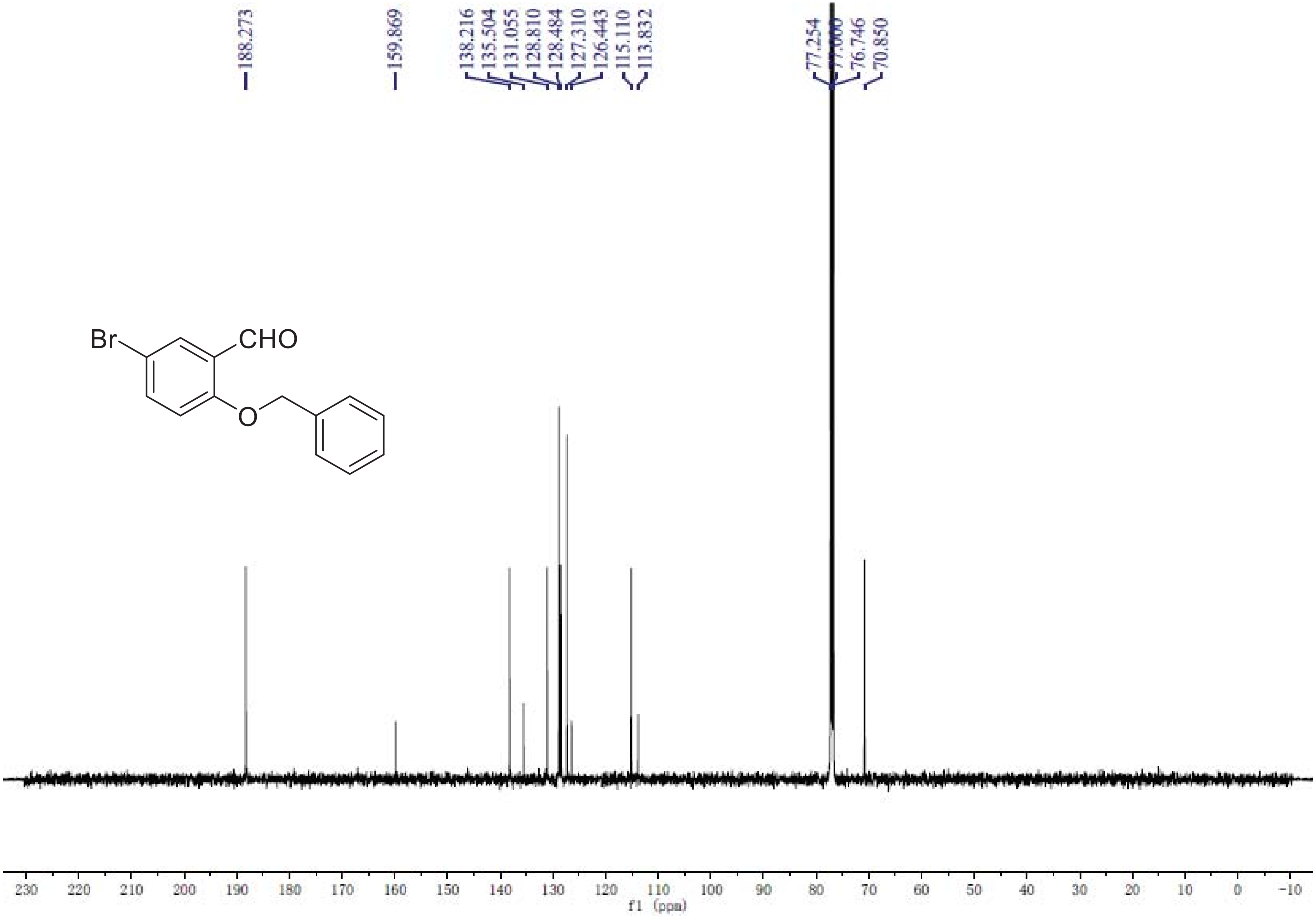


2-(benzyloxy)-5-bromobenzaldehyde



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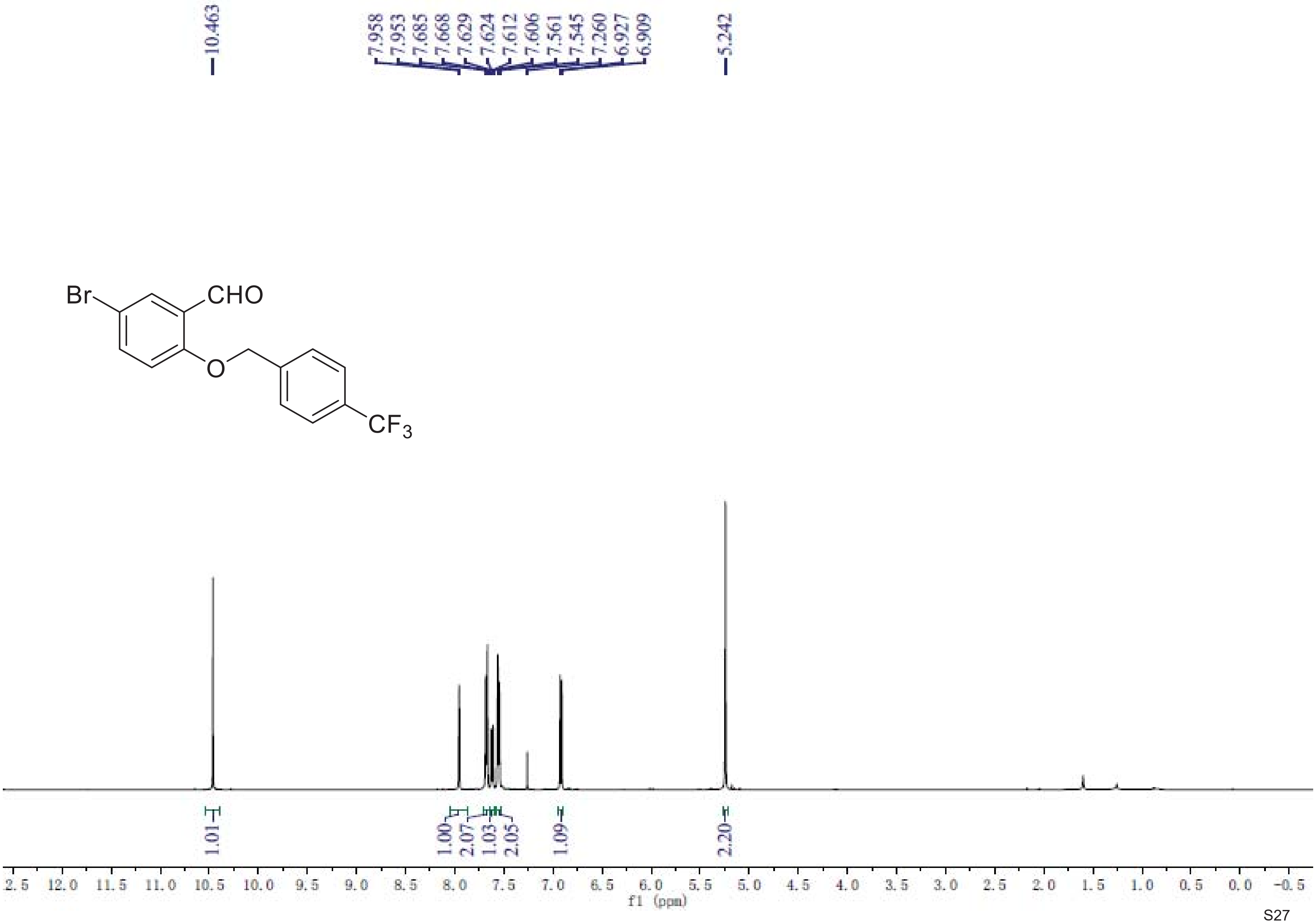
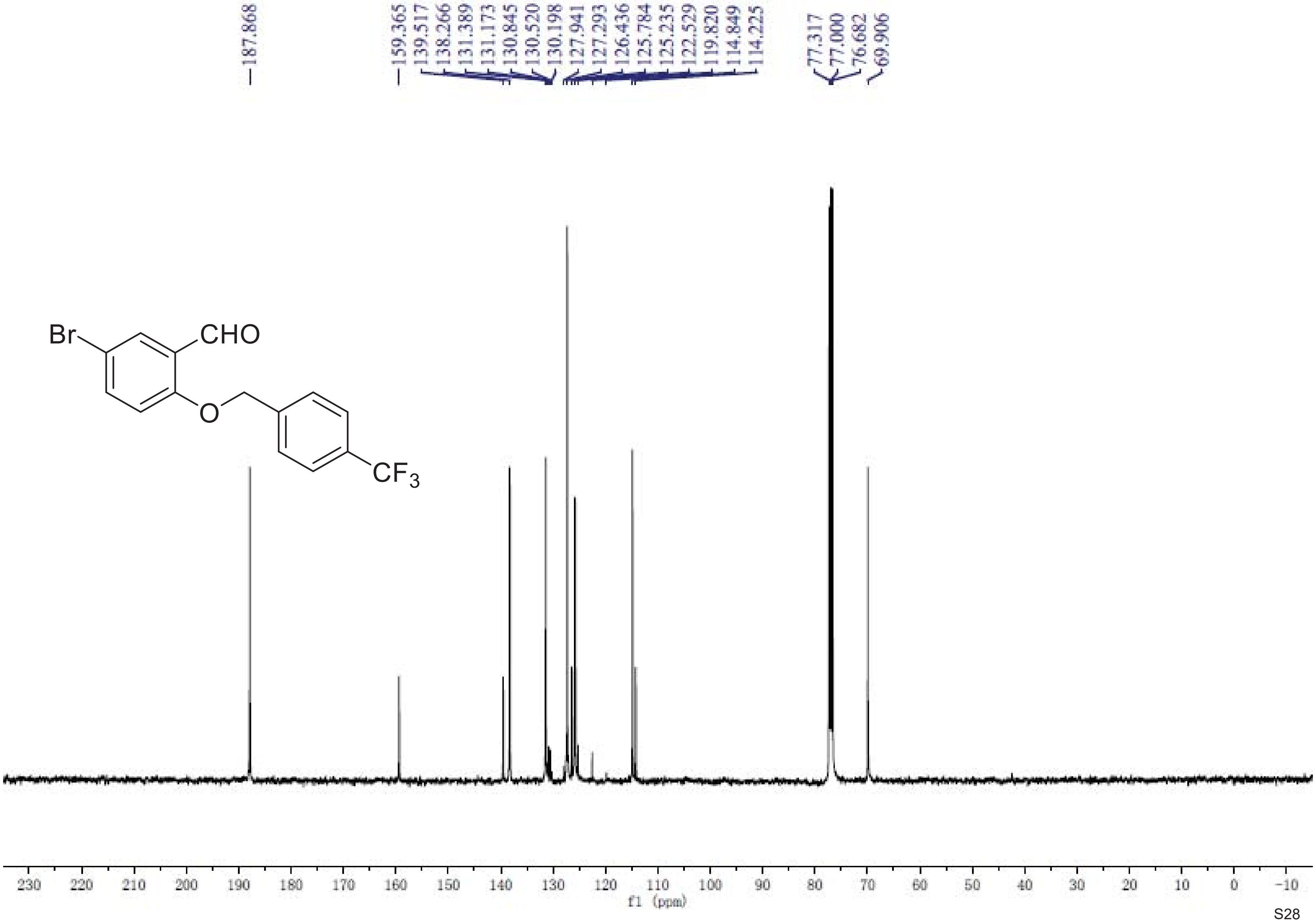


5-bromo-2-((4-(trifluoromethyl)benzyl)oxy)benzaldehyde



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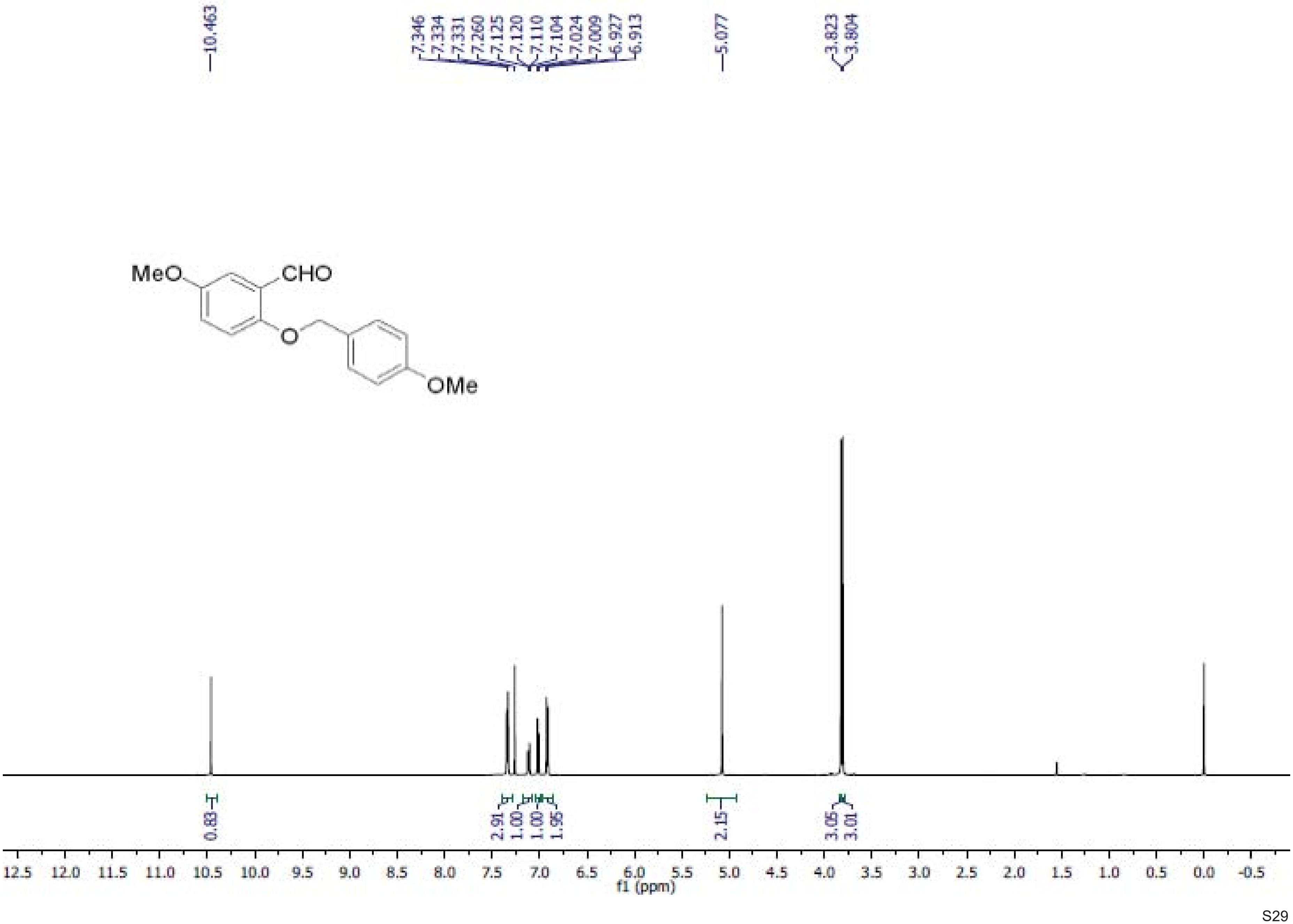
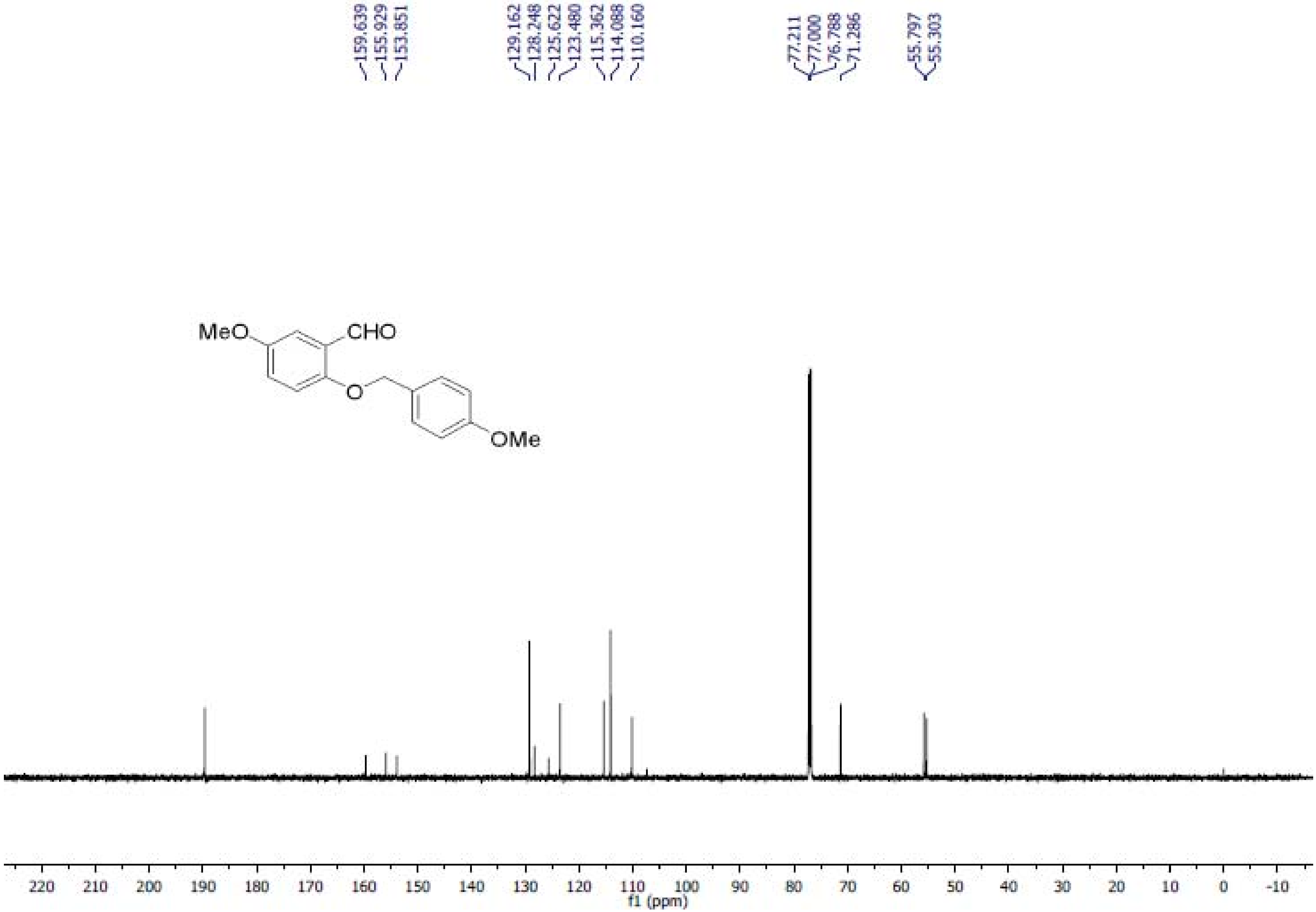
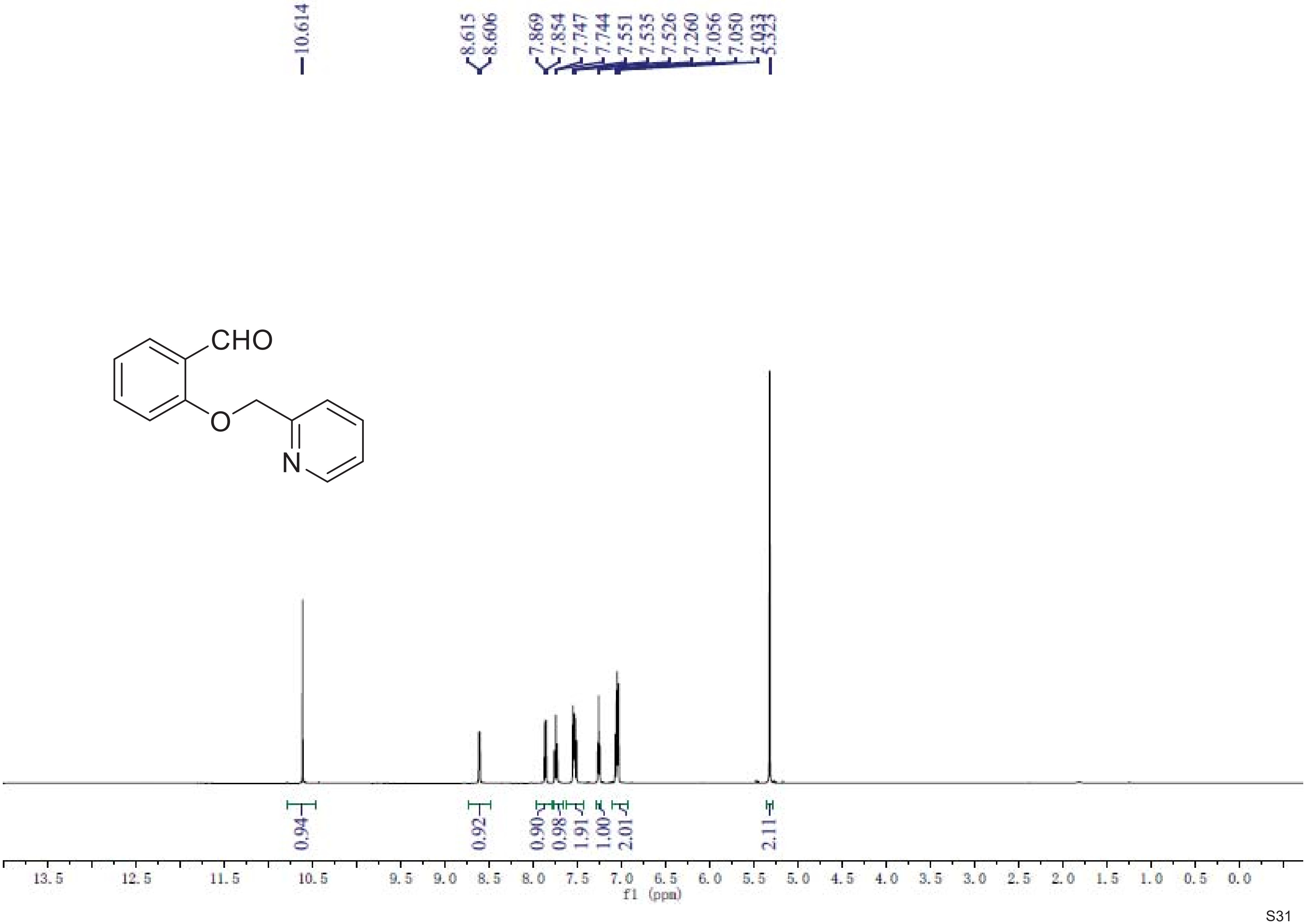


5-methoxy-2-((4-methoxybenzyl)oxy)benzaldehyde



2-(pyridin-2-ylmethoxy)benzaldehyde



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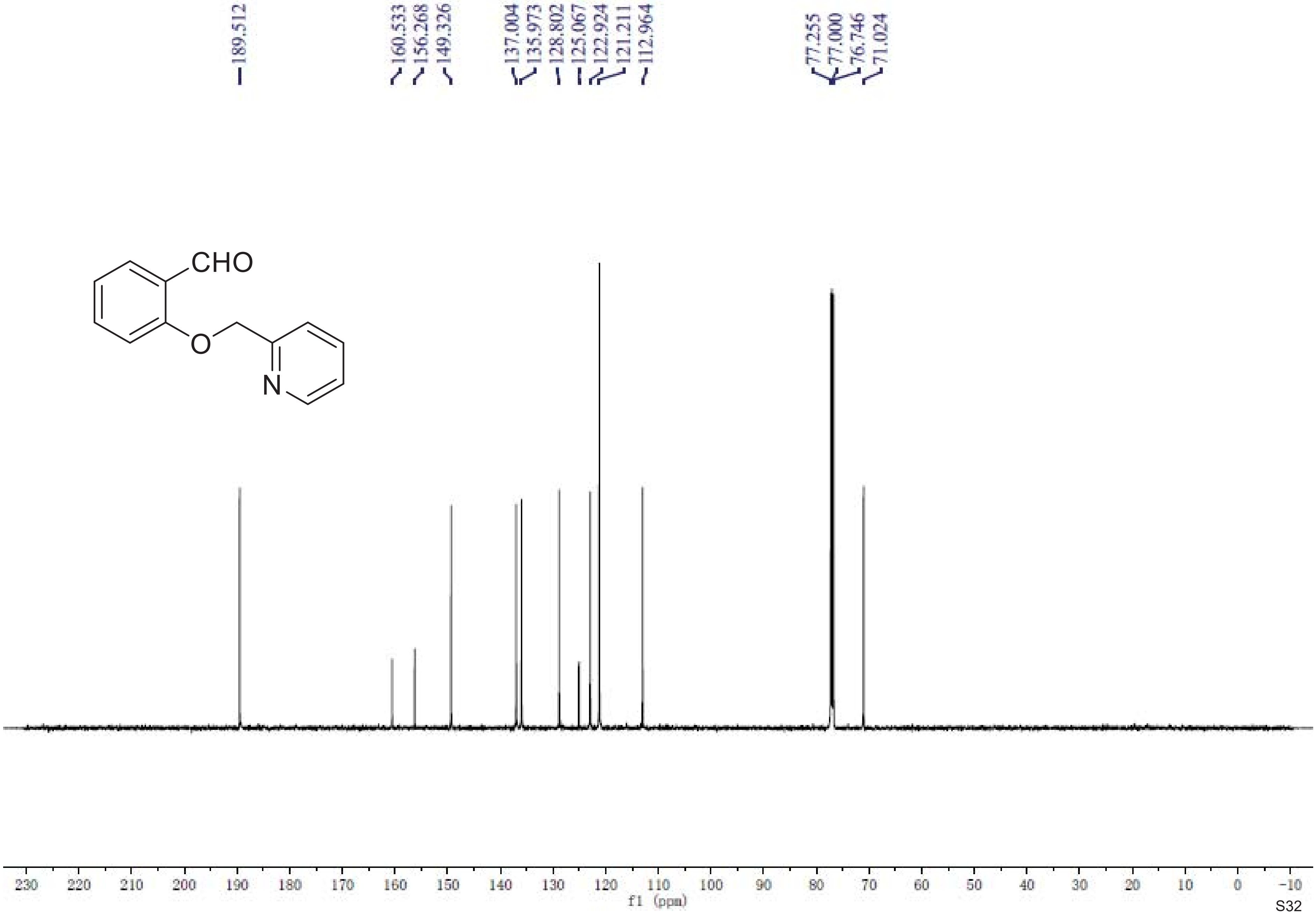

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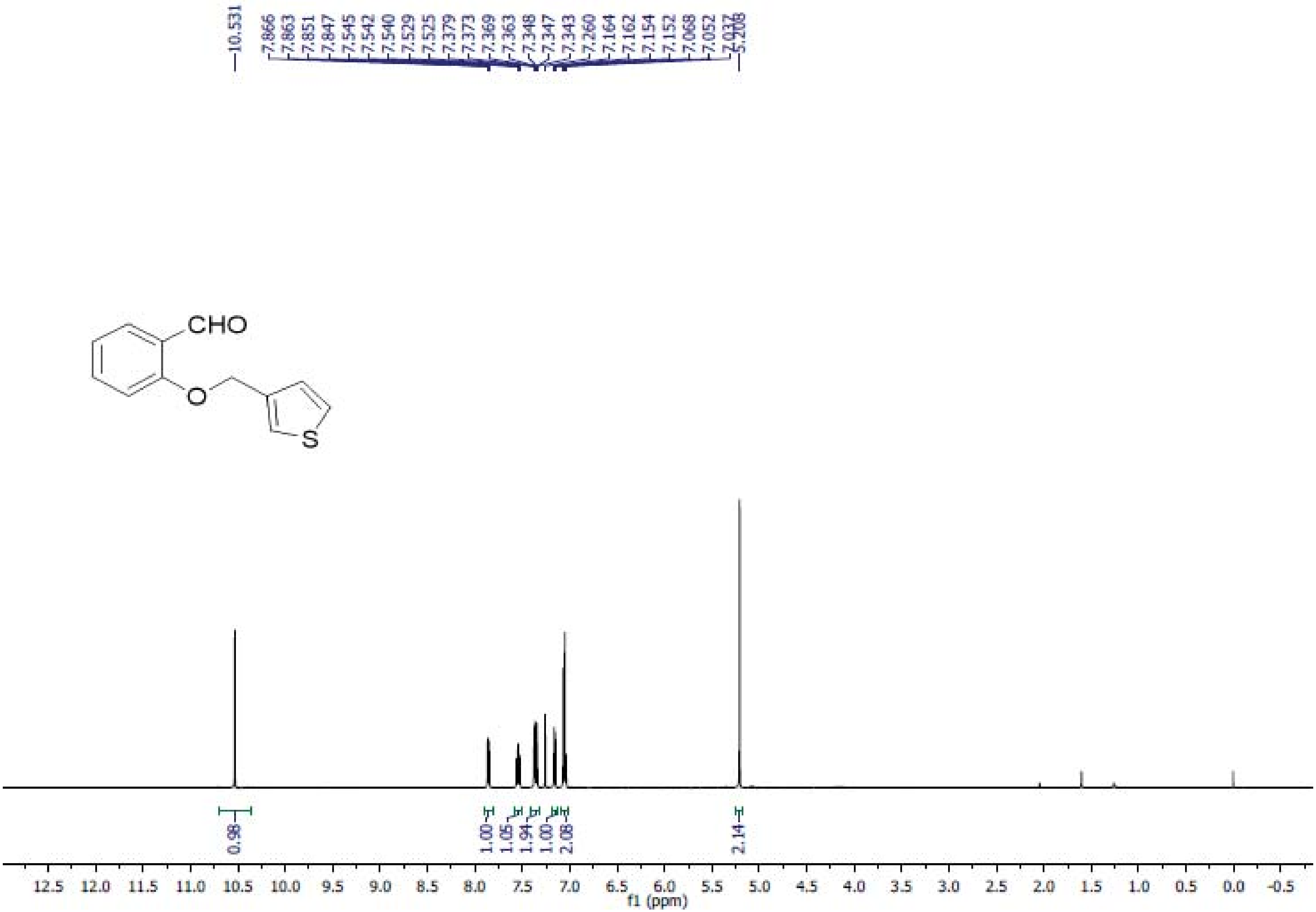
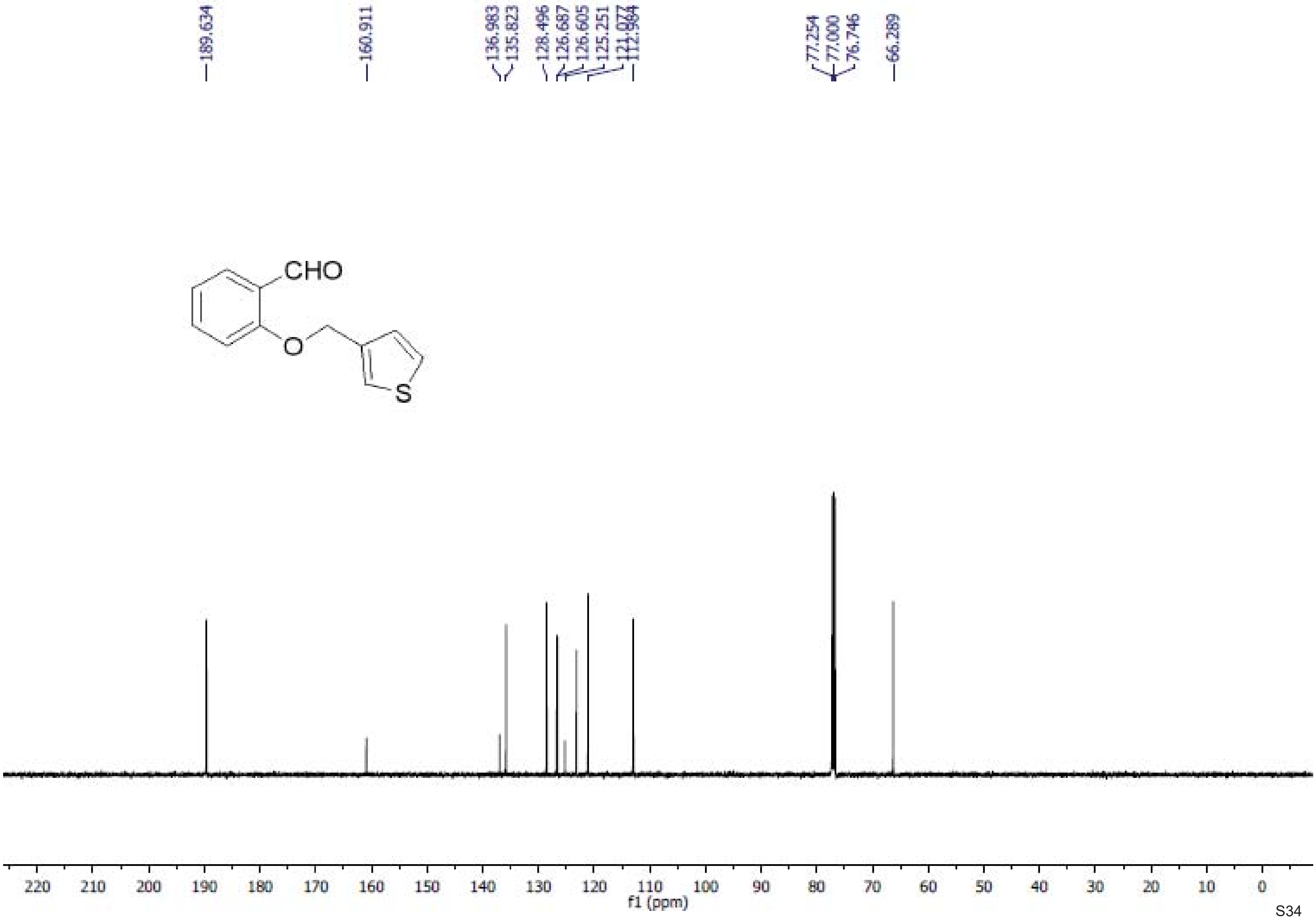


2-(thiophen-3-ylmethoxy)benzaldehyde



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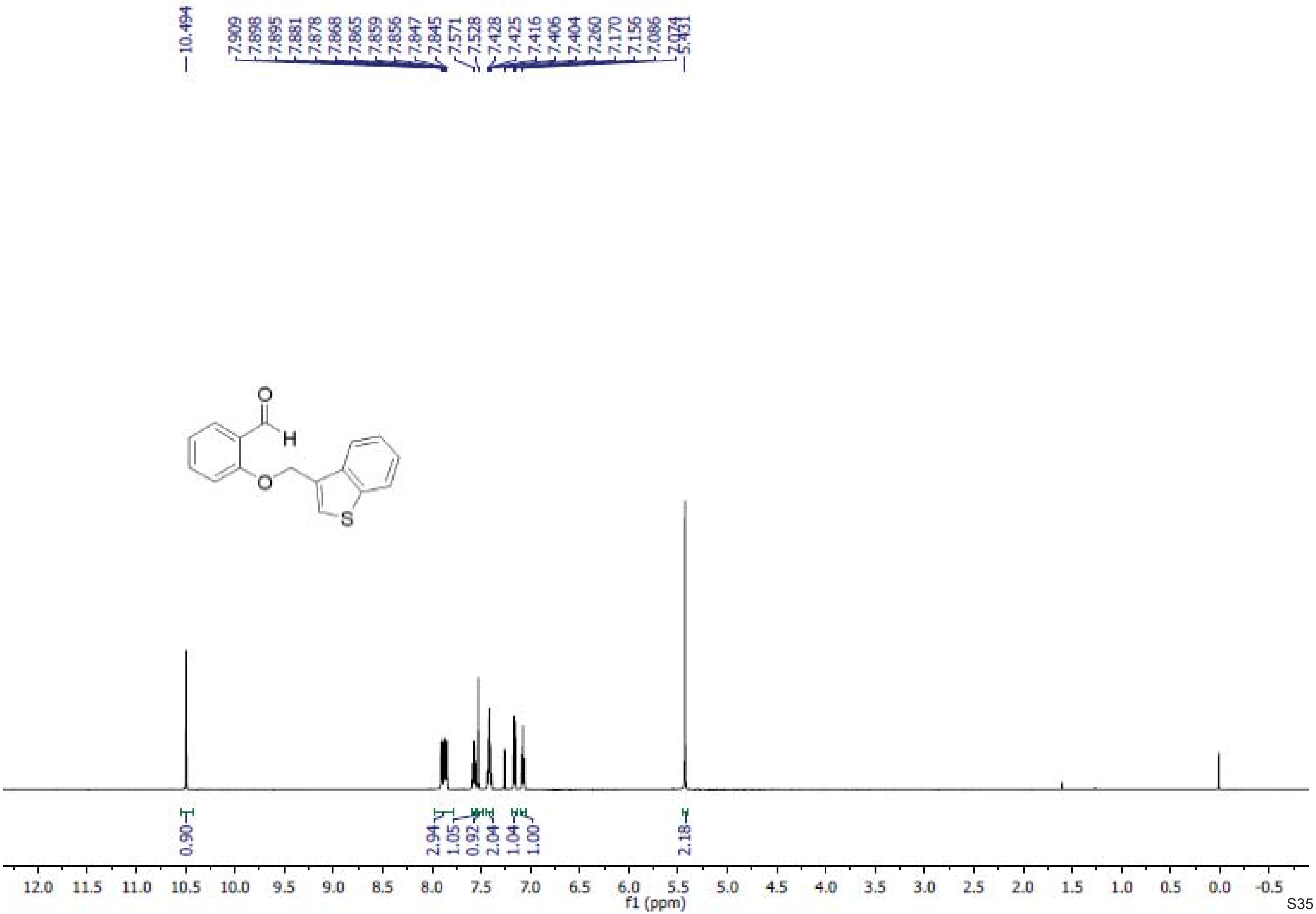
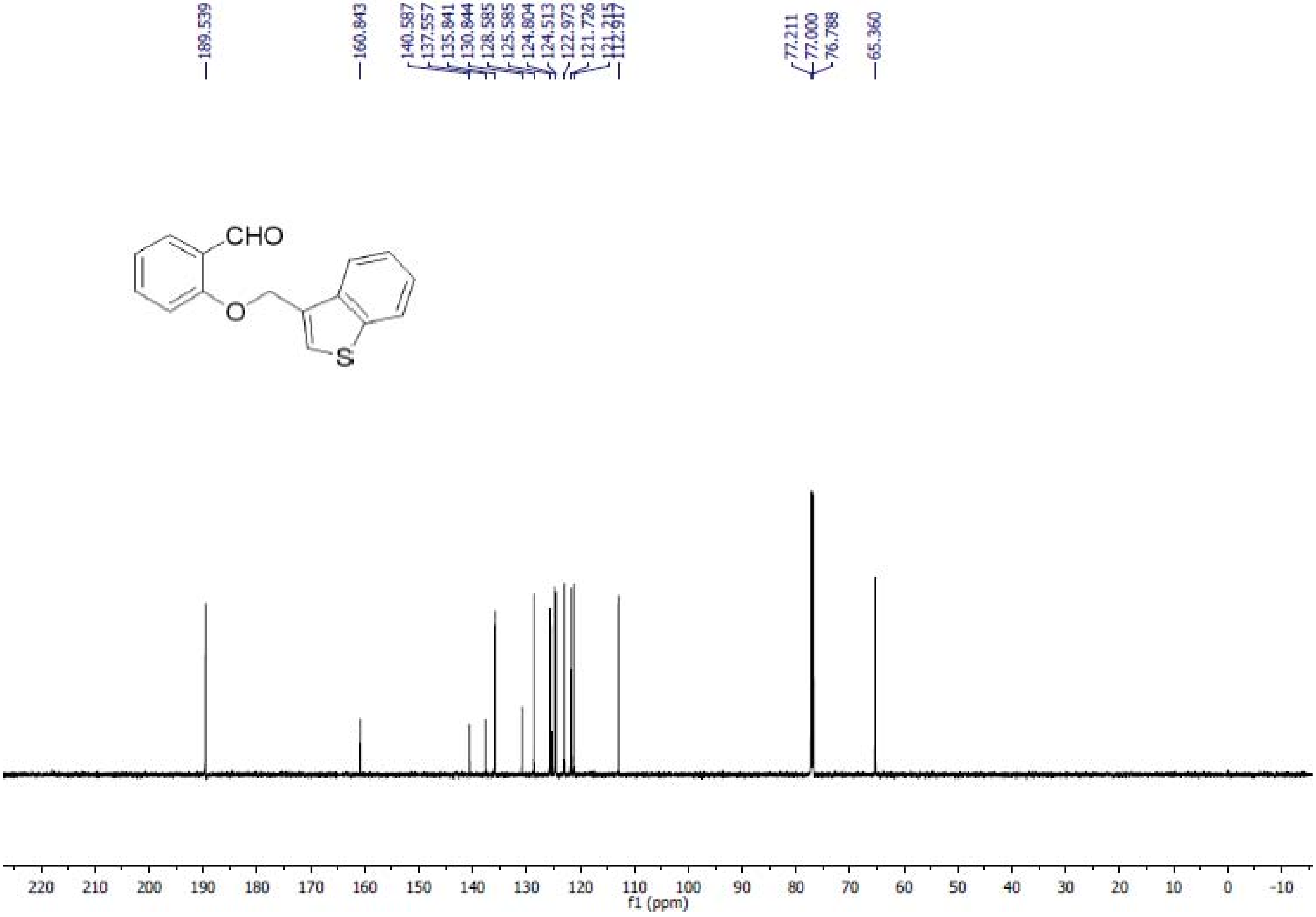
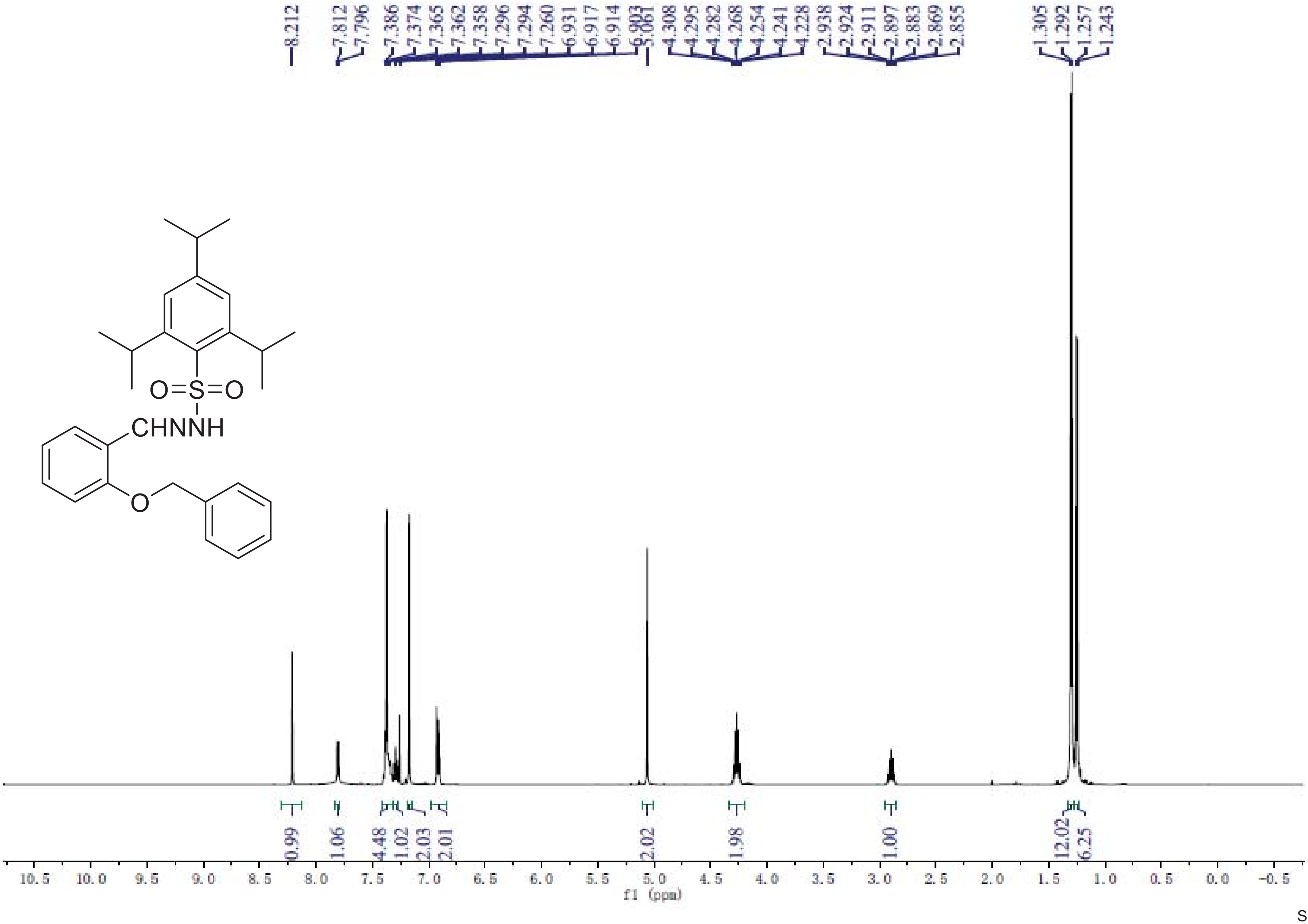


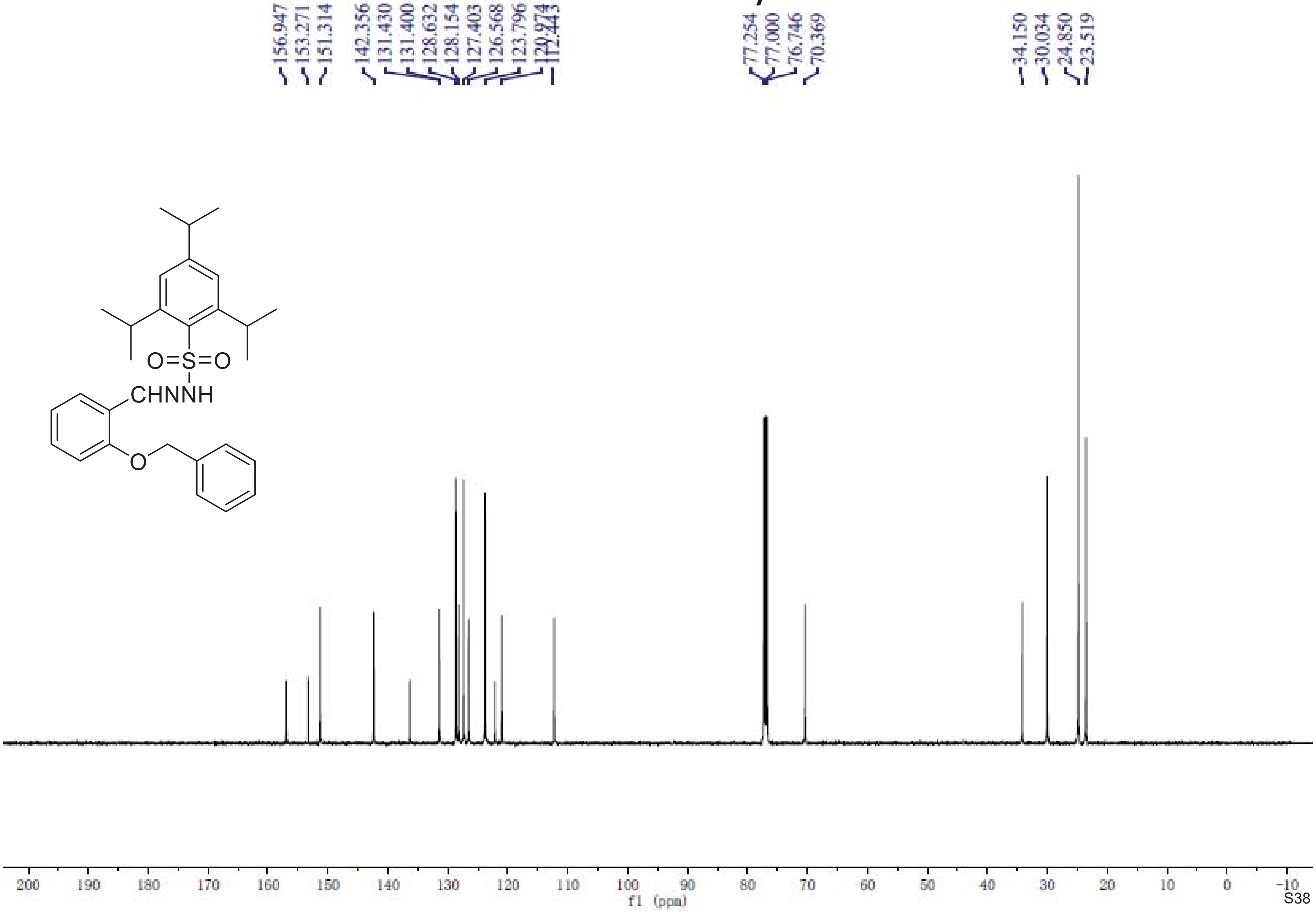
2-(benzo[b]thiophen-3-ylmethoxy)benzaldehyde



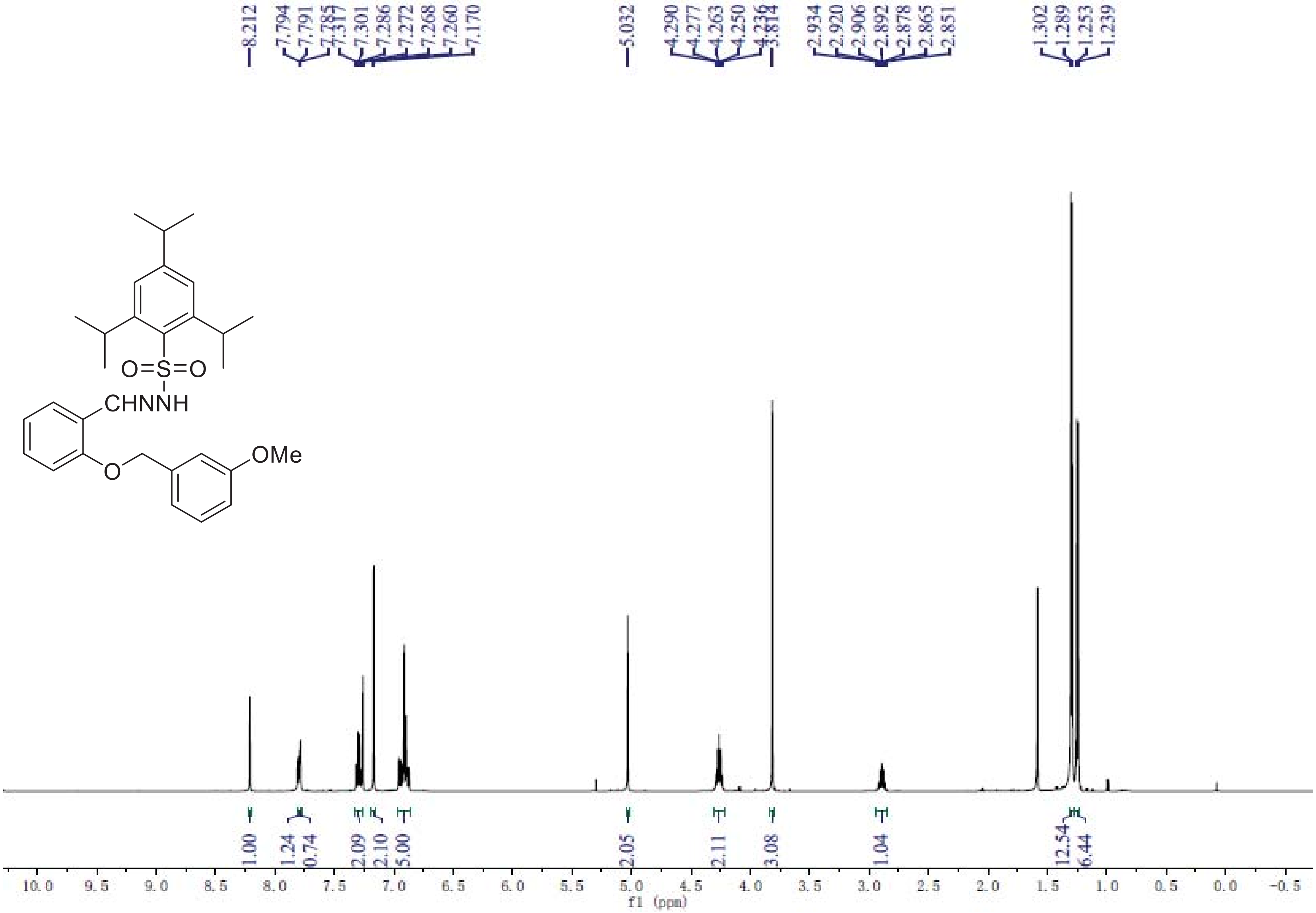
N'-(2-(benzyloxy)benzylidene)-2,4,6-triisopropyl-benzenesulfonohydrazide



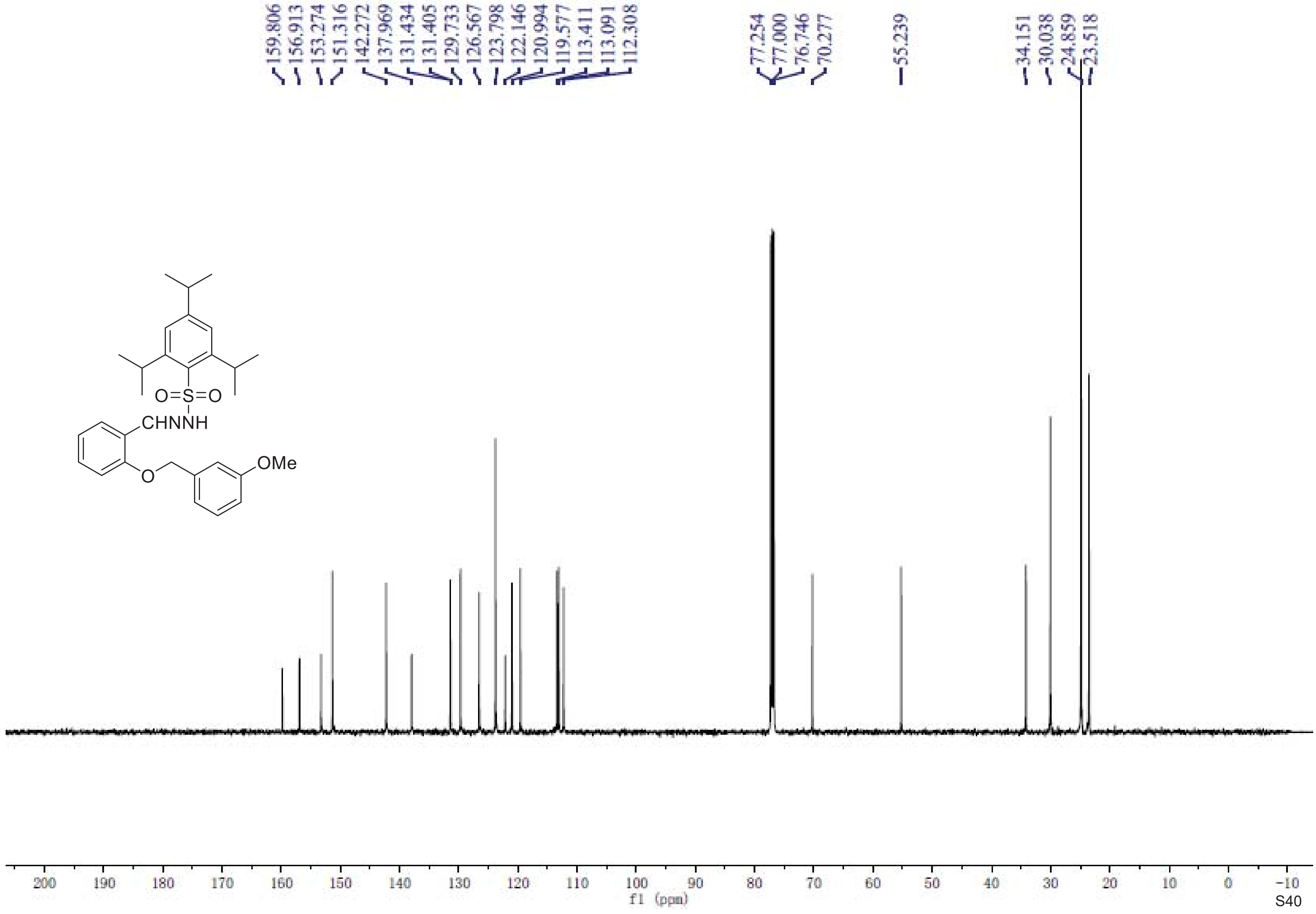
N'-(2-(benzyloxy)benzylidene)-2,4,6-triisopropyl-benzenesulfonohydrazide



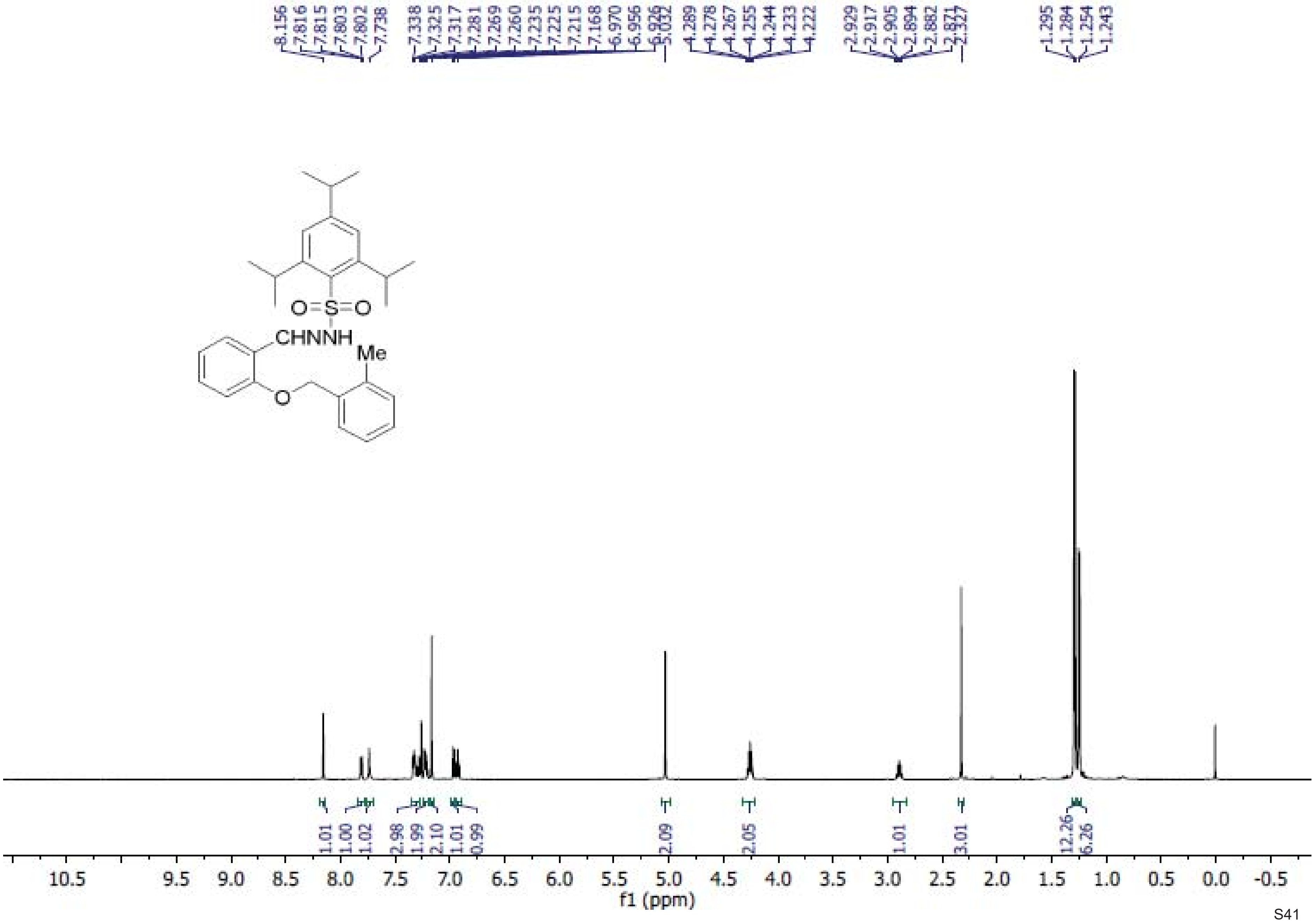
2,4,6-triisopropyl-N'-(2-((3-methoxybenzyl)oxy)benzylidene) benzenesulfonohydrazide



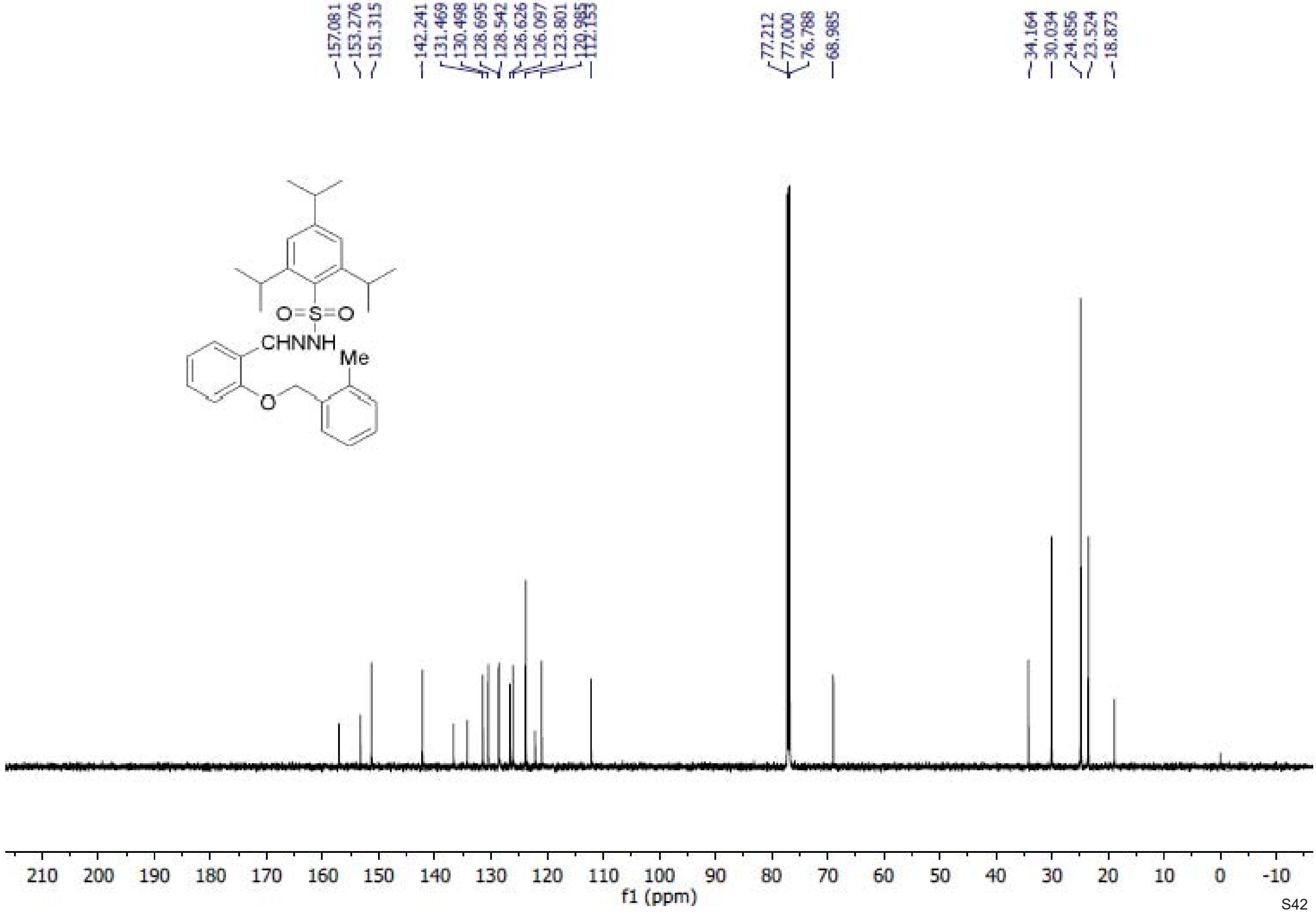
2,4,6-triisopropyl-N'-(2-((3-methoxybenzyl)oxy)benzylidene) benzenesulfonohydrazide



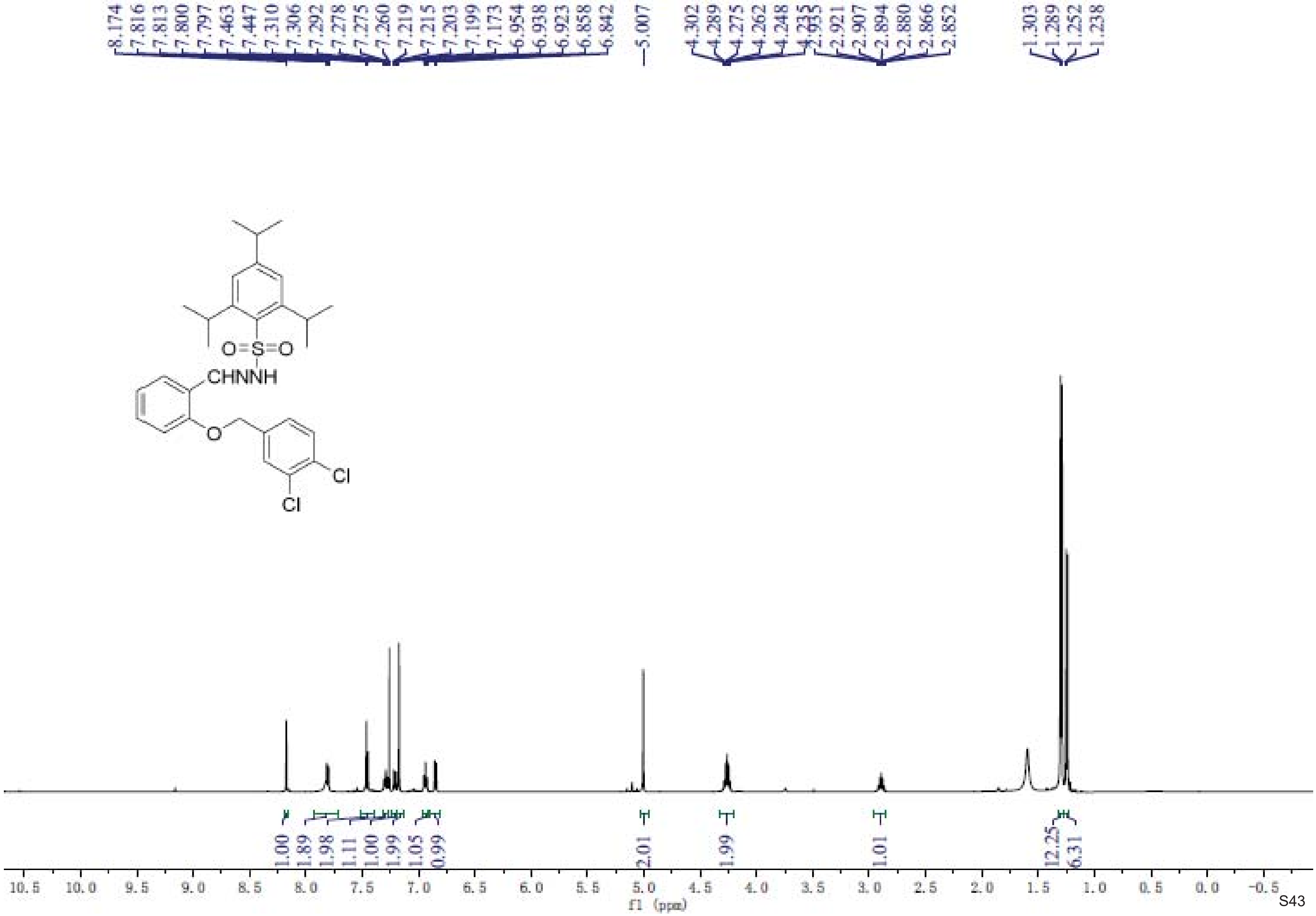
2,4,6-triisopropyl-N'-(2-((2-methylbenzyl)oxy)benzylidene)benzenesulfonohydrazide



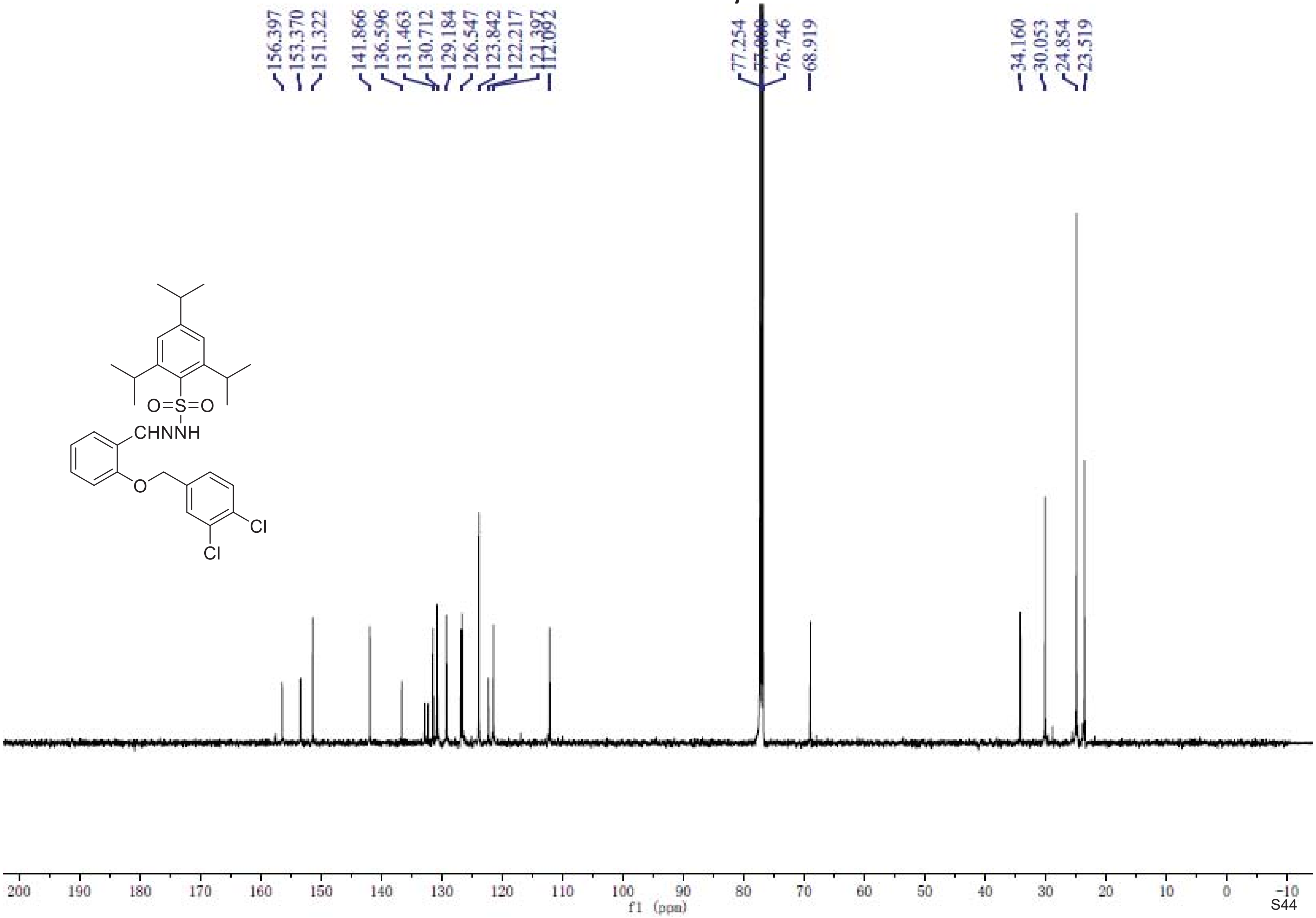
2,4,6-triisopropyl-N'-(2-((2-methylbenzyl)oxy)benzylidene)benzenesulfonohydrazide



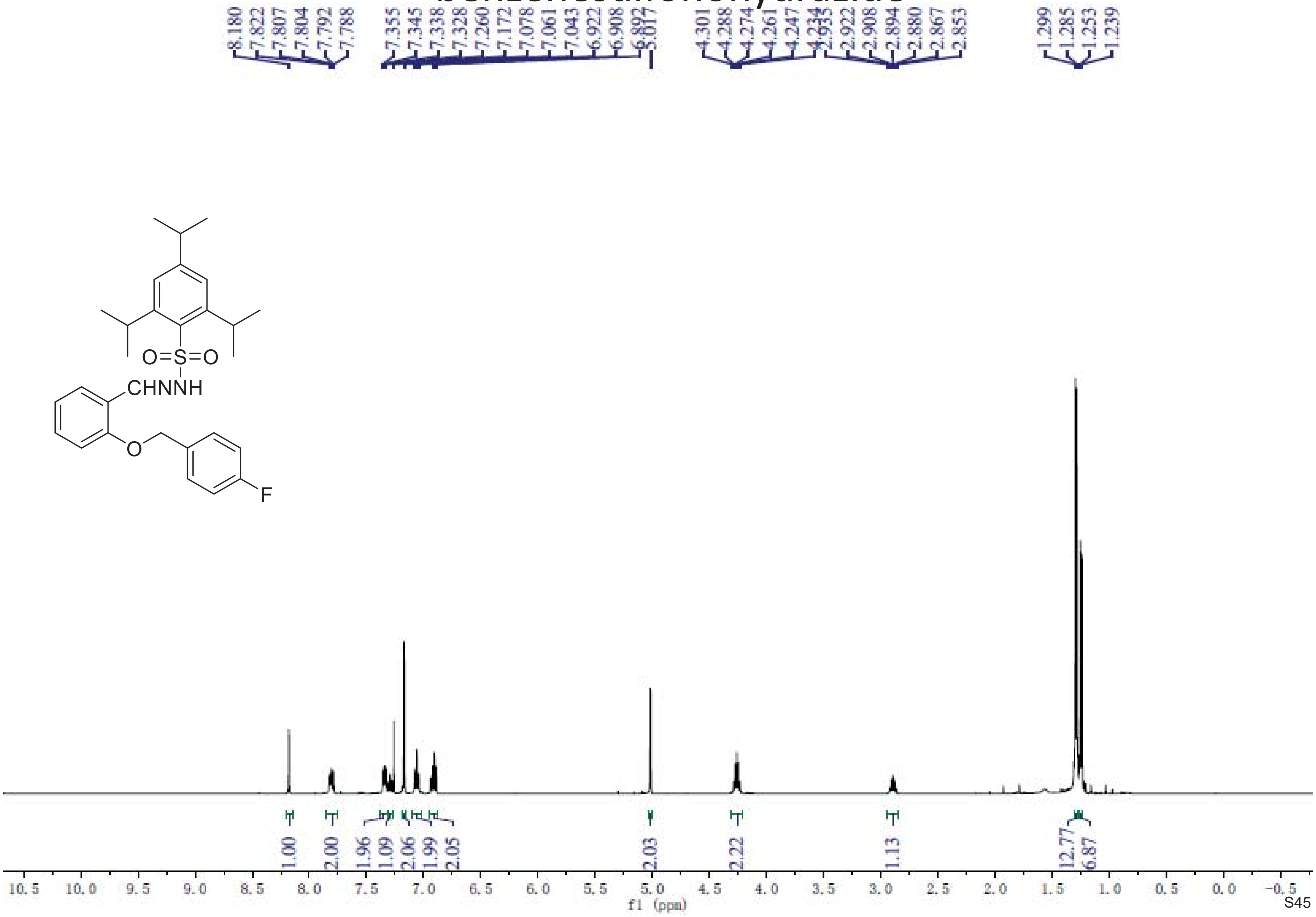
N'-(2-((3,4-dichlorobenzyl)oxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



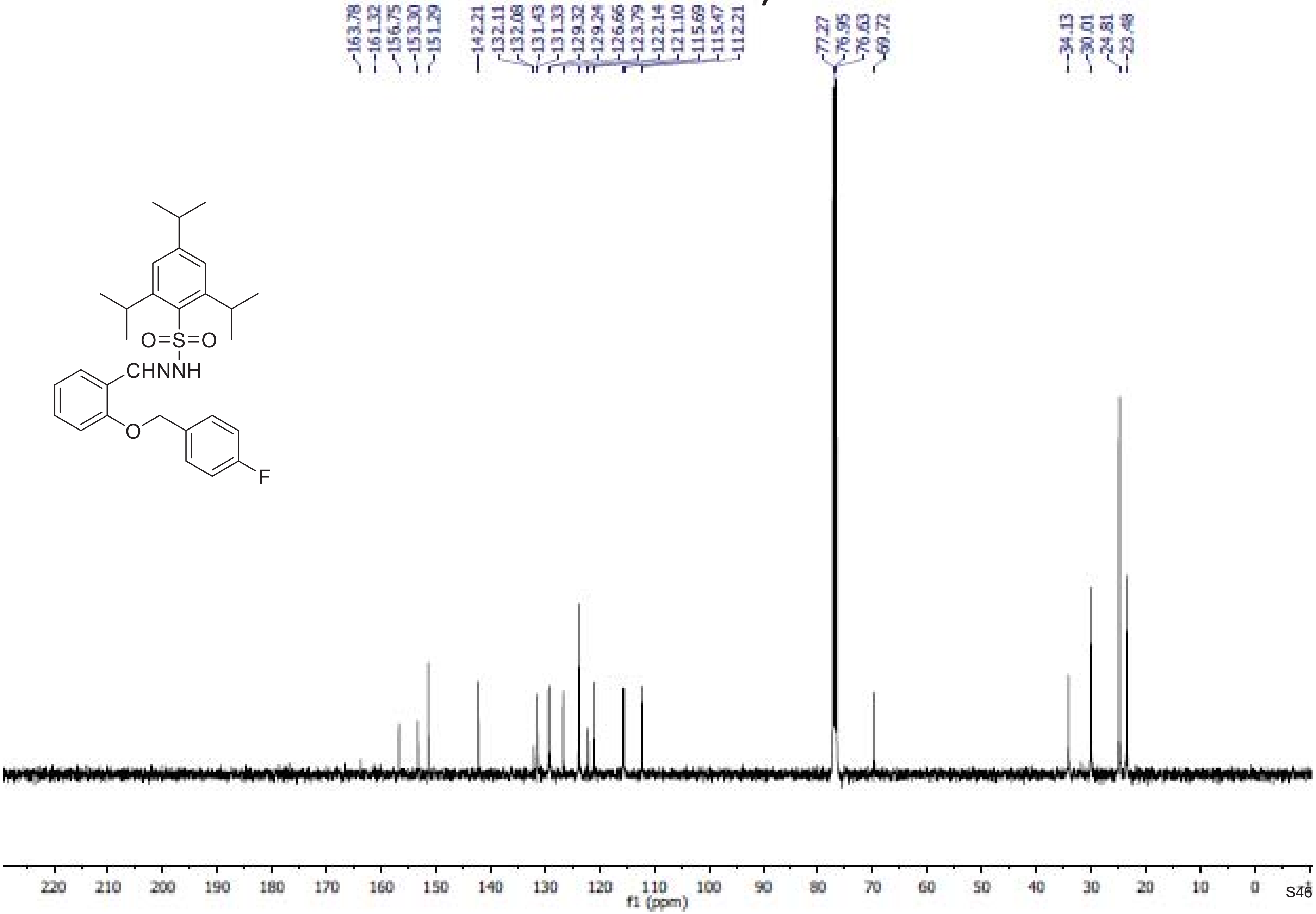
N'-(2-((3,4-dichlorobenzyl)oxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



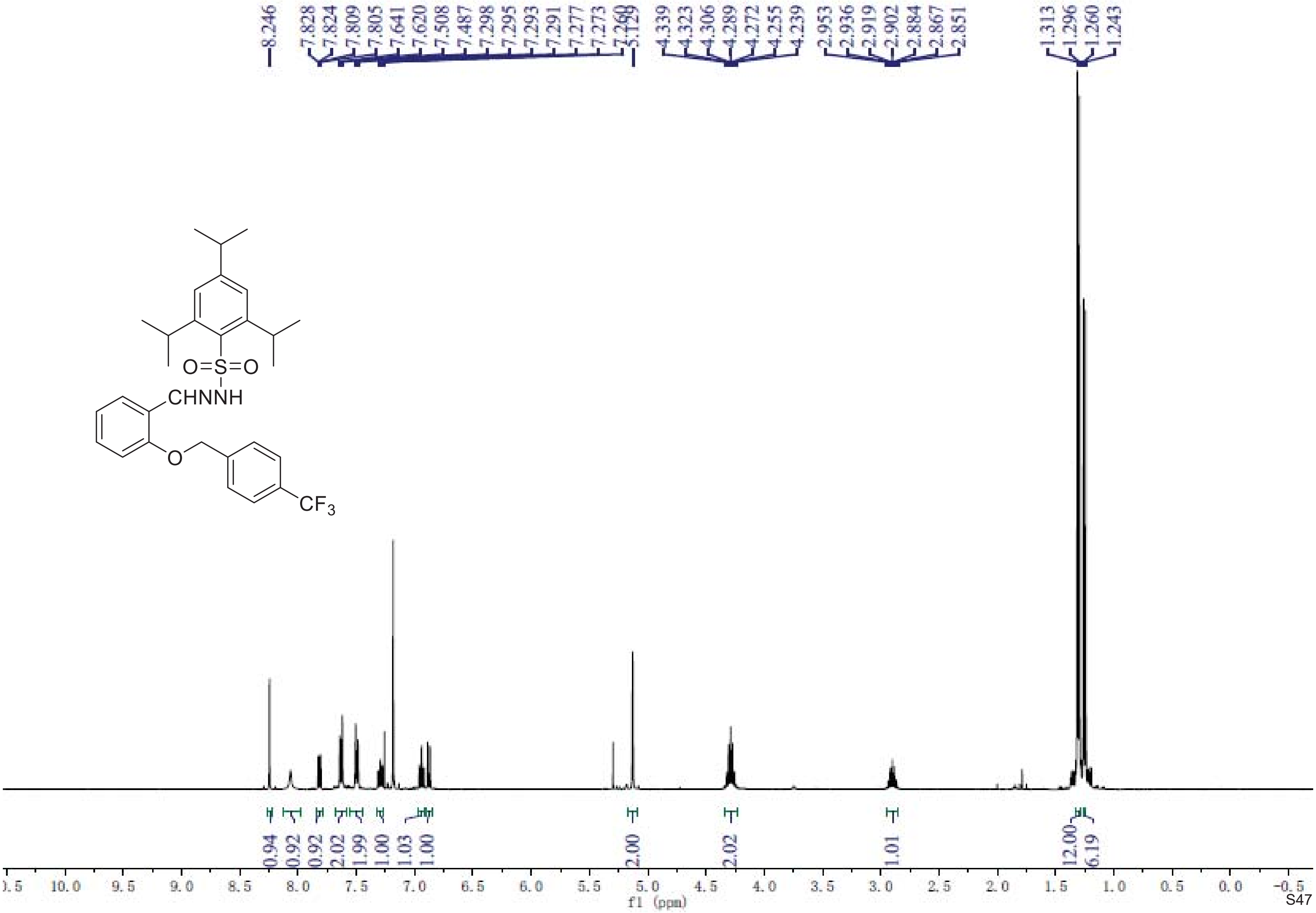
N'-(2-(benzyloxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



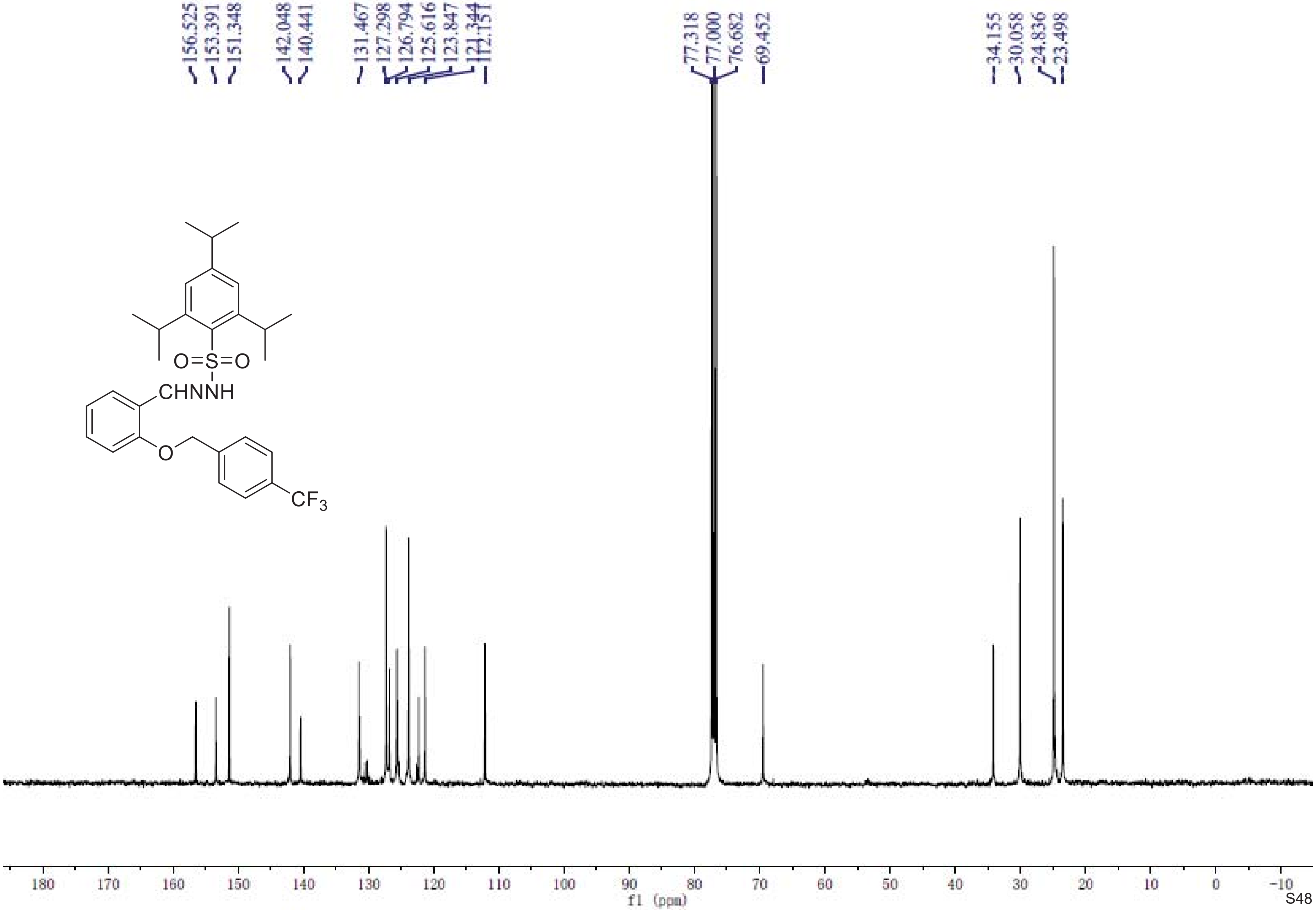
N'-(2-(benzyloxy)benzylidene)-2,4,6-triisopropyl-benzenesulfonohydrazide



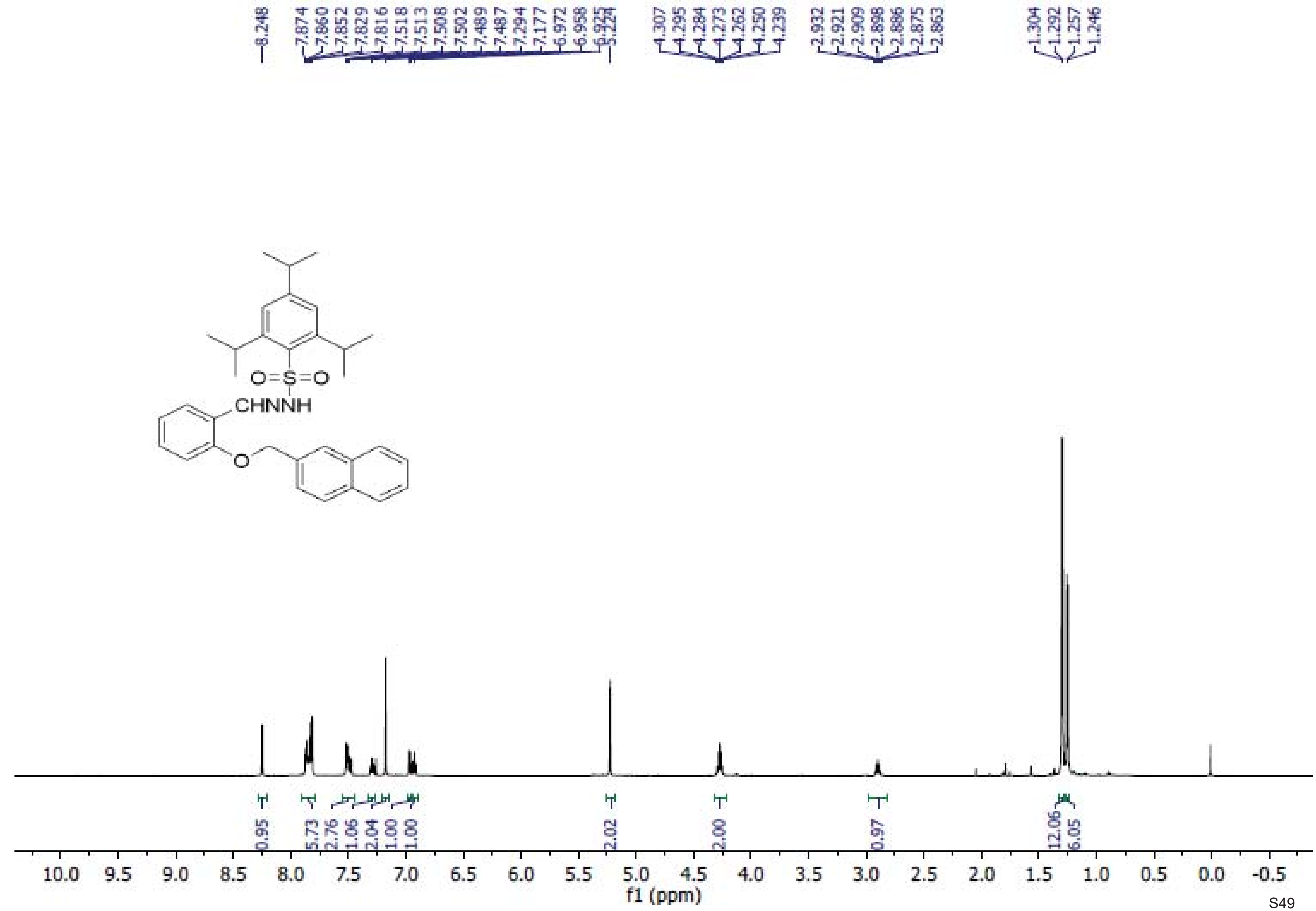
2,4,6-triisopropyl-N'-(2-((4-(trifluoromethyl)benzyl)oxy)benzylidene)benzenesulfonohydrazide



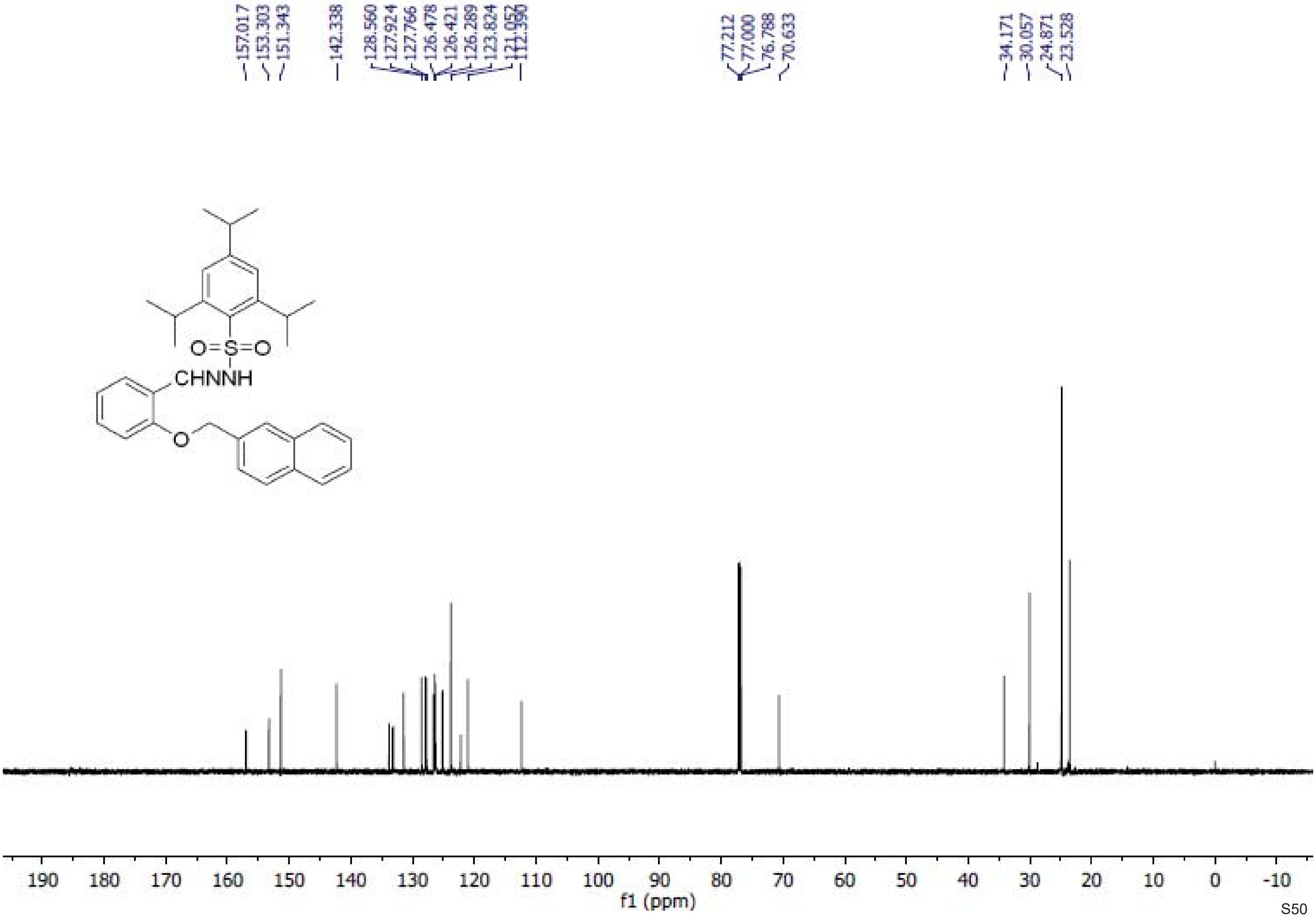
2,4,6-triisopropyl-N'-(2-((4-(trifluoromethyl)benzyl)oxy) benzylidene)benzenesulfonohydrazide



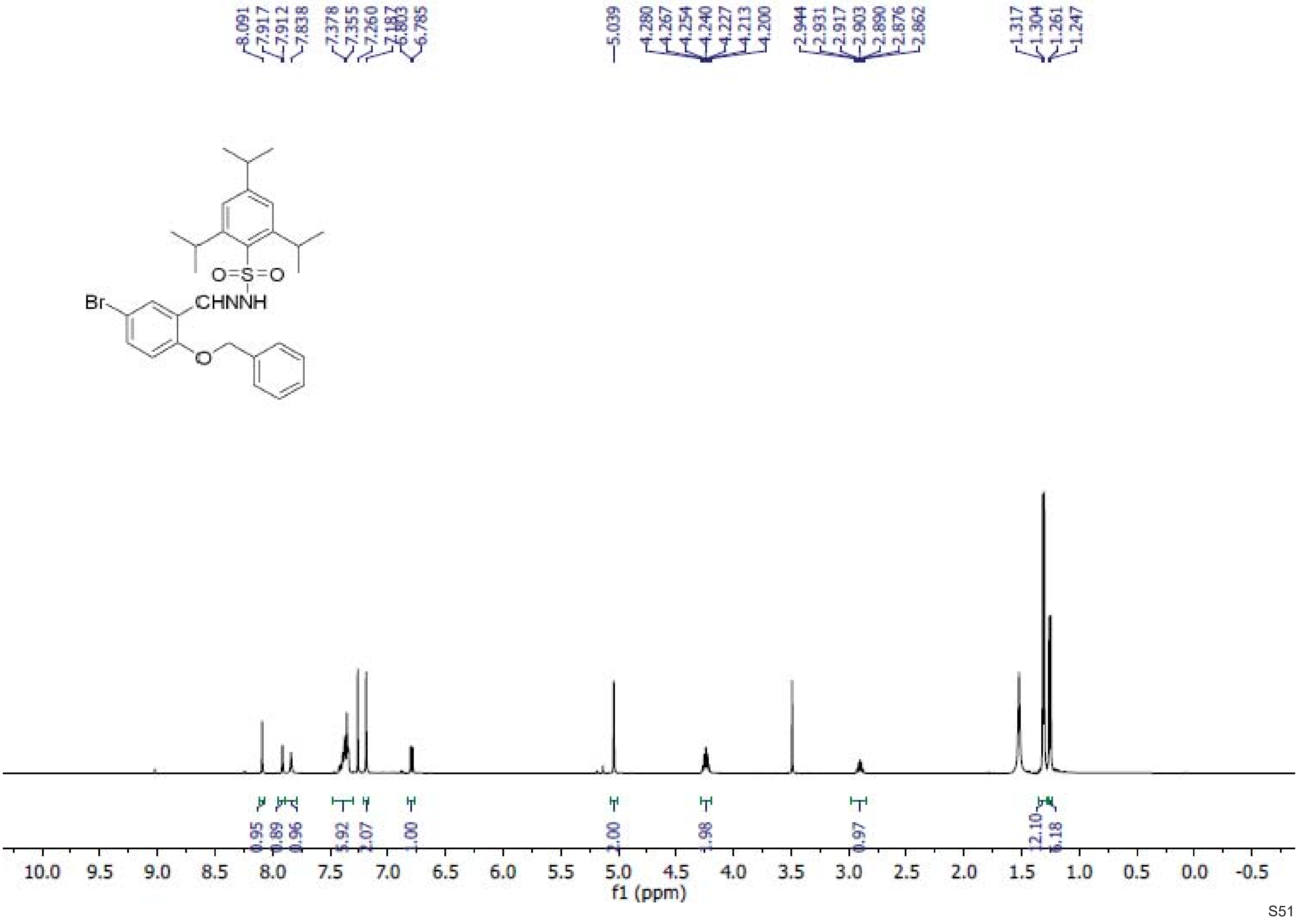
2,4,6-triisopropyl-N'-(2-(naphthalen-2-ylmethoxy)benzylidene)benzenesulfonohydrazide



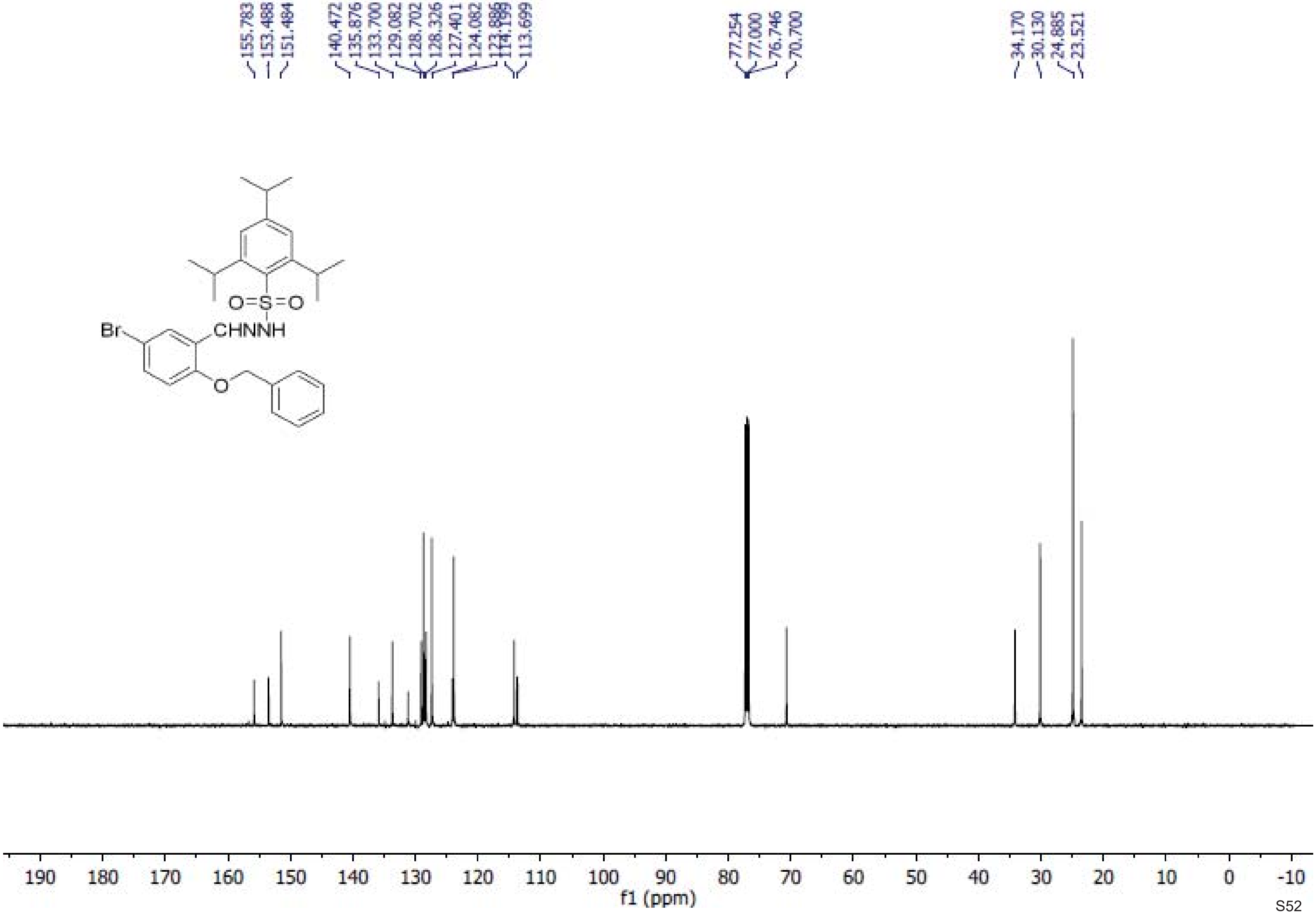
2,4,6-triisopropyl-N'-(2-(naphthalen-2-ylmethoxy)benzylidene)benzenesulfonohydrazide



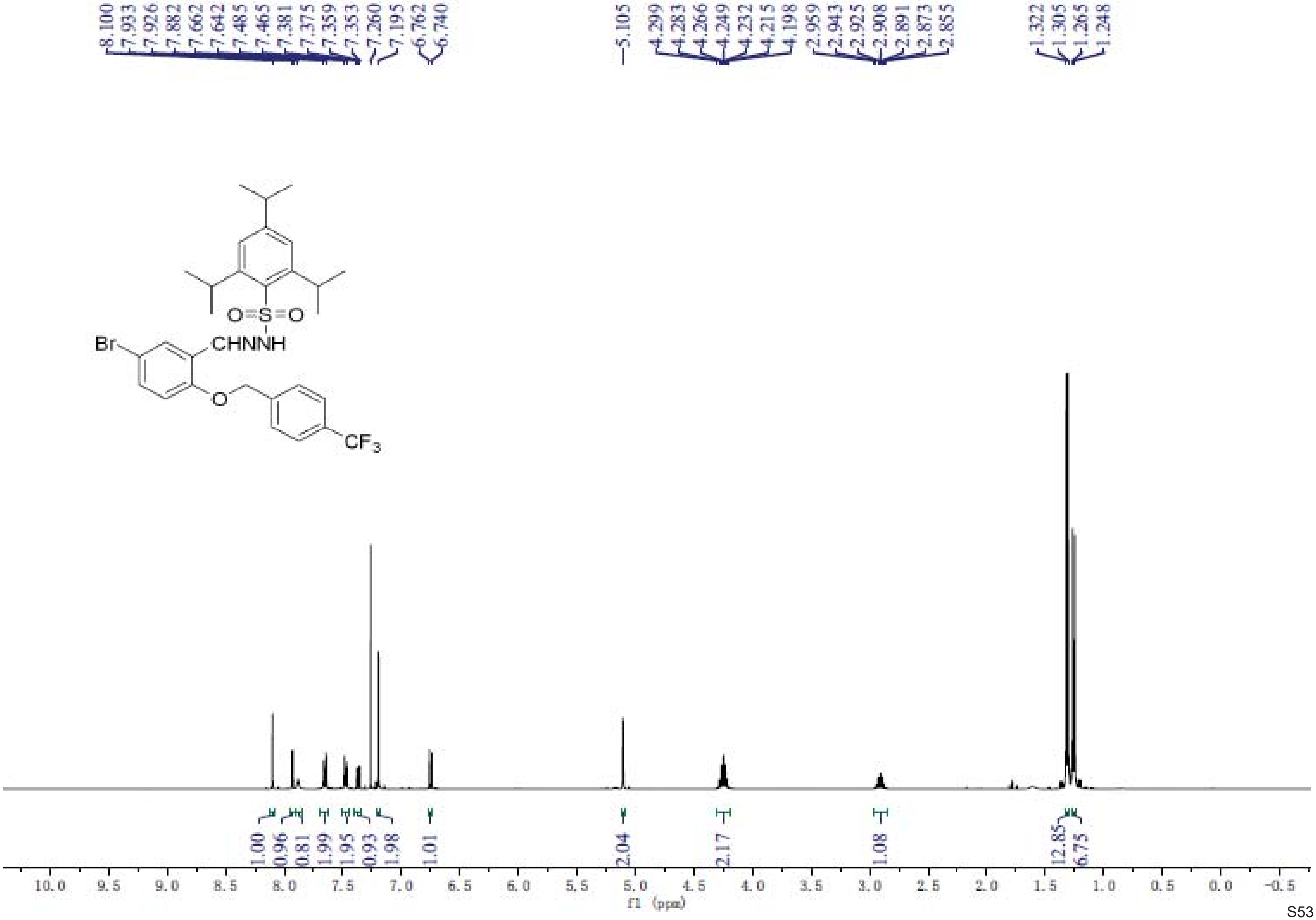
N'-(2-(benzyloxy)-5-bromobenzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



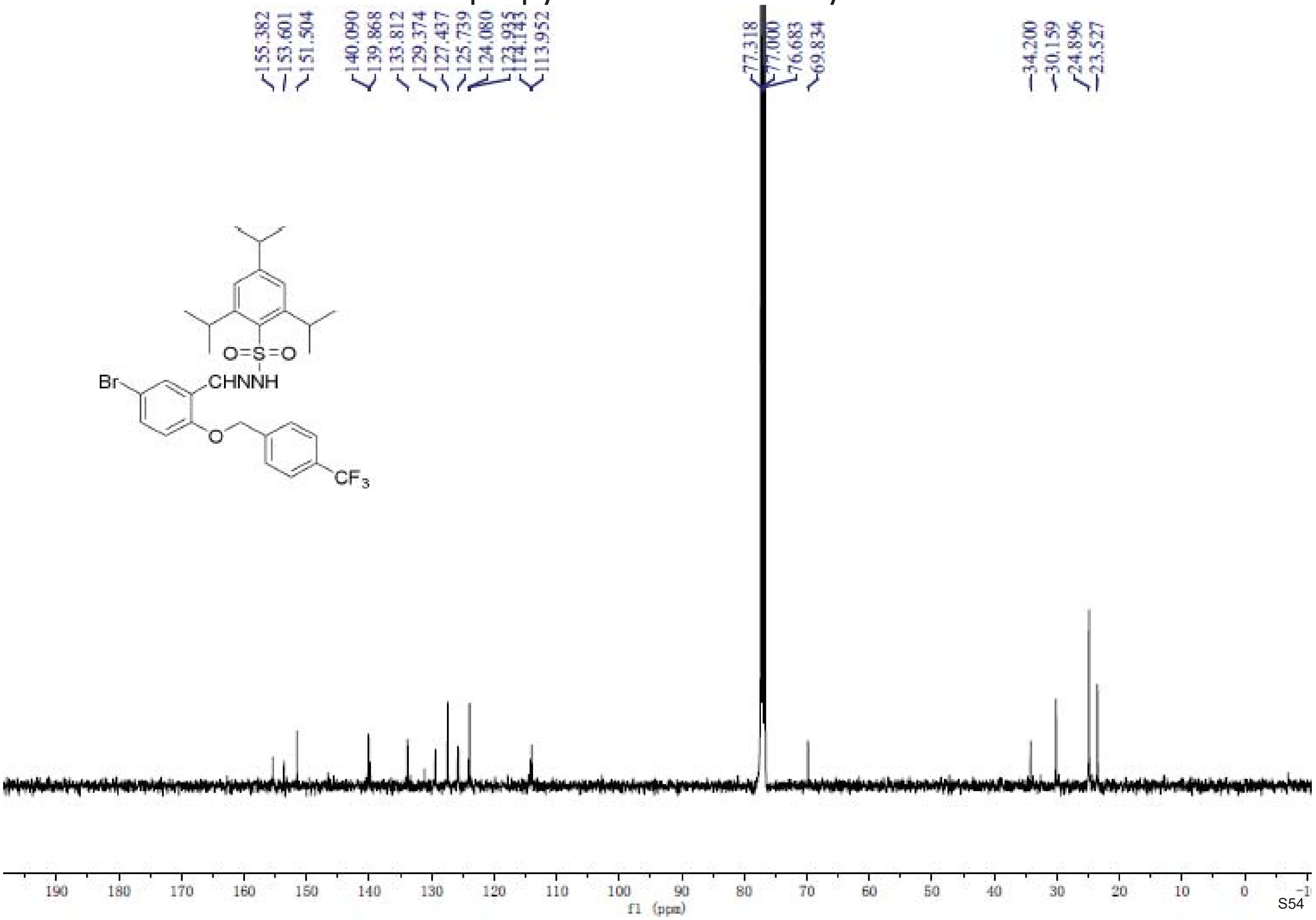
N'-(2-(benzyloxy)-5-bromobenzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



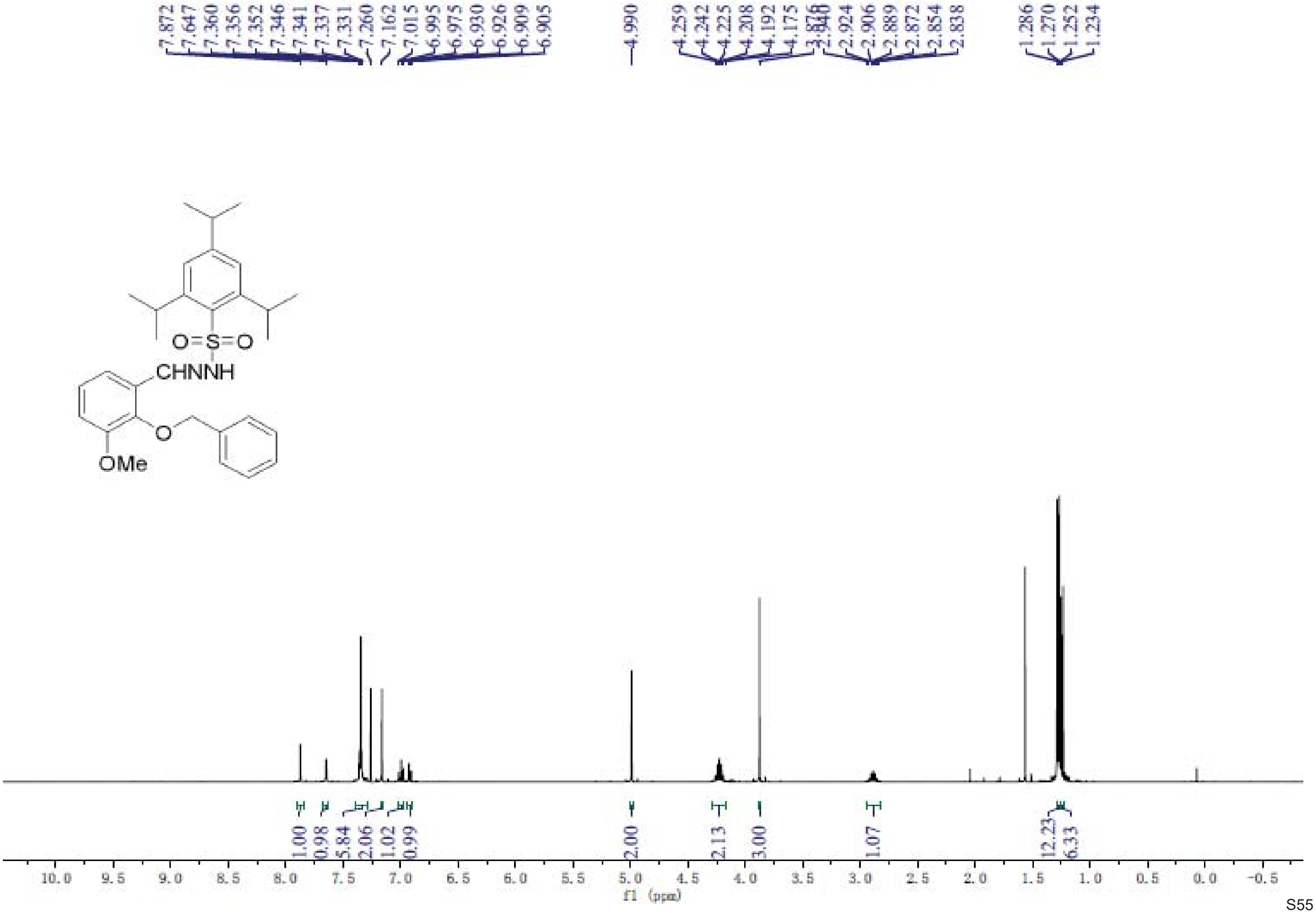
N'-(5-bromo-2-((4-(trifluoromethyl)benzyl)oxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



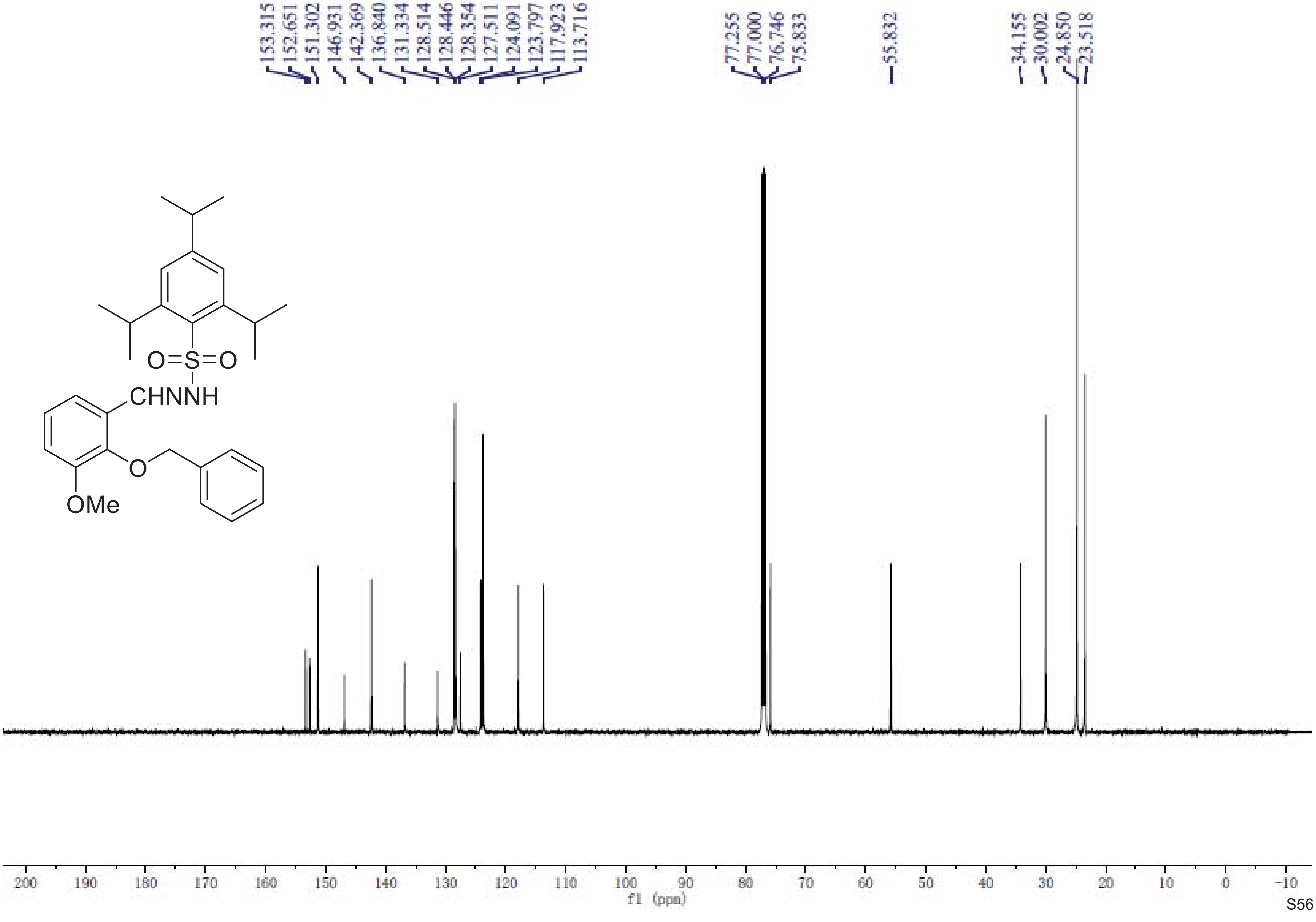
N'-(5-bromo-2-((4-(trifluoromethyl)benzyl)oxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



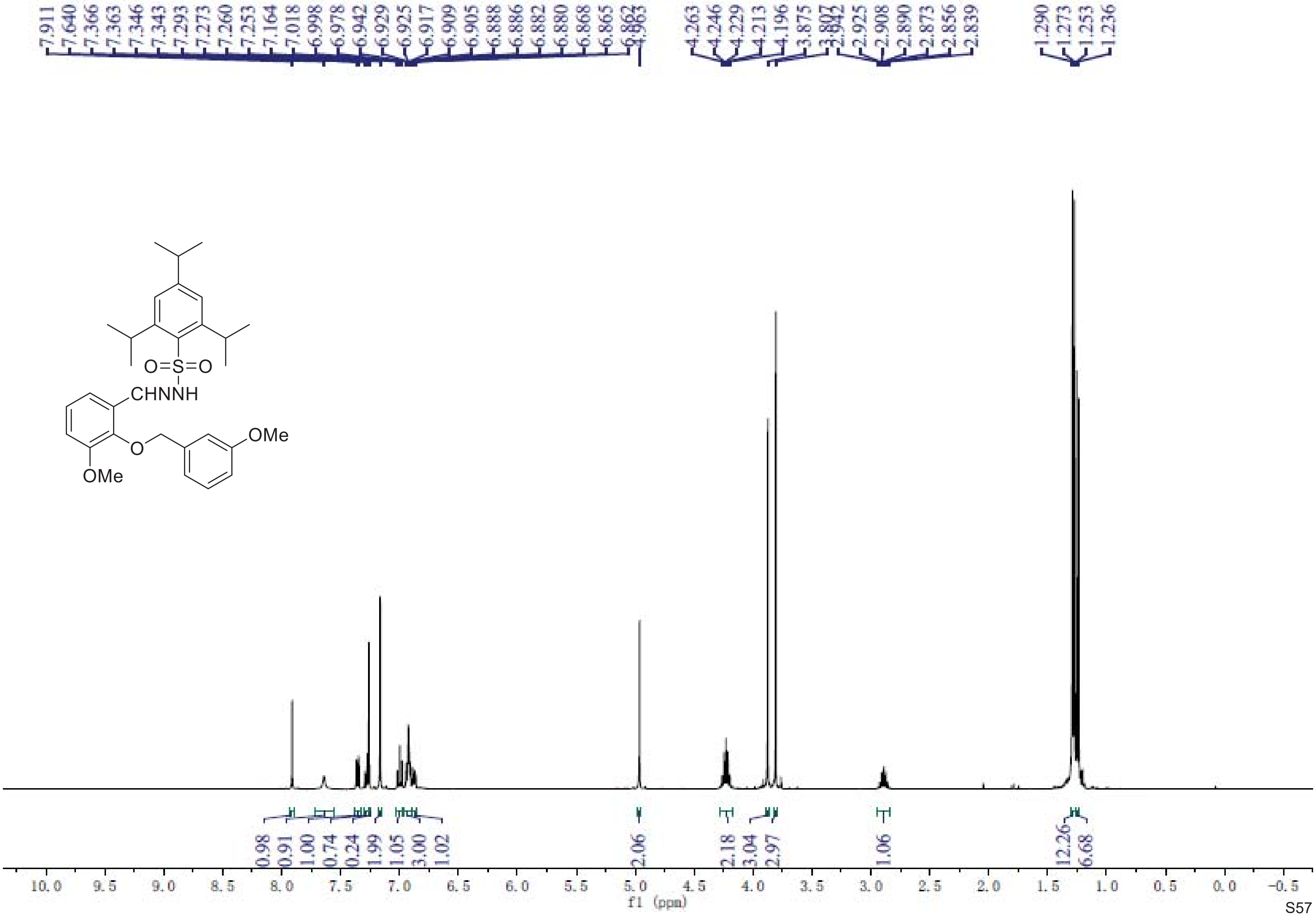
N'-(2-(benzyloxy)-3-methoxybenzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



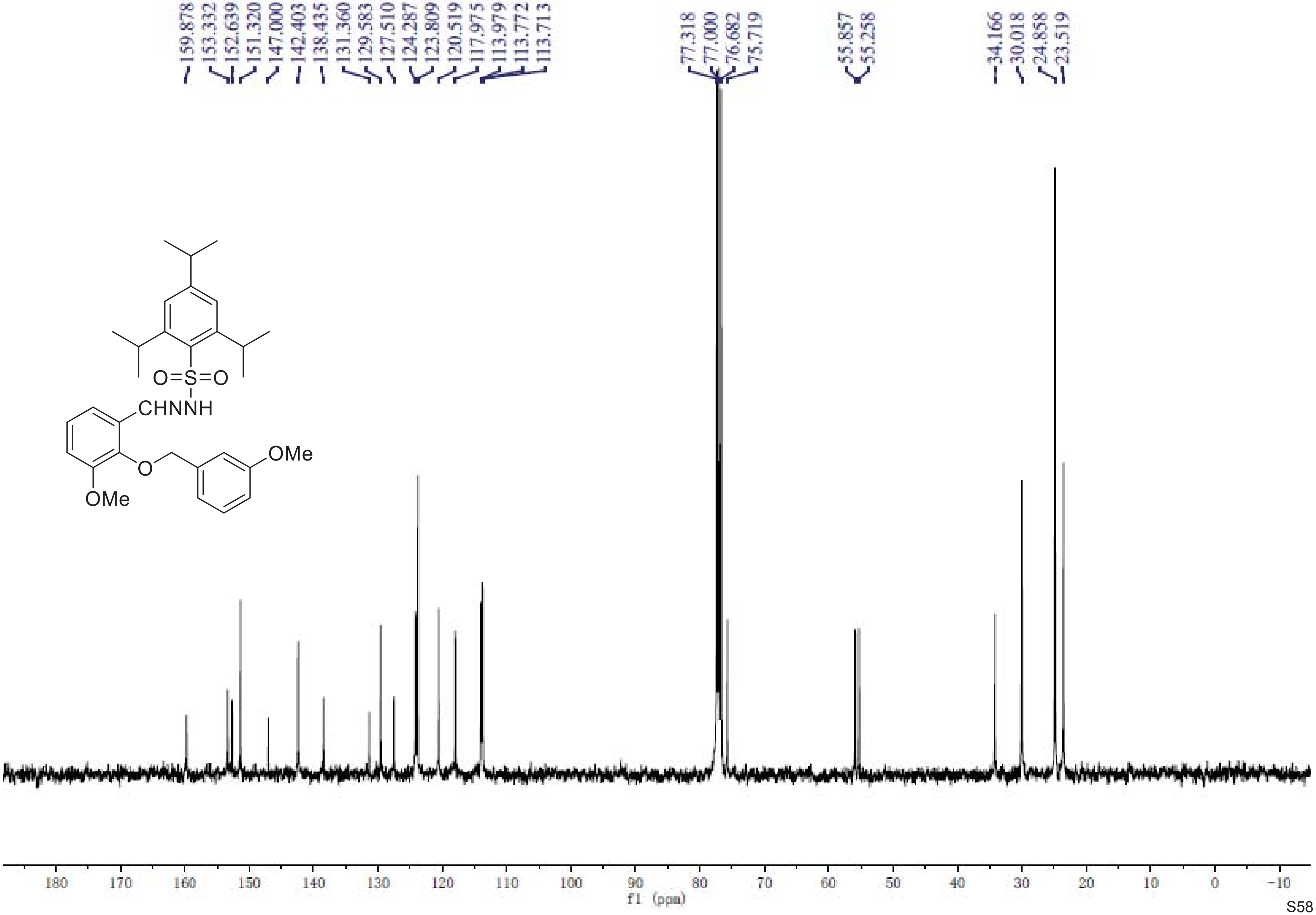
(E)-N'-(2-(benzyloxy)-3-methoxybenzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



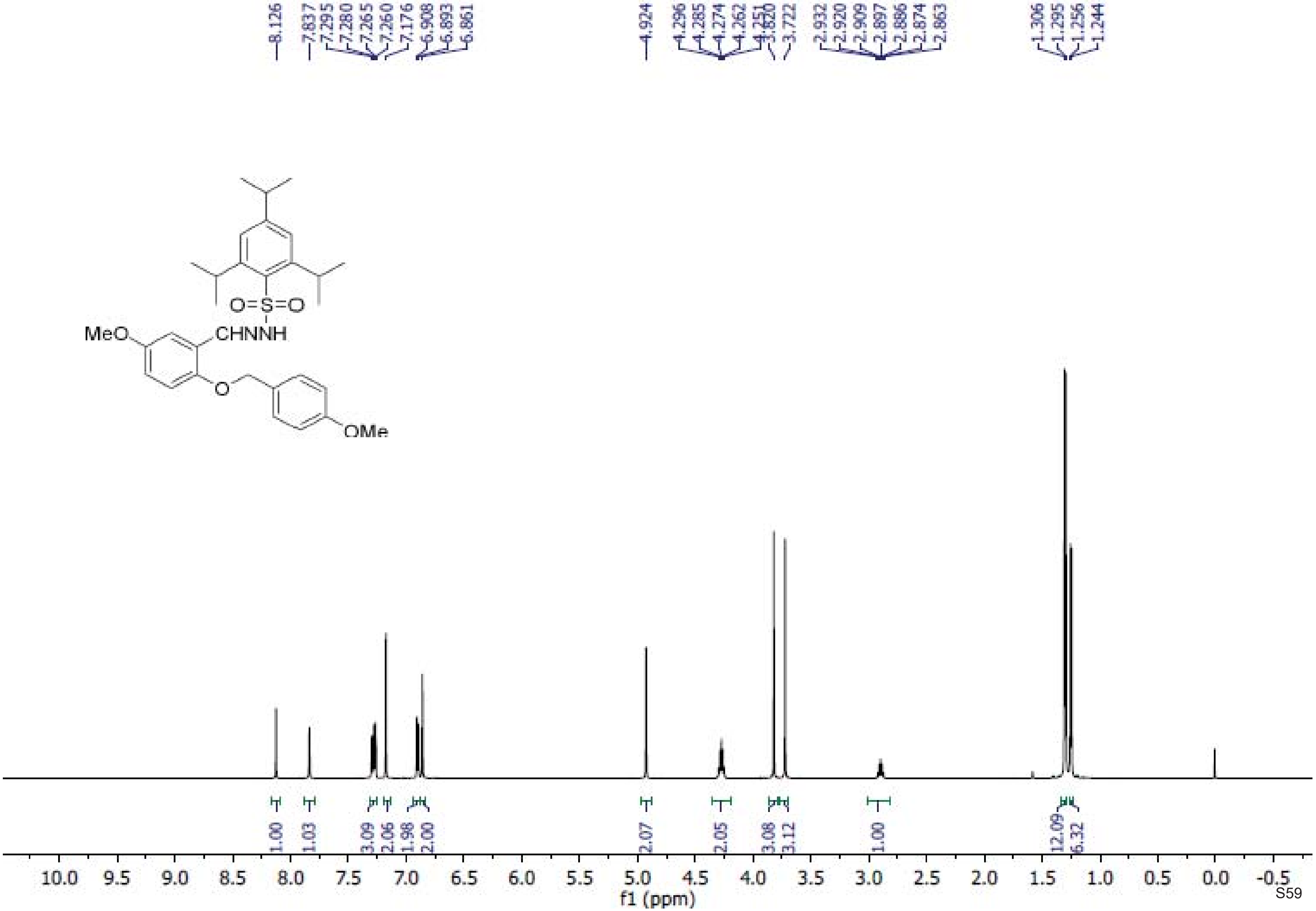
2,4,6-triisopropyl-N'-(3-methoxy-2-((3-methoxybenzyl)oxy)benzylidene)benzenesulfonohydrazide



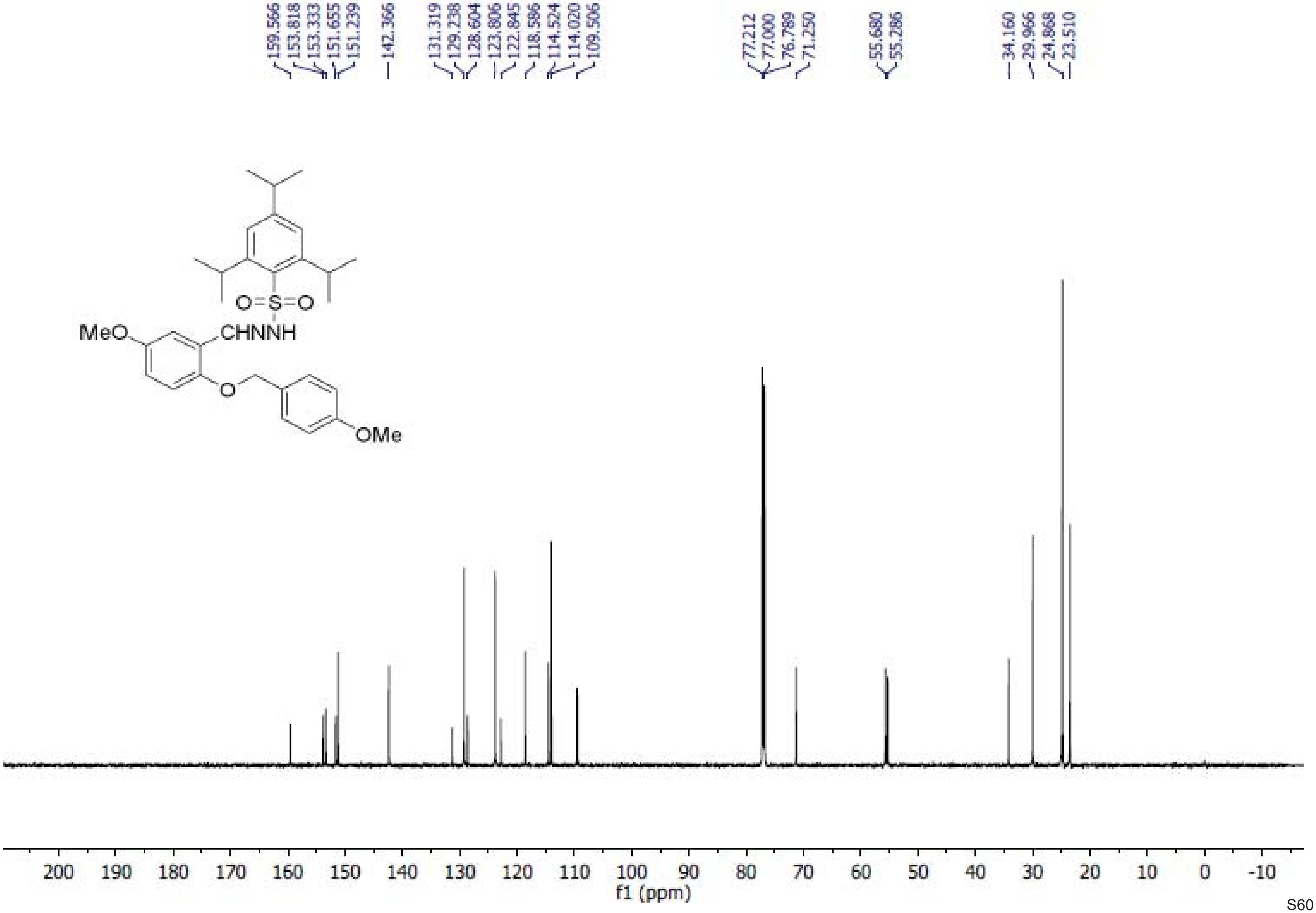
2,4,6-triisopropyl-N'-(3-methoxy-2-((3-methoxybenzyl)oxy)benzylidene)benzenesulfonohydrazide



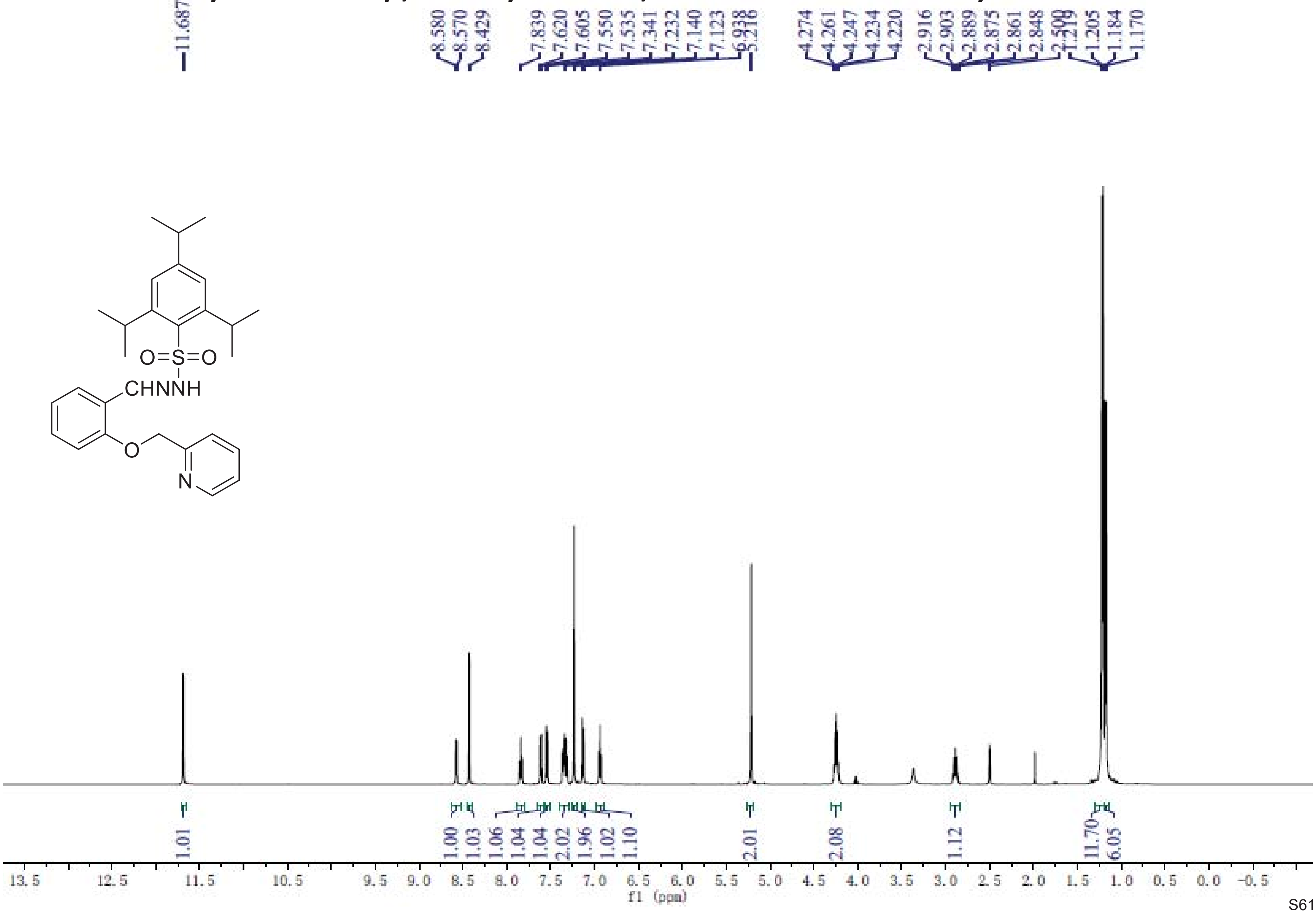
2,4,6-triisopropyl-N'-(5-methoxy-2-((4-methoxybenzyl)oxy)benzylidene)benzenesulfonohydrazide



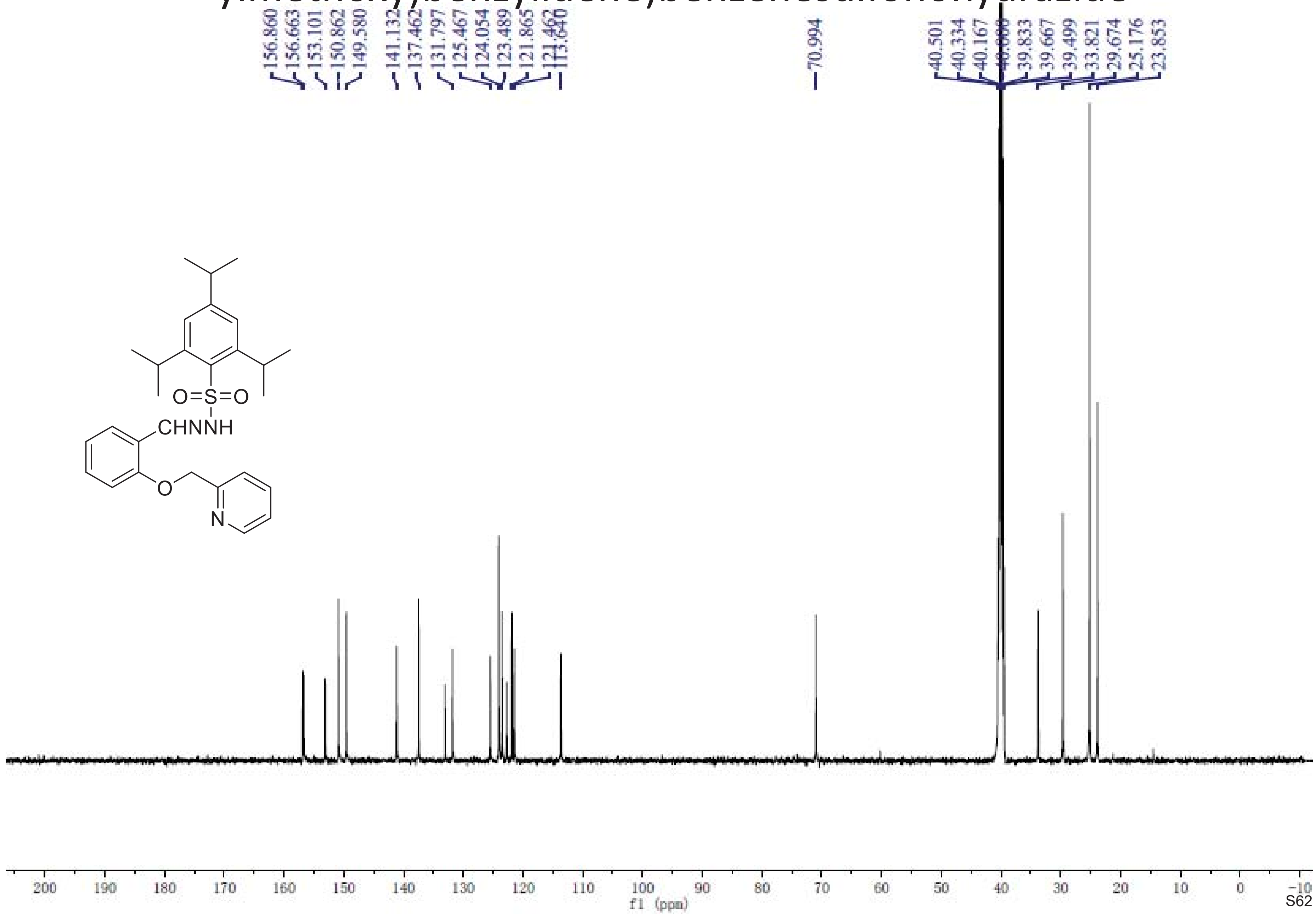
2,4,6-triisopropyl-N'-(5-methoxy-2-((4-methoxybenzyl)oxy)benzylidene)benzenesulfonohydrazide



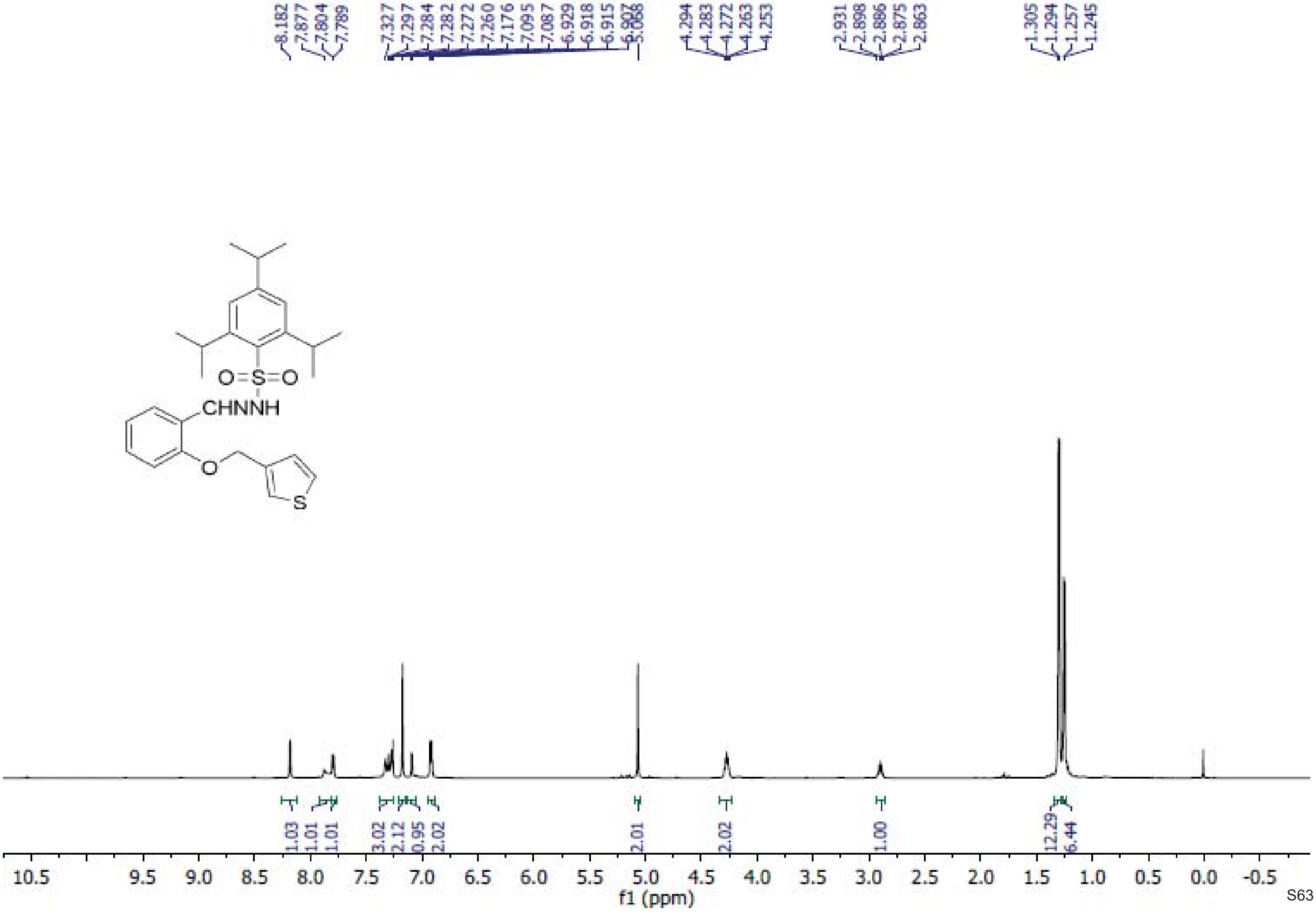
2,4,6-triisopropyl-N'-(2-(pyridin-2-ylmethoxy)benzylidene)benzenesulfonohydrazide



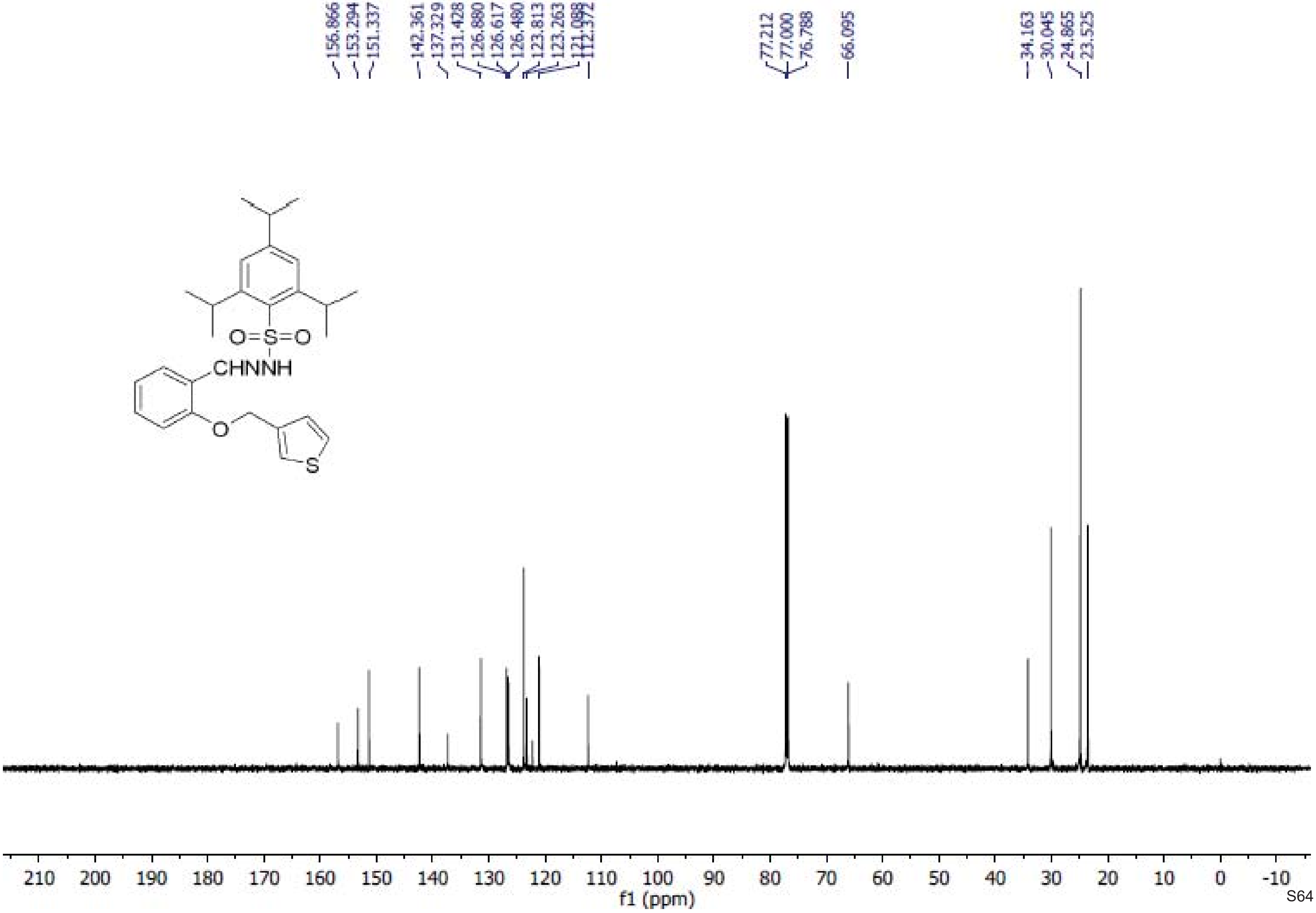
2,4,6-triisopropyl-N'-(2-(pyridin-2-ylmethoxy)benzylidene)benzenesulfonohydrazide



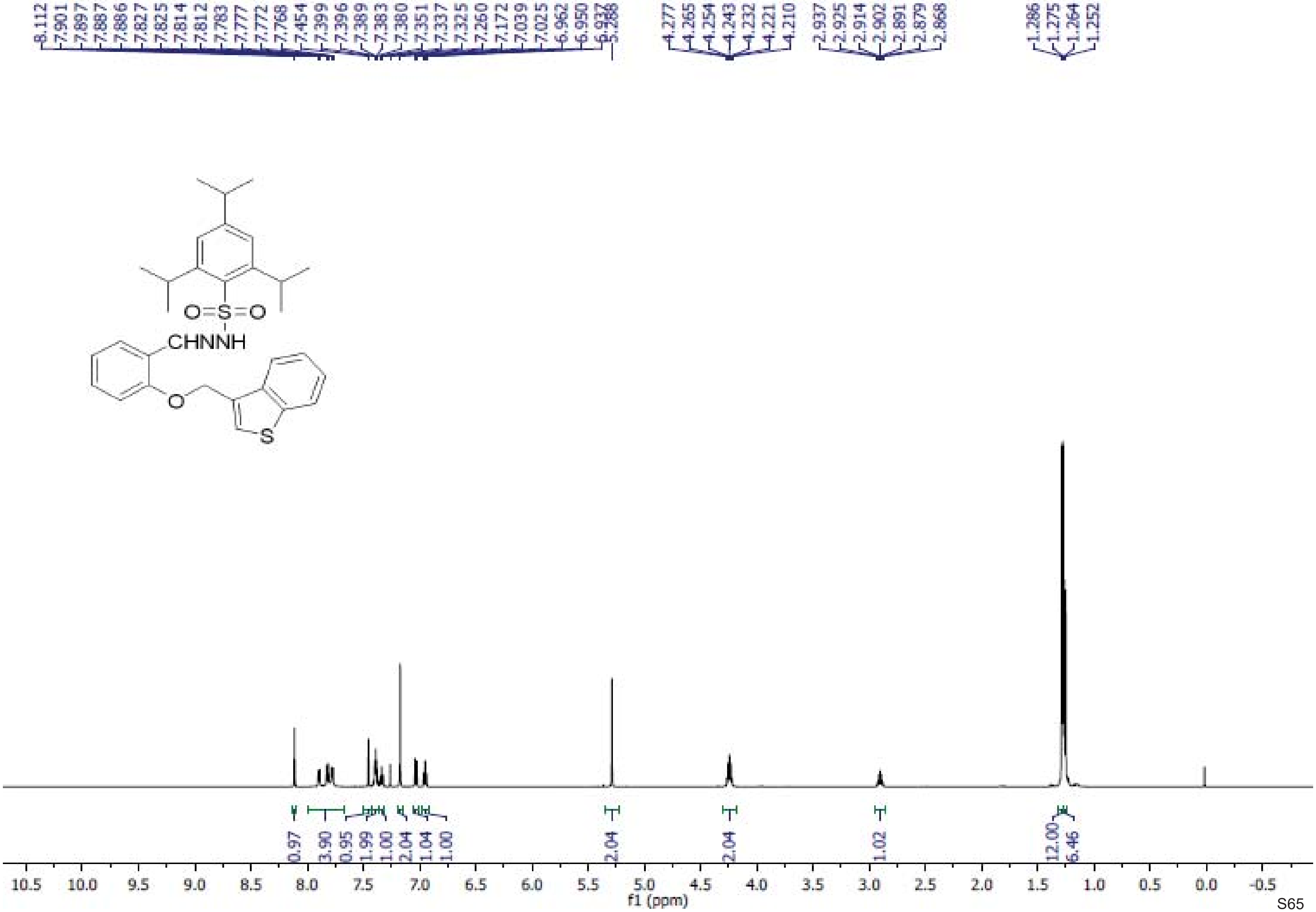
2,4,6-triisopropyl-N'-(2-(thiophen-3-ylmethoxy)benzylidene)benzenesulfonohydrazide



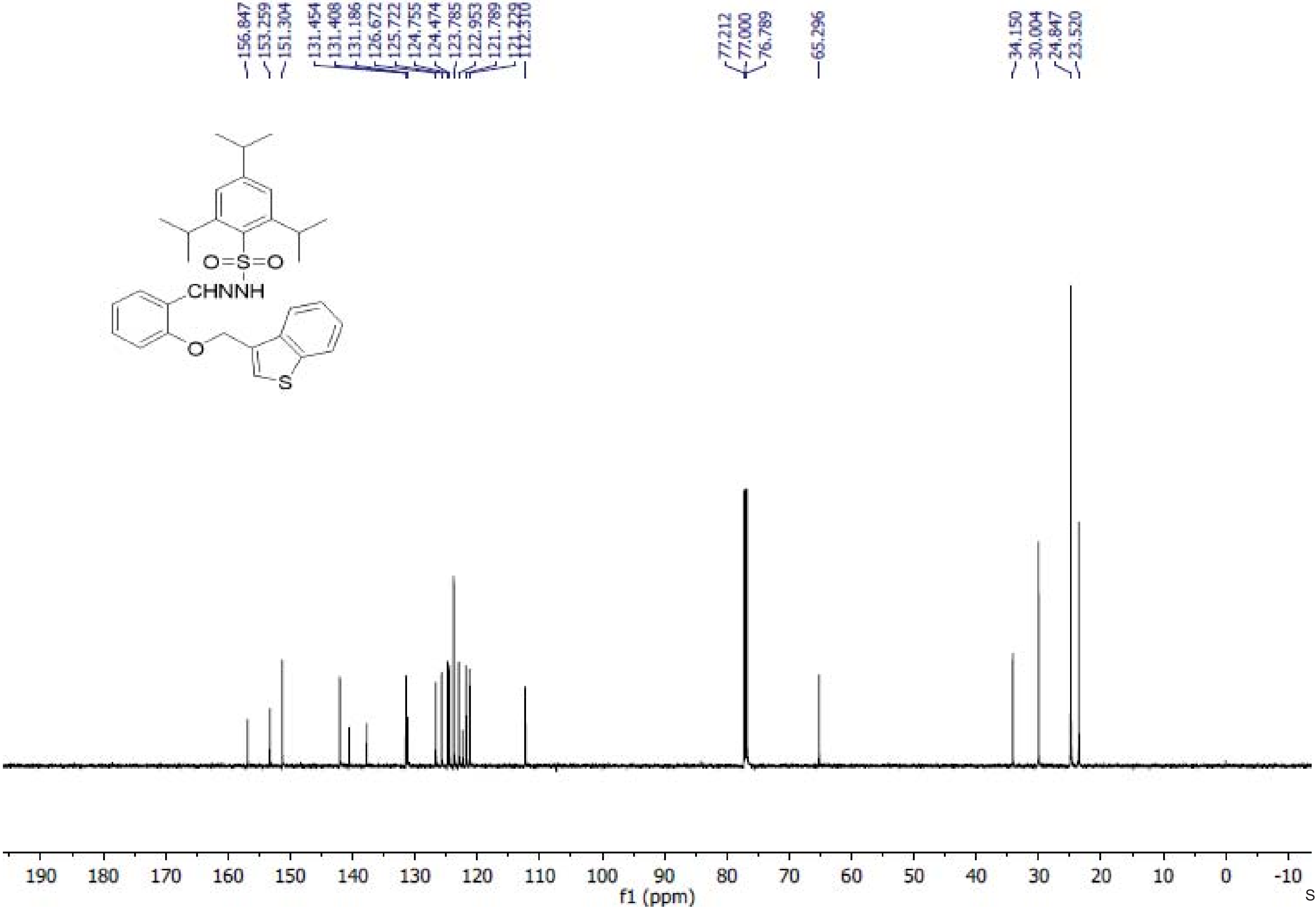
2,4,6-triisopropyl-N'-(2-(thiophen-3-ylmethoxy)benzylidene)benzenesulfonohydrazide



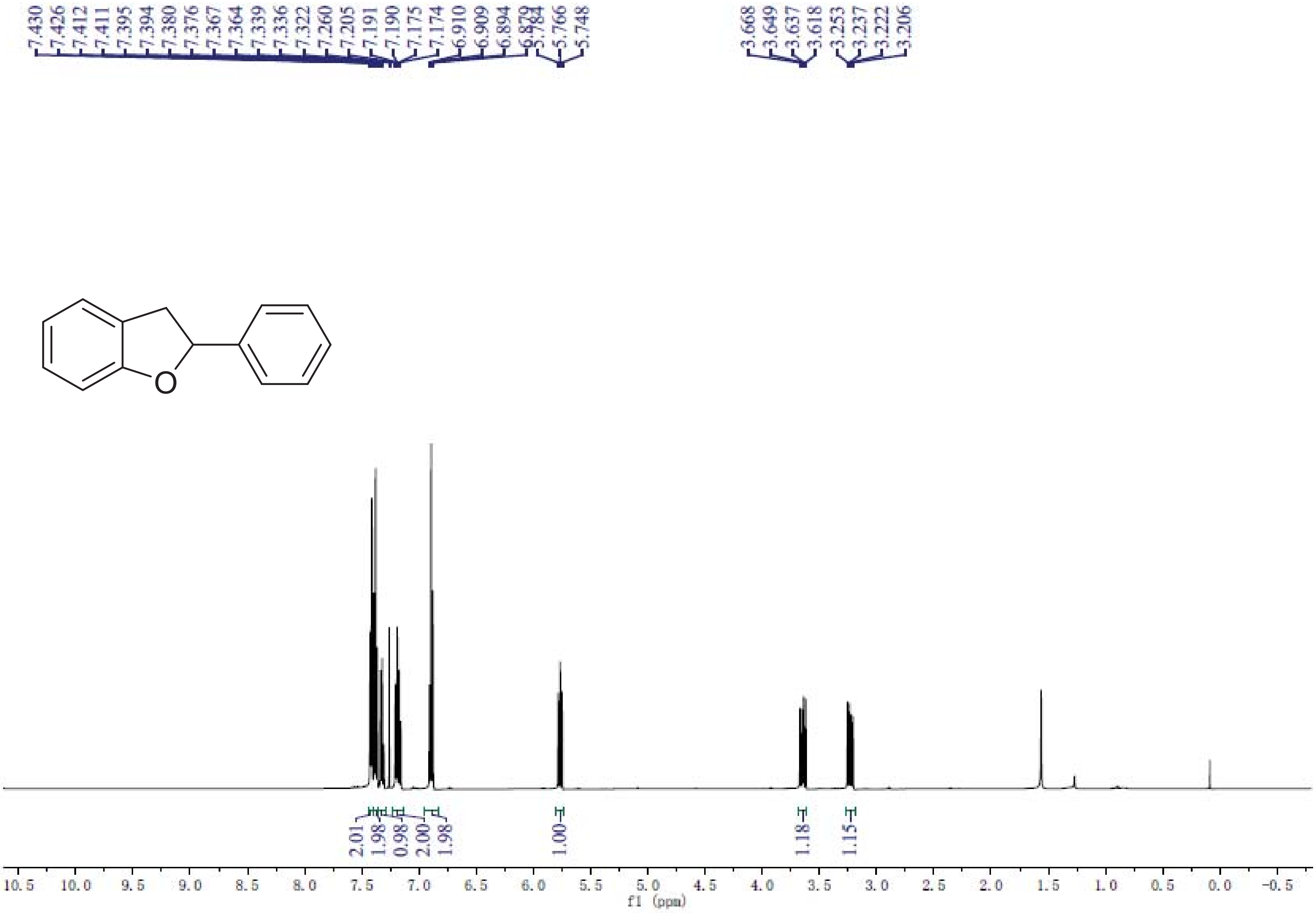
N'-(2-(benzo[b]thiophen-3-ylmethoxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



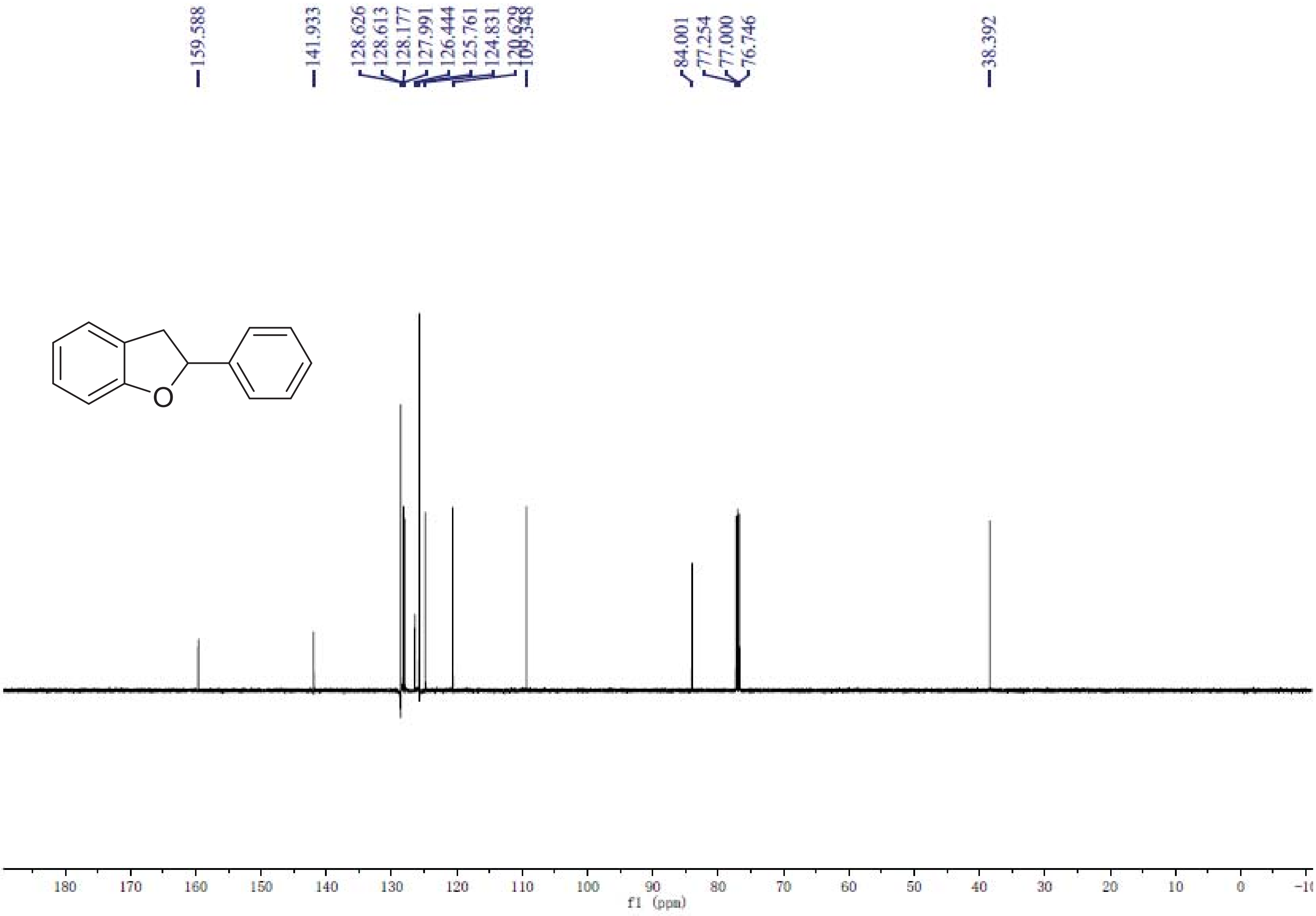
N'-(2-(benzo[b]thiophen-3-ylmethoxy)benzylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



(S)-2-phenyl-2,3-dihydrobenzofuran **2a**

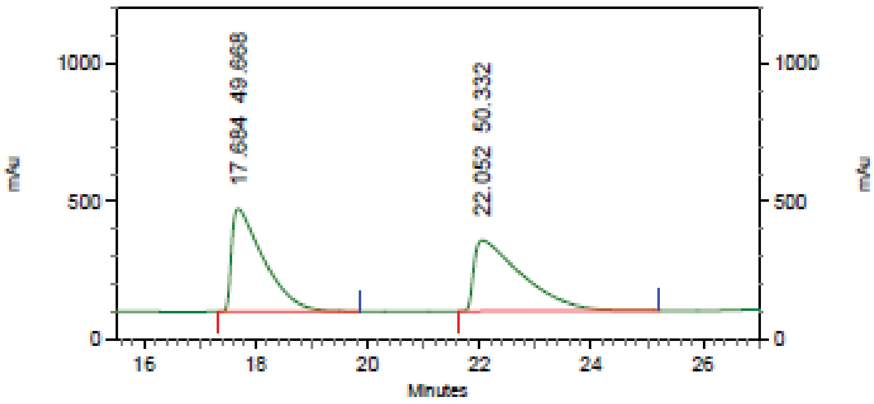


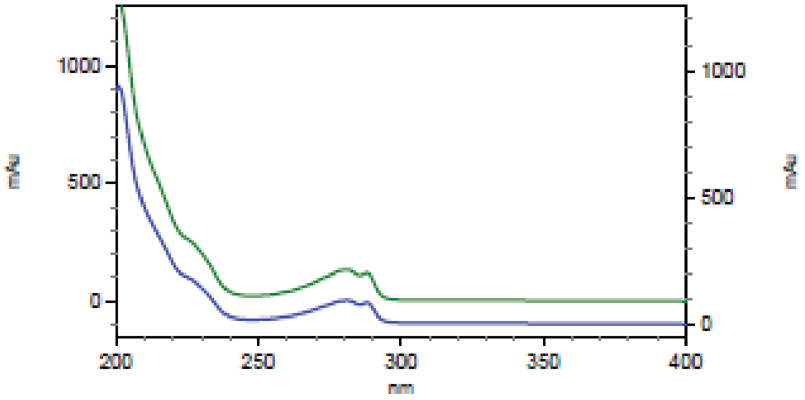
(S)-2-phenyl-2,3-dihydrobenzofuran **2a**



(S)-2-phenyl-2,3-dihydrobenzofuran **2a**

```
XW-I-102-ADH 0.8% 1mL
C:\EZStart\Projects\Default\Method\ywang0.8-1.0%.met
C:\EZStart\Projects\Default\Data\XW-I-102-ADH 0%-NEW 0.8mL
```

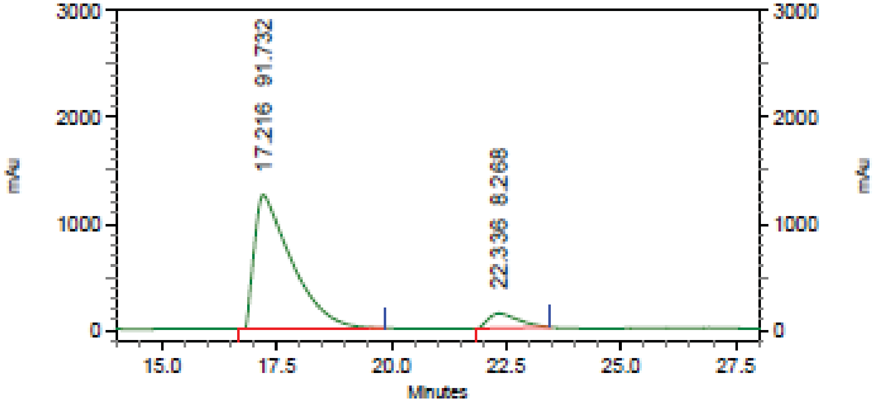


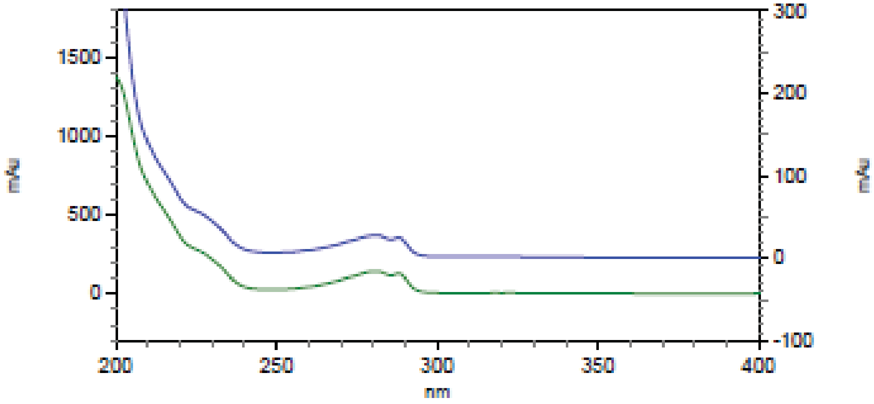


```
3: 231 nm, 4 nm
 Results
                Pk # Name                      Retention Time        Area Percent
                   1                                   17.684              49.668
                   2                                   22.052              50.332

           Totals
                                                                          100.000
```

(S)-2-phenyl-2,3-dihydrobenzofuran **2a**

```
XW-I-190-MEOCHEN-OLD ADH 0%0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\XW-I-190-MEOCHEN-OLD ADH 0%0.8 mL
```



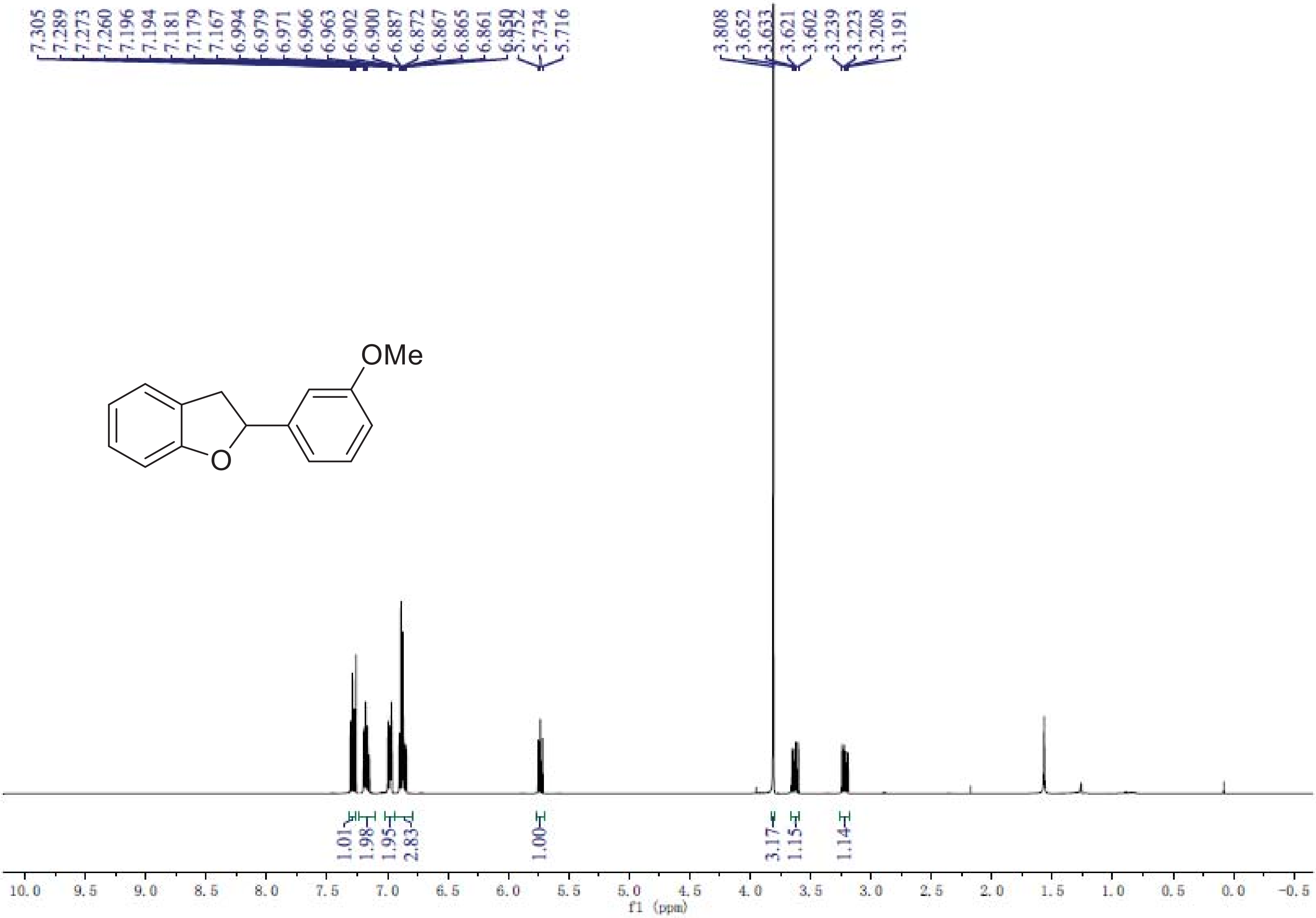


3: 227 nm, 4 nm

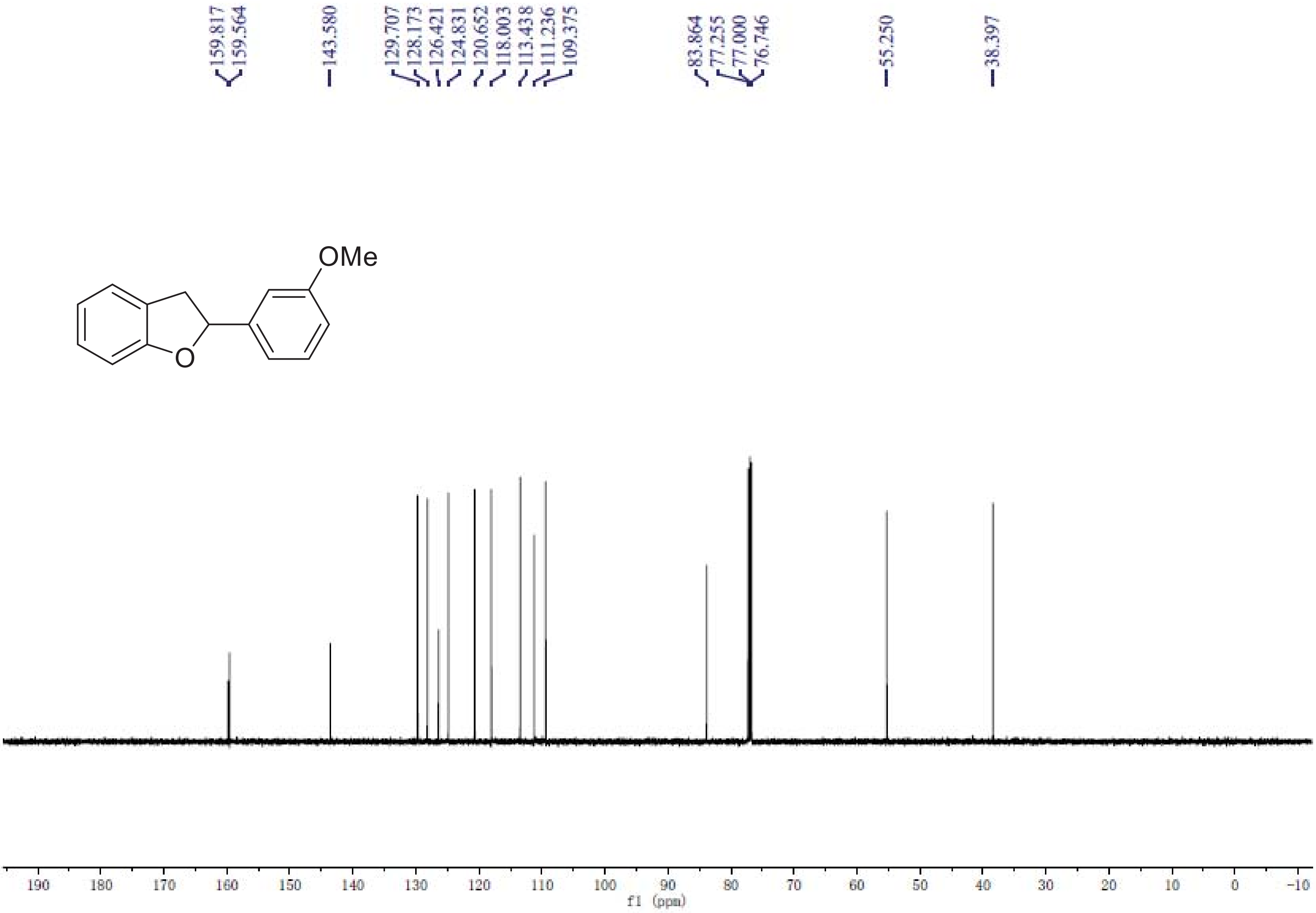
Results

Pk # Name	Retention Time	Area Percent
1	17.216	91.732
2	22.336	8.268
Totals		100.000

(S)-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran **2b**

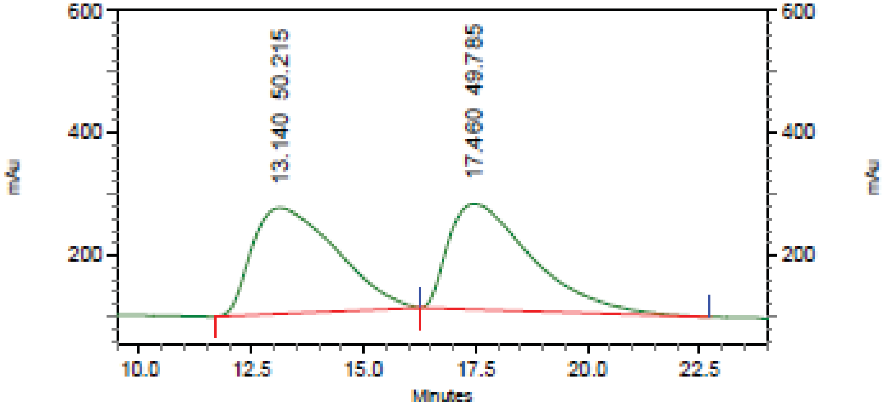


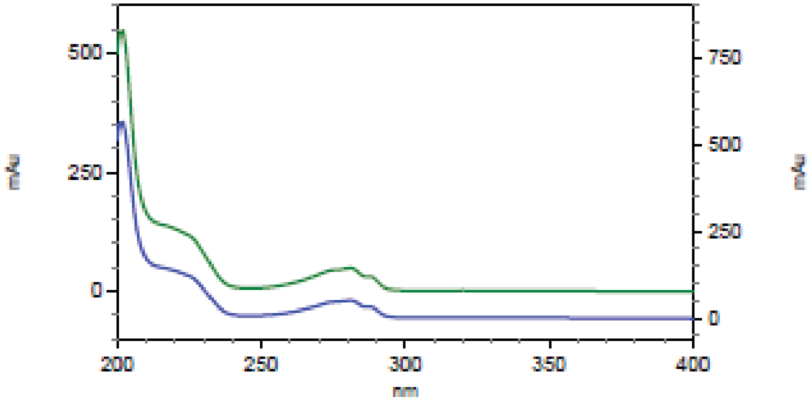
(S)-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran **2b**



(S)-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran **2b**

```
XW-I-196-ADH-1-0.9% 1mL
C:\EZStart\Projects\Default\Method\xinwen2.met
C:\EZStart\Projects\Default\Data\XW-I-196-ADH-2-0.9% 1mL
```



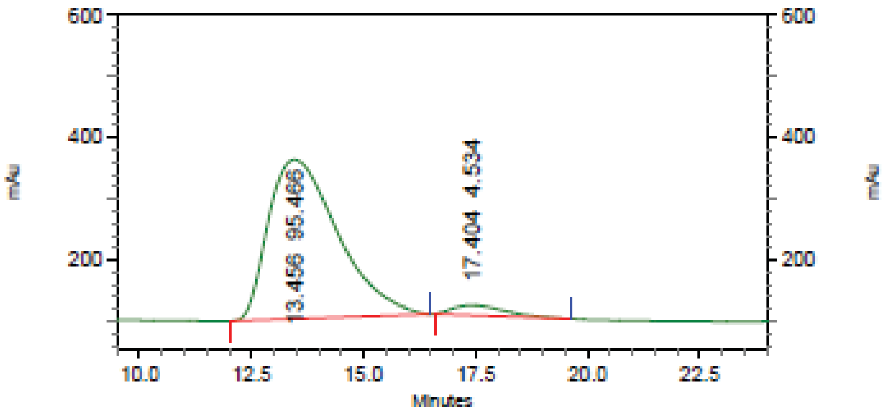


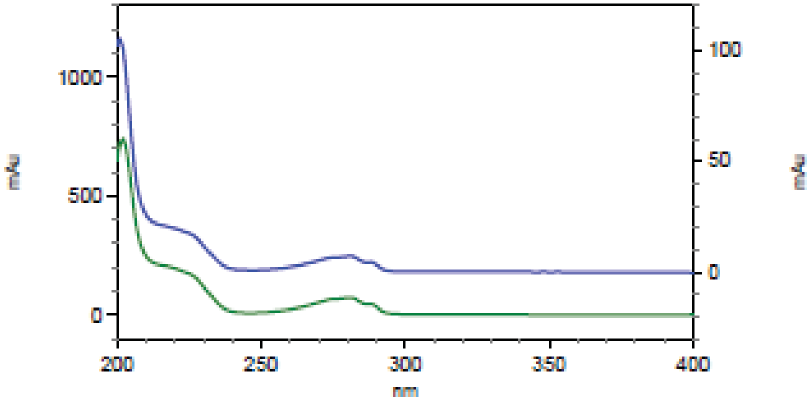
```
10: 229 nm, 4 nm
 Results
```

Pk #	Name	Retention Time	Area Percent
1		13.140	50.215
2		17.460	49.785
Totals			100.000

(S)-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran **2b**

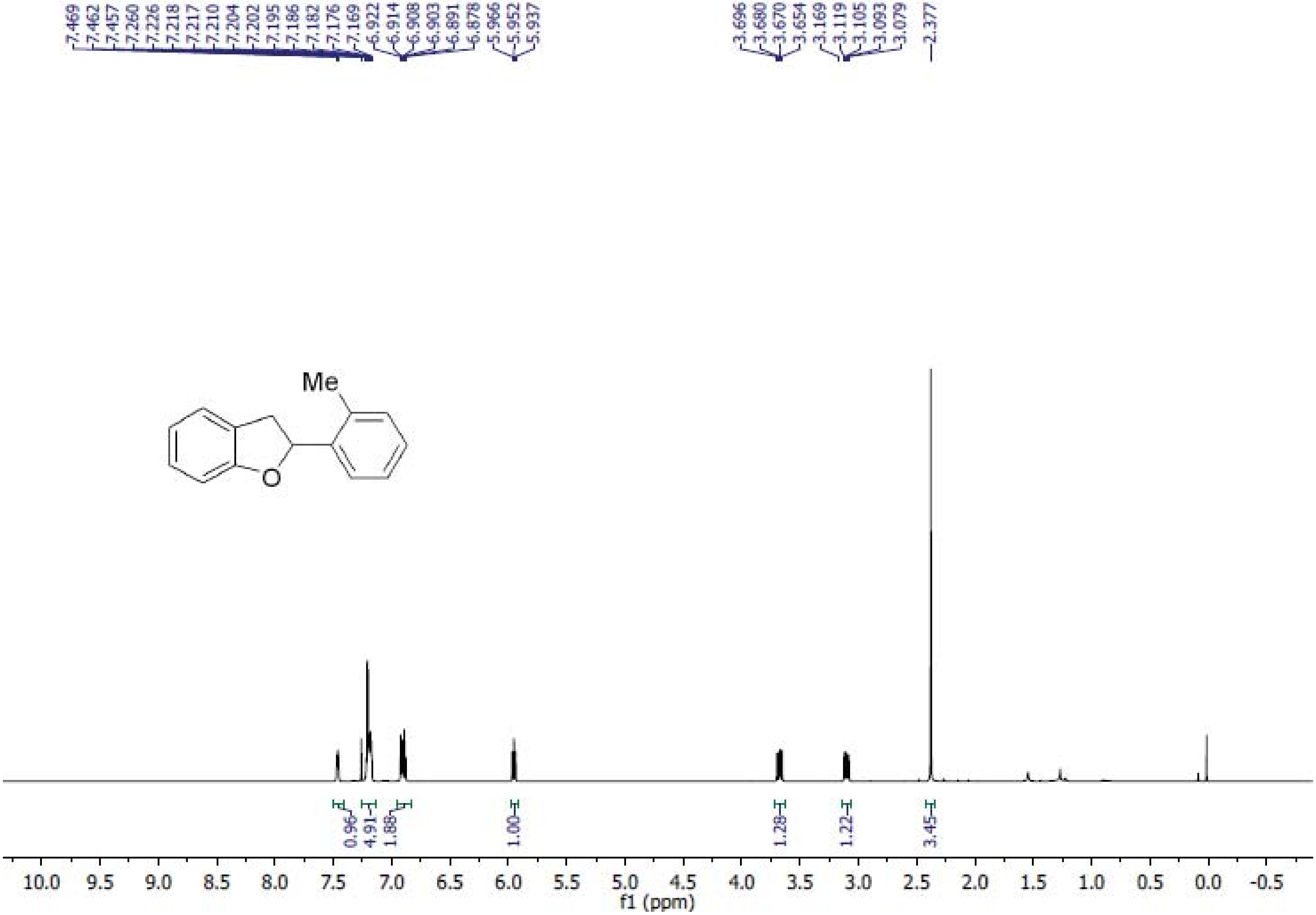
```
XW-II-110-ADH-1-0.9% 1mL
C:\EZStart\Projects\Default\Method\xinwen2.met
C:\EZStart\Projects\Default\Data\XW-II-110-ADH-1-0.9% 1mL
```



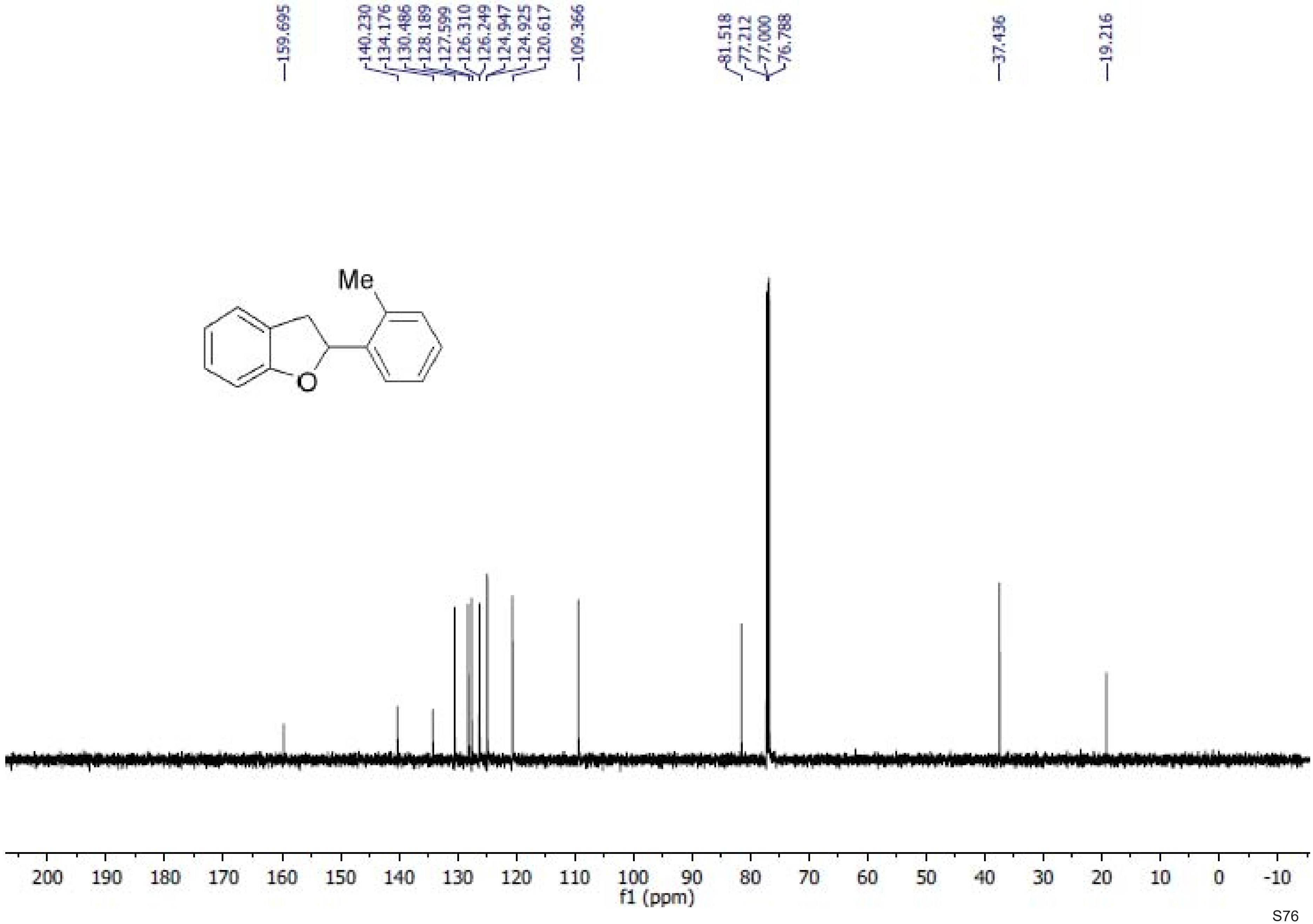


```
10: 229 nm, 4 nm
 Results
              Pk # Name                    Retention Time          Area Percent
-------------------------------------------------------------------------------
                 1                                 13.456                95.466
                 2                                 17.404                 4.534

 Totals
                                                                        100.000
```

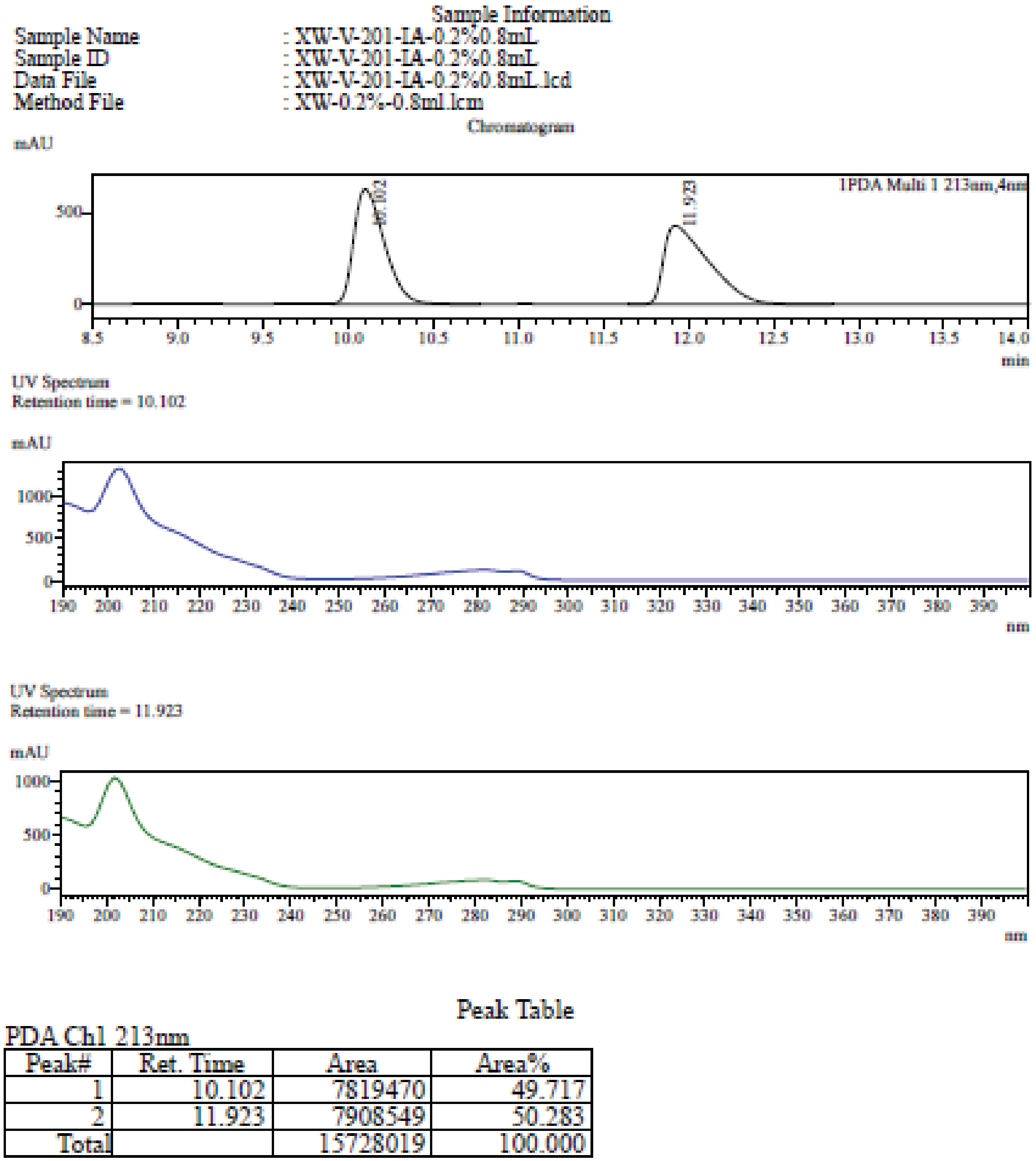
(S)-2-(o-tolyl)-2,3-dihydrobenzofuran **2c**



(S)-2-(o-tolyl)-2,3-dihydrobenzofuran **2c**



(S)-2-(o-tolyl)-2,3-dihydrobenzofuran **2c**



Sample Information

Sample Name	: XW-V-201-IA-0.2%0.8mL
Sample ID	: XW-V-201-IA-0.2%0.8mL
Data File	: XW-V-201-IA-0.2%0.8mL.lcd
Method File	: XW-0.2%-0.8ml.lcm

Chromatogram

UV Spectrum
Retention time = 10.102

UV Spectrum
Retention time = 11.923

Peak Table

PDA Ch1 213nm

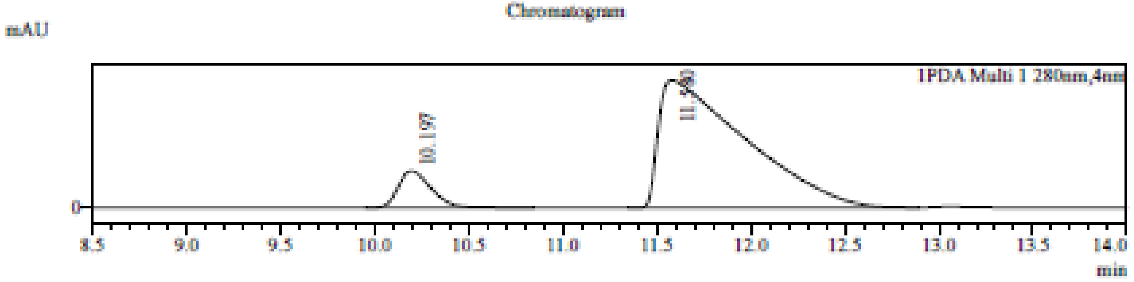
Peak#	Ret. Time	Area	Area%
1	10.102	7819470	49.717
2	11.923	7908549	50.283
Total		15728019	100.000

(S)-2-(o-tolyl)-2,3-dihydrobenzofuran **2c**

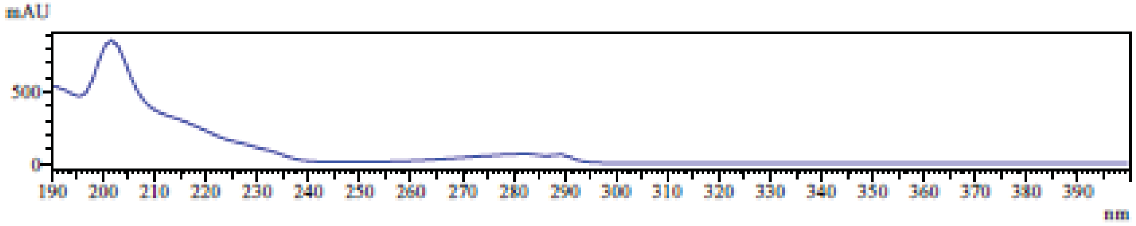
Sample Information

Sample Name : XW-V-202-IA-0.2%0.8mL
Sample ID : XW-V-202-IA-0.2%0.8mL
Data File : XW-V-202-IA-0.2%0.8mL.lcd
Method File : XW-0.2%-0.8ml.lcm

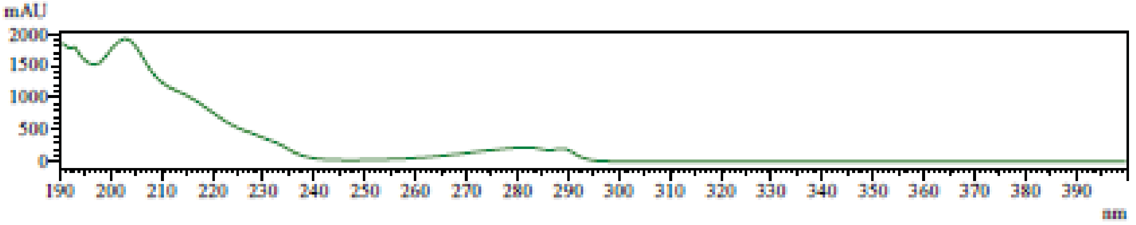
Chromatogram



UV Spectrum
Retention time = 10.197



UV Spectrum
Retention time = 11.580

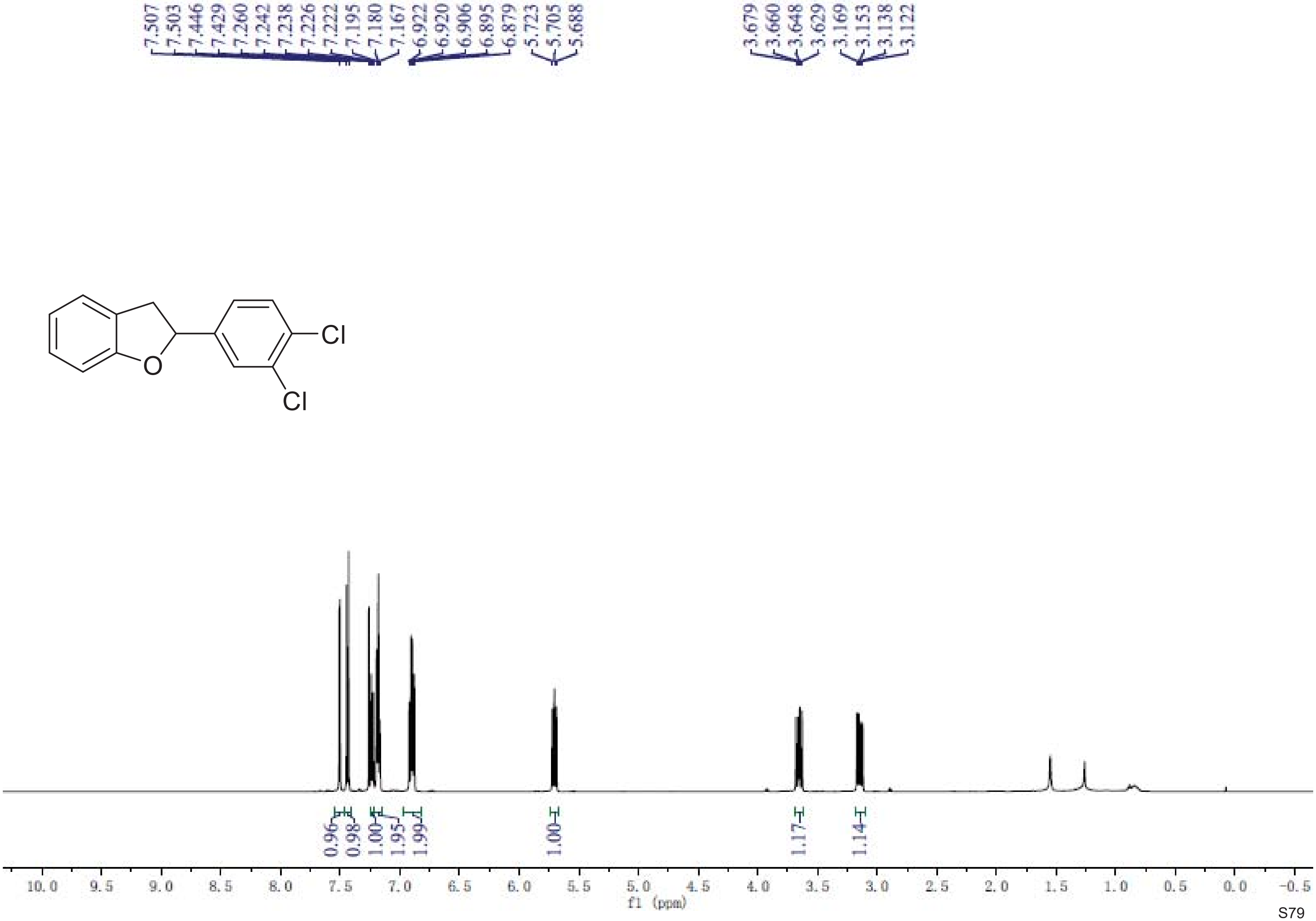


Peak Table

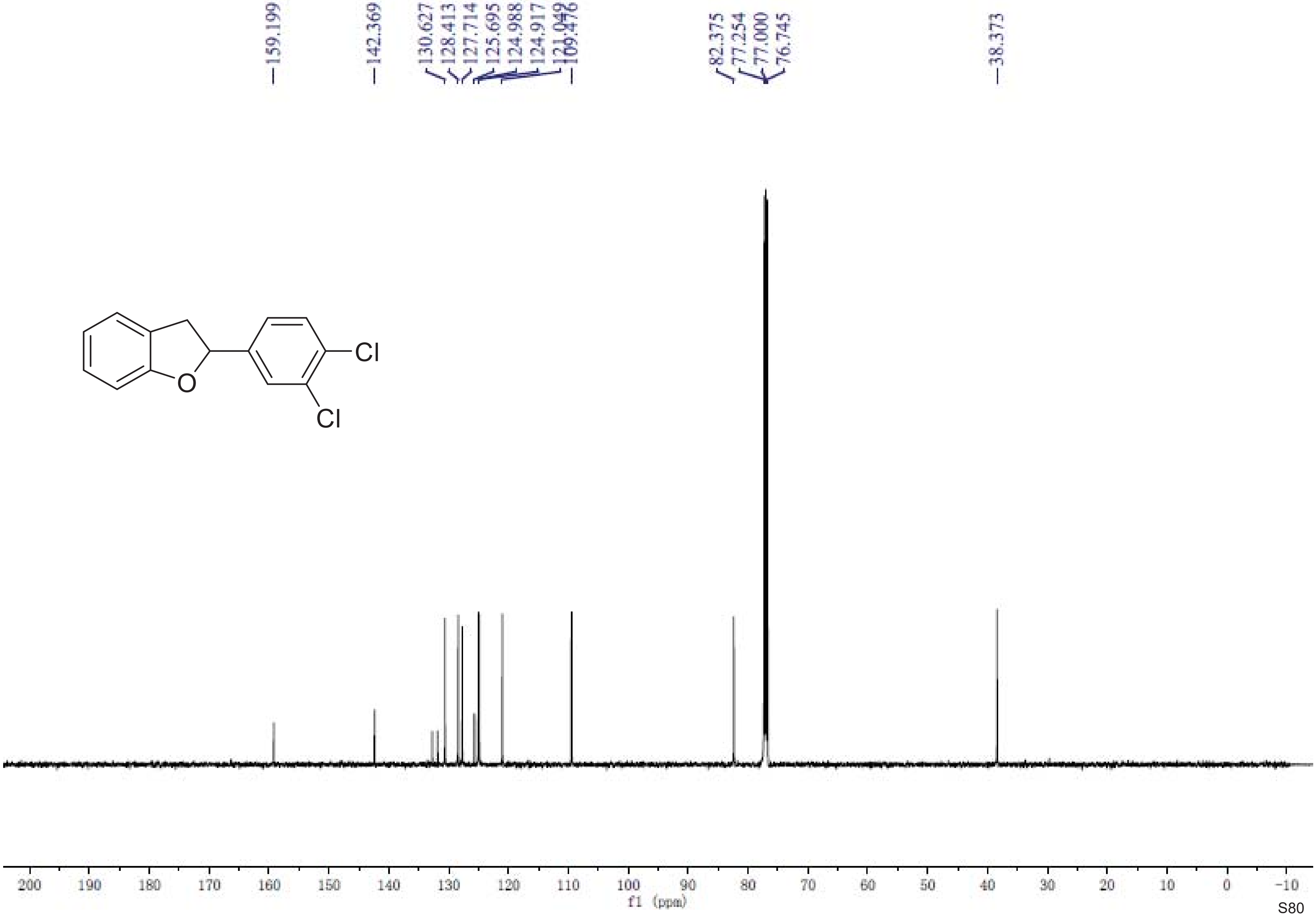
PDA Ch1 280nm

Peak#	Ret. Time	Area	Area%
1	10.197	775622	9.916
2	11.580	7046169	90.084
Total		7821791	100.000

(S)-2-(3,4-dichlorophenyl)-2,3-dihydrobenzofuran **2d**

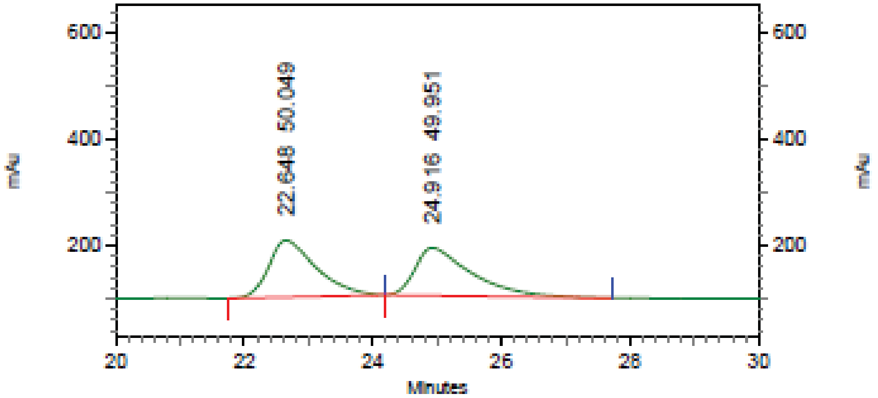


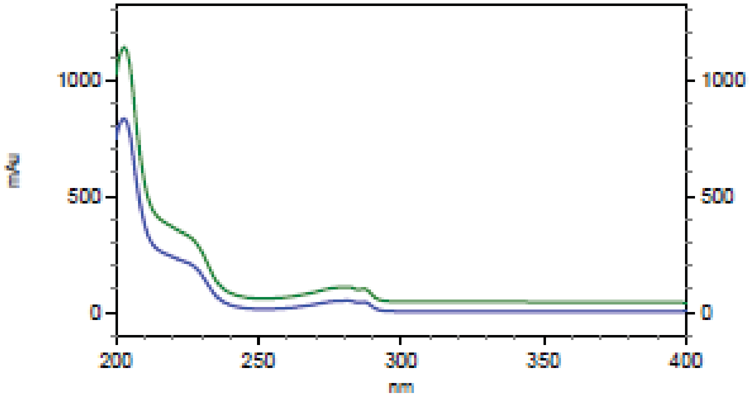
(S)-2-(3,4-dichlorophenyl)-2,3-dihydrobenzofuran **2d**



(S)-2-(3,4-dichlorophenyl)-2,3-dihydrobenzofuran **2d**

```
XW-I-228-OJH-1-1% 1mL
C:\EZStart\Projects\Default\Method\ywang0.8-1.0%.met
C:\EZStart\Projects\Default\Data\XW-I-228-OJH-1-1% 1mL
```

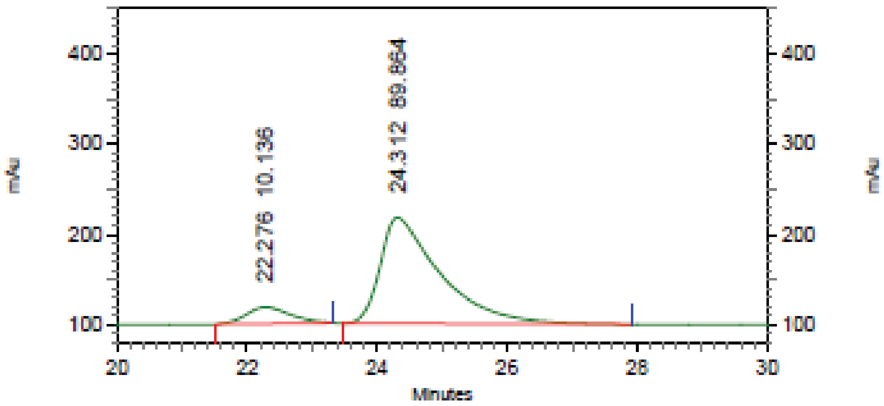


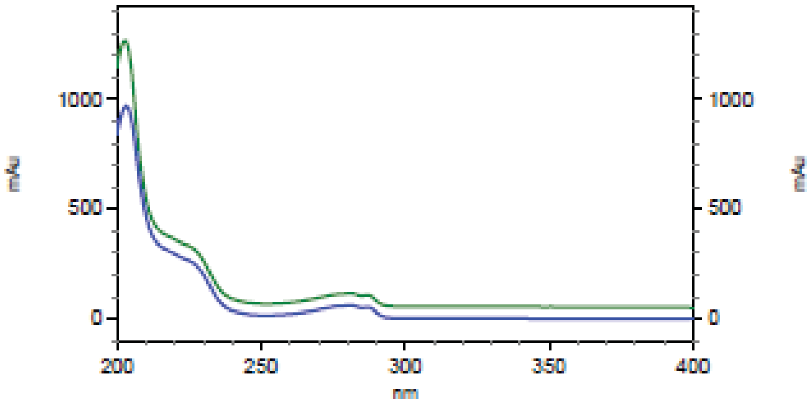


```
3: 278 nm, 4 nm
 Results
                    Pk # Name                        Retention Time          Area Percent
                       1                                     22.648                50.049
                       2                                     24.916                49.951

          Totals
                                                                                  100.000
```

(S)-2-(3,4-dichlorophenyl)-2,3-dihydrobenzofuran **2d**

XW-II-80-OJH-1-1% 1mL
C:\EZStart\Projects\Default\Method\ywang0.8-1.0%.met
C:\EZStart\Projects\Default\Data\XW-II-80-OJH-1-1% 1mL

