

Homogeneous nickel(II) catalysed transfer hydrogenation of unsaturated compounds

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Thesis accepted in fulfilment of the requirements for the degree
Doctor of Philosophy in Science with Chemistry at the North-
West University

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Graduation June 2022

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Declaration

I, Vincent Vermaak, declare that this thesis, entitled: "*Homogeneous nickel(II) catalysed transfer hydrogenation of unsaturated compounds*", submitted in fulfilment of the requirements for the degree *Doctor of Philosophy in Science with Chemistry*, is my own work, except where acknowledged in the text, and has not been submitted in whole or in part to any other tertiary institution.

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Yours sincerely,

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Abstract

A variety of well-known N-donor ligands, some synthesised, i.e. bis(pyrazolyl-1-methyl)pyridine (**L3.1**, **L4.1**, **L5.1**) and bis(2,5-dimethylpyrazolyl-1-methyl)pyridine (**L3.2**, **L4.2**), and others commercially sourced, i.e. phenanthroline (**L3.3**), bipyridine (**L3.4**), 2,2'-dipyridylamine (**L3.5**), ethylene diamine (**L3.6**, **L4.4**, **L5.2**), 1,2-diaminocyclohexane (**L5.3**) and ortho-phenylenediamine (**L5.4**) were combined with $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ and other nickel(II) salts to generate *in situ* Ni(II) pre-catalysts. All ligands synthesised in this study were characterised with Fourier transform infrared (FT-IR) and nuclear magnetic resonance (NMR) spectroscopy as well as atmospheric pressure chemical ionisation mass spectrometry (APCI-MS). The *in situ* Ni(II) pre-catalysts were used in the transfer hydrogenation (TH) of quinolines, nitriles and alkenes with ammonia borane (AB) serving as the source of H_2 . Optimisation of the reaction conditions for quinoline TH showed that 1 mol% of Ni/**L3.1** combined with one equivalent of AB could successfully convert quinoline to 1,2,3,4-tetrahydroquinoline (97% conversion, 90% isolated yield) in 30 minutes at 25 °C. Several quinoline derivatives formed part of the study with moderate to high yields (26 - 90%) obtained for the desired products. Investigation into the TH mechanism of quinoline illustrated the presence of a 1,4-dihydroquinoline intermediate with Ni(II)-hydride species responsible for the high activity observed. Further evaluation, using the same optimised reaction conditions as mentioned above, for the TH of nitriles revealed the versatility of the *in situ* prepared Ni/**L4.1** and Ni/**L4.4** pre-catalysts. Various nitriles could successfully undergo chemoselective TH to their secondary amine products (40 - 97% yields). A very high turnover number (TON) of 5100 was achieved with Ni/**L4.1** using only 0.01 mol% of the pre-catalyst. Using α -picoline borane (without dissociable protons) and external dihydrogen (H_2) during mechanistic elucidation, enabled the postulation of a two-step TH mechanism of benzonitrile, i.e. i) AB dehydrogenation followed by ii) benzonitrile hydrogenation. The dehydrogenation of AB to determine the potential amount of H_2 that can be released was investigated and revealed that an almost quantitative amount (2.96 equivalents) of H_2 was produced using 1 mol% of Ni/**L4.1**. Finally, the TH of aromatic- and aliphatic alkenes along with α,β -unsaturated esters were investigated using 1 mol% of Ni/**L5.2**. Successful conversion of aromatic alkenes (97 - 100% yield) was observed at 50 °C in 30 minutes, whereas the aliphatic alkenes only required 25 °C to be converted in 75 to 99% yields after one hour. Chemoselective TH of α,β -unsaturated esters to saturated esters (35 - 100% yield) was achieved under the same reaction conditions as those used for the aromatic alkenes. Mechanistic elucidation of the TH of styrene was conducted in the same manner as was done for benzonitrile. It was again concluded that borane activates H_2 leading to the postulation of a two-step TH mechanism, which is responsible for the conversion of styrene to ethylbenzene using AB as the source of H_2 .

Key terms: homogeneous, transfer hydrogenation, nickel(II), ammonia borane, quinoline, nitrile, alkene.

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List of abbreviations

^1H or ^{13}C NMR	proton or carbon-13 nuclear magnetic resonance
AB	ammonia borane ($\text{H}_3\text{N}-\text{BH}_3$)
Cy	cyclohexyl
DACH	1,2-diaminocyclohexane
DMAB	dimethylamine borane
dpa	diphenyl acetylene
ee	enantiomeric excess
FA	formic acid
FT-IR	Fourier transform infrared
GBL	γ -butyrolactone
GC	Gas chromatography
ICP-AES	inductively coupled plasma - atomic emission spectrometry
ICP-MS	inductively coupled plasma - mass spectrometry
^iPr , ^tBu	isopropyl, tert-butyl
Me, Ph	methyl, phenyl
Mes	mesitylene
MS	mass spectrometry
NP	nanoparticle
NR	no reaction
OAc	acetate
RT	room temperature
TH	transfer hydrogenation
TON	turnover number
Tp	tris(3,5-dimethylpyrazolyl)borate
triphos	bis(2-diphenylphosphinoethyl)phenyl-phosphine
XRD	x-ray diffraction

Preface

Format of thesis

This thesis is being submitted in article format, as allowed by the North-West University (NWU). The different manuscripts - published and unpublished - that have been prepared form part of the study utilising homogeneous Ni(II) pre-catalysts for the transfer hydrogenation of unsaturated compounds (Chapters 3 - 5). In addition to these manuscripts, an introduction and problem statement for the study (Chapter 1), a literature overview (Chapter 2, review article) and a summary of the findings and future recommendations (Chapter 6) have been included in the thesis.

According to the Quality Manual 2020 for the Faculty of Natural and Agricultural Sciences at the North-West University (NWU), the publication of the manuscripts is not a prerequisite for submitting a *Doctor of Philosophy* thesis in article format. However, at least one of the manuscripts should have been accepted for publication. Therefore, the prerequisite of the NWU was exceeded.

Format of numbering and referencing

It should be noted that the formatting, referencing style, the numbering of tables, figures and schemes, numbering of the ligands and the general outline of the manuscripts were adapted to ensure uniformity throughout the thesis. The format of the manuscripts, which have been submitted and/or published adheres to the author guidelines as stipulated by each peer-reviewed journal and may appear in a different format to what is presented in this thesis. The headings and original technical content of the manuscripts were not modified from the submitted and/or published versions, and only minor spelling and typographical errors were corrected.

Consent by co-authors

The co-authors listed below were informed and gave consent that Vincent Vermaak may submit this thesis, entitled: "*Homogeneous nickel(II) catalysed transfer hydrogenation of unsaturated compounds*", in article format for the degree *Doctor of Philosophy in Science with Chemistry*, at the North-West University:

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Contributions by authors

- Vincent Vermaak: Responsible for conceptualisation, idea generation, decisions/interpretation, acquisition of data and compilation of articles.
- Prof. Andrew J. Swarts (promoter): Responsible for the origin of this work, substantiated by ideas and recommendations.
- Prof. Hermanus C.M. Vosloo (co-promoter): Responsible for additional recommendations and corrections.

Research outputs

The (un)published article(s)/manuscript(s) as mentioned below form part of this thesis entitled: “Homogeneous nickel(II) catalysed transfer hydrogenation of unsaturated compounds”, and contribute towards the article format used. Below each published article, the author guidelines for the specified journal can be found.

Chapter 2 (review article)

V. Vermaak, H.C.M. Vosloo and A.J. Swarts. The development and application of homogeneous nickel catalysts for (de)hydrogenation reactions. Submitted to *Catalysis Reviews*. Status: Under review.

<https://www.tandfonline.com/action/authorSubmission?show=instructions&journalCode=lcitr20>

Chapter 3 (research article)

V. Vermaak, H.C.M. Vosloo, A.J. Swarts. Fast and efficient nickel(II)-catalysed transfer hydrogenation of quinolines with ammonia borane. *Adv. Synth. Catal.* **2020**, 362, 5788. DOI: 10.1002/adsc.202001147.

https://onlinelibrary.wiley.com/page/journal/16154169/homepage/2258_author.html

Chapter 4 (research article)

V. Vermaak, H.C.M. Vosloo, A.J. Swarts. Chemoselective transfer hydrogenation of nitriles to secondary amines with nickel(II) catalysts. *Mol. Catal.* **2021**, 511, 111738. DOI: 10.1016/j.mcat.2021.111738.

<https://www.elsevier.com/journals/molecular-catalysis/2468-8231/guide-for-authors>

Chapter 5 (research article)

V. Vermaak, H.C.M. Vosloo, A.J. Swarts. An inexpensive and simple nickel(II) catalysed transfer hydrogenation of alkenes with ammonia borane. Submitted as a Research Article to *Organic Chemistry Frontiers*.

https://publish.acs.org/publish/author_guidelines?coden=orlef7

Chapter 1

Introduction towards the Ni(II)-catalysed
transfer hydrogenation of quinolines, nitriles
and alkenes with ammonia borane

1.1 Problem statement and research justification

Homogeneous transfer hydrogenation (TH) reactions have become an invaluable method for organic chemists to transform unsaturated compounds to their respective hydrogenated products.¹ This method finds application in several industry-relevant processes, resulting in fine chemicals for the pharmaceutical and agricultural environments.² It is preferred above direct hydrogenation with dihydrogen (H₂) gas due to its flammability and danger caused by pressurised cylinders being stored over prolonged periods.³ Additional advantages include the use of H₂-donors that are readily available, inexpensive and easy to handle.⁴ Transfer hydrogenation reactions utilise an H₂-donor to either i) directly transfer the H₂ from the donor to the substrate (first illustrated by the Meerwein-Ponndorf-Verley reduction)⁵ or ii) hydrogenate the substrate via the formation of a metal-hydride intermediate.⁶

Different sources of H₂-donors, including alcohols, formic acid (FA), primary amines, Hantzsch ester, formate salts and dienes, have been utilised for TH reactions with great success.^{4, 6-7} Most recently, amine borane adducts⁸ have also been investigated and shown to be successful in the catalyst-mediated TH of several unsaturated compounds, i.e. alkenes,⁹ alkynes,^{9c, 10} nitriles,^{9b, 11} N-heteroaromatics,^{9a, 12} imines^{9b, 13} and nitroarenes.^{11c, 11d, 14} These transformations are dominated by Co(II)-, Cu(I)-, Bi(I), Pd(II), Re(II) and borane catalysts.

Unfortunately, the homogeneous AB-facilitated TH of unsaturated compounds using Ni(II) pre-catalysts seems to be scarce. Some examples of heterogeneous Ni catalysed TH of nitro-, nitrile-, alkyne- and quinoline-containing compounds with AB do exist.^{11a, 11c, 15} However, drawbacks include excess amounts (3 - 10 equivalents) of AB required and noble-metal impregnation (Pd) when heterogeneous Ni catalysts are used.

The only example employing a homogeneous Ni catalyst with AB as the source of H₂ is a study by García and Barrios-Francisco.¹⁶ They investigated the TH of alkynes using a 2-bis(diisopropylphosphino)ethane ligated Ni(0) complex. The long reaction times (72 hours) and elevated reaction temperatures (80 °C) required were, however, drawbacks. The use of phosphine ligands is also regarded as a problem due to their toxicity, laborious preparation, cost and sensitivity to moisture.¹⁷

From the above-mentioned studies, it can be seen that Ni might serve as a promising non-noble transition metal to be used in TH reactions, where AB functions as the source of H₂. Further evidence is found in its ability to catalyse the dehydrogenation of AB¹⁸ and act as a successful hydrogenation catalyst.¹⁹ The involvement of Ni in both of these reactions

provides a precedent that Ni would be able to catalyse the TH of unsaturated compounds using AB as the source of H₂. Further exploration of Ni as a homogeneous catalyst for the TH of compounds containing unsaturated C-N- and C-C bonds, i.e. quinolines, nitriles and alkenes, therefore needs to be conducted.

1.2 Aim and objectives

The aim of this study is to utilise various *in situ* prepared N-donor (bidentate and tridentate) ligated Ni(II) pre-catalysts for the TH of quinolines, nitriles and alkenes using AB as the source of H₂.

The objectives that are set to achieve this aim are as follows:

- a) Synthesis and characterisation of bis(pyrazolyl-1-methyl)pyridine ligands.
- b) Optimisation of reaction conditions for the TH of quinolines using *in situ* prepared N-donor ligated Ni(II) pre-catalysts, followed by a substrate scope evaluation.
- c) Evaluation of *in situ* prepared N-donor ligated Ni(II) pre-catalysts in the TH of nitriles using the optimised conditions found in b).
- d) Evaluation of *in situ* prepared N-donor ligated Ni(II) pre-catalysts in the TH of alkenes using the optimised conditions found in b).
- e) Mechanistic elucidation to identify intermediates and active species formed during the TH of quinolines, nitriles and alkenes.

1.3 Outline of thesis

In *Chapter 2*, the history and development of Ni catalysts used in (transfer) hydrogenation and dehydrogenation reactions are described. It will illustrate the growth in knowledge with regard to ligand and Ni catalyst design used for both reactions moving towards less expensive and hazardous reaction conditions.

In *Chapter 3*, the Ni(II)-catalysed TH of quinolines using ammonia borane as the source of H₂ is described. An investigation into the mechanism will be discussed with observations made with regard to intermediate and active species formation.

In *Chapter 4*, the chemoselective TH of nitriles to secondary amines catalysed by an *in situ* prepared N-donor ligated Ni(II) pre-catalyst will be described. Mechanistic elucidation with regard to deuterium labelling and the potential of the pre-catalysts to release H₂ from ammonia borane will also be discussed.

In *Chapter 5*, the Ni(II) catalysed TH of aromatic- and aliphatic alkenes, along with the chemoselective TH of α,β -unsaturated esters to their respective products, using AB as the source of H_2 , are described. The importance of the borane moiety and how it contributes to the description of a two-step TH process are also discussed.

In *Chapter 6*, the final conclusions and contributions to the scientific community will be discussed. Methods and ideas to improve upon the current research will also be outlined and discussed.

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Chapter 2

The development and application of
homogeneous nickel catalysts for
(de)hydrogenation reactions

2.1 Introduction

Being one of the earliest metals incorporated in catalysis, nickel (Ni) enjoys much attention as a versatile catalyst. Its first isolation dates back to 1751, with the purification and application thereof more than a century later (1897), when Sabatier utilised it as catalyst for heterogeneous ethylene hydrogenation. For this research, he was awarded the 1912 Nobel Prize in Chemistry.¹ The importance of Ni is evidenced by the 2.7 million tonnes of Ni that was produced worldwide in 2019, which represents a twofold increase in production since 2000 (Figure 2.1).² Throughout the last few decades, great advancements have been made utilising Ni in several chemical transformations such as cross-coupling,³ nucleophilic allylation and reductive coupling reactions.⁴

In addition, reactions focusing on (de)hydrogenation with homogeneous Ni complexes have received increased attention.⁵ The advantages of these homogeneous systems compared to similar heterogeneous systems is the increase in activity observed for certain reactions, decreased catalyst loadings, less additives required and more benign reaction conditions that include lower temperatures and pressures.⁶

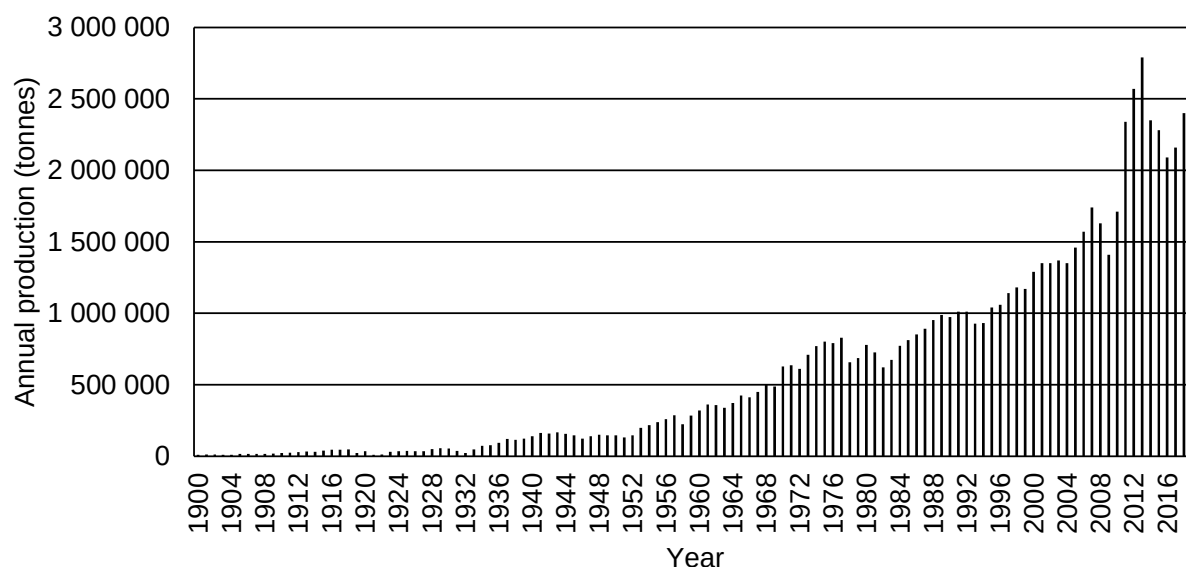


Figure 2.1 Annual worldwide nickel production from 1900 to 2019 measured in tonnes.²

Ni remains of great importance due to its availability, cheapness and low toxicity. Although it is identifiable as a first-row transition metal, it shares catalytic properties with the platinum group metals (PGM's), thereby making it a good candidate for chemical transformations such as hydrogenation and dehydrogenation,⁴ as will be described in further sections.

Describing each chemical transformation that has been accomplished by Ni would be exhaustive. Accordingly, the focus of this review will direct the reader's attention to the various homogeneous Ni complexes that have been developed over the last three decades and have found application in the hydrogenation of alkynes, alkenes, ketones, aldehydes, CO₂, nitriles, imines, hydrazones and nitro compounds. The dehydrogenation of alcohols, amines and FA, with an emphasis on H₂ production, will also be discussed. The importance of Ni complexes and how its intrinsic properties contribute to its versatility will be illustrated.

2.2 Hydrogenation

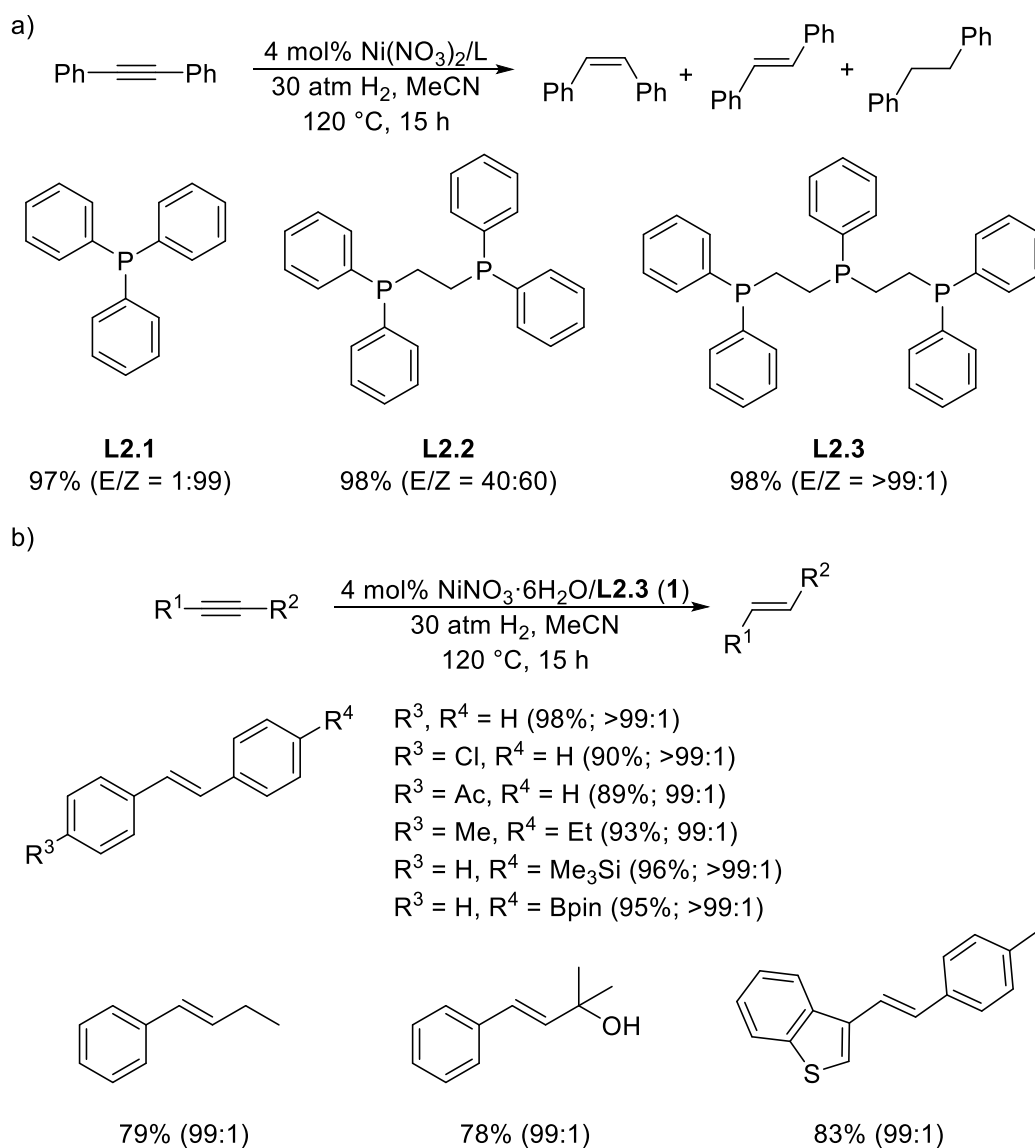
A broad scope of homogeneous Ni catalysed hydrogenation research is available describing the transformation of a variety of C-C- (alkynes, alkenes), C-N- (nitriles, imines, hydrazones), C-O- (ketones, aldehydes, CO₂) and N-O (nitro) containing compounds into their respective alkene, alkane, amine and alcohol products. For most hydrogenation reactions, hydrogen gas (H₂) remains the major hydrogen source to reduce unsaturated compounds.⁷ However, an alternative approach towards hydrogenation, i.e. transfer hydrogenation (TH), has become an important methodology with the application of alcohols, amines, ammonia borane (AB) and FA as sources of hydrogen. These sources are a greener and ultimately less hazardous option leading more research groups to redirect their focus towards transfer hydrogenation reactions. This section describes the research that has been conducted with homogenous Ni catalysts for the hydrogenation and TH of i) C=C-, ii) C≡C- iii) C-N-, vi) C-O- and v) N-O containing compounds.

2.2.1 Hydrogenation and transfer hydrogenation of C-C bonds

2.2.1.1 Hydrogenation and transfer hydrogenation of alkynes

The synthesis of compounds with C=C bonds remains important due to their high reactivity and being constituents of bioactive molecules in the pharmaceutical industry.⁸ The first known homogeneous Ni catalysed study on the semihydrogenation of alkynes toward stereodivergent alkenes employing H₂ was conducted in 2019.⁹ Beller's group found that an *in situ* prepared bis(2-diphenylphosphinoethyl)phenyl-phosphine (triphos, **L2.3**) ligated Ni(NO₃)₆·6H₂O pre-catalyst, **1** (4 mol%), activated by 30 atm H₂ at 120 °C, could convert (98%) diphenyl acetylene to E-stilbene (>99:1) in 15 hours. Stereoselectivity could be altered to Z-stilbene (99:1) by using monodentate phosphines, i.e. triphenylphosphine (PPh₃, **L2.1**) (Scheme 2.1a). Various alkynes were evaluated with high yields (79 - 98%) and E:Z ratios of >99:1 being obtained (Scheme 2.1b). Mechanistic investigations showed that isomerisation of an initially formed Z-alkene to E-alkene via a Ni(II) hydride is followed. Ligand-free Ni(II)

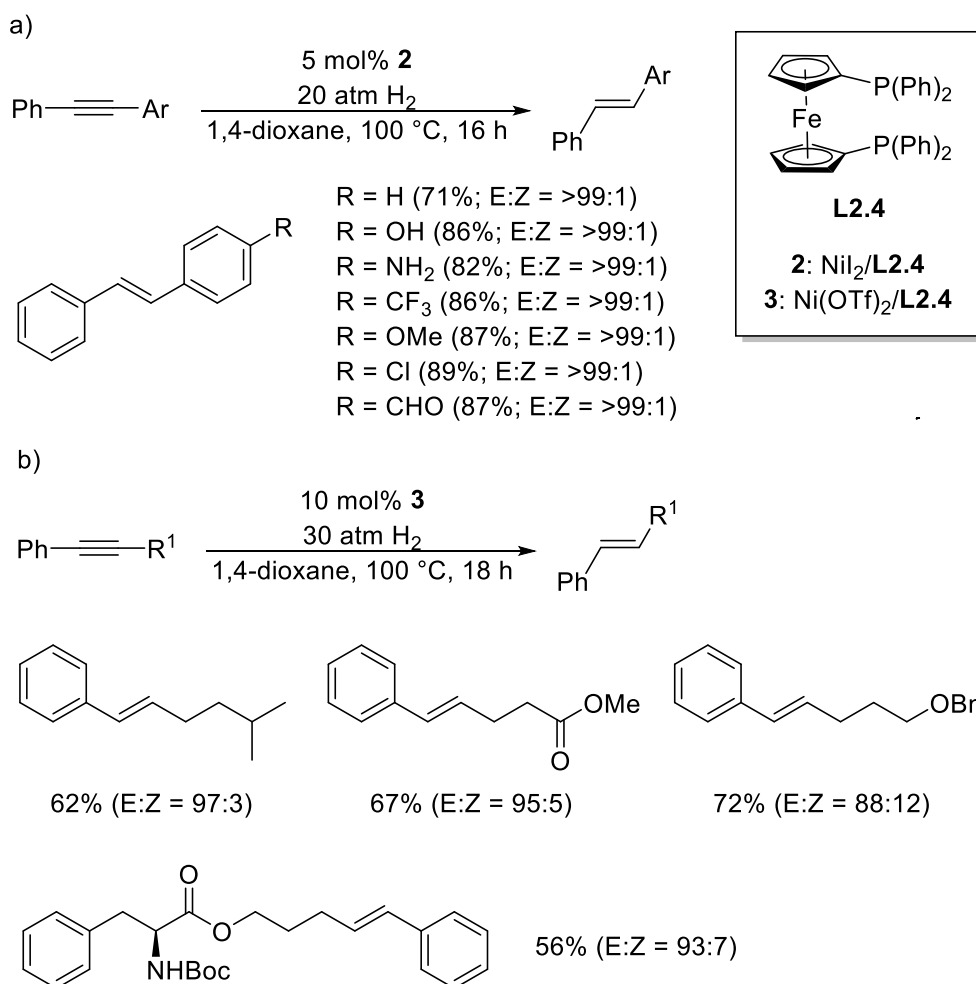
salt utilisation also displayed great activity (70 - 95% yield) and selectivity towards Z-alkenes (>99:1) under the same conditions, but was found to be heterogeneous in nature, corresponding to previously conducted heterogeneous studies.¹⁰



Scheme 2.1 Semihydrogenation of alkynes towards stereodivergent alkenes with a) different phosphine ligated Ni pre-catalysts and b) with **1**. Percentages are representative of GC yields.⁹

More recently, Thiel and co-workers followed a similar methodology towards the synthesis of E-alkenes from alkyne semihydrogenation employing a commercially available Ni catalyst.¹¹ A 1,1'-bis(diphenylphosphino)ferrocene (**L2.4**) ligated NiI_2 pre-catalyst, **2** (5 mol%), was used with 20 atm H_2 at 100 °C to hydrogenate several aromatic and aliphatic alkynes towards E-selective alkynes in 16 hours (Scheme 2.2a). Yields of up to 89% could be obtained with an E:Z ratio of >99:1. An increase in the catalyst loading (10 mol% using $\text{Ni}(\text{OTf})_2/\text{L2.4}$, **3**), H_2

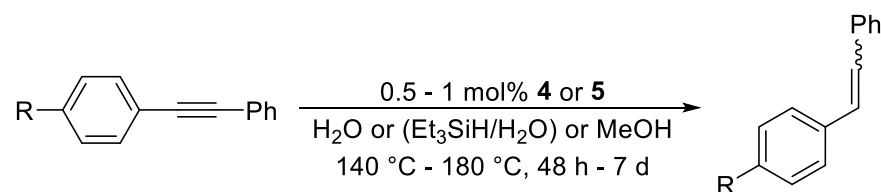
pressure (30 atm) and reaction time (18 hours) led to similar yields, however the E:Z ratio decreased significantly in some occasions (30:70) (Scheme 2.2b). Mechanistic evaluation corresponded with the study from Beller, confirming initial Z-alkene formation with subsequent isomerisation to E-alkenes via a proposed Ni(II) hydride.



Scheme 2.2 Semihydrogenation of alkynes towards E-selective alkenes with **2** and **3**. Percentages are representative of isolated yields.¹¹

The use of hydrogen donors for transfer hydrogenation has also been investigated for the hydrogenation of alkynes to alkenes. Barrios-Francis and García employed 1,2-bis(diisopropyl-phosphino)ethane (and tert-butyl derivative) ligated Ni(η^2 -C,C-alkyne) complexes, **4** and **5**, for the transfer hydrogenation of diphenyl acetylene (dpa) (Scheme 2.3).¹² H₂O, Et₃SiH/H₂O and MeOH were evaluated as hydrogen sources. Using 0.5 mol% of **4** or **5** with 350 equivalents of water in toluene-d₈ at 140 °C exclusive E-stilbene formation could be acquired after 12 days following a metal-mediated mechanism. With Et₃SiH/H₂O, under similar conditions, stereoselectivity was changed to Z-stilbene formation (98 % yield) at 180 °C in 48 hours, but a Cl-substituted dpa substrate resulted in the E-stilbene product. The

use of MeOH as alternative hydrogen source displayed the highest activity, yielding 99.5% of E-stilbene at 140 °C in 48 hours. Mechanistic elucidation revealed the isomerisation of Z-stilbene to E-stilbene for the H₂O and MeOH systems.



In Et₃SiH or H₂O:

R = CHO (100%; E:Z = 0:100)

R = OMe (20%; E:Z = 0:20)

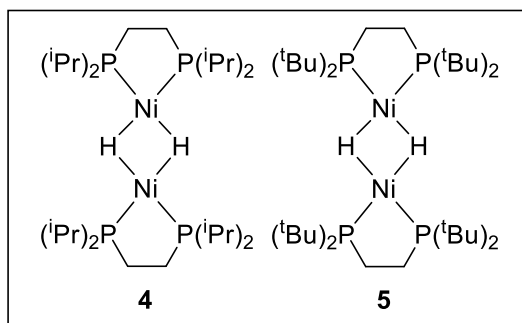
R = Cl (100%; E:Z = 99:1)

In MeOH:

R = CHO (100%; E:Z = 85:0)

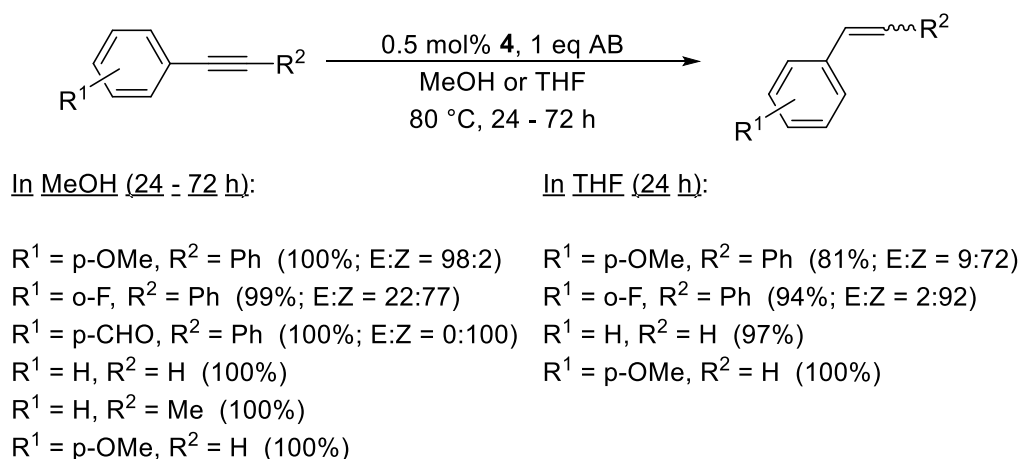
R = OMe (91%; E:Z = 90:1)

R = Cl (100%; E:Z = 99:1)



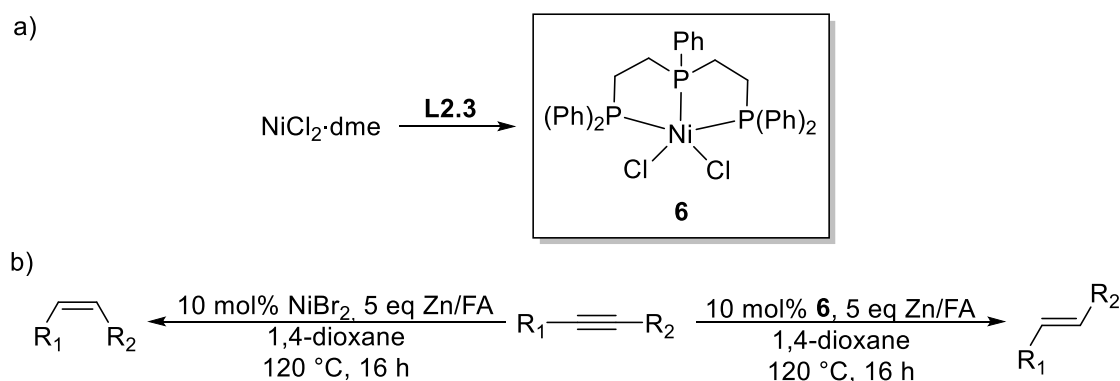
Scheme 2.3 Transfer hydrogenation of alkynes to stereodivergent alkenes with **4** and **5**. Percentages are representative of GC- and ¹H NMR yields.¹²

In a follow-up study, the same group utilised AB and NaBH₄ as alternative hydrogen sources for alkyne transfer hydrogenation.¹³ The *in situ* generated Ni(II) pre-catalyst **4** (0.5 mol%) was used with one equivalent of AB at 80 °C for 24 to 72 hours to convert alkynes to Z/E-alkenes (Scheme 2.4). When methanol was used as a solvent, it resulted in E-stilbene formation (86%), whereas coordinating and etheric solvents, i.e. THF, 1,4-dioxane, toluene and acetonitrile delivered Z-stilbene (75 - 90%). Thereafter, a few internal, terminal and substituted alkynes were evaluated using MeOH and THF as solvents with AB as the H₂ source. In MeOH, electron-withdrawing substituents on the phenyl group switched the stereoselectivity towards the Z-alkene. The use of NaBH₄ in MeOH/THF at 80°C for 72 hours mostly yielded Z-stilbene (80 - 100%), but an increase in the amount of NaBH₄ from one to two equivalents altered the stereoselectivity to the E-stilbene.



Scheme 2.4 Transfer hydrogenation of alkynes to stereodivergent alkenes with **4**. Percentages are representative of GC yields.¹³

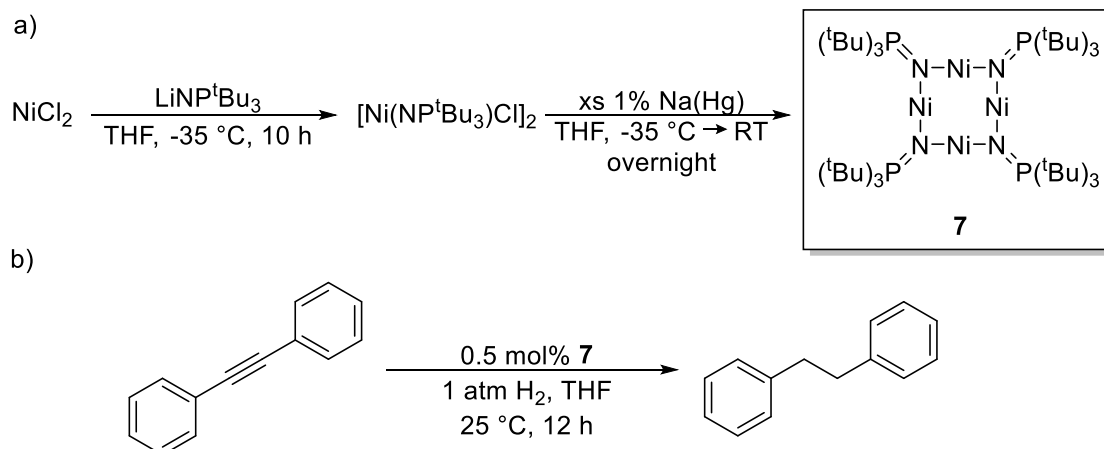
Richmond and Moran developed a different strategy by utilising Zn with FA as a hydrogen source.¹⁴ The introduction of **L2.3** (Scheme 2.5a) altered the stereoselectivity to E-alkenes (>95%) via Z-alkene isomerisation whereas using ligand-free NiBr₂ resulted in Z-alkenes (>95%) (Scheme 2.5b), similar to that observed by Beller.⁹ An *in situ* prepared pre-catalyst, **6** (10 mol%) with five equivalents of Zn and FA in 1,4-dioxane at 120 °C for 16 hours was required for both instances (pre-catalyst and ligand-free). The system could be applied to internal and terminal alkynes with high isolated yields and selectivity up to 99% and 95%, respectively. Alkynes with aliphatic substituents, however, delivered lower yields (20 - 77%) with selectivity towards the Z-alkene (>95%) for both instances.



Scheme 2.5 a) Formation of **6** and b) transfer hydrogenation of alkynes to Z- and E-selective alkenes.¹⁴

A novel tetrameric tri-tert-butylphosphoranimido ligated Ni(I) complex, [Ni(μ₂-NP^tBu₃)]₄, **7** (Scheme 2.6a), synthesised by Bunquin, Ferguson and Stryker, was able to catalyse the first complete hydrogenation of dpa (Scheme 2.6b).¹⁵ Using 1 atm of H₂ and 0.5 mol% catalyst in THF, dpa could be completely hydrogenated at 25 °C in 12 hours to produce 100% of 1,2-

diphenylethane. Further investigation with IR spectroscopy suggested the formation of terminal and bridging hydride ligands after exposure to H₂.



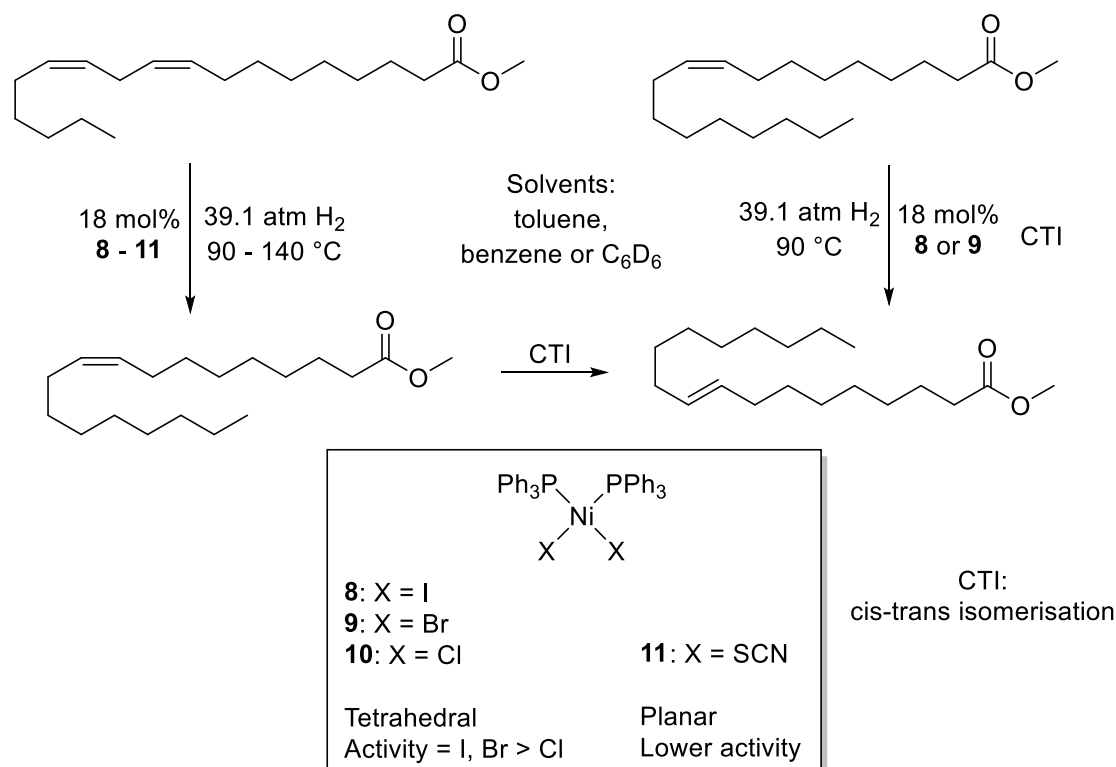
Scheme 2.6 a) Synthesis of **7** and b) complete hydrogenation of dpa towards 1,2-diphenylethane.¹⁵

2.2.1.2 Hydrogenation and transfer hydrogenation of alkenes

Alkenes can similarly undergo hydrogenation, compared to alkynes, and ultimately form alkane products, which find application in the petrochemical and pharmaceutical industry¹⁶. The earliest known study with a homogeneous Ni(II) catalyst towards alkene hydrogenation was conducted by Itatani and Bailar.¹⁷ Methyl linoleate and methyl oleate were subjected to mono-alkene hydrogenation under 40 atm of H₂ using 18 mol% of bis(triphenylphosphine)nickel halide (I, Br and Cl) complexes, **8** to **10**, at 90 to 140 °C for 3 to 12 hours (Scheme 2.7). For **8** and **9**, infrared analysis illustrated the formation of trans isomers in 23.9 to 84.7%, with selectivity for the desired product between 22.4 and 100%. Results obtained from catalysis with **10** was significantly lower at 2.1 to 6% product with 1.6% selectivity. The SCN complex, **11**, was ineffective, yielding only 1.5% of the trans product from methyl linoleate hydrogenation due to insufficient solubility in the benzene solvent.

During an initial study by Angulo, Kluwer and Bouwman, various *in situ* prepared bis(phosphine) ligated Ni(OAc)₂ complexes, **12**, **19** - **25** and **29**, were evaluated against 1-octene hydrogenation (Scheme 2.8).¹⁸ Using a catalyst loading of 0.2 mol% with 50 atm H₂ at 25 to 50 °C, TONs of up to 460 could be achieved in one hour in MeOH or EtOH. Comparative analysis revealed that the complexes with aliphatic substituents, **25** and **29**, show an increase in activity when a smaller ligand backbone (two carbons vs three carbons) is present. For the complexes containing aromatic substituents, **12** and **19**, this phenomenon

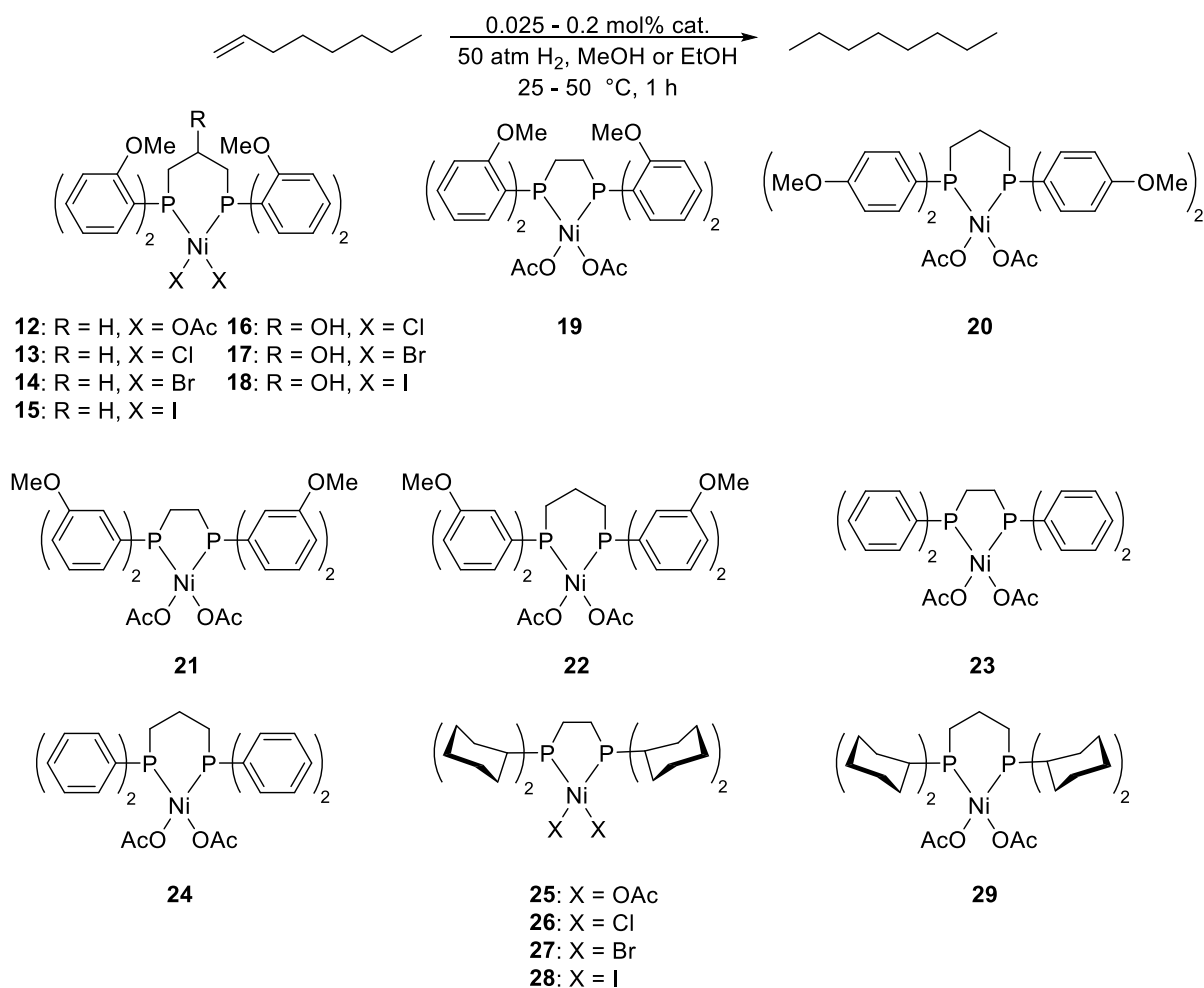
is inverted. Comparing the complexes with smaller backbones, **25** and **19**, illustrated that the aliphatic substituents increased the activity of the complex.



Scheme 2.7 Hydrogenation of methyl linoleate and methyl oleate with **8 - 11**.¹⁷

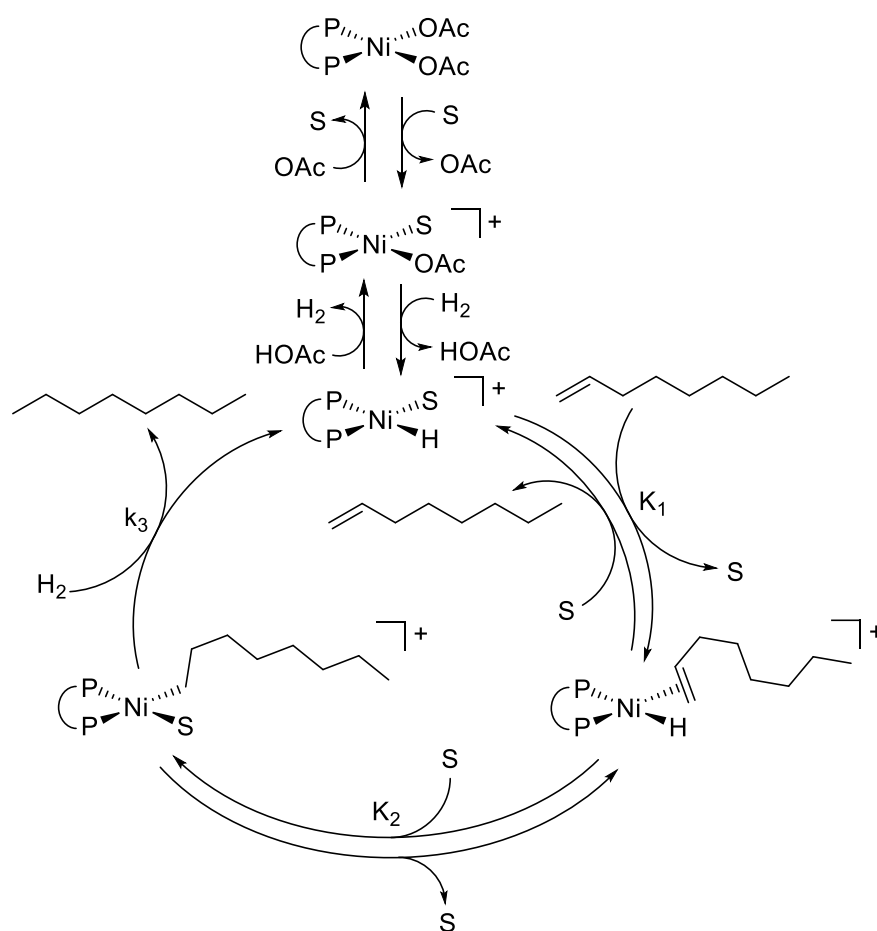
The same research group evaluated the kinetics of the hydrogenation of 1-octene and other alkenes by employing an *in situ* generated Ni(II) pre-catalyst, **12**.¹⁹ Various reaction parameters, i.e. temperature (30 - 60 °C), H₂ pressure (30 - 60 atm), Ni (0.35 - 2.81 mM, 0.05 - 0.5 mol%) and substrate (0.98 - 3.91 mM) concentration were studied in CH₂Cl₂. It was found that the hydrogenolysis termination step (k_3) served as the rate-determining step with catalytic rate constant (k_{cat}) values of up to 0.053 L²/(mol²s) (with 1-octene) (Scheme 2.10). Other alkene substrates, i.e. ethane, cyclooctene and 1,7-octadiene were also successfully hydrogenated (Scheme 2.9).

In a follow-up study by the same group, Ni(II) pre-catalysts, **13** to **18** and **26** to **28**, were characterised and investigated against 1-octene hydrogenation.²⁰ *In situ* generated **25** still displayed the highest activity (TON = 3000, 0.025 mol%) at 50 °C in MeOH with 50 atm of H₂ after one hour. The other pre-catalysts displayed activity under the same conditions, in decreasing order, as follows: **28** > **15** > **18**. In contrast, the chloride- and bromide derivatives displayed lower activity (Cl < Br < OAc¹⁹ > I), with 0.05 mol% catalyst under the same conditions.

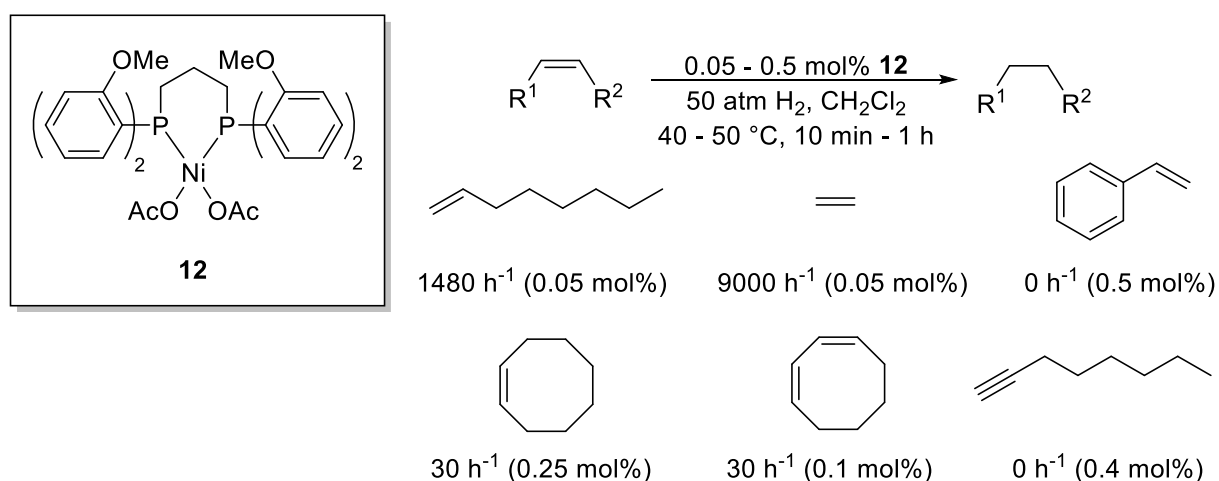


Scheme 2.8 Various diphosphine ligated Ni(II) pre-catalysts, **12** - **29**, used for the hydrogenation of 1-octene.

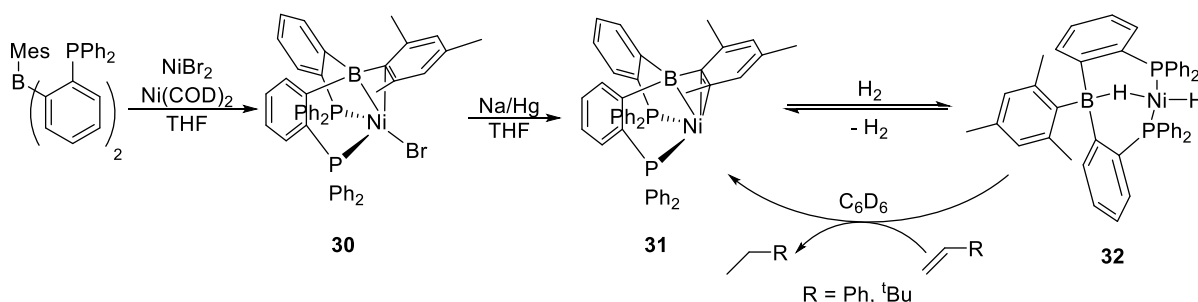
Harman and Peters illustrated the facile activation of H₂ via a Ni(II) borane complex.²¹ A B-mesityl derivative, [MesDPB^{Ph}]₂Ni, **31**, from a reduced 2-diphenylphosphinobenzyl ligated Ni(II) complex, **30**, was able to reversibly activate H₂ through oxidative addition to produce active Ni(II) hydride species, **32** (Scheme 2.11). Complex **32** (1 mol%) exhibited activity towards the hydrogenation of styrene and tert-butylethylene on NMR scale in C₆D₆ using 1 atm of H₂ at room temperature resulting in the rapid formation of ethylbenzene and 2,2-dimethylbutane in one hour.



Scheme 2.9 Proposed catalytic cycle of alkene hydrogenation with diphosphine ligated Ni(II) pre-catalysts.¹⁹

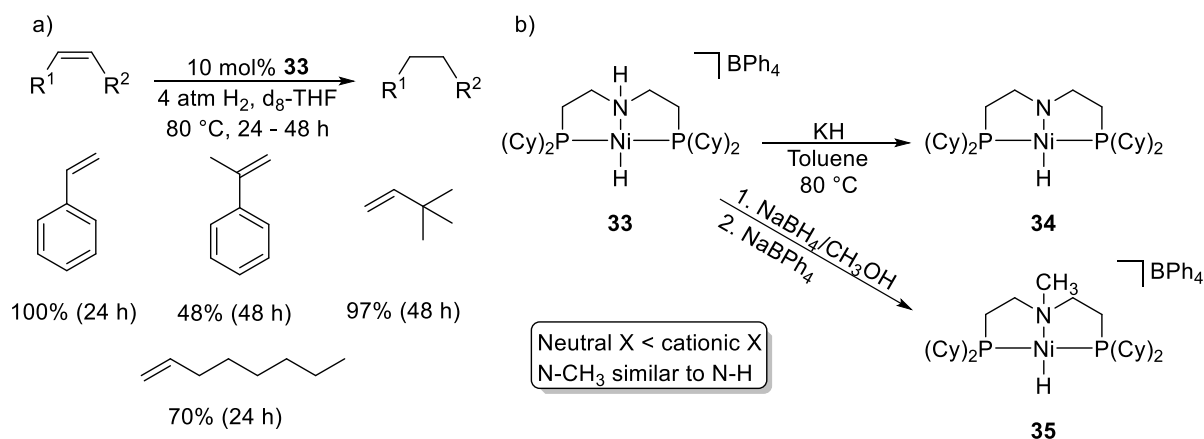


Scheme 2.10 Hydrogenation of alkenes with **12**.¹⁹ TOFs for each substrate are shown.



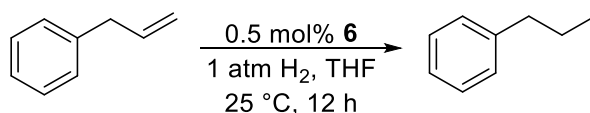
Scheme 2.11 Synthesis of [MesDPBPh]Ni, **31**, applied in the hydrogenation of styrene and tert-butylethylene.²¹

The alkene hydrogenation activity of Ni was also illustrated by Vasudevan, Scott and Hanson when they employed a cationic Ni(II) hydride complex, (PNHP^{Cy})Ni(H)]BPh₄, **33**, in alkene hydrogenation.²² The authors hypothesised that metal-ligand cooperativity may play a role in dihydrogen activation, as motivation for their catalyst design strategy. Terminal alkenes were subjected to hydrogenation with 10 mol% of **33** in d₈-THF at 80 °C using 4 atm H₂ for 24 to 48 hours yielding 48 to 100% alkane products (Scheme 2.12a). Upon treatment of the cationic complex with KH in toluene, a neutral Ni(II) hydride complex, **34**, was afforded but did not fare as well (Scheme 2.12b). Under the same reaction conditions, styrene was hydrogenated to ethylbenzene in 30% yield compared to 100% for the cationic complex. Complex **33** was methylated to form **35**, which displayed similar activity, suggesting that the cooperative interaction of N-H is not required for hydrogenation.



Scheme 2.12 a) Hydrogenation of alkenes with **33** and b) difference in catalytic activity between **33**, **34** and **35**. Percentages are representative of ¹H NMR yields.²²

A previously mentioned tetrameric tri-tert-butylphosphoranimido ligated Ni(I) complex, **6**, responsible for complete alkyne hydrogenation, was also successfully utilised in the hydrogenation of allylbenzene (Scheme 2.13).¹⁵ Propylbenzene was formed in 100% yield using 1 atm of H₂ with 0.5 mol% catalyst at 25 °C in 12 hours.



Scheme 2.13 Hydrogenation of allylbenzene with **6**.¹⁵

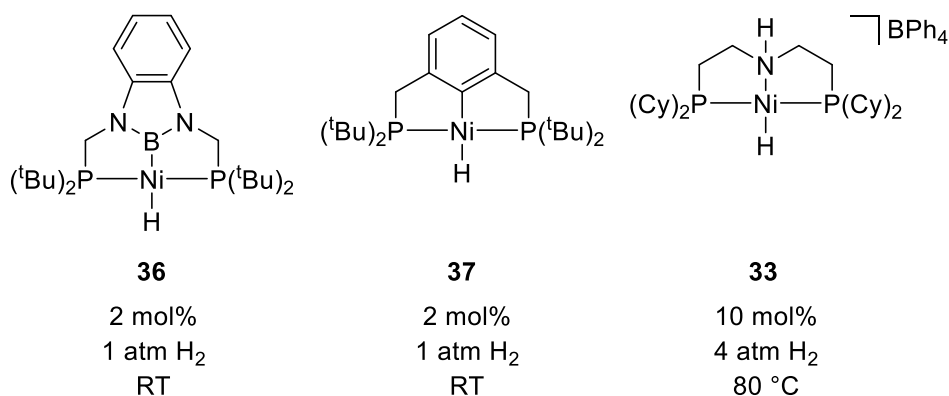


Figure 2.2 Ni complexes, **36**, **37** and **33** used for comparative analysis in alkene hydrogenation.

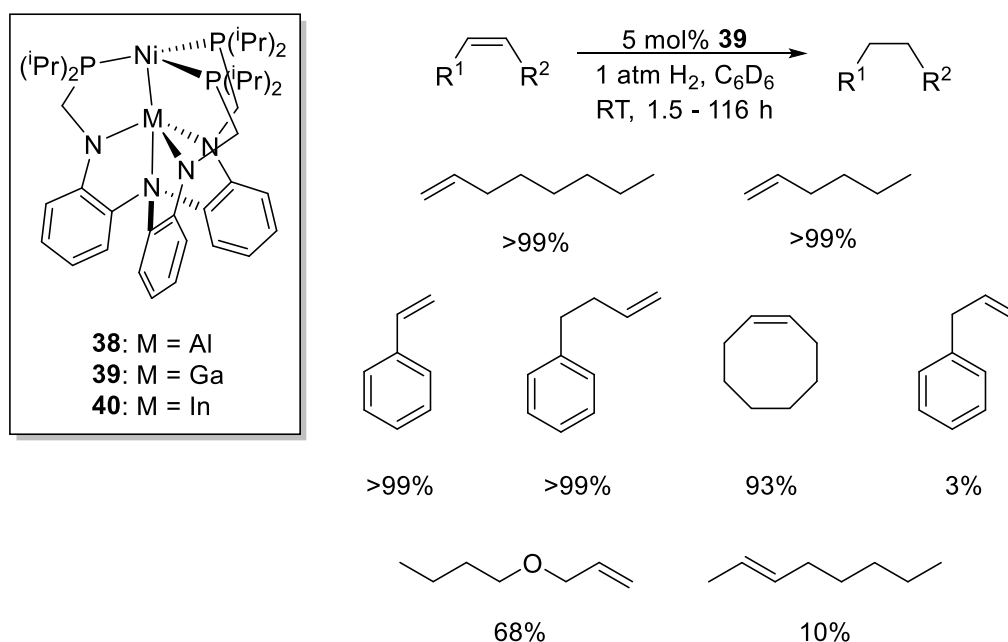
Table 2.1 Comparative analysis of reported TOFs of alkene hydrogenation with complexes **36**, **37** and **33**.

Substrate	36 ²³	37 ²³	33 ²⁴
	25 h ⁻¹ (100%)	0.7 h ⁻¹ (100%)	0.4 h ⁻¹ (100%)
	25 h ⁻¹ (64%)	0 h ⁻¹	0.4 h ⁻¹ (70%)
	5 h ⁻¹ (100%)	0 h ⁻¹	0.2 h ⁻¹ (97%)
	0.6 h ⁻¹ (100%)	0 h ⁻¹	not reported

TOF values given in h⁻¹ with ¹H NMR yield of corresponding alkane product in parenthesis.

Peters' group later developed boryl-containing complexes displaying enhanced activity towards the hydrogenation of alkenes with reversible H₂ activation.²³ Comparative analysis of the activity (TOF/h⁻¹) of three isostructural Ni-hydride complexes, (tBuPBP)NiH (**36**), (tBuPCP)NiH (**37**), (CyPnHP)NiH⁺ (**33**, from Hanson's group) (Figure 2.2), was evaluated

against terminal and internal alkenes, using 1 atm H₂ with 2 mol% catalyst in C₆D₆. The complex containing the boryl moiety, **36**, displayed the highest activity with a TOF of 0.6 to 25 h⁻¹ compared to 0 to 0.7 h⁻¹ achieved by **33** and **37**, which is attributed to the boryl-Ni cooperativity (Table 2.1). This is achieved by the strong trans influence of the boryl ligand, leading to strong σ -donation, ultimately destabilising the Ni-H bond. Migratory insertion of the alkene therefore becomes more favourable.

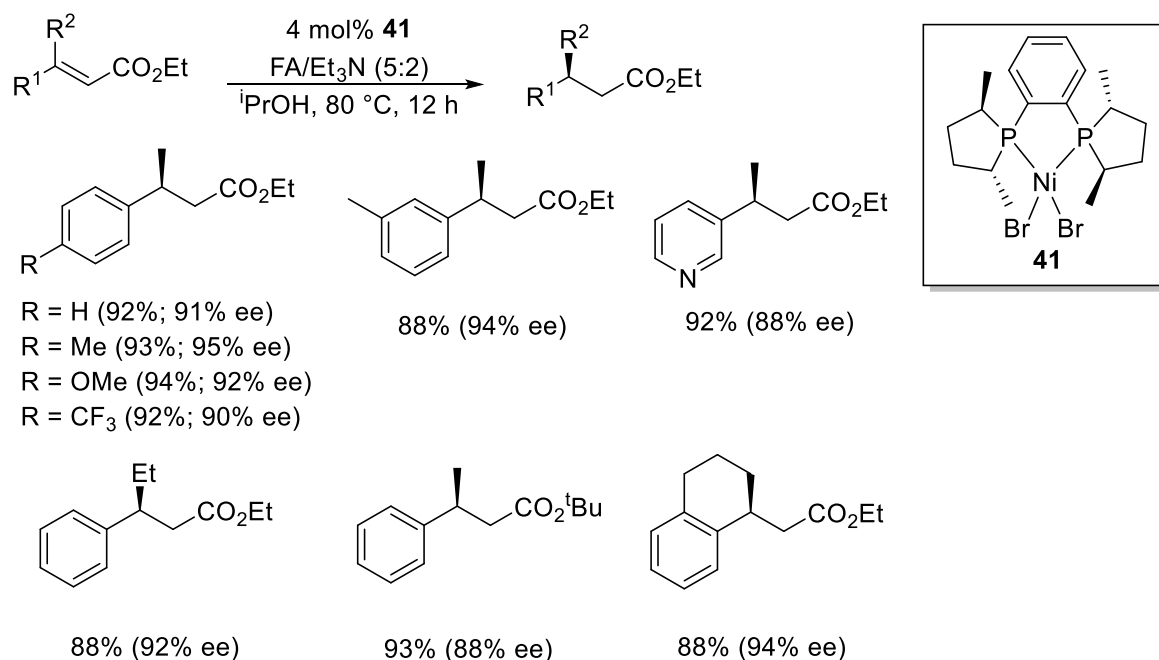


Scheme 2.14 Hydrogenation of alkenes with **39**. Percentages are representative of GC- and ¹H NMR yield of alkane product.²⁵

Cammarota and Lu exploited the boryl complexes from the above-mentioned studies to investigate the effect of other group 13 metals (Al, Ga and In) on the hydrogenation of alkenes.²⁵ Using 5 mol% of complexes **38** to **40** with 1 atm of H₂ at room temperature for 24 hours in C₆D₆, the only complexes that delivered significant hydrogenation results against styrene were those containing Ga (**39**, >99% yield) and In (**40**, 12% yield). Other alkenes were also evaluated and delivered good yields of up to 99% (Scheme 2.14). Complex **40** delivered divergent results for 1-octene due to the formation of octane and an isomer, 2-octene, with cis:trans ratio of 1:4. The difference in observed activity was thought to be reflected in the difference in their tendency to stabilise a HNi(μ -H)M intermediate because M-H can be destabilised as you progress down group 13.²⁶

Guo, Yang and Zhou investigated the asymmetric transfer hydrogenation of electron-deficient alkenes with an *in situ* prepared (R)-Me-Duphos ligated NiBr₂(DME) pre-catalyst, **41**, using FA/Et₃N (5:2) as the source of H₂ (Scheme 2.15).²⁷ Screening of several chiral

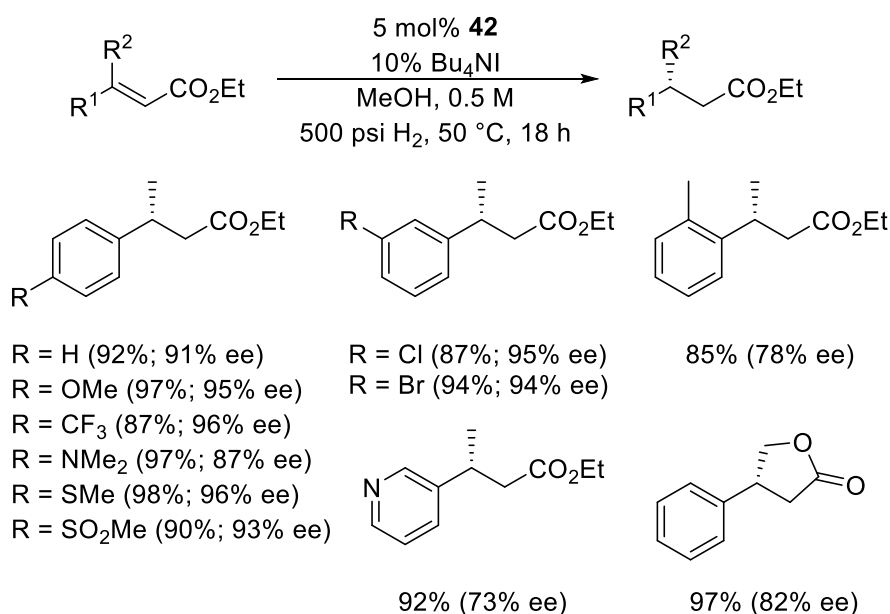
bisphosphines against β -methylcinnamate in *i*PrOH at 80 °C for 12 hours using 4 mol% pre-catalyst, revealed that the (R)-Me-Duphos ligand delivered the best results with 92% product yield and an ee of 91%. Several alkenes with varying phenyl substituents, electron-deficient moieties and chiral carbon substituents were evaluated and converted in high yields and % ee.



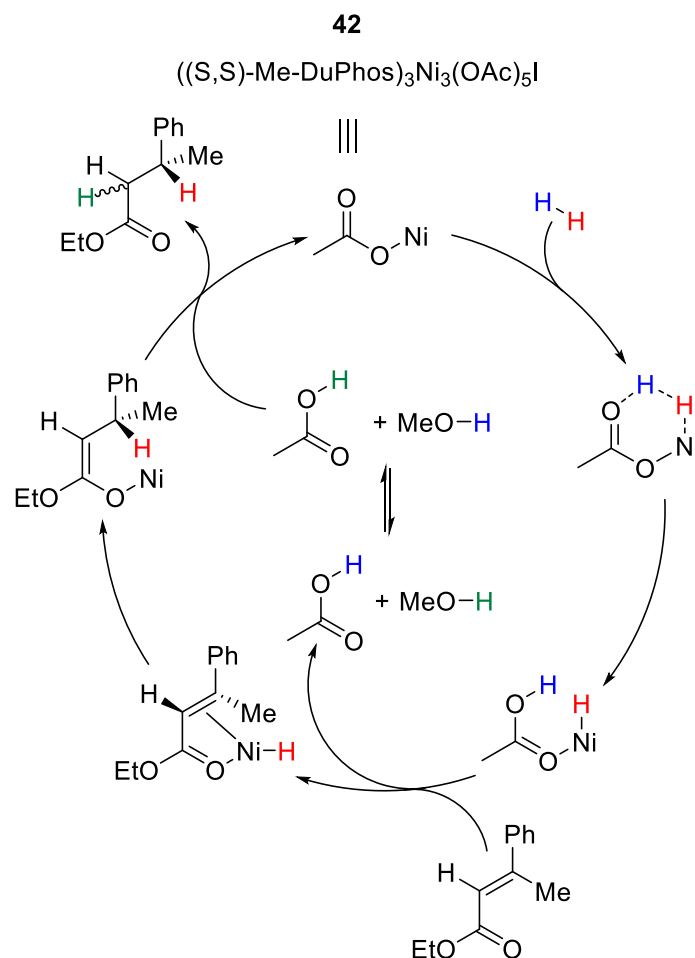
Scheme 2.15 Asymmetric transfer hydrogenation of electron-deficient alkenes with **41**. Percentages are representative of isolated yields.²⁷

A trimeric (Me-DuPhos)₃Ni₃(OAc)₅I pre-catalyst, **42**, activated by H₂, was utilised by Shevlin and co-workers for the first direct asymmetric hydrogenation of α,β -unsaturated esters (Scheme 2.16).²⁸ A high-throughput method was used to examine 192 chiral bidentate phosphine ligands (5.25 mol%) in combination with Ni(OAc)₂ (5 mol%) at 34 atm of H₂ and 50 °C in 4 days. It was seen that Me-DuPhos delivered the best ee (83%), nonetheless, with a low conversion of 44%. Various Bu₄NX (X = Cl, Br, I or OAc) additives were subsequently evaluated. Optimal results were obtained with the addition of 10% Bu₄NI, which increased conversion and ee to 100 and 94%, respectively, with a reduced reaction time of 18 hours being required. Addition of Bu₄NI altered the stereoselectivity of the dihydrocinnamate products when compared to the above-mentioned study by Guo and co-workers. Various enantioselective products could be produced following this method. Evaluation of NMR, X-ray diffraction (XRD) and MS data revealed that the resting state of the pre-catalyst is trimeric in equilibrium with mono- and dimeric Ni species (Scheme 2.17).

Yang, Xu and Zhou decided to focus on the asymmetric transfer hydrogenation of prochiral alkenes with FA/Et₃N towards the production of chiral α- and β-amino acid derivatives.²⁹ Numerous chiral phosphine ligands were screened with Ni(OAc)₂ for the hydrogenation of dehydro-β-acetamidobutyrate, and (S)-Binapine was found to be most effective (99% yield, 96% ee). A substrate scope towards the formation of β-acylamidoesters and α-acetamidoesters was performed using 5 mol% of **43** at 60 to 90 °C for 36 to 48 hours with 2-5:2 of FA:Et₃N (number is equivalent amount to the substrate) resulting in ee values of up to 99% (Scheme 2.18). Mechanistic evaluation revealed asymmetric hydride insertion followed by a protonation step of the Ni enolate species.



Scheme 2.16 Asymmetric hydrogenation of α,β-unsaturated esters with **42**. Percentages are representative of isolated yields.²⁸

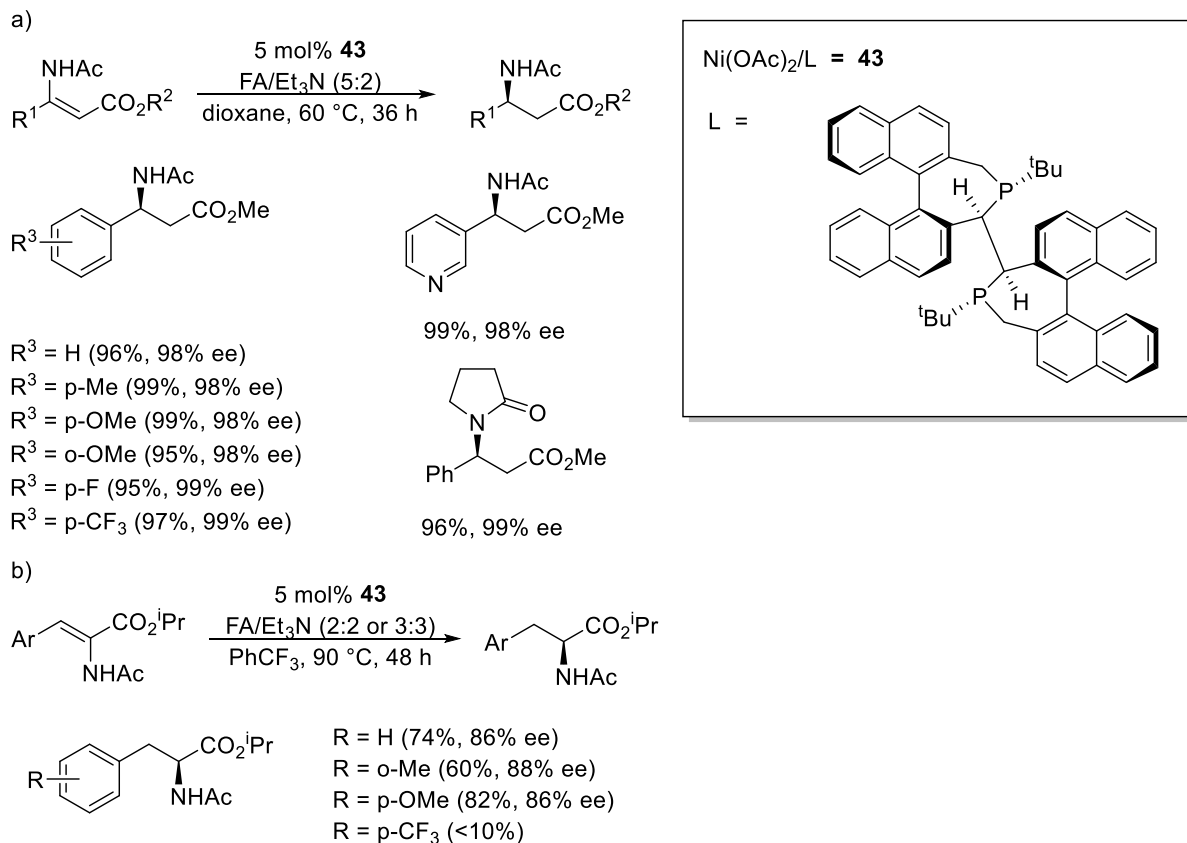


Scheme 2.17 Proposed catalytic cycle followed by **42** for the hydrogenation of α,β -unsaturated esters.²⁸

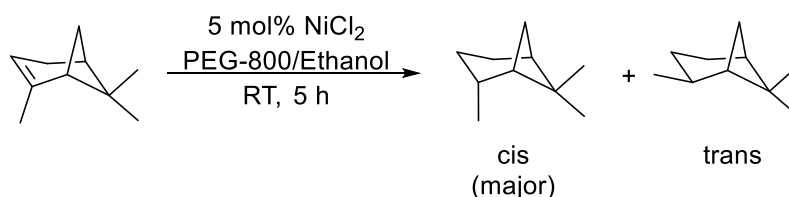
Li and co-workers focused their attention on the hydrogenation of α -pinene to cis-pinane with NaBH_4 as the source of H_2 .³⁰ An *in situ* combination of $\text{NiCl}_2 \cdot \text{H}_2\text{O}$ (5 mol%) and PEG-800 in EtOH could hydrogenate α -pinene (97%) to cis-pinane (98% selectivity) in five hours at room temperature using 50 mol% NaBH_4 (Scheme 2.19). The effects of the PEG chain length, solvent, different Ni salts and hydrogen sources were evaluated. Poisoning experiments revealed that one equivalent of CS_2 inhibits the reaction, indicating a heterogeneous system. However, the authors suggest that the active catalyst is still homogeneous in nature with Ni NPs *in situ* acting as a reservoir for the catalytic species.

α,β -Unsaturated enones (containing two alkene functionalities) also became a potential substrate to undergo hydrogenation. The group of García investigated the transfer hydrogenation of α,β -unsaturated enones with a previously utilised dimeric $\text{Ni}(0)$ catalyst, **4**.³¹ By using di(*p*-methoxybenzylidene)acetone as a model substrate with MeOH as the source of H_2 source, 1 mol% of **4** could catalytically convert the substrate (47%) in 48 h at 120 °C, yielding i, ii, iii or iv (Scheme 2.20). Tandem hydrogenation and alkylation were

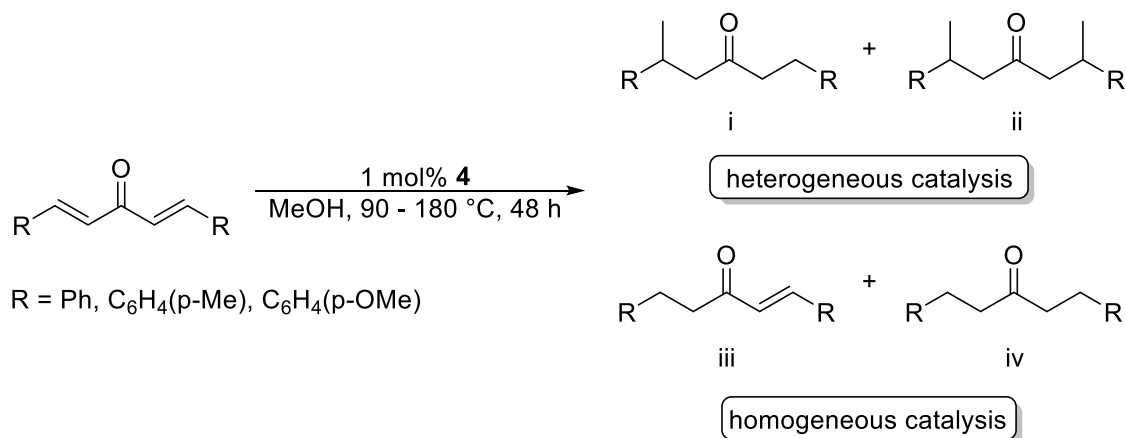
observed, suggesting that homogeneous and heterogeneous processes were followed, respectively. An increase in reaction temperature led to a more heterogeneous system being followed.



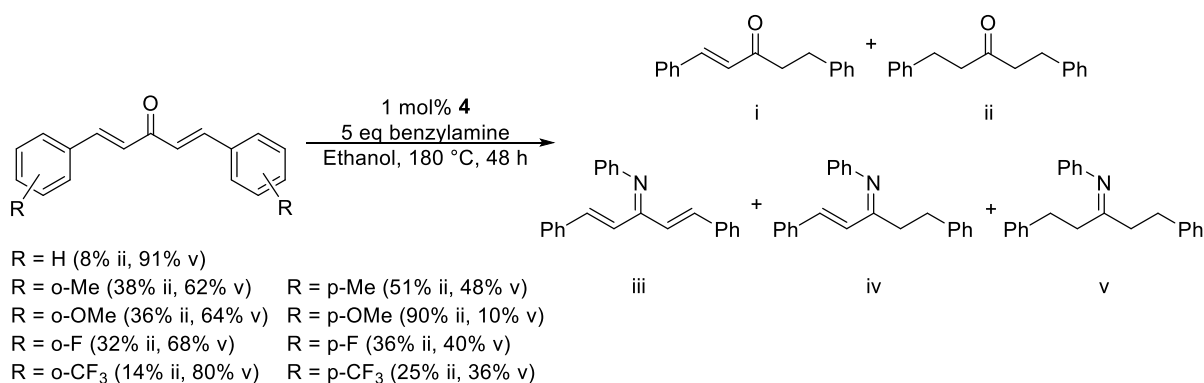
Scheme 2.18 Asymmetric transfer hydrogenation of prochiral alkenes with **43**. Percentages are representative of GC yields.²⁹



Scheme 2.19 Asymmetric hydrogenation of α -pinene to cis-pinane.³⁰



Scheme 2.20 Transfer hydrogenation of α,β-unsaturated enones with **4**.³¹



Scheme 2.21 Transfer hydrogenation of α,β-unsaturated enones with **4**. Percentages are representative of GC yields.³²

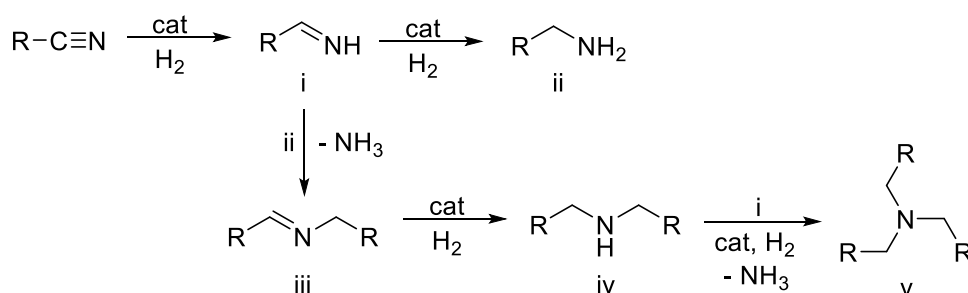
In a follow-up study, MeOH as the source of H₂ was exchanged for primary and secondary amines delivering interesting results.³² A mixture of hydrogenated and/or imine products (i - v) was formed, depending on the reaction conditions that were used, with ii and v being the major products (Scheme 2.21). After evaluation of several α,β-unsaturated enones, ancillary ligands and benzylamine as hydrogen donors, saturated imines remained the major product. This led the authors to propose a catalytic cycle describing the hydrogenation of the alkene groups via Ni(II) hydride intermediates and subsequent imine formation with a primary amine.

2.2.2 Hydrogenation and transfer hydrogenation of C-N bonds

2.2.2.1 Hydrogenation and transfer hydrogenation of nitriles

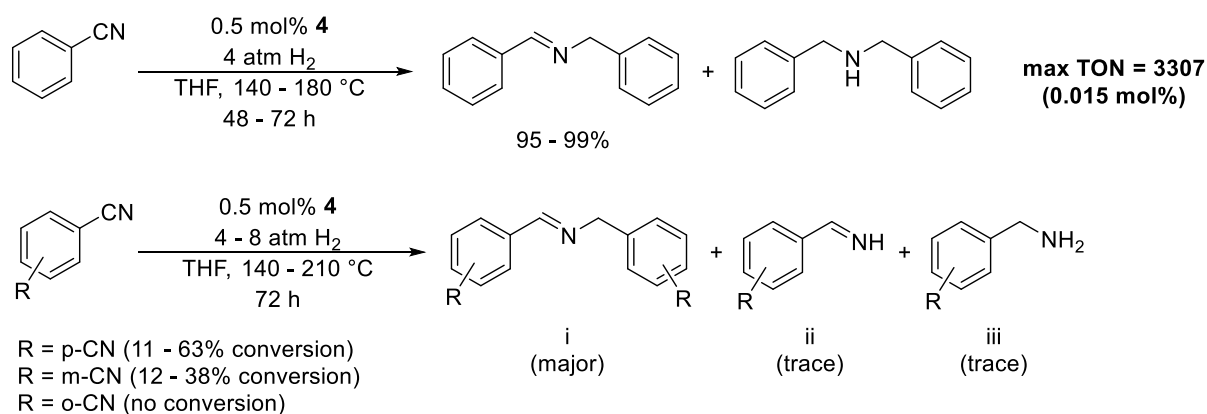
The hydrogenation of nitriles towards the formation of amines and imines has become an essential chemical transformation that finds application in various chemical industries, i.e. agrochemicals and pigments.³³ Their structure and reactivity also make them viable

candidates for use in the pharmaceutical industry as intermediates.³⁴ The downside concerning nitrile hydrogenation, however, is the problems experienced with product selectivity (Scheme 2.22).³⁵ Intermolecular side-reactions occur during the initial hydrogenation step leading to a variety of imines and amines being produced. The challenge remains to develop catalysts capable of selective product formation.



Scheme 2.22 Intermolecular side-reactions present during nitrile hydrogenation.

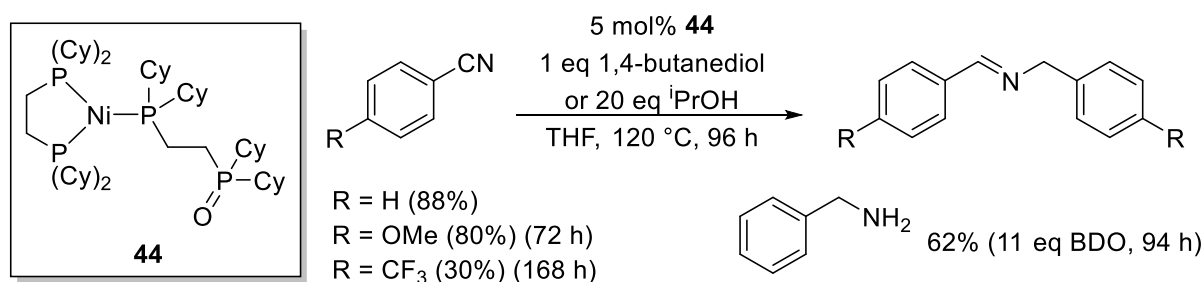
The group of García redirected their focus towards the use of H_2 for the selective hydrogenation of nitriles to their imine products.³⁶ Benzonitrile and its 1,2-, 1,3- and 1,4-dinitrile derivatives were subjected to hydrogenation using *in situ* prepared **4** (0.5 mol%) with 4 atm H_2 at 140 to 210 °C for 24 to 72 hours (Scheme 2.23). Benzonitrile underwent hydrogenation the easiest (100% conversion), with the 1,4-dinitrile derivative second (62% conversion), 1,3-dinitrile third (30% conversion) and the 1,2-dinitrile derivative showing no conversion.



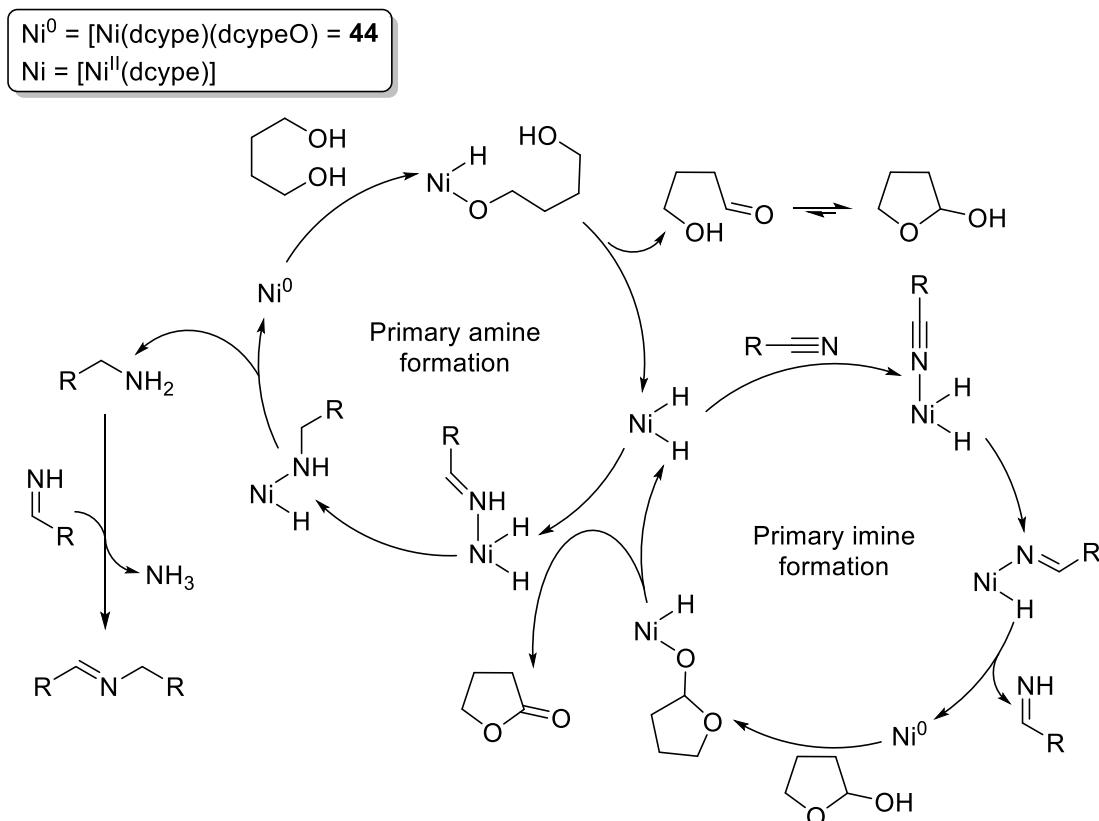
Scheme 2.23 Hydrogenation of benzonitriles with **4**.³⁶

The group decided to research cleaner and alternative ways of nitrile hydrogenation by employing alcohols as hydrogen donors.³⁷ 1,4-Butanediol (BDO) was evaluated as a hydrogen donor due to its capability of producing two equivalents of H_2 via dehydrogenation towards γ -butyrolactone (GBL). A dcype/dcypeO ligated $Ni(COD)_2$ catalyst, **44** (5 mol%),

was utilised for the hydrogenation of benzonitrile (BN) with 11 equivalents of BDO at 120 °C for 94 hours to produce 62% dibenzylamine (DBA) and 38% by-products (Scheme 2.24). Lowering the BDO amount to one equivalent altered the selectivity to 85% imine product (88% conversion). The same result was achieved with ⁱPrOH, albeit using 20 equivalents. Mechanistic insights illustrated the presence of an active dihydrido-Ni(II) intermediate (Scheme 2.25).



Scheme 2.24 Transfer hydrogenation of benzonitriles with **44**. Percentages are representative of GC yields.³⁷

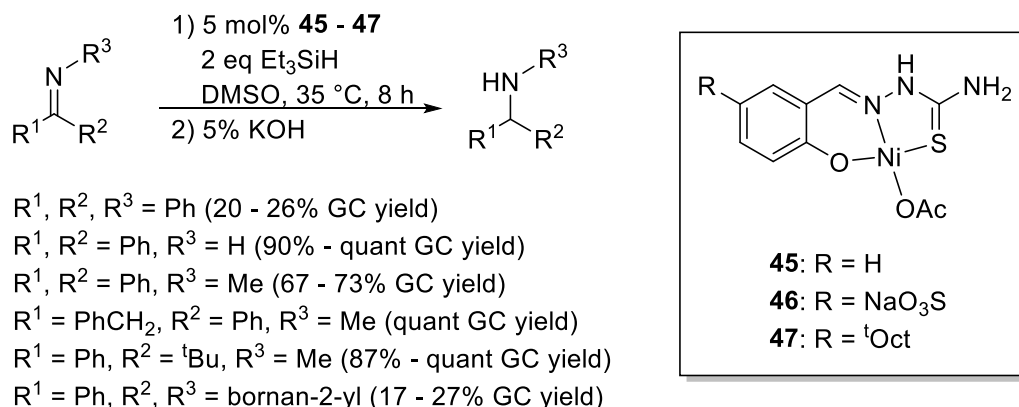


Scheme 2.25 Proposed catalytic cycle for the dehydrogenation of BDO and hydrogenation of nitriles with **44**.³⁷

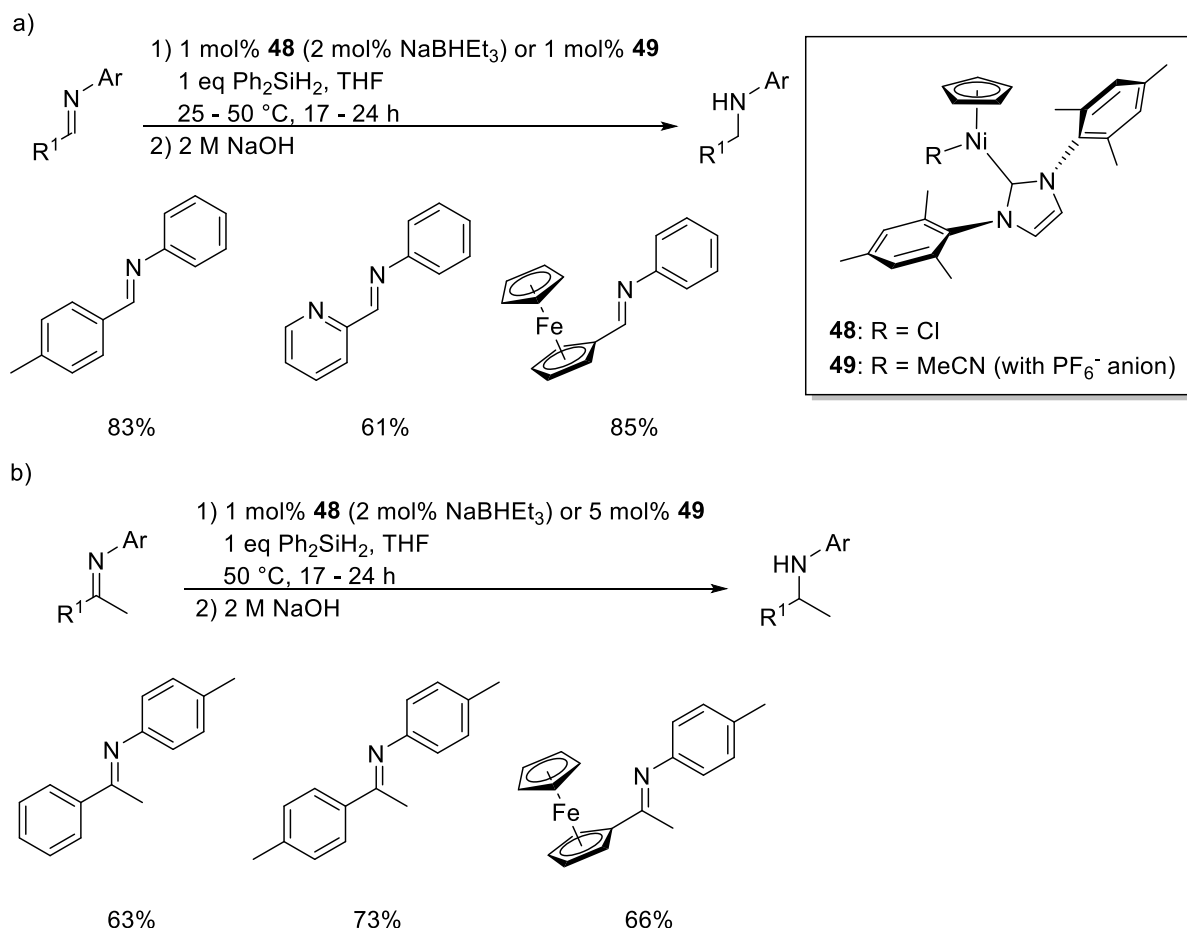
2.2.2.2 Transfer hydrogenation of imines and hydrazones

The first attempt at imine hydrogenation with a homogeneous Ni catalyst was conducted in 1995 by Vetter and Berkessel.³⁸ *In situ* pre-catalysts, **45** to **47**, used for the hydrosilylation of imines were prepared by combining Ni(OAc)₂ and thiosemicarbazones of o-hydroxy aromatic aldehydes. 5 mol% of **45** to **47** with two equivalents of Et₃SiH at 35 °C in DMSO were used for eight hours, after which protodesilylation afforded the corresponding secondary amines in up to 98% isolated yields (racemic mixtures) (Scheme 2.26). Activity for the three pre-catalysts in decreasing order were as follows: **45** > **46** > **47**, which may be ascribed to a difference in the polarity of each ligand, ultimately affecting the pre-catalyst's solubility.

