STEREOSELECTIVE SYNTHESIS OF SUBSTITUTED

HEXAHYDRO-3a,4a-DIAZACYCLOPENTAPHENANTHREN-4-ONES

AND AMINOFERROCENES

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Abstract

This thesis explored the development of several methodologies for the stereoselective construction of ligand frameworks and some of their applications. The first segment concerns the application of an enantioselective lithiation at an sp^3-hybridized position adjacent to nitrogen by means of the widely used and typically highly effective enantioselective lithiation with (−)-sparteine. This investigation was intended to develop a method to install chirality into a system that would be converted into a family of diaminoylidenes for use as phosphine mimics in transition metal catalysis or as nucleophilic reagents. Molecular modeling of the system revealed some key interactions between the substrate and (−)-sparteine that provided general insight into the diamine's mode of action and should lend some predictive value to its future applications.

The second portion focuses on the development of methods to access 1,2-disubstituted aminoferrocenes, an underexplored class of metallocenes possessing planar chirality. Two routes were examined involving a diastereoselective and an enantioselective pathway, where the latter method made use of the first BF_3-mediated lithiation-substitution to install planar chirality. Key derivatives such as 1,2-aminophosphines, made readily accessible by the new route, were evaluated as ligands for Pd(II), Pt(II) and Ir(I). These complexes show activity in a number of transformations with both achiral and prochiral substrates. Optimization experiments were conducted to prepare enantiomerically enriched 2-substituted-1-aminoferrocenes by direct asymmetric lithiation of BF_3-coordinated tertiary aminoferrocenes. A predictive computational model describing the transition state of this reaction was developed in collaboration with Professor Travis Dudding's group (Department of Chemistry, Brock University). The

predicted stereochemistry of the process was confirmed by single-crystal X-ray analysis of a 2-phosphino-1-dimethylaminoferrocene derivative. Enantiomerically pure samples of the aminophosphine ligands derived from this new process have given promising preliminary results in the enantioselective hydrogenation of prochiral alkenes and warrant further study in metal-mediated catalysis.

To my family

Acknowledgements

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Abbreviations

Ac	acetyl
aq.	aqueous
BAr^F	tetra[3,5-bis(trifluoromethylphenyl)]borate
BINAL-H	lithium 2,2'-dihydroxy-1,1'-binaphthylethoxyaluminum hydride
BINAM	2,2'-bis(dimethylamino)-1,1'-binaphthyl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Boc	*t*-butyloxycarbonyl
Bn	benzyl
Bu	butyl
c	*cyclo*
C	concentration
CbzCl	benzyl chloroformate
cod	1,5-cyclooctadiene
conv.	conversion
Cp	cyclopentadienyl
CSP	chiral stationary phase
d	days
D	sodium D line (589 nm)
DBU	1,8-diaza[5.4.0]bicycloundec-7-ene
DIPA	diisopropylamine
DMAE	dimethylaminoethanol
DME	1,2-dimethoxyethane
DMAP	4-dimethylaminopyridine
DMF	*N,N*-dimethylformamide
DMPU	*N,N*-dimethylpropylene urea
DMSO	dimethylsulfoxide
DPPA	diphenylphosphorylazide
de	diastereomeric excess
dr	diastereomeric ratio
ee	enantiomeric excess
equiv.	equivalents
er	enantiomeric ratio
Et	ethyl
E$^+$	electrophile
h	hours
HMPA	hexamethylphosphoramide
HPLC	high pressure liquid chromatography
i	iso
IR	infrared
LHMDS	lithium hexamethyldisilazane
L*	chiral ligand
LDA	lithium diisopropylamide

LTMP	lithium 2,2,6,6-tetramethylpiperidide
Me	methyl
min	minutes
n	normal
nbd	norbornadiene
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
o.p.	optical purity
OAc	acetoxy
o	ortho
p	para
quant.	quantitative
pent	pentyl
Ph	phenyl
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
Pr	propyl
PTSA	pyridium *p*-toluenesulfonate
py	pyridine
rt	room temperature
s	secondary
t	tertiary
tbf	*t*-butylformamidine
TBME	*t*-butyl methyl ether
TES	triethylsilyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMCDA	tetramethylcyclohexanediamine
TMEDA	tetramethylethylenediamine
TMS	trimethylsilyl
TrocCl	trichloroethylchloroformate
Ts	toluenesulfonyl
TS	transition state

Introduction

There is an increasing interest in chiral compounds, frequently as a single enantiomer. This increased demand comes from materials science applications, the flavour and fragrance industry, agrochemical synthesis, but in large part from the pharmaceutical industry, where many of today's prescription drugs are manufactured as enantiomerically pure compounds. Asymmetric synthesis may be achieved by using chiral starting materials from nature as building blocks, resolution of a racemic mixture or by asymmetric catalysis, where stereogenic elements are established by the use of a chiral catalyst. Since the 1970s, asymmetric catalysis has become an intensely investigated discipline of synthetic chemistry. The focus of research in the Metallinos group is directed toward the development of new classes of reagents for use in asymmetric synthesis and catalysis. Currently, these efforts are currently focused on two main areas: (i) the development chiral imidazolium and imidazolinium salts for use as precursors to diaminoylidenes, and (ii) the synthesis and investigation of 1,2-disubstituted aminoferrocenes.

Part 1 of this dissertation will discuss an enantioselective synthesis of a benzimidazolylidene precursor starting from inexpensive and readily available 1,10-phenanthroline, utilizing a (−)-sparteine-mediated enantioselective lithiation as the key step. This approach is unique as it represents the first documented case of lithiation of a benzo-fused piperidine and demonstrates the feasibility of ureas as directing groups for enantioselective lithiation. Given that piperidines are typically difficult substrates for enantioselective lithiation, a collaborative computational investigation was undertaken

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and offers insight into the nature of the transition state, where key interactions of potentially general application were observed between (−)-sparteine and the substrate.

Part 2 will outline two fundamentally different approaches to this problem and provide evidence to support the future investigation of aminoferrocenes by demonstrating their utility in several metal-mediated catalytic processes. First, a diastereoselective synthesis of aminoferrocenes will be approached by partial reduction of already known *N*-ferrocenyl phthalimide and subsequent use of chiral phthalimidine as an unprecedented nitrogen-based directing group for ferrocenes. The use of this directing group will allow conversion to the primary amine after the lithiation-substitution has been carried out and thus allow complete manipulation at nitrogen. Second, a route involving lithiation-substitution of a tertiary aminoferrocene-BF_3 complex will be described. Products from this lithiation-substitution sequence, specifically 1,2-aminophosphines, will then be structurally characterized and used as ligands for palladium(II), platinum(II) and iridium(I), illustrating their competence as useful reagents. Lastly, work towards an enantioselective BF_3-activated lithiation using chiral diamines will be presented, which allows for the synthesis of either enantiomer of these compounds, along with an assignment of absolute stereochemistry for the substitution products and a computational assessment of the transition state for deprotonation.

1 Enantioselective Synthesis of Chiral C_I-Symmetric Benzimidazolium Salts

1.1 Historical

1.1.1 Azolium Salts & Their Corresponding Diaminoylidenes

Carbenes are defined as molecules containing a divalent and formally neutral carbon atom bearing six valence electrons, which were originally thought to be too unstable to allow isolation.[1] This has not always proven to be true, such as in the case of diaminoylidenes, a class belonging to the carbene family where the carbene carbon is situated between two nitrogen atoms. Diaminoylidenes may gain stability by steric shielding of the carbene carbon by large substituents on the nitrogen atoms and electronically by the electron-donating ability of the flanking nitrogen atoms. Diaminoylidenes may behave as nucleophilic compounds, which differs from the electrophilic reactivity of traditional carbenes. This is indicated by resonance forms **1a-c** in **Scheme 1**, where structure **1** will be used to represent the average of **1a-c**.
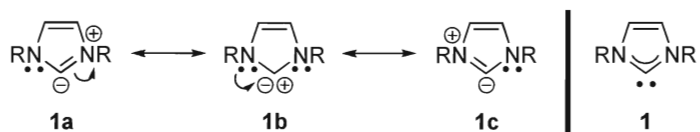
Scheme 1. Diaminoylidene resonance structures.

Diaminoylidenes were first investigated by Wanzlick[2] in the early 1960s, where he postulated the existence of stable carbenes. Shortly thereafter, he[3] and Öfele[4] independently prepared metal complexes (**3** and **5** respectively) of diaminoylidenes (**Scheme 2**).
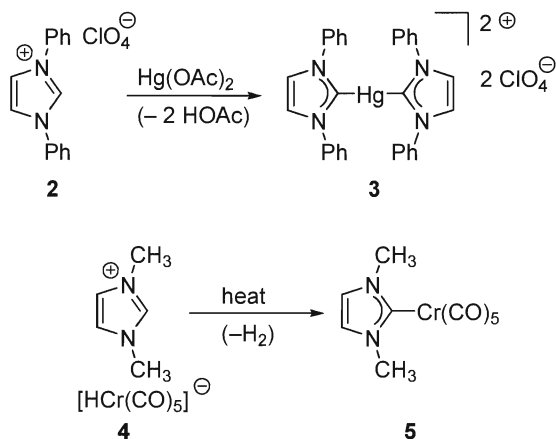
Scheme 2. Wanzlick and Öfele's pioneering syntheses of diaminoylidene-metal complexes.

In the following 20 years, few efforts followed these two seminal reports. It was not until 1991, when Arduengo reported "*A Stable Crystalline Carbene*"[5] that the chemical community took note. Treatment of bis-adamantyl-substituted imidazolium chloride **6** with a combination of sodium hydride and catalytic DMSO led to diaminoylidene **7** (**Scheme 3**), which could be isolated and even stored (in the absence of oxygen and moisture).
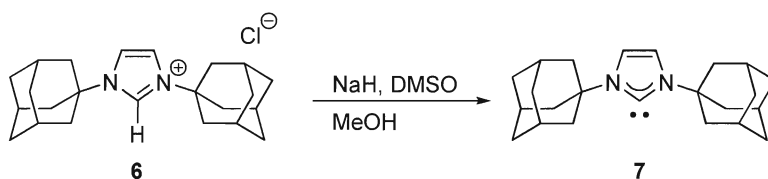
Scheme 3. Arduengo's isolation of the first stable diaminoylidene.

In the years following Arduengo's report and leading to the present, there has been a surge of interest in nucleophilic carbenes, particularly 5-membered cyclic diaminoylidenes. These may be further classified into three general groups: imidazolylidenes (**8**) with an unsaturated backbone, the benzo-fused

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benzimidazolylidenes (**9**) and imidazolinylidenes (**10**) with a saturated backbone (**Figure 1**). These may be arranged according to nucleophilicity/basicity or stability. Imidazolinylidenes (**8**) are typically the most reactive and least stable of the group.

increasing nucleophilicity/basicity

RN NR   RN NR   RN NR
  ..   ..   ..

  8   9   10

increasing stability
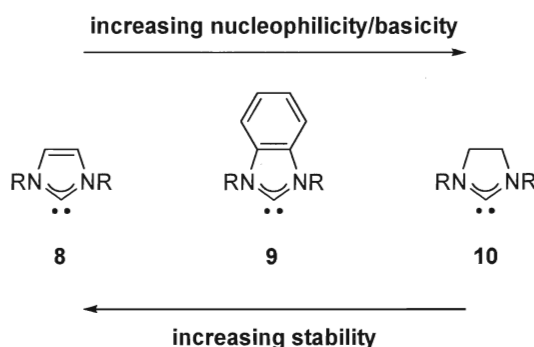
Figure 1. Comparison of the three main types of 5-membered diaminoylidenes.

Diaminoylidenes are most commonly obtained from their azolium salts by deprotonation, although they may be obtained by other methods (e.g. reduction of thioureas, elimination of volatile compounds such as $CHCl_3$ or MeOH, etc.) and have proven useful as phosphine mimics for ligands in transition metal-mediated transformations[6] and as nucleophilic catalysts.[7] A few selected applications are shown in **Scheme 4**. The first report[8] using a chiral diaminoylidene ligand in an asymmetric transformation was mediated by Rh complex **13** and although only modest selectivity was achieved in the hydrosilylation, it marked the onset of a rapid development for this class of ligands. On the topic of selectivity, it should be noted that there is little consensus in peer-reviewed literature when reporting selectivities (i.e. as enantiomeric ratios or enantiomeric excesses) in asymmetric transformations. Some researchers[9] have chosen to support the use of enantiomeric ratios and for the purposes of this thesis, enantiomeric ratios will be used predominantly, but enantiomeric excesses will be given for convenience. The

palladium complex of spirocyclic ligand **17**, generated *in situ* by treatment with KH and

catalytic *t*-BuOK, was shown to serve as a catalyst for very difficult Suzuki-Miyaura

couplings to give tetra-*ortho*-substituted biaryls (**16**) as products.[10] Most recently,

diaminoylidenes have found application as catalysts themselves, such as in the

transformation of cinnamaldehyde (**18**) and *p*-bromobenzaldehyde (**19**) into γ-

butyrolactone **20**.[11]
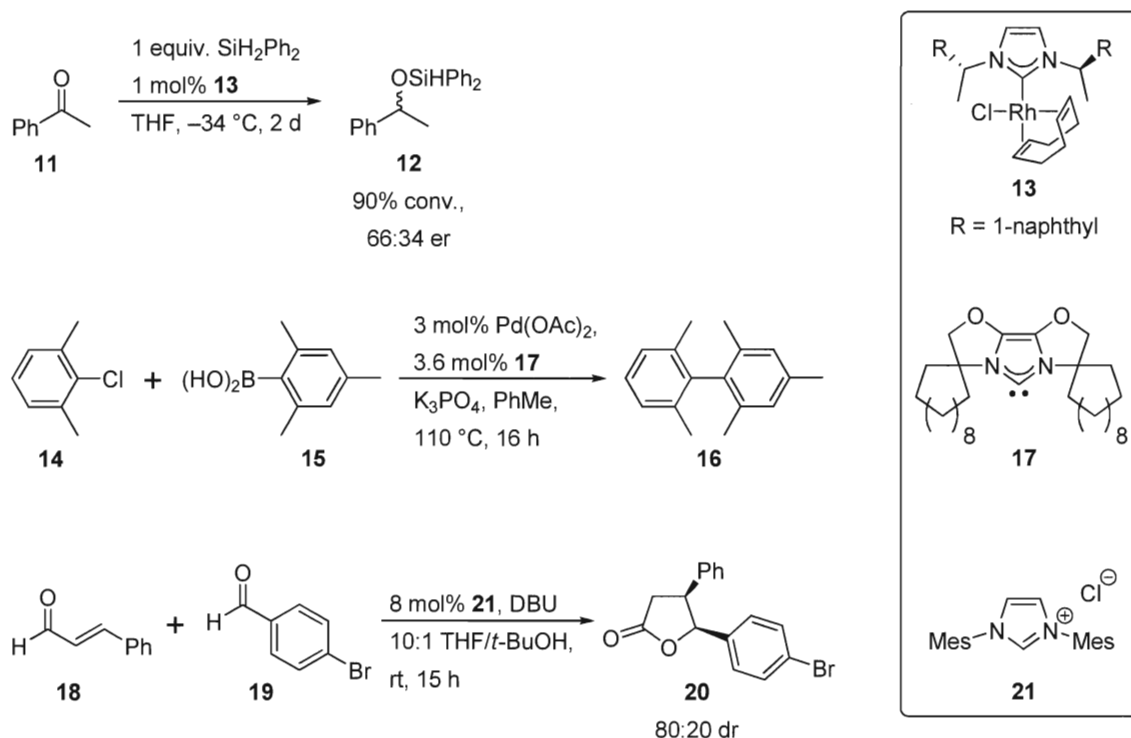
Scheme 4. Selected reactions using diaminoylidenes as ligands or catalysts.

Within the continuum of ylidenes illustrated in **Figure 1**, nearly all of the

investigations reported up to 2006 have focused on the species at either end (i.e. **8** and

10). At the end of 2002, only one researcher reported the synthesis of chiral

benzimidazolylidenes, but none of these had been applied to an organic transformation at

that point. Diver prepared benzimidazolium salts **23a-d** and **25** by Buchwald-Hartwig

aryl amination of 1,2-dibromobenzene, followed by cyclization of the two secondary amines and quaternization methods respectively (**Scheme 5**).[12]
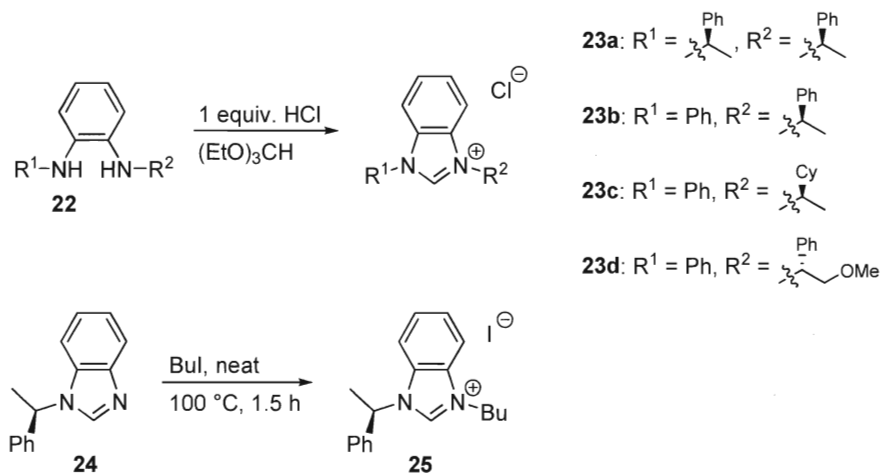
Scheme 5. Benzimidazolium salts prepared by Diver.

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Since that time, only a handful of other chiral benzimidazolium salts have been reported, such as **26**,[13] containing a pendant chiral dioxane, and the bis(benzimidazolium) salts **27**[14] and **28**,[15] containing central and axial chirality in the tether linking the two benzimidazolium fragments (**Figure 2**).
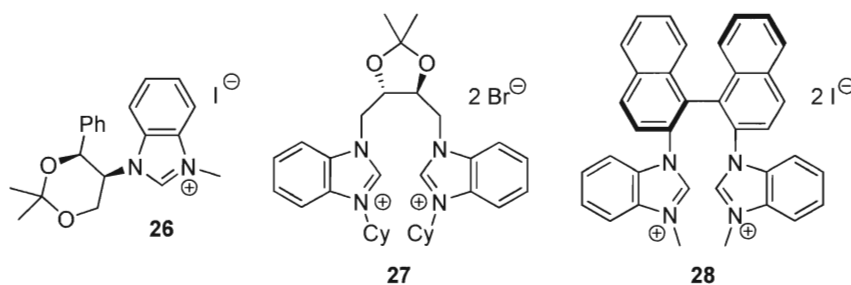
Figure 2. Other reported chiral benzimidazolium salts.

The preparation of salts **23a-d** and **26-28** all relied on the same cyclization and quaternization techniques, necessitating that the chirality be positioned at either freely

rotating sites, or sites remote to the future site of reaction or metal attachment (i.e. the ylidene carbon). In contrast to the synthesis of chiral imidazolylidenes and imidazolinylidenes, which may be prepared by condensation reactions, the synthetic limitation of preparing benzimidazolylidenes by aryl amination or nitrogen quaternization methods was most likely responsible for the previous lack of investigation into this subclass of reagents or ligands.

1.1.2 Methods for Preparing Chiral Octahydrophenanthrolines: Azolium Salt Precursors

Given the lack of structural diversity in the benzimidazolylidene class, the Metallinos group has made an effort to fill this void, particularly with a focus on increasing the rigidity of derived systems to affect greater selectivity in asymmetric reactions. The Metallinos group began addressing this issue by reporting a benzimidazolylidene synthesis starting from ubiquitous phenanthrolines, made by reduction of the pyridyl rings and subsequent formylative cyclization, providing a tetracyclic framework for the benzimidazolium salt.[16] Methods relating to and for the preparation of chiral derivatives of this system are briefly described in the following sections.

1.1.2.1 Diastereoselective Reduction

Substitution of phenanthroline, itself a common chelating ligand for metals,[17] by nucleophilic aromatic substitution[18] (**Scheme 6, A**) or Friedländer Condensation[19] (**Scheme 6, B**) led to the 2,9- and 2,3-substituted derivatives respectively (**30** and **34, 35**).
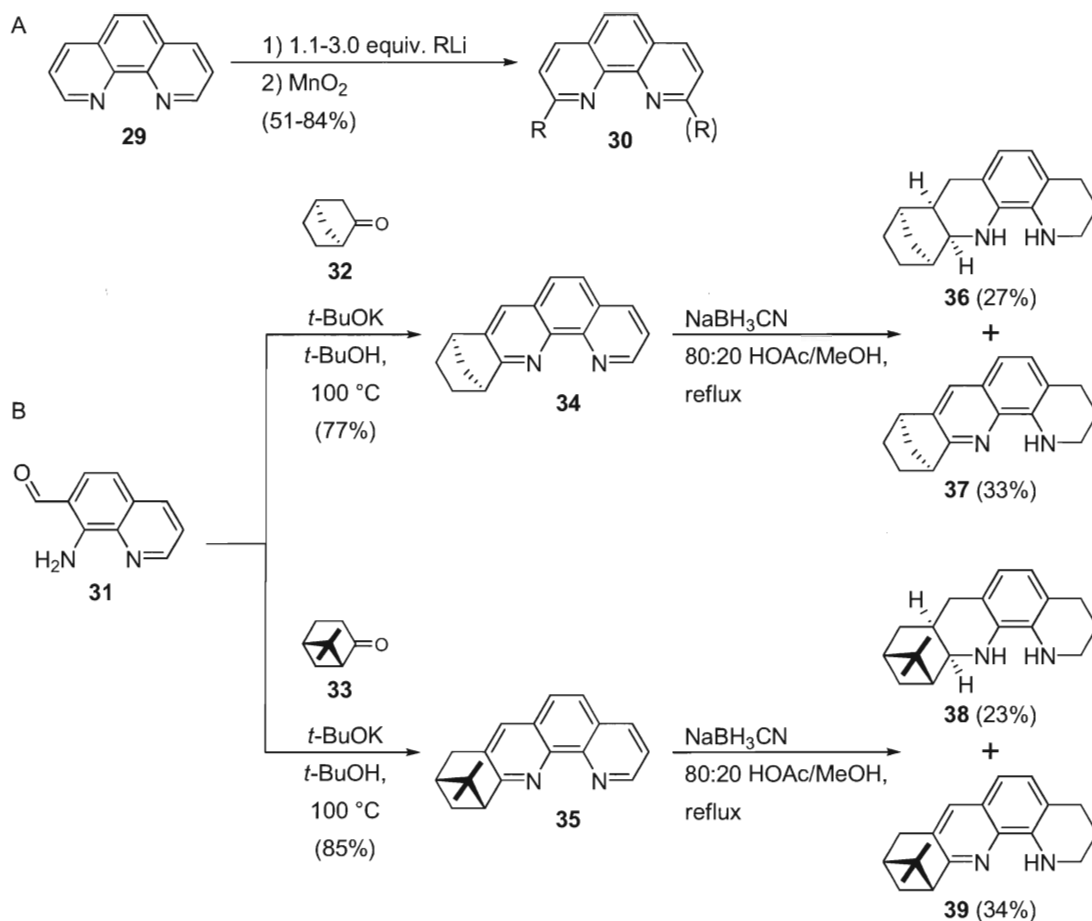
Scheme 6: Nucleophilic aromatic substitution (**A**) and
Friedländer Condensation (**B**) routes to variously substituted phenanthrolines.

Adducts **34** and **35** were subjected to NaBH₃CN in HOAc/MeOH at reflux and provided diamines **36** and **38** in low yields, accompanied by similar amounts of the tetrahydrophenanthrolines (**37** and **39** respectively) resulting from reduction of the unsubstituted pyridyl ring (**Scheme 6**).[20] It was also demonstrated that secondary diamines **36** and **38** could be converted to the target benzimidazolium salts, which now contain rigidified α-stereocentres in a tetracyclic framework, by standard cyclization with triethyl orthoformate and one equivalent of acid.

1.1.2.2 Resolution & Asymmetric Reduction

Diamines derived from the reduction of 2- or 2,9-disubstituted phenanthrolines may also be reduced in a fashion analogous to that used for 2,3-disubstituted derivatives **34** and **35**, providing the corresponding mono- or disubstituted octahydrophenanthrolines in greater than 62% yield (with the exception of the 2-*tert*-butyl-substituted case) as a racemic mixture (plus *meso* isomer for the disubstituted derivatives).[20] Enantiopure material, in these cases, would need to be obtained through a classical resolution. As efforts to separate diastereomeric salts with chiral counterions were unsuccessful,[21] resolution of covalent diastereomers was pursued.[20,22] A procedure developed for the resolution of 2,2'-bipiperidine by Herrmann was applied to the mixture of stereoisomers. Thus, cyclization of stereomeric mixture **40** with PCl₃, followed by addition of (−)-menthol and oxidation of the intermediate phosphorodiamidites with sulphur gave adduct **41** with all three diastereomers in roughly equal quantities according to ³¹P NMR analysis (**Scheme 7**). This mixture was separated by fractional crystallization from methanol to yield the pure stereoisomers. Removal of the phosphoryl group with LiAlH₄ provided the enantiopure diamines (**40**), which were converted to the desired benzimidazolium salts under standard conditions.

Although resolution provided the desired enantiopure benzimidazolium salts, it is not the most direct way to obtain them. More ideal would be an asymmetric reduction of the appropriately substituted phenanthroline. Toward this goal, several approaches for the reduction of quinolines are worthy of discussion. Firstly, Zhou developed an iridium-catalyzed hydrogenation using chiral phosphine ligands that produced the desired 2- and 2,6-disubstituted tetrahydroquinolines in high yields and selectivites (**Scheme 8**).[23]
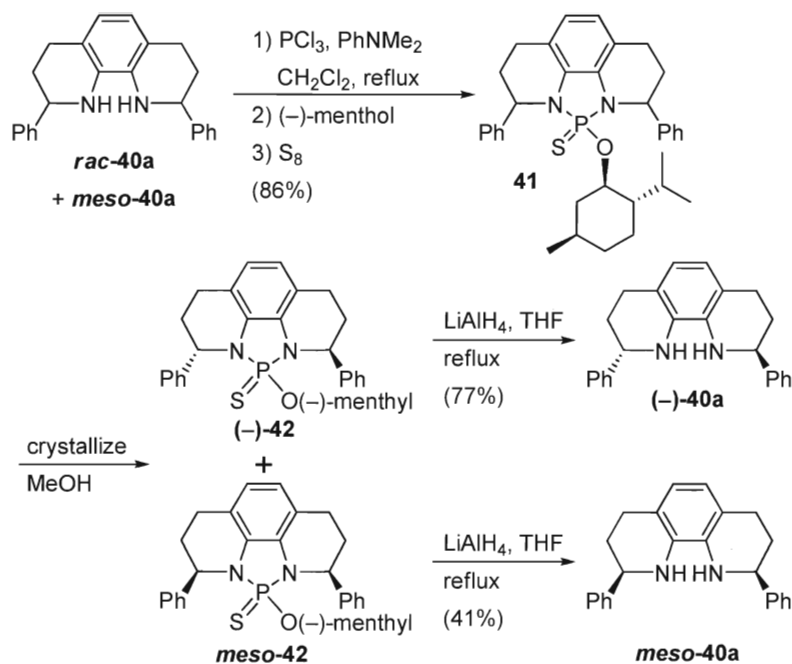
Scheme 7. Resolution of 2,9-diphenyl-octahydrophenanthroline (**40**).
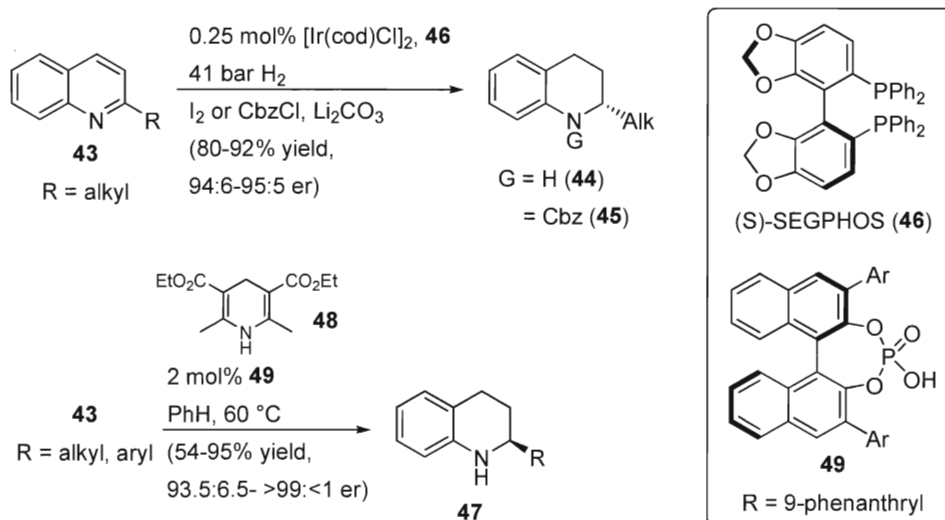
Scheme 8. Zhou and Rueping's methods for quinoline reduction.

Zhou's original method used molecular iodine to activate the substrate, but a later, more general procedure employed CbzCl and base, thus affording protected

tetrahydroquinolines **45**. The major drawback to this procedure is its lack of tolerance for 2-arylated substrates; however in their final report,[23a] Zhou *et al.* reported the reduction of 2-phenylquinoline with moderate success, where the reduction product (**45**, R = Ph) was obtained in 41% yield and 90:10 er (with opposite stereochemistry from all other products).

Secondly and concurrent with Zhou, Rueping disclosed an organocatalytic reduction of 2-substituted quinolines with a broader substrate scope.[24] When a catalytic amount of 3,3'-diarylbinaphthylphosphoric acid **49** (2-naphthyl groups provided slightly lower, but acceptable, selectivity) was used to protonate the quinolines and form a tight ion pair, 2.4 equivalents of Hantzsch dihydropyridine **48** allowed for complete reduction of the pyridyl ring. The only substrates tested that provided any resistance to the method were those with bulky aryl substituents (*o*-tolyl, 54%, and 2,6-xylyl, 65%).

Based on these results, Rueping's method was applied to 2- and 2,9-disubstituted octahydrophenanthrolines (**30**).[25] As has been observed by the Metallinos group, transformations of phenanthrolines compared to the analogous quinolines (and pyridines) often prove more difficult. When R^1 is an alkyl substituent with minimal steric bulk, the reduction products are obtained in ~50% yield with a 90:10 er; after isolation of the diamine products (**40**), conversion to ureas **50** facilitated measurement of enantioselectivity by chiral HPLC (**Scheme 9**). Upon introduction of bulkier groups, the yields and selectivities decreased (R^1 = *i*-Pr: 28% yield, 70:30 er). In contrast, 2,9-dialkylphenanthrolines (R^1, R^2 = Me, *n*-Bu) were reduced in 72-88% yield with near perfect selectivity (and a diastereomeric ratio of 3:2 *ent:meso*). 2-Phenyl phenanthroline was reduced in low yield but excellent er, while 2,9-diphenylphenanthroline underwent

reduction of only one pyridyl ring in high yield and low er. While the results were not definitive, a secondary interaction such as π-stacking, was suggested as being responsible for the switch in yield and selectivity of the phenyl-substituted derivatives.
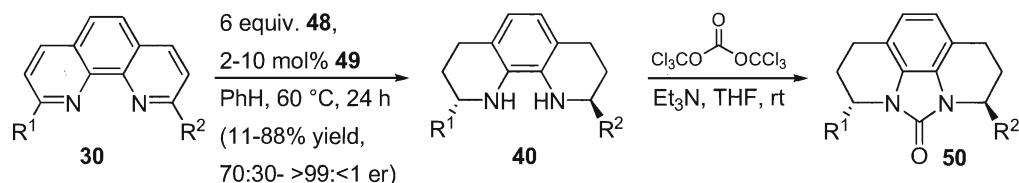
Scheme 9. Organocatalytic reduction of 2- and 2,9-disubstituted phenanthrolines.

Substrates that gave lower yields were accompanied by significant amounts of partially reduced material, where one substituted pyridyl ring was left intact. In summary, this method proved capable of producing sterically unencumbered alkyl-substituted octahydrophenanthrolines (2- or 2,9-) in good yields and with high selectivities.

1.1.2.3 Asymmetric α-Induction

One additional method that was considered for the preparation of chiral octahydrophenanthrolines with stereogenic centres α to nitrogen was the direct installation of substituents at an adjacent sp^3-hybridized C-H bond.[26]

Shono and Matsumura have developed a procedure to electrochemically oxidize *N*-carbomethoxypyrrolidines[27] and piperidines[28] at the α-position in good yields. The *N,O*-acetal (**52**) generated from the piperidine was used to efficiently access methylphenidate (Ritalin®, **54**) through a diastereoselective TiCl₄-mediated C-C bond-forming reaction (**Scheme 10**). Attempts to carry out the analogous transformation on biscarbamate **55** to generate aminal **57** were unsuccessful.[29]
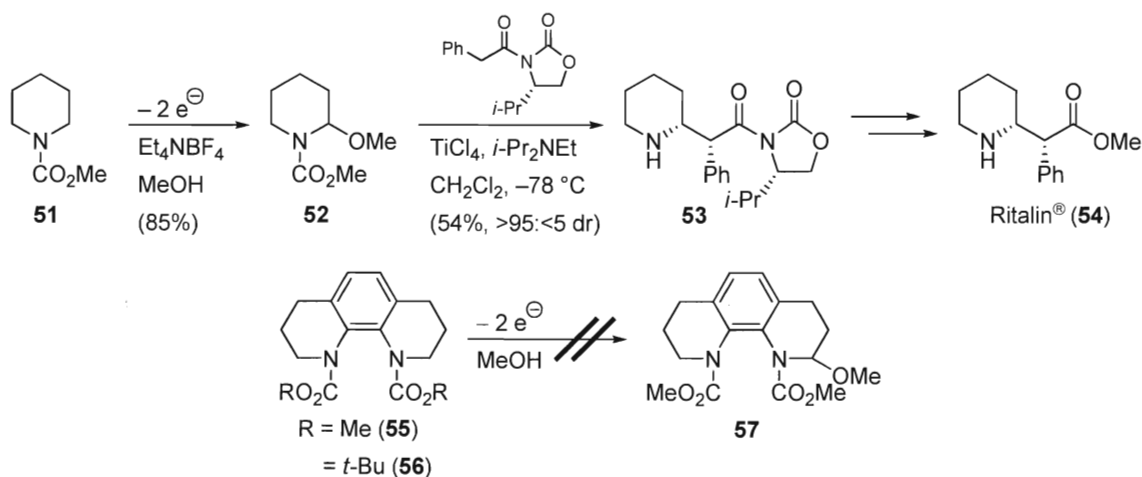
Scheme 10. Electrochemical C-H activation of protected *N*-heterocycles.

Alternatively to electrochemical activation, Davies has developed a great deal of C-H insertion chemistry using chiral rhodium prolinate complexes such as Rh₂[(*S*)-DOSP]₄ (**64**) and Rh₂[(*S*)-biDOSP]₂ (**65**), for pyrrolidine, piperidine and indoline systems.[30] Davies observed that even at low temperatures, Rh-catalyzed decomposition of methylaryldiazoacetates in the presence of *N*-Boc pyrrolidine (**58**) resulted in the formation of C-H insertion product **59** with excellent enantio- and diastereoselectivity. Even double C-H insertions were possible, leading to 2,5-disubstituted pyrrolidines. Screening of catalysts, solvents and stoichiometry were required to achieve reasonable selectivities for the reaction with *N*-Boc piperidines (**60**), as notable differences in reactivity were displayed compared to 5-membered ring analogue **58**. This trend was also observed for benzofused *N*-Boc indoline (**62**); however very good selectivities were still obtained, despite the need to use elevated reaction temperatures. When Rh-catalyst **64** was used to decompose methylphenyldiazoacetate in the presence of protected

octahydrophenanthrolines **55** or **56**, no reaction was observed and only the starting material could be partially recovered.[31]
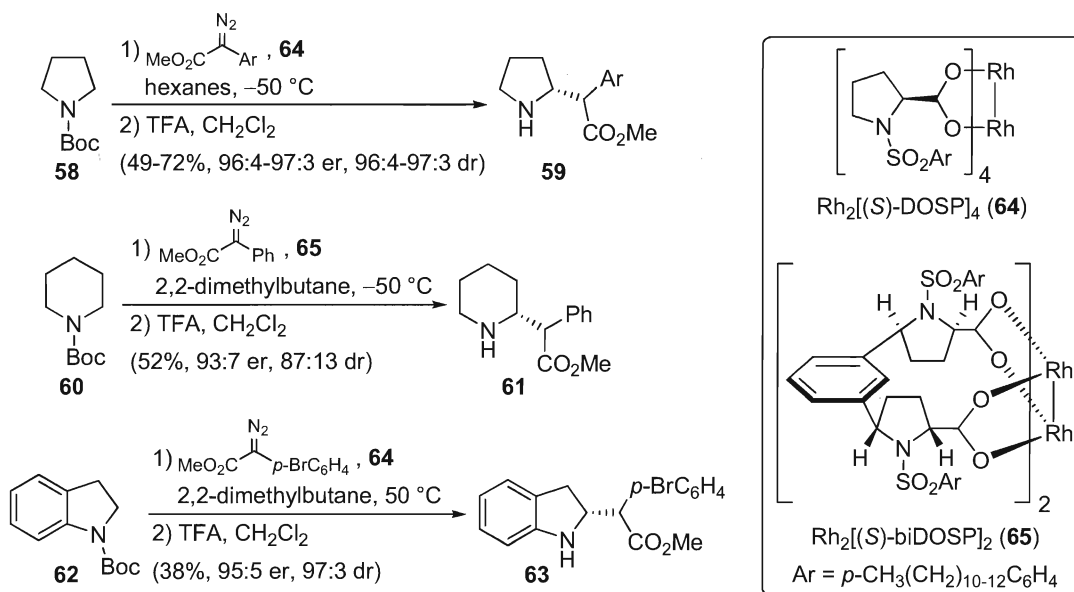
Scheme 11. Rh-catalyzed C-H activation of protected *N*-heterocycles.

Last, consideration should also be given to asymmetric deprotonation-electrophilic substitution reactions at sp^3-positions α to heteroatoms (i.e. nitrogen), discussed in detail in the following section.

1.1.3 Organolithium Compounds

1.1.3.1 Organolithiums

The earliest report of an organolithium compound, prepared by transmetalation of dimethylmercury, was made by Schlenk and Holtz[32] in the early twentieth century and marked the beginning of this branch of chemistry. Subsequently, the first report of metalation with an organolithium was made, whereby 9-fluorenyllithium was produced by the action of ethyllithium on fluorene.[33] Following these discoveries, Ziegler[34],

Wittig[35] and Gilman[36] showed that organolithiums could also be conveniently generated by reaction of lithium metal with organic halides. In the 1970s, the investigation of organolithiums as polymerization catalysts[37] for unsaturated hydrocarbons led to their commercialization, increasing availability and thus allowing further development of the field into a fundamental part of contemporary synthetic chemistry. The chemistry of organolithium compounds has since been greatly developed and various aspects have been reviewed.[38]

The strongly polarized nature of organolithiums is responsible for their typical behaviour as strong nucleophiles in addition reactions (to carbon-carbon double bonds, carbonyls, imines and other functionalities, such as epoxides and oxetanes) and exchange reactions (Sn→Li, P→Li, S→Li, Se→Li, Te→Li, Br→Li, I→Li), or as strong bases for deprotonation. Nearly 45 years elapsed from the first report of an organolithium to their application in an enantioselective process. In the late 1960s, Nozaki and coworkers reported their seminal work on the asymmetric synthesis of allenes from *gem*-dibromocyclopropanes[39a] and additions to carbonyls[39b] in the presence of the bidentate diamine (−)-sparteine (**66**), of which one conformer (**66a**) may act as a ligand for lithium (**Figure 3**).
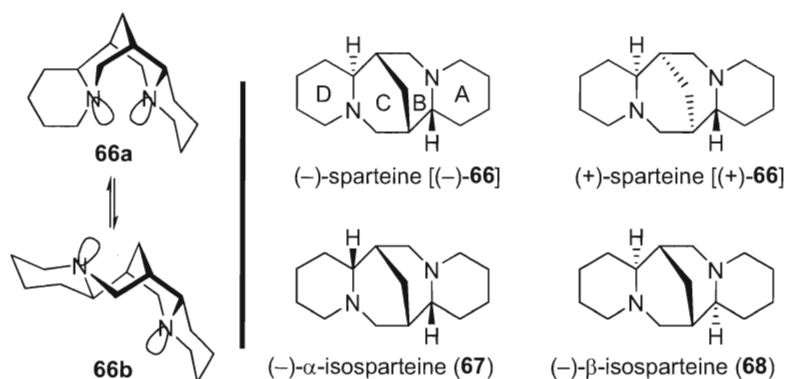
Figure 3. (−)-Sparteine conformers and isomers from the Lupin family of alkaloids.

Following sporadic research in the 1970s, Hoppe reported the first breakthroughs in asymmetric deprotonation-electrophile trapping with (−)-sparteine [(−)-**66**] in the late 1980s, where *O*-alkyl carbamate carbanions (**70**) were generated and shown to react with various electrophiles with a high degree of enantioselectivity (**Scheme 12**).[40] This work garnered much interest from the synthetic community, as it gave rise to new methods for preparing compounds with sp^3-hybridized chiral centres beside heteroatoms.[41]
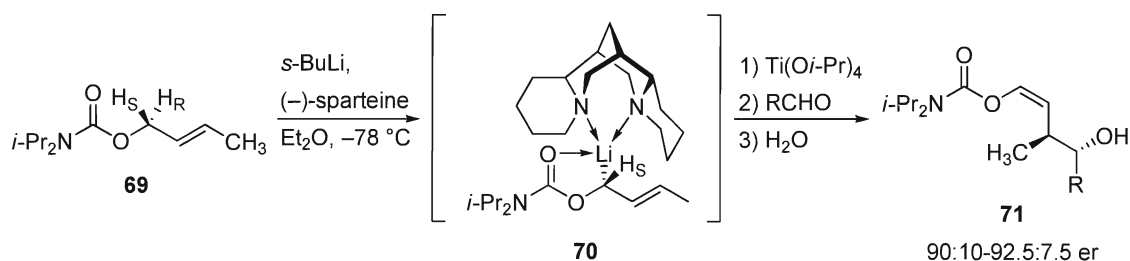
Scheme 12. First reported use of (−)-sparteine in highly enantioselective deprotonation.

Industrial interest in anionic polymerization also led to the finding that small amounts of Lewis base additives could significantly alter the reactivity of organolithiums. Most of these additives are bidentate and contain tertiary amines,[42] ethers, alkoxides or a combination thereof, although some tridentate ligands are used as well. (−)-Sparteine[43] [(−)-**66**], or lupinidine, is the predominant alkaloid in *Lupinus mutabilis* and a member of the Lupin family (**Figure 3**) of alkaloids. It is the most widely used and studied ligand for asymmetric transformations that use organolithium reagents. A major drawback of enantioselective (−)-sparteine-mediated transformations leading to a configurationally stable single-enantiomer intermediate is that one would require (+)-sparteine [(+)-**66**], or pachycarpine, to access the opposite enantiomer. (−)-Sparteine [(−)-**66**] was first isolated[44] in 1851 and is available commercially, readily isolated in large quantities from

the extracts of bitter lupin seeds, whereas the (+)-**66** is much less abundant and is more often (semi)synthesized.[45] This has led to considerable interest in methods[46] to circumvent this shortcoming and, more generally, the search for effective (+)-sparteine surrogates.[47]

1.1.3.2 α-Lithioamines: Lithiation of 5- & 6-Membered *N*-Heterocycles

Shortly after Hoppe's disclosure of the high enantioselectivity provided by (−)-sparteine [(−)-**66**] in the lithiation-substitution of *O*-alkyl carbamates (**69**), Beak reported an equally successful synthesis of enriched 2-substituted *N*-Boc pyrrolidines (**58**).[48] There is strong evidence to support an asymmetric deprotonation step leading to α-lithiopyrrolidine (**72**), which may then be trapped with various electrophiles in typically good yields and excellent enantioselectivities, furnishing the enriched 2-substituted pyrrolidines (**73a-e**, **Scheme 13**).
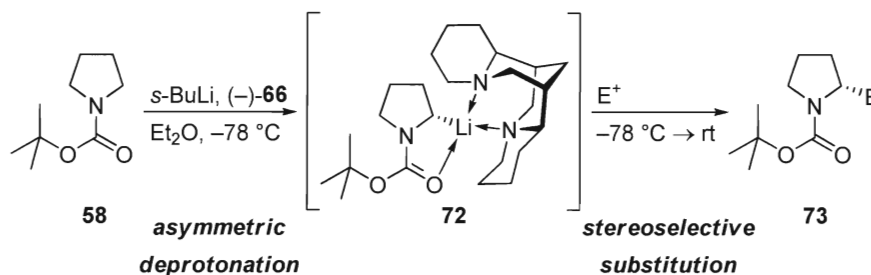
Product	E	Yield (%)	er (% ee)
73a	CH$_3$	88	3:97 (94)
73b	CO$_2$H	55	6:94 (88)
73c	C(OH)Ph$_2$	75	5:95 (90)
73d	SnBu$_3$	83	2:98 (96)
73e	SiMe$_3$	87	2:98 (96)

Scheme 13. (−)-Sparteine-mediated enantioselective substitution of *N*-Boc pyrrolidine.

While exploring the reaction parameters,[48b] what are now typical trends were observed: if the reaction was carried out at temperatures higher than −78 °C, erosion of selectivity occurred. Sub-stoichiometric amounts of the ligand or strongly coordinating solvents, THF[49] in particular, also led to significant losses in er due to competitive coordination with the alkyllithium.

A number of ligands (**Figure 4**) were screened[48b,50] in addition to (−)-sparteine [(−)-**66**]. Of these, only two, pyrrolidine derivative **74** and bispidine **88**, provided the 2-SiMe$_3$ product (**73e**) with selectivities approaching that of (−)-**66** but in diminished yields. Of note are the C_2-symmetric ligands[51] (−)-α-isosparteine (**67**) and (*R,R*)-TMCDA [(*R,R*)-**87**]. (−)-α-Isosparteine (**67**) provided only a small amount of **73e**, albeit with moderate enantioselectivity. Beak attributed this lack of reactivity to an overly crowded transition state where the Li atom becomes too encapsulated to be reactive, which becomes apparent from analysis of simple space-filling models (**Figure 5**). (*R,R*)-TMCDA [(*R,R*)-**87**] provided an excellent yield, but with no asymmetric induction detected. Wiberg and Bailey conducted a computational study, where this lack of selectivity was ascribed to a lack of steric interaction between (*R,R*)-**87** and *N*-Boc pyrrolidine (**58**).[52] It was suggested that a *trans*-diaminocyclohexane bearing branched alkyl groups might improve this.
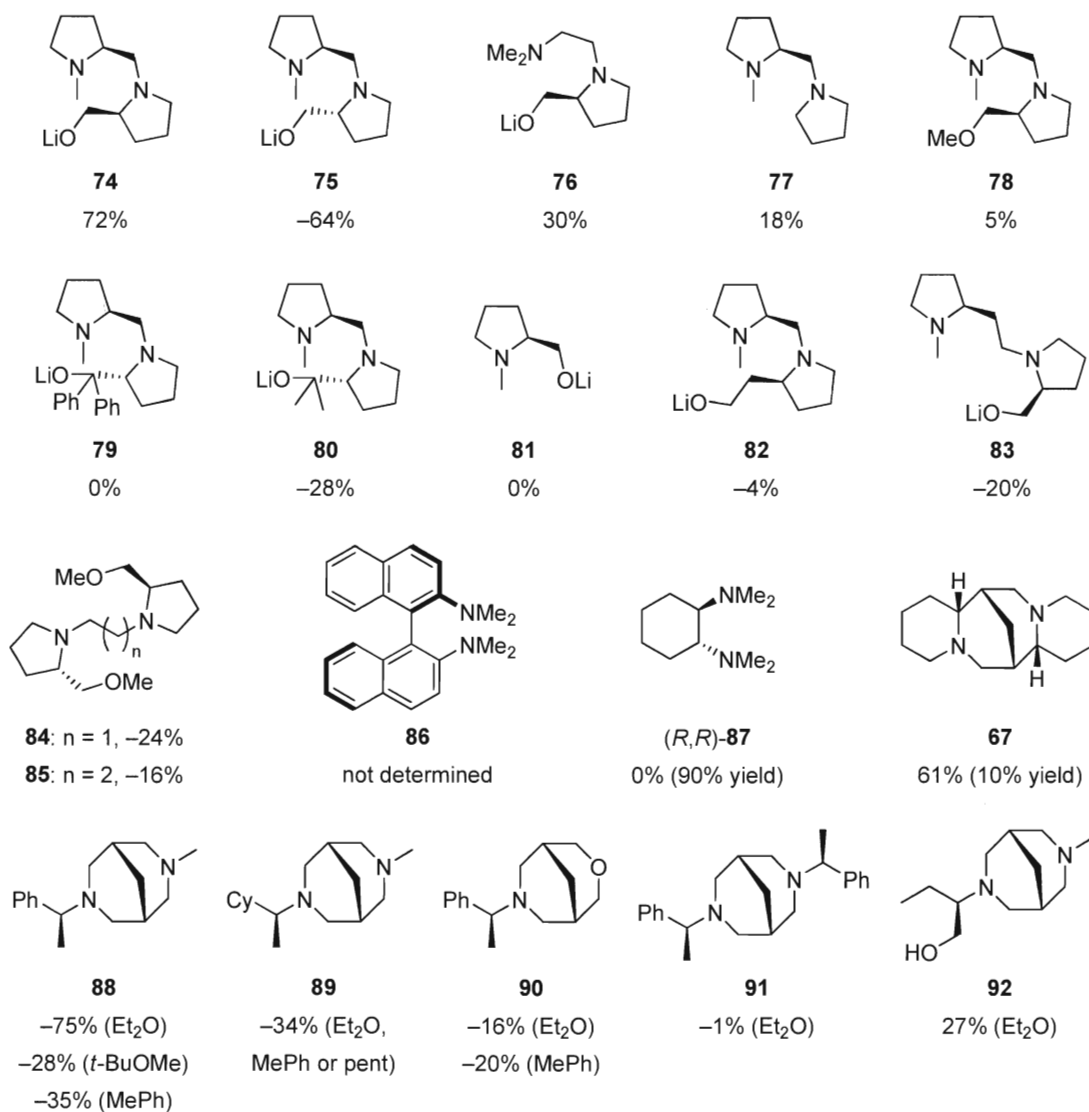
Figure 4. Ligands screened in enantioselective substitution of *N*-Boc pyrrolidine.

Lithiation and electrophile-trapping of piperidines is also possible.[53] The homologous *N*-Boc piperidine (**93**), however, does not behave analogously in an asymmetric environment.[54] Deprotonation is considerably slower and less selective relative to **58**, providing only about 8% of 2-TMS piperidine **94** with an er of 13:87.
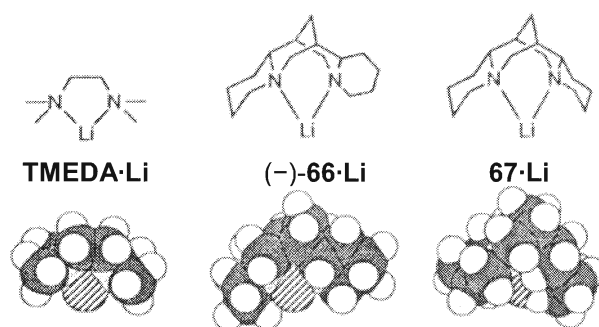
Figure 5. Space-filling models of diamine·Li complexes illustrating the extent of encapsulation of the Li atom.[50]

The major product of the reaction was enamine **95** (43%), along with an isomeric mixture of ketone **96** (9%) resulting from the attack of *s*-BuLi on the carbonyl of the Boc group (**Scheme 14**). The sense of enantioselection was confirmed by X-ray diffraction analysis of the *p*-bromobenzamide derivative (**97**) and shown to be the same (*S*)-configuration as the substituted *N*-Boc pyrrolidines (**73a-e**). That is, treatment with *s*-BuLi·(−)-sparteine involves the preferential abstraction of the (equatorial) pro-*S* hydrogen. Again, alternative ligands (−)-TMCDA [(−)-**87**] and (+)-sparteine surrogate **98**[47a,c-e] were only able to offer better chemical yields, with no improvement in selectivity.
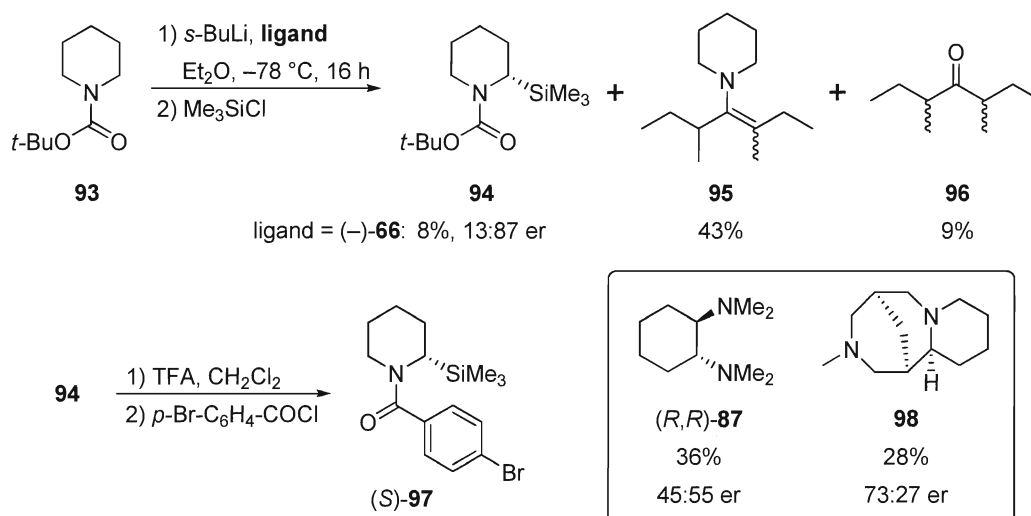
Scheme 14. Enantioselective substitution of *N*-Boc piperidine (**93**) and absolute stereochemical determination *via* bromobenzamide (*S*)-**97**.

Directed lithiation using Boc carbamates has also been applied to benzo-fused systems, such as the tetrahydroquinolines and indoline derivatives. Meyers carried out numerous comprehensive studies on the lithiation of nitrogen-containing heterocycles. It was demonstrated that the Boc group predominantly directs lithiation to the 8-position of **99** under achiral conditions, producing only small amounts of **99-d_1**.[55a] Substitution at C2 only proved significant if C7 was already substituted. Treatment of **99-d_1** under the typical metalation conditions for 6 h, followed by quenching with MeOD, led to **99-d_2** in 90% yield (**Scheme 15**). In contrast, metalation of the *t*-butylformamidine derivative (**100**) first took place at C2 to give **100-d_1**.
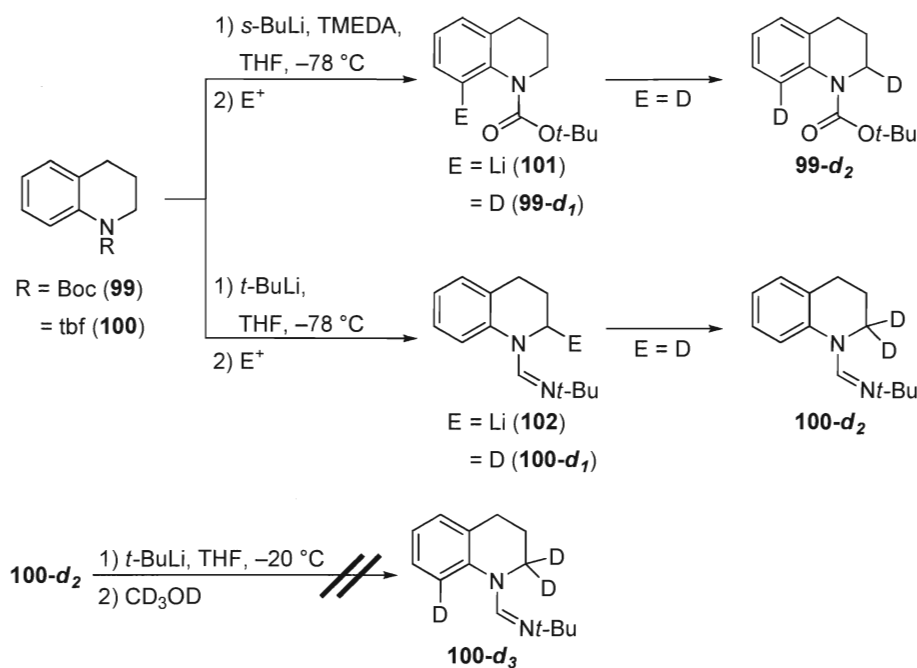
Scheme 15. Contrasting regioselectivity for Boc- (**99**) and tbf-protected (**100**) tetrahydroquinoline derivatives in lithiation-substitution.

Interestingly, exposure of **100-d_1** to metalation and MeOD quench provided the *gem*-dideuterated product (**100-d_2**) exclusively, which would not undergo further substitution (at C8) to form **100-d_3** even after an extended reaction time of 18 h. Only recovered

starting material and/or decomposition products were observed in this case. A point of difference betweeen **100** and **99** is that the tbf derivatives required the reaction to be carried out with *t*-BuLi in THF at −20 °C, while reaction of the Boc derivative could be performed with *s*-BuLi and TMEDA in Et$_2$O at −78 °C, thus precluding a direct comparison. Comparison of the Boc and *t*-butylformamidine derivatives led Meyers to suggest that conformational populations, in addition to the electronic nature of the directing groups and the metalation conditions, played an important role in the kinetic acidities of the protons in question.

Results for the Boc (**103**) and tbf indoline derivatives mirrored those described for the tetrahydroquinolines derivatives above (**99**, **100**). Subsequently, Beak described the enantioselective substitution of *N*-Boc indoline (**103**) and *N*-Boc-7-chloroindoline (**104**) in which metalation on the arene *ortho* to the directing group was blocked.[56] Selected results for the enantioselective lithiation-substitution of **103** and **104** leading to the (*S*)-configured products are shown in **Scheme 16**. Although the er is typically higher for **105a-c**, lithiation of **104** appears to be easier judging by the shorter reaction times. This fact is supported by a competition experiment where a mixture of **103** and **104** was exposed to lithiation (*s*-BuLi, (−)-**66**, *i*-PrPh, −78 °C) in which **104** reacted nearly eight times faster than **103**, where the 7-chloro substituent was absent. Of note is the aspect of regioselectivity in the lithiation of **103** compared to the above results of Meyers; whereas he obtained predominantly 8-substituted tetrahydroquinoline products upon lithiation-substitution of **99** using TMEDA, Beak observed mostly substitution at the indoline 2-position with (−)-sparteine [(−)-**66**] with < 5% of the 7-substituted regioisomer. Again, given that the reaction solvents are not the same, a definite conclusion cannot be made.

	for **103**: *s*-BuLi, (−)-**66**			Product	E	Yield (%)	er (% *ee*)

for **103**: *s*-BuLi, (−)-**66**
i-PrPh, −78 °C, 6 h
for **104**: *s*-BuLi, (−)-**66**
t-BuOMe, −78 °C, 3 h
then E⁺

R = H (**103**)
= Cl (**104**)

R = H (**105**)
= Cl (**106**)

Product	E	Yield (%)	er (% *ee*)
105a	SnMe₃	70	1:99 (98)
106a	SnMe₃	75	13:87 (74)
105b	C(OH)Ph₂	11	7.5:92.5 (85)
106b	C(OH)Ph₂	77	14:86 (72)
105c	CH₂CH=CH₂	28	32:68 (36)
106c	CH₂CH=CH₂	32	45:55 (10)
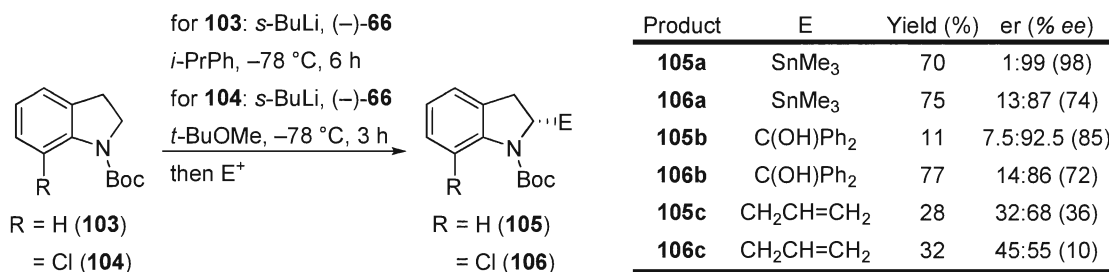
Scheme 16. (−)-Sparteine-mediated enantioselective substitution of *N*-Boc indolines.

A set of experiments where **104** was treated under achiral conditions (*s*-BuLi, TMEDA, Et₂O, −78 °C, 1 h) provided (±)-**106** in 79-89% yield (with the exception of MeI and CH₂=CHCH₂Br as electrophiles), which further illustrates that blocking a competitively lithiated position is a viable way to achieve regioselective substitution.

1.1.4 Ureas as Directing Groups for Lithiation

Although only tbf and carbamoyl directing groups have been used for lithiation of saturated *N*-heterocycles, many others are possible for any given substrate.[38g,i] The urea functionality is one group that has been sparsely applied as a directing group in lithiation chemistry and, to the best of our knowledge, never in a (−)-sparteine-mediated reaction with a prochiral substrate. Reported examples for non-prochiral substrates include indolyl-*N*,*N*-diethylurea (**107**),[57] *N*-aryltetrahydropyrimidinones (**108**),[58] *N'*-aryl-*N*,*N*-dimethylureas (**109**)[59] and diaryl ureas **110**[60] and **111** by Clayden (**Scheme 17**). Shortly after reporting the chemistry on **110**, Clayden's group discovered a highly stereoselective rearrangement of lithiated intermediate **111**, which proceeds by N-to-C aryl migration when the reaction was carried out in the presence of DMPU. This methodology was

extended to the synthesis of chiral diarylmethylamines (**114**) by subsequent cleavage of

the urea (**113**).[61]
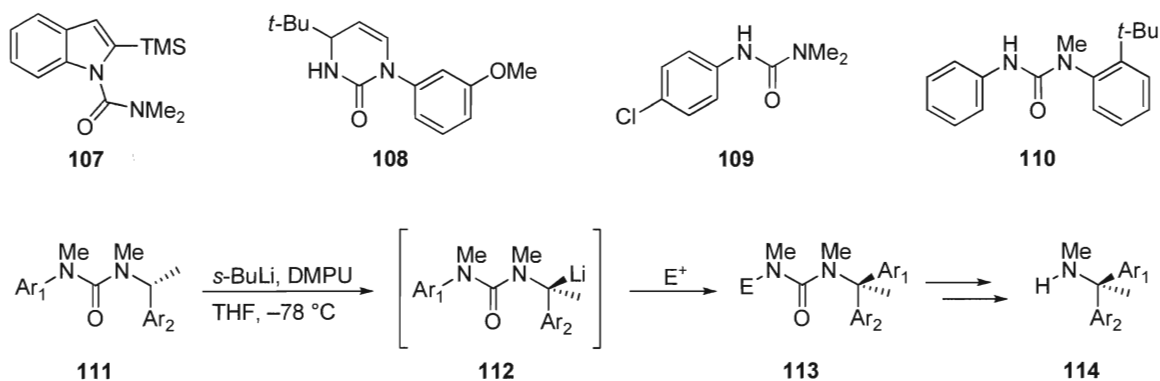
Scheme 17. Previously employed urea directing groups (**107-111**), and
rearrangement of lithiated intermediate **112**.

1.2 Aims & Objectives

The aim of the work that follows was to explore the feasibility of a new method, namely asymmetric α-induction by deprotonation-electrophile quench, for the preparation of chiral C_1- and possibly C_2-symmetric benzimidazolium salts based on the octahydrophenanthroline framework. This route would complement those already discussed: diastereoselective reduction (Section 1.1.2.1), reduction-resolution, asymmetric reduction (Section 1.1.2.2) and asymmetric α-induction by Rh-catalyzed C-H activation (1.1.2.3). The objectives are as follows:

1. To find a suitable group to direct lithiation to the position α to nitrogen.

2. To optimize and define the scope of the reaction in terms of asymmetric induction and electrophiles.

3. To determine the absolute stereochemistry of the substituted products.

4. To find a method to convert the chiral products to ylidene precursors (preferably benzimidazolium salts).

1.3 Results & Discussion

1.3.1 Lithiation of Octahydrophenanthroline Derivatives: Access to Chiral 2-Substituted Benzimidazolium Salts

At the onset of a program directed towards the use of reduced phenanthrolines in asymmetric catalysis,[16,62] (–)-sparteine-mediated enantioselective lithiation appeared to be a direct path to rigid C_1-, and possibly, C_2-symmetric molecules. Moreover, the urea functionality would serve as a useful directing group for post-substitution modification to potentially interesting compounds (e.g. ylidenes or phosphorodiamidites) for catalytic applications. A former undergraduate student conducted some substrate preparation and preliminary experiments for this work.[63] Considering the amount of work reported on the lithiation of Boc carbamates, the most logical derivative to test was bis-*N*-Boc octahydrophenanthroline (**117**). This was synthesized by heating a mixture of Boc$_2$O and octahydrophenanthroline (**116**),[62d] which was prepared from readily available 1,10-phenanthroline (**115**) by reduction (**Scheme 18**). The use of any solvents in the Boc protection step afforded mixtures of mono- and bis-protected products. The broadened NMR spectra of **117** clearly showed the presence of rotamers. The spectra may have been complicated further by steric interactions between the two bulky *tert*-butyloxycarbonyl groups projecting towards each other in the "bay region" of the molecule. Lithiation of **117** under standard (1.2 equivalents *s*-BuLi, TMEDA, −78 °C, THF) or more forcing conditions (3.2 equivalents *s*-BuLi, TMEDA, −78 °C) provided no evidence of α-substituted products (**117-d_1**, **118**) after quench with MeOD. Trials using (–)-sparteine [(–)-**66**] in Et$_2$O and methyl iodide to quench the putative carbanion also resulted only in recovery of **117**.
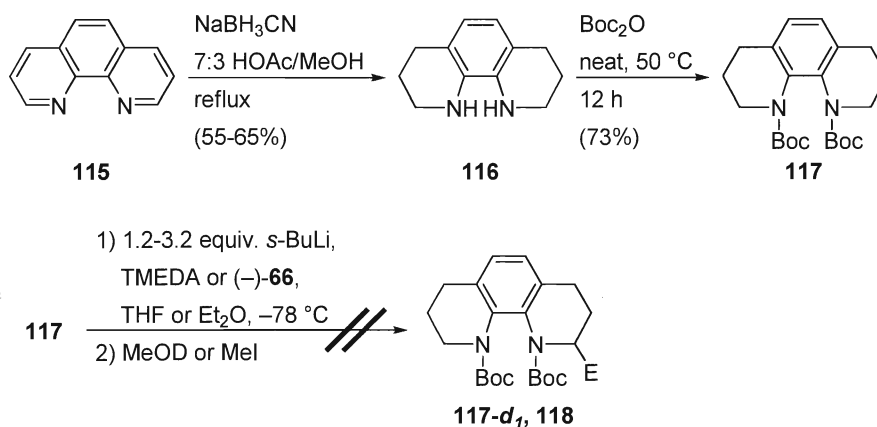
Scheme 18. Preparation and attempted lithiation of bis *N*-Boc substrate **117**.

The difficulty faced in the lithiation of **117** suggested that the Boc directing groups were unable to adopt the required conformations in which the coordinated alkyllithium was in close enough proximity to abstract one of the α-hydrogens.[64] Molecular modeling with Spartan02 provided support for this by allowing calculation of the ground state conformers for **117** based on a Boltzmann distribution. Four distinct conformational populations (**117a-d**, **Scheme 19**) were found to reside within 1 kcal/mol of the global energy minimum, and visual inspection revealed that both faces of the ring system were significantly blocked by the two Boc groups. The Boc groups were oriented above and below the mean plane of the piperidyl rings by a gear-like interaction enforced by their steric bulk. This conformational arrangement inhibited close approach of the *s*-BuLi·diamine complex to an α-hydrogen, thus preventing lithiation.
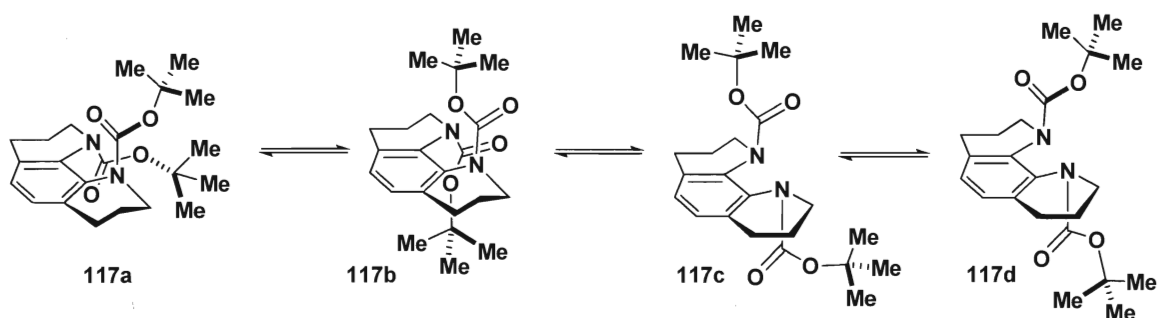
Scheme 19. Boltzmann-based conformational states of **117**.

To facilitate lithiation at the 2-position, a smaller directing group would be required, one that could bring the organolithium-diamine complex in proximity to the α-hydrogens. Bridging the two nitrogens with a carbonyl to make a urea would place the carbonyl in the plane of the rings and provide a favourable geometry to allow for deprotonation. To this end, cyclization of diamine **116** with triphosgene provided **119** as a highly crystalline compound in good yield. When subjected to asymmetric lithiation conditions, **119** gratifyingly afforded monodeuterated **119-d_1** in 50% yield with >95% D-incorporation. Some ring-opened amide **121** (**Scheme 20**) was also isolated from the reaction mixture (18%). Notably, 2.2 equivalents of alkyllithium were required for complete consumption of starting material, as incomplete deuteration was observed when only 1.2 equivalents of base were used. The high yield of **119-d_1** relative to Beak's 2-TMS substituted *N*-Boc piperidine (8%) was encouraging initially. However, the use of MeI as electrophile in this transformation gave methyl adduct **120a** in lower yield (25-30%) an er of 20:80. The enantioselectivity could be improved somewhat to 16:84 when *i*-PrLi was employed as the alkyllithium. Trapping of the intermediate carbanion with benzophenone gave similar results. Attempts to improve the yield and enantioselecivity of these reactions by addition of pre-complexed *i*-PrLi·(−)-**66** to the substrate (entries 5 and 6) were not fruitful. In

addition, reproducibly better yields and enantiomeric ratios were obtained by transferring the putative carbanion to a solution of either electrophile in THF at −78 °C. This observation may be attributed to displacement of (−)-sparteine from the carbanion by THF, implying that the intermediate possessed configurational stability and that the deprotonation step was enantiodetermining, as with N-Boc pyrrolidine (**58**). Attempts to use Me$_3$SiCl or CH$_2$=CHCH$_2$Br as electrophiles gave only trace amounts of the products, a phenomenon that had been observed before with N-Boc piperazines.[65]

Product	RLi	E⁺	E	Yield (%)	er (% ee)
119-d_1	s-BuLi	MeOD[a]	D	50	n.d.
120a	s-BuLi	MeI	Me	25-30	20:80 (60)
120a	i-PrLi	MeI	Me	25-30	16:84 (68)
120b	i-PrLi	Ph₂CO	C(OH)Ph₂	17-27	16.5:83.5 (67)
120a	i-PrLi[b]	MeI	Me	12	19:81 (62)
120b	i-PrLi[b]	Ph₂CO	C(OH)Ph₂	18	19:81 (62)

[a] the reaction was allowed to warm to rt after CH₃OD addition.
[b] i-PrLi and (−)-**66** were mixed at −78 °C prior to addition to **119**.
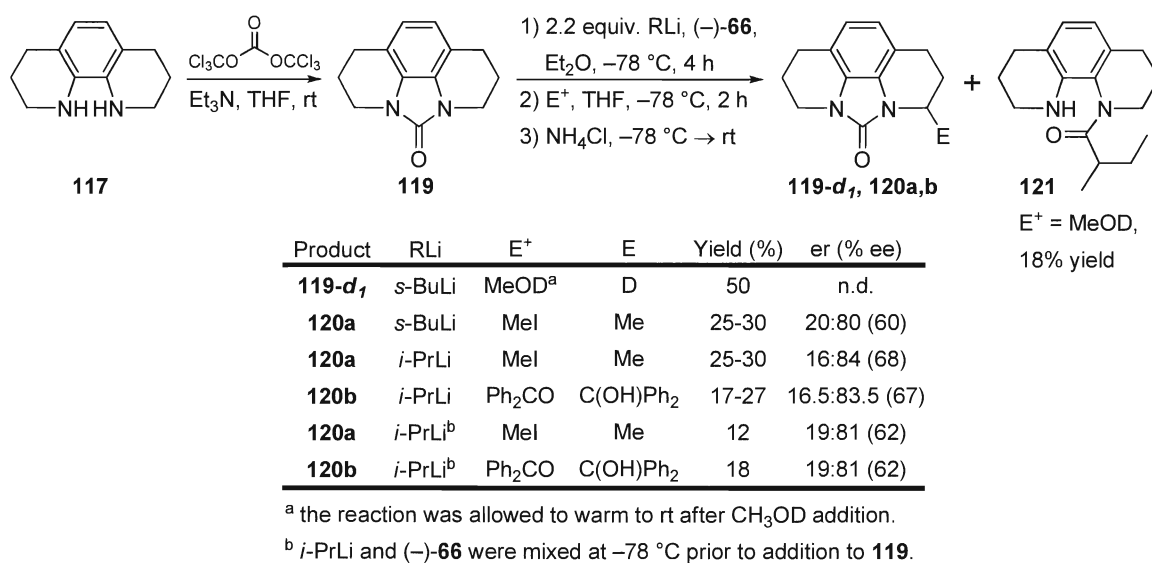
Scheme 20. Enantioselective lithiation-electrophile quench of urea **119**.

The preparation of two heavy atom derivatives of **120a** was pursued in order to determine the stereochemistry of the products by X-ray crystallography. In the first case, reduction of urea **120a** with LiAlH₄ at reflux gave an aminal that proved surprisingly difficult to hydrolyze to diamine **122**, which nonetheless afforded the 2-methylated benzimidazolium iodide (**123**) under standard conditions with HC(OEt)₃. All attempts to grow X-ray quality single crystals of **123** (including preparation and crystallization of the bromide salt) were unsuccessful.
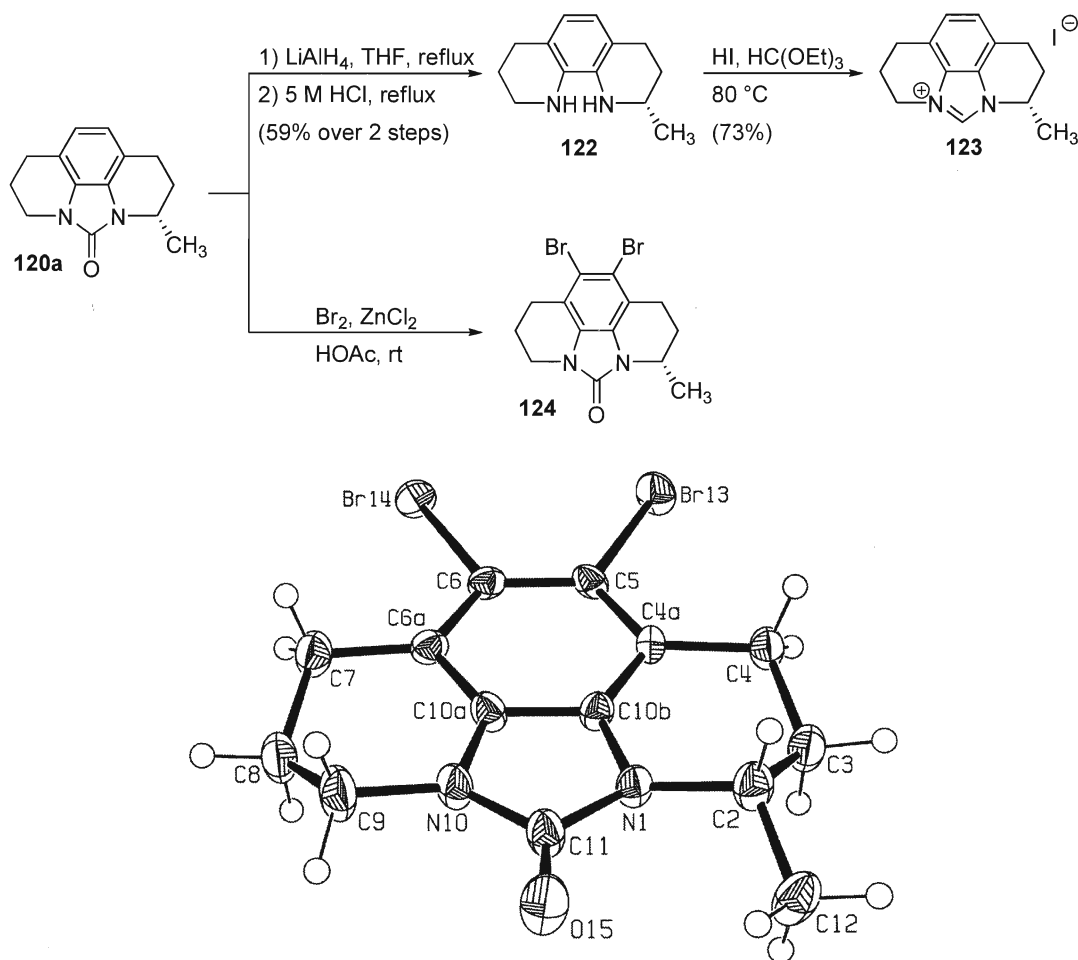
Scheme 21. Derivatization of **120a** and ORTEP plot of **124** with 50% probability ellipsoids showing absolute stereochemistry.

Attempts to prepare a bis(*p*-bromobenzamide) analogous to Beak's 2-TMS benzamide (**97**) was, not surprisingly, thwarted by steric congestion that would be imposed by these groups. Electrophilic bromination of the aromatic ring of **120a** was affected by exporsure to Br_2 and $ZnCl_2$ in acetic acid. This transformation proceeded in high yield and without erosion of the er to give dibromide **124**. Single crystals of the dibromide (**124**) were grown from EtOAc and determination of the absolute stereochemistry by anomalous scattering X-ray diffraction confirmed that it had the (*S*)-configuration, the same relative

streochemistry as *p*-bromobenzoyl-protected 2-TMS piperidine **94**. It may also be assumed that product **120b** has the same relative configuration as **120a**.

1.3.2 Computational Studies for Deprotonation of 1,2,3,5,6,7-Hexahydro-3a,4a-diazacyclopenta[*def*]phenanthren-4-one (119)

To aid in our understanding of the stereochemical course of lithiation of **119** with *i*-PrLi·(−)-sparteine [(−)-**66**], a transition state analysis was undertaken in collaboration with Professor Travis Dudding who used Gaussian '03.[66] Sixteen different transition state geometries were considered for the α-deprotonation of **119** with the C_1-symmetric complex *i*-PrLi·(−)-**66**, in which the relative orientations of the A and D rings of (−)-**66** were exchanged by a rotation of 180° with respect to the principal axis of the urea. Each transition state was optimized at the B3LYP[67]/6-31G(d,p)[68] level and verified as a first-order saddle point by frequency calculations. Finally, single-point MP2/6-31G(d) calculations were carried out to obtain a more accurate description of the energies involved.

Inspection of **TS1** and **TS2** (**Figure 6**) provided some revealing details. **TS1** shows (−)-sparteine and urea in a more sterically encumbered arrangement, with the diamine lying over the site of proton transfer. When aligned like this, it is notable that the A ring β-methylene hydrogens of (−)-sparteine are quite close to core of the urea and appear to be influential in the selectivity. A close contact of 2.18 Å in **TS1** is measured for the distance between the axial hydrogen of the urea and a β-methylene hydrogen, which leads to a destabilizing interaction in this transition state.
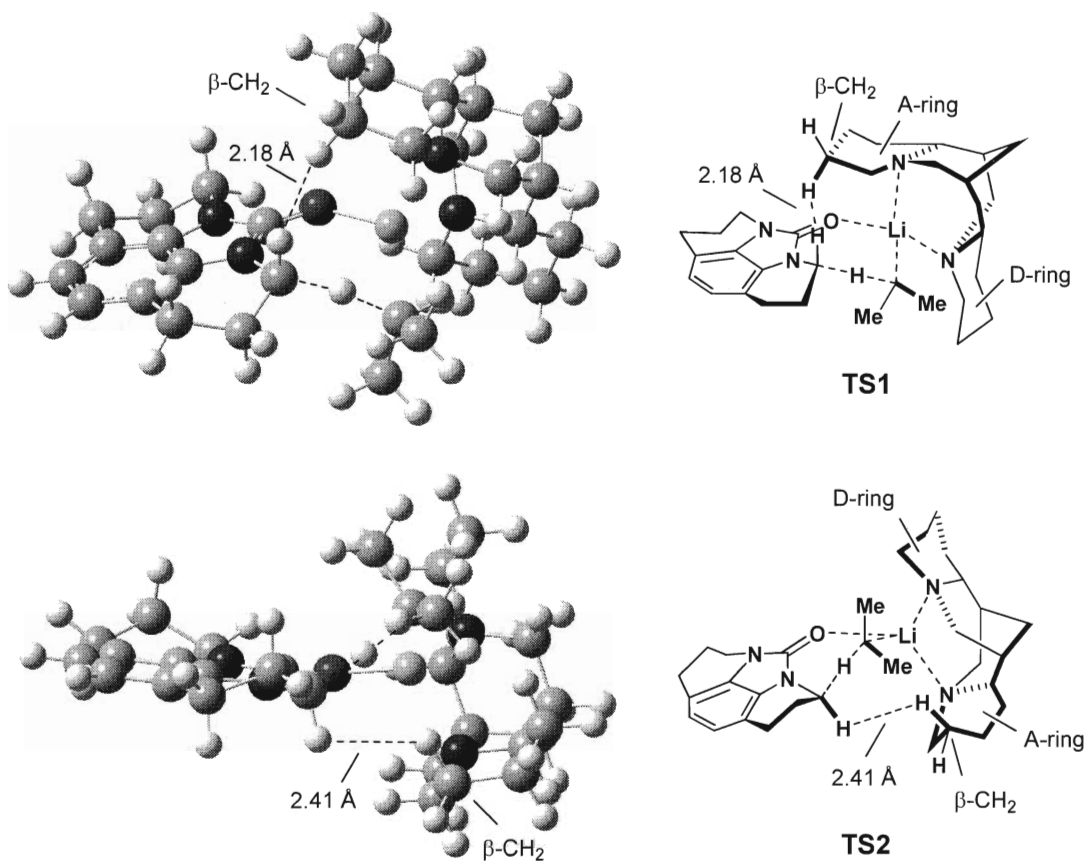
Figure 6. Transition state models leading to pro-*R* (**TS1**) and observed pro-*S* (**TS2**) deprotonation of **119**.

Conversely, the analogous closest contact in **TS2** is 2.41 Å, which is greater than the sum of the radii of two hydrogens (at 2.40 Å).[69] These results are in accord with precedent suggesting the necessity for the presence of the A ring in obtaining high selectivity in lithiation-substitution reactions.[70] These observations may translate to a predictive tool for assessing the performance of (−)-sparteine in future reactions.

1.4 Conclusions and Future Work

It was demonstrated that the urea functional group may serve as a directing group for the (−)-sparteine-mediated asymmetric lithiation of benzo-fused piperidines and a sequence developed for the conversion of the products to benzimidazolium salts. Compared to the analogous lithiation of *N*-Boc piperidine (**93**), yields for the reaction were slightly higher, while enantioselectivities were marginally lower. By X-ray diffraction studies of dibromide **124**, the sense of asymmetric induction was shown to be the same as for **93**; that is, abstraction of the pro-*S* hydrogen α to nitrogen was preferred, which is consistent with previous results on *N*-Boc pyrrolidines and piperidines.

Molecular modeling indicated that the pro-*S* the transition state was favoured over pro-*R* deprotonation in a ratio of 87:13. The difference in transition states appeared to arise from a repulsive interaction between (−)-sparteine's β-methylene group and an axial hydrogen α to nitrogen, an observation that may correlate well with other systems

In terms of the synthetic route used to access benzimidazolium salt **123**, transformation of the urea directly to a chloroimidazolium salt with POCl₃ should be investigated, as was demonstrated in a recently published paper by Metallinos and Xu.[71] Using the urea directing group, it was shown that 5-5 fused systems (**124** and **125**) underwent the lithiation-substitution reactions with high selectivities, just as in the case of Beak's 5-5 fused carbamates,[72] to generate α-substituted products **126** and **127** (**Scheme 22**). Treatment with POCl₃ and anion exchange allowed conversion to diaminoylidene precursors **128** and **129** without removal of the urea carbon. The 5-5 systems would also stand to be improved by the development of a protocol that would allow removal of the substituent (i.e. *t*-butyl) on nitrogen or employ a latent substituent.[73]

This could be achieved through dealkylation, which proved problematic for Metallinos and Xu,[71] or through latent protection and subsequent lithiation-quench. Essentially, this would provide more flexibility for the preparation of derivatives of **128** and **129**, namely *N*-arylated compounds.
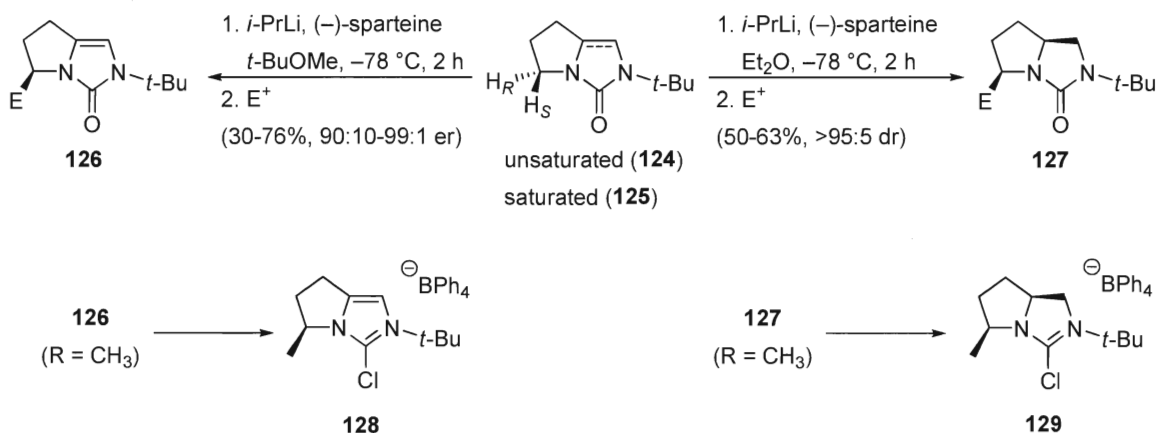
Scheme 22. Enantio- and diastereoselective lithiation-substitution of pyrrole[1,2-c]imidazol-3-ones and conversion to chloroimidazol(in)ium salts **128** and **129**.

