Development of 1,4-Azaborine-Derived Biaryl Phosphine Ligands with P-central and Axial Chirality

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New P-central and axially chiral 1,4-azaborine-derived biaryl phosphine Senphos ligand were designed and synthesized. The separation of diastereomers and enantiomers of those ligands was achieved through preparative recycling HPLC, and the separation efficiency was increased via the use of a borane protecting group. The effect of solvents and diamine ligands in enantioselective ligand synthesis was examined. The absolute configuration of the key enantiomer was confirmed via X-ray crystallography analysis. The catalytic performance of these newly synthesized ligands was evaluated through several benchmark reactions, demonstrating their potential in enantioselective catalysis.

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LIST OF ABBREVIATIONS

Å: Angstrom

Ac: acetyl

Ar: aryl

ASE: aromatic stabilization energy

BDE: bond dissociation energy

BeneP*: 1,2-bis((*R*)-*tert*-butyl(methyl)phosphaneyl)benzene

BIAN: bis(aryl)acenaphthenequinonediimine

BINAP: (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl

BSA: Bis(trimethylsilyl)acetamide

cat.: catalyst

COD: cyclooctadiene

Cy: cyclohexyl

DABCO: 1,4-diazabicyclo[2.2.2]octane

DART: direct analysis in real time

DFT: Density functional theory

DIOP: (2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane)

DIPAMP: (Ethane-1,2-diyl)bis[(2-methoxyphenyl)(phenyl)phosphane]

EDC: 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide

ee: enantiomeric excess

equiv.: equivalent(s)

Et: ethyl

h: hour(s)

HPLC: high performance liquid chromatography

HRMS: high resolution mass spectroscopy

Hz: hertz

IPA: isopropanol

*i*Pr: isopropyl

IR: infrared spectroscopy

JosiPhos: (2*R*)-1-[(1*R*)-1-(Dicyclohexylphosphino)ethyl]-2-

(diphenylphosphino)ferrocene

kcal: kilocalorie

L: ligand

L-DOPA: L-3,4-dihydroxyphenylalanine

M: molar

Me: methyl

min: minute(s)

mL: milliliter

mmol: millimole

MOP: 2-(diphenylphosphino)-2'-methoxy-1,1'-binaphthyl

mppp: (*S*)-methyl(phenyl)(propyl)phosphane

MS: mass spectroscopy

nm: nanometers

NMR: nuclear magnetic resonance spectroscopy

nPr: propyl

OAc: acetoxyl

OMe: methoxyl

OTf: trifluoromethanesulfonate

Ph: phenyl

PHANEPHOS: (*R*)-(–)-4,12-Bis(diphenylphosphino)-[2.2]-paracyclophane

PHMS: Polymethylhydrosiloxane

PHOX: (*R*)-(−)-2-[2-(Diphenylphosphino)phenyl]-4-phenyl-2-oxazoline

ppm: parts per million

rt: room temperature

SDP: 7,7′-Bis(diphenylphosphino)-2,2′,3,3′-tetrahydro-1,1′-spirobiindene

*t*Bu: tert-butyl

THF: tetrahydrofuran

TMS: trimethylsilyl

t_r: retention time

TS: transition state

μmol: micromole

μg: microgram

ACKNOWLEDGEMENT

With the completion of my studies at Boston College, my days as a student are officially coming to an end. This 18-year journey has encompassed most of my life thus far, and it is quite emotional to realize that I am transitioning from being a student to an adult, embarking on the second phase of my life. This transition comes slightly earlier than I imagined, and while it may seem sudden to others, I think it is time to make a change.

I'm very pleased to have spent the last two years of my student life at Boston College. During this time, I had my first experience as a teaching assistant, experienced the daily life of a working professional. I frequently switched between the roles of student and TA, living a somewhat "conflicted" life, but this is much like life itself. I am fortunate to have joined the Liu group and to have met so many experienced seniors, whose advice has been invaluable. I am grateful to my advisor, Prof. Shih-Yuan Liu, for his guidance, not only in my research projects but also in greatly improving my study habits and capabilities. I appreciate my mentor, Max, for his help with my research projects and experimental techniques. Special thanks to Dr. Ziyong Wang, Dr. Yanrong Li, Max, Tomoya, Jiangpeng and Changhang for reviewing my thesis. I also extend my thanks to Hannah, Nick, Skylar, Kevin, Ricky, Jennifer, and all the undergraduates in the Liu group for making life lively and fulfilling!

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Thanks to Mayday, whose music has been a constant companion since my youth. I remember Ashin once said, “The past is gone, and the future is always coming. Perhaps you will feel that your future does not quite match your expectations, and as you become an adult, it may not be as you imagined. The adult world is actually quite good, but if you ever feel a bit down, put on your headphones, and Mayday will always be there with you!” With your music, I stayed true to myself, walked the path I wanted, enjoyed my love, and finally, I found the courage to overturn all my life plans and start anew. Thank you for your music, which has given me the courage to believe in myself in this turbulent world.

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I am grateful to my parents, Mr. Xudong Huang and Mrs. Peiyu Qiu. Eleven years ago, we decided together to leave the traditional education system and pursue international education, which was quite an unconventional decision at the time. Over the years, from Shanghai to Manchester, to London, and then to Boston, we have made many decisions, big and small. Thank you for always respecting my ideas and providing financial and emotional support. Today, I have become the person I wanted to be. I also thank all my relatives and elders for their advice and help throughout my growth!

Lastly, inevitably, I must thank my husband, Mr. Caiyue Lai. Thanks for our acquaintance and love, for the trust between us that allowed us to endure five years of long-distance relationship, for the fate that brought us together in Boston, and for our final union in marriage. Over eight years, we have grown up from high school students into adults. We studied together, graduated together, traveled together, applied to new schools together, met each other's families together, made many decisions together, and finally, pledged to be married. Since we met, you have been a part of my life every single day, and I believe we will support each other through the long years ahead.

To youth, to friends, to families, and to undying love.

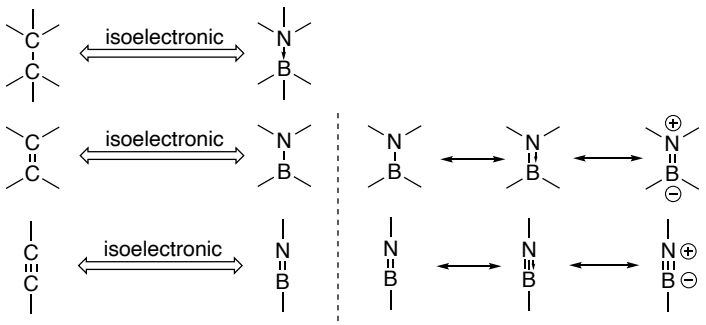
1.0 Chapter 1

Development of 1,4-Azaborine-Derived Biaryl Phosphine Ligands with P-central and Axial Chirality

1.1 INTRODUCTION

BN/CC isosterism represents the replacement of carbon-carbon bond unit with an isoelectronic boron-nitrogen unit (Scheme 1.1). Boron has three valence electrons and nitrogen has five valence electrons, which indicates a BN unit has the same valence electron number as a CC unit.[1] This demonstrates the isoelectronic nature between BN and CC units.

Scheme 1.1. BN/CC isosterism.

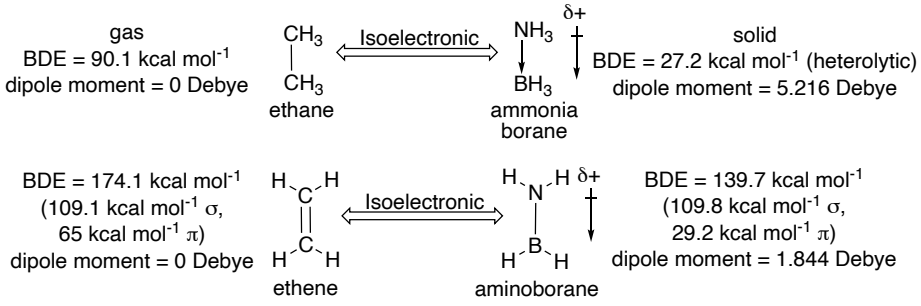


Different molecular properties can be expected when a BN unit is utilized to replace the corresponding CC unit in a molecule, even if the numbers of valence electrons are the same. Take ethane versus ammonia borane and ethene versus aminoborane as examples (Scheme 1.2); ethane is a volatile gas (b.p. = –89 ℃), with 90.1 kcal/mol of C-C bond dissociation energy (BDE)[2] and 0 Debye of dipole moment.[3] However, its corresponding BN isostere ammonia borane is a solid at room temperature

(1) (a) Z. Liu and T. B. Marder, *Angew. Chem. Int. Ed*. **2008**, *47*, 242–244. (b) M. J. D. Bosdet and W. E. Piers, *Can. J. Chem*. **2009**, *87*, 8–29. (c) P. G. Campbell, A. J. V. Marwitz and S. Y. Liu, *Angew. Chem. Int. Ed*. **2012**, *51*, 6074–6092. (d) Z. X. Giustra and S. Y. Liu, *J. Am. Chem. Soc*. **2018**, *140*, 1184–1194.
(2) Pritchard, R. H.; Kern, C.W. *J. Am. Chem. Soc.* **1969**, *91*, 1631 – 1635.
(3) Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255 – 263.

(m.p. = 104 ℃), with a lower bond dissociation energy (27.2 kcal/mol)[4] and a bigger dipole moment (5.2 Debye).[5] The C=C bond dissociation energy of the thermal stable ethene is 174.1 kcal/mol, of which 109.1 kcal/mol is attributed to the σ bond and 65 kcal/mol is due to π contribution.[4] Ethane also has no effective dipole moment.[5,6] On the other hand, aminoborane (the BN isostere of ethene) is reactive toward polymerization and oligomerization,[7] and it has a lower bond dissociation energy of 139.7 kcal/mol (109.8 kcal/mol is attributed to the σ bond, and 29.2 kcal/mol is due to π contribution)[4] and a higher dipole moment (1.8 Debye)[7] than ethene. Overall, boron is less electronegative, and nitrogen is more electronegative than carbon, resulting in BN units being more reactive than corresponding CC units. The BN/CC isosterism concept has demonstrated the potential to broaden the chemical diversity of compounds and has been widely applied in materials and biomedical research.[8]

Scheme 1.2. Molecular consequence of BN/CC isosterism.

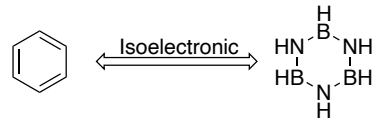


Comparing to the sp^3- and sp-type BN/CC isosterism, the sp^2-type has received the most attention (Scheme 1.1) since it could be applied to isosteres of aromatic

(4) Grant, D. J.; Dixon, D. A. *J. Phys. Chem.* **2006**, *110*, 12955 – 12962.
(5) Thorne, L. R.; Suenram, R. D.; Lovas, F. J. *J. Chem. Phys.* **1983**, *78*, 167 – 171.
(6) Alkorta, I.; Elguero, J. *Struct. Chem.* **1998**, *9*, 59 – 63.
(7) Sugie, M.; Takeo, H.; Matsumura, C. *Chem. Phys. Lett.* **1979**, *64*, 573 – 575.
(8) For representative examples, see: (a) Patani, G. A.; LaVoie, E. *J. Chem. Rev.* **1996**, *96*, 3147–3176. (b) Zhao, P.; Nettleton, D. O.; Karki, R. G.; Zecri, F. J.; Liu, S.–Y. *ChemMedChem* **2017**, *12*, 358–361. (c) Chen, C.; Zhang, Y.; Wang, X.–Y.; Wang, J.-Y.; Pei, J. *Chem. Mater.* **2023**, *35*, 24, 10277–10294. (d) Chen, C.; Chang, Z.-D.; Guo, Y.-K.; Huang, Y.-B.; Wang, X.-Y. *Chem. Int. Ed.* **2024**, *63*, e202316596 (e) Grams, R. J.; Santos, W. L.; Scorei, I. R.; Abad-García, A.; Rosenblum, C. A.; Bita, A.; Cerecetto, H.; Viñas, C.; Soriano-Ursúa, M. A. *Chem. Rev.* **2024**, *124*, 2441−2511.

systems. In 1926, Stock et al. successfully synthesized borazine ($B_3N_3H_6$) as the first example of a BN/CC isostere of an arene (Scheme 1.3).[9] Borazine is also known as the "inorganic benzene", but its aromatic stabilization energy (ASE) of ~ 10.0 kcal/mol is lower than that of benzene (ASE = ~ 34 kcal/mol)[10,11]. Borazine's low aromaticity is attributed to the electronegativity difference between nitrogen and boron, and localization of electron density near the nitrogen atom.[10]

Scheme 1.3. BN/CC isosterism between benzene and borazine.

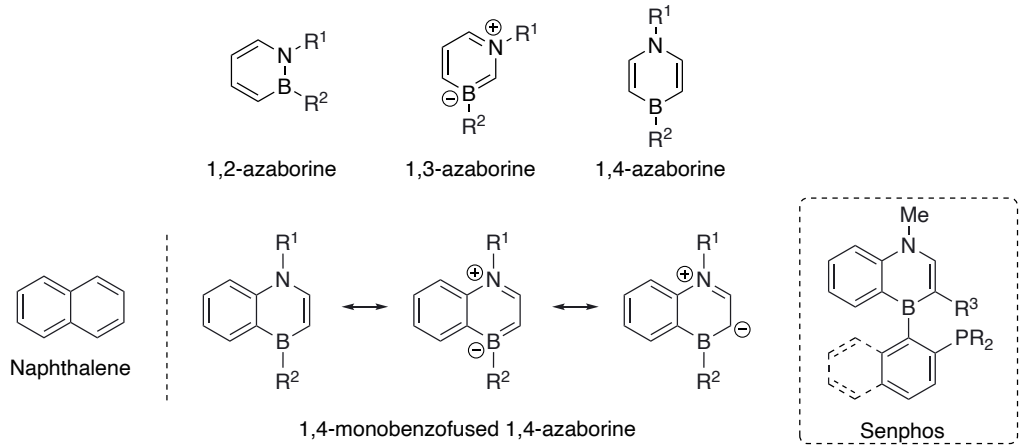


After Stock's work, development of carbon–boron–nitrogen (CBN) heterocycles (aromatic systems with carbons partially substituted with boron and nitrogen) became popular. Replacing carbons on arene with one BN unit would produce three possibilities, namely 1,2-azaborine, 1,3-azaborine and 1,4-azaborine (Scheme 1.4), depending on the relative position of boron and nitrogen atom. One of the applications of the azaborine motif is ligand development,[12] since the BN/CC isosterism would contribute to ligand diversification through electronic tuning, leading to homogeneous catalysis with new reactivity and selectivity. Naphthalene is a very common moiety in ligands.[13] Well known ligand families such as BINOL,[14] BINAP,[15] MOP[16] and many others[17] contain a naphthalene substructure. Therefore, the

(9) A. Stock, E. Pohland, Ber. Dtsch. *Chem. Ges.* **1926**, *59*, 2210 –2215.
(10) (a) Fink, W. H.; Richards, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 3385–3393. (b) Schleyer, P. v. R.; Jiao, H.; Hommes, N. J. R. v. E.; Malkin, V. G.;Malkina, O. L. *J. Am. Chem. Soc.* 1**997**, *119*, 12669–12670. (c) Marwitz, A. J. V.; Matus, M. H.; Zakharov, L. N.; Dixon, D. A.; Liu,S.-Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 973–977. (d) Lisovenko, A. S.; Timoshkin, A. Y. *Inorg. Chem.* **2010**, *49*, 10357–10369.
(11) Aromatic stabilization energy (ASE) was converted from kJ mol^{-1} to kcal mol^{-1}.
(12) McConnell, C. R.; Campbell, P. G.; Fristoe, C. R.; Memmel, P.; Zakharov, L. N.; Li, B.; Darrigan, C.; Chrostowska, A.; Liu, S.-Y. *Eur. J. Inorg. Chem.* **2017**, *2017*, 2207–2210.
(13) Kočovský, P.; Vyskočil, Š.; Smrčina, M. *Chem. Rev.* **2003**, *103*, 3213–3246.
(14) (a) Von Richter, V. *Chem. Ber.* **1873**, *6*, 1252 (b) Brunel, J. M. *Chem. Rev.* **2005**, *105*, 857–898.
(15) Berthod, M.; Mignani, G.; Woodward, G.; Lemaire, M. *Chem. Rev.* **2005**, *105*, 1801–1836.
(16) Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354–362.
(17) Parmar, D.; Sugiono, E.; Raja, S.; Rueping, M. *Chem. Rev.* **2014**, *114*, 9047–9153.

application of BN/CC isosterism to the naphthalene scaffold should expand the scope of ligand development. The Senphos ligand, which is a monobenzofused 1,4-azaborine mono/biaryl mono-phosphines, is a specific example (Scheme 1.4). This thesis explores the development of Senphos ligands with axial chirality and central chirality on phosphine, for enantioselective ligand-supported transition metal catalysis.

Scheme 1.4. 1,2-, 1,3- and 1,4-azaborine, and application of 1,4-azaborine in ligand development.

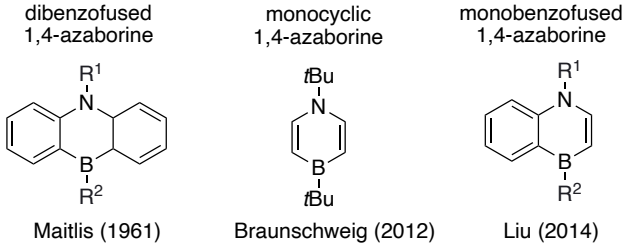


1.1.1 Development of 1,4-azaborine

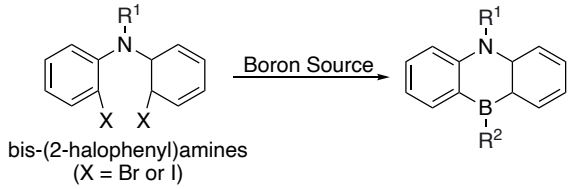
Several 1,4-azaborines have been synthesized and they can be classified as dibenzofused, monobenzofused and monocyclic 1,4-azaborine (Scheme 1.5). The first synthesis of 1,4-azaborine was reported by Maitlis *et al.* in 1961.[18] The dibenzofused framework was constructed by using bis-(2-halophenyl)amines (where X = Br or I) as starting materials (Scheme 1.6).

(18) Maitlis, P. M. *J. Chem. Soc.* **1961**, 425–429.

Scheme 1.5. Dibenzofused, monobenzofused and monocyclic 1,4-azaborine.

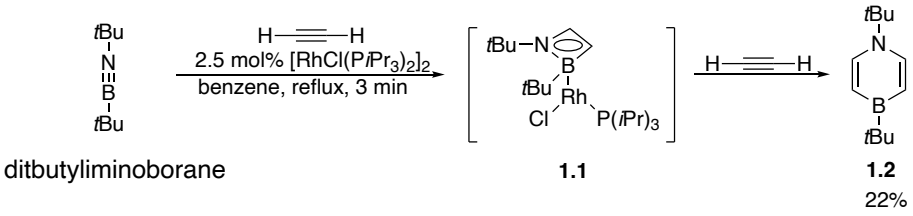


Scheme 1.6. Synthesis of dibenzofused 1,4-azaborine (Maitlis 1961).



In 2012, inspired by substituted benzene formation through [2+2+2] alkyne cyclotrimerization,[19a] Braunschweig reported the first synthetic route to monocyclic 1,4-azaborine (Scheme 1.7).[19b] Braunschweig's monocyclic 1,4-azaborine was made by initial [2+2] cycloaddition of di(*t*-butyl)iminoborane with acetylene to generate a rhodium η^4-1,2-azaborete intermediate **1.1**, which then **1.1** undergoes a [4+2] cycloaddition with acetylene to give 1,4-azaborine **1.2**.

Scheme 1.7. Synthesis of monocyclic 1,4-azaborine (Braunschweig 2012).

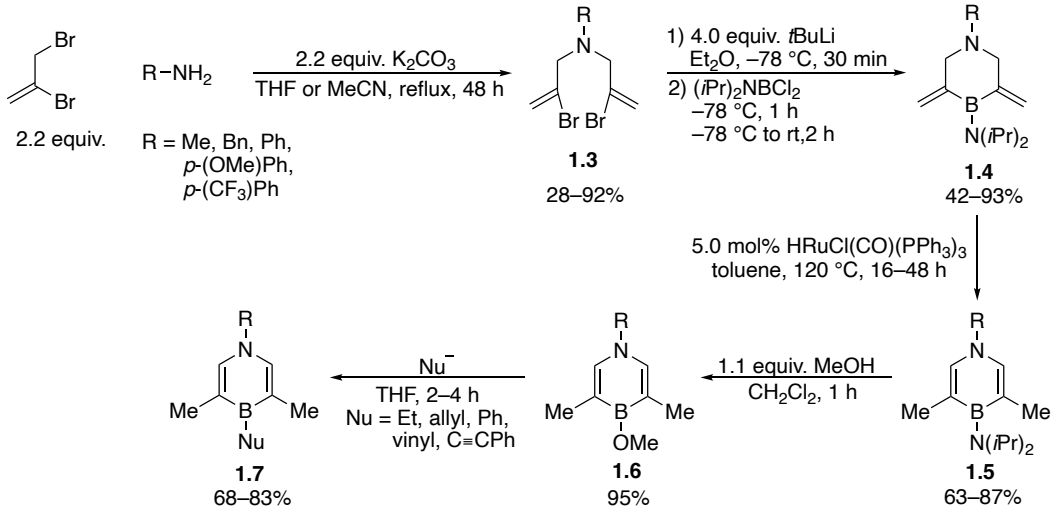


The Liu group also reported an alternative synthetic method to monocyclic 1,4-azaborine, which enables diversification of both boron and nitrogen substituents

(19) (a) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901–2915. (b)Braunschweig, H.; Damme, A.; Jimenez-Halla, J. O. C.; Pfaffinger, B.; Radacki, K.; Wolf, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 10034–10037.
(20) Liu, X.; Zhang, Y.; Li, B.; Zakharov, L. N.; Vasiliu, M.; Dixon, D. A.; Liu, S.-Y. *Angew. Chem., Int. Ed.* **2016**, *55*, 8333–8337.

(Scheme 1.8).[20] Dialkylation of amine gives compound **1.3**, then **1.3** undergoes double lithium-halogen exchange followed by quenching with (diisopropylamino)boron dichloride to give **1.4**. Ruthenium-hydride complex $HRuCl(CO)(PPh_3)_3$ then isomerizes the exo-cyclic alkene **1.4** to endo-cyclic alkene **1.5**. Monocyclic 1,4-azaborine **1.7** is then generated by methanolysis of **1.5** followed by nucleophilic substitution, which would allow various substituents on boron.

Scheme 1.8. Synthesis of monocyclic 1,4-azaborine (Liu 2016).

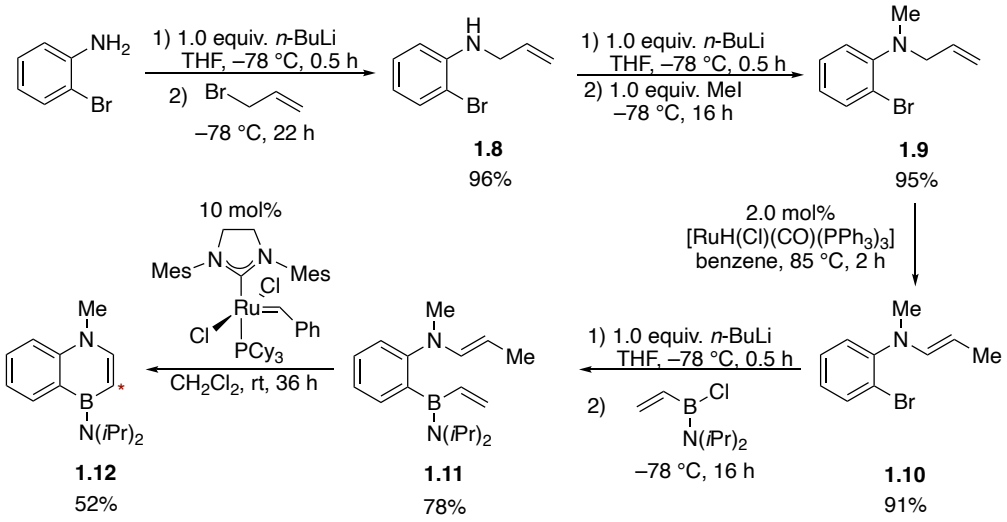


Compared with the dibenzofused 1,4-azaborine, monobenzofused 1,4-azaborine was less explored because the synthesis of enamine precursor is challenging.[21] The Liu group reported the first synthesis of monobenzofused 1,4-azaborine in 2014 (Scheme 1.9). 2-Bromoaniline undergoes allylation to give **1.8**, followed by methylation to generate **1.9**. Then **1.9** undergoes isomerization to form the key precursor enamine **1.10** in the presence of ruthenium-hydride complex. Lithiation of **1.10** followed by reacting with (diisopropylamino)boron dichloride generated **1.11**,

(21) Xu, S. M.; Haeffner, F.; Li, B.; Zakharov, L. N.; Liu, S. Y. *Angew. Chem., Int. Ed.* **2014**, *53*, 6795–6799.

then it undergoes ring closing metathesis (RCM) with Grubbs 2nd generation catalyst to give the monobenzofused 1,4-azaborine **1.12**.

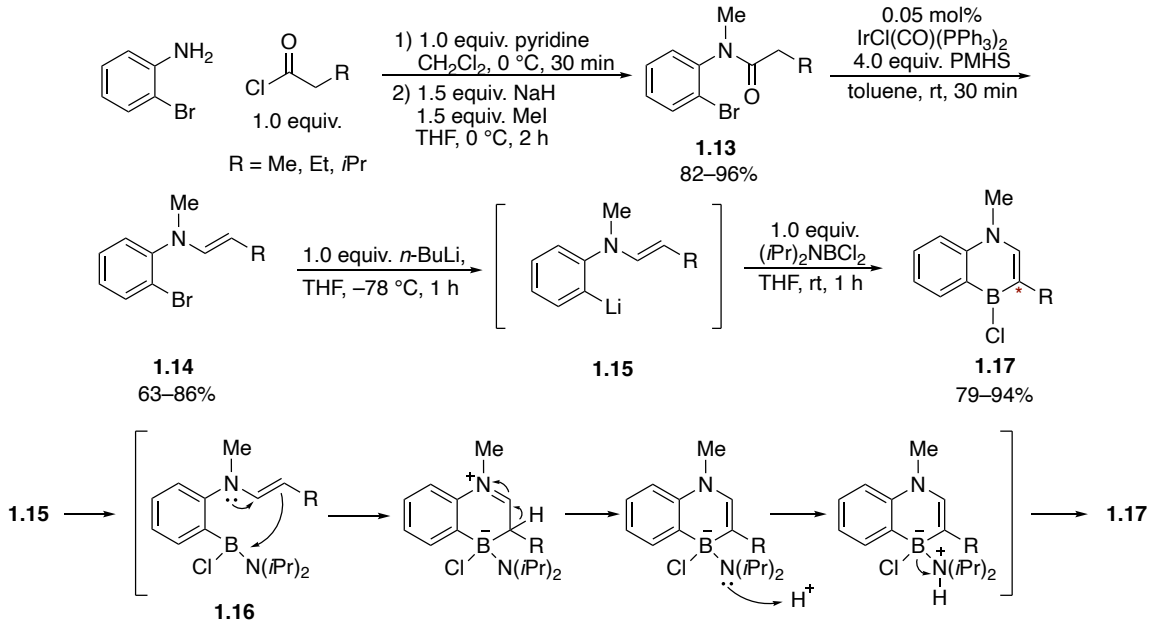
Scheme 1.9. Synthesis of monobenzofused 1,4-azaborine (Liu 2014).



Despite **1.12** could be prepared in decent yield, it was challenging to scale up, and the C(3) position (labelled as *), which was expected to affect the activation of metal catalyst in reaction, was hard to functionalize. Thus, in 2016, Liu group developed a new synthetic route to generate monobenzofused 1,4-azaborine that allows different C(3) substitution (Scheme 1.10).[22] Again, 2-bromoaniline was used as a starting material; acylation of aniline with different acyl chloride allows variation of C(3) substituents. Subsequent methylation gives amide **1.13**. Treating amide **1.13**. with Vaska's complex ($IrCl(CO)(PPh_3)_2$) and PMHS (polymethylhydrosiloxane) gives Enamine **1.14**.[23] Lithiation of **1.14** followed by adding (diisopropylamino)boron dichloride generates intermediate **1.16**, and its subsequent cyclization[24] forms the C(3) functionalized monobenzofused 1,4-azaborine with a labile B-Cl bond, which would facilitate further functionalization.

(22) Xu, S. M.; Zhang, Y. Z.; Li, B.; Liu, S. Y. *J. Am. Chem. Soc.* **2016**, *138*, 14566–14569.
(23) Motoyama, Y.; Aoki, M.; Takaoka, N.; Aoto, R.; Nagashima, H. *Chem. Commun.* **2009**, 1574–1576.
(24) Dewar, M. J. S.; Dietz, R., *J. Chem. Soc.* **1959**, 2728–2730.

Scheme 1.10. Synthesis of monobenzofused 1,4-azaborine (Liu 2016).

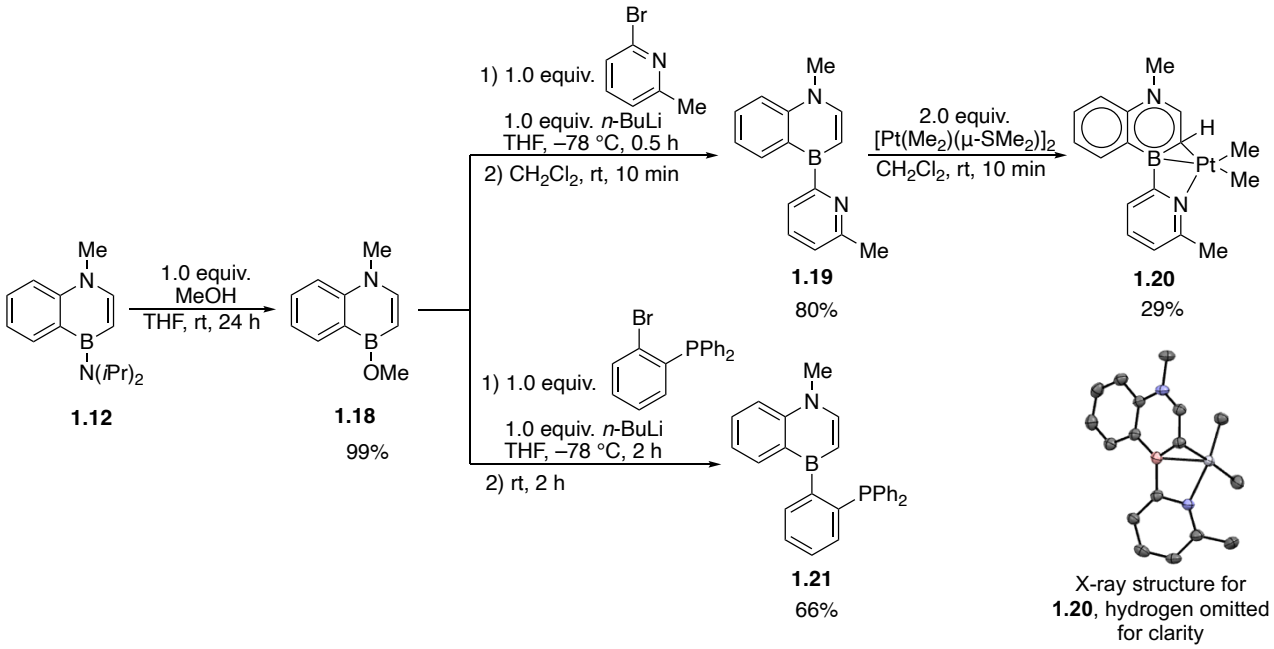


1.1.2 Development of Senphos ligands

The Liu group developed Senphos ligands based on the framework of monobenzofused 1,4-azaborine. The initial study of Senphos ligands started from 1,4-azaborine **1.12** (Scheme 1.11).[21] Methanolysis of **1.12** gives **1.18** with a labile B-OMe bond which allows further functionalization. Nucleophilic substitution of **1.18** with different substrates leads to two ligands, a B-pyridyl ligand **1.19** and a B-arylphosphine ligand **1.21**. Moreover, ligand **1.19** coordinates with platinum complex in a unique κ^2-N-η^2-BC mode, as demonstrated by X-ray crystallography analysis. Monobenzofused 1,4-azaborine phosphine ligands structurally analogous to ligand **1.21** are named as Senphos ligands to recognize the contribution of the original developer Dr. Senmiao Xu.

