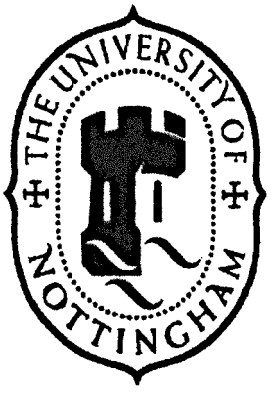
# Planar Chiral Ferrocene Lithium Amide Bases: A New Generation of Bases for Asymmetric Synthesis

by Jennifer Charlotte Arnall-Culliford, MChem

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# 1 Contents

## 2 Abstract

The design and preparation of a new class of planar chiral ferrocenyl lithium amide bases is described. Work commenced on preparing *N,N*-dimethyl-1-ferrocenylethylamine derivatives. Electrophilic amination was attempted with a variety of reagents, but no diamines were ever obtained. The introduction of a boronic acid group was also attempted, but no products were isolated. Finally, nitration followed by reduction was investigated, but again proved unsuccessful, resulting only in the preparation of a dimer of the starting amine, 2,2'-bis-[1-(*N,N*-dimethylamino)-ethyl]-1,1'-biferrocenyl.

Our attention turned to derivatives of *N,N*-diisopropylferrocene carboxamide. Metallation, followed by quenching with iodine gave *N,N*-diisopropyl-2-iodoferrocene carboxamide. Copper(I) oxide mediated coupling of the iodide with either acetic acid or phthalimide gave access to *ortho*-oxygen and nitrogen donor groups. A new class of planar chiral bases (*N*-alkyl-(2-alkoxyferrocenyl)methylamines) were prepared from this starting material by reduction of the amide, followed by substitution of the diisopropylamine with a range of primary amines.

Assays were carried out using the deprotonation of 4-*tert*-butylcyclohexanone and trapping of resultant enolate with TMSCl. Bases having a plane of chirality as the only stereochemical element, disappointingly, gave nearly racemic silyl enol ether, however low optical purities were recorded for bases consisting of both central and planar chirality. A non-chelating planar chiral lithium amide base was prepared ($_p$*S*)-*N*-*tert*-butyl-(2-methylferrocenyl)-

methylamine, however this too gave nearly racemic silyl enol ether in the assay reaction.

The synthesis of planar chiral azaferrocenyl bases was attempted by sequential complexation of lithiated pyrrole-2-methanol and lithium pentamethyl-cyclopentadienide with iron(II) chloride, followed by acylation of the pendant alcohol. However, all attempts to substitute the acetate with an amine proved unsuccessful.

# 3 Acknowledgements

Millions of thanks to my supervisor, Dr Jim Anderson, for his boundless enthusiasm for chemistry and education in all its guises. Thank you for your belief in me, and your support throughout the last three years.

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Finally, to my husband Jim, you may be last in the list, but you are always foremost in my mind. You are my rock and without you, this endeavour would have been much less bearable. For this reason, and for the many reasons that I have no words for, I would like to dedicate this thesis to you.

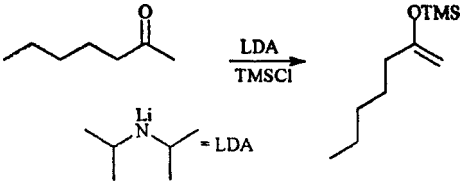
# 4 Abbreviations

| | |
|---|---|
| aq. | aqueous |
| BINAP | 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl |
| Boc | *tert*-butoxycarbonyl |
| BSA | *N,O*-bis(trimethylsilyl)acetamide |
| Cp | cyclopentadienyl |
| Cp* | 1,2,3,4,5-pentamethylcyclopentadienyl |
| dba | dibenzylideneacetone |
| DBU | 1,8-diazabicyclo[5.4.0]undec-7-ene |
| DCM | dichloromethane |
| *de* | diastereomeric excess |
| DIPA | *N,N*-diisopropylamine |
| DMAP | 4-*N,N*-dimethylaminopyridine |
| DME | ethylene glycol dimethyl ether |
| DMF | *N,N*-dimethylformamide |
| DPPF | 1,1'-bis(diphenylphosphino)ferrocene |
| *ee* | enantiomeric excess |
| ether | diethyl ether |
| eq | equivalents |
| Fmoc | 9-fluorenylmethoxycarbonyl |
| h | hours |
| HCLA | homochiral lithium amide |
| HMPA | hexamethylphosphoraminde |
| LDA | lithium diisopropylamide |
| nbd | 2,5-norbornadiene |
| min | minutes |
| pTSA | *para*-toluenesulfonic acid |
| r.t. | room temperature |
| sat. | saturated |
| t | time |
| THF | tetrahydrofuran |
| TMEDA | *N,N,N',N'*-tetramethylethylenediamine |
| TMS | trimethylsilyl |

# 5 Introduction

## *5.1 Homochiral Lithium Amide Bases*

Lithium amide bases are used in organic synthesis to carry out a range of transformations. The most familiar of this class of reagent is perhaps lithium diisopropylamide (LDA), which is well known for its use as a strong, non-nucleophilic, hindered base. It is widely used for the formation of enolates as well as in a number of other transformations (Equation 1).[1]




(1)

Since chiral lithium amide bases were first invented in 1980 by Whitesell and Felman,[2] their use in organic synthesis has continued to increase dramatically. There are many examples of bases giving excellent yields and enantiomeric excesses, but, no base gives good results across the full range of reactions. Homochiral lithium amides have seen most success in three major classes of transformation (Figure 1):[3] deprotonation of conformationally locked prochiral ketones (**A**); aromatic and benzylic functionalisation of ($\eta^6$-arene)chromium tricarbonyl complexes (**B**); and rearrangement of epoxides to allylic alcohols (**C**).

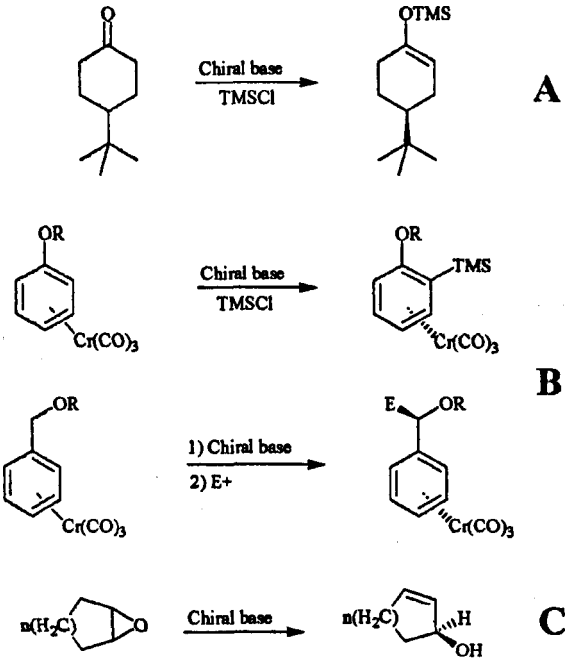



**Figure 1:** Classes of chiral base reactions

All of these reactions are examples of asymmetric desymmetrisation. Although good results have been obtained in all of these classes of reaction, there is still a need to develop a homochiral base that will be effective across the range of transformations.

The bases developed to date can be divided into three broad categories, and each of these groups are efficient in different classes of transformation.

The HCLAs developed by Whitesell[2] and Simpkins[4] (Figure 2) are all based on α-methylbenzylamine, and are efficient bases for the deprotonation of conformationally locked prochiral ketones, as well as for aromatic[5] and benzylic[6] functionalisation of ($\eta^6$-arene)chromium tricarbonyl complexes (Figure 1). Some of these bases are $C_2$ symmetric, and none of them have a neutral donor group.

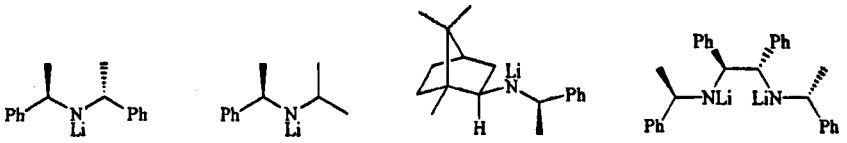


**Figure 2:** Homochiral lithium amides based on α-methylbenzylamine

Figure 3 shows a representative group of the lithium amides developed by Koga.[7] These are all derived from phenylglycine and are highly effective for the deprotonation of conformationally locked ketones. Common features of these bases also include the presence of either piperidine or piperazine moieties, which provide an extra donor group.

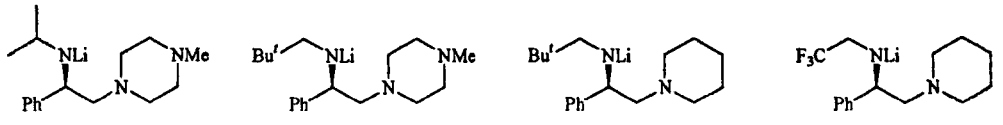


**Figure 3:** Homochiral lithium amides derived from phenylglycine

The group of bases shown in figure 4 is more disparate than in the preceding two groups. Indeed, they were developed by a variety of research groups, and are all effective in the rearrangement of epoxides.[8] These bases all include some form of secondary donor group, usually a nitrogen or oxygen functionality, and a saturated nitrogen containing heterocycle is a common feature.[3]

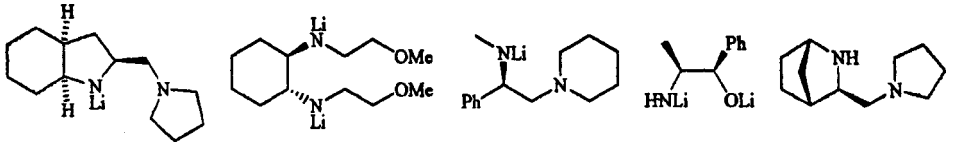
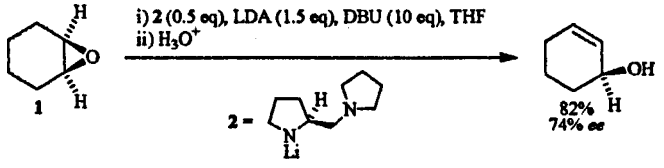


**Figure 4:** Homochiral lithium amides for the rearrangement of epoxides

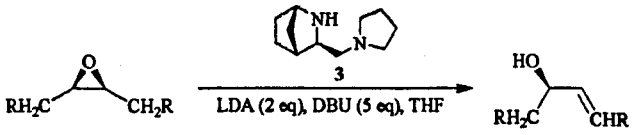
Despite the differences between these groups of bases, there are two features that are common to the majority of them: the presence of a secondary donor group in a 1,2-relationship with the lithium amide; and the inclusion of a saturated nitrogen heterocycle.

There has been some interest in the development of a cataytic version of the reaction, and it is hoped that this technology might be applicable to our systems. Asami *et al.*[9] published the first report of the catalytic use of homochiral lithium amide bases in 1994.



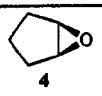
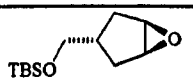
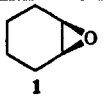
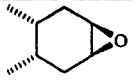
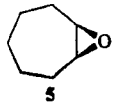
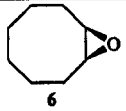

(2)

Their work focussed on the rearrangement of cyclohexene oxide (**1**) using sub-stoichiometric lithium (*S*)-2-(pyrrolidin-1-ylmethyl)pyrrolidide (**2**) and excess LDA in the presence of DBU (Equation 2). They obtained allylic alcohol with an enantiomeric excess approaching that obtained with stoichiometric chiral base (74% *ee* cf. 81% *ee*). More recently, Andersson *et al.*[10] report high enantiomeric excesses for the rearrangement of epoxides to form allylic alcohols, using a catalytic amount of diamine **3** as well as a stoichiometric quantity of LDA (Equation 3; Table 1).




(3)

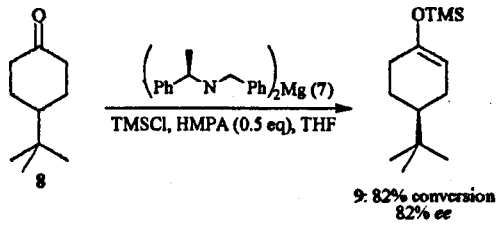
**Table 1:** Catalytic asymmetric rearrangement of epoxides

| Entry | Epoxide | Catalyst (mol%) | Temp. (°C) / time (h) | Yield (%) | *ee* (%) |
|---|---|---|---|---|---|
| 1 |  4 | 20 | rt / 24 | 67 | 49 |
| 2 |  TBSO | 20 | rt / 48 | 42 | 95 |
| 3 |  1 | 5 | 0 / 6 | 91 | 96 |
| 4 |  | 5 | 0 / 6 | 95 | 94 |
| 5 |  5 | 5 | 0 / 6 | 89 | 96 |
| 6 |  6 | 5 | 0 / 36 | 81 | 78 |

Using this system, cyclohexene and cycloheptene oxides (**1** and **5**) give better results than cyclopentene or cyclooctene oxides (**4** and **6**) (see entries 3 and 5 compared with 1 and 6). However, good results were achieved on a variety of substrates, and previously, no other reported lithium amide base had gained >90% *ee* for more than one substrate.

Recently, the exclusive role of lithium has been challenged by the work of Kerr *et al.*[11] on homochiral magnesium bisamide bases. They gain significant levels of selectivity, in the deprotonation of conformationally locked prochiral ketones with a very simple magnesium amide. Treatment of 2 equivalents of (*R*)-*N*-benzyl-α-methylbenzylamine with dibutylmagnesium in hexane gave

the desired magnesium bisamide **7**, which was then assayed using the deprotonation of 4-*tert*-butylcyclohexanone (**8**) (Equation 4).




**(4)**

This result, using a very simple amine ligand, approaches the level of enantioselectivity obtained for far more complex lithium amide base systems.

### *5.2 Axial and Planar Chiral Compounds in Organic Synthesis*

Some of the most efficient chiral ligands and reagents reported to date rely on axes and planes, rather than centres of chirality, to transmit their stereochemical information. A few examples are given below.

#### 5.2.1 BINAP

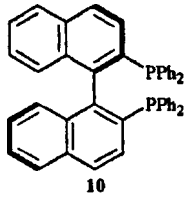
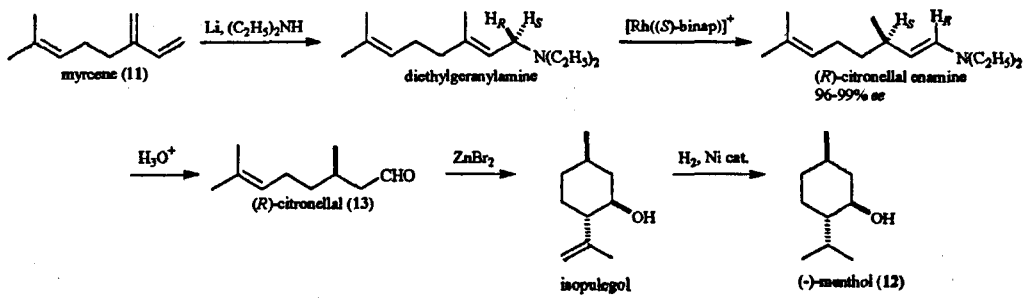



**Figure 5: (*R*)-(+)-BINAP (10)**

BINAP (**10**) is a chelating phosphine ligand with an axis of chirality and is commercially available in both enantiomeric forms. It was developed by Noyori and co-workers[12] during the late 1970s as part of ongoing studies into asymmetric hydrogenation. Since the first reproducible, non-racemic preparation in 1978, BINAP (**10**) has been used for an enormous range of asymmetric hydrogenation reactions. As a ligand for rhodium, it has been used industrially in the preparation of (-)-menthol (**12**) from myrcene (**11**) (Scheme 1).




**Scheme 1:** The Takasago International Co. synthesis of (-)-menthol[12b]

The asymmetric step in the industrial production of (-)-menthol (**12**) is carried out on nine-ton scale, and subsequent hydrolysis produces (*R*)-citronellal (**13**) in 96 – 99% *ee*. This is far superior to the 80% *ee* of the naturally occurring product from rose oil. To this point, asymmetric hydrogenation had been predominantly limited to the synthesis of amino acids. One of the most significant breakthroughs in the use of BINAP (**10**) as a ligand, resulted from the change of metal from the more commonly used rhodium to ruthenium. The BINAP-$Ru^{II}$ dicarboxylate complexes, developed by Noyori and co-workers in 1986,[12b] proved to be excellent catalysts for asymmetric hydrogenation of a wide range of functionalised olefins (Figure 6).

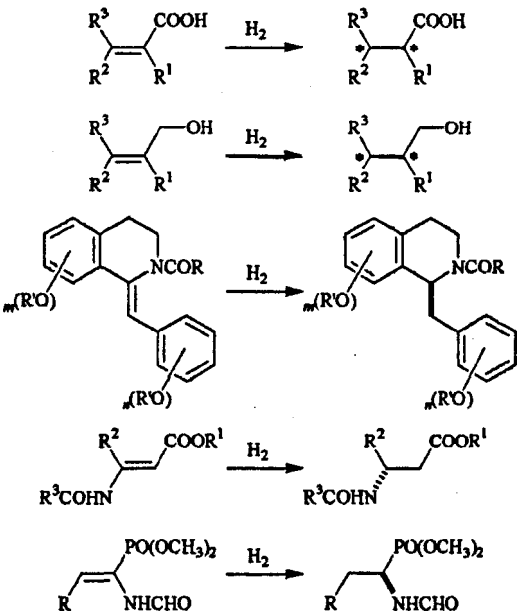


**Figure 6:** Asymmetric hydrogenation of functionalised olefins catalysed by $[Ru(OAc_2)((S)\text{-BINAP})]$[12b]

The use of a ruthenium-BINAP-halogen system allowed the hydrogenation of some functionalised ketones to their corresponding alcohols (Figure 7). However, the presence of coordinative nitrogen, oxygen or halogen atoms near to the ketone were necessary in order to direct the reactivity and stereochemical outcome of the reaction.

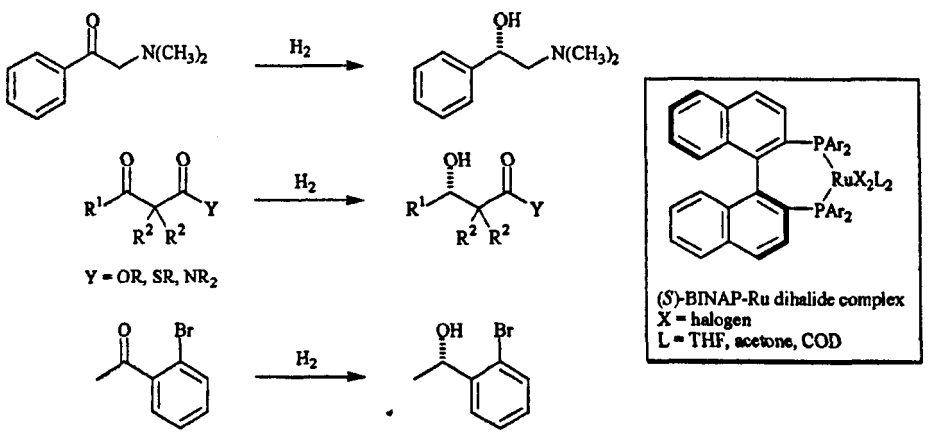



**Figure 7:** Asymmetric hydrogenation of functionalised ketones[12b]

Until the development of a BINAP/diamine ruthenium complex by Noyori and co-workers in 1995, the reduction of simple ketones had been largely

dominated by metal hydride technology and selective catalytic hydrogenation reactions had not generally been achieved (Figure 8).