Lastly, this methodology should be extended to other fused systems and the influence of (−)-sparteine's A-ring β-methylene group should be investigated for its substrate generality and reaction scope.

1.5 Experimental Procedures

General. All reagents were purchased from Aldrich, Fisher Scientific, Acros or Strem and used as received unless otherwise indicated. Tetrahydrofuran was freshly distilled from sodium/benzophenone ketyl under an atmosphere of nitrogen. Diethyl ether was distilled from LiAlH$_4$ under an atmosphere of argon. Dichloromethane was distilled from CaH$_2$ under an atmosphere of nitrogen. Organolithium reagents were titrated against *N*-benzylbenzamide[74] to a blue endpoint. All reactions were performed under argon in flame- or oven-dried glassware using syringe-septum cap techniques unless otherwise indicated. TLC was performed on silica gel unless otherwise stated. Column chromatography was performed on Silicycle silica gel 60 (70-230 mesh) unless otherwise stated. NMR spectra were obtained on a Bruker Avance 300 or Avance 600 instrument and are referenced to tetramethylsilane or to the residual proton signal of the deuterated solvent for ^{1}H spectra, and to the carbon multiplet of the deuterated solvent for ^{13}C spectra according to values given in *Spectrometric Identification of Organic Compounds, Seventh Edition*, p. 200 and p. 240. Spectroscopic data are reported as follows: (multiplicity, number of protons, coupling constant). FTIR spectra were recorded on an ATI Mattson Research Series spectrometer. Low and high-resolution mass spectral data were obtained on a Kratos Concept 1S Double Focusing spectrometer. Enantiomeric ratios were determined on an Agilent 1100 HPLC system using either Chiralpak AS-H or Chiralcel OD-H columns, and are compared to racemic material. It should be noted for HPLC measurements that response factors were not obtained for each enantiomer and the reported enantiomeric ratios are not calibrated. Optical rotations were measured on a Rudolph Research Autopol III automatic polarimeter. Elemental analyses were performed

by Atlantic Microlab, Inc., Norcross, GA, USA. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected.

1,2,3,4,7,8,9,10-Octahydro-1,10-phenanthroline (116).
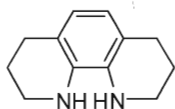
This compound was prepared according to a modification of a reported procedure.[75] NaBH$_3$CN (2.00 g, 31.8 mmol) was carefully added to a stirring solution of 1,10-phenanthroline (2.00 g, 10.1 mmol) in 7:3 HOAc/MeOH at room temperature. The resulting deep red mixture was then heated at reflux and additional NaBH$_3$CN (2.00 g, 31.8 mmol) was added every 2 h until 4 additions had been made in total (8.00 g, 127 mmol). With each addition, the colour of the reaction mixture became more yellow. 2 h after the last addition, the reaction was cooled to 0 °C, made strongly alkaline (pH >12) with aq. 6 M NaOH and the volatiles were removed on a rotary evaporator. The separated solids and aqueous layer were extracted with CH$_2$Cl$_2$ (3 × 30 mL) and the combined organics washed with brine (1 × 30 mL), dried over anhyd. Na$_2$SO$_4$ and concentrated to dryness under reduced pressure. The remaining yellowish oil was preadsorbed on silica and subjected to flash chromatography (97:3 PhMe/Et$_3$N), which afforded diamine **116** (1.18 g, 62%) as a waxy, slightly yellowish solid that was stored at −20 °C under argon and used without further purification: R$_f$ = 0.22 (97:3 PhMe/Et$_3$N); mp 66-67 °C (lit. 70 °C[76]); IR (KBr) v_{max} 3249, 3035, 2923, 2834, 1615, 1583, 1496, 1438, 1327, 1262, 1112, 782 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 6.23 (s, 2H), 3.68 (b, 2H), 3.26-3.21 (m, 4H), 2.62 (t, 4H, J = 5.8 Hz), 1.78 (quintet, 4H, J = 5.9 Hz); ^{13}C NMR (75.5 MHz, acetone-d_6) δ 133.4, 119.9, 119.1, 43.1, 27.9, 23.4; EIMS [m/z(%)] 188 (M$^+$, 100); HRMS (EI) calcd for C$_{12}$H$_{16}$N$_2$: 188.1313; found 188.1315.

2,3,4,7,8,9-Hexahydro-1,10-phenanthroline-1,10-dicarboxylic acid di-*tert*-butyl ester (117).
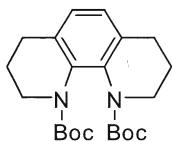
A round-bottomed flask was charged with diamine **116** (315 mg, 1.67 mmol) and di-*tert*-butyl dicarbonate (730 mg, 3.35 mmol), and heated to 50 °C for 12 h. After cooling to room temperature, column chromatography (SiO$_2$, 20% EtOAc/hex, R$_f$ 0.29) gave crude **117** as a yellow-orange semisolid that solidified on standing. Recrystallization from petroleum ether gave biscarbamate **117** as an amorphous off-white solid (473 mg, 73%): mp 113-114 °C (pet. ether); IR (KBr) v_{max} 3017, 2984, 2962, 2950, 2931, 2841, 1680, 1457, 1370, 1351, 1159, 1133 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$, rotameric) δ 6.83 (s, 2H), 4.08-3.93 (b, 2H), 3.39 (b, 2H), 2.62 (b, 4H), 2.07 (b, 2H), 1.70 (b, 2H), 1.44 (s, 18H); ^{13}C NMR (150.9 MHz, CDCl$_3$, rotameric) δ 153.6, 152.8, 134.8, 133.6, 133.3, 131.7, 124.3, 123.6, 122.8, 80.0, 79.3, 45.2, 43.2, 41.6, 28.2, 26.7, 24.7, 24.4; EIMS [m/z(%)] 214(M$^+$, 100), 185(12); HRMS (EI) calcd for C$_{22}$H$_{32}$N$_2$O$_4$: 388.2362; found 388.2359.

1,2,3,5,6,7-Hexahydro-3a,4a-diazacyclopenta[*def*]phenanthren-4-one (119).
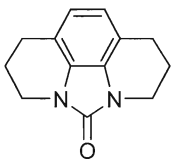
A solution of diamine **117** (1.63 g, 8.65 mmol) and triphosgene (2.57 g, 8.65 mmol) in dry THF (180 mL) was treated carefully (exothermic) with anhydrous triethylamine (2.40 mL, 17.3 mmol), and the resulting mixture was stirred at room temperature for 12 h. Water (50 mL) was added and the THF was removed *in vacuo*. The remaining aqueous mixture was extracted with CH$_2$Cl$_2$ (3 x 20 mL) and the combined extracts washed with water (20 mL) and brine (20

mL), dried over anhydrous MgSO$_4$, filtered, and concentrated to approximately 10% of its original volume. The concentrated solution was passed through a short column of SiO$_2$, eluting with 1:1 EtOAc/hex (R$_f$ 0.19) to give the crude product as an off-white solid. Recrystallization from EtOAc/hex gave urea **119** as colorless needles (1.58 g, 85%) in two crops; mp 160-162 °C (EtOAc/hex); IR (KBr) v_{max} 3053, 2954, 2920, 2857, 1701, 1631, 1514, 1411, 1342, 1230 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.75 (s, 2H), 3.85 (t, 4H, $J = 5.6$ Hz), 2.81 (t, 4H, $J = 6.3$ Hz), 2.12 (quintet, 4H, $J = 5.7$ Hz); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 152.9, 125.1, 118.4, 116.9, 38.9, 23.3, 22.7; EIMS [m/z(%)] 214(M$^+$, 100), 185(12); HRMS (EI) calcd for C$_{13}$H$_{14}$N$_2$O: 214.1106; found 214.1109; Anal. calcd for C$_{13}$H$_{14}$N$_2$O: C, 72.87; H, 6.59; found C, 72.75; H, 6.61.

3-Deutero-1,2,3,5,6,7-hexahydro-3a,4a-diazacyclopenta[*def*]phenanthren-4-one (119-*d₁*) and 1-(2,3,4,7,8,9,10-Heptahydro-[1,10]phenanthrolin-1-yl)-2-methylbutan-1-one (121).

A solution of urea **119** (107 mg, 0.5 mmol) and (−)-sparteine (0.25 mL, 1.1 mmol) in Et$_2$O (15 mL) under argon was cooled to −78 °C with stirring. The resulting suspension was treated with a solution of *s*-BuLi (0.93 mL, 1.18 M, 1.1 mmol) added dropwise over 10 min, giving a red-brown solution that was stirred for 4 h. Methanol-d_4 (0.45 mL) was added to quench the reaction mixture, resulting in a rapid change in color to pale yellow, and the mixture was allowed to warm to room temperature. Water (10 mL) was added, and the reaction mixture was extracted with Et$_2$O (3 x 10 mL) and CH$_2$Cl$_2$ (1 x 10 mL). The combined organic extracts were washed with water (10 mL), dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated *in vacuo*. Column chromatography (SiO$_2$, 64:35:1

hexanes:EtOAc:MeOH) gave, sequentially, amide **121** (24 mg, 18%) and urea **119-d_1** (54 mg, 50%, >95% monodeuterated).

121. off-white solid; R$_f$ 0.40 (SiO$_2$, 64:35:1 hexanes:EtOAc:MeOH); mp 84-85 °C; IR (KBr) ν_{max} 3393, 2957, 2931, 2872, 2839, 1643 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6, rotameric) δ 6.71 (d, 0.5 H, J = 7.2 Hz), 6.69 (d, 0.5 H, J = 7.5 Hz), 6.33 (d, 0.5 H, J = 7.2 Hz), 6.31 (d, 0.5 H, J = 7.5 Hz), 5.25 (b, 0.5 H), 5.16 (b, 0.5H), 4.60-4.51 (m, 1H), 3.23-3.11 (m, 2H), 2.68-2.39 (m, 4H), 2.28-2.21 (m, 1H), 2.08-2.02 (m, 1H), 1.79-1.65 (m, 3H), 1.52-1.47 (m, 1H), 1.25-1.09 (m, 2H), 1.04 (d, 1.5H, J = 6.6 Hz), 0.81 (t, 1.5H, J = 7.5 Hz), 0.66 (d, 1.5H, J = 7.2 Hz), 0.52 (t, 1.5H, J = 7.5 Hz); ^{13}C NMR (75.5 MHz, DMSO-d_6, rotameric) δ 176.9, 176.5, 140.1, 139.9, 134.6, 134.5, 127.1, 127.0, 125.0, 124.8, 119.5, 119.3, 114.0, 113.9, 41.1, 40.9, 40.7, 38.4, 37.8, 27.6, 27.0, 26.9, 26.3, 25.8, 25.5, 23.93, 23.88, 21.6, 18.0, 17.1, 12.3, 11.4; EIMS [m/z(%)] 272(M$^+$, 26), 215(74), 187(100); HRMS (EI) calcd for C$_{17}$H$_{24}$N$_2$O: 272.1889; found 272.1900.
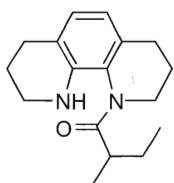
119-d_1. off-white solid; R$_f$ 0.10 (SiO$_2$, 64:35:1 hexanes:EtOAc:MeOH); mp 156-158 °C; IR (KBr) ν_{max} 3054, 2953, 2922, 2854, 2162, 1703, 1631, 1510, 1415, 1343, 1228 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.74 (s, 2H), 3.86-3.81 (m, 3H), 2.81 (t, 4H, J = 5.9 Hz), 2.16-2.08 (m, 4H); ^{13}C NMR (150.9 MHz, CDCl$_3$) δ 153.0, 125.2, 118.4, 117.0, 39.0, 38.7 (t, $^1J_{^{13}\mathrm{C}\text{-}^2\mathrm{H}}$ = 21.9 Hz), 23.4, 23.3, 22.8, 22.7; EIMS [m/z(%)] 215(M$^+$, 100), 186(12); HRMS (EI) calcd for C$_{13}$H$_{13}$DN$_2$O: 215.1168; found 215.1163.
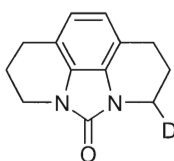
(+)-3-Methyl-1,2,3,5,6,7-hexahydro-3a,4a-diazacyclopenta[*def*]phenanthren-4-one (120a).
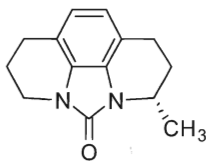
A solution of urea **119** (643 mg, 3.00 mmol) and (−)-sparteine (1.52 mL, 6.60 mmol) in dry Et$_2$O (70 mL) under argon was cooled to −78 °C with stirring. The resulting suspension was treated with a solution of *i*-PrLi in pentane (3.73 mL, 1.77 M, 6.60 mmol), added dropwise over 10 min, to give a red-brown solution that was stirred at −78 °C for 4 h. The reaction mixture was then transferred by cannula to a precooled (−78 °C) solution of iodomethane (0.65 mL, 10.5 mmol) in dry THF (80 mL), and stirred for a further 2 h. The resulting pale yellow solution was treated with saturated aqueous NH$_4$Cl solution (10 mL) and allowed to warm up to room temperature. Water (30 mL) was added, the phases were separated, and the remaining aqueous phase was extracted with Et$_2$O (3 x 20 mL). The combined organic layer was washed with 5% aqueous H$_3$PO$_4$ (2 x 10 mL) to remove (−)-sparteine, water (30 mL), brine (30 mL), dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated *in vacuo*. Column chromatography (SiO$_2$, 4:1 CH$_2$Cl$_2$/Et$_2$O, R$_f$ 0.32) gave **120a** (170 mg, 25%) as a pale yellow oil, which solidified on standing: CSP HPLC analysis (Chiralpak AS-H; eluent: 80:20 hexanes:*i*-PrOH, 1.0 mL/min) determined 84:16 er (68% ee) [t$_R$(major) = 11.03 min, t$_R$(minor) = 13.34 min]; [α]$_D^{20}$ = +21.0 (*c* = 4.37, CHCl$_3$); mp 57-59 °C; IR (KBr) v_{max} 2965, 2933, 2893, 1705, 1505, 1414, 1334, 1237 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.76 (s, 2H), 4.45-4.39 (m, 1H), 3.87-3.82 (m, 2H), 2.87-2.73 (m, 4H), 2.12 (quintet, 2H, *J* = 5.7 Hz), 2.07-1.99 (m, 2H), 1.40 (d, 3H, *J* = 6.3 Hz); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 152.6, 125.1, 118.4, 118.2, 116.9, 116.73, 116.66, 45.3, 38.9, 29.3, 23.3, 22.7, 20.1, 19.1; EIMS [*m/z*(%)] 228(M$^+$, 100), 213(87), 185(17); HRMS (EI)

calcd for $C_{14}H_{16}N_2O$: 228.1263; found 228.1260; Anal. calcd for $C_{14}H_{16}N_2O$: C, 73.66; H, 7.06; found C, 73.16; H, 7.01.

(−)-3-(Diphenylhydroxy)methyl-1,2,3,5,6,7-hexahydro-3a,4a-diazacyclopenta[*def*]phenanthren-4-one (120b).
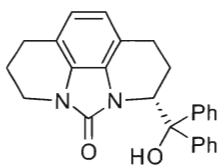
A solution of urea **119** (214 mg, 1.00 mmol) and (−)-sparteine (0.51 mL, 2.20 mmol) in dry Et_2O (25 mL) under argon was treated with a solution of *i*-PrLi in pentane (1.29 mL, 1.70 M, 2.20 mmol), added dropwise over 10 min, to give a red-brown solution that was stirred at −78 °C for 4 h. The reaction mixture was then transferred by cannula to a precooled (−78 °C) solution of benzophenone (638 mg, 3.50 mmol) in dry THF (18 mL) and stirred for a further 2 h. The resulting blue-green solution was treated with saturated aqueous NH_4Cl (3 mL) and allowed to warm to room temperature. Water (10 mL) was added, the phases were separated, and the resulting aqueous mixture was extracted with Et_2O (3 x 20 mL). The combined organic extract was washed with 5% aqueous H_3PO_4 (3 x 10 mL), water (15 mL) and brine (15 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. Column chromatography (SiO_2, 3:1 hexanes/EtOAc, R_f 0.23) gave **120b** as a colorless solid (107 mg, 27%); CSP HPLC analysis (Chiralcel OD-H; eluent: 90:10 hexanes:*i*-PrOH, 1.0 mL/min) determined 80:20 er (60% ee) [t_R(major) = 13.66 min, t_R(minor) = 22.64 min]; $[\alpha]_D^{20}$ = −75.9 (c = 0.2, $CHCl_3$). A recrystallized sample of **1.112b** (93% ee by CSP HPLC) had the following data: $[\alpha]_D^{20}$ = −122 (c = 0.10, $CHCl_3$) mp 257-259 °C (hexanes/EtOAc); IR (KBr) v_{max} 3387, 3056, 2963, 2938, 2912, 2883, 2831, 1689, 1501, 1349, 1234, 1165 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43-7.28 (m,

8H), 7.24-7.19 (m, 2H), 6.79 (d, 1H, J = 7.2 Hz), 6.71 (d, 1H, J = 8.1 Hz), 4.80 (dd, 1H, J = 8.1, 3.3 Hz), 3.84-3.70 (m, 2H), 2.92-2.73 (m, 2H), 2.54-2.25 (m, 3H), 2.20-2.03 (m, 2H), 1.77-1.67 (m, 1H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 154.3, 146.0, 143.9, 127.9, 127.8, 127.7, 127.5, 127.4, 127.2, 125.8, 125.4, 119.1, 118.6, 118.1, 117.0, 79.9, 62.7, 39.2, 27.1, 23.3, 23.0, 22.5; EIMS [m/z(%)] 396(M$^+$, 3), 378(16), 214(51), 105(57), 43(100); HRMS (EI) calcd for C$_{26}$H$_{24}$N$_2$O$_2$: 396.1838; found 369.1832; Anal. calcd for C$_{26}$H$_{24}$N$_2$O$_2$: C, 78.76; H, 6.10; found C, 78.23; H, 6.31.

(−)-2-Methyl-1,2,3,4,7,8,9,10-octahydro-1,10-phenanthroline (122).
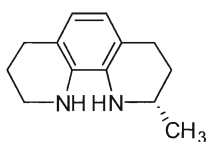
A stirred solution of urea **120a** (154 mg, 0.67 mmol) in THF (6.5 mL) under argon was cooled to 0 °C and treated with LiAlH$_4$ (128 mg, 3.37 mmol) in two portions. The resulting mixture was heated to reflux for 2 h. After cooling to room temperature, the reaction mixture was worked up by sequential addition of water (0.1 mL), 10% aqueous NaOH solution (0.1 mL), and water (0.3 mL). The precipitated aluminum salts were removed by filtration through Celite, and the filtrate was extracted with Et$_2$O (4 x 10 mL) and concentrated in vacuo. The resulting residue was treated with 5 M aqueous HCl solution (6.5 mL) and heated to 60 °C for 2 h. After cooling to room temperature, the mixture was made strongly alkaline with 10% aqueous NaOH (pH ≥ 12), and the product was extracted with CH$_2$Cl$_2$ (4 x 10 mL). The combined organic extract was dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated in vacuo. Column chromatography (SiO$_2$, 9:1 hexanes:EtOAc, R$_f$ 0.27) gave diamine **122** (80 mg, 59%) as a clear viscous oil; [α]$_D^{20}$ = −41.4 (c = 1.70, acetone); IR (KBr, neat) ν_{max} 3333, 3036, 2924, 2842, 1582, 1487, 1332, 1255 cm^{-1}; ^{1}H NMR (300 MHz, acetone-

d_6) δ 6.24 (ABq, 2H), 3.73 (b, 1H), 3.56 (b, 1H), 3.32-3.19 (m, 3H), 2.81-2.55 (m, 4H), 1.90-1.76 (m, 3H), 1.51-1.38 (m, 1H), 1.21 (d, 3H, J = 6.3 Hz); ^{13}C NMR (75.5 MHz, acetone-d_6) δ 133.5, 133.0, 119.9, 119.4, 119.0, 118.8, 48.4, 43.0, 31.2, 27.9, 27.5, 23.3, 22.8; EIMS [m/z(%)] 202(M$^+$, 100); HRMS (EI) calcd for $C_{13}H_{18}N_2$: 202.1470; found 202.1466.

(−)-Benzimidazolium iodide 123.
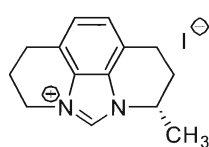
A solution of diamine **122** (31 mg, 0.15 mmol) in HC(OEt)$_3$ (3 mL) in a round-bottomed flask equipped with a reflux condenser under argon was treated with concentrated HI (21 μL, 0.15 mmol) and warmed to 80 °C for 1 h. The reflux condenser was removed, and heating was continued for an additional 2 h in the open air. After cooling to room temperature, the yellow reaction mixture was poured into Et$_2$O (15 mL), and the precipitated product was collected on a Hirsch funnel and dried in vacuo to give iodide **123** (37 mg, 73%) as an off-white powder: mp 219-221 °C (CH$_2$Cl$_2$/pent); [α]$_D^{20}$ = −3.8 (c = 0.40, CHCl$_3$); IR (KBr) ν_{max} 3091, 3064, 2963, 2917, 2838, 1509, 1320, 1200 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 10.69 (s, 1H), 7.25 (s, 2H), 4.90-4.85 (m, 1H), 4.74 (t, 2H, J = 6.0 Hz), 3.08-3.01 (m, 4H), 2.44-2.40 (m, 1H), 2.40-2.36 (m, 2H), 2.09 (sextet, 1H, J = 6.0 Hz), 1.85 (d, 3H, J = 6.0 Hz); ^{13}C NMR (150.9 MHz, CDCl$_3$) δ 137.4, 127.8, 127.4, 124.2 (2C), 122.8, 122.5, 52.6, 45.4, 30.7, 22.8, 22.7, 22.0, 20.3; FABMS [m/z(%)] 213(M–I$^-$, 100), HRMS (FAB) calcd for $C_{14}H_{17}N_2$: 213.1392; found 213.1384; Anal. calcd for $C_{14}H_{17}IN_2$: C, 49.43; H, 5.04; found C, 49.39; H, 5.06.

(−)-8,9-Dibromo-(3-*S*)-methyl-1,2,3,5,6,7-hexahydro-3a,4a-diaza-cyclopenta[def]phenanthren-4-one (124).
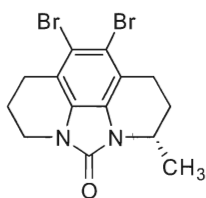
A solution of **120a** (228 mg, 1.00 mmol) in glacial acetic acid (5 mL) was treated with $ZnCl_2$ (290 mg, 2.13 mmol) and the mixture was stirred until a homogeneous solution had formed. The solution was then treated with Br_2 (0.11 mL, 2.1 mmol) by syringe and stirred at room temperature for 12 h. The slight excess of Br_2 persisted as an orange color in solution for the duration of the reaction. A solution of aqueous 50% Na_2SO_3 (10 mL), water (5 mL), and CH_2Cl_2 (20 mL) was added and the mixture was stirred at room temperature for approximately 20 min. The organic phase was collected and the remaining aqueous mixture was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extract was washed with 10% aqueous NaOH (3 x 10 mL), water (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was passed through a short column of SiO_2 eluting with CH_2Cl_2 to give dibromide **124** (370 mg, 96%) as a colorless oil that solidified on standing; CSP HPLC analysis (Chiralpak AS-H; eluent: 80:20 hexanes:*i*-PrOH, 1.0 mL/min) determined 84:16 er (68% ee) [t_R(major) = 13.48 min, t_R(minor) = 15.27 min]; $[\alpha]_D^{20}$ = (*c* = , $CHCl_3$); mp 119-123 °C (MeOH); X-Ray analysis (CCDC 620846) was performed on a colorless triangular needle fragment (0.22 × 0.14 × 0.12 mm), which was obtained by slow evaporation from EtOAc: $C_{14}H_{14}Br_2N_2O$: M = 385.08 g/mol, triclinic, $P1$, a = 7.7309(3) Å, b = 9.8742(4) Å, c = 10.3595(4) Å, V = 672.57(5) Å^3, α = 63.330(1)°, β = 85.655(1)°, γ = 72.561(1)°, Z = 2, D_c = 1.902 g/cm^3, F(000) = 378, T = 180(1) K. Data were collected on a Bruker APEX CCD system with graphite monochromated Mo Kα radiation (λ = 0.71073 Å); 7506 data were collected. The

structure was solved by Patterson and Fourier (SHELXTL) and refined by full-matrix least squares on F^2 resulting in final R, R_w and GOF [for 6187 data with F > 2σ(F)] of 0.0275, 0.0550 and 1.470, respectively, for solution using the *S* enantiomer model, Flack parameter = −0.031(7); IR (KBr) ν_{max} 2934, 2892, 1704, 1507, 1399, 1331 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.42-4.35 (m, 1H), 3.85-3.75 (m, 2H), 2.93-2.76 (m, 4H), 2.15 (quintet, 2H, *J* = 6.0 Hz), 2.08-2.04 (m, 2H), 1.38 (d, 3H, *J* = 6.5 Hz); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 152.1, 125.2, 124.7, 119.0, 118.9, 115.2 (2C), 45.2, 38.5, 29.2, 25.7, 22.7, 22.5, 18.9; EIMS [*m/z*(%)] 386(M$^+$, 100), 371(38), 185(17); HRMS (EI) calcd for C$_{14}$H$_{14}$^{79}Br^{81}BrN$_2$O: 385.9453; found 386.9454; Anal. calcd for C$_{14}$H$_{14}$Br$_2$N$_2$O: C, 43.55; H, 3.65; N, 7.26; found C, 43.69; H, 3.68.

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2 Stereoselective Synthesis of Aminoferrocenes

2.1 Historical

2.1.1 Ferrocenes: History, Synthesis & Applications

Bis(cyclopentadienyl)iron, or more commonly known as ferrocene, is the archetypal metallocene, where a transition metal is 'sandwiched' between two cyclopentadienyl rings. The account of its discovery and structural elucidation, which goes back to the early 1950s, is a complicated one that is still filled with debate.[1] Kealy & Pauson[2] (Duquesne University) and Miller, Tebboth & Tremaine[3] (British Oxygen Company) independently reported the synthesis of a stable orange compound with the chemical formula $C_{10}H_{10}Fe$, that both groups postulated as having two cyclopentadienyl (Cp) rings individually sigma bound to the Fe(II) centre (**130**). Immediately upon publication of these reports, researchers took interest in these compounds, as the study of aromaticity and non-benzenoid aromatics was of great interest at the time. Shortly after this period, Woodward & Wilkinson[4] and Fischer & Pfab[5] refuted the former structure and proposed a radical new one, where all five carbons of each Cp ring participated in bonding (η^5) to iron (**131**), as seen in **Scheme 23**. These proposals were independently confirmed by X-ray structural analysis.[6] Wilkinson and Fischer later shared the 1973 Nobel Prize for their work on metallocenes, which accelerated the development of the modern field of organometallic chemistry.

Interest in metallocenes, and ferrocenes in particular, has grown significantly since that time. Ferrocene is probably most notable for its use as a ligand scaffold, especially when bearing one or two phosphinyl groups on the cyclopentadienyl ring. The isolation of monosubstituted ferrocenes is not always a trivial task because of the

difficulty sometimes associated with their separation from 1,1'-disubstituted products, which form to various extents depending on the method of synthesis. Although ferrocenes behave as electron-rich aromatics and readily undergo electrophilic aromatic substitution processes, such as Friedel-Crafts and mercuration reactions, their susceptibility to oxidation precludes their use in electrophilic halogenation and nitration. Only radical and electrophilic substitution (under non-oxidizing conditions), borylation, lithiation/magnesiation and mercuration are used for the synthesis of monosubstituted ferrocenes. Researchers largely rely on lithiation to directly incorporate a heteroatom on the Cp ring, although this proved to require extensive investigation; it was originally circumvented by the preparation of ferrocene derivatives (i.e. **132-134**) that could be purified and subsequently converted to monolithioferrocene (**135**). For example, (chloromercurio)ferrocene (**132**) may be converted to **135** upon treatment with an alkyllithium, but this transformation proceeds in moderate yield and requires the handling of toxic mercury reagents.[7]

130

131

X = HgCl (**132**)
= Br (**133**)
= SnBu$_3$ (**134**)

X = HgCl, 65%
= Br, > 95%
= SnBu$_3$, > 95%

135
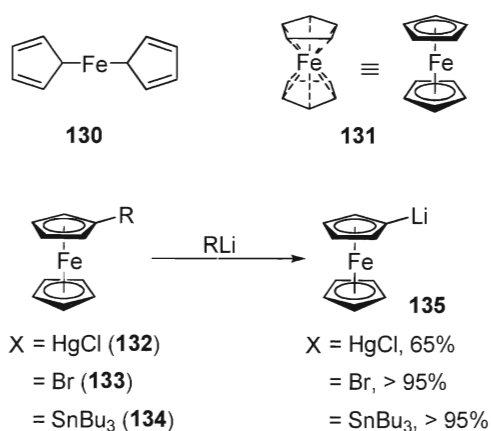
Scheme 23. Structures of ferrocene and generation of monolithioferrocene.

This approach was somewhat improved by derivatives **133**[8] and **134**, which undergo efficient exchange reactions with alkyllithiums at low temperatures. Stannane **134** may be prepared in up to a 20 g scale and is readily purified by distillation under reduced pressure.[9] Direct deprotonation of ferrocene (**131**) with *n*-BuLi yields mixtures of mono- and 1,1'-dilithiated species (**135** and **136** respectively). When *n*-BuLi is activated with TMEDA, a clean reaction occurs to yield **136** as a complex with TMEDA, which may be isolated as a pyrophoric orange solid.[10] Comprehensive studies on the lithiation of ferrocene and subsequent behaviour of **135** and **136** in solution did eventually lead a reliable procedure for the preparation of **135**.[11] In recent years, a more convenient preparation of **135** appeared, wherein ferrocene is treated with a sub-stoichiometric amount of *t*-BuLi at 0 °C. After a short time, hexanes are added and the mixture is cooled to −78 °C. The orange solids are collected by Schlenk filtration, yielding pure **135** as a pyrophoric orange solid that may be stored cold under an inert atmosphere (**Scheme 24**).[12]
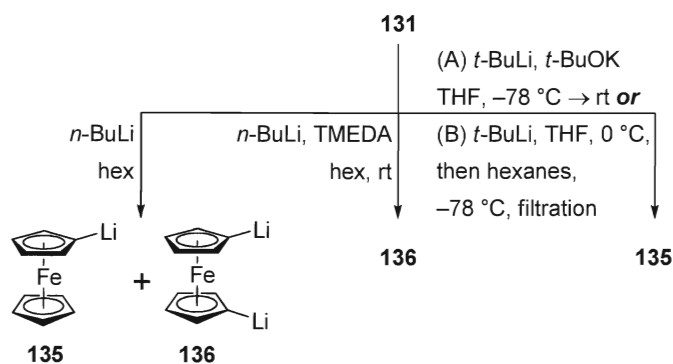
Scheme 24. Preparation of lithioferrocenes by reaction with alkyllithium reagents.

Ferrocenes have also been used in materials science applications and derivatives with biological activity have been prepared,[13] but they have garnered most of their utility

from the role they play in synthetic chemistry. Ferrocene derivatives have been used significantly as chiral ligands for metals[14] in asymmetric catalytic transformations and to some degree as nucleophilic catalysts.[15] Most notable are ferrocenyl diphosphines, which have seen extensive use and are particularly important in asymmetric hydrogenation processes. A recent example employs the biferrocene PhTRAP ligand (**139**) in the challenging asymmetric reduction of heterocycles, namely 2- and 3-substituted indoles (**138a,b**), which proceeds in good yield with excellent selectivity (**Scheme 25**).[16] These ligands have also been significant to industry; a group at Merck interested in the synthesis of anthrax LFI (**142**) employed JosiPhos ligand **143**, a commercially available ligand from Solvias, in the hydrogenation of tetrasubstituted alkene **140** as a model study to provide protected aminoacid **141**.[17] Arguably the most widely known industrial application is in the synthesis of Metolachlor (**146**), the active agent in the herbicide Dual®, which is produced in quantities greater than 20 000 tonnes/year.[18] The activity of the complex formed from Xyliphos (**147**) and the iridium salt is especially remarkable as only 1×10^{-7} mol% (or a substrate:catalyst ratio of 10^6) is required for the process, an important feature on this scale.
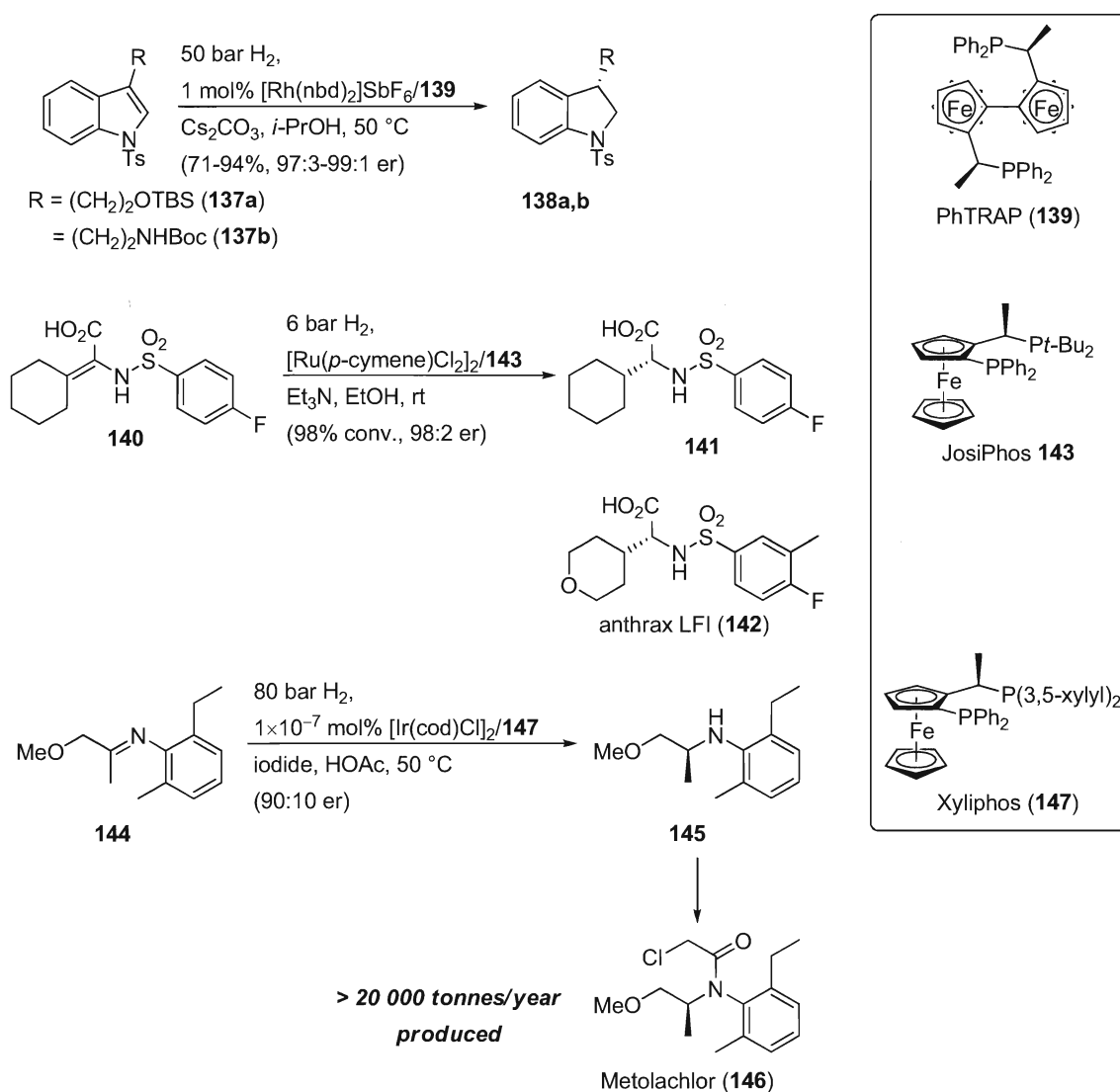
Scheme 25. Important ferrocenyl diphosphines in asymmetric hydrogenations.

Besides ferrocenyl ligands containing only *P*-donors, *N*-, *S*- and *O*-donors are also known (eg. **148-152**, **Scheme 26**), which are used in many other metal-catalyzed asymmetric reactions including cross-coupling, allylic alkylation/amination, hydroboration, additions to carbonyl compounds and cycloaddition reactions. *P*,*N*-ligands such as **148** and **149** have been shown to be capable of providing high selectivities, however ligands where the nitrogen is directly attached to the Cp ring as in

aminosulfoxide **152**, are generally uncommon. One of the few examples of their application is shown in **Scheme 26**, where aminosulfoxide **152** is used in the enantioselective addition of diethylzinc to aromatic aldehydes **153a-g**.[19] Considering the frequent use of nitrogen as a donating atom on ligands, it is surprising that the potential of aminoferrocenes in metal catalysis remains underexplored.

2.1.2 Aminoferrocenes

Aminoferrocene (**155**), which should be differentiated from other nitrogen-containing ferrocenes such as (dimethylamino)methylferrocene (**156**) and azaferrocene (**157**), contains a nitrogen atom directly attached to the Cp ring (**Scheme 27**).
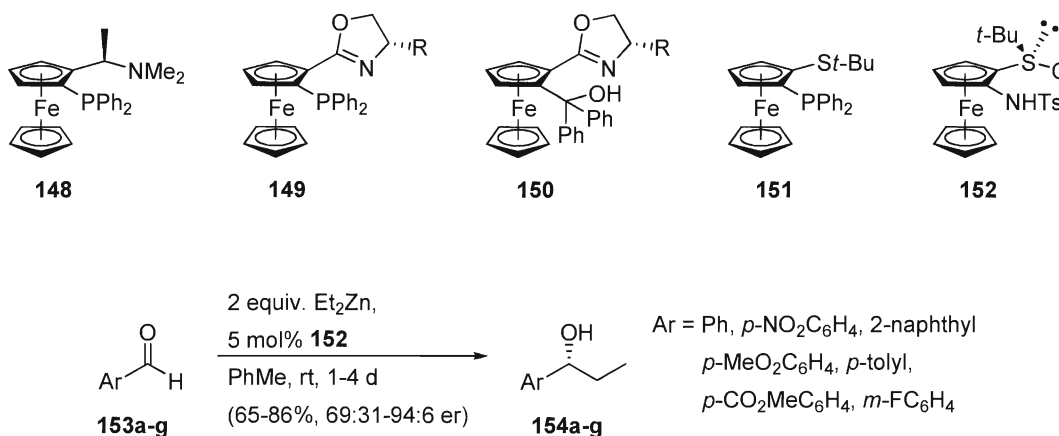
Scheme 26. Various heteroatom donors with a ferrocene backbone and application of an aminosulfoxide in diethylzinc addition.

Aminoferrocenes have long been a topic of interest to coordination chemists, yet this group of heteroatom-substituted compounds has lagged in development because of a lack of synthetic routes, especially for the preparation of planar chiral analogues. Aminoferrocene was first synthesized in 25% yield by Nesmeyanov in 1955[20a] (who laid much of the groundwork for early heteroatom-ferrocene chemistry), by reaction of

ferrocene with *O*-benzylhydroxylamine. Consequently, Nesmeyanov developed two alternative routes from bromoferrocene (**133**, **Scheme 27**): (i) treatment of **133** with NaN$_3$ under copper catalysis to give azidoferrocene (**158**)[20b] and subsequent reduction with LiAlH$_4$, and (ii) heating **133** with copper(I)-phthalimide as a melt to give *N*-ferrocenylphthalimide (**159**),[20d] which was easily deprotected with hydrazine monohydrate. These paths provided target amine **155** reproducibly, although a modification of the latter route by Sato using iodoferrocene, Cu$_2$O and phthalimide provides **155** more conveniently.[21]
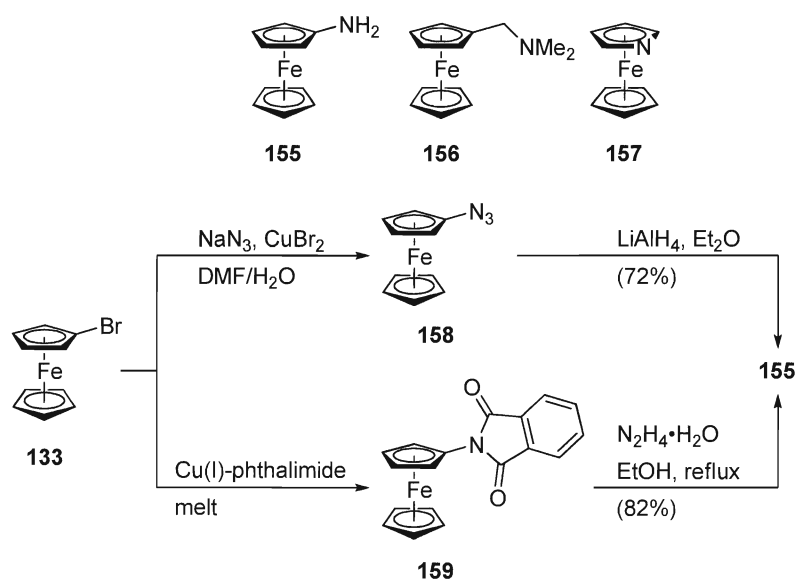
Scheme 27. Nitrogen-containing ferrocenes and aminoferrocene (**155**) syntheses.

Aminoferrocene is also available from ferrocenecarboxylic acid[22] through Curtius rearrangement of acyl azide **160**, trapping with acetic anhydride or alcohols and subsequent cleavage of the amide (**161**)[23] or carbamate (**162**, **163**).[24] Although the sequences involving phthalimide **159** and amide/carbamate **161-163** are capable of providing large quantities of stable precursors that are readily converted to **155**, more

synthetic steps are required in comparison to other routes. Perhaps the most convenient modern method for generating **155** is by quench of lithioferrocene (**135**) with α-azidostyrene at low temperature followed by acidic workup, which is based on a synthesis of aromatic amines by Hassner (**Scheme 28**).[25] Upon addition of aqueous HCl to the reaction mixture, acetophenone and N_2 are liberated from intermediate **164** to afford **155**.

Transition metal-catalyzed C-N bond-forming reactions have received much attention in recent years and researchers have applied them to ferrocene. Methods similar to the copper-catalyzed Gabriel reaction between FcBr (**133**) or FcI and phthalimide to form *N*-substituted aminoferrocene derivatives have been reported[26], however this has yet to be extended to a direct metal-catalyzed preparation of $FcNH_2$ (i.e. by coupling of NH_3).
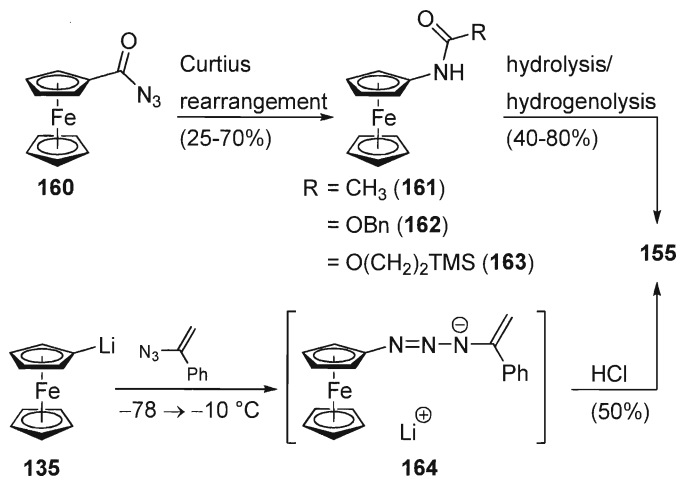
Scheme 28. Alternative preparations of aminoferrocene by Curtius rearrangement and trapping with an electrophilic source of nitrogen.

2.1.3 Diastereoselective Synthesis of Planar Chiral 2-Substituted Aminoferrocenes & Directing Group Manipulation

One of the most noteworthy attributes of 1,2- and 1,3-disubstituted ferrocenes is that they possess planar chirality, and thus potentially available as single enantiomers. As in the preparation of monosubstituted derivatives of ferrocene, lithiation-electrophile quench has proven to be an important tool and, in these cases, used almost exclusively. A number of carbon- (**165-169**),[27] sulphur- (**170**)[28] and phosphorus[29]-based (**171**) functionalities (**Figure 7**) have been employed as directing groups for lithiation to provide a diverse array of 1,2-disubstituted (and 1,2,1'-trisubstituted) ferrocenes.
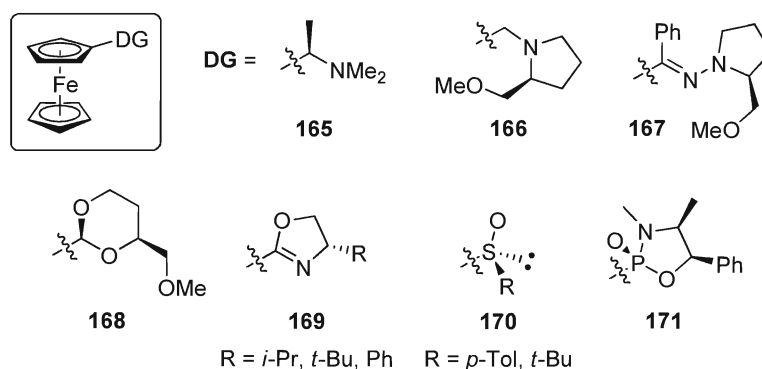
Figure 7. Some chiral directing groups for diastereoselective formation of 1,2-disubstituted ferrocenes.

The first highly diastereoselective induction of planar chirality in ferrocenes was reported by Ugi, who used α-ferrocenylethyldimethylamine as a substrate for lithiation [(*R*)-**165**].[27a] This starting material was prepared by substitution of the hydroxyl group of α-ferrocenylethanol with a dimethylamino group to yield (±)-**165**. Resolution of the racemate with (+)-tartaric acid gave (*R*)-**165**. When (*R*)-**165** was treated with *n*-BuLi, two diastereomeric intermediates, (*R*,*R*$_p$)-**172** and (*R*,*S*$_p$)-**172**, with a dr of 96:4 were produced

(**Scheme 30**). The lithiated interemediates have been shown as non-solvated monomers for simplification.
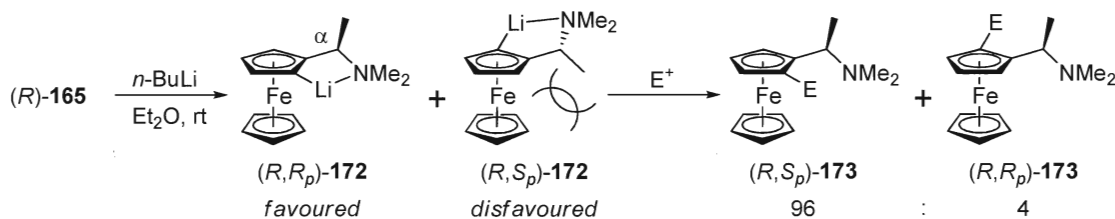
Scheme 29. Diastereoselective lithiation-substitution of ferrocenylethylamine (*R*)-**165**.

It was suggested that the high diastereoselectivity in the preceding lithiation originates from unfavourable steric interactions between the stereogenic α-methyl group and the lower Cp ring, as in (*R*,*S_p*)-**172**. Similar steric arguments have been used to explain the high diastereoselectivities (≥96:4) observed in lithiation-substitution of **166-171**. An exception to this guideline are oxazolines **169**, for which it has been postulated that coordination of the alkyllithium to nitrogen gives a less hindered and, therefore favoured transition state when the γ-stereogenic R group of the oxazoline points down towards the unsubstituted ring Cp ring as in (*S*,*R_p*)-**174** (**Scheme 30**).[27i]
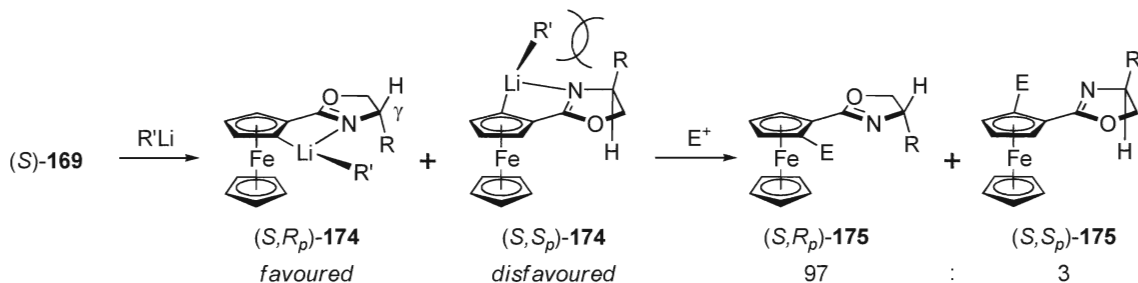
Scheme 30. Diastereoselective lithiation-substitution of ferrocenyl oxazoline (*S*)-**169**.

Despite the availability of synthetic methods that use chiral directing groups for diastereoselective lithiation, the structural diversity of enantiomerically pure 2-substituted

aminoferrocenes remains rather limited. To date, only a small number of planar chiral aminoferrocenes have been reported, several of which are shown in **Figure 8**. Despite the utility of *P,N*-ligands in catalysis, just four aminophosphine analogues of general structure **176** have been reported in a patent.[30] Compounds **177-180** have served as synthetic intermediates, while **181** was a target compound. Fu's planar chiral DMAP analogue (**182**)[15] and Stradiotto's aminophosphine (**183**)[31] rely on *de novo* syntheses for preparation to give racemic products that require resolution.
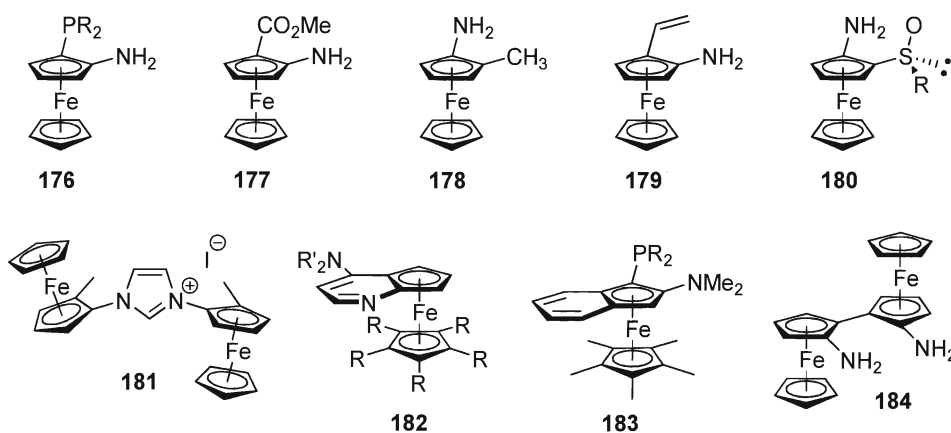
Figure 8. Representative chiral aminoferrocenes.

For resolution of **182**, researchers were forced to resort to preparative chiral HPLC to separate the enantiomers, whereas **183** has only been prepared as the racemate to date.

Apart from the *de novo* syntheses, the aforementioned planar chiral aminoferrocenes are typically prepared by installation of nitrogen into the 2-position of the Cp ring either directly of after subsequent reactions. For example, *en route* to amino acid analogues, amino ester **177** was synthesized by lithiation of oxazoline **169** (R = *i*-Pr) and quenching with N_2O_4 (**Scheme 31**) to give a photosensitive nitroferrocene (**185**).[32] A three-step transformation of the oxazoline auxiliary, followed by reduction of the nitro

group with Adam's catalyst, gave the primary amine (**177**). As there is no simple way to replace the CO$_2$R group with a heteroatom or some other functional group apart from Curtius rearragement, this method is not amenable to the synthesis of aminoferrocenes with non-carbon based functional groups beside the amine moiety.
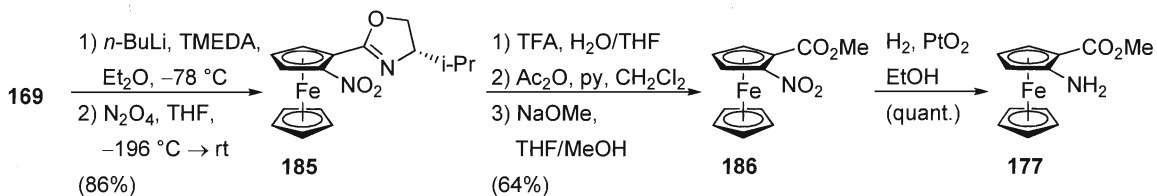
Scheme 31. The oxazoline directing group in the synthesis of amino ester **177**.

Imidazolium salt **181** represents the only reported case where chiral ferrocenyl groups are directly bound to the imidazolium nitrogens,[33] although Bildstein has reported the synthesis of similar imidazoliums and imidazoliniums from achiral aminoferrocene.[34] Kagan's acetal (**168**) was diastereoselectively lithiated and quenched with MeI to affordmethylated **187**. This step was followed by a five-step sequence of transformations, highlighted by a Curtius rearrangement of acyl azide **191**, to incorporate the Cp-amino group (**Scheme 32**). The difficulty associated with this transformation prompted Togni and co-workers to write, "…another major challenge in the present ligand synthesis was the generation of the nitrogen-ferrocene bond. Since aminoferrocenes serve as intermediates in the synthesis of various ligands and optically active materials, this problem has attracted considerable interest."[33]
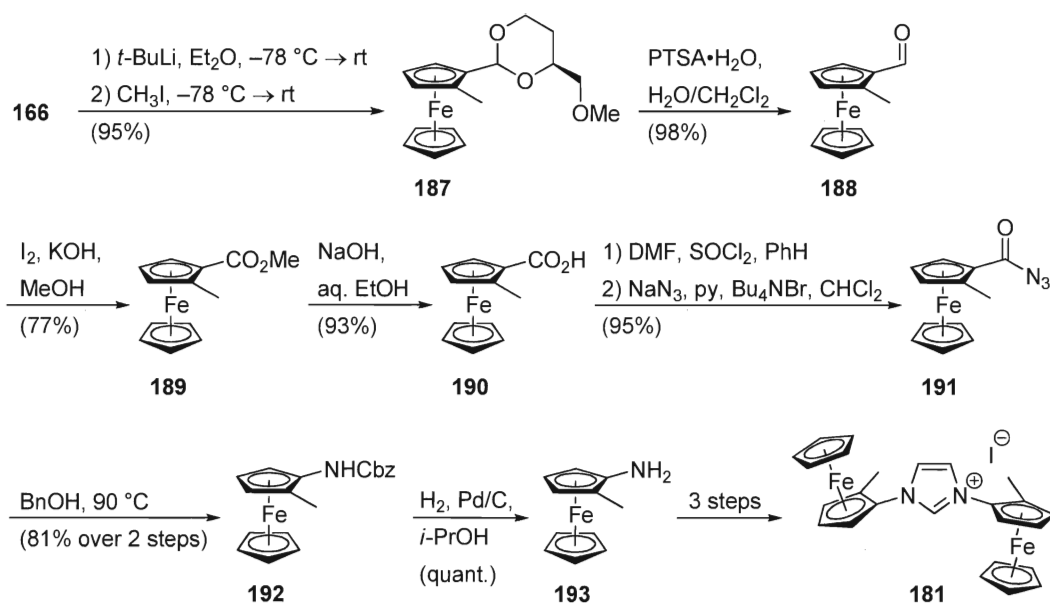
Scheme 32. The acetal directing group in the synthesis of imidazolium iodide 181.

Togni employed a similar strategy to prepare amine 198 starting from Ugi's amine (165).[35] In this case, quenching with CO_2 provided zwitterionic 194, and this was followed by elimination of the dimethylamino group and saponification of the ester to give 2-vinylferrocenecarboxylic acid (195, Scheme 33). Curtius rearrangement employing DPPA as an azide transfer reagent led to construction of the N-C(Cp) bond. Addition of nucleophiles (e.g. HPPh2, amines) across the double bond by acid catalysis and cleavage of carbamate 197 afforded free amine 198. Although this sequence reduced the number of operations (without purification of intermediates) from seven to five steps, it requires the preparation of DPPA and relies on a diastereoselective nucleophilic addition to the alkene addition, whose stereoselectivity varies with nucleophile. In addition, the overall route is still limited to the preparation of aminoferrocenes with branched alkyl groups beside nitrogen on the Cp ring.
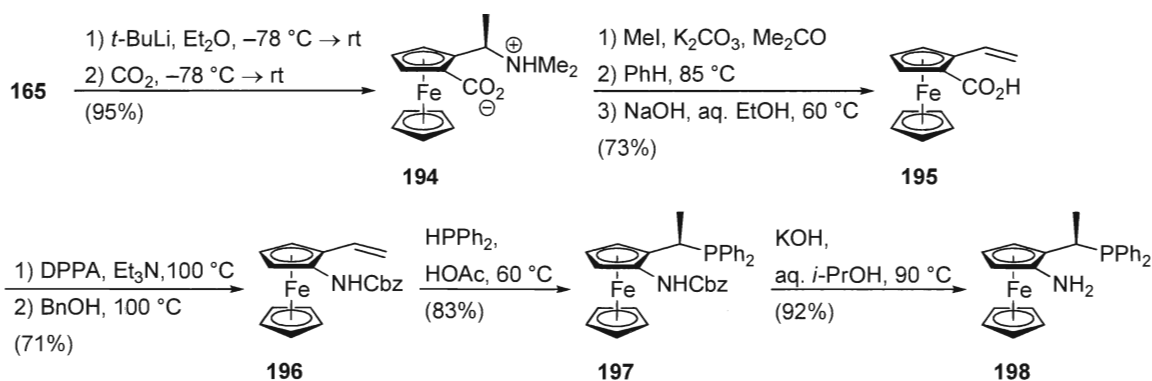
Scheme 33. Dimethylaminoethyl directing group in the synthesis of amine **198**.

The representative syntheses presented above show that although many chiral directing groups on ferrocenes allow for induction of planar chirality, they may not provide the desired functionality at the C2-position after metalation; they invariably require some degree of manipulation. In this respect, carbon-based directing groups **165-169** are useful as starting materials for the diastereoselective substitution of ferrocene as they provide the α-carbon atom in different oxidation states after removal of the auxiliary, usually under mild conditions so as not to affect the group introduced (i.e. **165/166**, alcohol oxidation state; **167**, ketone; **168**, aldehyde; **169**, carboxylic acid). Ideally, the directing group should be entirely removable. The one group that approaches this ideal is Kagan's sulfoxide (**170**, R = *p*-Tol), where treatment of the substituted sulfoxide **199** with *t*-BuLi results in sulfoxide-lithium exchange to generate a lithioferrocene that may be trapped with an appropriate electrophile (E^2X) to give **200** (**Scheme 34**).[36] However, the need to use organolithiums requires that the introduced substituent be stable to strong nucleophiles/bases or be suitably protected (e.g. when $E^1 =$ NH_2), which results in the introduction of additional steps to the overall route.
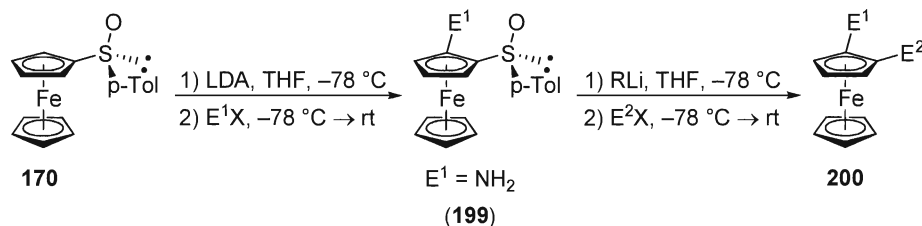
Scheme 34. Use of a *p*-tolyl sulfoxide group for preparing 1,2-disubstituted ferrocenes.

Knochel utilized Kagan's method to prepare ferrocenyl analogues of QUINAP (**205**).[37] Standard deprotonation of sulfoxide **170** with LDA, followed by transmetalation to the organozinc species and Pd-catalyzed Negishi coupling with 2-iodoisoquinoline, furnished biaryl sulfoxide **201** in good yield (**Scheme 35**). The conditions outlined in Kagan's original disclosure using *t*-BuLi provided the desired substitution product (**203**) in only 11% yield.
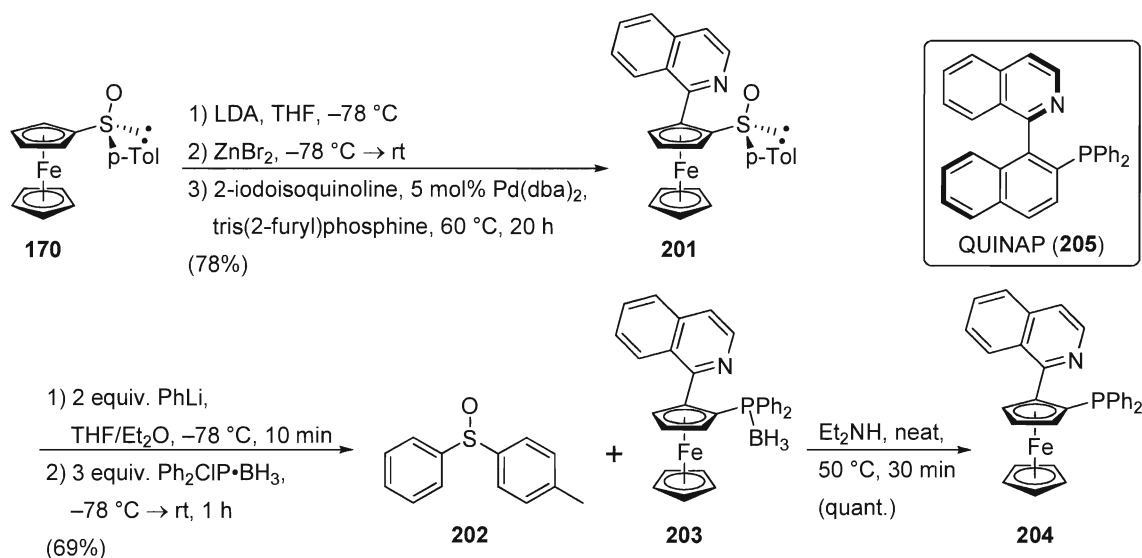
Scheme 35. Use of *p*-tolyl sulfoxide group to direct lithiation, followed by substitution of directing group.

Experimentation with other organolithiums to promote sulfur-lithium exchange revealed that inverse addition of PhLi was more effective, circumventing competitive reaction

with **202** to give **203** in nearly 70% yield. Deprotection of borane adduct **203** with diethylamine afforded free phosphine **204**. There was no explanation given for the lack of success with *t*-BuLi, although it is evident from Knochel's report that replacement of the sulfoxide is not always straightforward and success of the sulphur-lithium exchange is highly dependent on the other substituent(s) present.

2.1.4 Enantioselective Lithiation of Ferrocenes

Besides diastereoselective lithiation of ferrocenes, planar chirality may also be installed by enantioselective means, although this alternative is not as well developed. The origins of this approach can be traced to Nozaki in the early 1970s, who attempted the lithitation of isopropylferrocene (**205**) with an alkyllithium/(−)-sparteine complex.[38] Thus, exposure of **205** to 2.5 equivalents of *n*-BuLi and diamine (−)-**66** gave predominantly a 3,1'-dilithio intermediate, which was trapped with CO_2 or $ClSiMe_3$ (**Scheme 36**) to give products (**206**) in very low 3% enantiomeric excess. Moderate optical purities of up to 45% were obtained by partial resolution of the carboxylic acid products via comparison to tertiary alcohol **207**.

1) 2.5 equiv. *n*-BuLi,
2.5 equiv. (−)-**66**,
hexanes, −70 °C → rt
2. E⁺, 0 °C → rt
(45-85%, ≤ 45% o.p.)
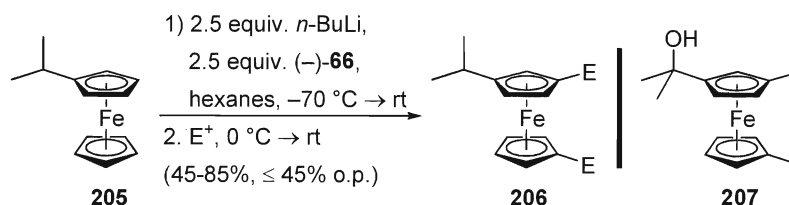
Scheme 36. Earliest report of asymmetric lithiation of a ferrocene derivative.

No further reports in this area were published until a resurgence of interest in planar chiral ferrocenes in the mid-1990s yielded three different studies within the span

of four months. Based on work carried out on (η^6-arene)chromium tricarbonyl complexes[39] where a chiral LDA analogue, Simpkins' base, gave good yields and enantioselectivities, Simpkins showed that silylation of prochiral substrates **208-210** could be carried out *in situ* with this base.[40] Although sulfone **208** and di(*iso*-propyl)carboxamide **209** only provided racemic products in this reaction, phosphine oxide **210** underwent silylation to give **211** in excellent yield and in moderate 77:23 er (**Scheme 37**). The stereochemical assignment was based on the earlier silylation work with chromium complexes and corroborated by circular dichroism data for **211** and the corresponding 2-SiMe$_3$-free phosphine, which were in accordance with close derivatives of the free phosphine. Attempts at installing groups more useful than trimethylsilyl by further metallation of **211** proved fruitless, even with alkyllithiums. However, reaction of the silyl group with a carbonyl proved possible in the presence of CsF under somewhat forceful conditions to give secondary alcohol **212** as a 1:1 mixture of diastereomers.
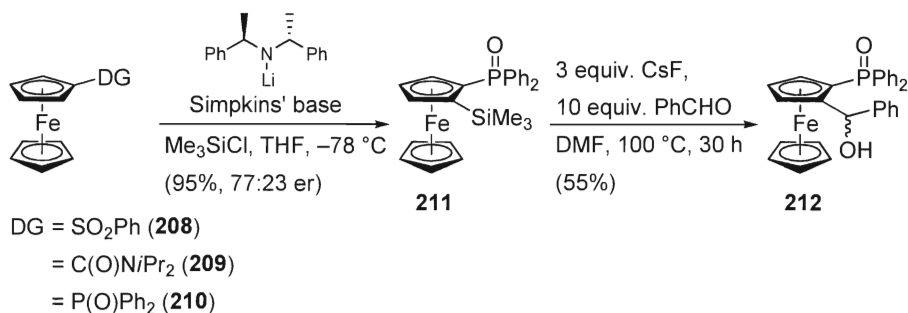
Scheme 37. Enantioselective lithiation of **210** with Simpkin's base.

A breakthrough occurred when carboxamide **209** was subjected to *n*-BuLi/(−)-sparteine lithiation to give the 2-SiMe$_3$-substituted derivative (**213a**) in excellent yield and an even more impressive enantiomeric ratio of 99:1.[41] Carbon- and heteratom-based electrophiles were installed with similar ease, and generally very high levels of

enantiomeric purity (**213b-e**, **Scheme 38**). In exploring the effects of base and solvent, it was noted that branched alkyllithiums such as *s*-BuLi gave lower yields and selectivities in both Et$_2$O (94%, 87:13 er) and *t*-BuOMe (97%, 78.5:11.5). Single-crystal X-ray diffraction analysis of the product resulting from 3-pentanone quench was used to confirm the stereochemistry of the products and indicated selective abstraction of the pro-(*S*) proton of the Cp ring.

Product	E$^+$	E	Yield 213 (%)	er (% ee)
213a	TMSCl	TMS	96	99:1 (98)
213b	Ph$_2$CO	C(OH)Ph$_2$	91	99.5:0.5 (99)
213c	B(OMe)$_3$	B(OH)$_2$	89	92.5:7.5 (95)
213d	I$_2$	I	85	98:2 (96)
213e	ClPPh$_2$	PPh$_2$	82	95:5 (90)

Ar = 2,4-diMeO-C$_6$H$_3$
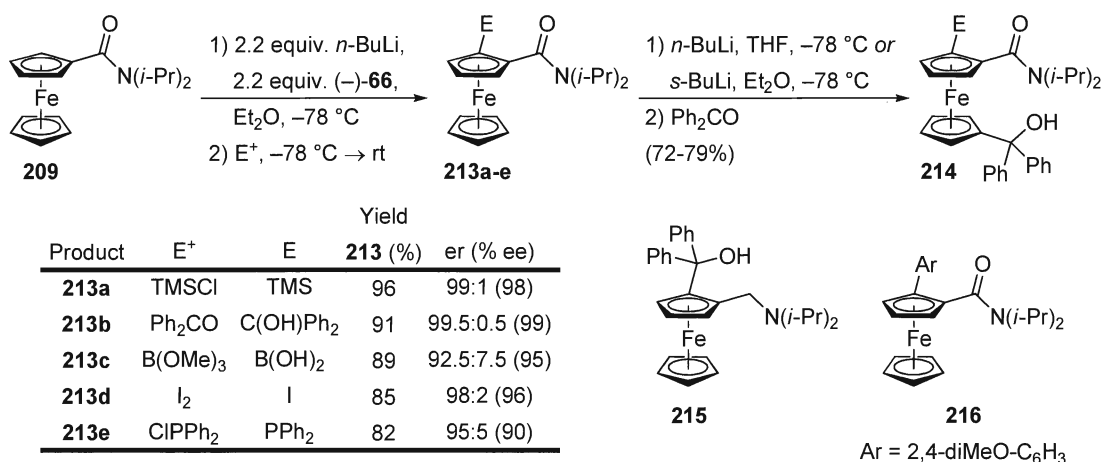
Scheme 38. Highly enantioselective substitution of ferrocenyl carboxamide **209**.

The products were subjected to subsequent lithiation with *n*- or *s*-BuLi, leading to substitution of the lower Cp ring to give alcohol **214** in good yields. The lack of reactivity of the remaining *ortho* proton on the substituted Cp ring has been attributed to the steric demand of the tertiary amido group, which forces the carbonyl to point towards the lower Cp ring, resulting in remote lithiation leading to the 1,2,1'-trisubstituted product.

Although hydrolysis of the tertiary amide can be difficult, BH$_3$ reduction of **213b** proceeded in 95% yield to give tertiary aminoalcohol **215** in excellent yield. Suzuki-Miyaura cross-coupling of **213d** afforded a moderate yield of biaryl **216**. It should be noted that to allow for further manipulation of the tertiary carboxamide, enantioselective

lithiation was extended to N-cumyl-N-ethylferrocenecarboxamide[42] which gave enantiomeric ratios of 94:6-98:2 for secondary N-ethylcarboxamides after N-dealkylation.

The other report of enantioselective ferrocene lithiation from this time was disclosed by Uemura, who carried out lithiation-substitutions on (dialkylamino)methylferrocenes (**156, 218, 220, 222**) and ferrocenyl sulfones.[43] The sulfones (FcSO$_2$t-Bu and FcSO$_2$p-Tol) provided the 2-substituted products in good yields (plus tolyl-substituted regioisomers for that case), but in racemic form upon DMF quench.[44] More interestingly, it was found that treatment of amine **217** with 1.5 equivalents of n-BuLi·(R,R)-**87** complex for 5 h at 0 °C gave a 26% yield of known phosphine **217a** with an er of 72:28 (entry 1) in favour of the (R)-isomer as determined by comparison of the optical rotations (**Scheme 39**).

RLi (equiv.)	L* (equiv.)	Yield **217a** (%)	er (% ee)
n-BuLi (1.5)	(R,R)-**87** (1.5)	26	72.5:28.5 (43)
s-BuLi (1.5)	(R,R)-**87** (1.5)	38	74:26 (48)
t-BuLi (1.5)	(R,R)-**87** (1.5)	trace	n.d.
n-BuLi (1.5)	(R,R)-**87** (2.0)	49	81:19 (62)
n-BuLi (3.0)	(R,R)-**87** (3.0)	31	78.5:21.5 (57)
n-BuLi (1.5)	(−)-**66** (2.0)	trace	n.d.
n-BuLi (1.5)	(S)-**86** (2.0)	40	50:50 (0)
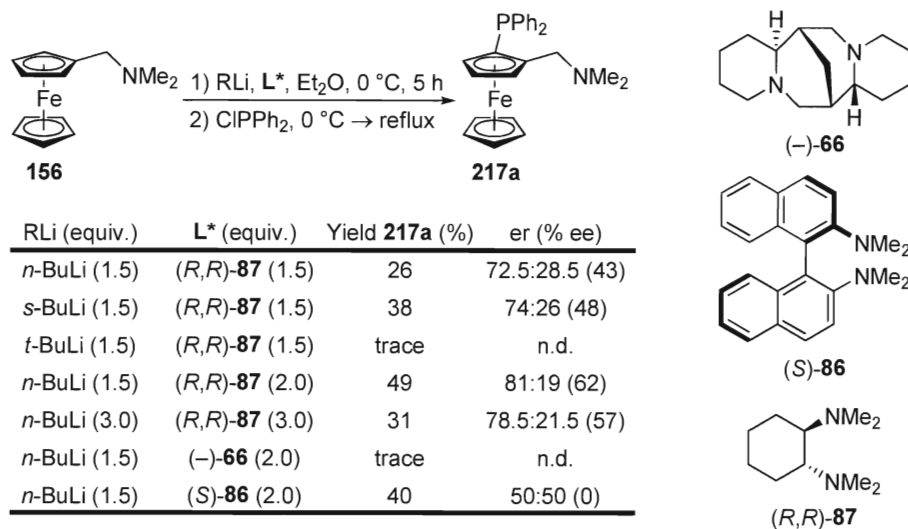
Scheme 39. Enantioselective lithiation of (dimethylaminomethyl)ferrocene (**156**).

Carrying out the reaction in THF or PhMe gave lower yields (< 13%) and er (< 60:40), as did using the bulkier alkyllithiums s- and t-BuLi (entries 2 and 3). Three equivalents of n-BuLi·(R,R)-**87** marginally increased the yield and er (entry 5), but the best results were

obtained when a slight excess of the ligand was present (entry 4). Interestingly, this is a case where (−)-sparteine [(−)-**66**] gave uncharacteristically poor results, while BINAM derivative (*S*)-**86** was no better (entries 6 and 7).

Uemura tested several additional tertiary amines (**Scheme 40**) to determine their effect on the reaction and although the yields stayed around 40% for the formyl derivative, the er gradually declined from 90:10 for the dimethyl derivative (**217b**) to 86.5:13.5 (**219b**) and 83.5:16.5 for the pyrrolidinyl derivative and morpholinyl derivatives (**221b**) respectively. Di(isopropyl) derivative **222** was almost completely resistant to lithiation under these conditions.

Compound	R	Product	Yield (%)	er (% ee)
156	—NMe$_2$	**217b**	41	90:10 (80)
218	—N (pyrrolidine)	**219b**	40	86.5:13.5 (73)
220	—N O (morpholine)	**221b**	42	83.5:16.5 (67)
222	—Ni-Pr$_2$	**223b**	trace	n.d.
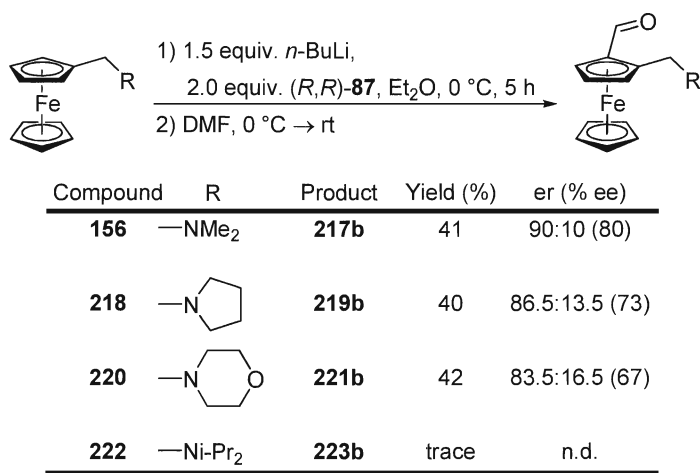
Scheme 40. Enantioselective lithiation of (dialkylaminomethyl)ferrocenes.

2.1.5 Nitrogen-Based Directing Groups in Lithiation-Substitution Reactions

2.1.5.1 Lithiation-Substitution of Imides & Phthalimidines

Nitrogen-based directing groups are common in arene lithiation and metal-catalyzed C-H activation; however they have not been used in ferrocene substitution. Amides and carbamates are most commonly used in lithiation chemistry, although imides have seen sporadic use as well. Simpkins has developed an interesting method for the

lithiation-substitution of bridgehead positions in bicyclic imides.[45] Phenyl-substituted imide **224** was shown to undergo racemic deprotonation using LTMP in the presence of LiCl and Me$_3$SiCl to furnish (±)-**225a** in 47% yield. Encouraged by this result, (*S,S*)-**213** was used as base in its place where a highly enantioselective silylation ensued to give **225a** in excellent yield and 99:1 er (**Scheme 41**). This degree of selectivity was also observed for a range of carbon-based electrophiles. In addition to the [3.3.1] system, the method has been applied to [3.3.2] and the related bicyclic succinimide (**226**) systems.

Product	E$^+$	E	Yield **225** (%)	er (% ee)
225a	ClSiMe$_3$	SiMe$_3$	74	99:1 (98)
225b	MeI	Me	96	98.5:1.5 (97)
225c	BnBr	Bn	91	97.5:2.5 (95)
225d	BrCH$_2$CH=CH$_2$	CH$_2$CH=CH$_2$	89	97.5:2.5 (95)
225e	BCH$_2$CH=CMe$_2$	CH$_2$CH=CMe$_2$	85	99:1 (98)
225f	ClC(O)*t*-Bu	C(O)*t*-Bu	82	99:1 (98)

R = Ph, Bn, OBn

n = 1-3
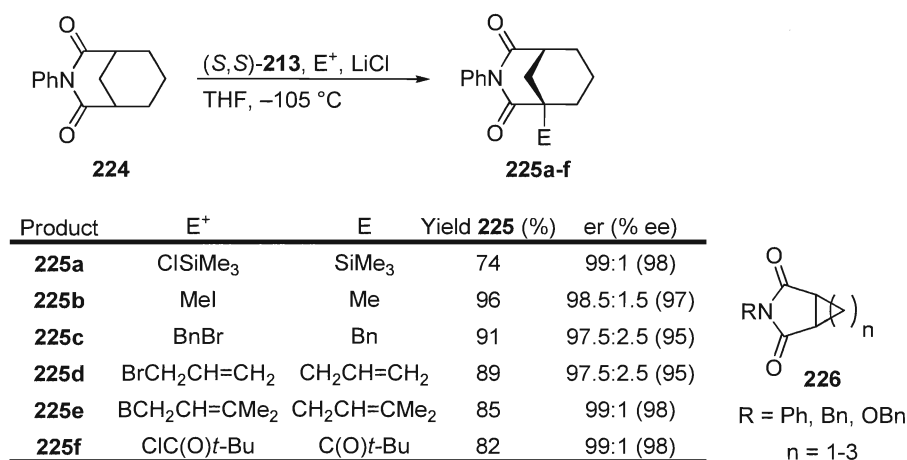
Scheme 41. Enantioselective bridgehead substitution using an imide directing group.

Related to Simpkins' studies are benzo-fused imides, namely phthalimide or isoindoline derivatives, variations of which have been used in Clayden's (±)-kainic acid synthesis and also by Weinreb for the generation of *N*-acyliminium[46] building blocks. Clayden displayed his dearomatizing cyclization method of *N*-benzylbenzamides in order to set the correct relative stereochemistry of kainic acid (**232**), a naturally occurring proline derivative with diverse biological activity.[47] Treatment of benzamide **227** with *t*-BuLi and HMPA expectedly affected benzylic deprotonation (**Scheme 42**). Upon prolonged reaction time, lithiated intermediate **228** added to the anisyl ring, causing

dearomatization and formation of lithium enolate **229**. Upon workup, phthalimidine

derivative **230** was initially obtained. *In situ* treatment with hydrochloric acid

transformed the enol to α,β-unsaturated ketone **231** in remarkable yield while setting

three contiguous stereocentres. A number of subsequent transformations were then

required to convert **231** into kainic acid (**232**).
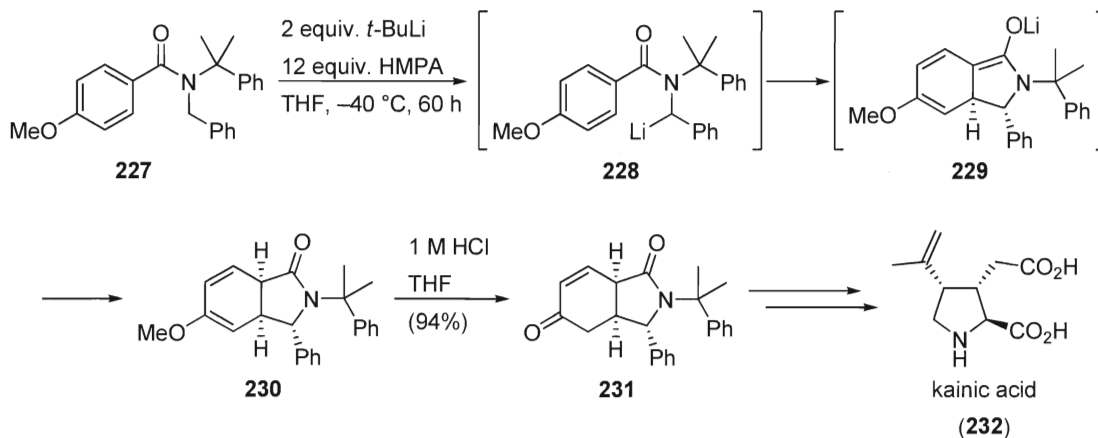
Scheme 42. Clayden's synthesis of (±)-kainic acid from *N*-benzyl-*N*-cumylbenzamide.

The same year, Weinreb investigated the synthesis of a number of *N*-cumyl-*N*-(α-

methoxy)benzamides and their subsequent derivatization by *N*-acyliminium ion

chemistry.[48] Substrates **233** and **235** were prepared by benzylic oxidation and it was

observed that treatment with $BF_3 \cdot OEt_2$ as a Lewis acid efficiently generated the iminium

ion (**Scheme 43**).
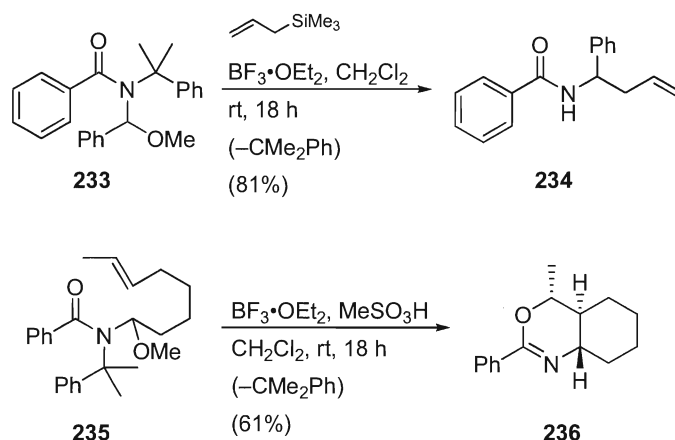
Scheme 43. Weinreb's use of α-methoxy benzamides as *N*-acyliminium precursors.

These reactive intermediates could be trapped by nucleophiles, as in the case of **233**, leading to homoallylic benzamide **234** in good yield. Tethered alkenes, such as **235**, could also be used to undergo cycloaddition with the acyliminum, producing bicyclic oxazine **236**.

In the original study, *N*-cumylphthalimidine (**237**) was subjected to lithiation with two equivalents of *s*-BuLi/TMEDA at low temperature (**Scheme 244**).[49] The resulting dianion was then trapped with excess ClSiMe₃ and allowed to warm to room temperature, giving disilylated **238** in excellent yield. Further manipulation of the phthalimidine portion served to illustrate conversion to the phthalimide (**239**) with relative ease.
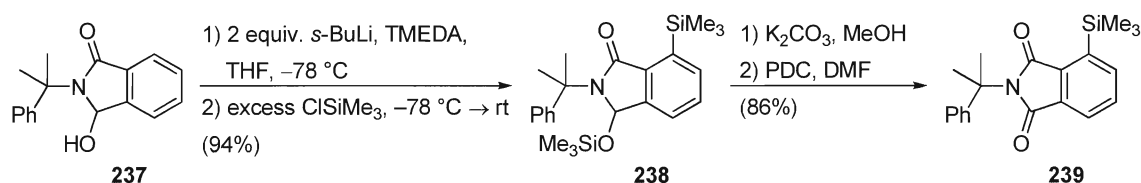
Scheme 44. Use of the phthalimidine moiety as a directing group.

2.1.5.2 Enantioselective Lithiation-Substitution of Cr(CO)$_3$-Complexed Anilides

Interest in planar chiral systems as a route to atropisomeric axial chiral amides prompted Uemura to study the lithiation-substitution of anilide (and benzamide) moieties of Cr(CO)$_3$ "piano-stool" complexes.[50] Attempts to distinguish between two enantiotopic methyl groups on the aromatic ring with *n*-BuLi and chiral diamines [such as (−)-sparteine, (*R*,*R*)-TMCDA and a chiral TMEDA analogue] only resulted in mediocre yields (24-50%) of (±)-**241a**. Chiral lithium amide ligands gave much improved results. The best results were obtained with (*S*)-phenylethylamine derivative **244d**, which afforded product **241a** in excellent yield as nearly pure (*R*)-enantiomer (**Scheme 45**).[51] Based on the ligands screened, the *N*-methyl and CH$_2$*t*-Bu portions of the chiral ligand (i.e. "X" and "R" of **244**) were key structural features of the reagent. A number of electrophiles could be introduced with similar selectivities.

Product	L*	E⁺	E	Yield 241/243 (%)	er (% ee)
241a	244a	MeI	Me	90	97.5:2.5 (95)
241b	244b	BnBr	Bn	90	98.5:1.5 (97)
241c	244c	Ph$_2$CO	C(OH)Ph$_2$	73	98:2 (96)
241d	244d	ClC(O)Ph	C(O)Ph	31	98.5:1.5 (97)
243a	244a	MeI	Me	73	98:2 (96)
243b	244b	BnBr	Bn	78	97:3 (94)

L*	X	R
244a	CH$_2$	*i*-Pr
244b	CH$_2$	CH$_2$*t*-Bu
244c	CH$_2$	CH$_2$O(CH$_2$)$_2$OCH$_3$
244d	NMe	CH$_2$*t*-Bu
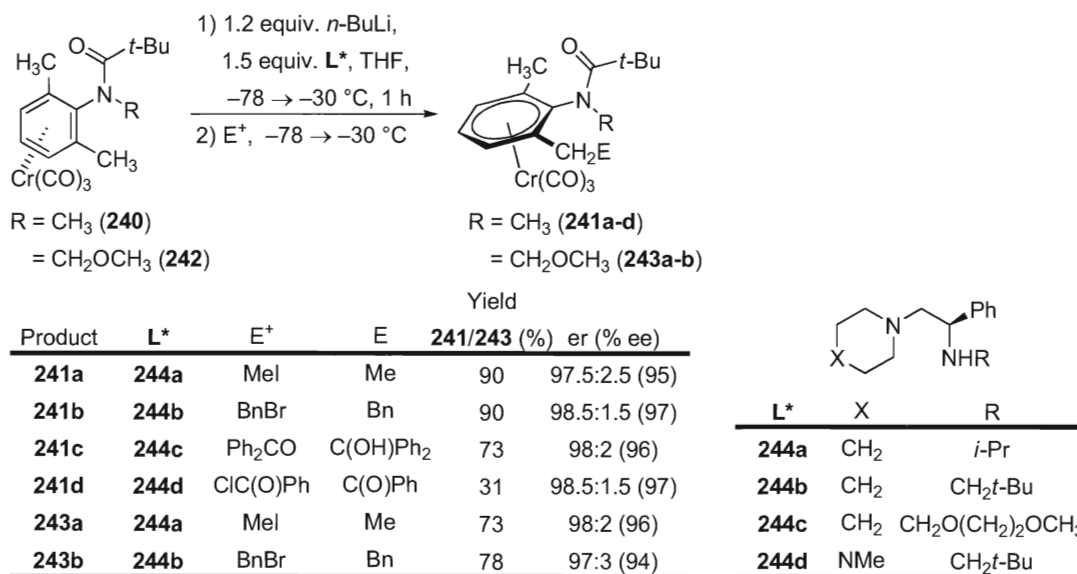
Scheme 45. Anilides as directing groups in chiral lithium amide-mediated deprotonation of benzylic groups.