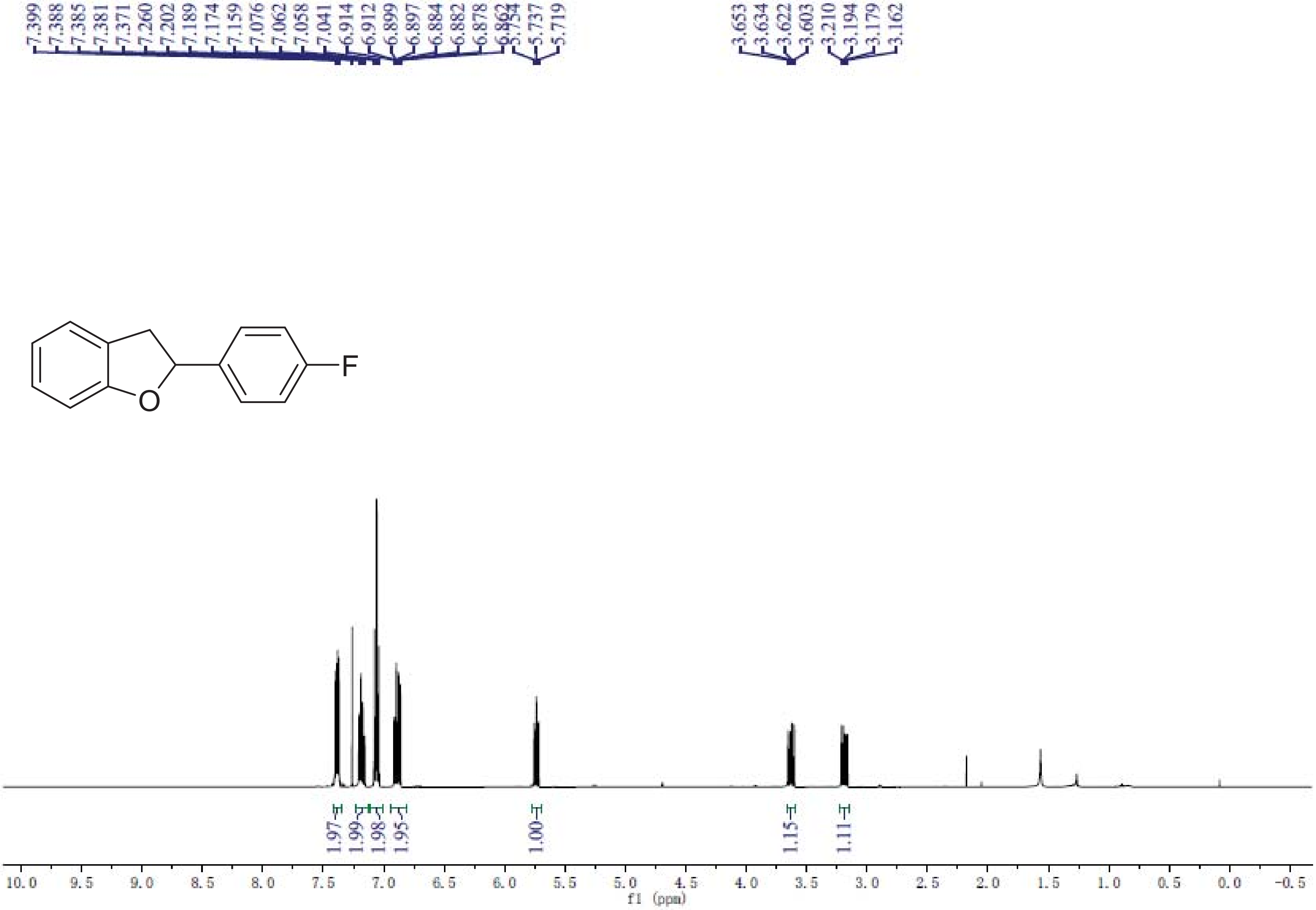




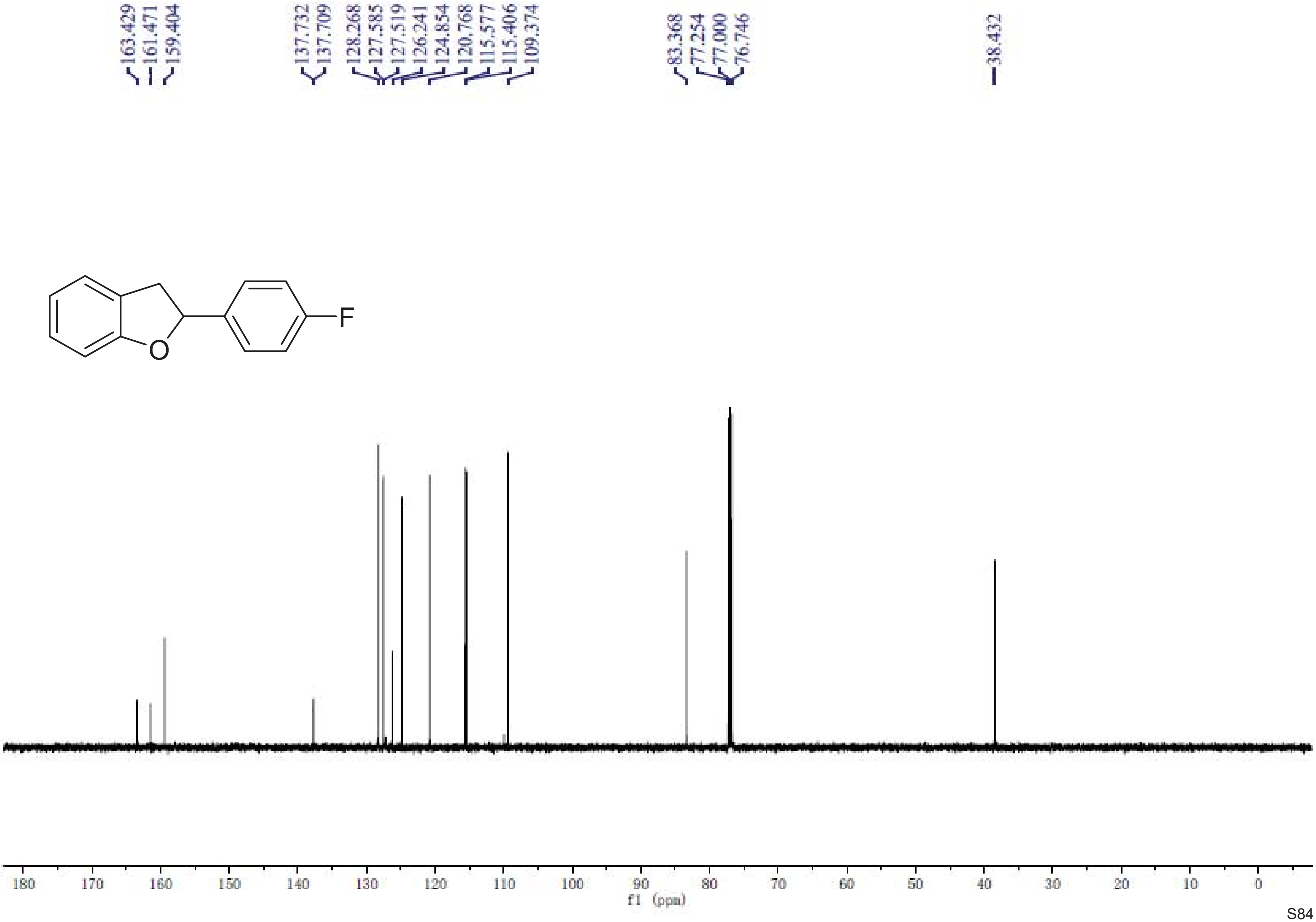
3: 278 nm, 4 nm
Results

Pk # Name	Retention Time	Area Percent
1	22.276	10.136
2	24.312	89.864
Totals		100.000

(S)-2-(4-fluorophenyl)-2,3-dihydrobenzofuran **2e**

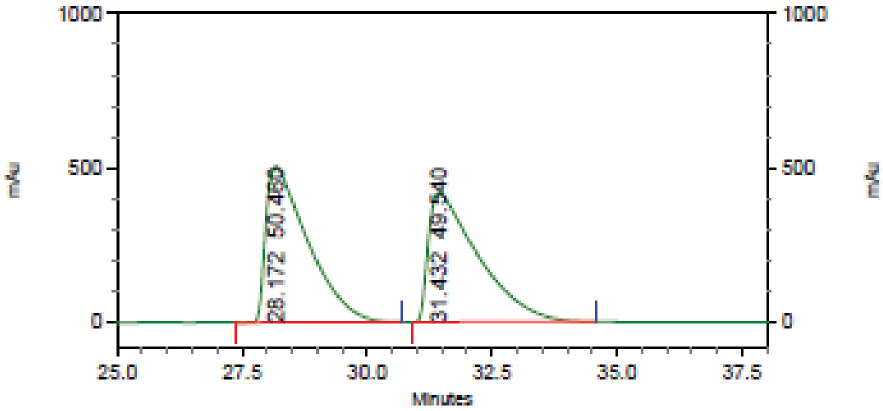


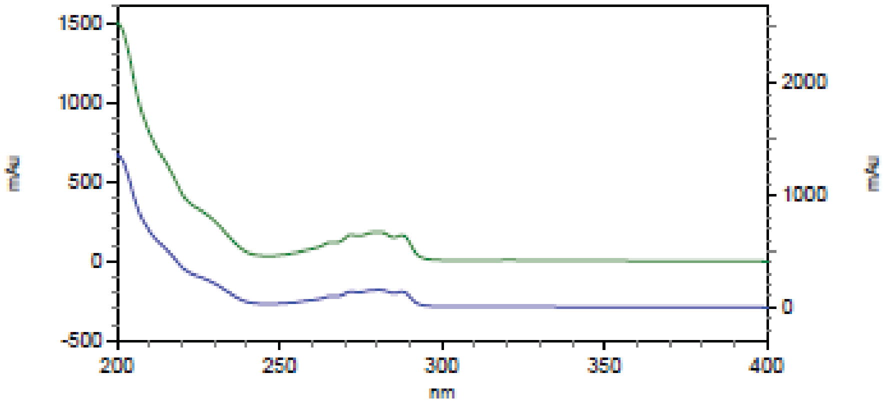
(S)-2-(4-fluorophenyl)-2,3-dihydrobenzofuran **2e**



(S)-2-(4-fluorophenyl)-2,3-dihydrobenzofuran **2e**

```
XW-I-163-ibu-F-60-ODH-3 0%0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\XW-I-163-ibu-F-60-ODH-3 0%0.8 mL
```



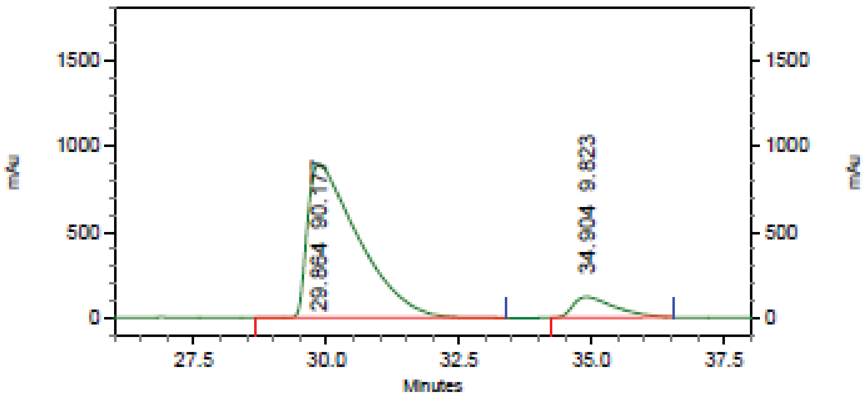


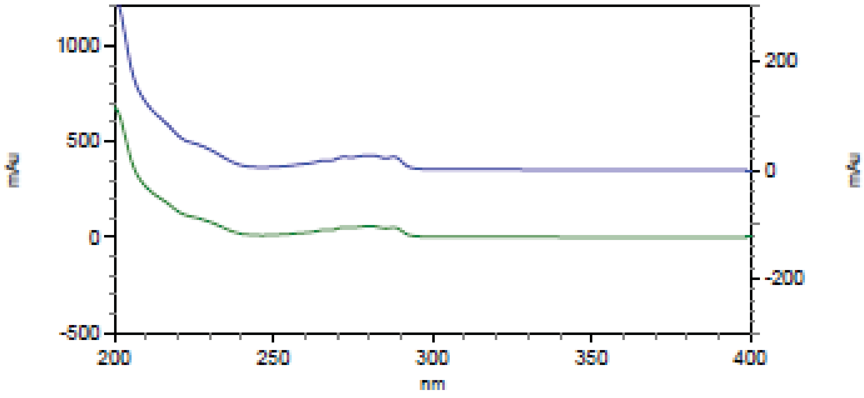
```
3: 276 nm, 4 nm
 Results
```

Pk #	Name	Retention Time	Area Percent
1		28.172	50.460
2		31.432	49.540
Totals			100.000

(S)-2-(4-fluorophenyl)-2,3-dihydrobenzofuran **2e**

```
XW-I-207-F-ODH 0%0.8 mL
C:\EZStart\Projects\Default\Method\JLM-ADH-0.2@-0.7mL.met
C:\EZStart\Projects\Default\Data\XW-I-207-F-ODH 0%0.8 mL
```

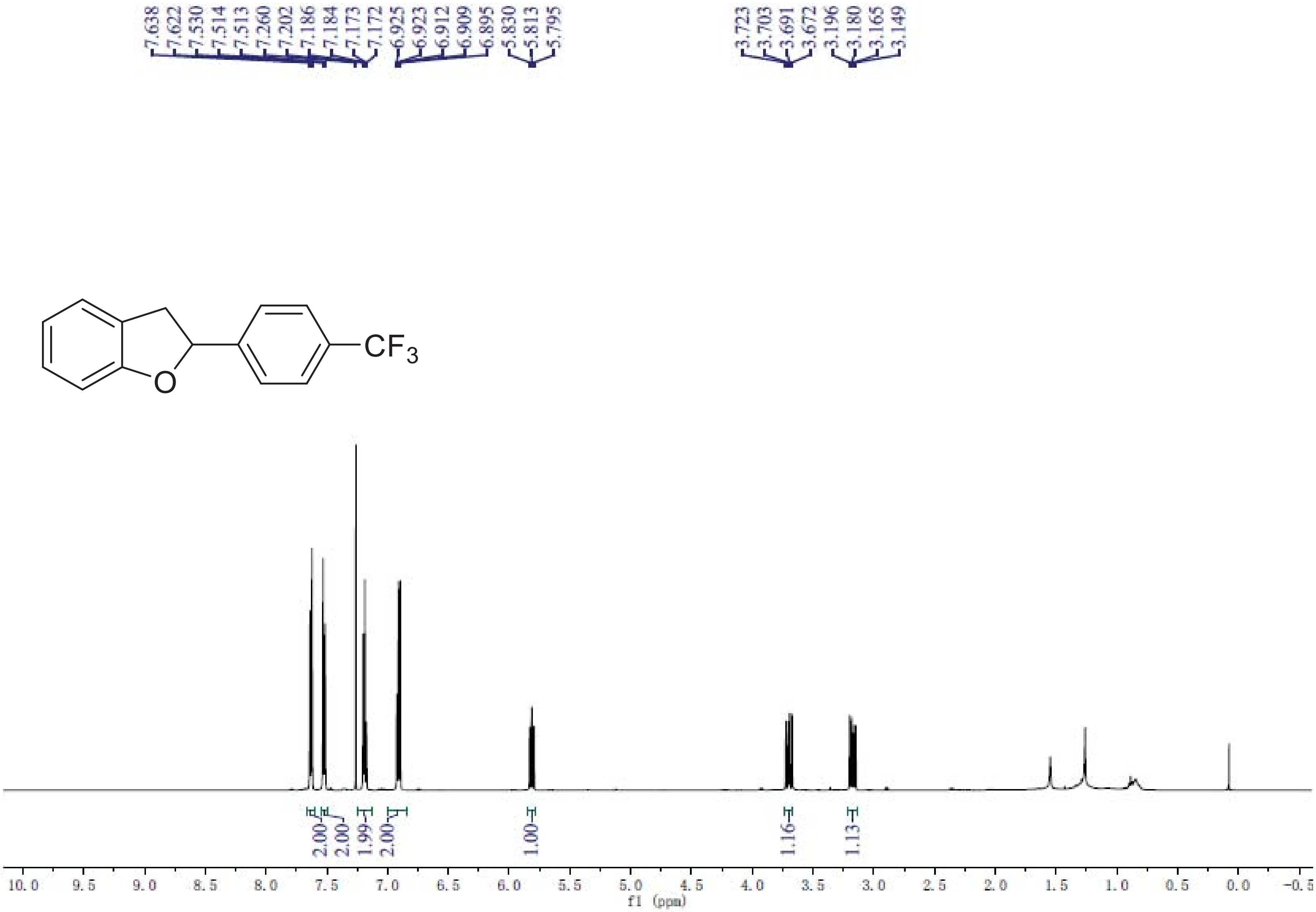




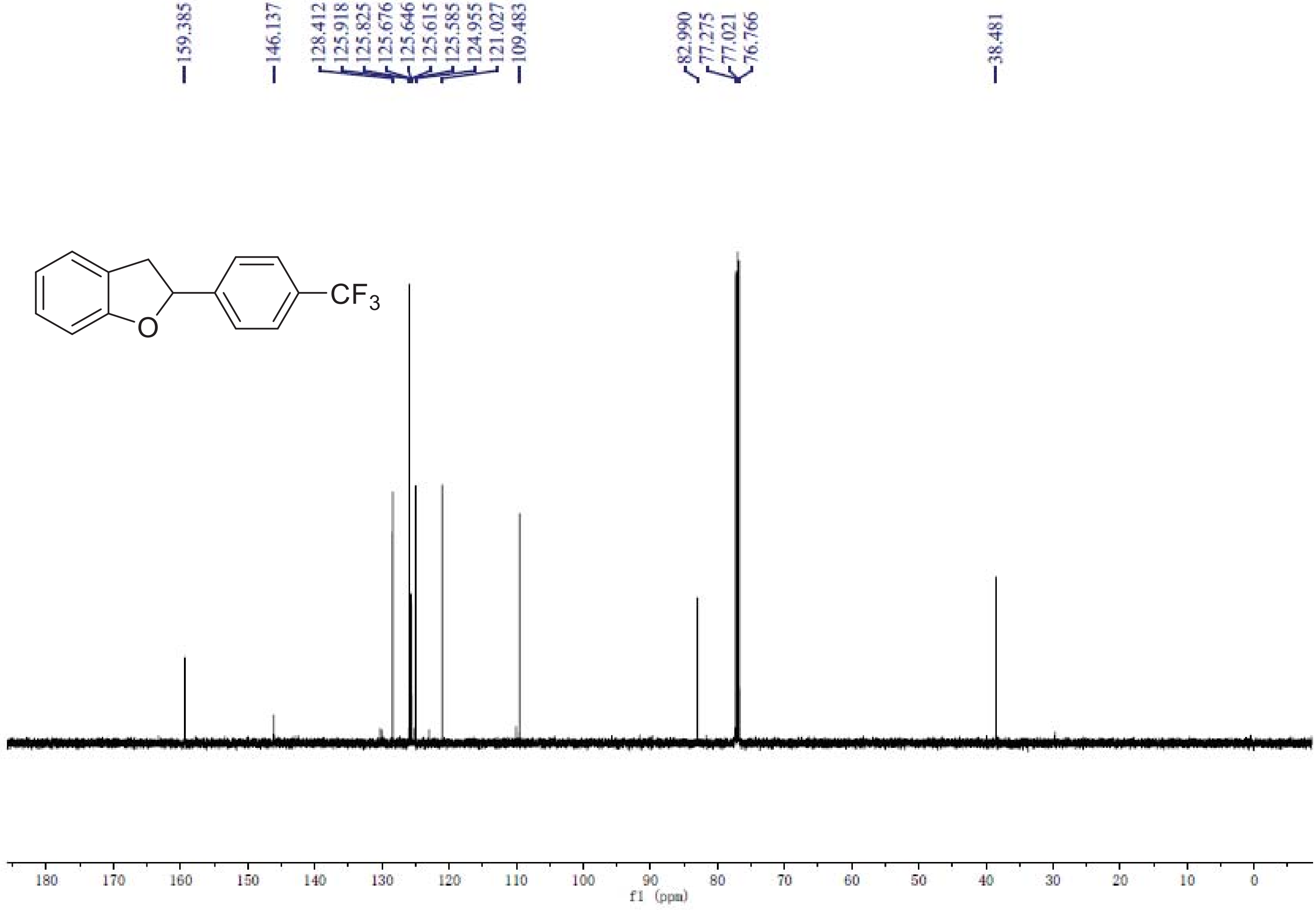
2: 229 nm, 4 nm
Results

Pk #	Name	Retention Time	Area Percent
1		29.864	90.177
2		34.904	9.823
Totals			100.000

(S)-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran **2f**

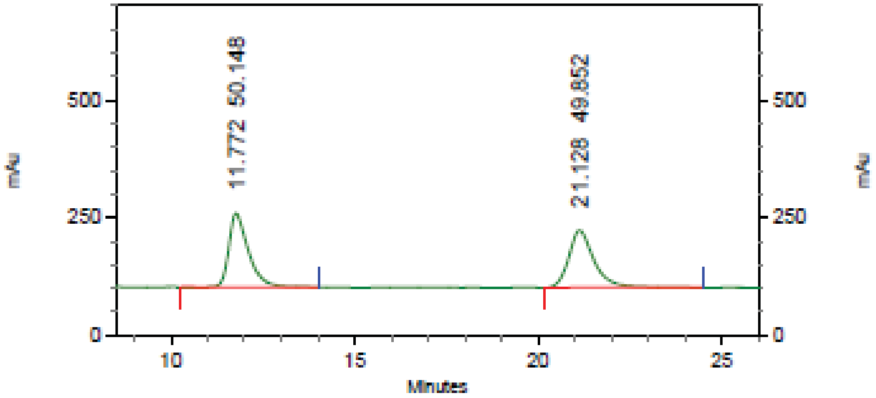


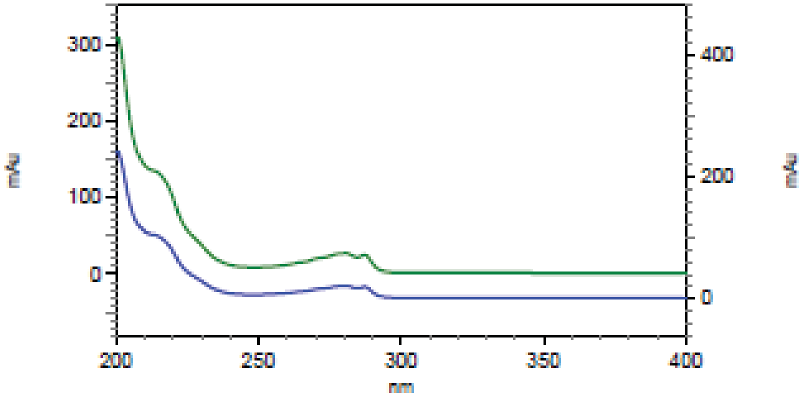
(S)-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran **2f**



(S)-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran **2f**

```
XW-I-180OJH-1-1% 1mL
C:\EZStart\Projects\Default\Method\ywang0.8-1.0%.met
C:\EZStart\Projects\Default\Data\XW-I-180OJH-1-1% 1mL
```

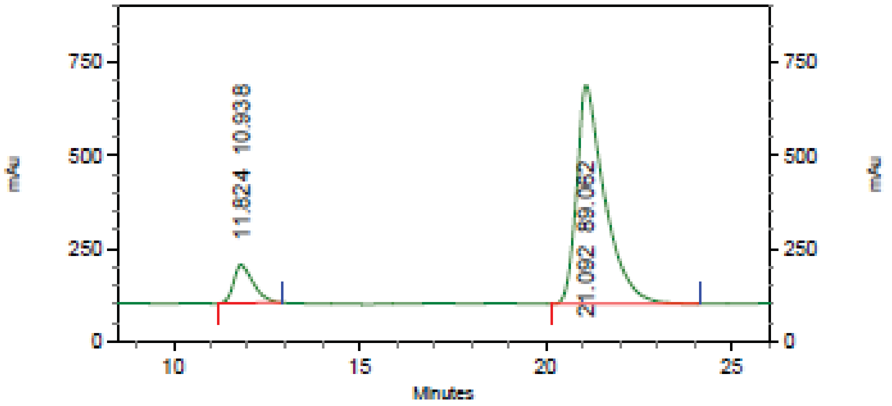


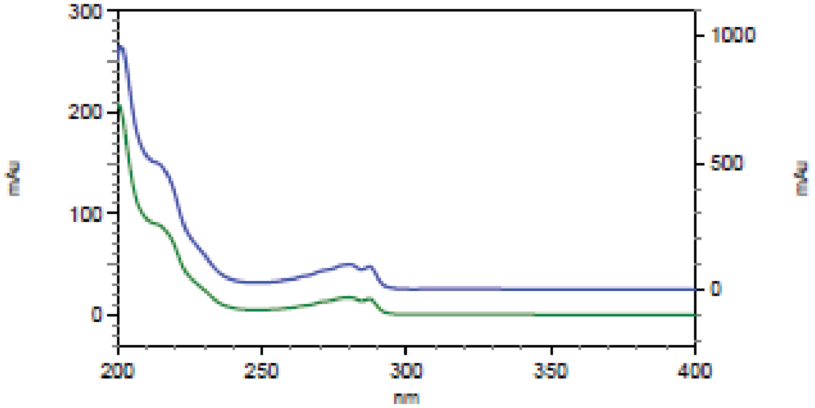


```
3: 222 nm, 4 nm
 Results
                Pk # Name                    Retention Time        Area Percent
-------------------------------------------------------------------------------
                   1                                 11.772              50.148
                   2                                 21.128              49.852

-------------------------------------------------------------------------------
|                Totals                                                       |
|                                                                     100.000 |
-------------------------------------------------------------------------------
```

(S)-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran **2f**

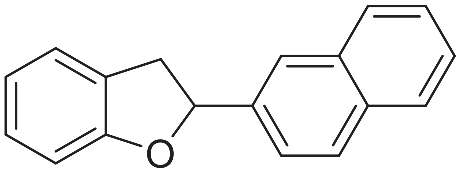
```
XW-II-117-OJH-1-1% 1mL
C:\EZStart\Projects\Default\Method\ywang0.8-1.0%.met
C:\EZStart\Projects\Default\Data\XW-II-117-OJH-1-1% 1mL
```

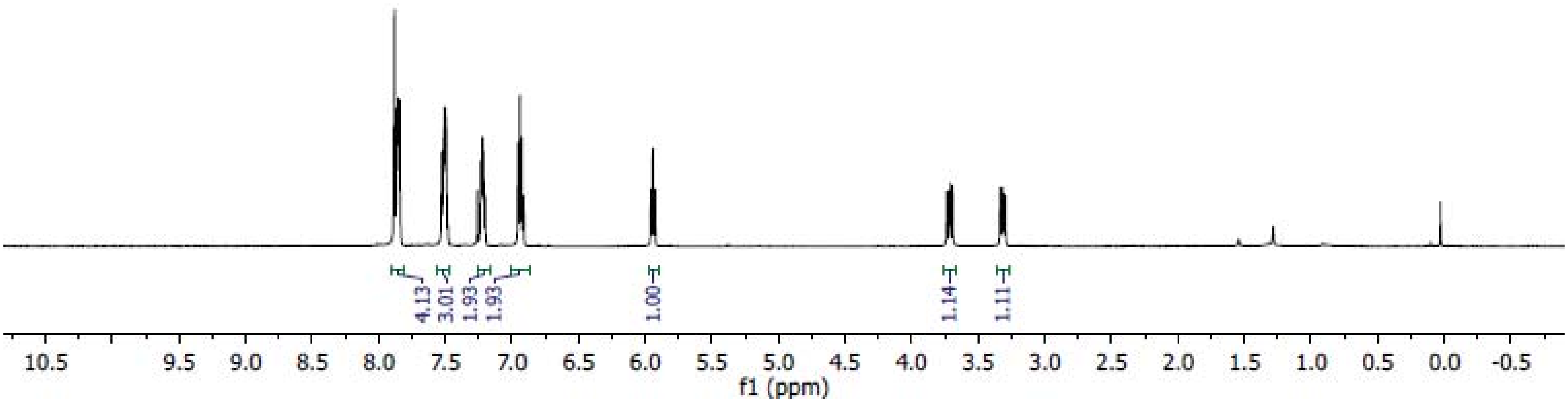




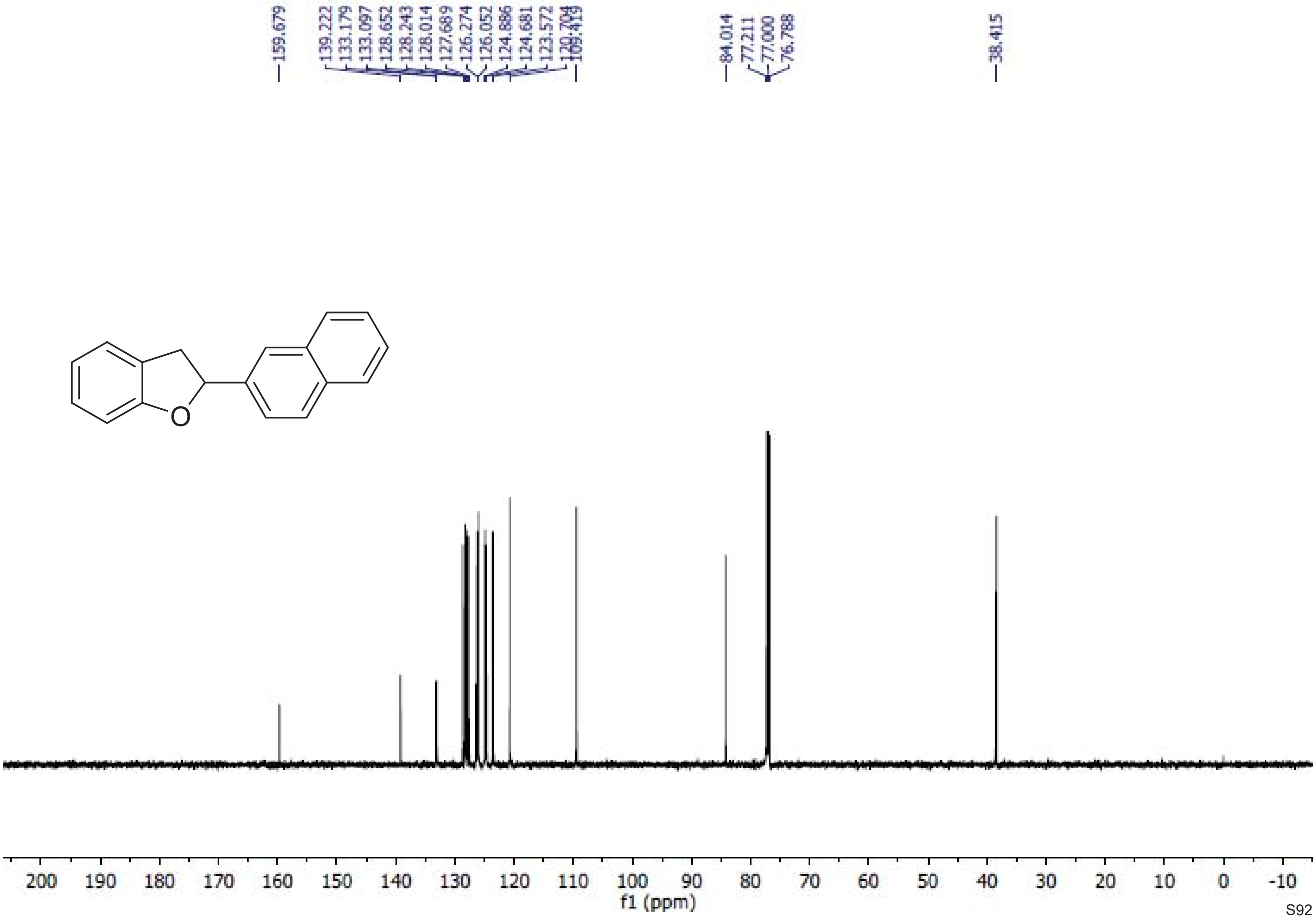
```
3: 222 nm, 4 nm
 Results
                    Pk # Name                        Retention Time        Area Percent
-------------------------------------------------------------------------------------------
                       1                                     11.824              10.938
                       2                                     21.092              89.062

 ------------------------------------------------------------------------------------------
|                 Totals                                                                    |
|                                                                                 100.000   |
 ------------------------------------------------------------------------------------------
```

(S)-2-(naphthalen-2-yl)-2,3-dihydrobenzofuran **2g**





(S)-2-(naphthalen-2-yl)-2,3-dihydrobenzofuran **2g**

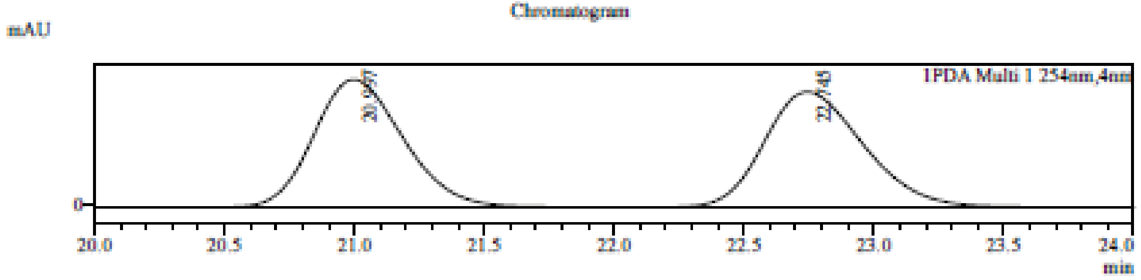


(S)-2-(naphthalen-2-yl)-2,3-dihydrobenzofuran **2g**

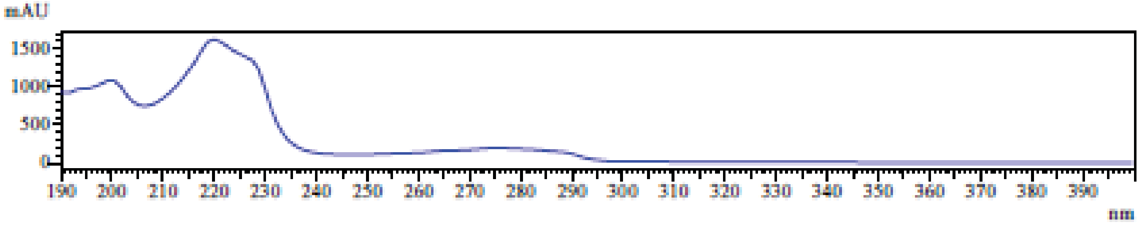
Sample Information

Sample Name	: XW-VI-9-IB-0.5%0.8mL
Sample ID	: XW-VI-9-IB-0.5%0.8mL
Data File	: XW-VI-9-IB-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

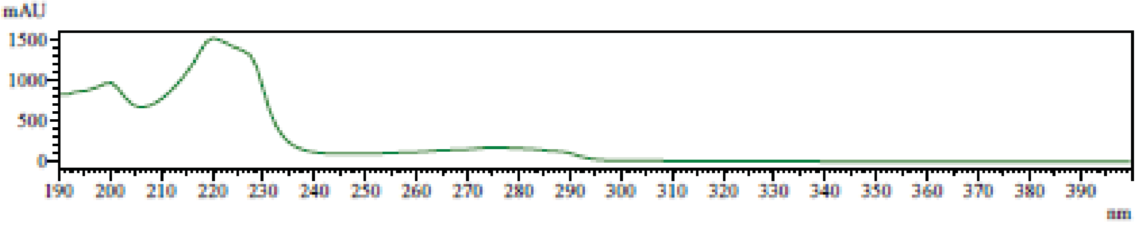
Chromatogram



UV Spectrum
Retention time = 20.997



UV Spectrum
Retention time = 22.745



Peak Table

PDA Ch1 254nm

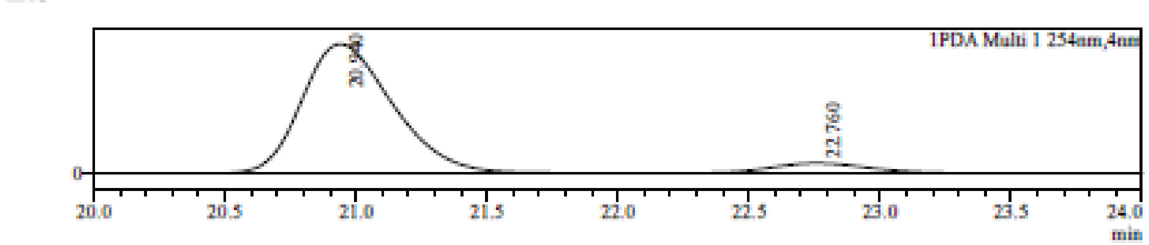
Peak#	Ret. Time	Area	Area%
1	20.997	2907159	50.011
2	22.745	2905854	49.989
Total		5813013	100.000

(S)-2-(naphthalen-2-yl)-2,3-dihydrobenzofuran **2g**

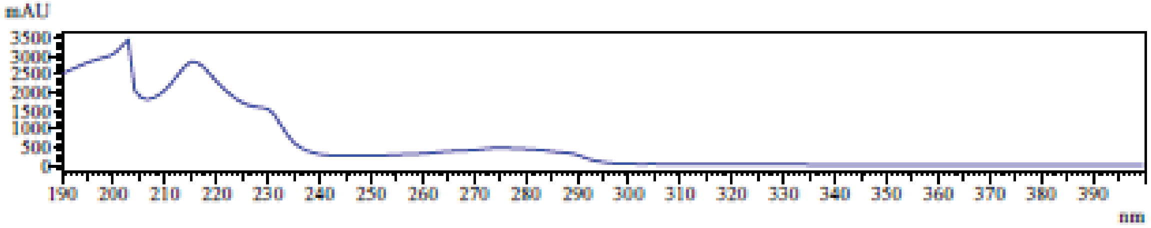
Sample Information

Sample Name	: XW-VI-10-NEW-IB-0.5%0.8mL
Sample ID	: XW-VI-10-NEW-IB-0.5%0.8mL
Data File	: XW-VI-10-NEW-IB-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

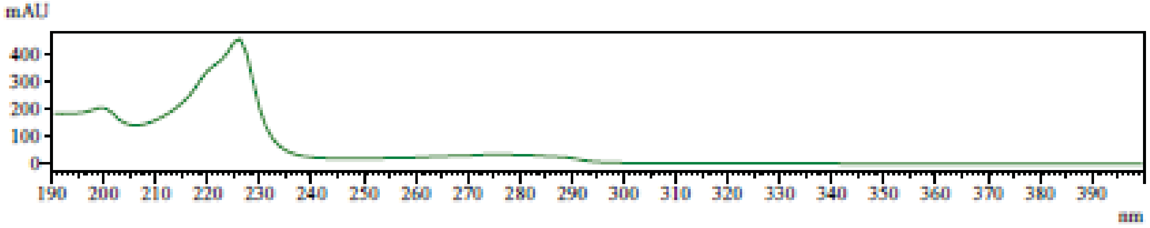
Chromatogram



UV Spectrum
Retention time = 20.940



UV Spectrum
Retention time = 22.760

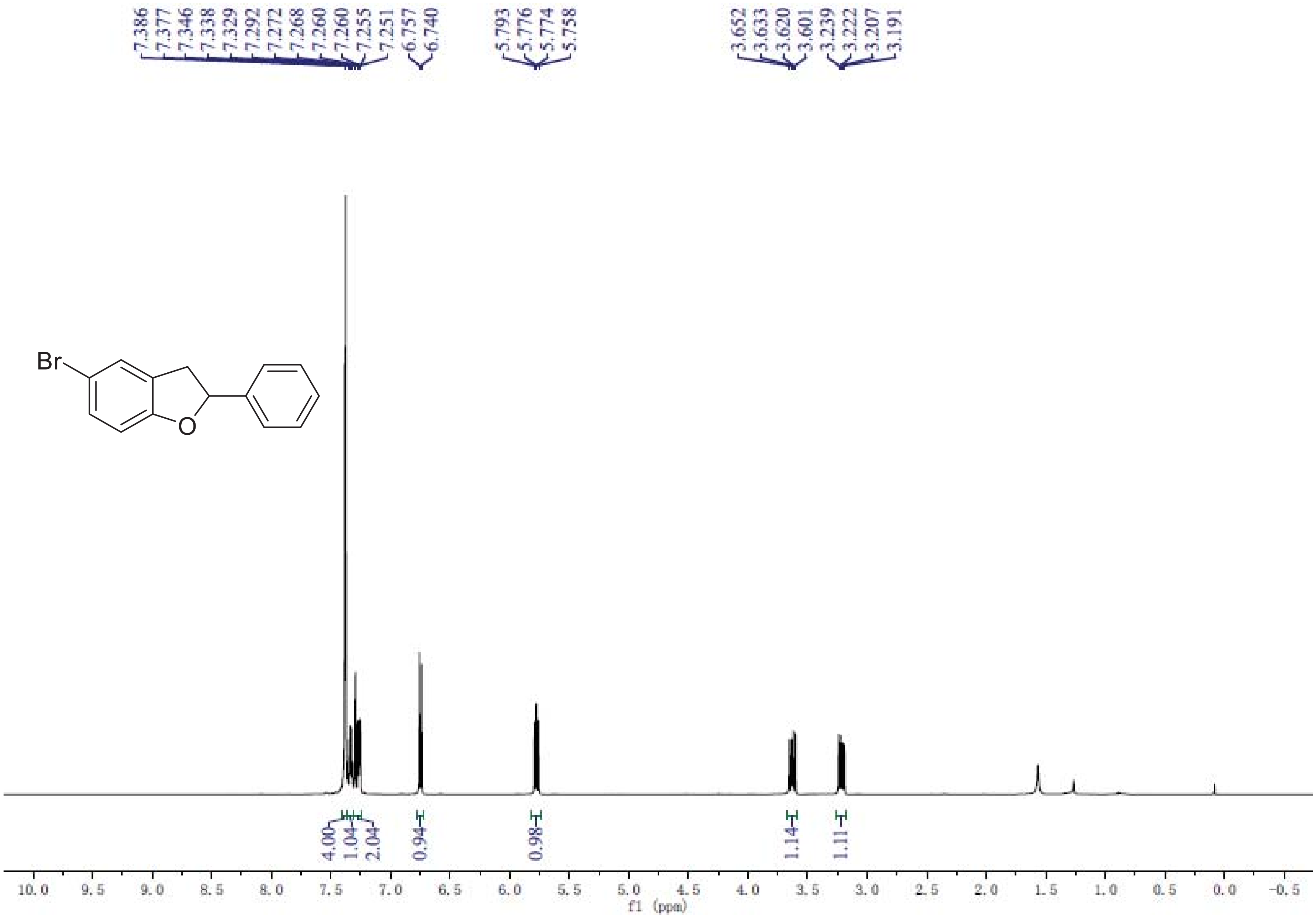


Peak Table

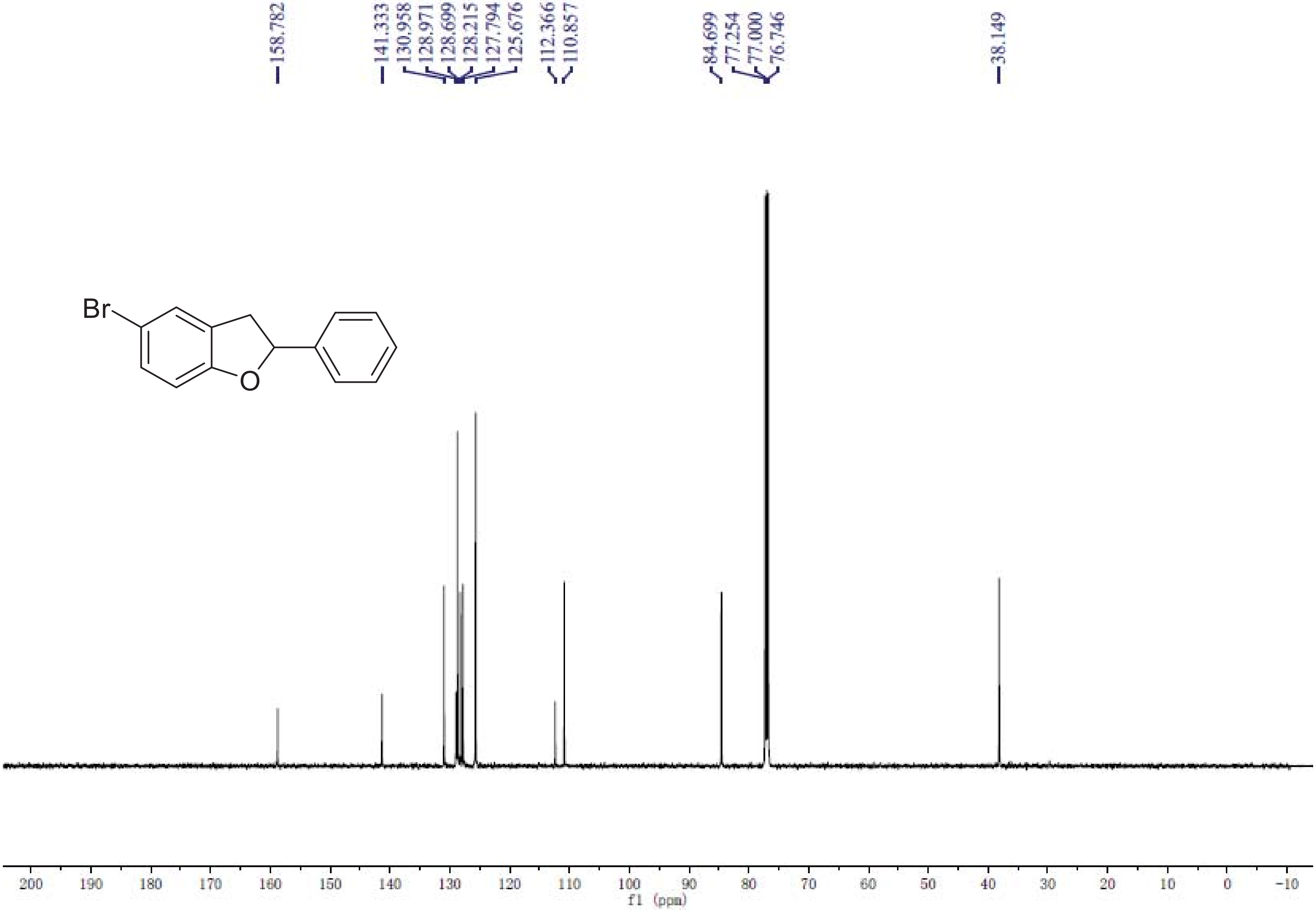
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	20.940	6948883	92.171
2	22.760	590267	7.829
Total		7539150	100.000

(S)-5-bromo-2-phenyl-2,3-dihydrobenzofuran **2h**

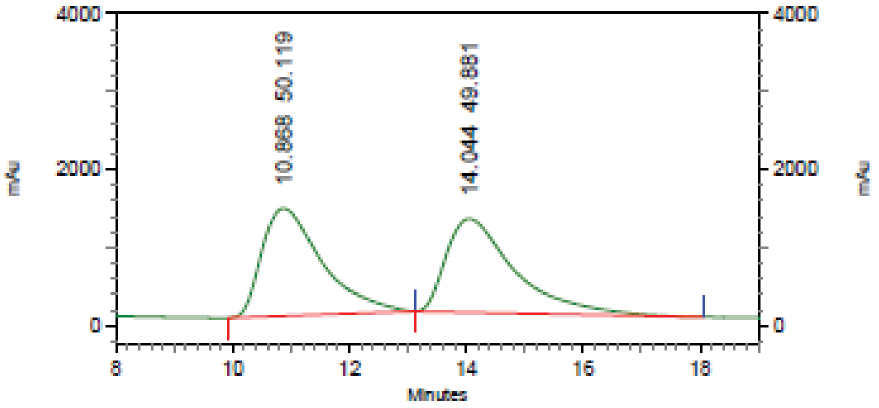


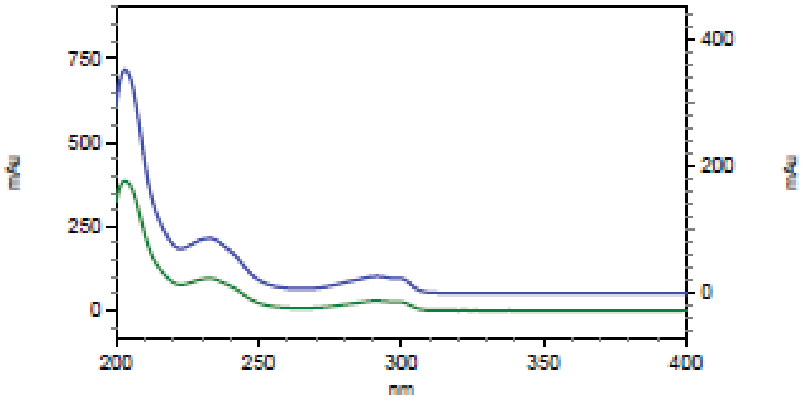
(S)-5-bromo-2-phenyl-2,3-dihydrobenzofuran **2h**



(S)-5-bromo-2-phenyl-2,3-dihydrobenzofuran **2h**

```
XW-II-8-ADH-1 1% 1mL
C:\EZStart\Projects\Default\Method\ywang1.met
C:\EZStart\Projects\Default\Data\XW-II-8-ADH-1 1% 1mL
```





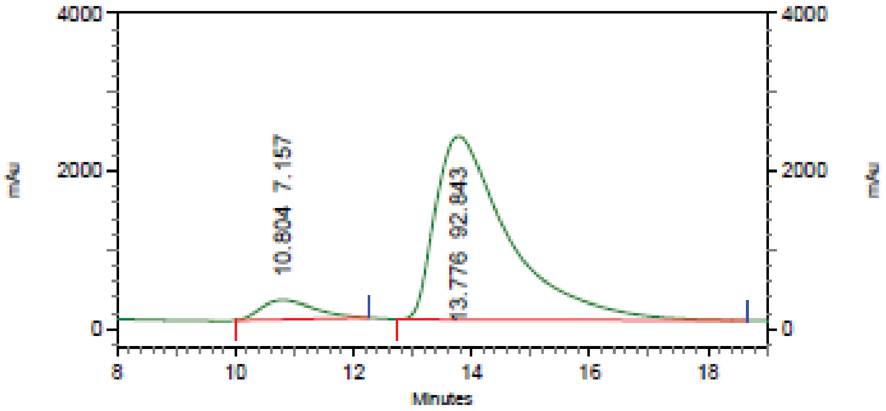
2: 234 nm, 4 nm

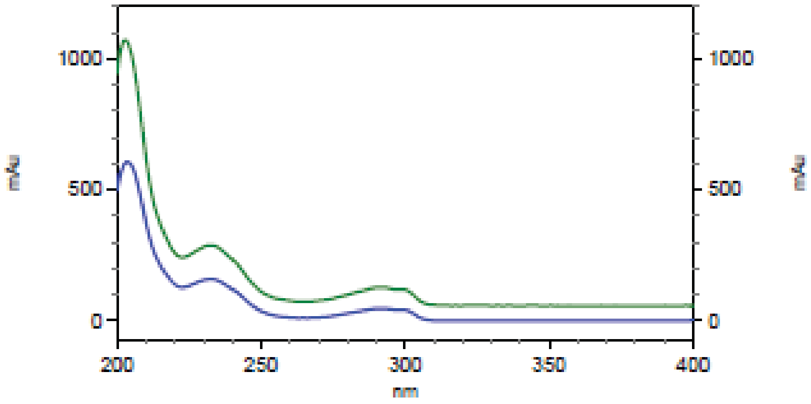
Results

Pk # Name	Retention Time	Area Percent
1	10.868	50.119
2	14.044	49.881
Totals		100.000

(S)-5-bromo-2-phenyl-2,3-dihydrobenzofuran **2h**

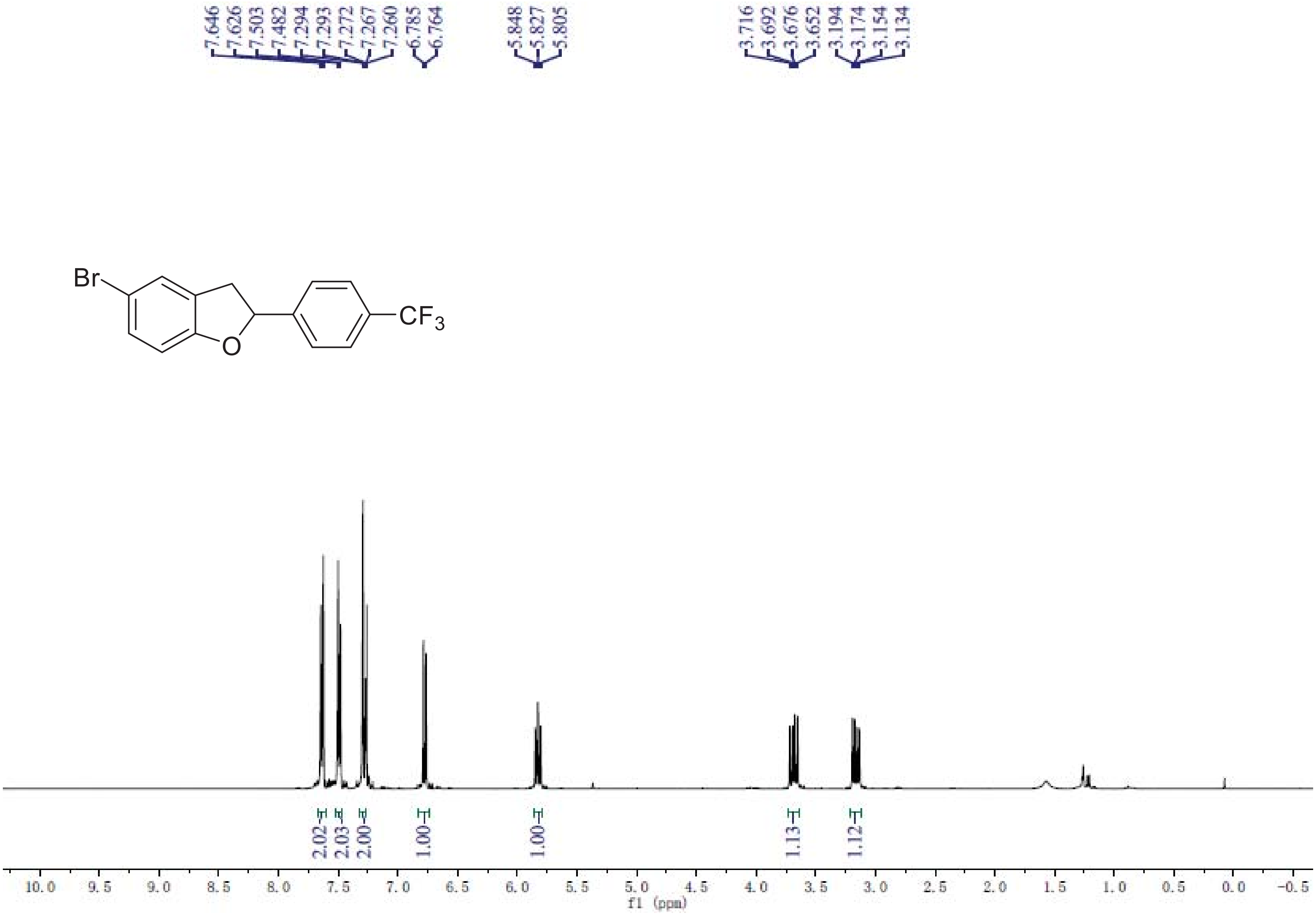
```
XW-II-83-ADH-1 1% 1mL
C:\EZStart\Projects\Default\Method\ywang1.met
C:\EZStart\Projects\Default\Data\XW-II-83-ADH-2 1% 1mL
```



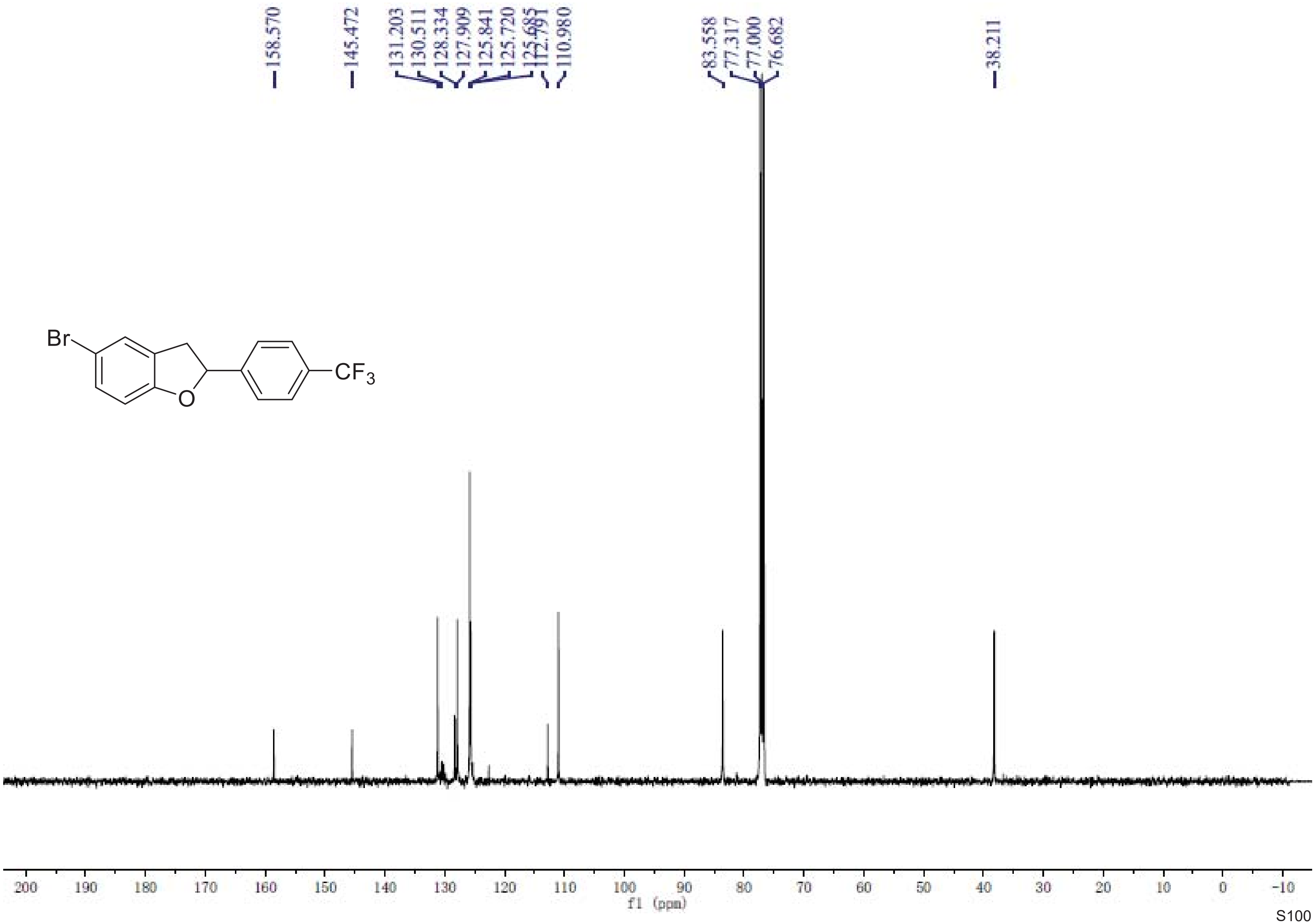


```
2: 234 nm, 4 nm
 Results
              Pk # Name                    Retention Time      Area Percent
 ---------------------------------------------------------------------------
                 1                                 10.804             7.157
                 2                                 13.776            92.843

            Totals
                                                                    100.000
```

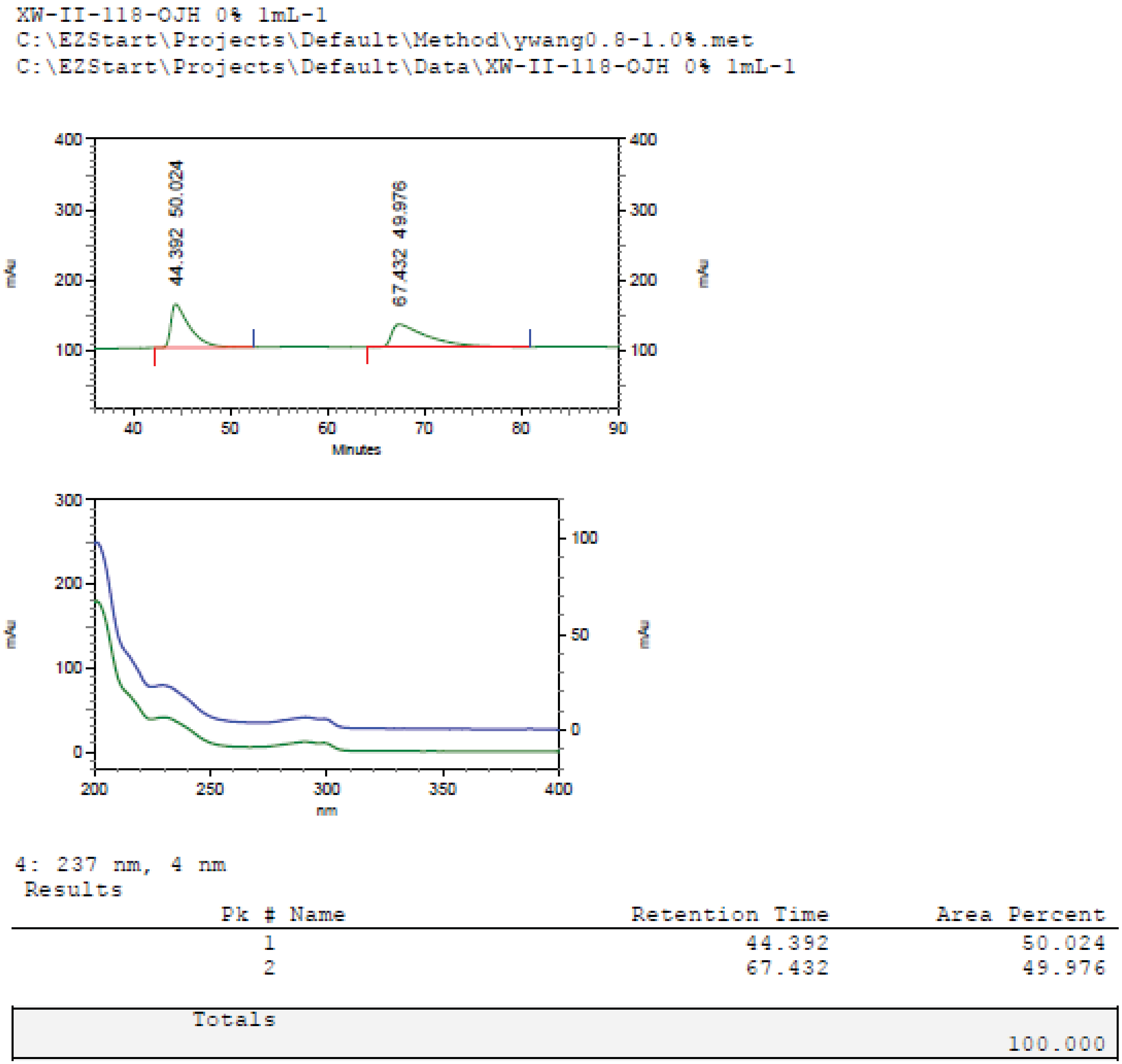
(S)-5-bromo-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran **2i**



(S)-5-bromo-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran **2i**



(S)-5-bromo-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran **2i**

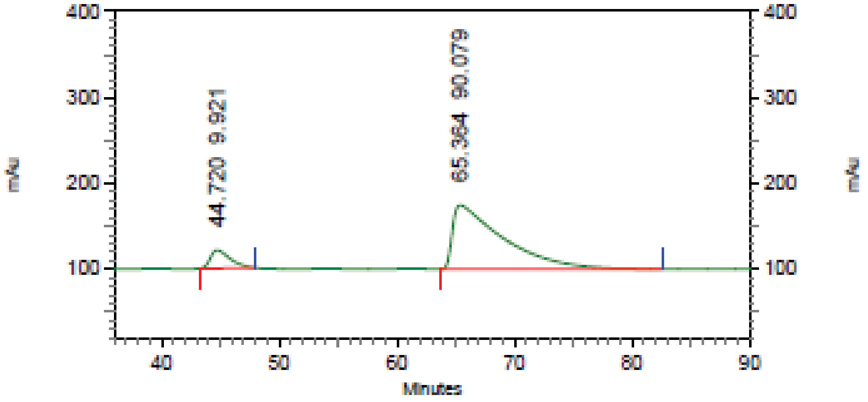


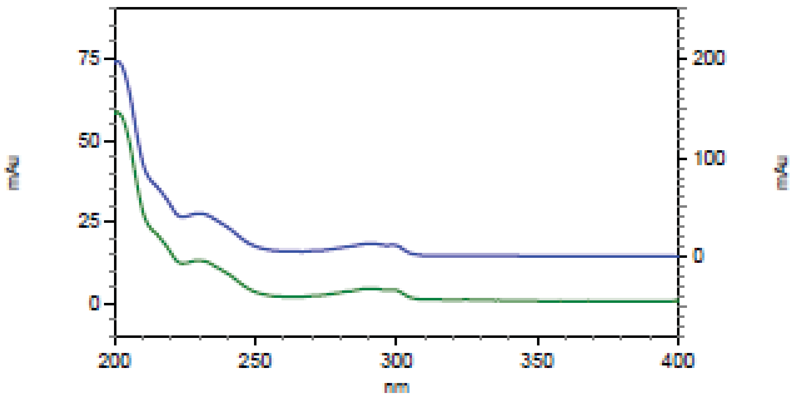
```
XW-II-118-OJH 0% 1mL-1
C:\EZStart\Projects\Default\Method\ywang0.8-1.0%.met
C:\EZStart\Projects\Default\Data\XW-II-118-OJH 0% 1mL-1
```

```
4: 237 nm, 4 nm
 Results
                  Pk # Name                     Retention Time       Area Percent
                     1                                  44.392             50.024
                     2                                  67.432             49.976

              Totals
                                                                          100.000
```

(S)-5-bromo-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran **2i**

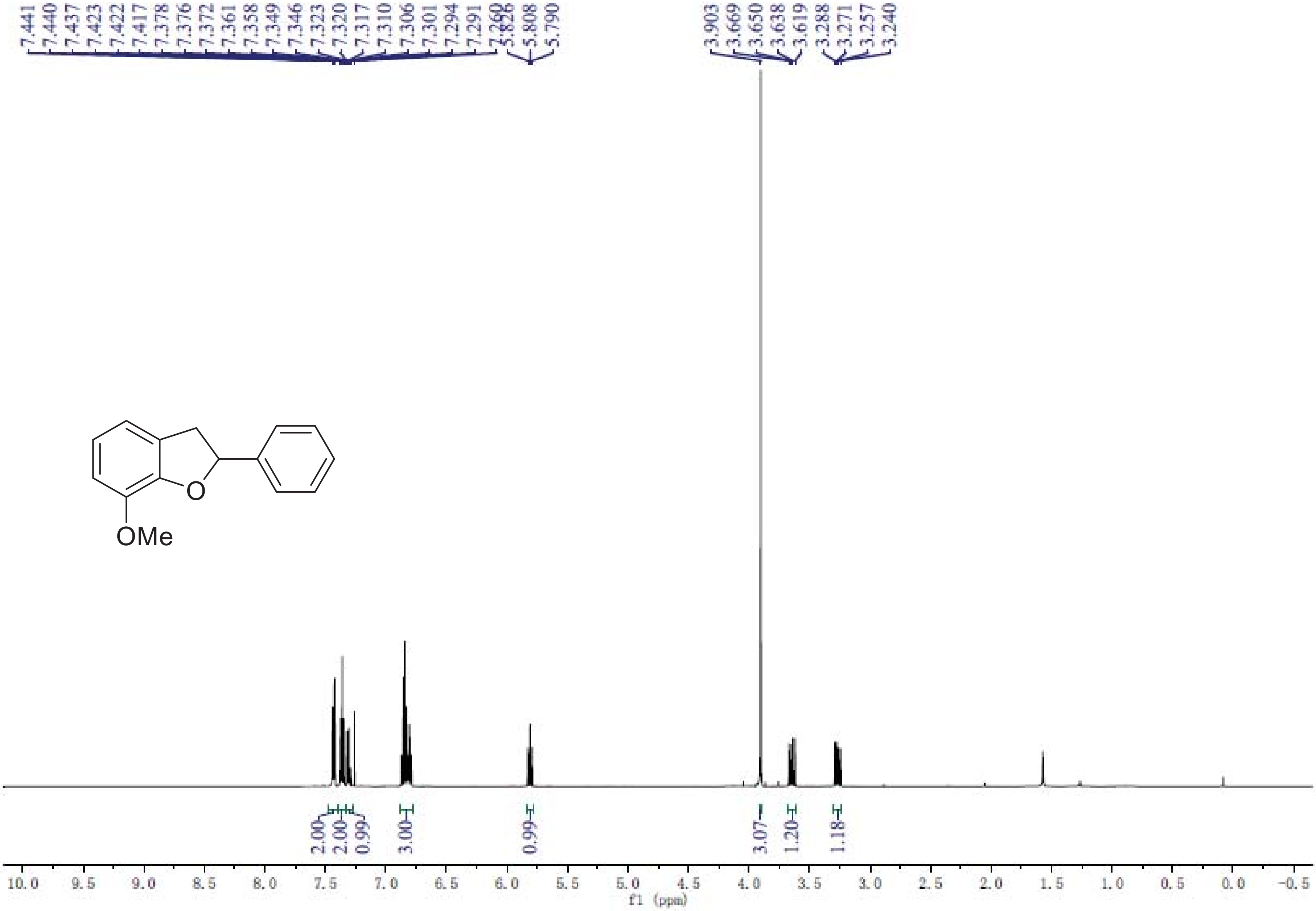
```
XW-II-119-OJH 0% 1mL-1
C:\EZStart\Projects\Default\Method\ywang0.8-1.0%.met
C:\EZStart\Projects\Default\Data\XW-II-119-OJH 0% 1mL-1
```



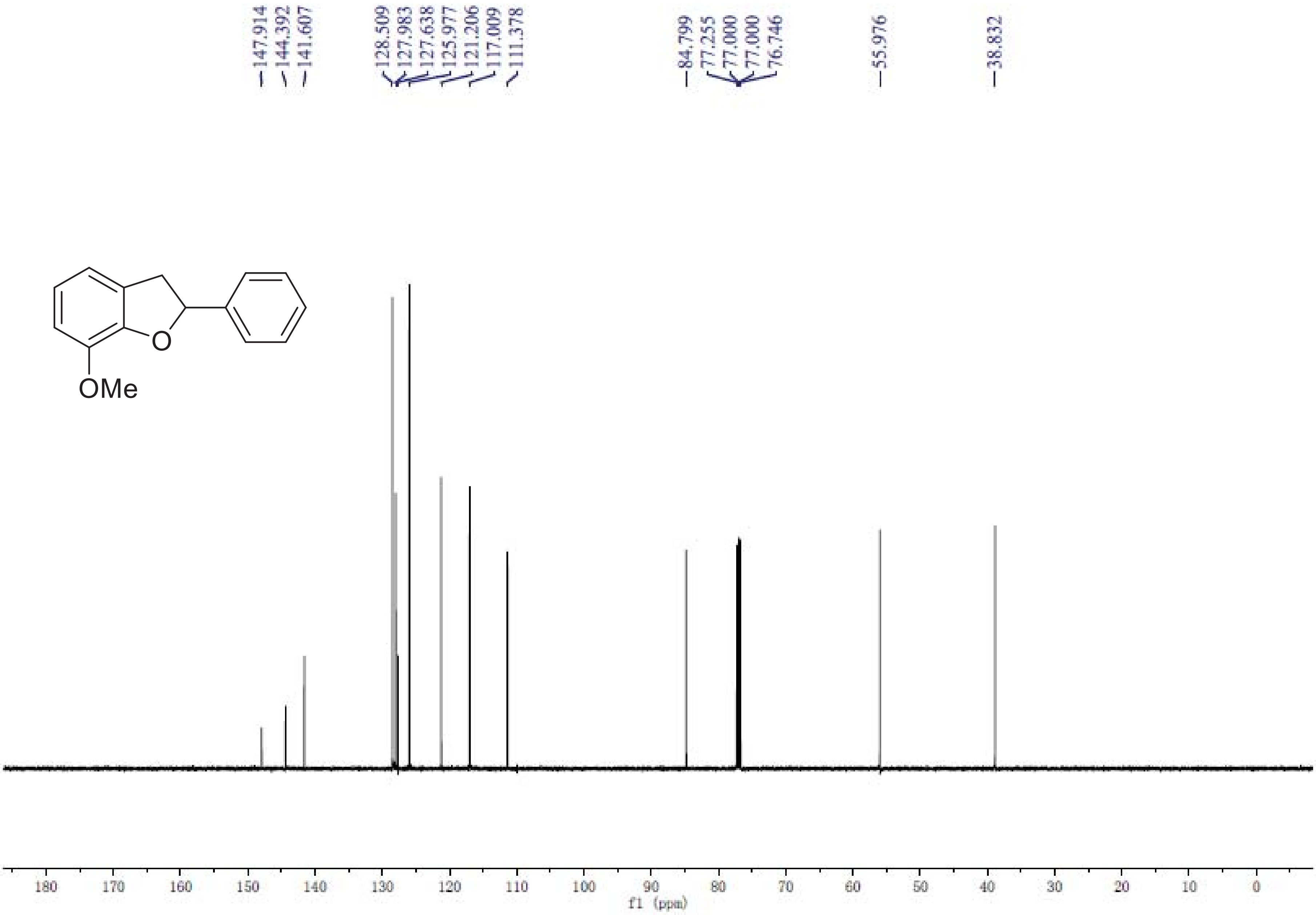


```
4: 236 nm, 4 nm
 Results
                 Pk # Name                      Retention Time      Area Percent
 ------------------------------------------------------------------------------
                    1                                   44.720             9.921
                    2                                   65.364            90.079

             Totals
                                                                         100.000
```

(S)-7-methoxy-2-phenyl-2,3-dihydrobenzofuran **2j**

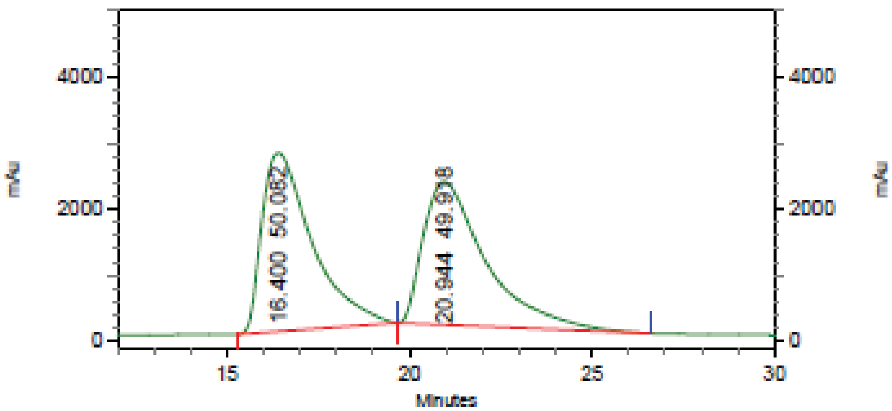


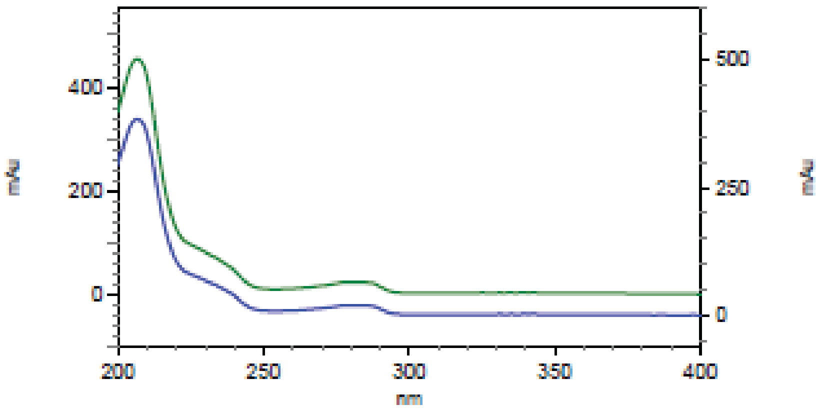
(S)-7-methoxy-2-phenyl-2,3-dihydrobenzofuran **2j**



(S)-7-methoxy-2-phenyl-2,3-dihydrobenzofuran **2j**

```
XW-I-193-ADH-1 1% 1mL
C:\EZStart\Projects\Default\Method\ywang1.met
C:\EZStart\Projects\Default\Data\XW-I-193-ADH-1 1% 1mL
```

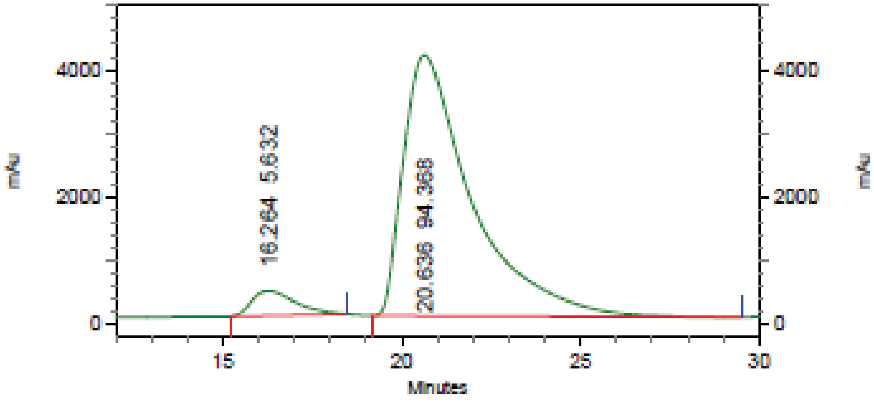


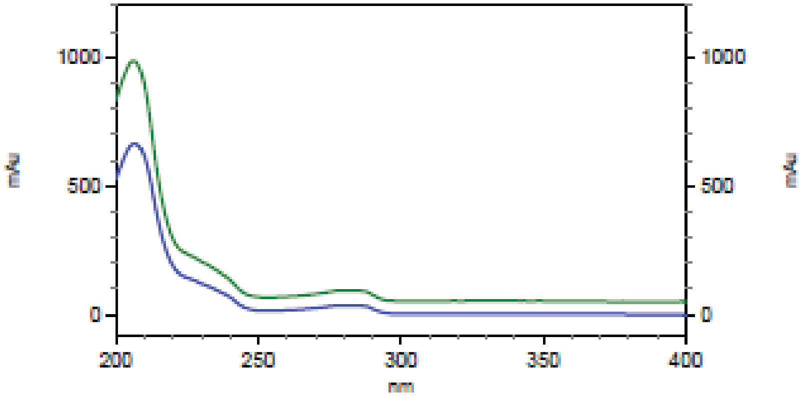


```
2: 217 nm, 4 nm
 Results
                 Pk # Name                      Retention Time          Area Percent
                    1                                   16.400                50.082
                    2                                   20.944                49.918

               Totals
                                                                             100.000
```

(S)-7-methoxy-2-phenyl-2,3-dihydrobenzofuran **2j**

```
XW-II-84-ADH-1 1% 1mL
C:\EZStart\Projects\Default\Method\ywang1.met
C:\EZStart\Projects\Default\Data\XW-II-83-ADH-1 1% 1mL
```

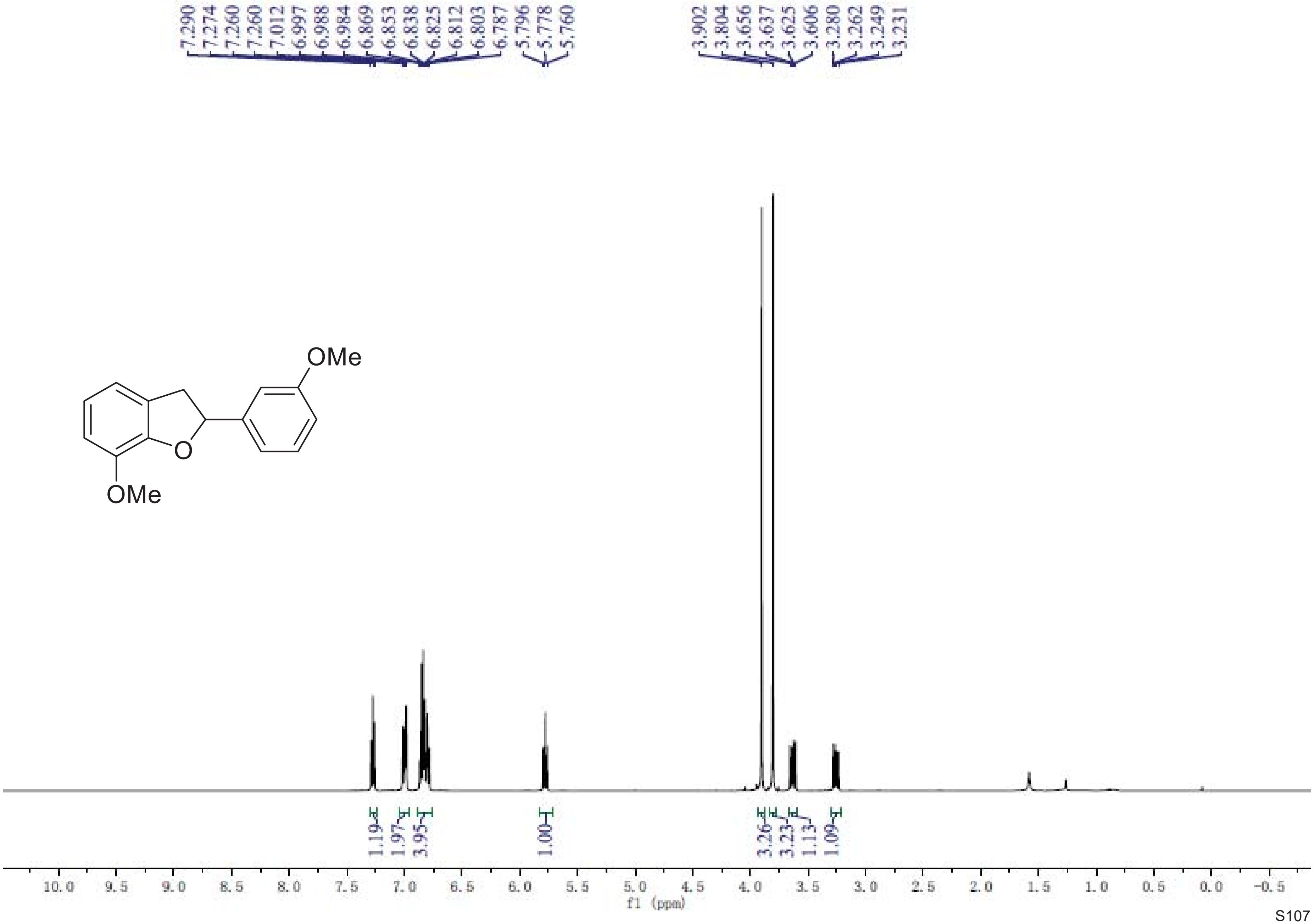




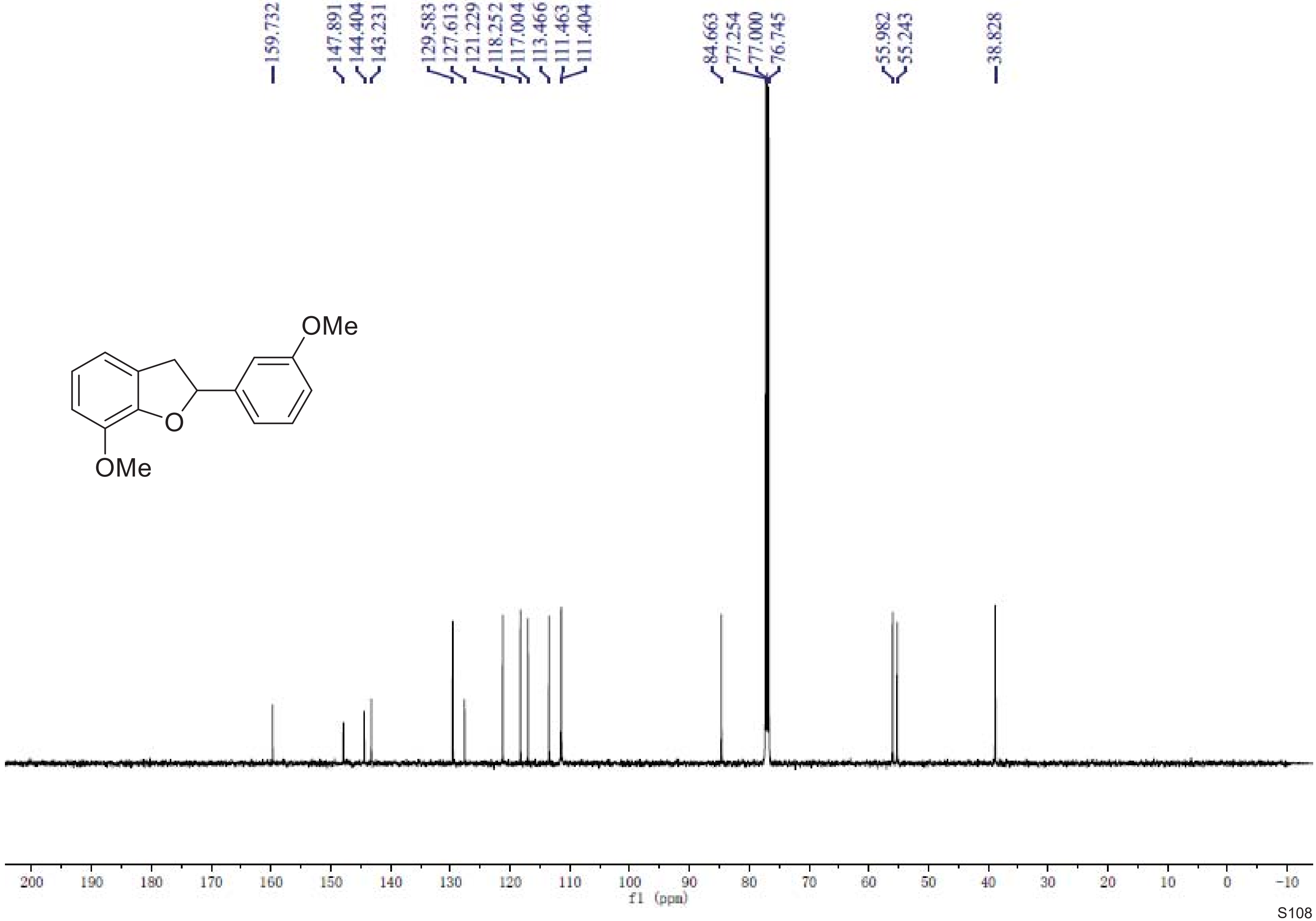
```
2: 217 nm, 4 nm
 Results
```

Pk #	Name	Retention Time	Area Percent
1		16.264	5.632
2		20.636	94.368
	Totals		100.000

(S)-7-methoxy-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran **2k**

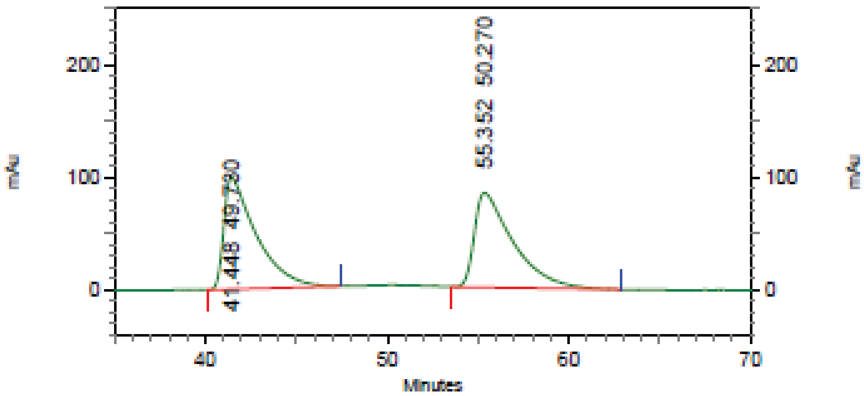


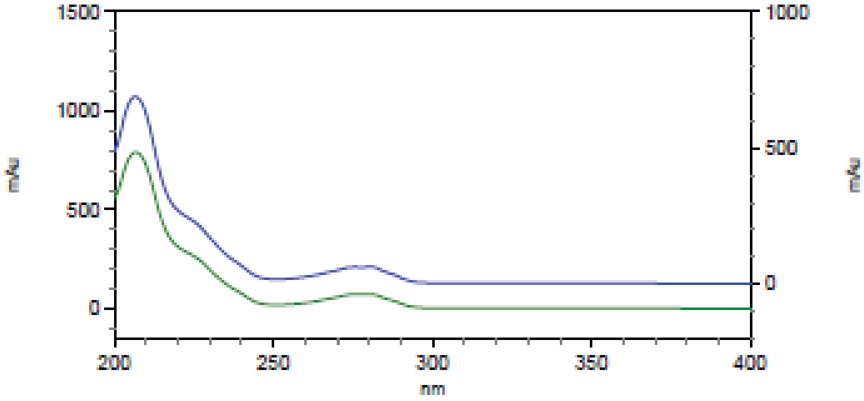
(S)-7-methoxy-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran **2k**



(S)-7-methoxy-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran **2k**

XW-II-6-OJH-2-2% 1mL
C:\EZStart\Projects\Default\Method\Joey-ODH-0.5%-0.8mL.met
C:\EZStart\Projects\Default\Data\XW-II-6-OJH-2-2% 1mL



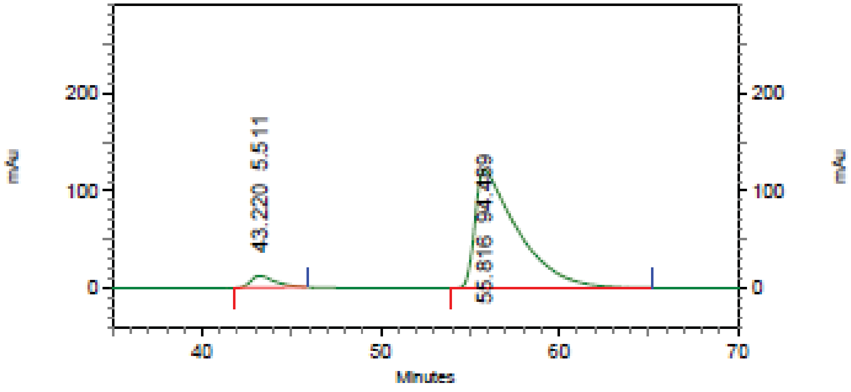


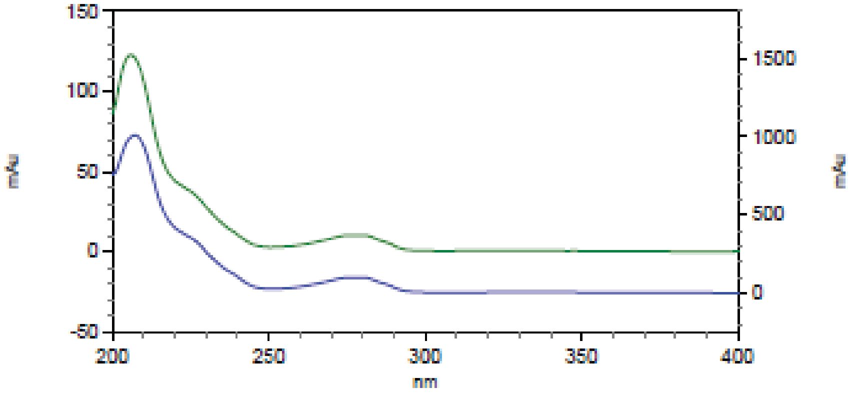
1: 232 nm, 4 nm
Results

Pk # Name	Retention Time	Area Percent
1	41.448	49.730
2	55.352	50.270
Totals		100.000

(S)-7-methoxy-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran **2k**

```
XW-II-126-1-OJH-1-2% 1mL
C:\EZStart\Projects\Default\Method\Joey-ODH-0.5%-0.8mL.met
C:\EZStart\Projects\Default\Data\XW-II-126-1-OJH-1-2% 1mL
```

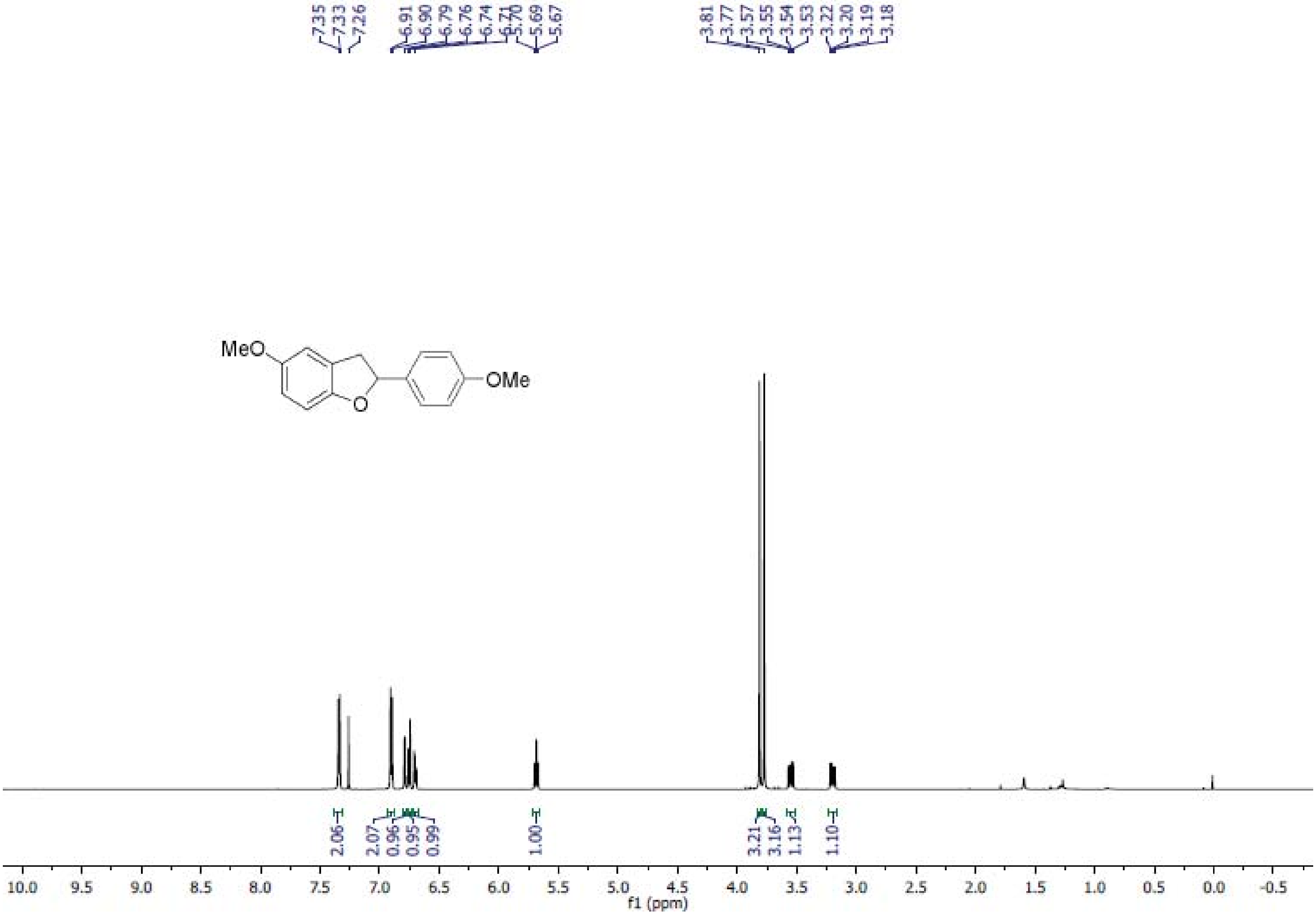




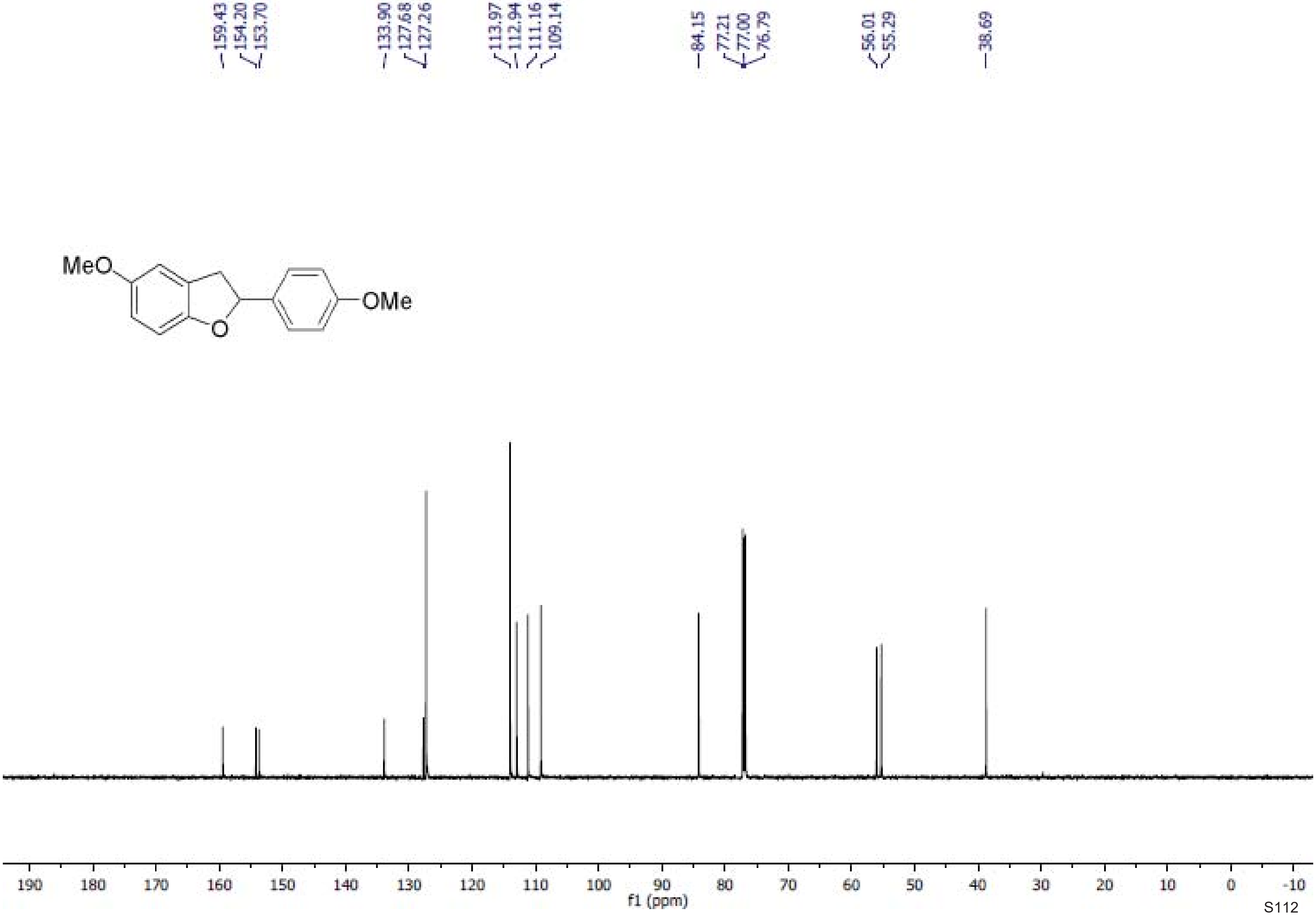
1: 233 nm, 4 nm
Results

Pk # Name	Retention Time	Area Percent
1	43.220	5.511
2	55.816	94.489
Totals		100.000

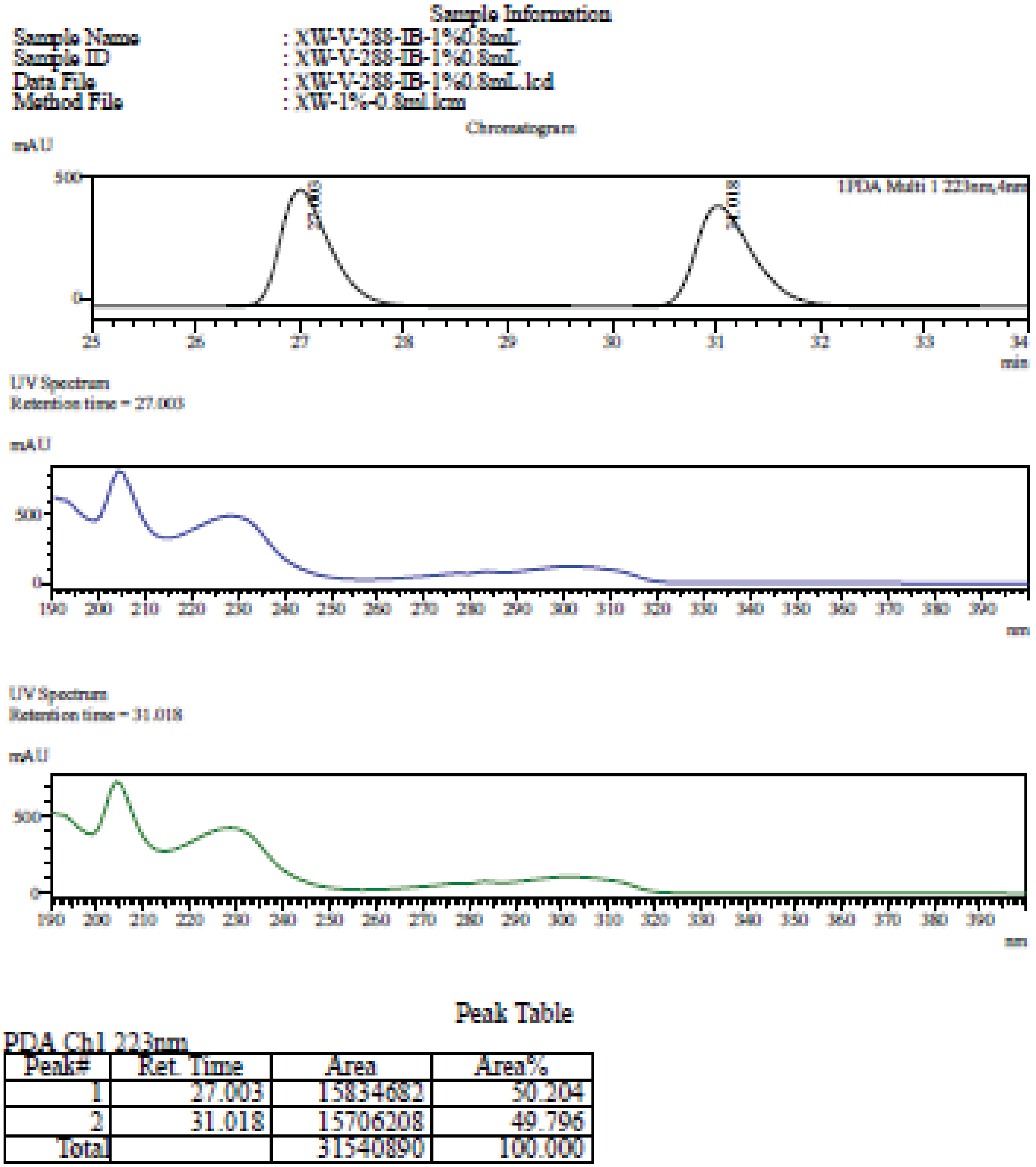
5-methoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran **2l**



5-methoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran **2l**



5-methoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran **2l**



Sample Information

Sample Name	: XW-V-288-IB-1%0.8mL
Sample ID	: XW-V-288-IB-1%0.8mL
Data File	: XW-V-288-IB-1%0.8mL.lcd
Method File	: XW-1%-0.8ml.lcm

Chromatogram

UV Spectrum
Retention time = 27.003

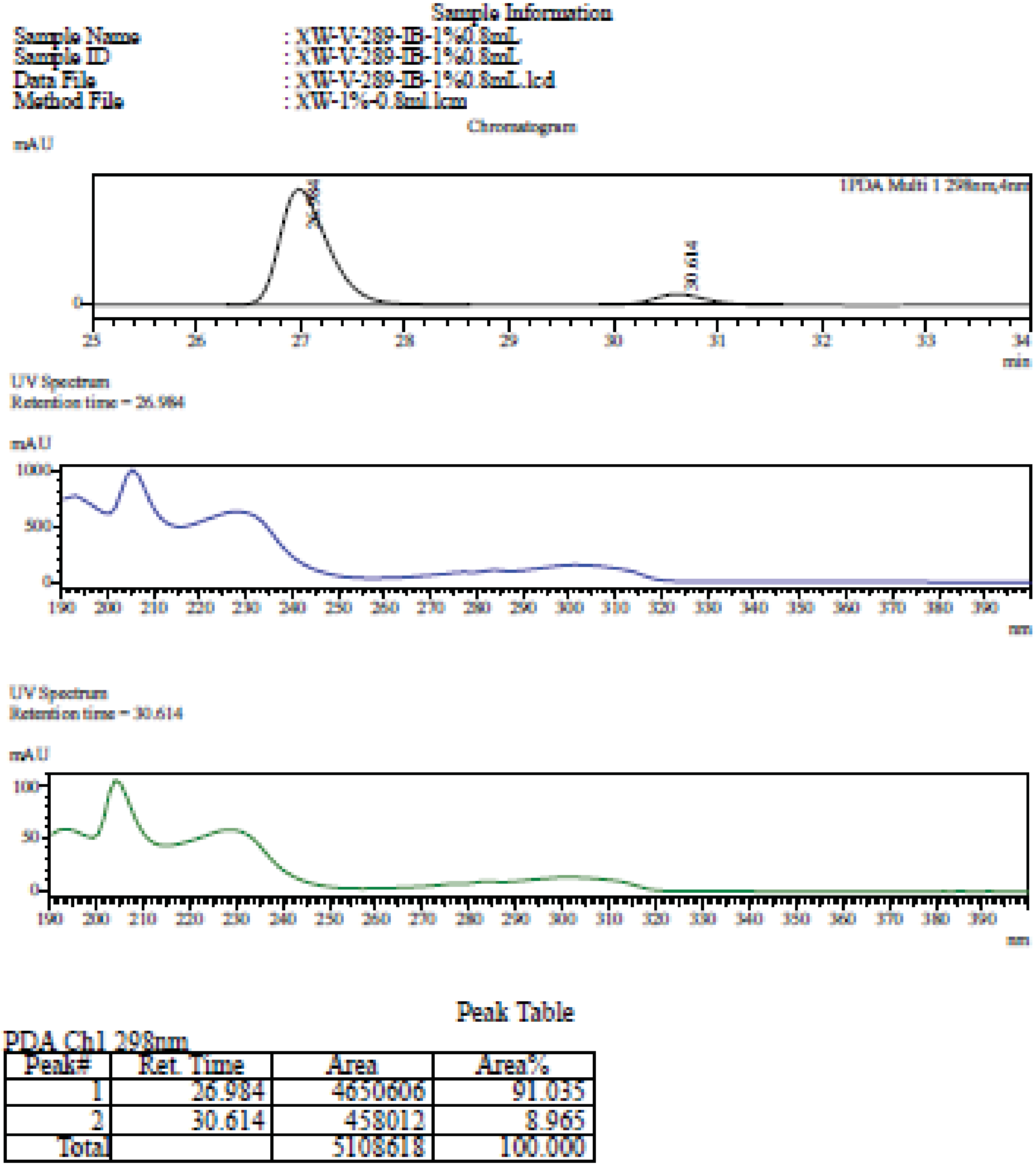
UV Spectrum
Retention time = 31.018

Peak Table

PDA Ch1 223nm

Peak#	Ret. Time	Area	Area%
1	27.003	15834682	50.204
2	31.018	15706208	49.796
Total		31540890	100.000

5-methoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran **2l**



Sample Information

Sample Name	: XW-V-289-IB-1%0.8mL
Sample ID	: XW-V-289-IB-1%0.8mL
Data File	: XW-V-289-IB-1%0.8mL.lcd
Method File	: XW-1%-0.8ml.lcm

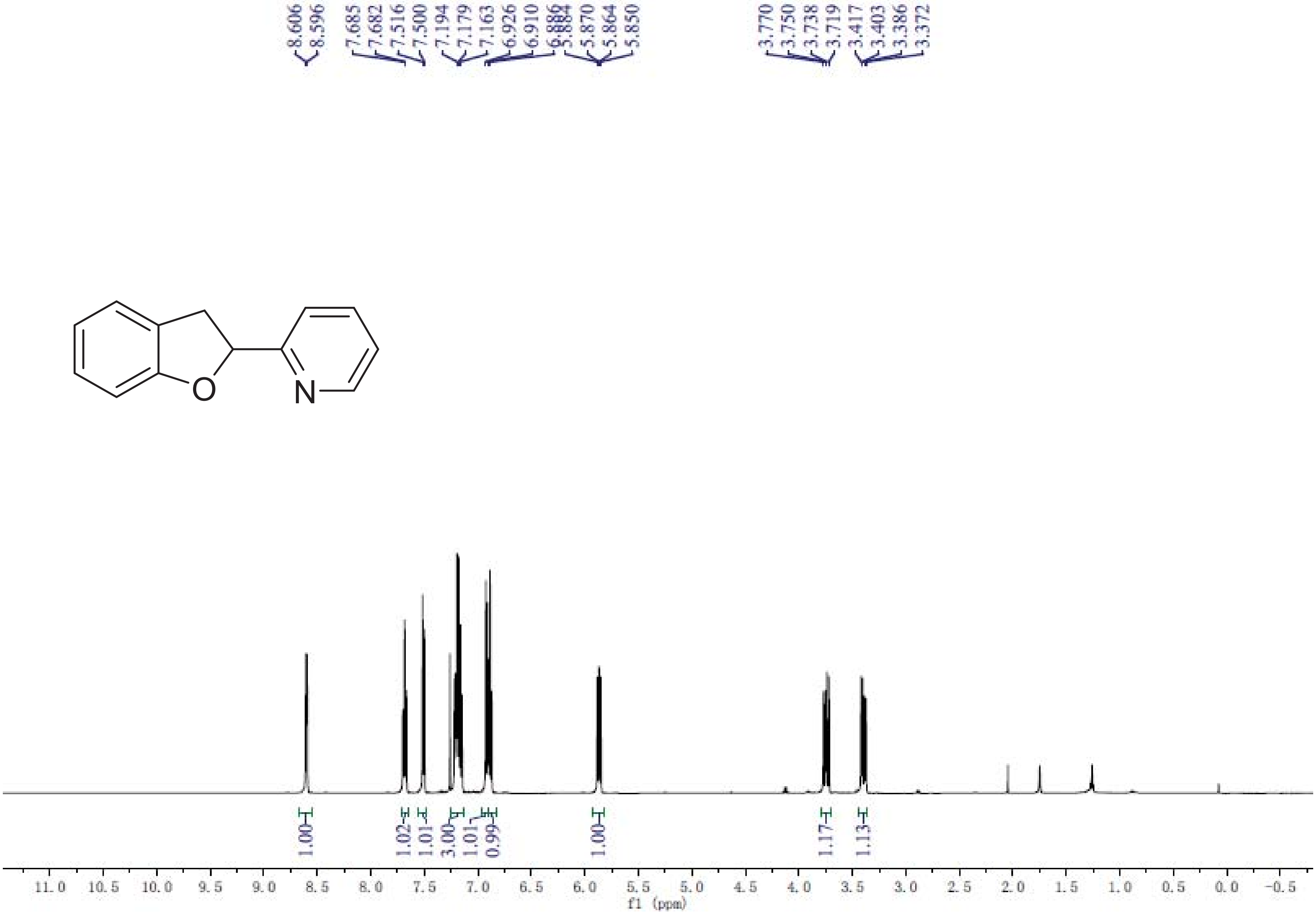
Peak Table

PDA Ch1 298nm

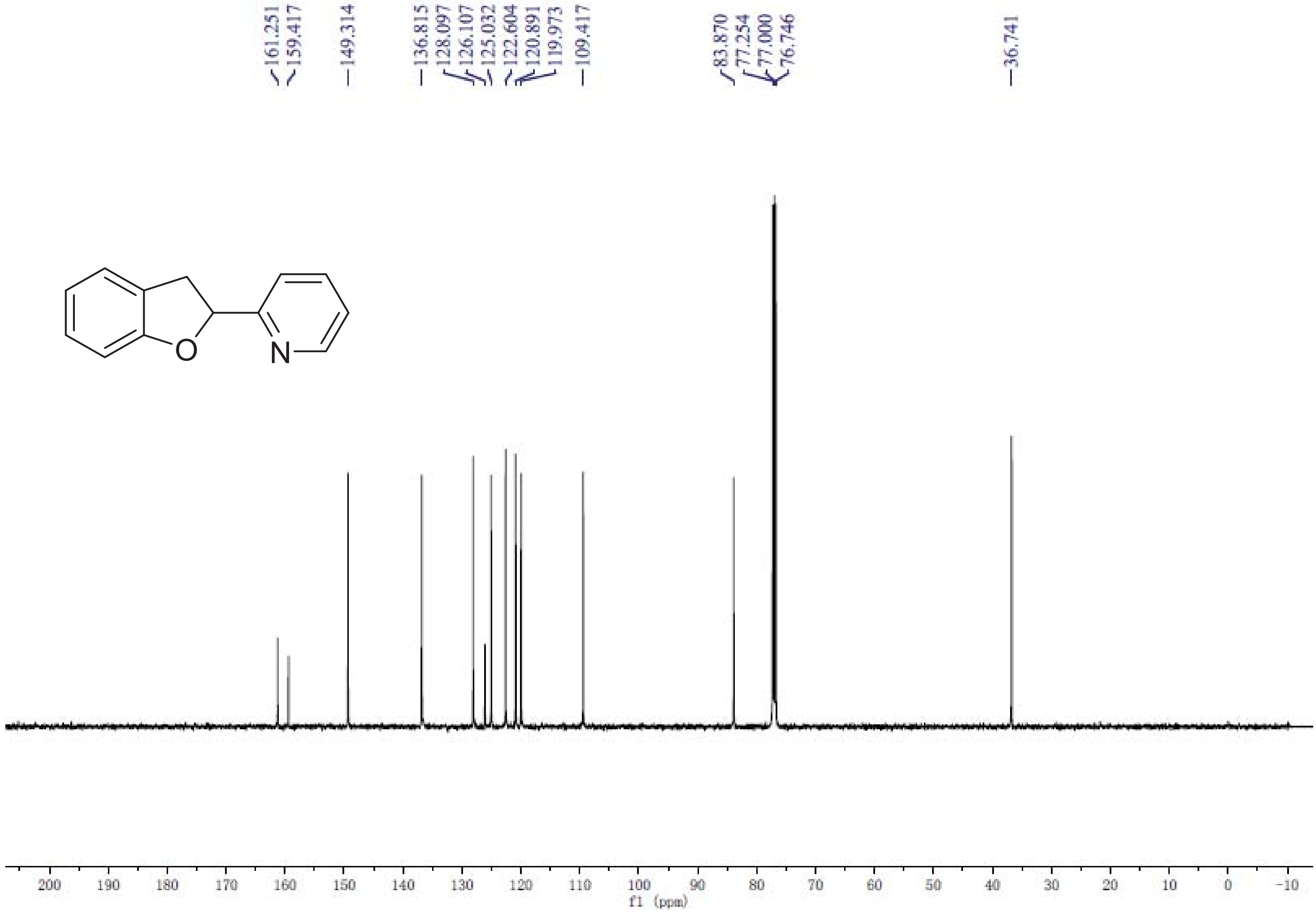
Peak#	Ret. Time	Area	Area%
1	26.984	4650606	91.035
2	30.614	458012	8.965
Total		5108618	100.000

5-methoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran **2l**

(S)-2-(2,3-dihydrobenzofuran-2-yl)pyridine **2m**

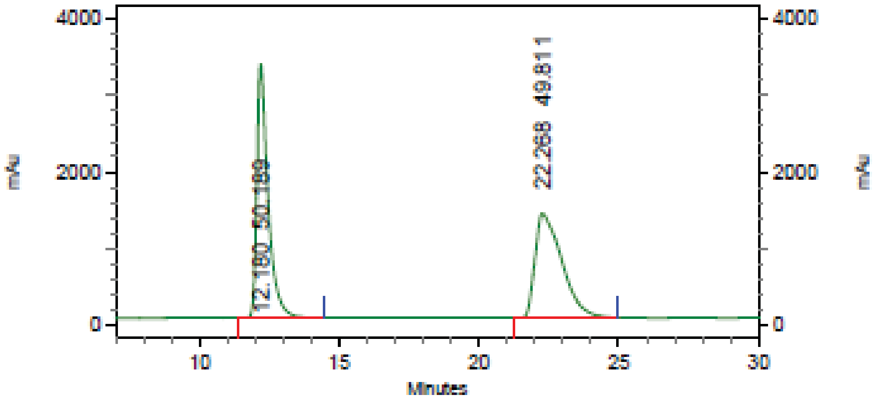


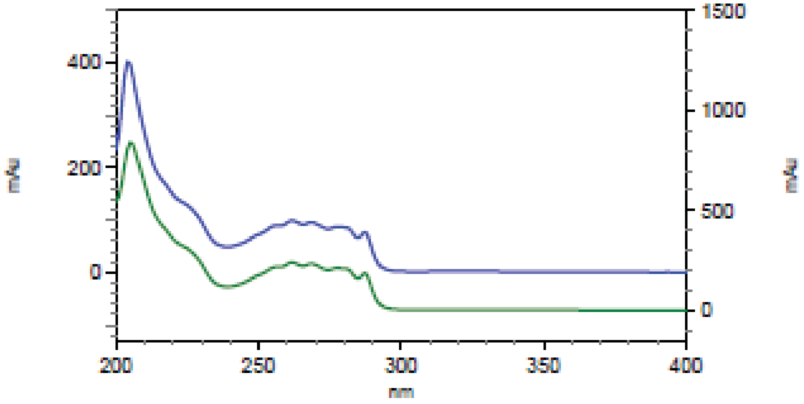
(S)-2-(2,3-dihydrobenzofuran-2-yl)pyridine **2m**



(S)-2-(2,3-dihydrobenzofuran-2-yl)pyridine **2m**

```
XW-II-181-OJH-1-3% 1mL
C:\EZStart\Projects\Default\Method\ywang0.8-1.0%.met
C:\EZStart\Projects\Default\Data\XW-II-181-OJH-1-3% 1mL
```



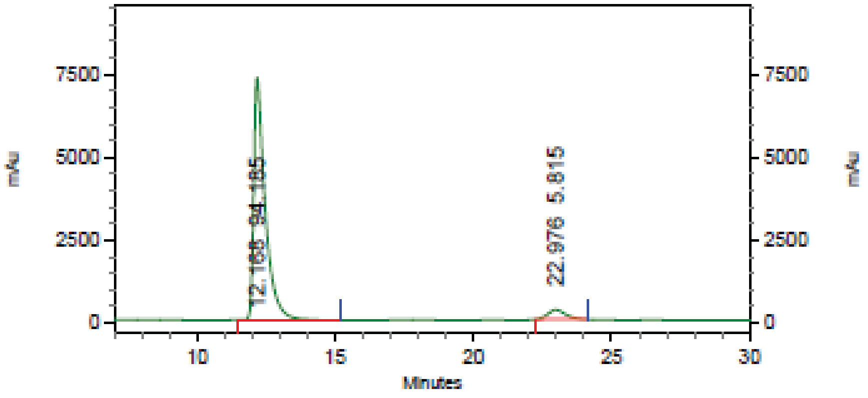


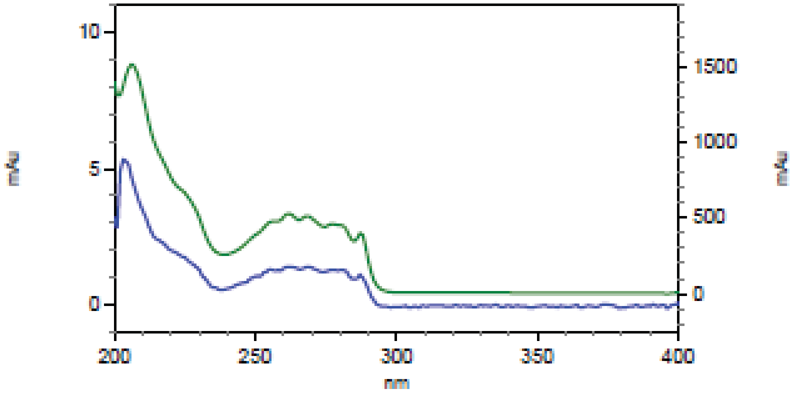
```
4: 271 nm, 4 nm
 Results
```

Pk # Name	Retention Time	Area Percent
1	12.180	50.189
2	22.268	49.811
Totals		100.000

(S)-2-(2,3-dihydrobenzofuran-2-yl)pyridine **2m**

```
XW-II-182-OJH-1-3% 1mL
C:\EZStart\Projects\Default\Method\ywang0.8-1.0%.met
C:\EZStart\Projects\Default\Data\XW-II-182-OJH-1-3% 1mL
```



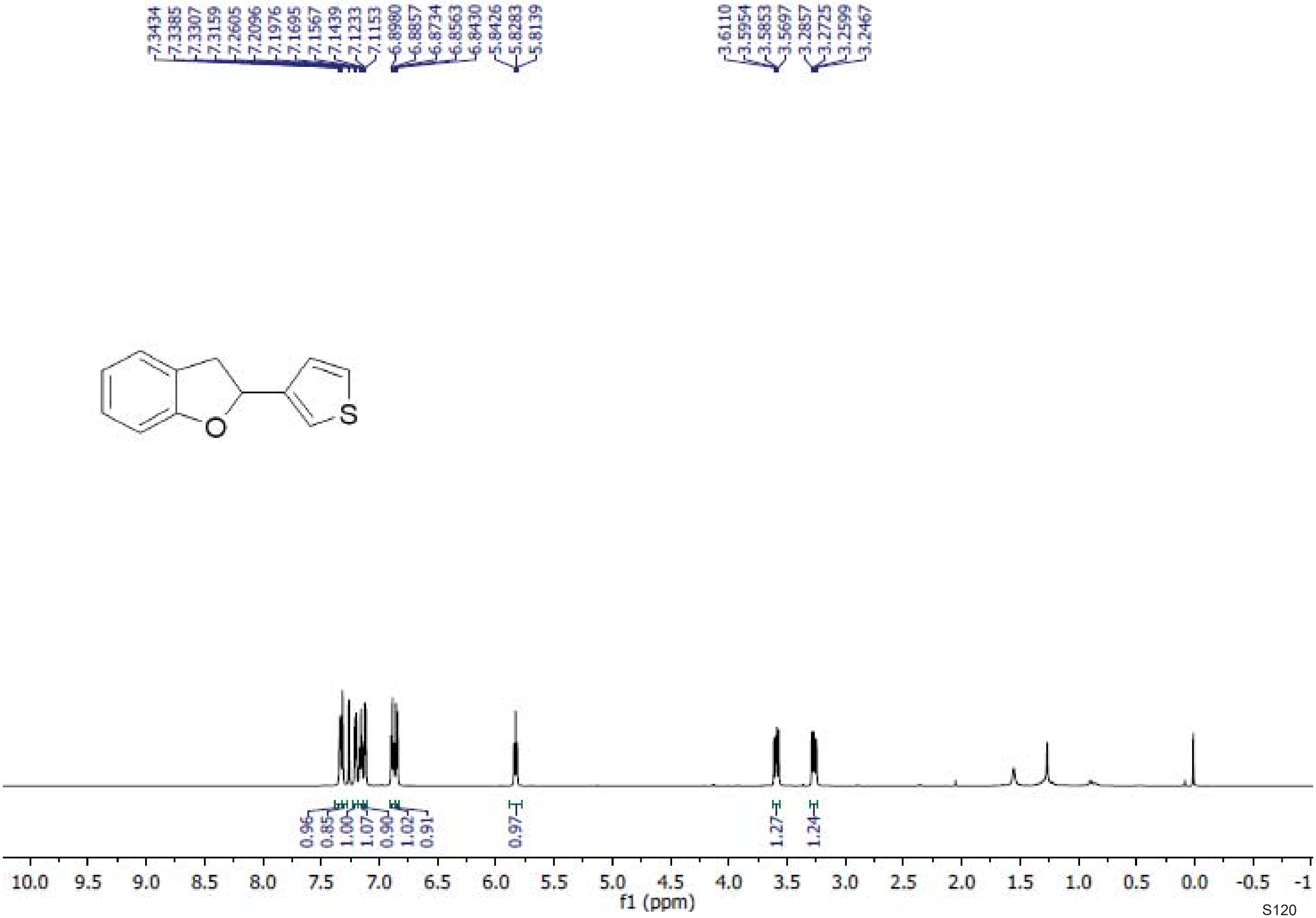


4: 271 nm, 4 nm

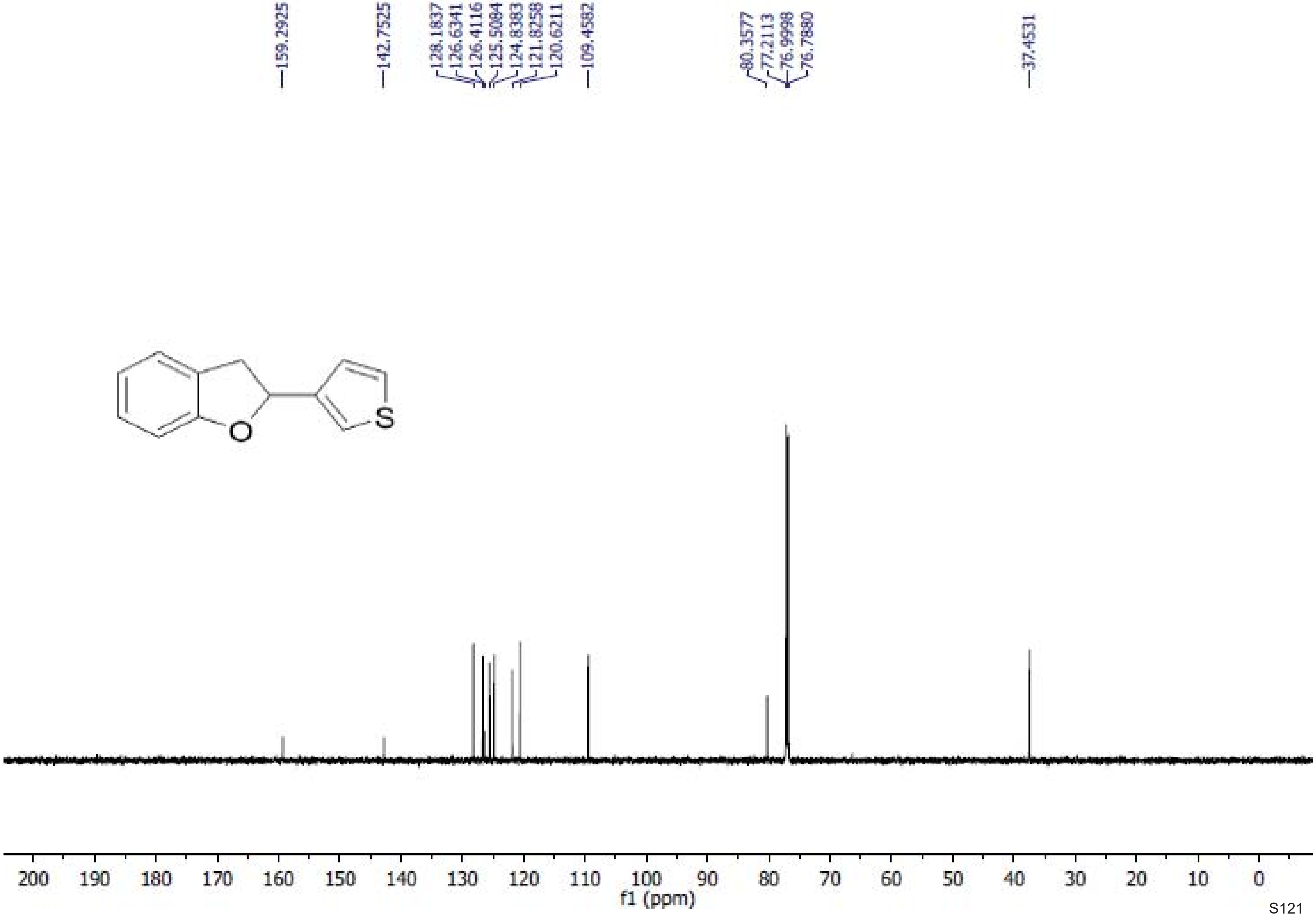
Results

Pk #	Name	Retention Time	Area Percent
1		12.168	94.185
2		22.976	5.815
Totals			100.000

2-(thiophen-3-yl)-2,3-dihydrobenzofuran **2n**



2-(thiophen-3-yl)-2,3-dihydrobenzofuran **2n**

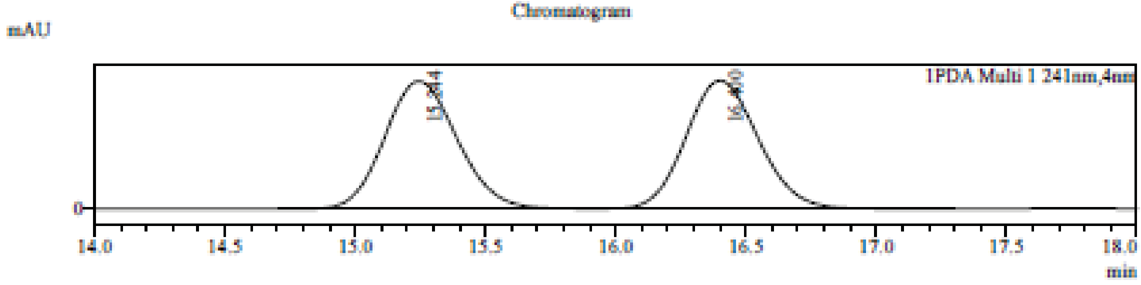


2-(thiophen-3-yl)-2,3-dihydrobenzofuran **2n**

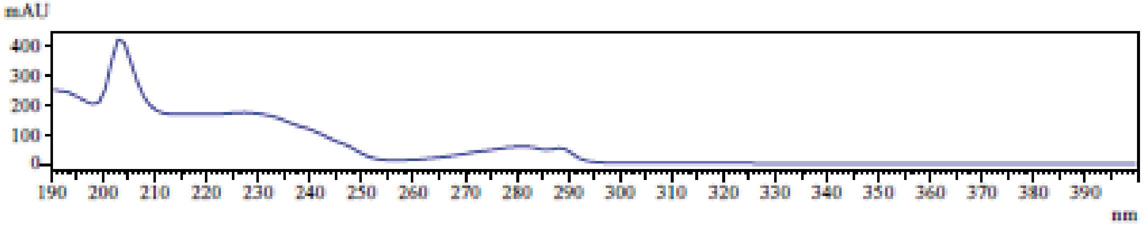
Sample Information

Sample Name	: XW-VI-16-ID-0.5%0.8mL-2
Sample ID	: XW-VI-16-ID-0.5%0.8mL-2
Data File	: XW-VI-16-ID-0.5%0.8mL-2.lcd
Method File	: XW-0.5%-0.8ml.lcm

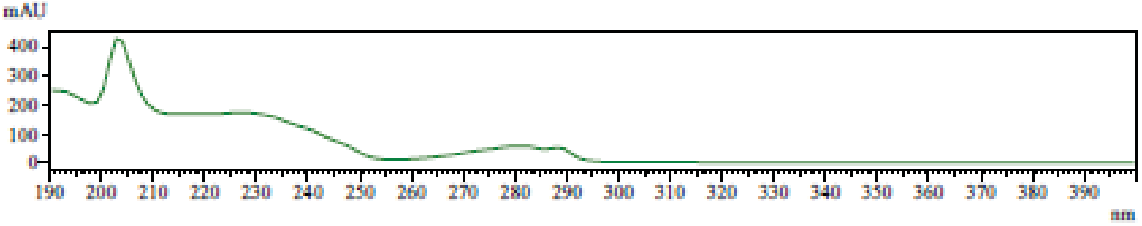
Chromatogram



UV Spectrum
Retention time = 15.244



UV Spectrum
Retention time = 16.400



Peak Table

PDA Ch1 241nm

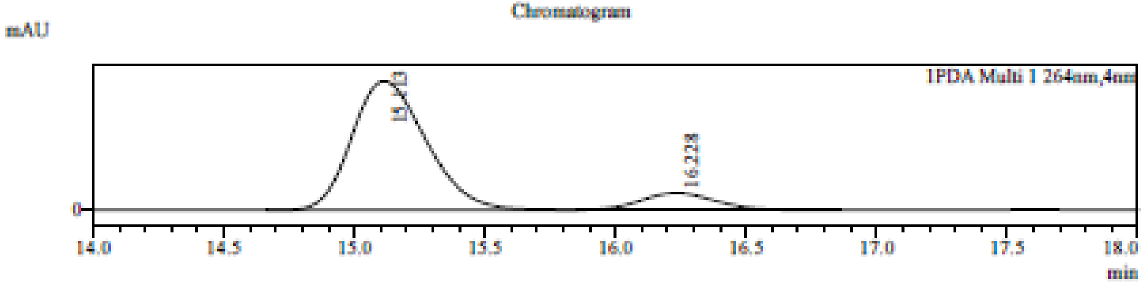
Peak#	Ret. Time	Area	Area%
1	15.244	2102491	49.951
2	16.400	2106628	50.049
Total		4209119	100.000

2-(thiophen-3-yl)-2,3-dihydrobenzofuran **2n**

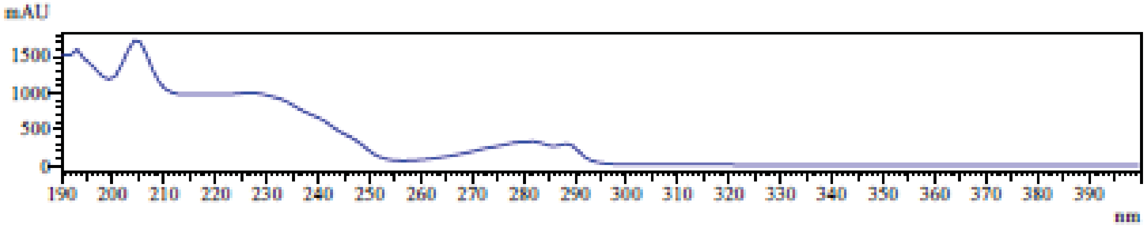
Sample Information

Sample Name : XW-VI-21-ID-0.5%0.8mL
Sample ID : XW-VI-21-ID-0.5%0.8mL
Data File : XW-VI-21-ID-0.5%0.8mL.lcd
Method File : XW-0.5%-0.8ml.lcm

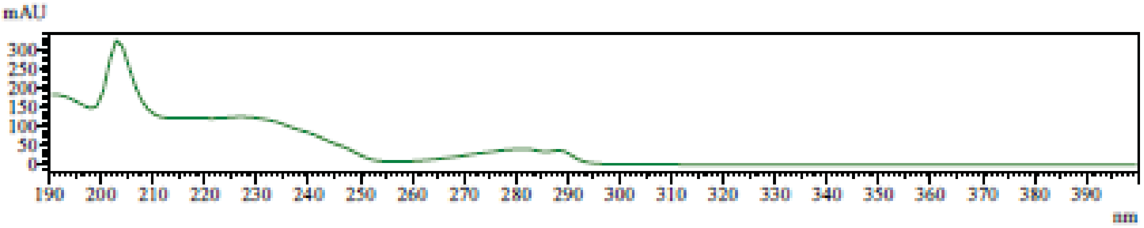
Chromatogram



UV Spectrum
Retention time = 15.113



UV Spectrum
Retention time = 16.228

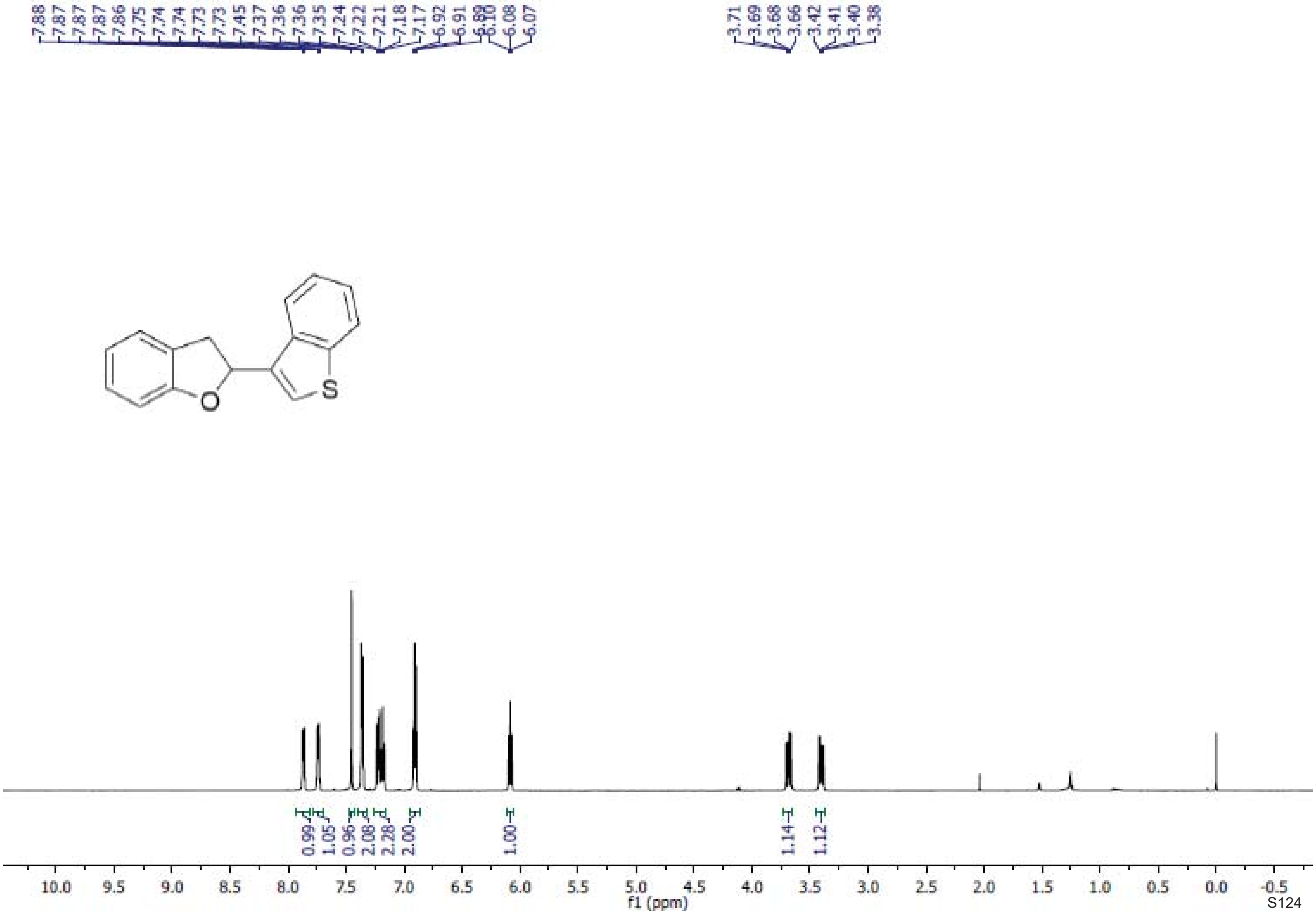


Peak Table

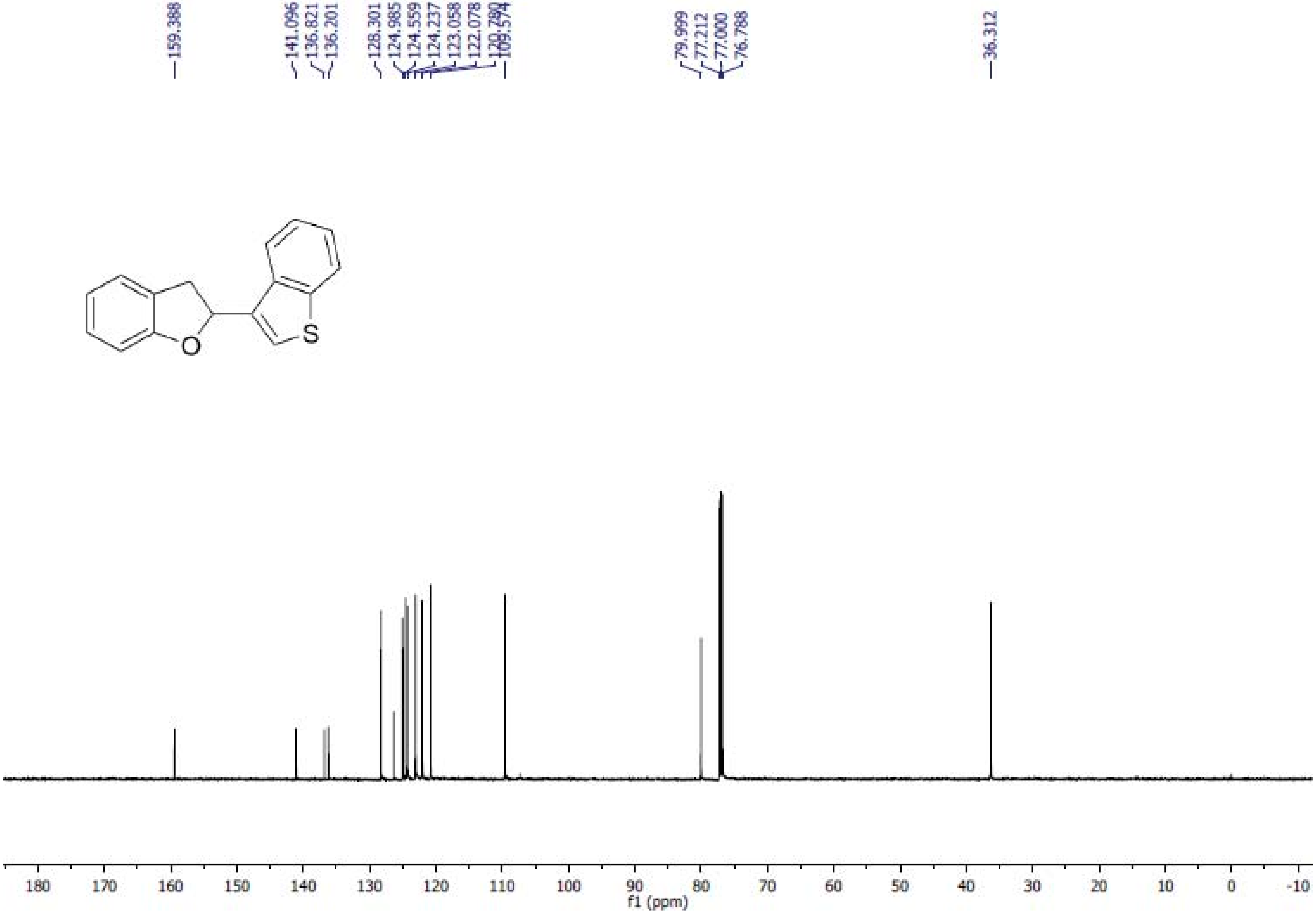
PDA Ch1 264nm

Peak#	Ret. Time	Area	Area%
1	15.113	2231895	88.285
2	16.228	296152	11.715
Total		2528047	100.000

2-(benzo[b]thiophen-3-yl)-2,3-dihydrobenzofuran **2o**



2-(benzo[b]thiophen-3-yl)-2,3-dihydrobenzofuran **2o**

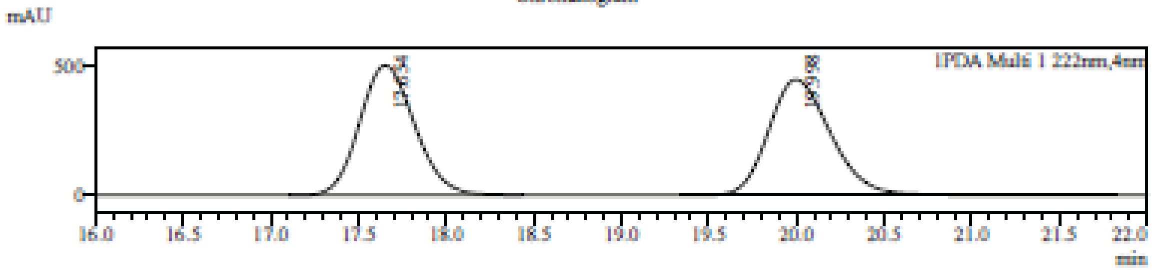


2-(benzo[b]thiophen-3-yl)-2,3-dihydrobenzofuran **2o**

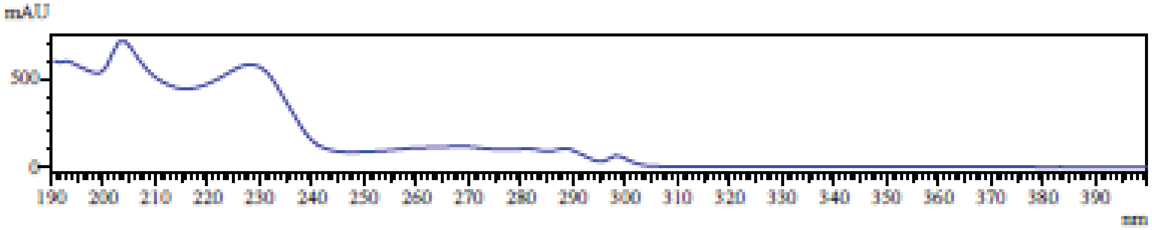
Sample Information

Sample Name	: XW-VI-19-ID-0.5%0.8mL
Sample ID	: XW-VI-19-ID-0.5%0.8mL
Data File	: XW-VI-19-ID-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

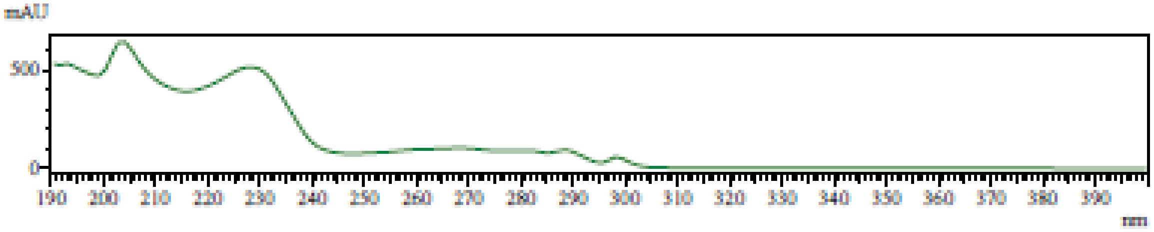
Chromatogram



UV Spectrum
Retention time = 17.654



UV Spectrum
Retention time = 19.998



Peak Table

PDA Ch1 222nm

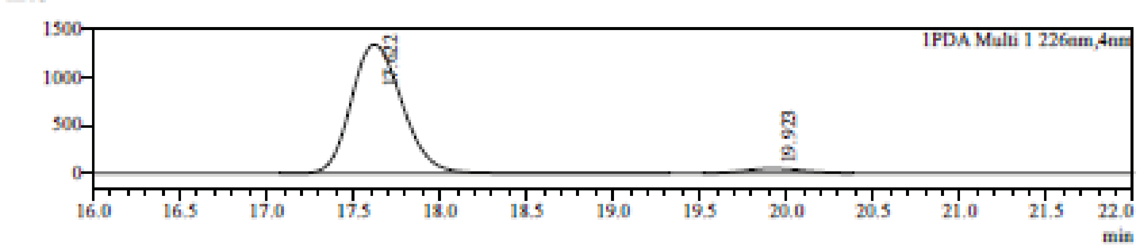
Peak#	Ret. Time	Area	Area%
1	17.654	10951793	49.749
2	19.998	11062129	50.251
Total		22013922	100.000

2-(benzo[b]thiophen-3-yl)-2,3-dihydrobenzofuran **2o**

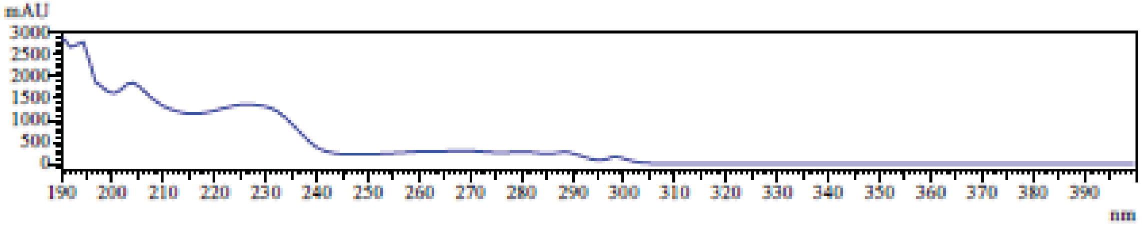
Sample Information

Sample Name : XW-VI-20-ID-0.5%0.8mL-2
Sample ID : XW-VI-20-ID-0.5%0.8mL-2
Data File : XW-VI-20-ID-0.5%0.8mL-2.lcd
Method File : XW-0.5%-0.8ml.lcm

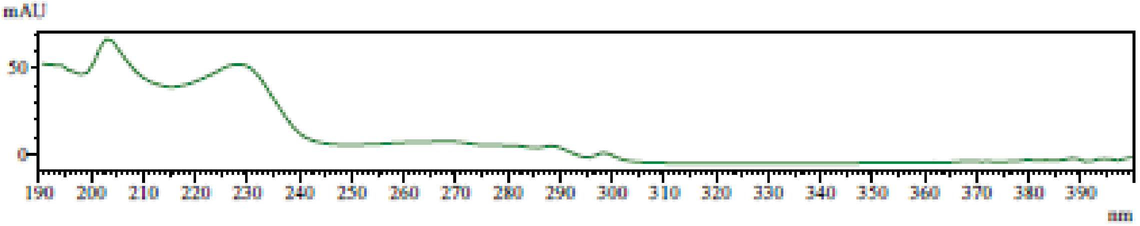
Chromatogram



UV Spectrum
Retention time = 17.622



UV Spectrum
Retention time = 19.923

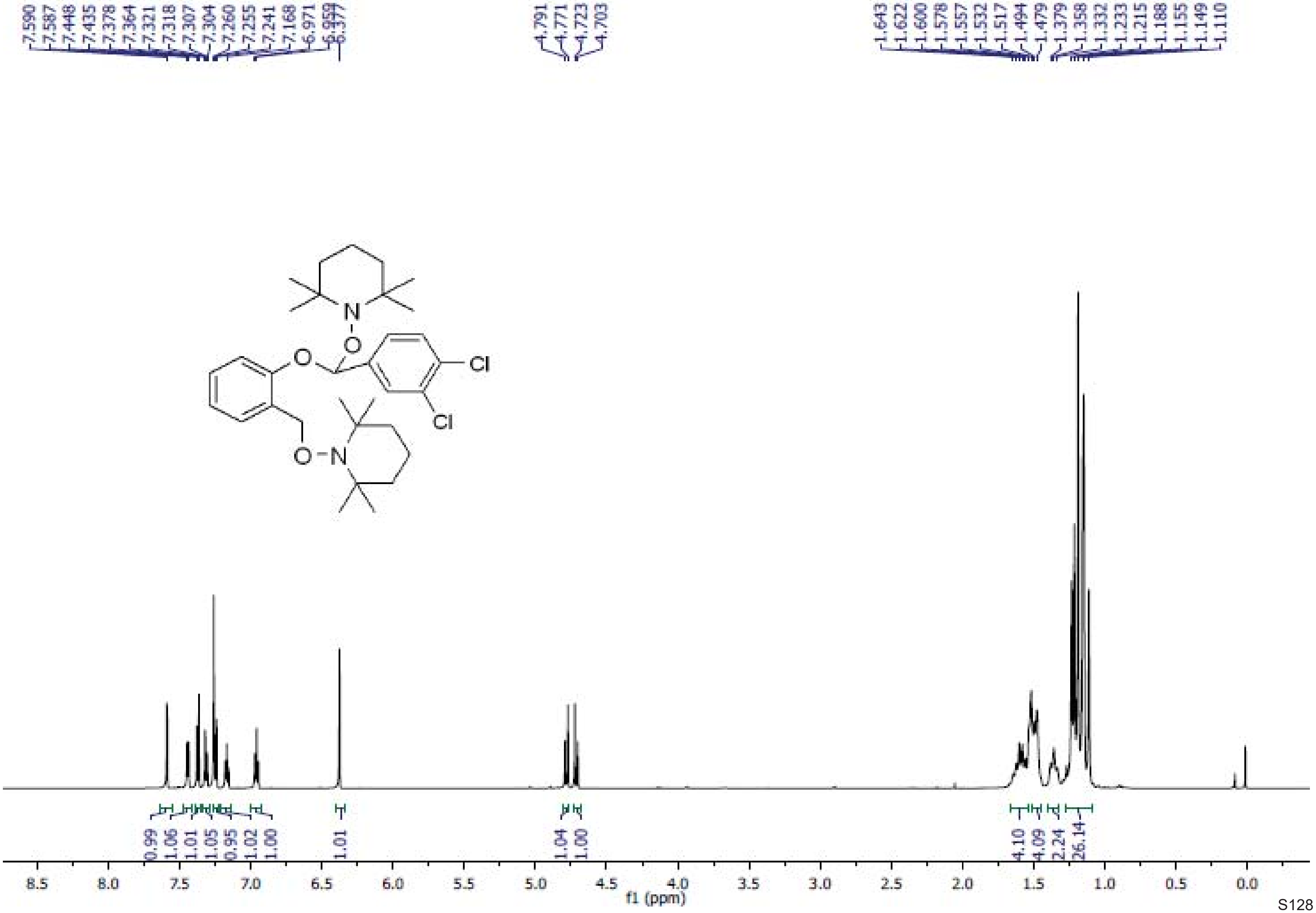


Peak Table

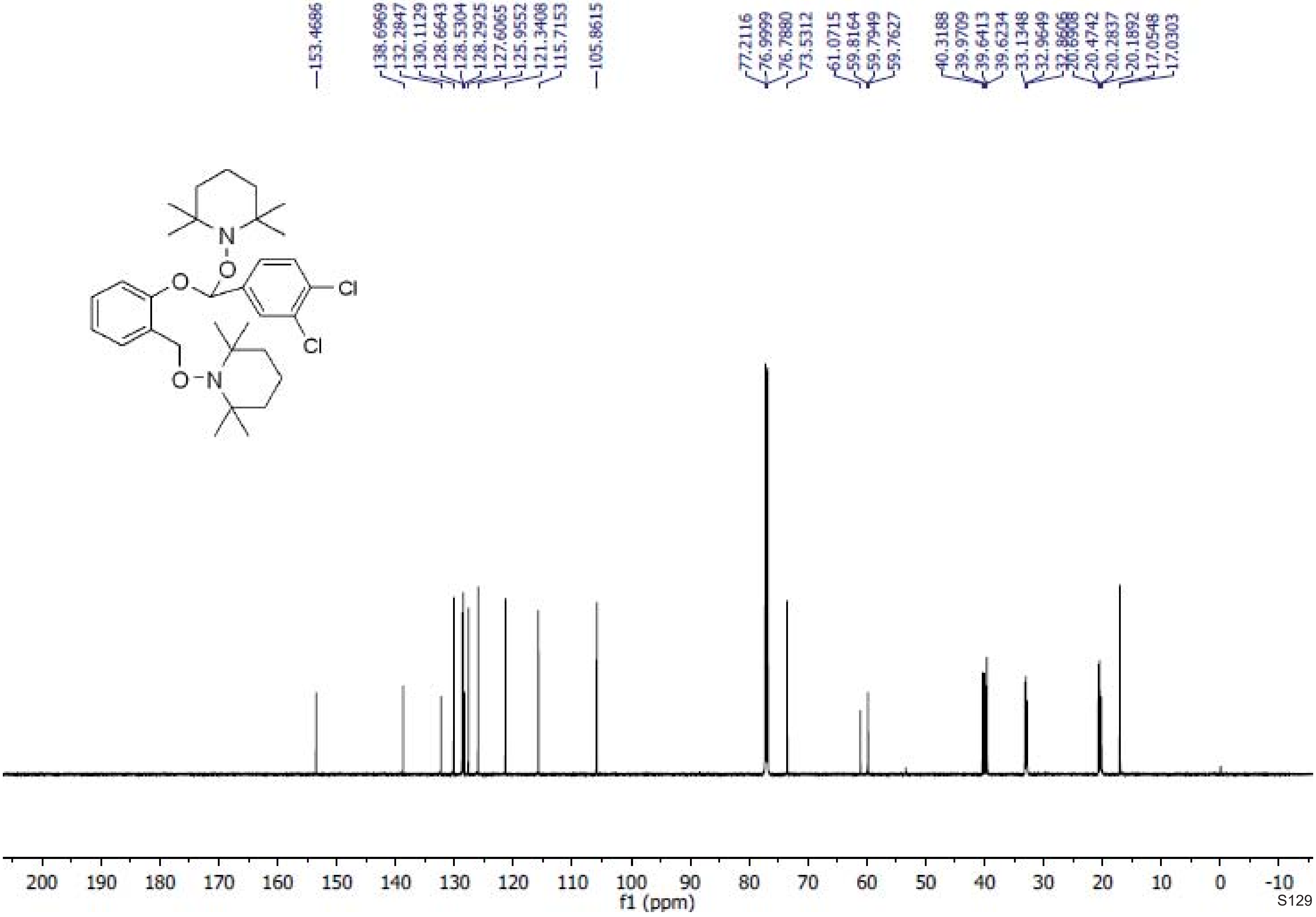
PDA Ch1 226nm

Peak#	Ret. Time	Area	Area%
1	17.622	27426213	96.214
2	19.923	1079194	3.786
Total		28505407	100.000

2,2,6,6-tetramethyl-1-((2-(phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methoxy)benzyl)oxy)piperidine **3d**



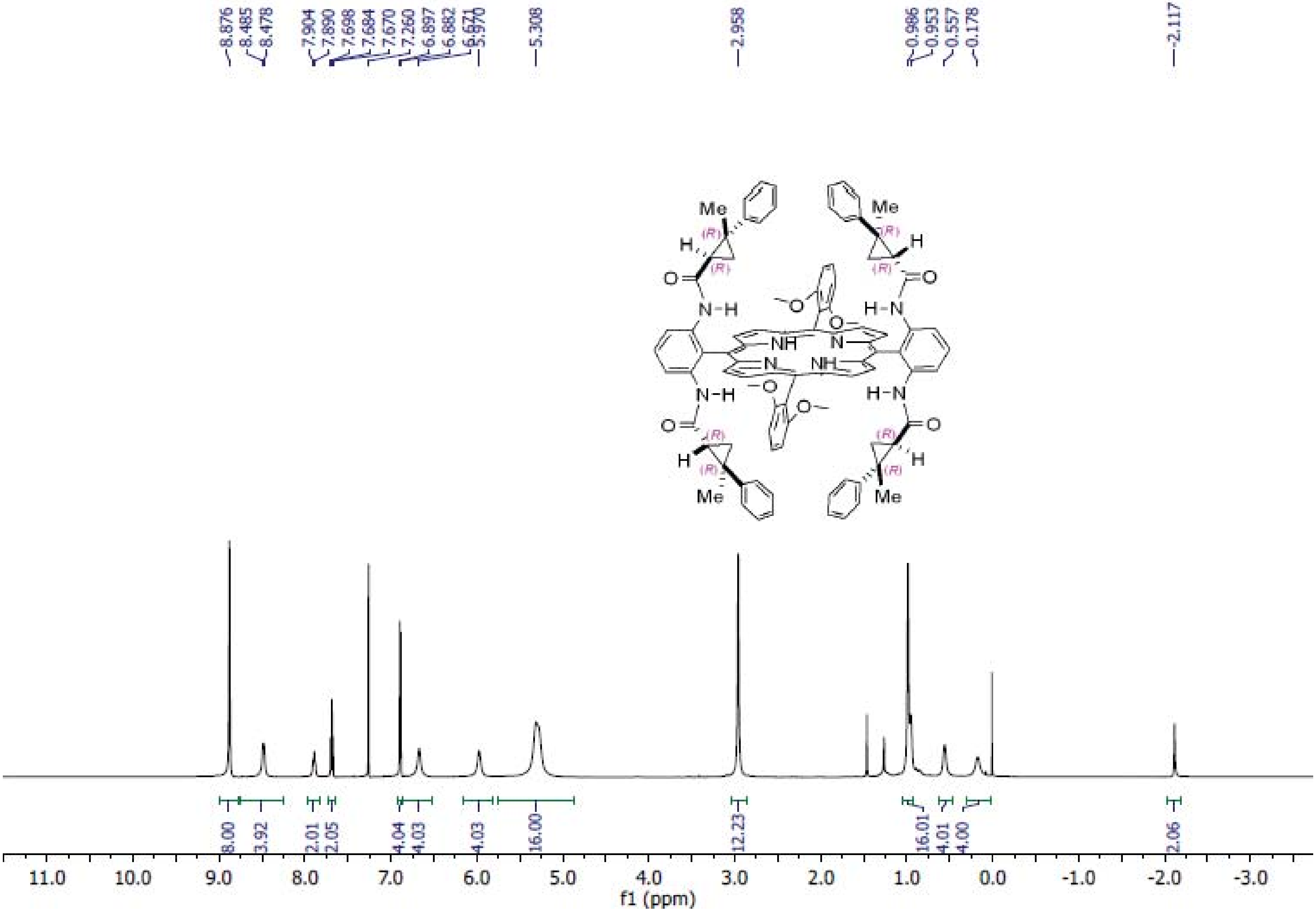
2,2,6,6-tetramethyl-1-((2-(phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methoxy)benzyl)oxy)piperidine **3d**



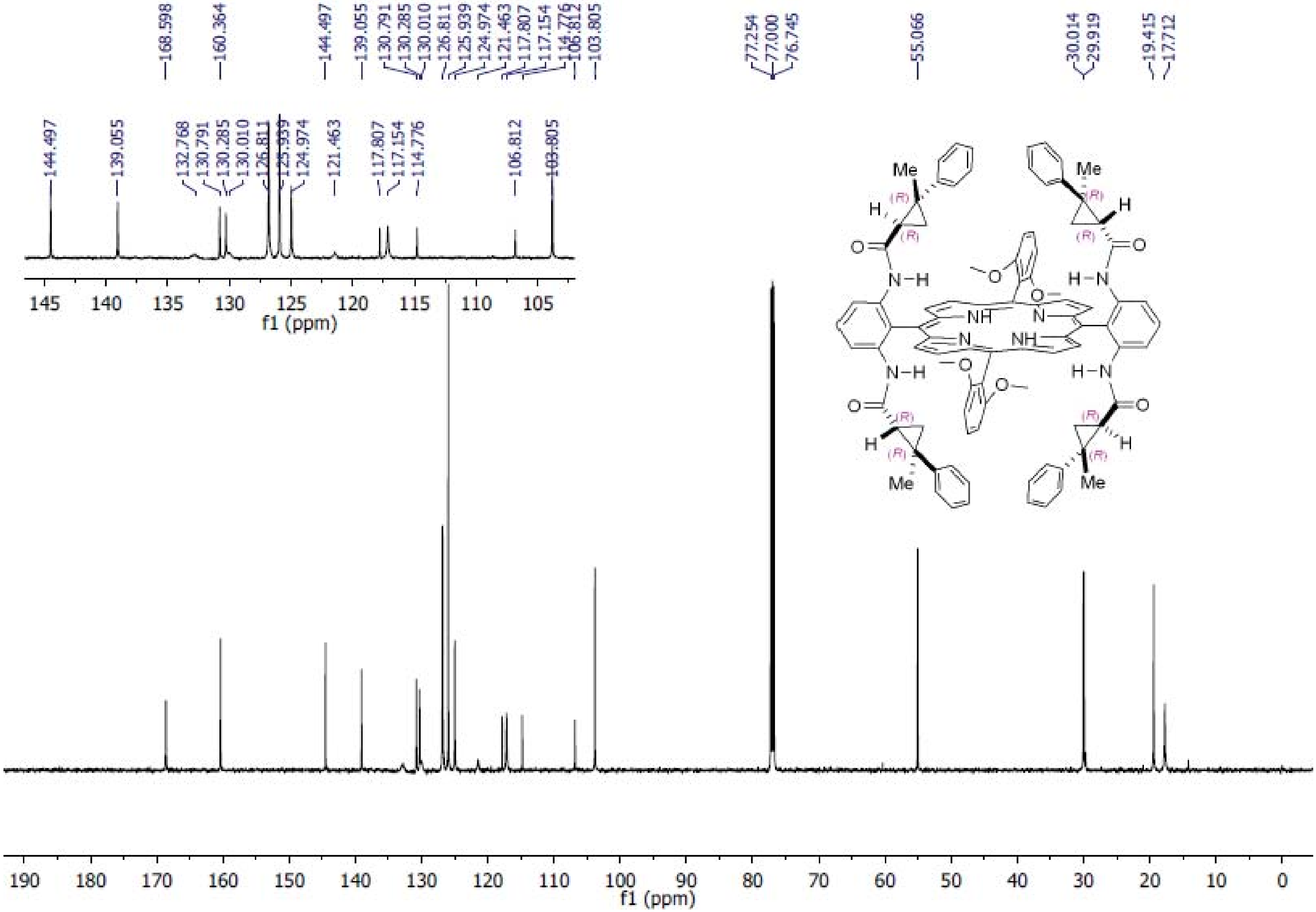
Spectral Data for Chapter 3

Enantioselective Radical Process for Synthesis of Chiral Indolines by Co(II)-Based Metalloradical Alkylation of Diverse C(sp^3)–H Bonds

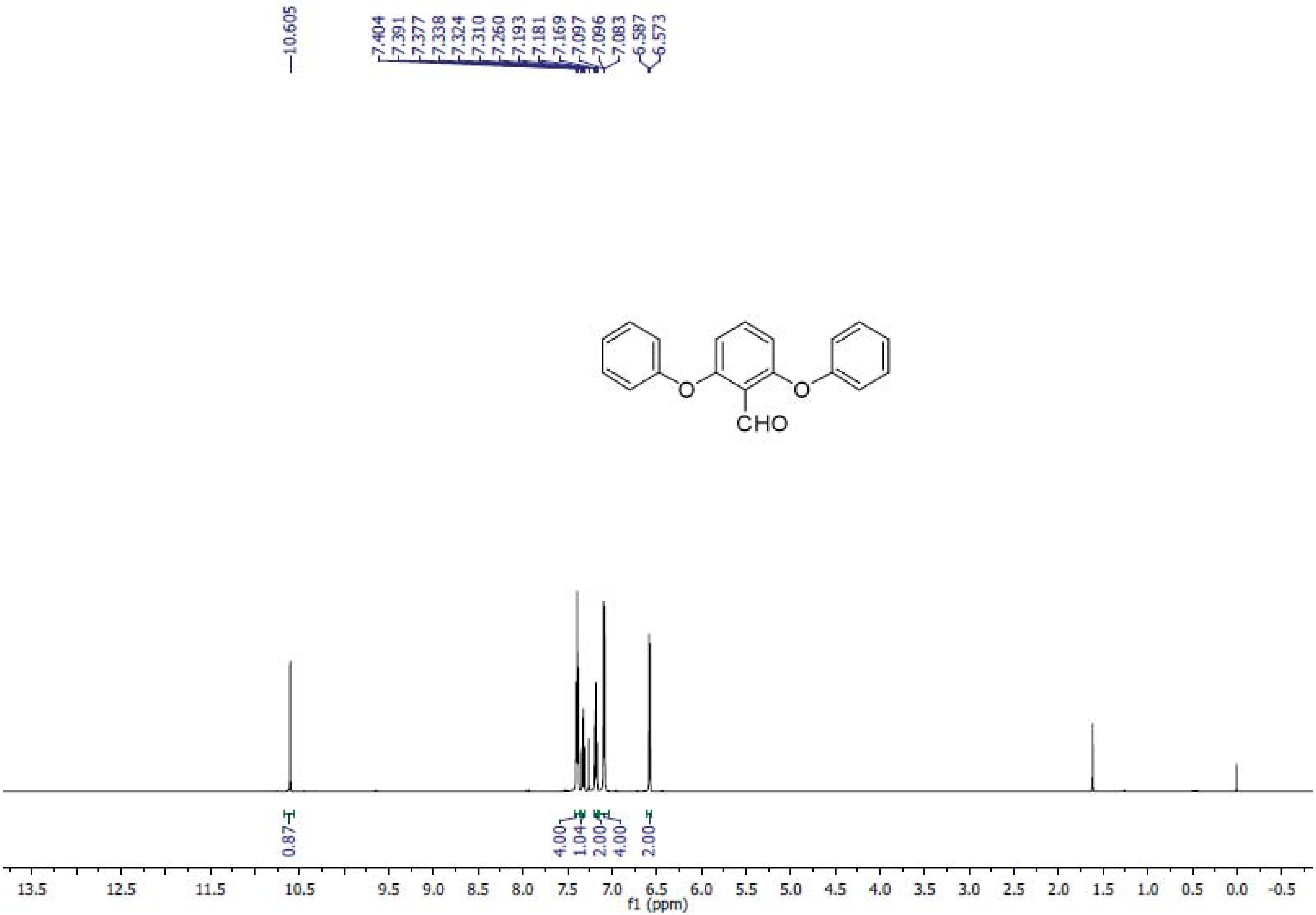
$[H_2(2,6\text{-DiMeO-QingPhyrin})]$ ($[H_2(P5)]$)



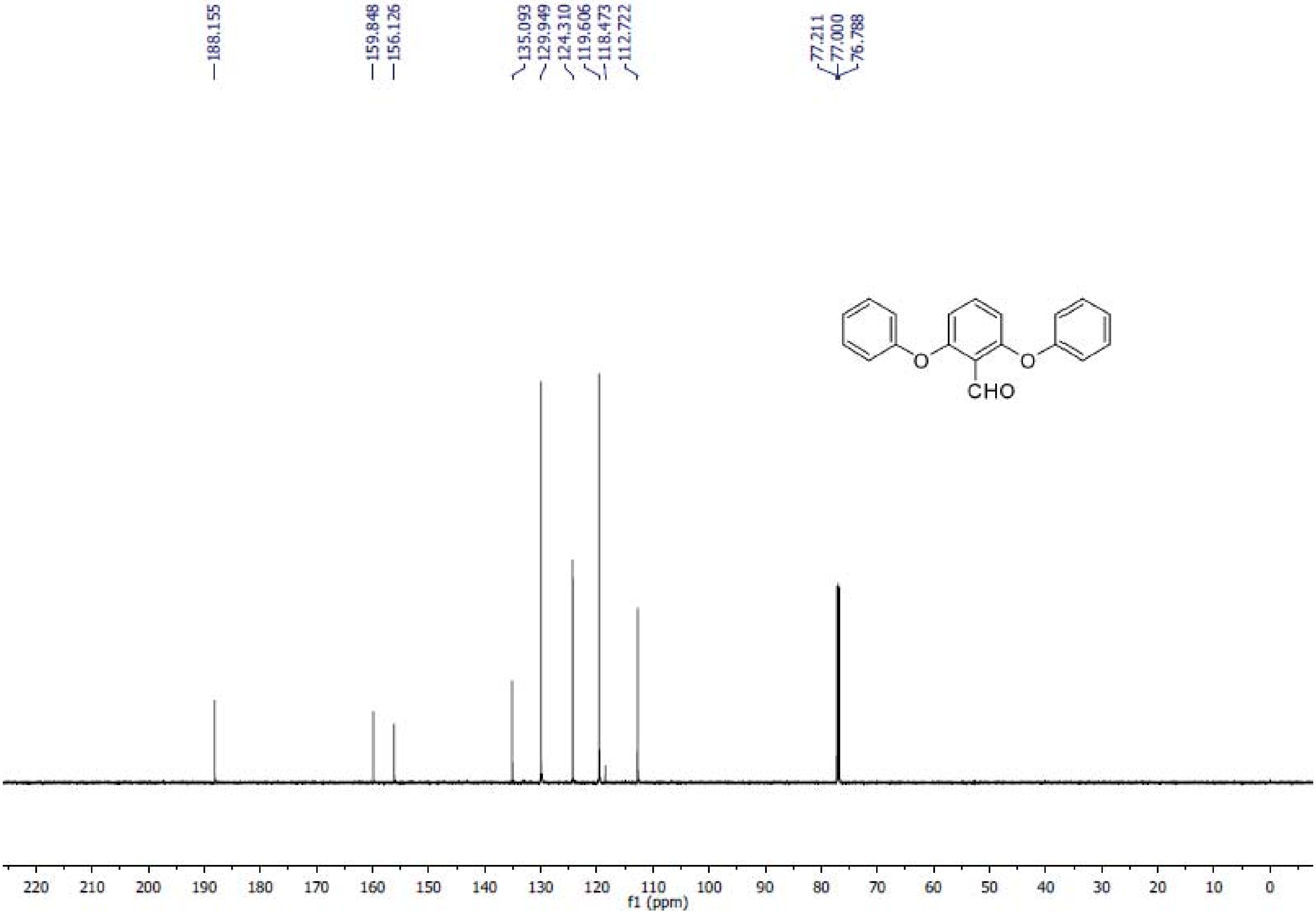
[H$_2$(2,6-DiMeO-QingPhyrin)] ([H$_2$(P5)])



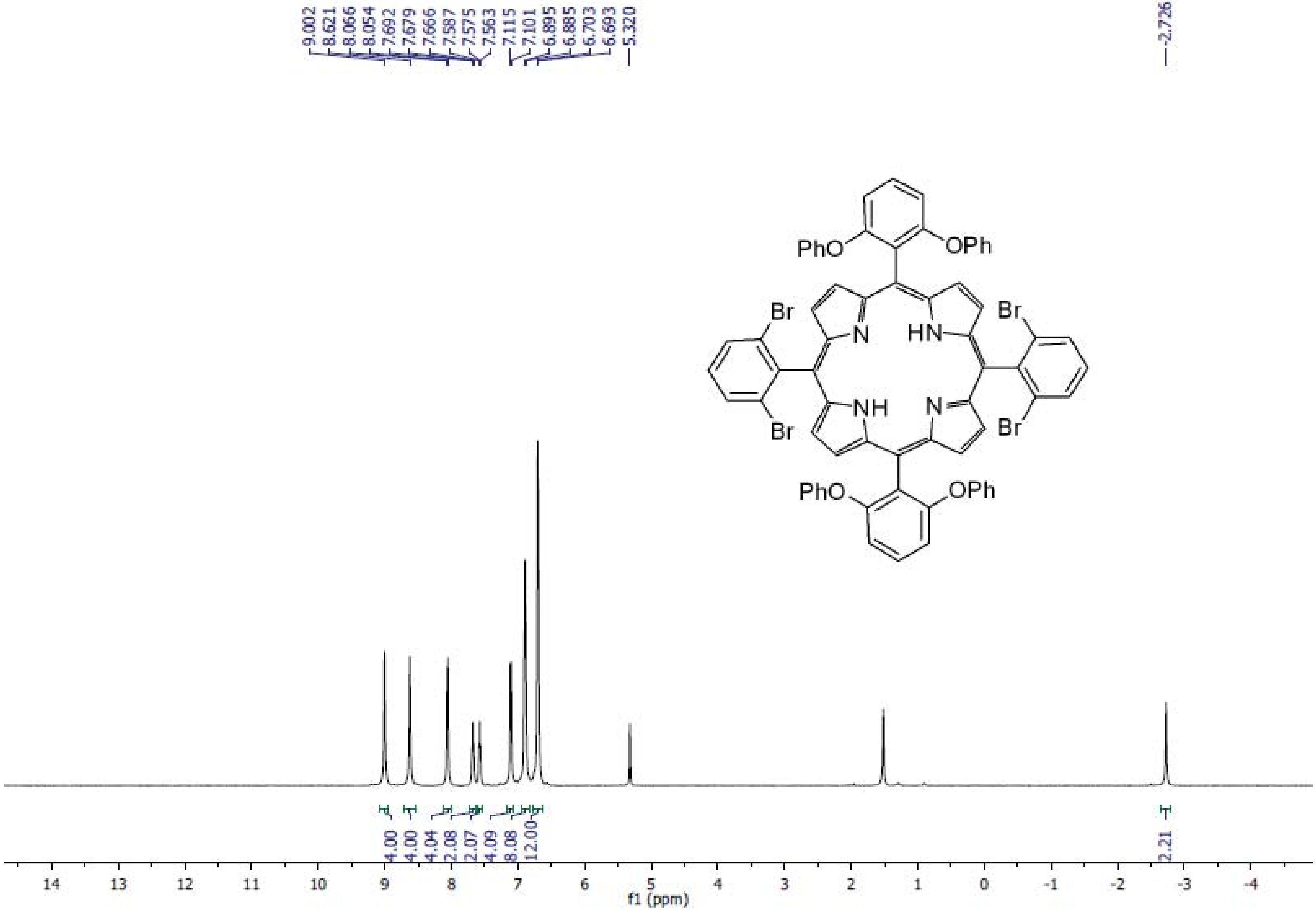
2,6-diphenoxybenzaldehyde



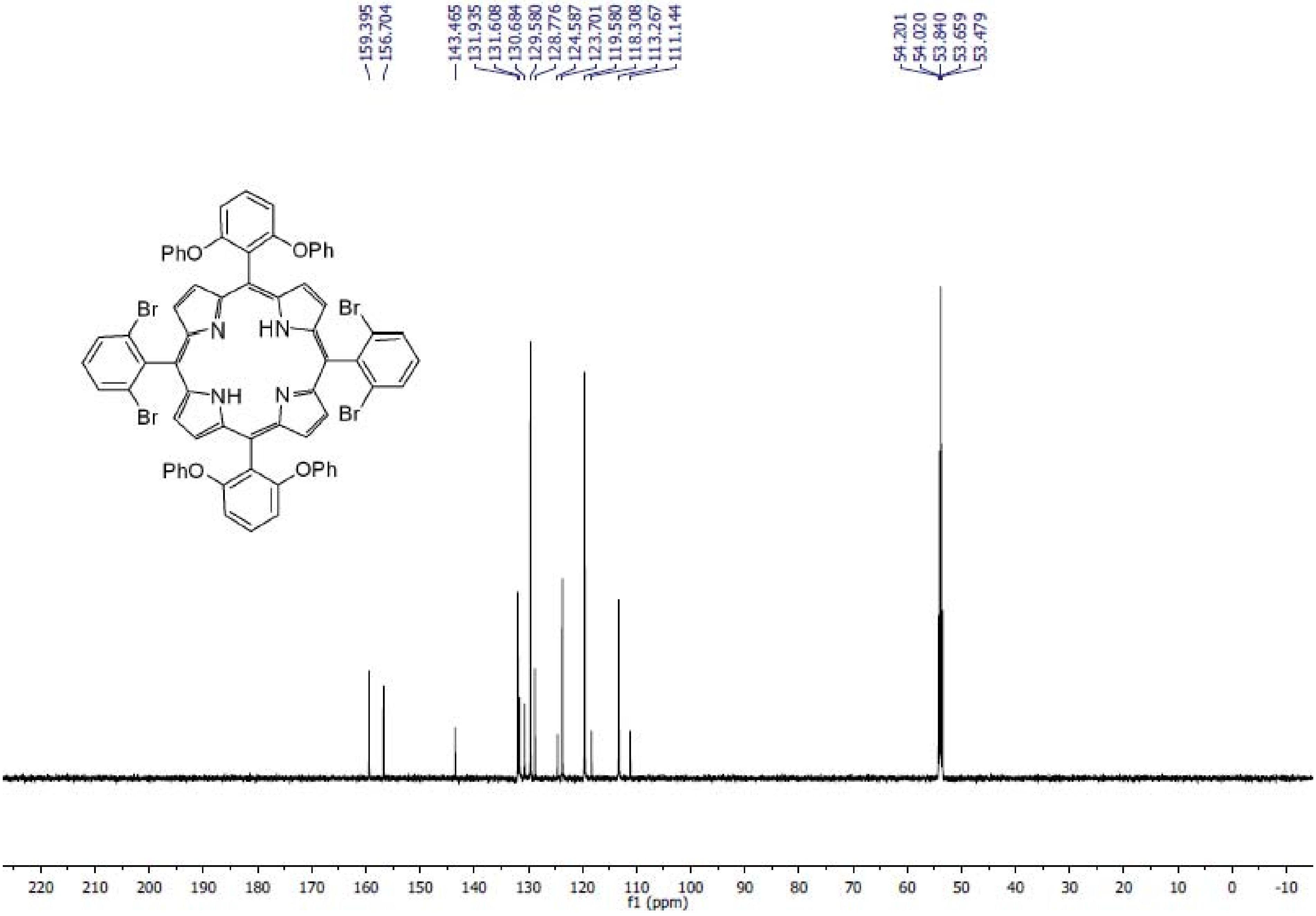
2,6-diphenoxybenzaldehyde



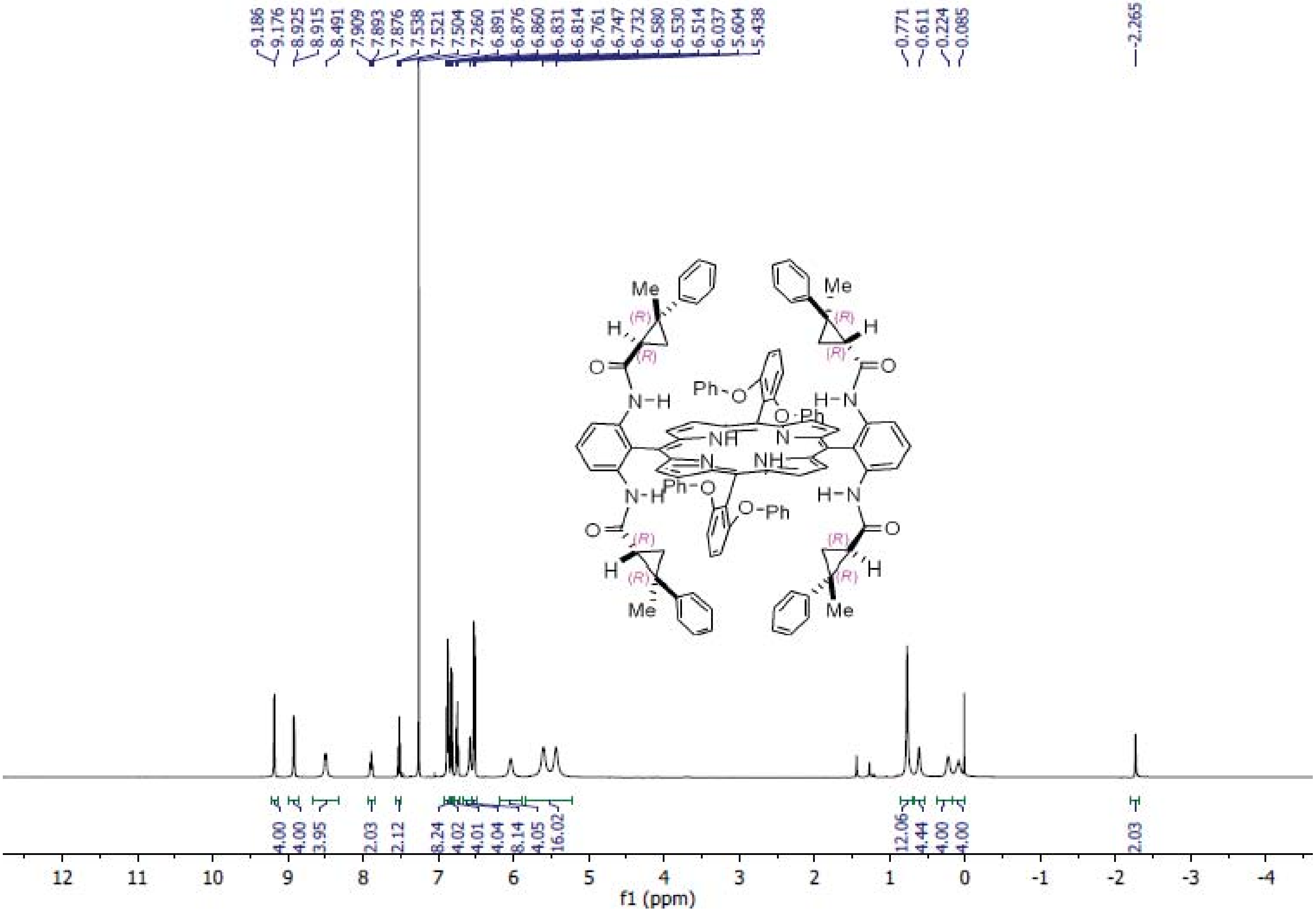
5,15-bis(2,6-dibromophenyl)-10,20-bis(2,6-diphenoxyphenyl)porphyrin in CD_2Cl_2



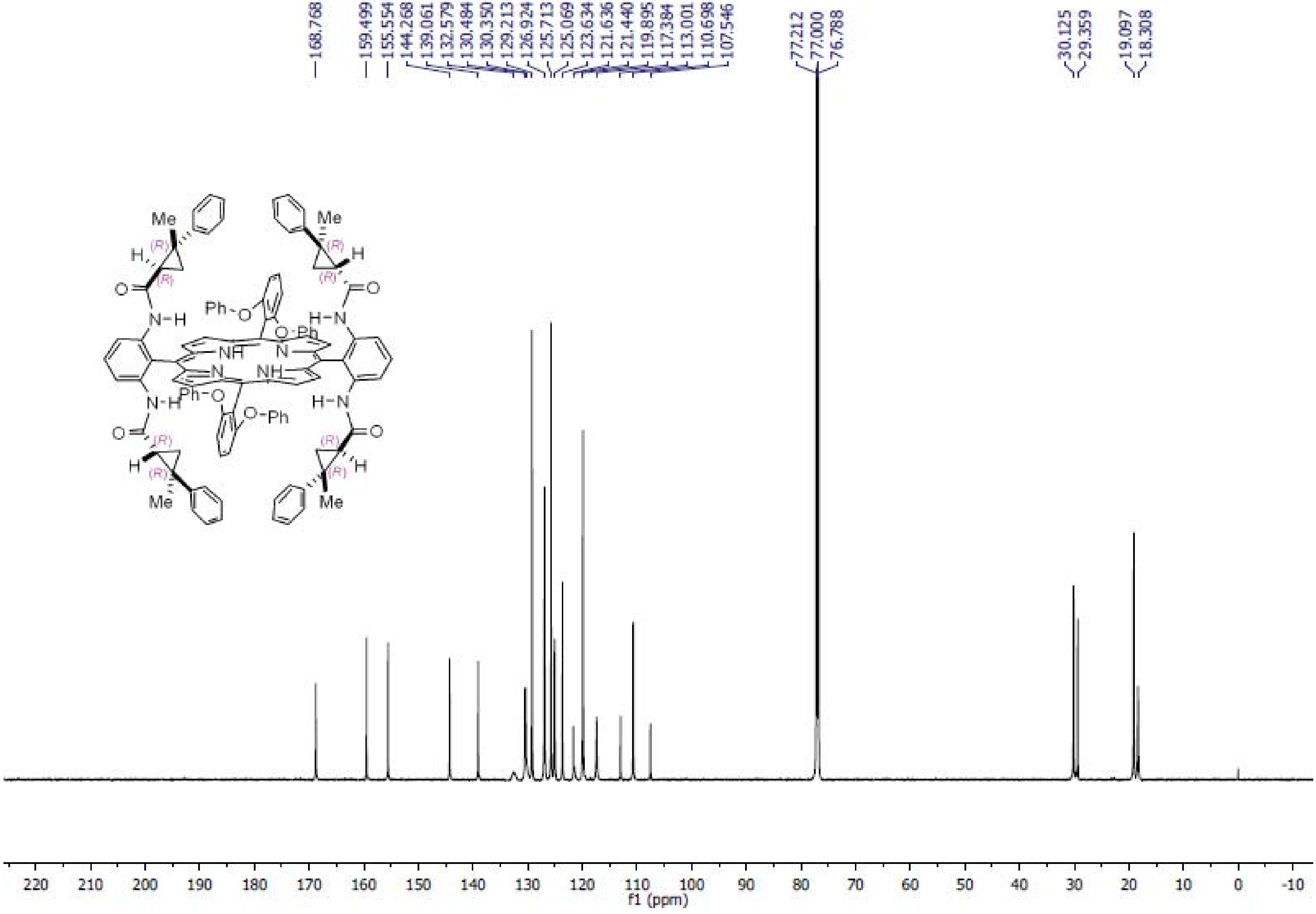
5,15-bis(2,6-dibromophenyl)-10,20-bis(2,6-diphenoxyphenyl)porphyrin in CD_2Cl_2



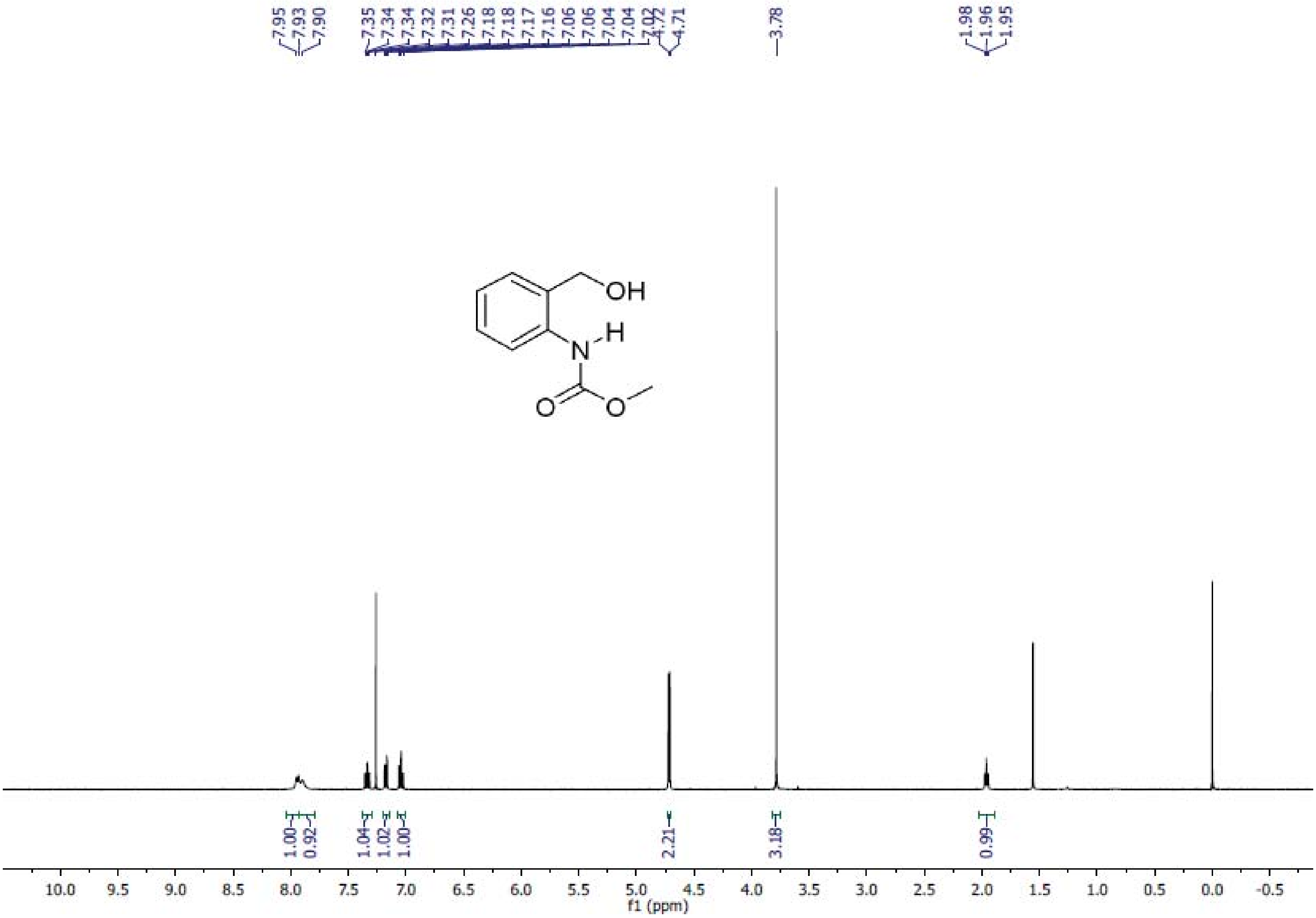
[H_2(2,6-DiPhO-QingPhyrin)] ([H_2(P6)])



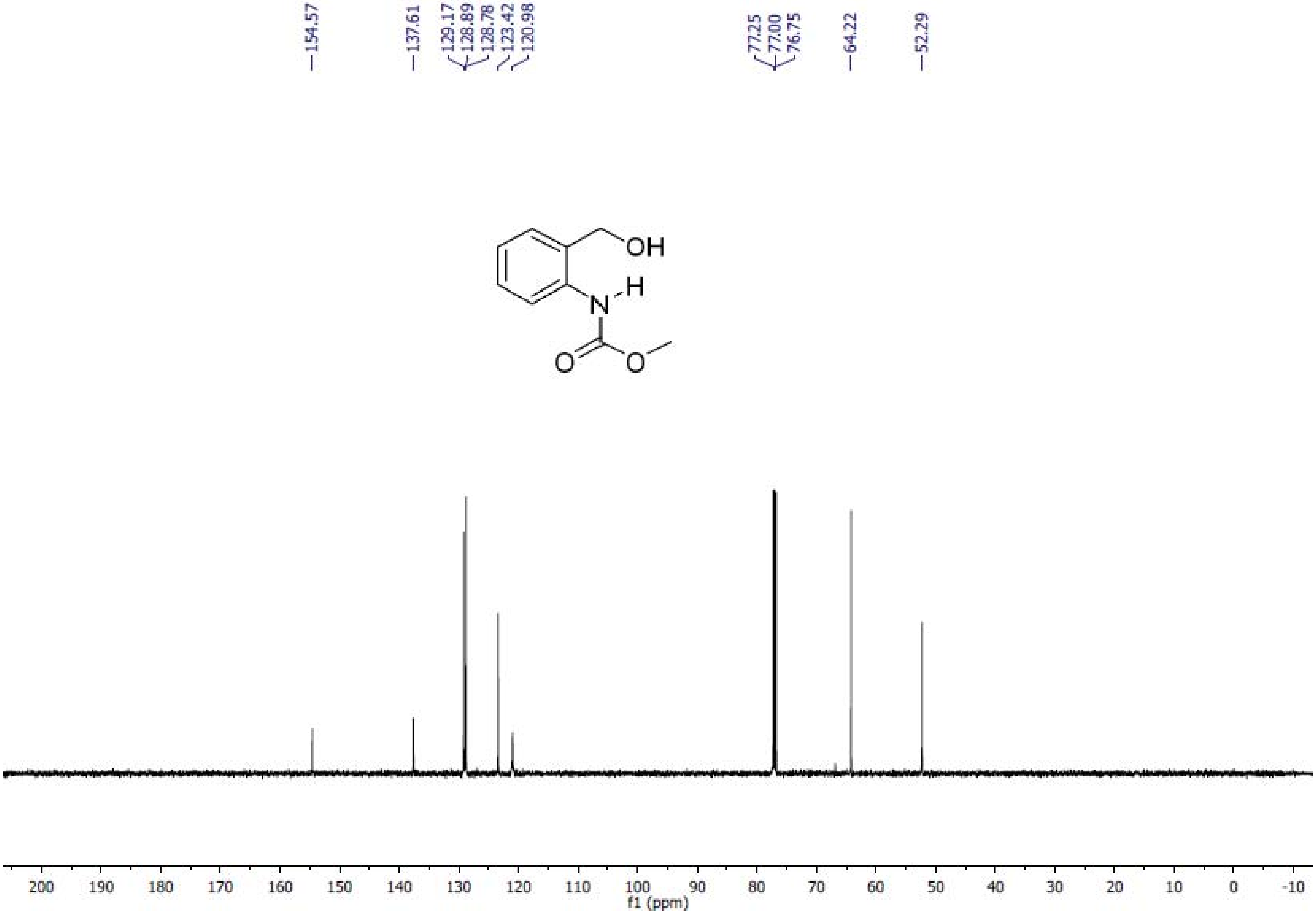
[H_2(2,6-DiPhO-QingPhyrin)] ([H_2(P6)])



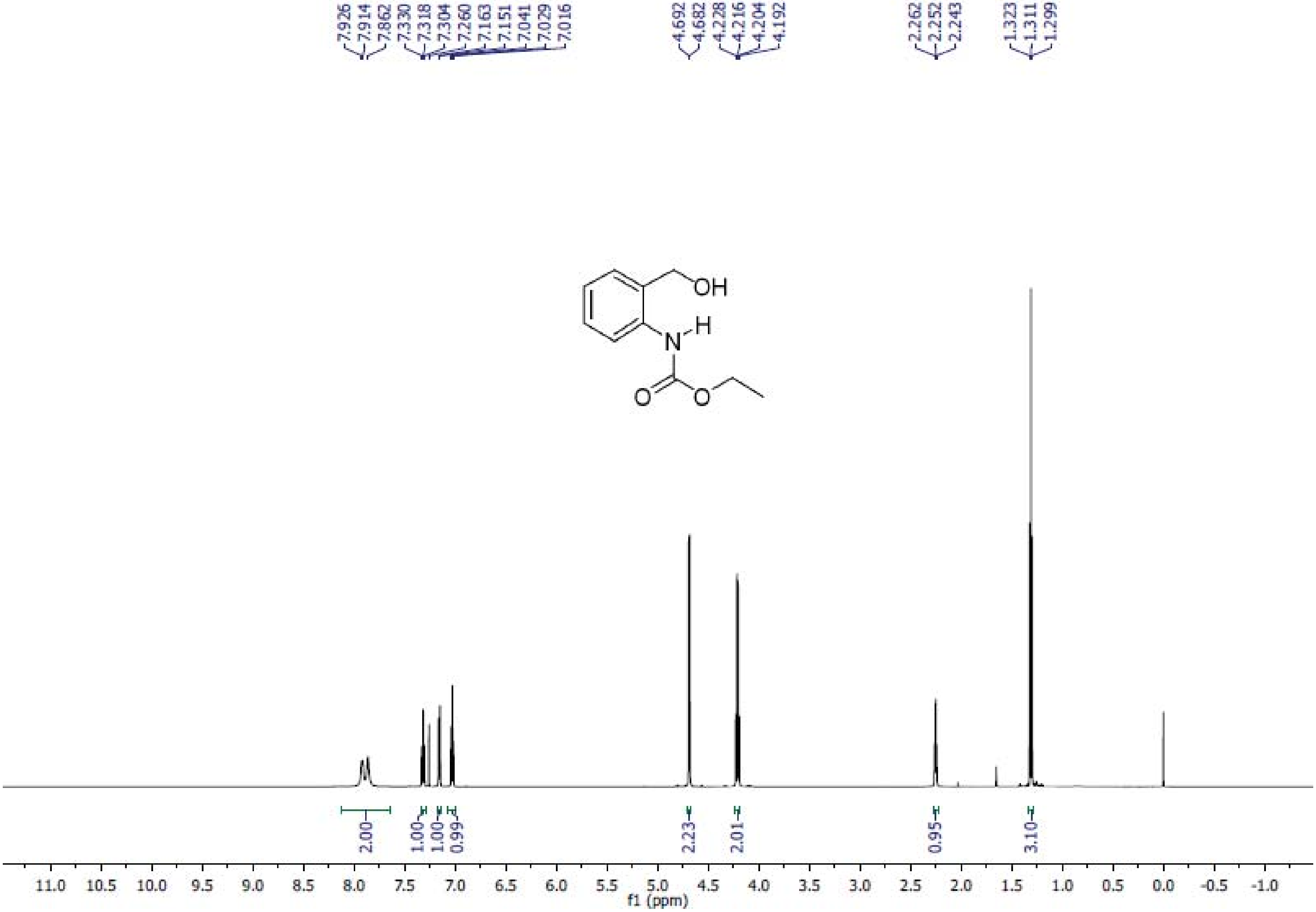
methyl (2-(hydroxymethyl)phenyl)carbamate s1-a



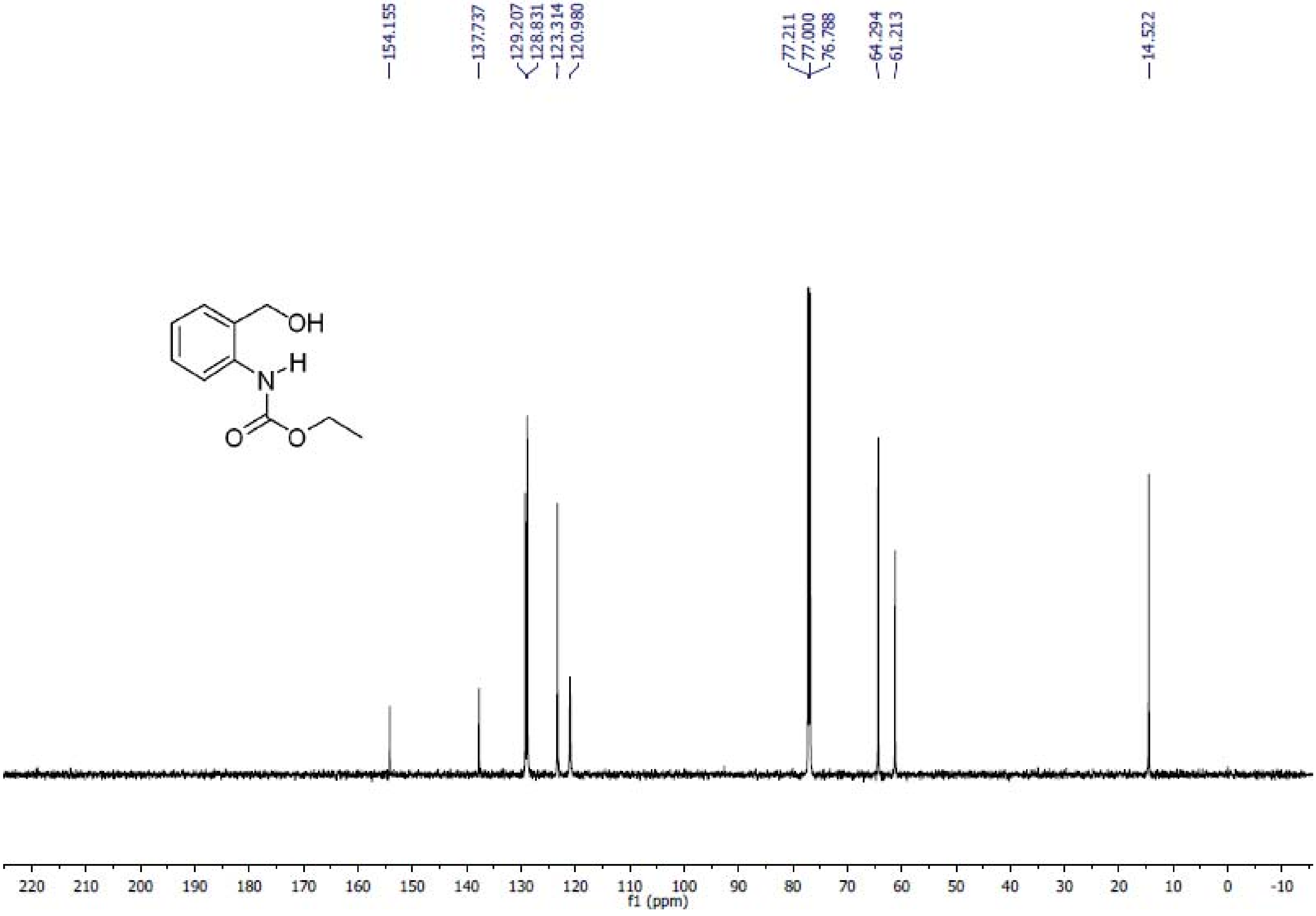
methyl (2-(hydroxymethyl)phenyl)carbamate s1-a



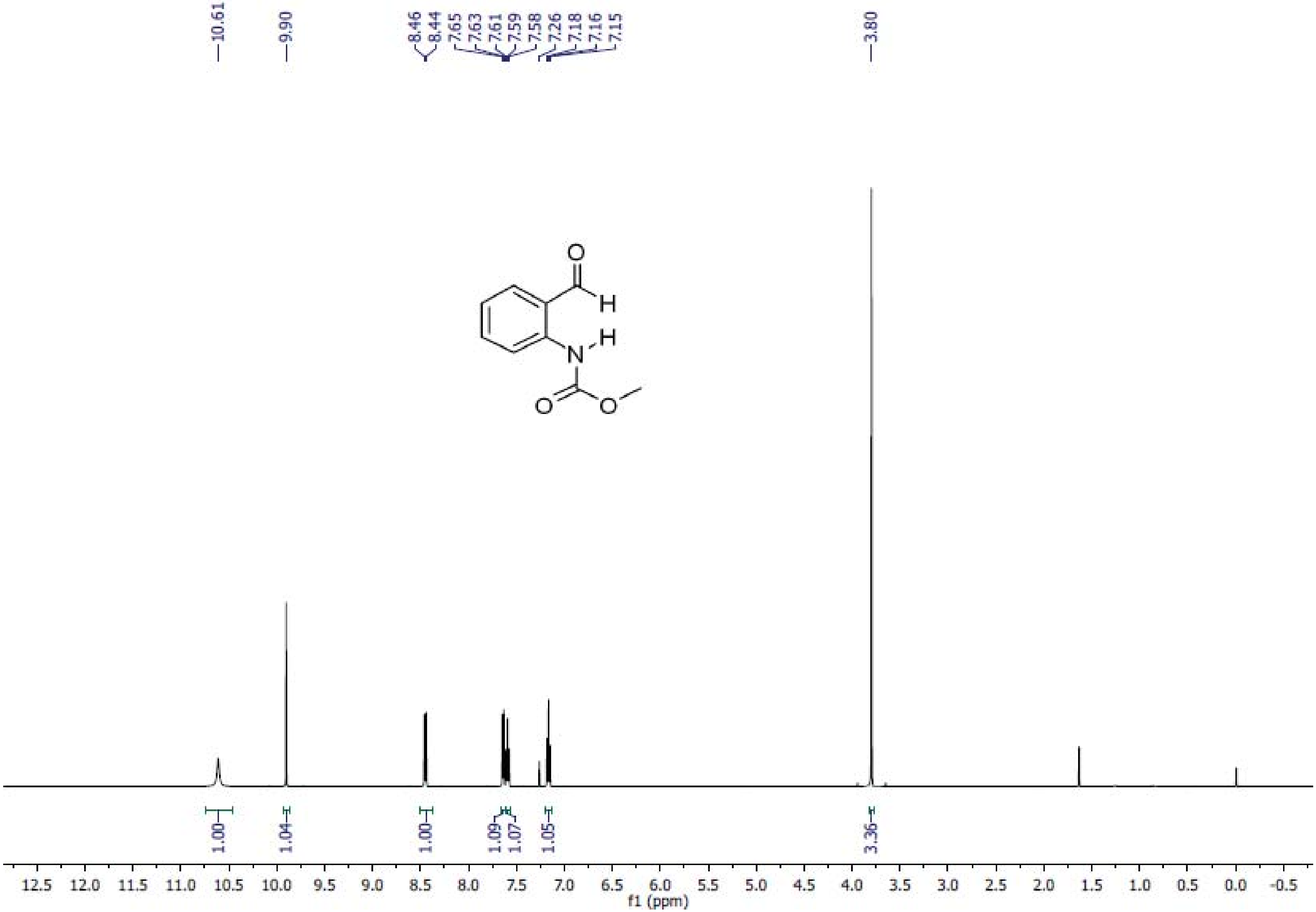
ethyl (2-(hydroxymethyl)phenyl)carbamate s1-b



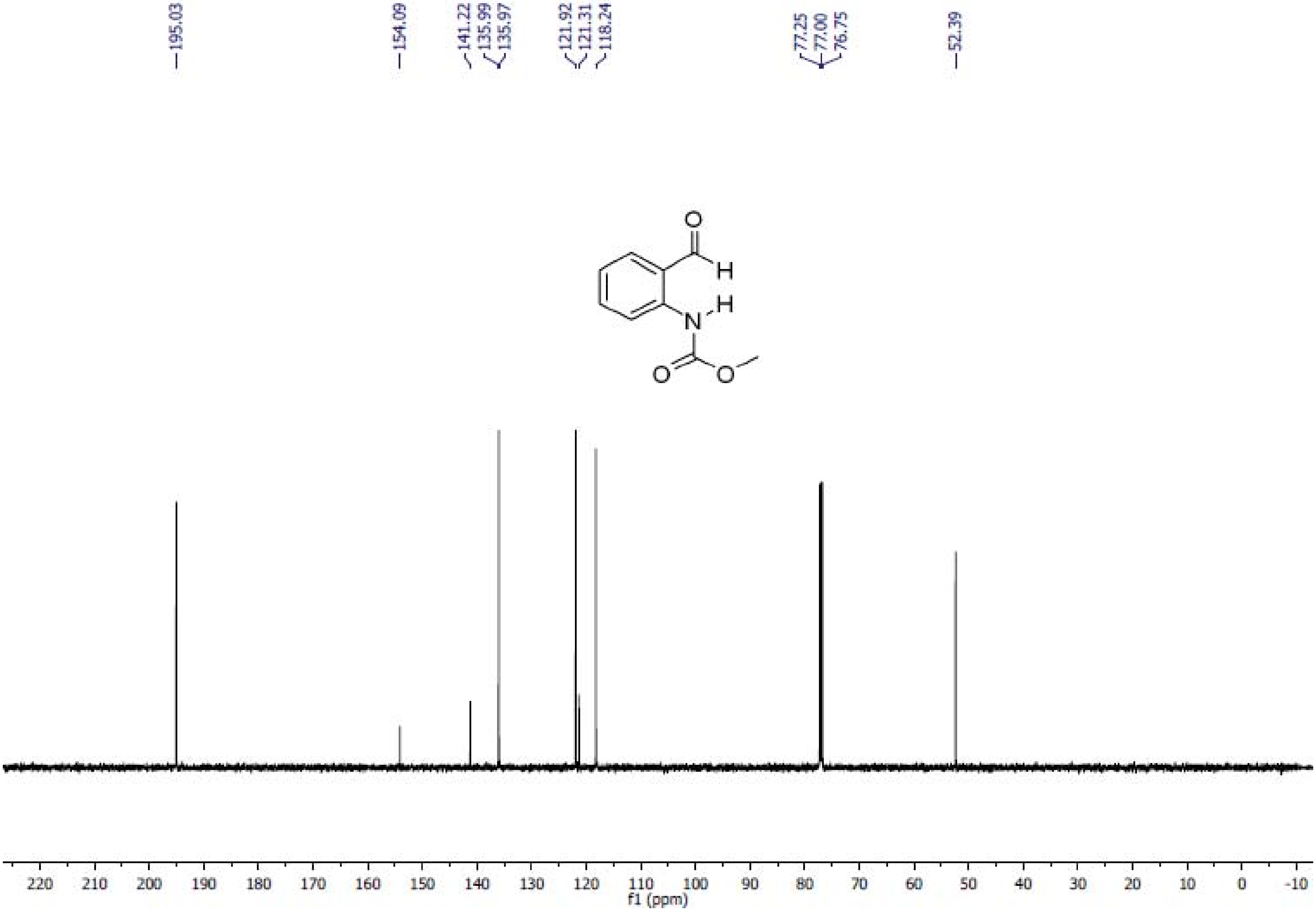
ethyl (2-(hydroxymethyl)phenyl)carbamate s1-b