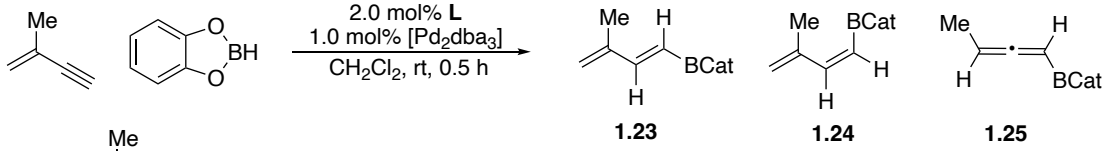
To demonstrate the application of 1,4-azaborine ligands, palladium-catalyzed hydroboration of an 1,3-enyne was investigated (Table 1.1).[21] The corresponding

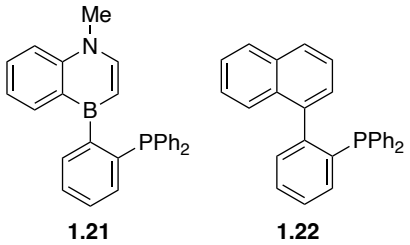
Scheme 1.11. Initial development of Senphos ligands.



all-carbon analogue ligand **1.22**, was used as a control ligand is monodentate triaryl phosphine ligand preferably forms allenylborane **1.25**, and the *cis*-hydroboration product **1.24** forms as a major product in the presence of bidentate bisphosphine ligands.[25] In contrast, when using Senphos ligand **1.21**, trans-hydroboration was dominant.

Table 1.1. Ligand effect on selectivity of Pd-catalyzed hydroboration





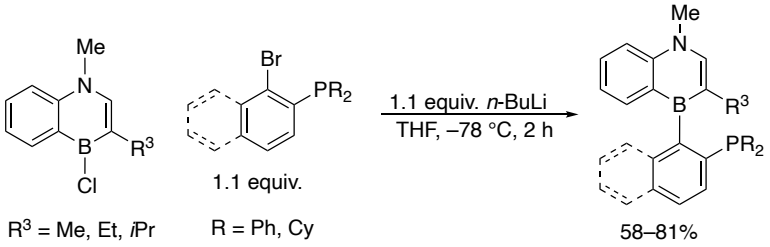
L	Yield (%)	ratio **1.23** / **1.24** / **1.25**
1.21	84	12 / 82 / 6
1.22	42	10 / 19/ 71

(25) (a) Y. Matsumoto, M. Naito, T. Hayashi, *Organometallics* **1992**, *11*, 2732 – 2734; (b) Y. Matsumoto, M. Naito, Y. Uozumi, T. Hayashi, *J. Chem. Soc. Chem. Commun.* **1993**, 1468 – 1469; (c) T. Hayashi, *Acc. Chem. Res.* **2000**, *33*, 354 – 362.

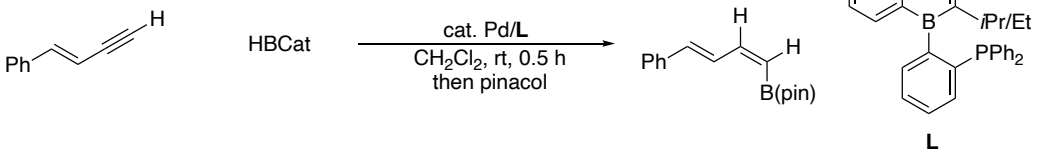
With these preliminary results in hand, in 2016, the Liu group optimized the synthetic route of ligand formation using C(3) substituted monobenzofused 1,4-azaborine as a starting material to generate C(3) substituted ligands (Scheme 1.12),[22] providing a general access to a diverse array (of C(3) and of phosphine) of Senphos ligand. To date, Senphos ligands are applied in Pd-catalyzed *tran*-hydroboration,[22] *trans*-cyanoboration,[26] *cis*-carboboration,[27] *trans*-hydroalkynylation[28] and hydroalkylation[29] reactions, resulting in excellent regio- and diastereoselectivities that are distinct from reactions supported by their corresponding carbonaceous control ligands.

(26) Zhang, Y.; Li, B.; Liu, S.-Y. *Angew. Chem., Int. Ed.* **2020**, *59*, 15928–15932.
(27) Wang, Z.; Wu, J.; Lamine, W.; Li, B.; Sotiropoulos, J.-M.; Chrostowska, A.; Miqueu, K.; Liu, S.-Y. *Angew. Chem. Int. Ed.* **2021**, *60*, 21231–21236.
(28) Wang, Z.; Zhang, C.; Wu, J.; Li, B.; Chrostowska, A.; Karamanis, P.; Liu, S.-Y. *J. Am. Chem. Soc.* **2023**, *145*, 5624–5630.
(29) Eaton, M.; Dai, Y.; Wang, Z.; Li, B.; Lamine, W.; Miqueu, K.; Liu, S.-Y. *J. Am. Chem. Soc.* **2023**, *145*, 21638−21645.

Scheme 1.12. Synthesis and application of Senphos ligands.

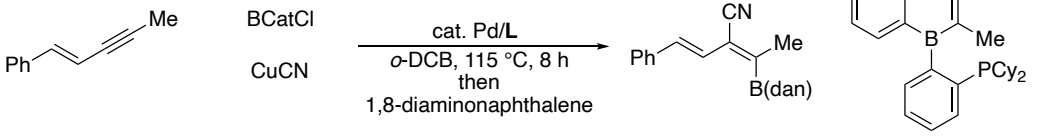


(a) *trans*-Hydroboration (Xu, S. et al. *J. Am. Chem. Soc.* **2016**, *138*, 14566–14569.)



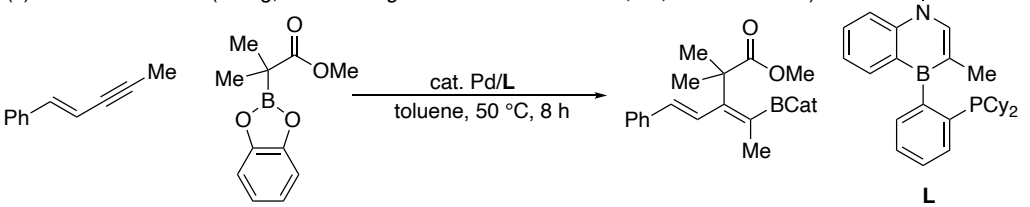
L

(b) *trans*-Cyanoboration (Zhang, Y. et al. *Angew. Chem., Int. Ed.* **2020**, *59*, 15928–15932.)



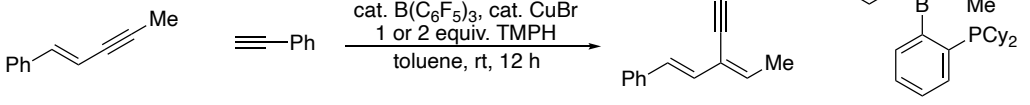
L

(c) *cis*-Carboboration (Wang, Z. et al. *Angew. Chem. Int. Ed.* **2021**, *60*, 21231–21236.)



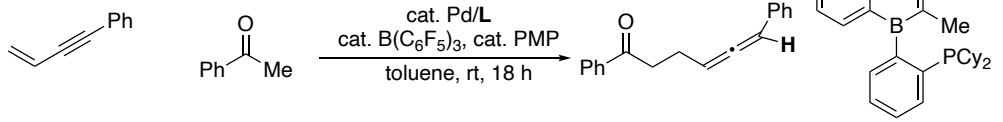
L

(d) *trans*-Hydroalkynylation (Wang, Z. et al. *J. Am. Chem. Soc.* **2023**, *145*, 5624–5630.)



L

(e) Hydroalkylation (Eaton, M. et al. *J. Am. Chem. Soc.* **2023**, *145*, 21638–21645.)

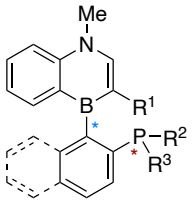


L

1.1.3 Development of chiral phosphine ligands

Although all the published Senphos ligand examples are racemic, they contain two stereogenic elements: axial chirality in the biaryl backbone and P-central chirality if the phosphorus atom is attached to three different groups. Therefore, it is possible to create chiral Senphos ligands (Scheme 1.13). Axial chirality can be achieved through the B-C axis (labeled with a blue star *), and it is also possible to create a Senphos ligand with a chiral phosphine group (labeled with a red star *).

Scheme 1.13. Senphos ligand with axial and P-central chirality.



Senphos

Phosphine ligands are ubiquitous, and they can easily coordinate with a metal to form a complex, such as Vaska's complex,[30] Crabtree's[31] and Wilkinson's catalyst,[32] and metal-phosphine complexes, play a vital role in homogeneous catalysis.

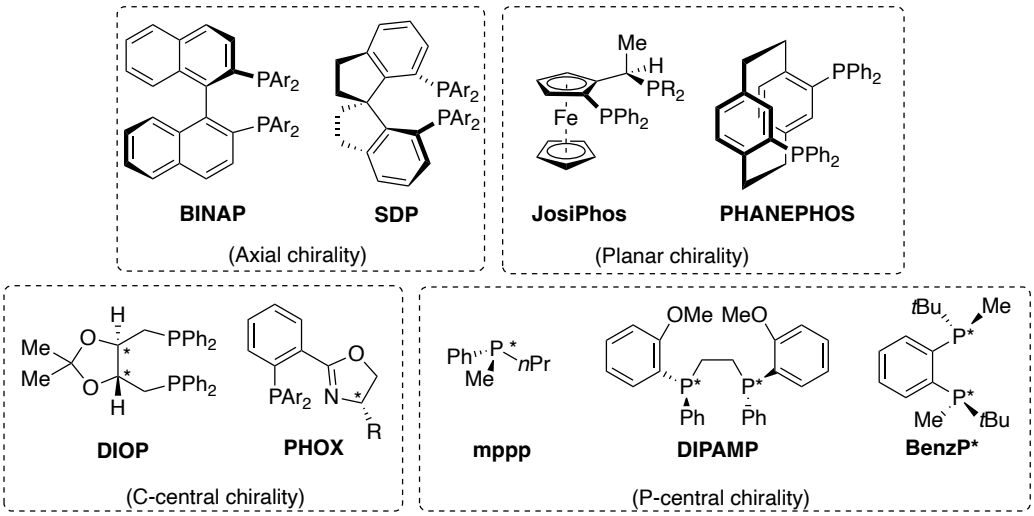
1.1.3.1 A historic overview of chiral phosphine ligands development

Chiral phosphine ligands could be categorized into four classes based on their chirality: axial chiral (e.g., BINAP[14, 33] and SDP[34]), planar chiral (e.g., JosiPhos[35] and

(30) Vaska, L.; DiLuzio; J. W. *J. Am. Chem. Soc.,* **1961**, *83*, 2784–2785.
(31) Crabtree, R. H. *Acc. Chem. Res.,* **1979**, *12*, 331–337.
(32) Young, J. F.; Osborn, J. A.; Jardine, F. H.; Wilkinson, G. *Chem. Commun.*, **1965**, 131–132.
(33) (a) Miyashita, A., Yasuda, A., Takaya, H., Toriumi, K., Ito, T., Souchi, T.; Noyori, R. *J. Am.Chem. Soc.* **1980**, *102*, 27, 7932–7934. (b) Ohta, T.; Takaya, H.; Noyori, R. *Inorg. Chem.* **1988**, *27*, 566–569. (c) Ohta, T.; Takaya, H.; Kitamura, M.; Nagai, K.; Noyori, R. *J. Org. Chem.* **1987**, *52*, 3174–3176. (d) Noyori, R. *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 2008–2022.
(34) Xie, J.; Duan, H.; Fan, B.; Cheng, X.; Wang, L.; Zhou, Q. *Adv. Synth. Catal.* **2004**, *346*, 625-632.

PHANEPHOS[36]), C-chirogenic (e.g., DIOP[37] and PHOX[38]) and P-chirogenic (e.g., mppp[39], DIPAMP[40] and BeneP*[41]) ligands (Scheme 1.14).

Scheme 1.14. Chiral phosphine ligands.



Development of chiral phosphine ligands[42] was started from late 1960s by Knowles[39a] and Horner.[39b] They reported the first asymmetric hydrogenation of olefin by replacing the triphenylphosphine ligand in Wilkinson's catalyst with enantiopure mppp ligand.[39,43] Although the enantiomeric excess (*ee*) was low (<15%), it marked a significant milestone in enantioselective hydrogenation. Later in 1971, Kagan developed the first bisphosphine ligand DIOP, and applied the ligand in Ru-catalyzed hydrogenation to achieve reasonable enantioselectivity (*ee* = 72%).[37] With Kagan's

(35) (a) Togni, A.; Breutel, U.; Schnyder, A.; Spindler, F.; Landert, H.; Tijiani, H. *J. Am. Chem. Soc.* **1994***, 116,* 4062–4066. (b) Blaser, H. U.; Brieden, W.; Pugin, B. *Topics in Catalysis*, **2002**, *19*, 3–16.
(36) (a) Pye, P. J.; Rossen, K.; Reamer, R. A.; Tsou, N. N.; Volante, R. P.; Reider, P. J. *J. Am. Chem. Soc.* **1997**, *119,* 6207–6208. (b) Pye, P. J.; Rossen, K.; Reamer, R. A.; Tsou, N. N.; Volante, R. P.; Reider, P. J. *Tetrahedron Lett.* **1998***, 39,* 4441–4444.
(37) Dand, T.P.; Kagan, H. B. *J. Chem. Soc. Chem. Commun.* **1971**, *10*, 481–481.
(38) (a) Koch, G.; Lloyd-Jones, G. C.; Loiseleur, O.; Pfaltz, A.; Prétôt, R.; Schaffner, S.; Schnider, P.; von Matt, P. *Recl. des Trav. Chim. des Pays-Bas.* **1995**, *114*, 206−210. (b) Connon, R.; Roche, B.; Rokade, B. V.; Guiry, P. J. *Chem. Rev.* **2021**, *121*, 6373−6521.
(39) (a) Knowles, W. S.; Sabacky, M. J. *Chem. Commun.* **1968**, 1445–1446. (b) Horner, L.; Siegel, H.; Büthe, H. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 941–973.
(40) (a) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, O. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946–5952. (b) Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106–112.
(41) Yamamoto, Y.; Koizumi, T.; Katagiri, K.; Furuya, Y.; Danjo, H.; Imamoto, T.; Yamaguchi, K. *Org. Lett.* **2006**, *8*, 6103–6106.
(42) Tang, W.; Zhang, X.; *Chem. Rev.* **2003**, *103*, 3029−3069.
(43) Knowles, W. S. *Angew. Chem. Int. Ed.* **2002**, *41*, 1998−2007.

pioneering work, bidentate bisphosphine ligands became predominant in the development of phosphine ligands.[44] Few years later, Knowles reported a C_2-symmetric chelating bisphosphine ligand DIPAMP, which gave 96% *ee* in Ru-catalyzed hydrogenation with high catalytic efficiency.[40] DIPAMP ligands were also used in commercial production of L-DOPA (L-3,4-dihydroxyphenylalanine), which contributes to the treatment of Parkinson's disease.[45] In 2001, Knowles was awarded the Nobel Prize in chemistry for his achievement in asymmetric hydrogenation.[43]

In late 1980s, Noyori reported the application of BINAP/Ru catalysts for enantioselective hydrogenation of olefins and reduction of ketones.[33] Later in 1995, Noyori developed a BINAP/diamine-Ru complex, which could hydrogenate unfunctionalized ketones with good enantioselectivity (*ee* > 99%).[46] Noyori's work inspired many researchers, leading to the development of numerous atropisomeric biaryl bisphosphine ligands.[42,47] Due to his significant contributions, Noyori was also awarded the Nobel Prize in Chemistry in 2001.

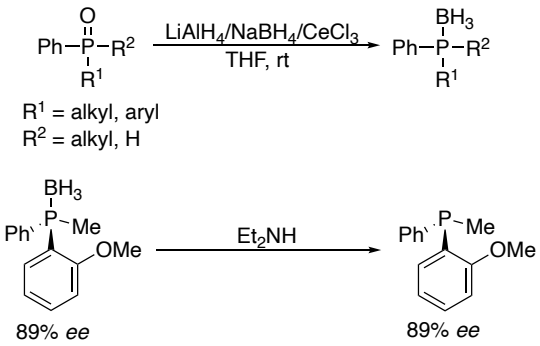
1.1.3.2 Imamoto's P-chirogenic ligands synthesis

Although the DIPAMP ligand was a significant success in the development of P-chirogenic ligands, P-chiral ligands have not been as widely applied as biaryl bisphosphine ligands. One of the biggest problems is the synthesis of optical pure phosphine. The phosphors (III) atom has a pyramidal geometry, and a phosphine with an electron-withdrawing group such as phenyl is easily racemized via pyramidal

(44) For examples, see: (a) Ansell, J.; Wills, M. *Chem. Soc. Rev.*, **2002**, *31*, 259–268. (b) Crépy, K.V.L., Imamoto, T. New P-Chirogenic Phosphine Ligands and Their Use in Catalytic Asymmetric Reactions. In *Top. in Curr. Chem.* Vol. 229. pp 1–40. (c) Guiry, P. J.; Saunders, C. P. *Adv. Synth. Catal.* **2004**, *346*, 497–537. (d) Goudriaan, P. E.; Leeuwen, P.; Birkholz, M.–N.; Reek, J. N. H. *Eur. J. Inorg. Chem.* **2008**, 2939–2958. (e) Clevenger, A. L.; Stolley, R. M.; Aderibigbe, J.; Louie, J. *Chem. Rev.* **2020**, *120*, 6124−6196.
(45) Knowles, W. S. *J. Chem. Educ.* **1986**, *63*, 222–225.
(46) Ohkuma, T.; Ooka, H.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 2675–2676.
(47) For examples, see (a) Shimizu, H.; Nagasaki, I.; Saito, T. *Tetrahedron 61*. **2005**, 5405–5432. (b) Zhang, W.; Chi, Y.; Zhang, X. *Acc. Chem. Res.* **2007**, *40*, 1278–1290. (c) Mino, T.; Naruse, Y.; Kobayashi, S.; Oishi, S.; Sakamoto, M.; Fujita, T. *Tetrahedron Lett. 50*. **2009**, 2239–2241.

inversion, even at room temperature.[48] In 1985, Imamoto found that using phosphine borane as an intermediate could lead to the formation of P-chiral phosphine ligands.[49] Imamoto's study was focused on developing organocerium reagents (e.g.; $CeCl_3$) to achieve carbonyl functionalization.[50] Once they applied this method to the reduction of phosphine oxide, and were surprised to find the formation of a phosphine borane complex upon treatment with a mixture of $LiAlH_4$, $NaBH_4$ and $CeCl_3$ (Scheme 1.15).[51] The formed complex is air and moisture stable, and compatible with strong acids and bases such as HCl and NaOH. The reactivities of the phosphine borane complex was also studied. The deprotection of borane can be achieved by treating the complex with an amine, without any erosion of enantiomeric excess.

Scheme 1.15. Formation and deprotection of phosphine borane complex.



Based on these preliminary results, Imamoto developed a series of P-chiral ligands with borane as a protecting group of phosphine, and those ligands are widely applied in Rh-catalyzed asymmetric hydrogenation.[48]

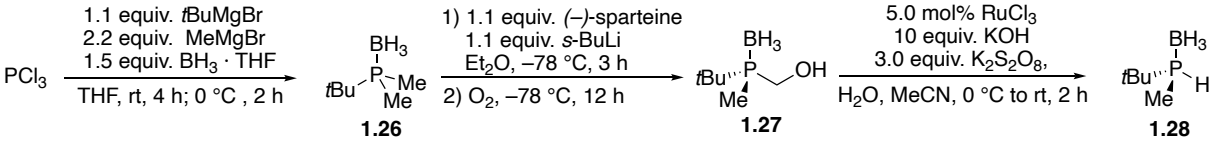
(48) (a) Imamoto T. *Chem. Rec.* **2016**, *16,* 2659–2673. (b) Imamoto T. *Proc. Jpn. Acad., Ser. B.* **2021***, 97,* 520–542.
(49) Imamoto, T.; Kusumoto, T.; Suzuki, N.; Sato, K. *J. Am. Chem. Soc.* **1985***, 107*, 5301–5303.
(50) Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904–3912.
(51) Imamoto, T.; Takeyama, T.; Kusumoto,T. *Chem. Lett.* **1985**, 1491–1492.

1.2 SYNTHESIS OF P-CHIROGENIC SENPHOS LIGANDS

1.2.1 Background

In 2000, Imamoto reported an efficient synthetic route to prepare enantiomerically pure secondary phosphine borane complex **1.28** in large scale (Scheme 1.16).[52] Secondary phosphine borane is electronically and structurally similar with phosphine oxide,[48a] and a previous study of Imamoto showed that enantiomerically enriched tertiary phosphine borane complexes could be obtained from phosphide anions derived from corresponding secondary phosphine boranes.[53] Therefore, secondary phosphine borane complex could be used as a key intermediate in the synthesis of chiral phosphine.

Scheme 1.16. Preparation of secondary phosphine borane complex.



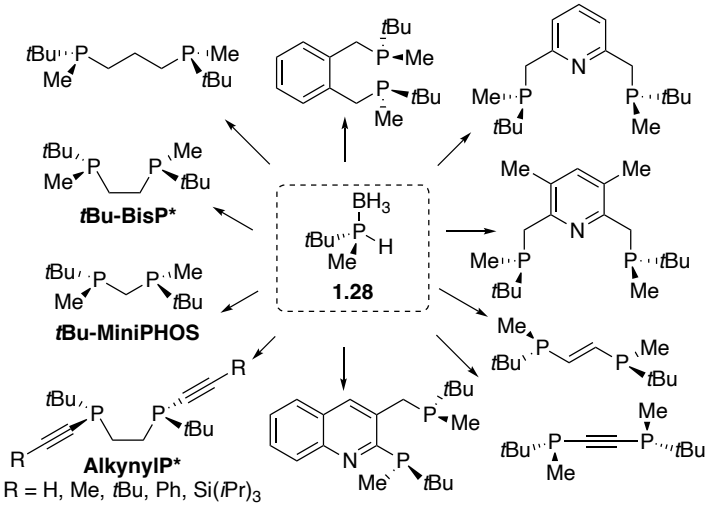
The synthesis of complex **1.28** started from commercially available phosphorus trichloride, two successive nucleophilic substitution by *t*BuMgBr and MeMgBr and borane protection leads to phosphine borane complex **1.26**. Then **1.26** could be selectively deprotonated by a combination of *(–)*-sparteine and *sec*-butyllithium, followed by oxidation to give optical pure complex **1.27**. The primary alcohol group of **1.27** is oxidized to carboxylic acid, followed by CO_2 elimination to form secondary phosphine borane complex **1.28**. This synthetic method is scalable, affording **1.28** in

(52) (a) Nagata, K.; Matsukawa, S.; Imamoto, T. *J. Org. Chem.* **2000**, *65*, 4185–4188. (b) Imamoto, T.; Tamura, K.; Ogura, T.; Ikematsu, Y.; Mayama, D.; Sugiya, Y. *Tetrahedron: Asymmetry* **2010**, *21*, 1522–1528.
(53) (a) Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.* **1990**, *112*, 5244–5252. (b) Oshiki, T.; Imamoto, T. *J. Am. Chem. Soc.* **1992**, *114*, 3975–3977.

gram scale. But one challenge is the stoichiometric use of the expensive *(–)*-sparteine reagent.

Further functionalization and borane group removal of complex **1.28** furnish P-chirogenic diphosphine ligands (Scheme 1.17), which have been utilized in catalytic asymmetric transformations.[48a,54]

Scheme 1.17. P-chirogenic diphosphine ligands from secondary phosphine borane **1.28**.



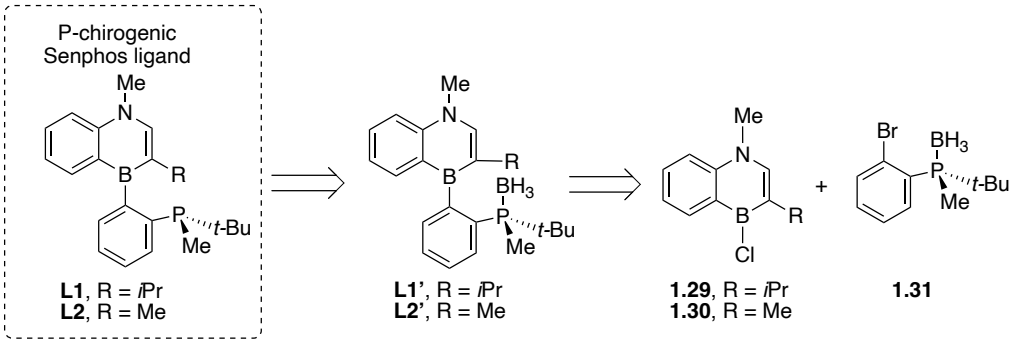
1.2.2 P-chirogenic Senphos ligands formation

Inspired by Imamoto's work, we designed a new Senphos ligand with a P-chirogenic phosphine group (Scheme 1.18). Methyl and *tert*-butyl groups were chosen since they were widely applied in Imamoto's ligand family. The designed ligand

(54) For examples, see (a) Imamoto, T.; Horiuchi, Y.; Hamanishi, E.; Takeshita, S.; Tamura, K.; Sugiya, M.; Yoshida, K. *Tetrahedron* **2015**, *71*, 6471–6480. (b) Miura, T.; Yamada, H.; Kikuchi, S.; Imamoto, T. *J. Org. Chem.* **2000**, *65*, 1877–1880. (c) Imamoto, T.; Tamura, K.; Ogura, T.; Ikematsu, Y.; Mayama, D.; Sugiya, M. *Tetrahedron: Asymmetry* **2010**, *21*, 1522–1528. (d) Gridnev, I. D.; Higashi, N.; Imamoto, T. *Organometallics* **2001**, *20*, 4542–4553. (e) Imamoto, T.; Saitoh, Y.; Koide, A.; Ogura, T.; Yoshida, K. *Angew. Chem. Int. Ed.* **2007**, *46*, 8636–8639. (f) Ding, B.; Zhang, Z.; Xu, Y.; Liu, Y.; Sugiya, M.; Imamoto, T.; Zhang, W. *Org. Lett.* **2013**, *15*, 5476–5479. (g) Yang, Z.; Xia, C.; Liu, D.; Liu, Y.; Sugiya, M.; Imamoto, T.; Zhang, W. *Org. Biomol. Chem.* **2015**, *13*, 2694–2702. (h) Yang, Z.; Liu, D.; Liu, Y.; Sugiya, M.; Imamoto, T.; Zhang, W. *Organometallics* **2015**, *34*, 1228–1237. (i) Yang, Z.; Wei, X.; Liu, D.; Liu, Y.; Sugiya, M.; Imamoto, T.; Zhang, W. *J. Organomet. Chem.* **2015**, *791*, 41–45. (j) *Xu, Y.; Yang, Z.; Ding, B.;* Liu, D.; Liu, Y.; Sugiya, M.; Imamoto, T.; Zhang, W. *Tetrahedron* **2015**, *71*, 6832–6839.

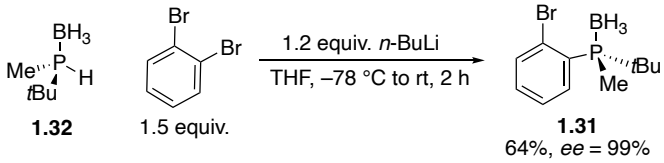
formation method was a bromo-lithium exchange of aryl bromide **1.31** followed by addition of 1,4-azaborine to give borane protected ligand, then the borane group can be removed by DABCO (1,4-diazabicyclo[2.2.2]octane) reagent.

Scheme 1.18. Retrosynthesis of P-chirogenic Senphos ligand.

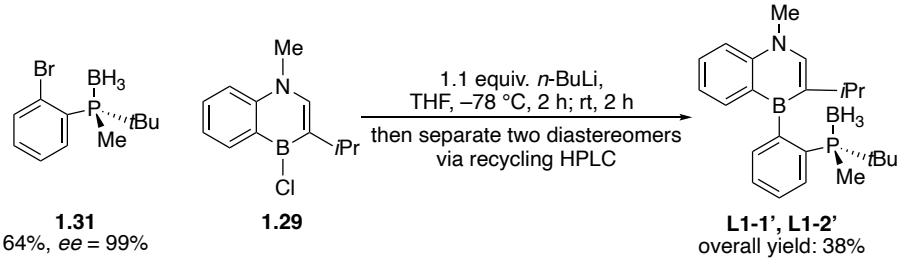


The aryl bromide **1.31** was made from secondary phosphine borane **1.32** via lithiation and nucleophilic addition (Scheme 1.19).[55] The *(R)*-enantiomer of secondary phosphine borane **1.32** was made via Imamoto's synthesis but with the less expensive ligand *(+)*-sparteine instead of *(–)*-sparteine. It is noteworthy that 78% of *(+)*-sparteine was recovered via acid-base work up, making this synthesis more sustainable. Then the ligand precursor **1.31** was obtained with 64% yield and 99% of *ee*.

Scheme 1.19. Synthesis of aryl bromide **1.31**.



Scheme 1.20. Ligand formation of **L1-1'** and **L1-2'**.

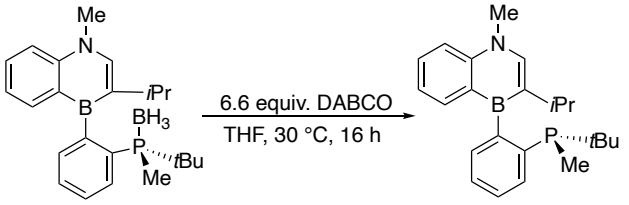


(55) Tamura, K.; Sugiya, M.; Yoshida, K.; Yanagisawa, A.; Imamoto, T. *Org. Lett.*, **2010**, *12*, 4400–4403.

The ligand formation (Scheme 1.20) leads to a mixture of two diastereomers **L1-1'** and **L1-2'**, which could be separated by recycling preparative HPLC. The two diastereomers can be distinguished by ^{1}H NMR (see NMR spectra).

With the successful synthesis and separation of borane-protected ligands, DABCO was utilized for the deprotection process. In our initial trial, we used an excess amount of DABCO in toluene as the solvent at room temperature (22 ℃). The reaction was monitored using ^{11}B and ^{31}P NMR spectroscopy. However, deprotection did not occur at this temperature. Subsequently, the reaction temperature was increased to 30 ℃, but this led to epimerization of the ligand (Scheme 1.21). Additionally, the deprotection remained incomplete due to insufficient heat.