Upon switching to α-alkoxy anilide **242**, an acyclic analogue of *O*-alkylated phthalimidines, the high reaction selectivity was retained. Finally, sunlight-induced decomplexation of products **241a-d** and **243a,b** gave the atropisomeric compounds as mixtures of *cis/trans* rotamers.

2.1.5.3 Lithiation-Substitution of Lewis Acid-Complexed Tertiary Amines

Many heteroatoms are known to increase the acidity of protons at adjacent sp^3-hydridized carbon atoms in heterocycles. Thus, O-, P- and S-containing compounds may be regioselectively deprotonated at the α-position upon treatment with strong bases, as the resulting carbanions are stabilized by a number of factors (i.e. inductive effect of heteroatom, polarizability and ability to accept negative charge density). In contrast *N*-containing hereocycles, and amines specifically are typically quite resistant to treatment with base and require forcing conditions to form α-carbanions. For example, deprotonation of *N*-methyl piperidines was only achieved with so-called superbases (*s*-BuLi and KO*t*-Bu) in neat amine.[52] These observations may be rationalized by considering that nitrogen is less polarizable that phosphorus or sulphur, its inductive effect is smaller than oxygen, and its lone pair creates a repulsive interaction with the adjacent carbanion.

In the past 20 years, it was found that prior complexation of amines with Lewis acids such as BH_3 or BF_3[53] facilitates α-deprotonation of heterocycles. Other Lewis acids, such as BH_2CN, BCl_3, $AlMe_3$ and $AlCl_3$ have also been screened in such reactions, but usually give inferior results. The method also proved amenable to the development of enantioselective variants by the use of chiral diamines. In one of the earlier examples,

Simpkins treated *N*-methylisoindoline (**245**) with borane and was able to isolate the resulting zwitterionic Lewis acid-base adduct (**246**), which are sometimes even stable to column chromatography on silica gel (**Scheme 46**).[54] Exposure of amine-borane complex **246** to excess *n*-BuLi in the presence of (−)-sparteine [(−)-**66**], followed by electrophile quench, produced the diastereomeric products (**247a-d**) with substitution occurring at the benzylic position. An important observation made here was that the major diastereomer was always the one where the newly introduced substituent was always *syn* to the borane moiety on nitrogen. Standard carbon-based electrophiles, such as methyl iodide and benzyl iodide, were introduced with good selectivity and yield, as were trimethylsilyl chloride and tributyltin chloride. Decomplexation of the products was effected in 62-94% yield by heating their ethanol solutions for five hours.

Product	E$^+$	E	Yield 247 (%)	er (% ee)
247a	MeI	Me	70	91.5:8.5 (83)
247b	BnBr	Bn	83	91.5:8.5 (83)
247c	ClSiMe$_3$	SiMe$_3$	84	92.5:7.5 (85)
247d	ClSnBu$_3$	SnBu$_3$	95	94.5:5.5 (89)
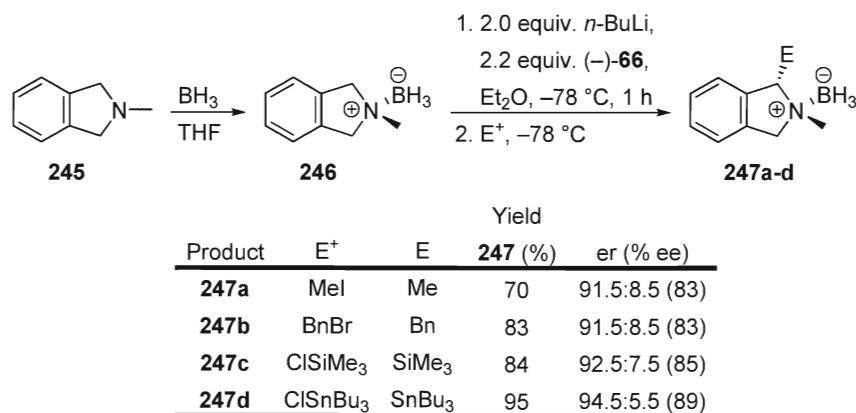
Scheme 46. BH$_3$-mediated enantioselective lithiation of *N*-methylisoindoline.

Kessar later reported the first stereoselective lithiation at non-benzylic *sp^3*-hybridized centres using this technique, and also provided the first computational analyses on Lewis acid-promoted lithiation.[55] It was demonstrated that BF$_3$-complexed *N*-ethylpyrrolidine (**2.113**) undergoes lithiation at low temperature when exposed to *s*-

BuLi·(−)-sparteine to produce tertiary alcohol (S)-**250** in low yield with an 85:15 er upon electrophile quench with benzophenone and aqueous work-up (**Scheme 47**). If lithiated intermediate **249** was subjected to a warm-cool cycle (−78 °C → 0 °C → −78 °C), followed by benzophenone quench, the er was inverted to 14:86. This result implied an initial lithiation *syn* to the BF_3 group followed by inversion of the carbanionic centre upon warming. Indolizidine complex **251**, which has a fixed stereocentre already in the molecule, corroborated this result since subjection of the carbanion to a warm-cool cycle changed the enantiomeric ratio of products from 97:3 → 41:59. DFT computational studies of gas phase intermediates with BF_3 showed one strong Li–F interaction (1.82 Å), while in the case of BH_3-coordinated intermediates, close contacts (1.92 and 2.01 Å) were seen between lithium and two hydrogens on boron.
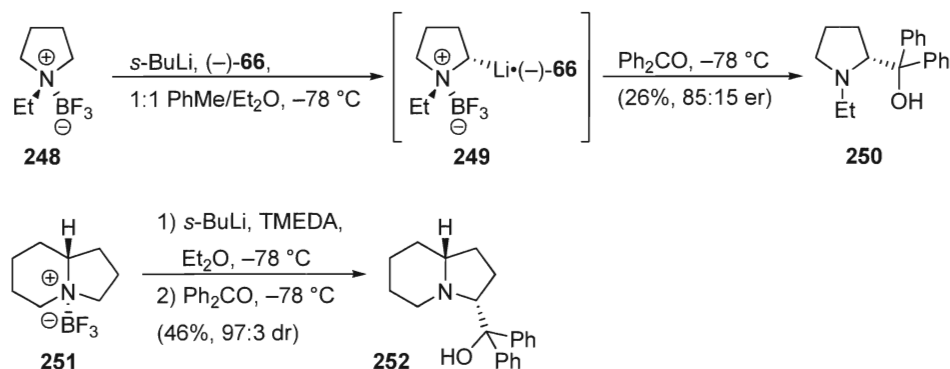
Scheme 47. BF_3-mediated stereoselective lithiation of
N-ethylpyrrolidine and isoindolizidine.

It was tentatively suggested that these types of interactions in a precomplex or transition state could be responsible for a kinetically controlled *syn* lithiation (CIPE).[56]

Another important example, reported by Kessar in early 2008, involved the application of his BF_3-mediated method to *N,N*-dimethylanilines **253-255**, compounds that have rather poor directing ability and are known to require rather harsh conditions

(alkyllithiums, hexane, reflux) to effect lithiation.[57] Complexation of the tertiary anilines to BF$_3$ allowed deprotonation to occur at -78 °C (**Scheme 48**). The putative *ortho*-lithiated zwitterions were trapped with CH$_3$OD, PhCHO or Ph$_2$CO to afford modest yields of the *ortho*-substituted anilines (**257a-c, 258a** and **259a**).[58] Despite the moderate yields of this process, *ortho* lithiation of BF$_3$-complexed dimethylanilines is actually quite remarkable as it allows complete regiocontrol even in the presence of the known methoxy and chloro substituents, which themselves may behave as directing groups.[59] It was originally thought that tertiary anilines would not be amenable to this method of lithiation as the zwitterionic intermediates would be prone to benzyne formation.

Product	E$^+$	E	Yield 257 (%)
257a	CH$_3$OD	D	40
257b	PhCHO	C(OH)HPh	51
257c	Ph$_2$CO	C(OH)Ph$_2$	41
258a	Ph$_2$CO	C(OH)Ph$_2$	40
259a	Ph$_2$CO	C(OH)Ph$_2$	30
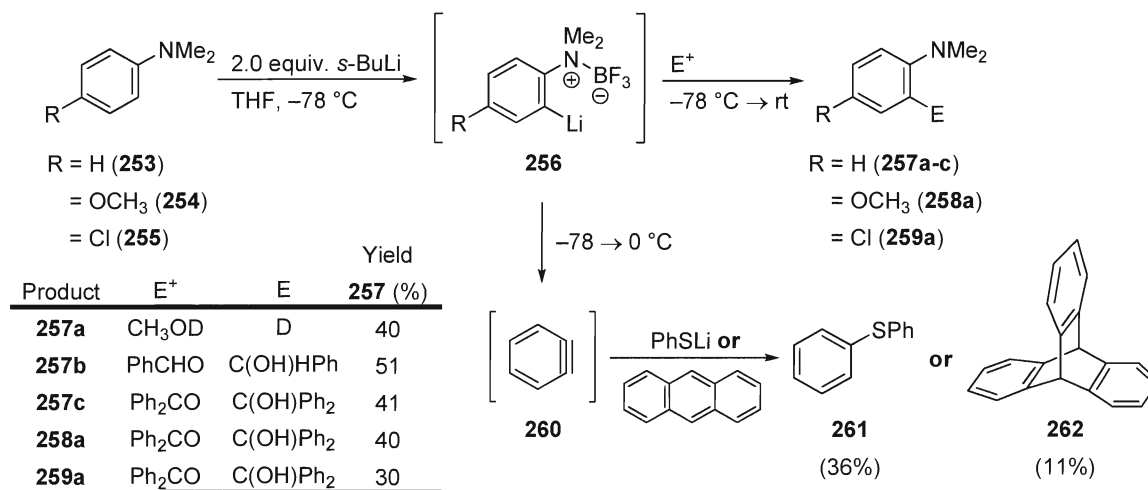
Scheme 48. BF$_3$-mediated lithiation of *N,N*-dimethylanilines and trapping of proposed benzyne intermediate.

Attempts to find eveidence of benzyne formation at low temperatures by addition of lithium thiophenolate and anthracene as a diene did not result in formation of a cycloadduct. However, upon warming the reaction mixture to 0 °C, some benzyne-derived products (**261** or **262**) were obtained in low yield.

Computational modeling of a simplified system with aniline and methyllithium once again revealed an important role for Li-F of Li-B interactions. As shown in **Figure 9**, when BH_3 is used a five-membered ring intermediate is predicted that has a Li-B contact of 2.21 Å (Li-H^1 and Li-H^2 contacts of 1.92 Å). On the other hand, a six-membered ring appears to be favoured when BF_3 is used, leading to a Li-F distance of 1.82 Å.

Lithiation-substitution of BF_{3-} of BH_3-complexed tertiary amines has also been carried out on aziridines,[60] Troger's base[61] (diastereoselective) and on sp^2-hybridized heterocycles, such as pyridines[62] and oxazoles.[63]
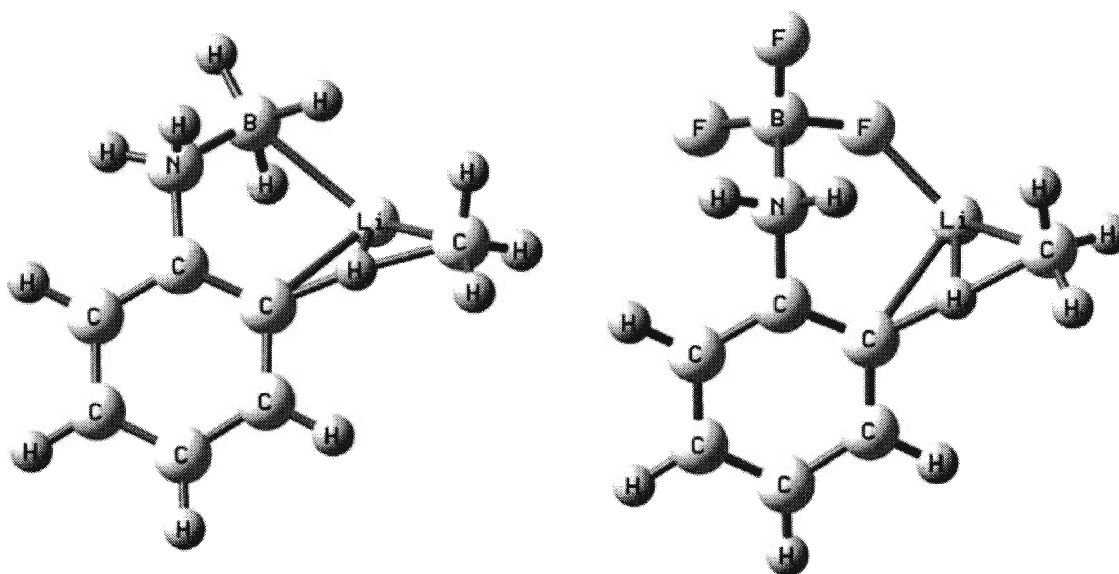
Figure 9. Kessar's modeling of BH_3- and BF_3-promoted lithiation of aniline.

2.2 Aims & Objectives

The aim of the current work is to develop a more direct method for the synthesis of 2-substituted aminoferrocenes possessing planar chirality. Historically, as lithiation-substitution has proven to be the most useful tactic to selectively substitute ferrocenes, this approach was taken. Two methods have been pursued: the first involved diastereoselective lithiation using a chiral directing group, while the second investigates enantioselective lithiation of a prochiral substrate. Both routes differ from previous aminoferrocene syntheses in that they use starting materials in which nitrogen is directly attached to the Cp ring. These approaches would obviate the need to introduce nitrogen into the products at a later stage of synthesis, thus avoiding cumbersome protection-deprotection sequences or the need for rearrangement reactions. With these issues in mind, the objectives of this work are to:

1. Investigate whether *N*-ferrocenyl phthalimide (**159**), a common and easily prepared precursor to aminoferrocene (**155**), can be reduced and protected as a phthalimidine (**263**), which would serve as a chiral directing group in the diastereoselective lithiation of the Cp ring (**Scheme 49**). Success in this endeavour would give access to primary aminoferrocenes (**265**) via standard deprotection of nitrogen using reducing agents or hydrazine (the latter after oxidation of 2-substituted product **264** to the phthalimide).
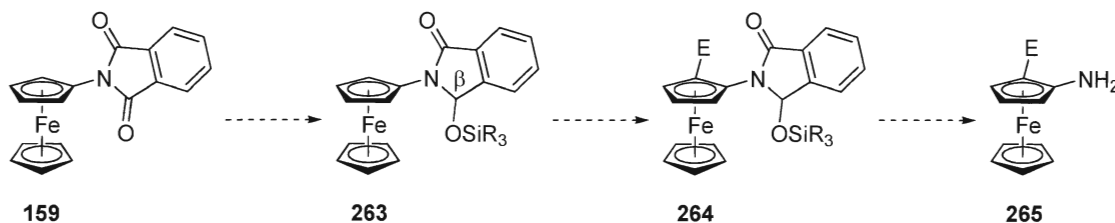
Scheme 49. Proposed use of phthalimidine as a removable, *N*-based directing group for the synthesis of 2-substituted aminoferrocenes.

2. See if Kessar's BF$_3$-mediated lithiaton methodology can be extended to tertiary aminoferrocenes (**266**, **Scheme 50**). The use of achiral substituents would allow for the development of enantioselective lithiation procedures in the presence of (−)-sparteine or other appropriate diamines. Moreover, in the case that the tertiary amine group is chiral (i.e. **269**), BF$_3$-activated lithiation may also be diastereoselective, since the chiral centre would be β- to the Cp ring, as in the proposed phthalimidine **263** above.
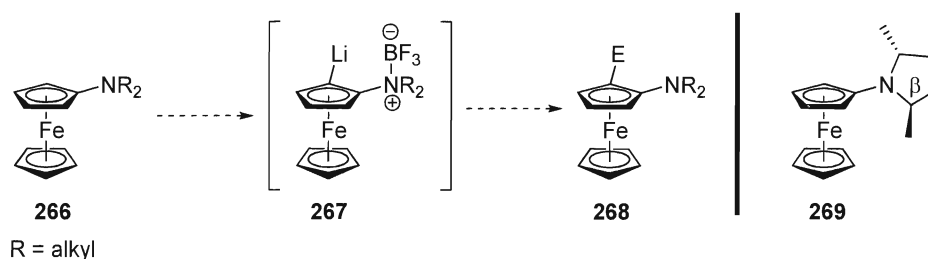
Scheme 50. Proposed BF$_3$-mediated lithiation of tertiary aminoferrocenes.

3. Given that many of the derivatives obtainable by the methods described above would be new or uncommon, especially with two heteroatoms on the Cp ring, the coordination chemistry of these new ligands is open for study (**271**, **Figure 10**). For example, to the best of our knowledge, Stradiotto's Rh complex **270**[31] is the only example thus far that contains a 2-phosphino-1-aminoferrocene ligand.
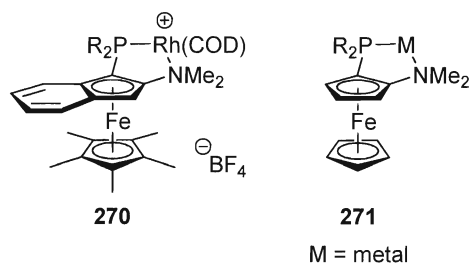
Figure 10. Ferrocenyl aminophosphine Rh and metal complexes.

2.3 Results & Discussion

2.3.1 Diastereoselective Lithiation-Substitution of Ferrocenyl Phthalimidines[64]

N-Ferrocenylphthalimide was prepared from ferrocene following the procedures of Bildstein[12] and Sato.[21] Thus, lithioferrocene (**135**) was generated with a slight excess of t-BuLi in THF at 0 °C, precipitated with hexane at −78 °C, and isolated while cold by filtration under inert atmosphere. Addition of iodine to lithioferrocene in THF at low temperature gave the iodide (**272**), which was converted to phthalimide **159** with Cu_2O in pyridine. The overall yield for this process was about 30%. Imide **159** was readily reduced to the phthalimidine (**273**) with $NaBH_4$ in MeOH/MeCN and the product was then O-silylated with either $ClSiMe_3$ or $ClSiEt_3$. The triethylsilyl adduct (**263b**) was stable to silica gel chromatography and generally easier to handle than the methyl analogue (**263a**).
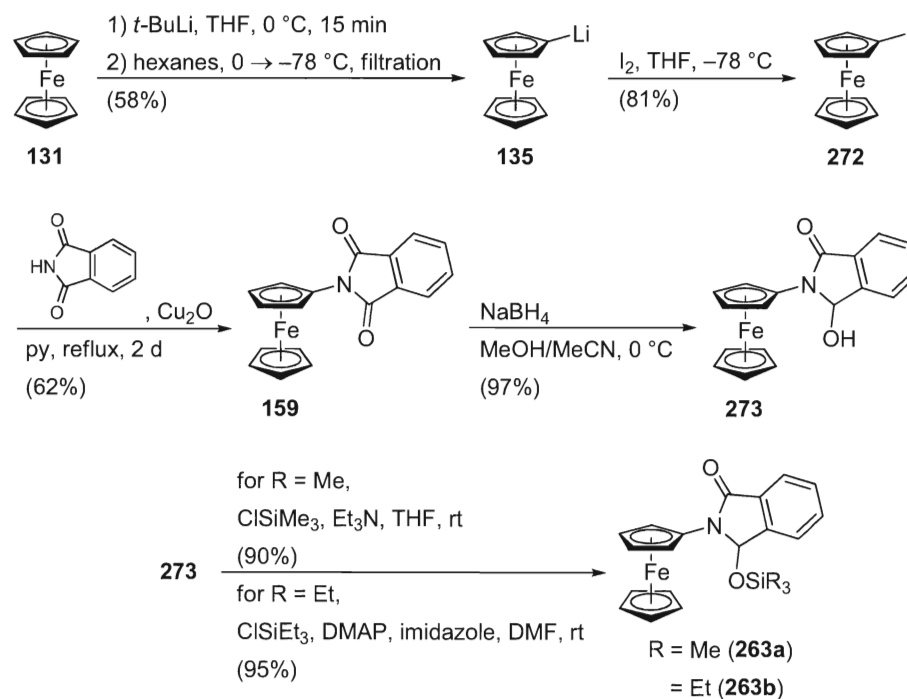
Scheme 51. Synthesis of N-ferrocenylphthalimidines.

Considering the position of the stereogenic centres in **165** and **169**, either alpha or gamma to the Cp ring, it was thought that silylated phthalimidines **263a,b** (**Figure 11**) would also provide diastereoselectivity during lithiation of the ferrocene core. The phthalimidines would be converted to primary amines after substitution at the 2-position of ferrocene.
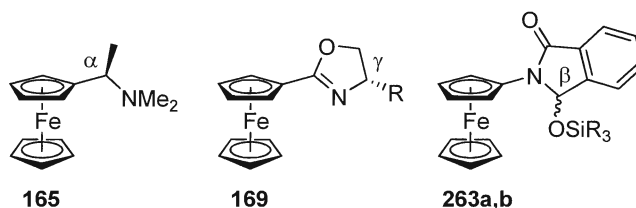
Figure 11. Comparison of stereogenic centres in chiral ferrocene directing groups.

Exposure of **273** to reaction conditions similar to those for *N*-cumylphthalimidine **237** (2.2 equiv. *s*-BuLi, 2.2 equiv. TMEDA, THF, −78 °C, then 2.2 equiv. ClSiMe₃, −78 °C) gave an inseparable mixture of compounds; however, it was clear from the SiMe₃ and Cp signals in ¹H NMR that the desired product was formed. It was thought a cleaner reaction may take place if the acidic hydroxyl group was protected with SiMe₃ (ClSiMe₃, Et₃N, THF, 0 °C) or SiEt₃ (ClSiEt₃, DMAP, imidazole, DMF, rt) group to generate silylethers **263a** and **263b** respectively.

Treatment of trimethylsilyl adduct **263a** with 2.5 equivalents of LDA and 4 equivalents of ClSiMe₃ *in situ* in THF at −78 °C and quenching with H₂O at low temperature gave the desired Cp-silylated product, which was difficult to isolate in pure form because of the lability of the *O*-trimethylsilyl group on silica gel. To alleviate this problem, the bulkier *O*-triethylsilyl derivative was used in its place. Under optimized

conditions, lithiation of **263b** (2.5 equivalents of LDA, 2.5 equivalents of ClSiMe$_3$, −78

°C, 2 h) and workup with water at low temperature gave the 2-silylated product (**274**) as

the major product (30%), along with an inseparable mixture of two aryl-silylated

products (**275** and **276**) in less than 5% combined yield (**Scheme 52**). More importantly,

according to ^{1}H and ^{13}C NMR, **274** appeared to be a diastereomerically pure compound,

as no other diastereomers could be detected. This implied that the lithiation occurred in ≥

95:5 diastereoselectivity,[65] which is a ratio comparable to those obtained from the use of

other chiral directing groups, such as oxazolines and Ugi's amine. Given a particular

configuration of the β-stereocentre, the conclusion may be drawn that the β-stereocentre

efficiently dictates the position of lithiation on the Cp ring (i.e. pro-*R* or pro-*S* lithiation

of the ferrocenyl moiety). This important result implied that if the phthalimidine starting

material (**263b**) was of a single stereochemical configuration, then deprotection of

nitrogen to the primary amine after Cp-silylation would afford an enantiomerically pure

product possessing only planar chirality.
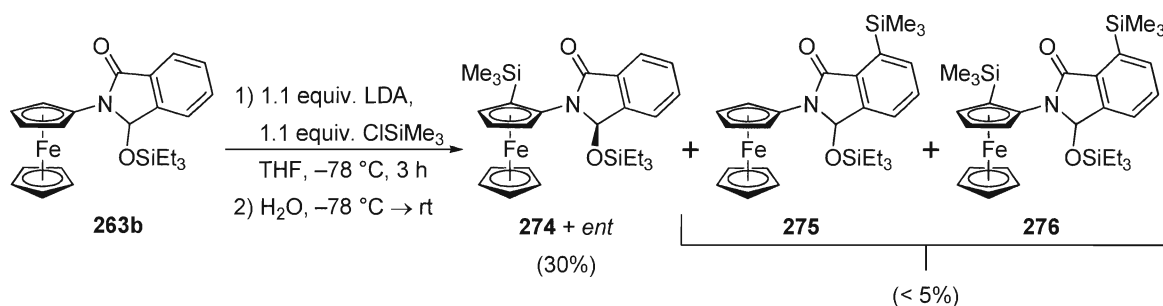
Scheme 52. Diastereoselective substitution of phthalimidines **263b**.

Encouraged by these results, the silyl ether of **274b** was manipulated further to

assess the ease with which the auxiliary could be removed. **274b** was easily desilylated

under standard conditions, revealing the free hydroxyl group. Attempts to oxidize

phthalimidine **277** to the phthalimide (**278**) with PDC or PCC caused significant decomposition of the starting marerial and provided only a trace amount of 2-SiMe₃ phthalimide **278**. That phthalimidine **277** was prone to irreversible oxidation to Fe(III) species was supported by voltammetry.[66] Even qualitatively, dark magnetic particles, presumably Fe(III) could be seen adhered to the stir bar during attempted oxidation with PDC or PCC. In contrast, classical Oppenauer conditions[67] [Al(O*i*-Pr)₃, cyclohexanone, PhH, reflux] provided the desired phthalimide (**278**) without decomposition, although the transformation was sluggish. Modified Oppenauer conditions[68] (AlMe₃, *p*-nitrobenzaldehyde, PhMe, 80 °C) gave **278** in a much improved yield of 60-70% in 16 h (**Scheme 53**). Removal of the phthalimide under standard conditions with hydrazine in refluxing ethanol for 1 h gave the simple, but as yet unreported, 2-trimethylsilyl primary aminoferrocene **279** in quantitative yield. The preceding sequence of transformations involving diastereoselective lithiation-substitution of the Cp ring, followed by *N*-deprotection to the primary amine under mild conditions seemed to prove, in principle, the feasibility of the approach.
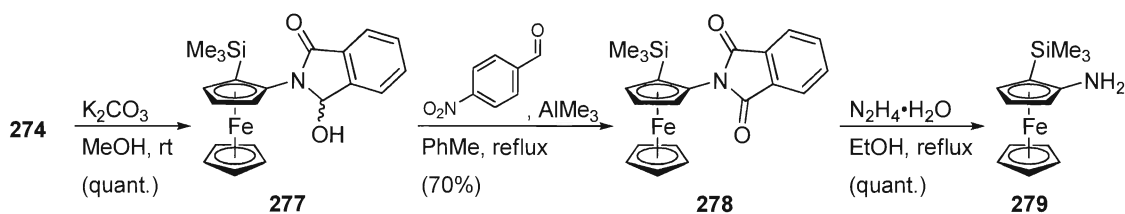
Scheme 53. Deprotection of phthalimidine **274** and
synthesis of 2-SiMe₃ aminoferrocene (**279**).

In addition, it may also be possible to use Ganem's approach in *N*-deprotection of phthalimidine **274**.[69] Specifically, it was found that sequential addition of K₂CO₃ to **263a** and NaBH₄ reduction gave the putative hydroxyamide **285**, which could be cleaved to

aminoferrocne and phthalide with *p*-toluenesulfonic acid (**Scheme 54**). This procedure avoids the requirement for a separate oxidation step.
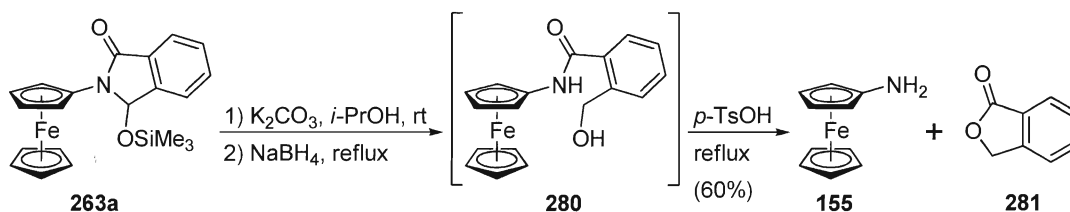
Scheme 54. Model study of one-pot deprotection of *O*-SiR$_3$ phthalimidines.

Attempts to control the absolute stereochemistry of the products by asymmetric reduction of the phthalimide (**159**) to the SiEt$_3$-protected phthalimidine (**263b**) were investigated next. Two reagents were employed for this purpose, namely BINAL-H and the Corey-Bakshi-Shibata oxazaborolidine. In these reactions, it was critical to maintain a basic environment until *O*-silylation occurred to avoid racemization of the hemiaminal. Both reactions provided some of the desired *O*-silylated phthalimidine (**263a,b**), which could not be separated from the starting material (**159**). The use of excess reagents did not lead to complete conversion of the starting material (**Scheme 55**). Metal-mediated hydrosilylation of the imide was briefly investigated as an alternative, considering that the product would be configurationally stable. Although the catalytic asymmetric hydrosilylation of imides (e.g. phthalimides) had no literature precedent, it is well established for ketones. It has been reported that Stryker's reagent[70], [(Ph$_3$P)CuH]$_6$, is capable of promoting such ketone hydrosilylations[71], with Et$_3$SiH, whereas many Rh-catalyzed[72] processes require dihydrosilanes as reagents. It was found that catalytic amounts of Stryker's reagent did not result in hydrosilylation of the phthalimidine. However, the combination of a stoichiometric amount of Stryker's reagent, dppf and

Et$_3$SiH gave the *O*-triethylsilyl phthalimidine **263b** in 60% yield. Attempts to perform

this reaction in asymmetric fashion by replacing dppf with MeO-BIPHEP or BINAP gave

no product (**Scheme 55**). Although these results were discouraging, the asymmetric

hydrosilylation of imides certainly warrants further investigation possibly with other

inexpensive metals (e.g. iron[73]) or even by organocatalytic methods.[74]
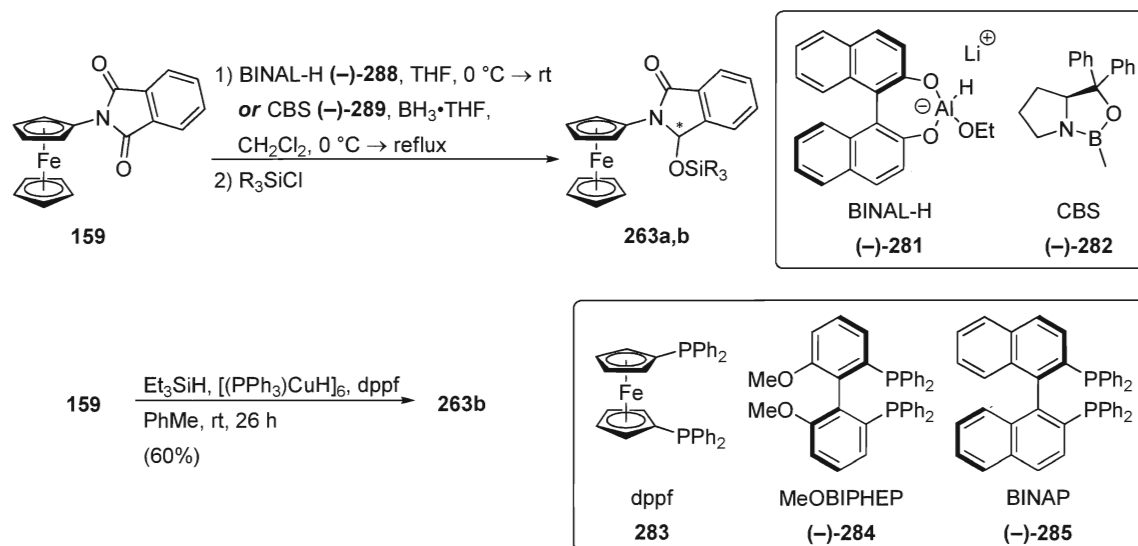
Scheme 55. Attempts at controlling phthalimidine absolute stereochemistry
by 2- and 1-step hydrosilylation processes.

One potential alternative to hydrosilylation is the control of absolute

stereochemistry of the phthalimidine by preparaing a hemiaminal from a chiral alcohol

such as (−)-menthol, as has been done with other imide derivatives.[75] In principle, these

products could be separated and independently subjected to the lithiation-substitution,

thereby providing access to both antipodes of the 2-substituted aminoferrocene.

In any case, it was also of interest to increase the scope of the reaction beyond

ClSiMe$_3$ to other electrophiles which are stable to lithium amide bases (such as ClSnBu$_3$

or B(O*i*-Pr)$_3$). Subjection of **263a** to LDA/B(O*i*-Pr)$_3$ conditions unfortunately gave the

undesired phenyl-substituted product (**286**). Similarly, the use of LTMP/ClSnBu$_3$ also

afforded only aryl-substituted stannane (**287**, **Scheme 56**). The reasons for this switch in regioselectivity were unclear. To better understand what was happening in these reactions, LTMP was used in combination with ClSiMe$_3$, which also afforded the benzene-substituted regioisomer (**275**) as the sole product in 85% yield. Although this was the undesired product, it was thought that disilylated compound **275** may serve as a blocked substrate which would be forced to undergo Cp ring deprotonation-silylation with LDA/TMSCl.
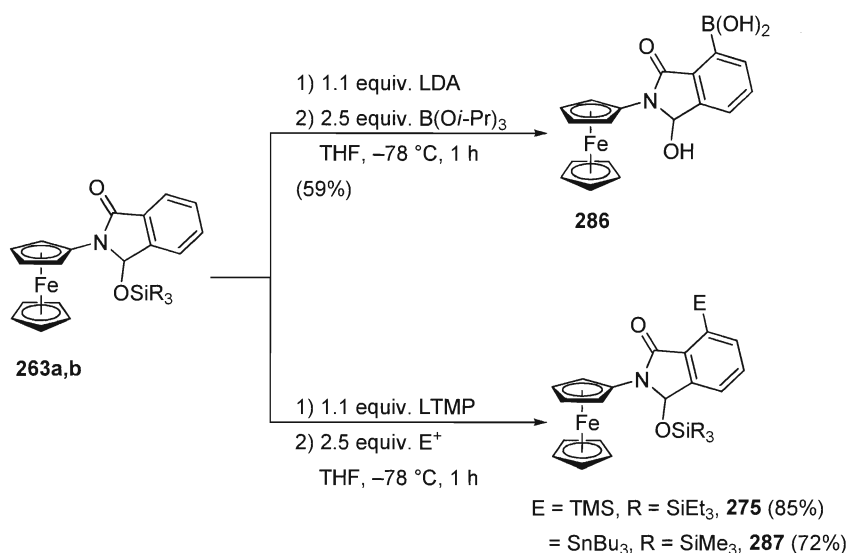
Scheme 56. Formation of regioisomeric products upon using different bases and/or electrophiles.

In fact, exposure of **275** to these conditions gave what has been tentatively assigned structure **289**, a constitutional isomer of the starting material, in a low yield. This product may have been formed by deprotonation of the methine proton at the benzylic centre, followed by equilibration of the anion and silyl migration (**Scheme 57**). All efforts to change this regioselectivity of the former reactions by using other bases (i.e. LiHMDS, LiBSBA,[76] i-PrMgCl·LiCl[77] or bimetallic bases[78]) proved fruitless.
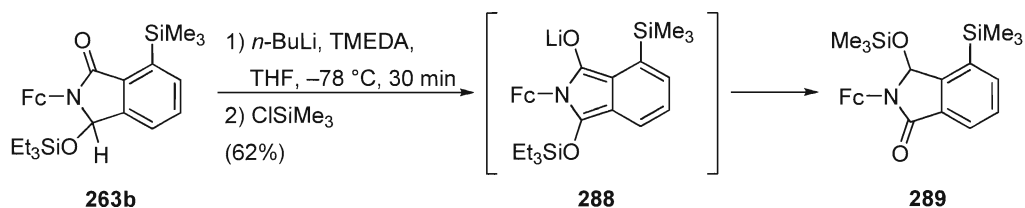
Scheme 57. Unanticipated potential formation of byproduct **289**.

TMS-substituted arenes are known to undergo halodesilylation reactions with various halogenating agents. Attempts were made at inducing *ipso*-substitution of **274** using ICl, which is known for electron-rich aromatics,[79] or carbodesilylation by *in situ* trapping with benzaldehyde as demonstrated by Simpkins (**Scheme 58**).[80] Both reactions led only to decomposition of **274**.
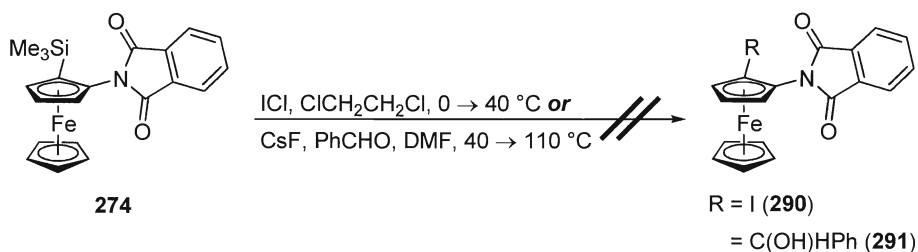
Scheme 58. Attempts at ipso-desilylation of phthalimide **274**.

The persisiting issues of electrophile scope and control of absolute sterochemistry of the starting material prompted an exploration of an alternative method for the synthesis of aminoferrocenes possessing planar chirality.

2.3.2 Boron Trifluoride-Activated Lithiation of Tertiary Aminoferrocenes

Ready access to aminoferrocene (**155**) *via* hydrazinolysis of phthalimide **159** allows for the preparation of any *N*-substituted aminoferrocene. Although the phthalimide

route to aminoferrocene reliably provides pure aminoferrocene, for the quantities that were required for this research, a more convenient preparation of **159** was sought. Although known for several years, Hessen's procedure[25a] for preparing aminoferrocene (**Scheme 59**) had been avoided because of the necessity to handle significant quantities of potentially explosive vinyl azide. Nevertheless, this route was reproduced on a small scale, validated, and then gruadually scaled up. All told, Hessen's procedure afforded aminoferrocene in 50-60% yield via quench of lithioferrocene with α-azidostyrene (**292**) and acid workup. The α-azidostyrene is readily prepared according to the route of Smolinski[81] from (1,2-dibromoethyl)benzene (**292**), by treatment with sodium azide in DMSO. The intermediate azidobromide (**293**) then undergoes elimination with sodium hydroxide (**Scheme 59**) to **294** at room temperature.
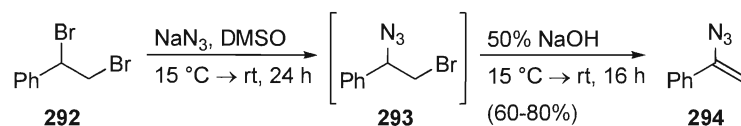
Scheme 59. One pot synthesis of α-azidostyrene (**294**).

With ample quantities of aminoferrocene on hand, *N,N*-dimethylaminoferrocene[82] (**295**) was prepared by reductive amination with paraformaldehyde and NaBH$_3$CN in acetic acid. Control experiments were conducted for the lithiation of dimethylaminoferrocene with *n*-BuLi in THF at 0 °C for three hours. Addition of ClSiMe$_3$ after this period did not show any sign of silylation of the Cp ring. This result was an unsurprising observation and is consistent with the recalcitrance of anilines to undergo lithiaition without the use of forcing conditions (alkyllithiums/refluxing hexanes,

vide supra).[57] Attempts to perform this lithiation at higher temperatures were not pursued as it was felt that these conditions were not conducive to good asymmetric induction.

To lower the temperature of the reaction while ensuring lithiation, pre-coordination of aminoferrocene **295** to a Lewis acid was pursued.[53]. In early experiments, dimethylaminoferrocene was coordinated to borane by addition of a 1 M solution of BH_3 in THF to the starting material at 0 °C. The putative $FcNMe_2 \cdot BH_3$ adduct (which was unstable to air, as observed previously for BH_3-complexed anilines[83]), underwent lithiation with *n*-BuLi at −78 °C which, following $ClSiMe_3$ quench, gave a trace amount of 2-trimethylsilyl derivative. Although the yield was low, this result was encouraging considering the temperature at which the reaction was conducted. Switching to the stronger Lewis acid $BF_3 \cdot OEt_2$ gave significantly better results. In this case, addition of an equimolar amount of $BF_3 \cdot OEt_2$ to dimethylaminoferrocene in THF at 0 °C resulted in a rapid colour change of the solution from orange to yellow-orange. The resulting solution of $FcNMe_2 \cdot BF_3$ was stirred for 10 minutes to ensure complete complexation of the reagents, and then cooled to −78 °C. At this point, 1.1 equivalents of *n*-BuLi was added, the mixture was stirred for 2 h and then quenched with $ClSiMe_3$ as before. Again, only a trace amount of product was obtained, along with recovery of the majority of starting material unchanged. As a result, the experiment was repeated, except that the reaction mixture was allowed to warm slowly from −78 C to −40 °C, at which point a discernible colour change had occurred from yellow-orange to red-orange. Addition of $ClSiMe_3$ to the mixture afforded 2-trimethylsilyl-1-dimethylaminoferrocene in 81% yield. To the best of our knowledge, this result represented the first example of a direct 2-lithiation of an aminoferrocene. This procedure was streamlined and repeated for many different

electrophiles. Thus, after coordination of the substrate with BF_3, the mixture was cooled to −78 °C, treated with n-BuLi and then warmed to −40 °C by transferring the reaction mixture to a different cold bath. The mixture was stirred at −40 °C for 1 h, cooled back to −78 °C, quenched with the appropriate electrophile, and then allowed to warm slowly to room temperature. Workup by addition of saturated aqueous sodium bicarbonate and purification of the products afforded 2-substituted aminoferrocenes **297a-k** in very good to excellent yields ranging from 76-94% (**Scheme 60**).[84] It was later found that it was unnecessary to cool the mixture to −78 °C and that the deprotonation-quench sequence could be carried out at −40 °C for the duration of the reaction with similar results. Notable substituents that could be installed included carbon-based groups such as formyl, amido and diphenylhydroxymethyl. Heteroatom substituents included boron, silyl, stannyl, iodo, sulfido and phosphino groups. It is noteworthy that these yields are significantly higher than what Kessar[58] obtained in BF_3-activated lithiation of dimethylanilines. The higher yields, in the case of dimethylaminoferrocene, may be tentatively attributed to the greater basicity of aminoferrocenes versus anilines, which may result in stronger coordination of the amine to BF_3.

Scheme reagents (left to right):

155 (Fe, NH$_2$) → (CH$_2$O)$_n$, NaBH$_3$CN, 50% HOAc (>90%) → **295** (Fe, NMe$_2$) → BF$_3\cdot$OEt$_2$, THF, 0 °C, 15 min → **296** [Fe, $\oplus$NMe$_2$·BF$_3^{\ominus}$] → 1) 1.1 equiv. n-BuLi, −40 °C, 1 h; 2) 1.2 equiv. E$^+$, −78 → rt → **297a-k** (Fe, E, NMe$_2$)
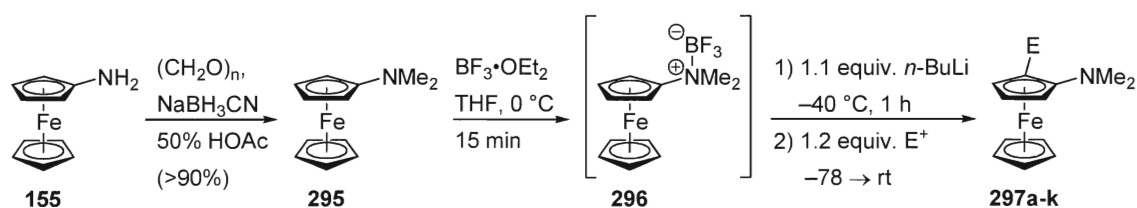
Product	E$^+$	E	Yield **297** (%)
297a	DMF	CHO	76
297b	Ph$_2$CO	C(OH)Ph$_2$	87
297c	PhCHO	C(OH)HPh	86[a]
297d	PhNCO	C(O)NHPh	93
297e	ClSiMe$_3$	SiMe$_3$	93
297f	ClSnMe$_3$	SnMe$_3$	91
297g	B(OEt)$_3$	Bpin	84[b]
297h	(SPh)$_2$	SPh	82
297i	ClPPh$_2$	PPh$_2$	77
297j	ClPCy$_2$	PCy$_2$	65
297k	I(CH$_2$)$_2$I	I	94

[a] separable 3:2 mixture of diastereomers.

[b] isolated as pinacol ester.

Scheme 60. Preparation of *N,N*-dimethylaminoferrocene and BF$_3$-mediated synthesis of (±)-2-substituted aminoferrocenes.

Many of these heteroatom-substituted products may be useful for further transformations, specifically stannane **297f**, boronate **297g** and iodide **297k**, as these are key intermediates for cross-coupling, transmetalation and metal-halogen exchange reactions. Unfortunately, attempts to incorporate bromine *via* quench with Br$_2$, 1,1,2,2-tetrabromoethane, 1,2-dibromo-1,1,2,2-tetrachloroethane or *N,N*-dibromodimethylhydantoin only led to decomposition and small amounts of recovered starting material. Similarly disappointing results were obtained when tellurium powder or BuTeBr[85] were used as electrophiles. In addition, tosyl azide quench, according to Carretero's procedure[19] also failed to give the azide.

Further elaboration of iodide **297k** was possible in a very fast reaction with Cu(OAc)$_2$ to provide 2-acetoxy derivative **298**, a rare *N,O*-substituted ferrocene (**Scheme**

61). In addition, copper-mediated Ullmann homocoupling[86] of the iodide gave a 1:1 mixture of separable *rac-* and *meso*-1,1"-diaminobiferrocenes (**299**) in 52% combined yield. It is noteworthy that *rac*-**299** is an unprecedented planar chiral analogue of axially chiral tetramethyl BINAM (**300**), which may have future applications in catalysis.
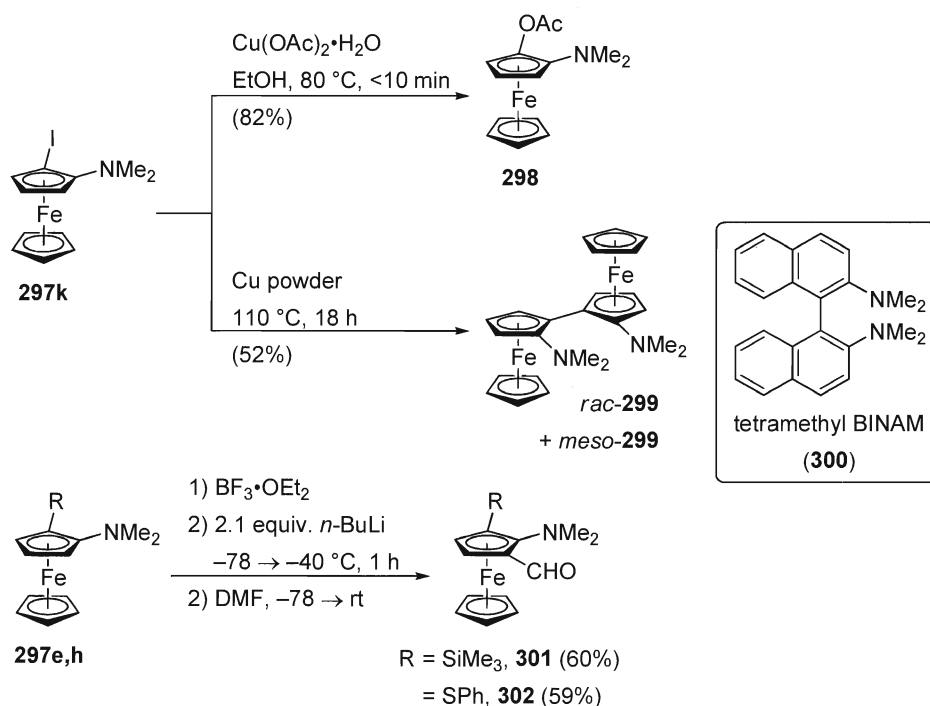
Scheme 61. Copper-mediated transformations of iodide **297k**
and consecutive lithiation-substitution of **297e,h**.

It was found that exposure of 2-SiMe$_3$ adduct **297e** or phenyl sulphide **297h** to an additional BF$_3$-activated lithiation sequence with 2.1 equivalents *n*-BuLi gave the contiguously 1,2,3-trisubstituted formyl adducts **301** and **302** after DMF quench.

Aldehyde **297a** also serves as a precursor to the alcohol, a synthetically useful intermediate. Thus, treatment with NaBH$_4$ afforded alcohol **303**, which readily undergoes S$_N$2-like substitution reactions, unlike Ugi's amine in which an α-ferrocenyl carbocation

is implicated. In this way, diamine **304**[87] and imidazole **305** may be prepared, the latter of

which may be a precursor to an imidazolylidene *via* imidazolium salt formation.
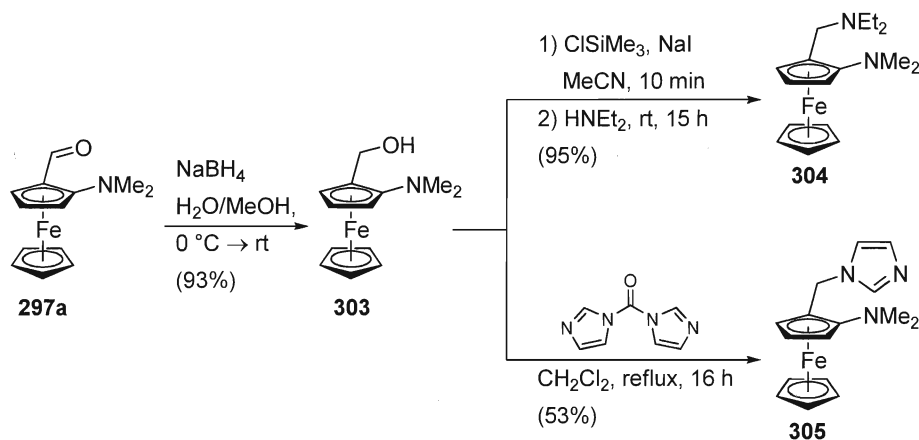
Scheme 62. Aldehyde **297a** as a precursor to bidentate ligands.

In addition, ferrocenyl iodide **297k** was subjected to Suzuki-Miyaura cross-coupling with arylboronic acids (**306a-e**), catalyzed by 10 mol% of Pd(PPh$_3$)$_4$ and aqueous NaOH to give the coupled products (**307a-e**) in 23-93% yield. The more typical phenylboronic acids are easier to install than the pyrrole moiety and the yields of these products compare favourably with previous Suzuki-Miyaura couplings of 2-substituted ferrocenes (**Scheme 63**).

ArB(OH)$_2$		Product	Yield **307** (%)
306a	(HO)$_2$B—phenyl	**307a**	80
306b	(HO)$_2$B—m-tolyl	**307b**	93
306c	MeO, (HO)$_2$B—o-anisyl	**307c**	87
306d	(HO)$_2$B—N-Boc-pyrrole	**307d**	23
306e	Br, (HO)$_2$B—o-bromophenyl	**307e**	46
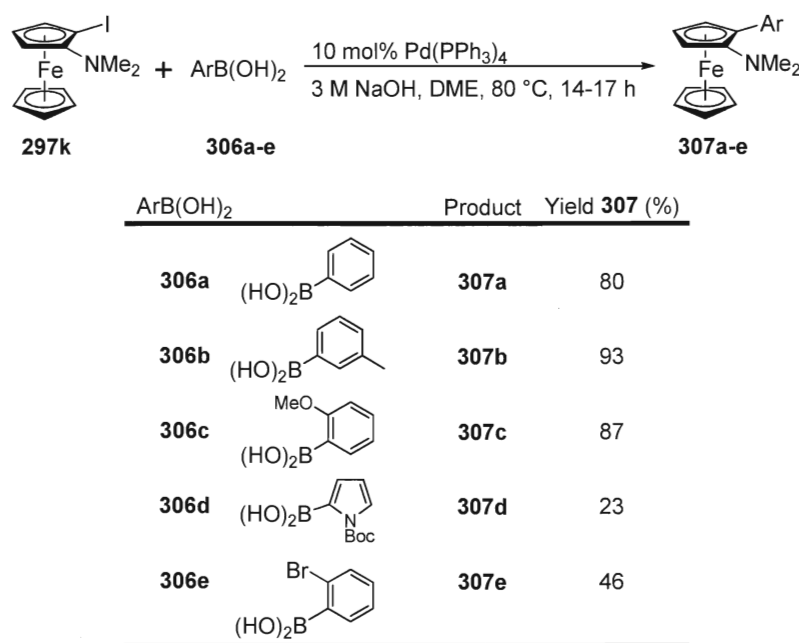
Scheme 63. Suzuki-Miyaura coupling of iodide **297k**.

Coupling of *N*-Boc 2-pyrrylboronic acid (**306d**), a challenging heterocyclic substrate for Suzuki-Miyaura reactions,[88] afforded 23% of the biaryl on the first attempt. Removal of the Boc group may allow installation of other groups on nitrogen such as phosphines. *o*-Bromophenylboronic acid (**306e**), prepared in one step by selective metal-halogen exchange of 1,2-dibromobenzene, was also a demanding coupling partner that provided **307e** in a moderate 46% yield, along with a small quantity of oligomers formed by further reaction of **307e** with the *o*-bromophenylboronic acid (**306e**). Overall, the yields obtained in these cross-couplings are quite respectable in comparison to other ferrocenyl biaryl bromides, which typically have relied on Negishi couplings of ferrocenyl zinc species. For example, Richards[89] and Weissensteiner[90] have reported yields of 27% and 27-45% for coupling of ferrocenylzinc chloride and 2-halozinc-1-ferrocenyl sulfoxides, respectively.

The bromobiaryl derivative **307e** was open to further manipulation via metal-halogen exchange. In this case, Br→Li exchange (*n*-BuLi, THF, −78 °C) proceeded very well, and addition of chlorodiphenylphosphine provided *P,N*-ligand **309** *via* the sulfide. The sulfide was prepared as an intermediate for ease of purification, and then reduced to the phosphine with Raney Ni (**Scheme 64**). Aminophosphine **309** is notably a planar chiral analogue of Buchwald's DavePhos (**310**),[91] a frequently used phosphine ligand for a number of transition metal-catalyzed processes.
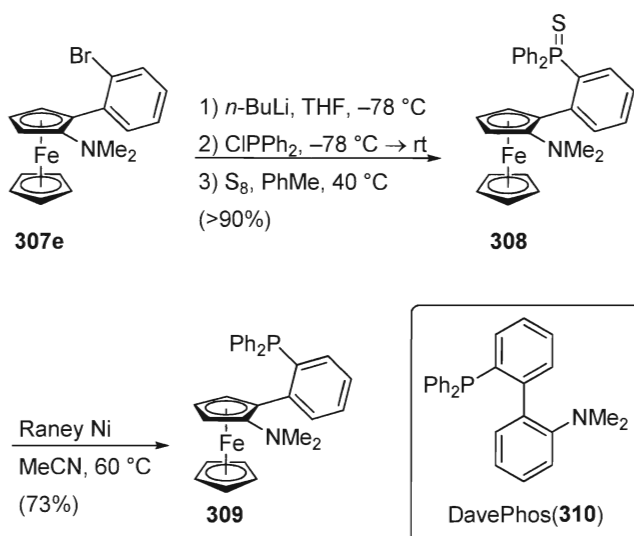
Scheme 64. Conversion of bromide **307e** to biaryl phosphine **309**.

2.3.3 Coordination Chemistry and Applications of 2-Phosphino-1-dimethylaminoferrocenes

The use of BF$_3$-mediated lithiation-substitution on dimethylaminoferrocene (**295**) gives access to rare 1,2-aminophosphines such as **297i,j** in short order. As Stradiotto has investigated the coordination chemistry of related indenyl-derived aminophosphine **270** with Rh(I) (*vide supra*), it was of interest to study the tendency of the new aminophosphines to chelate catalytically useful transition metals. For this purpose,

transition metals that favour square planar geometry such as palladium(II), platinum(II) and iridium(I) were studied. Thus, coordination of aminophosphines **297i,j** (R = Ph, Cy) to palladium was effected with Pd(MeCN)$_2$Cl$_2$ in CH$_2$Cl$_2$ at room temperature to give complexes **311a,b** in 87-91% yield (**Scheme 65**). In similar fashion, ligands **297i,j** were coordinated to platinum by heating the aminophosphines wtih Pt(COD)Cl$_2$ at reflux in toluene. Evidence for chelation of either ligand to the metals was provided by ^{1}H NMR in which the amino methyl groups were rendered non-equivalent, and by ^{31}P NMR where the phosphine chemical shifts moved significantly downfield in comparison to the free ligands.
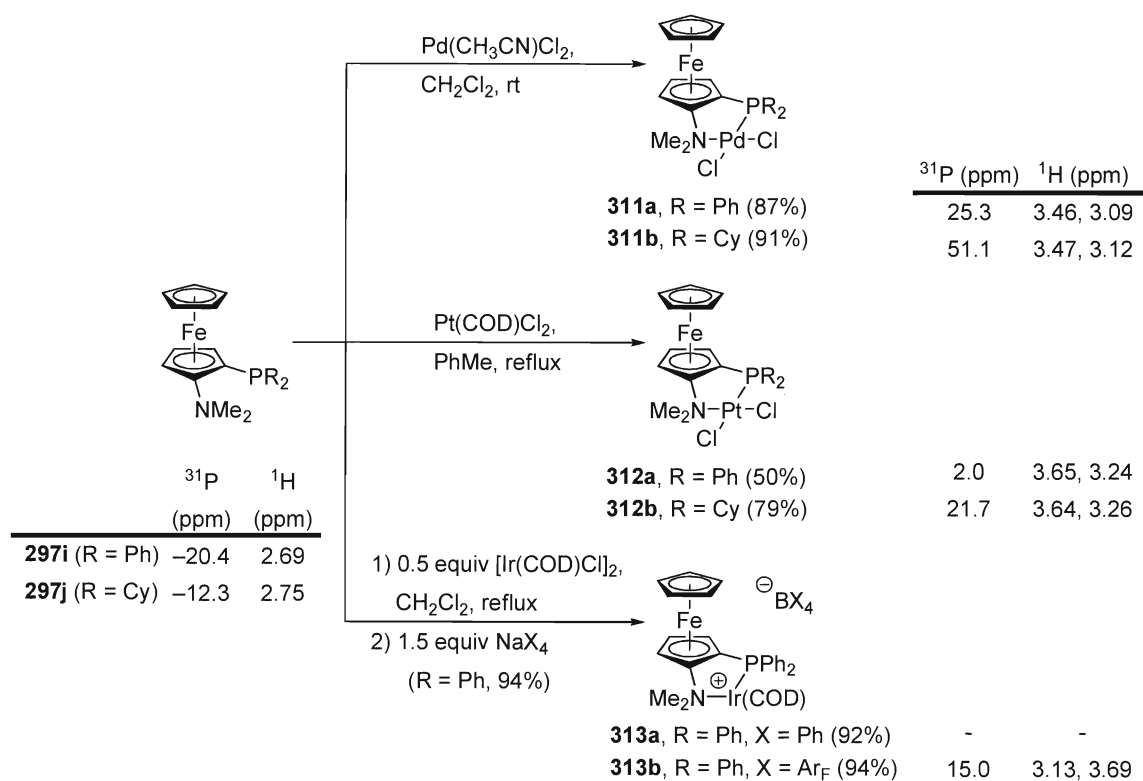
Scheme 65. Aminophosphine **297i,j** coordination to Pd(II), Pt(II) and Ir(I).

Specifically, upon coordination of diphenylphosphine derivative **297i** to Pd, the phosphorus signal moved from −20.4 ppm to 25.3 ppm and the NMe$_2$ singlet at 2.69 ppm from uncoordinated **297i** split into two signals at 3.46 and 3.09 ppm in ^{1}H NMR.

A cationic Ir(I) complex (**313a**) was formed by heating by heating a CH$_2$Cl$_2$ solution of **297i** with [Ir(COD)Cl]$_2$. The complex was isolated as the tetraphenylborate salt after anion exchange with NaBPh$_4$, but due to its insolubility, it was not fully characterized. Characterization of the cationic Ir(I) complex was carried out on the chloride and BAr$_F$ (**313b**) salts. The latter counterion is weakly coordinating and known to be beneficial in certain catalytic transformations performed concurrently in the Metallinos group.[92] Characterization, including a crystal structure, of **313b** will be presented in the M.Sc. thesis of Lori Van Belle.[93] The above Pt(II) and Ir(I) complexes (**312a,b** and **313b**) displayed the same ^{1}H and ^{31}P trends as in the Pd(II) complexes.

Key data from the X-ray analyses from the palladium and platinum complexes (**Figures 12** and **13** respectively) showed that the ligand chelates the metals with bite angles of 87.87(6)° for P1-Pd1-N2 and 88.78(5)° for P1-Pt1-N2, respectively. Because these values are close to orthogonal, no distortion from the ideal square planar geometry at the metal centre is observed. Pd complex **311a** and Pt complex **312a** were shown to be nearly isostructural. Both were characterized by staggered conformations of the Cp rings with dihedral angles (H4-C4-C4'-H4') of 32.27(14) and 28.59(13)° for **311a** and **312a** respectively.
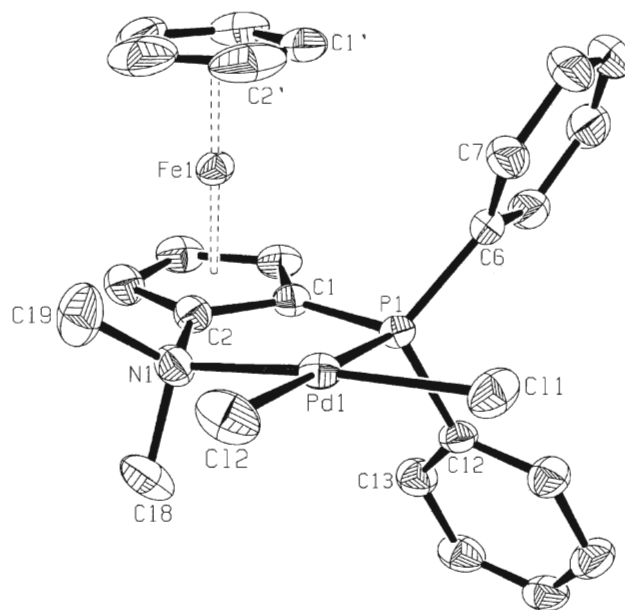
Figure 12. ORTEP plot of Pd complex **311a** at 50% probability.
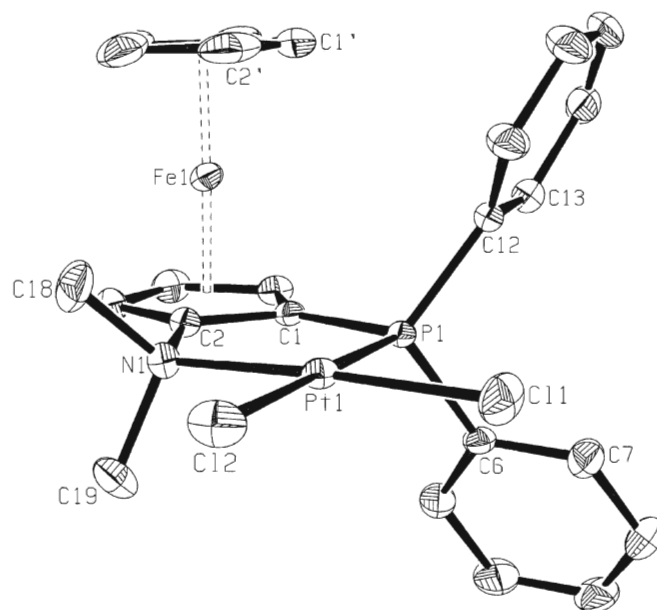
Figure 13. ORTEP plot of Pt complex **312a** at 50% probability.

The ability of both of the preceding aminophosphines to readily coordinate to palladium, platinum and iridium prompted a preliminary study of their catalytic potential in Suzuki-Miyaura[94] coupling, Buchwald-Hartwig[91a,95] amination and intramolecular hydroamination reactions. For Suzuki-Miyaura reactions, a number of aryl chlorides (**314a-f**), which are typically less reactive than bromides or iodides, were investigated. In this respect, cross coupling of phenylboronic acid with aryl chlorides **314a-f** catalyzed by 2 mol% Pd(OAc)$_2$, 4 mol% aminophosphine **297i** and three equivalents of CsF gave product yields ranging from 70-94% for all substrates, with the exception of **314f**, which afforded a moderate yield of 56% (**Scheme 66**). In addition, dibromide **314g**, provided by Professor Martin Lemaire's laboratory (Brock University), underwent double phenylation in 88% yield under the same conditions. Notably, double phenylation of **314g** with Pd(PPh$_3$)$_4$ afforded the product (**315g**) in less than 50% yield.

Aryl Halide	X	Yield **315** (%)
314a (G = 4-CF$_3$)	Cl	94
314b (G = 4-COMe)	Cl	88
314c (G = 4-CN)	Cl	92
314d (G = 2-NO$_2$)	Cl	73
314e (G = 4-OMe)	Cl	70
314f (G = 4-Me)	Cl	56
314g	-	88
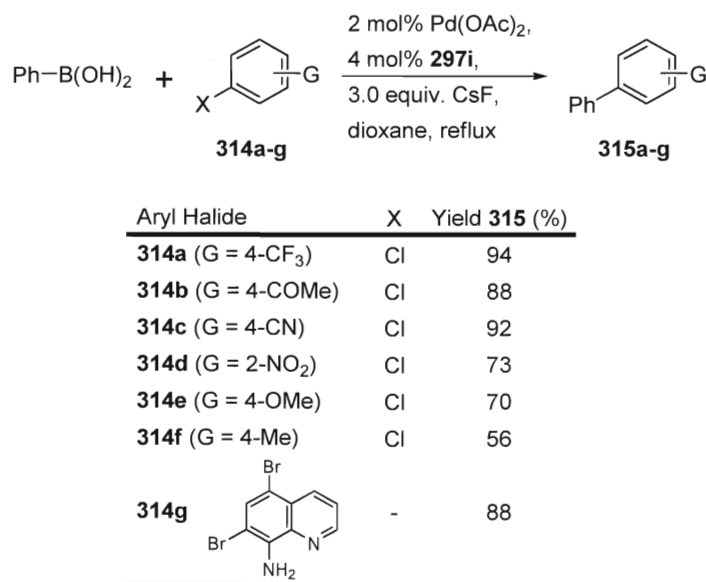
Scheme 66. Suzuki-Miyaura cross-coupling of PhB(OH)$_2$ using phosphine **297i**.

The aryl amination reactions proved more challenging. In this reaction, a 1:1 ratio of Pd:ligand was found to give better results. Acceptable yields of 74-77% for coupling products **317a,b** were obtained for electron deficient chlorides having 4-CF$_3$ or 4-C(O)Me groups. An *ortho*-substituent on the chloride (**316d**) adversely affected the reaction, providing 43% of the desired biaryl. Electron-rich or neutral substrates required the use of the corresponding aryl bromides (**316e,h**) to obtain reasonable yields.

Aryl Halide	X	Yield **317** (%)
316a (G = 4-CF$_3$)	Cl	77
316b (G = 4-COMe)	Cl	74
316d (G = 2-NO$_2$)	Cl	43
316e (G = 4-OMe)	Br	67
316h (G = H)	Br	82
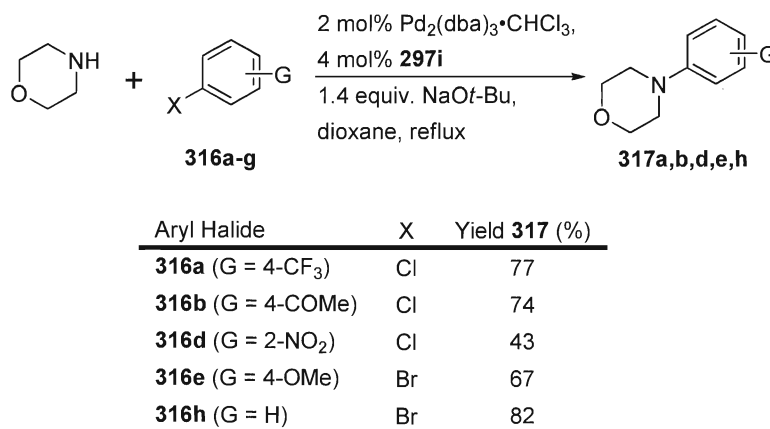
Scheme 67. Aryl amination of various aryl halides using phosphine **297i**.

In a subsequent test of catalytic competency, the late transition metal-catalyzed intramolecular hydroamination of unactivated alkenes[96] was briefly investigated. Widenhoefer[96d,e] has reported that a combination of PtCl$_2$ and Buchwald's biaryl aminophosphine ligand was able to catalyze the formation of pyrrolidine **319** from aminoalkene **318** in high yield. In our hands, the intramolecular hydroamination was first carried out using Pt(II) following Widenhoefer's reports, which after significant experimentation with solvents, Pt:ligand ratios and use of the discreet complex (**312a**), led only to a 27% yield of spirocyclic pyrrolidine **319** (**Scheme 68**). The corresponding cationic Ir(I) complex (**313b**) effected the same transformation in a much-improved 64%

yield of spirocycle **319**, along with an inseparable mixture of compounds that appeared to result from alkene isomerization and reduction. These byproducts may be diminished by the use of Rh(I) to catalyze this transformation, as shown by Hartwig.[96g] Nonetheless, this Ir(I)-catalyzed hydroamination was only the third of its type to be reported, following recent work by Stradiotto[96a,b] and Hollis.[96c]

Conditions	Yield (%)
5 mol% PtCl$_2$, 10 mol% **297i**, diethylene glycol, 100 °C, 48 h	27
2.5 mol% **297b**, dioxane, reflux, 22 h	64
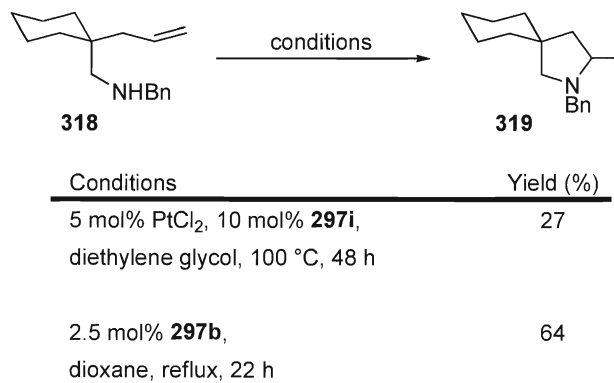
Scheme 68. Intramolecular hydroamination with Pt(II) and Ir(I).

2.3.4 Enantioselective Lithiation-Substitution of BF$_3$-Activated Tertiary Aminoferrocenes

As mentioned previously, asymmetric lithiation of BF$_3$- or BH$_3$-activated tertiary amines, such as isoindolines,[54] pyrrolidines[55] and aziridines[60a] has been established. In all of these cases, (–)-sparteine was used as a chiral diamine additive. When dimethylaminoferrocene was complexed as usual with BF$_3$·OEt$_2$, treated with n-BuLi·(–)-sparteine at –78 °C and the resulting mixture was warmed to –40 °C over 2 h, DMF quench gave formyl derivative **297a** in 43% yield but a disappointing 44:56 er. Replacing n-BuLi with s-BuLi or i-PrLi resulted in insignificant improvements to the stereoselectivity, prompting the investigation of other chiral diamine additives.

Recent reports by Alexakis[97] and O'Brien[98] have indicated that *trans*-cyclohexanediamines, which are available in either enantiomeric form by resolution of racemic **320** with tartaric acid, may serve as alternatives to (–)-sparteine for asymmetric reactions using organolithium reagents. Alexakis has shown that these additives afford moderate enantioselectivities in additions of alkyllithiums to imines, while O'Brien has used similar analogues as (+)-sparteine surrogates in lithiation of *N*-Boc pyrrolidine. 1,2-Diaminocyclohexane ligands (*S,S*)-**87** and **323-327** were prepared by resolution of (±)-*trans*-cyclohexanediamine [(±)-**320**] according to established procedures.[97,98] Eschweiler-Clarke methylation (CH$_2$O, HCO$_2$H, reflux) of the diastereomeric tartrate gave the *N,N,N',N'*-tetramethyl derivative; in this case, (*S,S*)-**321**·(–)-tartrate afforded (*S,S*)-**87** in good yield (**Scheme 69**).
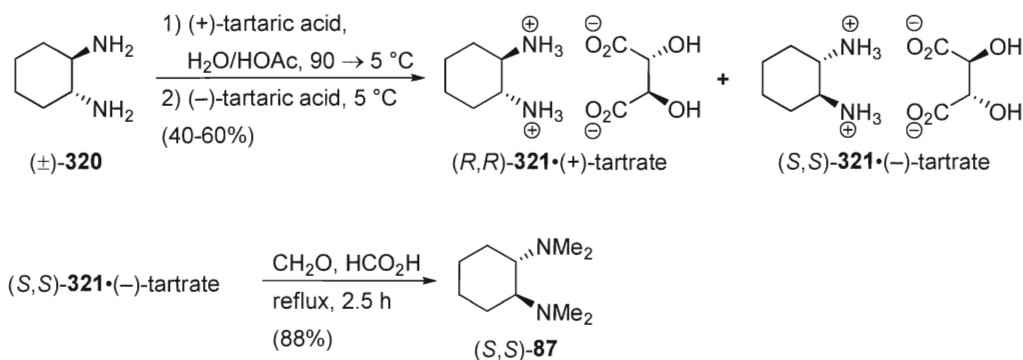
Scheme 69. Resolution of *trans*-(±)-cyclohexanediamine
and preparation of (*S,S*)-**87**.

Cyclohexanediamine ligands **323-327**, with two different *N*-substituents were prepared by modified syntheses, as outlined in **Scheme 70** below.
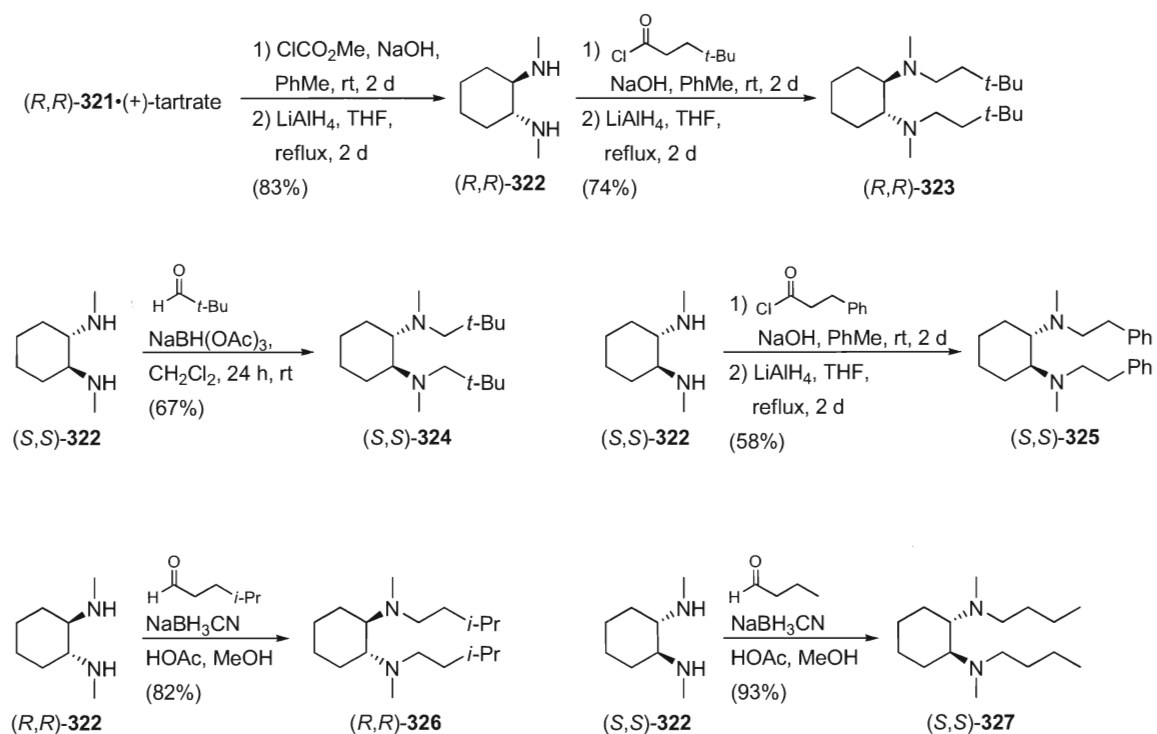
Scheme 70. Preparation of cyclohexanediamine ligands with different nitrogen substituents.

For example, **321** was transformed into the bis(carbamate), which was reduced with LiAlH$_4$ in THF in over 80% yield. (+)-Sparteine surrogate (*R,R*)-**323** and Ph-terminated ligand (*S,S*)-**325** were made in two steps from **321**, each by way of amide formation and subsequent reduction (LiAlH$_4$, THF, reflux, 2 d, 58-74%). It was found that reductive amination was more conveneient for the preparation of (*S,S*)-**324**, (*R,R*)-**326**, (*S,S*)-**327**.

Evans' bis(oxazoline) was also prepared for use in the BF$_3$-activated aminoferrocene lithiation as it has been reported to be effective in the cyclization of olefinic organolithiums by Bailey[99] and the enantioselective lateral lithiation of azaferrocenes.[100] According to Evans' procedure, the ligand was prepared from commercially available malonate **328**, which was saponified to dicarboxylic acid **329** (**Scheme 71**). Treatment with thionyl chloride, followed by addition of (*S*)-valinol gave

diol (*S,S*)-**330**. Formation of the bis(mesylate) (MsCl, Et₃N, CH₂Cl₂, 0 °C → rt) and treatment with NaOH at reflux effected ring closure to furnish bisoxazoline (*S,S*)-**331**.
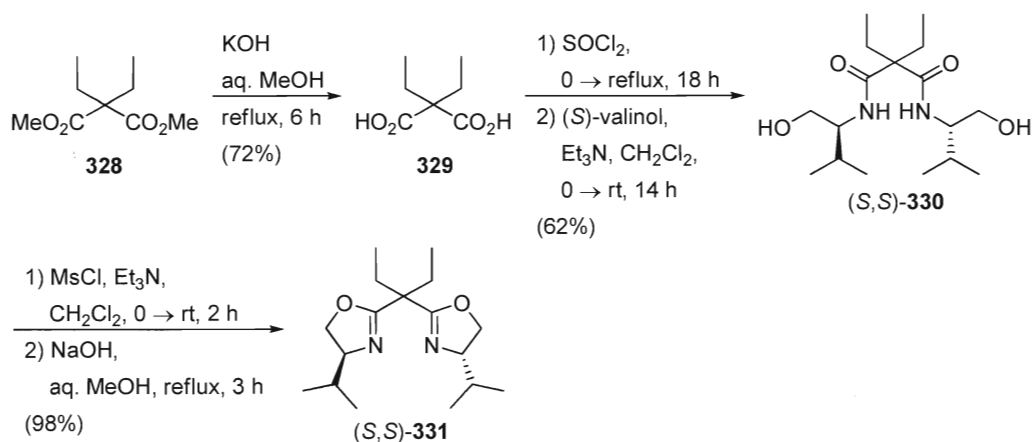
Scheme 71. Preparation of bis(oxazoline) ligand (*S,S*)-**331**.

With all of these diamines in hand, BF₃-mediated lithiation-substitution was systematically investigated.[101] The use of (*S,S*)-**87** in lithiation-substitution of dimethylaminoferrocene (**295**) provided a good yield of formyl derivative **297a**, but with a selectivity no better than that obtained with (−)-sparteine (entry 1, **Scheme 72**). Interestingly, (*R,R*)-**323** provided **297a** in 71% yield and 61:39 er *favouring the same enantiomer as that produced by the action of (−)-sparteine*. This result is in contrast to what was observed by O'Brien and coworkers in the asymmetric lithiation of *N*-Boc pyrrolidine, where (*R,R*)-**323** behaved as a (+)-sparteine surrogate.[98] Significant improvements in enantioselectivity were observed when (*R,R*)-**323** and secondary alkyllithiums were employed in this reaction. Lithiation of **295**·BF₃ with 1.1 equivalents of *s*-BuLi·(*R,R*)-**323** afforded the same product in 22% yield and 83:17 er in (entry 3). If 2.1 equivalents *s*-BuLi were used, the product was obtained in 35% yield, but marginally lower 80:20 er (entry 4). Further improvements in enantioselectivity were observed by

switching to *i*-PrLi. As in the experiments with *s*-BuLi, lithiation of **295**·BF$_3$ with 1.1 equivalents of *i*-PrLi·(*R,R*)-**323** gave a lower yield of product (36%, entry 5) than when 2.2 equivalents of reagent were used in entry 6. In both cases, similar enantioselectivities (86.5:13.5 and 86:14, respectively) were obtained for **297a**. Cyclopentyllithium did not lead to improvement in stereoselectivity, while *t*-BuLi showed poor reactivity and gave almost racemic product.

Scheme 72. Preliminary screening of chiral ligands and bases.
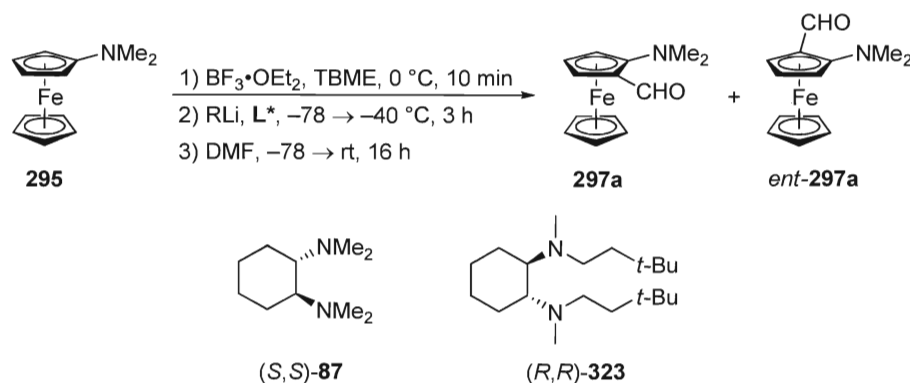
	Equiv. RLi	L*	Yield **297** (%)	er **297a**:*ent*-**297a** (% ee)	Recovered **295** (%)
1	2.1 *n*-BuLi	(*S,S*)-**87**	64	45:55 (10)	n.d.
2	2.1 *n*-BuLi	(*R,R*)-**323**	71	61:39 (22)	n.d.
3	1.1 *s*-BuLi	(*R,R*)-**323**	22	83:17 (66)	70
4	2.1 *s*-BuLi	(*R,R*)-**323**	35	80:20 (60)	25
5	1.1 *i*-PrLi	(*R,R*)-**323**	36	86.5:13.5 (73)	47
6	2.1 *i*-PrLi	(*R,R*)-**323**	56	86:14 (72)	20
7	1.1 *t*-BuLi	(*R,R*)-**323**	7	54.5:45.5 (9)	79
8	2.1 *t*-BuLi	(*R,R*)-**323**	10	53.5:46.5 (7)	79
9	1.1 *c*-PentLi	(*R,R*)-**323**	24	79.5:20.5 (59)	75
10	2.1 *c*-PentLi	(*R,R*)-**323**	56	78:22 (56)	40

In all of the preceding experiments, it appeared that deprotonation occurred upon slow warming of the reaction mixture from −78 to −40 °C. Allowing the reaction mixture to warm up to only −60 or −50 °C gave no appreciable improvement in selectivity and only

resulted in diminished yields of the product. This was likely, in part, a result of the reduced solubility of **295**·BF$_3$ at -78 to -78 °C. Switching to other solvents such as toluene, cumene or *i*-Pr$_2$O did not afford improved selectivities or only exacerbated the insolubility of **295**·BF$_3$. In fact, no reaction occurred in *i*-Pr$_2$O. For these reasons, TBME, or mixtures of TBME and other solvents, were used for subsequent optimization experiments.

Encouraged by the improved selectivity obtained in the reaction with *i*-PrLi· (*R,R*)-**323**, similar ligands (*S,S*)-**324**, (*S,S*)-**325**, (*R,R*)-**326** and (*S,S*)-**327** were investigated in this transformation (**Scheme 73**). (*S,S*)-**324** displayed very poor reactivity, resulting in very low conversion of the starting material, while (*S,S*)-**325** suffered from competitive benzylic deprotonation. Under the typical conditions using *i*-PrLi in TBME, bisoxazoline (*S,S*)-**331** only gave 13% yield. Thus, (*S,S*)-**324**, (*S,S*)-**325** and (*S,S*)-**331** were not investigated further.

In general, (*R,R*)-**326** and (*S,S*)-**327** provided better results than the previous chiral diamines that were tested. As expected, the primary alkyllithium *n*-BuLi did not provide adequate selectivity, even with alternative ligand (*S,S*)-**327** (**Scheme 73**, entry 1). An improved er of 89:11 was obtained upon switching to *i*-PrLi (entry 2). Direct comparison of (*S,S*)-**327** and (*R,R*)-**326** using *i*-PrLi showed that these two chiral diamines provided nearly the same results (entries 2 and 3) and could be used interchangeably. Other secondary alkyllithiums, such as *s*-BuLi and *c*-PentLi (entries 4 and 5), did not provide better results than *i*-PrLi. In an attempt to further improve on these results, reactions were run in mixtures of TBME with Et$_2$O, PhMe and *i*-PrPh (entries 6-8), with 1:1 TBME/Et$_2$O giving the best results (60% yield, 89:5:10.5 er).