Bheeter and co-workers continued work on the hydrosilylation of imines, but they employed N-heterocyclic carbene (NHC) ligated Ni(II) complexes for the catalytic reaction.³⁹ A neutral, **48**, and cationic Ni(II) complex, **49**, were successfully used as pre-catalysts for the hydrosilylation of various aldimines and ketimines (Scheme 2.27). Only 1 mol% of each complex was required with one equivalent of Ph₂SiH₂ at 25 to 50 °C to produce the corresponding secondary amines in isolated yields of up to 90% in 17 to 24 hours. Reaction of NaHBEt₃ with complex **48** or Ph₂SiH₂ with **49** resulted in the formation of an active Ni(II) hydride responsible for the high activity in the reaction.



Scheme 2.26 Hydrosilylation of imines with **45** - **47**.³⁸



Scheme 2.27 Hydrosilylation of a) aldimines and b) ketimines with **48** and **49**. Percentages are representative of isolated yields.³⁹

Kuhl, Schneider and Fort focused on NHC ligated Ni pre-catalysts but directed their attention to the transfer hydrogenation of imines.⁴⁰ Employing a variety of imidazolium salts as ligands, *in situ* Ni(0) pre-catalysts, **50** to **54** (5 mol%, Figure 2.3), were produced to catalyse the transfer hydrogenation of imines with five equivalents of pentan-3-ol (Et₂CHOH) as the hydrogen donor. Five equivalents of sodium hydride (NaH) were added as a reducing agent to convert i) Ni(acac)₂ to Ni(0) and ii) Et₂CHOH to Et₂CHONa. Pre-catalyst **50** displayed the highest activity (**50** > **52** > **53** > **54** > **51**) and was used for further evaluation of numerous imine substrates. Transfer hydrogenation of imines to secondary amines could be achieved in high yields (up to 99%) at 100 °C in 1 to 36 hours (Scheme 2.28). Although **50** showed tolerance towards sterically hindered substrates, dehalogenation was observed for a p-Cl derivative of N-Phenyl-N-(1-phenethyl)imine (last substrate in Scheme 2.28).

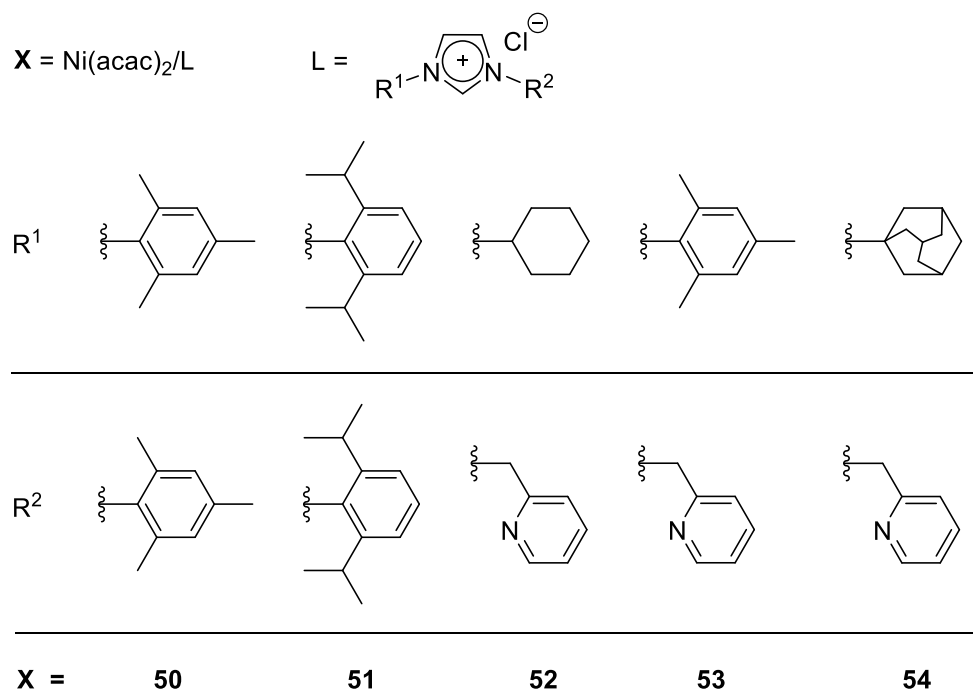
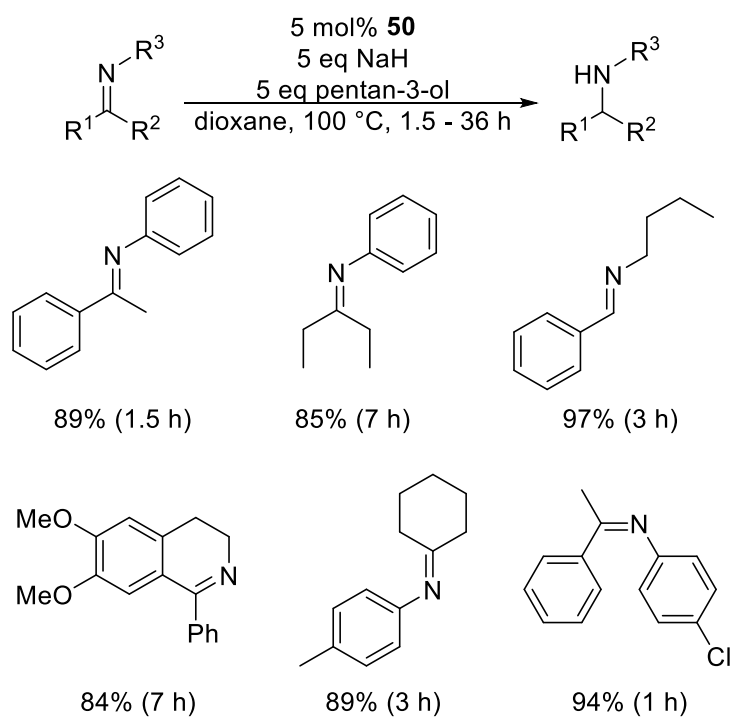
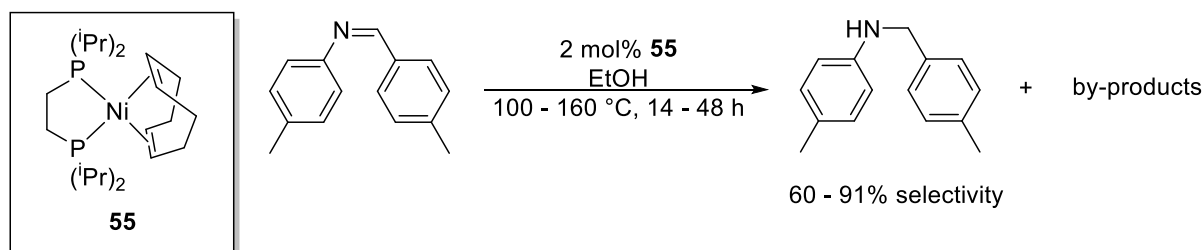


Figure 2.3 Different imidazolium salt ligated Ni(II) pre-catalysts, **50** - **54**, employed for imine transfer hydrogenation.⁴⁰

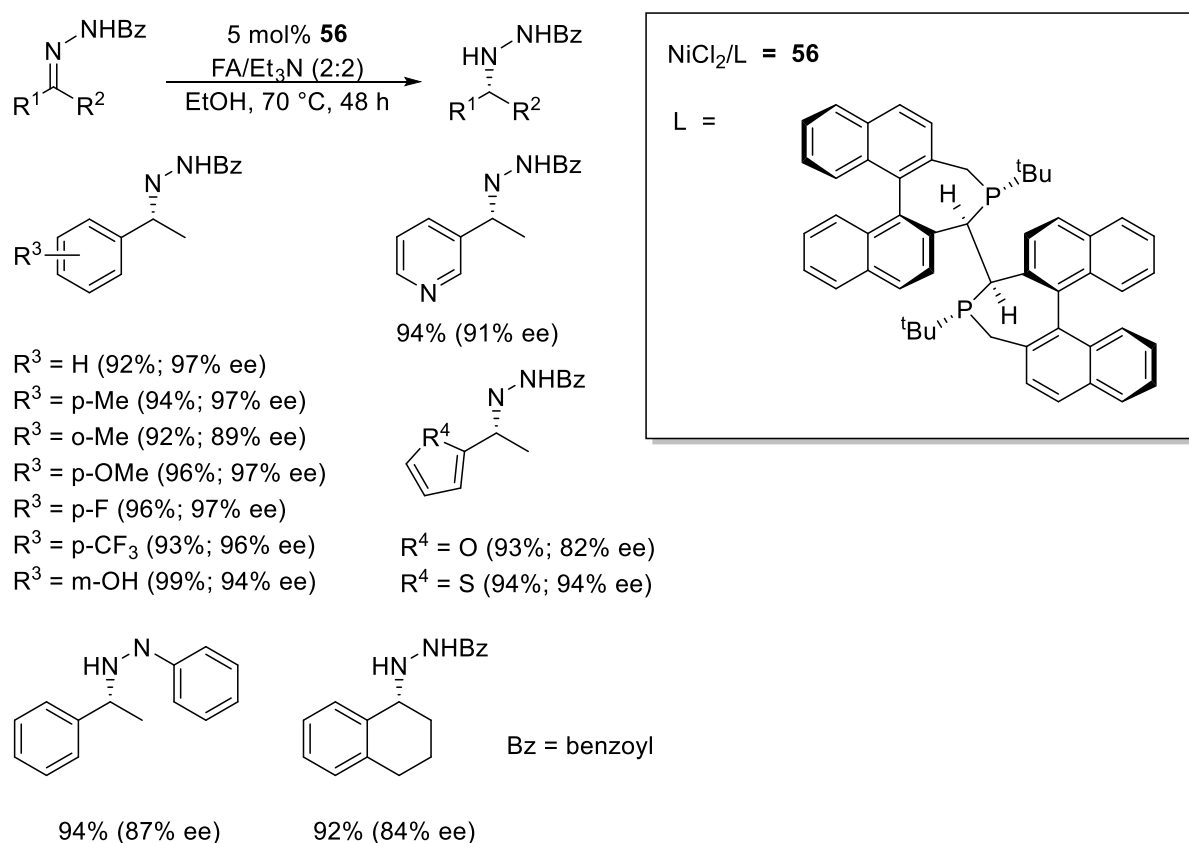


Scheme 2.28 Transfer hydrogenation of imines with **50**. Percentages are representative of isolated yields.⁴⁰

The same group continued their investigation towards the hydrogenation of imines.⁴¹ A dippe ligated $\text{Ni}(\text{COD})_2$ pre-catalyst, **55** (2 mol%), was utilised with EtOH, MeOH and *i*PrOH acting as hydrogen donors for the hydrogenation of (E)-N,1-di-*p*-tolylmethanimine to 4-methyl-N-(4-methylbenzyl)aniline (Scheme 2.29). At 150 °C after 24 hours, the conversions for different hydrogen donors were as follows: EtOH (98%), MeOH (83%) and *i*PrOH (78%). The introduction of molecular sieves (4 Å) to the reaction mixture led to hydrogenation and subsequent N-alkylation, producing 87 to 97% of the N-alkylated product.



Scheme 2.29 Transfer hydrogenation of (E)-N,1-di-*p*-tolylmethanimine with **55**.⁴¹

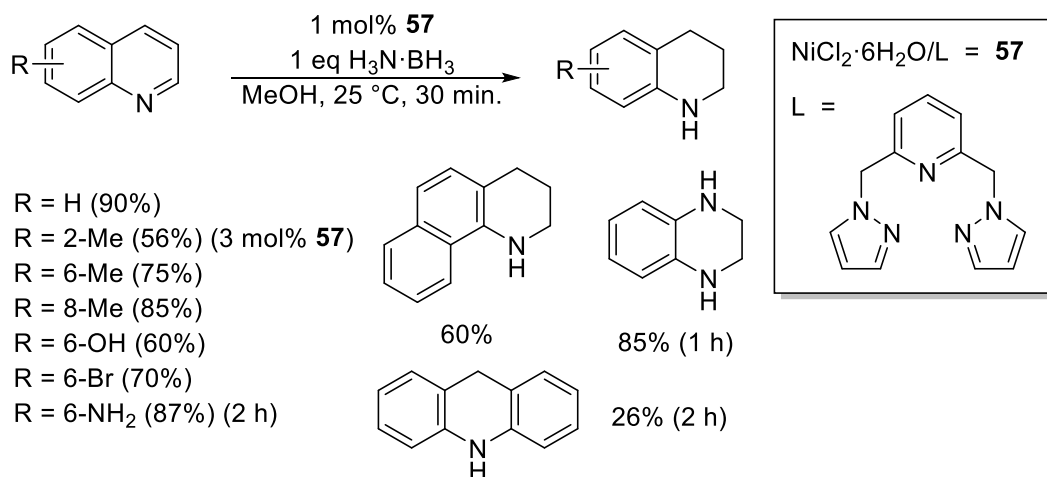


Scheme 2.30 Transfer hydrogenation of hydrazones and ketimines with **56**. Percentages are representative of GC yields.⁴²

Independently, the group of Zhou utilised their knowledge from the Ni(II)/binapine catalysed asymmetric transfer hydrogenation of prochiral alkenes with FA/Et₃N (mentioned above), for the transfer hydrogenation of hydrazones and ketimines (Scheme 2.30).⁴² Employing 5 mol% of *in situ* prepared pre-catalyst **56** with FA:Et₃N (2:2 equivalents) in EtOH for 24 - 48 hours at 70 to 80 °C, several aromatic and aliphatic hydrazones could undergo hydrogenation in 56 to 99% yield with 70 to 98% ee. Benzosultams were also successfully hydrogenated to their 2,3 dihydrobenzo[d]thiazole 1,1-dioxide products in 99% yield with 96% ee.

2.2.2.3 Transfer hydrogenation of quinolines

1,2,3,4-tetrahydroquinoline and other N-heteroaromatic compounds, generated from quinoline hydrogenation, have become important precursors in the synthesis of several pharmaceutical compounds.⁴³ The first and only known study that was conducted on the hydrogenation of quinolines with a homogeneous Ni catalyst was recently reported by Vermaak and co-workers (Chapter 3).⁴⁴ The transfer hydrogenation of various quinolines was achieved with 1 mol% of an *in situ* prepared NNN-tridentate ligated Ni(II) pre-catalyst with one equivalent of ammonia borane in MeOH at 25 °C in 30 minutes (Scheme 2.31). Mechanistic elucidation by NMR spectroscopy revealed the presence of active Ni(II) hydride species and a 1,4-dihydroquinoline intermediate.

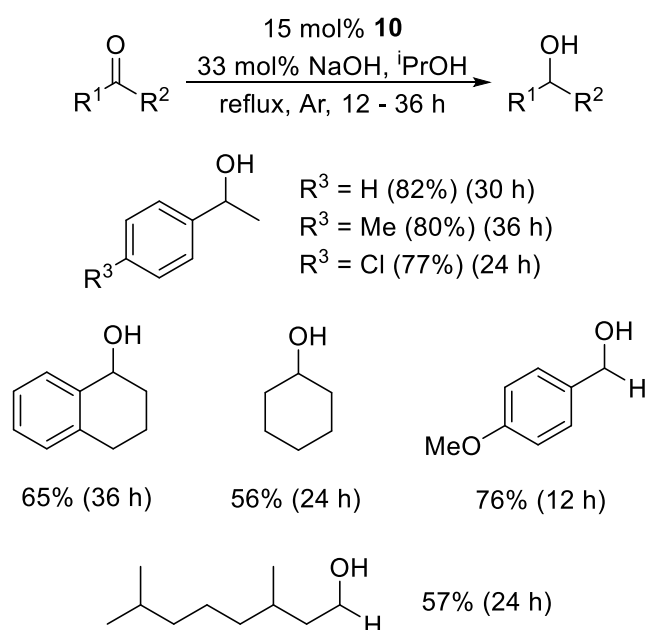


Scheme 2.31 Transfer hydrogenation of quinolines with **57**. Percentages are representative of isolated yields.⁴⁴

2.2.3 Hydrogenation and transfer hydrogenation of C-O bonds

2.2.3.1 Hydrogenation and transfer hydrogenation of ketones and aldehydes

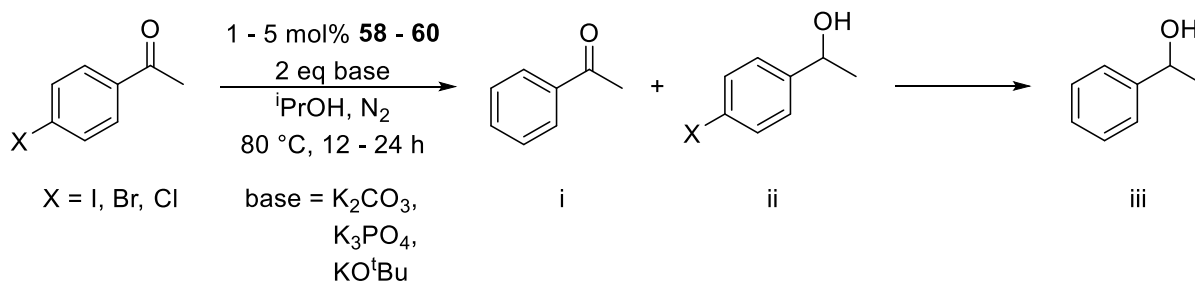
The hydrogenation of carbonyls to produce alcohols is an important and well-studied chemical transformation.⁴⁵ The alcohols that are obtained find application in the pharmaceutical and the chemical industry. The first known homogeneous Ni catalysed hydrogenation of carbonyls was conducted in 1995 by Iyer and Varghese when they employed a well-known $\text{NiCl}_2(\text{L2.1})_2$ complex, **10**, for the transfer hydrogenation of aldehydes and ketones.⁴⁶ Transfer hydrogenation was accomplished by refluxing $i\text{PrOH}$ (hydrogen donor) with 15 mol% of the Ni(II) catalyst and 33 mol% of NaOH as co-catalyst. Without NaOH, no activity was observed. Several benzylic and aliphatic ketones and aldehydes were hydrogenated to their corresponding secondary and primary alcohols in 12 to 36 hours with yields ranging from 51 to 82% via a proposed Ni(II) dihydride intermediate species (Scheme 2.32).



Scheme 2.32 Transfer hydrogenation of aldehydes and ketones with **10**. Percentages are representative of GC yields.⁴⁶

In a later study by Zhong and co-workers, novel salicylaldiminato-functionalised imidazolyl ligated heterometallic Ni complexes, **59** to **60** (Figure 2.4), were developed for the transfer hydrogenation of halo-acetophenones.⁴⁷ Heterometallic Ni/Ru, **59**, and Ni/Ir, **60**, (1 mol%) were evaluated against iodo-, bromo- and chloroacetophenone with $i\text{PrOH}$ as the hydrogen source at 80 °C for 12 to 24 hours (Scheme 2.33). Using two equivalents of K_2CO_3 and K_3PO_4 for the transfer hydrogenation of 4-iodoacetophenone produced 70 to 99% of the

halogenated alcohol product, but KO^tBu resulted in the dehalogenated alcohol product (99%). For the chloro- and bromo-derivatives, 89% and 31% halogenated alcohol was produced, respectively, after 24 hours, but an increase to 5 mol% catalyst led to 94% dehalogenated alcohol product from the bromo-derivative. Using 5 mol% of the monometallic Ni complex, **58**, 72% of the bromo alcohol was afforded, illustrating that the high activity of added noble metals causes dehalogenation.



Scheme 2.33 Transfer hydrogenation of ketones with **58 - 60**.⁴⁷

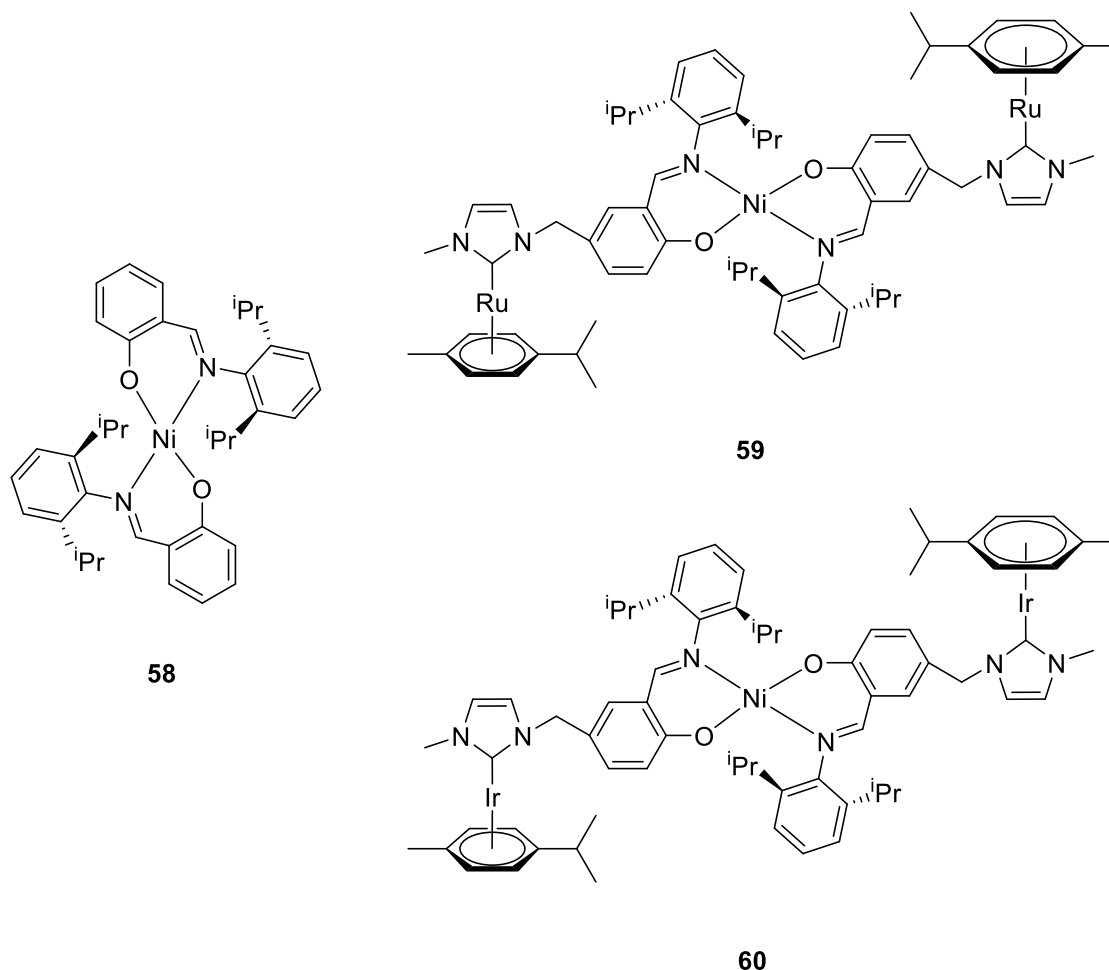


Figure 2.4 Novel salicylaldiminato-functionalised imidazolium salt ligated heterometallic Ni complexes, **58 - 59**, used for ketone transfer hydrogenation.⁵⁵

Chen and co-workers directed their attention to the hydrogenation of acetophenone with H₂ using six different diamine ligated Ni(II) complexes, **61** to **66** (Figure 2.5, Scheme 2.34).⁴⁸

Under a pressure of 50 atm H₂ at 80 °C with 0.1 mol% Ni(II) complex and 10 mol% KOH, acetophenone could be converted in 2.9 to 72.1% after five hours, with the bis(1,8-diaminonaphthalene) ligated Ni(II) complex, **65**, showing the highest activity. Employing KO^tBu as a base decreased the activity of **61** and **65**. Transfer hydrogenation with ⁱPrOH as hydrogen source was also evaluated with 1 mol% Ni(II) complex and 10 mol% KOH at 50 °C for 5 hours but low conversions of 0 to 4.3% were obtained. Evaluation of the transfer hydrogenation with FA/Et₃N showed no activity.

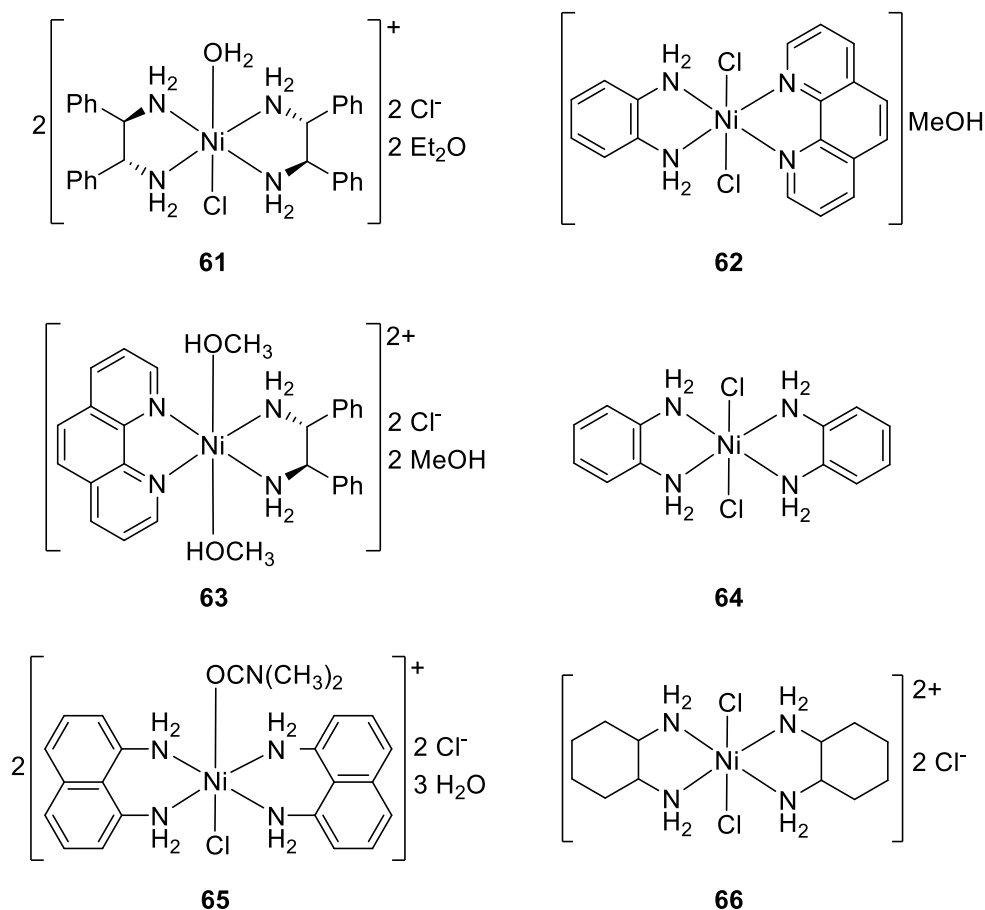
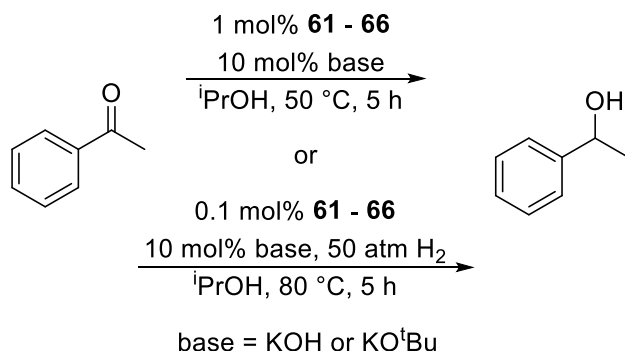


Figure 2.5 Diamine ligated Ni(II) complexes, **61** - **66**, employed for the transfer hydrogenation of acetophenone.⁴⁸

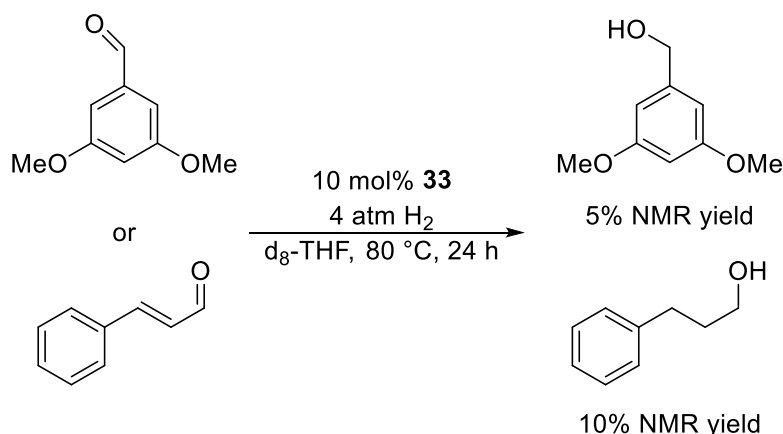
A previous study mentioned above, by the group of Hanson, also evaluated the hydrogenation of a few aldehyde substrates with H₂ using 10 mol% of **33**.²² Results, however, were not as good as those obtained for the alkene substrates. In 24 hours, hydrogenation of 3,5-dimethoxybenzaldehyde and cinnamaldehyde with 4 atm of H₂ at 80 °C resulted in only 5 and 10% of the corresponding alcohol product (Scheme 2.35).

Gao and co-workers decided to use ⁱPrOH as a hydrogen source in the asymmetric transfer hydrogenation of ketones using *in situ* prepared novel PNO-type ligated Ni(**L2.1**)Cl₂ pre-

catalysts, **67** to **69** (Scheme 2.36).⁴⁹ The different ligands were screened against the hydrogenation of propiophenone using 1 mol% pre-catalyst and 6 mol% KOH as the base at 70 °C for 20 to 22 hours. Pre-catalyst **69** afforded the best result with 93% yield, with its structure contributing to an increased enantioselectivity of the alcohol (84% ee). A decrease in reaction temperature to 25 °C resulted in no conversion. Using the optimal conditions, several aromatic and aliphatic ketones were hydrogenated to their corresponding alcohol products in 20 to 56 hours with yields and ee up to 99 and 84%, respectively.

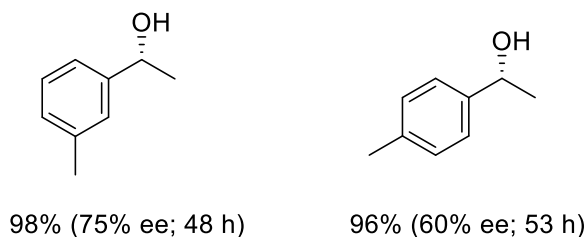
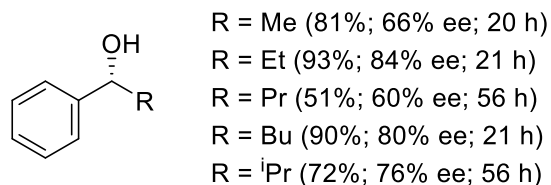
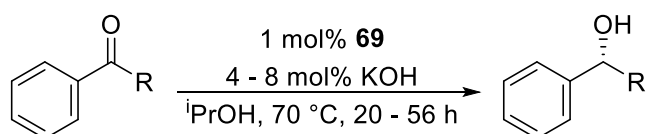
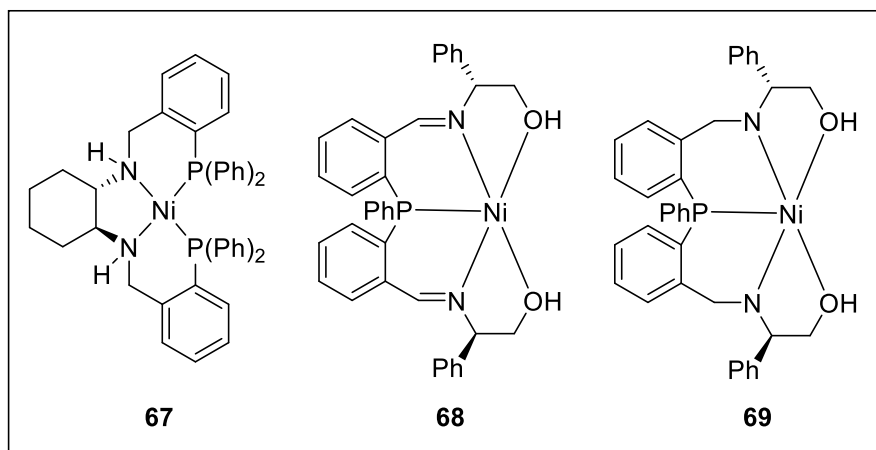


Scheme 2.34 Direct- and transfer hydrogenation of acetophenone with **61 - 66**.⁴⁸



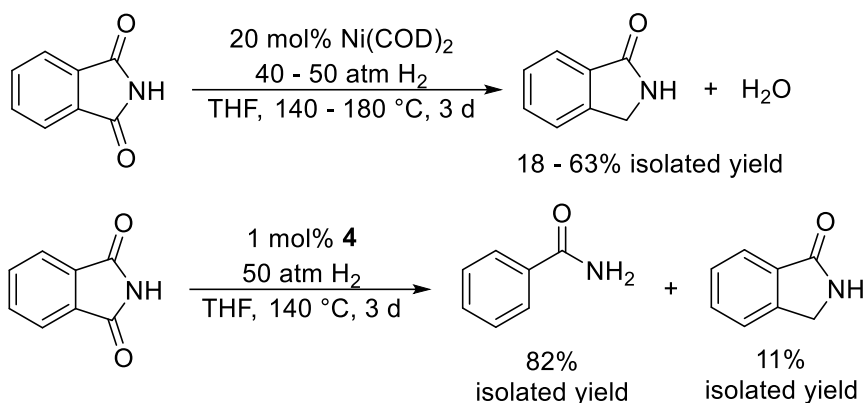
Scheme 2.35 Hydrogenation of 3,5-dimethoxybenzaldehyde and cinnamaldehyde with **33**.²²

A different approach was taken by the group of García for the hydrogenation of carbonyls by evaluating $Ni(COD)_2$ and **4** as catalytic precursors for the hydrogenation of phthalimide.⁵⁰ Employing 20 mol% of $Ni(COD)_2$ with 41 to 51 atm H_2 at 140 to 180 °C for 3 to 8 days, yielded 18 to 63% isoindolinone, which resulted from the complete reduction of C=O to CH_2 (Scheme 2.37). In comparison, 1 mol% of **4**, under similar conditions, resulted in 11% isoindolinone and 82% benzamide. Mechanistic elucidation revealed that κ^1 -N-phthalimide and η^2 -C,O-phthalimide intermediates are present during catalytic phthalimide hydrogenation.

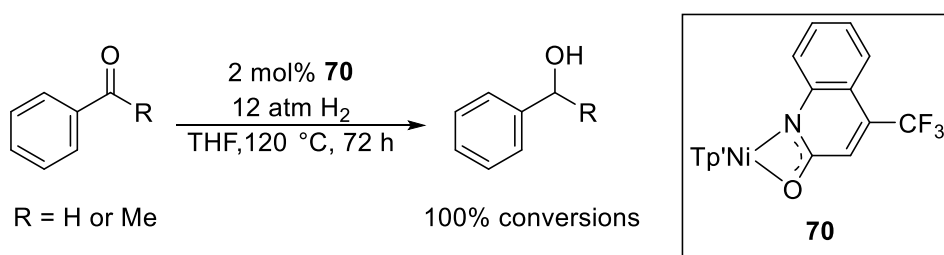


Scheme 2.36 Asymmetric transfer hydrogenation of ketones with **67** - **69**. Percentages are representative of GC yields.⁴⁹

While Chakraborty and co-workers used a tris(3,5-dimethylpyrazolyl)borate with ancillary 2-hydroxyquinoline ligated Ni(II) complex, **70**, for alcohol dehydrogenation, it was simultaneously used for the hydrogenation of benzaldehyde and acetophenone (Scheme 2.38).⁵¹ Using 5 mol% catalyst with 12 atm of H₂ at 120 °C, both substrates could be completely converted to their corresponding alcohol products in 72 hours. Lowering of the pressure to 5 atm resulted in no product formation concluding that there is a strong dependence on the pH₂ in the reaction.

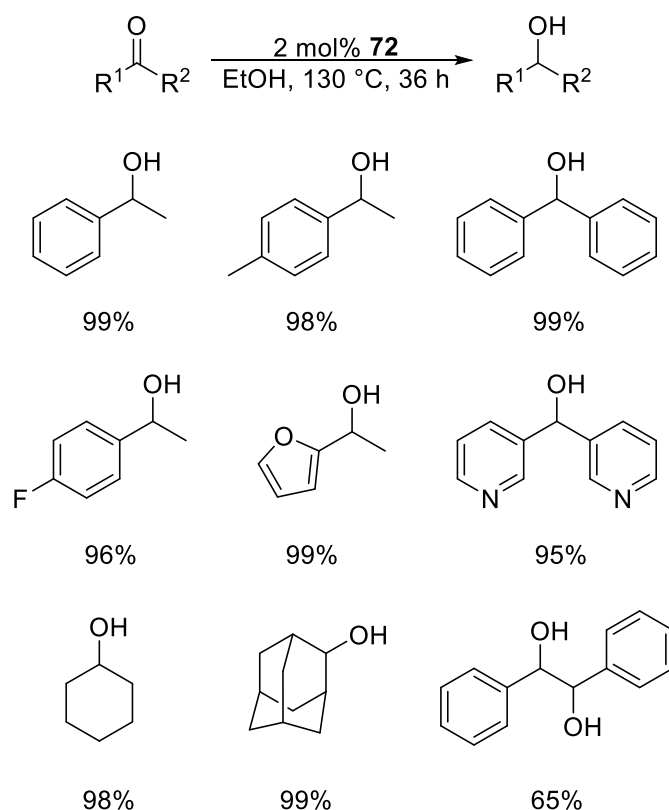


Scheme 2.37 Hydrogenation of phthalimide with Ni(COD)₂ and **4**.⁵⁰



Scheme 2.38 Hydrogenation of benzaldehyde and acetophenone with **70**.⁵¹

Later, the group of García applied their knowledge from the transfer hydrogenation of nitriles with dippe ligated Ni(COD)₂ pre-catalysts (Figure 2.6) to the transfer hydrogenation of ketones.⁵² Different alcohols were evaluated as hydrogen donors by using 2 mol% of **55** with acetophenone for 48 hours at 130 °C. Yields for the 1-phenylethanol product in different solvents were as follows: MeOH (13%), EtOH (95%), ⁱPrOH (4%), ⁱBuOH (53%). Evaluation of different *in situ* prepared pre-catalysts, **55**, **71** to **73**, with different phosphine ligands revealed that **72** displayed the highest activity at 130 °C for 36 hours, hydrogenating acetophenone to yield 99% alcohol product. A substrate scope of various (hetero)aromatic and aliphatic ketones was conducted with yields ranging from 95 to 99% for the corresponding alcohol product (Scheme 2.39). Benzil (a diketone) was also evaluated, but delivered a lower yield (65%). According to the authors, this was the first reported case of the transfer hydrogenation of ketones with a homogeneous Ni catalyst using EtOH as the hydrogen source.



Scheme 2.39 Transfer hydrogenation of ketones with **72**. Percentages are representative of GC yields.⁵²

Guan and co-workers developed an alternative strategy for carbonyl hydrogenation by following the hydrosilylation of aldehydes with PhSiH_3 and subsequent basic hydrolysis to produce the desired primary alcohol product.⁵³ POCOP-pincer ligated $\text{Ni}(\text{II})$ complexes, **74** to **76**, were synthesised and 0.2 mol% thereof was used along with 1.2 equivalents of PhSiH_3 at 25 to 70 $^\circ\text{C}$ for 1 to 24 hours to hydrogenate various aromatic and aliphatic aldehydes (Scheme 2.40). After complete conversion of the aldehyde, monitored by ^1H NMR spectroscopy, was observed, quenching of the silyl ether intermediate was conducted with 10% NaOH to afford 60 to 92% primary alcohol.

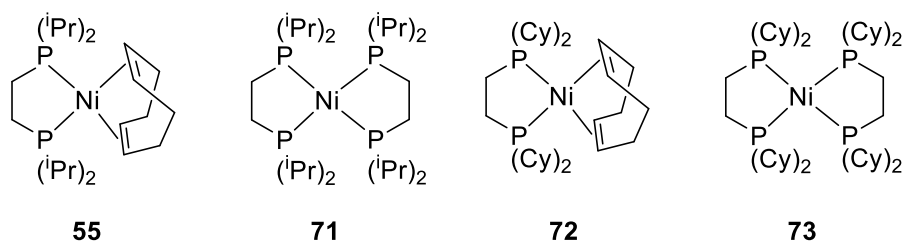
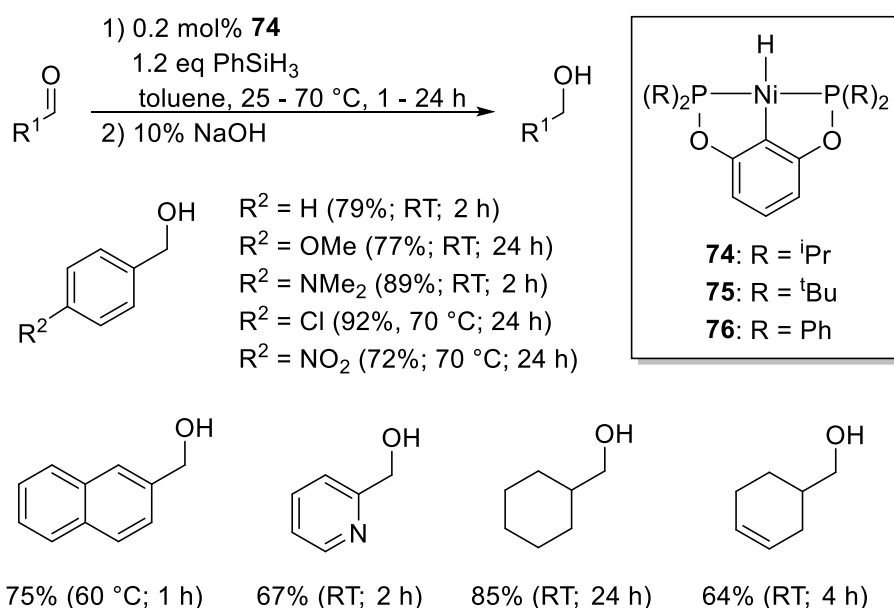


Figure 2.6 Different diphosphine ligated Ni pre-catalysts, **55**, **71** - **73**, employed for the transfer hydrogenation of ketones.⁵²



Scheme 2.40 Hydrosilylation of aldehydes with **74** - **76**. Percentages are representative of ^1H NMR yields.⁵³

Tran, Pink and Mindiola independently developed sterically demanding amidophosphine scaffolds for the synthesis of dimeric Ni complexes, **77** and **78** (Figure 2.7), which displayed activity towards the hydrosilylation of aromatic aldehydes and two ketones.⁵⁴ Benzaldehyde was evaluated as a benchmark substrate using 2 mol% of **77**, activating it with 4 mol% of KO^{*t*}Bu and employing 1.2 equivalents of Et₃SiH as the hydride source. Subsequent basic hydrolysis was not followed, but the yields of the silyl ether compounds (50 - 99%) are comparable to the yields of the alcohol products from previous studies (Scheme 2.41). A Ni(II) hydride intermediate was proposed as the possible active species responsible for the activity.

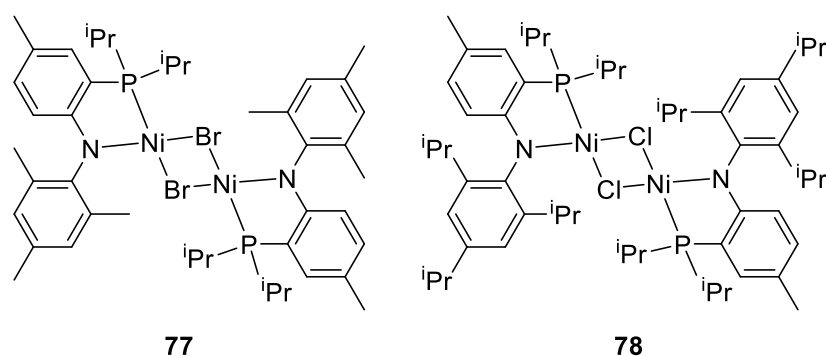
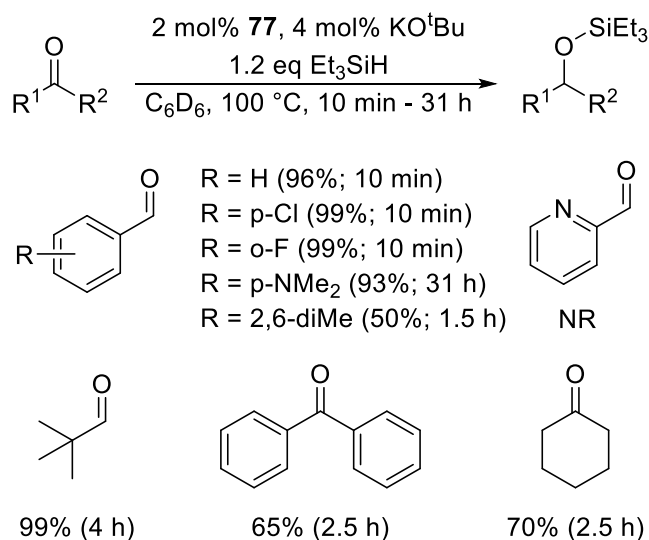


Figure 2.7 Ni complexes, **77** and **78**, with amidophosphine scaffolds used for hydrosilylation of aldehydes and ketones.⁵⁴



Scheme 2.41 Hydrosilylation of aldehydes and ketones with **77**. Percentages are representative of GC yields.⁵⁴

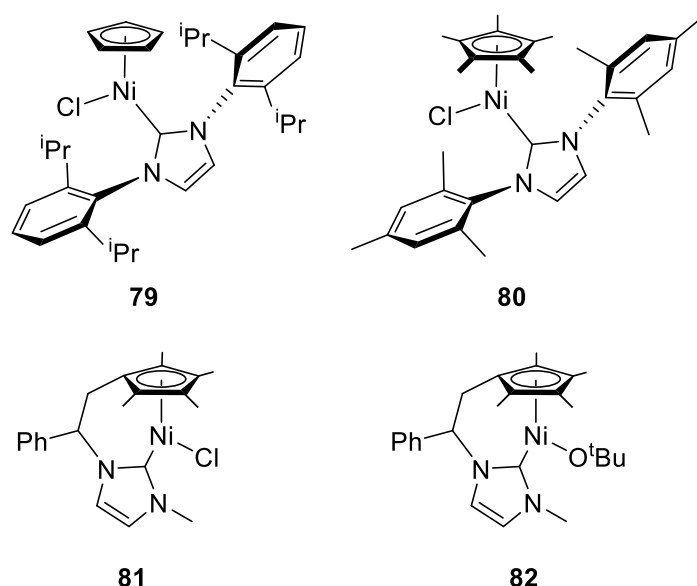
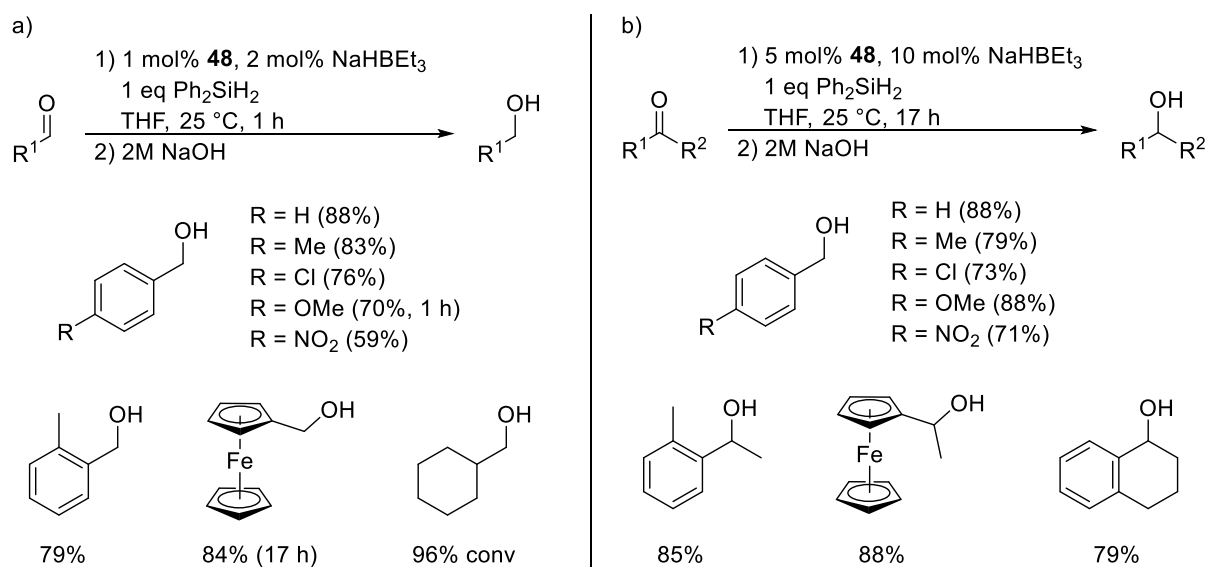


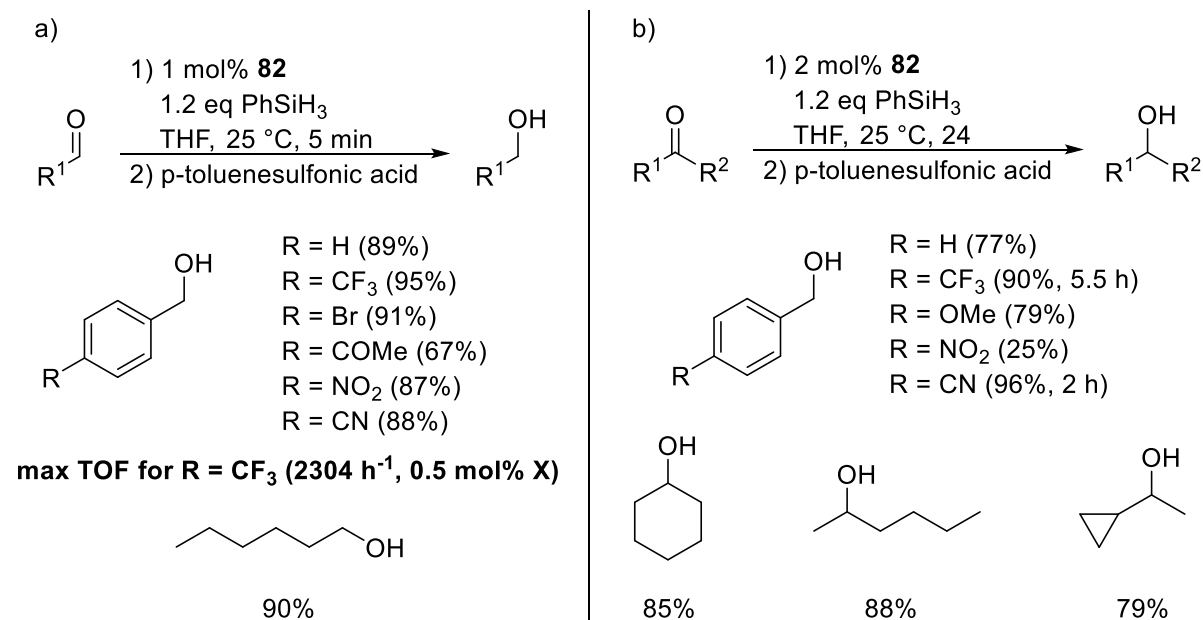
Figure 2.8 NHC ligated Ni complexes, **79** - **82**, employed for the hydrosilylation of aldehydes and ketones.⁵⁵⁻⁵⁶

A few years later, two groups (Bheeter and Postigo) independently conducted research on the hydrosilylation of aldehydes and ketones by employing similar Ni(II) complexes. A previously developed half-sandwich NHC Ni complex, **48**, with derivatives thereof, **79** and **80** (Figure 2.8), was used alongside PhSiH₂ for the hydrogenation of various aldehydes and ketones by Bheeter and co-workers.⁵⁵ Results indicated that complex **48** was the most active due to a less steric environment around the active centre. Further evaluation of an aldehyde substrate scope was conducted with 1 mol% of **48**, activated by 2 mol% of NaHBET₃, and

one equivalent of Ph_2SiH_2 at 25 °C for one hour (Scheme 2.42a). Primary alcohols could be isolated in 59 to 88% yields. Similar conditions were employed for the hydrogenation of ketone substrates, except with 5 mol% of **48** and 10 mol% NaHBEt_3 for 17 hours, which delivered 71 to 88% secondary alcohol yields (Scheme 2.42b).



Scheme 2.42 Hydrosilylation of a) aldehydes and b) ketones with **48**. Percentages are representative of isolated yields, unless stated otherwise.⁵⁵



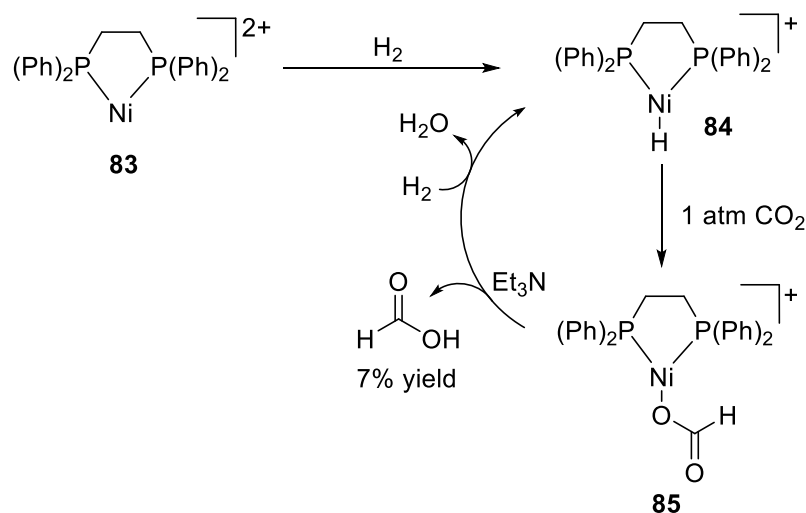
Scheme 2.43 Hydrosilylation of a) aldehydes and b) ketones with **82**. Percentages are representative of isolated yields.⁵⁶

Closely-related NHC half-sandwich ligated Ni(II) complexes, **81** and **82** (Figure 2.8), were synthesised by Postigo and Royo for the hydrosilylation of aldehydes and ketones.⁵⁶ Under

comparable conditions to that used by Bheeter, various aldehydes could be converted to their corresponding primary alcohols in very short reaction times (5 minutes), affording good yields of up to 95% (Scheme 2.43a). The alkoxide derivative, **82**, displayed higher catalytic activity compared to its Cl counterpart, **81**. With an increase in catalyst loading and reaction time, a ketone substrate scope was evaluated and delivered secondary alcohols, albeit with lower yields (Scheme 2.43b). Aliphatic ketones, except for cyclohexanone, did not fare as well as the aromatic ketones. Mechanistic elucidation again revealed the formation of an active nickel hydride intermediate.

2.2.3.2 Hydrogenation of CO₂ and carbonates

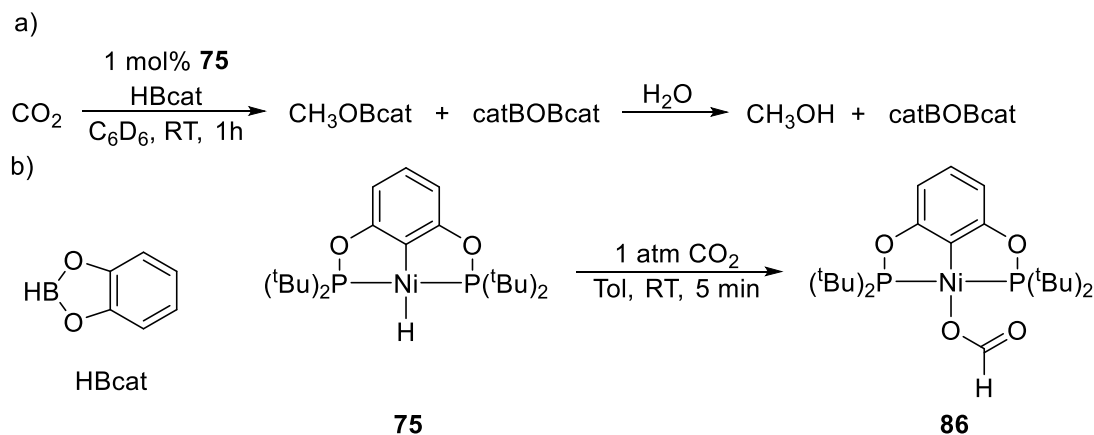
In the first study of catalytic fixation of CO₂, Inoue and co-workers utilised various phosphine ligated transition metal complexes to capture CO₂ and transform it into FA.⁵⁷ Among these complexes, Ni/**L2.2**, **83** (0.1 mmol) was employed with Et₃N (50 mmol) and 25 atm of H₂ to hydrogenate CO₂ (25 atm) at room temperature to FA (7% yield). Although no further experiments were conducted with **83**, an increase in the reaction temperature to 140 °C with Pd(**L2.2**)₂ yielded 70% FA, which delivered 12% at room temperature. A plausible mechanism (Scheme 2.44) was proposed following a Ni hydride intermediate, **84**, which could capture CO₂ to generate Ni formate species, **85**.



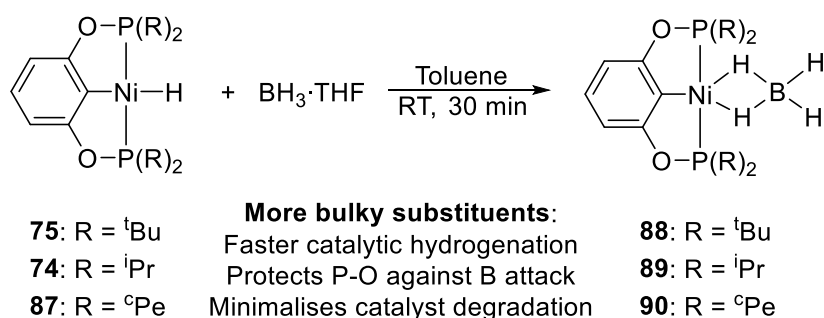
Scheme 2.44 Proposed mechanism for CO₂ hydrogenation with **83**.⁵⁷ No indication of the anions bonded to Ni was given in the article and is therefore excluded from this scheme. Ni will be taken as Ni(II) for mechanistic purposes.

Chakraborty and his group observed that a catalytic amount of ^tBuPOCOP^tBuNiH can convert CO₂ with catecholborane (HBcat) to CH₃OBcat, with hydrolysis thereof forming MeOH.⁵⁸ They continued their investigation into the hydrogenation of CO₂ with Ni(II) complex, **75**

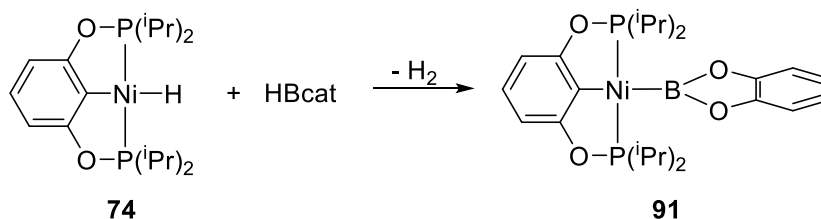
(Scheme 2.45a).⁵⁹ HBcat was chosen as the hydrogen source because it is an efficient reductant of Ni formates to MeOH derivatives and the precipitation of catBOBcat indicates a nearly complete reaction. With **75** (25 μ mol) and HBcat (2.5 mmol), 1 atm of CO₂ could be converted to MeOH derivatives in 45 minutes at room temperature via a Ni(II) formate intermediate, **86** (Scheme 2.45b).



Scheme 2.45 a) CO₂ hydrogenation with **75** using HBcat and b) Ni formate formation, **86**, from CO₂ capture.⁵⁸



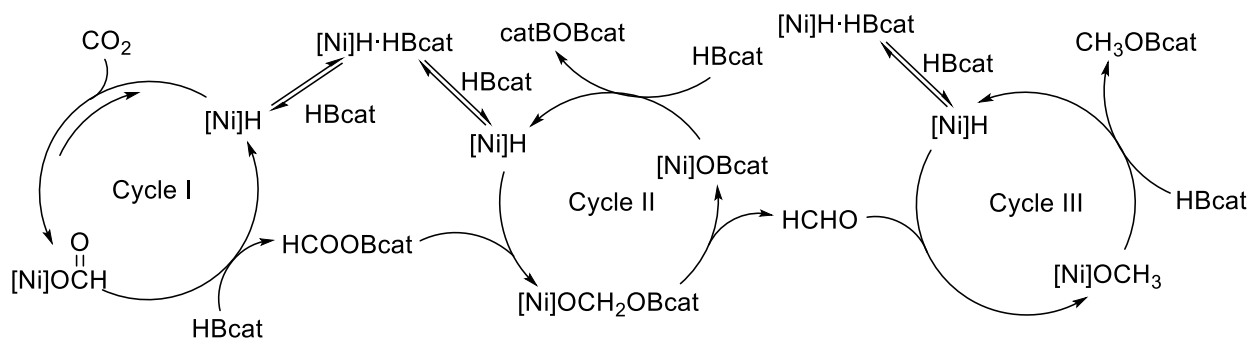
Scheme 2.46 Reaction of **75**, **74** and **87** with BH₃·THF.⁶⁰ ^cPe represents a cyclopentyl.



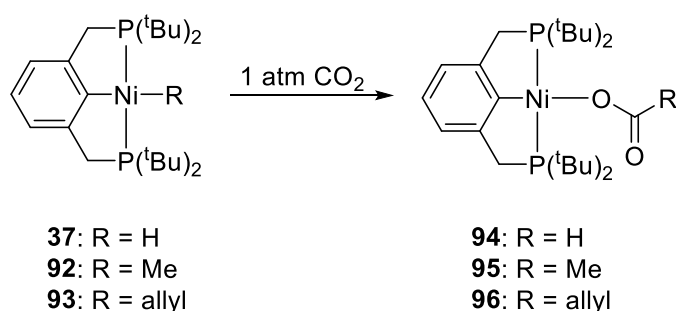
Scheme 2.47 Reaction of **74** with HBcat.⁶¹

Further investigations into the catalytic mechanism of CO₂ capture associated with Ni(II) complexes were conducted in a follow-up study (Scheme 2.48).^{60, 61} Reaction of **74**, **75** and **87** with BH₃·THF delivered borohydride complexes, **88** to **90**, which are irreversible at room

temperature, but reversible at 60 °C (Scheme 2.46). However, its capability to exchange H₂ results in its high activity. In comparison, the less bulky hydride complexes, **74** and **87**, produce η^2 -coordinated dihydridoborate complexes when reacted with 9-BBN and HBcat that are reversible at room temperature, but are less efficient (Scheme 2.47).



Scheme 2.48 Proposed catalytic cycle describing the hydrogenation CO₂ with Ni(II)-H species and HBcat.⁶⁰

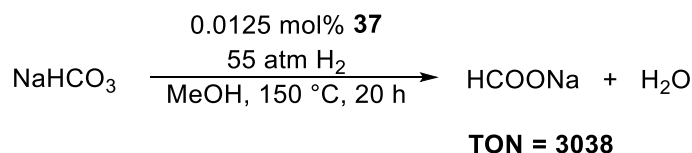


Scheme 2.49 Reaction of **37**, **92** and **93** with CO₂ towards the formation of Ni carboxylate species, **94** to **96**.⁶²

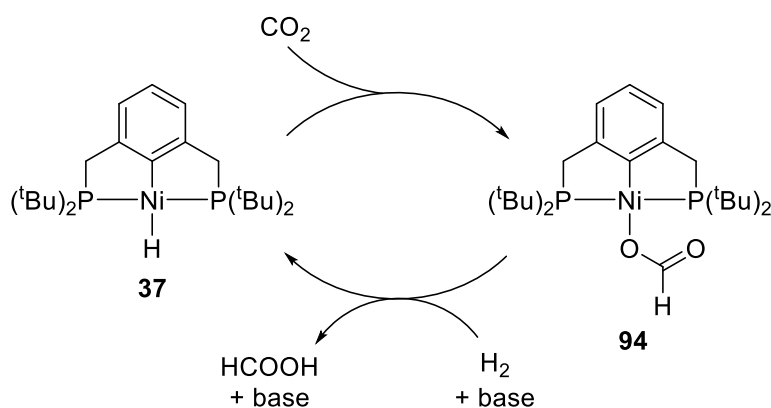
Schmeier and co-workers illustrated the involvement of Ni(II)-E (E = H, Me or allyl) σ -bonds in PCP ligated Ni complexes, **37**, **92** and **93**, during insertion of CO₂ for the generation of Ni carboxylates, **94** to **96** (Scheme 2.49).⁶² CO₂-bound products were evaluated with ¹H NMR-, IR spectroscopy and X-ray crystallography and confirmed the presence of the corresponding complexes. Computational investigations suggested different mechanistic pathways for each complex formation. For **94**, a four-centred transition state is generated resulting in Ni(II)-H bond scission and Ni(II)-O and C-H bonds formation. For **95** and **96**, no initial interaction between Ni and either O atoms from CO₂ occurs. CO₂ attack occurs on the Ni-bound C (**92**) and terminal olefin (**93**). After rearrangement and ligand substitution, respectively, the carboxylates are formed.⁶³

In 2015, Enthaler and co-workers also employed the same complex, **37**, for the hydrogenation of NaHCO₃ to HCOONa.⁶⁴ A low catalyst loading of 0.0125 mol% with 55 atm

of H₂ at 150 °C for 20 hours yielded HCOONa with a TON of 3038 (Scheme 2.50). Unfortunately, CO₂ could not be hydrogenated when the same conditions were followed, using nOctNMe₂ as the base. The Ni(II) formate intermediate, **94**, which was observed formed part of a hydrogen storage and release cycle (Scheme 2.51), with the latter part being discussed in a later section.

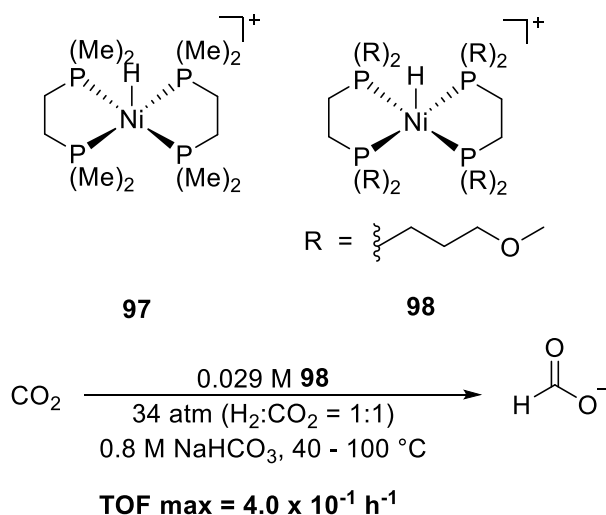


Scheme 2.50 Hydrogenation of NaHCO₃ with **37**.⁶⁴

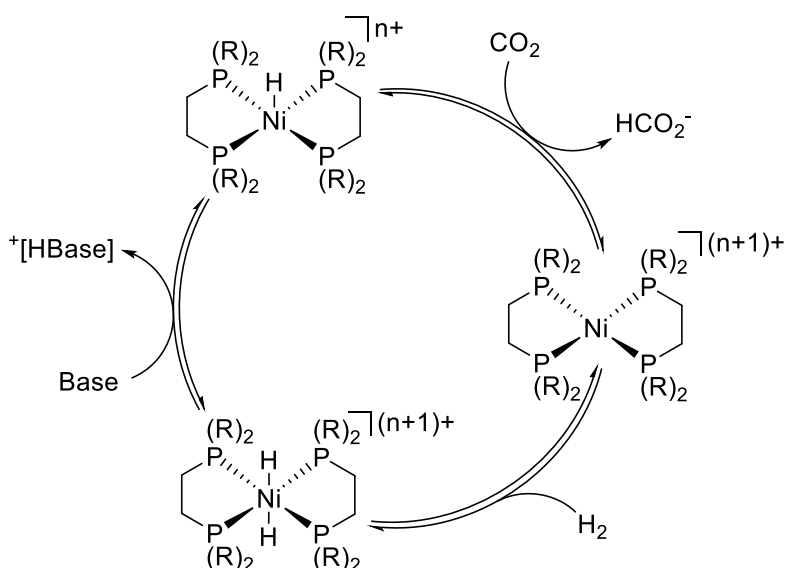


Scheme 2.51 CO₂ hydrogenation as part of a hydrogen storage and release cycle.⁶⁴

Burgess and co-workers managed to be the first group to successfully hydrogenate CO₂ in water as a green solvent.⁶⁵ A water-soluble bis(diphosphine) ligated Ni(II) complex, **98** (0.029 M), showed activity in combination with a 1:1 mixture of H₂:CO₂ (34 atm) buffered in a 0.8 M NaHCO₃ solution (Scheme 2.52). An increase in temperature from 40 to 100 °C increased the TOF from 0.022 to 0.6 h⁻¹. The success of the reaction was ascribed to the low energy requirement for hydride transfer between the Ni(II) hydride intermediate (HNiL₂⁺) and CO₂ (1 kcal/mol).



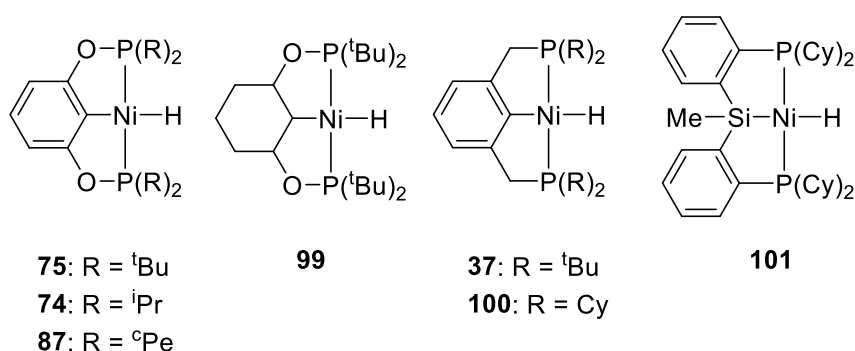
Scheme 2.52 Hydrogenation of CO₂ with **97** and **98**.⁶⁵



Scheme 2.53 Generalised description of CO₂ hydrogenation by disphosphine complexes.^{65, 70}

The kinetics of CO₂ insertion into Ni(II) complexes can differ quite drastically depending on the ligand coordinated to the Ni centre (Figure 2.9).⁶⁶ Ni(II) hydrides that are successful in the hydrogenation of CO₂ usually contain a POCOP- (with aromatic, **74**, **75**, **87** or aliphatic backbone, **99**)⁶⁷, PCP-, **37**, **100**,⁶² or PSiP, **101**,⁶⁸ pincer ligand and can facilitate rapid CO₂ insertion. In comparison, Ni hydride complexes containing PNP pincer ligands, **102** and **103**, are less active when it comes to CO₂ activation, and subsequent CO₂ insertion is much slower.⁶⁹

Fast CO₂ insertion



Slow CO₂ insertion

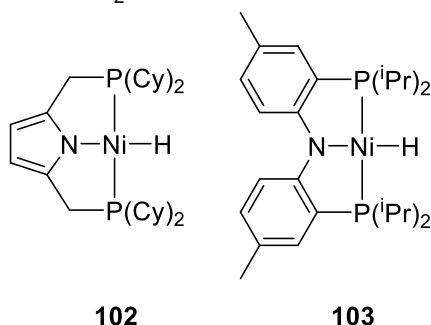
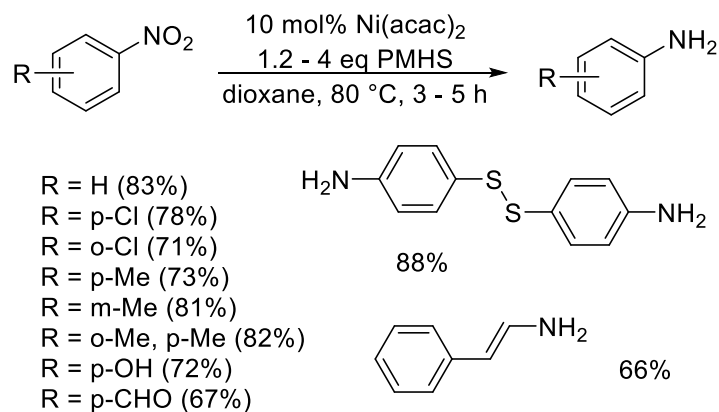


Figure 2.9 Difference in CO₂ insertion kinetics between different Ni(II)-H complexes, **37**, **74**, **75**, **87**, **99** - **103**.^{62, 66-69}

2.2.4 Transfer hydrogenation of N-O bonds

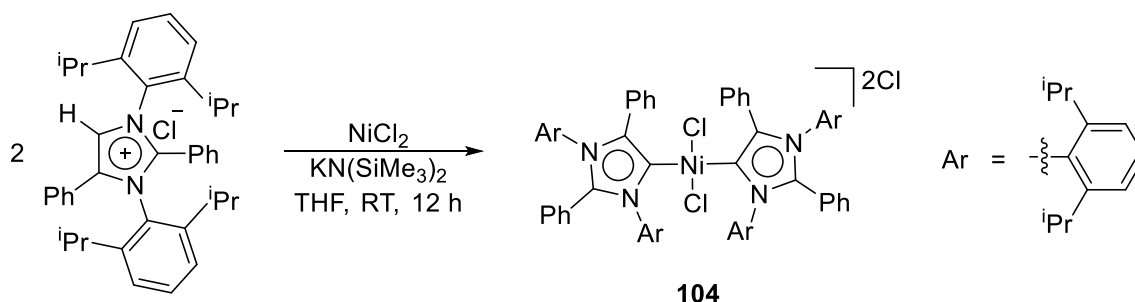
2.2.4.1 Transfer hydrogenation of nitro compounds

The first known hydrogenation of nitro compounds using a homogeneous Ni complex was conducted by Sun, Quan and Wang.⁷¹ They did, however, not employ H₂ but rather polymethylhydrosiloxane (PMHS), an air and moisture stable polymer containing 40 monomers, as the reductant. After Fe, Zn and Ni salts were screened, they found that Ni(acac)₂ (10 mol%) with 1.5 equivalents of PMHS in 1,4-dioxane at 80 °C could hydrogenate nitrobenzene in three hours to yield 81% of aniline. The methodology was extrapolated to various nitroarenes showing high chemoselectivity (Scheme 2.54). Several dihydropyrimidinones (DHPM), used for pyrimidine base synthesis,⁷² could also successfully undergo hydrogenation in yields of up to 93% while showing chemoselectivity for the nitro group.



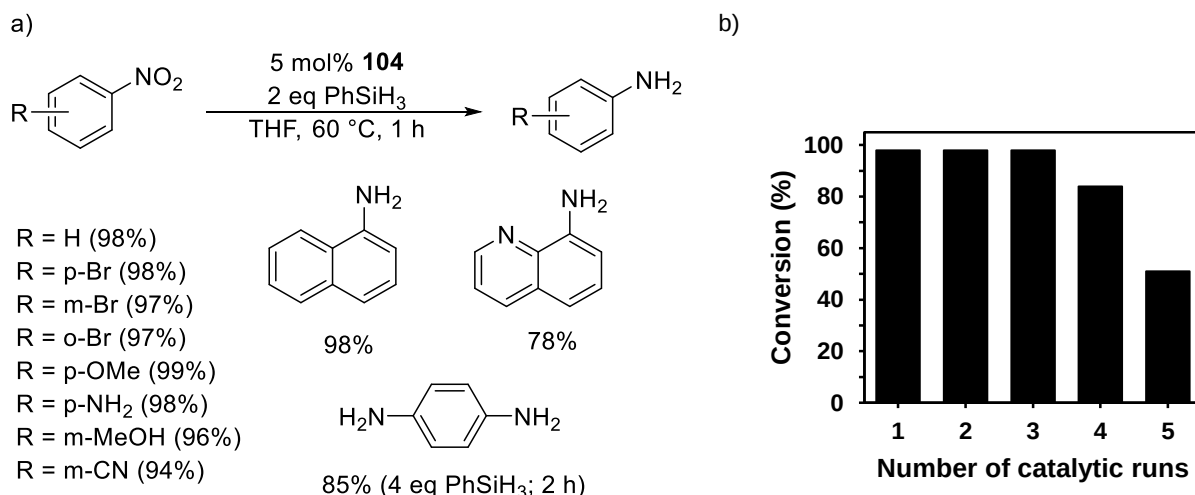
Scheme 2.54 Hydrosilylation of nitro compounds with Ni(acac)₂. Percentages are representative of isolated yields.⁷¹

Vijaykumar and Mandal continued work on the hydrogenation of nitroarenes with PhSiH₃ catalysed by a novel square planar bis(NHC) ligated Ni(II) complex, **104** (Scheme 2.55)⁷³ Using 5 mol% of **104** with two equivalents of PhSiH₃ at 60 °C, numerous nitroarenes could be hydrogenated to their corresponding amine products in one hour with yields between 64 and 98% (Scheme 2.56). A longevity assessment revealed that the catalyst remains active for three catalytic runs before it starts to lose activity.

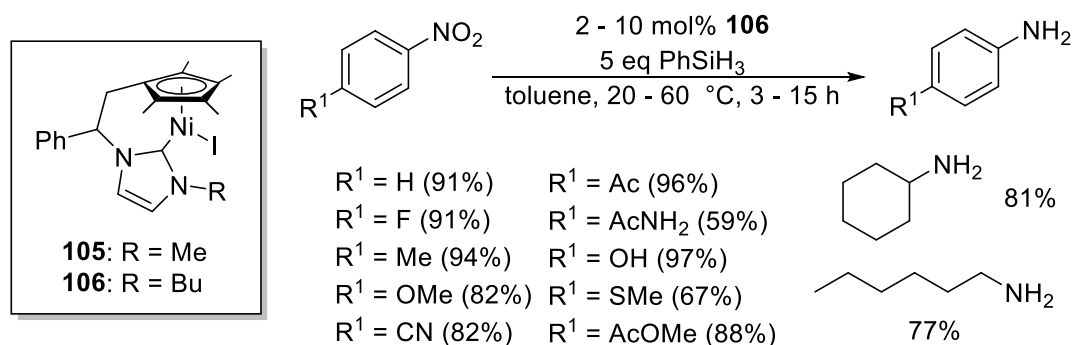


Scheme 2.55 Synthesis of novel square planar bis(N-heterocyclic carbene) ligated Ni(II) complex, **104**.⁷³

Royo and Pereira also utilised PhSiH₃ as a reductant for the hydrogenation of nitrocompounds with half-sandwich NHC ligated Ni complexes, **105** and **106** (Scheme 2.57).⁷⁴ Activity analysis of the complexes revealed that the complex containing a larger N-chain, **106**, was more active. By using 2 to 10 mol% of **106** with five equivalents of PhSiH₃, several aromatic and aliphatic nitro compounds could undergo hydrogenation in 3 to 15 hours at 20 to 60 °C. Notable chemoselectivity for the nitro group was observed in the presence of carbonyls and nitriles with tolerance to a variety of functional groups, i.e. halogens, hydroxides, amides, esters and methoxy groups. Mechanistic studies that were conducted did not reveal any insights into the nature of the active Ni species.



Scheme 2.56 Hydrosilylation of nitro compounds with **104**. Percentages are representative of isolated yields.⁷³



Scheme 2.57 Hydrosilylation of nitro compounds with **106**. Percentages are representative of isolated yields.⁷⁴

2.3 Dehydrogenation

Homogeneous Ni catalysed dehydrogenation reactions are less investigated compared to Ni catalysed hydrogenation reactions mentioned in this review. Although some TH reactions include a dehydrogenative step for H₂ production, exclusive studies on dehydrogenation remain scarce. This section will illustrate how homogeneous Ni catalysts are utilised for H₂ production from saturated compounds and how it compares to its heterogeneous counterparts. Much of the research that will be described employs alcohols as the substrate of choice for H₂ production along with coupling to amines/ketones for the production of quinolines. For other Ni catalysed dehydrogenative couplings not involving H₂ production, the reader is referred to literature.⁷⁵ Research depicting the dehydrogenation of AB, amines and FA will also be discussed.

2.3.1 Dehydrogenation of alcohols

Chakraborty and co-workers illustrated the versatility of tris(3,5-dimethylpyrazolyl)borate (Tp) and ancillary 2-hydroxyquinoline ligated Ni(II) complexes, **70**, **107** and **108** (5 mol%), in the acceptorless dehydrogenation of secondary- and primary alcohols to ketones and aldehydes, respectively (Scheme 2.58).⁵¹ Excellent yields between 75 and 95% could be achieved in 24 to 120 hours at 120 °C without the use of additives. Diols were also subjected to dehydrogenation and led to the formation of a lactone and two equivalents of H₂. Mechanistic studies illustrated the importance of the 2-hydroxyquinoline ancillary ligand for a concerted mechanism.

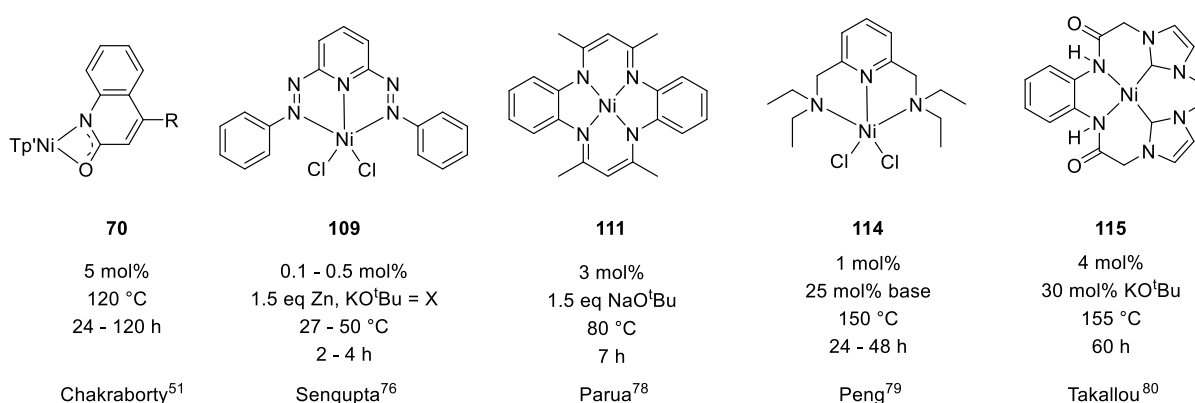
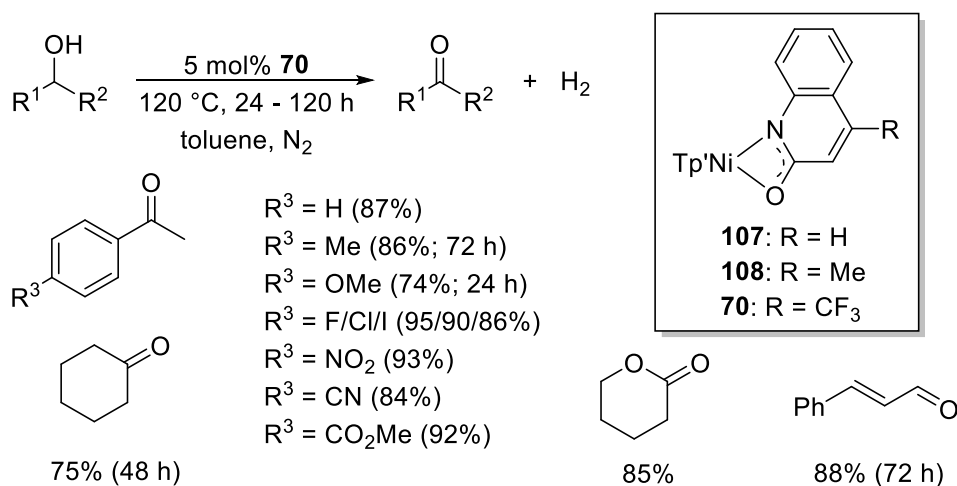
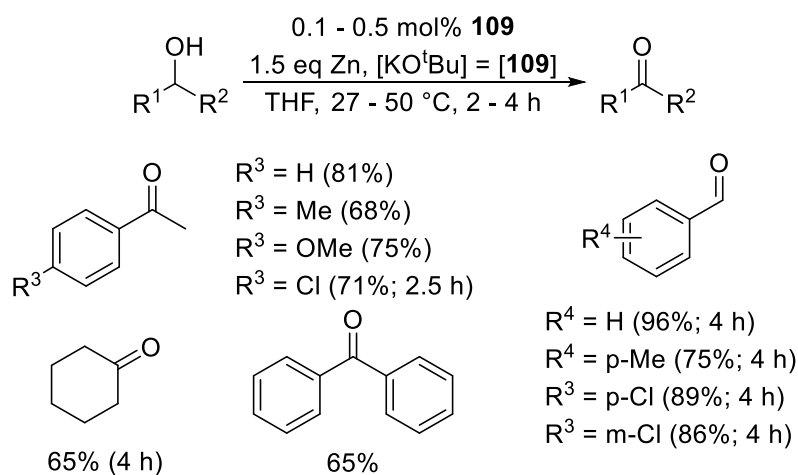


Figure 2.10 Ni complexes, **70**, **109**, **111**, **114** and **115** employed in the dehydrogenation of alcohols.

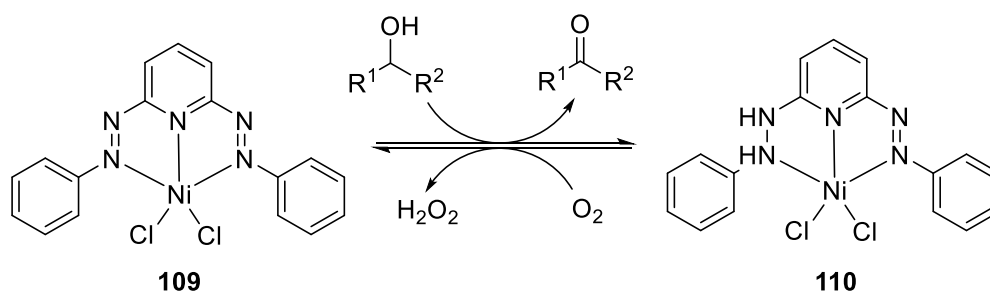
A year later, Sen Gupta and co-workers developed a 2,6-bis(phenylazo)pyridine ligated Ni(II) complex, **109**, which showed good activity towards the dehydrogenation of various primary- and secondary alcohols.⁷⁶ Although a smaller amount of catalyst (0.1 - 0.5 mol%) was required, 1.5 equivalents (compared to the substrate) of Zn dust and one equivalent (compared to the catalyst) KO^tBu were added to aid with the reaction. The reaction was done at 27 to 50 °C under a positive pressure of O₂ to yield 65 to 96% of the corresponding carbonyl products in two to four hours (Scheme 59). A ligand-mediated dehydrogenation mechanism generating **110**, was proposed, illustrating the importance of the azo-hydrazo couple (Scheme 2.60).



Scheme 2.58 Acceptorless dehydrogenation of secondary- and primary alcohols with **70**, **107** and **108**. Percentages are representative of isolated yields.⁵¹



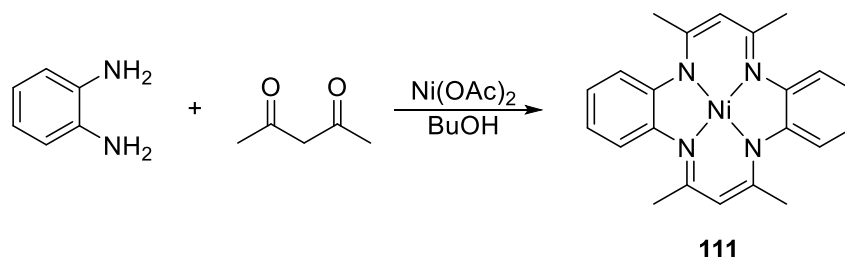
Scheme 2.59 Dehydrogenation of primary- and secondary alcohols with **109**. Percentages are representative of GC- and isolated yields.⁷⁶



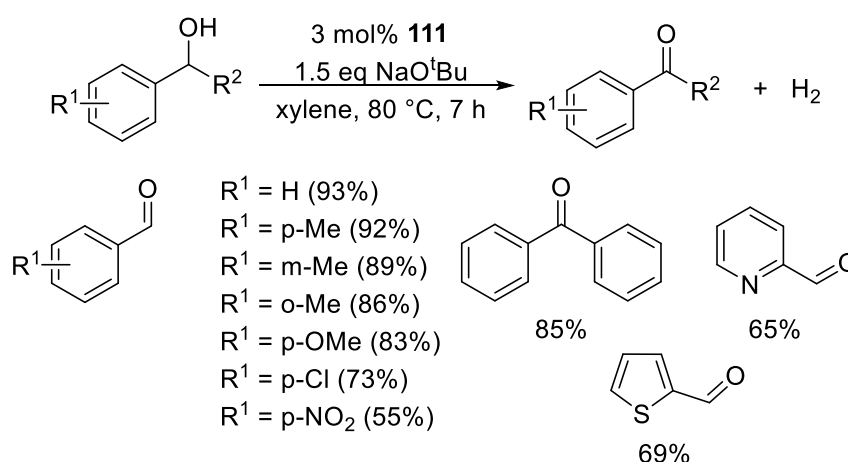
Scheme 2.60 Ligand-mediated dehydrogenation mechanism of alcohols illustrating azo-hydrazo couple.⁷⁶

Parua and co-workers illustrated the success of a previously synthesised tetramethyltetraaza[14]annulene (MeTAA) ligated Ni(II) complex, **111** (Scheme 2.61)⁷⁷, by

using 3 mol% of the complex with 1.5 equivalents of NaO^tBu in xylene at 80 °C for seven hours to dehydrogenate several benzylic alcohols in yields of 55 to 93% (Scheme 2.62).⁷⁸



Scheme 2.61 Synthesis of MeTAA ligated Ni(II) complex, **111**.⁷⁷



Scheme 2.62 Dehydrogenation of primary- and secondary alcohols with **111**. Percentages are representative of isolated yields.⁷⁸

The first occurrence of Ni catalysed alcohol dehydrogenation towards carboxylic acids was illustrated by Peng and co-workers a year later.⁷⁹ Three different *in situ* prepared N'N''N''' pincer ligated Ni(II) complexes, **112** to **114** (Figure 2.11), were evaluated with NiCl₂ against the dehydrogenation of primary alcohols, with complex **114** being the most active. A variety of benzyl- and aliphatic alcohols with their corresponding sodium alkoxide base (25 mol%) were evaluated with 1 mol% of **114** at 150 °C for 24 to 48 hours (Scheme 2.63). After extraction with HCl, the corresponding carboxylic acid products were isolated in 40 to 90% yields. The addition of 1 mL of mesitylene (Mes) increased the isolated yields between 10 and 20% (Scheme 2.63).

Most recently, the group of Takallou developed NHC ligated Ni(II) pre-catalysts, **115** to **118**, containing bis(amido-imidazolium)pyridyl ligands that were utilised for the dehydrogenation of secondary benzylic, cyclic and aliphatic alcohols to their respective ketone products in

yields of 47 to 87% (Scheme 2.64).⁸⁰ Unfortunately higher amounts of catalyst (4 mol%) were required, along with 30 mol% of KO^tBu for 60 hours at 155 °C.

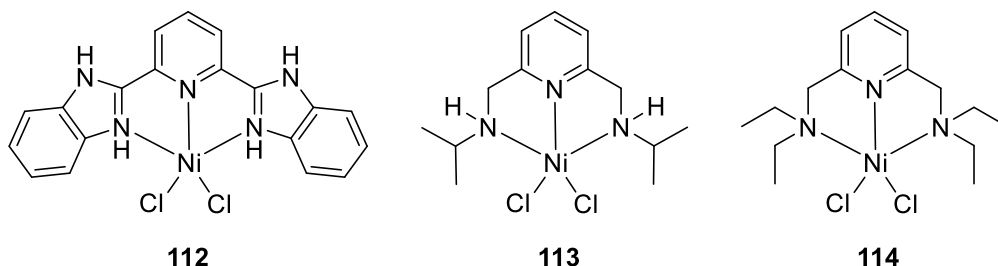
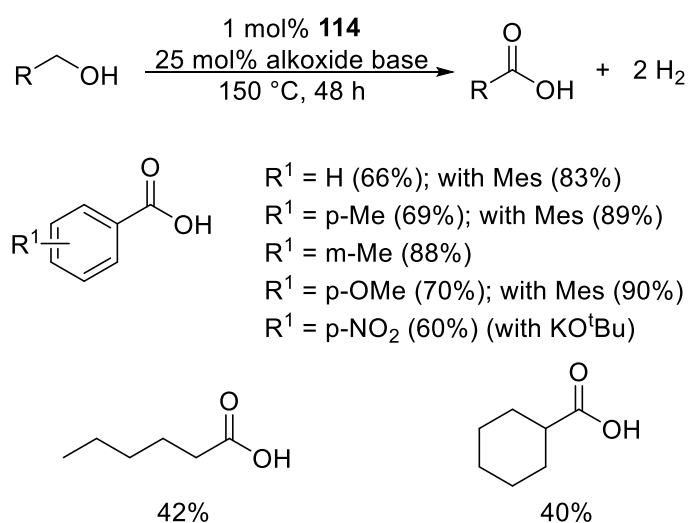
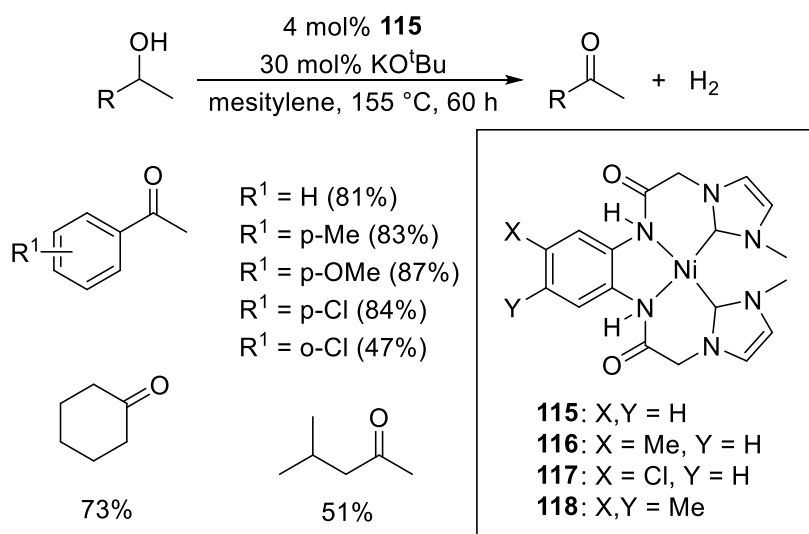


Figure 2.11 Ni complexes, **112** - **114**, evaluated against the dehydrogenation of primary alcohols to carboxylic acids.⁷⁹



Scheme 2.63 Dehydrogenation of primary alcohols to acids with **114**. Percentages are representative of isolated yields.⁷⁹



Scheme 2.64 Acceptorless dehydrogenation of secondary alcohols with **115** - **118**. Percentages are representative of isolated yields.⁸⁰

2.3.2 N-alkylation of amines and amides via dehydrogenative alcohol coupling

A year after Chakraborty and co-workers developed a homogeneous Ni catalyst for the dehydrogenation of alcohols, the group of Vellakkaran and Banerjee evaluated N-alkylation of anilines via i) an alcohol dehydrogenation step, ii) subsequent coupling to a primary amine and iii) *in situ* hydrogenation of the imine intermediate for the formation of a secondary amine.⁸¹ During preliminary optimisation, coordination of phenanthroline (phen) to NiBr₂ (10 mol%), generating **119**, yielded the best result to alkylate aniline with benzyl alcohol to form N-phenylbenzylamine using one equivalent of KO^tBu for 48 hours at 130°C (Scheme 2.65). Various benzylic, aliphatic and heteroaromatic alcohols were employed as alkylation agents for the N-alkylation of aniline and aniline derivatives and the products could be isolated in 32 to 99% yields.