Scheme 1.21. Borane deprotection of Senphos ligand.



L1-2'
d.r. > 99 : 1

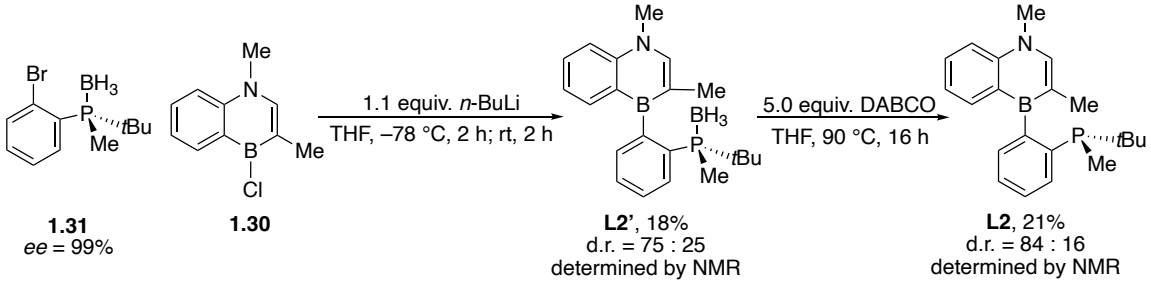
L1-2, 18%
d.r. = 94 : 6
determined by NMR

We hypothesize that the axially chiral configuration may be unstable under heat. To address this issue, two solutions were proposed: first, replacing the C(3) position with a smaller group and increasing the temperature during deprotection to allow the B-C axis to rotate freely and produce only one product as a result; second, replacing the bottom aryl phosphine group with a biaryl group to enhance the configuration stability of the chiral axis.

Therefore, the borane protected ligand **L2'**, which contains two diastereomers, was made in the same method with C(3)-Me 1,4-azaborine **1.30**. Then the ligand **L2'** was deprotected under 90 ℃ overnight to give **L2**. By ^{1}H and ^{31}P NMR, **L2** can still be observed as a mixture of two diastereomers (Scheme 1.22). But since the reaction was

heated to high temperature (90 ℃) and left for long time, the rotation of B-C axis should reach a thermodynamic equilibrium. The rotation is probably slower than the NMR time scale, indicate the observation of diastereomers in NMR.

Scheme 1.22. Ligand formation of **L2**.

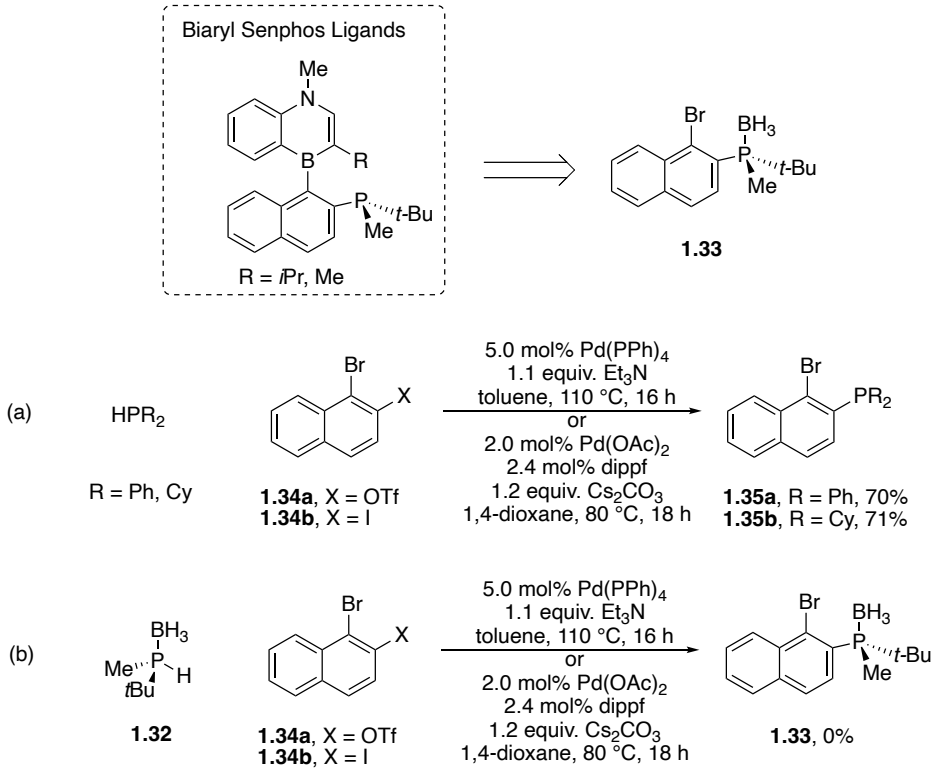


We later focused on the synthesis of binaphthyl Senphos ligands, starting with making ligand precursor **1.33**. Our group reported a few examples of binaphthyl Senphos ligands, [22, 29] Pd-catalyzed cross-coupling of naphthalene electrophile **1.34** with a secondary phosphine gives the precursor ligand **1.35**. (Scheme 1.23a).[56]

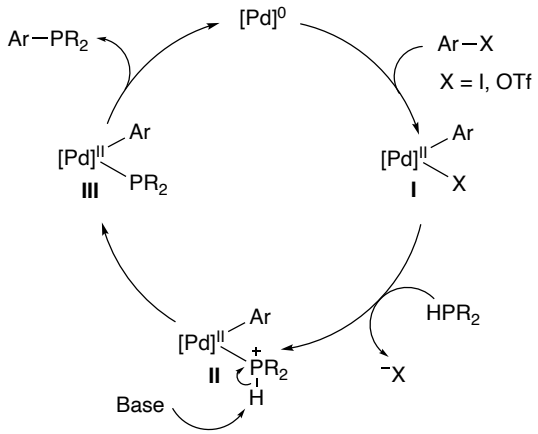
However, under the same conditions, the Pd-catalyzed cross-coupling did not succeed with the secondary phosphine **1.32**, only starting materials were recovered (Scheme 1.23b). A general mechanism of C-P coupling is shown in Scheme 1.24,[57] the $[Pd]^0$ catalyst undergoes an oxidative addition with Ar-X to give complex **I**, and then transmetallation takes place to give complex **II**, followed by deprotonation in the presence of base and reductive elimination to release the desired product. It may be challenging for compound **1.32** to coordinate with palladium since it has no lone pair, resulting in the failure of the C-P coupling. The borane complex **1.32** is deprotonated via *n*-butyllithium in the synthesis of ligand precursor **1.31** (Scheme 1.19). Thus, the deprotonation of secondary phosphine borane complex may need a very strong base.

(56) Murata, M.; Buchwald, S. L. *Tetrahedron 60* **2004**, 7397–7403.
(57) Tappe, F. M. J.; Trepohl, V.T.; Oestreich, M. *Synthesis* **2010**, *18,* 3037–3062.

Scheme 1.23. naphthyl Senphos ligands and the synthesis of ligand precursor.



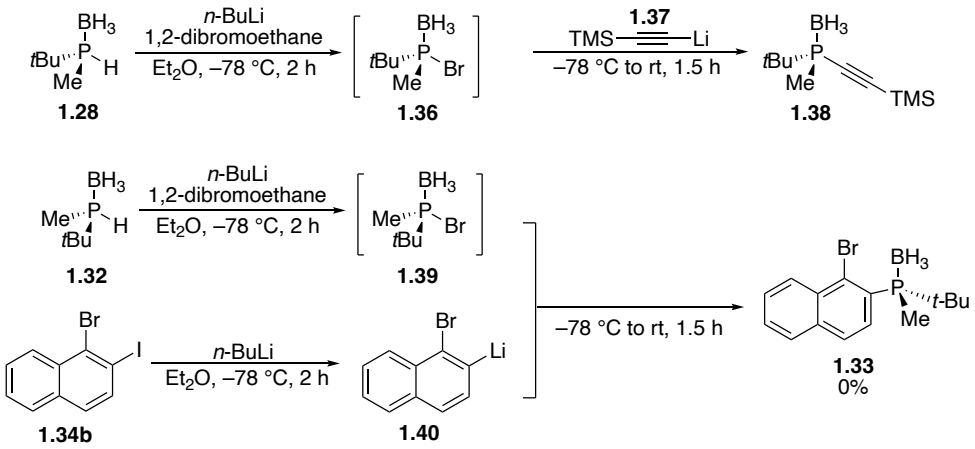
Scheme 1.24. General mechanism of C-P coupling.



In 2007, Imamoto reported a method to generate chiral phosphine borane from secondary phosphine borane **1.28** (Scheme 1.25).[54e] Treating the secondary phosphine borane **1.28** with *n*-butyllithium and 1,2-dibromoethane at –78 °C gives phosphine bromide **1.36**, then acetylide **1.37** was added to afford chiral phosphine **1.38** via a nucleophilic substitution. It is important to note that the phosphine bromide was configurationally unstable at room temperature, precluding isolation. The same method

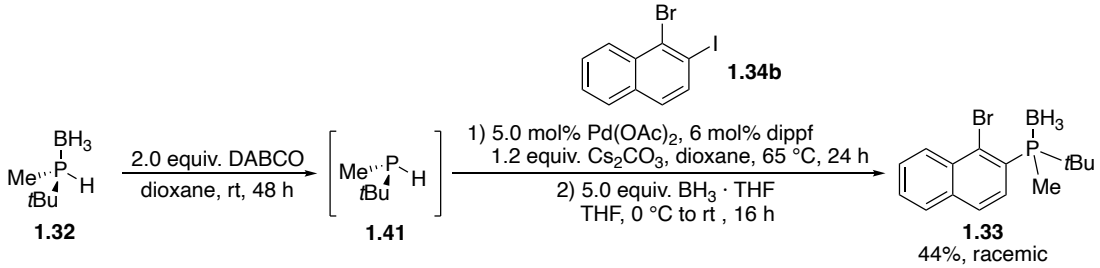
is applied to the synthesis of **1.33**. Lithiation and bromination of phosphine **1.32** leads to phosphine bromide **1.39** is, and at the same time, an iodo-lithium exchange of 1-bromo-2-iodonaphthalene **1.34b** gives the aryl lithium **1.40**. Then the reaction mixture of **1.40** is transferred into the phosphine bromide reaction flask by cannula transfer under –78 °C to prevent racemization, but this reaction leads to a complex mixture, and no desired product **1.33** was obtained.

Scheme 1.25. Imamoto's method to synthesis chiral phosphine borane.



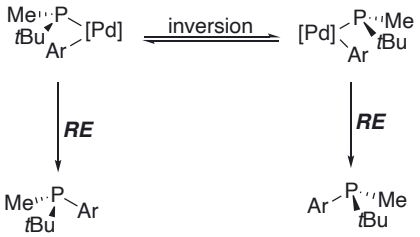
Therefore, we removed the borane group from **1.32** before conducting the cross-coupling with the aim to re-introduce the borane group after the coupling process to obtain biaryl phosphine borane **1.33**. The reaction is performed in one pot with 44% of yield, but the obtained naphthyl phosphine borane **1.33** was a racemic (Scheme 1.26).

Scheme 1.26. One pot synthesis of ligand precursor **1.33**.



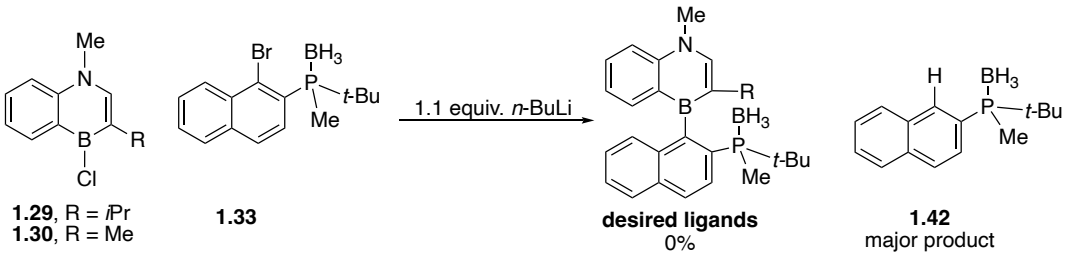
A study of Rheingold et al. shows that the pyramidal inversion of palladium-phosphine complex is faster than C-P bond formation (Scheme 1.27),[58] which is a possible reason for the epimerization of phosphine.

Scheme 1.27. Pyramidal inversion of palladium-phosphine complex and C-P bond formation.



We proceeded with attempts to form Senphos ligands using the racemized precursor **1.33** to assess the separability of the enantiomers and diastereomers via preparative recycling HPLC (Scheme 1.28). The standard conditions was applied in Senphos ligand synthesis, but instead of obtaining the desired ligands, we isolated the protonated product **1.42**. We also tested 1,4-azaborine derivatives with different C(3) substituents, but encountered similar outcomes.

Scheme 1.28. Ligand formation with biaryl phosphine borane **1.33**.

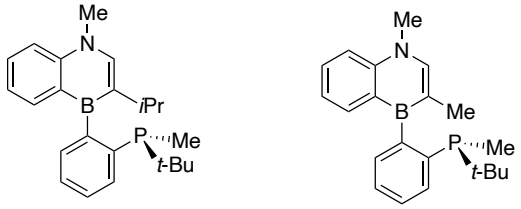


(58) BlankJillian, N. F.; Moncarz, J. R.; Brunker, T. J.; Scriban, C.; Anderson, B. J.; Amir, O.; Glueck, D. S.; Zakharov, L. N.; Golen, J. A.; Incarvito, C. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **2007**, *129*, 21, 6847–6858.

1.2.3 Ligands test

Since we have two enantiomerically enriched ligands **L1-2** and **L2** in hand, we chose the hydroalkylation of 1,3-enyne with simple ketone to evaluate their performance in enantiomeric catalysis.

Scheme 1.29. **L1-2** and **L2**.



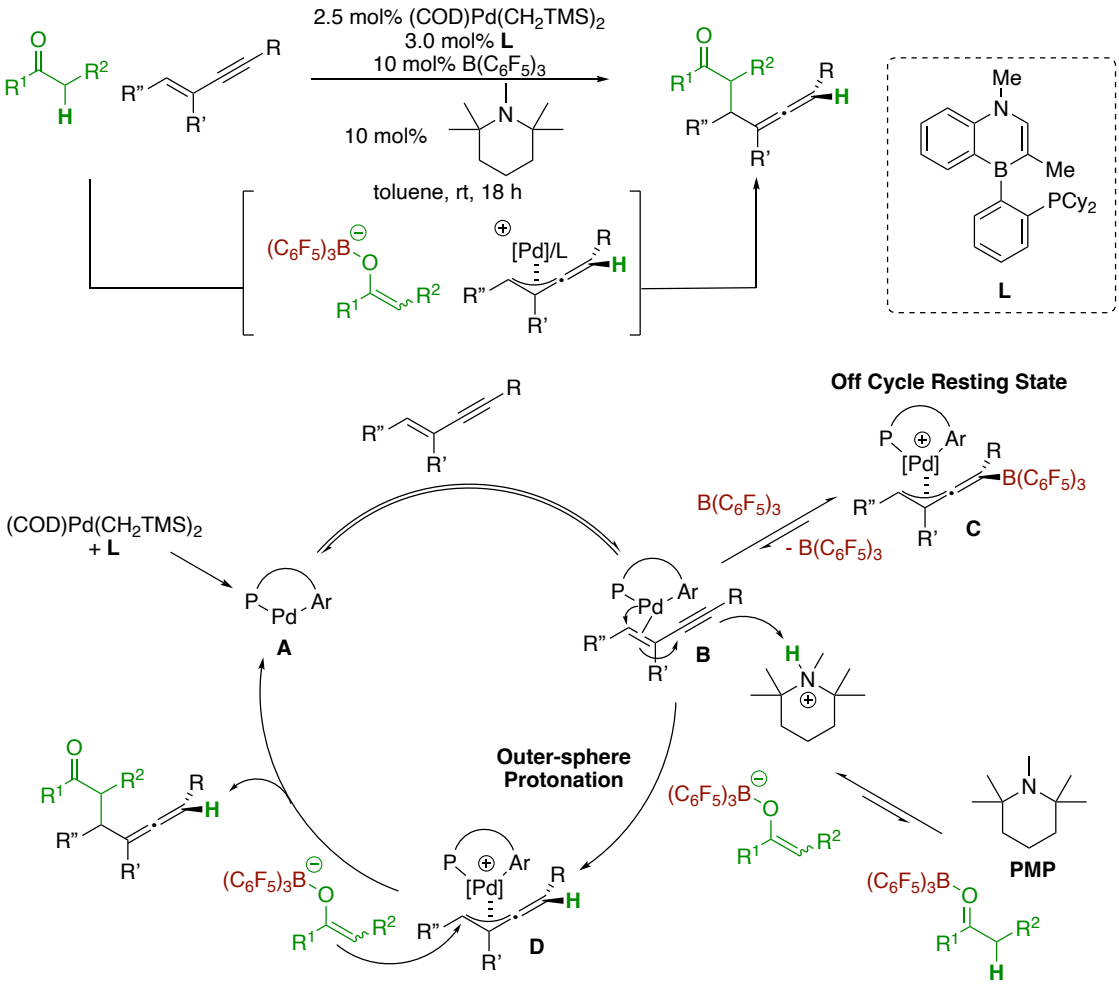
L1-2
d.r. = 94 : 6

L2
d.r. = 84 : 16

In 2023, our group reported the synthesis of allenes via hydroalkylation of 1,3-enyne via Pd/Senphos catalyst system. The reaction condition is mild, atom economical and tolerate a variety of ketones (Scheme 1.30).[29] However, the obtained allene product was a racemic mixture, due to the use of the racemic Senphos ligand. We hypothesized that employing chiral Senphos ligands would accomplish enantioselectivity in the hydroalkylation reaction.

The reaction mechanism of hydroalkylation is demonstrated in Scheme 1.30. The Pd precursor undergoes ligand exchange with Senphos ligands to form the complex **A**, followed by coordination with 1,3-enyne to afford complex **B**. Then the complex **B** reacts with $B(C_6F_5)_3$ to give the off cycle resting state **C** (supported by ^{31}P NMR and crystal structure). At the same time, $B(C_6F_5)_3$ catalyzes the deprotonation of ketone by **PMP** base, resulting in a boron-enolate and an ammonium species. Then, the outer-sphere deprotonation (rate-determining-step) affords complex **D**, followed by nucleophilic attacked of boron enolate to release the desired allene product.[29]

Scheme 1.30. Hydroalkylation of 1,3-enyne with simple ketone.



Our collaborator, Yuping Dai performed DFT calculations of SMD(Toluene)-WB97XD/SDD+f(Pd), 6-31+G**(other atoms) level to assess the feasibility of using P-chirogenic Senphos ligand to afford enantiopure allene product via hydroalkylation (Figure 1.1). The enantioselectivity is determined by the configuration of intermediate **D**: the **endo**-intermediate and **exo**-intermediate each would lead to *(R)*-allene and *(S)*-allene, respectively (Scheme 1.31). The **endo**- and **exo**-intermediate could isomerize via η^1-η^3 Pd migration/bond rotation. Assuming a Curtin-Hammett scenario, calculation predict that the attack of the nucleophile to the **exo**-isomer is favored by 5.1 kcal/mol (figure 1.1). Therefore, the computational result suggested that the chiral

Senphos ligand should enable an enantioselective hydroalkylation of 1,3-enyne process.

Scheme 1.31. Isomerization of **endo**-/**exo**-intermediates leads to *(R)* and *(S)* allenes.

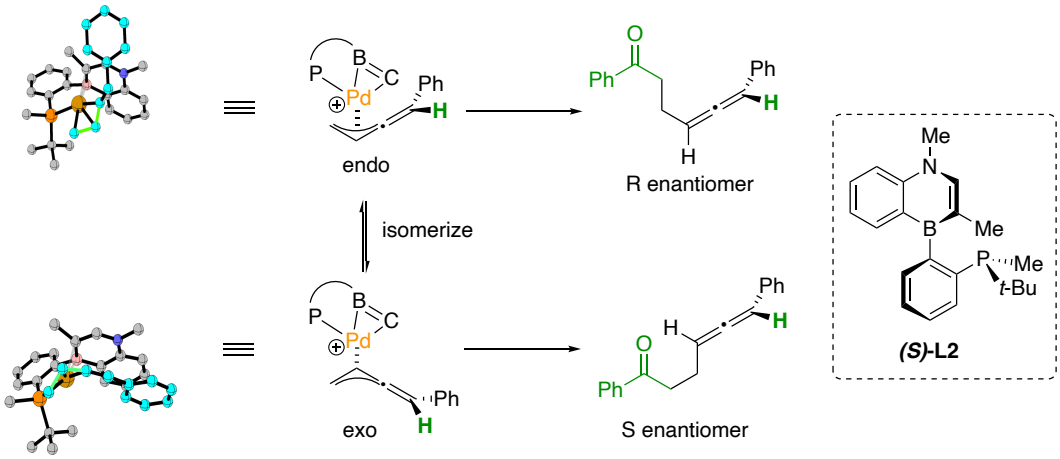
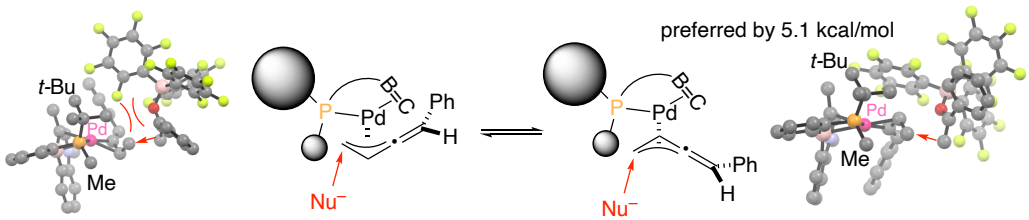


Figure 1.1. Energy profile for nucleophilic attack **endo**-intermediate and **exo**-intermediate.

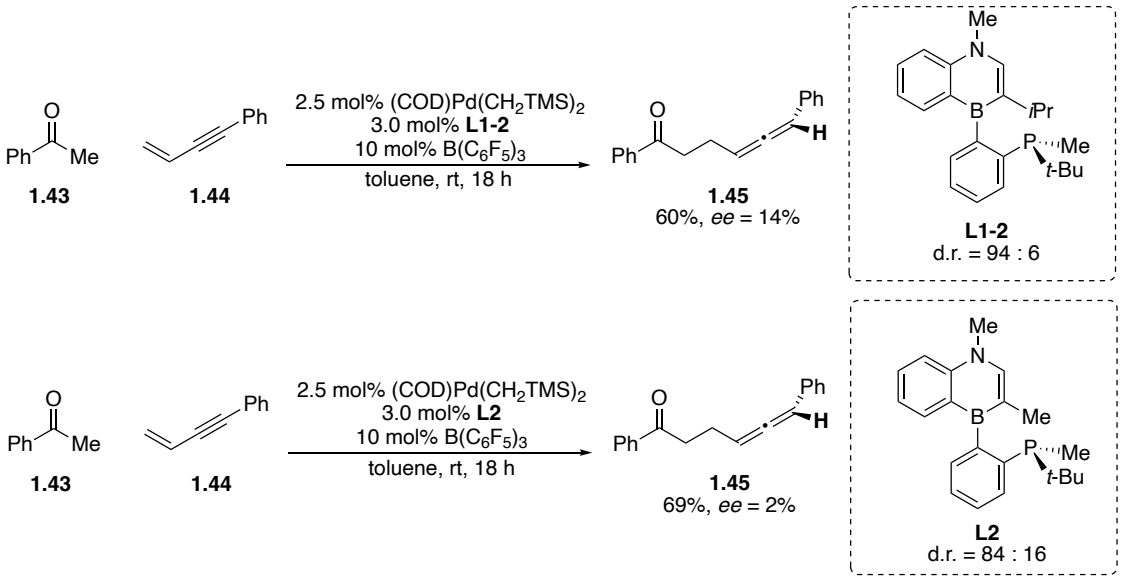


Even though the two ligands we obtained were not diastereomerically pure, we proceeded with the test reactions (Scheme 1.32). Both ligands are compatible with the standard conditions and provide decent yields. The reaction with ligand **L1-2** results in 14% of *ee*, which means either axial or P-chirality would affect the enantioselectivity. But when ligand **L2**, which has a P-chirogenic group but attenuated axial chirality, was used, the product allene was almost racemic.

The test results show that the axial chirality is likely more effective in controlling enantioselectivity compared with central chirality on phosphine, and points toward some deficiency in computational model. Based on these results and

the challenges encountered in forming biaryl P-chirogenic ligands, we have decided to prioritize the formation of axial chiral Senphos ligands.

Scheme 1.32. Tests of ligand **L1-2** and **L2** via hydroalkylation of 1,3-enyne.

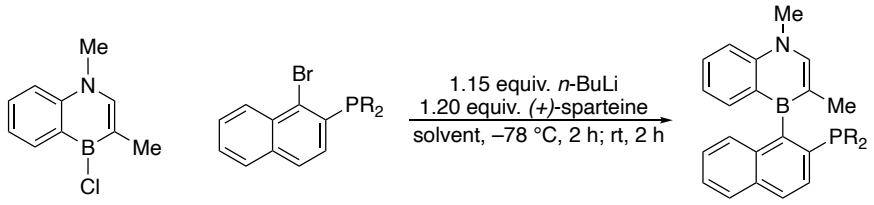


1.3 SYNTHESIS OF AXIAL CHIRAL SENPHOS LIGANDS

1.3.1 Solvent screening

The first trial we did to access the axial chirality of naphthyl Senphos ligand was to utilize *(+)*-sparteine as a chiral ligand in the ligand formation. The Pd-catalyzed C-P coupling affords dicyclohexyl phosphine **1.35a**,[23,51] and the standard conditions in the presence of *(+)*-sparteine gave the ligand **L3** with 17% *ee*. Later, the solvent effect on enantioselectivity was examined. 1,4-Dioxane, THF and toluene were used as the solvent in ligand formation (Table 1.2). The use of 1,4-dioxane did not yield the desired product. THF provided slightly higher yield, but lower enantiomeric excess (*ee*) compared to diethyl ether (Et_2O), which is the standard condition. Toluene as a solvent resulted in the formation of ligand **L3** with a low yield and *ee*.

Table 1.2. Solvent screening for axial chiral Senphos ligand formation.



1.30 1.1 equiv. | **1.35a** R = Cy, **1.35b** R = Ph | **L3** R = Cy, **L4** R = Ph

Entry	solvent	Yield of ligand (%)	*ee* of ligand (%)
1	Et_2O[a]	33	17
2	1,4-Dioxane[a]	N/A	N/A
3	THF[a]	36	11
4	Toluene[a]	10	4
5	THF[b]	66	21[c]

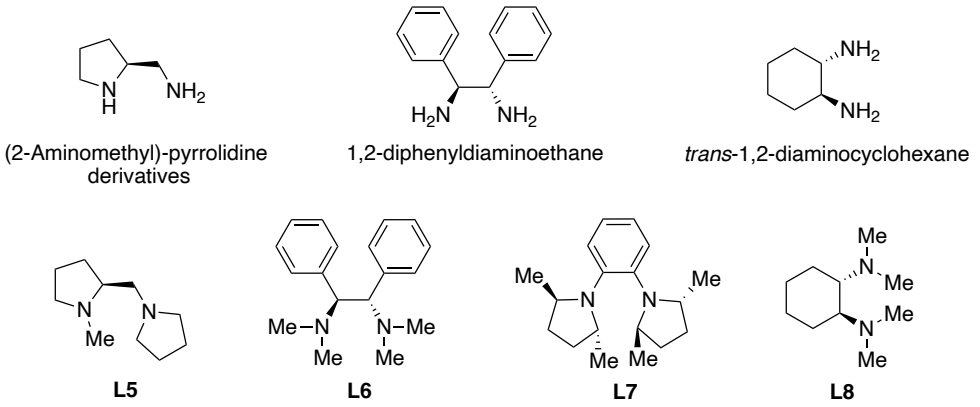
[a] Reaction conducted with phosphine **1.35a**; [b] Reaction conducted with phosphine **1.35b**; [c] *ee* was determined with borane protected ligands.

Due to the availability issue of dicyclohexyl phosphine, the starting material for ligand precursor **1.35a**, we had to switch our target ligand to **L4** with a diphenyl phosphine group. The Senphos ligand **L4** is more stable in air and moisture than **L3**, which avoids work-up in glovebox and simplifies the workflow.

1.3.2 Diamine ligands screening

To compare the ligand formation of **L3** and **L4**, **L4** in the presence of *(+)*-sparteine and THF (the ligand precursor **1.35b** is insoluble in Et_2O), resulted in 66% of yield and 21% of *ee* (Table 1.2 entry 5). This yield and *ee* were superior to those obtained for **L3** under the same conditions.

Scheme 1.33. Core structures of diamines.



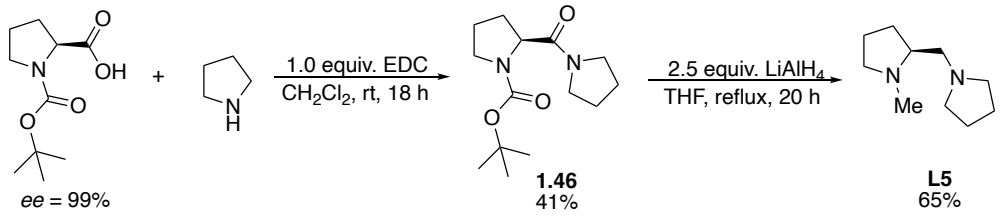
Given that *(+)*-sparteine exhibited some enantioselectivity in ligand formation, other chiral diamine ligands merit exploration. (2-Aminomethyl)-pyrrolidine derivatives, 1,2-diphenyldiaminoethane and *trans*-1,2-diaminocyclohexane are the most well-known core structures of diamines (Scheme 1.33).[59] However, due to the Lewis acidic and oxygen sensitive property of 1,4-azaborine **1.30**, the selection of diamine ligands is limited, necessitating avoidance

(59) Kizirian, J.–C. *Chem. Rev.* **2008**, *108,* 140-205.

of primary and secondary amines as well as amines containing carbonyl groups. Thus, ligands **L5**, **L6**, **L7** and **L8** were selected to evaluate their efficacy in synthesis of axial chiral Senphos ligands.

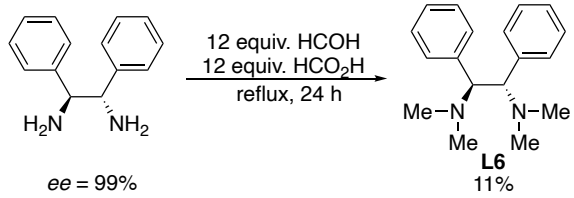
Boc-protected proline is a starting material to make diamine **L5**. (Scheme 1.34). The hydroxyl group is substituted by pyrrolidine to afford the amide **1.46**, then the Boc and carbonyl groups are reduced by $LiAlH_4$.[60]

Scheme 1.34. Synthesis of diamines **L5**.