Using Et$_2$O as the solvent (entry 9) provided comparable results to those from using 1:1 TBME/Et$_2$O. As anticipated, the use of THF as a solvent afforded nearly racemic product (entry 10), however the use of a ligand to base ratio of 3:2 (entry 11) gave similar results to the experiment conducted in Et$_2$O.
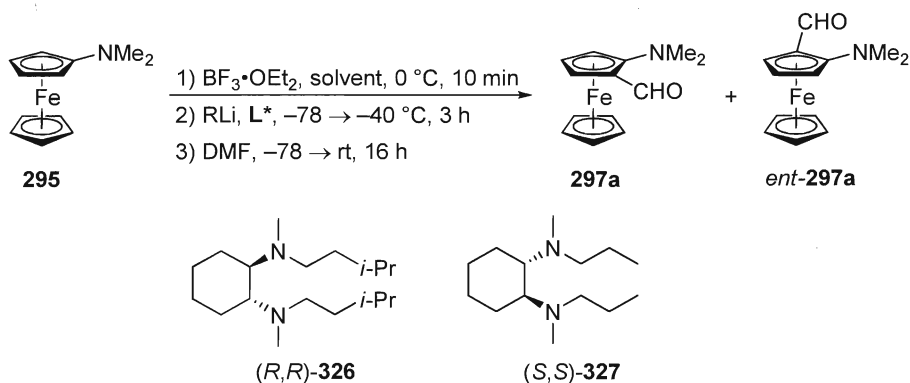
	Equiv. RLi	L*	Solvent	Yield **297a** (%)	er **297a**:*ent*-**297a** (%ee)	Recovered **295** (%)
1	2.1 *n*-BuLi	(*S,S*)-**327**	TBME	69	22.0:78.0 (56)	18
2	2.1 *i*-PrLi	(*S,S*)-**327**	TBME	44	11.0:89.0 (78)	37
3	2.1 *i*-PrLi	(*R,R*)-**326**	TBME	43	87.0:13.0 (74)	24
4	2.1 *s*-BuLi	(*R,R*)-**326**	TBME	30	85.5:14.5 (71)	52
5	2.1 *c*-PentLi	(*R,R*)-**326**	TBME	48	78.0:22.0 (56)	28
6	2.1 *i*-PrLi	(*R,R*)-**326**	1:1 TBME/Et$_2$O	60	89.5:10.5 (79)	4
7	2.1 *i*-PrLi	(*R,R*)-**326**	1:1 TBME/PhMe	45	90.5:9.5 (81)	10
8	2.1 *i*-PrLi	(*R,R*)-**326**	1:1 TBME/*i*-PrPh	47	90.5:9.5 (81)	10
9	2.1 *i*-PrLi	(*S,S*)-**327**	Et$_2$O	55	10.5:89.5 (79)	26
10	2.1 *i*-PrLi	(*R,R*)-**326**	THF	60	50.5:49.5 (1)	23
11	2.1 *i*-PrLi[a]	(*R,R*)-**326**[a]	TBME	56	90.0:10.0 (80)	28

[a] (*R,R*)-**326**:*i*-PrLi = 3:2

Scheme 73. Screening of additional chiral diamine ligands.

Dimethylaminoethanol (**333**)[102] and diisopropylamine (**334**)[103] have also been used as Lewis basic additives in asymmetric lithiation reactions. These additives have been reported to afford improved yields and selectivities in some cases; they also offer

the advantageous use of substoichiometric amounts of chiral diamine. The combination of various alkyllithium reagents with either **333** or **334** in the presence of chiral diamines maintained the level of selectivity and was able to marginally improve the yields. Notably, the higher reactivity[104] of this combination of reagents was observed by the isolation of some 1,2,1'-trisubstituted material (**332a**). Entries 1-4 (**Scheme 74**) show the combination of *n*-BuLi and DMAE or DIPA for comparison with the previous results using unbranched alkyllithiums. In the presence of these Lewis basic additives, it still proved beneficial to the yield to use additional alkyllithium (Entries 1-2). It was also observed that DMAE and DIPA produce similar results as additives to *n*-BuLi and (*S,S*)-**327** (entries 2 and 3). Entry 4 shows that the added steric bulk present in (*R,R*)-**326** was of no benefit and proved inferior to (*S,S*)-**327**. Entries 5-10, where *i*-PrLi was used in combination with **333** or **334**, serve to reinforce the necessity of using a more branched alkyllithium (i.e. *i*-PrLi) than *n*-BuLi. Entries 5 and 6 show that diamine (*S,S*)-**327** performed marginally better (76 and 79% ee respectively) than (*R,R*)-**326** with 1.65 equivalents *i*-PrLi. When the amount of *i*-PrLi was increased to 3.15 equivalents, (*S,S*)-**327** again proved to be slightly better than (*R,R*)-**326** (entries 7-8), giving respective selectivities of 82 and 78% ee. This trend also held for entries 9-10, where DIPA was used instead of DMAE. Thus, the conclusion may be drawn that DMAE is slightly better than DIPA and that (*S,S*)-**327** offers marginally better selectivity than (*R,R*)-**326** in the given system.

Scheme 74. Evaluation of achiral additives in the
(*R*,*R*)-326- and (*S*,*S*)-327-mediated lithiation of 295·BF$_3$.
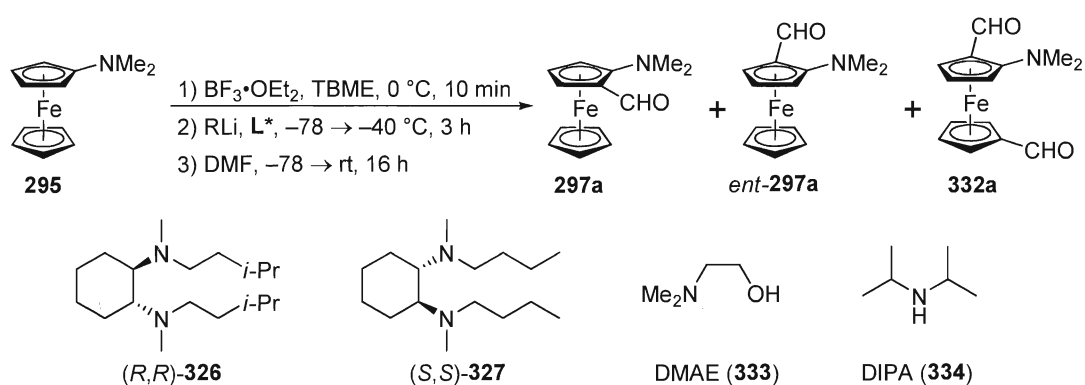
	Equiv. RLi	Equiv. L*	Yield 297a (%)	er 297a:ent-297a (%ee)	Yield 332a (%)	Recovered 295 (%)
1	1.65 *n*-BuLi	0.55 (*S*,*S*)-327 and DMAE	16	23.5:76.5 (53)	0	76
2	3.15 *n*-BuLi	1.05 (*S*,*S*)-327 and DMAE	67	23.5:76.5 (53)	<5	13
3	3.15 *n*-BuLi	1.05 (*S*,*S*)-327 and DIPA	64	22.5:77.5 (55)	0	24
4	3.15 *n*-BuLi	1.05 (*R*,*R*)-326 and DIPA	52	72.5:27.5 (45)	0	33
5	1.65 *i*-PrLi	0.55 (*R*,*R*)-326 and DMAE	43	88.0:12.0 (76)	7	48
6	1.65 *i*-PrLi	0.55 (*S*,*S*)-327 and DMAE	43	10.5:89.5 (79)	<5	32
7	3.15 *i*-PrLi	1.05 (*S*,*S*)-327 and DMAE	61	9.0:91.0 (82)	9	19
8	3.15 *i*-PrLi	1.05 (*R*,*R*)-326 and DMAE	41	89.0:11.0 (78)	21	9
9	3.15 *i*-PrLi	1.05 (*R*,*R*)-326 and 1.1 DIPA	24	89.0:11.0 (78)	9	26
10	3.15 *i*-PrLi	1.05 (*S*,*S*)-327 and DIPA	59	10.0:90.0 (80)	<5	26

The optimum conditions for lithiation-electrophile quench using electrophiles other than DMF varied somewhat (**Scheme 75**). Nevertheless, the carboxamide derived from PhNCO quench was produced by standard lithiation with *i*-PrLi·(*R*,*R*)-**323**. In the case of stannane **297f**, sulfide **297h** and iodide **297k**, the use of DMAE was beneficial to

avoid the production of trisubstituted material and led to more complete consumption of starting material. This was important for the purification of the major product, which invariably co-eluted with starting material and/or by product, depending on the electrophile used.

The enantiomeric ratio for stannane **297f** was measured *via* the formyl derivative (**297a**) by way of transmetalation and subsequent DMF quench (1. 2.1 equiv. MeLi, THF, −40 °C, 10 min; 2. DMF, −78 °C → rt). This result was also important, as it verified that products *ent*-**297a** and *ent*-**297f** possessed the same configuration, which was expected since both were obtained by asymmetric deprotonation of **295**·BF$_3$ with *i*-PrLi·(*S,S*)-**327**. The enantiomeric purity of the silane (**297e**) and phenyl sulfide (**297h**) derivatives was measured by conversion to trisubstituted formyl derivatives **301** and **302** by resubjection to BF$_3$-mediated lithiation as shown in **Scheme 61** (*vide supra*). Iodide **297k** was converted to *O*-acetate **298** for the same purpose (**Scheme 61**, *vide supra*). The development of an enantioselective protocol for the lithiation of **295** enabled the preparation of several enantiopure derivatives, such as tertiary alcohol ***ent*-297b** in **Scheme 75**, by way of crystallizaiton. In addition to *ent*-**297b**, biferrocene **299** was obtained in enantiopure form after two recrystallizations from *i*-PrOH. Importantly, phosphine **297i** could be recrystallized to enantiopurity as the phosphine sulfide·HBF$_4$ salt.[105]

Scheme 75. BF$_3$-mediated enantioselective deprotonation of dimethylaminoferrocene and quench with various electrophiles.
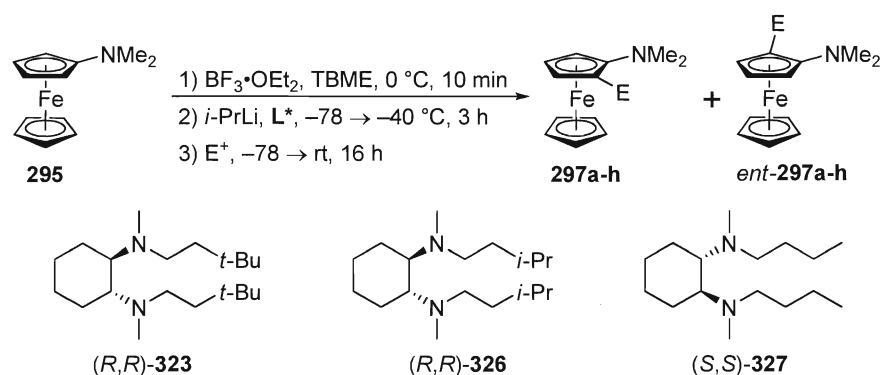
Product	Equiv. i-PrLi	Equiv. L*	E$^+$	E	Yield 297/ent-297 (%)	er 297:ent-297 (% ee)
297a	3.15	1.05 (S,S)-**327** and DMAE	DMF	CHO	61	9:91 (82)
297b	2.1	2.1 (S,S)-**327**	Ph$_2$CO	C(OH)Ph$_2$	74	ent-**297b**[a]
297d	2.1	2.1 (R,R)-**323**	PhNCO	C(O)NHPh	72	88:12 (76)
297e	2.1	2.1 (S,S)-**327**	ClSiMe$_3$	SiMe$_3$	39	11.5:88.5 (77)[b]
297f	2.4	0.80 (S,S)-**327** and DMAE	ClSnMe$_3$	SnMe$_3$	42	9:91 (82)[c]
297h	2.4	0.80 (S,S)-**327** and DMAE	(SPh)$_2$	SPh	71	12:88 (76)[b]
297i	3.15	1.05 (R,R)-**326** and DMAE	ClPPh$_2$	P(S)Ph$_2$[d]	50	88.5:11.5 (77)
297k	2.4	0.80 (S,S)-**327** and DMAE	(ICH$_2$)$_2$	I	47	12:88 (76)[e]

[a] Recrystallized to enantiomeric purity, configuration determined by X-ray.
[b] Measured by CSP HPLC analysis of the 1,2,3-trisubstituted formyl derivatives (i.e. **301**, **302**)
[c] Measured as formyl derivative **297a** by transmetalation-DMF quench of **297f**.
[d] Converted to phosphine sulphide for purification and CSP HPLC purposes.
[e] Measured as O-acetate **298**.

Single crystal X-ray analysis of ent-**297b** (**Figure 14**) and phosphine sulfide·HBF$_4$ **335** (**Figure 15**) determined that the compounds both had the (S)-absolute stereochemistry, but opposite relative stereochemistry. This was expected considering that the two derivatives were prepared by using different enantiomers of the chiral diamines, illustrating that both antipodes of the reaction products may be obtained

(**Scheme 76**). It is also clear from this data that the use of the (*S,S*)-cyclohexyl diamines favours abstraction of the pro-(*S*) hydrogen atom of the substituted Cp ring, while using (*R,R*)-diamines gives products of pro-(*R*) lithiation.
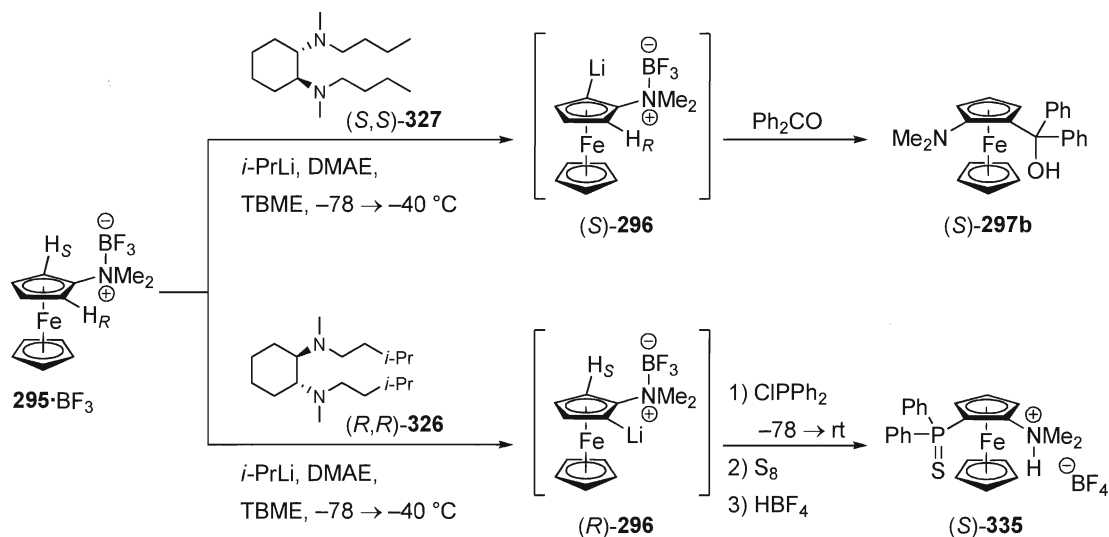
Scheme 76. (*S,S*)-**327**- and (*R,R*)-**326**-mediated lithiation of **295·BF₃**.

Figure 14. ORTEP plot of tertiary alcohol (*S*)-**297b** at 50% probability. All hydrogen atoms except H1 are omitted for clarity.
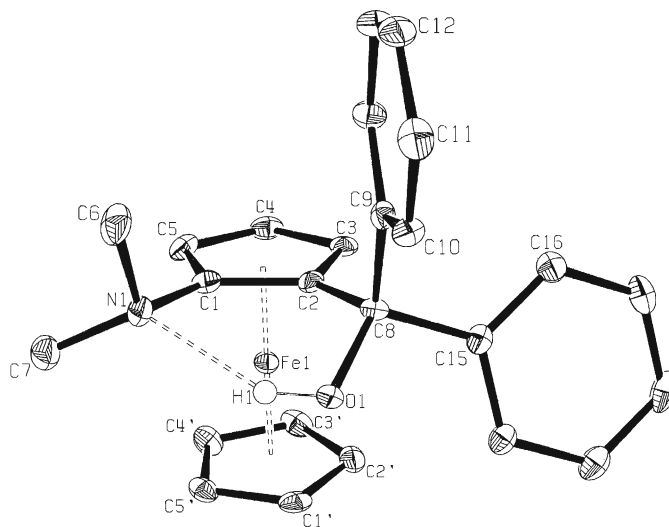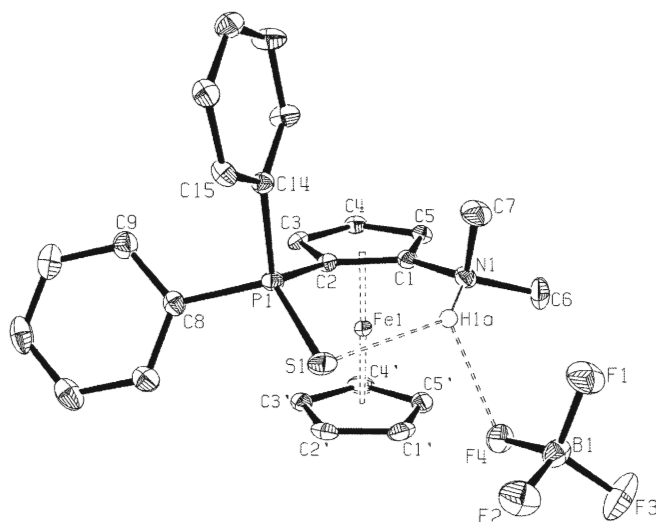
Figure 15. ORTEP plot of (*S*)-**335**·HBF$_4$ at 50% probability. All hydrogen atoms except H1a are omitted for clarity.

The stereochemistry of the reaction was also investigated by computational modeling, performed by Keivan Taban of Professor Travis Dudding's group (Brock University). Using Gaussian 09,[106] it was found that calculation of pro-(*R*) and pro-(*S*) transition states during lithiation of **295**·BF$_3$ with *i*-PrLi·(*S,S*)-**323** at the M06-2X[107]/6-311+g(2d,2p)[108] level predicted that abstraction of the pro-*S* hydrogen was favoured by 0.841 kcal/mol. This energy difference corresponds to a predicted er of 88:12 at −60 °C and 90:10 at −78 °C, which is consistent with experimental observations.

A key feature of the transition state models is the unsymmetrical coordination of chiral ligand (*S,S*)-**323** to lithium, which is apparent in the difference in the two N-Li bond distances. In the disfavoured pro-(*R*) transition state (**Figure 16**, left), the difference in distance between these bonds is 0.028 Å (based on contact distances of 2.041 and 2.069 Å). In the favoured pro-(*S*) transition state (**Figure 16**, right), the corresponding difference in these bonds is 0.071 Å (based on N-Li contact distances of 2.040 and 2.111

Å). Of further note is the *syn*-arrangement of the bulky *N*-3,3-dimethylbutyl groups of (*S,S*)-**323** and their orientation relative to FcNMe$_2$·BF$_3$. In the favoured transition state, the *N*-3,3-dimethylbutyl groups project out and away from *i*-PrLi and FcNMe$_2$·BF$_3$, while in the disfavoured one these same groups are oriented towards *i*-PrLi and the substrate. The latter arrangement leads to greater steric encumbrance around the site of deprotonation and appears to be a major factor in stereoselection. Other metrics in the pro-(*S*) transition state model, such as F-Li (1.621 Å) and N-B bonds distances (1.715 Å) are similar to Kessar's model of the (−)-sparteine-mediated lithiation of BF$_3$-activated *N*-ethylpyrrolidine.[55]
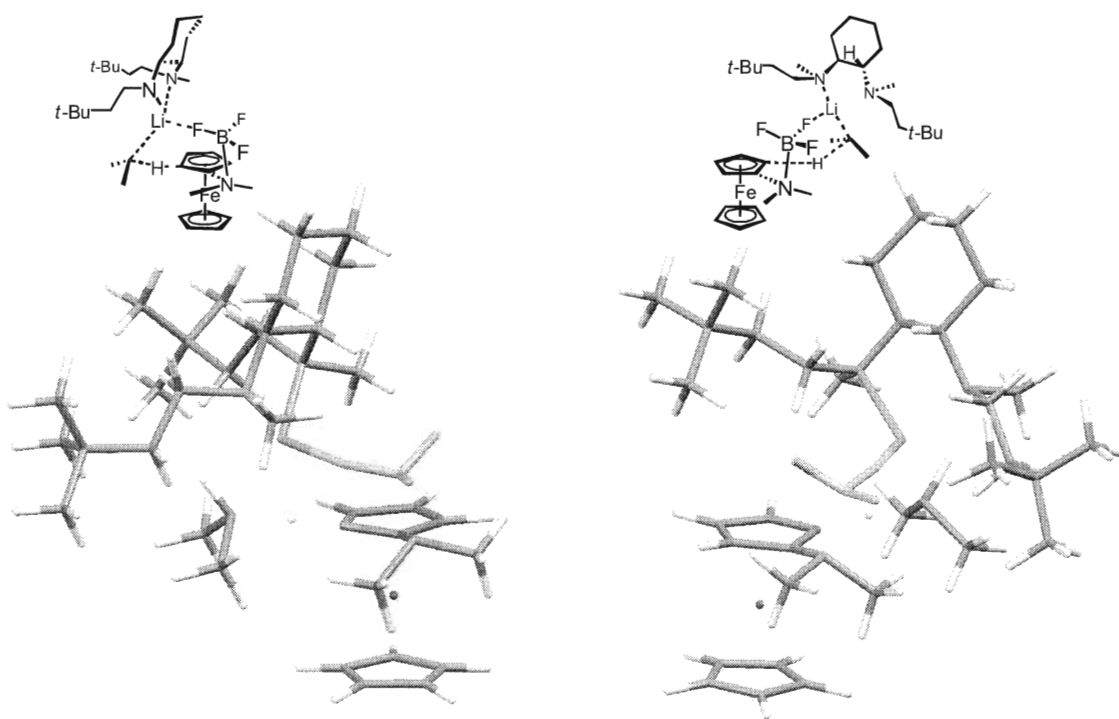
Figure 16. Lowest energy transition states for (disfavoured) pro-(*R*) deprotonation on the left and (favoured) pro-(*S*) deprotonation on the right using diamine (*S,S*)-**323**.

In an effort to investigate the regioselectivity of the lithiation and substrate scope, *N*-ferrocenyl pyrrolidine was synthesized (**Scheme 77**). Stirring aminoferrocene **155** and

succinic anhydride together, followed by heating the intermediate in buffered Ac$_2$O, gave a 78% yield of crystalline succinimide **336**. Reduction of the imide with LiAlH$_4$ provided the desired pyrrolidine (**337**), but in low yield and purity. Alternatively, using borane for the reduction gave **337** in high yield. On some occasions when conducting this reaction, a more polar compound (than **336** and **337**) was observed, which proved to be partially reduced pyrrolidone **336**.
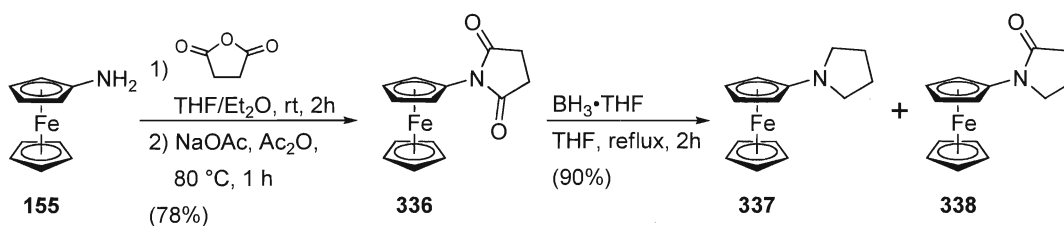
Scheme 77. Synthesis of pyrrolidinylferrocene.

Exposure of pyrroldinyl ferrocene (**337**) to similar conditions as used previously for lithiation of **295** gave the desired 2-substituted pyrrolidinyl ferrocenes (**339a,b**) in comparable yields and selectivities to the dimethylamino derivatives (**Scheme 78**). Thus, asymmetric lithiation of **337·**BF$_3$ (2.1 equiv i-PrLi, (R,R)-**323**, −78 → 40 °C, TBME), followed by DMF quench provided (R)-2-formyl pyrrolidinylferrocene [(R)-**339a**]. Iodo derivative (S)-**339b** was also prepared by lithiation [3.15 equiv. i-PrLi, 1.05 equiv. (R,R)-**326**, 1.05 equiv. DMAE] of **337·**BF$_3$ in 62% yield and 89:11 er (measured as the corresponding O-acetate). It is noteworthy that for this substrate deprotonation occured exclusively at the 2-position and not the α-methylene group of the pyrrolidinyl ring, which had been previously observed.[109] This observation may be due to the greater acidity of the Cp ring hydrogens compared to those of the pyrrolidinyl ring.
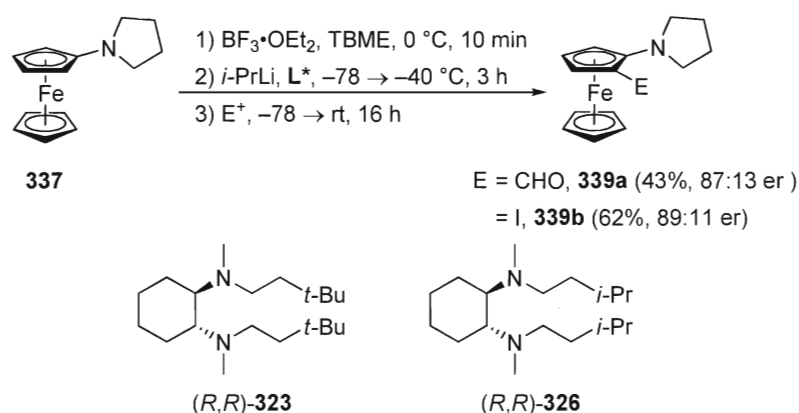
Scheme 78. Asymmetric lithiation of **337**·BF$_3$
using cyclohexyl diamines (*R,R*)-**323** and (*R,R*)-**326**.

The above result prompted an attempt at a diastereoselective lithiation of chiral *N*-ferrocenyl-(2*R*,5*R*)-dimethylpyrrolidine (**341**), for which the 1,1'-disubstituted version of this compound had been reported.[110] Following a procedure analogous to that reported for the 1,1'-disubstituted case gave unacceptable yields of less than 20% (although yields for the 1,1'-system were reportedly 18-24%). Sequential addition of *n*-BuLi and heating at reflux increased the yield to an acceptable 59% (**Scheme 79**).

Attempts to lithiate **341** by coordination of BF$_3$ to the substrate in THF, as used previously for dimethylaminoferrocene, resulted only in recovery of starting material. A lack of colour change or formation of precipitate seemed to indicate that coordination of BF$_3$ to the substrate may not have taken place. Switching to a noncoordinating solvent, such as PhMe, allowed formation of the putative zwitterion (as indicated by NMR spectrometry), but lithiation under a number of conditions (*n*-BuLi, *i*-PrLi; THF, TBME, PhMe; −78 → 0 °C) still returned unreacted starting material, probably owing to the lability of the **341**·BF$_3$ adduct in the presence of alkyllithiums. Based on the observed

weaker coordination of the amine (**341**) to BF$_3$, it was proposed that an unfavourable steric interaction was occurring between an α-methyl group and BF$_3$.
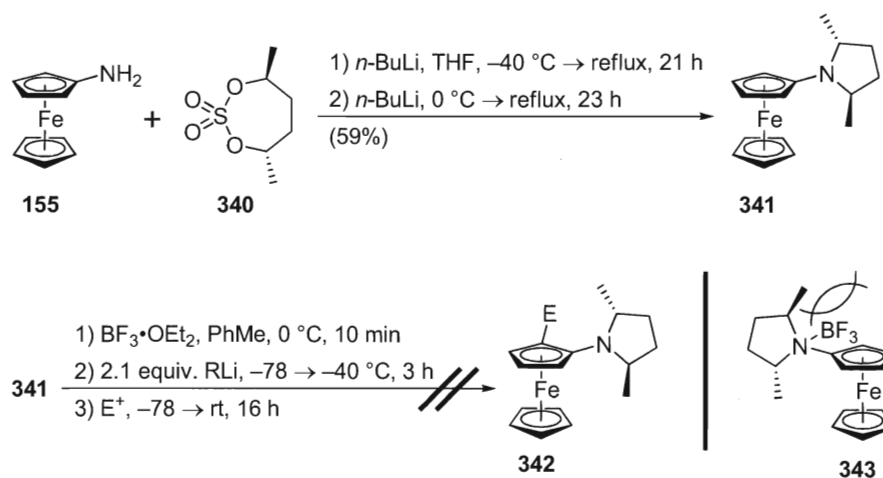
Scheme 79. Synthesis and attempted diastereoselective BF$_3$-mediated lithiation of a chiral *N*-ferrocenyl pyrrolidine (**341**).

2.4 Conclusions & Future Work

Two complementary approaches for the synthesis of 2-substituted aminoferrocenes have been developed. Both rely on a nitrogen-based directing group, which is unprecedented for aminoferrocene synthesis. The first approach described a modification of *N*-ferrocenyl phthalimide (**159**), a known and reliable precursor to aminoferrocene (**155**), to generate a chiral directing group that was removable and also served as the stereodetermining group. The simple, yet unreported, 2-trimethylsilylaminoferrocene (**279**) was synthesized to demonstrate this approach. Attempts to control the absolute stereochemistry of the phthalimidine by reduction of phthalimide **159** with standard reducing reagents were unsuccessful, but led to the interesting observation of a Cu-mediated imide hydrosilylation using Et$_3$SiH. To the best of our knowledge, imides are unknown hydrosilylation substrates and therefore warrant further investigation on this transformation as it may lead to valuable chiral building blocks Efforts to install groups other than SiMe$_3$ at the 2-position resulted in the formation of undesired arene-substituted regioisomers. The last two issues prompt consideration of an alternative route, one which would involve the union of two projects within the Metallinos group. Thus, transition metal-catalyzed coupling of previously reported[111] proline-derived bicyclic imide **344** to iodoferrocene (**272**), followed by reduction-silylation, would give **345**, which may undergo diastereoselective lithiation-substitution with an improved electrophile scope and little opportunity for the formation of regioisomers (**Scheme 80**).
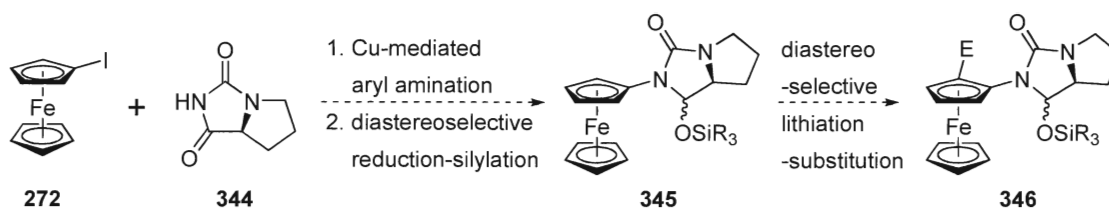
Scheme 80. Alternative imide-based route for
the diastereoselective synthesis of aminoferrocenes.

The problems associated with regiochemistry and electrophile scope for the phthalimidine project that could not be overcome at the time led to the development of the complementary BF$_3$-mediated enantioselective approach. Coordination of BF$_3$ to tertiary aminoferrocenes (**295** and **337**) facilitated a regioselective lithiation at the 2-position low temperature, allowing incorporation of various electrophiles in generally excellent yields and leading to many unusual aminoferrocenes that would be difficult to make by other means. This method gives access to a number of ferrocenyl aminophosphines, whose coordination chemistry with Pd(II), Pt(II) and Ir(I) was studied. The catalytic potential of those aminophosphines was briefly explored in several metal-mediated transformations with promising results.

The realization of an enantioselective version of the BF$_3$-mediatied lithiation-substitution of tertiary aminoferrocenes was also made, currently giving products in moderate yields and up to 90:10 er. Based on the computational results, a ligand based on a chiral bicyclic piperazine should be synthesized and tested in the enantioselective deprotonation of the BF$_3$-mediated substitution. The application of other enantiopure aminoferrocenes made available by this process, such as BINAM analogue **299**, should also be carried out as compounds of this type would be difficult to synthesize by other means. Aminophosphines and complexes thereof should most certainly be exploited as

ligands in asymmetric transformations. For example, complex **313b** has given some excellent preliminary results in the asymmetric hydrogenation of prochiral olefins (**347-349**, **Scheme 81**) and has therefore become a current project in the laboratory.[93]
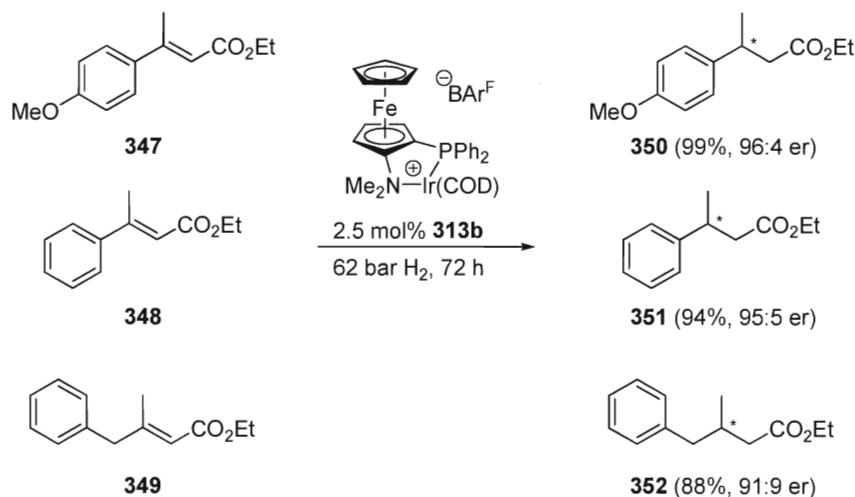
Scheme 81. Preliminary asymmetric hydrogenation results using aminophosphine-Ir complex **313b**.

Lastly, in an effort to improve the manipulability, some preliminary experiments were carried out to effect non-oxidative *N*-demethylation on some of the derivatives by using chloroformates. The most promising of those tried was 2,2,2-trichloroethylchloroformate (**Scheme 82**). When these reactions were conducted in solvents (MeCN, ClCH$_2$CH$_2$Cl), decomposition resulted. Upon reaction in neat TrocCl at 60 °C, the formation of a less polar compound was observed by TLC. Attempts to isolate carbamate **354** in pure form were unsuccessful, as residual TrocCl and trichloroethanol could not be removed from the desired product. Cleavage of carbamate **354** would give a 2-substituted secondary aminoferrocene (**355**) thereby increasing the number of possible derivatives and potential applications, making this a worthwhile addition to the BF$_3$-mediated methodology that was established in this thesis.
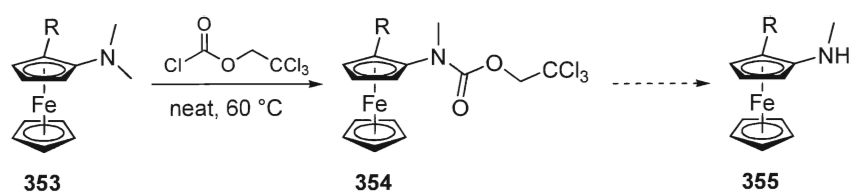
Scheme 82. TrocCl-mediated demethylation and carbamate hydrolysis of substituted dimethylaminoferrocenes.

2.5 Experimental Procedures

General. All reagents were purchased from Aldrich, Fisher Scientific, Acros or Strem and used as received unless otherwise indicated. Tetrahydrofuran, diethyl ether and 1,4-dioxane were freshly distilled from sodium/benzophenone ketyl under an atmosphere of nitrogen. Toluene was freshly distilled from sodium under an atmosphere of nitrogen. t-Butyl methyl ether was distilled from $LiAlH_4$ under an atmosphere of argon. Dichloromethane was distilled from CaH_2 under an atmosphere of nitrogen. i-PrLi was prepared according to the procedure in: Morrison, R. C.; Hall, R. W.; Schwindeman, J. A.; Kamienski, C. W.; Engel, J. F., European Patent 0525881, 1993 and *cyclo*-pentyllithium in analogous manner. Organolithium reagents were titrated against N-benzylbenzamide[112] to a blue endpoint. All reactions were performed under argon in flame- or oven-dried glassware using syringe-septum cap techniques unless otherwise indicated. TLC was performed on silica gel unless otherwise stated. Column chromatography was performed on Silicycle silica gel 60 (70-230 mesh) unless otherwise stated. NMR spectra were obtained on a Bruker Avance 300 or Avance 600 instrument and are referenced the residual proton signal of the deuterated solvent for ^{1}H spectra and to the carbon multiplet of the deuterated solvent for ^{13}C spectra according to values given in *Spectrometric Identification of Organic Compounds, Seventh Edition*, p. 200 and p. 240. Spectroscopic data are reported as follows: (multiplicity, number of protons, coupling constant), where s = singlet, d = doublet, t = triplet, q = quartet. FT-IR spectra were recorded on an ATI Mattson Research Series spectrometer. Low and high-resolution mass spectral data were obtained on a Kratos Concept 1S Double Focusing spectrometer. Enantiomeric ratios were determined on an Agilent 1100 HPLC system using either

Chiralpak AS-H or Chiralcel OD-H columns, and are compared to racemic material. It should be noted for HPLC measurements that response factors were not obtained for each enantiomer and the reported enantiomeric ratios are not calibrated. Optical rotations were measured on a Rudolph Research Autopol III automatic polarimeter. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA, USA. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected.

3-Hydroxy-2-ferrocenyl-2,3-dihydro-isoindol-1-one (273).
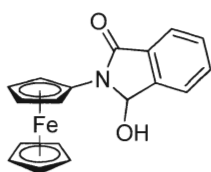
Phthalimide **159** (3.32 g, 10.0 mmol) was suspended in 1:1 MeOH/MeCN open to air and cooled to ~ 10 °C. NaBH$_4$ (0.76 g, 20.0 mmol) was added in one portion and stirred for 2.5 h, at which point TLC indicated completion of the reaction. The mixture was cooled to 0 °C, quenched with H$_2$O (50 mL) and allowed to warm to rt. The mixture was then cooled back to 0 °C, collected by suction filtration and washed with water (2 × 50 mL). After drying in air for 15 min, the resulting orange powder was recrystallized from i-PrOH/H$_2$O to give ferrocenylphthalimidine **273** (2.78 g, 93%) as red-orange crystals; R_f 0.09 (30:70 Et$_2$O/hexanes); mp 219-220 °C (i-PrOH/H$_2$O); IR (KBr) v_{max} 3276, 3115, 3094, 2931, 2875, 1664, 1498, 1054 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.74 (d, 1H, J = 7.2 Hz), 7.66-7.59 (m, 2H), 7.53-7.47 (m, 1H), 6.09 (d, 1H, J = 11.1 Hz), 5.08 (m, 1H), 4.85-4.85 (m, 1H), 4.16 (s, 5H), 4.12-4.10 (m, 2H), 2.90 (d, 1H, J = 11.1 Hz); EIMS [m/z(%)] 333 (M$^+$, 100); HRMS (EI) calcd for C$_{18}$H$_{15}$NO$_2$^{56}Fe: 333.0452; found 333.0454; Anal. calcd for C$_{18}$H$_{15}$NO$_2$Fe: C, 64.89; H, 4.54; found C, 64.64; H, 4.50.

2-Ferrocenyl-3-trimethylsilyloxy-2,3-dihydro-isoindol-1-one (263a).
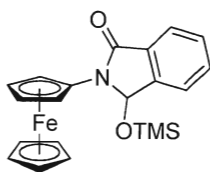
TMSCl (0.80 mL, 6.30 mmol) was added to an ice-cold solution of **273** (1.40 g, 4.20 mmol) and Et$_3$N (0.87 mL, 6.30 mmol) in THF (20 mL) and stirred at that temperature for 3 h. The reaction mixture was diluted with Et$_2$O, quenched with H$_2$O (15 mL) and allowed to warm to rt. The aqueous layer was extracted with Et$_2$O (1 × 15 mL) and the combined organic extracts were washed with brine, dried over anhyd. Na$_2$SO$_4$ and the volatiles were removed under reduced pressure. Recrystallization of the resulting orange solid from hexanes at −20 °C gave **263a** (1.54 g, 90%) as yellow-orange cyrstals in two crops; R_f 0.46 (30:70 Et$_2$O/hexanes); mp 94-96 °C (hexanes); IR (KBr) ν_{max} 3146, 3100, 3086, 2954, 2897, 1694, 1498, 1119, 1076 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.84 (d, 1H, J = 7.2 Hz), 7.62-7.52 (m, 3H), 6.31 (s, 1H), 5.40-5.38 (m, 1H), 4.62-4.60 (m, 1H), 4.17-4.15 (m, 1H), 4.15 (s, 5H), 4.09-4.07 (m, 1H), -0.16 (s, 9H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 165.8, 143.6, 132.2, 132.0, 130.0, 123.5, 123.4, 94.9, 84.2, 68.9, 65.4, 64.2, 61.8, 60.1, 1.0; EIMS [m/z(%)] 405 (M$^+$, 100), 195 (30), 167 (20); HRMS (EI) calcd for C$_{21}$H$_{23}$NO$_2$Si^{56}Fe: 405.8047; found 405.0840; Anal. calcd for C$_{21}$H$_{23}$NO$_2$SiFe: C, 62.22; H, 5.72; found C, 61.98; H, 5.70.

2-Ferrocenyl-3-triethylsilyloxy-2,3-dihydro-isoindol-1-one (263b).
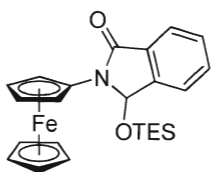
TESCl (1.73 mL, 10.3 mmol) was added to a suspension of **273** (3.12 g, 9.36 mmol), DMAP (0.12 g, 0.94 mmol) and imidazole (1.47 g, 21.5 mmol) in DMF (25 mL) at rt. Upon addition of TESCl, the starting material begins to go into solution. The mixture was stirred at rt for 18 h, then

diluted with Et$_2$O and quenched with H$_2$O (50 mL). The organic layer was then washed with H$_2$O (3 × 40 mL), brine, dried over anhyd. Na$_2$SO$_4$ and the volatiles were removed to get an orange solid as the crude. The crude was taken up in a minimum amount of hexanes and filtered through a pad of SiO$_2$ with 100% hexanes, which gave **263b** as orange crystals (3.99 g, 95%) in 2 crops; mp 83-85 °C (hexanes); IR (KBr) ν_{max} 3081, 3050, 2950, 2905, 2873, 1695, 1490, 1068 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.84 (d, 1H, J = 7.2 Hz), 7.62-7.52 (m, 3H), 6.32 (s, 1H), 5.39 (s, 1H), 4.60 (s, 1H), 4.15 (s, 1H), 4.14 (s, 5H), 4.06 (s, 1H), 0.73 (t, 9H, J = 7.8 Hz), 0.33-0.28 (m, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 165.9, 143.7, 132.2, 131.9, 130.0, 123.4, 94.8, 83.8, 68.9, 65.5, 64.0, 61.6, 60.4; EIMS [m/z(%)] 447 (M$^+$, 100), 103 (40), 75 (32); HRMS (EI) calcd for C$_{24}$H$_{29}$NO$_2$Si^{56}Fe: 447.1317; found 447.1309.

2-(2-Trimethylsilyl-1-ferrocenyl)-3-triethylsilyloxy-2,3-dihydro-isoindol-1-one (274).
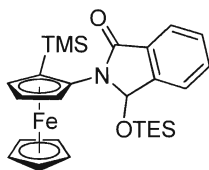
TMSCl (0.95 mL, 2.50 mmol) was added to a solution of **263b** (447 mg, 1.00 mmol) and LDA solution (1.64 mL, 1.52 M in THF/hexanes, 2.50 mmol) in THF (7 mL) at −78 °C and the resulting mixture was stirred for 2.5 h at that temperature. The reaction was quenched by addition of H$_2$O (5 mL) at −78 °C, then allowed to warm to rt. The reaction mixture was diluted with Et$_2$O, washed with H$_2$O (2 × 10 mL), brine, dried over Na$_2$SO$_4$ and the volatiles removed under reduced pressure to yield an orange oil as the crude. *Careful* column chromatography (SiO$_2$, 2:98 Et$_2$O/hexanes) gave regioisomer **275** (156 mg. 30%), followed by Cp-substituted product **274** (155 mg, 30%) as a waxy, orange solid and a mixture of **274** and unreacted **263b** (~1:4, 175 mg); R_f 0.58 (30:70 Et$_2$O/hexanes); mp

112-114 °C (hexanes); IR (KBr) ν_{max} 2953, 2908, 2874, 1712, 1454, 1065 cm^{-1}; ^{1}H NMR

(300 MHz, CDCl$_3$) δ 7.83 (d, 1H, J = 6.9 Hz), 7.62-7.50 (m, 3H), 6.28 (s, 1H), 4.42 (s,

1H), 4.38 (t, 1H, J = 2.4 Hz), 4.33 (s, 5H), 4.16 (m, 1H), 0.87 (t, 9H, J = 7.8 Hz), 0.52-

0.44 (m, 6H), 0.14 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 167.2, 143.5, 132.3, 131.9,

129.8, 123.5, 123.2, 97.4, 87.3, 72.3, 71.0, 69.4, 68.5, 68.1, 6.8, 5.8, 0.1; EIMS [m/z(%)]

519 (M$^+$, 14), 103 (100), 75 (92); HRMS (EI) calcd for C$_{27}$H$_{27}$NO$_2$Si$_2$^{56}Fe: 519.1712;

found 519.1705; Anal. calcd for C$_{29}$H$_{37}$NO$_2$Si$_2$Fe: C, 62.41; H, 7.18; found C, 62.63; H,

7.12.

3-Hydroxy-2-(2-trimethysilyl-1-ferrocenyl)-2,3-dihydro-isoindol-1-one (277).
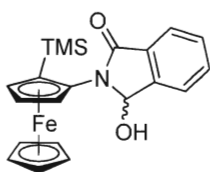
K$_2$CO$_3$ (166 mg, 1.20 mmol) was added to a solution of **274** (125 mg, 0.24 mmol) in MeOH (3 mL) and stirred at room temperature open to air. TLC indicated complete consumption of **274** after 2 h, at which point the volatiles were removed under reduced pressure. Gravity filtration of the mixture in CH$_2$Cl$_2$ gave, after removal of volatiles from the filtrate, Cp-substituted phthalimidine **277** (97 mg, quant.) as an orange solid; R_f 0.11 (20:80 EtOAc/hexanes); mp 105-110 °C (CHCl$_3$/hexanes); IR (KBr) ν_{max} 3355, 3083, 2952, 1689, 1454, 1405,

1371 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.78 (d, 1H, J = 7.8 Hz), 7.67-7.59 (m, 2H),

7.57 (t, 1H, 7.8 Hz), 4.43 (s, 1H), 4.37 (s, 1H), 4.35 (s, 1H), 3.55 (d, 1H, J = 7.2 Hz), 0.17

(s, 9H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 168.2, 142.7, 132.6, 131.8, 130.0, 123.6, 123.2,

96.2, 86.0, 72.6, 72.5, 69.7, 69.4, 69.3, −0.2; EIMS [m/z(%)] 405 (M$^+$, 47), 390 (17), 84

(100); HRMS (EI) calcd for C$_{21}$H$_{25}$NO$_2$Si^{56}Fe: 405.0847; found 405.0850.

2-(2-Trimethylsilyl-1-ferrocenyl)-isoindole-1,3-dione (278).
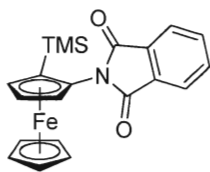
AlMe$_3$ (5 μL, 0.01 mmol) was added to a solution of phthalimidine **277** (34 mg, 0.08 mmol) in PhMe (0.75 mL) and stirred for 30 min. *p*-Nitrobenzaldehyde (38 mg, 0.25 mmol) was then added and the reaction mixture heated at reflux for 1 h. The reaction was quenched with H$_2$O (5 mL) and the aqueous extracted with CH$_2$Cl$_2$ (1 × 5 mL). The combined organics were washed with H$_2$O (1 × 5 mL), brine (1 × 5 mL), dried over Na$_2$SO$_4$ and concentrated to dryness. Column chromatography gave **278** (19 mg, 56%) as orange oil that solidified on standing; mp 124-126 °C (EtOAc/hexanes); IR (KBr) v_{max} 3428, 3350, 3093, 2954, 2896, 1613, 1463 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.92-7.89 (m, 2H), 7.77-7.74 (m, 2H), 4.45-4.44 (m, 1H), 4.40-4.39 (m, 1H), 4.34 (s, 5H), 4.22-4.19 (m, 1H), 0.23 (s, 9H); ^{13}C NMR (150.9 MHz, CDCl$_3$) δ 167.7, 134.2, 131.9, 123.3, 91.4, 72.4, 70.3, 69.8, 69.2, 67.8, 0.2; EIMS [*m/z*(%)] 403 (M$^+$, 100), 388 (47); HRMS (EI) calcd for C$_{21}$H$_{21}$NO$_2$Si^{56}Fe: 403.0691; found 403.0686; Anal. calcd for C$_{21}$H$_{21}$NO$_2$SiFe: C, 62.54; H, 5.25. Found: C, 62.48; H, 5.27.

2-Trimethylsilylaminoferrocene (279).
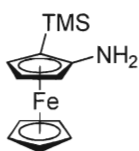
A solution of phthalimide **278** (42 mg, 0.10 mmol) and N$_2$H$_4$·H$_2$O (0.18 mL, 3.64 mmol) in stock EtOH (1 mL) was sparged with Ar for 10 min, followed by heating at reflux for 40 min. the mixture was cooled to room temperatue, H$_2$O (10 mL) was added and the aqueous extracted with Et$_2$O (2 × 10 mL). The combined organic layers were washed with H$_2$O, brine, dried over anhyd. Na$_2$SO$_4$ and the volatiles were removed under reduced pressure to give pure

aminoferrocene **279** (28 mg, quant.) as a yellow oil; R_f 0.45 (30:70 EtOAc/hexanes); ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.14 (s, 1H), 4.07 (s, 5H), 4.00 (s, 1H), 3.77 (s, 1H), 2.60 (b, 2H), 0.32 (s, 9H); 13C NMR (300 MHz, CDCl$_3$) 110.4, 69.0, 68.9, 65.6, 61.5, 59.7, 0.01; EIMS [m/z(%)] 273 (M$^+$, 100); HRMS (EI) calcd for C$_{13}$H$_{19}$NSi^{56}Fe: 273.0635; found 273.0639.

2-Ferrocenyl-3-triethylsilyloxy-7-trimethylsilylsoindol-1-one (275).
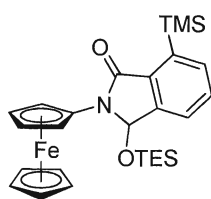
TMSCl (0.24 mL, 1.88 mmol) was added to a solution of **263b** (112 mg, 0.25 mmol) and LTMP solution (0.30 mL, 0.89 M in THF/hexanes, 0.26 mmol) in THF (2.5 mL) at -78 °C, which caused a colour change to dark orange-brown, and the resulting mixture was stirred for 110 min at that temperature. The reaction was quenched by addition of H$_2$O (5 mL) at -78 °C, then allowed to warm to rt. The reaction mixture was diluted with Et$_2$O, washed with H$_2$O (1 × 5 mL), brine, dried over Na$_2$SO$_4$ and the volatiles removed under reduced pressure. The crude was loaded on a column as a solution in hexanes and column chromatography (2:98 → 10:90 Et$_2$O/hexanes) gave **275** (116 mg, 89%) as an orange oil; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.69 (dd, 1H, $J = 6.9$, 1.8 Hz), 7.59-7.52 (m, 2H), 6.29 (s, 1H), 5.37 (s, 1H), 4.58 (s 1H), 4.13 (s, 6H), 4.05 (s, 1H), 0.72 (t, 9H, $J = 7.8$ Hz), 0.44 (s, 9H), 0.32-0.26 (m, 6H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 166.8, 143.7, 139.0, 136.4, 135.9, 130.8, 123.9, 95.7, 83.5, 69.1, 65.6, 64.1, 61.7, 60.5, 6.6, 5.4, -0.7; EIMS [m/z(%)] 519 (M$^+$, 100), 103 (82), 75 (66); HRMS (EI) calcd for C$_{27}$H$_{37}$NO$_2$Si$_2$^{56}Fe: 519.1712; found 519.1715.

(1-Hydroxy-2-ferrocenyl-3-oxoisoindolin-4-yl)boronic acid (286).
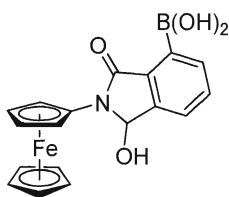
B(Oi-Pr)$_3$ (0.14 mL, 0.62 mmol) was added to a solution of **263a** (100 mg, 0.25 mmol) and LDA solution (0.22 mL, 1.25 M in THF/hexanes, 0.27 mmol) in THF (1.5 mL) at −78 °C, which caused a colour change to dark orange-brown, and the resulting mixture was stirred for 120 min at that temperature. The reaction was quenched by addition of HCl (1.00 mL, 1.00 M in H$_2$O) at −78 °C, then allowed to warm to rt. The reaction mixture was diluted with Et$_2$O, washed with H$_2$O (1 × 5 mL), brine, dried over Na$_2$SO$_4$ and the volatiles removed under reduced pressure. Column chromatography (30:70:0 → 25:70:5 Et$_2$O/hexanes/MeOH) of the residue gave 75 mg of an orange solid that was purified further by recrystallization from MeCN to give **286** (55 mg, 59%) as an orange powder; mp 185-188 °C (MeCN); ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.54 (s, 2H), 8.04 (d, 2H, J = 6.6 Hz), 7.74-7.68 (m, 2H), 6.95 (d, 1H, J = 10.2 Hz), 6.22 (d, 1H, J = 10.2 Hz), 5.11 (s, 1H), 4.91 (s, 1H), 4.20 (s, 6H), 4.16 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.1, 145.2, 137.5, 135.3, 131.9, 125.8, 94.0, 83.3, 69.2, 65.2, 64.8, 61.6, 60.5; EIMS [m/z(%)] 377 (M$^+$, 12), 331 (10), 41 (100); HRMS (EI) calcd for C$_{18}$H$_{16}$BNO$_4$^{56}Fe: 377.0523; found 377.0522.

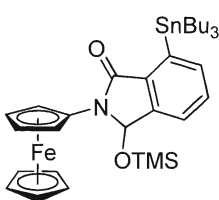## 2-Ferrocenyl-3-trimethylsilyloxy-7-tributylstannylisoindol-1-one (287).

Bu$_3$SnCl (0.16 mL, 0.62 mmol) was added to a solution of **263a** (100 mg, 0.25 mmol) and LTMP solution (0.69 mL, 0.89 M in THF/hexanes, 0.62 mmol) in THF (1.5 mL) at −78 °C, which caused a colour change to dark orange-brown, and the resulting mixture was stirred for 100 min at that temperature. The reaction was quenched by addition of a saturated aqueous solution

of NH$_4$Cl (1 mL) at −78 °C, then allowed to warm to rt. The reaction mixture was diluted with Et$_2$O, washed with H$_2$O (1 × 5 mL), brine, dried over Na$_2$SO$_4$ and the volatiles removed under reduced pressure. Column chromatography (alumina, hexanes) of the preadsorbed crude mixture gave **287** (115 mg, 72%) as an orange oil; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.73-7.64 (m, 1H), 7.55-7.51 (m, 1H), 6.31 (s, 1H), 5.40 (s, 1H), 4.59 (s, 1H), 4.12 (s, 6H), 4.06 (s, 1H), 1.55-1.50 (m, 6H), 1.35-1.28 (m, 6H), 1.22-1.18 (m, 6H), 0.87 (t, 9H, J = 7.2 Hz), −0.18 (s, 9H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 167.6, 142.7, 140.4, 138.0, 137.4, 131.0, 123.0, 95.2, 84.1, 68.8, 65.3, 64.0, 61.8, 60.0, 29.3, 27.4, 13.7, 10.5, 1.0; EIMS [m/z(%)] 638 (M$^+$, 18), 370 (100), 269 (88); HRMS (EI) calcd for C$_{29}$H$_{40}$NO$_2$Si^{56}FeSn: 638.1194; found 638.1199.

General Procedure for Lithiation-Electrophile Quench of *N,N*-Dimethylaminoferrocene.

To a solution of dimethylaminoferrocene **295** (1 equiv.) in THF (0.10 M) at 0 °C under argon was added BF$_3$·OEt$_2$ (1.05 equiv.). After stirring for 15 min, the yellow solution was cooled to −40 °C and treated with *n*-BuLi (1.10 equiv.). A distinct color change from yellow to orange-red was observed over a period of 1 h. The reaction mixture was then quenched with the desired electrophile (1.20 equiv.) and allowed to warm to room temperature. *Standard Workup*: The reaction mixture was diluted with Et$_2$O and a saturated solution of aq. NaHCO$_3$ was added. The phases were separated and the aqueous layer was extracted once with Et$_2$O. The combined organic extracts were washed with water, brine, dried over anhyd. Na$_2$SO$_4$ and volatiles were removed on a

rotary evaporator under reduced pressure. The crude product was purified by flash chromatography or recrystallized to give the desired 2-substituted product (**297a-k**).

(±)-2-Formyl-*N,N*-dimethylaminoferrocene (297a).
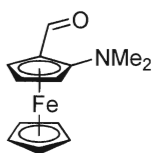
According to the General Procedure, a solution of **295** (100 mg, 0.44 mmol) in THF (5 mL) was sequentially treated with BF$_3$·OEt$_2$ (58 μL, 0.46 mmol), *n*-BuLi (0.51 mL, 1.70 M, 0.87 mmol) and DMF (0.17 mL, 2.18 mmol). Standard workup followed by gradient column chromatography (silica gel, 5:94:1→15:84:1 Et$_2$O/hexanes/Et$_3$N) gave **297a** (85 mg, 76%) as a red oil: IR (KBr, neat) v_{max} 3097, 2943, 2851, 2826, 2785, 1667 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 10.13 (s, 1H), 4.61 (m, 1H), 4.40 (t, 1H, J = 2.7 Hz), 4.29 (m, 1H), 4.27 (s, 5H), 2.70 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 192.8, 117.5, 71.8, 69.5, 67.7, 66.2, 60.2, 45.6; EIMS [*m/z*(%)] 257 (M$^+$, 100), 229 (13), 119 (54), 44 (66); HRMS (EI) calcd for C$_{13}$H$_{15}$NO^{56}Fe: 257.0503; found 257.0504.

(±)-2-[(Diphenylhydroxy)methyl]-*N,N*-dimethylaminoferrocene (297b).
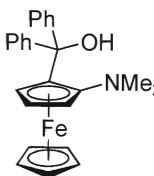
According to the General Procedure, **295** (229 mg, 1.00 mmol) in THF (10 mL) was sequentially treated with BF$_3$·OEt$_2$ (0.13 mL, 1.05 mmol), *n*-BuLi (0.59 mL, 1.86 M, 1.10 mmol) and quenched with a solution of benzophenone (218 mg, 1.20 mmol) in THF (8 mL). Standard workup and filtration through a plug of silica gel, eluting with Et$_2$O, gave an orange oil that solidified on standing. Recrystallization from Et$_2$O/hexanes afforded **297b** (358 mg, 87%) as a crystalline orange solid: mp 189-190 °C (Et$_2$O/hexanes); IR (KBr) v_{max} 3237, 3081, 2955,

2780 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.10 (s, 1H), 7.64-7.62 (m, 2H), 7.38-7.10 (m, 8H), 4.18 (m, 1H), 4.08 (m, 1H), 4.06 (s, 5H), 3.93 (m, 1H), 2.35 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 150.0, 146.1, 127.5, 127.2, 127.0, 126.9, 126.4, 126.2, 109.5, 91.8, 78.0, 69.8, 65.9, 63.8, 57.4, 46.7; EIMS [m/z(%)] 411 (M$^+$, 51), 273 (100); HRMS (EI) calcd for C$_{25}$H$_{25}$NO^{56}Fe: 411.1285; found 411.1282. Anal. calcd for C$_{25}$H$_{25}$NOFe: C, 73.00; H, 6.13. Found: C, 73.05; H, 6.15.

(±)-2-*N,N*-Dimethylamino-*N*-phenylferrocenecarboxamide (297d).
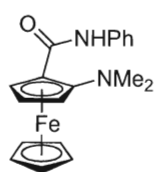
According to the General Procedure, a solution of **295** (115 mg, 0.50 mmol) in THF (5 mL) was sequentially treated with BF$_3$·OEt$_2$ (66 μL, 0.53 mmol), *n*-BuLi (0.23 mL, 2.45 M, 0.55 mmol) and quenched with PhNCO (65 μL, 0.60 mmol). Standard workup followed by column chromatography (silica gel, 30:70 Et$_2$O/hexanes) gave **297d** (162 mg, 93%) as an orange oil: R_f = 0.15 (30:70 Et$_2$O/hexanes); IR (KBr, neat) ν_{max} 3236, 3179, 3096, 3023, 3003, 2951, 2848, 2786, 1674, 1596, 1550 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 10.88 (b, 1H), 7.65 (d, 2H, J = 7.8 Hz), 7.36 (t, 2H, J = 7.5 Hz), 7.09 (t, 1H, J = 7.5 Hz), 4.89 (m, 1H), 4.31 (m, 1H), 4.28 (t, 1H, J = 2.7 Hz), 4.22 (s, 5H), 2.75 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 168.7, 139.2, 129.0, 123.2, 119.5, 112.5, 70.6, 69.2, 66.8, 66.1, 59.3, 46.8; EIMS [m/z(%)] 348 (M$^+$, 88), 43 (100); HRMS (EI) calcd for C$_{19}$H$_{20}$N$_2$O^{56}Fe: 348.0925; found 348.0931.

(±)-2-Trimethylsilyl-*N*,*N*-dimethylaminoferrocene (297e).
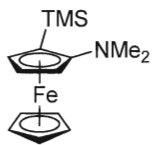
According to the General Procedure, a solution of **295** (229 mg, 1.0 mmol) in THF (10 mL) was sequentially treated with BF$_3$·OEt$_2$ (0.13 mL, 1.05 mmol), *n*-BuLi (0.48 mL, 2.30 M, 1.10 mmol) and quenched with TMSCl (0.15 mL, 1.20 mmol). Standard workup, followed by column chromatography (silica gel, 3:7 Et$_2$O/hexanes) gave **297e** (279 mg, 93%) as an orange oil: R_f = 0.68 (silica, 30:70 Et$_2$O/hexanes); IR (KBr, neat) v_{max} 3096, 2952, 2818, 2774, 1247 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.16 (s, 5H), 4.13 (t, 1H, J = 2.7 Hz), 4.10 (m, 1H), 3.86 (m, 1H), 2.57 (s, 6H), 0.33 (s, 9H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 120.1, 70.6, 68.5, 66.2, 65.9, 58.0, 46.1, 0.5; EIMS [*m/z*(%)] 301 (M$^+$, 100); HRMS (EI) calcd for C$_{15}$H$_{23}$N$_{28}$Si^{56}Fe: 301.0949; found 301.0945.

(±)-2-Trimethylstannyl-*N*,*N*-dimethylaminoferrocene (297f).
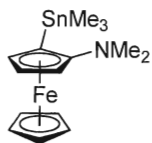
According to the General Procedure, a solution of **295** (300 mg, 1.31 mmol) in THF (13 mL) was sequentially treated with BF$_3$·OEt$_2$ (0.17 mL, 1.37 mmol), *n*-BuLi (0.59 mL, 2.45 M, 1.44 mmol) and Me$_3$SnCl (1.57 mL, 1.57 mmol). Standard workup followed by filtration through a plug of basic alumina, eluting with hexanes, gave **297f** (466 mg, 91%) as an orange oil; IR (KBr, neat) v_{max} 3093, 2980, 2940, 2910, 2825, 2775 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.16 (s, 6H), 4.06 (m, 1H), 3.81 (m, 1H), 2.59 (s, 6H), 0.32 (s, 9H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 120.2, 70.9, 67.8, 66.4, 60.4, 58.0, 45.1, −7.6; EIMS [*m/z*(%)] 393 (M$^+$, 100), 348 (88); HRMS (EI) calcd for C$_{15}$H$_{23}$N^{118}Sn^{56}Fe: 391.0198; found 391.0194.

**(±)-*N*,*N*-Dimethyl-2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-aminoferrocene (297g).**

According to the General Procedure, a solution of **295** (229 mg, 1.0 mmol) in THF (10 mL) was sequentially treated with $BF_3 \cdot OEt_2$ (0.13 mL, 1.05 mmol), *n*-BuLi (0.55 mL, 2.00 M, 1.10 mmol) and quenched with $B(OEt)_3$ (0.20 mL, 1.20 mmol). Standard workup gave the extract, to which was added pinacol (138 mg, 1.10 mmol) and stirred at room temperature for 5 min. After removal of volatiles under reduced pressure and column chromatography (basic alumina, hexanes) gave **297g** (298 mg, 84%) as an orange oil that solidified on standing: mp 75-76 °C (pentane); IR (KBr) v_{max} 3090, 2978, 2833, 2785, 1141, 1077 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 4.18 (s, 5H), 4.16 (s, 1H), 4.08 (s, 2H), 2.65 (s, 6H), 1.32 (s, 12H); ^{13}C NMR (75.5 MHz, acetone-d_6) δ 119.6, 82.7, 71.9, 68.3, 67.5, 66.0, 60.1, 43.7, 24.4, 24.1; EIMS [*m/z*(%)] 355 (M$^+$, 100), 255 (15), 121 (20); HRMS (EI) calcd for $C_{18}H_{26}BNO_2{}^{56}Fe$: 355.1406; found 355.1411. Anal. calcd for $C_{18}H_{26}BNO_2Fe$: C, 60.89; H, 7.38. Found: C, 60.96; H, 7.48.
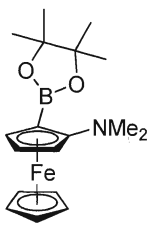
(±)-2-Thiophenyl-*N*,*N*-dimethylaminoferrocene (297h).

According to the General Procedure, a solution of **295** (229 mg, 1.00 mmol) in THF (10 mL) was sequentially treated with $BF_3 \cdot OEt_2$ (0.13 mL, 1.05 mmol), *n*-BuLi (0.51 mL, 2.15 M, 1.10 mmol) and quenched with a solution of $(PhS)_2$ (262 mg, 1.20 mmol) in THF (2 mL). Standard workup followed by gradient column chromatography (silica gel, 0:99:1 → 2:97:1 Et$_2$O/hexanes/Et$_3$N) gave **297h** (278 mg, 82%) as an orange oil that solidified on standing: mp 79-80 °C (pentane);

IR (neat) v_{max} 3098, 3087, 3055, 2967, 2847, 2785, 1498, 1002 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.20-7.15 (m, 2H), 7.08-7.01 (m, 3H), 4.32 (s, 5H), 4.22 (m, 1H), 4.16-4.12 (m, 2H), 2.66 (m, 6H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 140.8, 128.6, 125.3, 124.5, 115.9, 73.0, 69.2, 65.9, 64.5, 58.5, 44.4; EIMS [m/z(%)] 337 (M$^+$, 51), 229 (100); HRMS (EI) calcd for C$_{18}$H$_{19}$NS^{56}Fe: 337.0587; found 337.0588. Anal. calcd for C$_{18}$H$_{19}$NSFe: C, 64.10; H, 5.68. Found: C, 64.08; H, 5.61
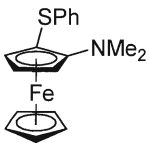
(±)-2-Diphenylphosphino-*N*,*N*-dimethylaminoferrocene (297i).
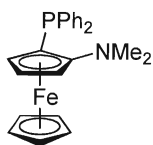
According to the General Procedure, a solution of **295** (229 mg, 1.00 mmol) in THF (10 mL) was sequentially treated with BF$_3$·OEt$_2$ (0.13 mL, 1.05 mmol), *n*-BuLi (0.45 mL, 2.45 M, 1.10 mmol) and quenched ClPPh$_2$ (0.22 mL, 1.20 mmol). Standard workup followed by filtration of the pre-adsorbed product through a plug of silica gel, eluting with Et$_2$O, gave an orange solid. Recrystallization from Et$_2$O afforded **297i** (317 mg, 77%) as orange needles in two crops: mp 146-148 °C (Et$_2$O); IR (KBr) v_{max} 3090, 3050, 2952, 2840, 2780, 1494 cm^{-1}; ^{31}P NMR (121.5 MHz, CDCl$_3$) δ –20.37; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.55-7.52 (m, 2H), 7.39 (m, 3H), 7.28 (m, 5H), 4.20 (s, 1H), 4.13 (s, 5H), 4.10 (t, 1H, J = 2.4 Hz), 3.50 (s, 1H), 2.69 (s, 6H); ^{13}C NMR (150.9 MHz, CDCl$_3$) δ 139.8 (d, J = 11.0 Hz), 137.9 (d, J = 10.6 Hz), 135.3 (d, J = 22.6 Hz), 132.4 (d, J = 18.1 Hz), 129.0, 128.1 (d), 128.0 (d), 127.8, 119.0 (d, J = 18.1 Hz), 68.7, 68.5 (d, J = 3.0 Hz), 65.9 (d, J = 10.6 Hz), 65.2, 60.1, 45.5; EIMS [m/z(%)] 413 (M$^+$, 100); HRMS (EI) calcd for C$_{24}$H$_{24}$NP^{56}Fe: 413.0995; found 413.0991. Anal. calcd for C$_{24}$H$_{24}$NPFe: C, 69.75; H, 5.85. Found: C, 69.87; H, 5.94.

2-Dicyclohexylphosphino-1-dimethylaminoferrocene (297j).
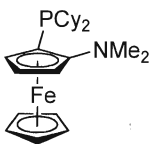
In a dry round bottom flask under argon, an ice-cold solution of dimethylaminoferrocene **295** (229 mg, 1.00 mmol) in THF (10 mL) was treated with $BF_3 \cdot OEt_2$ (0.13 mL, 1.05 mmol). After 15 min, the yellow solution was cooled to −40 °C and *n*-BuLi (0.46 mL of 2.40 M solution in hexanes, 1.10 mmol) was added by syringe to give an orange-red solution that was stirred for 1 h before $ClPCy_2$ (0.24 mL, 1.10 mmol) was added and the mixture was allowed to warm to room temperature. The reaction mixture was diluted with Et_2O (10 mL) and worked up with saturated aqueous $NaHCO_3$ solution (10 mL). The organic layer was washed with H_2O (1 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated to dryness. The residue was redissolved in pentane and chromatographed on silica gel (25 mL), eluting with 95:5 pentane/Et_2O to give 397 mg (77%) of the desired aminophosphine **297j** as a moderately air-sensitive viscous orange oil: R_f 0.50 (SiO_2, 90:10 hexanes/EtOAc); IR ($CHCl_3$): v_{max} 2920, 2848, 1489, 1446 cm^{-1}; ^{31}P NMR (121 MHz, acetone-d_6): δ −12.3; ^1H NMR (300 MHz, acetone-d_6): δ 4.22 (s, 5H), 4.15 (t, 1H, J = 1.1 Hz), 4.04 (t, 1H, J = 2.3 Hz), 3.92 (t, 1H, J = 1.7 Hz), 2.75 (s, 6H), 2.49-2.41 (m, 1H), 2.00-1.93 (m, 1H), 1.92-1.81 (m, 3H), 1.77-1.67 (m, 2H), 1.67-1.61 (m, 1H), 1.61-1.52 (m, 3H), 1.50-1.20 (m, 7H), 1.20-1.06 (m, 2H), 1.06-0.97 (m, 1H), 0.90-0.79 (m, 1H); ^{13}C NMR (75.5 MHz, acetone-d_6) δ 118.0 (d, $J^{13}_C{-}^{31}_P$ = 14.0 Hz), 67.5, 66.6 (d, $J^{13}_C{-}^{31}_P$ = 3.4 Hz), 63.3 (d, $J^{13}_C{-}^{31}_P$ = 25.3 Hz), 63.2, 61.3 (d, $J^{13}_C{-}^{31}_P$ = 1.5 Hz), 43.9 (d, $J^{13}_C{-}^{31}_P$ = 13.2 Hz), 35.0 (d, $J^{13}_C{-}^{31}_P$ = 15.9 Hz), 33.2 (d, $J^{13}_C{-}^{31}_P$ = 13.2 Hz), 32.2 (d, $J^{13}_C{-}^{31}_P$ = 20.6 Hz), 30.2 (d, $J^{13}_C{-}^{31}_P$ = 15.9 Hz), 29.5 (d, $J^{13}_C{-}^{31}_P$ = 10.8 Hz), 29.0, 27.3 (d, $J^{13}_C{-}^{31}_P$ = 11.8

Hz), 27.2 (d, $J^{13}_{C^-}{}^{31}_P$ = 6.5 Hz), 27.0 (d, $J^{13}_{C^-}{}^{31}_P$ = 12.8 Hz), 26.8 (d, $J^{13}_{C^-}{}^{31}_P$ = 8.3 Hz),

26.3 (d, $J^{13}_{C^-}{}^{31}_P$ = 15.5 Hz). EIMS (*m/z* (%)): 425 (M$^+$, 87), 130 (62), 55 (100), 41 (94);

HRMS (EI; *m/z*): calcd for C$_{24}$H$_{36}$NP^{56}Fe 425.1936; found 425.1934.

(±)-2-Iodo-*N,N*-dimethylaminoferrocene (297k).
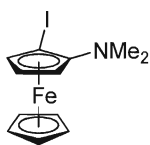
According to the General Procedure, a solution of **295** (250 mg, 1.09 mmol) in THF (10 mL) was sequentially treated with BF$_3$·OEt$_2$ (0.14 mL, 1.15 mmol), *n*-BuLi (0.49 mL, 2.45 M, 1.20 mmol) and quenched with a solution of ICH$_2$CH$_2$I (369 mg, 1.31 mmol) in THF (2 mL). Standard workup including an additional washing with sat. aq. Na$_2$S$_2$O$_3$ solution and filtration through silica, eluting with 2:98 Et$_2$O/pentane, gave **297k** (334 mg, 94%) as a moderately light-sensitive orange oil: IR (neat) v_{max} 3087, 2948, 2777, 1486 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.28 (m, 1H), 4.21 (s, 5H), 4.05 (t, 1H, *J* = 2.7 Hz), 4.02 (m, 1H), 2.69 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 113.4, 71.9, 71.1, 64.8, 56.3, 45.5, 38.7; EIMS [*m/z*(%)] 355 (M$^+$, 100), 290 (24); HRMS (EI) calcd for C$_{12}$H$_{14}$NI^{56}Fe: 354.9520; found 354.9517.

(±)-2-Acetoxy-*N,N*-dimethylaminoferrocene (298).
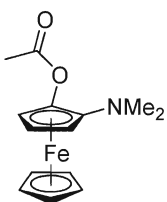
A solution of **297k** (144 mg, 0.41 mmol) in abs. EtOH (3 mL) was treated with Cu(OAc)$_2$·H$_2$O (95 mg, 0.50 mmol) and heated to reflux for 10 min to give a dark mixture. After cooling to room temperature, volatiles were removed under reduced pressure. The residue was dissolved in Et$_2$O and filtered through a pad of Celite in a sintered funnel to give **298** (99 mg, 86%) as an orange oil that solidified on standing: mp 52-54 °C (pentane); IR (KBr, neat) v_{max} 3103,

2974, 2851, 2793, 1752, 1210 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 4.29, 4.17 (dd, 1H, J = 2.4, 1.5 Hz), 3.78 (dd, 1H, J = 2.7, 0.9 Hz), 3.68 (t, 1H, J = 2.7 Hz), 2.61 (s, 6H), 2.15 (s, 3H); ^{13}C NMR (75.5 MHz, acetone-d_6) δ 169.8, 106.4, 69.2, 67.6, 60.0, 57.5, 55.4, 43.5, 21.2; EIMS [m/z(%)] 287 (M$^+$, 71), 245 (100); HRMS (EI) calcd for C$_{14}$H$_{17}$NO$_2$^{56}Fe: 287.0608; found 287.0606. Anal. calcd for C$_{14}$H$_{17}$NO$_2$Fe: C, 58.56; H, 5.97. Found: C, 58.56; H, 5.97.

N,N,N'',N''-Tetramethyl-2,2''-diamino-1,1''-biferrocene (299).

A mixture of **297k** (88 mg, 0.25 mmol), dichloromethane (5 mL) and purified Cu powder (787 mg, 12.4 mmol) was concentrated to dryness under reduced pressure. The resulting solid mass was heated under argon at 110 °C for 18 h. After cooling to room temperature, the solid mass was taken up in dichloromethane (20 mL) and filtered through a pad of Celite in a sintered funnel. Removal of volatiles from the filtrate under reduced pressure and gradient column chromatography (neutral alumina, 2:98→5:95 Et$_2$O/hexanes) sequentially gave *meso*-**299** (14 mg, 26%) and *rac*-**299** (15 mg, 26%) as orange solids.

meso-**299.** mp 198-200 °C (abs. EtOH); IR (KBr) ν_{max} 3088, 3073, 2999, 2940, 2822, 2780, 1472, 1411 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.88-4.86 (m, 2H), 4.14-4.13 (m, 2H), 4.05 (s, 10H), 3.99 (t, 2H, J = 2.7 Hz), 2.73 (s, 12H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 112.0, 76.4, 69.2, 66.4, 62.5, 57.7, 46.2; EIMS [m/z(%)] 456 (M$^+$, 100); HRMS (EI) calcd for C$_{24}$H$_{28}$N$_2$^{56}Fe$_2$: 456.0949; found 456.0950.
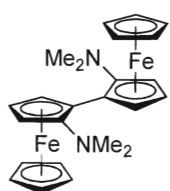
rac-**299.** ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.38- 4.37 (m, 2H), 4.32 (s, 10H), 3.93-3.92 (m, 4H), 2.38 (s, 12H); ^{13}C (150 MHz, CDCl$_3$) δ 114.7, 74.7, 71.2, 68.2, 61.2, 57.5, 43.9; EIMS [*m/z*(%)] 456 (M$^+$, 100); HRMS (EI) calcd for C$_{24}$H$_{28}$N$_2$^{56}Fe$_2$: 456.0949; found 456.0941.
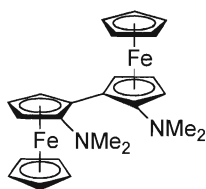
2-*N*,*N*-Dimethylamino-3-trimethylsilanyl-ferrocenecarboxaldehyde (301).
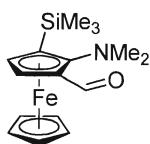
To a solution of dimethylaminoferrocene **297e** (81 mg, 0.27 mmol) in THF (2.5 mL) at 0 °C under argon was added BF$_3$·OEt$_2$ (35 μL, 0.28 mmol). After stirring for 15 min, the yellow solution was cooled to –78 °C, treated with *n*-BuLi (0.28 mL, 2.00 M, 0.56 mmol) and immediately warmed to –40 °C for 1 h. The reaction mixture was then cooled back to –78 °C before addition of DMF (52 μL, 0.67 mmol) and allowed to warm slowly to room temperature. Standard workup followed by gradient column chromatography (silica gel, 2:96:2→10:88:2 hexanes/Et$_2$O/Et$_3$N) gave **301** (53 mg, 60%) as a dark red oil; IR (KBr) v_{max} 3096, 2955, 2926, 2853, 2780, 1669 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 10.23 (s, 1H), 4.78 (s, 1H), 4.36 (s, 1H), 4.28 (s, 5H), 2.78 (s, 6H), 0.29 (s, 9H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 193.7, 120.5, 76.4, 75.5, 74.4, 70.3, 68.4, 47.3, 0.3; EIMS [*m/z*(%)] 329 (M$^+$, 100); HRMS (EI) calcd for C$_{16}$H$_{23}$NOSi^{56}Fe: 329.0898; found 329.0893.

2-*N*,*N*-Dimethylamino-3-thiophenyl-ferrocenecarboxaldehyde (302).
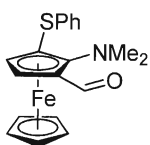
To a solution of dimethylaminoferrocene **297h** (81 mg, 0.27 mmol) in THF (2.5 mL) at 0 °C under argon was added BF$_3$·OEt$_2$ (35 μL, 0.28 mmol). After stirring for 15 min, the yellow solution was cooled to –78 °C,

treated with *n*-BuLi (0.28 mL, 2.00 M, 0.56 mmol) and immediately warmed to –40 °C for 1 h. The reaction mixture was then cooled back to –78 °C before addition of DMF (52 μL, 0.67 mmol) and allowed to warm slowly to room temperature. Standard workup followed by gradient column chromatography (silica gel, 2:96:2→10:88:2 hexanes/Et$_2$O/Et$_3$N) gave **302** (53 mg, 60%) as a dark red oil: IR (KBr) v_{max} 3073, 2927, 2853, 2787, 1669 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.28-7.15 (m, 2H), 7.15-7.03 (m, 3H), 4.83 (d, 1H, J = 2.7 Hz), 4.59 (d, 1H, J = 3.0 Hz), 4.36 (s, 5H), 2.82 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 193.0, 139.9, 128.8, 126.3, 125.4, 117.8, 76.7, 71.8, 71.5, 70.8, 65.2, 46.1; EIMS [*m/z*(%)] 365 (M$^+$, 100), 71 (58), 57 (69), 43 (53); HRMS (EI) calcd for C$_{19}$H$_{19}$NOS^{56}Fe: 365.0536; found 365.0535.

2-Hydroxymethyl-*N,N*-dimethylaminoferrocene (303).
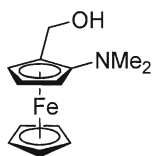
A solution of NaBH$_4$ (130 mg, 3.45 mmol) in H$_2$O (3.5 mL) was added to an ice-cold solution of **297a** (443 mg, 1.72 mmol) in MeOH (10 mL) that was open to air. After addition, a gradual colour change from red to orange was observed and the reaction mixture was allowed to warm to room temperature over 20 h. The reaction mixture was poured into a cold saturated solution of NH$_4$Cl (10 mL) and subsequently made weakly alkaline (pH 8) with a saturated solution of NaHCO$_3$ (xx mL). The resulting mixture was extracted with Et$_2$O (2 × 20 mL). The combined organic extracts were washed with H$_2$O (1 × 10 mL), brine (1 × 10 mL), dried over Na$_2$SO$_4$ and all volatiles were removed *in vacuo*. The crude was dissolved in Et$_2$O and filtered through a pad of silica, eluting with Et$_2$O. Evaporation of the filtrate afforded **303** (415 mg, 93%) as an orange oil: R_f = 0.12 (silica, 50:50 hexanes/EtOAc); IR (KBr,

neat) v_{max} 3369, 2943, 2851, 2785, 1485, 1455, 1422 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.46 (AB q, 1H, J = 12.3, 12.3 Hz), 4.21 (s, 5H), 4.12-3.98 (m, 1H), 3.97-3.94 (m, 1H), 3.93 (t, 1H, J = 2.4 Hz), 3.48 (br s, 1H), 2.60 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 112.1, 81.7, 68.7, 65.4, 62.8, 60.3, 56.2, 45.1; EIMS [m/z(%)] 259 (M$^+$, 25), 121 (66), 86 (65), 84 (100); HRMS (EI) calcd for C$_{13}$H$_{17}$NO^{56}Fe: 259.0659; found 259.0658.

2-Diethylaminomethyl-N,N-dimethylaminoferrocene (304).
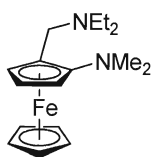
A stirred solution of alcohol **303** (90 mg, 0.35 mmol) and NaI (104 mg, 0.69 mmol) in MeCN (3 mL) under argon at room temperature was treated with ClSiMe$_3$ (0.11 mL, 0.87 mmol), resulting in the formation of fine precipitate. After stirring for 10 minutes, Et$_2$NH (0.14 mL, 1.39 mmol) was added and the reaction mixture left to stir for a further 15 h. CH$_2$Cl$_2$ (10 mL) was added and the mixture washed with H$_2$O (3 × 5 mL), brine (1 × 5 mL), dried over Na$_2$SO$_4$ and all volatiles were removed *in vacuo*. The crude mixture was dissolved in EtOAc and filtered through a pad of silica, eluting with 95:3:2 EtOAc/i-PrOH/Et$_3$N. Evaporation of the filtrate afforded the amine **304** (103 mg, 95%) as an orange oil: R_f = 0.25 (silica, 95:3:2 EtOAc/i-PrOH/Et$_3$N); IR (KBr, neat) v_{max} 3093, 2968, 2937, 2819, 2780, 1487,, 1452, 1421 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.13 (s, 5H), 3.97 (t, 1H, J = 1.8 Hz), 3.89 (t, 1H, J = 2.0 Hz), 3.86 (t, 1H, J = 2.4 Hz), 3.75 (AB d, 1H, J = 13.2 Hz), 3.12 (AB d, 1H, J = 12.9 Hz), 2.68 (s, 6H), 2.61 (dq, 2H, J = 13.8, 6.9 Hz), 2.41 (dq, 2H, J = 13.0, 7.1 Hz), 0.98 (t, 6H, J = 7.2); ^{13}C NMR (75 MHz, CDCl$_3$) δ 113.7, 76.6, 68.5, 68.3, 61.7, 56.9, 52.2, 45.9, 44.9, 11.2; EIMS [m/z(%)] 314 (M$^+$, 100), 241 (39), 121 (38); HRMS (EI) calcd for C$_{17}$H$_{26}$N$_2$^{56}Fe: 314.1445; found 314.1445.

2-Imidazolylmethyl-*N*,*N*-dimethylaminoferrocene (305).
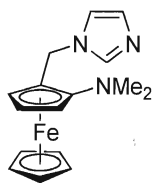
Alcohol **303** (60 mg, 0.23 mmol) and carbonyl diimidazole (47 mg, 0.29) were added to a round bottom flask, equipped with a condenser, under argon. CH_2Cl_2 (3 mL) was added, followed by heating at reflux for 16 h. After cooling to room temperature, the mixture was preadsorbed on silica and loaded on a column. Flash chromatography (silica, 98:0:2 $\rightarrow$ 93:5:2 EtOAc/MeOH/Et$_3$N) afforded the desired 2-substituted imidazole **305** as a yellow-brown oil (38 mg, 53%): R_f = 0.25 (silica, 93:5:2 EtOAc/MeOH/Et$_3$N); IR (KBr, neat) v_{max} 3100, 2949, 2848, 2784, 1504, 1421 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.50 (s, 1H), 7.00 (s, 1H), 6.92 (s, 1H), 5.11 (d, 1H, J = 14.1 Hz), 4.83 (d, 1H, J = 14.4 Hz), 4.16 (s, 5H), 4.10 (t, 1H, J = 1.8 Hz), 4.02-3.93 (m, 2H), 2.61 (s, 6H), 2.03 (s, 1H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 136.7, 129.1, 118.9, 113.4, 75.2, 68.9, 66.6, 63.5, 57.4, 45.5, 45.3; EIMS [*m/z*(%)] 309 (M$^+$, 48), 121 (100); HRMS (EI) calcd for C$_{16}$H$_{19}$N$_3$^{56}Fe: 309.0928; found 309.0930.