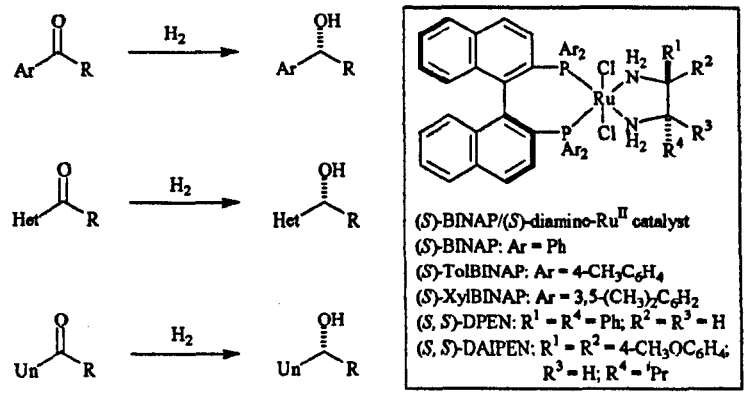



**Figure 8:** General asymmetric hydrogenation of simple ketones. Ar = aryl, Het = heteroaryl, Un = alkenyl[12b]

Ryoji Noyori won the 2001 Nobel Prize for Chemistry (along with K.B. Sharpless and W.S. Knowles) for his lifelong contribution to asymmetric organic synthesis. The enormous scope of reactions and excellent enantioselectivities imparted make BINAP (**10**) a remarkable ligand. Its use in asymmetric hydrogenation reactions has been outlined in some detail, but BINAP (**10**) is also highly effective in a wide range of other asymmetric transformations, including hydrosilylation and hydroboration of unsaturated compounds, epoxidation of allylic alcohols, hydroformylation, cyclopropanation and isomerism of olefins, allylic alkylation, aldol-type reactions and Diels-Alder reactions. It is the wide ranging reactivity and high selectivity of this ligand that sets it apart and it is the axis of chirality that must be responsible for the high enantioselectivities obtained, since BINAP (**10**) has no other chiral element.

### 5.2.2 Josiphos

The development of planar chiral phosphine compounds, such as Josiphos (**14**) (Figure 9), established another benchmark in the development of ligands for asymmetric synthesis.

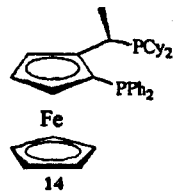



**Figure 9:** (*R*, $_p$*S*)-Josiphos (**14**)

When ferrocene has two different substituents on the same ring, two non-superimposable mirror images are possible and thus the compound is chiral (Figure 10).

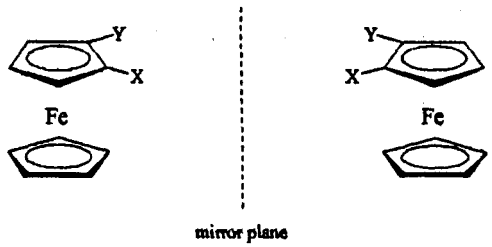



**Figure 10:** Planar chirality in ferrocenes

Josiphos (**14**) was developed by Togni and co-workers in 1994.[13] It is one example from a class of planar chiral ferrocenylamines and phosphines, derived from *N,N*-dimethyl-1-ferrocenylethylamine (**15**), that have been used as ligands in asymmetric synthesis. Earlier examples of planar chiral chelating phosphine ligands had been based on the following general structure (Figure 11).

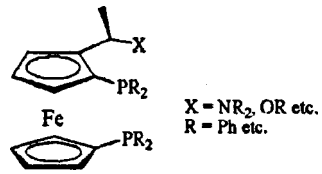
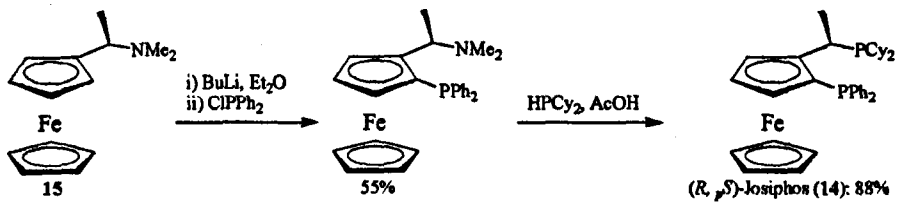


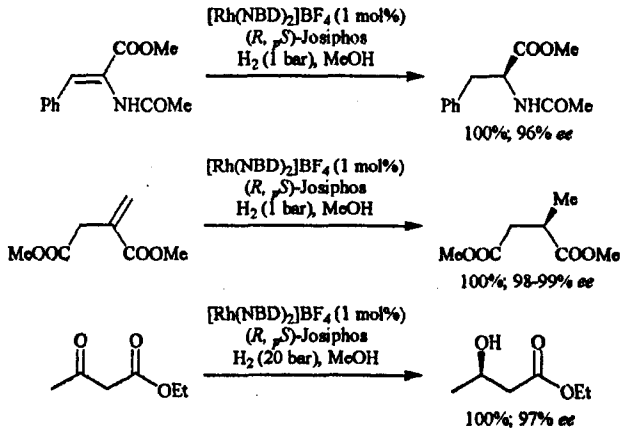

**Figure 11:** Planar chiral chelating phosphine ligands

In the vast majority of cases, the chelating phosphine groups were identical and usually diphenylphosphines.[14] The group present on the side chain of these ligands is introduced by a retentive nucleophilic displacement at the pseudo-benzylic position. Although these ligands give good enantioselectivities in several transition metal catalysed reactions, it was believed that modulating the steric and electronic factors around the phosphine groups would give better results. Josiphos (**14**) comprises two different phosphine groups, introduced in different reactions, thus allowing the ligands to be tuned for different catalytic properties.



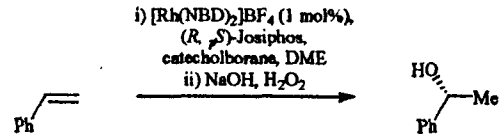

**Scheme 2:** Preparation of (*R*, *p*S)-Josiphos[13]

The plane of chirality is introduced *via* a diastereoselective *ortho*-lithiation followed by quench with chlorodiphenylphosphine.[14] The second phosphine group is introduced *via* a retentive substitution of the pendant dimethylamine, in good yield (88%). Josiphos (**14**) has been used to good effect in a number of asymmetric transformations. Like BINAP (**10**), it gives good results in asymmetric hydrogenation reactions, some of which are shown below (Scheme 3).



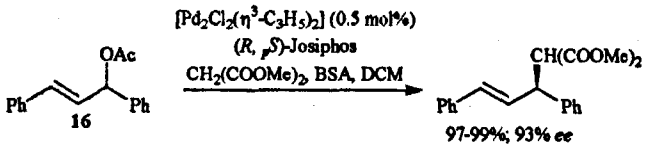

**Scheme 3:** Asymmetric hydrogenation reactions mediated by (*R*, *p*S)-Josiphos (**14**)[13]

High enantioselectivities have also been obtained for rhodium catalysed hydroboration reactions. The hydroboration of styrene with catecholborane, followed by oxidation with basic hydrogen peroxide, gives (*R*)-1-phenylethanol in 65% yield and 91% *ee* (Equation 5).




**(5)**[13]

Finally, good results have also been obtained for the palladium catalysed alkylation of an allylic acetate **16** (Equation 6).




**(6)**[13]

The enantioselectivity reported for this reaction is only slightly higher than that of the corresponding reaction with (*S*)-BINAP (**10**) (93% *ee*, cf. 89% *ee*), but, it is an order of magnitude faster. The above examples show the wide ranging reactivity and enantioselectivities obtained using the planar chiral Josiphos ligand (**14**).[13]

### 5.2.3 Planar Chiral DMAP

A wide range of compounds are known to be catalysed by nucleophiles (Lewis bases), however, there are far fewer examples of asymmetric Lewis base catalysis than there are of asymmetric Lewis acid catalysis. The most commonly encountered example of nucleophilic catalysis is, perhaps, the pyridine or DMAP mediated acylation of alcohols by anhydrides.

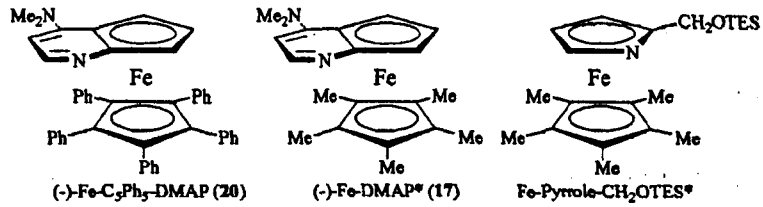



**Figure 12:** Fu's planar chiral nucleophilic catalysts

The planar chiral nucleophilic catalysts shown in figure 12 were developed by Fu and co-workers[15] and they have been shown to be effective nucleophilic catalysts for a range of reactions, including the acylation of alcohols, cyanosilylation of carbonyl groups, addition of alcohols to ketenes and the rearrangement of *O*-acylated enolates (Figure 13).[16]

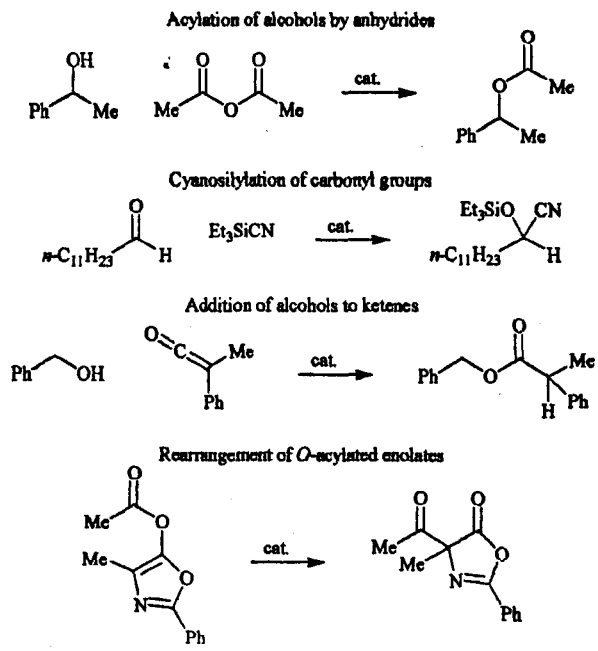
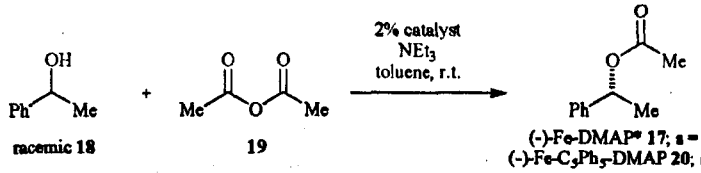


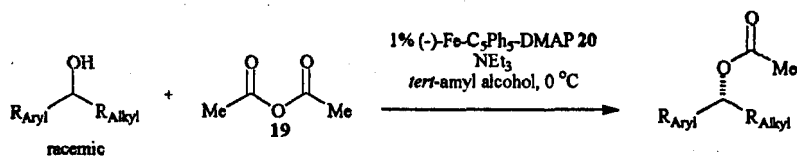

**Figure 13:** Examples of reactions catalysed by Lewis Bases

Preliminary investigations by Fu showed Fe-DMAP* **17** to be the most active of the catalysts in a variety of reactions. Racemic Fe-DMAP* **17** functions as an efficient catalyst for the acylation of 1-phenylethanol (**18**) with acetic anhydride (**19**). However, when enantiomerically pure material was used to carry out a kinetic resolution of alcohol **18**, the selectivity factor (a measure of the relative rate of reaction of the two isomers that needs to be at least 10 for the resolution to be effective) was only a disappointing 1.7 (Equation 7). Attempts to tune the reactivity of the catalyst led to the use of the more sterically demanding $C_5Ph_5$ ligand in place of Cp*.



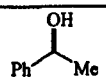
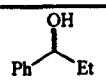
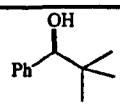
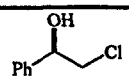
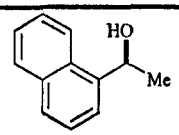
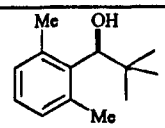

(7)[16]

This markedly increased the selectivity factor for the kinetic resolution of alcohol **18** with acetic anhydride (**19**) to 10 (Equation 7). The selectivity factor was increased further, to 43, by changing the solvent to *tert*-amyl alcohol and reducing the temperature to 0 °C (Equation 8; Table 2, Entry 1). Excellent results have also been obtained for a variety of other secondary alcohols (Table 2).




(8)

**Table 2:** Kinetic resolution of arylalkylcarbinols[16]

| Entry | Unreacted alcohol, major enantiomer | s | % *ee* | % conversion |
|---|---|---|---|---|
| 1 |  | 43 | 99 | 55 |
| 2 |  | 59 | 99 | 54 |
| 3 |  | 95 | 96 | 51 |
| 4 |  | 32 | 98 | 56 |
| 5 |  | 65 | 95 | 52 |
| 6 |  | >200 | 99 | 51 |

These results represent the highest values gained to date for the non-enzymatic resolution of secondary alcohols.

Since the only chiral element present in these compounds is their plane of chirality, this must be entirely responsible for the excellent results that have been achieved.

### 5.2.4 Summary and Conclusions

Despite the range of homochiral lithium amide bases developed to date, there is still scope to develop a base that would prove highly effective across the range of transformations. As the use of planar and axial chirality has been shown to be a highly efficient means of transmitting stereochemical information, it was hoped that by incorporating a planar chiral ferrocene core into a lithium amide

base, we could develop a new class of lithium amide. It was desirable that these bases would be highly effective across the range of possible transformations. It was also hoped that a catalytic system might be developed in order to make these compounds more attractive and efficient to use. The next section will provide a background to ferrocene chemistry.

### *5.3 Ferrocene Chemistry*

Since the discovery of ferrocene (**21**) in 1951, independently by both P. Pauson[17] and S. A. Miller,[18] there has been much interest in its properties and synthetic use. The key to understanding the reactivity of ferrocene lies in its structure and bonding. In fact, the early reports had incorrectly described ferrocene as a bis-σ-iron(II) structure and the correct "sandwich" structure of ferrocene was elucidated only later, independently by G. Wilkinson[19] and E. O. Fischer[20] (Figure 14).

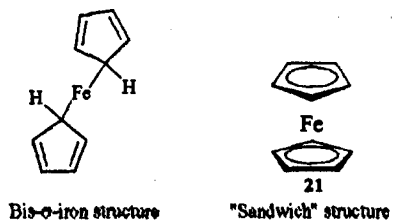



**Figure 14:** Proposed structures for ferrocene

#### 5.3.1 Structure and Bonding[21,22]

Ferrocene can be usefully described as two 6-electron π-donor $(C_5H_5)^-$ ligands interacting with $Fe^{+2}$ ($d^6$) metal centre, thus giving ferrocene a stable 18 valence electron configuration. The molecular orbital approach provides a detailed picture of the nature of structure and bonding in ferrocene. Ten delocalised $(C_5H_5)^-$ molecular orbitals are generated from the ten 2p atomic orbitals of the cyclopentadienide ligands, and these are combined with the 9

valence shell orbitals of the iron atom (5 × d-orbitals, 1 × s-orbital and 3 × p-orbitals), giving a total of 19 molecular orbitals for ferrocene. Six of these orbitals are strongly ring-metal bonding and have considerable ligand-based character. A further 3 orbitals are essentially non-bonding and have considerable metal-based character (Figure 15).

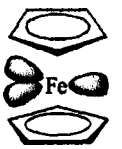



**Figure 15:** The 3 trigonally hybridised non-bonding orbitals of ferrocene.

These orbitals are trigonally hybridised around the metal and behave chemically as lone pairs. These orbitals play a key role in explaining the reactions of ferrocene. The remaining 10 orbitals are anti-bonding.

### 5.3.2 Physical and Chemical Properties of Ferrocene[21]

Ferrocene, unlike many other organometallic complexes, is an air- and moisture-stable solid. This makes it an attractive compound for the organic chemist, since for the most part it requires no specialised handling techniques. The Cp ligands do not dissociate from the metal centre as a result of the strong Cp-Fe bond (381 ± 13 kJ $mol^{-1}$).[23] This proves very important when preparing planar chiral complexes, as facile ligand dissociation would result in racemisation of compounds. Both proton and carbon-13 NMR spectra consist only of singlet resonances, therefore showing that all carbon and hydrogen atoms are equivalent, and that the delocalised aromatic character of the Cp anion persists on complexation.

Ferrocene is readily oxidised to the 17-electron ferricenium cation,[19] and although this reaction is reversible with mild reducing agents, it precludes the

use of oxidising reagents for synthesis. This inevitably means that many of the reagents used to carry out electrophilic aromatic substitution are not available to the ferrocene chemist.

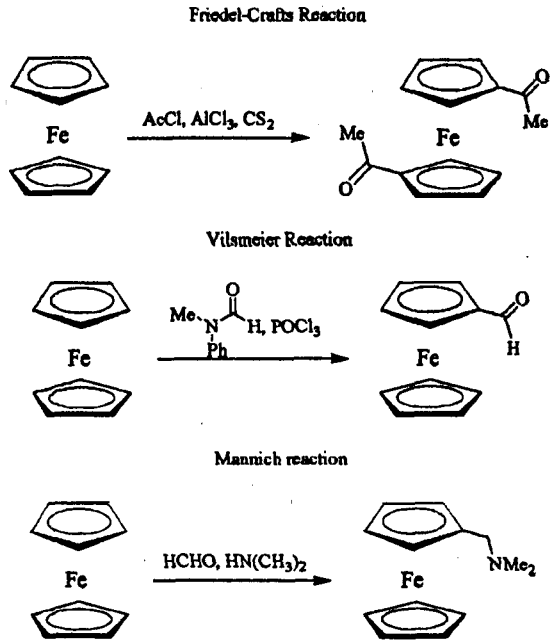
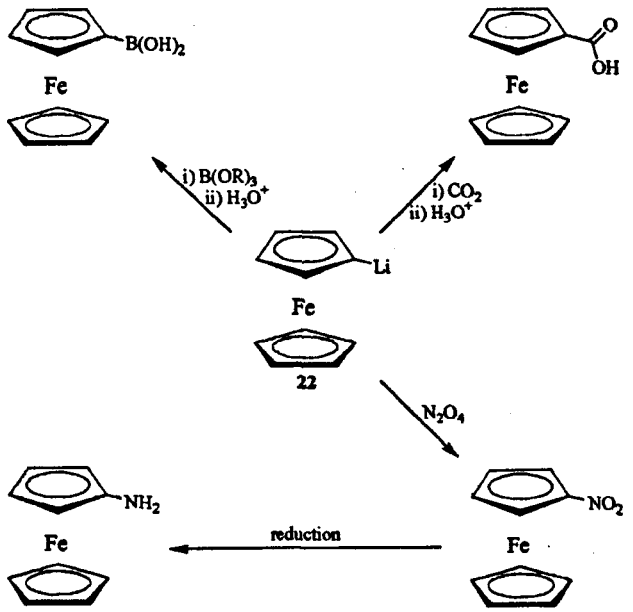



**Figure 16:** Electrophilic substitution reactions of ferrocene

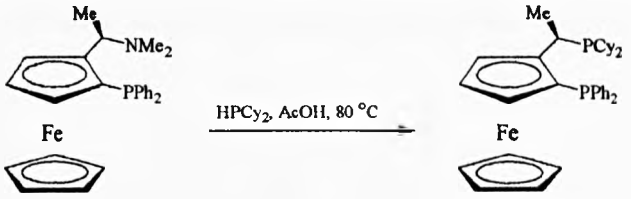
Among those reactions that are not possible are electrophilic nitration, halogenation and sulfonation. There is, however, a wide range of reactions that are easily carried out on ferrocene. In comparison with benzene, ferrocene is highly electron rich. Competition reactions have shown it to be ca. $3 \times 10^6$ times more reactive towards electrophilic substitution. Thus, Friedel-Crafts acylation occurs easily,[24] as do a variety of other reactions, including the Mannich reaction[25] and the Vilsmeier reaction[26] (Figure 16).