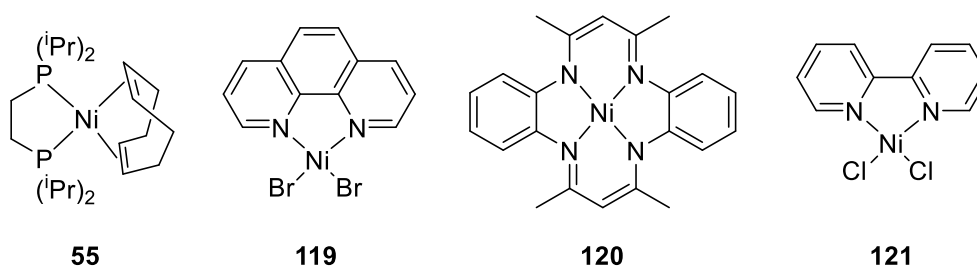
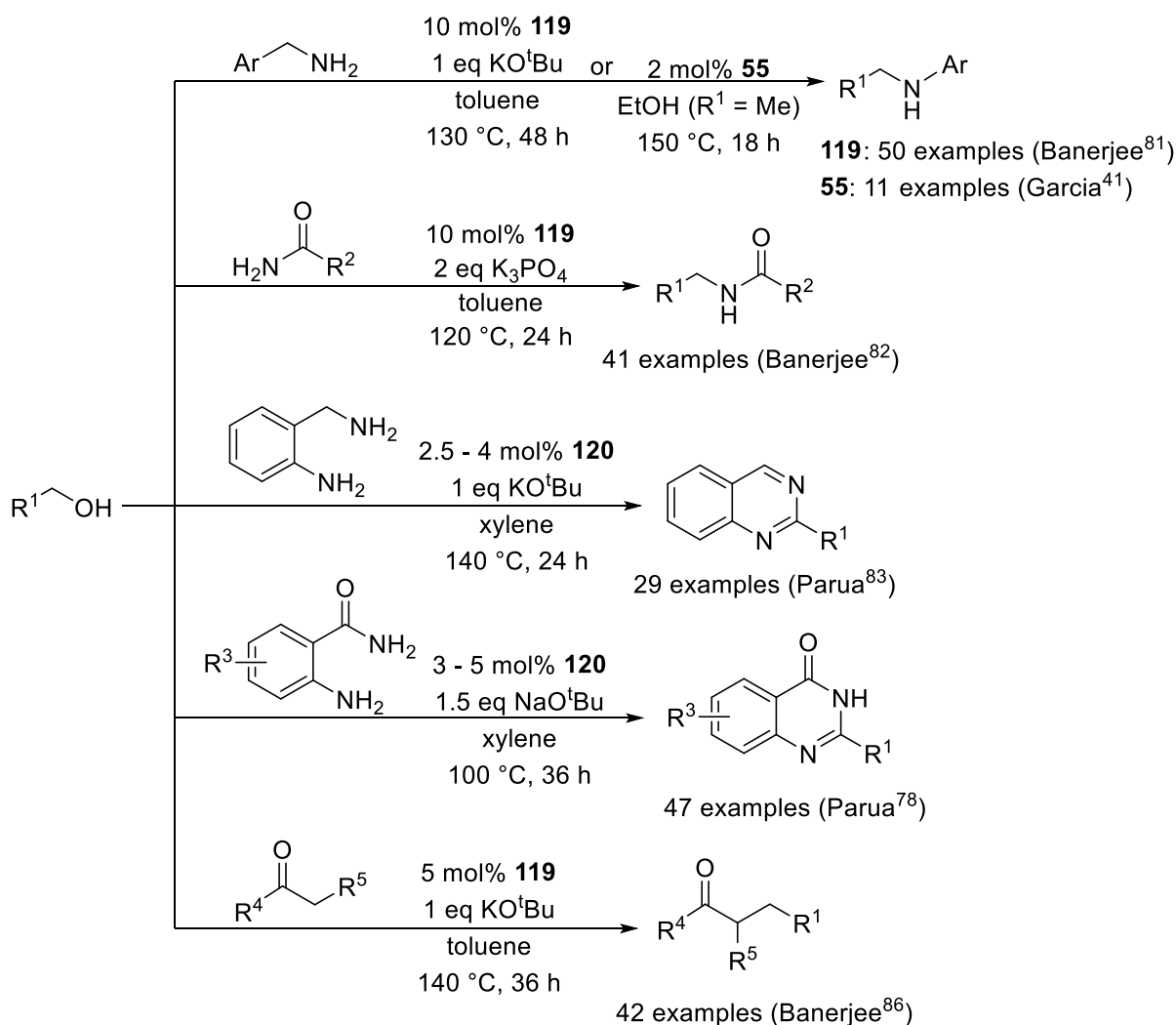


Figure 2.12 Ni complexes, **55**, **119** - **121**, which were used for dehydrogenative coupling between alcohols and amines.

Later, Benitez-Medina and García used a similar methodology for the N-alkylation of anilines with ethanol.⁴¹ Catalysed by 2 mol% of **55**, various anilines underwent N-alkylation with ethanol at 150 °C for 18 hours and no base was required (Scheme 2.65). Conversions of up to 100% were obtained.

The group of Banerjee continued their research on dehydrogenative coupling by conducting N-alkylation of amides and employing similar conditions to their previous research mentioned above, except for and the addition of two equivalents of K₃PO₄ (Scheme 2.65).⁸² Various primary alcohols and amides could be coupled dehydrogenatively in isolated yields of 13 to 92%.



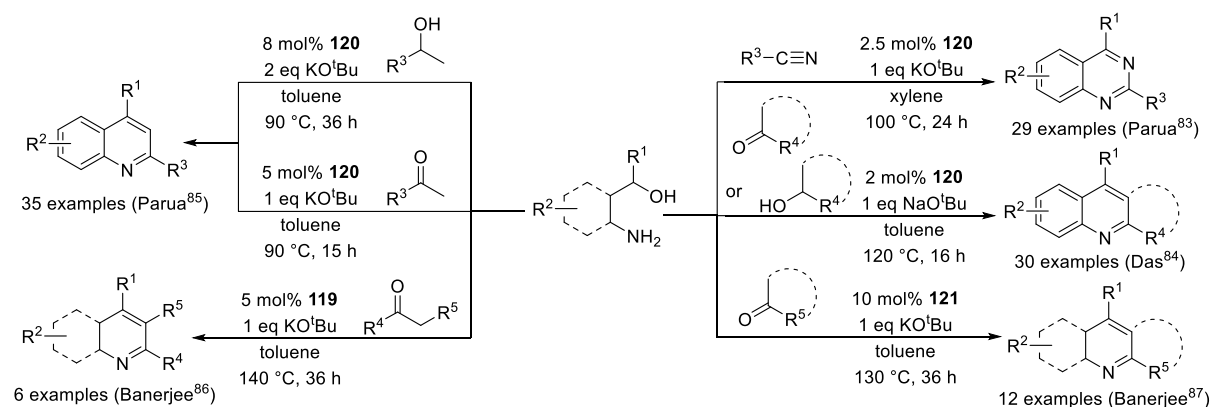
Scheme 2.65 Various dehydrogenative coupling reactions with Ni(II) complexes that required a simple alcohol.

In the same period, Parua and co-workers utilised the strategy of acceptorless dehydrogenative coupling between alcohols and amides for the synthesis of quinazoline-4(3H)-ones.⁷⁸ Employing 3 to 5 mol% of **120** with 1.5 equivalents of NaO^tBu aided in the coupling of a broad scope of benzylic alcohols and o-aminobenzamides in isolated yields of 50 to 90% at 100 °C for 36 to 60 hours (Scheme 2.65). Polysubstituted quinazolines could also be synthesised a year later by the same group using **120**, albeit with different substrates.⁸³ A combination of o-aminobenzylamines and benzylic alcohols (Scheme 2.65) or o-aminobenzylalcohols and benzonitriles (Scheme 2.66) could be coupled dehydrogenatively in xylene at 140°C for 24 hours with one equivalent of KO^tBu and 4 mol% or 2.5 mol% of complex, respectively.

Independently, Das, Maiti and De Sarkar used **120** (2 mol%) to dehydrogenatively couple o-aminobenzylalcohols with benzylalcohols or acetophenone to form polysubstituted

quinolines (Scheme 2.66).⁸⁴ In 16 hours at 120 °C with one equivalent of NaO^tBu various combinations of the previously mentioned substrates could produce the desired quinolines in 43 to 92% isolated yield.

The group of Parua could also synthesise polysubstituted quinolines (Scheme 2.66) employing the same strategy.⁸⁵ They, however, used 5 mol% of **120** at 90 °C for 15 hours with one equivalent of KO^tBu for the dehydrogenative coupling of o-aminobenzylalcohols and benzylic ketones (47 - 89% isolated yield). An alternative approach was to dehydrogenatively couple o-aminobenzylalcohols with benzylalcohols (29 - 83% isolated yield) using 8 mol% of **120** at 90 °C for 36 hours with two equivalents of KO^tBu. The former approach, utilising ketones, was the more effective choice as it resulted in higher yields compared to the latter approach.

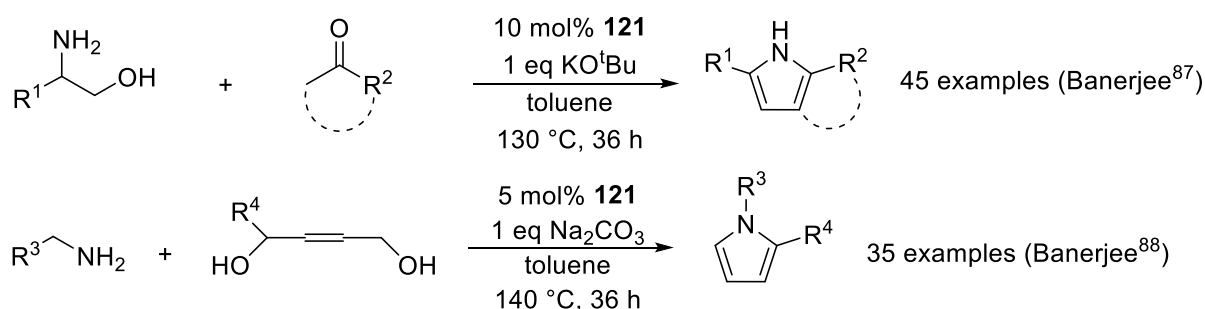


Scheme 2.66 Ni(II) catalysed dehydrogenative couplings requiring an aminoalcohol for the synthesis of substituted pyridines, quinolines and quinazolines.

The group of Banerjee was also successful in the synthesis of a few polysubstituted quinolines and pyridines following the former methodology by employing o-aminobenzylalcohols (or 3-aminopropanol) with benzylic ketones (Scheme 2.66).⁸⁶ However, 5 mol% of **119** was used with one equivalent of KO^tBu at 140 °C for 36 hours producing moderate isolated yields of 42 to 76%.

In the same study, dehydrogenative α -alkylation of ketones with primary alcohols was performed.⁸⁶ A variety of benzylketones could be alkylated with a scope of aromatic and aliphatic alcohols in 20 to 92% isolated yields using 5 mol% of **119** with one equivalent of KO^tBu at 140 °C for 36 hours (Scheme 2.65). A one-pot double alkylation of acetophenone could also be achieved under similar conditions in 48 hours. Afterward, this methodology was applied for the synthesis of a steroid hormone and Donepezil (an Alzheimer's drug); however, in 53 and 46% isolated yield.

The group of Banerjee employed the knowledge of dehydrogenative coupling to synthesise pyrroles (Scheme 2.67), pyridines and quinolines (Scheme 2.66).⁸⁷ They found that 10 mol% of a bipyridine (Bipy) ligated NiCl_2 pre-catalyst, **121**, with one equivalent of KO^tBu at 130°C could couple 2-aminopropan-1-ol and acetophenone to form 2-methyl-5-phenyl-1H-pyrrole in 36 hours. This strategy was utilised to dehydrogenatively couple various derivatives of the mentioned substrates to form the desired 2,5-disubstituted pyrroles. 2,3,5-Trisubstituted bi- and tricyclic pyrroles were also synthesised in this manner. Incorporating benzylic ketones instead of benzylalcohol, aided in the formation of C2-substituted quinoline and pyridine derivatives.



Scheme 2.67 Ni(II) catalysed dehydrogenative coupling reaction for the synthesis of pyrroles.

Afterwards, the same group developed a strategy employing cis-butene-1,4-diol with primary amines to dehydrogenatively synthesise N-substituted pyrroles (Scheme 2.67).⁸⁸ Only 5 mol% of **121** with one equivalent of Na_2CO_3 at 130°C was required to couple different benzylamines, aliphatic amines or anilines in 45 to 90% isolated product yields in 36 hours. Derivatives of cis-butene-1,4-diol were also investigated under the same conditions but lower yields of 31 to 40% were achieved.

2.3.3 Dehydrogenation of ammonia borane

Research conducted on the homogeneous Ni catalysed dehydrogenation of AB is rather scarce compared to that of other metals.⁸⁹ One of the first known homogeneous Ni catalysed AB dehydrogenation systems was developed by Keaton and co-workers in 2007.⁹⁰ Initial investigations into the most active NHC ligated Ni catalysed system were conducted with N,N'-bis(2,6-diisopropylphenyl)imidazole-2-ylidene (Idipp), N,N'-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene (Imes) and 1,3,4-triphenyl-4,5-dihydro-1H-1,2,4-triazol-5-ylidene (Enders' ligand)⁹¹ to determine the first-order rate constants (Figure 2.13). By employing 5 mol% of an *in situ* generated pre-catalyst, **122** to **124**, at 60°C , rate constants of 5.6, 7.3 and $64 \times 10^{-3} \text{ min}^{-1}$ were observed, respectively. Further studies with **124** (10 mol%) could generate more than 2.5 equivalents of H_2 gas (29 mL from a possible 31 mL) from AB in four

hours at 60 °C in C₆D₆ or diglyme (Scheme 2.68). Small amounts of borazine were present in the mixture originating from initial H₂N-BH₂ formation. A comparative study was made against [RuCl₂(p-cymene)]₂⁹² and [RhCl(coe)₂]₂⁹³ complexes (5 mol%) utilising Enders' ligand. It was found that **124** converted AB twice and four times faster compared to Ru and Rh, respectively.

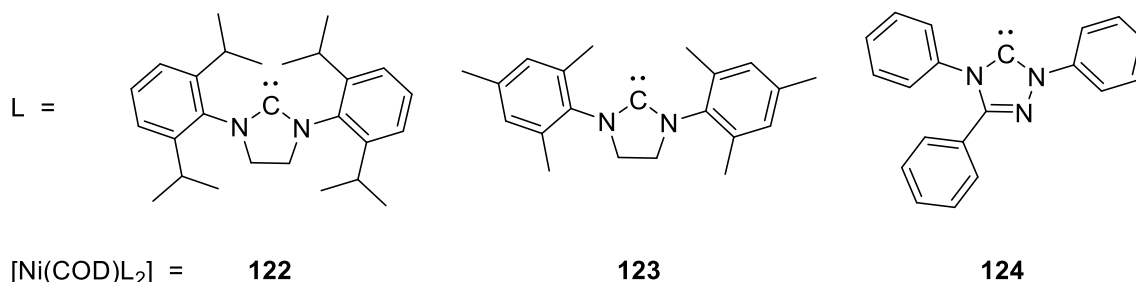
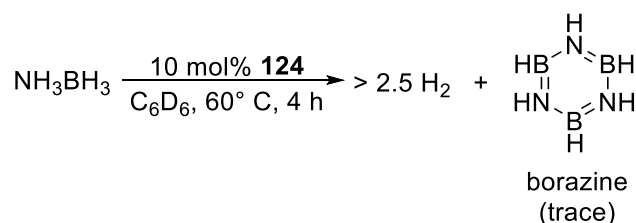
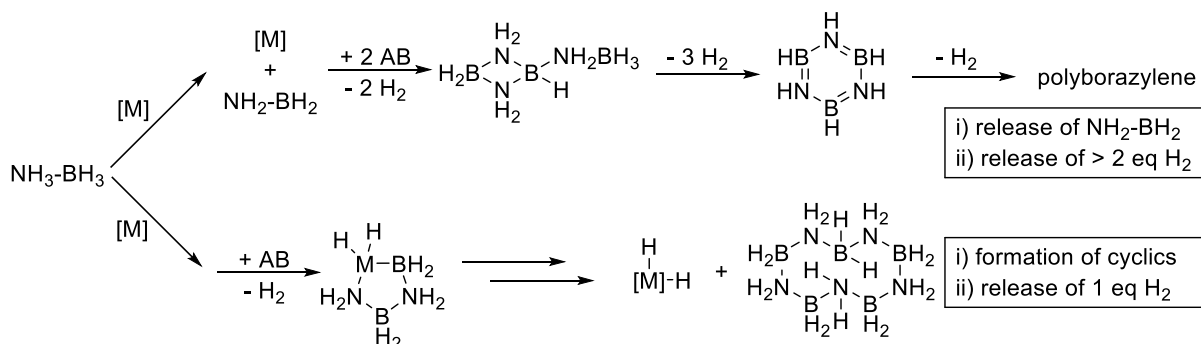


Figure 2.13 Ni(0) pre-catalysts, **122** - **124**, employed for the dehydrogenation of AB.⁹⁰



Scheme 2.68 Dehydrogenation of AB with **124**.⁹⁰

A year later, Pons and his team investigated a few metal complexes and how they influence the selectivity during AB dehydrogenation.⁹⁴ External trapping reactions with cyclohexene were performed illustrating that selectivity is determined by the coordination of aminoborane (NH₂BH₂) to the metal. AB dehydrogenation was followed with ¹¹B NMR spectroscopy using 10 mol% of an unspecified NHC ligated Ni(II) complex in diglyme at 25 °C. They observed that borazine was produced alongside a soluble polyborazylene resulting in more than two equivalents of H₂ being released, which confirms the results obtained by Keaton and co-workers mentioned above for the Ni catalysed dehydrogenation of AB (Scheme 2.69). An alternative route is followed by other metals via the formation of cyclic aminoboranes, resulting in the release of only one equivalent of H₂.

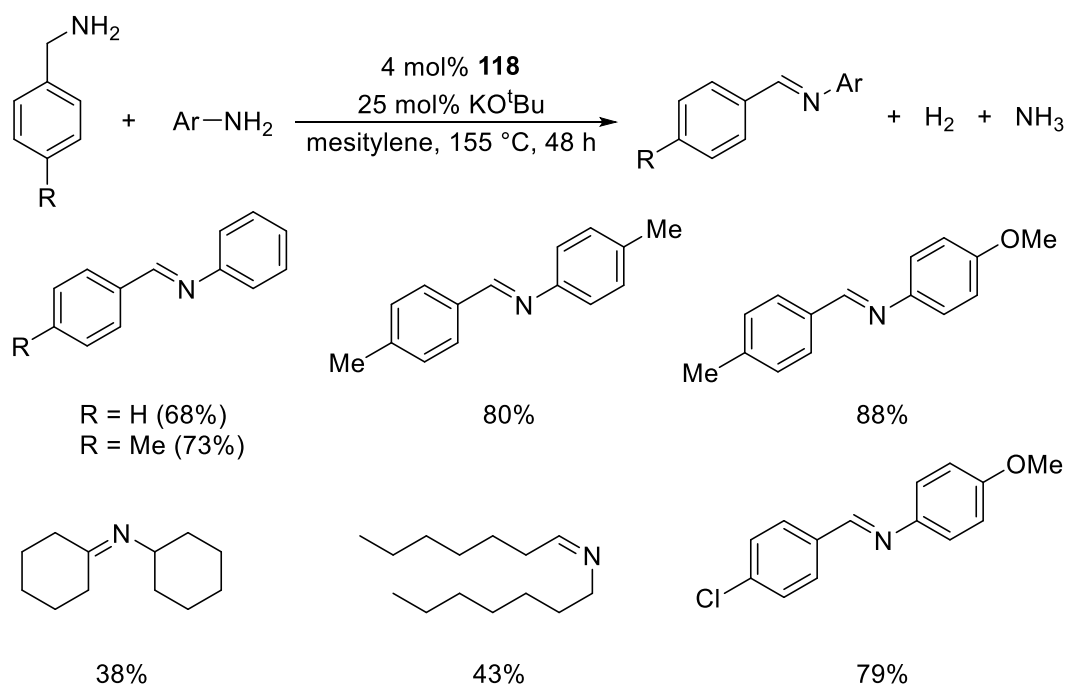


Scheme 2.69 Different pathways followed during AB dehydrogenation.⁹⁴

2.3.4 Dehydrogenation of primary amines

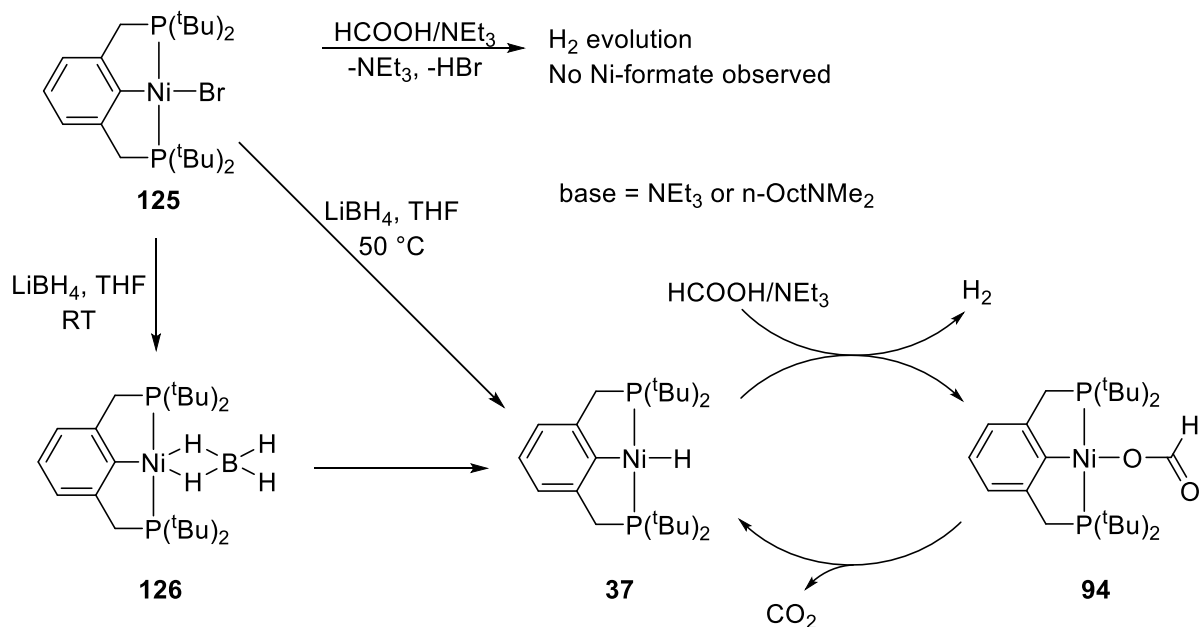
Not only has the dehydrogenation of AB been investigated, but studies conducted on the acceptorless dehydrogenation of amines, a structural analogue of AB, have also been performed.

Takallou and co-workers investigated the dehydrogenative coupling between primary amines and anilines resulting in the release of H_2 and NH_3 .⁸⁰ Several benzylic- and aliphatic amines were evaluated and seen to undergo dehydrogenative coupling to anilines by using 4 mol% of **118** with 25 mol% KO^tBu at 155 °C for 48 hours (Scheme 2.70). Isolated yields of up to 92% were afforded for the corresponding imine products.



Scheme 2.70 Acceptorless dehydrogenation of primary amines with **118**. Percentages are representative of isolated yields.⁸⁰

2.3.5 Dehydrogenation of formic acid



Scheme 2.71 Activation of **125** to generate Ni-H, **37**, for FA dehydrogenation and formation of **94**.⁶⁴

As previously illustrated, FA has been utilised in various catalytic transfer hydrogenation reactions due to its capability to produce H₂, but studies conducted on the exclusive use of FA for H₂ production remain scarce. The first and only study, to our knowledge, which is

reported on the homogeneous Ni(II) catalysed decomposition or dehydrogenation of FA for the liberation of H₂ and CO₂ was conducted by Enthaler and co-workers.⁶⁴ By employing 5.3 μmol of **37**, FA (11:10 ratio with n-OctNMe₂, 5 mL) could undergo dehydrogenation at 40 to 80 °C to produce up to 220 mL of H₂ in three hours with a maximum TON of 626. Mechanistic elucidation revealed the presence of a Ni(II) formate intermediate being formed during the catalytic cycle, with subsequent release of CO₂ (Scheme 2.71). Complexes **125** and **126** were also able to dehydrogenate FA, albeit with lower volumes of H₂ being produced.

2.4 Conclusions and outlook

Homogenous Ni catalysed hydrogenation and dehydrogenation reactions have seen remarkable progress in the last few decades. Various Ni pre-catalysts bearing bi-, tri- and tetradentate ligands have been developed and applied successfully in various (de)hydrogenation reactions. The utilisation of Ni in hydrogenation reactions seems to outnumber that which is present for dehydrogenation reactions, but growth in the latter research field is on the rise.

Homogeneous Ni pre-catalysts have been employed in the hydrogenation of C-C-, i.e. alkynes and alkenes, C-N-, i.e. nitriles, imines and hydrazones, C-O-, i.e. ketones, aldehydes and CO₂, and N-O, i.e. nitro-containing compounds. Various hydrogen sources have proven to be successful for these reactions and included not only the more commonly used H₂ gas, but also alcohols, amines, FA and silanes as less hazardous sources of H₂ during transfer hydrogenation reactions.

Dehydrogenation reactions of alcohols, amines, AB and FA have also been studied with great success. The dehydrogenation of alcohol has also been employed further in dehydrogenative coupling reactions with amine and amides towards valuable chemical intermediates and products.

From this literature review it was possible to identify three distinct pre-catalysts, **37**, **55** and **70**, which can catalyse both hydrogenation and dehydrogenation reactions. Other pre-catalysts utilised for transfer hydrogenation reactions also display the same properties and can consequently also fall into the same category.

A great deal of emphasis is still being placed on ligands containing phosphine moieties and although the corresponding Ni pre-catalysts display high activity, the use of phosphine for ligand synthesis remains laborious, toxic and they are sensitive to moisture. Greener ligands containing carbene or N-donors have shown to be effective in several (de)hydrogenation

reactions as seen in this review. It would therefore be advantageous to place more emphasis on the evaluation of these types of ligands as alternatives.

Although much research has been conducted on (de)hydrogenation reactions with homogeneous Ni pre-catalysts, opportunities remain concerning the evaluation of some substrates. Homogeneous (transfer) hydrogenation of esters with Ni complexes is non-existent and therefore provides an opportunity for further investigation.

AB has also become an important transfer hydrogenation agent in the last decade with an increase in research being conducted. The amount of research on the transfer hydrogenation of unsaturated compounds with homogeneous Ni complexes using AB as a source of H₂ is very scarce. Therefore, exploration in this field needs to be started as it will provide valuable insight into the formation of usable products.

Selectivity during nitrile hydrogenation remains a challenge, and it would consequently be a great opportunity to develop Ni complexes that are capable of chemoselective nitrile hydrogenation. Current pre-catalysts are only able to produce imine products but selectivity towards primary or secondary amines remains elusive. Further investigation using AB as the source of H₂ is required.

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Chapter 3

Fast and efficient nickel(II)-catalysed
transfer hydrogenation of quinolines with
ammonia borane

Fast and efficient nickel(II)-catalysed transfer hydrogenation of quinolines with ammonia borane

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Abstract: Herein we report the first Ni(II)-catalysed transfer hydrogenation of quinolines using ammonia borane (AB) as hydrogen (H₂) source. An *in situ* generated Ni(II)-bis(pyrazolyl)pyridine precatalyst could hydrogenate quinoline and its derivatives in excellent yields of up to 90% at 25 °C in 30 minutes. Spectroscopic studies revealed that a Ni (II)-hydride is responsible for the transfer hydrogenation of quinoline to 1,2,3,4-tetrahydroquinoline via a 1,4-dihydroquinoline intermediate.

Keywords: Nickel(II), ammonia borane, transfer hydrogenation, quinolines

3.1 Introduction

N-heterocyclic compounds, in particular 1,2,3,4-tetrahydroquinolines, are important precursors in the synthesis of various bioactive compounds used in the pharmaceutical industry,¹ i.e. farnesyltransferase inhibitors (antimalarial agents) that are highly cytotoxic to *Plasmodium falciparum*.²

The synthesis of 1,2,3,4-tetrahydroquinolines is possible utilising different approaches, i.e. cyclisation,³ rearrangements⁴ or partial reduction of quinoline and derivatives. Currently the partial reduction (hydrogenation) of N-heteroaromatics is preferred due to its simplicity.¹ Unfortunately elevated temperatures are required due to the increased stability associated with the aromaticity of the compound.⁵ Despite this drawback, several studies have been conducted on the hydrogenation of quinolines employing H₂ gas as reductant.⁶ The risks associated with H₂ gas, explosiveness and flammability, is a major concern while requiring very low temperatures (-253 °C) or very high pressures (350 - 700 atm) when stored.⁷ For these reasons alternative hydrogen sources such as ammonia borane (AB) are being utilised for transfer hydrogenation (TH) reactions. AB has a high gravimetric hydrogen storage density (19.6 wt%)

and is non-flammable.⁸ The catalytic dehydrogenation of one equivalent of AB has the potential to produce three equivalents of H₂ molecules, making it a viable candidate for TH reactions.

AB has been utilised in various TH reactions with great success. The produced H₂ gas from AB dehydrogenation is released *in situ*, facilitating catalyst-mediated hydrogenation of an unsaturated compound. Co (II)-, Cu(I)-, Bi(I)-, Pd(II)- and borane catalysts dominate the field of catalytic TH of unsaturated compounds with AB as H₂ source, i. e. nitriles,⁹ nitroarenes,¹⁰ N-heteroaromatics,¹¹ alkynes,¹² alkenes,¹¹ imines,¹³ and pyridines.¹⁴ These reactions are, however, still limited to long reaction times, elevated temperatures and excessive amounts of AB.

The use of Ni for the dehydrogenation of AB and subsequent hydrogenation of unsaturated compounds is rather scarce. Some examples of heterogeneous Ni-catalysts do exist but most of the reports evaluate bi- or trimetallic catalysts.¹⁵ Drawbacks include the excess of AB required (3 – 4 equivalents) and noble metal impregnation to ensure the success of the reaction. In particular, Yun *et. al.* recently reported a Ni@PC catalyst for the TH of quinolines with AB.^{15f} Their catalyst, while operating at room temperature required reaction times of three hours and 10 equivalents of AB. Some examples of homogeneous Ni-based catalyst systems have been reported for the TH of alkynes.¹⁶ These typically suffer from the use of phosphine moieties in the ligand, which are toxic, expensive and are laborious to synthesise. Also, reactions typically require prolonged reaction times (24 – 72 hours).^{12c,17}

In order to overcome the abovementioned drawbacks, we directed our research towards the development of a catalyst system comprising a cheap Ni(II) salt in combination with a bench stable tridentate bis(pyrazolyl)pyridine ligand for the TH of quinolines to their 1,2,3,4-tetrahydroquinoline products.

3.2 Results and discussion

3.2.1 Optimisation of reaction conditions for transfer hydrogenation of quinoline

Initially we were interested in finding a simple TH protocol that incorporated an earth-abundant metal and simple ligand system to hydrogenate quinoline under benign conditions. Evaluation of phenanthroline, a rigid and versatile ligand, with Co(II)-, Mn(II)-, Fe(II)-, Cu(II)- and Ni(II)-chloride salts (Table S1.1) indicated that Ni was the best candidate for further investigation. Bai and co-workers reported that a ligand-free Ni(II)-catalyst is very active during catalytic TH reactions with NaBH₄ and methanol serving as the source of H₂. It was, however, observed that Ni nanoparticles (NPs) are the active catalysts.^{15e} Various bi- and tridentate ligands were tested at reaction times of 16 hours and 30 minutes (Figure 3.1, Table S1.2).

Ligand **L3.1** led to higher conversion than **L3.2** (97% vs 73%, Table S1.2, entry 1 vs entry 2), attributed to a combination of steric and electronic effects leading to a sterically less accessible and less electrophilic nickel centre. Commercially available ligands, i.e. phenanthroline (**L3.3**), bipyridine (**L3.4**) and 2,2'-dipyridylamine (**L3.5**), led to lower conversions of 41, 49 and 10% respectively. Ethylenediamine (**L3.6**) led to a reasonably high conversion of 85% after 16 h, which can be ascribed to a higher pKa (9.69) compared to the former ligands, i.e. 4.27, 4.86 and 4.79. Conversion decreased significantly to 51% and TOF of 102 h⁻¹ after 30 minutes of reaction time. As such, **L3.1** displayed the highest conversion and TOF (194 h⁻¹) after 30 minutes (Table S1.2).

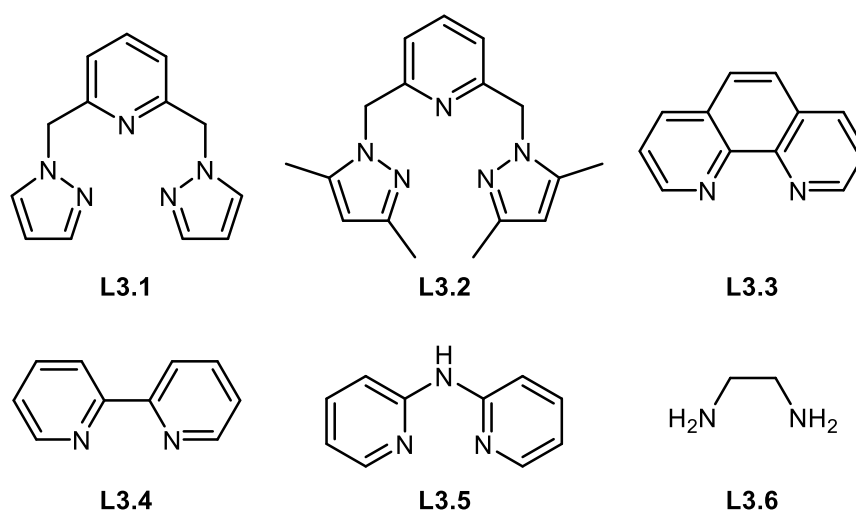
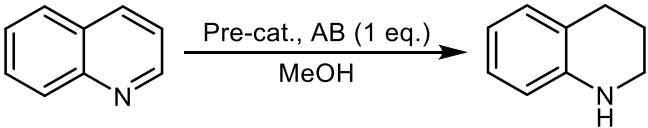


Figure 3.1 Bi- and tridentate N-donor ligands, **L3.1** - **L3.6**, used in this study.

To exclude the possibility of AB being solely responsible for the activity observed during the TH reaction, blank reactions, containing only AB and quinoline were performed. No conversion of quinoline was observed at 80 °C but at 25 °C only a trace amount of 1,2,3,4-tetrahydroquinoline was detected (Table 3.1, entry 1 and 2) due to slower decomposition of AB at lower temperatures.¹⁸ The addition of NiCl₂·6H₂O to the reaction, resulted in 63% conversion in 6 hours (Table 3.1, entry 3), significantly less than that reported by Bai and co-workers under similarly reaction conditions.^{15e} This provides further support that our catalyst system does not operate via Ni NP formation. With the addition of the best performing ligand, **L3.1**, the conversion increased to 96%, indicating enhanced activity in the presence of the ligand. A decrease in the catalyst concentration (1 mol%) and reaction time (0.5 hours), did not affect the conversion (Table 3.1, entry 7). Separate reactions containing only the pre-catalyst (Table 3.1, entry 9) or **L3.1** and AB (Table 3.1, entry 8), did not show any activity, indicating that both the pre-catalyst and AB are indeed necessary for the TH of quinoline to 1,2,3,4-tetrahydroquinoline. The homogeneity of the reaction was established by a mercury (Hg) drop test, with the

conversion of quinoline remaining unchanged after the addition of 500 equivalents of Hg (Table S1.5, entries 2 and 4), indicating that the reaction is indeed homogeneous in nature and no NP formation is present.

Table 3.1 Optimisation of quinoline transfer hydrogenation.

					
Entry	Pre-cat. (mol%)	AB (eq.)	T (°C)	t (h)	Conversion ^a (%)
1	-	1	80	24	-
2	-	1	25	24	3
3	NiCl ₂ ^b (3)	1	25	6	63
4	NiCl ₂ / L3.1 (3/3)	1	25	6	96
5	NiCl ₂ ^b (3)	1	25	0.5	56
6	NiCl ₂ / L3.1 (3/3)	1	25	0.5	96
7	NiCl ₂ / L3.1 (1/1)	1	25	0.5	97
8	L3.1 (1)	1	25	0.5	4
9	NiCl ₂ / L3.1 (1/1)	-	25	0.5	-

Reaction conditions: Under Ar atmosphere, ammonia borane (1 equivalent), quinoline (0.5 mmol), Ni(II) salt (x mol%) and **L3.1** (x mol%) in methanol (2 mL) were stirred at indicated temperature and time. ^a Conversion was determined by GC against biphenyl as the internal standard. ^b NiCl₂ denotes NiCl₂·6H₂O.

The composition of NiCl₂·6H₂O was evaluated with ICP (Table S1.6) and indicated that the relative amounts of PGMs present in the Ni(II) salt was extremely low (below 0.5 ppm). As such, the observed activity could be ascribed to Ni.

Next, we evaluated different Ni(II) salts using **L3.1** as the ligand of choice (Table S1.3). It was again seen that **L3.1** does indeed have an effect on the catalytic reaction because all of the reactions with added **L3.1** increased the percentage conversion of quinoline. The observed activity in decreasing order was as follows: NiCl₂·6H₂O > Ni(NO₃)₂·6H₂O > Ni(SO₄)₂·7H₂O. The result is advantageous due to the NiCl₂-precursor being the cheapest of the three. Next, we assessed the effect of the solvent on the reaction and observed that protic polar solvents, i.e. methanol and ethanol, are superior to aprotic polar and non-polar solvents (Table S1.4). Taking into account all of the abovementioned optimisation experiments, it was found that the NiCl₂·6H₂O precursor along with NNN-tridentate bis(pyrazolyl-1-methyl)pyridine ligand, **L3.1**, could effectively (97% conversion and 90% isolated yield) hydrogenate quinoline to 1,2,3,4-tetrahydroquinoline in 30 minutes at 25 °C, using one equivalent of AB as the H₂ source. To our

knowledge these conditions are the best reported for the TH of any substrate using AB operating under homogeneous conditions. Previous studies either required longer reaction times,¹¹ higher temperatures,^{12c} more than one equivalent of AB^{9a} or phosphine-containing ligands.^{9a} Further evaluation revealed that no dehydrogenation of 1,2,3,4-tetrahydroquinoline was observed when 1,2,3,4-tetrahydroquinoline was added to a methanol/toluene solution of the pre-catalyst at elevated (110 °C) temperatures. The abovementioned optimal reaction conditions were employed as the benchmark for the remainder of the study.

3.2.2 Transfer hydrogenation of quinoline derivatives with Ni(II)/L3.1

Using the optimised conditions, a series of quinoline derivatives were evaluated in TH to establish the substrate scope of our catalyst system. The percentage conversion and isolated yield of quinoline was used for comparison (Table 3.2, entry 1). Three different methyl-substituted quinolines were evaluated and it was found that the presence of methyl on C2 resulted in lower conversion due to an increased steric hindrance (Table 3.2, entry 2). However, increasing the reaction time (2 hours) and catalyst concentration (3 mol%), led to increased conversion and isolated yield of 64% and 56% respectively. A similar observation was noted during a study by Beller and co-workers where FA was used for the TH of quinoline derivatives.¹⁹ The presence of a methyl-substituent on C6 resulted in a high isolated yield of 75% (Table 3.2, entry 3), while changing the methyl-substituent to C8, increased the higher isolated yield to 85% (Table 3.2, entry 4).

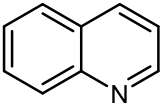
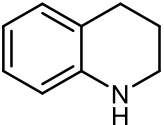
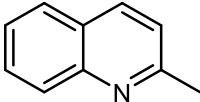
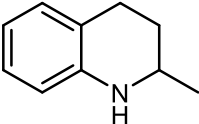
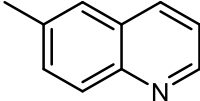
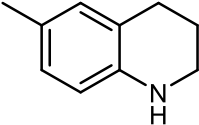
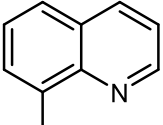
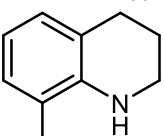
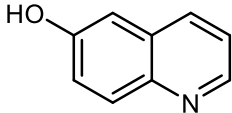
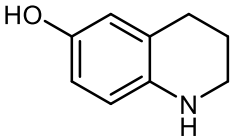
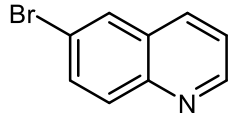
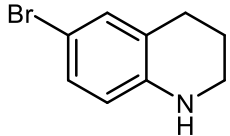
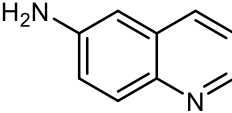
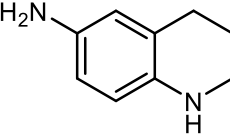
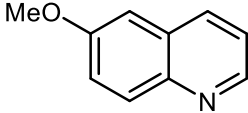
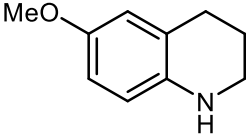
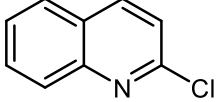
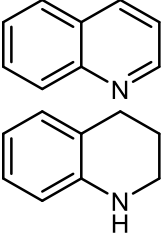
The presence of various electron acceptors and -donors on the C6 position were also evaluated. The hydroxyl substituent on C6 (Table 3.2, entry 5) showed a lower isolated yield compared to the methyl-substituted derivative (Table 3.2, entry 3), possibly due to a negative inductive effect from the OH group or hydrogen bonding to MeOH retarding hydrogenation.

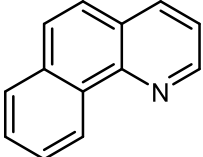
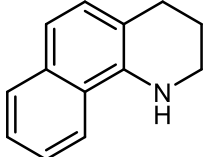
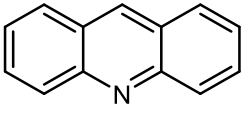
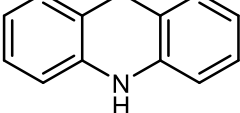
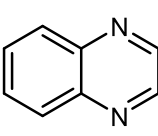
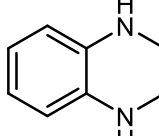
In contrast, the presence of a bromo substituent resulted in a slightly higher yield of 70% (Table 3.2, entry 6). A small amount (12%) of quinoline was present, indicative of dehalogenation. Amino-containing quinolines could be hydrogenated in 87% GC yield, when the reaction time was increased to two hours (Table 3.2, entry 7). 6-methoxyquinoline could be hydrogenated in 85% high isolated yield (Table 3.2, entry 8).

Unfortunately, low conversions were obtained for 2-chloroquinoline (Table 3.2, entry 9). Product analysis revealed that dehalogenation occurred, with no chlorinated 1,2,3,4-tetrahydroquinoline observed. Previous studies conducted on the hydrogenation of heteroaromatics have shown that dehalogenation is indeed possible.²⁰ Other quinoline derivatives, i. e. benzo[h]quinoline (Table 3.2, entry 10), acridine (Table 3.2, entry 11) and quinoxaline (Table 3.2, entry 12) were also evaluated. Benzo[h]quinoline could be hydrogenated in a moderate isolated yield of 60%,

with no increase after longer reaction times (2 hours) or higher catalyst loading (2 mol%). Acridine could not be converted further than 35%, even after increased reaction time (up to 6 hours), increased catalyst loading (up to 5 mol%) and temperature (80 °C), possibly due to the bulkiness of the second phenyl ring. Quinoxaline, showed a low conversion at first, however increasing the reaction time to 1 hour led to a very high yield, comparable to previous studies and in a much shorter reaction time.¹¹

Table 3.2 Ni(II)/L3.1 catalysed transfer hydrogenation of quinoline derivatives with AB.

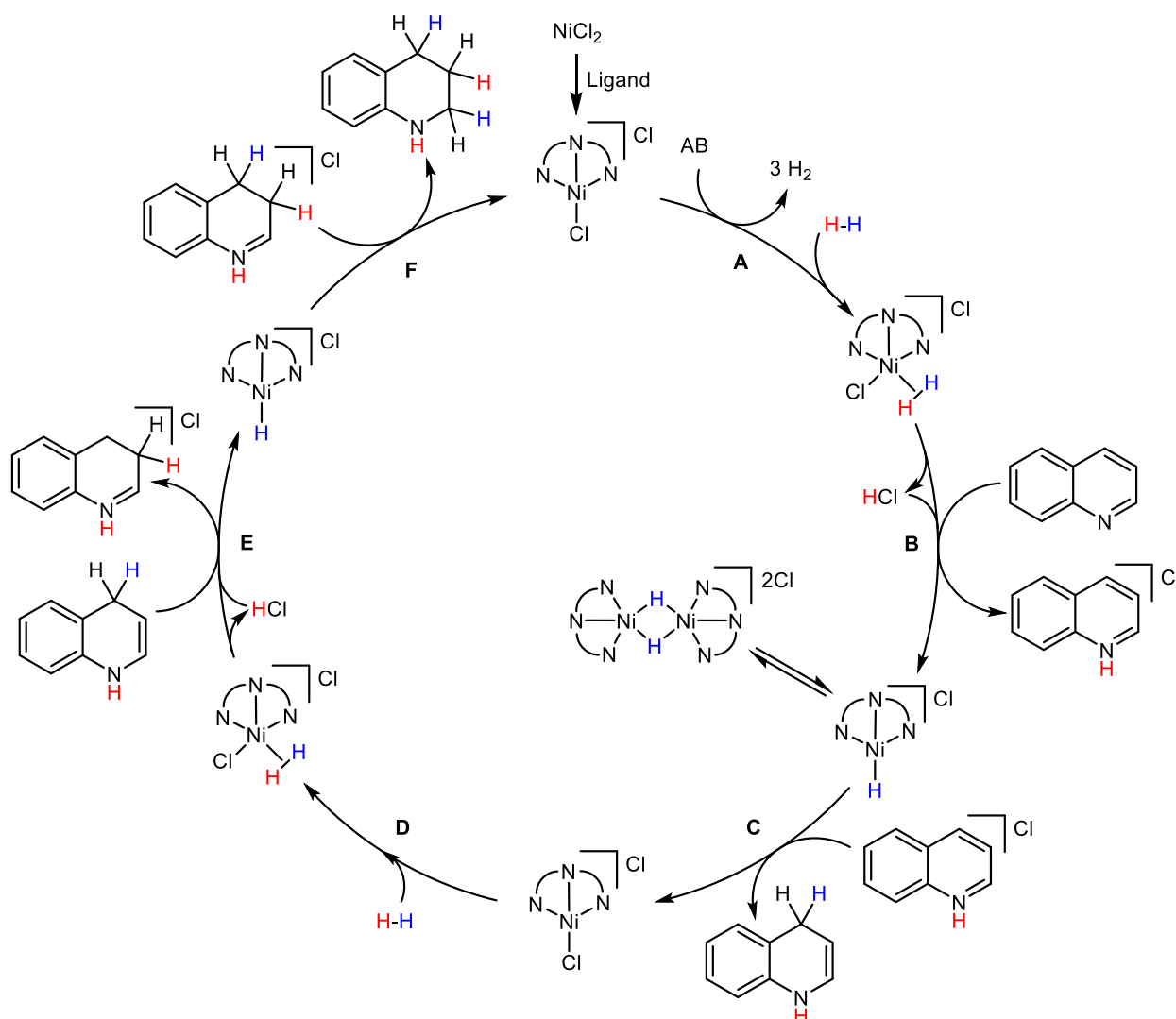
Entry	Substrate	Product	Conversion, % ^a (Isolated yield, %)
1			97 (90)
2			25, 64 ^b (56)
3			80 (75)
4			92 (85)
5			69 (60)
6			95 (70)
7			72, 87 ^{c, d}
8			96 (85)
9			19 (nd)

10			66 (60)
11			25, 35 ^e (26)
12			55, 94 ^f (85)

Reaction conditions: Under Ar atmosphere, ammonia borane (1 equivalent), substrate (0.5 mmol), Ni(II) salt (1 mol%) and **L3.1** (1 mol%) in methanol (2 mL) were stirred at 25 °C for 30 minutes. ^a Conversion was determined against biphenyl as internal standard. ^b 3 mol% pre-catalyst and 2 hours. ^c 2 hours. ^d GC-yield. ^e 2 hours. ^f 1 hour.

3.2.3 Mechanistic insights into the transfer hydrogenation of quinoline with Ni(II)/**L3.1**

NMR studies were conducted to elucidate the possible mechanism during which quinoline undergoes TH with AB. AB was subjected to dehydrogenation using NiCl₂·6H₂O and **L3.1**. Monitoring the ¹¹B NMR spectrum over time showed the disappearance of the AB quartet and emergence of a singlet at 14 ppm that was ascribed to the formation of trimethoxyborane (Figure S1.1).^{12c} Monitoring the ¹H NMR spectrum showed the presence of a broad upfield peak at -9.74 ppm and sharp peaks between 0 and 10 ppm that is due to the formation of a diamagnetic square planar Ni(II)-hydride species (Figure S1.2).²¹ The hydride signal disappeared when CD₃OD was used, illustrating Ni(II)-D formation. **L3.6** was used for comparison but did not show a hydride signal, indicating that **L3.1** has a greater stabilisation effect on the Ni(II)-hydride species. The presence of binuclear Ni(II)-hydride species in equilibrium with mononuclear species cannot be excluded.²¹ Broad downfield signals indicate the presence of NiCl₂/**L3.1** paramagnetic species²² due to incomplete conversion to the Ni(II)-hydride.



Scheme 3.1 Proposed mechanism for the transfer hydrogenation of quinoline to 1,2,3,4-tetrahydroquinoline.

Finally, we wanted to establish the type of hydrogenation pathway followed by quinoline en route to 1,2,3,4-tetrahydroquinoline. It was decided to use the optimum TH conditions and follow the reaction progress by NMR. The first ^{13}C NMR spectrum which could be recorded at time = six minutes showed complete conversion of quinoline. Additional spectra recorded as a function of time revealed a gradual increase in peak intensity for aliphatic and aromatic resonances that is indicative of the formation of 1,2,3,4-tetrahydroquinoline (Figure S1.3 and S1.4). Other peaks, which do not correspond to quinoline or the final product were also observed and gradually decreased in intensity over time. The peaks at 95.5 and 27.6 ppm were attributed to 1,4-dihydroquinoline (Figure S1.3 and S1.4), indicating that it serves as an intermediate between quinoline and 1,2,3,4-tetrahydroquinoline (Scheme 3.1). This result corresponds to a previous study where the mechanism of Ir-catalysed quinoline hydrogenation with H_2 gas was investigated.²³

Our results allow the conceptualisation of the mechanistic pathway illustrated in Scheme 3.1. Initial dehydrogenation of AB by Ni(II)/**L3.1** results in H₂ generation and subsequent H₂ addition to Ni(II)/**L3.1** (**A**). Protonation of quinoline occurs via a HCl pathway to produce the quinolinium species and the Ni(II)-hydride species (**B**).²⁴ Hydride addition to C4 follows, resulting in the observed 1,4-dihydroquinoline with concomitant formation of a coordinatively unsaturated Ni(II)-species (**C**). Coordination of another H₂ molecule occurs (**D**), followed by the step-wise protonation of C3 (**E**) and hydride addition to C2 (**F**) resulting in 1,2,3,4-dihydroquinoline and regeneration of the original Ni(II)-species (**E**). Our ¹³C NMR results suggests that **E** is the rate-limiting step due to the slow disappearance of the 1,4-dihydroquinoline intermediate.

3.3 Conclusion

In conclusion, we have demonstrated that an *in situ* prepared Ni(II)-bis(pyrazolyl)pyridine catalyst is capable of accelerating the methanolysis of AB to produce H₂ gas *in situ* that can subsequently be utilised for the hydrogenation of quinoline to 1,2,3,4-tetrahydroquinoline at ambient temperature and in a very short reaction time. High activity could be achieved in the absence of phosphine moieties or base additives. A variety of quinoline derivatives were converted and the products isolated in good to excellent yields. Mechanistic studies revealed the presence of a Ni(II)-hydride as well as 1,4-dihydroquinoline as key intermediates en route to produce 1,2,3,4-tetrahydroquinoline. We are currently exploring the TH of other unsaturated compounds utilising the optimised system from this study.

3.4 Experimental section

3.4.1 General procedure for the transfer hydrogenation of quinoline with Ni(II)/**L3.1**

Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under Ar atmosphere. Sequential addition of quinoline (60 µL, 0.5 mmol) and then NiCl₂ · 6H₂O (1.2 mg, 5 µmol) with **L3.1** (1.2 mg, 5 µmol) in methanol (2 mL) followed. The reaction mixture was allowed to stir at room temperature for 30 minutes where after it was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion.

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Chapter 4

Chemoselective transfer hydrogenation of
nitriles to secondary amines with nickel(II)
catalysts

Chemoselective transfer hydrogenation of nitriles to secondary amines with nickel(II) catalysts

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Notice: This chapter was originally published as a Full Paper article in *Molecular Catalysis (Mol. Catal., 2021, 511, 111738-111744)*. The format that follows, with regard to headings, has been changed to ensure consistency in this thesis.

Abstract: Herein we report the selective transfer hydrogenation (TH) of nitriles to secondary (2°) amines with simple Ni(II)-catalysts using ammonia borane (AB) as a source of hydrogen (H₂). A bis(pyrazolylmethyl)pyridine (**L4.1**) or ethylenediamine (**L4.4**) ligated Ni(II) pre-catalyst, created *in situ*, could hydrogenate several aromatic- and aliphatic nitriles in full conversions and isolated yields of up to 88% under ambient temperature and in very short reaction times. Deuterium labelling experiments illustrated the incorporation of a proton on the nitrogen and hydride on the α-carbon of dibenzylamine. Using α-picoline borane, containing no dissociable protons, assisted with the postulation of a two-step TH mechanism of benzonitrile. AB was subjected to dehydrogenation and it was observed that a maximum of 2.96 equivalents of H₂ gas could be generated from NiCl₂·6H₂O/**L4.1**.

Keywords: Transfer hydrogenation, nitriles, ammonia borane, nickel(II).

4.1 Introduction

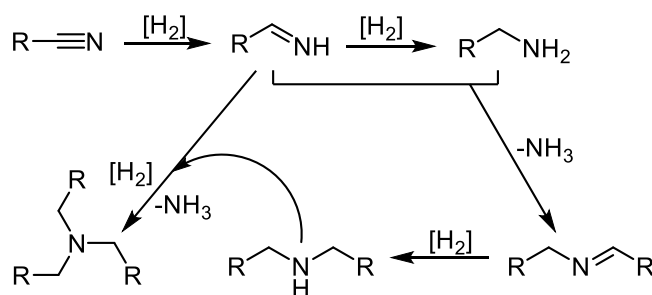
Amines are essential precursors for the production of several fine chemicals, particularly in the pharmaceutical industry.¹ The synthesis of amines can be performed following the reductive amination of ketones or aldehydes, but the catalytic hydrogenation of nitriles with molecular hydrogen (H₂) has received more attention as an environmentally friendlier route.² Nevertheless, a crucial drawback experienced with this method is poor chemoselectivity, resulting in a mixture of amine products (Scheme 4.1).³ It thus remains a challenge to control the selectivity of this reaction for the formation of a particular amine product.

Studies incorporating heterogeneous catalysts in the hydrogenation of nitriles with H₂ have focused more on primary (1°) amine formation⁴ with some showing that selective secondary (2°) amine and 1° aldimine formation is also possible.^{4a, 4c, 4e, 4f, 5} In homogeneous nitrile hydrogenation, catalysts containing Mn, Fe and Co outperform other transition metals.⁶ Regarding chemoselectivity, the emphasis is placed on 1° amine^{5a, 7} and -aldimine⁸ formation,

also when Ni is utilised.^{8a, 9} It seems as though studies focusing on selective 2° amine formation, which serve as important precursors for bioactive agents and ligands,¹⁰ are limited to noble metal catalysts.¹¹ Unfortunately the flammability and explosiveness of H₂ during storage, transport and operation is hazardous.¹² A greener alternative that has shown great efficiency in transfer hydrogenation reactions, is ammonia borane (AB).¹³ Advantages of AB include a high gravimetric hydrogen storage density (19.6 wt%) and it is a non-flammable solid.

AB can potentially release three equivalents of H₂, which can be applied in the catalytic hydrogenation of unsaturated compounds. Many examples are present in literature that illustrate the success of AB as hydrogen source, i.e. for alkynes,¹⁴ alkenes,¹⁵ nitroarenes,¹⁶ imines¹⁷ and heteroaromatics.^{15, 18} However, the transfer hydrogenation of nitriles with AB is scarce with only a few heterogeneous^{16b, 16c, 19} and homogeneous examples reported.²⁰ Although excellent results were obtained, excess amounts (1.6 - 4 equivalents) of AB and extended reaction times for homogeneous reactions (8 - 16 hours) were required. The presence of a toxic phosphine moiety as part of the ligand system is an additional drawback.

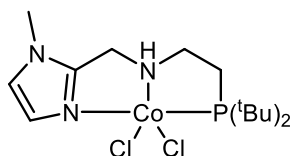
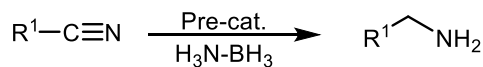
Shao and co-workers could chemodivergently hydrogenate several nitriles to 1° or 2° amines using a NNP-ligated Co(II)-catalyst and sacrificial AB.^{20b} Using expensive hexafluoroisopropanol (HFIP), 2° amines were generated in up to 95% isolated yield. However, changing the solvent to hexane resulted in selective 1° amine formation of up to 96% GC yield.



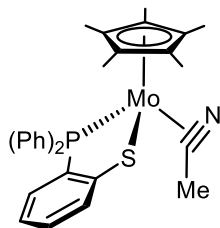
Scheme 4.1 Possible product formation during nitrile hydrogenation.

A. Previous work

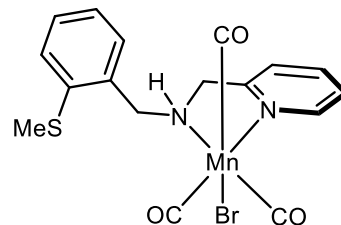
i) Primary amine synthesis



Shao et al. (2016)
1 mol% pre-cat., AB (1.6 eq.)
n-hexane, 50 °C, 16 h

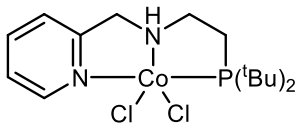
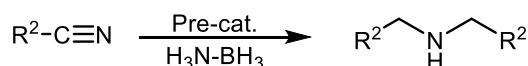


Hou et al. (2020)
2 mol% pre-cat., AB (2 eq.)
THF, RT, 8 h

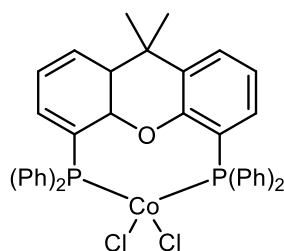


Sarkar et al. (2021)
1 mol% pre-cat., AB (3 eq.)
n-hexane, 60 °C, 6 h

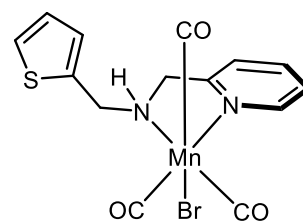
ii) Secondary amine synthesis



Shao et al. (2016)
0.5 mol% pre-cat., AB (1.6 eq.)
HFIP, RT, 13 h

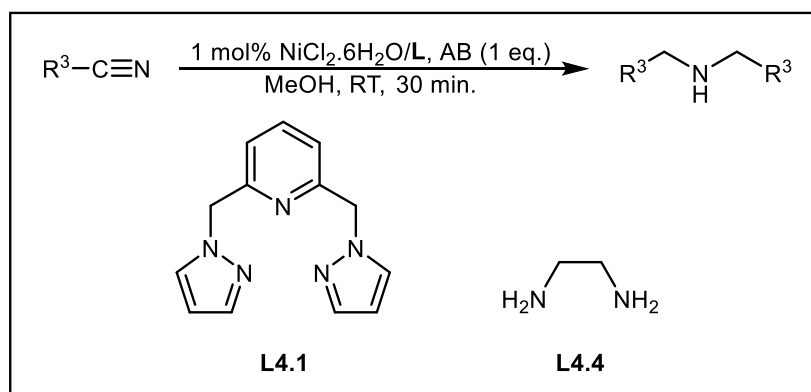


Sharma and Punji (2019)
1 mol% pre-cat., AB (2 eq.)
HFIP, 27 °C, 16 h



Sarkar et al. (2021)
1 mol% pre-cat., AB (3 eq.)
n-hexane, 60 °C, 12 h

B. Current work



Scheme 4.2 Previous and current work on the homogeneous transfer hydrogenation of nitriles with AB as the H₂ source.

Later Sharma and Punji utilised a 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (xantphos) ligated Co(II)-catalyst to hydrogenate nitriles with AB to 2° amines (up to 92% isolated yield)

under similar conditions to Shao.^{20c} Hou and co-workers showed that various nitriles could undergo chemoselective hydrogenation to 1° amines (up to 98% NMR yield) using a Cp*(1,2-Ph₂PC₆H₄S) ligated Mo(II)-catalyst with AB.^{20a} Most recently, Sarkar and co-workers followed a similar protocol to Shao et al. to chemoselectively hydrogenate nitriles to primary and secondary amines, using Mn(I) complexes.^{20d} To our knowledge, the chemoselective AB-facilitated transfer hydrogenation of nitriles with other homogeneous transition metals, i.e. Fe, Mn and Ni, has never been investigated.

Herein we report active and inexpensive catalyst systems comprising of cheap NiCl₂·6H₂O in combination with commercially available bis(pyrazolylmethyl)pyridine (**L4.1**) and ethylene diamine (**L4.4**) as ligands for the chemoselective TH of nitriles to their 2° amine products. This was achieved using a short reaction time and under ambient temperatures with AB as the source of H₂. We have previously observed that an active Ni(II)-hydride intermediate is responsible for the high TH activity^{18c} and the current study builds thereupon to investigate the TH of nitriles using NMR spectroscopy. In addition, the dehydrogenation of AB to determine the volume of H₂ released catalytically was also investigated.

4.2 Results and discussion

4.2.1 Optimisation of reaction conditions for transfer hydrogenation of benzonitrile

At the outset we decided to use the optimised conditions from our previous study that focused on the TH of quinolines^{18c} to evaluate the TH of benzonitrile with AB as a source of H₂. It was observed that AB cannot convert benzonitrile (Table 4.1, entry 1). The addition of ligand-free NiCl₂·6H₂O (Table 4.1, entry 2) led to full conversion of benzonitrile with a product distribution of benzylamine (**A**, 2%), N-benzylidenebenzylamine (**B**, 44%), dibenzylamine (**C**, 47%) and tribenzylamine (**D**, 7%). Using NiCl₂·6H₂O in combination with **L4.1** also resulted in complete conversion of benzonitrile but produced **C** selectively (Table 4.1, entry 3). This result indicates the importance of the ligand to enhance both the activity and selectivity of the catalyst during the reaction to ensure hydrogenation of **B** to **C**, which was the drawback in previous Ni catalysed nitrile hydrogenation studies.^{8a, 9} Employing only **L4.1** with AB did not convert benzonitrile (Table 4.1, entry 4).

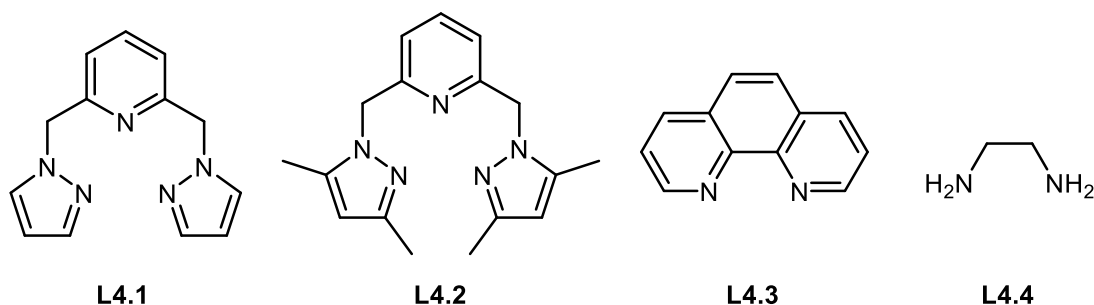


Figure 4.1 N-donor ligands, **L4.1** - **L4.4**, used in this study.

We decided to evaluate the effect of reaction time on the product distribution (Table S2.1). Complete conversion was observed after only five minutes albeit with slightly less 2° amine product of 67% (Table S2.1, entry 1). Increasing the reaction time to 10 and ultimately 30 minutes increased the selectivity (90%) towards **C** (Table S2.1, Entries 2 and 3).

Table 4.1 Optimisation of benzonitrile transfer hydrogenation conditions.^a

		A	B	C	D
Entry	Pre-cat.	Pre-cat. (mol%)	Time (min.)	Conversion (%) ^b	Prod. distr. ^c (A:B:C:D)
1	-	-	360	0	0
2	NiCl ₂ ·6H ₂ O	1	30	>99	2:44:47:7
3	NiCl ₂ ·6H ₂ O/ L4.1	1	30	>99	1:7:90:2
4	L4.1	1	30	0	0

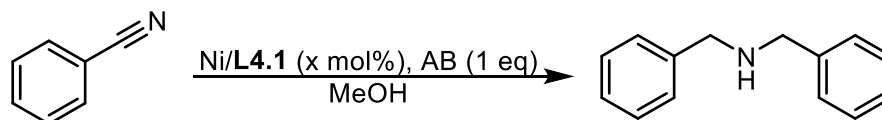
^a Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), benzonitrile (0.25 mmol), Ni(II) salt (1 mol%) and **L4.1** (1 mol%) in methanol (1 mL) were stirred at 25 °C for x minutes. ^b Conversion was determined by GC against biphenyl as the internal standard. ^c Product distribution was determined by GC-MS against internal standard.

Next we assessed the effect of the pre-catalyst (Table S2.2 and S2.3) on the reaction. Incorporation of ligands **L4.1**, **L4.2** and **L4.4**, resulted in full conversion of benzonitrile, with **L4.1** showing the highest selectivity towards **C** (90%). Using **L4.3** resulted in 41% conversion. Using CuCl₂·2H₂O/**L4.1** resulted in only 16% conversion. All Ni(II) salts evaluated could fully convert benzonitrile in 30 minutes at room temperature. However, only NiCl₂·6H₂O and NiSO₄·7H₂O showed good selectivity towards **C** of 90% and 78%, respectively, whereas NiNO₃·2H₂O

resulted in 59% **C** formation. Next we evaluated the effect of the solvent on selectivity (Table S2.4). Using EtOH as the solvent (Table S2.4, entry 2), resulted in 60% **B** formation. Changing the solvent to hexane, did not convert benzonitrile, contradictory to previous literature,^{20b} even at 50 °C, due to the insolubility of AB and the pre-catalyst (Table S2.4, entry 4). Previous studies have shown a change in selectivity towards the 1° amine, **A**, when small amounts of NH₃ are added to the reaction mixture.^{4a} Although a slight change in selectivity occurred when 5% v/v NH₃ was added (15 % **A**) (Table S2.4, entry 5), a further increase in NH₃ decreased activity and no conversion was observed (Table S2.4, entry 6).

We also investigated the effect of an open or closed reactor during the TH of benzonitrile (Table S2.5), which has not been evaluated before. Keeping the reactor open resulted in a slightly lower selectivity towards **C** (Table S2.5, entries 2 and 4) but good conversion, 88 - 100%, was still observed.

Next we determined the homogeneity of the reaction by conducting a mercury (Hg) drop test (Table S2.6). The assessment was done using both **L4.1** and **L4.4** as ligands with NiCl₂·6H₂O. Addition of 1000 equivalents of Hg did not reduce the percentage conversion or selectivity during the TH of benzonitrile (Table S2.6, entries 2 and 3), indicating that the reaction is homogeneous in nature.



0.025 mol%: Conversion = >99%, Selectivity = 67%
TON = 2680

0.01 mol%: Conversion = 69%, Selectivity = 74%
TON = 5100

Scheme 4.3 Maximum TON achieved during TH of benzonitrile with Ni/**L4.1**.

To evaluate the optimal efficiency and stability of our catalyst system, we decided to reduce the pre-catalyst loading as low as possible. We first mimicked the conditions used by Liu et al. by using 0.025 mol% of Ni/**L4.1**, which resulted in 100% conversion of benzonitrile with 67% dibenzylamine selectivity (TON = 2680) (Scheme 4.3).^{20b} Further reduction to 0.01 mol% of Ni/**L4.1** led to a 69% conversion with a 78% selectivity for **C**. This resulted in a maximum TON of 5100, the highest reported to date for an earth-abundant metal-based catalyst system evaluated in nitrile TH (Scheme 4.3).

From the abovementioned optimisation experiments, it was observed that $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}/\mathbf{L4.1}$ could completely (100% conversion and 90% selectivity) hydrogenate benzonitrile to dibenzylamine, **C**, in 30 minutes at 25 °C, with only one equivalent of AB being required. Due to $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}/\mathbf{L4.4}$ also showing good activity (100% conversion) and selectivity (79%) towards **C**, it was decided to also include it in further experiments, due to its low cost and commercial availability. To the best of our knowledge, the abovementioned conditions are the best reported for the TH of nitriles using AB operating under homogeneous conditions. Previous studies required higher temperatures, more than one equivalent of AB, longer reaction times, or toxic phosphine-containing ligands. The abovementioned optimal reaction conditions were employed as the benchmark for the remainder of the study.

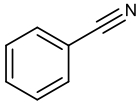
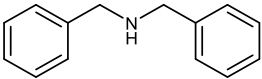
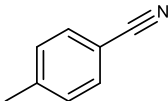
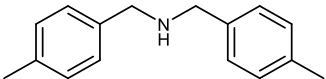
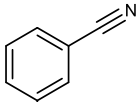
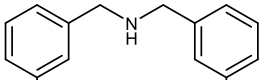
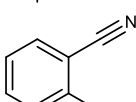
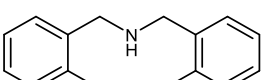
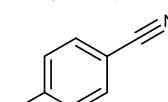
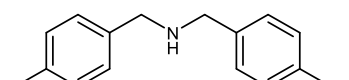
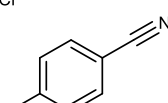
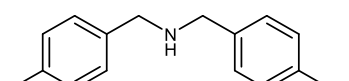
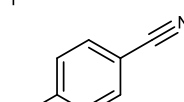
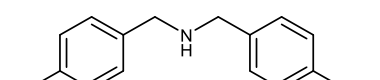
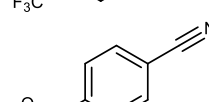
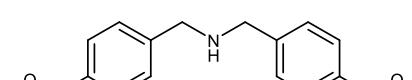
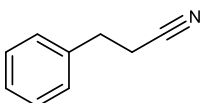
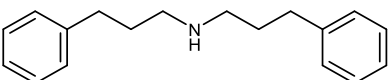
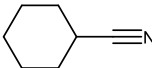
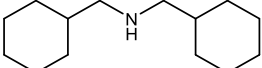
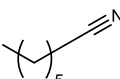
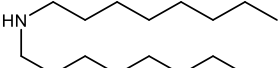
4.2.2 Transfer hydrogenation of benzonitrile derivatives with Ni(II)/L4.1** and Ni(II)/**L4.4****

We decided to evaluate a series of benzonitrile derivatives under the optimised conditions, as stated above, to establish the versatility of our catalyst system. In Table 4.2, the percentage conversion of the nitrile substrate, GC- and isolated yield of the 2° amine products are illustrated. Benzonitrile (Table 4.2, entry 1) is used as reference for comparison of other substrates.

Both $\text{Ni}/\mathbf{L4.1}$ and $\text{Ni}/\mathbf{L4.4}$ could convert the nitrile substrates to their respective 2° amine products in excellent percentage conversions of up to 100%, with $\text{Ni}/\mathbf{L4.1}$ showing quantitative conversion for all the nitrile substrates. For all the substrates except 2-methylbenzonitrile, $\text{Ni}/\mathbf{L4.1}$ showed the highest activity and selectivity towards the 2° amine products. A similar trend was observed for both pre-catalyst systems when selectivity is compared and therefore the focus of the discussion will be on $\text{Ni}/\mathbf{L4.1}$.

The presence of a methyl substituent on the 4- and 3-positions (Table 4.2, entries 2 and 3) resulted in an 80% and 70% selectivity, respectively, towards their respective 2° amines. Furthermore, a methyl substituent on the 2-position, not evaluated before with chemoselective secondary amine synthesis, resulted in a 40% selectivity toward 2° amine (Table 4.2, entry 4). Analysis of the product mixture revealed that 50% 1° amine had formed. For $\text{Ni}/\mathbf{L4.4}$, this was not the case as 60% 2° amine had formed. This difference in selectivity may be attributed to different steric environments imposed by **L4.1** relative to **L4.4**.

Table 4.2 Ni(II)/**L4.1** and Ni(II)/**L4.4**-catalysed transfer hydrogenation of benzonitrile derivatives.

Entry	Substrate	Product	Ni/ L4.1	Ni/ L4.4
			Conv. (%) ^a (GC yield, %) [IY, %] ^b	Conv. (%) ^a (GC yield, %)
1			>99 (90) [88]	>99 (79)
2			>99 (80) [75]	>99 (71)
3			>99 (71) [66]	>99 (56)
4			>99 (40) [55] ^c	>99 (60)
5			99 (97) [92]	67 (66)
6			>99 (93) [90]	>99 (94)
7			>99 (92) [86]	>99 (91)
8			>99 (90) [84] ^d	>99 (80)
9			>99 (77) [72]	>99 (70)
10			>99 (82) [78]	96 (72)
11			>99 (66) [63]	94 (65)

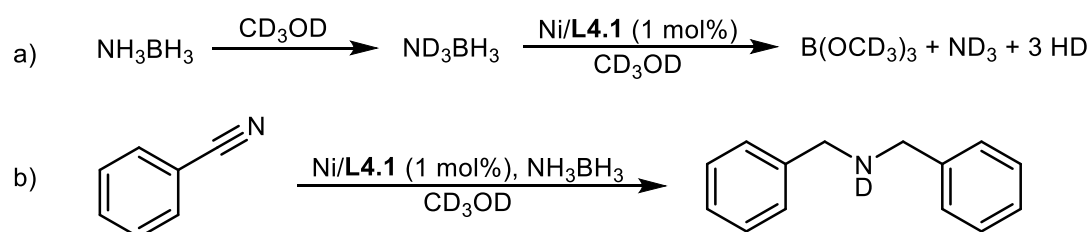
Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), substrate (0.25 mmol), NiCl₂·6H₂O (1 mol%) and **L4.1/L4.4** (1 mol%) in methanol (1 mL) were stirred at 25 °C for 30 minutes. ^a Percentage conversion and GC-yield (in parentheses) of 2° amine was determined against biphenyl as internal standard. ^b IY denotes isolated yield. ^c 1 hour. ^d 4 hours and 2 equivalents AB.

The pre-catalyst system also showed tolerance towards the presence of halide substituents, either -Cl or -F, on the 4-position of benzonitrile, which resulted in an excellent 2° amine selectivity of 97 and 93%, respectively (Table 4.2, entries 5 and 6). These results are superior to previous literature.^{20a, c, d} It is worth mentioning that no dehalogenation was observed. The presence of strong electron-withdrawing groups, -CF₃ and -COOMe, on the 4-position of benzonitrile was also tolerated but a longer reaction time (4 hours) and more AB (2 equivalents) were required for quantitative conversion (Table 4.2, entries 7 and 8). Under these reaction conditions, a high 2° amine selectivity (92 and 90%, respectively) was obtained, which is superior to previous studies.^{20a, c, d}

Three aliphatic nitriles, i.e. 3-phenylpropanenitrile, cyclohexanecarbonitrile and heptyl cyanide, not used in previous studies with regard to symmetric secondary amine synthesis, were also evaluated with the optimised pre-catalyst system (Table 4.2, entries 9 - 11). High selectivities (66 - 82%) towards their respective 2° amine products were obtained.

4.2.3 Mechanistic insights into the transfer hydrogenation of benzonitrile with Ni(II)/L4.1

To gain further insight into the benzonitrile TH mechanism, we decided to i) evaluate the direct hydrogenation of benzonitrile with the addition of borane and ii) use deuterium labelling to identify the position of proton and hydride insertion into the 2° amine product.



Scheme 4.4 a) Proton exchange and subsequent methanolysis of AB and b) deuterium incorporation during the transfer hydrogenation of benzonitrile with Ni/L4.1 and AB.

Initially 5 - 10 atm of H₂ with Ni/L4.1 was used to evaluate if the direct hydrogenation of benzonitrile occurs. No conversion was observed, even after an increase in the reaction temperature (60 °C) and reaction time (6 hours) (Table S2.8, entries 1 - 3). Addition of one equivalent of α-picoline borane, bearing no dissociable protons, with and without the addition of dihydrogen, resulted in <1% conversion (Table S2.8, entries 4 - 6). Increasing the reaction time (6 hours) and temperature (60 °C) led to an 80% conversion (Table S2.8, entry 7), whereas using only α-picoline borane with Ni/L4.1 under the same conditions, led to 31% conversion. These results indicated the importance of borane to activate dihydrogen for the formation of Ni(II)-hydride species, as previously observed (Figure S2.4).^{18c} Most importantly, it indicated

that the TH of benzonitrile with AB occurs via two separate steps, i.e. 1) dehydrogenation of AB and 2) subsequent hydrogenation of benzonitrile.^{14c, 18b}

Further investigation of the mechanism was conducted by applying deuterium labelling, which has not been evaluated before using AB as the source of H₂. Using the optimal conditions, separate reactions were conducted using MeOH and d₄-MeOH. From the ¹H NMR spectrum (Figure S2.1), the CH₂ protons for dibenzylamine, **C**, was observed as a singlet at 3.83 ppm and the NH proton as a broad singlet at 1.71 ppm. A singlet at 3.54 ppm was observed, corresponding to B(OMe)₃. Changing the solvent to d₄-MeOH resulted in the absence of a peak at 1.71 ppm, which can be attributed to deuterium incorporation on the 2° amine nitrogen (Scheme 4.4b). The peak at 3.83 ppm remained present, whereas the singlet at 3.54 ppm was also absent or very small. These observations can be ascribed to proton exchange of the ammonia protons from AB, resulting in the formation of D₃N-BH₃ and subsequent methanolysis with d₄-MeOH ultimately forming B(OCD₃)₃ (Scheme 4.4a).

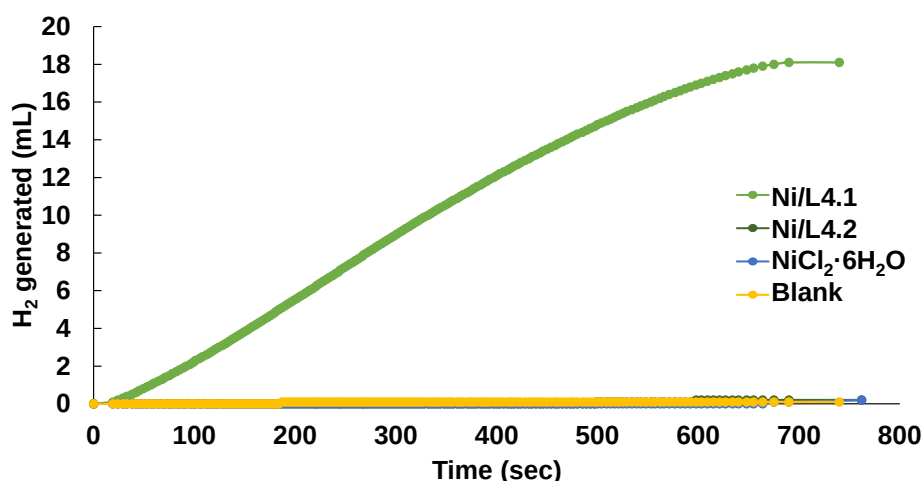


Figure 4.2 Total amount of H₂ gas generated during the dehydrogenation of 0.25 mmol of AB using 1 mol% of pre-catalyst in MeOH.

The high activity and conversion of nitriles to 2° amines led us to investigate the volume of H₂ that can be generated from ammonia borane. Catalytic non-hydrolytic dehydrogenation of AB results in the formation of B(OMe)₃ along with one equivalent of NH₃ and three equivalents of H₂ gas.^{14c, 22}

Utilising the optimal conditions as mentioned above, without benzonitrile and the pre-catalyst, little dehydrogenation (0.1 mL H₂ formation) was observed (Figure 4.2). Addition of NiCl₂·6H₂O to the solution increased the volume of H₂ to 0.2 mL. Using NiCl₂·6H₂O/L4.4 also yielded low H₂ evolution (0.2 mL). However, using NiCl₂·6H₂O/L4.1 as the pre-catalyst resulted in 18 mL of H₂

generated. This amounts to 2.96 equivalents of H₂ being formed, illustrating almost complete conversion of AB into H₂. This is the most H₂ generated compared to previous AB dehydrogenation studies with Ni or other homogeneous metals.²³ Formation of CDB, CTB and BCTB from AB, as previously seen, reduces the amount of H₂ that can potentially form and is also evident in our study. The increase in nitrogen donors in the ligand might influence the enhanced dehydrogenation of AB. Although NiCl₂·6H₂O resulted in low H₂ evolution, it could still successfully convert benzonitrile (100%) due to the coordinating benzonitrile and amine products. Contrary to this, NiCl₂·6H₂O/**L4.4** contains N-donors but the H₂ evolution was still low. However, the addition of benzonitrile resulted in full conversion. These observations illustrate that 1° amines are not good N-donors for AB dehydrogenation, whereas aromatic N-donors, i.e. pyridine and pyrazole, enhances the catalyst's AB dehydrogenation activity.

4.3 Conclusion

To summarise, we investigated the TH of benzonitrile and other aromatic and aliphatic nitriles using NiCl₂·6H₂O/**L4.1** and NiCl₂·6H₂O/**L4.4** as pre-catalysts with AB as the source of H₂. Complete conversion was achieved for almost all of the substrates with selectivity and isolated yields of up to 88% being obtained. Tolerance towards electron-donating and -withdrawing substituents was observed, with no dehalogenation occurring. Experimental insights into the TH of benzonitrile with AB revealed a two-step mechanism involving the incorporation of deuterium on the nitrogen with nucleophilic hydride attack on the α-carbon. Evaluation of AB dehydrogenation illustrated the high efficiency of NiCl₂·6H₂O/**L4.1**, which revealed its ability to produce 2.96 equivalents of H₂ gas. Currently, the optimised system from this study is being employed to evaluate the transfer hydrogenation of other unsaturated compounds with AB as the source of H₂.

4.4 Experimental section

4.4.1 General procedure for the transfer hydrogenation of benzonitrile with Ni(II)/L4.1****

Ammonia borane (8.6 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Addition of benzonitrile (25 µL, 0.25 mmol) and then NiCl₂·6H₂O (0.6 mg, 2.5 µmol) with **L4.1** (0.6 mg, 2.5 µmol) in methanol (1 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against biphenyl (internal standard) to determine percentage conversion. All catalytic runs were performed in duplicate. Additional experimental details are provided in the Supplementary Information

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Chapter 5

An inexpensive and simple nickel(II)
catalysed transfer hydrogenation of alkenes
with ammonia borane

An inexpensive and simple nickel(II) catalysed transfer hydrogenation of alkenes with ammonia borane

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Abstract: Herein we describe the catalytic transfer hydrogenation of alkenes (aromatic, aliphatic and α,β -unsaturated) to their respective alkane products utilising an ethylene diamine (**L5.2**) ligated Ni(II)-catalyst with ammonia borane (AB) as the source of hydrogen (H_2). Using only 1 mol% of the pre-catalyst at ambient conditions provided excellent conversions and isolated yields of the respective alkane products, with TON values up to 3960. The chemoselective hydrogenation of α,β -unsaturated esters was also achieved. Mechanistic elucidation revealed that borane activates dihydrogen, leading to the proposal of a two-step process during the transfer hydrogenation of styrene.

5.1 Introduction

The transition metal catalysed hydrogenation of unsaturated compounds containing π -systems remains an essential reaction in organic chemistry due to the valuable products resulting from it.¹ These reactions typically use dihydrogen (H_2) and have received particular attention in homogeneous Ni catalysed hydrogenations.² Some of these reactions do, however, suffer from high reaction temperatures, extended reaction times and high catalyst loadings. Furthermore, there is the added concern of flammability and explosiveness from pressurised cylinders.³ This resulted in research moving towards transfer hydrogenation (TH) reactions, which is a much safer method for the hydrogenation of unsaturated compounds.⁴

Several different sources of H_2 , including alcohols, formic acid, primary amines, Hantzsch esters, formate salts and dienes, have been utilised for TH reactions with great success.⁴⁻⁵ Recently, amine borane adducts⁶ have also been investigated and shown to be successful in the catalytic TH of several unsaturated compounds, i.e. alkenes,⁷ alkynes,^{7c, 8} nitriles,^{7b, 9} N-heteroaromatics,^{7a, 10} imines^{7b, 11} and nitroarenes.^{9c, 9d, 12} Amine-boranes, and specifically ammonia borane (AB), are more advantageous to use compared to other hydrogen sources because it is a non-flammable solid, which is safer to handle.⁶ AB also has a high gravimetric hydrogen storage density (19.6 wt%) and can potentially release up to three equivalents of H_2 , making it a suitable candidate for TH reactions.

Several successful attempts at the homogeneous TH of alkenes with AB as the source of H₂ have been reported. Studies focusing on metal-free alkene TH could only achieve success with activated alkenes,^{7e, 7h} whereas studies using Re(II)-catalysts had to use elevated reaction temperatures.^{7f, 7g} Most recently, a non-noble metal, i.e. Co(II), has also been used, but still suffered from long reaction times and high catalyst amounts.^{7a, 7c} Reports utilising other earth-abundant metals in a homogeneous fashion are scarce, with the above-mentioned drawbacks still present.

In an attempt to overcome all of these drawbacks, we decided to investigate the use of a simple and inexpensive pre-catalyst system comprising cheap NiCl₂·6H₂O in combination with commercially available ethylene diamine monohydrate (**L5.2**) as the ligand for the selective TH of aromatic- and aliphatic alkenes, and α,β -unsaturated esters to their respective hydrogenated products in a very short reaction time and under ambient conditions using AB as a source of H₂.

5.2 Results and discussion

5.2.1 Optimisation of reaction conditions for transfer hydrogenation of styrene

At the outset, we decided to use similar conditions from our previous studies^{10c} to explore the TH of styrene with AB as the source of H₂. We found that these conditions resulted in only 10% conversion (Table 5.1, entry 1). Increasing the temperature to 50 °C led to full conversion of styrene to ethylbenzene (Table 5.1, entry 2). Other bidentate N-donor ligands, **L5.2** to **L5.4** (Figure S3.1), were also evaluated as part of the pre-catalyst system and all resulted in >99% conversion (Table 5.1, entries 3 - 5). A ligand-free system also yielded the same results (Table 5.1, entry 6). Without any pre-catalyst, less than 1% of conversion was obtained (Table 5.1, entry 7).

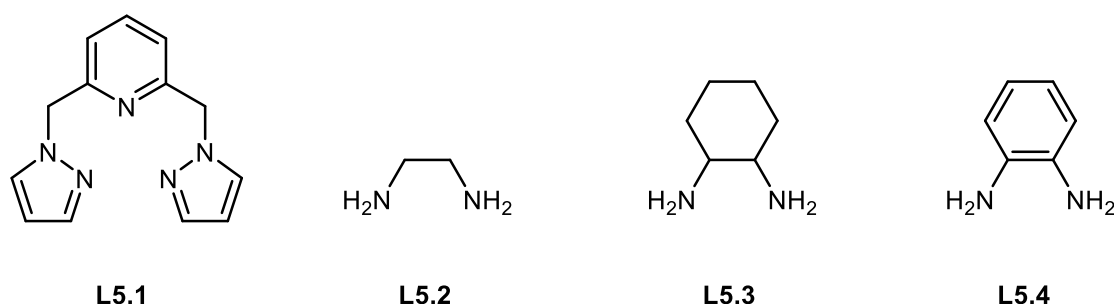


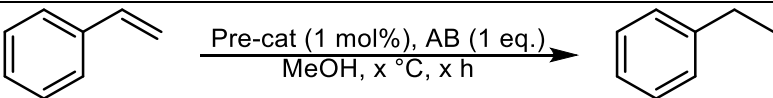
Figure 5.1 N-donor ligands, **L5.1** - **L5.4**, used in this study.

It was decided to evaluate the homogeneity of the catalytic system by incorporating 500 equivalents of Hg (Table S3.2). For all of the pre-catalysts, except Ni/**L5.2**, a drop in the

conversion was observed, establishing their heterogeneous nature. It was decided to continue with Ni/**L5.2** as the pre-catalyst of choice due to its homogeneous nature.

We also observed that using a lower purity of AB (90%) increased the conversion of styrene when the reaction was conducted at room temperature, compared to 97% AB under the same conditions (Table S3.3, entries 2 and 4). This observation was seen when utilising either Ni/**L5.1** or Ni/**L5.2** and illustrated the role of impurities in additives, particularly AB, and how they might influence reactions. For the remainder of the study, 97% AB was used.

Table 5.1 Evaluation of pre-catalyst, reaction time and temperature in styrene transfer hydrogenation.

				
Entry	Pre-cat	Temp. (°C)	Time (h)	Conversion ^a (%)
1	Ni/ L5.1	25	0.5	10
2	Ni/ L5.1	50	0.5	>99
3	Ni/ L5.2	50	0.5	>99
4	Ni/ L5.3	50	0.5	>99
5	Ni/ L5.4	50	0.5	>99
6	Ni	50	0.5	>99
7	-	50	0.5	<1

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), styrene (0.25 mmol), NiCl₂·6H₂O (1 mol%) and ligand (1 mol%) in methanol (1 mL) were stirred at indicated temperature and time. ^a Conversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs. Ni denotes NiCl₂·6H₂O.

As part of the optimisation studies, we evaluated the maximum turnover number (TON) that could be reached for the TH of styrene using AB as the source of H₂ (Table S3.4). Using 0.025 mol% of Ni/**L5.2**, a very high TON of 3960 was achieved (Table S3.4, entry 5), superior in comparison to most other transition metals used in TH and direct hydrogenation of alkenes (0.1 - 1000 TONs).^{2a, 13} Only one study fared better than our system, but a high H₂ pressure (30 atm) was required to achieve a TON of 10000 using 0.01 mol%.³⁶ We also evaluated the reaction on a 1 mmol scale, and Ni/**L5.2** was still able to convert styrene to ethylbenzene in 100% yield.

5.2.2 Transfer hydrogenation of styrene derivatives with Ni(II)/**L5.2**

Employing the conditions from Table 5.1, entry 3, we commenced evaluating a series of styrene derivatives, to establish the versatility of our catalyst system. Quantitative yields were achieved with the presence of a methyl substituent on the 4- and 3-positions (Table 5.2, entries 2 - 3,

respectively). Disubstituted styrene (Table 5.2, entry 4) could also be converted in >99% yield, with the addition of a bulky tert-butyl substituent on the 4-position (Table 5.2, entry 5) having no effect on the yield.

Table 5.2 Evaluation of Ni/**L5.2** in aromatic alkene transfer hydrogenation.

$\text{R}-\text{C}_6\text{H}_4-\text{CH=CH}_2 \xrightarrow[\text{MeOH, 50 } ^\circ\text{C, 30 min.}]{\text{Ni/L5.2 (1 mol\%), AB (1 eq.)}} \text{R}-\text{C}_6\text{H}_4-\text{CH}_2\text{CH}_3$				
Entry	Substrate	Product	Conversion ^a (%)	GC yield ^a (%)
1			>99	>99
2			>99	>99
3			>99	>99
4			>99	>99
5			>99	>99
6			>99	>99
7			>99	97
8			>99	>99
9			>99	>99

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), alkene (0.25 mmol), NiCl₂·6H₂O (1 mol%) and **L5.2** (1 mol%) in methanol (1 mL) were stirred at 50 °C for 30 minutes. ^a Conversion and GC yield were determined by GC against biphenyl as the internal standard and are the average of two independent runs.

The presence of electron-donating (MeO-) and -withdrawing (Cl-, AcO- and F₃C-) groups on the 4-position also had no influence, and the corresponding hydrogenated products were obtained in 97 to 100% yields (Table 5.2, entries 6 - 9). We did, however, observe that 4-ethylphenyl acetate starts to undergo methanolysis to 4-ethylphenol.

5.2.3 Transfer hydrogenation of aliphatic alkenes with Ni(II)/L5.2

Investigating the catalytic TH of unactivated aliphatic alkenes led to the observation that a lower temperature compared to the aromatic alkenes is required to achieve conversion (Table S3.5). Using Ni/L5.2 with AB at 25 °C, we could successfully convert 1-octene to octane (85% yield) in one hour.

Table 5.3 Evaluation of Ni/L5.2 in aliphatic alkene transfer hydrogenation.

$\text{R}-\text{CH}=\text{CH}_2 \xrightarrow[\text{MeOH, 25 } ^\circ\text{C, 1 h}]{\text{Ni/L5.2 (1 mol\%), AB (1 eq.)}} \text{R}-\text{CH}_2\text{CH}_3$					
Entry	Substrate	Product	Conversion ^a (%)	Selectivity ^b (%)	GC yield ^a (%)
1			91	>99	90
2			81	98	79
3			85	96	82
4			79	95	75
5			98	97	95
6			83	>99	82
7			76	>99	75
8			99	>99	99

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), alkene (0.25 mmol), NiCl₂·6H₂O (1 mol%) and L5.2 (1 mol%) in methanol (1 mL) were stirred at 25 °C for 1 hour. ^aConversion and GC yield were determined by GC against biphenyl as the internal standard and are the average of two independent runs. ^b Selectivity for the alkane product. Ni denotes NiCl₂·6H₂O.

We decided to evaluate other aliphatic alkenes using the optimised conditions. Seven different unactivated linear aliphatic alkenes differing in their chain length (C₆ - C₁₄) could all be converted in high yields between 75 and 95% (Table 5.3, entries 1 - 6). The selectivity for the linear alkane products was very high (95 - 99%), with little double bond isomerisation (1 - 5%), a usual occurrence with Ni catalysts,¹⁵ being observed. No significant correlation between carbon chain length and yield was observed. Vinylcyclohexane (Table 5.3, entry 7) and allylbenzene (Table 5.3, entry 8) could also undergo hydrogenation to yield 75 and 99% of their respective saturated products, with selectivity above 99% for both alkane products.