2-Phenyl-*N*,*N*-dimethylaminoferrocene (307a).
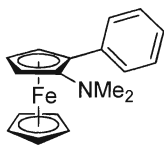
Iodoferrocene **297k** (89 mg, 0.25 mmol), PhB(OH)$_2$ (34 mg, 0.28 mmol) and Pd(PPh$_3$)$_4$ (29 mg, 2.51 x 10^{-2} mmol) were added to a dry Schlenk flask, followed by DME (2 mL) and an aqueous solution of 3 M NaOH (0.17 mL, 0.50 mmol). Argon was bubbled through the resulting mixture for 10 minutes, followed by heating the system at 55 °C for 14 h. The reaction was allowed to cool to room temperature, diluted with Et$_2$O, washed with water (1 $\times$ 5 mL), brine (1 $\times$ 5 mL), dried over Na$_2$SO$_4$ and all volatiles were removed *in vacuo*. Flash column

chromatography (silica, 98:2 hexanes/EtOAc) afforded biaryl **307a** (61 mg, 80%) as an orange oil: R_f 0.45 (90:10 hexanes/EtOAc); IR (KBr, CHCl$_3$) v_{max} 3091, 2941, 2852, 2779, 1601, 1491, 1444, 1416 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.80-7.74 (m, 2H), 7.36-7.19 (m, 3H), 4.28-4.25 (m, 1H), 4.18 (s, 5H), 4.15-4.11 (m, 1H), 4.05 (t, 1H, J = 2.7 Hz), 2.53 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 139.1, 128.4, 127.8, 125.9, 112.5, 78.1, 69.2, 66.5, 62.4, 58.0, 44.6; EIMS [m/z(%)] 305 (M$^+$, 100); HRMS (EI) calcd for C$_{18}$H$_{19}$N^{56}Fe: 305.0867; found 305.0864.

2-(3-Methylphenyl)-*N,N*-dimethylaminoferrocene (307b).
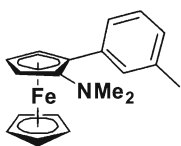
Iodoferrocene **297k** (102 mg, 0.29 mmol), PhB(OH)$_2$ (78 mg, 0.57 mmol) and Pd(PPh$_3$)$_4$ (33 mg, 2.86 x 10^{-2} mmol) were added to a dry Schlenk flask, followed by DME (3 mL) and an aqueous solution of 3 M aqueous NaOH (0.25 mL, 0.70 mmol). Argon was bubbled through the resulting mixture for 10 minutes, followed by heating the system at reflux for 17 h. The reaction was allowed to cool to room temperature, diluted with Et$_2$O, washed with water (1 × 5 mL), brine (1 × 5 mL), dried over Na$_2$SO$_4$ and all volatiles were removed *in vacuo*. Flash column chromatography (silica, 98:2 hexanes/EtOAc) afforded biaryl **307b** (85 mg, 93%) as an orange oil: R_f 0.41 (90:10 hexanes/EtOAc); IR (KBr, film from CHCl$_3$) v_{max} 3093, 2940, 2848, 2778, 1605, 1487, 1452, 1416 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.61 (d, 1H, J = 7.8 Hz), 7.49 (s, 1H), 7.23 (t, 1H, J = 7.5 Hz), 7.04 (d, 1H, J = 7.5 Hz), 4.23 (s, 1H), 4.18 (s, 5H), 4.11 (s, 1H), 4.02 (t, 1H, J = 2.7 Hz), 2.52 (s, 6H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 139.0, 137.1, 129.0, 127.7, 126.7, 125.7, 112.4, 77.9, 69.1,

66.7, 62.2, 58.1, 44.6, 21.5; EIMS [m/z(%)] 319 (M$^+$, 100); HRMS (EI) calcd for C$_{19}$H$_{21}$N^{56}Fe: 319.1023; found 319.1025.

2-(2-Methoxyphenyl)-*N,N*-dimethylaminoferrocene (307c).
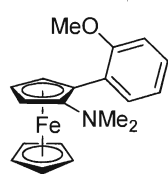
Iodoferrocene **297k** (101 mg, 0.28 mmol), 2-methoxyphenylboronic acid (86 mg, 0.57 mmol) and Pd(PPh$_3$)$_4$ (33 mg, 2.86 x 10^{-2} mmol) were added to a dry Schlenk flask, followed by DME (3 mL) and an aqueous solution of 3 M aqueous NaOH (0.24 mL, 0.70 mmol). Argon was bubbled through the resulting mixture for 10 minutes, followed by heating the system at reflux for 14 h. The reaction was allowed to cool to room temperature, diluted with Et$_2$O, washed with water (1 × 5 mL), brine (1 × 5 mL), dried over Na$_2$SO$_4$ and all volatiles were removed *in vacuo*. Flash column chromatography (silica, 98:2 → 95:5 hexanes/EtOAc) afforded biaryl **307c** (83 mg, 87%) as an orange oil that solidified on standing: R_f 0.19 (95:5 hexanes/EtOAc); mp 92-93 °C (hexanes); IR (KBr) ν_{max} 3082, 2941, 2833, 2776, 1597, 1450, 1411 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.09 (dd, 1H, J = 7.5, 1.8 Hz), 7.26 (td, 1H, J = 7.8, 1.8 Hz), 7.02 (td, 1H, J = 7.5, 0.9 Hz), 6.87 (d, 1H, J = 8.4 Hz), 4.27 (t, 1H, J = 3.6 Hz), 4.24 (s, 5H), 4.09 (t, 1H, J = 2.1 Hz), 4.05 (t, 1H, J = 2.7 Hz), 3.79 (s, 3H), 2.47 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 157.5, 132.6, 127.5, 127.0, 120.0, 113.1, 110.5, 75.5, 68.9, 66.8, 62.0, 56.8, 55.6, 44.1; EIMS [m/z(%)] 335 (M$^+$, 100), 229 (24); HRMS (EI) calcd for C$_{19}$H$_{21}$NO^{56}Fe: 335.0972; found 335.0978.

2-(*N*-Boc pyrrolyl)-*N*,*N*-dimethylaminoferrocene (307d).
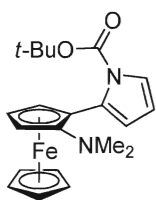
Iodoferrocene **297k** (107 mg, 0.30 mmol), 2-pyrrylboronic acid (95 mg, 0.45 mmol), K_3PO_4 (127 mg, 0.60 mmol) and $Pd(PPh_3)_4$ (35 mg, 0.03 mmol) were added to a dry Schlenk flask, which was evacuated and backfilled with argon (× 2). *n*-BuOH was added, followed by heating the system at 100 °C for 14 h. The reaction was allowed to cool to room temperature, diluted with Et_2O, washed with water (1 × 5 mL), brine (1 × 5 mL), dried over Na_2SO_4 and all volatiles were removed *in vacuo*. Flash column chromatography (silica, 97:3 hexanes/EtOAc) afforded biaryl **307d** (27 mg, 23%) as an orange oil: R_f 0.35 (90:10 hexanes/EtOAc); IR (KBr, film from $CHCl_3$) v_{max} 3094, 2979, 2951, 2851, 2787, 1736, 1731 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (t, 1H, J = 1.8 Hz), 6.44 (t, 1H, J = 2.4 Hz), 6.18 (t, 1H, J = 2.7 Hz), 4.31 (s, 5H), 4.01 (t, 1H, J = 1.8 Hz), 3.94-3.92 (m, 2H), 2.38 (s, 6H), 1.31 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.6, 130.2, 122.0, 115.7, 114.1, 110.0, 83.1, 69.2, 68.7, 68.0, 61.2, 58.3, 43.1, 27.5; EIMS [*m/z*(%)] 394 (M$^+$, 11), 294 (100), 229 (14); HRMS (EI) calcd for $C_{21}H_{26}N_2O_2{}^{56}Fe$: 394.1343; found 394.1340.

2-(2-Bromophenyl)-*N*,*N*-dimethylaminoferrocene (307e).
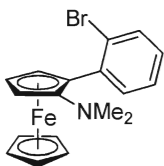
Iodoferrocene **297k** (355 mg, 1.00 mmol), 2-bromophenylboronic acid (210 mg, 1.05 mmol) and $Pd(PPh_3)_4$ (115 mg, 0.10 mmol) were added to a dry Schlenk flask, followed by DME (10 mL) and an aqueous solution of 3 M aqueous NaOH (0.50 mL, 1.50 mmol). Argon was bubbled through the resulting mixture for 10 minutes, followed by heating the system at reflux for 15 h. The reaction was allowed to cool to room temperature, diluted with Et_2O, washed with water (1 × 5

mL), brine (1 × 5 mL), dried over Na$_2$SO$_4$ and all volatiles were removed *in vacuo*. Flash column chromatography (silica, 97:3 → 95:5 TBME/hexanes) afforded biaryl **307e** (177 mg, 46%) as an orange oil: R_f 0.38 (90:10 hexanes/EtOAc); IR (KBr, CHCl$_3$) v_{max} 3091, 2947, 2846, 2783, 1587, 1502, 1485, 1416 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.12 (dd, 1H, J = 7.7, 1.5 Hz), 7.26 (dd, 1H, J = 8.1, 1.2 Hz), 7.34 (td, 1H, J = 7.5, 1.2 Hz), 7.13 (td, 1H, J = 7.8, 1.8 Hz), 4.32 (s, 5H), 4.13 (t, 1H, J = 1.8 Hz), 4.10-4.05 (m, 2H), 2.41 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 157.5, 132.6, 127.5, 127.0, 120.0, 113.1, 110.5, 75.5, 68.9, 66.8, 62.0, 56.8, 55.6, 44.1; EIMS [m/z(%)] 385 (^{81}Br M$^+$, 91), 383 (^{79}Br M$^+$, 100), 182 (62); HRMS (EI) calcd for C$_{18}$H$_{18}$N^{56}Fe^{79}Br: 382.9972; found 382.9974.

(±)-2-(2-Diphenylphosphinophenyl)-*N*,*N*-dimethylaminoferrocene (309).
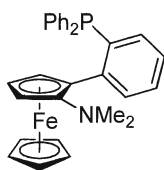
Bromoarene **307e** (194 mg, 0.51 mmol) was dissolved in THF (5 mL) in a Schlenk tube, cooled to −78 °C and treated with a solution of *n*-BuLi (0.28 mL, 0.56 mmol, 2.00 M in hexanes). After 10 minutes, ClPPh$_2$ (0.11 mL, 0.61 mmol) was added and the reaction mixture allowed to warm to room temperature over 2.5 h. The reaction mixture was diluted with Et$_2$O, washed with a saturated solution of NaHCO$_3$ (1 × 10 mL), water (1 × 10 mL), brine (1 × 10 mL), dried over Na$_2$SO$_4$ and all volatiles were removed *in vacuo*. The crude was dissolved in 75:25 Et$_2$O/pentane, filtered through a pad of silica, eluting with 75:25 Et$_2$O/pentane and evaporation of the filtrate afforded the crude. For the purpose of purification, the phosphine was treated with sulfur (19 mg, 0.60 mmol) in PhMe (5 mL) at 40 °C for 15 h. After cooling to room temperature, the mixture was preadsorbed on silica and loaded on a column. Flash column chromatography (silica, 85:15 pentane/Et$_2$O) afforded phosphine

sulfide **308** (274 mg, 96%) as an orange-red oil: R_f 0.18 (90:10 hexanes/EtOAc); IR (KBr, CHCl$_3$) ν_{max} 2918, 2848, 2779, 1481, 1437, 1097 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.56-8.51 (m, 1H), 7.87-7.81 (m, 2H), 7.69-7.63 (m, 2H), 7.50 (t, 1H, J = 3.6 Hz), 7.47-7.42 (m, 1H), 7.41-7.36 (m, 2H), 7.35-7.30 (m, 1H), 7.28-7.09 (m, 4H), 4.28 (s, 1H), 4.08 (s, 5H), 3.72 (s, 1H), 3.62 (t, 1H, J = 1.2 Hz), 2.39 (s, 6H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 142.1 (d, J^{13}_C-$^{31}_P$ = 9.0 Hz), 135.9 (d, J^{13}_C-$^{31}_P$ = 10.5 Hz), 134.1 (d, J^{13}_C-$^{31}_P$ = 84.0 Hz), 133.8 (d, J^{13}_C-$^{31}_P$ = 12.0 Hz), 133.4 (d, J^{13}_C-$^{31}_P$ = 58.5 Hz), 132.26 (d, J^{13}_C-$^{31}_P$ = 6.0 Hz), 132.22 (d, J^{13}_C-$^{31}_P$ = 27.0 Hz), 131.8 (d, J^{13}_C-$^{31}_P$ = 6.0 Hz), 131.3 (d, J^{13}_C-$^{31}_P$ = 3.0 Hz), 130.99 (d, J^{13}_C-$^{31}_P$ = 10.5 Hz), 130.91 (d, J^{13}_C-$^{31}_P$ = 3.0 Hz), 130.55 (d, J^{13}_C-$^{31}_P$ = 3.0 Hz), 130.27 (d, J^{13}_C-$^{31}_P$ = 1.5 Hz), 128.5 (d, J^{13}_C-$^{31}_P$ = 12.0 Hz), 128.03 (d, J^{13}_C-$^{31}_P$ = 12.0 Hz), 127.84 (d, J^{13}_C-$^{31}_P$ = 12.0 Hz), 126.0 (d, J^{13}_C-$^{31}_P$ = 13.5 Hz), 113.7, 81.8 (d, J^{13}_C-$^{31}_P$ = 4.5 Hz), 77.2, 76.9 (d, J^{13}_C-$^{31}_P$ = 31.5 Hz), 61.5, 55.8, 44.2; ^{31}P NMR (243 MHz, CDCl$_3$) δ 43.6; EIMS [m/z(%)] 521 (M$^+$, 50), 489 (10), 456 (39), 218 (100); HRMS (EI) calcd for C$_{30}$H$_{28}$NPS^{56}Fe: 521.1029; found 521.1027.

A portion of the aforementioned phosphine sulfide **308** (63 mg, 0.12 mmol) in MeCN (2 mL) was added to a suspension of activated Ni-Al catalyst [518 mg, 6.04 mmol activated by digesting with an aqueous solution of 6 M NaOH for 1 h at 50 °C (addition of NaOH solution is exothermic), followed by cooling to room temperature and successively washing the Ni-Al catalyst with H$_2$O (10 × 3 mL), MeOH (4 × 3 mL) and MeCN (3 × 3 mL)] in MeCN (3 mL) under argon. The resulting mixture was heated at 60 °C for 18 h. After cooling to room temperature, the mixture was filtered through a pad of Celite®, eluting with MeCN and all volatiles were removed *in vacuo*. The mixture was dissolved in 95:5 hexanes/EtOAc and carefully filtered through a pad of silica, eluting

with 95:5 hexanes/EtOAc, to afford biaryl phosphine **308** (43 mg, 73%) as a yellow-orange oil: R_f 0.35 (silica, 90:10 hexanes/EtOAc); IR (KBr, CHCl$_3$) ν_{max} 3070, 3051, 2948, 2849, 2781, 1499, 1480, 1434 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.20-8.16 (m, 1H), 7.42-7.38 (m, 1H), 7.31-7.25 (m, 6H), 7.23-7.15 (m, 5H), 7.02-6.99 (m, 1H), 4.28 (s, 5H), 4.05 (t, 1H, J = 1.8 Hz), 3.94 (t, 1H, J = 3.0 Hz), 3.85 (t, 1H, J = 1.2 Hz), 2.29 (s, 6H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 143.8 (d, J^{13}_C-$^{31}_P$ = 28.5 Hz), 138.4 (d, J^{13}_C-$^{31}_P$ = 13.5 Hz), 138.1 (d, J^{13}_C-$^{31}_P$ = 13.5 Hz), 135.7, 133.91, 133.76, 133.62, 133.53, 133.40, 132.84 (d, J^{13}_C-$^{31}_P$ = 6.0 Hz), 128.38, 128.15, 128.11, 128.04, 128.01, 128.00, 126.7, 125.5, 113.8, 80.93 (d, J^{13}_C-$^{31}_P$ = 10.5 Hz), 69.36 (d, J^{13}_C-$^{31}_P$ = 7.5 Hz), 68.5, 61.5, 56.8, 43.9; ^{31}P NMR (243 MHz, CDCl$_3$) δ −13.9; EIMS [m/z(%)] 489 (M$^+$, 2), 242 (40), 199 (100); HRMS (EI) calcd for C$_{30}$H$_{28}$NP^{56}Fe: 489.1308; found 489.1309.

2-Diphenylphosphino-1-dimethylaminoferrocene palladium dichloride (311a).

Representative procedure. A solution of aminophosphine **297i** (94 mg, 0.30 mmol) and Pd(MeCN)$_2$Cl$_2$ (58 mg, 0.30 mmol) in CH$_2$Cl$_2$ (2 mL) was stirred at room temperature in a dry flask under argon until TLC indicated consumption of the aminophosphine (75 min). The reaction mixture was then filtered through a pad of silica gel, eluting with 97:3 CH$_2$Cl$_2$/MeOH, and concentrated. Recrystallization from acetonitrile at −20 °C gave **311a** (154 mg, 87%) as a light orange powder in two crops. mp > 225 °C (decomp. at 210 °C); IR (KBr) ν_{max} 3448, 1460, 1434 cm^{-1}; ^{31}P NMR (243 MHz, CDCl$_3$): δ 25.3; ^{1}H NMR (600 MHz, CDCl$_3$): δ 8.11-8.05 (m, 2H), 7.63-7.58 (m, 1H), 7.58-7.52 (m, 4H), 7.51-7.46 (m, 1H), 7.39-7.34 (m, 2H), 4.74 (t, 1H J = 2.3 Hz), 4.53 (s, 1H), 4.21 (s, 1H), 4.00 (s, 5H), 3.46 (s, 3H),
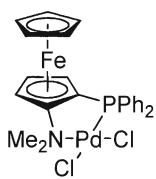
3.09 (s, 3H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 134.6 (d, $J^{13}{}_C$-$^{31}{}_P$ = 11.6 Hz), 132.2 (d, $J^{13}{}_C$-$^{31}{}_P$ = 2.2 Hz), 131.8 (d, $J^{13}{}_C$-$^{31}{}_P$ = 10.1 Hz), 131.4 (d, $J^{13}{}_C$-$^{31}{}_P$ = 57.8 Hz), 131.4 (d, $J^{13}{}_C$-$^{31}{}_P$ = 3.1 Hz), 129.4 (d, $J^{13}{}_C$-$^{31}{}_P$ = 67.7 Hz), 128.9 (d, $J^{13}{}_C$-$^{31}{}_P$ = 11.6 Hz), 128.6 (d, $J^{13}{}_C$-$^{31}{}_P$ = 12.1 Hz), 126.9 (d, $J^{13}{}_C$-$^{31}{}_P$ = 24.6 Hz), 75.2 (d, $J^{13}{}_C$-$^{31}{}_P$ = 6.1 Hz), 72.8 (d, $J^{13}{}_C$-$^{31}{}_P$ = 56.1 Hz), 63.9, 60.3 (d, $J^{13}{}_C$-$^{31}{}_P$ = 12.3 Hz), 58.2, 54.5. FABMS (m/z (%)): 591 (M$^+$, 14), 554 (90), 518 (84), 413 (77), 292 (73), 229 (85), 214 (81), 108 (100). Anal. calcd for C$_{24}$H$_{24}$NPCl$_2$FePd: C, 48.81; H, 4.10. Found: C, 49.04; H, 4.09.

2-Dicyclohexylphosphino-1-dimethylaminoferrocene palladium dichloride (311b).
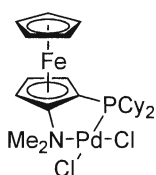
Prepared on a 0.22 mmol scale in a manner analogous to **311a** to give **311b** (121 mg, 91%) as rust-colored crystals after recrystallization from acetonitrile at −20 °C. mp > 225 °C (decomp. at 195 °C); IR (KBr): ν_{max} 2931, 2850, 1446 cm^{-1}; ^{31}P NMR (121.5 MHz, CDCl$_3$): δ 51.1; ^{1}H NMR (300 MHz, CDCl$_3$): δ 4.71 (s, 1H), 4.59 (s, 1H), 4.46 (s, 5H), 4.00 (s, 1H), 3.47 (s, 3H), 3.12 (s, 3H), 2.72-2.54 (m, 1H), 2.52-2.33 (m, 1H), 2.33-2.16 (m, 2H), 2.16-1.88 (m, 5H), 1.87-1.31 (m, 10H), 1.31-1.05 (m, 3H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 128.0 (d, $J^{13}{}_C$-$^{31}{}_P$ = 20.9 Hz), 74.6 (d, $J^{13}{}_C$-$^{31}{}_P$ = 5.6 Hz), 73.8, 73.3, 63.1, 60.4 (d, $J^{13}{}_C$-$^{31}{}_P$ = 10.6 Hz), 58.5, 56.7, 37.7 (d, $J^{13}{}_C$-$^{31}{}_P$ = 30.2 Hz), 35.1 (d, $J^{13}{}_C$-$^{31}{}_P$ = 30.2 Hz), 29.0 (d, $J^{13}{}_C$-$^{31}{}_P$ = 2.0 Hz), 28.7, 28.1, 28.0, 26.9 (d, $J^{13}{}_C$-$^{31}{}_P$ = 2.0 Hz), 26.7, 26.6 (d, $J^{13}{}_C$-$^{31}{}_P$ = 2.9 Hz), 26.5, 26.4, 25.8, 25.4; FABMS (m/z (%)): 603 (M$^+$, 8), 566 (81), 229 (100); Anal. calcd for C$_{24}$H$_{36}$NPCl$_2$FePd: C, 47.83; H, 6.02. Found: C, 47.77; H, 6.20.

2-Diphenylphosphino-1-dimethylaminoferrocene platinum dichloride (312a).
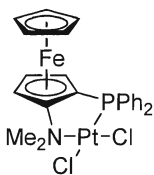
*Representative procedure.* A suspension of aminophosphine **297i** (100 mg, 0.24 mmol) and Pt(COD)Cl$_2$ (90 mg, 0.24 mmol) in PhMe (2.5 mL) was heated at reflux until TLC indicated consumption of the aminophosphine (1.5 h). The solvent was removed on a rotary evaporator, the residue redissolved in CH$_2$Cl$_2$, filtered through a pad of silica gel eluting with 97:3 CH$_2$Cl$_2$/MeOH, and concentrated again under reduced pressure. Recrystallization from acetone at −20 °C gave **312a** (82 mg, 50%) as fine orange crystals. mp > 225 °C (decomp. at 210 °C); IR (KBr): v_{max} 3469, 3421, 3048, 2925, 1435 cm^{-1}; ^{31}P NMR (243 MHz, CDCl$_3$): δ 2.01 (t, $J^{31}_{P-}{}^{195}_{Pt}$ = 1982 Hz); ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.18-8.06 (m, 2H), 7.63-7.40 (m, 6H), 7.39-7.30 (m, 2H), 4.92 (t, 1H, J = 2.6 Hz), 4.53 (s, 1H), 4.29 (t, 1H, J = 1.0 Hz), 3.94 (s, 5H), 3.65 (t, 3H, J = 16.6 Hz), 3.24 (t, 3H, J = 15.1 Hz); ^{1}H NMR (600 MHz, acetone-d$_6$): δ 8.24-8.17 (m, 2H), 7.70-7.60 (m, 3H), 7.59-7.53 (m, 2H), 7.53-7.48 (m, 1H), 7.45-7.39 (m, 2H), 5.08 (t, 1H, J = 2.3 Hz), 4.94 (s, 1H), 4.62 (t, 1H, J = 1.1 Hz), 4.01 (s, 5H), 3.66 (s, 3H), 3.22 (s, 3H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 134.5 (d, $J^{13}_{C-}{}^{31}_{P}$ = 11.9 Hz), 132.1 (d, $J^{13}_{C-}{}^{31}_{P}$ = 2.2 Hz), 131.5 (d, $J^{13}_{C-}{}^{31}_{P}$ = 10.3 Hz), 131.1 (d, $J^{13}_{C-}{}^{31}_{P}$ = 68.8 Hz), 130.9 (d, $J^{13}_{C-}{}^{31}_{P}$ = 2.7 Hz), 129.1 (d, $J^{13}_{C-}{}^{31}_{P}$ = 21.6 Hz), 128.9 (d, $J^{13}_{C-}{}^{31}_{P}$ = 73.8 Hz), 128.8 (d, $J^{13}_{C-}{}^{31}_{P}$ = 11.4 Hz), 128.6 (d, $J^{13}_{C-}{}^{31}_{P}$ = 12.3 Hz), 74.9 (d, $J^{13}_{C-}{}^{31}_{P}$ = 6.4 Hz), 74.0 (d, $J^{13}_{C-}{}^{31}_{P}$ = 66.7 Hz), 63.2, 59.7, 59.4 (d, $J^{13}_{C-}{}^{31}_{P}$ = 10.6 Hz), 55.6; FABMS (*m/z* (%)): 679 (M$^+$, 6), 643 (100), 605 (30), 486 (22); Anal. calcd for C$_{24}$H$_{24}$NPCl$_2$FePt: C, 42.44; H, 3.56. Found: C, 42.67; H, 3.56.

2-Dicyclohexylphosphino-1-dimethylaminoferrocene platinum dichloride (312b).

Prepared on a 0.19 mmol scale in a manner analogous to **312a** to give **312b** (101 mg, 79%) as orange crystals after recrystallization from CH$_2$Cl$_2$/EtOAc at -20 °C. mp > 225 °C (decomp. at 210 °C); IR (KBr): v_{max} 3448, 1460, 1434 cm^{-1}; ^{31}P NMR (121 MHz, CDCl$_3$): δ 21.7 (t, $J^{31}_{P^{-195}Pt}$ = 1898 Hz); ^{1}H NMR (600 MHz, CDCl$_3$): δ 4.86 (t, 1H, J = 2.5 Hz), 4.57 (s, 1H), 4.46 (s, 5H), 4.00 (s, 1H), 3.65 (t, 3H, J = 14.8 Hz), 3.26 (t, 3H, J = 14.3 Hz), 2.77-2.61 (m, 1H), 2.57-2.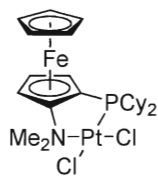39 (m, 1H), 2.31-2.17 (m, 1H), 2.14-1.75 (m, 8H), 1.74-1.53 (m, 4H), 1.50-1.30 (m, 3H), 1.30-1.05 (m, 4H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 129.9 (d, $J^{13}_{C^{-31}P}$ = 17.8 Hz), 74.5 (d, $J^{13}_{C^{-31}P}$ = 52.6 Hz), 74.3 (d, $J^{13}_{C^{-31}P}$ = 4.8 Hz), 71.5, 62.44, 59.4, 59.2 (d, $J^{13}_{C^{-31}P}$ = 8.9 Hz), 58.0, 36.1 (d, $J^{13}_{C^{-31}P}$ = 36.9 Hz), 33.0 (d, $J^{13}_{C^{-31}P}$ = 37.6 Hz), 28.9, 28.0, 27.6 (d, $J^{13}_{C^{-31}P}$ = 4.4 Hz), 27.0 (d, $J^{13}_{C^{-31}P}$ = 11.6 Hz), 26.8 (d, $J^{13}_{C^{-31}P}$ = 8.0 Hz), 26.6 (d, $J^{13}_{C^{-31}P}$ = 6.1 Hz), 26.5 (d, $J^{13}_{C^{-31}P}$ = 11.9 Hz), 26.1, 25.5; FABMS (*m/z* (%)): 691 (M$^+$, 8), 655 (100), 616 (59), 55 (76). Anal. calcd for C$_{24}$H$_{24}$NPCl$_2$FePd: C, 48.81; H, 4.10. Found: C, 49.04; H, 4.09.

General Procedure A (Suzuki-Miyaura Couplings). An oven-dried reaction tube under argon containing a mixture of phenylboronic acid (91 mg, 0.75 mmol), CsF (228 mg, 1.50 mmol), Pd(OAc)$_2$ (2 mg, 0.01 mmol) and **297i** (8 mg, 0.02 mmol) in dioxane (2.5 mL) was treated with an aryl halide **314a-g** (0.50 mmol) and stirred at room temperature for 5 min before heating to reflux for 22 h. After cooling to room temperature and diluting with Et$_2$O (7 mL), the mixture was filtered through a pipette containing a plug of silica gel and eluted with additional Et$_2$O. Evaporation of the solvent under reduced

pressure and recrystallization or column chromatography gave the purified products **315a-g**.

4-Trifluoromethylbiphenyl (315a).
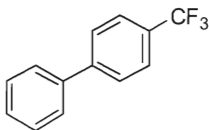
According to General Procedure A, a mixture of 4-chloro trifluoromethylbenzene (0.07 mL, 0.50 mmol), phenylboronic acid (91 mg, 0.75 mmol), CsF (228 mg, 1.50 mmol), Pd(OAc)$_2$ (2 mg, 0.01 mmol) and **297i** (8 mg, 0.02 mmol) in 1,4-dioxane (2.5 mL) was heated to reflux, cooled and filtered. Column chromatography (silica, 98:2 hexanes/EtOAc) gave **315a** (104 mg, 94%) as a colorless crystalline solid. mp 66-69 °C (95% EtOH) (lit.[113] 66-68 °C). Spectroscopic data matched literature reports.[114] ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.70 (s, 4H), 7.60 (d, 2H, J = 7.2 Hz), 7.50-7.41 (m, 3H).

4-Phenylacetophenone (315b).
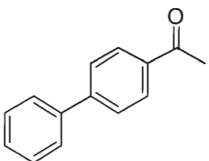
According to General Procedure A, a mixture of 4-chloroacetophenone (65 μL, 0.50 mmol), phenylboronic acid (91 mg, 0.75 mmol), CsF (228 mg, 1.50 mmol), Pd(OAc)$_2$ (2 mg, 0.01 mmol) and ligand **297i** (8 mg, 0.02 mmol) in 1,4-dioxane (2.5 mL) was heated to reflux, cooled and filtered. After evaporation of the solvent, recrystallization from hexanes containing a small amount of EtOAc gave **315b** (86 mg, 88%) as colorless crystals. Spectroscopic data matched literature reports.[115] ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.05 (d, 2H, J = 8.4 Hz), 7.69 (d, 2H, J = 8.4 Hz), 7.63 (d, 2H, J = 7.2 Hz), 7.50-7.40 (m, 3H), 2.64 (s, 3H); ^{13}C

NMR (75.5 MHz, CDCl$_3$) δ 197.7, 145.8, 139.8, 135.8, 128.93, 128.89, 128.2, 127.24, 127.20, 26.6.

4-Cyanobiphenyl (315c).
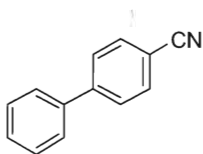
According to General Procedure A, a mixture 4-chlorobenzonitrile (69 mg, 0.50 mmol), phenylboronic acid (91 mg, 0.75 mmol), CsF (228 mg, 1.50 mmol), Pd(OAc)$_2$ (2 mg, 0.01 mmol) and **297i** (8 mg, 0.02 mmol) in 1,4-dioxane (2.5 mL) was heated to reflux, cooled and filtered. Evaporation of the solvent under reduced pressure and column chromatography of the pre-adsorbed crude material (silica, 95:5 hexanes/Et$_2$O) gave **315c** (83 mg, 92%) as a colorless solid. Spectroscopic data matched literature reports.[116] ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.69 (q, 4H, J = 6 Hz), 7.61-7.57 (m, 2H), 7.52-7.40 (m, 3H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 145.6, 139.1, 132.5, 129.0, 128.6, 127.6, 127.1, 118.8, 110.8.

2-Nitrobiphenyl (315d).
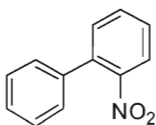
According to General Procedure A, a mixture of o-chloronitrobenzene (79 mg, 0.50 mmol), phenylboronic acid (91 mg, 0.75 mmol), CsF (228 mg, 1.50 mmol), Pd(OAc)$_2$ (2 mg, 0.01 mmol) and **297i** (8 mg, 0.02 mmol) in 1,4-dioxane (2.5 mL) has heated to reflux, cooled and filtered. Evaporation of the solvent under reduced pressure and column chromatography of the pre-adsorbed crude material (silica, 99:1 hexanes/Et$_2$O) gave **315d** (73 mg, 73%) as a bright yellow oil. Spectroscopic data matched literature reports.[117] ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.86 (d, 1H, J = 8.0 Hz), 7.62 (t, 1H, J = 7.5 Hz), 7.51-7.40 (m, 5H), 7.34-7.31

(m, 2H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 149.3, 137.4, 136.3, 132.2, 131.9, 128.7, 128.2, 128.1, 127.9, 124.0.

4-Methoxybiphenyl (315e).
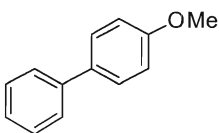
According to General Procedure A, a mixture of 4-chloroanisole (0.06 mL, 0.50 mmol), phenylboronic acid (91 mg, 0.75 mmol), CsF (228 mg, 1.50 mmol), Pd(OAc)$_2$ (2 mg, 0.01 mmol) and **297i** (8 mg, 0.02 mmol) in 1,4-dioxane (2.5 mL) was heated to reflux, cooled and filtered. Evaporation of the solvent under reduced pressure and column chromatography of the pre-adsorbed crude material (silica, 99.5:0.5 → 99:1 i-PrOH/hexanes) gave **315e** (64 mg, 70%) as a colorless solid. Spectroscopic data matched literature reports. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.54 (t, 4H, J = 6.8 Hz), 7.42 (t, 2H, J = 6.8 Hz), 7.32-7.26 (m, 1H), 6.99 (d, 2H, J = 8.7 Hz), 3.86 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 159.1, 140.8, 133.8, 128.7, 128.1, 126.7, 126.6, 114.2, 55.3.

4-Methylbiphenyl (315f).
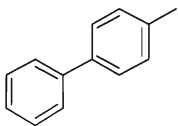
According to General Procedure A, a mixture of 4-chlorotoluene (59 µL, 0.50 mmol), phenylboronic acid (91 mg, 0.75 mmol), CsF (228 mg, 1.50 mmol), Pd(OAc)$_2$ (2 mg, 0.01 mmol) and **297i** (8 mg, 0.02 mmol) in 1,4-dioxane (2.5 mL) was heated to reflux, cooled and filtered. Evaporation of the solvent under reduced pressure and column chromatography of the pre-adsorbed crude material (silica, 99:1 hexanes/Et$_2$O) gave **315f** (47 mg, 56%) as a colorless solid. Spectroscopic data matched literature reports. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.59 (d, 2H,

J = 7.8 Hz), 7.51 (d, 2H, *J* = 7.8 Hz), 7.44 (d, 2H, *J* = 7.8 Hz), 7.35-7.24 (m, 3H), 2.41 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 141.1, 138.3, 137.0, 129.5, 128.7, 127.0, 126.9, 21.1.

5,7-Diphenyl-8-aminoquinoline (315g).
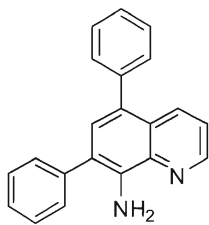
According to General Procedure A, a mixture of 5,7-dibromo-8-aminoquinoline (**314g**, 100 mg, 0.33 mmol), phenylboronic acid (60 mg, 0.50 mmol), CsF (150 mg, 0.99 mmol), Pd(OAc)$_2$ (1.3 mg, 0.007 mmol) and ligand **297i** (5.3 mg, 0.013 mmol) in 1,4-dioxane (2.5 mL) was heated to reflux, cooled and filtered. After evaporation of the solvent, recrystallization from Et$_2$O/hexanes gave **315g** (86 mg, 88%) as colorless crystals. mp: 100-102 °C (Et$_2$O/hexanes). IR (KBr): ν_{max} 3450, 3347, 3050, 3023, 1583 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.85-8.80 (m, 1H), 8.28 (dd, 1H, *J* = 8.4, 1.5 Hz), 7.66-7.63 (m, 2H), 7.54-7.44 (m, 6H), 7.42-7.34 (m, 4H), 5.32 (s, 2H). ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 147.5, 140.2, 139.9, 138.3, 134.2, 130.2, 130.0, 129.2, 129.0, 128.4, 128.2, 127.2, 126.8, 126.1, 121.7, 121.2. EIMS (m/z, (%)): 296 (72), 219 (24), 86 (100), 47 (85). HRMS (EI; m/z): calcd for C$_{21}$H$_{16}$N$_2$: 296.1314; found 296.1312.

General Procedure B (Buchwald-Hartwig Couplings). An oven-dried reaction tube under argon containing a mixture of Pd$_2$(dba)$_3$·CHCl$_3$ (10 mg, 0.01 mmol), **297i** (8 mg, 0.02 mmol) and NaO*t*-Bu (67 mg, 0.70 mmol) in PhMe (2.5 mL) was treated with an aryl halide (**316a,b,d,e,h**) (0.50 mmol) and morpholine (52 µL, 0.60 mmol). The resulting green-brown mixture was heated at 100 °C for 22 h. After cooling to room temperature,

the reaction mixture was diluted with Et$_2$O (5 mL) and filtered through a pipette containing a plug of silica gel while eluting with additional Et$_2$O. Evaporation of the solvent under reduced pressure and recrystallization or column chromatography of crude material gave products **317a,b,d,e,h**.

N-(4-Trifluoromethylphenyl)morpholine (317a).
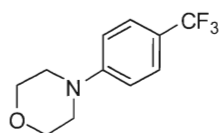
According to General Procedure B, a mixture of 4-chloro trifluoromethylbenzene (67 μL, 0.50 mmol), morpholine (52 μL, 0.60 mmol), NaO*t*-Bu (67 mg, 0.70 mmol), Pd$_2$(dba)$_3$·CHCl$_3$ (10 mg, 0.01 mmol) and **297i** (8 mg, 0.02 mmol) in PhMe (2.5 mL) was heated, cooled and filtered. Evaporation of the solvent under reduced pressure and column chromatography of the pre-adsorbed crude material (silica, 80:20 hexanes/Et$_2$O) gave **317a** (89 mg, 77%) as off-white crystals. Spectroscopic data matched literature reports.[114] ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.50 (d, 2H, *J* = 8.7 Hz), 6.92 (d, 2H, *J* = 8.7 Hz), 3.87 (t, 4H, *J* = 4.8 Hz), 3.24 (t, 4H, *J* = 5.1 Hz); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 153.3, 126.4 (q, *J* = 3 Hz), 124.6 (q, *J* = 271 Hz), 120.9 (q, *J* = 33 Hz) 114.3, 66.6, 48.1.

N-(4-Acetylphenyl)morpholine (317b).
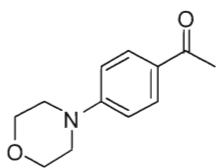
According to General Procedure B, a mixture of 4-chloroacetophenone (65 μL, 0.50 mmol), morpholine (52 μL, 0.60 mmol), NaO*t*-Bu (67 mg, 0.70 mmol), Pd$_2$(dba)$_3$·CHCl$_3$ (10 mg, 0.01 mmol) and **297i** (8 mg, 0.02 mmol) in PhMe (2.5 mL) was heated, cooled and filtered. Evaporation of the solvent under reduced pressure and column chromatography of the

pre-adsorbed crude material (silica, 83:15:2 to 78:20:2 hexanes/EtOAc/Et$_3$N) gave **317b** (76 mg, 74%) as a pale yellow solid. Spectroscopic data matched literature reports. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.90 (d, 2H, J = 9.0 Hz), 6.87 (d, 2H, J = 9.0 Hz), 3.86 (t, 4H, J = 4.8 Hz), 3.31 (t, 4H, J = 5.1 Hz), 2.53 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 196.4, 154.2, 130.3, 128.1, 113.2, 66.5, 47.5, 26.1.

N-(2-Nitrophenyl)morpholine (317d).
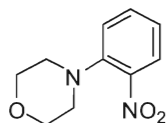
According to General Procedure B, a mixture of 2-nitro chlorobenzene (79 mg, 0.50 mmol), morpholine (52 μL, 0.60 mmol), NaO*t*-Bu (67 mg, 0.70 mmol), Pd$_2$(dba)$_3$·CHCl$_3$ (10 mg, 0.01 mmol) and **297i** (0.4 mL of 0.05 M solution in PhMe) in PhMe (2.5 mL) was heated, cooled and filtered. Evaporation of the solvent under reduced pressure and column chromatography of the pre-adsorbed crude material (silica, 40:60 Et$_2$Ohexanes) gave **317d** (45 mg, 43%) as a yellow oil. Spectroscopic data matched literature reports.[118] ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.79 (d, 1H, J = 8.1 Hz), 7.52-7.47 (m, 1H), 7.15 (d, 1H, J = 8.3 Hz), 7.10-7.06 (m, 1H), 3.85-3.83 (m, 4H), 3.07-3.04 (m, 4H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 145.8, 143.7, 133.5, 125.9, 122.3, 120.9, 66.8, 52.1.

N-(4-Methoxyphenyl)morpholine (317e).
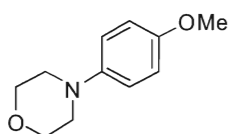
According to General Procedure B, a mixture of 4-bromoanisole (63 μL, 0.50 mmol), morpholine (52 μL, 0.60 mmol), NaO*t*-Bu (67 mg, 0.70 mmol), Pd$_2$(dba)$_3$·CHCl$_3$ (10 mg, 0.01 mmol), and **297i** (8 mg, 0.02 mmol) in PhMe (2.5 mL) was heated, cooled and filtered.

Evaporation of the solvent under reduced pressure and column chromatography of the pre-adsorbed crude material (silica, 50:48:2 Et$_2$O/hexanes/Et$_3$N) gave **317e** (64 mg, 67%) as an off-white solid. Spectroscopic data matched literature reports.[119] ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.92-6.84 (m, 4H), 3.86 (t, 4H, J = 4.8 Hz), 3.77 (s, 3H), 3.06 (t, 4H, J = 4.8 Hz); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 153.9, 145.5, 117.7, 114.4, 66.9, 55.5, 50.7.

N-Phenylmorpholine (317h).
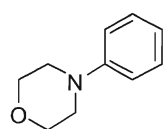
According to General Procedure B, a mixture of bromobenzene (53 µL, 0.50 mmol), morpholine (52 µL, 0.60 mmol), NaOt-Bu (67 mg, 0.70 mmol), Pd$_2$(dba)$_3$·CHCl$_3$ (10 mg, 0.01 mmol) and **297i** (8 mg, 0.02 mmol) in PhMe (2.5 mL), was heated, cooled and filtered. Column chromatography (silica, 93:6:1 hexanes/Et$_2$O/Et$_3$N) gave **317h** (67 mg, 82%) as a colorless solid. Spectroscopic data matched literature reports.[118] ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.32 (t, 2H, J = 4.2 Hz), 6.97-6.91 (m, 3H), 3.90 (t, 4H, J = 2.4 Hz), 3.19 (t, 4H, J = 2.4 Hz); ^{13}C NMR (150.9 MHz, CDCl$_3$) δ 151.3, 129.2, 120.1, 115.7, 67.0, 49.4.

(S)-2-Dimethylamino-1-ferrocenecarboxaldehyde [(S)-297a] and (S)-2-Dimethylamino-1,1'-ferrocene-dicarboxaldehyde [(S)-332a].
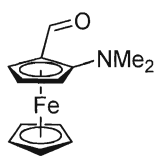
A solution of (S,S)-**327** (134 mg, 0.53 mmol) in t-BuOMe (4 mL) was cooled to –40 °C, treated with i-PrLi (1.18 mL, 1.34 M, 1.58 mmol) and a solution of DMAE (47 mg, 0.53 mmol) in t-BuOMe (1 mL), and the mixture was stirred for 20 min. This solution was transferred by cannula to a mixture of **295**·BF$_3$ at –78 °C [prepared by addition of BF$_3$·OEt$_2$ (66 µL, 0.53 mmol) to a solution of

295 (115 mg, 0.50 mmol) in *t*-BuOMe (5 mL) at 0 °C and stirring for 10 min]. After stirring for 10 min, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, the electrophile DMF (96 µL, 1.25 mmol) was added and the mixture was allowed to warm to room temperature over 16 h. The reaction mixture was diluted with Et$_2$O and worked-up by addition of a saturated solution of aqueous NaHCO$_3$. The aqueous layer was extracted with Et$_2$O (2 x 10 mL) and the combined organic extract was washed with H$_2$O (1 x 10 mL), saturated NaCl solution (1 x 10 mL), dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure on a rotary evaporator. Gradient flash column chromatography (95:5 to 90:10 to 80:20 CH$_2$Cl$_2$/Et$_2$O) gave, sequentially **295** (22 mg, 19%), (*S*)-**297a** (78 mg, 61%) as a red oil and (*S*)-**332a** (13 mg, 9%) as a red oil.

(*S*)-**297a.** CSP HPLC analysis (Chiralpak AS-H; eluent: 80:20 hexanes/*i*-PrOH, 1.0 mL/min) determined an enantiomeric ratio (er) of 91:9 (82% ee) [t_R(minor) = 12.48 min, t_R(major) = 26.38 min]. All other spectroscopic data matched racemic (±)-**297a** (*vide supra*).

(*S*)-**332a.** [α]$_D^{20}$ +118.9 (*c* 0.09, CHCl$_3$); CSP HPLC analysis (Chiralpak AS-H; eluent: 60:40 hexanes/*i*-PrOH, 1.0 mL/min) determined an er of 91.5:8.5 (83% ee) [t_R(minor) = 28.19 min, t_R(major) = 40.3 min]; IR (KBr): v_{max} 3113, 3099, 2959, 2870, 2806, 1644, 1522, 1233, 1034 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 10.13 (s, 1H), 9.93 (s, 1H), 4.90-4.89 (m, 1H), 4.86-4.85 (m, 1H), 4.70-4.66 (m, 2H), 4.43 (t, 1H, *J* = 2.7 Hz), 4.27 (dd, 1H, *J* = 2.7, 1.8 Hz), 2.73 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 192.8, 192.1, 119.6, 80.2, 74.1, 73.5, 70.65, 70.60, 70.4,

68.5, 67.3, 60.1, 44.6; EIMS [m/z, (%)] 285 (100), 119 (35); HRMS (EI) calcd for $C_{14}H_{15}NO_2{}^{56}Fe$: 285.0452; found 285.0446.

(S)-2-[(Diphenylhydroxy)methyl]-1-dimethylaminoferrocene [(S)-297b].
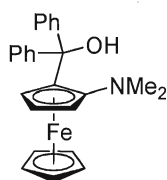
A solution of (S,S)-**327** (267 mg, 1.05 mmol) in t-BuOMe (5 mL) was cooled to –40 °C, treated with i-PrLi (0.42 mL, 2.49 M in pentane, 1.05 mmol), and the mixture was stirred for 20 min. This solution was transferred by cannula to a mixture of **295**·BF₃ at –78 °C [prepared by addition of BF₃·OEt₂ (66 μL, 0.53 mmol) to a solution of **295** (115 mg, 0.50 mmol) in t-BuOMe (5 mL) at 0 °C and stirring for 10 min]. After stirring for 10 min, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, an ice-cooled solution of benzophenone (200 mg, 2.20 mmol) in MTBE (5 mL) was added by cannula, and the mixture was allowed to warm to room temperature over 19 h. The reaction mixture was diluted with Et₂O and worked-up by addition of a saturated aqueous solution of NaHCO₃. The aqueous layer was extracted with Et₂O (1 x 10 mL) and the combined organic extract was washed with H₂O (1 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure on a rotary evaporator. The crude mixture was dissolved in 1:1 THF/MeOH (10 mL) and treated with an aqueous solution of NaBH₄ (42 mg, 1.10 mmol) at room temperature for 16 h to reduce excess benzophenone. The reaction mixture was then poured into an ice-cold solution of saturated aqueous NH₄Cl and subsequently brought to pH 8 by addition of saturated aqueous NaHCO₃. Solvents were removed on a rotary evaporator and the remaining aqueous layer was extracted with Et₂O (2 x 10 mL). The

combined organic extract was washed with H_2O (1 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash column chromatography (silica gel, 98:2 hexanes/Et_2O) gave alcohol (S)-**297b** (152 mg, 74%) as an orange powder: mp 189-192 °C; $[\alpha]_D^{20}$ +45.8 (c 1.0, $CHCl_3$). Determination of the enantiomeric ratio by CSP HPLC using Daicel Chiralpak AS-H, or Chiralcel OD-H or OB-H columns with mixtures of hexanes, i-PrOH, EtOAc or t-BuOMe as eluents, was unsuccessful; however, one recrystallization from Et_2O at −20 °C afforded orange cubes of constant melting point and optical rotation that were homochiral by X-ray diffraction: mp 191-192 °C; $[\alpha]_D^{20}$ +69.0 (c 1.0, $CHCl_3$); X-Ray analysis was performed on an orange block (0.17 × 0.15 × 0.05 mm^3): $C_{25}H_{25}FeNO$: M = 411.31 g/mol, monoclinic, $P2_1$, a = 9.415(3) Å, b = 10.637(4) Å, c = 10.440(4) Å, V = 997.6(6) Å^3, α = 90 °, β = 107.404(6) °, γ = 90 °, Z = 2, D_c = 1.369 g/cm^3, F(000) = 432, T = 100(2) K; 13421 data were collected. The structure was solved by Direct Methods (SHELXTL) and refined by full-matrix least squares on F^2 resulting in final R, R_w and GOF [for 4424 data with F > 2σ(F)] of 0.0328, 0.0646 and 1.01, respectively, for solution using the (S)-enantiomer model [Flack parameter = 0.010(13)]. All other spectroscopic data matched (±)-**297b** (vide supra).

(R)-2-Dimethylamino-1-(N-phenylferrocenecarboxamide) [(R)-297d].
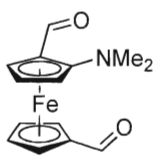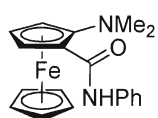

A solution of (R,R)-**323** (327 mg, 1.05 mmol) in t-BuOMe (3 mL) was cooled to –40 °C, treated with i-PrLi (1.05 mL, 1.00 M, 1.05 mmol), and the mixture was stirred for 20 min. This solution was transferred by cannula to a mixture of **295**·BF_3 at –78 °C [prepared by addition of BF_3·OEt_2 (66 μL, 0.53 mmol) to a solution of **295** (115 mg, 0.50 mmol) in t-BuOMe (5 mL) at 0 °C and stirring for 10 min].

After stirring for 10 min, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, the phenylisocyanate (0.14 mL, 1.25 mmol) was added and the mixture was allowed to warm to room temperature over 16 h. The reaction mixture was diluted with Et_2O and worked-up by addition of a saturated solution of aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O (2 x 10 mL) and the combined organic extract was washed with H_2O (1 x 10 mL), saturated NaCl solution (1 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure on a rotary evaporator. Flash column chromatography (88:10:2 hexanes/EtOAc/Et_3N) gave carboxamide (*R*)-**297d** (172 mg, 72%) as a dark orange oil.

(*R*)-**297d**. CSP HPLC analysis (Chiralcel OD-H; eluent: 99:1 hexanes/*i*-PrOH, 1.0 mL/min) determined an enantiomeric ratio (er) of 88:12 (76% ee) [t_R(minor) = 17.60 min, t_R(major) = 18.80 min]. All other spectroscopic data matched (±)-**297d** (*vide supra*).

(*R*)-2-Trimethylsilyl-*N,N*-dimethylaminoferrocene [(*R*)-297e].

A solution of (*S,S*)-**327** (267 mg, 1.05 mmol) in *t*-BuOMe (5 mL) was cooled to –40 °C, treated with *i*-PrLi (0.42 mL, 2.49 M in pentane, 1.05 mmol), and the mixture was stirred for 20 min. This solution was transferred by cannula to a mixture of **295**·BF_3 at –78 °C [prepared by addition of BF_3·OEt_2 (66 µL, 0.53 mmol) to a solution of **295** (115 mg, 0.50 mmol) in *t*-BuOMe (5 mL) at 0 °C and stirring for 10 min]. After stirring for 10 min, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, $ClSiMe_3$ (0.16 mL, 1.25 mmol) was added and the mixture

was allowed to warm to room temperature over 19 h. The reaction mixture was diluted with Et_2O and worked-up by addition of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O (1 x 10 mL) and the combined organic extract was washed with H_2O (1 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash column chromatography (silica gel, 95:5 hexanes/EtOAc) gave silane (R)-**297e** (58 mg, 39%) as an orange oil: $[\alpha]_D^{20}$ −128 (c 1.0, $CHCl_3$); for er determination, see (R)-**301**; All other spectroscopic data matched (±)-**297e** (*vide supra*).

(R)-3-Trimethylsilyl-2-dimethylamino-1-ferrocenecarboxaldehyde [(R)-301].
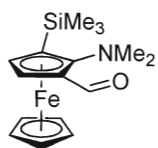
To a solution of enriched silane (R)-**297d** (58 mg, 0.19 mmol) in THF (2 mL) at 0 °C under argon was added $BF_3 \cdot OEt_2$ (25 μL, 0.20 mmol). After stirring for 10 min, the yellow solution was cooled to −78 °C, treated with *n*-BuLi (0.22 mL, 1.79 M in hexanes, 0.39 mmol) and immediately warmed to −40 °C for 1 h. The reaction mixture was then cooled back to −78 °C before addition of DMF (37 μL, 0.48 mmol) and allowed to warm slowly to room temperature. After addition of Et_2O, the reaction mixture was worked-up by addition of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O (1 x 10 mL) and the combined organic extract was washed with H_2O (1 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash column chromatography (silica gel, 90:10 hexanes/EtOAc) gave the title compound, (R)-**301** (35 mg, 56%) as a dark red oil: $[\alpha]_D^{20}$ −557 (c 0.18, $CHCl_3$); CSP HPLC (Chiralpak AS-H, 95:5 hexanes/*i*-PrOH, 1.0 mL/min) determined an er of 88.5:11.5 [t_R(minor) = 6.36 min, t_R(major) = 8.63 min]. All other spectroscopic data matched (±)-**301** (*vide supra*).

(*R*)-2-Trimethylstannyl-1-dimethylaminoferrocene [(*R*)-297f)].
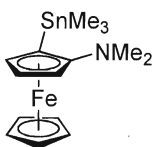
A solution of (*S,S*)-**327** (102 mg, 0.40 mmol) in *t*-BuOMe (4 mL) was cooled to –40 °C, treated with *i*-PrLi (0.90 mL, 1.34 M, 1.20 mmol) and as solution of dimethylaminoethanol (DMAE, 36 mg, 0.40 mmol) in *t*-BuOMe (1 mL), and the mixture was stirred for 20 min. This solution was transferred by cannula to a mixture of **295**·BF$_3$ at –78 °C [prepared by addition of BF$_3$·OEt$_2$ (66 µL, 0.53 mmol) to a solution of **295** (115 mg, 0.50 mmol) in *t*-BuOMe (5 mL) at 0 °C and stirring for 10 min]. After stirring for 10 min, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, chlorotrimethylstannane (1 mL, 1.0 M solution in hexane, 1.0 mmol) was added and the mixture was allowed to warm to room temperature over 16 h. The reaction mixture was diluted with Et$_2$O and worked-up by addition of a saturated solution of aqueous NaHCO$_3$. The aqueous layer was extracted with Et$_2$O (2 x 10 mL) and the combined organic extract was washed with 10% aqueous potassium fluoride solution (2 x 10 mL), H$_2$O (1 x 10 mL) and saturated NaCl solution (1 x 10 mL), dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure on a rotary evaporator. Gradient flash column chromatography (98:2 to 95:5 hexanes/EtOAc) gave, (*R*)-**297f** (83 mg, 42%) as a red oil. All other spectroscopic data of (*R*)-**297f** matched (±)-**297f** (*vide supra*).

Transmetalation: The enantiomeric purity of (*R*)-**297f** was determined by conversion of the stannane to the aldehyde. A solution of (*R*)-**297f** (13 mg, 0.00372 mmol) in THF (1 mL) at –40 °C was treated with methyllithium (61 µL, 1.15 M in Et$_2$O, 0.00697 mmol) and stirred for 1 h. Dimethylformamide (6 µL, 0.008 mmol) was added

and the mixture was left to warm slowly to room temperature. The reaction mixture was diluted with Et$_2$O and worked-up by addition of a saturated solution of aqueous NaHCO$_3$. The aqueous layer was extracted with Et$_2$O (2 x 10 mL) and the combined organic extract was washed with 10% aqueous potassium fluoride solution (2 x 10 mL), H$_2$O (1 x 10 mL) and saturated NaCl solution (1 x 10 mL), dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure on a rotary evaporator. The mixture was filtered through a pad of silica gel, eluting with Et$_2$O to give (S)-**297a** (8 mg, 89%) as a red oil CSP HPLC analysis (Chiralpak AS-H; eluent: 80:20 hexanes/i-PrOH, 1.0 mL/min) determined an enantiomeric ratio (er) of 91:9 (82% ee) [t_R(minor) = 13.9 min, t_R(major) = 29.2 min]. All other spectroscopic data matched (±)-**297a** (*vide supra*).

(*R*)-2-Thiophenyl-1-dimethylaminoferrocene [(*R*)-297h].
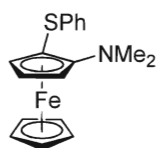
A solution of (*S,S*)-**327** (102 mg, 0.40 mmol) in t-BuOMe (5 mL) was cooled to –40 °C, treated with i-PrLi (0.53 mL, 2.25 M in pentane, 1.20 mmol) and a solution of dimethylaminoethanol (36 mg, 0.40 mmol) in t-BuOMe (1 mL), and the mixture was stirred for 20 min. This solution was transferred by cannula to a mixture of **295·BF$_3$** at –78 °C [prepared by addition of BF$_3$·OEt$_2$ (66 µL, 0.53 mmol) to a solution of **295** (115 mg, 0.50 mmol) in t-BuOMe (5 mL) at 0 °C and stirring for 10 min]. After stirring for 10 min, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, a solution of phenyl disulfide (273 mg, 1.25 mmol) in $t$-BuOMe (5 mL) was added over 2 min and the mixture was allowed to warm to room temperature over 16 h. The reaction mixture was diluted with Et$_2$O and worked-up by addition of saturated

aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O (1 x 10 mL) and the combined organic extract was washed with water (1 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash column chromatography (silica gel, 99:1 hexanes/EtOAc) gave (R)-**297h**, (120 mg, 71%) as an orange oil: $[\alpha]_D^{20}$ −43.6 (c 1.0, $CHCl_3$); for er determination, see (R)-**302.** All other spectroscopic data matched (±)-**297h** (*vide infra*).

(R)-3-Thiophenyl-2-dimethylamino-1-ferrocenecarboxaldehyde [(R)-302].

To a solution of enriched sulfide (R)-**297h** (41 mg, 0.12 mmol) in THF (1 mL) at 0 °C under argon was added BF_3·OEt_2 (16 µL, 0.13 mmol). After stirring for 10 min, the yellow solution was cooled to −78 °C, treated with *n*-BuLi (0.12 mL, 1.95 M in hexanes, 0.24 mmol) and immediately warmed to −40 °C for 1 h. The reaction mixture was then cooled back to −78 °C before addition of DMF (23 µL, 0.30 mmol) and allowed to warm slowly to room temperature. The reaction mixture was diluted with Et_2O and worked-up by addition of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O (1 x 10 mL) and the combined organic extract was washed with H_2O (1 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash column chromatography (silica gel, 90:10 hexanes/EtOAc) gave (R)-**302** (14 mg, 32%) as a dark red oil: $[\alpha]_D^{20}$ −175 (c 0.14, $CHCl_3$); CSP HPLC (Chiralpak AS-H, 90:10 hexanes/*i*-PrOH, 1.0 mL/min) determined an er of 88:12 [t_R(minor) = 13.04 min, t_R(major) = 16.85 min]. All other spectroscopic data matched (±)-**302** (*vide supra*).

Preparation of (*S*)-[2-(Diphenylphosphinothioyl)ferrocenyl]-1-dimethylamine [(*S*)-297i].
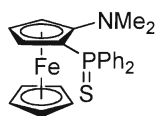
A solution of (*R,R*)-**326** (390 mg, 1.38 mmol) in *t*-BuOMe (3 mL) was cooled to –40 °C, treated sequentially with *i*-PrLi (2.23 mL, 1.85 M in pentane, 4.13 mmol) and dimethylaminoethanol (124 mg, 1.39 mmol) in *t*-BuOMe (3 mL), and stirred for 20 min at that temperature. The solution was transferred by cannula to a pre-formed mixture of **295**·BF_3 at –78 °C [prepared by addition of BF_3·OEt_2 (175 μL, 1.39 mmol) to a solution of $FcNMe_2$ (300 mg, 1.31 mmol) in *t*-BuOMe (13 mL) at 0 °C and stirring for 10 min]. After stirring for 10 min at –78 °C, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, $ClPPh_2$ (600 μL, 3.27 mmol) was added and the mixture was allowed to warm slowly to room temperature. The reaction mixture was diluted with Et_2O and worked-up by addition of a saturated solution of aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O (3 x 15 mL) and the combined organic extract was washed with H_2O (1 x 15 mL), brine (1 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure on a rotary evaporator to afford the crude aminophosphine. To the crude mixture in a dry round bottom flask was added sulfur powder (1.59 g, 49.6 mmol) under argon. Toluene (25 mL) was added and the reaction mixture heated at 40 °C for 2 h. The reaction mixture was gravity filtered to remove excess sulfur and pre-adsorbed on silica gel. Flash column chromatography (90:10 pentane/diethyl ether) gave (*S*)-**297i** (285 mg, 50%) as an orange foam. $[\alpha]^{20}_D$ +38.5 (*c* 1.0, $CHCl_3$); CSP HPLC analysis (Chiralpak OD-H; eluent: 99:1 hexanes/*i*-PrOH, 1.0 mL/min) determined a 88.5:11.5 er (77% ee) [t_R(minor) = 6.74 min, t_R(major) = 7.23

min]; IR (KBr) ν_{max} 3394, 2950, 2788, 1494, 1419 cm^{-1}; ^{31}P NMR (121.5 MHz, CDCl$_3$) 44.2 ppm; ^{1}H NMR (300 MHz, CDCl$_3$) 8.00-7.88 (m, 2H), 7.79-7.71 (m, 2H), 7.48-7.36 (m, 6H), 4.33 (s, 5H), 4.29 (s, 1H), 4.13 (s, 1H), 3.81 (s, 1H), 2.50 (s, 6H) ppm; ^{13}C NMR (75 MHz, CDCl$_3$) 135.4 (d, J = 87.5 Hz), 133.5 (d, J = 86.8 Hz), 132.6 (d, J = 10.6 Hz), 131.8 (d, J = 10.6 Hz), 131.1 (d, J = 2.3 Hz), 130.8 (d, J = 2.3 Hz), 127.9 (d, J = 12.8 Hz), 117.2 (d, J = 9.1 Hz), 72.3 (d, J = 13.6 Hz), 69.9, 67.1 (d, J = 92.8 Hz), 65.3 (d, J = 11.3 Hz), 61.8 (d, J = 8.3 Hz), 46.0 ppm; EIMS [m/z(%)] 445 (M$^+$, 100), 413 (32); HRMS (EI) calcd for C$_{24}$H$_{24}$NP^{56}Fe: 445.07161; found 445.07158. Anal. Calcd for C$_{24}$H$_{24}$NPSFe: C, 64.73; H, 5.43. Found: C, 64.79; H, 5.44.

(*R*)-2-Iodo-1-dimethylaminoferrocene [(*R*)-297k].
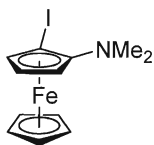
A solution of (*S,S*)-**327** (204 mg, 0.80 mmol) in *t*-BuOMe (5 mL) was cooled to –40 °C, treated with *i*-PrLi (1.79 mL, 1.34 M, 2.40 mmol) and as solution of dimethylaminoethanol (DMAE, 71 mg, 0.80 mmol) in *t*-BuOMe (1 mL), and the mixture was stirred for 20 min. This solution was transferred by cannula to a mixture of **295**·BF$_3$ at –78 °C [prepared by addition of BF$_3$·OEt$_2$ (0.13 mL, 1.05 mmol) to a solution of **295** (229 mg, 1.00 mmol) in *t*-BuOMe (8 mL) at 0 °C and stirring for 10 min]. After stirring for 10 min, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, a solution of 1,2-diiodoethane (705 mg, 2.5 mmol) in *t*-BuOMe (5 mL) was added over 2 min and the mixture was allowed to warm to room temperature over 16 h. The reaction mixture was diluted with Et$_2$O and worked-up by addition of a saturated solution of aqueous NaHCO$_3$. The aqueous layer was extracted with Et$_2$O (2 x 10 mL)

and the combined organic phase was washed with saturated sodium thiosulfate solution (2 x 10 mL), water (2 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure on a rotary evaporator. The reaction mixture was dissolved in 95:5 pentane/Et^2O and filtered through a pad of silica gel. Concentration of the filtrate in vacuo gave (R)-**297k** (168 mg, 47%). Spectroscopic data of (R)-**297k** matched (±)-**297k** (*vide supra*).

The enantiomeric purity of (R)-**297k** was determined by conversion of the iodide to the acetate. A solution of (R)-**297k** (11 mg, 0.031 mmol) in absolute EtOH (0.5 mL) was treated with $Cu(OAc)_2 \cdot H_2O$ (8 mg, 0.039 mmol) and heated at reflux for 10 min to give a dark mixture. After cooling to room temperature, the mixture was concentrated under reduced pressure. The residue was dissolved in Et_2O and filtered through a pipette of silica gel and the filtrate was concentrated to give (R)-**298** (7 mg, 78%) as a yellow film; CSP HPLC analysis (Chiralcel OD-H; eluent: 95:5: hexanes/i-PrOH, 1.0 mL/min) determined an enantiomeric ratio (er) of 88:12 (76% ee) [t_R(minor) = 8.4 min, t_R(major) = 10.4 min]. All other spectroscopic data of (R)-**298** matched (±)-**298** (*vide supra*).

Preparation of N,N,N'',N''-Tetramethyl-2,2''-diamino-1,1''-biferrocene (R,R)-299.
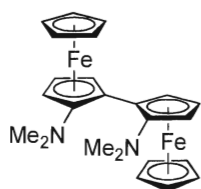
A mixture of (S)-**297k** (96 mg, 0.27 mmol), dichloromethane (5 mL) and purified Cu powder (860 mg, 13.5 mmol) was concentrated to dryness under reduced pressure. The resulting solid mass was heated under argon at 110 °C for 17 h. After cooling to room temperature, the solid mass was taken up in dichloromethane (20 mL) and filtered through Celite in a sintered funnel. Concentration of the filtrate under reduced pressure and gradient column chromatography

(neutral alumina, 99:1 to 95:5 hexanes/Et$_2$O) gave, sequentially, *meso*-**299** (11 mg, 18%) as red-orange solid, and (*R,R*)-**299** (35 mg, 56%) as a yellow-orange solid;

(*R,R*)-**299**. mp 115-116 °C; [α]$_D^{20}$ –517 (*c* 1, CHCl$_3$). Two recrystallizations from isopropanol afforded (*R,R*)-**299** with the following physical data: mp 143-145 °C (isopropanol); [α]$_D^{20}$ – 695° (c = 1 CHCl$_3$). All other spectroscopic data of (*R,R*)-**299** matched that of (±)-**299** (*vide supra*).

N-Ferrocenylsuccinimide (336).
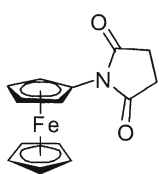
A solution of succinic anhydride (378 mg, 3.78 mmol) in THF (10 mL) was added to a solution of aminoferrocene **155** (760 mg, 3.78 mmol) in Et$_2$O (25 mL) and stirred for 2 h, at which point the mixture was concentrated on a rotary evaporator to yield a viscous brown oil as the intermediate amide. To this was added a suspension of NaOAc (310 mg, 3.78 mmol) in Ac$_2$O (8 mL) and the resulting mixture was heated at 80 °C for 1 h. The reaction mixture was poured into an ice cold solution of saturated aqueous NaHCO$_3$ (20 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with H$_2$O (1 × 20 mL), brine (1 × 20 mL), dried over anhydrous Na$_2$SO$_4$ and all volatiles were removed *in vacuo*. The residue was preadsorbed on silica and filtered through a pad of silica, eluting with 50:50 hexanes/EtOAc. Concentration of the filtrate and recrystallization from hexanes/EtOAc gave ferrocenyl succinimide **336** (838 mg, 78%) as dark orange crystals; R_f 0.53 (75:25 EtOAc/hexanes); mp 187-189 °C (EtOAc/hexanes); IR (KBr) v_{max} 3147, 2970, 1707, 1468, 1149 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.90 (t, 2H, *J* = 2.0 Hz), 4.19 (s, 5H), 4.16 (t, 2H, *J* = 2.0 Hz), 2.77 (s, 4H); ^{13}C NMR (300 MHz, CDCl$_3$) δ 175.6,

88.7, 69.6, 65.6, 63.1, 28.2; EIMS [m/z(%)] 283 (M$^+$, 100), 218 (22); HRMS (EI) calcd for C$_{14}$H$_{13}$NO$_2$^{56}Fe: 283.0295; found 283.0293; Anal. calcd for C$_{14}$H$_{13}$NO$_2$Fe: C, 59.40; H, 4.63; Found: C, 59.31; H, 4.58.

N-Ferrocenylpyrrolidine (337).
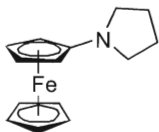
A solution of BH$_3$·THF (5.02 mL, 0.80 M in THF, 4.00 mmol) was added to a room temperature solution of succinimide **336** (284 mg, 1.00 mmol) in THF (5 mL) and the resulting mixture heated at reflux for 2 h. The reaction mixture was then cooled to 0 °C, diluted with Et$_2$O and quenched with aq. 10% NaOH until gas evolution ceased. The layers were separated and the organic washed with H$_2$O (1 × 10 mL), brine (1 × 10 mL), dried over anhydrous Na$_2$SO$_4$ and all volatiles removed *in vacuo*. The crude was taken up in hexanes, filtered through a pad of basic alumina and concentrated. Recrystallization from hexanes gave *N*-ferrocenyl pyrrolidine **337** (232 mg, 91%) in two crops; R_f 0.63 (30:70 Et$_2$O/hexanes); mp 105-106 °C (hexanes); IR (KBr) v_{max} 2964, 2904, 2872, 2810, 1510 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 4.16 (s, 5H), 3.83 (t, 2H, J = 1.8 Hz), 3.69 (t, 2H, J = 2.1 Hz), 3.03-2.88 (m, 4H), 1.96-1.84 (m, 4H); ^{13}C NMR (300 MHz, CDCl$_3$) δ 115.0, 67.9, 64.0, 56.4, 51.6, 25.8; EIMS [m/z(%)] 255 (M$^+$, 100); HRMS (EI) calcd for C$_{14}$H$_{17}$N^{56}Fe: 255.0710; found 255.0703; Anal. calcd for C$_{14}$H$_{17}$NFe: C, 65.91; H, 6.72; Found: C, 65.67; H, 6.63.

N-Ferrocenylpyrrolidin-2-one (338).
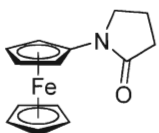
On several occasions during the preparation of **337**, a more polar reduction product was also observed (in up to 50% yield) and assigned the

structure of *N*-Ferrocenylpyrrolidin-2-one (**338**). It appeared as yellow plates after recrystallization from EtOAc/hexanes and had the following properties: R_f 0.35 (75:25 EtOAc/hexanes); mp 134-135 °C (EtOAc/hexanes); IR (KBr) v_{max} 2977, 2933, 2880, 1683, 1499 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.69 (t, 2H, *J* = 2.1 Hz), 4.14 (s, 5H), 4.01 (t, 2H, *J* = 1.8 Hz), 3.65 (t, 2H, *J* = 6.9 Hz), 2.44 (t, 2H, *J* = 8.1 Hz), 2.10 (q, 2H, *J* = 3.9 Hz); ^{13}C NMR (300 MHz, CDCl$_3$) δ 173.5, 96.2, 68.6, 64.6, 60.1, 48.5, 32.2, 18.1; EIMS [*m/z*(%)] 269 (M$^+$, 100), 204 (68); HRMS (EI) calcd for C$_{14}$H$_{15}$NO^{56}Fe: 269.0503; found 269.0508.

(*R*)-2-Pyrrolidinyl-1-ferrocenecarboxaldehyde [(*R*)-339a].
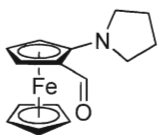
A solution of ligand (*R,R*)-**323** (256 mg, 0.82 mmol) in *t*-BuOMe (2.5 mL) was cooled to –40 °C, treated with *i*-PrLi (0.82 mL, 1.00 M, 0.82 mmol) and stirred for 20 min at that temperature. The solution was transferred by cannula to a mixture of **337**·BF$_3$ at –78 °C [prepared by addition of BF$_3$·OEt$_2$ (52 µL, 0.41 mmol) to a solution of **337** (100 mg, 0.39 mmol) in *t*-BuOMe (4 mL) at 0 °C and stirring for 10 min]. After stirring for 10 min, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, DMF (75 µL, 0.98 mmol) was added and the reaction mixture was allowed to warm to room temperature over 16 h. The reaction mixture was diluted with Et$_2$O and worked-up by addition of saturated aqueous NaHCO$_3$. The aqueous layer was extracted with Et$_2$O (1 x 10 mL) and the combined organic extract was washed with H$_2$O (1 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na$_2$SO$_4$ and concentrated in vacuo. Flash column chromatography (silica gel, 95:5 CH$_2$Cl$_2$/Et$_2$O) gave (*R*)-**339a** (47

mg, 43%) as a red oil that crystallized on standing; mp 78-80 °C (hexanes); $[\alpha]_D^{20}$ –264 (c = 0.10 CHCl$_3$); CSP HPLC analysis (Chiralpak AS-H; eluent: 80:20 hexanes/i-PrOH, 1.0 mL/min) determined an er of 87:13 (74% ee) [t_R(major) = 21.42 min, t_R(minor) = 27.32 min]; IR (KBr) v_{max} 3442, 2956, 2875, 2823, 1648 cm^{-1}; ^{1}H NMR (600 MHz, acetone-d_6) δ 10.23 (s, 1H), 4.59 (s, 1H), 4.37 (s, 1H), 4.28 (s, 6H), 3.26 (m, 2H) 3.16 (m, 2H), 1.99-1.96 (m, 4H); ^{13}C NMR (150.9 MHz, acetone-d_6) δ 193.8, 115.7, 69.34, 69.29, 68.3, 65.9, 61.8, 53.5, 26.1; EIMS [m/z(%)] 283 (M+, 100), 145 (53); HRMS (EI) calcd for C$_{15}$H$_{17}$NO^{56}Fe: 283.0660; found 283.0659.

(S)-N-(2-iodoferrocenyl)pyrrolidine [(S)-339b].
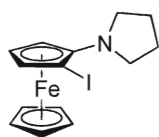
This procedure is best conducted in subdued light. A solution of (R,R)-326 (155 mg, 0.55 mmol) in t-BuOMe (6 mL) was cooled to –40 °C, treated with i-PrLi (0.67 mL, 2.45 M in pentane, 1.65 mmol) and a solution of dimethylaminoethanol (50 mg, 0.55 mmol) in t-BuOMe (1 mL), and the mixture was stirred for 20 min. This solution was transferred by cannula to a mixture of 337·BF$_3$ at –78 °C [prepared by addition of BF$_3$·OEt$_2$ (90 µL, 0.72 mmol) to a solution of 337 (175 mg, 0.69 mmol) in t-BuOMe (6 mL) at 0 °C and stirring for 10 min]. After stirring for 10 min, the mixture was allowed to warm slowly to –40 °C over 2 h and then held at that temperature for an additional hour. After cooling back to –78 °C, a solution of 1,2-diiodoethane (329 mg, 1.17 mmol) in t-BuOMe (5 mL) was added over 2 min and the mixture was allowed to warm to room temperature over 16 h. The reaction mixture was diluted with Et$_2$O and worked-up by addition of saturated aqueous NaHCO$_3$. The aqueous layer was extracted with Et$_2$O (1 x 10 mL) and the combined organic phase was washed

with saturated aqueous sodium thiosulfate (2 x 10 mL), water (2 x 10 mL), brine (1 x 10 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The reaction mixture was dissolved in 95:5 pentane/Et_2O and filtered through a pad of silica gel. Concentration of the filtrate in vacuo gave (*S*)-**339b** (161 mg, 62%) as an orange oil: $[\alpha]_D^{20}$ +3.0 (*c* 1.0, acetone); for er determination, the iodide was converted to the corresponding *O*-acetate (*vide infra*); IR (KBr, neat) v_{max} 3092, 2965, 2872, 2812, 1492, 1477, 1459 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 4.22 (s, 5H), 4.17-4.12 (m, 1H), 4.00 (t, 1H, J = 3.0 Hz), 3.95-3.89 (m, 1H), 3.38-3.24 (m, 2H), 3.17-3.06 (m, 2H), 1.98-1.77 (m, 4H); ^{13}C NMR (75 MHz, acetone-d_6) δ 111.8, 71.9, 69.9, 63.9, 57.7, 52.0, 31.4, 24.5; EIMS [*m/z*(%)] 381 (M$^+$, 100); HRMS (EI) calcd for $C_{14}H_{16}N^{56}FeI$: 380.9676; found 380.9672.

A solution of (*S*)-**339b** (77 mg, 0.20 mmol) in absolute EtOH (2.0 mL) was treated with $Cu(OAc)_2 \cdot H_2O$ (50 mg, 0.25 mmol) and heated at reflux for 20 min to give a dark mixture. After cooling to room temperature, the volatiles were removed in vacuo. The residue was dissolved in Et_2O, filtered through a pad of silica gel and the filtrate was concentrated to give (*S*)-*N*-(2-acetoxyferrocenyl)pyrrolidine (21 mg, 33%) as a yellow-brown oil: $[\alpha]_D^{20}$ −60.6 (*c* 0.50, acetone); CSP HPLC analysis (Chiralcel OD-H; eluent: 95:5: hexanes/*i*-PrOH, 1.0 mL/min) determined an enantiomeric ratio of 89:11 (78% ee) [t_R(major) = 7.6 min, t_R(minor) = 19.1 min]; IR (KBr, neat) v_{max} 3095, 2968, 2931, 2871, 2834, 1757, 1520, 1205 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 4.22 (s, 5H), 3.65 (t, 1H, J = 3.0 Hz), 3.12-2.95 (m, 4H), 2.13 (s, 3H), 1.95-1.78 (m, 4H); ^{13}C NMR (75 MHz, acetone-d_6) δ 170.2, 105.6, 104.6, 69.3, 59.4, 57.7, 55.0, 52.0, 25.7, 21.4; EIMS [*m/z*(%)] 313 (M$^+$, 91), 271 (100), 145 (71); HRMS (EI) calcd for $C_{16}H_{19}NO_2^{56}Fe$: 313.0765; found 313.0760.

(+)-*N*-Ferrocenyl-(2*R*,5*R*)-dimethylpyrrolidine (341).
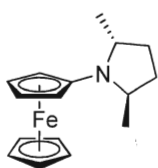
Aminoferrocene **155** (302 mg, 1.50 mmol) was dissolved in THF (8 mL) in a round bottom flask, fitted with a condenser, under argon and cooled to 0 °C. *n*-BuLi (0.75 mL, 2.00 M in hexanes, 1.50 mmol) was added and the mixture stirred 15 minutes at that temperature. The mixture was cooled to −40 °C and a room temperature solution of cyclic sulfate **340**[120] (270 mg, 1.50 mmol) in THF (2 mL) was added by cannula. After warming to room temperature over 30 minutes, the mixture was heated at reflux for 21 h, cooled back to 0 °C and treated with an additional portion of *n*-BuLi (0.75 mL, 2.00 M in hexanes, 1.50 mmol). After warming to room temperature over 30 minutes, the mixture was heated at reflux for 23 h. After cooling to room temperature, the mixture was diluted with Et_2O and quenched with a saturated solution of $NaHCO_3$ (10 mL). The aqueous layer was extracted with Et_2O (1 × 10 mL) and the combined organic extracts were washed with H_2O (1 × 10 mL), brine (1 × 10 mL), dried over Na_2SO_4 and all volatiles were removed *in vacuo*. The crude was dissolved in pentane and filtered through a pad of neutral alumina, eluting with the same solvent, and evaporation of the filtrate afforded dimethylpyrrolidine **341** (250 mg, 59%) as an orange oil; R_f 0.73 (50:50 EtOAc/hexanes); $[\alpha]_D^{20}$ +20.9 (*c* 1.00, hexanes); IR (KBr) v_{max} 3092, 2959, 2925, 2870, 1519 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 4.00 (s, 5H), 3.86-3.79 (m, 2H), 3.72 (s, 1H), 3.63 (s, 1H), 3.55 (t, 2H, *J* = 6.0 Hz); ^{13}C NMR (75 MHz, acetone-d_6) 112.2, 69.3, 63.6, 63.0, 56.0, 55.0, 54.0, 31.7, 19.7; EIMS [*m/z*(%)] 283 (M^+, 100), 268 (74), 121 (43); HRMS (EI) calcd for $C_{16}H_{21}N^{56}Fe$: 283.1023; found 283.1024.

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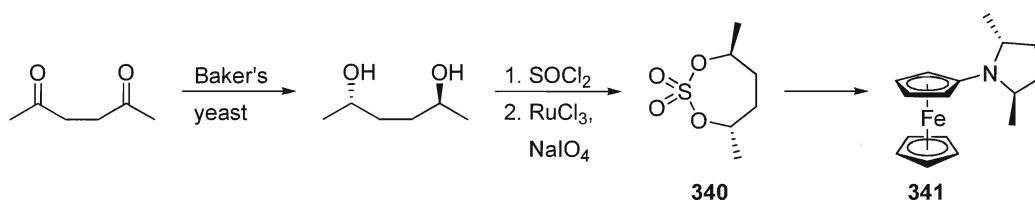
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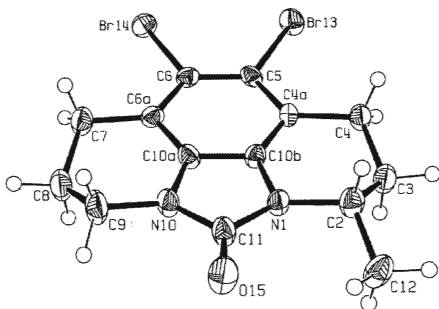
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expression of F^2^ > 2sigma(F^2^) is used only for calculating R-
factors(gt) etc. and is not relevant to the choice of reflections
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198

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C6A 0.0239(17) 0.0244(16) 0.0205(15) -0.0080(12) 0.0008(13) -
0.0059(13)
C7 0.048(2) 0.0289(18) 0.0241(17) -0.0127(14) 0.0040(15) -0.0084(16)
C8 0.062(3) 0.032(2) 0.0297(19) -0.0190(16) 0.0049(18) -0.0045(18)
C9 0.072(3) 0.0248(18) 0.0325(19) -0.0177(15) 0.0051(19) -0.0100(18)
N10 0.0473(19) 0.0175(13) 0.0234(13) -0.0098(11) 0.0045(13) -
0.0073(13)
C10A 0.0309(18) 0.0193(15) 0.0223(15) -0.0087(12) 0.0055(13) -
0.0045(13)
C10B 0.0266(17) 0.0234(16) 0.0192(15) -0.0095(13) 0.0044(13) -
0.0084(14)
C11 0.044(2) 0.0221(16) 0.0248(16) -0.0106(13) 0.0084(15) -
0.0095(15)
C12 0.063(3) 0.0330(19) 0.0240(17) -0.0098(15) 0.0035(17) -
0.0197(19)
O15 0.084(2) 0.0221(12) 0.0283(13) -0.0070(10) 0.0080(13) -
0.0186(13)
N16 0.0378(17) 0.0233(13) 0.0175(13) -0.0097(11) 0.0049(12) -
0.0074(12)
C17 0.049(2) 0.0271(18) 0.0227(17) -0.0070(14) 0.0053(16) -
0.0104(16)
C18 0.055(2) 0.0226(17) 0.0244(17) -0.0065(13) 0.0016(16) -
0.0119(17)
C19 0.047(2) 0.0231(16) 0.0241(17) -0.0115(14) 0.0042(16) -
0.0134(15)
C19A 0.0268(18) 0.0225(16) 0.0193(15) -0.0069(13) 0.0024(13) -
0.0113(14)
C20 0.0297(18) 0.0259(16) 0.0234(15) -0.0162(13) 0.0026(13) -
0.0090(14)
C21 0.0281(18) 0.0304(17) 0.0159(14) -0.0111(13) 0.0038(13) -
0.0085(14)
C21A 0.0341(19) 0.0261(16) 0.0194(15) -0.0086(13) 0.0029(13) -
0.0058(14)
N25 0.056(2) 0.0191(13) 0.0222(14) -0.0099(11) 0.0053(13) -
0.0023(14)
C25A 0.036(2) 0.0215(15) 0.0225(15) -0.0109(13) 0.0033(14) -
0.0045(14)
C25B 0.0295(18) 0.0223(16) 0.0150(14) -0.0059(12) 0.0011(13) -
0.0053(13)
C26 0.047(2) 0.0266(17) 0.0194(15) -0.0097(13) -0.0009(15)
0.0012(16)

C27 0.068(3) 0.0324(19) 0.0222(17) -0.0088(15) 0.0087(18) -
0.0162(19)
O30 0.085(2) 0.0305(14) 0.0249(13) -0.0149(11) 0.0086(14) 0.0001(14)

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 All esds (except the esd in the dihedral angle between two l.s.
planes) are estimated using the full covariance matrix. The cell
esds are taken into account individually in the estimation of esds
in distances, angles and torsion angles; correlations between esds
in cell parameters are only used when they are defined by crystal
symmetry. An approximate (isotropic) treatment of cell esds is used
for estimating esds involving l.s. planes.
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N1 C11 1.394(4) . ?
N1 C2 1.475(4) . ?
C2 C3 1.502(5) . ?
C2 C12 1.505(5) . ?
C3 C4 1.539(4) . ?
C4 C4A 1.509(4) . ?
C4A C10B 1.369(4) . ?
C4A C5 1.408(4) . ?
C5 C6 1.398(4) . ?
C6 C6A 1.402(4) . ?
C6A C10A 1.374(4) . ?
C6A C7 1.505(4) . ?
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C8 C9 1.524(5) . ?
C9 N10 1.454(4) . ?
N10 C10A 1.380(4) . ?
N10 C11 1.391(4) . ?
C10A C10B 1.371(4) . ?
C11 O15 1.216(4) . ?
N16 C25B 1.379(4) . ?
N16 C26 1.393(4) . ?
N16 C17 1.476(4) . ?
C17 C27 1.489(5) . ?
C17 C18 1.507(5) . ?
C18 C19 1.534(4) . ?
C19 C19A 1.512(4) . ?
C19A C25B 1.359(4) . ?
C19A C20 1.405(4) . ?

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C20 C21 1.409(4) . ?
C21 C21A 1.390(4) . ?
C21A C25A 1.365(4) . ?
C21A C22Y 1.487(7) . ?
C21A C22X 1.574(8) . ?
C22X C23X 1.548(11) . ?
C23X C24X 1.528(10) . ?
C24X N25 1.505(8) . ?
C22Y C23Y 1.570(9) . ?
C23Y C24Y 1.573(9) . ?
C24Y N25 1.452(7) . ?
N25 C25A 1.377(4) . ?
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C26 O30 1.220(4) . ?