The reactions of metallated ferrocene derivatives provide alternative methods for functionalisation. Monolithioferrocene (**22**) is prepared from ferrocene in moderate yields by lithiation with *tert*-butyl lithium in THF.[27] A wide range of reactions are then available, allowing access to compounds not obtainable by direct electrophilic substitution.




**Scheme 4:** Indirect substitution reactions of lithioferrocene (**22**)[26,29,30]

Crucial to the syntheses of many useful ferrocene based ligands has been the ability of the ferrocenyl group to stabilise electron deficient centres α- to the ring system. Here, a comparison should be drawn with the acidity of the benzylic position, since the pseudo-benzylic α-position in ferrocenyl compounds is deprotonated with difficulty, and requires some stabilisation of the resultant carbanion.[31] Nucleophilic substitutions at this position occur readily, and when the α-position is chiral, the intermediate carbocation is chiral[32] and the substitution proceeds with retention of stereochemistry.[33] This effect has been used in the synthesis of many chiral ferrocene derivatives. For example, the final step in the synthesis of the highly effective Josiphos (**14**) ligand consists of the retentive substitution of a dimethylamino group with a dicyclohexylphosphine group (Equation 9).[13]




(9)

(*R*, *pS*)-Josiphos (14)

The explanation for both the α-effect and the facile substitutions at the α-position lies in the nature of the stabilisation provided by the ferrocenyl group. When this effect was first noticed, two possible mechanisms were invoked to explain the stabilisation.

The first explanation was that of direct stabilisation with a through-space interaction between the iron-based non-bonding orbitals and the vacant p-orbital of an α-carbocation.[34]

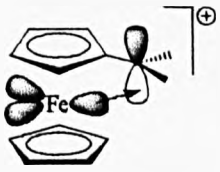



**Figure 17:** Direct stabilisation of an α-carbocation

An indirect stabilisation mechanism was also suggested, with the iron centre able to transfer electron density to the π-system of the Cp ring, which can then overlap with the vacant p-orbital.[34]

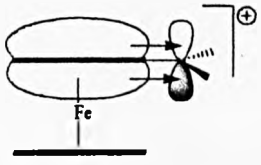



**Figure 18:** Indirect stabilisation of an α-carbocation

The explanation now widely accepted, favours the direct participation of the iron atom in charge delocalisation (Figure 17). When this occurs, the two cyclopentadienyl rings become slightly tilted away from parallel, and the

carbocationic substituent is bent out of the plane of the ring, towards the iron atom (Figure 19).

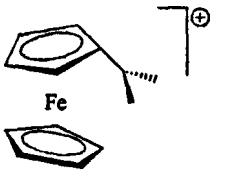



**Figure 19:** Structure of ferrocenylalkylcarbocation

This result was predicted by theoretical calculations[35] and has been confirmed by X-ray structural analysis.[36] As a result of this, rotation around the bond between the ring and the cationic centre is hindered, and thus α-ferrocenylethyl carbocations exist as enantiomers with a low tendency for racemisation.[37] This explains the retention of configuration in nucleophilic substitution reactions, since stereochemical and kinetic evidence indicates that the reaction proceeds by an $S_N1$ mechanism.

### 5.3.3 Applications of Ferrocene Derivatives

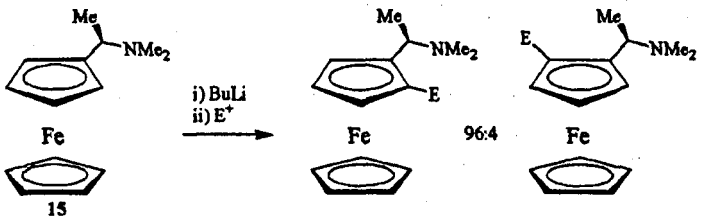
One of the most diverse areas in which ferrocene derivatives have been utilised has been as ligands for asymmetric synthesis, where planar chiral ligands are regularly used. Planar chiral ferrocene-based catalysts have also been prepared, most notably the analogues of DMAP introduced by Fu *et al.*[16] (see section 5.2.3).

### 5.3.4 Preparation of Planar Chiral Ferrocene Complexes

As shown above, planar chiral ferrocene derivatives have found much use in asymmetric organic synthesis. It is, therefore, not surprising that there are a number of methods available for the asymmetric introduction of a second ring substituent, thus creating a plane of chirality.

### 5.3.4.1 Ligands Derived From *N,N*-Dimethyl-1-ferrocenylethylamine (15)

The development, by Ugi and co-workers,[32,33] of *N,N*-dimethyl-1-ferrocenylethylamine (**15**) as a starting material for chiral ligand synthesis, was a real breakthrough. It allowed the reliable preparation of compounds containing a plane of chirality by diastereoselective *ortho*-lithiation (Equation 10).




(10)

The amine itself is easily prepared and can be resolved using tartaric acid, to give good yields of both enantiomers.[38] The high diastereoselectivity (92% *de*) results from the rigid transition state where the dimethylamino group directs lithiation to the *ortho*-position. Of the two diastereomeric transition states, the one where the methyl group points away from the ferrocenyl system is more favourable, and thus gives the major diastereoisomer (Figure 20).

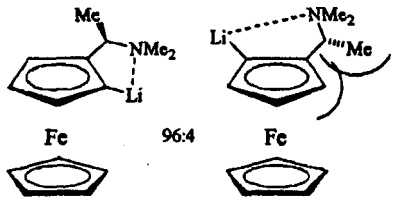



**Figure 20:** Diastereomeric lithiated intermediates

An enormous number of chiral ligands are derived from *N,N*-dimethyl-1-ferrocenylethylamine (**15**), both from the introduction of an electrophile to the ferrocenyl lithium, and also the retentive nucleophilic displacement of the pendant amine.

### 5.3.4.2 Other Chiral *ortho*-Directing Groups

Following on from the success of *N,N*-dimethyl-1-ferrocenylethylamine (**15**) as a diastereoselective *ortho*-directing ferrocene template, many other chiral *ortho*-directing groups and auxiliaries were introduced. Some of these have advantages over Ugi's amine **15**, as they do not require the incorporation of a centre of chirality or contain unwanted carbon fragments.

Kagan and co-workers introduced two highly successful diastereoselective *ortho*-directing groups. The first was a chiral acetal derived from ferrocene carboxaldehyde[39] and the second utilised a chiral sulfoxide.[40]

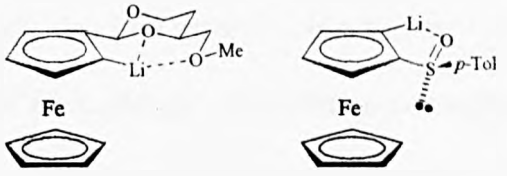



**Figure 21:** Acetal and sulfoxide *ortho*-directing groups

Both of these directing groups allow the introduction of a wide range of electrophiles in excellent yield and enantiomeric excess. The chiral sulfoxide has the extra advantage of being readily substituted itself. Treatment of an *ortho*-substituted sulfoxide with *tert*-butyl lithium in ether yields racemic sulfoxide and a planar chiral lithio-ferrocene, which can be trapped with a range of electrophiles. This allows the stereoselective introduction of two different electrophiles and thus widens the range of planar chiral ferrocene derivatives available.

Chiral oxazolines have been prepared in good yield from ferrocene carboxylic acid and the corresponding amino alcohol.[41] These compounds direct *ortho*-lithiation by coordination to the nitrogen atom (Figure 22).

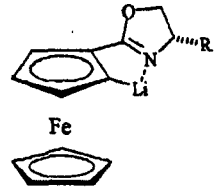
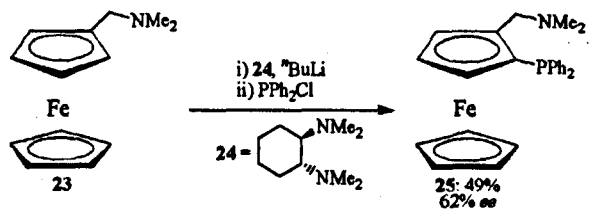



**Figure 22:** An oxazoline *ortho*-directing group

Oxazoline ligands have been prepared with an *ortho*-phosphine group, and these give excellent enantiomeric excesses for a range of reactions.[42] Alternatively, the oxazoline unit may be removed to give an *ortho*-substituted carboxylic acid.

### 5.3.4.3 Non-auxiliary Enantioselective *ortho*-Functionalisation

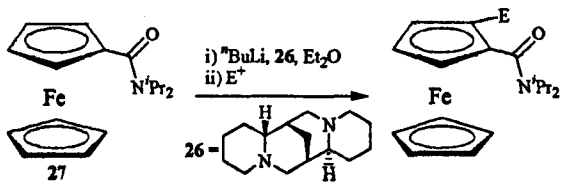
Stereoselective introduction of a second ring substituent has also been carried out using chiral base methodology. A common strategy has been the use of butyl lithium with a chiral amine, such as (-)-sparteine (**26**) or *N,N,N',N'*-tetramethyl-1(*R*),2(*R*)-cyclohexanediamine (**24**). For this strategy to work, the ferrocene derivative needs an *ortho*-directing substituent, such as an amine or amide. Work by Uemura *et al.*,[43] published in 1996, showed the use of ((*N,N*-dimethylamino)methyl)ferrocene (**23**) with butyl lithium and the chiral cyclohexanediamine **24**, to give a diphosphino amino ferrocene **25** in moderate yield and enantiomeric excess (Equation 11).




**(11)**

This result was quickly surpassed by Snieckus and co-workers, who used butyl lithium and (-)-sparteine (**26**) to stereoselectively deprotonate *N,N*-diisopropylferrocene carboxamide (**27**).[44,45] Subsequent quench with

electrophiles gave planar chiral ferrocenyl amides in excellent yield and enantiomeric excess (Scheme 5).




| $E^+$ | E | Yield / % | ee / % |
|---|---|---|---|
| TMSCl | TMS | 96 | 98 |
| MeI | Me | 91 | 94 |
| $I_2$ | I | 85 | 96 |
| $B(OMe)_3$ | $B(OH)_3$ | 65 | 85 |

**Scheme 5**

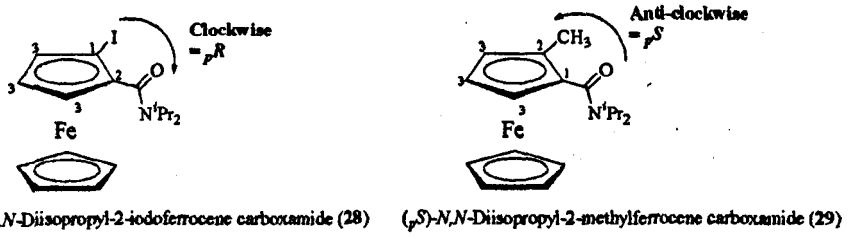
The strategies outlined above give access to a wide range of planar chiral ferrocene compounds, some that incorporate both central and planar chirality, and others with just a plane of chirality.

The final part of this introduction clarifies the nomenclature that will be used for chirality descriptors of planar chiral ferrocenes.

### 5.3.5 Assignment of Chirality Descriptors for Planar Chiral Ferrocenes[46]

The observer regards the ferrocenyl compound from the side of the ring to be assigned (the "upper" ring). The ring substituents are then analysed for priority using the Cahn-Ingold-Prelog rules. If the shortest path from the highest to the next highest priority substituent is clockwise, the chirality descriptor is (*R*), if it is anti-clockwise it is (*S*). In cases where both rings have two or more substituents, the ring bearing the highest priority substituent is considered first, and the molecule is inverted before assigning the second ring. Where both central and planar chiral elements are present, convention states that the descriptor of central chirality precedes that of planar chirality. For example, (*R*, *S*) should mean a compound with central chirality of (*R*) configuration and planar chirality of (*S*) configuration. In practice, planar chiral descriptors ($_p$*R* and $_p$*S*) are often used to clarify that the planar chiral system is being used. All

non-racemic chiral compounds will be assigned according to the above system (Figure 23).



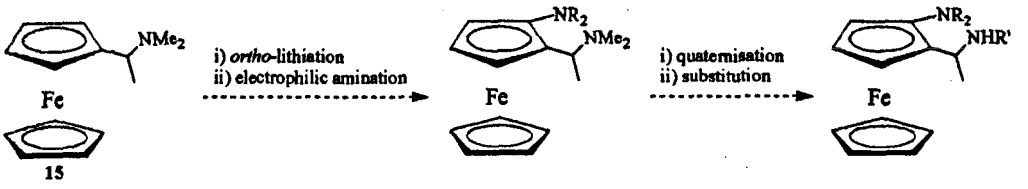

($_pR$)-*N,N*-Diisopropyl-2-iodoferrocene carboxamide (28) ($_pS$)-*N,N*-Diisopropyl-2-methylferrocene carboxamide (29)

**Figure 23:** Examples of assignment of planar chiral descriptors

In the original paper by Cahn, Ingold and Prelog,[47] they stated that metallocene stereochemistry could be described as central chirality. The highest priority substituent is considered as being bonded to the carbon atoms in the Cp ring as well as to the central metal atom, thus making a distorted tetrahedral system that can be assigned in the normal way. This system is not commonly used for ferrocene compounds, but, care needs to be taken, since it can give the opposite descriptor to that given by the planar chiral approach.

# 6 Results and Discussion

It was proposed initially, that the desired bases could be derived from Ugi's amine **15**. This would provide a flexible starting point, since both enantiomers are available in high yield, and our proposed route would allow modification of both amine functions (Scheme 6).




**Scheme 6:** Proposed route to planar chiral lithium amides

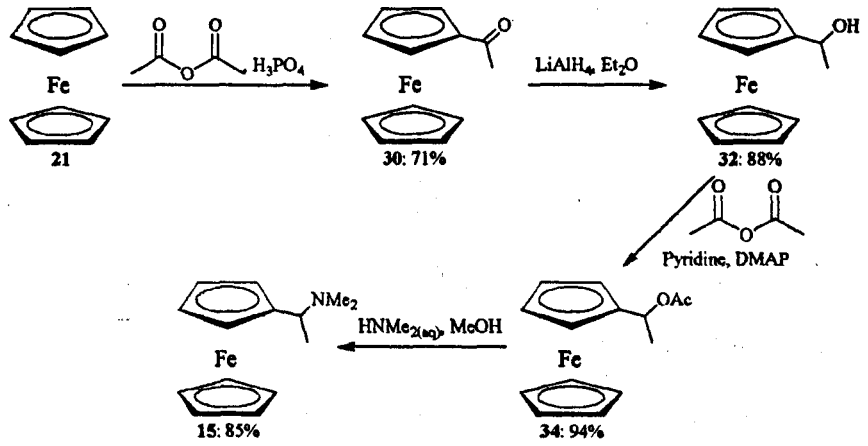
Diastereoselective *ortho*-lithiation followed by quenching with an electrophilic aminating agent would allow the introduction of an *ortho*-amine group. Subsequent quaternisation and substitution of the pendant amine with a primary amine would give the lithium amide centre. Variation of the amino groups used would allow tuning of the lithium amide, as well as scope to investigate the effect of swapping the donor group and lithium amide positions.

## *6.1 Studies Based on* N,N-*Dimethyl-1-ferrocenylethylamine (15)*

### 6.1.1 Preparation of N,N-Dimethyl-1-ferrocenylethylamine (15)

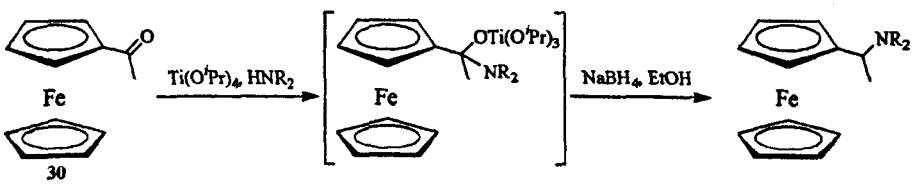
Racemic *N,N*-dimethyl-1-ferrocenylethylamine (**15**) was prepared from ferrocene (**21**) in good yield (50% over 4 steps) (Scheme 7). This synthesis is loosely based on a procedure published by Gokel and Ugi.[38] Acetylferrocene (**30**) was prepared, using the procedure of Graham *et al.*,[48] from ferrocene in 71% yield, with only 1% of the diacylated 1,1'-diacetylferrocene (**31**) byproduct. The mono-acylated product **30** was then reduced with lithium aluminium hydride, using a procedure by Arimoto and Haven,[49] to give α-

ferrocenylethanol (**32**) in 88% yield, with a small amount of ethylferrocene (**33**) (8%) as a byproduct. The published acylation procedure[49] was modified, by addition of a catalytic quantity of DMAP, and yielded α-ferrocenylethylacetate (**34**) in 94% yield. Substitution of the acetate with dimethylamine in methanol yielded *N,N*-dimethyl-1-ferrocenylethylamine (**15**) in 85% yield.[38]



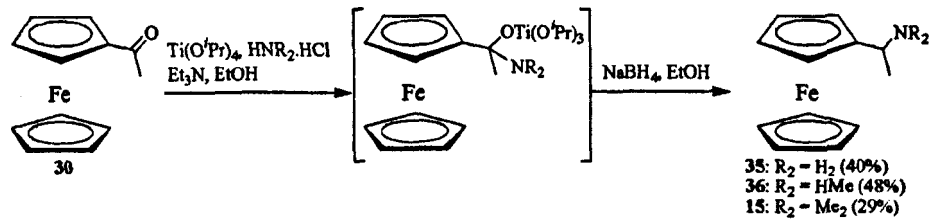

**Scheme 7**

In order to cut down on the number of synthetic steps, an alternative route to *N,N*-dialkyl-1-ferrocenylethylamines was investigated. The reductive amination of acetylferrocene (**30**) was reported by Bhattacharyya[50] in 1994 (Scheme 8), but the desired dimethyl compound (**15**) was not reported. An analogous preparation was attempted, using a solution of dimethylamine in THF or in methanol, in place of the neat amines used by Bhattacharyya. Despite varying reaction time and order of addition, α-ferrocenylethanol (**32**) was the only product recovered from these reactions.




**Scheme 8**

In order to see if the problem resulted from the use of a solution of amine, the known reactions with diethylamine and morpholine were attempted, but, again the only product isolated was $\alpha$-ferrocenylethanol (**32**). A modified procedure for reductive amination using titanium(IV) isopropoxide[51] was later obtained and this modification was also reported for the preparation of 1-ferrocenylethylamine (**35**).[52]




**Scheme 9**

This modified procedure was used successfully with ammonium chloride (**35**: 40%, lit.[52] yield = 75%), methylamine hydrochloride (**36**: 48%) and dimethylamine hydrochloride (**15**: 29%) (Scheme 9). Despite the low yields, this route provides a useful alternative to our original synthesis, as it may allow greater flexibility in the amine groups introduced.