We continued our investigation into the TH of internal alkenes. Unfortunately, after several attempts using different substrates and reaction conditions, conversions remained low to moderate (5 - 50%). These results do, however, correspond with previous reports,^{7c} illustrating the difficulty of hydrogenating internal alkenes using AB as the source of H₂, with some direct hydrogenation studies showing similar observations.¹⁶

5.2.4 Transfer hydrogenation of α,β -unsaturated alkenes with Ni(II)/L5.2

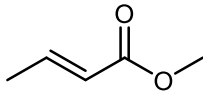
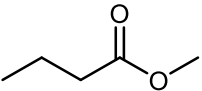
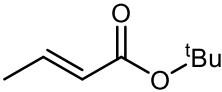
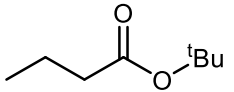
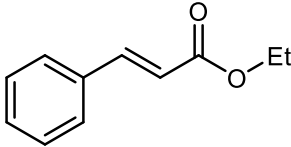
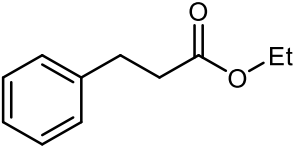
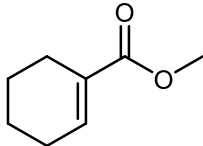
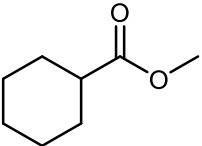
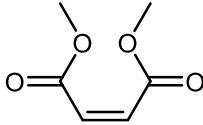
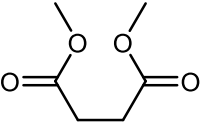
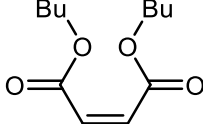
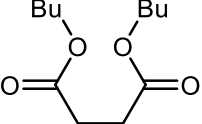
Although internal alkenes might prove to be challenging, previous literature has illustrated the importance of electron-withdrawing groups and their advantage when performing transfer hydrogenations with AB.^{7e, 7h} Activation of alkenes, particularly with an electron-withdrawing group, improves the kinetics of the reaction to such a point that metal-free conditions can be used. This observation corresponds with the difference in reaction conditions observed between aromatic and aliphatic alkenes above. Using this principle, we decided to evaluate the TH of α,β -unsaturated esters using the same reaction conditions that were utilised for the TH of aromatic alkenes.

Under these conditions, methyl crotonate could undergo complete TH to yield >99 methyl butanoate (Table 5.4, entry 1). Further investigation using different substituents on either side of the ester group was conducted to determine the versatility of our pre-catalyst system. A bulky tert-butyl group had no influence on the activity, and tert-butyl butanoate was obtained in 98% yield (Table 5.4, entry 2). The presence of a phenyl substituent did, however, result in a lower conversion (80%) due to electron donation towards the C-C double bond (Table 5.4, entry 3). Increasing the reaction time to one hour yielded 95% of the hydrogenated product. Although methyl cyclohex-1-ene-1-carboxylate could only be converted in 36% (Table 5.4, entry 4), the presence of the ester group did indeed increase the conversion by 30% compared to cyclooctene.

Further investigation was conducted on diesters, with dimethyl maleate and dibutyl maleate being converted in 90 and 86%, respectively (Table 5.4, entries 5 and 6). Increasing the reaction time to one hour for both substrates, resulted in >99 and 96% yields, respectively.

Table 5.4 Evaluation of Ni/L5.2 in α,β -unsaturated esters transfer hydrogenation.

$ \begin{array}{c} \text{O} \\ \parallel \\ \text{R}^1\text{-CH=CH-C-O-R}^2 \end{array} \xrightarrow[\text{MeOH, 50 }^\circ\text{C, 30 min.}]{\text{Ni/L5.2 (1 mol\%), AB (1 eq.)}} \begin{array}{c} \text{O} \\ \parallel \\ \text{R}^1\text{-CH}_2\text{-CH}_2\text{-C-O-R}^2 \end{array} $				
Entry	Substrate	Product	Conversion ^a (%)	GC yield ^b (%)

1			>99	>99
2			98	98
3			80	95 ^c (90)
4			36	35
5			90	>99 ^c (92)
6			86	96 ^c (91)

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), alkene (0.25 mmol), NiCl₂·6H₂O (1 mol%) and **L5.2** (1 mol%) in methanol (1 mL) were stirred at 50 °C for 30 minutes. ^a Conversion and GC yield were determined by GC against biphenyl as the internal standard and are the average of two independent runs. ^b Isolated yields are shown in parentheses. ^c 1 hour.

It is noteworthy that all of the α,β -unsaturated esters underwent chemoselective hydrogenation at the alkene position. No hydrogenation of the ester group was observed.

5.2.5 Transfer hydrogenation of biologically important alkenes

Using the optimised conditions mentioned above, we decided to evaluate biologically important alkene substrates. Eugenol, an important compound found in cloves and utilised in the medicinal industry,¹⁷ and stearyl methacrylate, a monomer for polymerisation,¹⁸ were subjected to TH. Both compounds were converted successfully resulting in >99% yields. The products, 2-methoxy-4-propylphenol and octadecyl isobutanoate, were isolated and obtained in 94 and 96% yields, respectively (Figure 5.1). The 2-methoxy-4-propylphenol product is found in Bordeaux wines attracting fruit flies,¹⁹ with a smell similar to eugenol, but sweeter. The octadecyl isobutanoate product is a known aggregation pheromone released by the male *Riptortus clavatus* (bean bug).²⁰

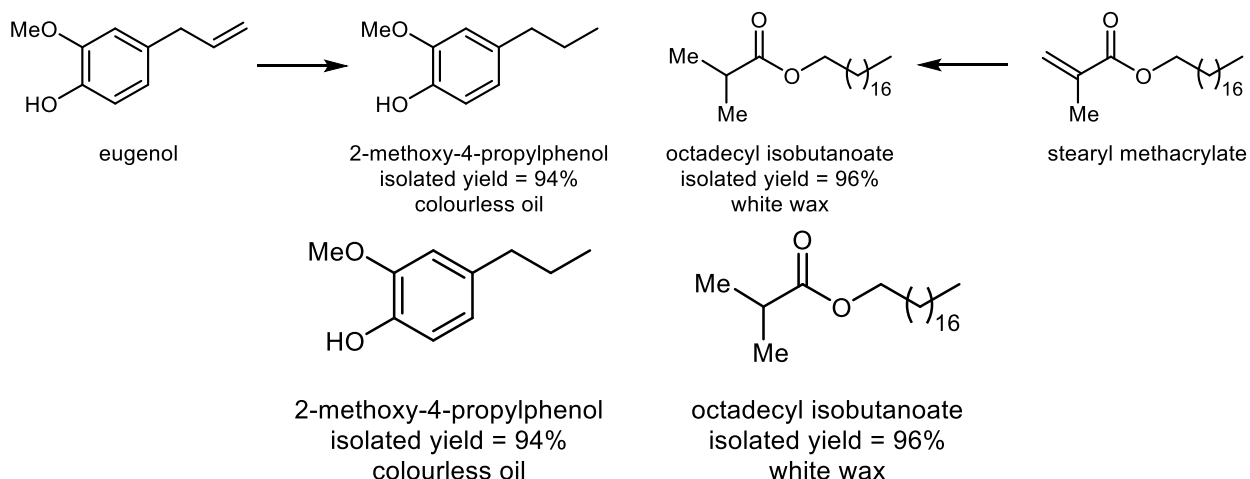
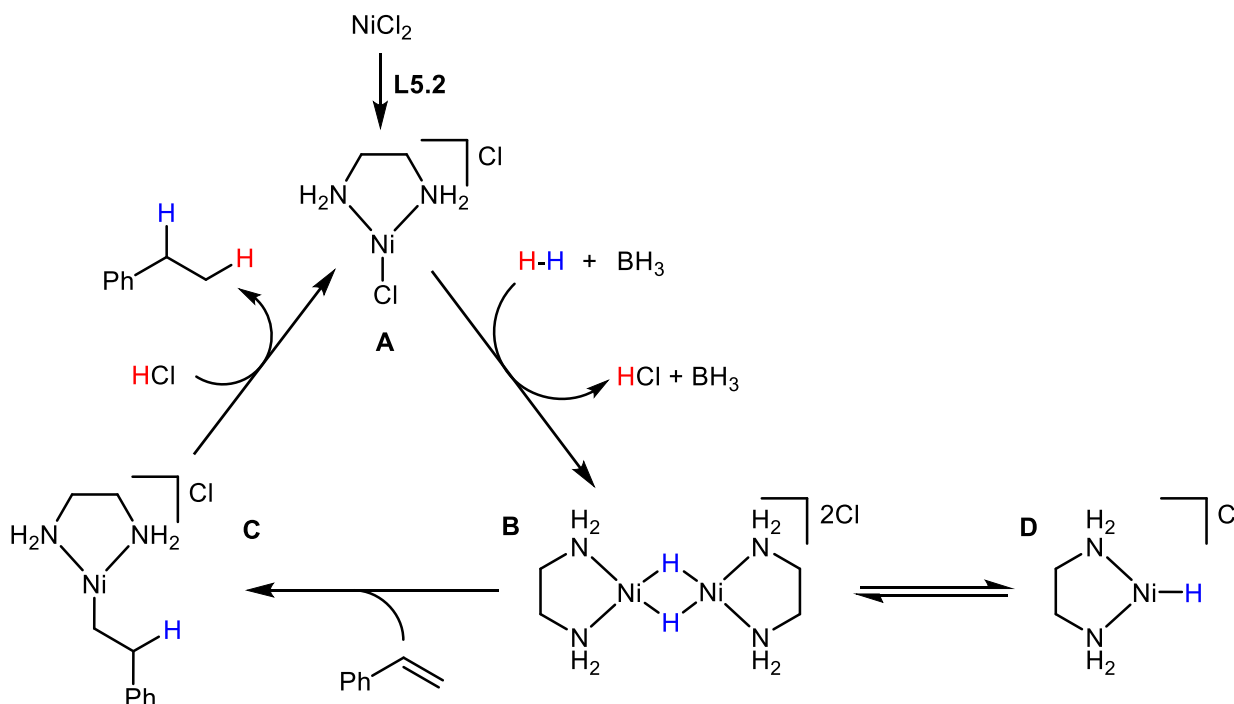


Figure 5.2 Biological important alkanes formed via the TH of alkenes with Ni/L5.2 and AB.

5.2.6 Mechanistic insights into the transfer hydrogenation of styrene with Ni(II)/L5.2

To gain further insight into the TH mechanism of styrene, we first decided to subject styrene to direct hydrogenation with H_2 . Using 10 atm of H_2 for six hours at 60 °C resulted in only 1% of ethylbenzene. However, addition of one equivalent of a borane adduct, with no dissociable protons (α -picoline borane), assisted Ni/L5.2 and H_2 in successfully hydrogenating styrene to 100% ethylbenzene (Table S3.8, entry 1). Using only one equivalent of α -picoline borane with Ni/L5.2, in the absence of H_2 , resulted in only 14% of the product (Table S3.8, entry 2). These results indicate the importance of borane as an activator of dihydrogen (Scheme 5.1),²¹ illustrating that molecular H_2 is necessary during this process.

It can therefore be concluded that a two-step transfer hydrogenation process, i.e. i) AB dehydrogenation and ii) substrate hydrogenation, is followed for the TH of styrene using Ni/L5.2 with AB as the source of H_2 active Ni(II)-hydride species.^{10c} A plausible mechanism is presented in Scheme 5.1, illustrating the activation of H_2 with borane to produce active Ni(II) hydride species (**B**), which are in equilibrium with its monomeric form (**D**). Subsequent coordination of styrene to Ni(II)-hydride occurs with hydride transfer, resulting in the formation of a Ni(II) alkyl intermediate (**C**). Finally, protonation results in the release of ethylbenzene and formation of original Ni(II) pre-catalyst (**A**).



Scheme 5.1 Proposed mechanism of styrene hydrogenation with H_2 and α -picoline borane, illustrating the activation role of borane. α -Picoline has been omitted from the scheme for simplicity.

5.3 Conclusion

In conclusion, we investigated the transfer hydrogenation of alkenes (aromatic, aliphatic and α,β -unsaturated esters) using a simple and inexpensive ethylene diamine-ligated (**L5.2**) Ni(II) pre-catalyst under ambient conditions with AB as the source of H_2 . Aromatic alkenes could be converted in excellent yields between 97 and >99%, while inactivated linear aliphatic alkenes could also be hydrogenated resulting in 75 to 99% yields with >95% selectivity. We also illustrated the chemoselective hydrogenation of α,β -unsaturated esters resulting in excellent yields of up to >99%. Investigation into the importance of borane during the TH of styrene showed that it acts as an activator of dihydrogen to form Ni(II)-hydride species confirming a two-step transfer hydrogenation process.

5.4 Experimental section

5.4.1 General procedure for the transfer hydrogenation of aromatic alkenes and α,β -unsaturated esters with Ni(II)/**L5.2**

Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under Ar atmosphere. Sequential addition of alkene (0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with **L5.2** (0.6 mg, 2.5 μmol) in methanol (1 mL) followed. The reaction mixture was

allowed to stir at 50 °C for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate. Additional experimental details are provided in the Supplementary Information.

5.4.2 General procedure for the transfer hydrogenation of aliphatic alkenes with Ni(II)/L5.2

Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under Ar atmosphere. Sequential addition of alkene (0.25 mmol) and then NiCl₂·6H₂O (0.6 mg, 2.5 µmol) with **L5.2** (0.6 mg, 2.5 µmol) in methanol (1 mL) followed. The reaction mixture was allowed to stir at 50 °C for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate. Additional experimental details are provided in the Supplementary Information.

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Chapter 6

Concluding remarks and
recommendations for future work

6.1 General summary

Chemical transformations involving the hydrogenation of π -unsaturated bonds are still important in the formation of various saturated compounds utilised in the different chemical industries we see today. Dihydrogen (H_2) remains the main hydrogenation agent in this transformation, but a few drawbacks are present during the use and storage thereof. The flammability of H_2 serves as a hazard whenever it is used, with the prolonged storage of high pressurised cylinders serving as an additional safety concern. Most of the reactions requiring H_2 are usually conducted at high temperatures, with high H_2 pressures adding to the previously mentioned drawbacks.

Ongoing research towards a safer environment has led to the development of transfer hydrogenation (TH) reactions using H_2 transfer agents instead of hazardous H_2 .¹ These transfer agents can be stored for prolonged periods of time without the added concern of combustion due to pressurisation. They are solvents and solids, which make them easy to handle in open atmosphere. Recently, noticeable attention has been given to a new transfer agent, i.e. ammonia borane (AB), which has been used successfully in the catalyst-mediated TH of several unsaturated compounds.²

Unfortunately, the homogeneous AB facilitated TH of unsaturated compounds using Ni(II) pre-catalysts is scarce.³ Long reaction times (6 - 72 hours), elevated reaction temperatures (50 - 80 °C) and excess amounts of AB (0.6 - 3 equivalents) contribute to the drawbacks observed with other transition metals. The use of phosphine ligands is also regarded as a problem due to their toxicity, laborious preparation, cost and sensitivity to moisture.⁴

This study aimed to overcome the above-mentioned drawbacks and contribute towards the development of Ni catalysis in AB-facilitated TH reactions of quinolines, nitriles and alkenes. Simple, inexpensive and commercially available bi- and tridentate N-donor ligands were utilised to develop *in situ* prepared Ni(II) pre-catalysts. We aimed to evaluate the versatility of the pre-catalysts, using AB as the source of H_2 , against several quinolines, nitriles, aromatic- and aliphatic alkenes, and α,β -unsaturated ester substrates. Further improvement of the reaction conditions compared to previous literature was an additional objective, with elucidation of the TH mechanism for the different substrates also forming part of the study. Additional evaluation of AB dehydrogenation was also conducted to determine the potential H_2 amount that can be released using the *in situ* prepared Ni(II) pre-catalysts.

6.2 Final conclusions

Two known N'N''N'''-tridentate ligands, i.e. bis(pyrazolyl-1-methyl)pyridine (**L3.1**, **L4.1**, **L5.1**) and bis(3,5-dimethylpyrazolyl-1-methyl)pyridine (**L3.2**, **L4.2**), were synthesised according to

literature. They were characterised using FT-IR and ^1H and ^{13}C NMR spectroscopic techniques, with APCI mass spectrometry contributing to the ligands' identification. The above-mentioned ligands and other well-known, commercially available bi- and tridentate N-donor ligands, i.e. phenanthroline (**L3.3**), bipyridine (**L3.4**), 2,2'-dipyridylamine (**L3.5**), ethylene diamine (**L3.6**, **L4.4**, **L5.2**), 1,2-diaminocyclohexane (**L5.3**) and ortho-phenylenediamine (**L5.4**), were combined with $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ to prepare various *in situ* Ni(II) pre-catalysts. No separate complexes were isolated. The pre-catalysts were used in combination with AB, a source of dihydrogen (H_2), for the transfer hydrogenation (TH) of quinolines, nitriles, aromatic- and aliphatic alkenes, and α,β -unsaturated esters.

Preliminary investigations into quinoline TH and optimisation of the reaction conditions were performed using the Ni/**L3.1** pre-catalyst and one equivalent of AB in MeOH. Different ligands (**L3.1** - **L3.6**), Ni(II) salts, metal(II) salts and solvents were evaluated during optimisation. Optimisation towards the reaction time and -temperature was also conducted. The optimal conditions, including 1 mol% of Ni/**L3.1** and one equivalent of AB in methanol could successfully convert quinoline to 1,2,3,4-tetrahydroquinoline (97% conversion and 90% isolated yield) at 25 °C in 30 minutes. Under these conditions, several quinoline derivatives, containing electron-donating and -withdrawing groups at different positions, were evaluated. Moderate to high isolated yields (60 - 90%) were obtained, illustrating the versatility and effectiveness of the pre-catalyst under these conditions. Mechanistic elucidation using ^1H and ^{13}C NMR spectroscopy revealed the presence of active Ni(II)-hydride species responsible for the high activity seen during TH. Further investigations illustrated the formation of a 1,4-dihydroquinoline intermediate during quinoline's transformation to 1,2,3,4-tetrahydroquinoline.

The above-mentioned system was expanded to the chemoselective TH of nitriles to secondary amines using Ni/**L4.1** under the same reaction conditions. Initially, optimisation of the TH of benzonitrile was conducted following the same protocol as mentioned above. Results showed that 1 mol% of the Ni/**L4.1** with one equivalent of AB at 25 °C could fully convert benzonitrile to 90% dibenzylamine in 30 minutes. A very high TON of 5100 was achieved using only 0.01 mol% of this pre-catalyst. Apart from this system, EDA combined with $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, Ni/**L4.4**, under the same reaction conditions, produced good results, with full conversion of benzonitrile to 79% dibenzylamine. Both pre-catalyst systems were further evaluated against the TH of various aromatic- and aliphatic nitriles, with the effect of electron-donating and -withdrawing groups being investigated. Full conversion was achieved for most of the substrates with yields between 40 and 97% obtained. Experimental insights into the TH of benzonitrile followed showing deuterium labelling on the nitrogen and nucleophilic hydride attack on the α -carbon. Using α -picoline borane (with no dissociable protons) and external H_2 , a two-step TH

mechanism was postulated. Finally, dehydrogenation of AB was conducted to investigate the potential H₂ gas that can be released when Ni/**L4.1** is used. It was observed that an almost quantitative yield (2.96 equivalents) of H₂ gas is released in less than 15 minutes.

Research into the Ni(II)-catalysed TH reaction continued towards aromatic- and aliphatic alkenes as well as α,β -unsaturated esters. During optimisation, it was found that an increase in the temperature (50 °C), compared to the above-mentioned studies, was required to fully convert styrene to ethylbenzene (100% yield) in 30 minutes using 1 mol% of Ni/**L5.1**. It was, however, seen that only Ni/**L5.2** displayed a homogeneous nature, with all of the other pre-catalysts (Ni/**L5.1**, Ni/**L5.3** and Ni/**L5.4**) behaving in a heterogeneous manner. Investigation therefore continued with Ni/**L5.2**. Several aromatic alkenes, containing electron donating and -withdrawing groups, could be successfully converted in 97 to 100% yields. Unactivated aliphatic alkenes required a longer reaction time, but 25 °C was sufficient for successful TH. The linear aliphatic alkenes differing in their chain length (C₆ - C₁₄) could be converted in high yields of 75 to 95%. Unfortunately, internal alkenes did not fare as good with percentage conversions obtained between 5 and 50%. Evaluation of α,β -unsaturated esters followed, using the same reaction conditions as mentioned for the aromatic alkenes. The α,β -unsaturated esters could undergo chemoselective conversion in very high yields of up to 100%, with the ester group remaining intact. Two biologically important compounds, i.e. eugenol and stearyl methacrylate, were also investigated and could be fully converted to their respective products in 94 and 96% isolated yields, respectively. Mechanistic insights, similar to the TH of benzonitrile with α -picoline borane, were conducted. Again, a two-step TH mechanism for styrene was postulated.

6.3 Scientific contributions

With regard to the catalytic TH using homogenous Ni catalysts, the following accomplishments during the current study have been made and are important contributions to the scientific community:

- Research conducted on the TH of quinolines, nitriles and alkenes with a homogeneous Ni(II) catalyst using AB as the source of H₂ is a first for this research field. In particular, the use of stable, inexpensive and commercially available N-donor ligands for this purpose provides a greener alternative to the expensive, toxic and air sensitive phosphine ligands that are normally used.
- Although the TH of quinolines, with AB as the source of H₂, has been conducted previously, more benign reaction conditions were used during this study.^{2v} Only 1 mol% of an N-donor (**L3.1**) ligated non-noble transition metal (Ni) pre-catalyst and one equivalent of AB were required for successful conversion of quinoline to 1,2,3,4-

tetrahydroquinoline at a lower temperature (25 °C) and shorter reaction time (30 minutes), which is superior to previous studies.^{2a, 2t, 2u}

- Mechanistic elucidation using Ni/**L3.1** for AB dehydrogenation illustrated the presence of active Ni(II)-hydride species, which has not been investigated before with other TH studies using AB as the source of H₂. The presence of a 1,4-dihydroquinoline intermediate, only speculated about before during quinoline hydrogenation,⁵ has been confirmed with NMR spectroscopy in this study, leading to a proposed TH mechanism.
- Two separate pre-catalysts, i.e. Ni/**L4.1** and Ni/**L4.4**, were capable of chemoselective TH of nitriles to secondary amines. Previous studies using Ni(II) catalysts for TH could only produce aldimines and/or primary amines.⁶ This is the first time that chemoselective TH of nitriles to secondary amines was achieved with high yields of 60 to 97% being obtained.
- More benign reaction conditions for the chemoselective TH of nitriles compared to previous studies of the same kind have been utilised, i.e. lower reaction temperature (25 °C), shorter reaction time (30 minutes) and a smaller amount of AB (one equivalent). Usual reaction conditions included 25 to 50 °C, 8 to 16 hours and 1.6 to 4 equivalents of AB.^{2p-r} The yields obtained for all the secondary amines bearing electron-withdrawing groups (90 - 97%) are superior to previous studies (65 - 86%).^{2q-s}
- The highest TON (5100) for chemoselective nitrile TH with AB as the source of H₂ was observed using 0.01 mol% of Ni/**L4.1**, which is superior to previous studies (TON = 2259).^{2q}
- Four new nitrile substrates, i.e. 2-methylbenzonitrile, 3-phenylpropanenitrile, cyclohexanecarbonitrile and heptyl cyanide, which have not been investigated before in previous TH studies using AB as the source of H₂, have been evaluated with the optimised system mentioned above.
- During a study on the mechanistic insights into the hydrogenation of benzonitrile using direct H₂ with α -picoline borane, the importance of the borane species in activating H₂ for the generation of Ni(II) hydride species was illustrated, which has not been investigated before.
- Dehydrogenation of AB to investigate the potential amount of H₂ gas that can be released illustrated that Ni/**L4.1** was able to release 2.96 equivalents of H₂. This corresponds to an almost quantitative yield (3 equivalents), and is the highest amount of H₂ released by any pre-catalyst seen before.
- Shorter reaction times (0.5 - 1 hour) with excellent yields (75 - 100%) could be achieved for aromatic- and aliphatic alkene TH with 1 mol% of Ni/**L5.2** and one equivalent of AB,

compared to previous studies using longer reaction times (6 - 16 hours) and higher catalyst loadings (5 mol%).^{2a, 7}

- The chemoselective TH of α,β -unsaturated esters using 1 mol% of Ni/L5.2 (inexpensive and easy to prepare) yielded up to 100% of the desired ester products at 50 °C in 30 minutes. These reaction conditions are better than previous studies that required longer reaction times (1 - 16 hours) and a metal-free catalyst demanding laborious preparation.⁸

6.4 Future recommendations

The current study on TH reactions has created new opportunities for future researchers that may be investigated to answer relevant questions and expand the knowledge in this particular field.

6.4.1 Transfer hydrogenation of quinolines and other N-heteroaromatics

Further investigation into the TH mechanism of quinolines is required. A recommendation towards a deuterium labelling study would be beneficial in illustrating the position of a nucleophilic hydride attack on the quinoline to further strengthen the proposed mechanism.

Evaluation of other N-heteroaromatic substrates similar to quinolines, i.e. pyridines, imidazoles, pyrazoles and indoles, could be investigated under similar reactions conditions or with the same pre-catalyst. Previous studies have shown success with pyridine TH using borane catalysts⁹ and could be investigated further with the use of transition metal catalysts using AB as the source of H₂.

6.4.2 Synthesis of asymmetric secondary amines

The study described in Chapter 4 of this thesis illustrated the chemoselective TH of nitriles to symmetric secondary amines. There is, however, a synthetic approach to asymmetric secondary amines as well as utilising the TH of nitriles with the addition of a primary amine.^{2q-s} It was a challenge during the current study using a Ni(II) pre-catalyst, because the formation of the symmetric amine was favoured above that of the asymmetric amine. Optimisation of the reaction conditions or addition of additives may deliver the desired asymmetric product.

6.4.3 Transfer hydrogenation of esters

During this study, the TH of esters was not investigated, but some ester hydrogenation (1%) was observed during the TH of ethyl cinnamate, an α,β -unsaturated ester (Chapter 5). It is believed that the TH of esters using a Ni(II) pre-catalyst with AB as the source of H₂ is indeed

possible upon optimisation of the reaction conditions. It would, however, require harsher reaction conditions compared to that used during this study.

6.4.4 Transfer hydrogenation using other amino borane adducts

During the current study, AB was used as the source of H₂, but another source, i.e. dimethylamine borane (Me₂NH-BH₃, DMAB), has also been applied successfully in the field of homogeneous TH.^{2f, 2g, 10} Although a higher reaction temperature (70 - 85 °C), noble metals (Re, Rh) and an excess amount of DMAB (1 - 4 equivalent) are required to ensure TH, it still has an advantage with regard to cost effectiveness. Additional research conducted but not discussed in this thesis, illustrated that two equivalents of DMAB with 1 mol% of Ni/**L5.2** were enough to successfully convert styrene to ethylbenzene (100% yield) at 70 °C in 30 minutes. It would consequently be prudent to explore this field towards cheaper sources of H₂ using non-noble metals as pre-catalysts.

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Supplementary information
for Chapter 3, 4 and 5

Supplementary information for Chapter 3

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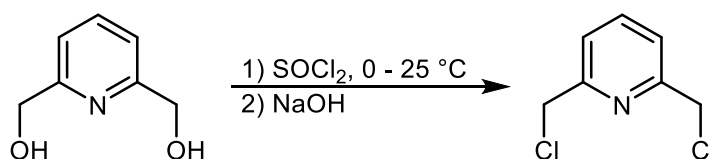
S1.1 General considerations

All chemicals were obtained from commercial sources, i.e. Sigma-Aldrich, Merck and Rochelle Chemicals and used as received. Ammonia borane ($\text{H}_3\text{N-BH}_3$, 97%) was stored in a MBraun glove box under an Ar atmosphere. The $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ salt (98%) sent for ICP-analysis was digested with 2% HNO_3 (Ultra-pure grade) and analysed against NIST standards. ICP-AES analysis (Al to Zn) were conducted using a Thermo iCAP 6000 spectrometer and ICP-MS analysis (Ru to Au) on an Agilent 7900 spectrometer. FT-IR spectra were recorded on a Bruker Alpha-P range infrared instrument equipped with an ATR accessory as neat samples in the range of 400 to 4000 cm^{-1} . APCI-MS characterisation was conducted on a Bruker microTOF-Q II mass spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Ultrashield Plus (600 and 151 MHz, respectively) in 5 mm cylindrical glass tubes. Gas chromatographic analysis, GC and GC-MS, were performed on an Agilent 6890N Series GC System with a HP-5 and HP-5MS columns respectively, with the following column dimensions: 30 m in length, 0.320 mm internal diameter and 0.25 mm film thickness. The GC-MS was equipped with an Agilent 5973N mass detector. Rinsing solutions included MeOH (GC and GC-MS) with N_2 (GC) or He (GC-MS) serving as the carrier gas and biphenyl as an internal standard.

S1.2 Synthesis of N,N,N-tridentate ligands, L3.1 & L3.2

Synthesis of ligands, **L3.1** and **L3.2**, were conducted following methods previously described.¹⁻² The other ligands, **L3.3** to **L3.6**, were commercially available and used as received.

S1.2.1 Synthesis of 2,6-bis(chloromethyl)pyridine

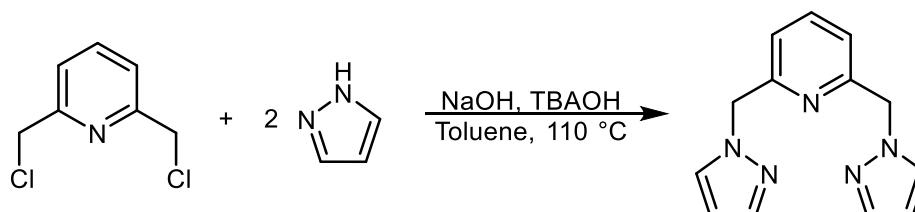


Scheme S1.1 Synthesis of 2,6-bis(chloromethyl)pyridine.

A round-bottomed flask, connected to a NaOH trap, was charged with 2,6-pyridinedimethanol (1.0011 g, 7.051 mmol) and placed in an ice bath. While stirring, cold thionyl chloride (5 mL, 66.86 mmol) was added dropwise over 30 minutes, through a septum. The reaction mixture was allowed to gradually warm to room temperature over a period of 2 hours. The mixture was cooled and toluene (15 mL) was added. The white salt was filtered, washed with 2 x 5 mL portions of cold toluene and diethyl ether (10 mL) and dried under vacuum. The salt was dissolved in water and NaOH (0.6032 g, mmol) added to neutralise the salt. The suspension was cooled in an ice bath, the crystals filtered and washed with 2 x 10 mL portions of H_2O . The

crude product was recrystallized from petroleum ether to obtain colourless crystals (1.0335 g, 83%). FT-IR (ATR) ν , cm^{-1} : 2965, 3022, 1591, 1576, 671. ^1H NMR (600 MHz, CDCl_3 , ppm) δ : 7.76 (t, $J = 7.8$ Hz, 1H), 7.44 (d, $J = 7.8$ Hz, 2H), 4.66 (s, 4H). ^{13}C NMR (151 MHz, CDCl_3 , ppm) δ : 156.53, 138.27, 122.23, 46.57.

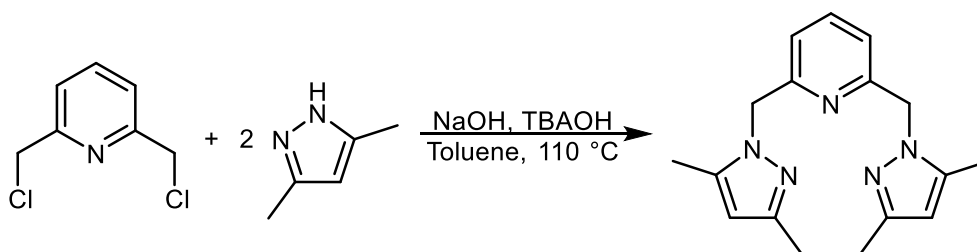
S1.2.2 Synthesis of 2,6-bis((1H-pyrazol-1-yl)methyl)pyridine (L3.1)



Scheme S1.2 Synthesis of ligand **L3.1**.

In a round-bottomed flask 2,6-bis(chloromethyl)pyridine (0.3010 g, 1.710 mmol) and pyrazole (0.2385 g, 3.433 mmol) were dissolved in toluene (20 mL). A 40% NaOH solution (12 mL) and 10 drops of TBAOH were added to the mixture. The mixture was heated to 110 °C and stirred for 23 hours. After the allotted time, the solution was cooled down to room temperature, the organic layer was separated and washed with 3 x 10 mL portions of H_2O . The combined organic layers were dried over MgSO_4 , filtered and the solvent removed under vacuum to obtain a pale yellow oil (0.3250 g, 79%) (**L3.1**). FT-IR (ATR) ν , cm^{-1} : 3437, 3107, 3008, 2936, 1594, 1575. ^1H NMR (600 MHz, CDCl_3 , ppm) δ : 7.59 – 7.49 (m, 5H), 6.83 (d, $J = 7.8$ Hz, 2H), 6.31 (t, $J = 2.1$ Hz, 2H), 5.44 (s, 4H). ^{13}C NMR (151 MHz, CDCl_3 , ppm) δ : 156.68, 140.09, 138.22, 130.12, 120.62, 106.37, 57.50. APCI-MS (m/z): 240.1250 [$\text{M} + \text{H}$] $^+$.

S1.2.3 Synthesis of 2,6-bis((3,5-dimethyl-1H-pyrazol-1-yl)methyl)pyridine (L3.2)

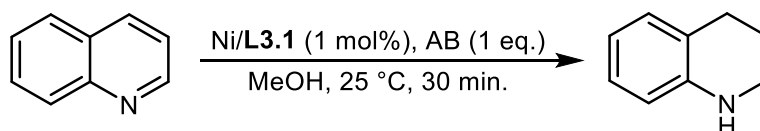


Scheme S1.3 Synthesis of ligand **L3.2**.

The same procedure described for the synthesis of **L3.1**, was followed for **L3.2** using 2,6-bis(chloromethyl)pyridine (0.3050 g, 1.733 mmol) and 3,5-dimethyl pyrazole (0.3345 g, 3.444 mmol). The product was recrystallized from petroleum ether and isolated as white crystals (0.4595 g, 90%) (**L3.2**). FT-IR (ATR) ν , cm^{-1} : 2980, 2956, 2930, 2912, 2862, 1596, 1579. ^1H

NMR (600 MHz, CDCl_3 , ppm) δ : 7.50 (t, $J = 7.8$ Hz, 1H), 6.67 (d, $J = 7.8$ Hz, 2H), 5.85 (s, 2H), 5.29 (s, 4H), 2.23 (s, 6H), 2.16 (s, 6H). ^{13}C NMR (151 MHz, CDCl_3 , ppm) δ : 157.27, 148.21, 139.87, 138.14, 119.75, 105.82, 54.51, 13.62, 11.17. APCI-MS (m/z): 296.1856 $[\text{M} + \text{H}]^+$.

S1.3 General procedure for the transfer hydrogenation of quinoline



Scheme S1.4 General procedure for the transfer hydrogenation of quinoline.

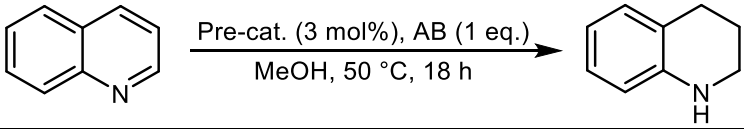
Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under Ar atmosphere. Sequential addition of quinoline (60 μL , 0.5 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1.2 mg, 5 μmol) with **L3.1** (1.2 mg, 5 μmol) in methanol (2 mL) followed. The reaction mixture was allowed to stir at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

S1.4 Optimisation of reaction conditions for transfer hydrogenation of quinoline

S1.4.1 General procedure to evaluate different metal(II) salts

Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under Ar atmosphere. Sequential addition of quinoline (60 μ L, 0.5 mmol) and then metal(II) salt (15 μ mol) with **L3.3** (2.7 mg, 15 μ mol) in methanol (2 mL) followed. The reaction mixture was stirred at 50 °C for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

Table S1.1 Evaluation of metal(II)-salts against quinoline transfer hydrogenation.

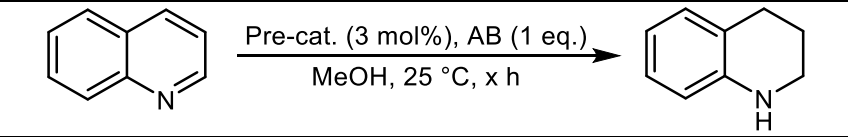
		
Entry	Pre-catalyst	Conversion ^a (%)
1	CoCl ₂ ·6H ₂ O/ L3.3	40
2	MnCl ₂ ·4H ₂ O/ L3.3	11
3	FeCl ₂ ·4H ₂ O/ L3.3	4
4	CuCl ₂ ·2H ₂ O/ L3.3	43
5	NiCl ₂ ·6H ₂ O/ L3.3	56

Reaction conditions: Under Ar atmosphere, ammonia borane (1 equivalent), quinoline (0.5 mmol), metal(II) salt (3 mol%) and **L3.3** (3 mol%) in methanol (2 mL) were stirred at 50 °C for 18 hours. ^a Conversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs.

S1.4.2 General procedure to evaluate different ligands

Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under Ar atmosphere. Sequential addition of quinoline (60 μ L, 0.5 mmol) and then Ni(II) salt (3.6 mg, 15 μ mol) with ligand (15 μ mol) in methanol (2 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

Table S1.2 Evaluation of ligands against quinoline transfer hydrogenation.

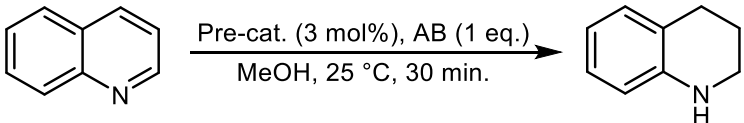
			
Entry	Ligand	Time (h)	Conversion ^a (%)
1	L3.1	0.5	97
		16	96
2	L3.2	0.5	73
3	L3.3	16	41
4	L3.4	16	49
5	L3.5	16	10
6	L3.6	16	85

Reaction conditions: Under Ar atmosphere, ammonia borane (1 equivalent), quinoline (0.5 mmol), NiCl₂·6H₂O (3 mol%) and ligand (3 mol%) in methanol (2 mL) were stirred at 25 °C for 0.5/16 hours. ^aConversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs.

S1.4.3 General procedure to evaluate different Ni(II) salts

Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under Ar atmosphere. Sequential addition of quinoline (60 μ L, 0.5 mmol) and then Ni(II) salt (15 μ mol) with/without **L3.1** (3.6 mg, 15 μ mol) in methanol (2 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

Table S1.3 Evaluation of Ni(II) salts against quinoline transfer hydrogenation.

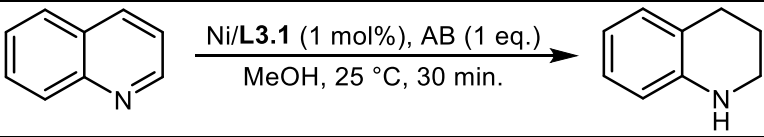
		
Entry	Pre-catalyst	Conversion ^a (%)
1	NiCl ₂ ·6H ₂ O	56
2	Ni(NO ₃) ₂ ·6H ₂ O	53
3	Ni(SO ₄) ₂ ·7H ₂ O	15
4	NiCl ₂ ·6H ₂ O/ L3.1	97
5	Ni(NO ₃) ₂ ·6H ₂ O/ L3.1	90
6	Ni(SO ₄) ₂ ·7H ₂ O/ L3.1	80

Reaction conditions: Under Ar atmosphere, ammonia borane (1 equivalent), quinoline (0.5 mmol), Ni(II) salt (3 mol%) and **L3.1** (3 mol%) in methanol (2 mL) were stirred at 25 °C for 30 minutes. ^a Conversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs.

S1.4.4 General procedure to evaluate influence of solvent

Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under Ar atmosphere. Sequential addition of quinoline (60 μ L, 0.5 mmol) and then NiCl₂·6H₂O (1.2 mg, 5 μ mol) with **L3.1** (1.2 mg, 5 μ mol) in solvent (2 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

Table S1.4 Evaluation of solvent influence against quinoline transfer hydrogenation.

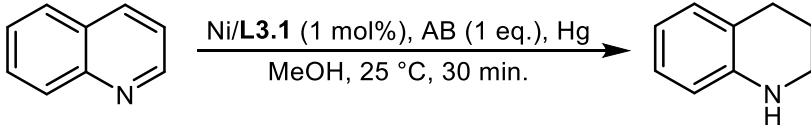
		
Entry	Solvent	Conversion ^a (%)
1	Methanol	97
2	Acetonitrile	3
3	DCM	-
4	THF	4
5	Toluene	-
6	Ethanol	57
7	CHCl ₃	-
8	Hexane	-
9	H ₂ O	2

Reaction conditions: Under Ar atmosphere, ammonia borane (1 equivalent), quinoline (0.5 mmol), NiCl₂·6H₂O (1 mol%) and **L3.1** (1 mol%) in solvent (2 mL) were stirred at 25 °C for 30 minutes. ^a Conversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs.

S1.5 Evaluating homogeneity of catalyst with Hg drop test

Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under Ar atmosphere. Sequential addition of quinoline (60 μ L, 0.5 mmol) and then NiCl₂·6H₂O (1.2 mg, 5 μ mol) with **L3.1** (1.2 mg, 5 μ mol) and Hg (0.486 g, 2.42 mmol) in methanol (2 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

Table S1.5 Evaluating the effect of Hg on the transfer hydrogenation of quinoline.

			
Entry	Additive	Equivalents to Ni	Conversion ^a (%)
1	-	-	97
2	Hg	500	97

Reaction conditions: Under Ar atmosphere, ammonia borane (1 equivalent), quinoline (0.5 mmol), NiCl₂·6H₂O (1 mol%), **L3.1** (1 mol%) and Hg (0 or 500 eq. to Ni) in methanol (2 mL) were stirred at 25 °C for 30 minutes.

^a Conversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs.

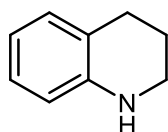
S1.6 Evaluating possible dehydrogenation of 1,2,3,4-dehydroquinoline

A 50 mL Schlenk tube was charged with NiCl₂·6H₂O (6 mg, 25 μ mol) with **L3.1** (6 mg, 25 μ mol) in methanol:toluene (2 mL:2 mL) and 1,2,3,4-tetrahydroquinoline (0.5 mmol) was added. The mixture was refluxed at 110 °C for 24 hours. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl). No conversion (0%) and product (0%) was observed.

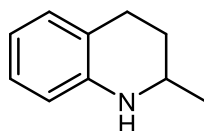
S1.7 Evaluating transfer hydrogenation of quinoline derivatives with ammonia borane

Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor vial under Ar atmosphere. Sequential addition of quinoline-derivative (0.5 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1.2 mg, 5 μmol) with **L3.1** (1.2 mg, 5 μmol) in methanol (2 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

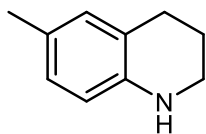
To obtain isolated products after the transfer hydrogenation reaction, the reaction mixture was quenched with 32% HCl (to decompose any residual AB and/or borane-adducts that might have formed) until bubbling ceased and sequentially neutralised with a saturated sodium carbonate (Na_2CO_3) solution. The aqueous layer was extracted with 3 x 5mL portions of DCM. The combined organic layers were dried over MgSO_4 . Filtration and subsequent removal of the solvent resulted in the crude product. Purification was done by column chromatography on silica employing an eluent as indicated below.

S1.7.1 1,2,3,4-tetrahydroquinoline

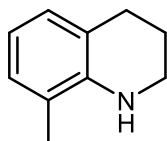
Isolated as a yellow oil (79.5 mg; 64 %). Eluent: DCM/Petroleum ether (9:1). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 6.96 (ddd, J = 7.4, 3.9, 2.6 Hz, 2H), 6.61 (td, J = 7.4, 1.1 Hz, 1H), 6.49 – 6.45 (m, 1H), 3.79 (bs, 1H), 3.34 – 3.28 (m, 2H), 2.77 (t, J = 6.4 Hz, 2H), 1.99 – 1.92 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 144.96, 129.63, 126.87, 121.61, 117.13, 114.34, 42.20, 27.18, 22.43. FT-IR (ATR) ν , cm^{-1} : 3404 (N-H). Analytical data is in accordance with that previously reported in literature.³

S1.7.2 2-methyl-1,2,3,4-tetrahydroquinoline

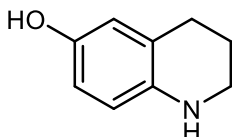
Isolated as a colourless oil (40.6 mg; 56 %). Eluent: Pentane/ Et_2O (4:1). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 6.96 (t, J = 6.5 Hz, 2H), 6.60 (t, J = 7.4 Hz, 1H), 6.47 (d, J = 8.2 Hz, 1H), 3.44 – 3.36 (m, 1H), 2.86 – 2.71 (m, 2H), 1.66 – 1.51 (m, 2H), 1.21 (d, J = 6.3 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 144.92, 129.40, 126.83, 121.25, 117.12, 114.13, 47.31, 30.29, 26.75, 22.76. FT-IR (ATR) ν , cm^{-1} : 3392 (N-H). Analytical data is in accordance with that previously reported in literature.³

S1.7.3 6-methyl-1,2,3,4-tetrahydroquinoline

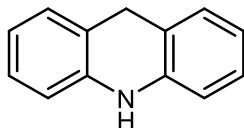
Isolated as a colourless oil (56.4 mg; 75 %). Eluent: Et₂O. ¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.77 (s, 2H), 6.41 (d, *J* = 8.6 Hz, 1H), 3.31 – 3.23 (m, 2H), 2.73 (t, *J* = 6.5 Hz, 2H), 2.20 (s, 3H), 1.97 – 1.89 (m, 2H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 142.55, 130.21, 127.37, 126.40, 121.74, 114.59, 42.33, 27.06, 22.59, 20.54. FT-IR (ATR) ν, cm⁻¹: 3399 (N-H). Analytical data is in accordance with that previously reported in literature.⁴

S1.7.4 8-methyl-1,2,3,4-tetrahydroquinoline

Isolated as a colourless oil (62.4 mg; 85 %). Eluent: Pentane/Et₂O (4:1). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.86 (dd, *J* = 16.3, 7.4 Hz, 2H), 6.55 (t, *J* = 7.4 Hz, 1H), 3.39 – 3.36 (m, 2H), 2.79 (t, *J* = 6.4 Hz, 2H), 2.08 (s, 3H), 1.95 (dd, *J* = 11.5, 6.0 Hz, 2H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 142.55, 130.21, 127.37, 126.40, 121.74, 114.59, 42.33, 27.06, 22.59, 20.54. FT-IR (ATR) ν, cm⁻¹: 3424 (N-H). Analytical data is in accordance with that previously reported in literature.⁵

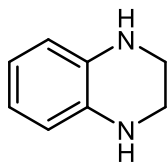
S1.7.5 8-hydroxy-1,2,3,4-tetrahydroquinoline

Isolated as white crystals (44.7 mg; 60 %). Eluent: Et₂O. ¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.50 (d, *J* = 9.5 Hz, 2H), 6.40 (d, *J* = 8.2 Hz, 1H), 3.28 – 3.20 (m, 2H), 2.72 (t, *J* = 6.5 Hz, 2H), 1.97 – 1.86 (m, 2H). ¹³C NMR (151 MHz, (CD₃)₂CO) δ (ppm): 148.38, 139.61, 131.93, 125.09, 122.89, 116.14, 42.89, 28.01, 23.52. FT-IR (ATR) ν, cm⁻¹: 3285 (N-H). Analytical data is in accordance with that previously reported in literature.³

S1.7.6 9,10-dihydroacridine

Isolated as yellow crystals (23.0 mg; 26 %). Eluent: DCM/Petroleum ether (9:1). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.09 (dd, *J* = 16.9, 7.9 Hz, 4H), 6.85 (t, *J* = 7.4 Hz, 2H), 6.67 (d, *J* = 7.9 Hz, 2H), 5.95 (s, 1H), 4.06 (s, 2H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 140.27, 128.74, 127.13, 120.78, 120.18, 113.57, 77.37, 77.16, 76.95, 31.54. FT-IR (ATR) ν, cm⁻¹: 3372 (N-H). Analytical data is in accordance with that previously reported in literature.⁶

S1.7.7 1,2,3,4-tetrahydroquinoxaline



Isolated as an orange solid (56.3 mg; 85 %). Eluent = Et₂O/TEA (19:1), MeOH. ¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.58 (dd, *J* = 5.7, 3.4 Hz, 2H), 6.49 (dd, *J* = 5.6, 3.5 Hz, 2H), 3.42 (s, 4H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 133.8, 118.90, 114.85, 41.51. FT-IR (ATR) ν, cm⁻¹: 3233 (N-H). Analytical data is in accordance with that previously reported in literature.³

S1.8 Elucidation of the transfer hydrogenation mechanism of quinoline

All reactions pertaining to the elucidation of the mechanism were conducted in a 5 mm Wilmad® high-pressure/vacuum (HPV) J. Young NMR tube.

S1.8.1 Dehydrogenation of ammonia borane

Ammonia borane (15.4 mg, 0.5 mmol, 100 eq. to catalyst) was added to an NMR tube under an Ar atmosphere. After the addition of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1.2 mg, 5 μmol) with **L3.1** (1.2 mg, 5 μmol) in CD_3OD (0.7 mL) the mixture was analysed with ^{11}B NMR spectroscopy from 8 - 60 minutes. Results indicated that B(OMe)_3 had formed at 14.23 ppm.⁷

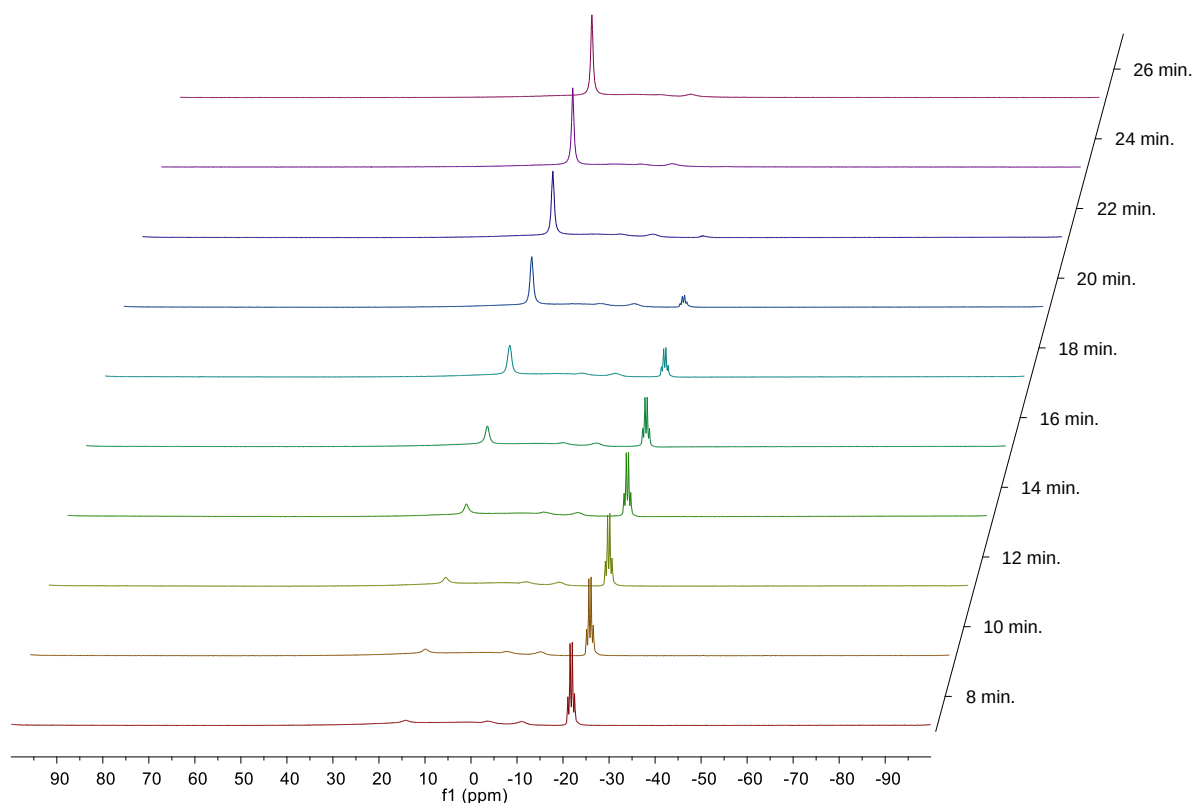


Figure S1.1 Time-dependent ^{11}B NMR (193 MHz, CD_3OD) spectrum depicting the catalytic dehydrogenation of AB and the formation of trimethoxyborane from 8 - 26 minutes in CD_3OD at 25 °C. Low-intensity overlapping resonances at -3.5 and -11 ppm were attributed to of the presence of cyclodiborazanyl (CDB) and cyclotriborazanyl (CTB) (-12.5 ppm) and B-(cyclotriborazanyl)amine-borane (BCTB, -5 ppm).^{4, 8-9}

S1.8.2 Detection of the Ni(II)-hydride species

Ammonia borane (6 mg, 0.19 mmol, 6 eq. to catalyst) was added to a NMR tube under Ar atmosphere. After addition of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (7.5 mg, 0.03 mmol) with **L3.1** (7.5 mg, 0.03 mmol) in MeOH (0.62 mL) and CD_3OD (0.08 mL) the mixture was analysed with ^1H NMR spectroscopy from 10 - 60 minutes. The chemical shifts and peak intensity remained constant from 10 - 60 minutes and only the spectrum at 10 minutes is shown.

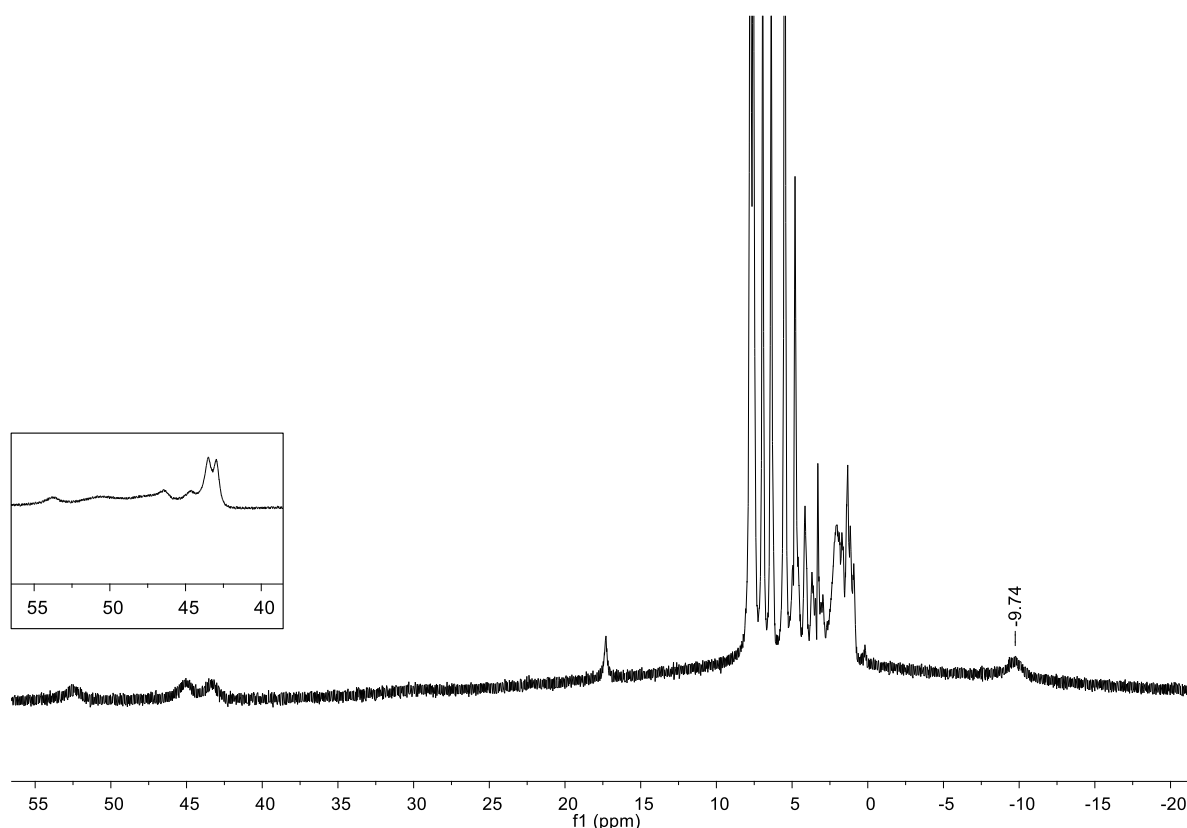


Figure S1.2 ^1H NMR (600 MHz, CD_3OD) spectrum illustrating the presence of a Ni-H species after 10 minutes at 25 °C. Inset shows region of ^1H NMR from $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ /**L3.1** (in MeOH) indicating paramagnetism due to signal broadening.

S1.8.3 Stepwise hydrogenation of quinoline

Ammonia borane (6 mg, 0.19 mmol) was added to a NMR tube under Ar atmosphere. After addition of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (7.5 mg, 0.03 mmol) with **L3.1** (7.5 mg, 0.03 mmol) and quinoline (20 μL , 0.17 mmol) in MeOH (0.62 mL) and CD_3OD (0.08 mL) the solution turned black. The mixture was analysed with ^{13}C NMR spectroscopy from 6 - 45 minutes. All spectra are referenced against the resonance for CH_3OH observed at 49.00 ppm (heptet).

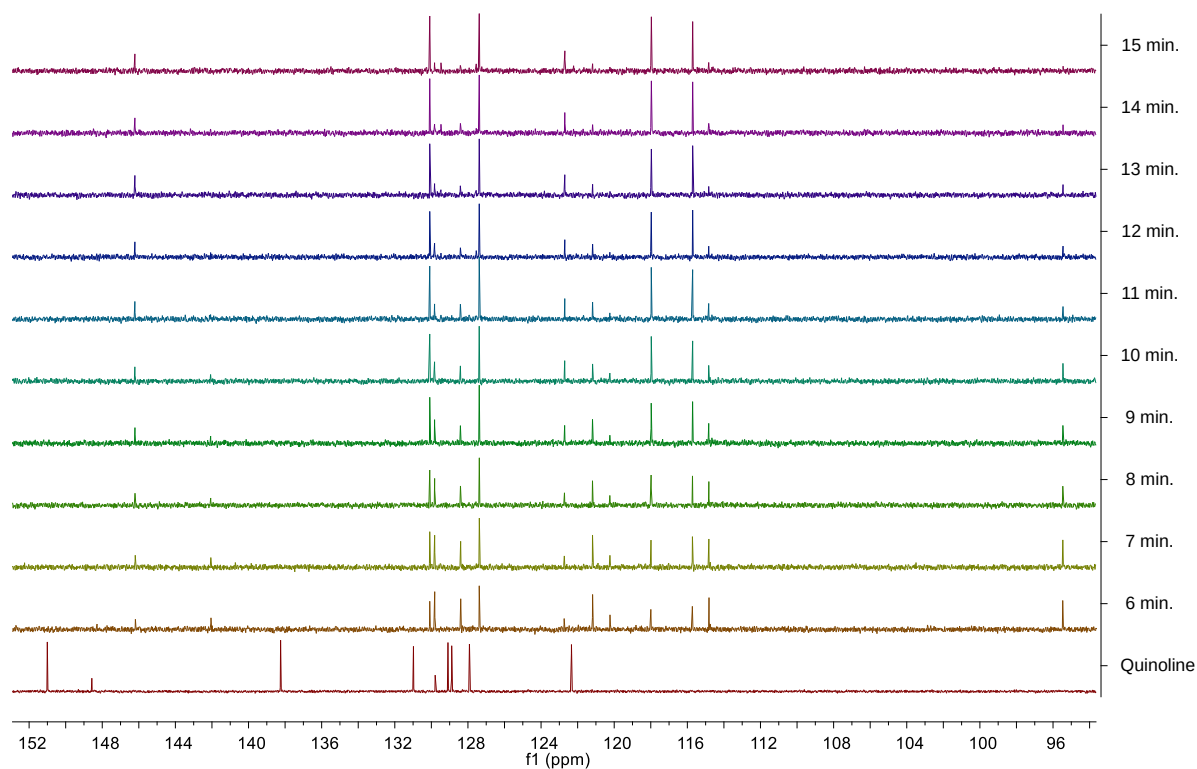


Figure S1.3 Time-dependent ^{13}C NMR (151MHz, CD_3OD) spectrum of the aromatic region during the catalytic transfer hydrogenation of quinoline from 6 - 15 minutes at 25 °C.

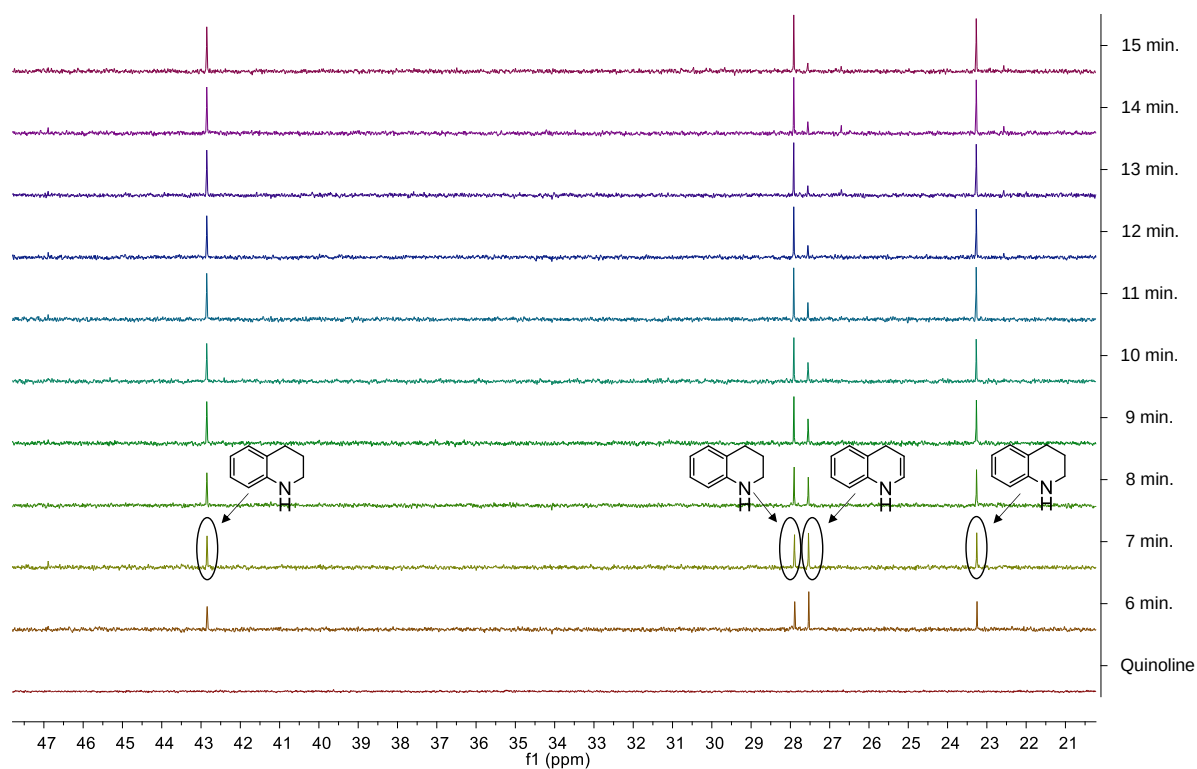


Figure S1.4 Time-dependent ^{13}C NMR (151 MHz, CD_3OD) spectrum of the aliphatic region during the transfer hydrogenation of quinoline from 6 - 15 minutes at 25 °C.

S1.9 ICP-AES and ICP-MS analysis of NiCl₂·6H₂O salt**Table S1.6** Concentration (in ppb) and relative concentration of metal relative to Ni.

Element	Concentration (ppb) (µg/kg)	Relative to Ni (element/Ni)
Al	BDL (<5570)	-
B	3400	1.12E-05
Ba	BDL (<1860)	-
Ca	BDL (<18570)	-
Co	22800	7.54E-05
Cr	7600	2.51E-05
Cu	BDL (<1860)	-
Fe	6400	2.12E-05
K	BDL (<18570)	-
Mg	BDL (<18570)	-
Mn	BDL (<1860)	-
Na	908700	3.00E-03
Ni	302451000	1.00
P	150900	4.99E-04
Pb	28400	9.39E-05
Si	BDL (<18570)	-
Sr	BDL (<930)	-
Zn	BDL (<1860)	-
Ru*	BDL (<1.41)	-
Rh*	232.7	7.69E-07
Re*	BDL (<0.7)	-
Os*	BDL (<11.33)	-
Ir*	436	1.44E-06
Pt*	381	1.26E-06
Au*	207	6.84E-07

* Analysed with ICP-MS. BDL = below detection limit

S1.10 Analytical data of ligands L3.1, L3.2 and hydrogenated quinoline products

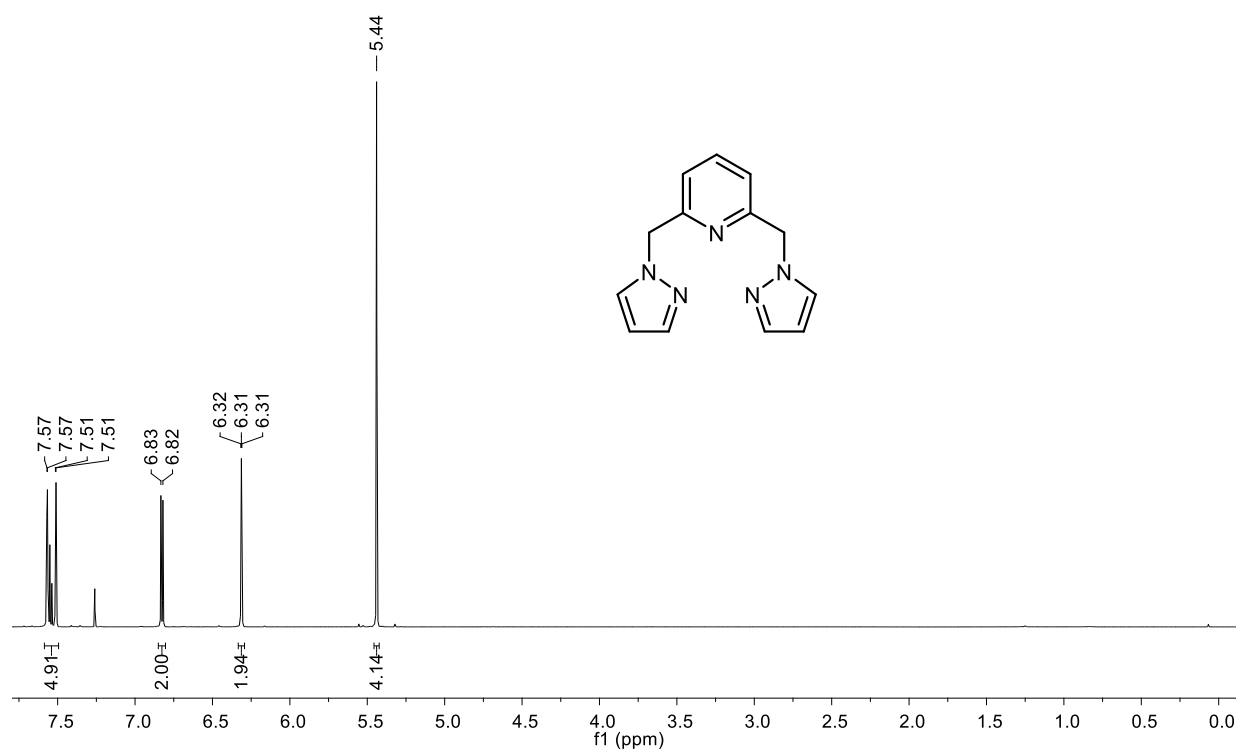


Figure S1.5 ^1H NMR (600 MHz, CDCl_3) spectrum of ligand L3.1.

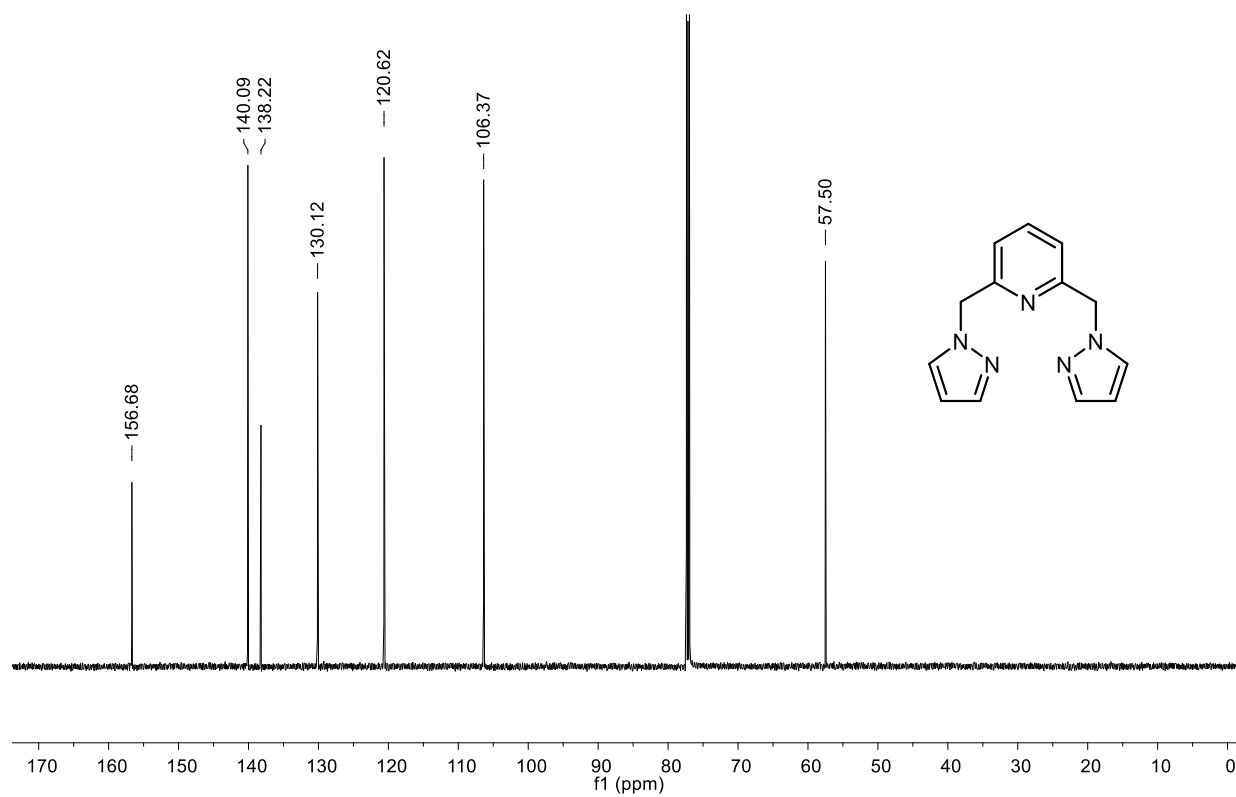


Figure S1.6 ^{13}C NMR (151 MHz, CDCl_3) spectrum of ligand L3.1.

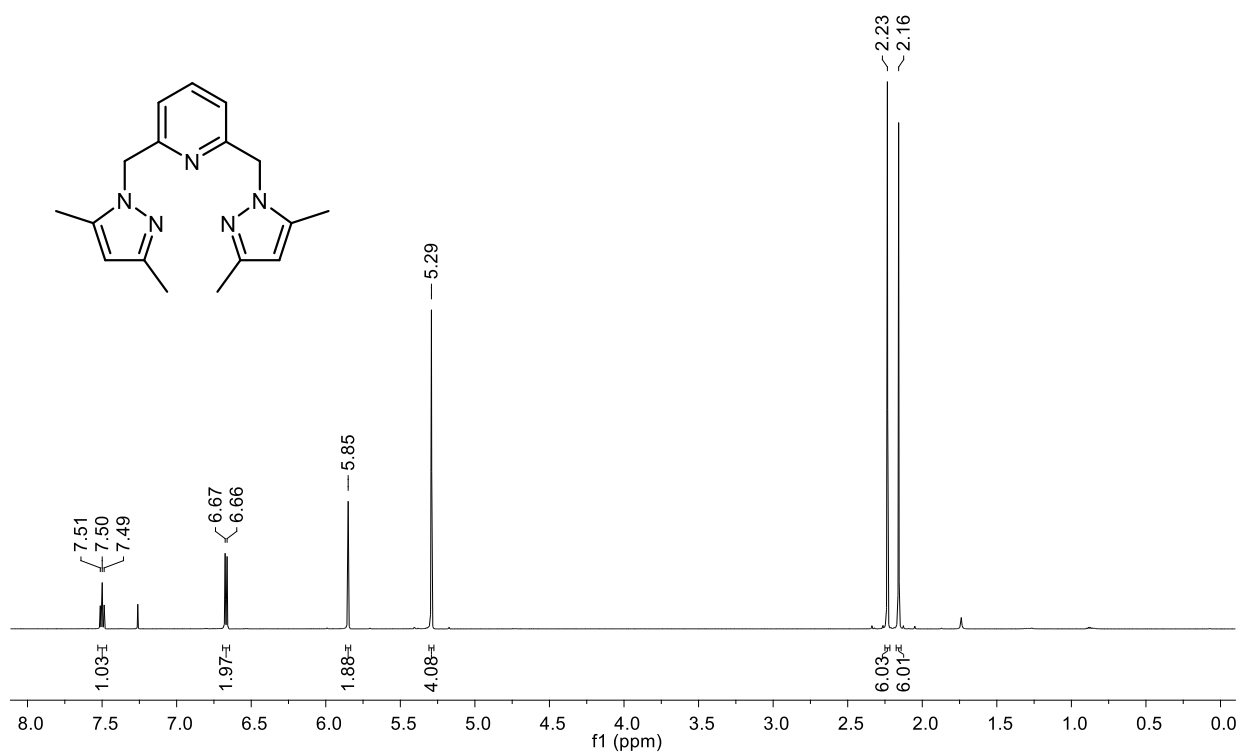


Figure S1.7 ¹H NMR (600 MHz, CDCl₃) spectrum of ligand **L3.2**.

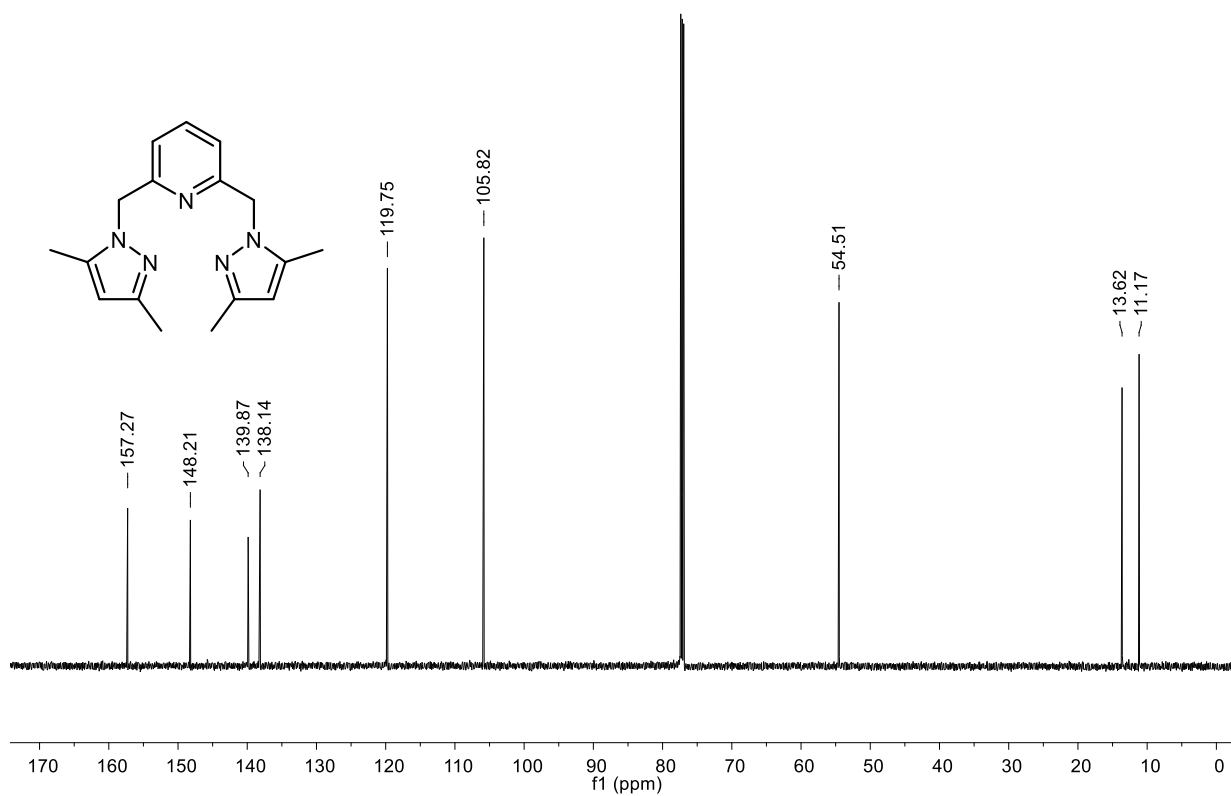


Figure S1.8 ¹³C NMR (151 MHz, CDCl₃) spectrum of ligand **L3.2**.

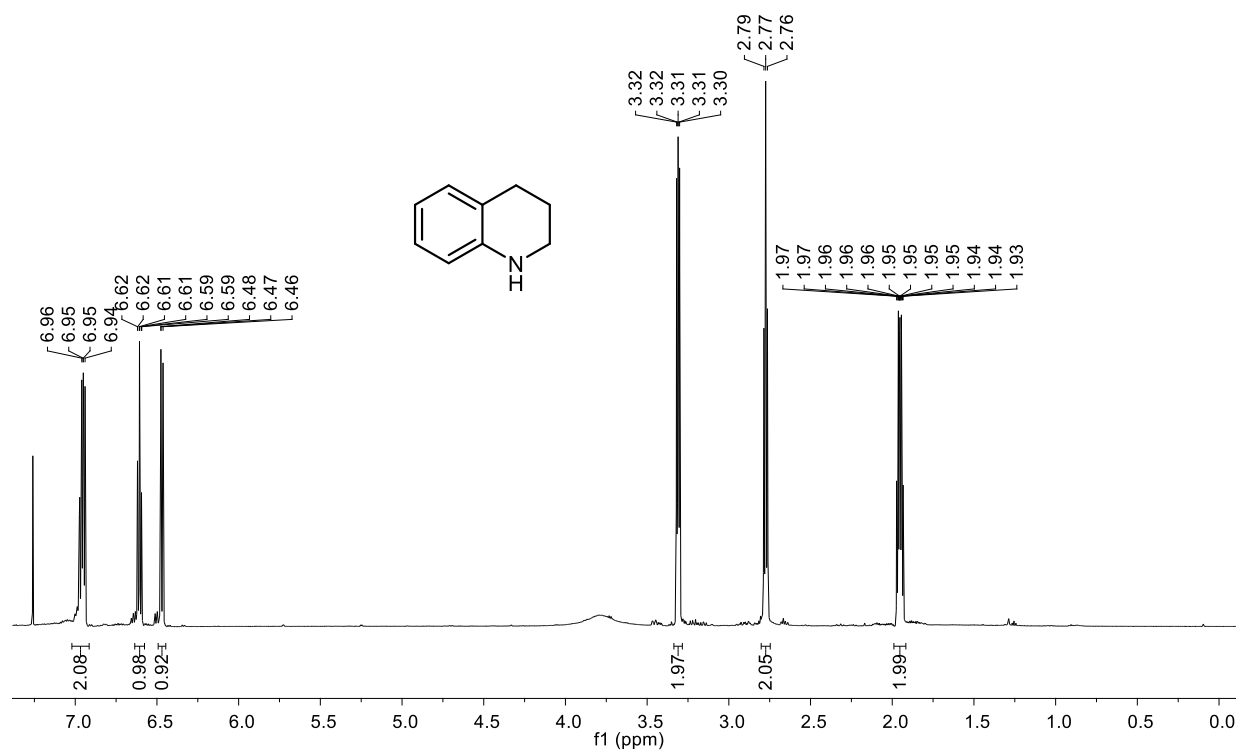


Figure S1.9 ¹H NMR (600 MHz, CDCl₃) spectrum of 1,2,3,4-tetrahydroquinoline.

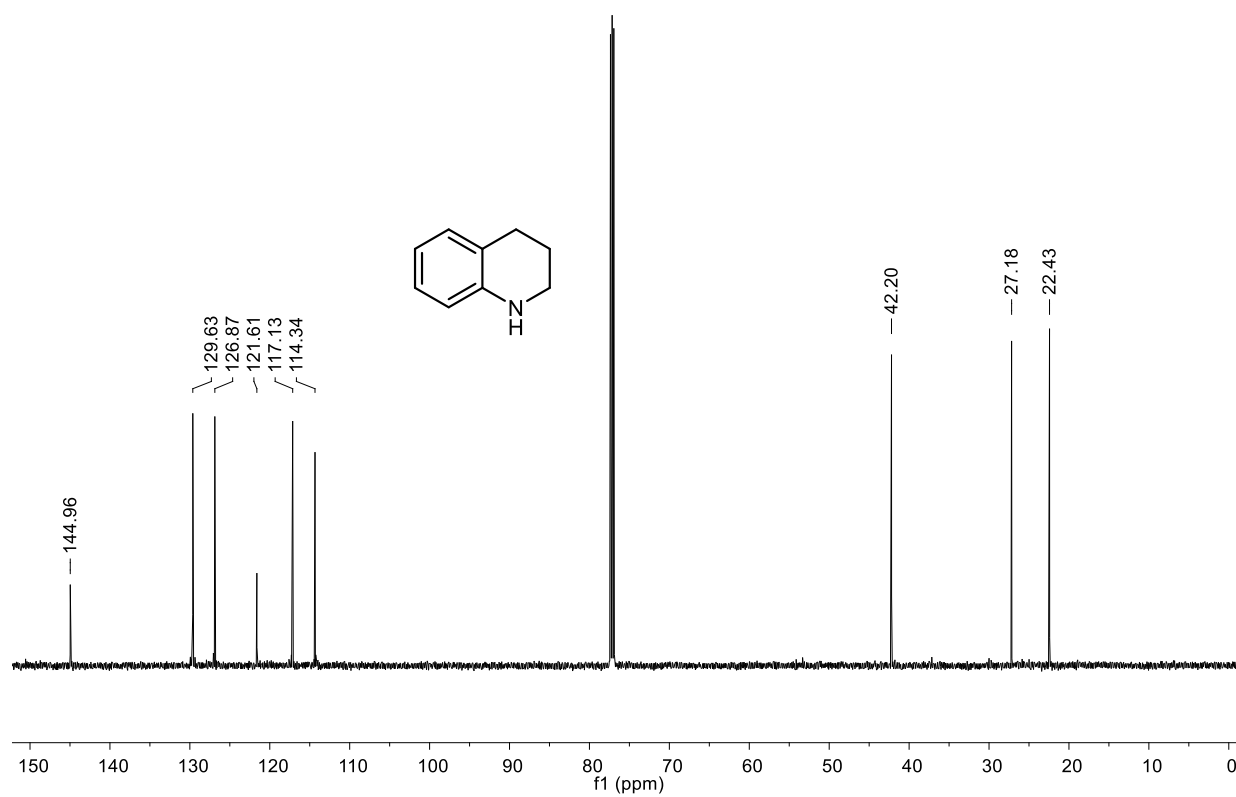


Figure S1.10 ¹³C NMR (151 MHz, CDCl₃) spectrum of 1,2,3,4-tetrahydroquinoline.

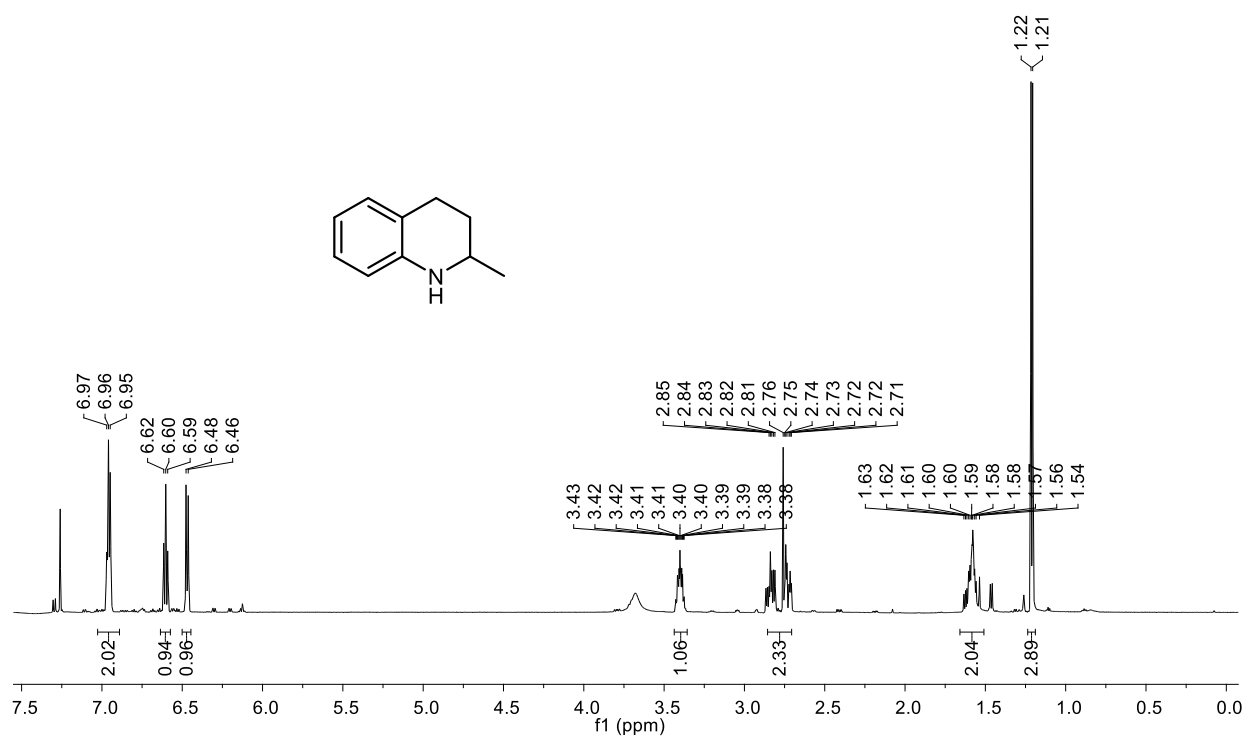


Figure S1.11 ¹H NMR (600 MHz, CDCl₃) spectrum of 2-methyl-1,2,3,4-tetrahydroquinoline.

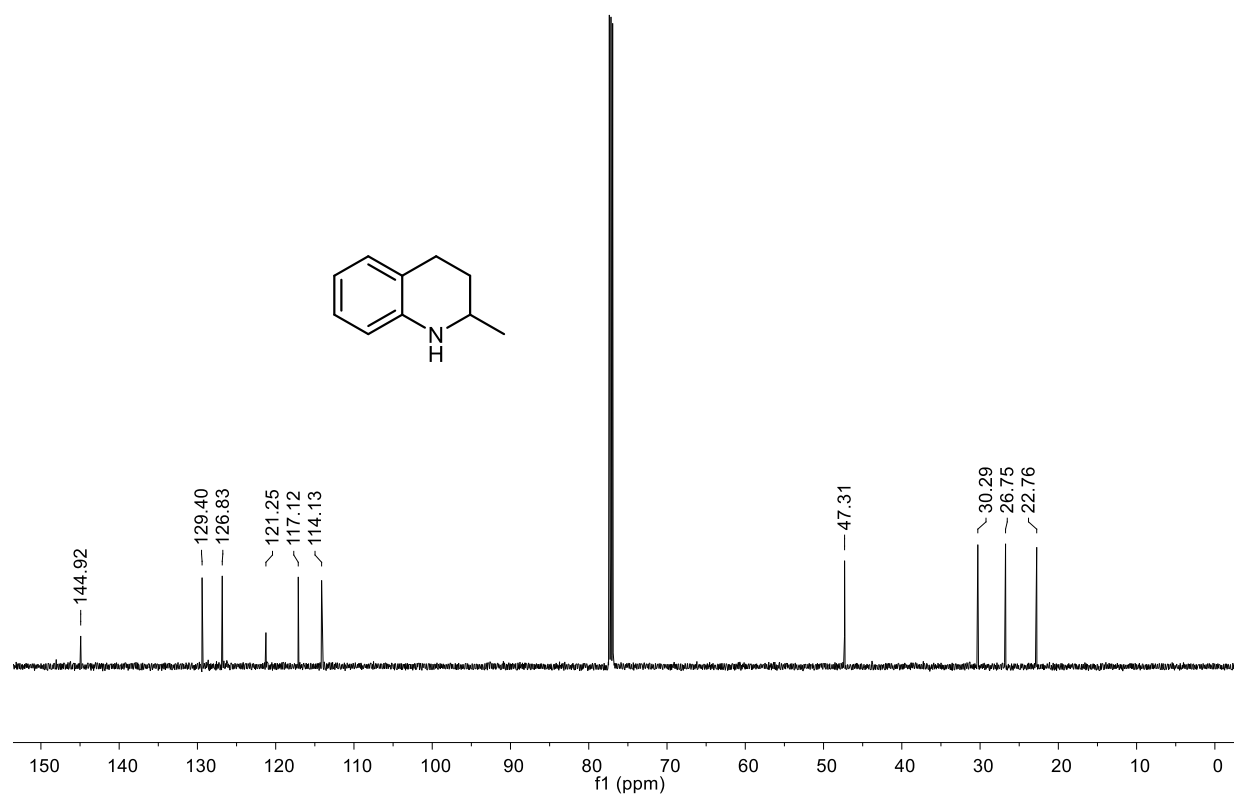


Figure S1.12 ¹³C NMR (151 MHz, CDCl₃) spectrum of 2-methyl-1,2,3,4-tetrahydroquinoline.

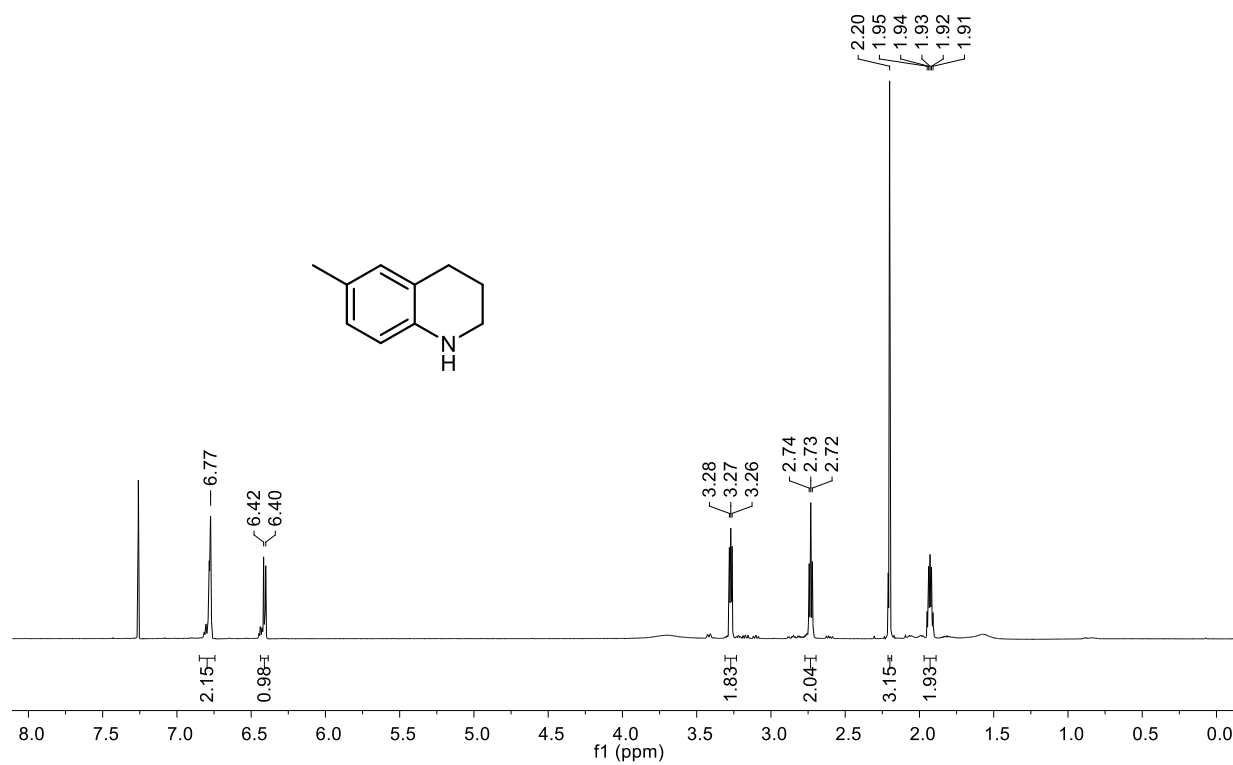


Figure S1.13 ^1H NMR (600 MHz, CDCl_3) spectrum of 6-methyl-1,2,3,4-tetrahydroquinoline.

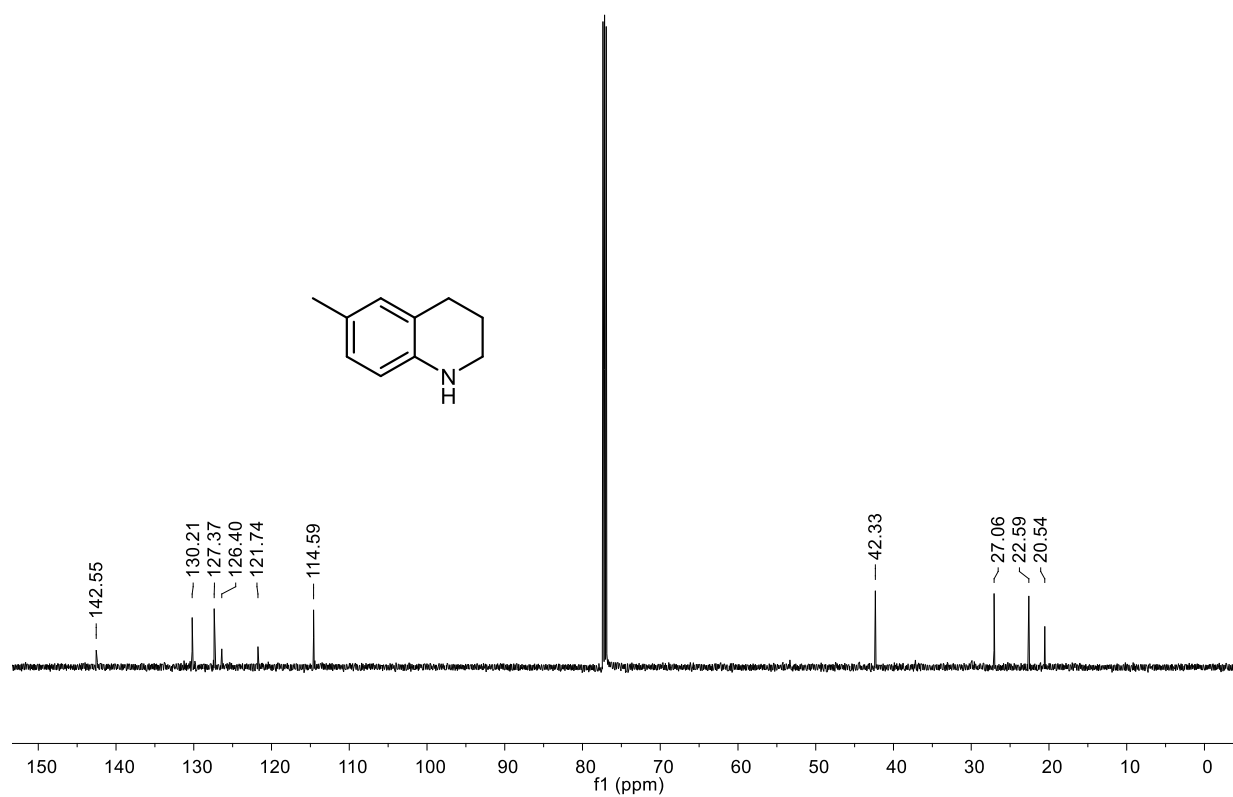


Figure S1.14 ^{13}C NMR (151 MHz, CDCl_3) spectrum of 6-methyl-1,2,3,4-tetrahydroquinoline.