Methylation of 1,2-diphenylethylenediamine with formaldehyde and formic acid under heating conditions leads to diamine **L6** (Scheme 1.35).[61]

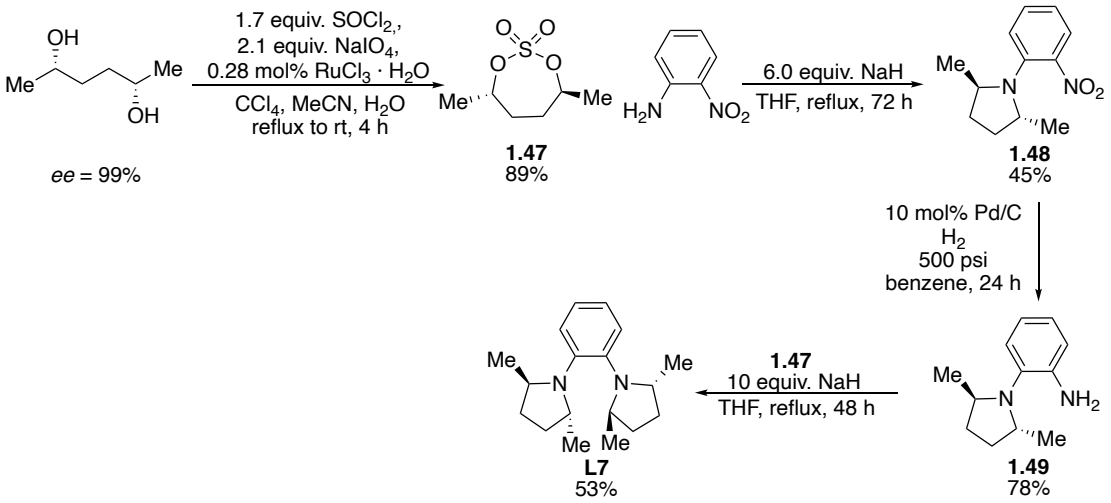
Scheme 1.35. Synthesis of diamines **L6**.



An intramolecular cyclization of hexanediol followed by oxidation to give cyclic sulfate **1.47** (Scheme 1.33).[62] Nucleophilic substitution between **1.47** and 2-nitroaniline in the presence of NaH affords **1.48**, which is reduced by Pd/C catalyzed hydrogenation to give amine **1.49**. Finally, another substitution with cyclic sulfate **1.47** furnishes diamine **L7**.[63]

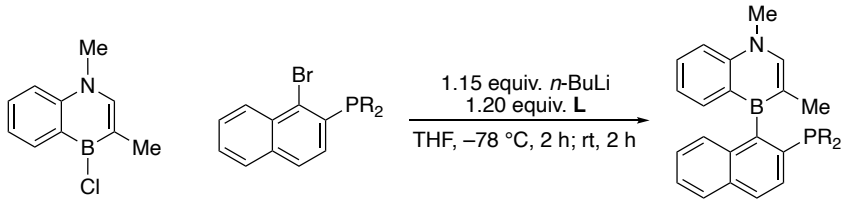
(60) Pérez-Botella, E.; Martínez-Franco, R.; González-Camuñas, N.; Cantín, Á.; Palomino, M.; Moliner, M.; Valencia, S.; Rey, F. *Front Chem.* **2020**, *8*, 588712.
(61) Shang, M.; Wang, X.; Koo, S. M.; Youn, J.; Chan, J. Z.; Yao, W.; Hastings B. T.; Wasa, M. *J. Am. Chem. Soc.* **2017**, *139*, 1, 95–98.
(62) Zhang, A., Rajanbabu, T. V. *Org. Lett.* **2004**, *6*, 9, 1515–1517.
(63) Illesinghe, J.; Ebeling, R.; Ferguson, B.; Patel, J.; Campi, E. M.; Jackson, W. R.; Robinson, A. J. *Aust. J. Chem.* **2004**, *57*, 167–176.

Scheme 1.36. Synthesis of diamines **L7**.



After successfully synthesizing the diamine ligands, we evaluated their efficacy in forming axial chiral Senphos ligands. **L5** yielded the desired ligand in 37% yield but with only 3% *ee* (Table 1.3, entry 1). **L6** provided ligands with a decent yield and 43% *ee* (Table 1.3, entry 2). **L7** resultes in a 48% yield and 13% *ee* (Table 1.3, entry 3). The commercially available diamine **L8** produce the Senphos ligand with 43% yield and 16% of *ee* (Table 1.3, entry 4).

Table 1.3. Diamine ligands screening for axial chiral Senphos ligand formation.



Entry	Ligand	Yield of ligand (%)	*ee* of ligand (%)
1	**L5**[a]	37	3[c]
2	**L6**[a]	56	43[c]
3	**L7**[a]	48	13[c]
4	**L8**[b]	43	16

[a] Reaction conducted with phosphine **1.35b**; [b] Reaction conducted with phosphine **1.35a**; [c] *ee* was determined with borane protected ligands.

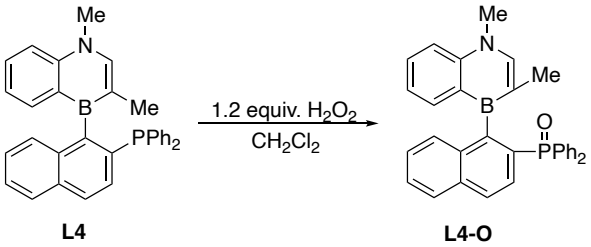
In summary, we tested diamine ligands containing common core structures in axial chiral Senphos ligand synthesis, but none of them yielded satisfactory results. Further optimization with regard to the N-substituents might lead to improvement.

1.3.3 Preparative recycling HPLC separation

Since the two diastereomers of the P-chirogenic Senphos ligand (**L1-1** and **L1-2**) were successfully separated via preparative recycling HPLC, we hypothesize that a similar approach could be applied to achieve Senphos ligands with axial chirality.

However, after screening HPLC conditions, neither **L3** (PR_2 where R = Cy) nor **L4** (PR_2 where R = Ph) show a good separation. Consequently, we explored the addition of protecting groups to the ligand to facilitate the separation process. Initially, we tried to oxidize the ligand with H_2O_2 (Scheme 1.37),[64] resulting in a phosphine oxide ligand **L4-O**. **L4-O** gives a better HPLC separation (t_r = 47 min and 50 min; for HPLC trace, see Experimental), however, the difference in retention times remained too small to allow for effective separation.

Scheme 1.37. Oxidation of **L4**.



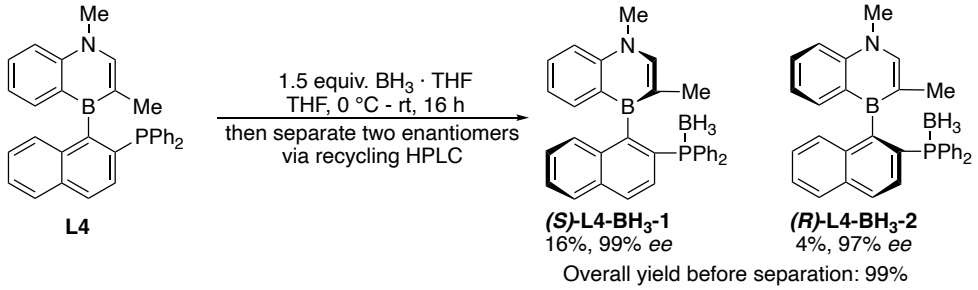
L4 **L4-O**

Moreover, ligand **L4** was protected with a borane group with borane · THF complex. This protection ligand that was amenable to separation via recycling HPLC, with retention times of 19 minutes and 30 minutes respectively (for HPLC trace, see

(64) Kostas, I. D.; Antonopoulou, G.; Ioannou, P.–C.; Ferentinos, E.; Kyritsis, P. *Results in Chemistry* **2022**, *4*, 100525.

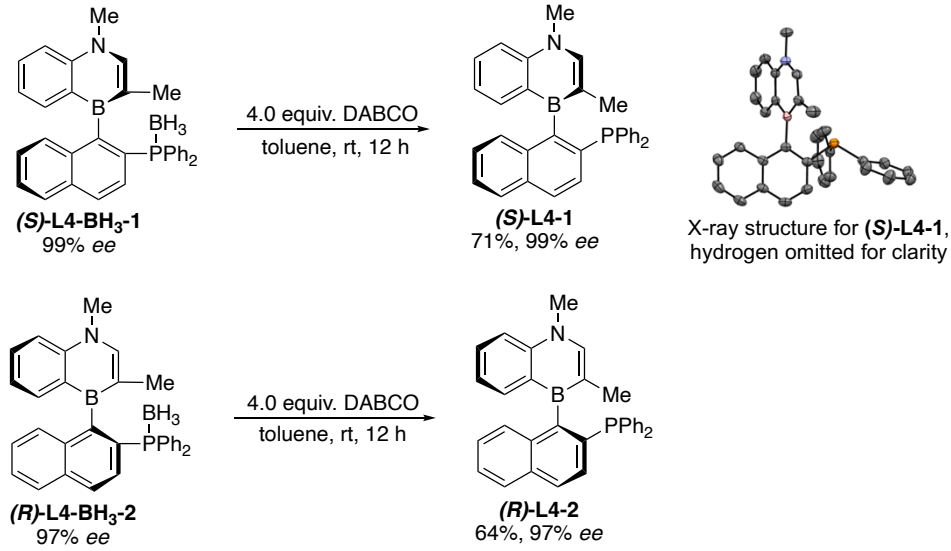
Experimental). Consequently, we successfully isolated the two enantiomers **(*S*)-L4-BH$_3$-1** and **(*R*)-L4-BH$_3$-2** (Scheme 1.38).

Scheme 1.38. Borane protection of **L4**.



Subsequently, the borane protecting group was removed by DABCO (Scheme 1.39). Notably, the borane deprotection reaction was successfully conducted at room temperature, therefore minimizing the risk of racemization. Both enantiomers **(*S*)-L4-BH$_3$-1** and **(*R*)-L4-BH$_3$-2** exhibit remarkable deprotection yields, with the enantiomeric excess (*ee*) remaining unaffected. In addition, the absolute configuration of one of the enantiomers, **(*S*)-L4-1**, was determined through single crystal X-ray crystallography analysis.

Scheme 1.39. Borane deprotection of **L4**.



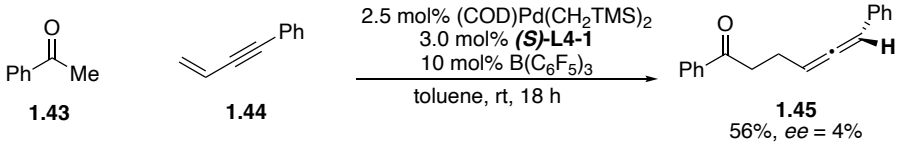
1.3.4 Benchmark reactions

To evaluate the catalytic efficiency and enantioselectivity of the obtained enantiopure axial chiral Senphos ligands, we performed three benchmark reactions. The first one is the hydroalkylation, the ligand ***(S)*-L4-1** is compatible with standard conditions, affords the desired allene in 56% yield, but only with 4% *ee* (Scheme 1.40a). The second benchmark reaction is the Pd-catalyzed allylic substitution, which is the most commonly applied chiral ligand benchmark reaction.[65] The reaction between allylic acetate **1.50** and diethyl malonate gives product **1.51** in 82% yield and 71% *ee* (Scheme 1.40b). This result supports the potential of axially chiral Senphos ligands in facilitating enantioselective reactions. The last benchmark reaction is the Ru-catalyzed nucleophilic addition of naphthyl aldehyde **1.52** by phenylboronic acid, a reaction previously reported by Li et al. as a benchmark reaction to test their new ligand.[65a] The reaction produces desired alcohol **1.53** in 28% yield and 20% *ee* when using ligand ***(S)*-L4-1** (Scheme 1.40c).

(65) (a) Wang, P.; Wu, H.; Zhang, X.–P.; Huang, G.; Crabtree, R. H.; Li, X. *J. Am. Chem. Soc.* **2023**, *145*, 8417−8429. (b) Pàmies, O.; Margalef, J.; Cañellas, S.; James, J.; Judge, E.; Guiry, P. J.; Moberg, C.; Bäckvall, J.–E.; Pfaltz, A.; Pericàs, M. A.; Diéguez, M. *Chem. Rev.* **2021**, *121,* 4373−4505.

Scheme 1.40. Benchmark reactions with ligand ***(S)*-L4-1**.

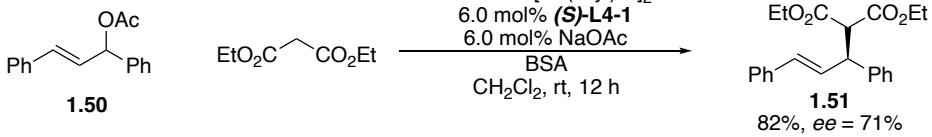
(a) Hydroalkylation



1.43 **1.44** **1.45**

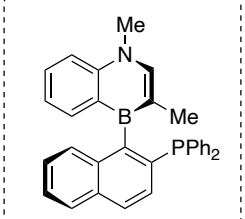
56%, *ee* = 4%

(b) Allylic substitution



1.50 **1.51**

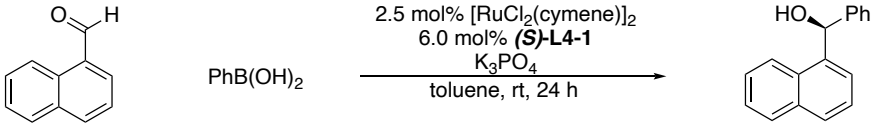
82%, *ee* = 71%



***(S)*-L4-1**

ee = 99%

(c) Ru-catalyzed nucleophilic substituton



1.52 **1.53**

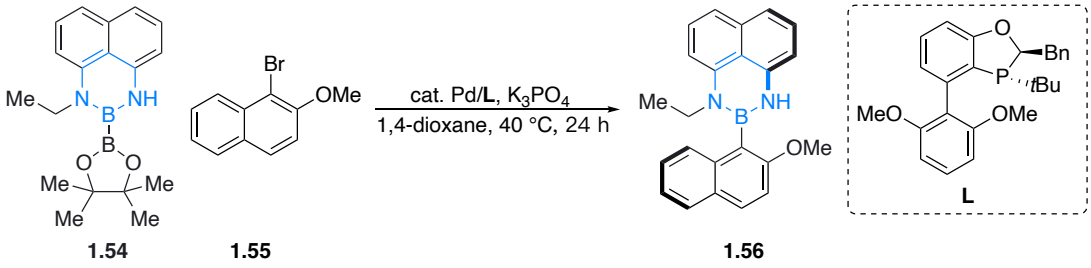
28%, *ee* = 20%

1.4 SUMMARY AND FUTURE DIRECTIONS

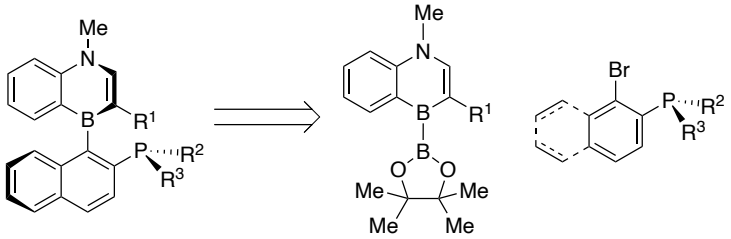
In summary, we made two P-chirogenic Shenphos ligand **L1-2** and **L2**, and two axial chiral Shenphos ligand ***(S)*-L4-1** and ***(R)*-L4-2**, and the results from benchmark reaction supports that the axial chiral Shenphos ligands could be applied in enantioselective reactions.

However, one of the disadvantages to make the axial chiral Shenphos ligands is the preparative recycling HPLC separation, which requires long time to proceed and high waste of sample. In 2021, Song *et al.* reported an atroposelective Miyaura borylation to form axial biaryl compound **1.56** from diazaborine **1.54** and biaryl bromide **1.55**, via utilization of chiral ligand (Scheme 1.41).[66] The substrates used in Song's Miyaura borylation are similar to the materials for Senphos formation, therefore this borylation represents a potential new strategy to make Senphos ligand with axial or even central chirality.

Scheme 1.41. Atroposelective Miyaura borylation (Song 2021).



Scheme 1.42. New strategy of Senphos ligands formation.



(66) Yang, K.; Mao, Y.; Xu, J.; Wang, H.; He, Y.; Li, W.; Song, Q. *J. Am. Chem. Soc.* **2021**, *143,* 10048−10053.

1.5 EXPERIMENTAL

General Information

All oxygen- and moisture-sensitive manipulations were carried out under an inert atmosphere using either standard Schlenk techniques or a glove box. Unless otherwise noted, all reagents were obtained from commercial sources and used as received. Bulk volumes of diethyl ether, dichloromethane, pentane, toluene and tetrahydrofuran were passed through an alumina column and dispensed from a solvent purification system under argon.

(COD)Pd($CH_2TMS)_2$ was prepared as previously reported[67] and stored under inert atmosphere at –35 °C. Tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) was purchased from Strem and stored under inert atmosphere at –35 °C.

^1H, ^{13}C, ^{11}B and ^{31}P NMR spectra were measured on Varian 400, 500 or 600 MHz spectrometers at the Boston College nuclear magnetic resonance facility. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constant (Hz). ^1H and ^{13}C spectra were internally referenced to residual solvent peaks (^1H $CDCl_3$: δ = 7.26 ppm, ^{13}C $CDCl_3$: δ = 77.16 ppm); ^{11}B spectra were externally referenced to $BF_3 \cdot Et_2O$ (δ = 0.0 ppm), ^{31}P spectra were externally referenced to 0.1 M H_3PO_4 (δ = 0.0 ppm).

$CDCl_3$ was purchased from Cambridge Isotope, distilled under N_2 and stored over activated 4 Å molecular sieves prior to use. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific) in air unless otherwise noted.

All IR spectra were measured on a Bruker Alpha-P FT-IR equipped with a single crystal diamond ATR module, and values are reported in cm^{-1}. High-resolution

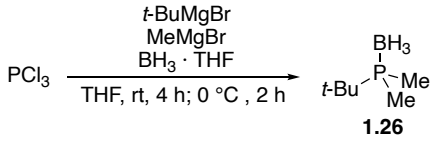
(67) Lee, H. G.; Milner, P. J.; Buchwald, S. L. *Org. Lett.* **2013**, *15*, 5602-5605.

mass spectrometry (HRMS) data were generated in Boston College facilities using direct analysis in real-time (DART) on a JEOL AccuTOF DART spectrometer.

Single-crystal X-ray diffraction data were generated in Boston College facilities from measurements with a Bruker Kappa Apex Duo fully automated diffractometer.

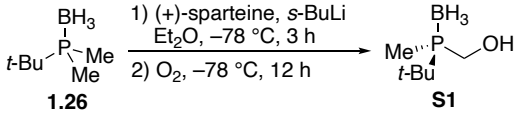
Synthesis of ligand precursors

Compound **1.34b** was prepared according to previously reported procedures.[29]



1.26

Compound **1.26** was prepared according to literature procedure.[68] To a stirred solution of phosphorus trichloride (6.52 mL, 74.6 mmol, 1.00 equiv.) and THF (100 mL) was added *t*-butylmagnesium chloride (41 mL of 2.0 M THF solution, 82 mmol, 1.1 equiv.) in dropwise at –78 °C. The resulting mixture was allowed to warm to room temperature then stir for 1 hour. The mixture was allowed to cool to 0 °C and methylmagnesium chloride (59.7 mL of 3.0 M THF solution, 179 mmol, 2.20 equiv.) was added dropwise. The mixture was allowed to stir for 1 hour at room temperature. The mixture was allowed to cool to 0 °C and BH_3·THF complex (112 mL of 1.00 M THF solution, 112 mmol, 1.50 equiv.) was added. The resulting mixture was then allowed to stir at 0 °C for 1 hour. At the conclusion of the reaction, the mixture was slowly added to vigorously stirred iced water (100 mL) containing conc. HCI (20 mL), and the mixture was extracted with EtOAc (3 x 100 mL). The combined organic phase was washed with brine (100 mL), dried over Na_2SO_4 and then concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (10% EtOAc/hexanes) to afford the desired product as white solid (5.02 g, 38.1 mmol, 51% yield). Spectral data match those previously reported.[68]

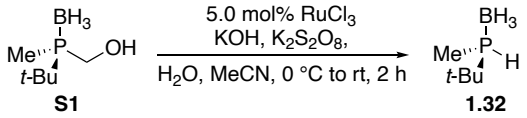


1.26 **S1**

Compound **S1** was prepared according to literature procedure.[52a] To a stirred solution

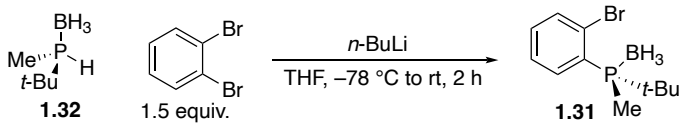
(68) Imamoto, T.; Watanabe, J.; Wada, Y.; Masuda, H.; Yamada, H.; Tsuruta, H.; Matsukawa, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **1998**, *120*, 1635-1636.

of *(+)*-sparteine (9.38 g, 40.0 mmol, 1.2 equiv.) in Et_2O (90 mL) was added *s*-BuLi (26.2 mL of a 1.4 M solution in cyclohexane, 36.7 mmol, 1.1 equiv.) dropwise at –78 °C. The reaction mixture was allowed to stir at that temperature for 15 minutes, then a solution of phosphine-borane complex **1.21** (4.41 g, 33.4 mmol, 1.00 equiv.) in Et_2O (10 mL) was added dropwise over 10 minutes. The resulting mixture was allowed to stir at –78 °C for 3 hours. Oxygen gas was blown through the solution with vigorous stirring at –78 °C for 1 hour. At the conclusion of the reaction, 1 M HCl (50 mL) and EtOAc (50 mL) was added, layers were separated and the aqueous layer was extracted with EtOAc (100 mL x 3). The combined organic phase was washed with 1 M HCl (aq) (100 mL), water (100 mL) and brine (100 mL), dried over Na_2SO_4 and then concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (30% EtOAc/hexanes) to afford the desired product as white solid (3.51 g, 23.6 mmol, 71% yield). Spectral data match those previously reported.[52a]

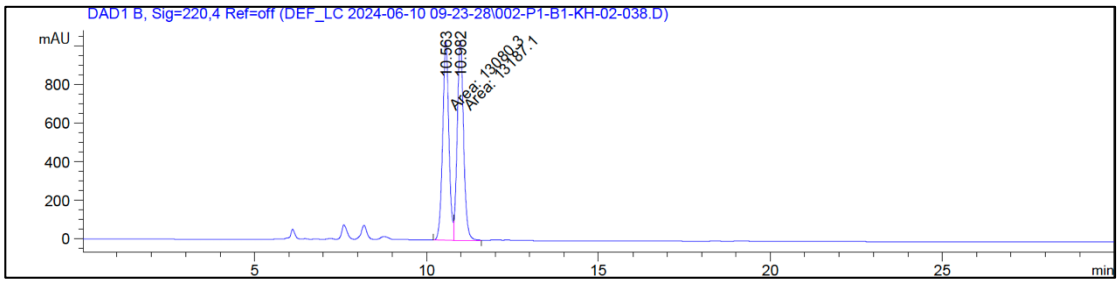


Compound **1.32** was prepared according to literature procedure.[52a] To a stirred solution of solution of potassium hydroxide (13.25 g, 236 mmol, 10.0 equiv.) and potassium persulfate (19.2 g, 70.9 mmol, 3.00 equiv.) in water (140 mL) was added ruthenium trichloride trihydrate (252 mg, 2.57 mmol, 10.0 mol%) at 0 °C. The reaction mixture was allowed to stir for 15 minutes, then a solution of phosphine-borane complex **S1** (3.51 g, 23.6 mmol, 1.00 equiv.) in acetonitrile (80.0 mL) was added dropwise. The mixture was allowed to stir at room temperature for two hours. At the conclusion of the reaction, the reaction was quenched with 1 M HCl (50 mL). The resulting mixture was extracted with diethyl ether (50 mL x 3). The combined organic phase was passed through a Celite pad to remove any residual ruthenium, washed with brine (50 mL),

dried over Na_2SO_4, and then concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (5% Et_2O/pentane) to give product as colorless solid (2.23 g, 10.8 mol, 80% yield). Spectral data match those previously reported.[52a]



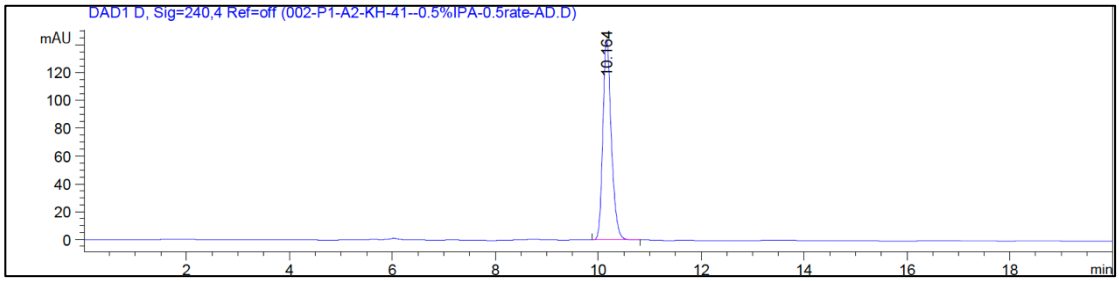
Compound **1.31** was prepared according to literature procedure.[55] To a stirred solution of phosphine-borane complex **1.32** (1.61 g, 13.6 mmol, 1.00 equiv.) in THF (18 mL) was added *n*-BuLi (6.0 mL of 2.5 M hexane solution, 15 mmol, 1.1 equiv.) dropwise at –78 °C. To the resulting solution was added a solution of 1,2-dibromobenzene (4.80 g, 20.4 mmol, 1.50 equiv.) in THF (7 mL) during 15 minutes. The bath temperature was gradually elevated to 0 °C during 2 hours. At the conclusion of the reaction, the reaction was quenched with water (30 mL), and the resulting mixture was extracted with EtOAc (30 mL x 3). The combined organic phase was washed with brine (30 mL), dried over Na_2SO_4 and then concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (2% Et_2O/hexanes) and recrystallization from pantane/Et_2O to afford the desired product as white solid (2.38 g, 38.1 mmol, 64% yield, *ee* = 99%). Spectral data match those previously reported.[55] **Chiral HPLC**: 99% *ee*. AD-H (IPA/hexane = 0.5/99.5, 0.5 mL/min, 220 nm): t_r (major) = 10.5 min, t_r (minor) = 10.9 min (The racemic product was obtained without *(+)*-sparteine).



Signal 2: DAD1 B, Sig=220,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.563	MF	0.2103	1.30803e4	1036.51208	49.7967
2	10.982	FM	0.2119	1.31871e4	1037.27795	50.2033

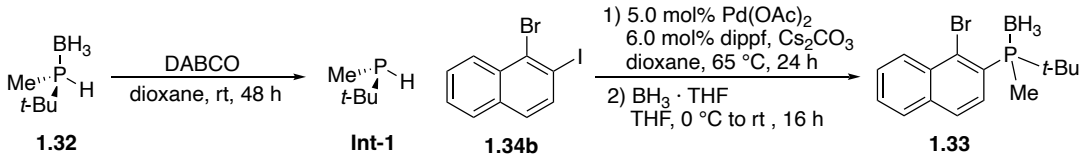
Totals : 2.62675e4 2073.79004



Signal 4: DAD1 D, Sig=240,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.164	BB	0.1738	1648.48267	143.77501	100.0000

Totals : 1648.48267 143.77501



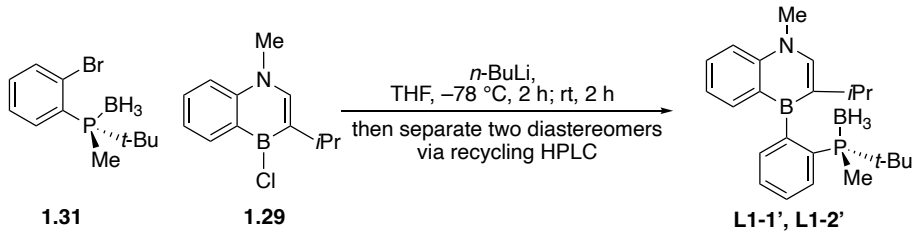
To a 20 mL pressure vessel was charged with a stir bar was added Cs_2CO_3 (1.8 g, 5.5 mmol, 1.2 equiv.), $Pd(OAc)_2$ (52 mg, 0.23 mmol, 5.0 mol%), and dippf ligand (116 mg, 0.277 mmol, 6.0 mol%) and dioxane (15 mL). The mixture was allowed to stir for 10 minutes, then aryl iodide **1.34b** (1.53 g, 4.61 mmol, 1.0 equiv.) and phosphine-borane complex **1.32** (480 mg, 4.61 mmol, 1.0 equiv.) was added. The vial was sealed and heated to 65 °C for 24 hours. The mixture was then allowed to cool to 0 °C, BH_3·THF complex (23 mL of 1.0 M solution in THF, 1.0 mmol, 5 equiv.) was added, then the reaction mixture was allowed to stir for 16 h. At the conclusion of the reaction, the mixture was filtered through a glass frit eluting with CH_2Cl_2. The resulting solution was concentrated under reduced pressure, and the crude materials was purified by silica gel column chromatography (20% CH_2Cl_2 in hexanes) to afford the product as

yellow solid (905 mg, 2.80 mmol, 60% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.47 (ddd, *J* = 7.9, 1.8, 0.7 Hz, 1H), 8.05 (dd, *J* = 11.3, 8.6 Hz, 1H), 7.88 – 7.84 (m, 2H), 7.68 – 7.61 (m, 2H), 2.02 (d, *J* = 9.8 Hz, 3H), 1.25 (d, *J* = 14.3 Hz, 9H), 1.22 – 0.54 (m, 3H) ppm. **^{13}C-NMR** (126 MHz, $CDCl_3$) δ132.7, 132.6, 128.4, 128.2, 128.0 (d, *J* = 3.6 Hz), 127.1 (d, *J* = 11.4 Hz), 31.7 (d, *J* = 31.4 Hz), 26.0 (d, *J* = 2.9 Hz), 10.0 (d, *J* = 37.3 Hz) ppm. **^{31}P-NMR** (202 MHz, $CDCl_3$) δ 39.9 (d, *J* = 92.4 Hz) ppm. **^{11}B-NMR** (160 MHz, $CDCl_3$) δ -36.2 (d, *J* = 79.9 Hz), -37.0 ppm. **FTIR** (thin film) 3199, 2974, 2959, 2368, 2340, 1711, 1546, 1495, 1413, 1395, 1364, 1295, 1190, 1145, 1066, 1017, 959, 888, 865, 811, 771, 746, 713, 666, 644, 620, 533 cm^{-1}. **HRMS** (DART) m/z: $[M\text{-}BH_2]^+$ calcd for $C_{15}H_{19}BrP$ 309.0402; found 309.0418.

Synthesis of ligands

Compound **1.29,**[22] **1.30,**[22] **1.35a,**[29] **1.35b**[22] were prepared according to previously reported procedures.



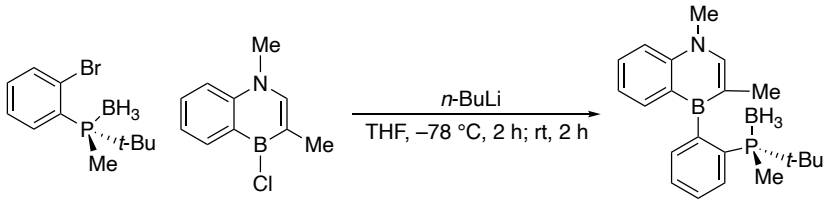
1.31 **1.29** **L1-1', L1-2'**

To a 20 mL round-bottom flask charged with phosphine-borane complex **1.31** (819 mg, 3.00 mmol, 1.10 equiv.) and Et_2O (60 mL) was added *n*-BuLi (1.2 mL, 2.5 M in hexanes, 0.30 mmol, 1.1 equiv.) dropwise at –78 °C. The resulting mixture was allowed to stir at –78 °C for 1 hour. 1,4-Azaborine **1.29** (599 mg, 2.73 mmol, 1.00 equiv.) in THF (5.0 mL) was then added. The resulting mixture was allowed to stir at −78 °C for 1 h and then at room temperature for 1 h. At the conclusion of the reaction, volatiles were removed under reduced pressure. The resulting crude residue was purified by silica gel column chromatography (hexanes/THF =10:1) to afford a mixture of ligand **L1-1'** and **L1-2'** as white powder (400 mg, 1.06 mmol, 38% yield). Ligand **L1-1'** and **L1-2'** were separated by recycling HPLC (IA column, IPA/ hexane = 1.5/ 98.5).