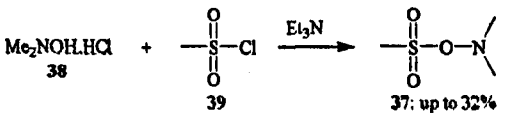
## 6.1.2 Introduction of Nitrogen Functionality

### 6.1.2.1 Electrophilic Amination of *N,N*-Dimethyl-1-ferrocenylethylamine

Having successfully prepared *N,N*-dimethyl-1-ferrocenylethylamine (**15**), the aim was to aminate the *ortho* position of the cyclopentadienyl ring, thus introducing the second amine functionality. Diastereoselective *ortho*-lithiation of **15** was reported by Ugi *et al.*[33] in 1970, and the resulting lithiated ferrocenylamine was reacted with a variety of electrophiles. It was hoped that Ugi's strategy could be employed to introduce the desired nitrogen functionality using an electrophilic aminating agent. The first such agent that

was investigated was *N,N*-dimethyl-*O*-(methylsulfonyl)hydroxylamine (**37**). Bernheim and Boche reported the use of **37** to aminate cyclopentadienyl lithium,[53] and so it seemed reasonable that amination of the ferrocenyl compound **15** would be possible.

*N,N*-Dimethyl-*O*-(methylsulfonyl)hydroxylamine (**37**) was prepared from *N,N*-dimethyl-hydroxylamine hydrochloride (**38**) and methane sulfonyl chloride (**39**) (Equation 12) in an analogous reaction to that reported by Boche *et al.*[54]




**(12)**

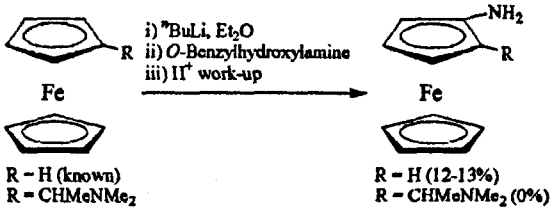
The highest yield obtained for this reaction was 32%, but it consistently yielded less than 20% of the desired product.

Electrophilic amination of *N,N*-dimethyl-1-ferrocenylethylamine (**15**) was then attempted using **37**, but all attempts resulted in the quantitative recovery of **37** and ferrocenylamine **15**. In order to verify that the lithiation was taking place, the reaction mixture was quenched with $D_2O$, yielding 93% of deuterated product **40**. The cyclopentadienyl peaks for *N,N*-dimethyl-1-ferrocenylethylamine (**15**) appear as a multiplet, integrating for 9, at δ 4.1 in the $^1$H NMR spectrum. The $^1$H NMR spectrum recorded for the deuterated product **40** showed the expected reduction in the integration for the cyclopentadienyl protons at δ 4.1 and the mass spectrum showed the molecular ion peak to be 258 *m/z*. This showed that lithiation was occurring, so it was decided to investigate alternative aminating reagents.

Dialkyl azodicarboxylates have been shown to act as electrophilic aminating agents for chiral enolates.[55] The electrophilic amination reaction was repeated

using di-*tert*-butylazodicarboxylate as the aminating agent, and in this case the reaction yielded an unidentifiable mixture of products that decomposed on silica.

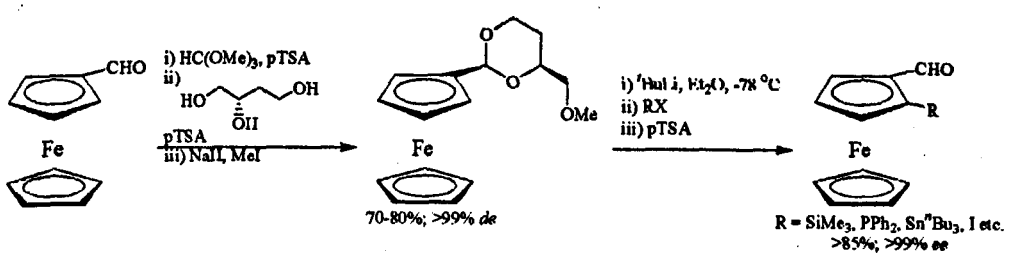
Amination of lithio-ferrocene (**22**) has been carried out successfully using *O*-benzylhydroxylamine, albeit in only 12 – 13% yield.[56,57] Use of *O*-benzylhydroxylamine to attempt amination of lithiated *N,N*-dimethyl-1-ferrocenylethylamine (**15**) simply yielded starting material (Equation 13). This reaction may have been unsuccessful due to coordination of the ferrocenyl lithium by the pendant dimethylamine. This coordination may provide too much stabilisation to the carbanion rendering it unreactive towards *O*-benzylhydroxylamine as an electrophile.




(13)

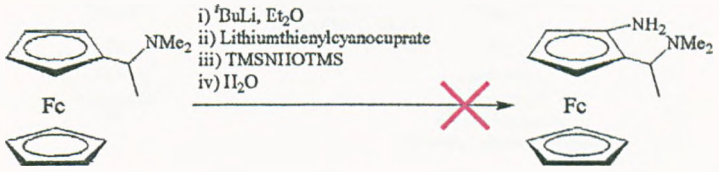
### 6.1.2.2 Other Methods for the Introduction of Amine Functionality

Since electrophilic amination proved unsuccessful, it was decided to investigate alternative routes to our desired compounds. Work by Kagan *et al.*[58] on *ortho*-directing chiral acetalferrocenes, reported the introduction of a range of electrophiles (Scheme 10).




**Scheme 10**

In addition to simple electrophiles they also reported the use of organocuprates, prepared from the lithiated ferrocene species, to introduce amine functionality. Attempted amination of the ferrocenylamine **15** *via* an organocuprate (Equation 14) was unsuccessful, probably due to the high affinity of amines for copper.

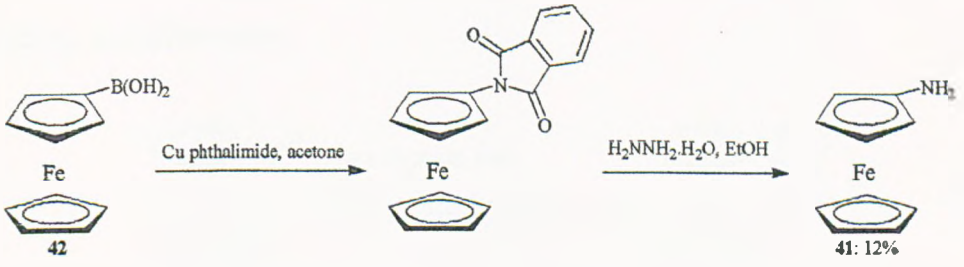



**(14)**

The reaction yielded mostly ferrocenylamine **15** with a small quantity of another unidentifiable product also formed.

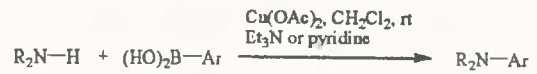
Kagan *et al.* also described the preparation of a ferrocenylboronic acid. which led us to consider using a coupling reaction to introduce the amine group.[58]

Montserrat *et al.*[59] have reported the preparation of aminoferrocene (**41**) from ferrocene (**21**), in 3 steps with an overall yield of 13%. The reaction proceeds *via* the coupling of ferrocene boronic acid (**42**) with copper phthalimide, followed by cleavage of the phthalimide group to unmask the amine functionality (Scheme 11).



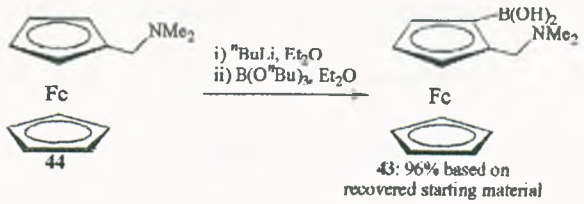

**Scheme 11:** Montserrat's synthesis of aminoferrocene (**41**)

Recent work by Chan *et al*[60] on the *N*-arylation of phenylboronic acids (Equation 15), also supported the proposal that the ferrocene boronic acid **45** could undergo a coupling reaction to introduce an amine group.



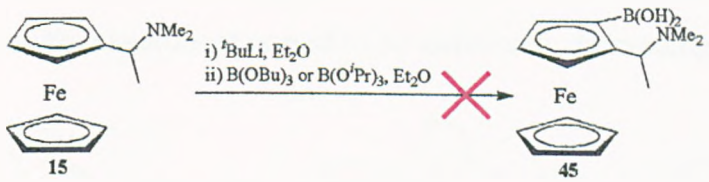

(15)

The preparation of 2-(*N,N*-dimethylaminomethyl)ferrocene boronic (**43**) acid from the corresponding ferrocenylamine **44** has been reported by Marr *et al.*[61] (Equation 16).



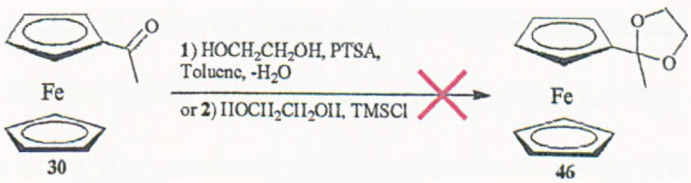

(16)

Attempts to prepare a ferrocenylboronic acid **45** following Marr's methodology, using both tributyl borate and triisopropyl borate, failed, with starting material **15** the only identifiable product (Equation 17).




(17)

The Lewis basic nature of the amine group could account for the lack of success of both the boronic acid preparation and the organocuprate work. It was, therefore, decided to try to prepare an acetalferrocene **46** as this would be expected to exhibit reactivity more similar to that of Kagan's chiral *ortho*-directing acetalferrocene.



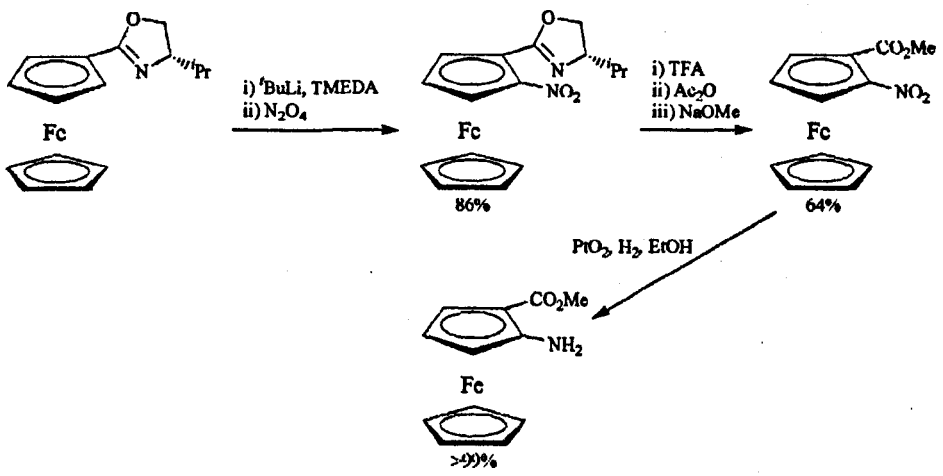

(18)

Attempts to form the acetal using Dean-Stark dehydration conditions yielded only starting material, whereas Chan's procedure[62] yielded starting material **30** and three other products, one of which was obtained cleanly by column

chromatography, but remains unidentified (Equation 18). The chiral acetal prepared by Kagan was derived from an aldehyde, and the lesser reactivity of ketones may account for the difficulty we encountered in trying to protect acetylferrocene.

### 6.1.2.3 Nitration of *N,N*-Dimethyl-1-ferrocenylethylamine (15)

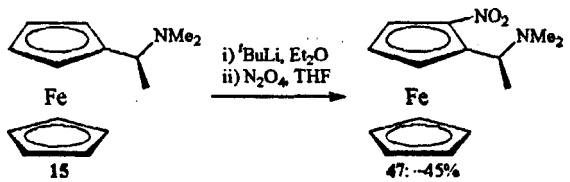
The preparation of 2-aminoferrocenecarboxylic acids via 2-nitroferrocenyloxazolines was reported by Richards *et al*[63] (Scheme 12) and provided us with a viable alternative route to our desired compounds. Mechanistic evidence for the nitration step, reported by Eaton *et al.*,[64] suggests that the reaction takes place at the melting THF/$N_2O_4$ interface. They postulate that the rate of delivery of the reactants is controlled by the melting process. This meant that the experiment proved to be technically demanding.




**Scheme 12:** Richards' preparation of ferrocenylaminoacids

Nitration of lithiated *N,N*-dimethyl-1-ferrocenylethylamine (**15**) using $N_2O_4$ was attempted using the procedure of Richards *et al.*[63] The THF solution of lithiated ferrocenyl amine (**15**) was frozen in a thin layer around the sides of the reaction flask and then reacted with a known quantity of dinitrogen tetraoxide gas. The first few attempts at this reaction yielded black, insoluble

material, thought to be an oxidation product due to the paramagnetic nature of the $^1$H NMR spectrum. By reducing the number of equivalents of $N_2O_4$, and improving the technique for freezing the reaction mixture around the walls of the flask, the quantity of oxidation product was reduced and a red oil was isolated. Purification of the products by flash column chromatography was moderately successful, but the products were highly sensitive to oxidation, turning from red oils to black insoluble tar. Therefore, despite several attempts to isolate the products of this reaction, only clean proton and carbon-13 NMR spectra have been obtained. These spectra appear to show a 1:1 mixture of starting material and an *ortho*-substituted ferrocenylamine with an electron withdrawing group.




(19)

This would seem to be consistent with the desired product **47** present in 45% yield based on mass balance and $^1$H NMR (Equation 19). Due to loss of material through oxidation, especially in solution, it was decided to hydrogenate the crude reaction mixture.

Column chromatography of the hydrogenation products yielded *N,N*-dimethyl-1-ferrocenylethylamine (**15**) (27% recovery) followed by an orange solid. Initial NMR analysis seemed to suggest an *N,N*-dimethyl-1-ferrocenylethylamine with one *ortho*-substituent. However, mass spectrum, elemental analysis and single crystal x-ray diffraction studies showed the product to be a dimer of the starting amine **48** (Figure 24).

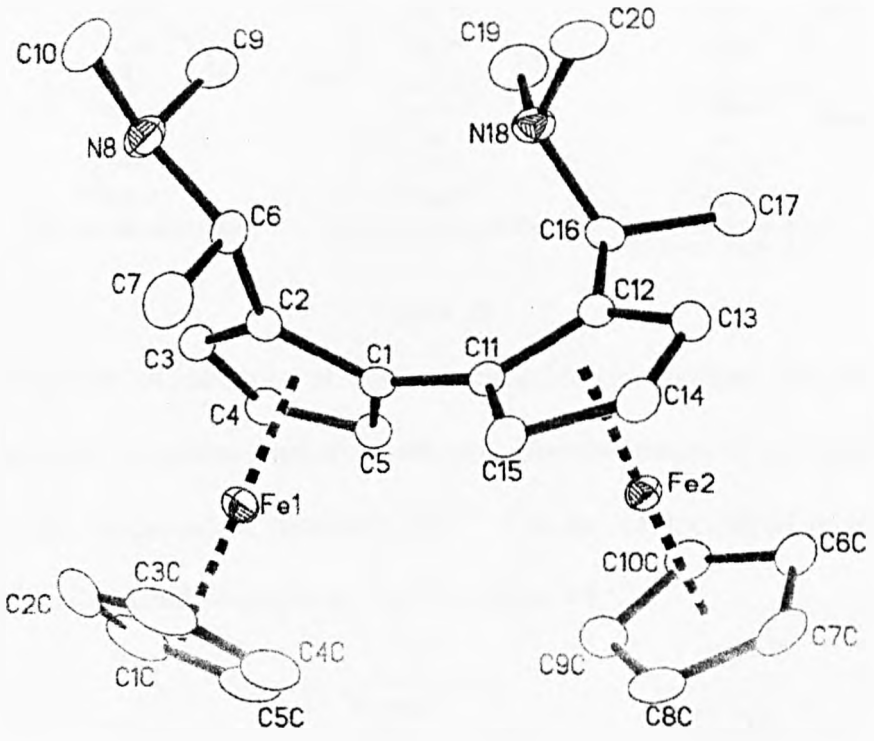



**Figure 24:** Single crystal x-ray diffraction structure

Diastereoisomers of the dimer can exhibit central, axial and planar chirality. The $^1$H NMR spectrum shows the compound to have a high level of symmetry. Schlögl *et al.*[65] report the formation of two isomers of 2,2'-bis-[1-(N,N-dimethylamino)-ethyl]-1,1'-biferrocenyl, *via* the reaction of lithiated ferrocenyl amine with cobalt(II) chloride. They assign these as an achiral *meso* form (**49**) and a chiral heterocoupled product formed from the major and minor diastereoisomers of the preceding *ortho*-lithiation step (**50**) (Figure 25). Our data did not agree with that reported by Schlögl *et al.*, however, on inspection of the single crystal x-ray diffraction structure obtained for our compound, it is assigned as a racemic, planar chiral and centrally chiral, $C_2$ symmetric isomer (**48**). For clarity, the enantiomers are not shown.

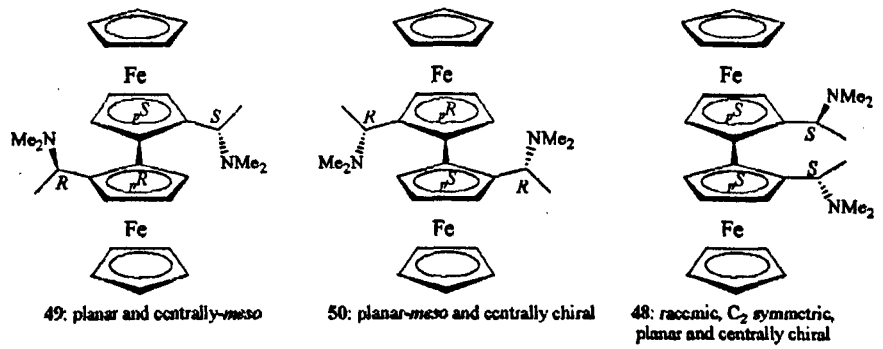
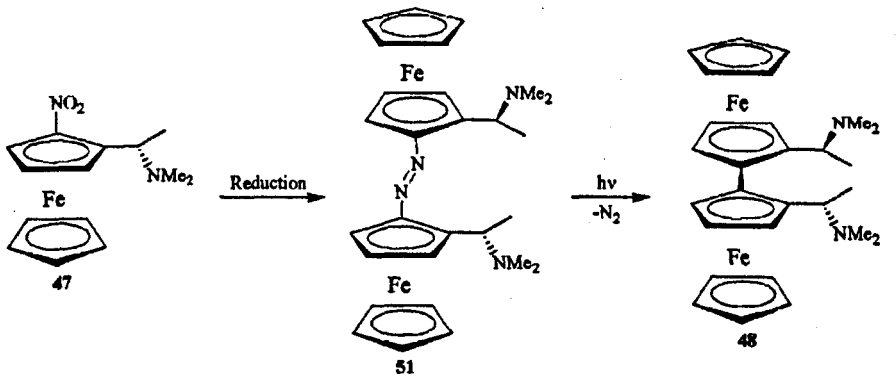



**Figure 25**

The mechanism of formation of this compound remains unclear. We postulate that under reducing conditions the ferrocenyl nitro compound **47** is transformed into an azo compound **51** (Equation 20).[66] The azo compound **51** might then photolytically extrude nitrogen to yield the dimer **48**.[67,68]

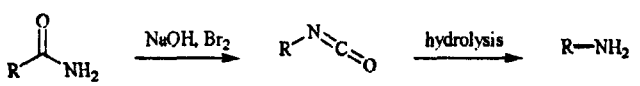



**(20)**

Despite the preparation of this interesting diamino ferrocenyl dimer **48**, preparation of an *ortho*-amino compound had still not been realised, therefore our attention turned to other possible methods for the introduction of an amine.