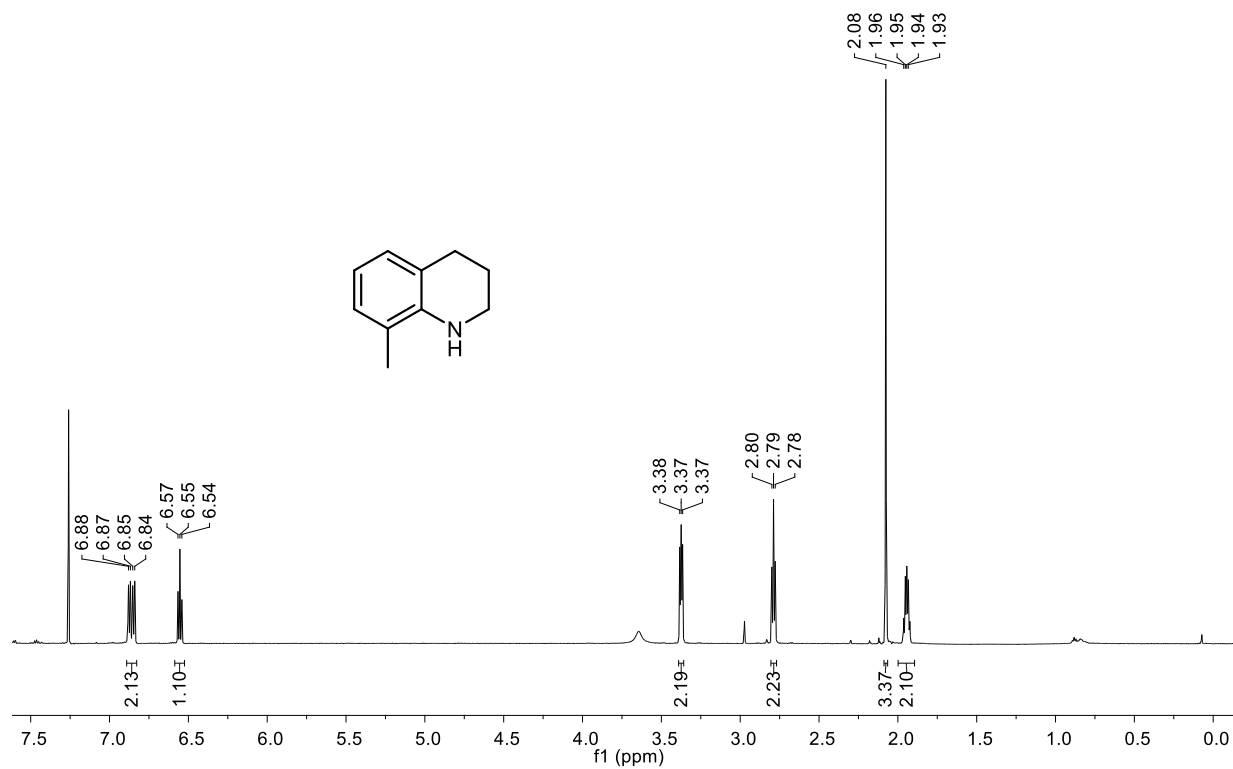


Figure S1.15 ¹H NMR (600 MHz, CDCl₃) spectrum of 8-methyl-1,2,3,4-tetrahydroquinoline.

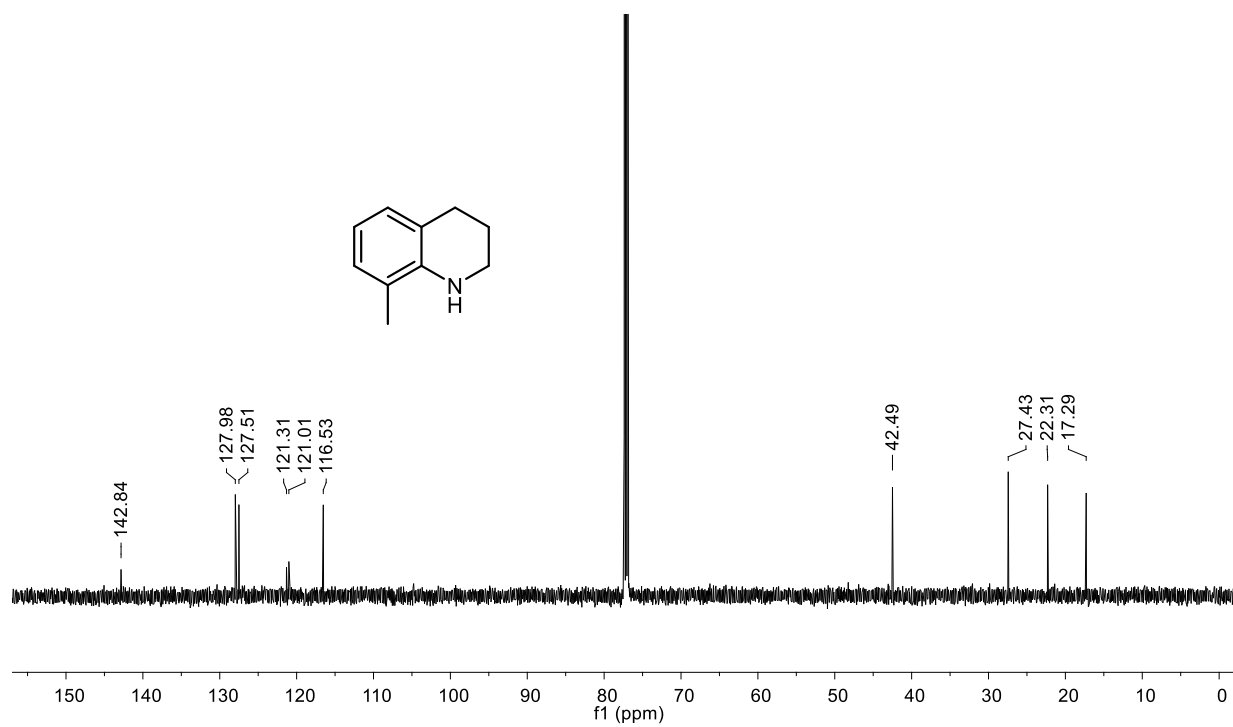


Figure S1.16 ¹³C NMR (151 MHz, CDCl₃) spectrum of 8-methyl-1,2,3,4-tetrahydroquinoline.

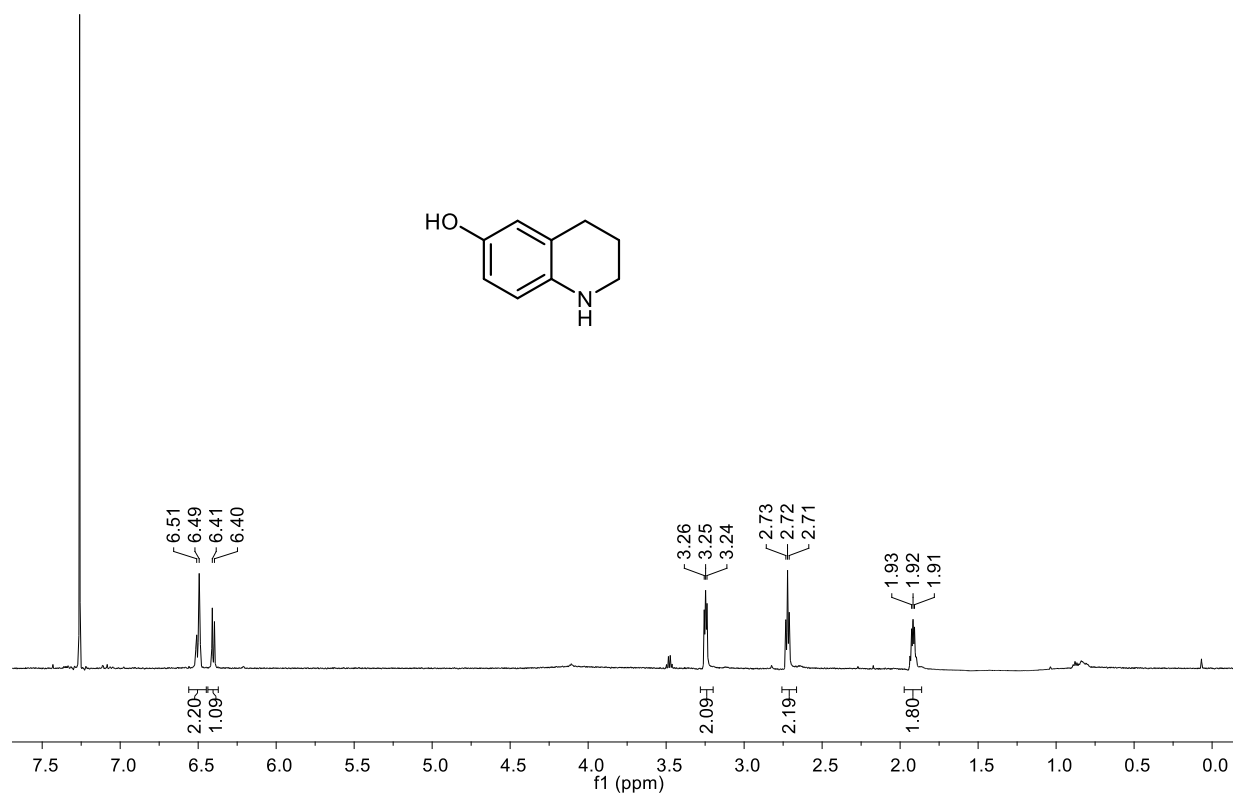


Figure S1.17 ^1H NMR (600 MHz, CDCl_3) spectrum of 6-hydroxy-1,2,3,4-tetrahydroquinoline.

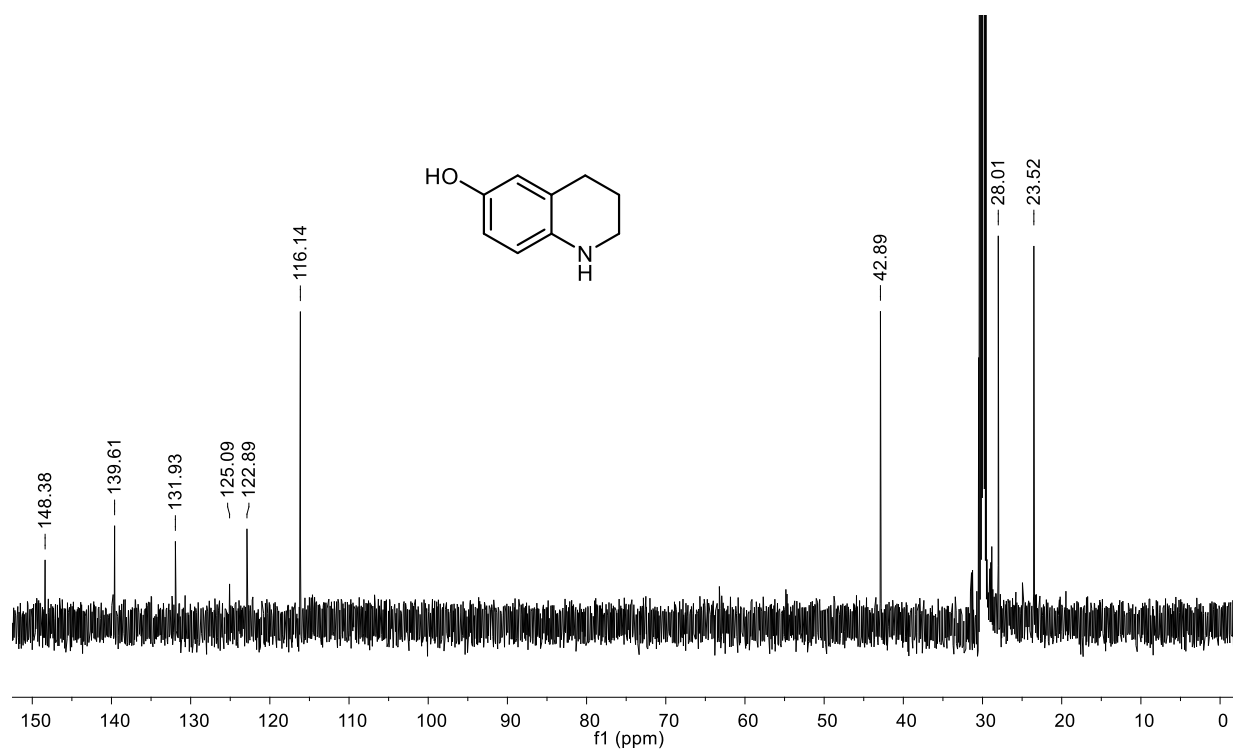


Figure S1.18 ^{13}C NMR (151 MHz, CDCl_3) spectrum of 6-hydroxy-1,2,3,4-tetrahydroquinoline.

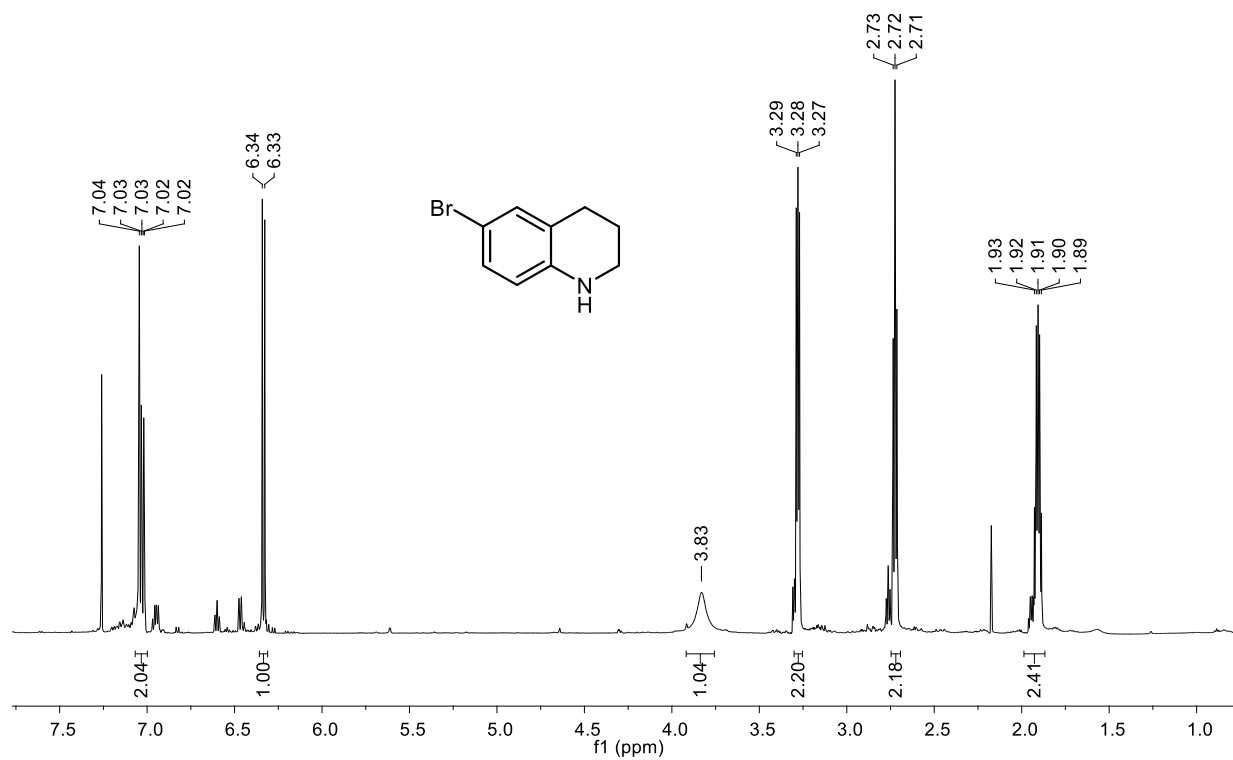


Figure S1.19 ¹H NMR (600 MHz, CDCl₃) spectrum of 6-bromo-1,2,3,4-tetrahydroquinoline.

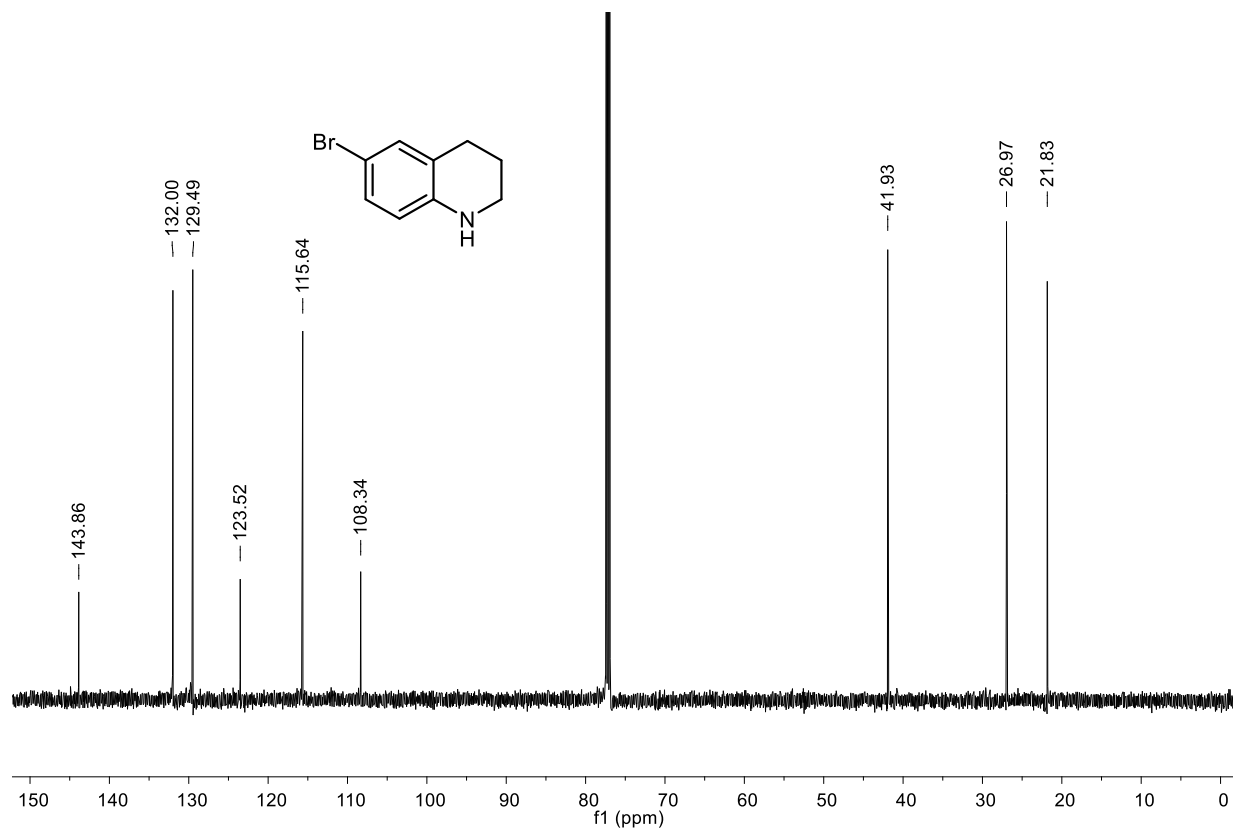


Figure S1.20 ¹³C NMR (151 MHz, CDCl₃) spectrum of 6-bromo-1,2,3,4-tetrahydroquinoline.

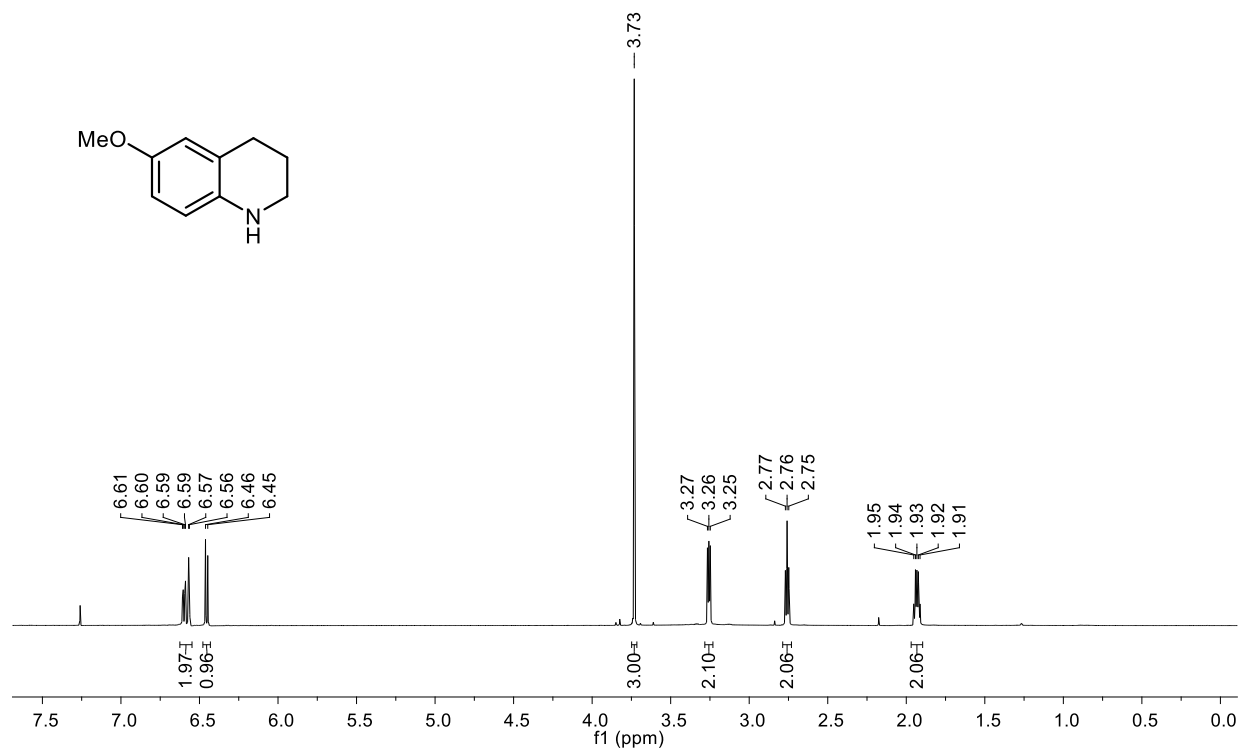


Figure S1.21 ¹H NMR (600 MHz, CDCl₃) spectrum of 6-methoxy-1,2,3,4-tetrahydroquinoline.

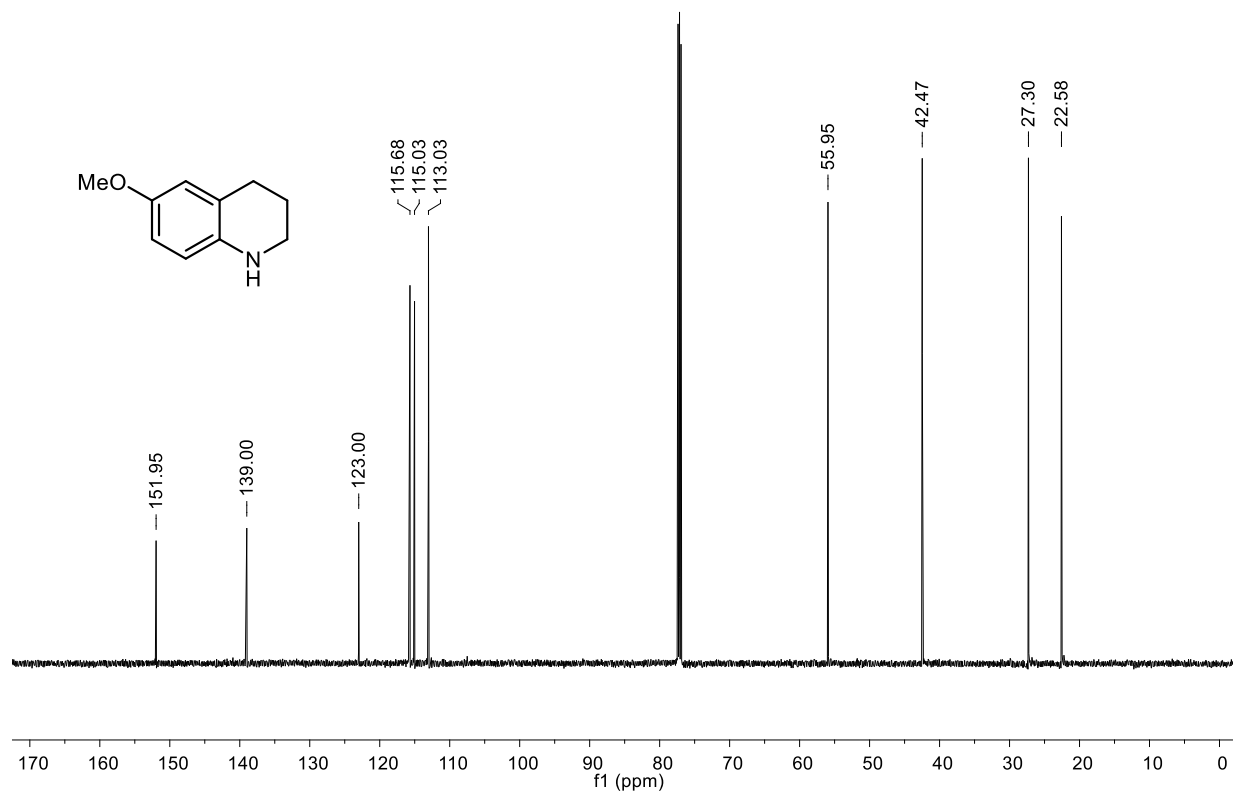


Figure S1.22 ¹³C NMR (151 MHz, CDCl₃) spectrum of 6-methoxy-1,2,3,4-tetrahydroquinoline.

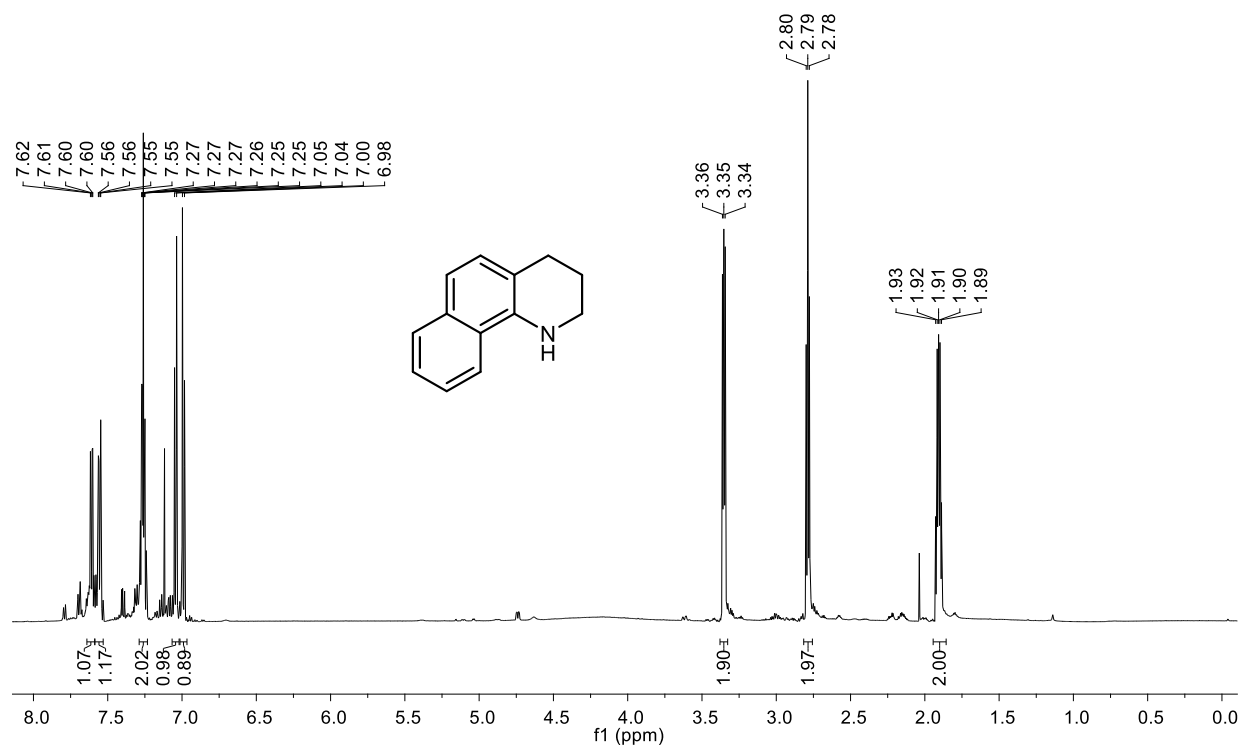


Figure S1.23 ¹H NMR (600 MHz, CDCl₃) spectrum of 1,2,3,4-tetrahydrobenzo[h]quinoline.

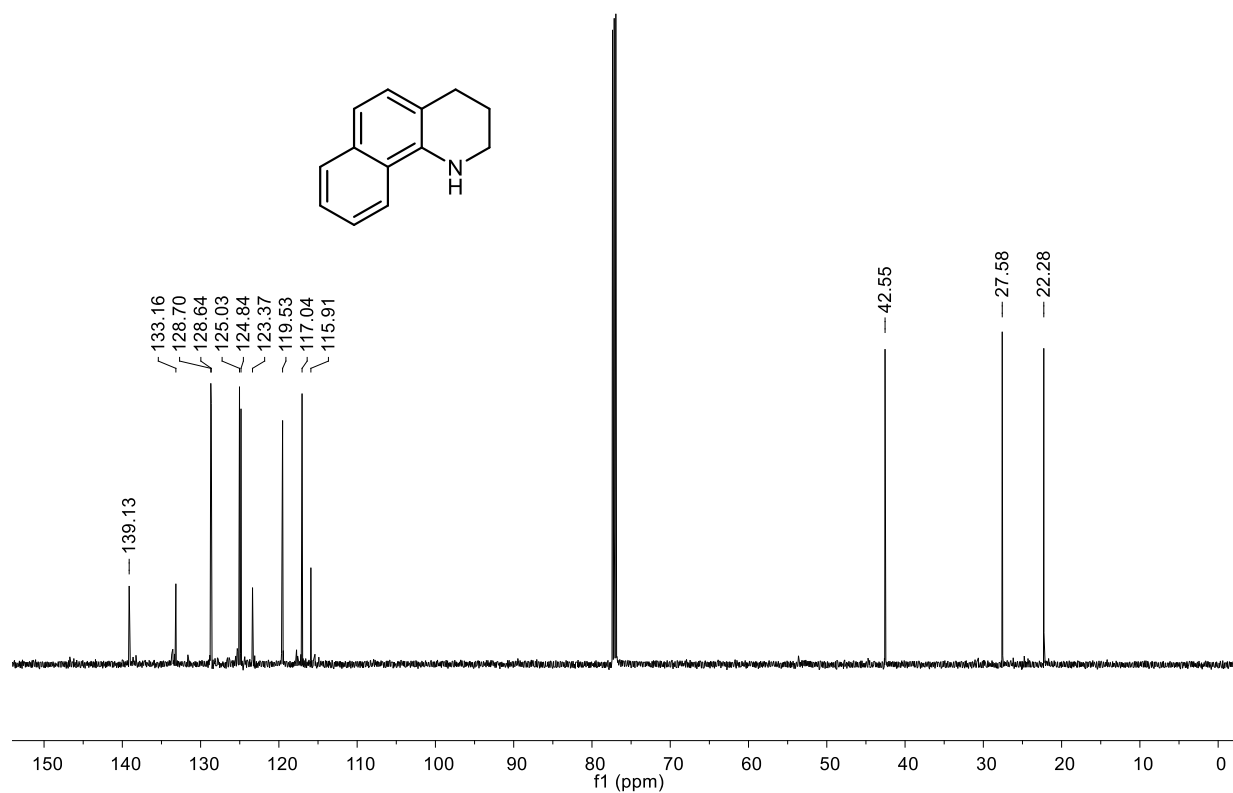


Figure S1.24 ¹³C NMR (151 MHz, CDCl₃) spectrum of 1,2,3,4-tetrahydrobenzo[h]quinoline.

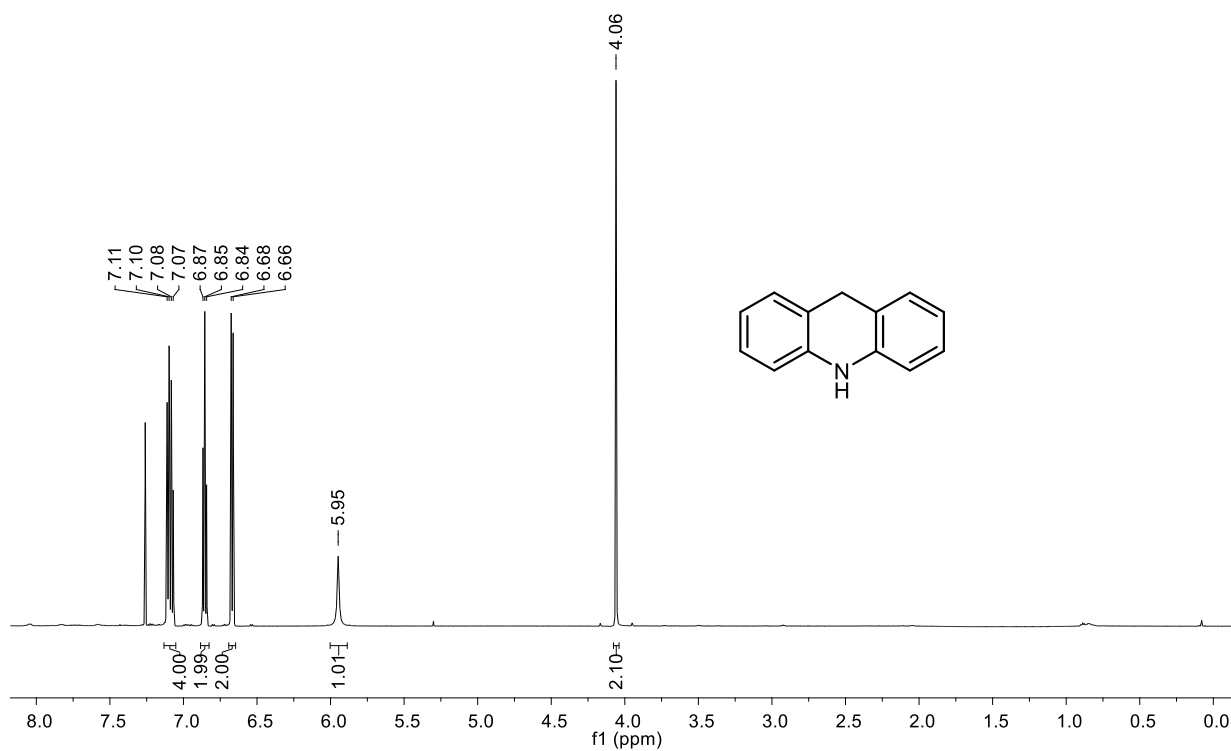


Figure S1.25 ¹H NMR (600 MHz, CDCl₃) spectrum of 9,10-dihydroacridine.

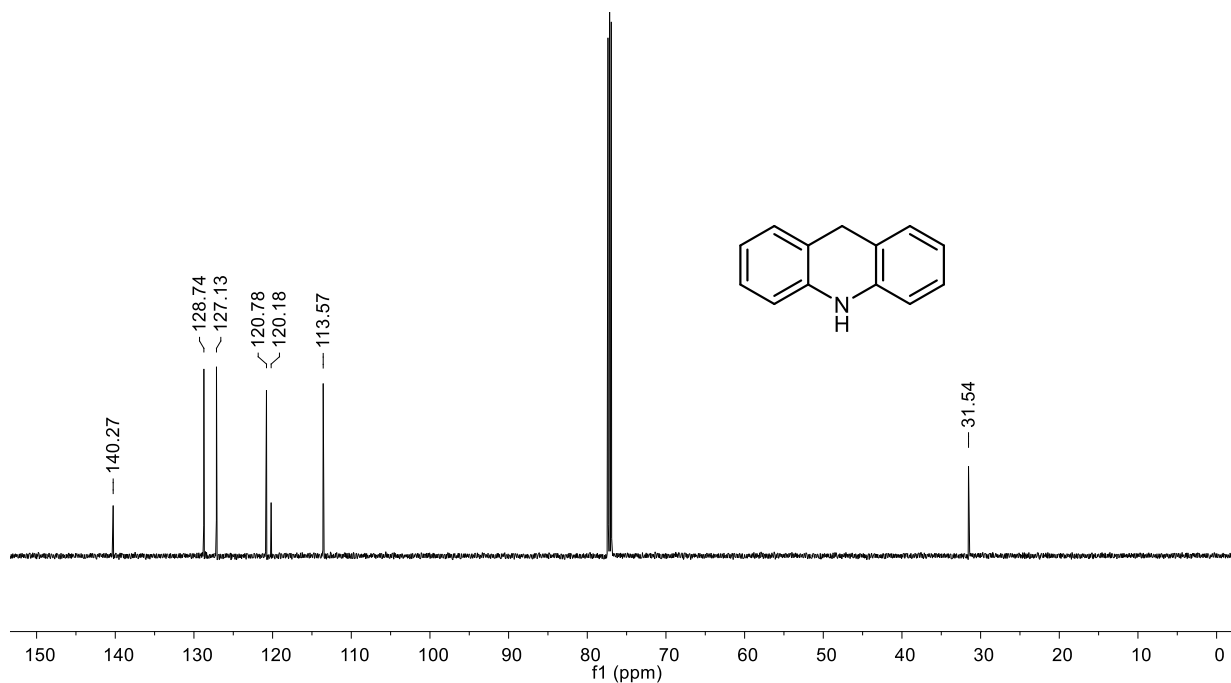


Figure S1.26 ¹³C NMR (151 MHz, CDCl₃) spectrum of 9,10-dihydroacridine.

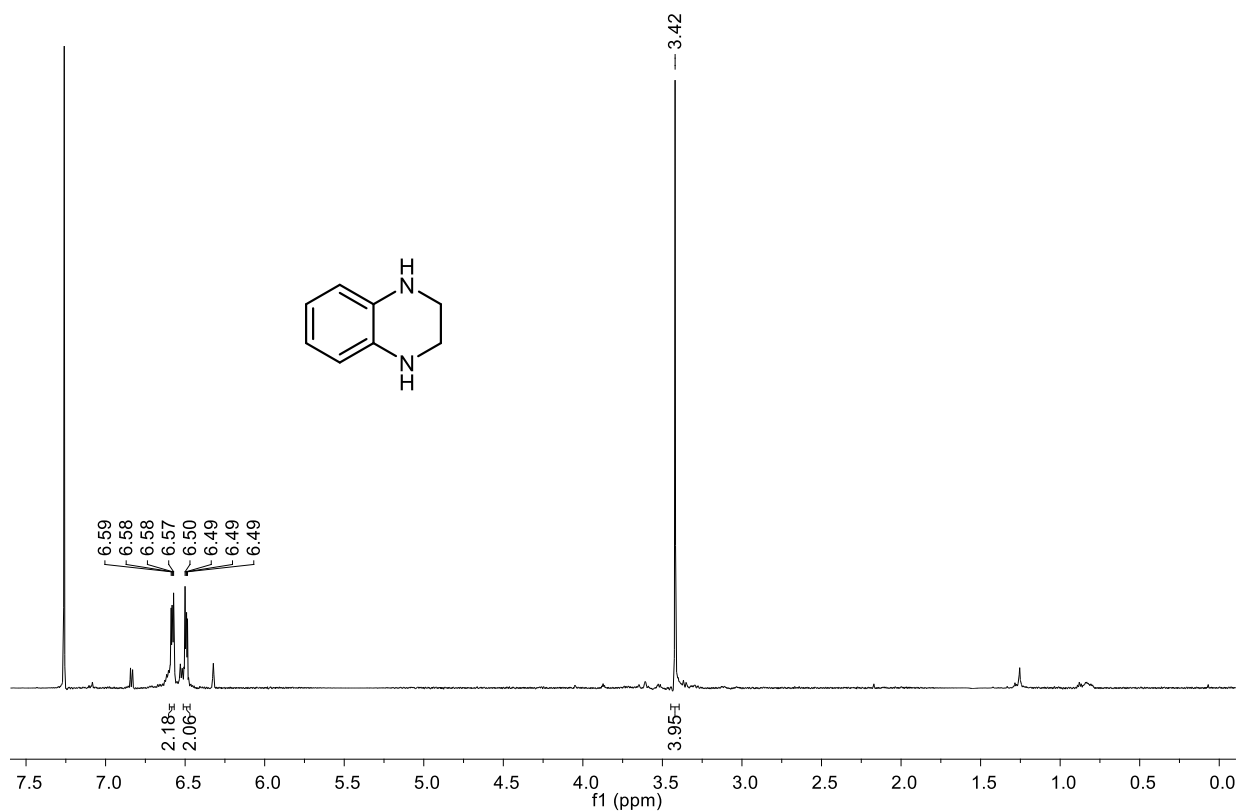


Figure S1.27 ¹H NMR (600 MHz, CDCl₃) spectrum of 1,2,3,4-tetrahydroquinoxaline.

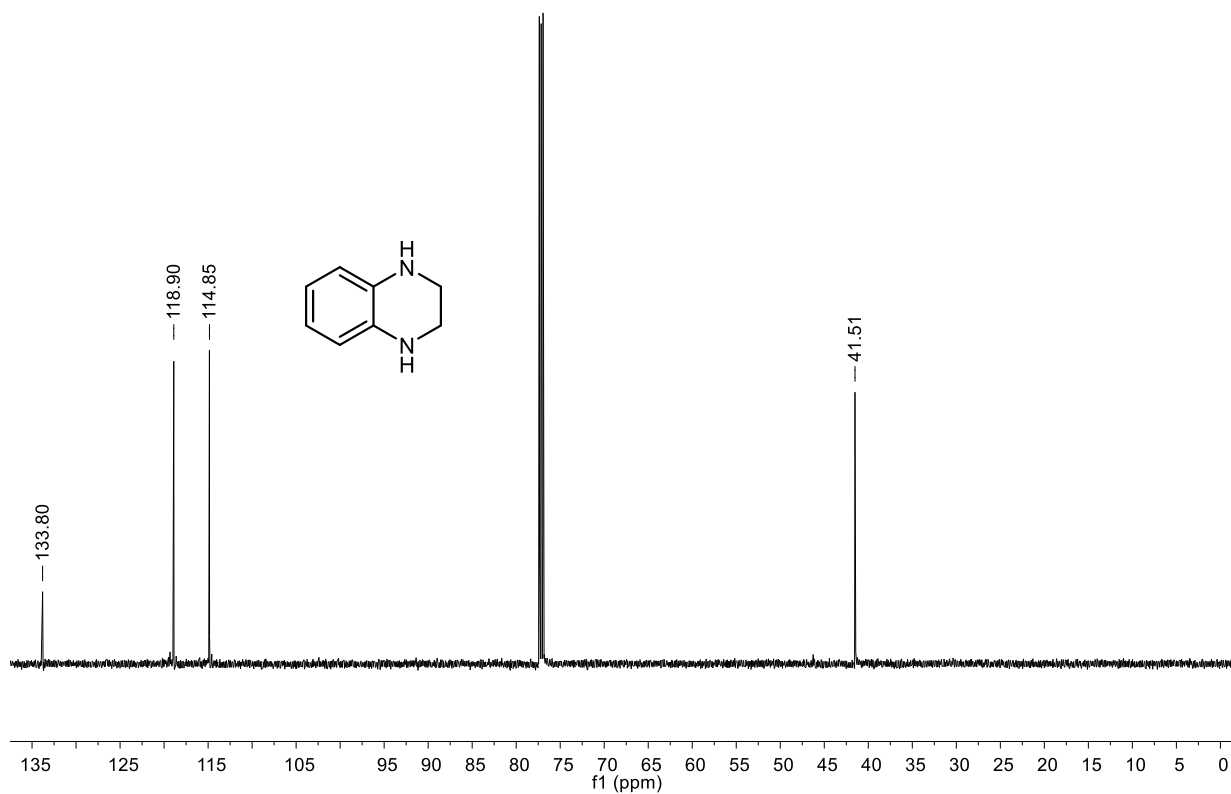


Figure S1.28 ¹³C NMR (151 MHz, CDCl₃) spectrum of 1,2,3,4-tetrahydroquinoxaline.

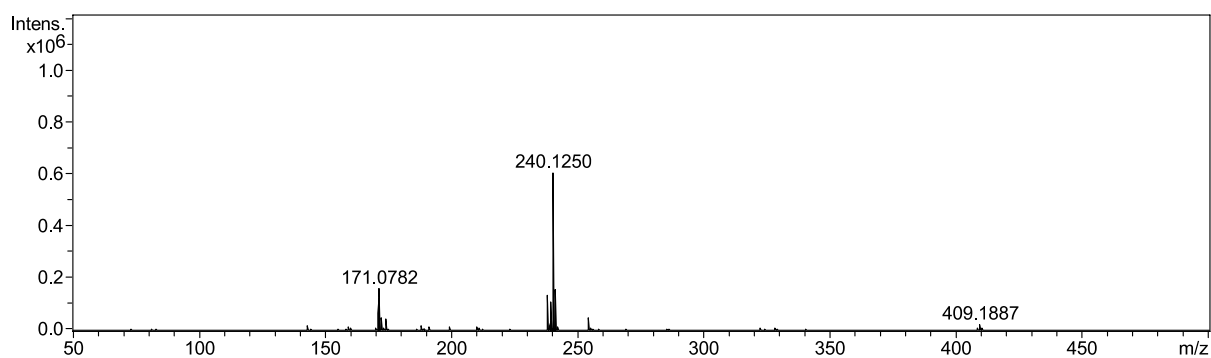


Figure S1.29 APCI-MS spectrum of **L3.1** recorded in positive ion mode. Isotope cluster found at m/z of 240.1250 corresponding to the $[M + H]^+$ ion.

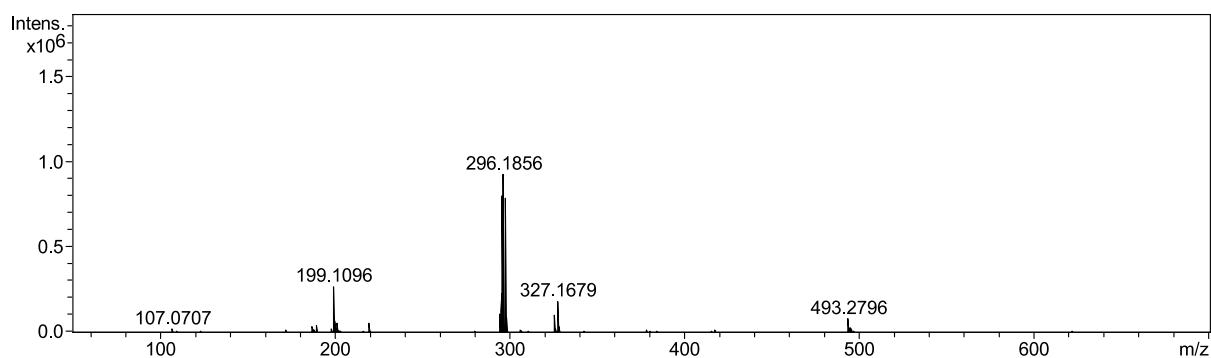


Figure S1.30 APCI-MS spectrum of **L3.2** recorded in positive ion mode. Isotope cluster found at m/z of 296.1856 corresponding to the $[M + H]^+$ ion.

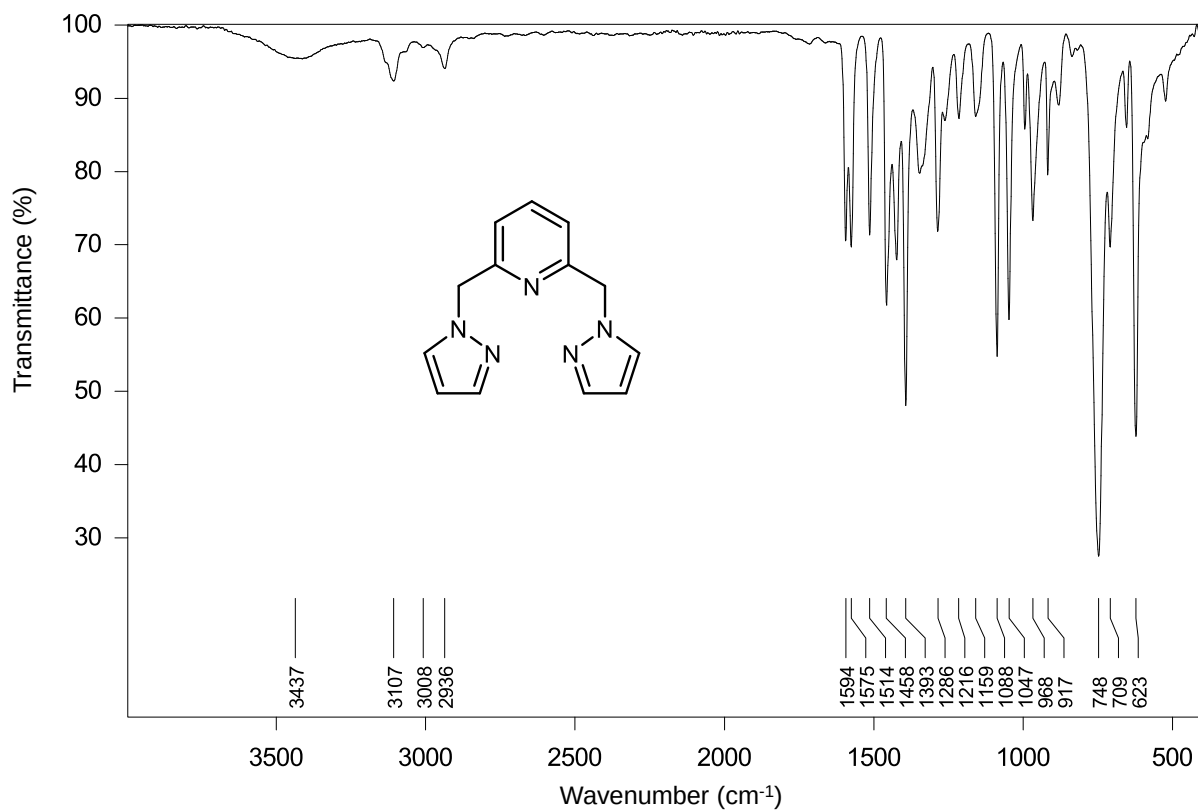


Figure S1.31 FT-IR spectrum of ligand **L3.1**.

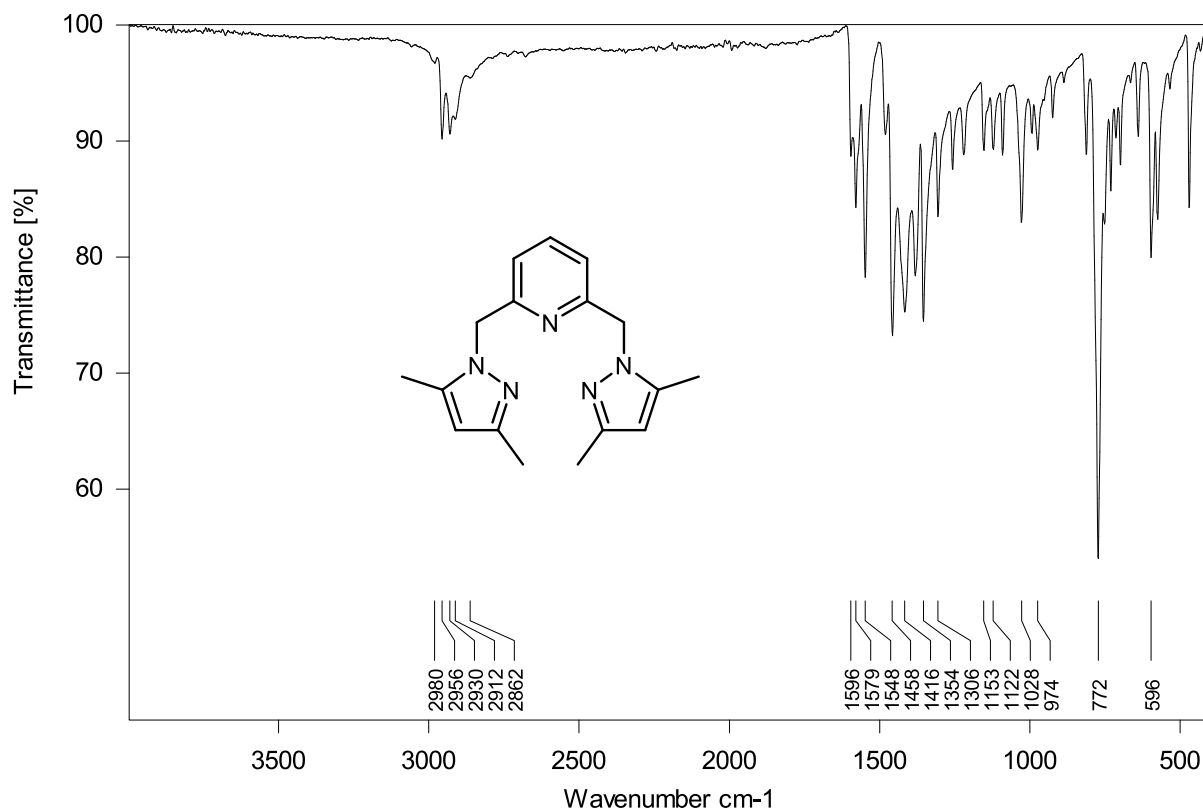


Figure S1.32 FT-IR spectrum of ligand **L3.2**.

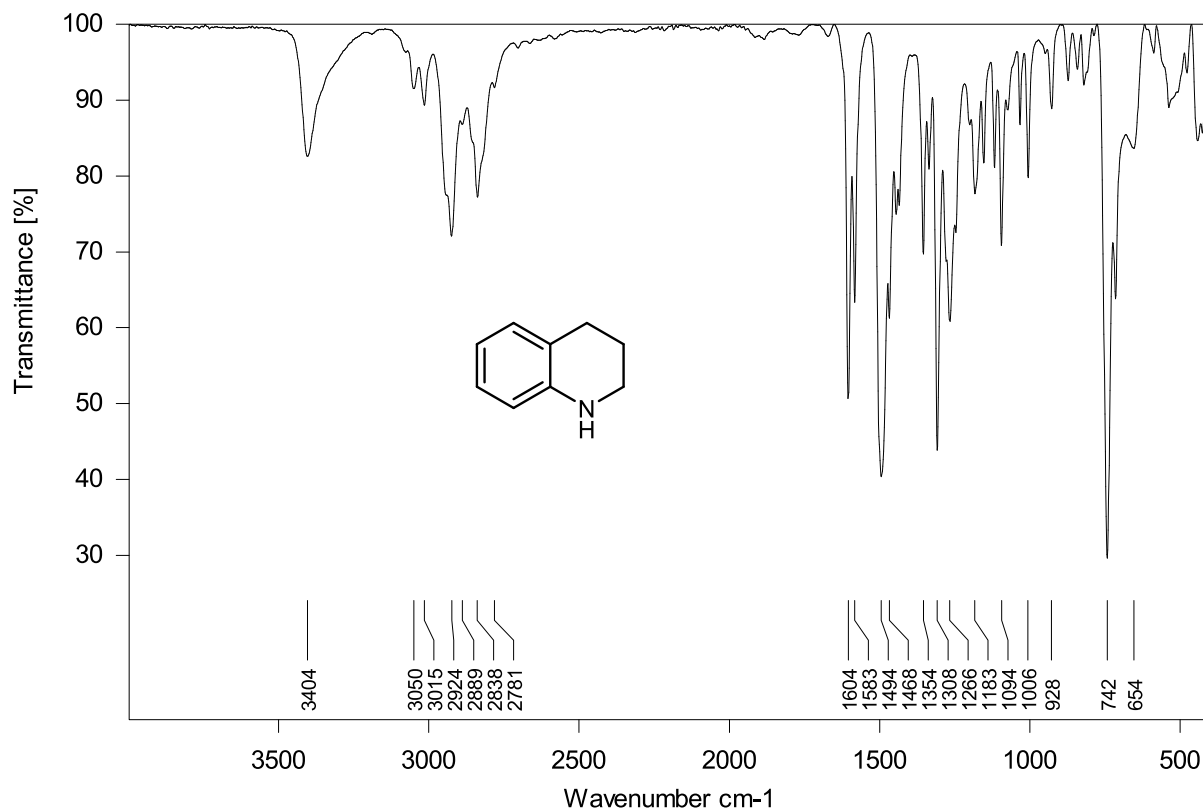


Figure S1.33 FT-IR spectrum of isolated product 1,2,3,4-tetrahydroquinoline.

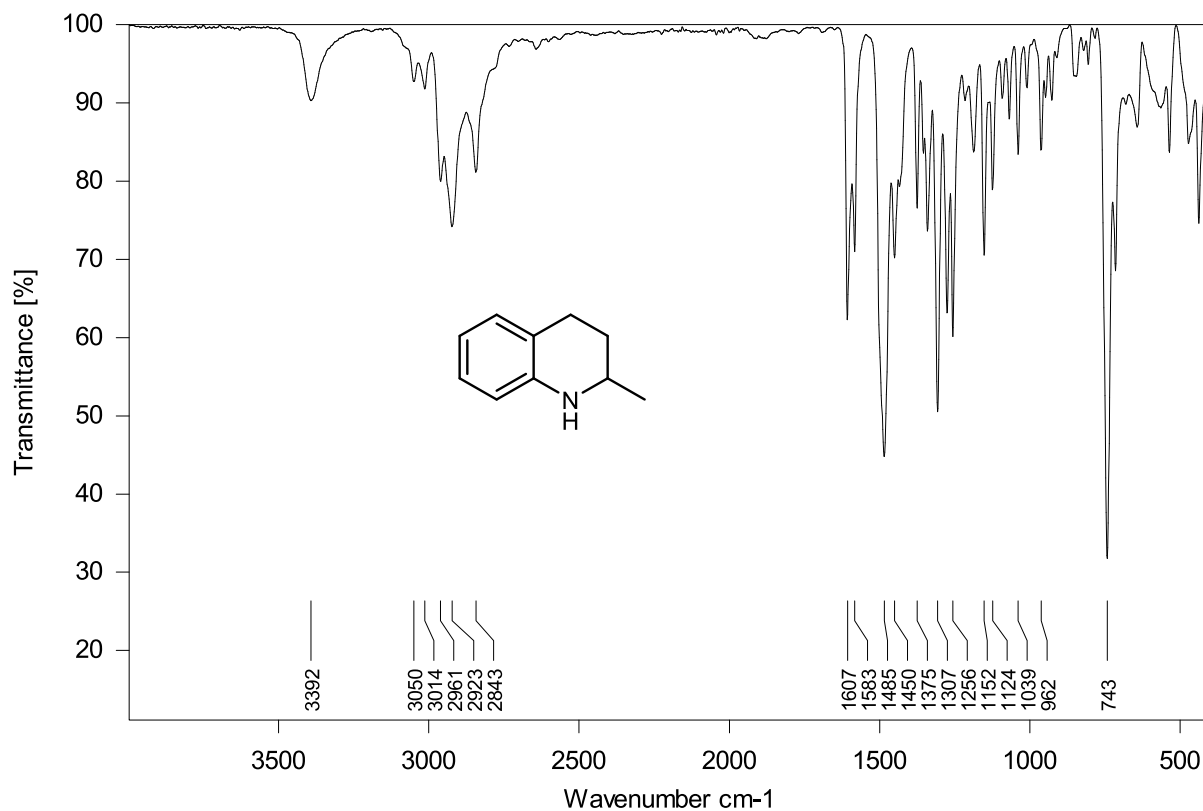


Figure S1.34 FT-IR spectrum of isolated product 2-methyl-1,2,3,4-tetrahydroquinoline.

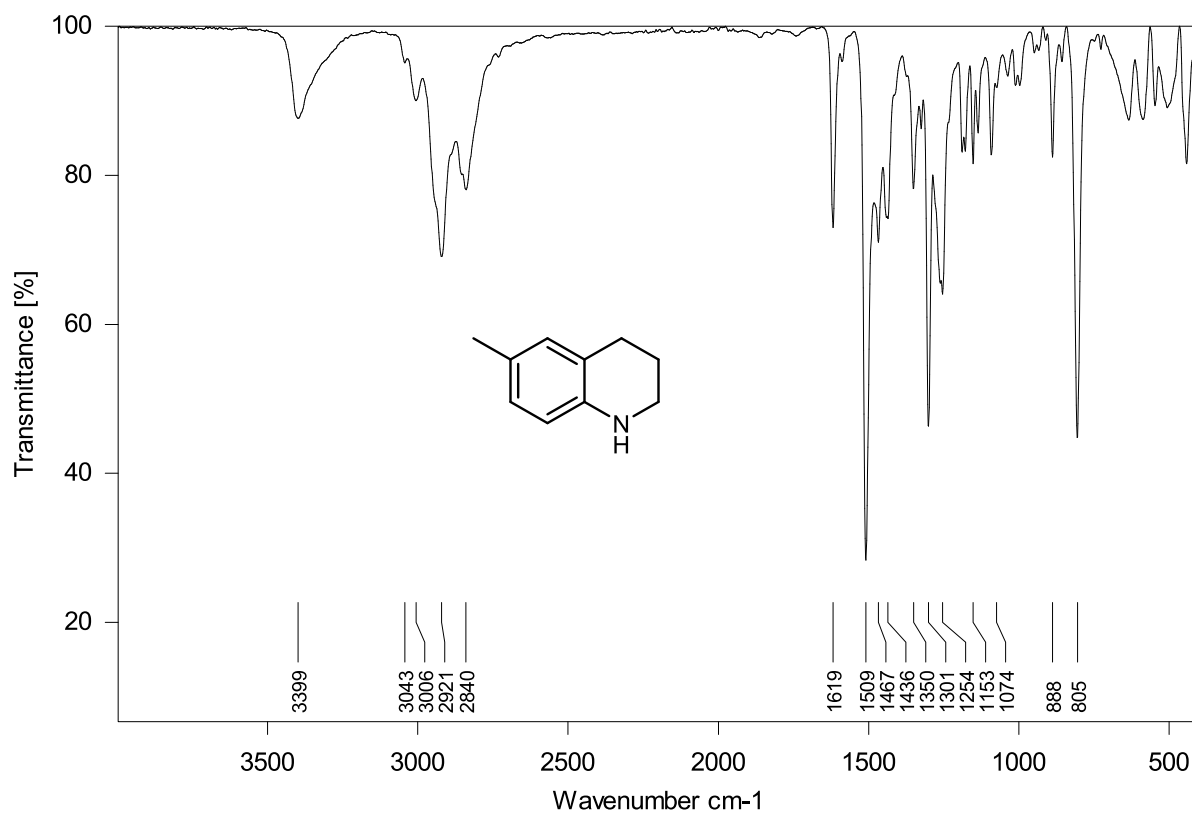


Figure S1.35 FT-IR spectrum of isolated product 6-methyl-1,2,3,4-tetrahydroquinoline.

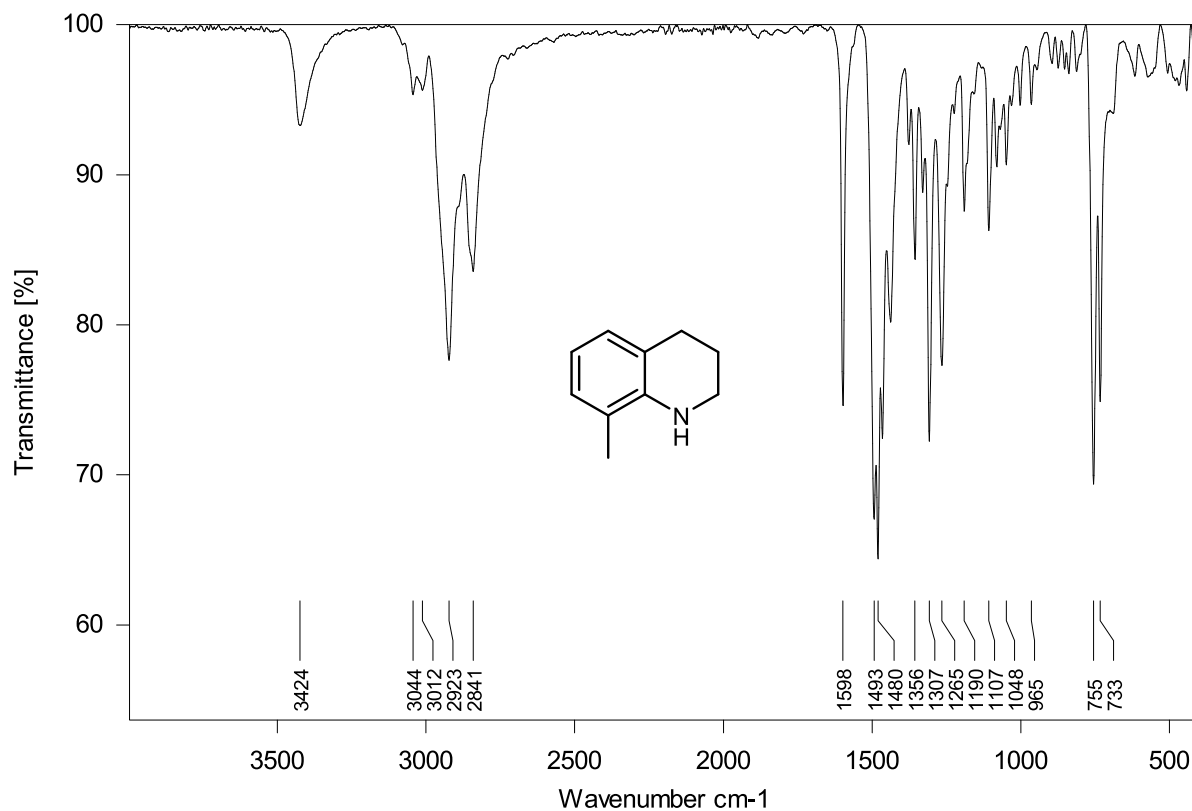


Figure S1.36 FT-IR spectrum of isolated product 8-methyl-1,2,3,4-tetrahydroquinoline.

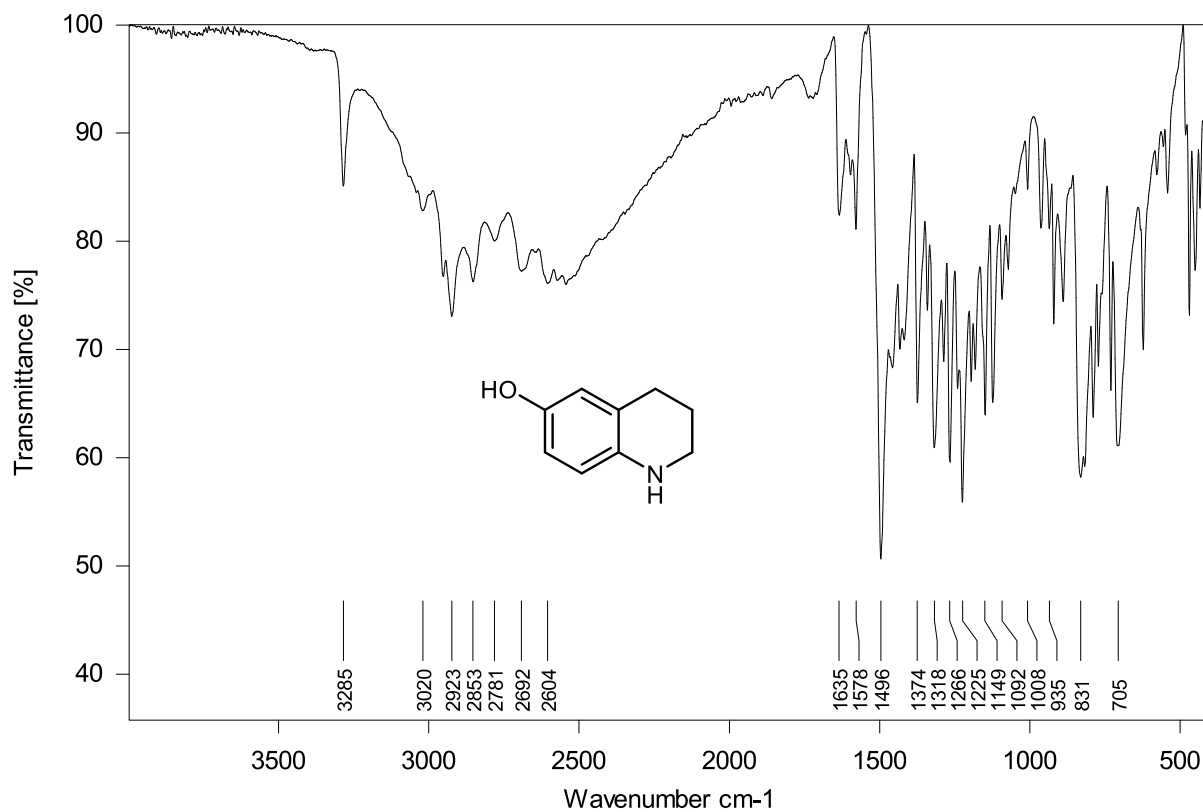


Figure S1.37 FT-IR spectrum of isolated product 6-hydroxy-1,2,3,4-tetrahydroquinoline.

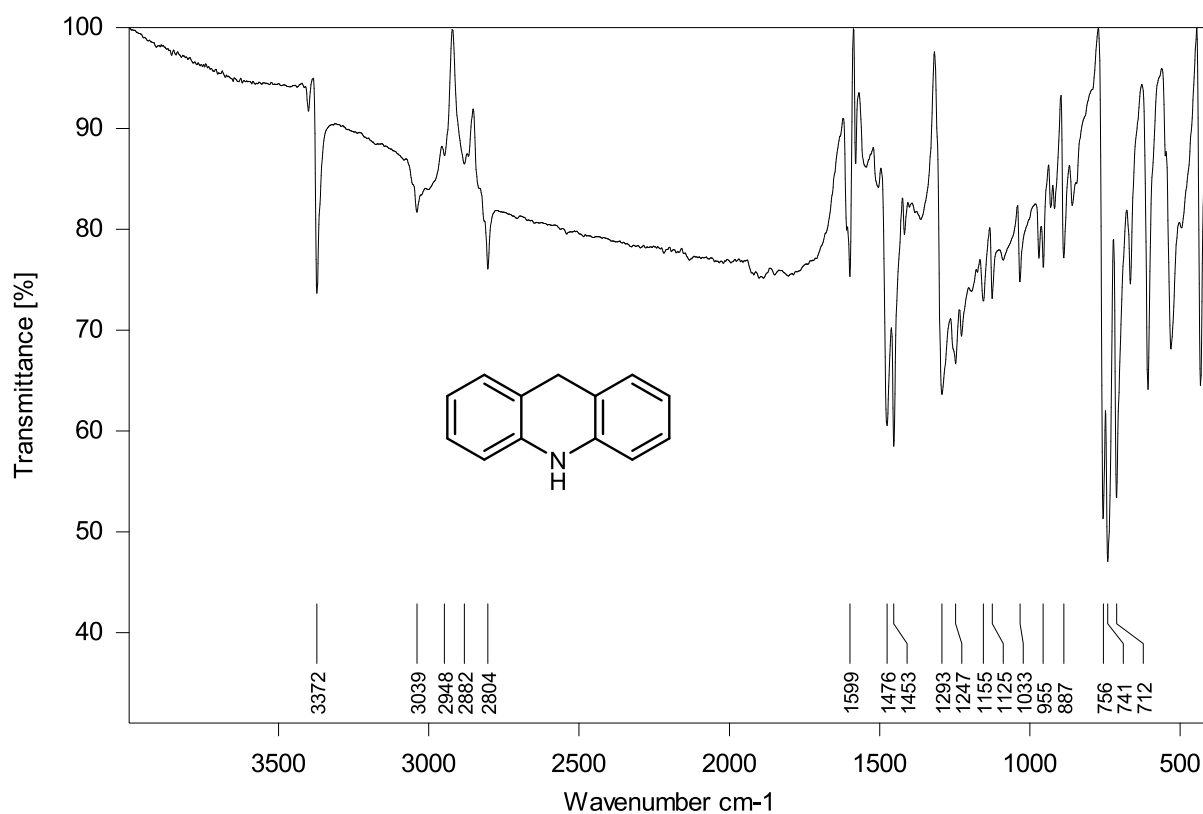


Figure S1.38 FT-IR spectrum of isolated product 9,10-dihydroacridine.

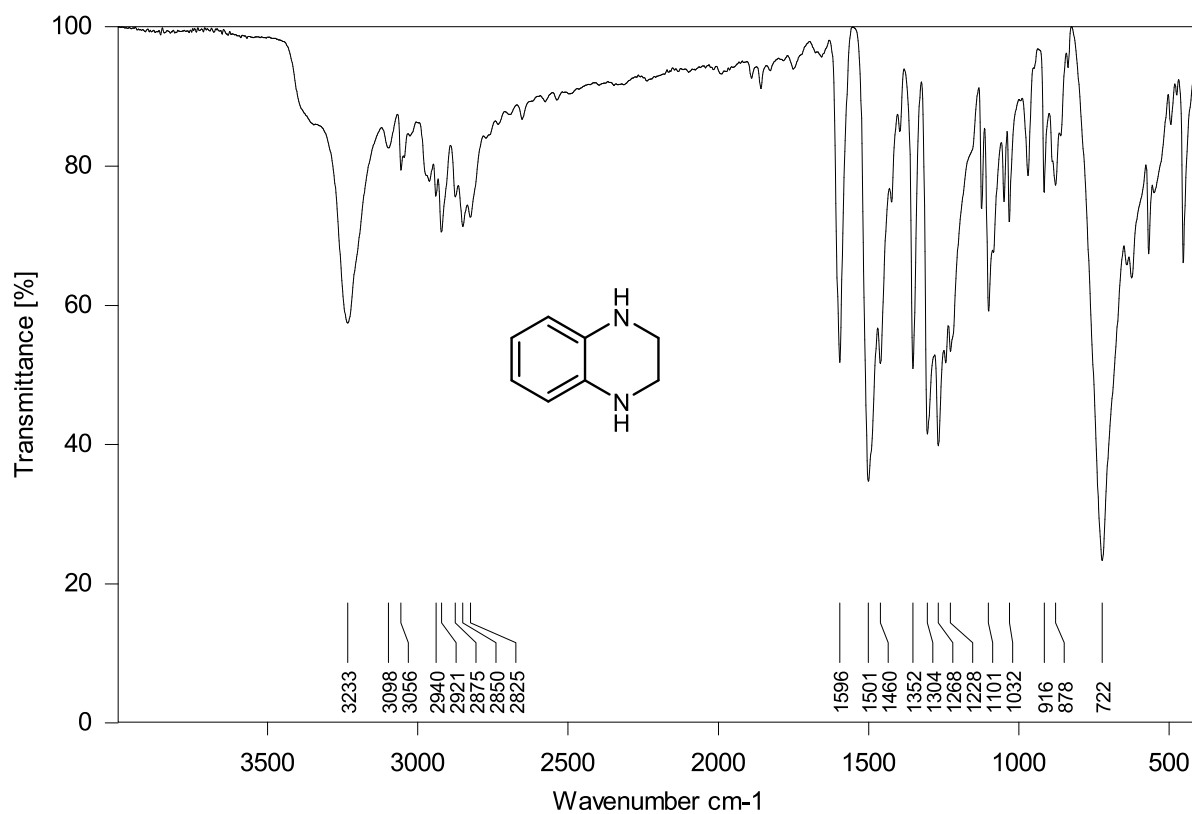


Figure S1.39 FT-IR spectrum of isolated product 1,2,3,4-tetrahydroquinoxaline.

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Supplementary information for Chapter 4

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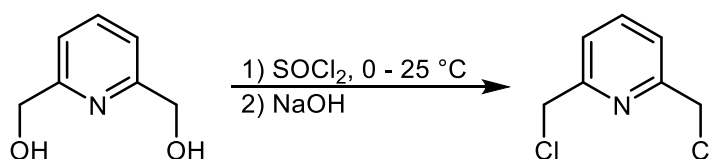
S2.1 General considerations

All chemicals were sourced from commercial suppliers, i.e. Sigma-Aldrich, Merck and Rochelle Chemicals and used as received. Ammonia borane ($\text{H}_3\text{N}-\text{BH}_3$, AB) was stored in a MBraun glove box under an Ar atmosphere. No difference in activity was found between 90% (8.6 mg, 1 eq.) and 97% (7.7 mg, 1 eq.) AB used in this study. The $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ salt (98%) sent for ICP-analyses was digested with 2% HNO_3 (Ultra-pure grade) and analysed against NIST standards. ICP-AES analysis (Al to Zn) were conducted using a Thermo Scientific iCAP 6000 ICP-AES spectrometer and ICP-MS analysis (Ru to Au) on an Agilent 7900 spectrometer. FT-IR spectra were recorded on a Bruker Alpha-P range infrared instrument equipped with an ATR accessory as neat samples in the range of 400 to 4000 cm^{-1} . APCI-MS characterisation was conducted on a Bruker microTOF-Q II mass spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Ultrashield Plus (600 and 151 MHz, respectively) in 5 mm cylindrical glass tubes. Gas chromatographic analysis, GC and GC-MS, were performed on an Agilent 6890N Series GC system with HP-5 and HP-5MS columns respectively, with the following column dimensions: 30 m in length, 0.320 mm internal diameter and 0.25 mm film thickness. The GC and GC-MS were equipped with a FID and Agilent 5973N mass detector, respectively. The rinsing solution included MeOH (GC and GC-MS) with N_2 (GC) or He (GC-MS) used as the carrier gas and biphenyl serving as an internal standard.

S2.2 Synthesis of N,N,N-tridentate ligands, L4.1 & L4.2

Synthesis of ligands, **L4.1** and **L4.2**, were conducted following methods previously described.¹ The other ligands, **L4.3** to **L4.6**, were commercially available and used as received.

S2.2.1 Synthesis of 2,6-bis(chloromethyl)pyridine

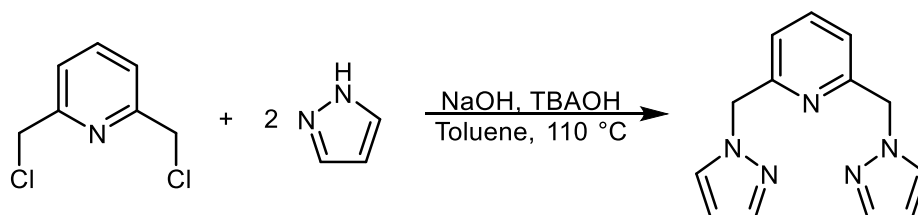


Scheme S2.1 Synthesis of 2,6-bis(chloromethyl)pyridine.

A round-bottomed flask, connected to a NaOH trap, was charged with 2,6-pyridinedimethanol (1.0011 g, 7.051 mmol) and placed in an ice bath. While stirring, cold thionyl chloride (5 mL, 66.86 mmol) was added slowly over 30 minutes, through a septum. The reaction mixture was allowed to gradually warm to room temperature over a period of 2 hours. The mixture was cooled and toluene (15 mL) was added. The white salt was filtered, washed with 2 x 5 mL portions of cold toluene and diethyl ether (10 mL) and dried under vacuum. The salt was

dissolved in water and NaOH (0.6032 g, mmol) added to neutralise the salt. The suspension was cooled in an ice bath, the crystals filtered and washed with 2 x 10 mL portions of H₂O. The crude product was recrystallized from petroleum ether to obtain colourless crystals (1.0335 g, 83%). FT-IR (ATR) ν , cm⁻¹: 2965, 3022, 1591, 1576, 671. ¹H NMR (600 MHz, CDCl₃, ppm) δ : 7.76 (t, J = 7.8 Hz, 1H), 7.44 (d, J = 7.8 Hz, 2H), 4.66 (s, 4H). ¹³C NMR (151 MHz, CDCl₃, ppm) δ : 156.53, 138.27, 122.23, 46.57.

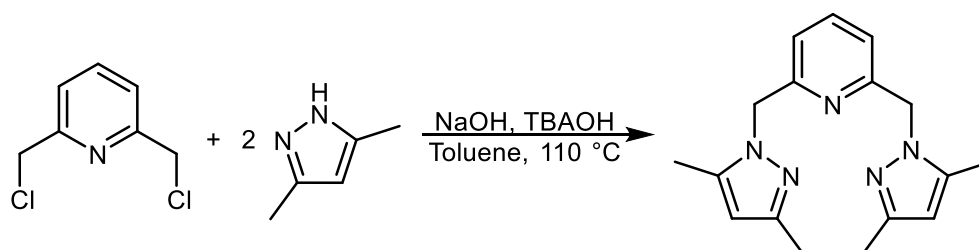
S2.2.2 Synthesis of 2,6-bis((1H-pyrazol-1-yl)methyl)pyridine (L4.1)



Scheme S2.2 Synthesis of ligand **L4.1**.

In a round-bottomed flask 2,6-bis(chloromethyl)pyridine (0.3010 g, 1.710 mmol) and pyrazole (0.2385 g, 3.433 mmol) were dissolved in toluene (20 mL). A 40% NaOH solution (12 mL) and 10 drops of TBAOH were added to the mixture. The mixture was heated to 110 °C and stirred for 23 hours. After the allotted time, the solution was cooled down to room temperature, the organic layer was separated and washed with 3 x 10 mL portions of H₂O. The organic layers were combined, dried over MgSO₄, filtered and the solvent removed under vacuum to obtain a pale yellow oil (0.3250 g, 79%) (**L4.1**). FT-IR (ATR) ν , cm⁻¹: 3437, 3107, 3008, 2936, 1594, 1575. ¹H NMR (600 MHz, CDCl₃, ppm) δ : 7.59 – 7.49 (m, 5H), 6.83 (d, J = 7.8 Hz, 2H), 6.31 (t, J = 2.1 Hz, 2H), 5.44 (s, 4H). ¹³C NMR (151 MHz, CDCl₃, ppm) δ : 156.68, 140.09, 138.22, 130.12, 120.62, 106.37, 57.50. APCI-MS (m/z): 240.1250 [$M + H$]⁺.

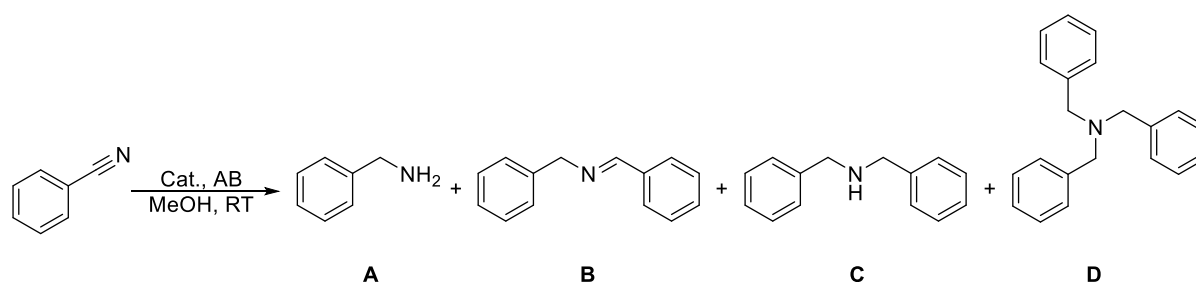
S2.2.3 Synthesis of 2,6-bis((3,5-dimethyl-1H-pyrazol-1-yl)methyl)pyridine (L4.2)



Scheme S2.3 Synthesis of ligand **L4.2**.

The same procedure described for the synthesis of **L4.1**, was followed for **L4.2** using 2,6-bis(chloromethyl)pyridine (0.3050 g, 1.733 mmol) and 3,5-dimethyl pyrazole (0.3345 g, 3.444 mmol). The product was recrystallized from petroleum ether and isolated as white crystals (0.4595 g, 90%) (**L4.2**). FT-IR (ATR) ν , cm^{-1} : 2980, 2956, 2930, 2912, 2862, 1596, 1579. ^1H NMR (600 MHz, CDCl_3 , ppm) δ : 7.50 (t, $J = 7.8$ Hz, 1H), 6.67 (d, $J = 7.8$ Hz, 2H), 5.85 (s, 2H), 5.29 (s, 4H), 2.23 (s, 6H), 2.16 (s, 6H). ^{13}C NMR (151 MHz, CDCl_3 , ppm) δ : 157.27, 148.21, 139.87, 138.14, 119.75, 105.82, 54.51, 13.62, 11.17. APCI-MS (m/z): 296.1856 $[\text{M} + \text{H}]^+$.

S2.3 General procedure for the transfer hydrogenation of benzonitrile



Scheme S2.4 Transfer hydrogenation of benzonitrile with possible product formation.

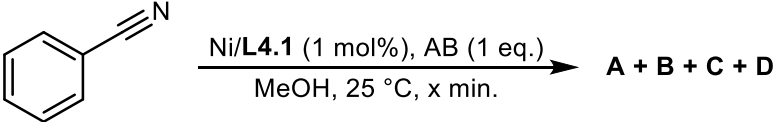
Ammonia borane (8.6 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile (25 μL , 0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with **L4.1** (0.6 mg, 2.5 μmol) in methanol (1 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

S2.4 Optimisation of reaction conditions for transfer hydrogenation of benzonitrile

S2.4.1 General procedure to evaluate influence of reaction time

Ammonia borane (8.6 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile (25 μ L, 0.25 mmol) and then Ni(II) salt (2.5 μ mol) with **L4.1** (0.6 mg, 2.5 μ mol) in methanol (1 mL) followed. The reaction mixture was stirred at room temperature for the time indicated. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

Table S2.1 Evaluation of reaction time influence against benzonitrile transfer hydrogenation.

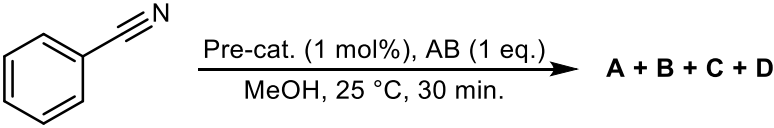
			
Entry	Time (minutes)	Conversion ^a (%)	Prod. distr. ^a (A:B:C:D)
1	5	>99	1:31:67:1
2	10	>99	1:13:85:1
3	30	>99	1:7:90:2

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), benzonitrile (0.25 mmol), NiCl₂·6H₂O (1 mol%) and **L4.1** (1 mol%) in methanol (1 mL) were stirred at 25 °C for the time indicated. ^a Conversion and product distribution was determined by GC and GCMS against biphenyl as the internal standard and is the average of two independent runs.

S2.4.2 General procedure to evaluate different ligands

Ammonia borane (8.6 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile (25 μ L, 0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μ mol) with ligand (2.5 μ mol) in methanol (1 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

Table S2.2 Evaluation of ligands against benzonitrile transfer hydrogenation.

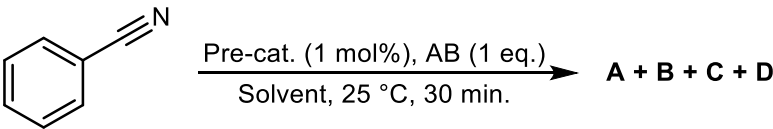
			
Entry	Ligand	Conversion ^a (%)	Prod. distr. ^a (A:B:C:D)
1	L4.1	>99	1:7:90:2
2	L4.2	>99	3:18:77:2
3	L4.3	41	0:23:13:5
4	L4.4	>99	3:13:79:5

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), benzonitrile (0.25 mmol), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1 mol%) and ligand (1 mol%) in methanol (1 mL) were stirred at 25 °C for 30 minutes. ^aConversion and product distribution were determined by GC against biphenyl as the internal standard and is the average of two independent runs.

S2.4.3 General procedure to evaluate different Ni(II) salts

Ammonia borane (8.6 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile (25 μ L, 0.25 mmol) and then Ni(II) salt (2.5 μ mol) with **L4.1** (0.6 mg, 2.5 μ mol) in methanol (1 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

Table S2.3 Evaluation of Ni(II) salts against benzonitrile transfer hydrogenation.

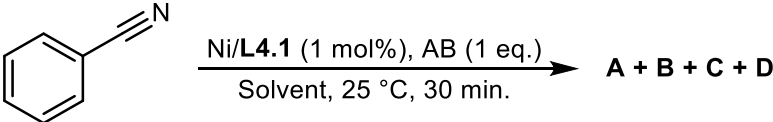
			
Entry	Pre-catalyst	Conversion ^a (%)	Prod. distr. ^a (A:B:C:D)
1	NiCl ₂ ·6H ₂ O/ L4.1	>99	1:7:90:2
2	Ni(NO ₃) ₂ ·6H ₂ O/ L4.1	>99	1:40:59:0
3	Ni(SO ₄) ₂ ·7H ₂ O/ L4.1	>99	1:19:78:2

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), benzonitrile (0.25 mmol), Ni(II) salt (1 mol%) and **L4.1** (1 mol%) in methanol (1 mL) were stirred at 25 °C for 30 minutes. ^a Conversion and product distribution was determined by GC and GCMS against biphenyl as the internal standard and is the average of two independent runs.

S2.4.4 General procedure to evaluate influence of solvent

Ammonia borane (8.6 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile (25 μ L, 0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μ mol) with **L4.1** (0.6 mg, 2.5 μ mol) in solvent (1 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

Table S2.4 Evaluation of solvent influence against benzonitrile transfer hydrogenation.

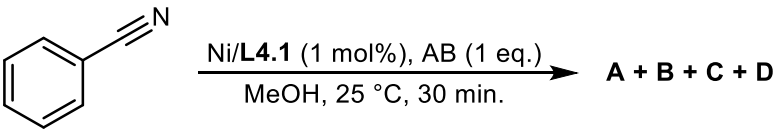
			
Entry	Solvent	Conversion ^a (%)	Prod. distr. ^a (A:B:C:D)
1	Methanol	>99	1:7:90:2
2	Ethanol	>99	1:60:39:0
3	<i>i</i> PrOH	44	0:6:38:0
4 ^b	Hexane	0	-
5	MeOH/NH ₃ (1.9/0.1)	>99	15:56:29:0
6	MeOH/NH ₃ (1.5/0.5)	0	0
7	MeOH/H ₂ O (7/3)	>99	0:32:66:2
8	MeOH/H ₂ O (1/1)	15	0:0:11:4

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), benzonitrile (0.25 mmol), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1 mol%) and **L4.1** (1 mol%) in solvent (1 mL) were stirred at 25 °C for 30 minutes. ^a Conversion and product distribution was determined by GC and GCMS against biphenyl as the internal standard and is the average of two independent runs. ^b Carried out at 50 °C for 3 hours.

S2.4.5 General procedure to evaluate influence of open or closed reactor

Ammonia borane (8.6 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile (25 μ L, 0.25 mmol) and then Ni(II) salt (2.5 μ mol) with **L4.1** (0.6 mg, 2.5 μ mol) in methanol (1 mL) followed. The reaction mixture was stirred at room temperature for the time indicated. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

Table S2.5 Evaluation of open/closed reactor influence against benzonitrile transfer hydrogenation.

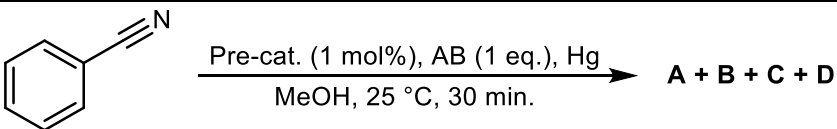
				
Entry	Conditions	Time (minutes)	Conversion ^a (%)	Prod. distr. ^a (A:B:C:D)
1	Closed	5	>99	1:31:67:1
2	Open	5	88	4:43:37:4
3	Closed	30	>99	1:7:90:2
4	Open	30	>99	7:18:77:2

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), benzonitrile (0.25 mmol), NiCl₂·6H₂O (1 mol%) and **L4.1** (1 mol%) in methanol (1 mL) were stirred at 25 °C for the time indicated. ^aConversion and product distribution was determined by GC and GCMS against biphenyl as the internal standard and is the average of two independent runs.

S2.4.6 Evaluating homogeneity of catalyst with Hg drop test

Ammonia borane (8.6 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile (25 μ L, 0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μ mol) with **L4.1** (0.6 mg, 2.5 μ mol) and Hg (0.486 g, 2.42 mmol) in methanol (1 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

Table S2.6 Evaluating the effect of Hg on the transfer hydrogenation of benzonitrile.

				
Entry	Additive	Equivalents to Ni	Conversion ^a (%)	Prod. distr. ^a (A:B:C:D)
1	-	-	>99	1:7:90:2
2 ^b	Hg	1000	>99	1:trace:98:1
3 ^c	Hg	1000	>99	3:trace:94:3

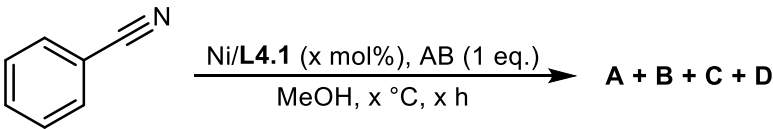
Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), benzonitrile (0.25 mmol), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1 mol%), **L4.1/L4.4** (1 mol%) and Hg (0 or 1000 eq. to Ni) in methanol (1 mL) were stirred at 25 °C for 30 minutes.

^a Conversion and product distribution were determined by GC against biphenyl as the internal standard and is the average of two independent runs. ^b **L4.1**. ^c **L4.4**.

S2.4.7 Evaluating maximum TON of NiCl₂·6H₂O/L4.1 pre-catalyst

Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile (50 μ L, 0.5 mmol) and then NiCl₂·6H₂O with **L4.1** in methanol (2 mL) followed. The reaction mixture was stirred at room temperature (or 50 °C) for 6 - 24 hours. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

Table S2.7 Evaluating the maximum TON of the transfer hydrogenation of benzonitrile.

						
Entry	Pre-cat load. (mol%)	Temperature (°C)	Time (hours)	Conversion ^a (%)	Prod. distr. ^a (A:B:C:D)	TON ^b
1	1	25	0.5	>99	1:7:90:2	100 (90)
2	0.025	25	6	>99	trace:20:67:13	4000 (2680)
3	0.01	50	24	69	4:trace:51:14	6900 (5100)

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), benzonitrile (0.5 mmol), NiCl₂·6H₂O (indicated mol%), **L4.1** (indicated mol%) in methanol (2 mL) were stirred at indicated temperature and time.

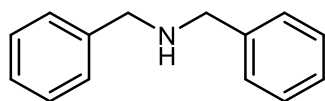
^a Conversion and product distribution was determined by GC against biphenyl as the internal standard and is the average of two independent runs. ^b Numbers in brackets indicate TON with regard to secondary amine yield.

S2.5 Evaluating transfer hydrogenation of benzonitrile derivatives

Ammonia borane (8.6 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile-derivative (0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with **L4.1** (0.6 mg, 2.5 μmol) in methanol (1 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

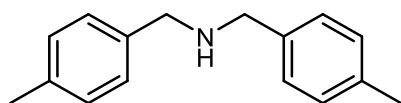
To obtain isolated products after the transfer hydrogenation reaction, the reaction mixture was quenched with 32% HCl (to decompose any residual AB and/or borane-adducts that might have formed) until bubbling ceased and sequentially neutralised with a saturated sodium carbonate (Na_2CO_3) solution. The aqueous layer was extracted with 3 x 5mL portions of DCM. The combined organic layers were dried over NaSO_4 . Filtration and subsequent removal of the solvent resulted in the crude product. Purification was done by column chromatography on silica employing an eluent as indicated below.