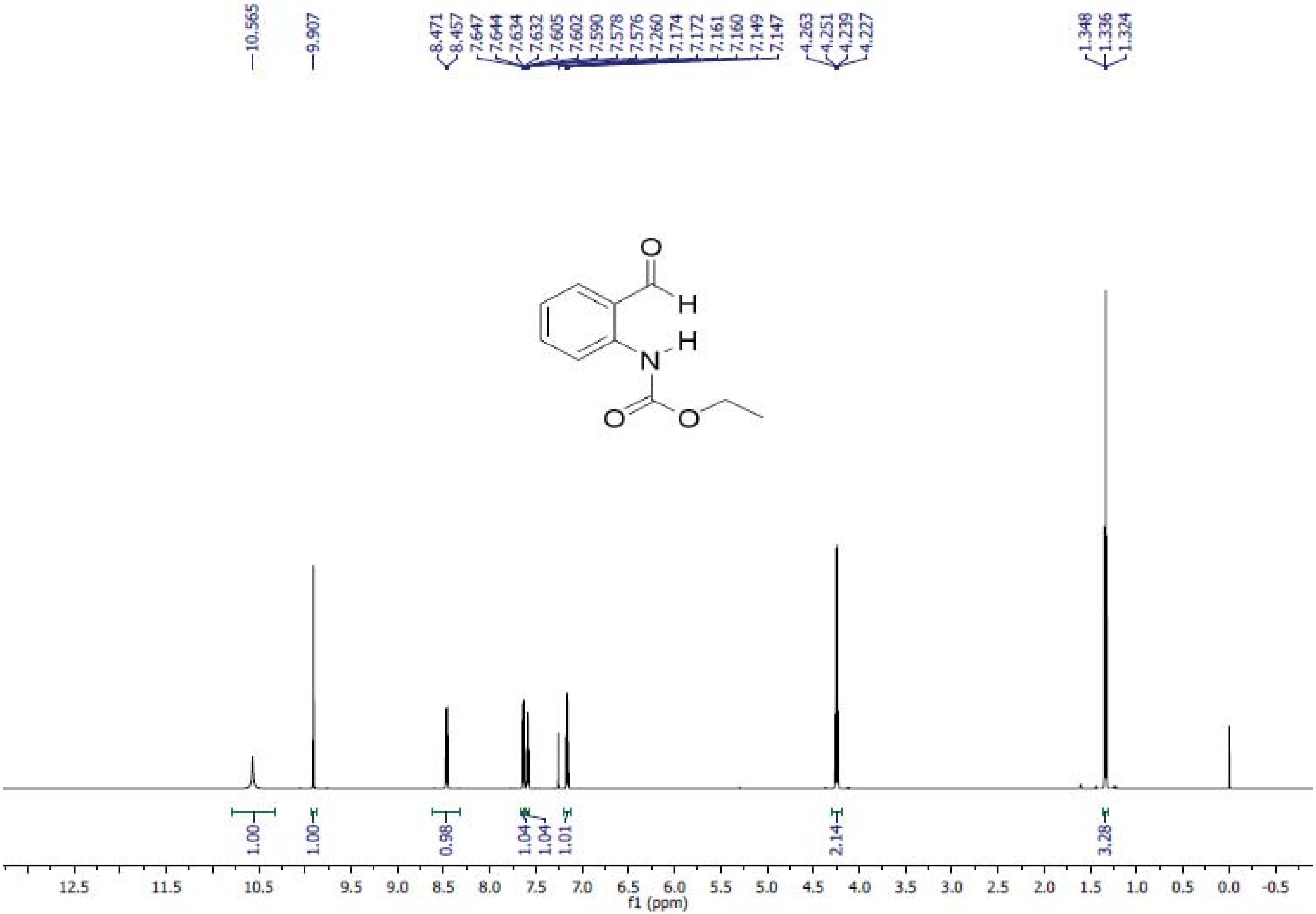
methyl (2-formylphenyl)carbamate s2-a



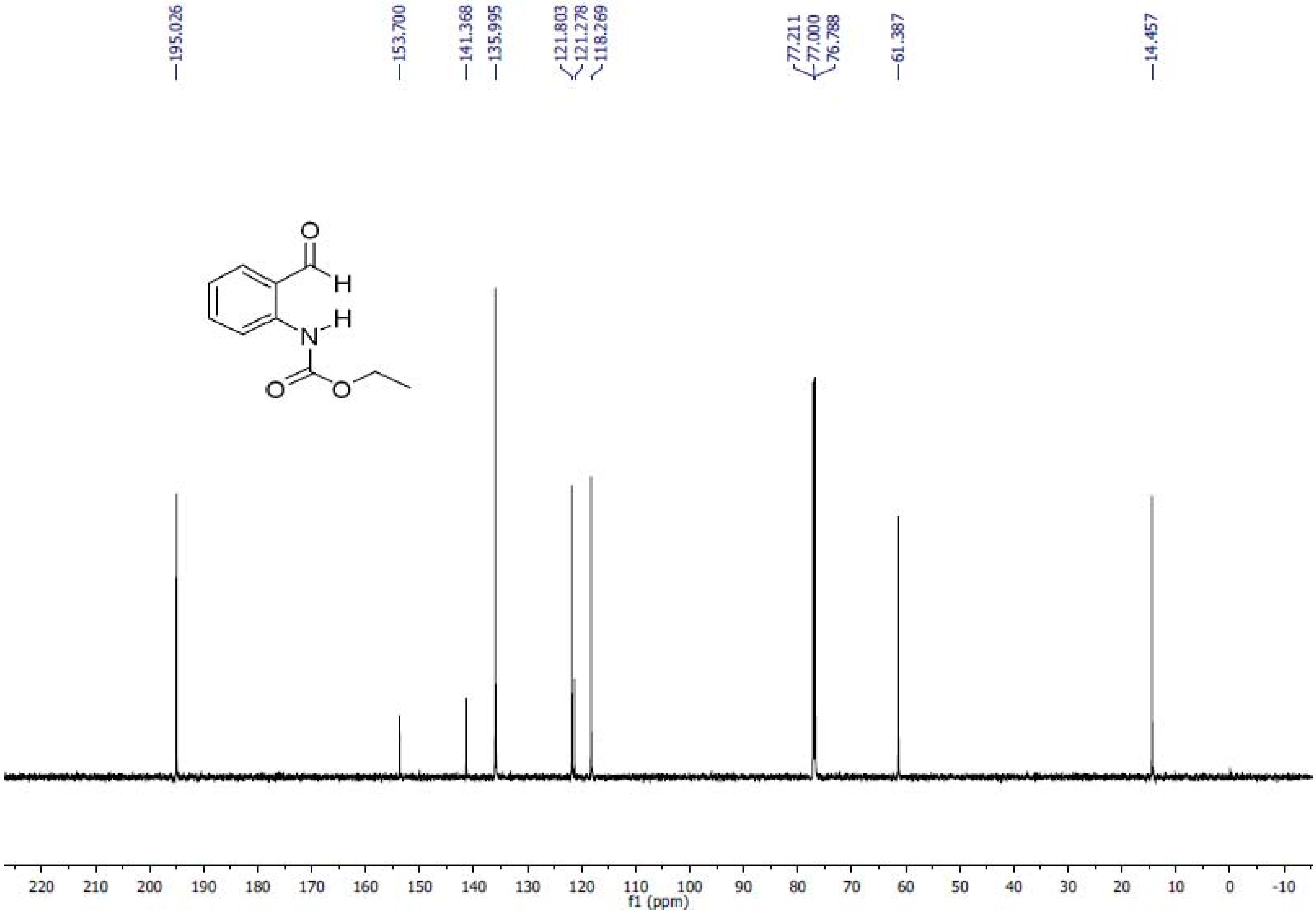
methyl (2-formylphenyl)carbamate s2-a



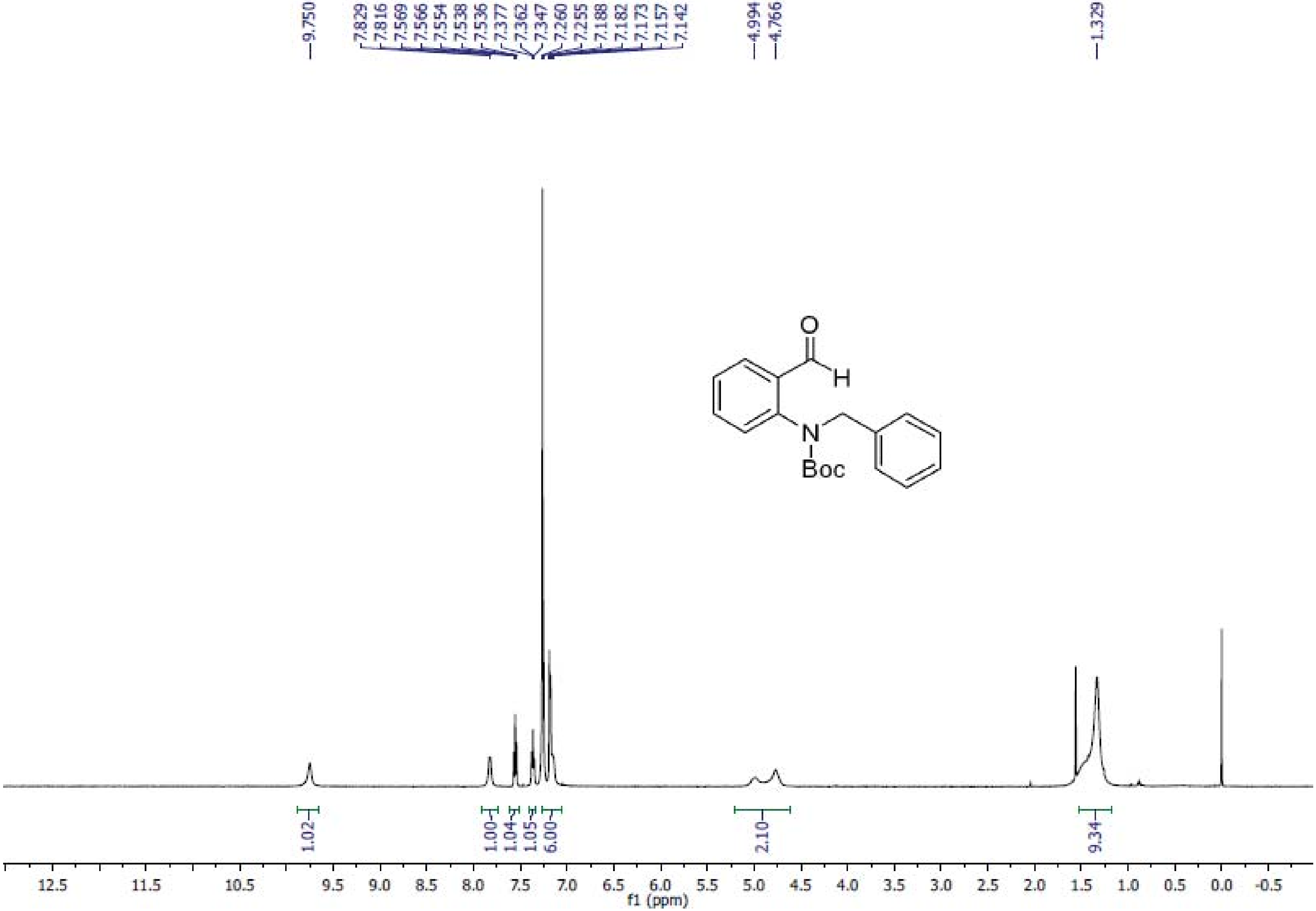
ethyl (2-formylphenyl)carbamate s2-b



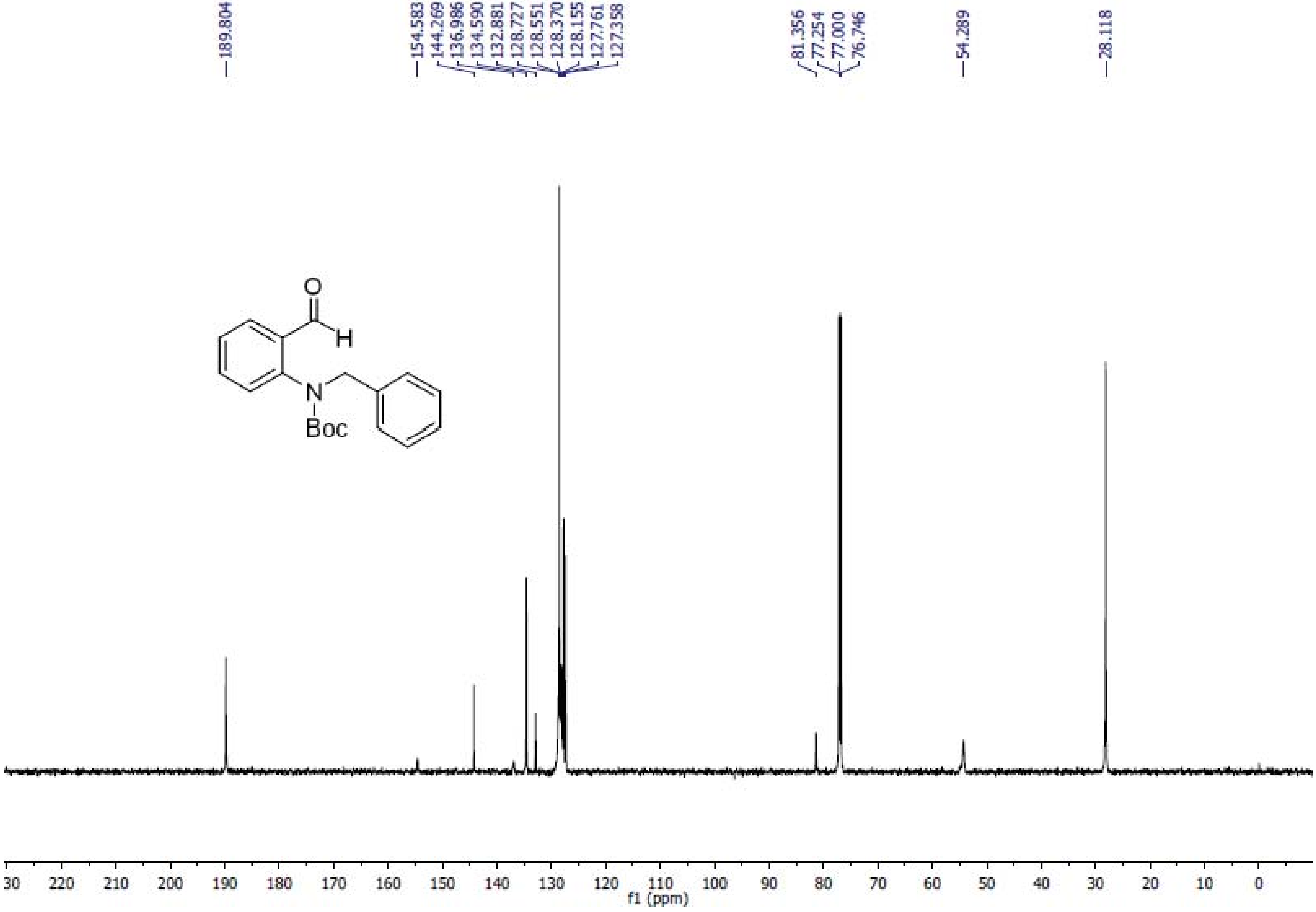
ethyl (2-formylphenyl)carbamate s2-b



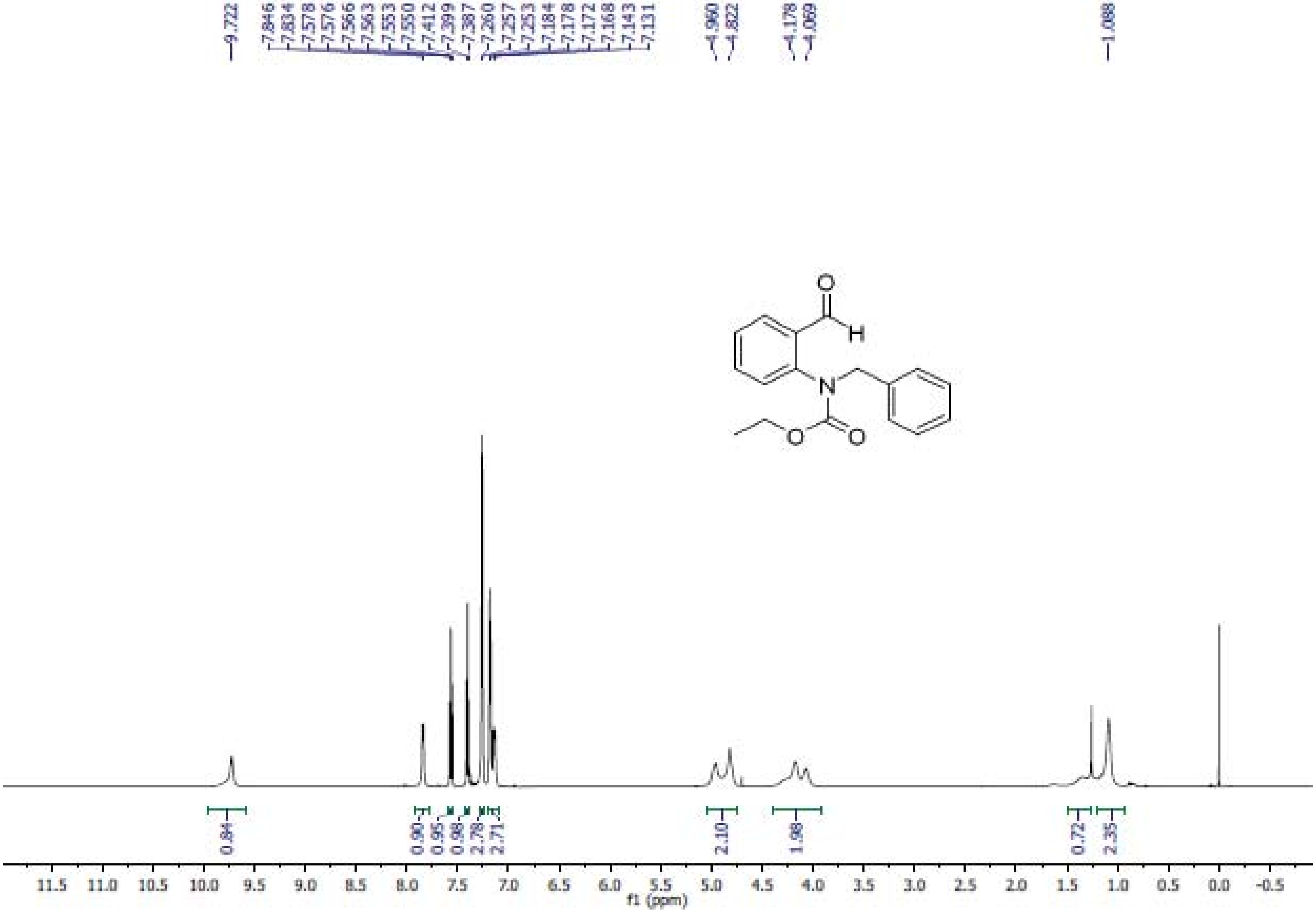
tert-butyl benzyl(2-formylphenyl)carbamate s3-a



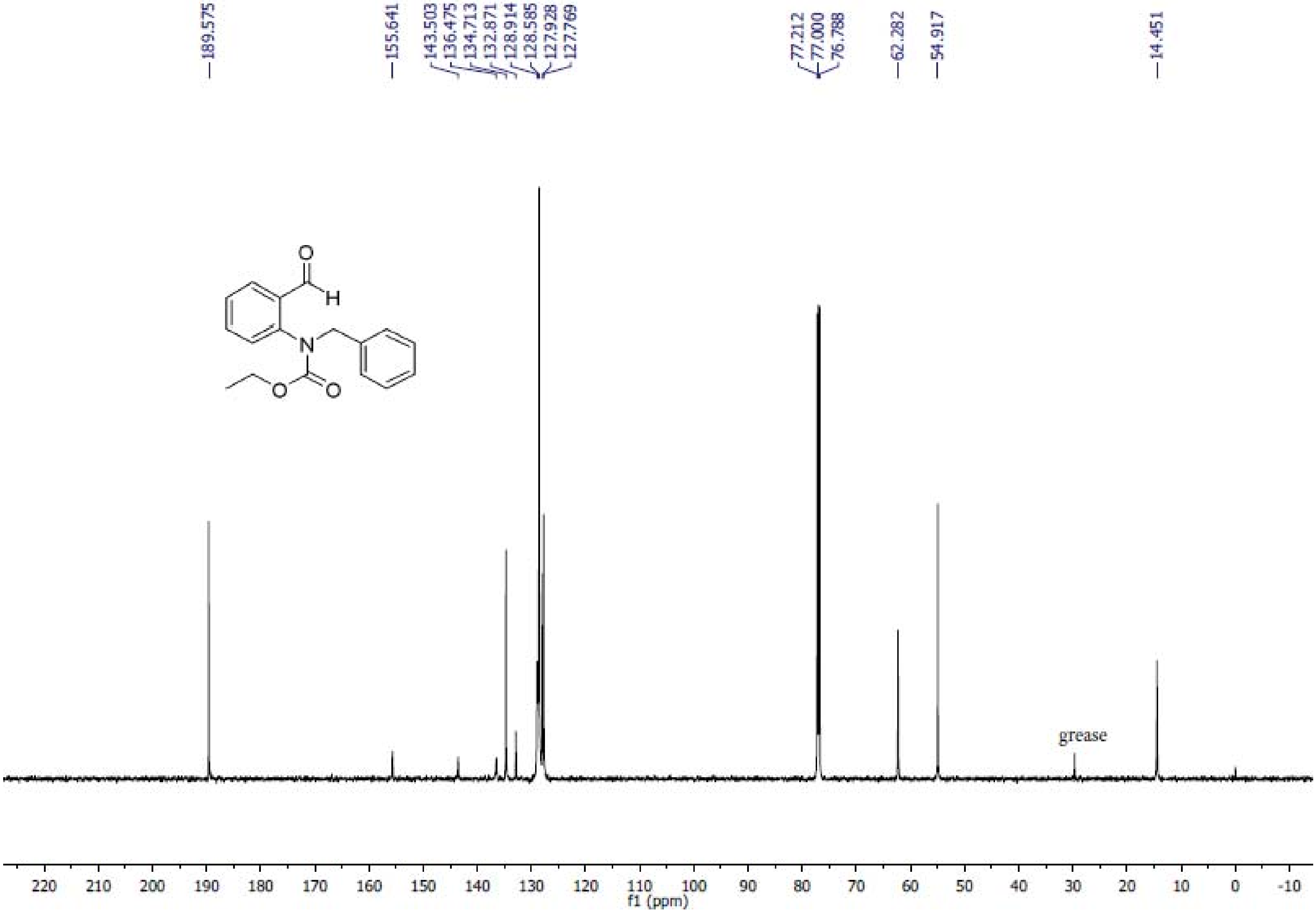
tert-butyl benzyl(2-formylphenyl)carbamate s3-a



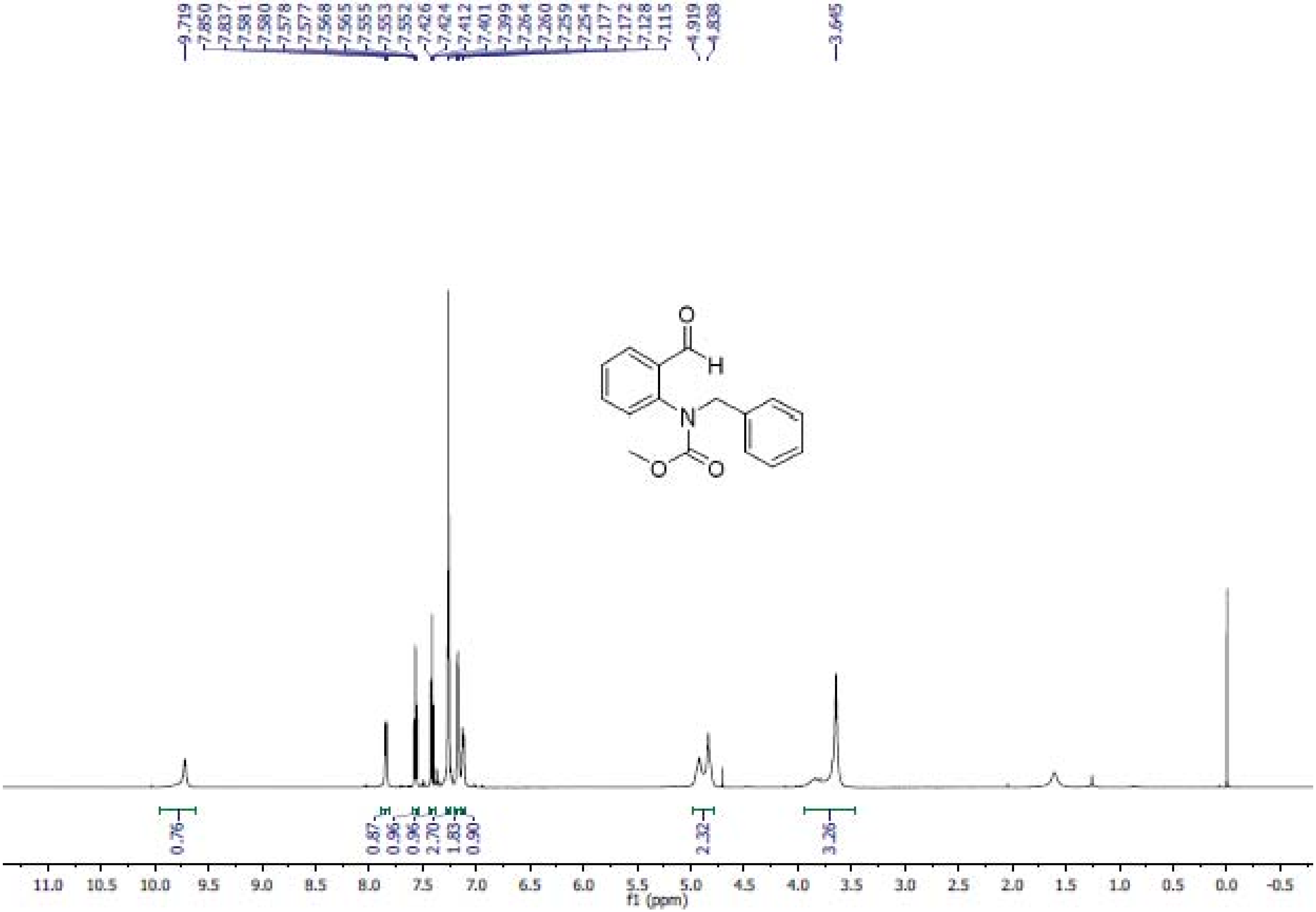
ethyl benzyl(2-formylphenyl)carbamate s3-b



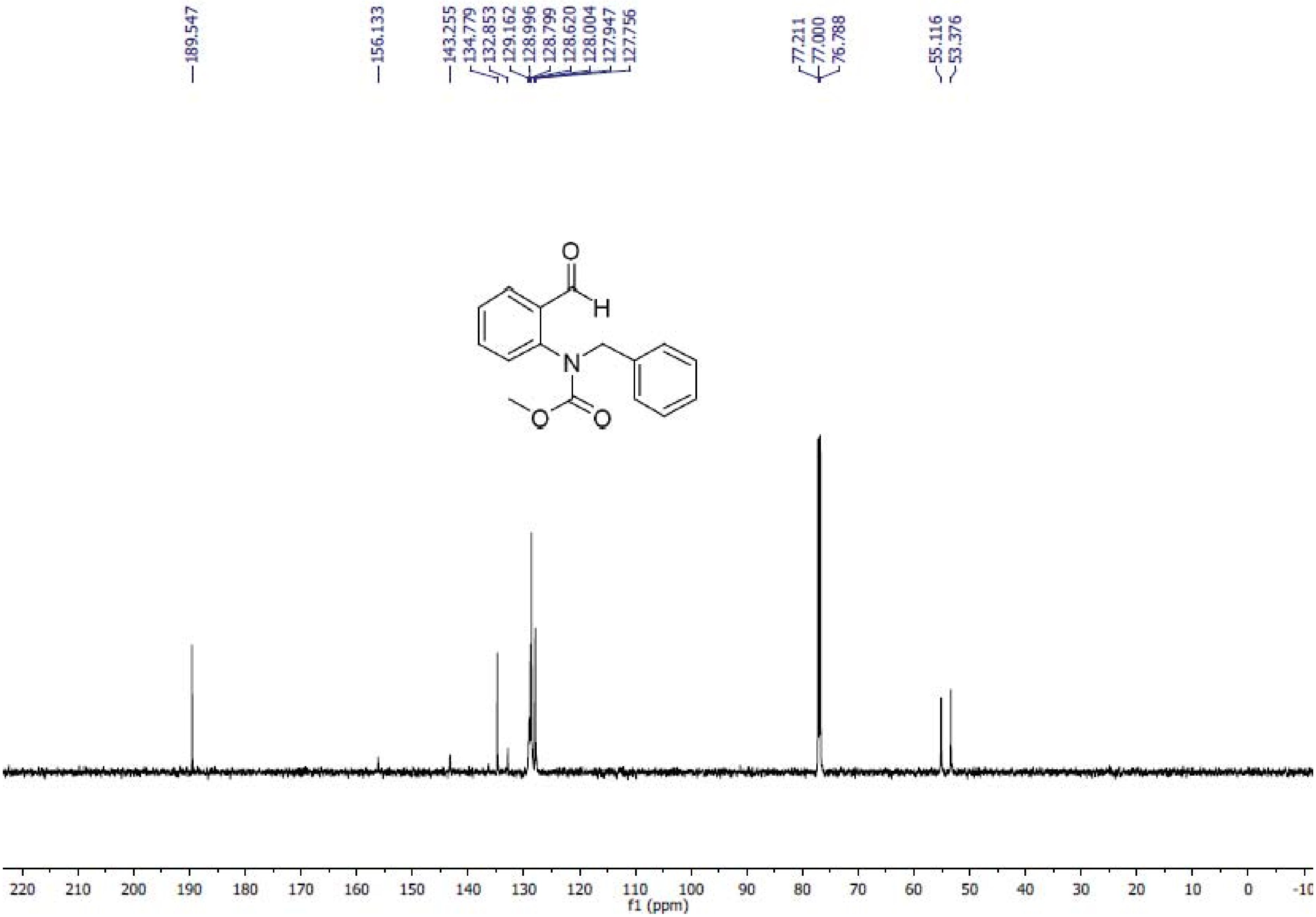
ethyl benzyl(2-formylphenyl)carbamate s3-b



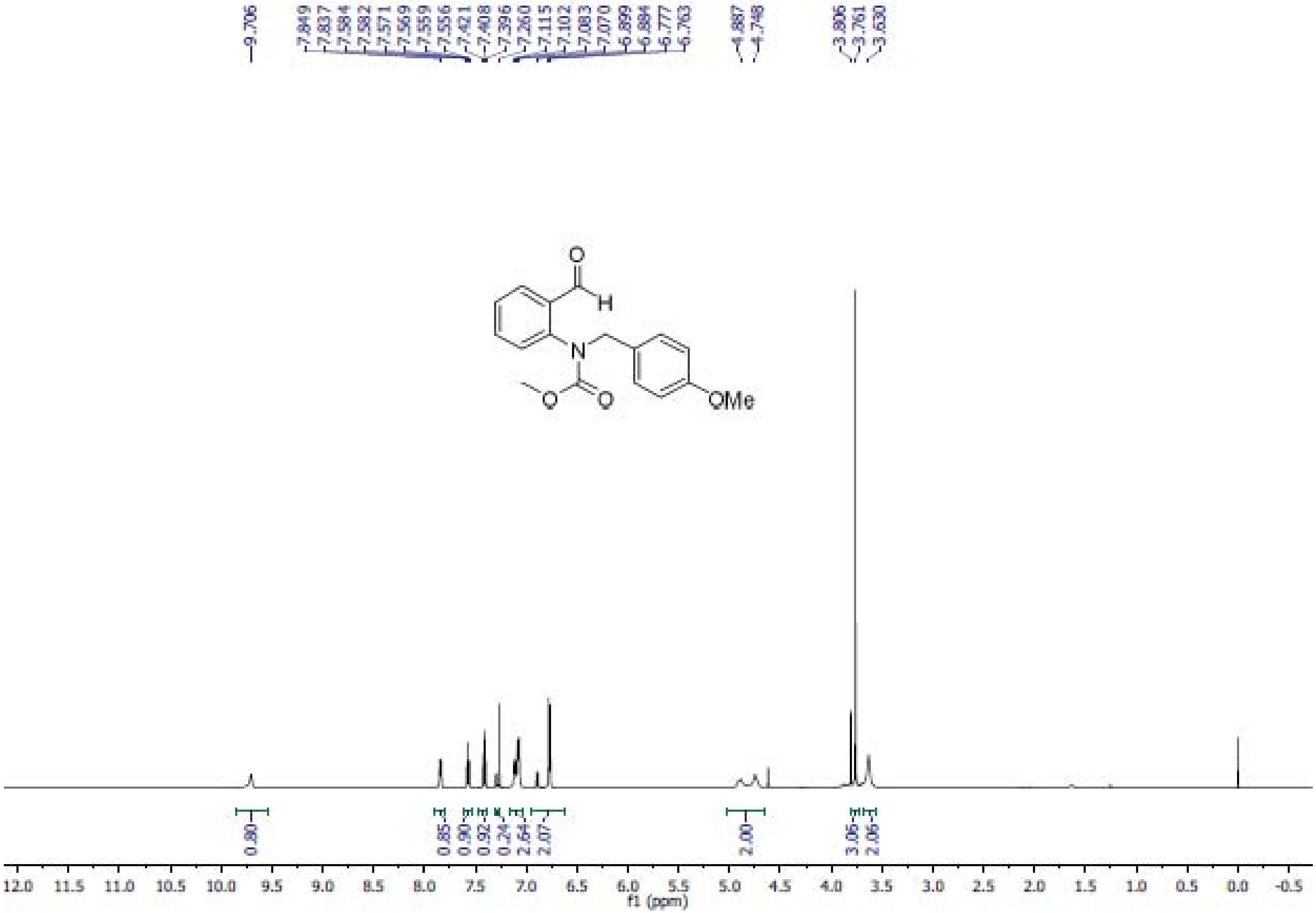
methyl benzyl(2-formylphenyl)carbamate s3-c



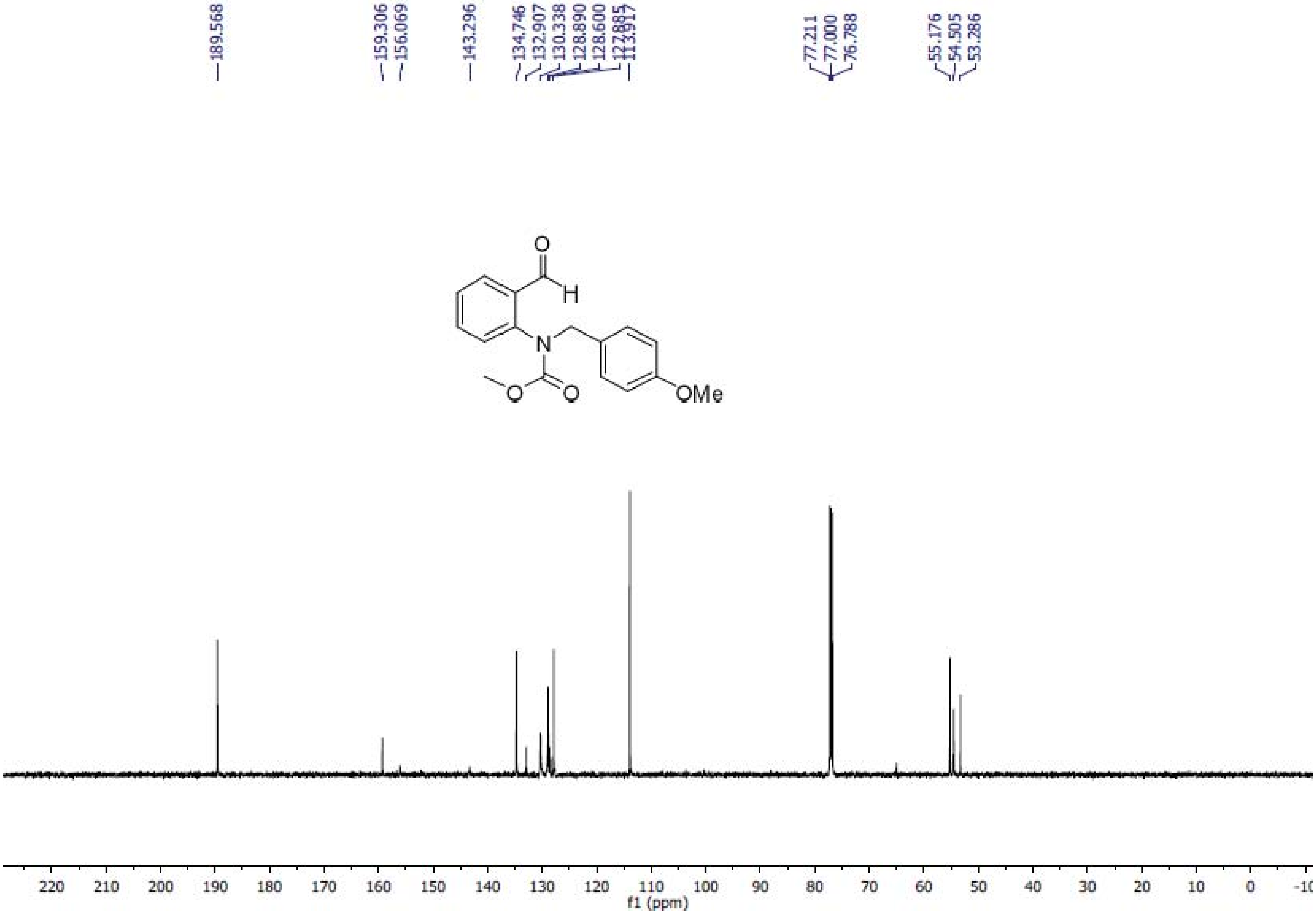
methyl benzyl(2-formylphenyl)carbamate s3-c



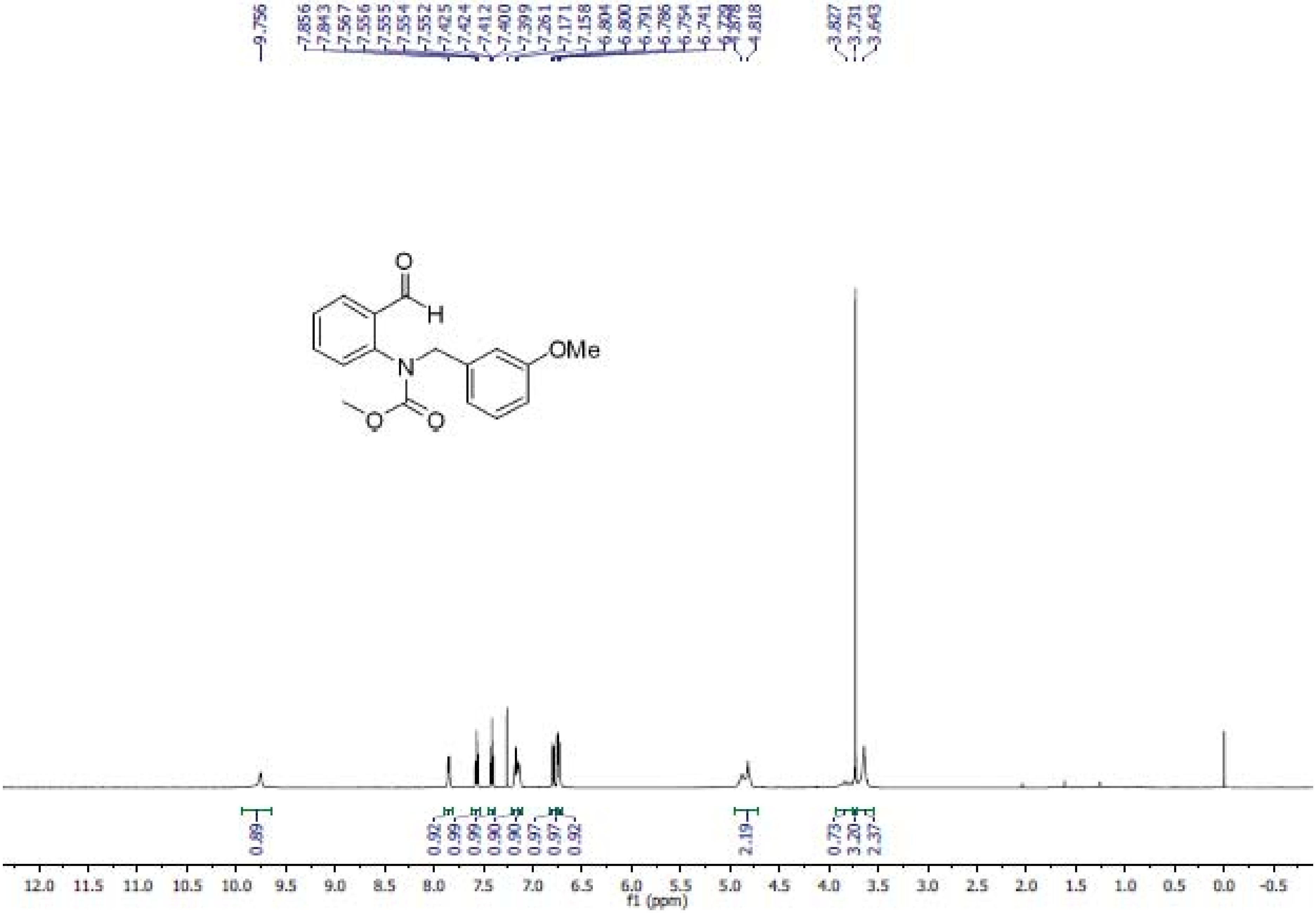
methyl (2-formylphenyl)(4-methoxybenzyl)carbamate s3-d



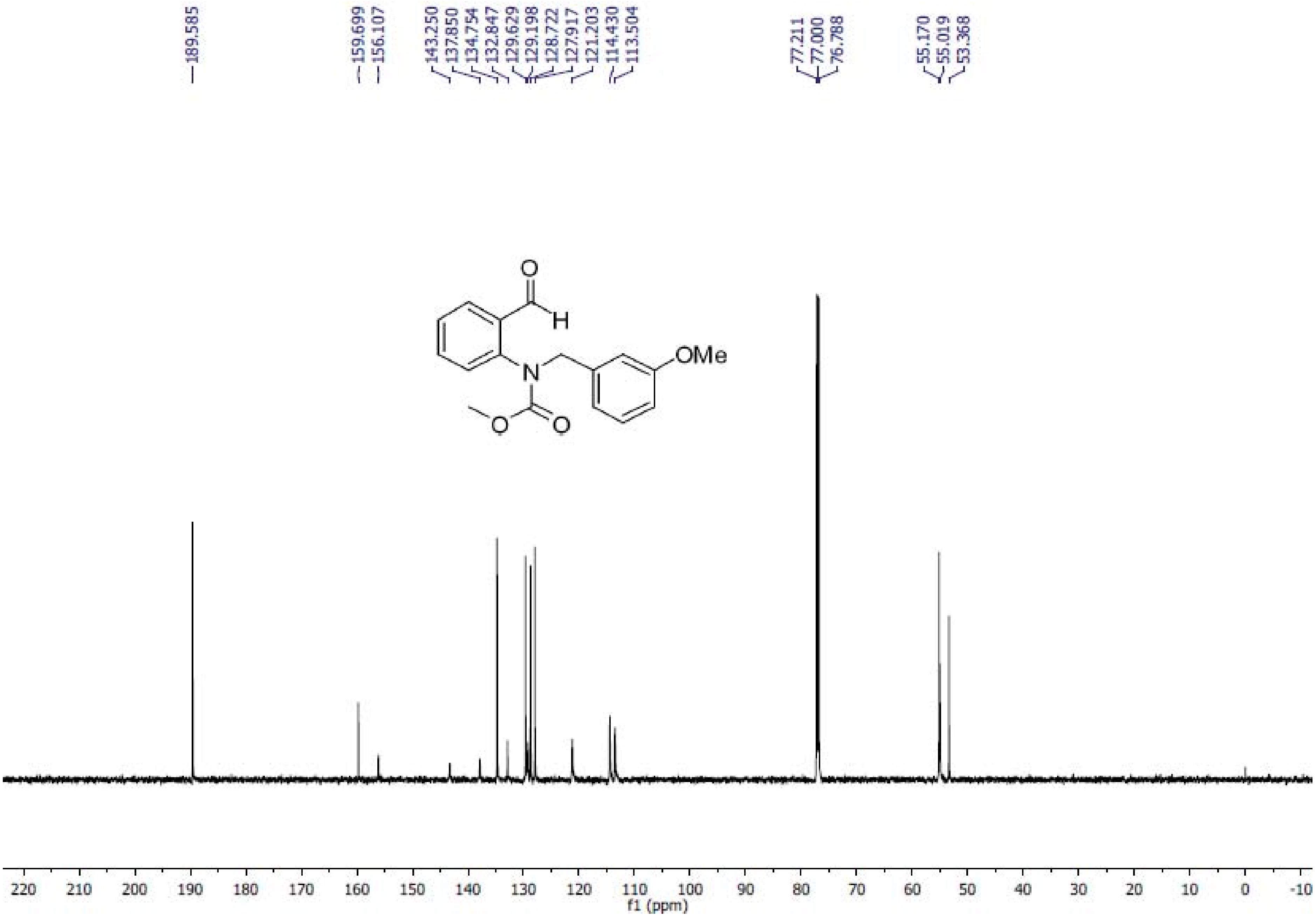
methyl (2-formylphenyl)(4-methoxybenzyl)carbamate s3-d



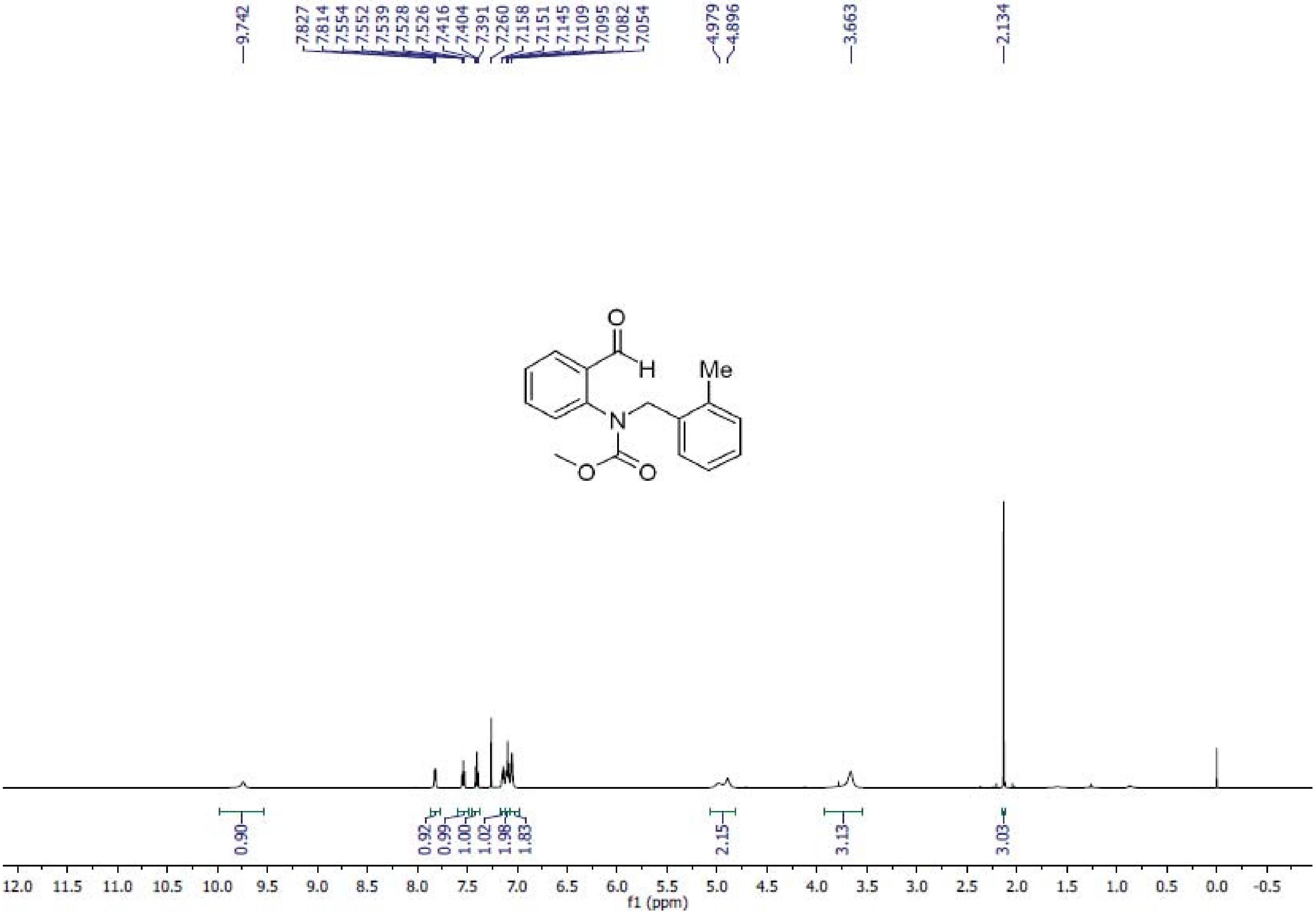
methyl (2-formylphenyl)(3-methoxybenzyl)carbamate s3-e



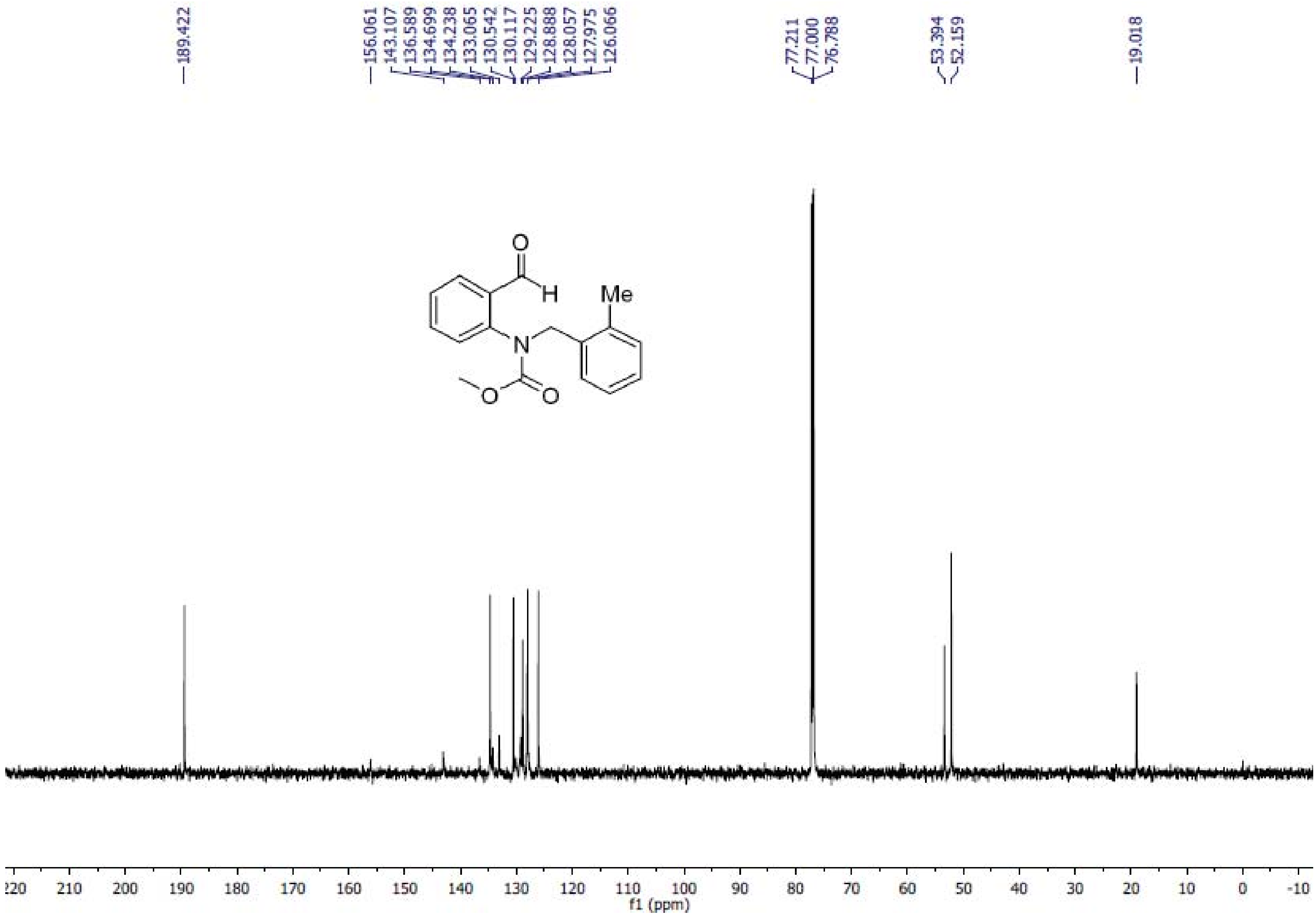
methyl (2-formylphenyl)(3-methoxybenzyl)carbamate s3-e



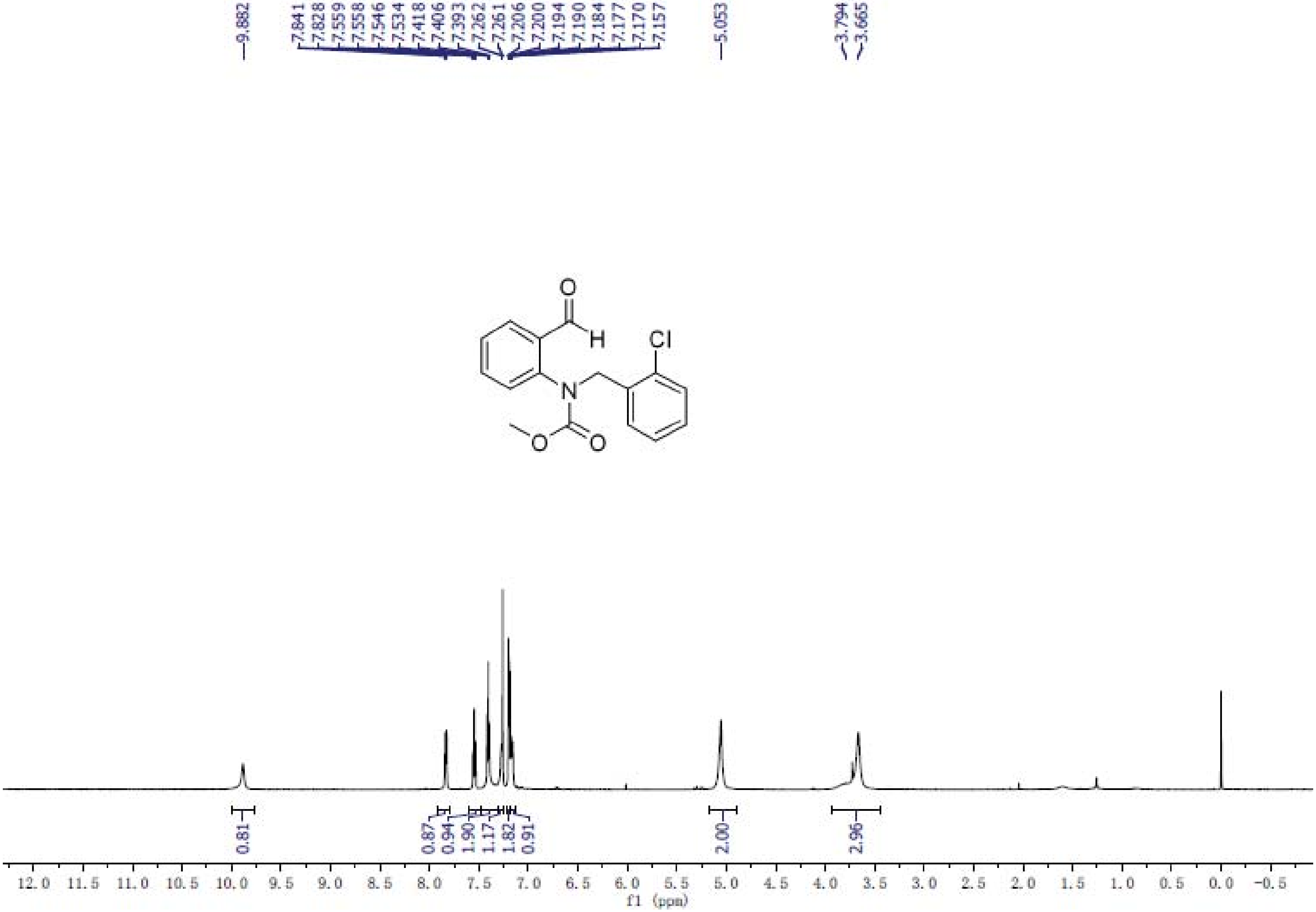
methyl (2-formylphenyl)(2-methylbenzyl)carbamate s3-f



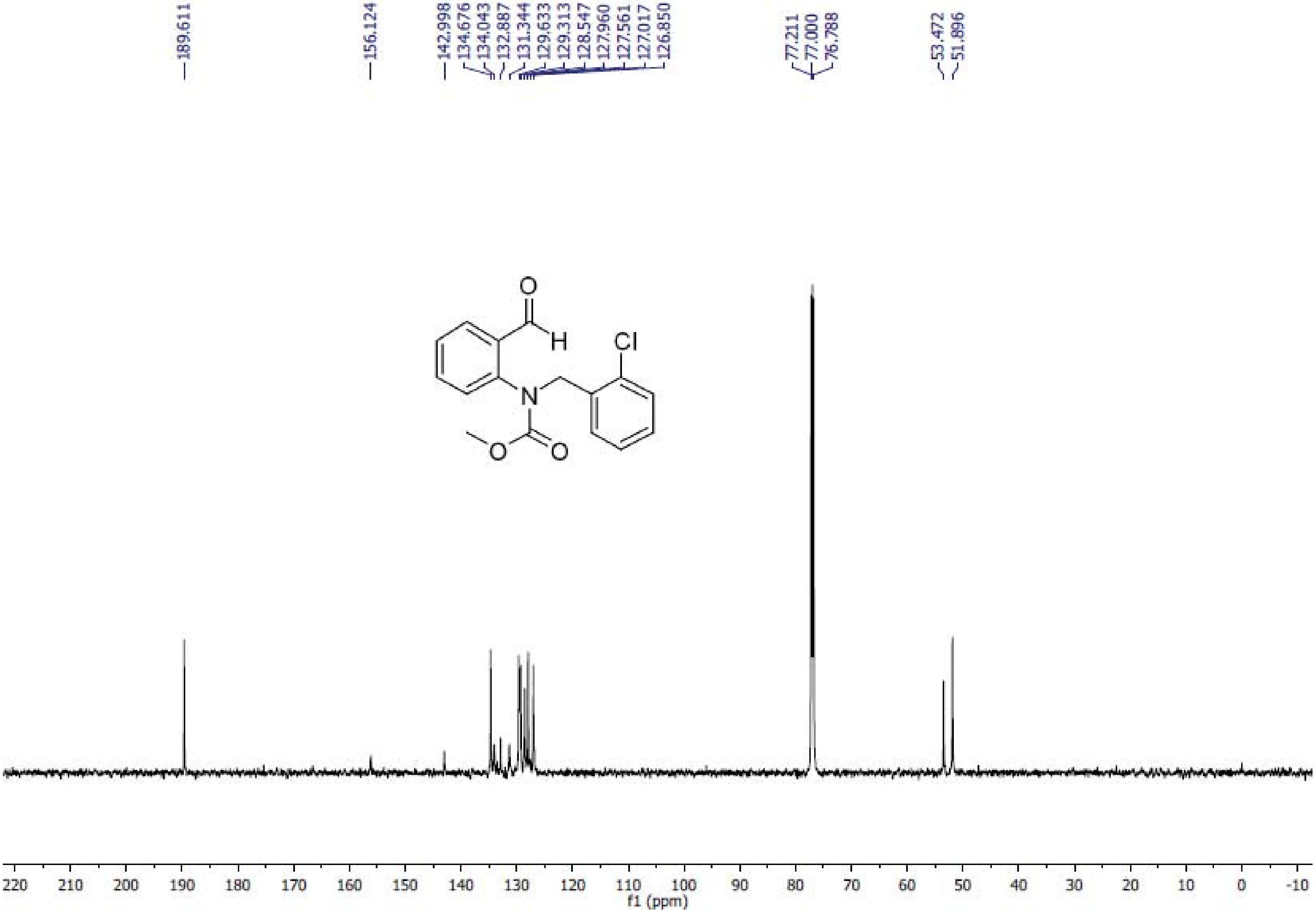
methyl (2-formylphenyl)(2-methylbenzyl)carbamate s3-f



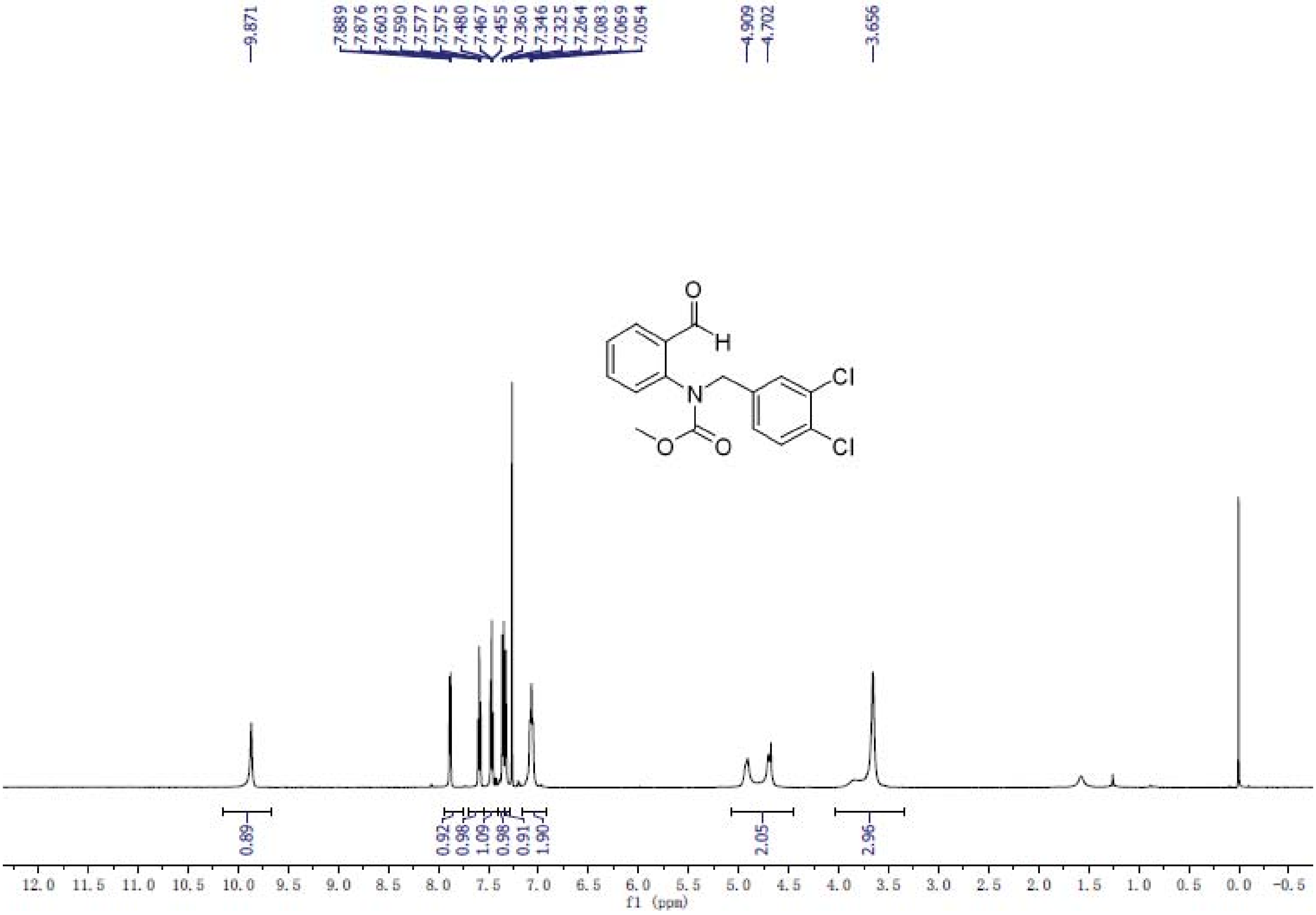
methyl (2-chlorobenzyl)(2-formylphenyl)carbamate s3-g



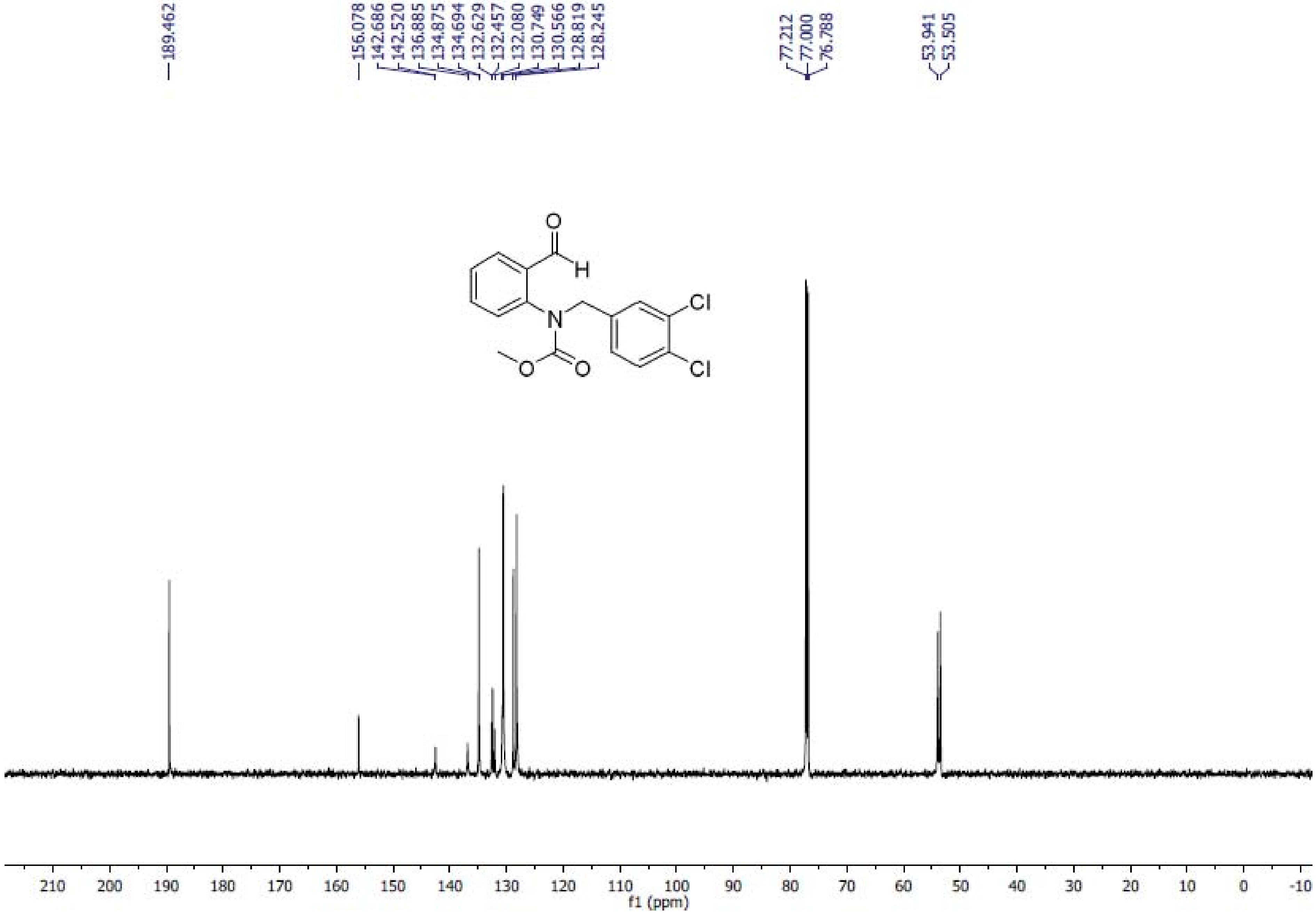
methyl (2-chlorobenzyl)(2-formylphenyl)carbamate s3-g



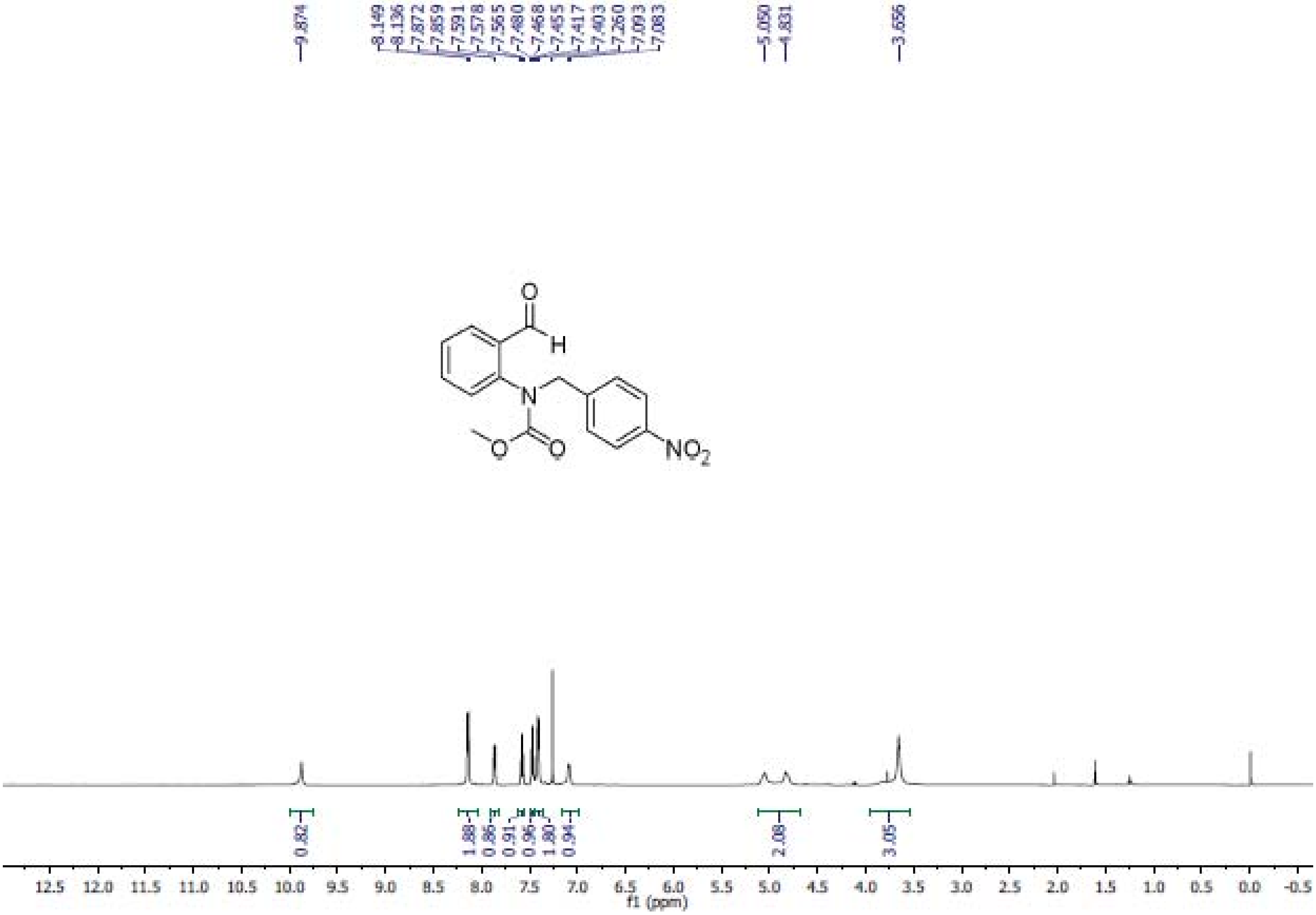
methyl (3,4-dichlorobenzyl)(2-formylphenyl)carbamate s3-h



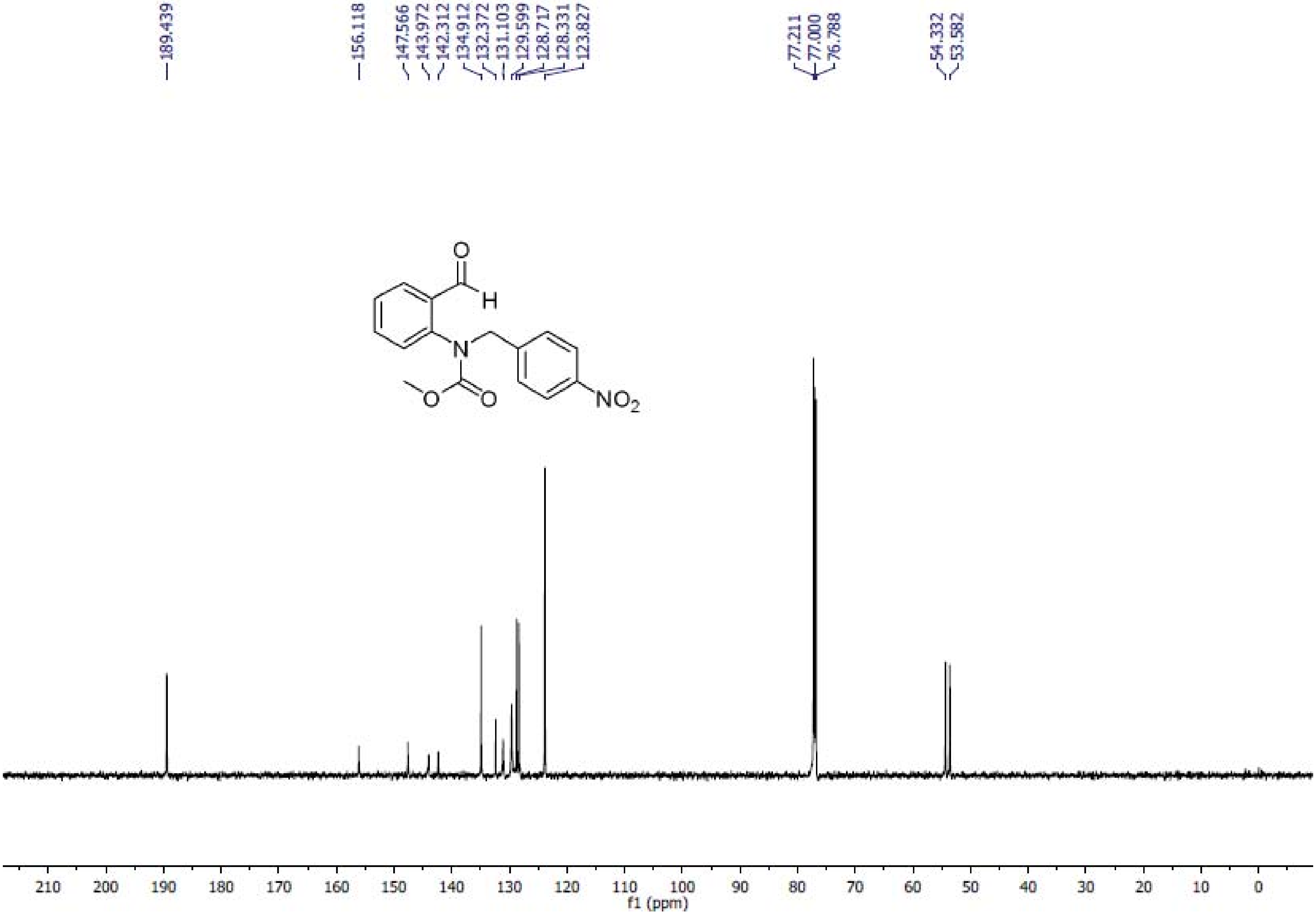
methyl (3,4-dichlorobenzyl)(2-formylphenyl)carbamate s3-h



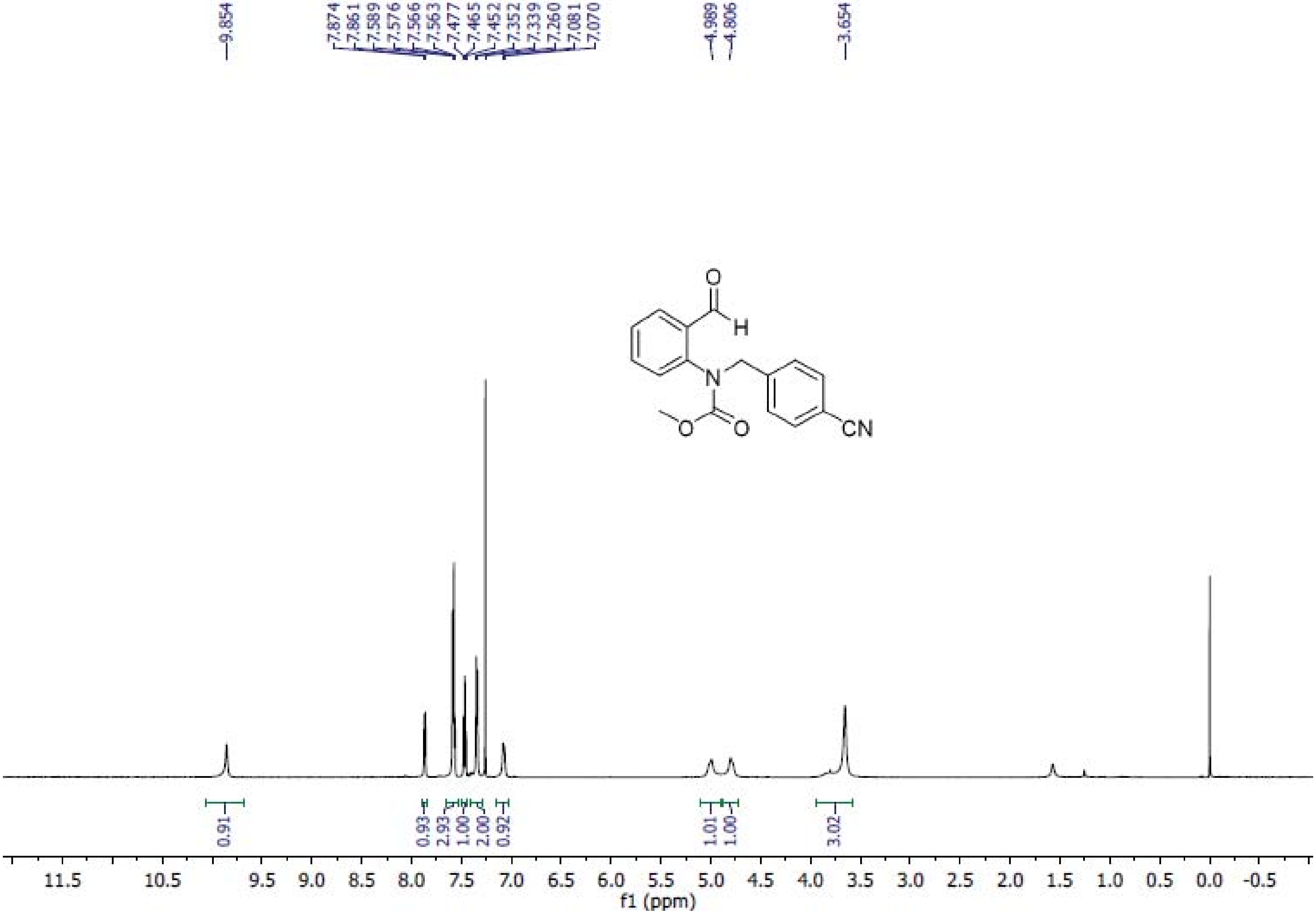
methyl (2-formylphenyl)(4-nitrobenzyl)carbamate s3-i



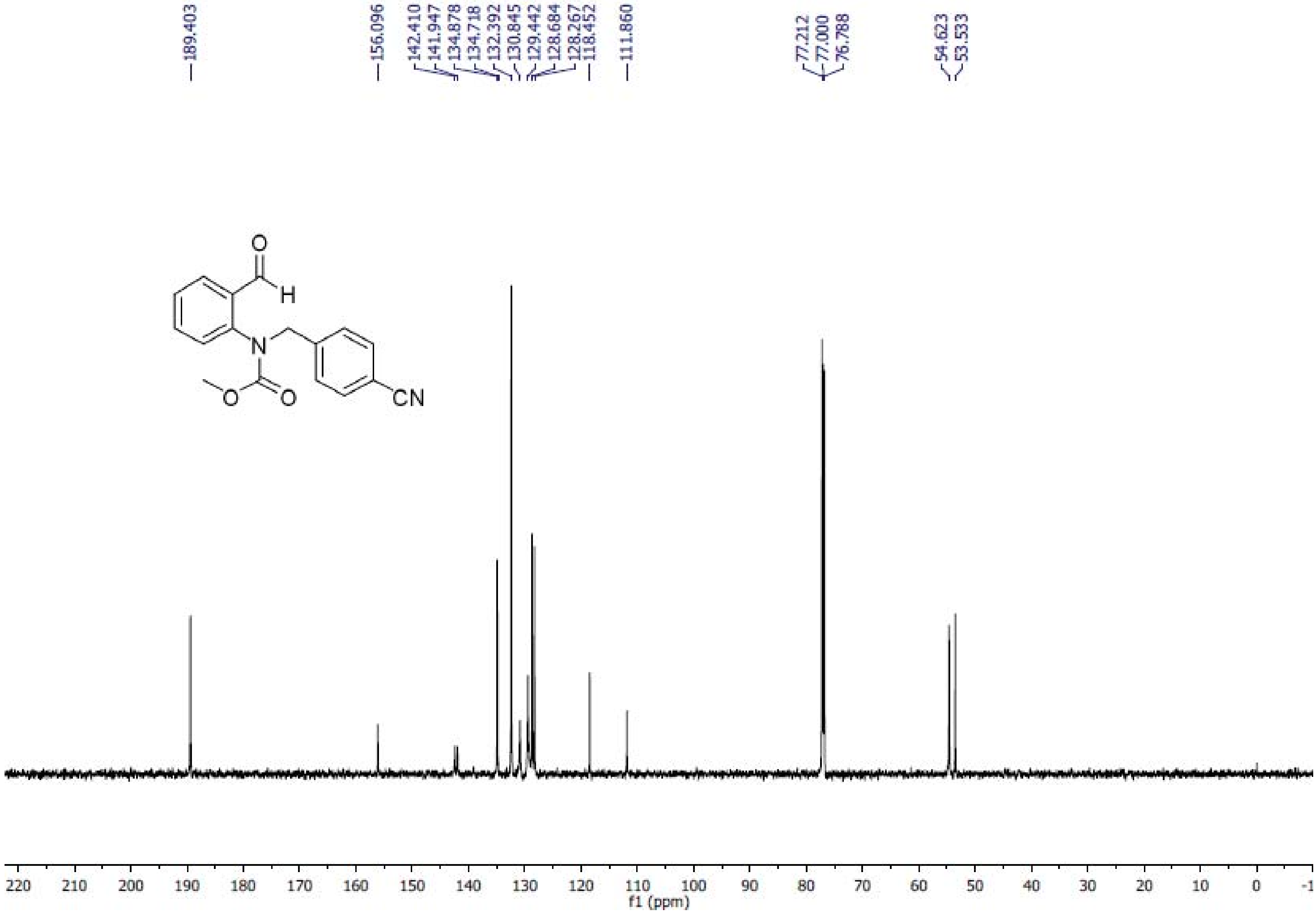
methyl (2-formylphenyl)(4-nitrobenzyl)carbamate s3-i



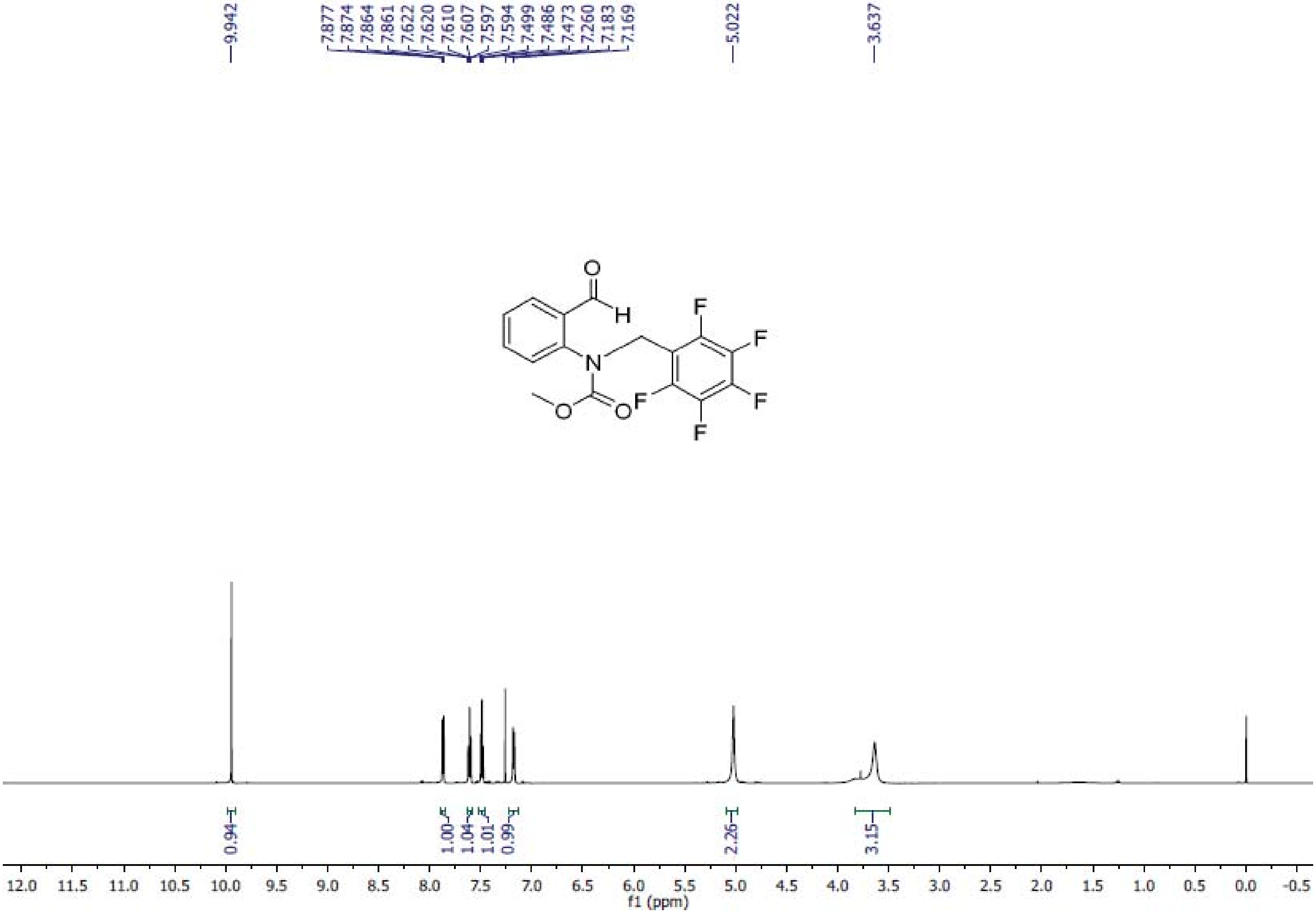
methyl (4-cyanobenzyl)(2-formylphenyl)carbamate s3-j



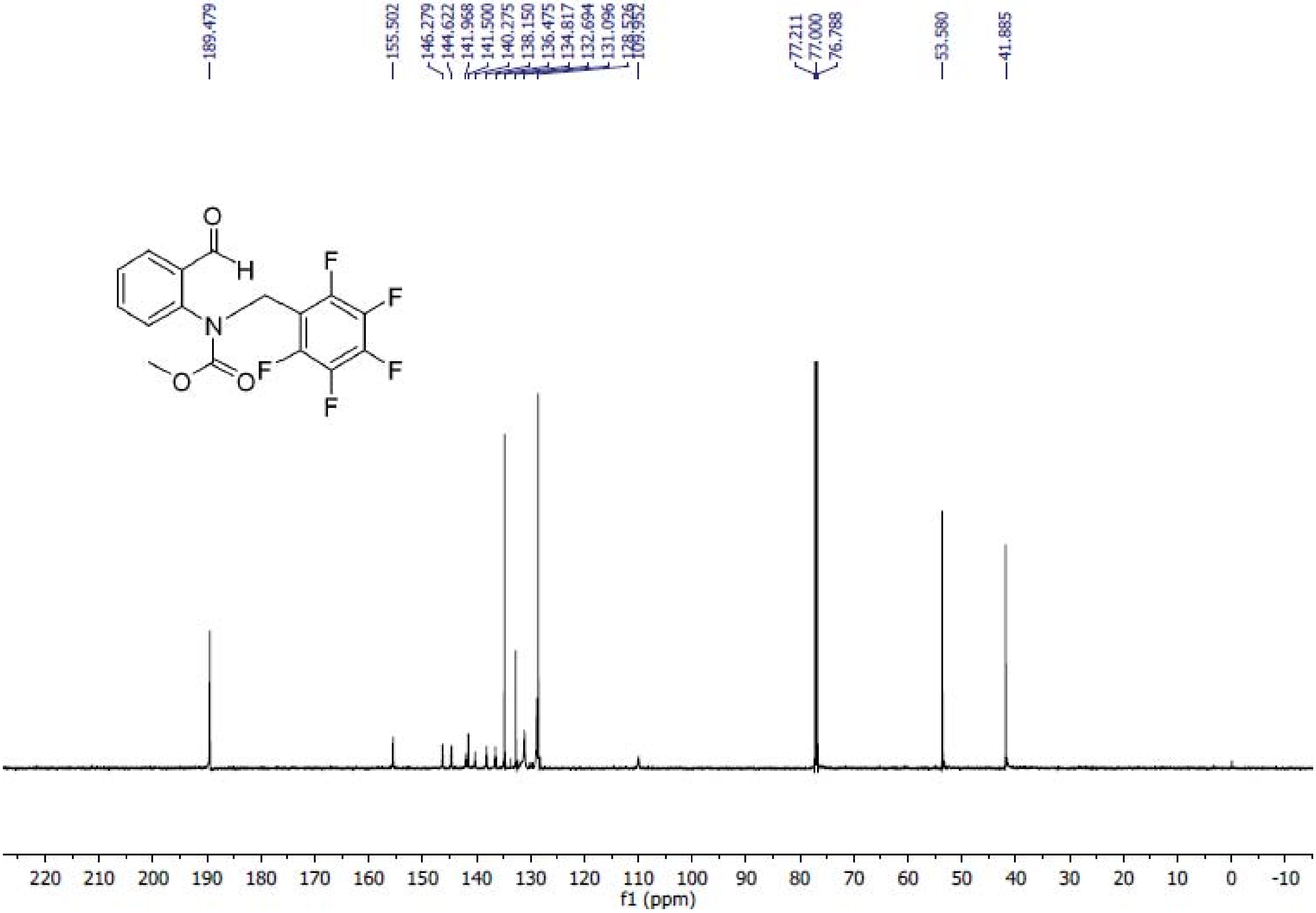
methyl (4-cyanobenzyl)(2-formylphenyl)carbamate s3-j



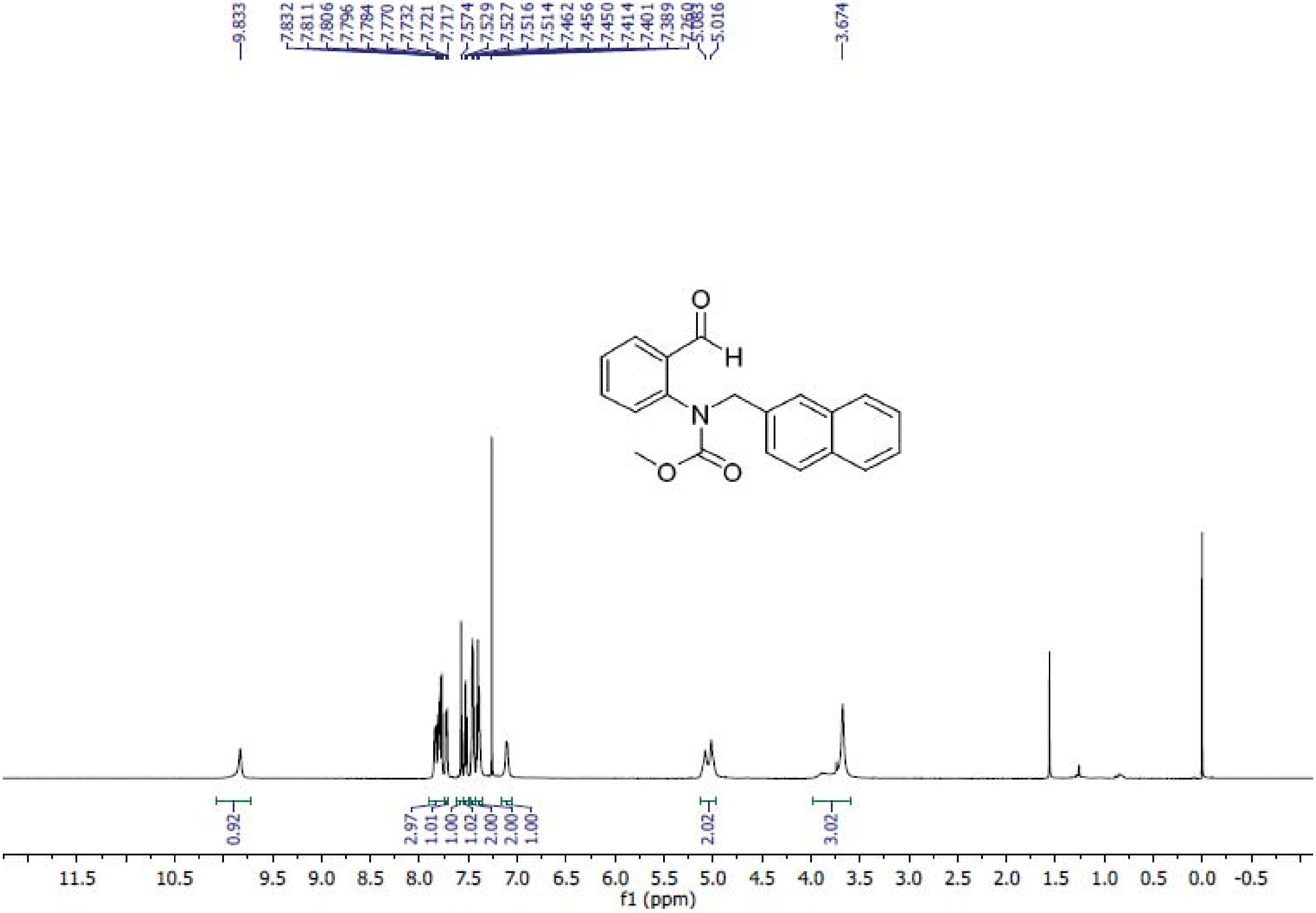
methyl (2-formylphenyl)((perfluorophenyl)methyl)carbamate s3-k



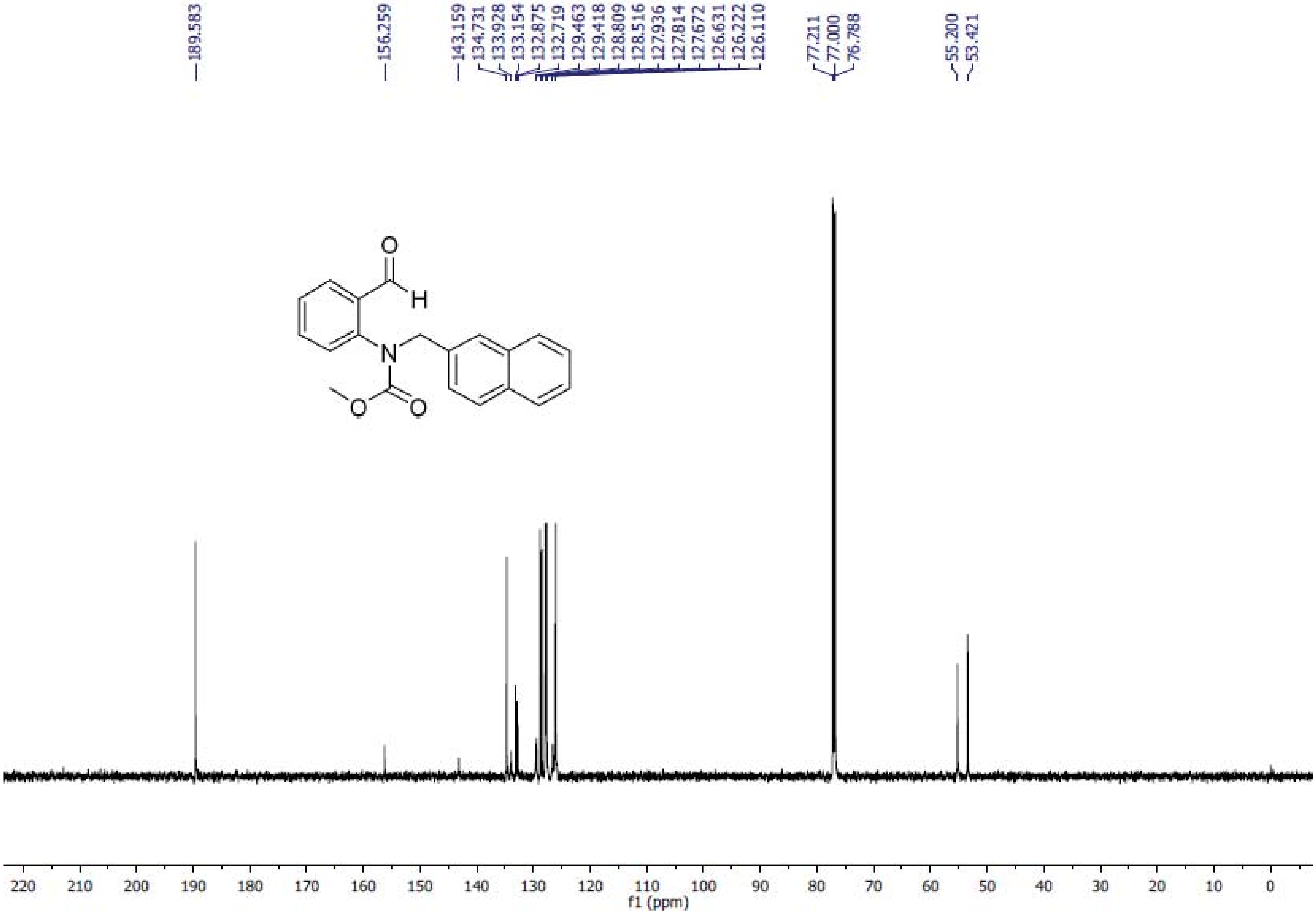
methyl (2-formylphenyl)((perfluorophenyl)methyl)carbamate s3-k



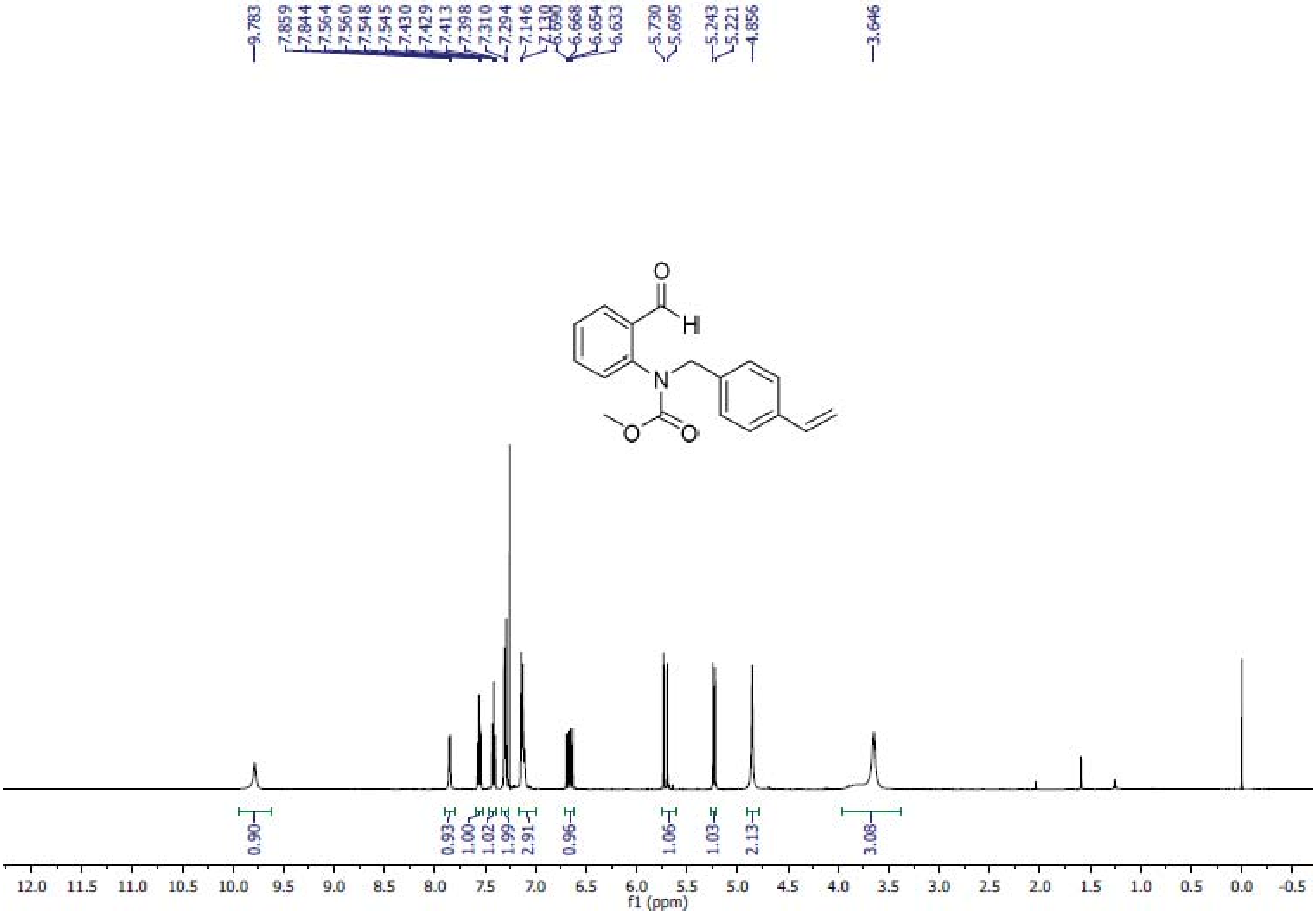
methyl (2-formylphenyl)(naphthalen-2-ylmethyl)carbamate s3-l



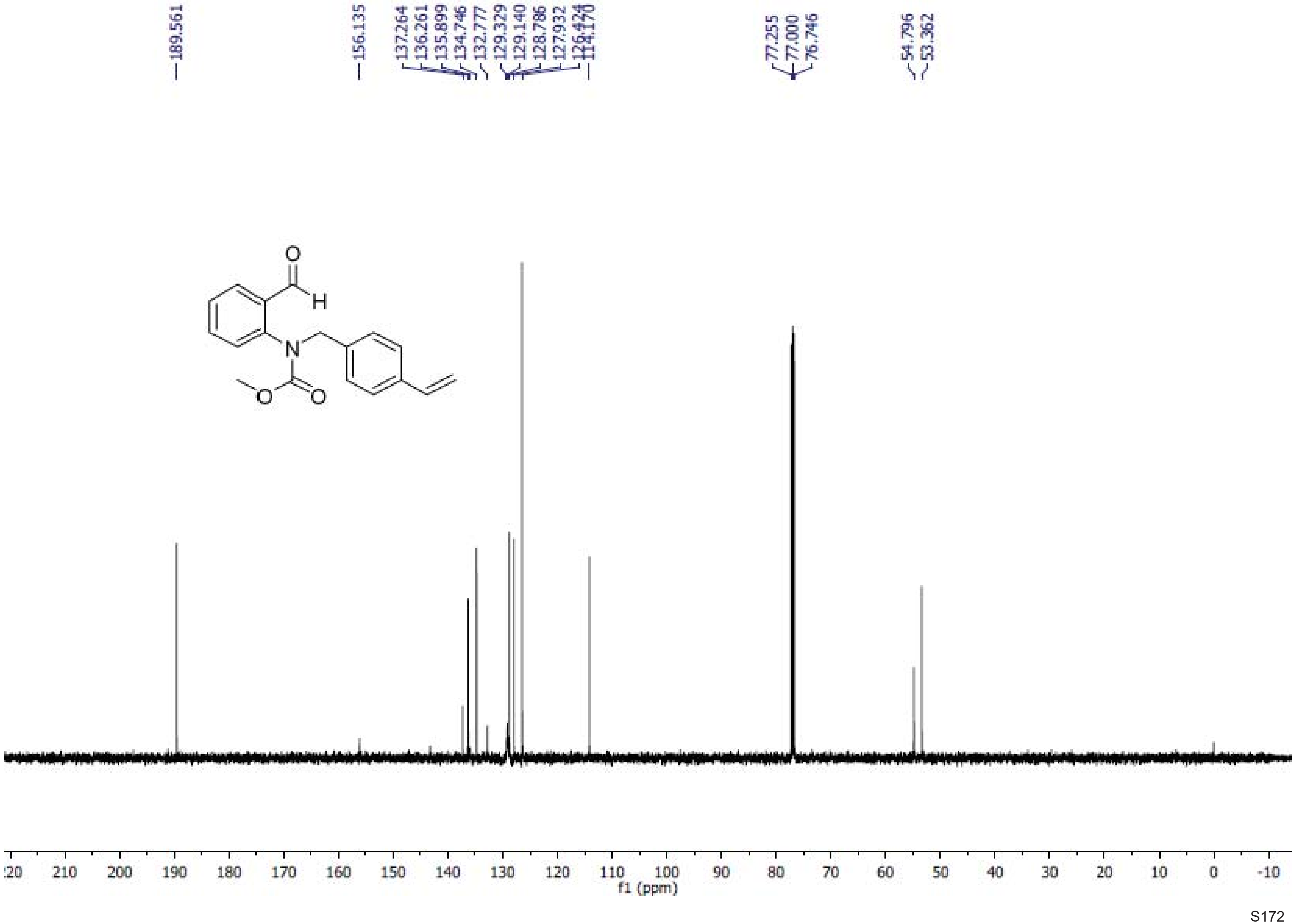
methyl (2-formylphenyl)(naphthalen-2-ylmethyl)carbamate s3-l



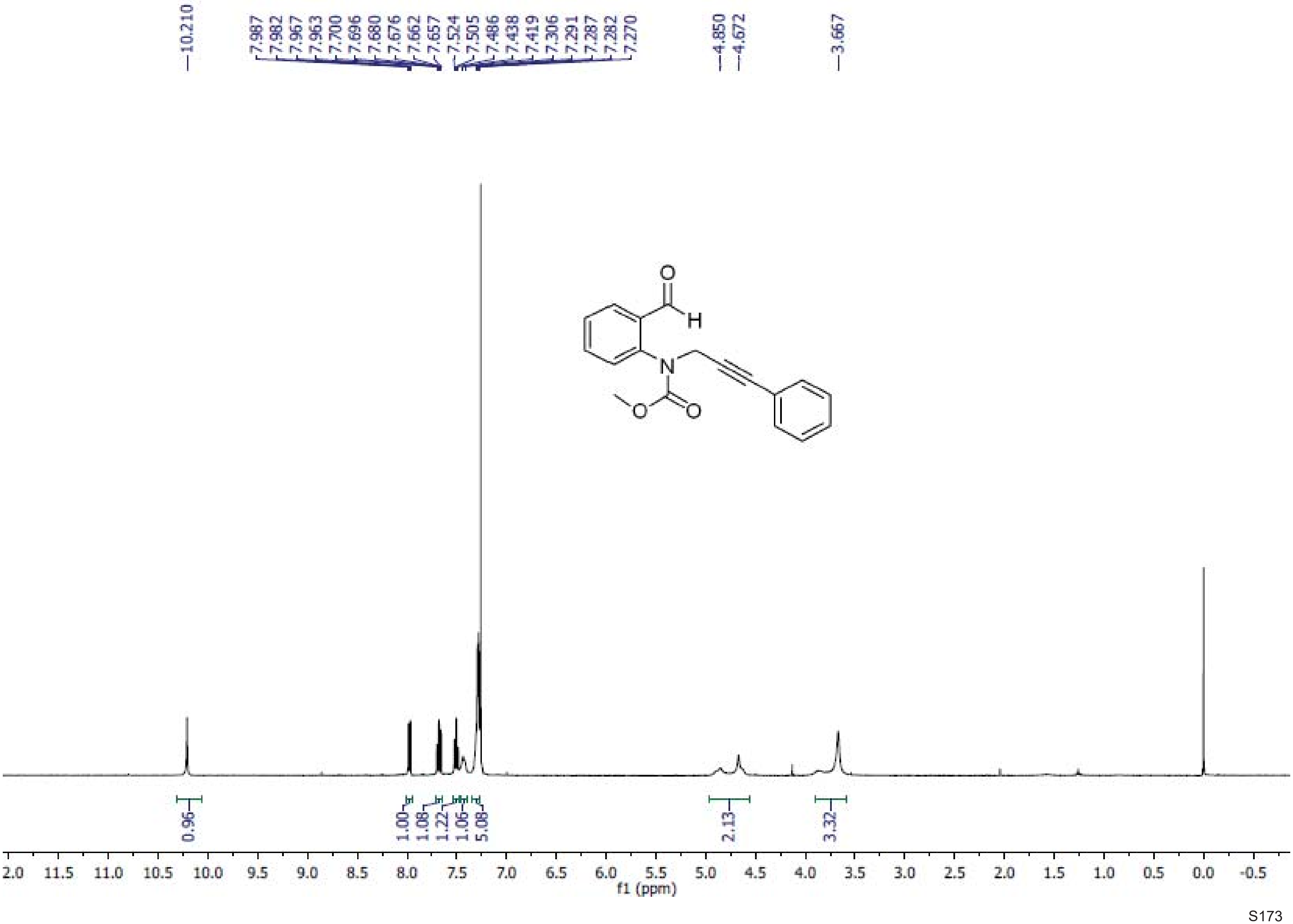
methyl (2-formylphenyl)(4-vinylbenzyl)carbamate s3-m



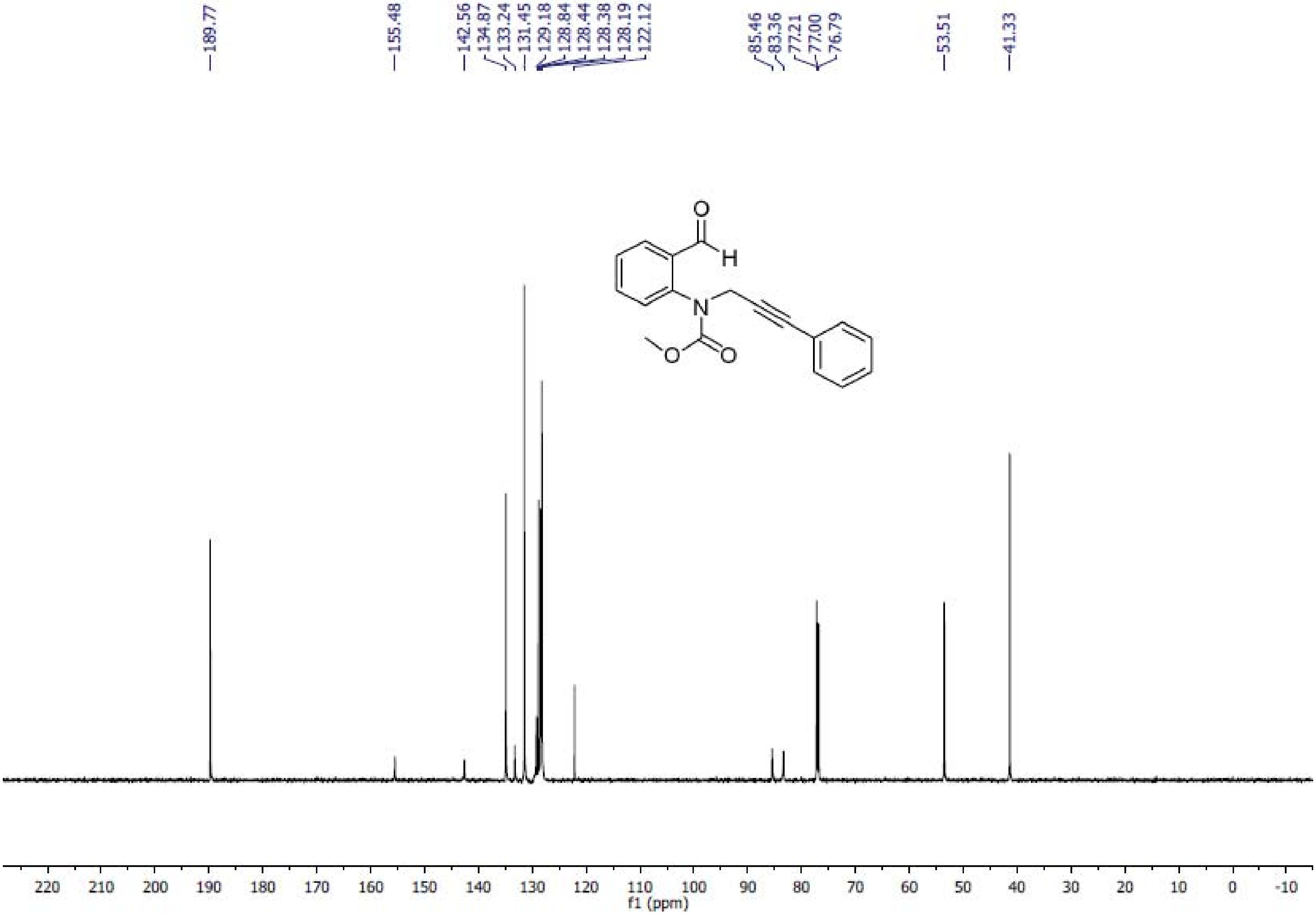
methyl (2-formylphenyl)(4-vinylbenzyl)carbamate s3-m



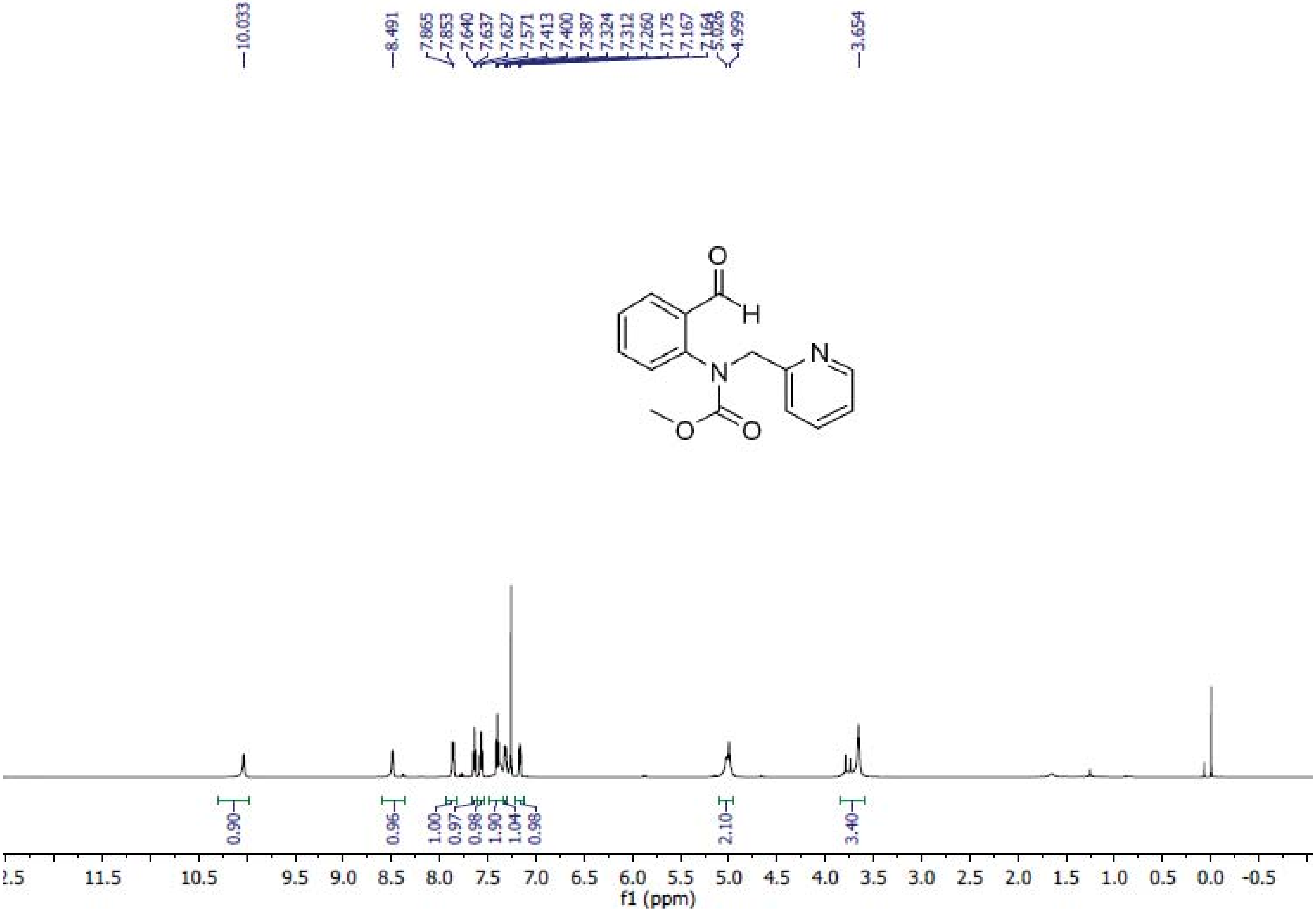
methyl (2-formylphenyl)(3-phenylprop-2-yn-1-yl)carbamate s3-n



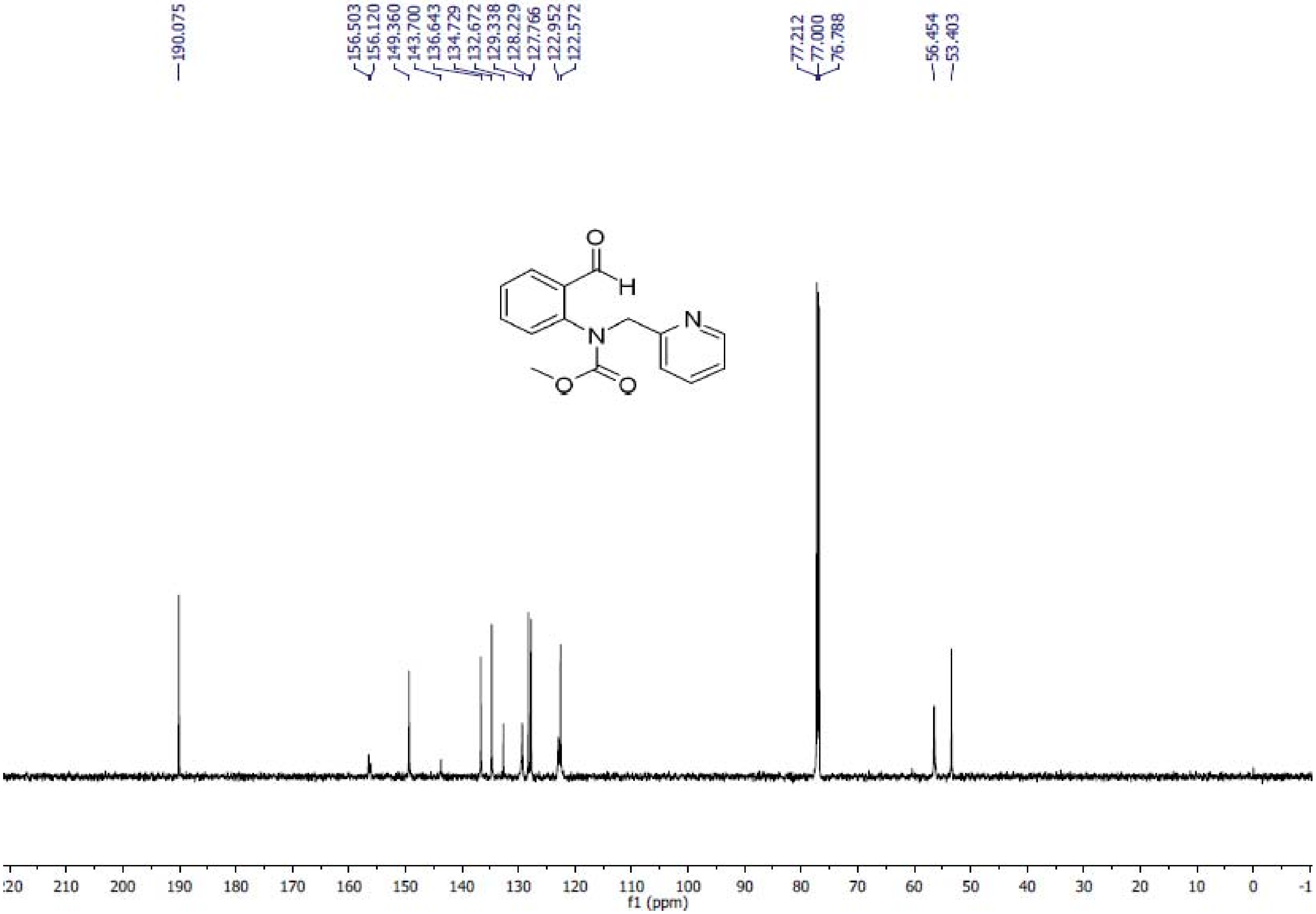
methyl (2-formylphenyl)(3-phenylprop-2-yn-1-yl)carbamate s3-n



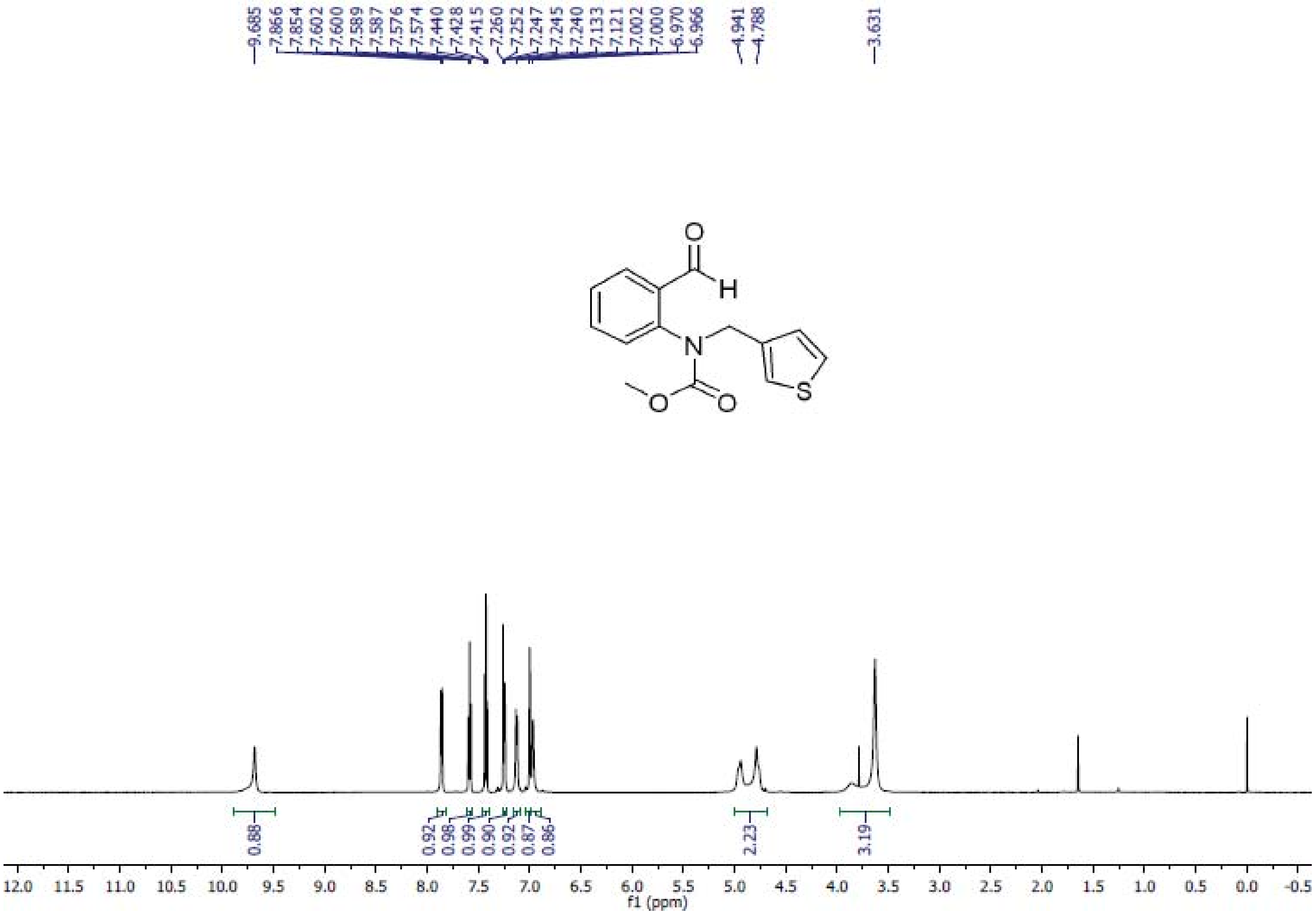
methyl (2-formylphenyl)(pyridin-2-ylmethyl)carbamate s3-o



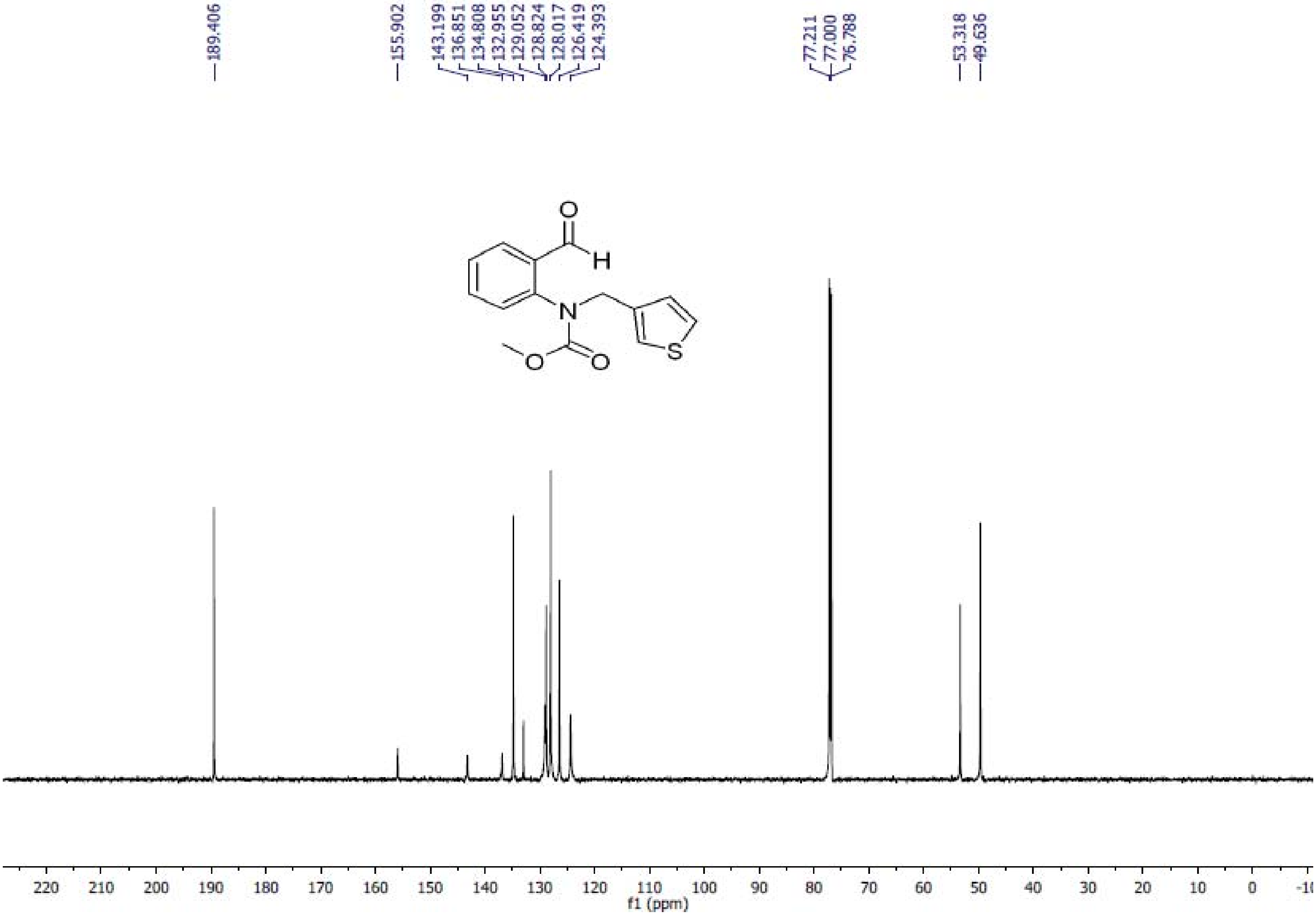
methyl (2-formylphenyl)(pyridin-2-ylmethyl)carbamate s3-o



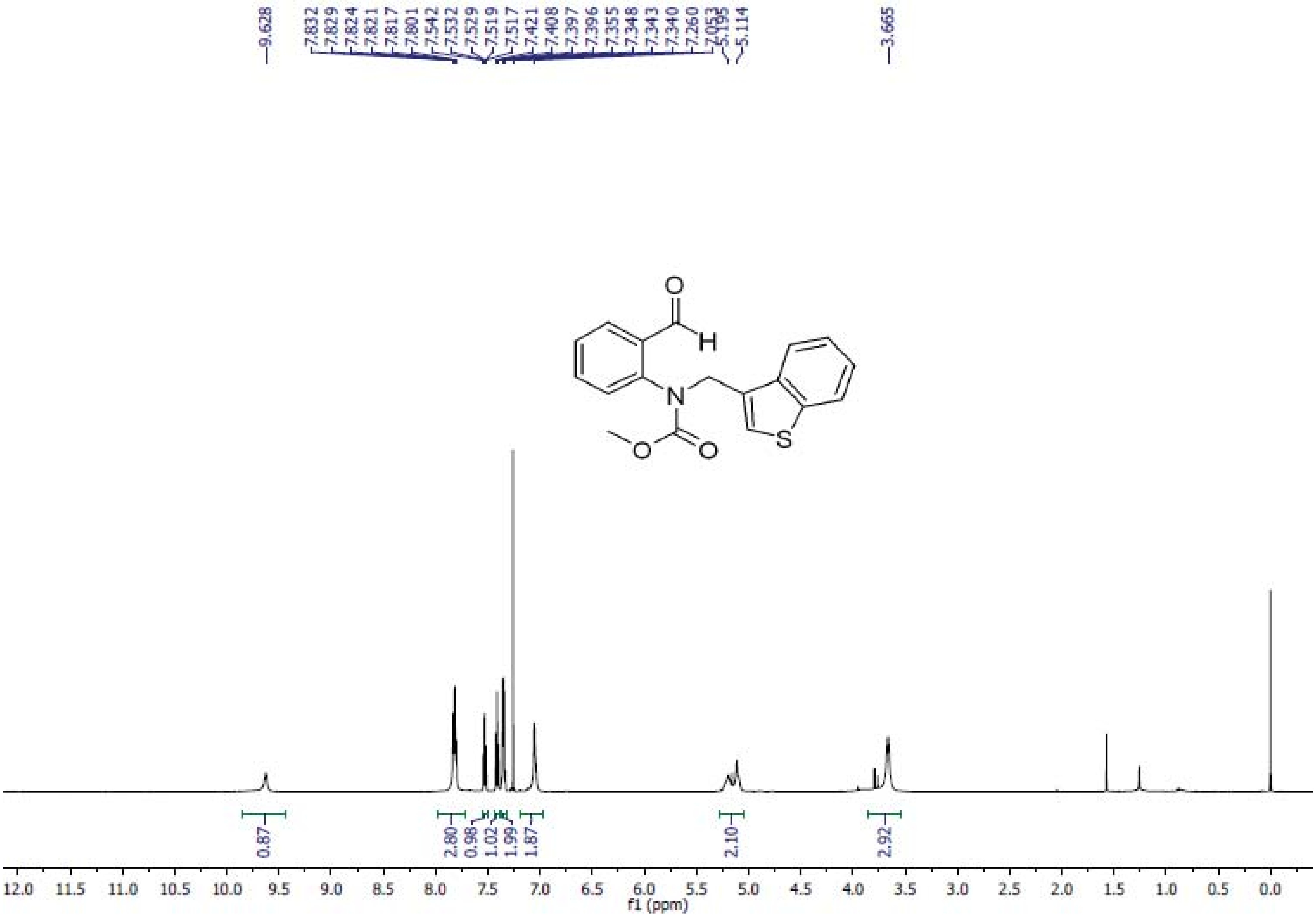
methyl (2-formylphenyl)(thiophen-3-ylmethyl)carbamate s3-p



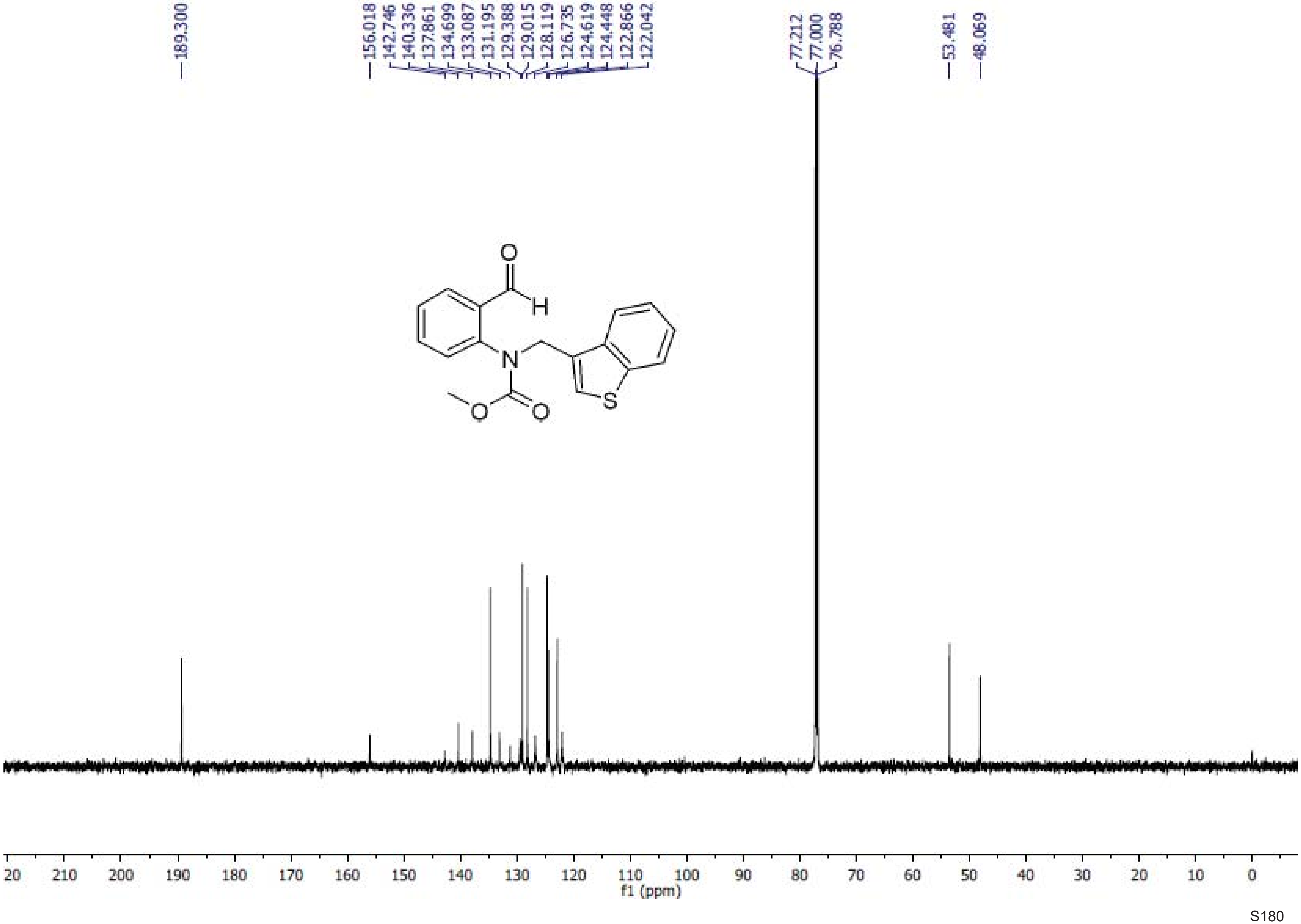
methyl (2-formylphenyl)(thiophen-3-ylmethyl)carbamate s3-p



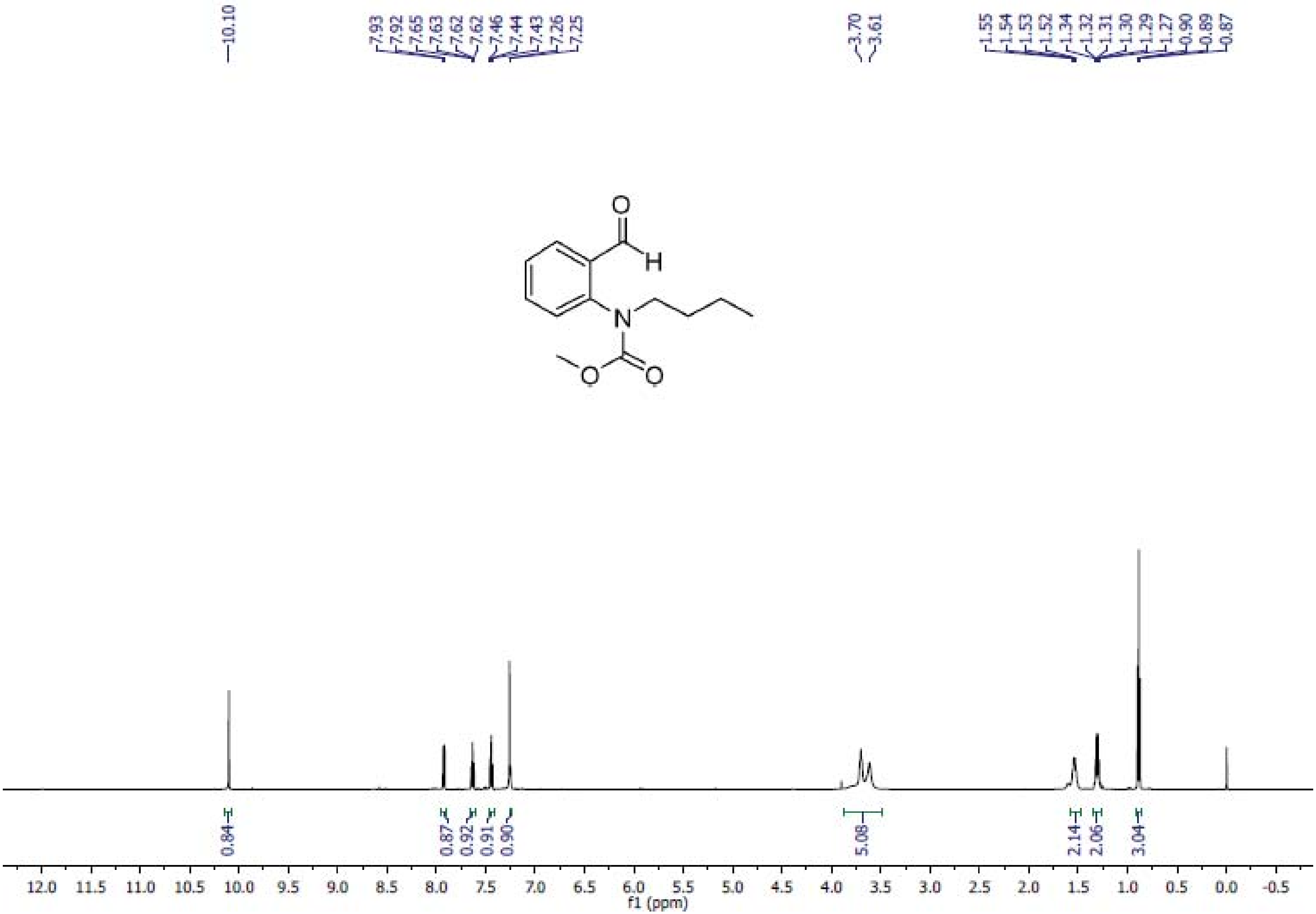
methyl (benzo[*b*]thiophen-3-ylmethyl)(2-formylphenyl)carbamate s3-q



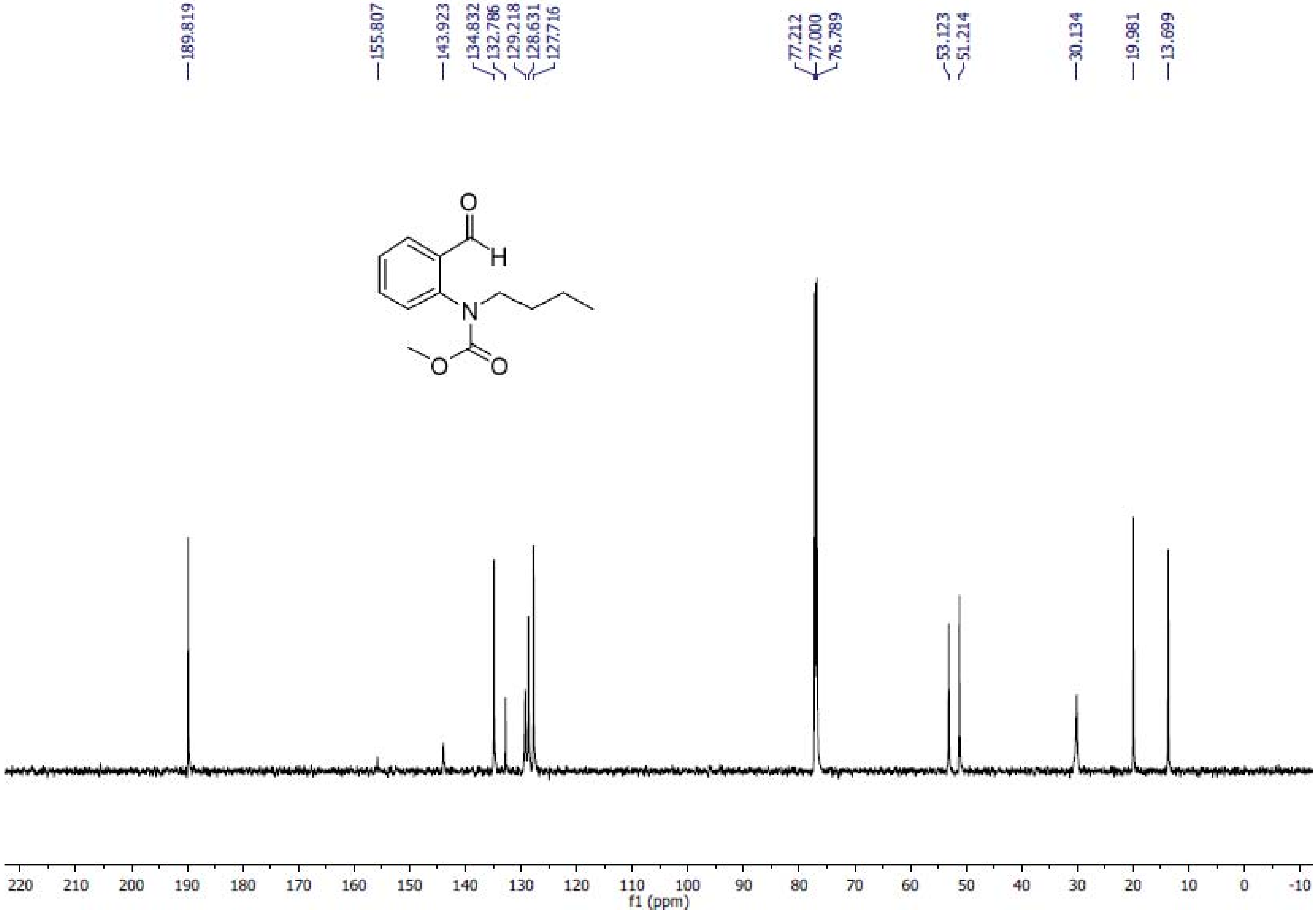
methyl (benzo[*b*]thiophen-3-ylmethyl)(2-formylphenyl)carbamate s3-q



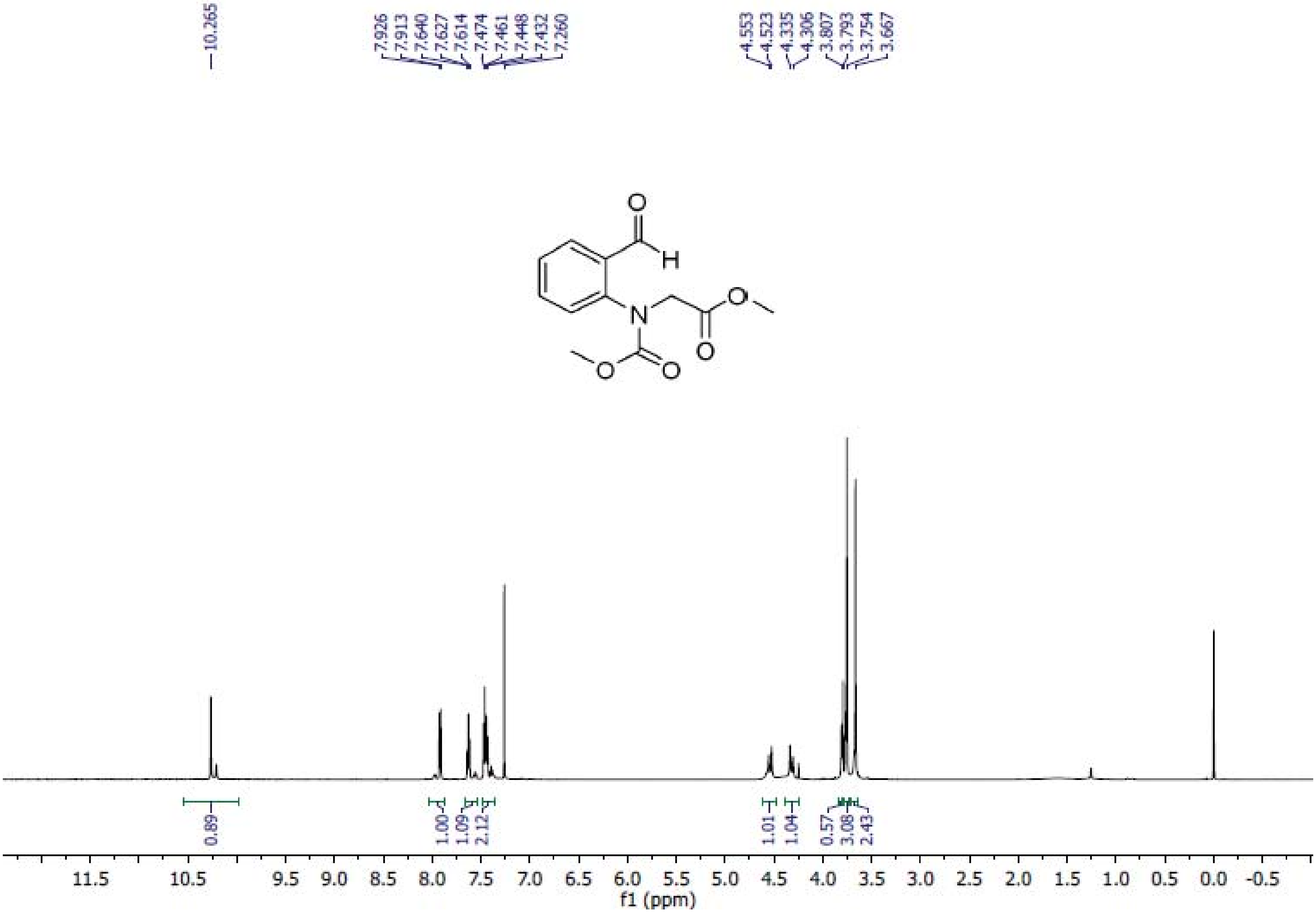
methyl butyl(2-formylphenyl)carbamate s3-r



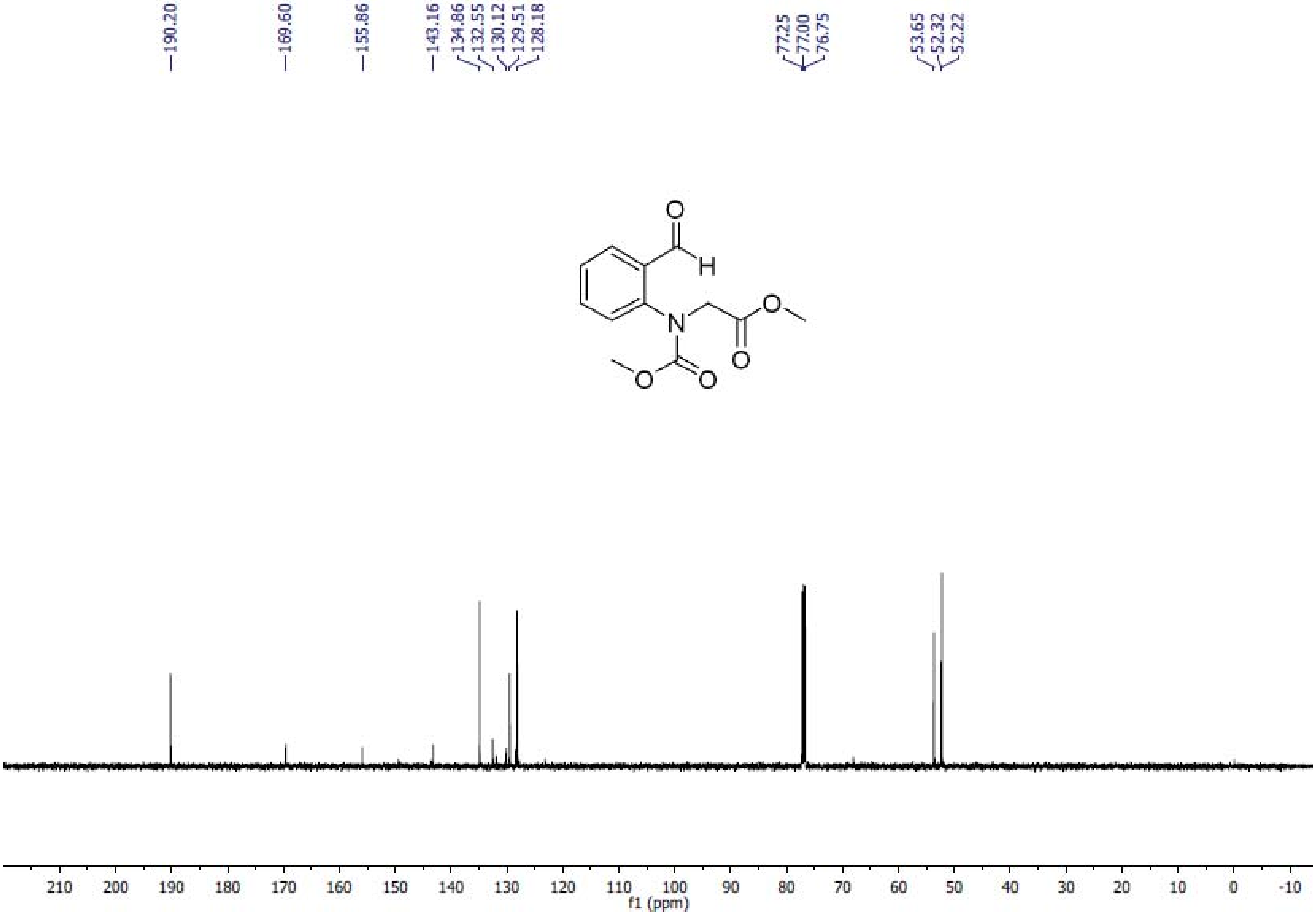
methyl butyl(2-formylphenyl)carbamate s3-r



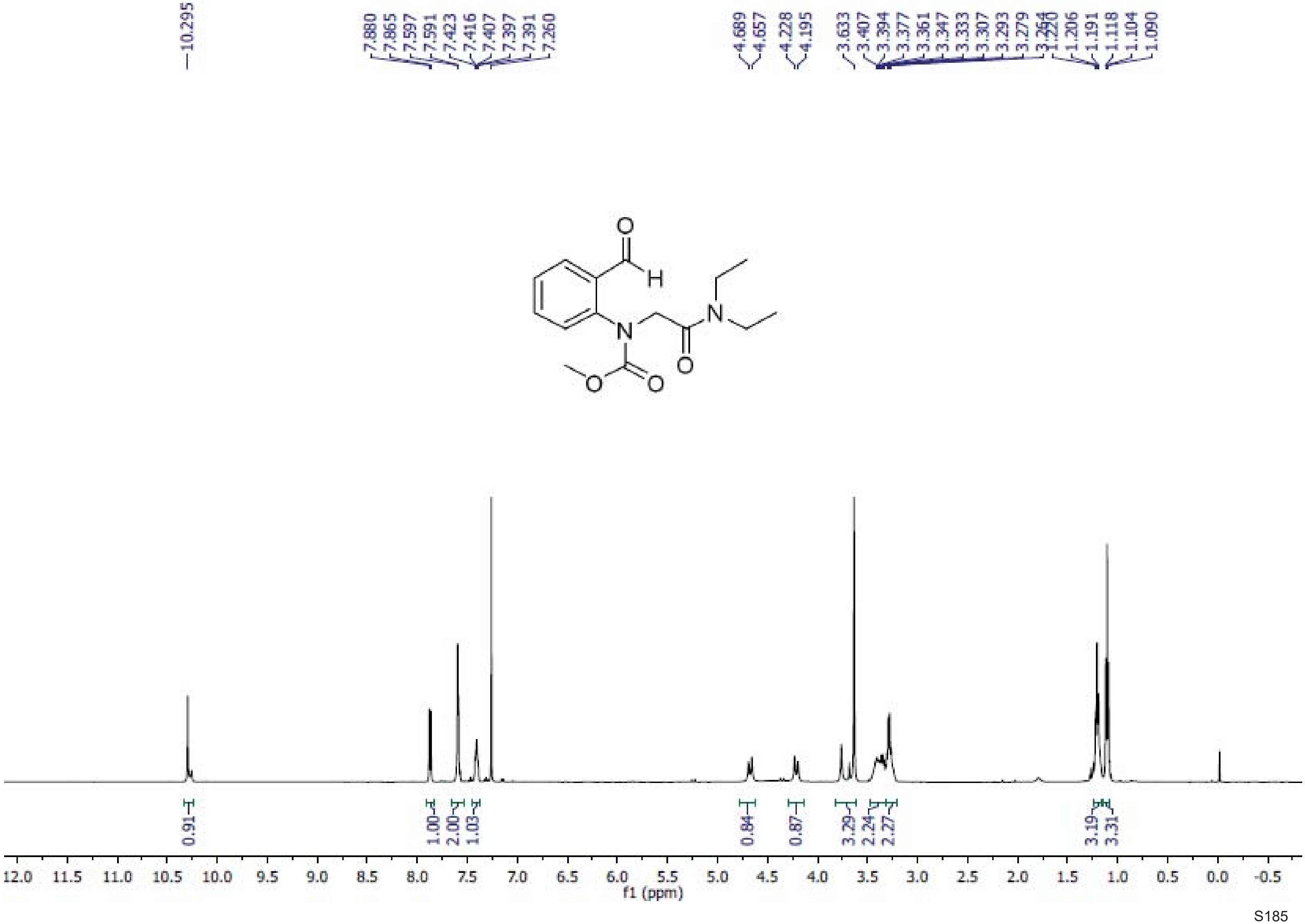
methyl *N*-(2-formylphenyl)-*N*-(methoxycarbonyl)glycinate s3-s



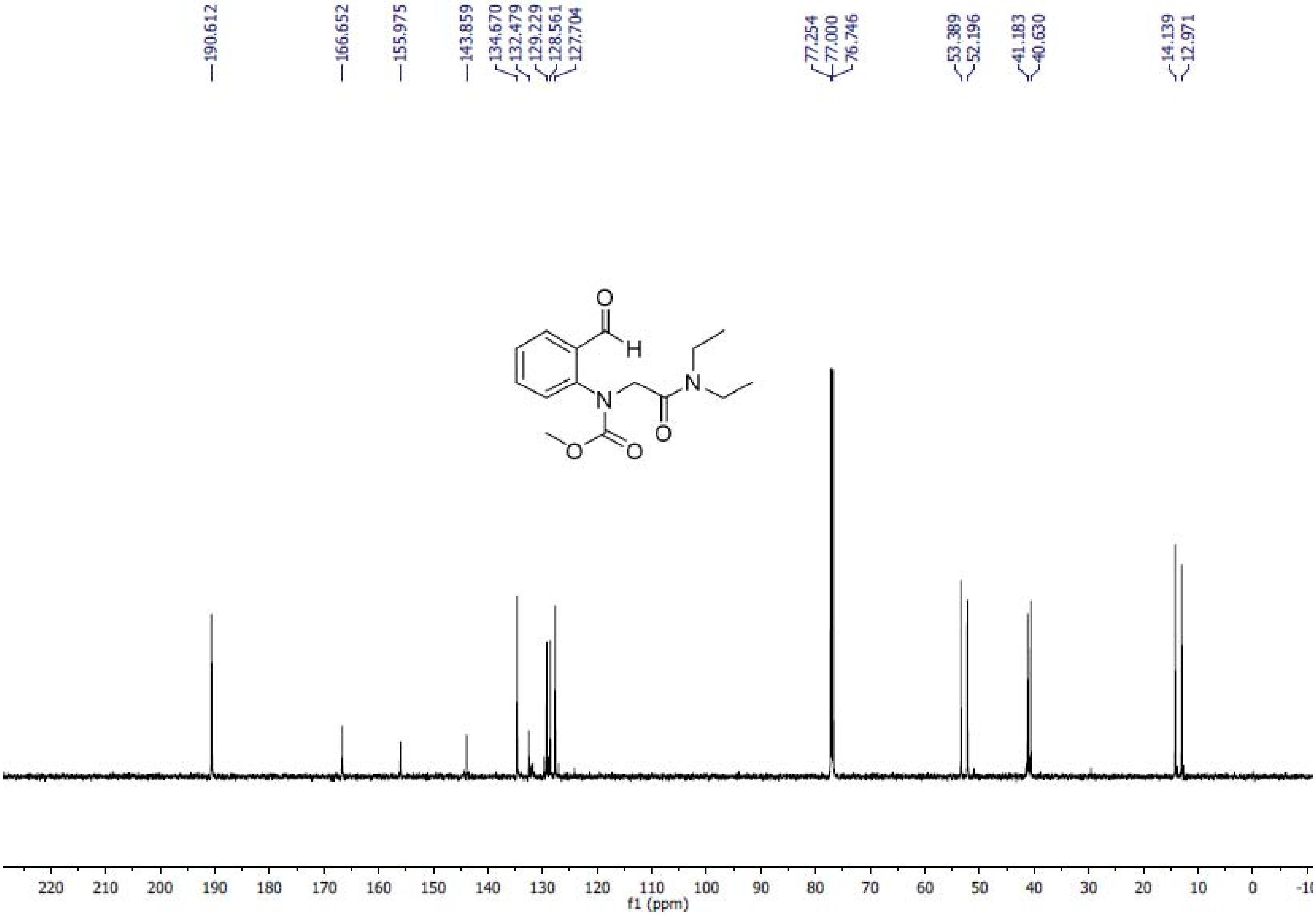
methyl *N*-(2-formylphenyl)-*N*-(methoxycarbonyl)glycinate s3-s



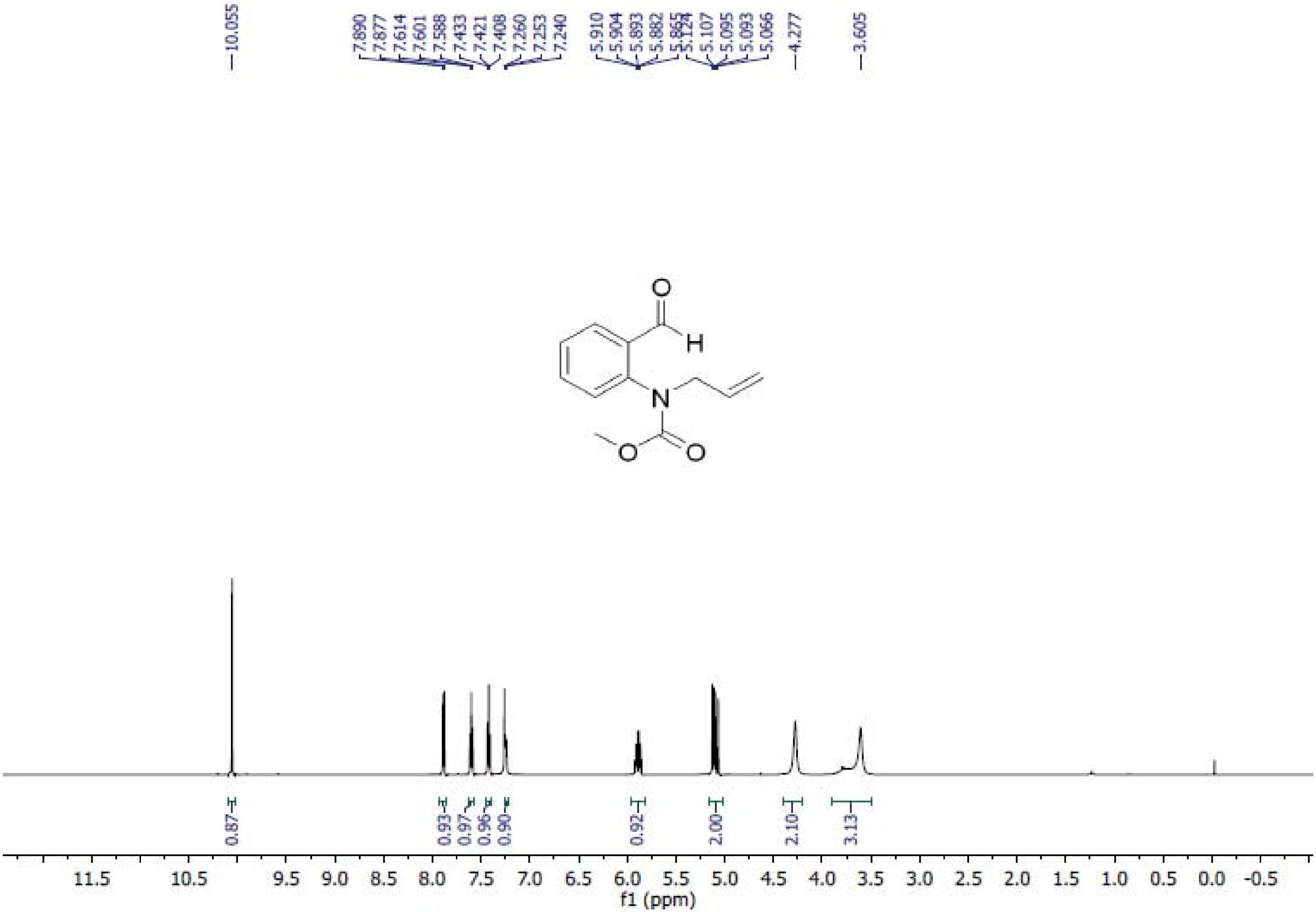
methyl (2-(diethylamino)-2-oxoethyl)(2-formylphenyl)carbamate s3-t



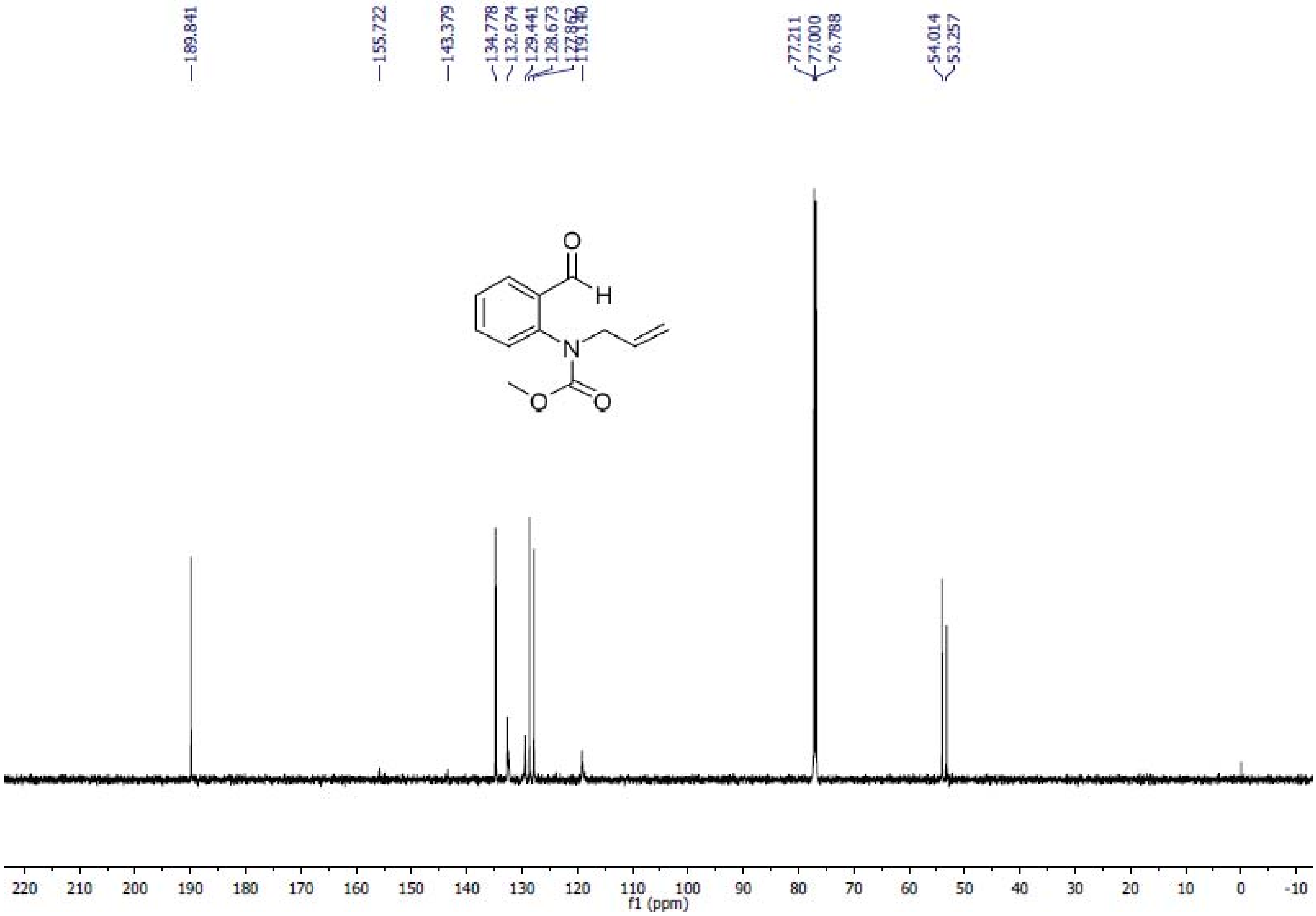
methyl (2-(diethylamino)-2-oxoethyl)(2-formylphenyl)carbamate s3-t



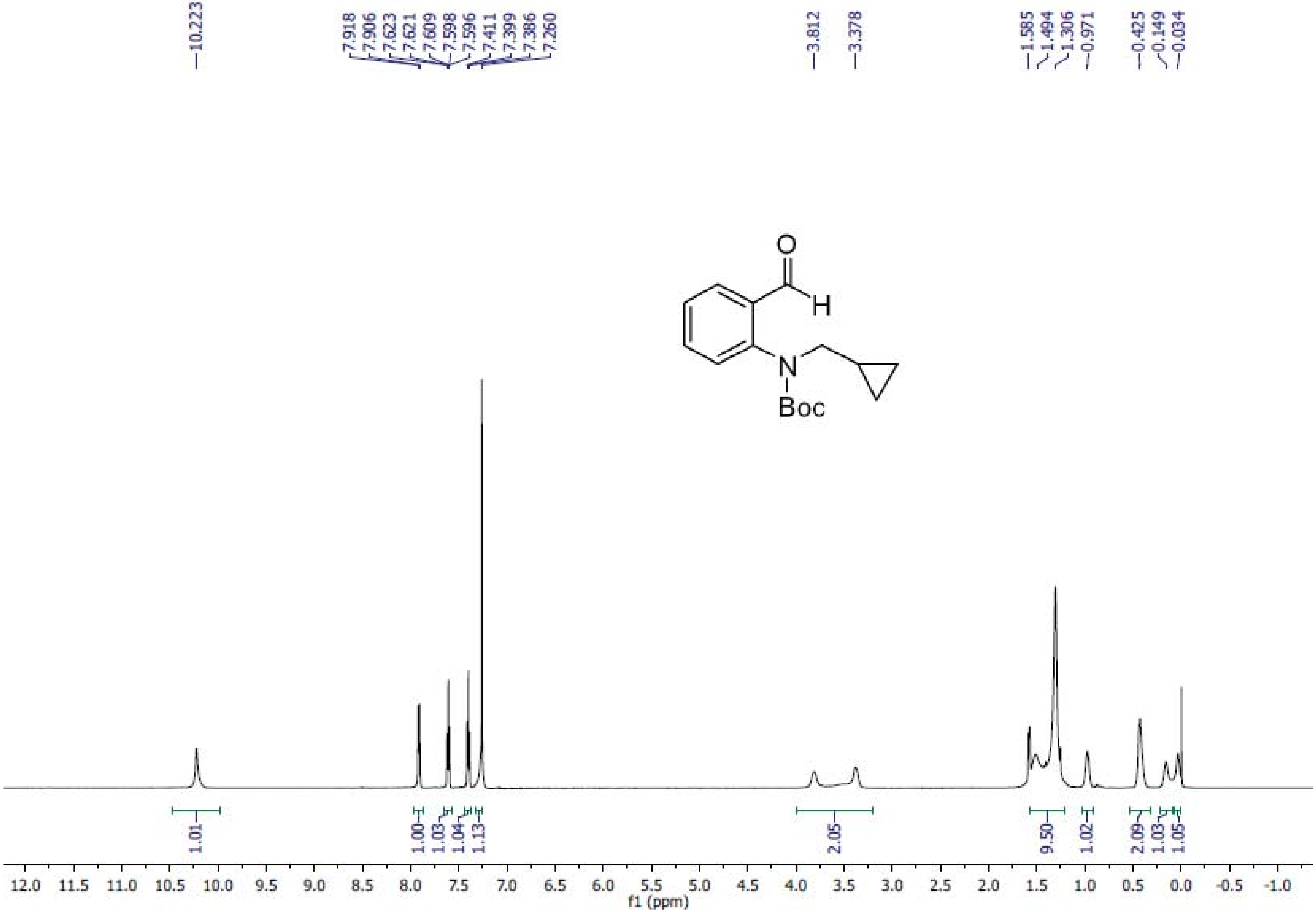
methyl allyl(2-formylphenyl)carbamate s3-u



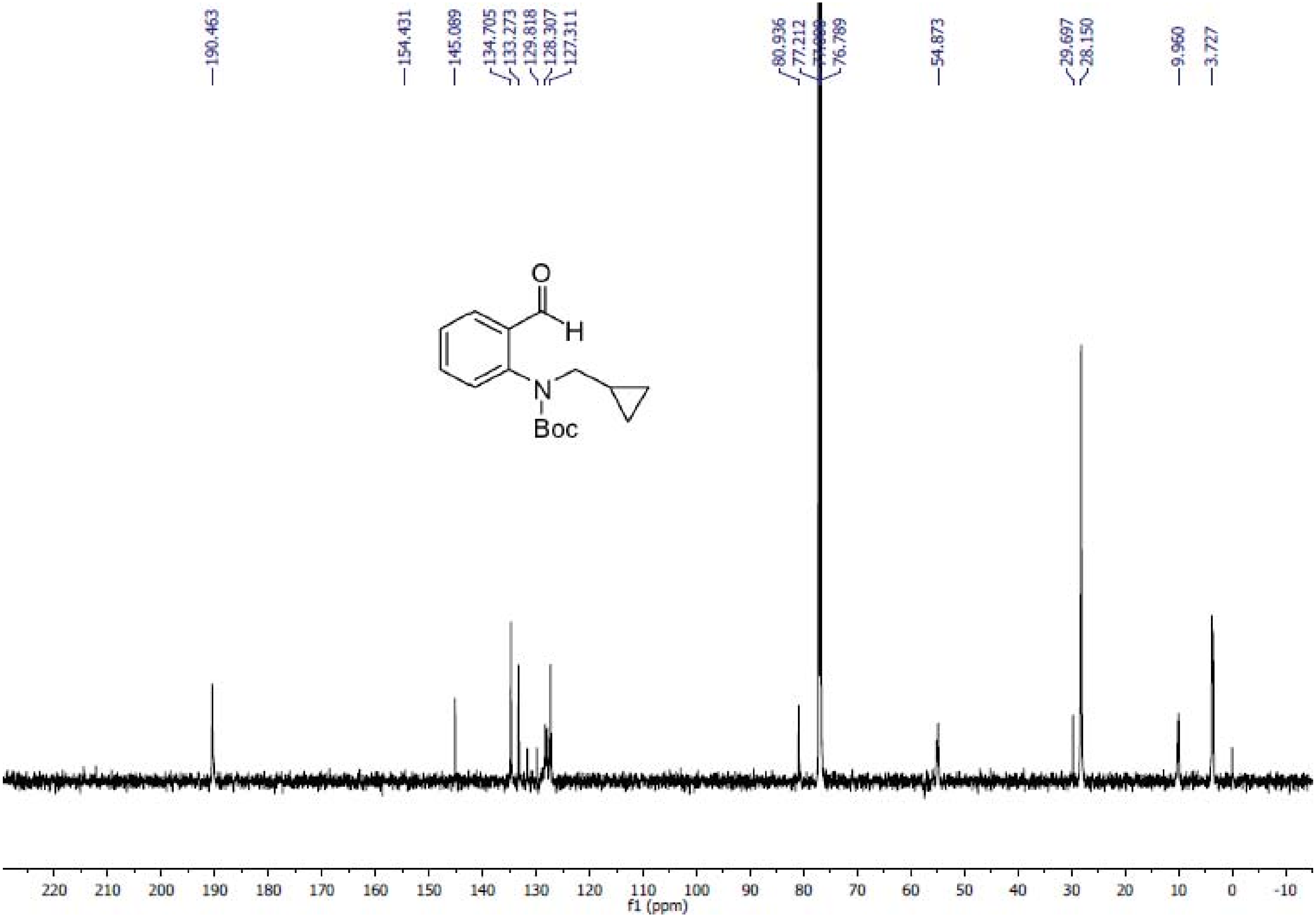
methyl allyl(2-formylphenyl)carbamate s3-u



tert-butyl (cyclopropylmethyl)(2-formylphenyl)carbamate s3-v

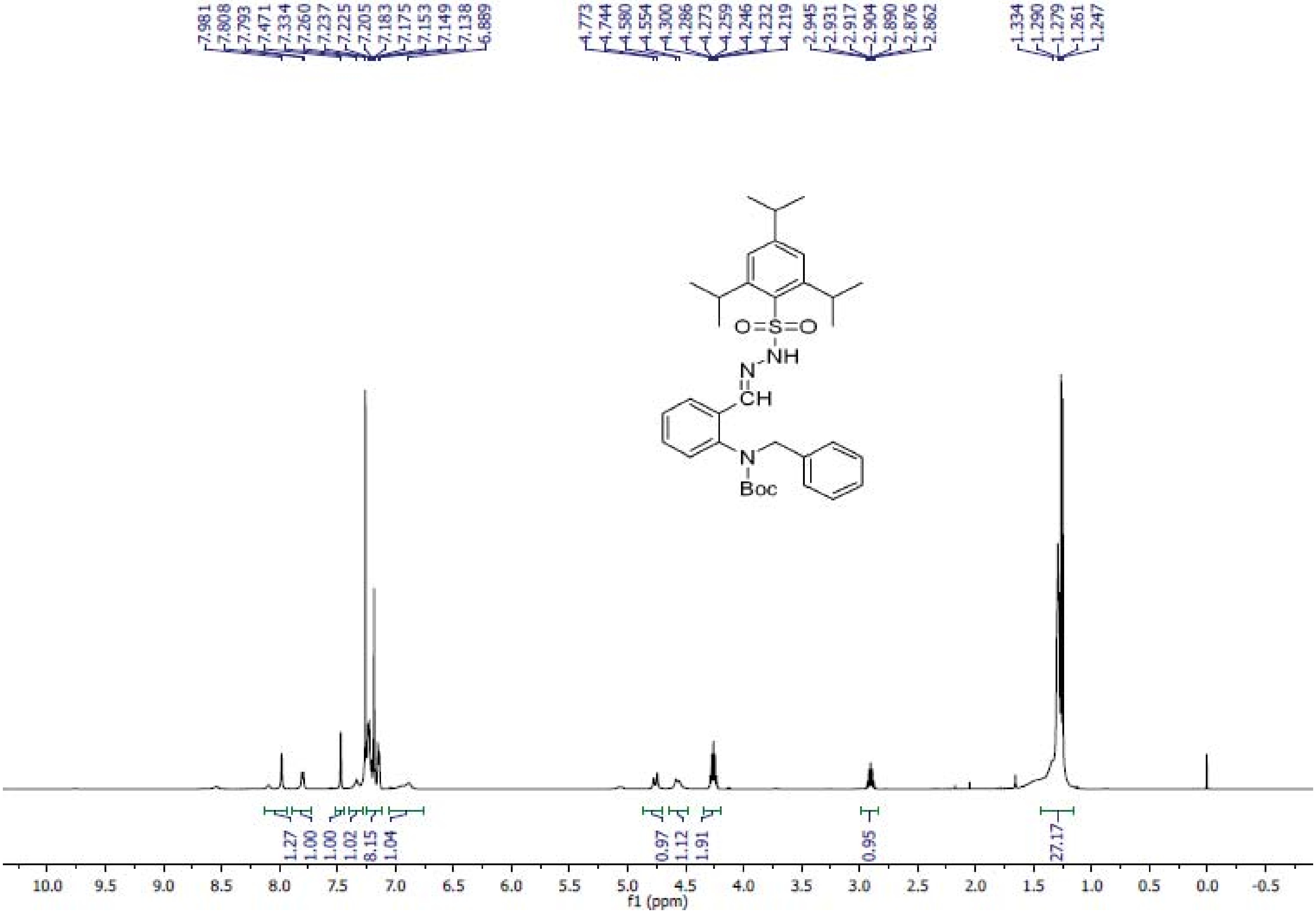


tert-butyl (cyclopropylmethyl)(2-formylphenyl)carbamate s3-v

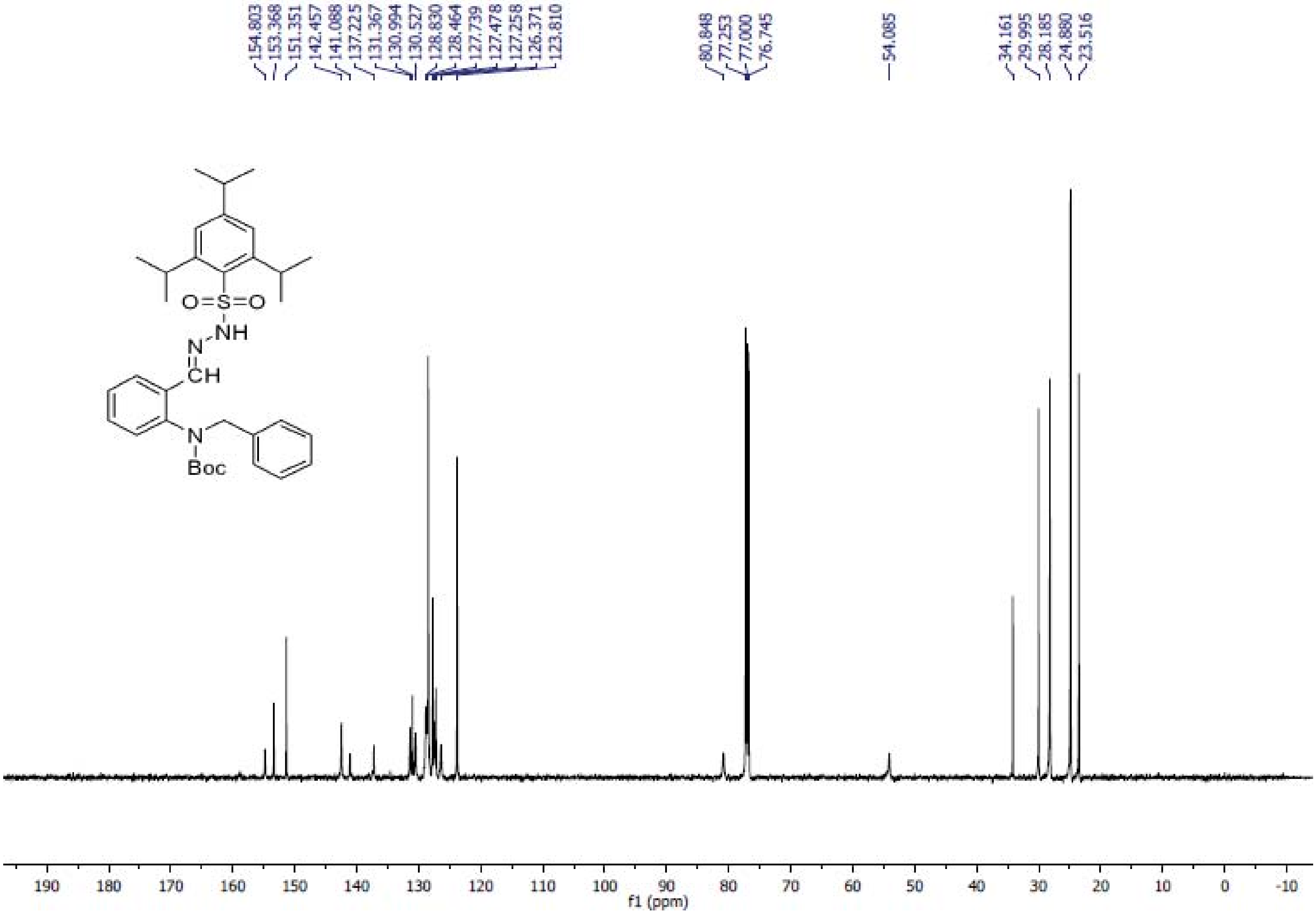


Note: The spectrum contains a mixture of amide rotamers and the major rotamer was labelled.