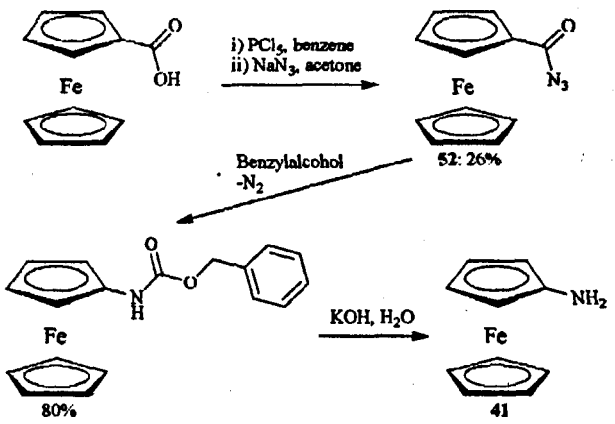
### 6.1.2.4 Hofmann Rearrangement

Our final attempt to introduce an *ortho*-amine involved the use of the Hofmann rearrangement (Scheme 13).[69]




**Scheme 13:** Hofmann Rearrangement

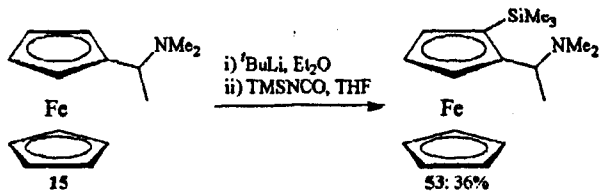
Arimoto and Haven report the use of a Curtius rearrangement to give aminoferrocene (41) in less than 20% yield (Scheme 14).[49]




**Scheme 14**

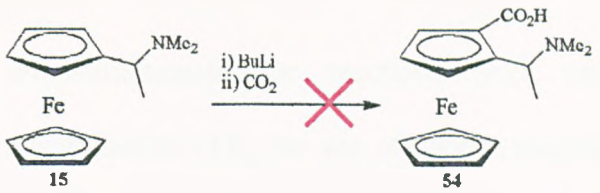
Since the Hofmann rearrangement proceeds *via* a similar mechanism, it was anticipated that this could allow the introduction of the amine functionality.

Primary amides are known to be accessible from Grignard reagents on treatment with TMS-isocyanate.[70] It was therefore hoped that a similar preparation might be possible from our lithiated ferrocenyl amine. However, the only isolated product from the reaction was α-(2-trimethylsilylferrocenyl)ethyldimethylamine (**53**) (Equation 21).




**(21)**

Preparation of an amino acid **54** in order to make an amino ferrocenyl acid azide for use in the Curtius rearrangement was not a possible strategy since research within our group[71] had shown that these compounds were not readily available (Equation 22).

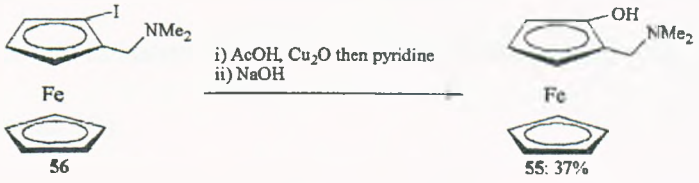



(22)

Due to our lack of success in introducing an *ortho*-amine group, our attention turned to alternative donor groups.

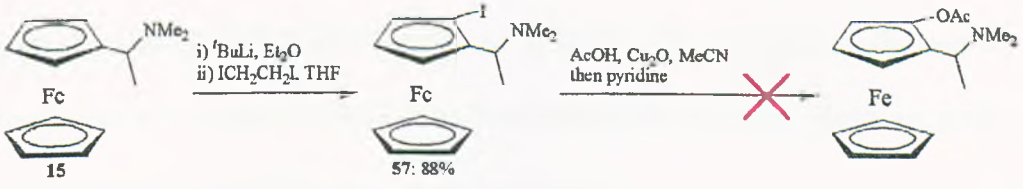
### 6.1.3 Introduction of Oxygen Functionality

Besides amine functionality, the next most common secondary donor group found in lithium amide bases is the methoxy group. Onishi *et al.*[72] have reported the preparation of a 2-hydroxyferrocenylamine **55** *via* a coupling reaction of the corresponding iodide **56** (Equation 23).




(23)

The procedure used is based on a more general coupling of carboxylic acids with ferrocenyl iodides as reported by Akabori, Sato and Ebine in 1981.[73] Preparation of 2-iodo-*N,N*-dimethyl-1-ferrocenylethylamine (**57**) from Ugi's amine **15** proceeded smoothly and gave **57** in 88% yield (Scheme 15).




**Scheme 15**

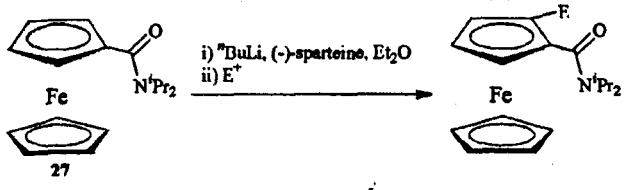
However, when the iodide **57** was subjected to the coupling conditions, none of the desired acetate was isolated, only an intractable mixture of products that were not separable by column chromatography. It is assumed that the amine sequesters the copper salt, despite treatment with pyridine at reflux.

### 6.1.4 Conclusions

Although many *ortho*-functionalisation reactions work well with *N,N*-dimethyl-1-ferrocenylethylamine (**15**), the use of copper reagents is precluded due to unfavourable interactions. The introduction of a boronic acid group *ortho*- to the pendant amine, and all attempts at electrophilic amination of the lithiated ferrocenylamine proved unsuccessful.

## *6.2 Studies Based on* N,N-*Diisopropylferrocene carboxamide (27)*

A procedure, pioneered by Snieckus *et al.*,[44] involving asymmetric deprotonation of *N,N*-diisopropylferrocene carboxamide (**27**) using *n*-butyl lithium and (-)-sparteine (**26**), appeared to be an attractive alternative to our earlier strategy. Quenching the resultant anion with a variety of electrophiles gave planar chiral ferrocene derivatives in excellent yields and enantiomeric excesses (Scheme 16).




| $E^+$ | E | Yield / % | ee / % |
|---|---|---|---|
| TMSCl | TMS | 96 | 98 |
| MeI | Me | 91 | 94 |
| $I_2$ | I | 85 | 96 |
| $B(OMe)_3$ | $B(OH)_3$ | 65 | 85 |

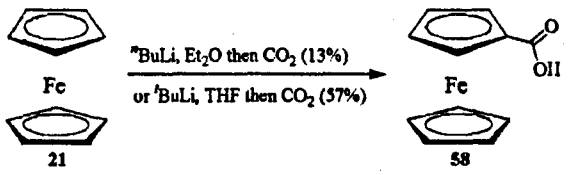
**Scheme 16**

It was expected that our previous problems, encountered using copper or boron reagents, should be avoided when using an amide in place of the amine. Reduction of the amide after *ortho*-functionalisation should yield an amine which could then be substituted in the usual way.

### 6.2.1 Preparation of *N,N*-Diisopropylferrocene Carboxamide (27)

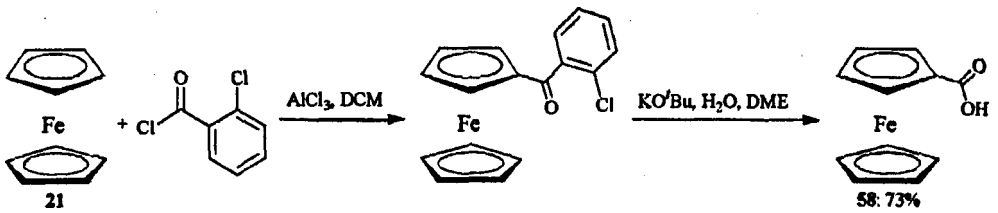
Lithiation of ferrocene (**21**) with *n*-butyl lithium in ether, followed by quenching with dry ice, has been reported for the preparation of ferrocene

carboxylic acid (58).[28] The maximum yield we obtained was 13%, compared to the literature yield of 25%, however, the reaction often gave far lower yields. Kagan *et al.*[27] reported an improved method for the mono-lithiation of ferrocene, using *tert*-butyl lithium in THF, giving yields up to 70%. Use of this method provided higher yields of acid **58** (57% in multi-gram quantities), however the procedure was still cumbersome and unreliable (Equation 24).



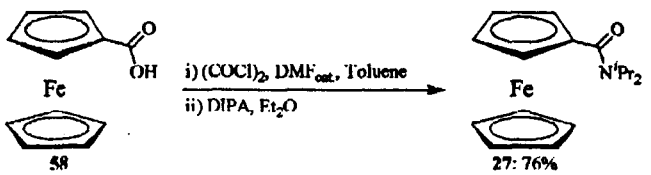

**(24)**

An alternative two step procedure, consisting of a Friedel-Crafts acylation followed by cleavage with potassium *tert*-butoxide and water, gave **58** in an overall yield of 73%.[74] This is our method of choice for the preparation of ferrocene carboxylic acid (**58**) since both steps are high yielding and reliable (Scheme 17).



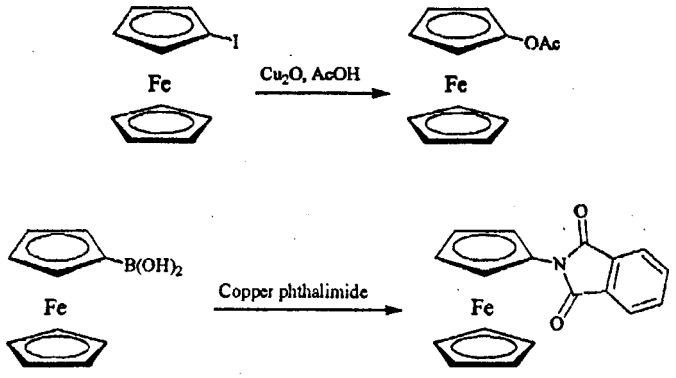

**Scheme 17:** Preparation of ferrocene carboxylic acid

Conversion of ferrocene carboxylic acid (**58**) to its acid chloride, followed by reaction with diisopropylamine furnished *N,N*-diisopropylferrocene carboxamide (**27**) in 76% yield (Equation 25).



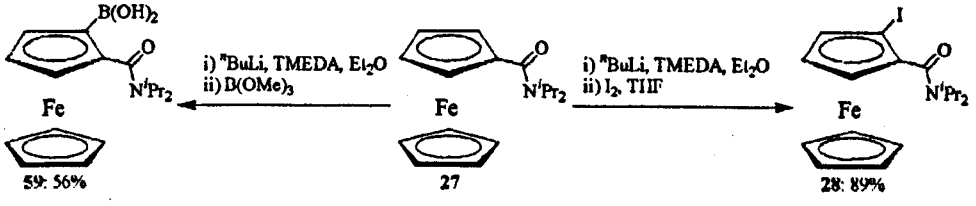

**(25)**

The two most promising routes for the introduction of an *ortho*-heteroatom, based on our work on *N,N*-dimethyl-1-ferrocenylethylamine (**15**), were then studied. Investigation was thus focussed on the introduction of oxygen functionality *via* the copper mediated coupling of a ferrocenyl iodide with acetic acid, and the introduction of nitrogen functionality *via* the coupling of a boronic acid with copper phthalimide (Scheme 18).




**Scheme 18:** Strategies for the introduction of oxygen[73] and nitrogen[69] functionalities

Racemic *N,N*-diisopropyl-2-iodoferrocene carboxamide (**28**) and 2-(*N,N*-diisopropylamido)-ferrocene boronic acid (**59**) were successfully prepared using *n*-butyl lithium in the presence of TMEDA for the deprotonation step, in a modification of Snieckus' method (Scheme 19).[44]

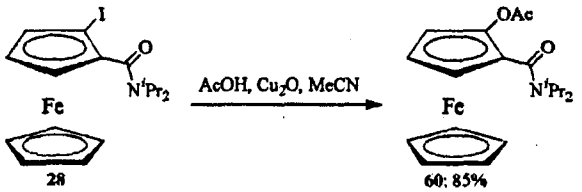



**Scheme 19**

Since the iodide **28** was prepared more cleanly and in higher yield, than the boronic acid, initial efforts were concentrated on the introduction of an *ortho*-oxygen functionality.

### 6.2.2 Introduction of Oxygen Functionality and Elaboration to give first Potential Bases

Coupling of *N,N*-diisopropyl 2-iodoferrocenecarboxamide **28** with acetic acid was performed using the procedure of Akabori *et al.*,[73] to give the novel 2-(*N,N*-diisopropylamido) ferrocenylacetate (**60**) in 85% yield after recrystallisation (Equation 26).

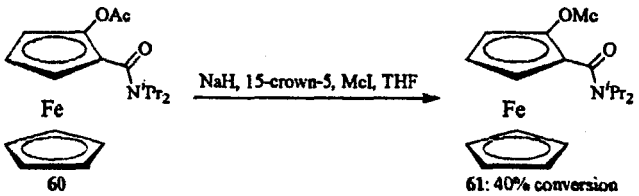



28 60: 85%

**(26)**

Reduction of this compound **60**, directly to the hydroxyamine was attempted, but the product proved to be unstable and decomposed during work-up.

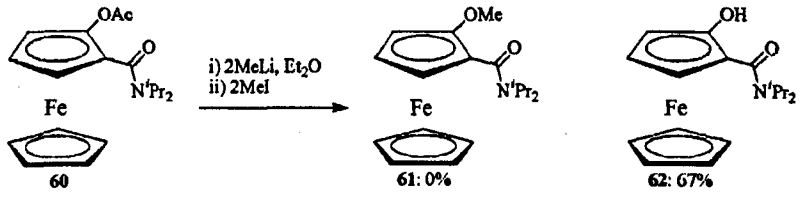
The aerobic instability of hydroxyferrocene and 1,1'-dihydroxyferrocene is well known.[75] To avoid isolation of the hydroxyferrocene derivative **62**, a protocol developed by Akabori *et al.*[73] to deprotect the acetate *in situ* and directly form the methoxyamide **61** was attempted. However, this procedure gave a disappointing 40% conversion to the ferrocenyl ether **61** and was not investigated further (Equation 27).




60 61: 40% conversion

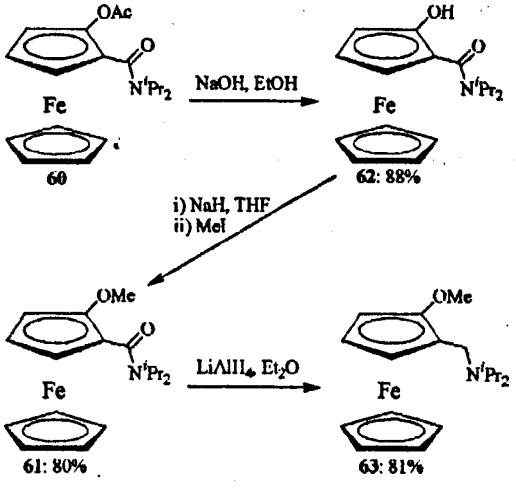
**(27)**

An alternative direct conversion was tried, using 2 equivalents of methyllithium followed by 2 equivalents of iodomethane. Surprisingly, the product isolated from this reaction was *N,N*-diisopropyl 2-hydroxyferrocenecarboxamide (**62**) (67%) (Scheme 20).




**Scheme 20**

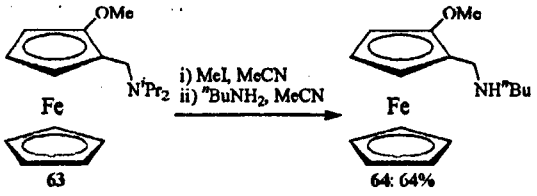
This compound was more stable than anticipated, although noticeable decomposition occurred after 2 days in air at room temperature. The stability may be attributed to favourable hydrogen bonding between the hydroxyl and the amide carbonyl group, since the hydroxyl proton appears at δ 9.68 in the $^1$H NMR spectrum. Indeed, other examples of hydroxyferrocenes are known where a neighbouring group can participate in hydrogen bonding.[76] Saponification of 2-(*N,N*-diisopropylamido)ferrocenylacetate (**60**) gave *N,N*-diisopropyl-2-hydroxyferrocene carboxamide (**62**) in 88% yield (Scheme 21). Some mass was lost due to decomposition of the product during recrystallisation.




**Scheme 21**

Methylation of the hydroxyl group gave the more stable *N,N*-diisopropyl-2-methoxyferrocenecarboxamide (**61**) in 80% yield after recrystallisation. Reduction of the amide functionality gave *N,N*-diisopropyl-(2-

methoxyferrocenyl)-methylamine (**63**) in 81% yield (Scheme 21). To gain our required lithium amide precursor, the final reaction required the substitution of the diisopropylamine with a primary amine.




63 64: 64% **(28)**

This was successfully performed by quaternisation of the amine **63** with methyl iodide followed by introduction of *n*-butylamine to furnish *N*-butyl-(2-methoxyferrocenyl)methylamine (**64**) in 64% yield (Equation 28). This reaction is analogous to many reported by Kumada *et al.*.[14]

Thus our first potential planar chiral lithium amide base was obtained in 15% yield over 8 steps.

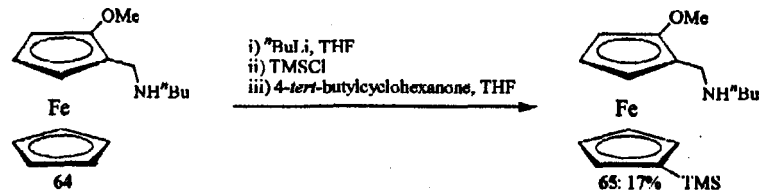
### 6.2.3 Preliminary Base Reactions

The deprotonation of 4-*tert*-butylcyclohexanone (**8**), and subsequent quench with chlorotrimethylsilane was chosen as our preliminary base assay reaction (Equation 29). There is much data available in the literature for this reaction, thus enabling us to compare our results with those of other bases.[4,7,11,77,78,79,80,81]


8 9 **(29)**

Corey's internal quench conditions were used,[1] since previous data suggested that they should give the best results.[4] Our first attempt yielded none of the desired silyl enol ether **9**, and when the base **64** was recovered some material

resulting from silylation on the "lower" cyclopentadienyl ring was identified (Equation 30).




(30)

An explanation for the silylation of the lower ring is the coordination of a second equivalent of butyl lithium, which can then deprotonate the lower Cp ring (Figure 26).

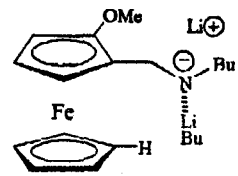
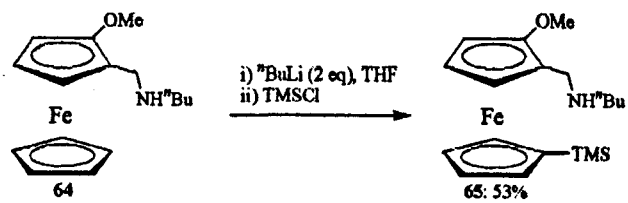



**Figure 26:** Deprotonation of the "lower" Cp ring

To test this hypothesis, the base **64** was reacted with 2 equivalents of *n*-butyl lithium and quenched with chlorotrimethylsilane. This reaction yielded 53% silylated base **65**, 21% recovered starting material **64** and a small quantity of a mixture of other silylated products (Equation 31).