S2.5.1 Dibenzylamine



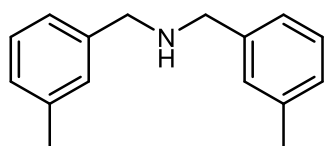
Isolated as a pale yellow oil (21.1 mg; 88%). Eluent: EtOAc/Petroleum ether (4:1). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.29 – 7.23 (m, 10H), 3.73 (s, 4H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 140.44, 129.07, 128.35, 127.10, 53.31. Analytical data is in accordance with that previously reported in literature.²

S2.5.2 Bis(4-methylbenzyl)amine



Isolated as a colourless oil (20.6 mg; 75%). Eluent: EtOAc/Petroleum ether (4:1). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.23 (d, J = 7.6 Hz, 4H), 7.15 (d, J = 7.5 Hz, 4H), 3.77 (s, 4H), 2.35 (s, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 137.45, 136.55, 129.15, 128.20, 52.94, 21.20. Analytical data is in accordance with that previously reported in literature.²⁻³

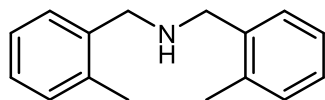
S2.5.3 Bis(3-methylbenzyl)amine



Isolated as a colourless oil (28.2 mg; 66%). Eluent: EtOAc/Petroleum ether (4:1). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.25 – 7.21 (m, 2H), 7.18 – 7.14 (m, 4H), 7.08 (d, J = 7.4 Hz, 2H), 3.79 (s, 4H), 2.37 (s, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm):

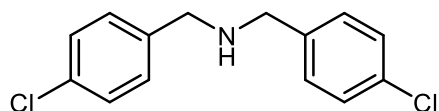
140.37, 138.09, 129.02, 128.37, 127.75, 125.27, 53.36, 21.50. Analytical data is in accordance with that previously reported in literature.²

S2.5.4 Bis(2-methylbenzyl)amine



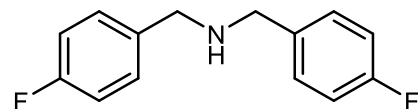
Isolated as a colourless oil (18.2 mg; 40%). Eluent: EtOAc/Petroleum ether (4:1). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.36 – 7.32 (d, 2H), 7.19 – 7.14 (m, 6H), 3.84 (s, 4H), 2.35 (s, 6H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 138.47, 136.62, 130.39, 128.60, 127.11, 125.99, 51.64, 19.07. Analytical data is in accordance with that previously reported in literature.⁴

S2.5.5 Bis(4-chlorobenzyl)amine



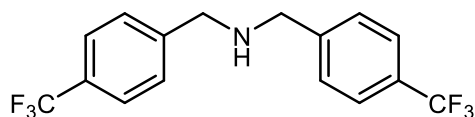
Isolated as colourless oil (30.6 mg; 92%). Eluent: EtOAc/Petroleum ether (4:1). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.29 (dd, J = 9.5 Hz, 8H), 3.75 (s, 4H). ¹³C NMR (151 MHz, (CD₃)₂CO) δ (ppm): 138.71, 132.80, 129.54, 128.63, 52.43. Analytical data is in accordance with that previously reported in literature.²⁻³

S2.5.6 Bis(4-fluorobenzyl)amine



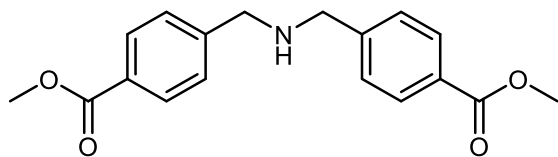
Isolated as colourless oil (25.7 mg; 90%). Eluent: MeOH. ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.35 – 7.29 (m, 4H), 7.06 – 7.00 (m, 4H), 3.79 (s, 4H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 162.80, 161.18, 135.97, 135.95, 129.61, 129.56, 115.21, 115.07, 52.37. Analytical data is in accordance with that previously reported in literature.³

S2.5.7 Bis(4-trifluoromethylbenzyl)amine



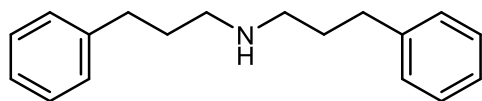
Isolated as pale yellow oil (35.5 mg; 86%). Eluent: MeOH. ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.62 (d, J = 8.1 Hz, 4H), 7.50 (d, J = 8.0 Hz, 4H), 3.90 (s, 4H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 144.15, 128.26, 125.35 (q, J = 3.8 Hz), 125.12, 123.32, 52.63. Analytical data is in accordance with that previously reported in literature.³

S2.5.8 Dimethyl 4,4'-(azanediylbis(methylene))dibenzoate



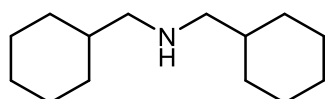
Isolated as pale yellow crystals (32.7 mg; 84%). Eluent: EtOAc/Petroleum ether (4:1). ^1H NMR (600 MHz, CDCl_3) δ (ppm):. ^{13}C NMR (151 MHz, $(\text{CD}_3)_2\text{CO}$) δ (ppm):. Analytical data is in accordance with that previously reported in literature.

S2.5.9 Bis(3-phenylpropyl)amine



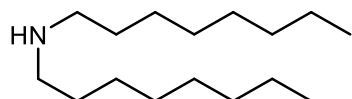
Isolated as a pale yellow oil (24.1 mg; 72%). Eluent = EtOAc/Petroleum ether (4:1). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.28 (d, J = 7.8 Hz, 4H), 7.18 (t, J = 8.1 Hz, 6H), 2.64 – 2.58 (m, 4H), 2.49 – 2.43 (m, 4H), 1.79 – 1.69 (m, 4H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 142.63, 128.52, 128.42, 125.81, 53.77, 33.94, 29.06. Analytical data is in accordance with that previously reported in literature.

S2.5.10 Dicyclohexylamine



Isolated as colourless oil (20.4 mg; 78%). Eluent: EtOAc/Petroleum ether (4:1). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 2.47 (d, J = 6.8 Hz, 4H), 1.80 – 1.62 (m, 10H), 1.53 (ddd, J = 11.1, 7.5, 3.9 Hz, 2H), 1.28 – 1.10 (m, 6H), 0.91 (qd, J = 12.4, 3.2 Hz, 4H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 56.48, 37.32, 31.56, 26.73, 26.12. Analytical data is in accordance with that previously reported in literature.⁵

S2.5.11 Dioctylamine



Isolated as a colourless oil (19.2 mg; 63%). Eluent = DCM/MeOH (1:1). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 2.40 – 2.36 (m, 4H), 1.32 – 1.23 (m, 10H), 0.88 (t, J = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 54.41, 32.03, 29.77, 29.49, 27.85, 22.83, 14.26. Analytical data is in accordance with that previously reported in literature.⁶

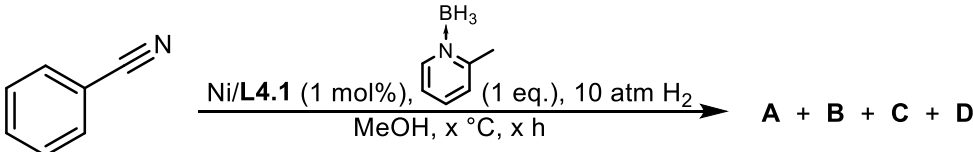
S2.6 Experimental insights into the transfer hydrogenation mechanism of benzonitrile

All reactions pertaining to the elucidation of the mechanism were conducted in a 5 mm Wilmad® high-pressure/vacuum (HPV) J. Young NMR tube.

S2.6.1 Direct hydrogenation of benzonitrile with NiCl₂·6H₂O/L4.1 and H₂

In a 50 mL steel Parr reactor (or 5 mL screw-capped mini-reactor), NiCl₂·6H₂O (1.2 mg, 5 μmol) with **L4.1** (1.2 mg, 5 μmol), α-picoline borane (APB, 53.4 mg, 0.5 mmol) and styrene (0.5 mmol) was dissolved in MeOH (2 mL). The reactor was flushed three times with H₂ and then pressurised with 10 atm H₂. After the indicated reaction time at the indicated reaction temperature, the mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion. The reaction was done in duplicate.

Table S 2.8 Evaluation of H₂ pressure and α-picoline borane on the transfer hydrogenation of benzonitrile.

						
Entry	α-picoline borane (eq.)	pH ₂ (atm)	Temp. (°C)	Time (h)	Conv. ^a (%)	Prod. distr. ^a (A:B:C:D)
1	-	5	25	0.5	0	0
2	-	5	25	4	0	0
3	-	10	60	6	0	0
4	1	-	25	0.5	<1%	nd
5	1	-	50	1	<1%	nd
6	1	10	25	0.5	<1%	nd
7	1	10	60	6	80%	0:31:48:1
8	1	-	60	6	31%	0:4:26:1

Reaction conditions: Benzonitrile (0.5 mmol), NiCl₂·6H₂O (1 mol%), **L4.2** (1 mol%) and α-picoline borane (0.5 mmol) in MeOH (2 mL) were stirred at indicated reaction time and temperature at specified pH₂. ^a Conversion and product distribution were determined by GC against biphenyl as the internal standard and is the average of two independent runs.

S2.6.2 Deuterium labelling studies

Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of benzonitrile (0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with **L4.1** (0.6 mg, 2.5 μmol) in $\text{CH}_3\text{OH}/\text{CD}_3\text{OD}$ (0.8 mL) followed. The reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed with ^1H NMR spectroscopy.

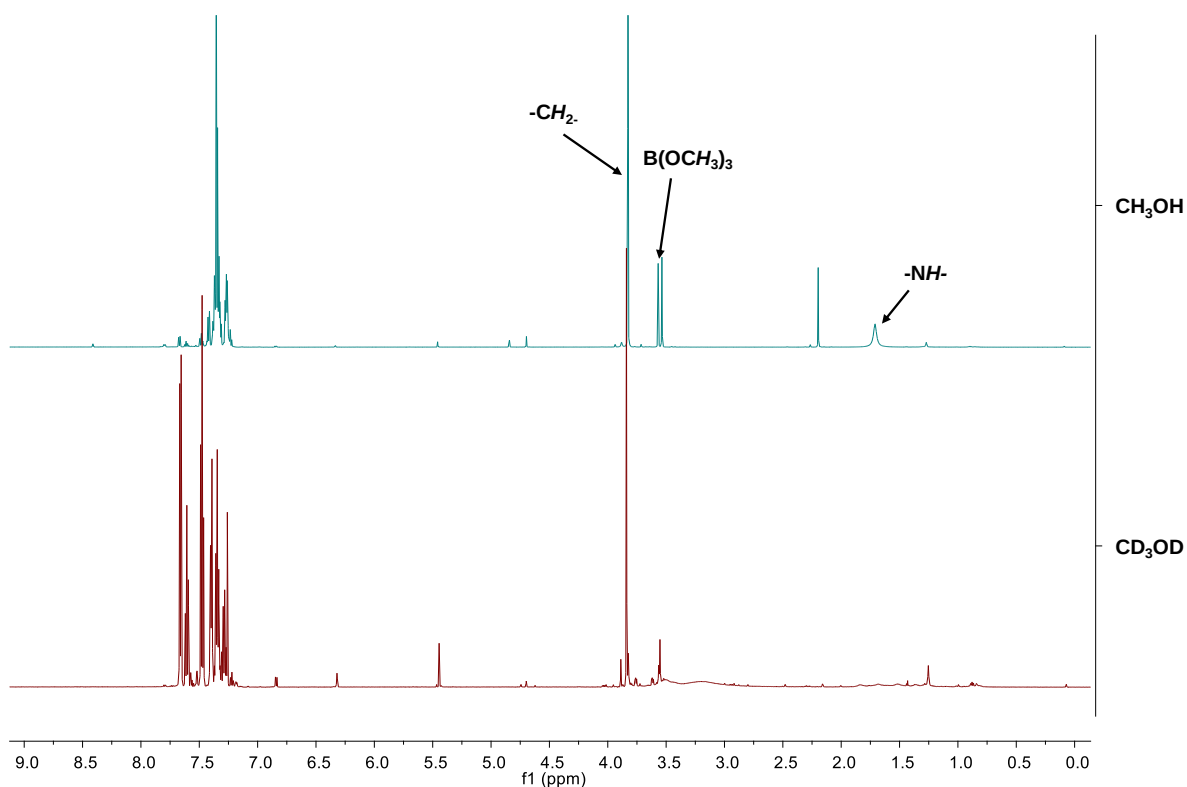


Figure S2.1 Deuterium labelling study depicting the ^1H NMR (600 MHz, CDCl_3) spectra of benzonitrile transfer hydrogenation reaction mixtures which were conducted in i) CH_3OH and ii) CD_3OD .

S2.7 Dehydrogenation of ammonia borane

Ammonia borane (7.7 mg, 0.25 mmol, 100 eq. to catalyst) was added to a 20 mL test tube connected to a burette filled with silicon oil (Figure S). After the addition of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with **L4.1** (0.6 mg, 2.5 μmol) in CH_3OH (1 mL) through a septum, the solution turned a dark yellow colour and bubbling started. The volume of H_2 formed was measured with the burette from 0 - 15 minutes. The same reaction was conducted in a J. Young NMR tube and subsequently analysed with ^1H NMR spectroscopy, which provided evidence of H_2 gas formation at 4.5 ppm.⁷

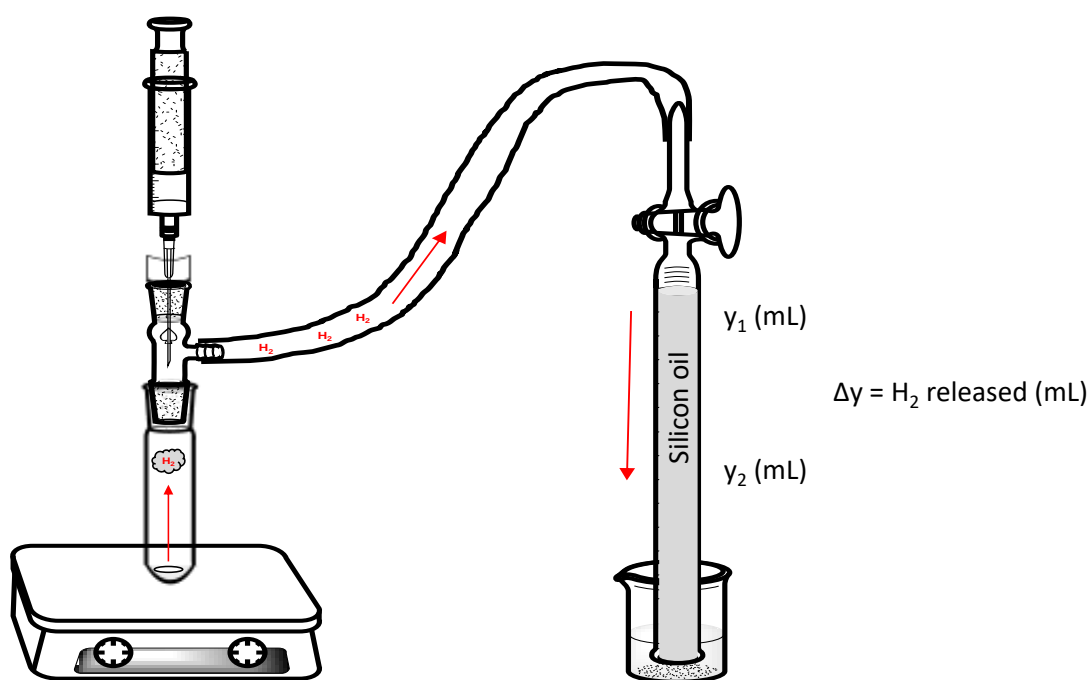
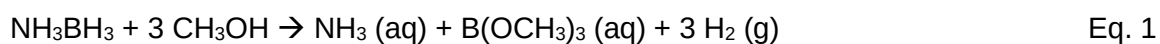


Figure S2.2 Experimental setup to determine the amount of H_2 generated during the dehydrogenation of AB.



$$pV = nRT \quad \text{Eq. 2}$$

p = atm pressure on the day - vapour pressure of silicon oil

$$= 761 \text{ mmHg} - 5 \text{ mmHg} = 756 \text{ mmHg}$$

$$n = \frac{pV}{RT} = \frac{100792 \times 18 \times 10^{-6}}{8.314 \times 295} = 0.7397 \text{ mmol } \text{H}_2 \text{ generated}$$

$$\frac{0.7397}{0.7500} \times 3 = 2.959 \text{ equivalents of } \text{H}_2 \text{ generated}$$

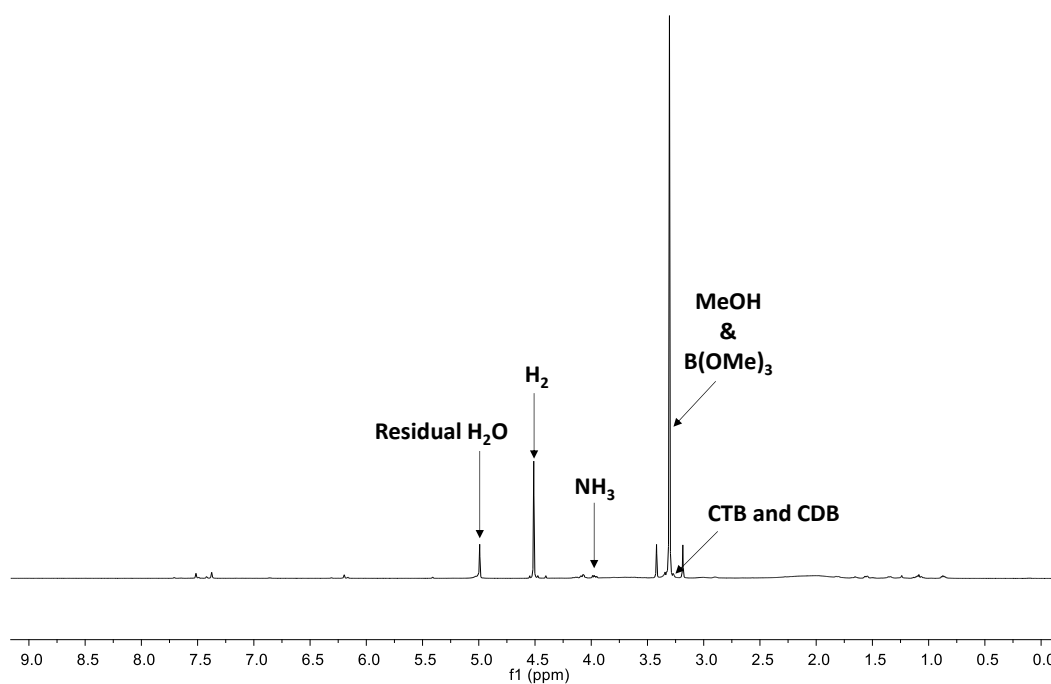


Figure S2.3 ^1H NMR (600 MHz, CD_3OD) spectrum of reaction mixture after AB (0.25 mmol) dehydrogenation with $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1 mol%) and L4.1 (1 mol%) in MeOH after 50 minutes at 25 °C. Chemical shifts originating from protons on MeOH, H_2 gas, $\text{B}(\text{OMe})_3$, CTB and CDB are illustrated. Due to deuterium exchange between NH_3 and CD_3OD , only trace amounts of NH_3 were detected.⁸

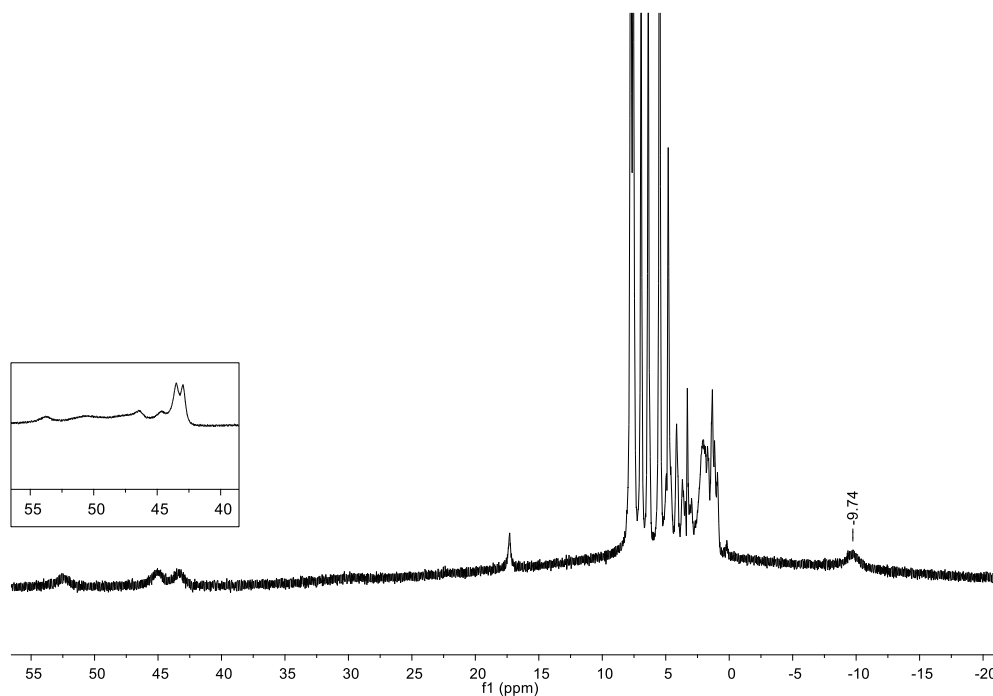


Figure S2.4 ^1H NMR (600 MHz, CD_3OD) spectrum illustrating the presence of a Ni-H species after 10 minutes at 25 °C. Inset shows region of ^1H NMR from $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ /L1 (in MeOH) indicating paramagnetism due to signal broadening.

S2.8 ICP-AES and ICP-MS analysis of NiCl₂·6H₂O salt**Table S2.9** Concentration (in ppb) and relative concentration of metal relative to Ni.

Element	Concentration (ppb) (µg/kg)	Relative to Ni (element/Ni)
Al	BDL (<5570)	-
B	3400	1.12E-05
Ba	BDL (<1860)	-
Ca	BDL (<18570)	-
Co	22800	7.54E-05
Cr	7600	2.51E-05
Cu	BDL (<1860)	-
Fe	6400	2.12E-05
K	BDL (<18570)	-
Mg	BDL (<18570)	-
Mn	BDL (<1860)	-
Na	908700	3.00E-03
Ni	302451000	1.00
P	150900	4.99E-04
Pb	28400	9.39E-05
Si	BDL (<18570)	-
Sr	BDL (<930)	-
Zn	BDL (<1860)	-
Ru*	BDL (<1.41)	-
Rh*	232.7	7.69E-07
Re*	BDL (<0.7)	-
Os*	BDL (<11.33)	-
Ir*	436	1.44E-06
Pt*	381	1.26E-06
Au*	207	6.84E-07

* Analysed with ICP-MS. BDL = below detection limit

S2.9 Analytical data of ligands L4.1, L4.2 and secondary amine products

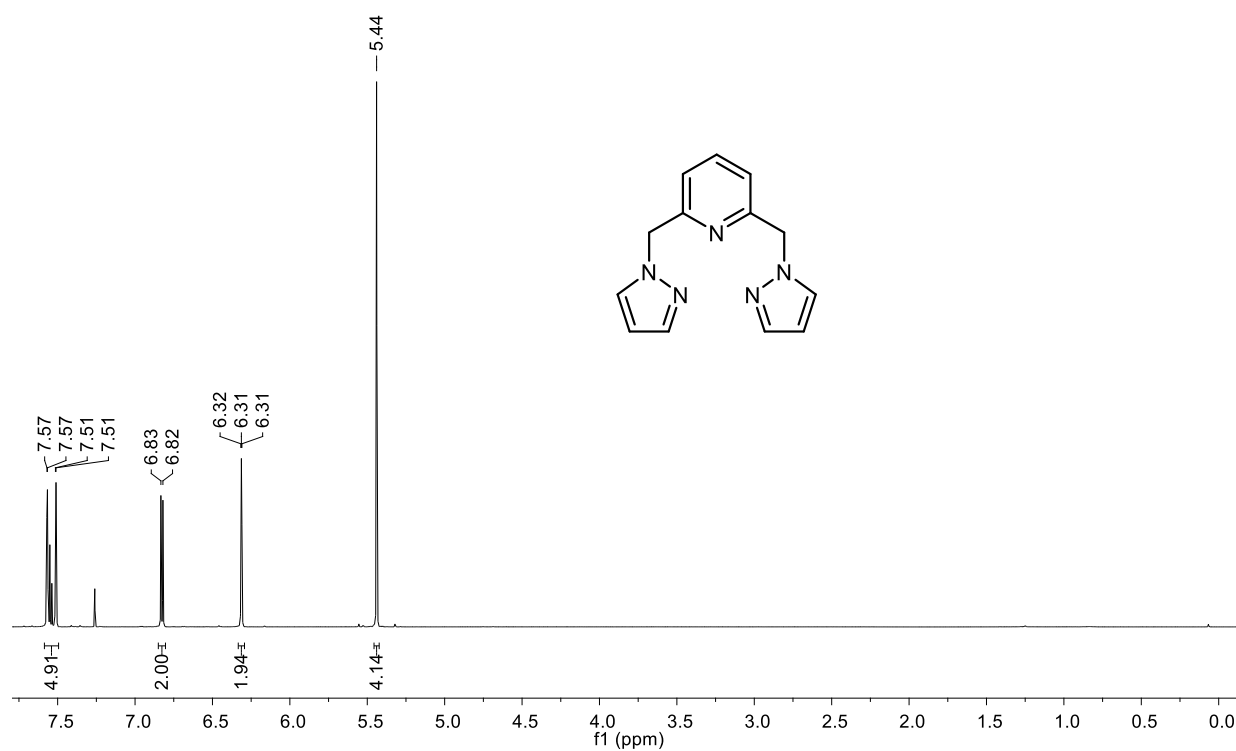


Figure S2.5 ¹H NMR (600 MHz, CDCl₃) spectrum of ligand **L4.1**.

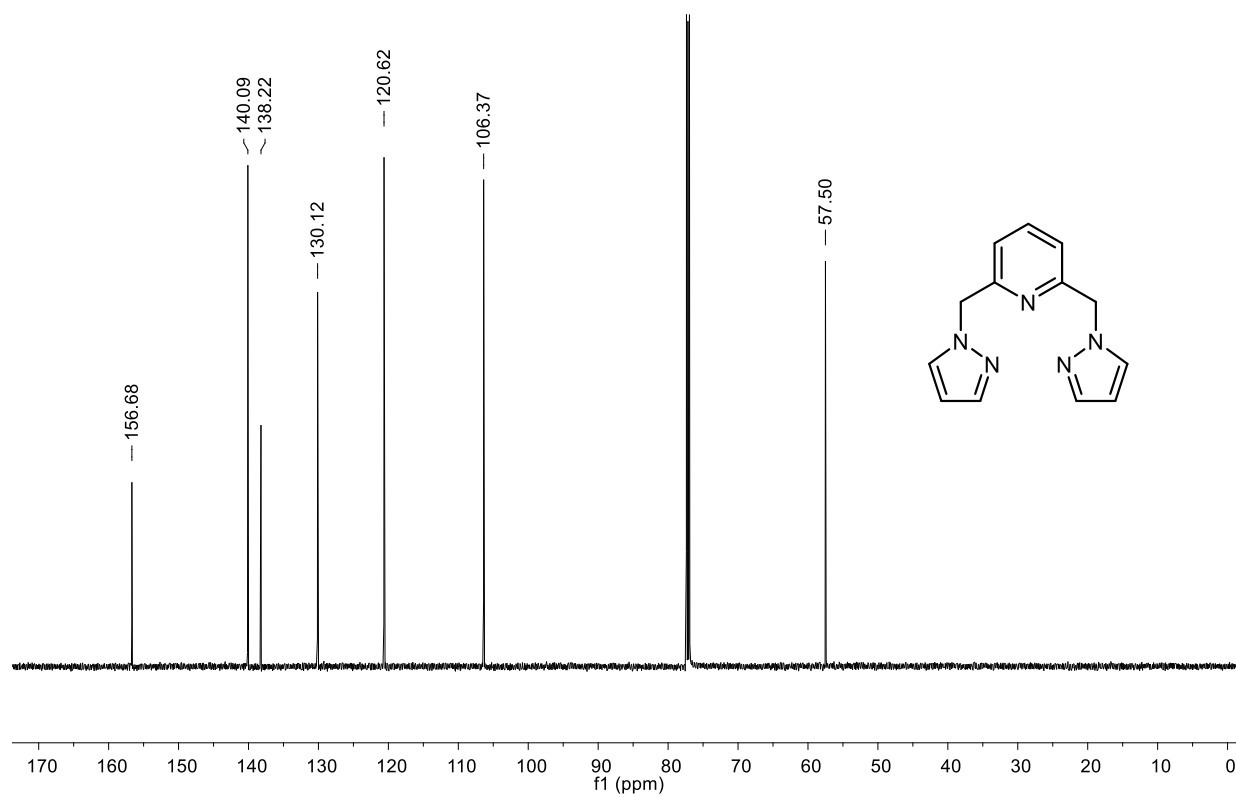


Figure S2.6 ¹³C NMR (151 MHz, CDCl₃) spectrum of ligand **L4.1**.

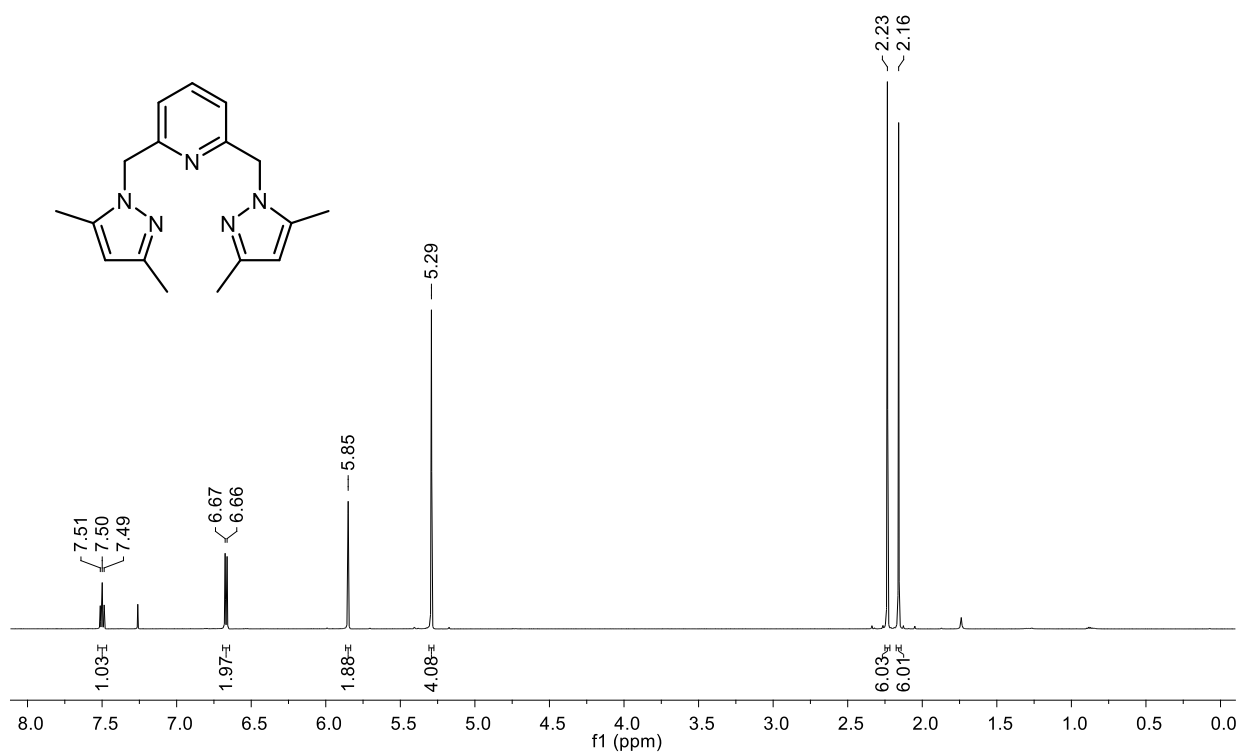


Figure S2.7 ¹H NMR (600 MHz, CDCl₃) spectrum of ligand **L4.2**.

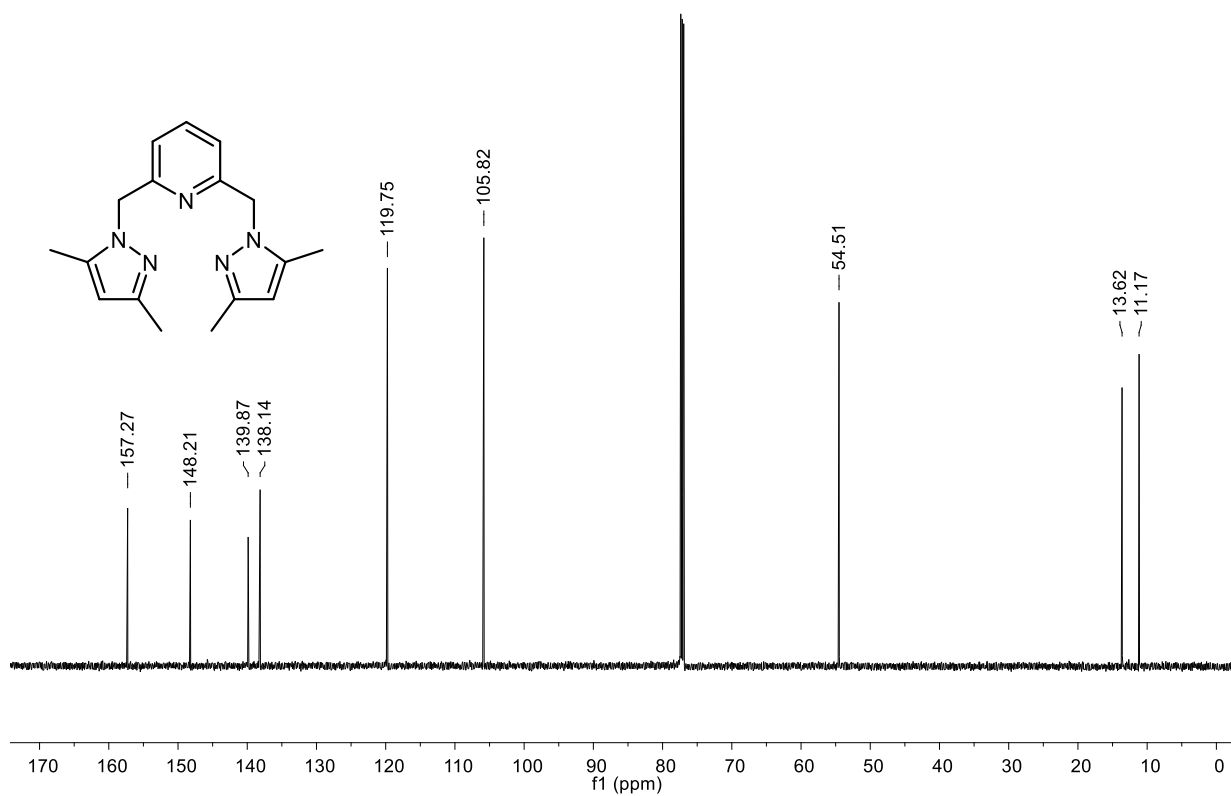


Figure S2.8 ¹³C NMR (151 MHz, CDCl₃) spectrum of ligand **L4.2**.

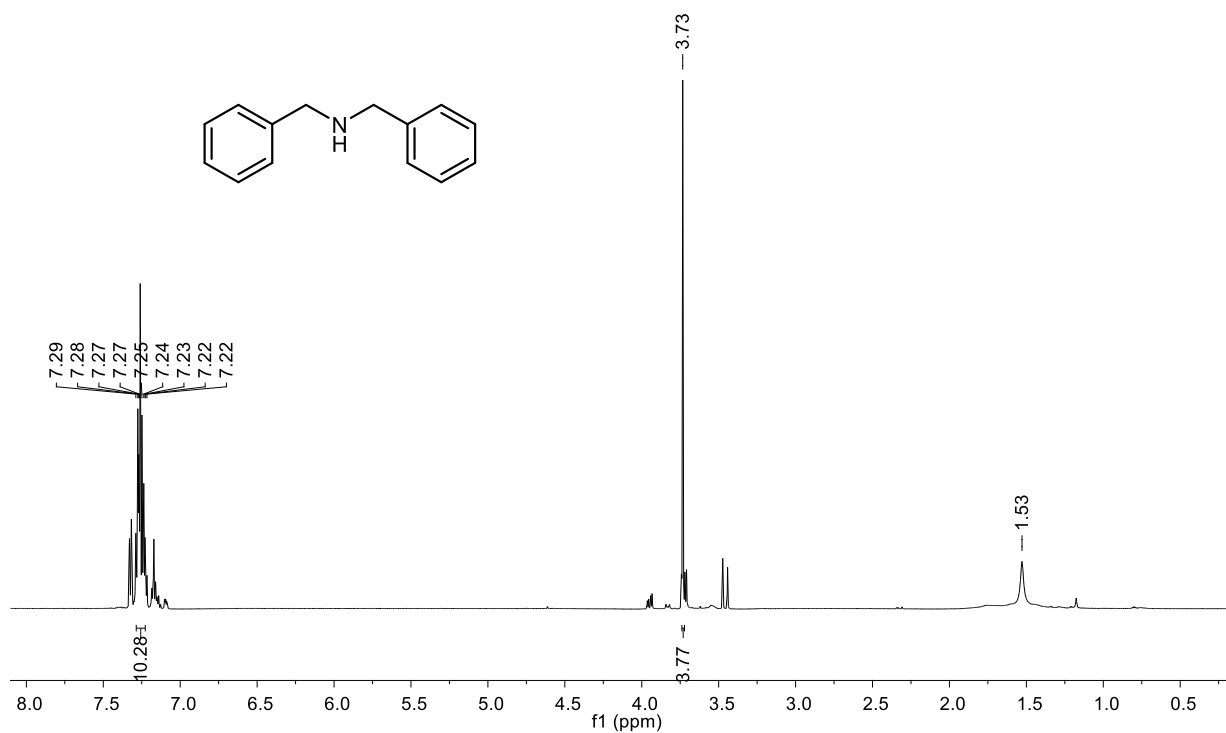


Figure S2.9 ¹H NMR (600 MHz, CDCl₃) spectrum of dibenzylamine.

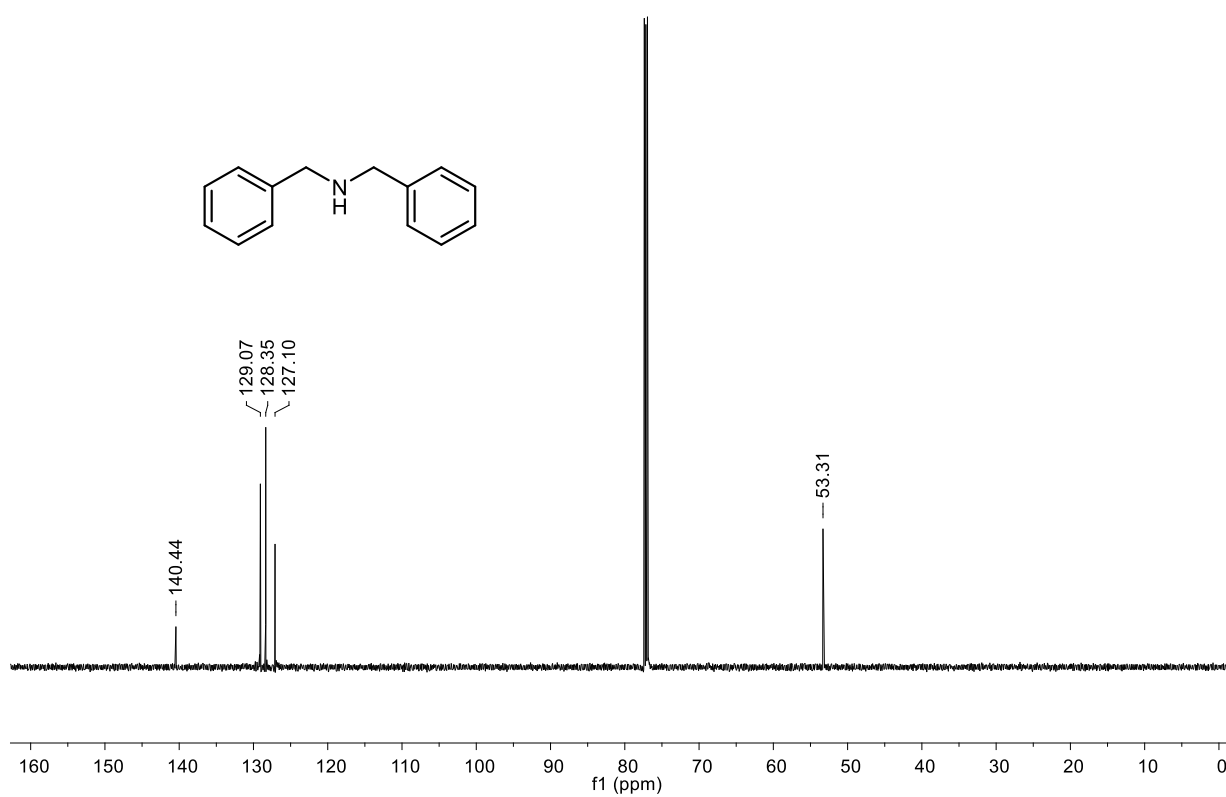


Figure S2.10 ¹³C NMR (151 MHz, CDCl₃) spectrum of dibenzylamine.

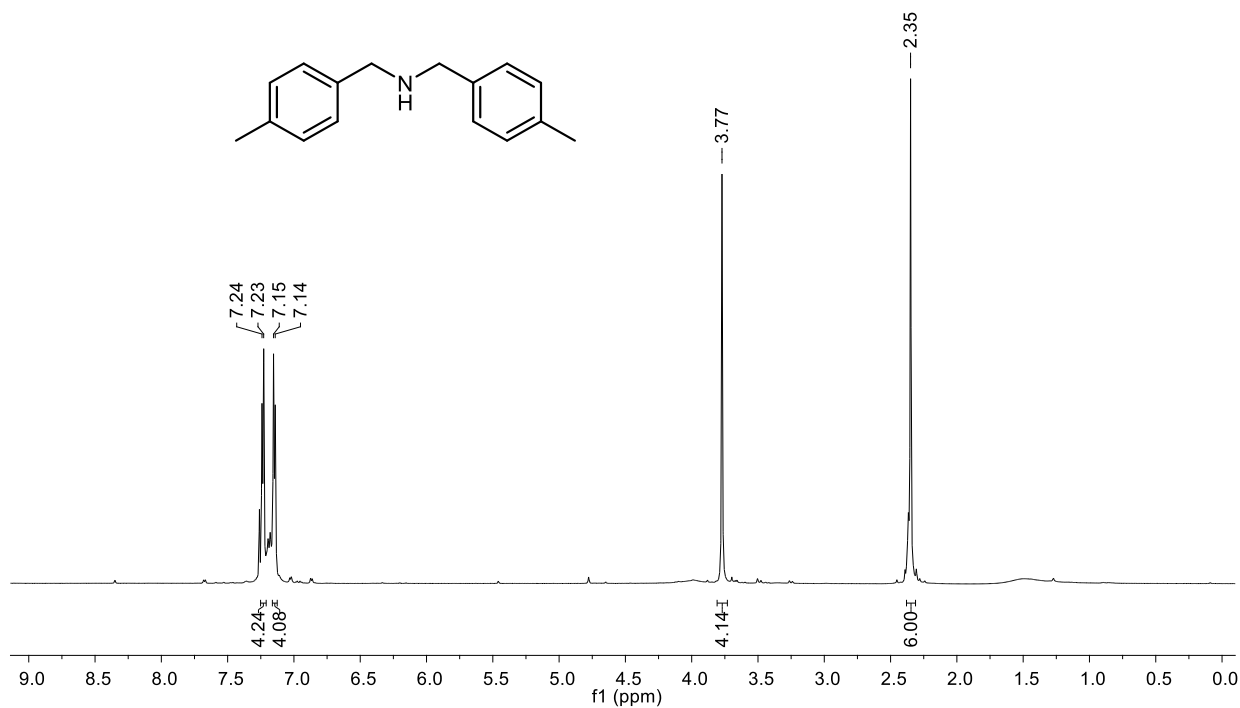


Figure S2.11 ¹H NMR (600 MHz, CDCl₃) spectrum of bis(4-methylbenzyl)amine.

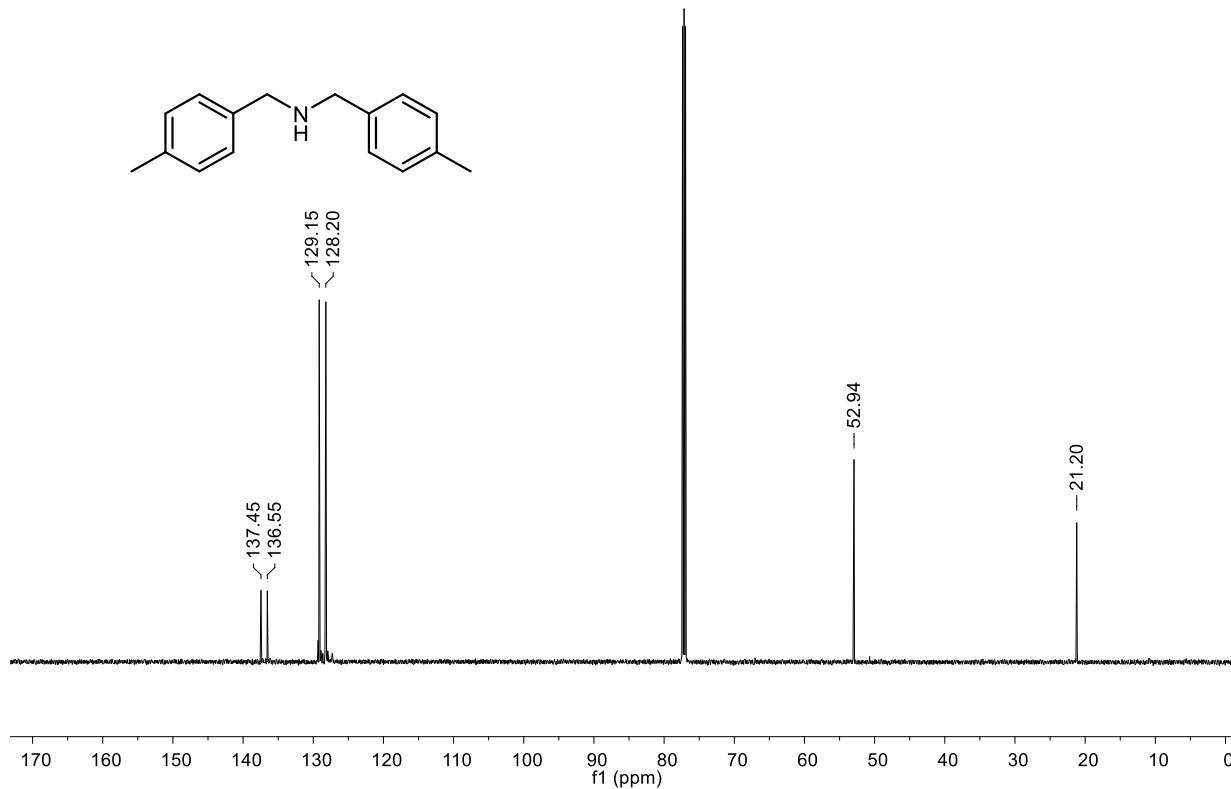


Figure S2.12 ¹³C NMR (151 MHz, CDCl₃) spectrum of bis(4-methylbenzyl)amine.

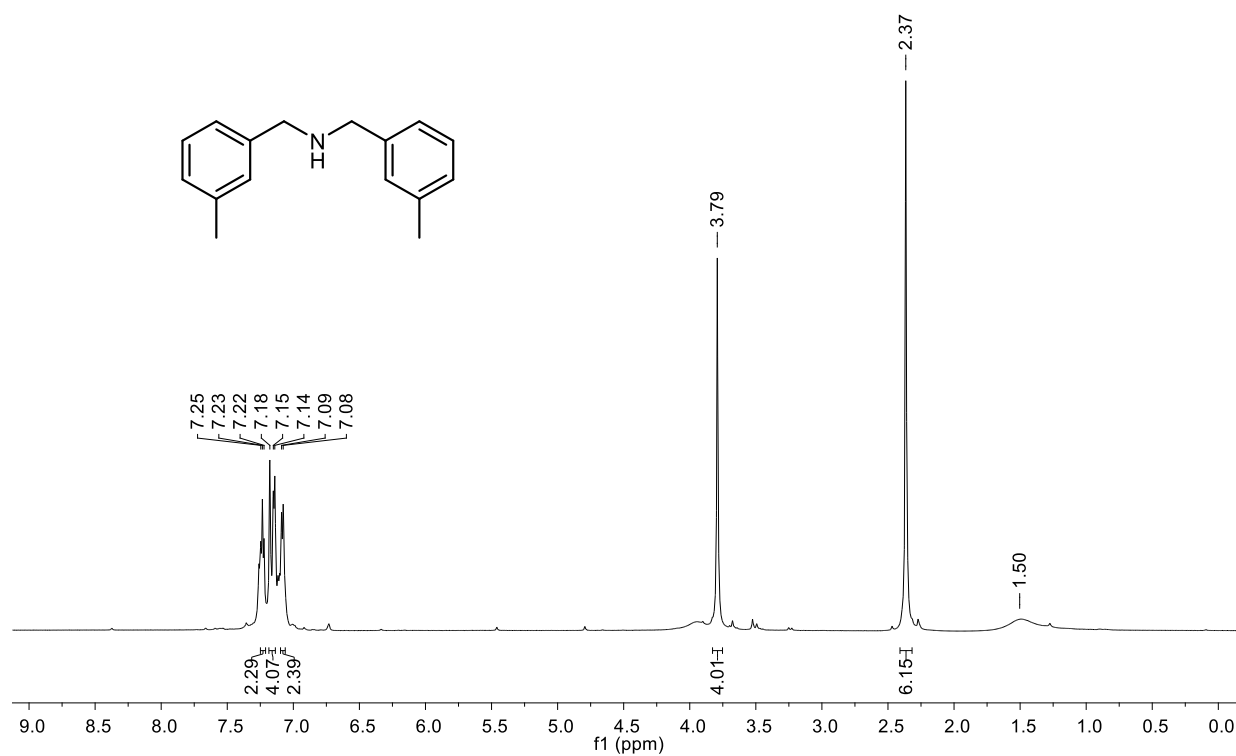


Figure S2.13 ¹H NMR (600 MHz, CDCl₃) spectrum of bis(3-methylbenzyl)amine.

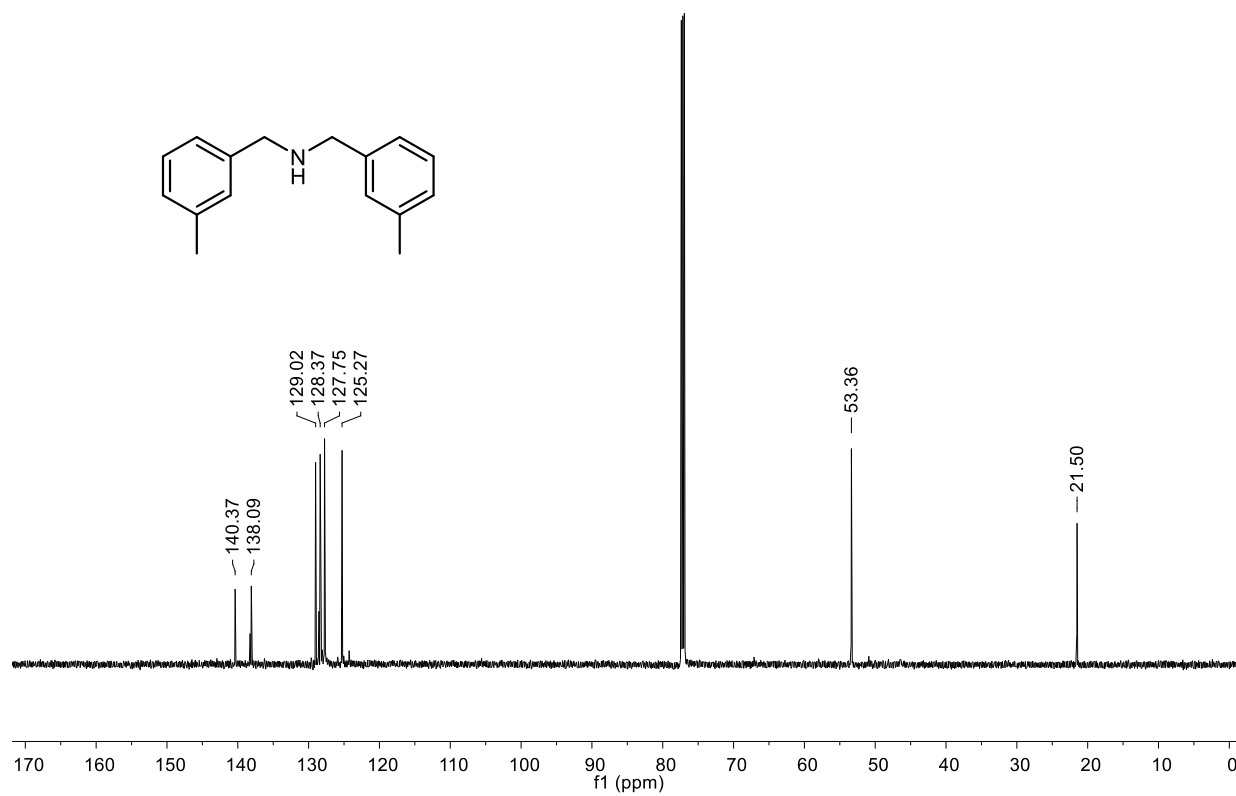


Figure S2.14 ¹³C NMR (151 MHz, CDCl₃) spectrum of bis(3-methylbenzyl)amine.

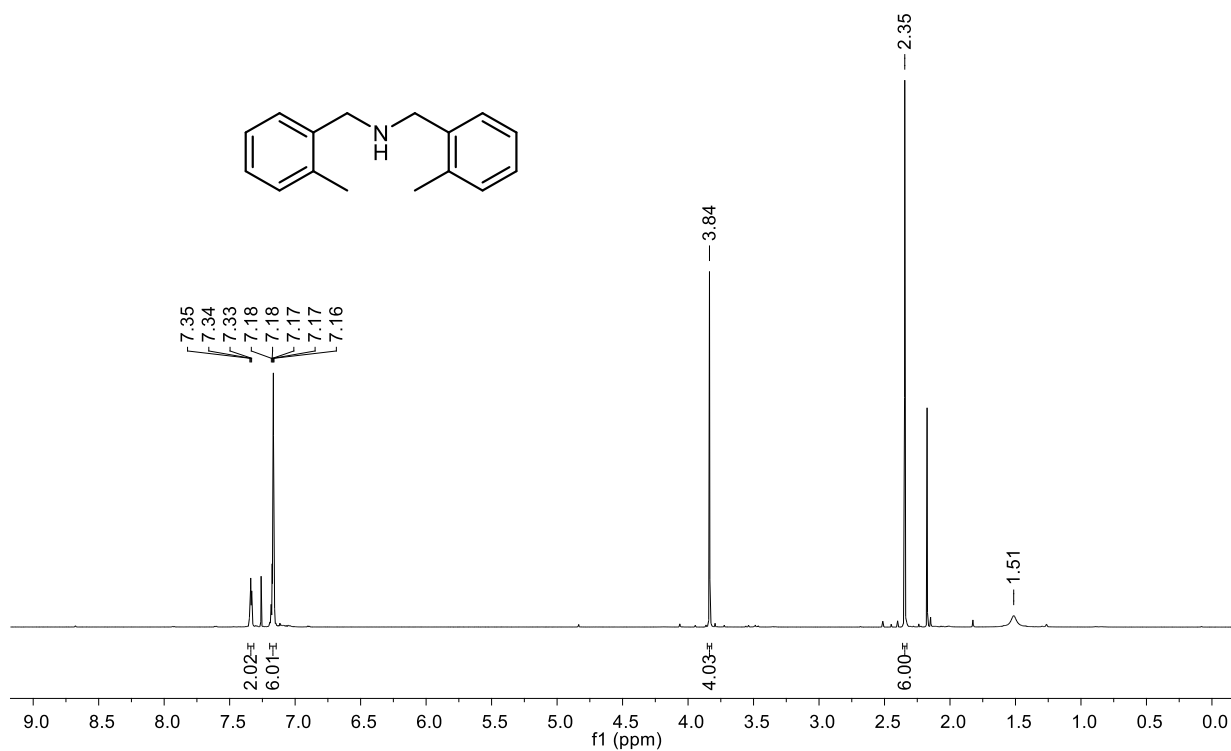


Figure S2.15 ¹H NMR (600 MHz, CDCl₃) spectrum of bis(2-methylbenzyl)amine.

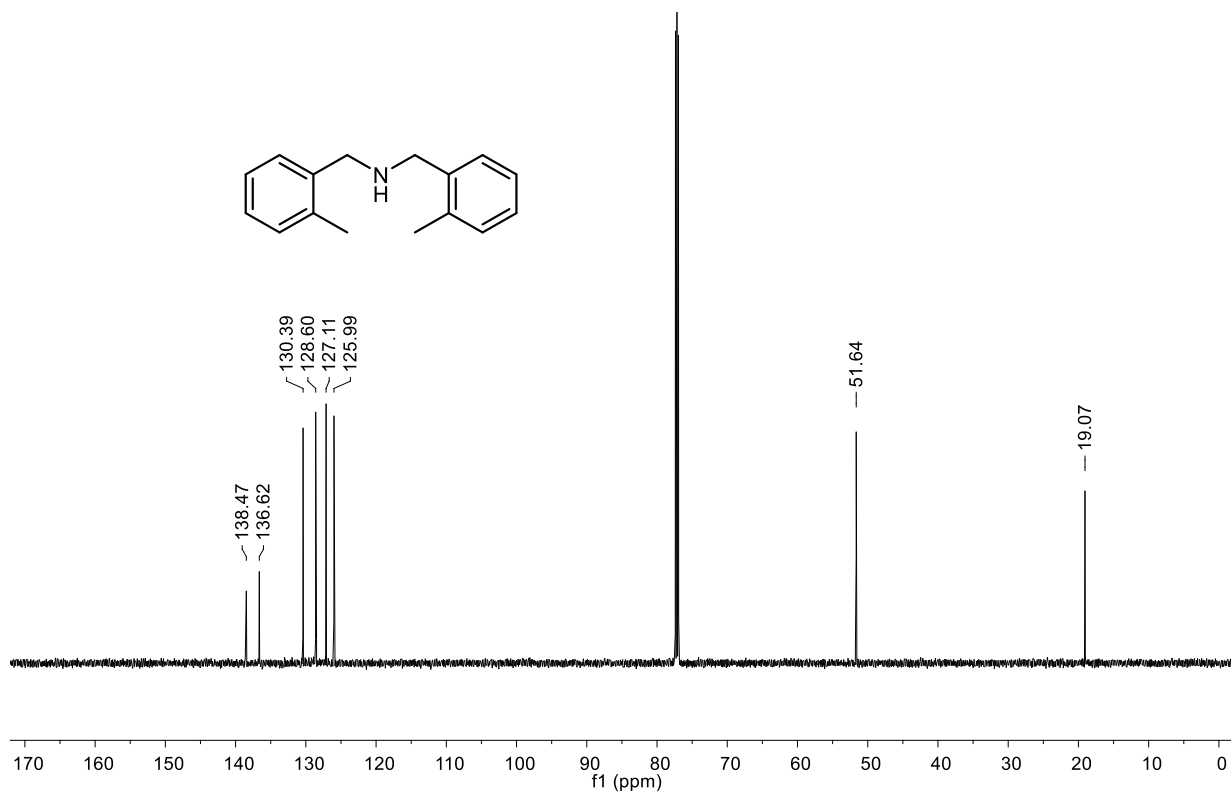


Figure S2.16 ¹³C NMR (151 MHz, CDCl₃) spectrum of bis(2-methylbenzyl)amine.

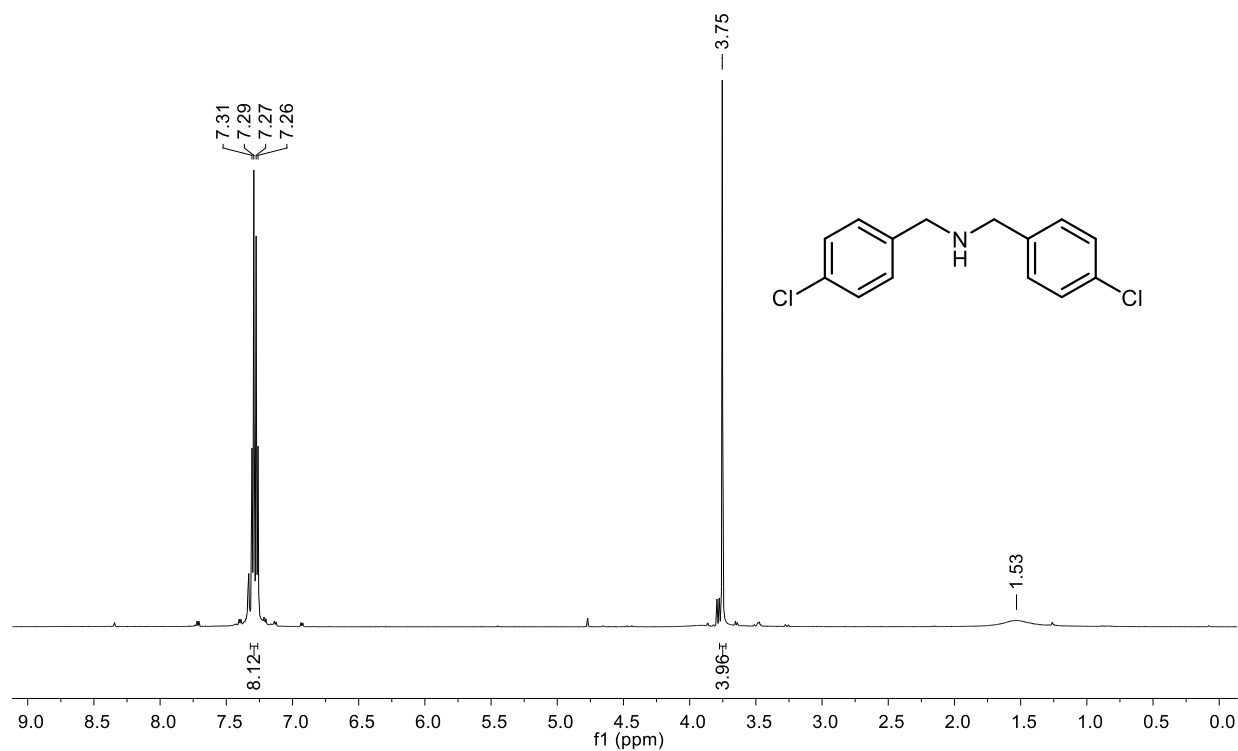


Figure S2.17 ¹H NMR (600 MHz, CDCl₃) spectrum of bis(2-chlorobenzyl)amine.

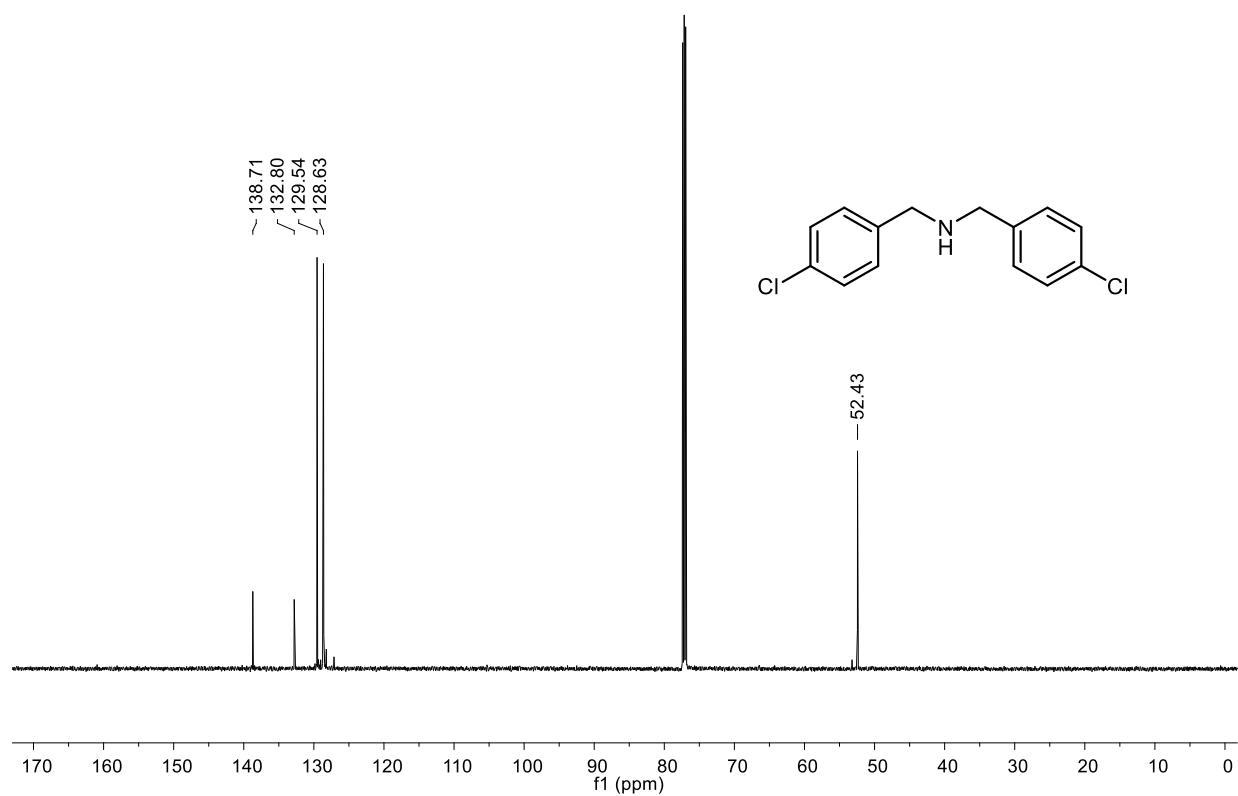


Figure S2.18 ¹³C NMR (151 MHz, CDCl₃) spectrum of bis(2-chlorobenzyl)amine.

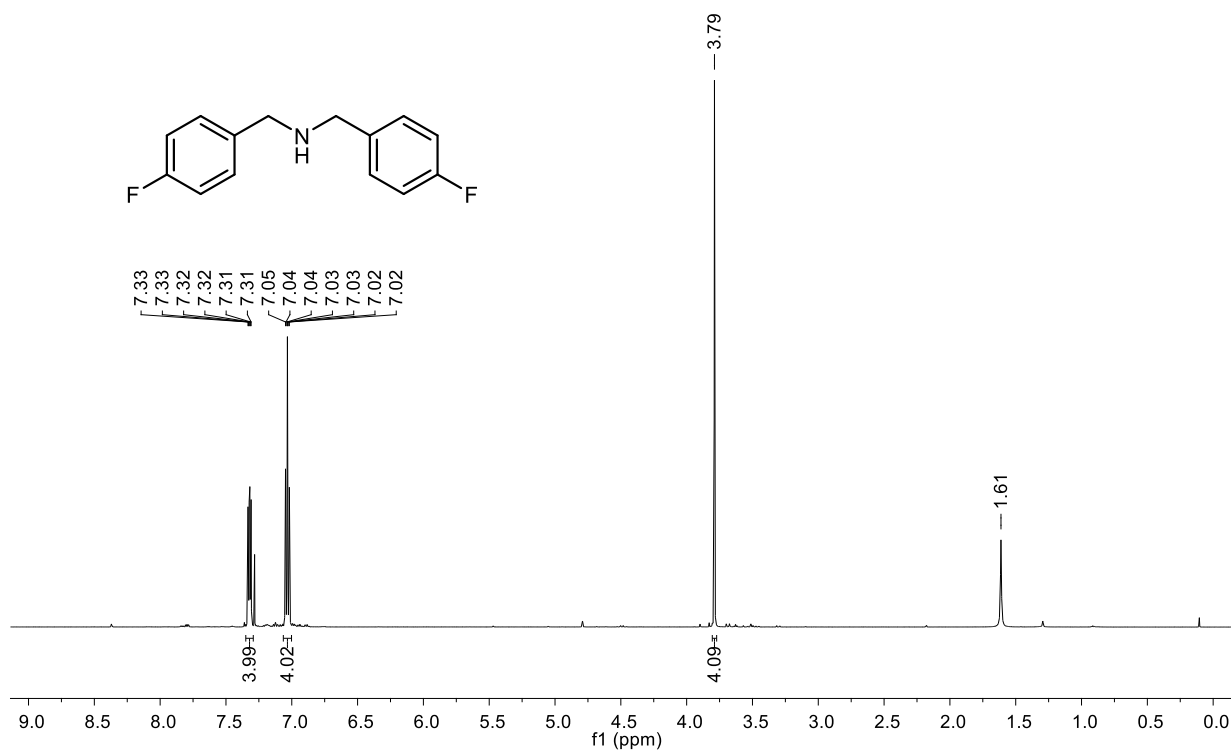


Figure S2.19 ¹H NMR (600 MHz, CDCl₃) spectrum of bis(2-fluorobenzyl)amine.

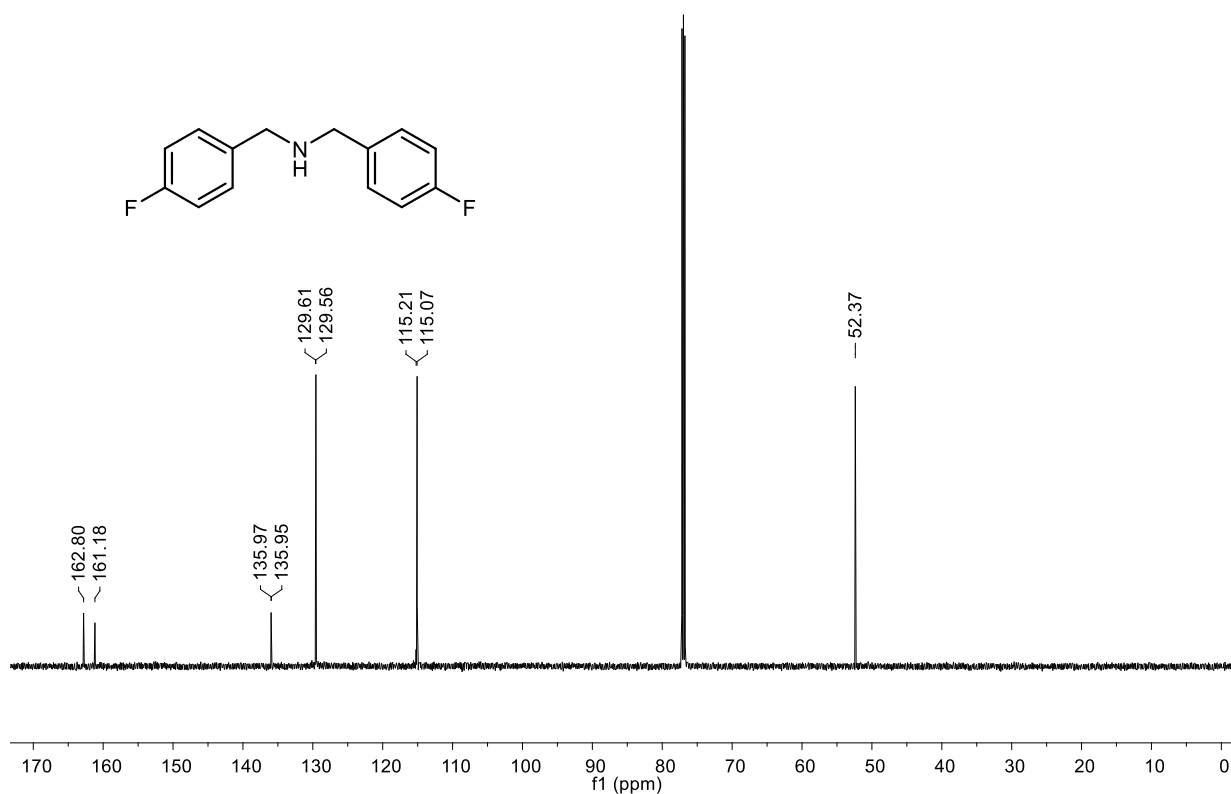


Figure S2.20 ¹³C NMR (151 MHz, CDCl₃) spectrum of bis(2-fluorobenzyl)amine.

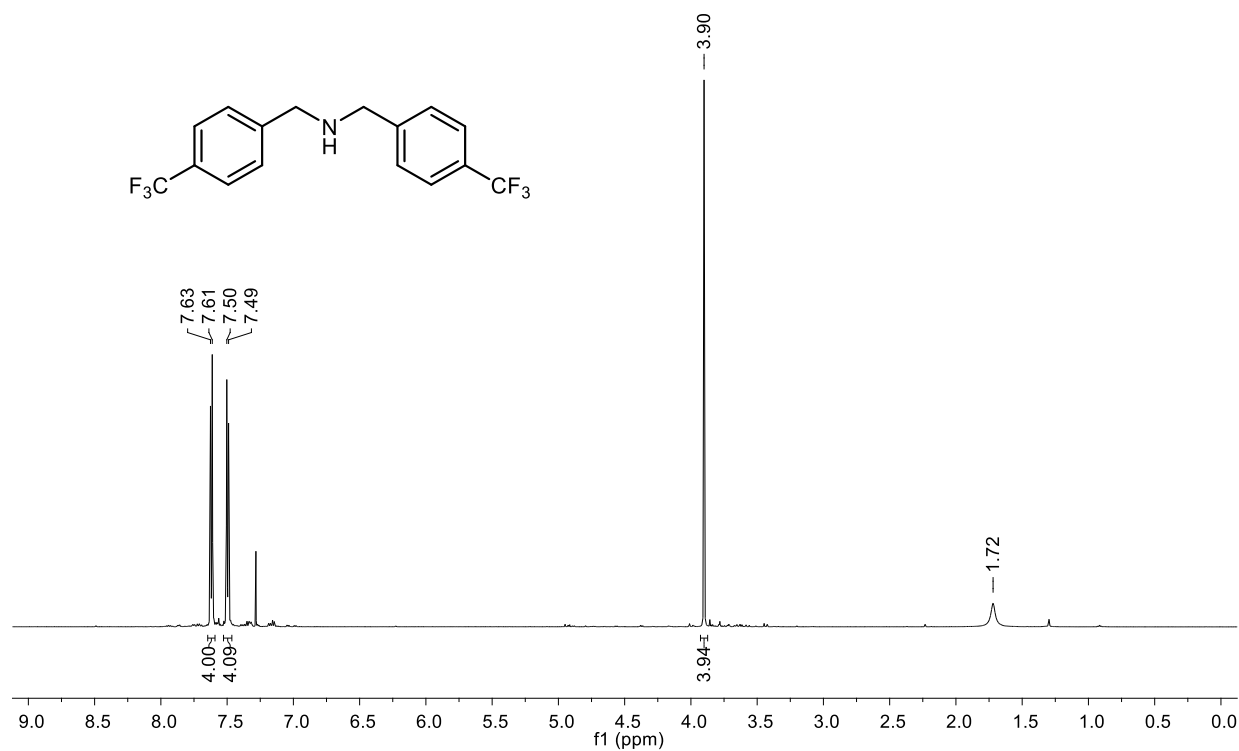


Figure S2.21 ¹H NMR (600 MHz, CDCl₃) spectrum of bis(4-(trifluoromethyl)benzyl)amine.

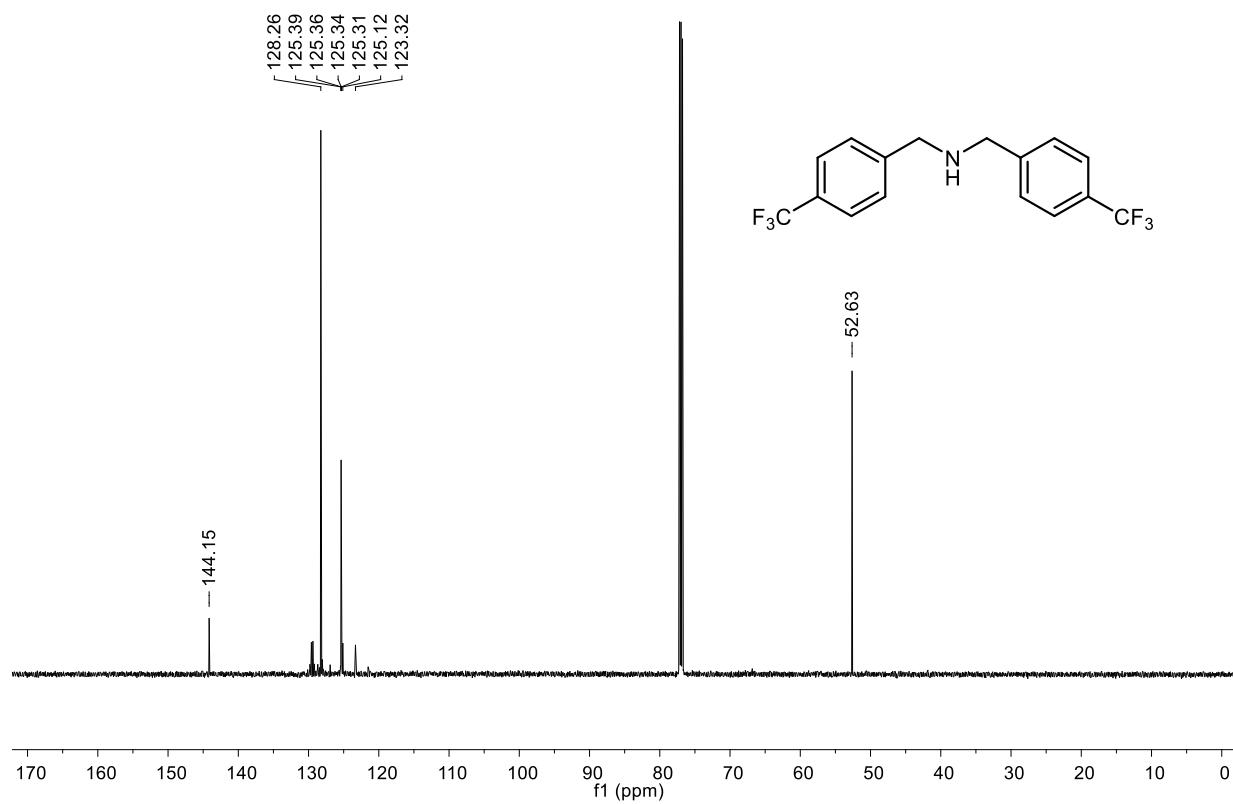


Figure S2.22 ¹³C NMR (151 MHz, CDCl₃) spectrum of bis(4-(trifluoromethyl)benzyl)amine.

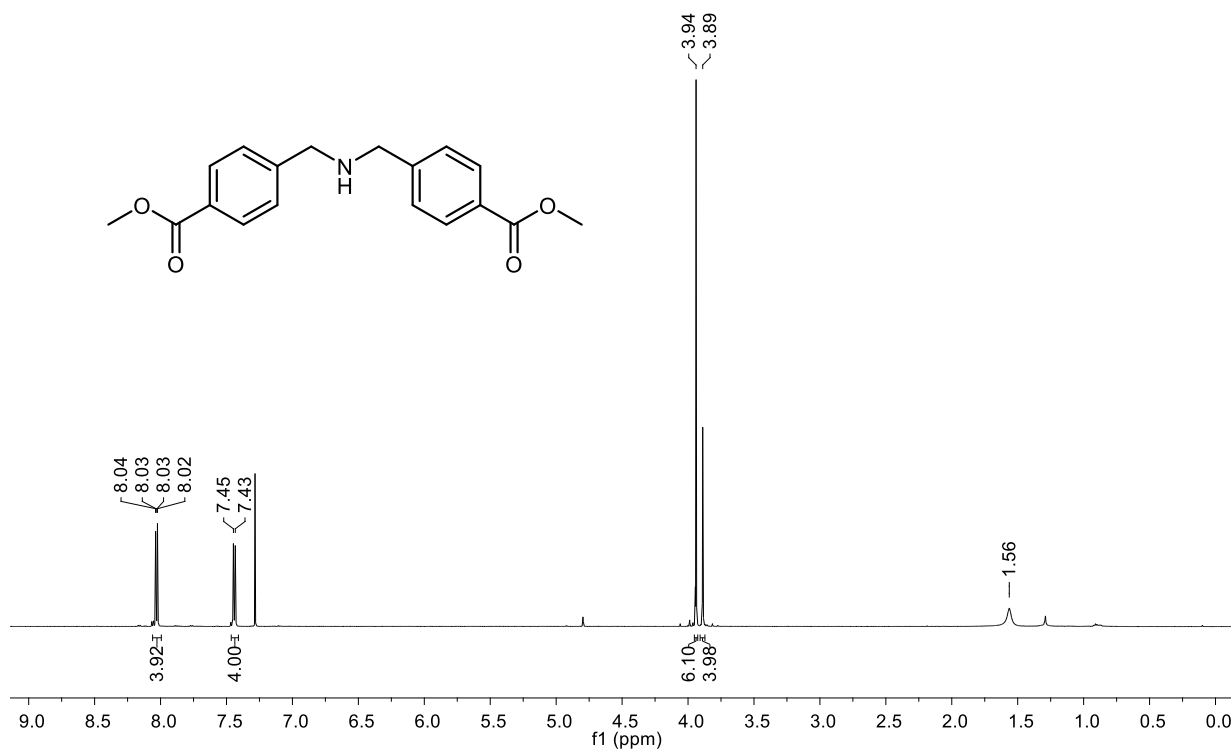


Figure S2.23 ¹H NMR (600 MHz, CDCl₃) spectrum of dimethyl 4,4'-(azanediylbis(methylene))dibenzoate.

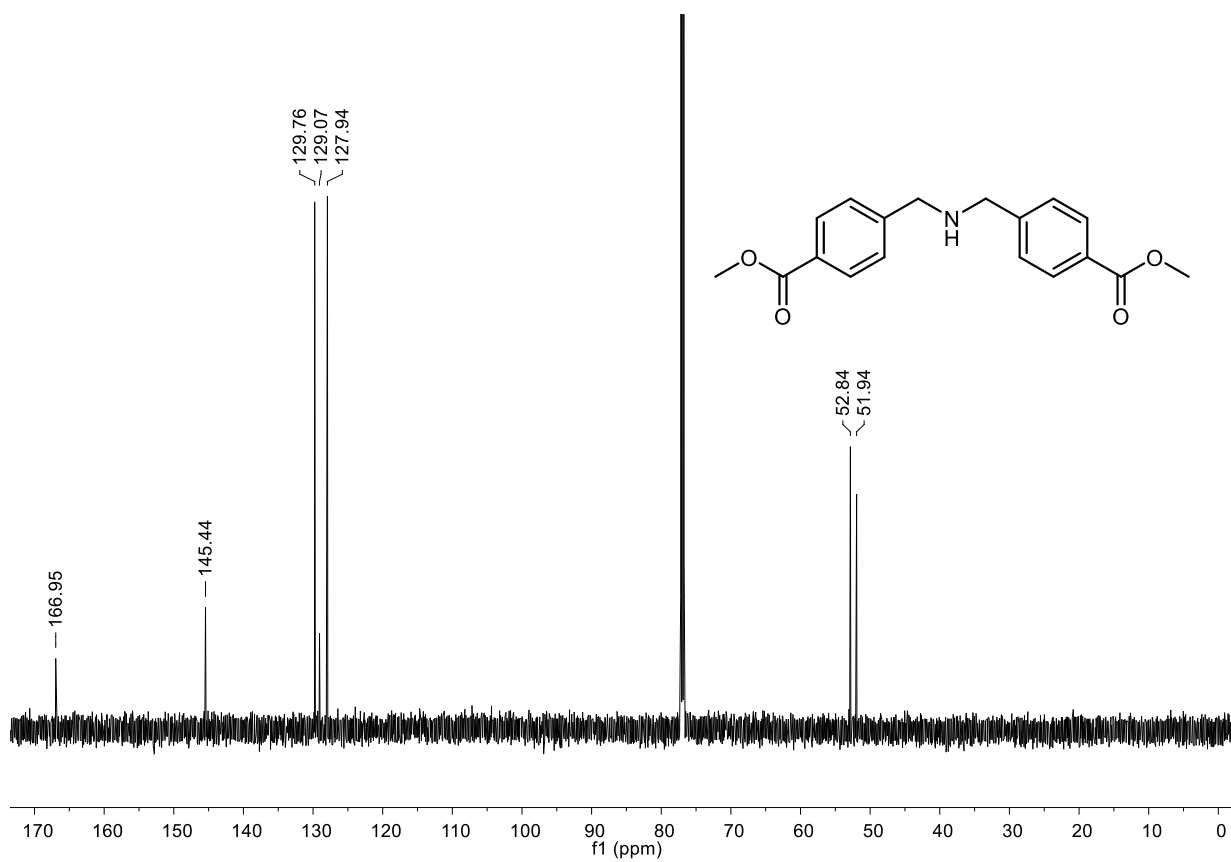


Figure S2.24 ¹³C NMR (151 MHz, CDCl₃) spectrum of dimethyl 4,4'-(azanediylbis(methylene))dibenzoate

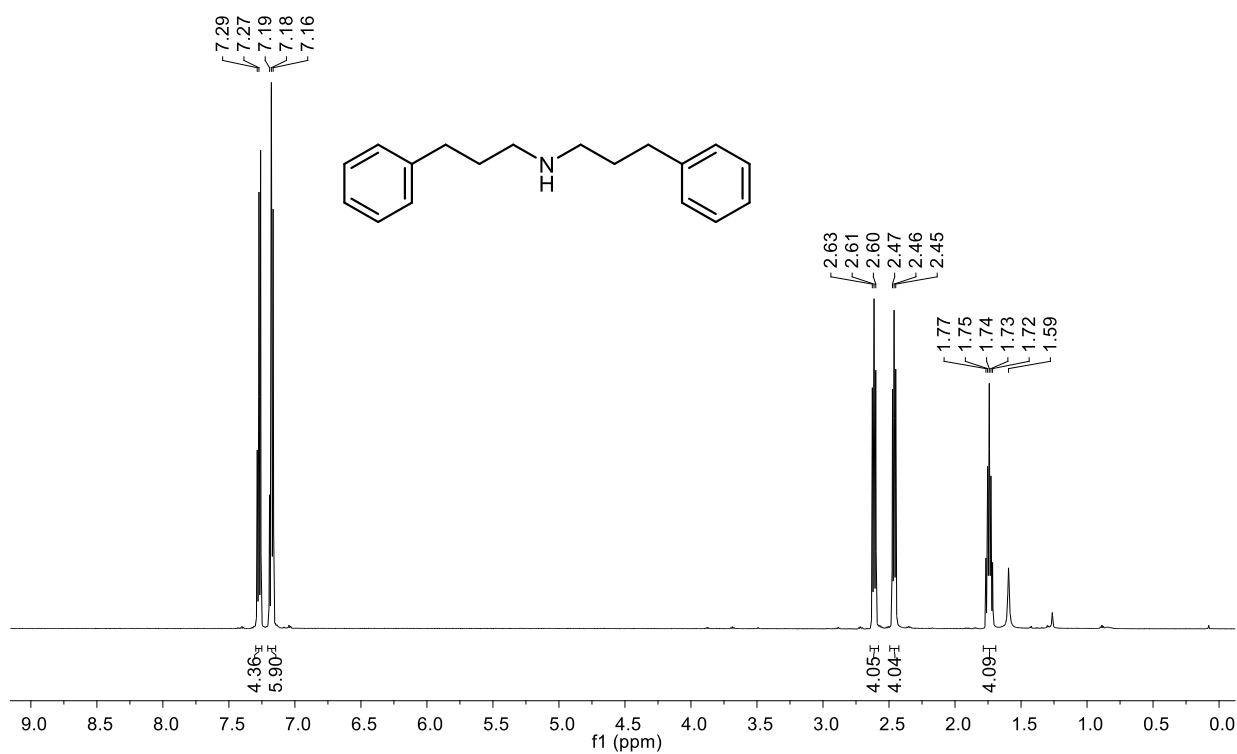


Figure S2.25 ¹H NMR (600 MHz, CDCl₃) spectrum of bis(3-phenylpropyl)amine.

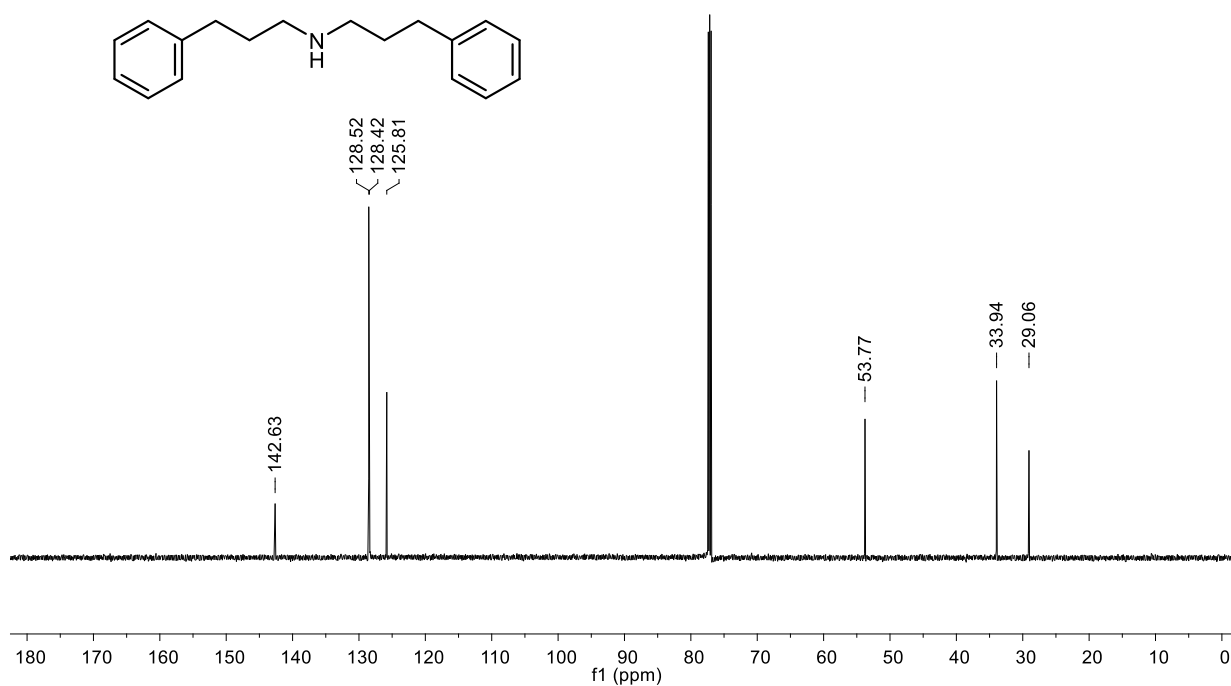


Figure S2.26 ¹³C NMR (151 MHz, CDCl₃) spectrum of bis(3-phenylpropyl)amine.

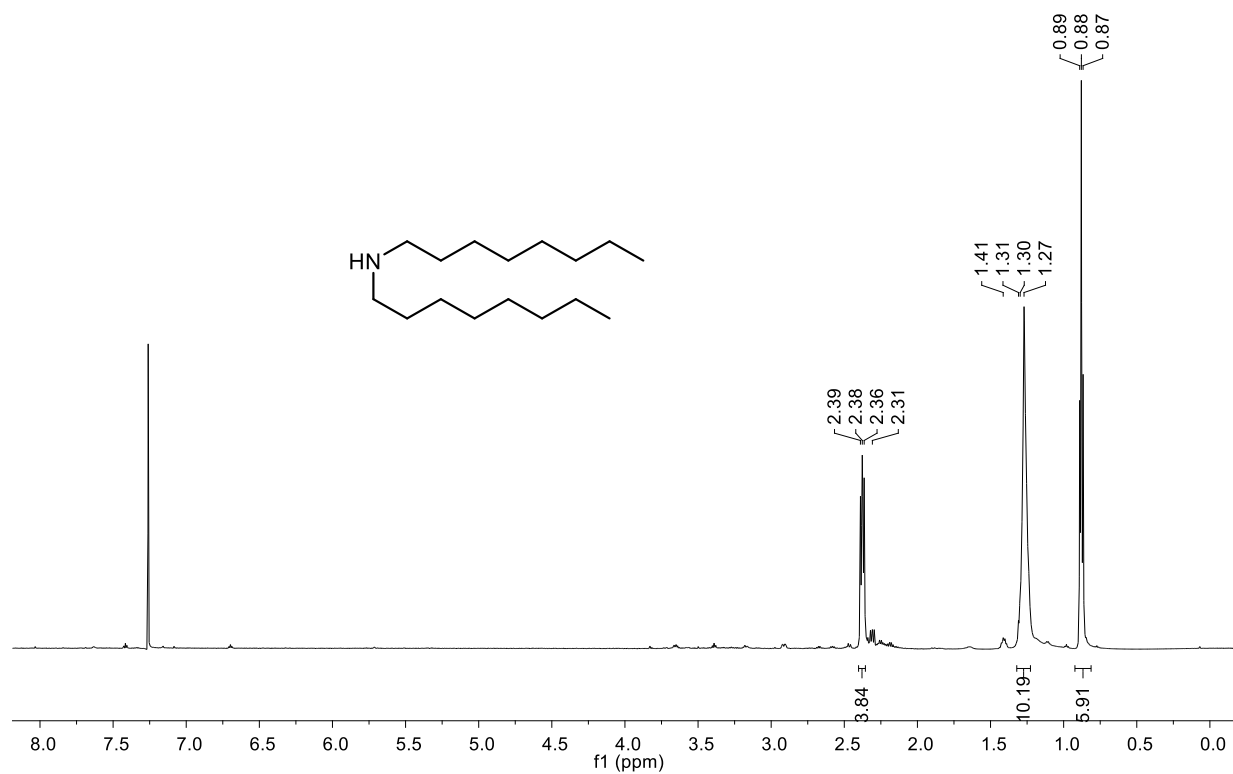


Figure S2.27 ^1H NMR (600 MHz, CDCl_3) spectrum of dioctylamine.

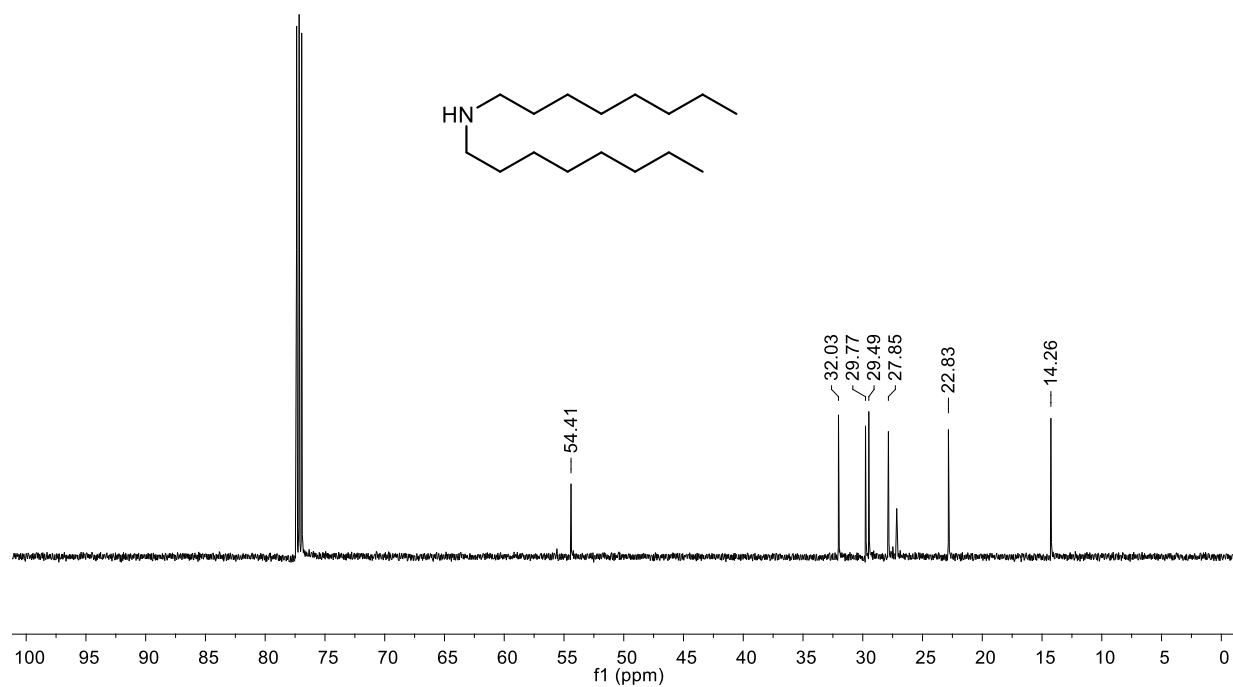


Figure S2.28 ^{13}C NMR (151 MHz, CDCl_3) spectrum of dioctylamine.