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C10B N1 C2 117.8(3) . . ?
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N1 C2 C12 112.2(3) . . ?
C3 C2 C12 113.3(3) . . ?
C2 C3 C4 117.6(3) . . ?
C4A C4 C3 110.8(3) . . ?
C10B C4A C5 114.4(3) . . ?
C10B C4A C4 117.1(3) . . ?
C5 C4A C4 128.5(3) . . ?
C6 C5 C4A 122.0(3) . . ?
C6 C5 Br13 120.9(2) . . ?
C4A C5 Br13 117.0(2) . . ?
C5 C6 C6A 122.4(3) . . ?
C5 C6 Br14 120.6(2) . . ?
C6A C6 Br14 116.9(2) . . ?
C10A C6A C6 113.5(3) . . ?
C10A C6A C7 117.0(3) . . ?
C6 C6A C7 129.4(3) . . ?
C6A C7 C8 111.0(3) . . ?
C9 C8 C7 115.4(3) . . ?
N10 C9 C8 108.5(3) . . ?
C10A N10 C11 109.6(3) . . ?
C10A N10 C9 119.6(3) . . ?
C11 N10 C9 129.5(3) . . ?
C10B C10A C6A 124.5(3) . . ?
C10B C10A N10 107.8(3) . . ?
C6A C10A N10 127.5(3) . . ?
C4A C10B C10A 123.1(3) . . ?
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C4A C10B N1 128.9(3) . . ?
C10A C10B N1 107.8(3) . . ?
O15 C11 N10 125.8(3) . . ?
O15 C11 N1 128.6(3) . . ?
N10 C11 N1 105.6(2) . . ?
C25B N16 C26 109.3(2) . . ?
C25B N16 C17 118.6(3) . . ?
C26 N16 C17 130.4(3) . . ?
N16 C17 C27 112.9(3) . . ?
N16 C17 C18 108.0(3) . . ?
C27 C17 C18 113.5(3) . . ?
C17 C18 C19 118.5(3) . . ?
C19A C19 C18 110.6(3) . . ?
C25B C19A C20 114.6(3) . . ?
C25B C19A C19 117.7(3) . . ?
C20 C19A C19 127.6(3) . . ?
C19A C20 C21 121.9(3) . . ?
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C21 C20 Br28 120.3(2) . . ?
C21A C21 C20 121.6(3) . . ?
C21A C21 Br29 117.7(2) . . ?
C20 C21 Br29 120.3(2) . . ?
C25A C21A C21 114.6(3) . . ?
C25A C21A C22Y 117.0(4) . . ?
C21 C21A C22Y 127.3(4) . . ?
C25A C21A C22X 114.9(4) . . ?
C21 C21A C22X 130.2(4) . . ?
C22Y C21A C22X 15.2(4) . . ?
C23X C22X C21A 109.4(5) . . ?
C24X C23X C22X 115.3(7) . . ?
N25 C24X C23X 105.8(5) . . ?
C21A C22Y C23Y 107.2(5) . . ?
C22Y C23Y C24Y 111.4(5) . . ?
N25 C24Y C23Y 104.9(5) . . ?
C25A N25 C26 109.9(3) . . ?
C25A N25 C24Y 118.9(3) . . ?
C26 N25 C24Y 128.4(3) . . ?
C25A N25 C24X 120.1(4) . . ?
C26 N25 C24X 129.3(4) . . ?
C24Y N25 C24X 22.6(4) . . ?
C21A C25A C25B 124.0(3) . . ?
C21A C25A N25 128.6(3) . . ?
C25B C25A N25 107.2(3) . . ?
C19A C25B C25A 123.1(3) . . ?
C19A C25B N16 128.7(3) . . ?
C25A C25B N16 108.2(3) . . ?
O30 C26 N16 129.1(3) . . ?
O30 C26 N25 125.7(3) . . ?
N16 C26 N25 105.2(3) . . ?


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_refine_diff_density_max     0.573
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Appendix B. X-ray Crystallographic Data for Pd Complex **311a**.
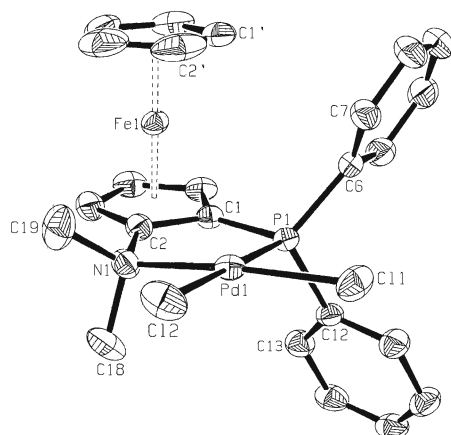

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data_costa3


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_chemical_name_common           ?

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  'C24 H24 Cl2 Fe N P Pd'

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 _atom_type_description

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'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

'N'   'N'    0.0061    0.0033

'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

'P'   'P'    0.1023    0.0942

'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

'Cl'  'Cl'   0.1484    0.1585

'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

'Fe'  'Fe'   0.3463    0.8444

'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

'Pd'  'Pd'  -0.9988    1.0072

'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'


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_symmetry_space_group_name_H-M    Pbca
_symmetry_space_group_name_Hall   '-P 2ac 2ab'


loop_

 _symmetry_equiv_pos_as_xyz

 'x, y, z'

 '-x+1/2, -y, z+1/2'

 '-x, y+1/2, -z+1/2'

 'x+1/2, -y+1/2, -z'
```

```
'-x, -y, -z'

'x-1/2, y, -z-1/2'

'x, -y-1/2, z-1/2'

'-x-1/2, y-1/2, z'


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_cell_length_c                      18.736(3)

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_cell_angle_beta                    90.00

_cell_angle_gamma                   90.00

_cell_volume                        4603.8(11)

_cell_formula_units_Z               8

_cell_measurement_temperature       296(2)

_cell_measurement_reflns_used       9897

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_exptl_crystal_description          block

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_exptl_crystal_size_max             0.24

_exptl_crystal_size_mid             0.22

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_exptl_crystal_density_meas         'not measured'

_exptl_crystal_density_diffrn       1.704

_exptl_crystal_density_method       'not measured'

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_diffrn_radiation_type                 MoK\a

_diffrn_radiation_source               'fine-focus sealed tube'

_diffrn_radiation_monochromator        graphite

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_diffrn_measurement_method             'phi and omega scans'

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_diffrn_reflns_number                  61593

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_computing_molecular_graphics       'Bruker SHELXTL'

_computing_publication_material     'Bruker SHELXTL'


_refine_special_details

;

 Refinement of F^2^ against ALL reflections.  The weighted R-factor
wR and goodness of fit S are based on F^2^, conventional R-factors R
are based on F, with F set to zero for negative F^2^. The threshold
expression of F^2^ > 2sigma(F^2^) is used only for calculating R-
factors(gt) etc. and is not relevant to the choice of reflections
for refinement.  R-factors based on F^2^ are statistically about
twice as large as those based on F, and R-factors based on ALL data
will be even larger.

;
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_refine_ls_weighting_details

 'calc w=1/[\s^2^(Fo^2^)+(0.0453P)^2^+4.3915P] where
P=(Fo^2^+2Fc^2^)/3'

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_atom_sites_solution_secondary     difmap

_atom_sites_solution_hydrogens     geom

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_refine_ls_extinction_method       none

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_refine_ls_number_parameters       271

_refine_ls_number_restraints       0

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_atom_site_refinement_flags

_atom_site_disorder_assembly

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. . .

Fe1 Fe -0.223663(19) 0.30664(2) 0.386286(19) 0.02496(9) Uani 1 1 d .
. .

Cl1 Cl 0.08702(4) 0.31026(5) 0.26013(4) 0.03760(15) Uani 1 1 d . . .

Cl2 Cl 0.10650(4) 0.26315(5) 0.43328(4) 0.04278(17) Uani 1 1 d . . .

P1 P -0.08581(3) 0.25004(4) 0.26510(3) 0.02198(12) Uani 1 1 d . . .

N1 N -0.07195(12) 0.18816(15) 0.41890(11) 0.0292(4) Uani 1 1 d . . .

C1 C -0.16637(13) 0.21721(16) 0.31890(13) 0.0237(4) Uani 1 1 d . . .

C2 C -0.15094(14) 0.19456(16) 0.39204(13) 0.0267(5) Uani 1 1 d . . .

C3 C -0.22136(15) 0.17132(18) 0.42634(16) 0.0340(6) Uani 1 1 d . . .

H3A H -0.2280 0.1528 0.4764 0.041 Uiso 1 1 calc R . .

C4 C -0.28010(15) 0.18027(18) 0.37462(17) 0.0350(6) Uani 1 1 d . . .

H4A H -0.3351 0.1703 0.3836 0.042 Uiso 1 1 calc R . .

C5 C -0.24805(14) 0.20914(17) 0.30820(15) 0.0294(5) Uani 1 1 d . . .

H5A H -0.2761 0.2207 0.2637 0.035 Uiso 1 1 calc R . .
```

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C1'  C  -0.2310(2)   0.4428(2)   0.3485(2)    0.0542(10) Uani 1 1 d . . .

H1'A H  -0.2219      0.4628      0.2992       0.065 Uiso 1 1 calc R . .

C2'  C  -0.1767(2)   0.4377(2)   0.4012(3)    0.0602(11) Uani 1 1 d . . .

H2'A H  -0.1222      0.4538      0.3961       0.072 Uiso 1 1 calc R . .

C3'  C  -0.2125(2)   0.4075(2)   0.4644(2)    0.0639(11) Uani 1 1 d . . .

H3'A H  -0.1878      0.3992      0.5109       0.077 Uiso 1 1 calc R . .

C4'  C  -0.2913(2)   0.3923(2)   0.44845(19)  0.0499(9) Uani 1 1 d . . .

H4'A H  -0.3314      0.3720      0.4819       0.060 Uiso 1 1 calc R . .

C5'  C  -0.30122(19) 0.4155(2)   0.37689(19)  0.0473(8) Uani 1 1 d . . .

H5'A H  -0.3500      0.4128      0.3507       0.057 Uiso 1 1 calc R . .

C6   C  -0.11006(14) 0.35730(17) 0.21677(13)  0.0272(5) Uani 1 1 d . . .

C7   C  -0.07686(15) 0.44371(18) 0.23497(15)  0.0339(6) Uani 1 1 d . . .

H7A  H  -0.0379      0.4461      0.2689       0.041 Uiso 1 1 calc R . .

C8   C  -0.10206(19) 0.5264(2)   0.20228(18)  0.0450(7) Uani 1 1 d . . .

H8A  H  -0.0804      0.5841      0.2150       0.054 Uiso 1 1 calc R . .

C9   C  -0.1592(2)   0.5232(2)   0.15102(17)  0.0492(8) Uani 1 1 d . . .

H9A  H  -0.1757      0.5788      0.1293       0.059 Uiso 1 1 calc R . .

C10  C  -0.19188(19) 0.4379(2)   0.13183(16)  0.0458(7) Uani 1 1 d . . .

H10A H  -0.2301      0.4360      0.0971       0.055 Uiso 1 1 calc R . .

C11  C  -0.16752(17) 0.3540(2)   0.16470(14)  0.0358(6) Uani 1 1 d . . .

H11A H  -0.1895      0.2965      0.1519       0.043 Uiso 1 1 calc R . .

C12  C  -0.07348(14) 0.15933(16) 0.19731(13)  0.0259(5) Uani 1 1 d . .
     .

C13  C  -0.11928(16) 0.07812(18) 0.19619(14)  0.0328(5) Uani 1 1 d . .
     .

H13A H  -0.1582      0.0704      0.2297       0.039 Uiso 1 1 calc R . .

C14  C  -0.10652(17) 0.00863(18) 0.14464(15)  0.0367(6) Uani 1 1 d . .
     .
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H14A H -0.1377 -0.0448 0.1434 0.044 Uiso 1 1 calc R . .

C15 C -0.04807(18) 0.0189(2) 0.09566(14) 0.0371(6) Uani 1 1 d . . .

H15A H -0.0394 -0.0282 0.0620 0.045 Uiso 1 1 calc R . .

C16 C -0.00217(16) 0.0986(2) 0.09616(15) 0.0371(6) Uani 1 1 d . . .

H16A H 0.0372 0.1051 0.0629 0.044 Uiso 1 1 calc R . .

C17 C -0.01506(16) 0.1697(2) 0.14681(14) 0.0327(5) Uani 1 1 d . . .

H17A H 0.0153 0.2238 0.1468 0.039 Uiso 1 1 calc R . .

C18 C -0.04941(18) 0.0857(2) 0.42006(19) 0.0447(7) Uani 1 1 d . . .

H18A H -0.0828 0.0518 0.4519 0.067 Uiso 1 1 calc R . .

H18B H 0.0028 0.0800 0.4362 0.067 Uiso 1 1 calc R . .

H18C H -0.0538 0.0599 0.3729 0.067 Uiso 1 1 calc R . .

C19 C -0.0675(2) 0.2261(3) 0.49333(16) 0.0484(8) Uani 1 1 d . . .

H19A H -0.1039 0.1936 0.5230 0.073 Uiso 1 1 calc R . .

H19B H -0.0792 0.2925 0.4930 0.073 Uiso 1 1 calc R . .

H19C H -0.0165 0.2167 0.5118 0.073 Uiso 1 1 calc R . .

loop_

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Pd1 0.02144(10) 0.02180(10) 0.02897(12) -0.00220(7) -0.00238(6) 0.00202(6)

Fe1 0.02444(17) 0.02114(16) 0.02929(19) -0.00300(13) 0.00521(13) -0.00197(12)

Cl1 0.0274(3) 0.0412(3) 0.0443(4) −0.0063(3) 0.0099(3) −0.0038(3)

Cl2 0.0362(3) 0.0394(3) 0.0527(4) 0.0025(3) −0.0196(3) 0.0011(3)

P1 0.0222(3) 0.0210(3) 0.0228(3) −0.0019(2) 0.0005(2) 0.0017(2)

N1 0.0316(11) 0.0284(10) 0.0276(11) 0.0042(8) −0.0030(9) 0.0024(8)

C1 0.0227(10) 0.0209(10) 0.0273(12) −0.0025(9) 0.0001(9) 0.0002(8)

C2 0.0284(11) 0.0224(10) 0.0292(13) 0.0011(9) 0.0021(9) −0.0021(9)

C3 0.0368(14) 0.0272(12) 0.0379(15) 0.0062(11) 0.0078(11) −
0.0030(10)

C4 0.0272(12) 0.0235(11) 0.0543(17) −0.0026(11) 0.0058(12) −
0.0059(9)

C5 0.0233(11) 0.0238(10) 0.0413(15) −0.0054(10) −0.0020(10) −
0.0004(9)

C1' 0.081(3) 0.0244(13) 0.057(2) 0.0019(13) 0.0313(19) 0.0129(15)

C2' 0.0395(17) 0.0295(14) 0.112(3) −0.0248(18) 0.0190(19) −
0.0057(13)

C3' 0.088(3) 0.0452(18) 0.058(2) −0.0300(17) −0.031(2) 0.0263(19)

C4' 0.061(2) 0.0312(14) 0.058(2) −0.0068(13) 0.0342(17) 0.0020(13)

C5' 0.0448(16) 0.0340(14) 0.063(2) −0.0187(14) −0.0083(15)
0.0139(13)

C6 0.0307(12) 0.0262(11) 0.0247(12) 0.0019(9) 0.0063(9) 0.0048(9)

C7 0.0338(13) 0.0284(12) 0.0395(15) 0.0051(11) 0.0058(11) −
0.0010(10)

C8 0.0523(18) 0.0281(13) 0.0545(19) 0.0108(13) 0.0125(15) 0.0000(12)

C9 0.064(2) 0.0385(16) 0.0449(18) 0.0158(13) 0.0114(15) 0.0171(15)

C10 0.0532(18) 0.0550(18) 0.0291(15) 0.0054(13) −0.0005(13)
0.0221(15)

C11 0.0417(15) 0.0370(14) 0.0285(13) −0.0020(11) −0.0012(11)
0.0102(12)

C12 0.0307(12) 0.0240(10) 0.0228(11) −0.0041(9) −0.0035(9) 0.0073(9)

C13 0.0383(14) 0.0272(11) 0.0330(14) −0.0018(10) −0.0019(11)
0.0006(10)

C14 0.0463(16) 0.0237(11) 0.0402(15) -0.0057(11) -0.0100(12)
0.0025(11)

C15 0.0492(17) 0.0342(13) 0.0280(13) -0.0087(10) -0.0099(12)
0.0143(12)

C16 0.0408(15) 0.0434(16) 0.0270(14) -0.0082(11) 0.0012(11)
0.0097(12)

C17 0.0375(14) 0.0324(13) 0.0282(13) -0.0055(10) -0.0006(10)
0.0012(11)

C18 0.0399(15) 0.0340(14) 0.060(2) 0.0190(14) -0.0044(14) 0.0057(12)

C19 0.0451(17) 0.072(2) 0.0281(15) -0.0017(14) -0.0071(13)
0.0001(16)

_geom_special_details

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 All esds (except the esd in the dihedral angle between two l.s.
planes) are estimated using the full covariance matrix. The cell
esds are taken into account individually in the estimation of esds
in distances, angles and torsion angles; correlations between esds
in cell parameters are only used when they are defined by crystal
symmetry. An approximate (isotropic) treatment of cell esds is used
for estimating esds involving l.s. planes.

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loop_

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Pd1 N1 2.135(2) . ?
Pd1 P1 2.2185(7) . ?
Pd1 Cl1 2.2857(7) . ?
Pd1 Cl2 2.3788(7) . ?
Fe1 C2 2.030(2) . ?
Fe1 C2' 2.044(3) . ?
Fe1 C1 2.046(2) . ?

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Fe1 C4 2.050(2) . ?
Fe1 C4' 2.051(3) . ?
Fe1 C3' 2.052(3) . ?
Fe1 C5' 2.054(3) . ?
Fe1 C5 2.055(3) . ?
Fe1 C1' 2.056(3) . ?
Fe1 C3 2.056(3) . ?
P1 C1 1.787(2) . ?
P1 C6 1.816(2) . ?
P1 C12 1.818(2) . ?
N1 C2 1.465(3) . ?
N1 C19 1.496(4) . ?
N1 C18 1.500(3) . ?
C1 C2 1.433(3) . ?
C1 C5 1.438(3) . ?
C2 C3 1.421(3) . ?
C3 C4 1.413(4) . ?
C3 H3A 0.9800 . ?
C4 C5 1.423(4) . ?
C4 H4A 0.9800 . ?
C5 H5A 0.9800 . ?
C1' C2' 1.368(6) . ?
C1' C5' 1.385(5) . ?
C1' H1'A 0.9800 . ?
C2' C3' 1.403(6) . ?
C2' H2'A 0.9800 . ?
C3' C4' 1.418(5) . ?
C3' H3'A 0.9800 . ?
C4' C5' 1.391(5) . ?
C4' H4'A 0.9800 . ?
C5' H5'A 0.9800 . ?
C6 C7 1.394(4) . ?
C6 C11 1.397(4) . ?
C7 C8 1.391(4) . ?
C7 H7A 0.9300 . ?
C8 C9 1.382(5) . ?
C8 H8A 0.9300 . ?
C9 C10 1.382(5) . ?
C9 H9A 0.9300 . ?
C10 C11 1.401(4) . ?
C10 H10A 0.9300 . ?
C11 H11A 0.9300 . ?
C12 C17 1.396(4) . ?
C12 C13 1.397(4) . ?
C13 C14 1.396(4) . ?
C13 H13A 0.9300 . ?
C14 C15 1.376(4) . ?
C14 H14A 0.9300 . ?
C15 C16 1.381(4) . ?
C15 H15A 0.9300 . ?
C16 C17 1.400(4) . ?
C16 H16A 0.9300 . ?
C17 H17A 0.9300 . ?
C18 H18A 0.9600 . ?
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C18 H18B 0.9600 . ?
C18 H18C 0.9600 . ?
C19 H19A 0.9600 . ?
C19 H19B 0.9600 . ?
C19 H19C 0.9600 . ?


loop_

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N1 Pd1 P1 87.87(6) . . ?
N1 Pd1 Cl1 172.65(6) . . ?
P1 Pd1 Cl1 87.78(3) . . ?
N1 Pd1 Cl2 93.37(6) . . ?
P1 Pd1 Cl2 178.58(3) . . ?
Cl1 Pd1 Cl2 91.05(3) . . ?
C2 Fe1 C2' 116.88(13) . . ?
C2 Fe1 C1 41.16(10) . . ?
C2' Fe1 C1 116.80(12) . . ?
C2 Fe1 C4 67.86(10) . . ?
C2' Fe1 C4 174.73(12) . . ?
C1 Fe1 C4 68.17(10) . . ?
C2 Fe1 C4' 142.00(13) . . ?
C2' Fe1 C4' 67.38(13) . . ?
C1 Fe1 C4' 174.07(13) . . ?
C4 Fe1 C4' 107.53(12) . . ?
C2 Fe1 C3' 116.49(12) . . ?
C2' Fe1 C3' 40.06(17) . . ?
C1 Fe1 C3' 145.46(14) . . ?
C4 Fe1 C3' 136.62(17) . . ?
C4' Fe1 C3' 40.42(15) . . ?
C2 Fe1 C5' 176.78(12) . . ?
C2' Fe1 C5' 66.04(14) . . ?
C1 Fe1 C5' 136.88(12) . . ?
C4 Fe1 C5' 109.29(12) . . ?
C4' Fe1 C5' 39.61(14) . . ?
C3' Fe1 C5' 66.54(13) . . ?
C2 Fe1 C5 69.04(10) . . ?
C2' Fe1 C5 142.03(15) . . ?
C1 Fe1 C5 41.06(9) . . ?
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C4  Fe1 C5  40.58(11) . . ?
C4' Fe1 C5  133.04(13) . . ?
C3' Fe1 C5  173.43(13) . . ?
C5' Fe1 C5  107.86(12) . . ?
C2  Fe1 C1' 142.05(12) . . ?
C2' Fe1 C1' 38.98(16) . . ?
C1  Fe1 C1' 113.40(11) . . ?
C4  Fe1 C1' 138.60(15) . . ?
C4' Fe1 C1' 66.81(13) . . ?
C3' Fe1 C1' 66.43(16) . . ?
C5' Fe1 C1' 39.40(14) . . ?
C5  Fe1 C1' 111.76(14) . . ?
C2  Fe1 C3  40.70(10) . . ?
C2' Fe1 C3  141.82(16) . . ?
C1  Fe1 C3  68.93(10) . . ?
C4  Fe1 C3  40.27(11) . . ?
C4' Fe1 C3  110.72(12) . . ?
C3' Fe1 C3  112.63(15) . . ?
C5' Fe1 C3  137.89(13) . . ?
C5  Fe1 C3  68.86(11) . . ?
C1' Fe1 C3  177.24(12) . . ?
C1  P1  C6  108.45(11) . . ?
C1  P1  C12 107.65(11) . . ?
C6  P1  C12 105.56(11) . . ?
C1  P1  Pd1 100.59(8) . . ?
C6  P1  Pd1 119.16(9) . . ?
C12 P1  Pd1 114.76(8) . . ?
C2  N1  C19 110.3(2) . . ?
C2  N1  C18 108.0(2) . . ?
C19 N1  C18 108.6(2) . . ?
C2  N1  Pd1 110.69(15) . . ?
C19 N1  Pd1 113.43(18) . . ?
C18 N1  Pd1 105.55(17) . . ?
C2  C1  C5  107.5(2) . . ?
C2  C1  P1  116.81(17) . . ?
C5  C1  P1  135.7(2) . . ?
C2  C1  Fe1 68.84(14) . . ?
C5  C1  Fe1 69.80(13) . . ?
P1  C1  Fe1 124.68(12) . . ?
C3  C2  C1  108.9(2) . . ?
C3  C2  N1  129.6(2) . . ?
C1  C2  N1  121.2(2) . . ?
C3  C2  Fe1 70.63(15) . . ?
C1  C2  Fe1 70.01(13) . . ?
N1  C2  Fe1 130.53(17) . . ?
C4  C3  C2  106.9(2) . . ?
C4  C3  Fe1 69.65(15) . . ?
C2  C3  Fe1 68.68(14) . . ?
C4  C3  H3A 126.5 . . ?
C2  C3  H3A 126.5 . . ?
Fe1 C3  H3A 126.5 . . ?
C3  C4  C5  110.0(2) . . ?
C3  C4  Fe1 70.08(15) . . ?
C5  C4  Fe1 69.88(14) . . ?
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C3 C4 H4A 125.0 . . ?
C5 C4 H4A 125.0 . . ?
Fe1 C4 H4A 125.0 . . ?
C4 C5 C1 106.7(2) . . ?
C4 C5 Fe1 69.54(15) . . ?
C1 C5 Fe1 69.13(13) . . ?
C4 C5 H5A 126.7 . . ?
C1 C5 H5A 126.7 . . ?
Fe1 C5 H5A 126.7 . . ?
C2' C1' C5' 108.4(3) . . ?
C2' C1' Fe1 70.05(19) . . ?
C5' C1' Fe1 70.24(18) . . ?
C2' C1' H1'A 125.8 . . ?
C5' C1' H1'A 125.8 . . ?
Fe1 C1' H1'A 125.8 . . ?
C1' C2' C3' 108.6(3) . . ?
C1' C2' Fe1 70.97(19) . . ?
C3' C2' Fe1 70.27(19) . . ?
C1' C2' H2'A 125.7 . . ?
C3' C2' H2'A 125.7 . . ?
Fe1 C2' H2'A 125.7 . . ?
C2' C3' C4' 107.3(3) . . ?
C2' C3' Fe1 69.67(19) . . ?
C4' C3' Fe1 69.78(18) . . ?
C2' C3' H3'A 126.3 . . ?
C4' C3' H3'A 126.3 . . ?
Fe1 C3' H3'A 126.3 . . ?
C5' C4' C3' 106.6(3) . . ?
C5' C4' Fe1 70.29(17) . . ?
C3' C4' Fe1 69.80(18) . . ?
C5' C4' H4'A 126.7 . . ?
C3' C4' H4'A 126.7 . . ?
Fe1 C4' H4'A 126.7 . . ?
C1' C5' C4' 109.1(3) . . ?
C1' C5' Fe1 70.36(18) . . ?
C4' C5' Fe1 70.10(18) . . ?
C1' C5' H5'A 125.5 . . ?
C4' C5' H5'A 125.5 . . ?
Fe1 C5' H5'A 125.5 . . ?
C7 C6 C11 119.7(2) . . ?
C7 C6 P1 120.9(2) . . ?
C11 C6 P1 119.1(2) . . ?
C8 C7 C6 119.9(3) . . ?
C8 C7 H7A 120.0 . . ?
C6 C7 H7A 120.0 . . ?
C9 C8 C7 120.3(3) . . ?
C9 C8 H8A 119.8 . . ?
C7 C8 H8A 119.8 . . ?
C10 C9 C8 120.3(3) . . ?
C10 C9 H9A 119.8 . . ?
C8 C9 H9A 119.8 . . ?
C9 C10 C11 120.0(3) . . ?
C9 C10 H10A 120.0 . . ?
C11 C10 H10A 120.0 . . ?
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C6 C11 C10 119.7(3) . . ?
C6 C11 H11A 120.2 . . ?
C10 C11 H11A 120.2 . . ?
C17 C12 C13 119.4(2) . . ?
C17 C12 P1 119.05(19) . . ?
C13 C12 P1 121.5(2) . . ?
C14 C13 C12 119.9(3) . . ?
C14 C13 H13A 120.0 . . ?
C12 C13 H13A 120.0 . . ?
C15 C14 C13 120.3(3) . . ?
C15 C14 H14A 119.9 . . ?
C13 C14 H14A 119.9 . . ?
C14 C15 C16 120.5(2) . . ?
C14 C15 H15A 119.7 . . ?
C16 C15 H15A 119.7 . . ?
C15 C16 C17 119.9(3) . . ?
C15 C16 H16A 120.1 . . ?
C17 C16 H16A 120.1 . . ?
C12 C17 C16 120.0(3) . . ?
C12 C17 H17A 120.0 . . ?
C16 C17 H17A 120.0 . . ?
N1 C18 H18A 109.5 . . ?
N1 C18 H18B 109.5 . . ?
H18A C18 H18B 109.5 . . ?
N1 C18 H18C 109.5 . . ?
H18A C18 H18C 109.5 . . ?
H18B C18 H18C 109.5 . . ?
N1 C19 H19A 109.5 . . ?
N1 C19 H19B 109.5 . . ?
H19A C19 H19B 109.5 . . ?
N1 C19 H19C 109.5 . . ?
H19A C19 H19C 109.5 . . ?
H19B C19 H19C 109.5 . . ?


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N1 Pd1 P1 C1 11.11(10) . . . . ?
Cl1 Pd1 P1 C1 -174.81(8) . . . . ?
N1 Pd1 P1 C6 129.35(11) . . . . ?
Cl1 Pd1 P1 C6 -56.58(9) . . . . ?
N1 Pd1 P1 C12 -104.10(11) . . . . ?
Cl1 Pd1 P1 C12 69.97(9) . . . . ?
P1 Pd1 N1 C2 -15.87(15) . . . . ?
Cl2 Pd1 N1 C2 163.44(15) . . . . ?
P1 Pd1 N1 C19 -140.43(19) . . . . ?
Cl2 Pd1 N1 C19 38.88(19) . . . . ?
P1 Pd1 N1 C18 100.76(17) . . . . ?
Cl2 Pd1 N1 C18 -79.93(17) . . . . ?
C6 P1 C1 C2 -131.81(18) . . . . ?
C12 P1 C1 C2 114.43(19) . . . . ?
Pd1 P1 C1 C2 -6.01(19) . . . . ?
C6 P1 C1 C5 46.2(3) . . . . ?
C12 P1 C1 C5 -67.6(3) . . . . ?
Pd1 P1 C1 C5 172.0(2) . . . . ?
C6 P1 C1 Fe1 -49.98(18) . . . . ?
C12 P1 C1 Fe1 -163.74(14) . . . . ?
Pd1 P1 C1 Fe1 75.82(14) . . . . ?
C2' Fe1 C1 C2 101.1(2) . . . . ?
C4 Fe1 C1 C2 -80.86(16) . . . . ?
C3' Fe1 C1 C2 62.2(3) . . . . ?
C5' Fe1 C1 C2 -176.19(18) . . . . ?
C5 Fe1 C1 C2 -119.1(2) . . . . ?
C1' Fe1 C1 C2 144.14(18) . . . . ?
C3 Fe1 C1 C2 -37.46(14) . . . . ?
C2 Fe1 C1 C5 119.1(2) . . . . ?
C2' Fe1 C1 C5 -139.9(2) . . . . ?
C4 Fe1 C1 C5 38.20(15) . . . . ?
C3' Fe1 C1 C5 -178.8(2) . . . . ?
C5' Fe1 C1 C5 -57.1(2) . . . . ?
C1' Fe1 C1 C5 -96.80(19) . . . . ?
C3 Fe1 C1 C5 81.61(16) . . . . ?
C2 Fe1 C1 P1 -108.7(2) . . . . ?
C2' Fe1 C1 P1 -7.6(2) . . . . ?
C4 Fe1 C1 P1 170.46(19) . . . . ?
C3' Fe1 C1 P1 -46.5(3) . . . . ?
C5' Fe1 C1 P1 75.1(2) . . . . ?
C5 Fe1 C1 P1 132.3(2) . . . . ?
C1' Fe1 C1 P1 35.5(2) . . . . ?
C3 Fe1 C1 P1 -146.14(18) . . . . ?
C5 C1 C2 C3 0.9(3) . . . . ?
P1 C1 C2 C3 179.40(17) . . . . ?
Fe1 C1 C2 C3 60.19(18) . . . . ?
C5 C1 C2 N1 174.6(2) . . . . ?
P1 C1 C2 N1 -6.8(3) . . . . ?
Fe1 C1 C2 N1 -126.0(2) . . . . ?
C5 C1 C2 Fe1 -59.33(16) . . . . ?

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P1 C1 C2 Fe1 119.21(15) . . . . . ?
C19 N1 C2 C3 -44.6(3) . . . . . ?
C18 N1 C2 C3 74.0(3) . . . . . ?
Pd1 N1 C2 C3 -170.9(2) . . . . . ?
C19 N1 C2 C1 143.1(2) . . . . . ?
C18 N1 C2 C1 -98.4(3) . . . . . ?
Pd1 N1 C2 C1 16.7(3) . . . . . ?
C19 N1 C2 Fe1 53.5(3) . . . . . ?
C18 N1 C2 Fe1 172.1(2) . . . . . ?
Pd1 N1 C2 Fe1 -72.8(2) . . . . . ?
C2' Fe1 C2 C3 139.7(2) . . . . . ?
C1 Fe1 C2 C3 -119.5(2) . . . . . ?
C4 Fe1 C2 C3 -37.80(17) . . . . . ?
C4' Fe1 C2 C3 52.6(3) . . . . . ?
C3' Fe1 C2 C3 94.6(2) . . . . . ?
C5 Fe1 C2 C3 -81.56(17) . . . . . ?
C1' Fe1 C2 C3 179.6(2) . . . . . ?
C2' Fe1 C2 C1 -100.85(19) . . . . . ?
C4 Fe1 C2 C1 81.70(16) . . . . . ?
C4' Fe1 C2 C1 172.12(19) . . . . . ?
C3' Fe1 C2 C1 -145.93(19) . . . . . ?
C5' Fe1 C2 C1 54(2) . . . . . ?
C5 Fe1 C2 C1 37.94(14) . . . . . ?
C1' Fe1 C2 C1 -60.9(3) . . . . . ?
C3 Fe1 C2 C1 119.5(2) . . . . . ?
C2' Fe1 C2 N1 13.6(3) . . . . . ?
C1 Fe1 C2 N1 114.5(3) . . . . . ?
C4 Fe1 C2 N1 -163.8(3) . . . . . ?
C4' Fe1 C2 N1 -73.4(3) . . . . . ?
C3' Fe1 C2 N1 -31.5(3) . . . . . ?
C5' Fe1 C2 N1 168(2) . . . . . ?
C5 Fe1 C2 N1 152.4(2) . . . . . ?
C1' Fe1 C2 N1 53.5(3) . . . . . ?
C3 Fe1 C2 N1 -126.0(3) . . . . . ?
C1 C2 C3 C4 -0.4(3) . . . . . ?
N1 C2 C3 C4 -173.5(2) . . . . . ?
Fe1 C2 C3 C4 59.40(18) . . . . . ?
C1 C2 C3 Fe1 -59.80(17) . . . . . ?
N1 C2 C3 Fe1 127.1(3) . . . . . ?
C2 Fe1 C3 C4 -118.6(2) . . . . . ?
C2' Fe1 C3 C4 172.3(2) . . . . . ?
C1 Fe1 C3 C4 -80.70(17) . . . . . ?
C4' Fe1 C3 C4 93.0(2) . . . . . ?
C3' Fe1 C3 C4 136.6(2) . . . . . ?
C5' Fe1 C3 C4 57.1(2) . . . . . ?
C5 Fe1 C3 C4 -36.54(16) . . . . . ?
C2' Fe1 C3 C2 -69.1(3) . . . . . ?
C1 Fe1 C3 C2 37.87(15) . . . . . ?
C4 Fe1 C3 C2 118.6(2) . . . . . ?
C4' Fe1 C3 C2 -148.46(18) . . . . . ?
C3' Fe1 C3 C2 -104.9(2) . . . . . ?
C5' Fe1 C3 C2 175.63(18) . . . . . ?
C5 Fe1 C3 C2 82.03(16) . . . . . ?
C2 C3 C4 C5 -0.2(3) . . . . . ?
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```
Fe1 C3 C4 C5 58.57(18) . . . . . ?
C2 C3 C4 Fe1 -58.78(17) . . . . . ?
C2 Fe1 C4 C3 38.19(15) . . . . . ?
C1 Fe1 C4 C3 82.74(17) . . . . . ?
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C3' Fe1 C4 C3 -67.5(2) . . . . . ?
C5' Fe1 C4 C3 -143.40(18) . . . . . ?
C5 Fe1 C4 C3 121.4(2) . . . . . ?
C1' Fe1 C4 C3 -176.16(18) . . . . . ?
C2 Fe1 C4 C5 -83.20(16) . . . . . ?
C1 Fe1 C4 C5 -38.65(14) . . . . . ?
C4' Fe1 C4 C5 137.02(17) . . . . . ?
C3' Fe1 C4 C5 171.11(18) . . . . . ?
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C1' Fe1 C4 C5 62.5(2) . . . . . ?
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C3 C4 C5 C1 0.7(3) . . . . . ?
Fe1 C4 C5 C1 59.42(16) . . . . . ?
C3 C4 C5 Fe1 -58.69(19) . . . . . ?
C2 C1 C5 C4 -1.0(3) . . . . . ?
P1 C1 C5 C4 -179.1(2) . . . . . ?
Fe1 C1 C5 C4 -59.68(17) . . . . . ?
C2 C1 C5 Fe1 58.72(16) . . . . . ?
P1 C1 C5 Fe1 -119.4(2) . . . . . ?
C2 Fe1 C5 C4 80.02(16) . . . . . ?
C2' Fe1 C5 C4 -172.8(2) . . . . . ?
C1 Fe1 C5 C4 118.0(2) . . . . . ?
C4' Fe1 C5 C4 -62.8(2) . . . . . ?
C5' Fe1 C5 C4 -99.05(18) . . . . . ?
C1' Fe1 C5 C4 -140.85(18) . . . . . ?
C3 Fe1 C5 C4 36.27(15) . . . . . ?
C2 Fe1 C5 C1 -38.02(14) . . . . . ?
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C4 Fe1 C5 C1 -118.0(2) . . . . . ?
C4' Fe1 C5 C1 179.14(17) . . . . . ?
C5' Fe1 C5 C1 142.91(17) . . . . . ?
C1' Fe1 C5 C1 101.11(17) . . . . . ?
C3 Fe1 C5 C1 -81.77(15) . . . . . ?
C2 Fe1 C1' C2' -65.4(3) . . . . . ?
C1 Fe1 C1' C2' -104.3(2) . . . . . ?
C4 Fe1 C1' C2' 172.7(2) . . . . . ?
C4' Fe1 C1' C2' 82.2(2) . . . . . ?
C3' Fe1 C1' C2' 38.0(2) . . . . . ?
C5' Fe1 C1' C2' 119.2(3) . . . . . ?
C5 Fe1 C1' C2' -148.9(2) . . . . . ?
C2 Fe1 C1' C5' 175.40(19) . . . . . ?
C2' Fe1 C1' C5' -119.2(3) . . . . . ?
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C3' Fe1 C1' C5' -81.2(2) . . . . . ?
C5 Fe1 C1' C5' 92.0(2) . . . . . ?
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Fe1 C1' C2' C3' -60.5(2) . . . . . ?
```

```
C5' C1' C2' Fe1 60.0(2) . . . . . ?
C2 Fe1 C2' C1' 141.16(18) . . . . . ?
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C3' Fe1 C2' C1' -118.8(3) . . . . . ?
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Fe1 C2' C3' C4' -59.9(2) . . . . . ?
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C1 Fe1 C3' C2' 60.5(3) . . . . . ?
C4 Fe1 C3' C2' -173.8(2) . . . . . ?
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C2' Fe1 C3' C4' 118.3(3) . . . . . ?
C1 Fe1 C3' C4' 178.84(19) . . . . . ?
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C3 Fe1 C3' C4' -95.8(2) . . . . . ?
C2' C3' C4' C5' -1.2(3) . . . . . ?
Fe1 C3' C4' C5' -61.0(2) . . . . . ?
C2' C3' C4' Fe1 59.8(2) . . . . . ?
C2 Fe1 C4' C5' -175.55(19) . . . . . ?
C2' Fe1 C4' C5' 79.2(2) . . . . . ?
C4 Fe1 C4' C5' -99.3(2) . . . . . ?
C3' Fe1 C4' C5' 117.1(3) . . . . . ?
C5 Fe1 C4' C5' -62.0(2) . . . . . ?
C1' Fe1 C4' C5' 36.8(2) . . . . . ?
C3 Fe1 C4' C5' -141.91(19) . . . . . ?
C2 Fe1 C4' C3' 67.3(3) . . . . . ?
C2' Fe1 C4' C3' -37.9(2) . . . . . ?
C4 Fe1 C4' C3' 143.6(2) . . . . . ?
C5' Fe1 C4' C3' -117.1(3) . . . . . ?
C5 Fe1 C4' C3' -179.1(2) . . . . . ?
C1' Fe1 C4' C3' -80.3(3) . . . . . ?
C3 Fe1 C4' C3' 101.0(2) . . . . . ?
C2' C1' C5' C4' -0.3(3) . . . . . ?
Fe1 C1' C5' C4' 59.6(2) . . . . . ?
C2' C1' C5' Fe1 -59.9(2) . . . . . ?
C3' C4' C5' C1' 0.9(3) . . . . . ?
Fe1 C4' C5' C1' -59.8(2) . . . . . ?
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C3' C4' C5' Fe1 60.7(2) . . . . . ?
C2' Fe1 C5' C1' 36.9(2) . . . . . ?
C1 Fe1 C5' C1' -67.4(3) . . . . . ?
C4 Fe1 C5' C1' -145.7(2) . . . . . ?
C4' Fe1 C5' C1' 119.9(3) . . . . . ?
C3' Fe1 C5' C1' 80.9(3) . . . . . ?
C5 Fe1 C5' C1' -102.8(2) . . . . . ?
C3 Fe1 C5' C1' 179.2(2) . . . . . ?
C2' Fe1 C5' C4' -82.9(2) . . . . . ?
C1 Fe1 C5' C4' 172.76(18) . . . . . ?
C4 Fe1 C5' C4' 94.4(2) . . . . . ?
C3' Fe1 C5' C4' -39.0(2) . . . . . ?
C5 Fe1 C5' C4' 137.34(19) . . . . . ?
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C3 Fe1 C5' C4' 59.4(3) . . . . . ?
C1 P1 C6 C7 108.0(2) . . . . . ?
C12 P1 C6 C7 -136.9(2) . . . . . ?
Pd1 P1 C6 C7 -6.1(2) . . . . . ?
C1 P1 C6 C11 -66.6(2) . . . . . ?
C12 P1 C6 C11 48.5(2) . . . . . ?
Pd1 P1 C6 C11 179.28(17) . . . . . ?
C11 C6 C7 C8 1.2(4) . . . . . ?
P1 C6 C7 C8 -173.4(2) . . . . . ?
C6 C7 C8 C9 -0.9(4) . . . . . ?
C7 C8 C9 C10 0.1(5) . . . . . ?
C8 C9 C10 C11 0.4(5) . . . . . ?
C7 C6 C11 C10 -0.7(4) . . . . . ?
P1 C6 C11 C10 174.0(2) . . . . . ?
C9 C10 C11 C6 -0.1(4) . . . . . ?
C1 P1 C12 C17 178.3(2) . . . . . ?
C6 P1 C12 C17 62.6(2) . . . . . ?
Pd1 P1 C12 C17 -70.6(2) . . . . . ?
C1 P1 C12 C13 -4.0(2) . . . . . ?
C6 P1 C12 C13 -119.7(2) . . . . . ?
Pd1 P1 C12 C13 107.1(2) . . . . . ?
C17 C12 C13 C14 -0.3(4) . . . . . ?
P1 C12 C13 C14 -178.0(2) . . . . . ?
C12 C13 C14 C15 1.2(4) . . . . . ?
C13 C14 C15 C16 -1.1(4) . . . . . ?
C14 C15 C16 C17 0.0(4) . . . . . ?
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_diffrn_reflns_theta_full   29.00

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Appendix C. X-ray Crystallographic Data for Pt Complex **312a**.
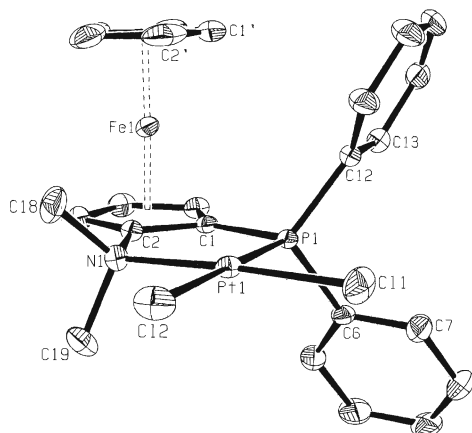

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'H'  'H'   0.0000   0.0000
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'N'  'N'   0.0061   0.0033
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'P'  'P'   0.1023   0.0942
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'Cl'  'Cl'   0.1484   0.1585
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'Fe'  'Fe'   0.3463   0.8444
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'Pt'  'Pt'  -1.7033   8.3905
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
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_symmetry_space_group_name_H-M        'P21/n'

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 'x, y, z'
 '-x+1/2, y+1/2, -z+1/2'
 '-x, -y, -z'
 'x-1/2, -y-1/2, z-1/2'


_cell_length_a                        9.9906(18)
_cell_length_b                        14.365(3)
_cell_length_c                        16.145(3)
_cell_angle_alpha                     90.00
_cell_angle_beta                      90.946(6)
_cell_angle_gamma                     90.00
_cell_volume                          2316.7(8)
_cell_formula_units_Z                 4
_cell_measurement_temperature         150(2)
_cell_measurement_reflns_used         1051
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_cell_measurement_theta_max           28.21

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_exptl_crystal_density_diffrn         1.947
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_diffrn_standards_number              ?
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_computing_cell_refinement           'Bruker SMART'
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_computing_molecular_graphics        'Bruker XP'
_computing_publication_material      'Bruker SHELXTL'

_refine_special_details
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 Refinement of F^2^ against ALL reflections.  The weighted R-factor
wR and goodness of fit S are based on F^2^, conventional R-factors R
are based on F, with F set to zero for negative F^2^. The threshold
expression of F^2^ > 2sigma(F^2^) is used only for calculating R-
factors(gt) etc. and is not relevant to the choice of reflections
for refinement.  R-factors based on F^2^ are statistically about
twice as large as those based on F, and R-factors based on ALL data
will be even larger.
;

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_refine_ls_weighting_details
 'calc w=1/[\s^2^(Fo^2^)+(0.0119P)^2^+2.1255P] where
P=(Fo^2^+2Fc^2^)/3'
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_refine_ls_extinction_method      none
_refine_ls_extinction_coef        ?
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 _atom_site_occupancy
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Fe1 Fe 0.70060(3) 0.707433(19) 0.250826(18) 0.01847(6) Uani 1 1 d .
. .
P1 P 0.38932(5) 0.79566(3) 0.28436(3) 0.01382(9) Uani 1 1 d . . .
N1 N 0.52127(16) 0.81816(12) 0.11836(10) 0.0187(3) Uani 1 1 d . . .
Cl1 Cl 0.10400(5) 0.77267(4) 0.19118(4) 0.03055(12) Uani 1 1 d . . .
Cl2 Cl 0.25147(6) 0.79049(4) 0.01369(3) 0.02926(11) Uani 1 1 d . . .
C1 C 0.56517(18) 0.81112(12) 0.27339(12) 0.0151(4) Uani 1 1 d . . .
C2 C 0.61237(18) 0.81551(13) 0.19024(12) 0.0169(4) Uani 1 1 d . . .
C3 C 0.75339(19) 0.82884(14) 0.19273(13) 0.0223(4) Uani 1 1 d . . .
H3 H 0.8090 0.8345 0.1474 0.027 Uiso 1 1 calc R . .
C4 C 0.79324(19) 0.83189(14) 0.27768(14) 0.0238(4) Uani 1 1 d . . .
H4 H 0.8804 0.8401 0.2974 0.029 Uiso 1 1 calc R . .
C5 C 0.67890(18) 0.82051(14) 0.32749(13) 0.0195(4) Uani 1 1 d . . .
H5 H 0.6781 0.8194 0.3851 0.023 Uiso 1 1 calc R . .
C6 C 0.32754(19) 0.89095(13) 0.34680(12) 0.0176(4) Uani 1 1 d . . .
C7 C 0.4033(2) 0.97012(14) 0.36252(14) 0.0264(4) Uani 1 1 d . . .
H7 H 0.4893 0.9749 0.3418 0.032 Uiso 1 1 calc R . .
C8 C 0.3507(3) 1.04243(16) 0.40935(15) 0.0350(5) Uani 1 1 d . . .
H8 H 0.4016 1.0956 0.4196 0.042 Uiso 1 1 calc R . .
C9 C 0.2233(3) 1.03535(16) 0.44058(15) 0.0341(5) Uani 1 1 d . . .
H9 H 0.1885 1.0836 0.4721 0.041 Uiso 1 1 calc R . .
C10 C 0.1476(2) 0.95709(17) 0.42518(15) 0.0340(5) Uani 1 1 d . . .
H10 H 0.0617 0.9527 0.4462 0.041 Uiso 1 1 calc R . .
C11 C 0.1986(2) 0.88445(15) 0.37842(14) 0.0264(4) Uani 1 1 d . . .
H11 H 0.1471 0.8317 0.3682 0.032 Uiso 1 1 calc R . .
C12 C 0.36069(19) 0.69452(13) 0.34804(12) 0.0183(4) Uani 1 1 d . . .
C13 C 0.4086(2) 0.69414(14) 0.42975(13) 0.0227(4) Uani 1 1 d . . .

H13 H 0.4468 0.7475 0.4526 0.027 Uiso 1 1 calc R . .
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C14  C  0.3990(2)  0.61339(16)  0.47687(14)  0.0293(5)  Uani  1  1  d  .  .  .
H14  H  0.4322  0.6124  0.5310  0.035  Uiso  1  1  calc  R  .  .
C15  C  0.3400(2)  0.53475(16)  0.44333(16)  0.0340(5)  Uani  1  1  d  .  .  .
H15  H  0.3326  0.4812  0.4753  0.041  Uiso  1  1  calc  R  .  .
C16  C  0.2922(2)  0.53510(16)  0.36277(17)  0.0346(5)  Uani  1  1  d  .  .  .
H16  H  0.2528  0.4817  0.3407  0.042  Uiso  1  1  calc  R  .  .
C17  C  0.3023(2)  0.61470(14)  0.31436(14)  0.0263(4)  Uani  1  1  d  .  .  .
H17  H  0.2703  0.6147  0.2599  0.032  Uiso  1  1  calc  R  .  .
C19  C  0.5674(2)  0.75278(18)  0.05251(13)  0.0304(5)  Uani  1  1  d  .  .  .
H19A  H  0.6594  0.7654  0.0404  0.046  Uiso  1  1  calc  R  .  .
H19B  H  0.5135  0.7612  0.0033  0.046  Uiso  1  1  calc  R  .  .
H19C  H  0.5590  0.6898  0.0716  0.046  Uiso  1  1  calc  R  .  .
C18  C  0.5253(2)  0.91516(15)  0.08383(14)  0.0282(5)  Uani  1  1  d  .  .  .
H18A  H  0.5031  0.9589  0.1264  0.042  Uiso  1  1  calc  R  .  .
H18B  H  0.4619  0.9205  0.0388  0.042  Uiso  1  1  calc  R  .  .
H18C  H  0.6136  0.9282  0.0642  0.042  Uiso  1  1  calc  R  .  .
C1'  C  0.6527(3)  0.58226(16)  0.30451(18)  0.0399(6)  Uani  1  1  d  .  .  .
H1'  H  0.5888  0.5733  0.3450  0.048  Uiso  1  1  calc  R  .  .
C2'  C  0.6296(3)  0.57776(16)  0.21904(19)  0.0428(7)  Uani  1  1  d  .  .  .
H2'  H  0.5480  0.5654  0.1928  0.051  Uiso  1  1  calc  R  .  .
C3'  C  0.7517(3)  0.59516(17)  0.17979(16)  0.0403(6)  Uani  1  1  d  .  .  .
H3'  H  0.7653  0.5963  0.1230  0.048  Uiso  1  1  calc  R  .  .
C4'  C  0.8498(2)  0.61060(16)  0.24219(18)  0.0374(6)  Uani  1  1  d  .  .  .
H4'  H  0.9397  0.6239  0.2339  0.045  Uiso  1  1  calc  R  .  .
C5'  C  0.7875(3)  0.60235(17)  0.31882(16)  0.0383(6)  Uani  1  1  d  .  .  .
H5'  H  0.8289  0.6091  0.3705  0.046  Uiso  1  1  calc  R  .  .

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0.00060(2)
Fe1  0.01710(12)  0.01497(13)  0.02342(14)  -0.00028(11)  0.00283(10)
0.00325(10)
P1  0.0142(2)  0.0105(2)  0.0168(2)  0.00006(17)  0.00218(16)  0.00013(16)
N1  0.0188(8)  0.0191(8)  0.0183(8)  0.0011(6)  0.0029(6)  -0.0004(6)
Cl1  0.0152(2)  0.0355(3)  0.0409(3)  -0.0026(2)  -0.0002(2)  -0.00126(19)
Cl2  0.0378(3)  0.0267(3)  0.0229(3)  -0.0025(2)  -0.0112(2)  0.0011(2)
C1  0.0159(8)  0.0106(8)  0.0189(9)  -0.0002(7)  0.0016(7)  0.0014(6)
C2  0.0171(8)  0.0145(9)  0.0191(9)  0.0011(7)  0.0022(7)  0.0003(7)
C3  0.0197(9)  0.0199(10)  0.0277(11)  0.0035(8)  0.0067(8)  -0.0010(7)
C4  0.0166(9)  0.0196(10)  0.0352(12)  -0.0006(9)  -0.0012(8)  -0.0015(7)
C5  0.0196(9)  0.0158(9)  0.0229(10)  -0.0010(8)  -0.0020(7)  0.0011(7)
C6  0.0233(9)  0.0125(9)  0.0172(9)  -0.0002(7)  0.0029(7)  0.0032(7)
C7  0.0306(11)  0.0171(10)  0.0319(12)  -0.0019(9)  0.0087(9)  -0.0017(8)
C8  0.0477(14)  0.0160(10)  0.0414(14)  -0.0069(10)  0.0072(11)  -
0.0001(10)
C9  0.0502(14)  0.0223(11)  0.0303(12)  -0.0047(9)  0.0111(10)  0.0125(10)
```

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C11 0.0256(10) 0.0226(11) 0.0314(11) -0.0031(9) 0.0075(8) 0.0009(8)
C12 0.0171(8) 0.0144(9) 0.0237(10) 0.0026(7) 0.0060(7) 0.0014(7)
C13 0.0234(10) 0.0204(10) 0.0243(10) 0.0010(8) 0.0057(8) 0.0026(8)
C14 0.0316(11) 0.0300(12) 0.0268(11) 0.0097(9) 0.0099(9) 0.0107(9)
C15 0.0326(11) 0.0237(11) 0.0461(14) 0.0179(10) 0.0155(10) 0.0044(9)
C16 0.0320(11) 0.0192(11) 0.0529(15) 0.0053(10) 0.0060(10) -0.0058(9)
C17 0.0267(10) 0.0182(10) 0.0339(12) 0.0011(9) 0.0012(8) -0.0033(8)
C19 0.0327(11) 0.0392(13) 0.0196(11) -0.0056(10) 0.0074(9) 0.0052(10)
C18 0.0300(11) 0.0249(11) 0.0296(12) 0.0107(9) -0.0004(9) -0.0051(9)
C1' 0.0439(14) 0.0190(11) 0.0575(17) 0.0109(11) 0.0231(12) 0.0120(10)
C2' 0.0364(13) 0.0159(11) 0.076(2) -0.0073(12) -0.0097(13) 0.0029(9)
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C4' 0.0242(11) 0.0213(12) 0.0671(18) -0.0009(11) 0.0116(11) 0.0093(9)
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 All esds (except the esd in the dihedral angle between two l.s.
planes) are estimated using the full covariance matrix. The cell
esds are taken into account individually in the estimation of esds
in distances, angles and torsion angles; correlations between esds
in cell parameters are only used when they are defined by crystal
symmetry. An approximate (isotropic) treatment of cell esds is used
for estimating esds involving l.s. planes.
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Pt1 Cl1 2.2862(6) . ?
Pt1 Cl2 2.3542(7) . ?
Fe1 C2 2.0286(19) . ?
Fe1 C4' 2.046(2) . ?
Fe1 C3' 2.049(2) . ?
Fe1 C1 2.0490(18) . ?
Fe1 C5' 2.051(2) . ?
Fe1 C3 2.053(2) . ?
Fe1 C2' 2.055(2) . ?
Fe1 C5 2.056(2) . ?
Fe1 C1' 2.056(2) . ?
Fe1 C4 2.056(2) . ?

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C6 C11 1.396(3) . ?
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C14 C15 1.380(4) . ?

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C2 Fe1 C3' 116.29(9) . . ?
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C3' Fe1 C1 147.49(10) . . ?
C2 Fe1 C5' 176.46(9) . . ?
C4' Fe1 C5' 39.95(10) . . ?
C3' Fe1 C5' 67.23(10) . . ?
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C4' Fe1 C2' 67.39(10) . . ?
C3' Fe1 C2' 40.08(11) . . ?
C1 Fe1 C2' 118.50(9) . . ?
C5' Fe1 C2' 66.91(11) . . ?
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C2 Fe1 C5 68.67(8) . . ?
C4' Fe1 C5 131.50(9) . . ?
C3' Fe1 C5 171.44(10) . . ?
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C5' Fe1 C5 107.89(9) . . ?
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C3' Fe1 C1' 67.01(11) . . ?
C1 Fe1 C1' 113.69(8) . . ?
C5' Fe1 C1' 39.65(11) . . ?
C3 Fe1 C1' 177.14(9) . . ?
C2' Fe1 C1' 39.72(11) . . ?
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C2 Fe1 C4 68.08(8) . . ?
C4' Fe1 C4 106.24(9) . . ?
C3' Fe1 C4 133.40(10) . . ?
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C2 C3 Fe1 68.69(11) . . ?
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C11 C6 P1 118.49(15) . . ?
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C9 C8 C7 120.1(2) . . ?
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C10 C11 C6 119.8(2) . . ?
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C16 C17 C12 119.4(2) . . ?
C5' C1' C2' 108.5(2) . . ?
C5' C1' Fe1 69.97(14) . . ?
C2' C1' Fe1 70.11(14) . . ?
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Appendix D. X-ray Crystallographic Data for Alcohol (*S*)-**297b**.
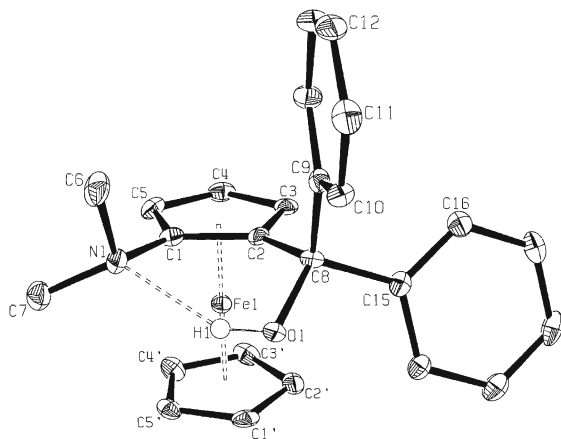

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 'C25 H25 Fe N O'

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'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

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'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

'Fe'  'Fe'   0.3463    0.8444

'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'


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loop_

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'x, y, z'

'-x, y+1/2, -z'


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_exptl_special_details

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 Refinement of F^2^ against ALL reflections.  The weighted R-factor
wR and goodness of fit S are based on F^2^, conventional R-factors R
are based on F, with F set to zero for negative F^2^. The threshold
expression of F^2^ > 2sigma(F^2^) is used only for calculating R-
factors(gt) etc. and is not relevant to the choice of reflections
for refinement.  R-factors based on F^2^ are statistically about
twice as large as those based on F, and R-factors based on ALL data
will be even larger.

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_refine_ls_weighting_details

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P=(Fo^2^+2Fc^2^)/3'

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 'Flack H D (1983), Acta Cryst. A39, 876-881'

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N1 N 0.6189(2) -0.14447(19) 0.86024(19) 0.0165(4) Uani 1 1 d . . .

C1 C 0.5900(3) -0.0149(2) 0.8244(2) 0.0143(5) Uani 1 1 d . . .

C1' C 0.4750(3) -0.0302(3) 0.4668(2) 0.0172(6) Uani 1 1 d . . .

H1A H 0.548(3) -0.082(3) 0.454(3) 0.027(8) Uiso 1 1 d . . .

C2 C 0.6879(2) 0.0615(3) 0.77453(17) 0.0120(4) Uani 1 1 d . . .

C2' C 0.4594(3) 0.1011(2) 0.4453(2) 0.0195(6) Uani 1 1 d . . .

H2A H 0.523(3) 0.151(3) 0.420(3) 0.015(7) Uiso 1 1 d . . .

C3' C 0.3290(3) 0.1406(3) 0.4761(2) 0.0197(6) Uani 1 1 d . . .

H3A H 0.295(4) 0.223(3) 0.468(3) 0.040(9) Uiso 1 1 d . . .

C3 C 0.6276(3) 0.1861(2) 0.7562(2) 0.0144(5) Uani 1 1 d . . .

H3 H 0.667(3) 0.256(3) 0.721(2) 0.013(6) Uiso 1 1 d . . .

C4' C 0.2657(3) 0.0334(2) 0.5176(2) 0.0186(6) Uani 1 1 d . . .

H4A H 0.184(3) 0.033(3) 0.548(2) 0.029(8) Uiso 1 1 d . . .

C4 C 0.4934(3) 0.1858(2) 0.7920(2) 0.0179(5) Uani 1 1 d . . .

H4 H 0.425(3) 0.256(3) 0.786(3) 0.020(7) Uiso 1 1 d . . .

C5 C 0.4698(2) 0.0636(3) 0.83453(19) 0.0170(4) Uani 1 1 d . . .

H5 H 0.387(3) 0.042(3) 0.859(2) 0.025(7) Uiso 1 1 d . . .