(31)

It is quite unlikely that it is the lithium amide base itself which is deprotonating the lower ring, since the p$K_a$ of ferrocene is 39.[82]

Addition of an equivalent of a coordinating solvent, such as HMPA or TMEDA, should sequester the lithium cation and thus prevent the undesired deprotonation, and this was found to be the case, but, there was still no silyl enol ether **9** formation (Equation 32).


**(32)**

Since deprotonation of the ketone **8** was not occurring, it was considered that the nitrogen atom could attack the carbonyl in a nucleophilic manner, to form the hemiaminal (Figure 27). The use of lithium amides as nucleophiles for the *in situ* protection of carbonyl groups has been reported.[83]

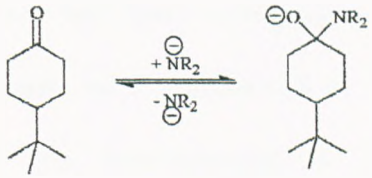
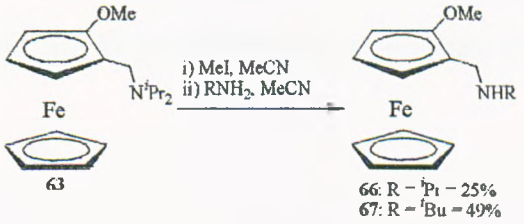



**Figure 27:** Nucleophilic attack at the carbonyl

In an attempt to prevent this, the steric bulk at the lithium amide centre could be increased by the use of a more hindered primary amine in the final displacement reaction.

### 6.2.4 Preparation and Assay of More Hindered Planar Chiral Lithium Amide Bases

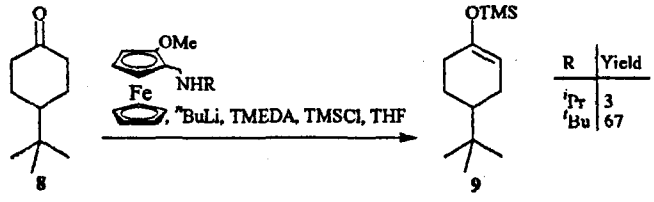
Two new potential bases were prepared, using isopropylamine and *tert*-butylamine in the final substitution reaction (Equation 33).




**(33)**

The bases thus prepared; *N*-isopropyl-(2-methoxyferrocenyl)methylamine (**66**) and *N-tert*-butyl-(2-methoxy-ferrocenyl)methylamine (**67**) were then assayed

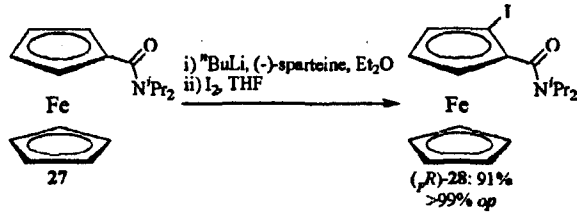
under the standard conditions with addition of 1 equivalent of TMEDA (Equation 34).




(34)

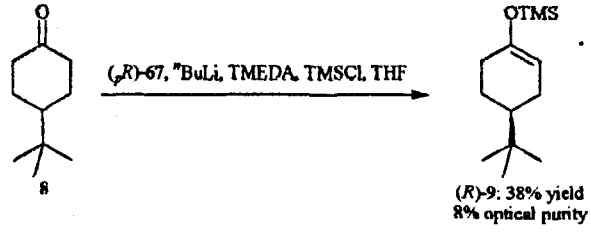
The isopropyl base **66** yielded only 3% of silyl enol ether **9**, however, increasing the bulk further, to *tert*-butyl, gave a much improved 67% yield.

Now that a successful base had been identified, homochiral material was needed. The required bases were synthesised by using (-)-sparteine (**26**) instead of TMEDA in the deprotonation of *N,N*-diisopropylferrocene carboxamide (**27**), following Snieckus' procedure.[44] After recrystallisation from hexane, optical purity was >99% (Equation 35).




(35)

All following synthetic steps proceeded in comparable yields to their racemic counterparts. It is presumed that no erosion of enantiomeric excess occurs, since racemisation would require dissociation of the substituted Cp ligand from the metal centre and the Cp-Fe bond is known to be particularly strong, 381 ± 13 kJ mol$^{-1}$.[23]




(36)

The assay reaction was repeated using ($_p$*R*)-*N*-*tert*-butyl-(2-methoxyferrocenyl)methylamine (**67**), and yielded 38% of silyl enol ether (*R*)-**9** with an optical rotation of $[\alpha]_D^{23} = +6.35$ (c = 1.150, $CHCl_3$). This corresponds to an optical purity of 8% (based on Simpkins' results[77]) (Equation 36). The chemical yield was not as good as that recorded in the racemic case, and the optical purity was disappointing.

When the recovered ferrocenyl bases were purified by column chromatography, a small portion of each base was discovered to have undergone silylation of the "lower" ring (**68**: R = $^i$Pr: yield = 18%; (±)-**69**: R = $^t$Bu: yield = 10%; ($_p$*R*)-69: R = $^t$Bu: yield = 14%) (Figure 28). It was therefore decided to use HMPA as the coordinating solvent as its effect on the lithium cation was expected to be stronger.

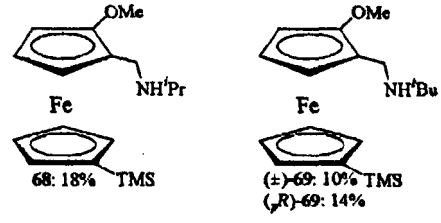


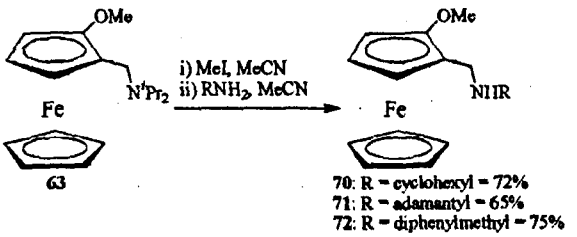

**Figure 28**

Work commenced on preparation of a variety of bases with different donor groups and different groups at the lithium amide centre.

### 6.2.5 Preparation of a Series of Potential Bases

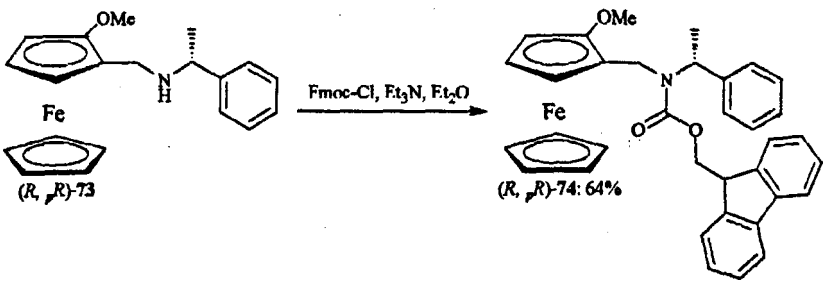
#### 6.2.5.1 Variation at the Lithium Amide Centre

In an attempt to further understand the steric requirements at the lithium amide centre, a range of analogues were prepared, each using a different base in the substitution step.




(37)

Cyclohexylamine, adamantanamine and aminodiphenylmethane were employed in the substitution steps to give good yields of the corresponding ferrocenyl bases (Equation 37). Bases were also prepared from (*R*)- and (*S*)-α-methylbenzylamine, however, in these cases great difficulty was encountered in their purification. Both diastereoisomers of product **73** co-ran with the starting material **63** in all the solvent systems that were investigated. Enough clean (*S*, $_p$*R*)-*N*-α-methylbenzyl-(2-methoxyferrocenyl)methylamine ((*S*, $_p$*R*)-**73**) was obtained to run an assay, however some material remained inseparable from the starting material **63**. However, the base derived from (*R*)-α-methylbenzylamine (*R*, $_p$*R*)-**73** proved entirely inseparable from the starting material **63**. Therefore, the mixture of starting material **63** and product (*R*, $_p$*R*)-**73** was treated with 9-fluorenylmethyl-chloroformate (Fmoc-Cl) and triethylamine in ether, to give the Fmoc derivative **74** in moderate yield (Equation 38).[84]



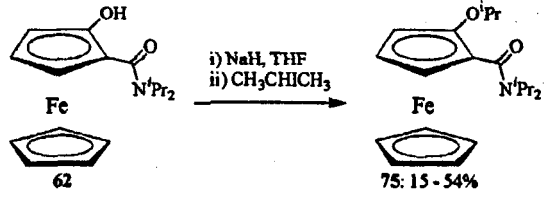

(38)

The Fmoc derivative **74** was easily separable from the tertiary amine impurity. The $^1$H NMR, of the product, in $CDCl_3$ at room temperature was exceedingly broad, this was assumed to be due to rotameric forms present at this

temperature. Therefore, a spectrum was recorded in $d_6$-DMSO at 90 °C, at which point the it became possible to assign the signals. The Fmoc group was cleaved by simple treatment of a DMF solution with piperidine to yield (*R*, $_p$*R*)-*N*-α-methylbenzyl-(2-methoxyferrocenyl)methylamine (*R*, $_p$*R*)-**73** (85%).

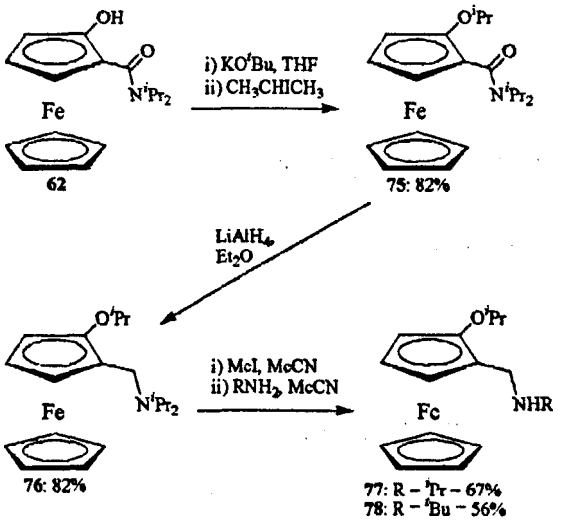
### 6.2.5.2 Variation of the Donor Group

To investigate the steric effect of the donor group, bases were prepared with an isopropoxy group, which was introduced in an analogous manner to the methoxy group. Treatment of ($_p$*R*)-*N*,*N*-diisopropyl-2-hydroxyferrocene carboxamide (**62**) with sodium hydride in THF, followed by addition of 2-iodopropane gave the desired product **75** in a variable yield of 15 to 54% (Equation 39).




**(39)**

The base was changed from sodium hydride to potassium *tert*-butoxide, in the hope that the potassium counter-ion might increase the reactivity of the oxygen anion. The change did indeed have the desired effect, and treatment of the hydroxide **62** with potassium *tert*-butoxide in THF followed by 2-iodopropane gave ($_p$*R*)-*N*,*N*-diisopropyl-2-isopropoxyferrocene carboxamide (**75**) in 82% yield.




**Scheme 22**

Reduction of the resulting amide **75** proceeded in good yield (82%), and subsequent quaternisation and substitution of the pendant amine **76** to introduce isopropyl and *tert*-butyl groups was successful (Scheme 22).

### 6.2.6 Introduction of Nitrogen Functionality

The introduction of an *ortho*-amine donor group had been a long-term aim of the project, due to the fact that the majority of successful lithium amide bases possessing a donor group, have an amine donor group. The introduction of an *ortho*-amine would also allow us to compare the effect of swapping the positions of the lithium amide and donor groups (Figure 29).

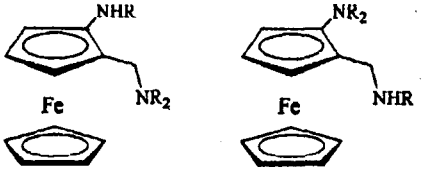


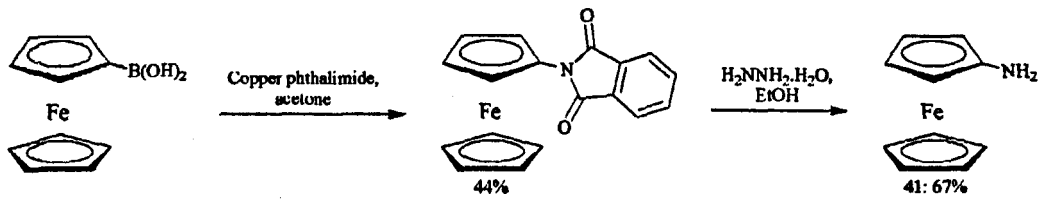

**Figure 29**

Three strategies for the introduction of *ortho*-nitrogen functionality were investigated: the coupling of a boronic acid with copper phthalimide; a more general strategy, using Buchwald-Hartwig technology[85] to aminate a

haloferrocene; and a copper mediated coupling of phthalimide and a haloferrocene.

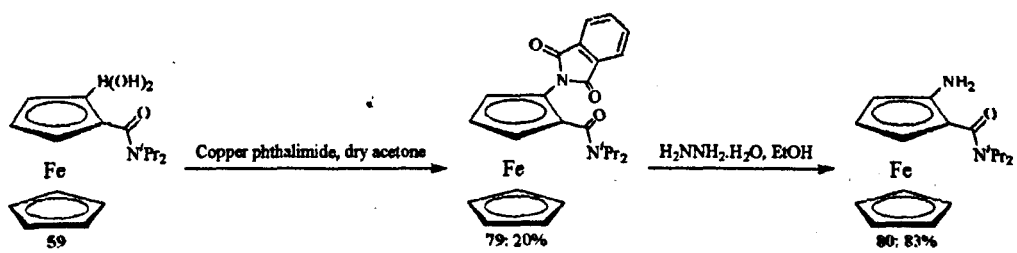
### 6.2.6.1 Boronic Acid Coupling Strategy

Since aminoferrocene (41) has been prepared *via* boronic acid coupling with copper phthalimide, we investigated this route first (Scheme 23).[59]




**Scheme 23**

Treatment of 2-(*N,N*-diisopropylamido)-ferrocene boronic acid (59) with copper phthalimide in refluxing acetone yielded a disappointing 20% of the desired product, 2-(*N,N*-diisopropylamido)ferrocenylphthalimide (79). The phthalimide 79 was successfully unmasked to give the amine (80) in 83% yield, by refluxing with hydrazine hydrate in ethanol (Scheme 24).



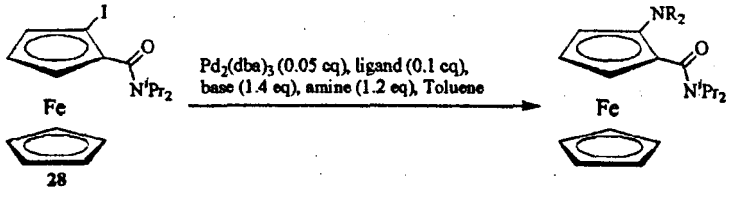

**Scheme 24**

Despite the low overall yield of this amine 80 (5% from ferrocene), it was decided to scale the synthesis up in order to prepare enough amine 80 to attempt alkylation reactions. Frustratingly, increasing the scale markedly decreased the yields for the preparation of the boronic acid 59 and the phthalimide 79 (31% and 2% respectively). This rendered the route unworkable, so alternative strategies were considered. Since an iodoferrocenyl

amide **28** had been prepared in good yield, it was decided to investigate the use of palladium catalysed amination reactions as a method for the introduction of an amine group.

### 6.2.6.2 Buchwald-Hartwig Aryl-Amination Reactions

Investigations into the use of Buchwald-Hartwig technology[85] for the amination of haloferrocenes commenced. Preliminary work in this area focussed on assaying a range of ligands, bases, and amines. There are many different combinations used in the literature, so some representative examples were tried (Equation 40, Table 3).




(40)

**Table 3:** Results of palladium catalysed coupling reactions

| Entry | Amine | Base | Ligand | Conditions | Result |
|---|---|---|---|---|---|
| 1 | $Et_2NH$ | $Cs_2CO_3$ | BINAP | Reflux, 48 h | Loss of S.M. |
| 2 | $Et_2NH$ | $Cs_2CO_3$ | $PBu_3$ | Reflux, 18 h | No reaction |
| 3 | $^iPr_2NH$ | $Cs_2CO_3$ | BINAP | r.t. 18 h | No reaction |
| 4 | $^iPr_2NH$ | $NaO^tBu$ | BINAP | r.t. 18 h | No reaction |
| 5 | $^iPr_2NH$ | $NaO^tBu$ | DPPF | r.t. 18 h | No reaction |
| 6 | BnMeNH | $NaO^tBu$ | BINAP | Reflux, 18 h | Loss of S.M. |

No reaction occurred at room temperature (Entries 3 – 5), and when the mixture was warmed to reflux, still no product was observed, although starting material was consumed (Entries 1 and 6). When starting material was consumed, the only identifiable product was the reduced starting material, *N,N*-diisopropylferrocene carboxamide (**27**), which leads to the hypothesis that β-hydride elimination is occurring, thus preventing product formation.

Therefore, amines that are unable to undergo this side reaction could be investigated, such as aniline or *tert*-butylamine.

Another possible explanation for the lack of success, is the electron-rich nature of our aryl halide **28**, since problems have been reported with electron rich aryl halides, with significant quantities of reduced arene side product observed.[85d]

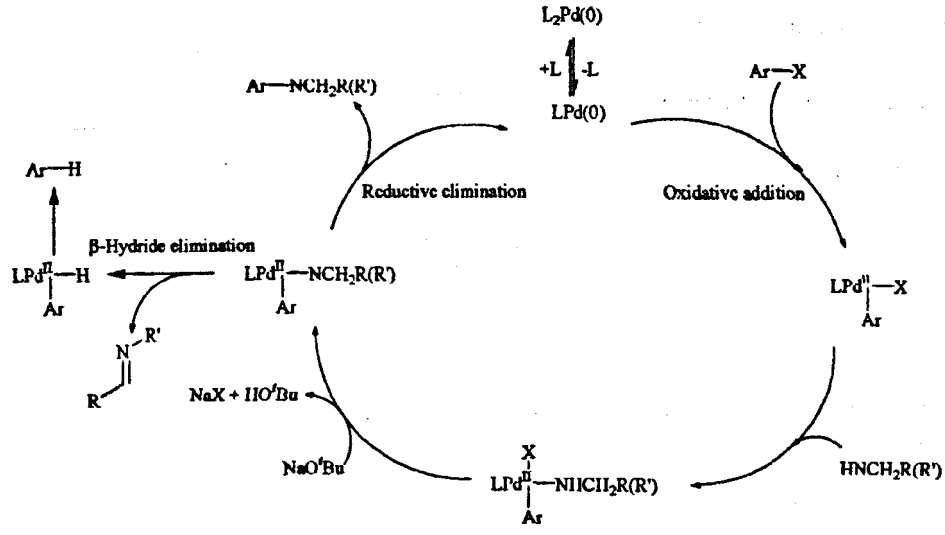



**Figure 30:** Catalytic cycle for the palladium catalysed amination of aryl halides[86]

Indeed, it has been reported that the palladium catalysed coupling of bromoferrocene and *para*-tolylamine was unsuccessful due to the electron rich nature of the ferrocene system.[87] Production of reduced arene product is thought to be caused by the over stabilisation of the aryl-aminopalladium(II) complex (Figure 30), thus making β-hydride elimination more favourable than reductive elimination. In an attempt to combat this problem, a less electron donating and chelating ligand than BINAP (**10**), for example, PPF-OMe or PPFA could be used (Figure 31).