L1-1': ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.02 (ddd, *J* = 12.3, 6.3, 2.9 Hz, 1H), 7.80 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.40 (ddd, *J* = 4.7, 3.3, 1.7 Hz, 2H), 7.25 (t, *J* = 2.4 Hz, 1H), 7.17 (ddd, *J* = 7.8, 6.9, 1.0 Hz, 1H), 3.99 (s, 3H), 2.70 (p, *J* = 6.9 Hz, 1H), 1.21 (d, *J* = 7.0 Hz, 3H), 1.00 (dd, *J* = 11.8, 4.1 Hz, 12H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.68 (m, 3H) ppm. **^{13}C-NMR** (126 MHz, $CDCl_3$) δ 144.2, 143.3, 137.3, 135.0 (d, *J* = 18.1 Hz), 132.6 (d, *J* = 10.2 Hz), 131.2, 128.5, 125.8 (d, *J* = 12.4 Hz), 120.8, 114.6, 42.5, 30.0, 26.6, 26.2 (d, *J* = 2.5 Hz), 22.5, 7.8 (d, *J* = 36.5 Hz) ppm (signals for two carbons next to boron not observed). **^{31}P-NMR** (202 MHz, $CDCl_3$) δ 32.3 (d, J = 86.5 Hz) ppm. ^{11}B NMR (160 MHz, $CDCl_3$) δ 47.3, -38.4 (t, J = 85.0 Hz)

ppm. **FTIR** (thin film) 2954, 2927, 2372, 2358, 1584, 1492, 1384, 1373, 1267, 1222, 1082, 1067, 1020, 900, 885, 767, 755 cm^{-1}. **HRMS** (DART) m/z: $[M\text{-}BH_2]^+$ calcd for $C_{23}H_{32}NBP$ 364.2359; found 364.2362.

L1-2': ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.09 – 7.99 (m, 1H), 7.82 (s, 1H), 7.60 (ddd, *J* = 8.7, 6.9, 1.7 Hz, 1H), 7.51 (d, *J* = 8.6 Hz, 1H), 7.46 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.41 (dtd, *J* = 6.2, 3.7, 2.2 Hz, 2H), 7.30 (dt, *J* = 5.8, 2.9 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 3.99 (d, *J* = 1.5 Hz, 3H), 2.99 – 2.88 (m, 1H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.14 (d, *J* = 6.7 Hz, 3H), 1.07 (dd, *J* = 13.3, 1.6 Hz, 9H), 0.88 (d, *J* = 10.0 Hz, 3H), 0.67 (d, *J* = 83.9 Hz, 3H) ppm. **^{13}C-NMR** (126 MHz, $CDCl_3$) δ 146.0, 136.7, 135.3 (d, *J* = 17.3 Hz), 132.3 (d, *J* = 10.4 Hz), 131.0 128.6, 125.9, 125.7, 121.8, 114.4, 42.6, 29.9, 29.7, 27.8, 26.0 (d, *J* = 2.4 Hz), 23.5, 8.2 (d, *J* = 36.6 Hz) ppm (signals for two carbons next to boron not observed). **^{31}P-NMR** (202 MHz, $CDCl_3$) δ 32.0 ppm. **^{11}B-NMR** (160 MHz, $CDCl_3$) δ 46.3, -20.8 – -68.9 (m) ppm. **FTIR** (thin film) 2954, 2926, 2373, 1583, 1456, 1384, 1373, 1218, 1067, 900, 766, 756 cm^{-1}. **HRMS** (DART) m/z: $[M\text{-}BH_2]^+$ calcd for $C_{23}H_{32}NBP$ 364.2359; found 364.2347.

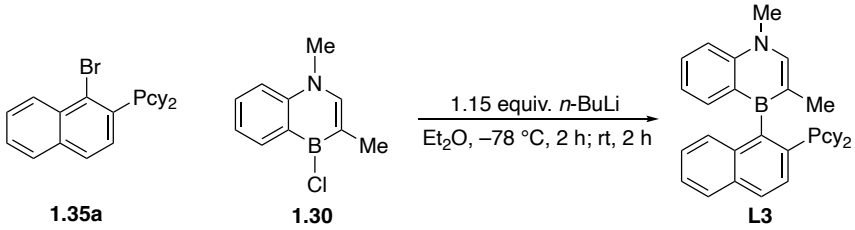


1.31 **1.30** **L2'**
d.r. = 67 : 33
determined by NMR

To a 20 mL round-bottom flask charged with phosphine-borane complex **1.31** (100 mg, 0.366 mmol, 1.10 equiv.) and Et_2O (6.0 mL) was added *n*-BuLi (0.15 mL, 2.5 M in hexanes, 0.37 mmol, 1.1 equiv.) dropwise at –78 °C. The resulting mixture was allowed to stir at –78 °C for 1 hour. 1,4-Azaborine **1.30** (64 mg, 0.33 mmol, 1.0 equiv.) in THF (3.0 mL) was then added. The resulting mixture was allowed to stir at −78 °C for 1 h and then at room temperature for 1 h. At the conclusion of the reaction, volatiles were

removed under reduced pressure. The resulting crude residue was purified by silica gel column chromatography (10% EtOAc in hexanes) to afford the product as white powder (21 mg, 60 μmol, 18% yield).

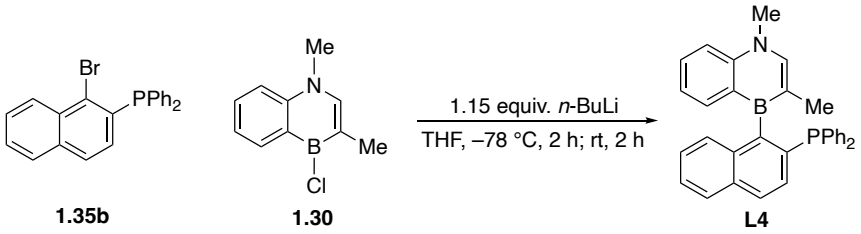
^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.04 – 7.98 (m, 1H), 7.82 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.69 – 7.62 (m, 2H), 7.56 (d, *J* = 8.7 Hz, 1H), 7.41 (tt, *J* = 6.9, 1.9 Hz, 2H), 7.21 – 7.15 (m, 2H), 3.96 (s, 4H), 2.18 (s, 3H), 1.90 (s, 3H), 1.02 (d, *J* = 13.4 Hz, 9H), 0.87 – 0.71 (m, 3H) ppm. **^{13}C-NMR** (126 MHz, $CDCl_3$) δ 147.9, 146.3, 137.1, 136.5, 135.2 (d, *J* = 17.2 Hz), 131.8 (d, *J* = 10.5 Hz), 130.9, 129.0 (d, *J* = 2.7 Hz), 125.8 (d, *J* = 12.2 Hz), 121.7, 120.9, 114.6, 114.4, 42.1, 26.0 (dd, *J* = 17.9, 2.5 Hz), 19.0, 8.1 (d, *J* = 36.7 Hz) ppm (signals for two carbons next to boron not observed). **^{31}P-NMR** (202 MHz, $CDCl_3$) δ 31.6 (d, *J* = 107.4 Hz) ppm. **^{11}B-NMR** (160 MHz, $CDCl_3$) δ 47.2, -38.8 ppm. **FTIR** (thin film) 2925, 2865, 2363, 1585, 1455, 1365, 1246, 1215, 1102, 1066, 941, 897, 884, 763, 748, 660, 631, 561 cm^{-1}. **HRMS** (DART) m/z: $[M-H]^-$ calcd for $C_{21}H_{29}NB_2P$ 348.2218; found 348.2209.



1.35a **1.30** **L3**

Compound **L3** was prepared according to literature procedure.[29] To a stirred solution of phosphine **1.35a** (79 mg, 0.20 mmol, 1.0 equiv.) and Et_2O (2.0 mL) was added *n*-BuLi (0.14 mL, 1.6 M in hexanes, 0.23 mmol, 1.15 equiv.) dropwise at −78 °C. The resulting mixture was allowed to stir at –78 °C for 1 hour. 1,4-Azaborine **1.30** (41 mg, 0.22 mmol, 1.1 equiv.) in Et_2O (2.0 mL) was then added. The resulting mixture was allowed to stir at −78 °C for 1 h and then at room temperature for 1 h. At the conclusion of the reaction, volatiles were removed under reduced pressure. The mixture was then passed through a plug of silica gel eluting with CH_2Cl_2. The resulting mixture was

concentrated under reduced pressure, and the oily residue was recrystallized from Et_2O/pentane to afford the product as colorless solid (42 mg, 88 μmol, 44% yield). Spectral data match those previously reported.[29]



1.35b **1.30** **L4**

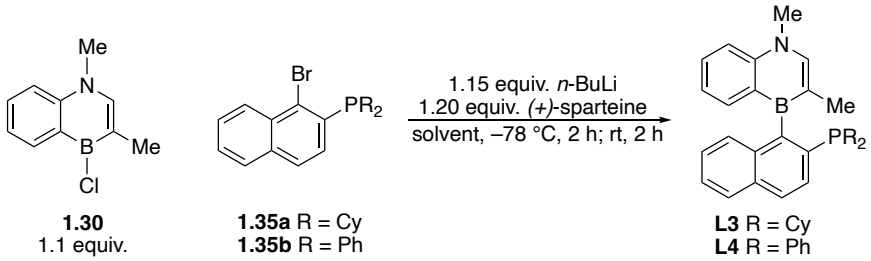
Compound **L4** was prepared according to literature procedure.[22] To a stirred solution of phosphine **1.35b** (400 mg, 1.02 mmol, 1.00 equiv.) and THF (10 mL) was added *n*-BuLi (0.45 mL, 2.5 M in hexanes, 1.12 mmol, 1.15 equiv.) dropwise at −78 °C. The resulting mixture was allowed to stir at –78 °C for 1 hour. 1,4-Azaborine **1.30** (200 mg, 1.10 mmol, 1.10 equiv.) in THF (2.0 mL) was then added. The resulting mixture was allowed to stir at −78 °C for 1 h and then at room temperature for 1 h. At the conclusion of the reaction, volatiles were removed under reduced pressure. The mixture was then passed through a plug of silica gel eluting with CH_2Cl_2. The resulting mixture was concentrated under reduced pressure, and the oily residue was recrystallized from THF/hexanes to afford the product as colorless solid (383 mg, 0.734 mmol, 71% yield). Spectral data match those previously reported.[22]

General procedure for solvent screening

To a stirred solution of *(+)*-sparteine (53 mg, 0.24 mmol, 1.5 equiv.) and solvent (2.0 mL) was added *n*-BuLi (110 μL, 1.60 M in hexanes, 170 μmol, 1.15 equiv.) dropwise at −78 °C. Then phosphine (60 mg, 0.15 mmol, 1.0 equiv.) was added. The resulting mixture was allowed to stir at –78 °C for 1 hour. 1,4-Azaborine **1.30** (432 mg, 0.16 mmol, 1.1 equiv.) in solvent (2.0 mL) was then added. The resulting mixture was allowed to stir at −78 °C for 1 h and then at room temperature for 1 h. At the conclusion

of the reaction, volatiles were removed under reduced pressure. The mixture was then passed through a plug of silica gel eluting with CH_2Cl_2. The resulting mixture was concentrated under reduced pressure, and the oily residue was recrystallized from Et_2O/pentane to afford the product as colorless solid.

Table S1. Solvent screening for axial chiral Senphos ligand formation.



1.30 1.1 equiv. | **1.35a** R = Cy, **1.35b** R = Ph | **L3** R = Cy, **L4** R = Ph

Entry	solvent	Yield of ligand (%)	*ee* of ligand (%)
1	Et_2O[a]	33	17
2	1,4-Dioxane[a]	N/A	N/A
3	THF[a]	36	11
4	Toluene[a]	10	4
5	THF [b]	66	21[c]

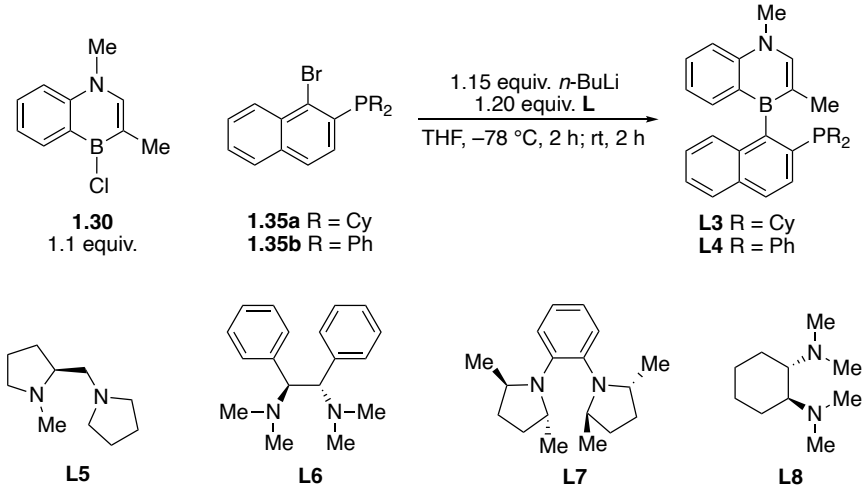
[a] Reaction conducted with phosphine **1.35a**; [b] Reaction conducted with phosphine **1.35b**; [c] *ee* was determined with borane protected ligands.

General procedure for diamine ligand screening

To a stirred solution of **L** (0.24 mmol, 1.5 equiv.) and THF (2.0 mL) was added *n*-BuLi (0.11 mL, 1.6 M in hexanes, 0.17 mmol, 1.15 equiv.) dropwise at −78 °C. Then phosphine (0.15 mmol, 1.0 equiv.) was added. The resulting mixture was allowed to stir at –78 °C for 1 hour. 1,4-Azaborine **1.30** (432 mg, 0.16 mmol, 1.1 equiv.) in THF (2.0 mL) was then added. The resulting mixture was allowed to stir at −78 °C for 1 h and then at room temperature for 1 h. At the conclusion of the reaction, volatiles were removed under reduced pressure. The mixture was then passed through a plug of silica gel eluting with CH_2Cl_2. The resulting mixture was concentrated under reduced pressure, and the oily residue was recrystallized from THF/hexanes to afford the

product as a colorless solid.

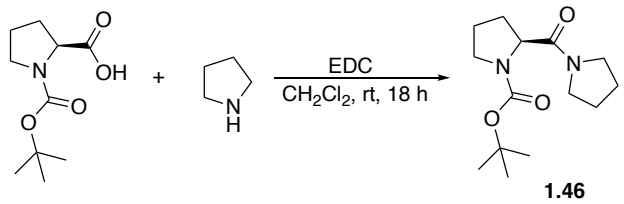
Table S2. Diamine ligands screening for axial chiral Senphos ligand formation.



Entry	Ligand	Yield of ligand (%)	*ee* of ligand (%)
1	**L5**[a]	37	3[c]
2	**L6**[a]	56	43[c]
3	**L7**[a]	48	13[c]
4	**L8**[b]	43	16

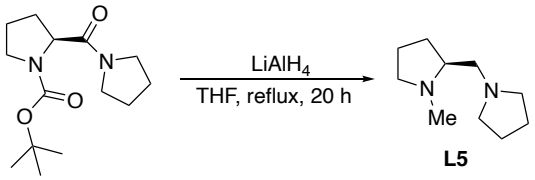
[a] Reaction conducted with phosphine **1.35b**; [b] Reaction conducted with phosphine **1.35a**; [c] *ee* was determined with borane protected ligands.

Synthesis of diamine ligands



1.46

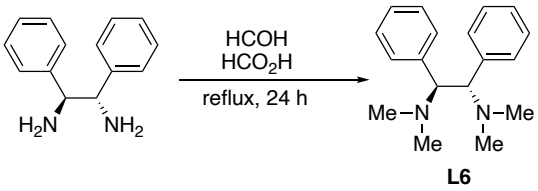
Compound **1.46** was prepared according to literature procedure.[60] To a solution of Boc-(L)-Proline (3.0 g, 14 mmol, 1.0 equiv.) in CH_2Cl_2 (15 mL) was added a solution of EDC (2.67 g, 13.9 mmol, 1.00 equiv.) in CH_2Cl_2 (5 mL) at 0º C. The resulting mixture was allowed to stir at 0 °C for 30 minutes. Then a solution of pyrrolidine (1.2 mL, 14 mmol, 1.0 equiv.) in CH_2Cl_2 (6 mL) was added dropwise at 0º C. The resulting mixture was allowed to stir at 0 °C for 15 minutes then warmed to room temperature for 16 hours. At the conclusion of the reaction, volatiles were removed under reduced pressure. The mixture was then passed through a plug of silica gel eluting with CH_2Cl_2. The resulting mixture was washed with 1M HCl (30 mL), saturated $NaHCO_3$ (30 mL) and brine (30 mL), dried over Na_2SO_4 and then concentrated under reduced pressure to afford the product as white solid (1.54 g, 5.57 mmol, 41% yield). Spectral data match those previously reported.[60]



1.46 **L5**

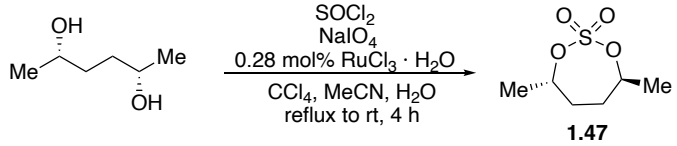
Ligand **L5** was prepared according to literature procedure.[60] To a solution of $LiAlH_4$ (502 mg, 13.2 mmol, 2.5 equiv.) in THF (6 mL) was added a solution of amide **1.46** in THF (6 mL) dropwise at 0º C. The resulting mixture was allowed to stir at room temperature for 30 minutes, then heated under reflux for 20 hours. At the conclusion of the reaction, the reaction mixture was cooled to 0º C and quenched with 1 M NaOH (6 mL). The resulting mixture was allowed to stir at room temperature for 30 minutes,

then passed through a plug of celite eluting with EtOAc. The resulting mixture was washed with brine (30 mL), dried over Na_2SO_4 and then concentrated under reduced pressure to afford the product as white solid (579 mg, 3.44 mmol, 65% yield). Spectral data match those previously reported.[60]



L6

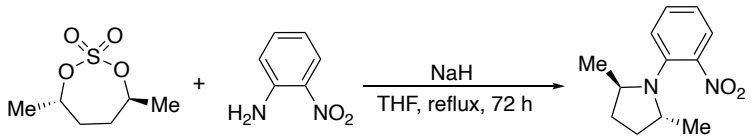
Ligand **L6** was prepared according to literature procedure.[61] To a solution of 1,2-diphenylethylenediamine (1.0 g, 4.7 mmol, 1.0 equiv.) in HCHO (37 % aq., 2.2 mL, 57 mmol, 12 equiv.) was added HCOOH (80 % aq., 4.3 mL, 57 mmol, 12 equiv.). The resulting mixture was allowed to stir under reflux for 16 hours. At the conclusion of the reaction, the reaction mixture was allowed to cool to 0 °C, then saturated Na_2CO_3 (aq.) (20 mL) was added dropwise. The resulting mixture was then diluted with water (10 mL), then extracted with CH_2Cl_2 (20 mL x 3). The combined organic phase was washed with brine (30 mL), dried over Na_2SO_4, and then concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (60% EtOAc in hexanes with 3% TEA) to afford product as white solid (128 mg, 0.477 mol, 11% yield). Spectral data match those previously reported.[61]



1.47

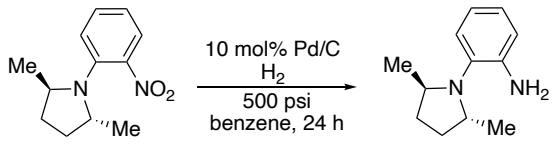
Compound **1.47** was prepared according to literature procedure.[62] To a solution of ()-*(S, S)*-hexanediol (2.0 g, 17 mmol, 1.0 equiv.) in CCl_4 (10 mL) was added thionyl chloride (2.03 mL, 27.9 mmol, 1.65 equiv.) dropwise. The resulting mixture was allowed to heat under reflux for 1.5 hour. The resulting mixture was allowed to cool to room temperature then concentrated under reduced pressure to afford a brown oil. The

oil was then dissolved in a mixture of CCl_4 (10 mL), MeCN (10 mL) and water (15 mL). $RuCl_3$ (11 mg, 47 μmol, 0.28 mol%) and $NaIO_4$ (7.6 g, 36 mmol, 2.1 equiv.) was added to the mixture at 0 °C. The reaction was allowed to stir at room temperature for 1 h. At the conclusion of the reaction, the reaction mixture was quenched with water, then extracted with Et_2O (30 mL x 3). The combined organic phase was washed with brine (30 mL), dried over Na_2SO_4, passed through a plug of silica gel eluting with Et_2O, then concentrated under reduced pressure to afford product as white solid (2.74 g, 15.2 mol, 89% yield). Spectral data match those previously reported.[62]



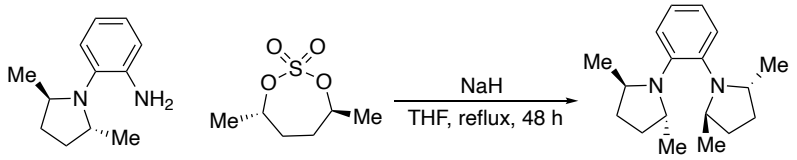
1.47 **1.48**

Compound **1.48** was prepared according to literature procedure.[63] To a solution of cyclic sulfate **1.47** (1.00 g, 5.55 mmol, 1.00 equiv.) in THF (200 mL) was added 2-nitroanaline (767 mg, 5.55 mmol, 1.00 equiv.). The resulting mixture was allowed to heat under reflux for 48 hours, then sodium hydride (1.33 g, 60% in mineral oil, 33.3 mmol, 6.00 equiv.) was added. The resulting mixture was allowed to heat under reflux for further 24 hours. At the conclusion of the reaction, the reaction mixture was quenched with NH_4Cl, then concentrated under reduced pressure. The resulting mixture was extracted with CH_2Cl_2 (50 mL x 3), the combined organic phase was washed with water (50 mL) and brine (50 mL), dried over Na_2SO_4, and then concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (10% EtOAc in hexanes) to afford product as orange solid (538 mg, 2.44 mol, 45% yield). Spectral data match those previously reported.[63]



1.48 **1.49**

Compound **1.49** was prepared according to literature procedure.[63] To a solution of nitrophenyl pyrrolidine **1.48** (538 mg, 2.44 mmol, 1.0 equiv.) in benzene (10 mL) was added Pd/C (259 mg, 244μmol, 10 mol%). The reaction mixture was allowed to pressurize with hydrogen gas to 500 psi and stir for 16 hours. At the conclusion of the reaction, mixture was then passed through a plug of Celite eluting with EtOAc. The resulting mixture was concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography (10% EtOAc in hexanes) to afford product as orange solid (365 mg, 1.92 mmol, 78% yield). Spectral data match those previously reported.[63]

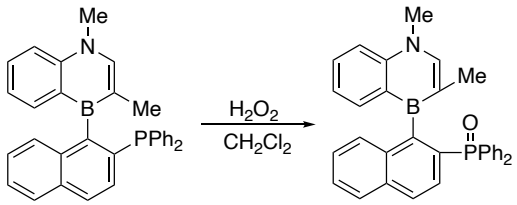


1.49 **1.47** **L7**

Ligand **L7** was prepared according to literature procedure.[63] To a solution of cyclic sulfate **1.47** (692 mg, 3.84 mmol, 2.00 equiv.) in THF (100 mL) was added amine **1.49** (365 mg, 1.92 mmol, 1.00 equiv.) and sodium hydride (768 mg, 60% in mineral oil, 19.2 mmol, 10.0 equiv.). The resulting mixture was allowed to heat under reflux for 48 hours. At the conclusion of the reaction, the mixture was quenched with NH_4Cl. then concentrated under reduced pressure. The resulting mixture was extracted with CH_2Cl_2 (50 mL x 3), the combined organic phase was washed with water (50 mL) and brine (50 mL), dried over Na_2SO_4, and then concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (10% EtOAc in hexanes) to

afford product as brown solid (279 mg, 1.02 mmol, 53% yield). Spectral data match those previously reported.[63]

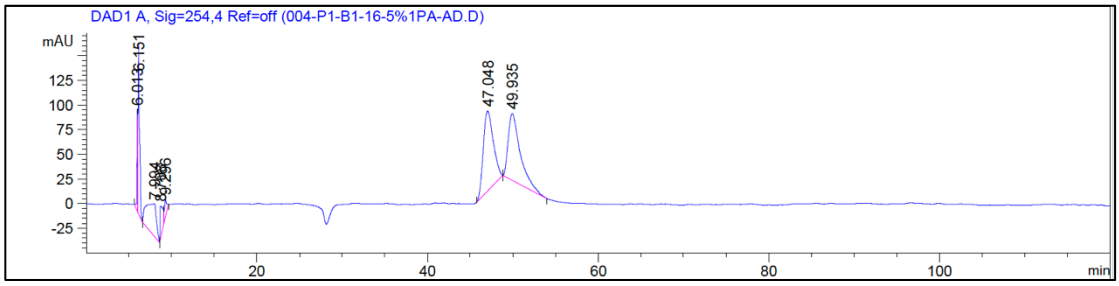
Protection of ligands



L4 **L4-O**

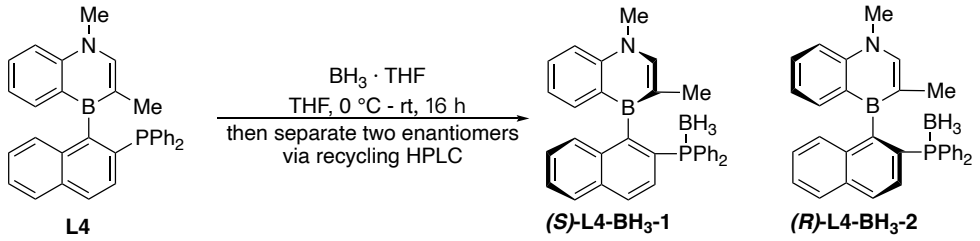
To a solution of **L4** (47 mg, 2.9 mmol, 1.0 equiv.) in CH_2Cl_2 (1 mL) was added H_2O_2 (30 % w/w, 0.10 mL, 0.12 mmol, 1.2 equiv.) dropwise. The reaction mixture was allowed to stir at room temperature for 1 hour. At the conclusion of the reaction, the mixture was quenched with aqueous $Na_2S_2O_3$. The resulting mixture was extracted with CH_2Cl_2 (10 mL x 3), the combined organic phase was washed with brine (10 mL), dried over Na_2SO_4, and then concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (50% EtOAc in hexanes) to afford product as white solid (25 mg, 52 μmol, 51% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 2H), 7.68 – 7.62 (m, 3H), 7.60 – 7.54 (m, 3H), 7.53 – 7.37 (m, 6H), 7.36 – 7.28 (m, 4H), 7.24 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.14 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.76 (ddd, *J* = 7.7, 6.9, 1.0 Hz, 1H), 3.78 (s, 3H), 1.74 (d, *J* = 1.1 Hz, 3H) ppm. **^{13}C-NMR** (126 MHz, $CDCl_3$) δ 142.5, 136.1, 132.5, 132.4, 132.3, 132.3, 131.9, 131.7, 130.4, 129.3, 128.5, 128.4, 128.3, 128.2, 128.1, 127.6, 127.0, 126.9, 126.1, 126.0, 126.0, 119.6, 113.3, 41.3, 19.5 ppm (signals for two carbons next to boron not observed). **^{31}P-NMR** (202 MHz, $CDCl_3$) δ 34.7 ppm. **^{11}B-NMR** (160 MHz, $CDCl_3$) δ 38.6 ppm. **FTIR** (thin film) 3052, 2920, 2849, 1587, 1456, 1435, 1368, 1212, 1182, 1118, 1098, 1046, 1022, 863, 809, 723, 692, 667, 646, 610, 537, 515 cm^{-1}. **HRMS** (DART) m/z: $[M+H]^+$ calcd for $C_{32}H_{28}NBPO$ 484.1996; found 484.1983. **Chiral HPLC**: racemic (for preparative recycling HPLC condition screening) AD-H (IPA/hexane = 5/95, 0.5 mL/min, 220 nm): t_r = 47.0 min and 49.9 min.



Signal 1: DAD1 A, Sig=254,4 Ref=off

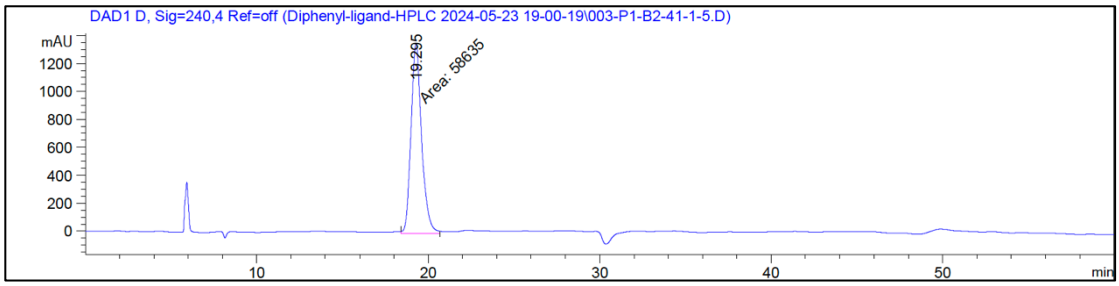
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.013	BV	0.0867	604.92676	102.66988	3.1031
2	6.151	VB	0.1604	2059.16772	173.53751	10.5631
3	7.994	BB	0.9611	2551.52612	32.88860	13.0888
4	8.708	BV	0.2712	703.03442	33.73021	3.6064
5	9.296	VB	0.2416	306.67209	17.74433	1.5732
6	47.048	BB	1.2354	6604.72168	80.99273	33.8808
7	49.935	BB	1.4227	6663.92139	67.68166	34.1845
Totals :				1.94940e4	509.24491	



To a solution of **L4** (155 mg, 0.332 mmol, 1.0 equiv.) and THF (1 mL) was added BH_3·THF complex (0.5 mL, 0.5 mmol, 1.5 equiv.) at 0 °C. The mixture was allowed to stir for 16 hours at room temperature. At the conclusion of the reaction, volatiles were removed under reduced pressure. The mixture was then passed through a plug of silica gel eluting with CH_2Cl_2. The resulting mixture was concentrated under reduced pressure to afford the product as white solid (160 mg, 0.331 mmol, 99% yield). Ligand **L4-BH$_3$-1** and **L4-BH$_3$-2** were separated by recycling HPLC (IA column, IPA / henane = 1/ 99 with 3% THF).