C5' C 0.3553(3) -0.0718(2) 0.5110(2) 0.0165(5) Uani 1 1 d . . .

```
H5A  H  0.335(3)  -0.153(3)  0.530(2)  0.010(6)  Uiso  1  1  d  .  .  .

C6   C  0.7171(3)  -0.1585(3)  0.9987(3)  0.0230(6)  Uani  1  1  d  .  .  .

H6C  H  0.677(3)  -0.122(3)  1.067(3)  0.032(8)  Uiso  1  1  d  .  .  .

H6B  H  0.730(3)  -0.243(3)  1.018(3)  0.022(8)  Uiso  1  1  d  .  .  .

H6A  H  0.811(3)  -0.126(3)  1.004(3)  0.020(7)  Uiso  1  1  d  .  .  .

C7   C  0.4828(3)  -0.2181(3)  0.8442(3)  0.0210(5)  Uani  1  1  d  .  .  .

H7C  H  0.425(3)  -0.207(2)  0.761(3)  0.014(6)  Uiso  1  1  d  .  .  .

H7B  H  0.512(3)  -0.309(3)  0.862(2)  0.024(7)  Uiso  1  1  d  .  .  .

H7A  H  0.432(3)  -0.194(3)  0.916(3)  0.027(8)  Uiso  1  1  d  .  .  .

C8   C  0.8346(2)  0.0185(2)  0.7568(2)  0.0122(4)  Uani  1  1  d  .  .  .

C9   C  0.9593(2)  0.0219(2)  0.8930(2)  0.0126(5)  Uani  1  1  d  .  .  .

C10  C  1.0830(3)  -0.0556(2)  0.9110(2)  0.0161(5)  Uani  1  1  d  .  .  .

H10  H  1.086(3)  -0.105(2)  0.842(2)  0.014(7)  Uiso  1  1  d  .  .  .

C11  C  1.1950(3)  -0.0567(2)  1.0331(2)  0.0194(5)  Uani  1  1  d  .  .  .

H11  H  1.277(3)  -0.107(3)  1.045(3)  0.028(8)  Uiso  1  1  d  .  .  .

C12  C  1.1853(3)  0.0192(2)  1.1370(2)  0.0193(5)  Uani  1  1  d  .  .  .

H12  H  1.264(3)  0.014(3)  1.216(3)  0.030(8)  Uiso  1  1  d  .  .  .

C13  C  1.0659(3)  0.0989(2)  1.1193(2)  0.0205(6)  Uani  1  1  d  .  .  .

H13  H  1.059(3)  0.149(2)  1.192(3)  0.018(7)  Uiso  1  1  d  .  .  .

C14  C  0.9529(3)  0.1002(2)  0.9965(2)  0.0168(5)  Uani  1  1  d  .  .  .

H14  H  0.866(3)  0.159(2)  0.988(2)  0.013(6)  Uiso  1  1  d  .  .  .

C15  C  0.8807(2)  0.1009(2)  0.6553(2)  0.0135(5)  Uani  1  1  d  .  .  .

C16  C  0.9556(3)  0.2140(2)  0.6949(2)  0.0170(5)  Uani  1  1  d  .  .  .

H16  H  0.978(3)  0.243(3)  0.781(3)  0.037(9)  Uiso  1  1  d  .  .  .

C17  C  0.9954(3)  0.2892(2)  0.6025(3)  0.0203(5)  Uani  1  1  d  .  .  .

H17  H  1.043(3)  0.363(3)  0.625(3)  0.023(7)  Uiso  1  1  d  .  .  .

C18  C  0.9616(3)  0.2529(2)  0.4692(2)  0.0211(6)  Uani  1  1  d  .  .  .
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H18 H 0.9900 0.3041 0.4064 0.025 Uiso 1 1 calc R . .

C19 C 0.8862(3) 0.1417(2) 0.4289(2) 0.0190(5) Uani 1 1 d . . .

H19 H 0.864(3) 0.119(2) 0.337(3) 0.020(7) Uiso 1 1 d . . .

C20 C 0.8462(2) 0.0650(3) 0.52082(19) 0.0148(4) Uani 1 1 d . . .

H20 H 0.797(3) -0.014(2) 0.493(2) 0.013(6) Uiso 1 1 d . . .

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O1 0.0161(8) 0.0120(8) 0.0123(8) -0.0025(6) 0.0044(7) -0.0028(7)

N1 0.0190(10) 0.0175(10) 0.0141(9) 0.0024(8) 0.0063(8) -0.0032(8)

C1 0.0158(12) 0.0166(12) 0.0093(10) -0.0012(9) 0.0019(9) 0.0003(10)

C1' 0.0125(12) 0.0259(15) 0.0105(11) -0.0066(10) -0.0007(9) -
0.0002(11)

C2 0.0123(9) 0.0156(9) 0.0073(8) -0.0003(12) 0.0017(7) -0.0007(13)

C2' 0.0214(13) 0.0233(15) 0.0110(11) 0.0006(9) 0.0004(9) -0.0089(10)

C3' 0.0214(13) 0.0149(13) 0.0160(12) 0.0016(10) -0.0043(10)
0.0001(11)

C3 0.0165(12) 0.0159(12) 0.0083(10) -0.0015(9) 0.0000(9) -0.0015(10)

C4' 0.0114(11) 0.0198(17) 0.0216(11) -0.0013(9) 0.0004(9) -0.0008(9)

C4 0.0179(12) 0.0200(13) 0.0157(11) -0.0058(9) 0.0050(10) 0.0035(10)

C5 0.0170(10) 0.0233(11) 0.0125(9) 0.0000(13) 0.0069(8) 0.0017(15)

C5' 0.0166(12) 0.0152(13) 0.0135(11) −0.0010(10) −0.0019(9) −0.0022(10)

C6 0.0241(14) 0.0244(15) 0.0195(12) 0.0107(11) 0.0052(11) −0.0006(12)

C7 0.0234(13) 0.0200(14) 0.0191(12) 0.0037(10) 0.0055(11) −0.0030(11)

C8 0.0127(10) 0.0117(10) 0.0109(9) −0.0025(8) 0.0017(8) 0.0004(8)

C9 0.0116(10) 0.0143(11) 0.0110(10) 0.0031(8) 0.0022(8) −0.0010(8)

C10 0.0187(12) 0.0173(12) 0.0127(11) −0.0012(9) 0.0052(9) −0.0011(10)

C11 0.0150(12) 0.0203(13) 0.0202(12) 0.0070(10) 0.0013(10) 0.0020(10)

C12 0.0187(12) 0.0231(13) 0.0115(10) 0.0018(9) −0.0021(9) −0.0025(9)

C13 0.0236(13) 0.0235(14) 0.0128(10) −0.0044(9) 0.0029(9) −0.0033(10)

C14 0.0169(11) 0.0164(12) 0.0153(10) −0.0009(8) 0.0020(9) 0.0014(9)

C15 0.0099(10) 0.0169(11) 0.0133(10) 0.0027(8) 0.0027(8) 0.0018(8)

C16 0.0162(12) 0.0173(13) 0.0160(12) 0.0019(9) 0.0027(10) −0.0001(10)

C17 0.0162(12) 0.0159(13) 0.0287(13) 0.0039(11) 0.0063(10) −0.0019(10)

C18 0.0181(13) 0.0253(14) 0.0226(13) 0.0135(10) 0.0104(10) 0.0055(10)

C19 0.0188(12) 0.0238(13) 0.0156(12) 0.0047(10) 0.0068(10) 0.0046(10)

C20 0.0132(9) 0.0174(10) 0.0144(9) 0.0017(12) 0.0049(7) 0.0024(13)

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 All esds (except the esd in the dihedral angle between two l.s.
planes) are estimated using the full covariance matrix. The cell
esds are taken into account individually in the estimation of esds
in distances, angles and torsion angles; correlations between esds

in cell parameters are only used when they are defined by crystal
symmetry. An approximate (isotropic) treatment of cell esds is used
for estimating esds involving l.s. planes.

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Fe1 C3 2.038(2) . ?
Fe1 C2 2.0454(18) . ?
Fe1 C2' 2.040(3) . ?
Fe1 C5 2.047(2) . ?
Fe1 C3' 2.049(2) . ?
Fe1 C4' 2.055(2) . ?
Fe1 C1 2.057(2) . ?
Fe1 C1' 2.056(3) . ?
Fe1 C5' 2.065(2) . ?
O1 C8 1.436(3) . ?
O1 H1 0.84(3) . ?
N1 C1 1.433(3) . ?
N1 C6 1.472(3) . ?
N1 C7 1.468(3) . ?
C1 C2 1.438(3) . ?
C1 C5 1.435(4) . ?
C1' C5' 1.411(4) . ?
C1' C2' 1.416(4) . ?
C1' H1A 0.92(3) . ?
C2 C3 1.431(4) . ?
C2 C8 1.518(3) . ?
C2' C3' 1.422(4) . ?
C2' H2A 0.90(3) . ?
C3' C4' 1.413(4) . ?
C3' H3A 0.93(3) . ?
C3 C4 1.421(4) . ?
C3 H3 0.95(3) . ?
C4' C5' 1.416(3) . ?
C4' H4A 0.91(3) . ?
C4 C5 1.412(4) . ?
C4 H4 0.98(3) . ?
C5 H5 0.91(3) . ?
C5' H5A 0.92(3) . ?

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C6  H6C  0.98(3)  .  ?
C6  H6B  0.92(3)  .  ?
C6  H6A  0.93(3)  .  ?
C7  H7C  0.88(3)  .  ?
C7  H7B  1.01(3)  .  ?
C7  H7A  1.03(3)  .  ?
C8  C15  1.534(3)  .  ?
C8  C9  1.550(3)  .  ?
C9  C14  1.380(3)  .  ?
C9  C10  1.393(3)  .  ?
C10  C11  1.390(3)  .  ?
C10  H10  0.90(3)  .  ?
C11  C12  1.377(4)  .  ?
C11  H11  0.92(3)  .  ?
C12  C13  1.375(3)  .  ?
C12  H12  0.93(2)  .  ?
C13  C14  1.401(3)  .  ?
C13  H13  0.94(3)  .  ?
C14  H14  1.01(3)  .  ?
C15  C16  1.393(3)  .  ?
C15  C20  1.397(3)  .  ?
C16  C17  1.389(4)  .  ?
C16  H16  0.91(3)  .  ?
C17  C18  1.386(4)  .  ?
C17  H17  0.90(3)  .  ?
C18  C19  1.379(4)  .  ?
C18  H18  0.9500  .  ?
C19  C20  1.395(4)  .  ?
C19  H19  0.95(3)  .  ?
C20  H20  0.96(3)  .  ?


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C3  Fe1  C2  41.04(11)  .  .  ?
C4  Fe1  C2'  127.56(11)  .  .  ?
C3  Fe1  C2'  107.25(10)  .  .  ?
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C2 Fe1 C2' 117.48(10) . . ?
C4 Fe1 C5 40.55(13) . . ?
C3 Fe1 C5 68.61(11) . . ?
C2 Fe1 C5 69.03(8) . . ?
C2' Fe1 C5 165.71(12) . . ?
C4 Fe1 C3' 104.89(11) . . ?
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C2 Fe1 C4' 170.86(12) . . ?
C2' Fe1 C4' 67.96(11) . . ?
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C3' Fe1 C4' 40.28(10) . . ?
C4 Fe1 C1 68.72(10) . . ?
C3 Fe1 C1 68.81(9) . . ?
C2 Fe1 C1 41.04(10) . . ?
C2' Fe1 C1 151.82(11) . . ?
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C3' Fe1 C1 167.25(11) . . ?
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C2' Fe1 C1' 40.43(12) . . ?
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C2 Fe1 C5' 133.20(12) . . ?
C2' Fe1 C5' 67.61(10) . . ?
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C3' Fe1 C5' 67.64(12) . . ?
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C1 Fe1 C5' 111.66(10) . . ?
C1' Fe1 C5' 40.05(10) . . ?
C8 O1 H1 107(2) . . ?
C1 N1 C6 111.63(19) . . ?
C1 N1 C7 113.1(2) . . ?
C6 N1 C7 109.2(2) . . ?
N1 C1 C2 123.1(2) . . ?
N1 C1 C5 129.3(2) . . ?
C2 C1 C5 107.6(2) . . ?
N1 C1 Fe1 128.95(15) . . ?
C2 C1 Fe1 69.06(11) . . ?
C5 C1 Fe1 69.15(12) . . ?
C5' C1' C2' 107.8(3) . . ?
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C5' C1' H1A 124.4(19) . . ?
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C2' C1' H1A 127.8(19) . . ?
Fe1 C1' H1A 127.0(17) . . ?
C3 C2 C1 107.5(2) . . ?
C3 C2 C8 126.9(2) . . ?
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C1' C2' C3' 108.1(2) . . ?
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C1' C2' H2A 125.6(18) . . ?
C3' C2' H2A 126.2(18) . . ?
Fe1 C2' H2A 123.2(17) . . ?
C4' C3' C2' 107.7(2) . . ?
C4' C3' Fe1 70.08(14) . . ?
C2' C3' Fe1 69.33(14) . . ?
C4' C3' H3A 129(2) . . ?
C2' C3' H3A 124(2) . . ?
Fe1 C3' H3A 127(2) . . ?
C4 C3 C2 108.1(2) . . ?
C4 C3 Fe1 69.15(14) . . ?
C2 C3 Fe1 69.75(13) . . ?
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C2 C3 H3 125.9(16) . . ?
Fe1 C3 H3 124.0(15) . . ?
C3' C4' C5' 108.1(2) . . ?
C3' C4' Fe1 69.63(14) . . ?
C5' C4' Fe1 70.28(14) . . ?
C3' C4' H4A 126.1(19) . . ?
C5' C4' H4A 125.8(19) . . ?
Fe1 C4' H4A 123.4(15) . . ?
C5 C4 C3 108.7(2) . . ?
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C3 C4 Fe1 69.93(14) . . ?
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C3 C4 H4 127.0(17) . . ?
Fe1 C4 H4 123.9(15) . . ?
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C1 C5 Fe1 69.91(12) . . ?
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C1 C5 H5 129(2) . . ?
Fe1 C5 H5 123.8(14) . . ?
C1' C5' C4' 108.3(2) . . ?
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C4' C5' Fe1 69.53(14) . . ?
C1' C5' H5A 126.7(16) . . ?
C4' C5' H5A 124.9(16) . . ?
Fe1 C5' H5A 128.4(14) . . ?
N1 C6 H6C 113.9(16) . . ?
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H6C C6 H6B 107(2) . . ?
N1 C6 H6A 109.3(16) . . ?
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H6C C6 H6A 112(2) . . ?
H6B C6 H6A 107(2) . . ?
N1 C7 H7C 107.7(17) . . ?
N1 C7 H7B 107.9(15) . . ?
H7C C7 H7B 112(2) . . ?
N1 C7 H7A 111.2(16) . . ?
H7C C7 H7A 113(2) . . ?
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O1 C8 C2 109.39(19) . . ?
O1 C8 C15 107.40(17) . . ?
C2 C8 C15 111.59(19) . . ?
O1 C8 C9 108.93(17) . . ?
C2 C8 C9 110.38(17) . . ?
C15 C8 C9 109.08(18) . . ?
C14 C9 C10 118.82(19) . . ?
C14 C9 C8 122.28(19) . . ?
C10 C9 C8 118.90(19) . . ?
C11 C10 C9 120.2(2) . . ?
C11 C10 H10 122.0(16) . . ?
C9 C10 H10 117.8(16) . . ?
C12 C11 C10 120.4(2) . . ?
C12 C11 H11 119.2(18) . . ?
C10 C11 H11 120.3(18) . . ?
C13 C12 C11 120.0(2) . . ?
C13 C12 H12 124.2(17) . . ?
C11 C12 H12 115.8(17) . . ?
C12 C13 C14 119.7(2) . . ?
C12 C13 H13 119.2(16) . . ?
C14 C13 H13 121.1(16) . . ?
C9 C14 C13 120.8(2) . . ?
C9 C14 H14 122.0(13) . . ?
C13 C14 H14 117.2(14) . . ?
C16 C15 C20 118.6(2) . . ?
C16 C15 C8 120.7(2) . . ?
C20 C15 C8 120.6(2) . . ?
C17 C16 C15 120.6(2) . . ?
C17 C16 H16 117(2) . . ?
C15 C16 H16 122(2) . . ?
C16 C17 C18 120.5(2) . . ?
C16 C17 H17 122.7(18) . . ?
C18 C17 H17 116.7(18) . . ?
C19 C18 C17 119.2(2) . . ?
C19 C18 H18 120.4 . . ?
C17 C18 H18 120.4 . . ?
C18 C19 C20 120.8(2) . . ?
C18 C19 H19 117.9(15) . . ?
C20 C19 H19 121.3(16) . . ?
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C6 N1 C1 C2 84.8(3) . . . . ?
C7 N1 C1 C2 -151.6(2) . . . . ?
C6 N1 C1 C5 -92.5(3) . . . . ?
C7 N1 C1 C5 31.1(3) . . . . ?
C6 N1 C1 Fe1 173.55(19) . . . . ?
C7 N1 C1 Fe1 -62.9(3) . . . . ?
C4 Fe1 C1 N1 161.6(2) . . . . ?
C3 Fe1 C1 N1 -154.4(2) . . . . ?
C2 Fe1 C1 N1 -116.3(3) . . . . ?
C2' Fe1 C1 N1 -67.3(3) . . . . ?
C5 Fe1 C1 N1 124.3(3) . . . . ?
C3' Fe1 C1 N1 99.7(5) . . . . ?
C4' Fe1 C1 N1 57.4(3) . . . . ?
C1' Fe1 C1 N1 -28.3(3) . . . . ?
C5' Fe1 C1 N1 15.5(2) . . . . ?
C4 Fe1 C1 C2 -82.17(17) . . . . ?
C3 Fe1 C1 C2 -38.12(16) . . . . ?
C2' Fe1 C1 C2 49.0(3) . . . . ?
C5 Fe1 C1 C2 -119.5(2) . . . . ?
C3' Fe1 C1 C2 -144.0(4) . . . . ?
C4' Fe1 C1 C2 173.68(17) . . . . ?
C1' Fe1 C1 C2 87.94(18) . . . . ?
C5' Fe1 C1 C2 131.73(16) . . . . ?
C4 Fe1 C1 C5 37.32(17) . . . . ?
C3 Fe1 C1 C5 81.37(18) . . . . ?
C2 Fe1 C1 C5 119.5(2) . . . . ?
C2' Fe1 C1 C5 168.5(2) . . . . ?
C3' Fe1 C1 C5 -24.5(5) . . . . ?
C4' Fe1 C1 C5 -66.8(2) . . . . ?
C1' Fe1 C1 C5 -152.57(17) . . . . ?
C5' Fe1 C1 C5 -108.79(18) . . . . ?
C4 Fe1 C1' C5' -138.8(4) . . . . ?
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C3 Fe1 C1' C5' 175.58(15) . . . . . ?
C2 Fe1 C1' C5' 132.99(16) . . . . . ?
C2' Fe1 C1' C5' −118.9(2) . . . . . ?
C5 Fe1 C1' C5' 48.3(3) . . . . . ?
C3' Fe1 C1' C5' −80.89(18) . . . . . ?
C4' Fe1 C1' C5' −37.26(15) . . . . . ?
C1 Fe1 C1' C5' 88.31(17) . . . . . ?
C4 Fe1 C1' C2' −19.9(6) . . . . . ?
C3 Fe1 C1' C2' −65.5(2) . . . . . ?
C2 Fe1 C1' C2' −108.08(18) . . . . . ?
C5 Fe1 C1' C2' 167.23(18) . . . . . ?
C3' Fe1 C1' C2' 38.04(16) . . . . . ?
C4' Fe1 C1' C2' 81.67(17) . . . . . ?
C1 Fe1 C1' C2' −152.76(15) . . . . . ?
C5' Fe1 C1' C2' 118.9(2) . . . . . ?
N1 C1 C2 C3 −177.13(19) . . . . . ?
C5 C1 C2 C3 0.6(2) . . . . . ?
Fe1 C1 C2 C3 59.24(13) . . . . . ?
N1 C1 C2 C8 −1.9(3) . . . . . ?
C5 C1 C2 C8 175.90(18) . . . . . ?
Fe1 C1 C2 C8 −125.5(2) . . . . . ?
N1 C1 C2 Fe1 123.6(2) . . . . . ?
C5 C1 C2 Fe1 −58.59(15) . . . . . ?
C4 Fe1 C2 C3 −37.54(14) . . . . . ?
C2' Fe1 C2 C3 84.92(16) . . . . . ?
C5 Fe1 C2 C3 −81.11(17) . . . . . ?
C3' Fe1 C2 C3 46.8(2) . . . . . ?
C1 Fe1 C2 C3 −118.77(19) . . . . . ?
C1' Fe1 C2 C3 128.94(15) . . . . . ?
C5' Fe1 C2 C3 169.15(16) . . . . . ?
C4 Fe1 C2 C1 81.22(15) . . . . . ?
C3 Fe1 C2 C1 118.77(19) . . . . . ?
C2' Fe1 C2 C1 −156.31(14) . . . . . ?
C5 Fe1 C2 C1 37.66(16) . . . . . ?
C3' Fe1 C2 C1 165.61(19) . . . . . ?
C1' Fe1 C2 C1 −112.29(15) . . . . . ?
C5' Fe1 C2 C1 −72.08(17) . . . . . ?
C4 Fe1 C2 C8 −158.9(3) . . . . . ?
C3 Fe1 C2 C8 −121.4(3) . . . . . ?
C2' Fe1 C2 C8 −36.5(3) . . . . . ?
C5 Fe1 C2 C8 157.5(3) . . . . . ?
C3' Fe1 C2 C8 −74.5(4) . . . . . ?
C1 Fe1 C2 C8 119.9(3) . . . . . ?
C1' Fe1 C2 C8 7.6(3) . . . . . ?
C5' Fe1 C2 C8 47.8(3) . . . . . ?
C5' C1' C2' C3' −0.1(3) . . . . . ?
Fe1 C1' C2' C3' −60.06(17) . . . . . ?
C5' C1' C2' Fe1 59.93(17) . . . . . ?
C4 Fe1 C2' C1' 174.63(15) . . . . . ?
C3 Fe1 C2' C1' 134.03(16) . . . . . ?
C2 Fe1 C2' C1' 90.82(18) . . . . . ?
C5 Fe1 C2' C1' −155.1(4) . . . . . ?
C3' Fe1 C2' C1' −118.8(2) . . . . . ?
C4' Fe1 C2' C1' −81.09(17) . . . . . ?
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C1 Fe1 C2' C1' 56.9(3) . . . . ?
C5' Fe1 C2' C1' -37.52(15) . . . . ?
C4 Fe1 C2' C3' -66.60(19) . . . . ?
C3 Fe1 C2' C3' -107.19(16) . . . . ?
C2 Fe1 C2' C3' -150.41(16) . . . . ?
C5 Fe1 C2' C3' -36.4(5) . . . . ?
C4' Fe1 C2' C3' 37.68(15) . . . . ?
C1 Fe1 C2' C3' 175.6(2) . . . . ?
C1' Fe1 C2' C3' 118.8(2) . . . . ?
C5' Fe1 C2' C3' 81.25(17) . . . . ?
C1' C2' C3' C4' 0.5(3) . . . . ?
Fe1 C2' C3' C4' -59.84(16) . . . . ?
C1' C2' C3' Fe1 60.32(18) . . . . ?
C4 Fe1 C3' C4' -110.03(17) . . . . ?
C3 Fe1 C3' C4' -152.50(15) . . . . ?
C2 Fe1 C3' C4' 175.85(19) . . . . ?
C2' Fe1 C3' C4' 118.8(2) . . . . ?
C5 Fe1 C3' C4' -71.8(2) . . . . ?
C1 Fe1 C3' C4' -51.8(5) . . . . ?
C1' Fe1 C3' C4' 81.01(17) . . . . ?
C5' Fe1 C3' C4' 37.62(16) . . . . ?
C4 Fe1 C3' C2' 131.17(15) . . . . ?
C3 Fe1 C3' C2' 88.70(16) . . . . ?
C2 Fe1 C3' C2' 57.0(3) . . . . ?
C5 Fe1 C3' C2' 169.40(17) . . . . ?
C4' Fe1 C3' C2' -118.8(2) . . . . ?
C1 Fe1 C3' C2' -170.6(4) . . . . ?
C1' Fe1 C3' C2' -37.80(16) . . . . ?
C5' Fe1 C3' C2' -81.18(16) . . . . ?
C1 C2 C3 C4 -1.0(2) . . . . ?
C8 C2 C3 C4 -176.14(19) . . . . ?
Fe1 C2 C3 C4 58.69(15) . . . . ?
C1 C2 C3 Fe1 -59.67(14) . . . . ?
C8 C2 C3 Fe1 125.18(18) . . . . ?
C2 Fe1 C3 C4 -119.7(2) . . . . ?
C2' Fe1 C3 C4 128.05(16) . . . . ?
C5 Fe1 C3 C4 -37.45(15) . . . . ?
C3' Fe1 C3 C4 85.00(17) . . . . ?
C4' Fe1 C3 C4 52.1(2) . . . . ?
C1 Fe1 C3 C4 -81.54(15) . . . . ?
C1' Fe1 C3 C4 166.21(16) . . . . ?
C4 Fe1 C3 C2 119.7(2) . . . . ?
C2' Fe1 C3 C2 -112.29(14) . . . . ?
C5 Fe1 C3 C2 82.22(14) . . . . ?
C3' Fe1 C3 C2 -155.33(13) . . . . ?
C4' Fe1 C3 C2 171.78(16) . . . . ?
C1 Fe1 C3 C2 38.12(13) . . . . ?
C1' Fe1 C3 C2 -74.13(17) . . . . ?
C2' C3' C4' C5' -0.6(3) . . . . ?
Fe1 C3' C4' C5' -60.01(17) . . . . ?
C2' C3' C4' Fe1 59.37(17) . . . . ?
C4 Fe1 C4' C3' 84.56(18) . . . . ?
C3 Fe1 C4' C3' 50.0(3) . . . . ?
C2' Fe1 C4' C3' -38.05(16) . . . . ?
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C5 Fe1 C4' C3' 127.53(18) . . . . . ?
C1 Fe1 C4' C3' 166.71(16) . . . . . ?
C1' Fe1 C4' C3' -81.87(18) . . . . . ?
C5' Fe1 C4' C3' -119.0(2) . . . . . ?
C4 Fe1 C4' C5' -156.45(15) . . . . . ?
C3 Fe1 C4' C5' 169.03(18) . . . . . ?
C2' Fe1 C4' C5' 80.93(17) . . . . . ?
C5 Fe1 C4' C5' -113.48(18) . . . . . ?
C3' Fe1 C4' C5' 119.0(2) . . . . . ?
C1 Fe1 C4' C5' -74.30(19) . . . . . ?
C1' Fe1 C4' C5' 37.12(16) . . . . . ?
C2 C3 C4 C5 0.9(2) . . . . . ?
Fe1 C3 C4 C5 60.00(16) . . . . . ?
C2 C3 C4 Fe1 -59.06(15) . . . . . ?
C3 Fe1 C4 C5 -119.5(2) . . . . . ?
C2 Fe1 C4 C5 -81.81(15) . . . . . ?
C2' Fe1 C4 C5 168.98(14) . . . . . ?
C3' Fe1 C4 C5 130.72(15) . . . . . ?
C4' Fe1 C4 C5 88.96(15) . . . . . ?
C1 Fe1 C4 C5 -37.67(14) . . . . . ?
C1' Fe1 C4 C5 -174.9(4) . . . . . ?