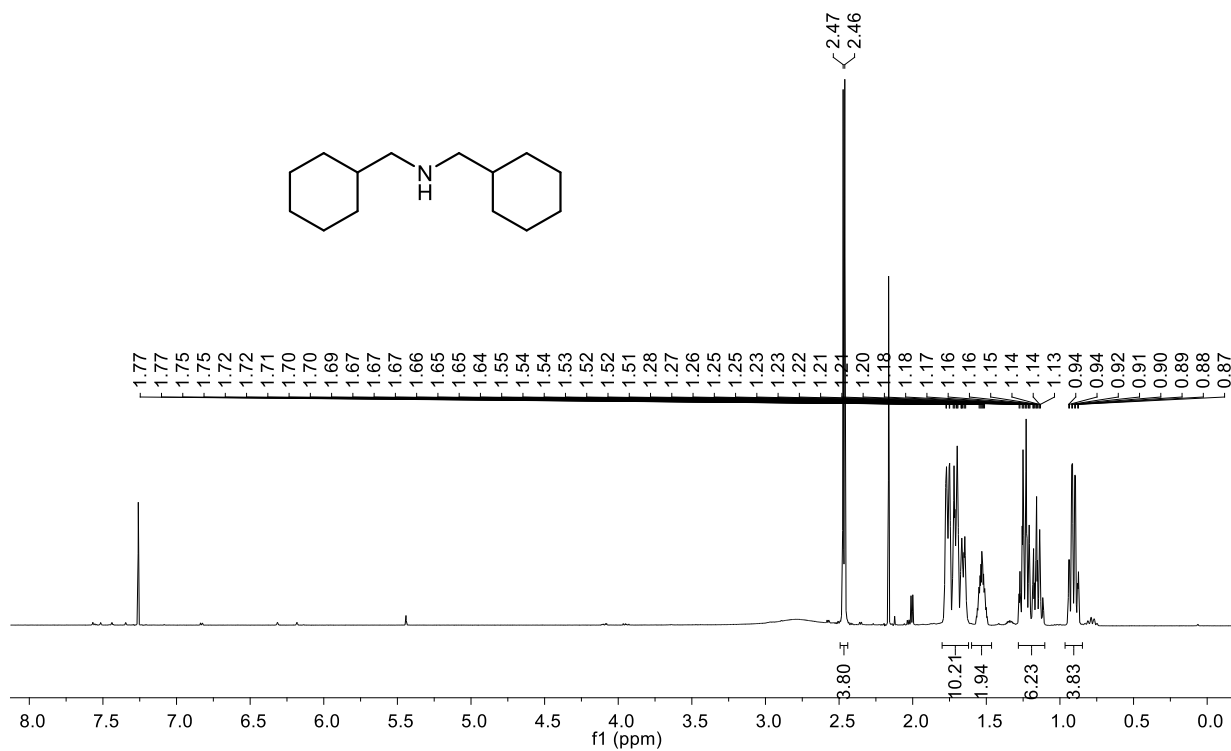


Figure S2.29 ¹H NMR (600 MHz, CDCl₃) spectrum of dicyclohexylamine.

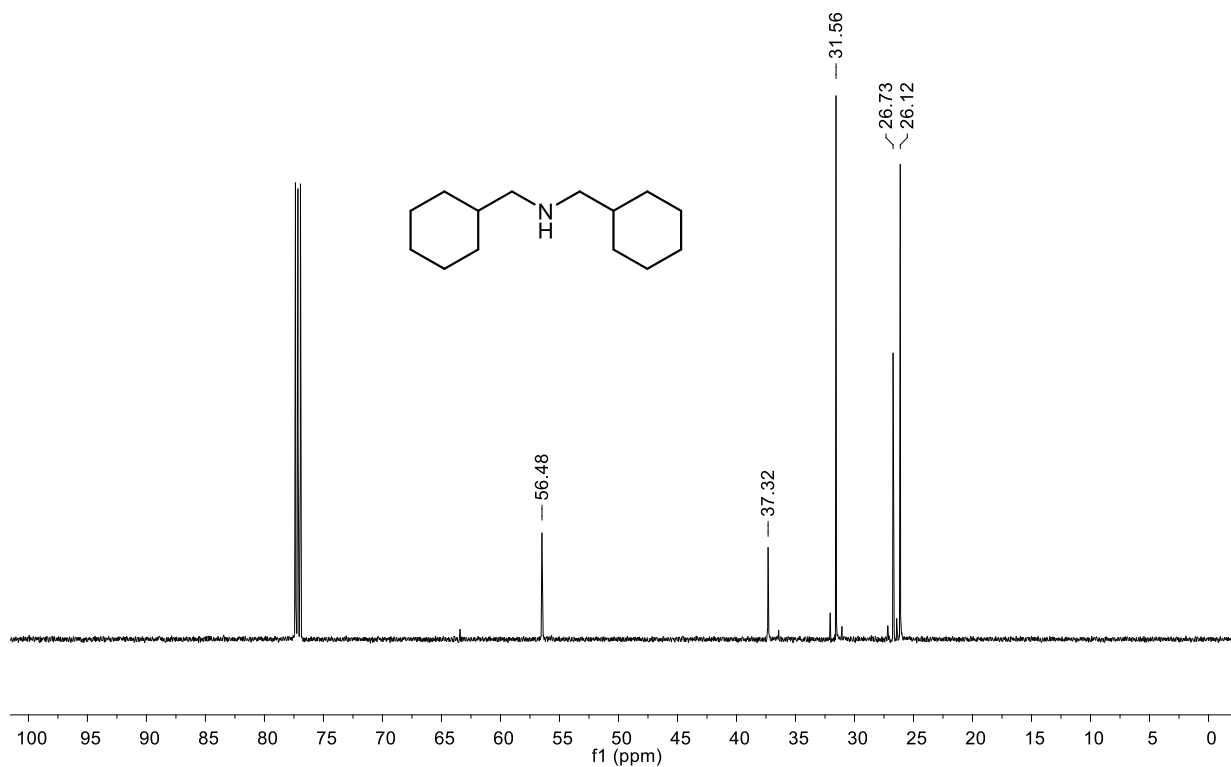


Figure S2.30 ¹³C NMR (151 MHz, CDCl₃) spectrum of dicyclohexylamine.

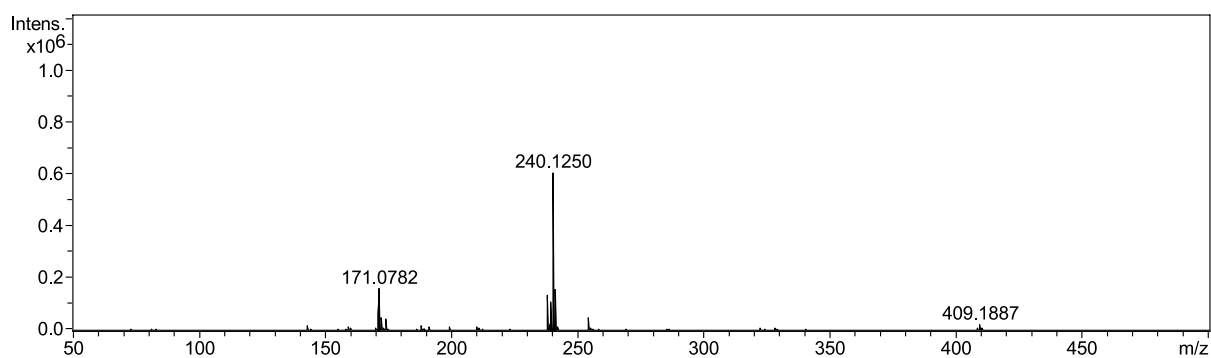


Figure S2.31 APCI-MS spectrum of **L4.1** recorded in positive ion mode. Isotope cluster found at m/z of 240.1250 corresponding to the $[M + H]^+$ ion.

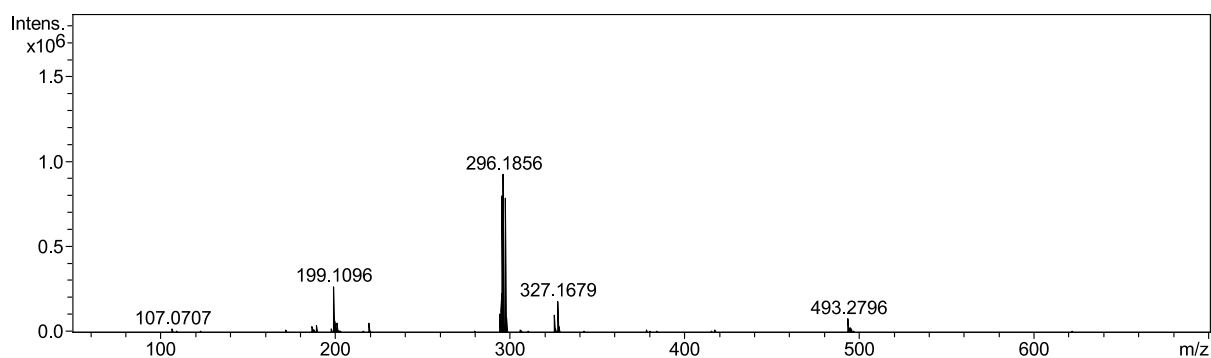


Figure S2.32 APCI-MS spectrum of **L4.2** recorded in positive ion mode. Isotope cluster found at m/z of 296.1856 corresponding to the $[M + H]^+$ ion.

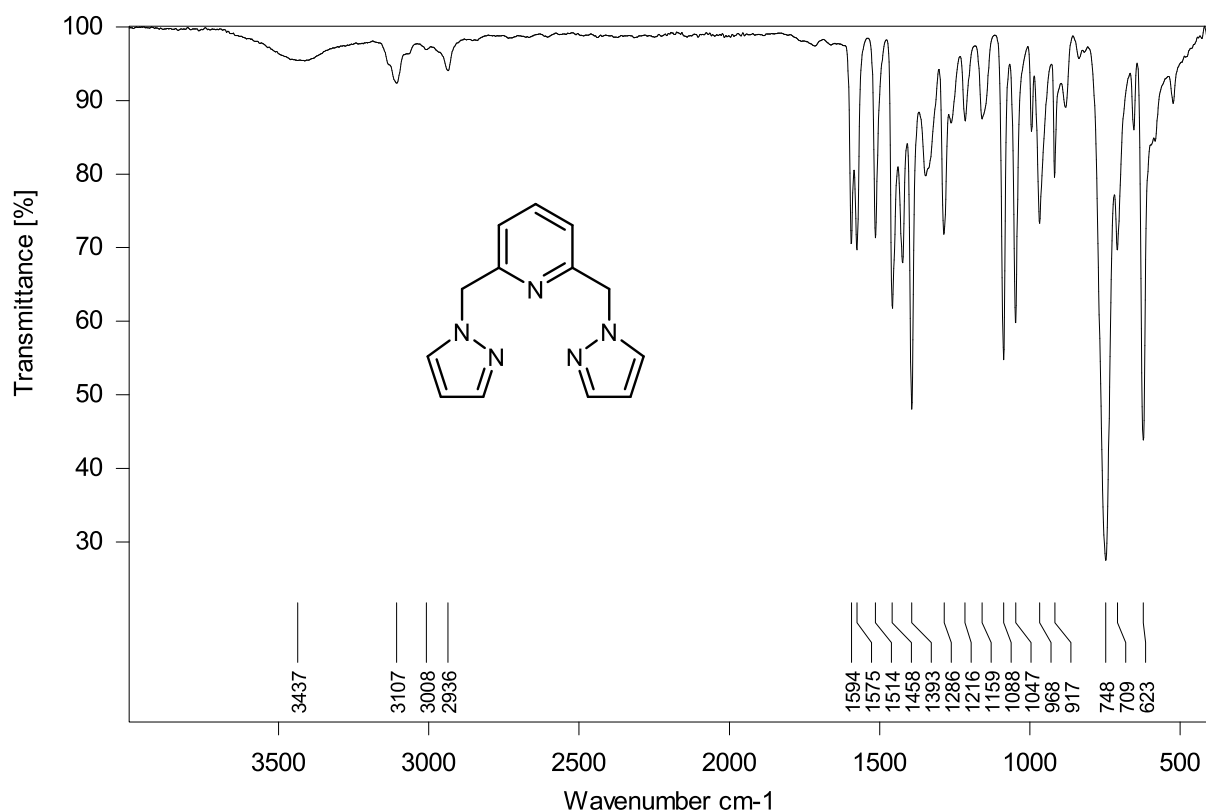


Figure S2.33 FT-IR spectrum of ligand **L4.1**.

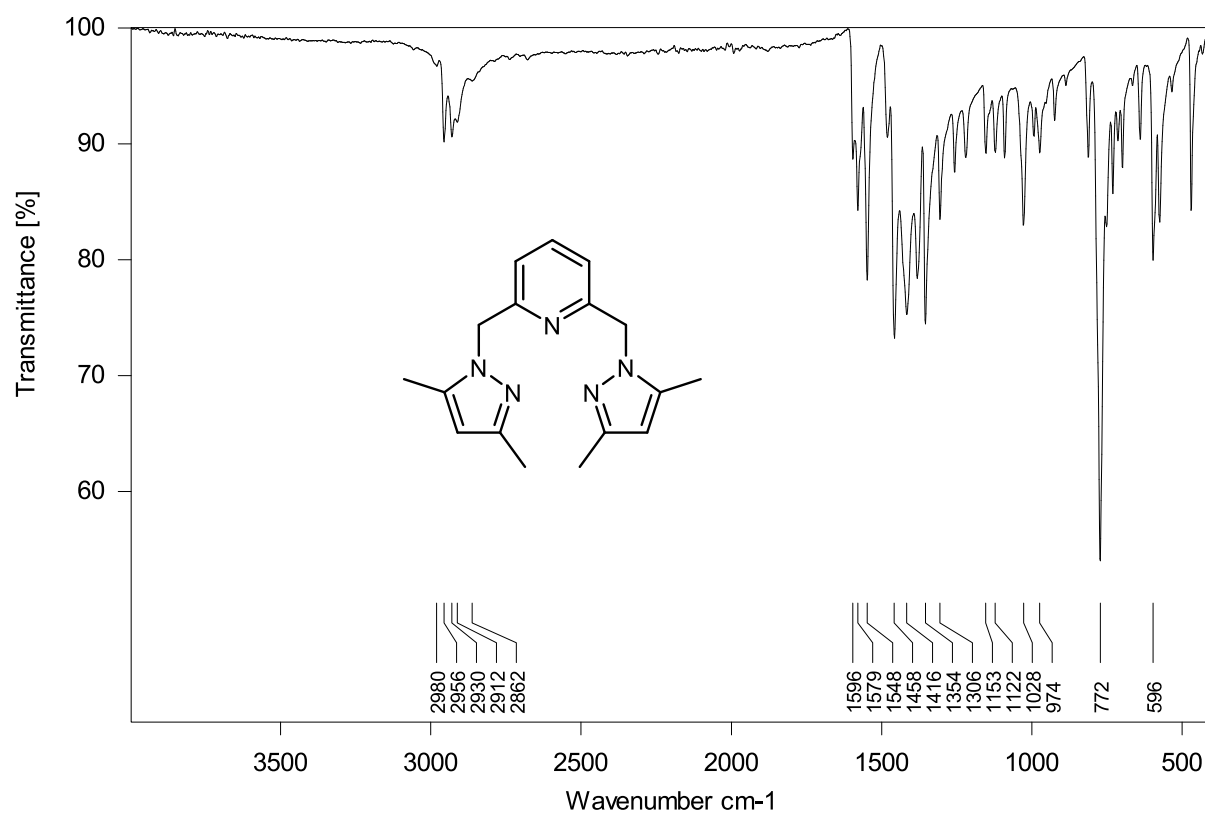


Figure S2.34 FT-IR spectrum of ligand **L4.2**.

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Supplementary information for Chapter 5

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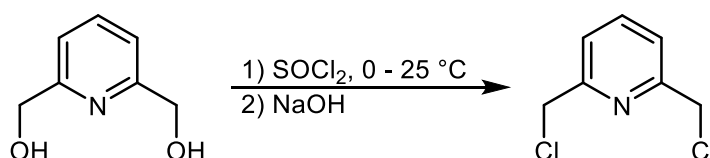
S3.1 General considerations

All chemicals were obtained from commercial sources, i.e. Sigma-Aldrich, Merck and Rochelle Chemicals and used as received. Ammonia borane ($\text{H}_3\text{N-BH}_3$, AB) was stored in a MBraun glove box under an Ar atmosphere. The $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ salt (98%) sent for ICP-analyses was digested with 2% HNO_3 (Ultra-pure grade) and analysed against NIST standards. ICP-AES analysis (Al to Zn) were conducted using a Thermo Scientific iCAP 6000 ICP-AES spectrometer and ICP-MS analysis (Ru to Au) on an Agilent 7900 spectrometer. FT-IR spectra were recorded on a Bruker Alpha-P range infrared instrument equipped with an ATR accessory as neat samples in the range of 400 to 4000 cm^{-1} . APCI-MS characterisation was conducted on a Bruker microTOF-Q II mass spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Ultrashield Plus (600 and 151 MHz, respectively) in 5 mm cylindrical glass tubes. Gas chromatographic analysis, GC and GC-MS, were performed on an Agilent 6890N Series GC system with HP-5 and HP-5MS columns respectively, with the following column dimensions: 30 m in length, 0.320 mm internal diameter and 0.25 mm film thickness. The GC and GC-MS were equipped with a FID and Agilent 5973N mass detector, respectively. The rinsing solution included MeOH (GC and GC-MS) with N_2 (GC) or He (GC-MS) used as the carrier gas and biphenyl serving as an internal standard.

S3.2 Synthesis of N,N,N-tridentate ligand, L5.1

Synthesis of ligand, **L5.1**, were conducted following methods previously described.¹ The other ligands, **L5.2** to **L5.4**, were commercially available and used as received.

S3.2.1 Synthesis of 2,6-bis(chloromethyl)pyridine

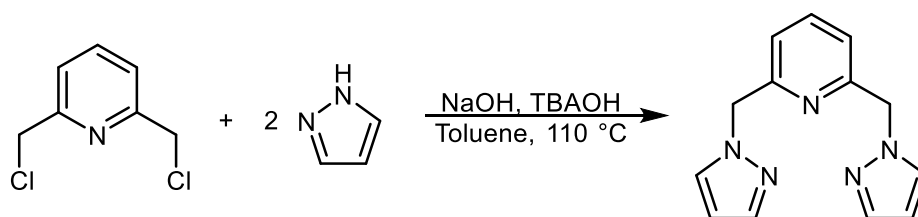


Scheme S3.1 Synthesis of 2,6-bis(chloromethyl)pyridine.

A round-bottomed flask, connected to a NaOH trap, was charged with 2,6-pyridinedimethanol (1.0011 g, 7.051 mmol) and placed in an ice bath. While stirring, cold thionyl chloride (5 mL, 66.86 mmol) was added dropwise over 30 minutes, through a septum. The reaction mixture was allowed to gradually warm to room temperature over a period of 2 hours. The mixture was cooled and toluene (15 mL) was added. The white salt was filtered, washed with 2 x 5 mL

portions of cold toluene and diethyl ether (10 mL) and dried under vacuum. The salt was dissolved in water and NaOH (0.6032 g, mmol) added to neutralise the salt. The suspension was cooled in an ice bath, the crystals filtered and washed with 2 x 10 mL portions of H₂O. The crude product was recrystallized from petroleum ether to obtain colourless crystals (1.0335 g, 83%). FT-IR (ATR) ν , cm⁻¹: 2965, 3022, 1591, 1576, 671. ¹H NMR (600 MHz, CDCl₃, ppm) δ : 7.76 (t, J = 7.8 Hz, 1H), 7.44 (d, J = 7.8 Hz, 2H), 4.66 (s, 4H). ¹³C NMR (151 MHz, CDCl₃, ppm) δ : 156.53, 138.27, 122.23, 46.57.

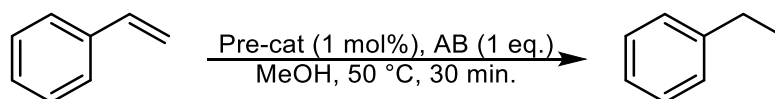
S3.2.2 Synthesis of 2,6-bis((1H-pyrazol-1-yl)methyl)pyridine (L5.1)



Scheme S3.2 Synthesis of ligand **L5.1**.

In a round-bottomed flask 2,6-bis(chloromethyl)pyridine (0.3010 g, 1.710 mmol) and pyrazole (0.2385 g, 3.433 mmol) were dissolved in toluene (20 mL). A 40% NaOH solution (12 mL) and 10 drops of TBAOH were added to the mixture. The mixture was heated to 110 °C and stirred for 23 hours. After the allotted time, the solution was cooled down to room temperature, the organic layer was separated and washed with 3 x 10 mL portions of H₂O. The combined organic layers were dried over MgSO₄, filtered and the solvent removed under vacuum to obtain a pale yellow oil (0.3250 g, 79%) (**L5.1**). FT-IR (ATR) ν , cm⁻¹: 3437, 3107, 3008, 2936, 1594, 1575. ¹H NMR (600 MHz, CDCl₃, ppm) δ : 7.59 – 7.49 (m, 5H), 6.83 (d, J = 7.8 Hz, 2H), 6.31 (t, J = 2.1 Hz, 2H), 5.44 (s, 4H). ¹³C NMR (151 MHz, CDCl₃, ppm) δ : 156.68, 140.09, 138.22, 130.12, 120.62, 106.37, 57.50. APCI-MS (m/z): 240.1250 [$M + H$]⁺.

S3.3 General procedure for the transfer hydrogenation of styrene



Scheme S3.3 General procedure for the transfer hydrogenation of styrene.

Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of styrene (30 μ L, 0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μ mol) with **L5.2** (0.2 mg, 2.5 μ mol) in methanol (1 mL) followed. The reaction mixture was stirred at 50 $^\circ\text{C}$ for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

S3.4 Optimisation of reaction conditions for transfer hydrogenation of styrene

S3.4.1 Evaluating the effect of pre-catalyst, reaction time and temperature

Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of styrene (30 μ L, 0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μ mol) with ligand (2.5 μ mol) in methanol (1 mL) followed. The reaction mixture was stirred at indicated temperature and time. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

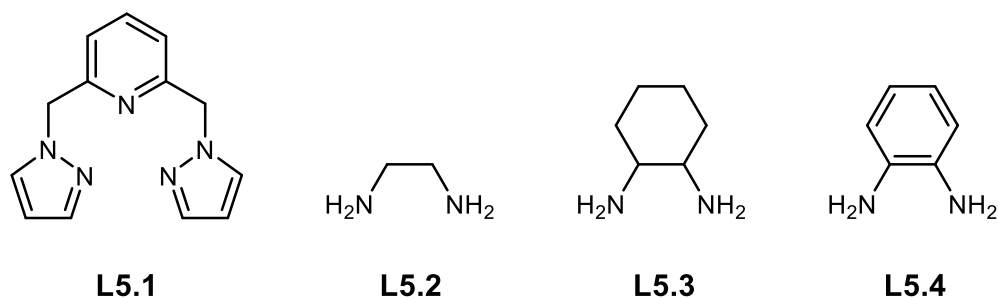
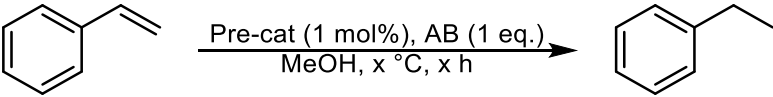


Figure S3.1 Ligands used in this study.

Table S3.1 Evaluation of pre-catalyst, reaction time and temperature in styrene transfer hydrogenation.

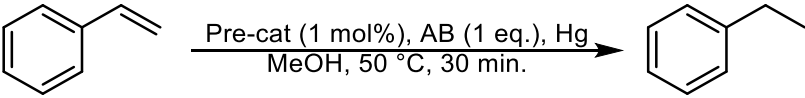
				
Entry	Pre-cat	Temp. (°C)	Time (h)	Conversion ^a (%)
1	Ni/L5.1	25	0.5	10
2	Ni/L5.1	50	2	>99
3	Ni/L5.2	50	2	>99
4	Ni/L5.1	50	1	>99
5	Ni/L5.2	50	1	>99
6	Ni/L5.1	50	0.5	>99
7	Ni/L5.2	50	0.5	>99
8	Ni/L5.3	50	0.5	>99
9	Ni/L5.4	50	0.5	>99
10	Ni	50	0.5	>99
11	-	50	0.5	<1

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), styrene (0.25 mmol), NiCl₂·6H₂O (1 mol%) and ligand (1 mol%) in methanol (1 mL) were stirred at indicated temperature and time. ^a Conversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs. Ni denotes NiCl₂·6H₂O.

S3.4.2 Evaluating homogeneity of catalyst with Hg drop test

Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of alkene (0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with ligand (2.5 μmol) in methanol (1 mL) followed. The reaction mixture was stirred at 50 °C for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

Table S3.2 Evaluating the effect of Hg in the transfer hydrogenation of styrene.

			
Entry	Pre-cat	Conversion ^a (%)	
		No Hg	Hg added
1	Ni/L5.1	>99	45
2	Ni/L5.2	>99	>99
3	Ni/L5.3	>99	56
4	Ni/L5.4	>99	30
5	Ni	98	14

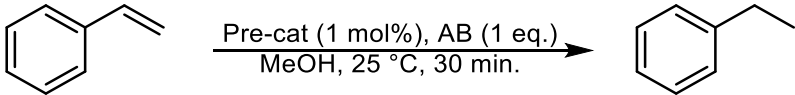
Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), styrene (0.25 mmol), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1 mol%), ligand (1 mol%) and Hg (0 or 500 eq. to Ni) in methanol (1 mL) were stirred at 50 °C for 30 minutes.

^a Conversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs. Ni denotes $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$.

S3.4.3 Evaluating the effect of ammonia borane purity

Ammonia borane (0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of styrene (30 μ L, 0.25 mmol) and then NiCl₂·6H₂O (0.6 mg, 2.5 μ mol) with **L5.1/L5.2** (2.5 μ mol) in methanol (1 mL) followed. The reaction mixture was stirred at 25 °C for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

Table S3.3 Evaluating the effect of ammonia borane purity in the transfer hydrogenation of styrene.

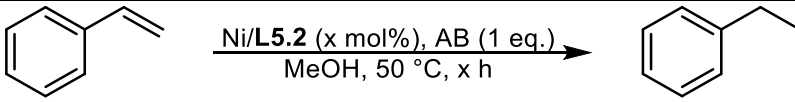
			
Entry	Pre-cat	AB (% purity)	Conversion ^a (%)
1	Ni/ L5.1	97	10
2	Ni/ L5.1	90	>99
3	Ni/ L5.2	97	44
4	Ni/ L5.2	90	>99

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), styrene (0.25 mmol), NiCl₂·6H₂O (1 mol%) and **L5.1/L5.2** (1 mol%) in methanol (1 mL) were stirred at 25 °C for 30 minutes. ^aConversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs. Ni denotes NiCl₂·6H₂O.

S3.4.4 Evaluating maximum TON of NiCl₂·6H₂O/L2 pre-catalyst

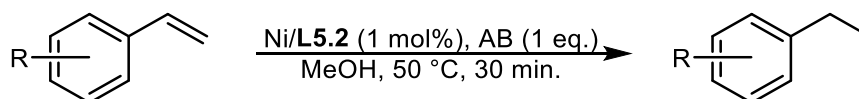
Ammonia borane (15.4 mg, 0.5 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of styrene (60 μ L, 0.5 mmol) and then NiCl₂·6H₂O with **L5.2** in methanol (2 mL) followed. The reaction mixture was stirred at 50 °C for indicated time. The reaction mixture was filtered through a Celite plug and analysed by GC against an internal standard (biphenyl) to determine percentage conversion. All catalytic runs were performed in duplicate.

Table S3.4 Evaluating the maximum TON of the transfer hydrogenation of styrene.

						
Entry	Pre-cat load. (mol%)	Temperature (°C)	Time (hours)	Conversion ^a (%)	GC yield ^a (%)	TON ^b
1	1	50	0.5	>99	>99	100
2	0.1	50	24	>99	>99	1000
3	0.05	50	24	56	56	1120
4	0.025	50	24	42	42	1680
5	0.025	50	48	99	99	3960
6	0.01	50	24	4	4	400

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), styrene (0.5 mmol), NiCl₂·6H₂O (indicated mol%), **L5.2** (indicated mol%) in methanol (2 mL) were stirred at 50 °C and indicated time. ^a Conversion and GC yield were determined by GC against biphenyl as the internal standard and is the average of two independent runs. ^b Numbers in brackets indicate TON with regard to ethylbenzene. TON calculated using TON = (mol ethylbenzene formed)/(mol pre-catalyst used).

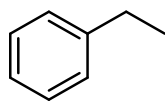
S3.5 Evaluating transfer hydrogenation of styrene derivatives



Scheme S3.4 General procedure for the transfer hydrogenation of aromatic alkenes.

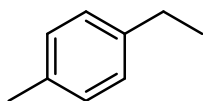
Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of alkene (0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with **L5.2** (0.2 mg, 2.5 μmol) in methanol (1 mL) followed. The reaction mixture was stirred at 50 $^\circ\text{C}$ for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate. For NMR analysis of product 3.5.1 to 3.5.9, the reaction mixture was filtered through a Celite plug and 0.2 mL CDCl_3 was added to the filtrate. The signals in the spectra at 2.9 ppm (^1H NMR) and 48.4 ppm (^{13}C NMR) originate from MeOH.

S3.5.1 Ethylbenzene



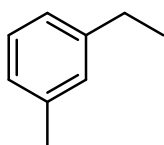
^1H NMR (600 MHz, CDCl_3) δ (ppm): 6.79 – 6.73 (m, 2H), 6.72 – 6.67 (m, 2H), 6.65 (t, J = 7.3 Hz, 1H), 2.15 (q, J = 7.6 Hz, 2H), 0.75 (t, J = 7.6 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 143.56, 127.51, 127.00, 124.80, 28.10, 14.57. Analytical data is in accordance with that previously reported in literature.²

S3.5.2 1-Ethyl-4-methylbenzene



^1H NMR (600 MHz, CDCl_3) δ (ppm): 6.55 (s, 4H), 2.08 (q, J = 7.6 Hz, 2H), 1.79 (d, J = 10.0 Hz, 3H), 0.70 (t, J = 7.6 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 140.48, 134.15, 128.13, 126.88, 27.65, 19.52, 14.65. Analytical data is in accordance with that previously reported in literature.³

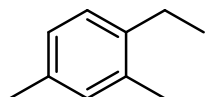
S3.5.3 1-Ethyl-3-methylbenzene



^1H NMR (600 MHz, CDCl_3) δ (ppm): 6.66 (t, J = 7.5 Hz, 1H), 6.52 (s, 1H), 6.49 (dd, J = 7.4, 2.2 Hz, 2H), 2.12 (q, J = 7.6 Hz, 2H), 1.83 (s, 3H), 0.74 (t, J = 7.6 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 143.51, 137.01, 127.78, 127.43, 125.50, 124.05, 28.05, 19.96,

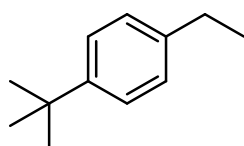
14.62. Analytical data is in accordance with that previously reported in literature.³

S3.5.4 1-Ethyl-2,4-dimethylbenzene



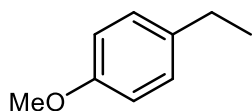
¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.52 (d, *J* = 7.6 Hz, 1H), 6.48 – 6.41 (m, 2H), 2.11 (q, *J* = 7.6 Hz, 2H), 1.79 (d, *J* = 1.6 Hz, 6H), 0.70 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 138.48, 134.57, 134.25, 129.97, 127.11, 125.84, 24.99, 19.46, 17.65, 13.48.⁴

S3.5.5 1-(tert-Butyl)-4-ethylbenzene



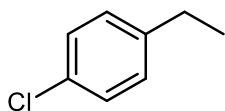
¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.87 – 6.80 (m, 2H), 6.66 (d, *J* = 8.3 Hz, 2H), 2.16 (q, *J* = 7.6 Hz, 2H), 0.86 (s, 9H), 0.77 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (151 MHz, (CD₃)₂CO) δ (ppm): 147.63, 140.52, 126.74, 124.40, 33.44, 30.33, 27.58, 14.61. Analytical data is in accordance with that previously reported in literature.⁵

S3.5.6 1-Ethyl-4-methoxybenzene



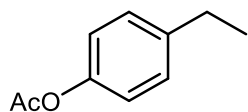
¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.61 (d, *J* = 8.7 Hz, 2H), 6.36 – 6.31 (m, 2H), 3.28 (s, 3H), 2.10 (q, *J* = 7.6 Hz, 2H), 0.72 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 157.20, 135.74, 127.88, 112.98, 54.04, 27.21, 14.81. Analytical data is in accordance with that previously reported in literature.⁶

S3.5.7 1-Chloro-4-ethylbenzene



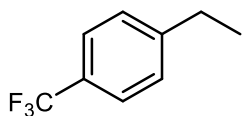
¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.75 (d, *J* = 8.4 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 2.13 (q, *J* = 7.6 Hz, 2H), 0.73 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 142.22, 130.54, 128.54, 127.54, 27.43, 14.38. Analytical data is in accordance with that previously reported in literature.⁷

S3.5.8 4-Ethylphenyl acetate



^1H NMR (600 MHz, CDCl_3) δ (ppm): 6.74 (d, J = 8.5 Hz, 2H), 6.53 – 6.50 (m, 2H), 2.19 (q, J = 7.6 Hz, 2H), 1.81 (s, 3H), 0.77 (t, J = 7.6 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 169.75, 148.22, 141.31, 127.97, 120.64, 27.53, 19.56, 14.59. Analytical data is in accordance with that previously reported in literature.⁸

S3.5.9 1-Ethyl-4-trifluoromethylbenzene

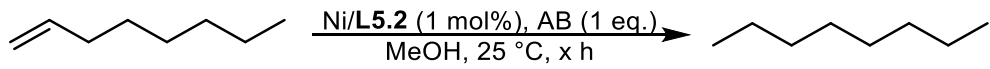


^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.07 (d, J = 8.1 Hz, 2H), 6.89 (d, J = 8.0 Hz, 2H), 2.26 (q, J = 7.6 Hz, 2H), 0.80 (t, J = 7.6 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 148.04, 127.58, 124.89, 124.43 (q, J = 3.8 Hz), 123.10, 27.96, 14.18. Analytical data is in accordance with that previously reported in literature.⁹

S3.6 Optimisation of reaction conditions for transfer hydrogenation of aliphatic alkenes

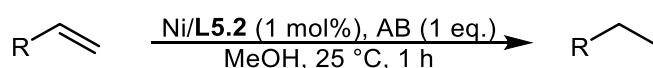
Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of 1-octene (0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with **L5.2** (0.2 mg, 2.5 μmol) in methanol (1 mL) followed. The reaction mixture was stirred at 25 °C for 0.5 - 1 hours. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate.

Table S3.5 Evaluation of pre-catalyst, reaction time and temperature in styrene transfer hydrogenation.

			
Entry	Temp. (°C)	Time (h)	Conversion ^a (%)
1	25	0.5	56
2	25	1	85

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), 1-octene (0.25 mmol), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (1 mol%) and **L5.2** (1 mol%) in methanol (1 mL) were stirred at indicated temperature and time. ^a Conversion was determined by GC against biphenyl as the internal standard and is the average of two independent runs. Ni denotes $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$.

S3.7 Evaluating transfer hydrogenation of aliphatic alkenes

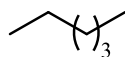


Scheme S3.5 General procedure for the transfer hydrogenation of aliphatic alkenes.

Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of alkene (0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with **L5.2** (0.2 mg, 2.5 μmol) in methanol (1 mL) followed. The reaction mixture was stirred at 25 °C for 1 hour. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate. For NMR analysis of product 3.7.1 to 3.7.6, the reaction mixture was filtered through a Celite plug and 0.2 mL CDCl_3

was added to the filtrate. The signals in the spectra at 2.9 ppm (^1H NMR) and 48.4 ppm (^{13}C NMR) originate from MeOH.

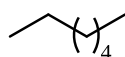
S3.7.1 Hexane



^1H NMR (600 MHz, CDCl_3) δ (ppm): 0.88 – 0.74 (m, 8H), 0.41 (t, J = 7.0 Hz, 6H).

^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 30.91, 21.89, 12.82. Analytical data is in accordance with that previously reported in literature.¹⁰

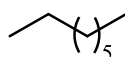
S3.7.2 Heptane



^1H NMR (600 MHz, CDCl_3) δ (ppm): 0.89 – 0.76 (m, 10H), 0.42 (t, J = 7.1 Hz, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 31.23, 28.34, 21.95, 12.86. Analytical

data is in accordance with that previously reported in literature.¹⁰

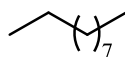
S3.7.3 Octane



^1H NMR (600 MHz, CDCl_3) δ (ppm): 0.89 – 0.75 (m, 12H), 0.43 (t, J = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 31.28, 28.64, 21.96, 12.88. Analytical

data is in accordance with that previously reported in literature.¹⁰

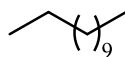
S3.7.4 Decane



^1H NMR (600 MHz, CDCl_3) δ (ppm): 0.88 – 0.77 (m, 16H), 0.42 (t, J = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 31.28, 28.98, 28.68, 21.96, 12.88.

Analytical data is in accordance with that previously reported in literature.¹¹

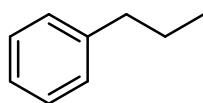
S3.7.5 Dodecane



^1H NMR (600 MHz, CDCl_3) δ (ppm): 0.89 – 0.78 (m, 20H), 0.43 (t, J = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 31.30, 29.04, 28.99, 28.71, 21.98,

12.91. Analytical data is in accordance with that previously reported in literature.¹²

S3.7.6 Propylbenzene

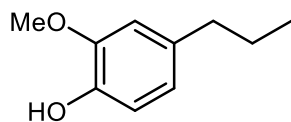


^1H NMR (600 MHz, CDCl_3) δ (ppm): 6.78 (dd, J = 10.5, 4.6 Hz, 2H), 6.68 (dd, J = 13.3, 7.2 Hz, 3H), 2.14 – 2.09 (t, 2H), 1.23 – 1.13 (m, 2H), 0.48 (t, J

= 7.4 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 141.93, 127.68, 127.44,

124.86, 37.34, 23.97, 12.55. Analytical data is in accordance with that previously reported in literature.¹³

S3.7.7 2-Methoxy-4-propylphenol



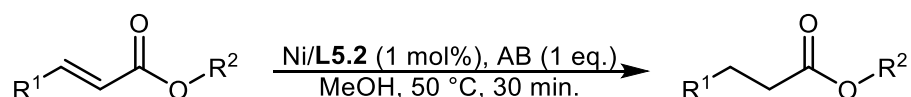
Isolated as a colourless oil (40.2 mg, 94%). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.86 (d, *J* = 7.8 Hz, 1H), 6.75 – 6.68 (m, 2H), 5.53 (s, 1H), 3.91 (s, 3H), 2.58 – 2.52 (m, 2H), 1.70 – 1.60 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 146.30, 143.54, 134.72, 120.99, 114.10, 111.06, 55.86, 37.77, 24.86, 13.80. Analytical data is in accordance with that previously reported in literature.¹⁴

Table S3.6 Evaluation of Ni/**L5.1** in aliphatic alkene transfer hydrogenation.

$\text{R}-\text{CH}=\text{CH}_2 \xrightarrow[\text{MeOH, 25 } ^\circ\text{C, 1 h}]{\text{Ni/L5.1 (1 mol\%), AB (1 eq.)}} \text{R}-\text{CH}_2\text{CH}_3$				
Entry	Substrate	Product	Conversion ^a (%)	GC yield ^a (%) Selectivity ^b [%]
1			>99	>99 [>99]
2			97	96 [99]
3			95	91 [96]
4			98	95 [97]
5			98	>99 [>99]
6			80	76 [95]

Reaction conditions: Under an Ar atmosphere, ammonia borane (1 equivalent), alkene (0.25 mmol), NiCl₂·6H₂O (1 mol%) and **L5.1** (1 mol%) in methanol (1 mL) were stirred at 25 °C for 1 hour. ^a Conversion and GC yield were determined by GC against biphenyl as the internal standard and is the average of two independent runs. ^b Selectivity for alkane product. Ni denotes NiCl₂·6H₂O.

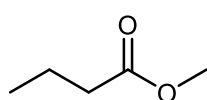
S3.8 Evaluating transfer hydrogenation of α,β -unsaturated alkenes



Scheme S3.6 General procedure for the transfer hydrogenation of α,β -unsaturated alkenes.

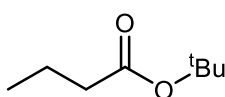
Ammonia borane (7.7 mg, 0.25 mmol, 1 eq.) was added to a 5 mL screw-capped mini-reactor under an Ar atmosphere. Sequential addition of alkene (0.25 mmol) and then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.6 mg, 2.5 μmol) with **L5.2** (0.2 mg, 2.5 μmol) in methanol (1 mL) followed. The reaction mixture was stirred at 50 $^\circ\text{C}$ for 30 minutes. The reaction mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion and GC-yield. All catalytic runs were performed in duplicate. For NMR analysis of product 3.8.1 and 3.8.2, the reaction mixture was filtered through a Celite plug and 0.2 mL CDCl_3 was added to the filtrate. The signals in the spectra at 2.9 ppm (^1H NMR) and 48.4 ppm (^{13}C NMR) originate from MeOH.

S3.8.1 Methyl butanoate



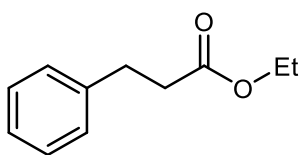
^1H NMR (600 MHz, CDCl_3) δ (ppm): 3.19 (s, 3H), 1.82 (t, $J = 7.4$ Hz, 2H), 1.16 (h, $J = 7.4$ Hz, 2H), 0.47 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 174.16, 50.35, 35.04, 17.64, 12.34. Analytical data is in accordance with that previously reported in literature.¹⁵

S3.8.2 tert-Butyl butanoate



^1H NMR (600 MHz, CDCl_3) δ (ppm): 1.72 (t, $J = 7.3$ Hz, 2H), 1.13 (h, $J = 7.4$ Hz, 2H), 0.97 (s, 9H), 0.46 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 173.31, 79.64, 36.70, 26.83, 17.84, 12.30. Analytical data is in accordance with that previously reported in literature.¹⁶

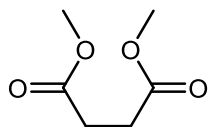
S3.8.3 Ethyl 3-phenylpropanoate



Isolated as a colourless oil (37.8 mg; 90%). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.31 (dd, $J = 9.7, 5.4$ Hz, 2H), 7.26 – 7.19 (m, 3H), 4.16 (q, $J = 7.1$ Hz, 2H), 2.98 (t, $J = 7.9$ Hz, 2H), 2.68 – 2.62 (m, 2H), 1.26 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ (ppm): 172.92, 140.60, 128.48, 128.31, 126.23, 60.41, 35.96, 30.99, 14.21. Analytical data is in accordance with that previously reported in

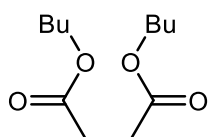
literature.¹⁷

S3.8.4 Dimethyl succinate



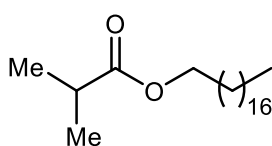
Isolated as a colourless oil (31.2 mg; 90%). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 3.71 (s, 6H), 2.65 (s, 4H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 172.74, 51.84, 28.89. Analytical data is in accordance with that previously reported in literature.¹⁸

S3.8.5 Dibutyl succinate



Isolated as a colourless oil (52.6 mg; 91%). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 4.10 (t, *J* = 6.7 Hz, 4H), 2.62 (s, 4H), 1.65 – 1.57 (m, 4H), 1.41 – 1.35 (m, 4H), 0.94 (t, *J* = 7.4 Hz, 6H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 172.37, 64.58, 30.61, 29.20, 19.08, 13.66. Analytical data is in accordance with that previously reported in literature.¹⁹

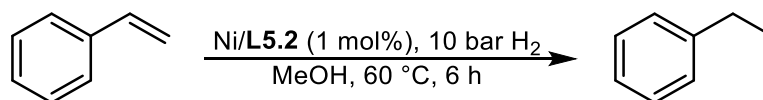
S3.8.6 Octadecyl isobutanoate



Isolated as a transparent-white wax (81.8 mg; 96%). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 4.04 (t, *J* = 6.7 Hz, 2H), 2.52 (dt, *J* = 14.0, 7.0 Hz, 1H), 1.65 – 1.56 (m, 2H), 1.37 – 1.22 (m, 30H), 1.15 (d, *J* = 7.0 Hz, 6H), 0.87 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 177.35, 64.53, 34.19, 32.08, 29.85, 29.82, 29.81, 29.79, 29.72, 29.67, 29.51, 29.40, 28.80, 26.05, 22.83, 19.14, 14.24.²⁰

S3.9 Experimental insights into the TH mechanism of styrene

S3.9.1 Direct hydrogenation of styrene with NiCl₂·6H₂O/L5.2 and H₂



Scheme S3.7 General procedure for direct hydrogenation of styrene with H₂.

In a 50 mL steel Parr reactor, NiCl₂·6H₂O (1.2 mg, 5 μmol) with **L5.2** (0.4 mg, 5 μmol) and styrene (0.5 mmol) was dissolved in MeOH (2 mL). The reactor was flushed three times with H₂ and then pressurised with 10 atm H₂. After 6 hours at 60 °C the mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to yield (GC) 1% of ethylbenzene. The reaction was done in duplicate.

S3.9.2 Importance of borane in transfer hydrogenation of styrene

In a 50 mL steel Parr reactor (or 5 mL screw-capped mini-reactor), NiCl₂·6H₂O (1.2 mg, 5 μmol) with **L5.2** (0.4 mg, 5 μmol), α-picoline borane (APB, 53.4 mg, 0.5 mmol) and styrene (0.5 mmol) was dissolved in MeOH (2 mL). The reactor was flushed three times with H₂ and then pressurised with 10 atm H₂. After 30 minutes at 50 °C the mixture was filtered through a Celite plug and analysed by GC and GCMS against an internal standard (biphenyl) to determine percentage conversion. The reaction was done in duplicate.

Table S 3.7 Evaluation of H₂ pressure and α-picoline borane in the transfer hydrogenation of styrene.

Entry	α-picoline borane (eq.)	pH ₂ (atm)	Time (h)	Yield ^a (%)
1	1	10	0.5	>99
2	1	-	0.5	14

Reaction conditions: Styrene (0.5 mmol), NiCl₂·6H₂O (1 mol%), **L5.2** (1 mol%) and α-picoline borane (0.5 mmol) in MeOH (2 mL) were stirred at 50 °C for 30 min. at specified pH₂. ^aYield was determined by GC against biphenyl as the internal standard and is the average of two independent runs.

S3.10 ICP-AES and ICP-MS analysis of NiCl₂·6H₂O salt**Table S3.8** Concentration (in ppb) and relative concentration of metal relative to Ni.

Element	Concentration (ppb) (µg/kg)	Relative to Ni (element/Ni)
Al	BDL (<5570)	-
B	3400	1.12E-05
Ba	BDL (<1860)	-
Ca	BDL (<18570)	-
Co	22800	7.54E-05
Cr	7600	2.51E-05
Cu	BDL (<1860)	-
Fe	6400	2.12E-05
K	BDL (<18570)	-
Mg	BDL (<18570)	-
Mn	BDL (<1860)	-
Na	908700	3.00E-03
Ni	302451000	1.00
P	150900	4.99E-04
Pb	28400	9.39E-05
Si	BDL (<18570)	-
Sr	BDL (<930)	-
Zn	BDL (<1860)	-
Ru*	BDL (<1.41)	-
Rh*	232.7	7.69E-07
Re*	BDL (<0.7)	-
Os*	BDL (<11.33)	-
Ir*	436	1.44E-06
Pt*	381	1.26E-06
Au*	207	6.84E-07

* Analysed with ICP-MS. BDL = below detection limit

S3.11 Analytical data of ligand L5.1 and hydrogenated alkene products

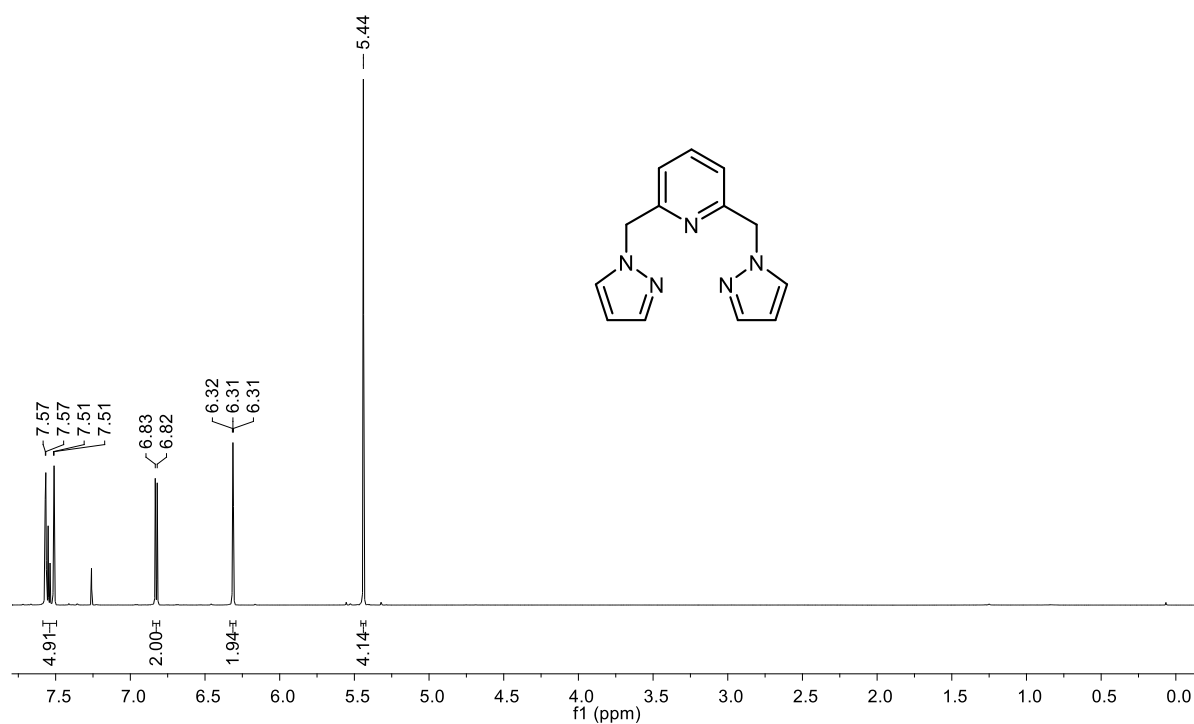


Figure S3.2 ¹H NMR (600 MHz, CDCl₃) spectrum of ligand L5.1.

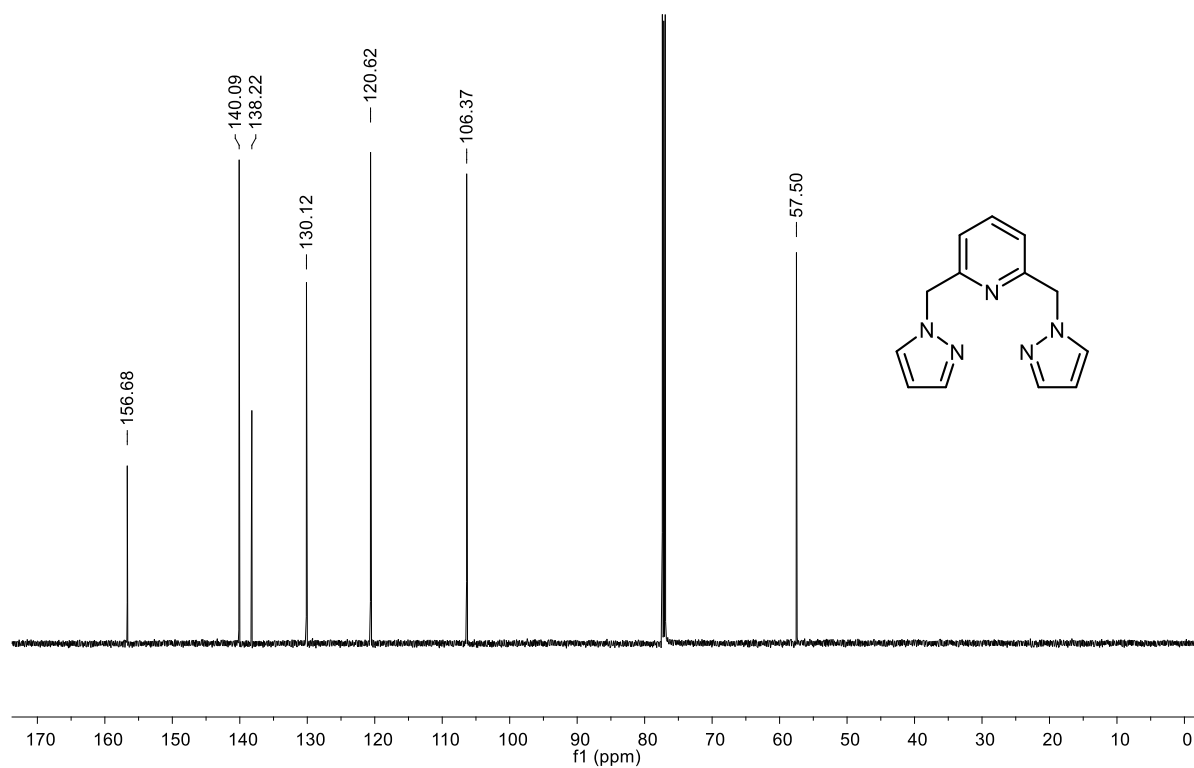


Figure S3.3 ¹³C NMR (151 MHz, CDCl₃) spectrum of ligand L5.1.

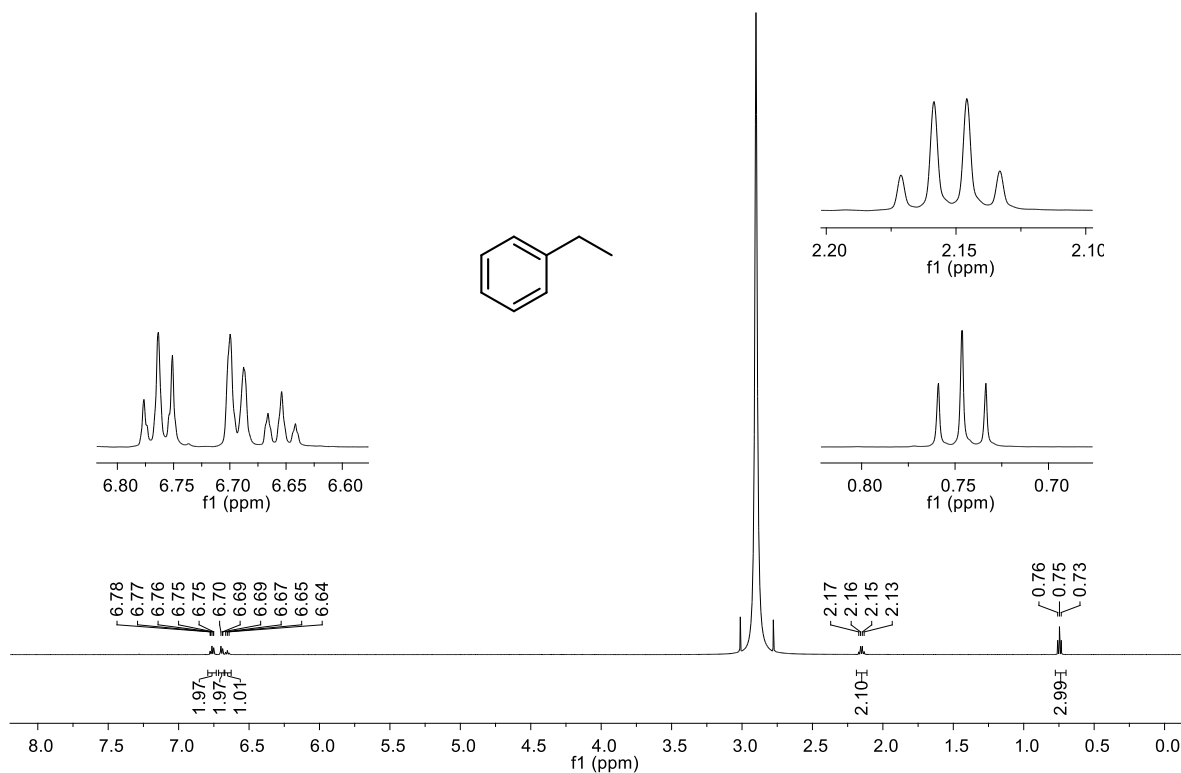


Figure S3.4 ¹H NMR (600 MHz, CDCl₃) spectrum of ethylbenzene in MeOH.

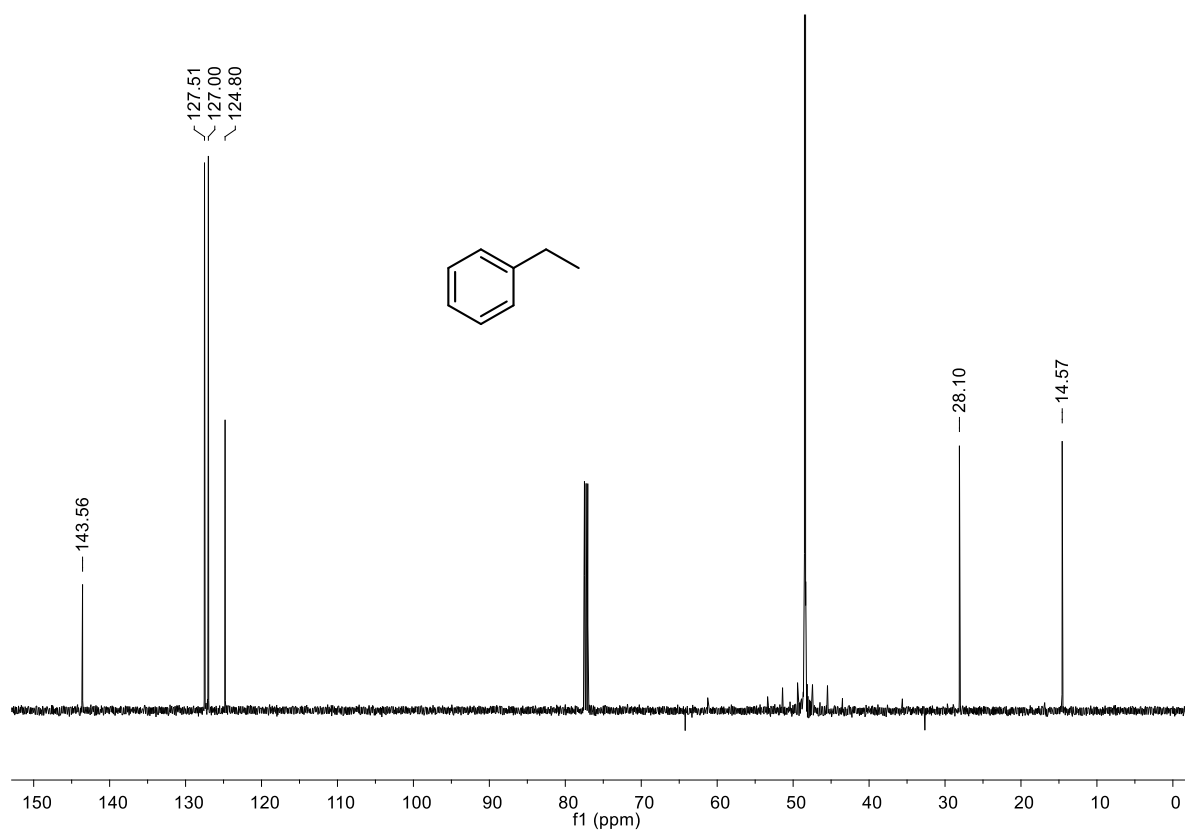


Figure S3.5 ¹³C NMR (151 MHz, CDCl₃) spectrum of ethylbenzene in MeOH.

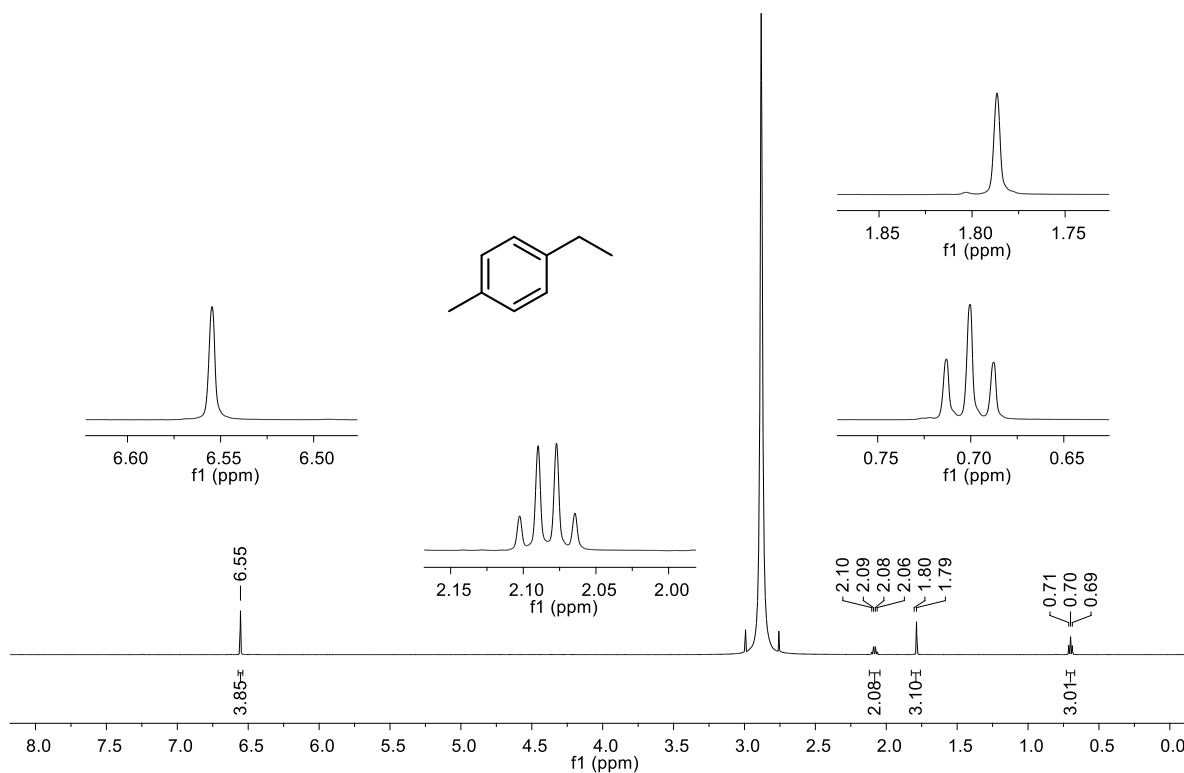


Figure S3.6 ¹H NMR (600 MHz, CDCl₃) spectrum of 1-ethyl-4-methylbenzene in MeOH.

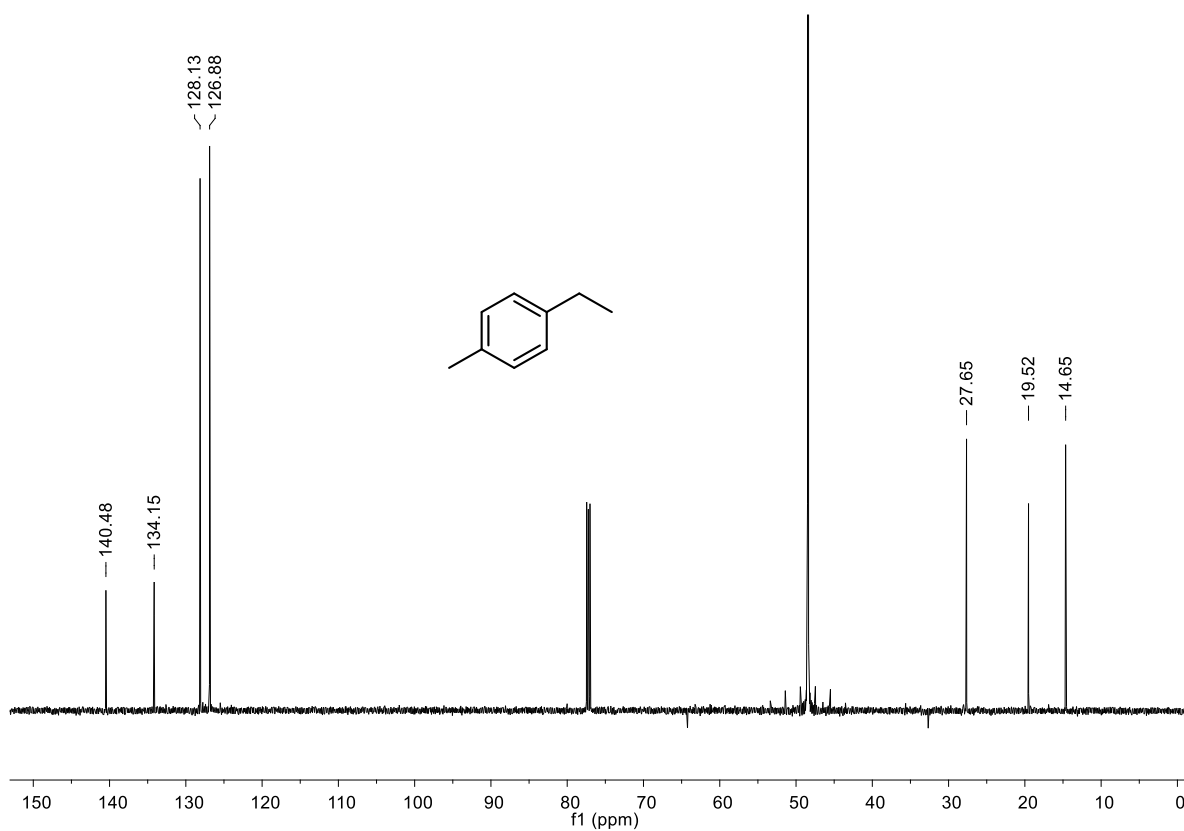


Figure S3.7 ¹³C NMR (151 MHz, CDCl₃) spectrum of 1-ethyl-4-methylbenzene in MeOH.

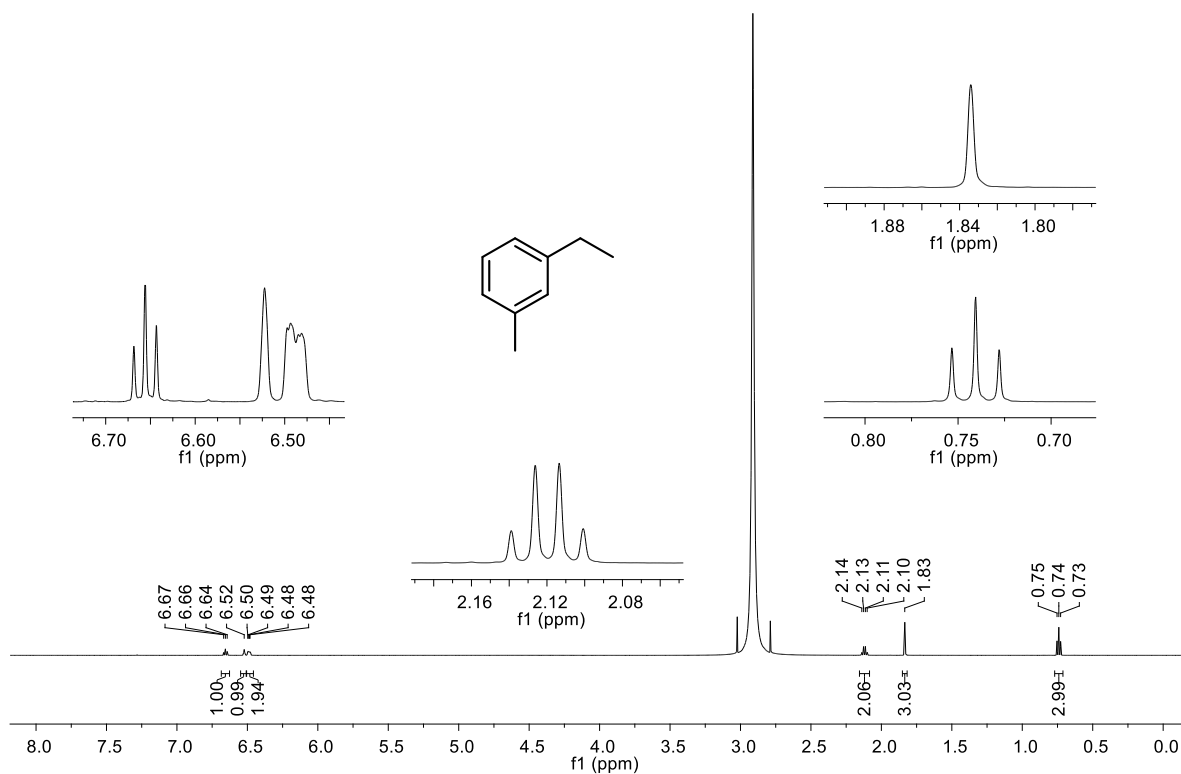


Figure S3.8 ¹H NMR (600 MHz, CDCl₃) spectrum of 1-ethyl-3-methylbenzene in MeOH.

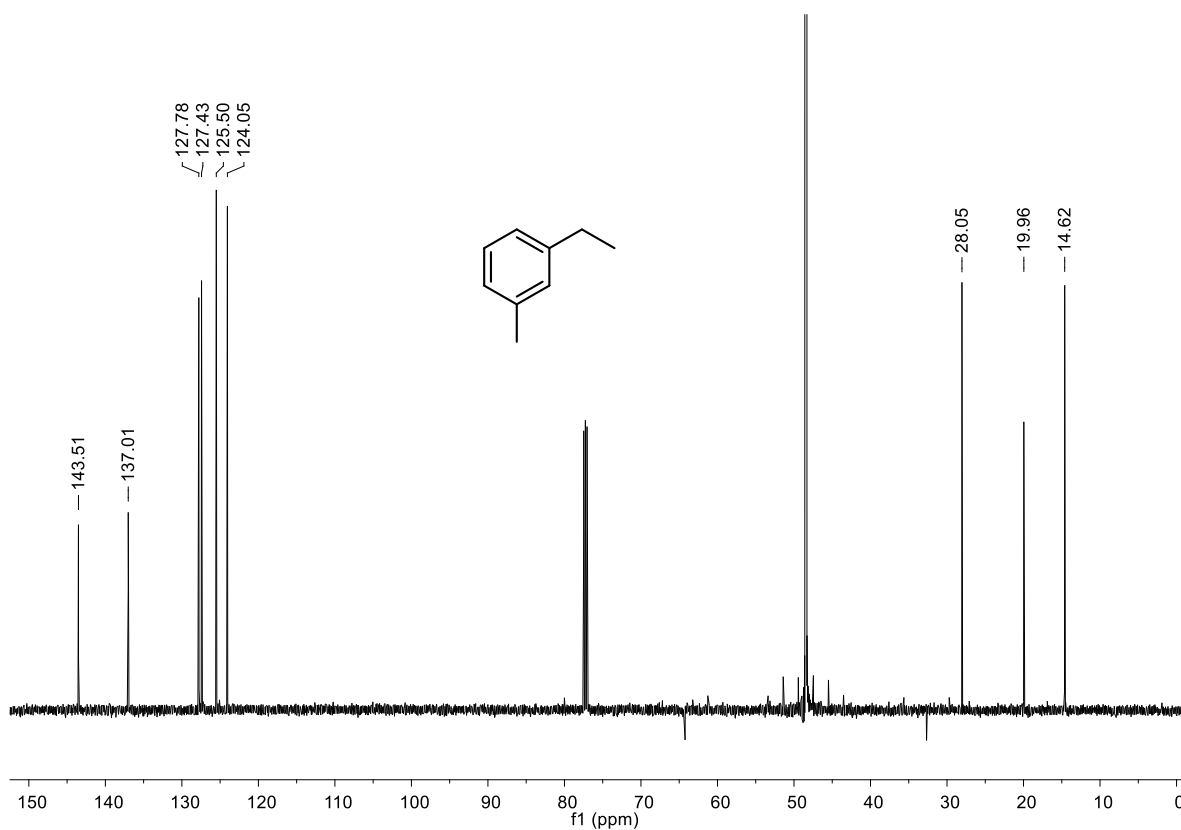


Figure S3.9 ¹³C NMR (151 MHz, CDCl₃) spectrum of 1-ethyl-3-methylbenzene in MeOH.

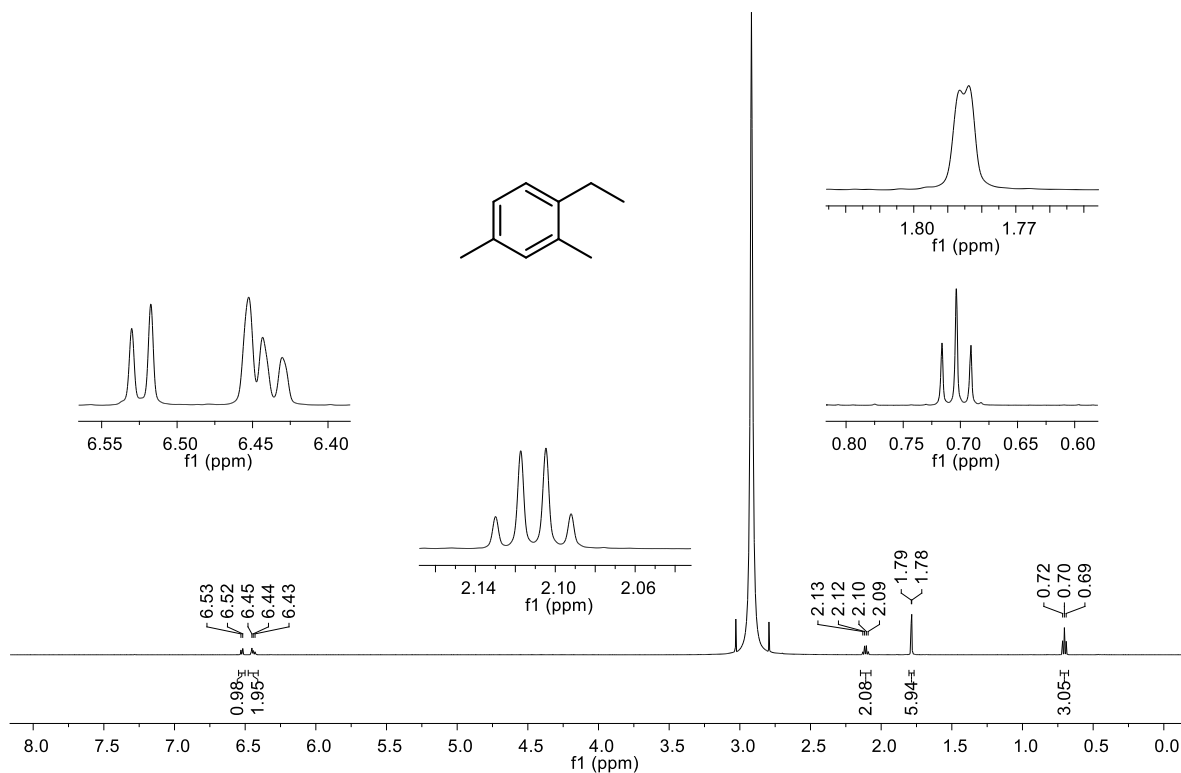


Figure S3.10 ¹H NMR (600 MHz, CDCl₃) spectrum of 1-ethyl-2,4-dimethylbenzene in MeOH.

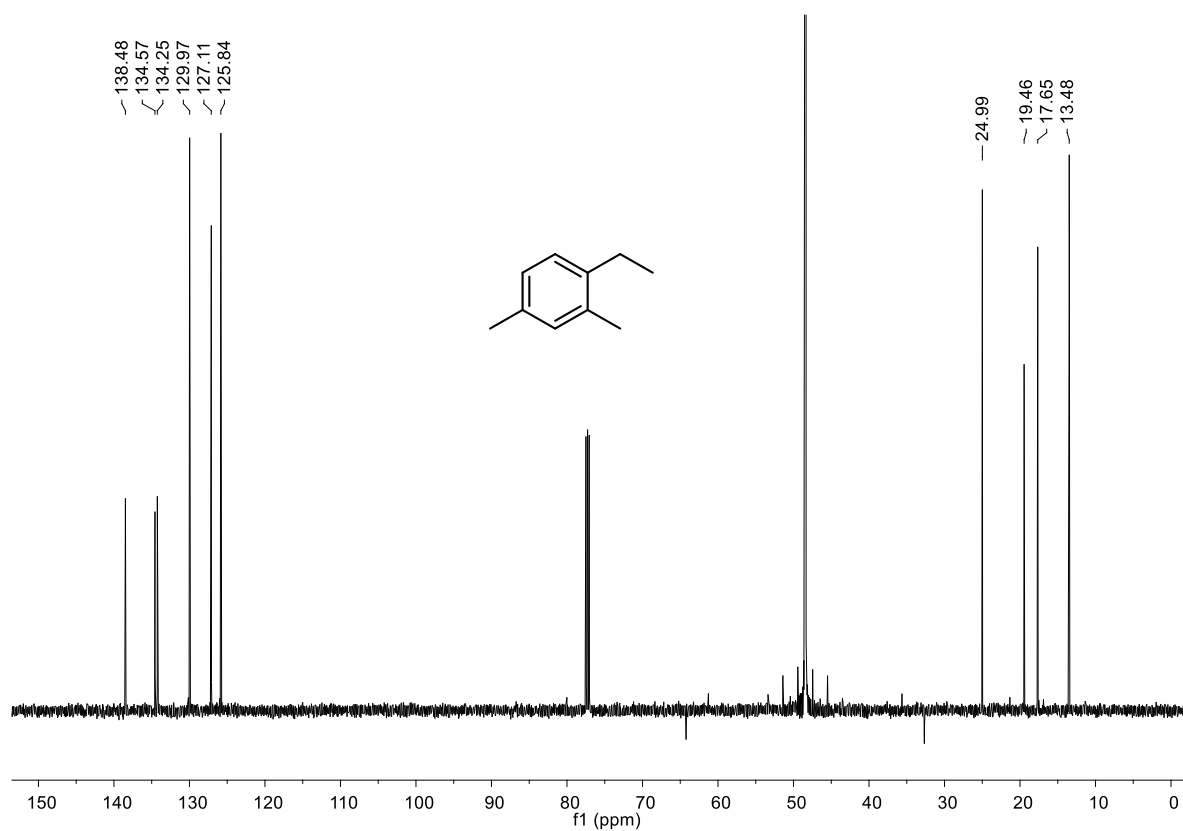


Figure S3.11 ¹³C NMR (151 MHz, CDCl₃) spectrum of 1-ethyl-2,4-dimethylbenzene in MeOH.

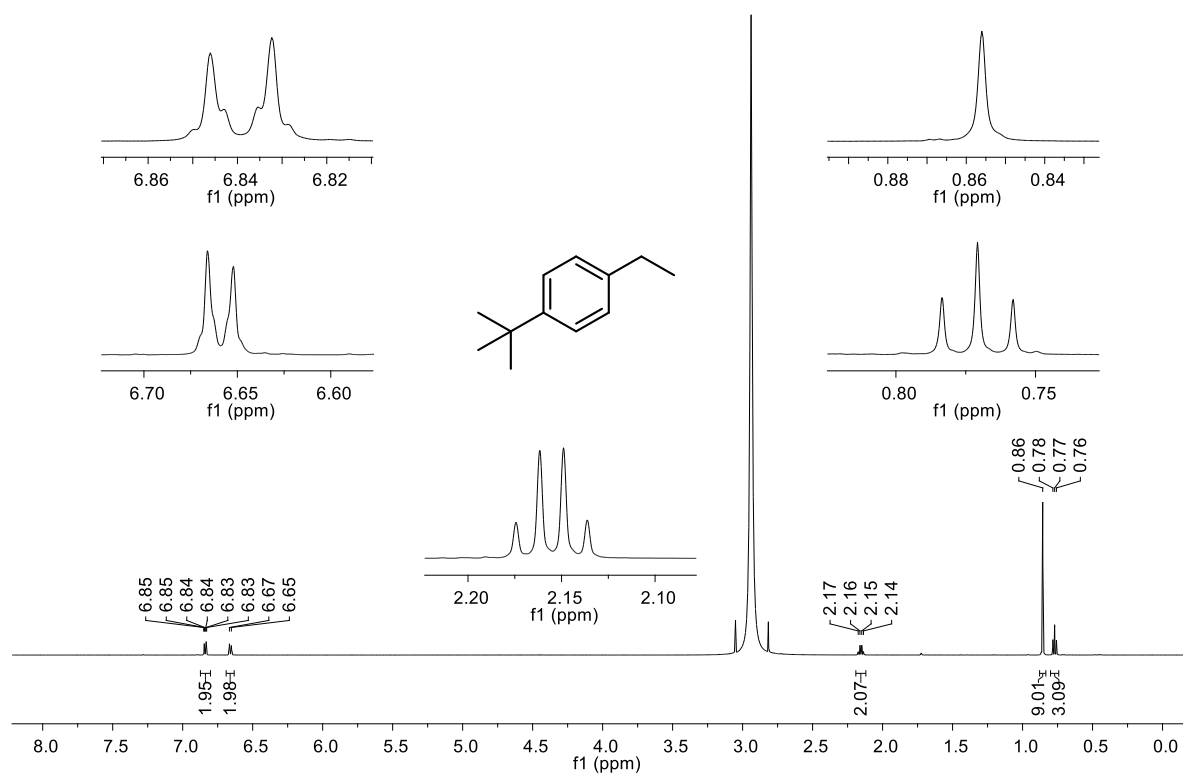


Figure S3.12 ^1H NMR (600 MHz, CDCl_3) spectrum of 1-(tert-butyl)-4-ethylbenzene in MeOH.

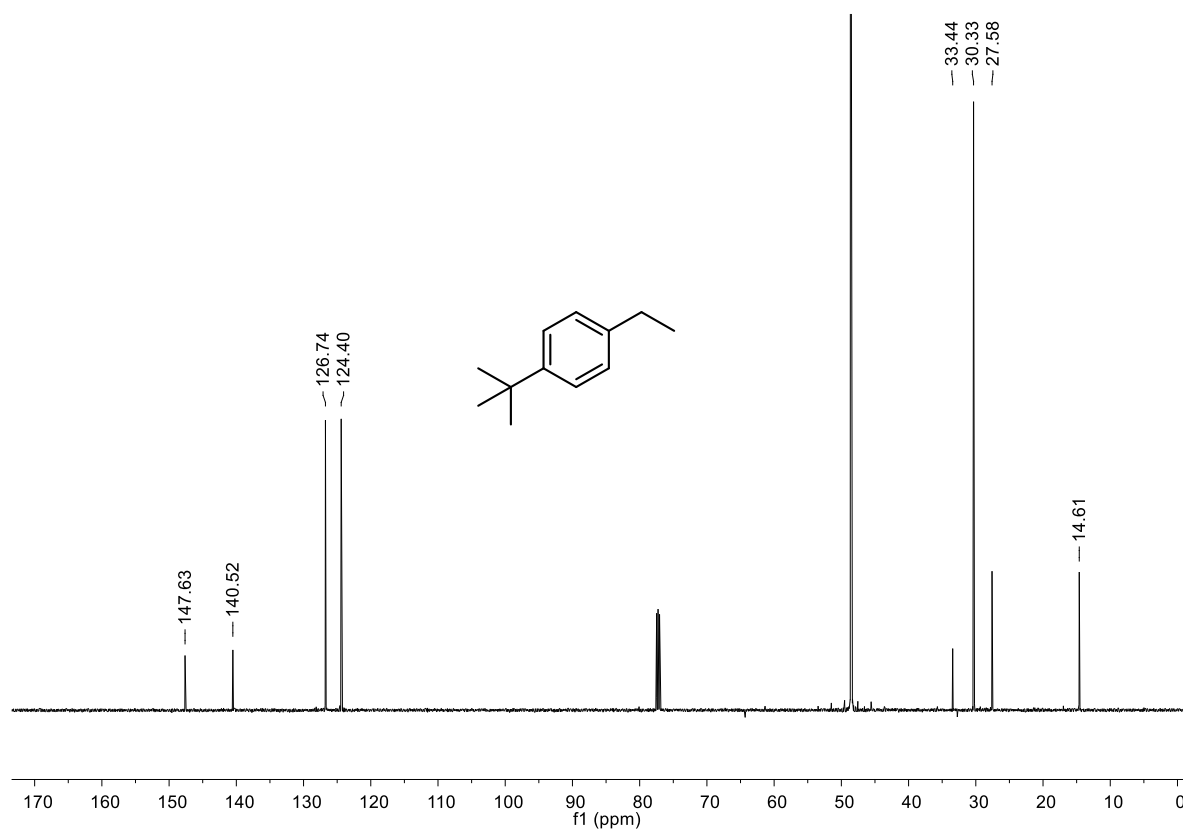


Figure S3.13 ^{13}C NMR (151 MHz, CDCl_3) spectrum of 1-(tert-butyl)-4-ethylbenzene in MeOH.

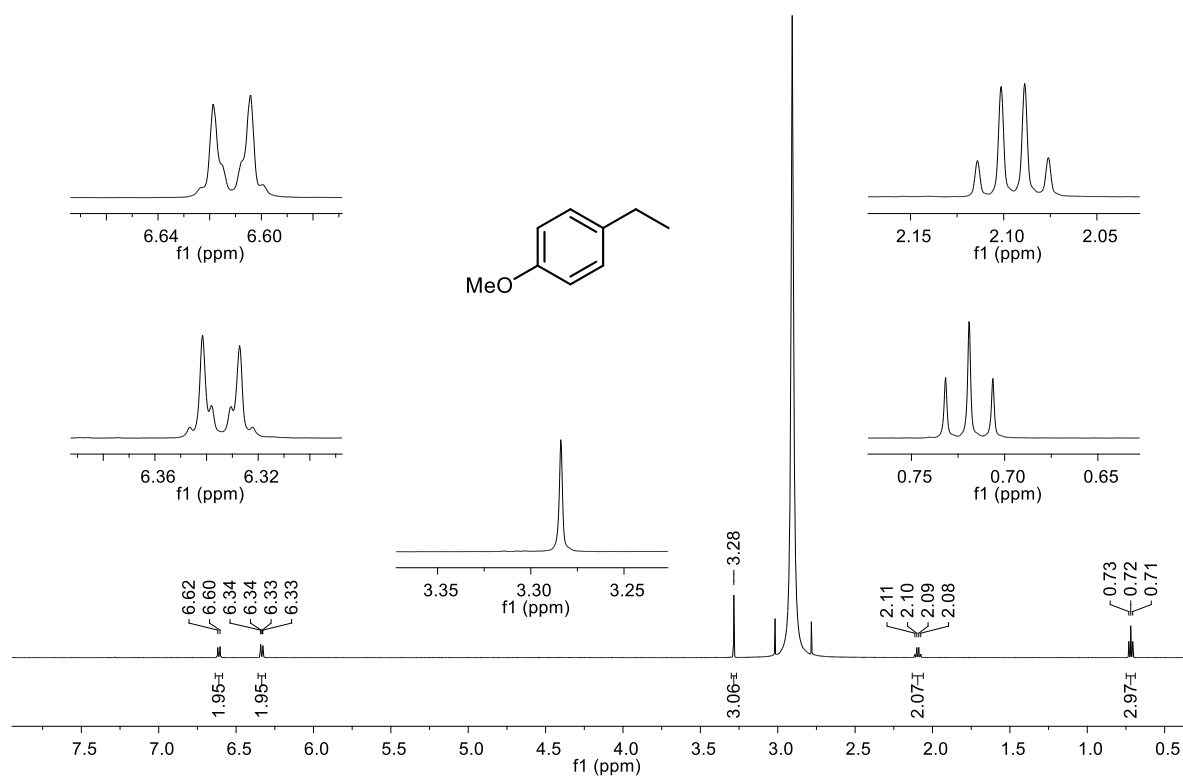


Figure S3.14 ^1H NMR (600 MHz, CDCl_3) spectrum of 1-ethyl-4-methoxybenzene in MeOH.

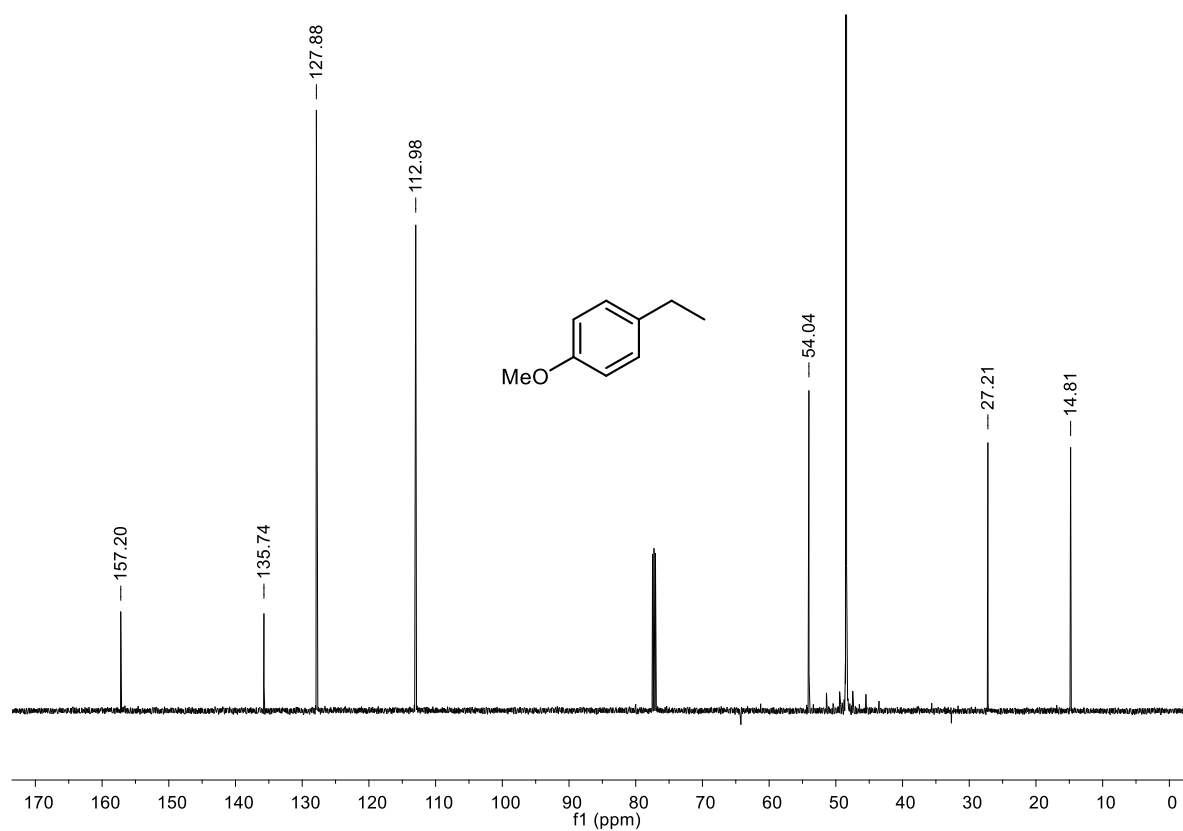


Figure S3.15 ^{13}C NMR (151 MHz, CDCl_3) spectrum of 1-ethyl-4-methoxybenzene in MeOH.

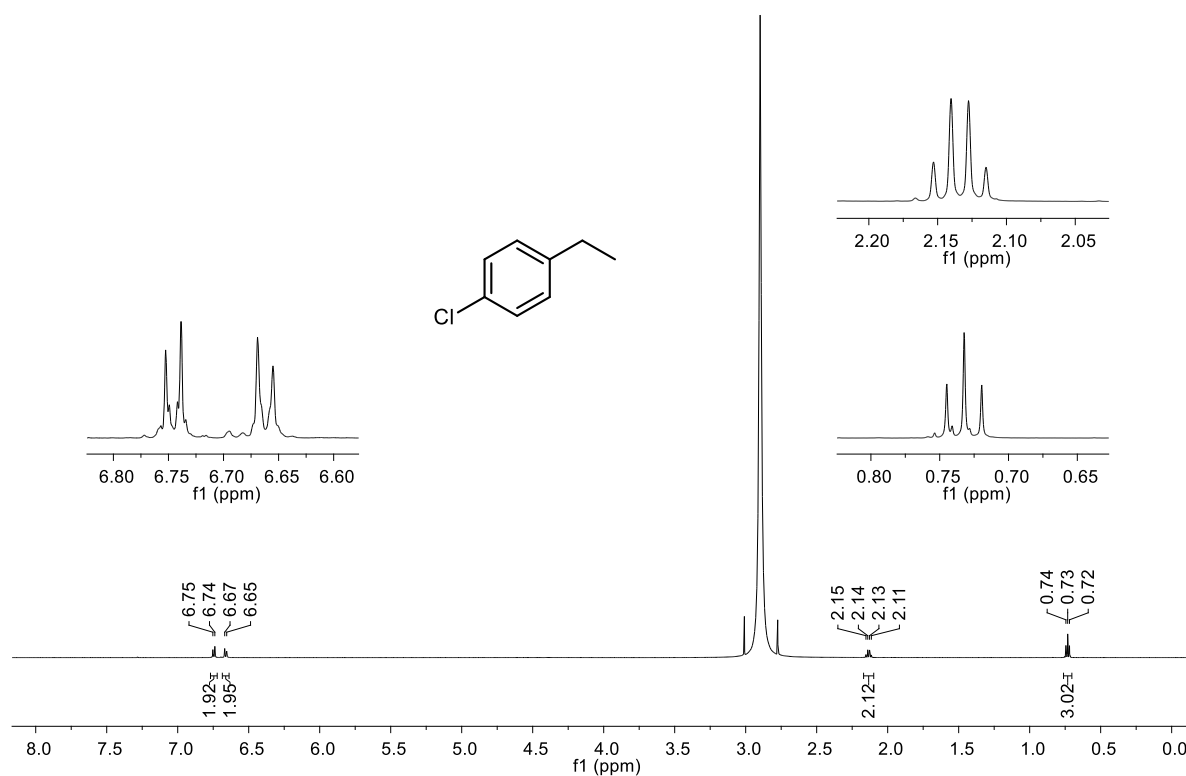


Figure S3.16 ¹H NMR (600 MHz, CDCl₃) spectrum of 1-chloro-4-ethylbenzene in MeOH.

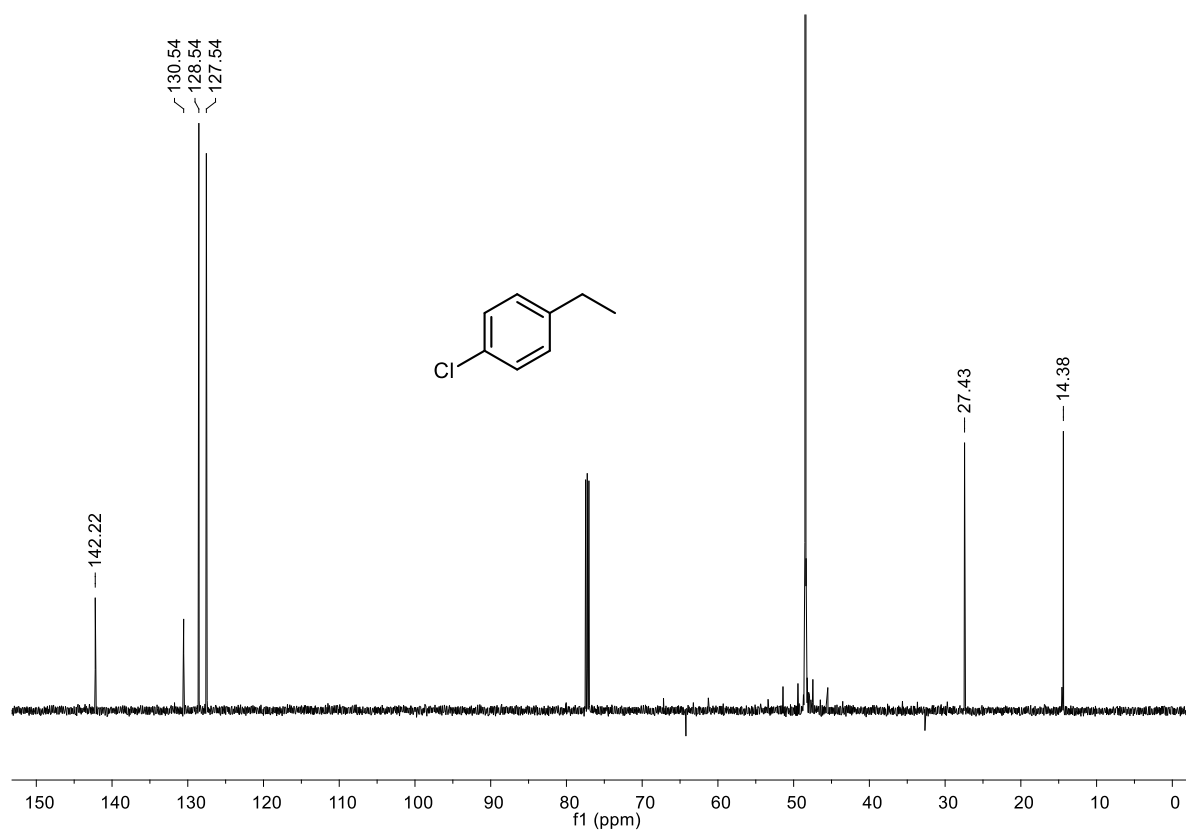


Figure S3.17 ¹³C NMR (151 MHz, CDCl₃) spectrum of 1-chloro-4-ethylbenzene in MeOH.