L4-BH$_3$-1: **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.86 (ddd, *J* = 8.6, 4.7, 1.7 Hz, 2H), 7.76 (dd, *J* = 11.0, 8.7 Hz, 1H), 7.51 (ddd, *J* = 8.6, 6.9, 1.7 Hz, 1H), 7.47 (ddd, *J* = 8.1, 6.7, 1.2 Hz, 1H), 7.44 – 7.32 (m, 7H), 7.30 – 7.23 (m, 3H), 7.18 (ddd, *J* = 8.3, 6.7, 1.3 Hz,

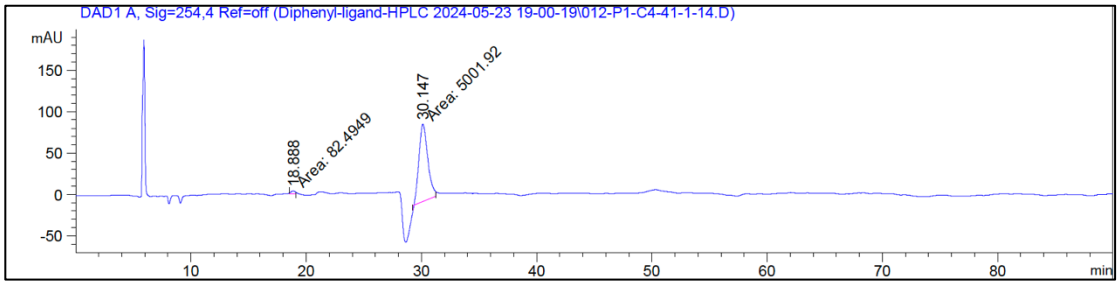
1H), 7.04 (td, J = 7.8, 2.3 Hz, 4H), 6.92 (ddd, J = 7.7, 6.8, 0.9 Hz, 1H), 3.80 (s, 3H), 1.78 (d, J = 0.9 Hz, 3H), 1.38 – 0.95 (m, 3H) ppm. **^{13}C-NMR** (126 MHz, $CDCl_3$) δ 145.0, 142.1, 136.6, 134.3, 134.2, 134.0, 133.9, 130.6, 130.3, 130.2 (d, J = 4.3 Hz), 130.0, 129.9, 128.2, 127.8 (d, J = 4.2 Hz), 127.8 (d, J = 3.9 Hz), 127.1, 126.8, 126.7, 125.6, 120.7, 114.0, 41.7, 19.3 ppm (signals for two carbons next to boron not observed). **^{31}P-NMR** (202 MHz, $CDCl_3$) δ 24.0 ppm. **^{11}B-NMR** (160 MHz, $CDCl_3$) δ 48.2, -35.9 ppm. **FTIR** (thin film) 2922, 2376, 2343, 1585, 1490, 1456, 1435, 1371, 1218, 1207, 1131, 1104, 1057, 1027, 903, 856, 811, 760, 735, 689, 676, 492, 447, 423 cm^{-1}. **HRMS** (DART) m/z: $[M-H]^-$ calcd for $C_{32}H_{29}NB_2P$ 480.2218; found 480.2225. **Chiral HPLC**: 99% *ee*. AD-H (IPA/hexane = 5/95, 0.5 mL/min, 220 nm): t_r (major) = 19.2 min, t_r (minor) = 30.7 min. $[\alpha]_D^{22}$ = +42.4 (c = 1.0, $CHCl_3$).



Signal 4: DAD1 D, Sig=240,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.295	MM	0.7173	5.86350e4	1362.38928	100.0000
Totals :				5.86350e4	1362.38928	

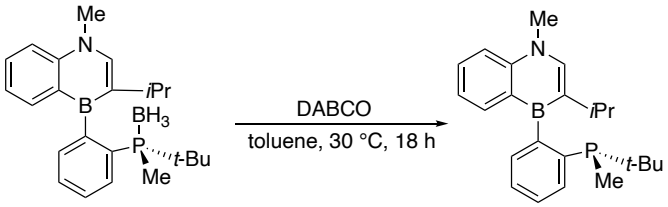
L4-BH_3-2: spectral data match with **L4-BH_3-1**. **Chiral HPLC**: 97% *ee*. AD-H (IPA/hexanes = 5/95, 0.5 mL/min, 220 nm): t_r (major) = 18.9 min, t_r (minor) = 30.1 min (*ee* was determined by re-adding BH_3 group to the ligand). $[\alpha]_D^{22}$ = -36.4 (c = 1.0, $CHCl_3$).



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.888	MM	0.4235	82.49490	3.24640	1.6225
2	30.147	MM	0.8935	5001.91895	93.29852	98.3775
Totals :				5084.41385	96.54492	

Deprotection of ligands

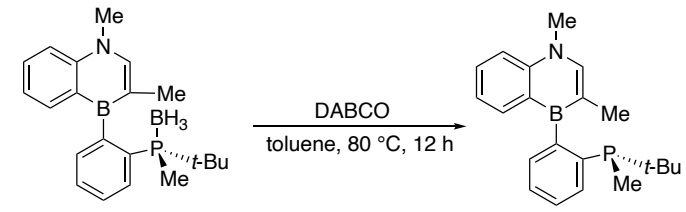


L1-2'
d.r. > 99 : 1

L1-2
d.r. = 94 : 6
determined by NMR

In the glovebox, to a 20 mL vial charged with the ligand **L1-2'** (25 mg, 66 mmol, 1.0 equiv.) added DABCO (49 mg, 0.44 mmol, 6.6 equiv.) and toluene (0.5 mL). The reaction mixture was transferred into a J-young tube and allowed to stir for 18 hours at 30 °C. At which point the crude ^{31}P and ^{11}B NMR showed full conversion to the free phosphine, the resulting mixture was concentrated under reduced pressure, and the crude mixture was purified by silica gel column chromatography (10% Et_2O in pentane) in glovebox to afford product as white solid (4.2 mg, 12 μmol, 18% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.69 – 7.57 (m, 3H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.38 – 7.27 (m, 3H), 7.11 (t, *J* = 7.4 Hz, 1H), 3.94 (s, 3H), 2.72 (p, *J* = 6.9 Hz, 1H), 1.28 (d, *J* = 4.0 Hz, 3H), 1.23 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 11.9 Hz, 9H) ppm. **^{13}C-NMR** (126 MHz, $CDCl_3$) δ 145.9, 143.5, 137.4, 131.6 (d, *J* = 16.2 Hz), 131.0, 130.4, 127.8, 125.7, 120.2, 114.1, 41.8, 30.0, 29.7, 29.5, 29.4, 27.5 (d, *J* = 13.8 Hz), 24.7, 19.4 (d, *J* = 8.8 Hz), 7.4 (d, *J* = 18.3 Hz) ppm (signals for two carbons next to boron not observed). **^{31}P-NMR** (202 MHz, $CDCl_3$) δ -17.5 ppm. **^{11}B-NMR** (160 MHz, $CDCl_3$) δ 46.6 ppm. **FTIR** (thin film) 2950, 2929, 2860, 1605, 1585, 1490, 1457, 1429, 1382, 1372, 1264, 1224, 765, 750 cm^{-1}. **HRMS** (DART) m/z: $[M+H]^+$ calcd for $C_{23}H_{32}NBP$ 364.2359; found 364.2354.

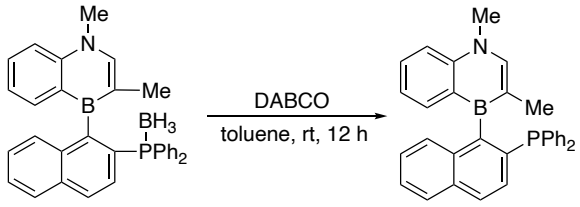


L2'
d.r. = 67 : 33
determined by NMR

L2
d.r. = 80 : 20
determined by NMR

In the glovebox, to a 20 mL vial charged with the ligand **L2'** (21 mg, 0.061 mmol, 1.0 equiv.) was added DABCO (34 mg, 0.30 mmol, 5.0 equiv.) and toluene (0.5 mL). The reaction mixture was transferred into a J-young tube and allowed to stir for 12 hours at 80 °C. At which point the crude ^{31}P and ^{11}B NMR showed full conversion to the free phosphine, the resulting mixture was concentrated under reduced pressure, and the crude mixture was purified by silica gel column chromatography (10% Et_2O in pentane) in glovebox to afford product as a white solid (4.3 mg, 13 μmol, 21% yield).

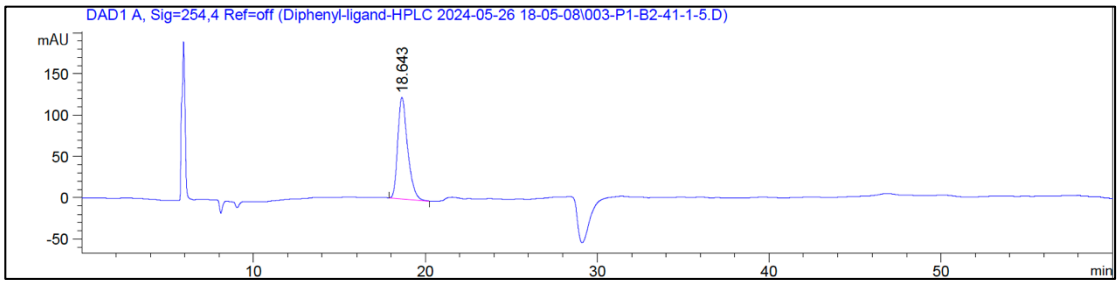
^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.65 – 7.57 (m, 3H), 7.51 – 7.47 (m, 1H), 7.38 – 7.33 (m, 2H), 7.24 (d, *J* = 5.5 Hz, 1H), 7.13 (t, *J* = 7.3 Hz, 1H), 3.90 (s, 3H), 1.96 (s, 3H), 1.34 (d, *J* = 3.9 Hz, 3H), 0.79 (d, *J* = 12.0 Hz, 9H) ppm. **^{13}C-NMR** (126 MHz, $CDCl_3$) δ 146.0, 143.6, 137.6, 131.8, 131.7, 131.1, 130.5, 127.9, 125.8, 120.3, 114.3, 41.9, 29.7, 27.6 (d, *J* = 13.8 Hz), 24.8, 19.6 (d, *J* = 8.8 Hz), 7.5 (d, *J* = 18.3 Hz) ppm (signals for two carbons next to boron not observed). **^{31}P-NMR** (202 MHz, $CDCl_3$) δ -15.9 ppm. **^{11}B-NMR** (160 MHz, $CDCl_3$) δ 47.0 ppm. **FTIR** (thin film) 2926, 2856, 1604, 1587, 1490, 1471, 1457, 1370, 1270, 1218, 1118, 1102, 1052, 890, 752 cm^{-1}. **HRMS** (DART) m/z: $[M+H]^+$ calcd for $C_{21}H_{28}NBP$ 336.2046; found 336.2042.



***(S)*-L4-BH_3-1** and ***(R)*-L4-BH_3-2**

***(S)*-L4-1** and ***(R)*-L4-2**

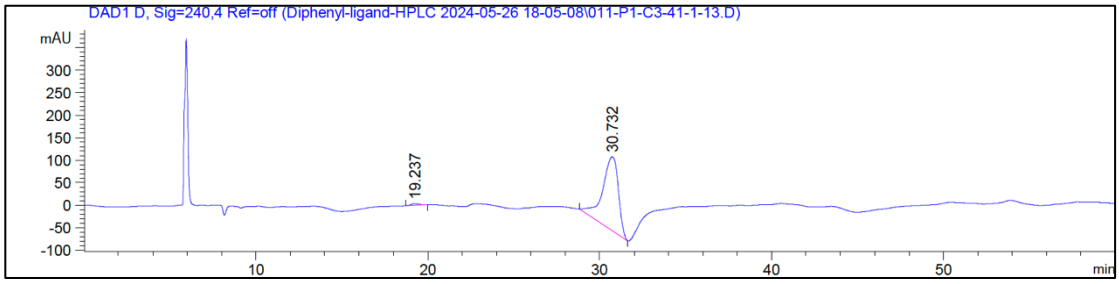
In the glovebox, to a 25 mL round-bottom-flask charged with the ligand ***(S)*-4-BH_3-1** (26 mg, 54 µmol, 1.0 equiv.) added DABCO (24 mg, 0.22 mmol, 4.0 equiv.) and toluene (2.0 mL). The reaction mixture was allowed to stir for 16 hours at room temperature. At the conclusion of the reaction, the resulting mixture was concentrated under reduced pressure, and the crude mixture was purified by silica gel column chromatography (30% CH_2Cl_2 in hexanes) to afford product as white solid (18 mg, 38 µmol, 71% yield). Spectral data match those previously reported. **Chiral HPLC**: 99% *ee*. AD-H (IPA/hexane = 5/95, 0.5 mL/min, 220 nm): t_r (major) = 18.6 min, t_r (minor) = 30.7 min (*ee* was determined by re-adding BH_3 group to the ligand). $[\alpha]_D^{22}$ = +39.2 (c = 1.0, $CHCl_3$).



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.643	BB	0.6038	4906.48047	122.89592	100.0000
Totals :				4906.48047	122.89592	

L4-BH_3-2: 30% CH_2Cl_2 in hexanes, white solid (4.4 mg, 9.4 µmol, 64% yield). Spectral data match those previously reported. **Chiral HPLC**: 97% *ee*. AD-H (IPA/hexanes = 5/95, 0.5 mL/min, 220 nm): t_r (major) = 30.7 min, t_r (minor) = 19.2 min (*ee* was determined by re-adding BH_3 group to the ligand). $[\alpha]_D^{22}$ = -36.1 (c = 1.0, $CHCl_3$).



Signal 4: DAD1 D, Sig=240,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.237	BB	0.4971	121.72308	3.55817	1.1608
2	30.732	BB	0.9696	1.03643e4	163.48090	98.8392
Totals :				1.04860e4	167.03907	

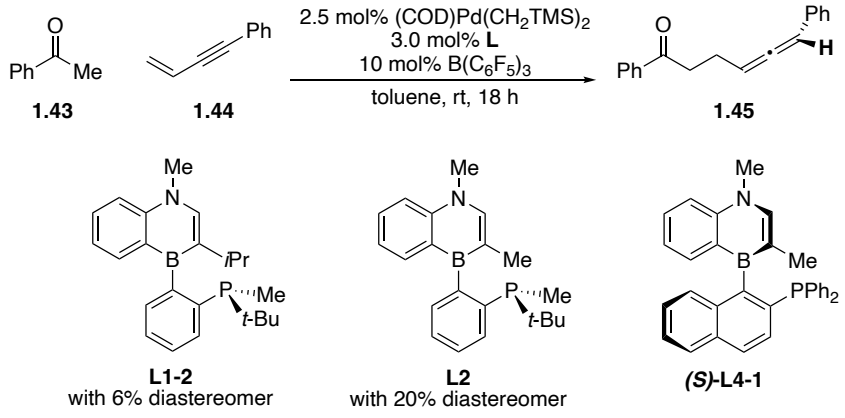
Benchmark reactions

Compound **1.44**[29] and **1.50**[69] was prepared according to previously reported procedures.

General procedure of hydroalkylation

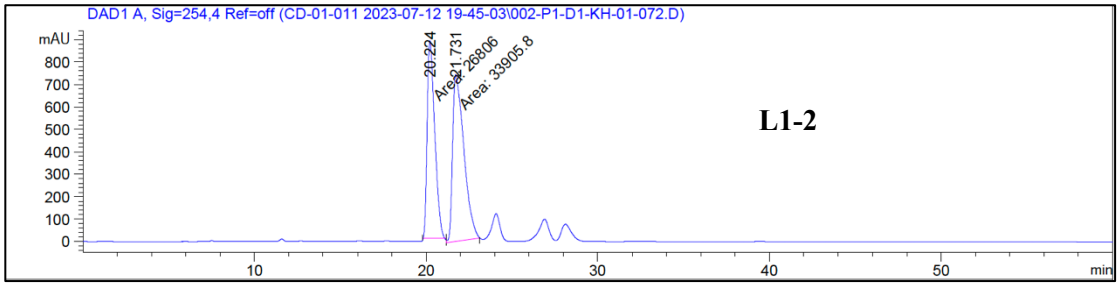
Compound **1.45** was prepared according to literature procedure.[29] In the glovebox, to an oven-dried 4 mL vial containing a stir bar was added (COD)Pd($CH_2TMS)_2$ (2.0 mg, 5.0 μmol, 2.5 mol%), ligand (6.0 μmol, 3.0 mol%), and toluene (0.2 mL). The solution was allowed to stir for 5 minutes, then acetophenone (60 mg, 0.50 mmol, 2.5 equiv.), $B(C_6H_5)_3$ (10mg, 0.020 mmol, 10 mol%), PMP (3.2 mg, 0.020 mmol, 10 mol%), and **1.39** (26 mg, 0.20 mmol, 1.0 equiv.) were added, and the solution was allowed to stir at room temperature for 18 hours. At the conclusion of the reaction, the reaction mixture was passed through a short plug of silica gel eluting with Et_2O (3 x 2 mL). The resulting mixture was concentrated under reduced pressure, and the crude mixture was purified by silica gel column chromatography (50% CH_2Cl_2 in hexanes) to afford product as orange solid. Spectral data match those previously reported.[29] **Chiral HPLC**: AD-H (IPA/hexanes = 0.5/99.5, 0.5 mL/min, 220 nm): t_r (major) = 21.7 min, t_r (minor) = 22.2 min.

Table S3. Hydroalkylation with different ligands.



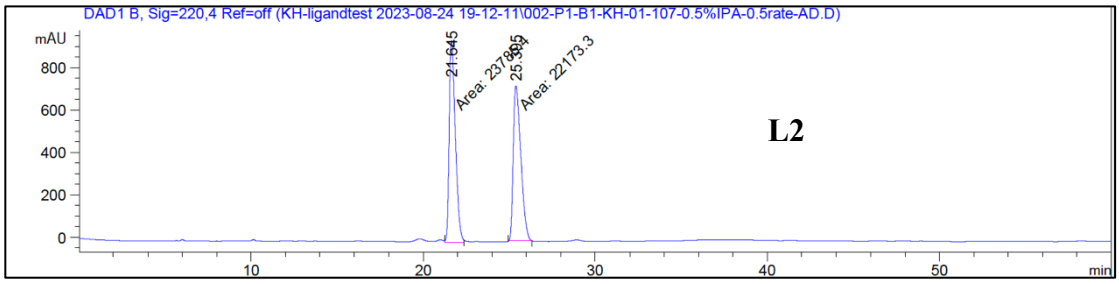
(69) Huo, X.; Yang, G.; Liu, D.; Liu, Y.; Gridnev, I. D.; Zhang, W. *Angew. Chem. Int. Ed.* **2014**, *53*, 6776 –6780.

Entry	Ligand	yield	*ee*
1	**L1-2**	60%	12%
2	**L2**	69%	2%
3	***(S)*-L4-1**	56%	4%



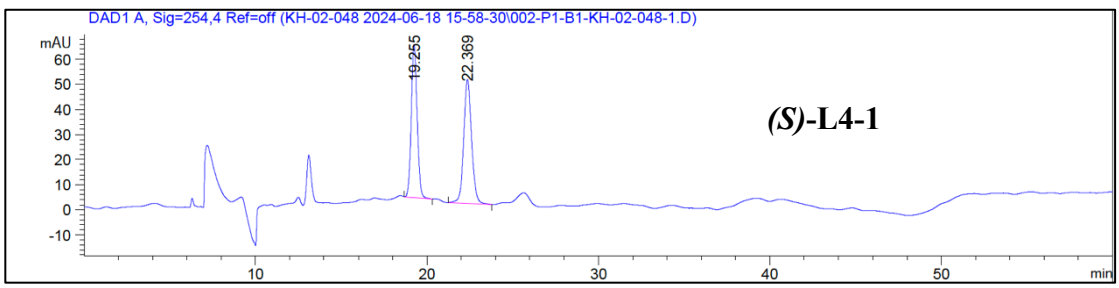
Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.224	MM	0.5078	2.68060e4	879.83807	44.1528
2	21.731	MM	0.7608	3.39058e4	742.79340	55.8472
Totals :				6.07118e4	1622.63147	



Signal 2: DAD1 B, Sig=220,4 Ref=off

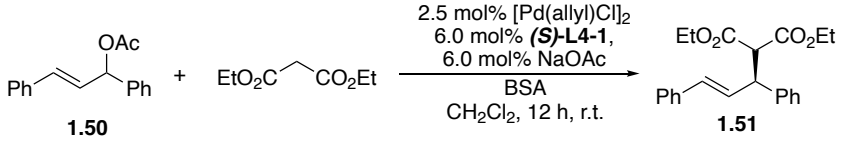
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.645	MM	0.4166	2.37854e4	951.53406	51.7539
2	25.395	MM	0.5074	2.21733e4	728.35315	48.2461
Totals :				4.59587e4	1679.88721	



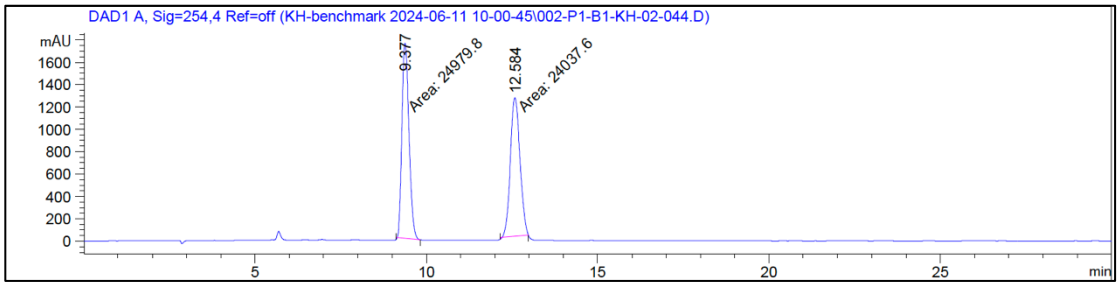
Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.255	BB	0.3672	1446.89429	60.89948	47.8201
2	22.369	BB	0.4885	1578.80823	49.44785	52.1799
Totals :				3025.70251	110.34734	

Allylic substitution

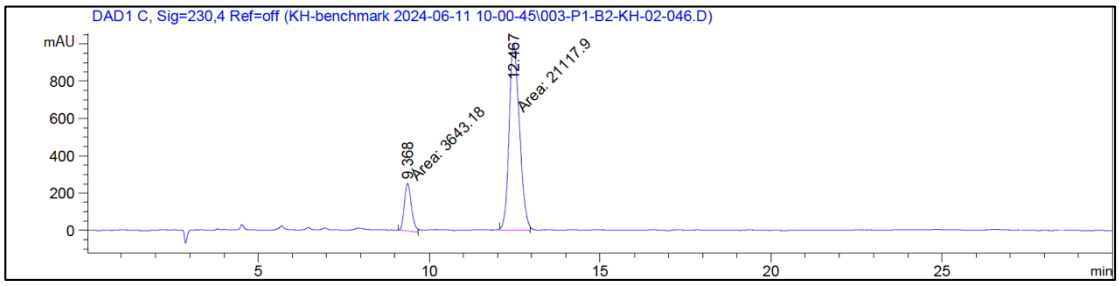


Compound **1.51** was prepared according to literature procedure.[65a] In the glovebox, to an oven-dried 4 mL vial containing a stir bar was added $[Pd(C_3H_5)Cl]_2$ (1.2 mg, 3.3 µmol, 2.5 mol%), ligand ***(S)*-L4-1** (3.7 mg, 7.9 µmol, 6.0 mol%) and CH_2Cl_2 (0.2 mL). The solution was allowed to stir for 30 minutes, then **1.50** (33 mg, 0.13 mmol, 1.0 equiv.), diethyl malonate (43 mg, 0.26 mmol, 2.0 equiv.), NaOAc (0.7 mg, 8 µmol, 6 mol%) and BSA (67 mg, 0.33 mmol, 2.5 equiv) were added, and the solution was allowed to stir at room temperature for 12 hours. At the conclusion of the reaction, the reaction mixture was diluted with EtOAc (5 mL), then saturated NH_4Cl (aq) (10 mL) was added. The mixture was extracted with EtOAc (3 x 10 mL), the combined organic phase was washed with brine (10 mL), dried over Na_2SO_4, and then concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (10% EtOAc in hexanes) to afford product as colorless oil (38 mg, 0.11 mmol, 82% yield). Spectral data match those previously reported.[64a] **Chiral HPLC**: 71% *ee*. AD-H (IPA/hexane = 10/90, 1.0 mL/min, 220 nm): t_r (major) = 12.5 min, t_r (minor) = 9.4 min (The racemic product was obtained with racemic **L4**).



Signal 1: DAD1 A, Sig=254,4 Ref=off

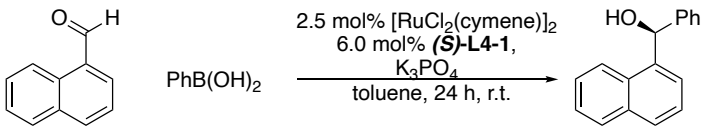
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.377	MM	0.2387	2.49798e4	1743.95483	50.9611
2	12.584	MM	0.3237	2.40376e4	1237.80066	49.0389
Totals :				4.90173e4	2981.75549	



Signal 3: DAD1 C, Sig=230,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.368	MM	0.2387	3643.18384	254.39006	14.7133
2	12.467	MM	0.3513	2.11179e4	1001.97150	85.2867
Totals :				2.47611e4	1256.36156	

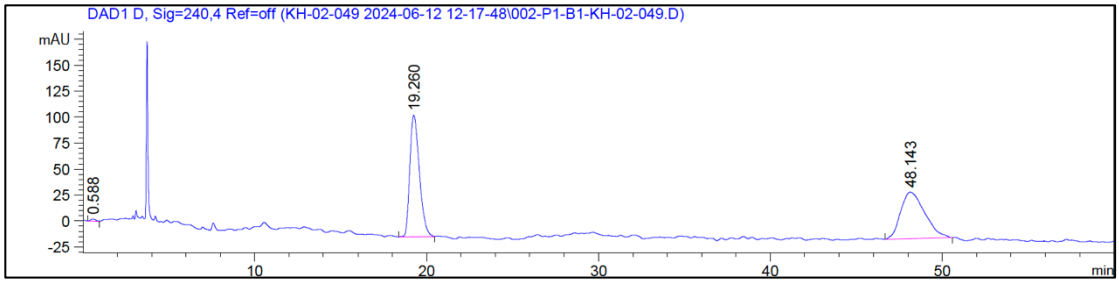
Ru-catalyzed nucleophilic addition



1.52 **1.53**

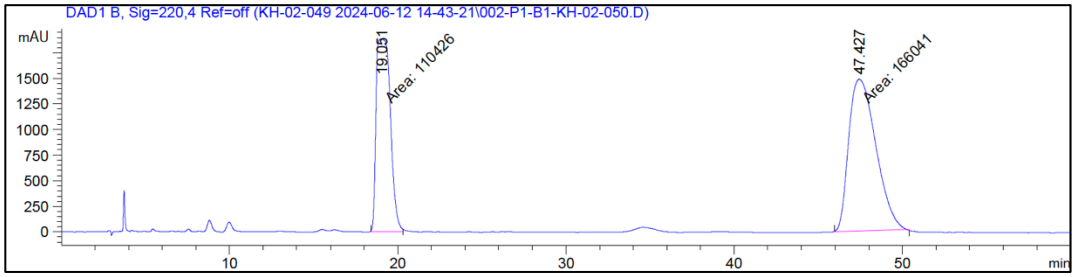
Compound **1.53** was prepared according to literature procedure.[65a] In the glovebox, to an oven-dried 4 mL vial containing a stir bar was added $[RuCl_2(cymene)]_2$ (5.5 mg, 9.0 μmol, 2.5 mol%), ligand ***(S)*-L4-1** (4.2 mg, 9.0 μmol, 6.0 mol%) and toluene (0.2 mL). The solution was allowed to stir for 30 minutes, then 1-naphthaldehyde **1.52** (24

mg, 0.15 mmol, 1.0 equiv.), boronic acids (37 mg, 0.30 mmol, 2.0 equiv.) and K_3PO_4 (64 mg, 0.30 mmol, 2.0 equiv.) were added, and the solution was allowed to stir at room temperature for 24 hours. At the conclusion of the reaction, the reaction mixture was passed through a short plug of silica gel eluting with CH_2Cl_2 (3 x 2 mL). The resulting mixture was concentrated under reduced pressure, and the crude mixture was purified by preparative TLC (10% EtOAc in hexane) to afford product as a white solid (10 mg, 43 μmol, 28%). Spectral data match those previously reported.[65a] **Chiral HPLC**: 20% *ee*. OD-H (IPA/hexanes = 5/95, 1.0 mL/min, 220 nm): t_r (major) = 47.4 min, t_r (minor) = 19.1 min (The racemic product was obtained with racemic **L4**).



Signal 4: DAD1 D, Sig=240,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.588	BB	0.2765	40.98396	2.14913	0.4571
2	19.260	BB	0.6014	4533.87207	117.16834	50.5695
3	48.143	BB	1.2202	4390.76904	45.00523	48.9734
Totals :				8965.62508	164.32270	

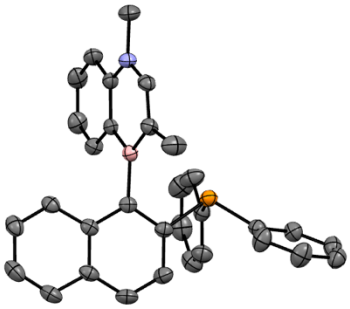


Signal 2: DAD1 B, Sig=220,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.051	MM	0.9769	1.10426e5	1883.85718	39.9418
2	47.427	MM	1.8665	1.66041e5	1482.67322	60.0582
Totals :				2.76467e5	3366.53040	

X-ray Crystallographic Data

Table S4. Crystal data and structure refinement for C32H27BNP.