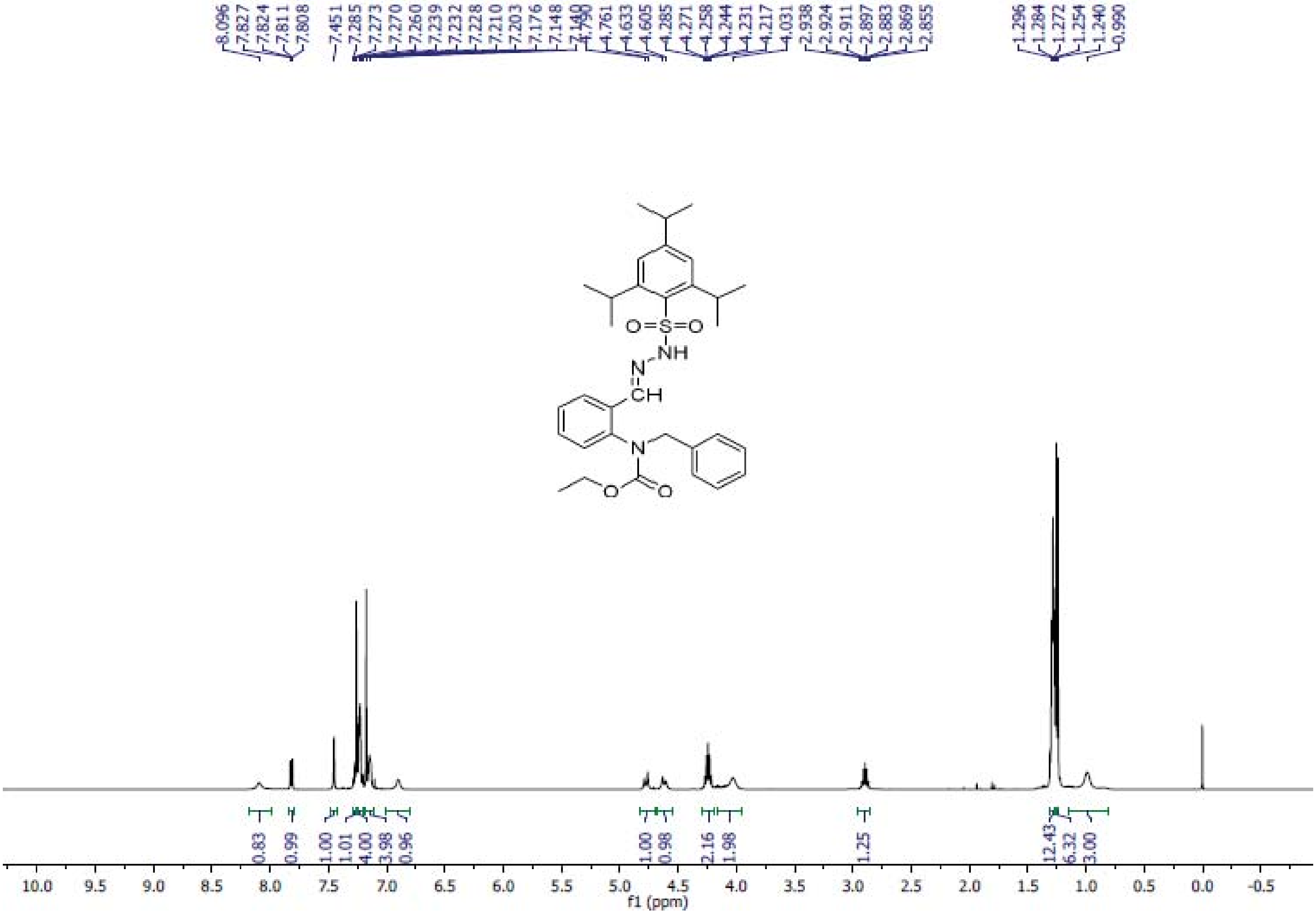
tert-butyl benzyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-a



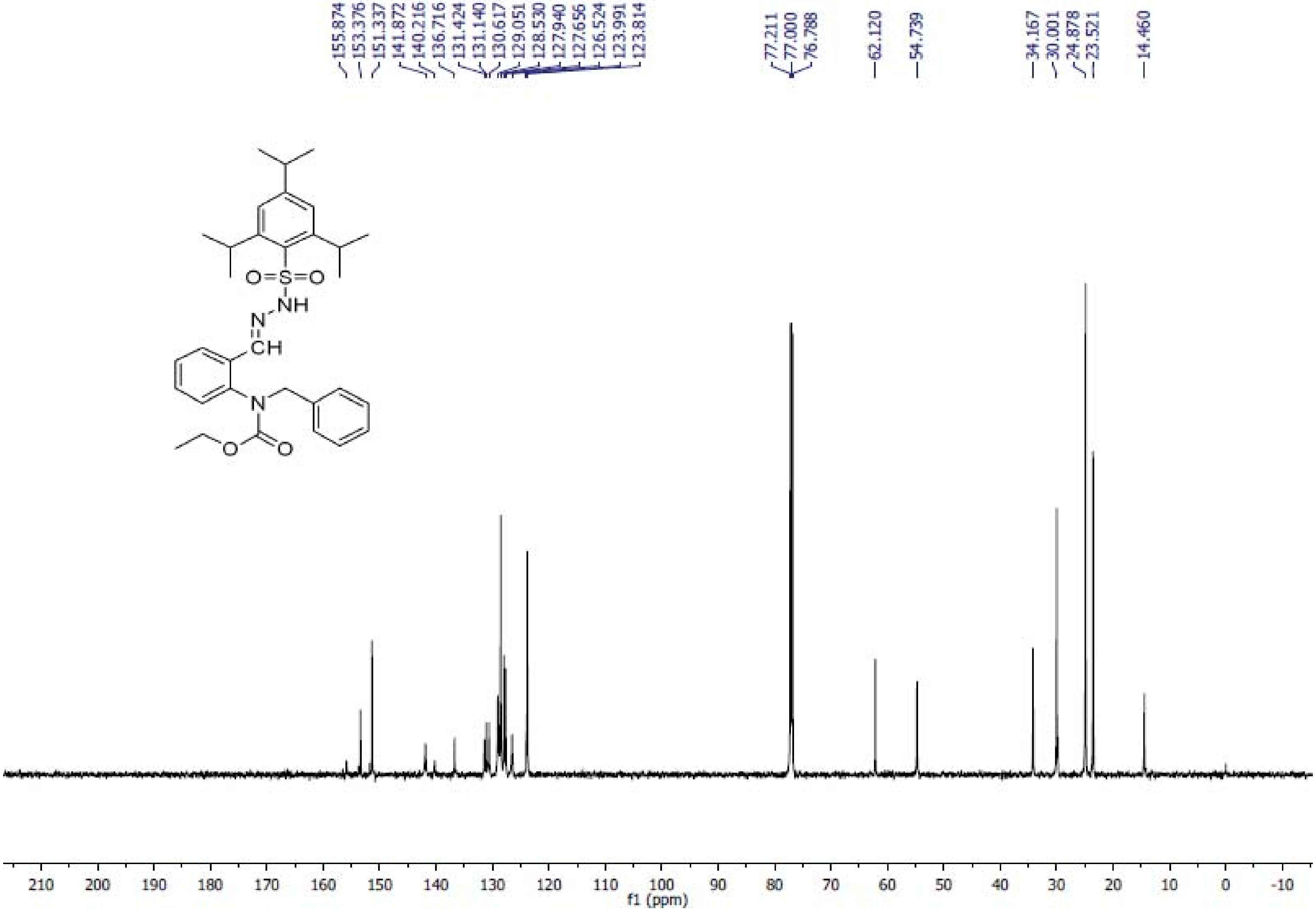
tert-butyl benzyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono) methyl)phenyl)carbamate 1-a



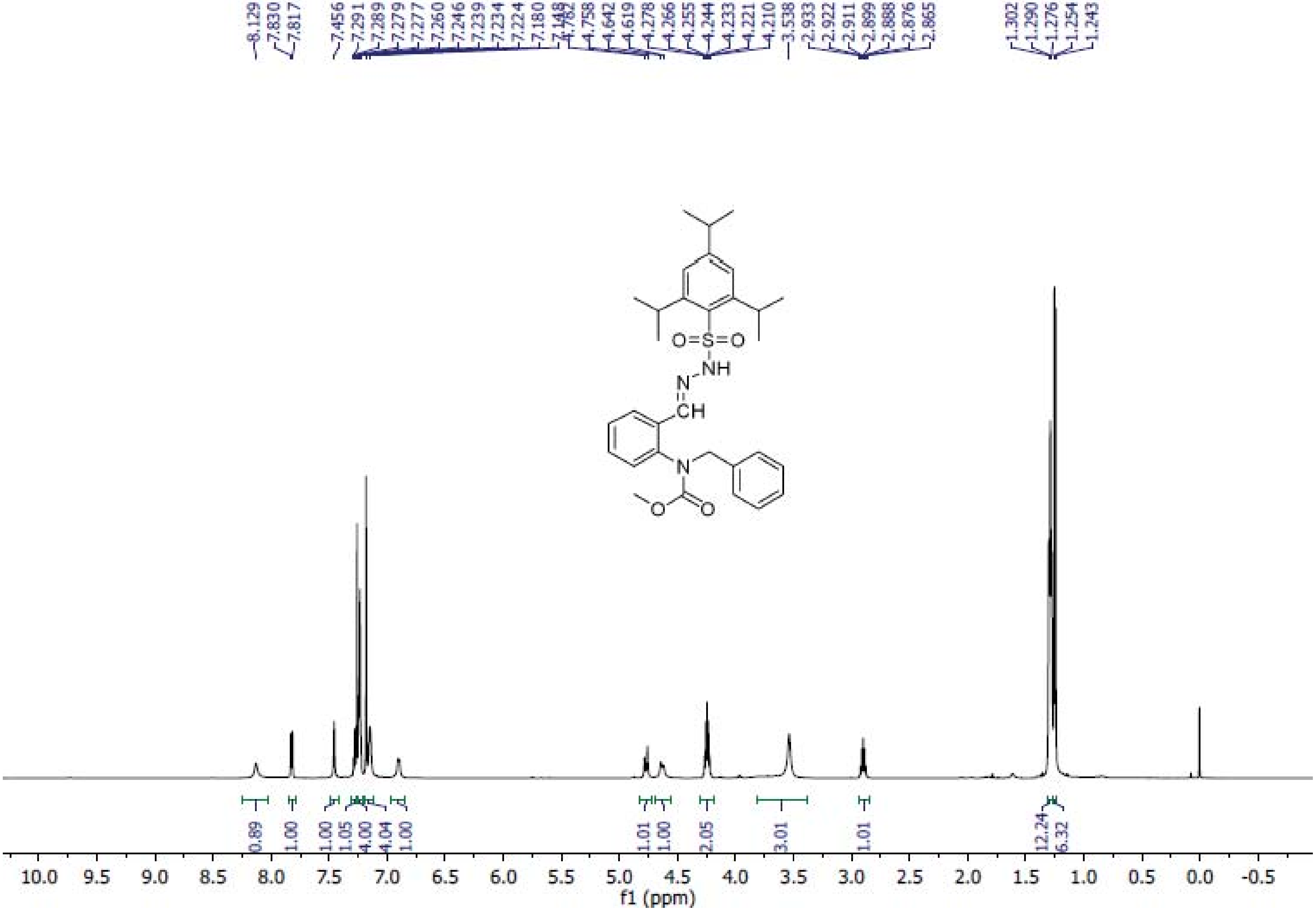
ethyl benzyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl) carbamate 1-b



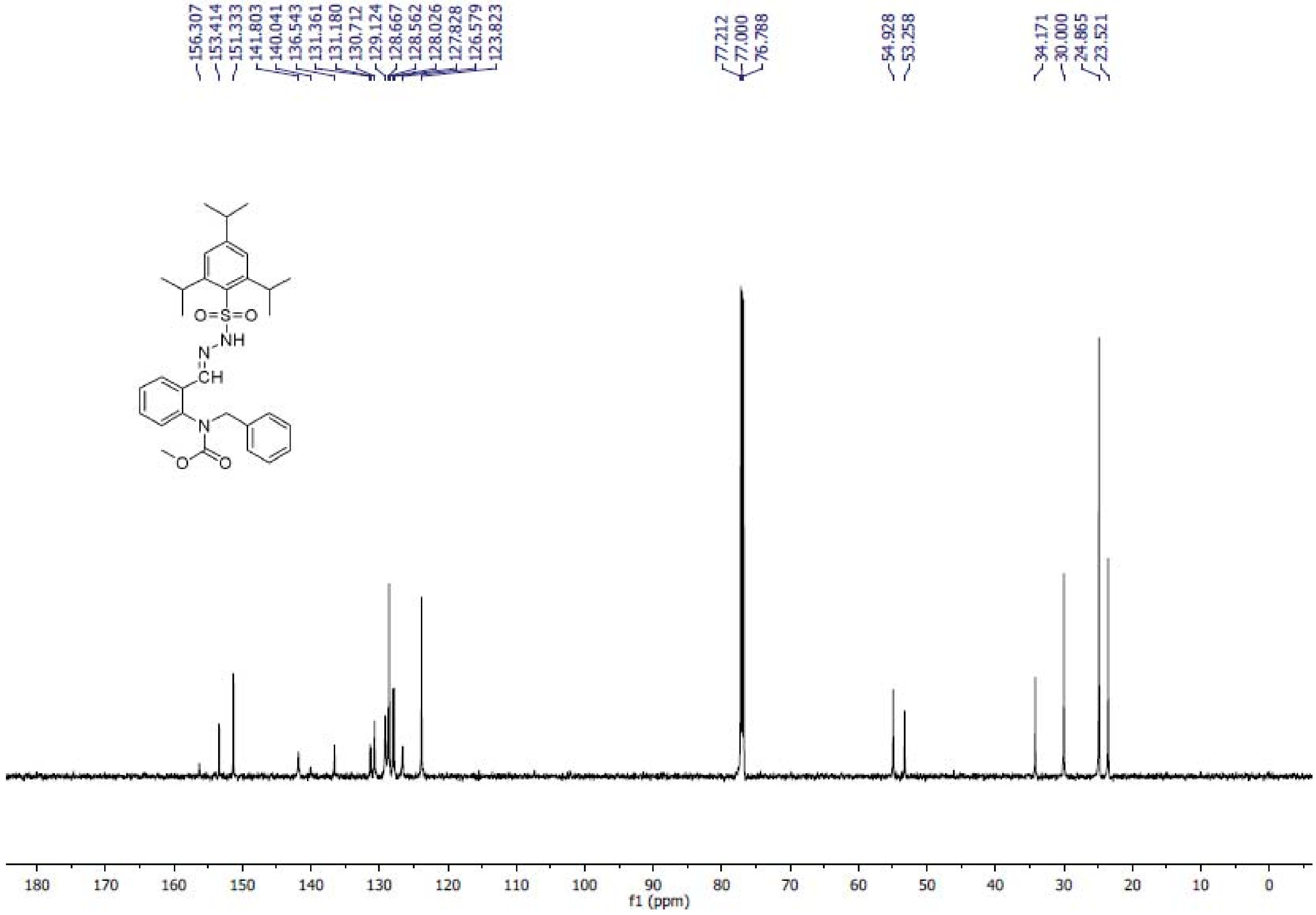
ethyl benzyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl) carbamate 1-b



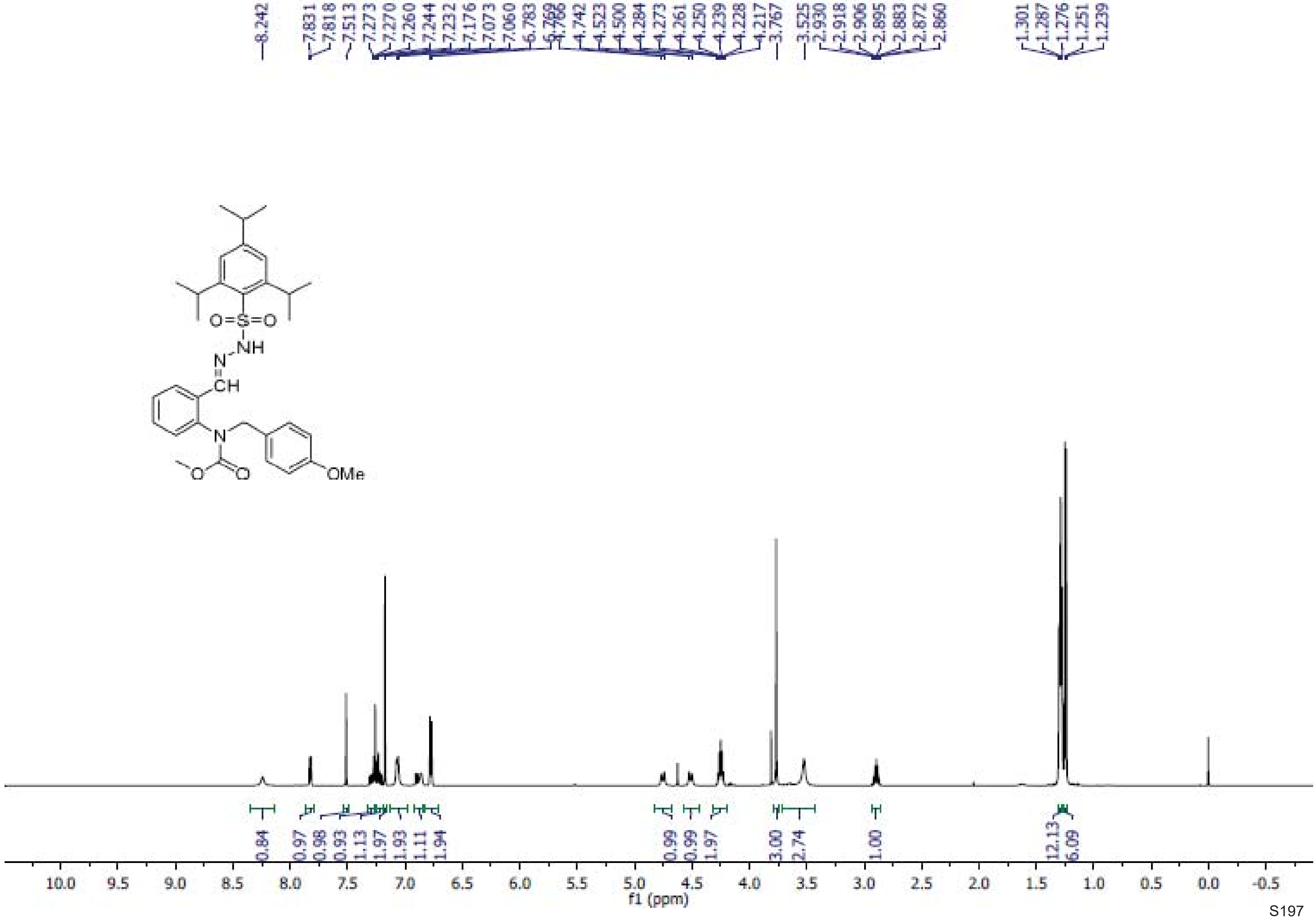
methyl benzyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-c



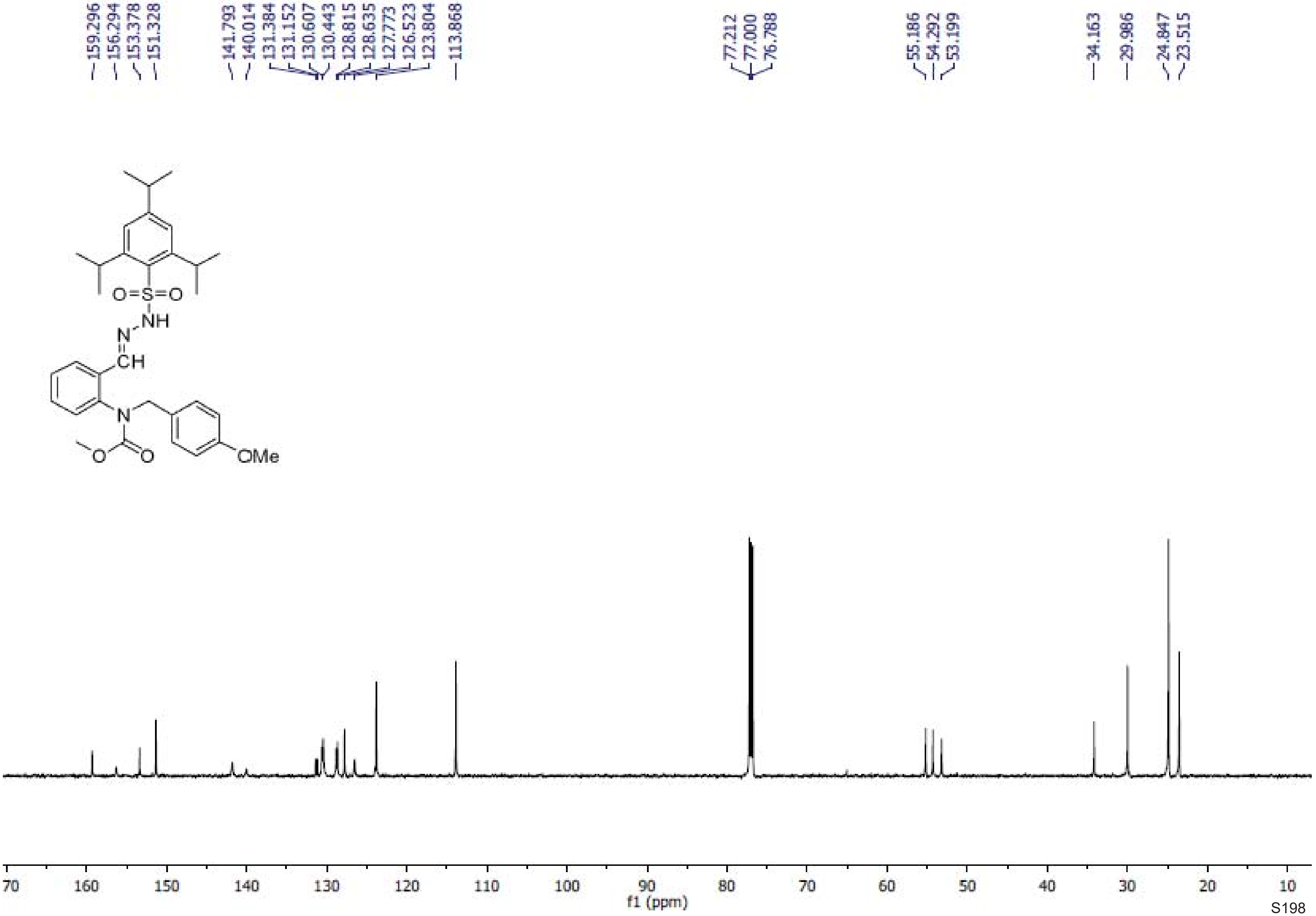
methyl benzyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-c



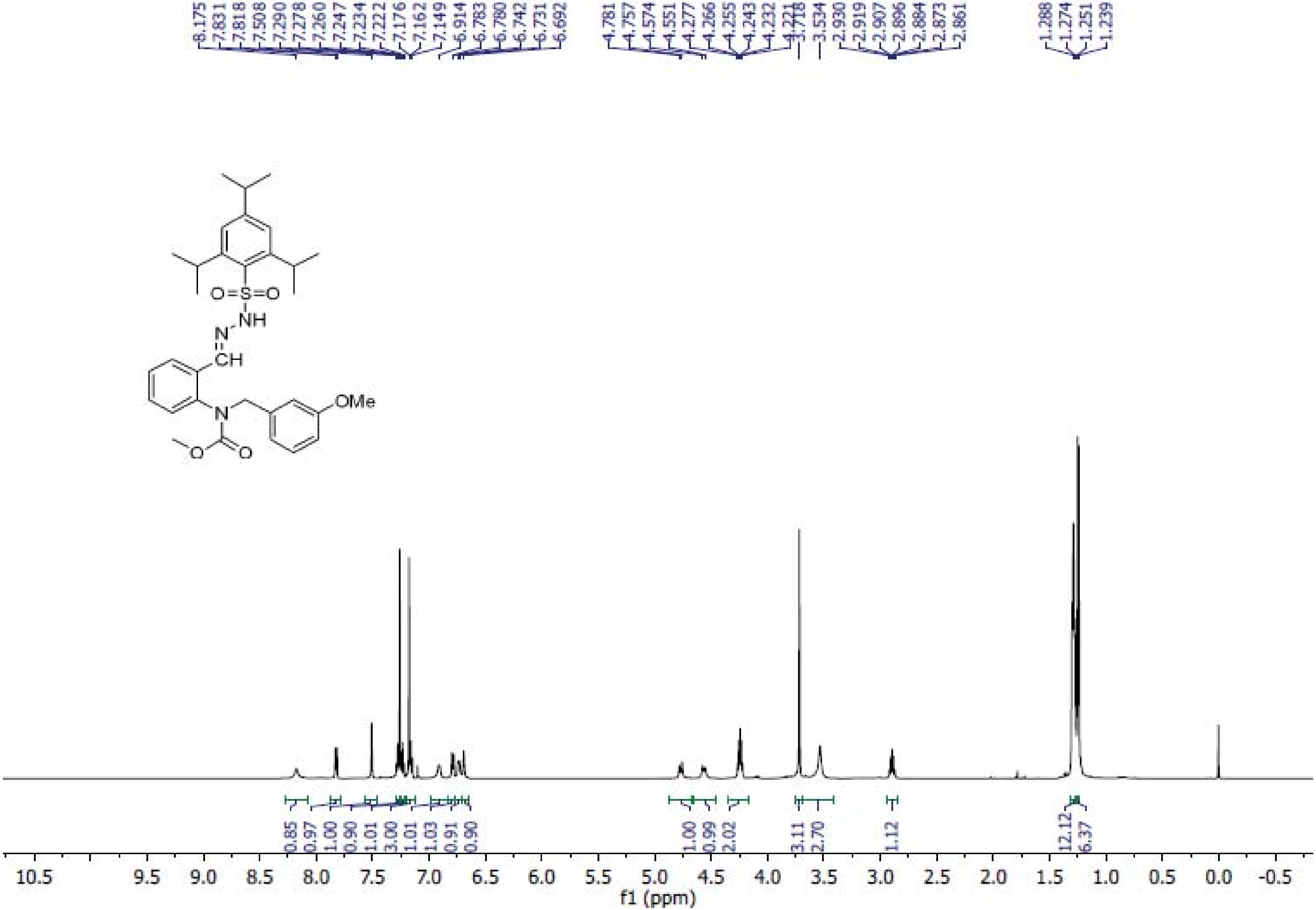
methyl (4-methoxybenzyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-d



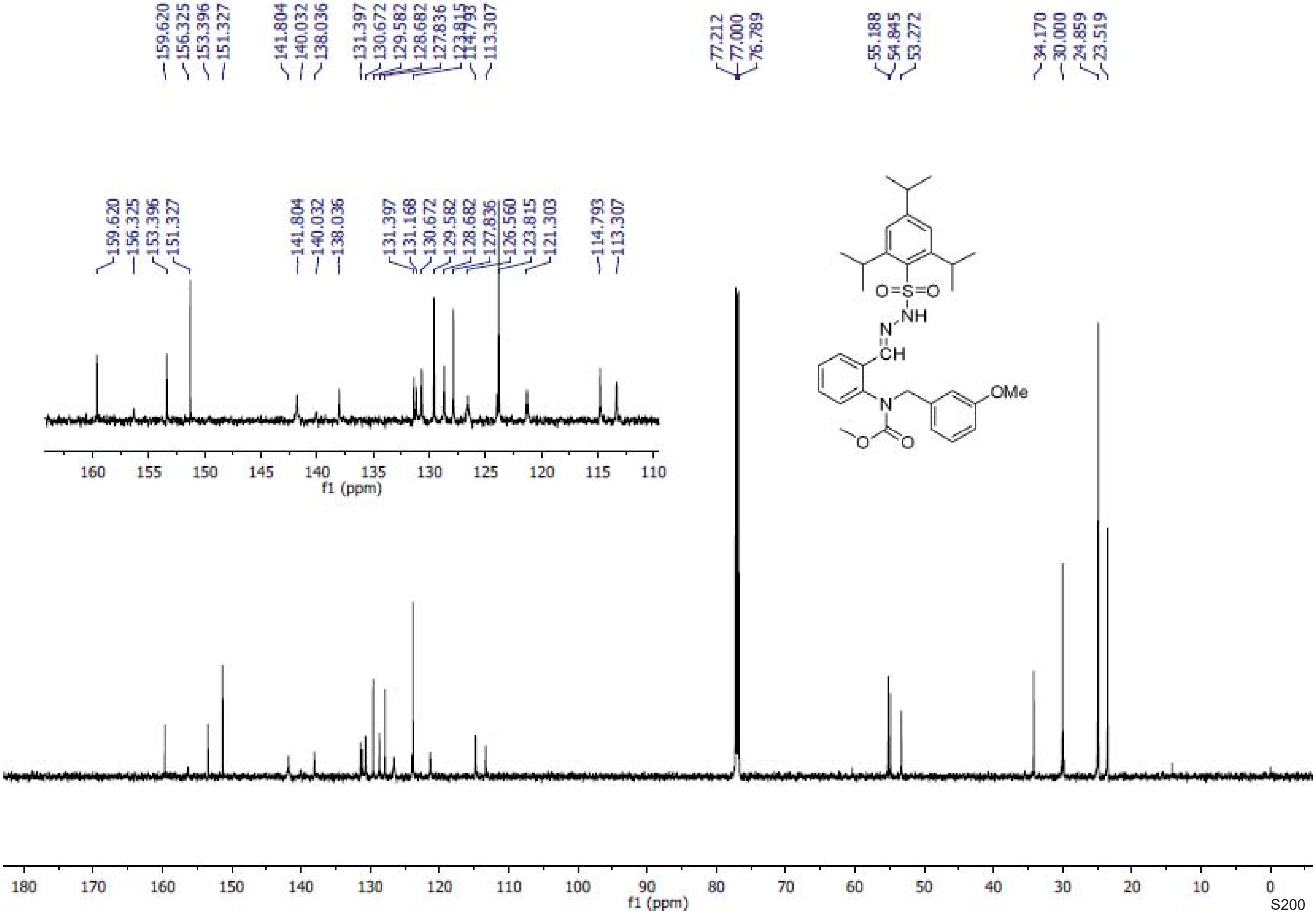
methyl (4-methoxybenzyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-d



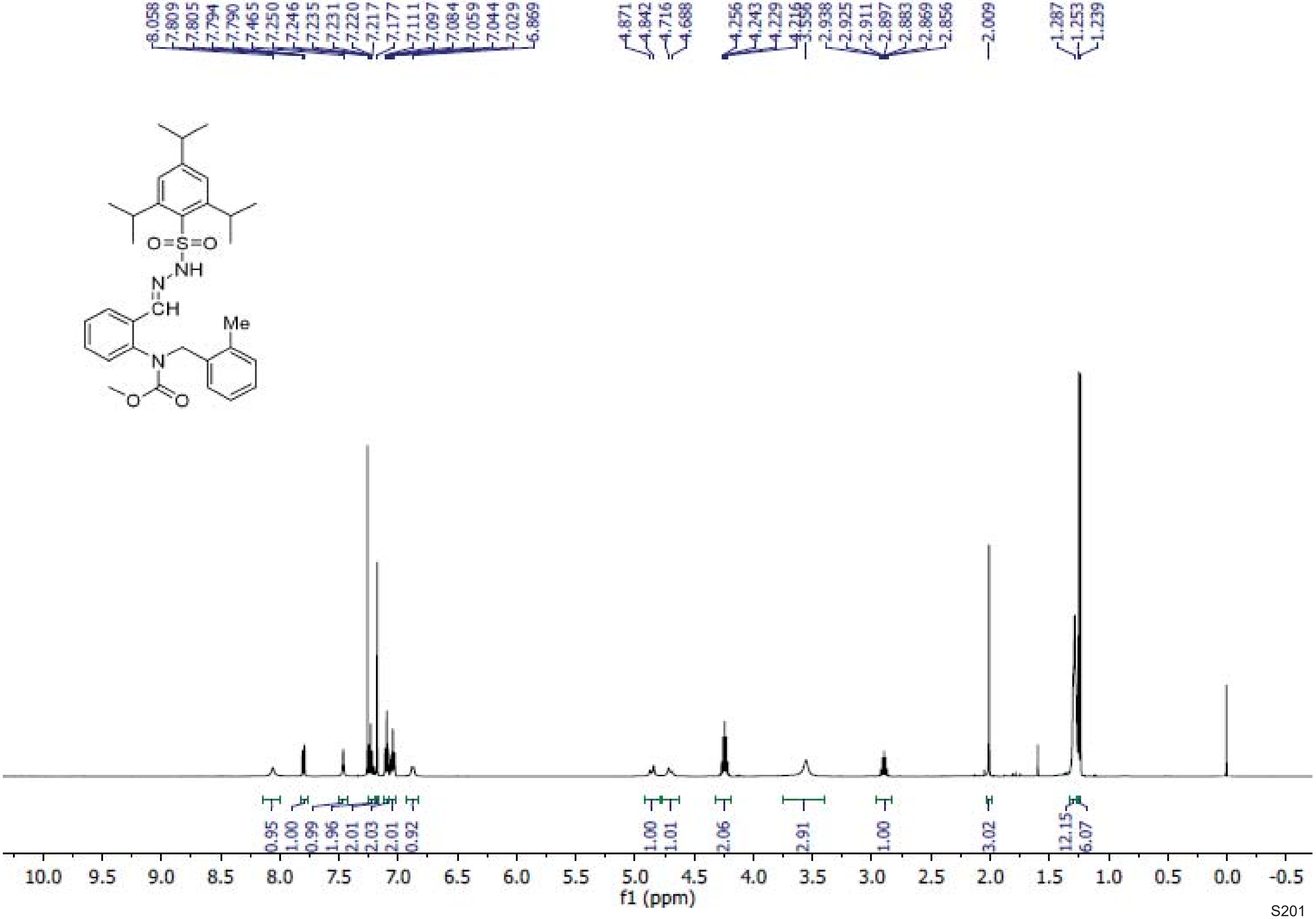
methyl (3-methoxybenzyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl) hydrazono)methyl)phenyl)carbamate 1-e



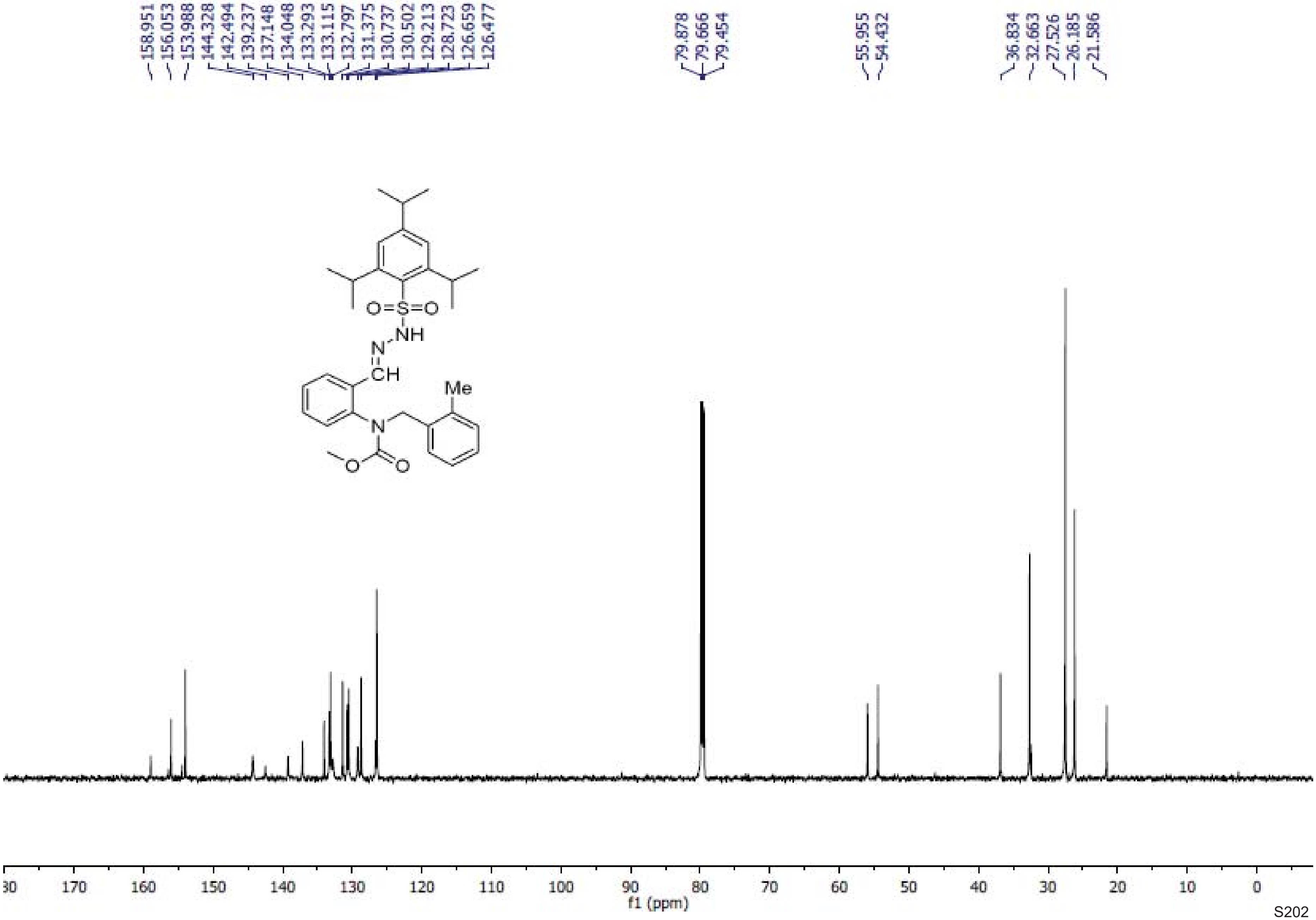
methyl (3-methoxybenzyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl) hydrazono)methyl)phenyl)carbamate 1-e



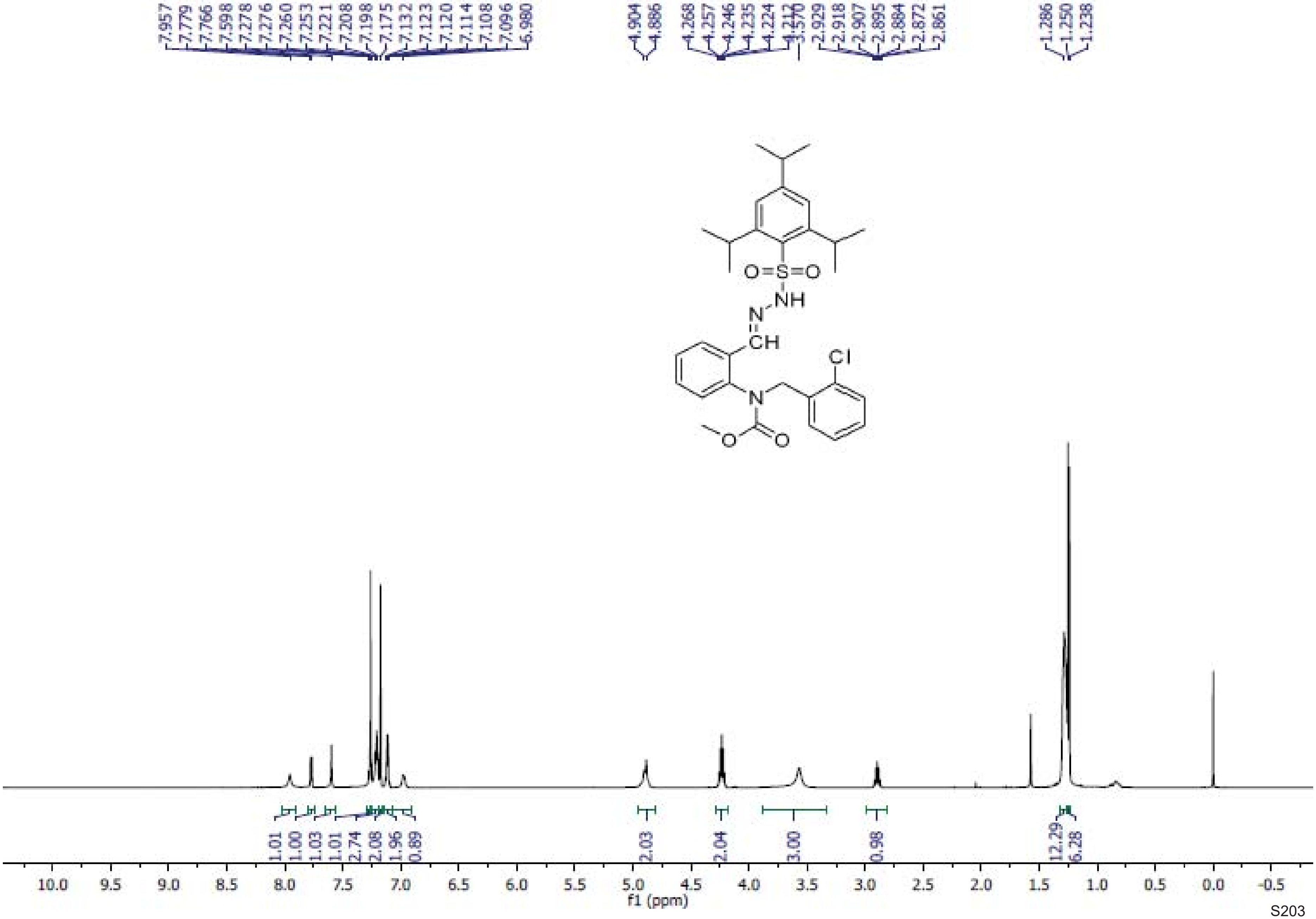
methyl (2-methylbenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-f



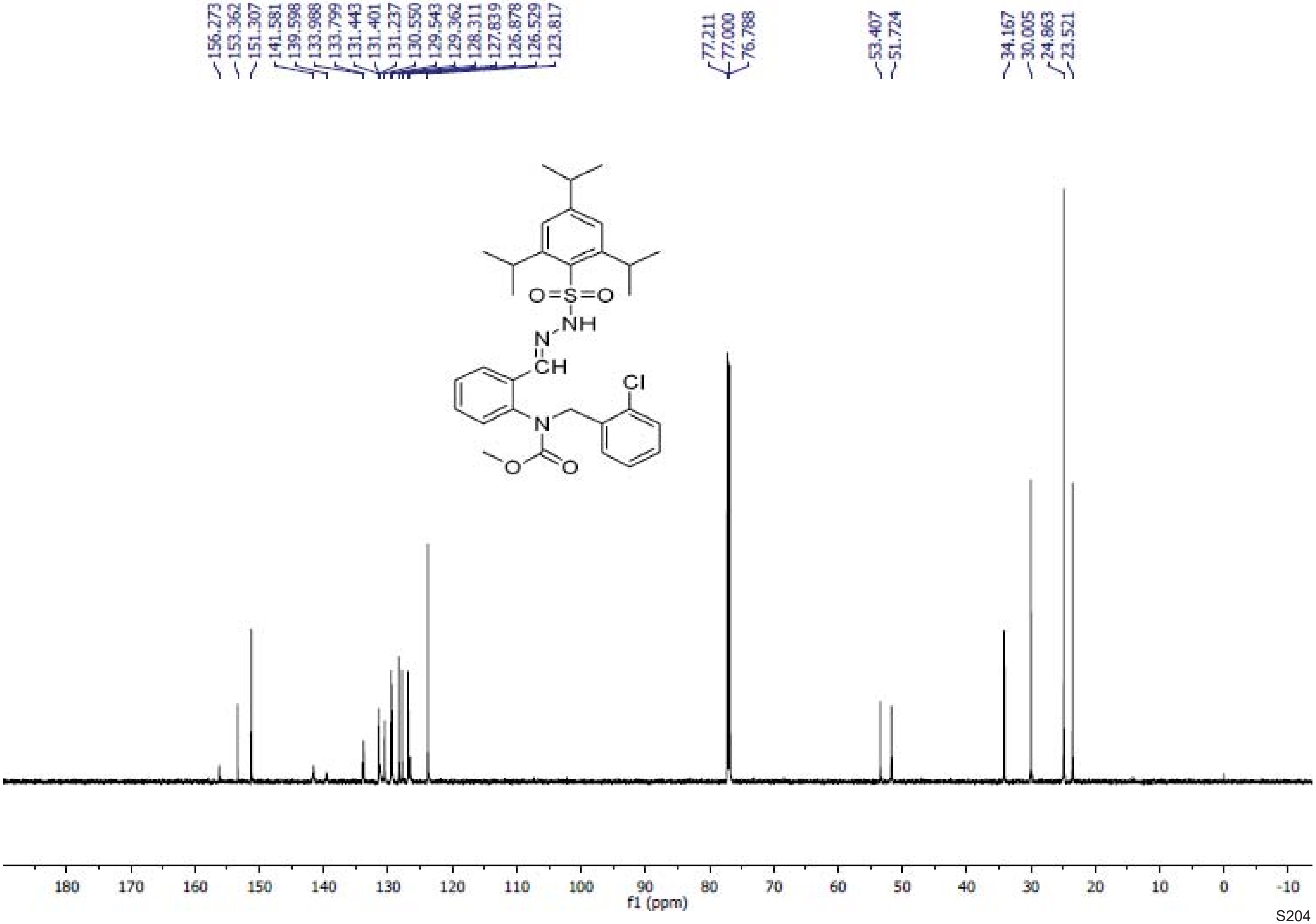
methyl (2-methylbenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-f



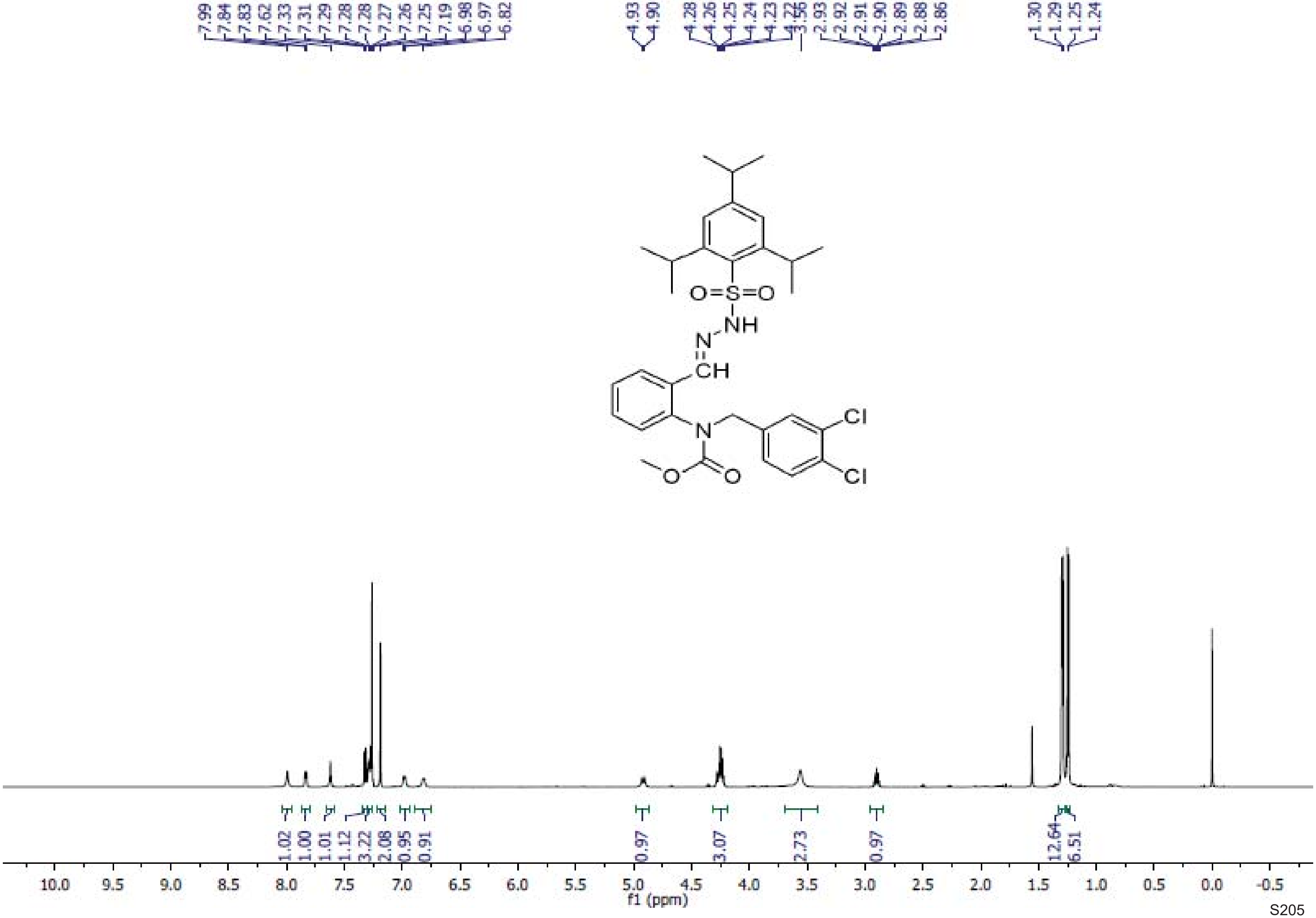
methyl (2-chlorobenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-g



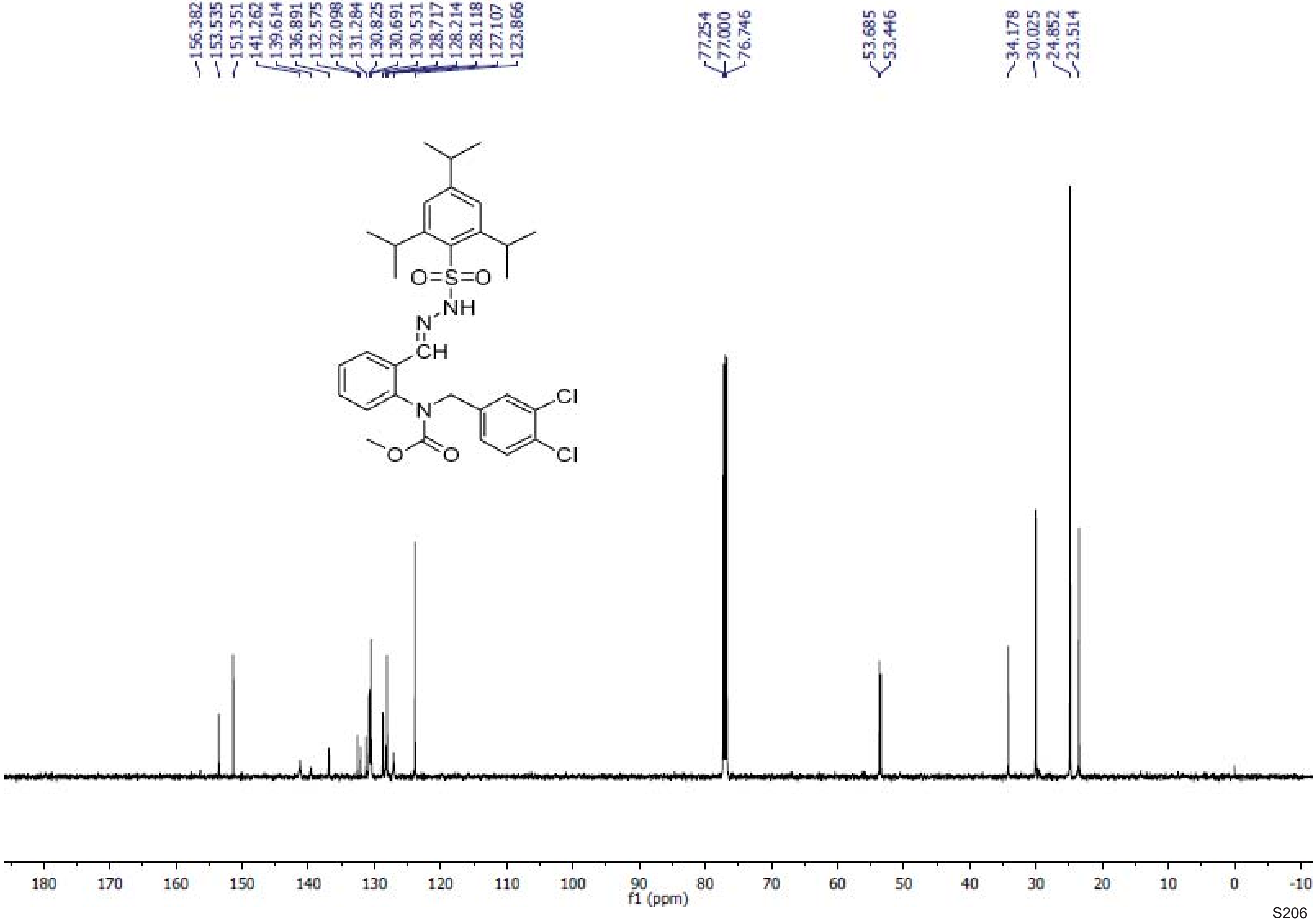
methyl (2-chlorobenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-g



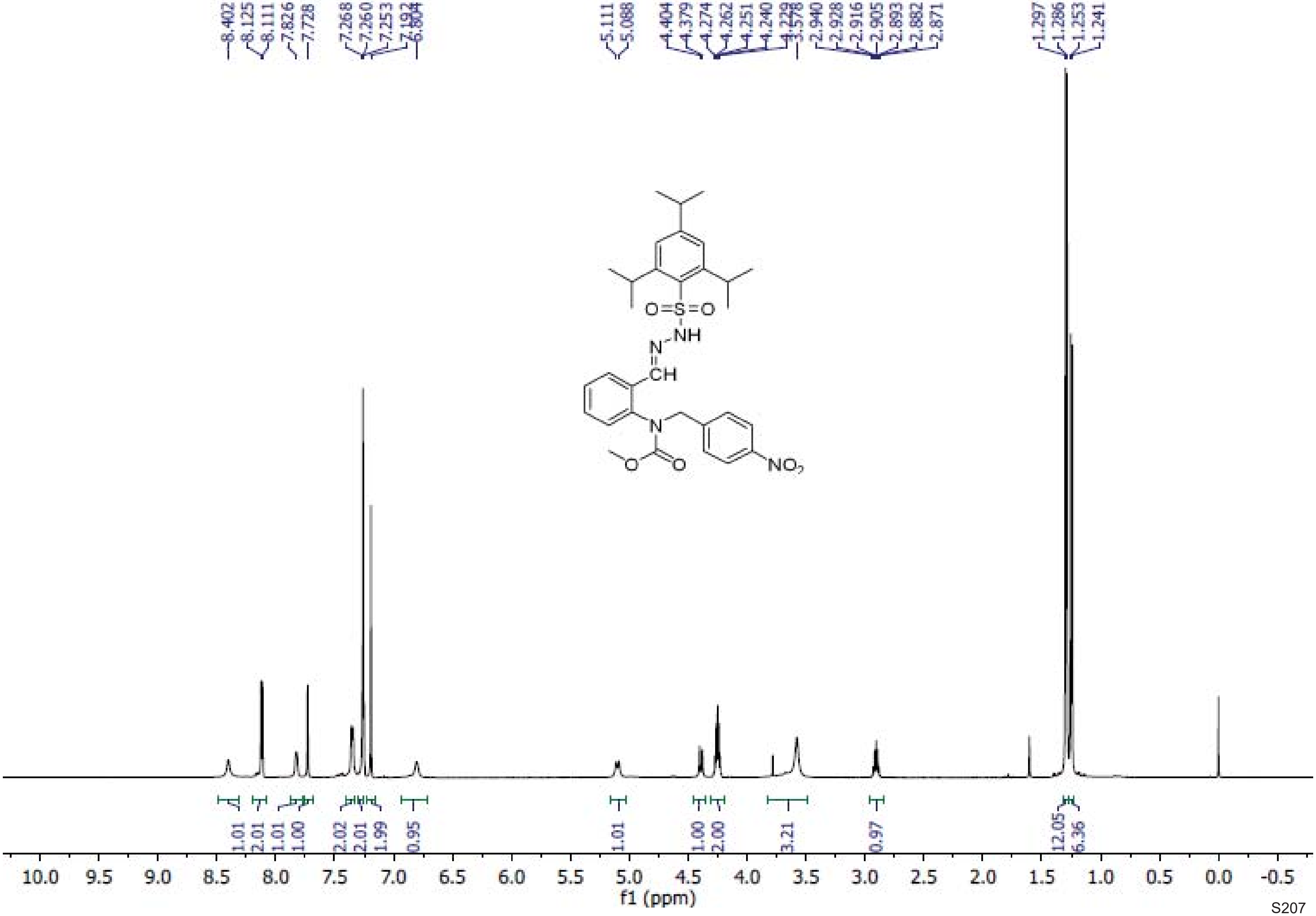
methyl (3,4-dichlorobenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-h



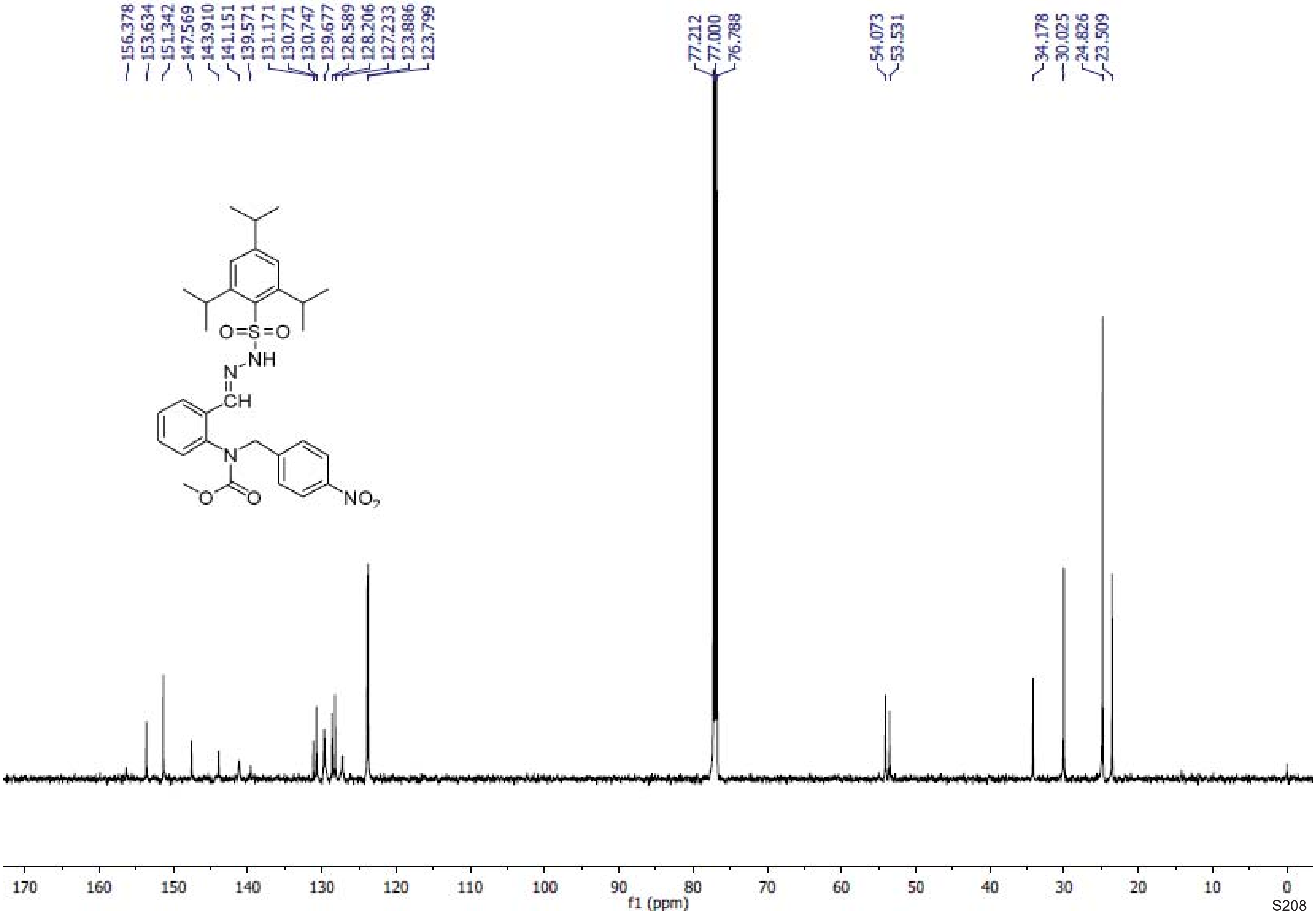
methyl (3,4-dichlorobenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-h



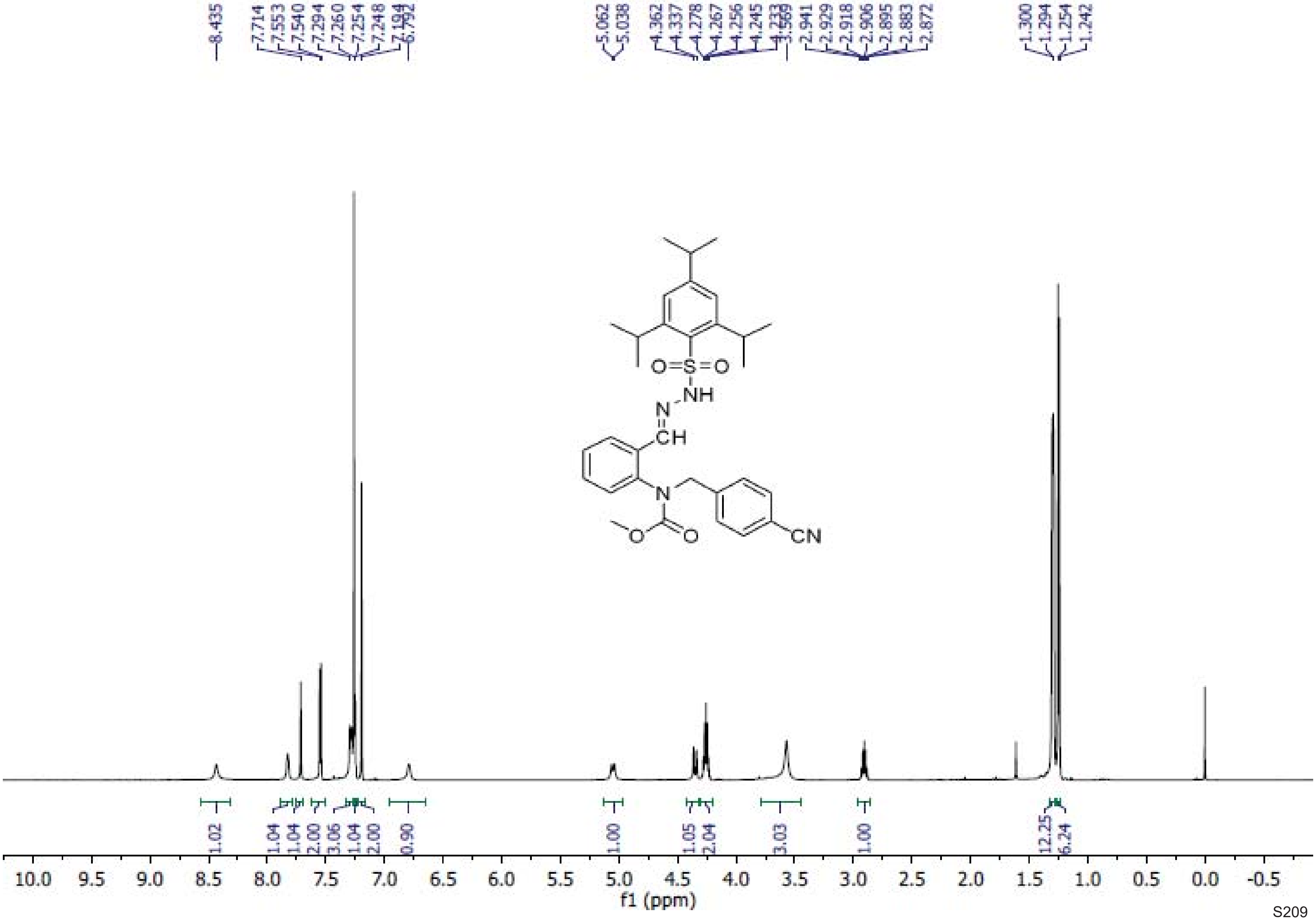
methyl (4-nitrobenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-i



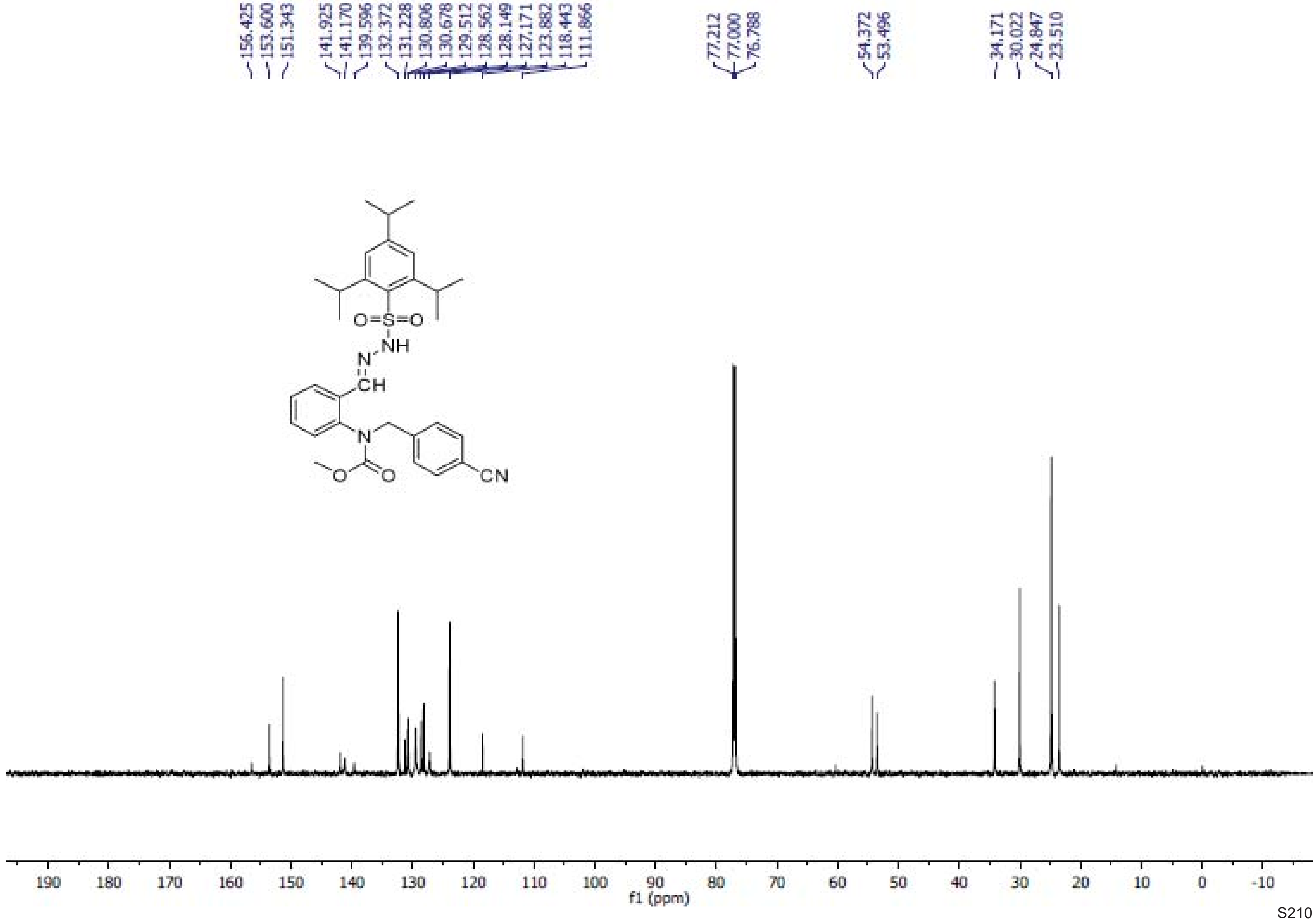
methyl (4-nitrobenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-i



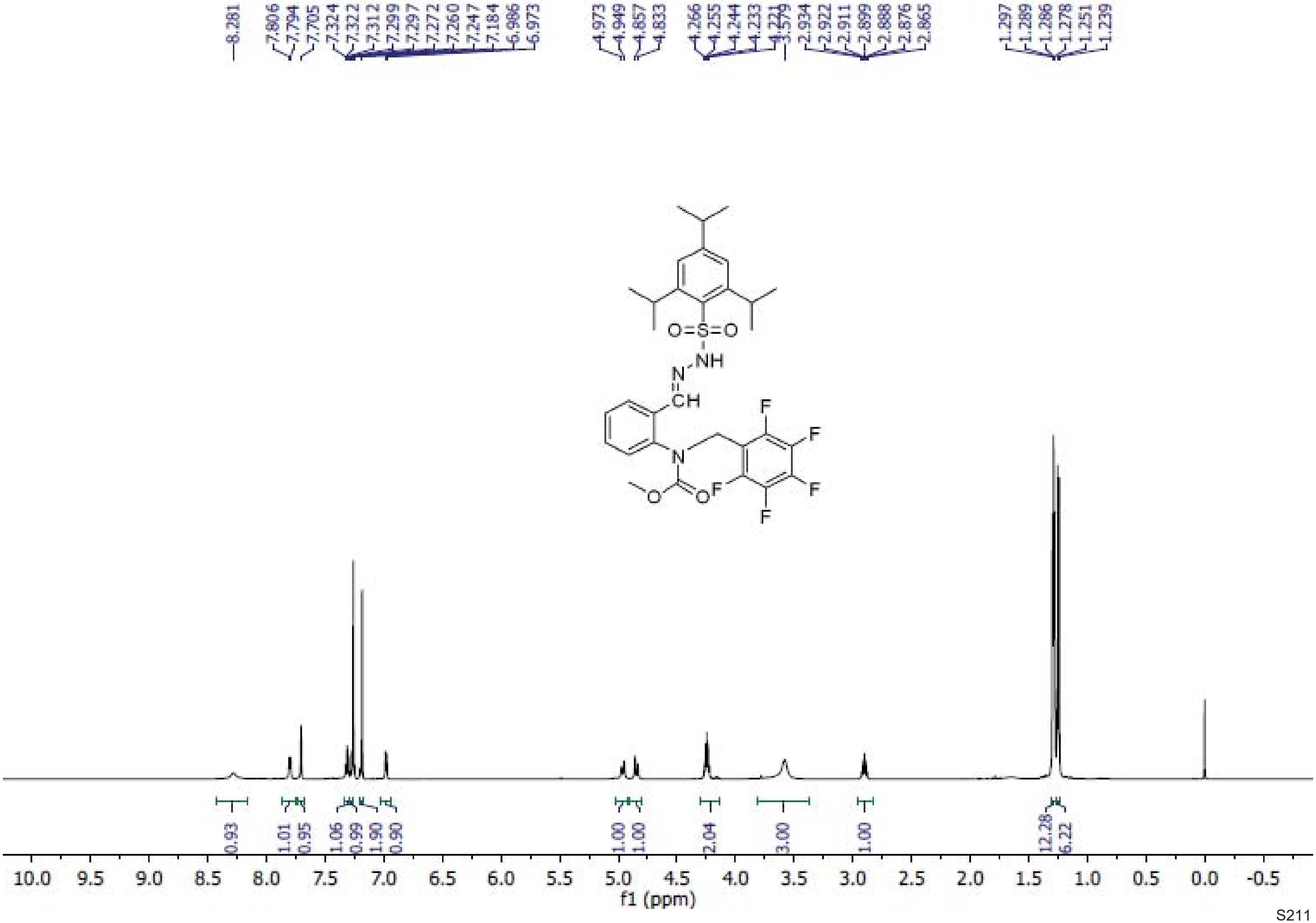
methyl (4-cyanobenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-j



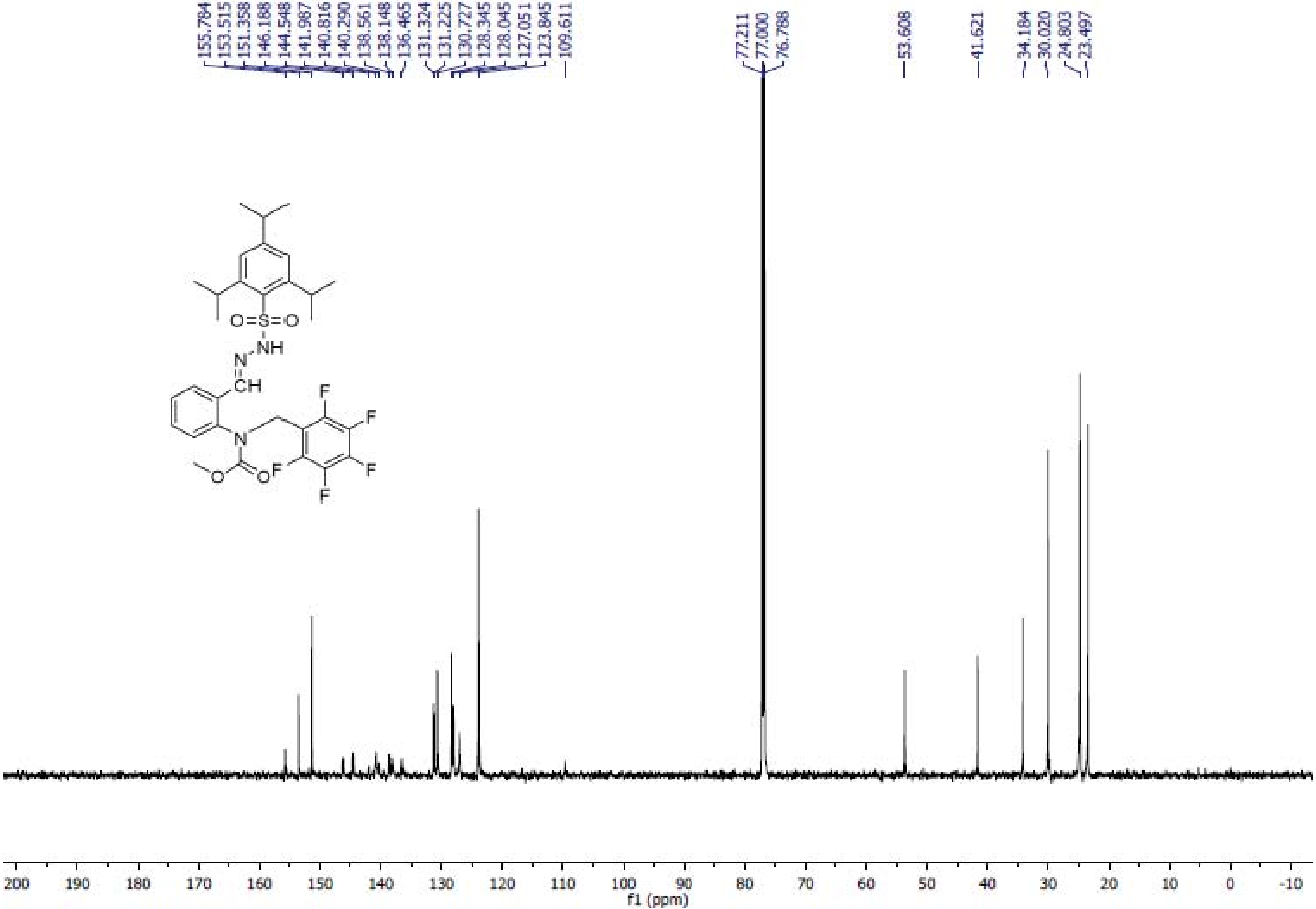
methyl (4-cyanobenzyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-j



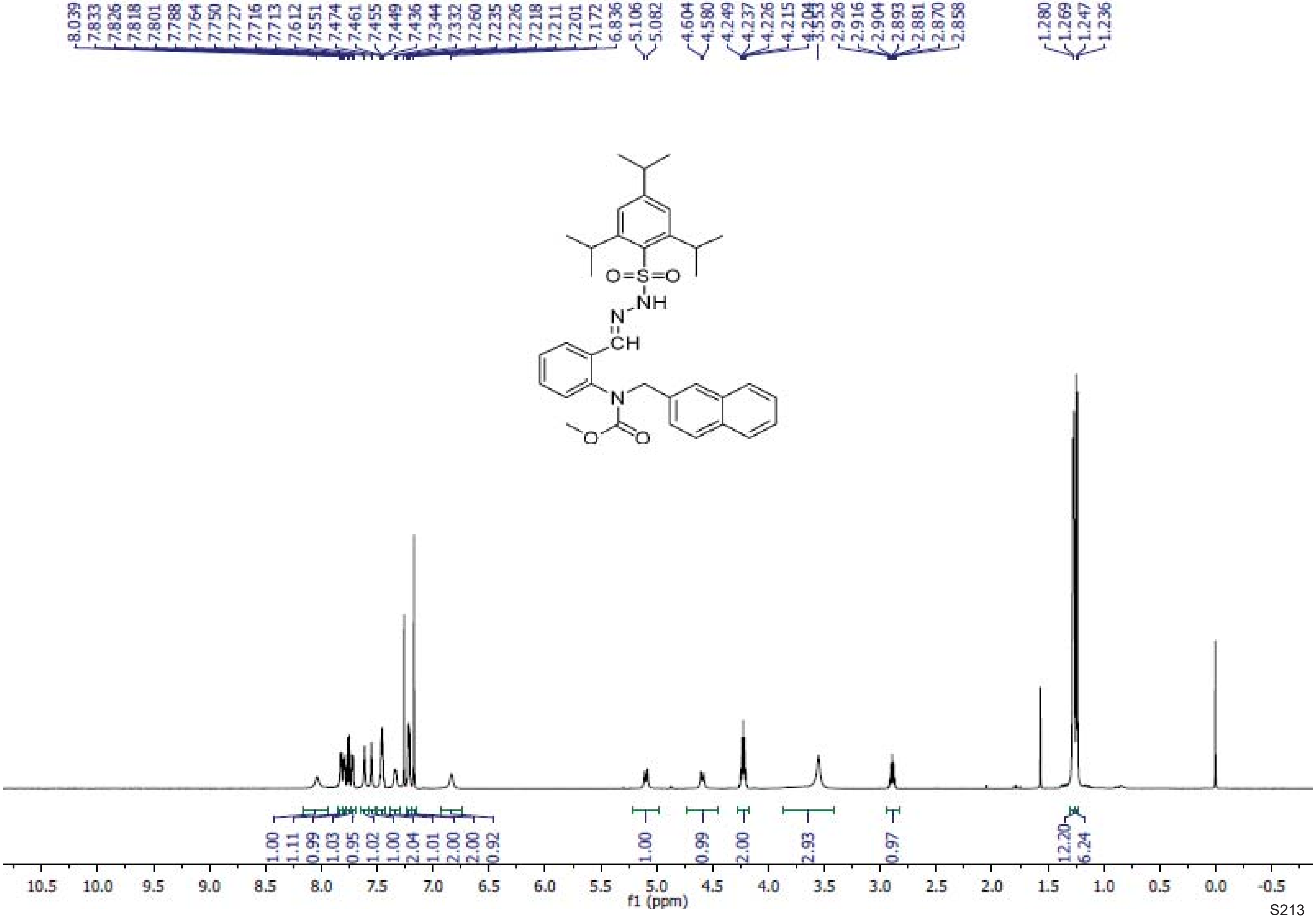
methyl ((perfluorophenyl)methyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-k



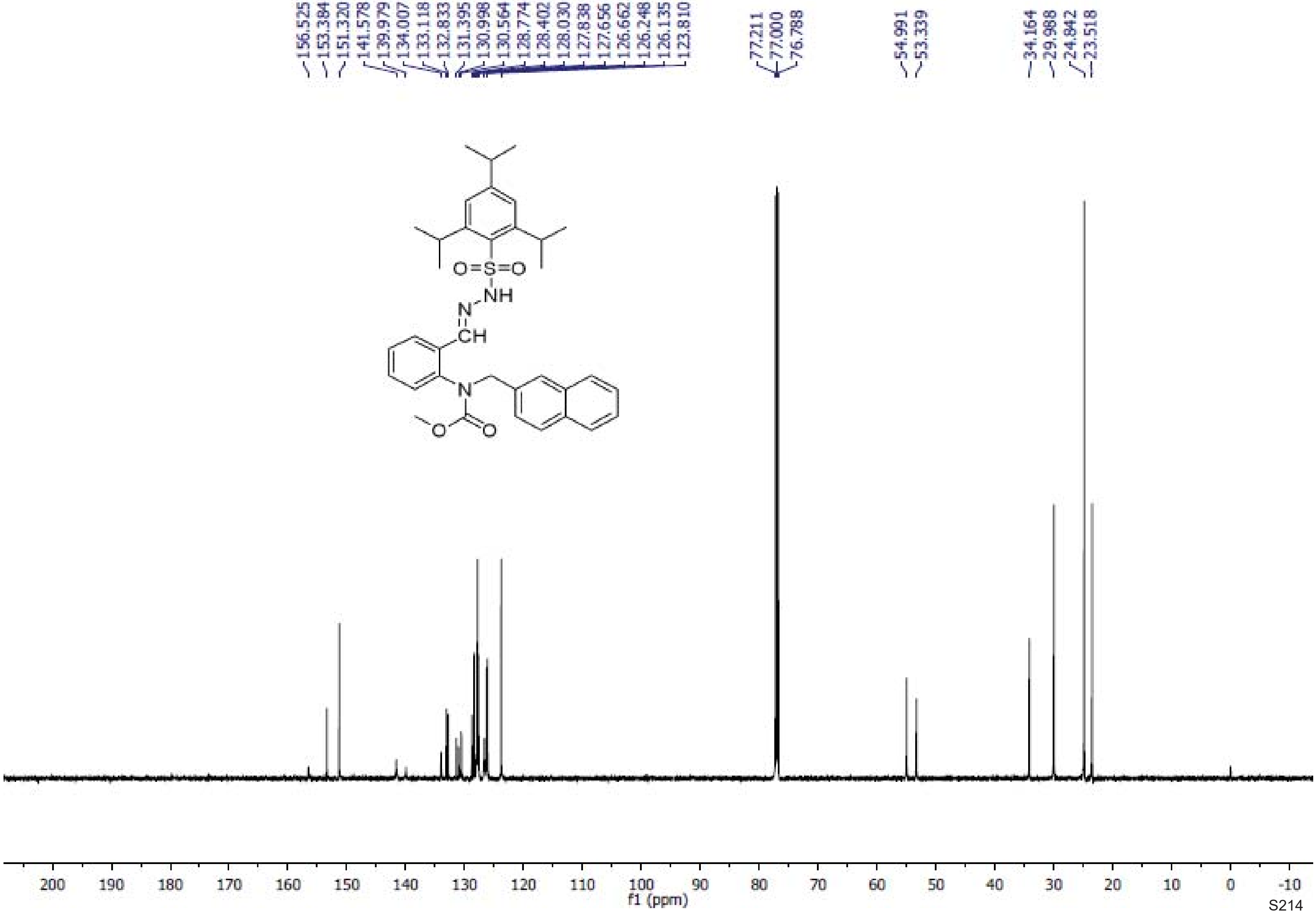
methyl ((perfluorophenyl)methyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-k



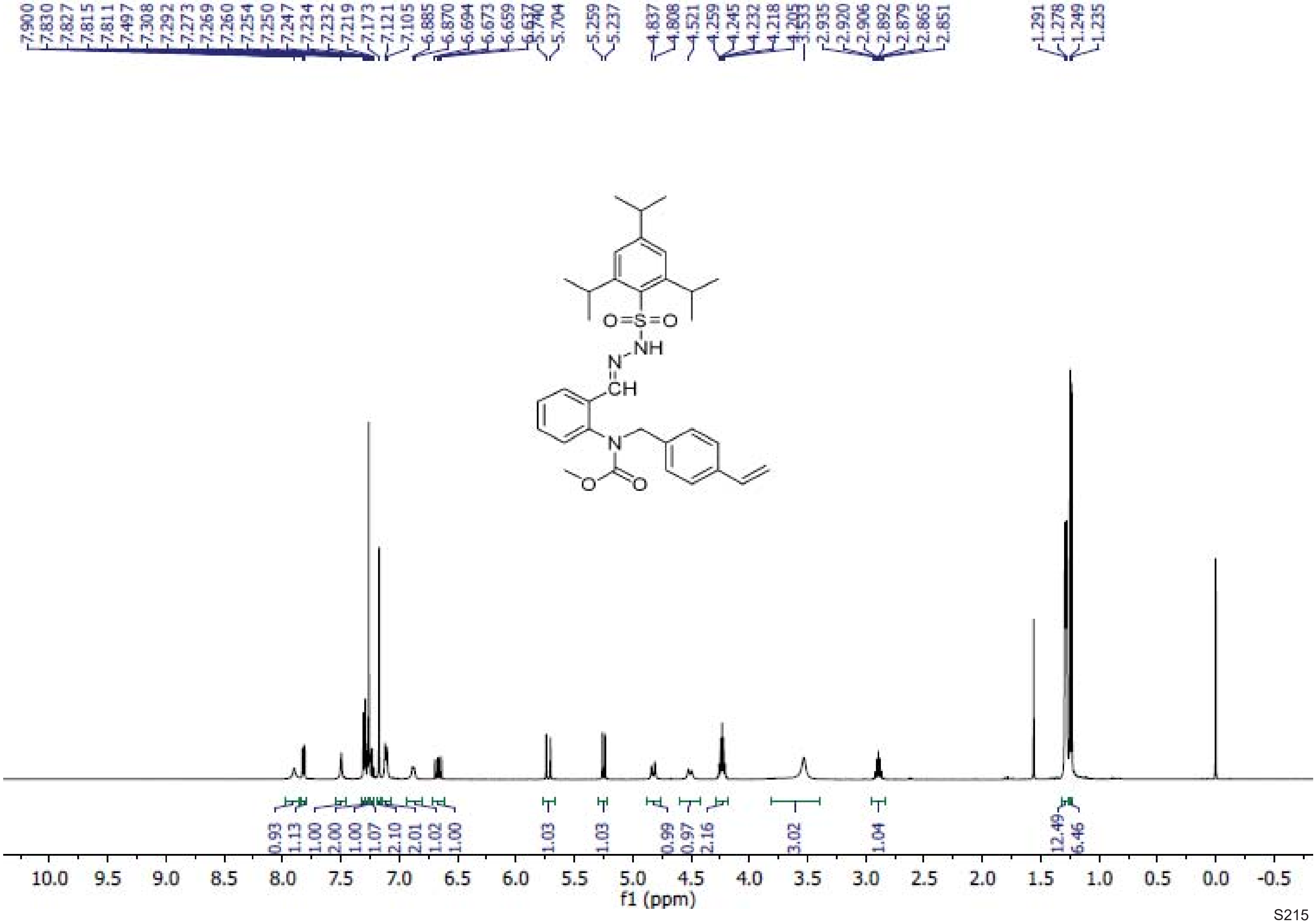
methyl (naphthalen-2-ylmethyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-l



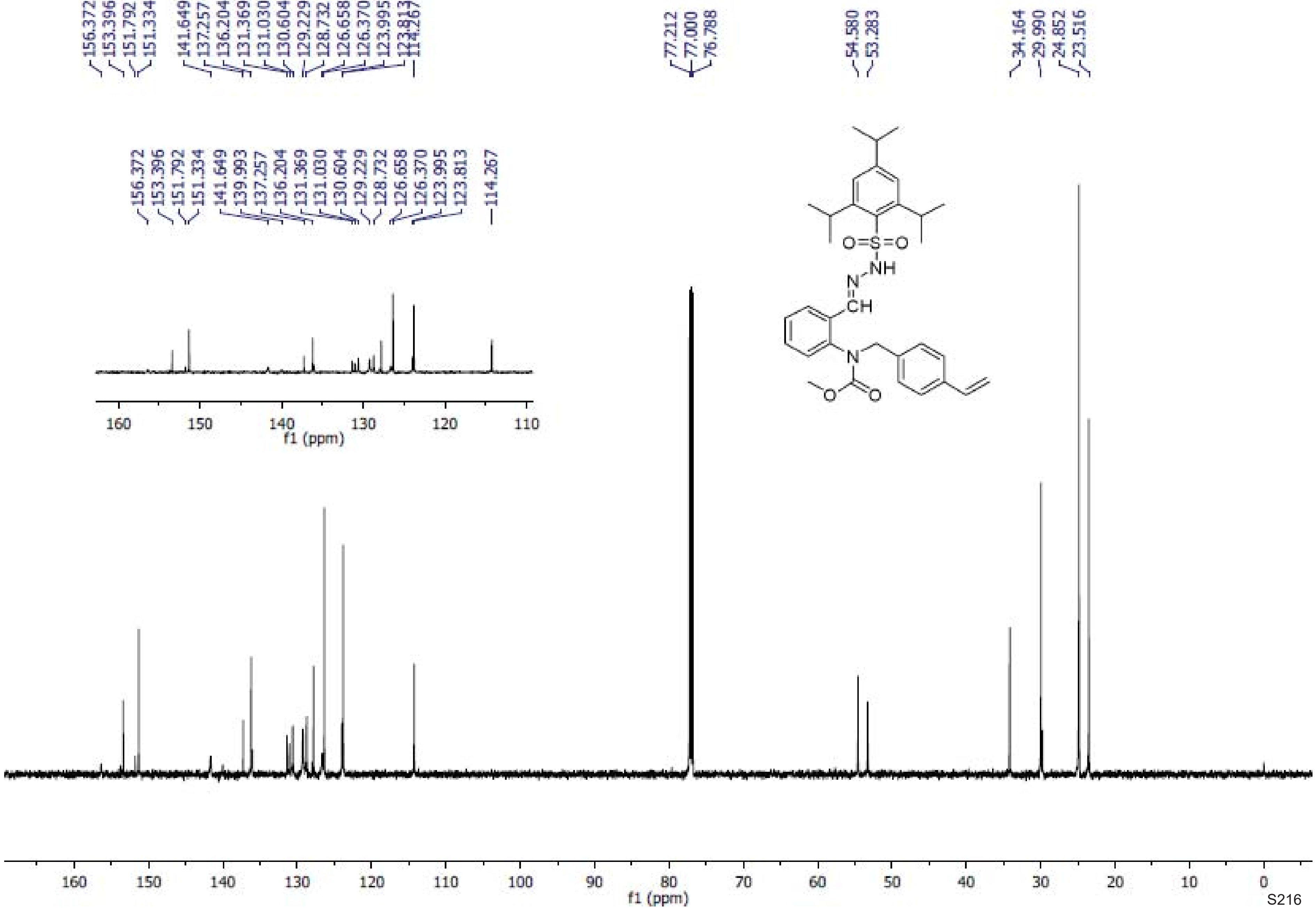
methyl (naphthalen-2-ylmethyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-l



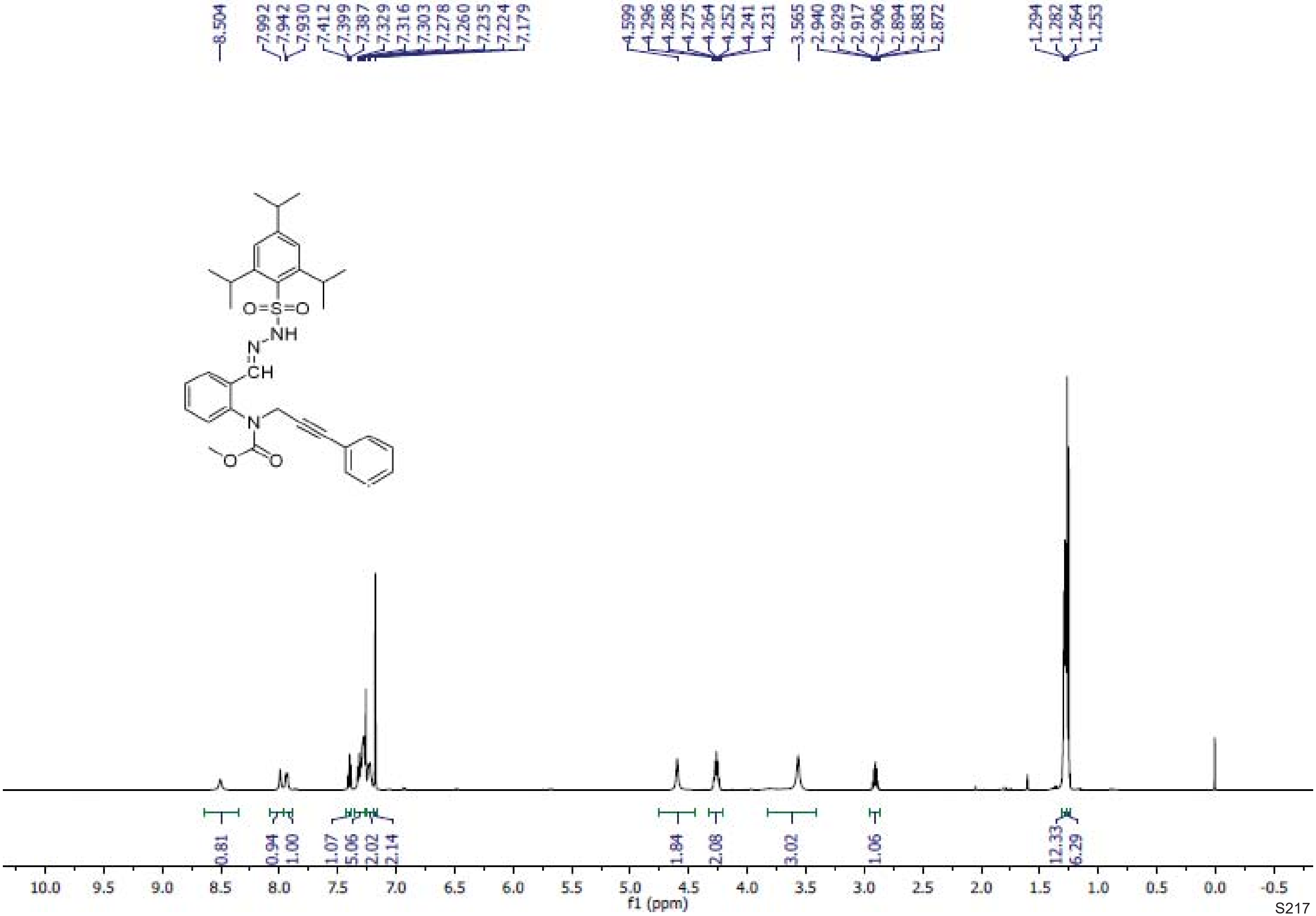
methyl (2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl) phenyl)(4-vinylbenzyl)carbamate 1-m



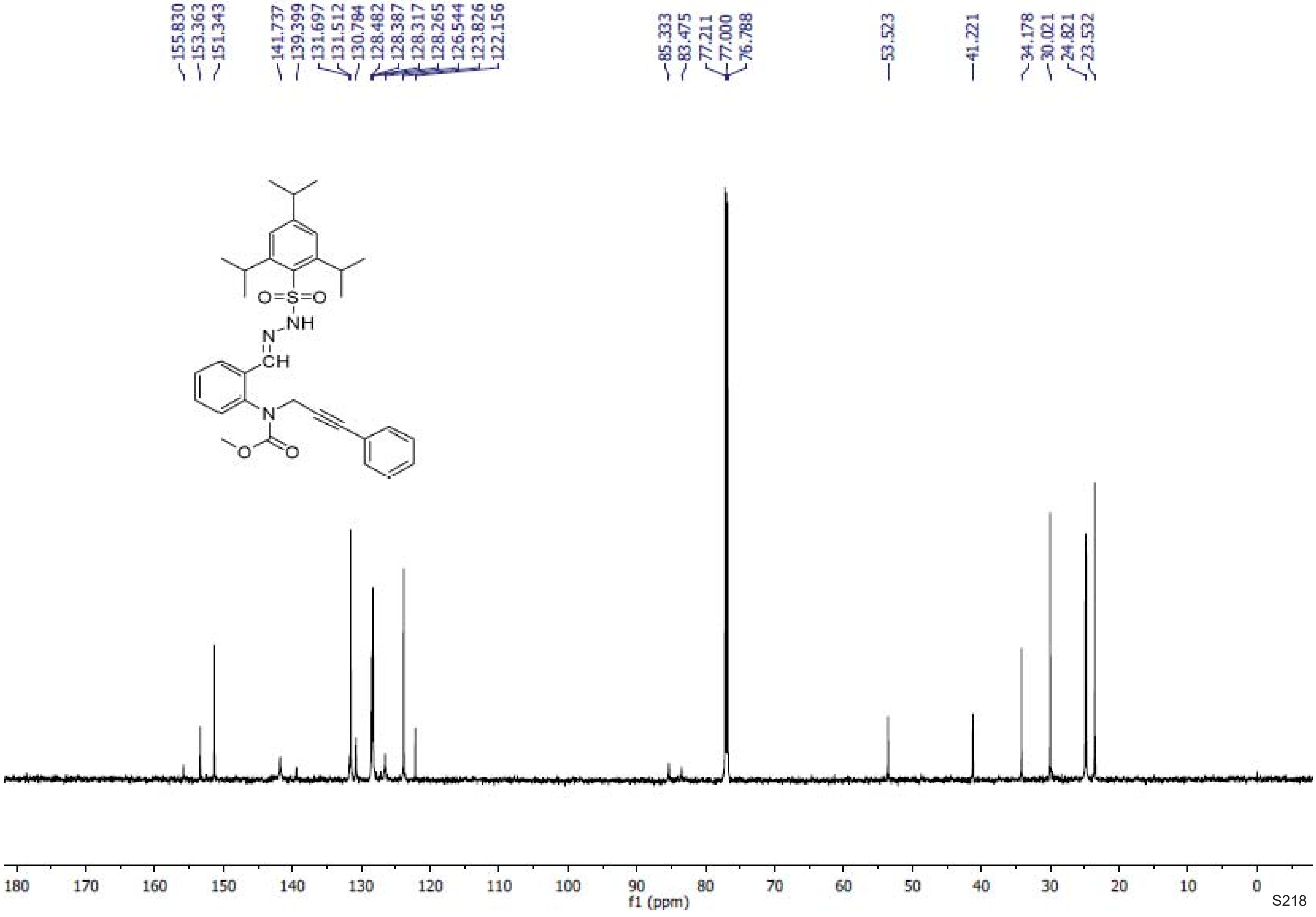
methyl (2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl) phenyl)(4-vinylbenzyl)carbamate 1-m



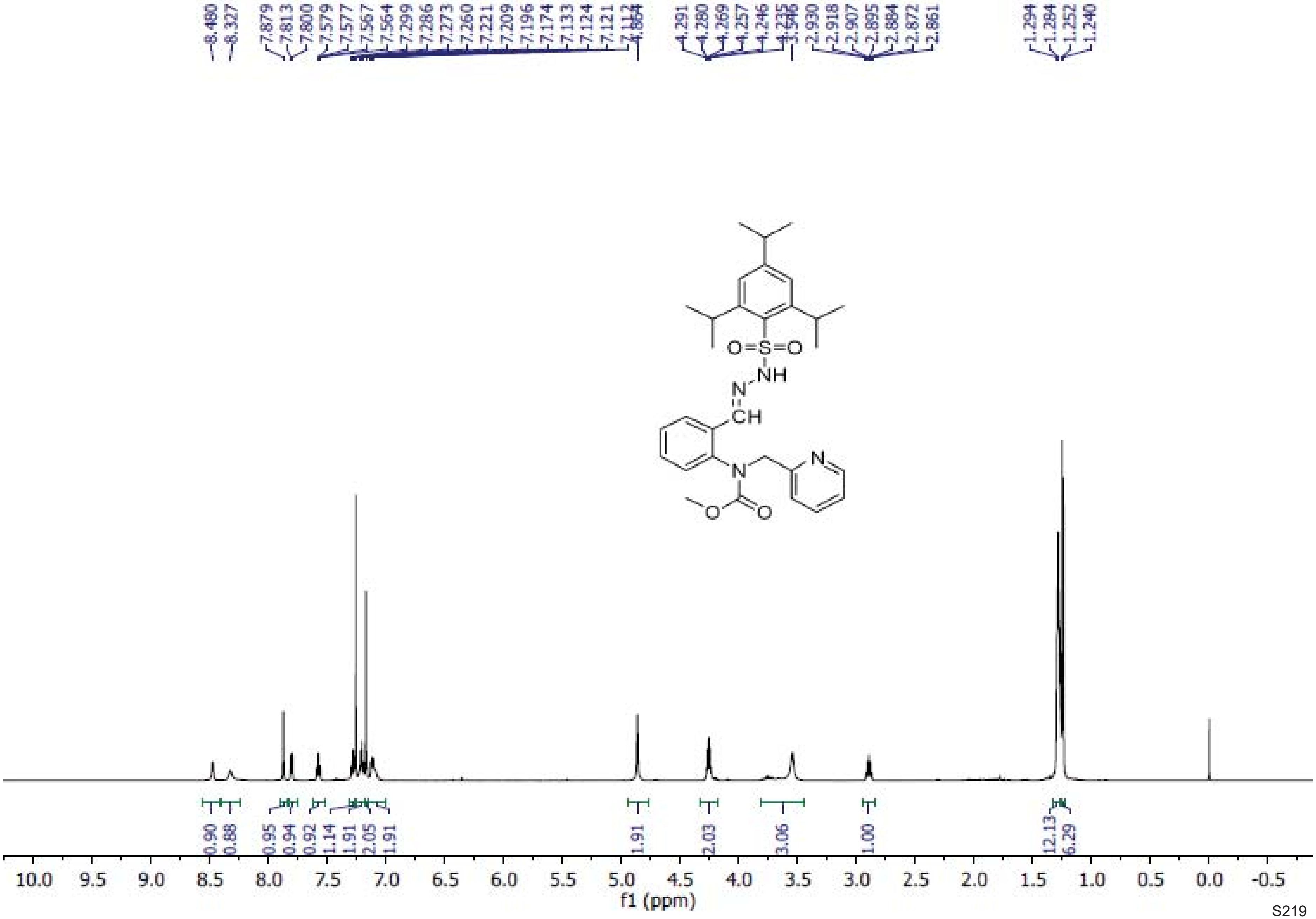
methyl (3-phenylprop-2-yn-1-yl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-n



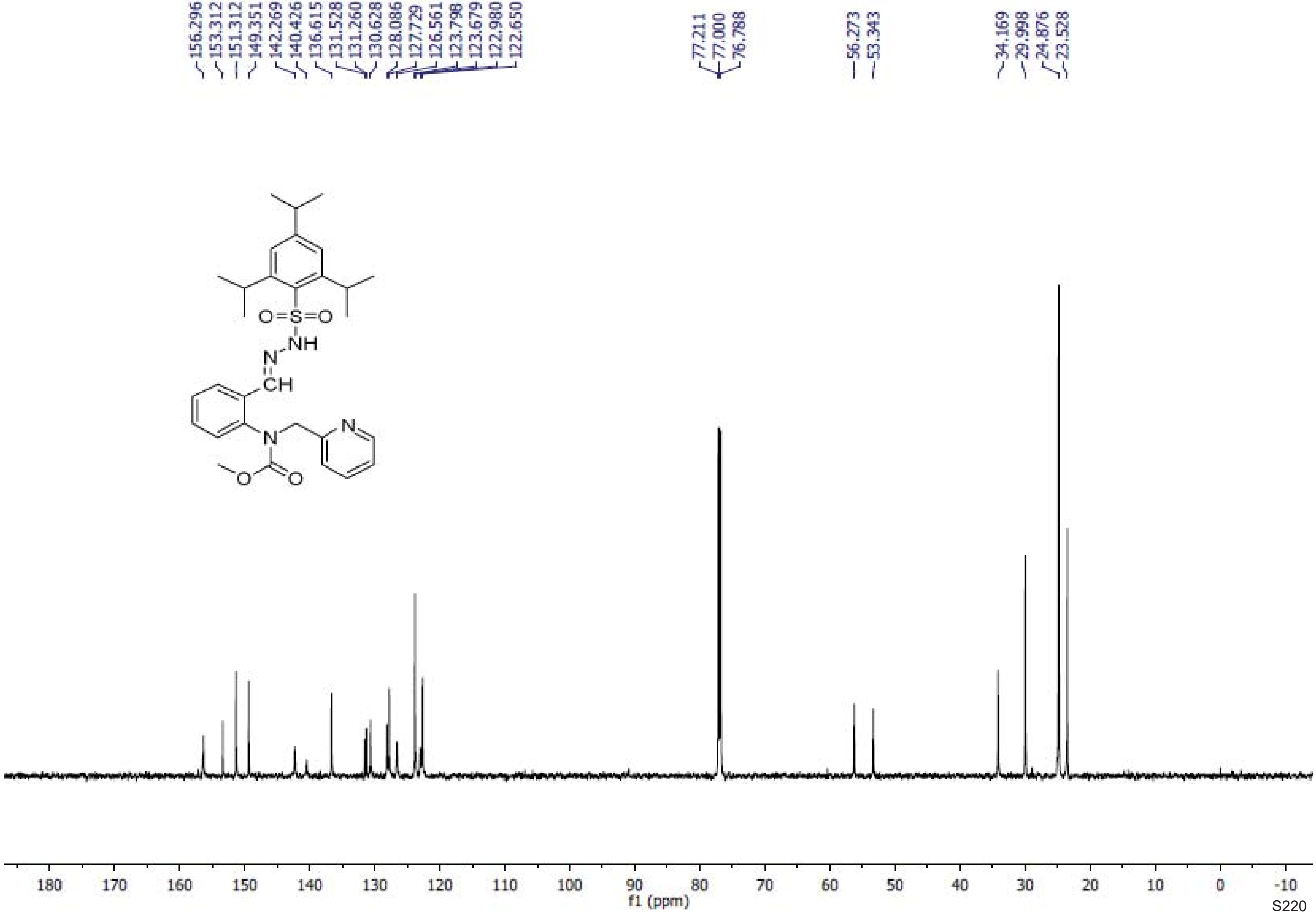
methyl (3-phenylprop-2-yn-1-yl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-n



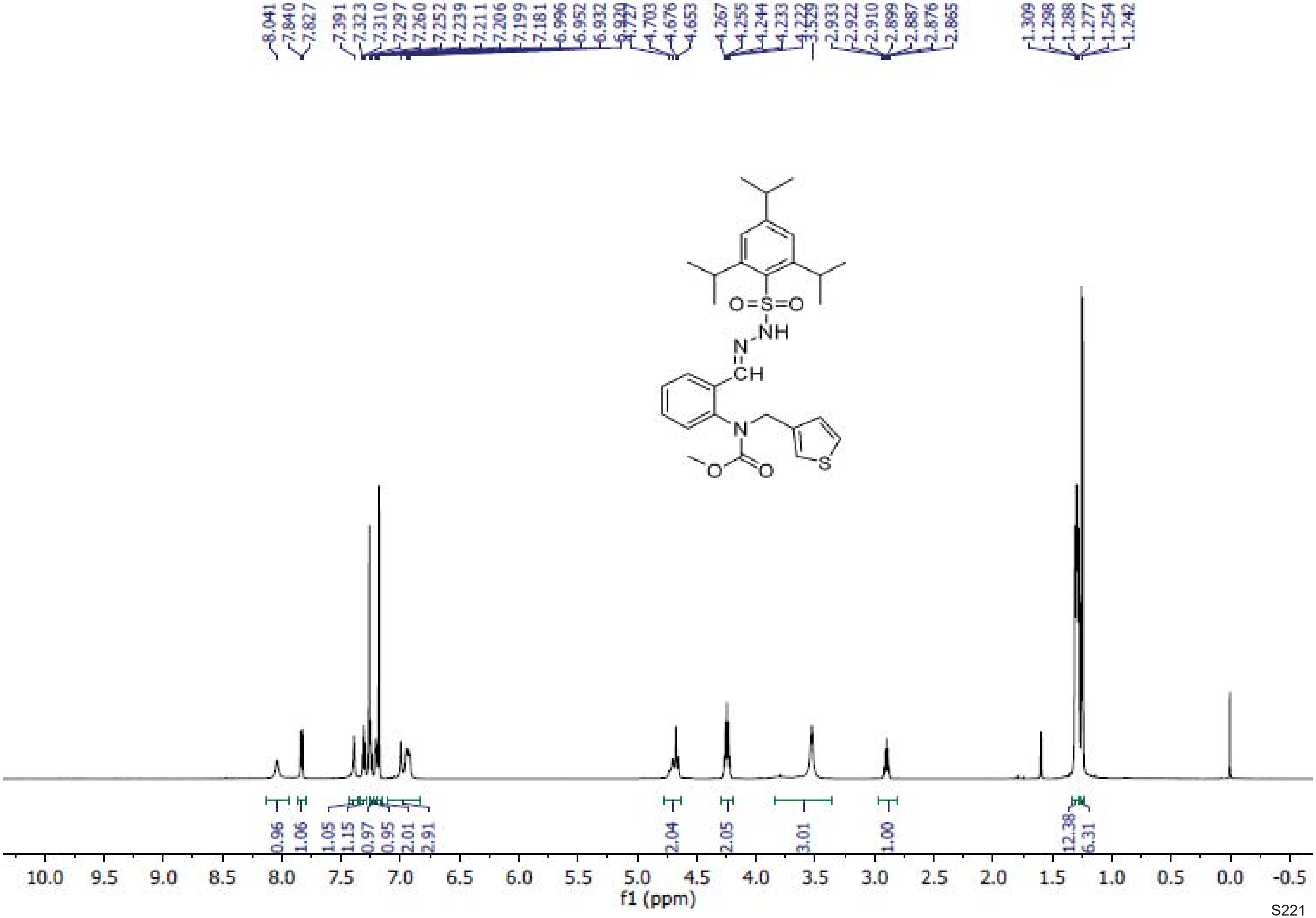
methyl (pyridin-2-ylmethyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-o



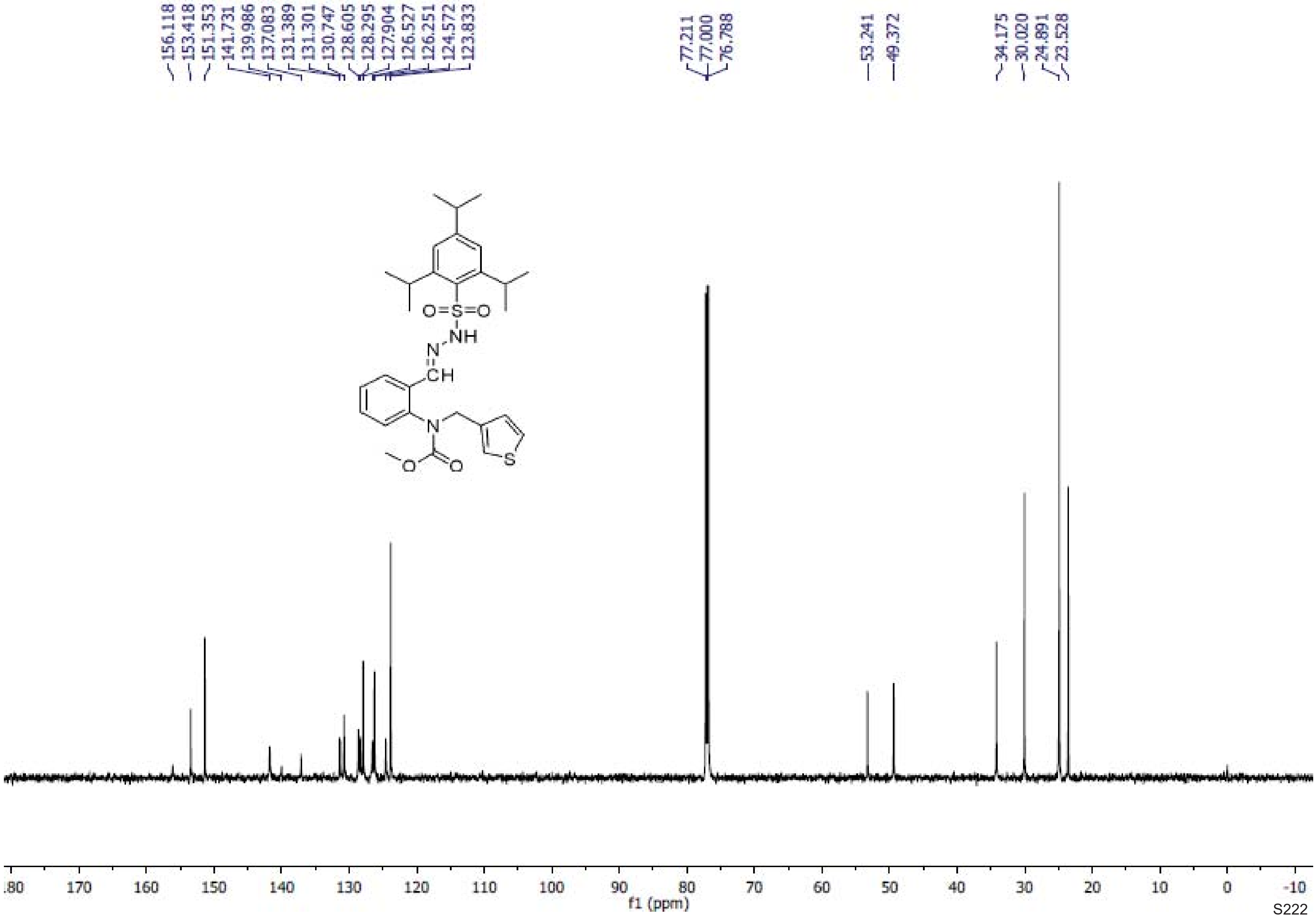
methyl (pyridin-2-ylmethyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-o



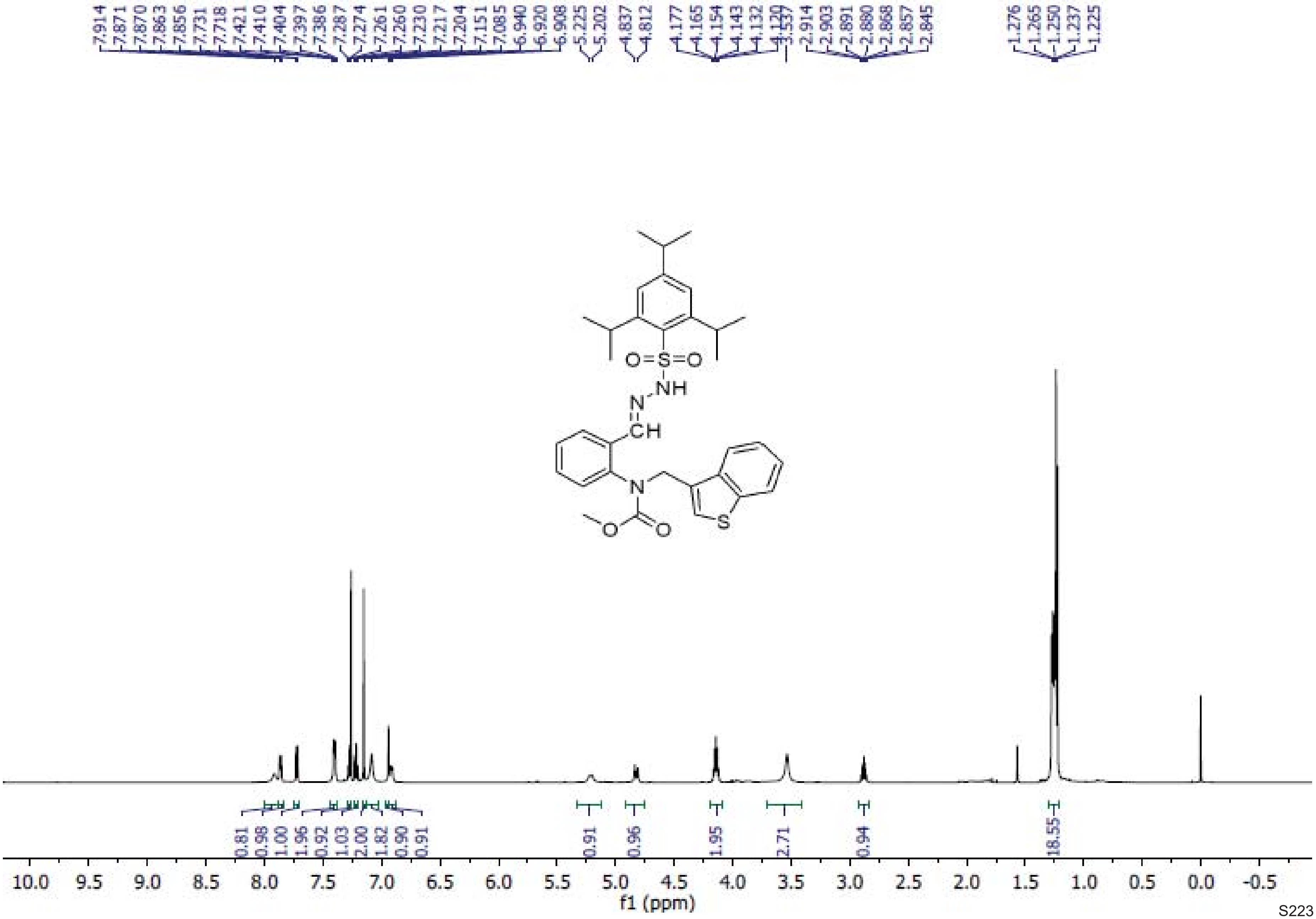
methyl (thiophen-3-ylmethyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-p



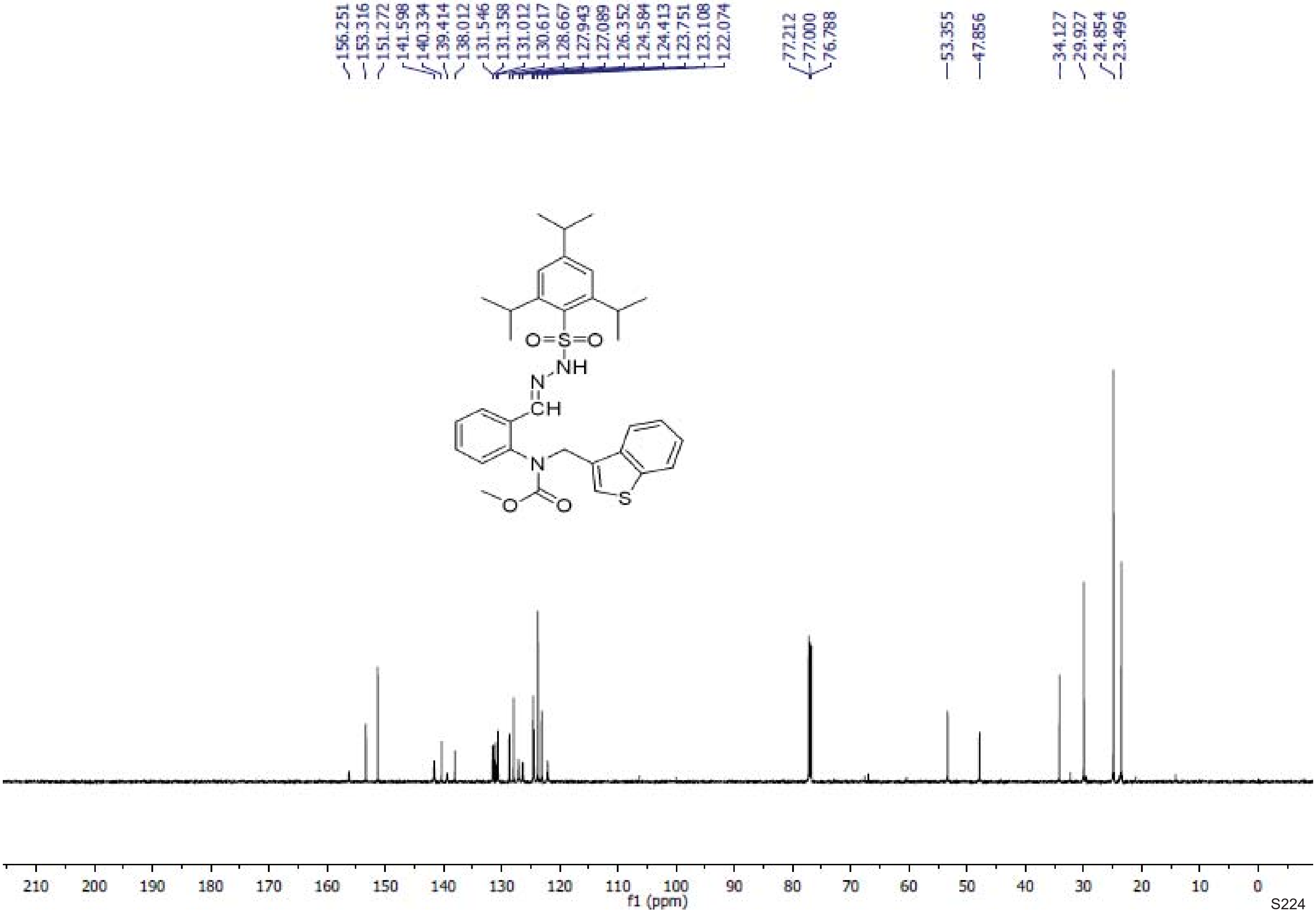
methyl (thiophen-3-ylmethyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-p



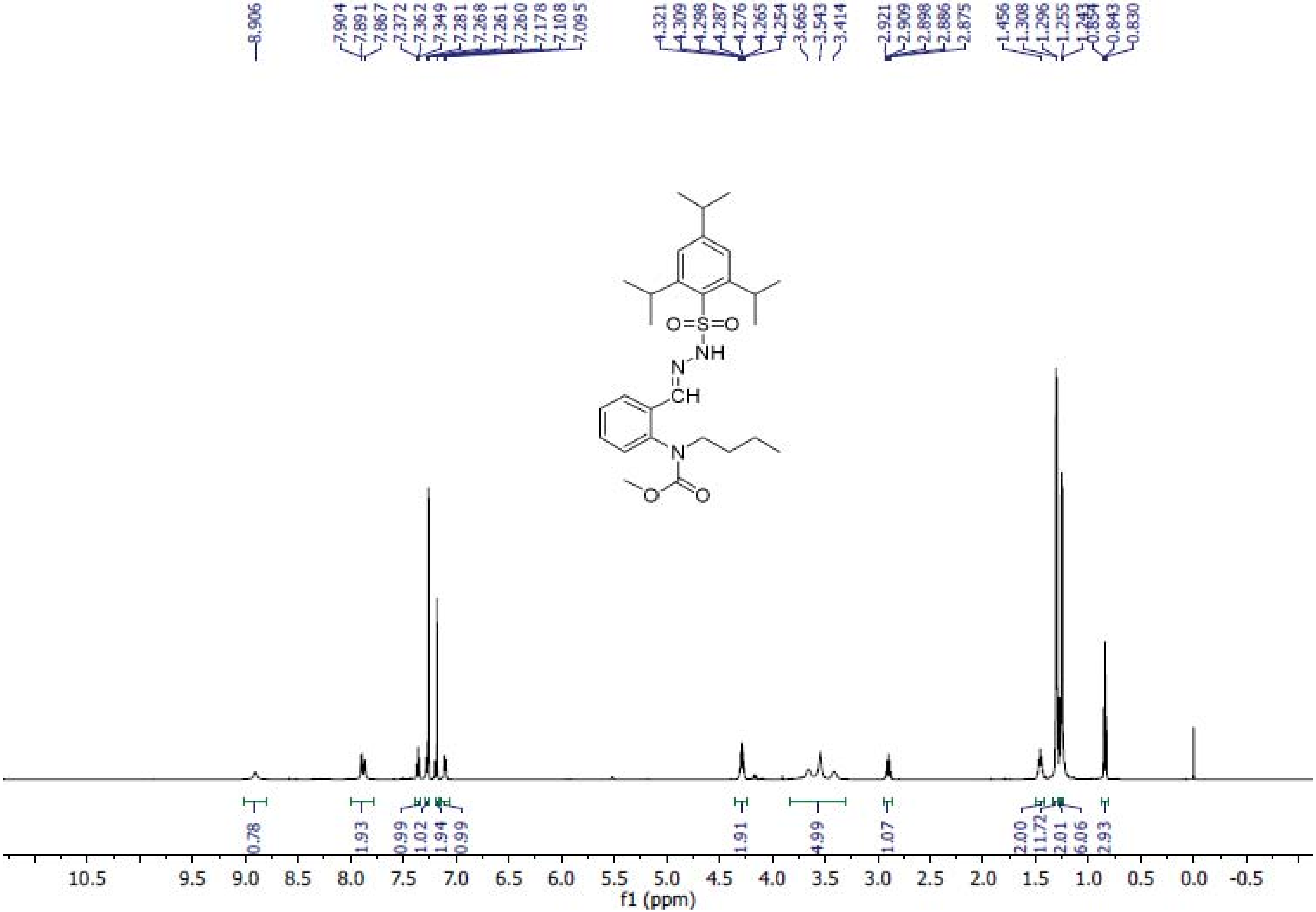
methyl (benzo[*b*]thiophen-3-ylmethyl)(2-((2-((2,4,6-triisopropyl phenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-q



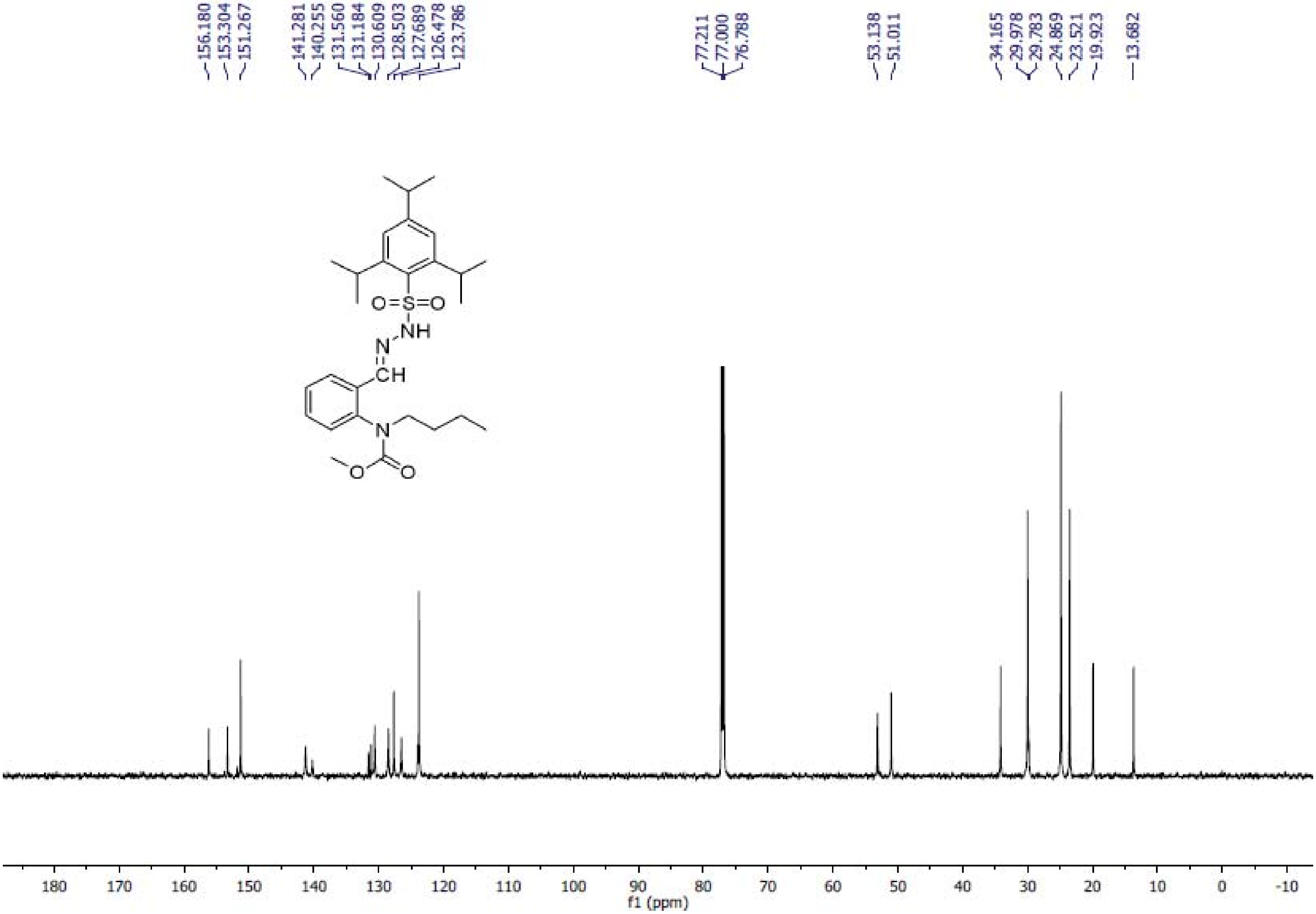
methyl (benzo[*b*]thiophen-3-ylmethyl)(2-((2-((2,4,6-triisopropyl phenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-q



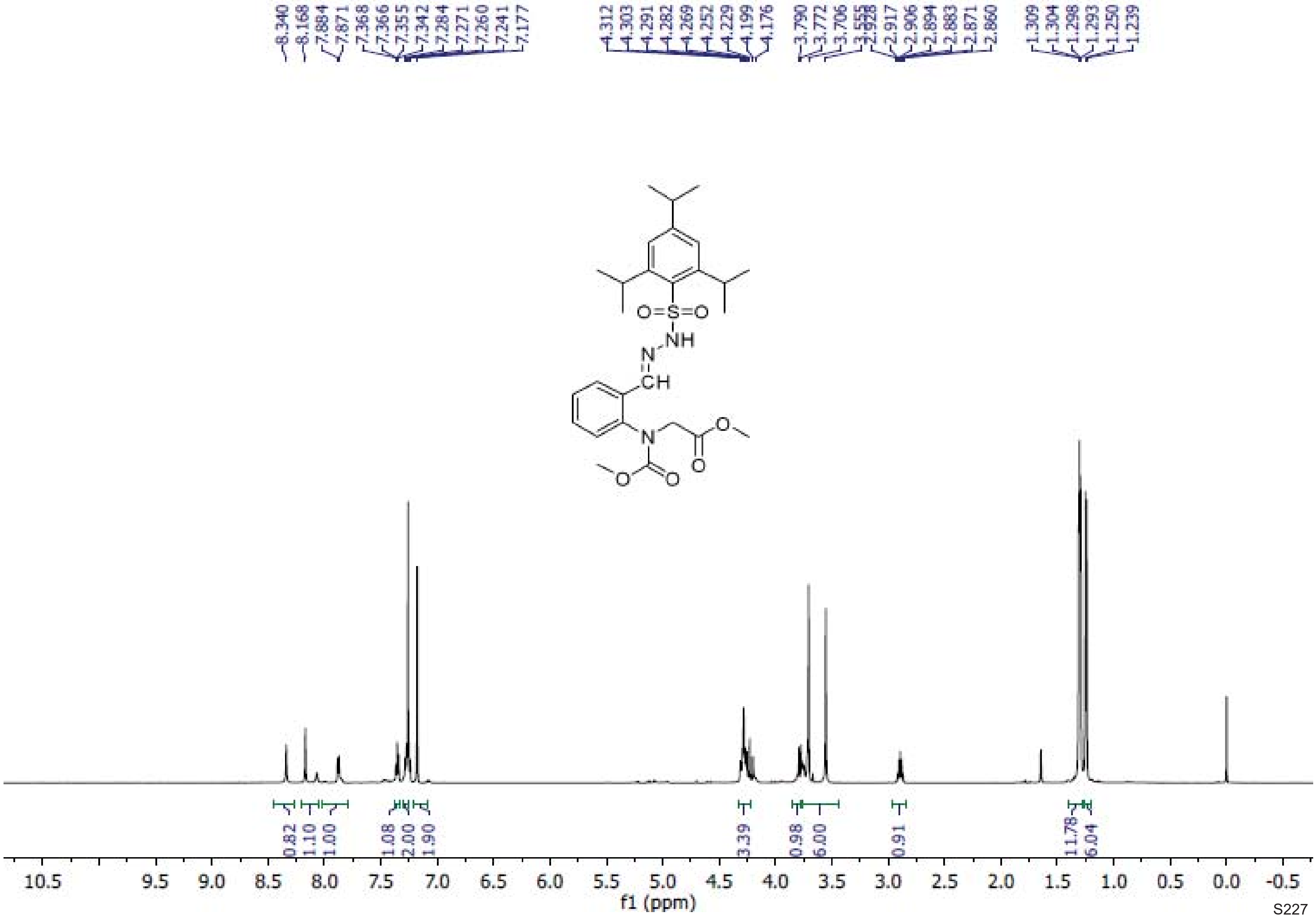
methyl butyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-r



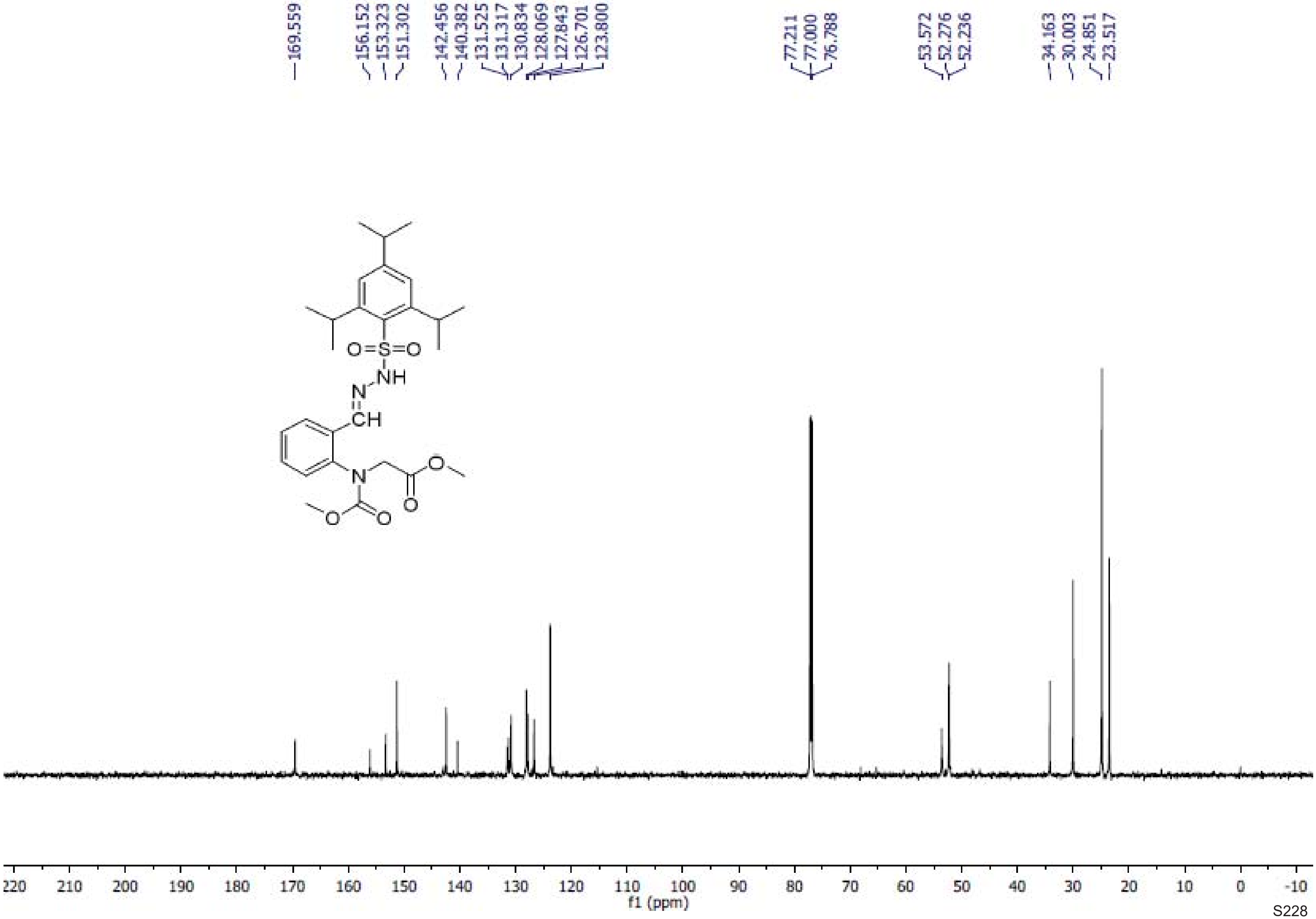
methyl butyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-r



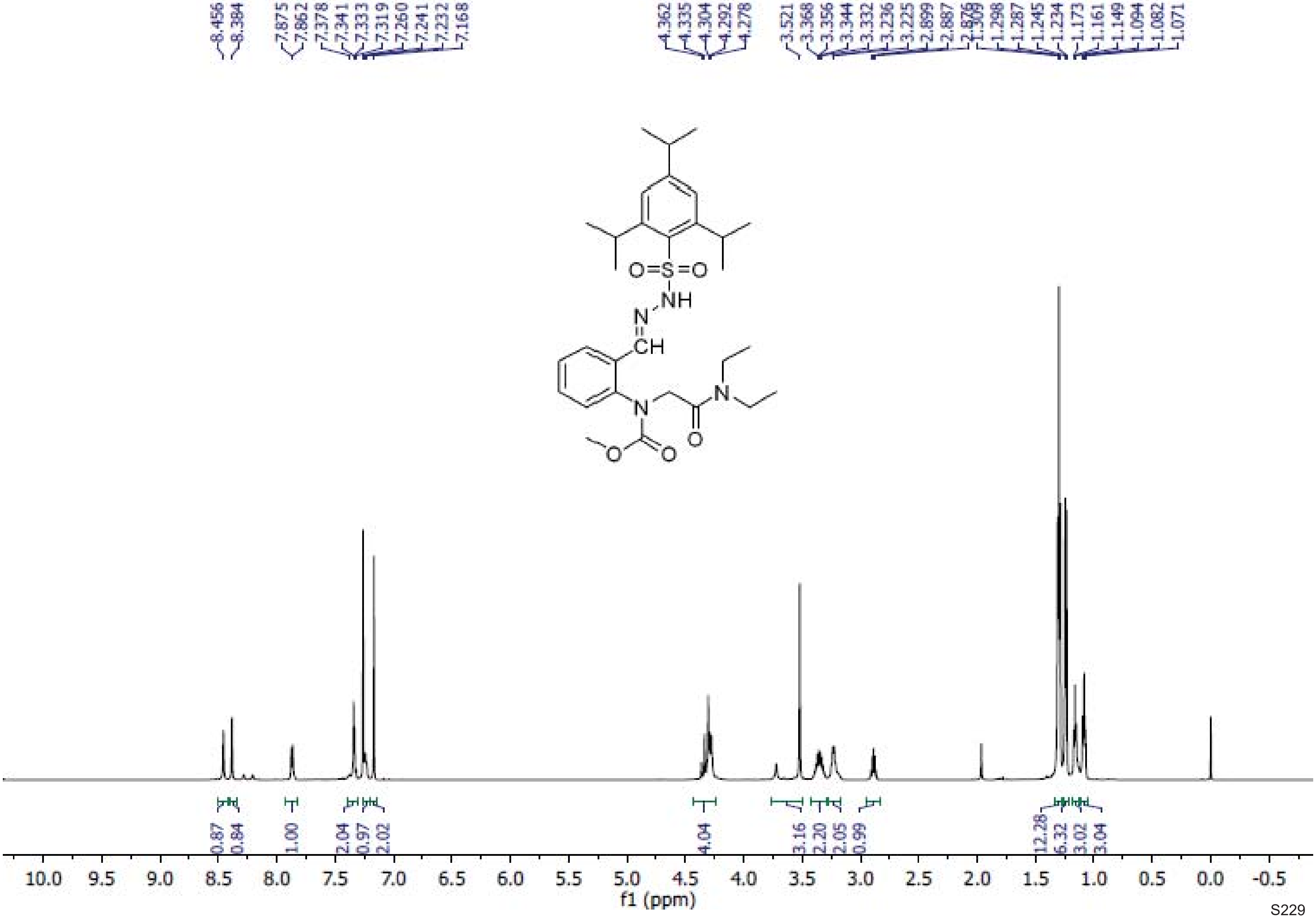
methyl *N*-(methoxycarbonyl)-*N*-(2-((2-((2,4,6-triisopropylphenyl) sulfonyl) hydrazono)methyl)phenyl)glycinate 1-s



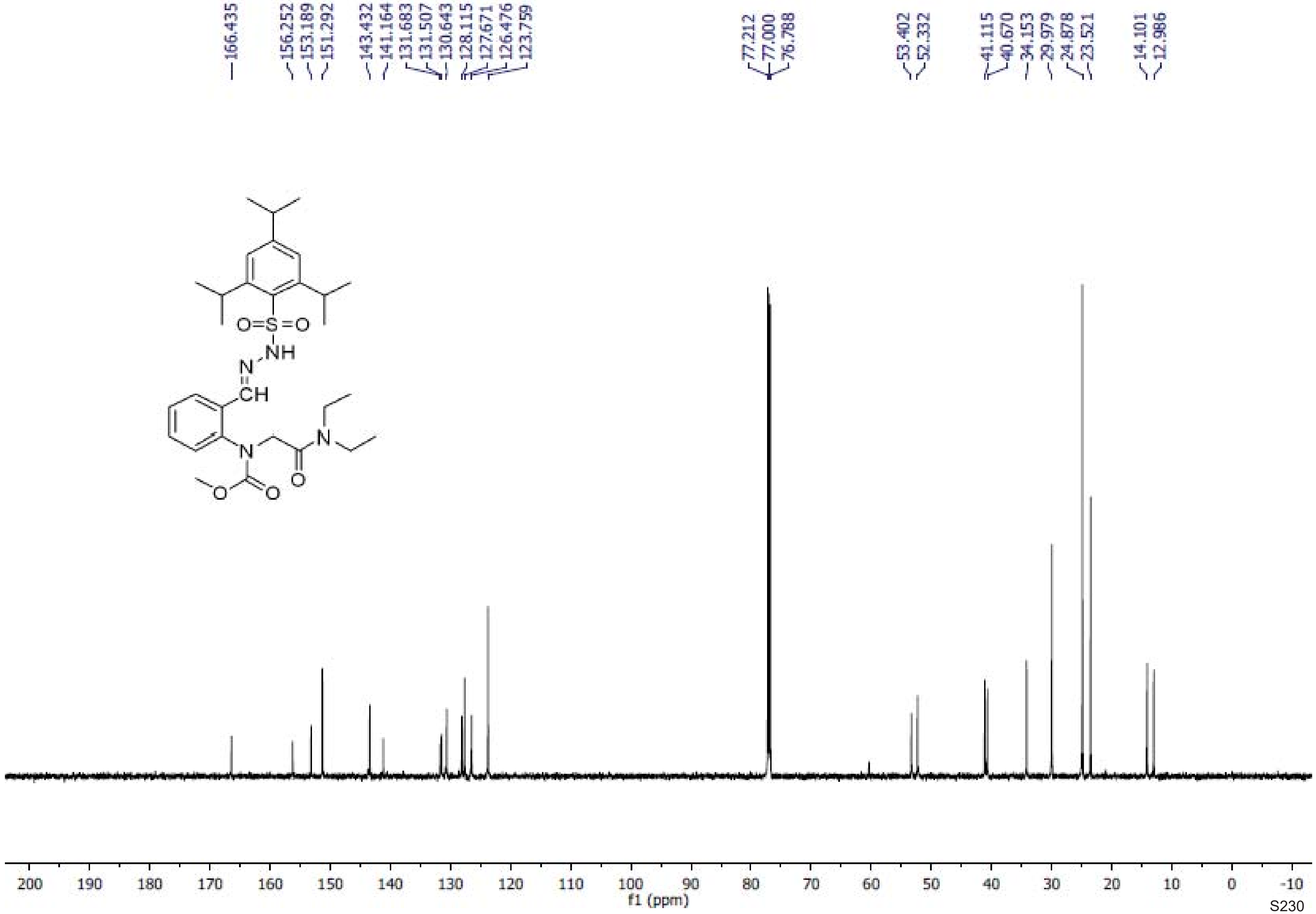
methyl *N*-(methoxycarbonyl)-*N*-(2-((2-((2,4,6-triisopropylphenyl) sulfonyl) hydrazono)methyl)phenyl)glycinate 1-s



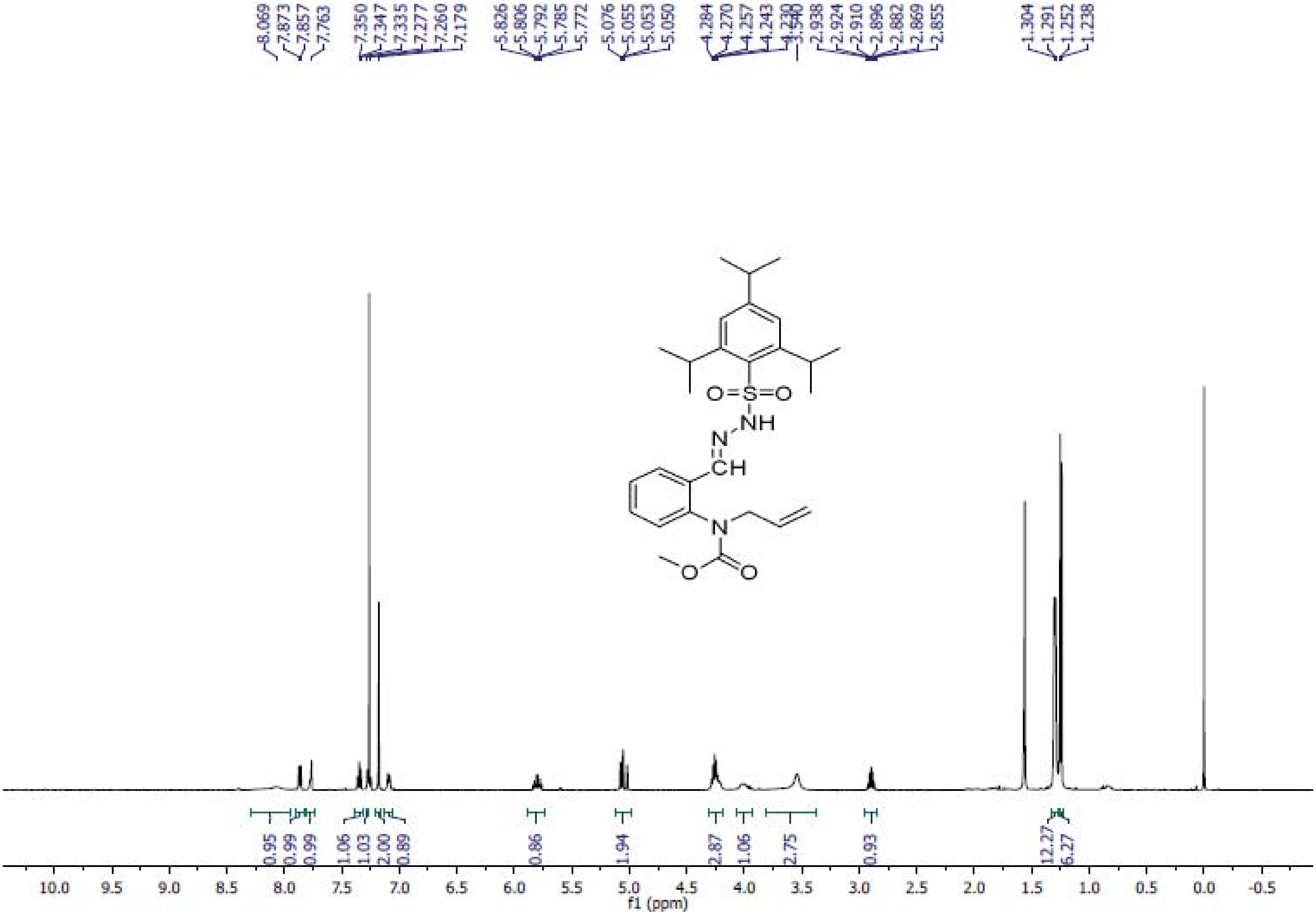
methyl (2-(diethylamino)-2-oxoethyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-t



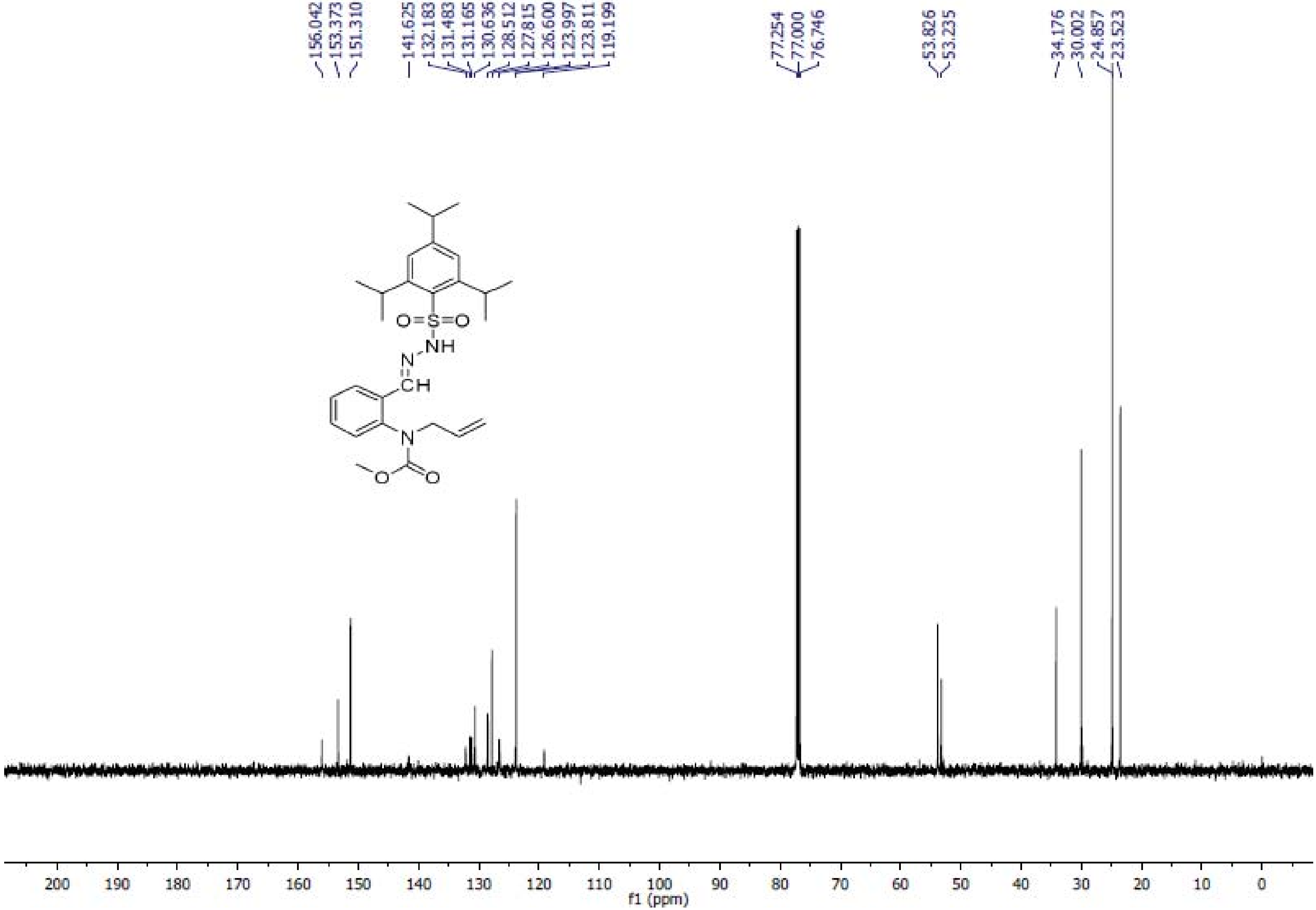
methyl (2-(diethylamino)-2-oxoethyl)(2-((2-((2,4,6-triisopropylphenyl) sulfonyl)hydrazono)methyl)phenyl)carbamate 1-t



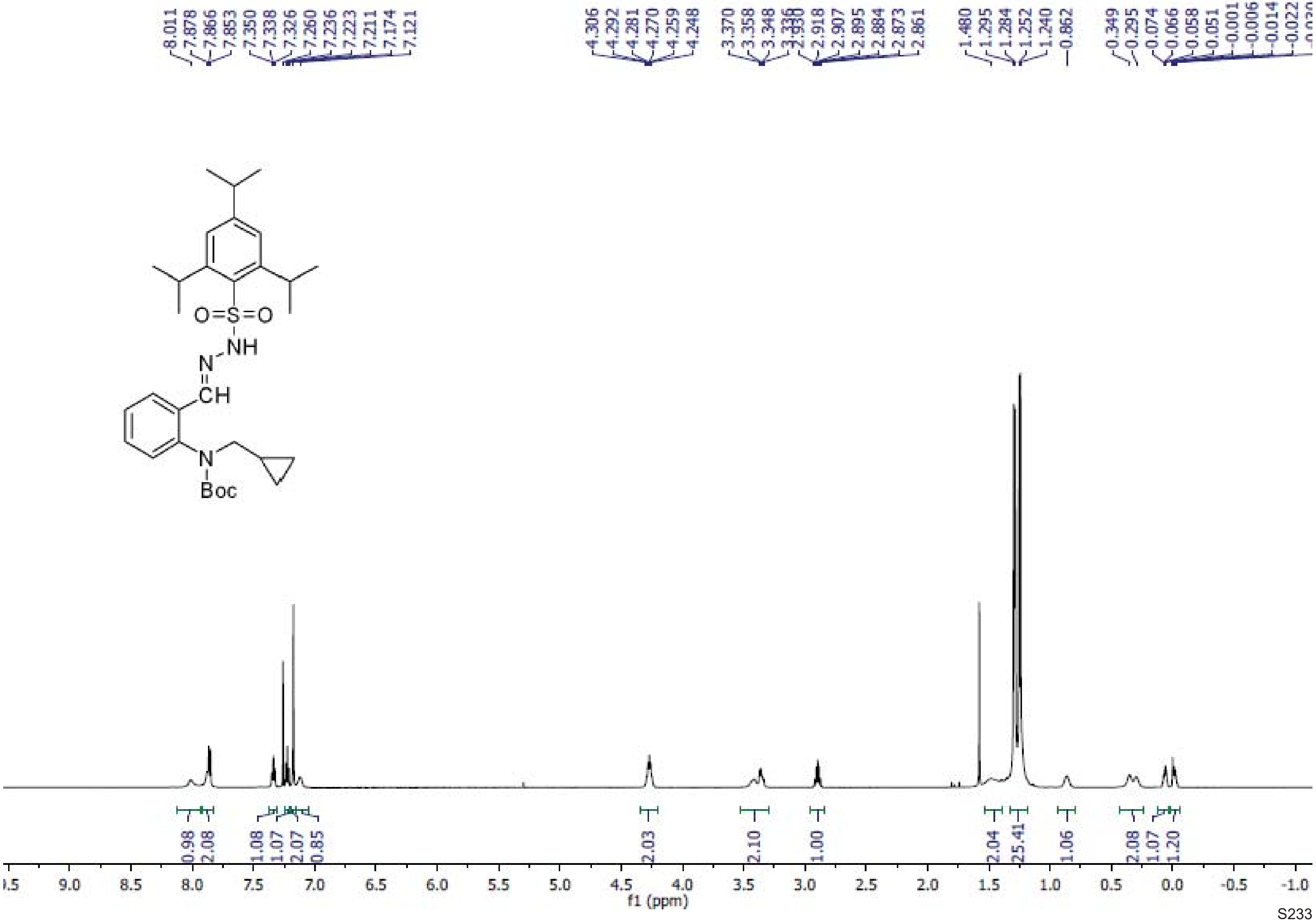
methyl allyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-u



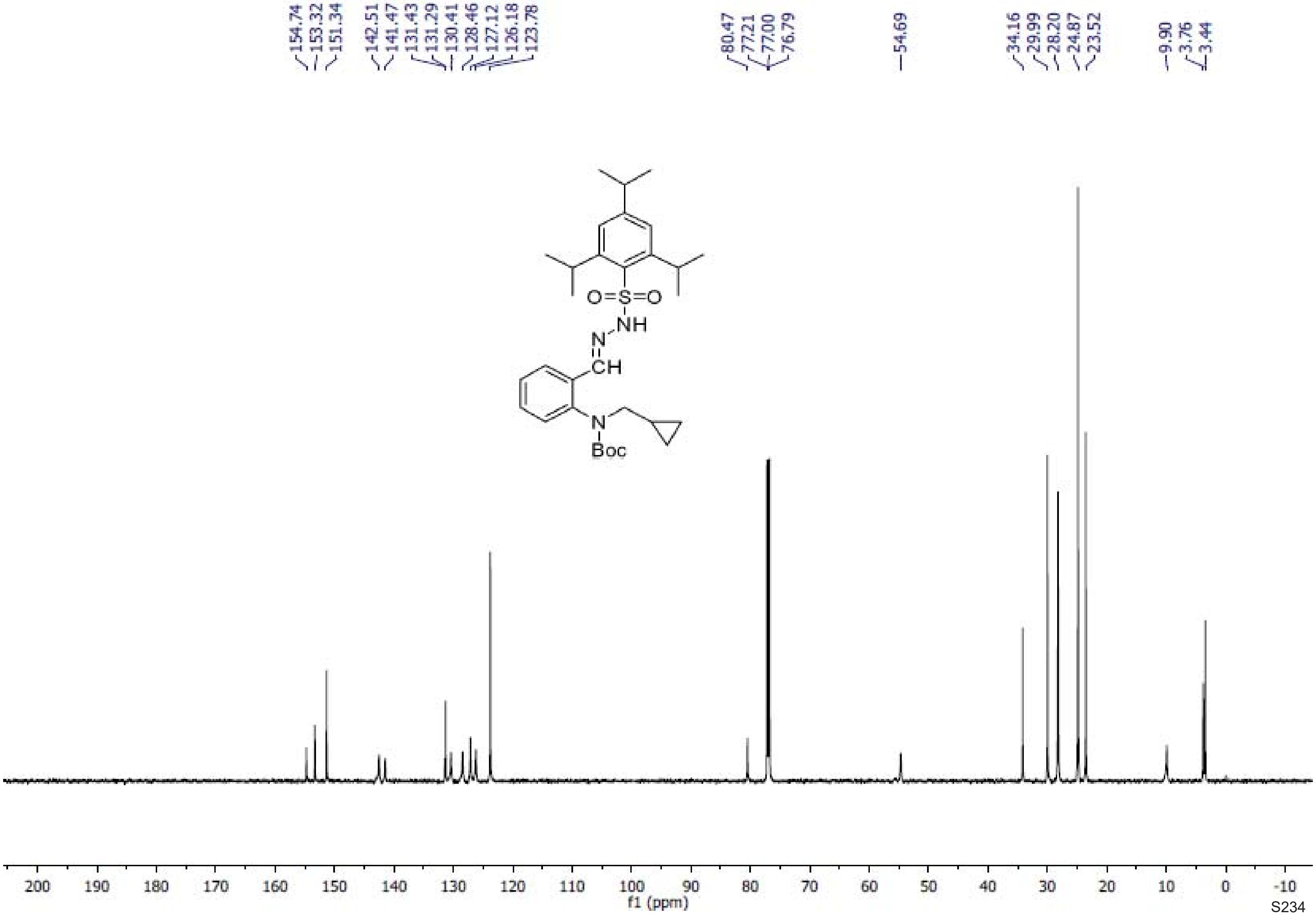
methyl allyl(2-((2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazono)methyl)phenyl)carbamate 1-u



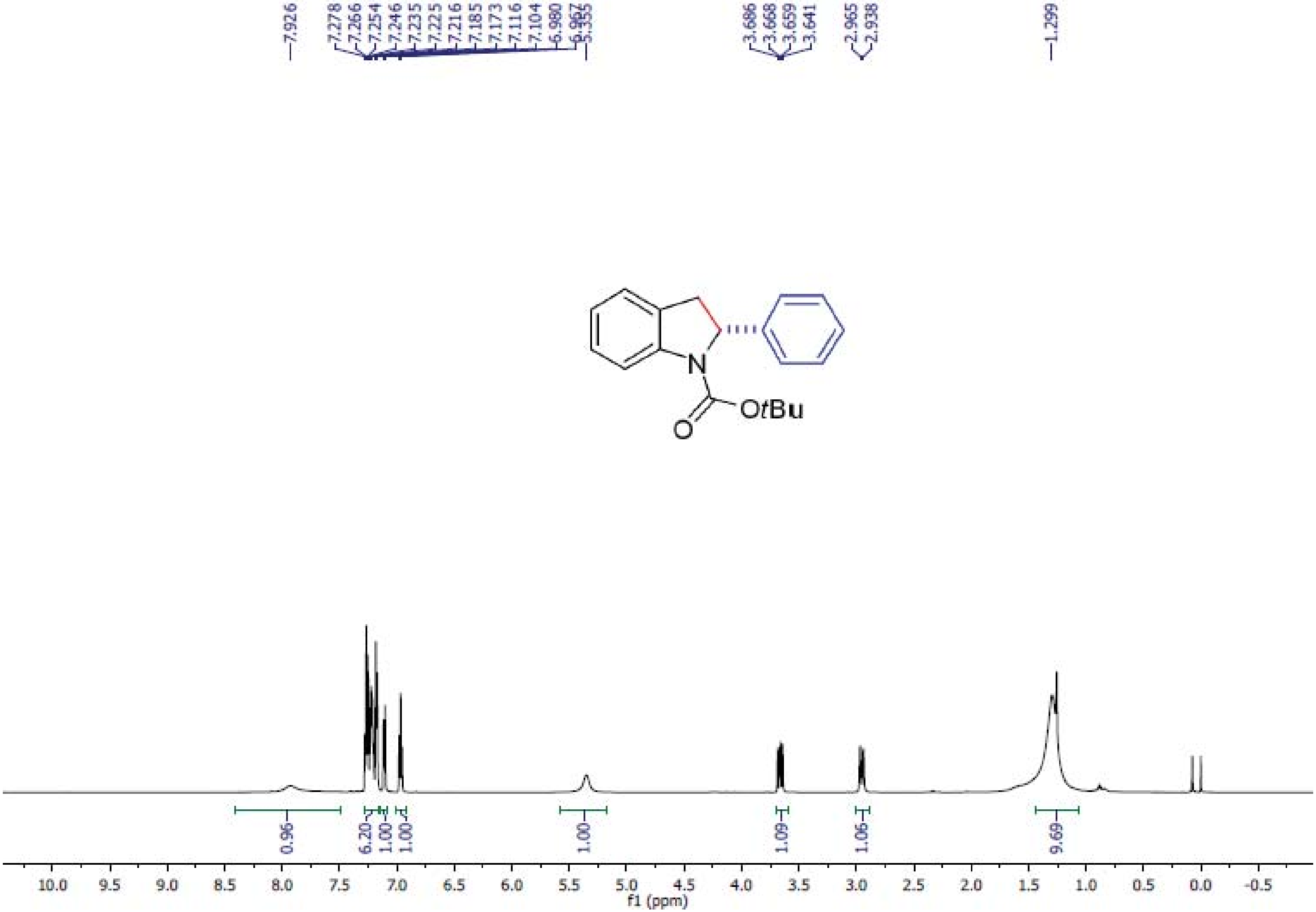
tert-butyl (cyclopropylmethyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-v



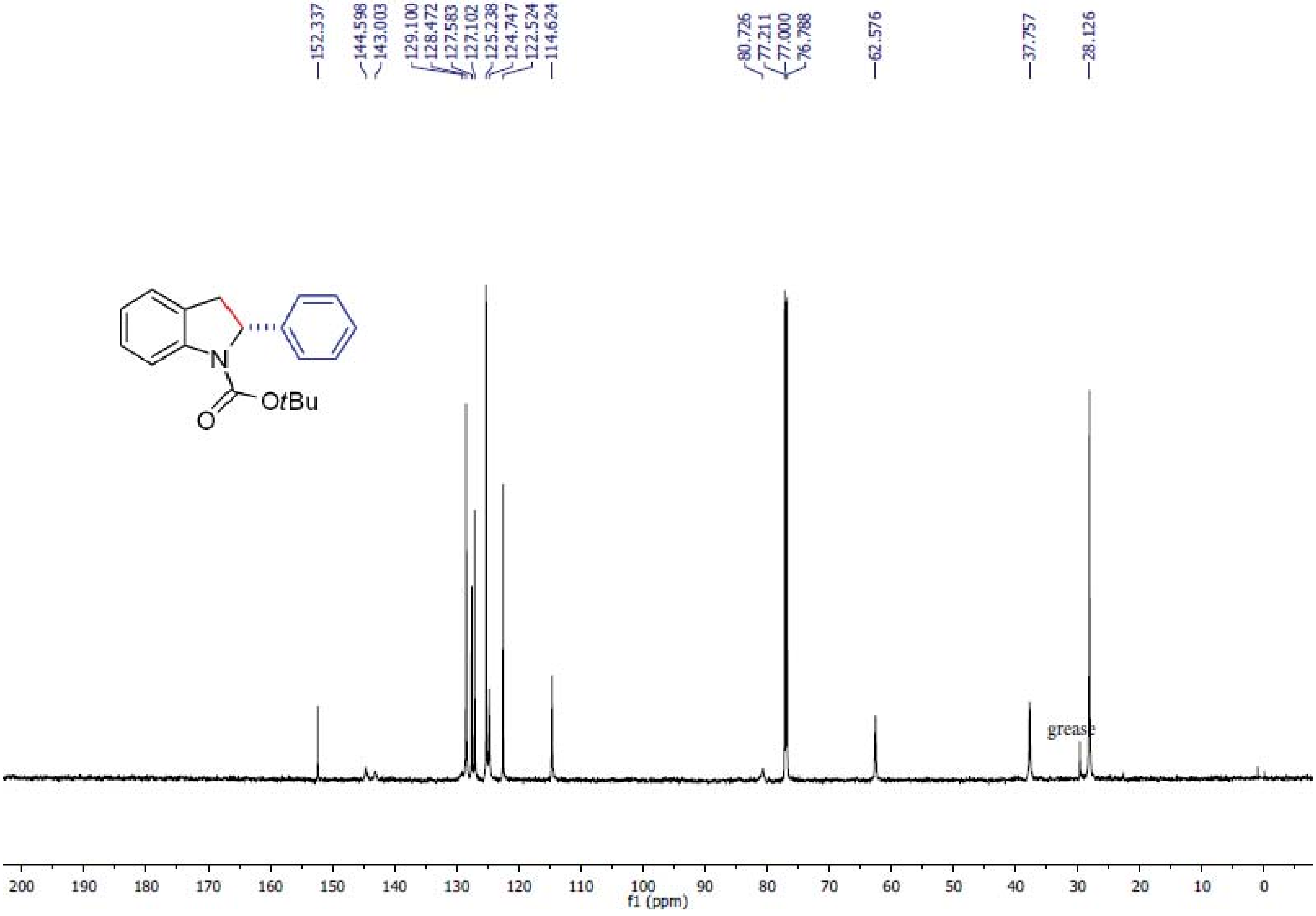
tert-butyl (cyclopropylmethyl)(2-((2-((2,4,6-triisopropylphenyl)sulfonyl) hydrazono)methyl)phenyl)carbamate 1-v



tert-butyl (*R*)-2-phenylindoline-1-carboxylate 2a



tert-butyl (*R*)-2-phenylindoline-1-carboxylate 2a

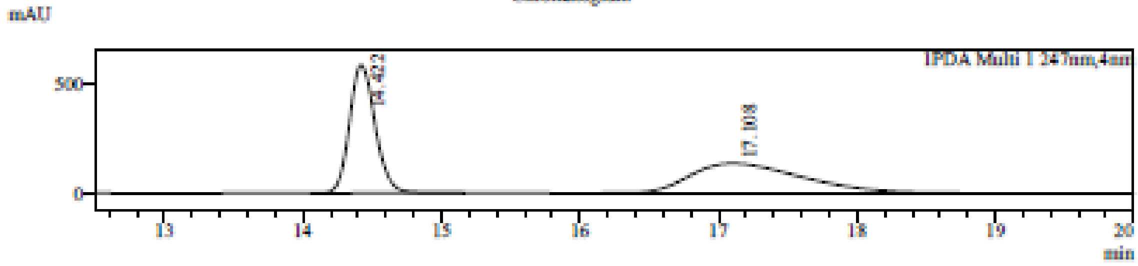


tert-butyl (*R*)-2-phenylindoline-1-carboxylate 2a

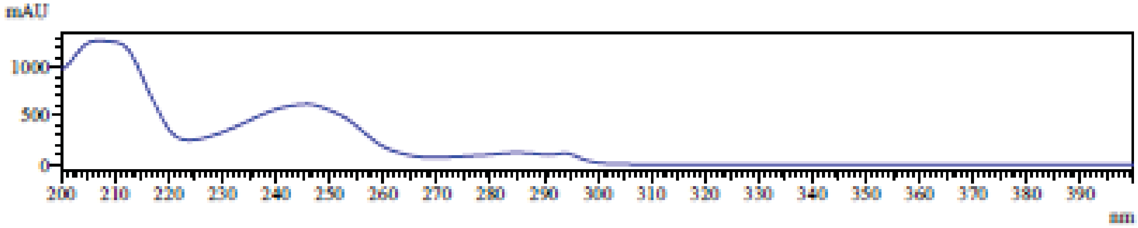
Sample Information

Sample Name	: XW-IV-8-IA-0.3%0.8mL-1
Sample ID	: XW-IV-8-IA-0.3%0.8mL-1
Data File	: XW-IV-8-IA-0.3%0.8mL-1.lcd
Method File	: XW-0.3%-0.8ml.lcm

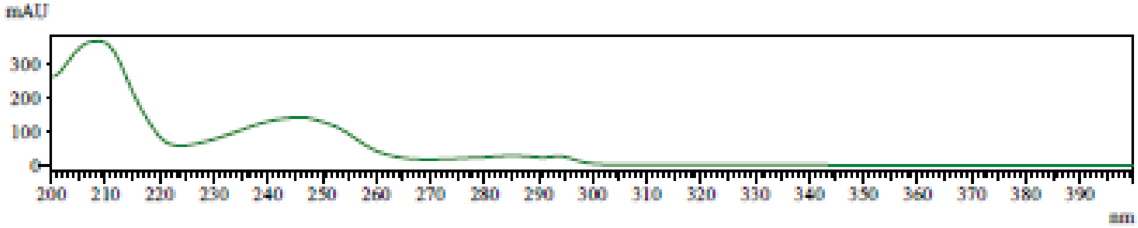
Chromatogram



UV Spectrum
Retention time = 14.422



UV Spectrum
Retention time = 17.108



Peak Table

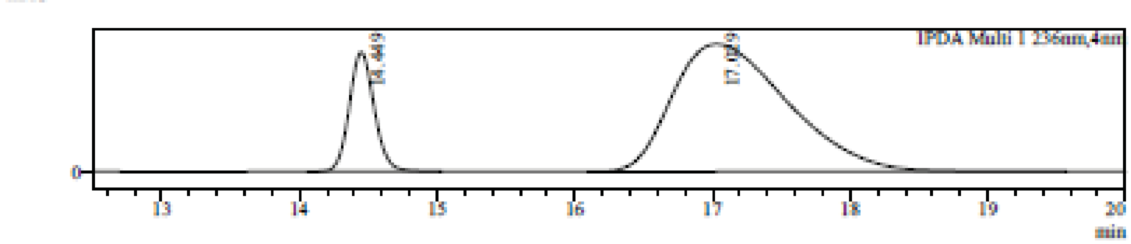
PDA Ch1 247nm

Peak#	Ret. Time	Area	Area%
1	14.422	7635869	49.725
2	17.108	7720233	50.275
Total		15356102	100.000

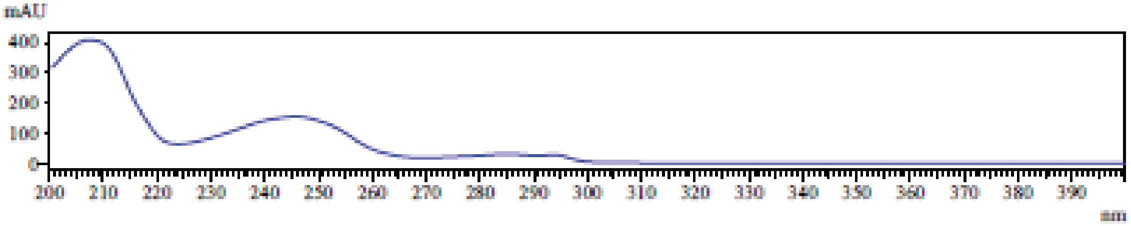
tert-butyl (*R*)-2-phenylindoline-1-carboxylate 2a

Sample Information
Sample Name : XW-IV-18-IA-0.3%0.8mL-1
Sample ID : XW-IV-18-IA-0.3%0.8mL-1
Data File : XW-IV-18-IA-0.3%0.8mL-1.lcd
Method File : XW-0.3%-0.8ml.lcm

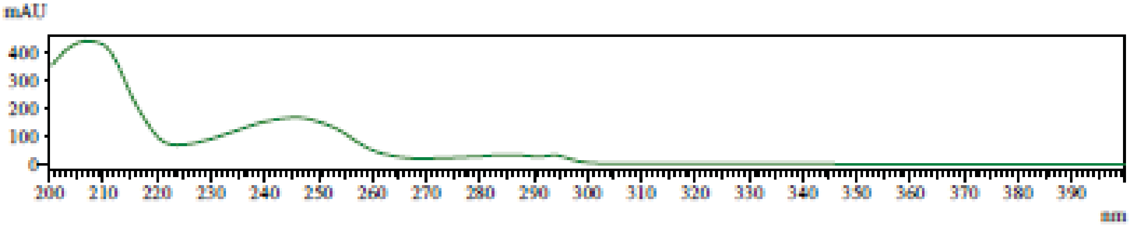
Chromatogram



UV Spectrum
Retention time = 14.449



UV Spectrum
Retention time = 17.029

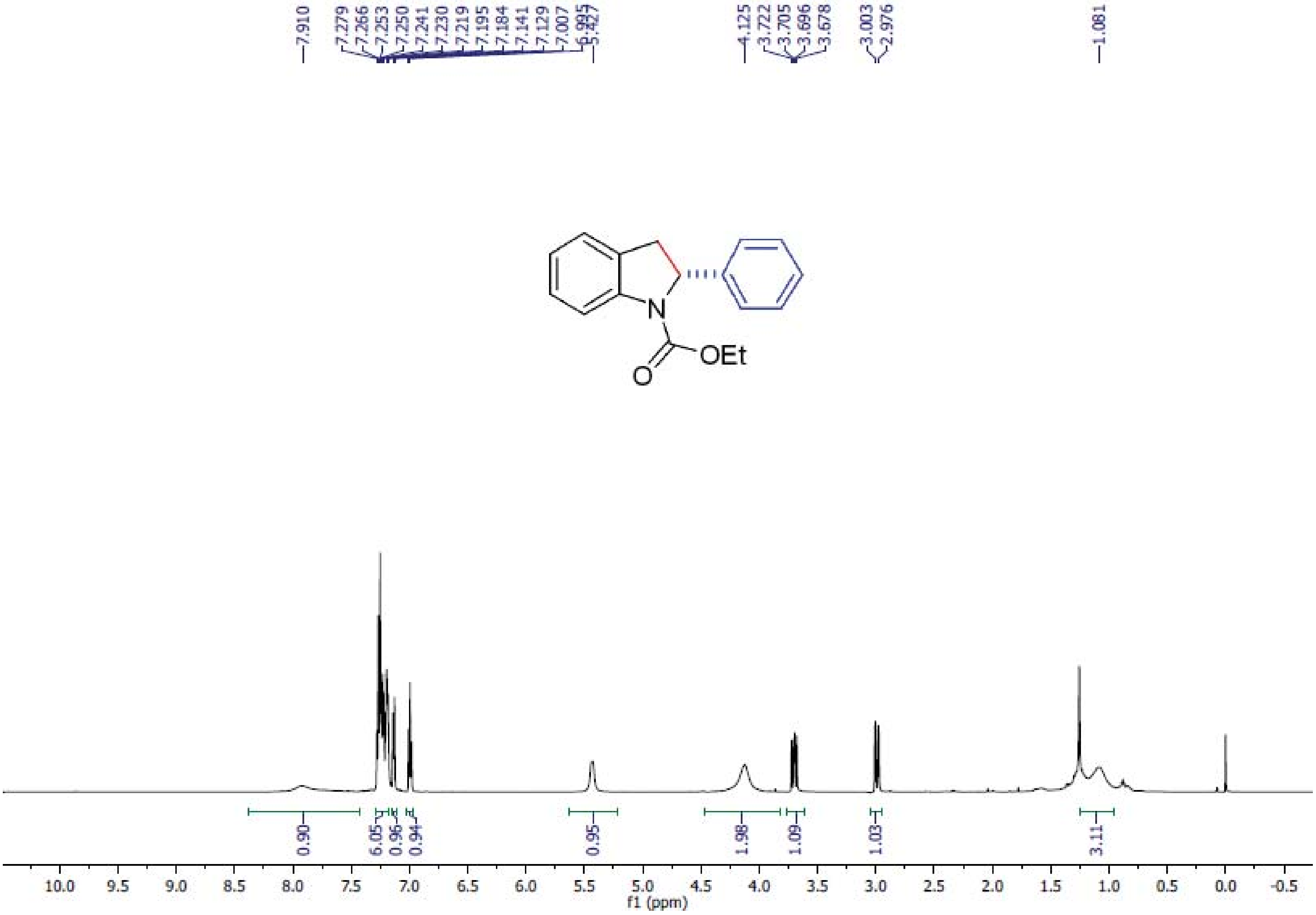


Peak Table

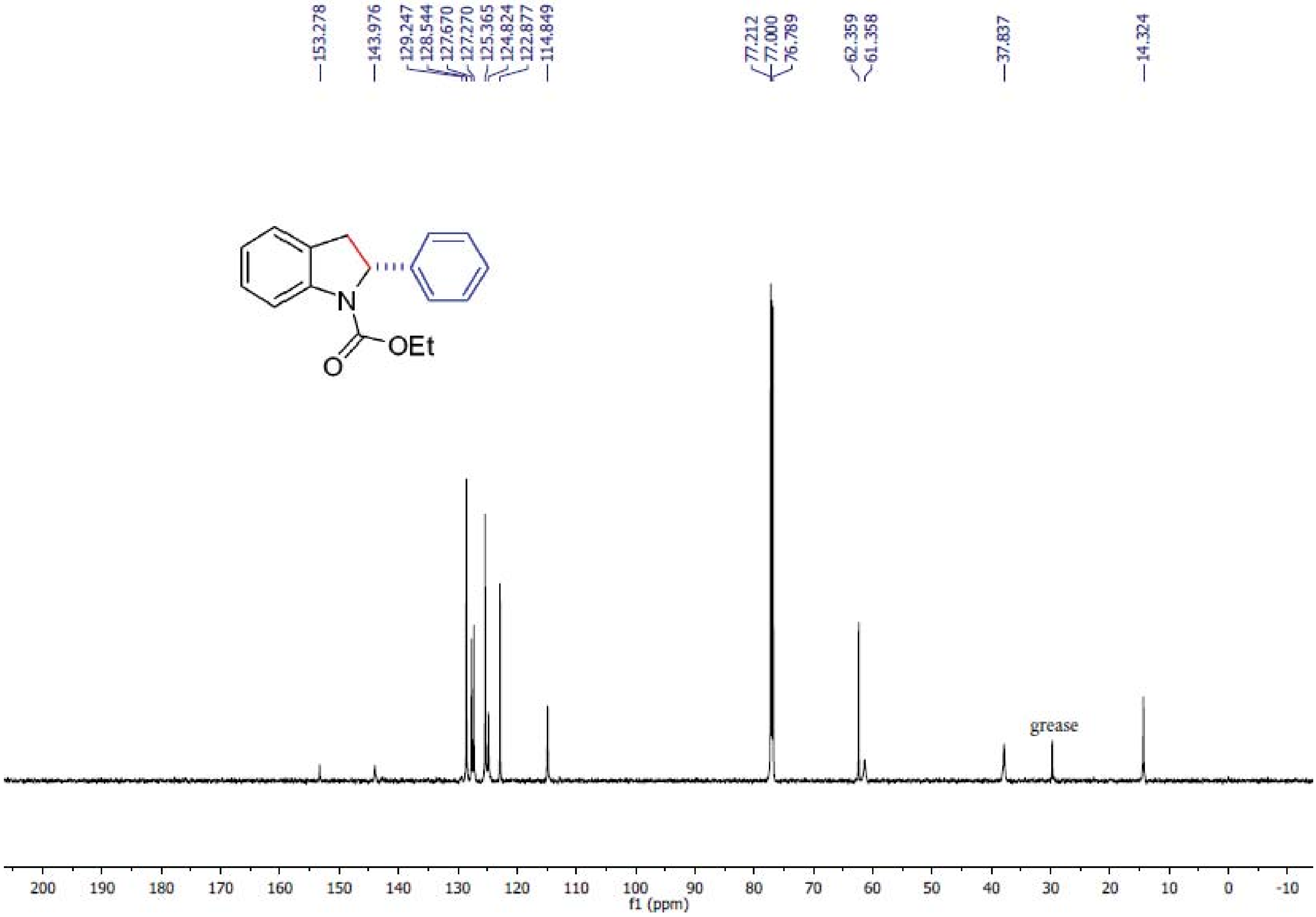
PDA Ch1 236nm

Peak#	Ret. Time	Area	Area%
1	14.449	1506306	16.837
2	17.029	7440359	83.163
Total		8946665	100.000

ethyl (*R*)-2-phenylindoline-1-carboxylate 2b



ethyl (*R*)-2-phenylindoline-1-carboxylate 2b

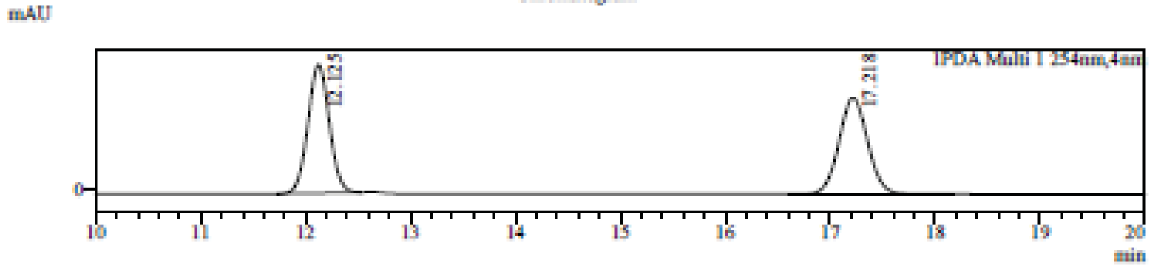


ethyl (*R*)-2-phenylindoline-1-carboxylate 2b

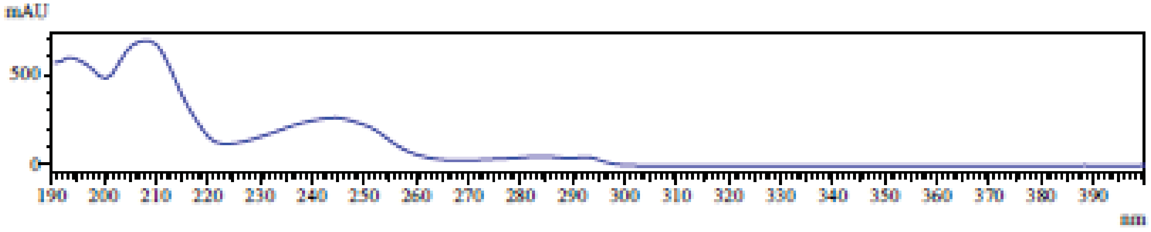
Sample Information

Sample Name	: XW-IV-268-IA-2-1%0.8mL
Sample ID	: XW-IV-268-IA-2-1%0.8mL
Data File	: XW-IV-268-IA-2-1%0.8mL.lcd
Method File	: XW-1%-0.8ml.lcm

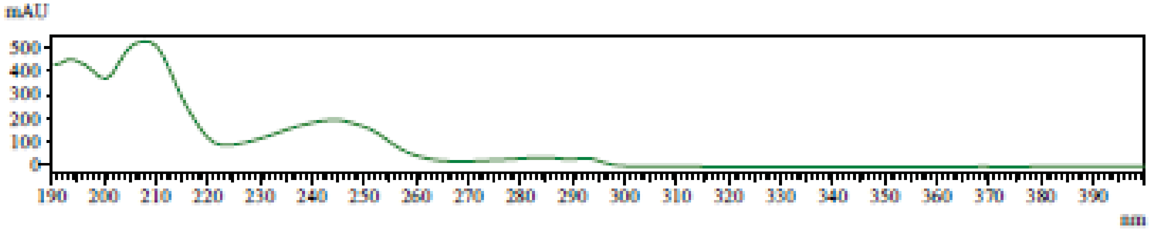
Chromatogram



UV Spectrum
Retention time = 12.125



UV Spectrum
Retention time = 17.218



Peak Table

PDA Ch1 254nm

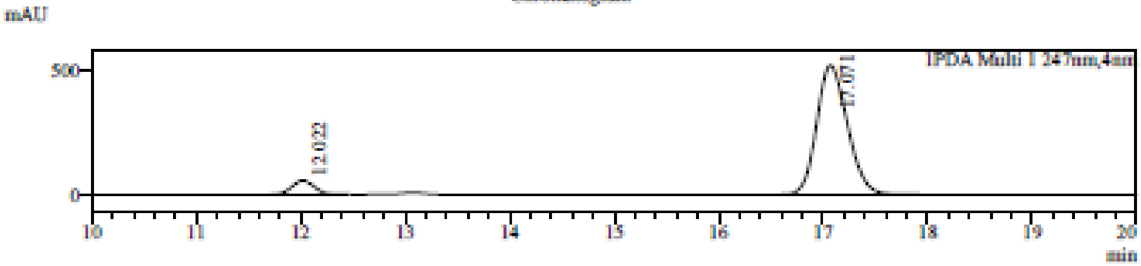
Peak#	Ret. Time	Area	Area%
1	12.125	2254333	49.762
2	17.218	2275872	50.238
Total		4530205	100.000

ethyl (*R*)-2-phenylindoline-1-carboxylate 2b

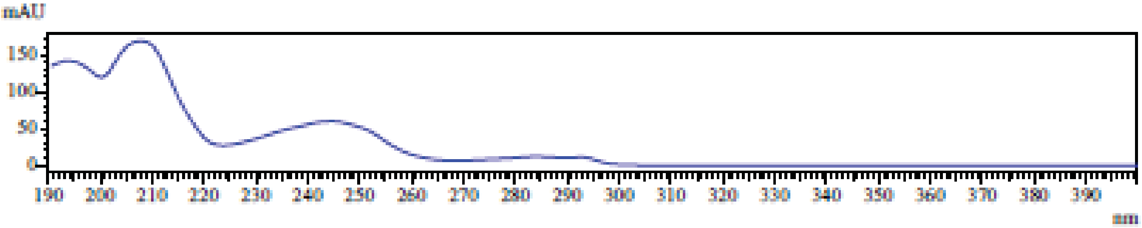
Sample Information

Sample Name	: XW-IV-269-IA-1%0.8mL
Sample ID	: XW-IV-269-IA-1%0.8mL
Data File	: XW-IV-269-IA-1%0.8mL.lcd
Method File	: XW-1%-0.8ml.lcm

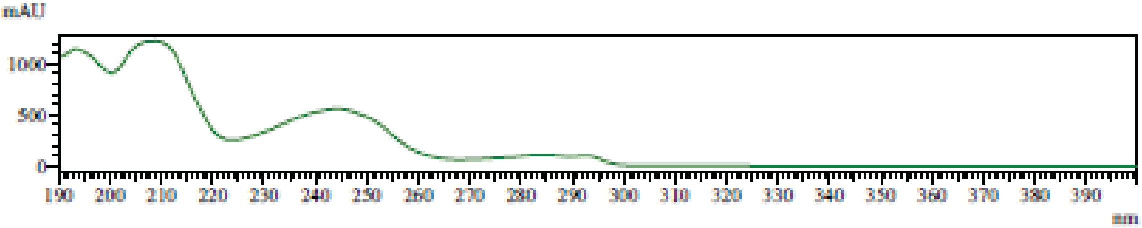
Chromatogram



UV Spectrum
Retention time = 12.022



UV Spectrum
Retention time = 17.071

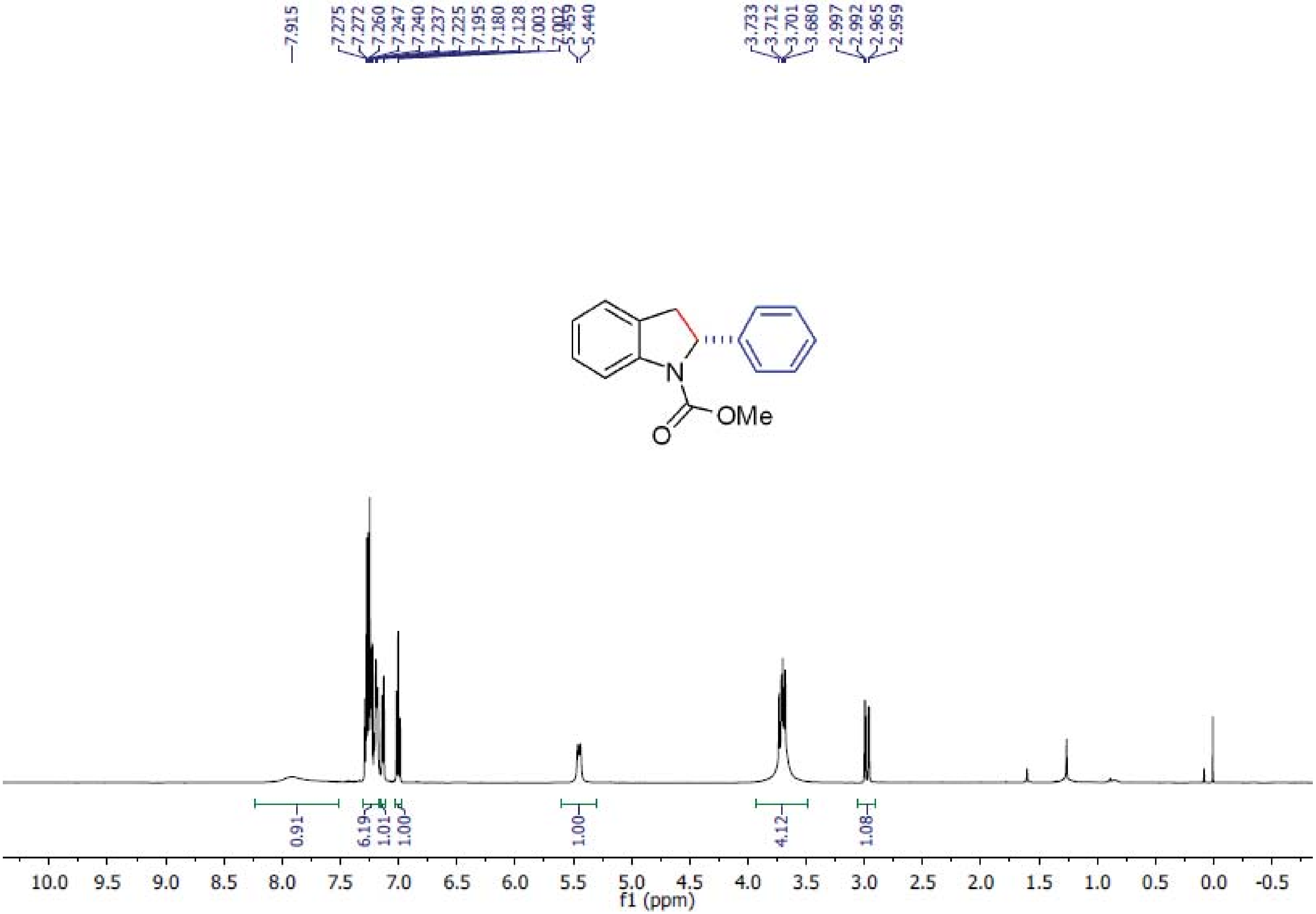


Peak Table

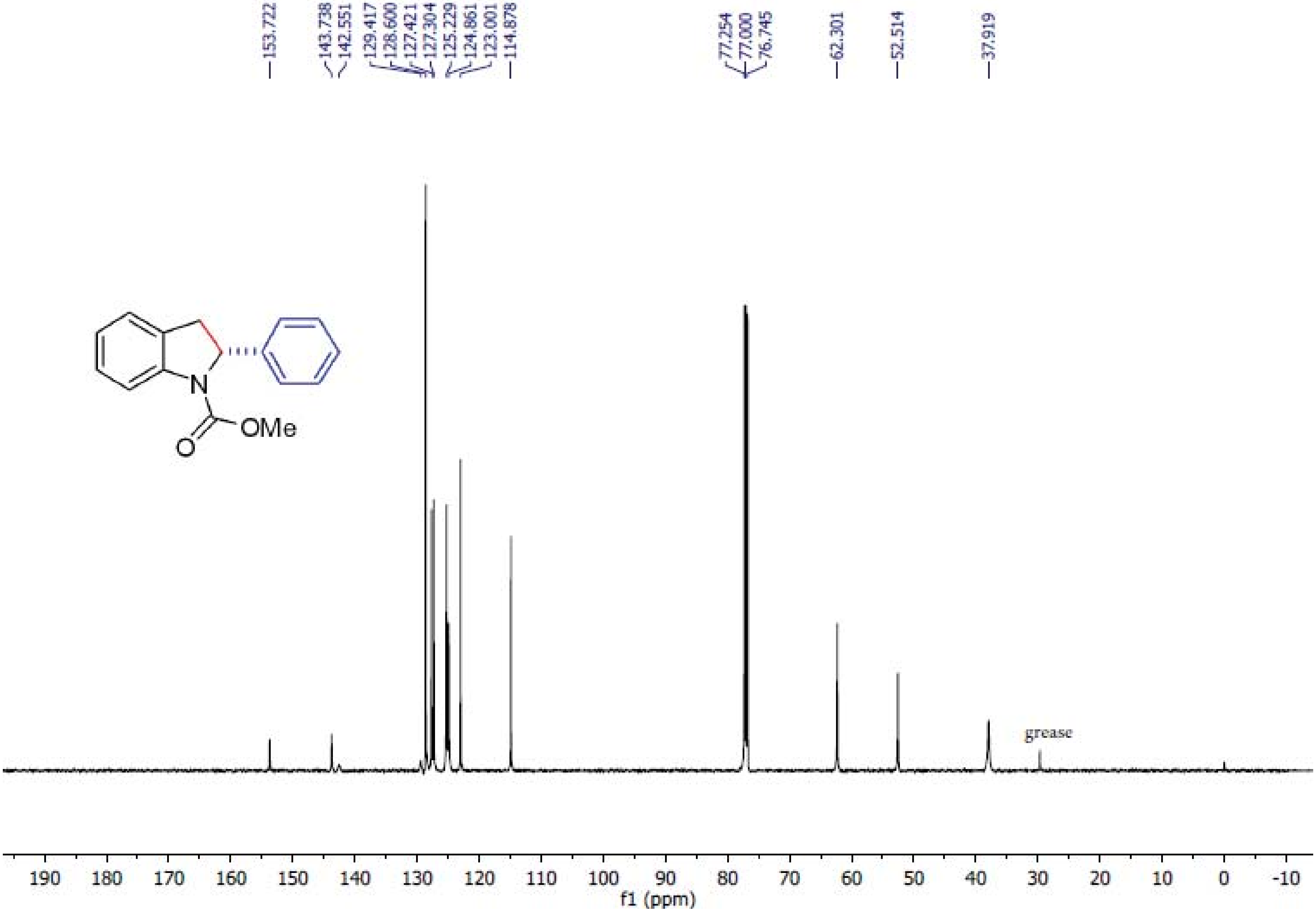
PDA Ch1 247nm

Peak#	Ret. Time	Area	Area%
1	12.022	837835	7.273
2	17.071	10682085	92.727
Total		11519920	100.000

methyl (*R*)-2-phenylindoline-1-carboxylate 2c



methyl (*R*)-2-phenylindoline-1-carboxylate 2c

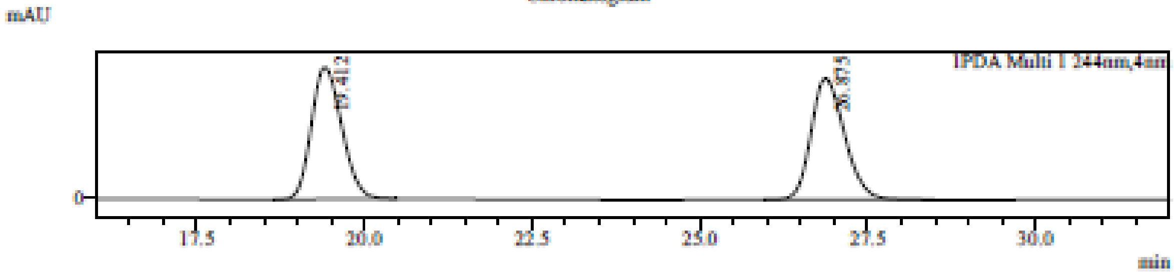


methyl (*R*)-2-phenylindoline-1-carboxylate 2c

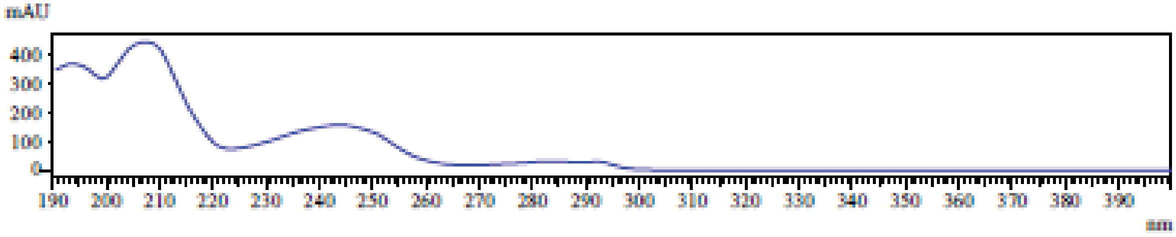
Sample Information

Sample Name	: XW-IV-246-IA-0.5%0.8mL
Sample ID	: XW-IV-246-IA-0.5%0.8mL
Data File	: XW-IV-246-IA-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

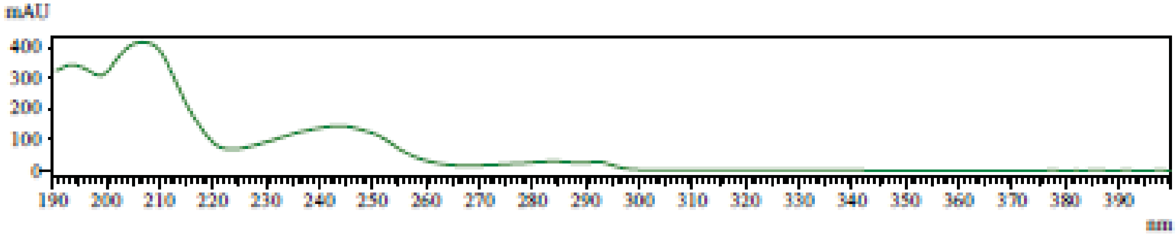
Chromatogram



UV Spectrum
Retention time = 19.412



UV Spectrum
Retention time = 26.875



Peak Table

PDA Ch1 244nm

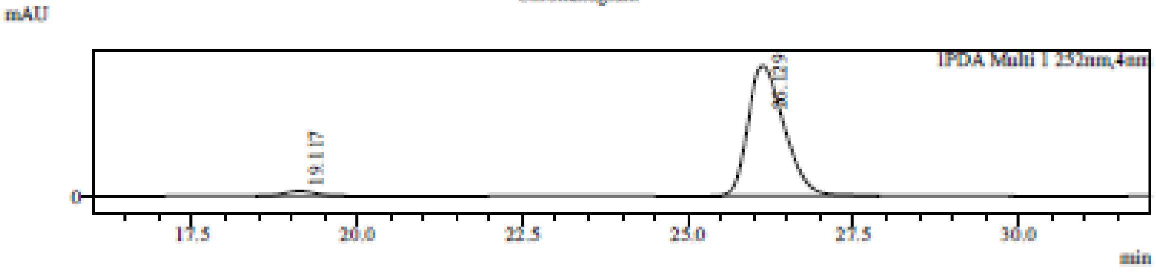
Peak#	Ret. Time	Area	Area%
1	19.412	4857504	49.571
2	26.875	4941667	50.429
Total		9799171	100.000

methyl (*R*)-2-phenylindoline-1-carboxylate 2c

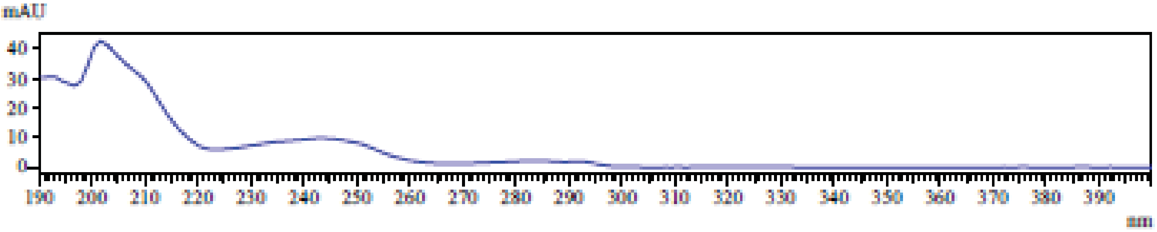
Sample Information

Sample Name	: XW-IV-283-MeOH-IA-0.5%0.8mL
Sample ID	: XW-IV-283-MeOH-IA-0.5%0.8mL
Data File	: XW-IV-283-MeOH-IA-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

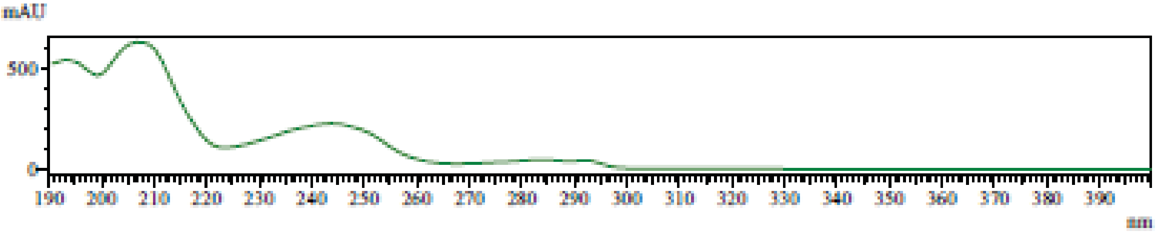
Chromatogram



UV Spectrum
Retention time = 19.117



UV Spectrum
Retention time = 26.129

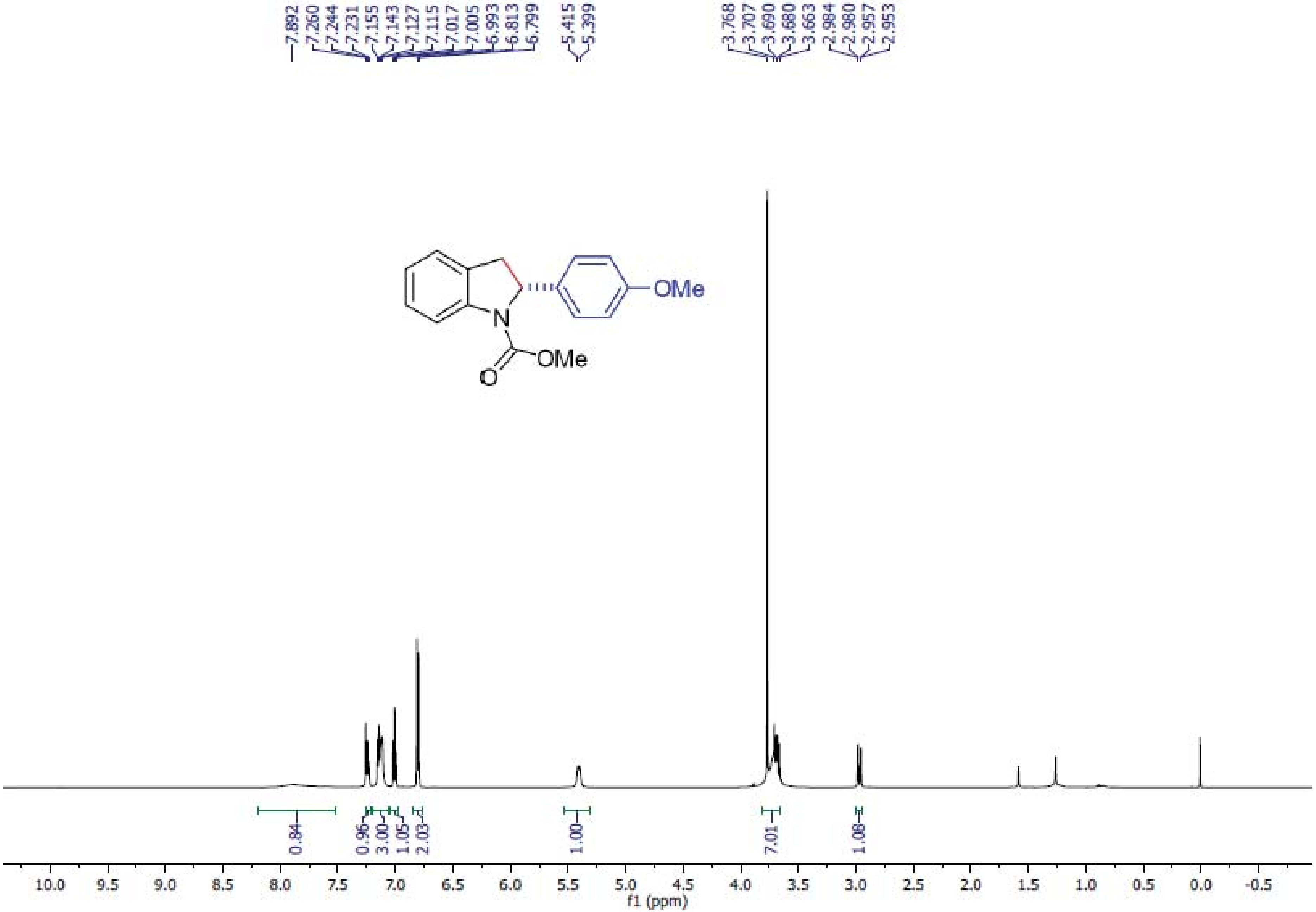


Peak Table

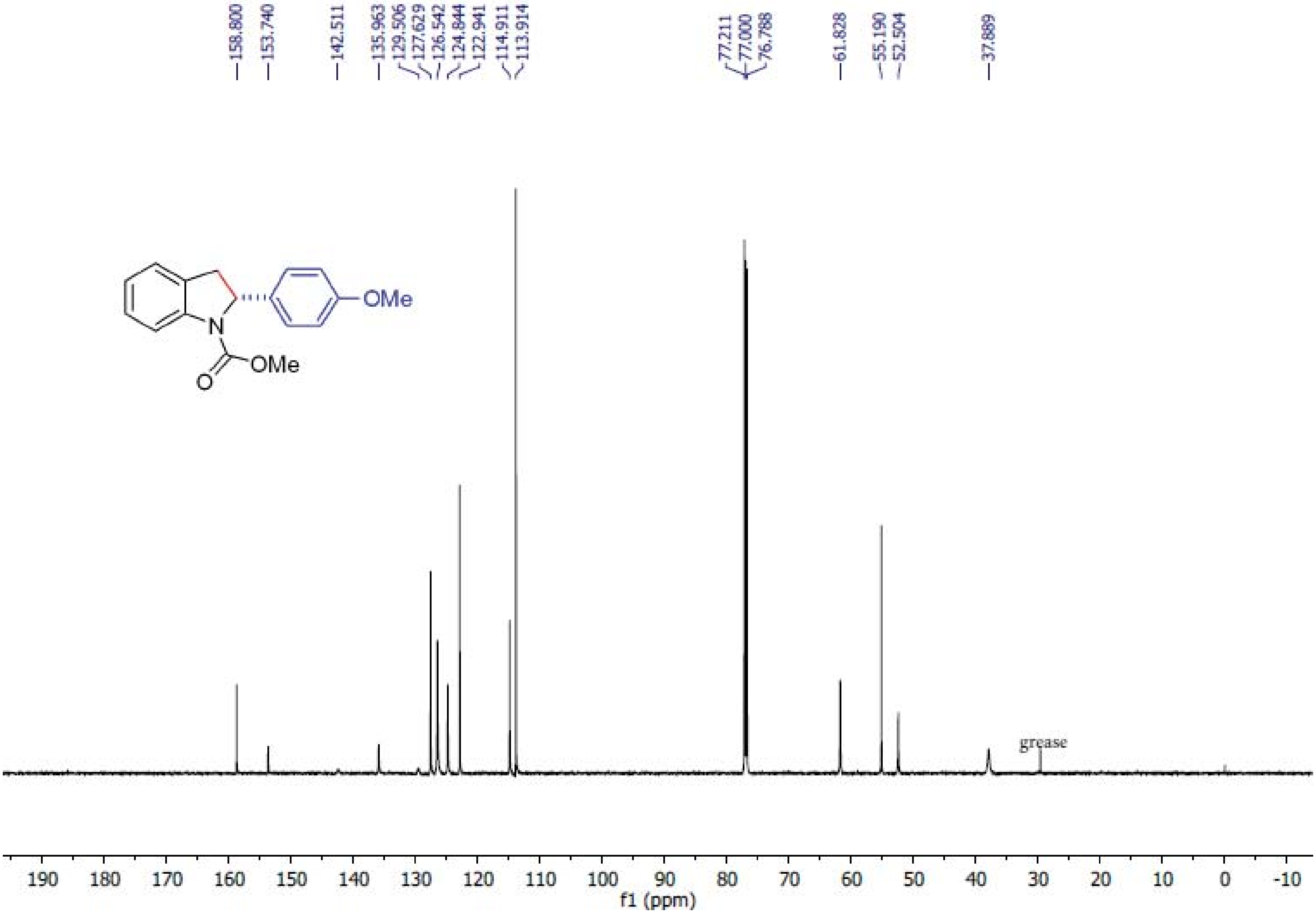
PDA Ch1 252nm

Peak#	Ret. Time	Area	Area%
1	19.117	190423	3.140
2	26.129	5873582	96.860
Total		6064005	100.000

methyl (*R*)-2-(4-methoxyphenyl)indoline-1-carboxylate 2d



methyl (*R*)-2-(4-methoxyphenyl)indoline-1-carboxylate 2d

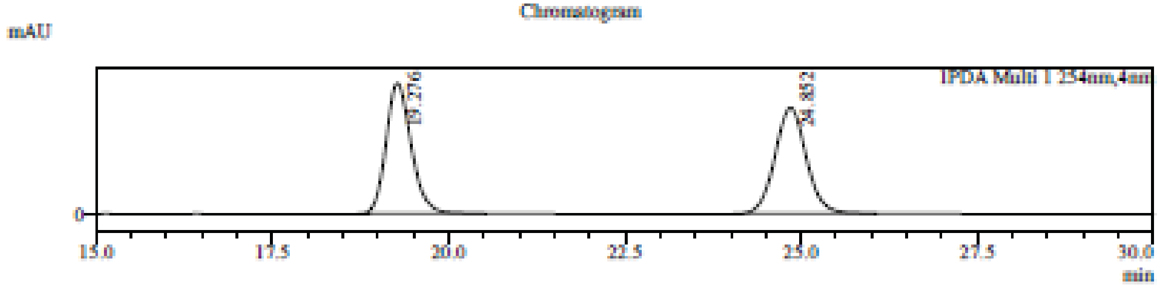


methyl (*R*)-2-(4-methoxyphenyl)indoline-1-carboxylate 2d

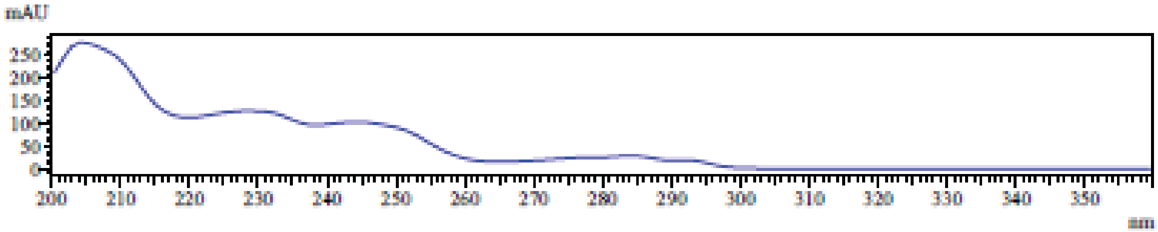
Sample Information

Sample Name	: XW-V-17-2-IA-1%1.0mL
Sample ID	: XW-V-17-2-IA-1%1.0mL
Data File	: XW-V-17-2-IA-1%1.0mL.lcd
Method File	: XW-1%-1.0ml.lcm

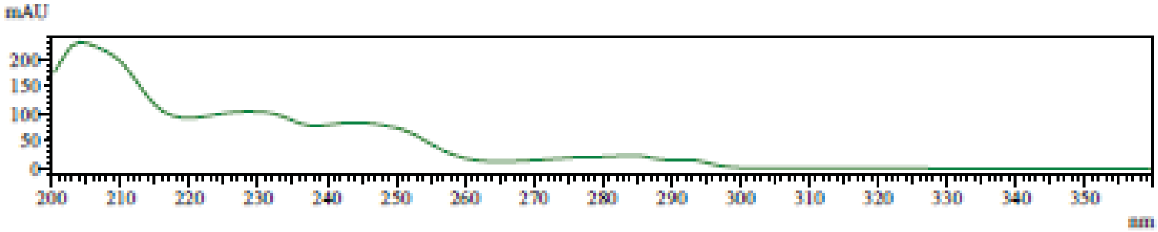
Chromatogram



UV Spectrum
Retention time = 19.276



UV Spectrum
Retention time = 24.852



Peak Table

PDA Ch1 254nm

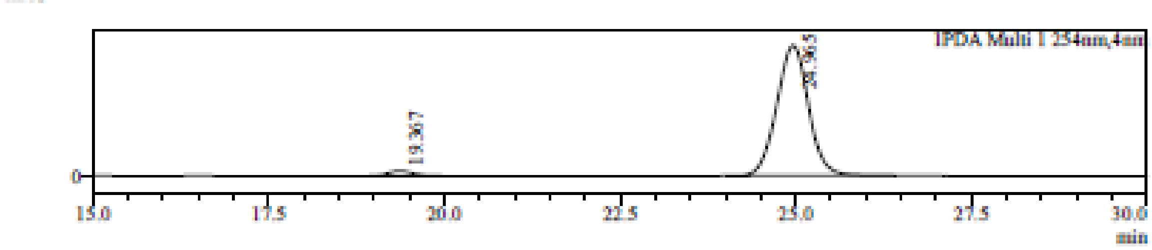
Peak#	Ret. Time	Area	Area%
1	19.276	1594697	49.760
2	24.852	1610066	50.240
Total		3204763	100.000

methyl (*R*)-2-(4-methoxyphenyl)indoline-1-carboxylate 2d

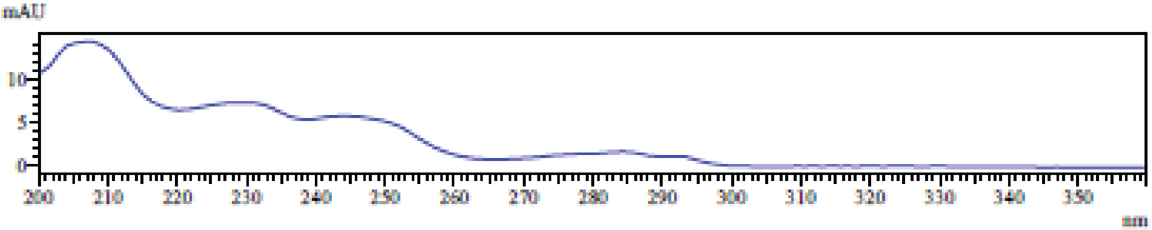
Sample Information

Sample Name : XW-V-18-new-IA-1%1.0mL
Sample ID : XW-V-18-new-IA-1%1.0mL
Data File : XW-V-18-new-IA-1%1.0mL.lcd
Method File : XW-1%-1.0ml.lcm

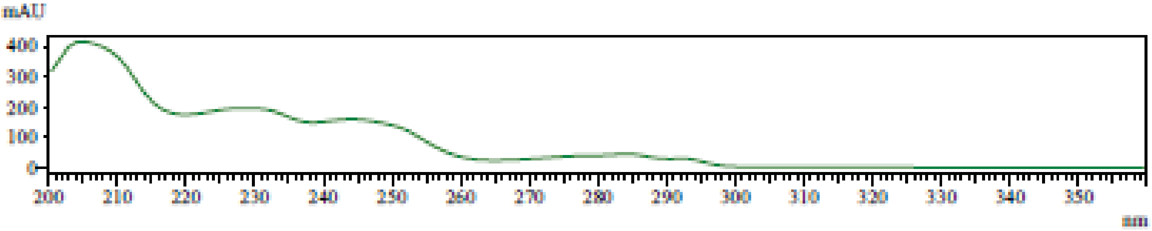
Chromatogram



UV Spectrum
Retention time = 19.367



UV Spectrum
Retention time = 24.965

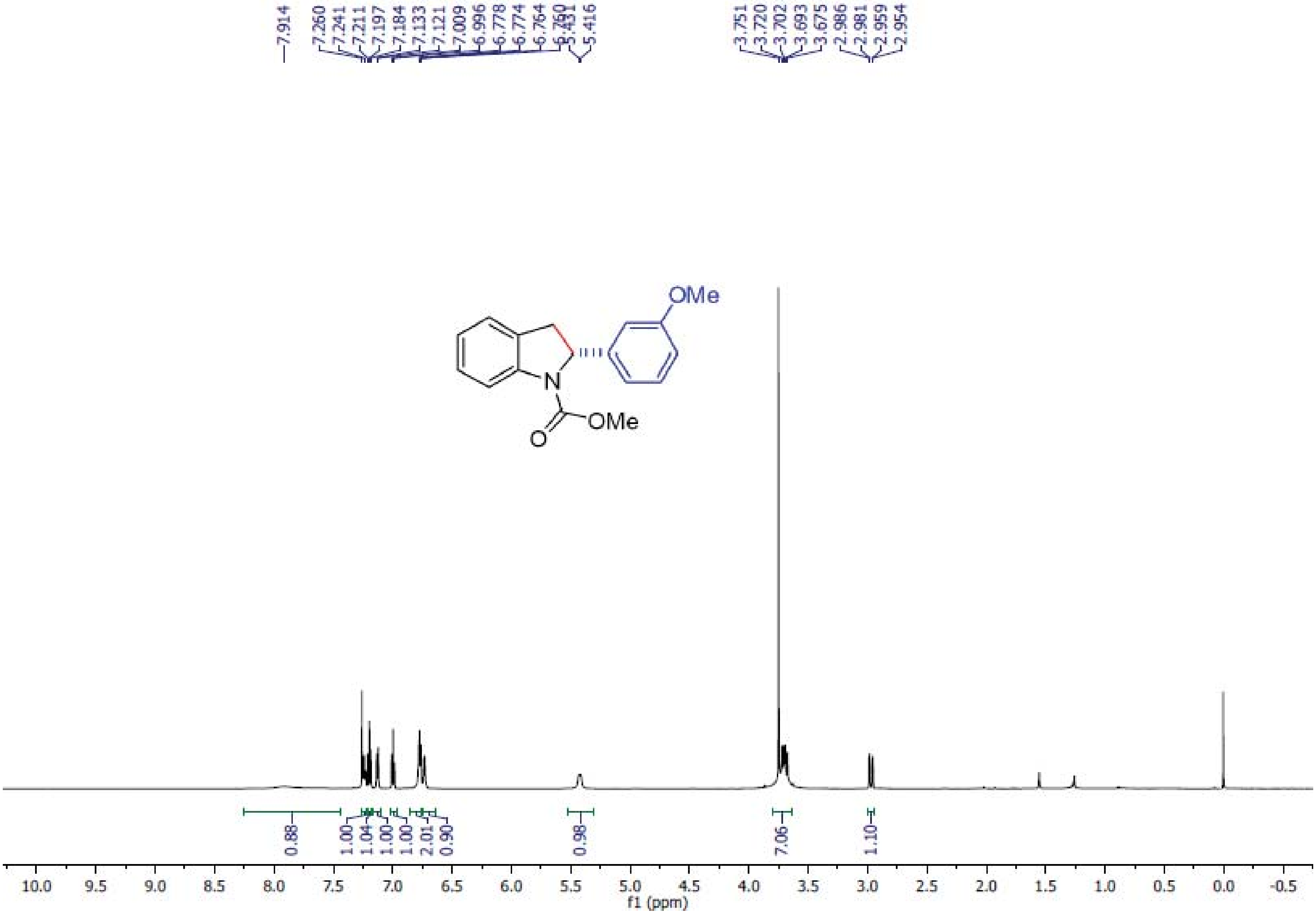


Peak Table

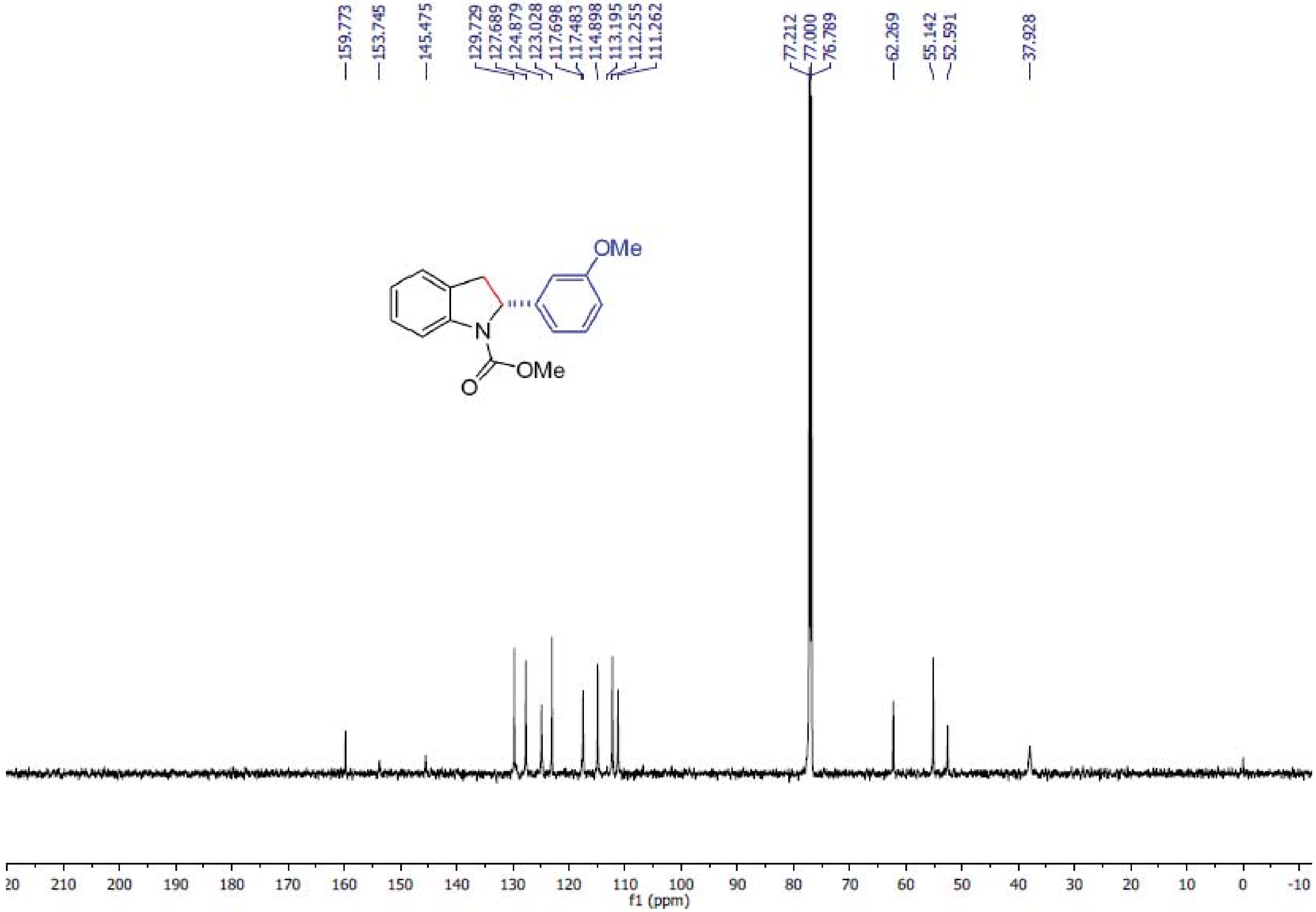
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	19.367	89446	2.820
2	24.965	3082787	97.180
Total		3172233	100.000

methyl (*R*)-2-(3-methoxyphenyl)indoline-1-carboxylate 2e



methyl (*R*)-2-(3-methoxyphenyl)indoline-1-carboxylate 2e

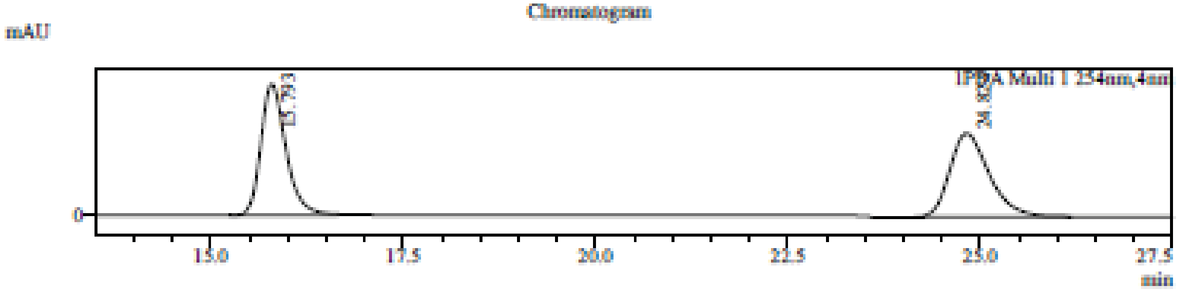


methyl (*R*)-2-(3-methoxyphenyl)indoline-1-carboxylate 2e

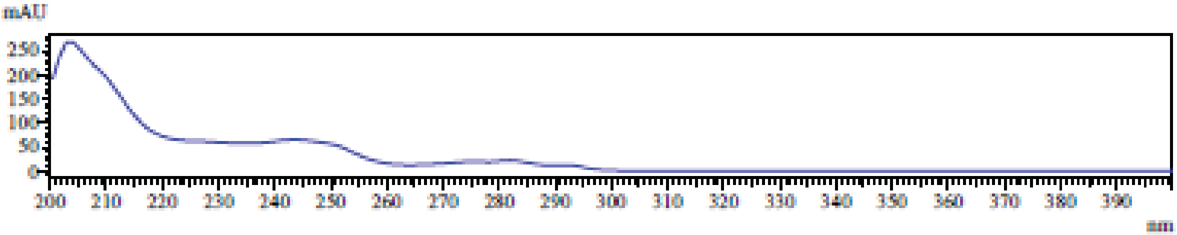
Sample Information

Sample Name : XW-V-7-IA-1%1.0mL
Sample ID : XW-V-7-IA-1%1.0mL
Data File : XW-V-7-IA-1%1.0mL.lcd
Method File : XW-1%-1.0ml.lcm

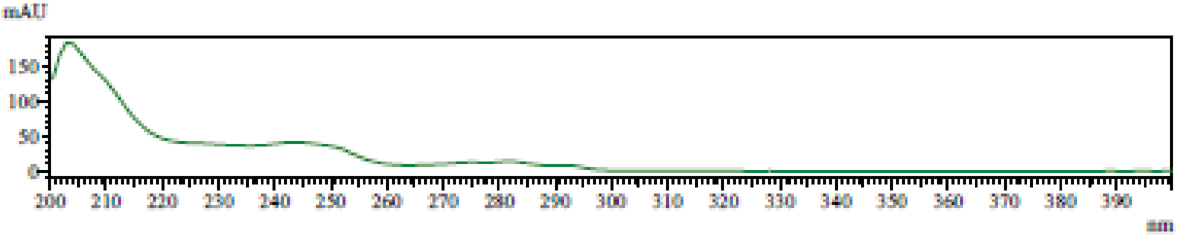
Chromatogram



UV Spectrum
Retention time = 15.793



UV Spectrum
Retention time = 24.824



Peak Table

PDA Ch1 254nm

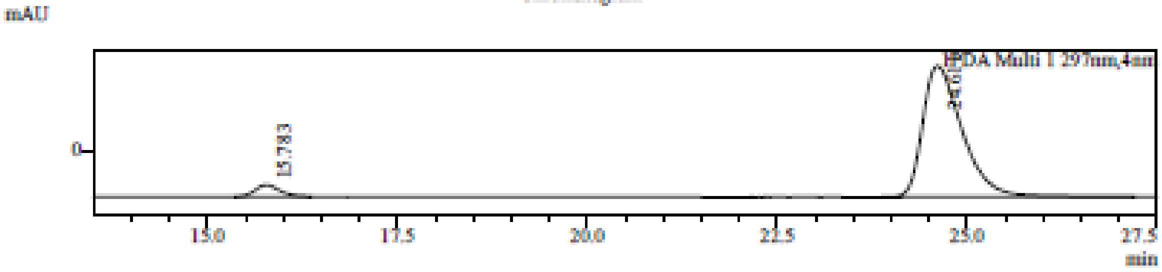
Peak#	Ret. Time	Area	Area%
1	15.793	875771	50.011
2	24.824	875394	49.989
Total		1751165	100.000

methyl (*R*)-2-(3-methoxyphenyl)indoline-1-carboxylate 2e

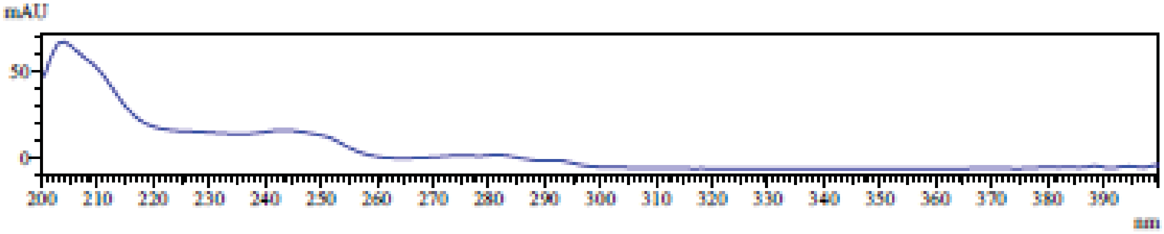
Sample Information

Sample Name : XW-V-8A-IA-1%1.0mL
Sample ID : XW-V-8A-IA-1%1.0mL
Data File : XW-V-8A-MeOH-IA-1%1.0mL.lcd
Method File : XW-1%-1.0ml.lcm

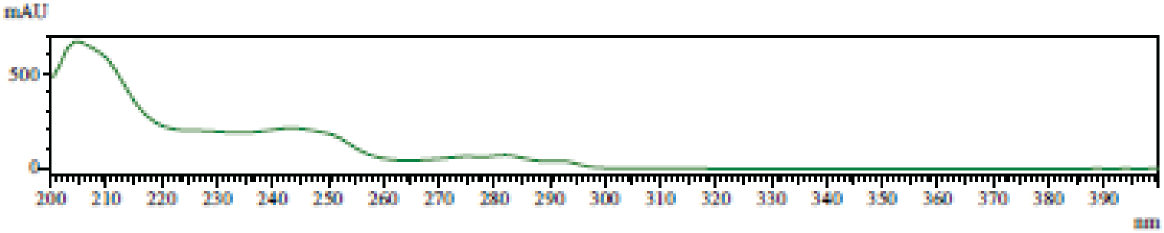
Chromatogram



UV Spectrum
Retention time = 15.783



UV Spectrum
Retention time = 24.611

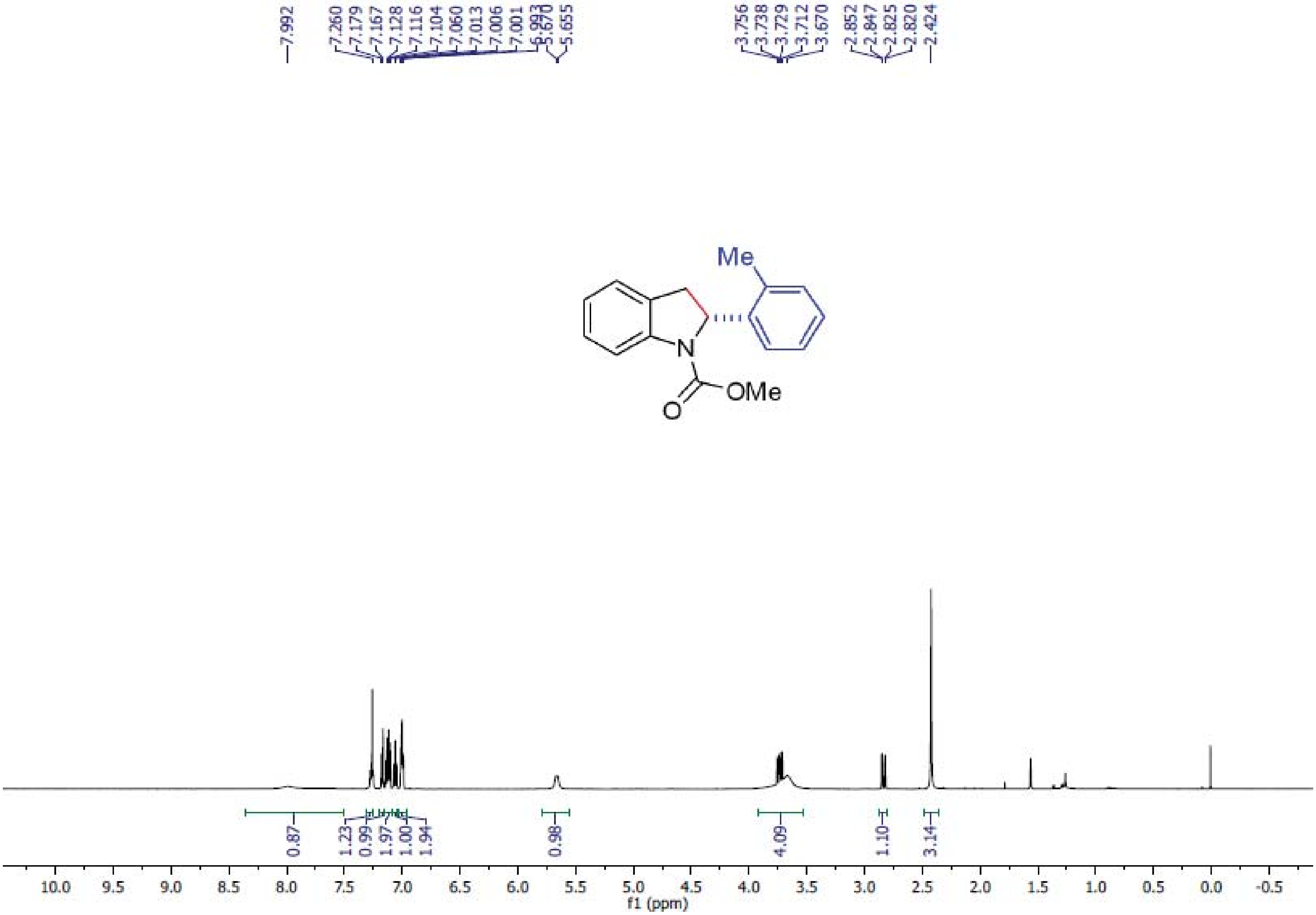


Peak Table

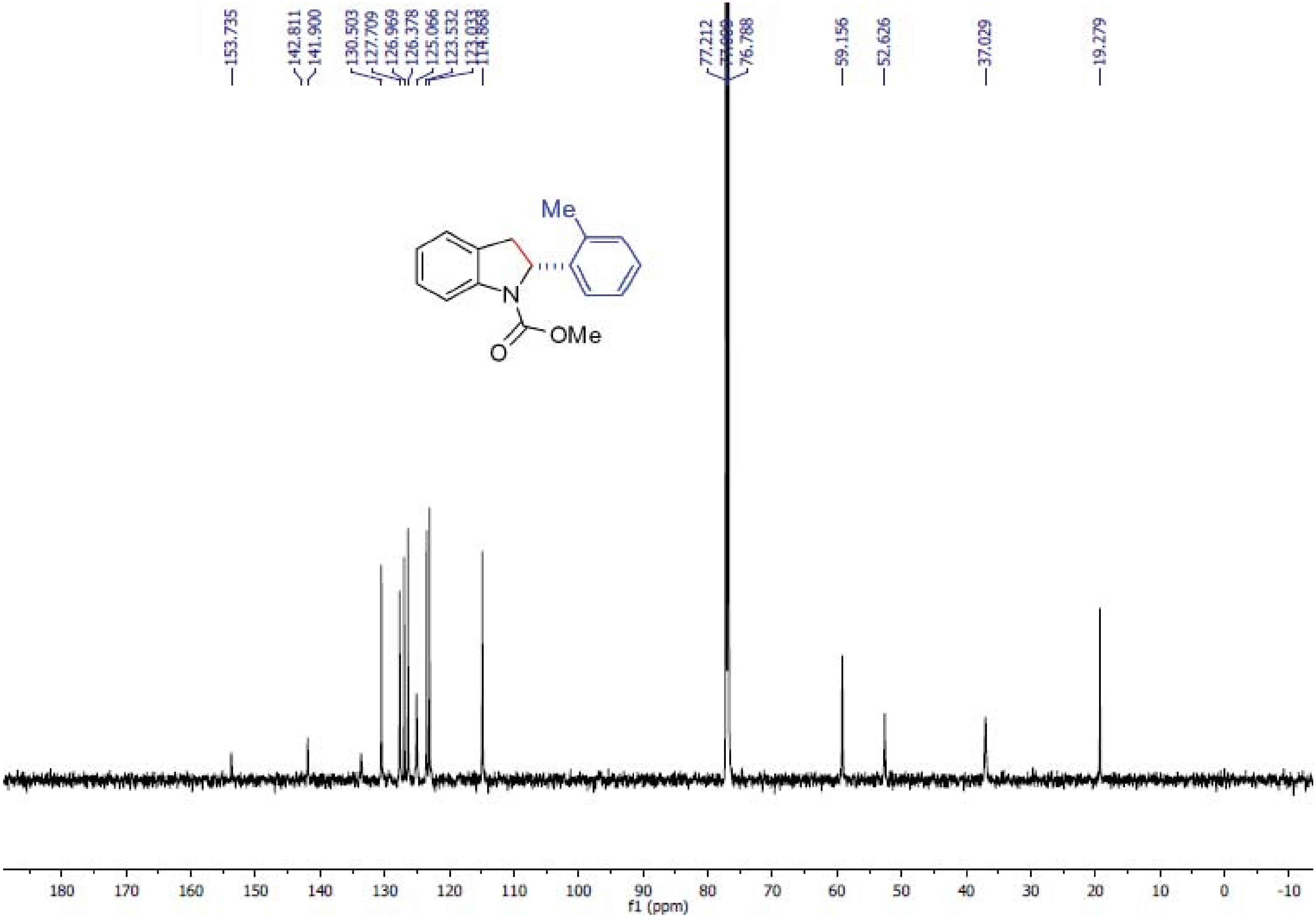
PDA Ch1 297nm

Peak#	Ret. Time	Area	Area%
1	15.783	34284	5.273
2	24.611	615910	94.727
Total		650195	100.000

methyl (*R*)-2-(o-tolyl)indoline-1-carboxylate 2f



methyl (*R*)-2-(o-tolyl)indoline-1-carboxylate 2f

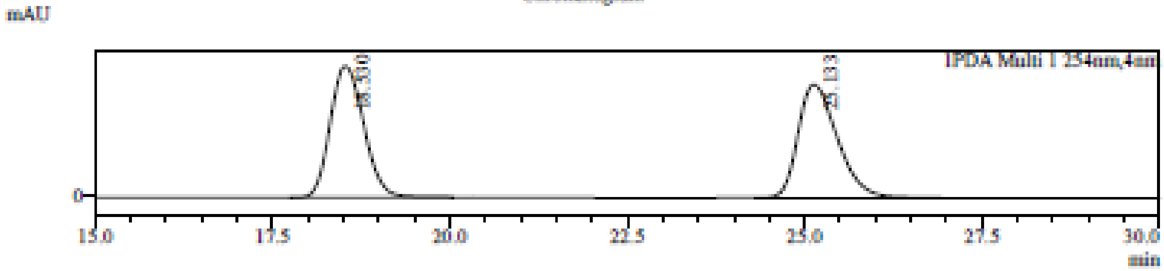


methyl (*R*)-2-(o-tolyl)indoline-1-carboxylate 2f

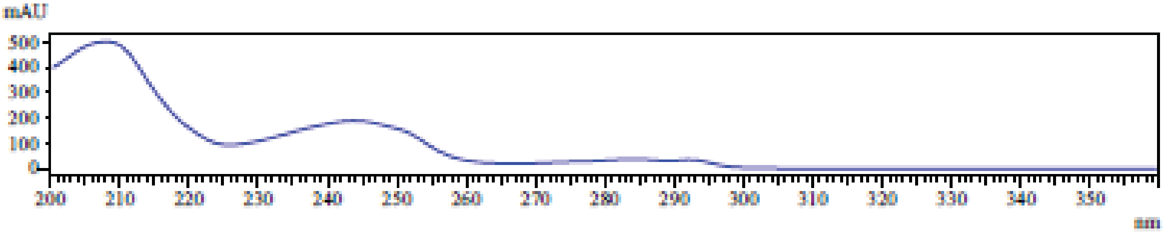
Sample Information

Sample Name	: XW-V-46-IA-0.5%0.8mL
Sample ID	: XW-V-46-IA-0.5%0.8mL
Data File	: XW-V-46-IA-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