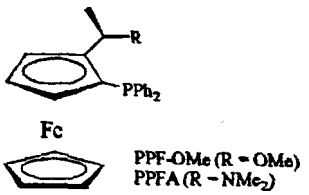


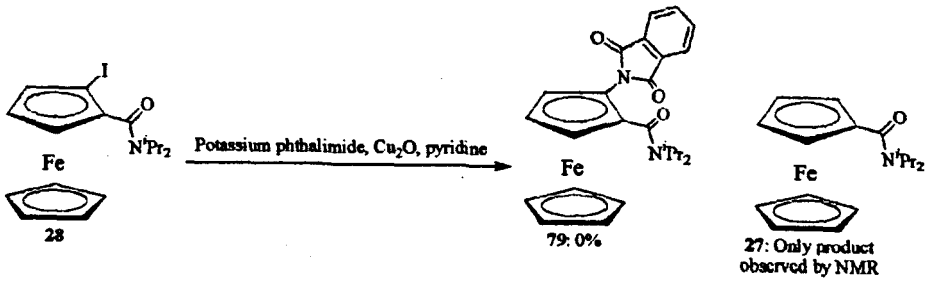

**Figure 31:** Alternative chelating ligands

The use of such a ligand should reduce the electron density at the palladium centre and thus make reductive elimination more favourable. These ligands work well for secondary acyclic amines, but have proved less successful with other classes of amine. They are especially unsuccessful with primary amines, since the weak binding group (OMe or $NMe_2$) can be displaced by the sterically unencumbered primary nitrogen atom, resulting in the formation of a catalytically inactive bis-amine complex.[85d]

Since other areas of investigation were proving more successful, work on palladium catalysed ferrocenyl aminations ceased.

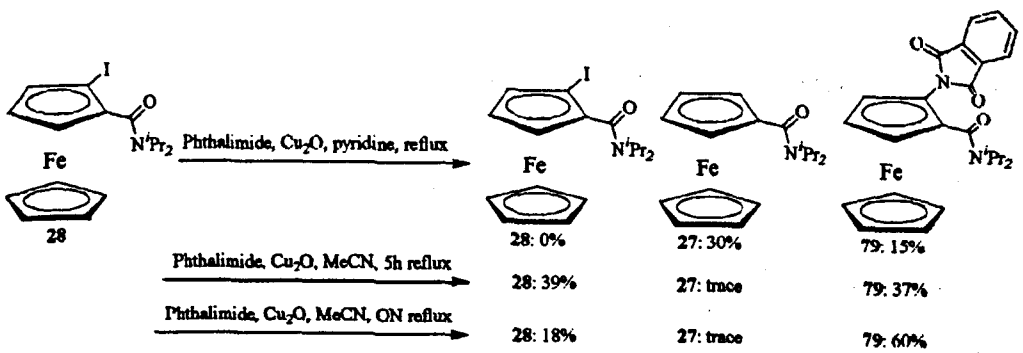
### 6.2.6.3 Alternative Phthalimide Coupling Strategies

Organic halides can be transformed to primary amines by reaction with potassium phthalimide, followed by hydrolysis.[88] This reaction takes place slowly with aryl halides, but can be accelerated by the addition of copper(I) salts.[89,90] This seemed to be a particularly attractive route for our purposes, since it would allow the use of *N,N*-diisopropyl-2-iodoferrocene carboxamide (**28**) (prepared in 89% yield) instead of 2-(*N,N*-diisopropylamido)ferrocene boronic acid (**59**) (prepared in 56% yield) and would negate the need to prepare copper phthalimide. However, when the reaction was attempted it yielded only the reduced starting material **27** (Scheme 25). This is a known side reaction for copper catalysed reactions of aryl halides with nucleophiles.[91]




**Scheme 25**

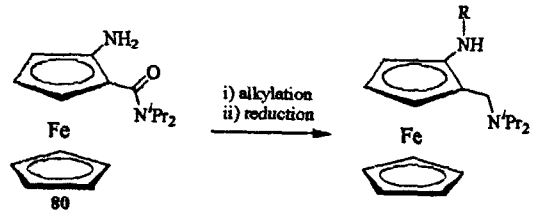
Ebine *et al.*[92] have reported the preparation of phthalimidoferrocenes in good yields *via* a copper(I) oxide mediated coupling of phthalimide and haloferrocenes. Indeed, when the reaction was attempted using the literature conditions, 15% yield of the desired phthalimidoferrocene **79** was obtained, as well as 30% yield of reduced starting material **27** (Scheme 26).




**Scheme 26**

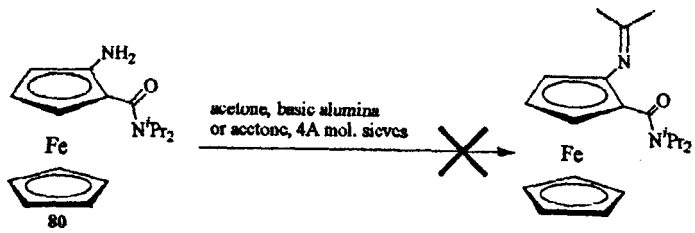
Since the reaction conditions were so similar to those of the acetate coupling reaction (Equation 26), it was decided to try changing the solvent from pyridine to acetonitrile. The change in solvent diminished the yield of reduced product **27** and increased the yield of the desired phthalimide **79**. Increasing the reaction time to overnight achieved a 60% yield of the desired product **79** (Scheme 26). This represents a significant improvement on the original route to phthalimidoferrocene **79** (53% from amide **27** *via* iodoferrocene **28** cf. 11% *via* boronic acid **59**).

As before, the primary amine group was unmasked using hydrazine hydrate in ethanol, to give ($_p$*R*)-2-(*N,N*-diisopropylamido)ferrocenylamine (**80**) in 83% yield (Scheme 24). Introduction of an alkyl group at the primary amine **80** was desirable, in order to make this the lithium amide centre (Equation 41). Therefore, a number of reactions were attempted to introduce an isopropyl or *tert*-butyl group.




(41)

The first alkylation strategy assayed was reductive amination. The reaction of 2-(*N,N*-diisopropylamido)ferrocenylamine (**80**) with acetone and sodium cyanoborohydride in methanol yielded only starting material **80** (42%) and a decomposition product. It was, therefore, decided to try to isolate the imine intermediate before reduction. Reactions in acetone with either basic alumina or crushed 4 Å molecular sieves failed with quantitative starting material **80** recovered (Equation 42).

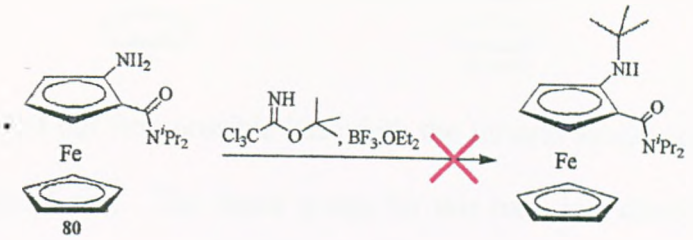



(42)

The low reactivity of the amine function can be explained by delocalisation with the cyclopentadienyl ring.

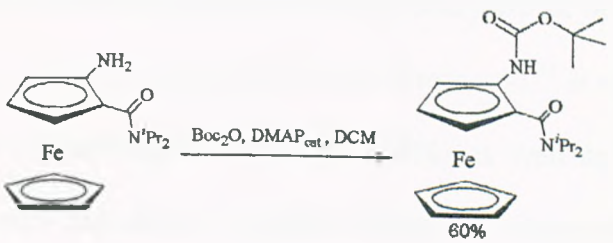
Previous work within our group has shown that treatment of anilines with trichloroacetimidate-*tert*-butoxide gives the *tert*-butyl aniline derivative in good yield.[93] Unfortunately, when this reaction was performed on our

ferrocenylamine **80** it caused total decomposition of the starting material (Equation 43).



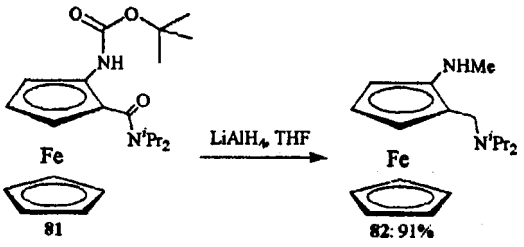

**(43)**

Since the $pK_a$ of the N-H of a Boc protected amine is similar to that of an O-H, an alternative alkylation strategy is to protect the amine **80** as its Boc derivative, then to deprotonate and quench with a suitable alkyl halide.




**(44)**

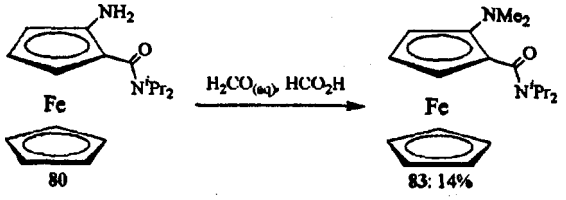
Protection of the primary amine **80** was carried out successfully using di-*tert*-butyl dicarbonate in DCM with a catalytic quantity of DMAP, to give ($_pR$)-*N*-Boc-2-(*N'*,*N'*-diisopropylamido)ferrocenylamine (**81**) in 60% yield (Equation 44). Treatment of the Boc-protected amine (**81**) with potassium tert-butoxide followed by 2-iodopropane led to an inseparable mixture of starting material **81** and possible product. Further attempts to alkylate the Boc derivative **81** were not carried out. Instead, the carbamate **81** was reduced using lithium aluminium hydride in THF to give ($_pR$)-2-(*N'*-methylamino)-(*N*,*N*-diisopropyl)-ferrocenylmethylamine (**82**) in 91% yield (Equation 45).




81 82: 91% (45)

This represented our first possible base with the lithium amide centre situated on the ferrocenyl ring. The donor group for this base is a diisopropylamine, and may be substituted by an amine or alkoxy group using standard methods.[14]

As well as preparing a base with the lithium amide centre on the Cp ring, it was desirable to use the *ortho*-amine functionality as a donor group. Investigations were carried out into the dimethylation of the primary amine **80**. Treatment of the amine **80** with aqueous formaldehyde and formic acid,[94] at reflux, yielded a small quantity of dimethylated product **83** (14%) as well as a dark brown product that proved impossible to separate from the silica used for column chromatography (Equation 46).

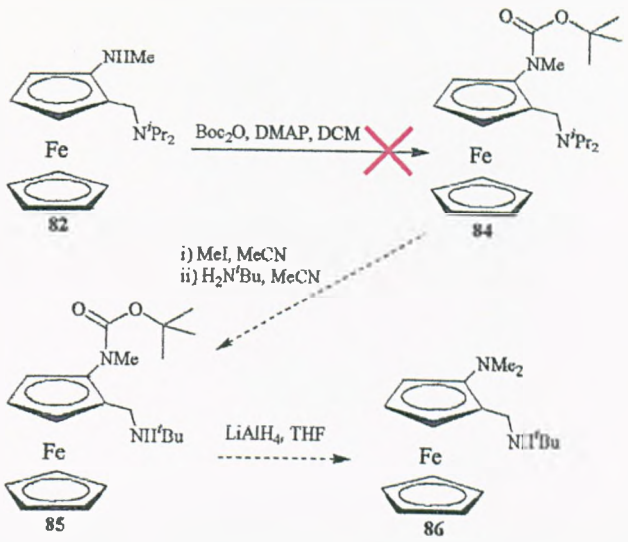



80 83: 14% (46)

In an attempt to reduce decomposition, the reaction was repeated at room temperature, but only decomposition products were formed and no starting material or desired product was isolated.

An alternative route to a dimethylated donor group was investigated. Since one methyl group had been introduced *via* the reduction of a Boc group, it was considered that the methylamine **82** could be further Boc protected. This compound **84** could then undergo a quaternisation and substitution procedure

to introduce the lithium amide centre **85** and finally be reduced to yield the desired base **86** (Scheme 27).




**Scheme 27**

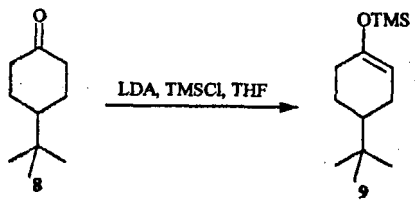
The Boc protection of ($_p$*R*)-2-(*N'*-methylamino)-(*N,N*-diisopropyl)ferrocenyl-methylamine (**82**) was attempted using standard procedures, but, no identifiable product was isolated from this reaction. A small quantity of starting material **82** was isolated (35%) but the other product was unidentifiable after column chromatography and recrystallisation.

Despite our success in introducing an *ortho*-amine group, we have been unsuccessful in introducing any groups other than methyl to provide a donor group. The dimethylation of the amine proceeded in very low yield (14%) and thus didn't provide a workable route. Methylation of the amine has been achieved by reduction of a Boc protecting group, thus providing a possible lithium amide base.

### 6.2.7 Base Assay Reactions

Assay reactions were performed on the bases reported above. It was discovered that the use of HMPA as a co-solvent was preventing the

deprotonation step from proceeding. Despite two successive distillations from sodium, and storage over activated molecular sieves, addition of HMPA appeared to prevent deprotonation from occurring. This would seem to imply that the HMPA was still wet, however, the same batch was used successfully by members of our research group carrying out aza-[2,3]-Wittig rearrangements, thus implying that this was not the problem.

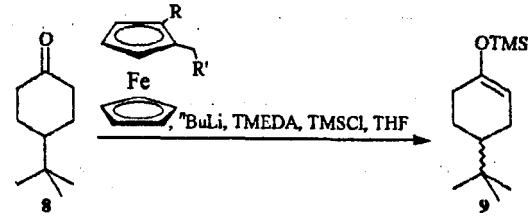



(47)

Control reactions were performed using LDA to study the effect of reaction additives and procedures (Equation 47). The results of these investigations are summarised below:

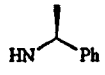
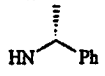
- THF must be freshly distilled.
- TMSCl must be distilled from $CaH_2$ onto polyvinylpyridine immediately prior to use.
- Ketone **8** must be recrystallised from hexane and stored under nitrogen in a desiccator.
- Addition of HMPA prevents formation of product.
- Addition of lithium chloride significantly reduces yield of product.
- Addition of TMEDA, distilled from $CaH_2$ onto activated 4 Å molecular sieves, does not affect the product yield.
- Quench with triethylamine, followed by a sat. solution of sodium bicarbonate, must be carried out at –78 °C.

Using these observations, an optimum procedure was devised and the bases were assayed (Equation 48; Table 4).




(48)

**Table 4:** Results of base assay reactions

| Entry | R | R' | Compound number | Chemical yield / % | Optical rotation* | Optical purity / %† |
|---|---|---|---|---|---|---|
| 1 | OMe | NH$^n$Bu | **64** | 0 | - | - |
| 2 | OMe | NH$^i$Pr | **66** | 3 | - | - |
| 3 | OMe | NH$^i$Pr | **66** | 51 | $[\alpha]_D^{27} = +1.81$ (c = 0.992) | 2 |
| 4 | OMe | NH$^t$Bu | **67** | 67 | - | - |
| 5 | OMe | NH$^t$Bu | **67** | 38 | $[\alpha]_D^{23} = +6.35$ (c = 1.150) | 8 |
| 6‡ | OMe | NH$^t$Bu | **67** | 15 | $[\alpha]_D^{25} = +9.85$ (c = 0.670) | 13 |
| 7 | OMe | NH$^t$Bu | **67** | 58 | $[\alpha]_D^{28} = +5.85$ (c = 0.975) | 7 |
| 8 | OMe | NH$^t$Bu | **67** | 49 | $[\alpha]_D^{28} = +4.32$ (c = 1.065) | 5 |
| 9 | OMe | NH$^t$Bu | **67** | 82 | $[\alpha]_D^{27} = +6.36$ (c = 1.195) | 8 |
| 10 | OMe |  | (*S*, $_p$*R*)-**73** | 40 | $[\alpha]_D^{26} = +22.3$ (c = 0.970) | 28 |
| 11 | OMe |  | (*R*, $_p$*R*)-**73** | 72 | $[\alpha]_D^{25} = -8.78$ (c = 0.980) | -11 |
| 12 | O$^i$Pr | NH$^i$Pr | **77** | 46 | - | - |
| 13 | O$^i$Pr | NH$^i$Pr | **77** | 0 | - | - |
| 14 | O$^i$Pr | NH$^t$Bu | **78** | 22 | - | - |
| 15 | O$^i$Pr | NH$^t$Bu | **78** | 67 | $[\alpha]_D^{27} = +4.87$ (c = 1.150) | 6 |
| 16 | NHMe | N$^i$Pr$_2$ | **82** | 0 | - | - |

* Where no optical rotation is recorded, racemic base was used.

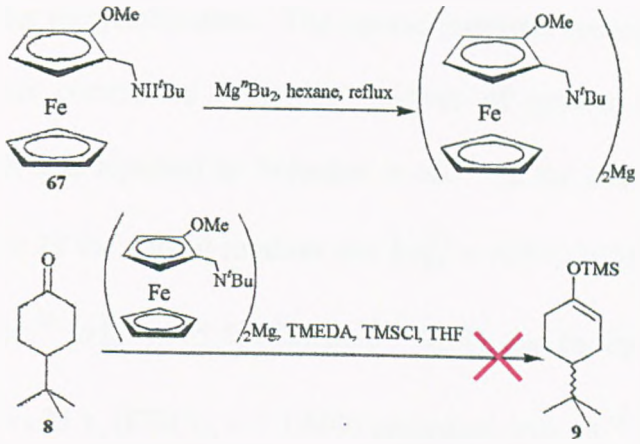
† Optical purities are by comparison with results reported by Simpkins et al.[77]

‡ Two equivalents of undistilled HMPA were used instead of TMEDA

No product was ever isolated from reactions using either **64** or **82** (Entries 1 and 16). The *n*-butyl base **64** is thought to be unreactive towards deprotonation for reasons given in section 6.2.3 (Entry 1). For base **82**, the negative charge on nitrogen may be involved in delocalisation with the Cp ring, thus reducing its basicity (Entry 16). It is difficult to draw conclusions about the steric requirements of these bases due to the lack of consistency of results. Where reactions have been repeated using identical conditions there is still a wide variation in results (Entries 4 – 5 and 7 – 9). The inconsistency in the chemical yield of these reactions is despite the stringent care taken over these reactions, and no obvious explanation seems likely. Both bases containing the α-methylbenzylamine motif **73** give reasonable yields (Entries 10 and 11), and give optical purities that are good in comparison with those for bases only having a plane of chirality. In the case of (*S*, $_p$*R*)-*N*-α-methylbenzyl-(2-methoxyferrocenyl)-methylamine (*S*, $_p$*R*)-**73**, the plane and centre of chirality appear to be matched and thus the highest optical purity obtained is recorded (28%) (Entry 10). The opposite enantiomer is obtained with (*R*, $_p$*R*)-*N*-α-methylbenzyl-(2-methoxyferrocenyl)methyl-amine (*R*, $_p$*R*)-**73**, but the optical purity is much lower (11%) suggesting that the plane and centre of chirality are mismatched (Entry 11). There appears to be no benefit in increasing the steric bulk of the donor group (OMe to O$^i$Pr), (compare entries 4 – 9 with entries 14 and 15). The most successful base only having a plane of chirality is **67**, which gives yields from 32 to 82% and optical purities from 5 to 8% (Entries 4 – 9). Entry 6 is interesting since the use of undistilled HMPA seems to give a higher optical purity (13%), but an understandably lower yield (15%). This is the

only time that product has been isolated from a reaction using HMPA, and proved irreproducible.