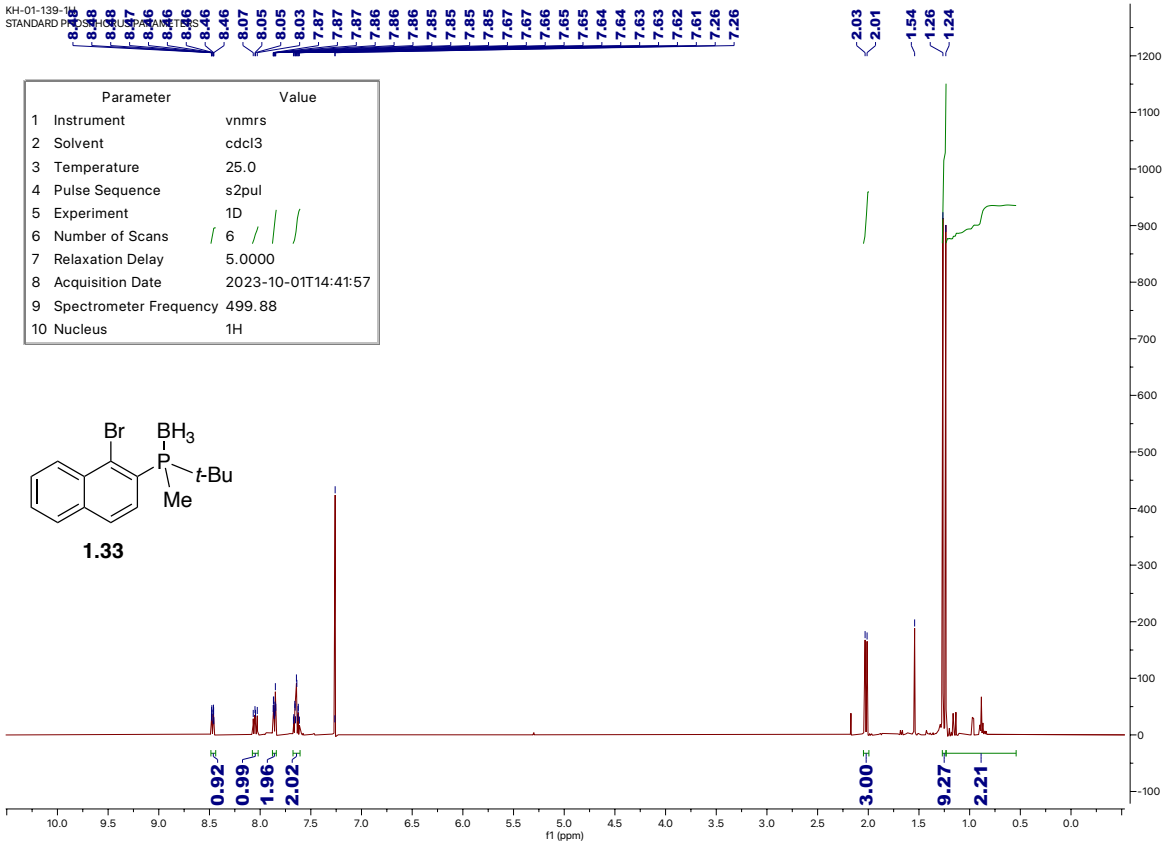


***(S)*-L4-1**

Identification code	C32H27BNP	
Empirical formula	C32 H27 B N P	
Formula weight	467.32	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 9.1852(4) Å	a= 90°.
	b = 13.0743(6) Å	b= 90°.
	c = 20.8776(9) Å	g = 90°.
Volume	2507.19(19) $Å^3$	
Z	4	
Density (calculated)	1.238 Mg/m^3	
Absorption coefficient	1.115 mm^{-1}	
F(000)	984	
Crystal size	0.280 x 0.160 x 0.080 mm^3	
Theta range for data collection	3.989 to 66.646°.	
Index ranges	-10<=h<=10, -13<=k<=15, -24<=l<=24	
Reflections collected	32822	
Independent reflections	4421 [R(int) = 0.0441]	
Completeness to theta = 66.646°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7528 and 0.6896	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4421 / 0 / 319
Goodness-of-fit on F^2	1.047
Final R indices [I>2sigma(I)]	R1 = 0.0284, wR2 = 0.0758
R indices (all data)	R1 = 0.0302, wR2 = 0.0771
Absolute structure parameter	0.04(2)
Extinction coefficient	n/a
Largest diff. peak and hole	0.325 and -0.125 e.$Å^{-3}$

NMR Spectra


KH-01-139-1H
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2.03 2.01 1.54 1.26 1.24
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2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 6
7 Relaxation Delay 5.0000
8 Acquisition Date 2023-10-01T14:41:57
9 Spectrometer Frequency 499.88
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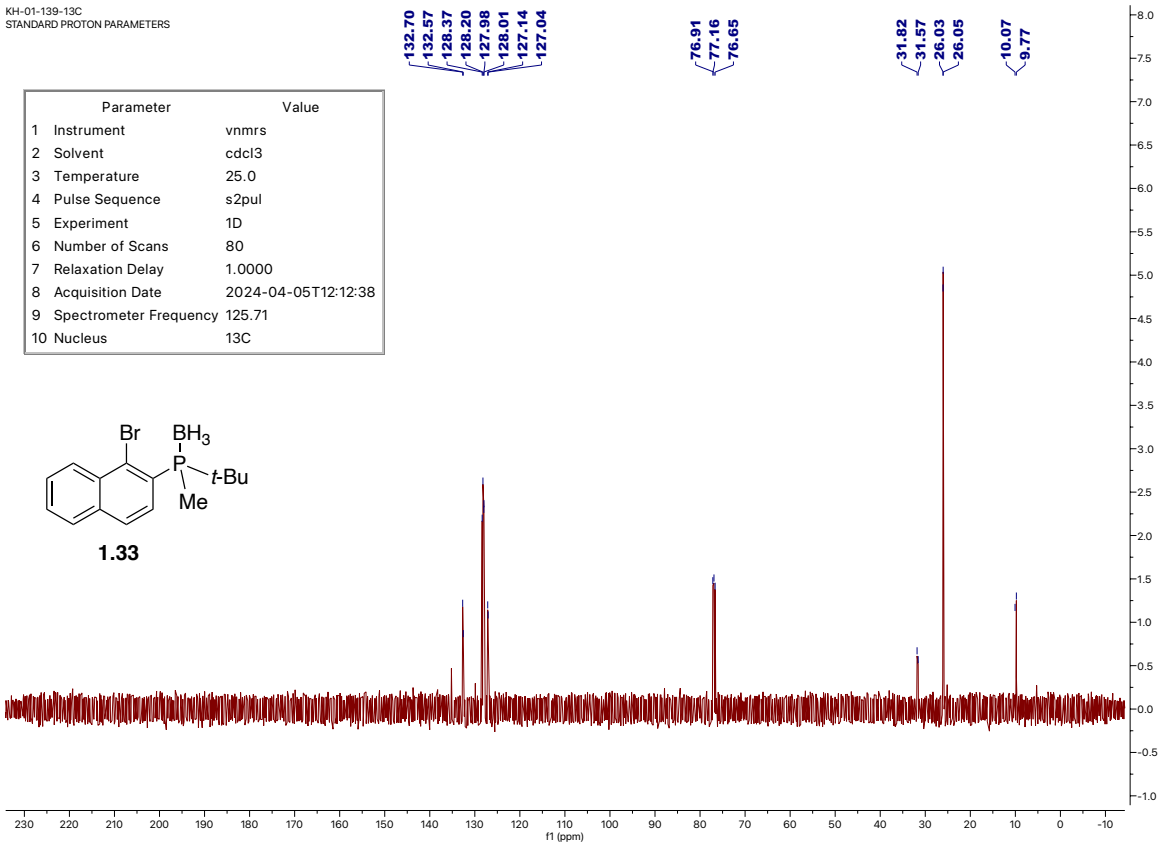
Br
BH3
P
t-Bu
Me
1.33
0.92 0.99 1.96 2.02 3.00 9.27 2.21
f1 (ppm)


KH-01-139-13C
STANDARD PROTON PARAMETERS
132.70 132.57 128.37 128.20 127.98 128.01 127.14 127.04
76.91 77.16 76.65
31.82 31.57 26.03 26.05 10.07 9.77
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 80
7 Relaxation Delay 1.0000
8 Acquisition Date 2024-04-05T12:12:38
9 Spectrometer Frequency 125.71
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Br
BH3
P
t-Bu
Me
1.33
f1 (ppm)

KH-01-139-31P-1
STANDARD PHOSPHORUS PARAMETERS

	Parameter	Value
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2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	26
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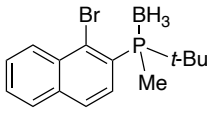
9	Spectrometer Frequency	202.37
10	Nucleus	31P



1.33

KH-01-139-11B
STANDARD PROTON PARAMETERS

	Parameter	Value
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2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	256
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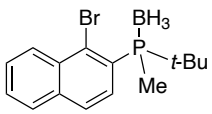
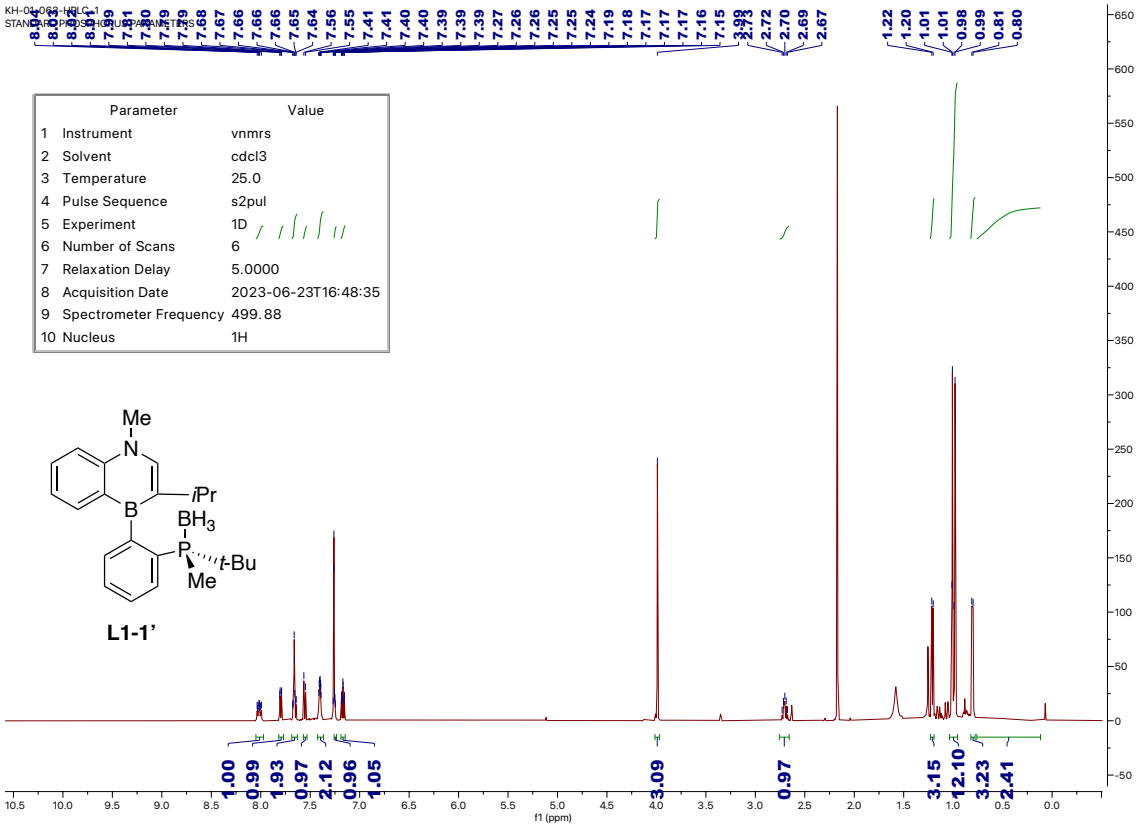
8	Acquisition Date	2023-10-01T14:47:02
9	Spectrometer Frequency	160.38
10	Nucleus	11B



1.33


KH-01-063-HRLC-1
STANDARD PROTON PARAMETERS
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
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6 Number of Scans 6
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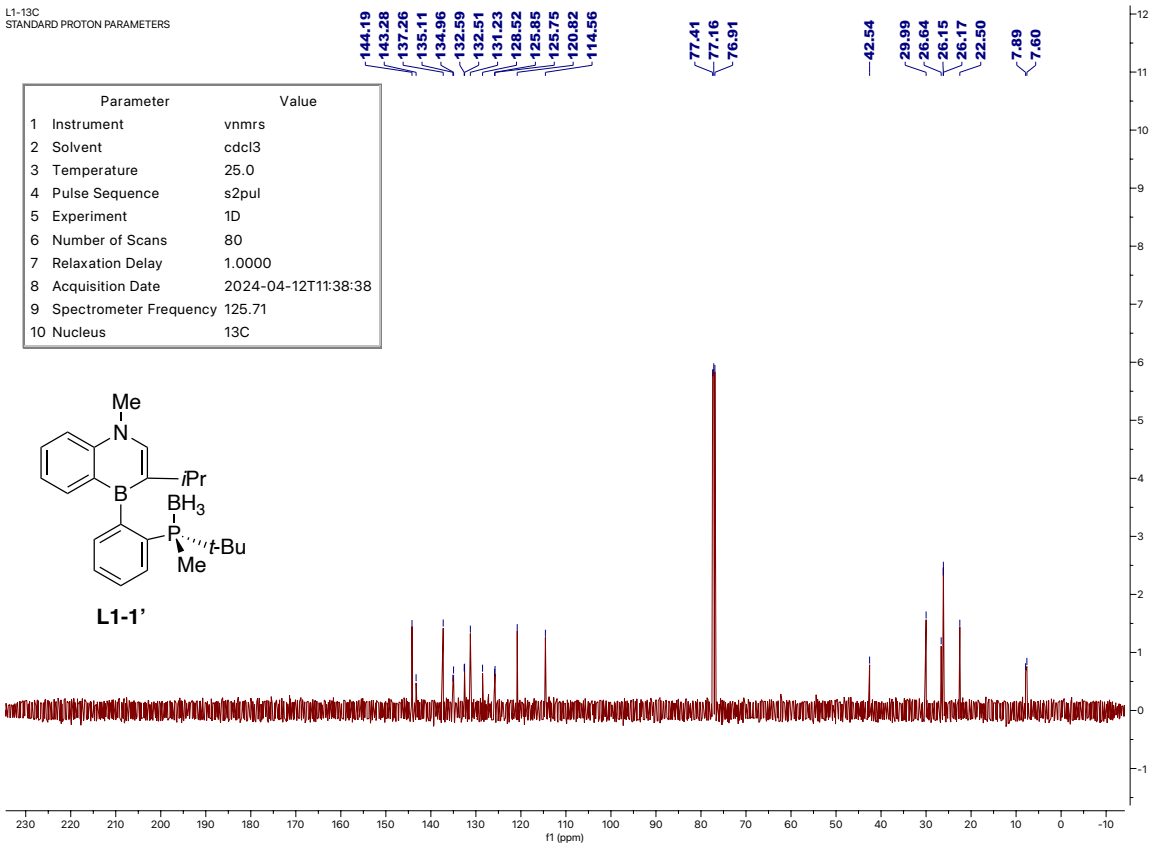
N
B
iPr
BH3
P
t-Bu
Me
L1-1'
f1 (ppm)


L1-13C
STANDARD PROTON PARAMETERS
Parameter Value
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2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 80
7 Relaxation Delay 1.0000
8 Acquisition Date 2024-04-12T11:38:38
9 Spectrometer Frequency 125.71
10 Nucleus 13C
Me
N
B
iPr
BH3
P
t-Bu
Me
L1-1'
f1 (ppm)

L1-31P
STANDARD PHOSPHORUS PARAMETERS

	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
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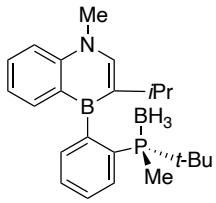
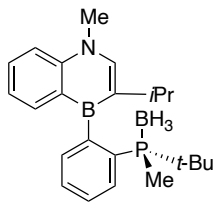
10	Nucleus	31P



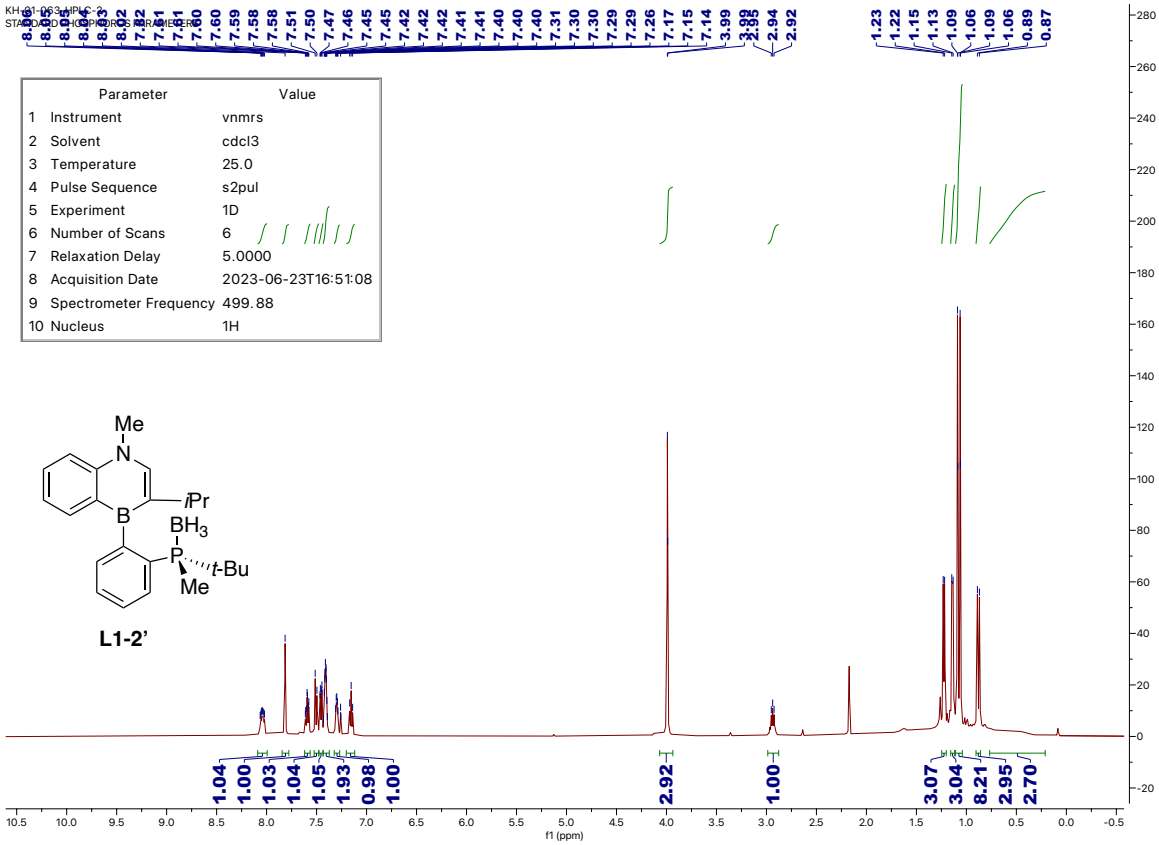
L1-1'

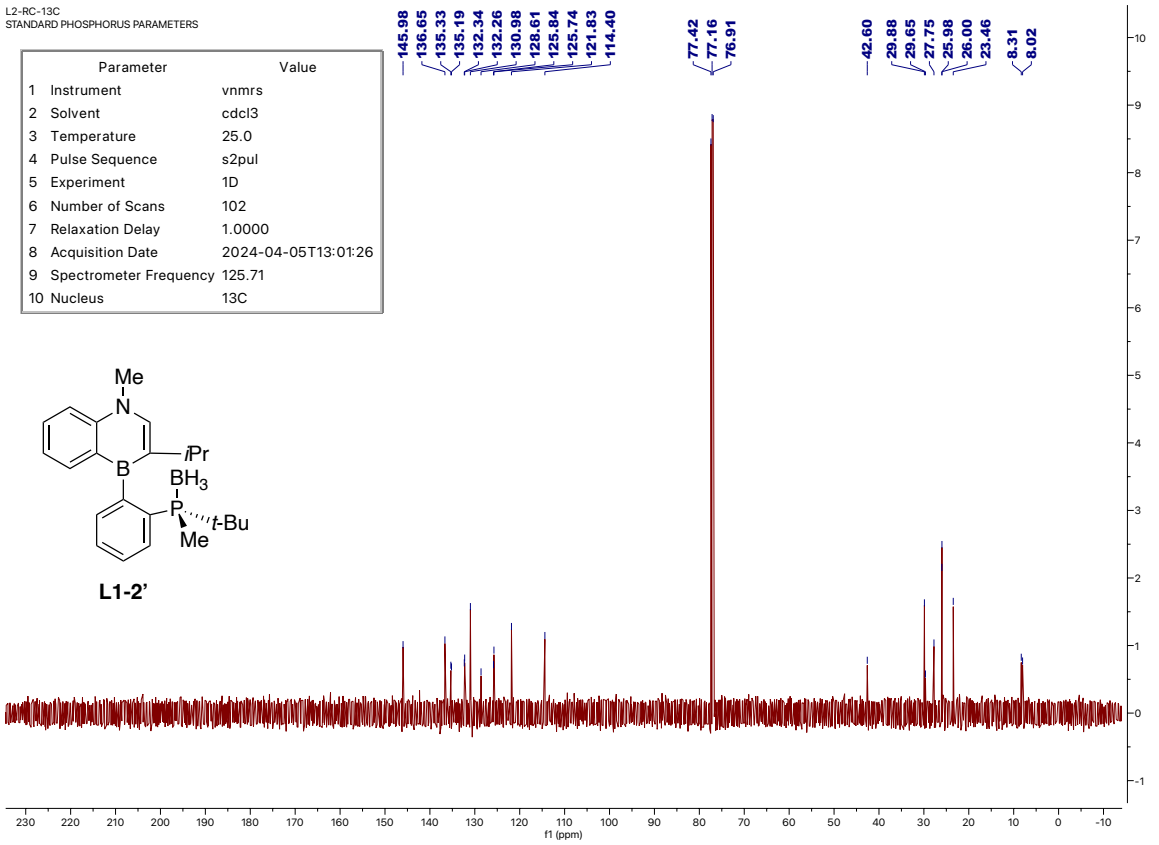
L1-11B
STANDARD PROTON PARAMETERS

	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	256
7	Relaxation Delay	0.0100
8	Acquisition Date	2024-04-12T10:17:48
9	Spectrometer Frequency	160.38
10	Nucleus	11B



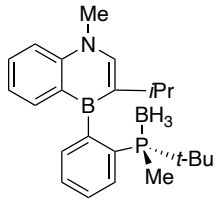
L1-1'


Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 6
7 Relaxation Delay 5.0000
8 Acquisition Date 2023-06-23T16:51:08
9 Spectrometer Frequency 499.88
10 Nucleus 1H
Me
N
B
iPr
BH3
P
t-Bu
Me
L1-2'
f1 (ppm)


L2-RC-13C
STANDARD PHOSPHORUS PARAMETERS
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 102
7 Relaxation Delay 1.0000
8 Acquisition Date 2024-04-05T13:01:26
9 Spectrometer Frequency 125.71
10 Nucleus 13C
Me
N
B
iPr
BH3
P
t-Bu
Me
L1-2'
f1 (ppm)

L2-RC-31P
STANDARD PHOSPHORUS PARAMETERS

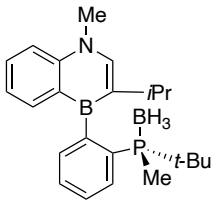
	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	32
7	Relaxation Delay	1.0000
8	Acquisition Date	2024-04-05T13:06:16
9	Spectrometer Frequency	202.37
10	Nucleus	31P



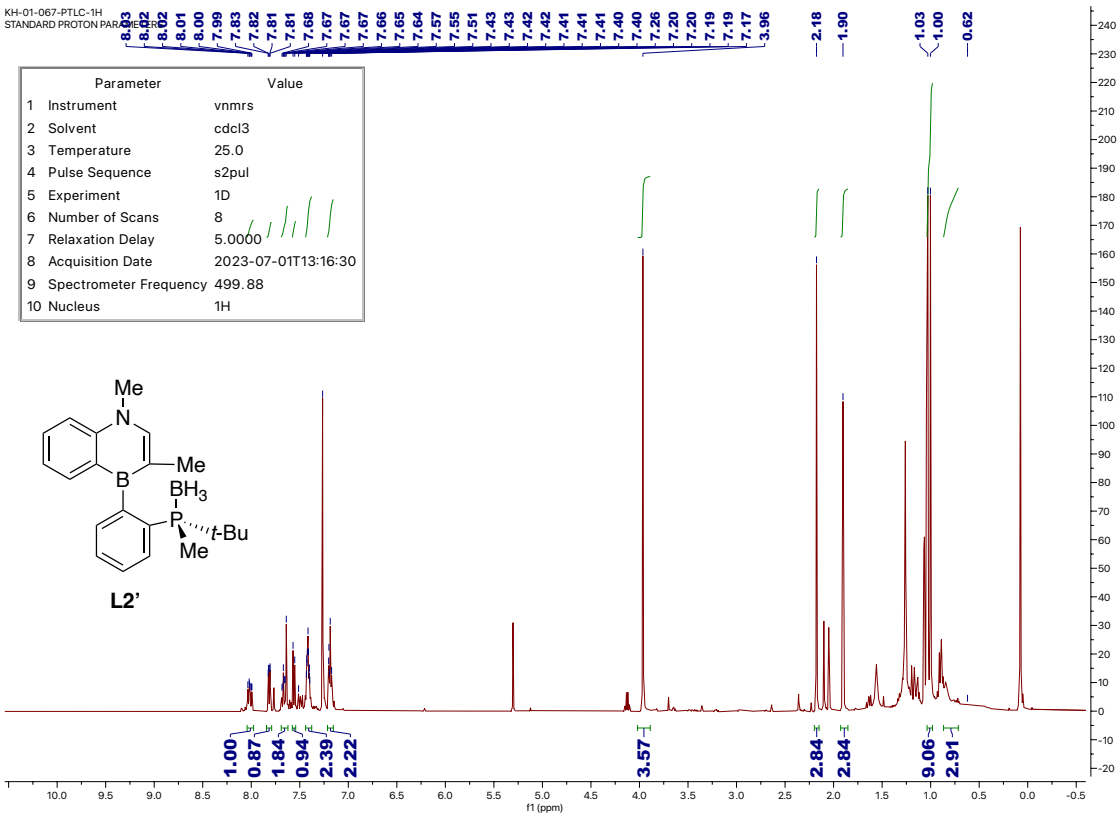
L1-2'

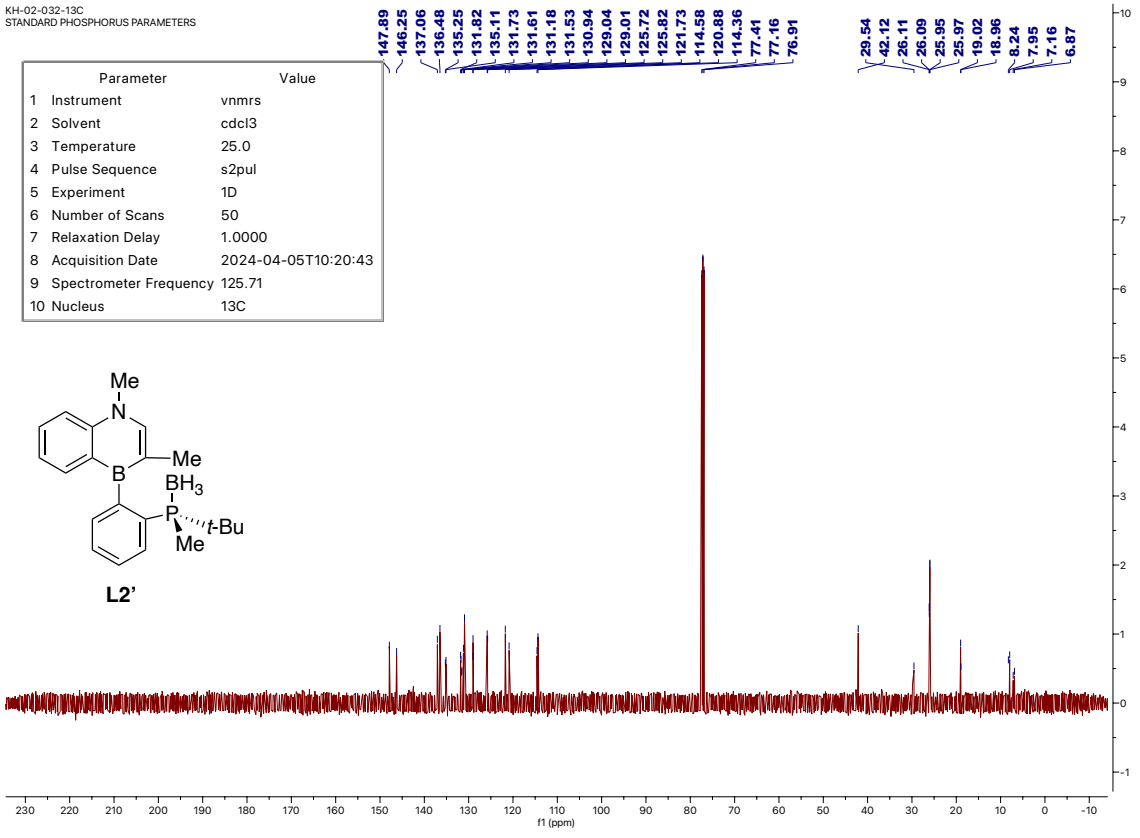
L2-RC-11B
STANDARD PROTON PARAMETERS

	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	256
7	Relaxation Delay	0.0100
8	Acquisition Date	2024-04-05T13:08:39
9	Spectrometer Frequency	160.38
10	Nucleus	11B



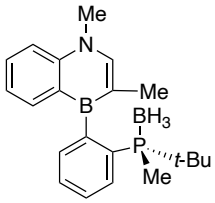
L1-2'


KH-01-067-PTLC-1H
STANDARD PROTON PARAMETERS
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 8
7 Relaxation Delay 5.0000
8 Acquisition Date 2023-07-01T13:16:30
9 Spectrometer Frequency 499.88
10 Nucleus 1H
Me
N
B
Me
BH3
P
t-Bu
Me
L2'
f1 (ppm)


KH-02-032-13C
STANDARD PHOSPHORUS PARAMETERS
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 50
7 Relaxation Delay 1.0000
8 Acquisition Date 2024-04-05T10:20:43
9 Spectrometer Frequency 125.71
10 Nucleus 13C
Me
N
B
Me
BH3
P
t-Bu
Me
L2'
f1 (ppm)

KH-02-032-31P
STANDARD PHOSPHORUS PARAMETERS

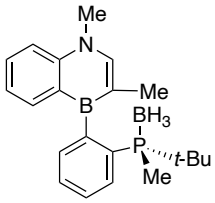
	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	30
7	Relaxation Delay	1.0000
8	Acquisition Date	2024-04-05T10:23:47
9	Spectrometer Frequency	202.37
10	Nucleus	31P



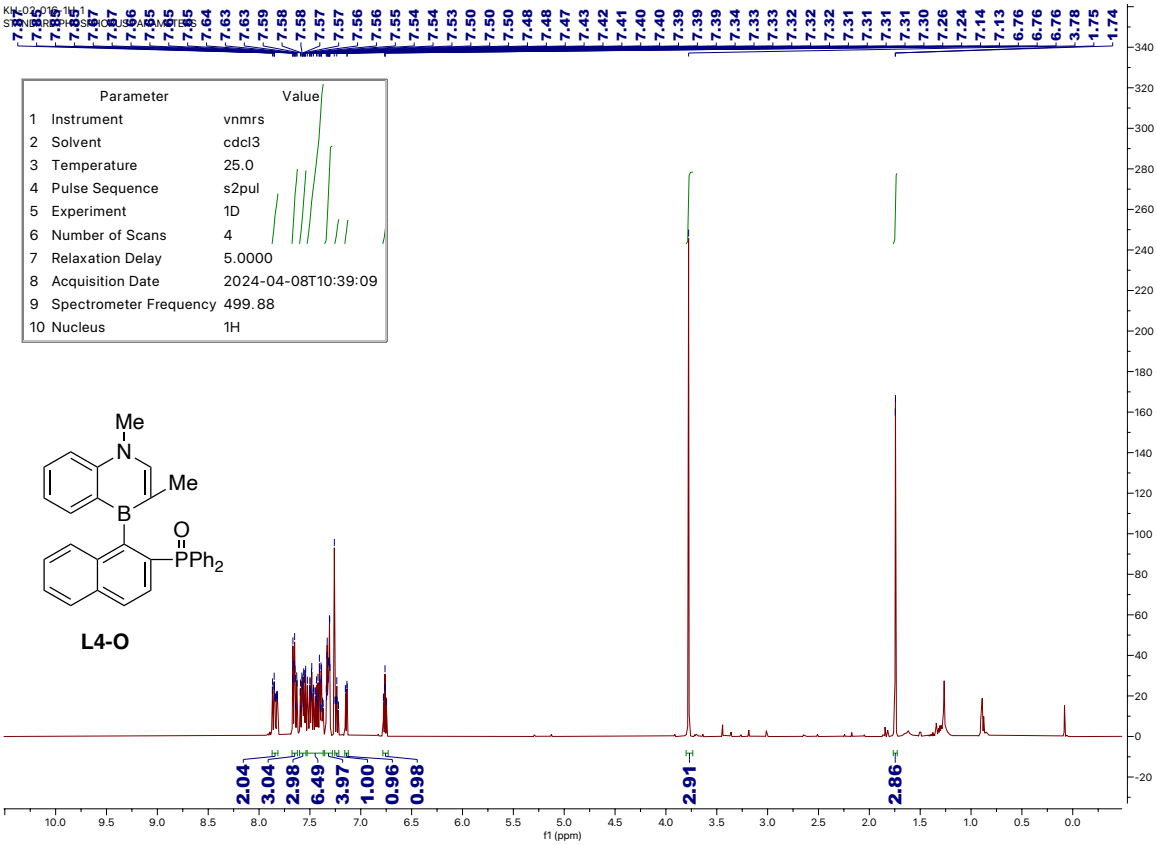
L2'