C5' Fe1 C4 C5 59.4(2) . . . . . ?
C2 Fe1 C4 C3 37.65(14) . . . . . ?
C2' Fe1 C4 C3 -71.57(19) . . . . . ?
C5 Fe1 C4 C3 119.5(2) . . . . . ?
C3' Fe1 C4 C3 -109.83(15) . . . . . ?
C4' Fe1 C4 C3 -151.59(14) . . . . . ?
C1 Fe1 C4 C3 81.79(15) . . . . . ?
C1' Fe1 C4 C3 -55.4(5) . . . . . ?
C5' Fe1 C4 C3 178.82(18) . . . . . ?
C3 C4 C5 C1 -0.5(2) . . . . . ?
Fe1 C4 C5 C1 59.15(15) . . . . . ?
C3 C4 C5 Fe1 -59.69(16) . . . . . ?
N1 C1 C5 C4 177.5(2) . . . . . ?
C2 C1 C5 C4 -0.1(2) . . . . . ?
Fe1 C1 C5 C4 -58.61(15) . . . . . ?
N1 C1 C5 Fe1 -123.9(2) . . . . . ?
C2 C1 C5 Fe1 58.53(15) . . . . . ?
C3 Fe1 C5 C4 37.77(14) . . . . . ?
C2 Fe1 C5 C4 81.93(17) . . . . . ?
C2' Fe1 C5 C4 -37.9(5) . . . . . ?
C3' Fe1 C5 C4 -66.93(19) . . . . . ?
C4' Fe1 C5 C4 -107.02(15) . . . . . ?
C1 Fe1 C5 C4 119.7(2) . . . . . ?
C1' Fe1 C5 C4 177.6(2) . . . . . ?
C5' Fe1 C5 C4 -149.29(14) . . . . . ?
C4 Fe1 C5 C1 -119.7(2) . . . . . ?
C3 Fe1 C5 C1 -81.90(16) . . . . . ?
C2 Fe1 C5 C1 -37.74(16) . . . . . ?
C2' Fe1 C5 C1 -157.6(4) . . . . . ?
C3' Fe1 C5 C1 173.39(15) . . . . . ?
C4' Fe1 C5 C1 133.30(15) . . . . . ?
C1' Fe1 C5 C1 57.9(2) . . . . . ?
C5' Fe1 C5 C1 91.03(16) . . . . . ?
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C2' C1' C5' C4' -0.3(3) . . . . . ?
Fe1 C1' C5' C4' 58.95(17) . . . . . ?
C2' C1' C5' Fe1 -59.23(17) . . . . . ?
C3' C4' C5' C1' 0.6(3) . . . . ?
Fe1 C4' C5' C1' -59.04(17) . . . . . ?
C3' C4' C5' Fe1 59.61(17) . . . . ?
C4 Fe1 C5' C1' 164.01(19) . . . . ?
C2 Fe1 C5' C1' -69.5(2) . . . . ?
C2' Fe1 C5' C1' 37.87(17) . . . . ?
C5 Fe1 C5' C1' -156.52(15) . . . . ?
C3' Fe1 C5' C1' 82.05(17) . . . . ?
C4' Fe1 C5' C1' 119.8(2) . . . . ?
C1 Fe1 C5' C1' -111.69(17) . . . . ?
C4 Fe1 C5' C4' 44.3(3) . . . . ?
C2 Fe1 C5' C4' 170.80(14) . . . . ?
C2' Fe1 C5' C4' -81.88(17) . . . . ?
C5 Fe1 C5' C4' 83.73(18) . . . . ?
C3' Fe1 C5' C4' -37.70(15) . . . . ?
C1 Fe1 C5' C4' 128.56(15) . . . . ?
C1' Fe1 C5' C4' -119.8(2) . . . . ?
C3 C2 C8 O1 -146.1(2) . . . . ?
C1 C2 C8 O1 39.6(3) . . . . ?
Fe1 C2 C8 O1 -53.1(3) . . . . ?
C3 C2 C8 C15 -27.4(3) . . . . ?
C1 C2 C8 C15 158.25(19) . . . . ?
Fe1 C2 C8 C15 65.6(3) . . . . ?
C3 C2 C8 C9 94.0(2) . . . . ?
C1 C2 C8 C9 -80.3(3) . . . . ?
Fe1 C2 C8 C9 -173.0(2) . . . . ?
O1 C8 C9 C14 -145.2(2) . . . . ?
C2 C8 C9 C14 -25.1(3) . . . . ?
C15 C8 C9 C14 97.8(2) . . . . ?
O1 C8 C9 C10 35.6(3) . . . . ?
C2 C8 C9 C10 155.7(2) . . . . ?
C15 C8 C9 C10 -81.3(2) . . . . ?
C14 C9 C10 C11 2.3(4) . . . . ?
C8 C9 C10 C11 -178.5(2) . . . . ?
C9 C10 C11 C12 -0.5(4) . . . . ?
C10 C11 C12 C13 -1.4(4) . . . . ?
C11 C12 C13 C14 1.4(4) . . . . ?
C10 C9 C14 C13 -2.3(3) . . . . ?
C8 C9 C14 C13 178.5(2) . . . . ?
C12 C13 C14 C9 0.4(4) . . . . ?
O1 C8 C15 C16 -156.3(2) . . . . ?
C2 C8 C15 C16 83.8(2) . . . . ?
C9 C8 C15 C16 -38.4(3) . . . . ?
O1 C8 C15 C20 24.8(3) . . . . ?
C2 C8 C15 C20 -95.1(2) . . . . ?
C9 C8 C15 C20 142.7(2) . . . . ?
C20 C15 C16 C17 -0.2(3) . . . . ?
C8 C15 C16 C17 -179.1(2) . . . . ?
C15 C16 C17 C18 -0.2(4) . . . . ?
C16 C17 C18 C19 0.8(4) . . . . ?
C17 C18 C19 C20 -1.1(4) . . . . ?
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C18 C19 C20 C15 0.7(4) . . . . ?
C16 C15 C20 C19 -0.1(3) . . . . ?
C8 C15 C20 C19 178.8(2) . . . . ?
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_diffrn_measured_fraction_theta_max   0.998

_diffrn_reflns_theta_full   28.39

_diffrn_measured_fraction_theta_full   0.998

_refine_diff_density_max   0.372

_refine_diff_density_min   -0.339

_refine_diff_density_rms   0.058

Appendix E: Selected Spectra

^{1}H and ^{13}C spectra for biscarbamate **117**.
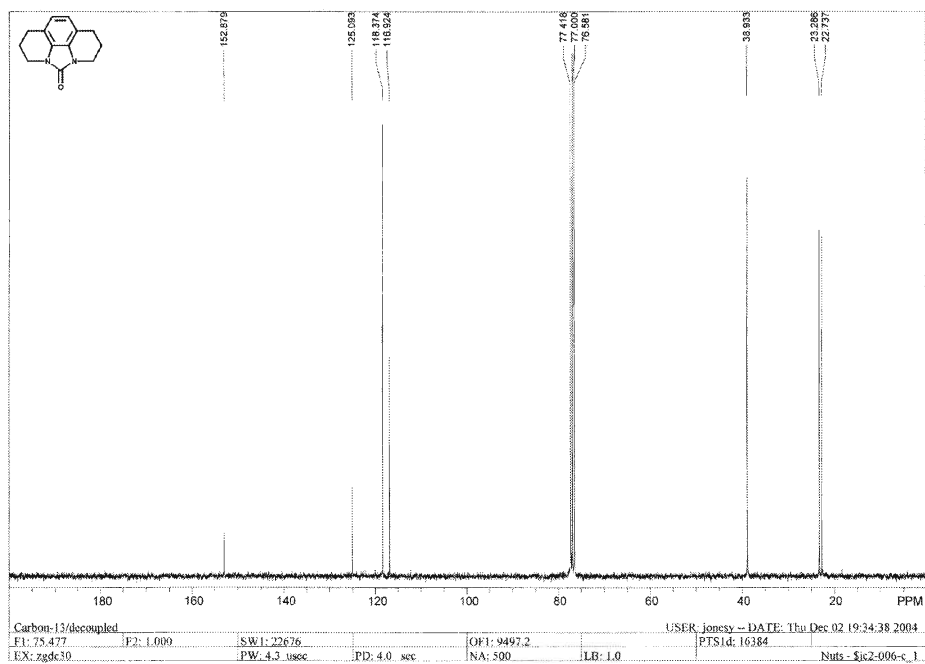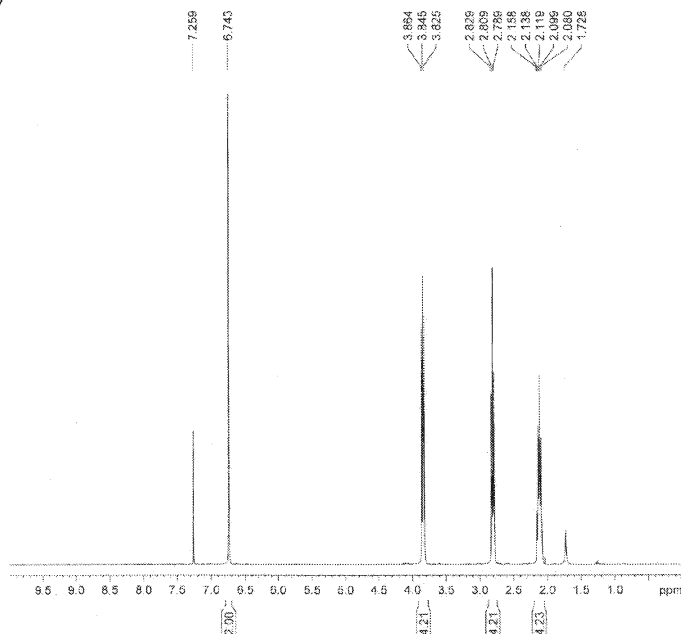
¹H and ¹³C spectra for urea **119**.
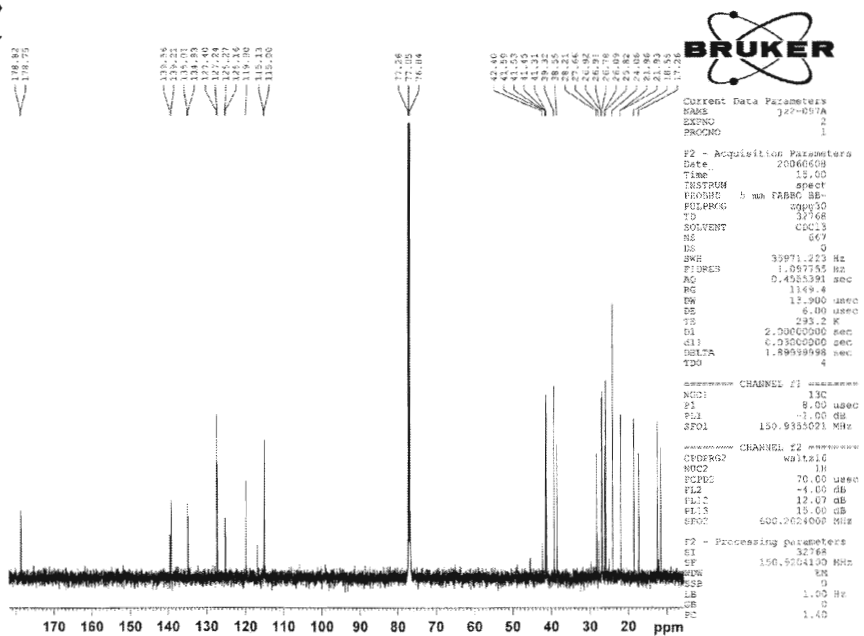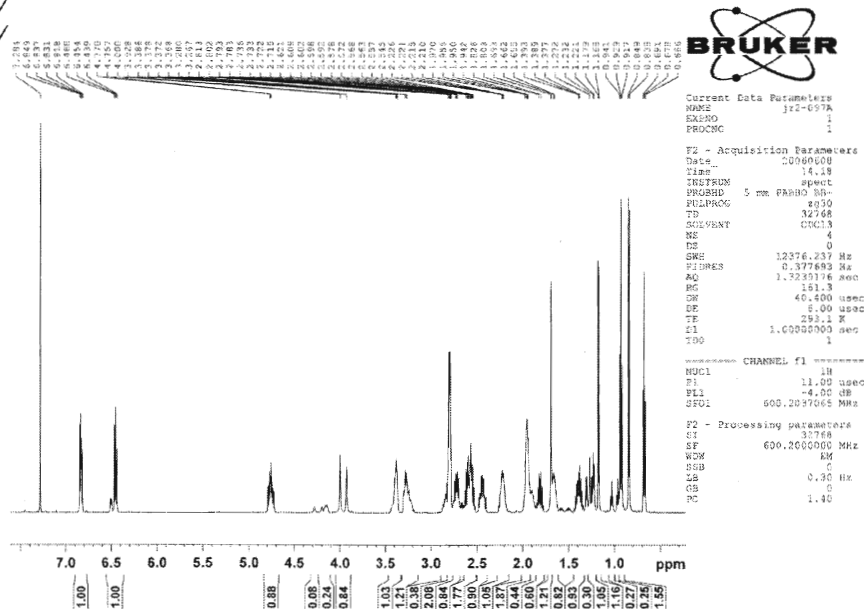
^{1}H and ^{13}C spectra for amide **121**

^{1}H and ^{13}C spectra for urea **119-*d₁***.
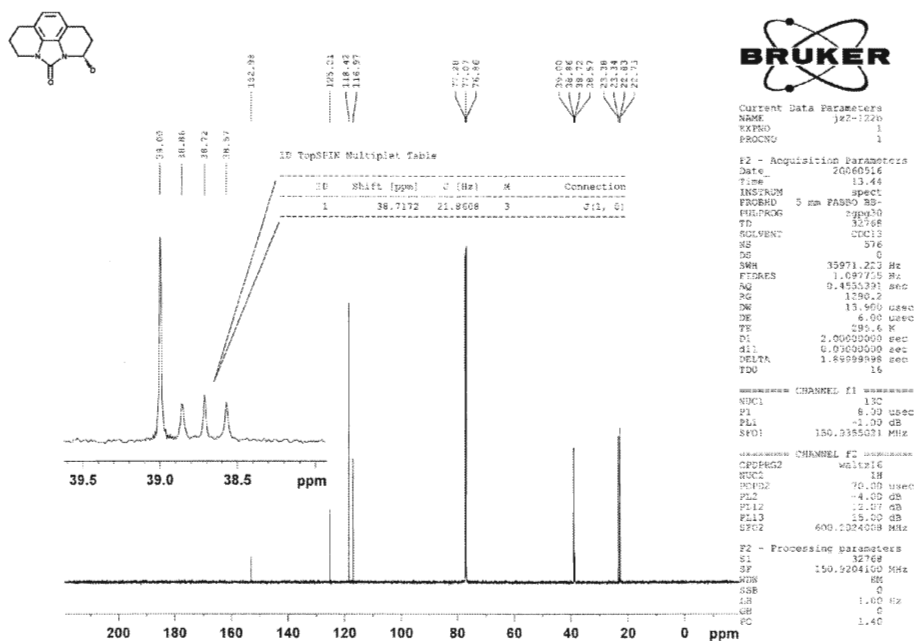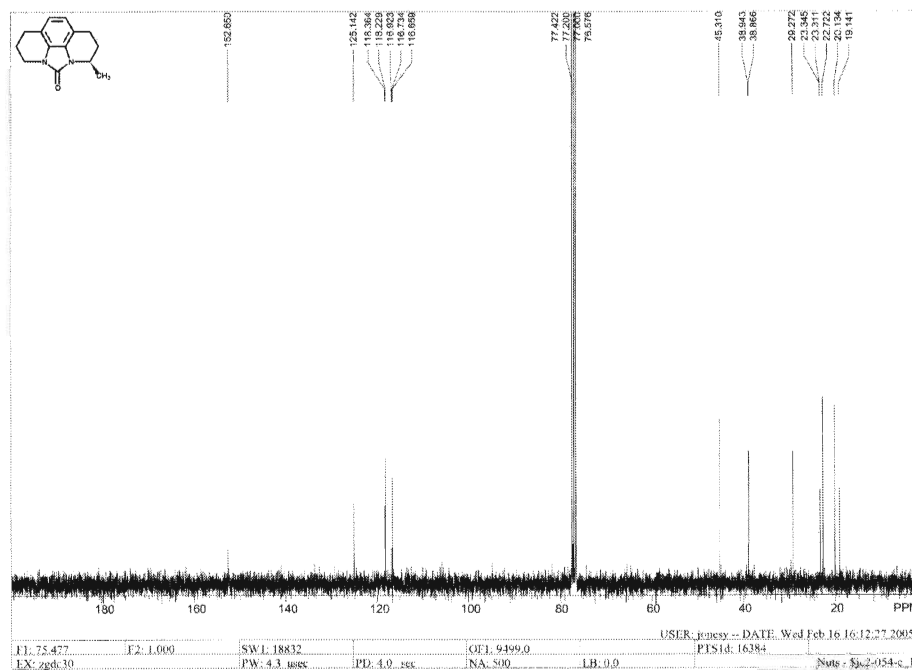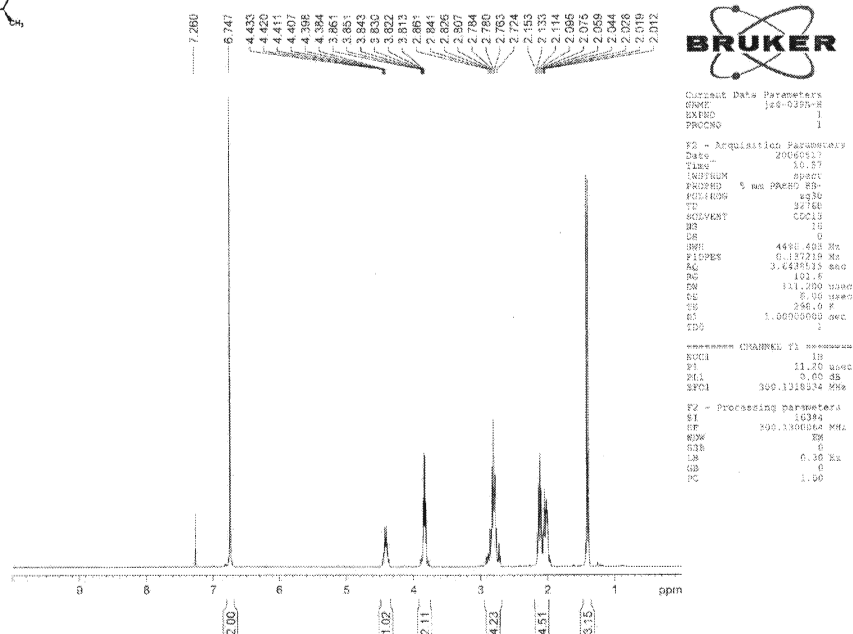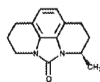
^{1}H and ^{13}C spectra for urea **119a**.

^{1}H and ^{13}C spectra for urea **119b**.
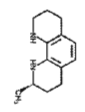
^{1}H and ^{13}C spectra for diamine **122**.

^{1}H and ^{13}C spectra for benzimidazolium iodide **123**.
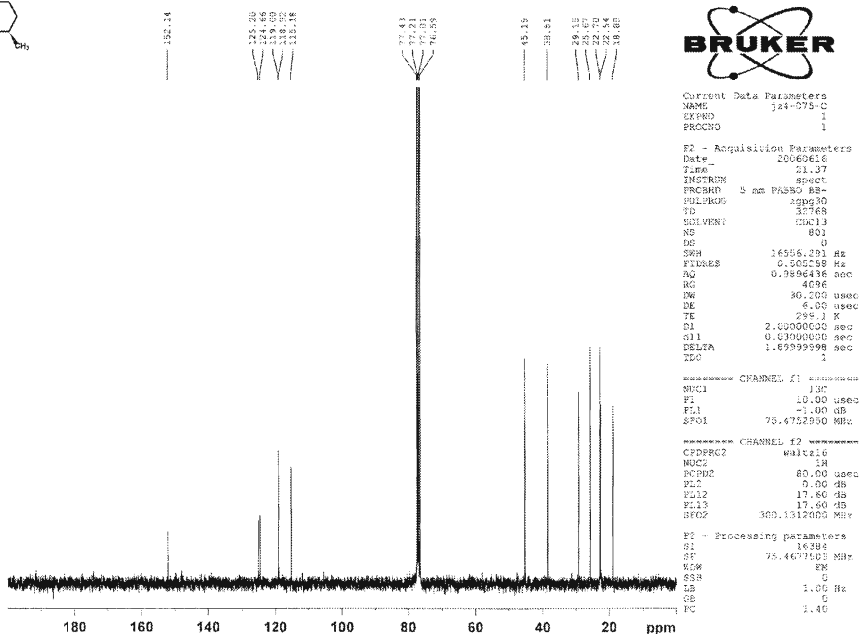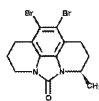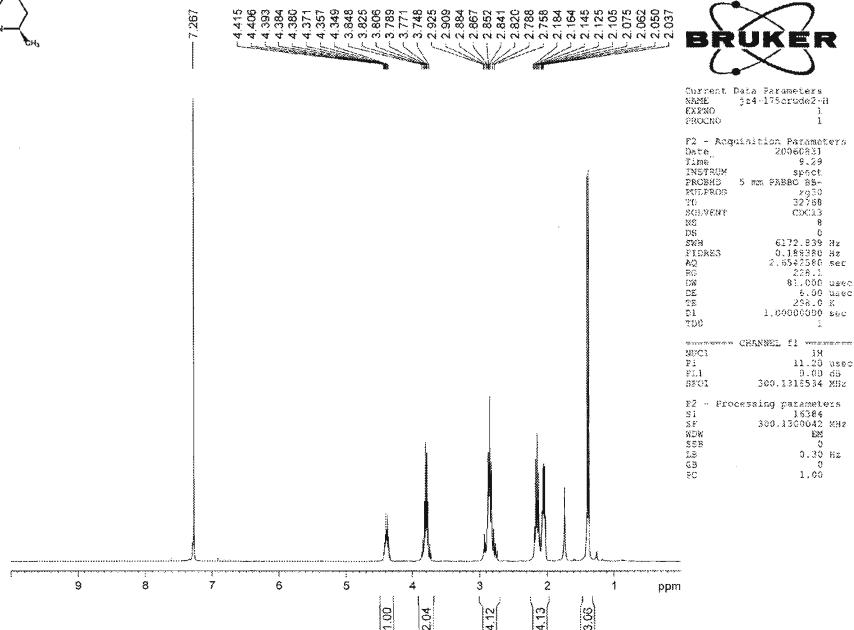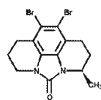
^{1}H and ^{13}C spectra for dibromide **124**.
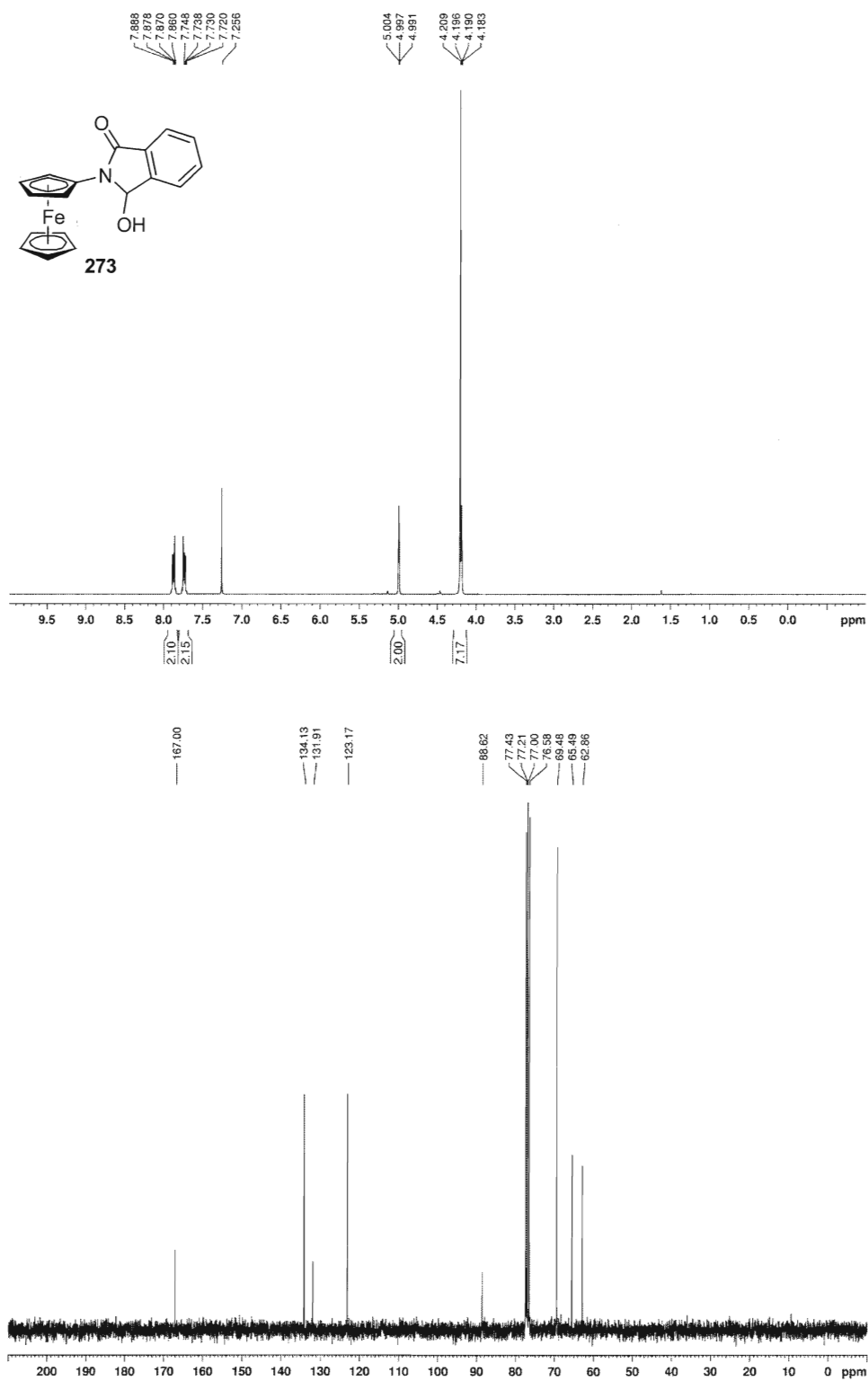
^{1}H and ^{13}C spectra for phthalimidine **273**.
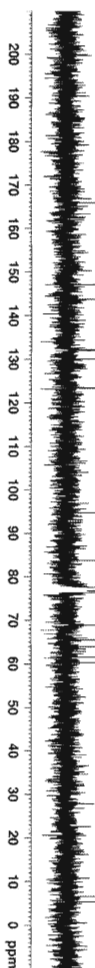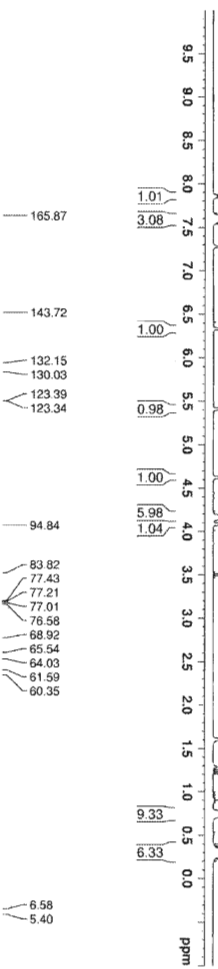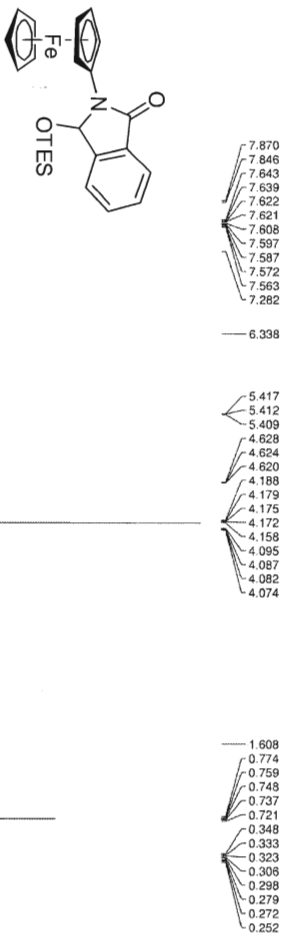
^{1}H and ^{13}C spectra for TES-protected phthalimidine **263b**.

263b

^{13}C peaks: 165.87, 143.72, 132.15, 130.03, 123.39, 123.34, 94.84, 83.82, 77.43, 77.21, 77.01, 76.58, 68.92, 65.54, 64.03, 61.59, 60.35, 6.58, 5.40

^{1}H peaks: 7.870, 7.846, 7.643, 7.639, 7.622, 7.621, 7.608, 7.597, 7.587, 7.572, 7.563, 7.282, 6.338, 5.417, 5.412, 5.409, 4.628, 4.624, 4.620, 4.188, 4.179, 4.175, 4.172, 4.158, 4.095, 4.087, 4.082, 4.074, 1.608, 0.774, 0.759, 0.748, 0.737, 0.721, 0.348, 0.333, 0.323, 0.306, 0.298, 0.279, 0.272, 0.252

Integrations: 1.01, 3.08, 1.00, 0.98, 1.00, 5.98, 1.04, 9.33, 6.33

267

^{1}H and ^{13}C NMR for phthalimidine **274**.

268
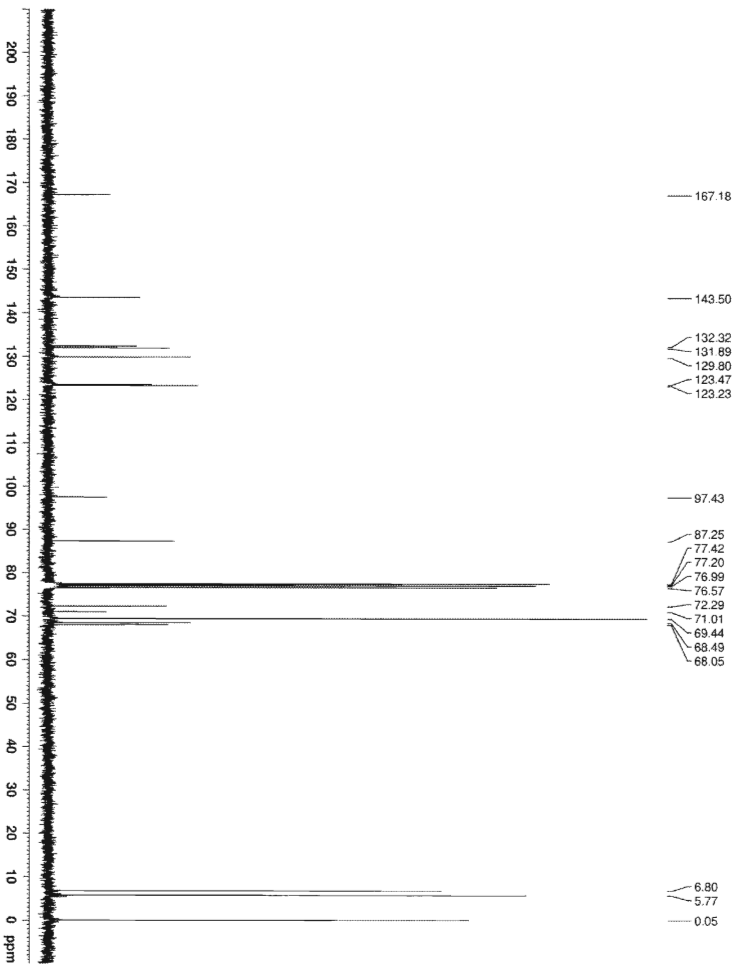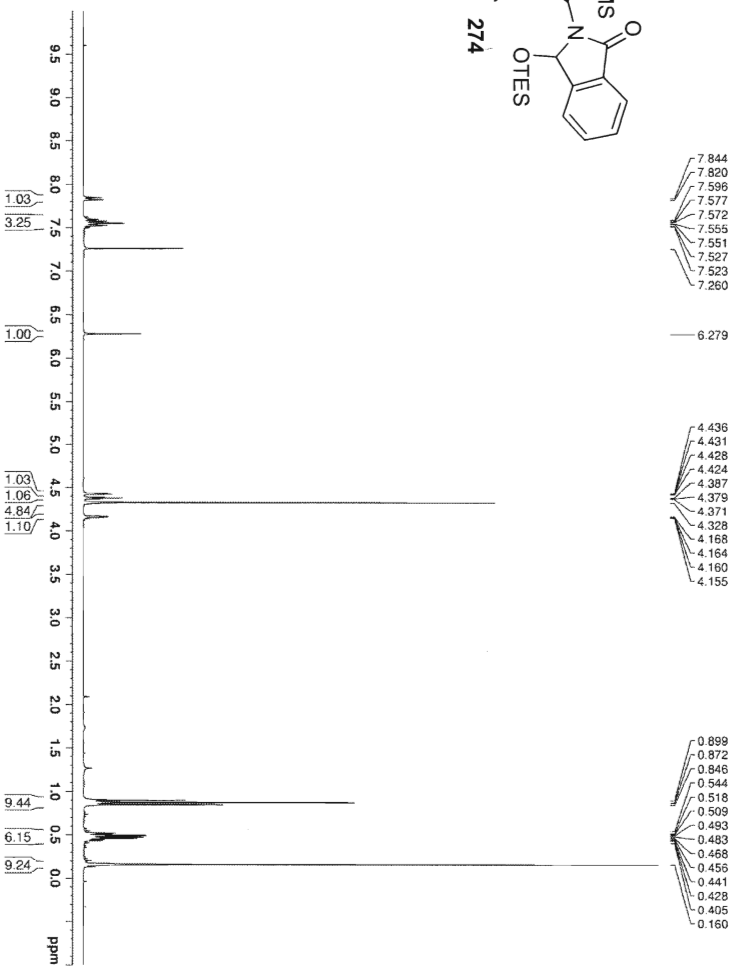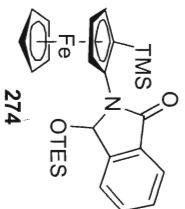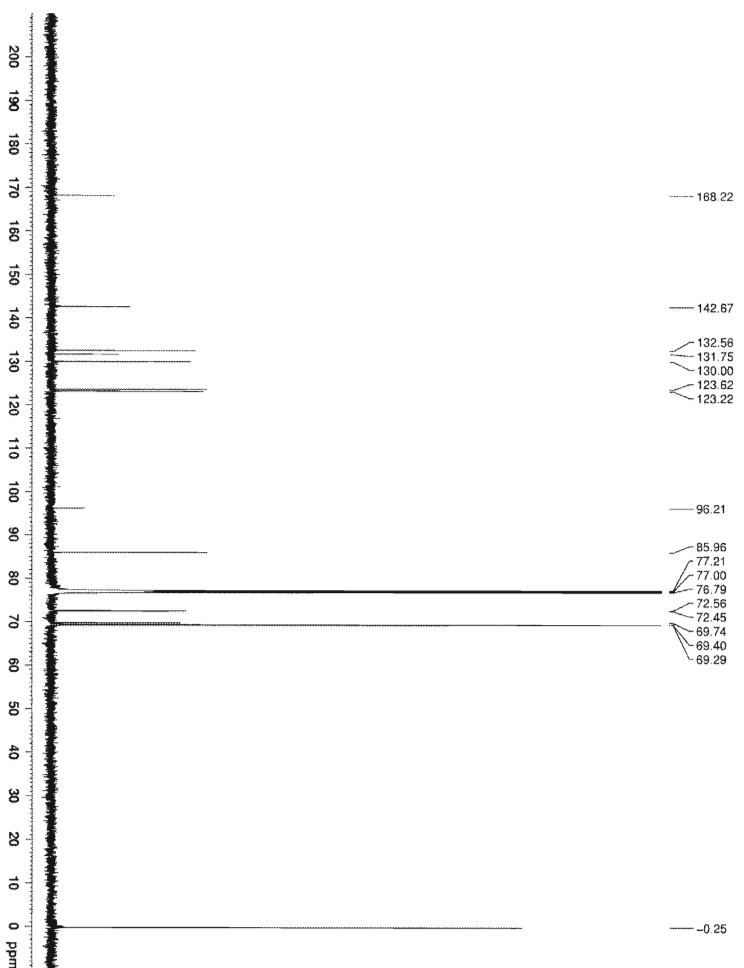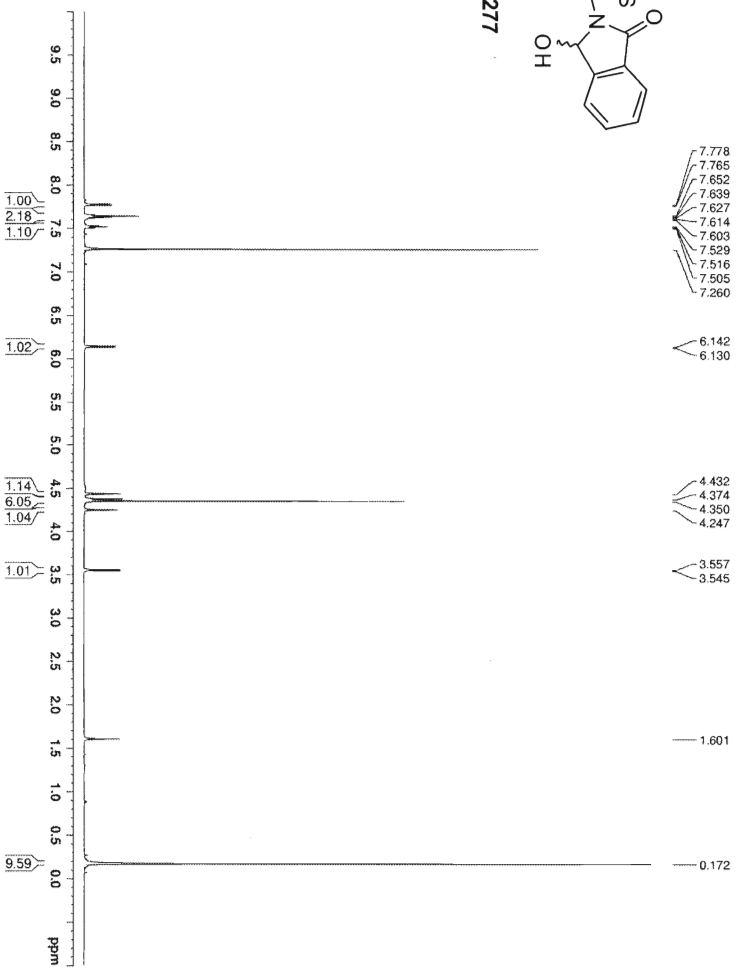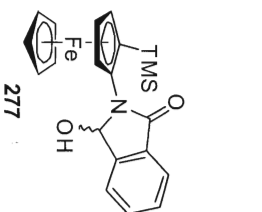
^{1}H and ^{13}C NMR for phthalimidine **277**.
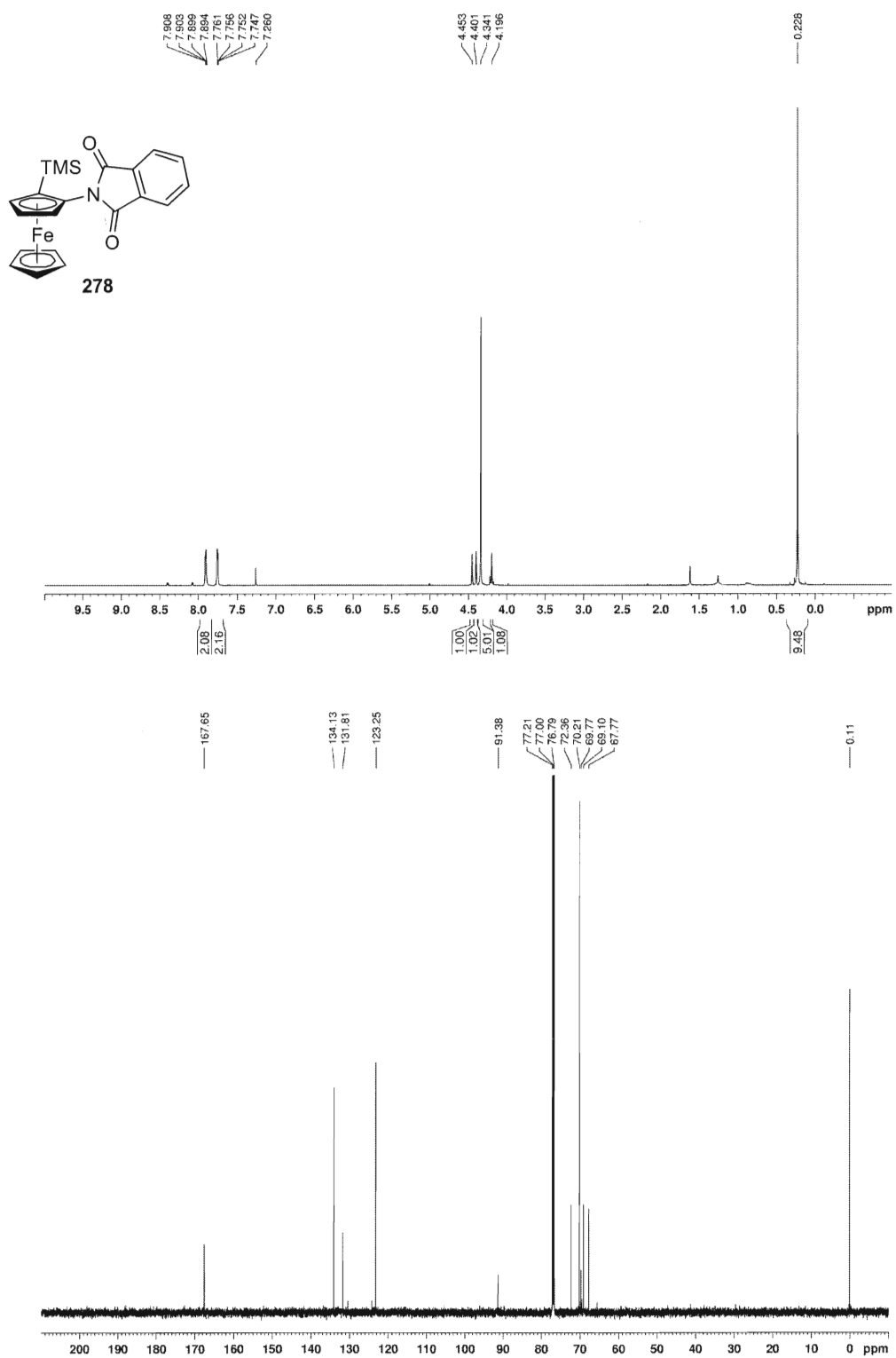
^{1}H and ^{13}C NMR for phthalimide **278**.
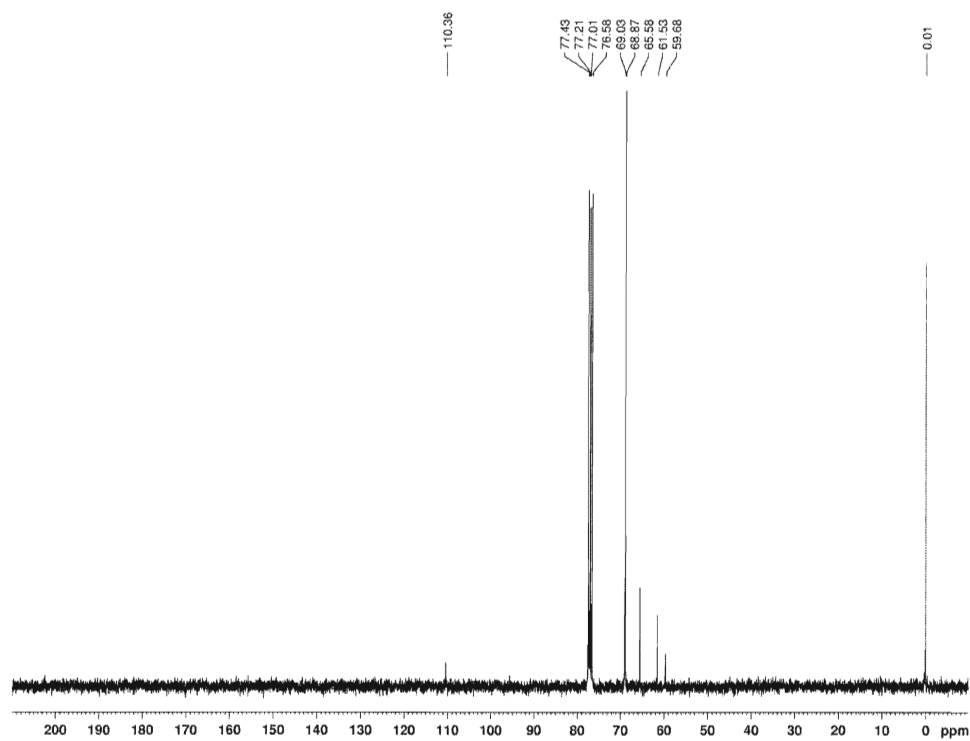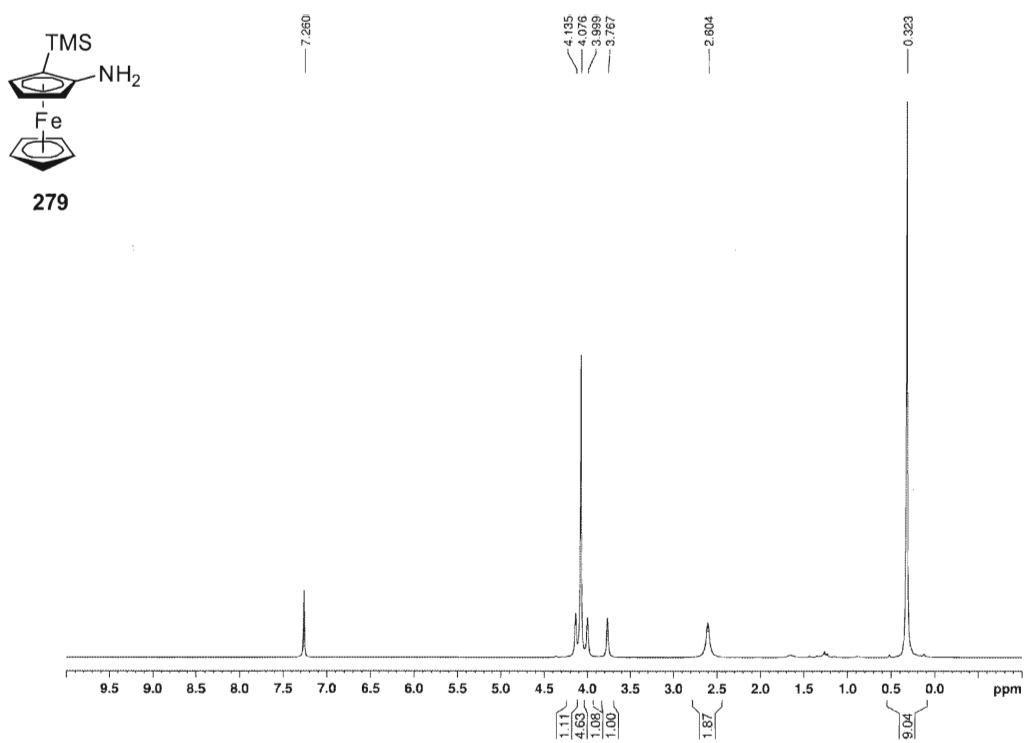
^{1}H and ^{13}C NMR for TMS-substituted aminoferrocene **279**.
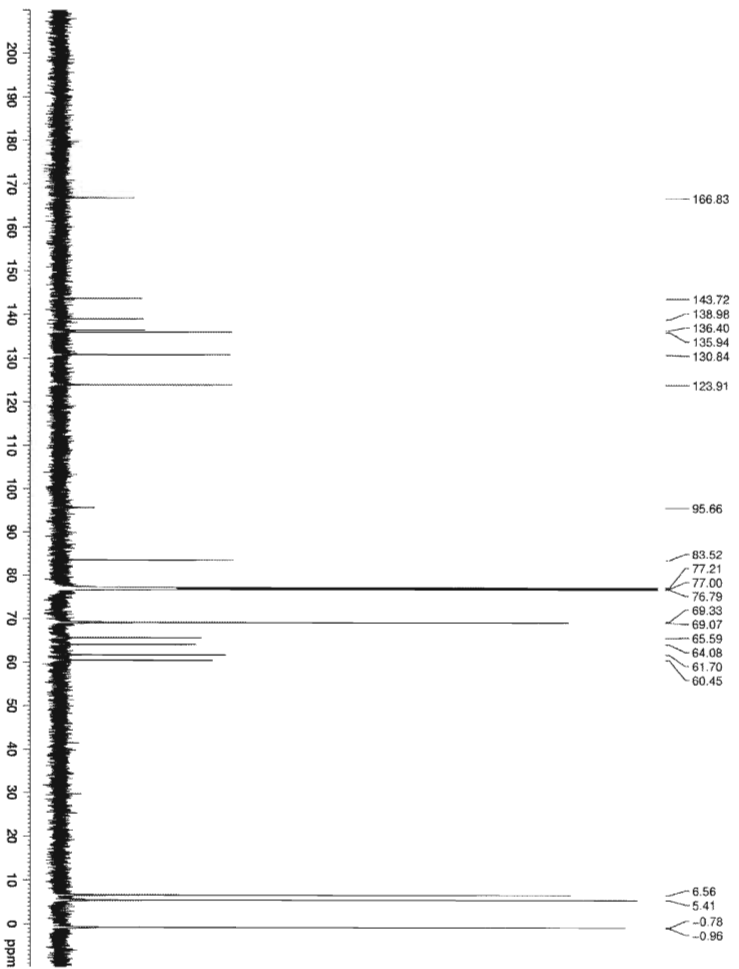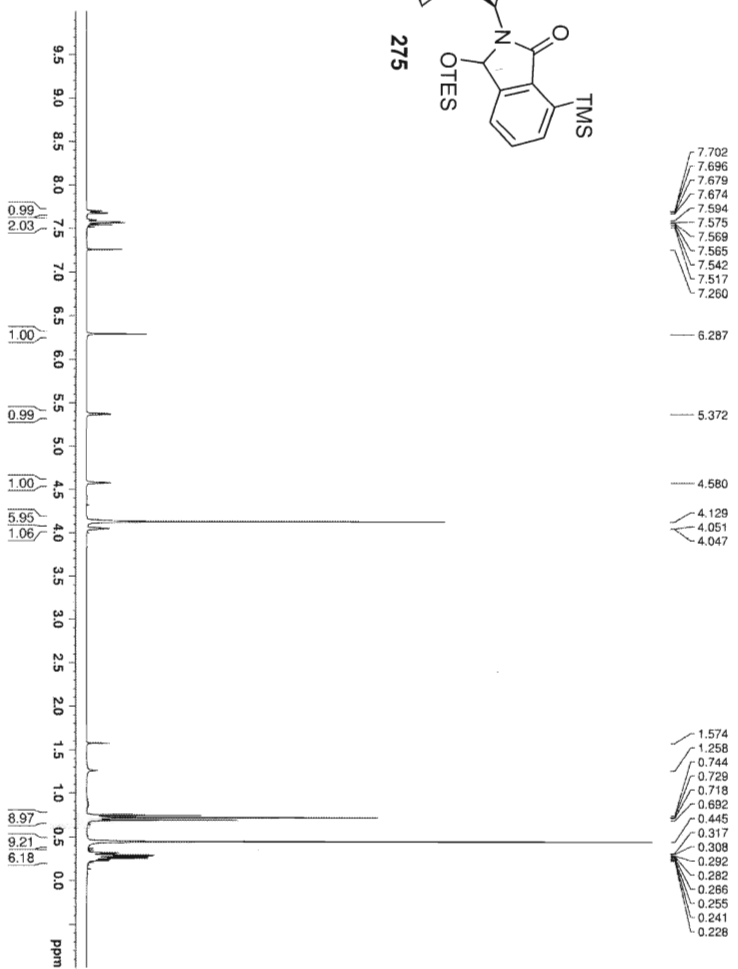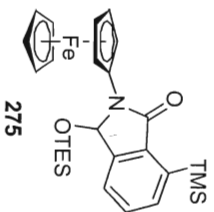
^{1}H and ^{13}C NMR for phthalimidine **275**.
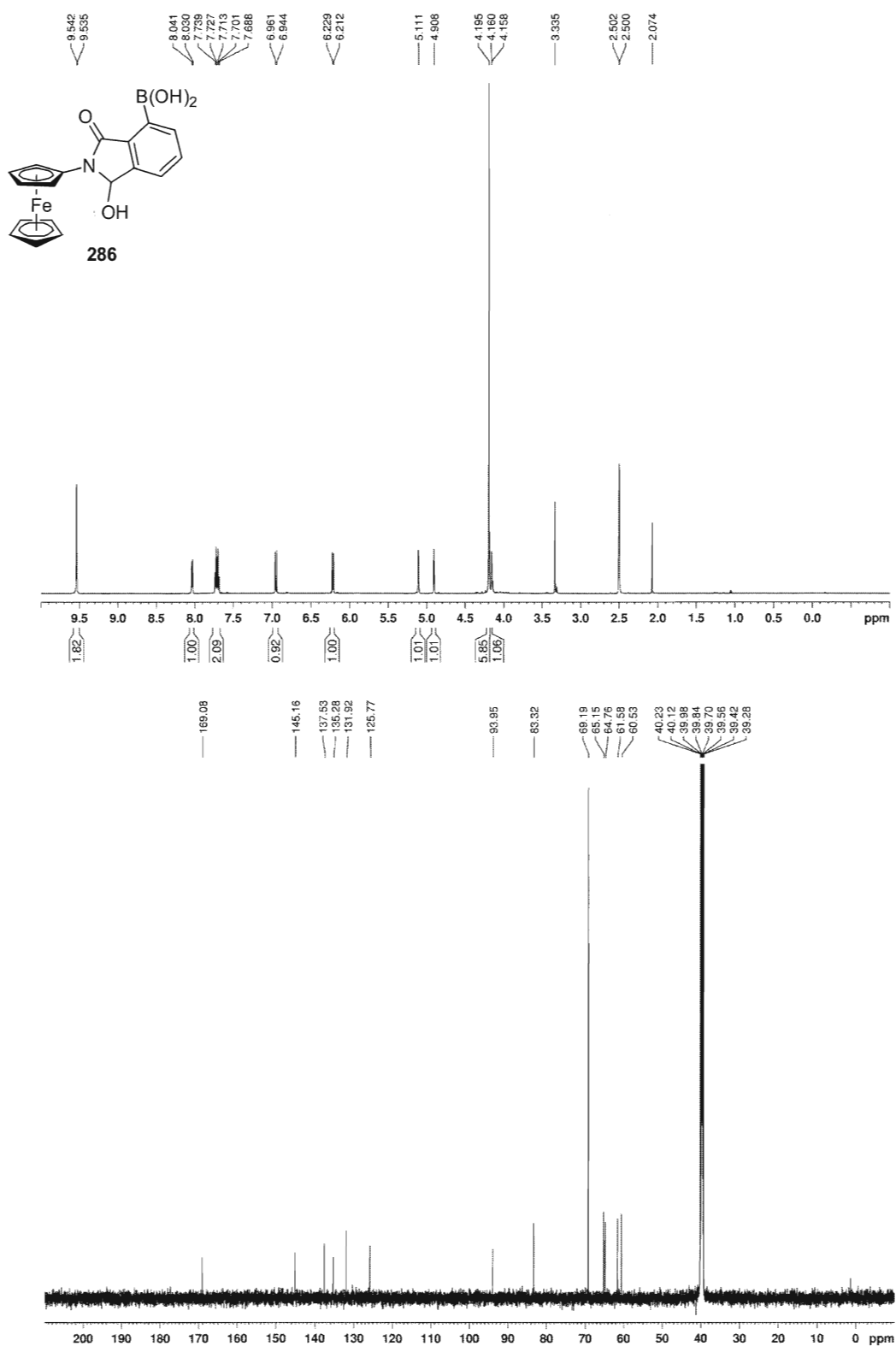
^{1}H and ^{13}C NMR for phthalimidine **286**.
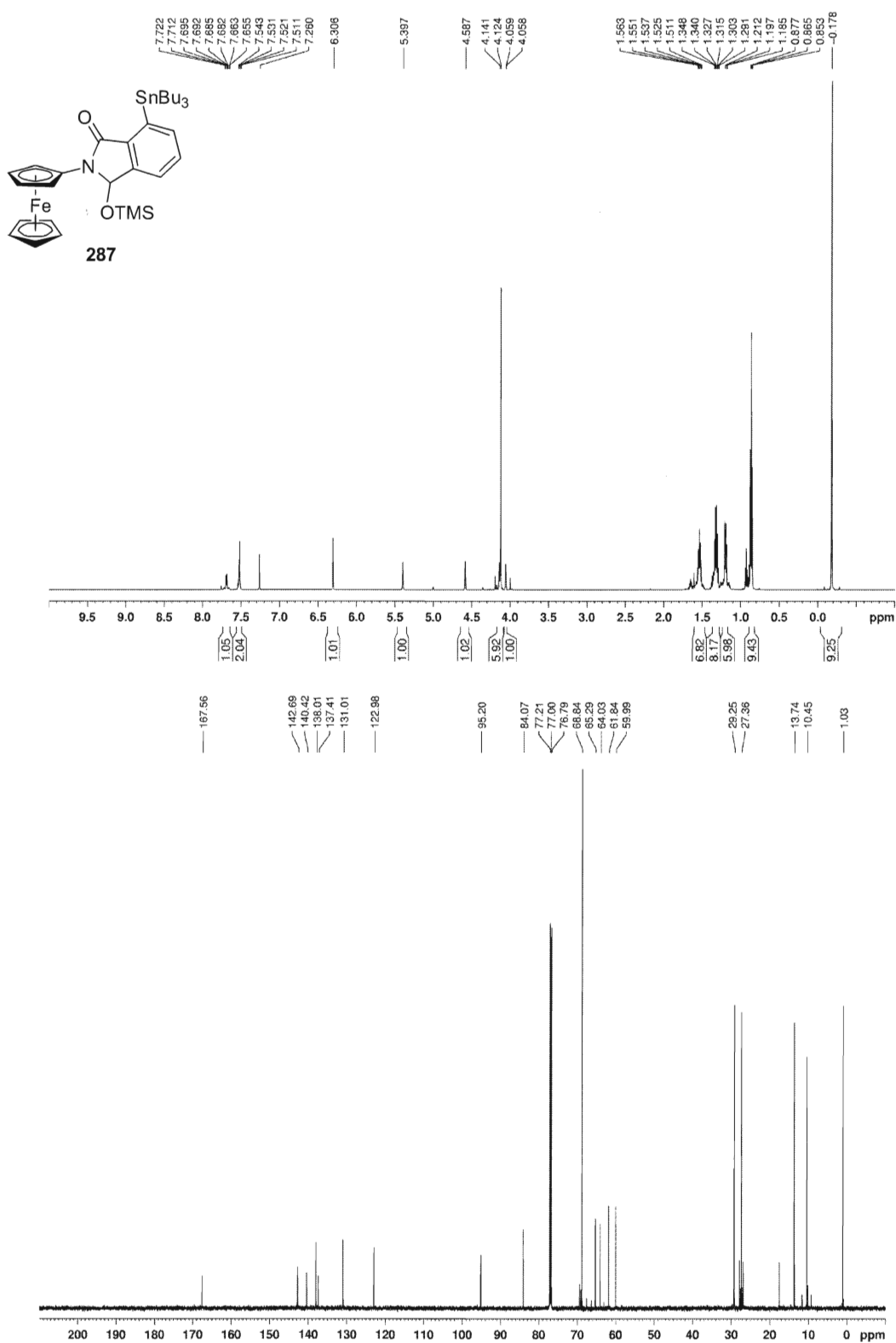
^{1}H and ^{13}C NMR for phthalimidine **287**.
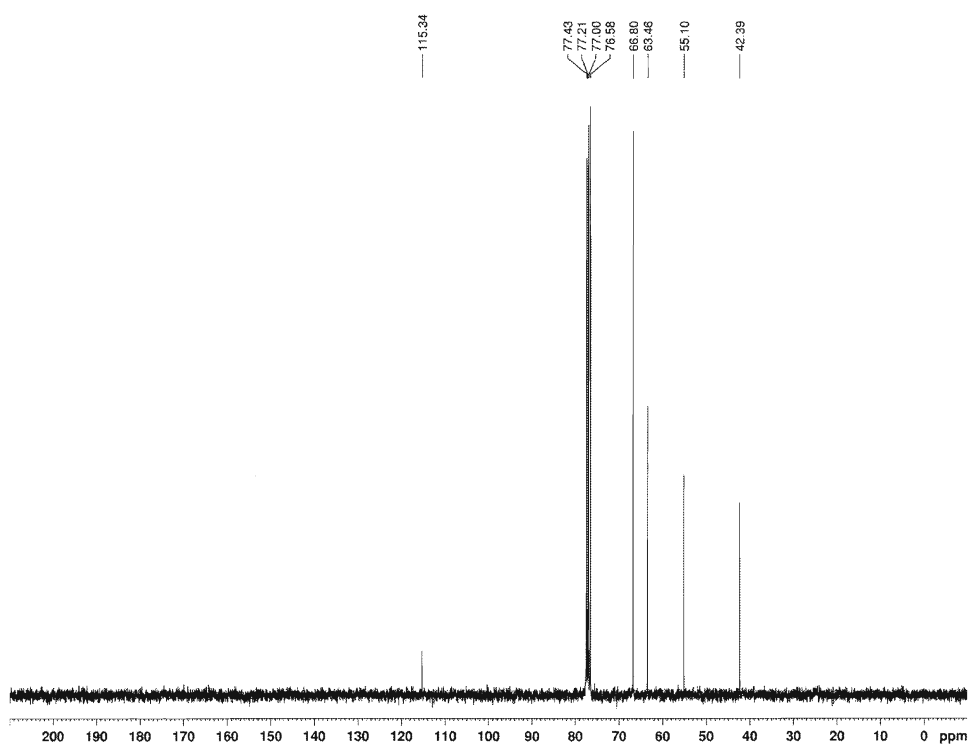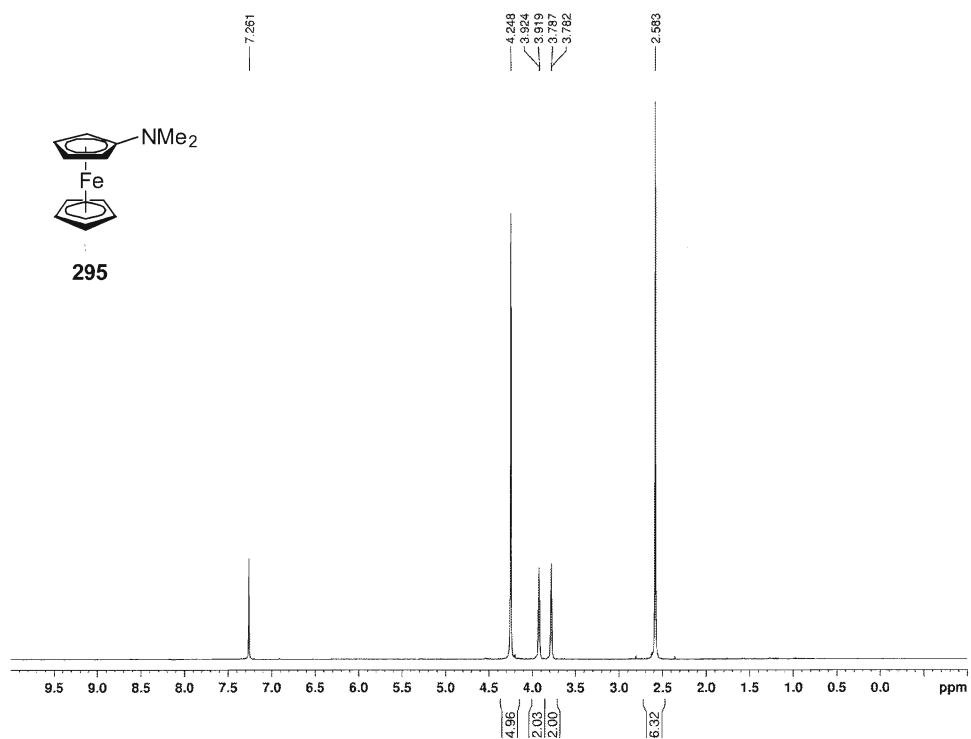
^{1}H and ^{13}C NMR for dimethylaminoferrocene **295**.
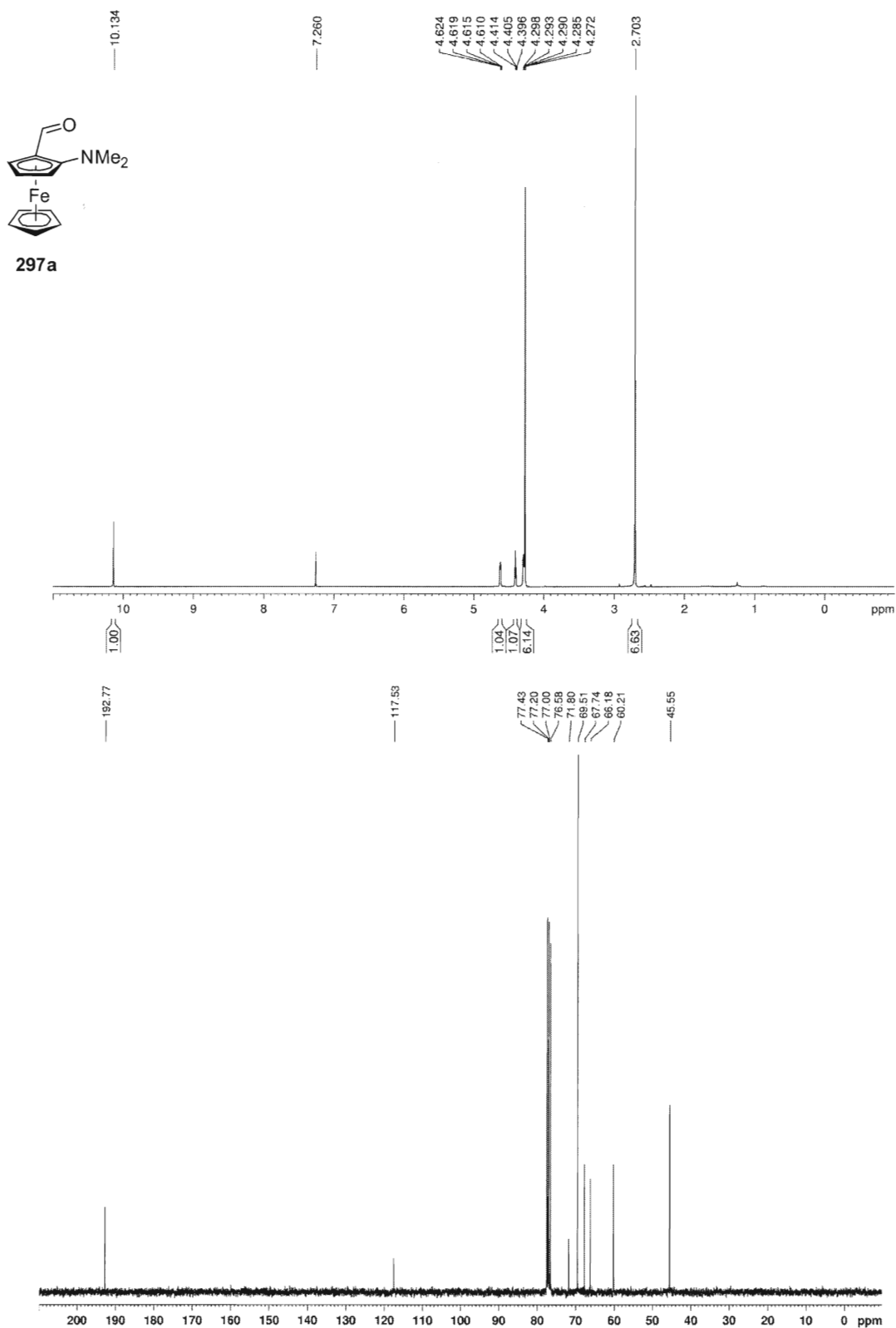
^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297a**.

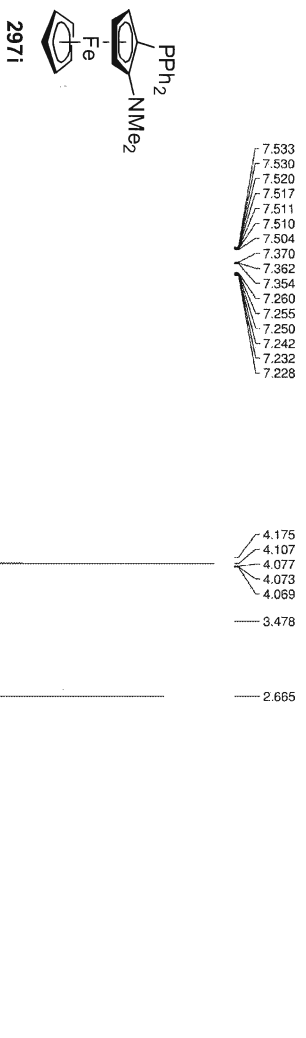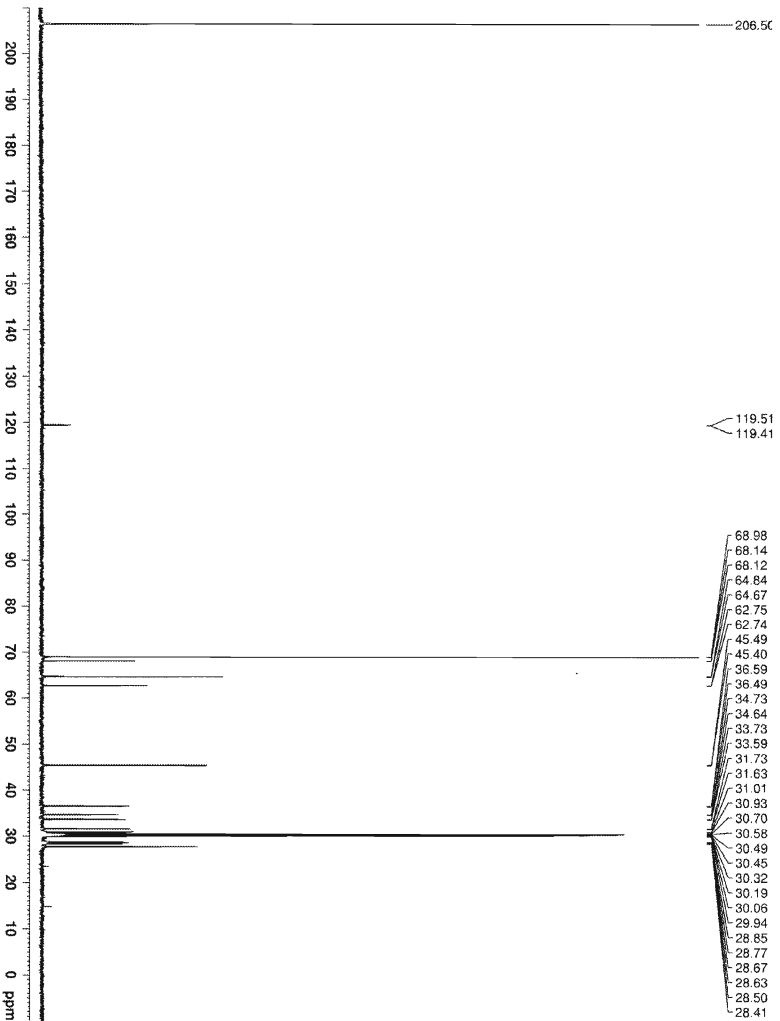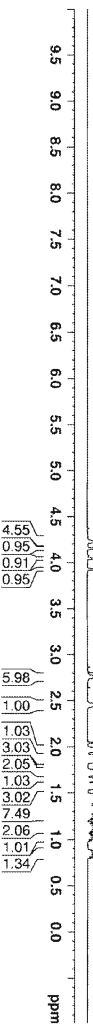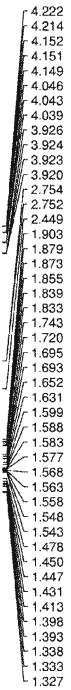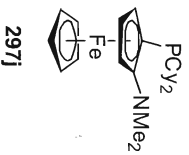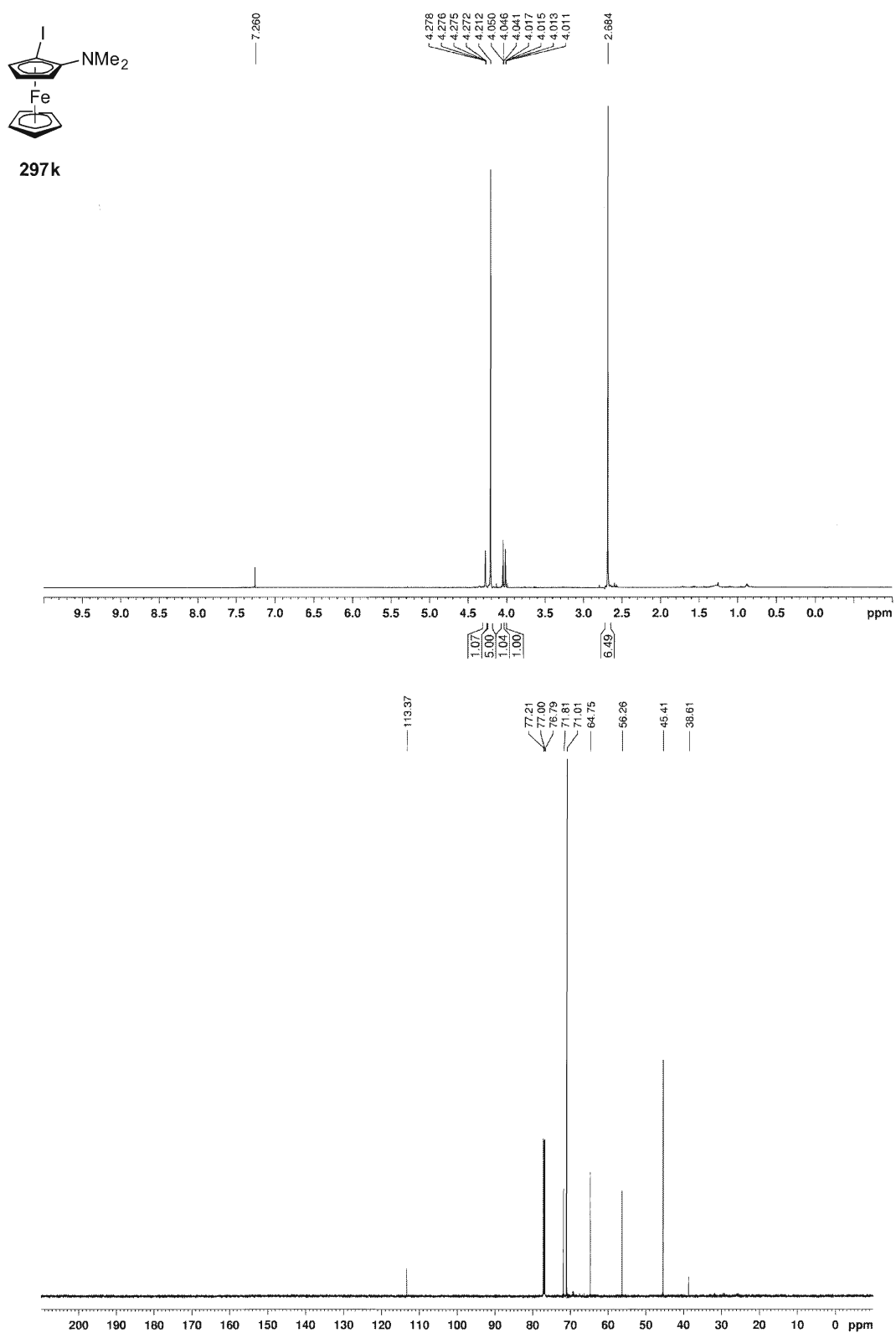^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297b**.

297b

13C NMR peaks:
150.04
146.13
127.48
127.15
127.03
126.87
126.41
126.23
109.52
91.82
78.03
77.43
77.21
77.00
76.58
69.81
65.93
63.84
57.43
46.67

1H NMR peaks:
8.097
7.645
7.641
7.617
7.375
7.351
7.329
7.306
7.259
7.234
7.226
7.220
7.214
7.210
7.198
7.173
7.152
7.138
7.129
7.105
4.186
4.182
4.178
4.174
4.088
4.079
4.061
3.937
3.932
3.928
3.924
2.353

Integrations: 1.01, 2.04, 8.39, 1.00, 5.82, 0.97, 6.17

Ph⏜OH

NMe₂

Fe

297c

(less polar)

7.529
7.505
7.410
7.386
7.361
7.321
7.297
7.260

5.676

5.226

4.218
4.061
3.906
3.889
3.613

2.615

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

2.06 2.22 1.01   1.00   1.03   4.88 1.01 1.03 1.00   6.46

144.94

127.94
126.65
125.76

110.91

85.63
77.42
77.20
77.00
76.58
72.67
69.75
65.30
63.63
56.90

46.46

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

¹H and ¹³C NMR for less polar 2-substituted aminoferrocene diastereomer **297c**.

278
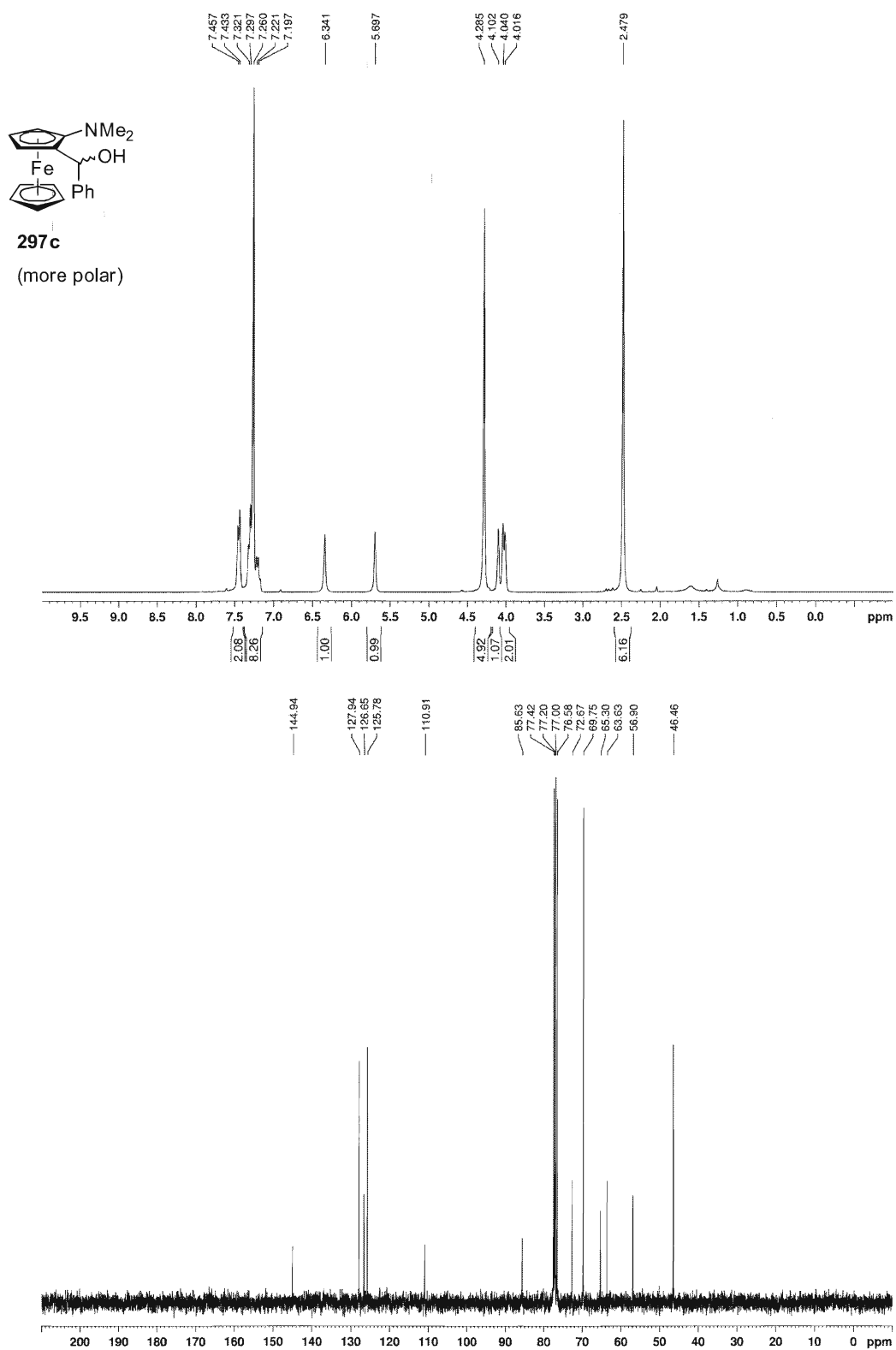
^{1}H and ^{13}C NMR for more polar 2-substituted aminoferrocene diastereomer **297c**.
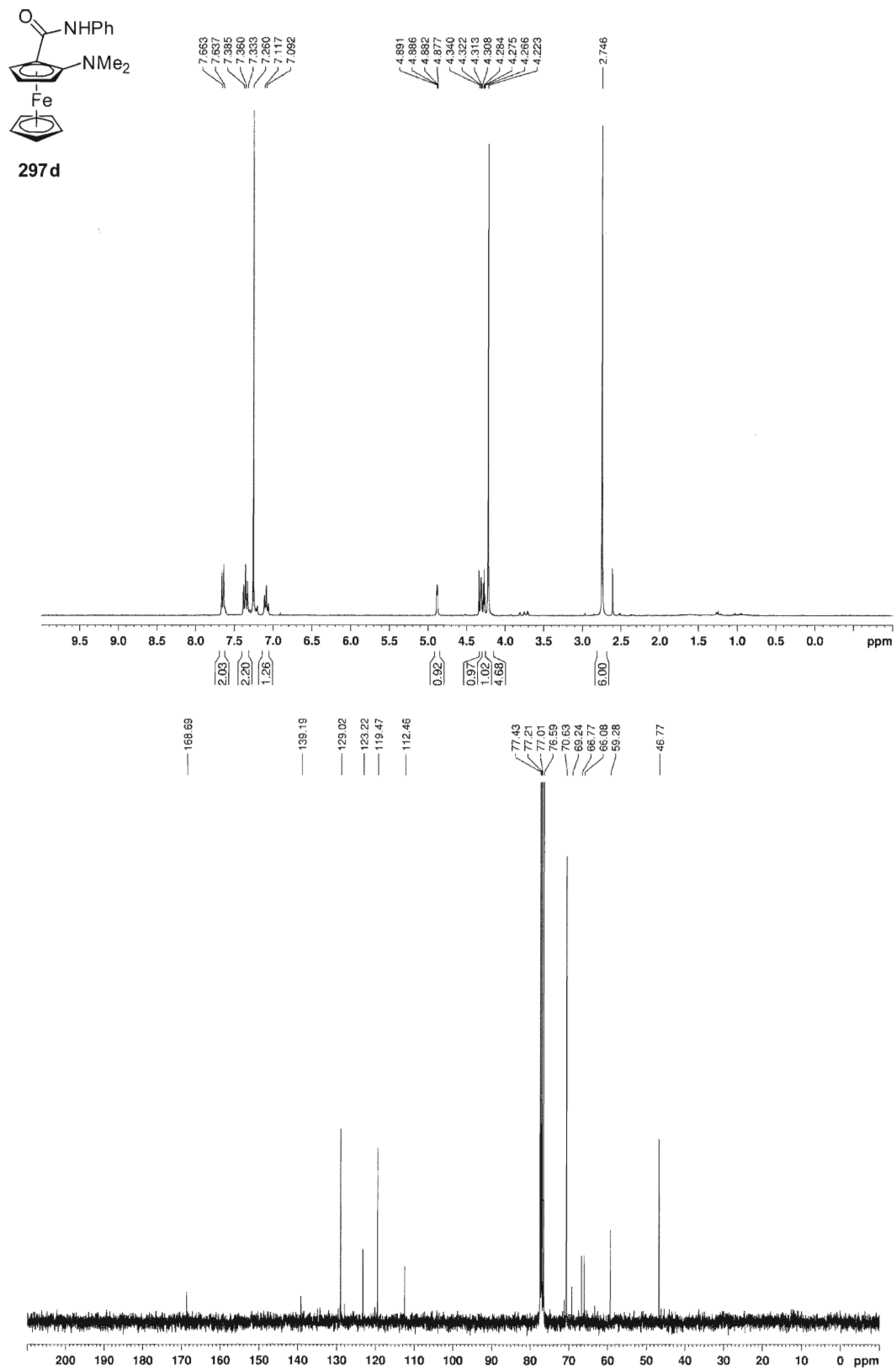
^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297d**.
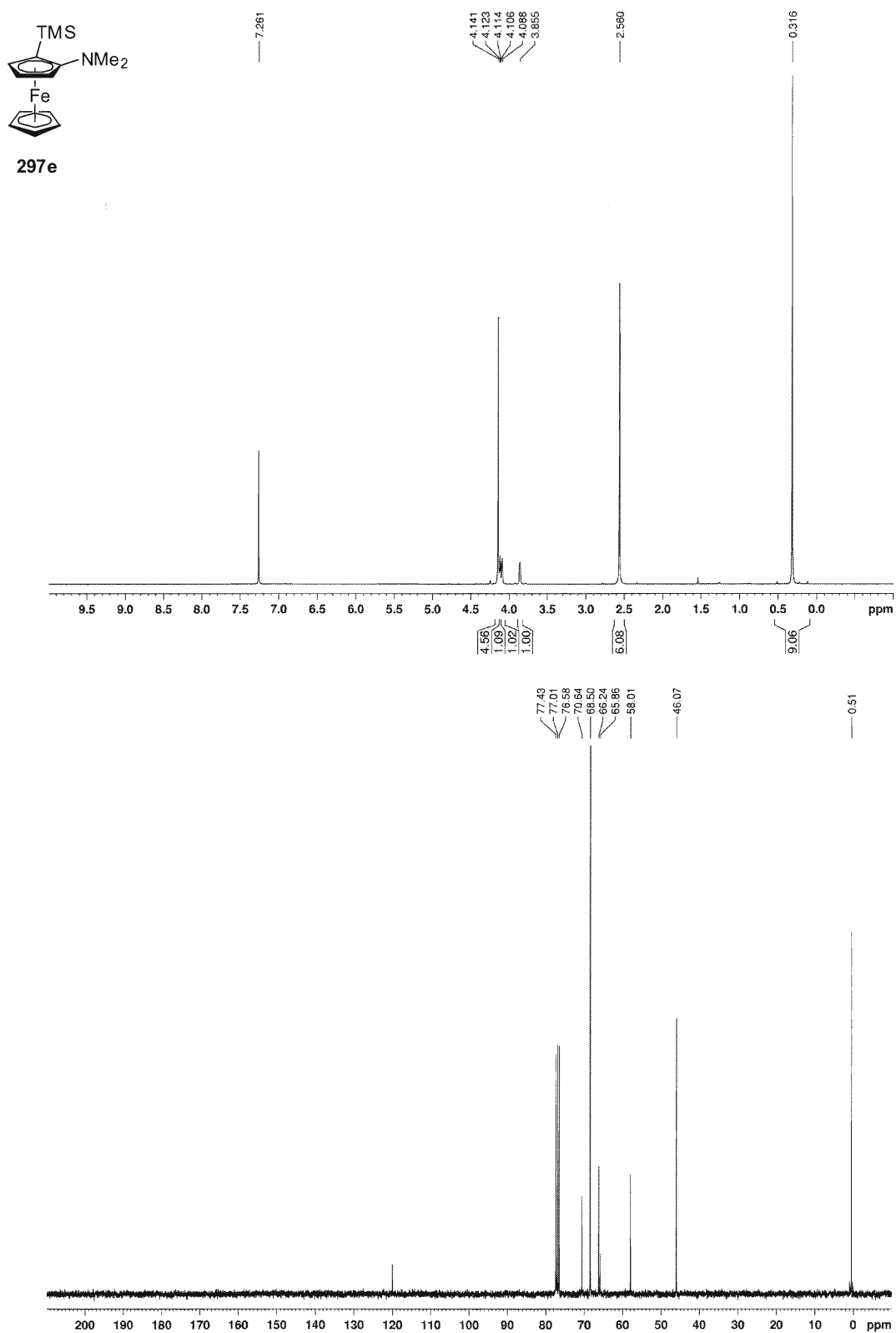
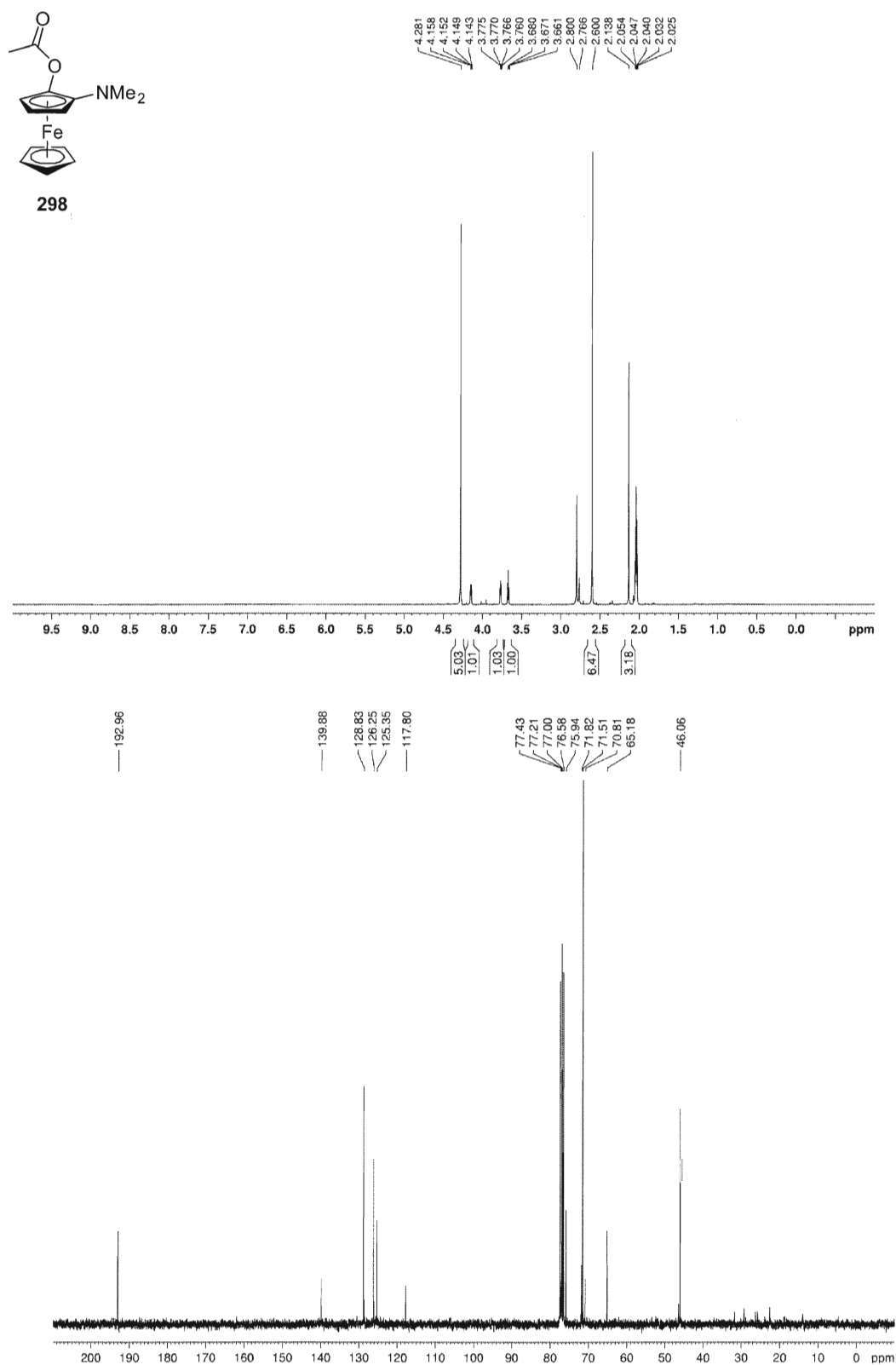^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297e**.
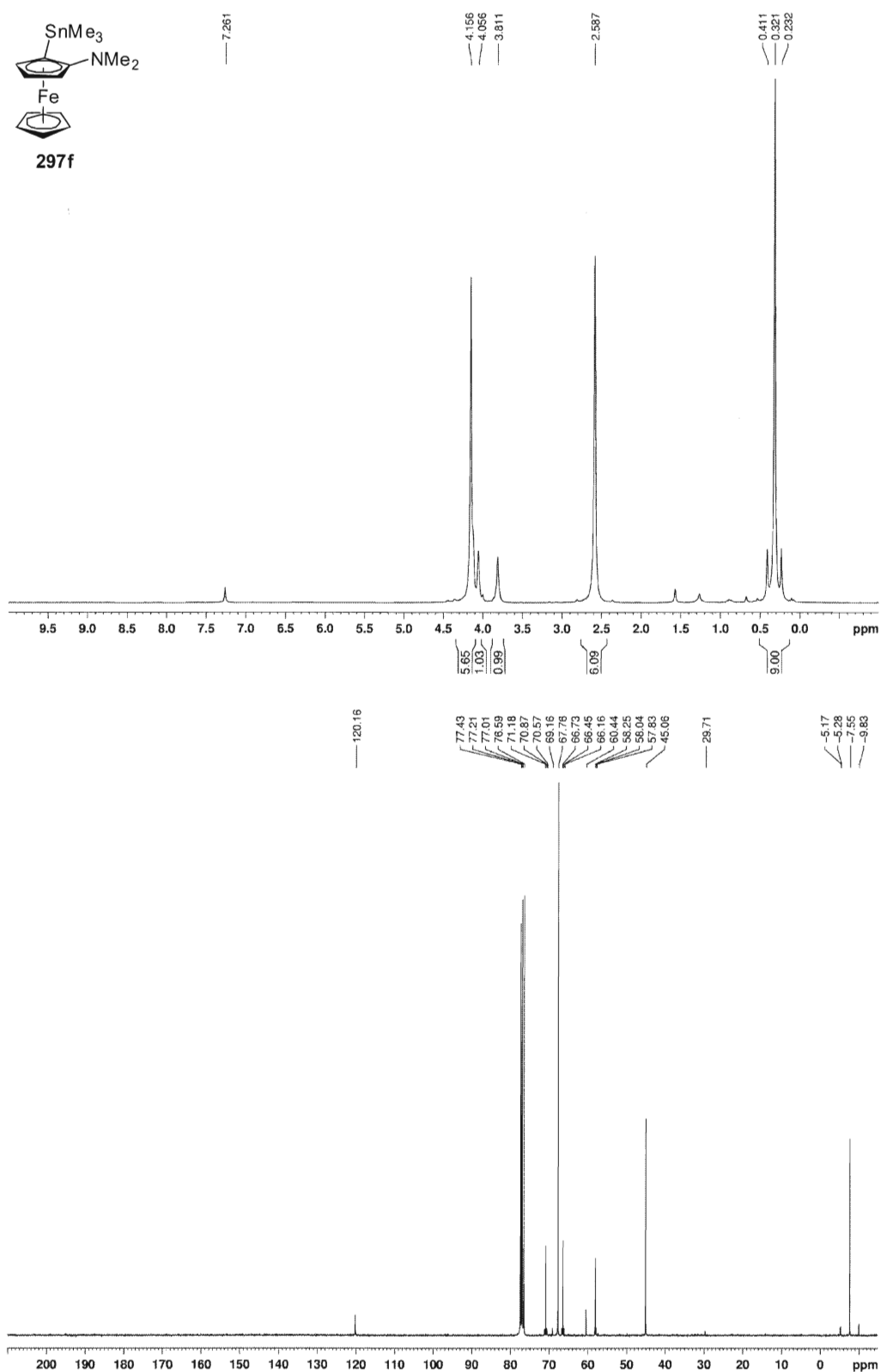
^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297f**.
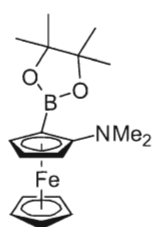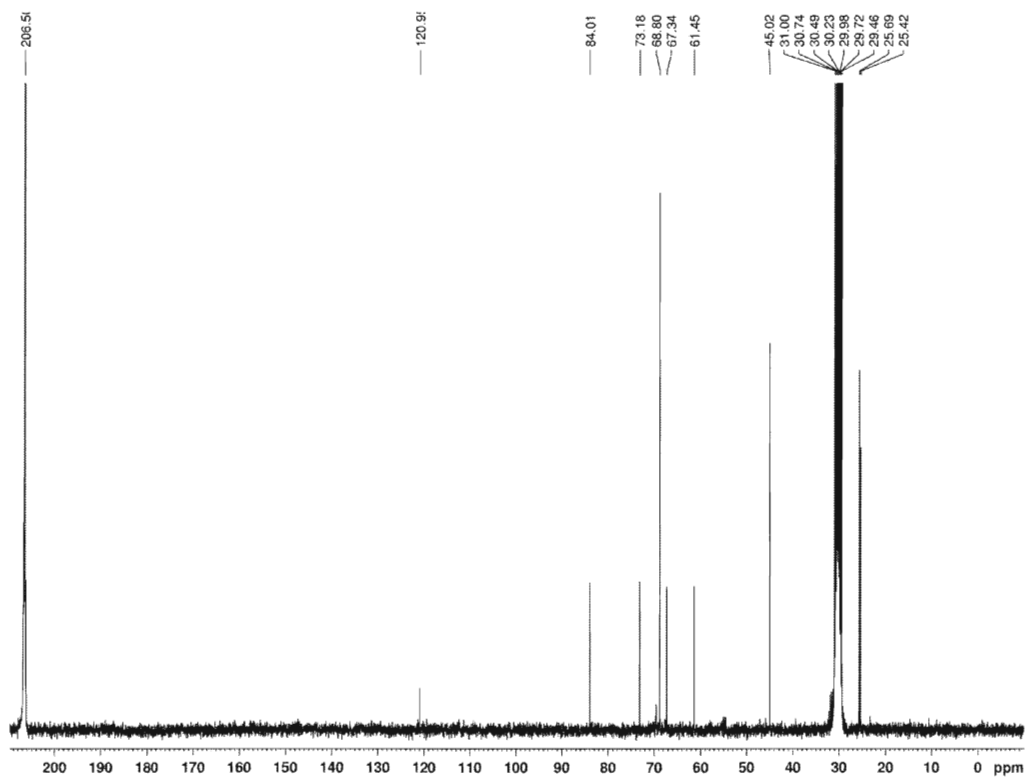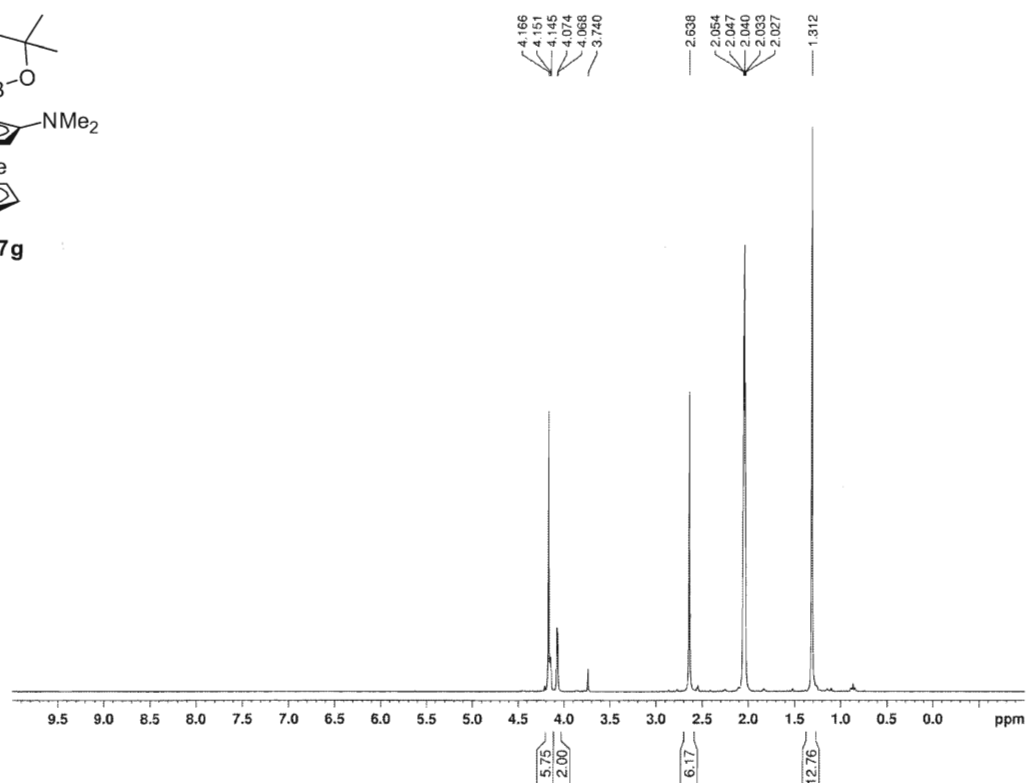
^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297g**.
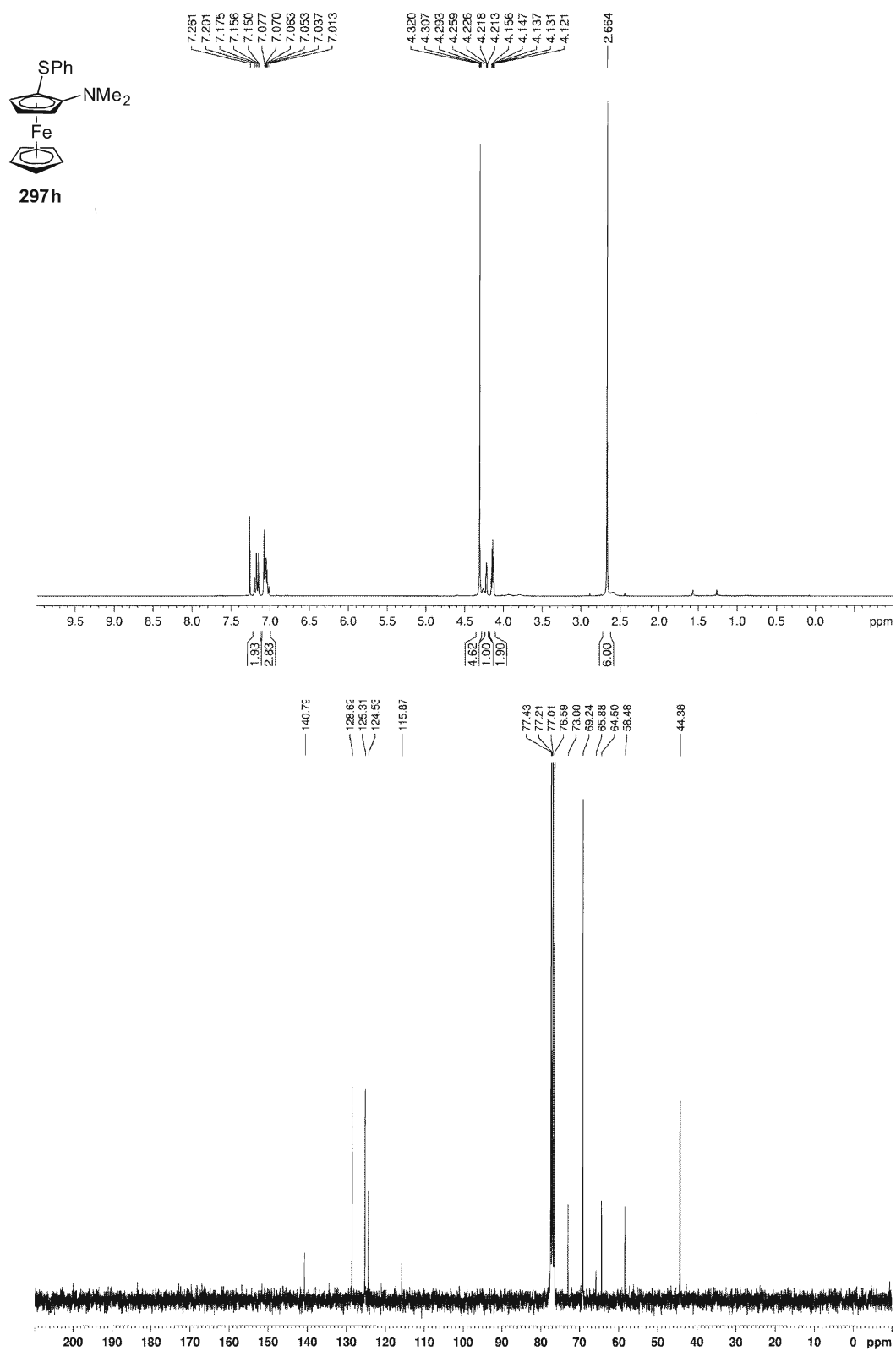
^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297h**.

^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297i**.

297i

PPh$_2$

NMe$_2$

Fe

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

139.79
139.71
137.89
137.82
135.34
135.20
132.45
132.33
129.01
128.08
128.05
128.02
127.96
127.75
119.00
118.88

77.22
77.00
76.79
68.66
68.51
68.48
65.98
65.91
65.16
60.07

45.51
45.45

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

7.533
7.530
7.520
7.517
7.511
7.510
7.504
7.370
7.362
7.354
7.260
7.255
7.250
7.242
7.232
7.228

4.175
4.107
4.077
4.073
4.069

3.478

2.665

2.00
2.96
6.51

1.04
5.68

1.05

6.05

297j

206.50

119.51
119.41

68.98
68.14
68.12
64.84
64.67
62.75
62.74
45.49
45.40
36.59
36.49
34.73
34.64
33.73
33.59
31.73
31.63
31.01
30.93
30.70
30.58
30.49
30.45
30.32
30.19
30.06
29.94
28.85
28.77
28.67
28.63
28.50
28.41

4.222
4.214
4.152
4.151
4.149
4.046
4.043
4.039
3.926
3.924
3.923
3.920
2.754
2.752
2.449
1.903
1.879
1.873
1.855
1.839
1.833
1.743
1.720
1.695
1.693
1.652
1.631
1.599
1.588
1.583
1.577
1.568
1.563
1.558
1.548
1.543
1.478
1.450
1.447
1.431
1.413
1.398
1.393
1.338
1.333
1.327

4.55
0.95
0.91
0.95
5.98
1.00
1.03
3.03
2.05
1.03
3.02
7.49
2.06
1.01
1.34

^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297j**.

286

^{1}H and ^{13}C NMR for 2-substituted aminoferrocene **297k**.

298

4.281
4.158
4.152
4.149
4.143
3.775
3.770
3.766
3.680
3.671
3.661
2.800
2.766
2.600
2.138
2.054
2.047
2.040
2.032
2.025

5.03
1.01
1.03
1.00
6.47
3.18

192.96
139.88
128.83
126.25
125.35
117.80
77.43
77.21
77.00
76.58
75.94
71.82
71.51
70.81
65.18
46.06

^{1}H and ^{13}C NMR for *O*-acetate **298**.
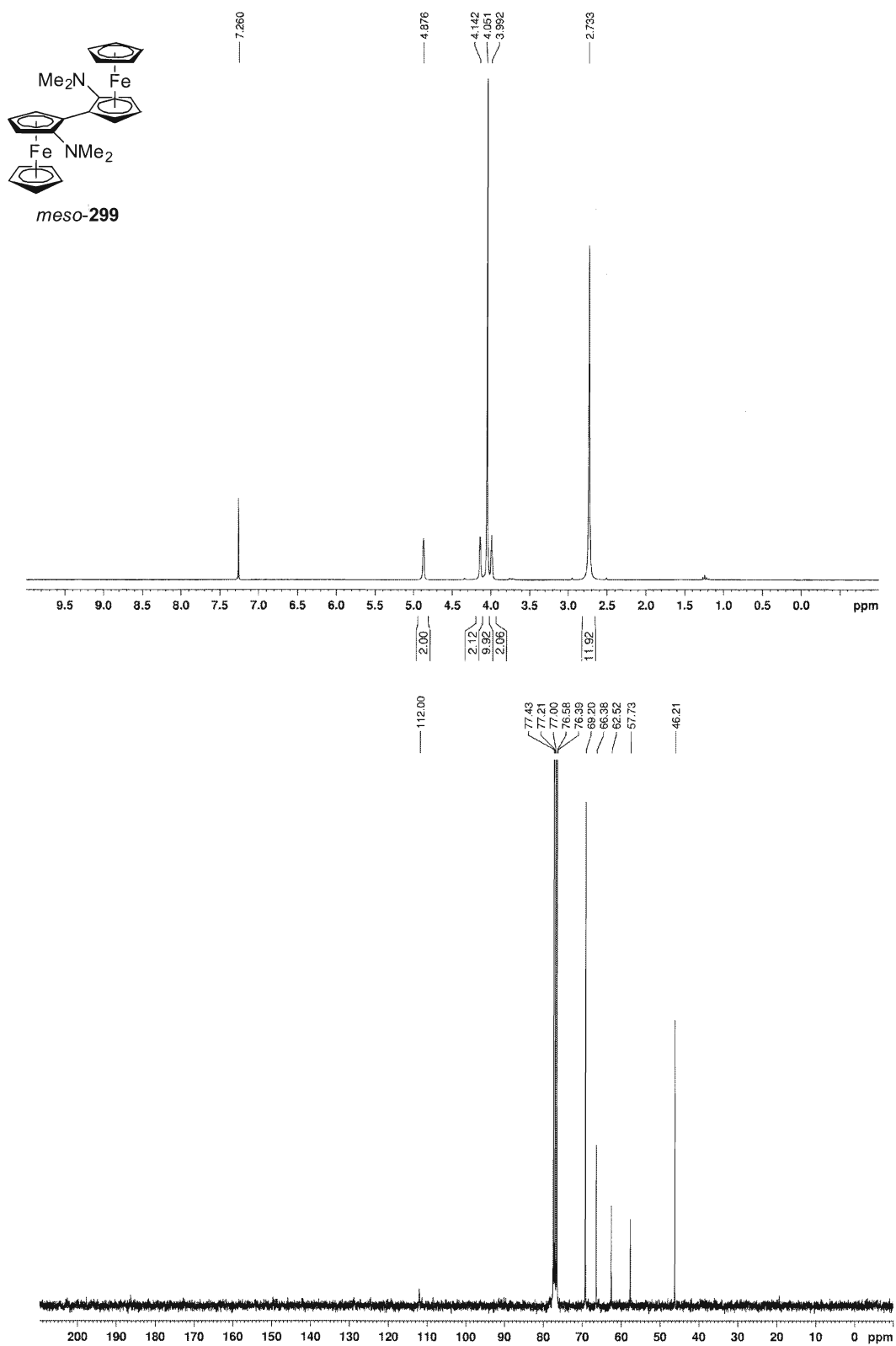
¹H and ¹³C NMR for *meso*-biferrocene **299**.
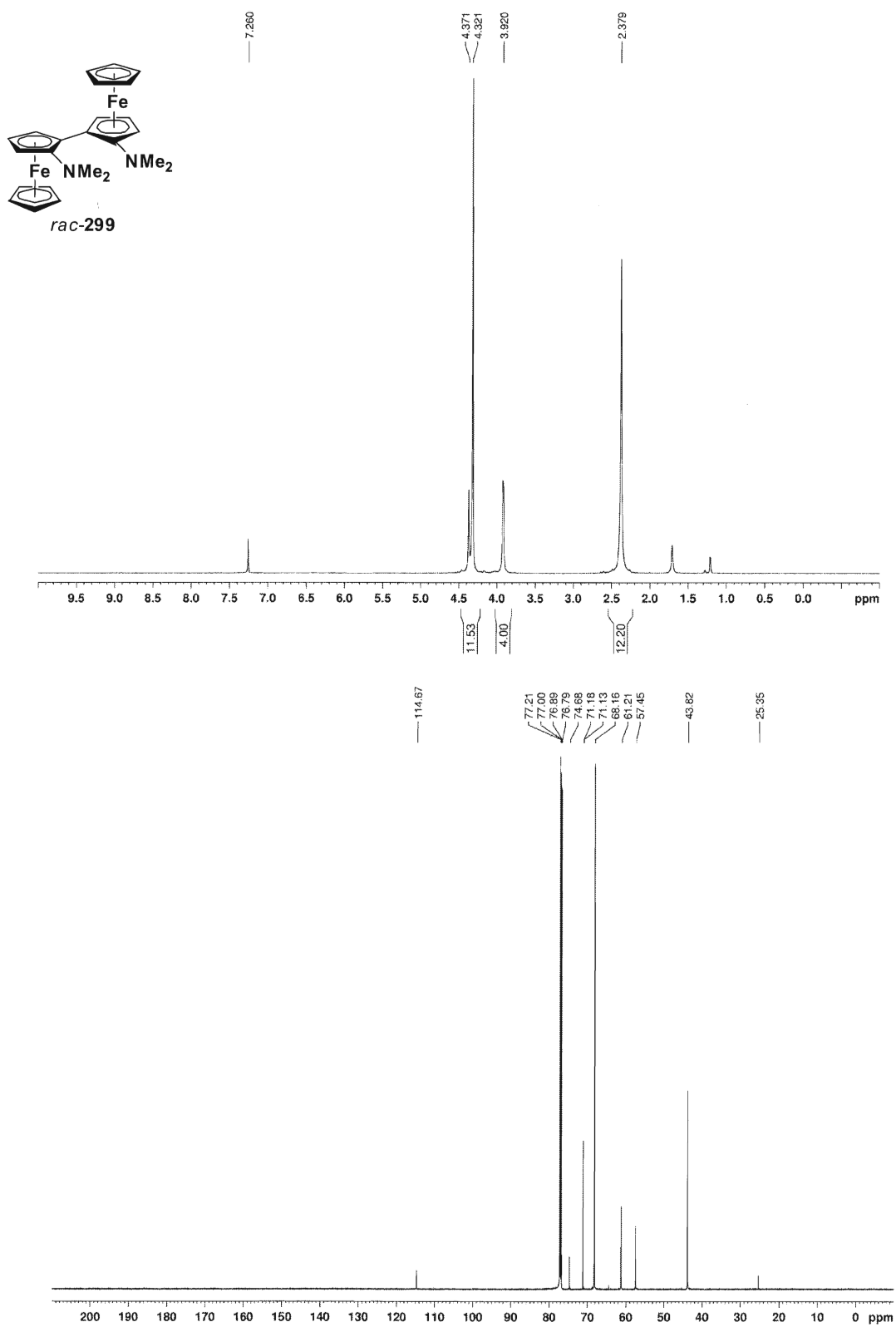
^{1}H and ^{13}C NMR for *rac*-biferrocene **299**.
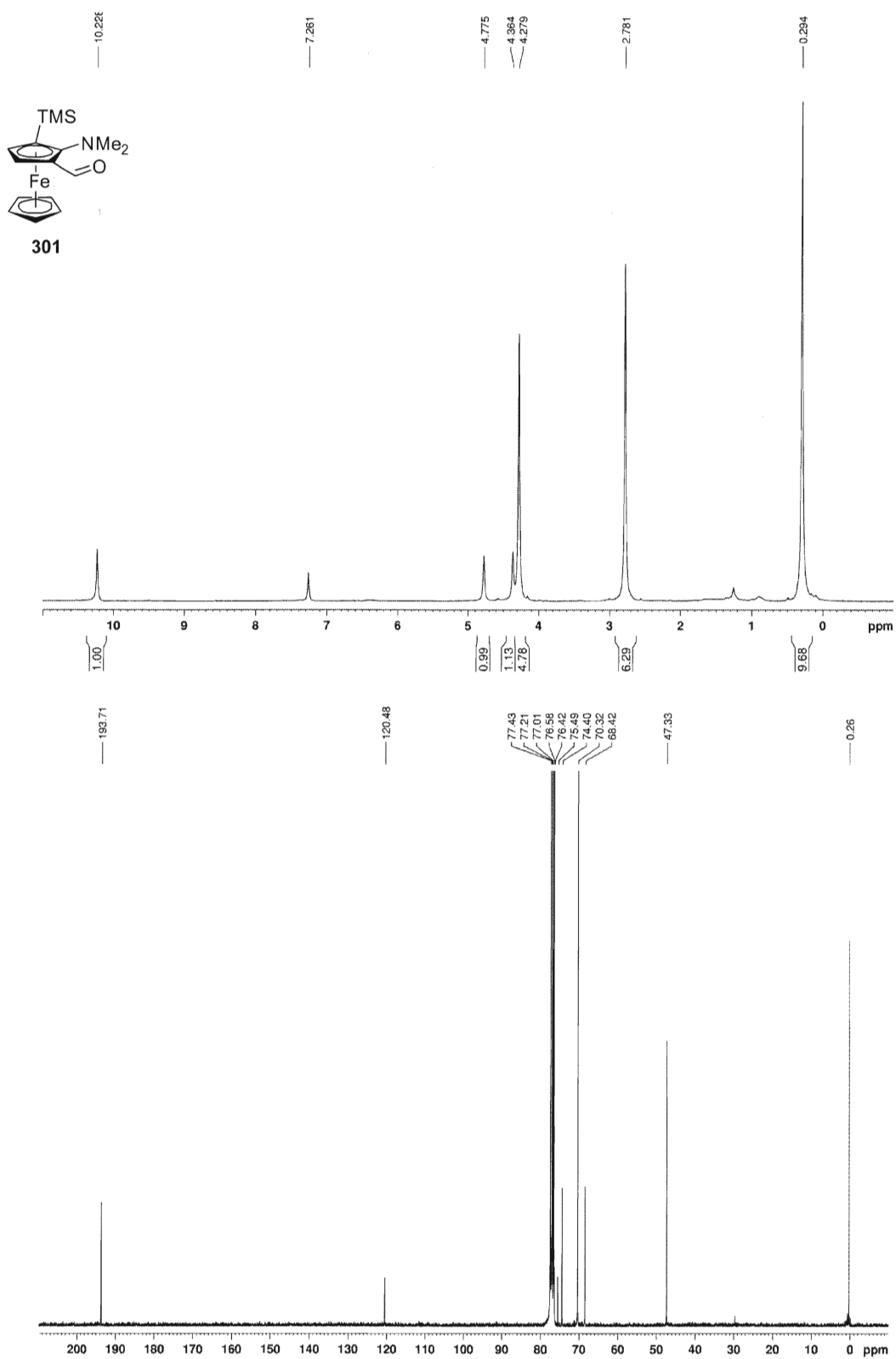
¹H and ¹³C NMR for trisubstituted aminoferrocene **301**.
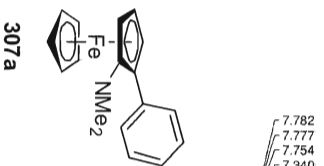
10.180

7.260
7.223
7.199
7.127
7.108
7.081

4.835
4.825
4.599
4.590
4.367

2.821

302

SPh
NMe₂
Fe
O

1.01

1.93
3.24

1.00
1.02
5.11

5.43

192.9

139.8

128.8
126.2
125.3

117.8

77.43
77.21
77.00
76.58
75.94
71.82
71.51
70.81
65.18

46.06
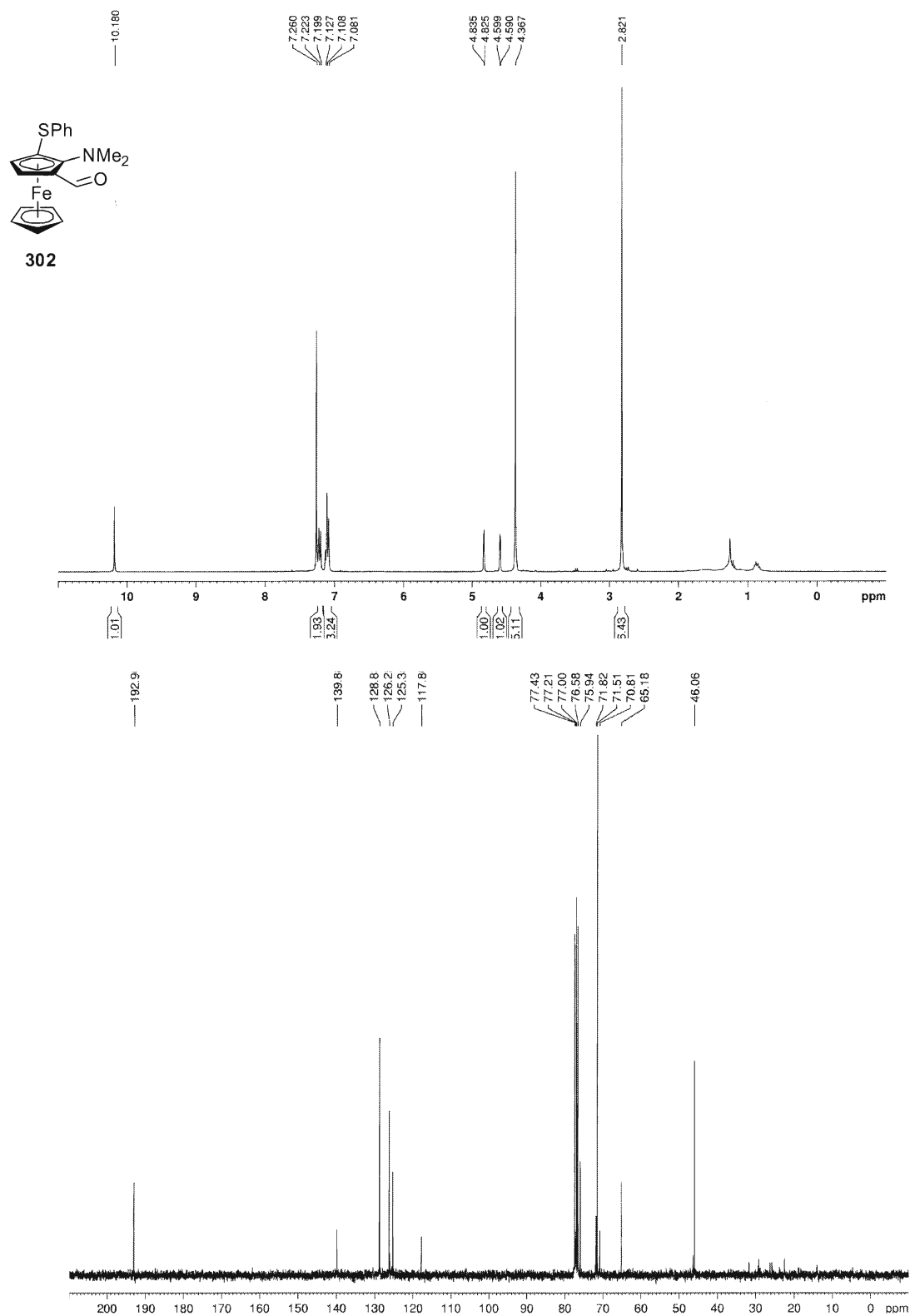
¹H and ¹³C NMR for trisubstituted aminoferrocene **302**.
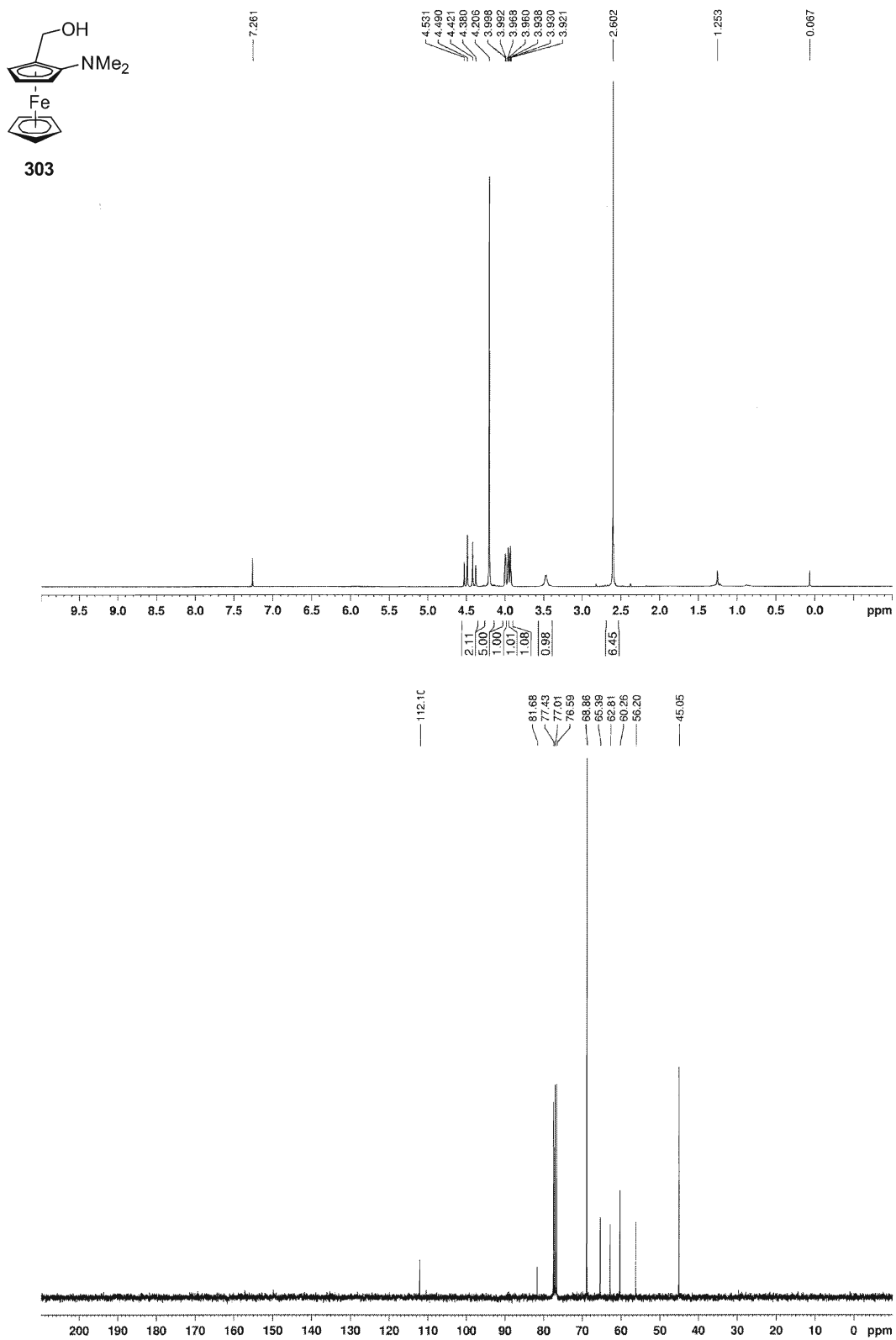
^{1}H and ^{13}C NMR for alcohol **303**.

^{1}H and ^{13}C NMR for diamine **304**.

304

7.260

4.133
4.119
3.972
3.966
3.958
3.896
3.888
3.883
3.865
3.857
3.848
3.770
3.726
3.146
3.103
2.682
2.653
2.633
2.629
2.609
2.585
2.562
2.469
2.446
2.422
2.402
2.379
2.356
1.001
0.978
0.954

4.84
1.01
1.00
1.03
1.04
1.01
6.23
2.10
2.13
6.17

113.73

77.42
77.20
77.00
76.64
76.58
68.47
68.34
61.70
56.90
52.20
45.92
44.91
11.12

7.499
7.260
7.000
6.924

5.138
5.091
4.854
4.806

4.164
4.040
4.019

2.474

305

1.01
2.04

1.00
1.00

5.00
2.99

6.01

136.73
129.08
118.76
113.43

77.42
77.20
77.00
76.57
75.20
68.93
66.63
63.48
57.45

45.46
45.30

^{1}H and ^{13}C NMR for imidazole **305**.
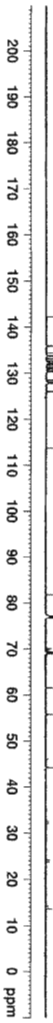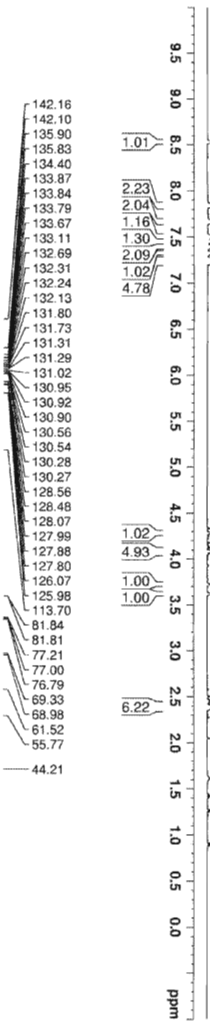
^{1}H and ^{13}C NMR for 2-aryl aminoferrocene **307a**.

307a

7.782
7.777
7.754
7.340
7.335
7.317
7.312
7.291
7.260
7.252
7.248
7.235
7.228
7.220
7.207
7.204

4.270
4.265
4.263
4.257
4.181
4.137
4.132
4.130
4.124
4.058
4.050
4.041

2.529

2.05
3.47
1.09
4.96
1.03
1.00
6.43

139.14
128.38
127.76
125.86
112.46
78.11
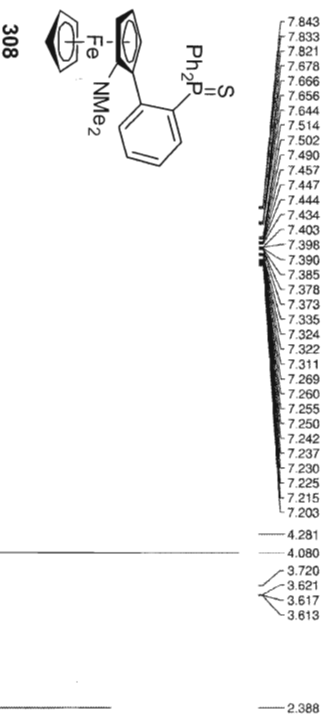77.42
77.20
77.00
76.58
69.24
66.50
62.39
58.03
44.61

307b

^{1}H and ^{13}C NMR for 2-aryl aminoferrocene **307b**.

7.647
7.621
7.517
7.365
7.359
7.260
7.229
7.204
7.075
7.050

4.258
4.253
4.250
4.245
4.215
4.203
4.188
4.136
4.130
4.128
4.122
4.053
4.045
4.036

2.539
2.408

1.03
1.02
1.87
1.01

1.08
4.93
1.03
1.00

6.38
3.11

138.99
137.12
129.00
127.66
126.66
125.72
112.37
77.94
77.42
77.20
77.00
76.58
69.13
66.73
62.24
58.09
44.56
21.49

^{1}H and ^{13}C NMR for 2-aryl aminoferrocene **307c**.

307c

MeO

Fe

NMe$_2$

8.107
8.101
8.082
8.076
7.289
7.283
7.260
7.237
7.231
7.029
7.026
7.004
7.001
6.979
6.976
6.878
6.877
6.851
6.849

4.278
4.273
4.265
4.253
4.239
4.096
4.088
4.082
4.062
4.053
4.044
3.790

2.474

1.00
1.57
1.02
1.01
6.14
1.00
1.00
3.17
6.06

157.48

132.60
127.46
126.95
120.02
113.13
110.54

77.42
77.00
76.57
75.49
68.85
62.02
56.75
55.55
44.08

^{1}H and ^{13}C NMR for 2-aryl aminoferrocene **307d**.

^{1}H and ^{13}C NMR for 2-aryl aminoferrocene **307e**.

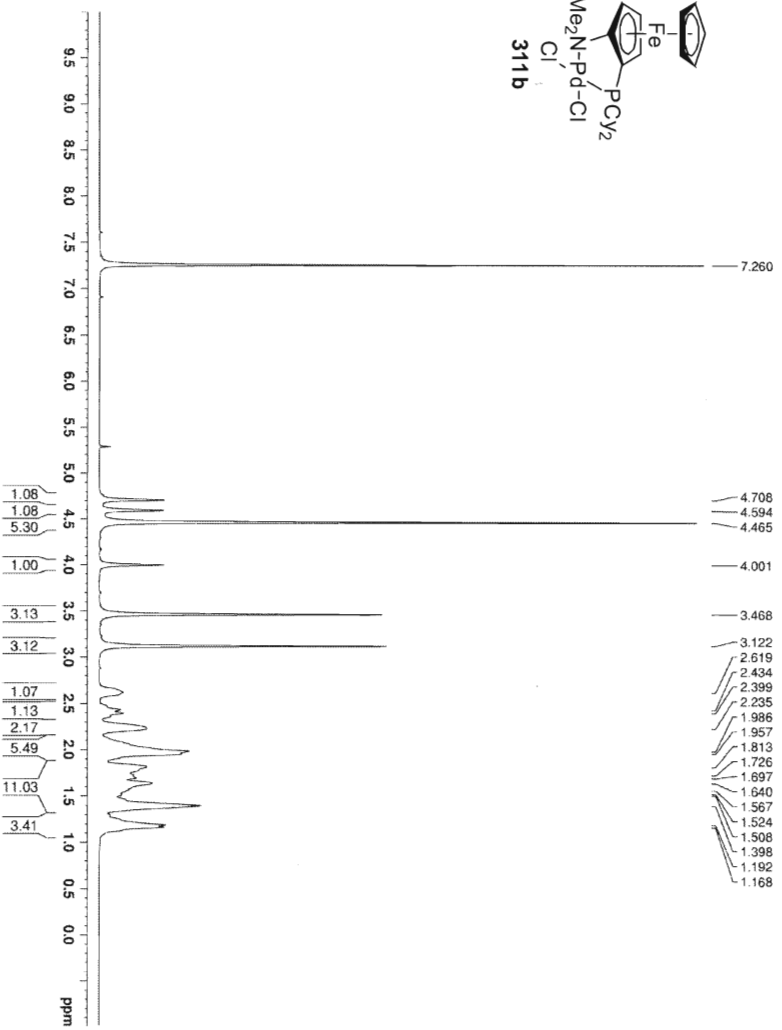## ¹H and ¹³C NMR for 2-aryl aminoferrocene 308.

308

¹³C NMR peaks:
142.16, 142.10, 135.90, 135.83, 134.40, 133.87, 133.84, 133.79, 133.67, 133.11, 132.69, 132.31, 132.24, 132.13, 131.80, 131.73, 131.31, 131.29, 131.02, 130.95, 130.92, 130.90, 130.56, 130.54, 130.28, 130.27, 128.56, 128.48, 128.07, 127.99, 127.88, 127.80, 126.07, 125.98, 113.70, 81.84, 81.81, 77.21, 77.00, 76.79, 69.33, 68.98, 61.52, 55.77, 44.21

¹H NMR peaks:
7.843, 7.833, 7.821, 7.678, 7.666, 7.656, 7.644, 7.514, 7.502, 7.490, 7.457, 7.447, 7.444, 7.434, 7.403, 7.398, 7.390, 7.385, 7.378, 7.373, 7.335, 7.324, 7.322, 7.311, 7.269, 7.260, 7.255, 7.250, 7.242, 7.237, 7.230, 7.225, 7.215, 7.203, 4.281, 4.080, 3.720, 3.621, 3.617, 3.613, 2.388

^{1}H and ^{13}C NMR for biaryl aminophosphine **309**.

309

Ph$_2$P

NMe$_2$

^{13}C NMR peaks:
143.88, 143.69, 138.42, 138.33, 138.15, 138.06, 135.70, 133.91, 133.76, 133.62, 133.53, 133.40, 132.86, 132.82, 128.38, 128.15, 128.11, 128.04, 128.01, 128.00, 126.71, 125.49, 113.81, 80.96, 80.89, 69.38, 69.33, 68.57, 68.55, 68.52, 68.49, 61.48, 56.76, 43.86

^{1}H NMR peaks:
8.179, 8.178, 8.174, 8.167, 7.413, 7.412, 7.401, 7.399, 7.388, 7.386, 7.293, 7.290, 7.283, 7.272, 7.268, 7.260, 7.225, 7.223, 7.212, 7.203, 7.199, 7.194, 7.188, 7.185, 7.177, 7.173, 7.168, 7.161, 7.015, 7.014, 7.008, 7.003, 6.997, 4.283, 4.058, 4.055, 4.052, 3.946, 3.941, 3.937, 3.851, 3.849, 3.847, 2.291

Integrations: 1.04, 1.16, 6.94, 5.43, 1.22, 4.93, 1.04, 1.02, 1.00, 6.76

311a

Me₂N–Pd–Cl
Cl
Fe
PPh₂

^{1}H and ^{13}C NMR for palladium complex **311a**.

¹H NMR peaks:
8.100, 8.088, 8.079, 8.066, 7.619, 7.609, 7.606, 7.596, 7.567, 7.561, 7.554, 7.549, 7.536, 7.503, 7.490, 7.479, 7.381, 7.377, 7.368, 7.364, 7.356, 7.351, 7.260

4.748, 4.744, 4.740, 4.535, 4.207, 3.995, 3.460, 3.095

Integrations: 2.00, 1.04, 4.01, 1.05, 2.03, 1.00, 1.01, 1.00, 4.98, 3.07, 3.06

¹³C NMR peaks:
134.68, 134.60, 132.23, 132.22, 131.88, 131.81, 131.55, 131.42, 131.40, 131.17, 129.65, 129.20, 128.94, 128.86, 128.68, 128.60, 126.96, 126.80, 77.21, 77.00, 76.79, 75.20, 75.16, 72.98, 72.61, 71.53, 71.52, 71.48, 71.45, 71.44, 63.94, 60.38, 60.30, 58.21, 54.48

^{1}H and ^{13}C NMR for palladium complex **311b**.

^{1}H and ^{13}C NMR for platinum complex **312a**.

312a

305

^{1}H and ^{13}C NMR for platinum complex **312b**.

312b

7.252

4.913

4.194
4.165

2.761

336

2.00

7.10

4.09

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
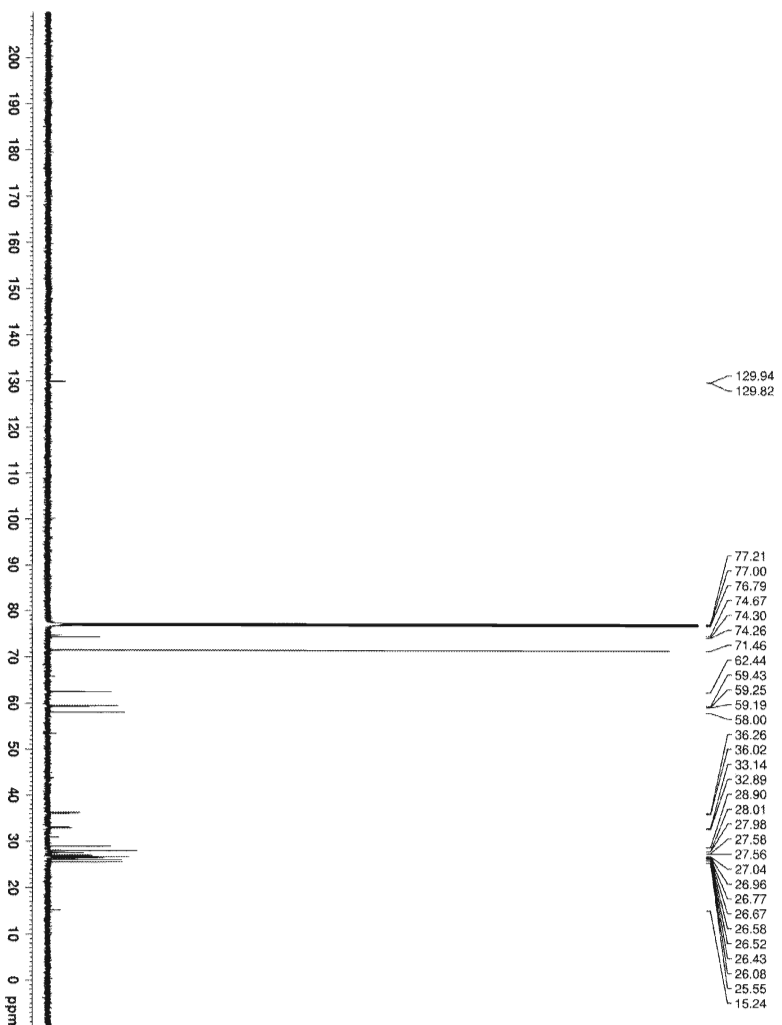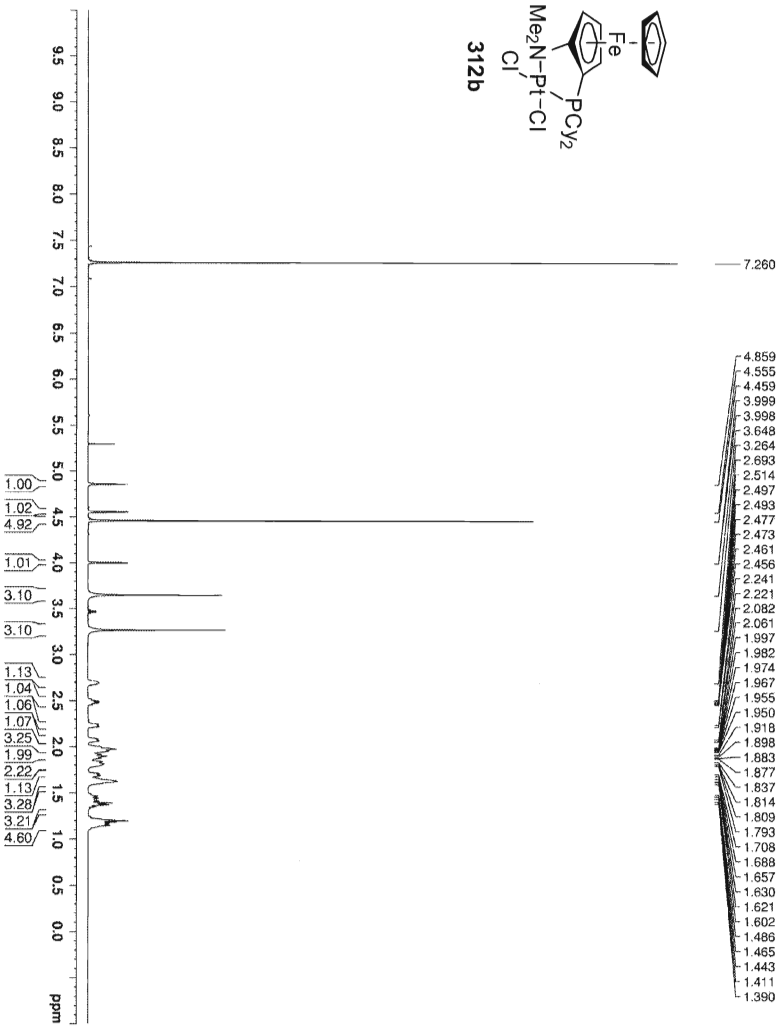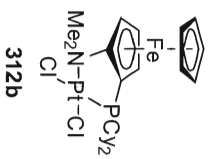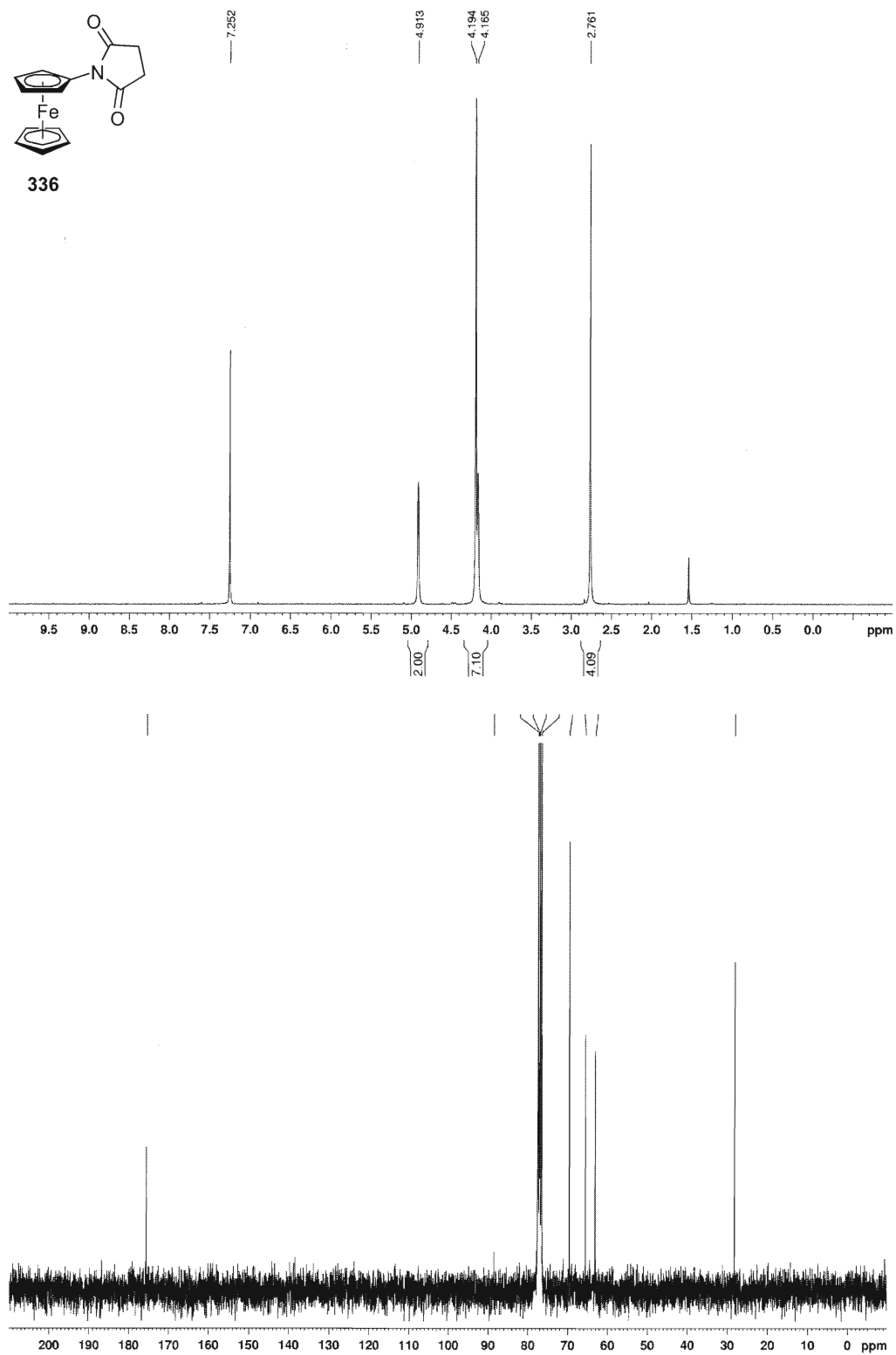
^{1}H and ^{13}C NMR for succinimide **336**.
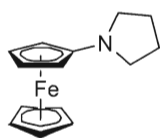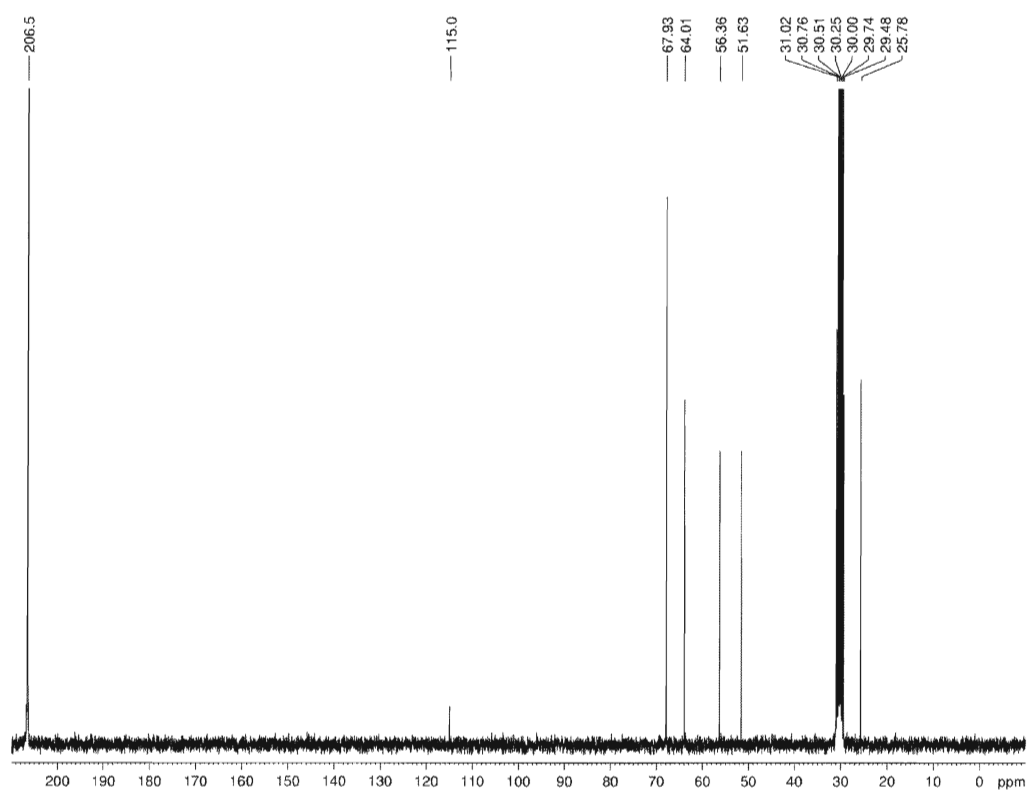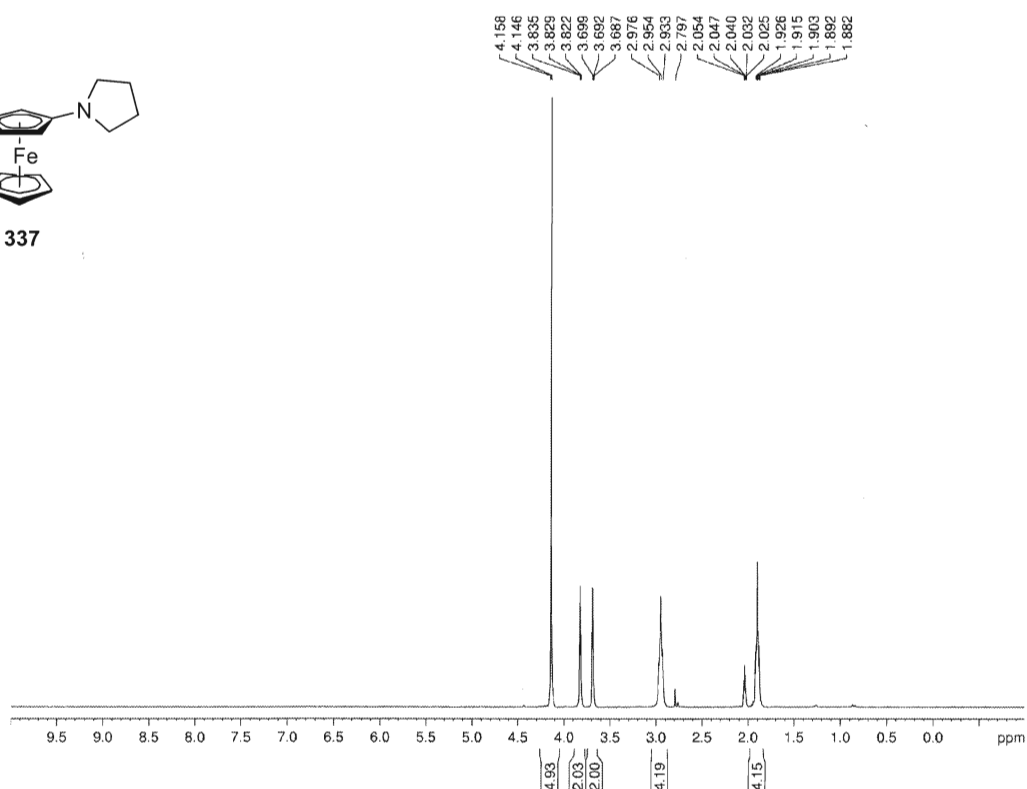
^{1}H and ^{13}C NMR for pyrrolidinyl ferrocene **337**.
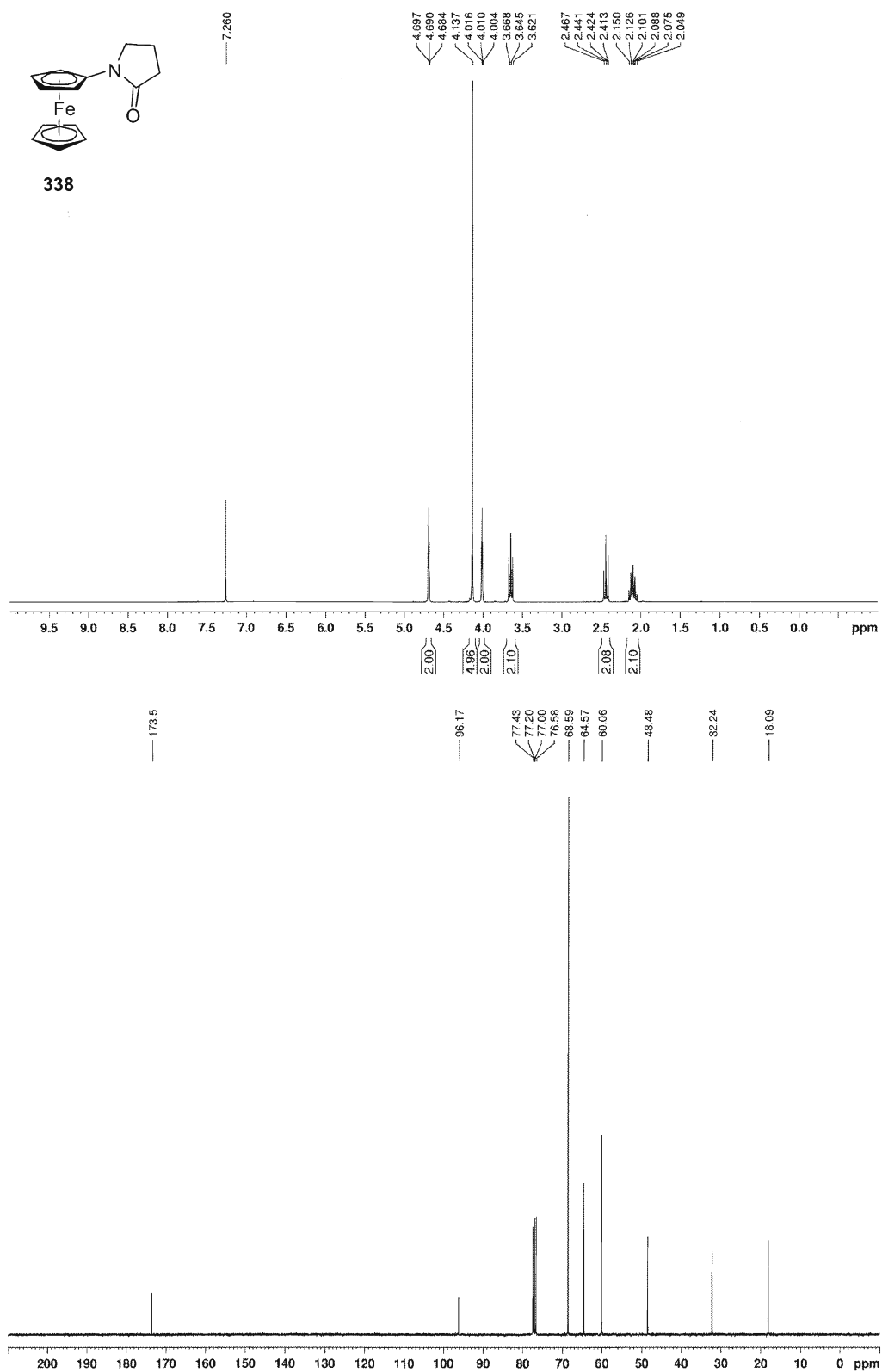
^{1}H and ^{13}C NMR for amide byproduct **338**.
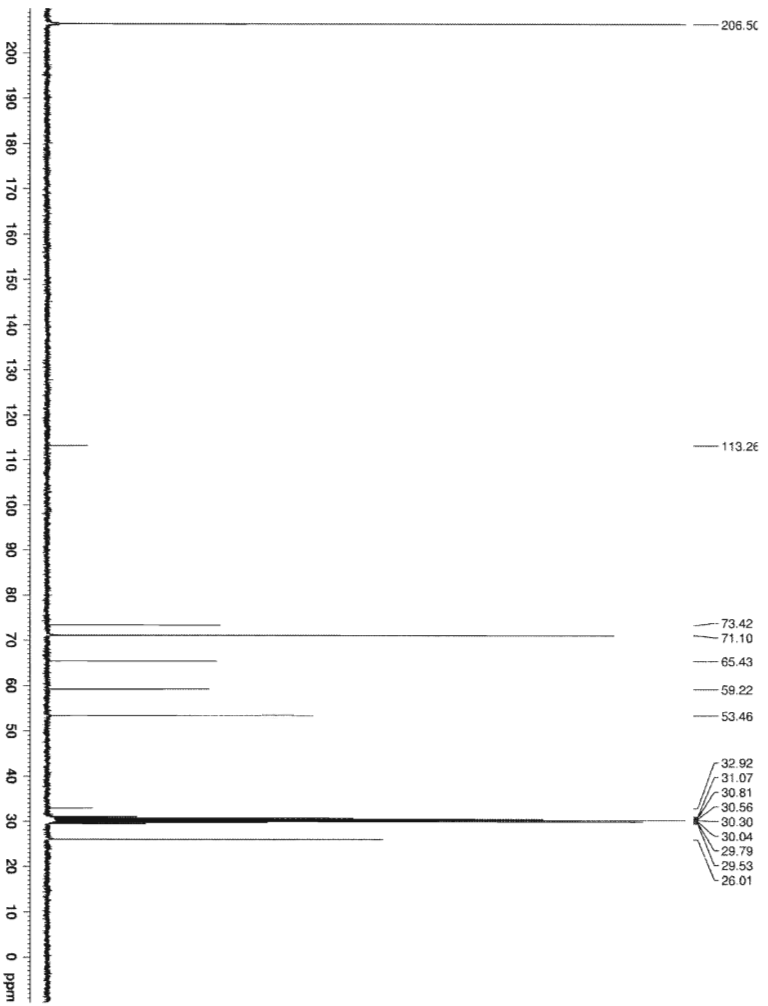
10.201

4.562
4.343
4.255

3.250
3.237
3.225
3.132
3.118

2.040
1.963
1.953
1.942
1.931

339a

10 9 8 7 6 5 4 3 2 1 0 ppm

1.00

0.96
1.03
5.61

2.11
2.08

4.06

206.50

193.83

115.66

69.34
69.29
68.27
65.90
61.80

53.49

30.59
30.47
30.34
30.21
30.08
29.95
29.82
26.10

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
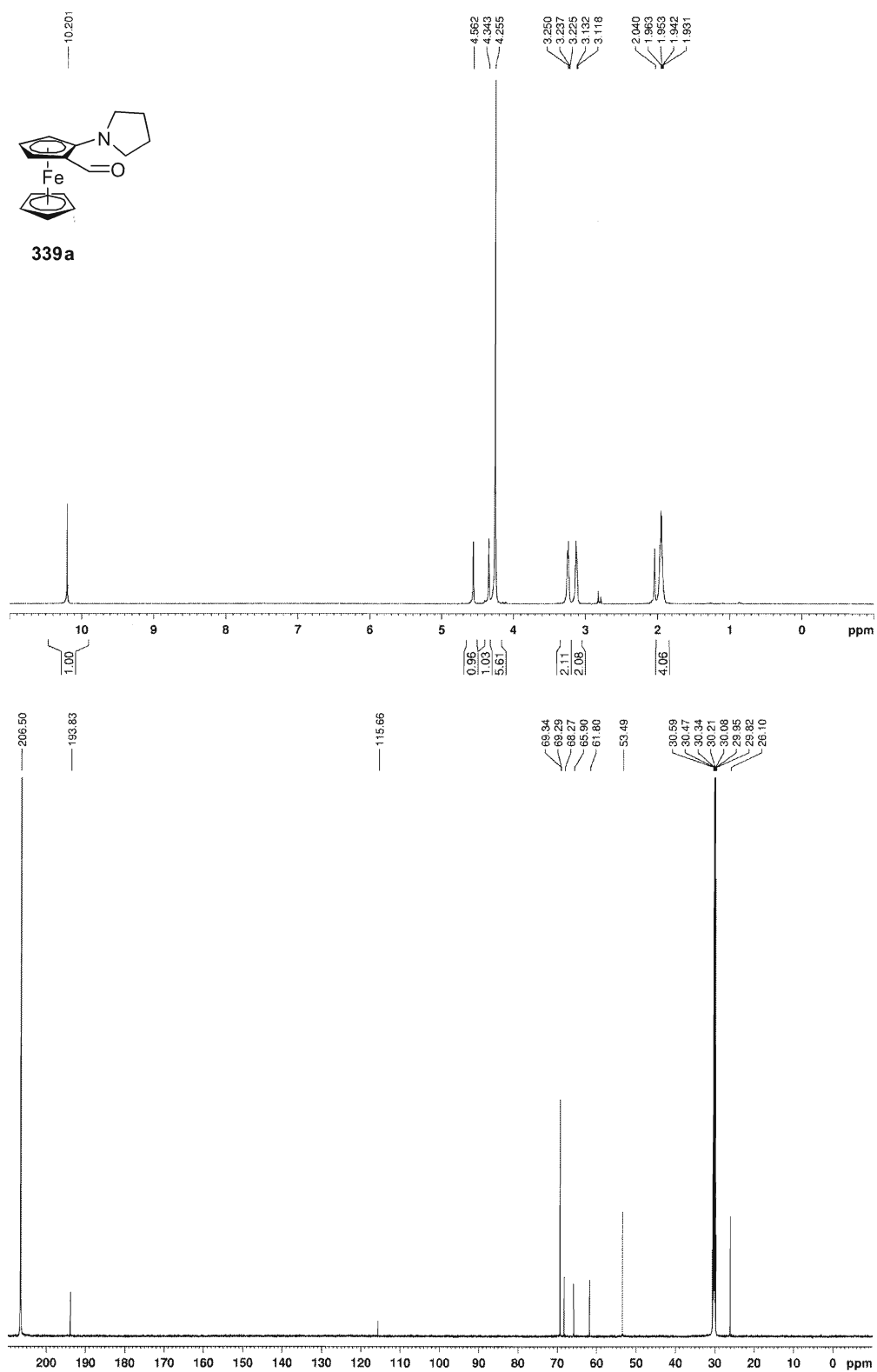
^{1}H and ^{13}C NMR for 2-substituted pyrrolidinyl ferrocene **339a**.
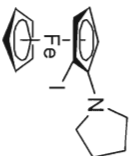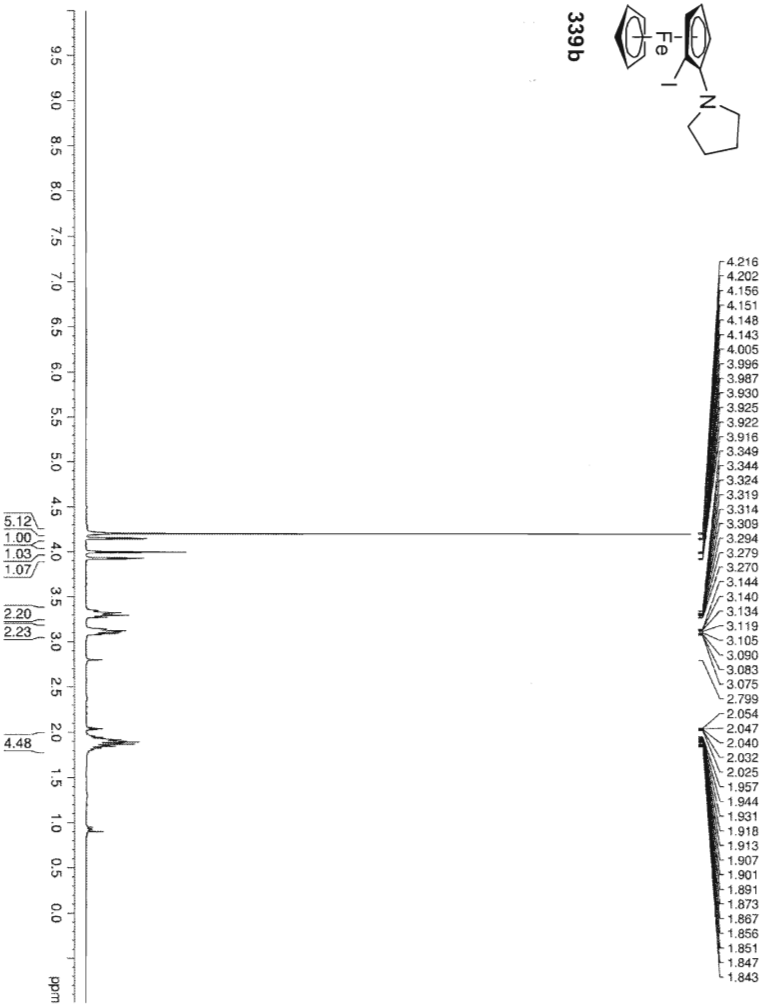
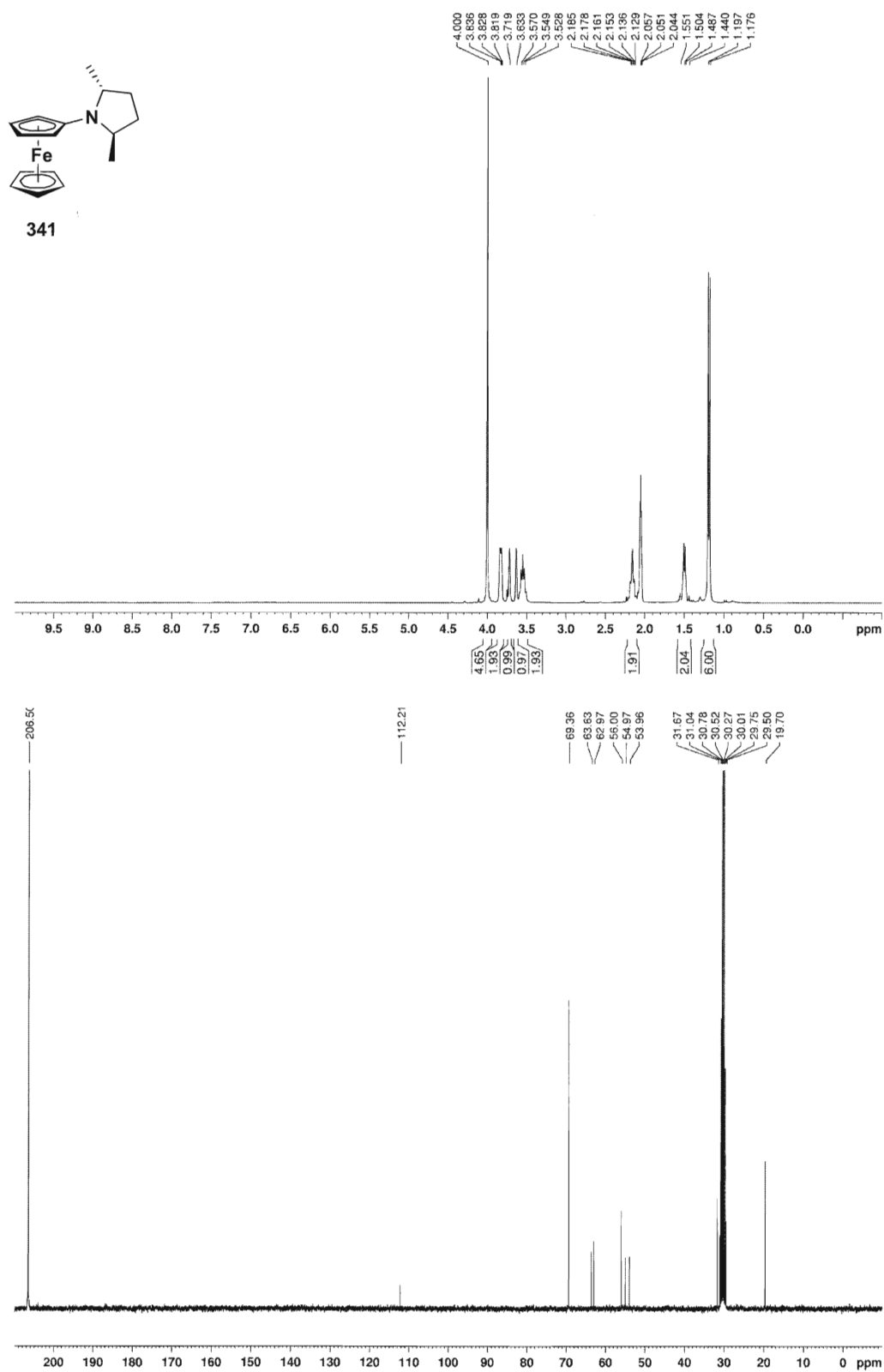^{1}H and ^{13}C NMR for 2-substituted pyrrolidinyl ferrocene **339b**.

339b
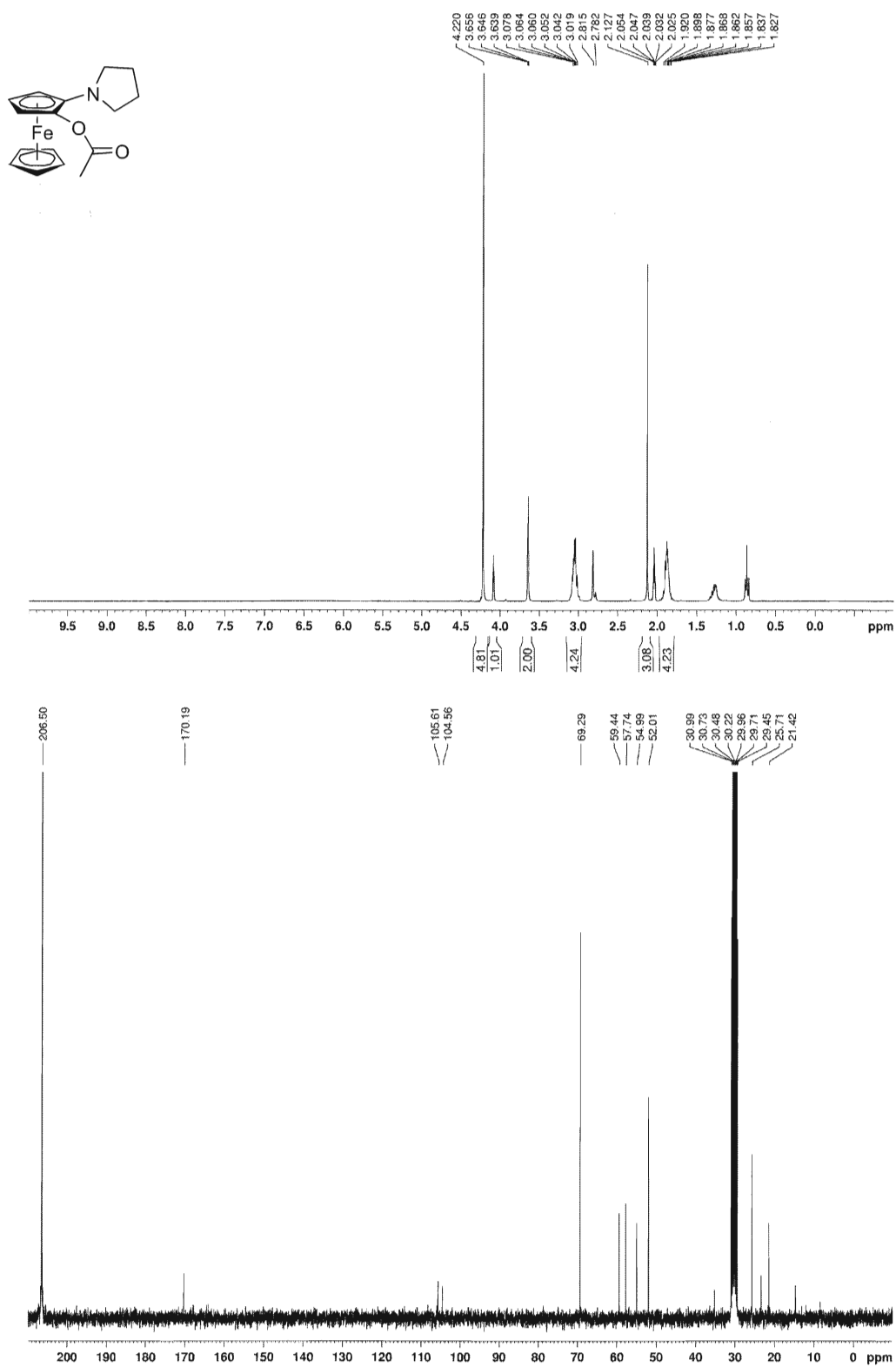
^{1}H and ^{13}C NMR for 2-acetoxy pyrrolidinyl ferrocene.

^{1}H and ^{13}C NMR for 2,5-dimethyl pyrrolidinyl ferrocene **341**.