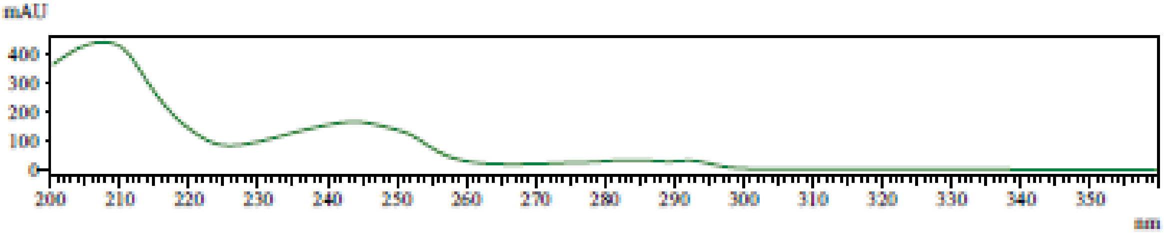
Chromatogram



UV Spectrum
Retention time = 18.530



UV Spectrum
Retention time = 25.133



Peak Table

PDA Ch1 254nm

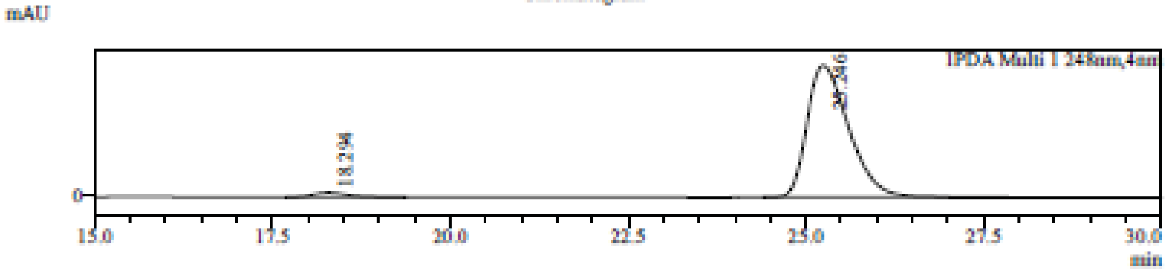
Peak#	Ret. Time	Area	Area%
1	18.530	3403363	49.929
2	25.133	3413071	50.071
Total		6816434	100.000

methyl (*R*)-2-(o-tolyl)indoline-1-carboxylate 2f

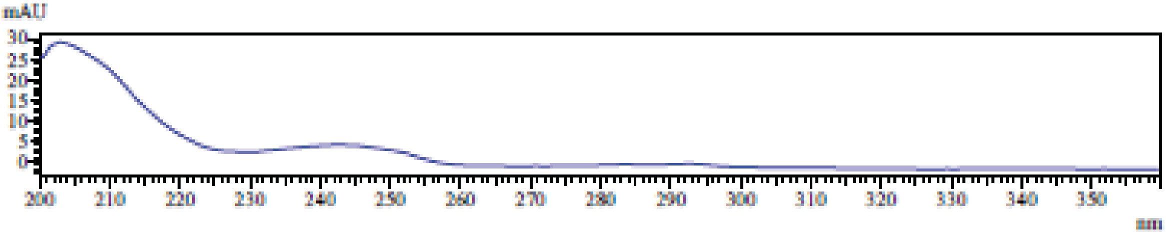
Sample Information

Sample Name : XW-V-47A-IA-0.5%0.8mL
Sample ID : XW-V-47A-IA-0.5%0.8mL
Data File : XW-V-47A-IA-0.5%0.8mL.lcd
Method File : XW-0.5%-0.8ml.lcm

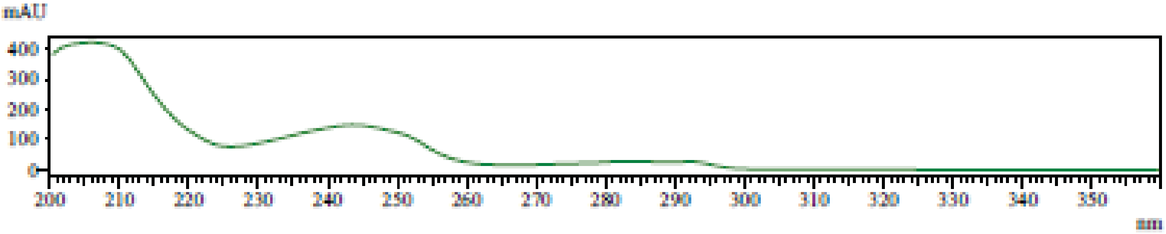
Chromatogram



UV Spectrum
Retention time = 18.294



UV Spectrum
Retention time = 25.246

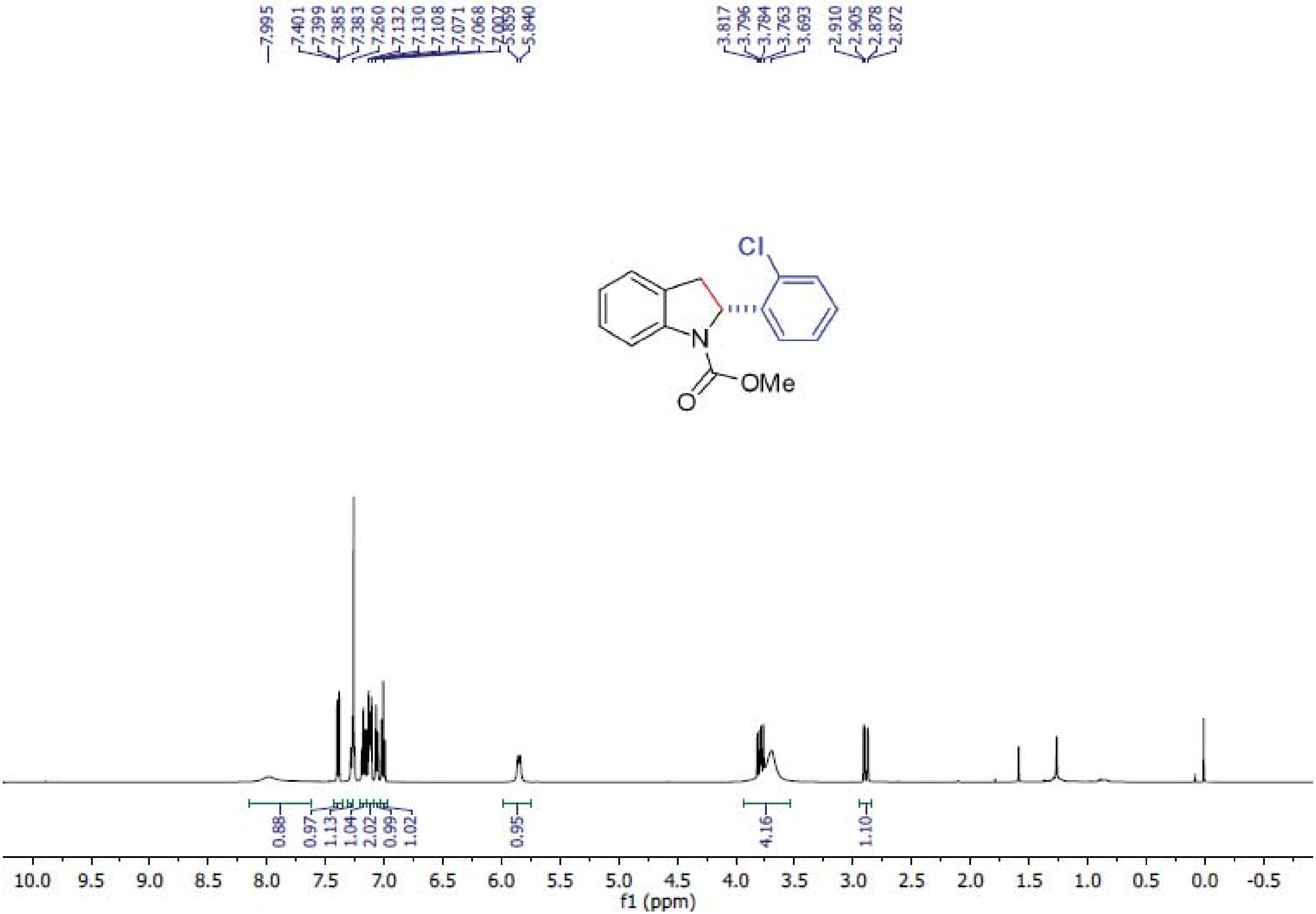


Peak Table

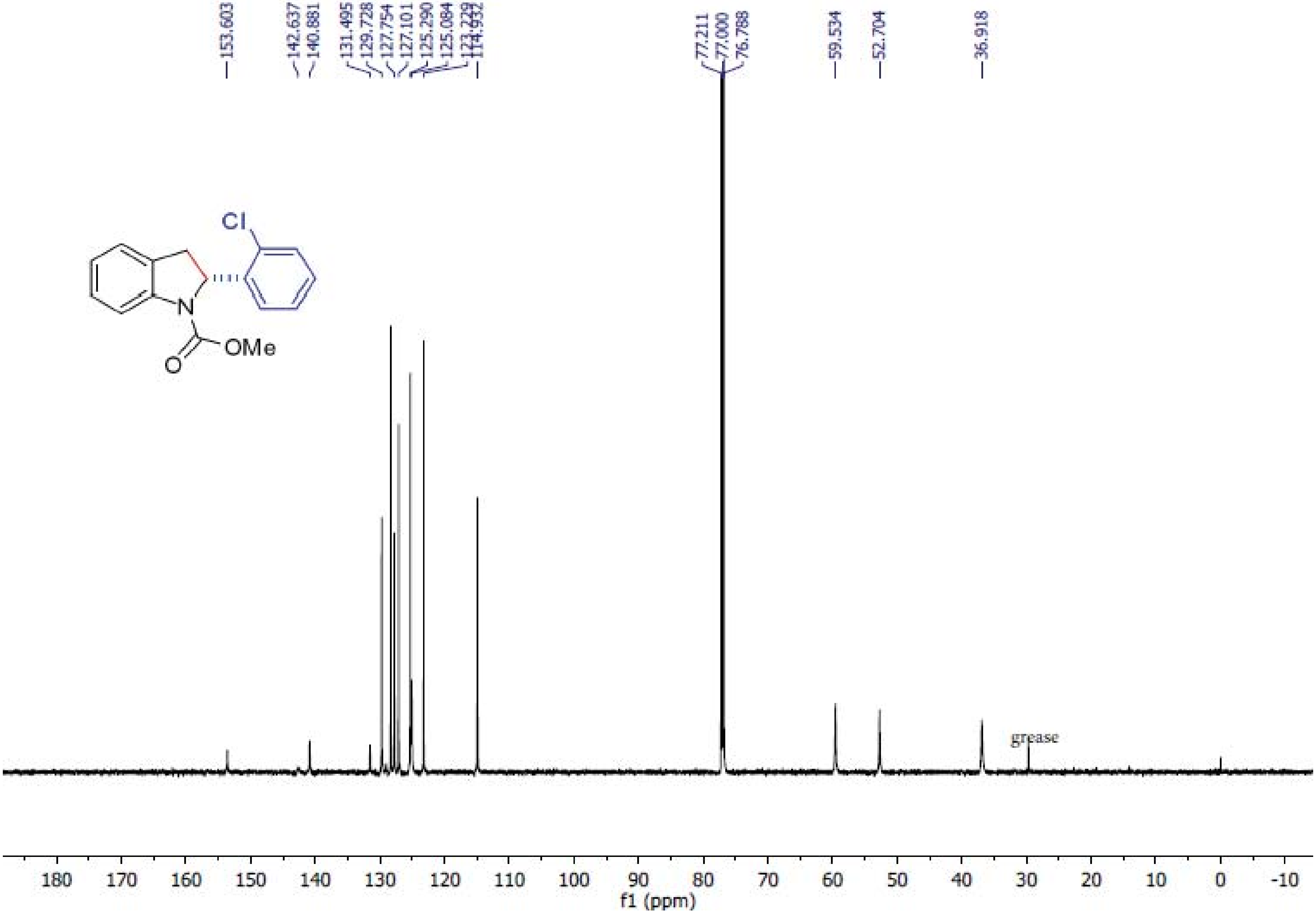
PDA Ch1 248nm

Peak#	Ret. Time	Area	Area%
1	18.294	164441	2.886
2	25.246	5533370	97.114
Total		5697811	100.000

methyl (*R*)-2-(2-chlorophenyl)indoline-1-carboxylate 2g



methyl (*R*)-2-(2-chlorophenyl)indoline-1-carboxylate 2g

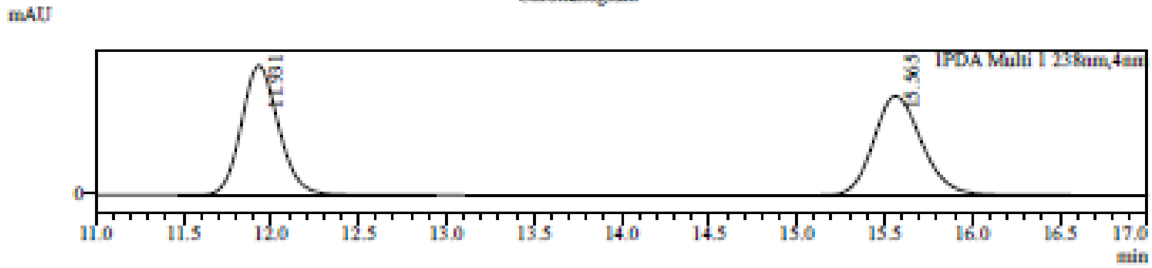


methyl (*R*)-2-(2-chlorophenyl)indoline-1-carboxylate 2g

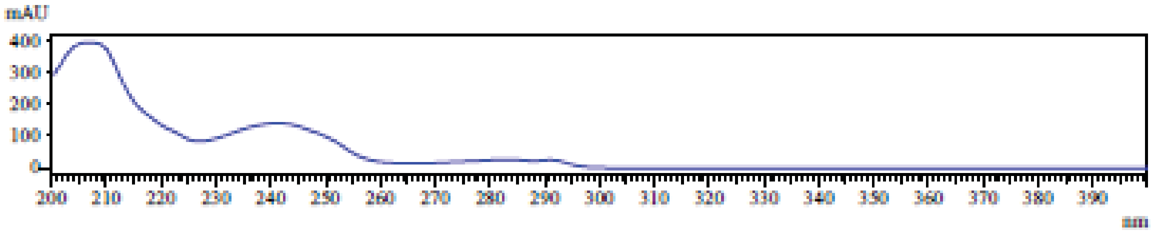
Sample Information

Sample Name	: XW-V-13-IA-1%0.8.0mL
Sample ID	: XW-V-13-IA-1%0.8.0mL
Data File	: XW-V-13-IA-1%0.8.0mL.lcd
Method File	: XW-1%-0.8ml.lcm

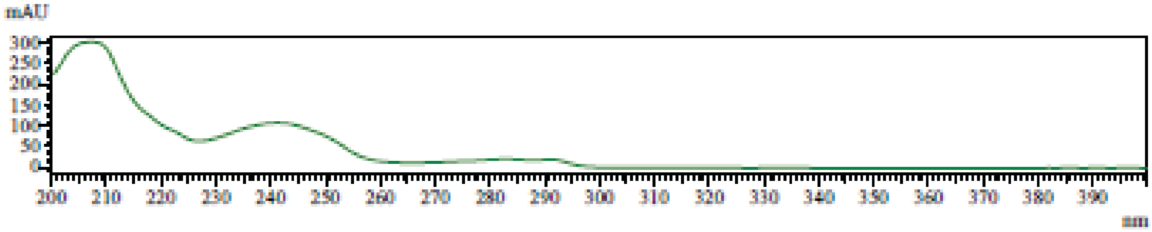
Chromatogram



UV Spectrum
Retention time = 11.931



UV Spectrum
Retention time = 15.565



Peak Table

PDA Ch1 238nm

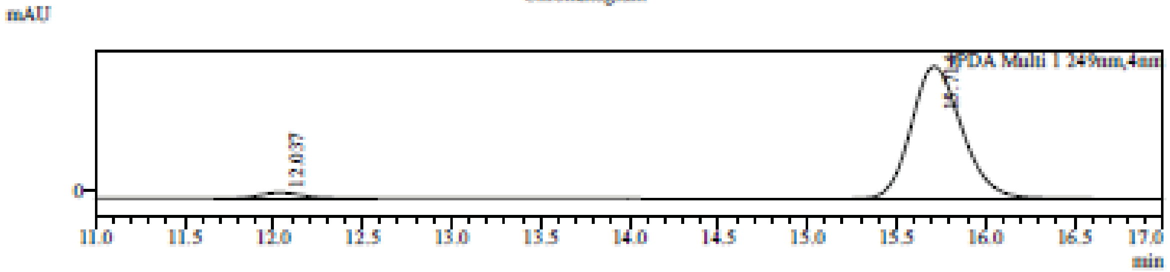
Peak#	Ret. Time	Area	Area%
1	11.931	2006931	50.175
2	15.565	1992922	49.825
Total		3999853	100.000

methyl (*R*)-2-(2-chlorophenyl)indoline-1-carboxylate 2g

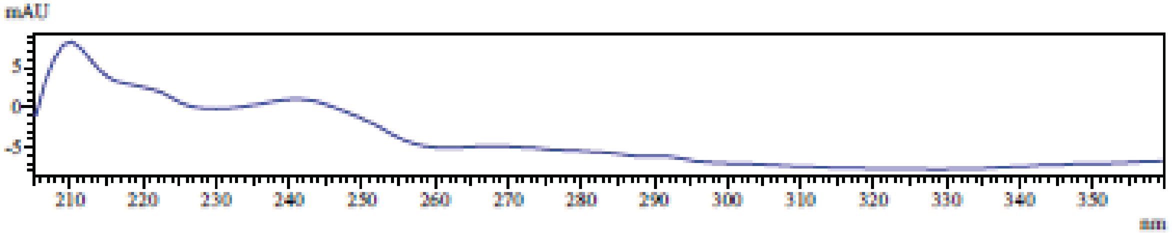
Sample Information

Sample Name : XW-V-11-MeOH-2-IA-1%0.8mL
Sample ID : XW-V-11-MeOH-2-IA-1%0.8mL
Data File : XW-V-11-MeOH-2-IA-1%0.8mL.lcd
Method File : XW-1%-0.8ml.lcm

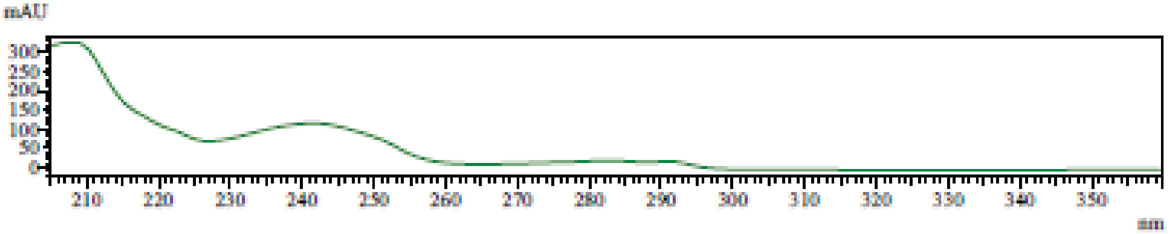
Chromatogram



UV Spectrum
Retention time = 12.037



UV Spectrum
Retention time = 15.714

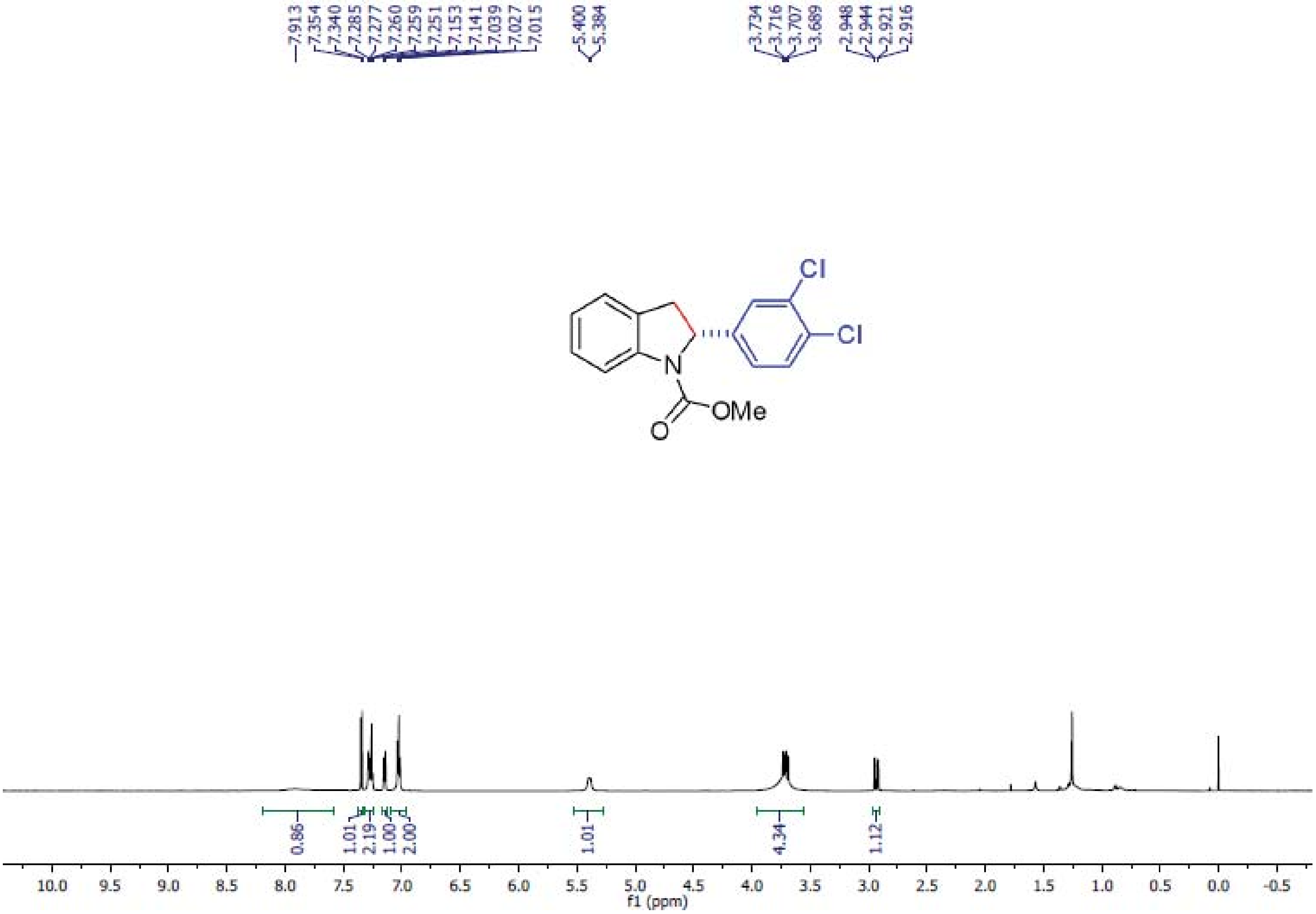


Peak Table

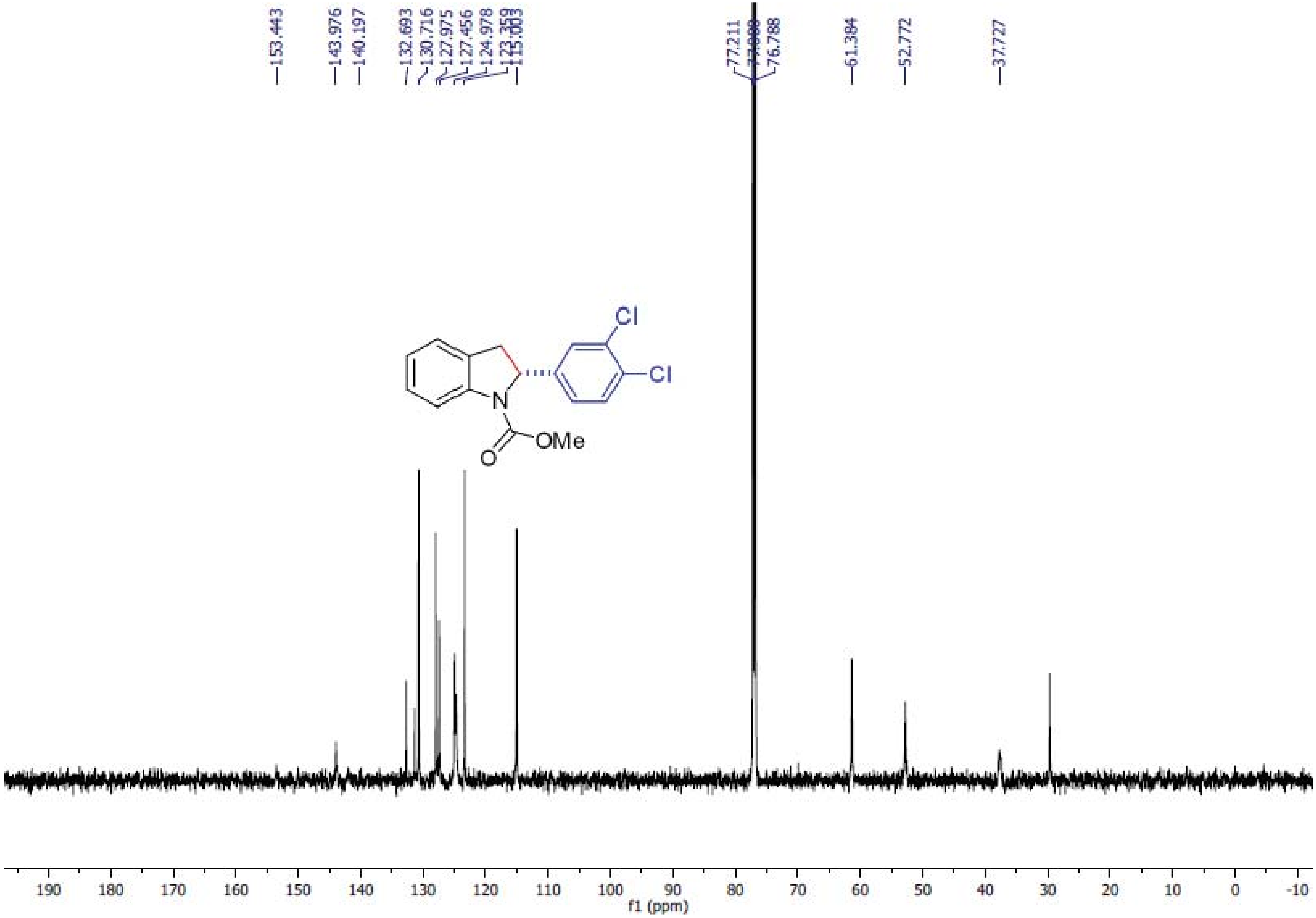
PDA Ch1 249nm

Peak#	Ret. Time	Area	Area%
1	12.037	64130	3.500
2	15.714	1768249	96.500
Total		1832379	100.000

methyl (*R*)-2-(3,4-dichlorophenyl)indoline-1-carboxylate 2h



methyl (*R*)-2-(3,4-dichlorophenyl)indoline-1-carboxylate 2h

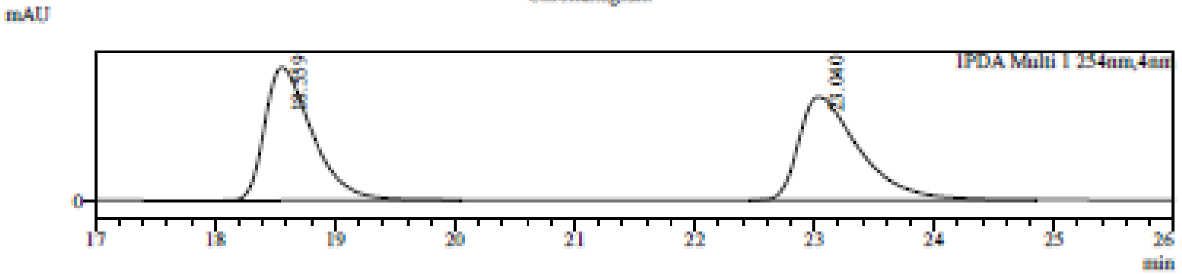


methyl (*R*)-2-(3,4-dichlorophenyl)indoline-1-carboxylate 2h

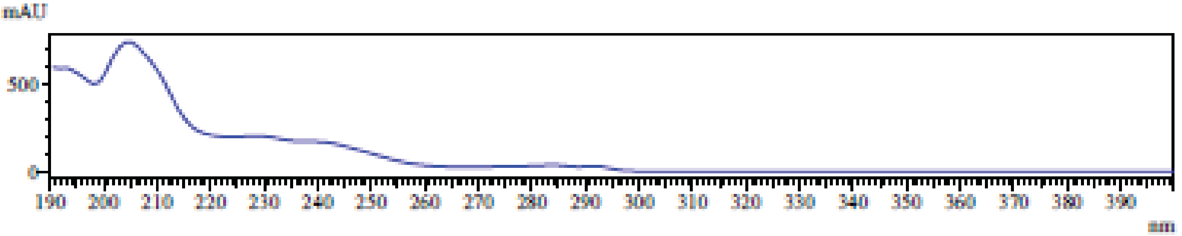
Sample Information

Sample Name	: XW-IV-262-2-IB-0.5%0.8mL
Sample ID	: XW-IV-262-2-IB-0.5%0.8mL
Data File	: XW-IV-262-2-IB-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

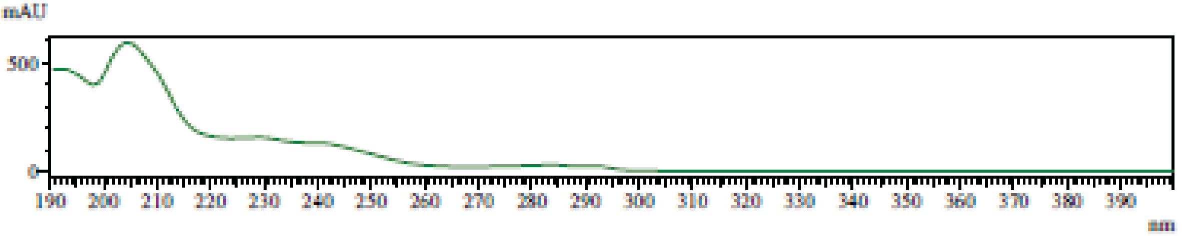
Chromatogram



UV Spectrum
Retention time = 18.559



UV Spectrum
Retention time = 23.040



Peak Table

PDA Ch1 254nm

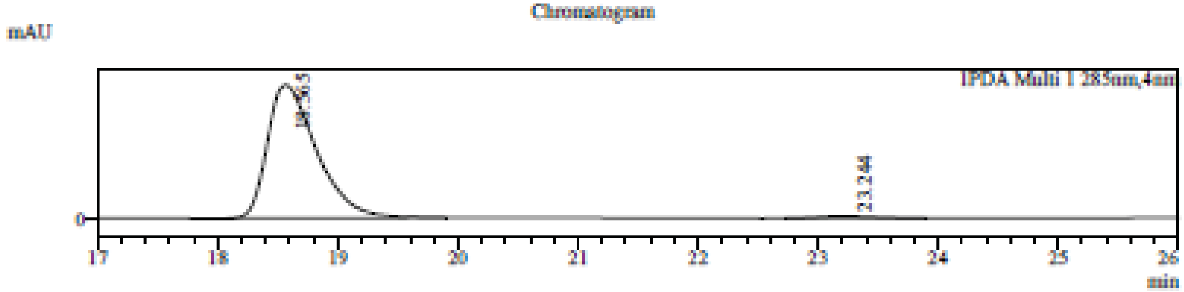
Peak#	Ret. Time	Area	Area%
1	18.559	1880586	50.371
2	23.040	1852905	49.629
Total		3733491	100.000

methyl (*R*)-2-(3,4-dichlorophenyl)indoline-1-carboxylate 2h

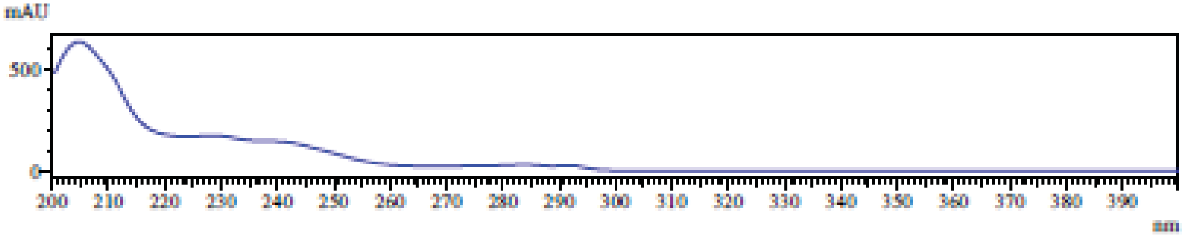
Sample Information

Sample Name : XW-IV-292B-MeOH-1-IB-0.5%0.8mL
Sample ID : XW-IV-292B-MeOH-1-IB-0.5%0.8mL
Data File : XW-IV-292B-MeOH-1-IB-0.5%0.8mL.lcd
Method File : XW-0.5%-0.8ml.lcm

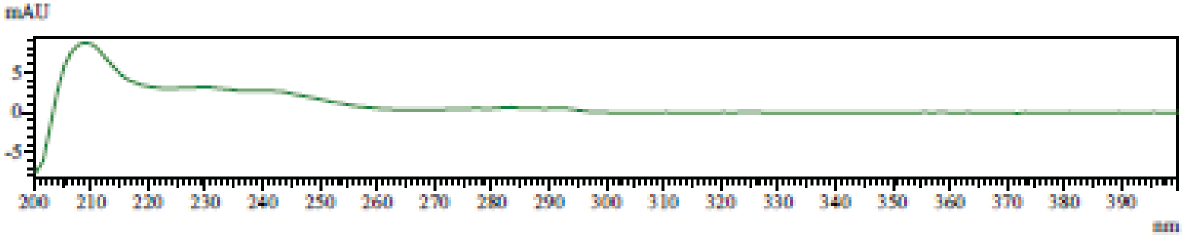
Chromatogram



UV Spectrum
Retention time = 18.565



UV Spectrum
Retention time = 23.244

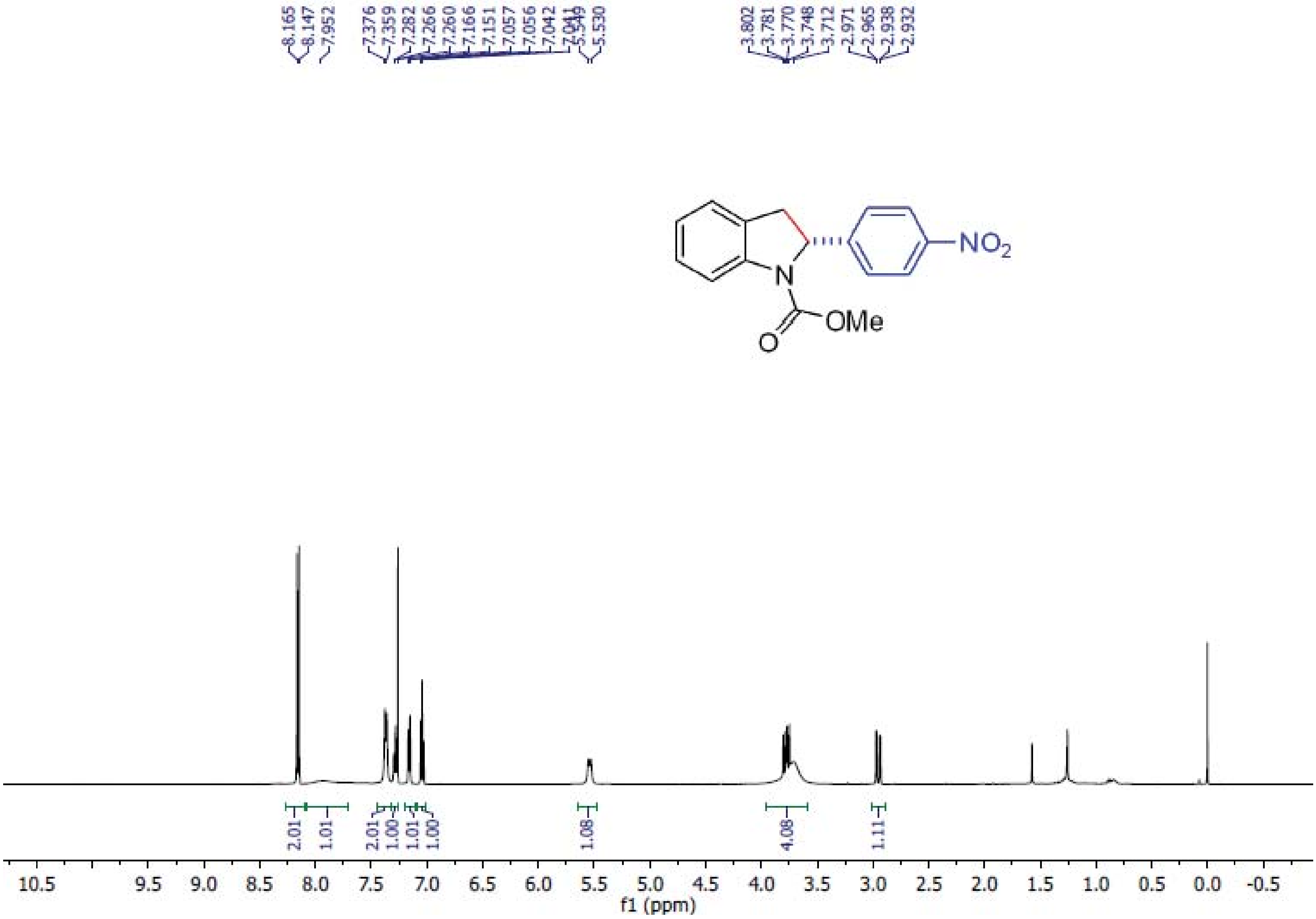


Peak Table

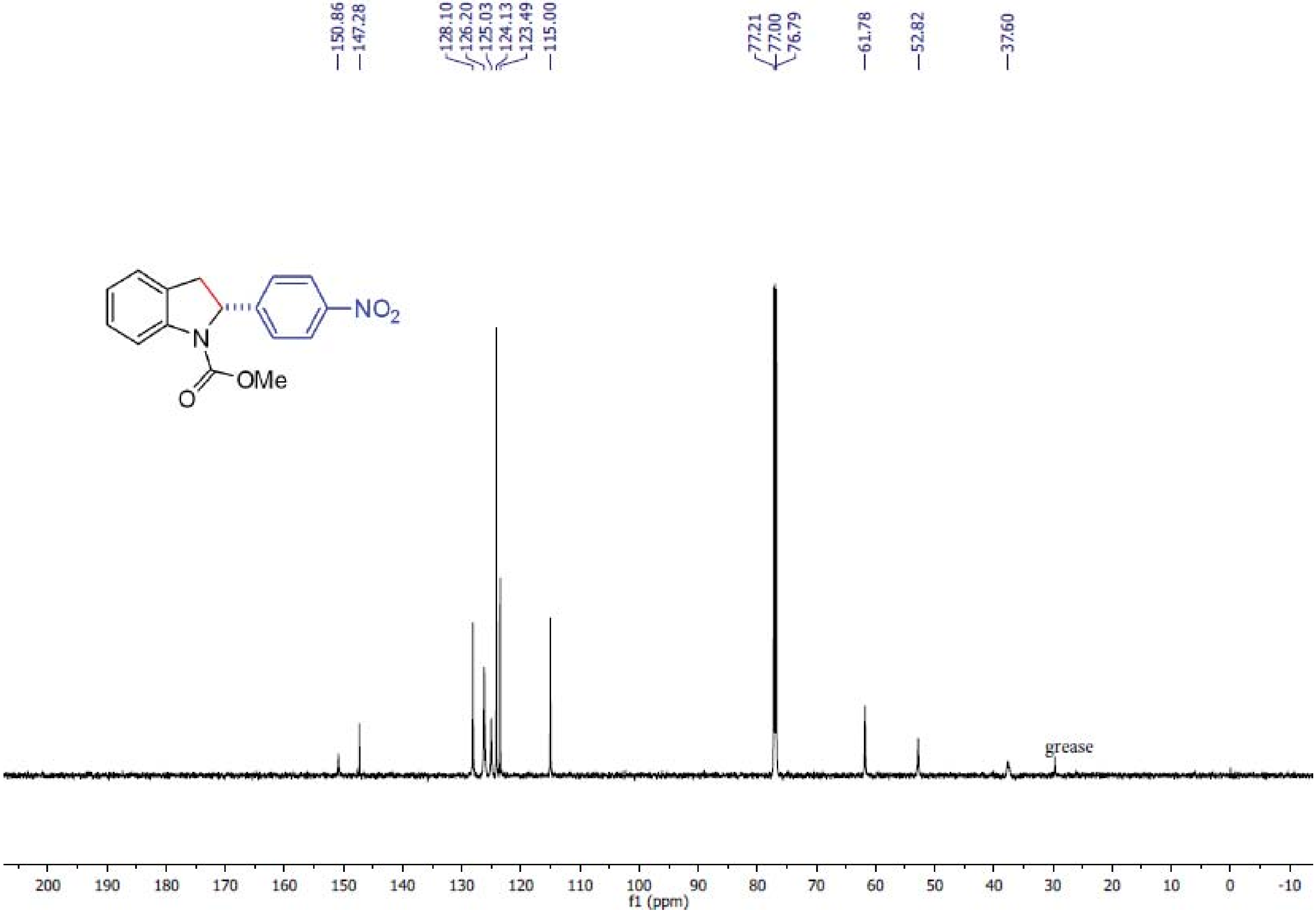
PDA Ch1 285nm

Peak#	Ret. Time	Area	Area%
1	18.565	849351	98.008
2	23.244	17267	1.992
Total		866618	100.000

methyl (*R*)-2-(4-nitrophenyl)indoline-1-carboxylate 2i



methyl (*R*)-2-(4-nitrophenyl)indoline-1-carboxylate 2i

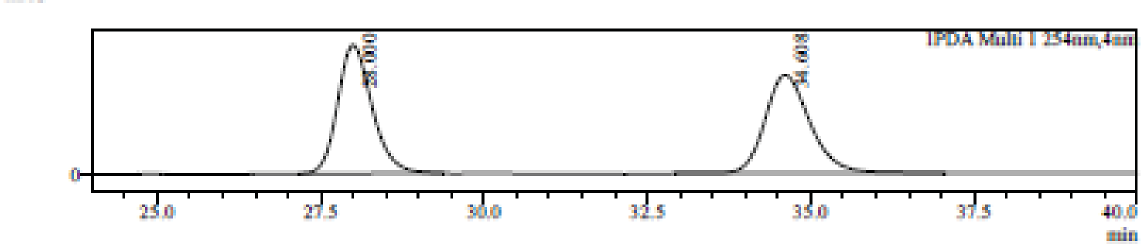


methyl (*R*)-2-(4-nitrophenyl)indoline-1-carboxylate 2i

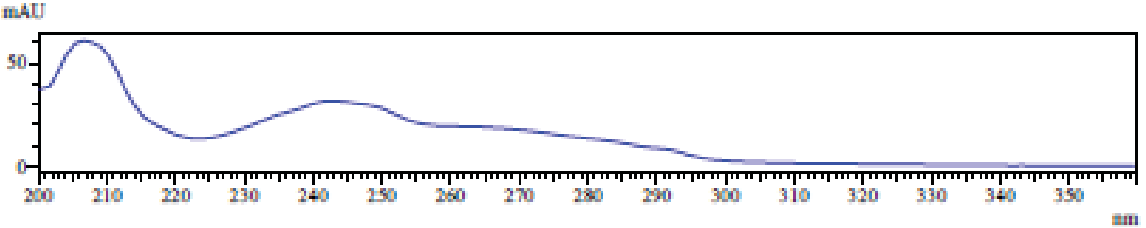
Sample Information

Sample Name : XW-V-31-2-IA-2%1.0mL
Sample ID : XW-V-31-2-IA-2%1.0mL
Data File : XW-V-31-2-IA-2%1.0mL.lcd
Method File : XW-2%-1ml.lcm

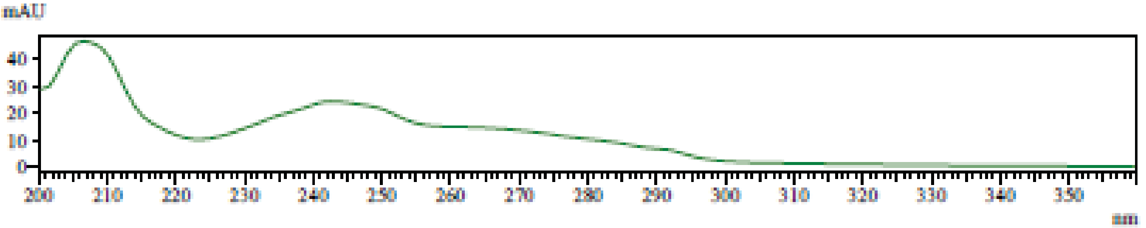
Chromatogram



UV Spectrum
Retention time = 28.000



UV Spectrum
Retention time = 34.608



Peak Table

PDA Ch1 254nm

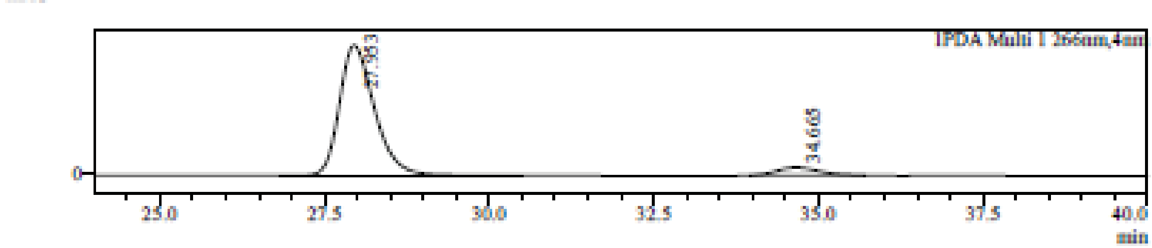
Peak#	Ret. Time	Area	Area%
1	28.000	824550	50.067
2	34.608	822338	49.933
Total		1646888	100.000

methyl (*R*)-2-(4-nitrophenyl)indoline-1-carboxylate 2i

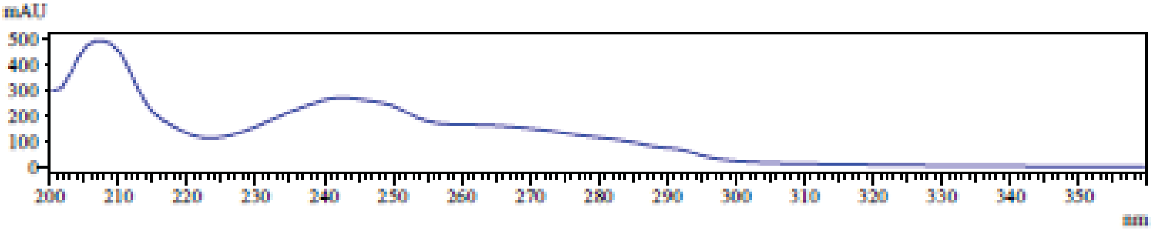
Sample Information

Sample Name	: XW-V-32A-IA-2%1.0mL
Sample ID	: XW-V-32A-IA-2%1.0mL
Data File	: XW-V-32A-IA-2%1.0mL.lcd
Method File	: XW-2%-1ml.lcm

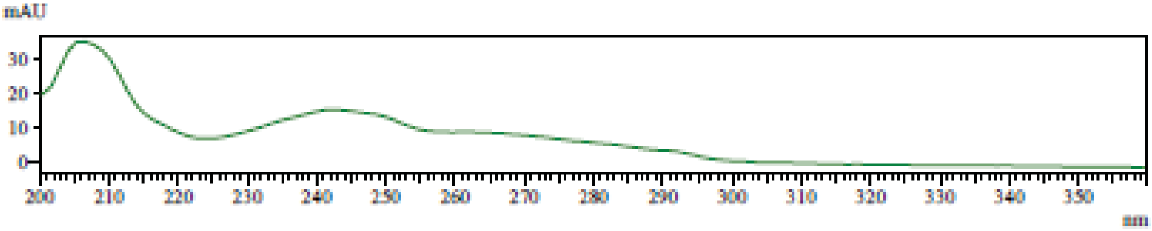
Chromatogram



UV Spectrum
Retention time = 27.953



UV Spectrum
Retention time = 34.665

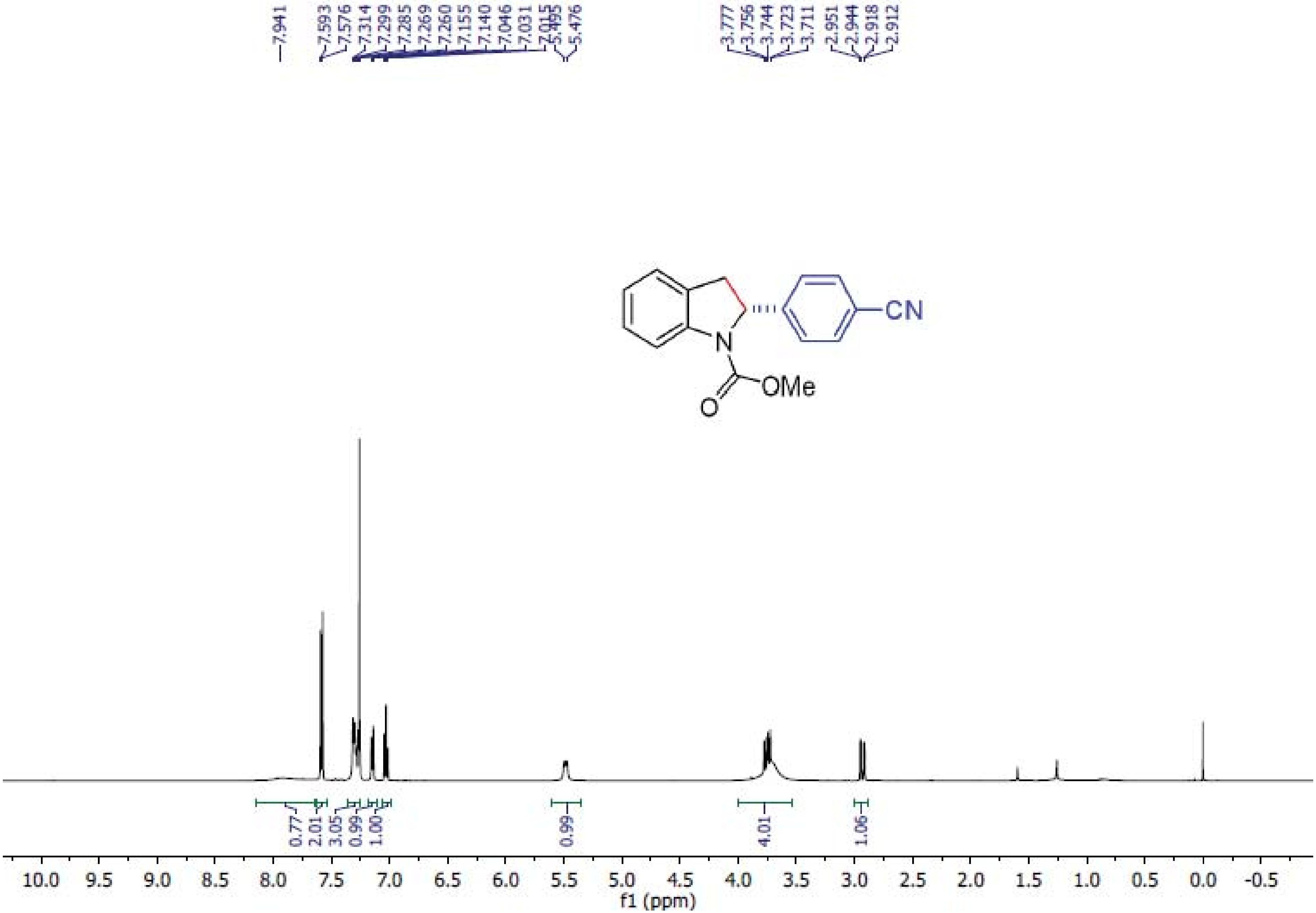


Peak Table

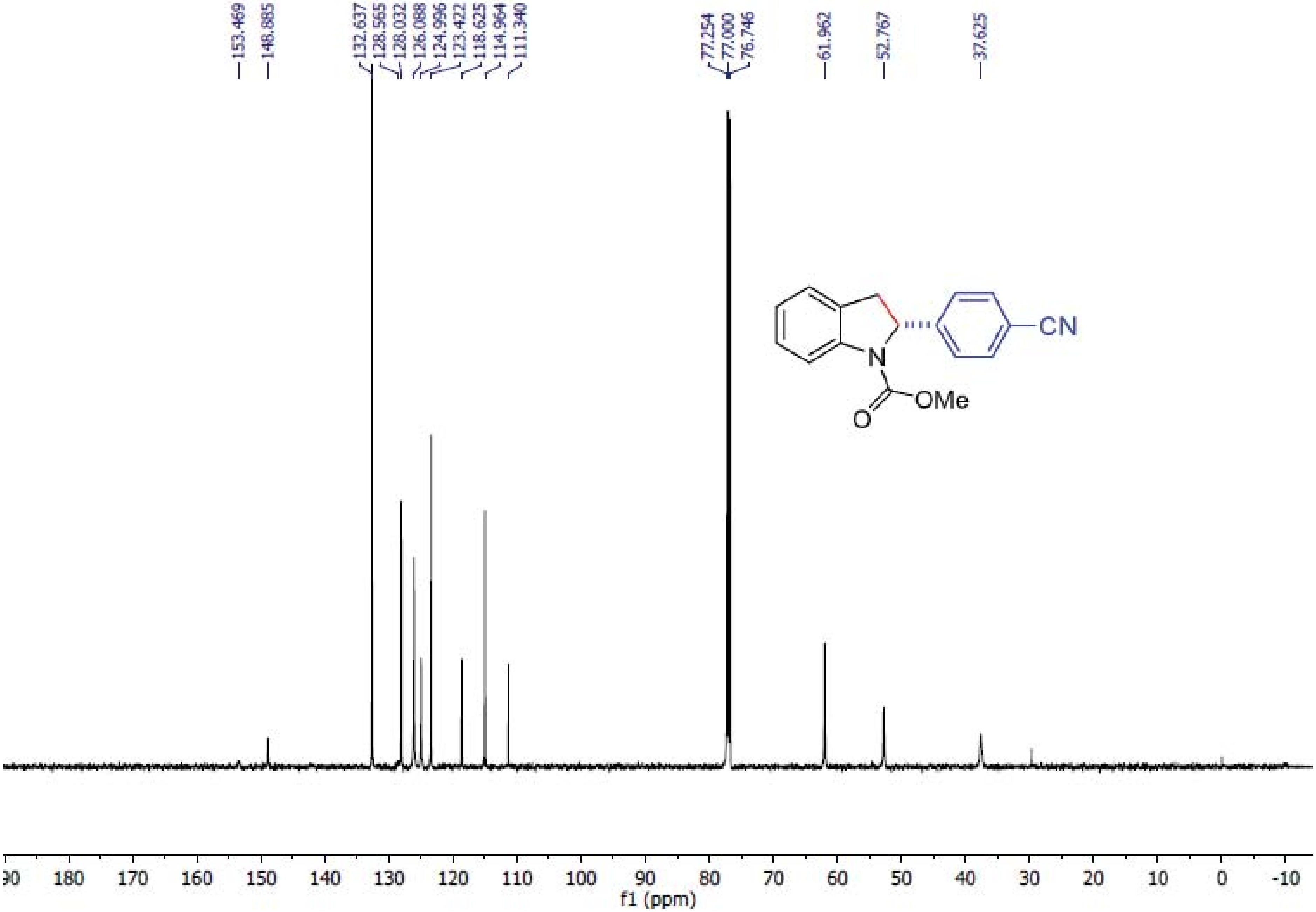
PDA Ch1 266nm

Peak#	Ret. Time	Area	Area%
1	27.953	5923290	93.377
2	34.665	420091	6.623
Total		6343381	100.000

methyl (*R*)-2-(4-cyanophenyl)indoline-1-carboxylate 2j



methyl (*R*)-2-(4-cyanophenyl)indoline-1-carboxylate 2j

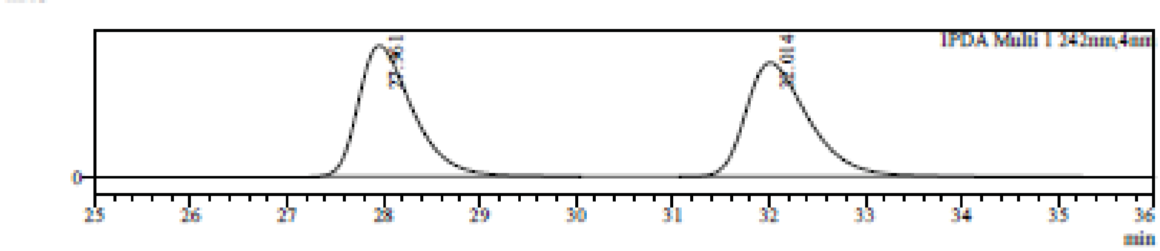


methyl (*R*)-2-(4-cyanophenyl)indoline-1-carboxylate 2j

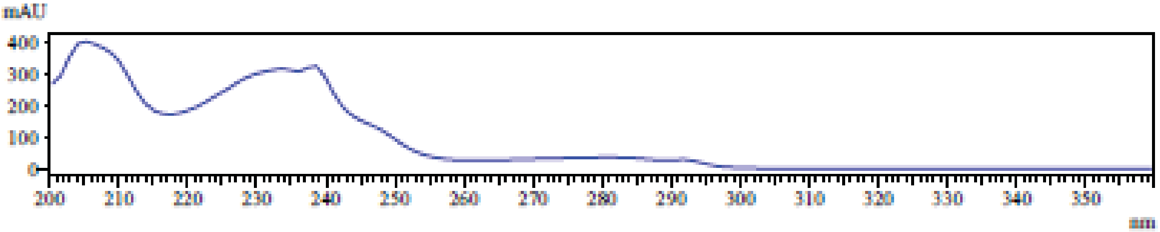
Sample Information

Sample Name : XW-V-19-IA-2%1.0mL
Sample ID : XW-V-19-IA-2%1.0mL
Data File : XW-V-19-IA-2%1.0mL.lcd
Method File : XW-2%-1ml.lcm

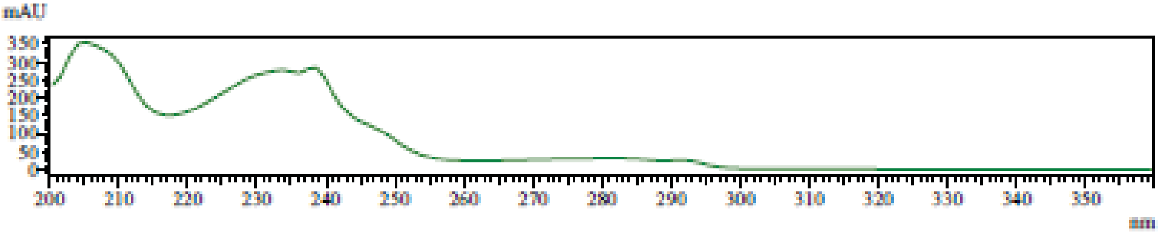
Chromatogram



UV Spectrum
Retention time = 27.961



UV Spectrum
Retention time = 32.014



Peak Table

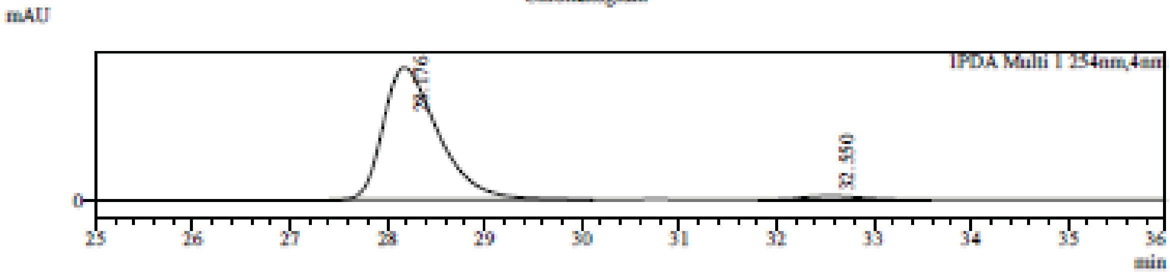
PDA Ch1 242nm

Peak#	Ret. Time	Area	Area%
1	27.961	9127467	49.823
2	32.014	9192143	50.177
Total		18319611	100.000

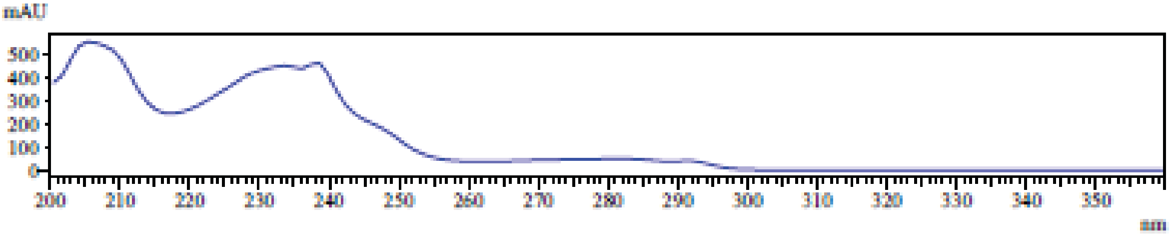
methyl (*R*)-2-(4-cyanophenyl)indoline-1-carboxylate 2j

Sample Information
Sample Name : XW-V-20-new-IA-2%1.0mL
Sample ID : XW-V-20-new-IA-2%1.0mL
Data File : XW-V-20-new-IA-2%1.0mL.lcd
Method File : XW-2%-1ml.lcm

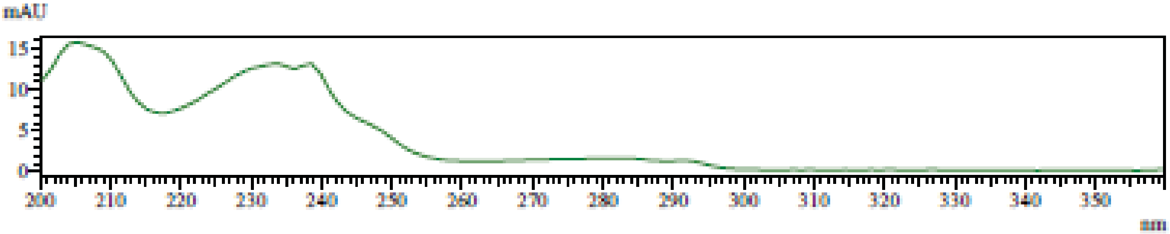
Chromatogram



UV Spectrum
Retention time = 28.176



UV Spectrum
Retention time = 32.550

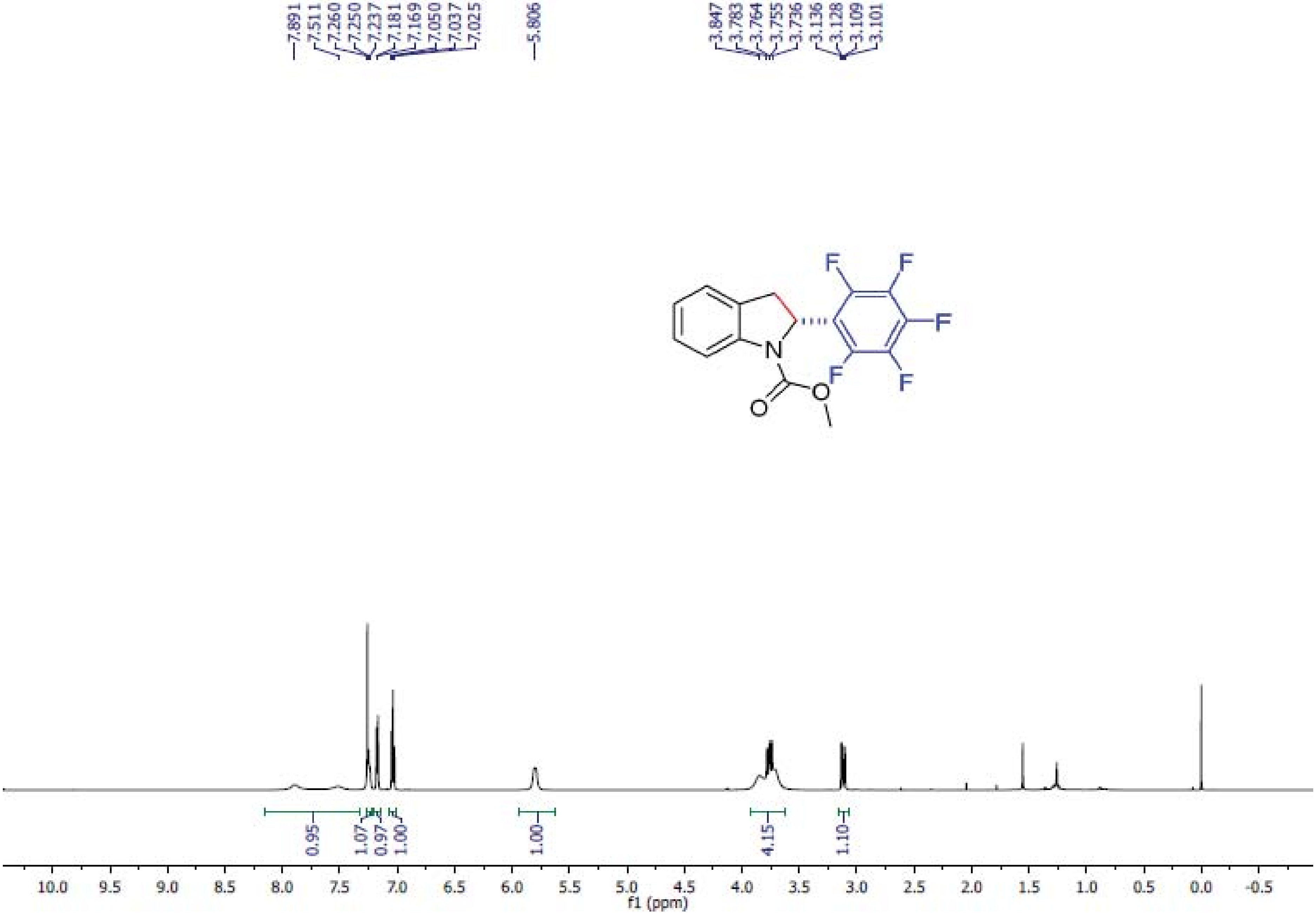


Peak Table

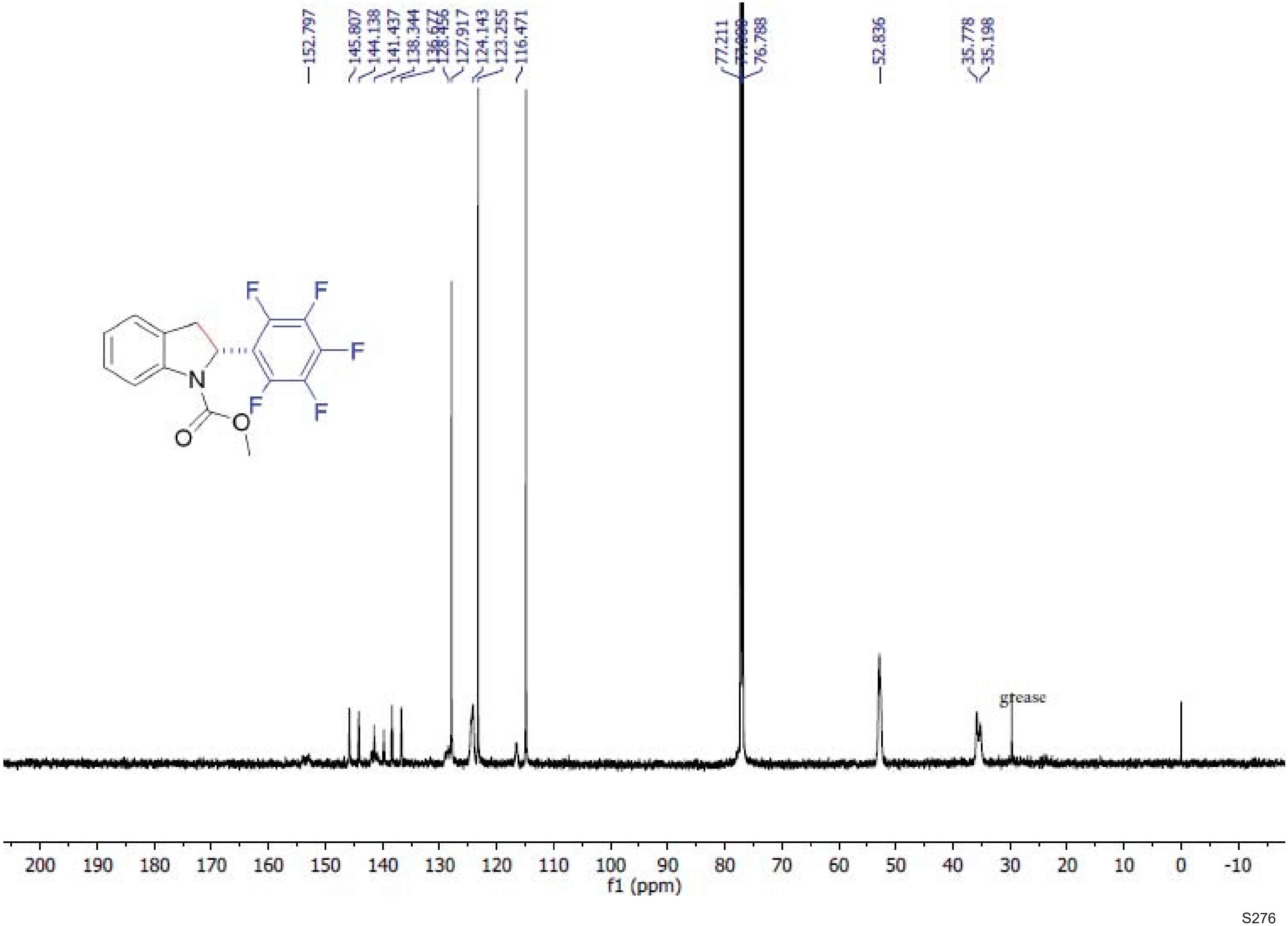
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	28.176	2751841	97.097
2	32.550	82286	2.903
Total		2834127	100.000

methyl (*R*)-2-(perfluorophenyl)indoline-1-carboxylate 2k



methyl (*R*)-2-(perfluorophenyl)indoline-1-carboxylate 2k

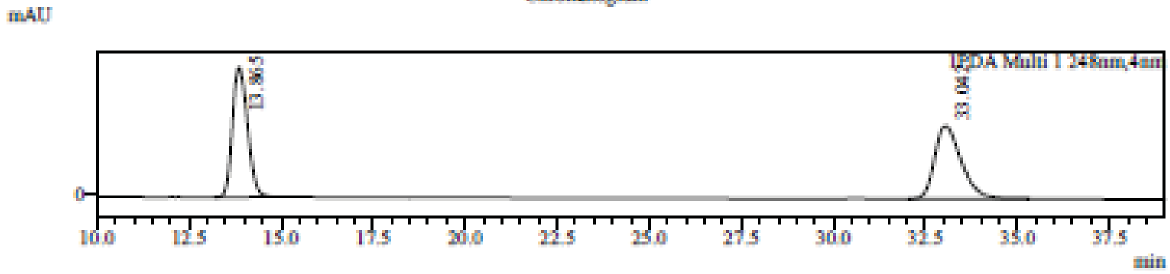


methyl (*R*)-2-(perfluorophenyl)indoline-1-carboxylate 2k

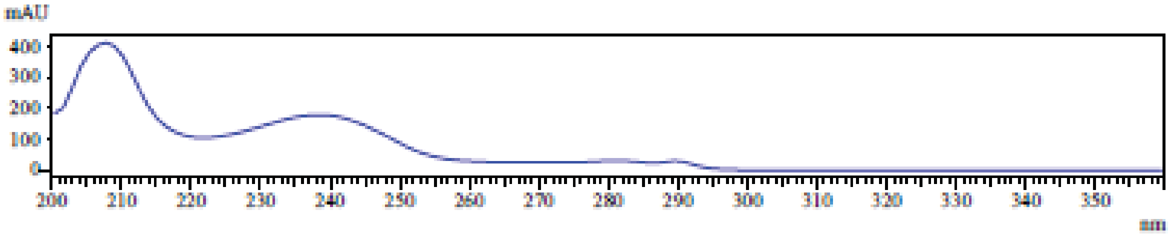
Sample Information

Sample Name	: XW-V-103-IA-0.5%0.8mL
Sample ID	: XW-V-103-IA-0.5%0.8mL
Data File	: XW-V-103-IA-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

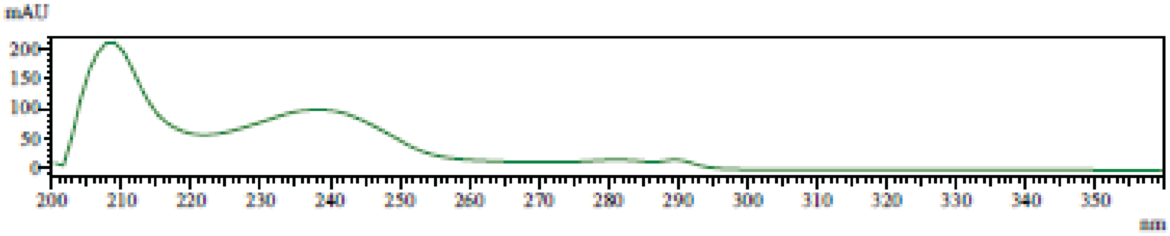
Chromatogram



UV Spectrum
Retention time = 13.865



UV Spectrum
Retention time = 33.042



Peak Table

PDA Ch1 248nm

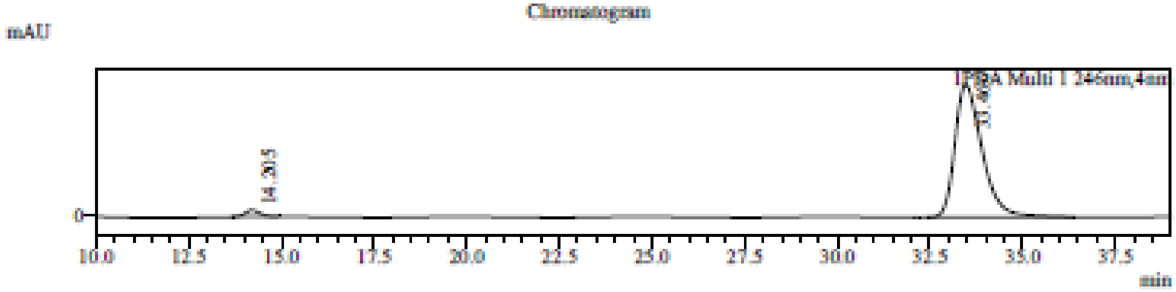
Peak#	Ret. Time	Area	Area%
1	13.865	3220132	50.366
2	33.042	3173293	49.634
Total		6393424	100.000

methyl (*R*)-2-(perfluorophenyl)indoline-1-carboxylate 2k

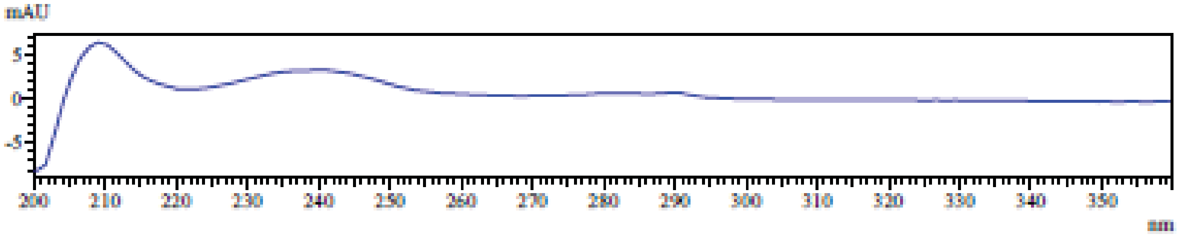
Sample Information

Sample Name : XW-V-104-old-IA-0.5%0.8mL
Sample ID : XW-V-104-old-IA-0.5%0.8mL
Data File : XW-V-104-old-IA-0.5%0.8mL.lcd
Method File : XW-0.5%-0.8ml.lcm

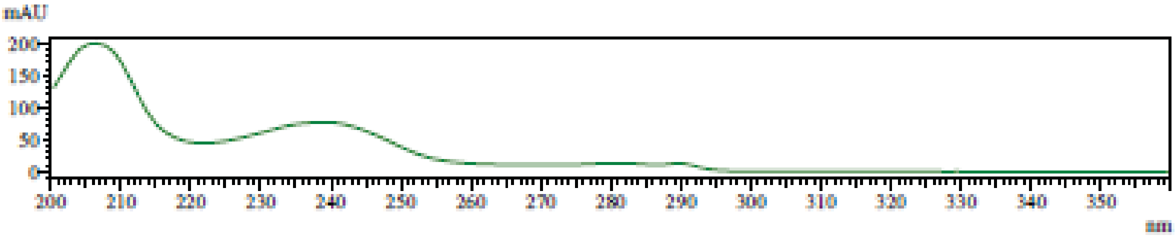
Chromatogram



UV Spectrum
Retention time = 14.205



UV Spectrum
Retention time = 33.466

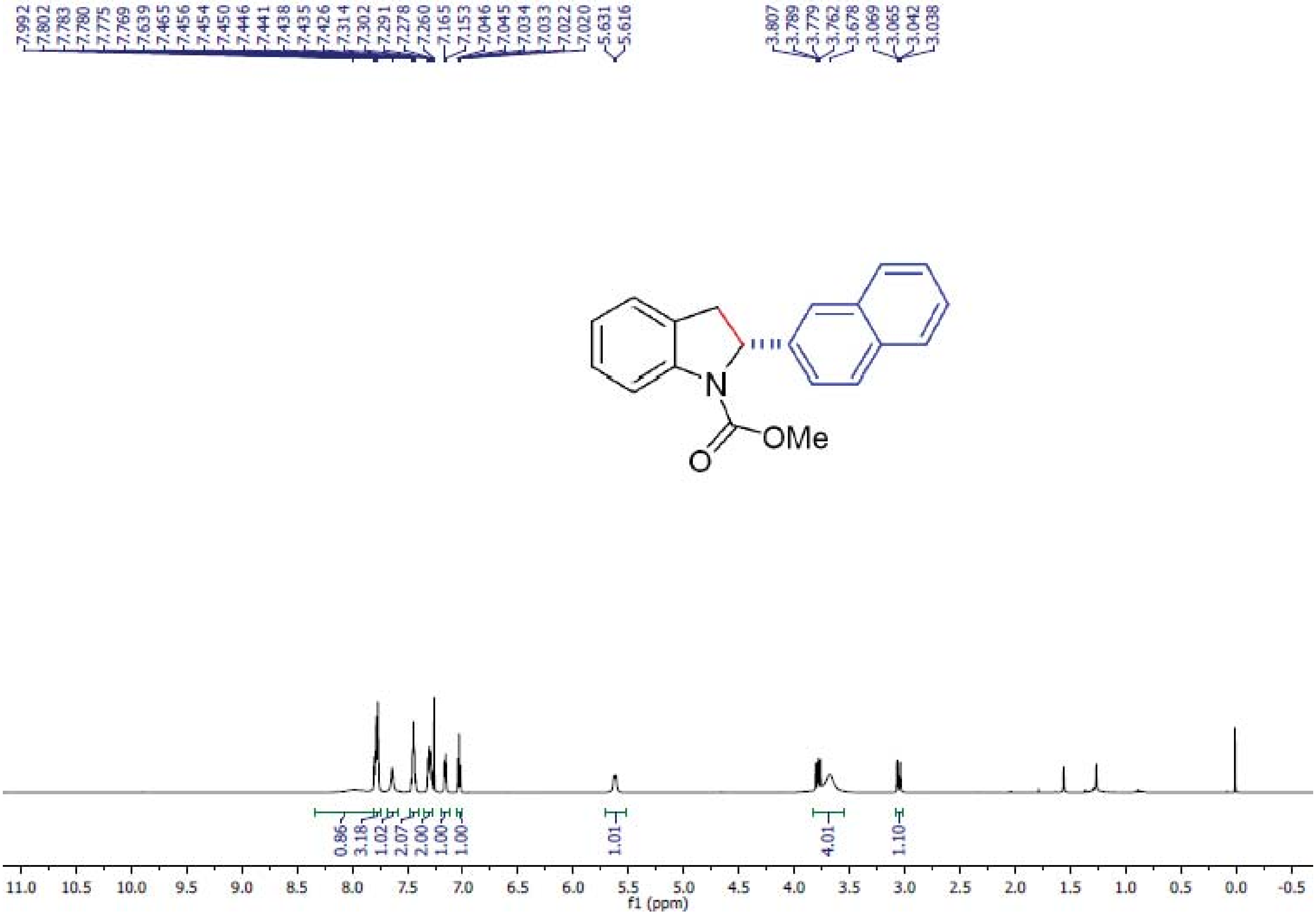


Peak Table

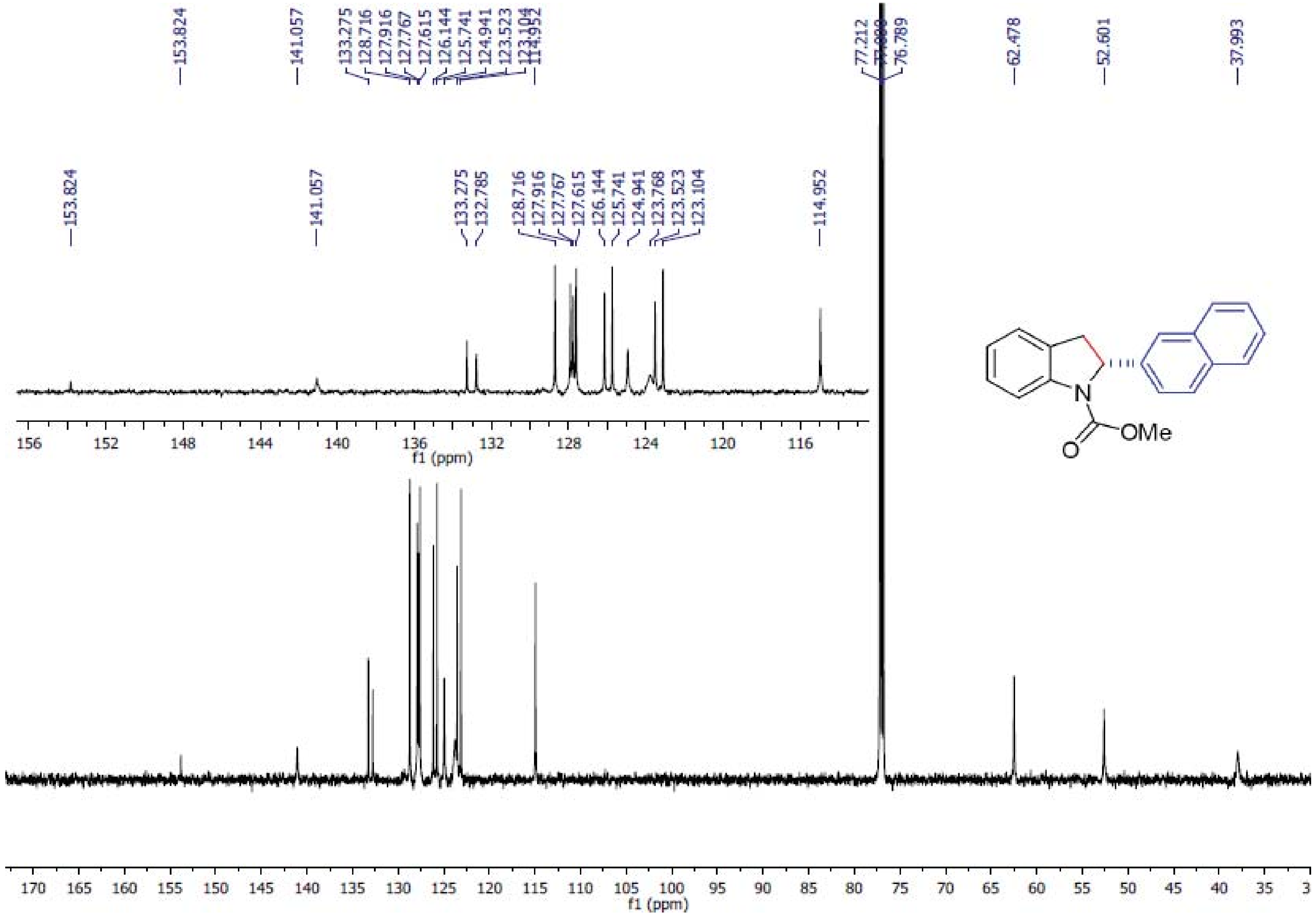
PDA Ch1 246nm

Peak#	Ret. Time	Area	Area%
1	14.205	79148	2.588
2	33.466	2979528	97.412
Total		3058675	100.000

methyl (*R*)-2-(naphthalen-2-yl)indoline-1-carboxylate 2l



methyl (*R*)-2-(naphthalen-2-yl)indoline-1-carboxylate 2l

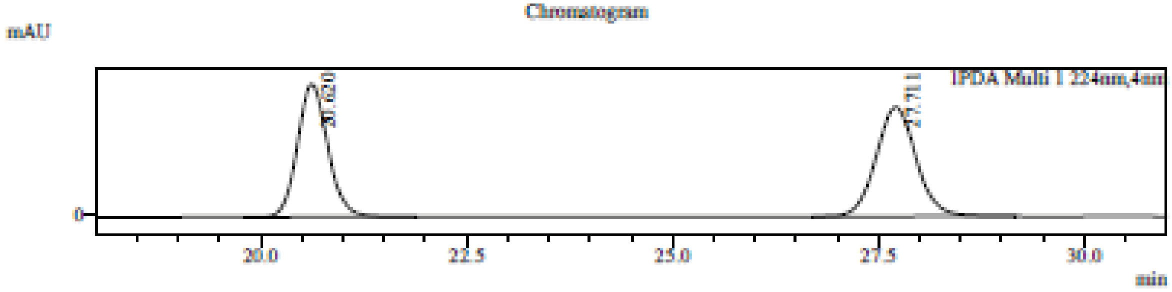


methyl (*R*)-2-(naphthalen-2-yl)indoline-1-carboxylate 2l

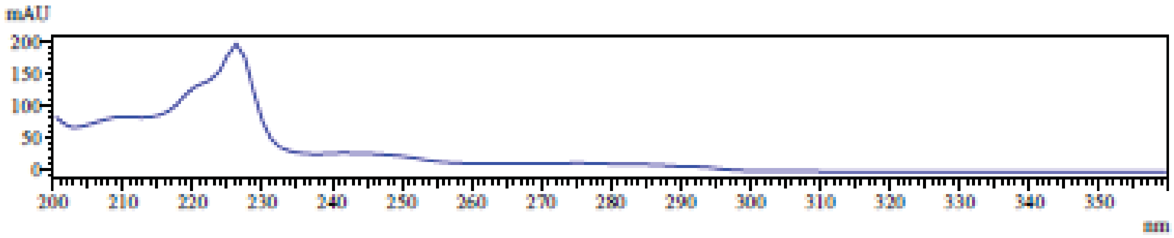
Sample Information

Sample Name : XW-V-98-1-IA-1%0.8mL
Sample ID : XW-V-98-1-IA-1%0.8mL
Data File : XW-V-98-1-IA-1%0.8mL.lcd
Method File : XW-1%-0.8ml.lcm

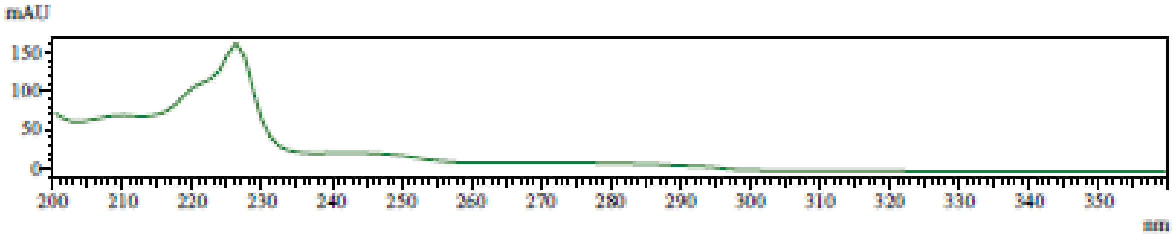
Chromatogram



UV Spectrum
Retention time = 20.620



UV Spectrum
Retention time = 27.711



Peak Table

PDA Ch1 224nm

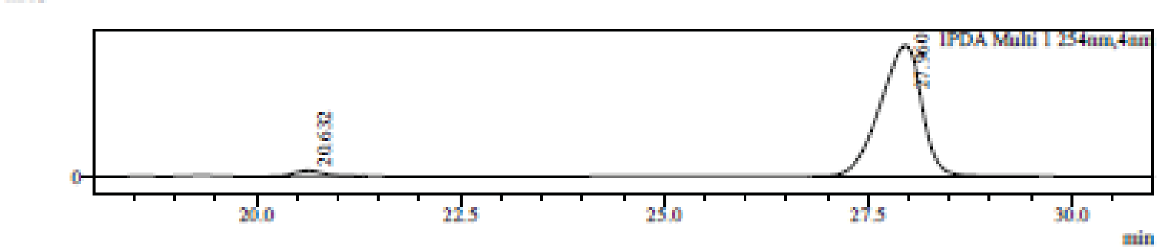
Peak#	Ret. Time	Area	Area%
1	20.620	4098843	48.021
2	27.711	4436621	51.979
Total		8535464	100.000

methyl (*R*)-2-(naphthalen-2-yl)indoline-1-carboxylate 2l

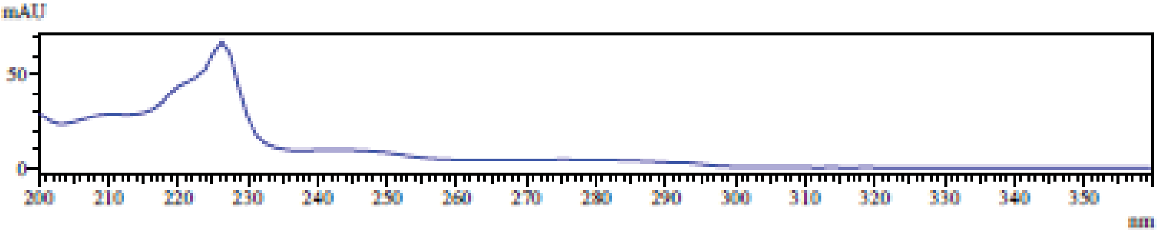
Sample Information

Sample Name	: XW-V-99-Old-IA-1%0.8mL
Sample ID	: XW-V-99-Old-IA-1%0.8mL
Data File	: XW-V-99-Old-IA-1%0.8mL.lcd
Method File	: XW-1%-0.8ml.lcm

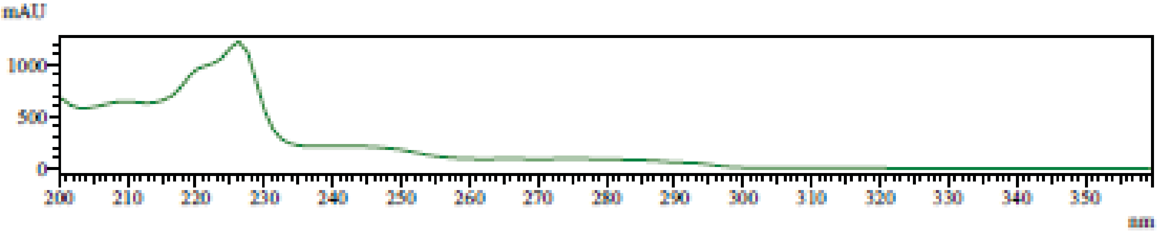
Chromatogram



UV Spectrum
Retention time = 20.632



UV Spectrum
Retention time = 27.960

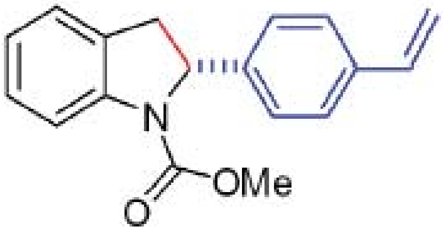


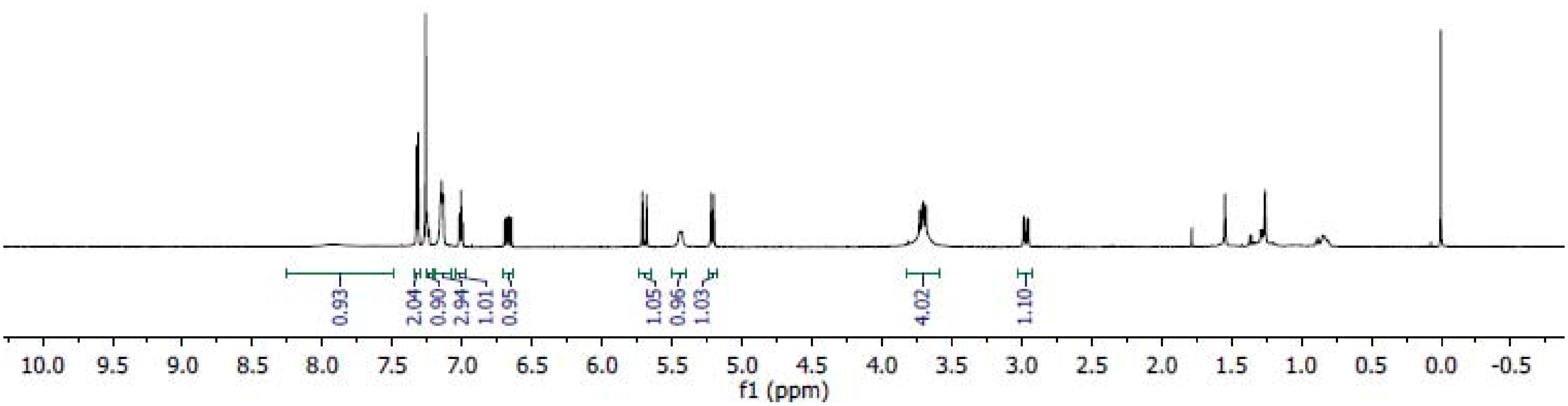
Peak Table

PDA Ch1 254nm

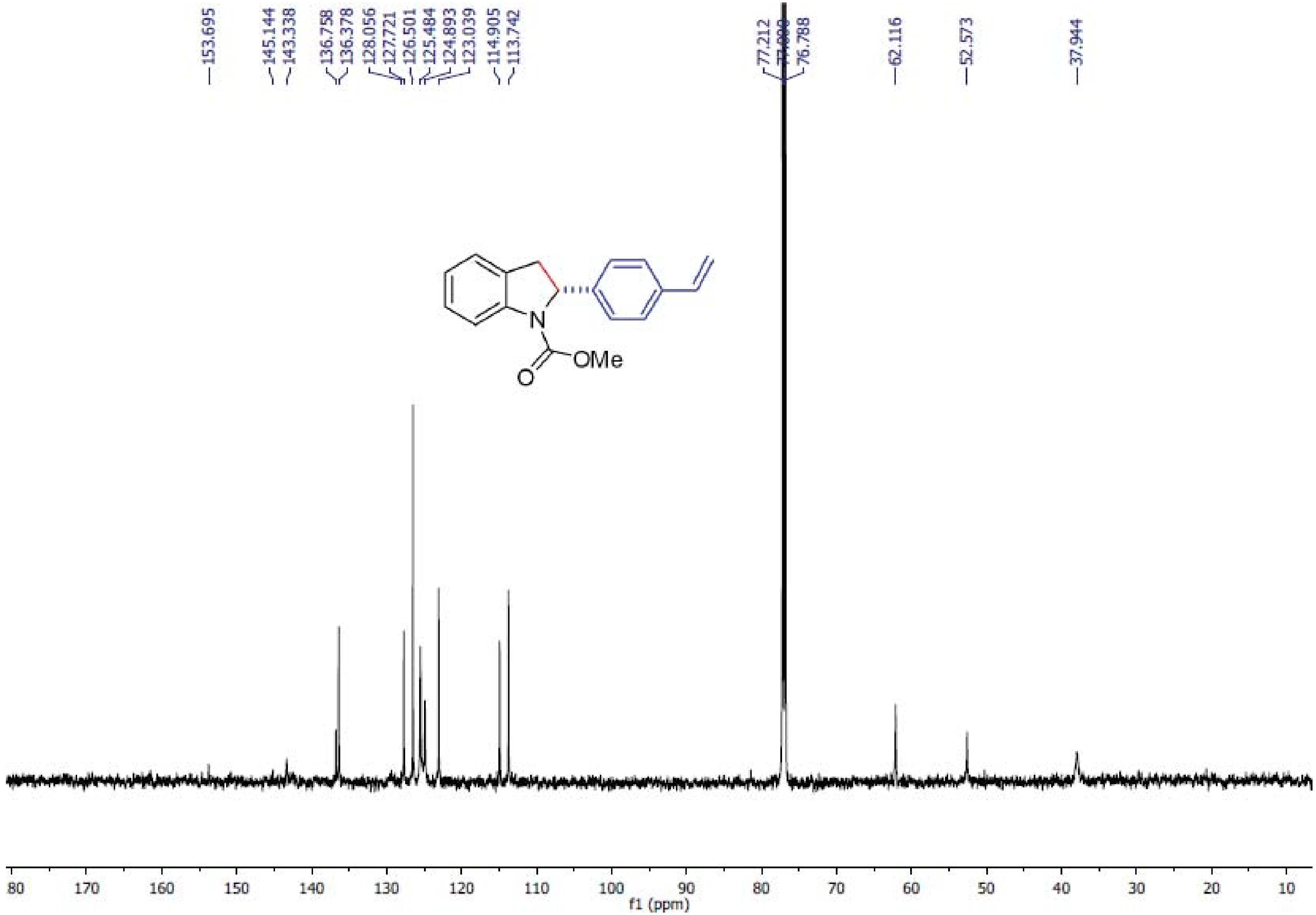
Peak#	Ret. Time	Area	Area%
1	20.632	145509	2.999
2	27.960	4706561	97.001
Total		4852070	100.000

methyl (*R*)-2-(4-vinylphenyl)indoline-1-carboxylate 2m





methyl (*R*)-2-(4-vinylphenyl)indoline-1-carboxylate 2m

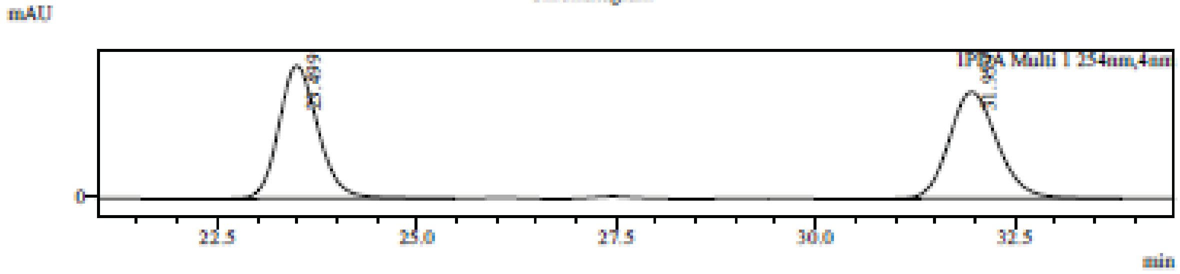


methyl (*R*)-2-(4-vinylphenyl)indoline-1-carboxylate 2m

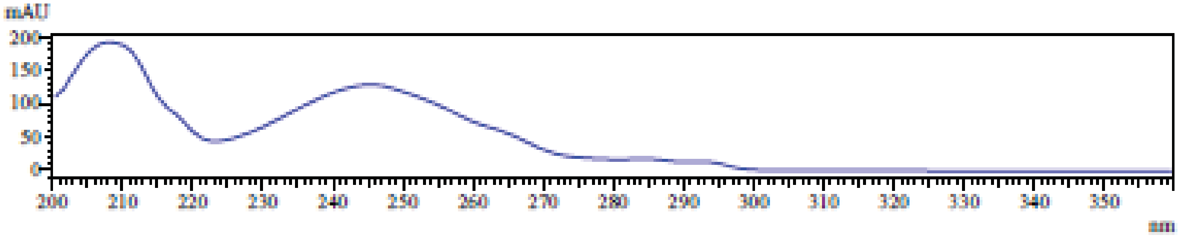
Sample Information

Sample Name	: XW-V-88-IA-0.5%0.8mL
Sample ID	: XW-V-88-IA-0.5%0.8mL
Data File	: XW-V-88-IA-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

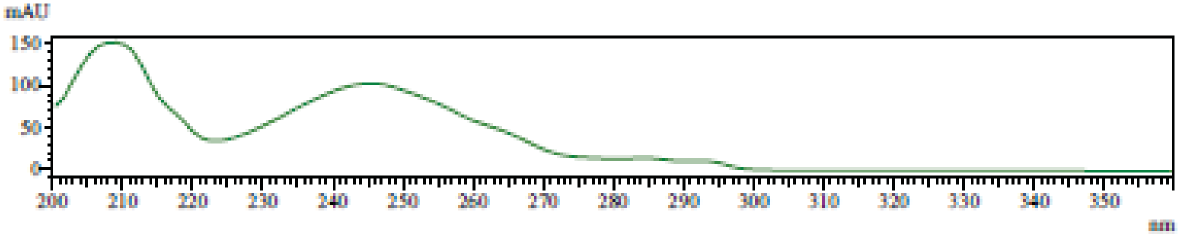
Chromatogram



UV Spectrum
Retention time = 23.499



UV Spectrum
Retention time = 31.959



Peak Table

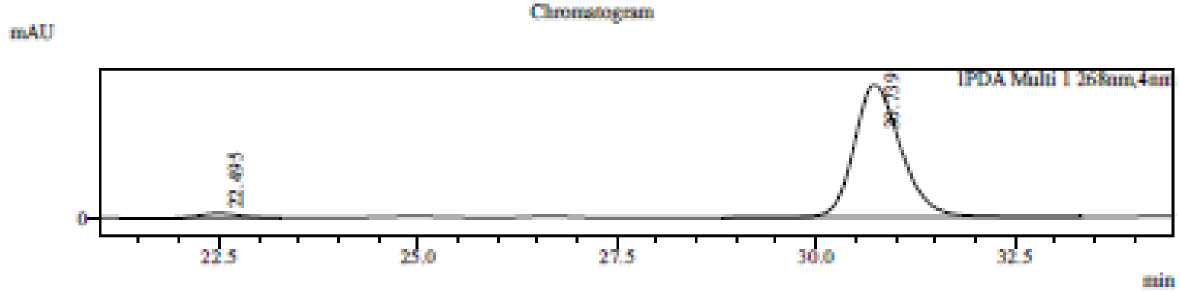
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	23.499	3519407	50.275
2	31.959	3480837	49.725
Total		7000243	100.000

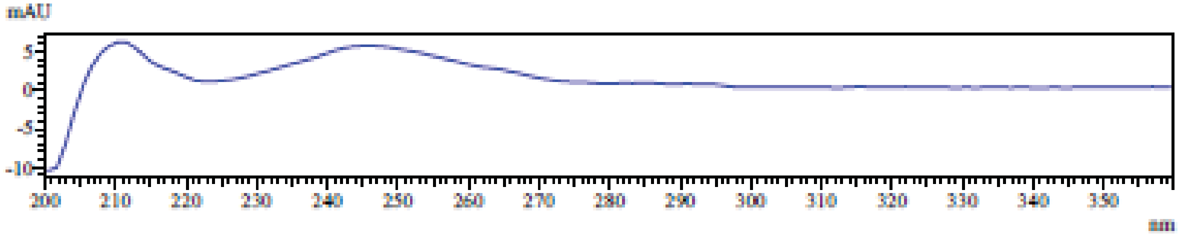
methyl (*R*)-2-(4-vinylphenyl)indoline-1-carboxylate 2m

Sample Information

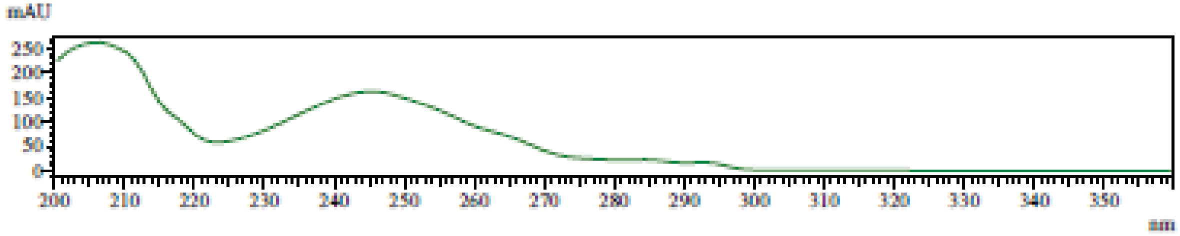
Sample Name	: XW-V-89-New-batch-IA-0.5%0.8mL
Sample ID	: XW-V-89-New-batch-IA-0.5%0.8mL
Data File	: XW-V-89-New-batch-IA-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm


Chromatogram

UV Spectrum
Retention time = 22.495



UV Spectrum
Retention time = 30.739

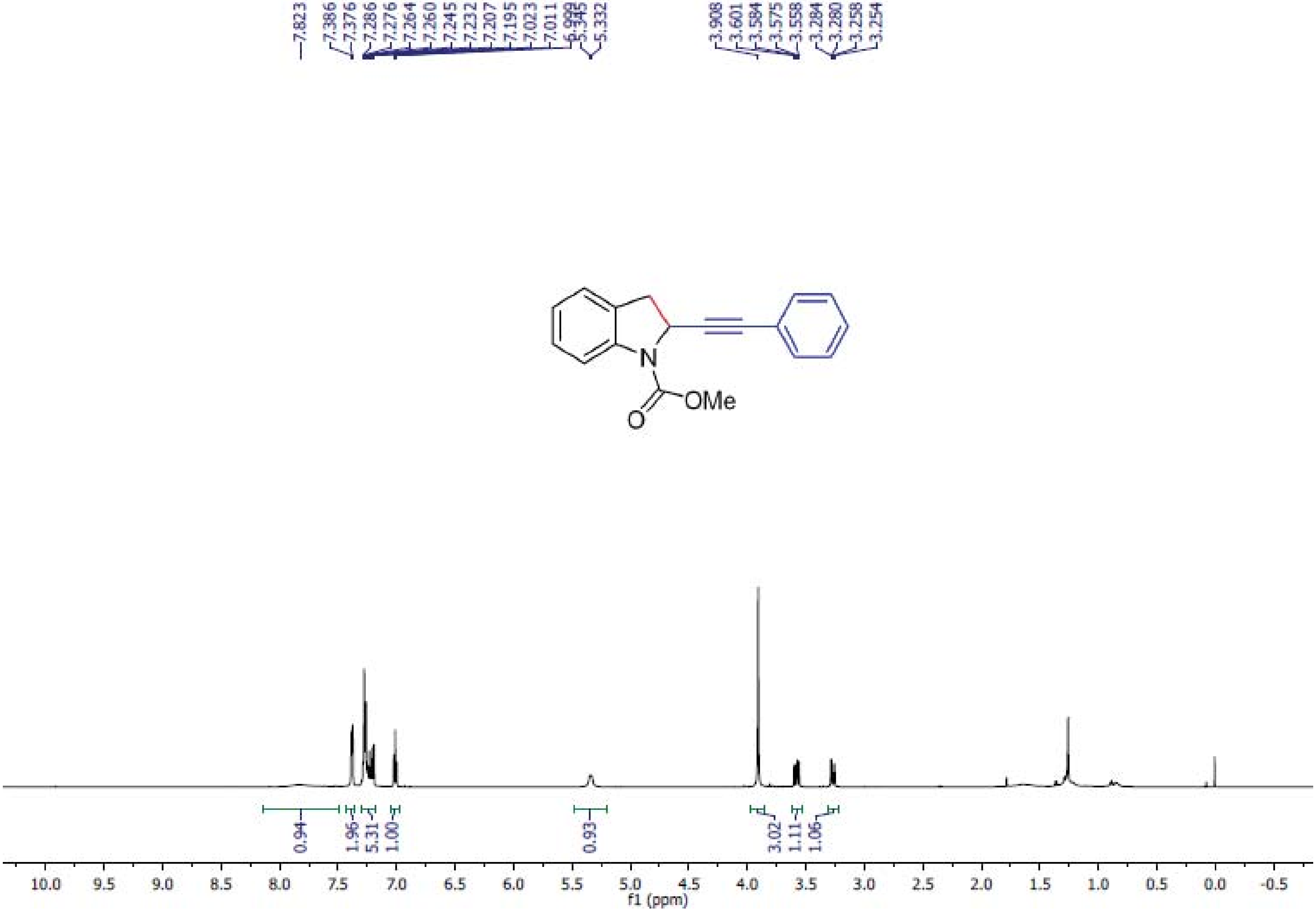


Peak Table

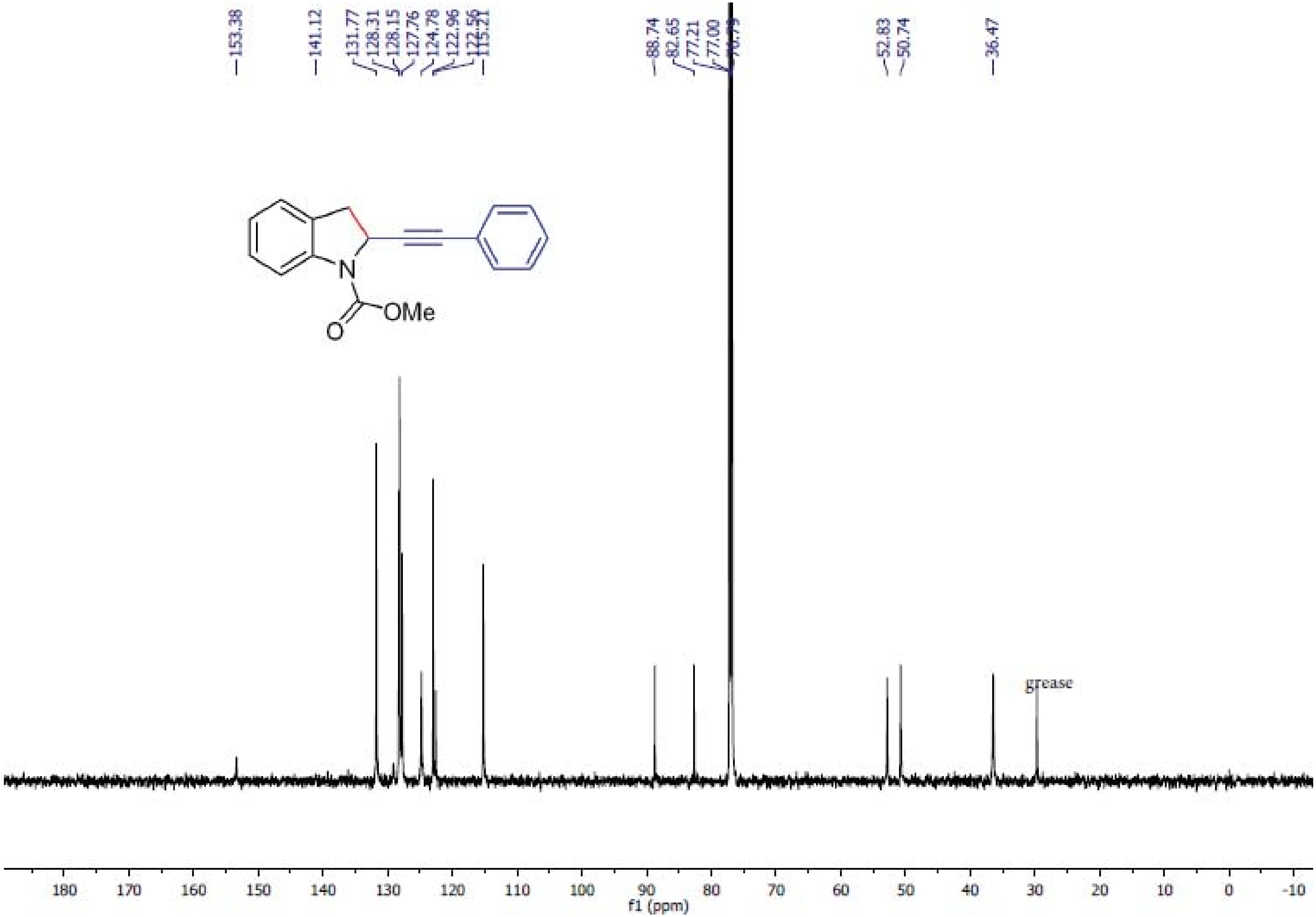
PDA Ch1 268nm

Peak#	Ret. Time	Area	Area%
1	22.495	62384	2.698
2	30.739	2250109	97.302
Total		2312493	100.000

methyl (R)-2-(phenylethynyl)indoline-1-carboxylate 2n



methyl (R)-2-(phenylethynyl)indoline-1-carboxylate 2n

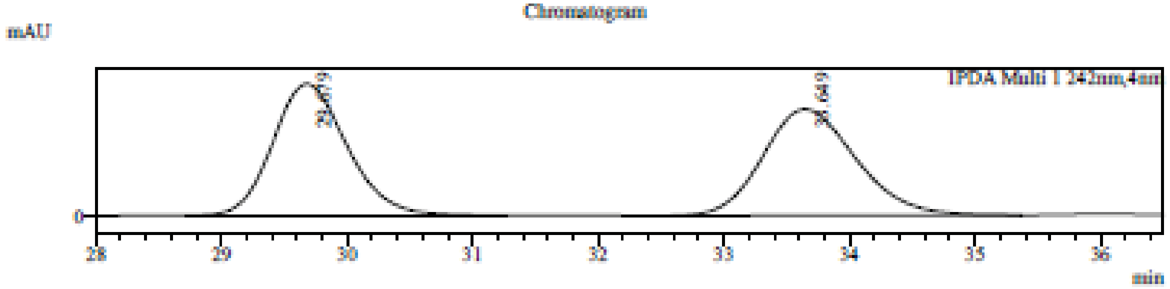


methyl (R)-2-(phenylethynyl)indoline-1-carboxylate 2n

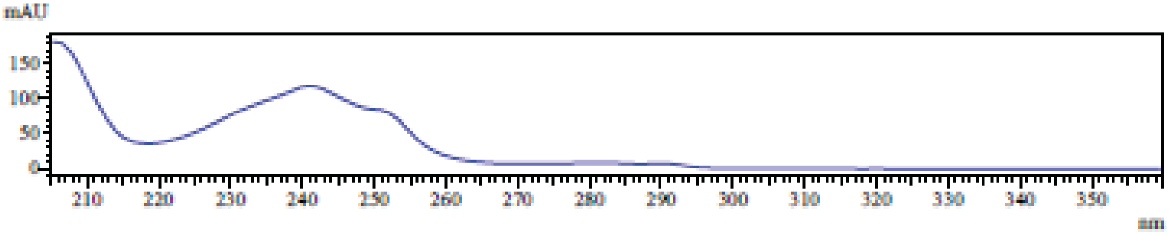
Sample Information

Sample Name : XW-V-132-IC-1%0.8mL
Sample ID : XW-V-132-IC-1%0.8mL
Data File : XW-V-132-IC-1%0.8mL.lcd
Method File : XW-1%-0.8ml.lcm

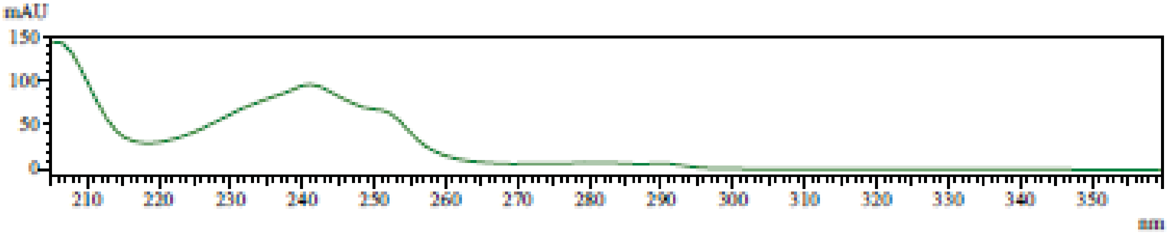
Chromatogram



UV Spectrum
Retention time = 29.679



UV Spectrum
Retention time = 33.649



Peak Table

PDA Ch1 242nm

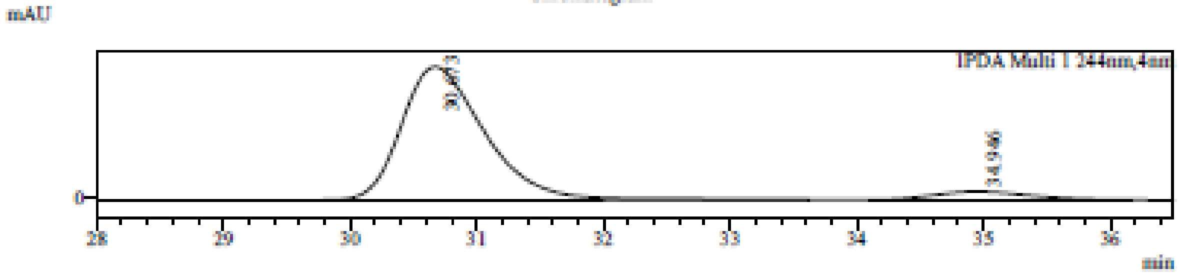
Peak#	Ret. Time	Area	Area%
1	29.679	4639557	49.555
2	33.649	4722845	50.445
Total		9362402	100.000

methyl (R)-2-(phenylethynyl)indoline-1-carboxylate 2n

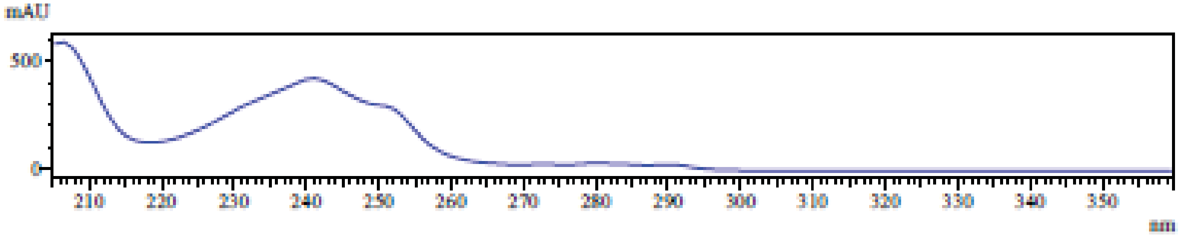
Sample Information

Sample Name	: XW-V-129B-IC-1%0.8mL
Sample ID	: XW-V-129B-IC-1%0.8mL
Data File	: XW-V-129B-IC-1%0.8mL.lcd
Method File	: XW-1%-0.8ml.lcm

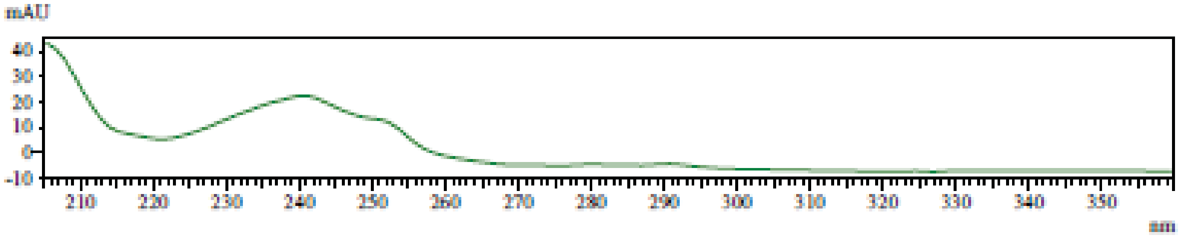
Chromatogram



UV Spectrum
Retention time = 30.673



UV Spectrum
Retention time = 34.946

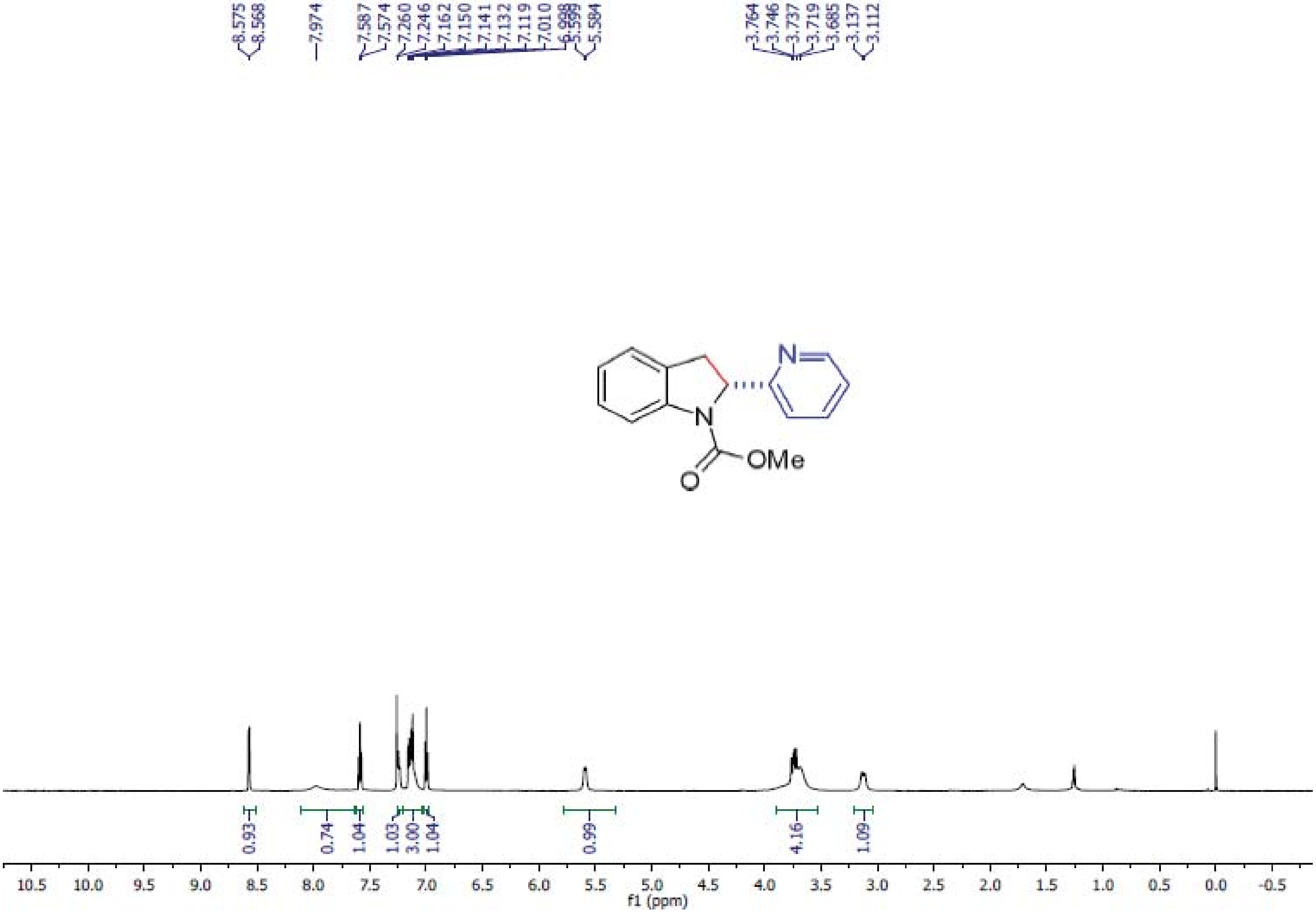


Peak Table

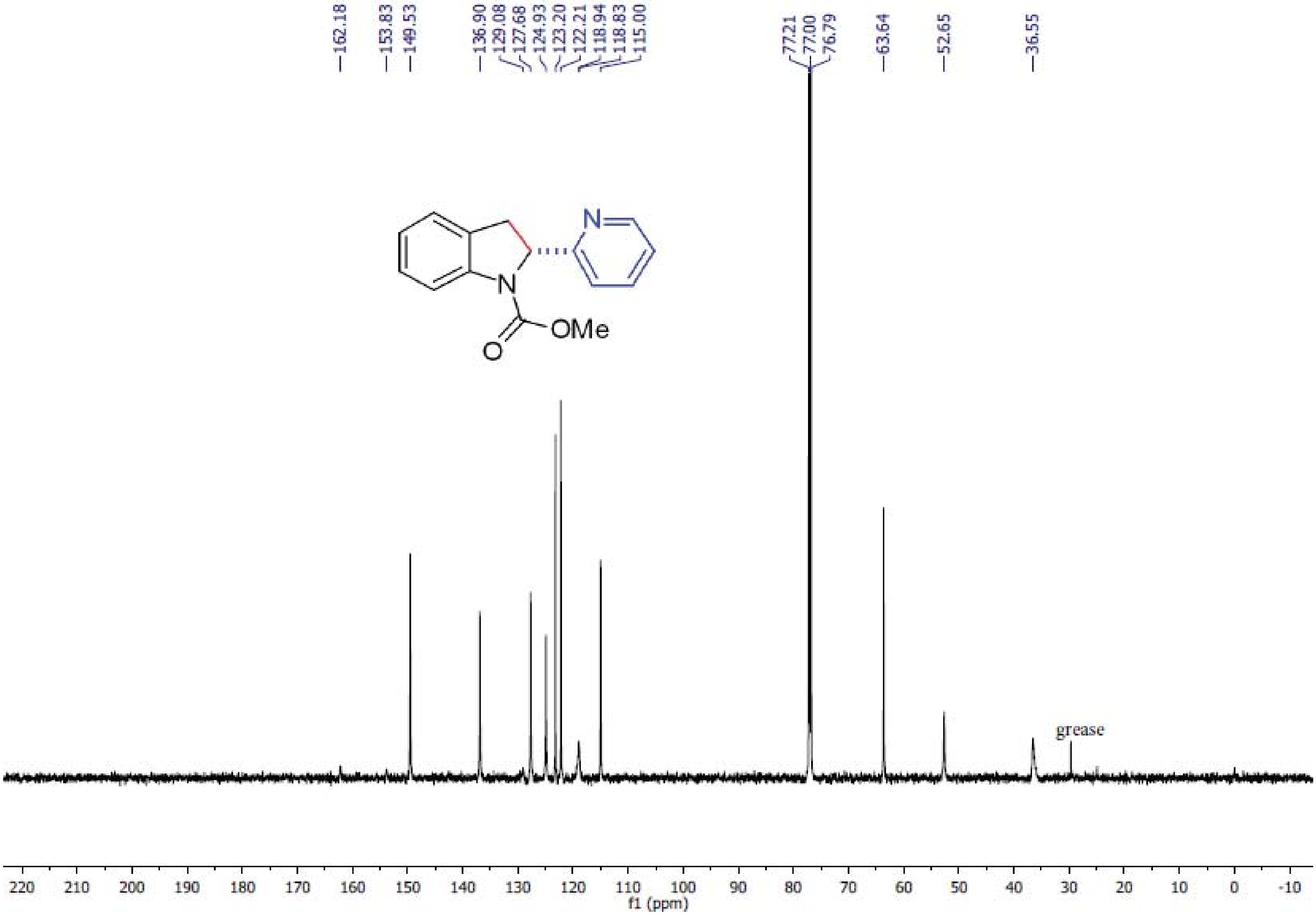
PDA Ch1 244nm

Peak#	Ret. Time	Area	Area%
1	30.673	17400671	93.483
2	34.946	1213004	6.517
Total		18613675	100.000

methyl (R)-2-(pyridin-2-yl)indoline-1-carboxylate 2o



methyl (R)-2-(pyridin-2-yl)indoline-1-carboxylate 2o

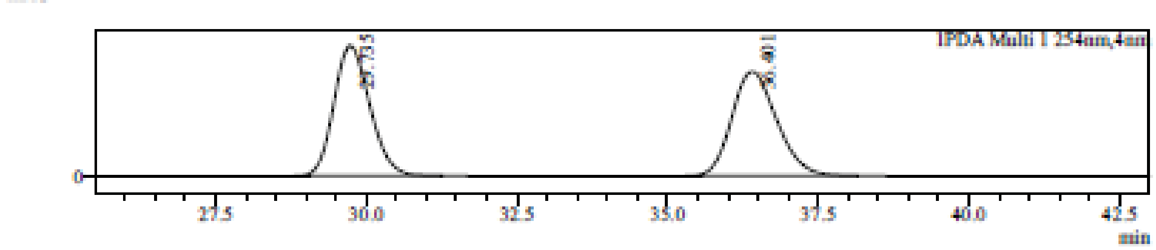


methyl (R)-2-(pyridin-2-yl)indoline-1-carboxylate 2o

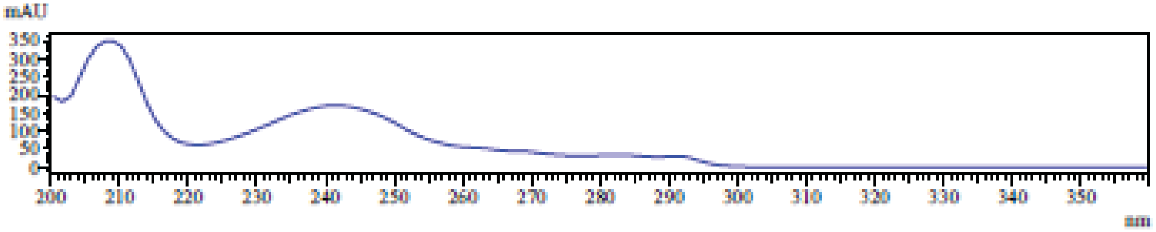
Sample Information

Sample Name	: XW-V-44-IC-5%1mL
Sample ID	: XW-V-44-IC-5%1mL
Data File	: XW-V-44-IC-5%1mL.lcd
Method File	: XW-5%-1ml.lcm

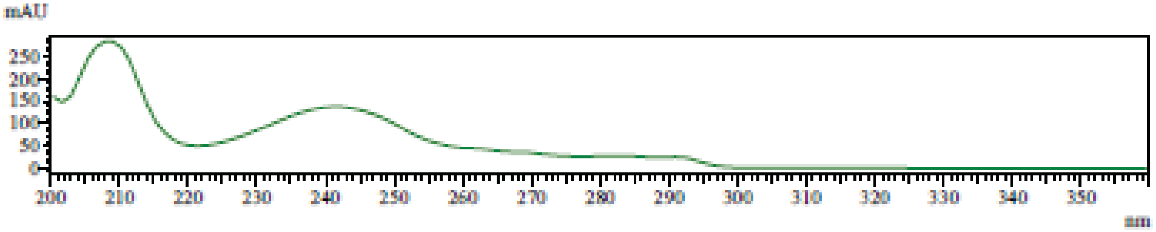
Chromatogram



UV Spectrum
Retention time = 29.735



UV Spectrum
Retention time = 36.401



Peak Table

PDA Ch1 254nm

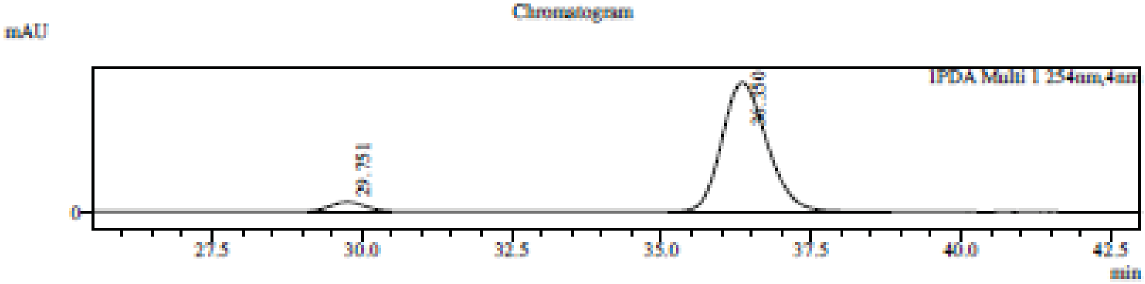
Peak#	Ret. Time	Area	Area%
1	29.735	3562726	50.034
2	36.401	3557929	49.966
Total		7120655	100.000

methyl (R)-2-(pyridin-2-yl)indoline-1-carboxylate 2o

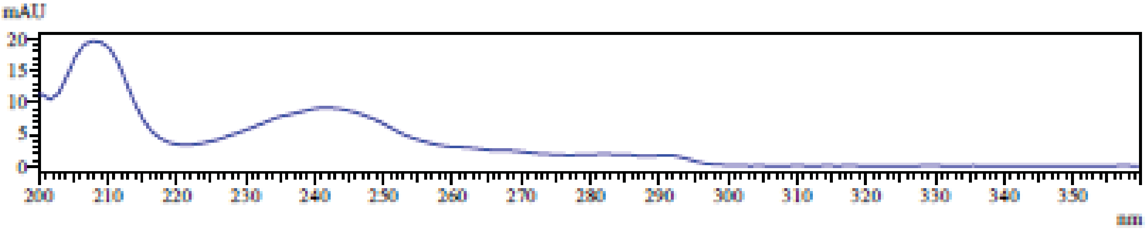
Sample Information

Sample Name : XW-V-45B-IC-5%1mL
Sample ID : XW-V-45B-IC-5%1mL
Data File : XW-V-45B-IC-5%1mL.lcd
Method File : XW-5%-1ml.lcm

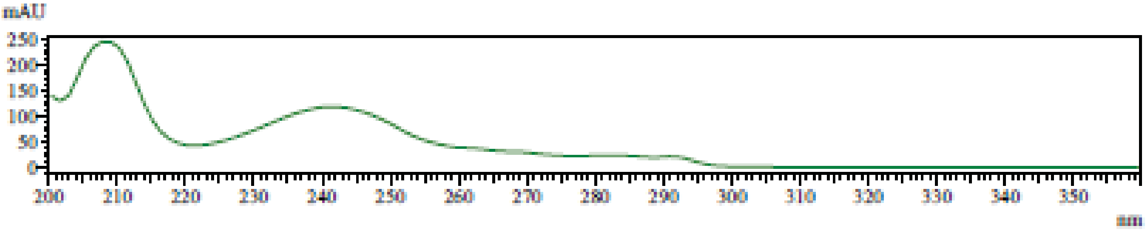
Chromatogram



UV Spectrum
Retention time = 29.751



UV Spectrum
Retention time = 36.350

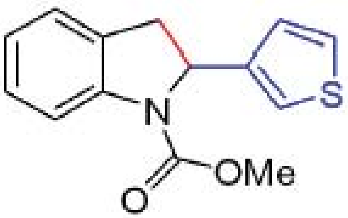


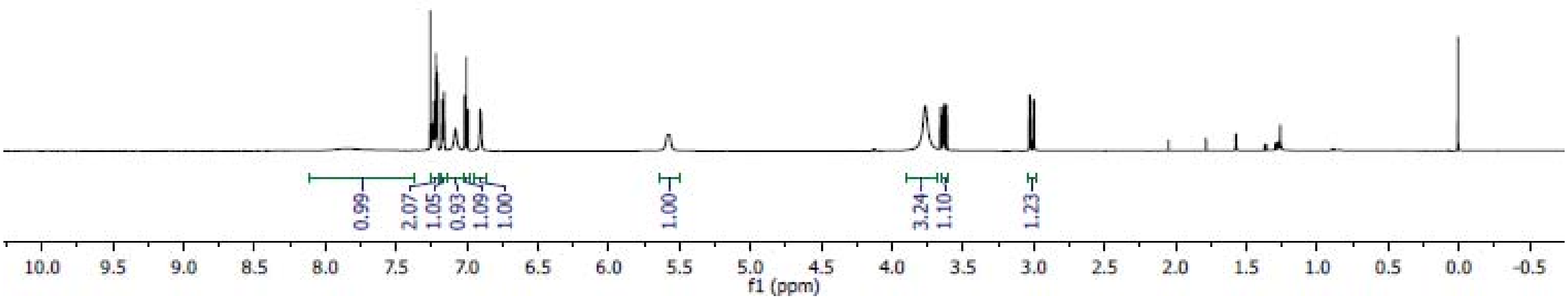
Peak Table

PDA Ch1 254nm

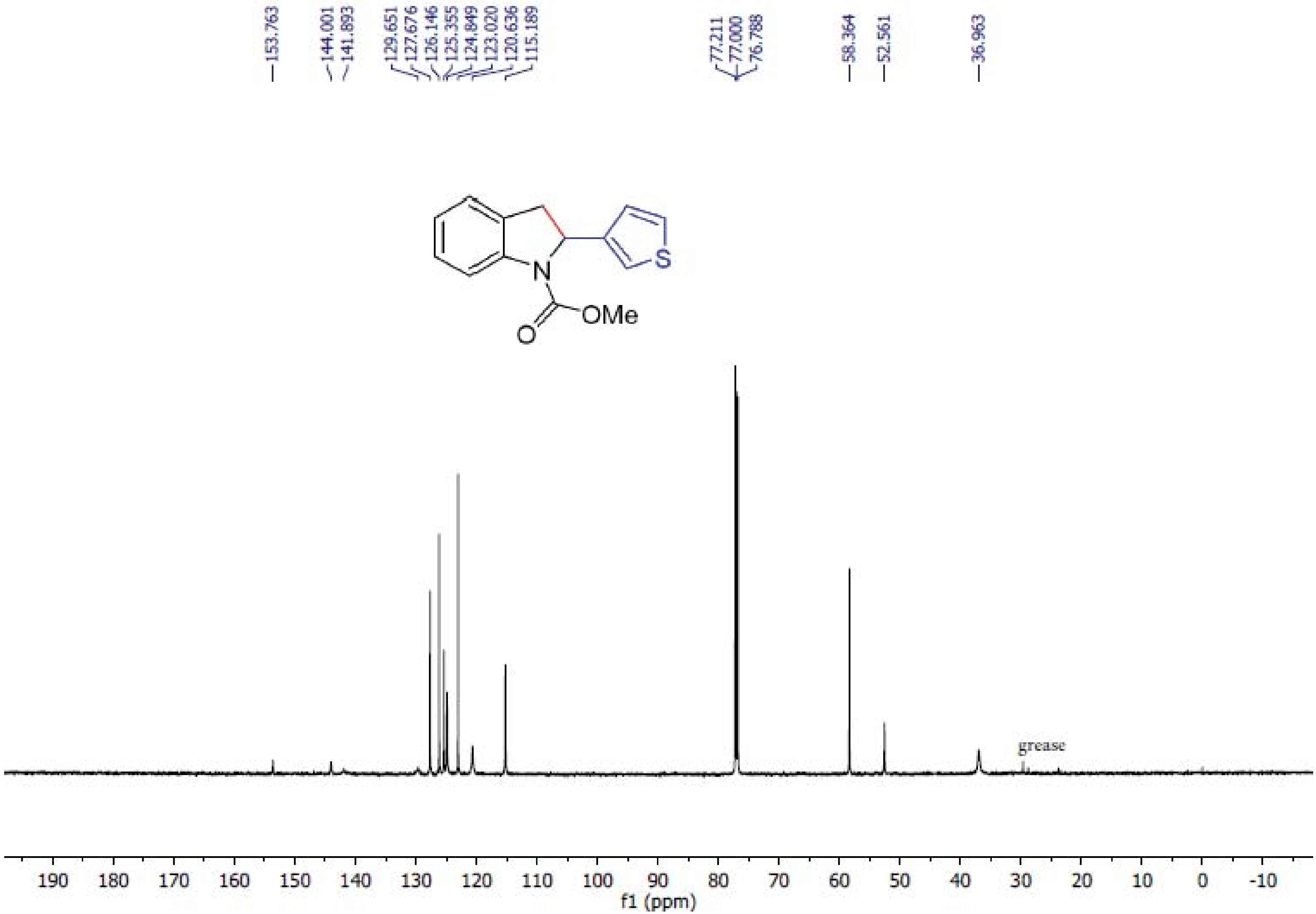
Peak#	Ret. Time	Area	Area%
1	29.751	165124	5.058
2	36.350	3099441	94.942
Total		3264565	100.000

methyl (*R*)-2-(thiophen-3-yl)indoline-1-carboxylate 2p





methyl (*R*)-2-(thiophen-3-yl)indoline-1-carboxylate 2p

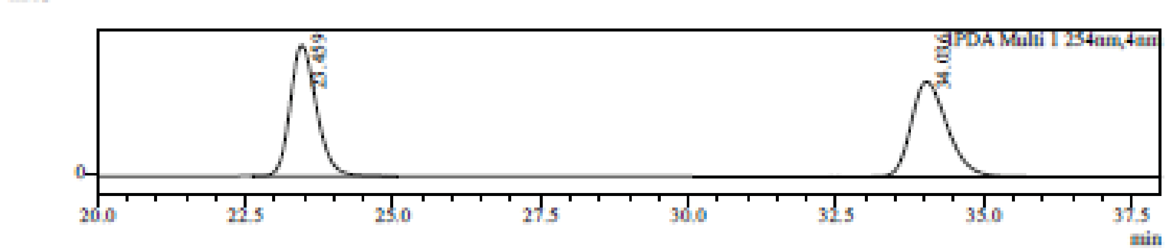


methyl (*R*)-2-(thiophen-3-yl)indoline-1-carboxylate 2p

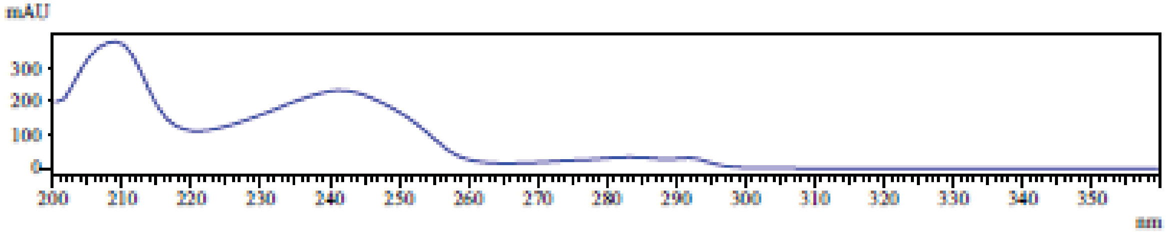
Sample Information

Sample Name	: XW-V-68-IA-0.5%0.8mL
Sample ID	: XW-V-68-IA-0.5%0.8mL
Data File	: XW-V-68-IA-0.5%0.8mL.lcd
Method File	: XW-0.5%-0.8ml.lcm

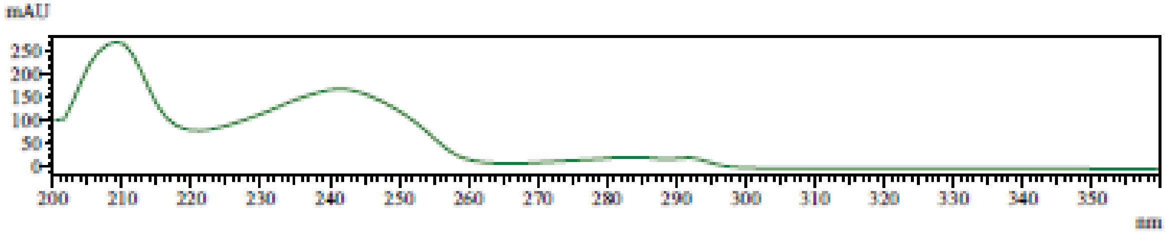
Chromatogram



UV Spectrum
Retention time = 23.459



UV Spectrum
Retention time = 34.036



Peak Table

PDA Ch1 254nm

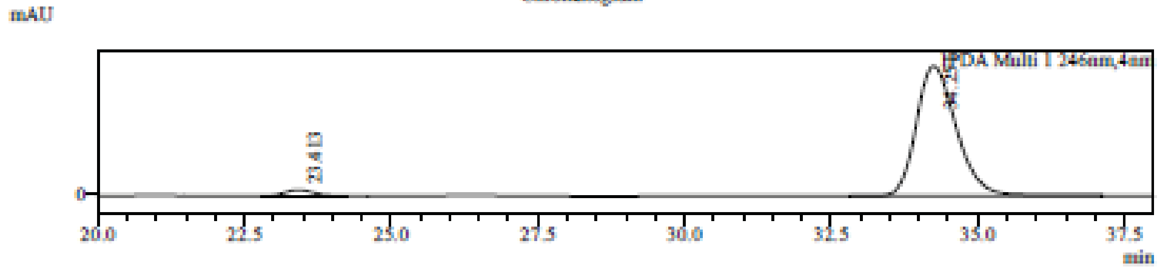
Peak#	Ret. Time	Area	Area%
1	23.459	3317129	50.079
2	34.036	3306717	49.921
Total		6623845	100.000

methyl (*R*)-2-(thiophen-3-yl)indoline-1-carboxylate 2p

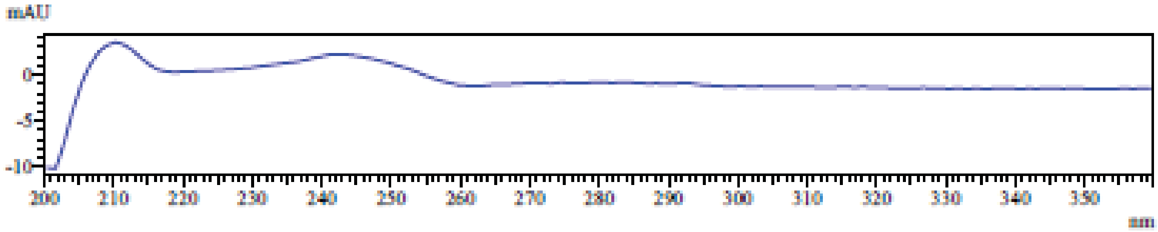
Sample Information

Sample Name : XW-V-69B-IA-0.5%0.8mL
Sample ID : XW-V-69B-IA-0.5%0.8mL
Data File : XW-V-69B-IA-0.5%0.8mL.lcd
Method File : XW-0.5%-0.8ml.lcm

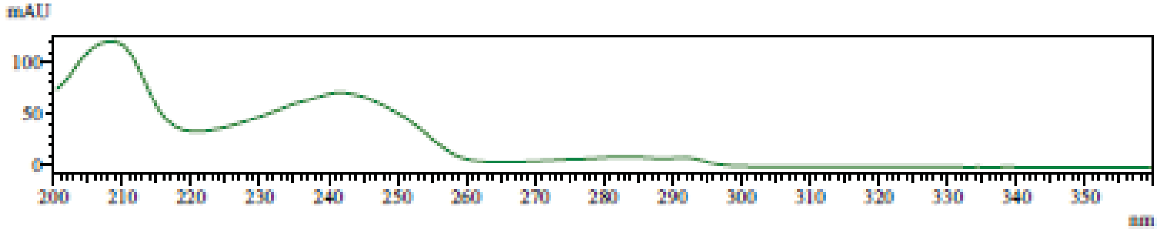
Chromatogram



UV Spectrum
Retention time = 23.413



UV Spectrum
Retention time = 34.251

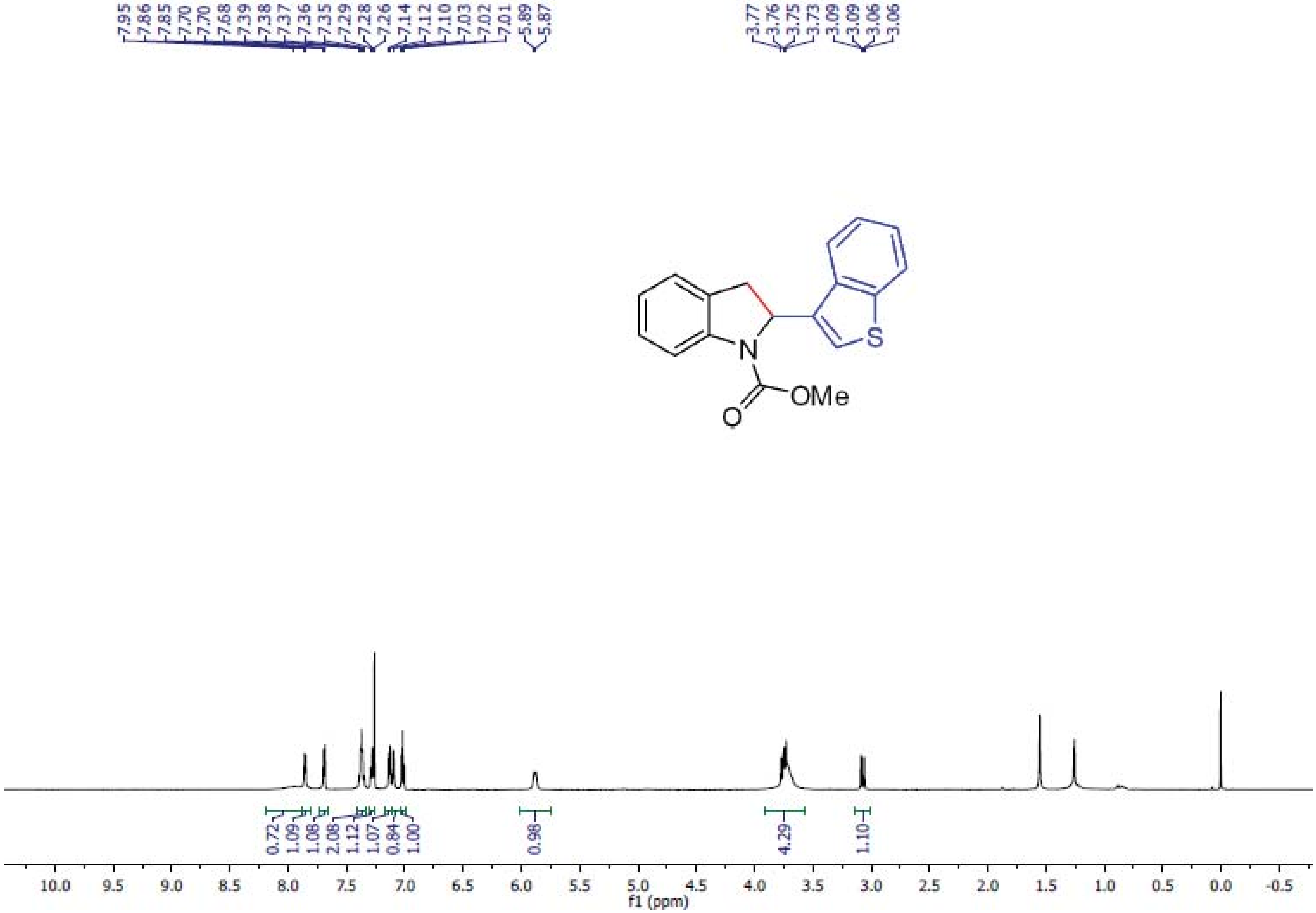


Peak Table

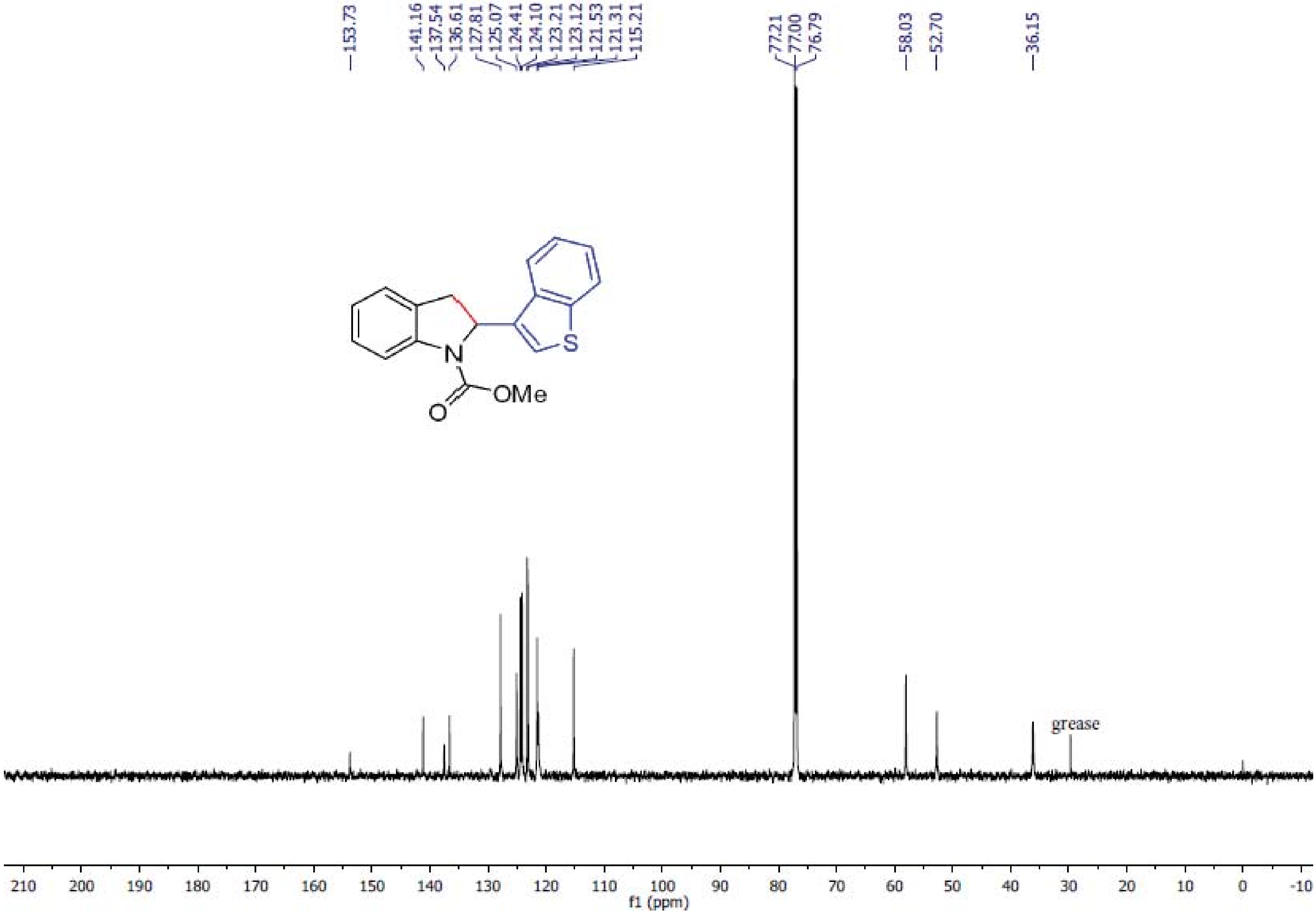
PDA Ch1 246nm

Peak#	Ret. Time	Area	Area%
1	23.413	99299	3.163
2	34.251	3040058	96.837
Total		3139357	100.000

methyl (*R*)-2-(benzo[*b*]thiophen-3-yl)indoline-1-carboxylate 2q



methyl (*R*)-2-(benzo[*b*]thiophen-3-yl)indoline-1-carboxylate 2q

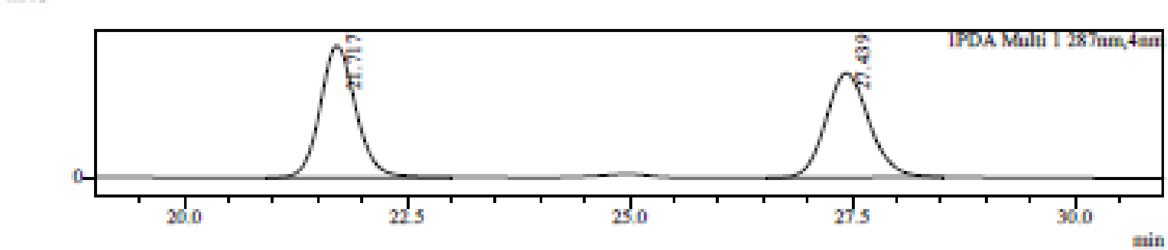


methyl (*R*)-2-(benzo[*b*]thiophen-3-yl)indoline-1-carboxylate 2q

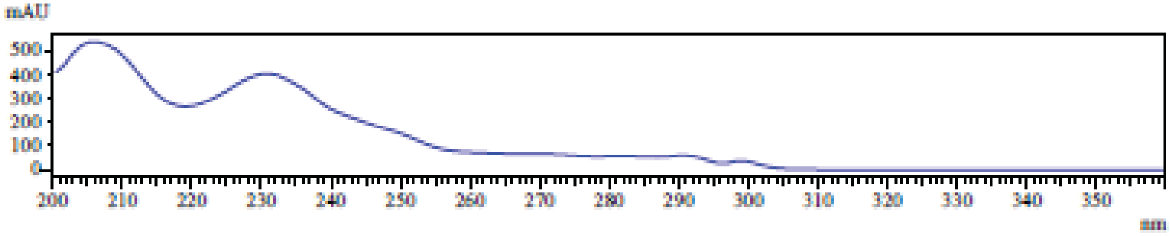
Sample Information

Sample Name : XW-V-116-IA-1%0.8mL
Sample ID : XW-V-116-IA-1%0.8mL
Data File : XW-V-116-IA-1%0.8mL.lcd
Method File : XW-1%-0.8ml.lcm

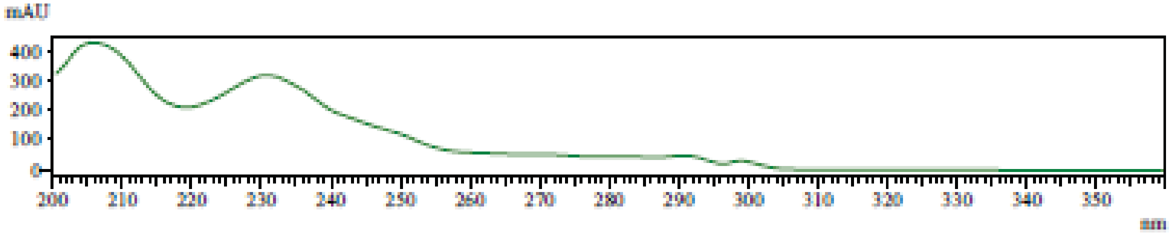
Chromatogram



UV Spectrum
Retention time = 21.717



UV Spectrum
Retention time = 27.439



Peak Table

PDA Ch1 287nm

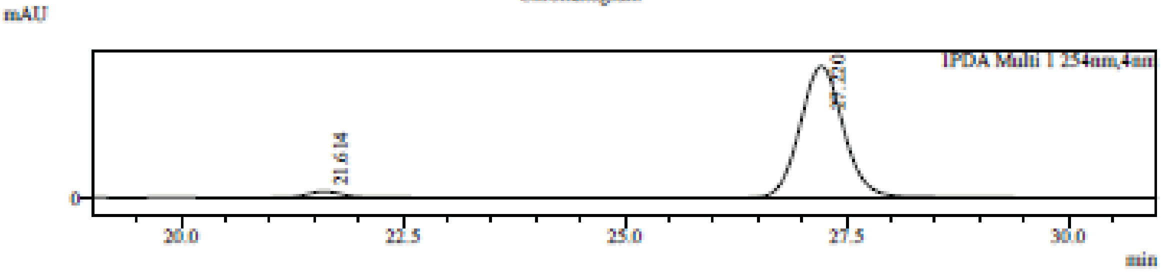
Peak#	Ret. Time	Area	Area%
1	21.717	1545390	50.918
2	27.439	1489687	49.082
Total		3035077	100.000

methyl (*R*)-2-(benzo[*b*]thiophen-3-yl)indoline-1-carboxylate 2q

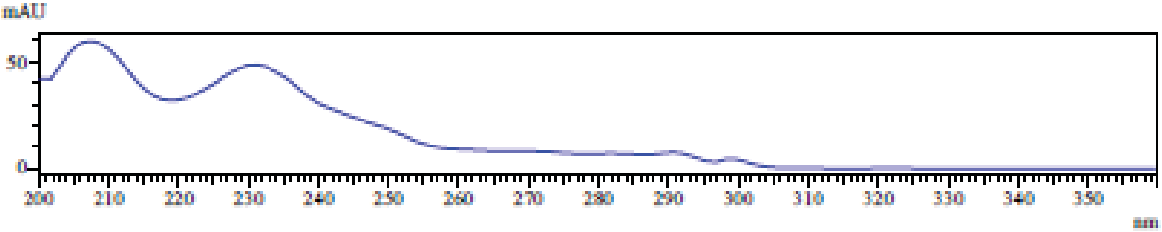
Sample Information

Sample Name : XW-V-117-old-IA-1%0.8mL
Sample ID : XW-V-117-old-IA-1%0.8mL
Data File : XW-V-117-old-IA-1%0.8mL.lcd
Method File : XW-1%-0.8ml.lcm

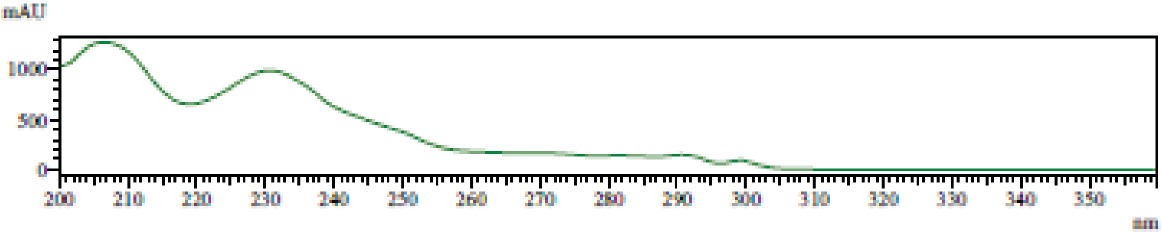
Chromatogram



UV Spectrum
Retention time = 21.614



UV Spectrum
Retention time = 27.220

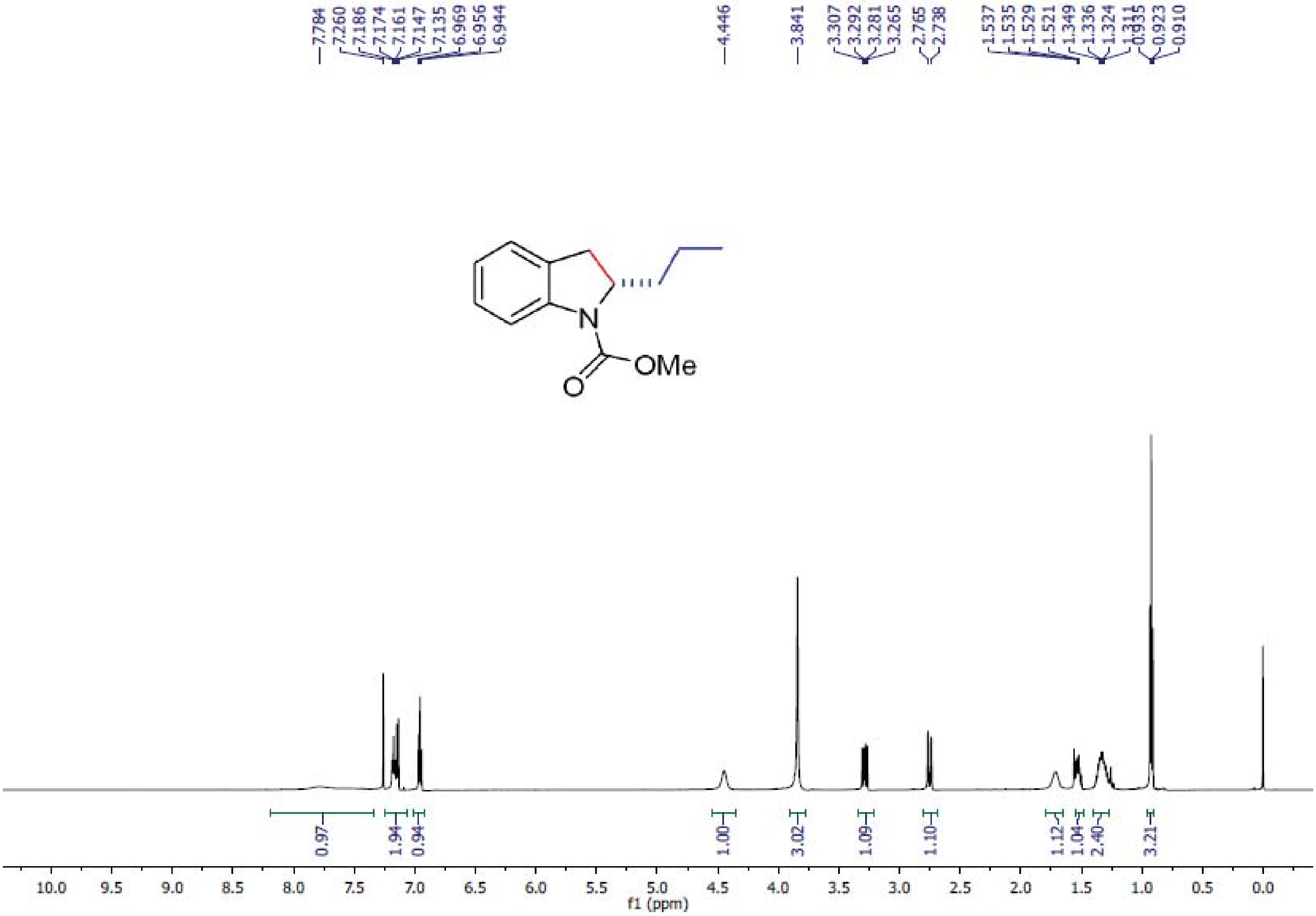


Peak Table

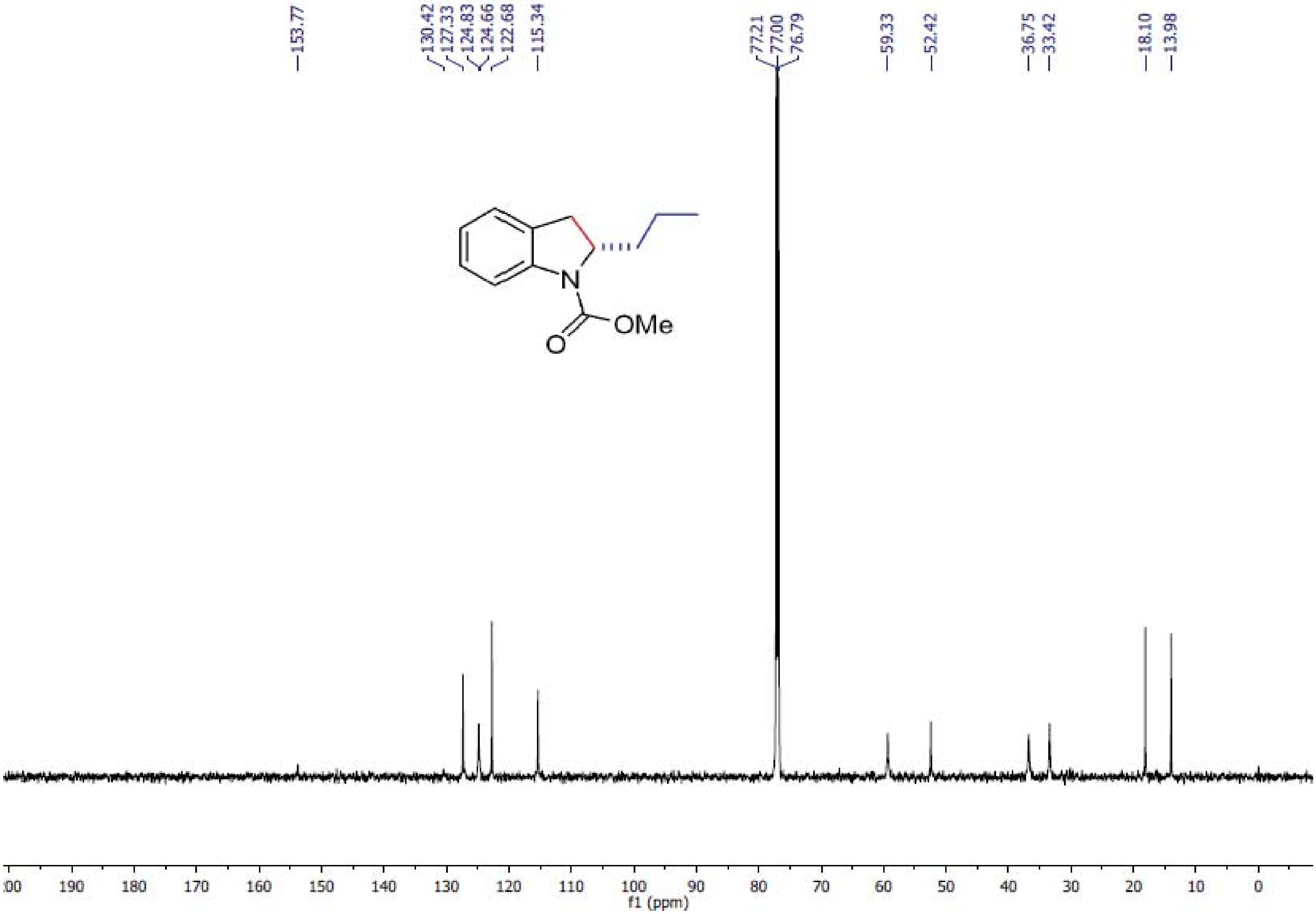
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	21.614	376448	3.980
2	27.220	9082278	96.020
Total		9458726	100.000

methyl (*S*)-2-propylindoline-1-carboxylate 2r



methyl (*S*)-2-propylindoline-1-carboxylate 2r

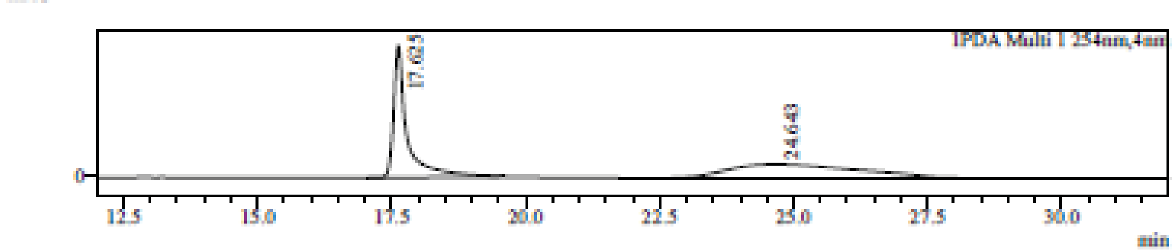


methyl (*S*)-2-propylindoline-1-carboxylate 2r

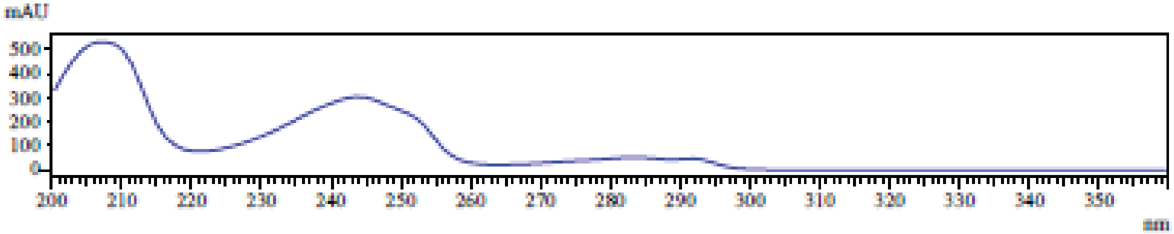
Sample Information

Sample Name : XW-V-52--2-IA-0.2%0.8mL
Sample ID : XW-V-52--2-IA-0.2%0.8mL
Data File : XW-V-52--2-IA-0.2%0.8mL.lcd
Method File : XW-0.2%-0.8ml.lcm

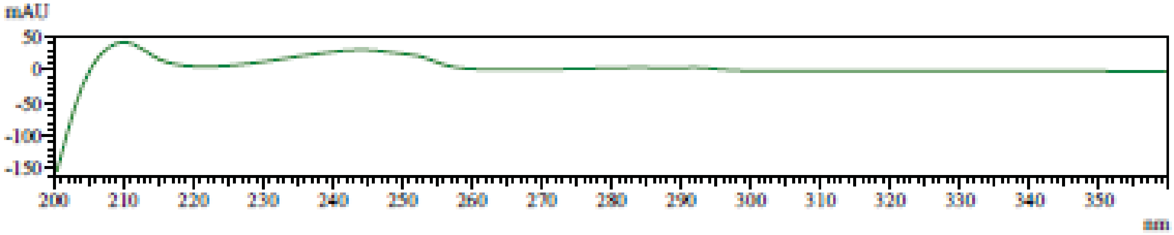
Chromatogram



UV Spectrum
Retention time = 17.625



UV Spectrum
Retention time = 24.643



Peak Table

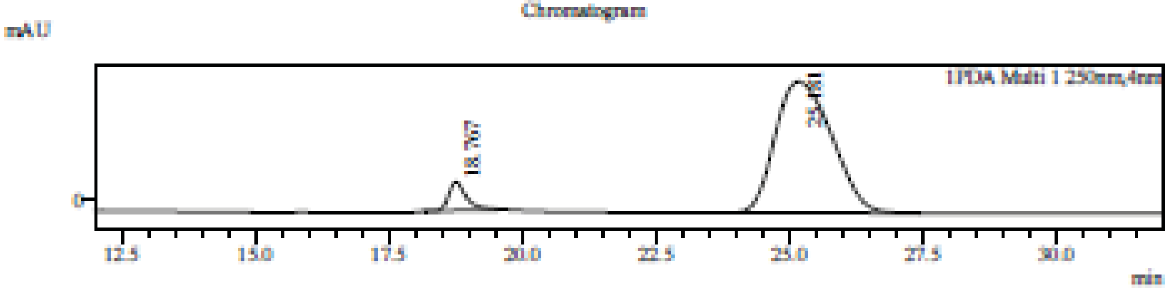
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.625	2722739	50.278
2	24.643	2692668	49.722
Total		5415407	100.000

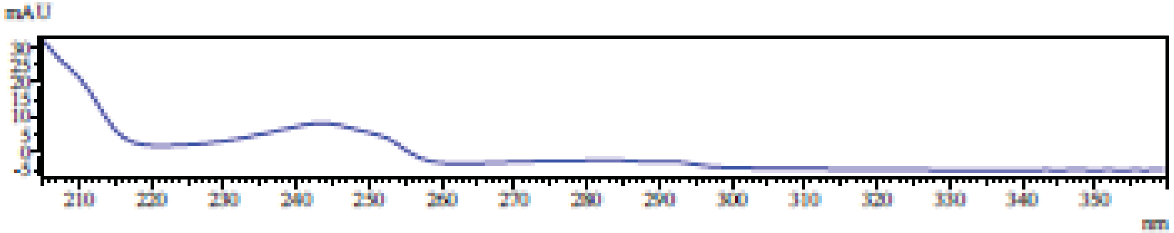
methyl (*S*)-2-propylindoline-1-carboxylate 2r

Sample Information

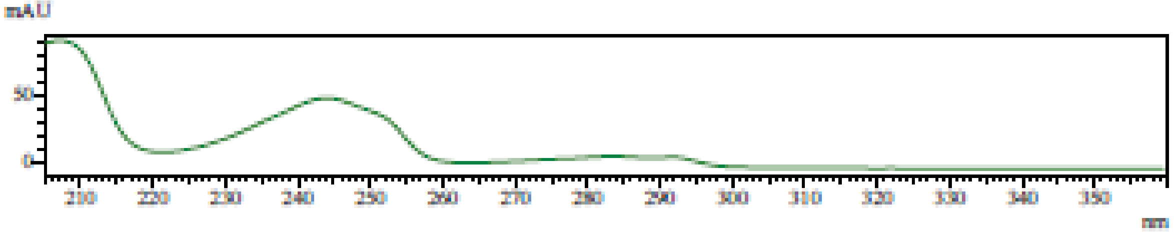
Sample Name	: XW-V-53-60oC-2-IA-0.2%0.8mL
Sample ID	: XW-V-53-60oC-2-IA-0.2%0.8mL
Data File	: XW-V-53-60oC-2-IA-0.2%0.8mL.lcd
Method File	: XW-0.2%-0.8ml.lcm



UV Spectrum
Retention time = 18.767



UV Spectrum
Retention time = 25.181

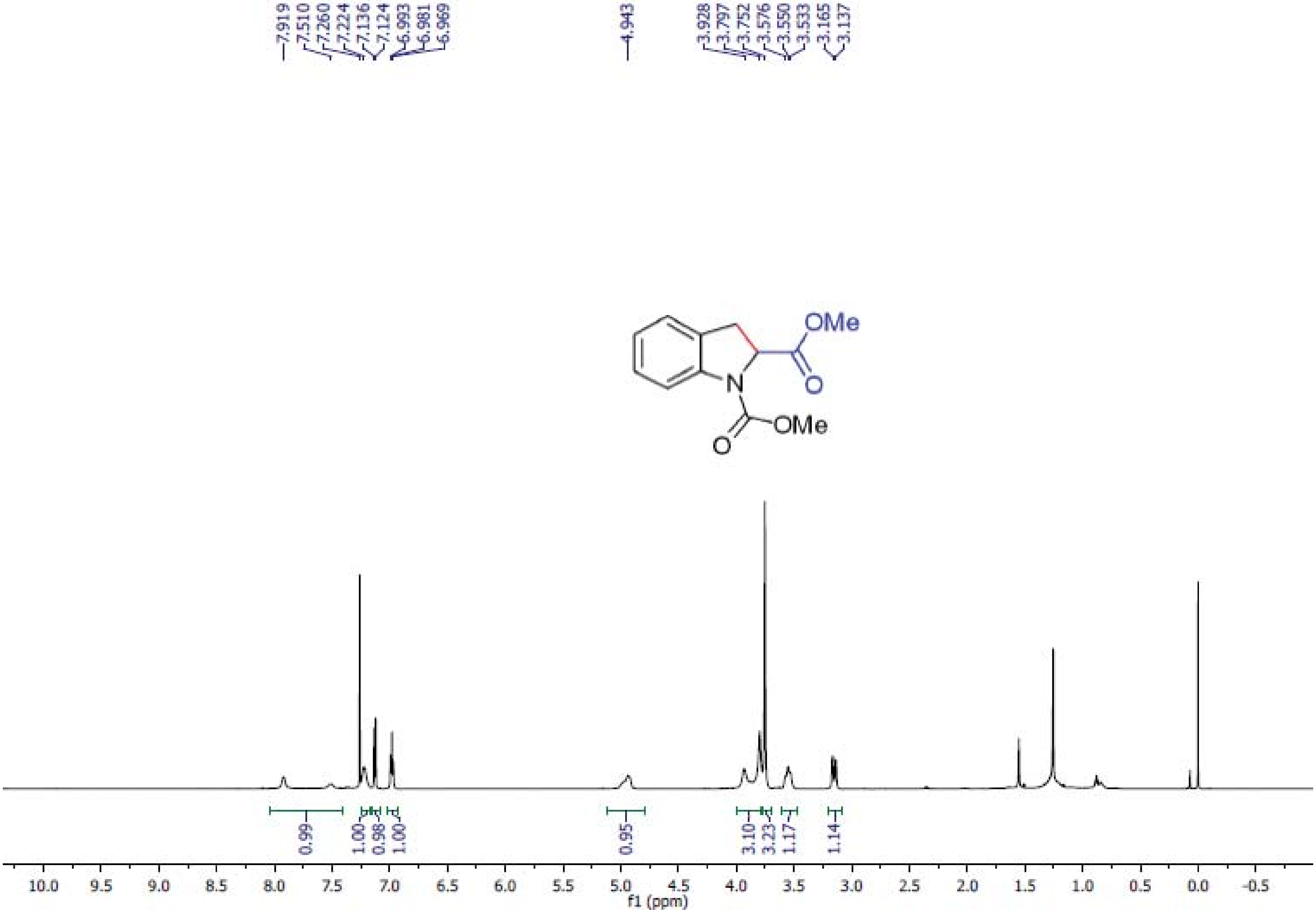


Peak Table

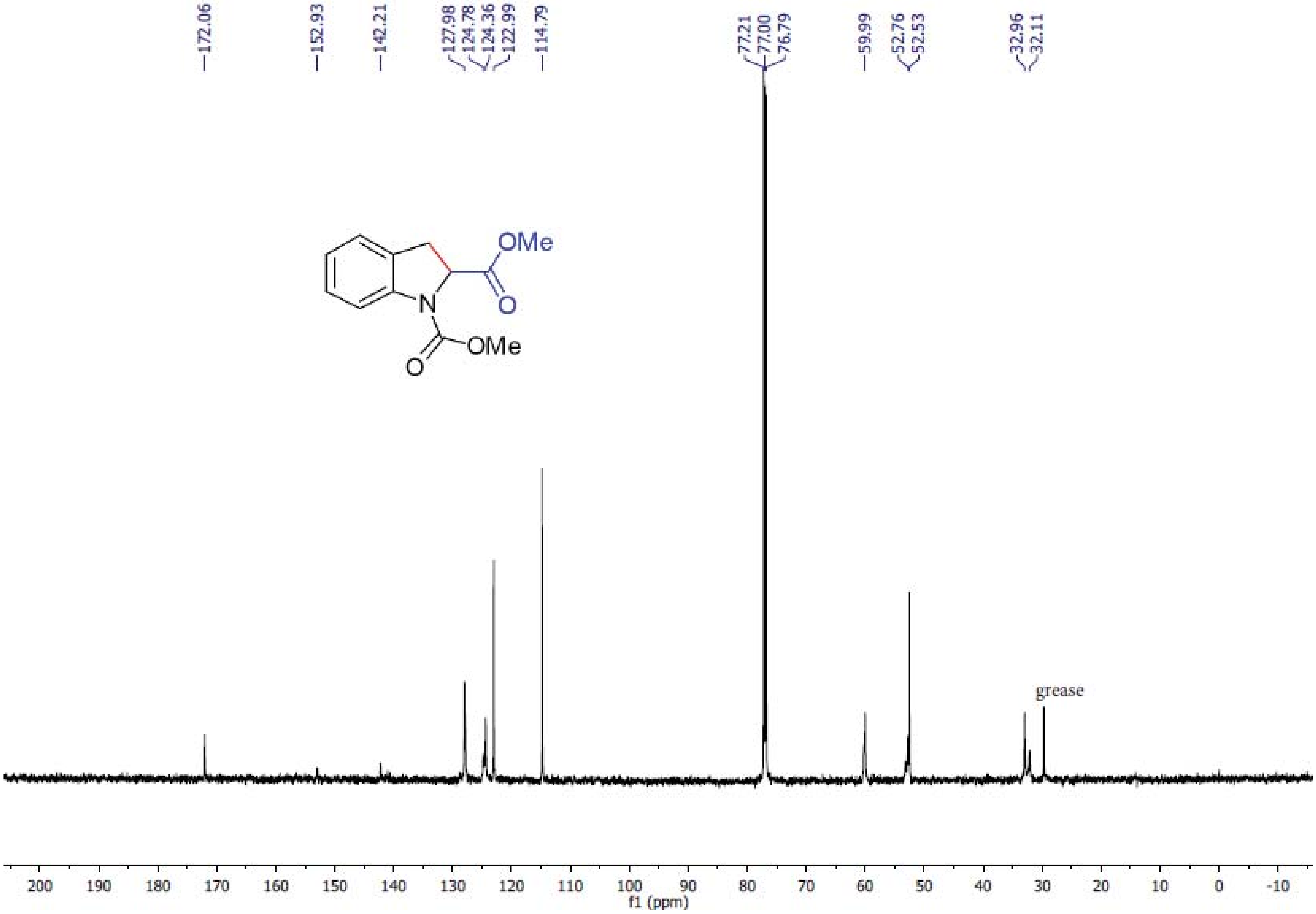
PDA Ch1 250nm

Peak#	Ret. Time	Area	Area%
1	18.767	213047	6.350
2	25.181	3142094	93.650
Total		3355141	100.000

dimethyl (*R*)-indoline-1,2-dicarboxylate 2s



dimethyl (*R*)-indoline-1,2-dicarboxylate 2s

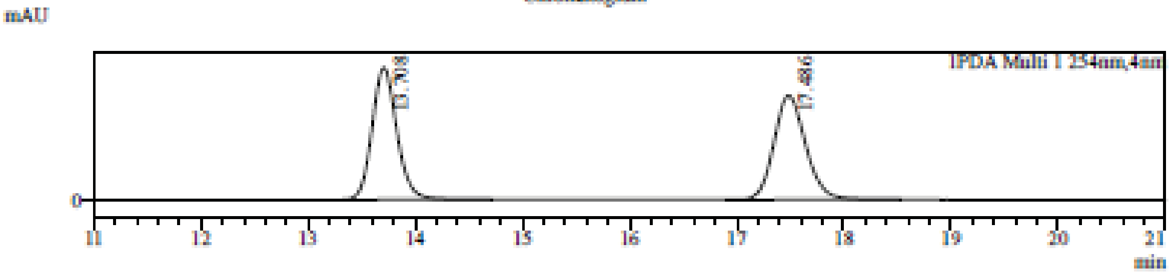


dimethyl (*R*)-indoline-1,2-dicarboxylate 2s

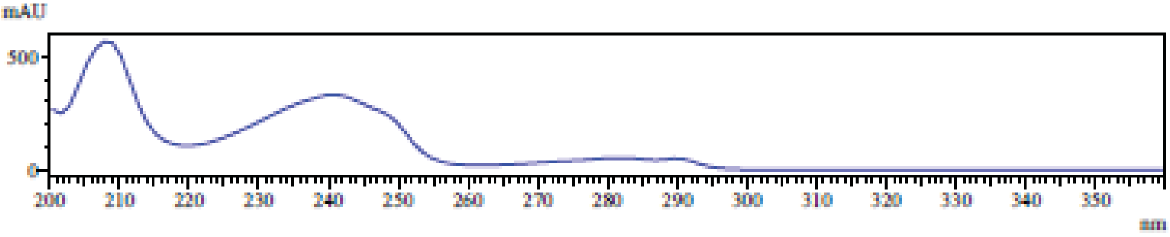
Sample Information

Sample Name	: XW-V-86-2-IA-5%0.8mL
Sample ID	: XW-V-86-2-IA-5%0.8mL
Data File	: XW-V-86-2-IA-5%0.8mL.lcd
Method File	: XW-5%-0.8ml.lcm

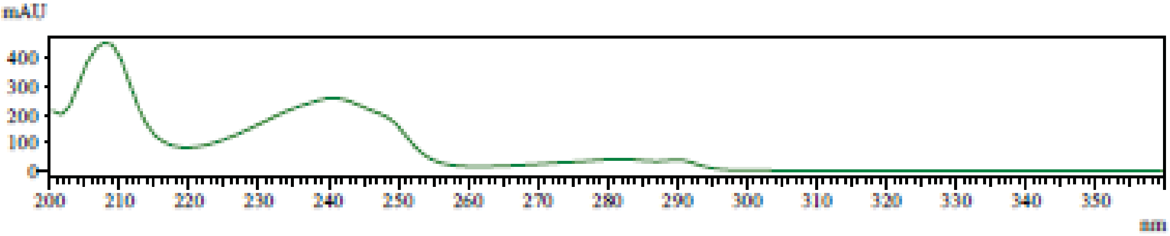
Chromatogram



UV Spectrum
Retention time = 13.708



UV Spectrum
Retention time = 17.486



Peak Table

PDA Ch1 254nm

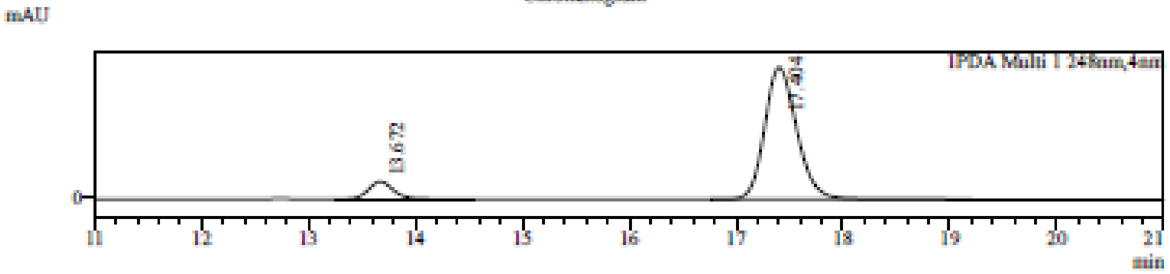
Peak#	Ret. Time	Area	Area%
1	13.708	1284010	49.832
2	17.486	1292669	50.168
Total		2576679	100.000

dimethyl (*R*)-indoline-1,2-dicarboxylate 2s

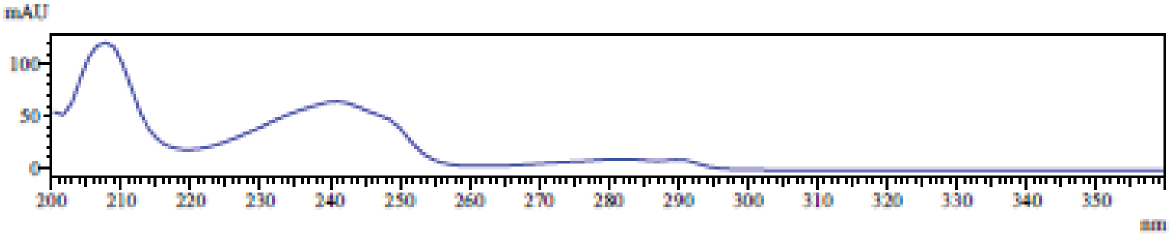
Sample Information

Sample Name : XW-V-87-40C-IA-5%0.8mL
Sample ID : XW-V-87-40C-IA-5%0.8mL
Data File : XW-V-87-40C-IA-5%0.8mL.lcd
Method File : XW-5%-0.8ml.lcm

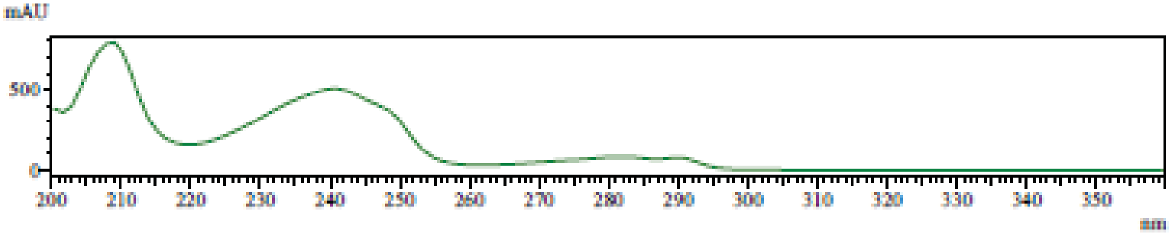
Chromatogram



UV Spectrum
Retention time = 13.672



UV Spectrum
Retention time = 17.404

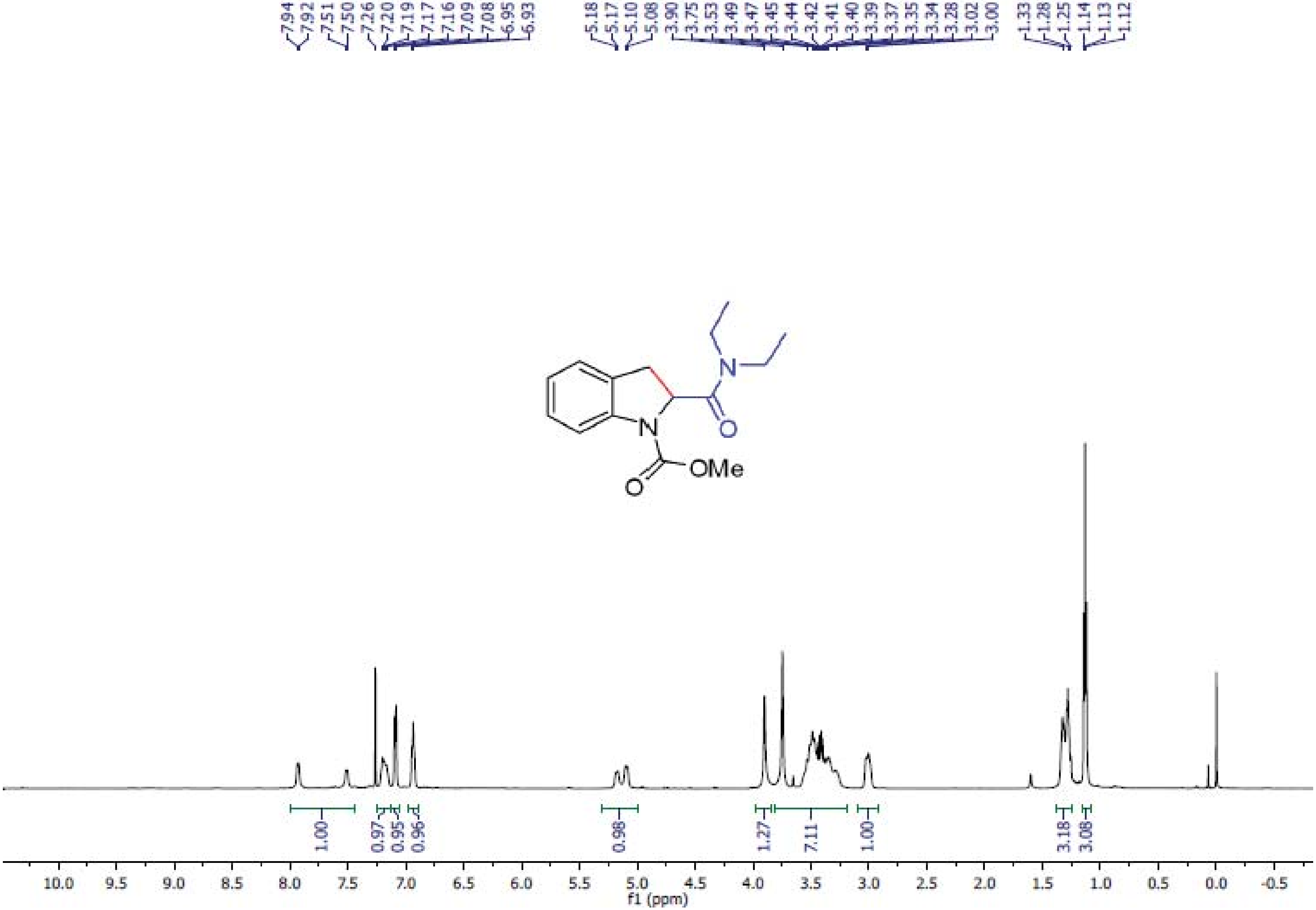


Peak Table

PDA Ch1 248nm

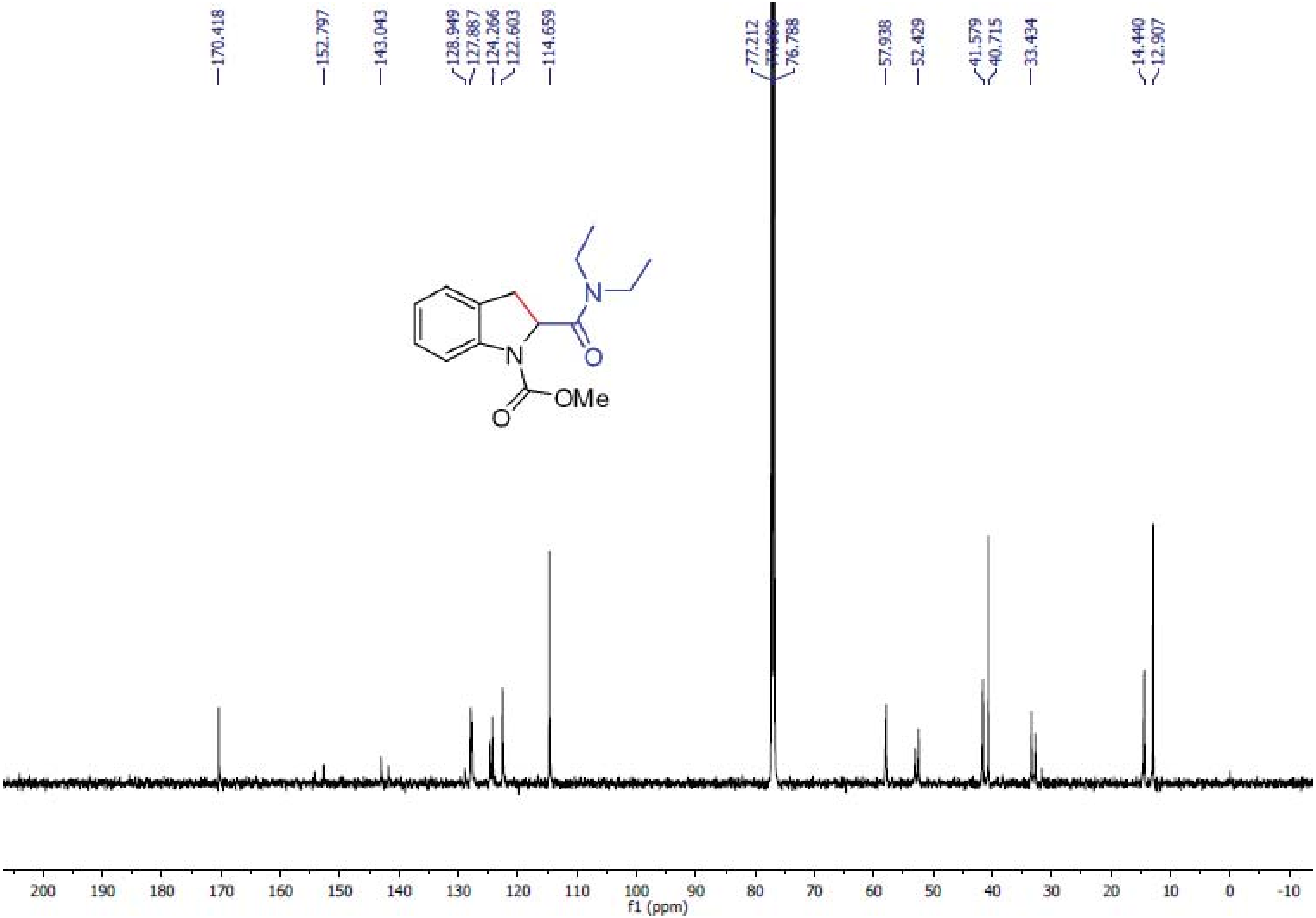
Peak#	Ret. Time	Area	Area%
1	13.672	799187	9.368
2	17.404	7731407	90.632
Total		8530593	100.000

methyl (*R*)-2-(diethylcarbamoyl)indoline-1-carboxylate 2t



Note: The broad spectrum was due to the amide rotamers

methyl (*R*)-2-(diethylcarbamoyl)indoline-1-carboxylate 2t



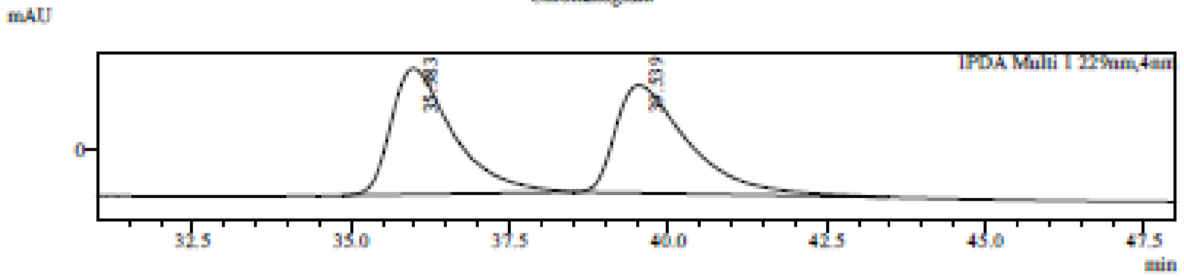
Note: The spectrum contains a mixture of amide rotamers and the major rotamer was labelled.

methyl (*R*)-2-(diethylcarbamoyl)indoline-1-carboxylate 2t

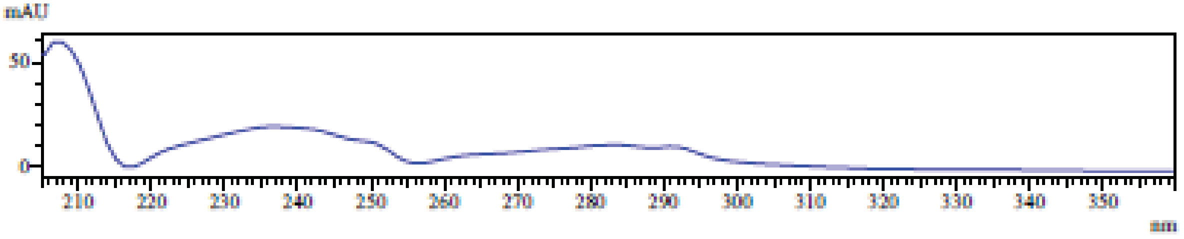
Sample Information

Sample Name : XW-V-111-IA-8%0.8mL
Sample ID : XW-V-111-IA-8%0.8mL
Data File : XW-V-111-IA-8%0.8mL001.lcd
Method File : XW-8%-0.8ml.lcm

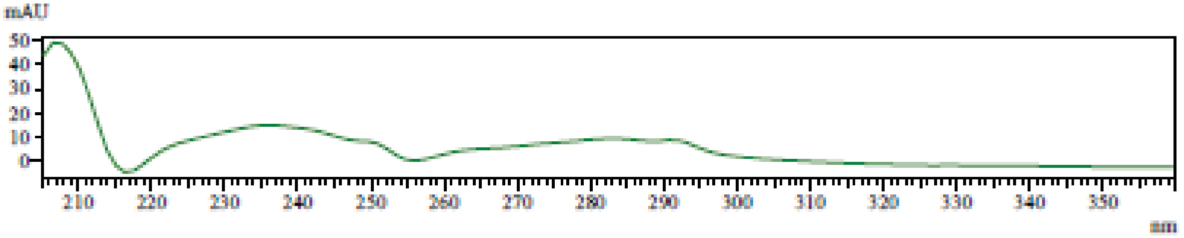
Chromatogram



UV Spectrum
Retention time = 35.983



UV Spectrum
Retention time = 39.539



Peak Table

PDA Ch1 229nm

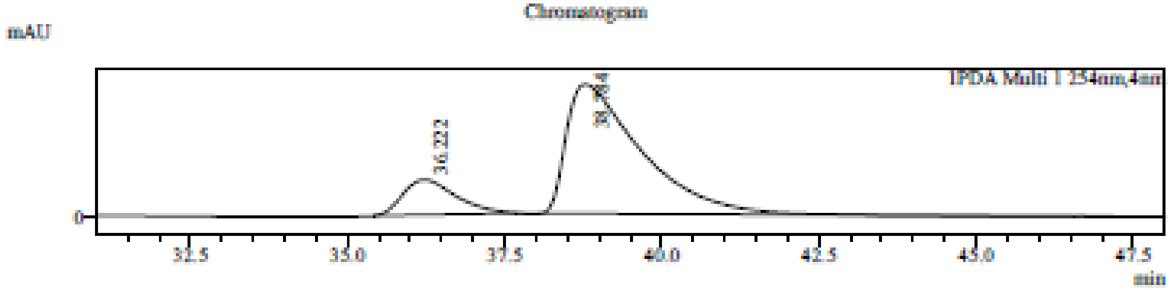
Peak#	Ret. Time	Area	Area%
1	35.983	1476682	49.895
2	39.539	1482878	50.105
Total		2959560	100.000

methyl (*R*)-2-(diethylcarbamoyl)indoline-1-carboxylate 2t

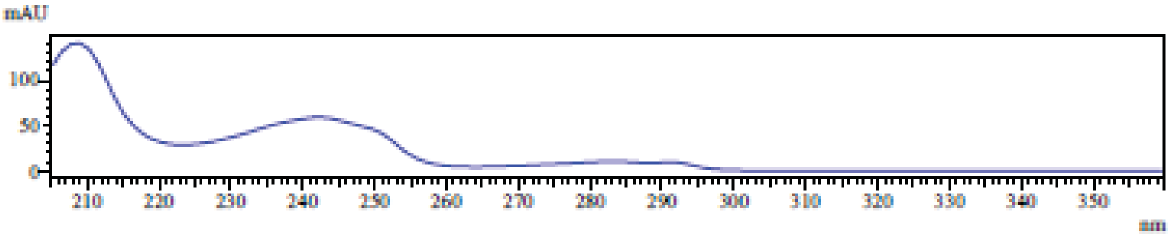
Sample Information

Sample Name	: XW-V-113-40C-IA-8%0.8mL
Sample ID	: XW-V-113-40C-IA-8%0.8mL
Data File	: XW-V-113-40C-IA-8%0.8mL.lcd
Method File	: XW-8%-0.8ml.lcm

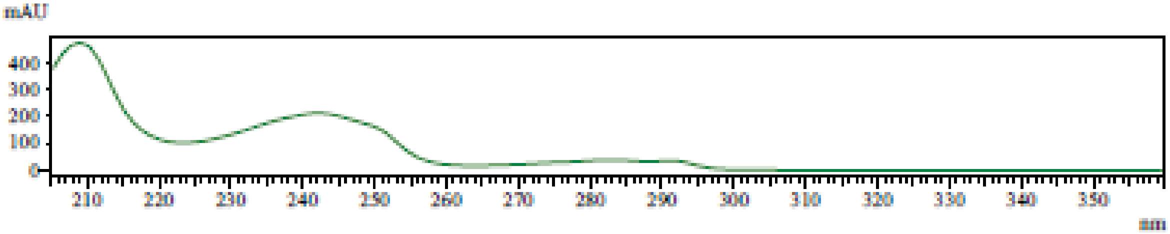
Chromatogram



UV Spectrum
Retention time = 36.222



UV Spectrum
Retention time = 38.784

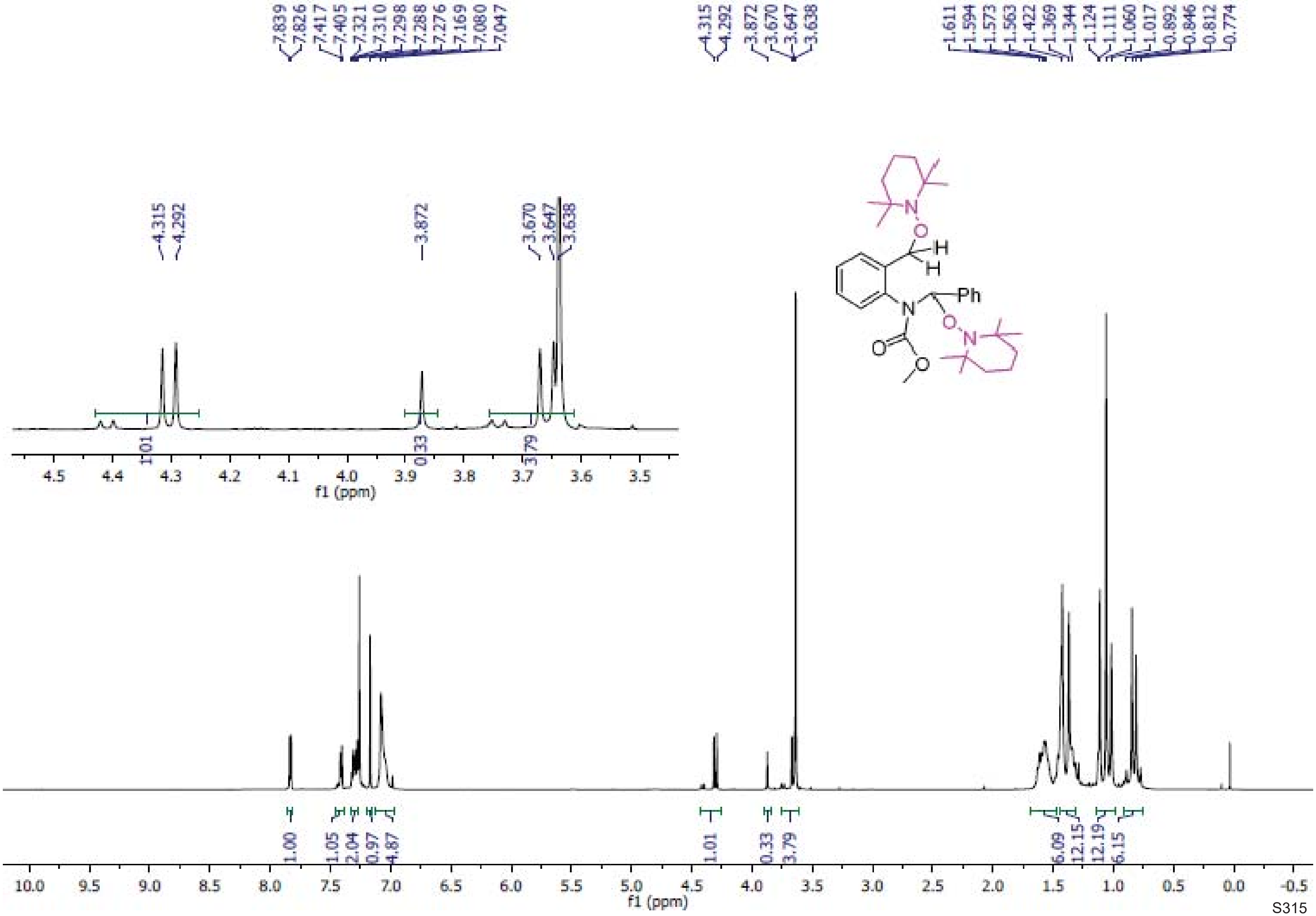


Peak Table

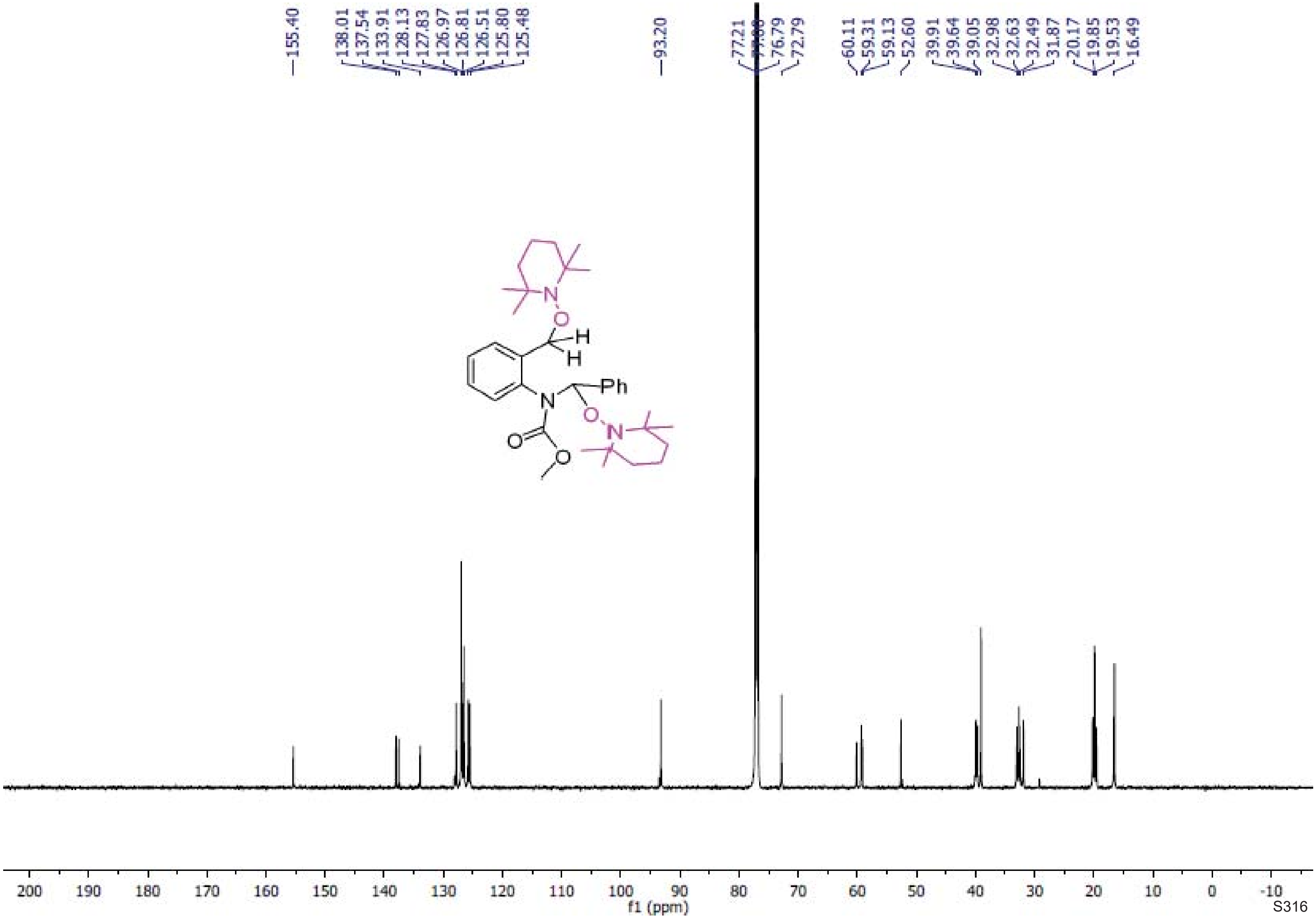
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	36.222	1352139	16.203
2	38.784	6992618	83.797
Total		8344758	100.000

methyl (phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)carbamate 3c



methyl (phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)carbamate 3c

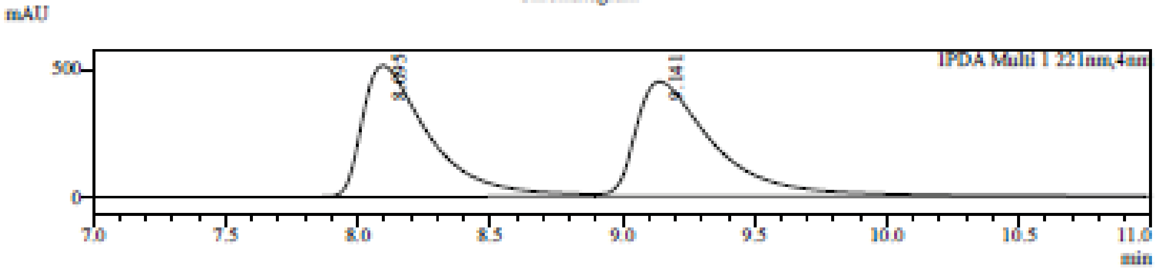


methyl (phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)carbamate 3c

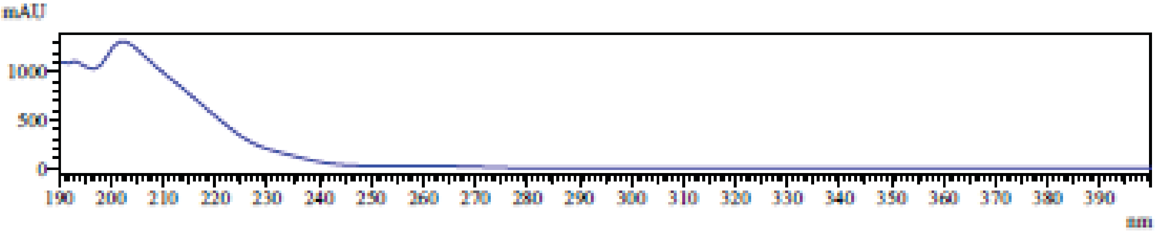
Sample Information

Sample Name : XW-V-127-IA-0.3%0.8mL-1
Sample ID : XW-V-127-IA-0.3%0.8mL-1
Data File : XW-V-127-IA-0.3%0.8mL-1.lcd
Method File : XW-0.3%-0.8ml.lcm

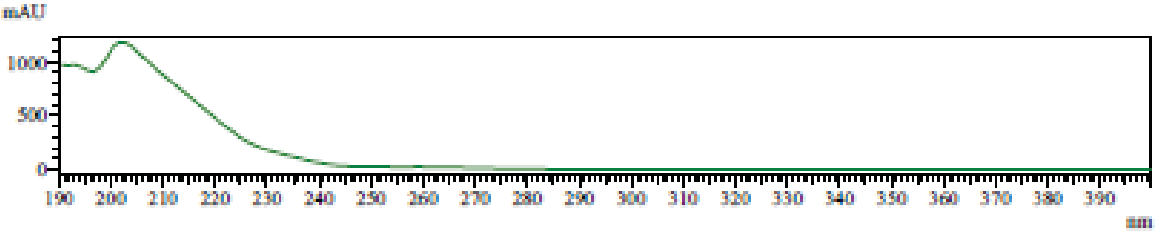
Chromatogram



UV Spectrum
Retention time = 8.095



UV Spectrum
Retention time = 9.141



Peak Table

PDA Ch1 221nm

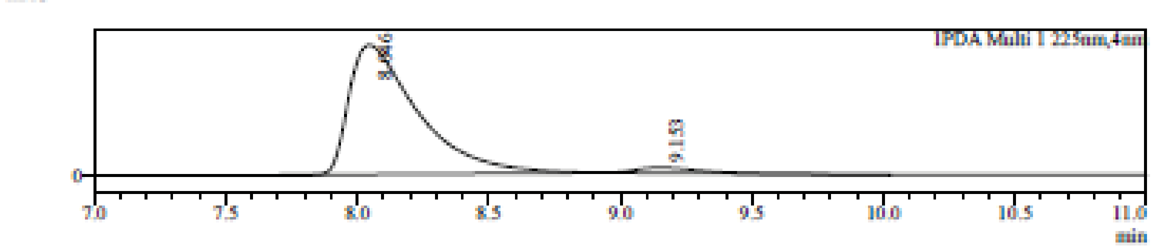
Peak#	Ret. Time	Area	Area%
1	8.095	9013766	49.278
2	9.141	9277793	50.722
Total		18291559	100.000

methyl (phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)(2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)carbamate 3c

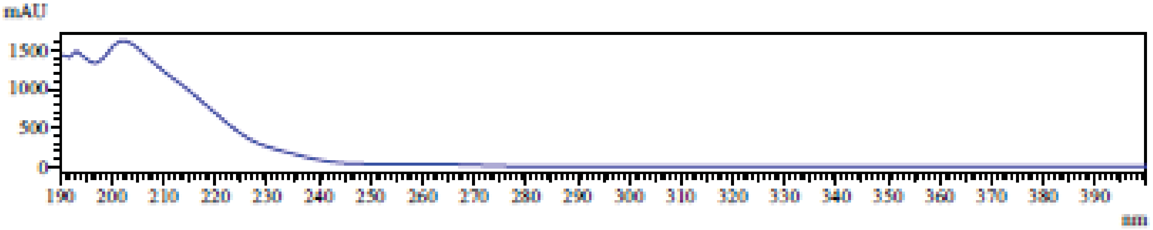
Sample Information

Sample Name : XW-V-137-IA-0.3%0.8mL-1
Sample ID : XW-V-137-IA-0.3%0.8mL-1
Data File : XW-V-137-IA-0.3%0.8mL-1.lcd
Method File : XW-0.3%-0.8ml.lcm

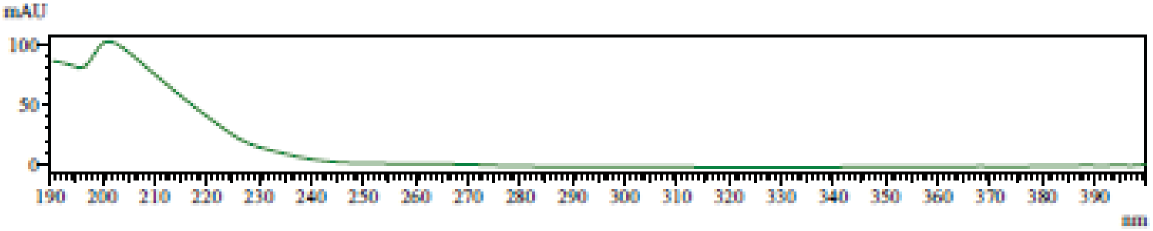
Chromatogram



UV Spectrum
Retention time = 8.046



UV Spectrum
Retention time = 9.153

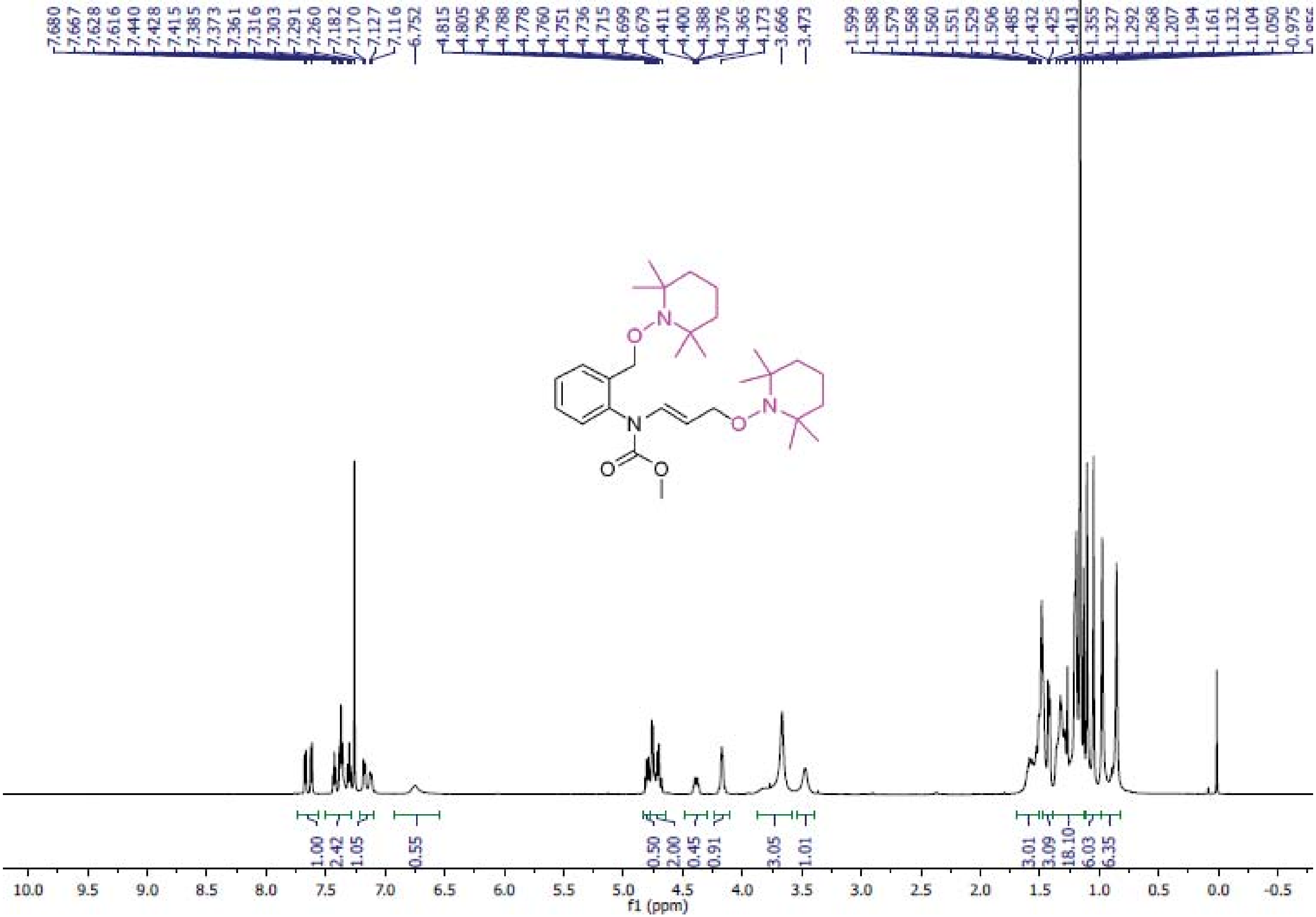


Peak Table

PDA Ch1 225nm

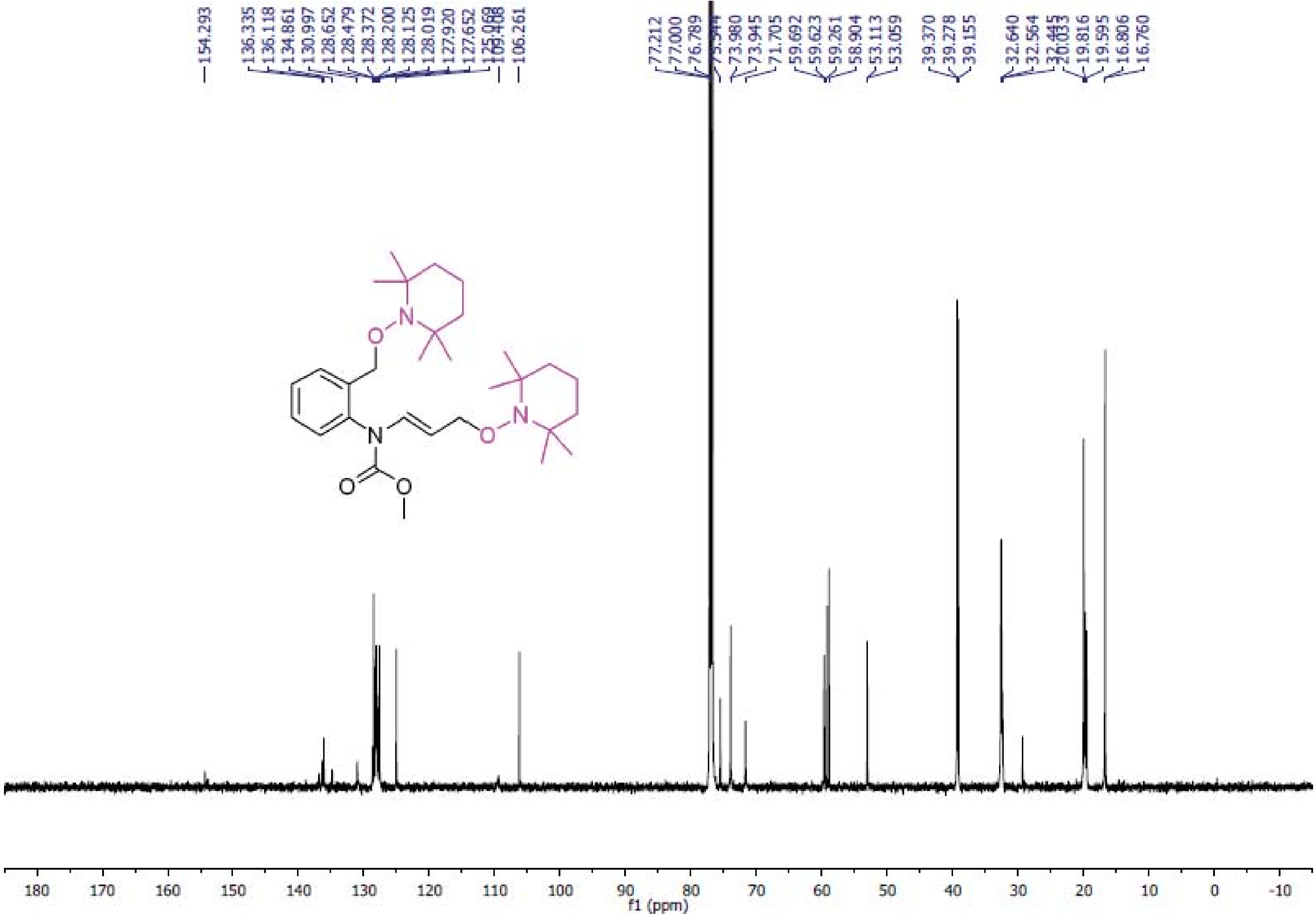
Peak#	Ret. Time	Area	Area%
1	8.046	7823322	96.446
2	9.153	288260	3.554
Total		8111582	100.000

methyl (2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl) phenyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)prop-1-en-1-yl)carbamate 3u



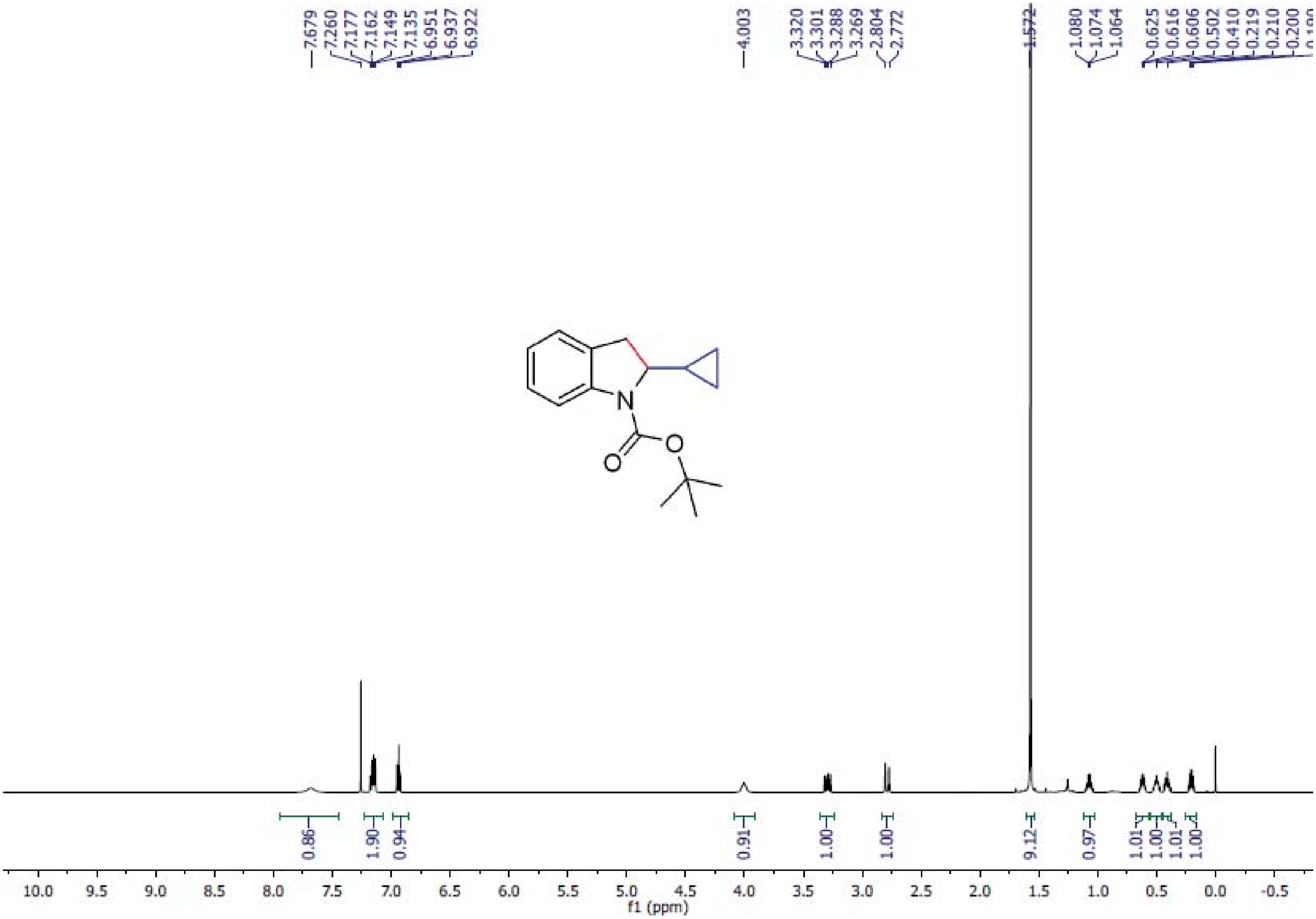
Note: The spectrum contains E/Z isomers of C=C bond.

methyl (2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl) phenyl)(3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)prop-1-en-1-yl)carbamate 3u

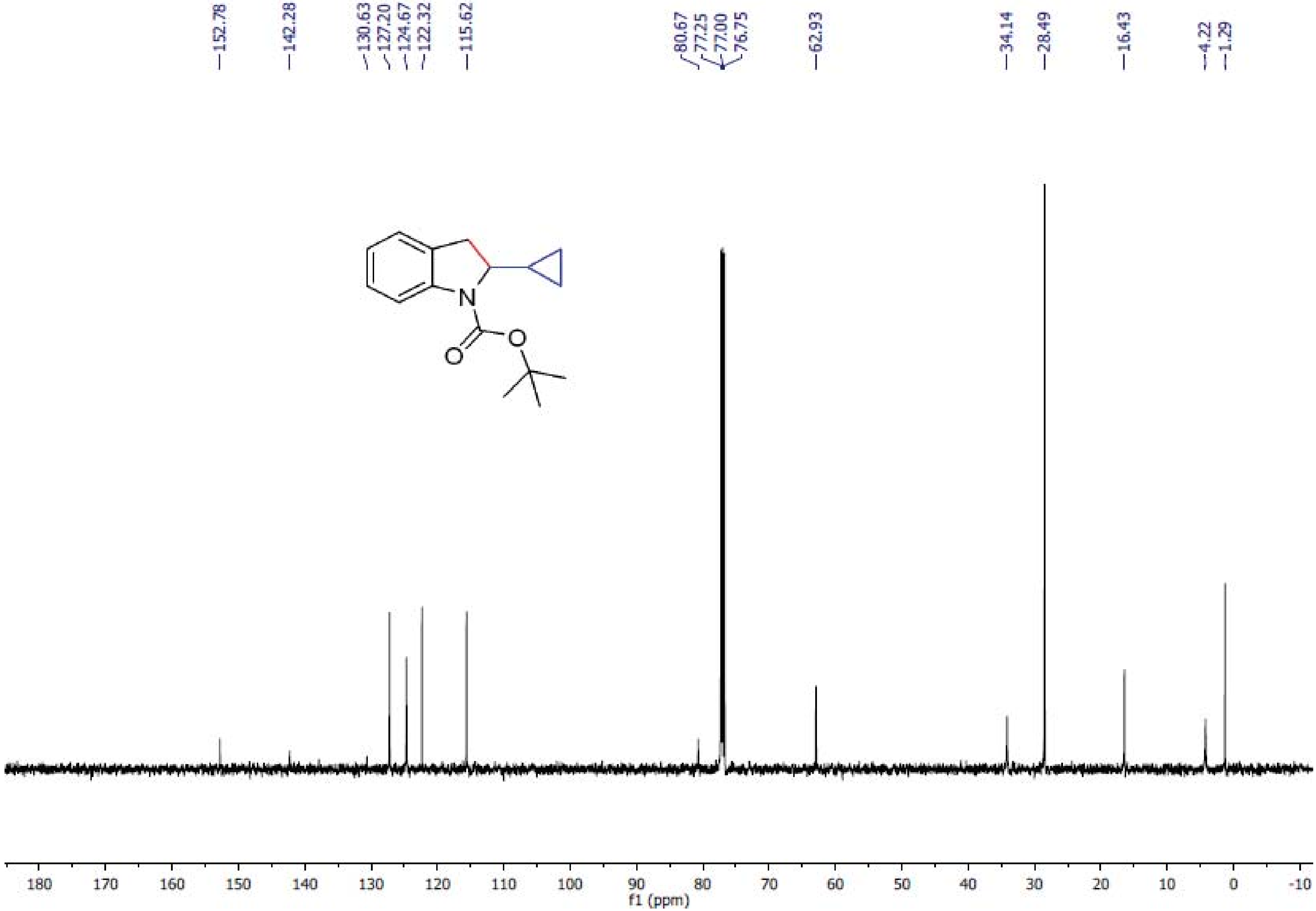


Note: The spectrum contains E/Z isomers of C=C bond.