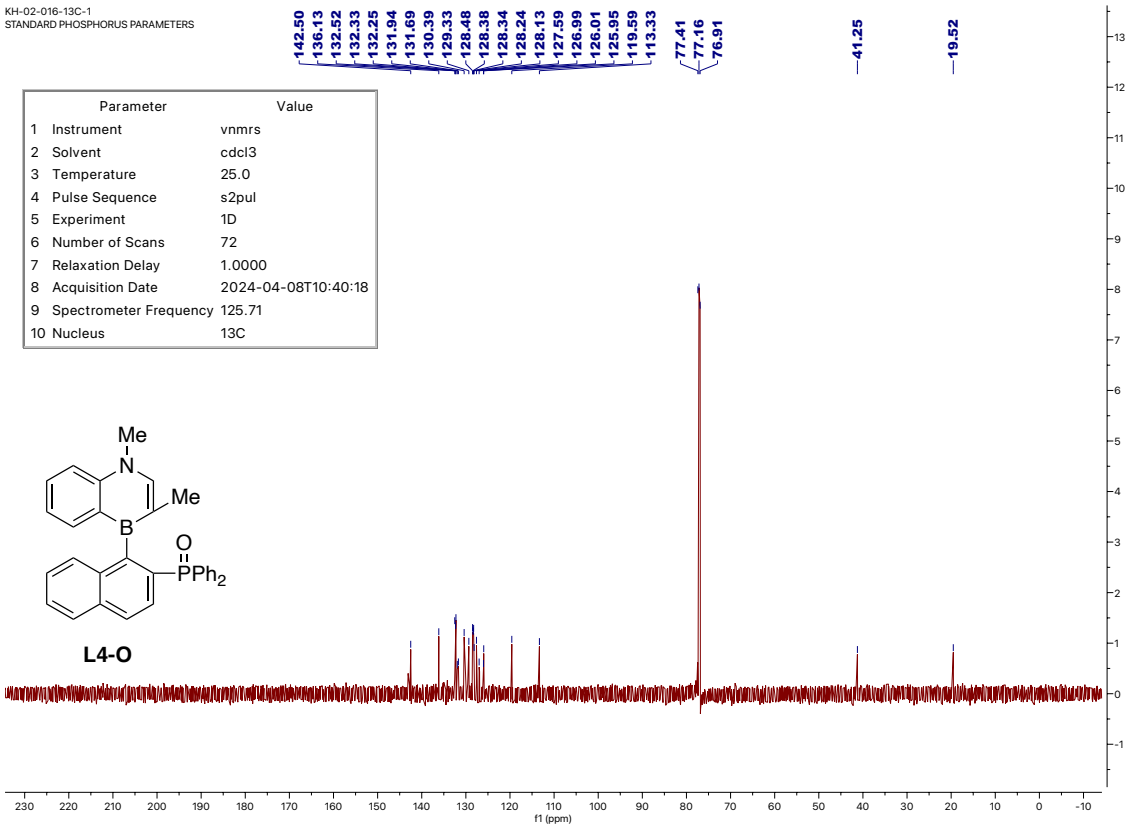
KH-01-067-PTLC-11B
STANDARD PROTON PARAMETERS

	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	256
7	Relaxation Delay	0.0100
8	Acquisition Date	2023-07-01T13:21:30
9	Spectrometer Frequency	160.38
10	Nucleus	11B



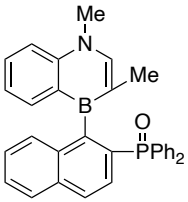
L2'


KH-02-016-1h-1
STANDARD PHOSPHORUS PARAMETERS
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 4
7 Relaxation Delay 5.0000
8 Acquisition Date 2024-04-08T10:39:09
9 Spectrometer Frequency 499.88
10 Nucleus 1H
Me
N
Me
B
O
PPh2
L4-O
2.04
3.04
2.98
6.49
3.97
1.00
0.96
0.98
2.91
2.86
f1 (ppm)


KH-02-016-13C-1
STANDARD PHOSPHORUS PARAMETERS
142.50
136.13
132.52
132.33
132.25
131.94
131.69
130.39
129.33
128.48
128.38
128.34
128.24
128.13
127.59
126.99
126.01
125.95
119.59
113.33
77.41
77.16
76.91
41.25
19.52
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 72
7 Relaxation Delay 1.0000
8 Acquisition Date 2024-04-08T10:40:18
9 Spectrometer Frequency 125.71
10 Nucleus 13C
Me
N
Me
B
O
PPh2
L4-O
f1 (ppm)

KH-02-016-31P
STANDARD PHOSPHORUS PARAMETERS

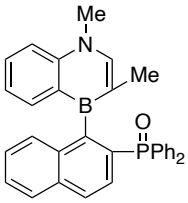
	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	10
7	Relaxation Delay	1.0000
8	Acquisition Date	2024-02-20T11:21:44
9	Spectrometer Frequency	202.37
10	Nucleus	31P



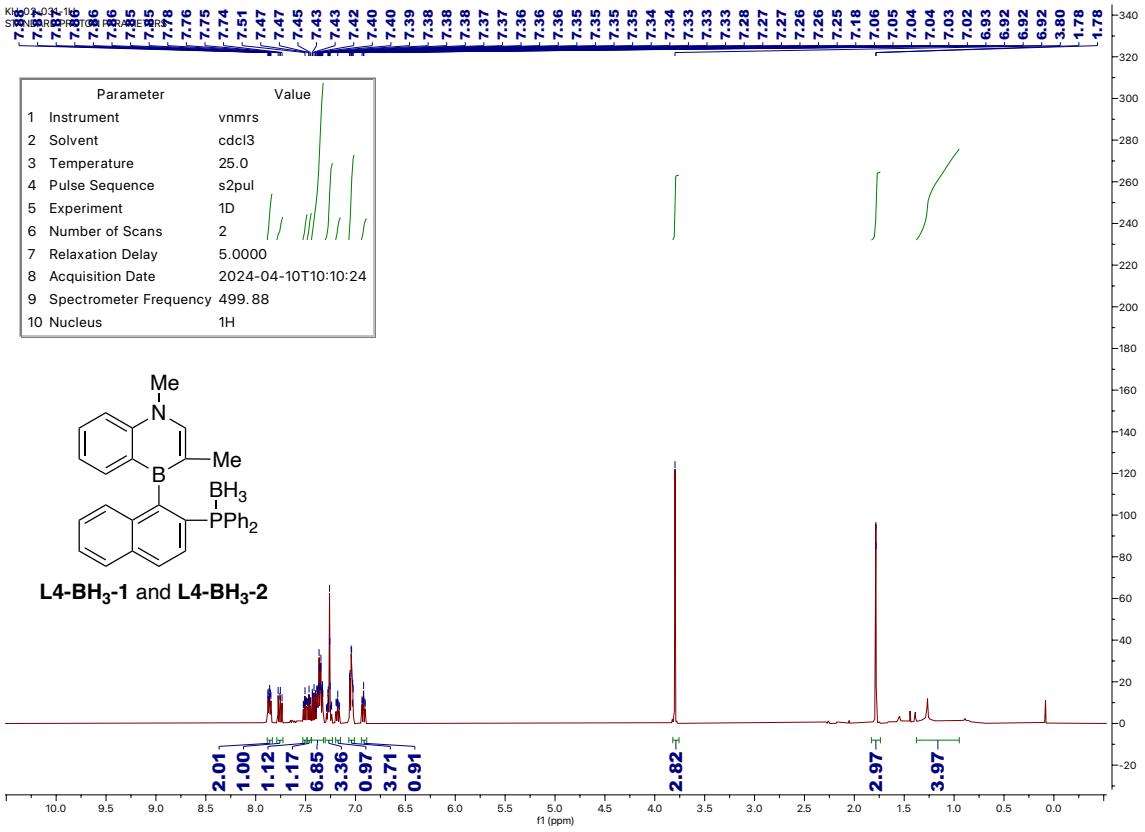
L4-O

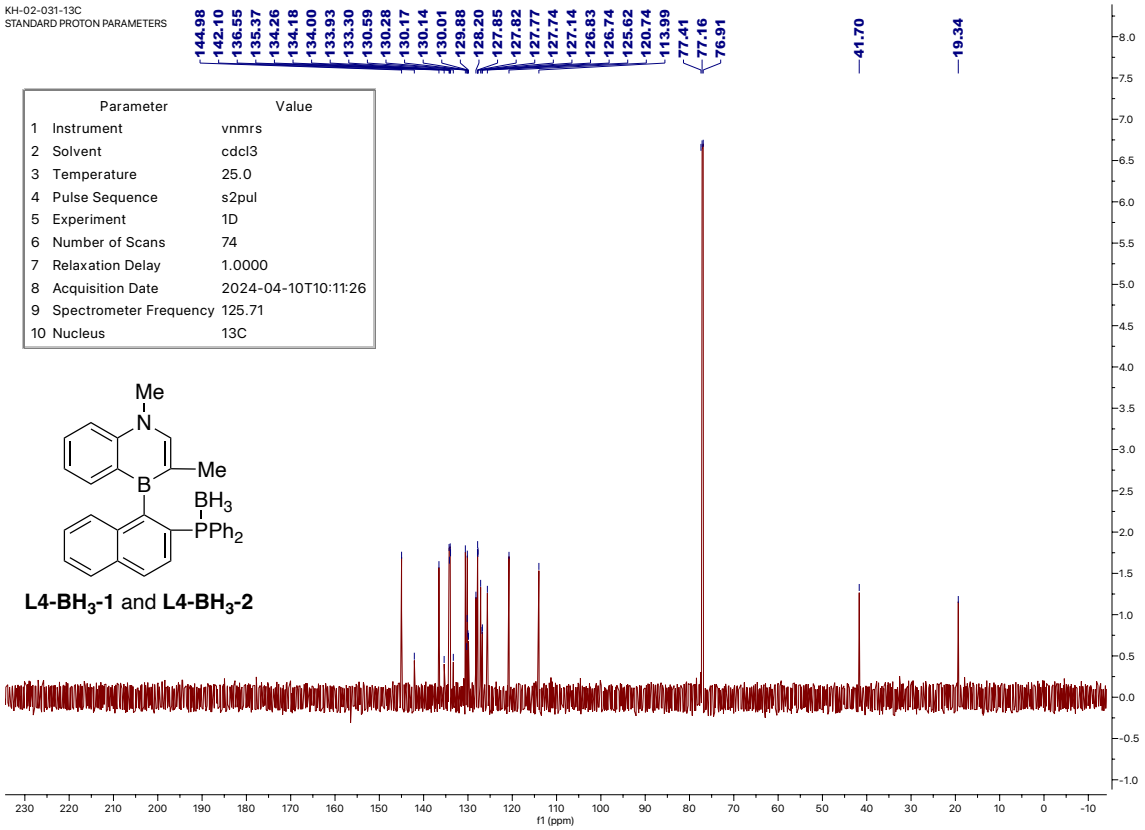
KH-02-016-11B
STANDARD PROTON PARAMETERS

	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	256
7	Relaxation Delay	0.0100
8	Acquisition Date	2024-02-20T11:23:37
9	Spectrometer Frequency	160.38
10	Nucleus	11B



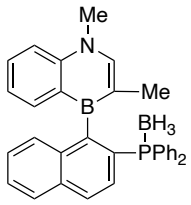
L4-O


KH-03-031-1H
STANDARD PROTON PARAMETERS
7.80 7.79 7.78 7.76 7.75 7.74 7.51 7.47 7.45 7.43 7.42 7.40 7.39 7.38 7.38 7.37 7.37 7.36 7.36 7.35 7.35 7.35 7.34 7.34 7.33 7.33 7.28 7.27 7.26 7.25 7.18 7.06 7.05 7.04 7.03 7.02 6.93 6.92 6.92 3.80 1.78
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 2
7 Relaxation Delay 5.0000
8 Acquisition Date 2024-04-10T10:10:24
9 Spectrometer Frequency 499.88
10 Nucleus 1H
Me
N
B
Me
BH3
PPh2
L4-BH3-1 and L4-BH3-2
2.01 1.00 1.12 1.17 6.85 3.36 0.97 3.71 0.91 2.82 2.97 3.97
f1 (ppm)


KH-02-031-13C
STANDARD PROTON PARAMETERS
144.98 142.10 136.55 135.37 134.26 134.18 134.00 133.93 133.30 130.59 130.28 130.17 130.14 130.01 129.88 128.20 127.85 127.82 127.77 127.74 127.14 126.83 126.74 125.62 120.74 113.99 77.41 77.16 76.91 41.70 19.34
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 74
7 Relaxation Delay 1.0000
8 Acquisition Date 2024-04-10T10:11:26
9 Spectrometer Frequency 125.71
10 Nucleus 13C
Me
N
B
Me
BH3
PPh2
L4-BH3-1 and L4-BH3-2
f1 (ppm)

KH-02-031-31P
STANDARD PHOSPHORUS PARAMETERS

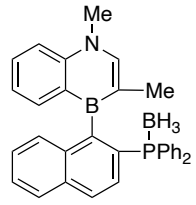
	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	12
7	Relaxation Delay	1.0000
8	Acquisition Date	2024-03-28T12:06:41
9	Spectrometer Frequency	202.37
10	Nucleus	31P



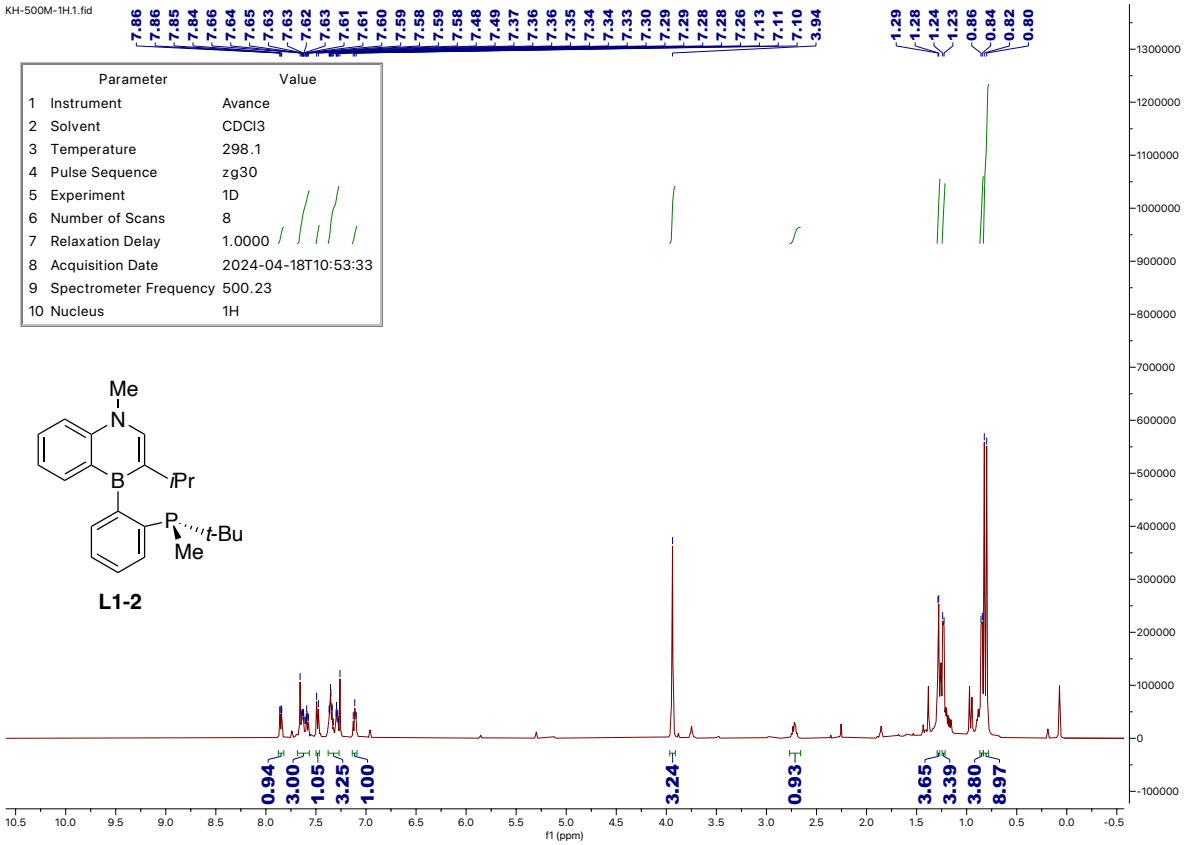
L4-BH_3-1 and **L4-BH_3-2**

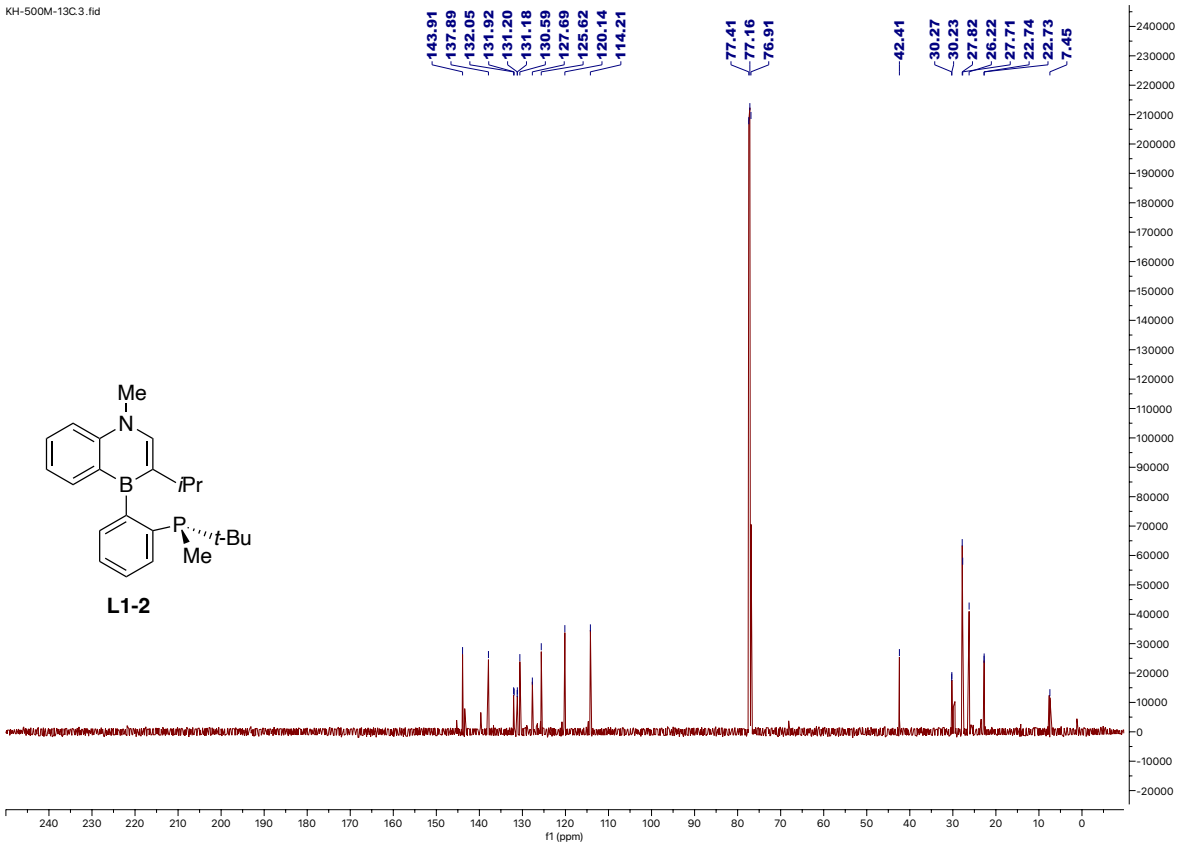
KH-02-031-11B-1
STANDARD PROTON PARAMETERS

	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	256
7	Relaxation Delay	0.0100
8	Acquisition Date	2024-04-10T10:16:59
9	Spectrometer Frequency	160.38
10	Nucleus	11B



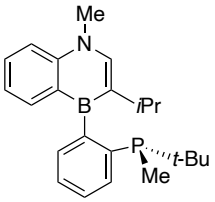
L4-BH_3-1 and **L4-BH_3-2**


KH-500M-1H.1.fid
7.86 7.86 7.85 7.84 7.66 7.64 7.65 7.63 7.63 7.62 7.63 7.61 7.61 7.60 7.59 7.58 7.59 7.58 7.48 7.49 7.37 7.36 7.36 7.35 7.34 7.34 7.33 7.30 7.29 7.29 7.28 7.28 7.26 7.13 7.11 7.10 3.94
1.29 1.28 1.24 1.23 0.86 0.84 0.82 0.80
Parameter Value
1 Instrument Avance
2 Solvent CDCl3
3 Temperature 298.1
4 Pulse Sequence zg30
5 Experiment 1D
6 Number of Scans 8
7 Relaxation Delay 1.0000
8 Acquisition Date 2024-04-18T10:53:33
9 Spectrometer Frequency 500.23
10 Nucleus 1H
Me
N
B
iPr
P
t-Bu
Me
L1-2
0.94 3.00 1.05 3.25 1.00 3.24 0.93 3.65 3.39 3.80 8.97
f1 (ppm)


KH-500M-13C.3.fid
143.91 137.89 132.05 131.92 131.20 131.18 130.59 127.69 125.62 120.14 114.21
77.41 77.16 76.91
42.41
30.27 30.23 27.82 26.22 27.71 22.74 22.73 7.45
Me
N
B
iPr
P
t-Bu
Me
L1-2
f1 (ppm)

KH-01-070-COL-11B
STANDARD PROTON PARAMETERS

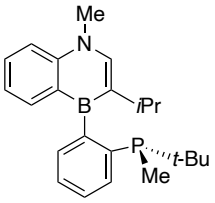
	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	256
7	Relaxation Delay	0.0100
8	Acquisition Date	2023-07-07T16:52:23
9	Spectrometer Frequency	160.38
10	Nucleus	11B



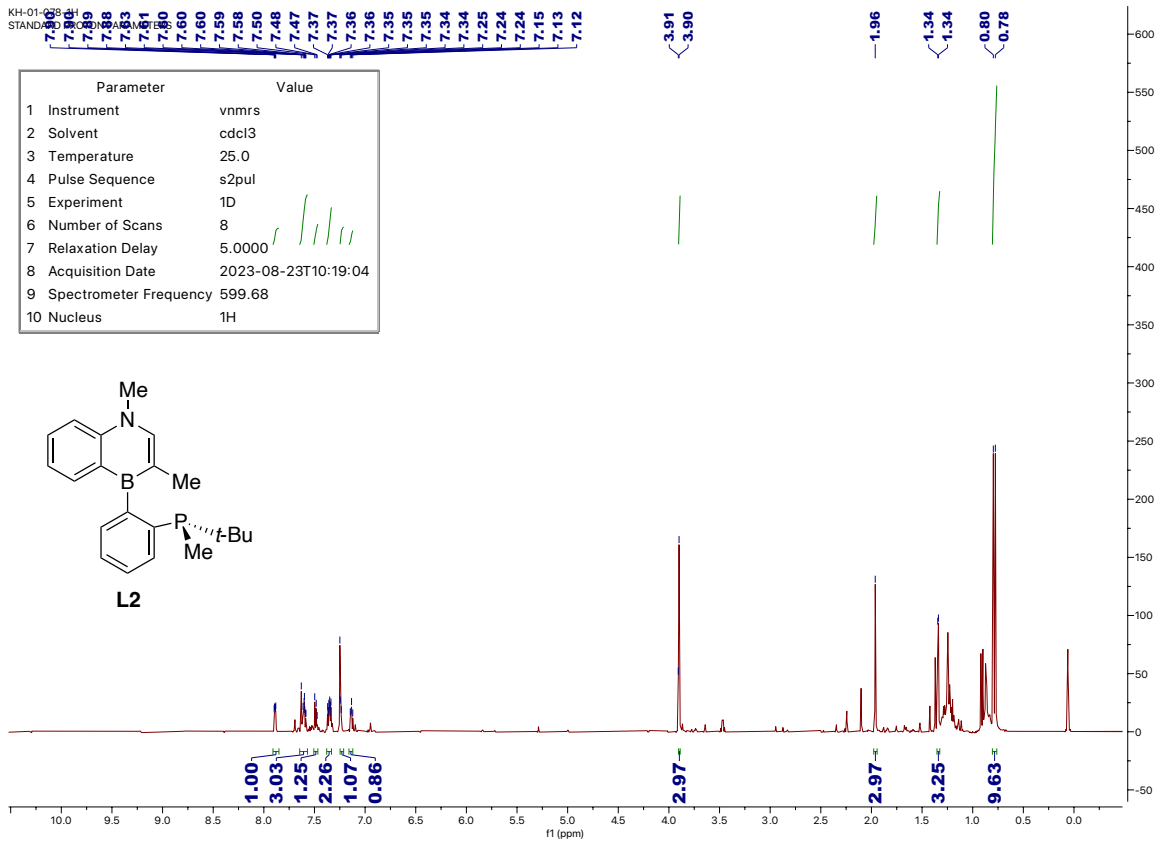
L1-2

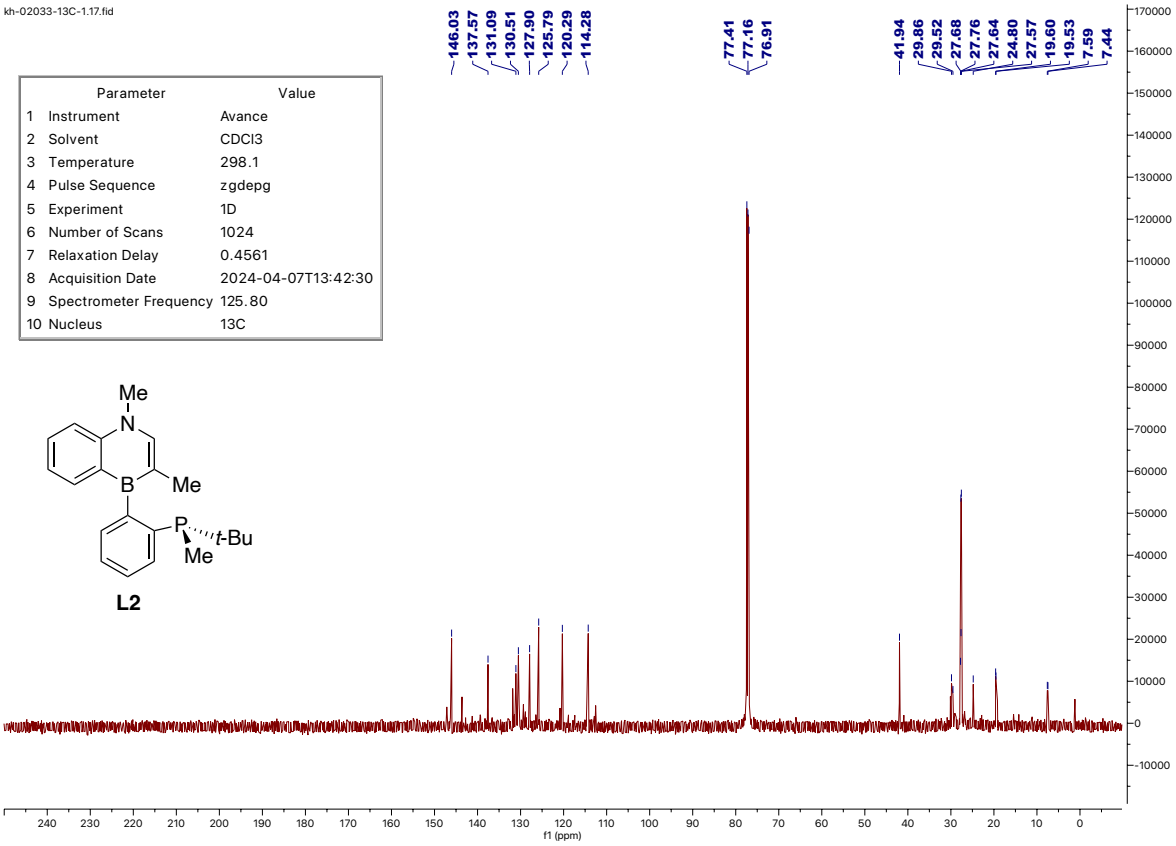
KH-01-070-COL-31P
STANDARD PHOSPHORUS PARAMETERS

	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	42
7	Relaxation Delay	1.0000
8	Acquisition Date	2023-07-07T16:49:49
9	Spectrometer Frequency	202.37
10	Nucleus	31P



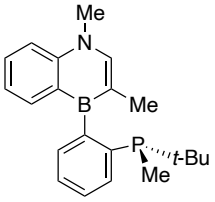
L1-2


KH-01-028-1H
STANDARD PROTON PARAMETERS
7.66 7.66 7.65 7.64 7.63 7.62 7.61 7.60 7.60 7.59 7.58 7.50 7.48 7.47 7.37 7.37 7.36 7.36 7.35 7.35 7.35 7.34 7.34 7.25 7.24 7.24 7.15 7.13 7.12
3.91 3.90
1.96
1.34 1.34
0.80 0.78
Parameter Value
1 Instrument vnmrs
2 Solvent cdcl3
3 Temperature 25.0
4 Pulse Sequence s2pul
5 Experiment 1D
6 Number of Scans 8
7 Relaxation Delay 5.0000
8 Acquisition Date 2023-08-23T10:19:04
9 Spectrometer Frequency 599.68
10 Nucleus 1H
Me
N
B
Me
P
t-Bu
Me
L2
1.00 3.03 1.25 2.26 1.07 0.86
2.97
2.97
3.25
9.63
f1 (ppm)


kh-02033-13C-1.17.fid
146.03 137.57 131.09 130.51 127.90 125.79 120.29 114.28
77.41 77.16 76.91
41.94 29.86 29.52 27.68 27.76 27.64 24.80 27.57 19.60 19.53 7.59 7.44
Parameter Value
1 Instrument Avance
2 Solvent CDCl3
3 Temperature 298.1
4 Pulse Sequence zgdepg
5 Experiment 1D
6 Number of Scans 1024
7 Relaxation Delay 0.4561
8 Acquisition Date 2024-04-07T13:42:30
9 Spectrometer Frequency 125.80
10 Nucleus 13C
Me
N
B
Me
P
t-Bu
Me
L2
f1 (ppm)

KH-02-033-31P-COL
STANDARD PHOSPHORUS PARAMETERS

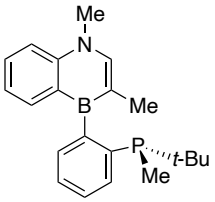
	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	12
7	Relaxation Delay	1.0000
8	Acquisition Date	2024-04-04T12:52:06
9	Spectrometer Frequency	202.37
10	Nucleus	31P



L2

KH-02-033-11B-COL
STANDARD PROTON PARAMETERS

	Parameter	Value
1	Instrument	vnmrs
2	Solvent	cdcl3
3	Temperature	25.0
4	Pulse Sequence	s2pul
5	Experiment	1D
6	Number of Scans	256
7	Relaxation Delay	0.0100
8	Acquisition Date	2024-04-04T12:53:54
9	Spectrometer Frequency	160.38
10	Nucleus	11B



L2