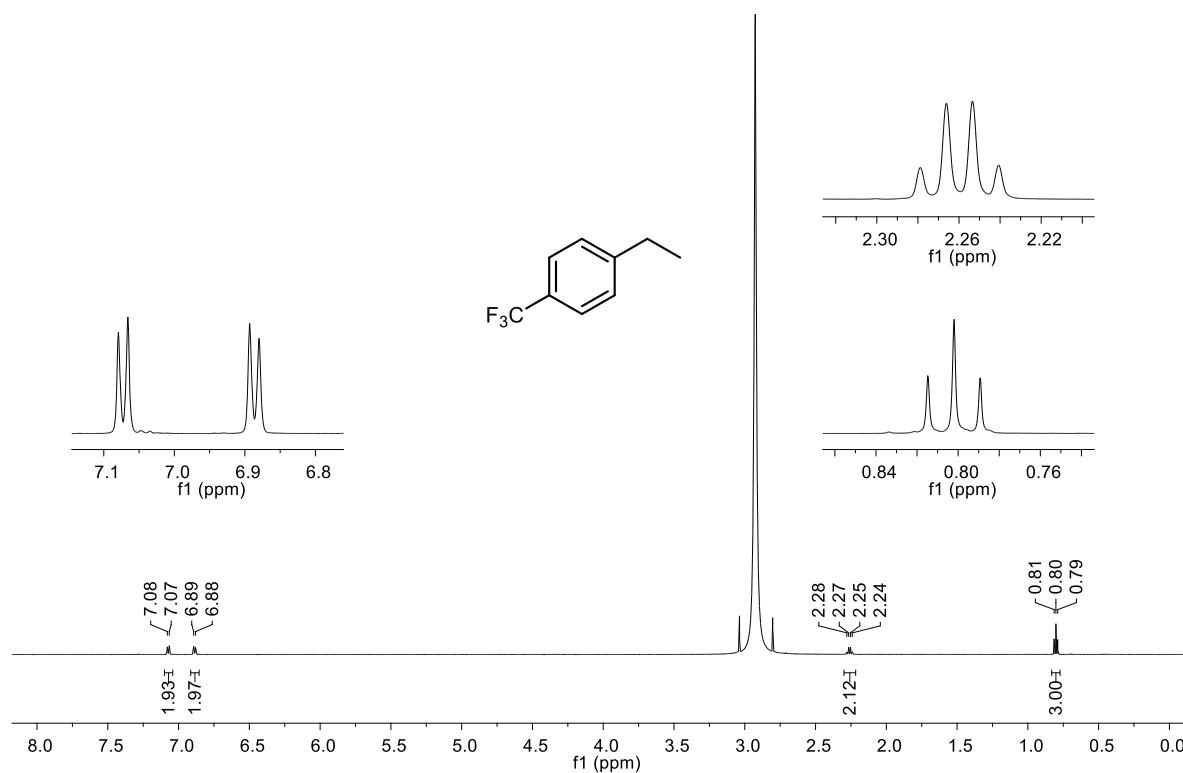


Figure S3.18 ¹H NMR (600 MHz, CDCl₃) spectrum of 1-ethyl-4-(trifluoromethyl)benzene in MeOH.

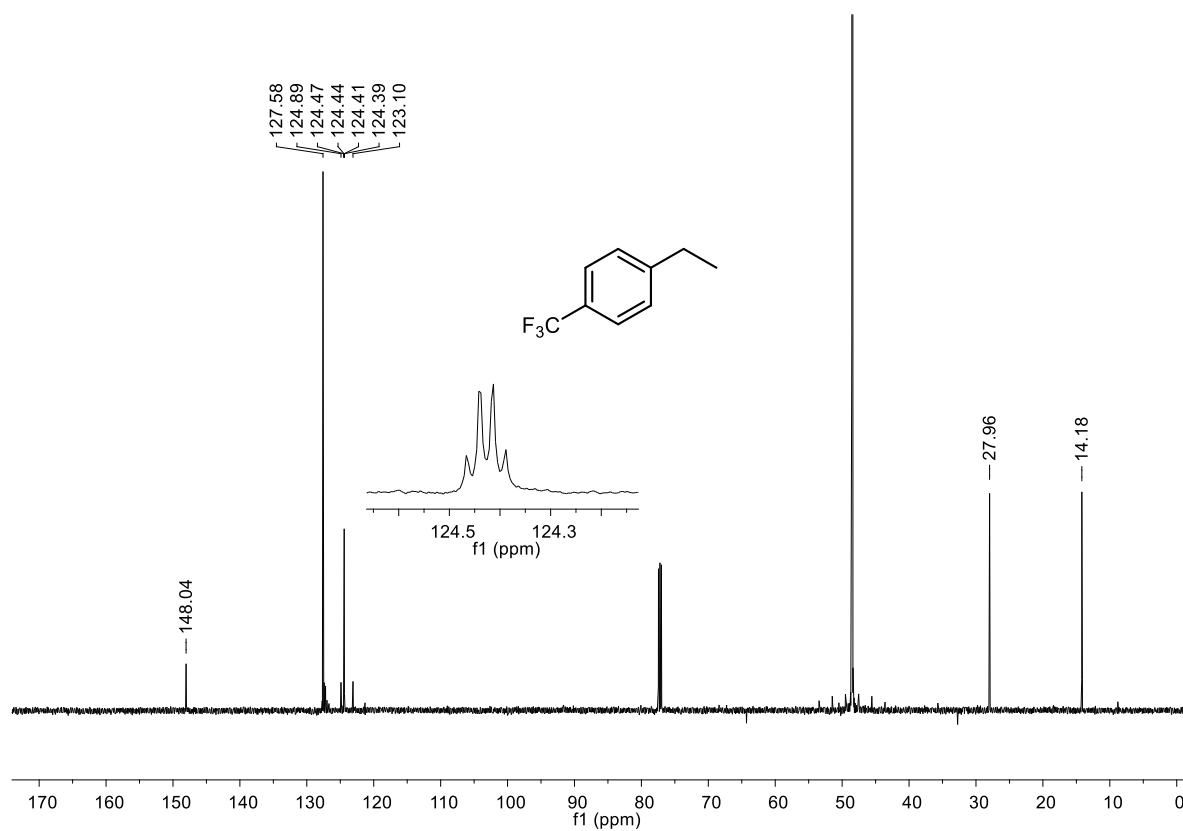


Figure S3.19 ¹³C NMR (151 MHz, CDCl₃) spectrum of 1-ethyl-4-(trifluoromethyl)benzene in MeOH.

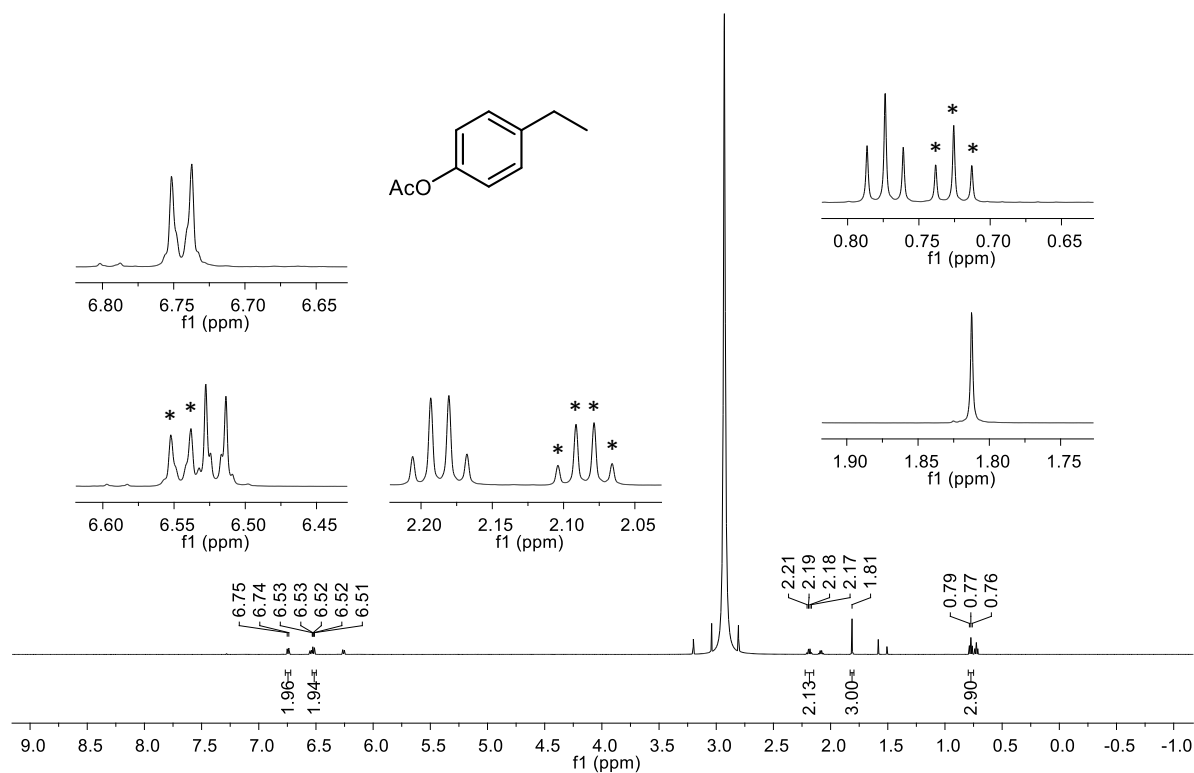


Figure S3.20 ^1H NMR (600 MHz, CDCl_3) spectrum of 4-ethylphenyl acetate in MeOH. * Indicates presence of 4-ethylphenol.

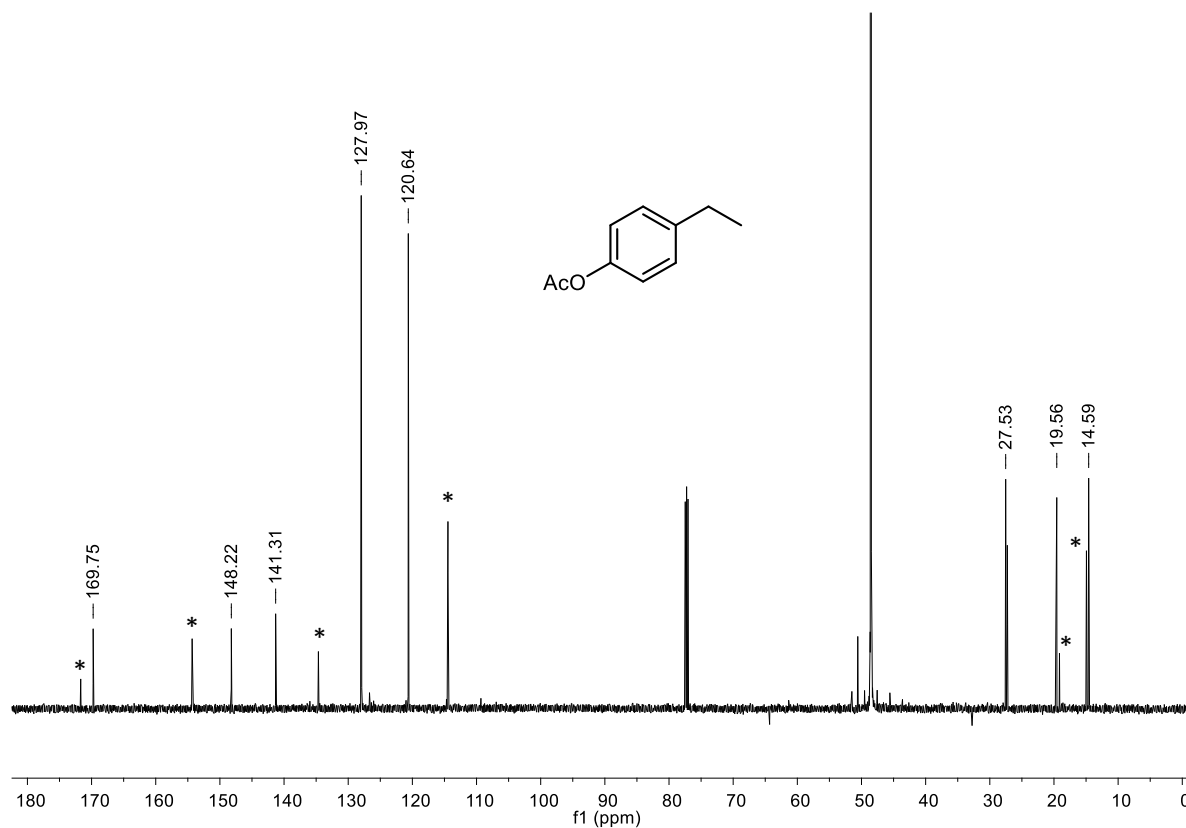


Figure S3.21 ^{13}C NMR (151 MHz, CDCl_3) spectrum of 4-ethylphenyl acetate in MeOH. * Indicates presence of 4-ethylphenol.

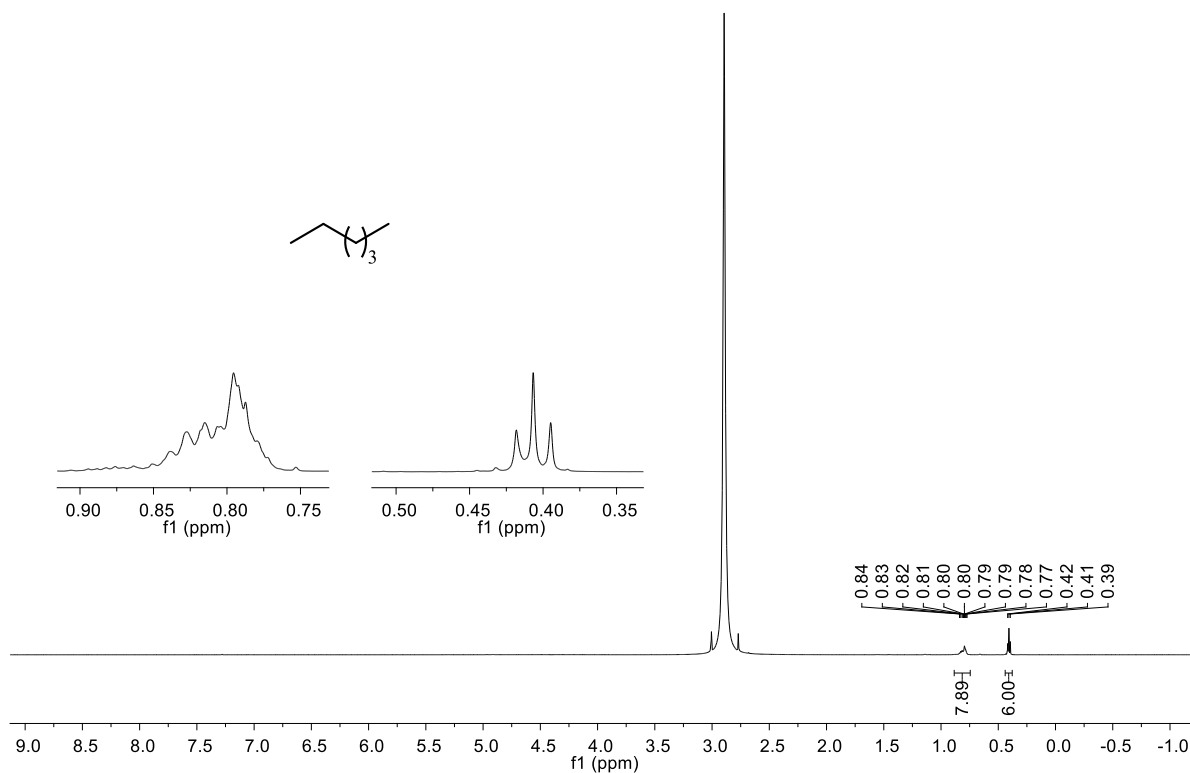


Figure S3.22 ¹H NMR (600 MHz, CDCl₃) spectrum of hexane in MeOH.

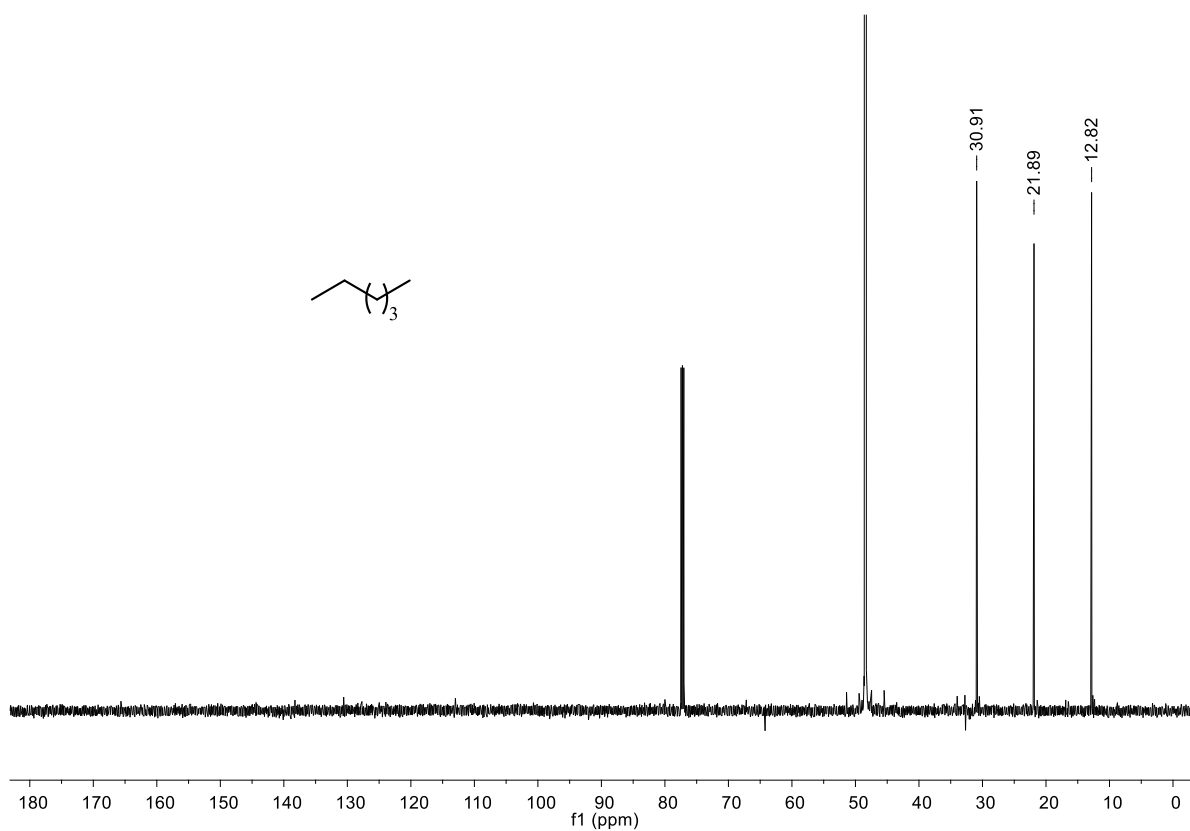


Figure S3.23 ¹³C NMR (151 MHz, CDCl₃) spectrum of hexane in MeOH.

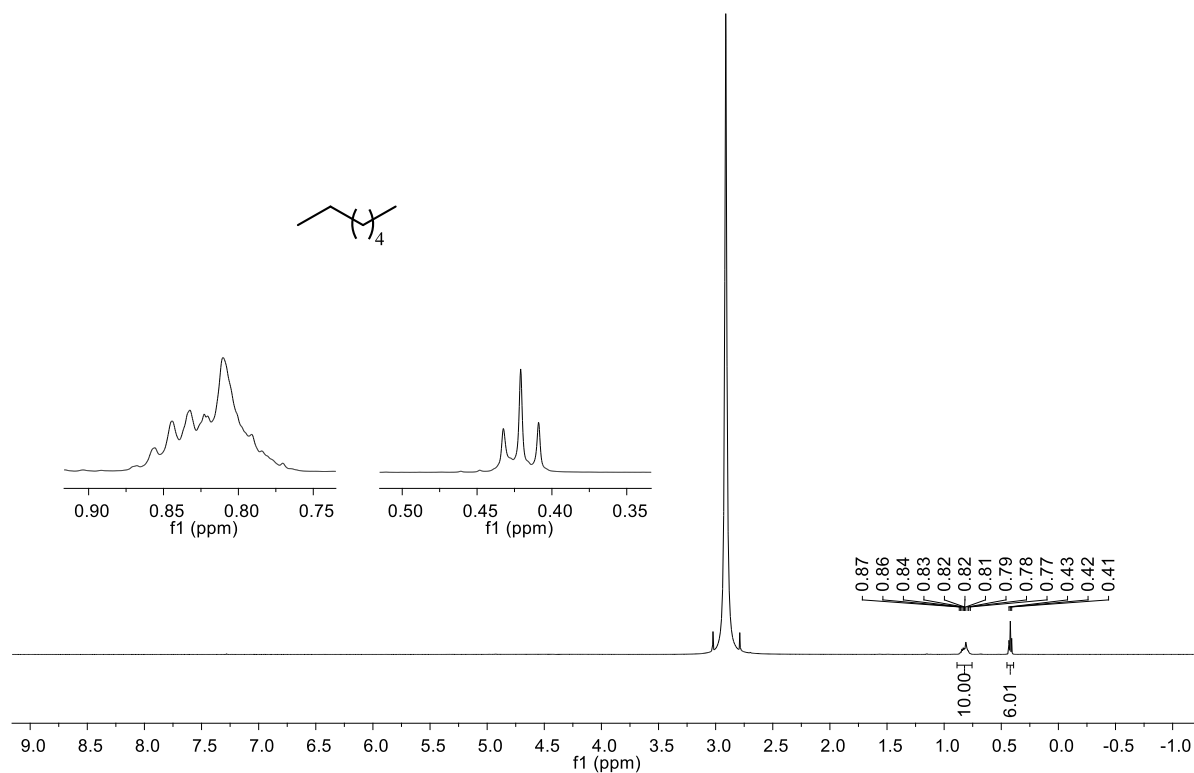


Figure S3.24 ¹H NMR (600 MHz, CDCl₃) spectrum of heptane in MeOH.

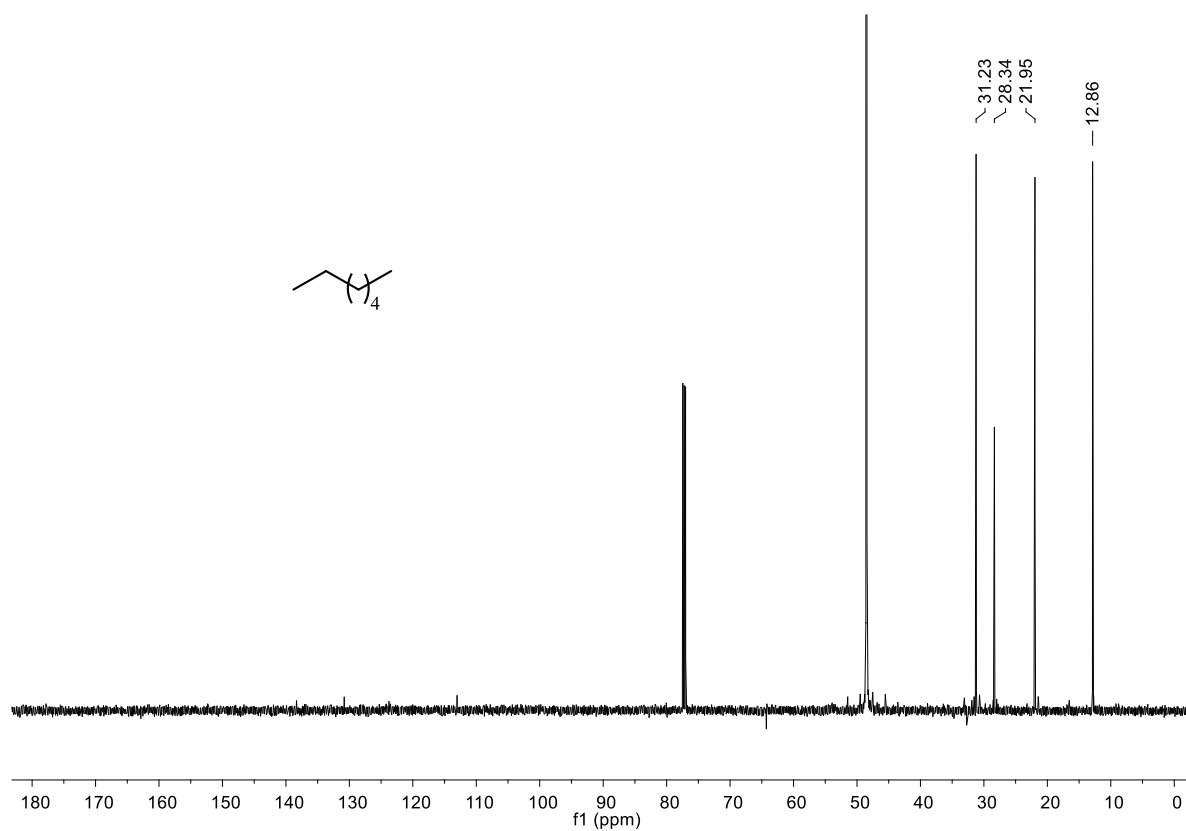


Figure S3.25 ¹³C NMR (151 MHz, CDCl₃) spectrum of heptane in MeOH.

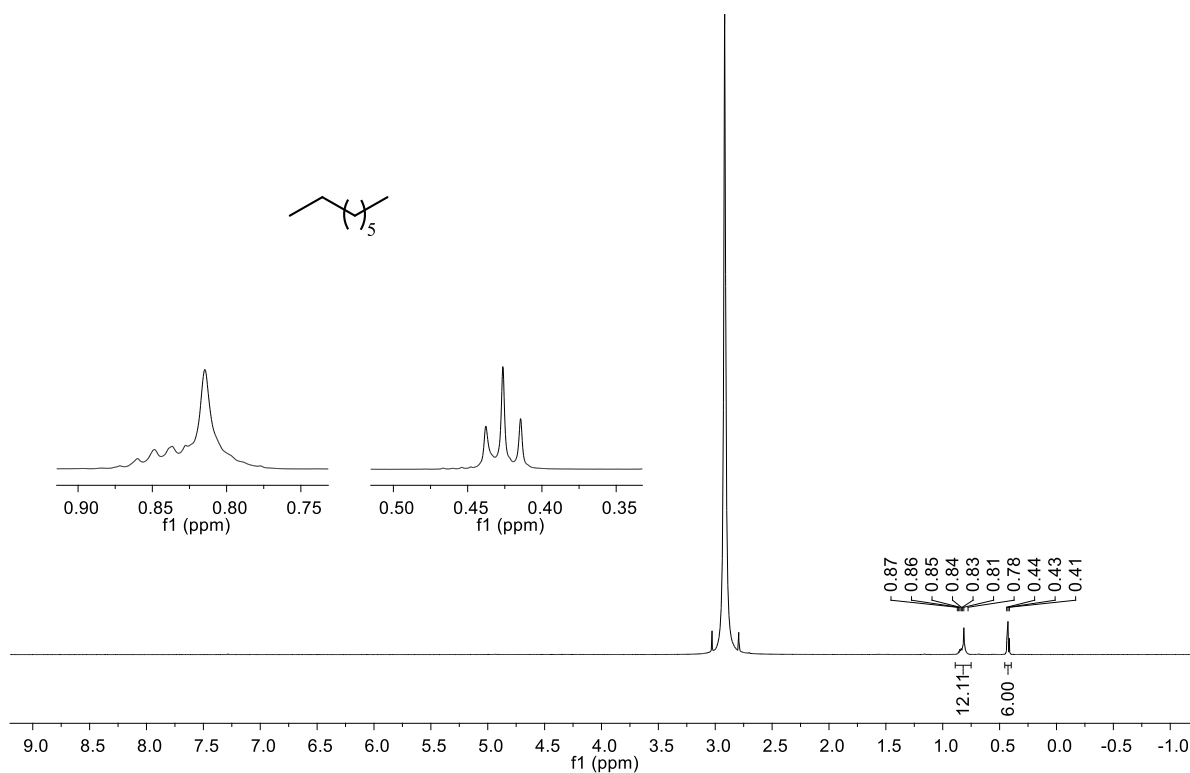


Figure S3.26 ¹H NMR (600 MHz, CDCl₃) spectrum of octane in MeOH.

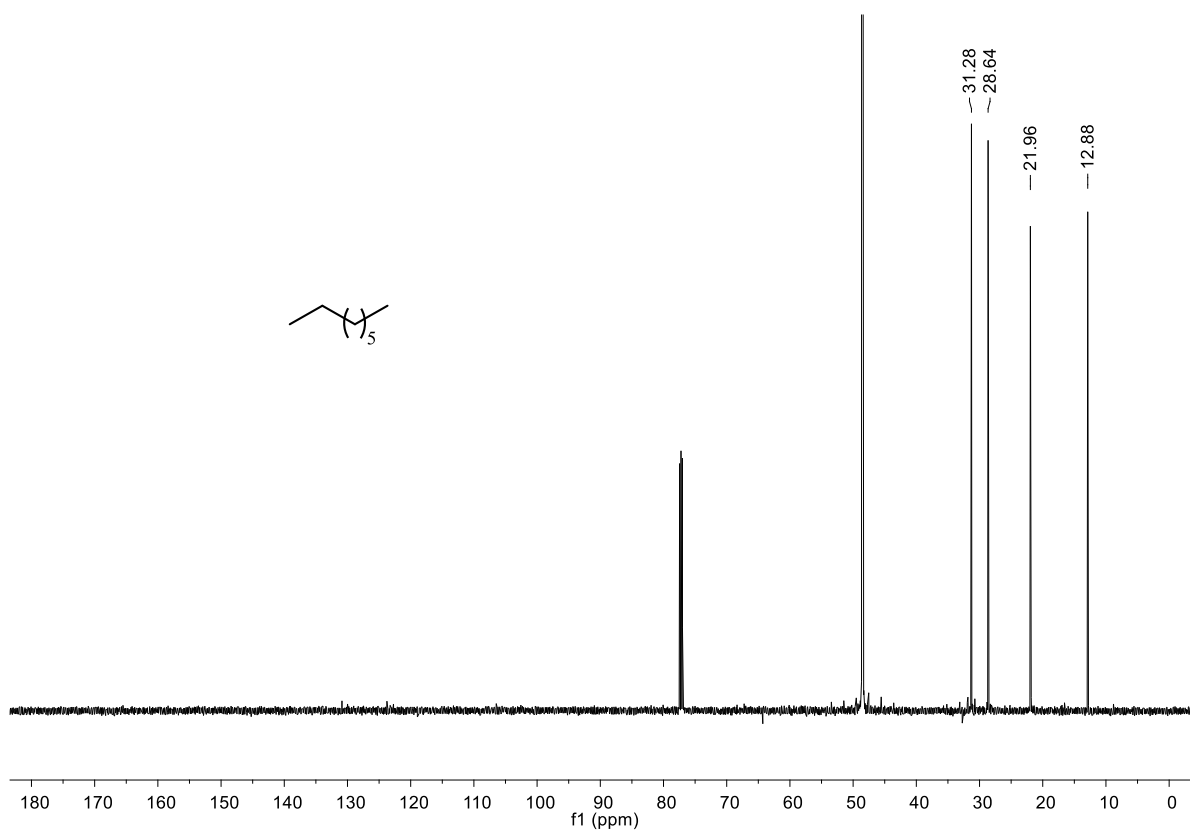


Figure S3.27 ¹³C NMR (151 MHz, CDCl₃) spectrum of octane in MeOH.

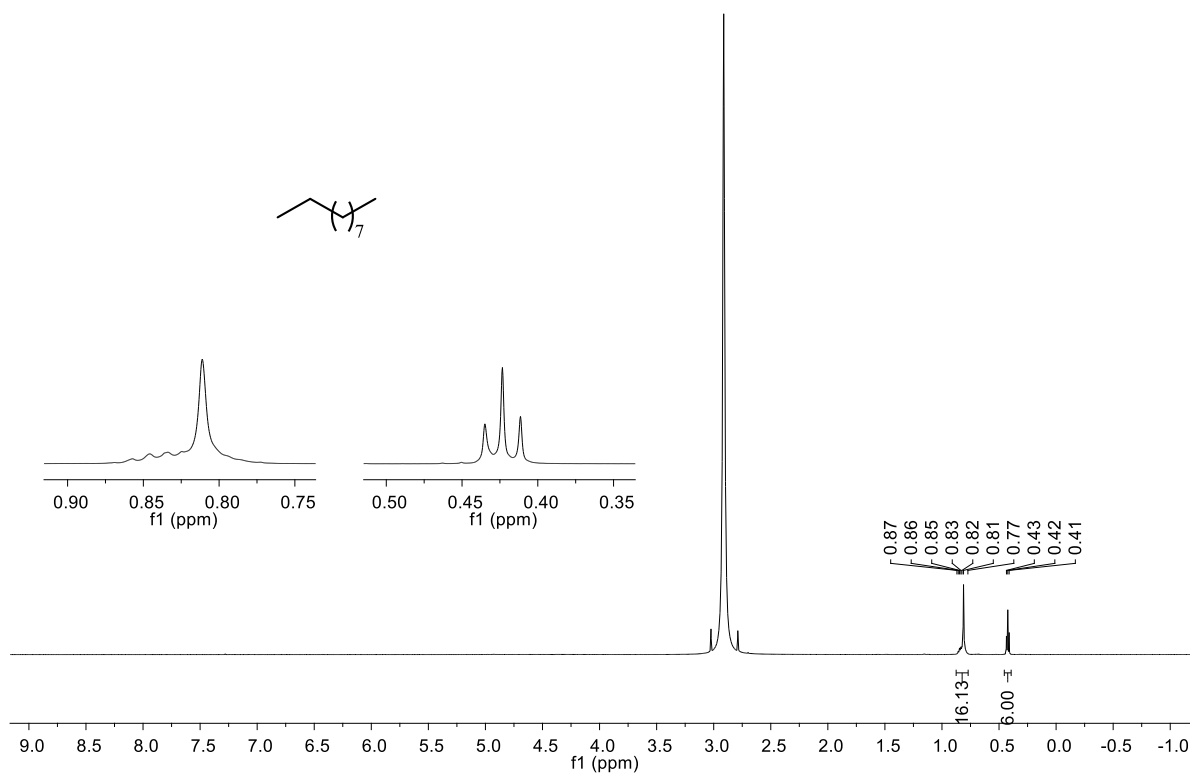


Figure S3.28 ¹H NMR (600 MHz, CDCl₃) spectrum of decane in MeOH.

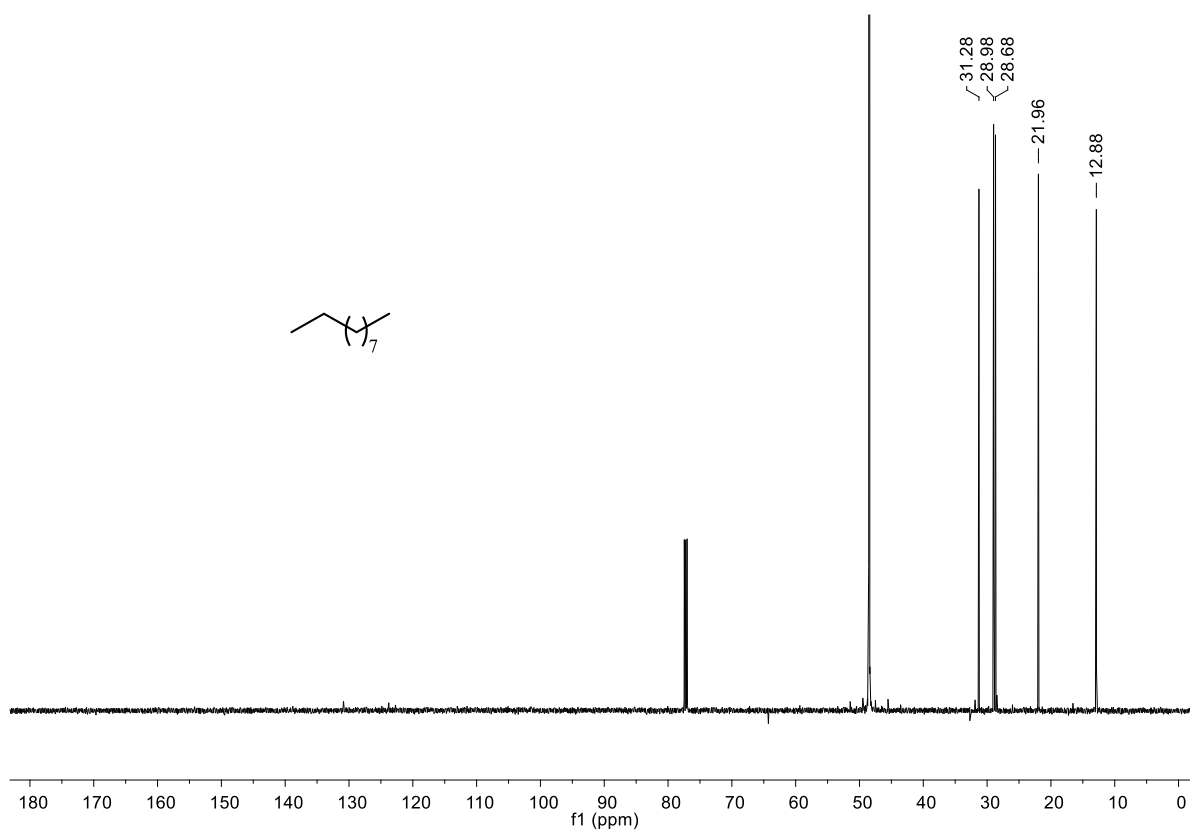


Figure S3.29 ¹³C NMR (151 MHz, CDCl₃) spectrum of decane in MeOH.

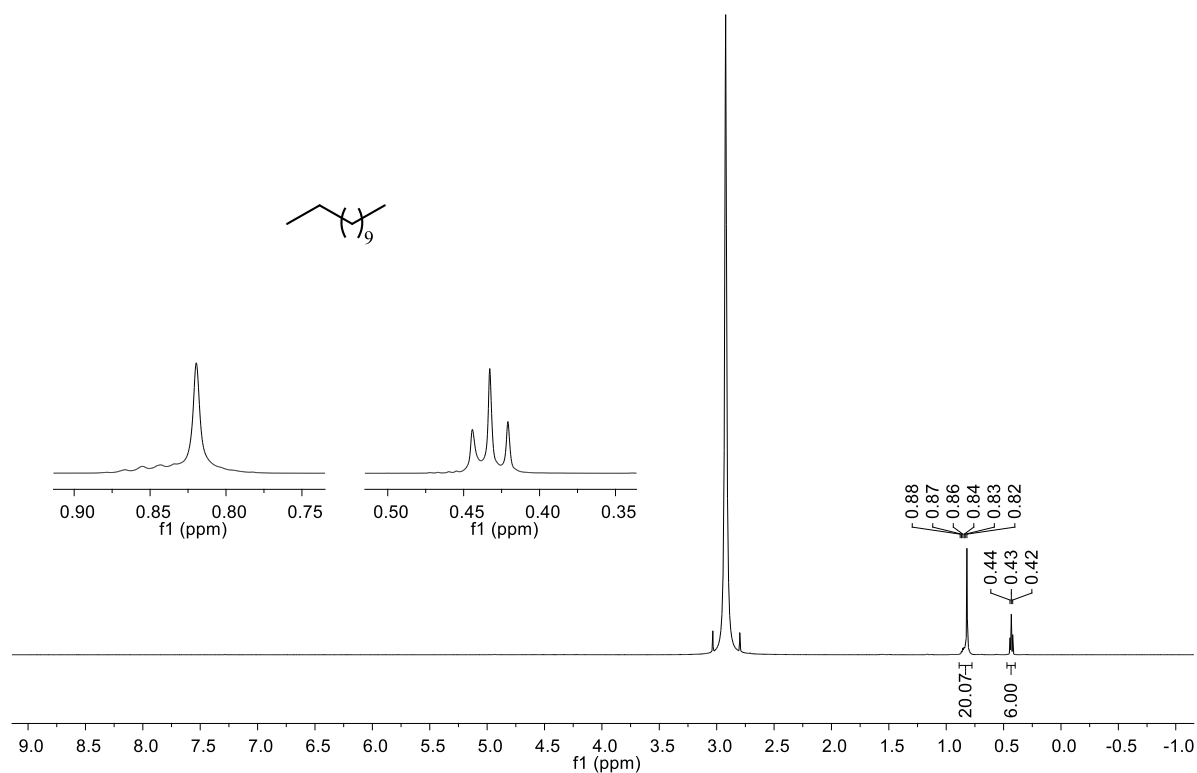


Figure S3.30 ¹H NMR (600 MHz, CDCl₃) spectrum of dodecane in MeOH.

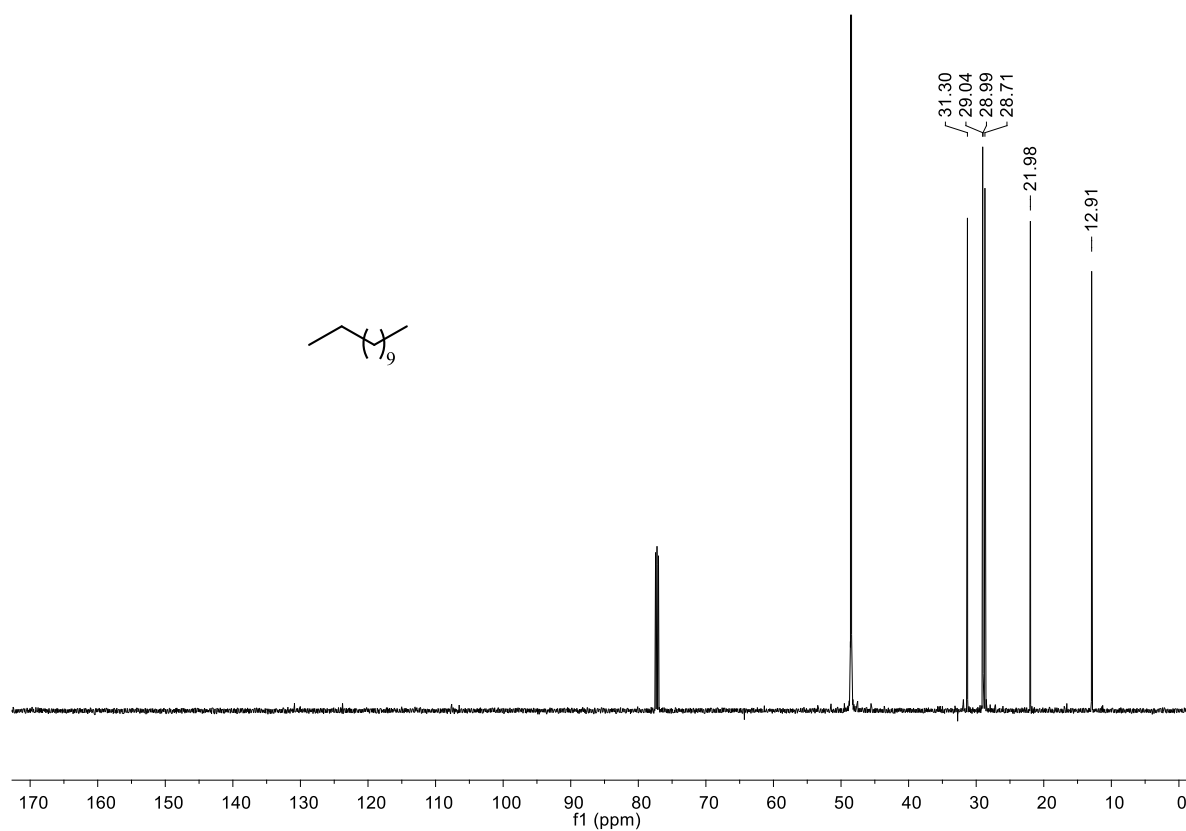


Figure S3.31 ¹³C NMR (151 MHz, CDCl₃) spectrum of dodecane in MeOH.

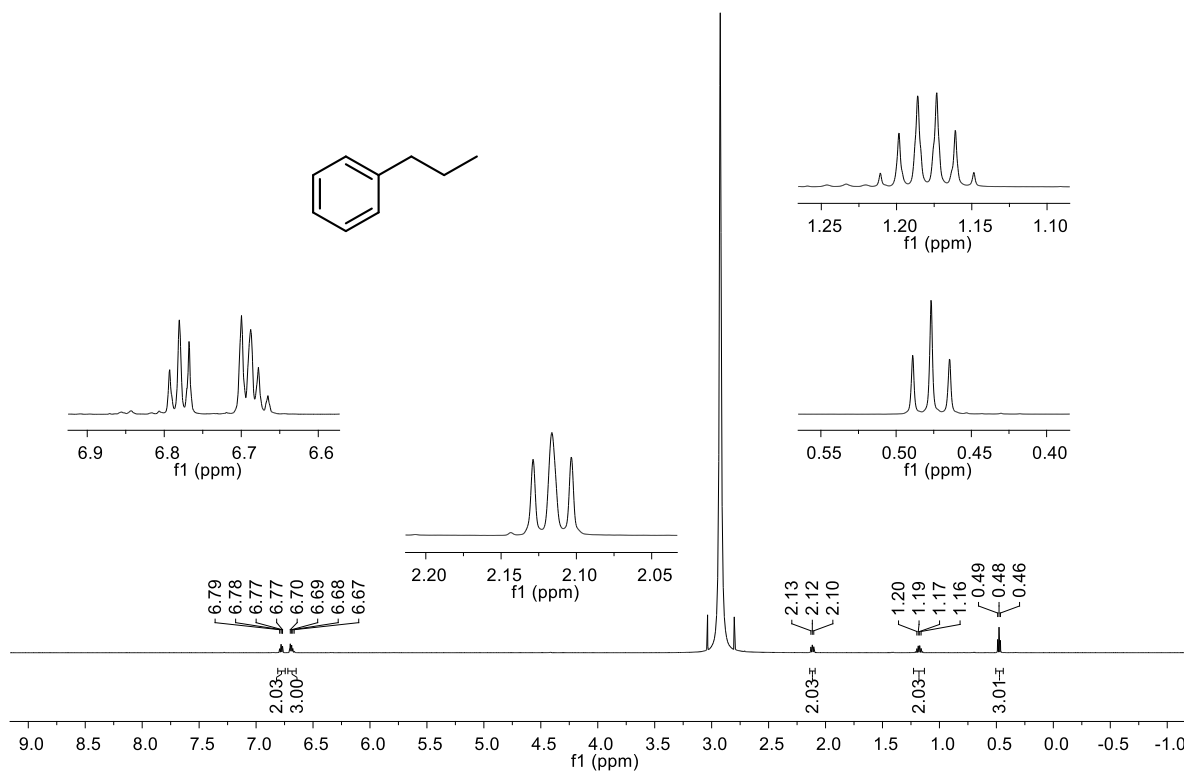


Figure S3.32 ¹H NMR (600 MHz, CDCl₃) spectrum of propylbenzene in MeOH.

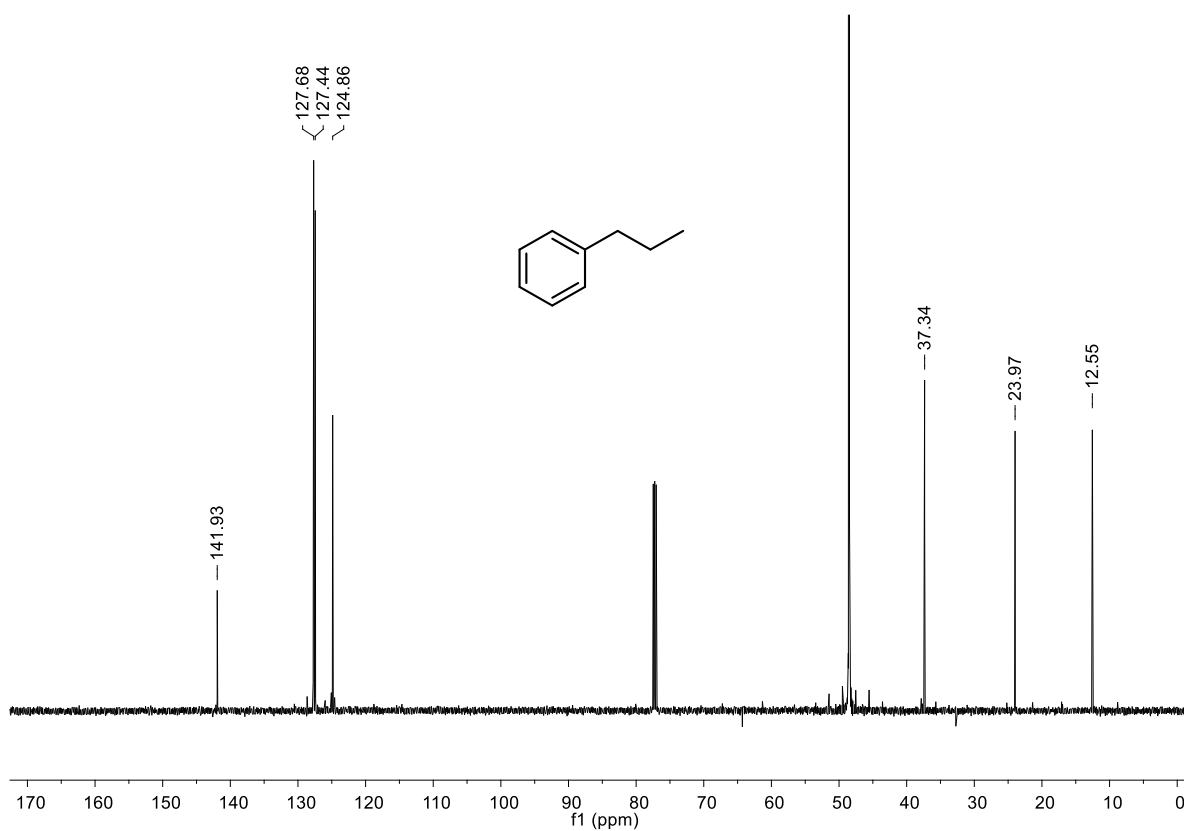


Figure S3.33 ¹³C NMR (151 MHz, CDCl₃) spectrum of propylbenzene in MeOH.

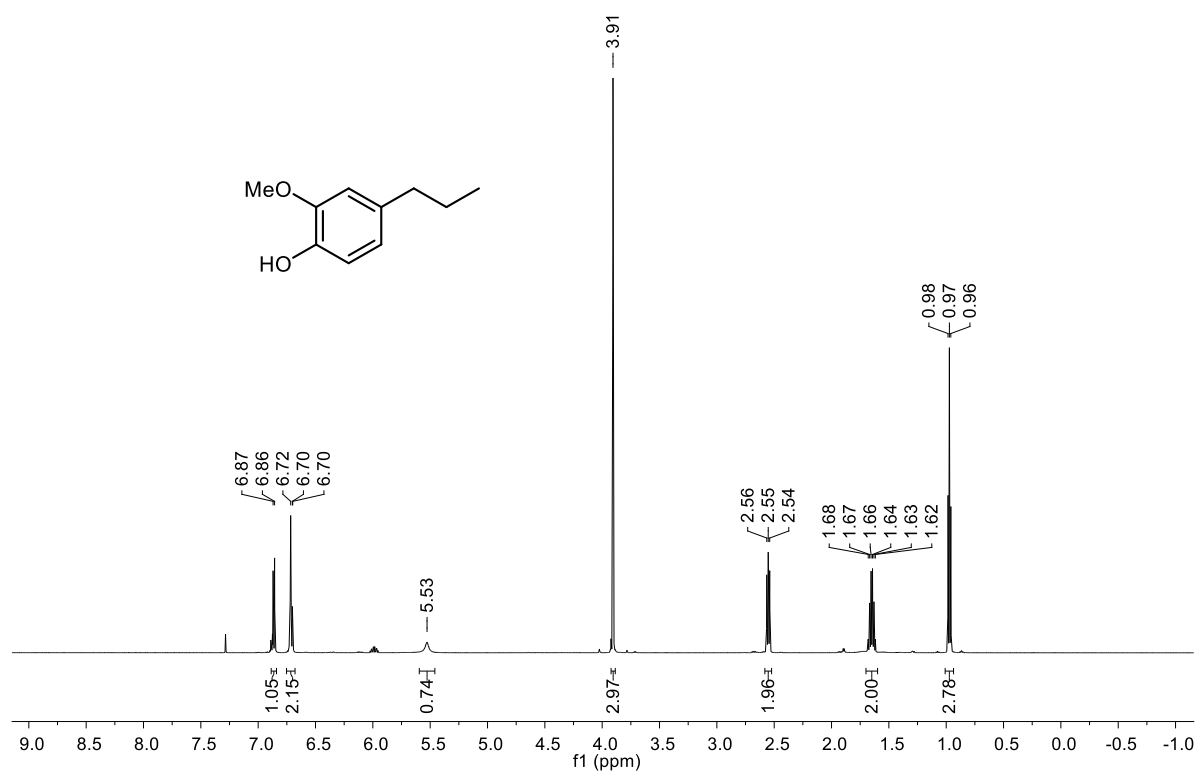


Figure S3.34 ¹H NMR (600 MHz, CDCl₃) spectrum of 2-methoxy-4-propylphenol.

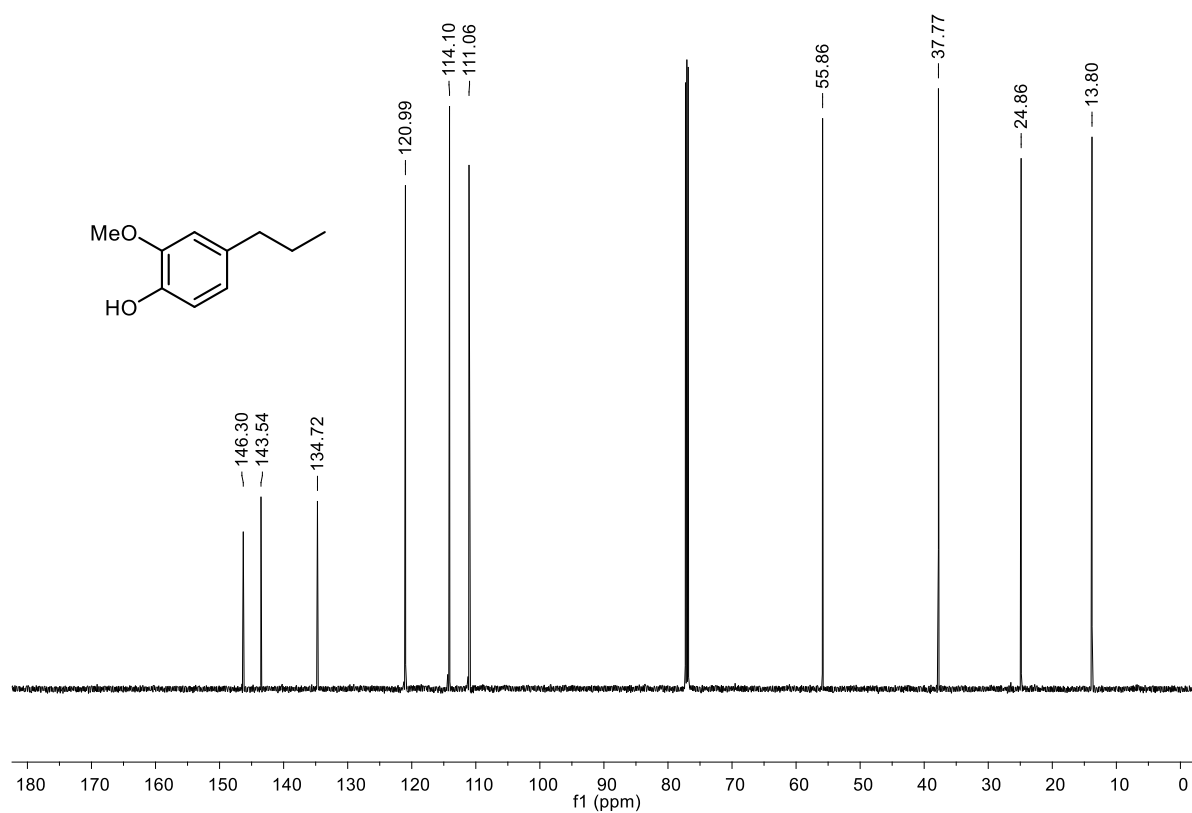


Figure S3.35 ¹³C NMR (151 MHz, CDCl₃) spectrum of 2-methoxy-4-propylphenol.

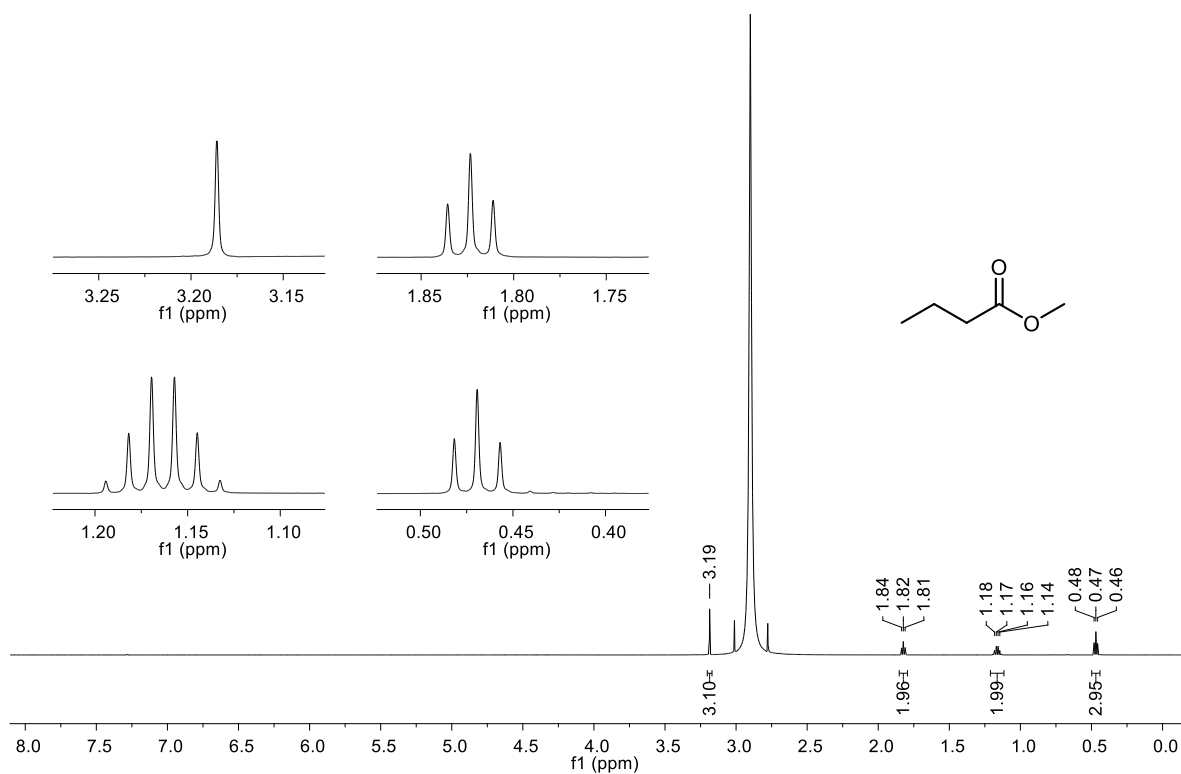


Figure S3.36 ^1H NMR (600 MHz, CDCl_3) spectrum of methyl butanoate in MeOH.

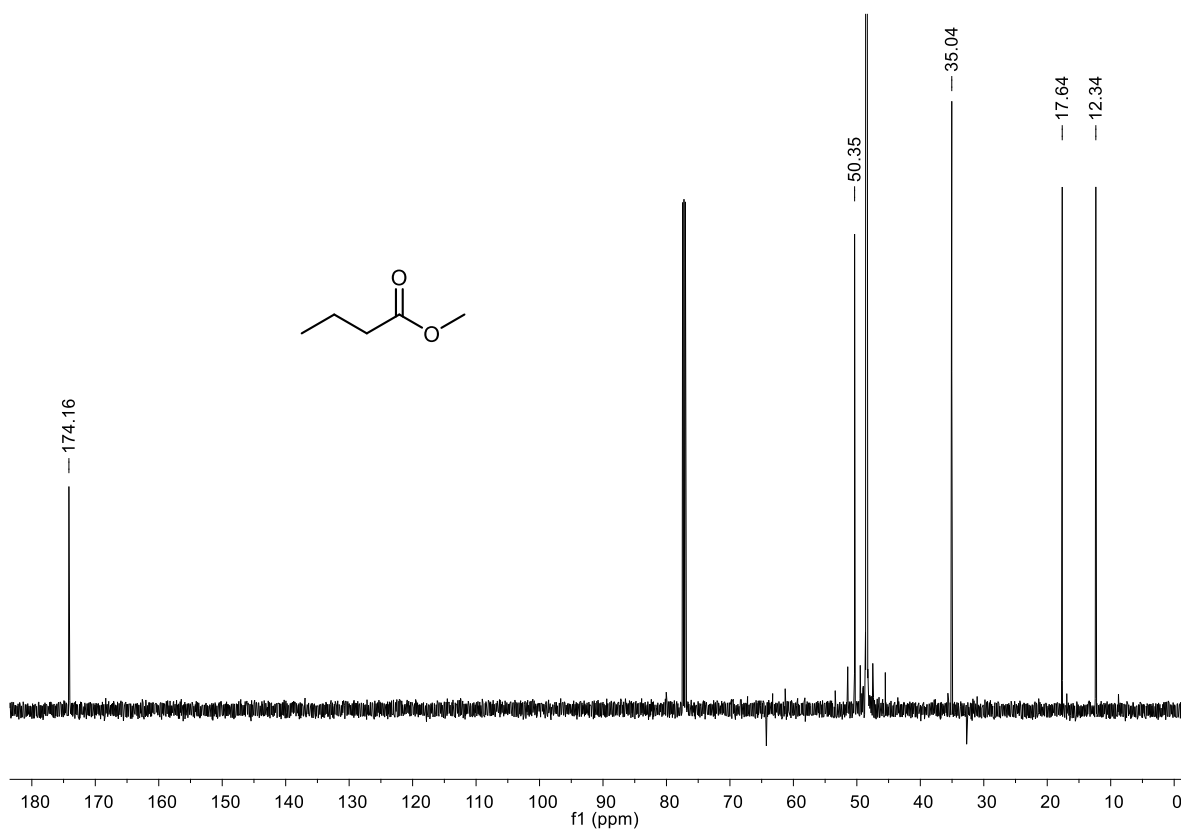


Figure S3.37 ^{13}C NMR (151 MHz, CDCl_3) spectrum of methyl butanoate in MeOH.

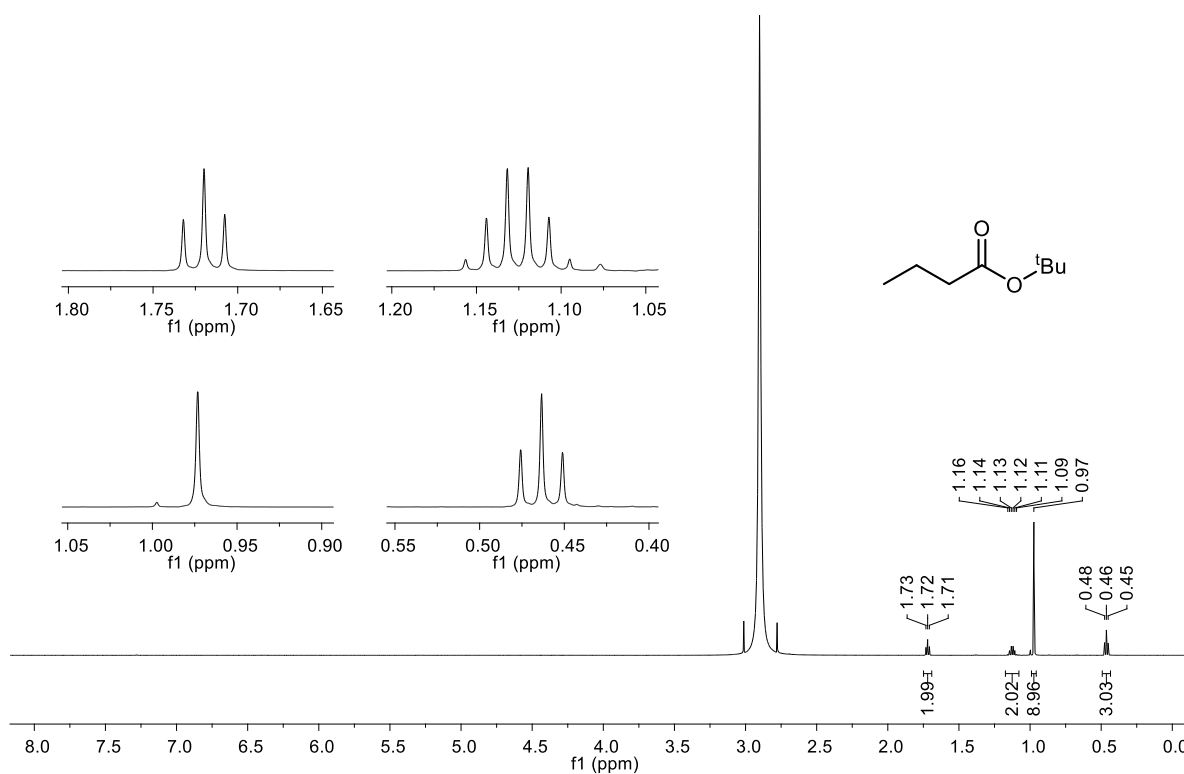


Figure S3.38 ^1H NMR (600 MHz, CDCl_3) spectrum of tert-butyl butanoate in MeOH.

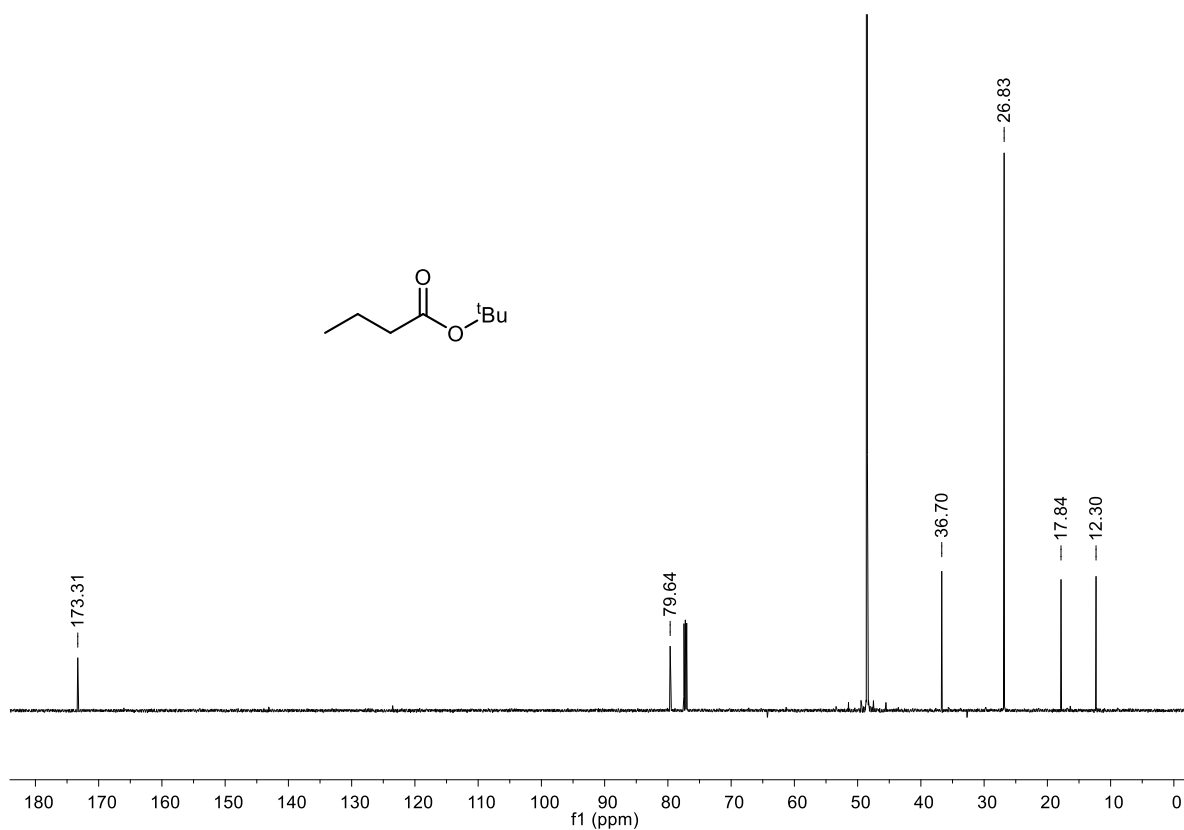


Figure S3.39 ^{13}C NMR (151 MHz, CDCl_3) spectrum of tert-butyl butanoate in MeOH.



Figure S3.40 ^1H NMR (600 MHz, CDCl_3) spectrum of ethyl 3-phenylpropanoate.

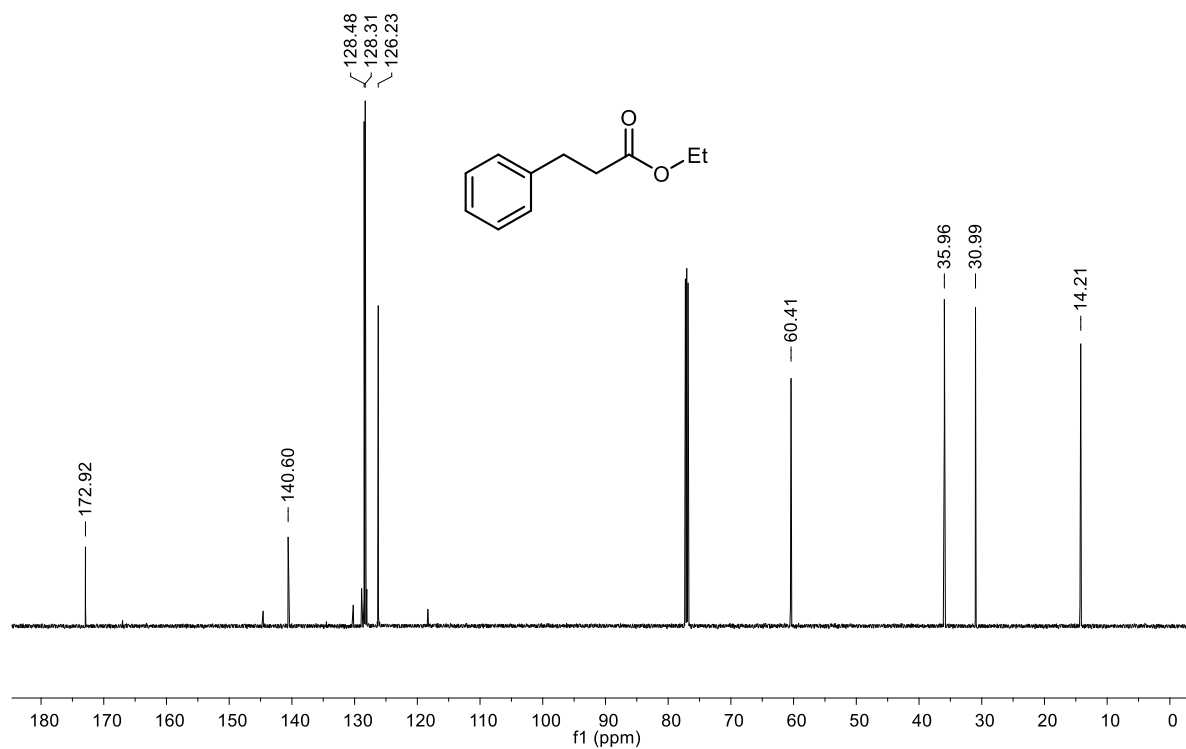


Figure S3.41 ^{13}C NMR (151 MHz, CDCl_3) spectrum of ethyl 3-phenylpropanoate.

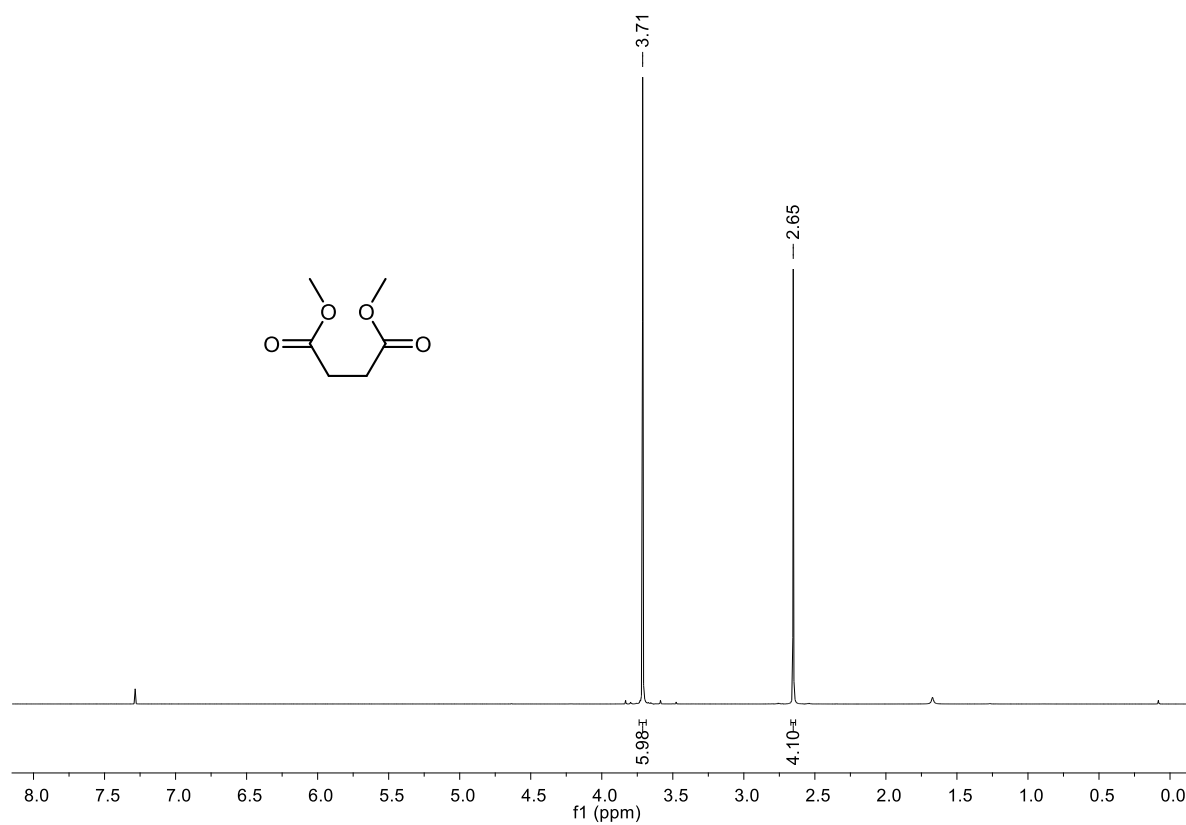


Figure S3.42 ^1H NMR (600 MHz, CDCl_3) spectrum of dimethyl succinate.

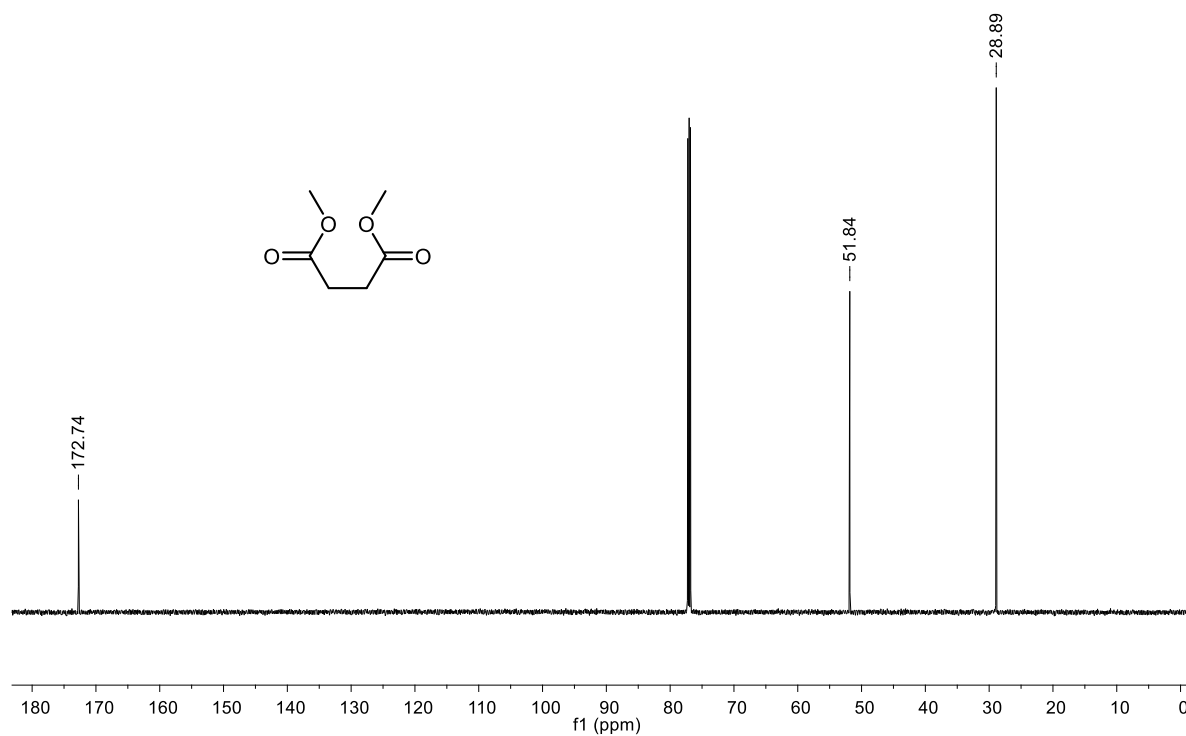


Figure S3.43 ^{13}C NMR (151 MHz, CDCl_3) spectrum of dimethyl succinate.

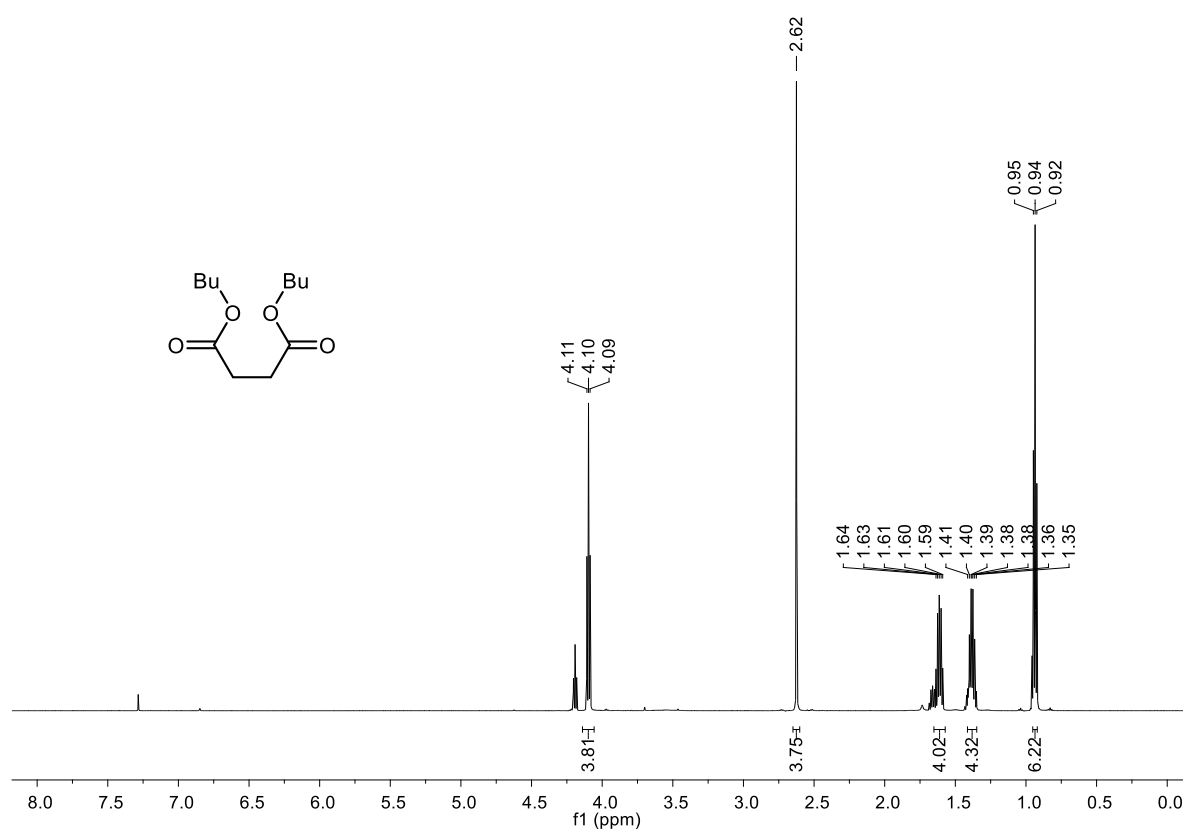


Figure S3.44 ¹H NMR (600 MHz, CDCl₃) spectrum of dibutyl succinate.

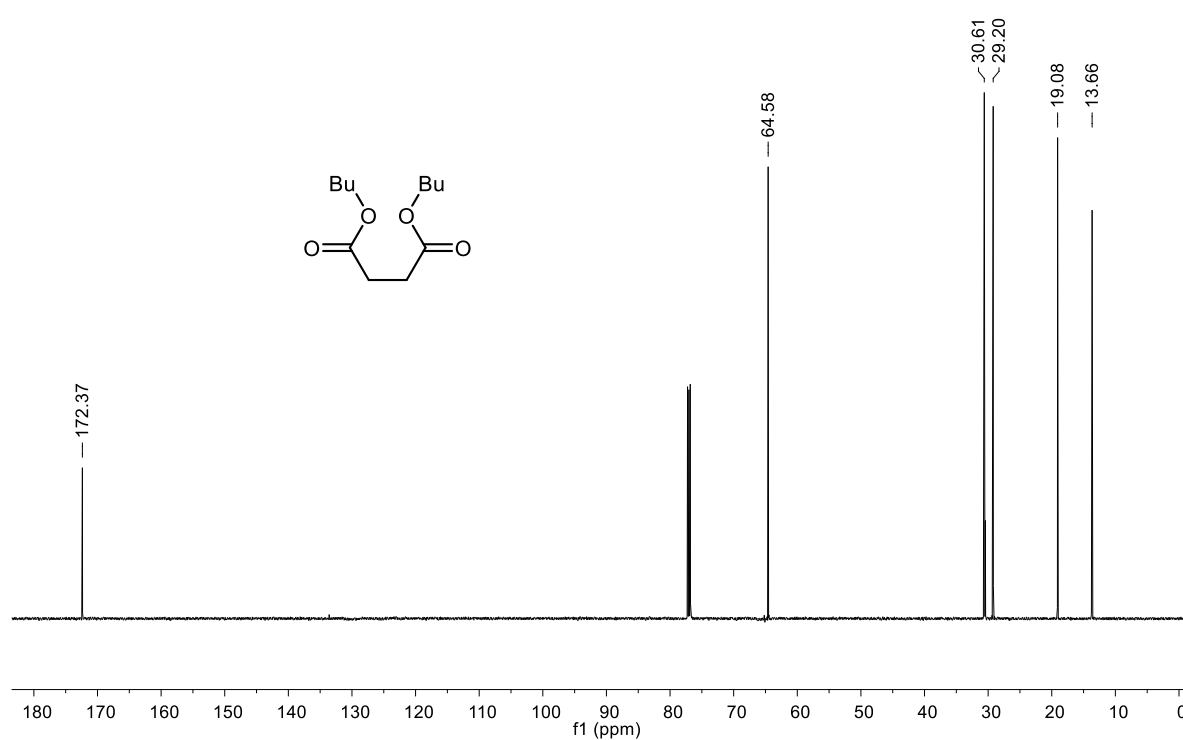


Figure S3.45 ¹³C NMR (151 MHz, CDCl₃) spectrum of dibutyl succinate.

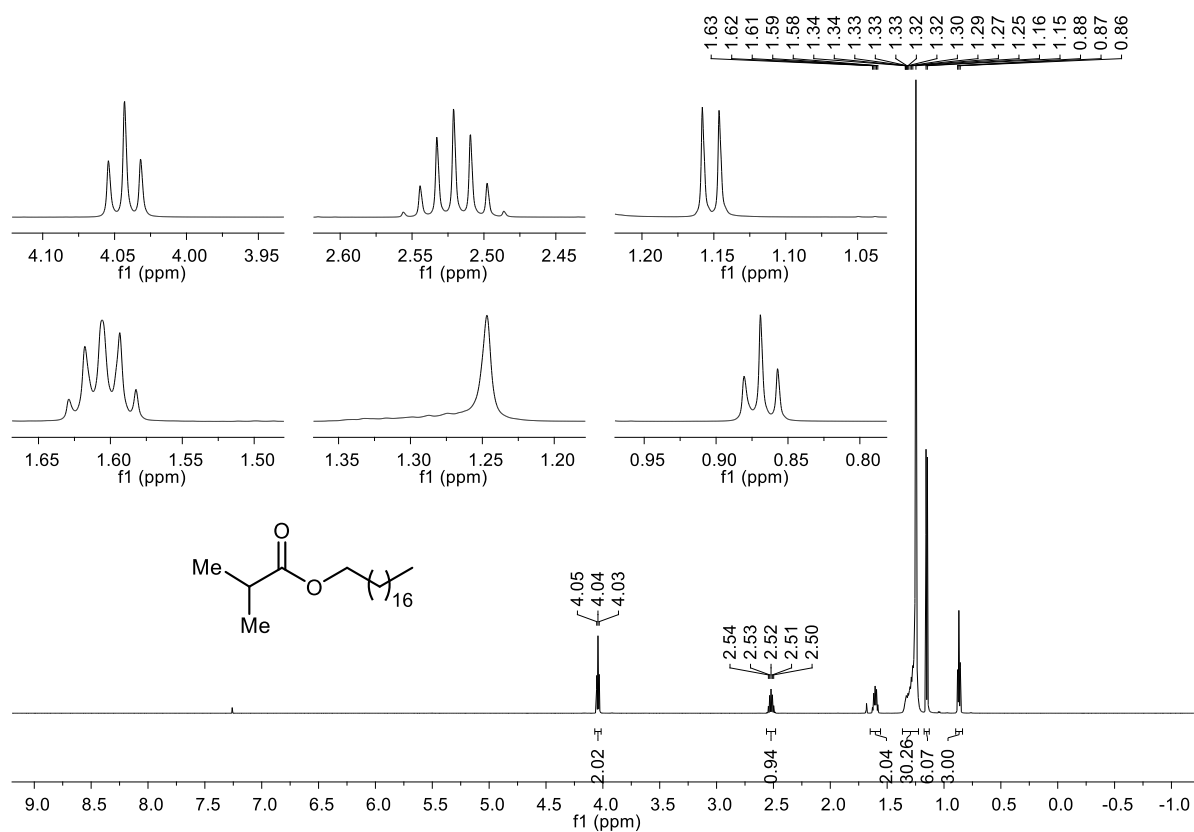


Figure S3.46 ^1H NMR (600 MHz, CDCl_3) spectrum of octadecyl isobutanoate.

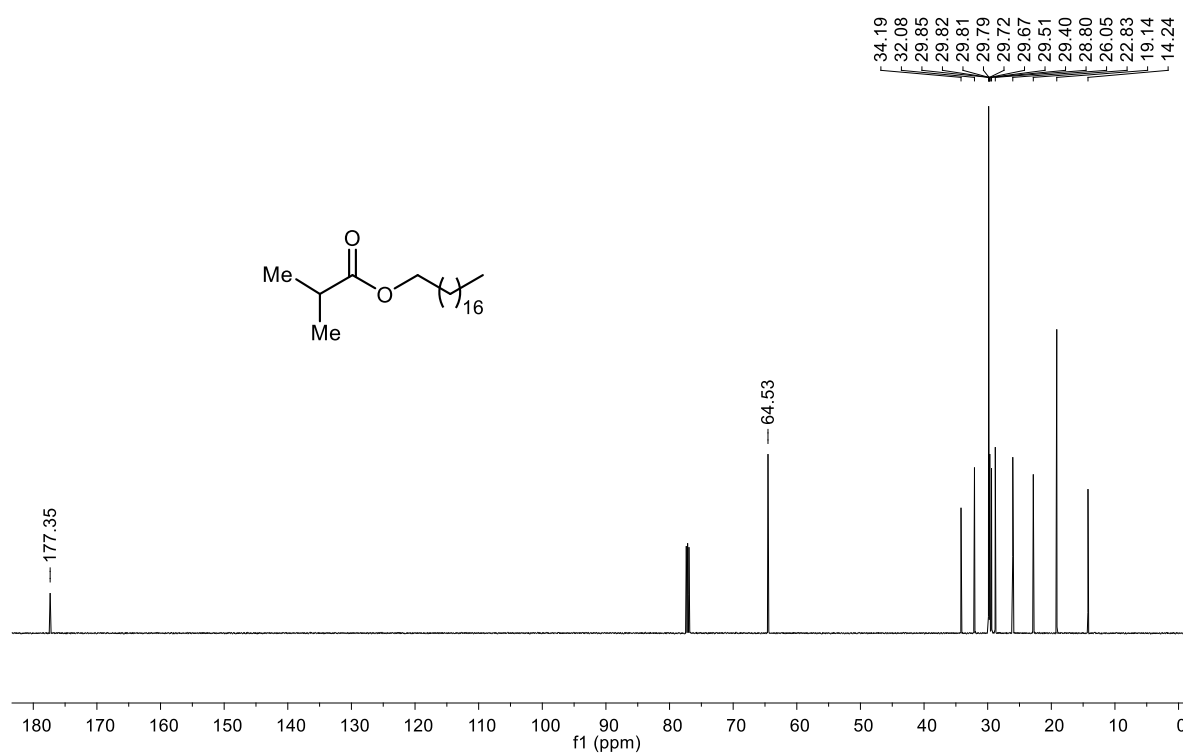


Figure S3.47 ^{13}C NMR (151 MHz, CDCl_3) spectrum of octadecyl isobutanoate.

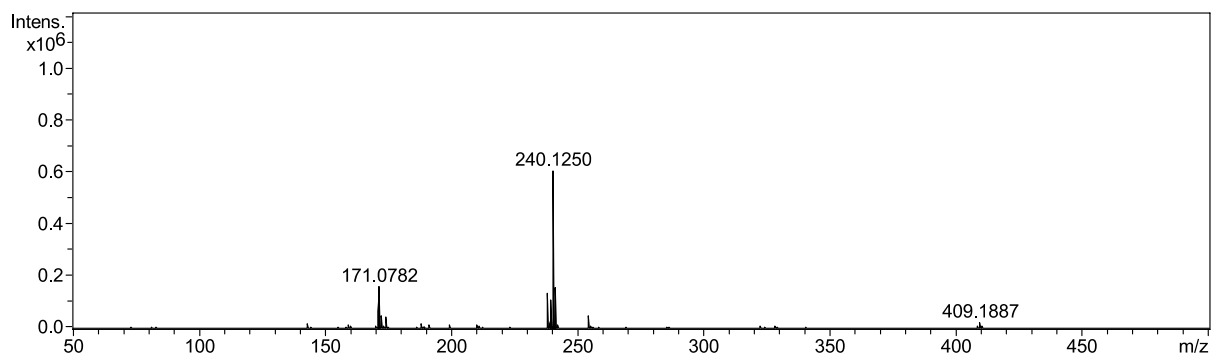


Figure S3.48 APCI-MS spectrum of **L5.1** recorded in positive ion mode. Isotope cluster found at m/z of 240.1250 corresponding to the $[M + H]^+$ ion.

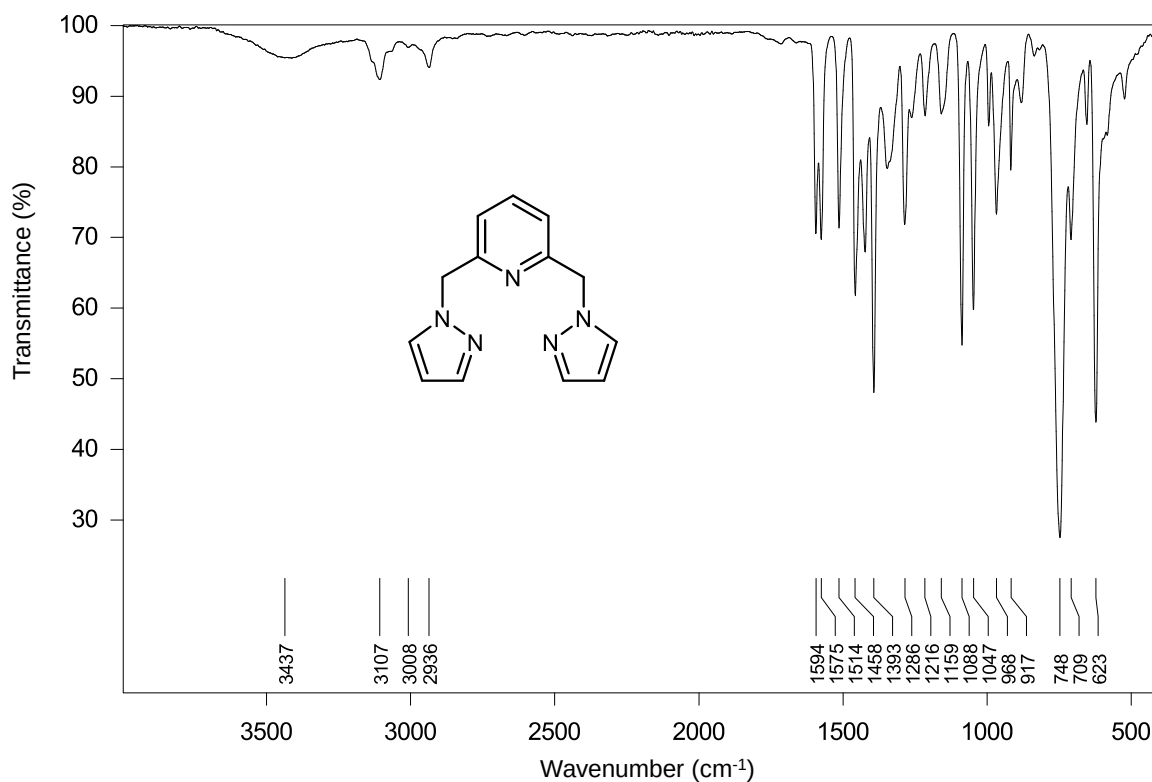


Figure S3.49 FT-IR spectrum of ligand **L5.1**.

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