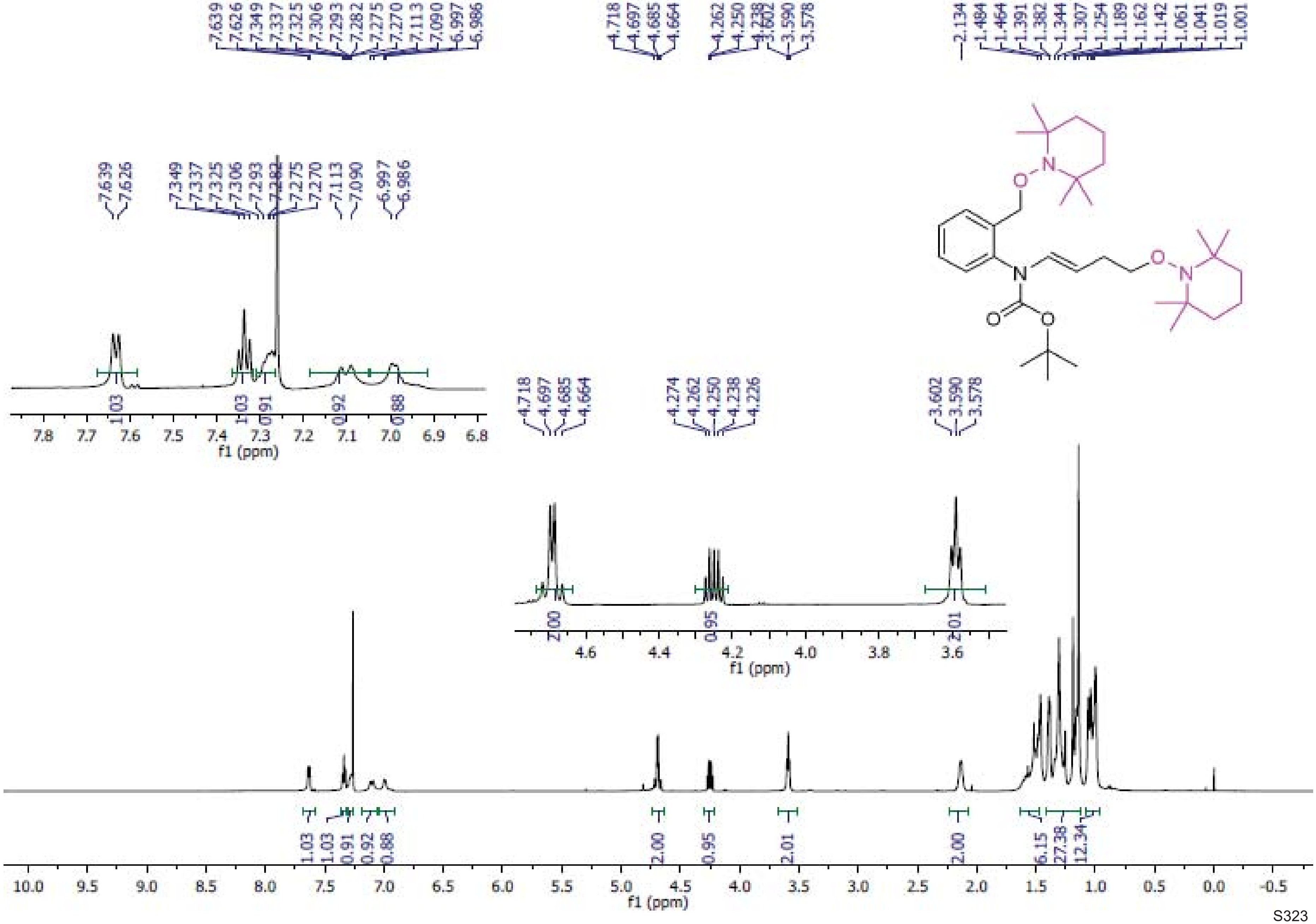
tert-butyl 2-cyclopropylindoline-1-carboxylate 2v



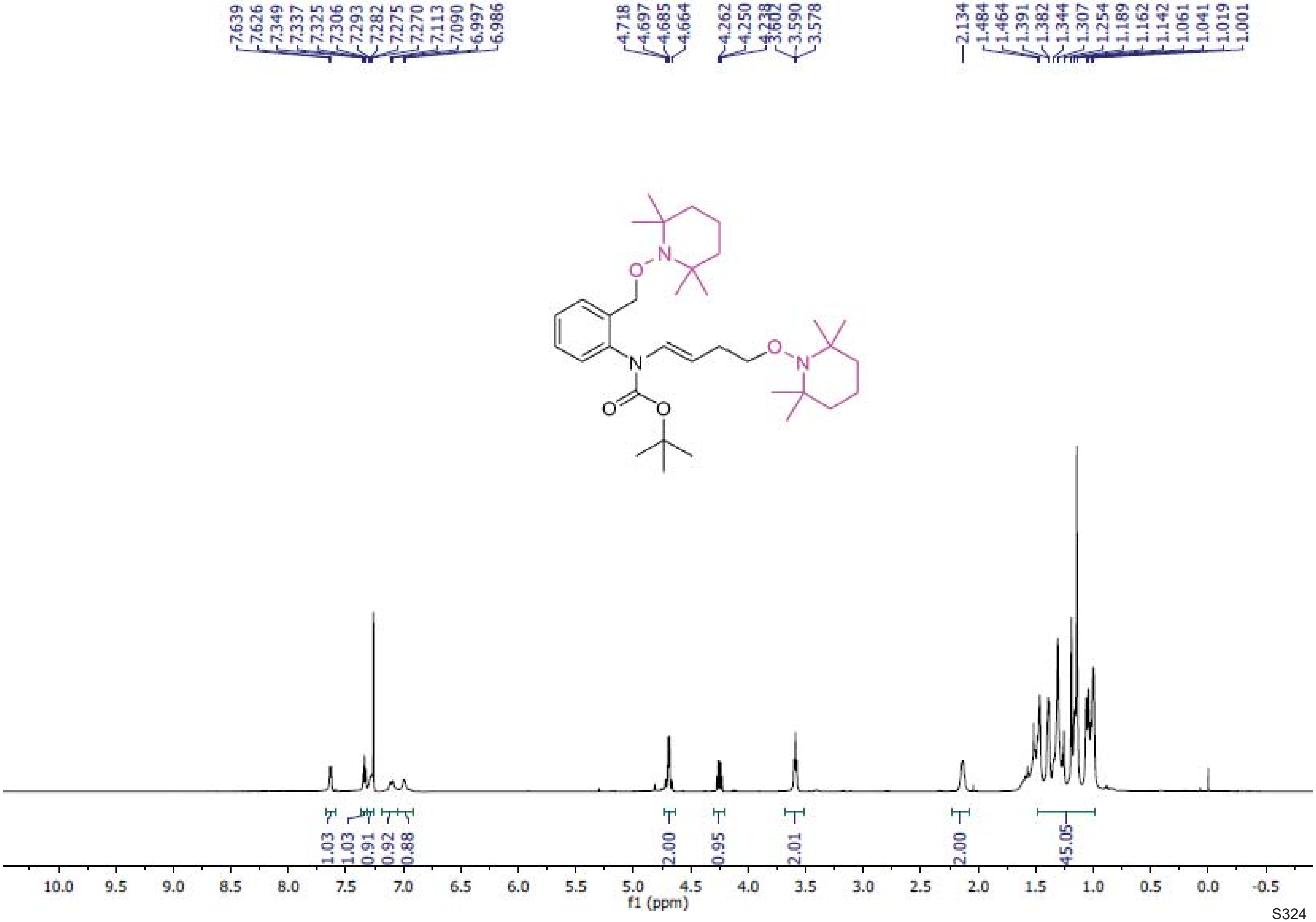
tert-butyl 2-cyclopropylindoline-1-carboxylate 2v



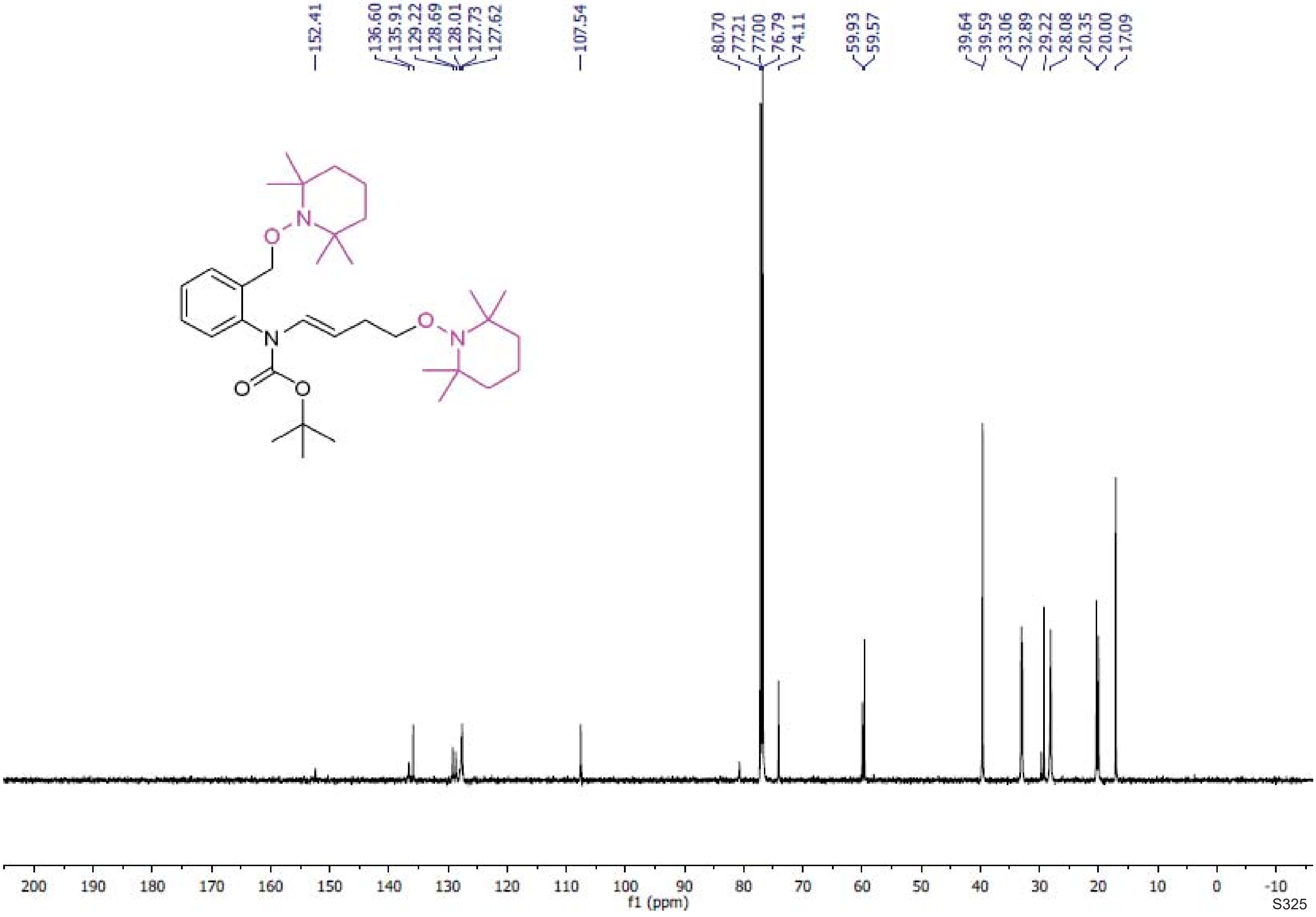
tert-butyl (4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)but-1-en-1-yl)(2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)carbamate 3v



tert-butyl (4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)but-1-en-1-yl)(2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)carbamate 3v



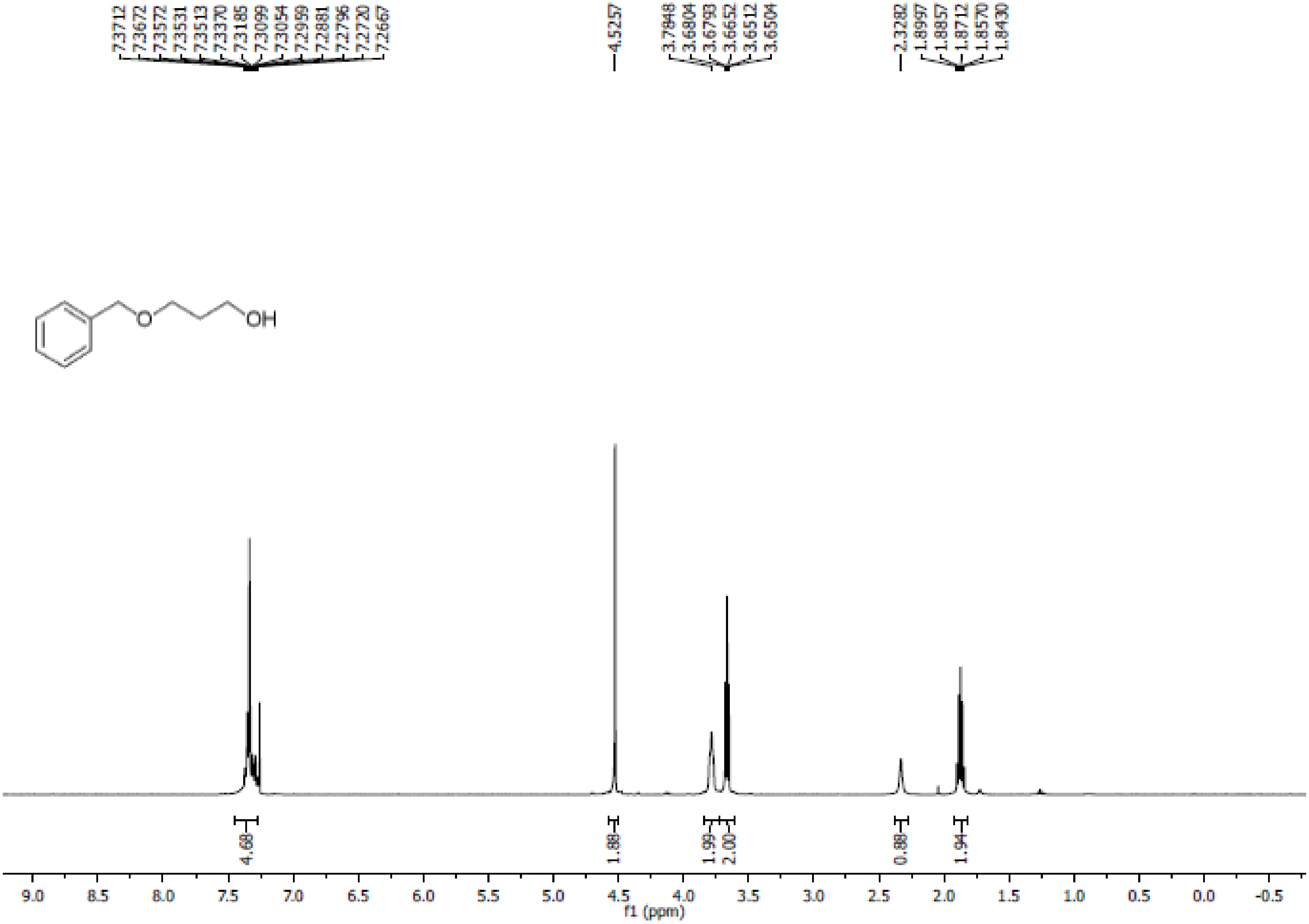
tert-butyl (4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)but-1-en-1-yl)(2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)phenyl)carbamate 3v



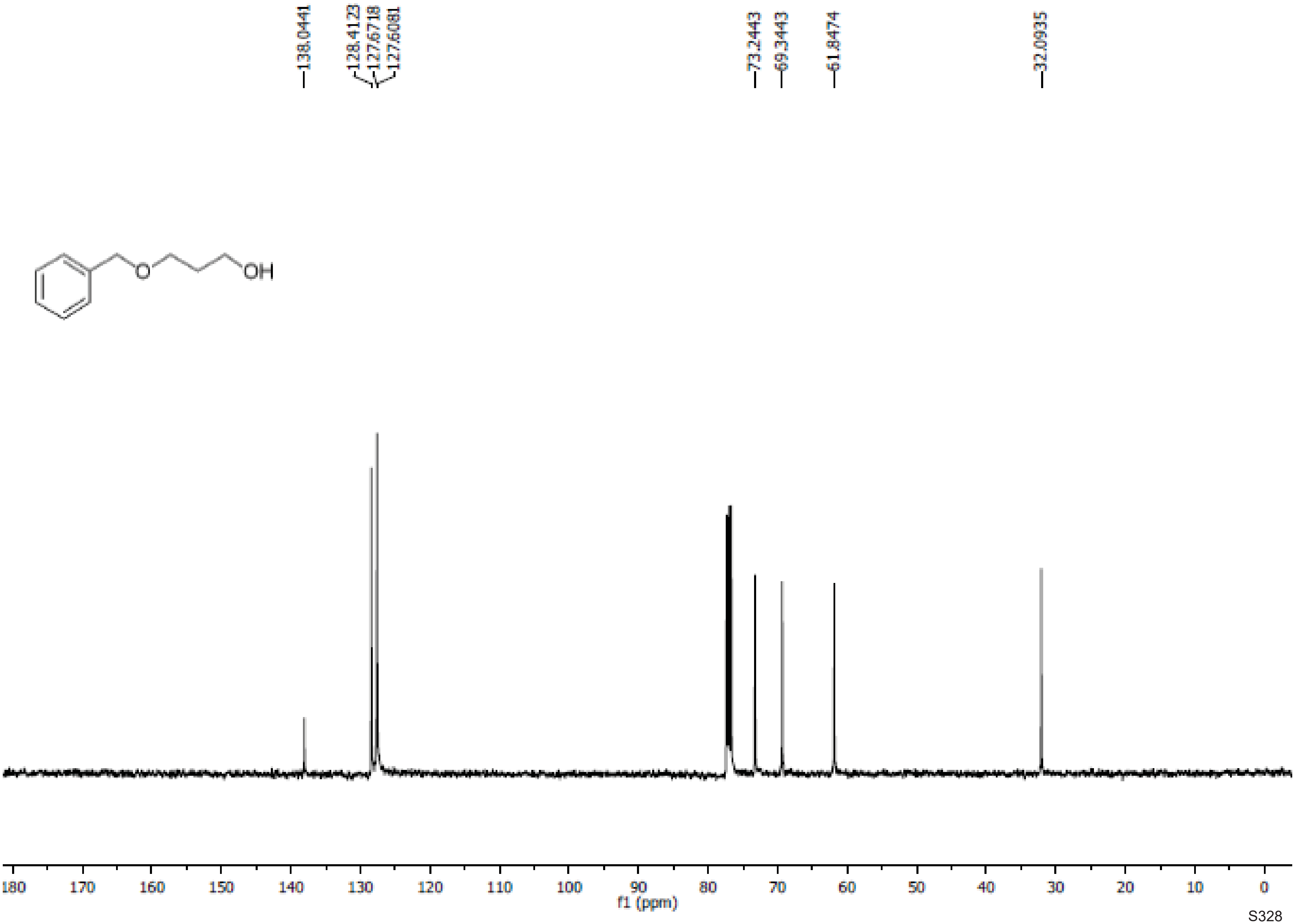
Spectral Data for Chapter 4

Enantioselective Synthesis of 2-Substituted Tetrahydrofurans via Co(II)-Catalyzed Radical C–H Alkylation

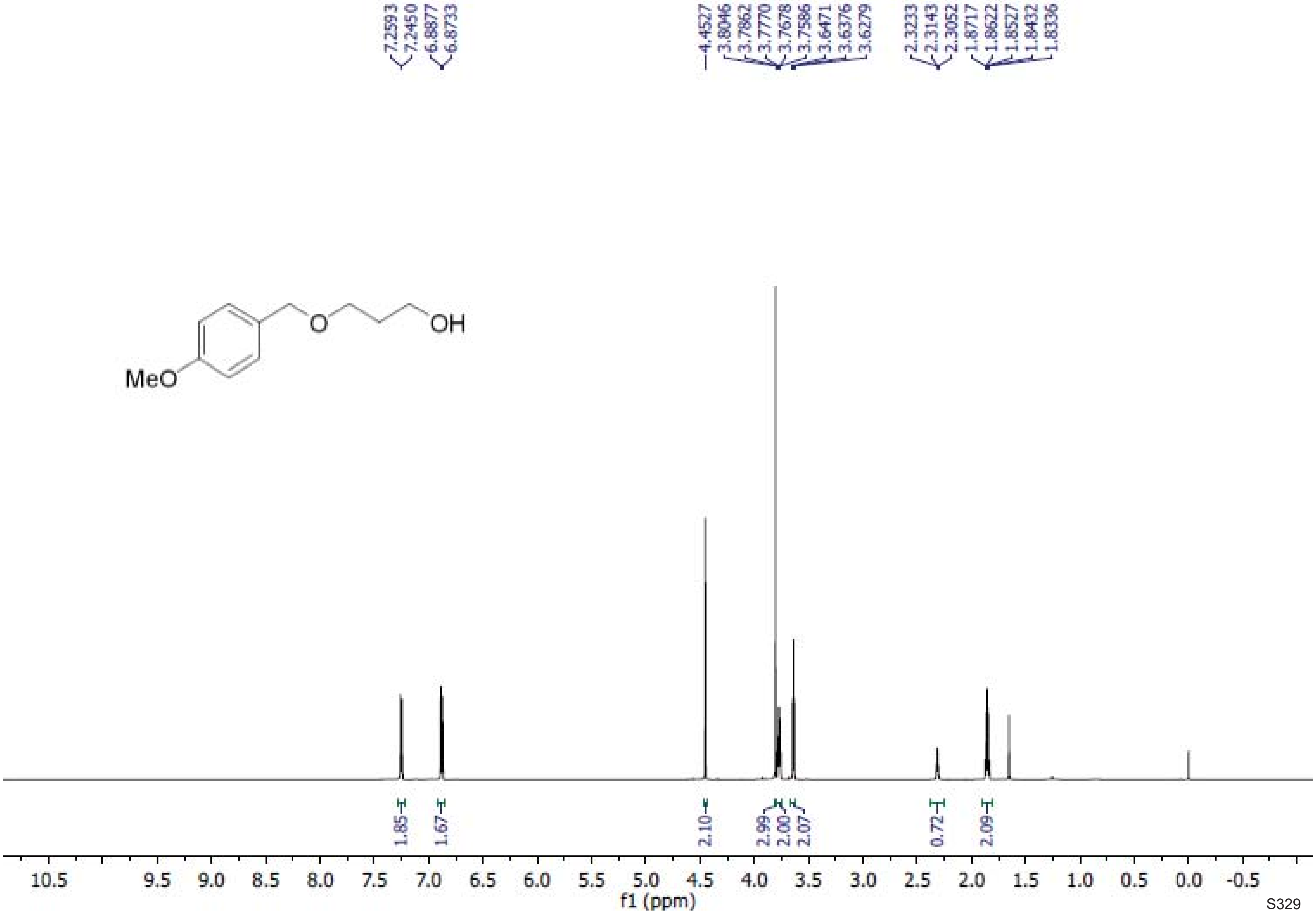
3-(benzyloxy)propan-1-ol



3-(benzyloxy)propan-1-ol



3-((4-methoxybenzyl)oxy)propan-1-ol



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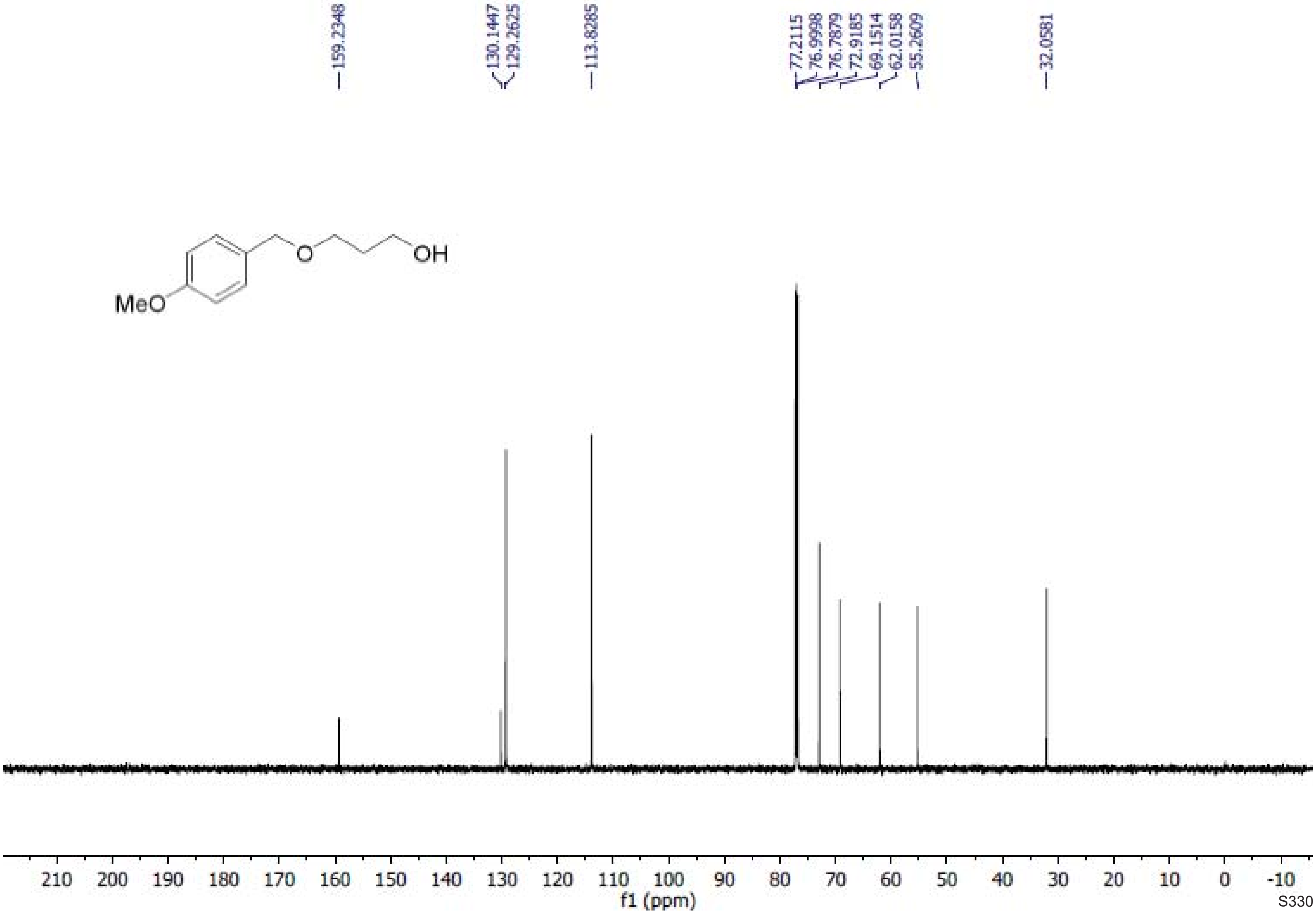
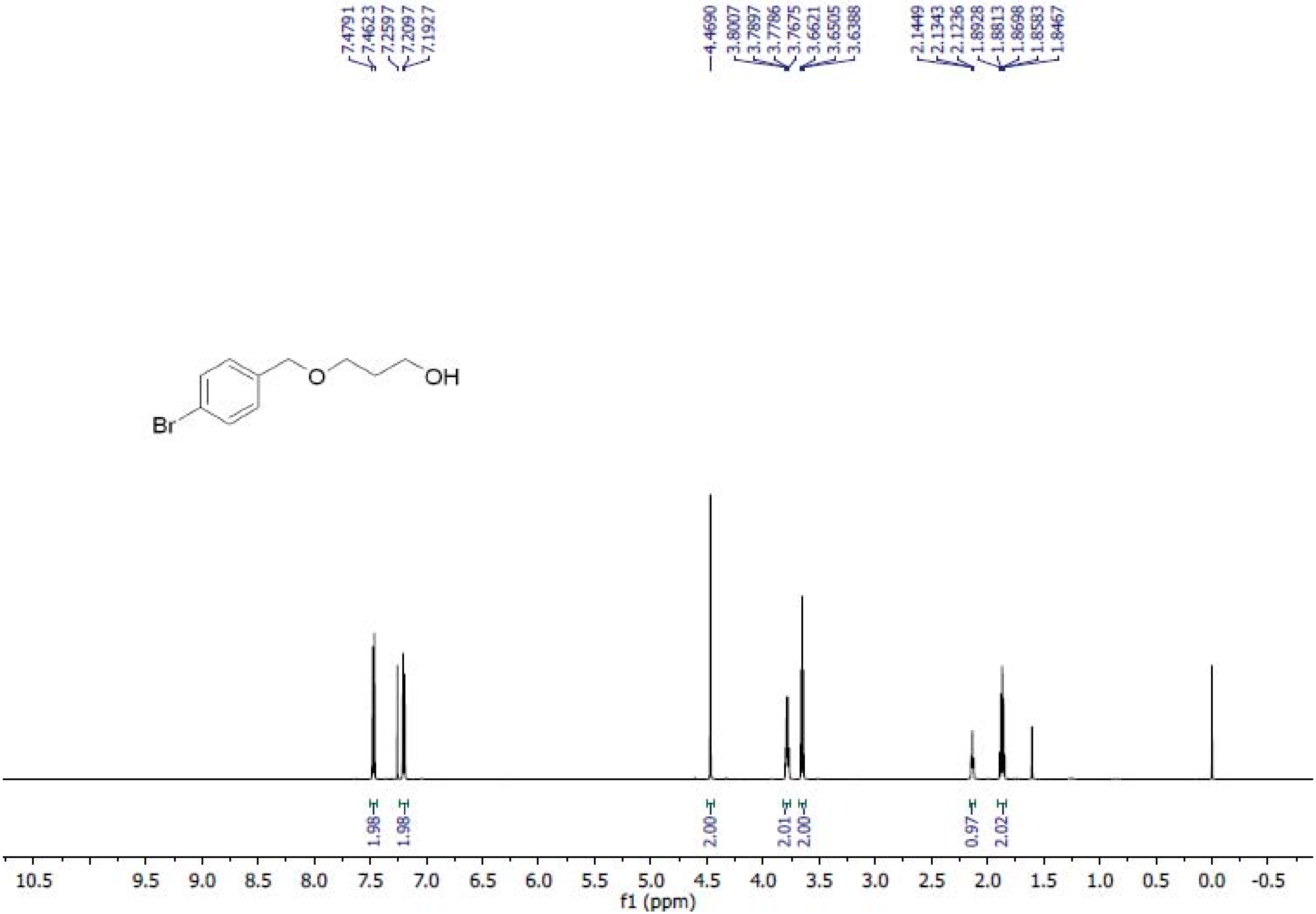


3-((4-bromobenzyl)oxy)propan-1-ol



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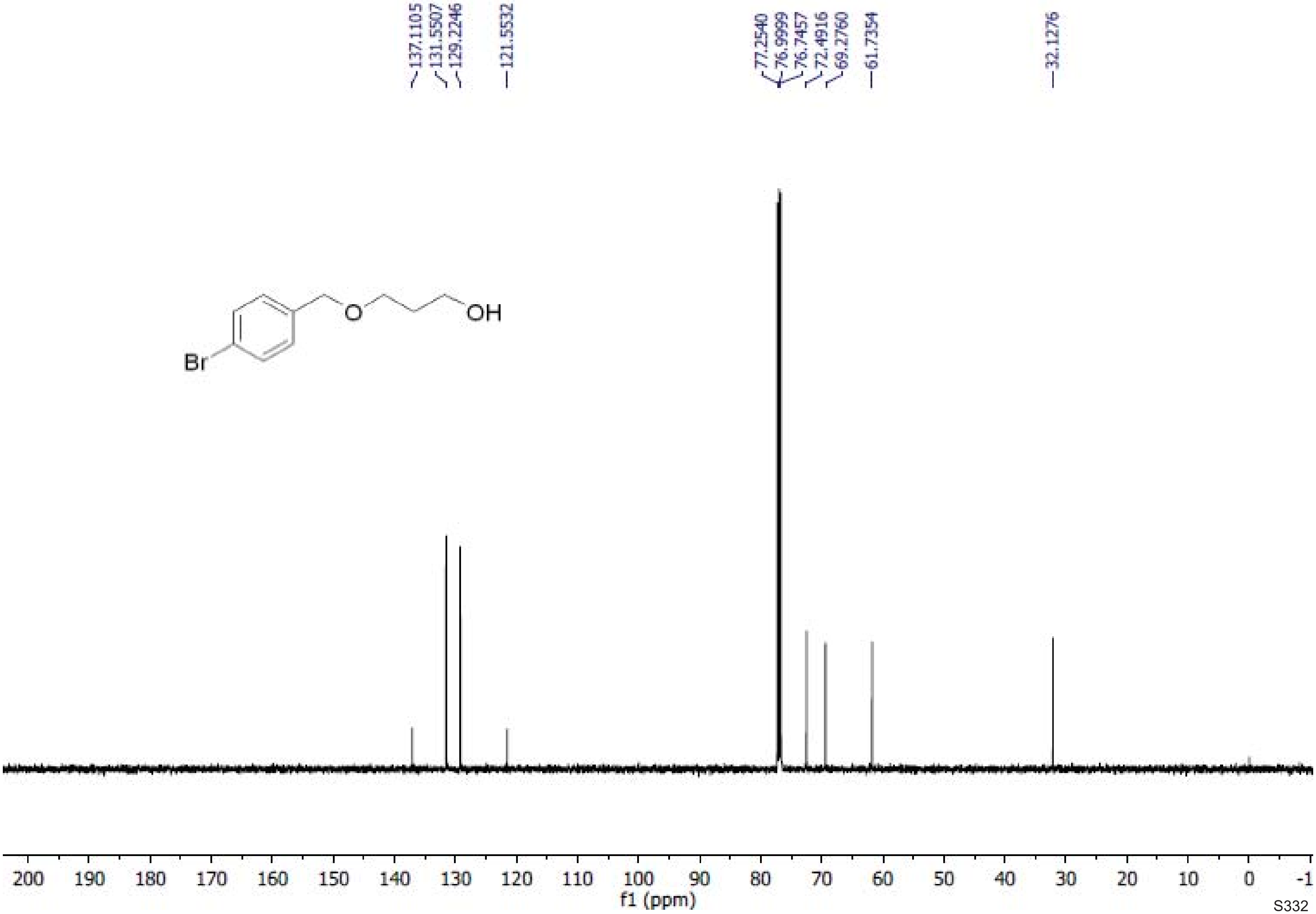
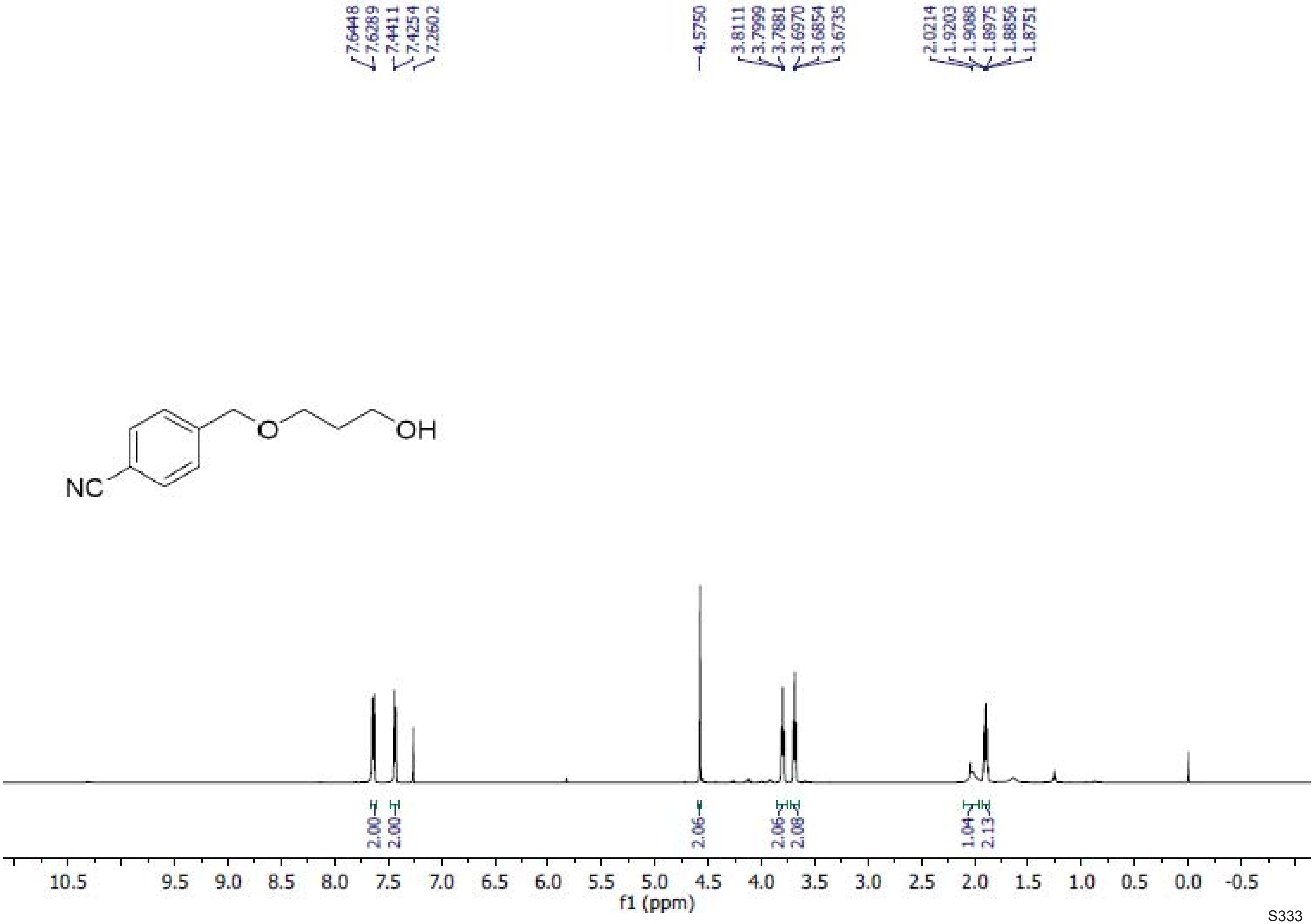
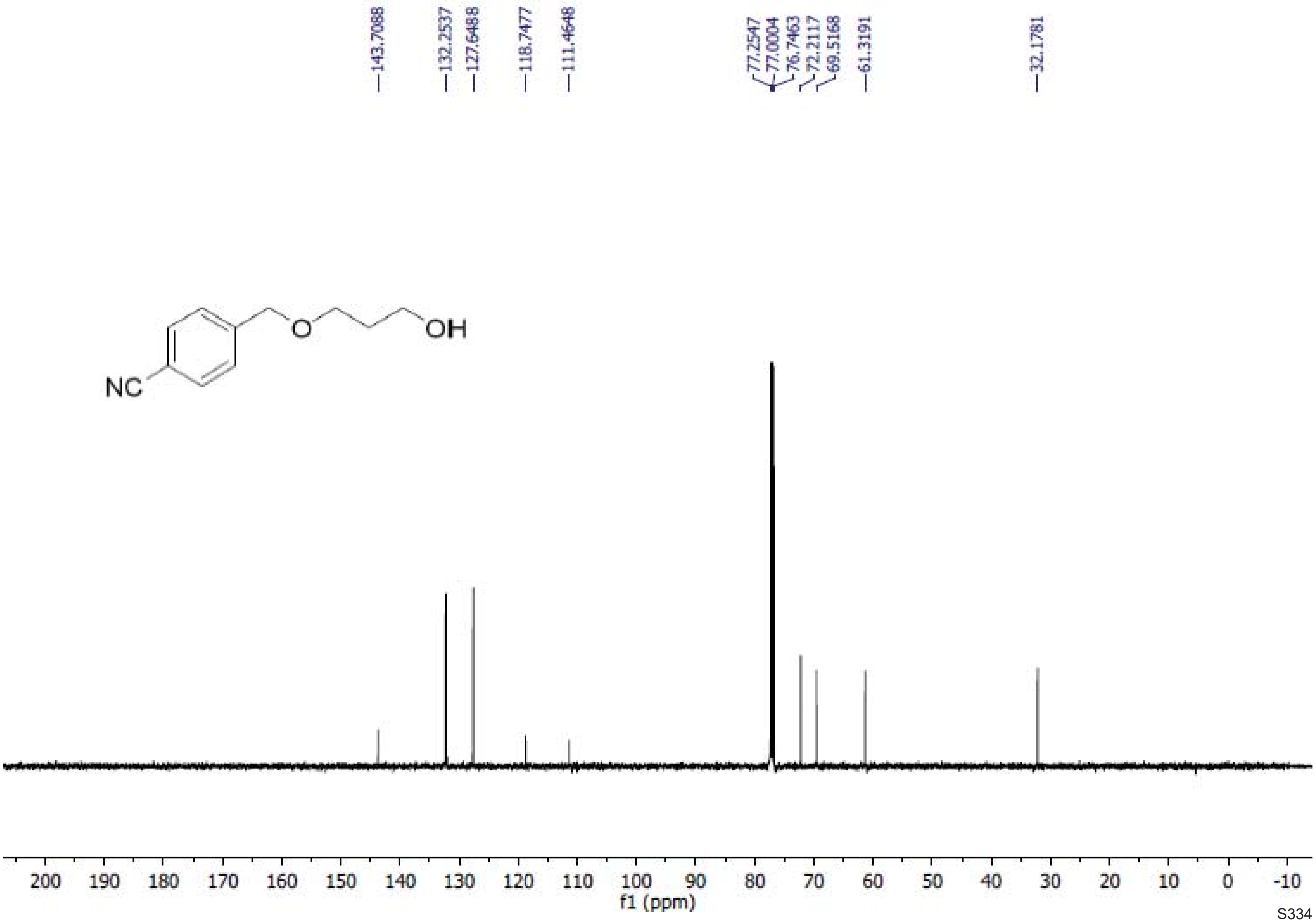


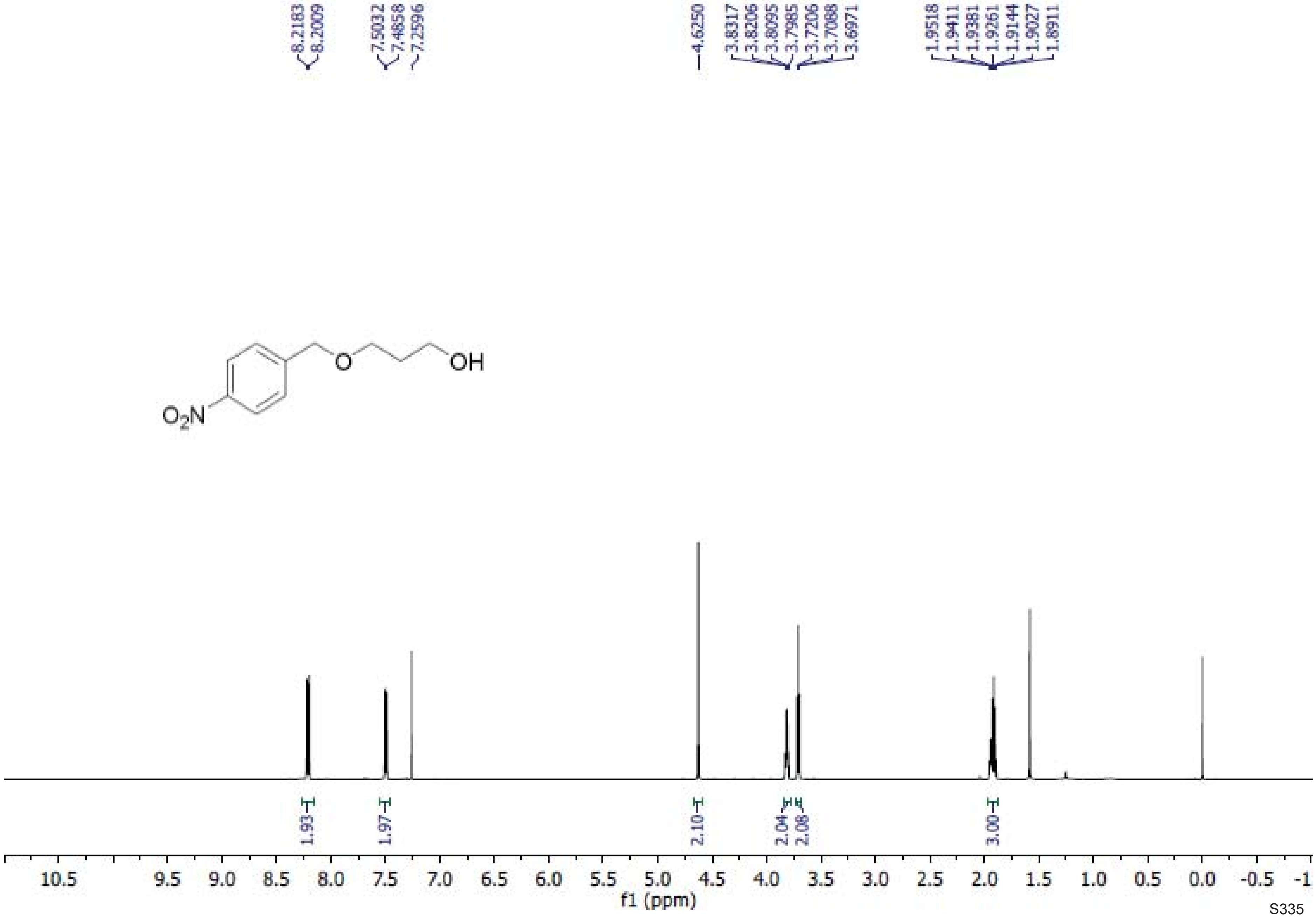
4-((3-hydroxypropoxy)methyl)benzonitrile



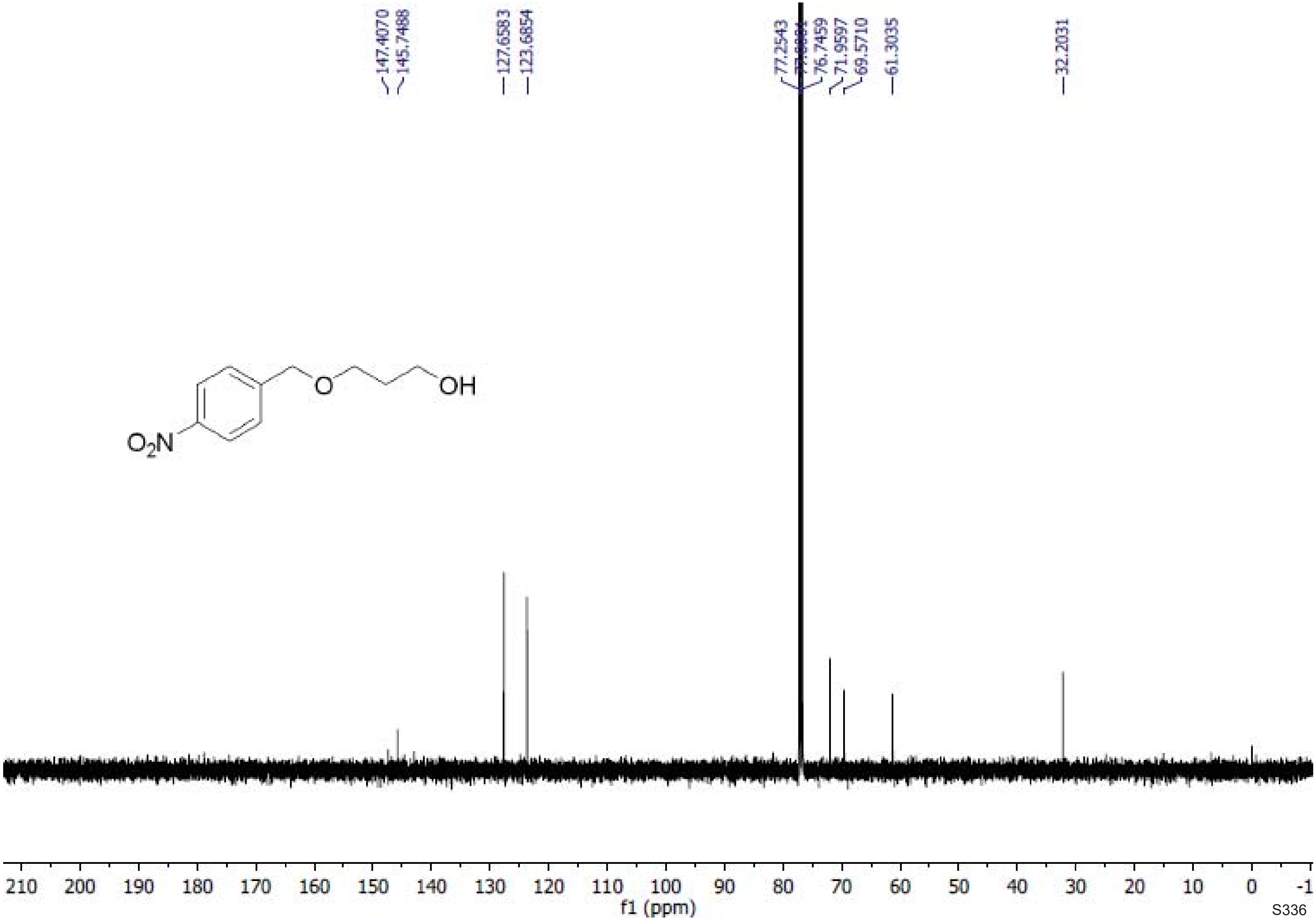
4-((3-hydroxypropoxy)methyl)benzonitrile



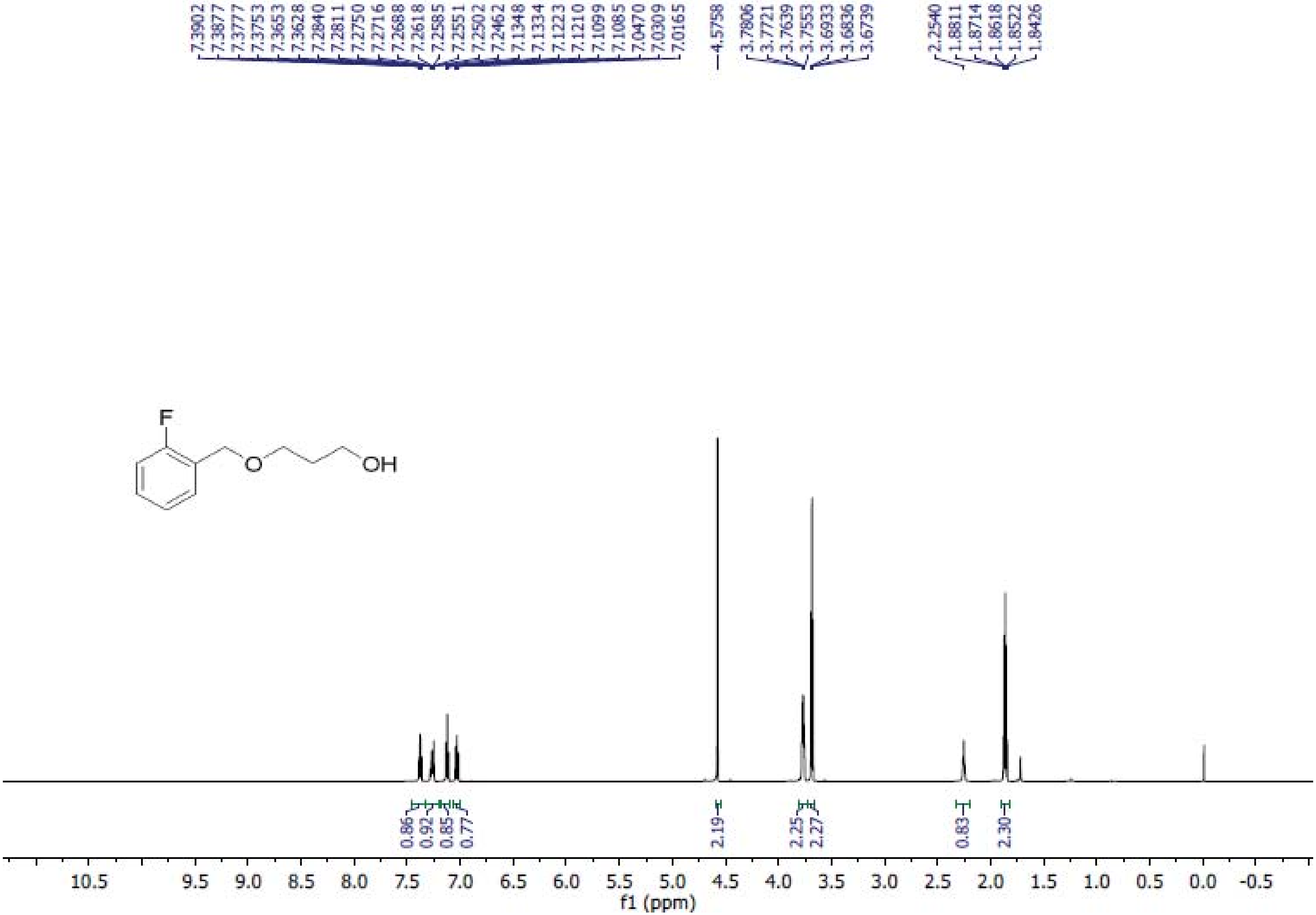
3-((4-nitrobenzyl)oxy)propan-1-ol



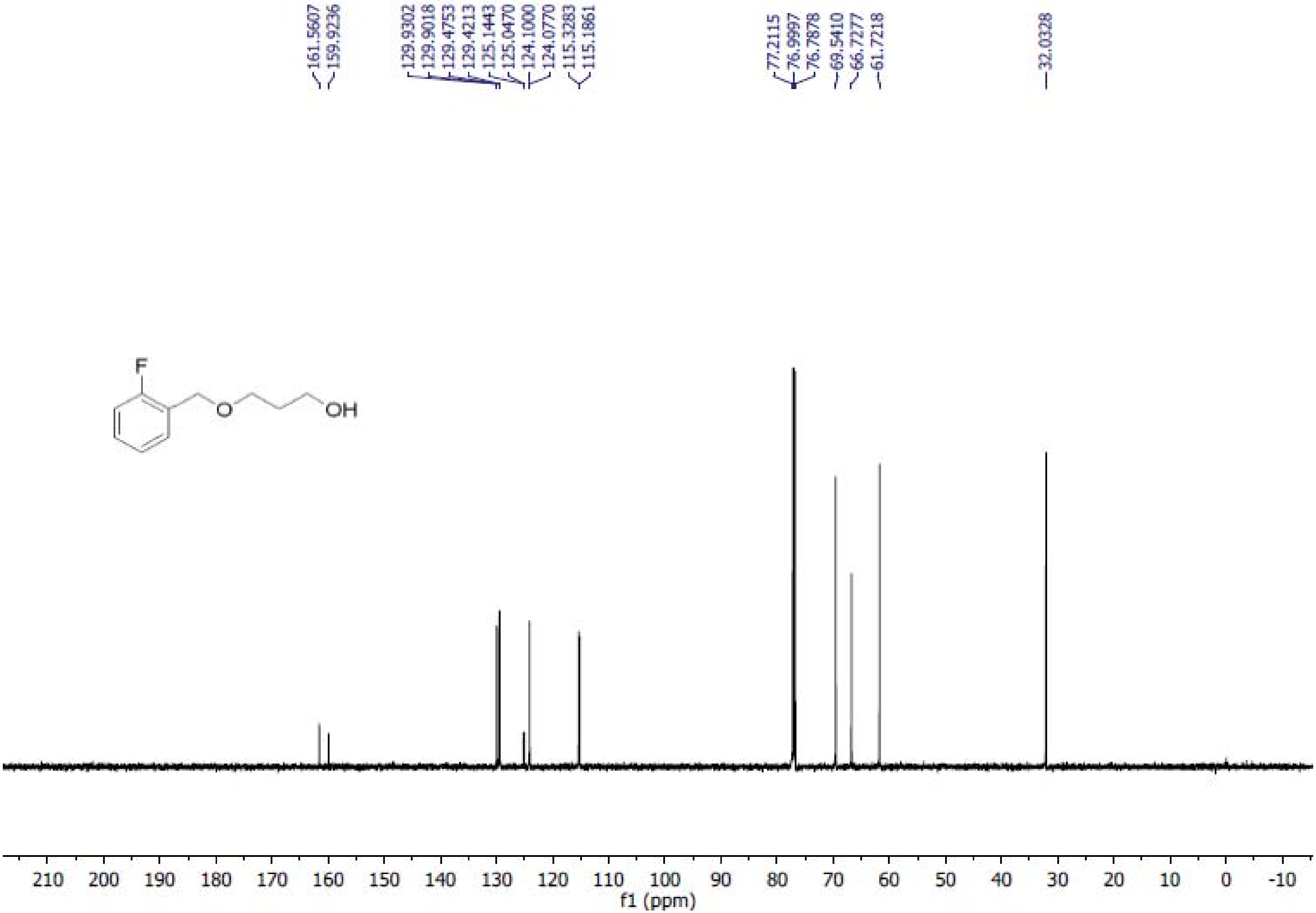
3-((4-nitrobenzyl)oxy)propan-1-ol



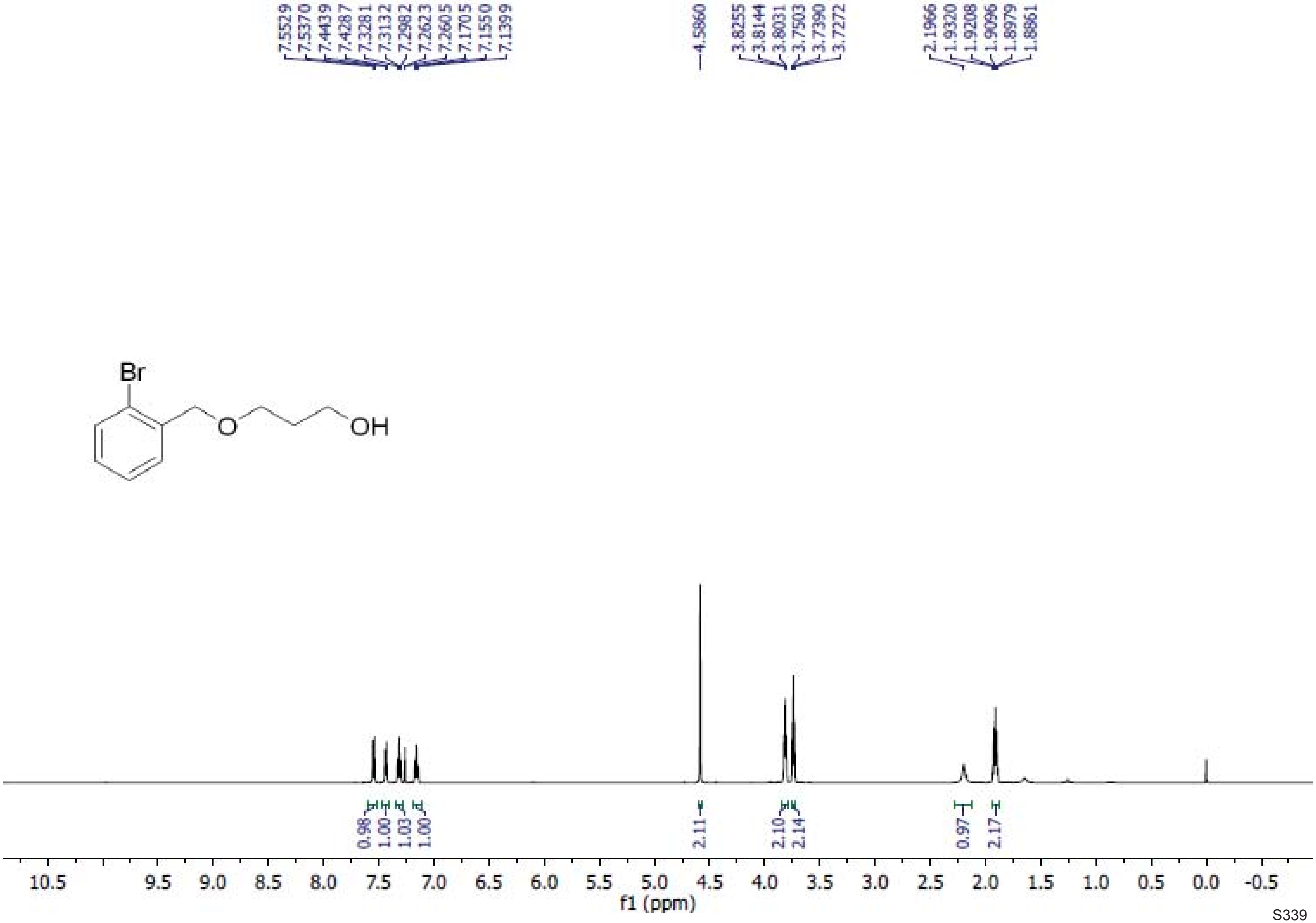
3-((2-fluorobenzyl)oxy)propan-1-ol



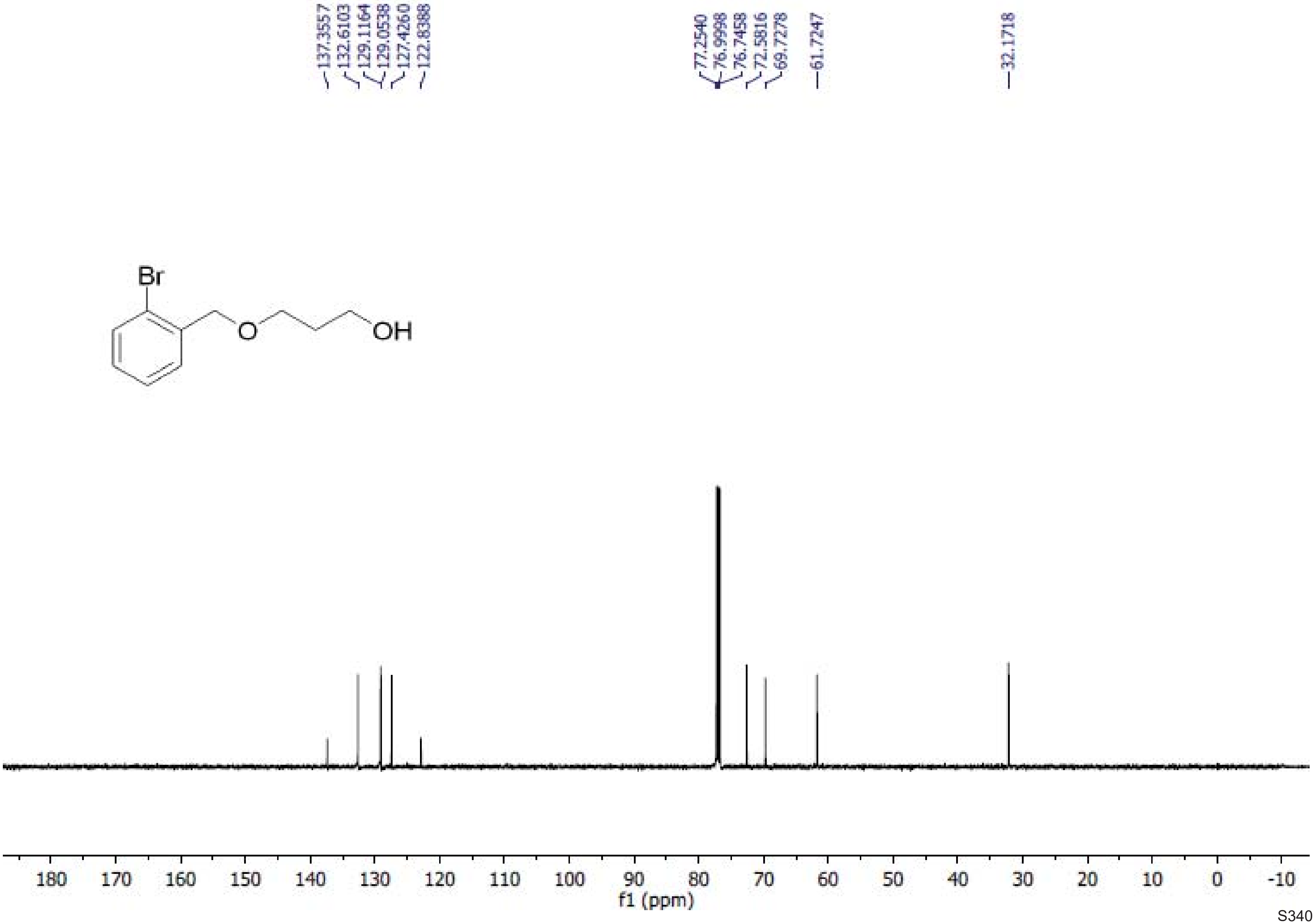
3-((2-fluorobenzyl)oxy)propan-1-ol



3-((2-bromobenzyl)oxy)propan-1-ol



3-((2-bromobenzyl)oxy)propan-1-ol



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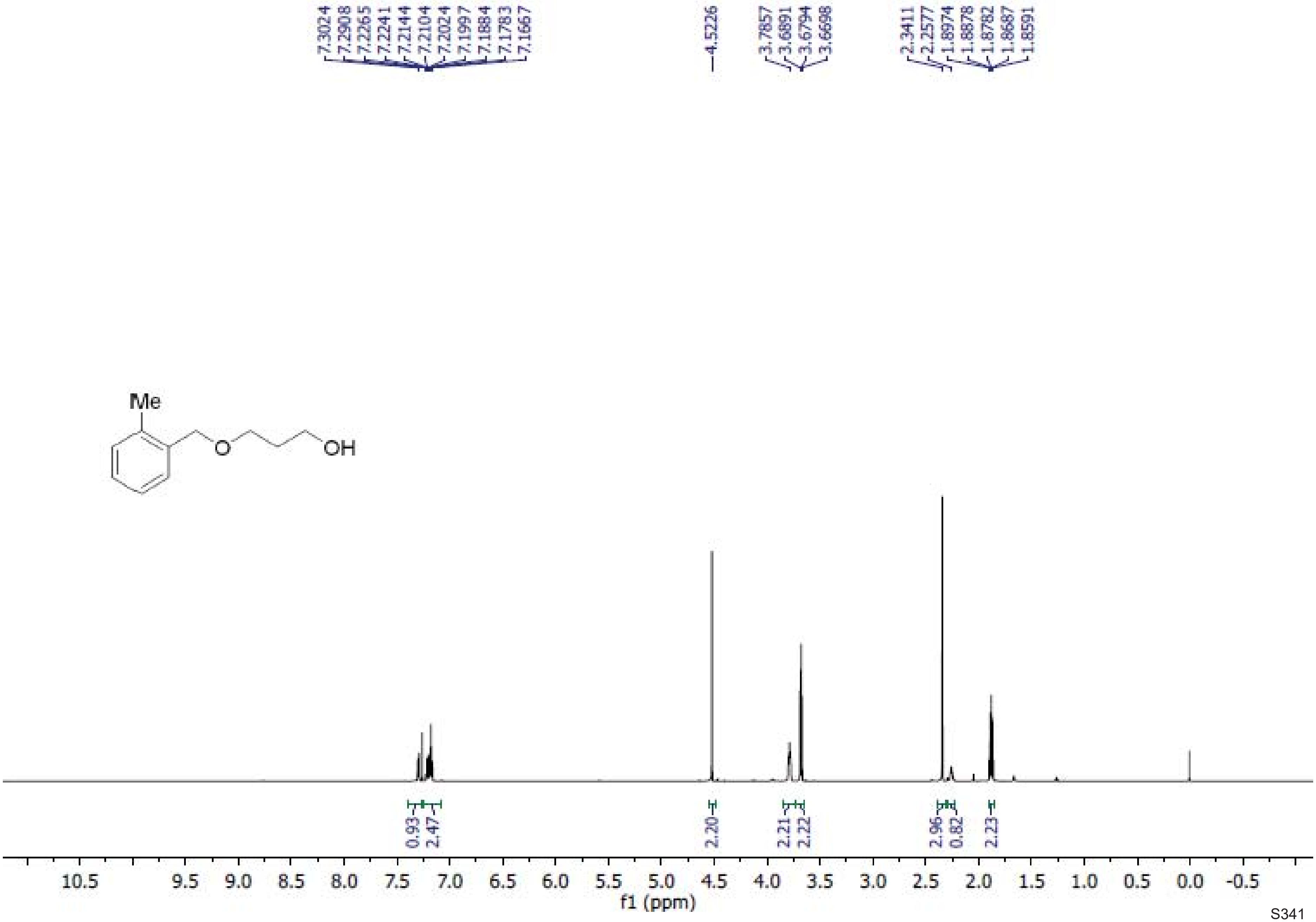
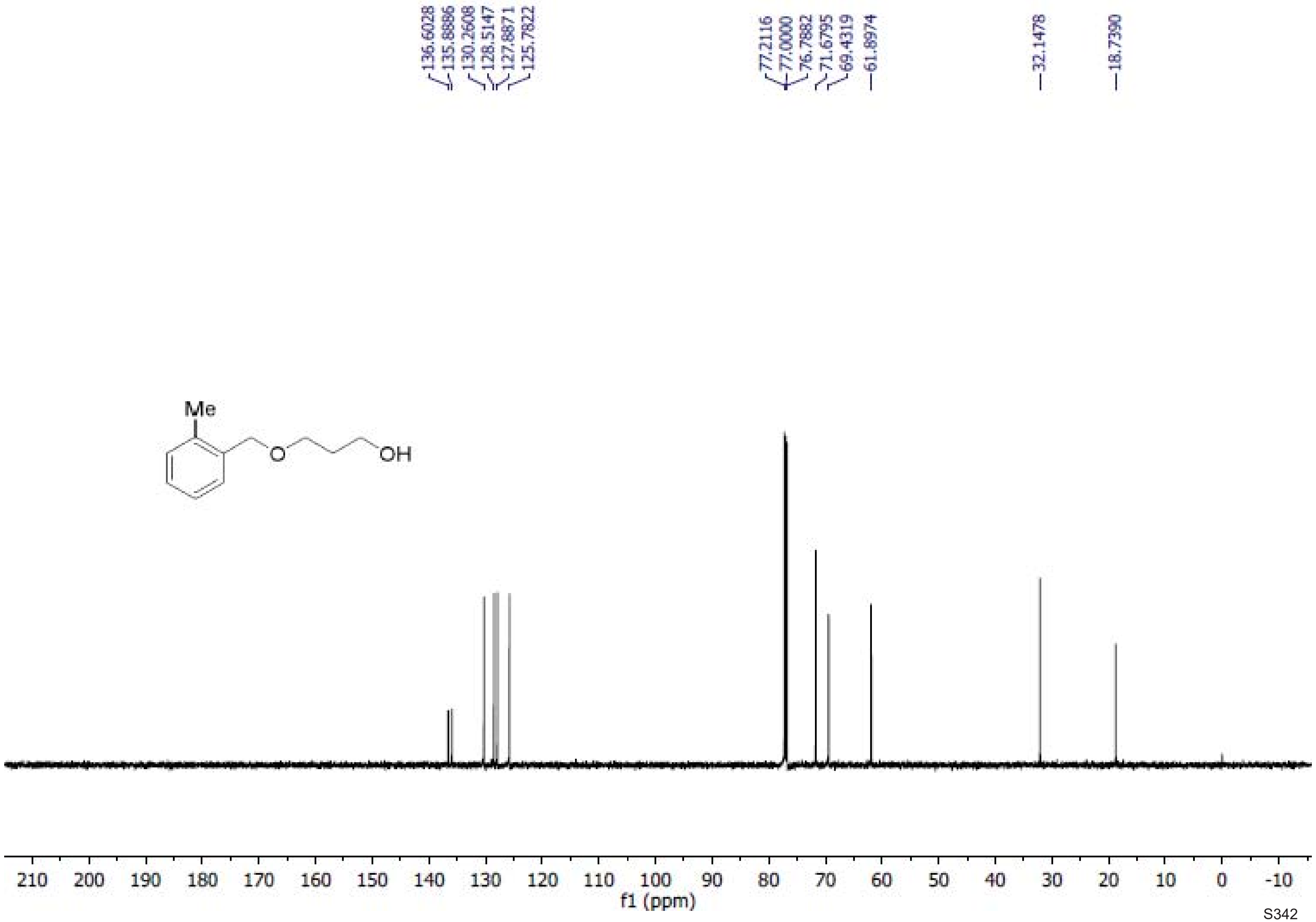
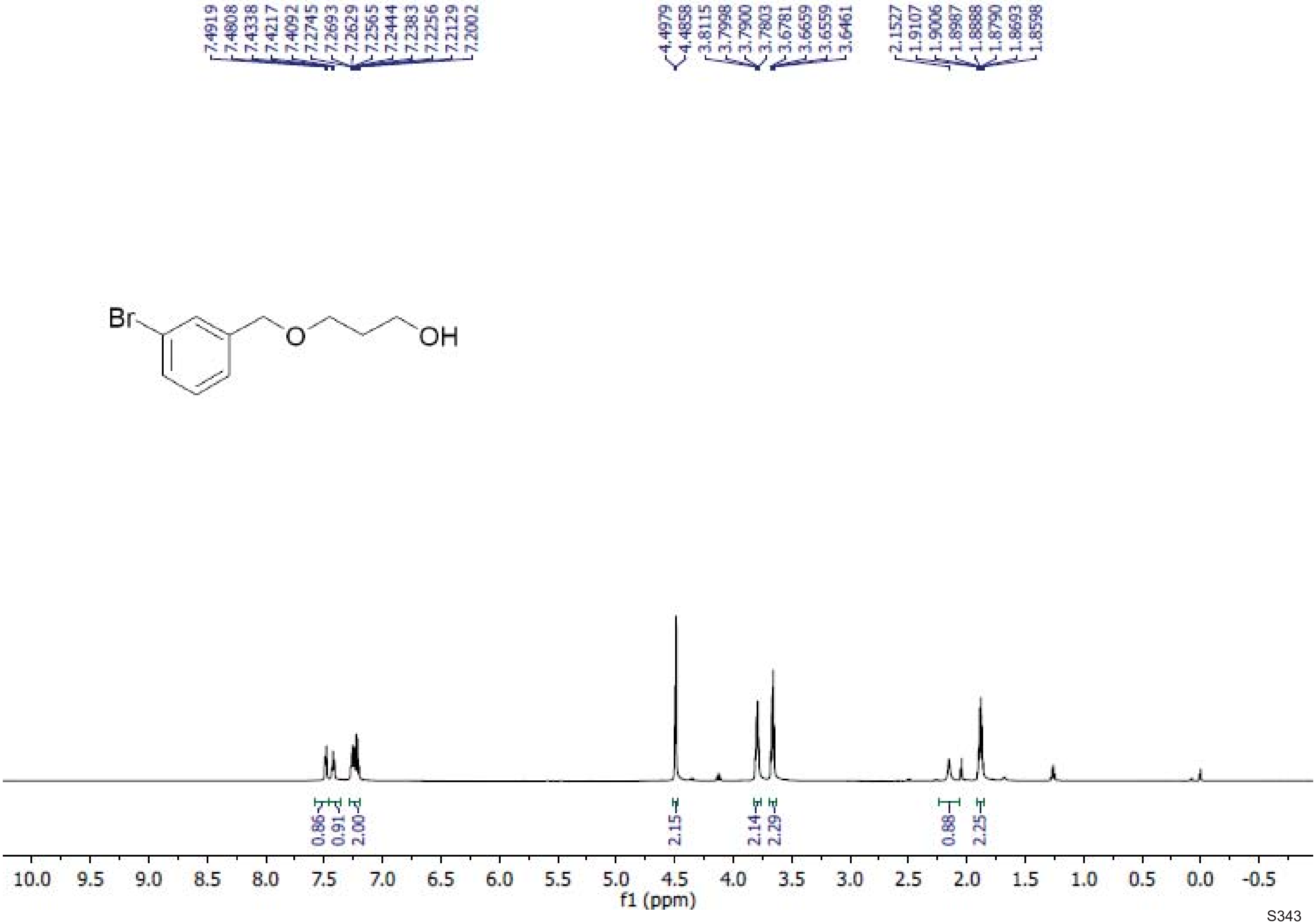


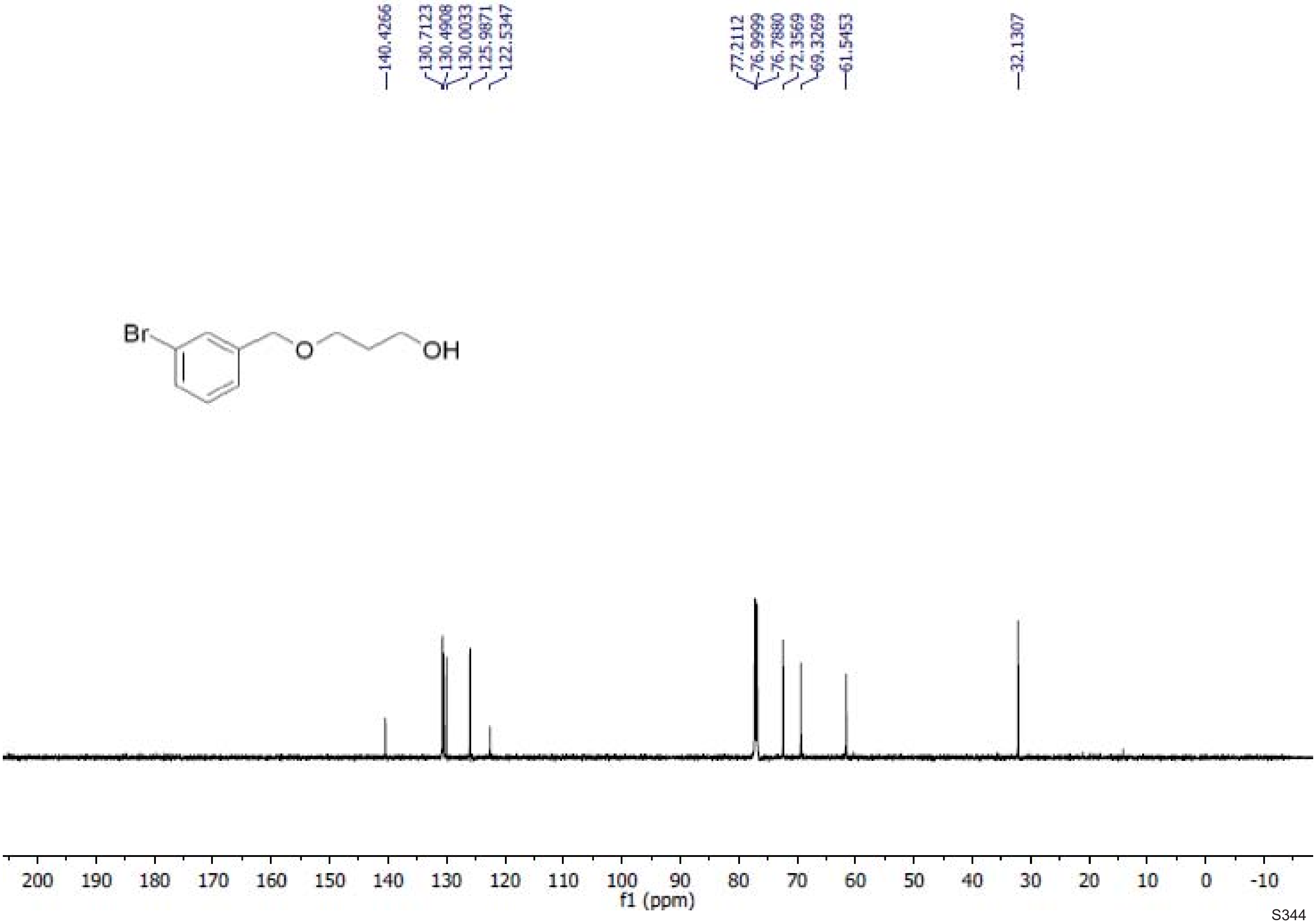
3-((2-methylbenzyl)oxy)propan-1-ol



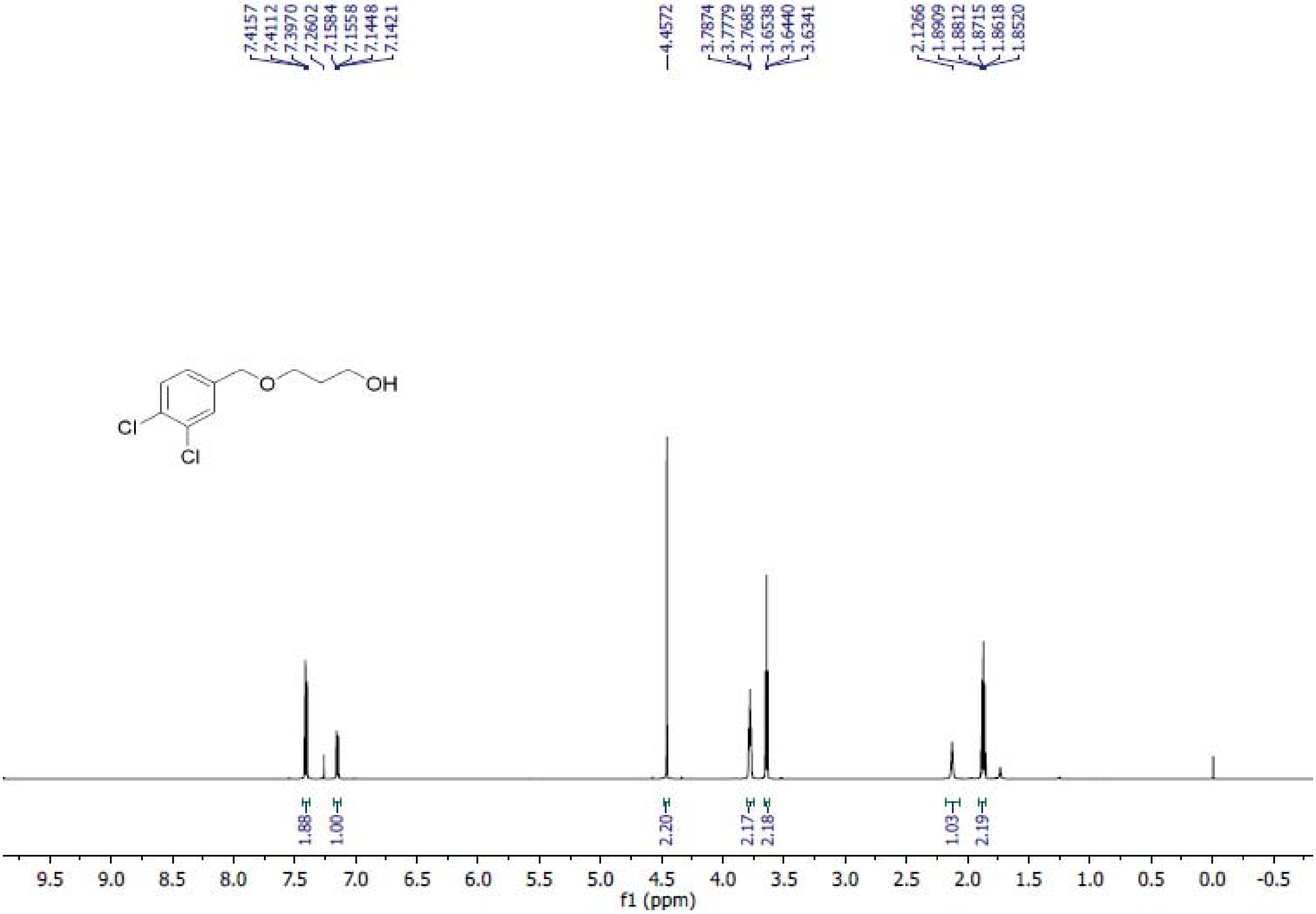
3-((3-bromobenzyl)oxy)propan-1-ol



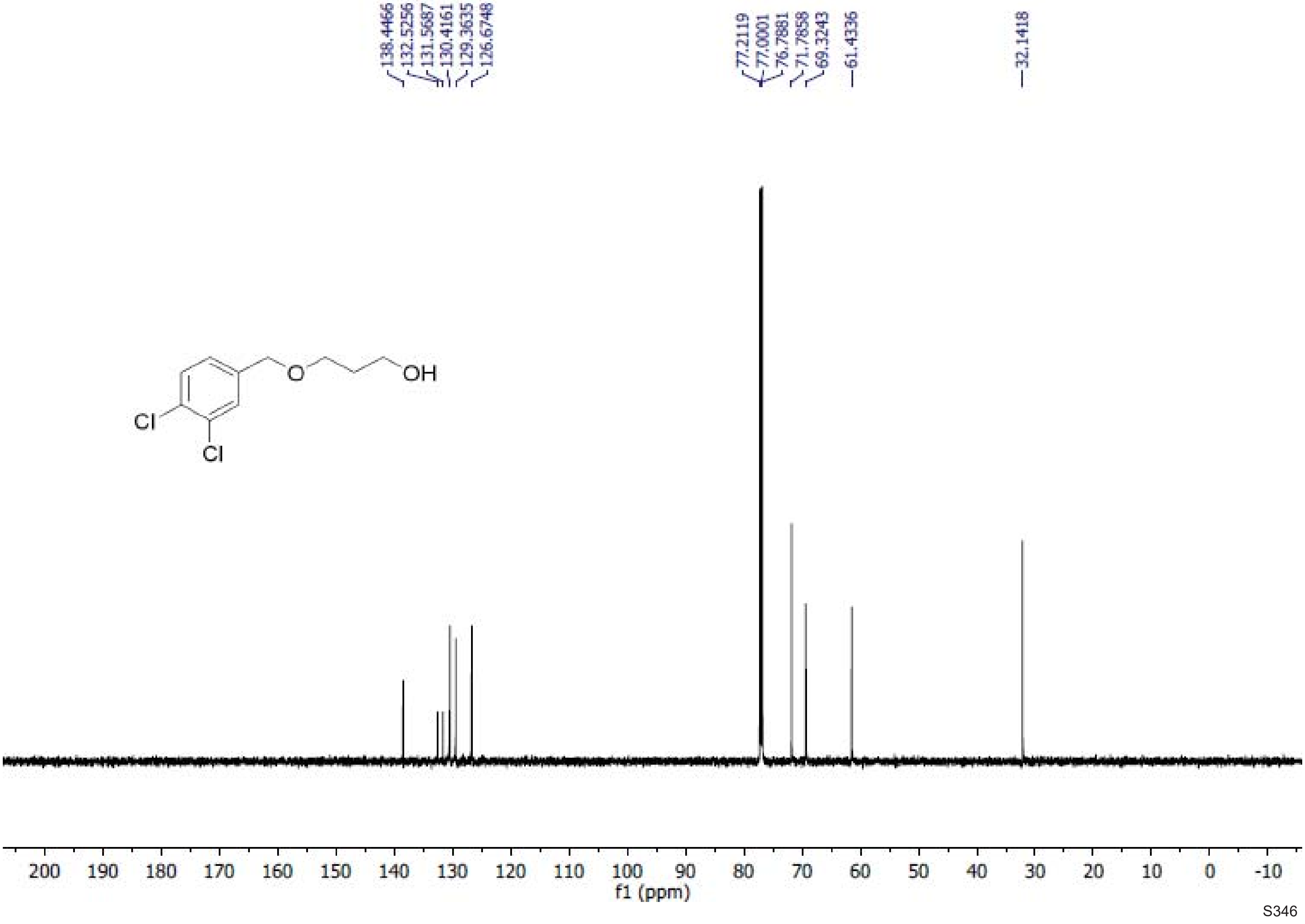
3-((3-bromobenzyl)oxy)propan-1-ol



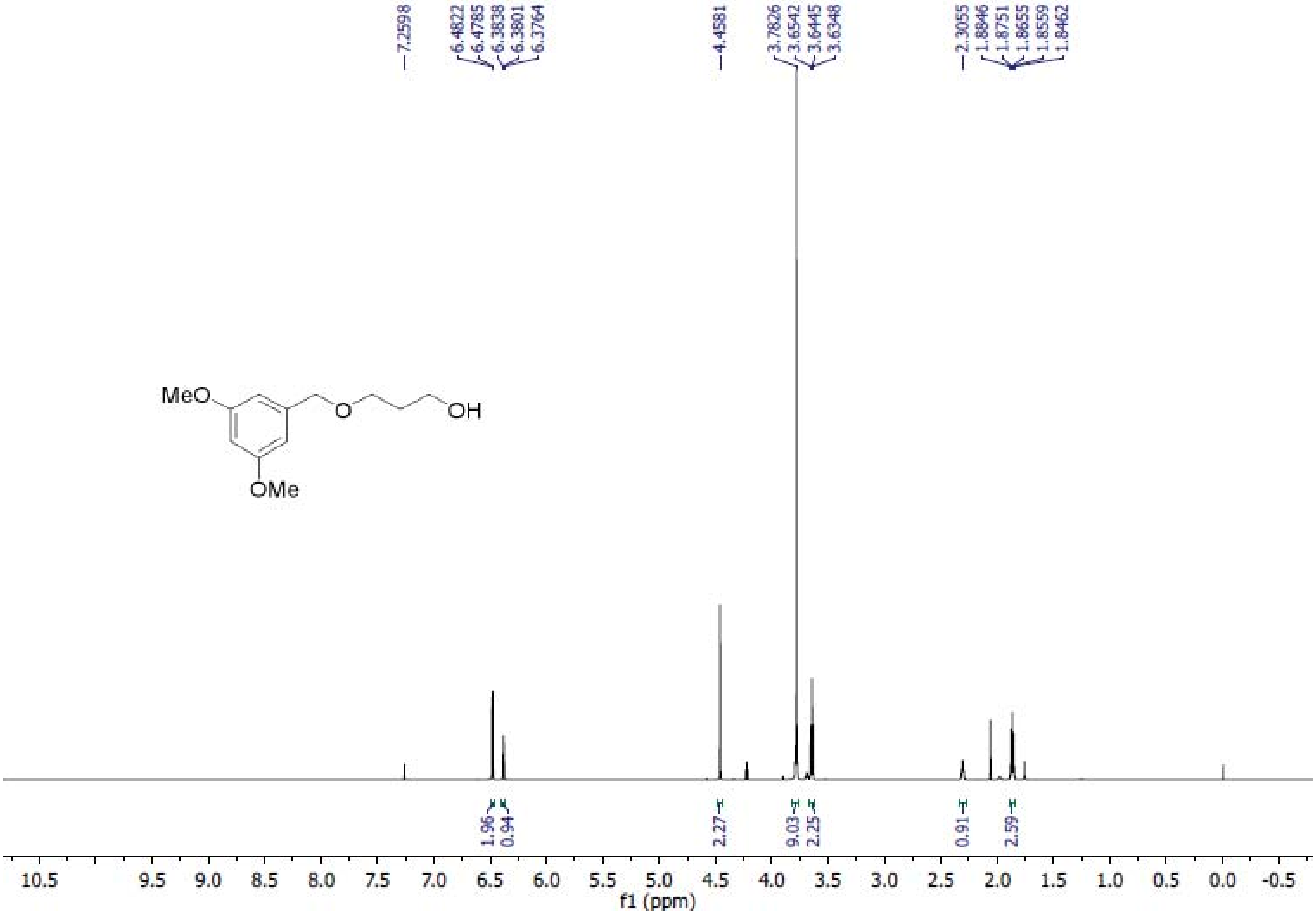
3-((3,4-dichlorobenzyl)oxy)propan-1-ol



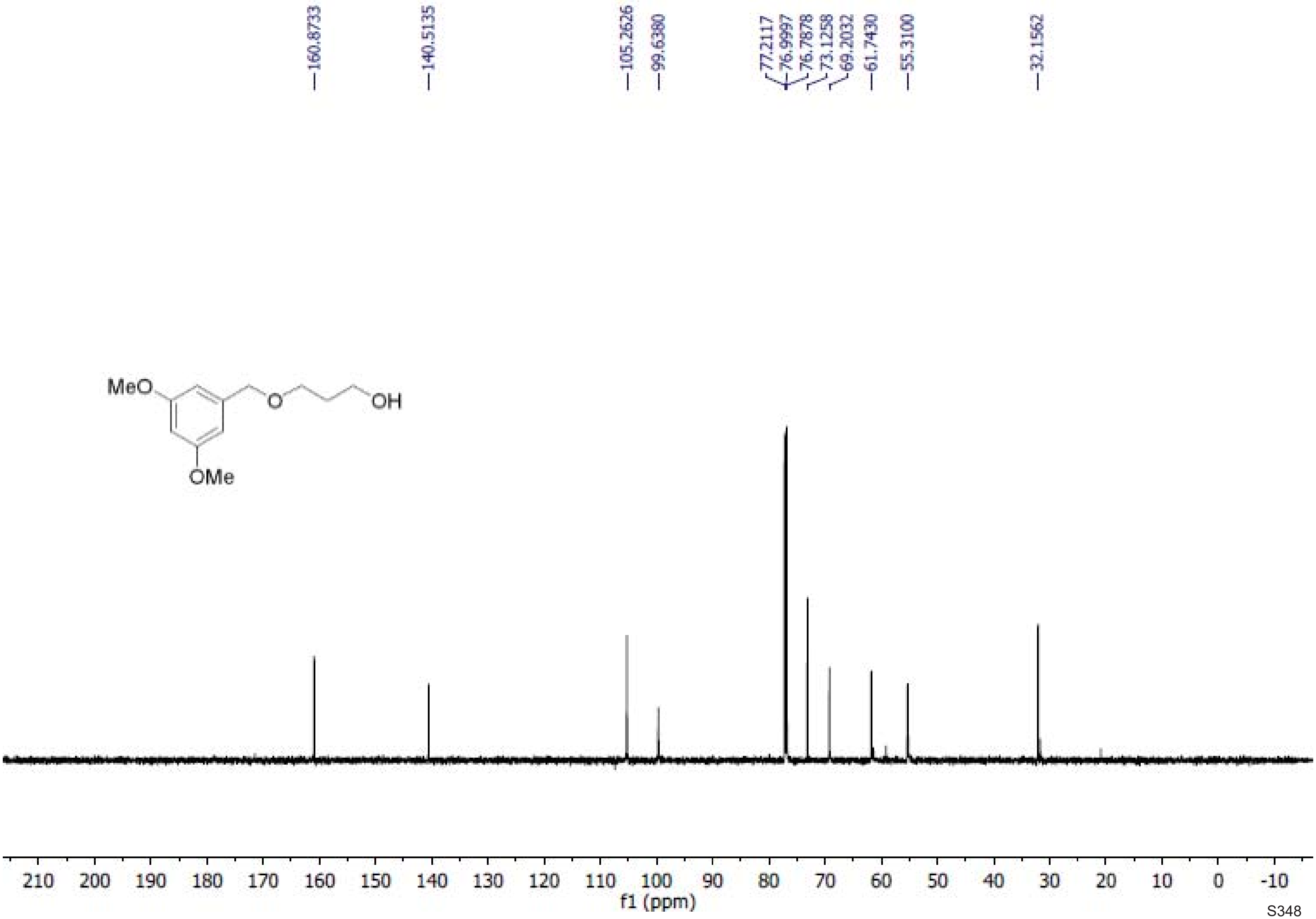
3-((3,4-dichlorobenzyl)oxy)propan-1-ol



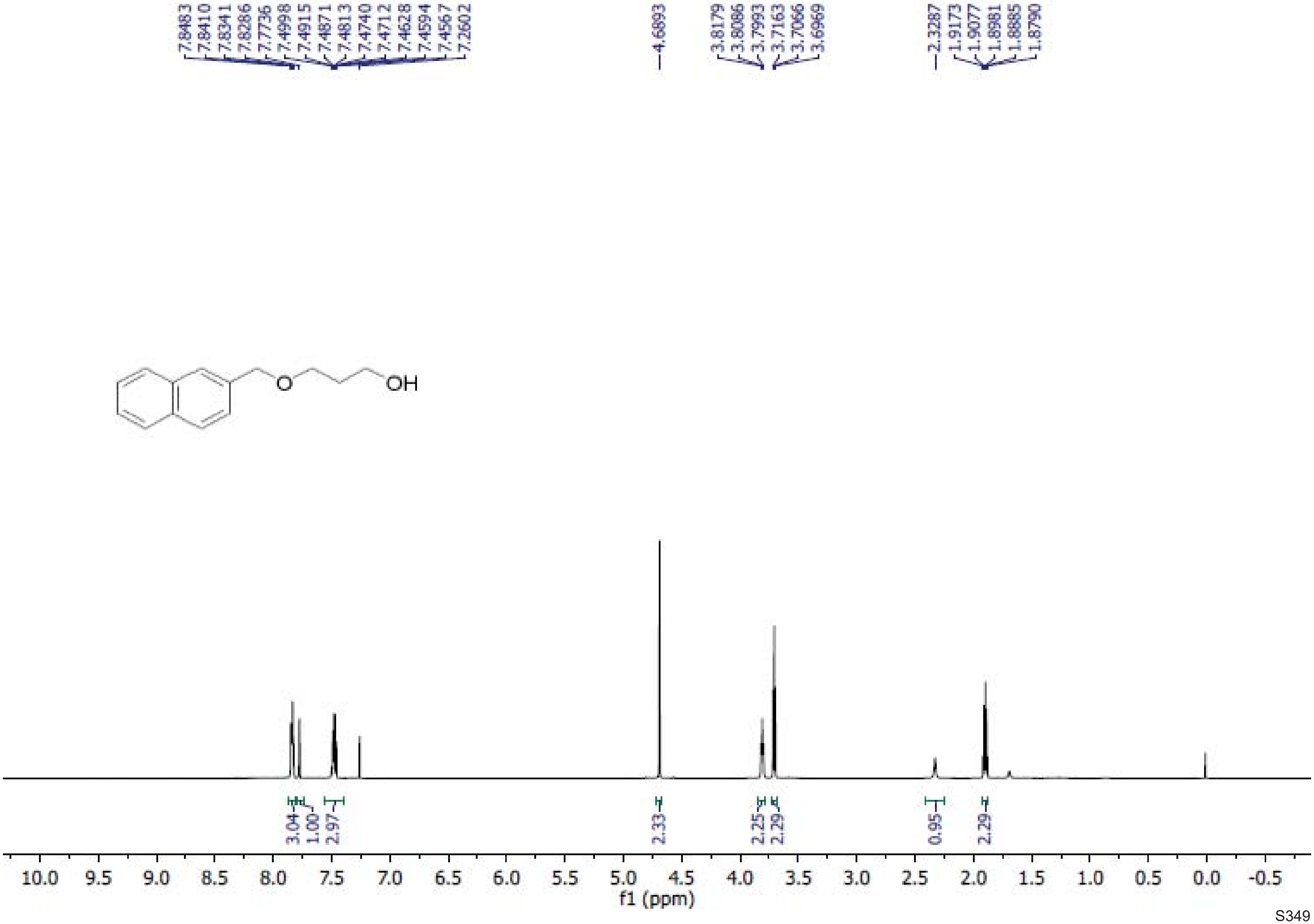
3-((3,5-dimethoxybenzyl)oxy)propan-1-ol



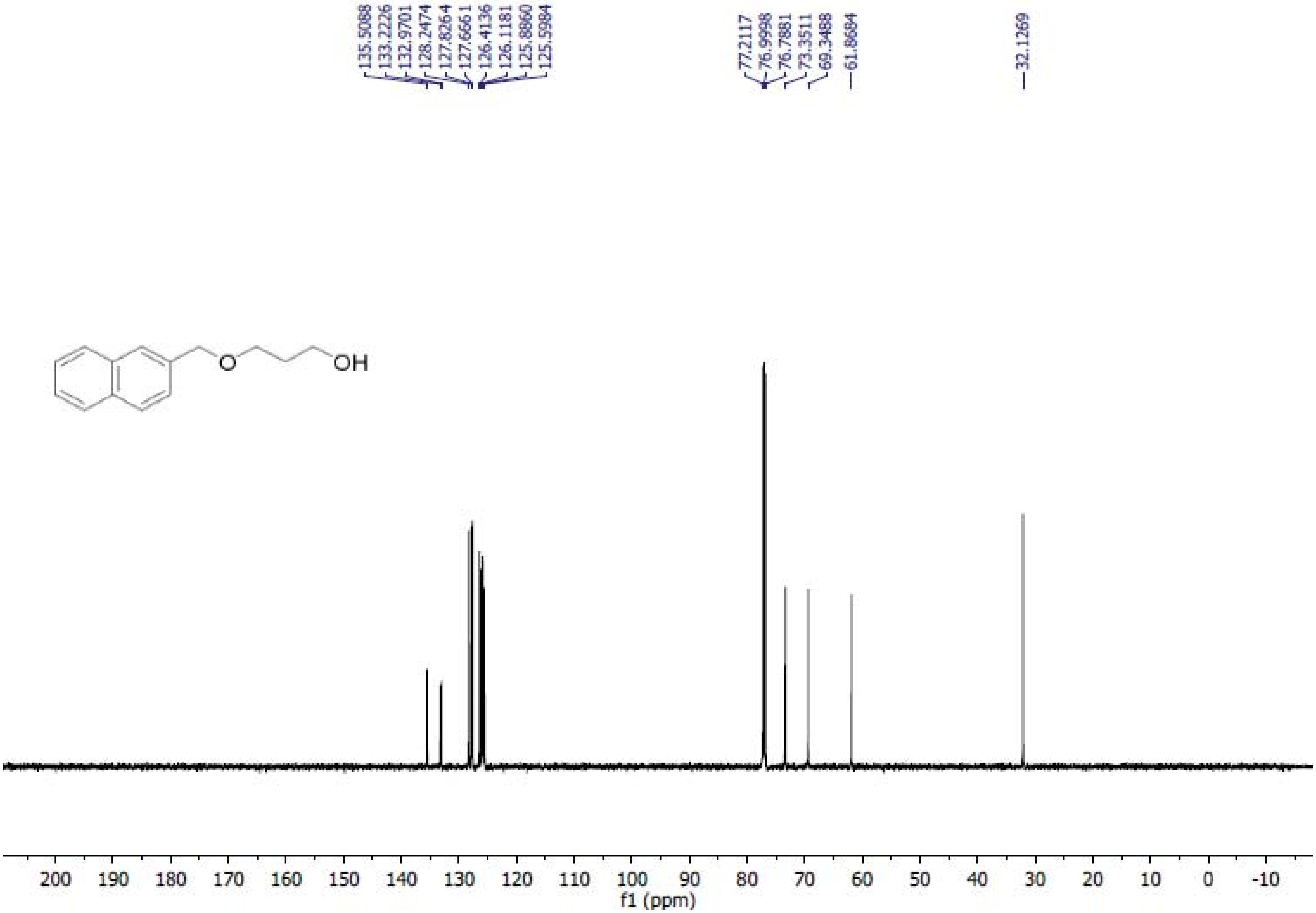
3-((3,5-dimethoxybenzyl)oxy)propan-1-ol



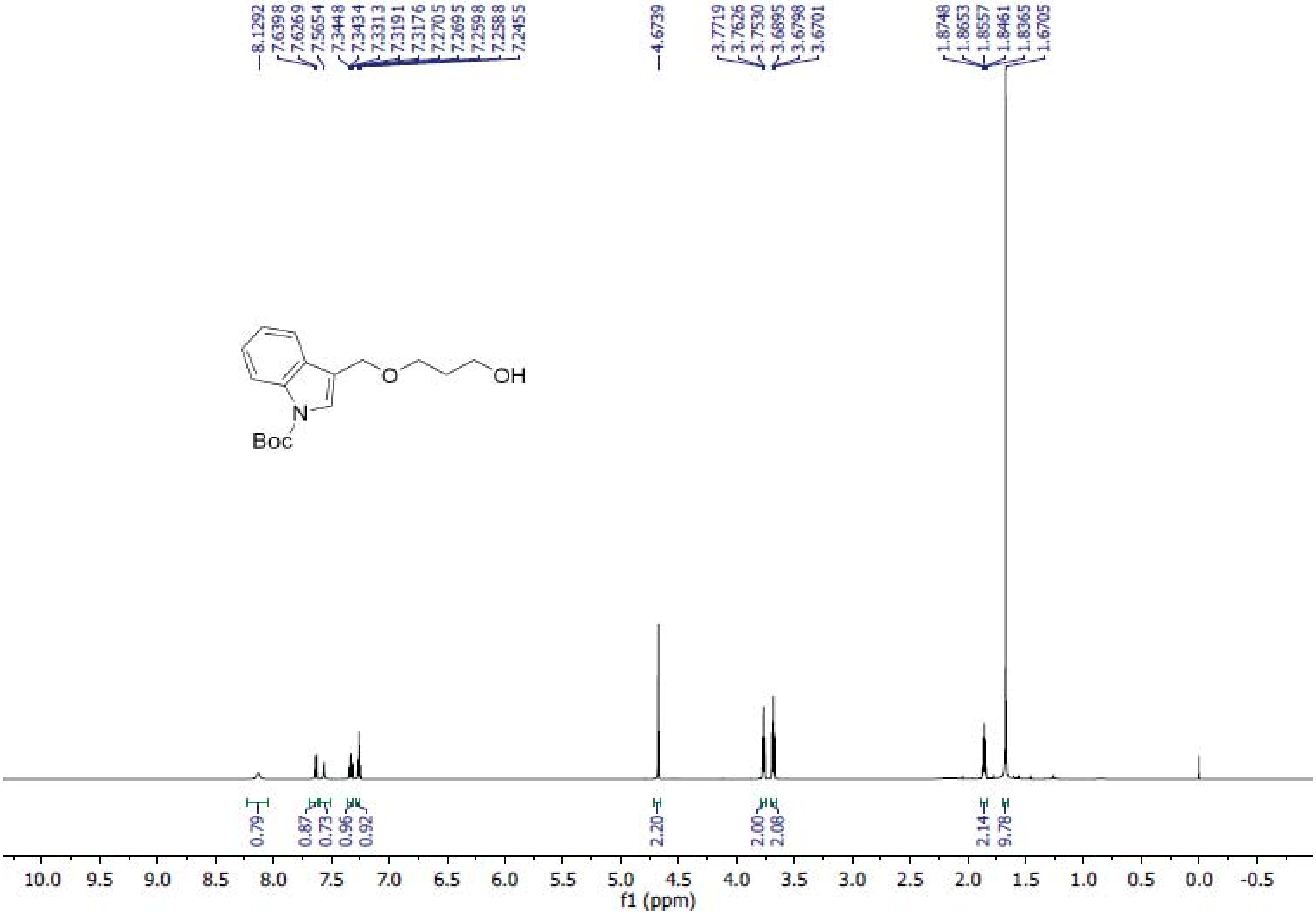
3-(naphthalen-2-ylmethoxy)propan-1-ol



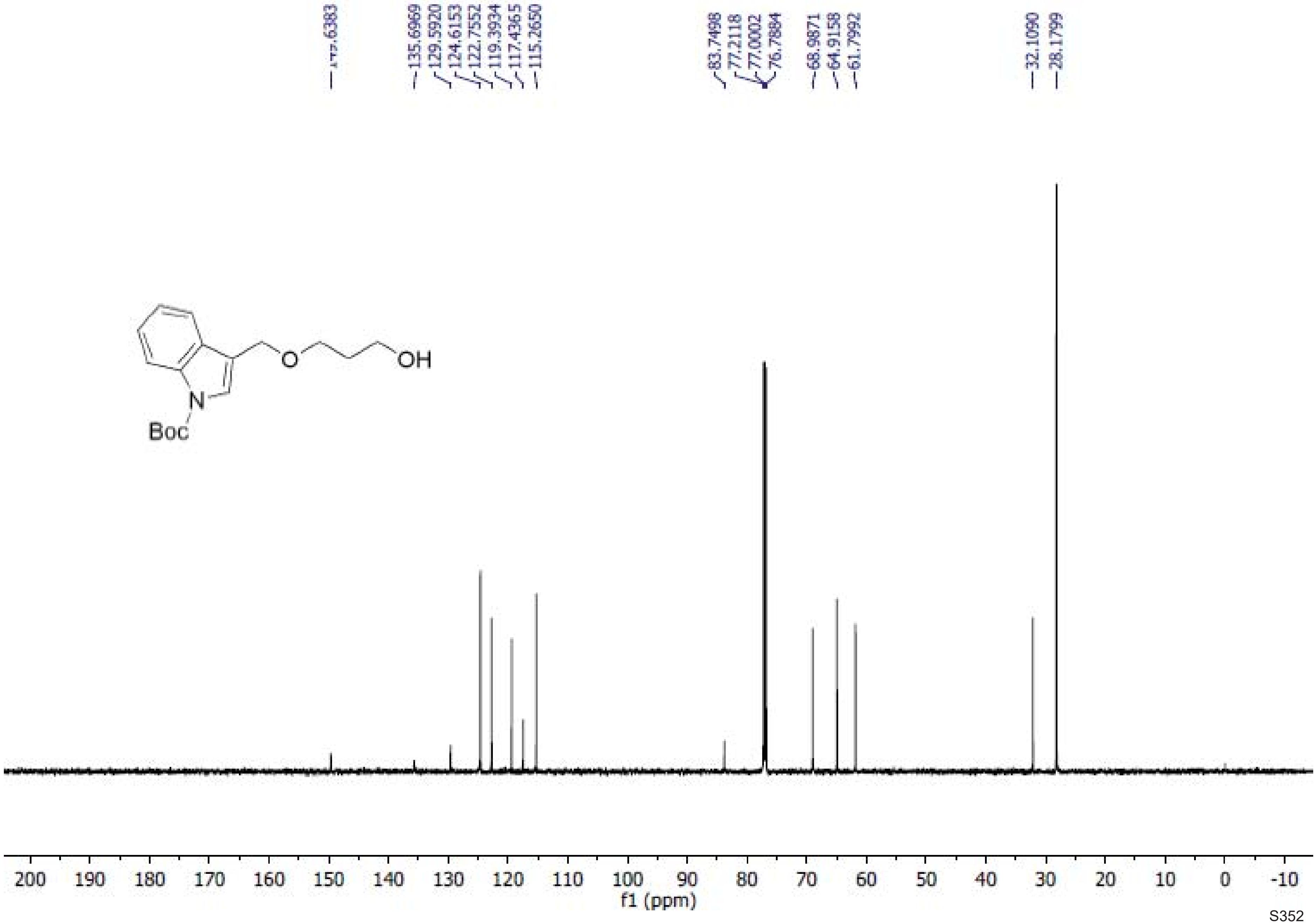
3-(naphthalen-2-ylmethoxy)propan-1-ol



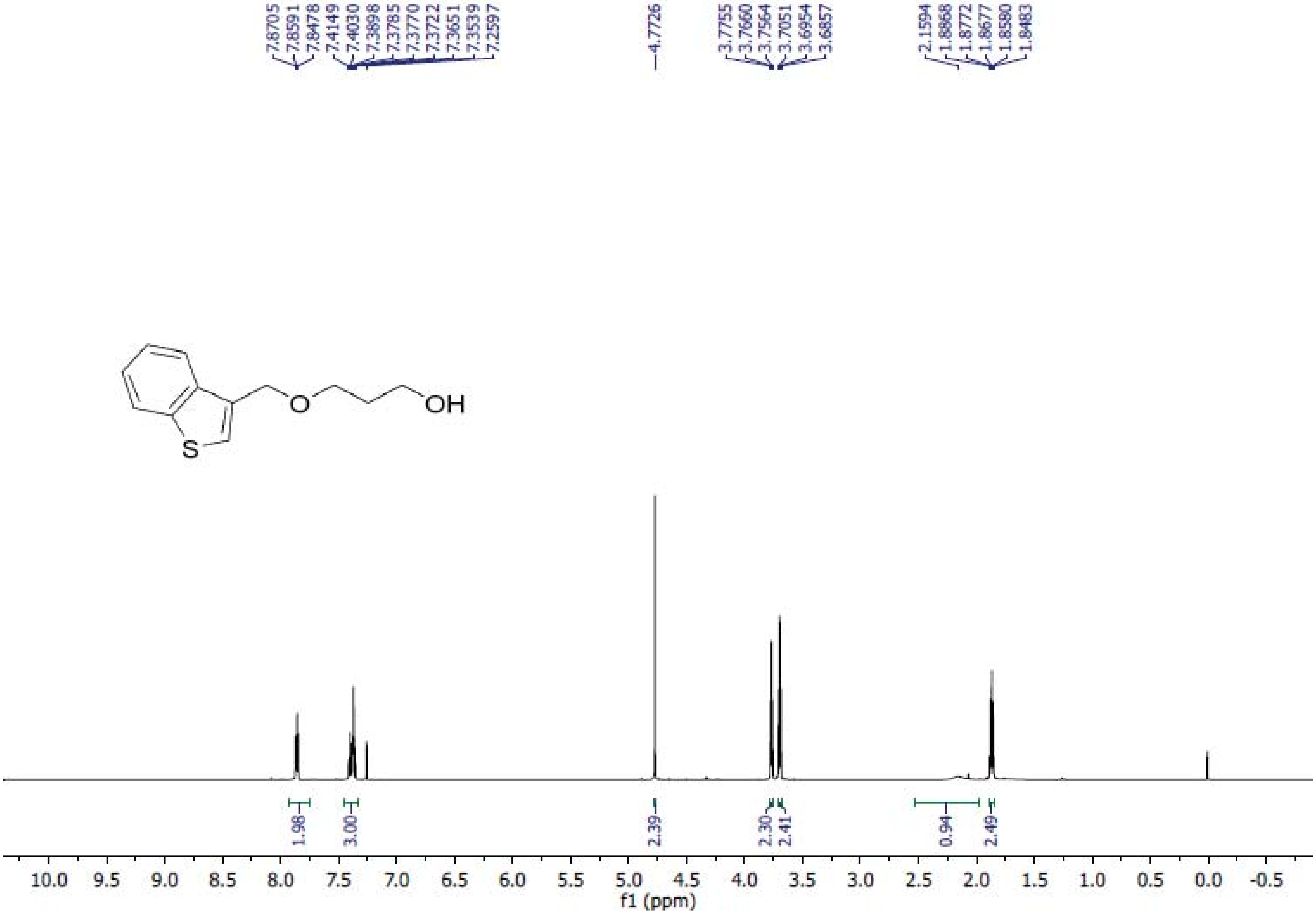
tert-butyl 3-((3-hydroxypropoxy)methyl)-1H-indole-1-carboxylate



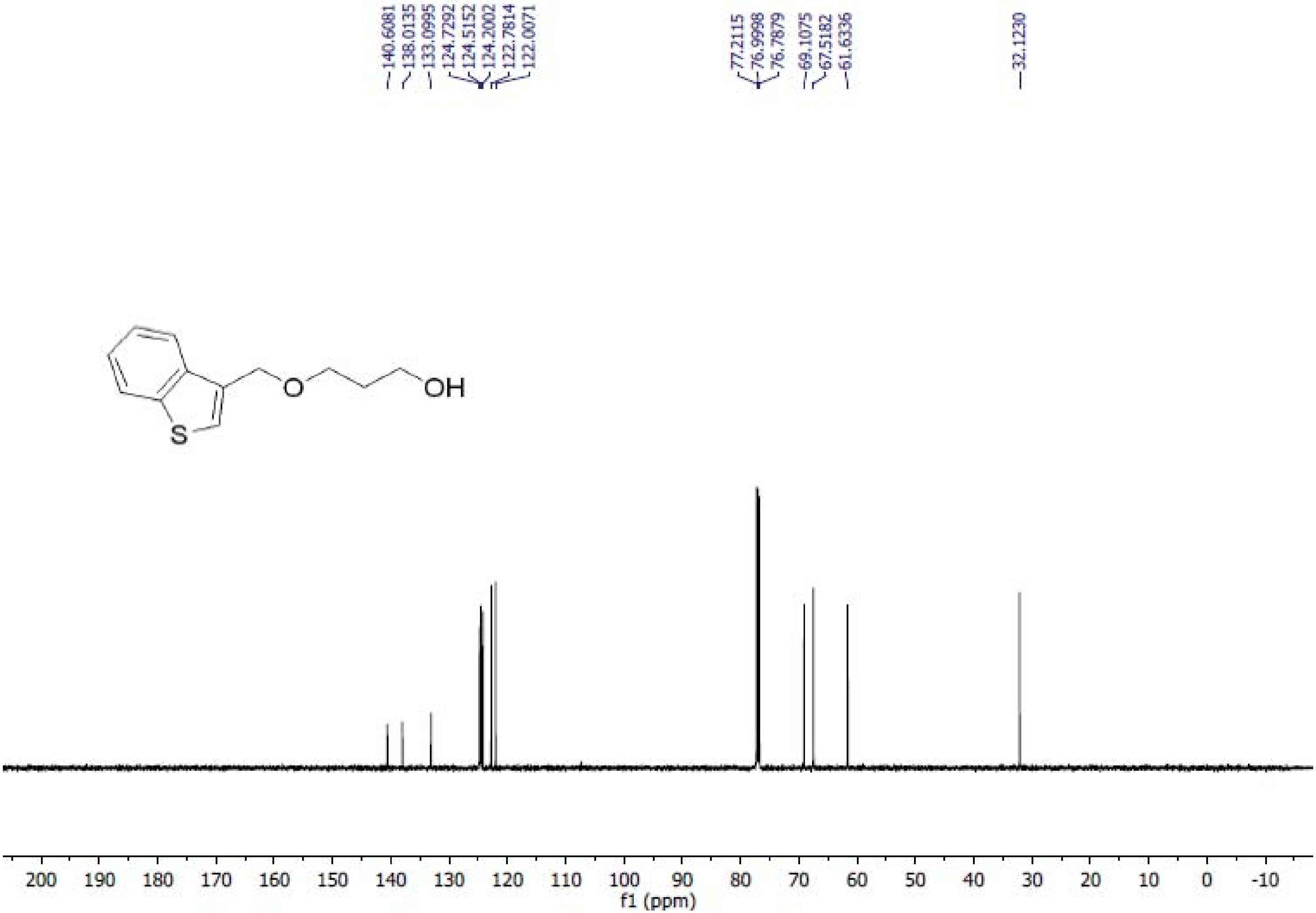
tert-butyl 3-((3-hydroxypropoxy)methyl)-1H-indole-1-carboxylate



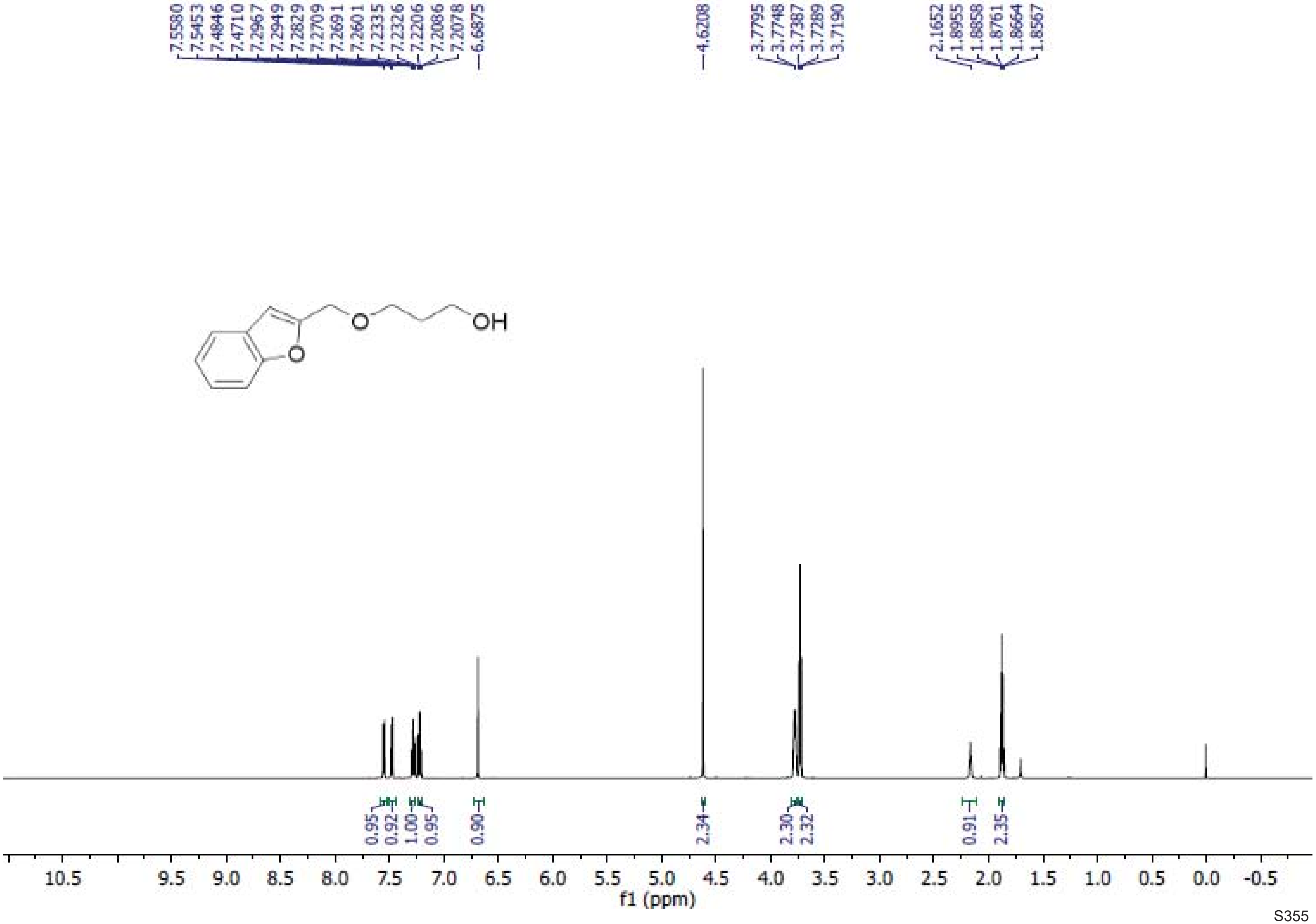
3-(benzo[b]thiophen-3-ylmethoxy)propan-1-ol



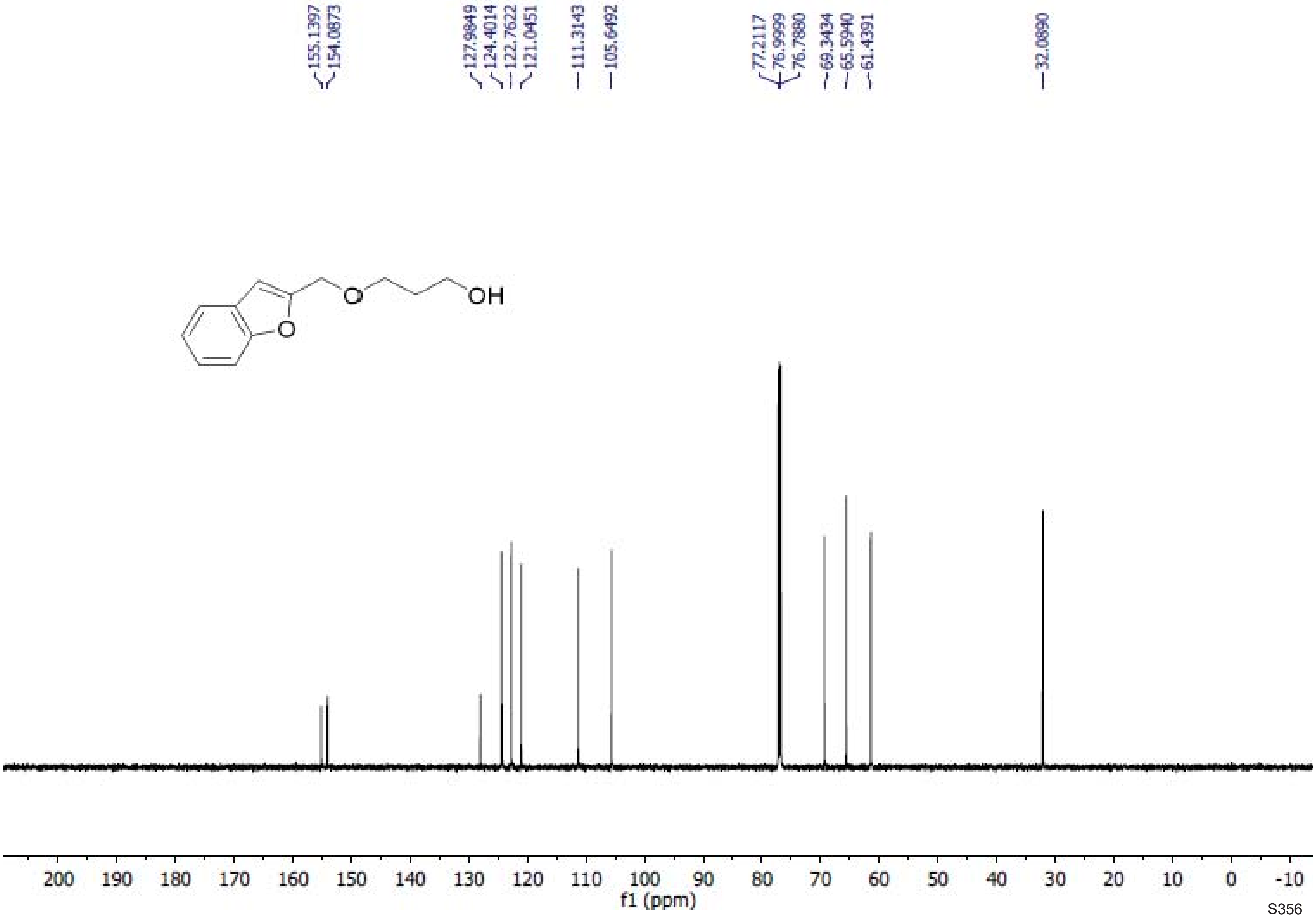
3-(benzo[b]thiophen-3-ylmethoxy)propan-1-ol



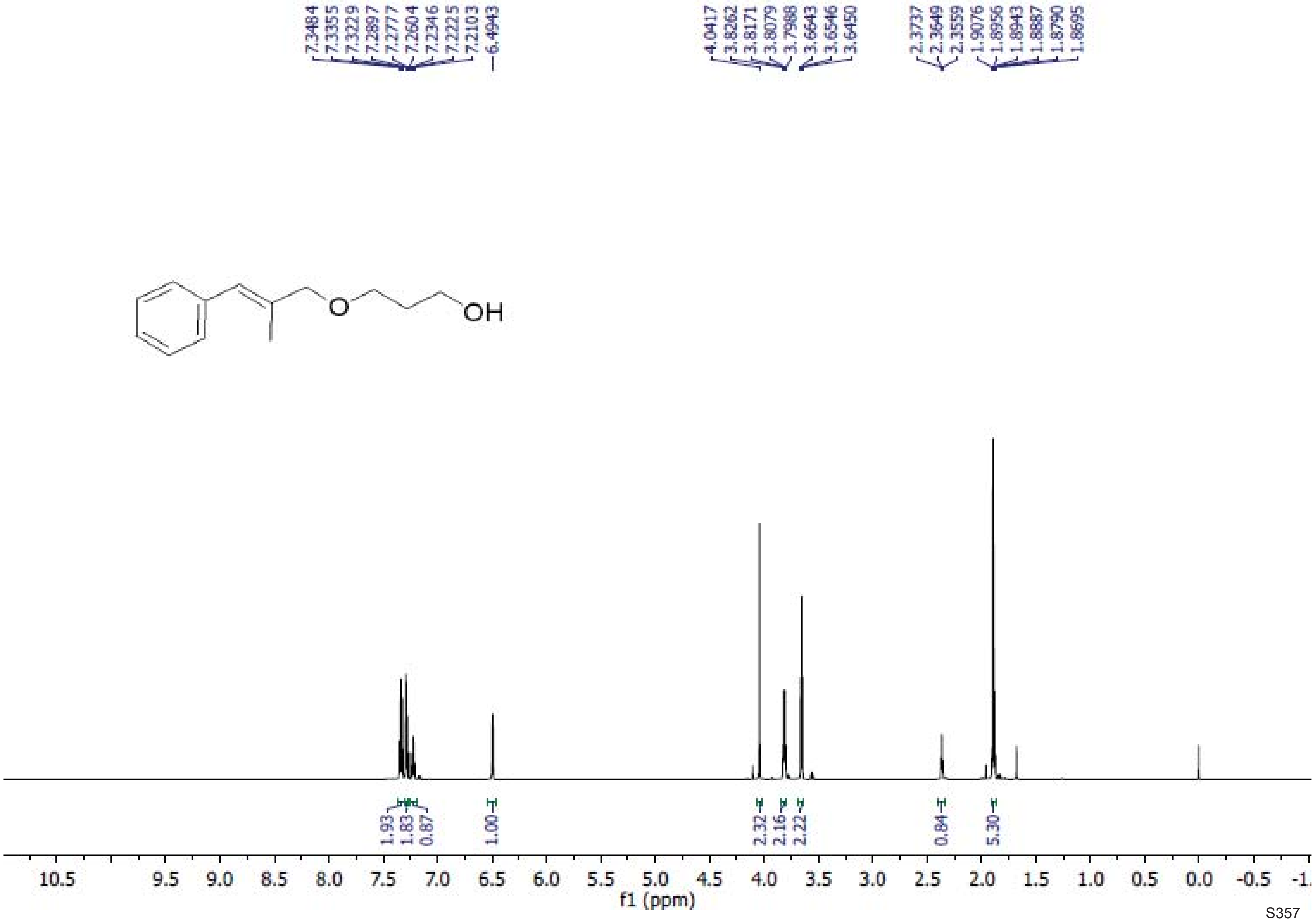
3-(benzofuran-2-ylmethoxy)propan-1-ol



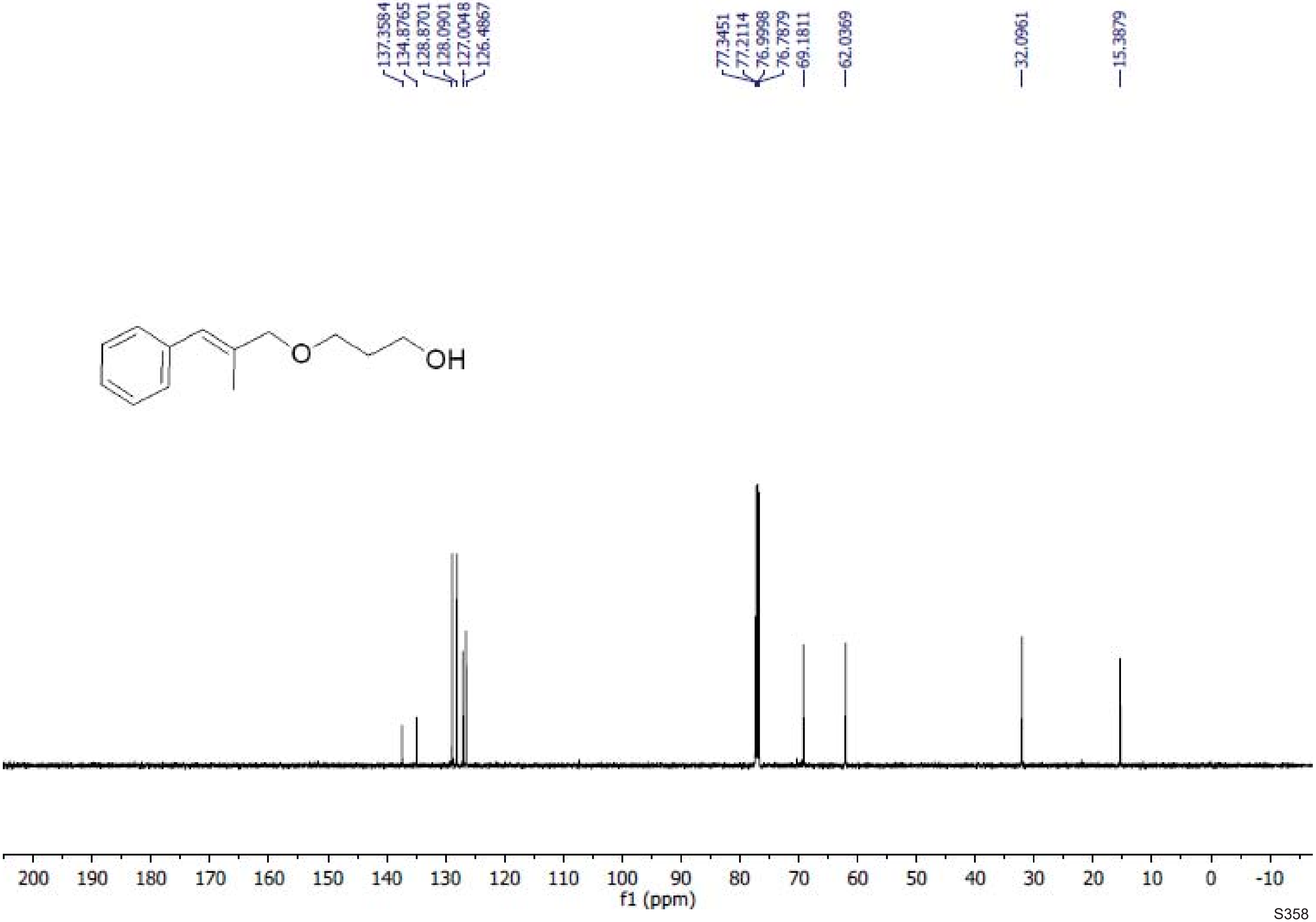
3-(benzofuran-2-ylmethoxy)propan-1-ol



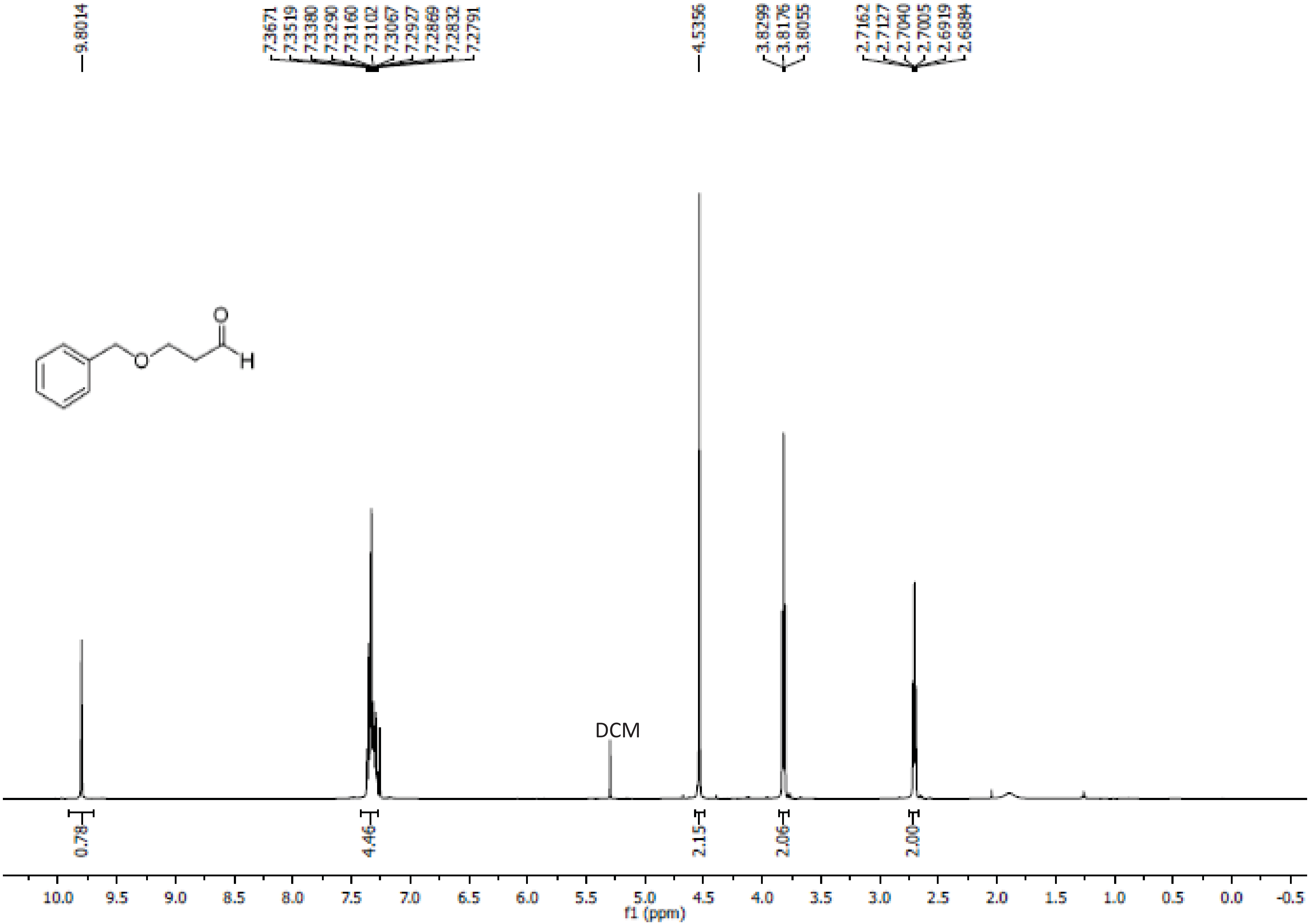
3-((2-methyl-3-phenylallyl)oxy)propan-1-ol



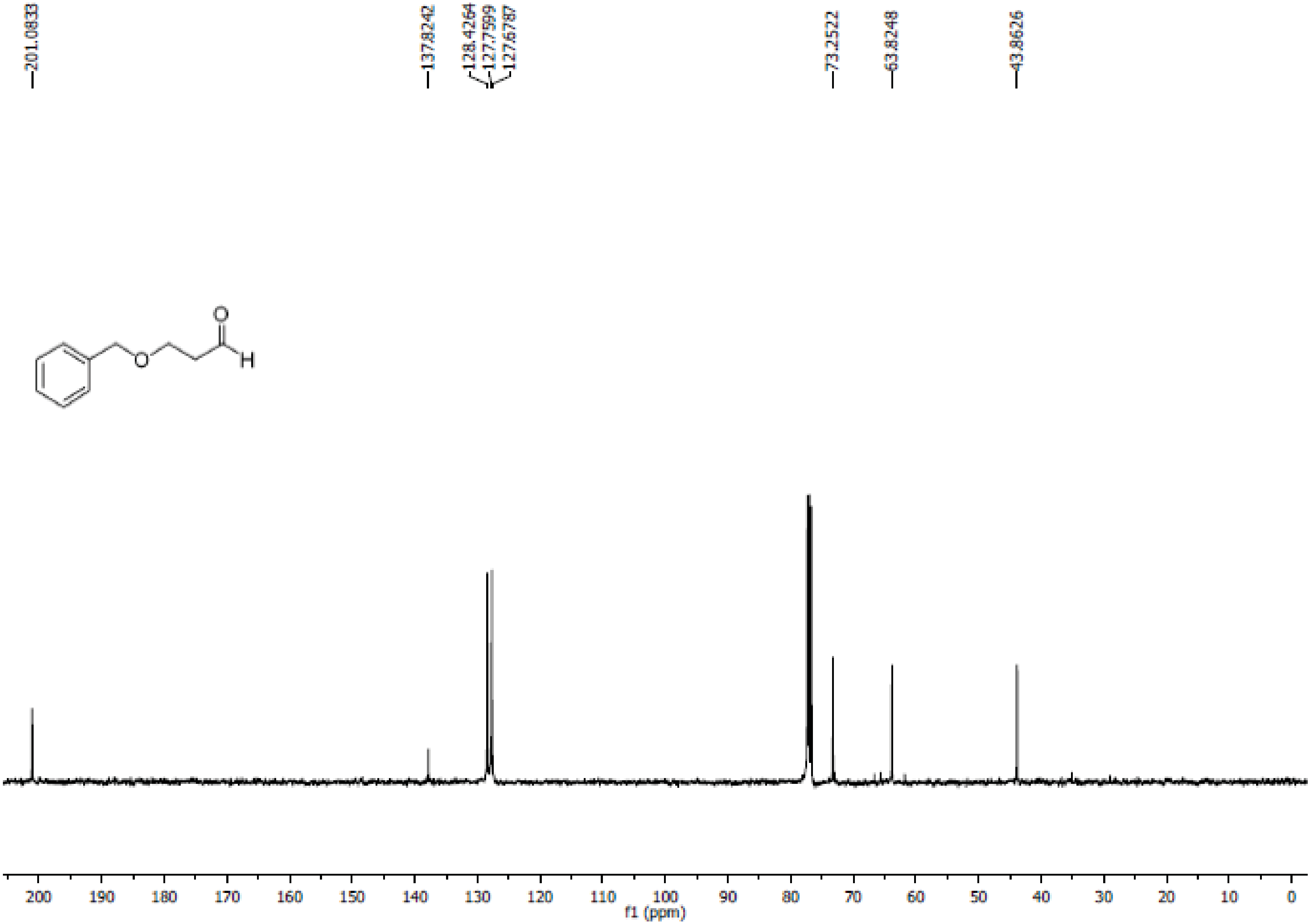
3-((2-methyl-3-phenylallyl)oxy)propan-1-ol



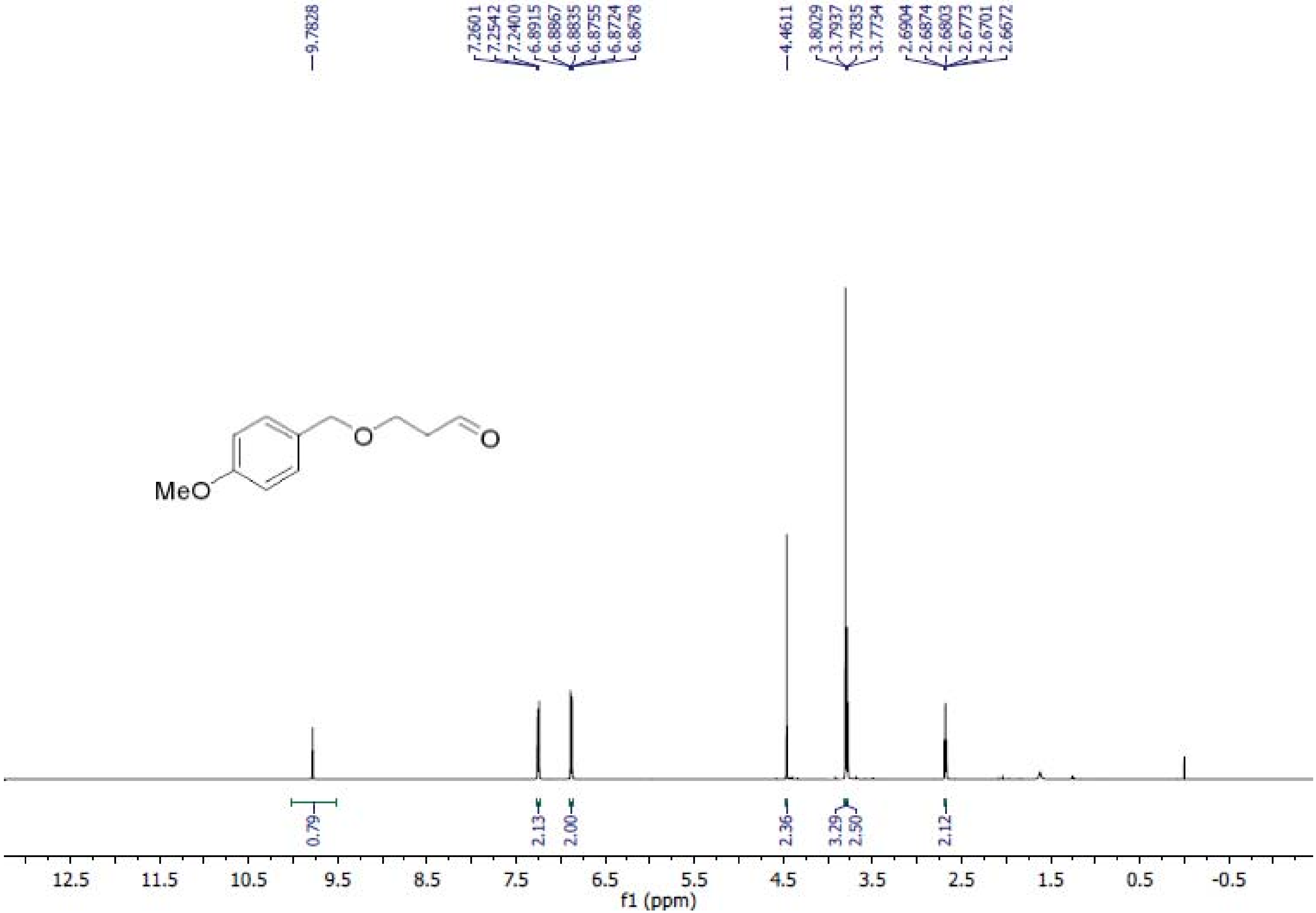
3-(benzyloxy)propanal



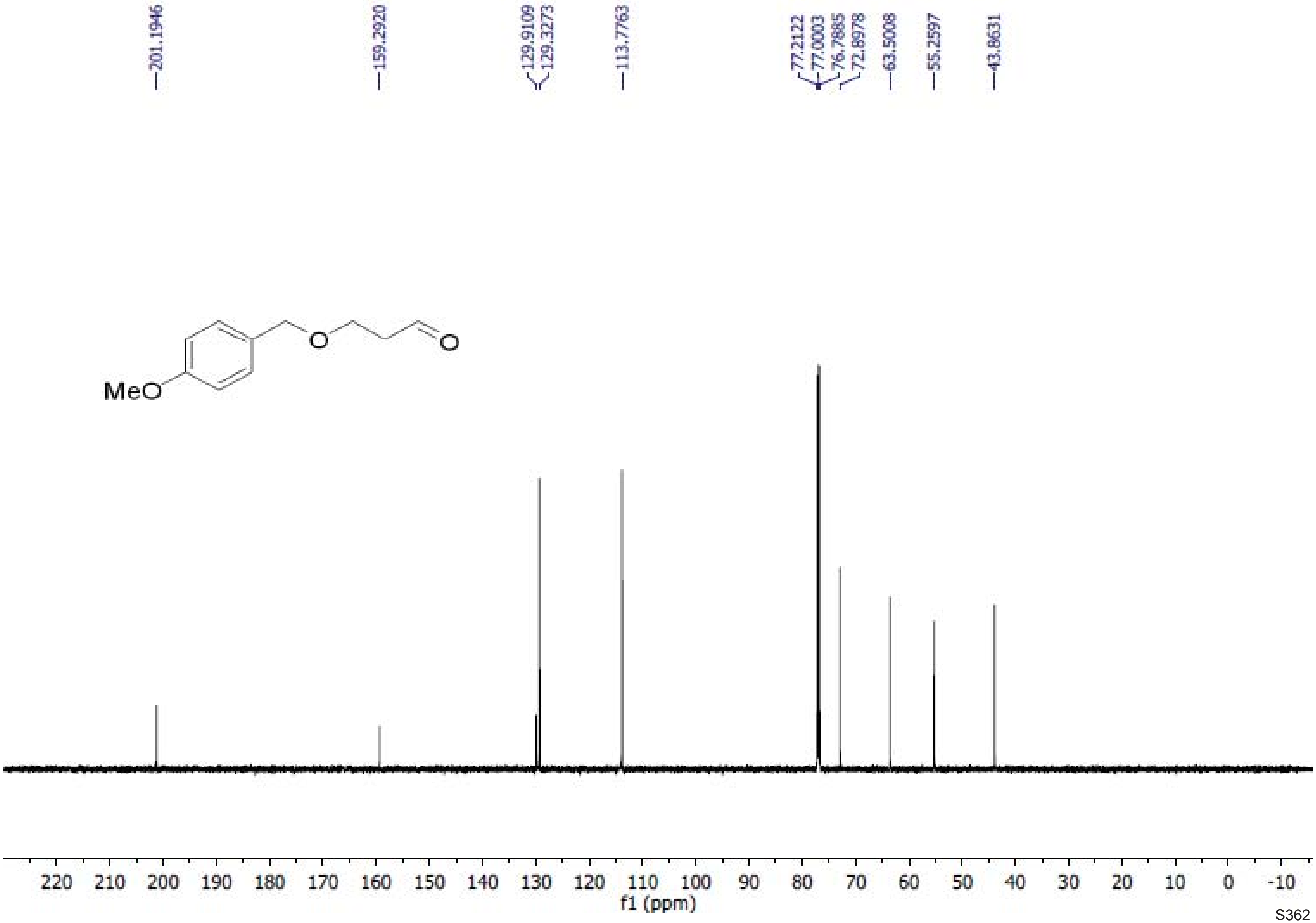
3-(benzyloxy)propanal



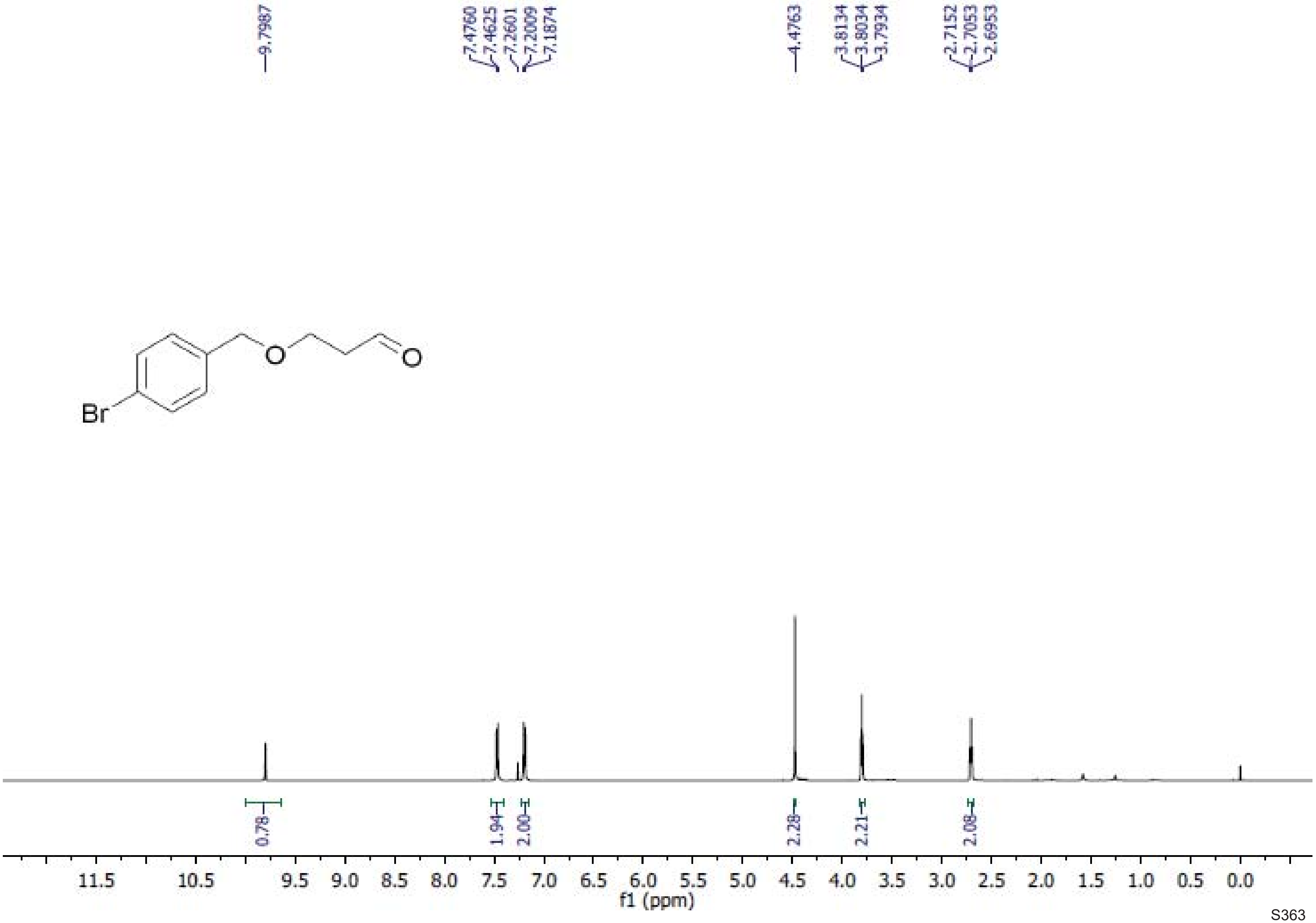
3-((4-methoxybenzyl)oxy)propanal



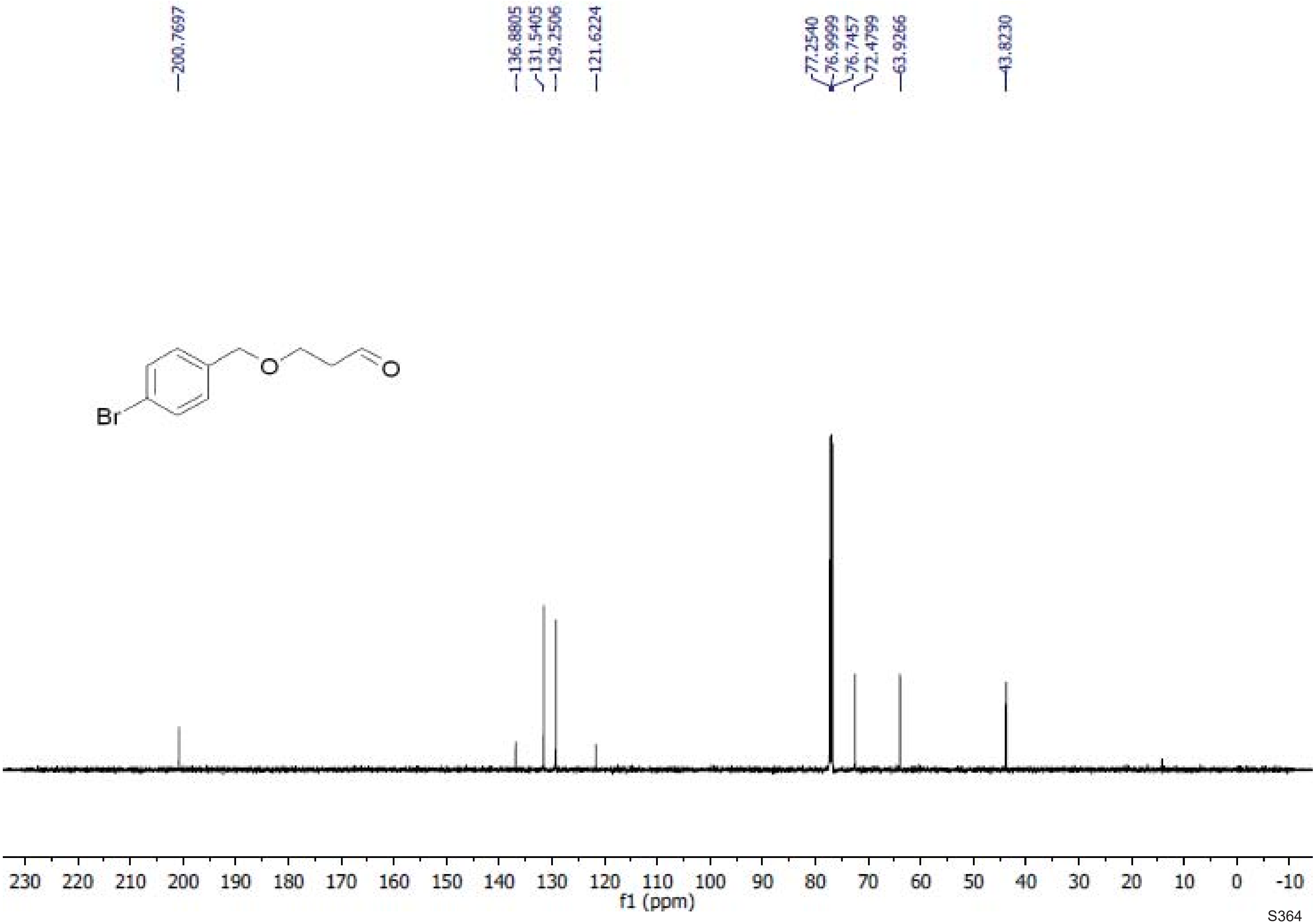
3-((4-methoxybenzyl)oxy)propanal



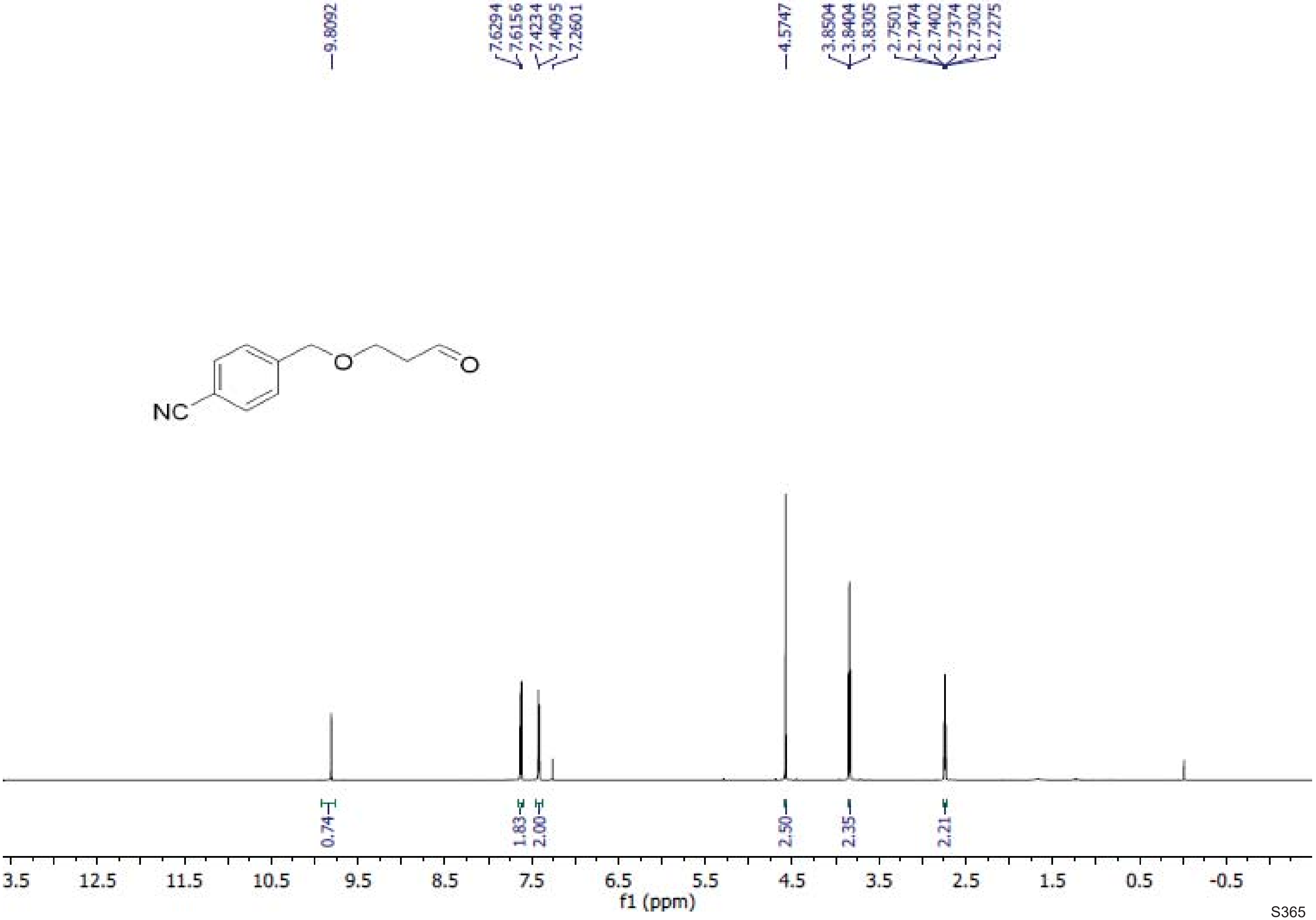
3-((4-bromobenzyl)oxy)propanal



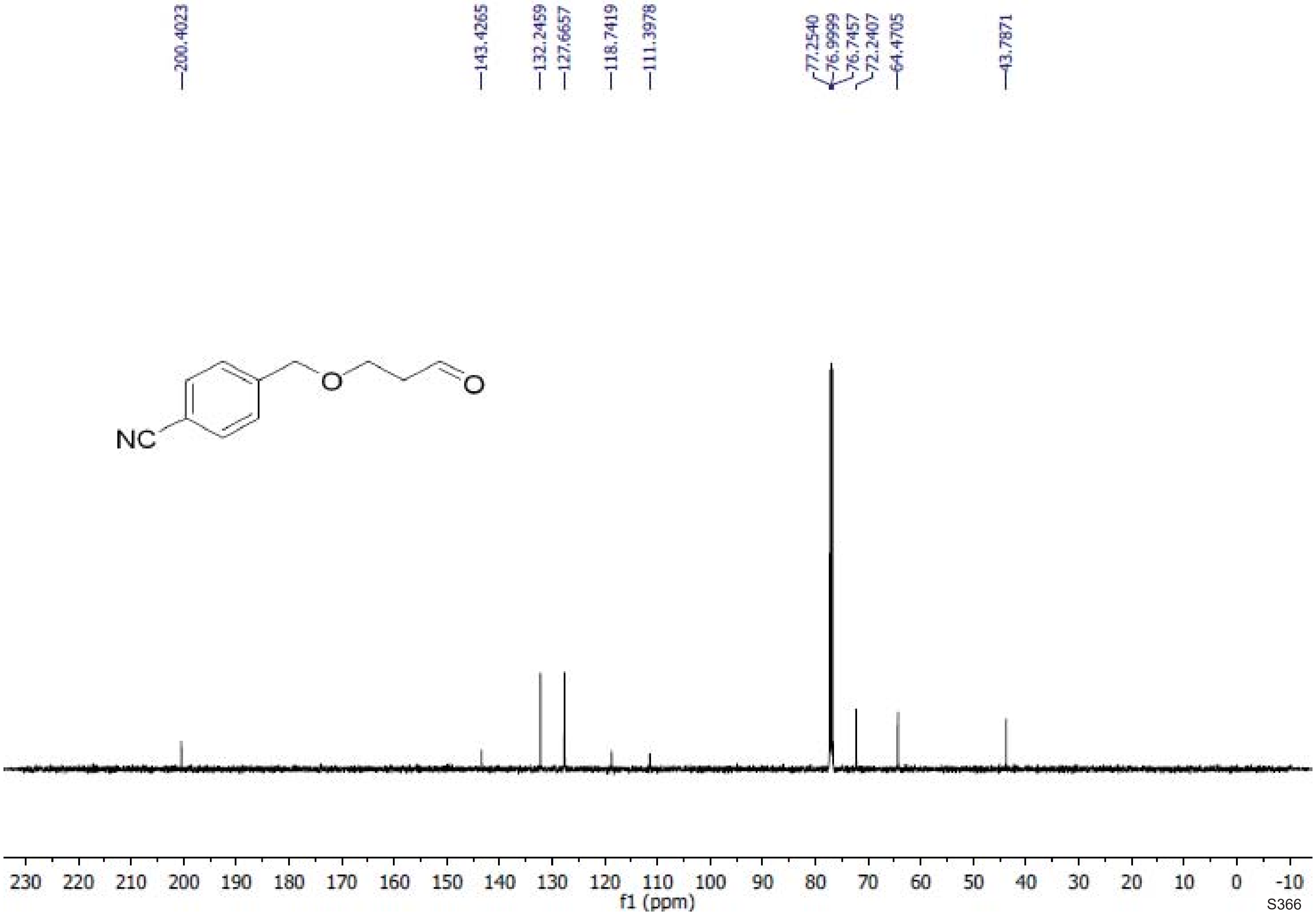
3-((4-bromobenzyl)oxy)propanal



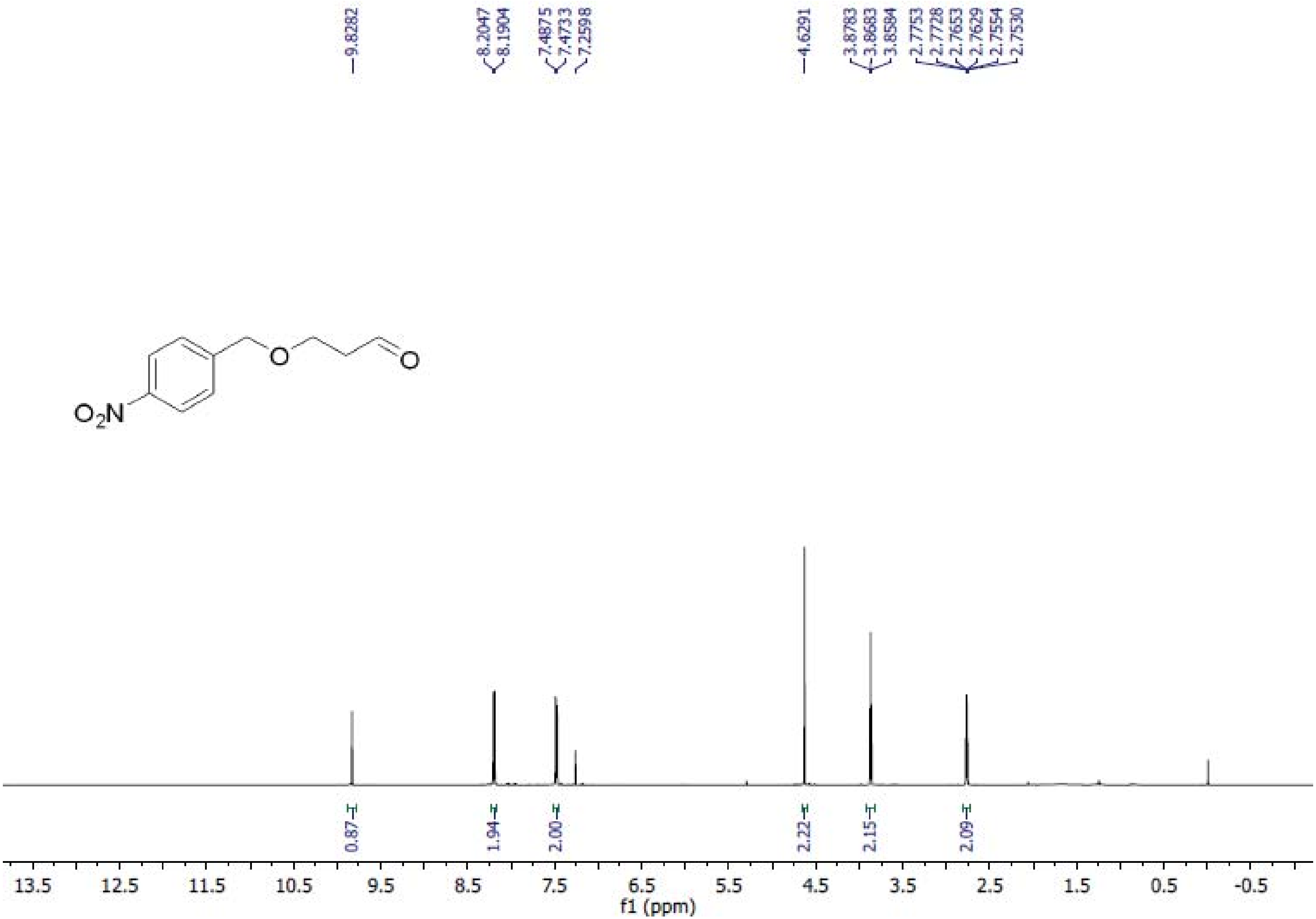
4-((3-oxopropoxy)methyl)benzonitrile



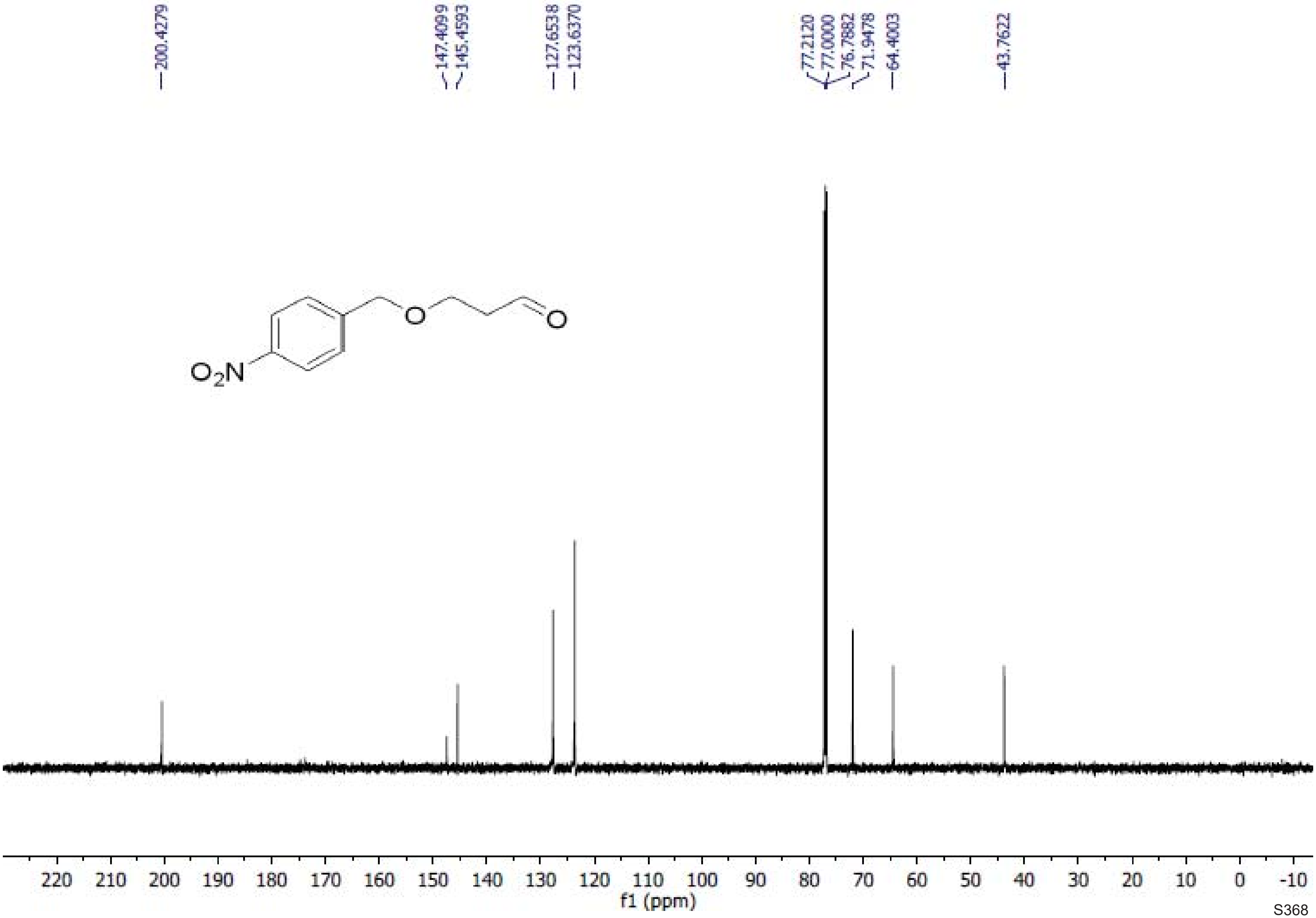
4-((3-oxopropoxy)methyl)benzonitrile



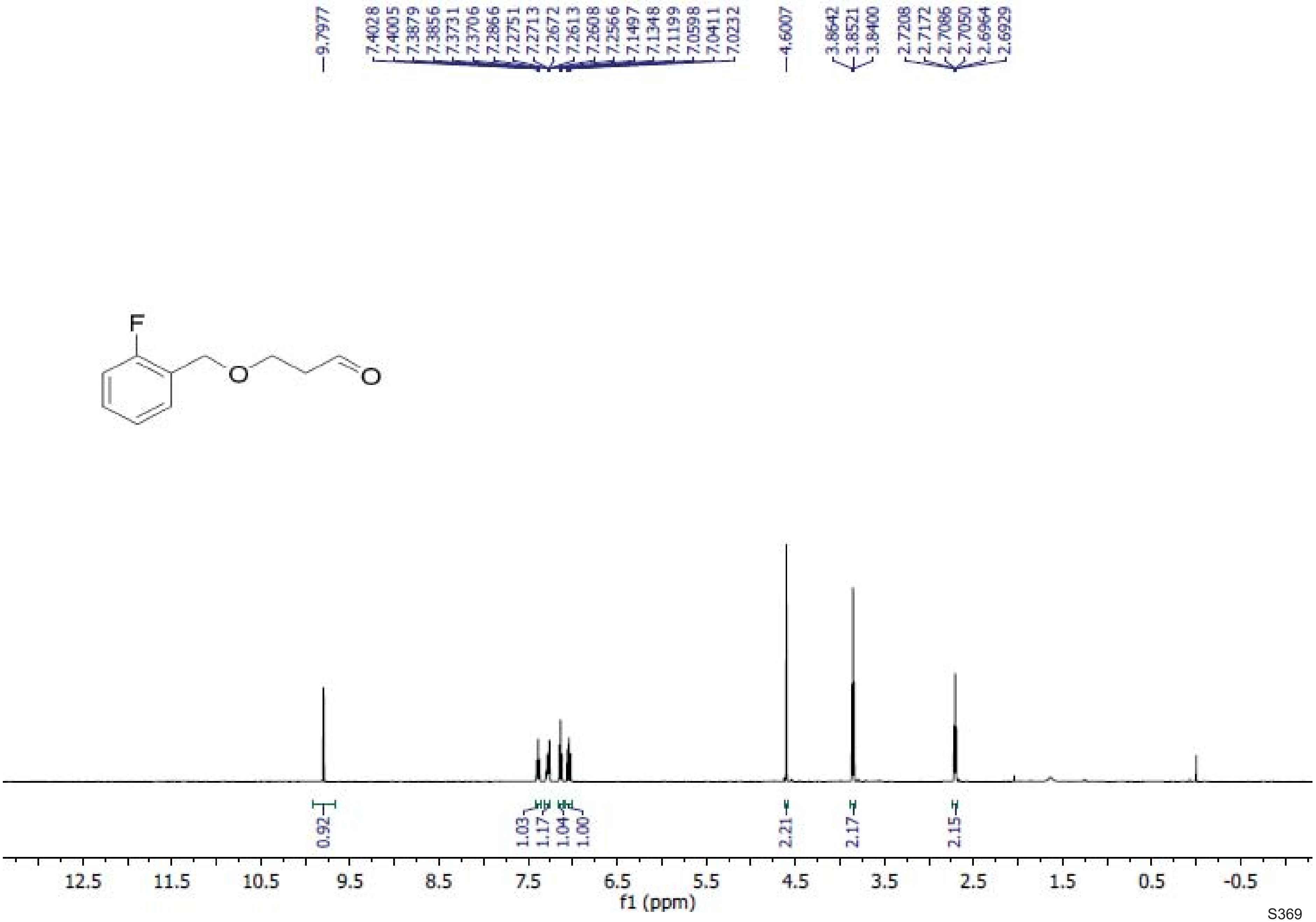
3-((4-nitrobenzyl)oxy)propanal



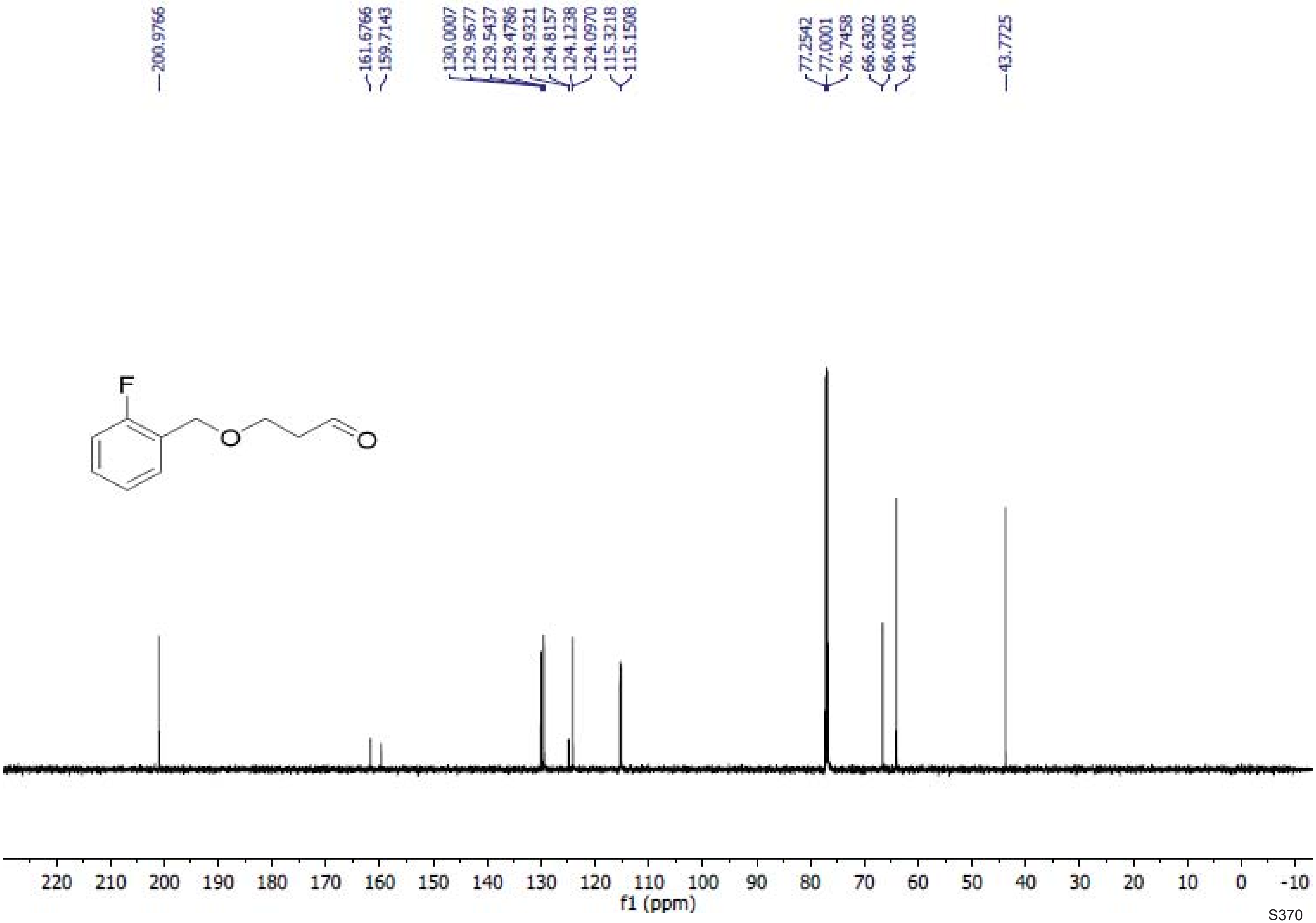
3-((4-nitrobenzyl)oxy)propanal



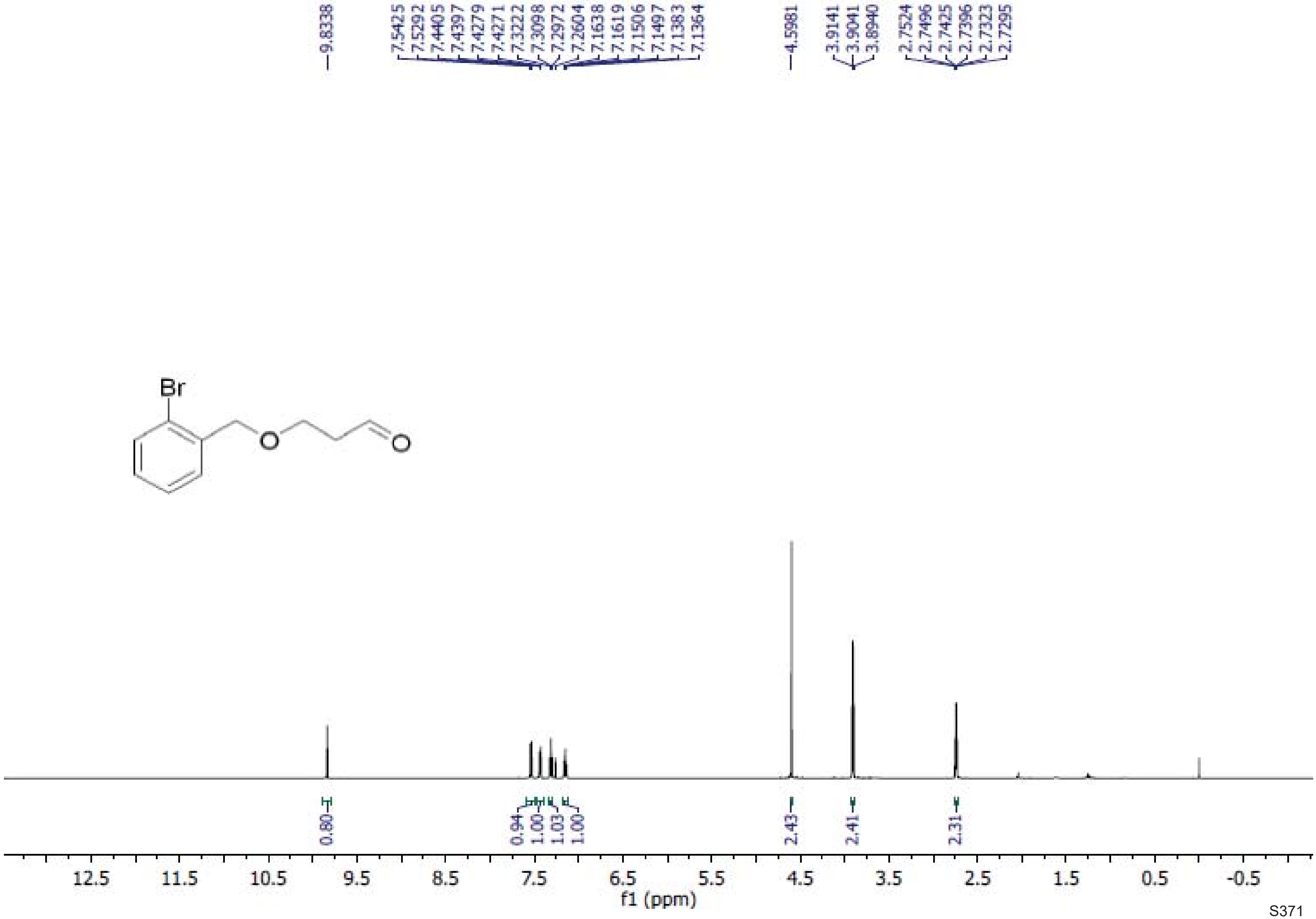
3-((2-fluorobenzyl)oxy)propanal



3-((2-fluorobenzyl)oxy)propanal



3-((2-bromobenzyl)oxy)propanal



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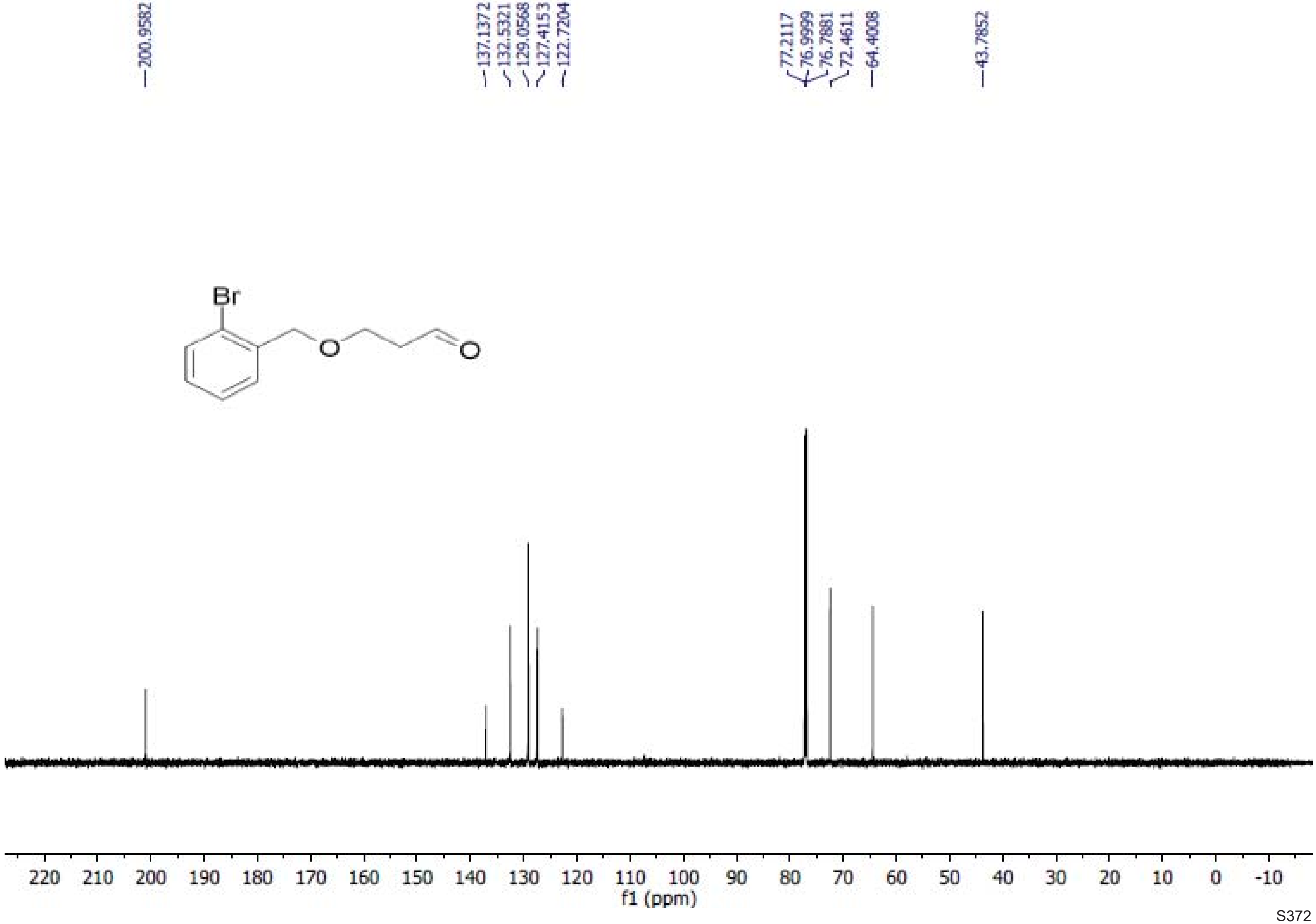
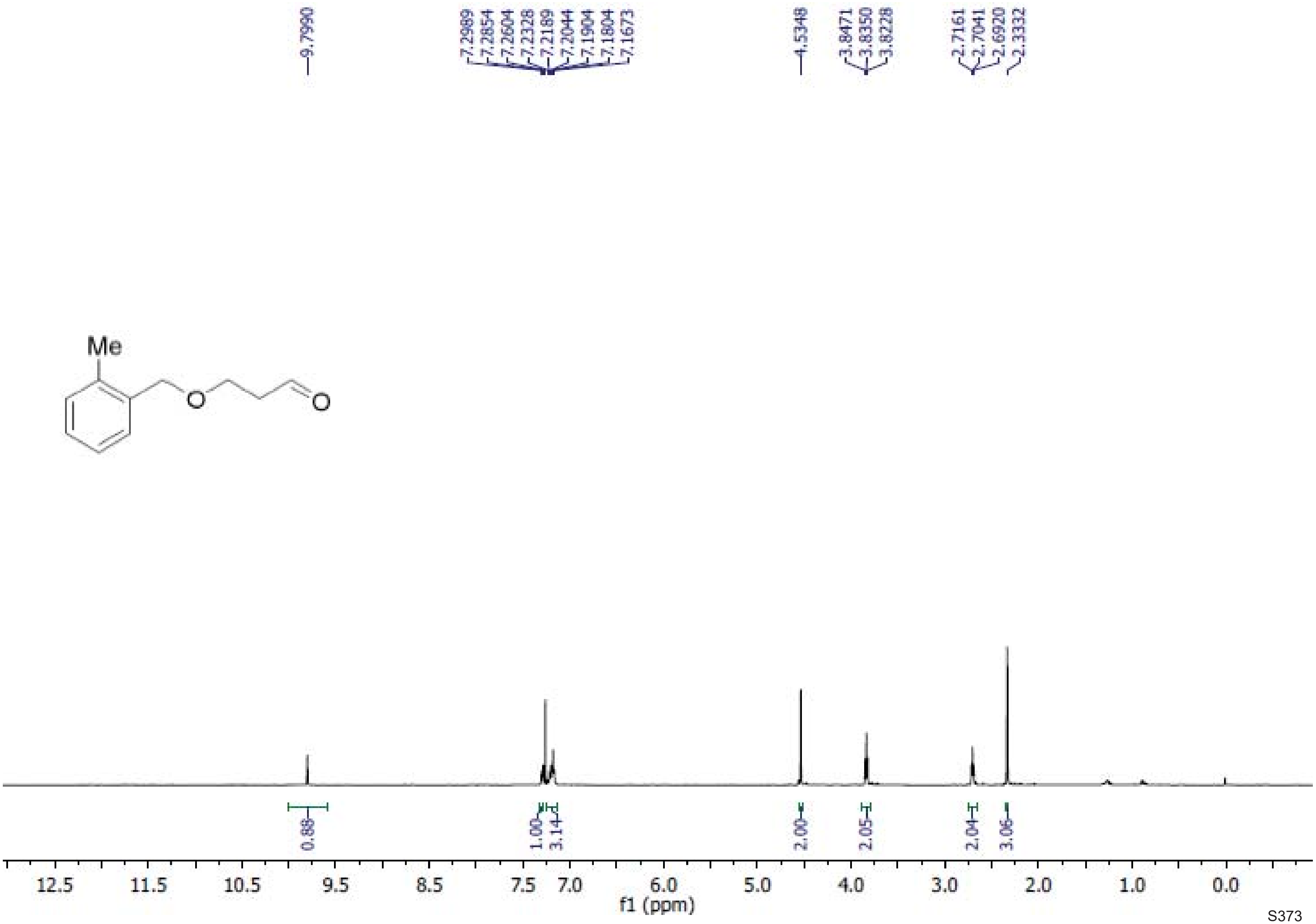
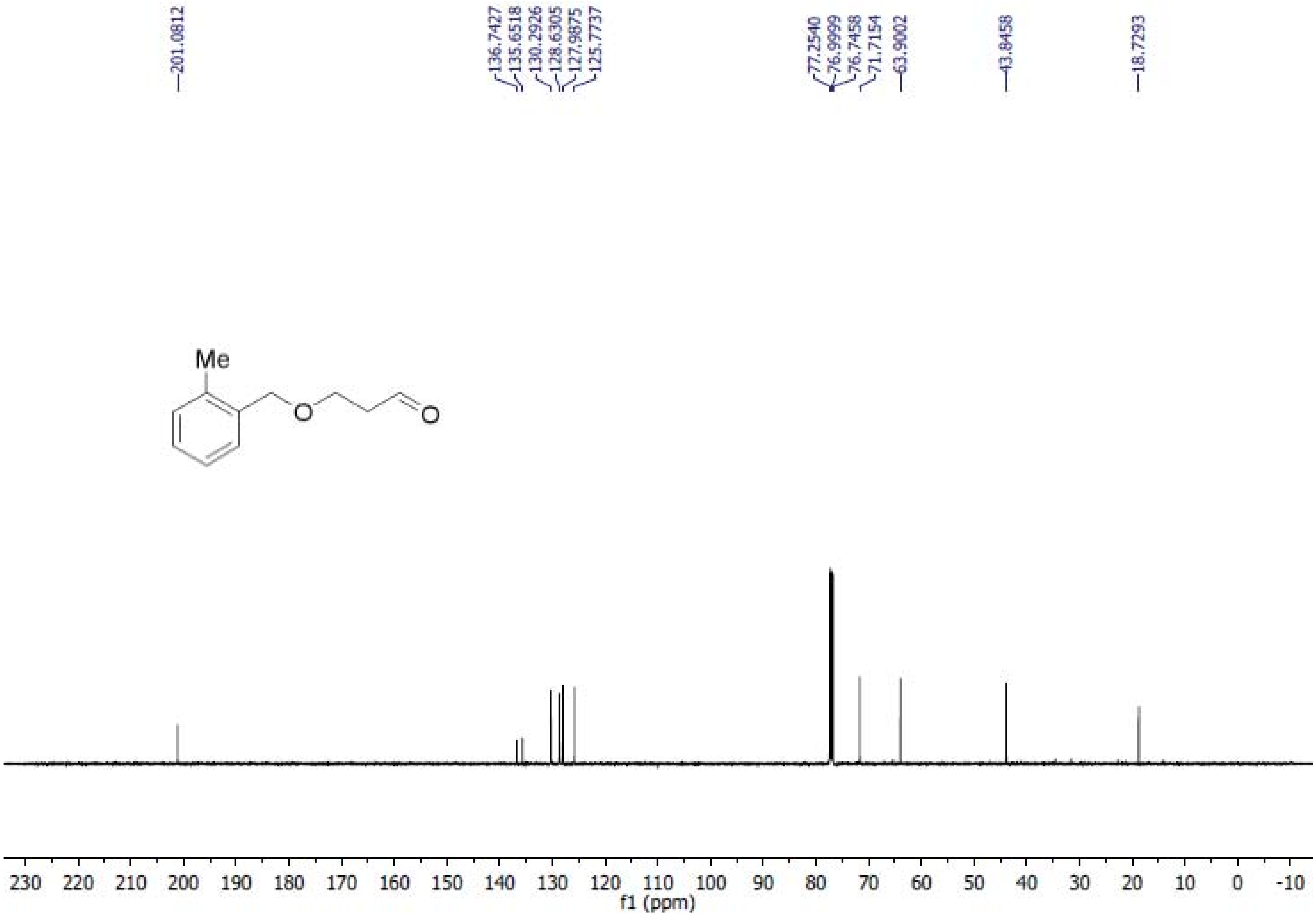


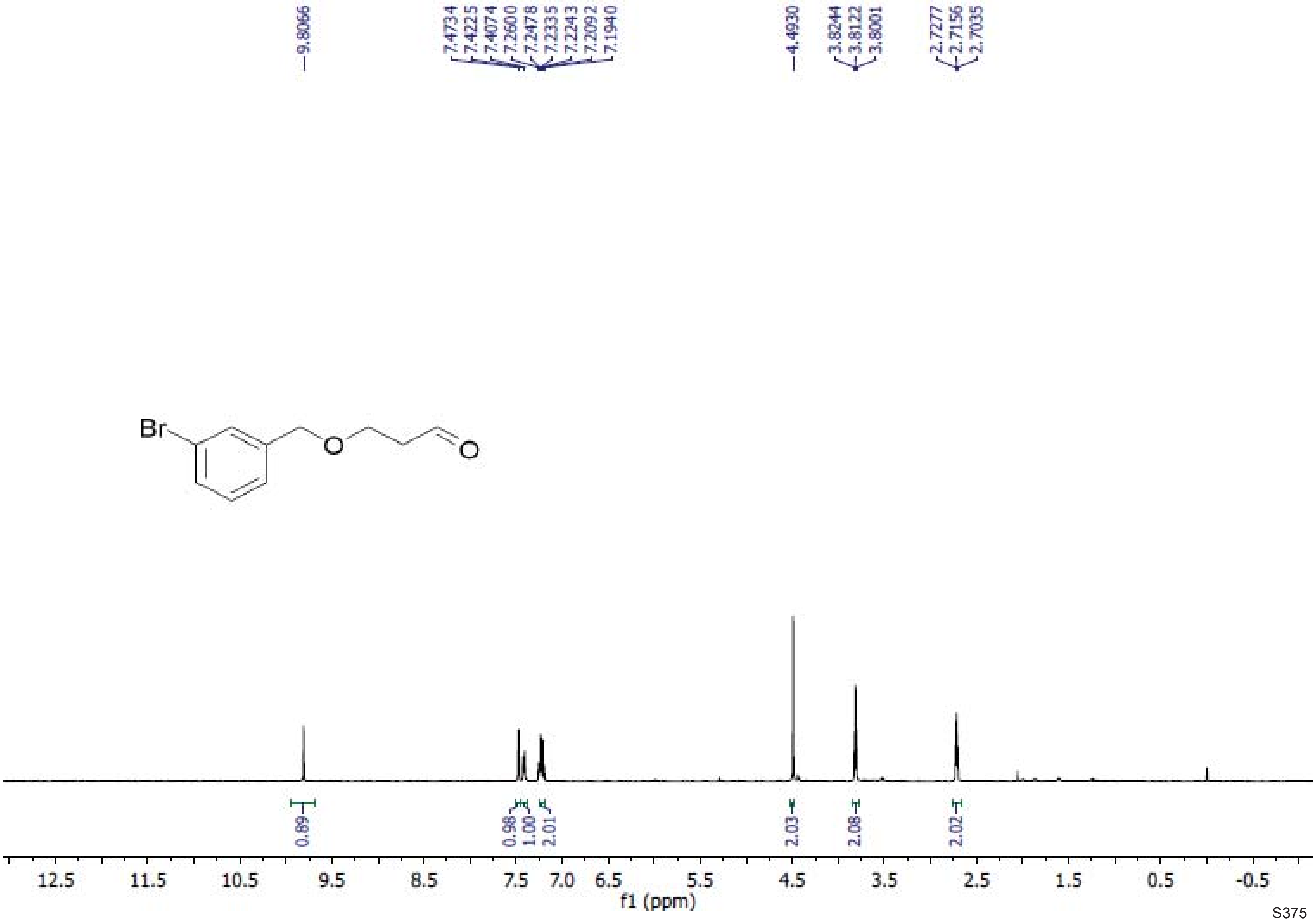
3-((2-methylbenzyl)oxy)propanal



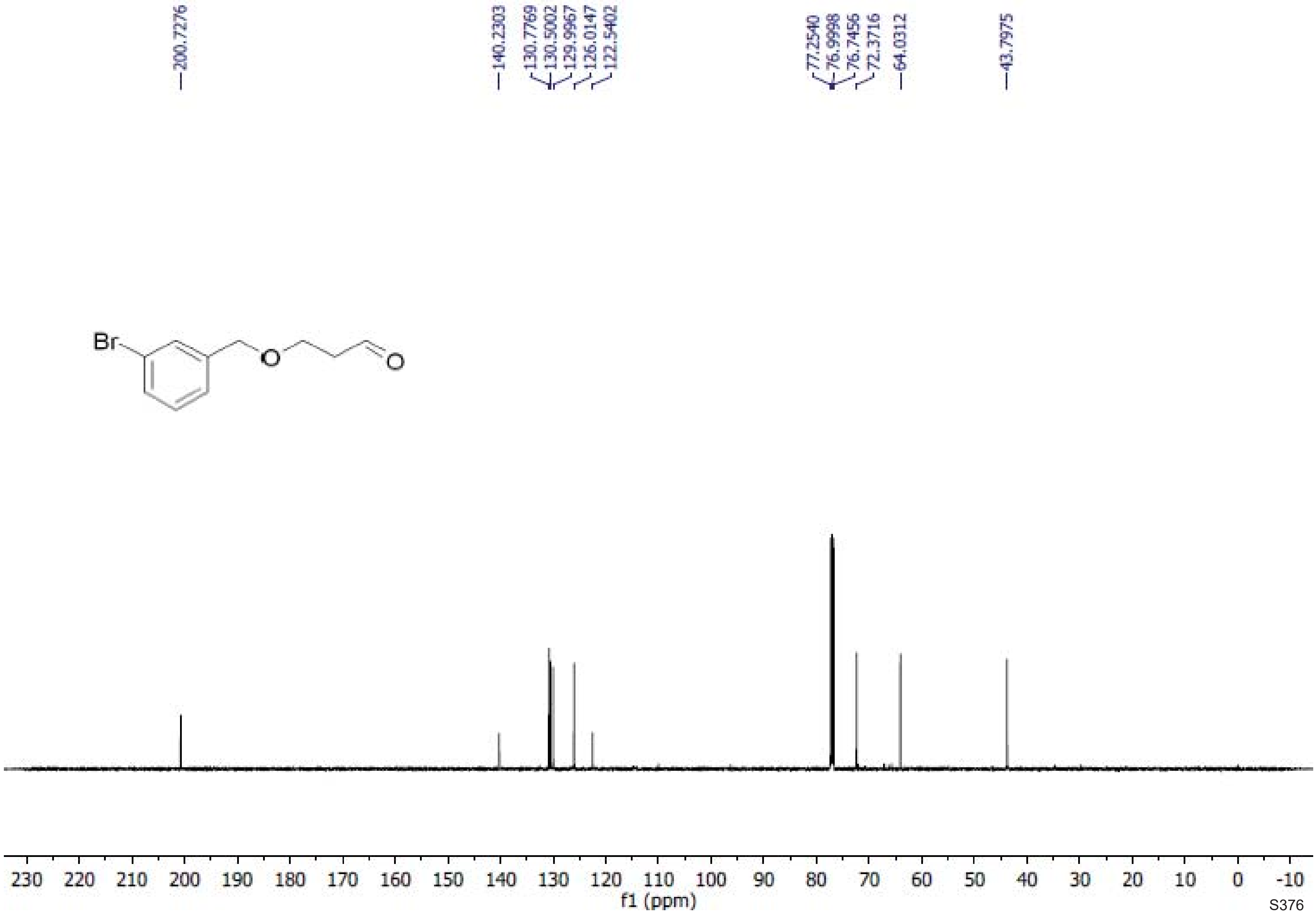
3-((2-methylbenzyl)oxy)propanal



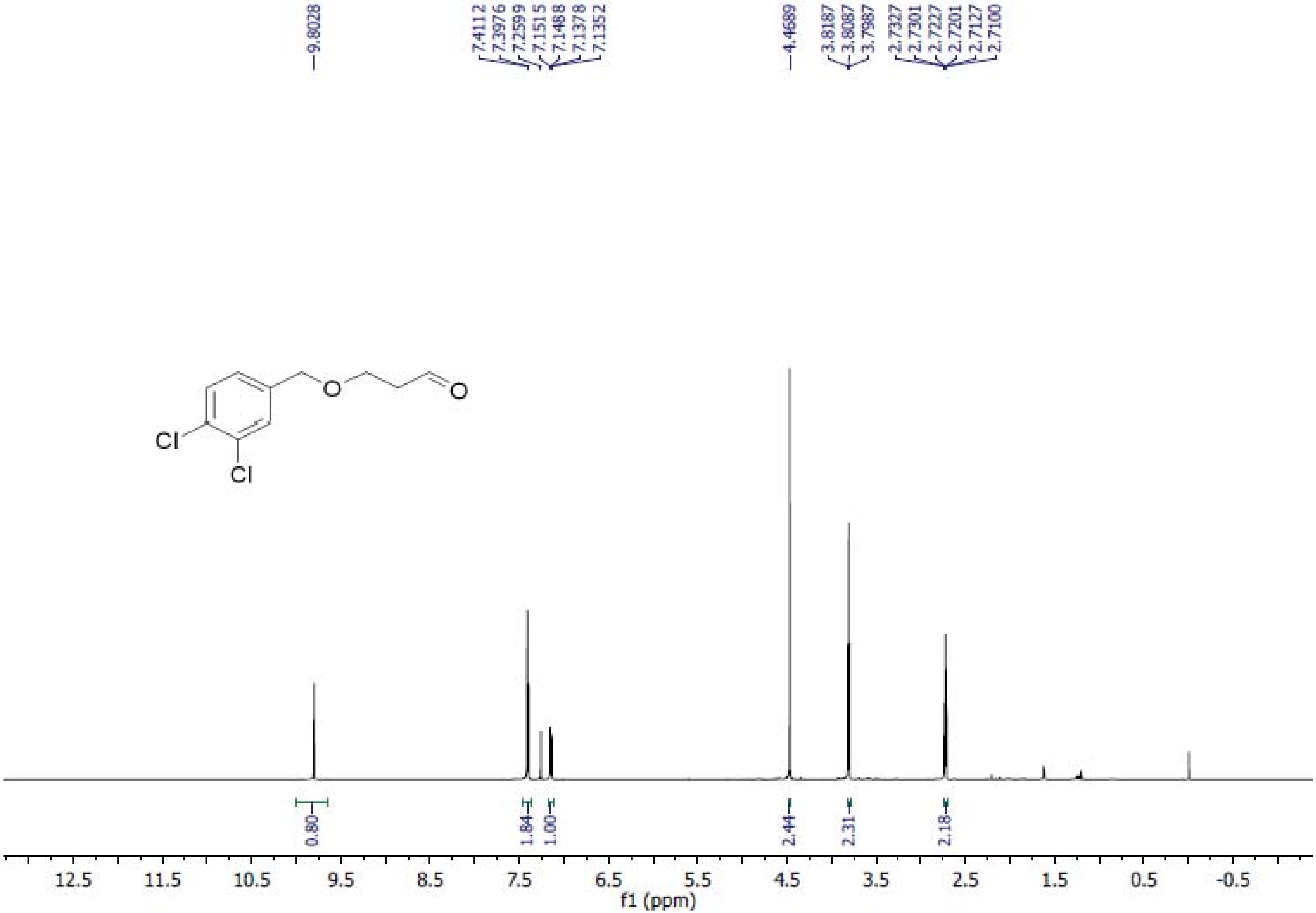
3-((3-bromobenzyl)oxy)propanal



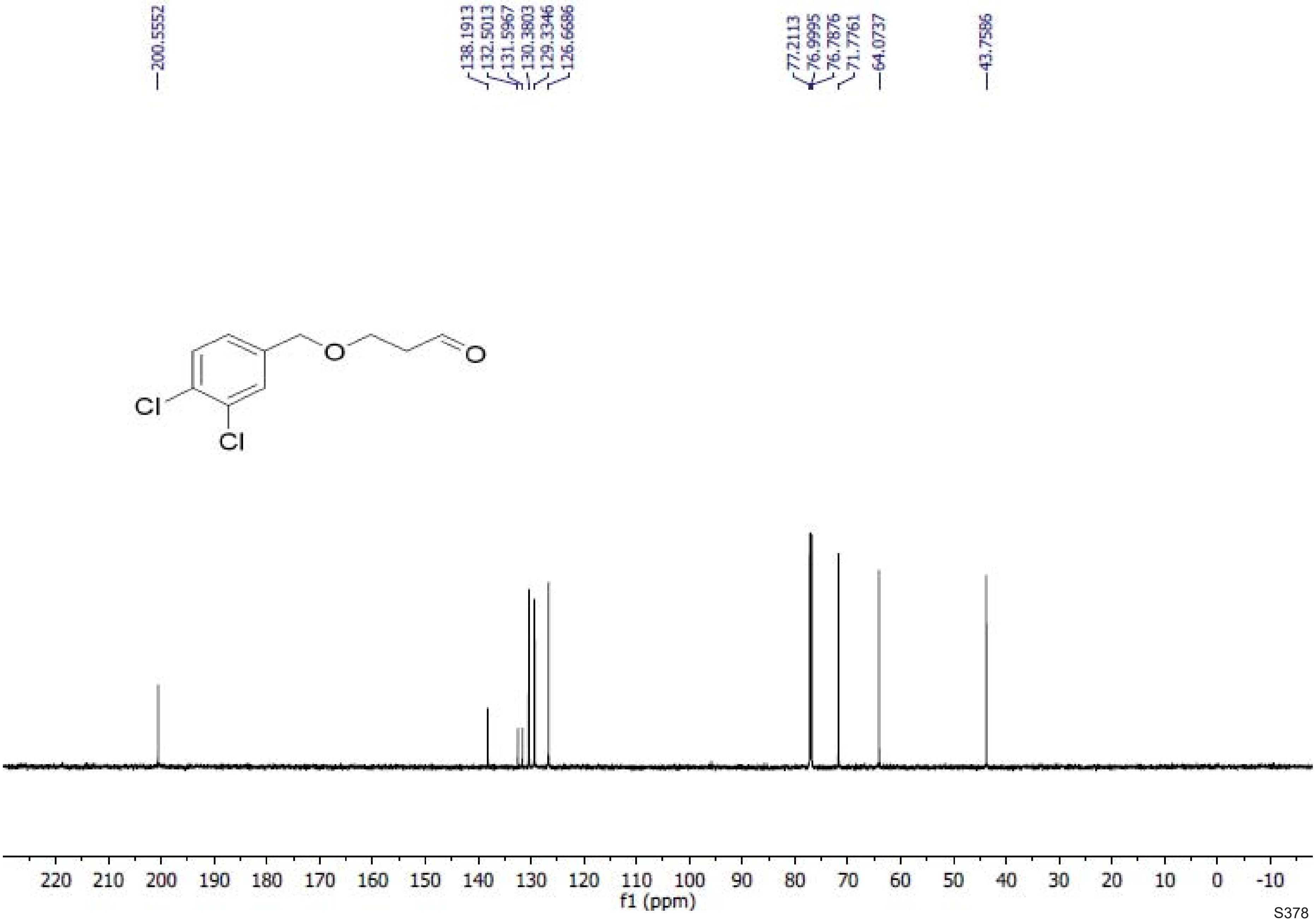
3-((3-bromobenzyl)oxy)propanal



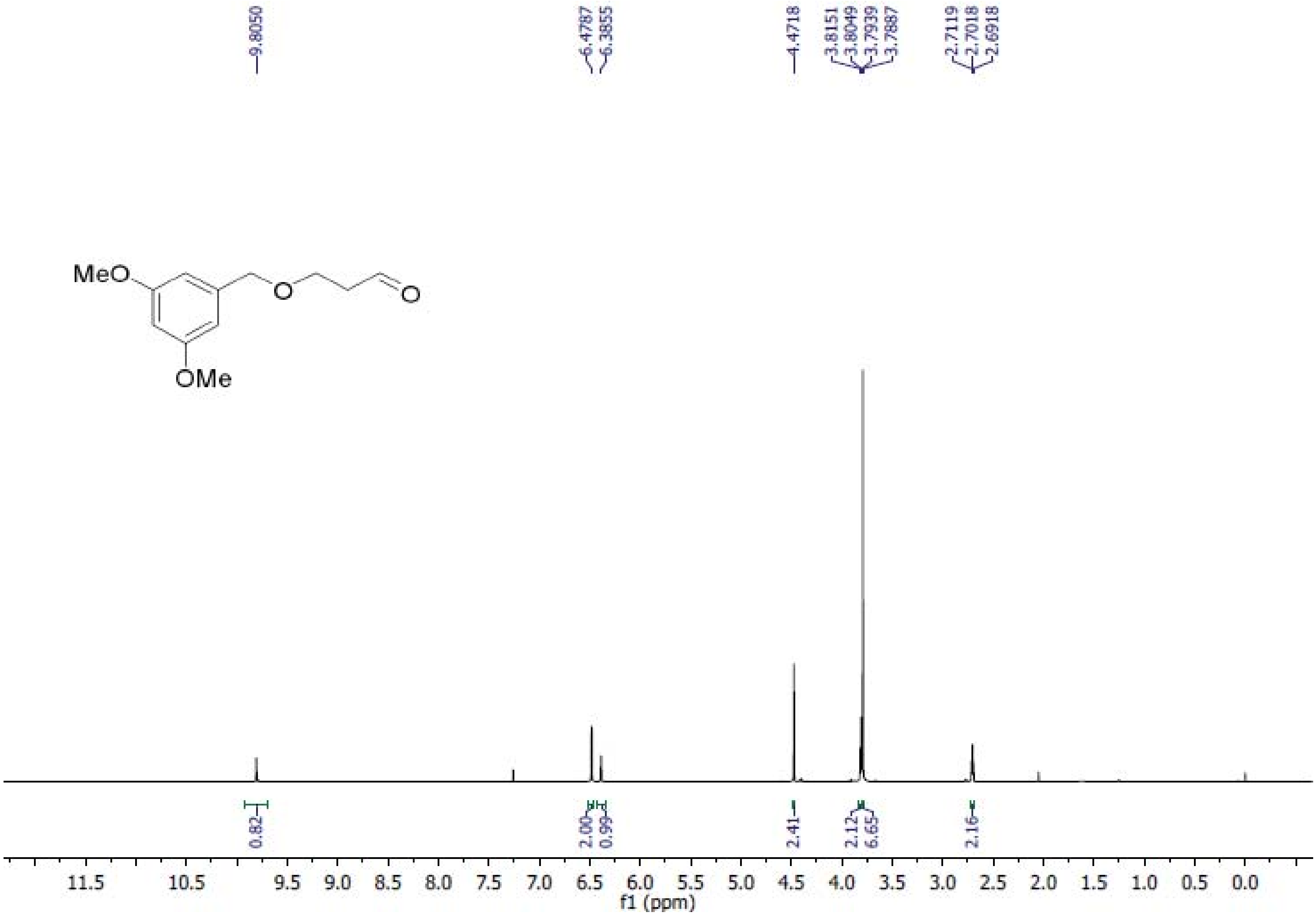
3-((3,4-dichlorobenzyl)oxy)propanal



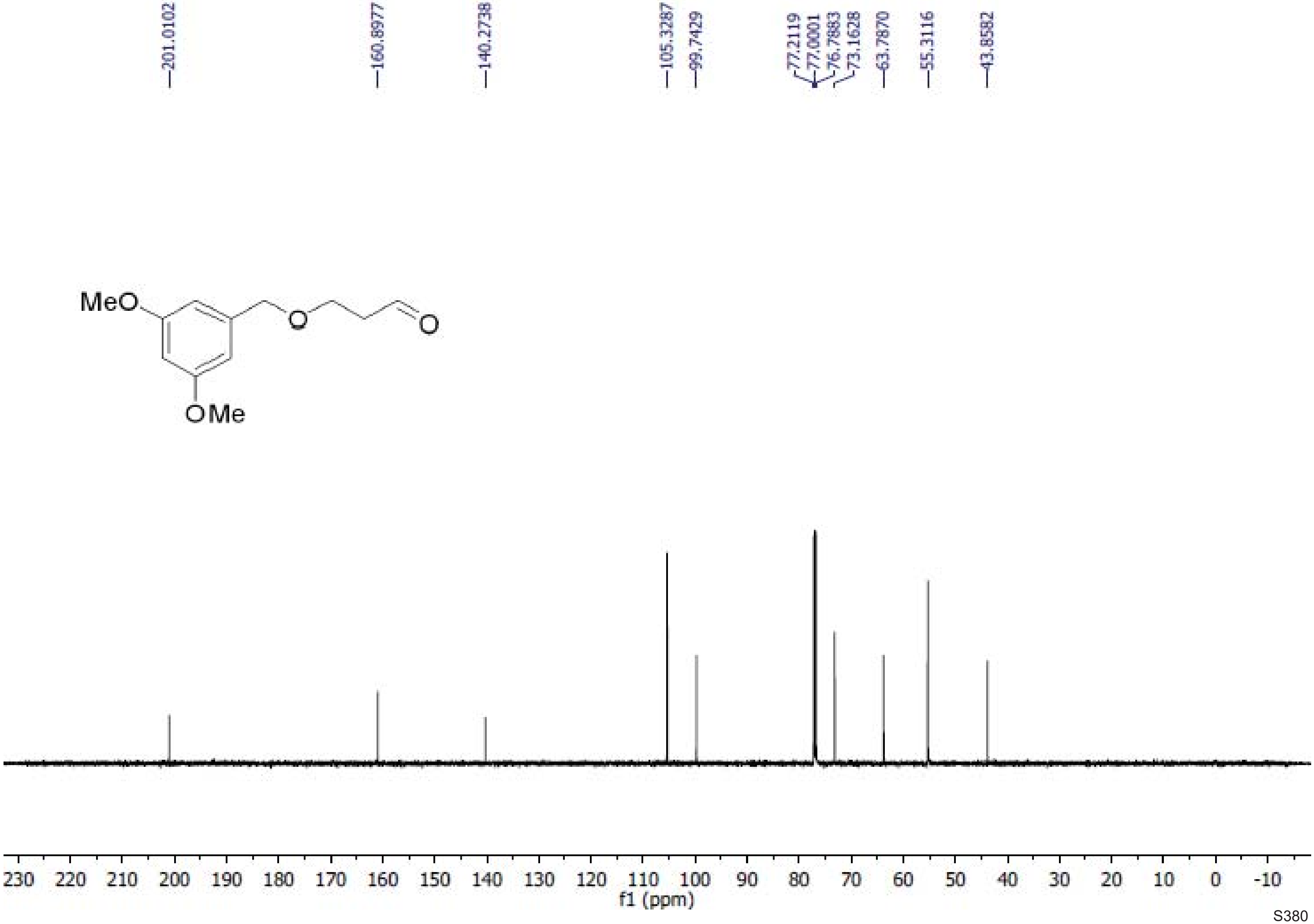
3-((3,4-dichlorobenzyl)oxy)propanal



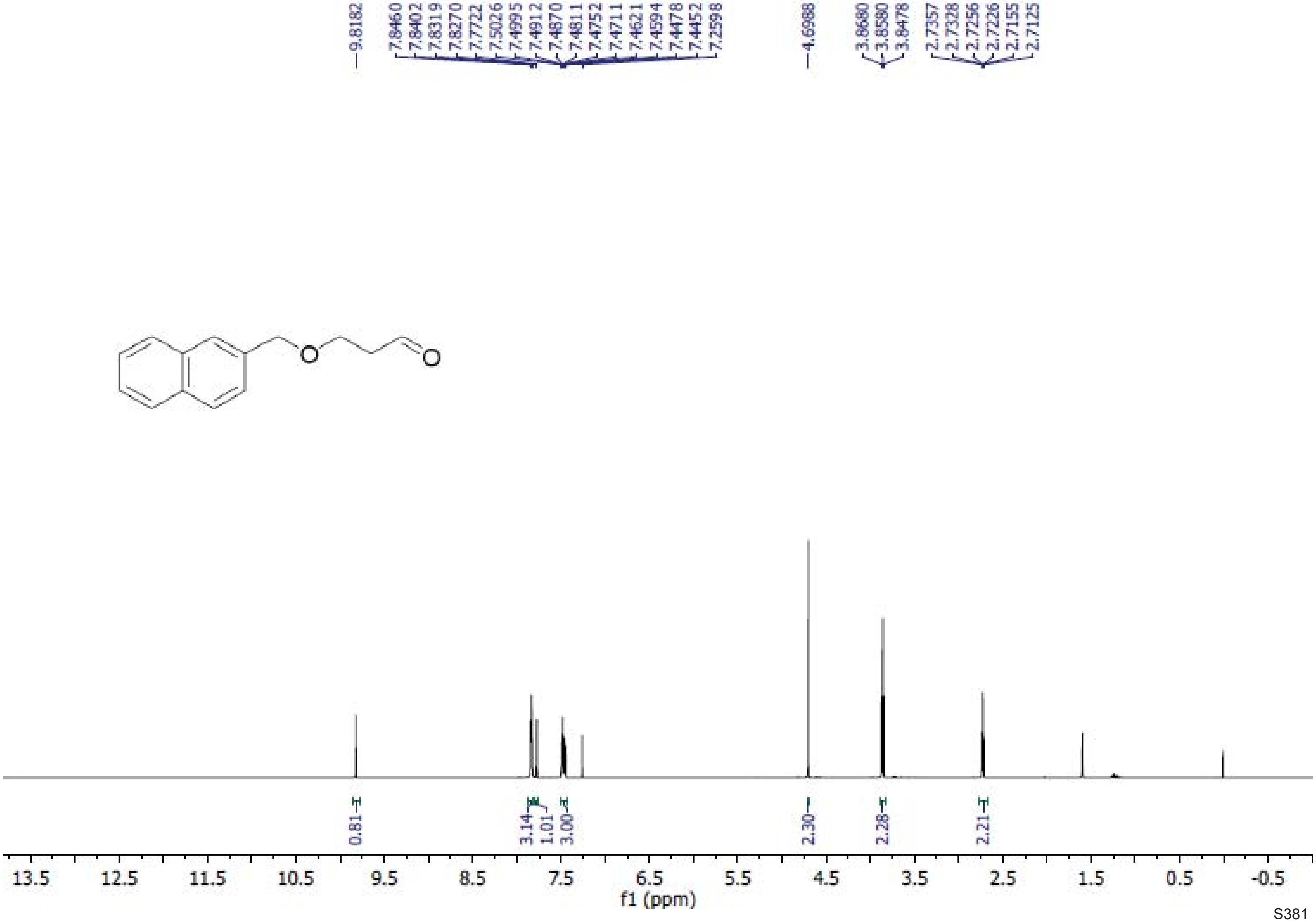
3-((3,5-dimethoxybenzyl)oxy)propanal



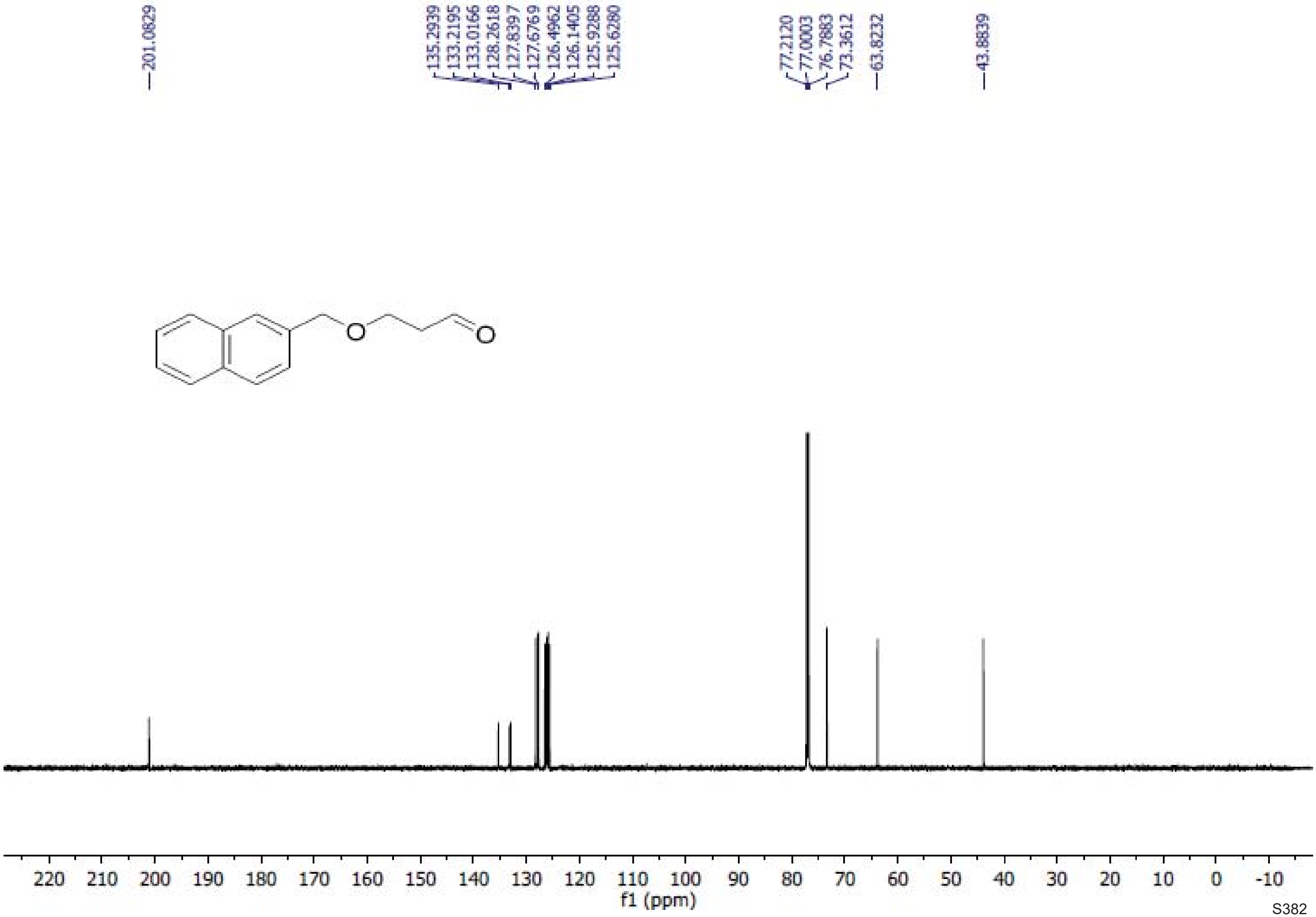
3-((3,5-dimethoxybenzyl)oxy)propanal



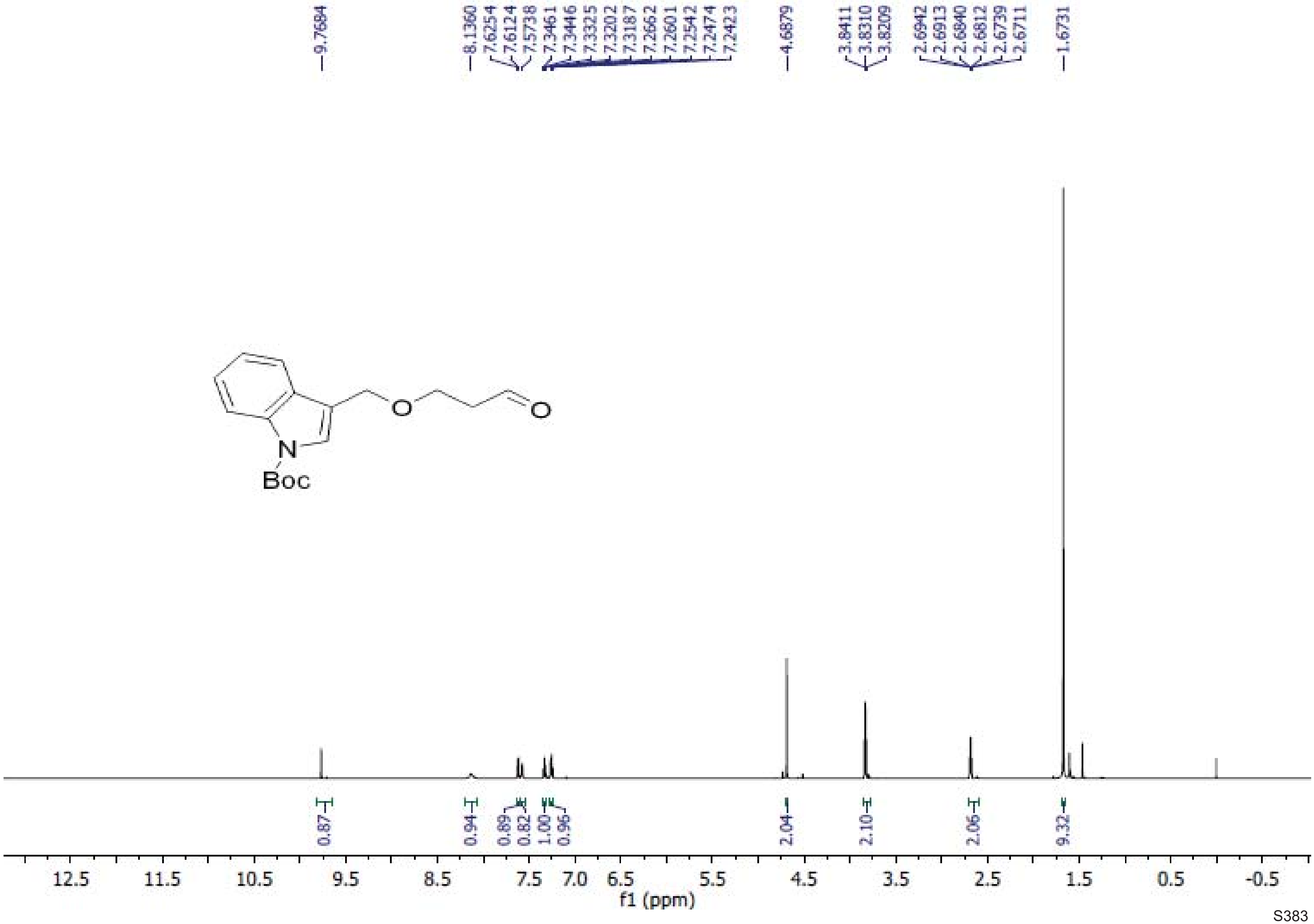
3-(naphthalen-2-ylmethoxy)propanal



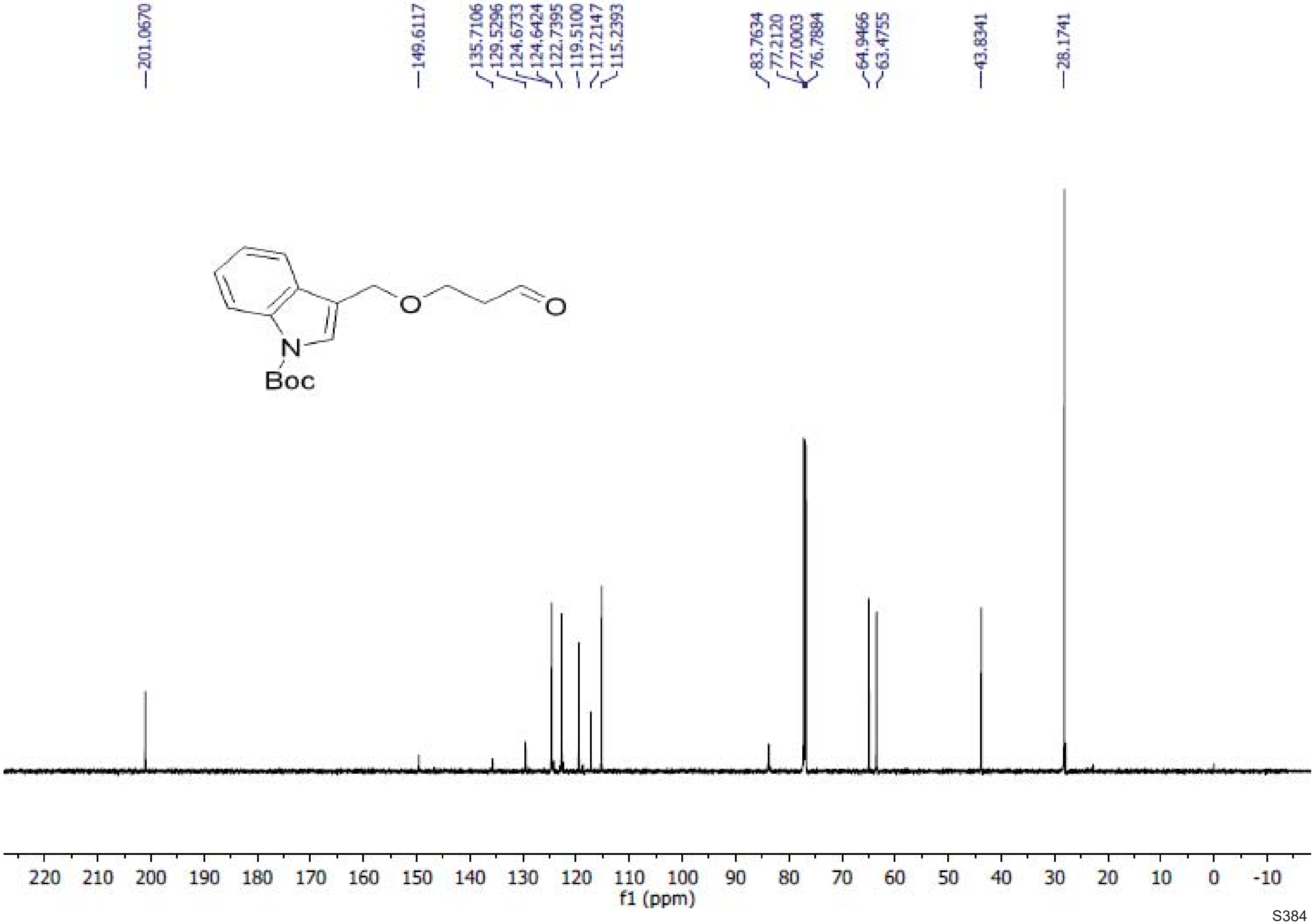
3-(naphthalen-2-ylmethoxy)propanal



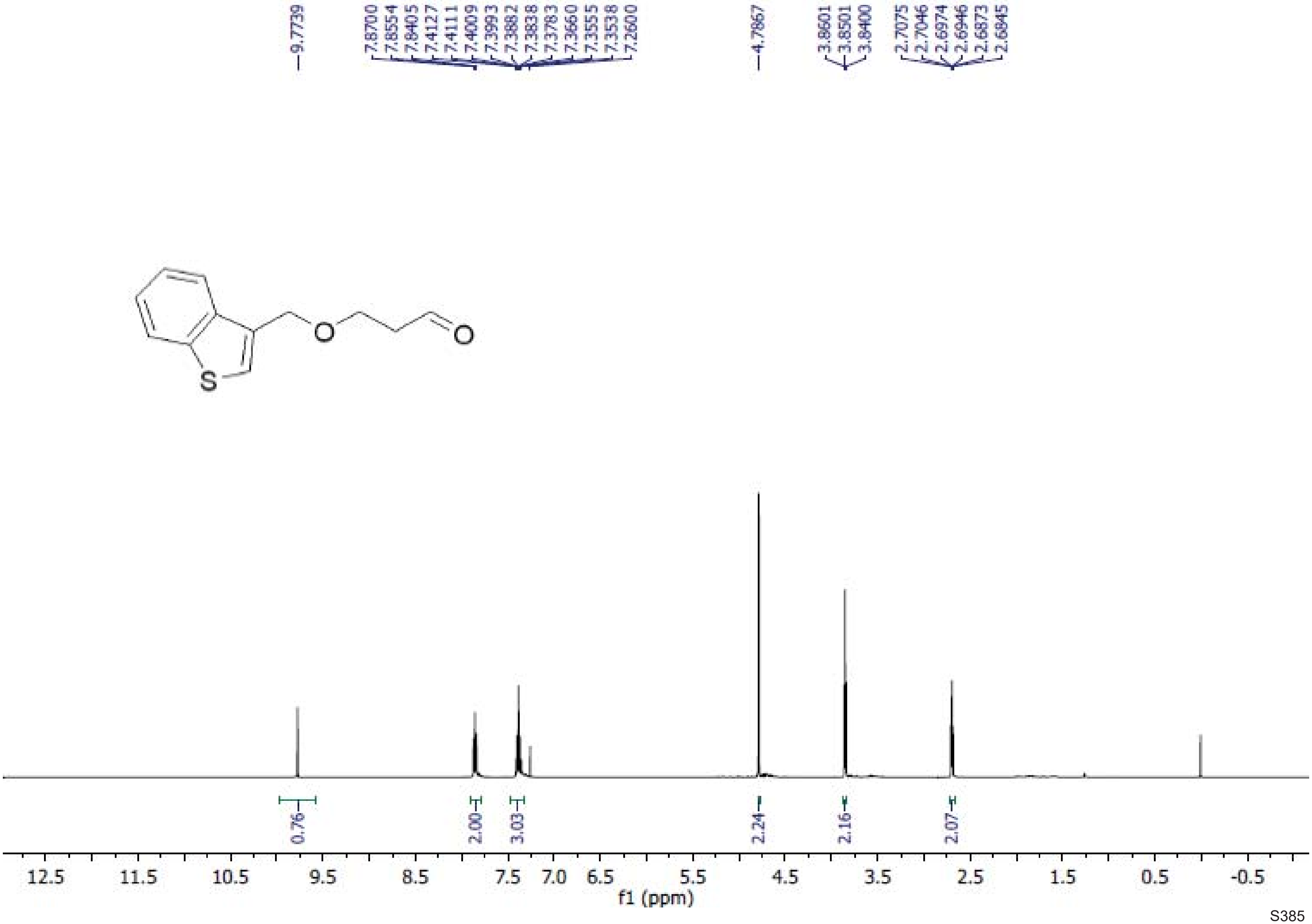
tert-butyl 3-((3-oxopropoxy)methyl)-1H-indole-1-carboxylate



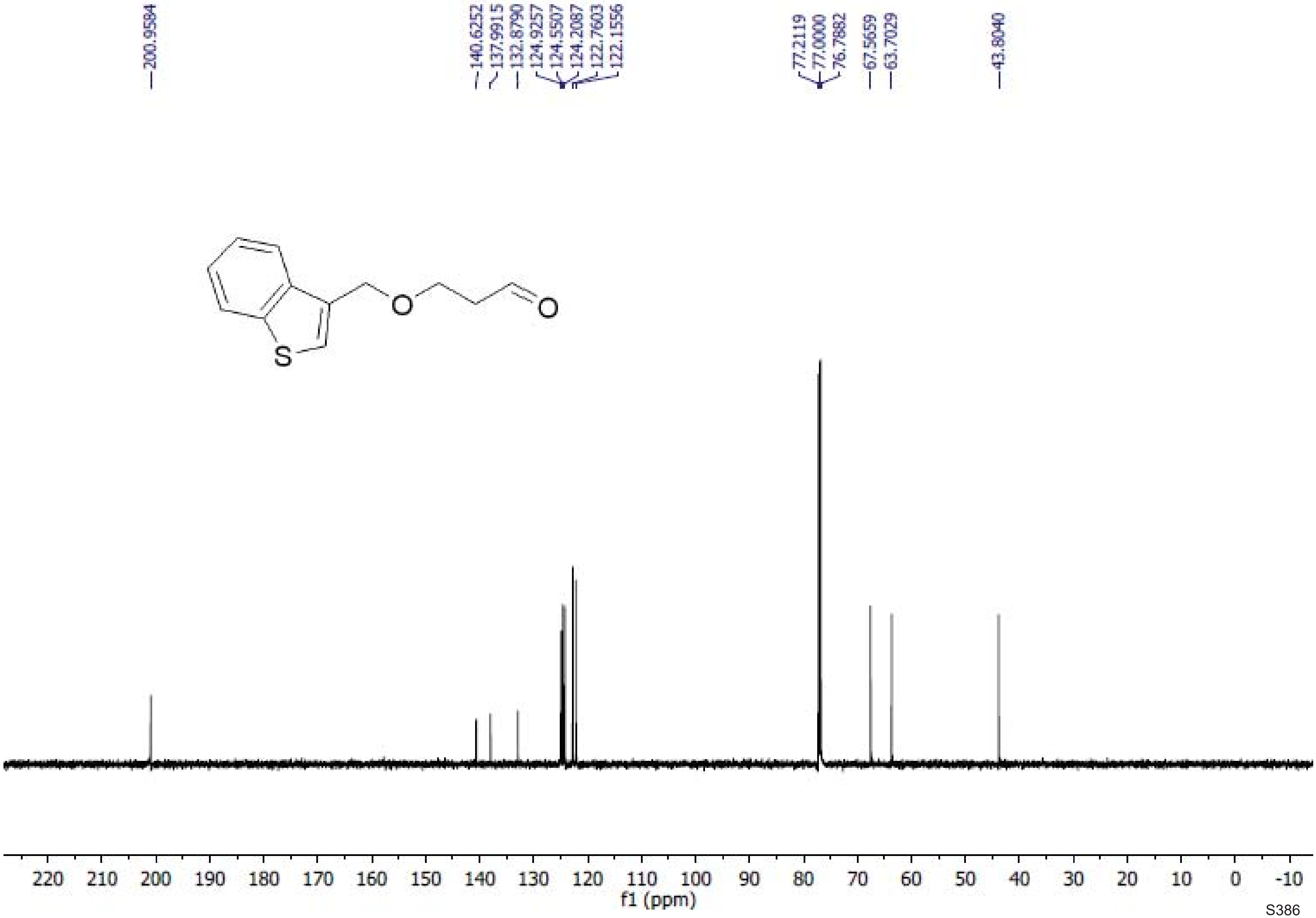
tert-butyl 3-((3-oxopropoxy)methyl)-1H-indole-1-carboxylate



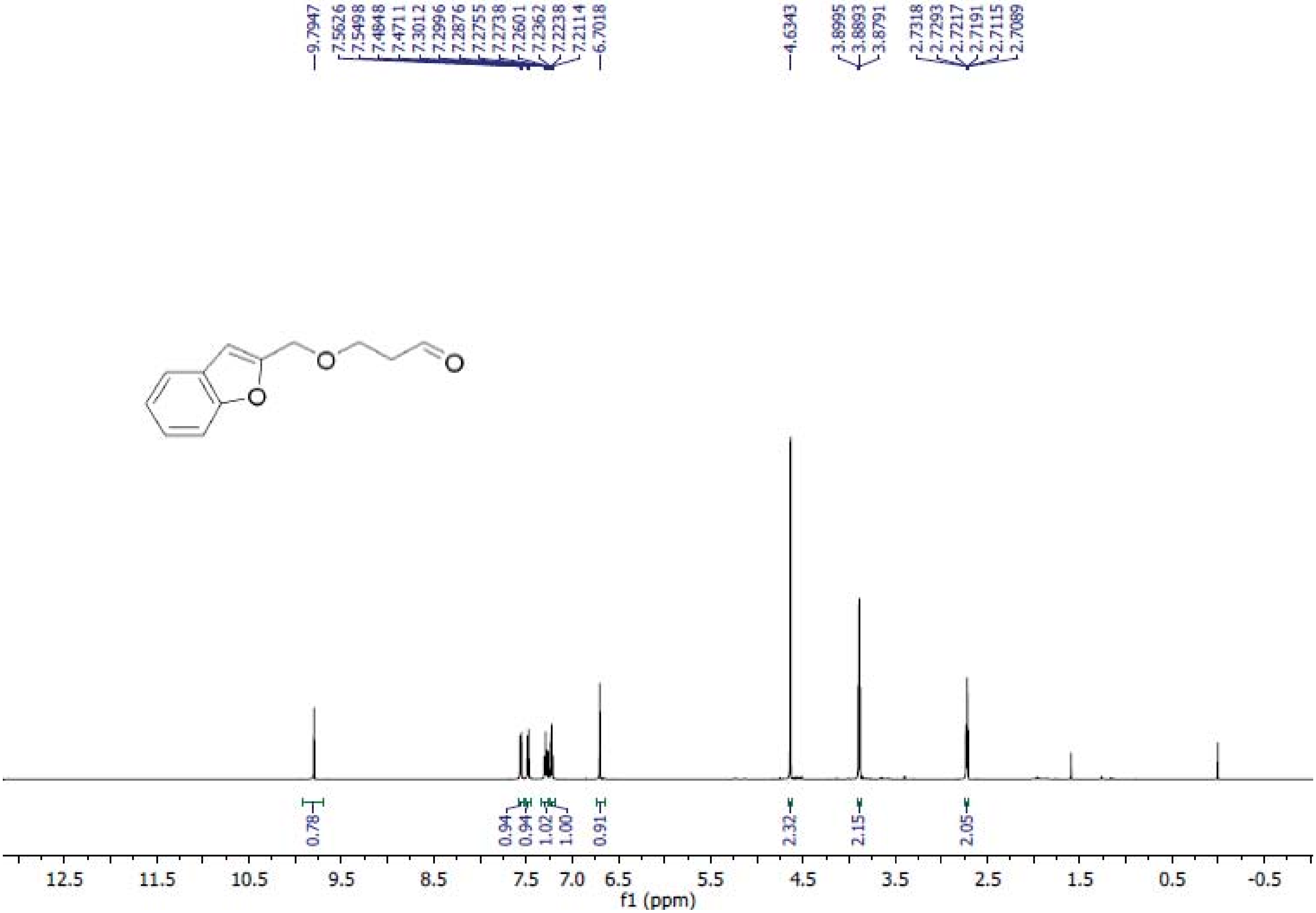
3-(benzo[b]thiophen-3-ylmethoxy)propanal



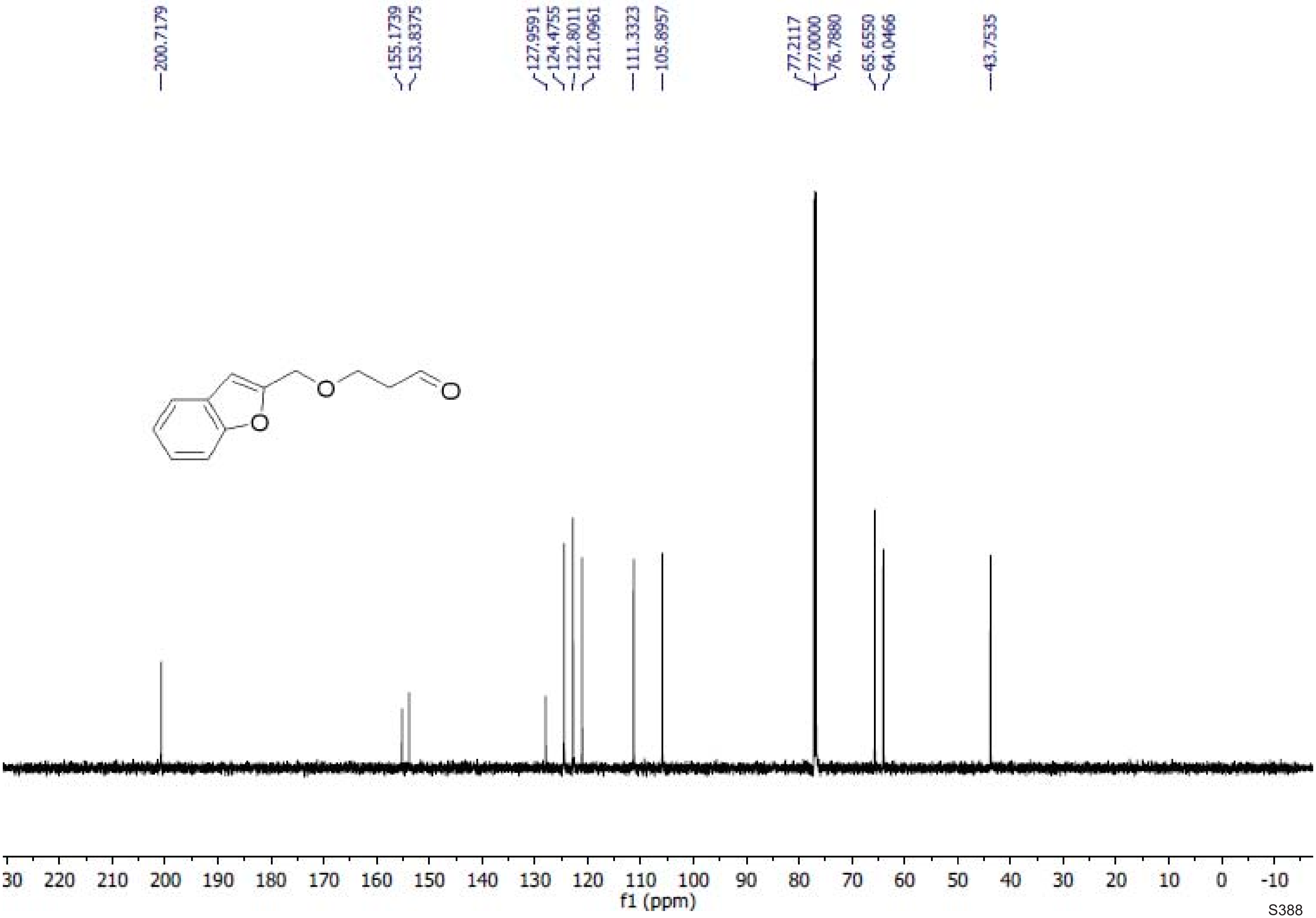
3-(benzo[b]thiophen-3-ylmethoxy)propanal



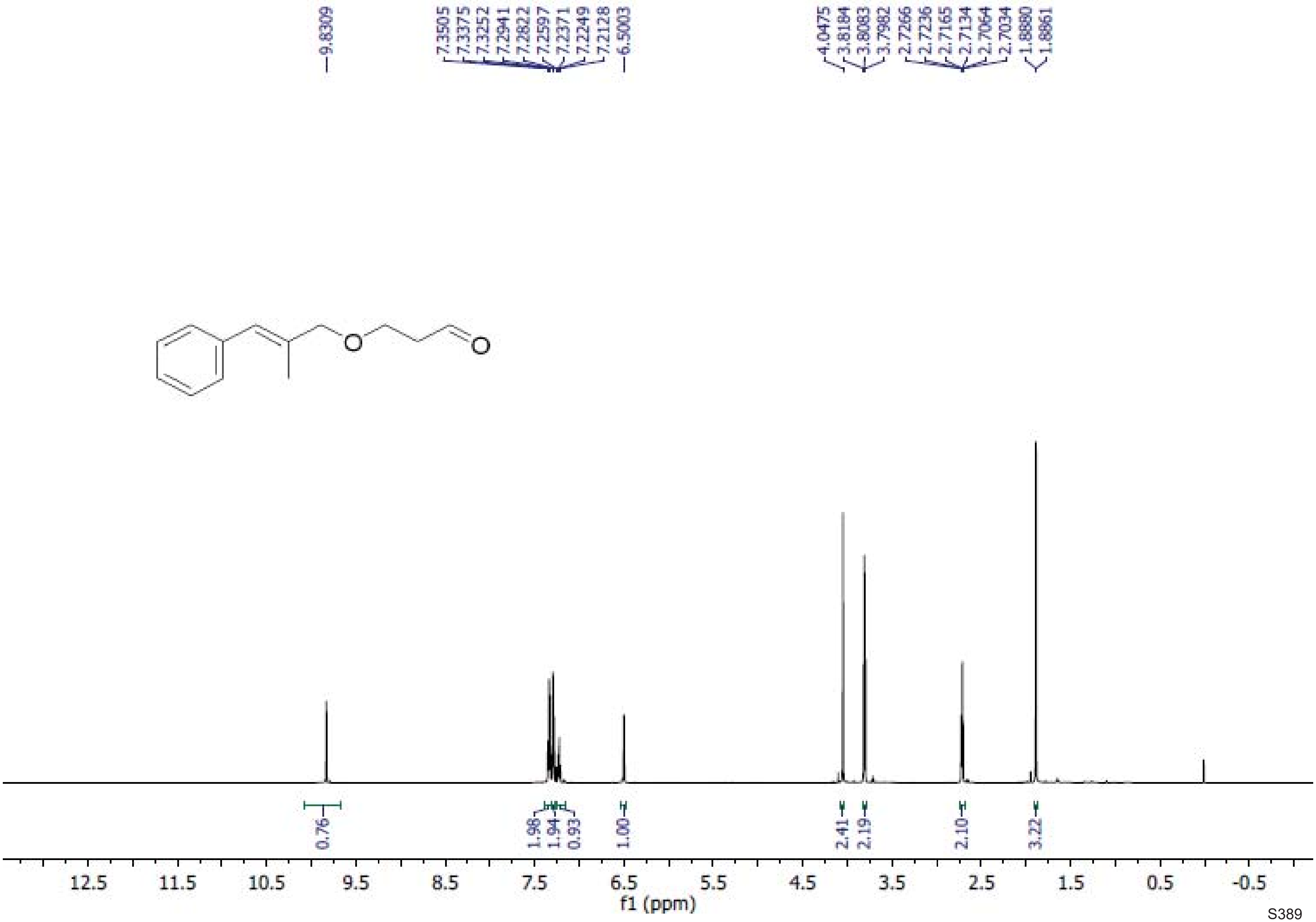
3-(benzofuran-2-ylmethoxy)propanal



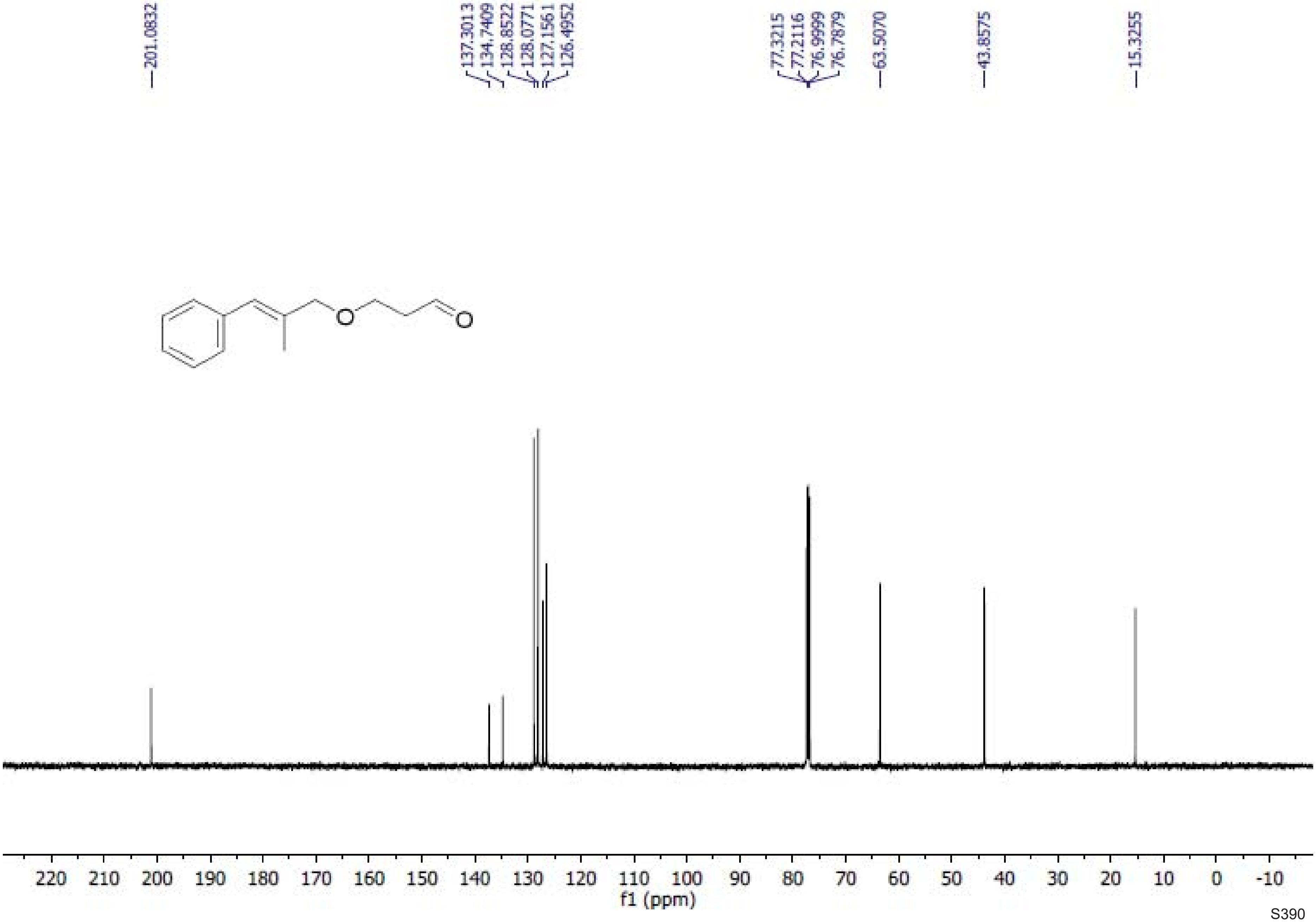
3-(benzofuran-2-ylmethoxy)propanal



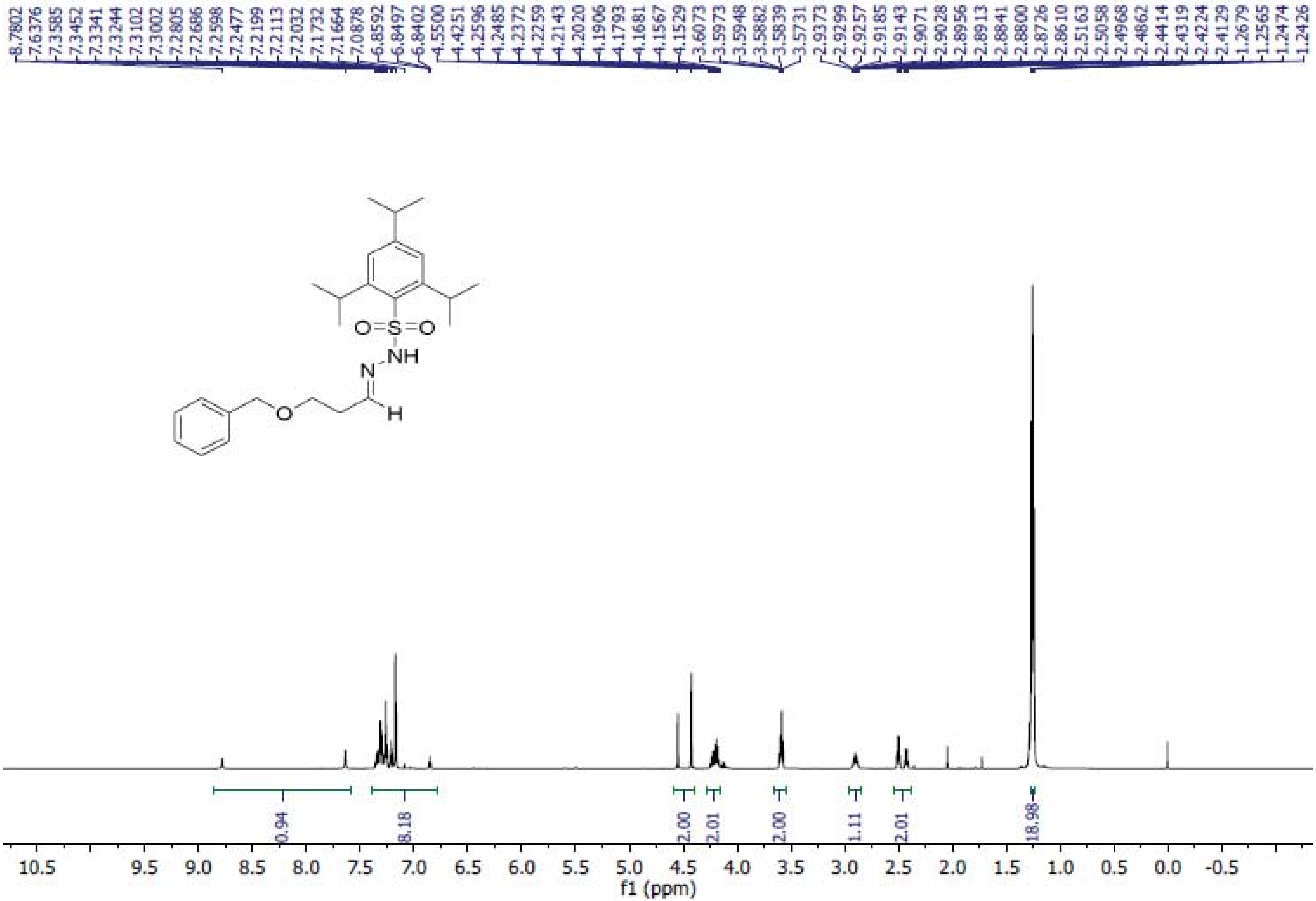
(E)-3-((2-methyl-3-phenylallyl)oxy)propanal



(E)-3-((2-methyl-3-phenylallyl)oxy)propanal

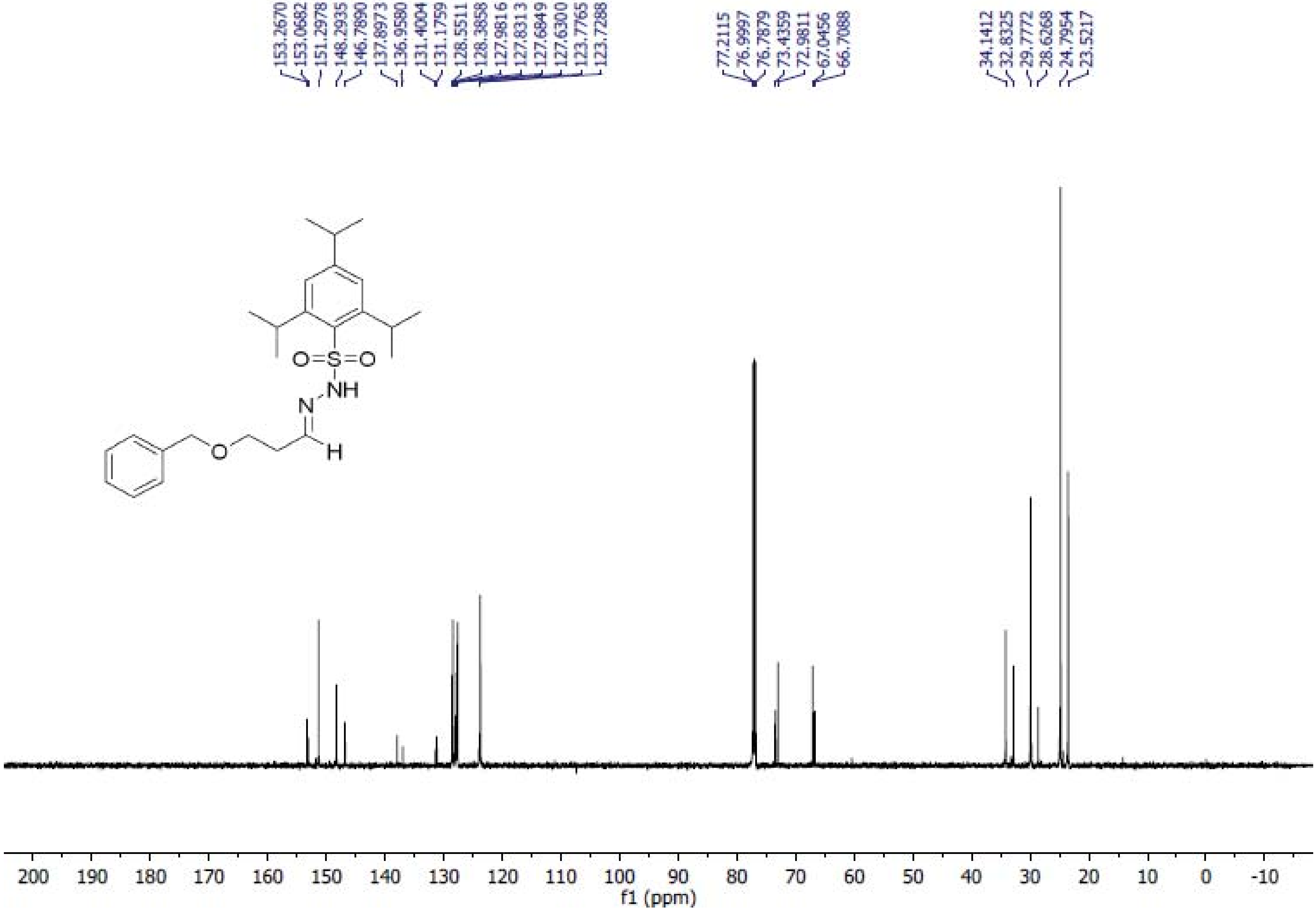


N'-(3-(benzyloxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



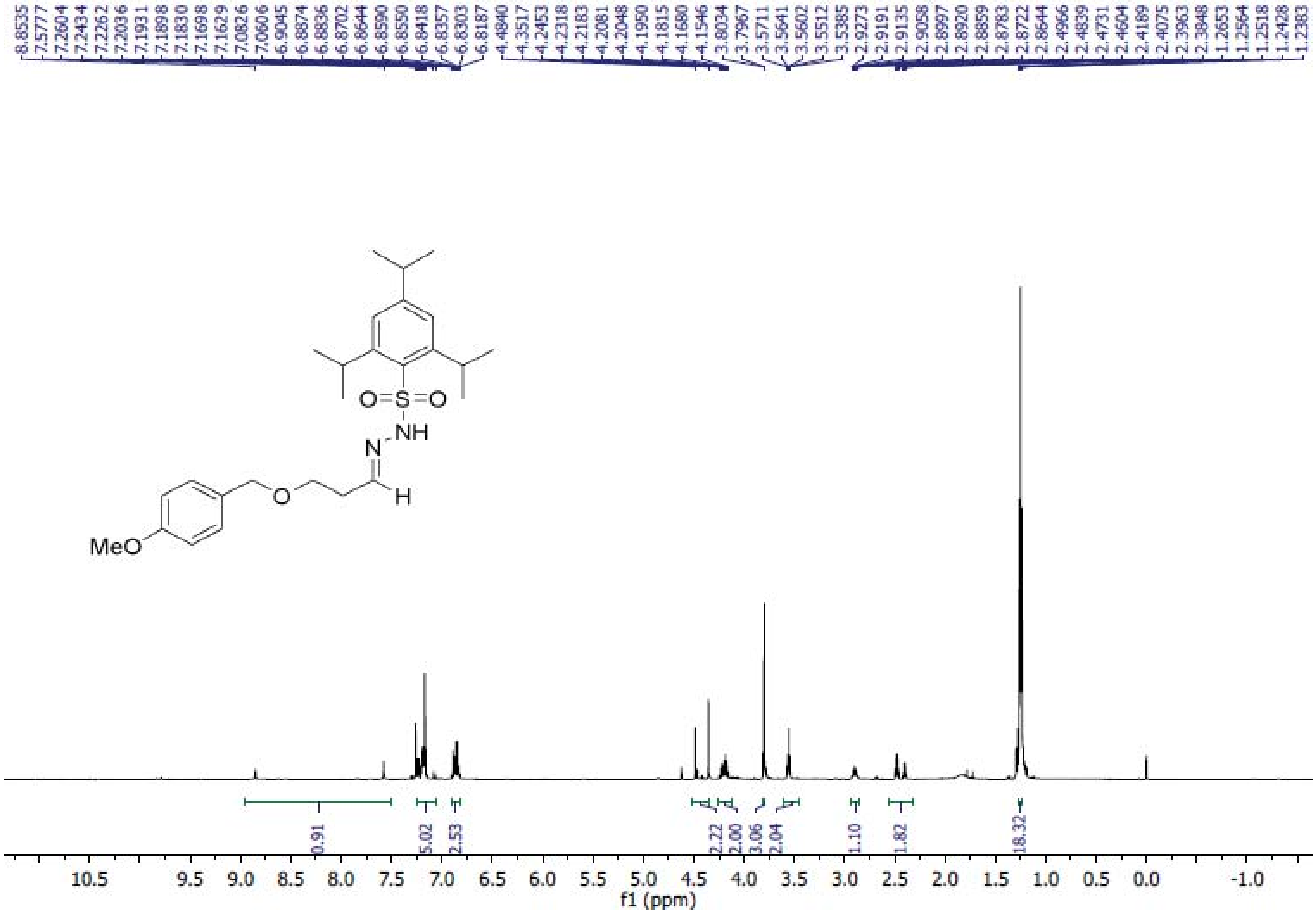
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-(benzyloxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



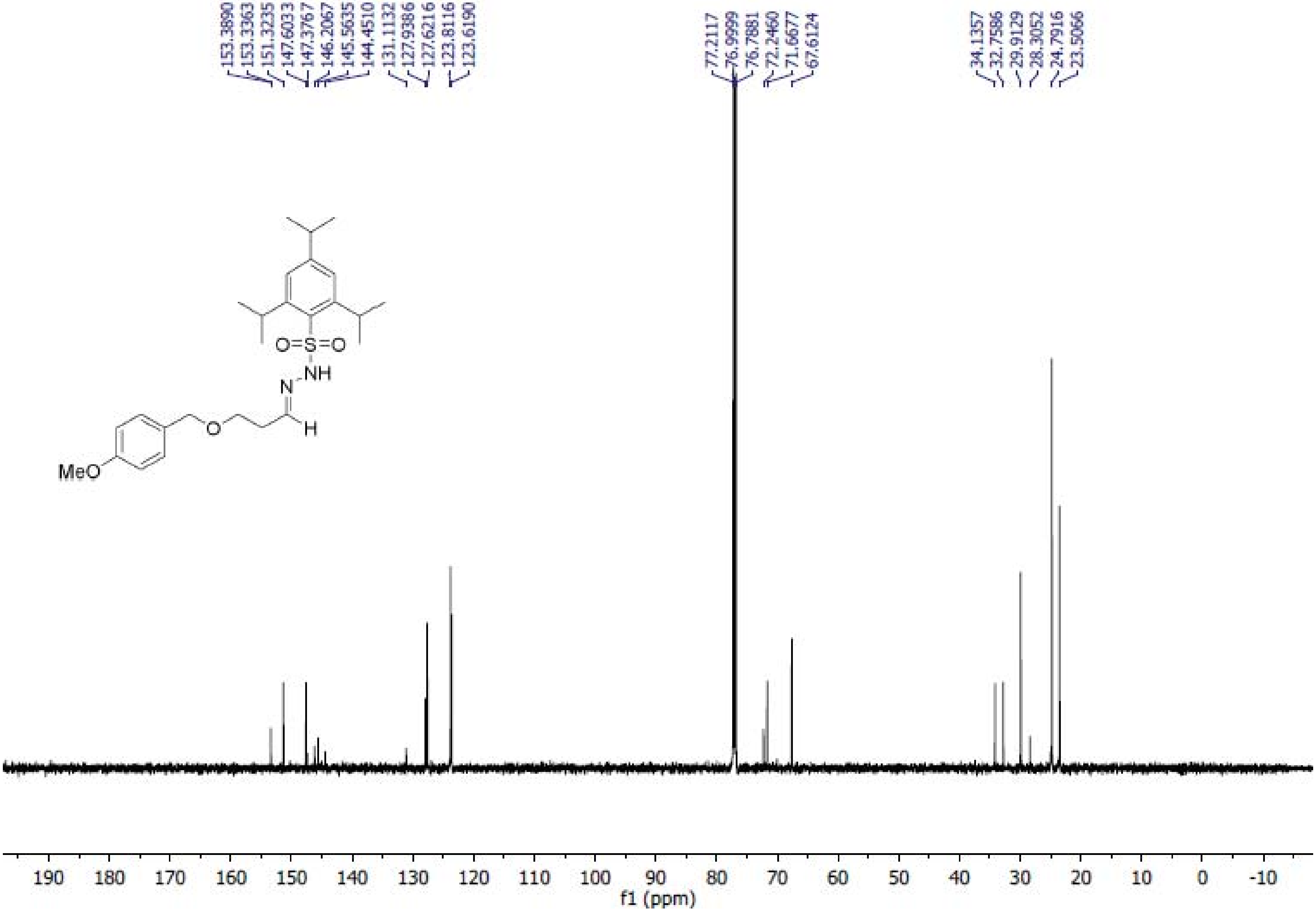
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-N'-(3-((4-methoxybenzyl)oxy)propylidene)benzenesulfonohydrazide



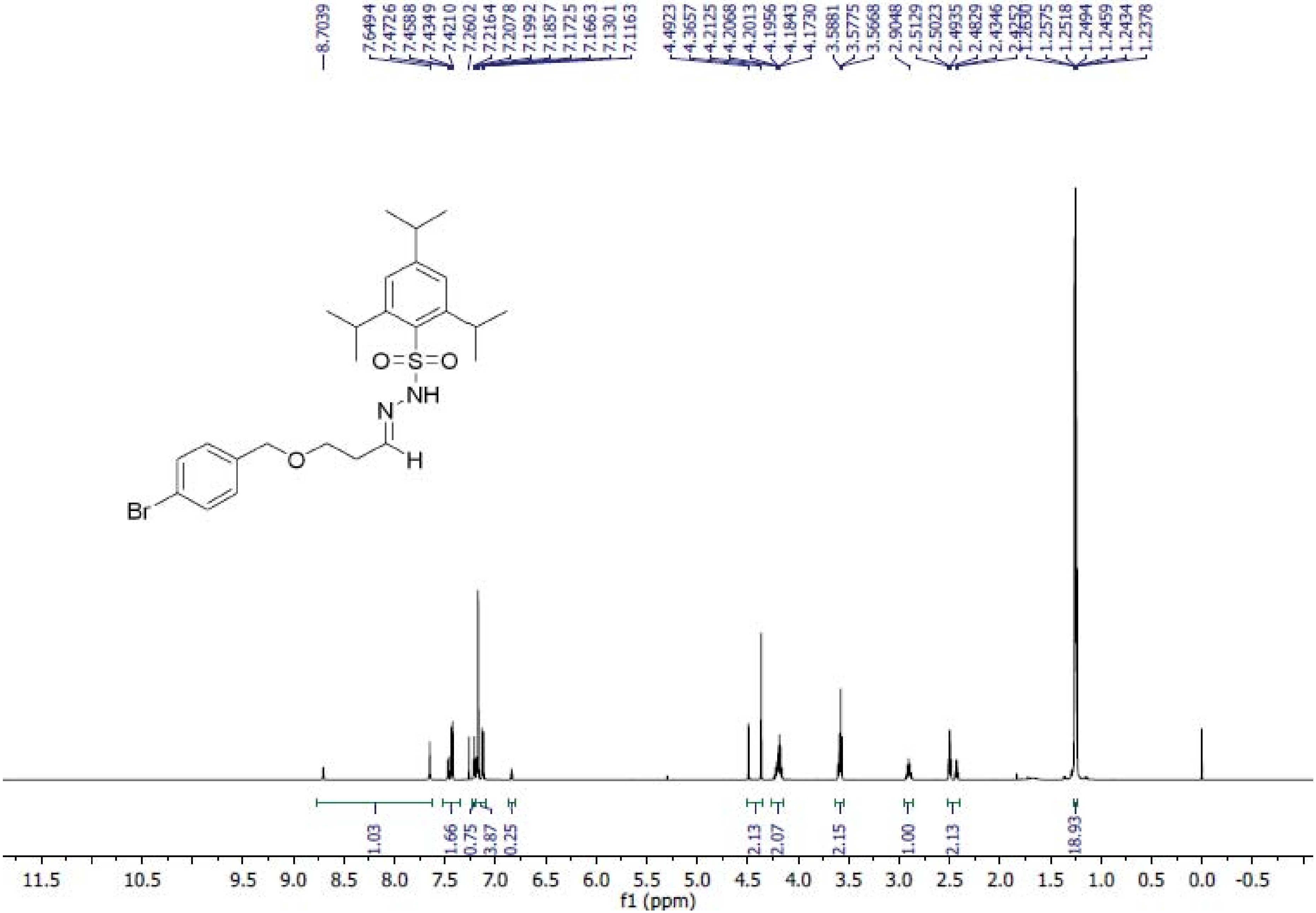
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-N'-(3-((4-methoxybenzyl)oxy)propylidene)benzenesulfonohydrazide



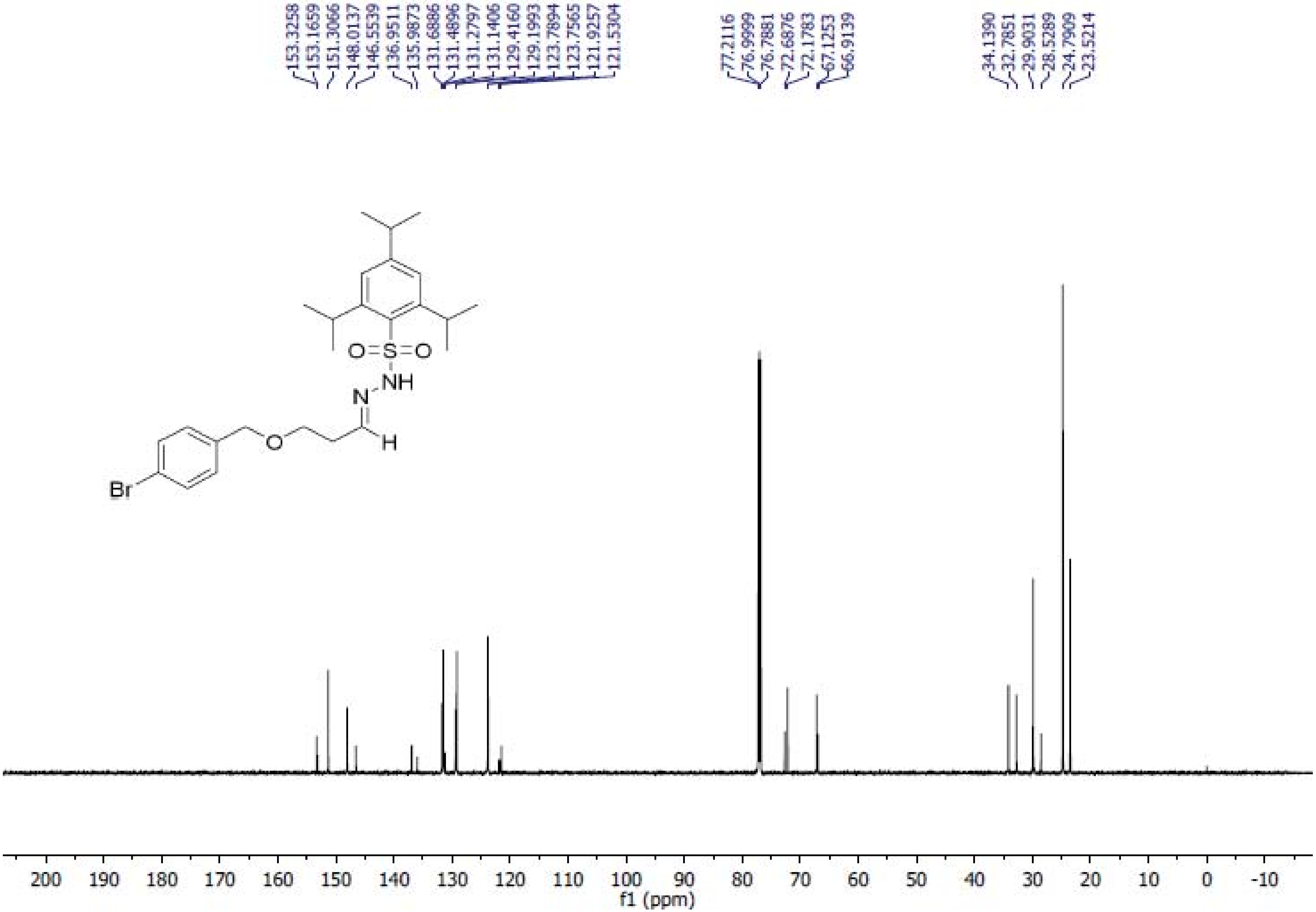
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((4-bromobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



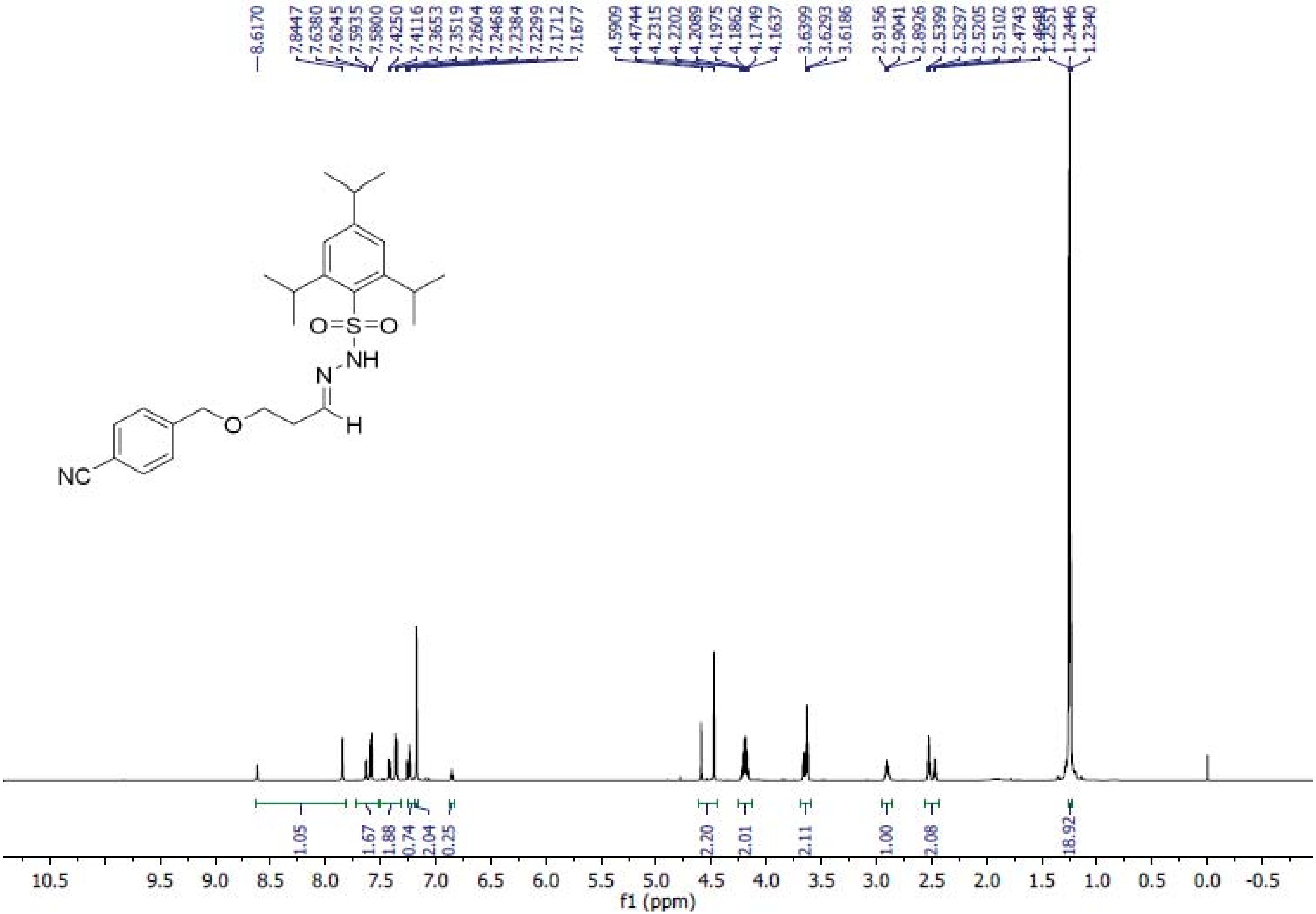
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((4-bromobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



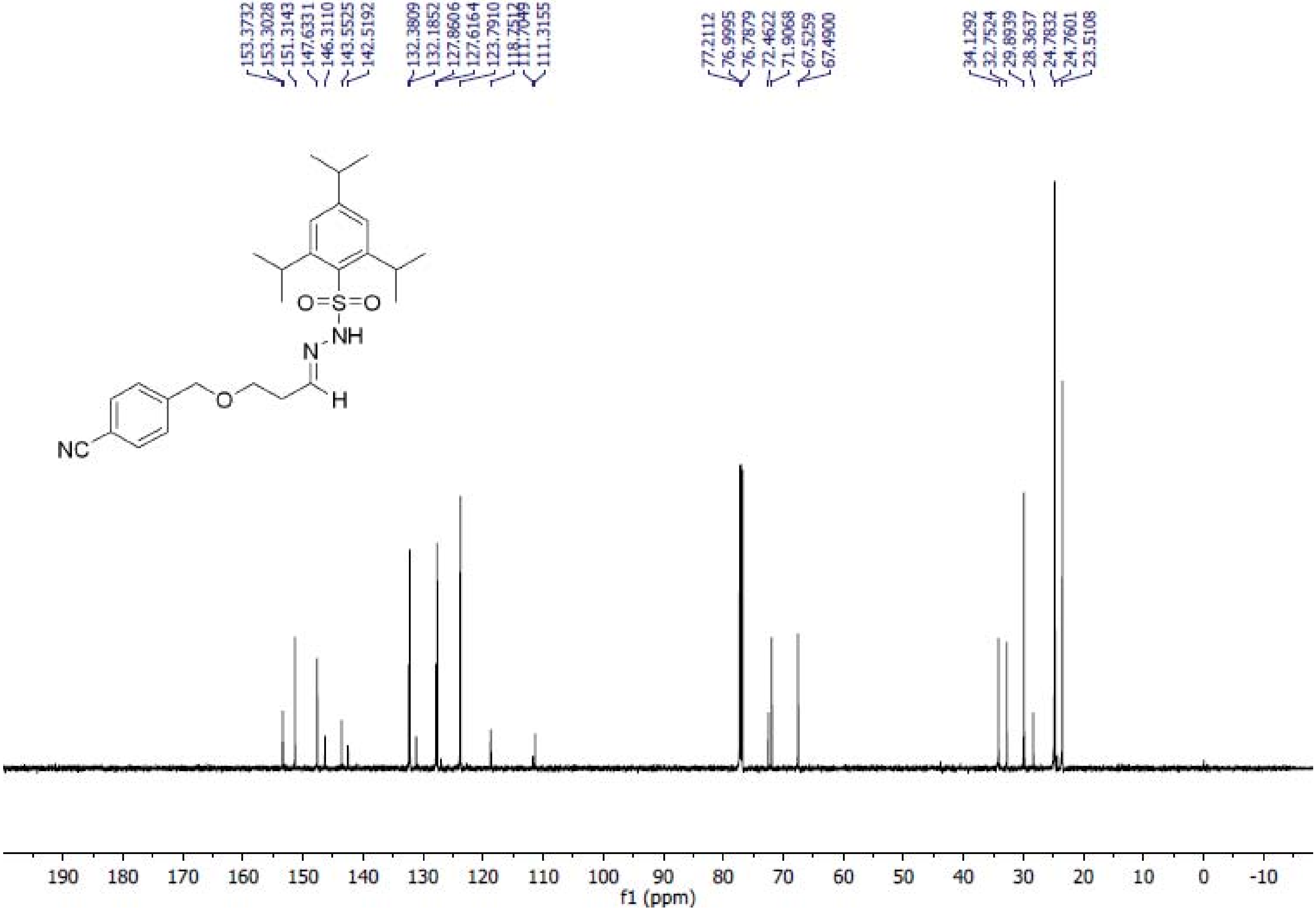
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((4-cyanobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



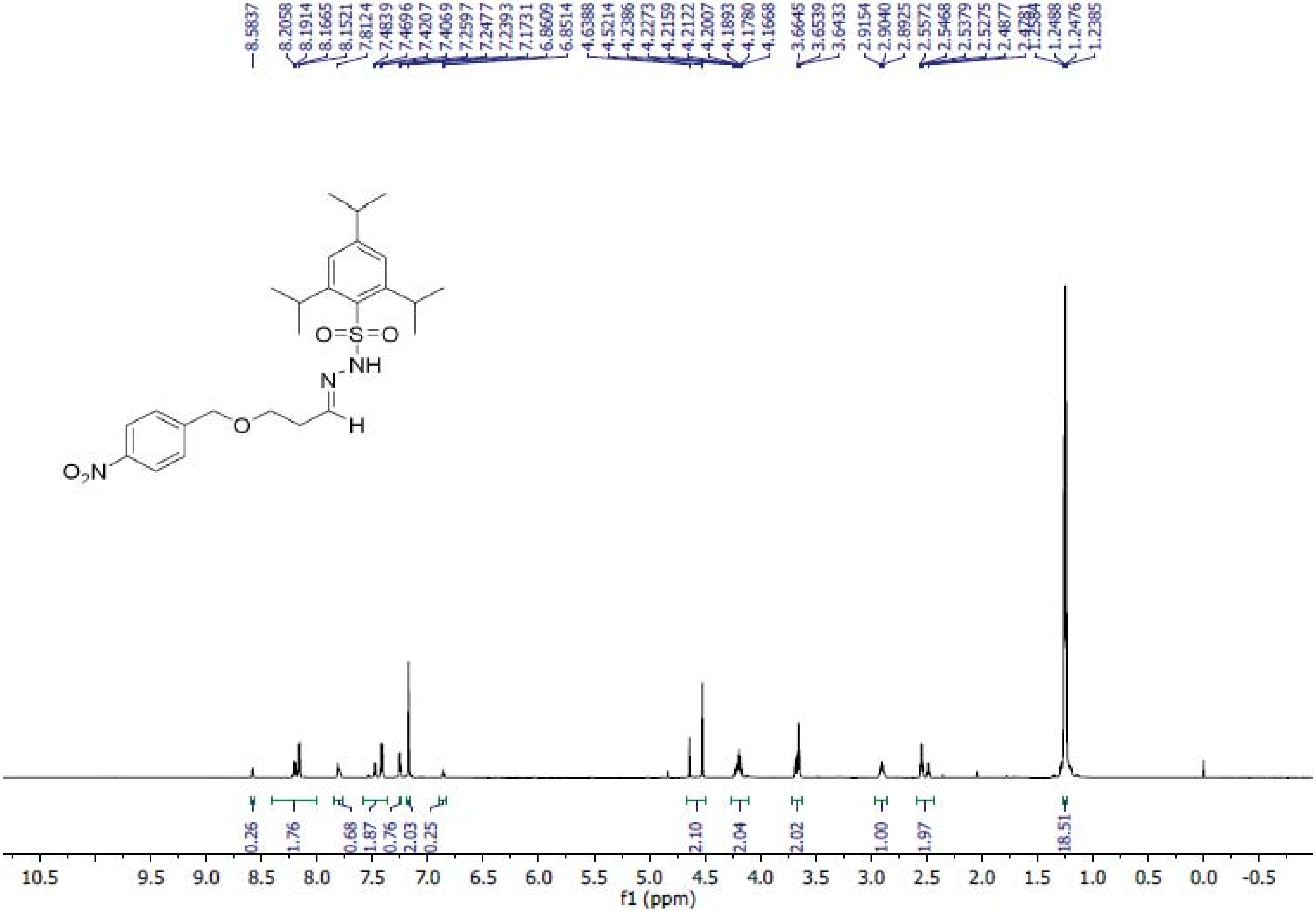
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((4-cyanobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



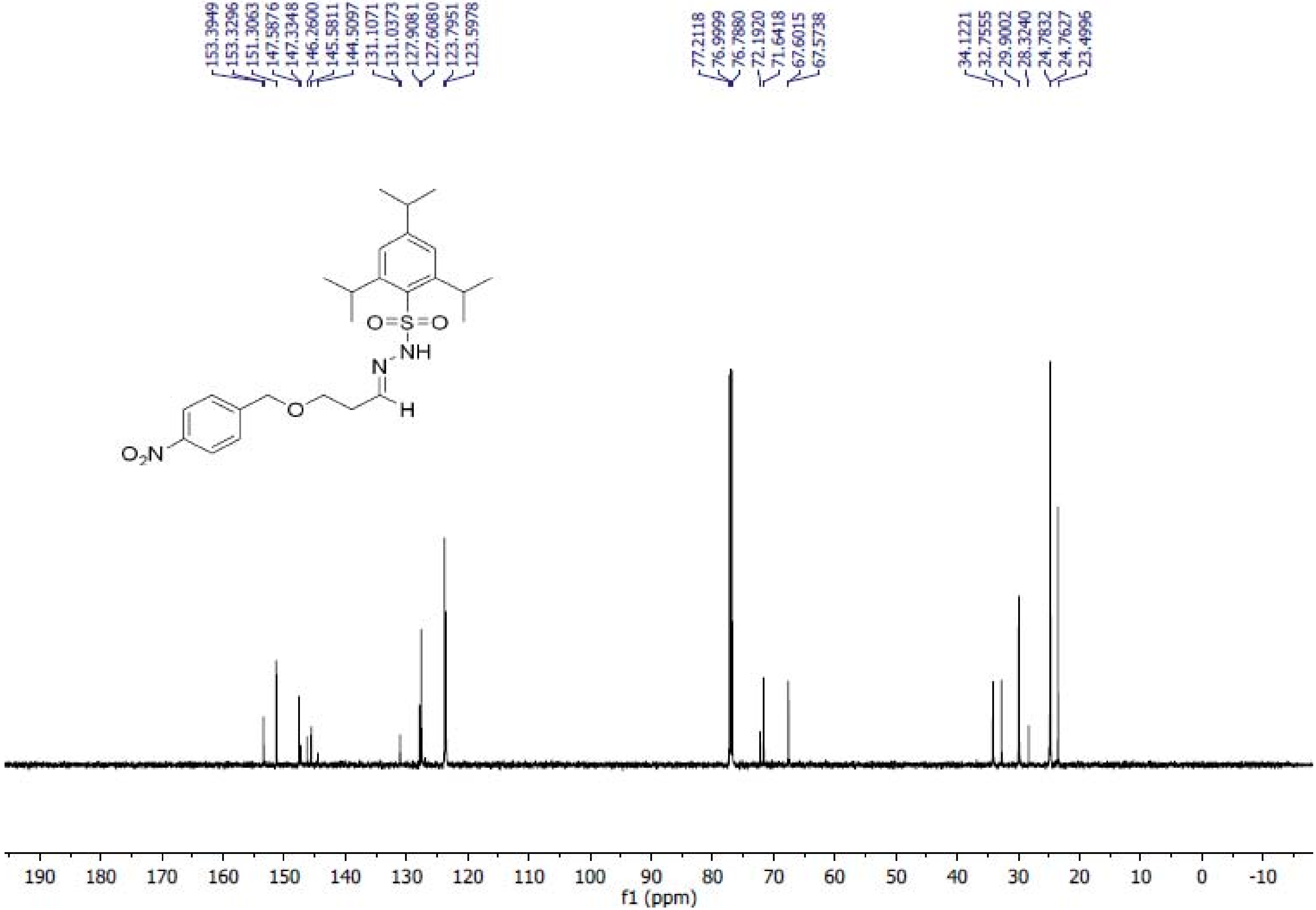
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-N'-(3-((4-nitrobenzyl)oxy)propylidene)benzenesulfonohydrazide



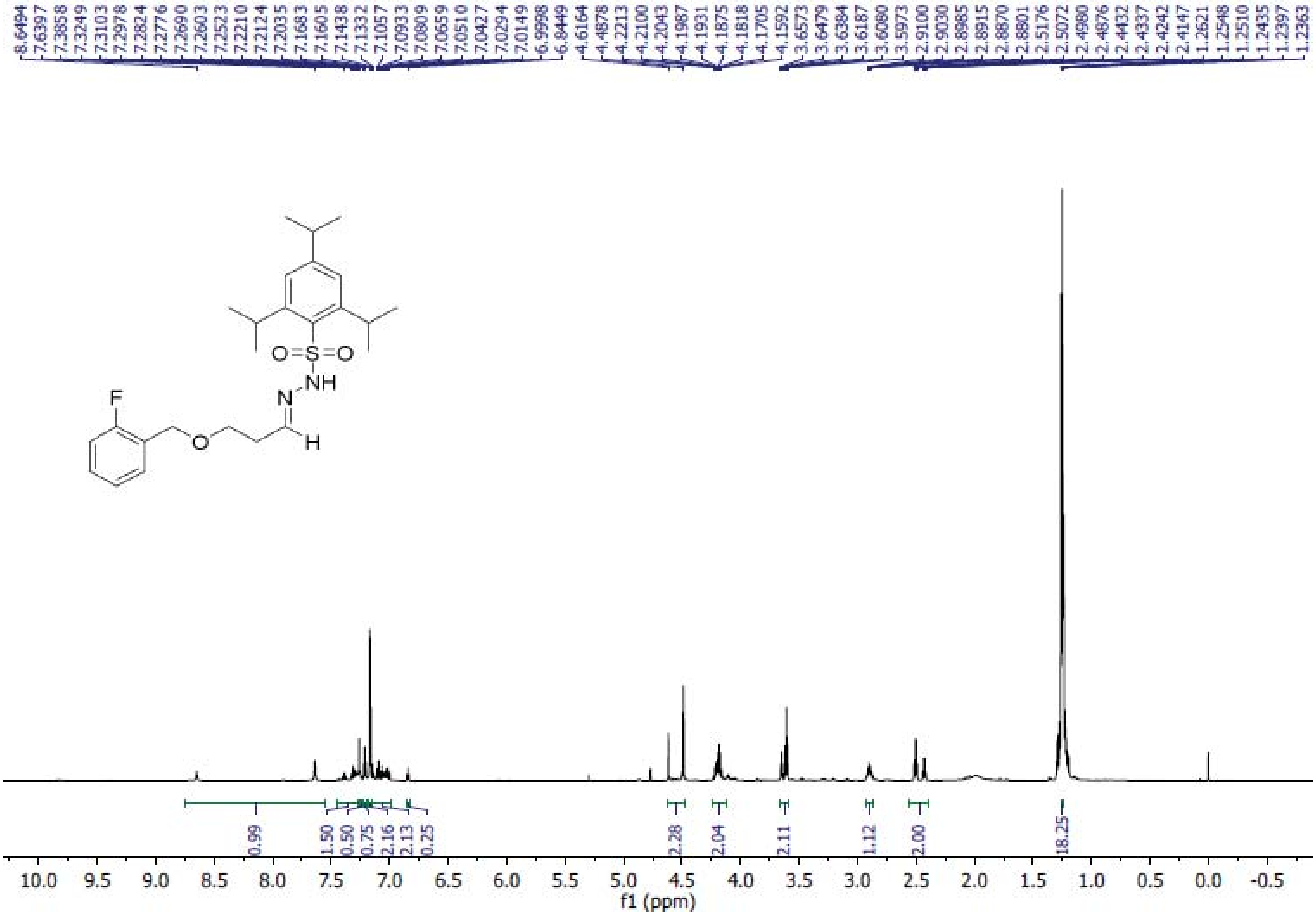
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-N'-(3-((4-nitrobenzyl)oxy)propylidene)benzenesulfonohydrazide



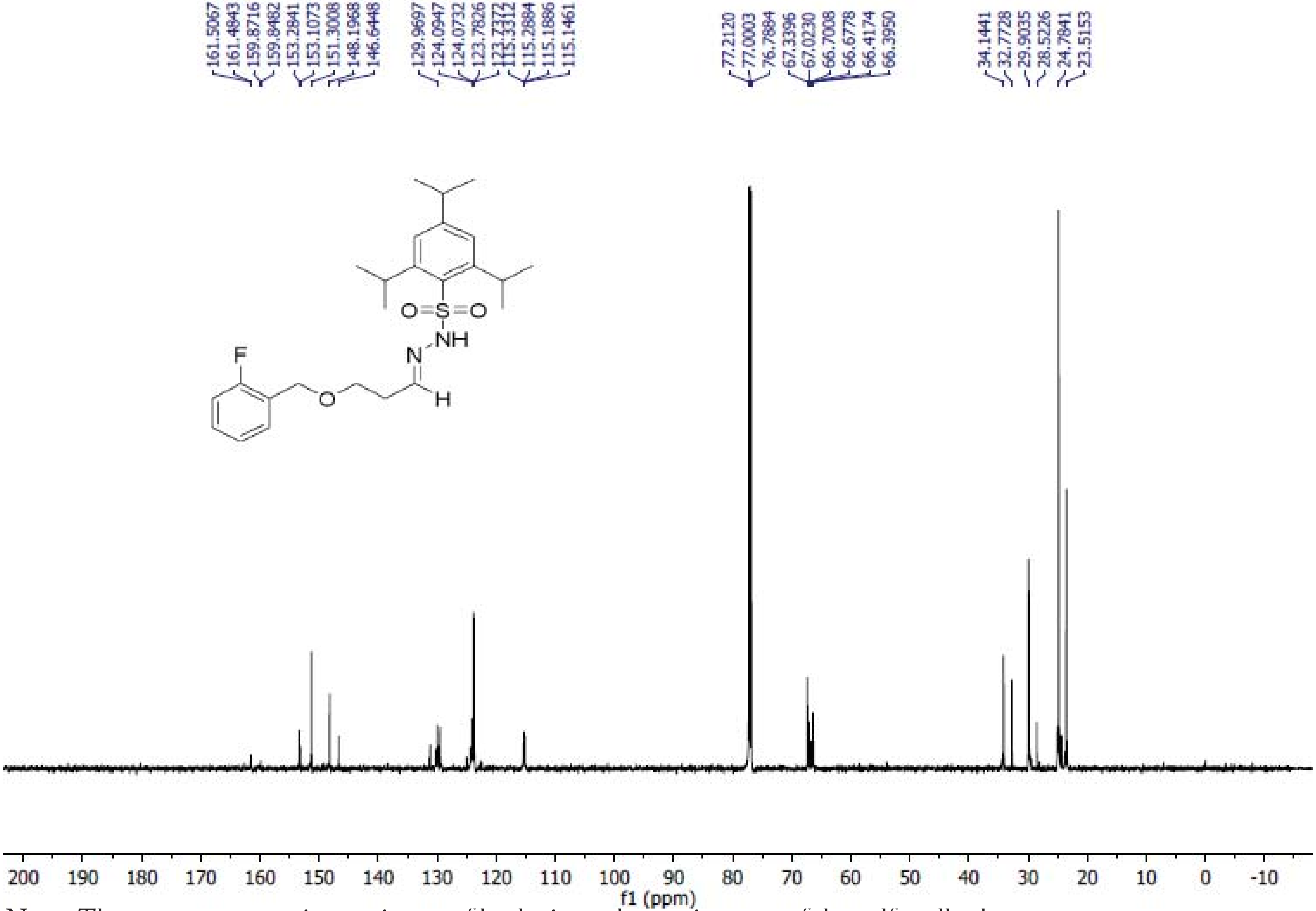
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((2-fluorobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



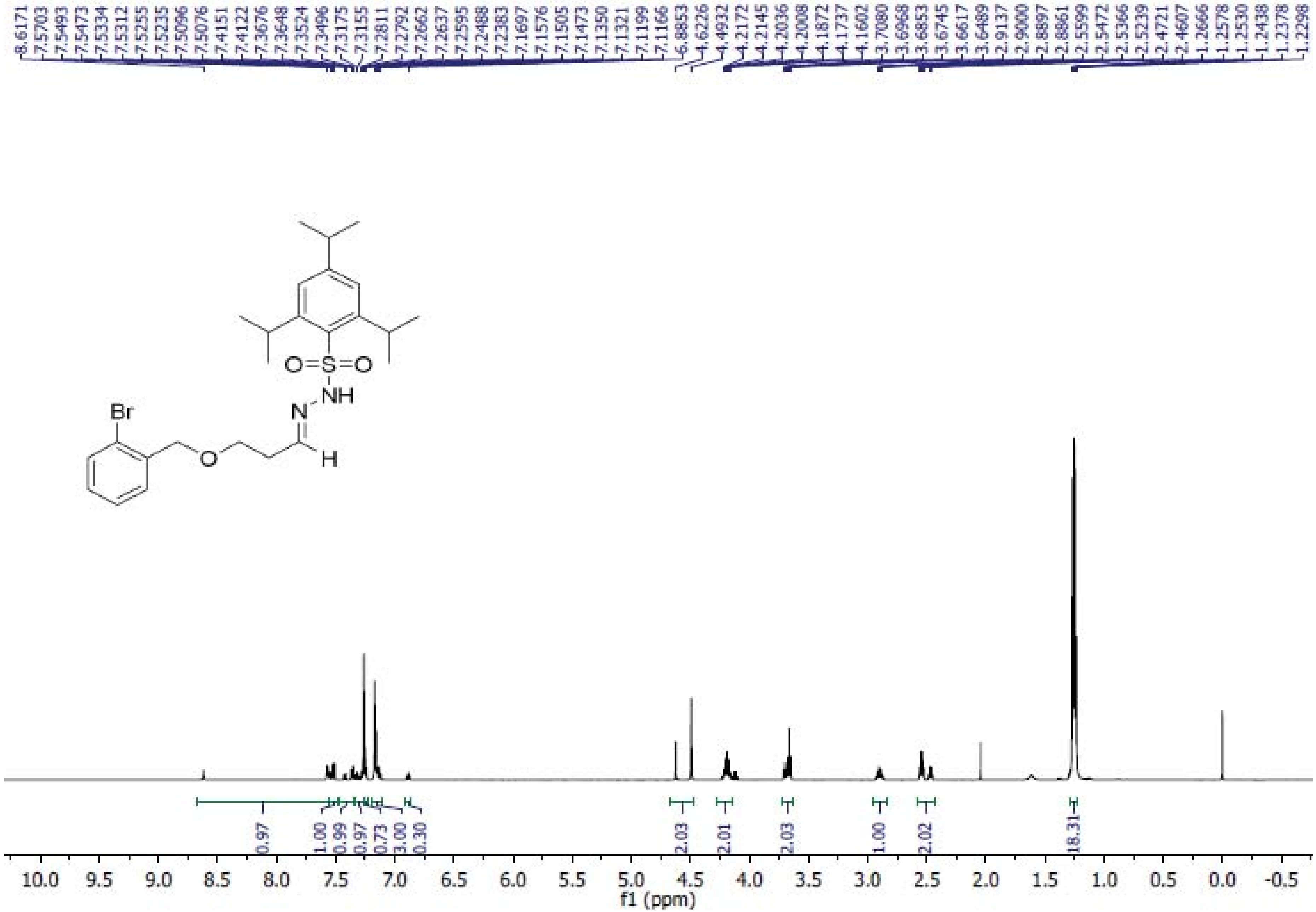
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((2-fluorobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



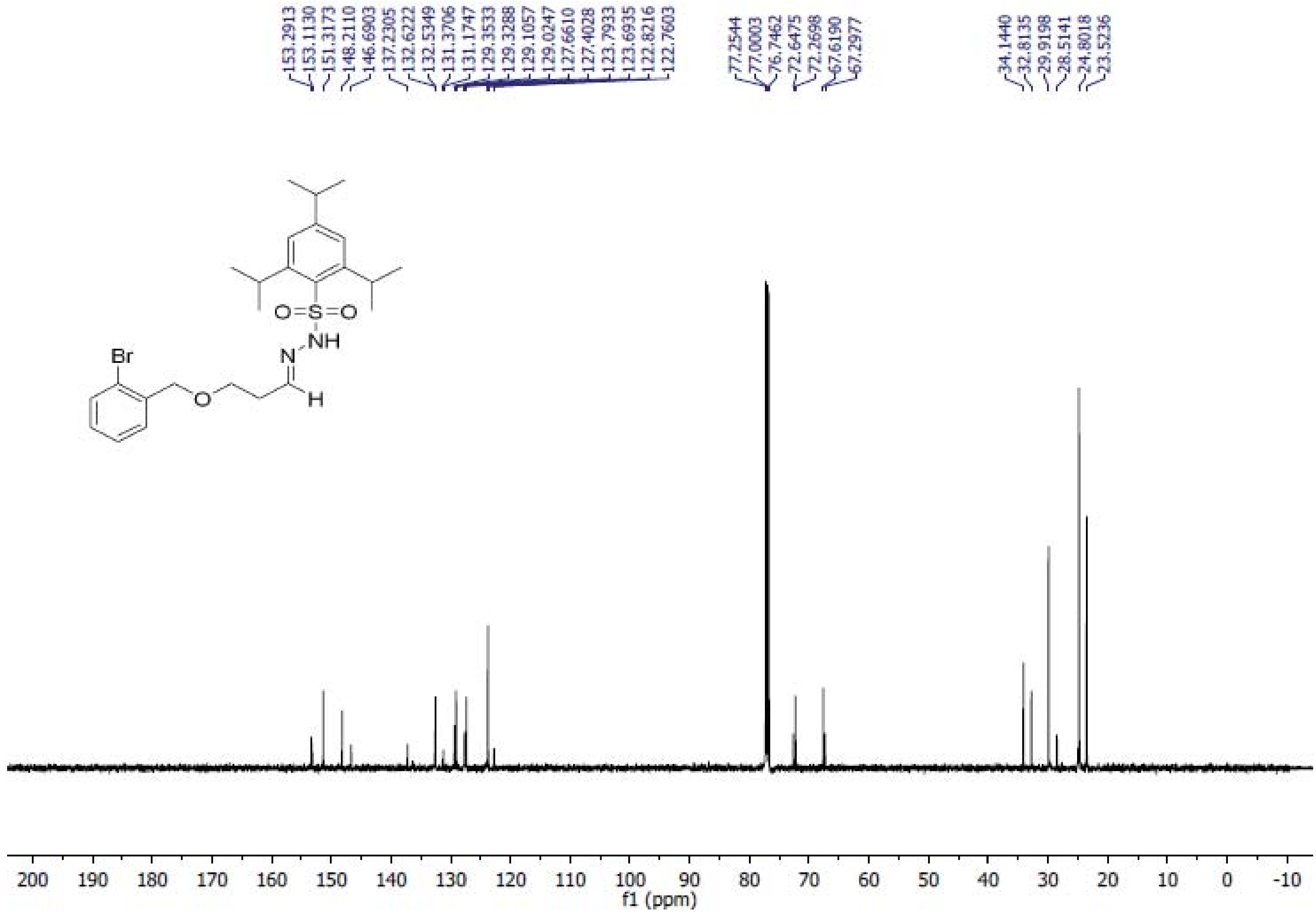
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((2-bromobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



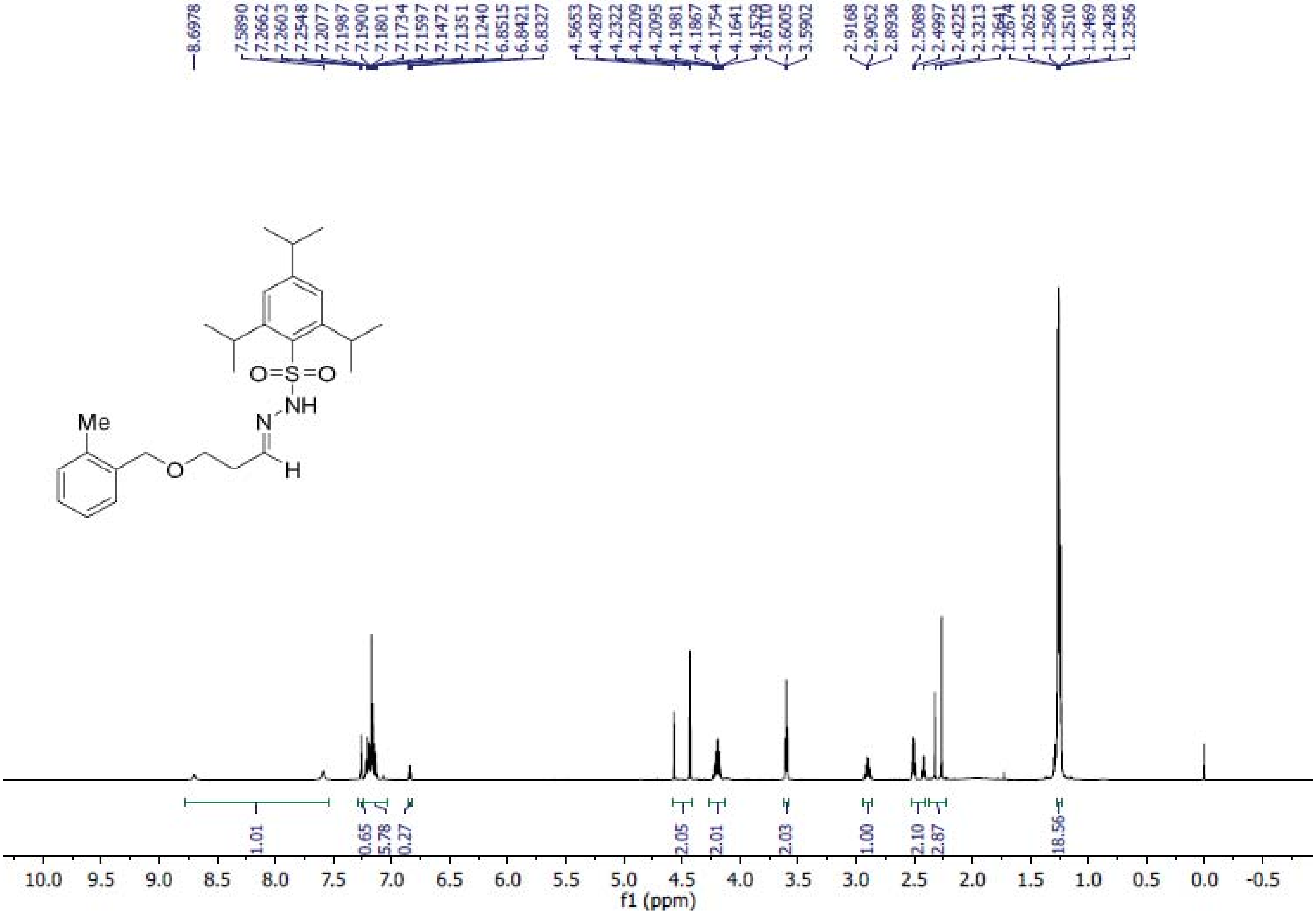
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((2-bromobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



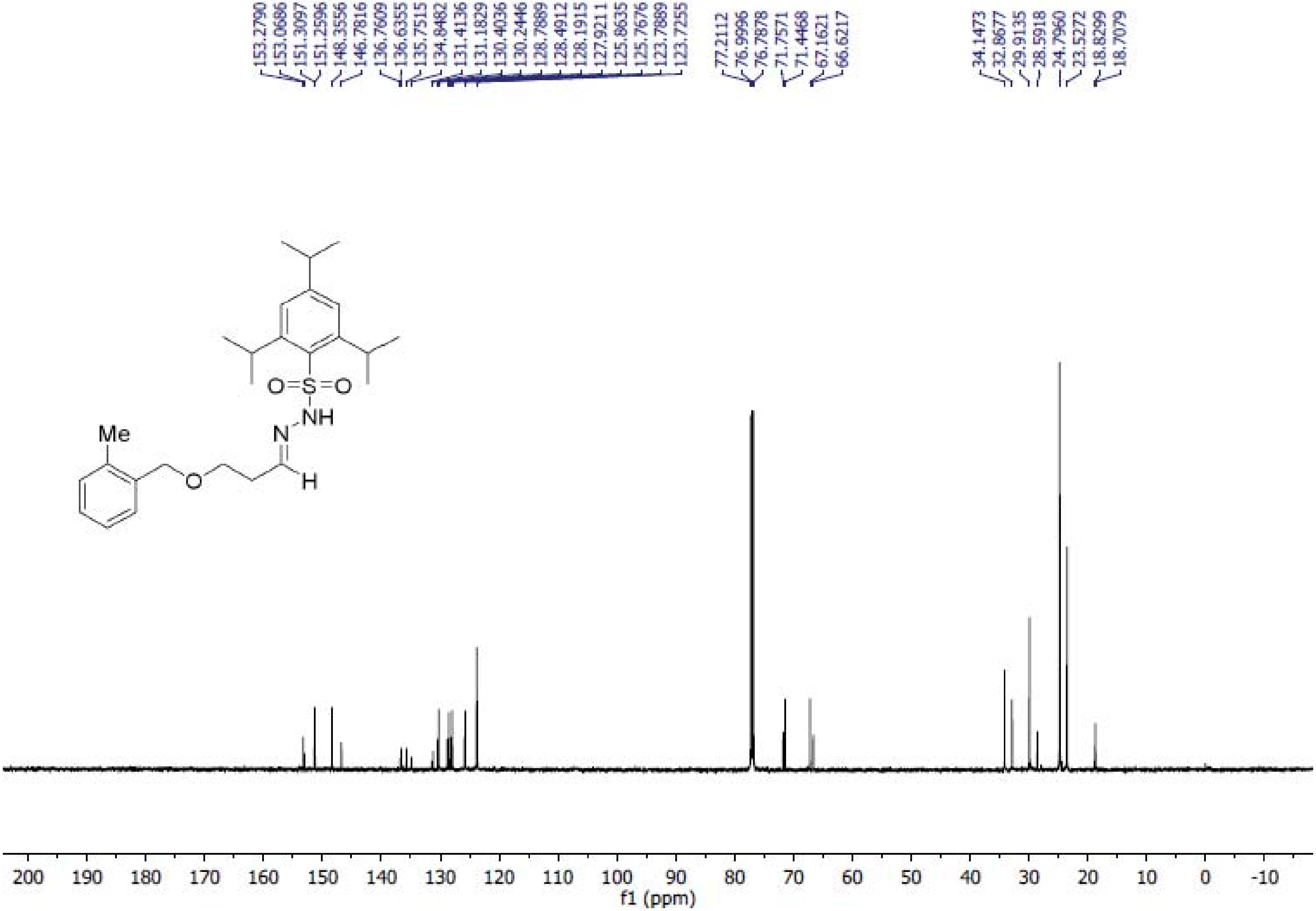
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-N'-(3-((2-methylbenzyl)oxy)propylidene)benzenesulfonohydrazide



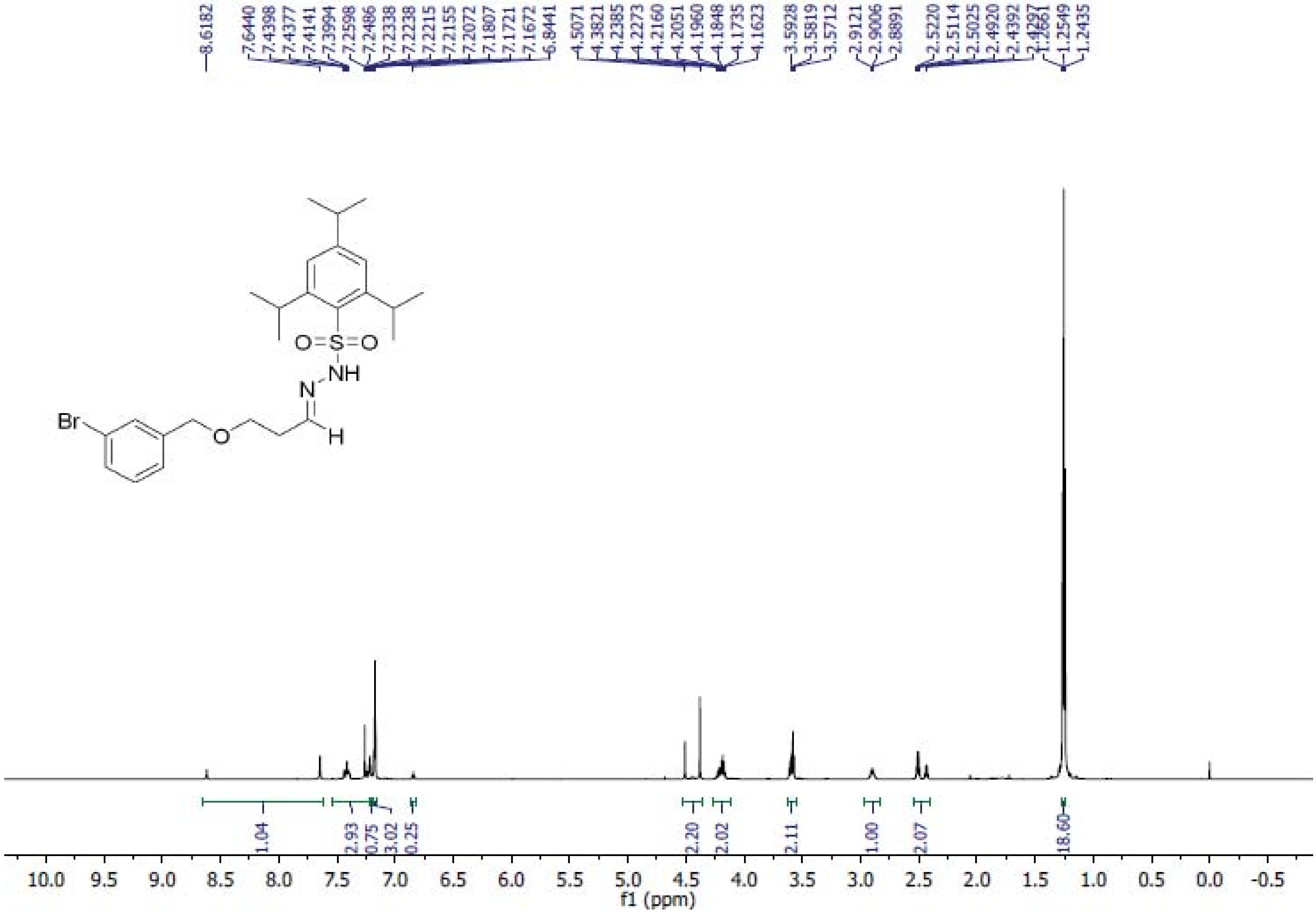
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-N'-(3-((2-methylbenzyl)oxy)propylidene)benzenesulfonohydrazide



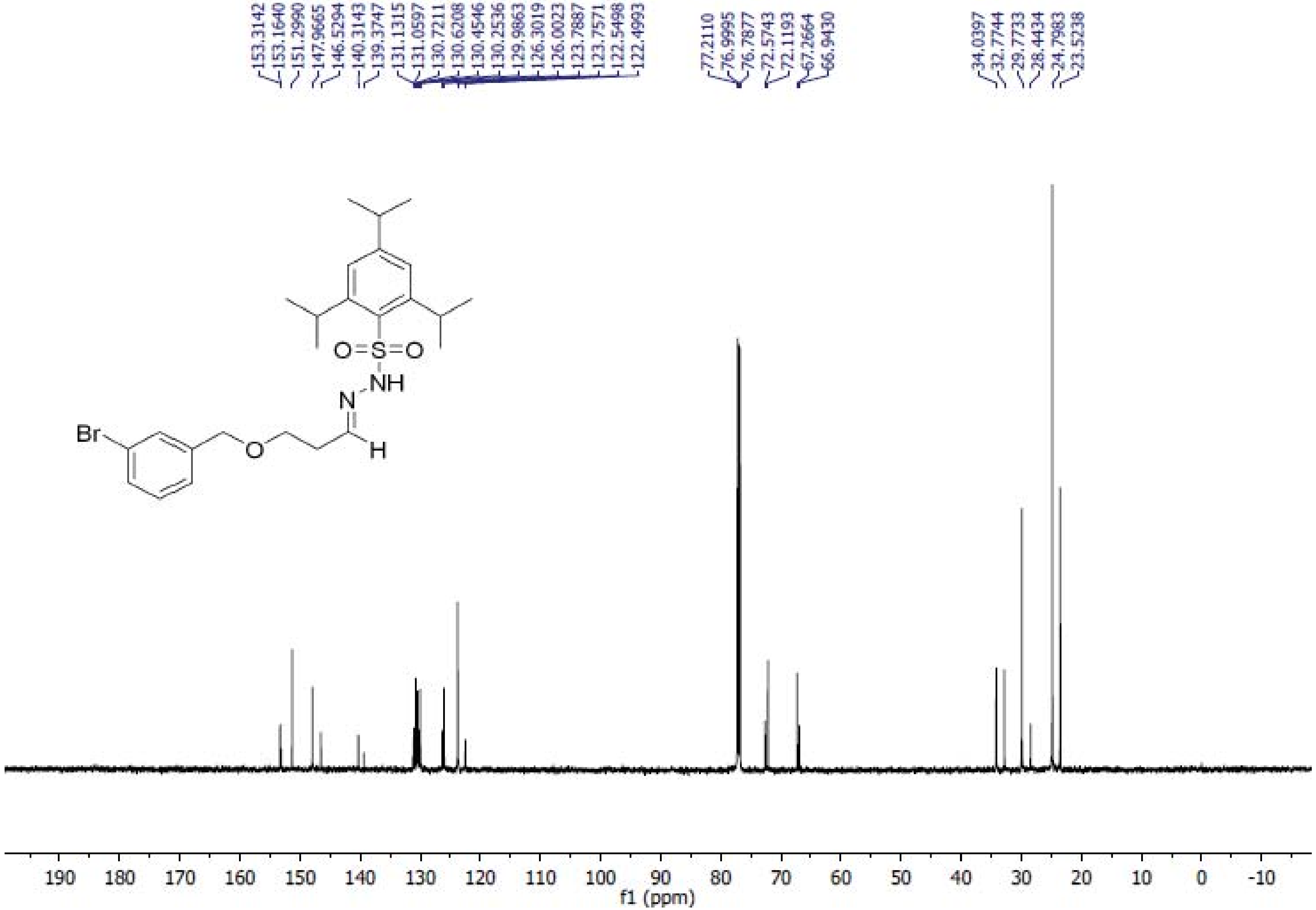
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((3-bromobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



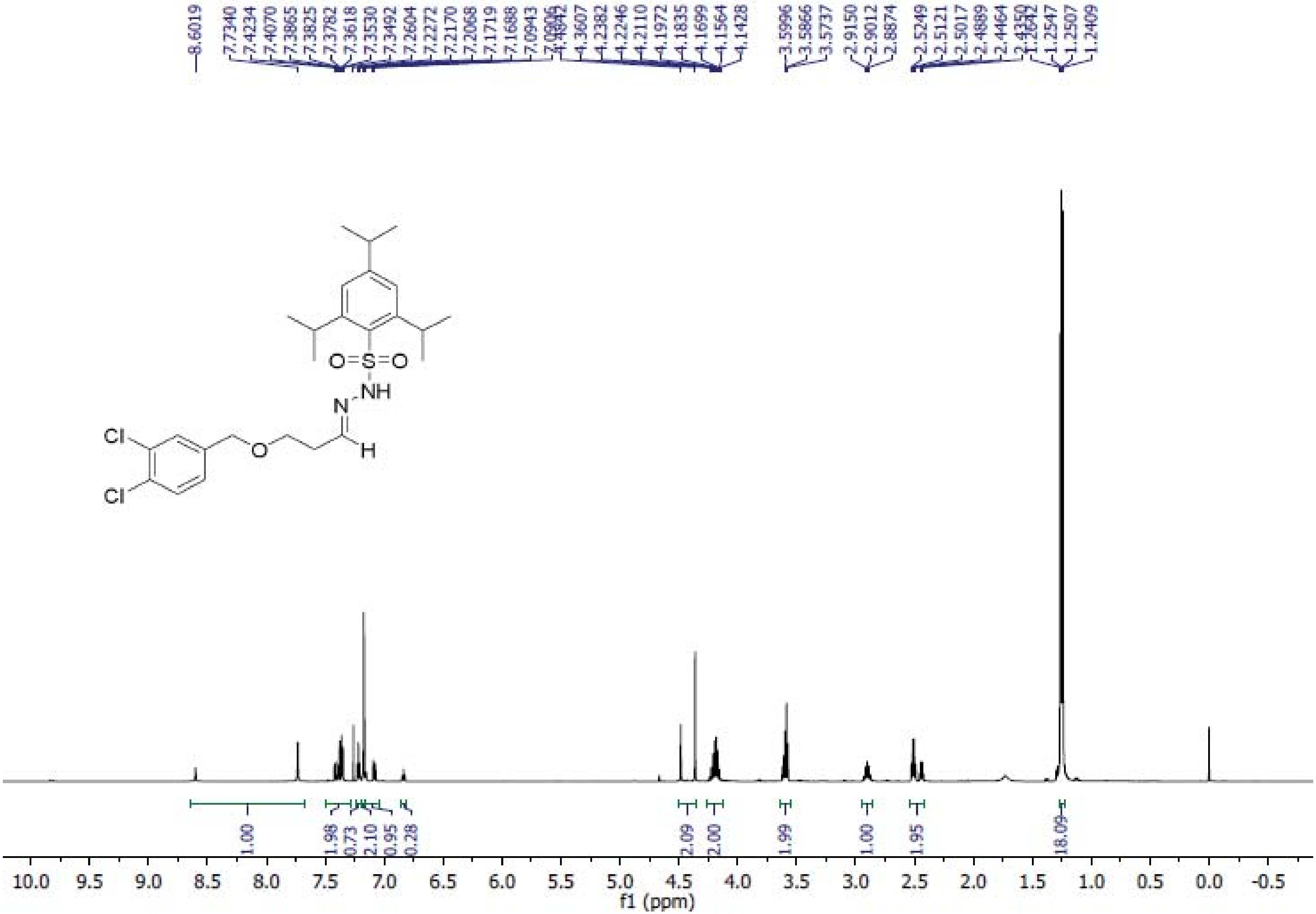
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((3-bromobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



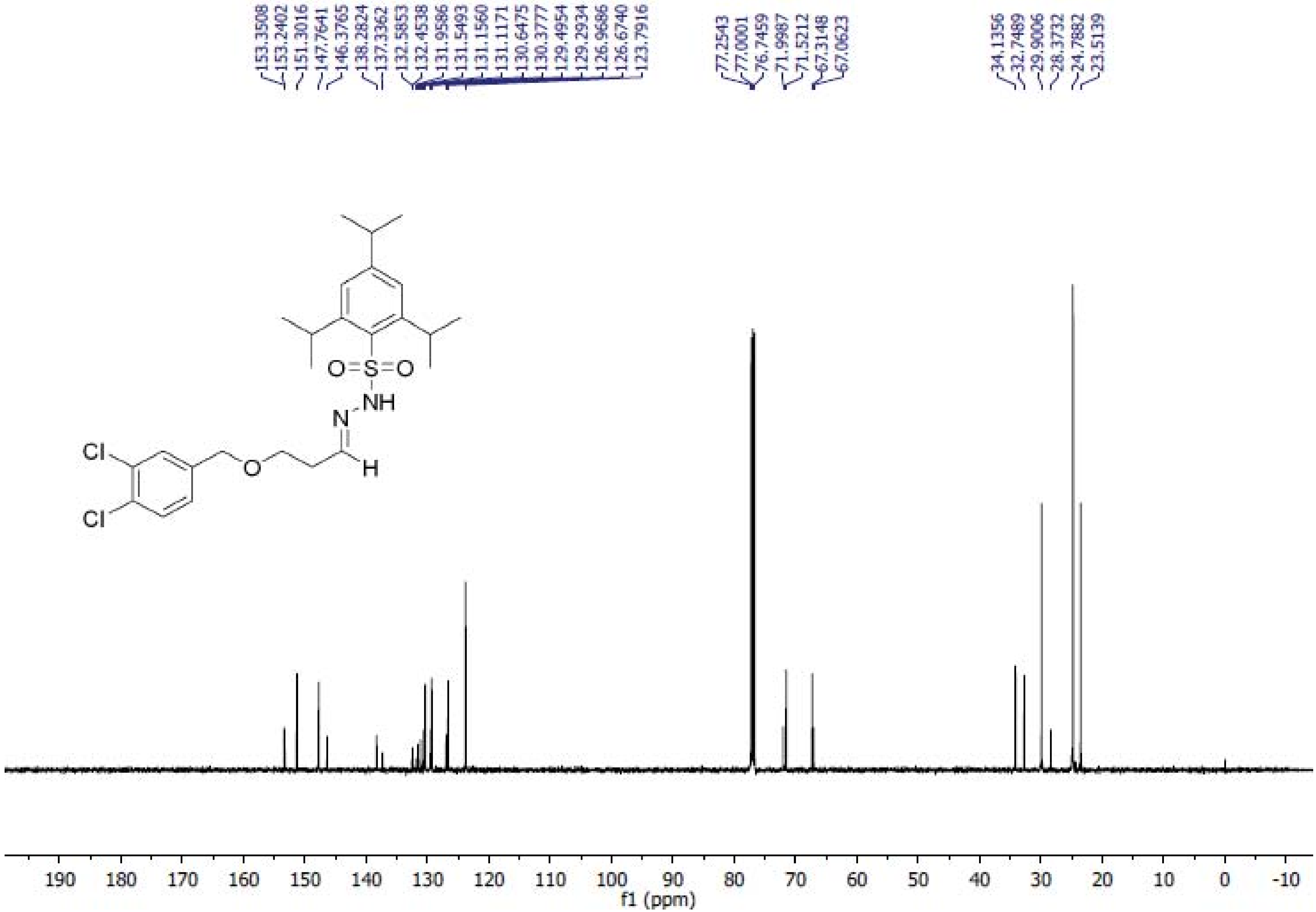
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((3,4-dichlorobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



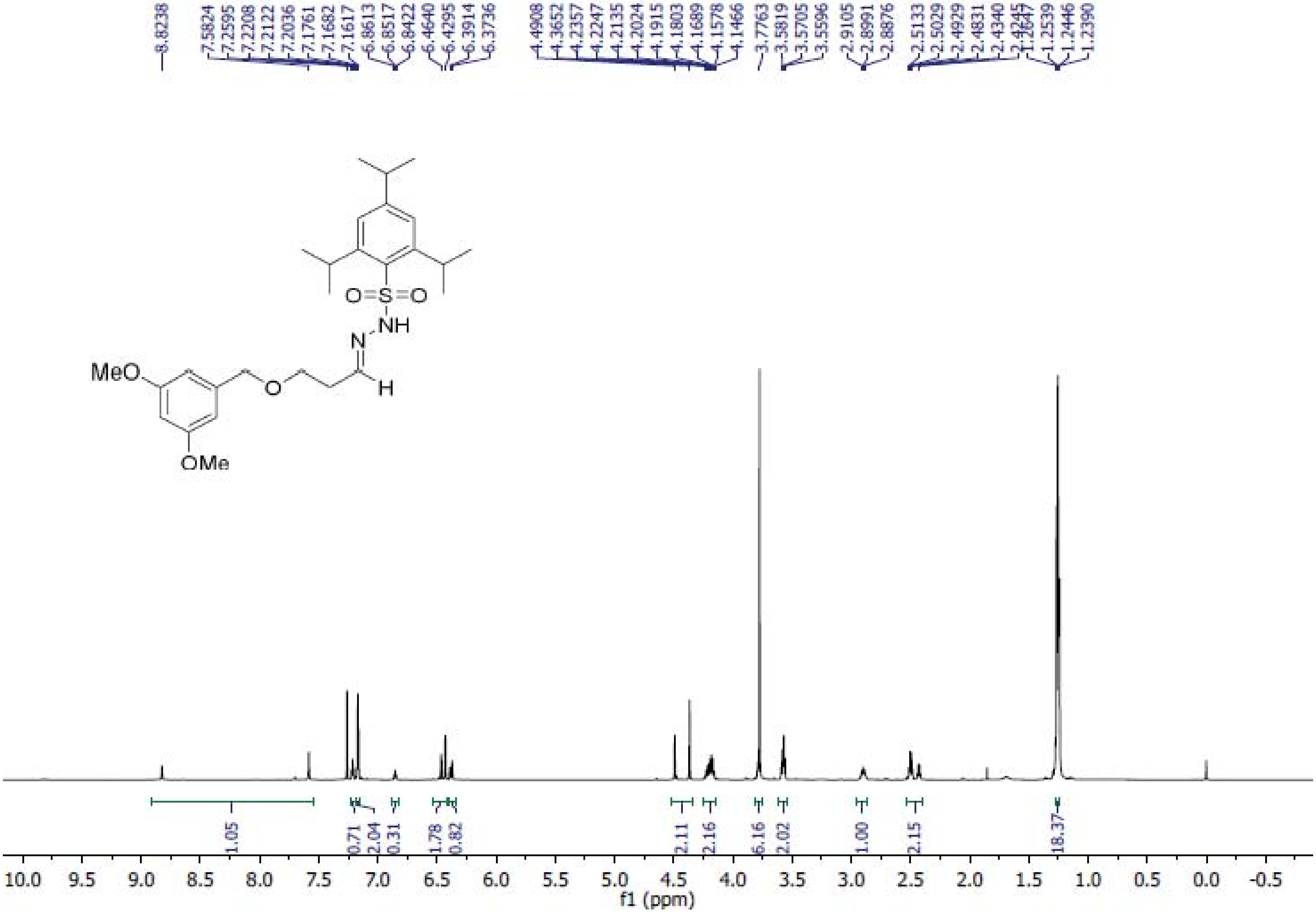
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((3,4-dichlorobenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



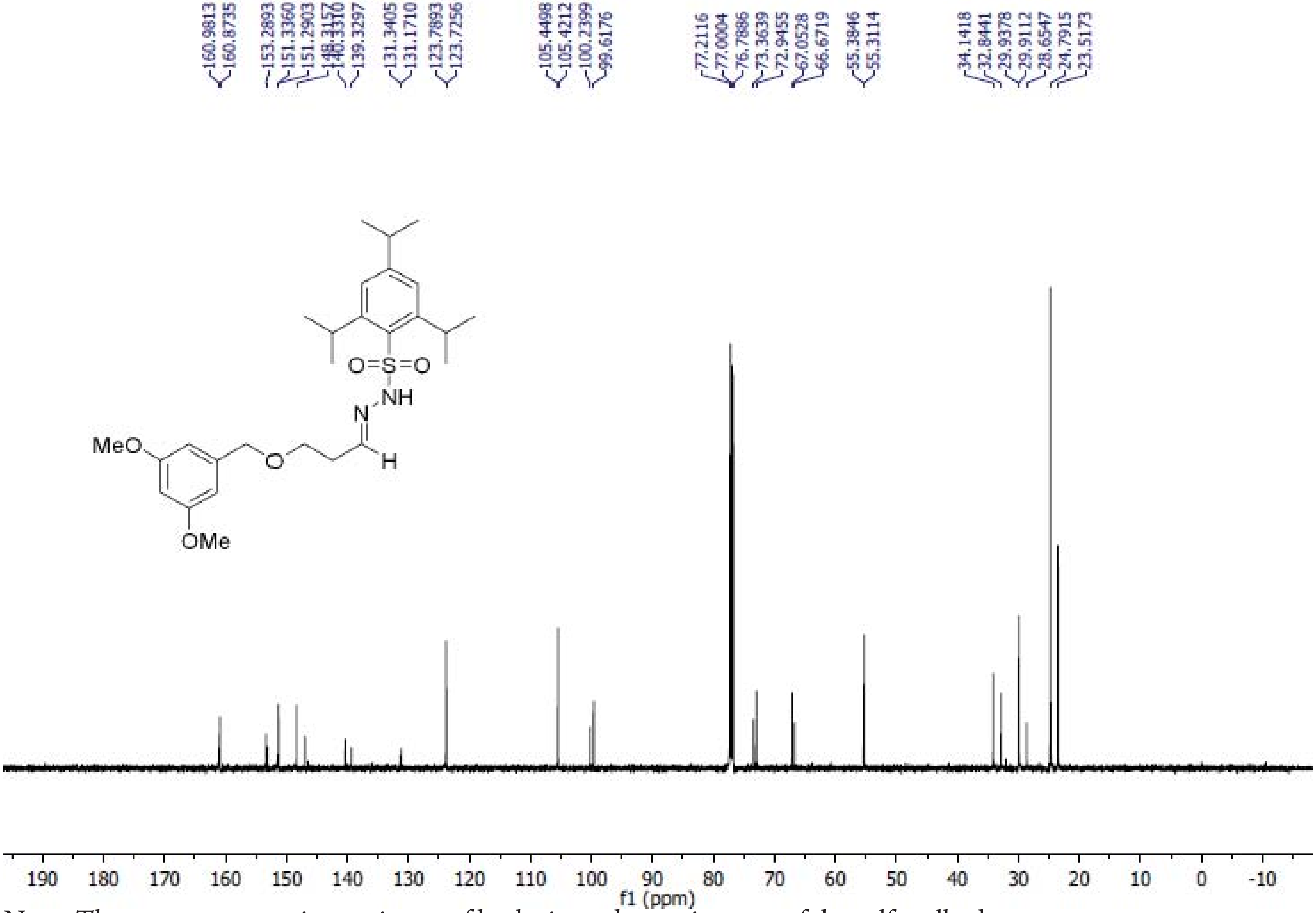
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((3,5-Dimethoxybenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



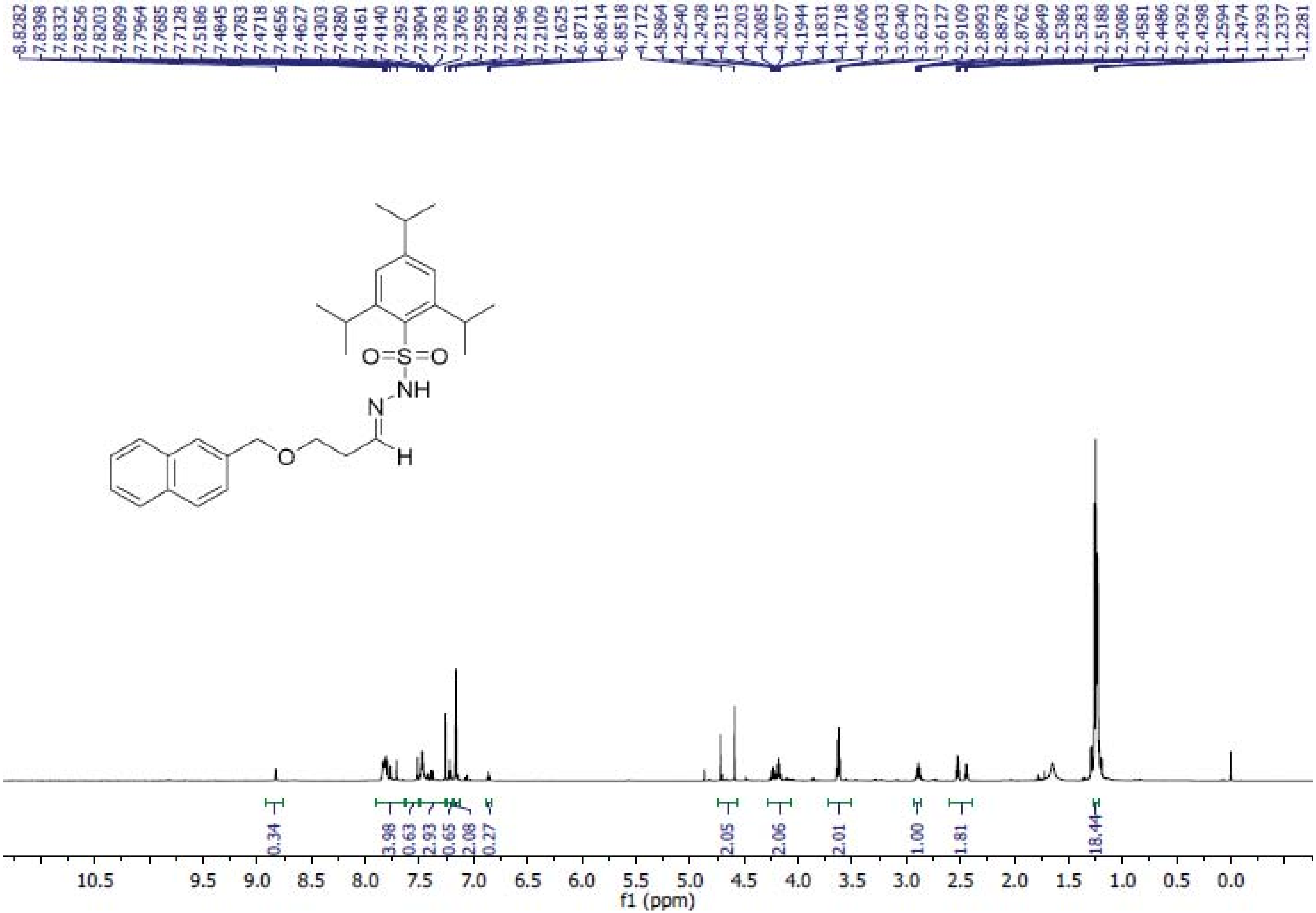
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-((3,5-Dimethoxybenzyl)oxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



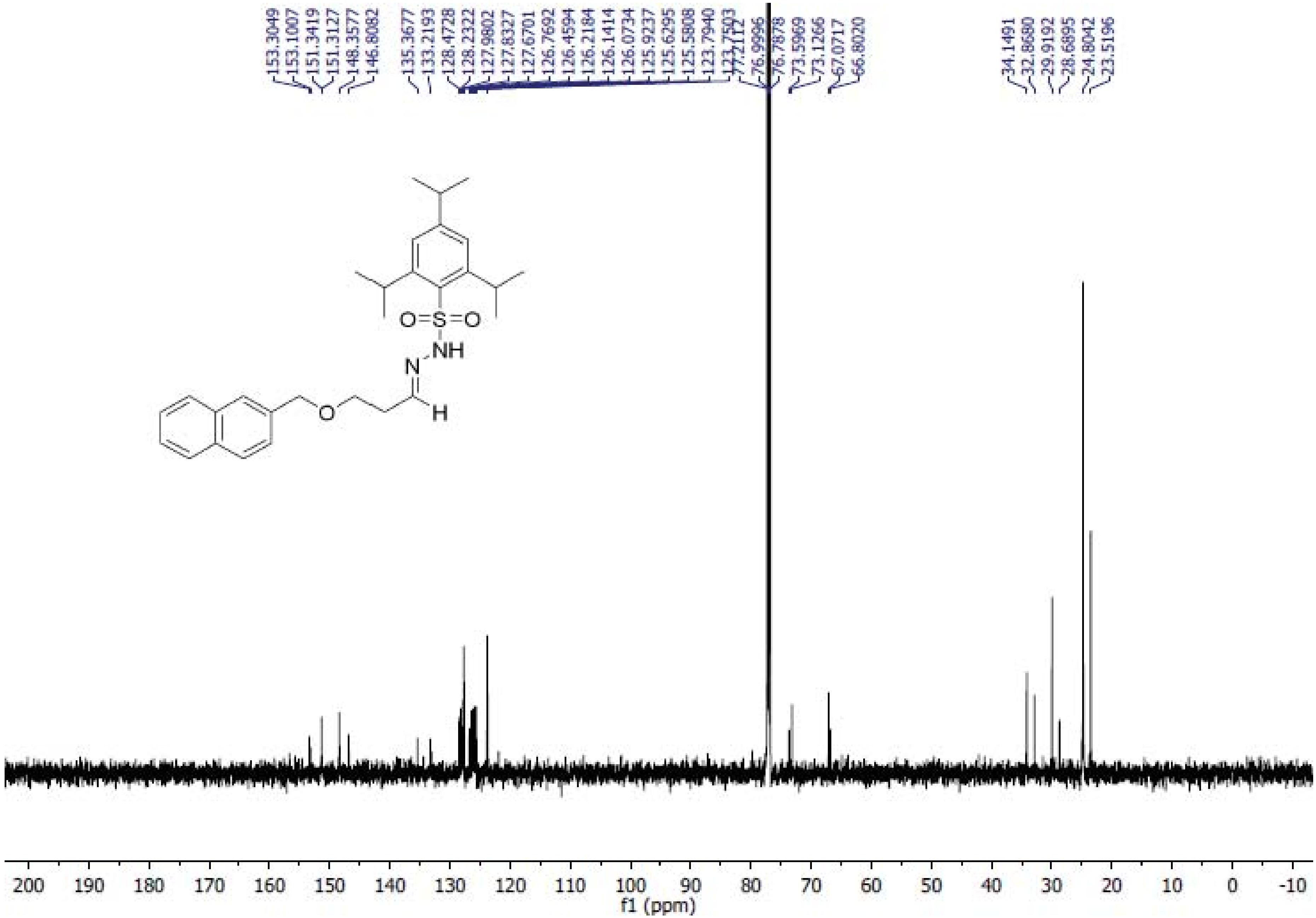
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-*N*'-(3-(naphthalen-2-ylmethoxy)propylidene)benzenesulfonohydrazide



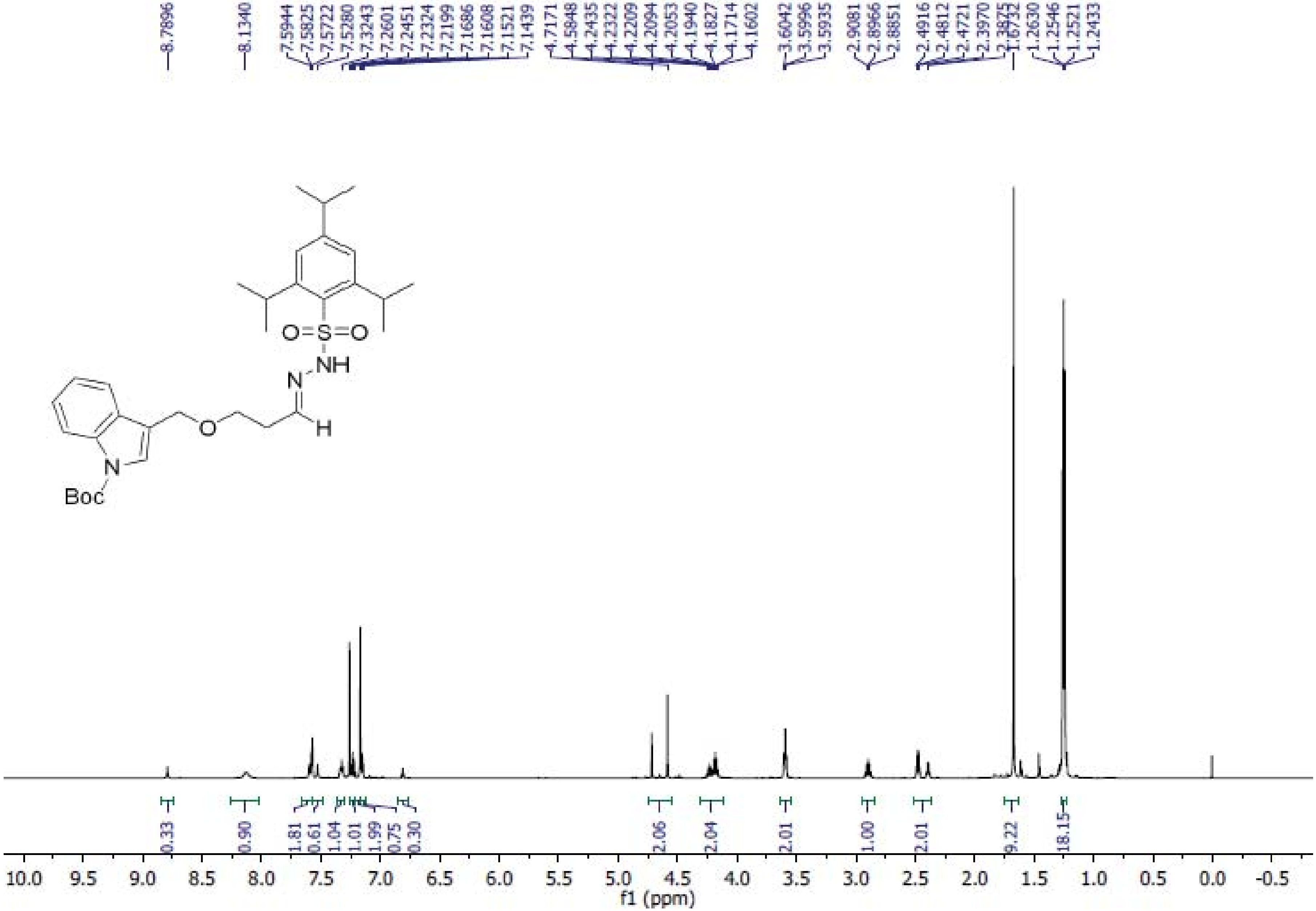
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-*N*'-(3-(naphthalen-2-ylmethoxy)propylidene)benzenesulfonohydrazide



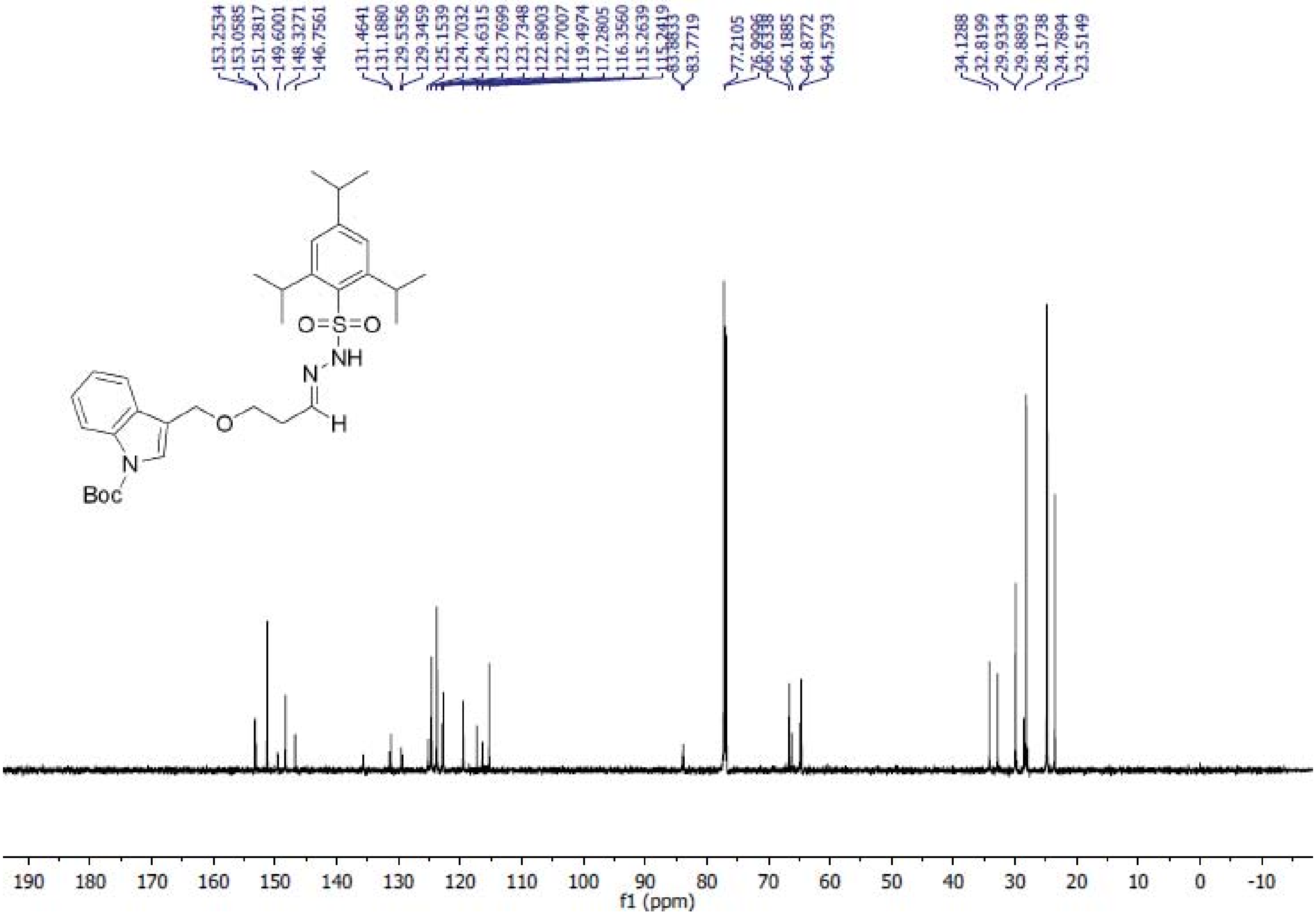
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

tert-butyl 3-((3-(2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazineylidene)propoxy) methyl)-1H-indole-1-carboxylate



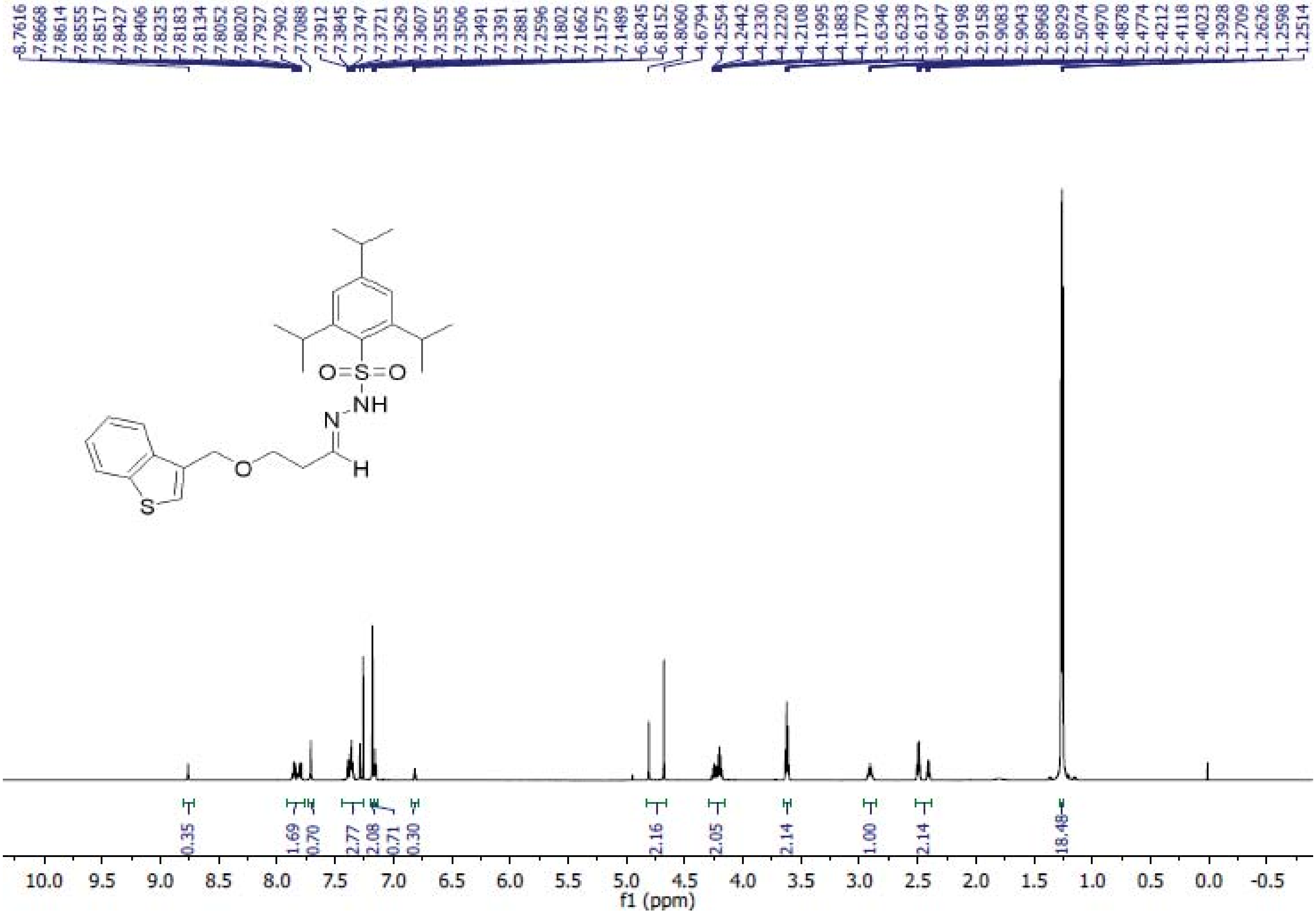
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

tert-butyl 3-((3-(2-((2,4,6-triisopropylphenyl)sulfonyl)hydrazineylidene)propoxy) methyl)-1H-indole-1-carboxylate



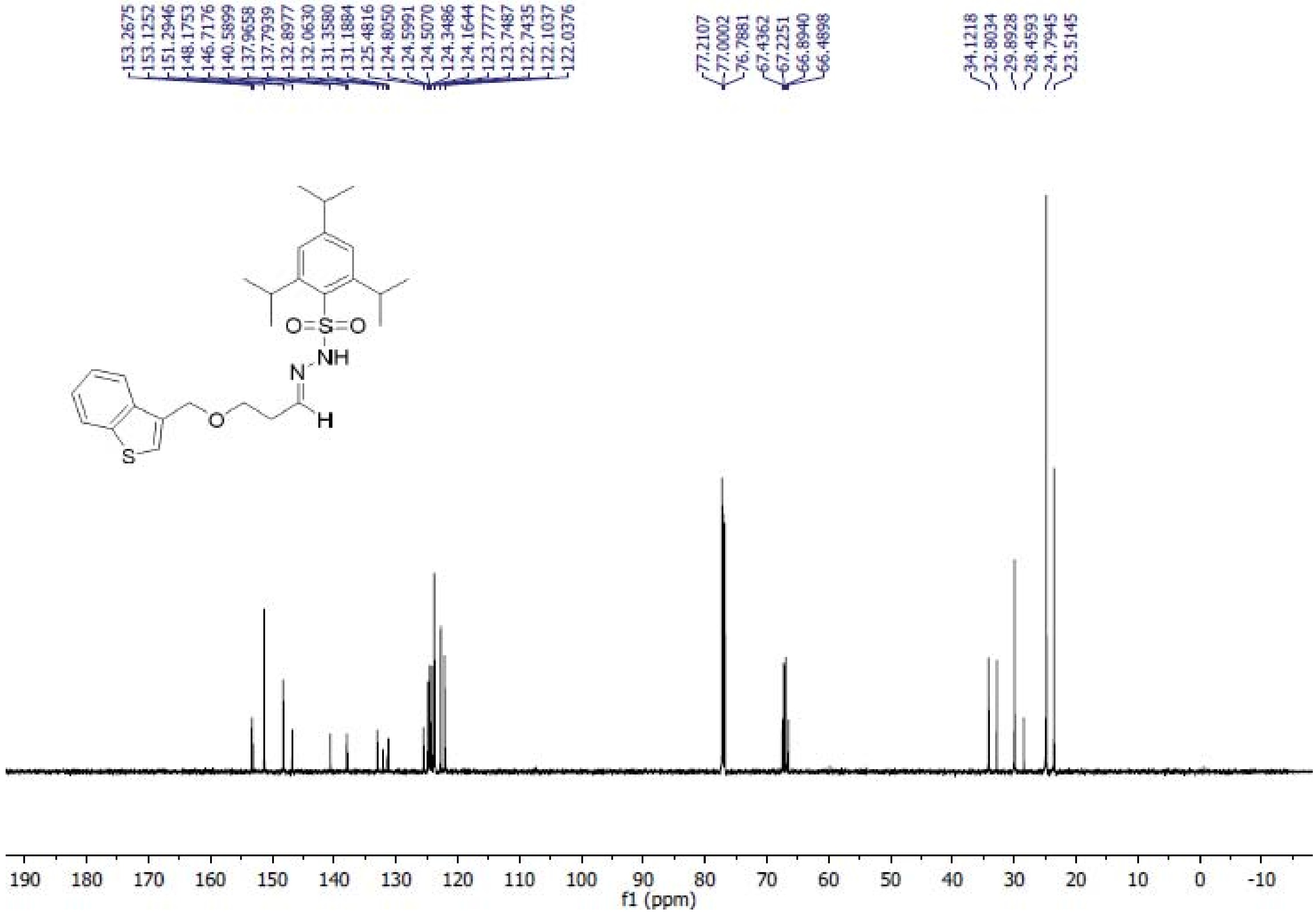
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-(benzo[b]thiophen-3-ylmethoxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



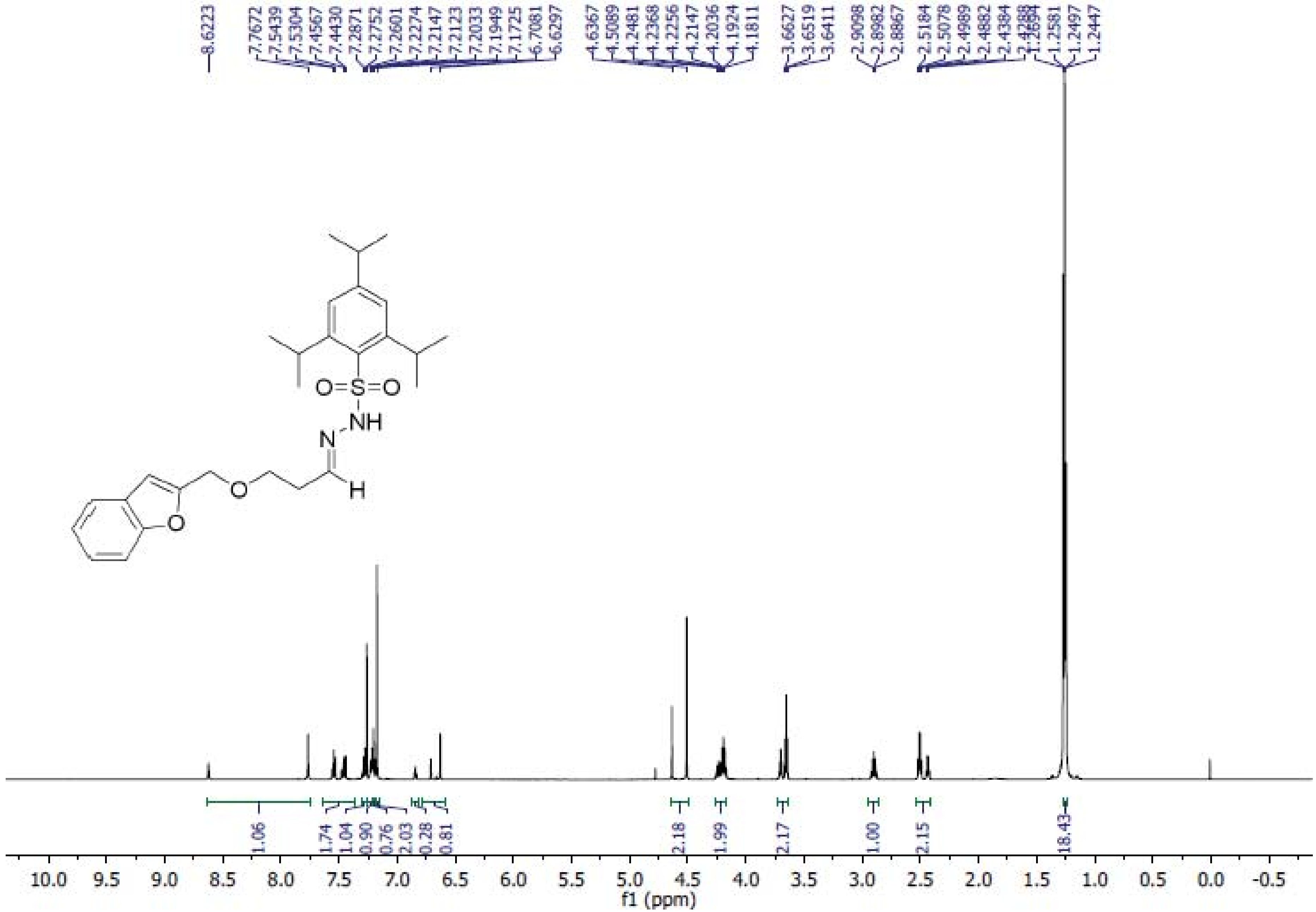
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-(benzo[b]thiophen-3-ylmethoxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



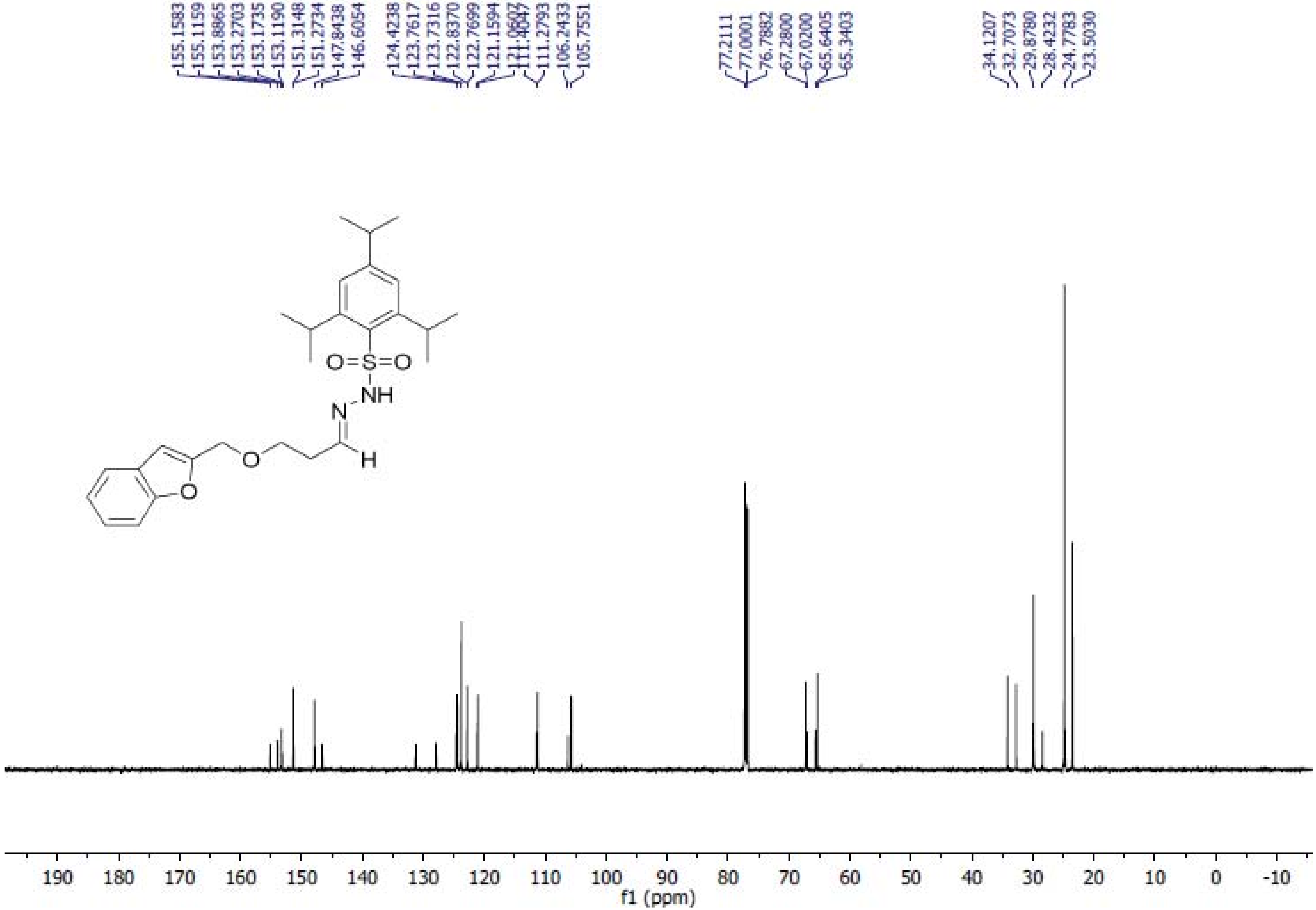
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-(benzofuran-2-ylmethoxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



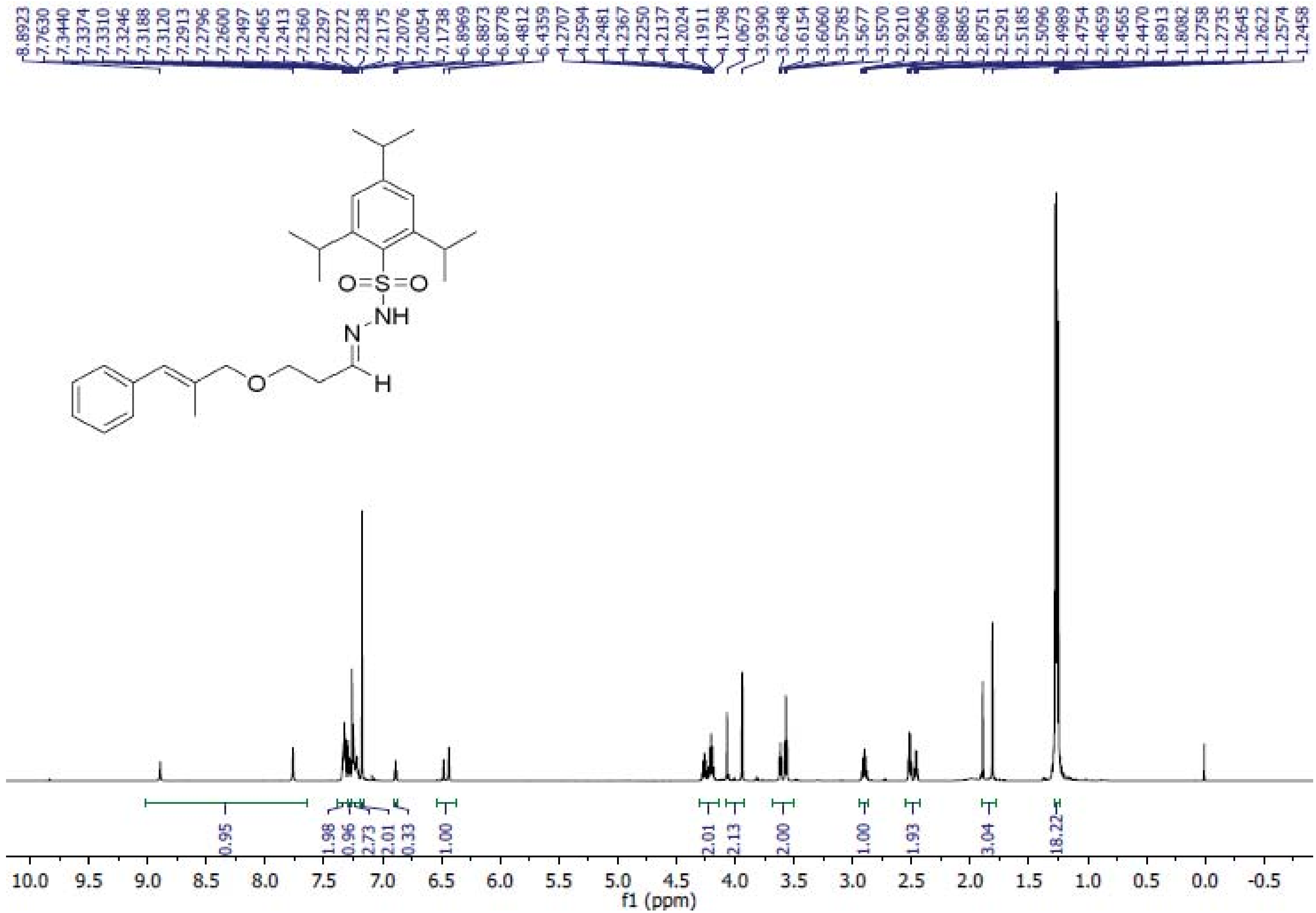
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

N'-(3-(benzofuran-2-ylmethoxy)propylidene)-2,4,6-triisopropylbenzenesulfonohydrazide



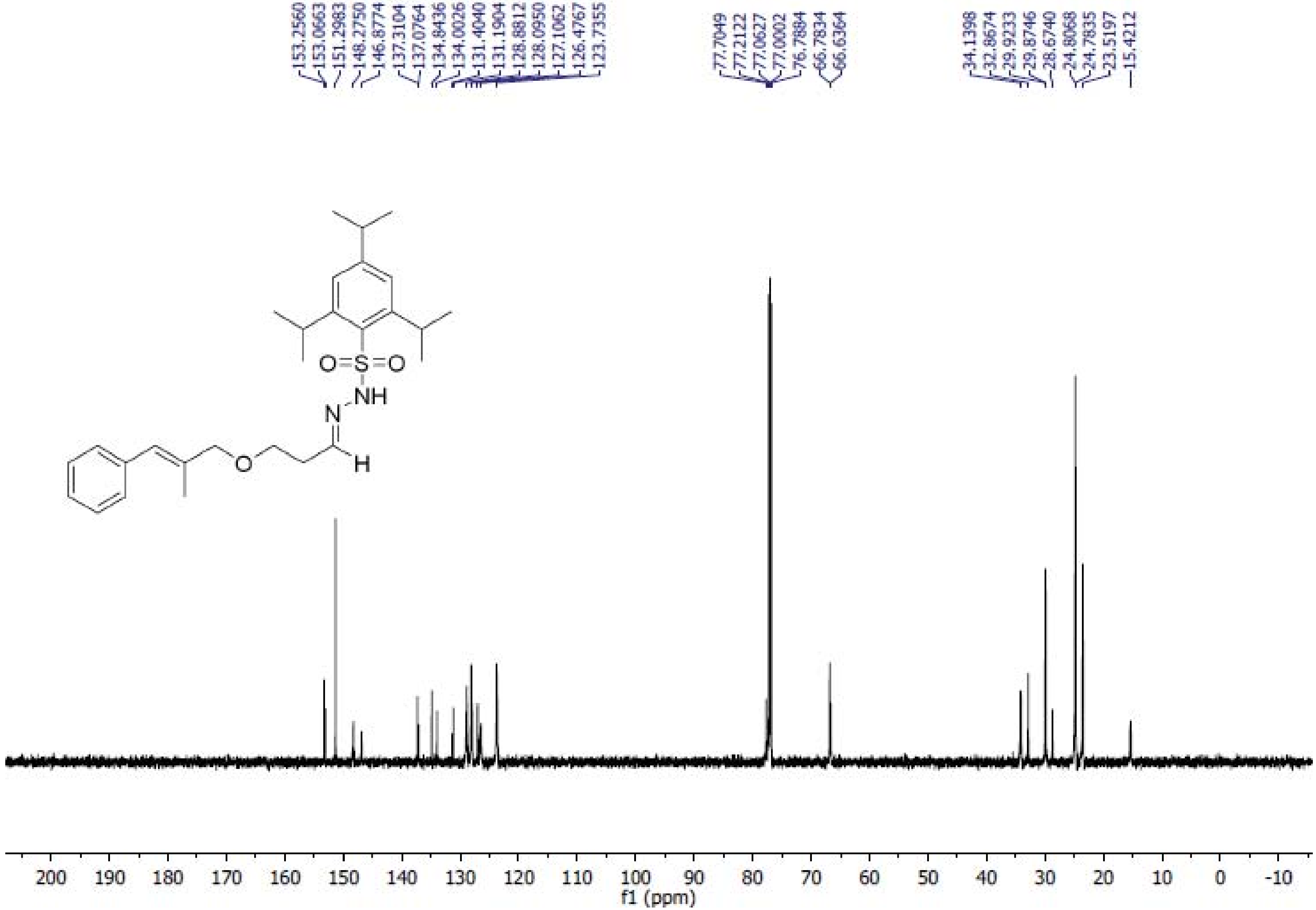
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-*N*'-(3-(((E)-2-methyl-3-phenylallyl)oxy)propylidene)benzenesulfonohydrazide



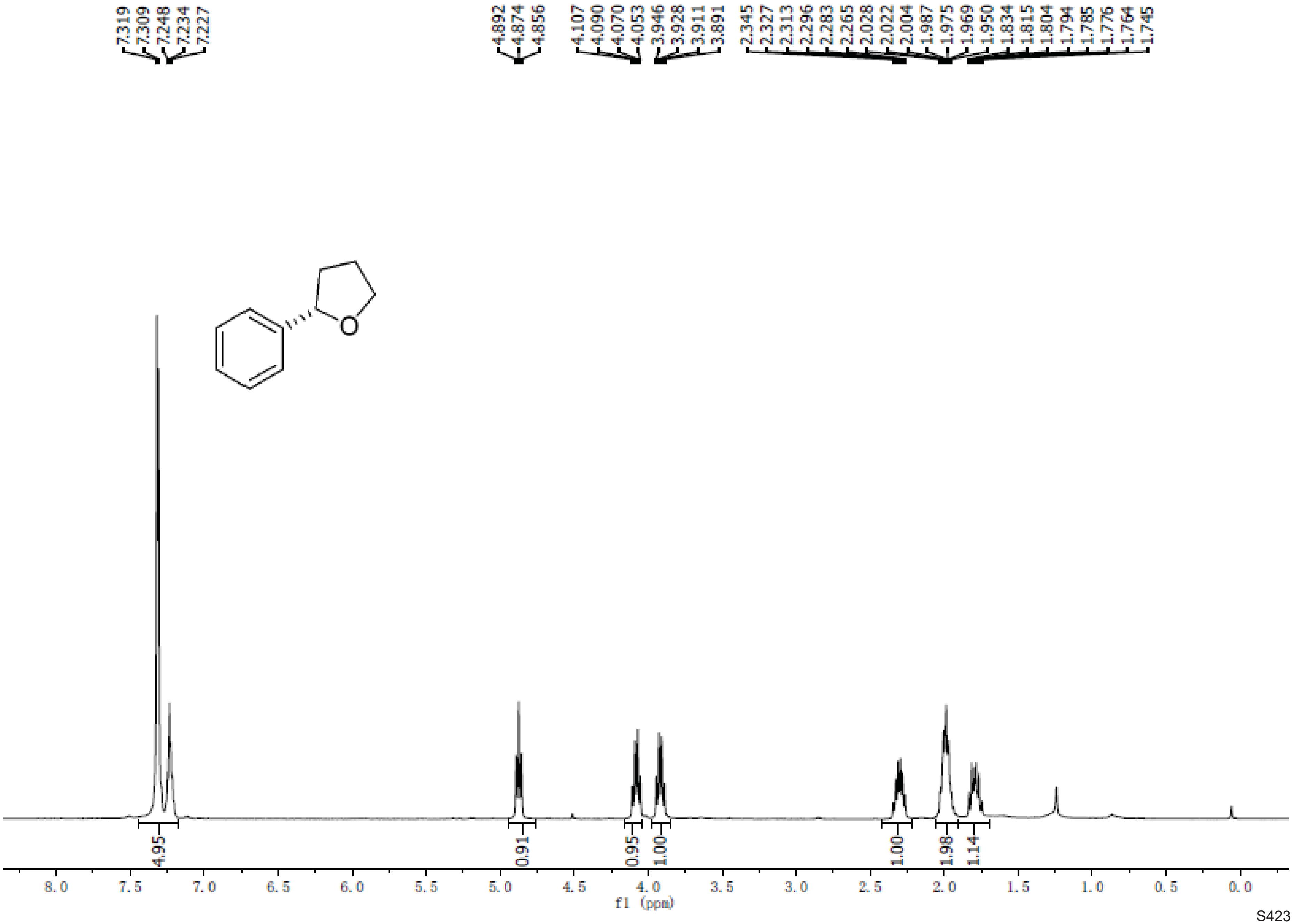
Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

2,4,6-triisopropyl-*N*'-(3-(((E)-2-methyl-3-phenylallyl)oxy)propylidene)benzenesulfonohydrazide

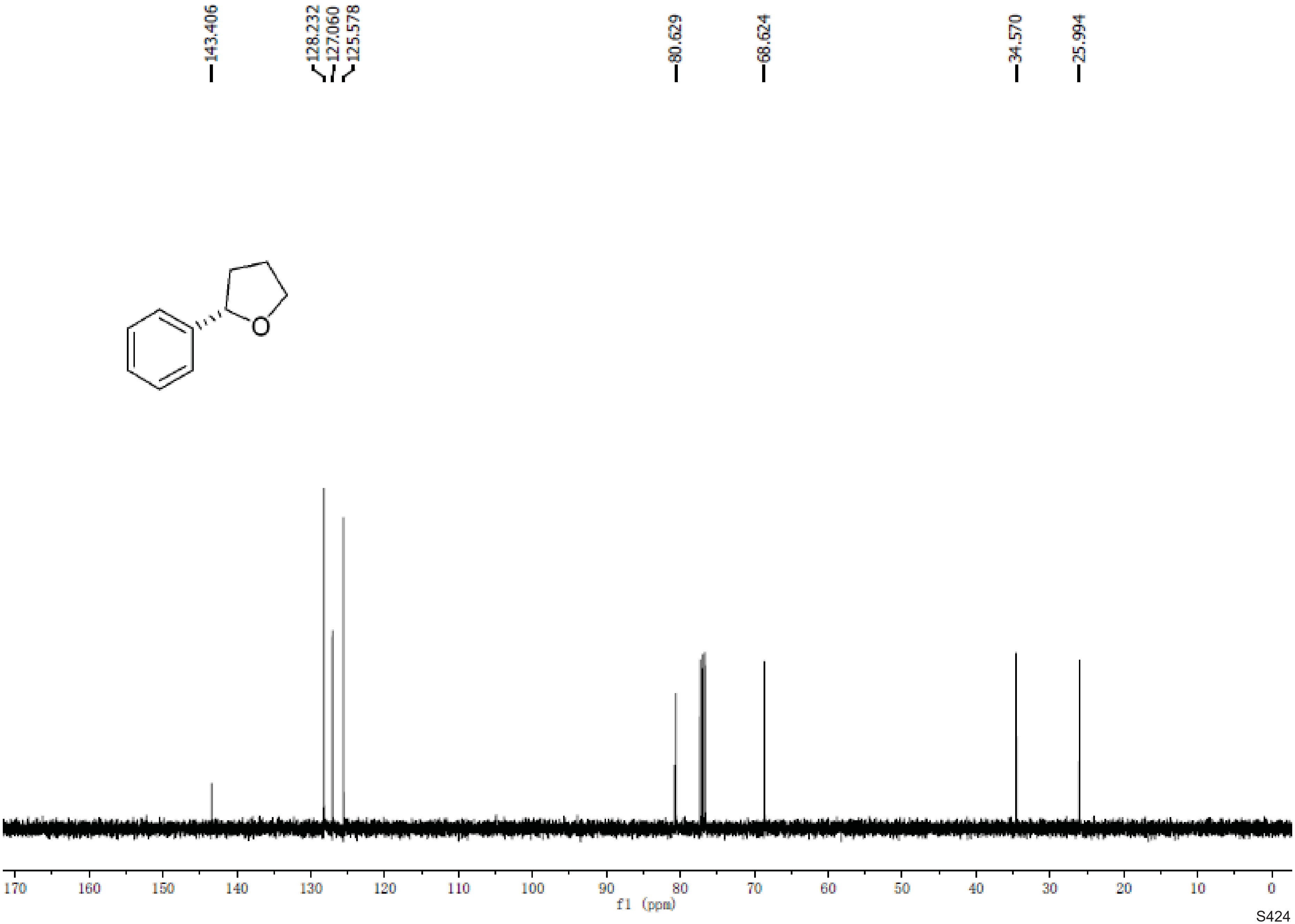


Note: The spectrum contains a mixture of both cis- and trans-isomers of the sulfonylhydrazones

(*S*)-2-phenyltetrahydrofuran



(*S*)-2-phenyltetrahydrofuran

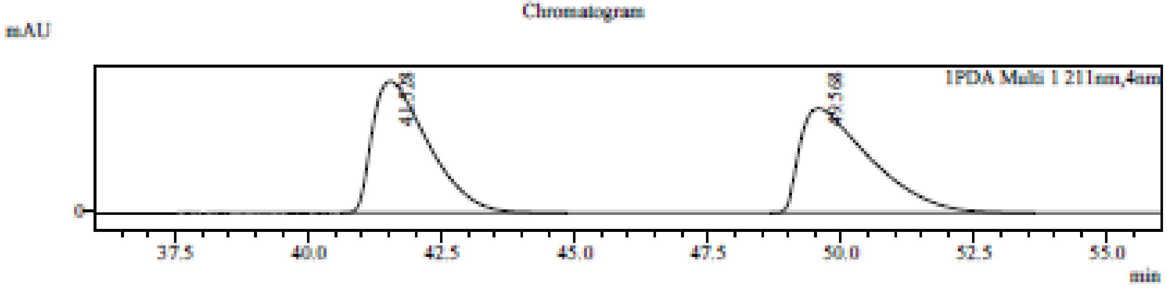


(*S*)-2-phenyltetrahydrofuran

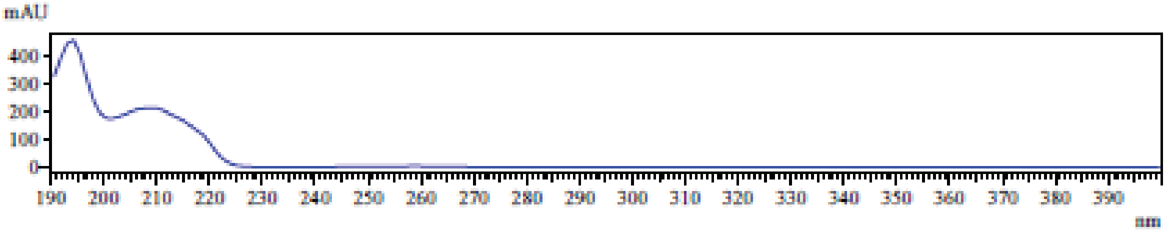
Sample Information

Data File	: XW-VI-160-ADH0%0.8mL-2.lcd
Sample Name	: XW-VI-160-ADH0%0.8mL-2
Sample ID	: XW-VI-160-ADH0%0.8mL-2
Method File	: XW-0%-0.8ml.lcm

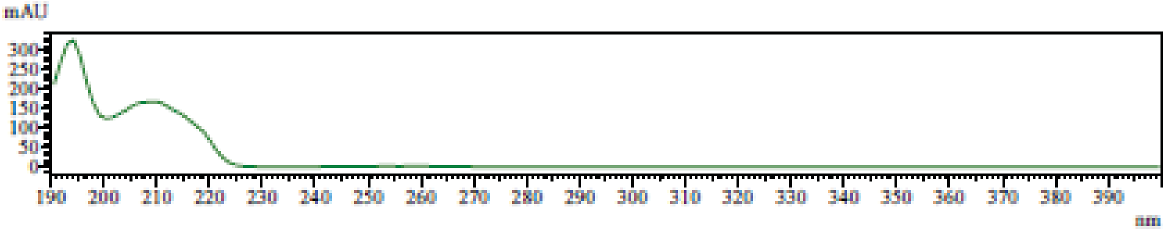
Chromatogram



UV Spectrum
Retention time = 41.528



UV Spectrum
Retention time = 49.568



Peak Table

PDA Ch1 211nm

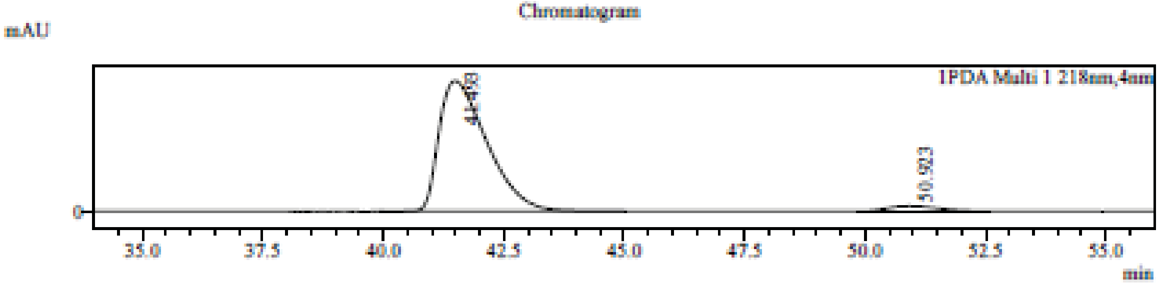
Peak#	Ret. Time	Area	Area%
1	41.528	14908960	49.979
2	49.568	14921672	50.021
Total		29830632	100.000

(*S*)-2-phenyltetrahydrofuran

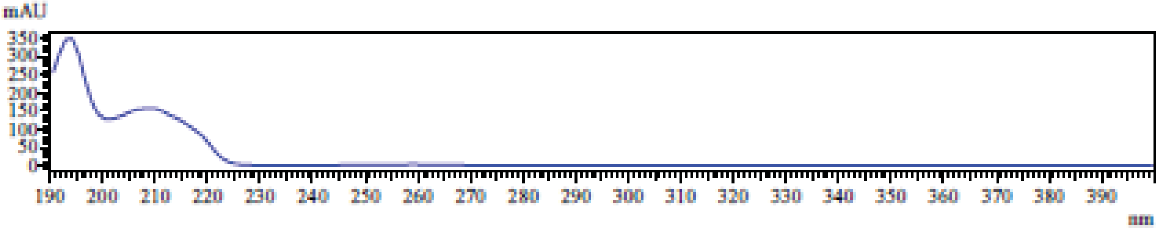
Sample Information

Data File : XW-VI-211-THF-ADH0%0.8mL-3.lcd
Sample Name : XW-VI-211-THF-ADH0%0.8mL-3
Sample ID : XW-VI-211-THF-ADH0%0.8mL-3
Method File : XW-0%-0.8ml.lcm

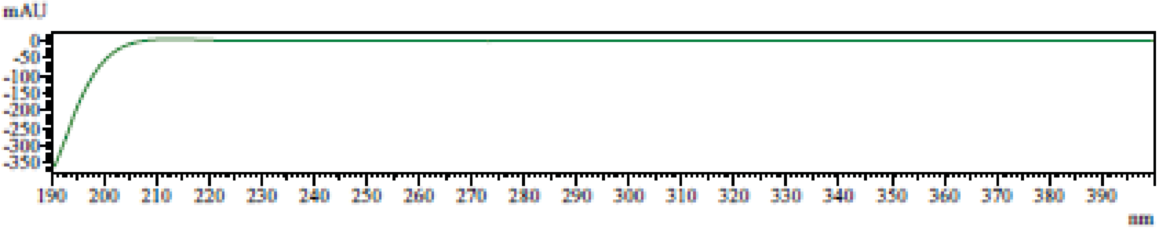
Chromatogram



UV Spectrum
Retention time = 41.493



UV Spectrum
Retention time = 50.923

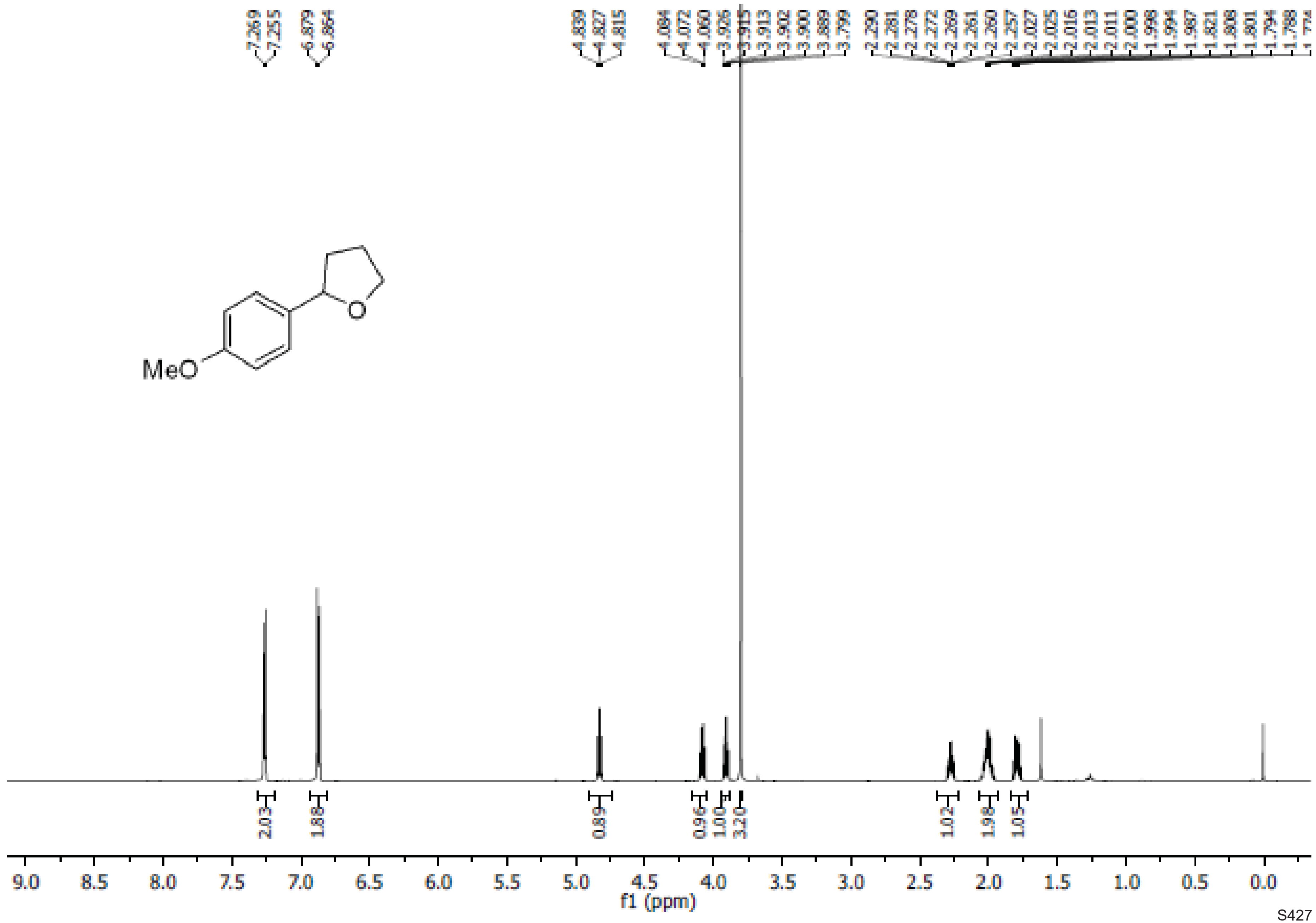


Peak Table

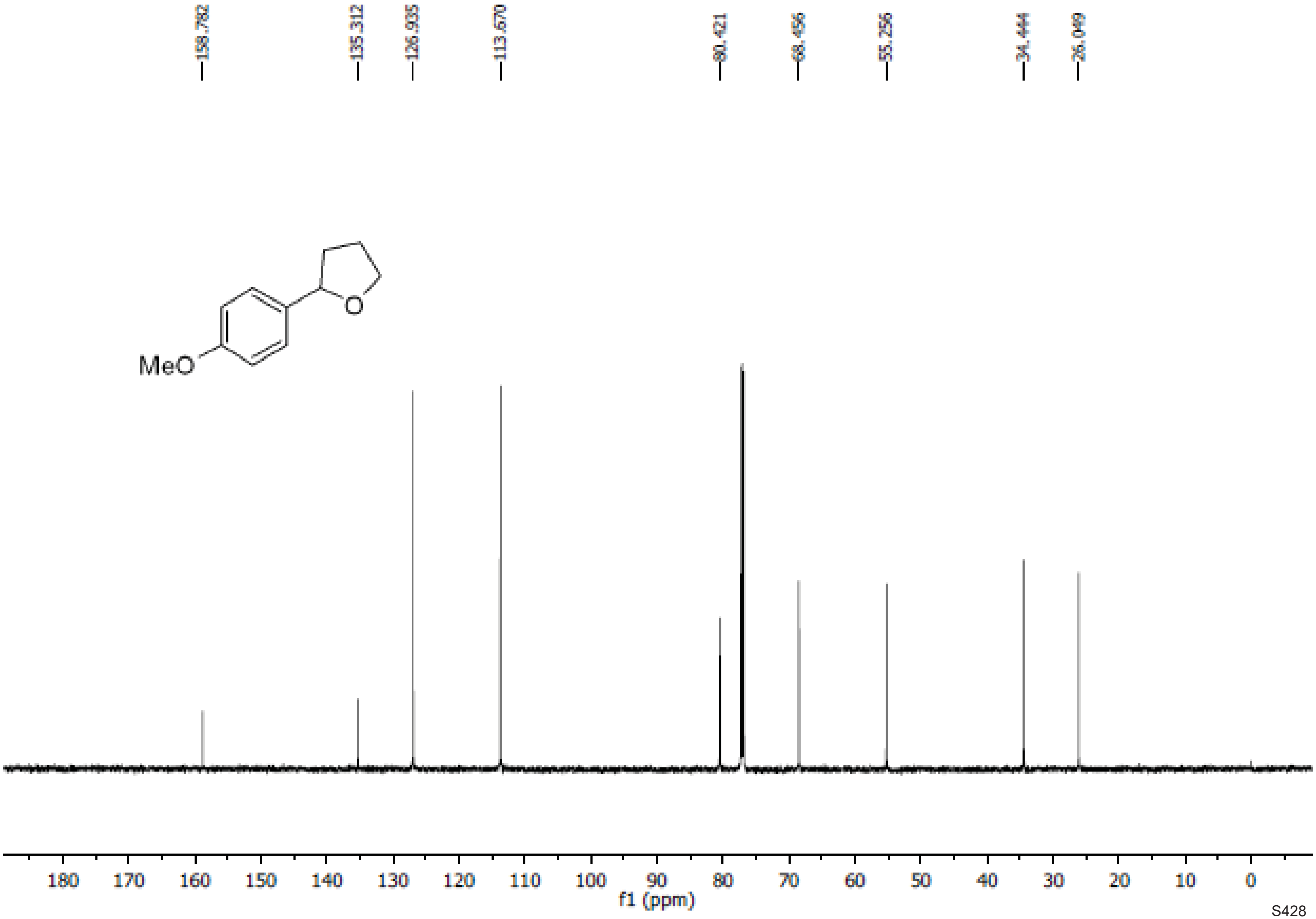
PDA Ch1 218nm

Peak#	Ret. Time	Area	Area%
1	41.493	5998629	95.956
2	50.923	252798	4.044
Total		6251427	100.000

(*S*)-2-(4-methoxyphenyl)tetrahydrofuran



(*S*)-2-(4-methoxyphenyl)tetrahydrofuran

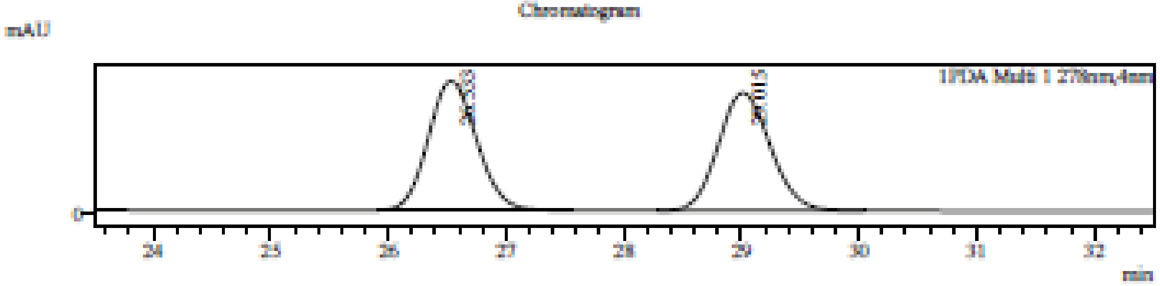


(*S*)-2-(4-methoxyphenyl)tetrahydrofuran

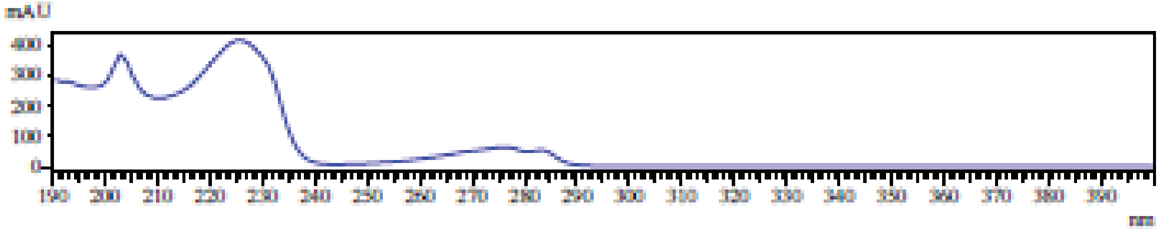
Sample Information

Data File : XW-VI-262-IF-1%0.8mL-2.lcd
Sample Name : XW-VI-262-IF-1%0.8mL-2
Sample ID : XW-VI-262-IF-1%0.8mL-2
Method File : XW-1%-0.8ml.lcm

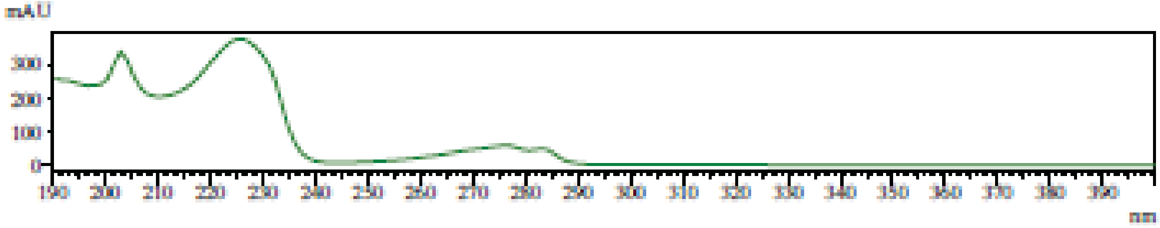
Chromatogram



UV Spectrum
Retention time = 26.533



UV Spectrum
Retention time = 29.015



Peak Table

PDA Ch1 278nm

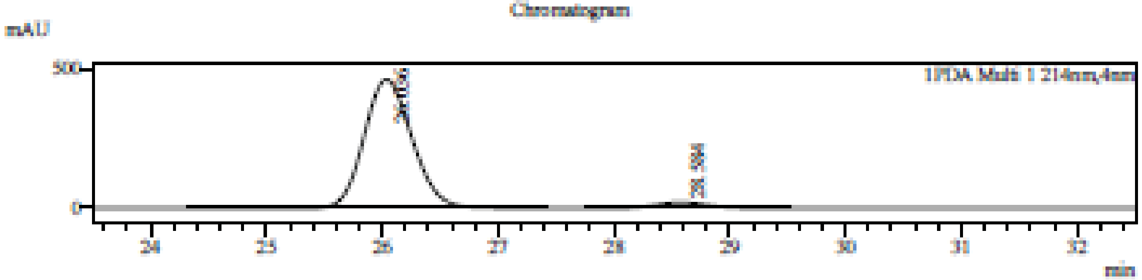
Peak#	Ret. Time	Area	Area%
1	26.533	1611421	50.468
2	29.015	1581557	49.532
Total		3192977	100.000

(*S*)-2-(4-methoxyphenyl)tetrahydrofuran

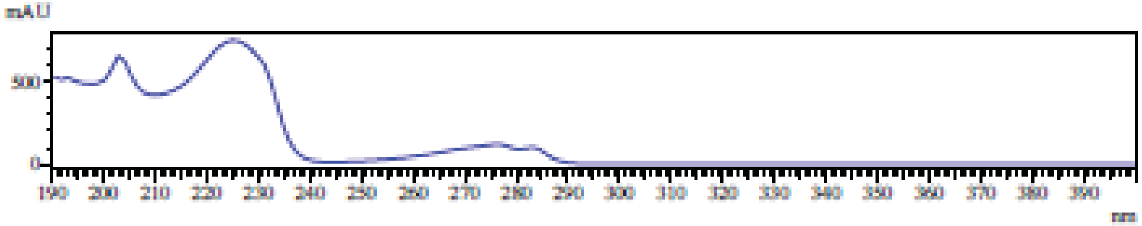
Sample Information

Data File : XW-VI-263b-IF-1%0.8mL.lcd
Sample Name : XW-VI-263b-IF-1%0.8mL
Sample ID : XW-VI-263b-IF-1%0.8mL
Method File : XW-1%-0.8ml.lcm

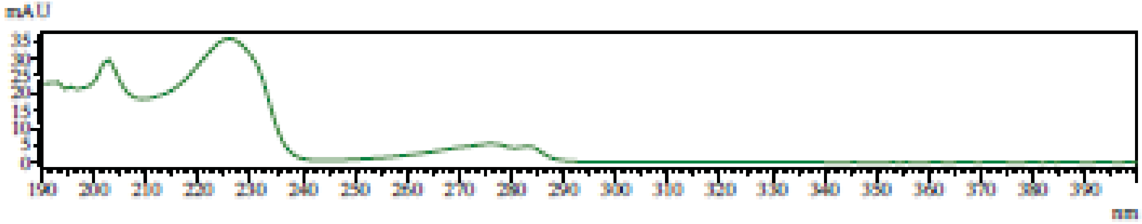
Chromatogram



UV Spectrum
Retention time = 26.036



UV Spectrum
Retention time = 28.584

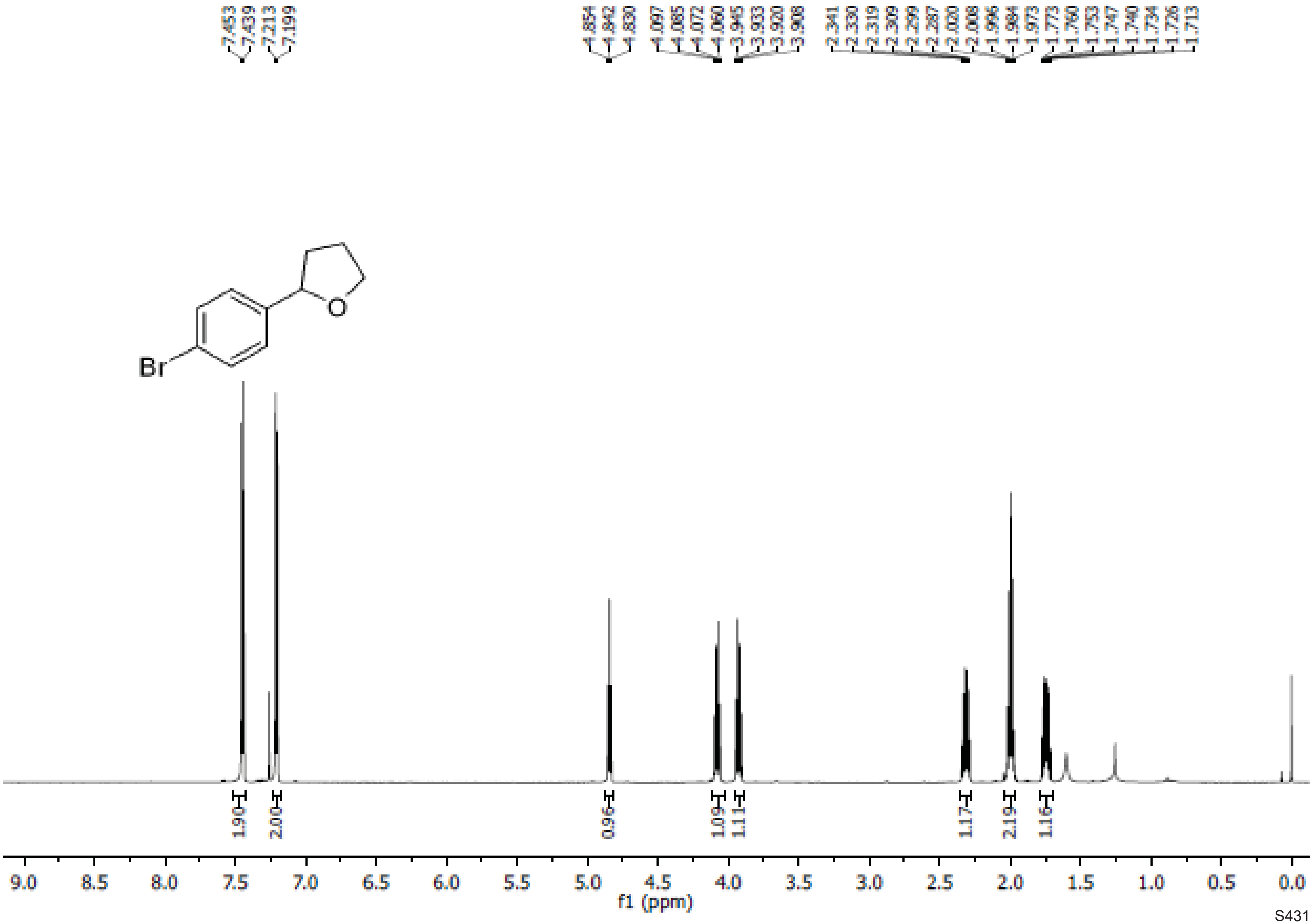


Peak Table

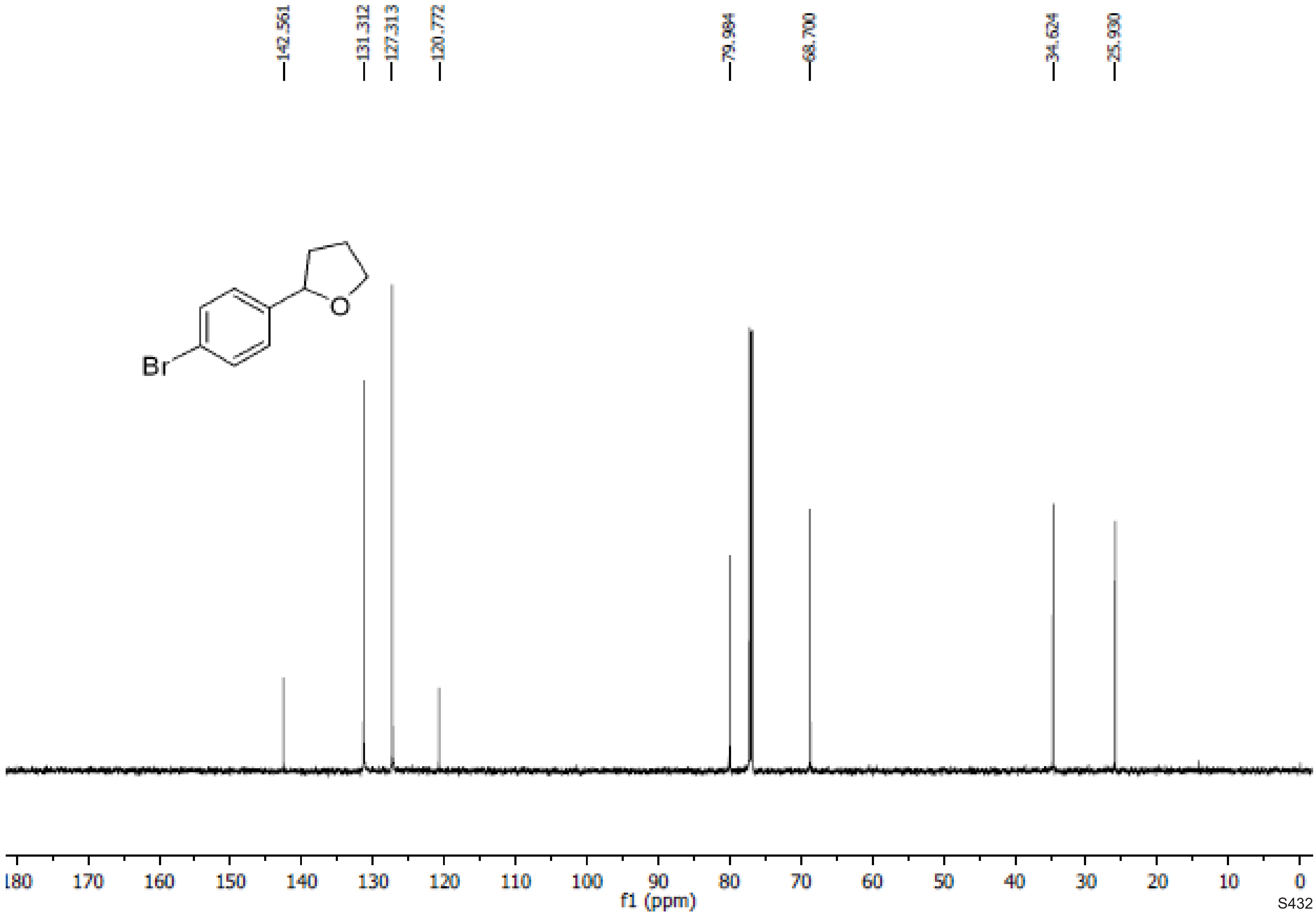
PDA Ch1 214nm

Peak#	Ret. Time	Area	Area%
1	26.036	13310402	95.424
2	28.584	638280	4.576
Total		13948683	100.000

(*S*)-2-(4-bromophenyl)tetrahydrofuran



(*S*)-2-(4-bromophenyl)tetrahydrofuran

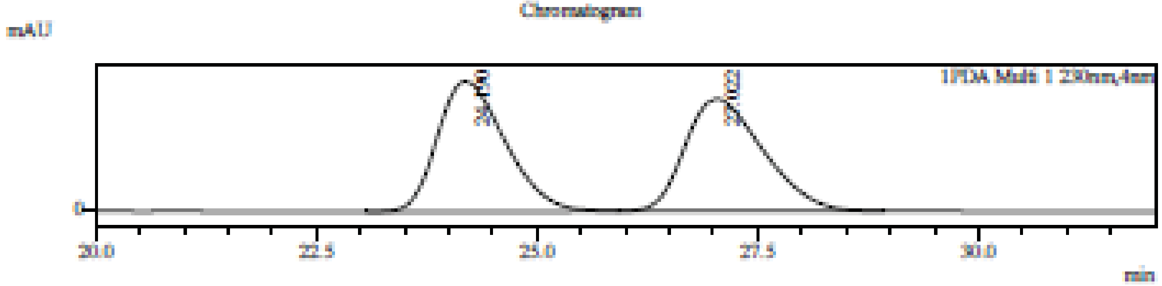


(*S*)-2-(4-bromophenyl)tetrahydrofuran

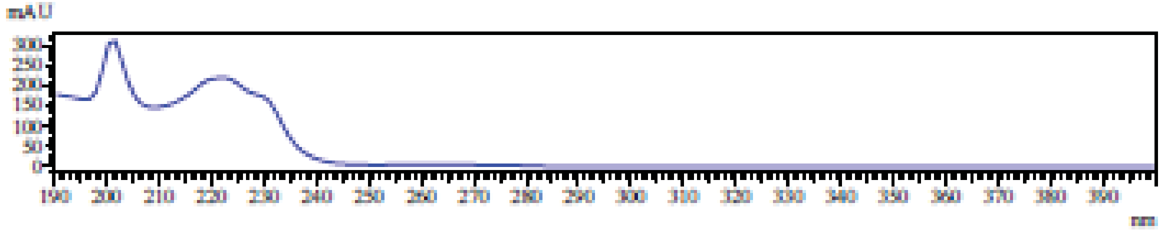
Sample Information

Data File : XW-VI-219-IE-0.2%0.8mL-3.lcd
Sample Name : XW-VI-219-IE-0.2%0.8mL-3
Sample ID : XW-VI-219-IE-0.2%0.8mL-3
Method File : XW-0.2%-0.8ml.lcm

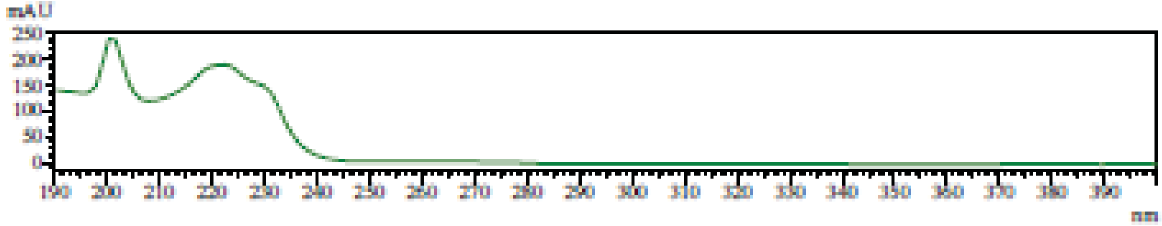
Chromatogram



UV Spectrum
Retention time = 24.190



UV Spectrum
Retention time = 27.022



Peak Table

PDA Ch1 230nm

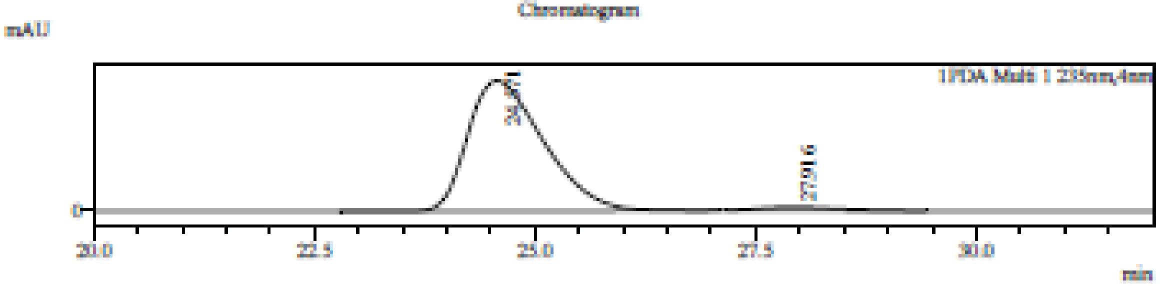
Peak#	Ret. Time	Area	Area%
1	24.190	8576599	50.126
2	27.022	8533465	49.874
Total		17110064	100.000

(*S*)-2-(4-bromophenyl)tetrahydrofuran

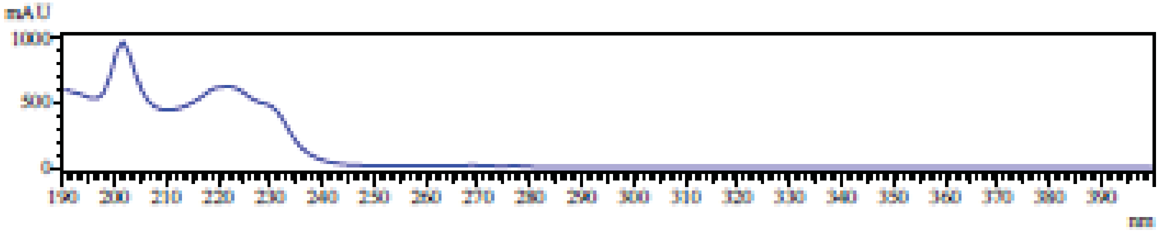
Sample Information

Data File : XW-VI-220b-IE-0.2%0.8mL-2.lcd
Sample Name : XW-VI-220b-IE-0.2%0.8mL-2
Sample ID : XW-VI-220b-IE-0.2%0.8mL-2
Method File : XW-0.2%-0.8ml.lcm

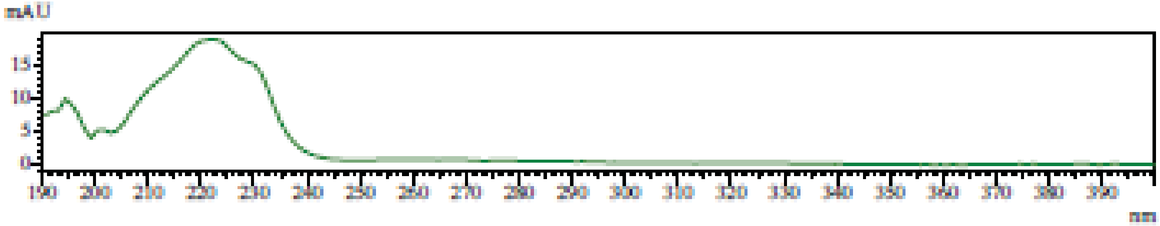
Chromatogram



UV Spectrum
Retention time = 24.571



UV Spectrum
Retention time = 27.916

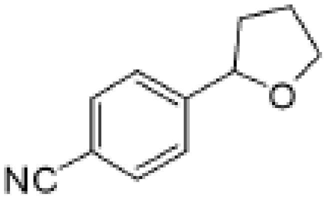


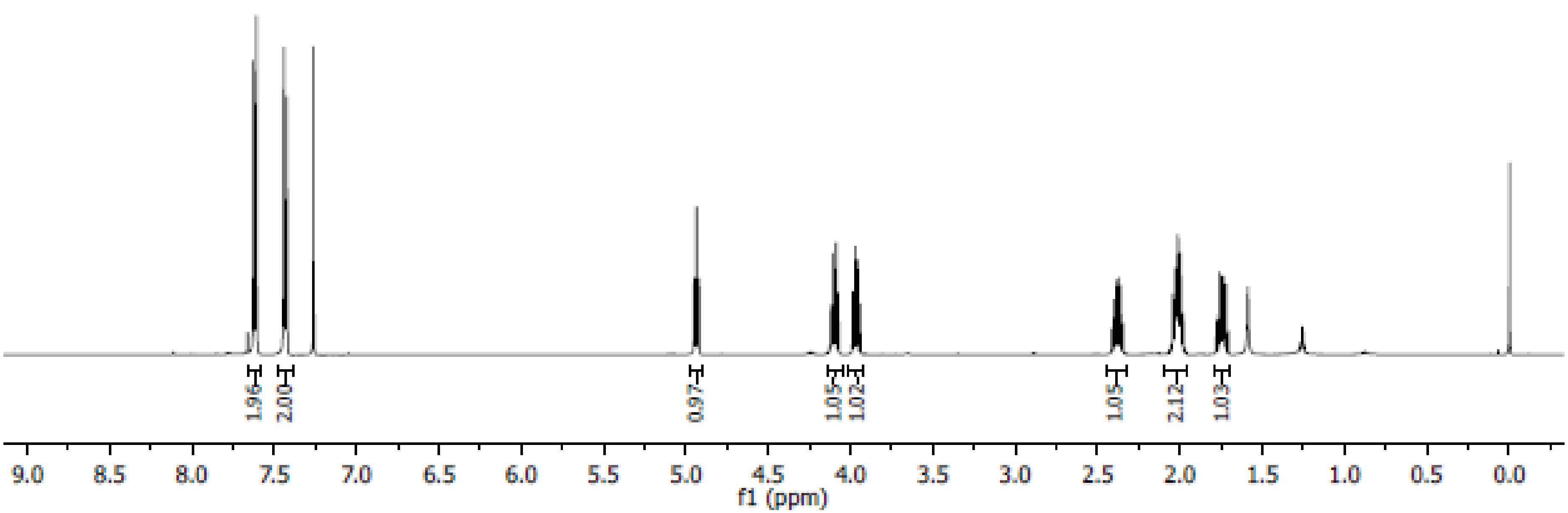
Peak Table

PDA Ch1 235nm

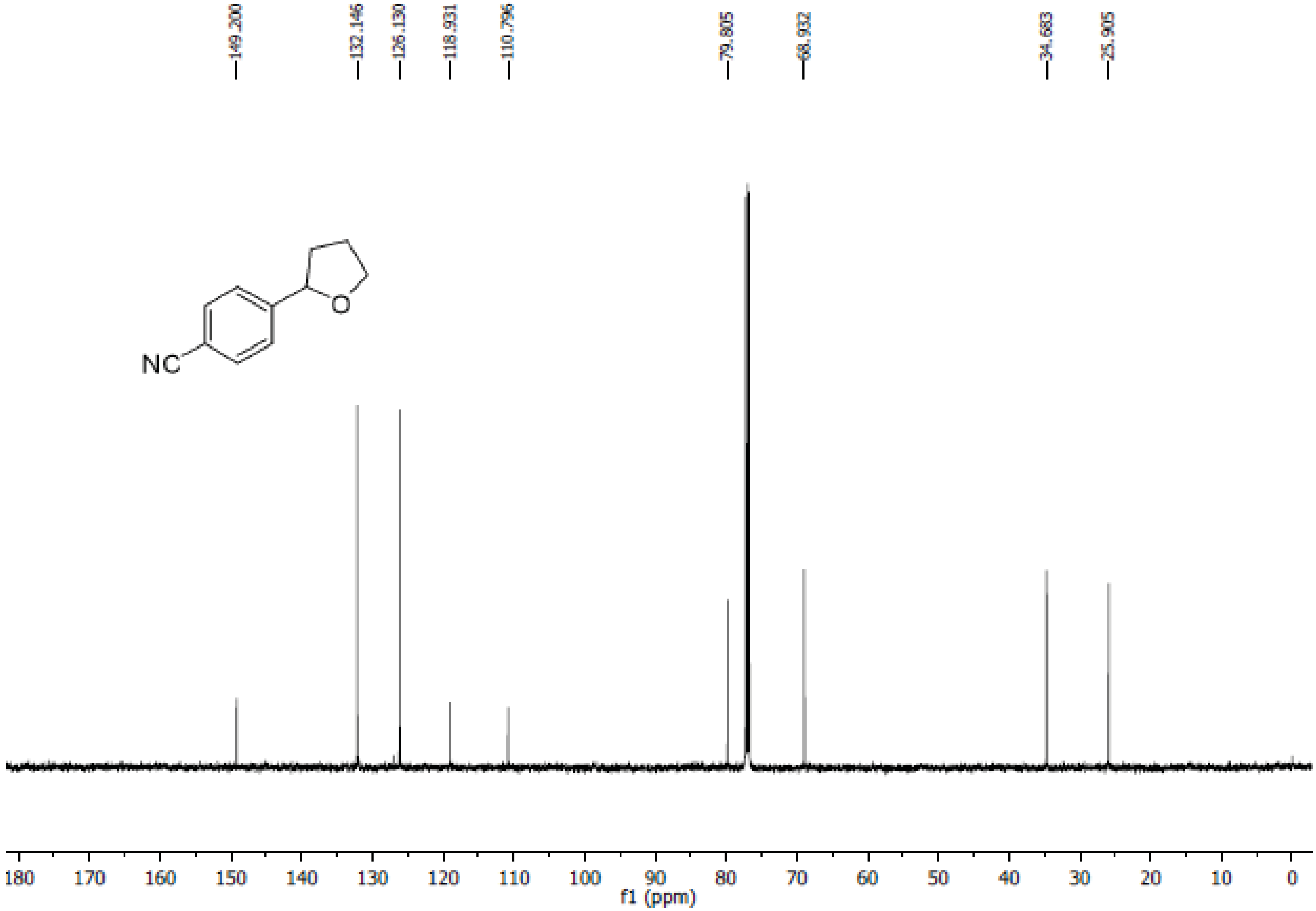
Peak#	Ret. Time	Area	Area%
1	24.571	13923202	97.214
2	27.916	399050	2.786
Total		14322252	100.000

(*S*)-4-(tetrahydrofuran-2-yl)benzonitrile





(*S*)-4-(tetrahydrofuran-2-yl)benzonitrile

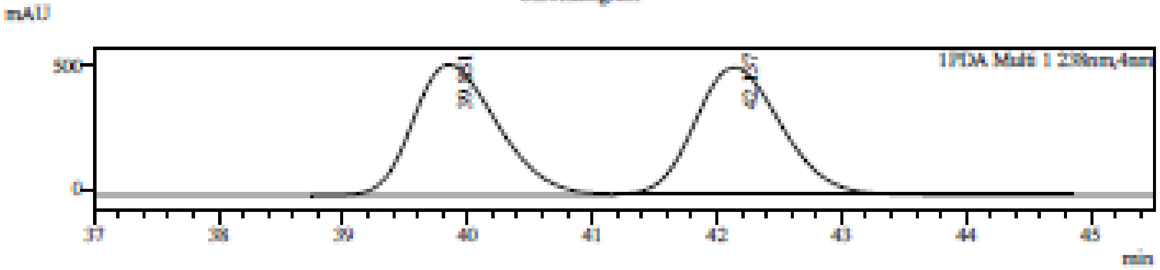


(*S*)-4-(tetrahydrofuran-2-yl)benzonitrile

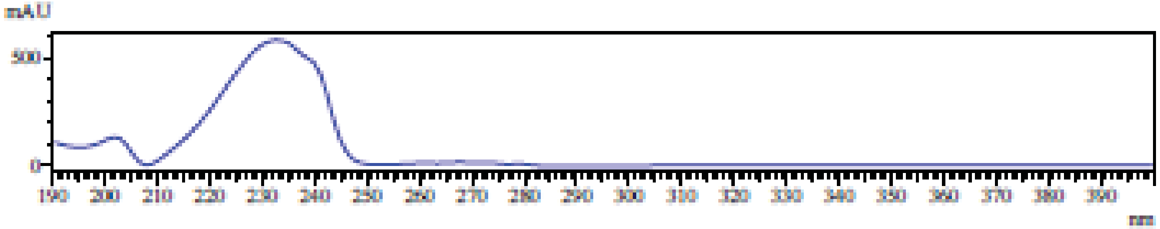
Sample Information

Data File : XW-VI-255-IF-1%0.8mL.lcd
Sample Name : XW-VI-255-IF-1%0.8mL
Sample ID : XW-VI-255-IF-1%0.8mL
Method File : XW-1%-0.8ml.lcm

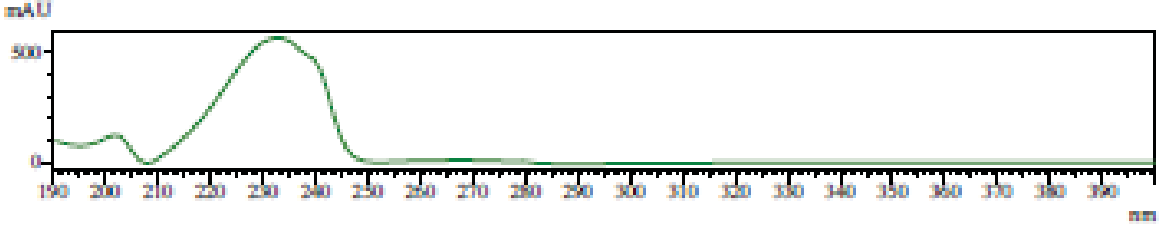
Chromatogram



UV Spectrum
Retention time = 39.851



UV Spectrum
Retention time = 42.137



Peak Table

PDA Ch1 238nm

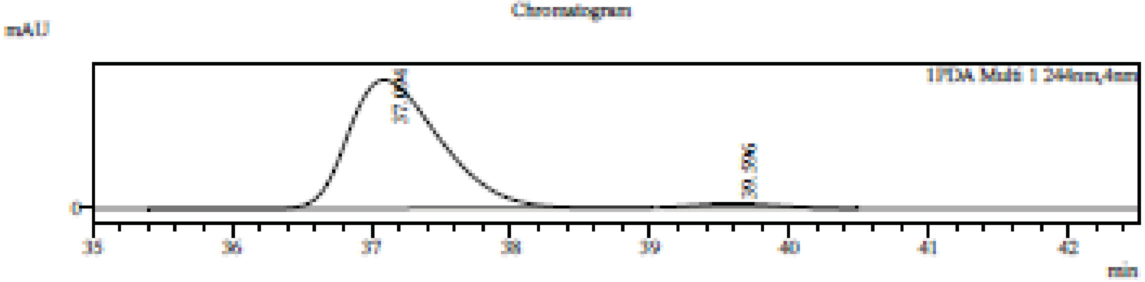
Peak#	Ret. Time	Area	Area%
1	39.851	25050504	49.826
2	42.137	25225077	50.174
Total		50275582	100.000

(*S*)-4-(tetrahydrofuran-2-yl)benzonitrile

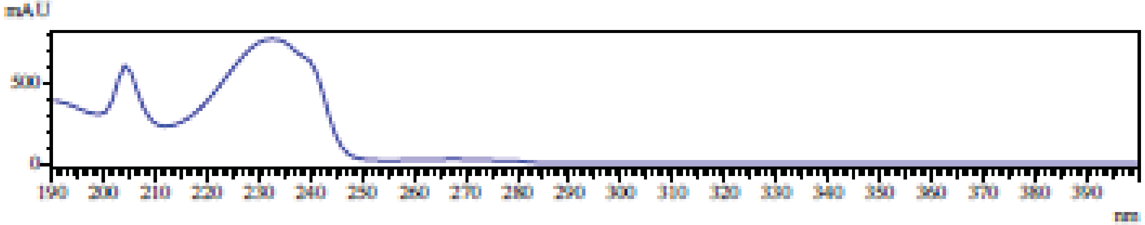
Sample Information

Data File	: XW-VI-256A-IF-1%0.8mL001.lcd
Sample Name	: XW-VI-256A-IF-1%0.8mL001
Sample ID	: XW-VI-256A-IF-1%0.8mL001
Method File	: XW-1%-0.8ml.lcm

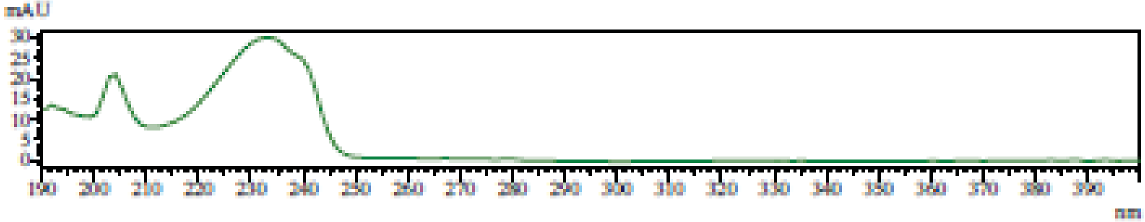
Chromatogram



UV Spectrum
Retention time = 37.094



UV Spectrum
Retention time = 39.596

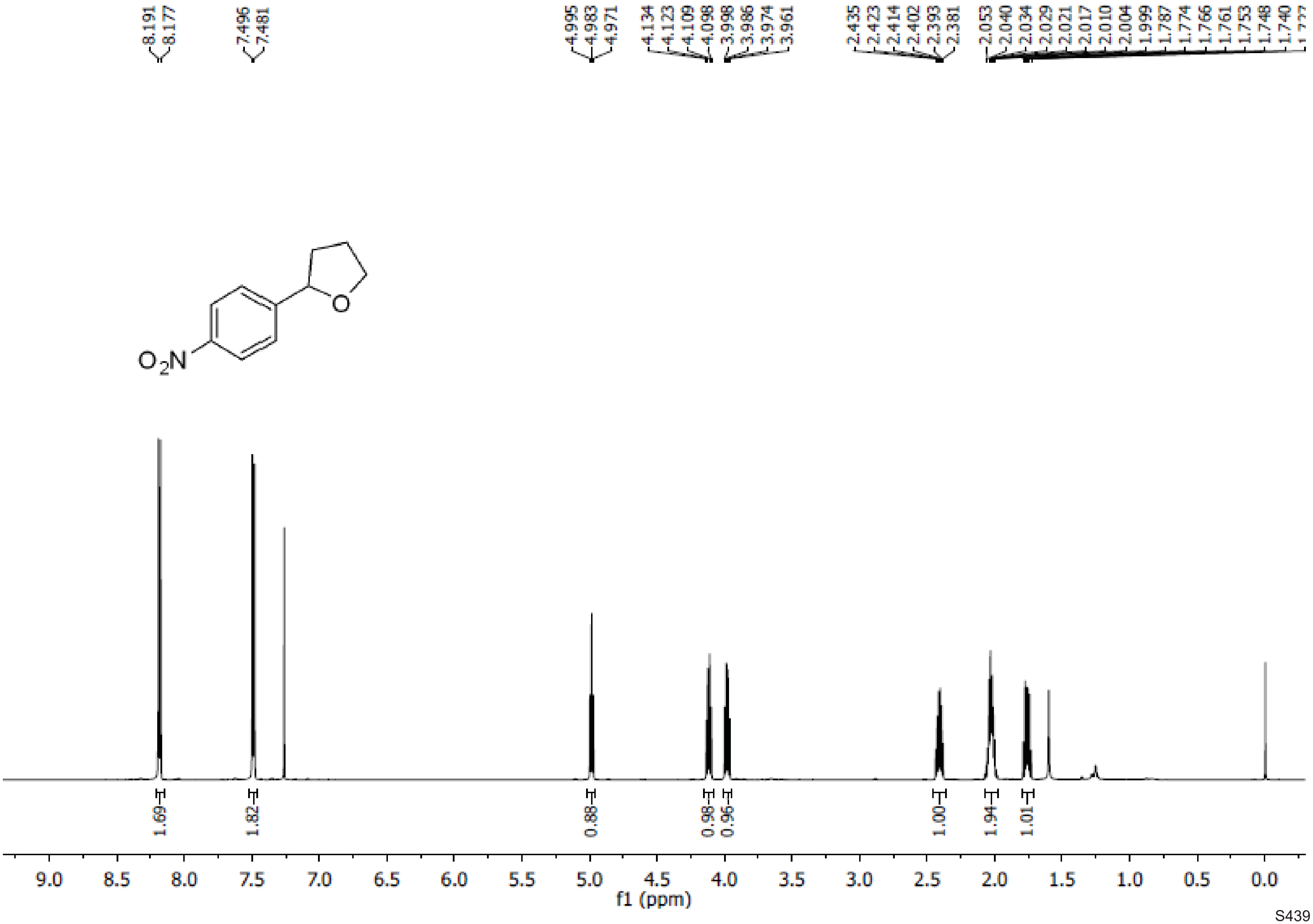


Peak Table

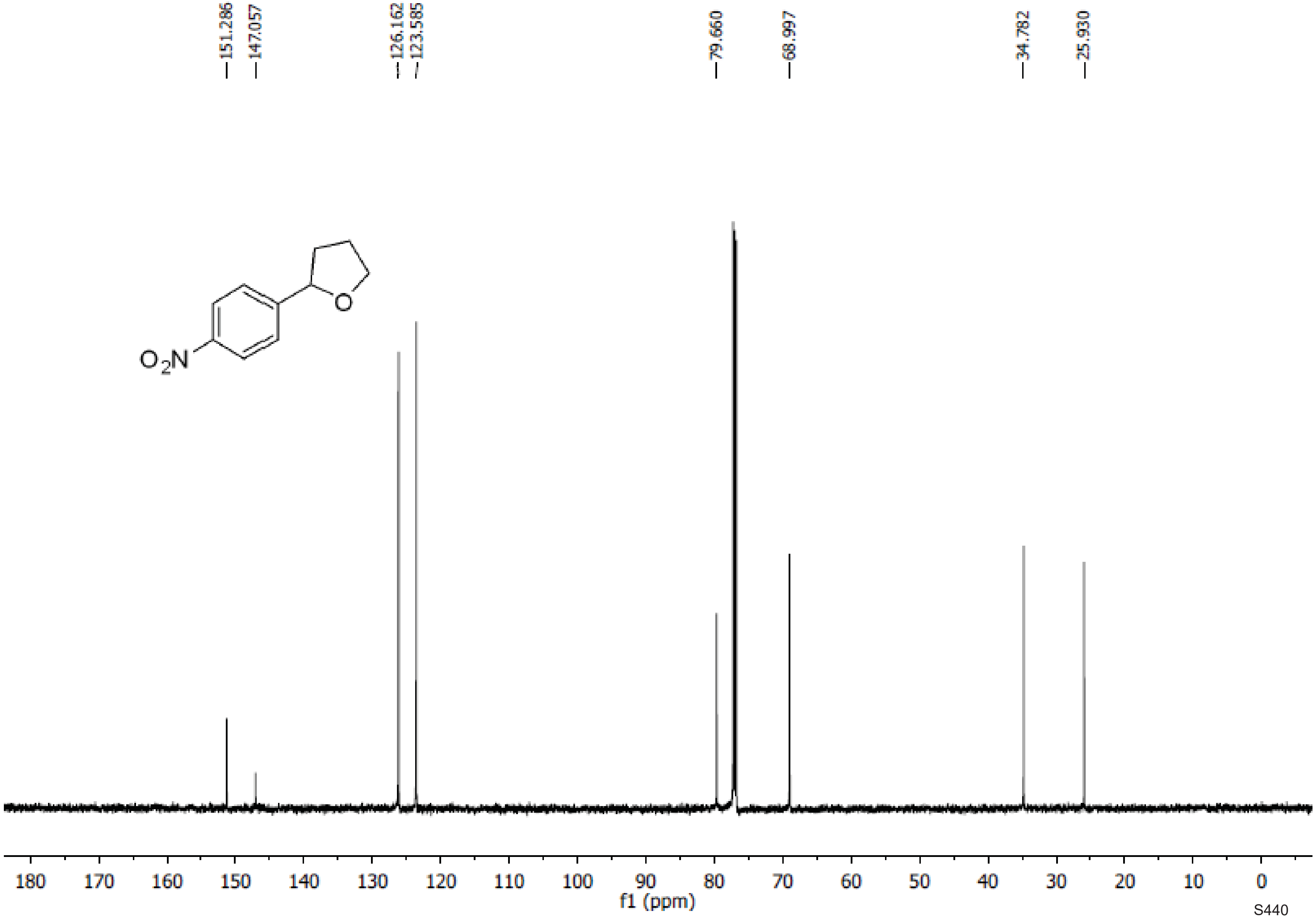
PDA Ch1 244nm

Peak#	Ret. Time	Area	Area%
1	37.094	12717600	97.266
2	39.596	357526	2.734
Total		13075126	100.000

(*S*)-2-(4-nitrophenyl)tetrahydrofuran



(*S*)-2-(4-nitrophenyl)tetrahydrofuran

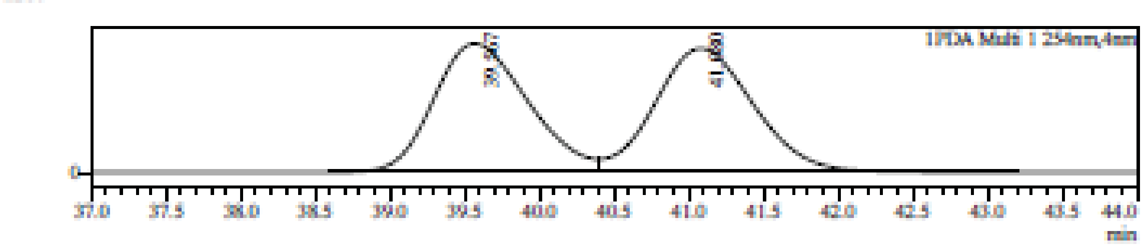


(*S*)-2-(4-nitrophenyl)tetrahydrofuran

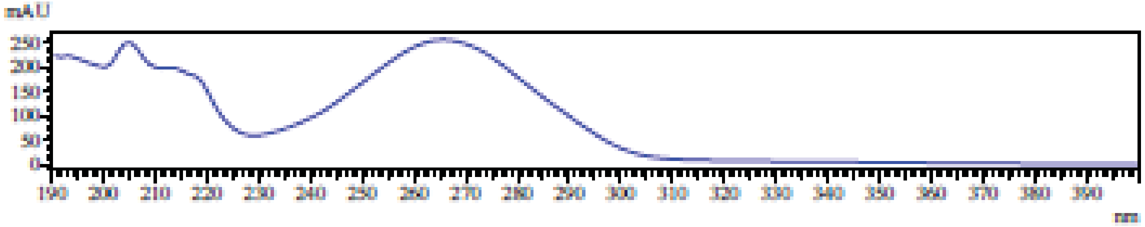
Sample Information

Data File	: XW-VI-264-IF-1%0.8mL-2.lcd
Sample Name	: XW-VI-264-IF-1%0.8mL-2
Sample ID	: XW-VI-264-IF-1%0.8mL-2
Method File	: XW-1%-0.8ml.lcm

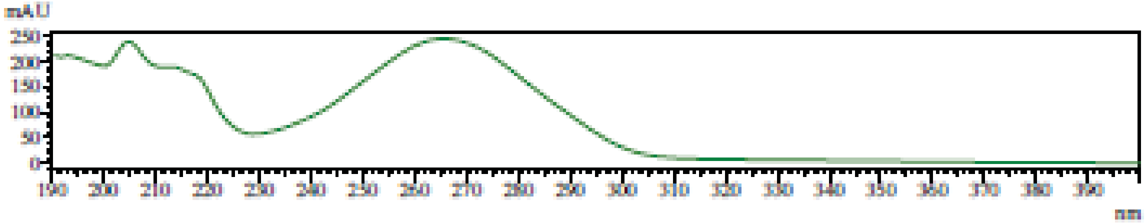
Chromatogram



UV Spectrum
Retention time = 39.567



UV Spectrum
Retention time = 41.080



Peak Table

PDA Ch1 254nm

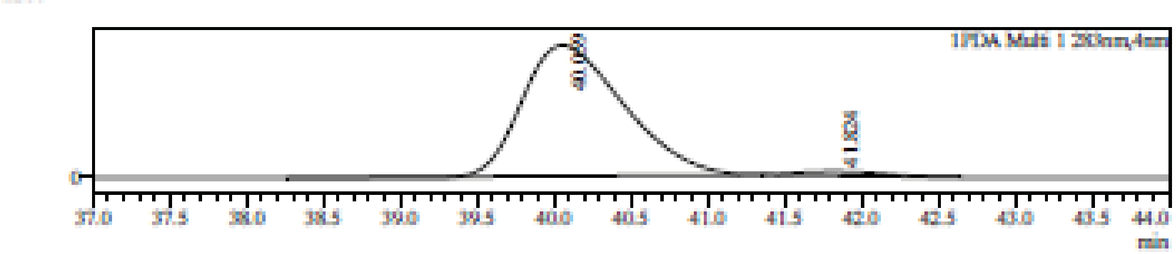
Peak#	Ret. Time	Area	Area%
1	39.567	8696739	49.765
2	41.080	8778873	50.235
Total		17475612	100.000

(*S*)-2-(4-nitrophenyl)tetrahydrofuran

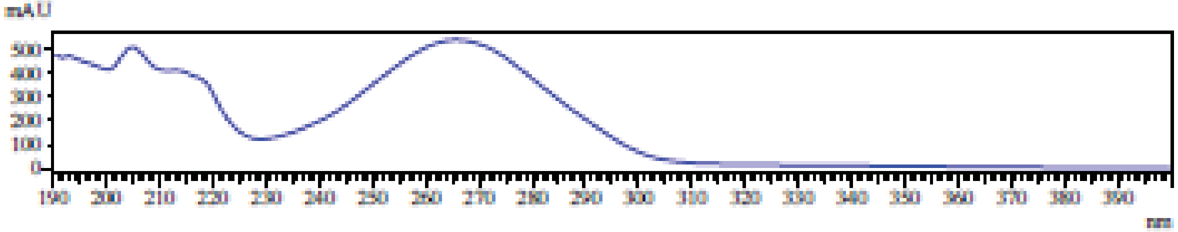
Sample Information

Data File : XW-VI-265a-IF-1%0.8mL.lcd
Sample Name : XW-VI-265a-IF-1%0.8mL
Sample ID : XW-VI-265a-IF-1%0.8mL
Method File : XW-1%-0.8ml.lcm

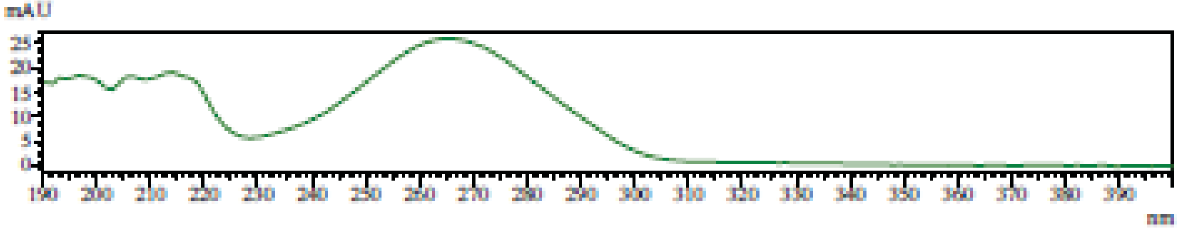
Chromatogram



UV Spectrum
Retention time = 40.059



UV Spectrum
Retention time = 41.824

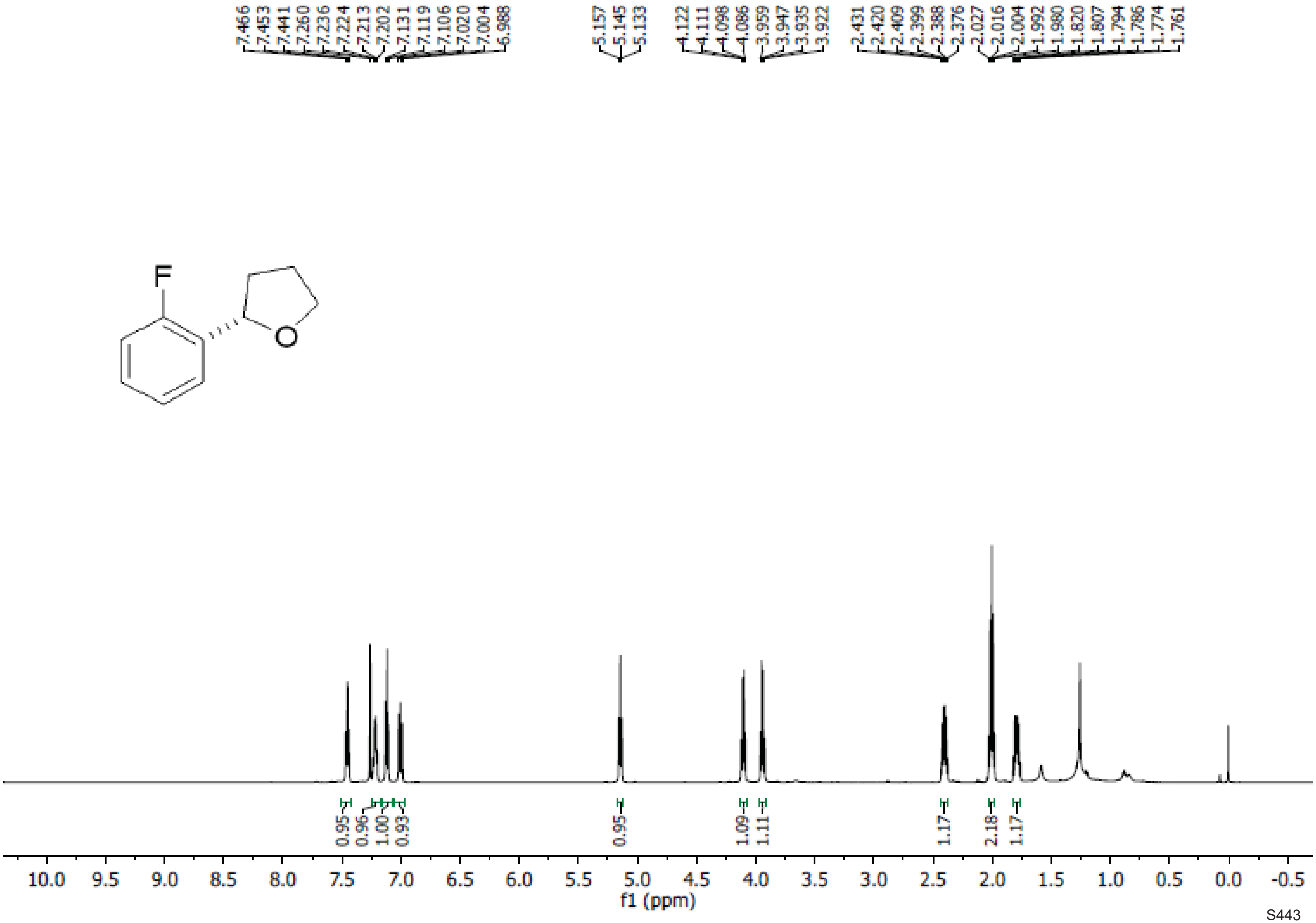


Peak Table

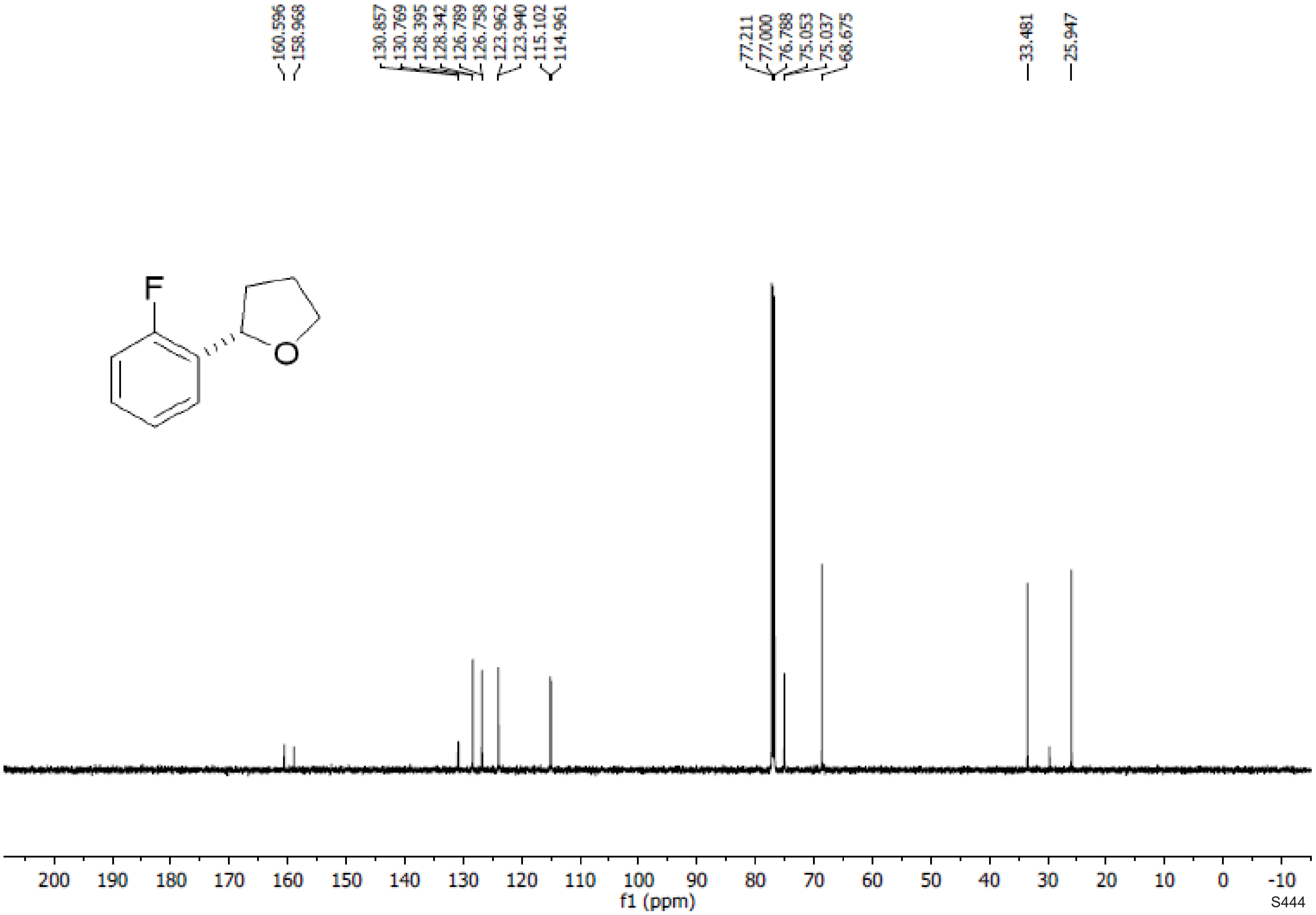
PDA Ch1 283nm

Peak#	Ret. Time	Area	Area%
1	40.059	14379431	97.456
2	41.824	375349	2.544
Total		14754780	100.000

(*S*)-2-(2-fluorophenyl)tetrahydrofuran



(*S*)-2-(2-fluorophenyl)tetrahydrofuran

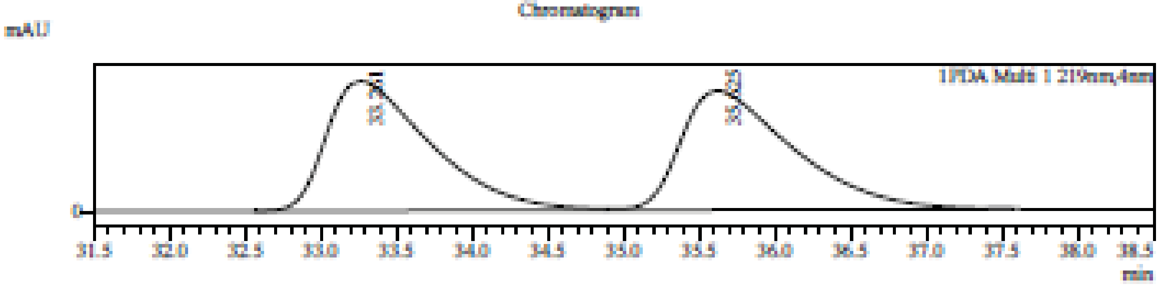


(*S*)-2-(2-fluorophenyl)tetrahydrofuran

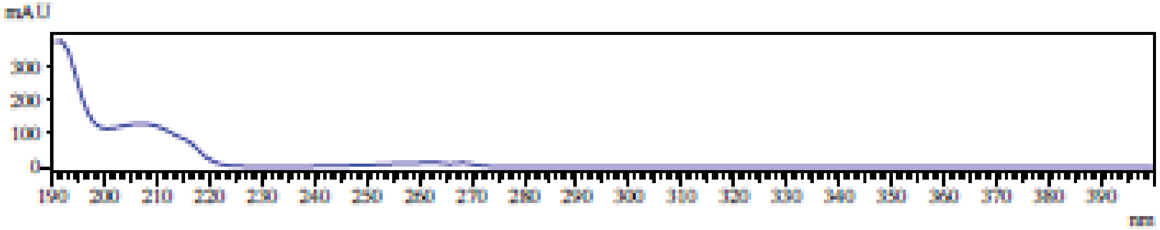
Sample Information

Data File	: XW-VI-248-IA-0%0.8mL-2.lcd
Sample Name	: XW-VI-248-IA-0%0.8mL-2
Sample ID	: XW-VI-248-IA-0%0.8mL-2
Method File	: XW-0%-0.8ml.lcm

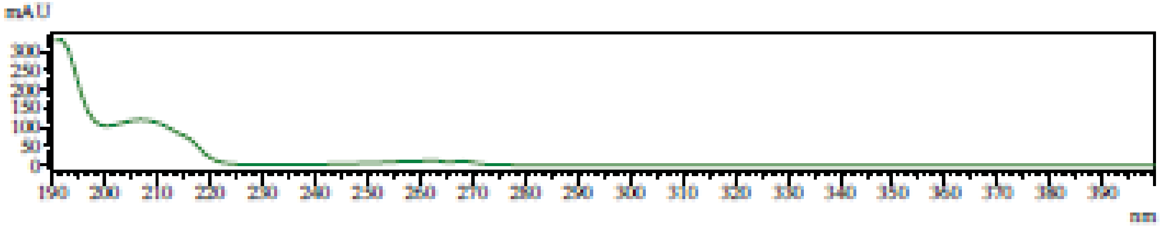
Chromatogram



UV Spectrum
Retention time = 33.261



UV Spectrum
Retention time = 35.625



Peak Table

PDA Ch1 219nm

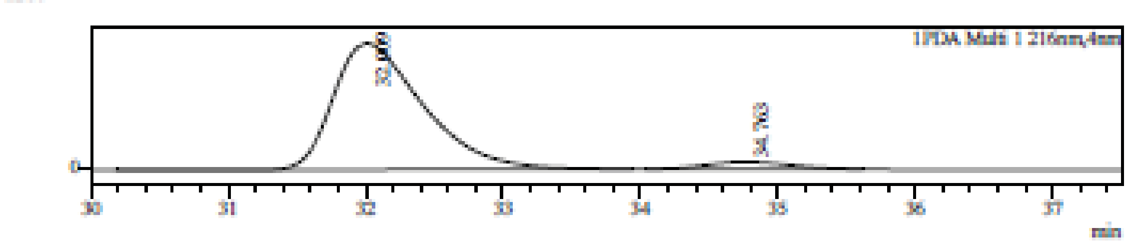
Peak#	Ret. Time	Area	Area%
1	33.261	1935519	50.256
2	35.625	1915768	49.744
Total		3851286	100.000

(*S*)-2-(2-fluorophenyl)tetrahydrofuran

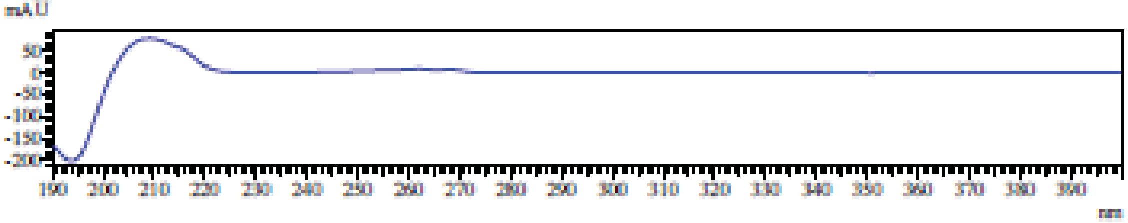
Sample Information

Data File : XW-VI-249B-IA-0%0.8mL-1.lcd
Sample Name : XW-VI-249B-IA-0%0.8mL-1
Sample ID : XW-VI-249B-IA-0%0.8mL-1
Method File : XW-0%-0.8ml.lcm

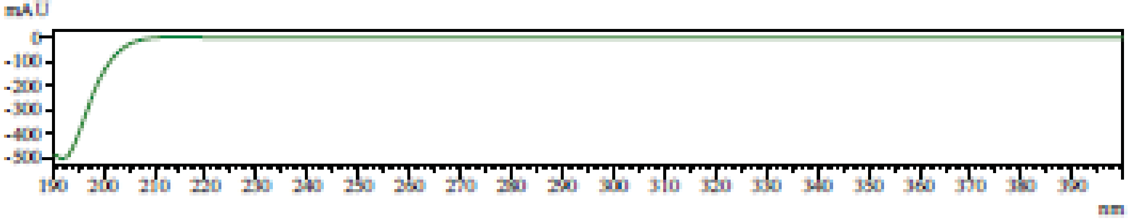
Chromatogram



UV Spectrum
Retention time = 32.009



UV Spectrum
Retention time = 34.763

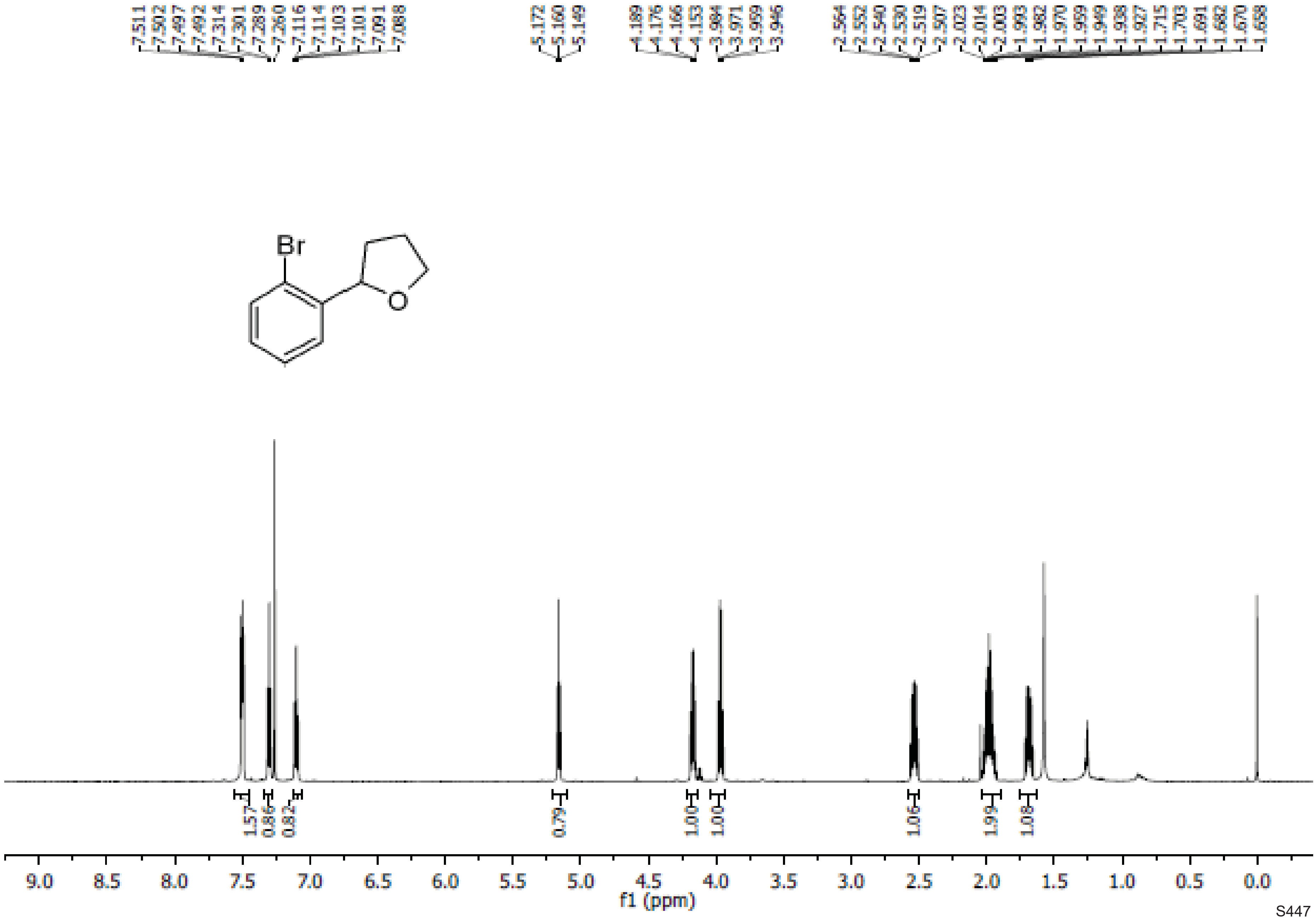


Peak Table

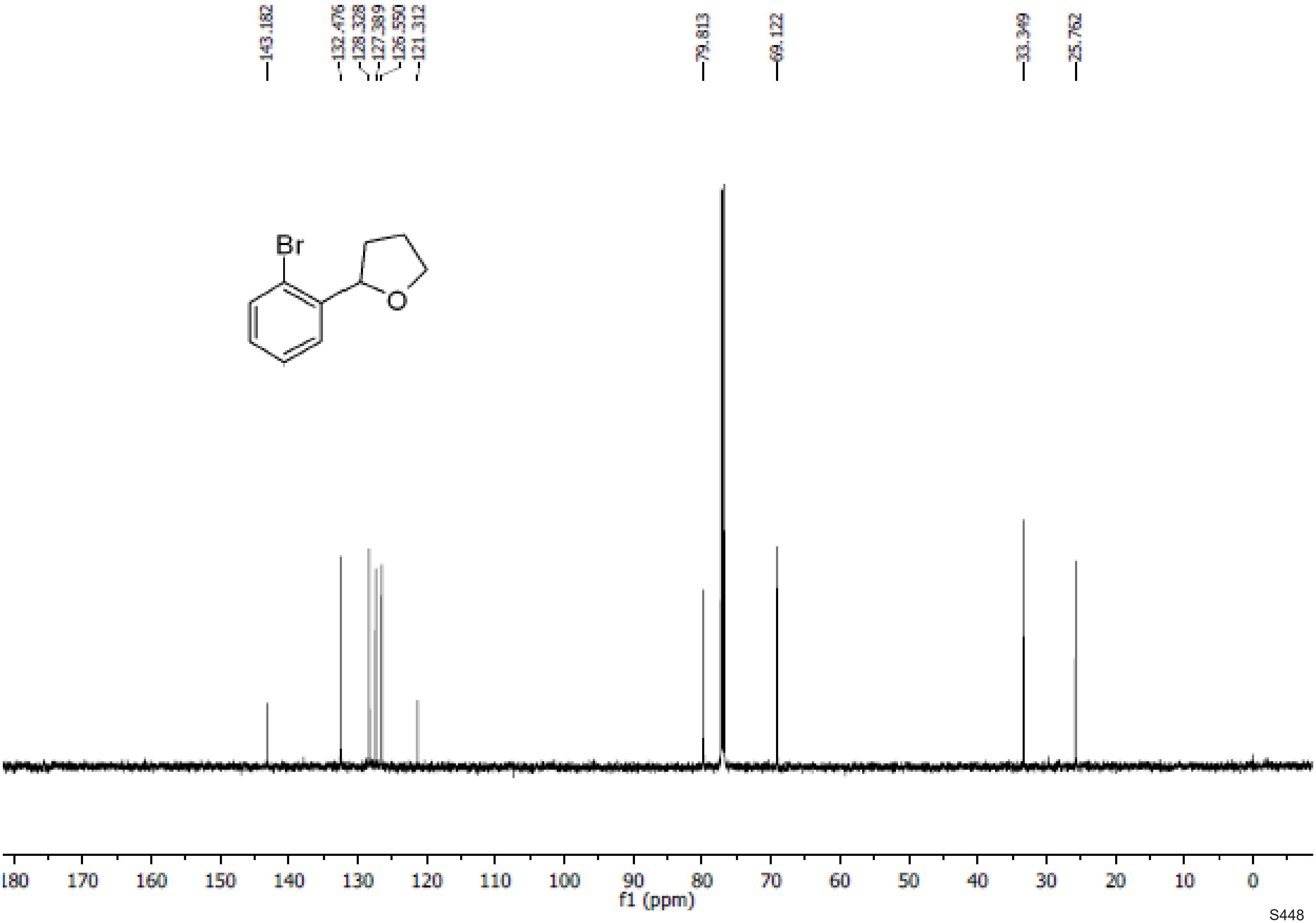
PDA Ch1 216nm

Peak#	Ret. Time	Area	Area%
1	32.009	2248948	94.965
2	34.763	119246	5.035
Total		2368194	100.000

(*S*)-2-(2-bromophenyl)tetrahydrofuran



(*S*)-2-(2-bromophenyl)tetrahydrofuran

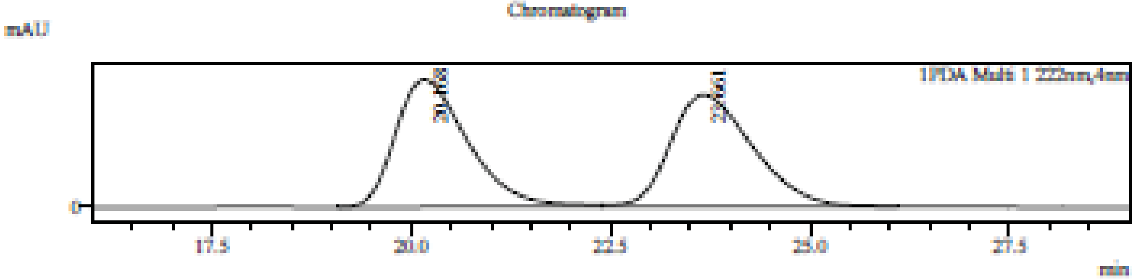


(S)-2-(2-bromophenyl)tetrahydrofuran

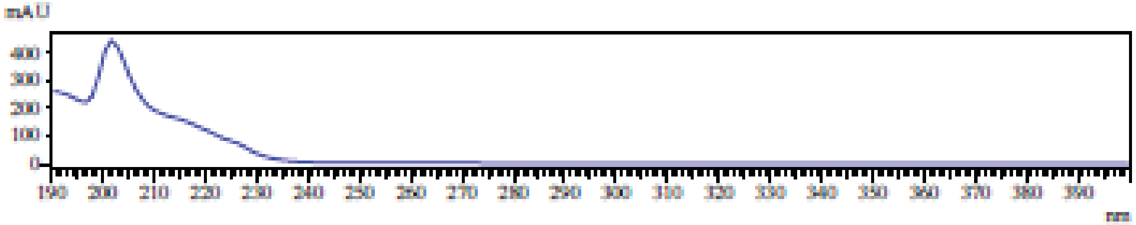
Sample Information

Data File : XW-VI-124-IE-0.2%0.8mL-2.lcd
Sample Name : XW-VI-124-IE-0.2%0.8mL-2
Sample ID : XW-VI-124-IE-0.2%0.8mL-2
Method File : XW-0.2%-0.8ml.lcm

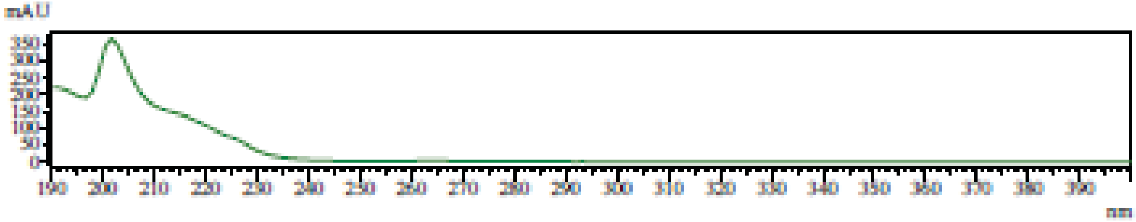
Chromatogram



UV Spectrum
Retention time = 20.168



UV Spectrum
Retention time = 23.661



Peak Table

PDA Ch1 222nm

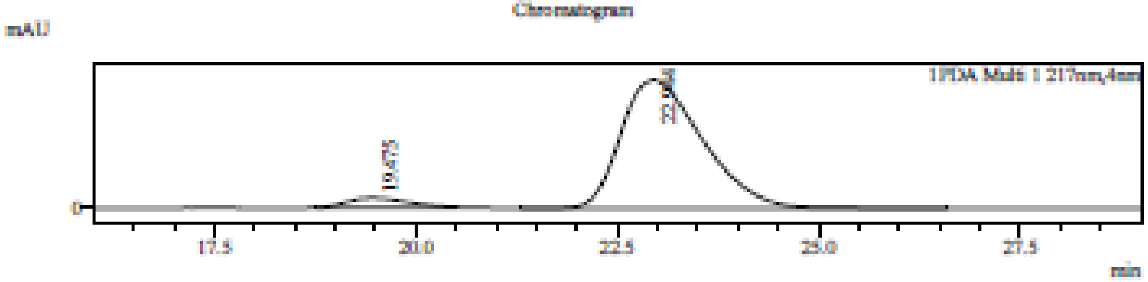
Peak#	Ret. Time	Area	Area%
1	20.168	6624131	50.120
2	23.661	6592353	49.880
Total		13216484	100.000

(S)-2-(2-bromophenyl)tetrahydrofuran

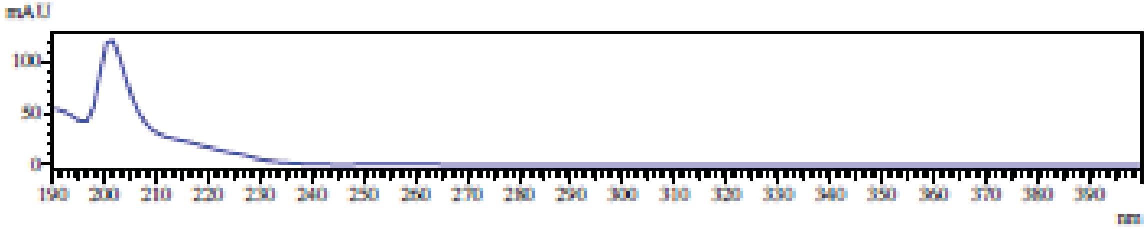
Sample Information

Data File : XW-VI-125b-IE-0.2%0.8mL-1.lcd
Sample Name : XW-VI-125b-IE-0.2%0.8mL-1
Sample ID : XW-VI-125b-IE-0.2%0.8mL-1
Method File : XW-0.2%-0.8ml.lcm

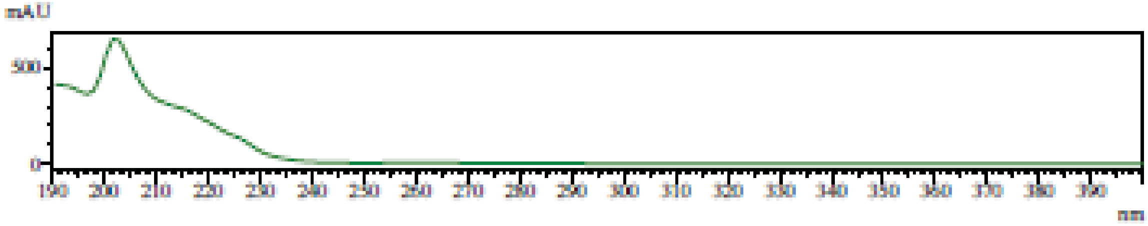
Chromatogram



UV Spectrum
Retention time = 19.475



UV Spectrum
Retention time = 22.944

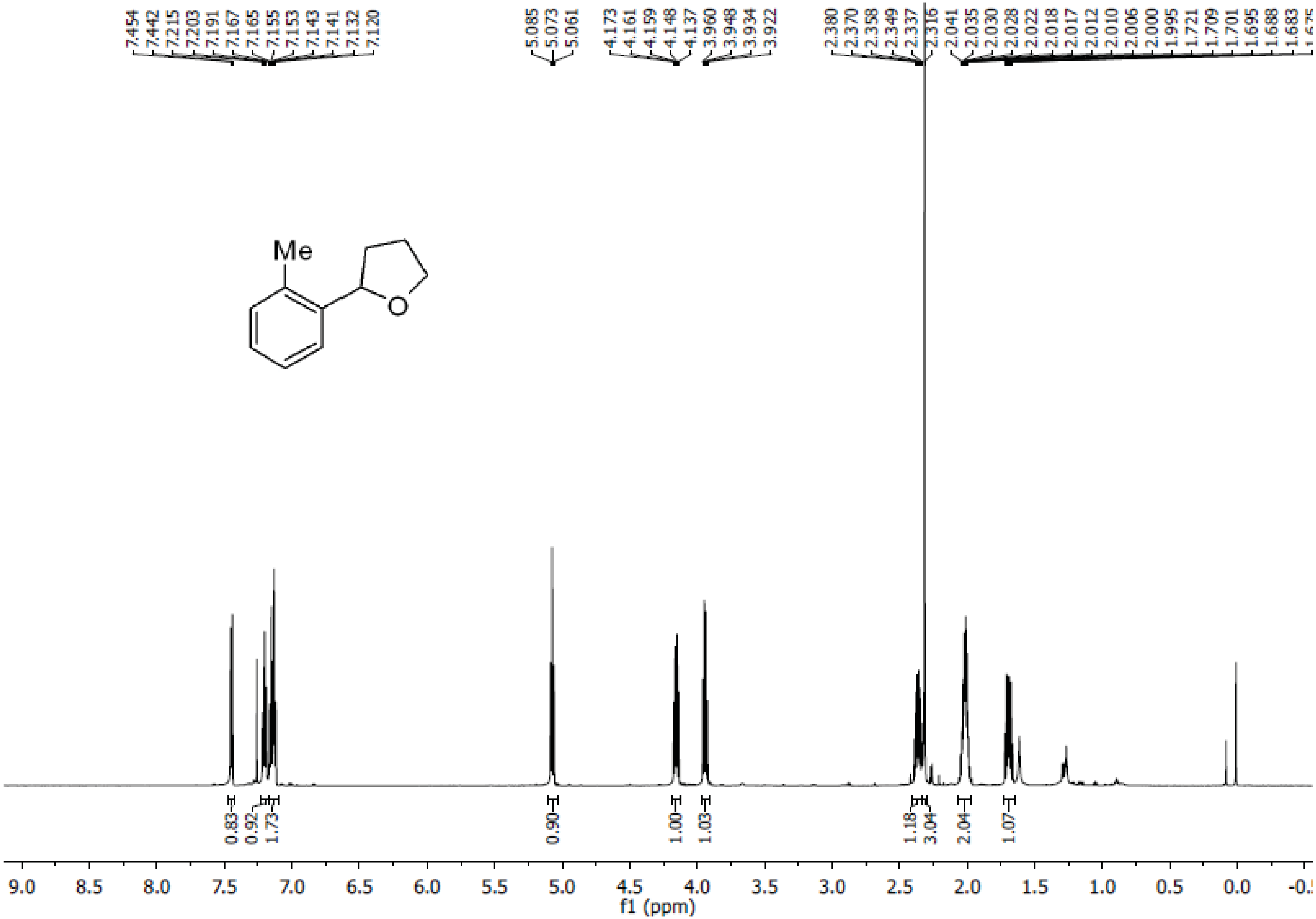


Peak Table

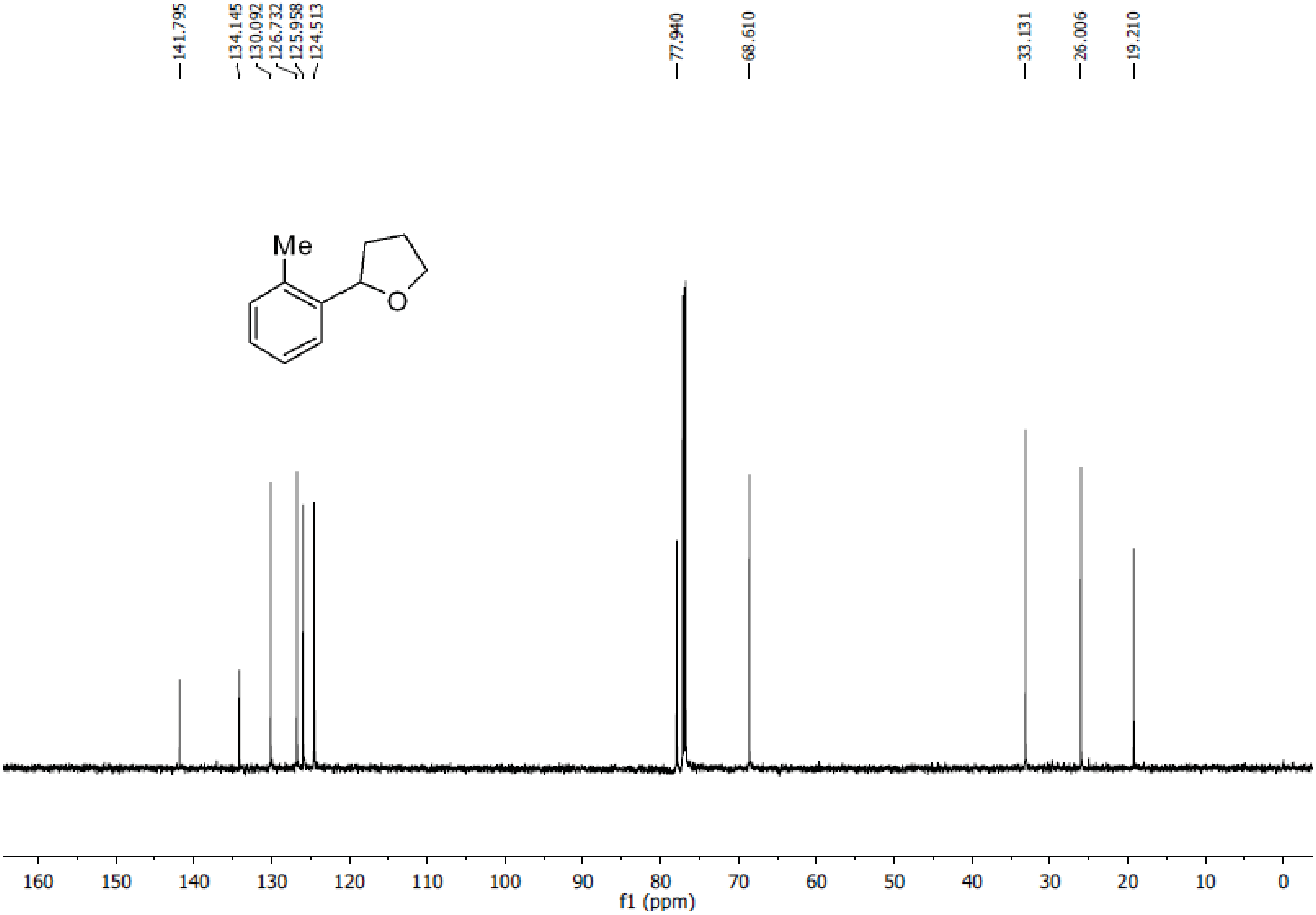
PDA Ch1 217nm

Peak#	Ret. Time	Area	Area%
1	19.475	976530	5.062
2	22.944	18314508	94.938
Total		19291037	100.000

(*S*)-2-(o-tolyl)tetrahydrofuran



(*S*)-2-(o-tolyl)tetrahydrofuran

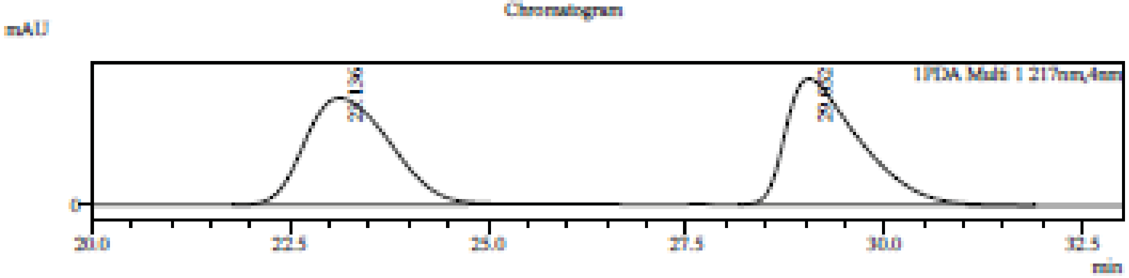


(*S*)-2-(o-tolyl)tetrahydrofuran

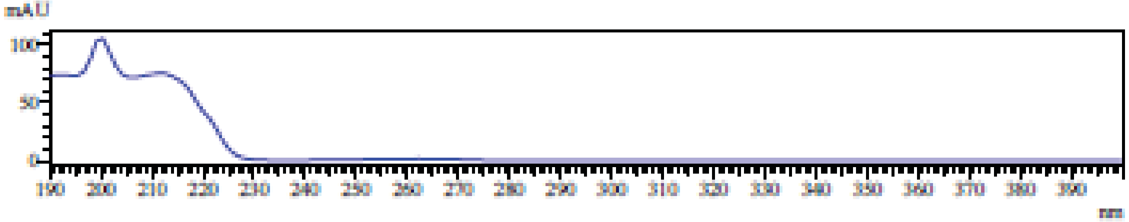
Sample Information

Data File	: XW-VI-224-IE-0.2%0.8mL-3.lcd
Sample Name	: XW-VI-224-IE-0.2%0.8mL-3
Sample ID	: XW-VI-224-IE-0.2%0.8mL-3
Method File	: XW-0.2%-0.8ml.lcm

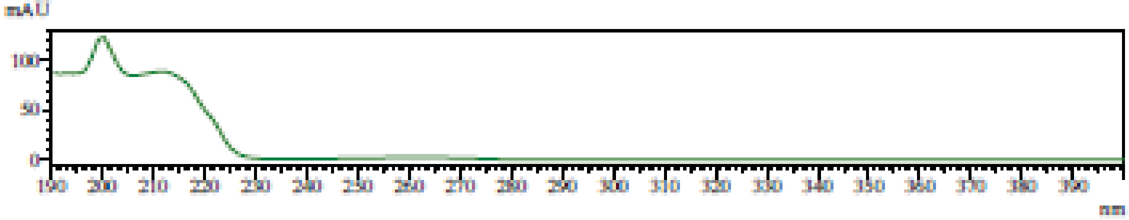
Chromatogram



UV Spectrum
Retention time = 23.136



UV Spectrum
Retention time = 29.052



Peak Table

PDA Ch1 217nm

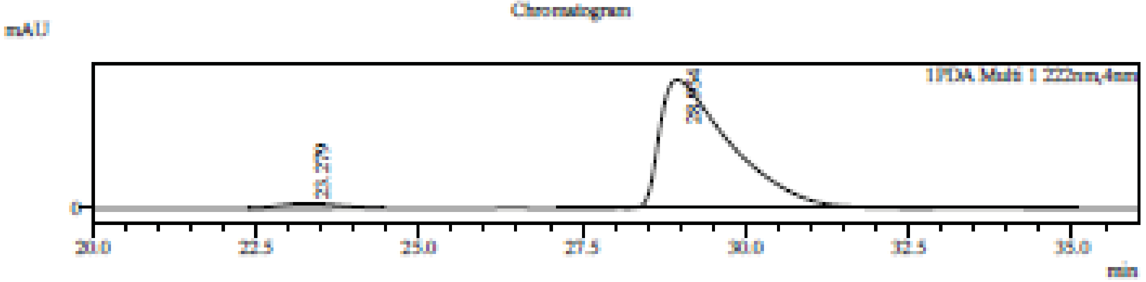
Peak#	Ret. Time	Area	Area%
1	23.136	4484265	49.705
2	29.052	4537461	50.295
Total		9021726	100.000

(*S*)-2-(o-tolyl)tetrahydrofuran

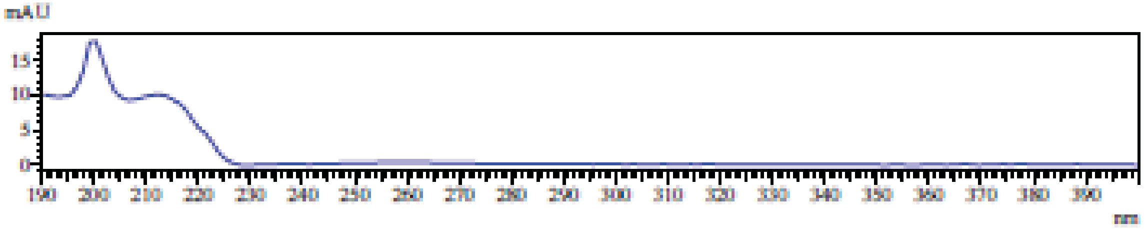
Sample Information

Data File	: XW-VI-225b-IE-0.2%0.8mL-1.lcd
Sample Name	: XW-VI-225b-IE-0.2%0.8mL-1
Sample ID	: XW-VI-225b-IE-0.2%0.8mL-1
Method File	: XW-0.2%-0.8ml.lcm

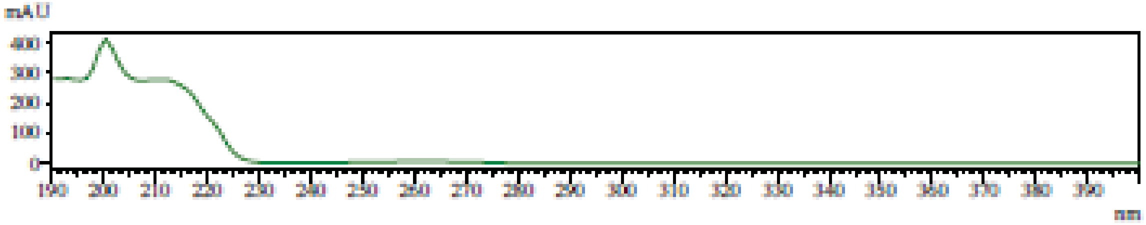
Chromatogram



UV Spectrum
Retention time = 23.279



UV Spectrum
Retention time = 28.954

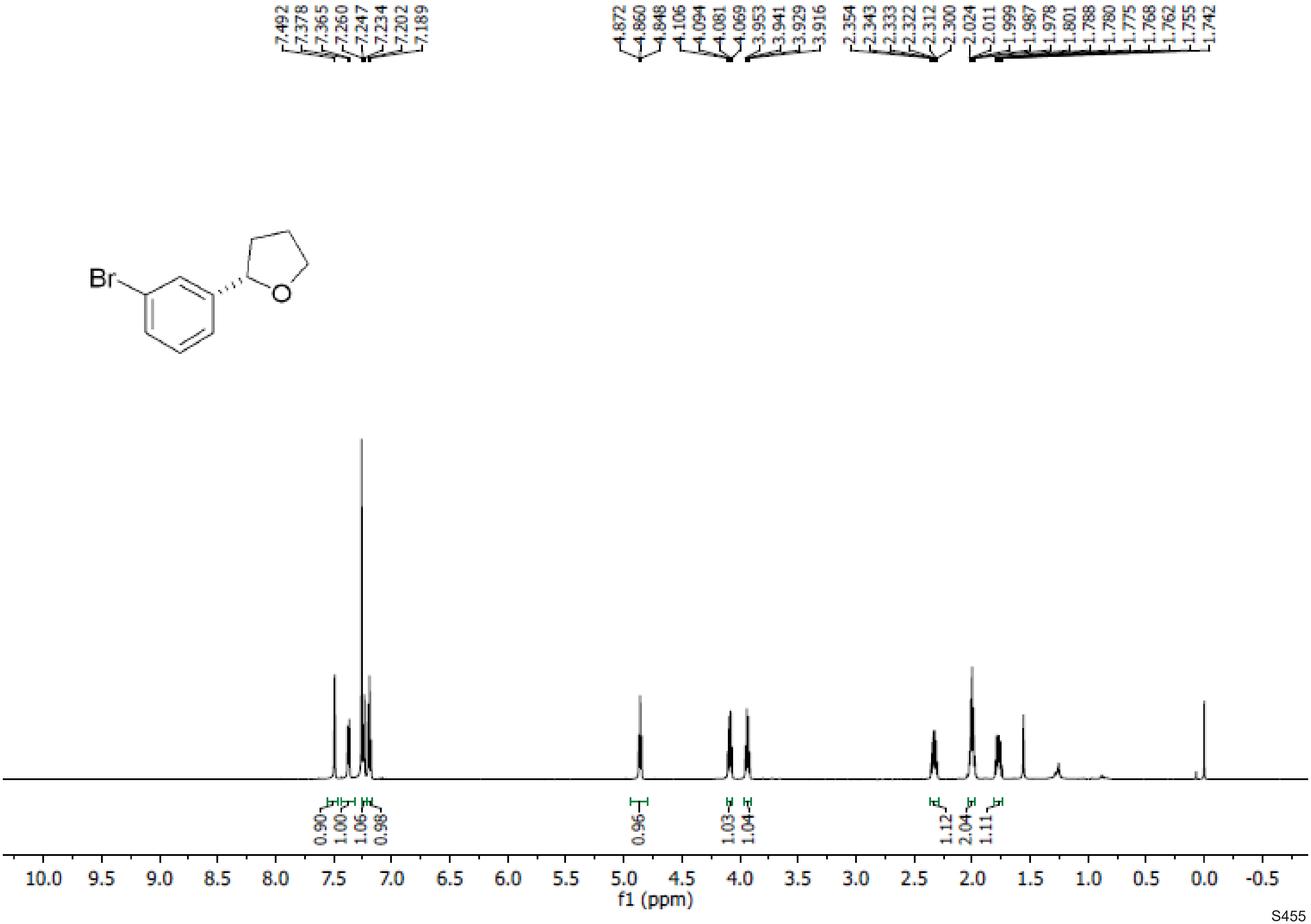


Peak Table

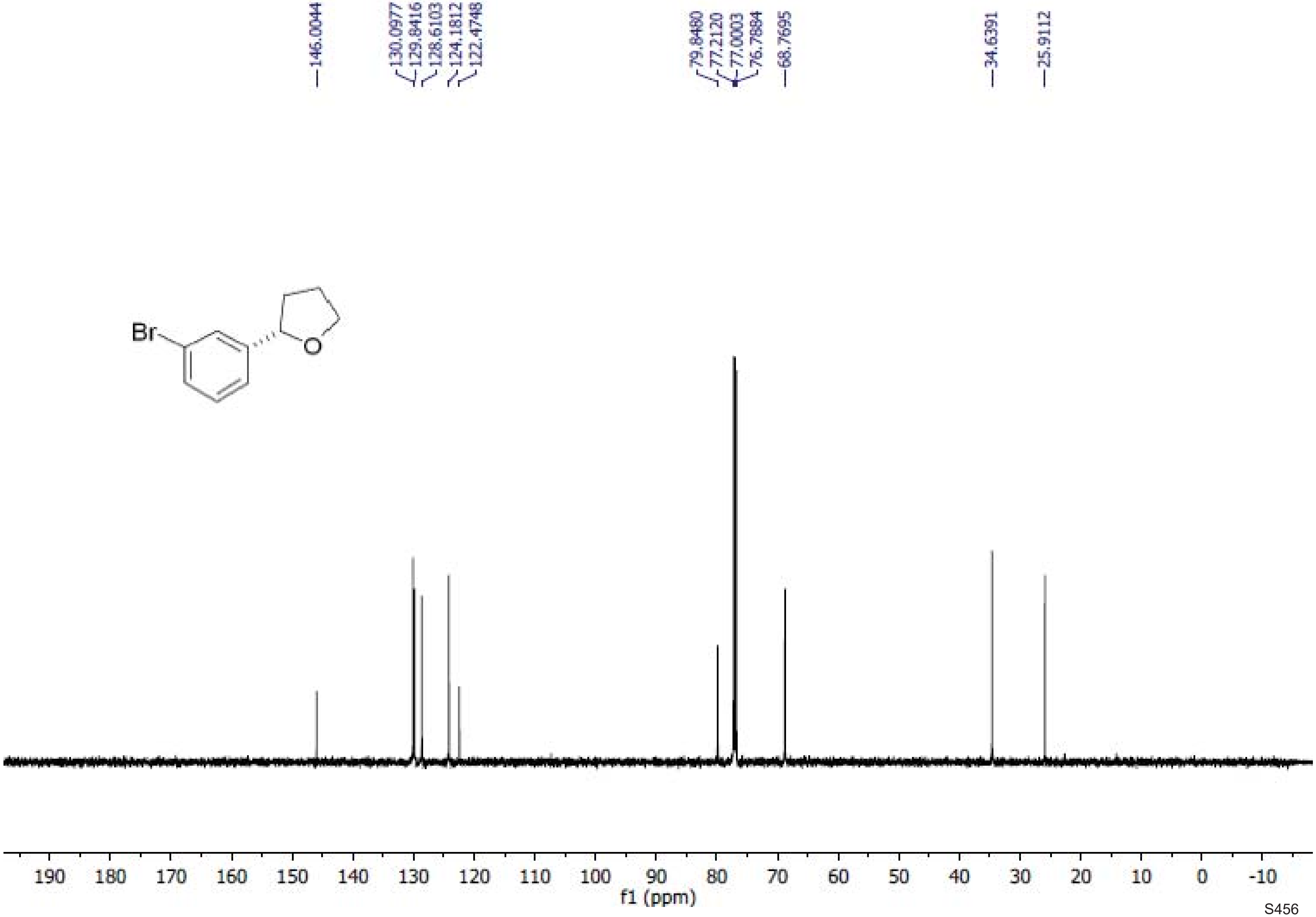
PDA Ch1 222nm

Peak#	Ret. Time	Area	Area%
1	23.279	264087	2.984
2	28.954	8585997	97.016
Total		8850084	100.000

(*S*)-2-(3-bromophenyl)tetrahydrofuran



(*S*)-2-(3-bromophenyl)tetrahydrofuran

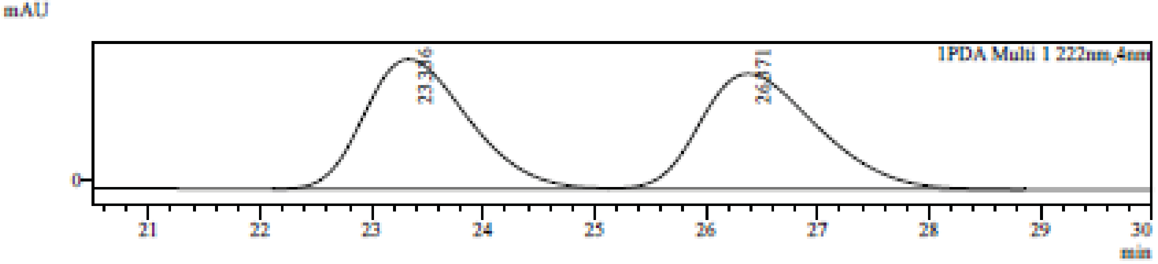


(*S*)-2-(3-bromophenyl)tetrahydrofuran

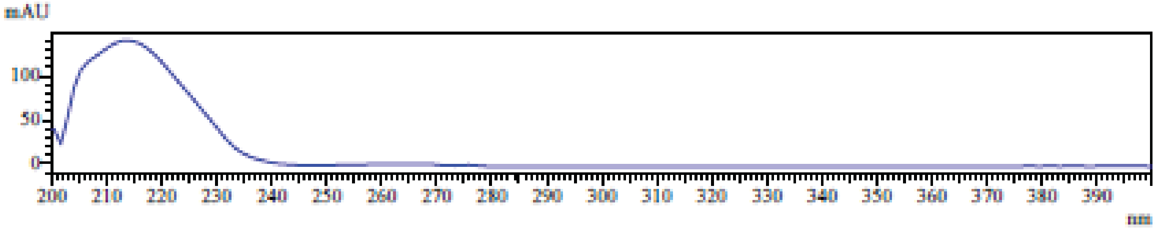
Sample Information

Data File : XW-VI-146-IE-0.2%0.8mL.lcd
Sample Name : XW-VI-146-IE-0.2%0.8mL
Sample ID : XW-VI-146-IE-0.2%0.8mL
Method File : XW-0.2%-0.8ml.lcm

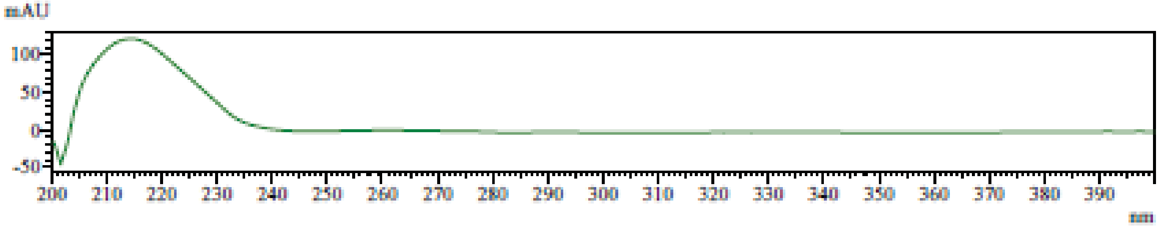
Chromatogram



UV Spectrum
Retention time = 23.336



UV Spectrum
Retention time = 26.371



Peak Table

PDA Ch1 222nm

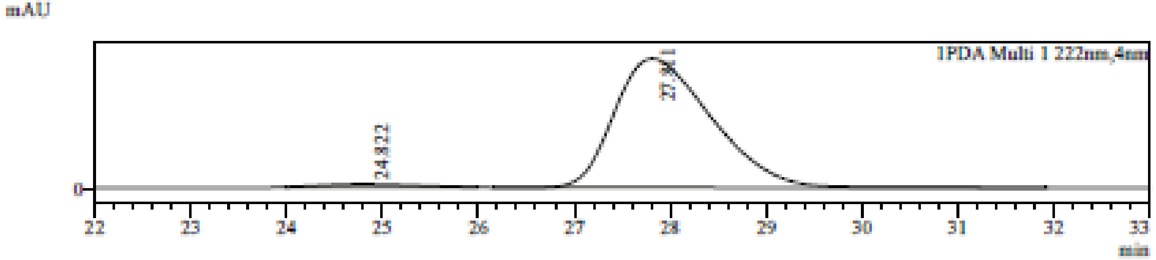
Peak#	Ret. Time	Area	Area%
1	23.336	7024308	49.986
2	26.371	7028189	50.014
Total		14052497	100.000

(*S*)-2-(3-bromophenyl)tetrahydrofuran

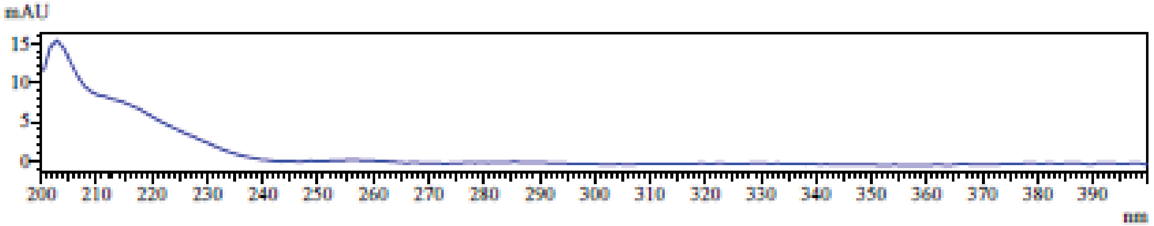
Sample Information

Data File : XW-VI-147a-IE-0.2%0.8mL.lcd
Sample Name : XW-VI-147a-IE-0.2%0.8mL
Sample ID : XW-VI-147a-IE-0.2%0.8mL
Method File : XW-0.2%-0.8ml.lcm

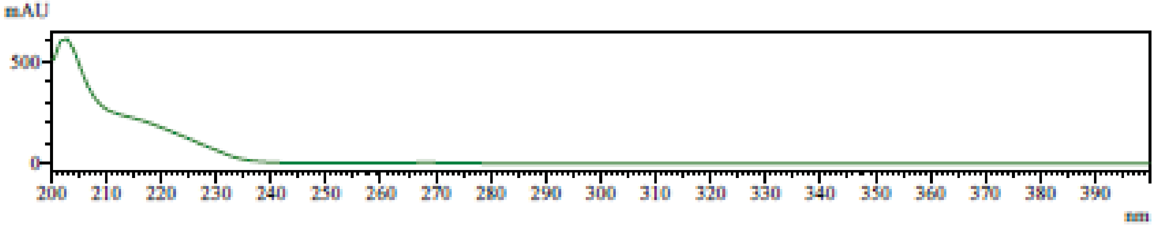
Chromatogram



UV Spectrum
Retention time = 24.822



UV Spectrum
Retention time = 27.811

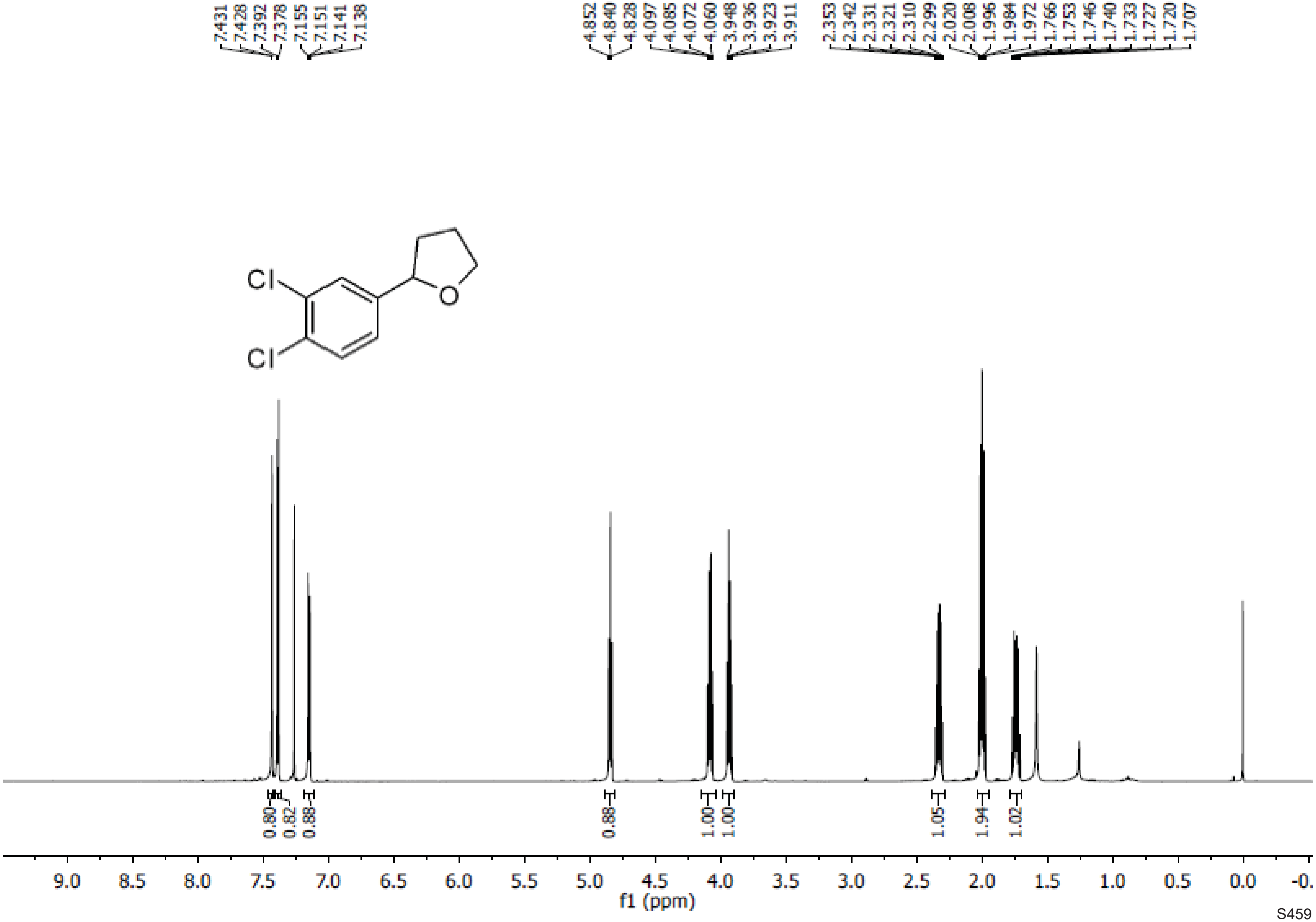


Peak Table

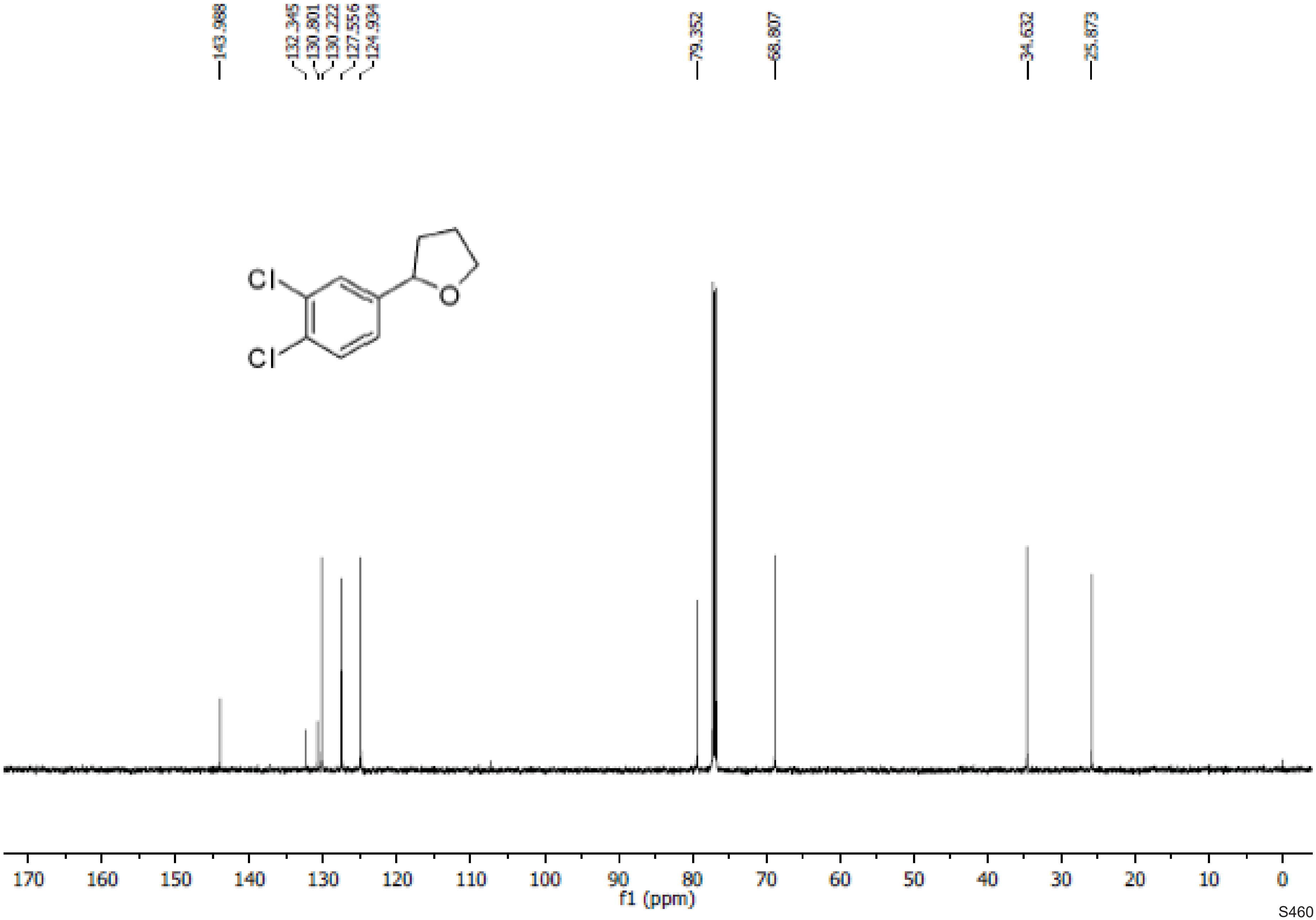
PDA Ch1 222nm

Peak#	Ret. Time	Area	Area%
1	24.822	248359	2.220
2	27.811	10938307	97.780
Total		11186665	100.000

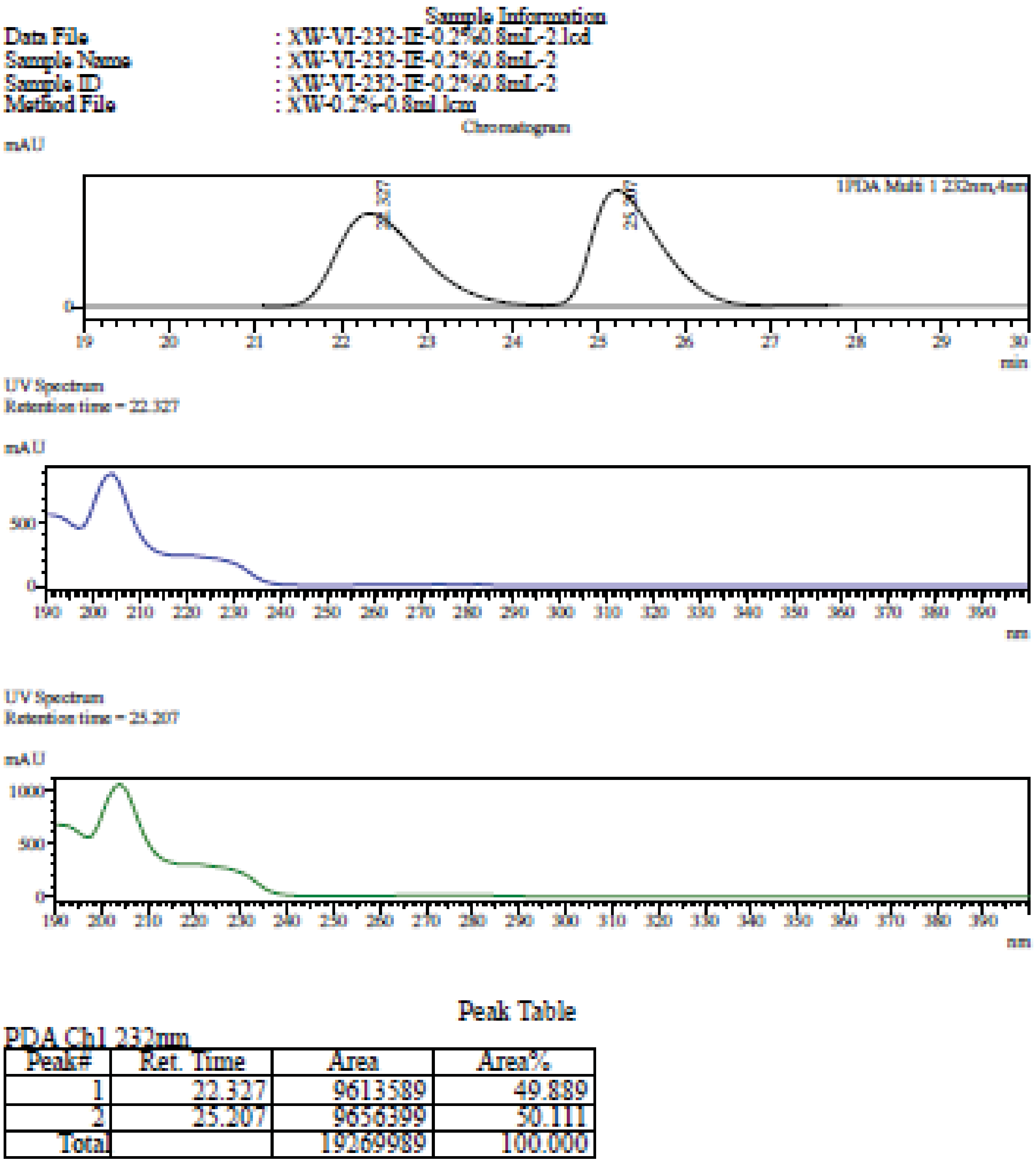
(*S*)-2-(3,4-dichlorophenyl)tetrahydrofuran



(*S*)-2-(3,4-dichlorophenyl)tetrahydrofuran



(*S*)-2-(3,4-dichlorophenyl)tetrahydrofuran



Sample Information

Data File	: XW-VI-232-IE-0.2%0.8mL-2.lcd
Sample Name	: XW-VI-232-IE-0.2%0.8mL-2
Sample ID	: XW-VI-232-IE-0.2%0.8mL-2
Method File	: XW-0.2%-0.8ml.lcm

Chromatogram

UV Spectrum
Retention time = 22.327

UV Spectrum
Retention time = 25.207

Peak Table

PDA Ch1 232nm

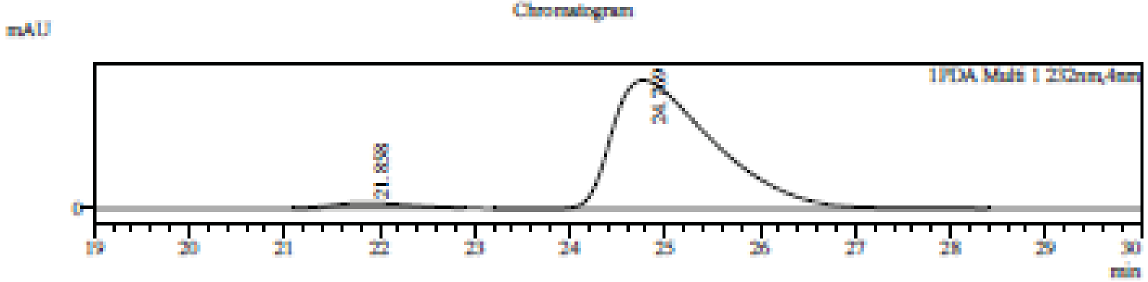
Peak#	Ret. Time	Area	Area%
1	22.327	9613589	49.889
2	25.207	9656399	50.111
Total		19269989	100.000

(*S*)-2-(3,4-dichlorophenyl)tetrahydrofuran

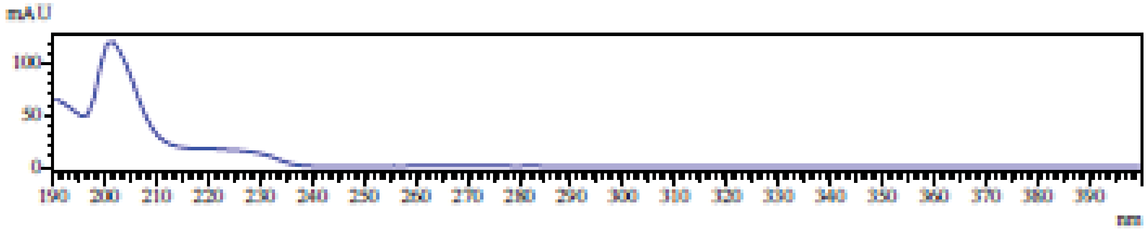
Sample Information

Data File	: XW-VI-233B-IE-0.2%0.8mL-1.lcd
Sample Name	: XW-VI-233B-IE-0.2%0.8mL-1
Sample ID	: XW-VI-233B-IE-0.2%0.8mL-1
Method File	: XW-0.2%-0.8ml.lcm

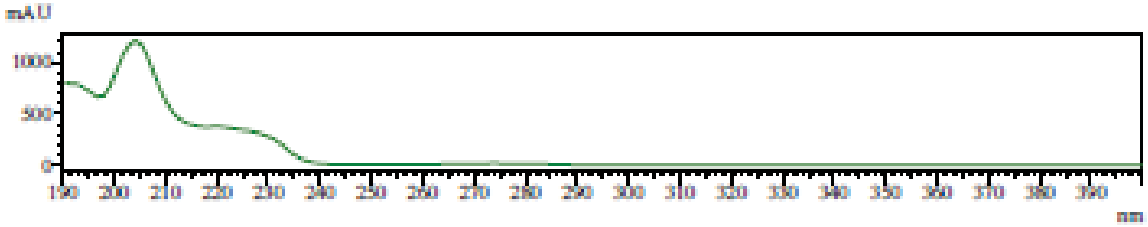
Chromatogram



UV Spectrum
Retention time = 21.858



UV Spectrum
Retention time = 24.769

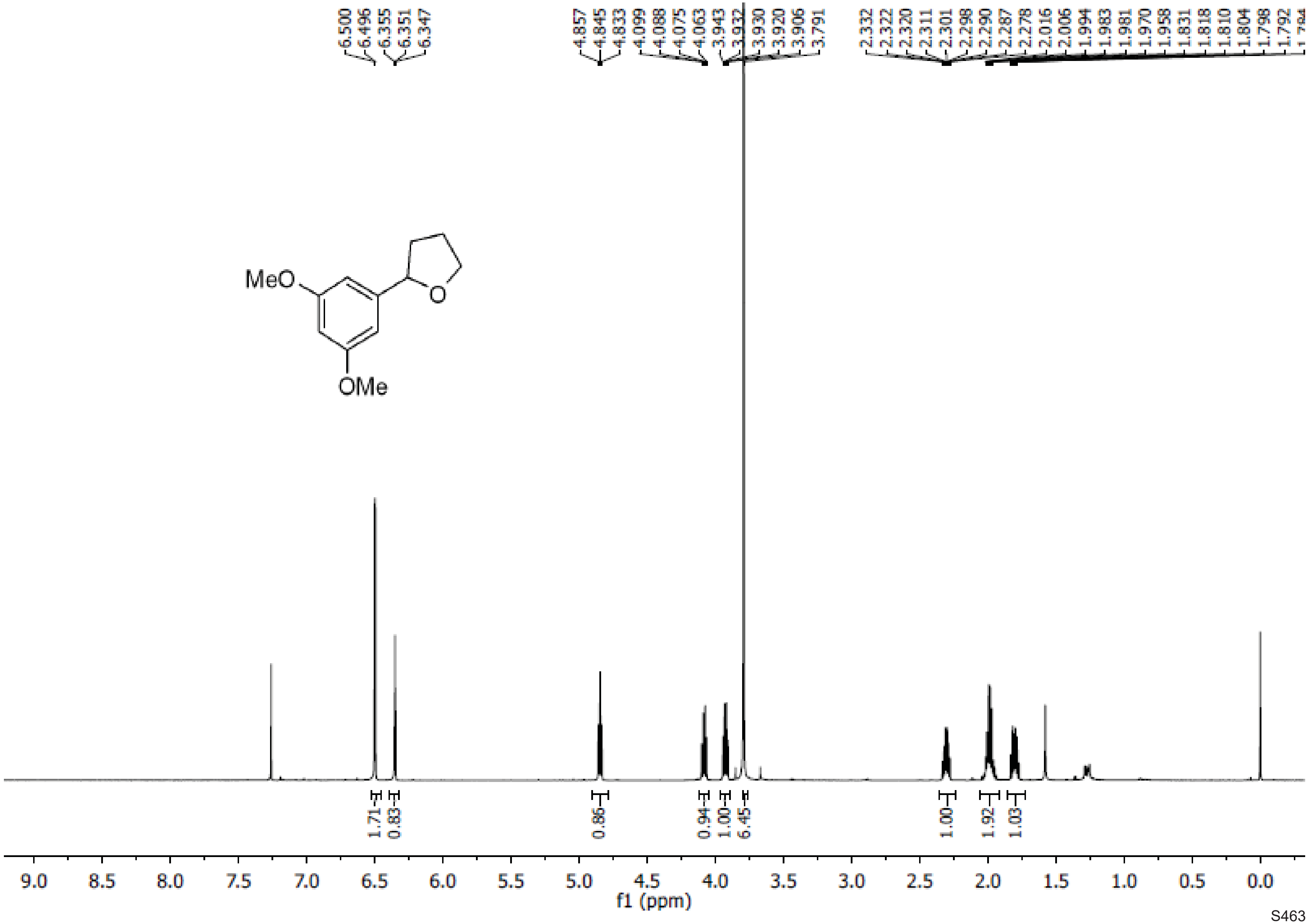


Peak Table

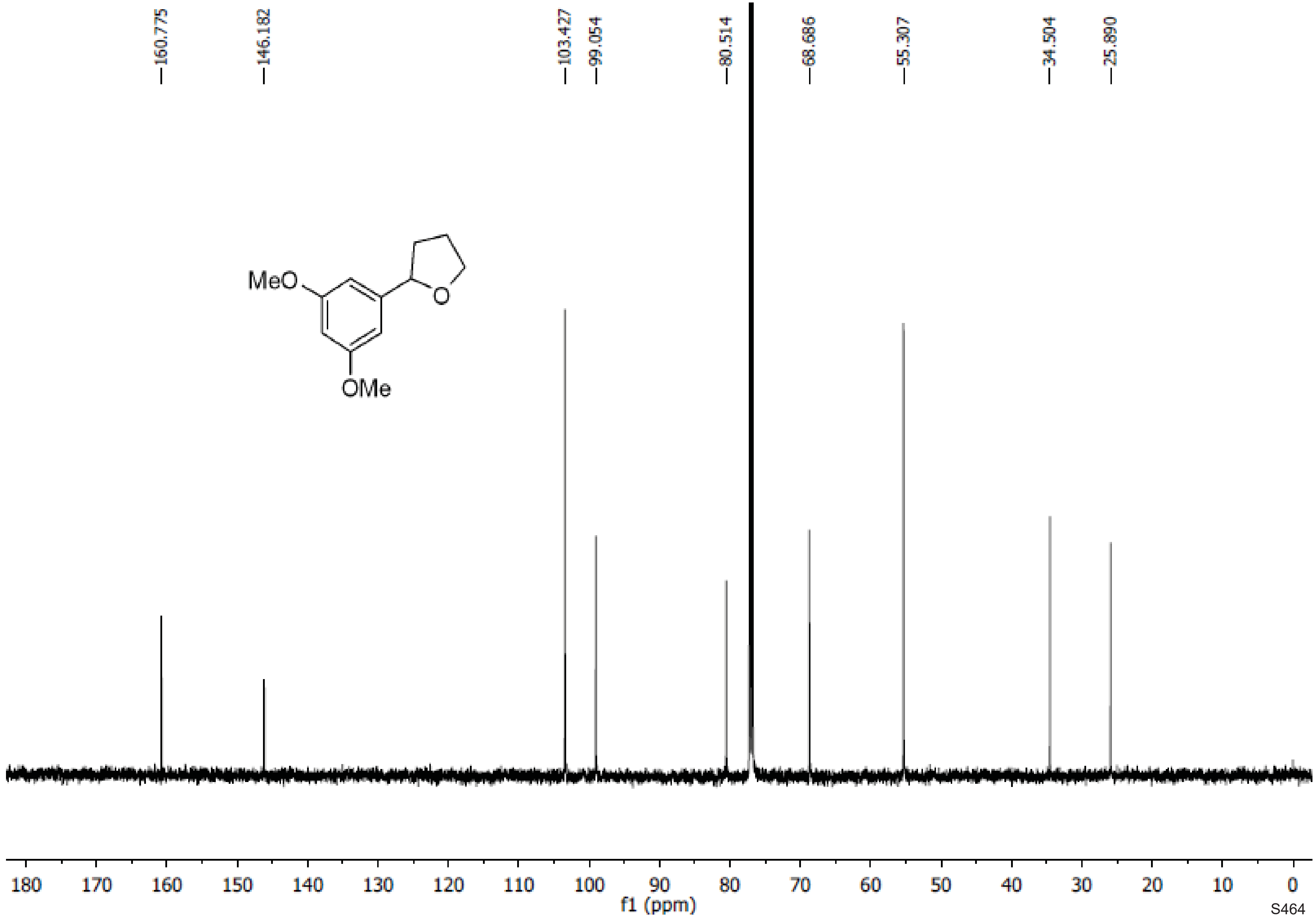
PDA Ch1 232nm

Peak#	Ret. Time	Area	Area%
1	21.858	496290	3.032
2	24.769	15870366	96.968
Total		16366656	100.000

(*S*)-2-(3,5-dimethoxyphenyl)tetrahydrofuran



(*S*)-2-(3,5-dimethoxyphenyl)tetrahydrofuran

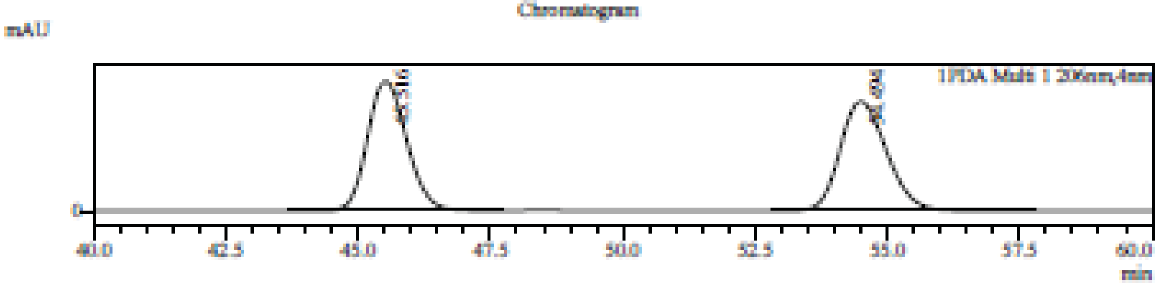


(*S*)-2-(3,5-dimethoxyphenyl)tetrahydrofuran

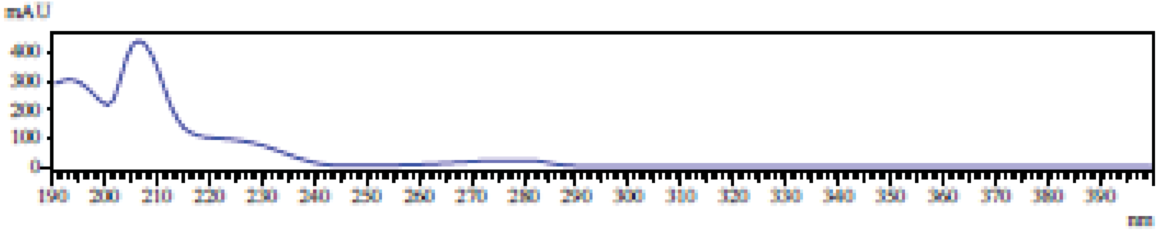
Sample Information

Data File : XW-VI-268-IF-1%0.8mL-2.lcd
Sample Name : XW-VI-268-IF-1%0.8mL-2
Sample ID : XW-VI-268-IF-1%0.8mL-2
Method File : XW-1%-0.8ml.lcm

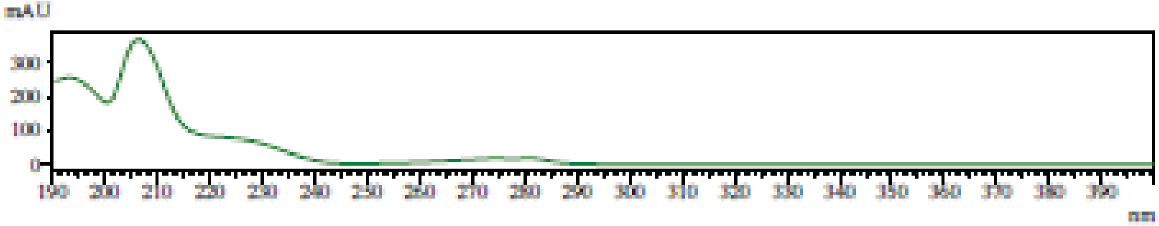
Chromatogram



UV Spectrum
Retention time = 45.516



UV Spectrum
Retention time = 54.494



Peak Table

PDA Ch1 206nm

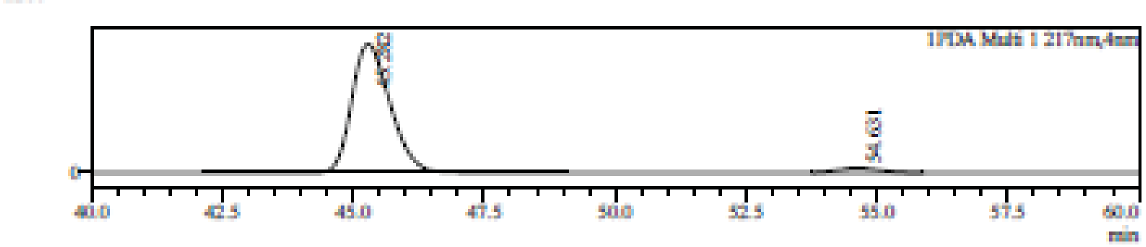
Peak#	Ret. Time	Area	Area%
1	45.516	20089542	50.032
2	54.494	20064172	49.968
Total		40153714	100.000

(*S*)-2-(3,5-dimethoxyphenyl)tetrahydrofuran

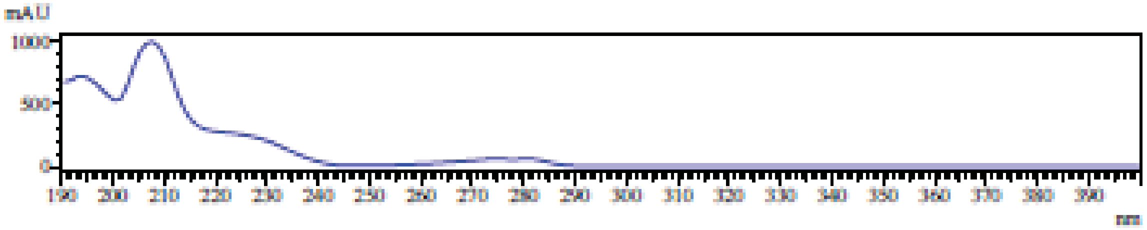
Sample Information

Data File	: XW-VI-269a-IF-1%0.8mL-1.lcd
Sample Name	: XW-VI-269a-IF-1%0.8mL-1
Sample ID	: XW-VI-269a-IF-1%0.8mL-1
Method File	: XW-1%-0.8ml.lcm

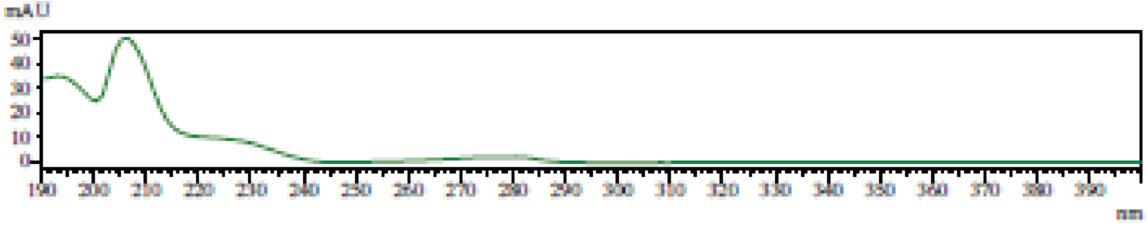
Chromatogram



UV Spectrum
Retention time = 45.282



UV Spectrum
Retention time = 54.631

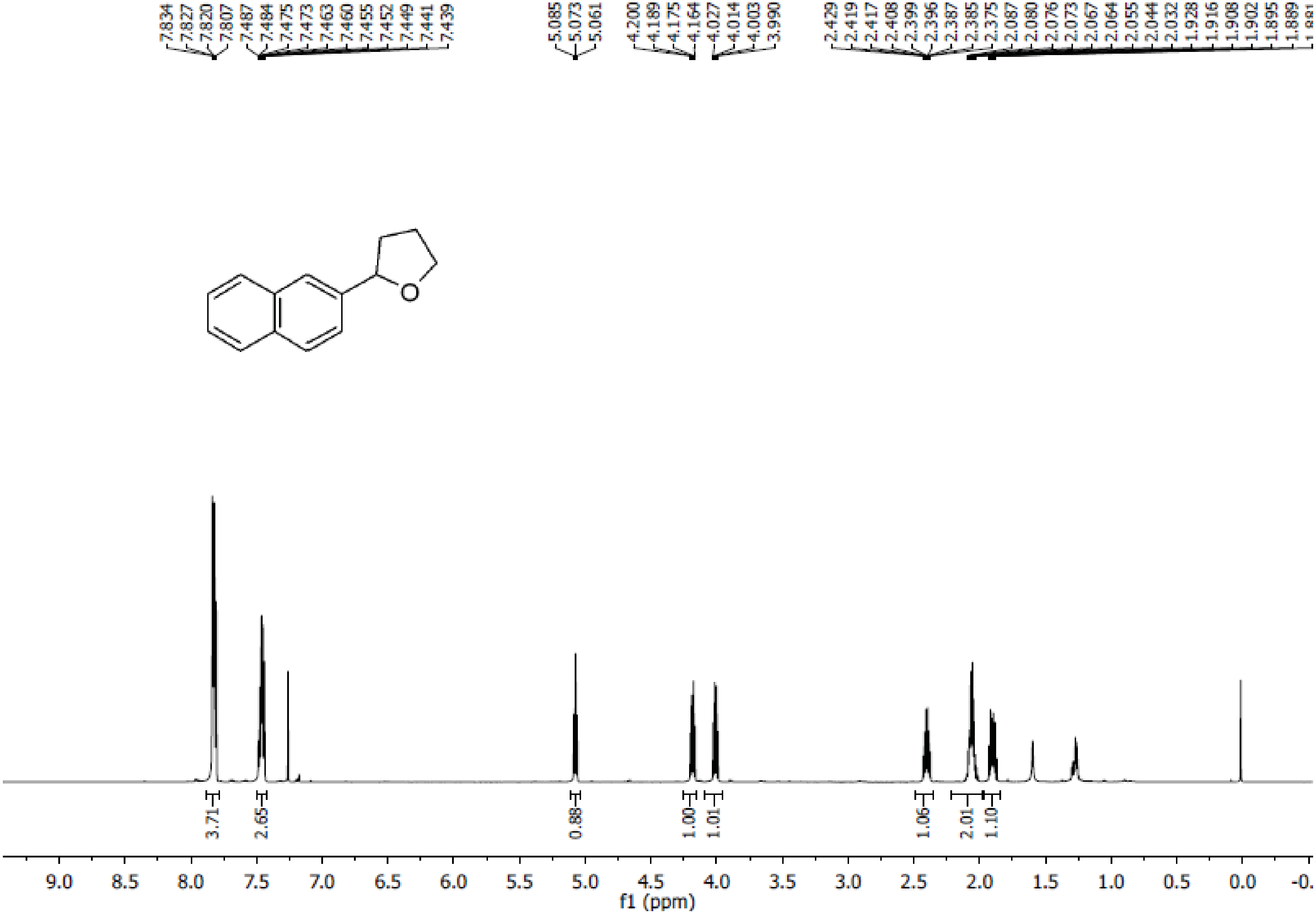


Peak Table

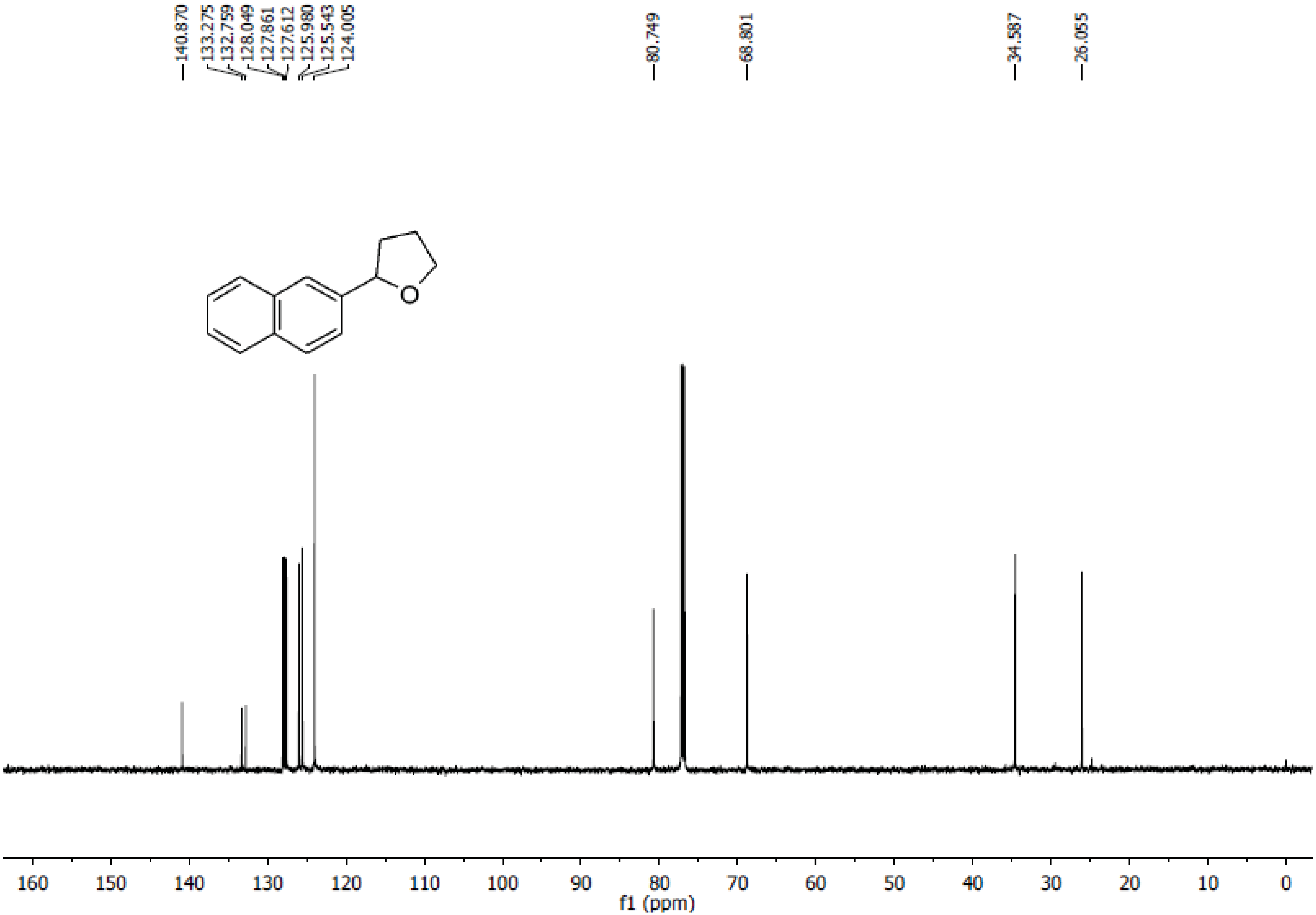
PDA Ch1 217nm

Peak#	Ret. Time	Area	Area%
1	45.282	17134792	96.086
2	54.631	698049	3.914
Total		17832841	100.000

(*S*)-2-(naphthalen-2-yl)tetrahydrofuran



(*S*)-2-(naphthalen-2-yl)tetrahydrofuran

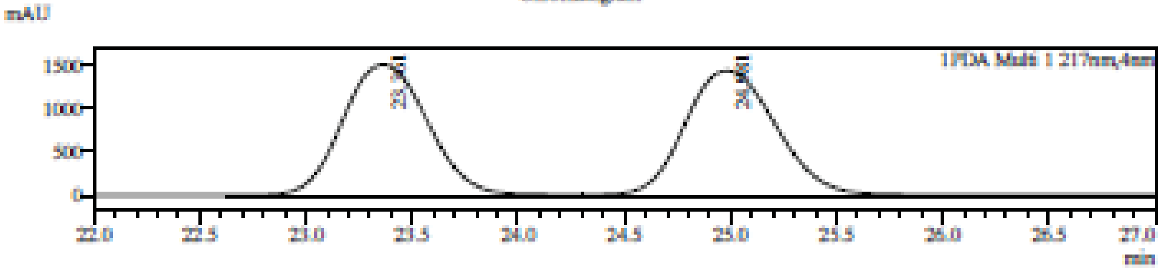


(*S*)-2-(naphthalen-2-yl)tetrahydrofuran

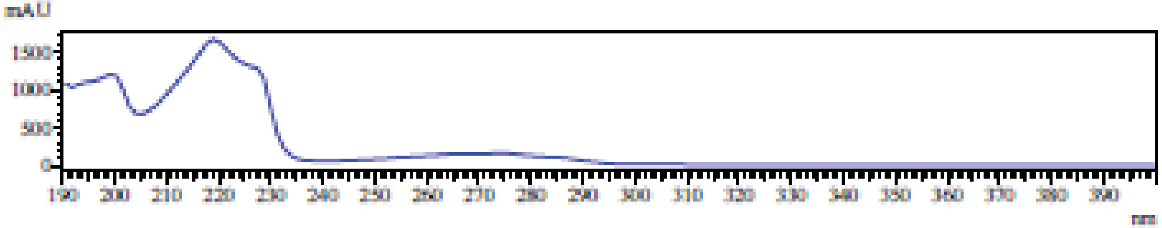
Sample Information

Data File	: XW-VI-266-IE-1%0.8mL-2.lcd
Sample Name	: XW-VI-266-IE-1%0.8mL-2
Sample ID	: XW-VI-266-IE-1%0.8mL-2
Method File	: XW-1%-0.8ml.lcm

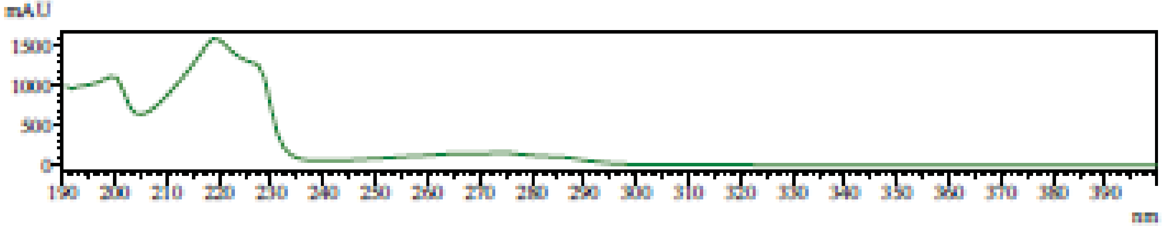
Chromatogram



UV Spectrum
Retention time = 23.361



UV Spectrum
Retention time = 24.981



Peak Table

PDA Ch1 217nm

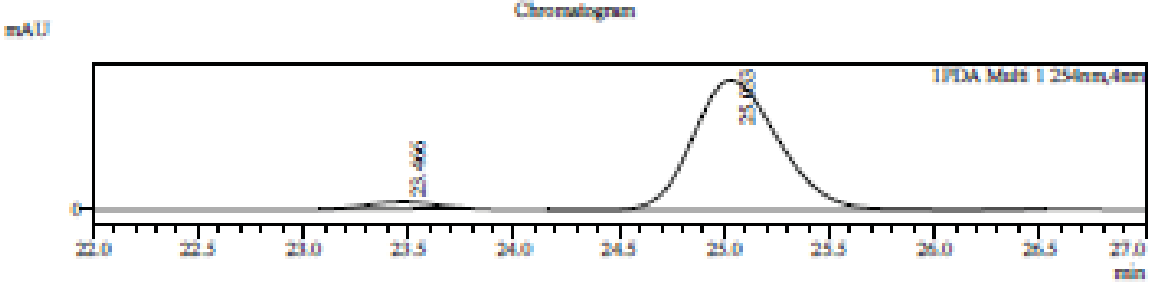
Peak#	Ret. Time	Area	Area%
1	23.361	41554286	49.437
2	24.981	42500044	50.563
Total		84054330	100.000

(*S*)-2-(naphthalen-2-yl)tetrahydrofuran

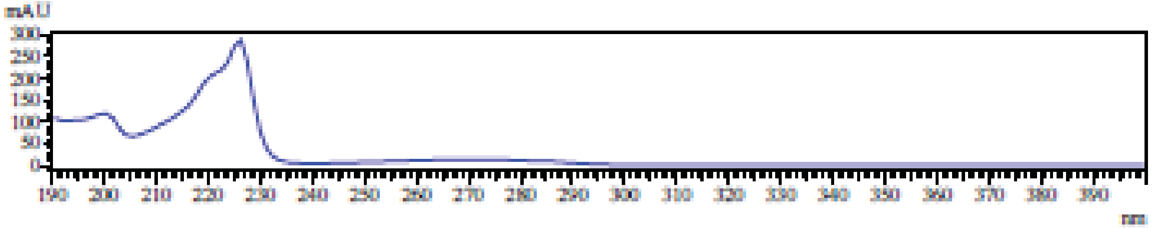
Sample Information

Data File	: XW-VI-267a-IE-1%0.8mL-1.lcd
Sample Name	: XW-VI-267a-IE-1%0.8mL-1
Sample ID	: XW-VI-267a-IE-1%0.8mL-1
Method File	: XW-1%-0.8ml.lcm

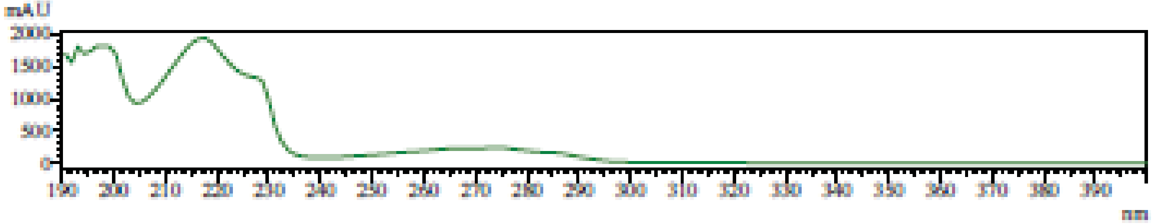
Chromatogram



UV Spectrum
Retention time = 23.466



UV Spectrum
Retention time = 25.033

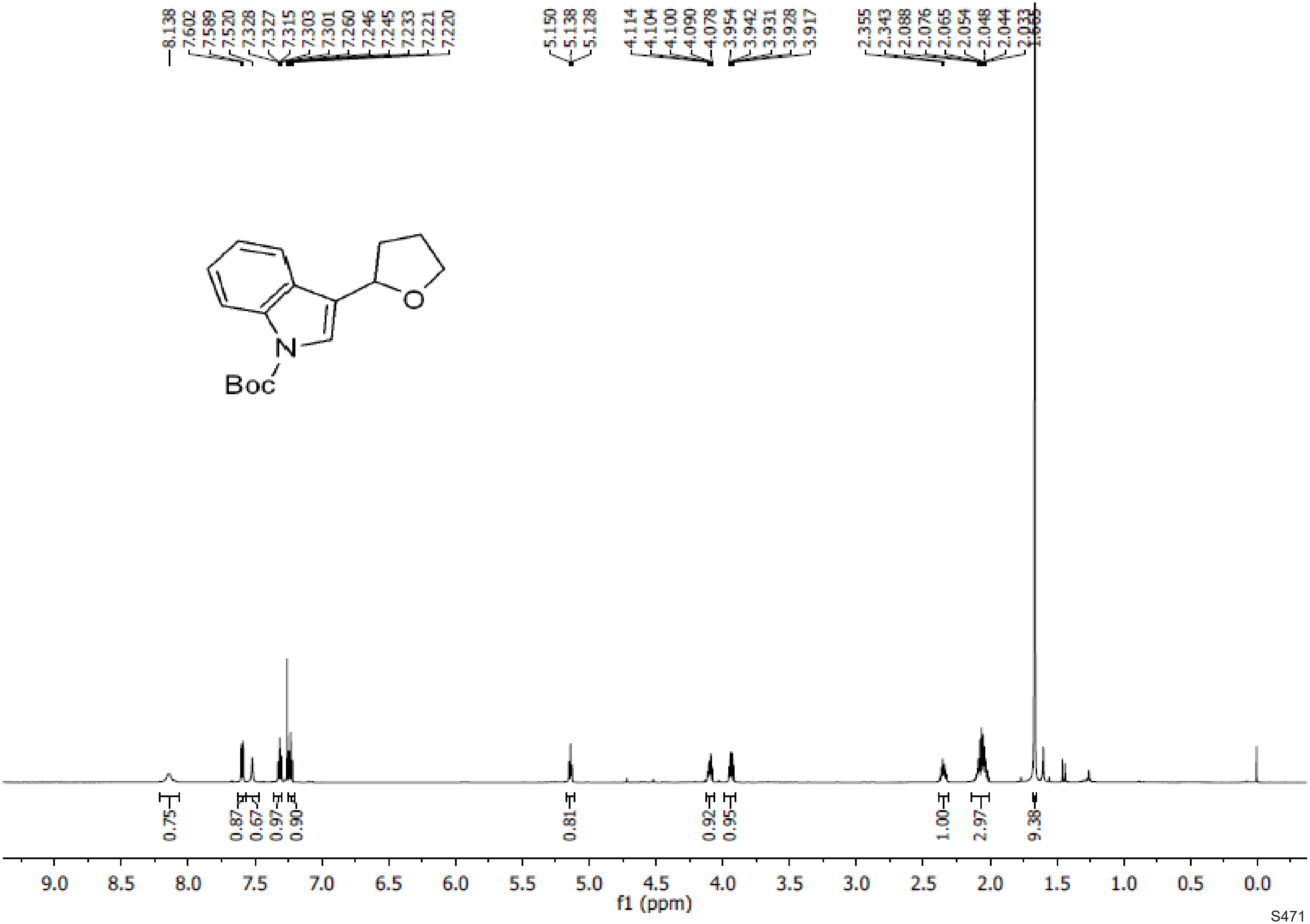


Peak Table

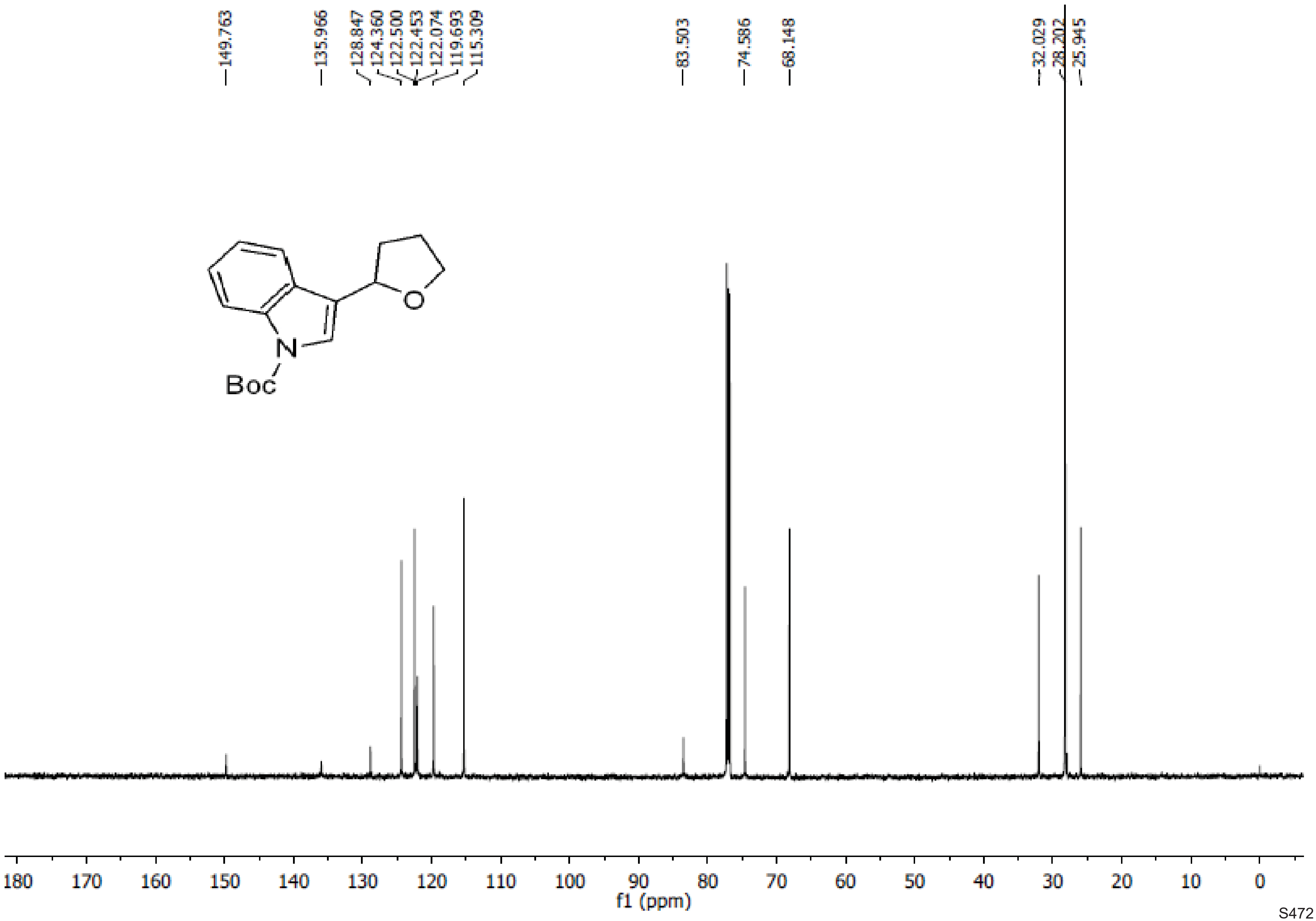
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	23.466	171433	3.886
2	25.033	4239951	96.114
Total		4411384	100.000

tert-butyl (*S*)-3-(tetrahydrofuran-2-yl)-1H-indole-1-carboxylate



tert-butyl (*S*)-3-(tetrahydrofuran-2-yl)-1H-indole-1-carboxylate

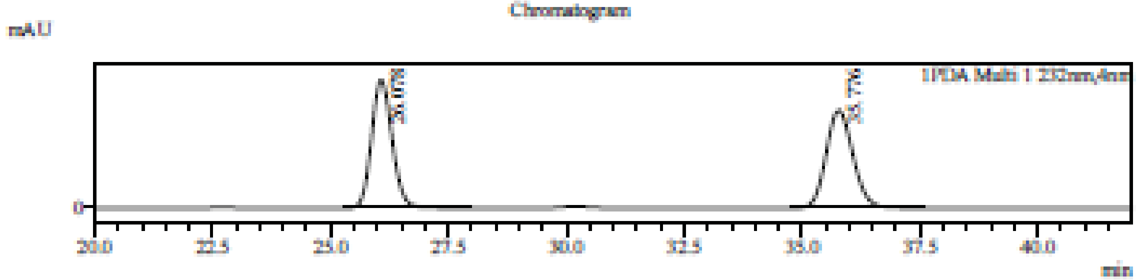


tert-butyl (*S*)-3-(tetrahydrofuran-2-yl)-1H-indole-1-carboxylate

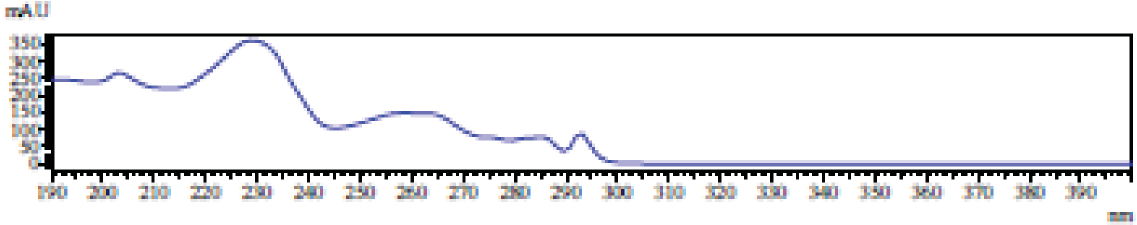
Sample Information

Data File : XW-VI-277-IF-1%0.8mL-2.lcd
Sample Name : XW-VI-277-IF-1%0.8mL-2
Sample ID : XW-VI-277-IF-1%0.8mL-2
Method File : XW-1%-0.8ml.lcm

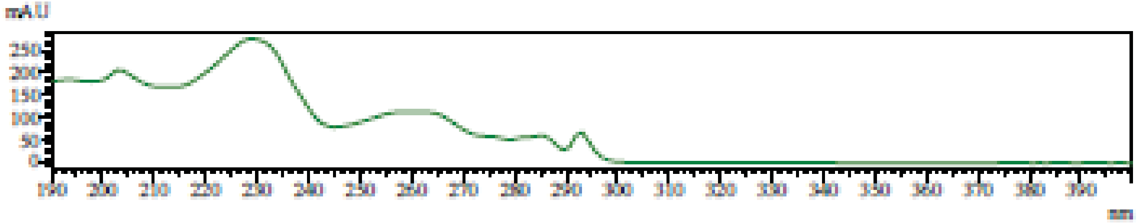
Chromatogram



UV Spectrum
Retention time = 26.078



UV Spectrum
Retention time = 35.776



Peak Table

PDA Ch1 232nm

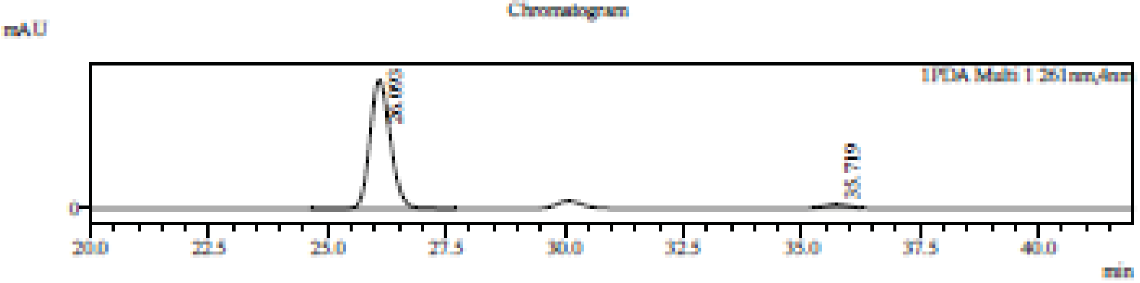
Peak#	Ret. Time	Area	Area%
1	26.078	10224867	50.007
2	35.776	10222164	49.993
Total		20447030	100.000

tert-butyl (*S*)-3-(tetrahydrofuran-2-yl)-1H-indole-1-carboxylate

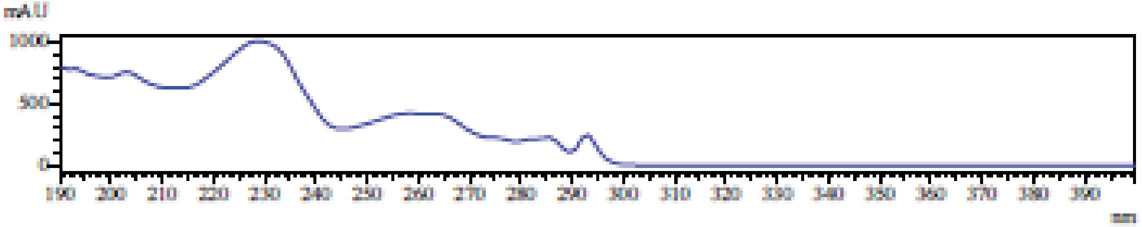
Sample Information

Data File	: XW-VI-278a-IF-1%0.8mL-1.lcd
Sample Name	: XW-VI-278a-IF-1%0.8mL-1
Sample ID	: XW-VI-278a-IF-1%0.8mL-1
Method File	: XW-1%-0.8ml.lcm

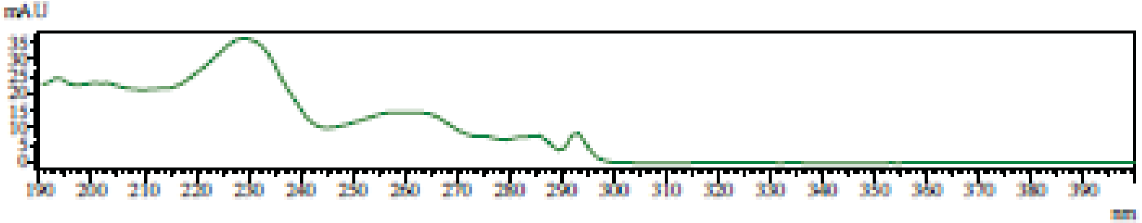
Chromatogram



UV Spectrum
Retention time = 26.093



UV Spectrum
Retention time = 35.719

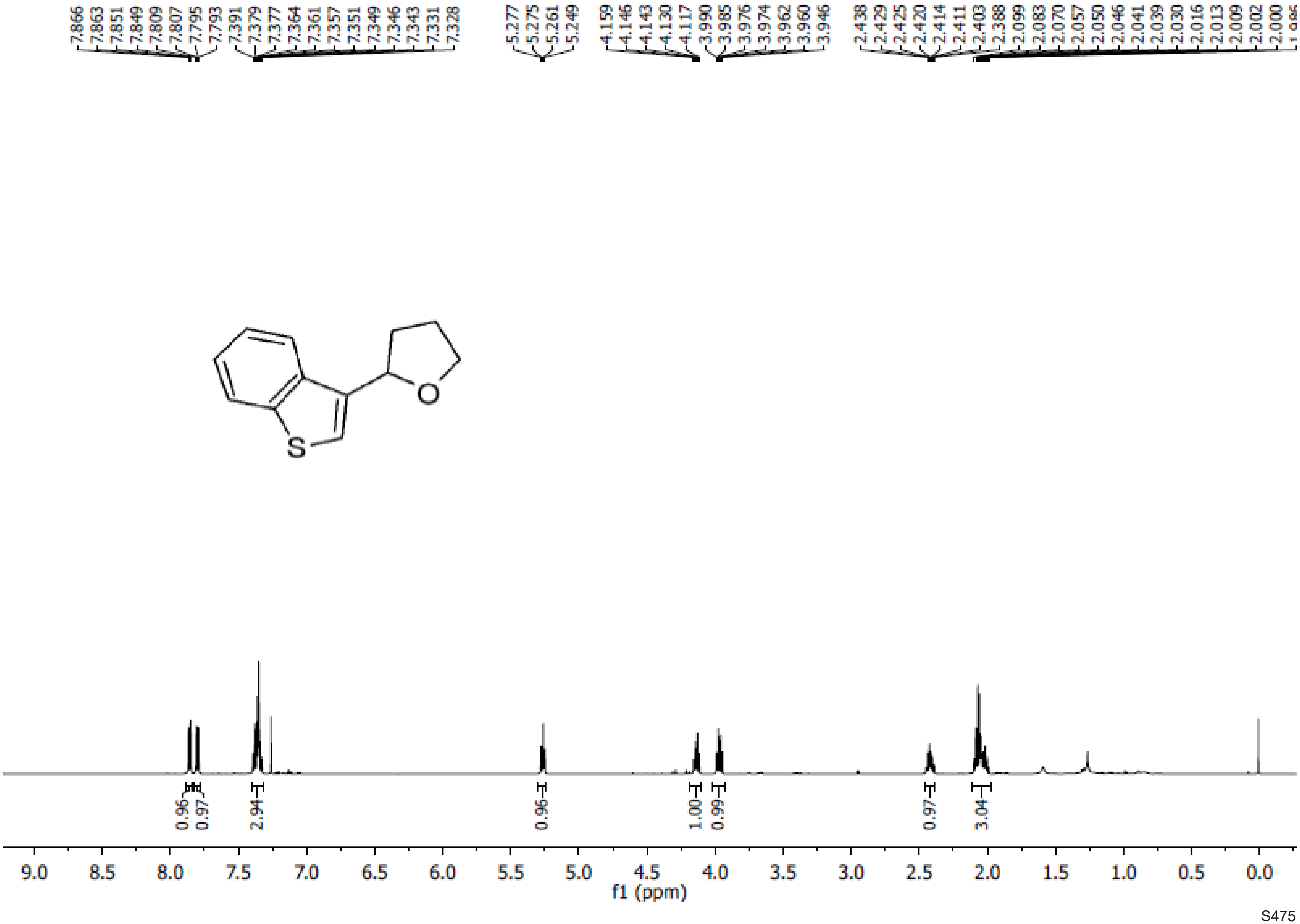


Peak Table

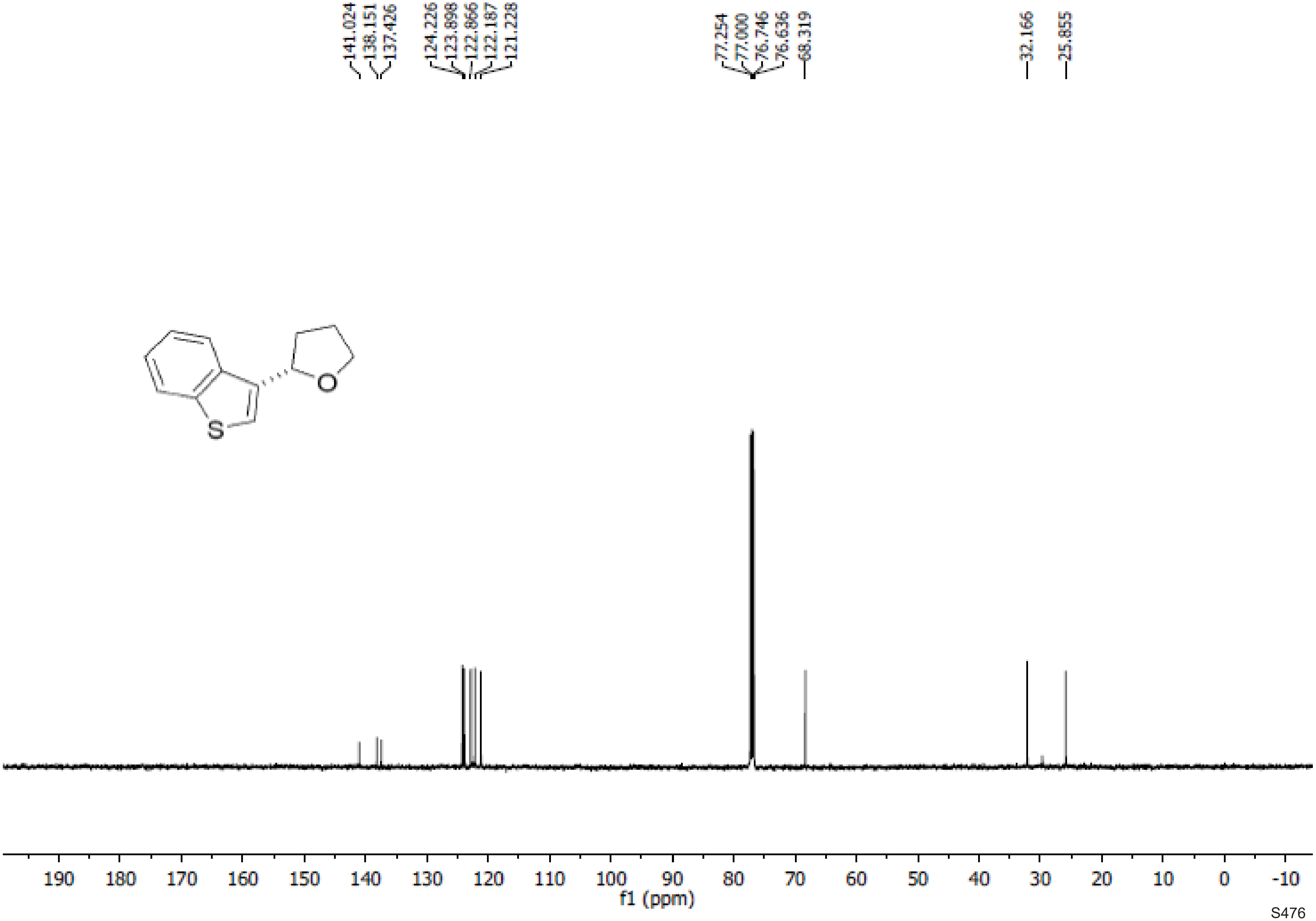
PDA Ch1 261nm

Peak#	Ret. Time	Area	Area%
1	26.093	12559168	96.820
2	35.719	412438	3.180
Total		12971605	100.000

(*S*)-2-(benzo[b]thiophen-3-yl)tetrahydrofuran



(*S*)-2-(benzo[b]thiophen-3-yl)tetrahydrofuran

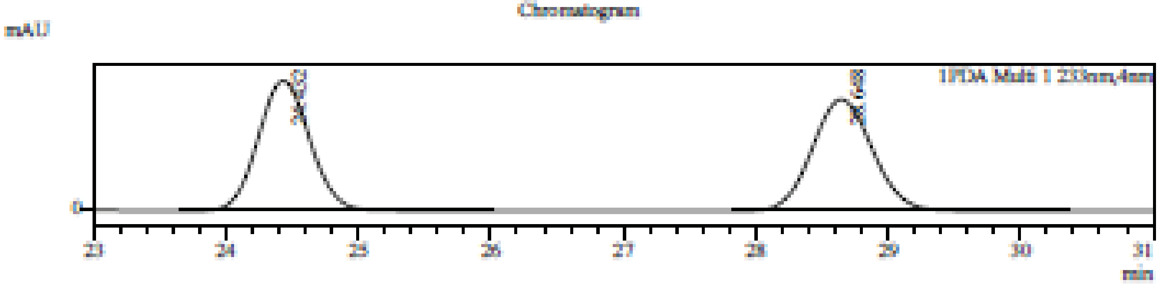


(*S*)-2-(benzo[b]thiophen-3-yl)tetrahydrofuran

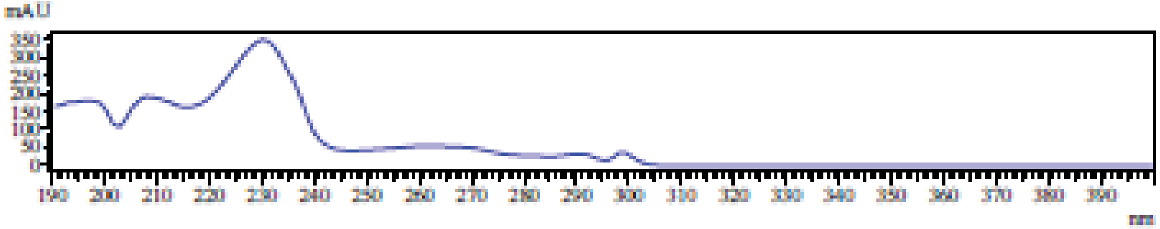
Sample Information

Data File : XW-VI-289-IF-0.5%0.8mL-1.lcd
Sample Name : XW-VI-289-IF-0.5%0.8mL-1
Sample ID : XW-VI-289-IF-0.5%0.8mL-1
Method File : XW-0.5%-0.8ml.lcm

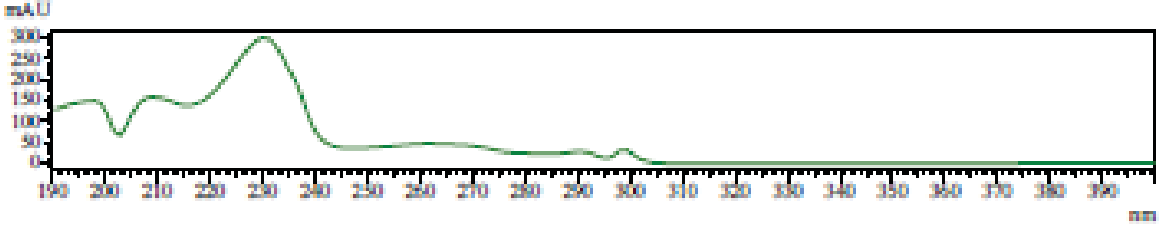
Chromatogram



UV Spectrum
Retention time = 24.432



UV Spectrum
Retention time = 28.648



Peak Table

PDA Ch1 233nm

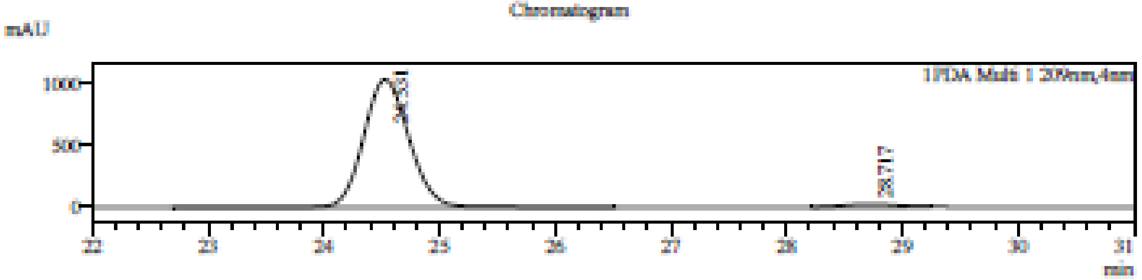
Peak#	Ret. Time	Area	Area%
1	24.432	8406974	49.990
2	28.648	8410363	50.010
Total		16817336	100.000

(*S*)-2-(benzo[b]thiophen-3-yl)tetrahydrofuran

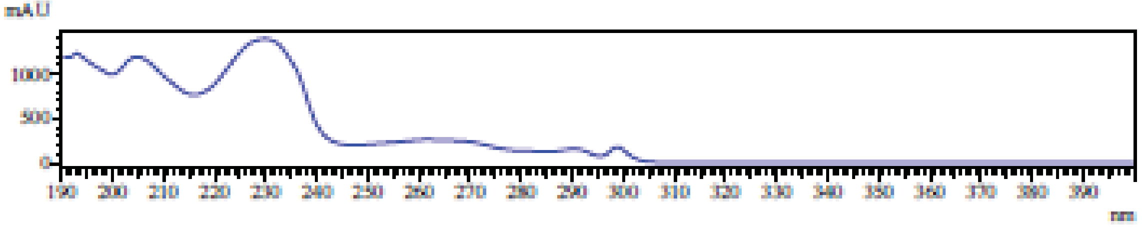
Sample Information

Data File	: XW-VI-290b-IF-0.5%0.8mL-1.lcd
Sample Name	: XW-VI-290b-IF-0.5%0.8mL-1
Sample ID	: XW-VI-290b-IF-0.5%0.8mL-1
Method File	: XW-0.5%-0.8ml.lcm

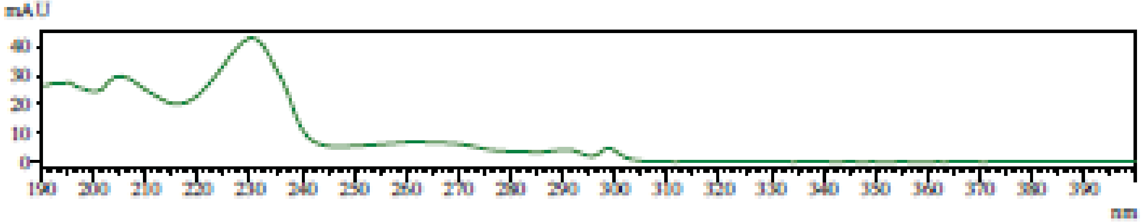
Chromatogram



UV Spectrum
Retention time = 24.531



UV Spectrum
Retention time = 28.717

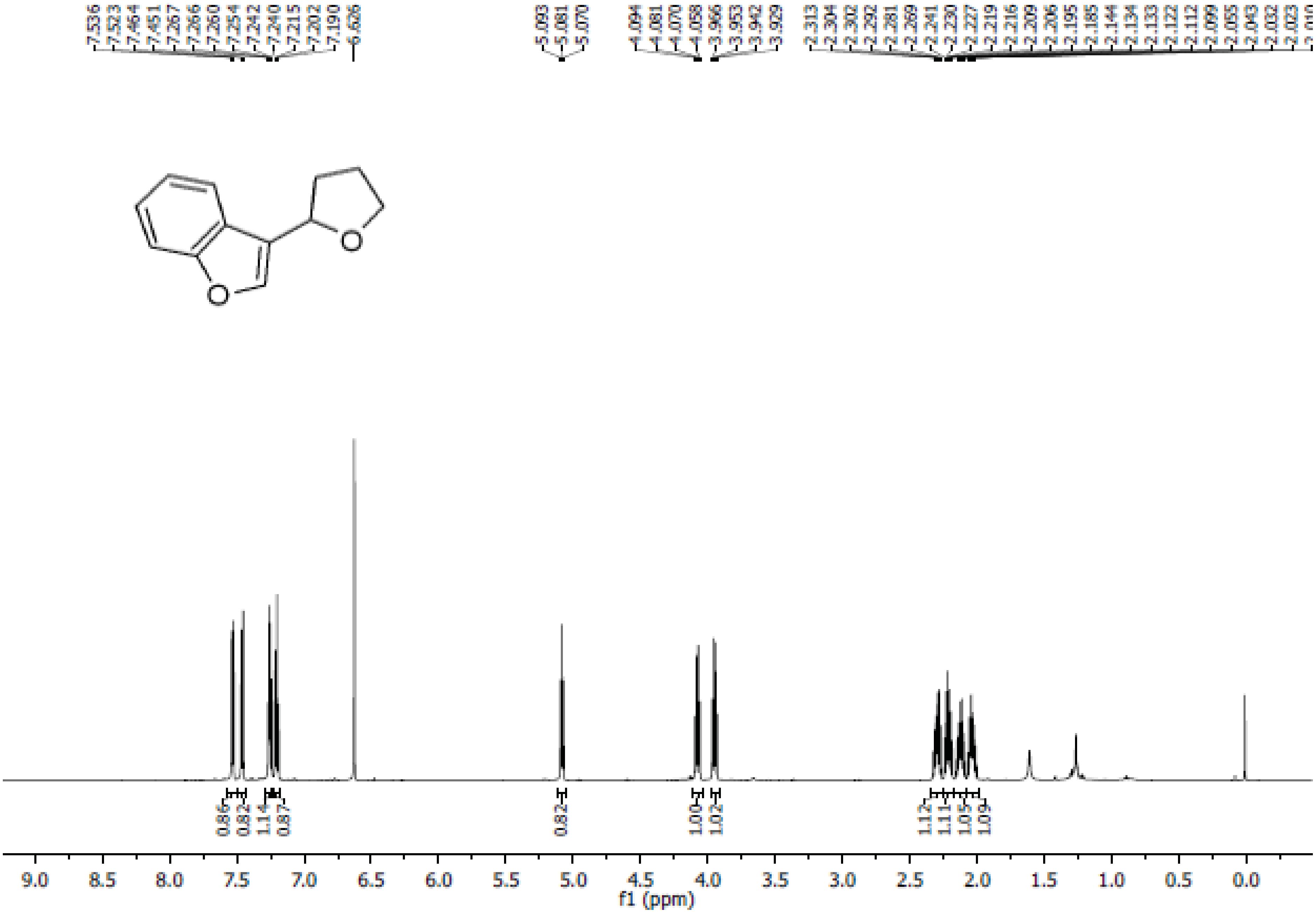


Peak Table

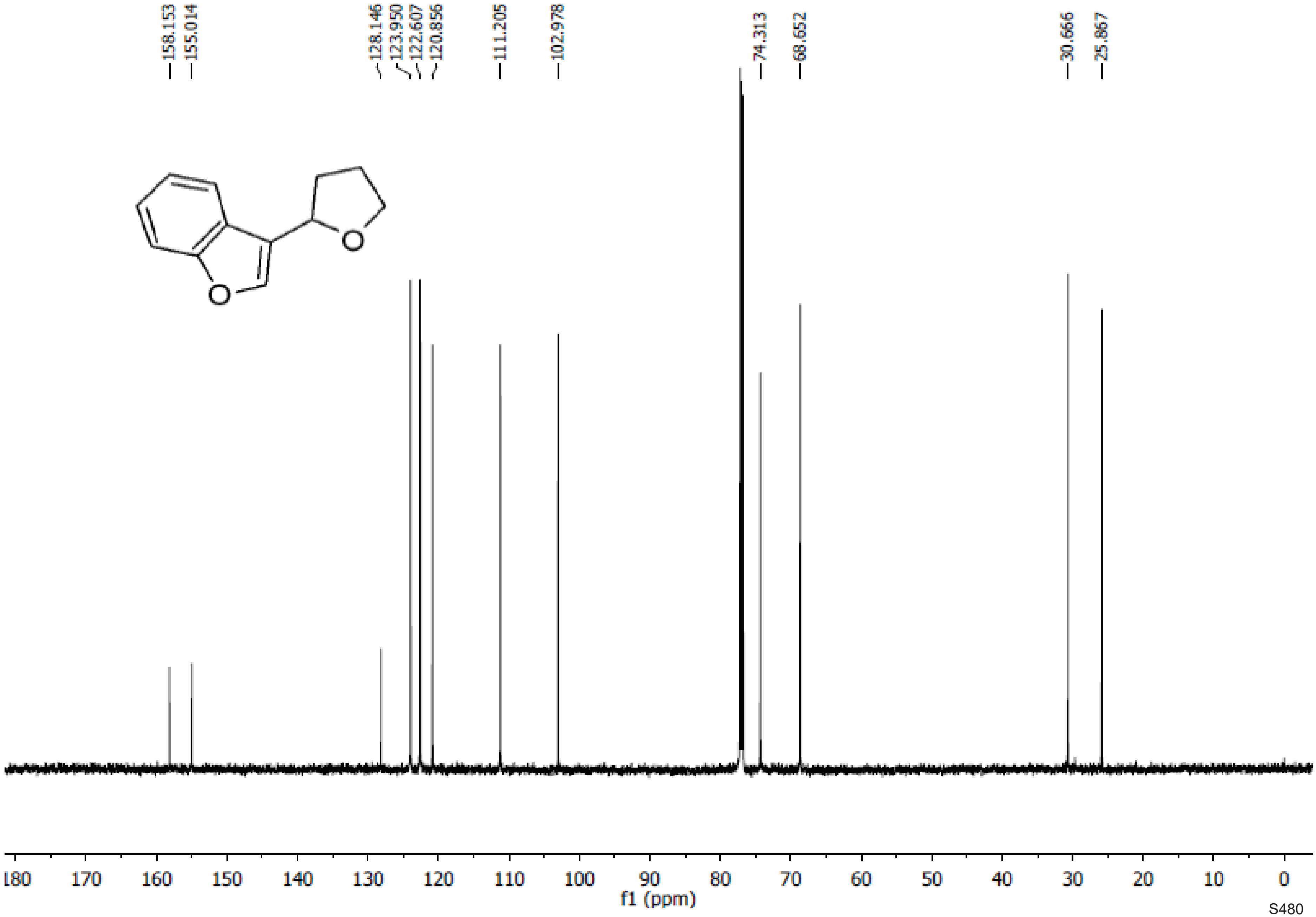
PDA Ch1 209nm

Peak#	Ret. Time	Area	Area%
1	24.531	28289435	97.405
2	28.717	753681	2.595
Total		29043116	100.000

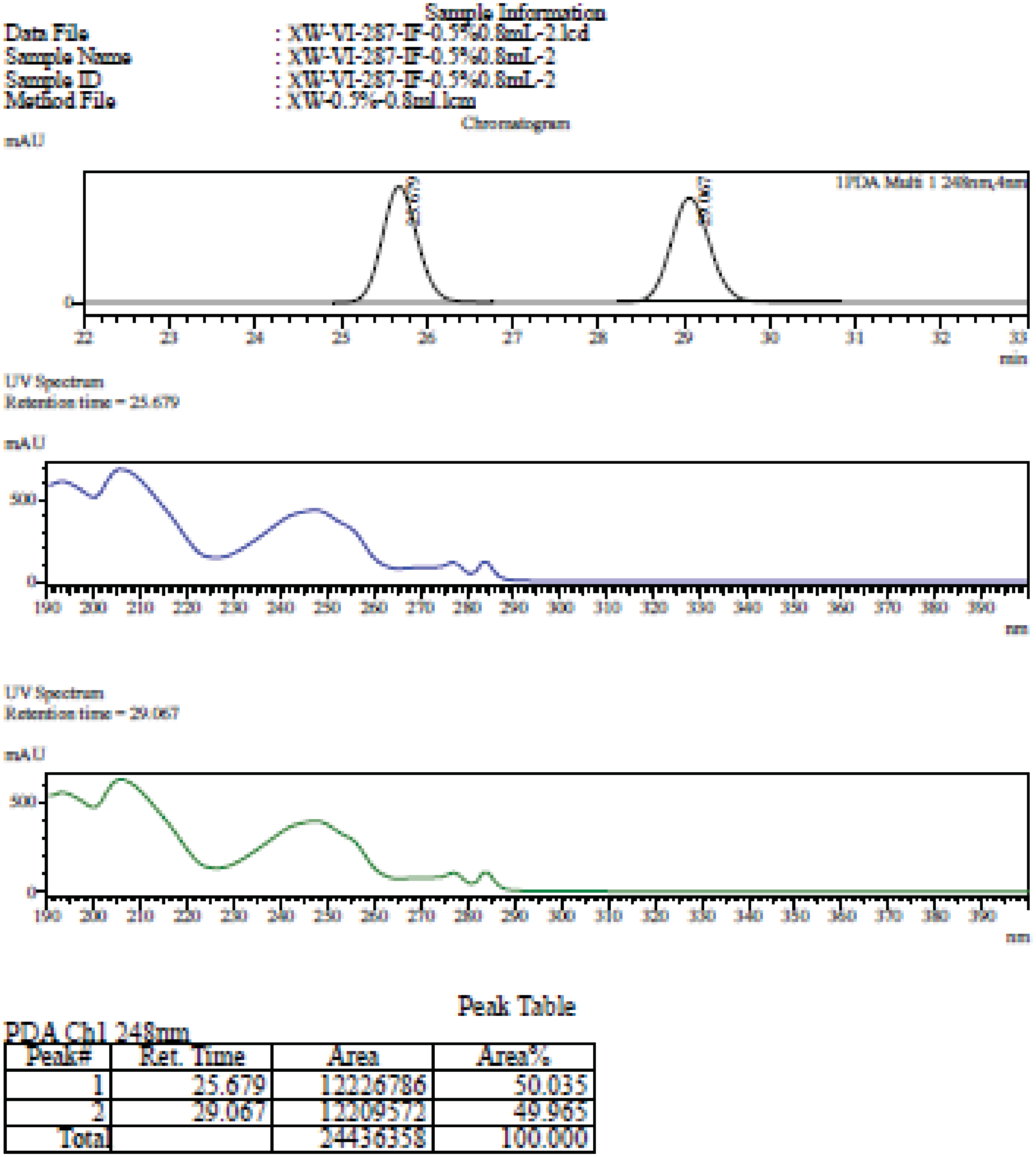
(*S*)-2-(tetrahydrofuran-2-yl)benzofuran



(*S*)-2-(tetrahydrofuran-2-yl)benzofuran



(*S*)-2-(4-methoxyphenyl)tetrahydrofuran



Sample Information

Data File : XW-VI-287-IF-0.5%0.8mL-2.lcd
Sample Name : XW-VI-287-IF-0.5%0.8mL-2
Sample ID : XW-VI-287-IF-0.5%0.8mL-2
Method File : XW-0.5%-0.8ml.lcm

UV Spectrum
Retention time = 25.679

UV Spectrum
Retention time = 29.067

Peak Table

PDA Ch1 248nm

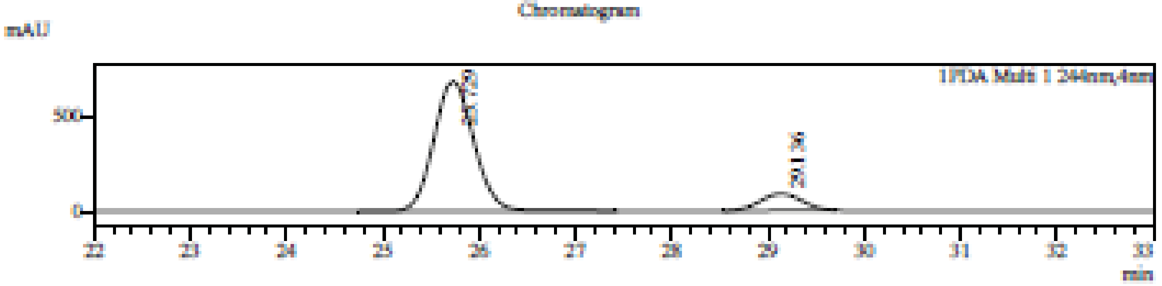
Peak#	Ret. Time	Area	Area%
1	25.679	12226786	50.035
2	29.067	12209572	49.965
Total		24436358	100.000

(S)-2-(tetrahydrofuran-2-yl)benzofuran

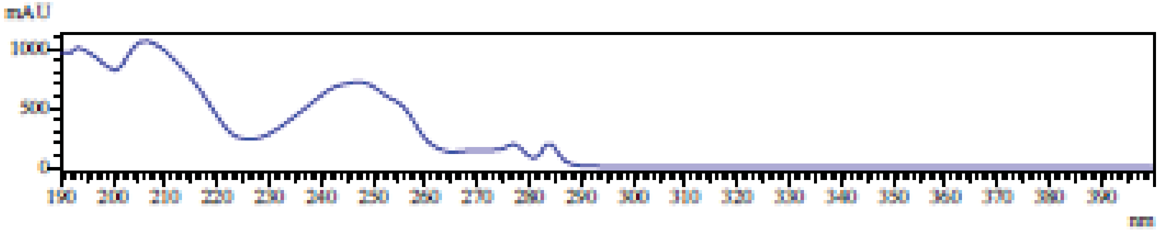
Sample Information

Data File	: XW-VI-288b-IF-0.5%0.8mL-1.lcd
Sample Name	: XW-VI-288b-IF-0.5%0.8mL-1
Sample ID	: XW-VI-288b-IF-0.5%0.8mL-1
Method File	: XW-0.5%-0.8ml.lcm

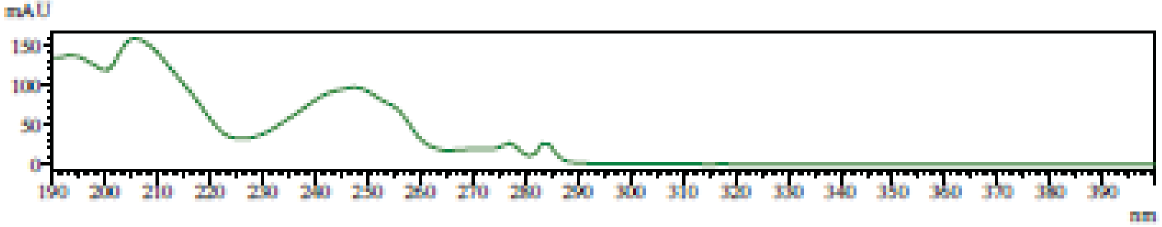
Chromatogram



UV Spectrum
Retention time = 25.729



UV Spectrum
Retention time = 29.136

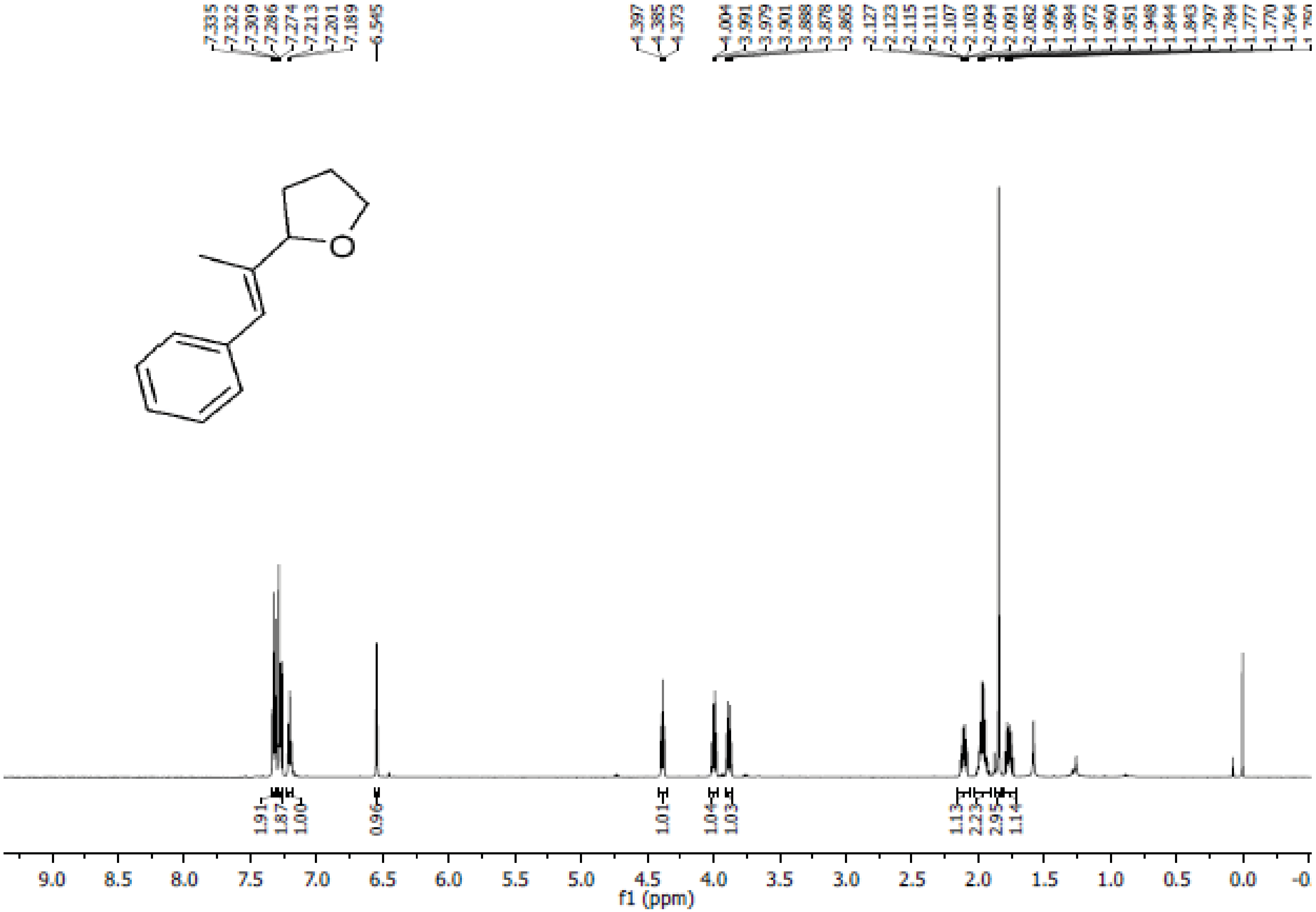


Peak Table

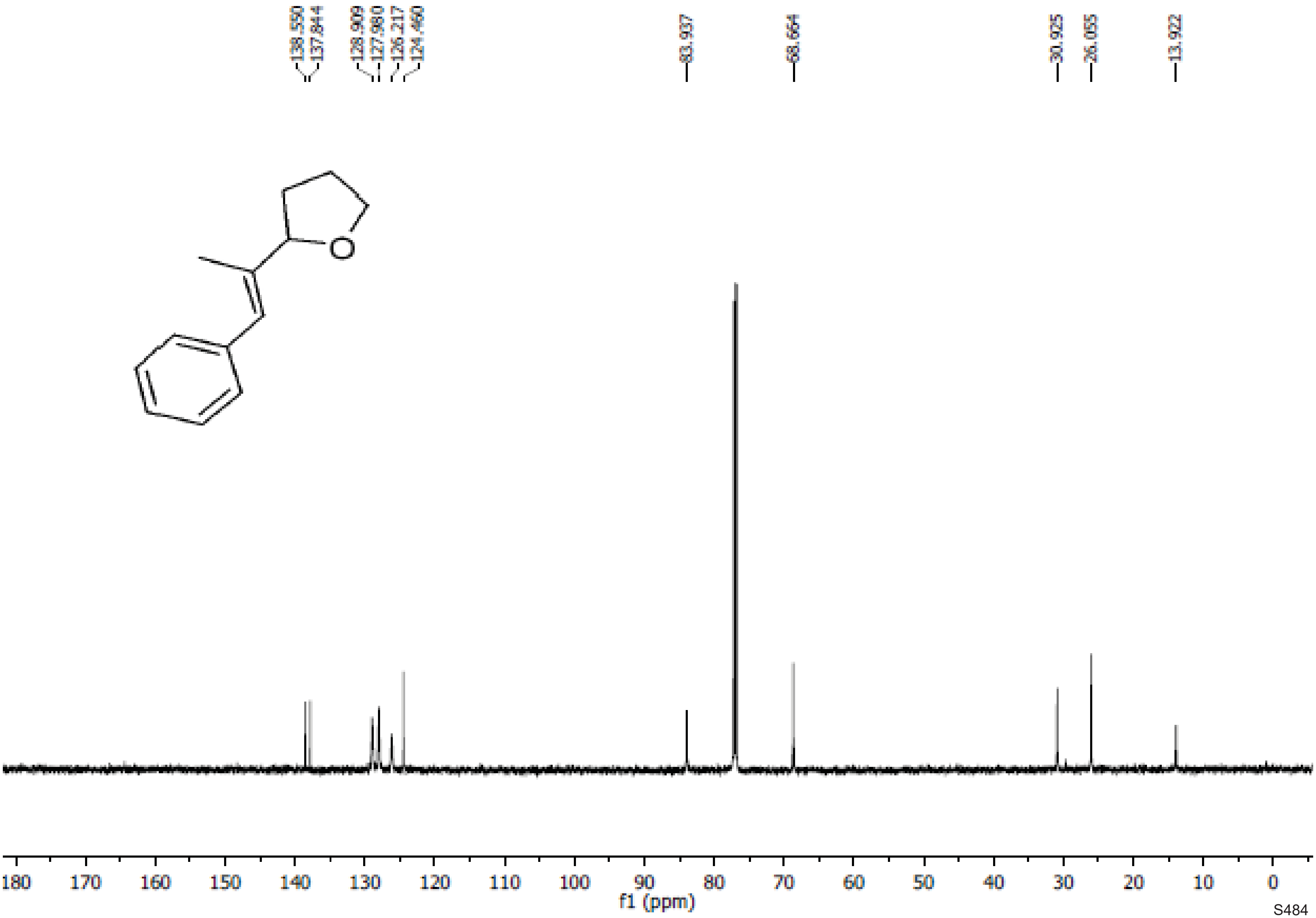
PDA Ch1 244nm

Peak#	Ret. Time	Area	Area%
1	25.729	19928231	87.984
2	29.136	2721588	12.016
Total		22649819	100.000

(*S,E*)-2-(1-phenylprop-1-en-2-yl)tetrahydrofuran



(*S,E*)-2-(1-phenylprop-1-en-2-yl)tetrahydrofuran

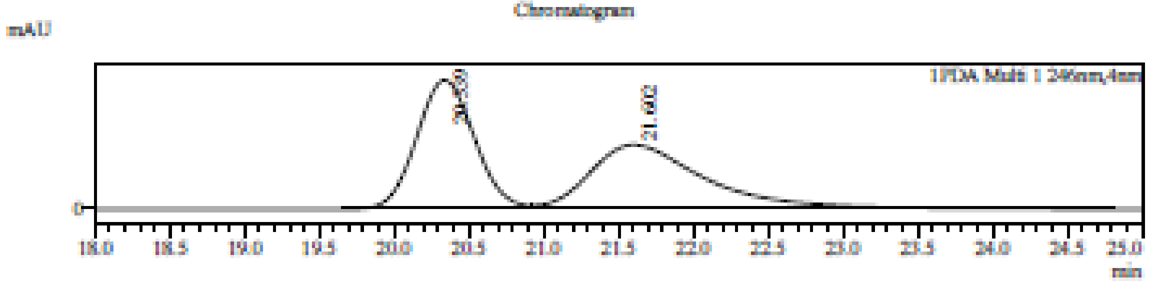


(*S,E*)-2-(1-phenylprop-1-en-2-yl)tetrahydrofuran

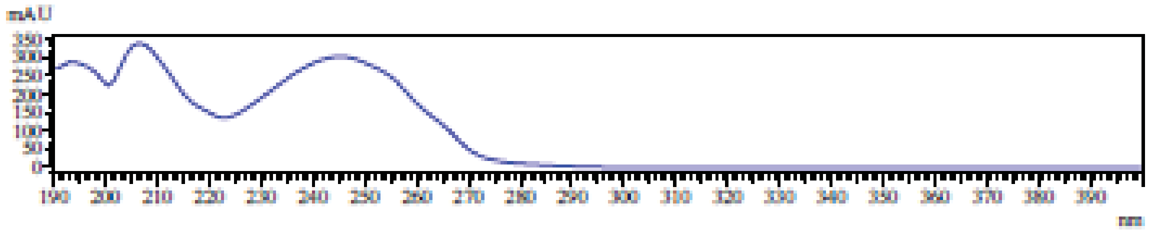
Sample Information

Data File	: XW-VI-198-ID-0.3%0.8mL-1.lcd
Sample Name	: XW-VI-188-ID-0.3%0.8mL-1
Sample ID	: XW-VI-188-ID-0.3%0.8mL-1
Method File	: XW-0.3%-0.8ml.lcm

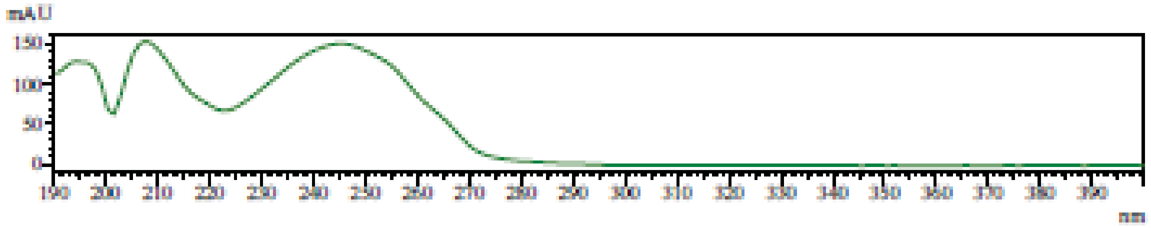
Chromatogram



UV Spectrum
Retention time = 20.339



UV Spectrum
Retention time = 21.602



Peak Table

PDA Ch1 246nm

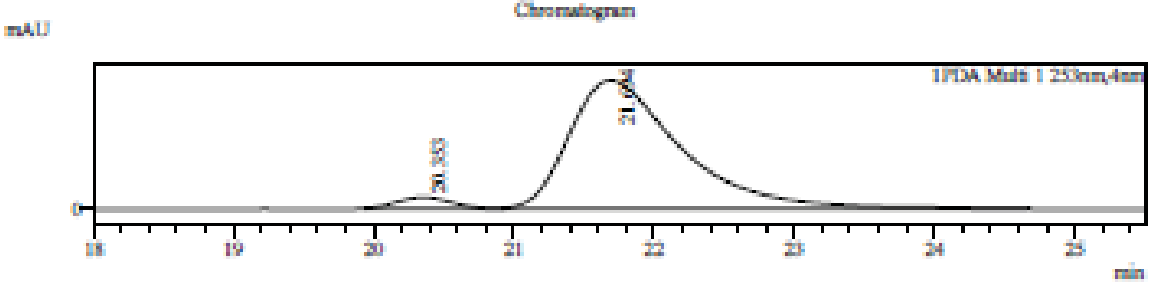
Peak#	Ret. Time	Area	Area%
1	20.339	8050369	49.934
2	21.602	8071703	50.066
Total		16122072	100.000

(*S,E*)-2-(1-phenylprop-1-en-2-yl)tetrahydrofuran

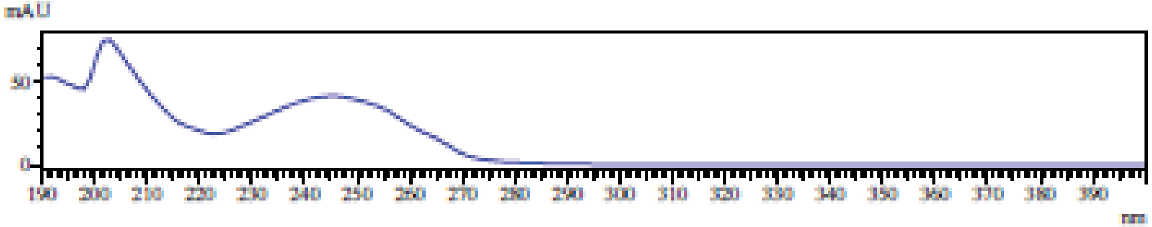
Sample Information

Data File : XW-VI-199b-ID-0.3%0.8mL-1.lcd
Sample Name : XW-VI-189b-ID-0.3%0.8mL-1
Sample ID : XW-VI-189b-ID-0.3%0.8mL-1
Method File : XW-0.3%-0.8ml.lcm

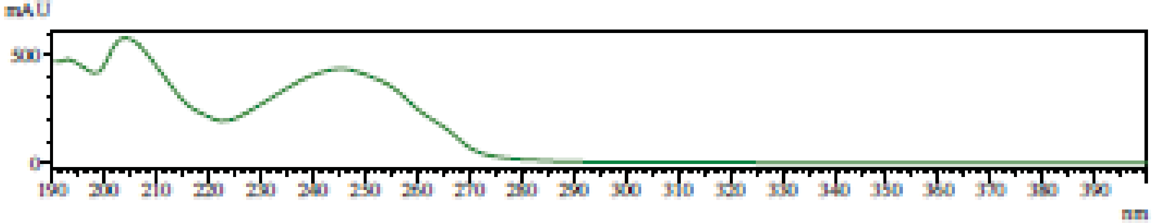
Chromatogram



UV Spectrum
Retention time = 20.353



UV Spectrum
Retention time = 21.694



Peak Table

PDA Ch1 253nm

Peak#	Ret. Time	Area	Area%
1	20.353	838882	3.891
2	21.694	20721822	96.109
Total		21560703	100.000