Work by Kerr *et al.*[11] reports that the use of magnesium as a counter-ion, rather than lithium, gives high enantioselectivities even with a very simple base. Our most successful planar chiral base **67** was tested using these conditions. The reaction was performed using the procedure of Kerr *et al.*, with the exception that one equivalent of TMEDA was used in place of HMPA, due to our earlier problems with HMPA.




**Scheme 28**

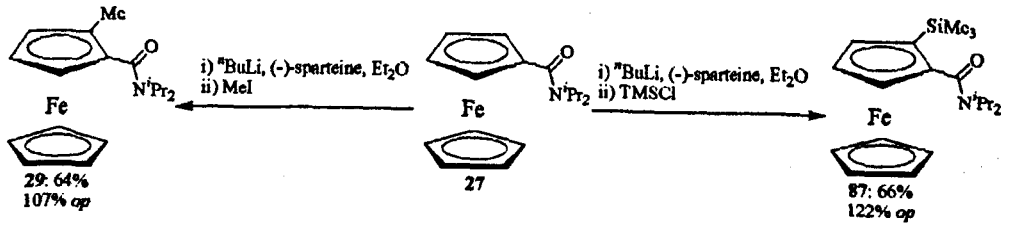
Sadly, no product was observed, and time constraints meant that the procedure was not repeated (Scheme 28).

At this point it was decided to investigate whether the presence of a donor group was desirable, or whether a simple non-donating *ortho*-group would give similar results.

### 6.2.8 Non-chelating Bases

In Snieckus' paper on planar chiral ferrocenes, he reports the introduction of a methyl group and a TMS group in the *ortho*-position.[44] Both of these would

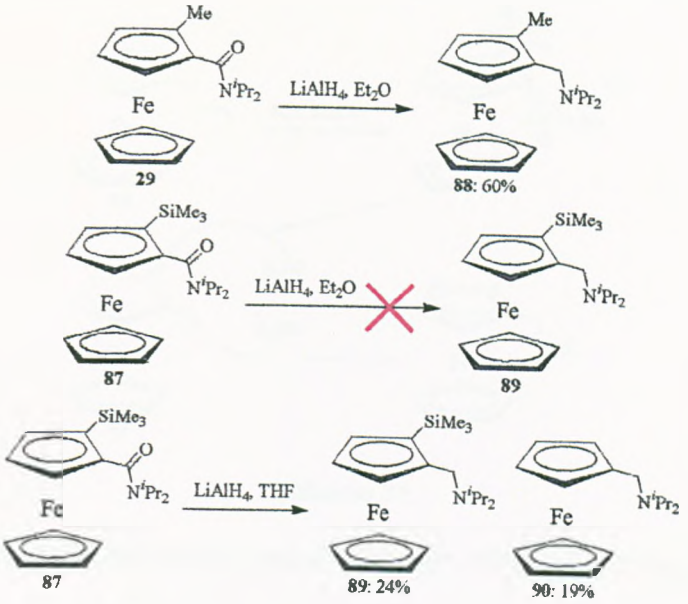
provide our bases with a plane of chirality and be suitable non-donating groups.




**Scheme 29**

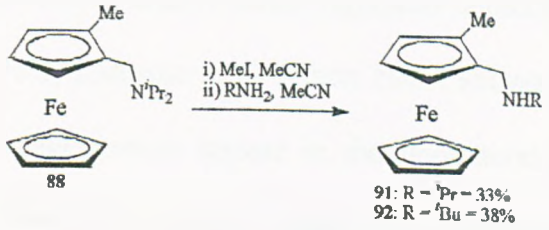
The *ortho*-methyl **29** and *ortho*-trimethylsilyl ferrocenyl amides **87** were prepared, according to the literature procedure, in 64 and 66% yields respectively, after recrystallisation. The optical rotations recorded for both of these compounds correspond to optical purities of greater than 100% in comparison with data reported by Snieckus *et al.*.[44] In the case of the methyl substituted amide **29** the optical rotation was $[\alpha]_D^{27} = +29.0$, ($CHCl_3$, c = 1.110) compared with lit.[44] $[\alpha]_D^{25} = +25.5$, ($CHCl_3$, c = 0.97), and for the trimethylsilyl amide **87** $[\alpha]_D^{27} = +25.1$, ($CHCl_3$, c = 1.000) compared with lit.[44] $[\alpha]_D^{25} = +20.2$, ($CHCl_3$, c = 0.97). The reason for this is not clear, although Snieckus reports column chromatography as the only purification in the experimental procedure, whereas our compounds are then recrystallised from hexane.

Both amides were treated with lithium aluminium hydride in ether. The methyl amide **29** was reduced in moderate yield to give the desired amine **88** (60%), however, the TMS substituted ferrocene **87** proved to be unreactive to these conditions (Scheme 30). Indeed, it was necessary to perform the reduction in THF, at reflux, to obtain the desired amine **89** (24%), with a significant quantity of desilylated amine **90** also recovered (19%). Despite these harsh conditions, starting material was still recovered **87** (32%).



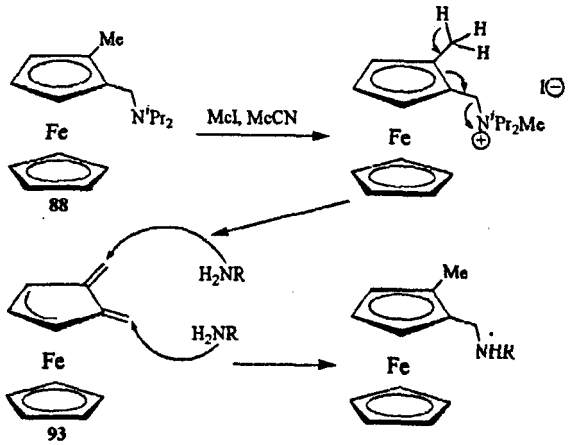

**Scheme 30**

Both of these diisopropyl amines now required substituting with a suitable amine to provide the lithium amide centre. Methyl amine **88** was treated with methyl iodide followed by either isopropylamine or *tert*-butylamine to yield the required amines **91** and **92** in 33 and 38% respectively (Equation 49). Steric hindrance by the methyl group may be causing these lower yields for the quaternisation and substitution reaction.



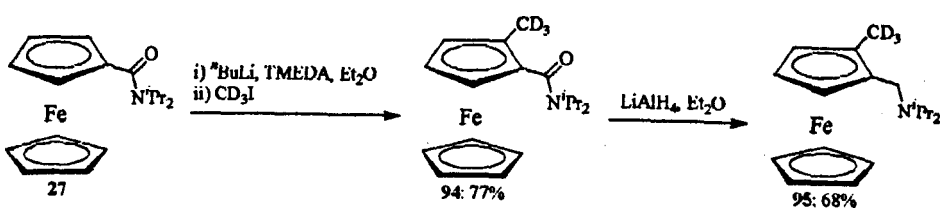

**(49)**

When the optical rotation of *tert*-butyl amine **92** was measured ($[\alpha]_D^{26} = -6.25$ (c = 1.072)), it concerned us to discover that it was two orders of magnitude smaller than that of the corresponding methoxy base. Although dissociation of the Cp ring can be ruled out as a mechanism for racemisation, we were still concerned that an alternative mechanism might be possible (Scheme 31).



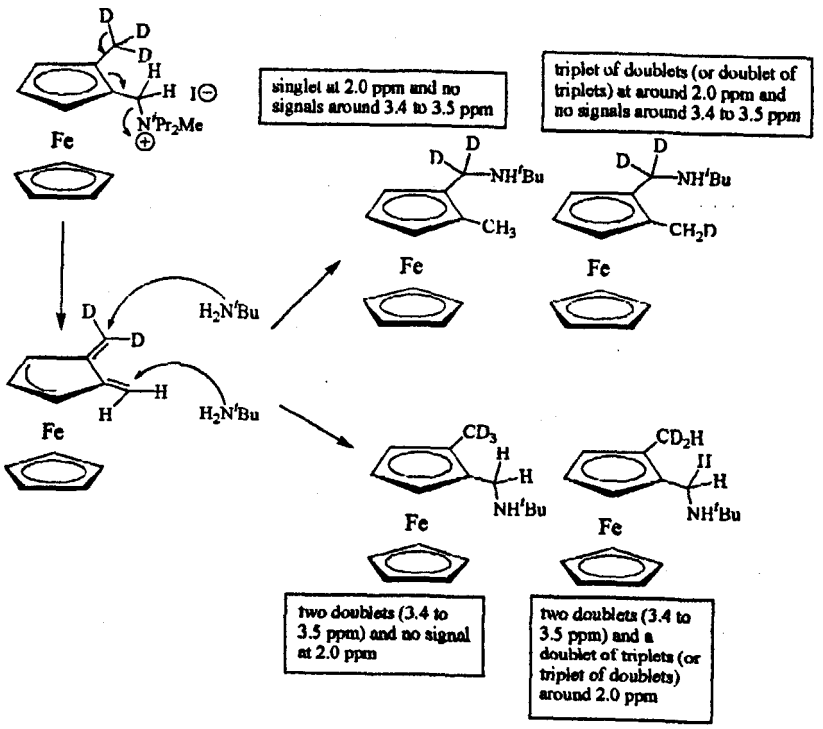

**Scheme 31**

It might be imagined that in the case of a methyl substituted compound, loss of a proton, from the methyl group, concomitant with loss of the quaternary amine would yield a symmetrical intermediate **93**. This intermediate **93** could then be attacked by the primary amine from either side, thus causing racemisation. The low yields of methyl substituted bases might also be explained by this unusual mechanism. To discover whether such a mechanism might be causing racemisation, a deuterated analogue was prepared. Treatment of *N,N*-diisopropylferrocene carboxamide (**27**) with $^n$BuLi in the presence of TMEDA followed by quench with $d_3$-methyl iodide furnished deuterated methyl amide **94** in good yield (77%) (Scheme 32). Proton NMR showed no peak at 2.05 ppm, where the methyl protons appear in the undeuterated compound **29**. Carbon-13 NMR showed the expected septet that is characteristic of a $CD_3$ fragment.



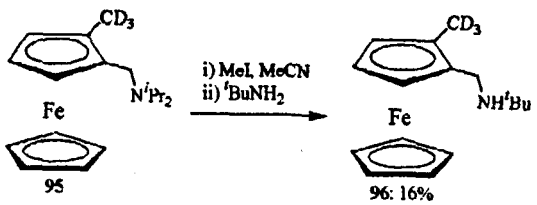

**Scheme 32**

Reduction of the amide **94** to form the corresponding amine **95** occurred smoothly in 68% yield and again, NMR studies confirmed the position of the deuterium atoms (Scheme 32). Finally, the pendant amine **95** was quaternised with methyl iodide and substituted with *tert*-butylamine. If the suspected racemisation had occurred it would be expected that the proton NMR would show signals for protons in both pseudo benzylic positions (Scheme 33).




**Scheme 33**

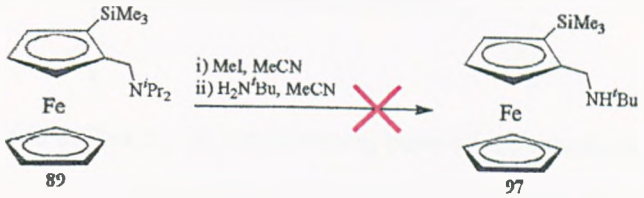
In actual fact, the $^1$H NMR spectrum was very simple, and consisted of the expected doublets for the C*H*$_2$NH$^t$Bu group (δ 3.46 and 3.53) and no signal in the region where the methyl group would be expected. The *tert*-butyl base **96** was obtained cleanly in 16% yield (Equation 50).




**(50)**

This result suggests that racemisation is not occurring by this mechanism, and therefore probably not occurring at all.

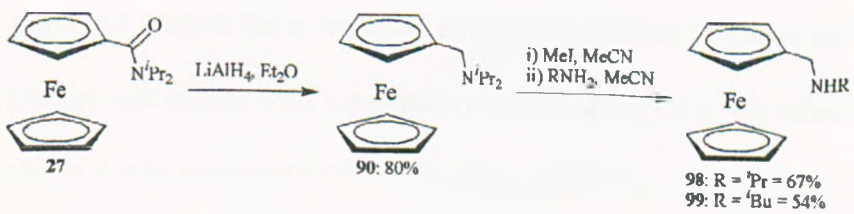
The last task was to quaternise and substitute the trimethylsilyl base **89**. This was attempted twice using the standard procedure, but each time no product **97** was isolated, and the starting material **89** was recovered quantitatively (Equation 51). Heating the reaction mixture to reflux at both steps of the reaction also failed to provide any product **97**.




**(51)**

The trimethylsilyl substituent is the most sterically demanding group that has been used in the *ortho*-position, and the conformation required for reaction to occur may be of such high energy that it becomes impossible.

Finally, two bases were prepared with no *ortho*-group and therefore no plane of chirality, to verify that steric bulk at the *ortho*-position was not adversely affecting the chemical yields of the base assay reactions. Reduction of *N,N*-diisopropylferrocene carboxamide **27** with lithium aluminium hydride in ether gave the desired amine **90** in good yield (80%). Quaternisation with methyl iodide followed by substitution with isopropylamine or *tert*-butylamine gave the required bases **98** and **99** in 67 and 54% yields respectively (Scheme 34).

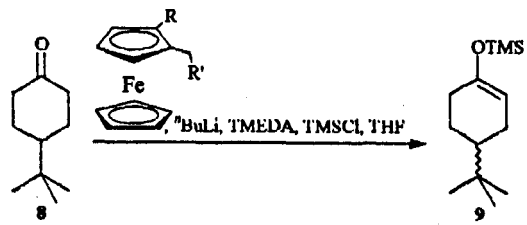



**Scheme 34**

These new bases, with no *ortho*-group, as well as the non-chelating *ortho*-methyl base **92**, were subjected to the base assay.

### 6.2.9 Non-chelating Base Assay Reactions

Base assays were performed using our optimised procedure (Equation 52; Table 5).




**(52)**

**Table 5:** Results of non-chelating base assay reactions

| Entry | R | R' | Compound number | Chemical yield / % | Optical rotation | Optical purity |
|---|---|---|---|---|---|---|
| 1 | Me | NH$^t$Bu | **92** | 78 | $[\alpha]_D^{25} = +7.54$ (c = 1.300) | 10 |
| 2 | H | NH$^i$Pr | **98** | 26 | - | - |
| 3 | H | NH$^t$Bu | **99** | 75 | - | - |

As before, the more hindered *tert*-butyl group gave a better chemical yield than isopropyl (Entries 2 and 3). Comparison of the results for the non-chelating methyl base **92** (Entry 1) and the analogous methoxy base **67** (Table 4, Entries 4 – 9) imply that chelation (if it is indeed occurring) is not improving either chemical yield or optical purity (78%; 10% *op* cf. 82%; 8% *op*).

## *6.3 Preliminary Investigations into Azaferrocene Bases*

To this point, all studies have focussed on the preparation of bases consisting of a lithium amide centre with a secondary donor group in a 1,3-relationship. This has been due to the constraints of finding a suitable planar chiral ferrocene backbone. It is therefore desirable to develop a planar chiral system that would

allow the presence of the donor group in a 1,2-relationship with the lithium amide centre, this being a property of successful bases reported to date in the literature.

The obvious 1,2-donor lithium amide system would consist of a ferrocene with two adjacent amine functionalities. Since we encountered great difficulty in introducing amine groups to the Cp ring, and even greater problems alkylating the resultant amines, this was not considered to be an option. The low basicity of the nitrogen anion connected directly to the Cp ring also means that these compounds would be unlikely to work well as bases.

Fu *et al.*[15,95,96] report the development of nucleophilic catalysts based on π-complexation of nitrogen heterocycles, such as pyrrole or pyridine. The development of these planar chiral DMAP and imidazole analogues led us to believe it would be possible to develop a planar chiral azaferrocene lithium amide system. Since the lone pair of the azaferrocene nitrogen is in the same plane as the pyrrole ring, and thus not involved in delocalisation with the π-orbital system, it should act as a far more effective donor group than our previous examples. Also, this donor group would now be in a 1,2-relationship with the lithium amide centre (Figure 32).

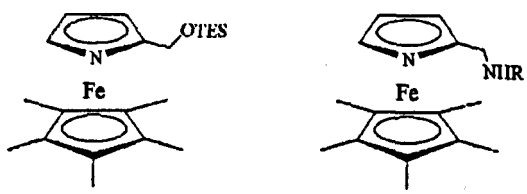



**Figure 32:** Fu's azaferrocene derivative and a desired azaferrocene lithium amide

Work by Fu *et al.*[97] on phosphaferrocene oxazolines **100**, as ligands for palladium catalysed enantioselective allylic alkylations, has shown that the plane of chirality is the dominant stereocontrol element. This is worth

contrasting with two related ligands; the bidentate P,N ligand **101** which furnishes exceptional stereocontrol (up to 99% *ee*'s) for palladium catalysed allylic alkylations[98] and the planar chiral ferrocenyl P,N, ligand **102**, where the chirality of the oxazoline subunit is dominant for asymmetric allylic alkylations[42] (Figure 33).

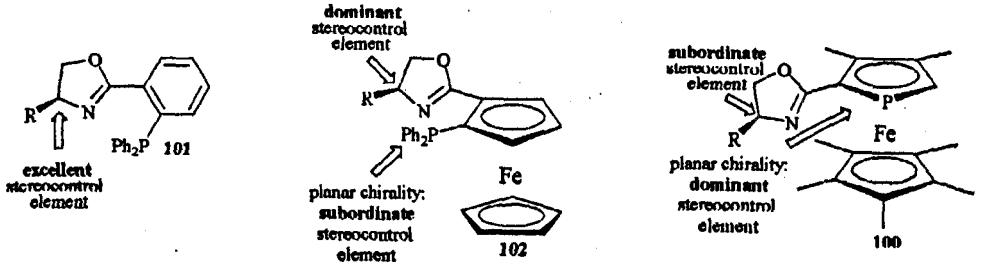



**Figure 33**

It is hoped that we will observe a similar improvement in stereocontrol on moving to an azaferrocene unit (Figure 34).

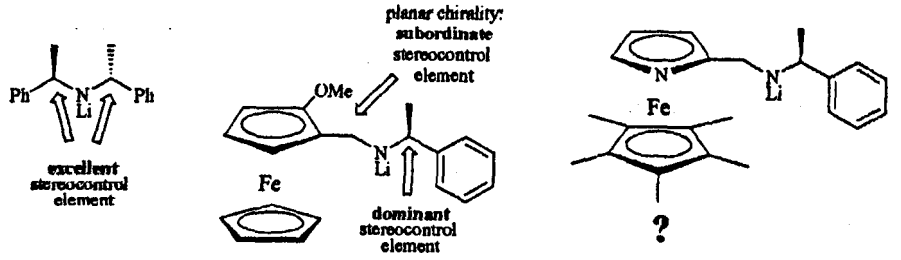
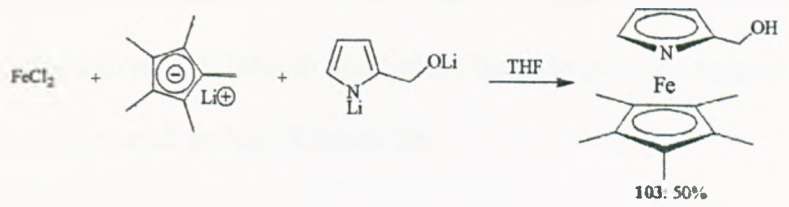


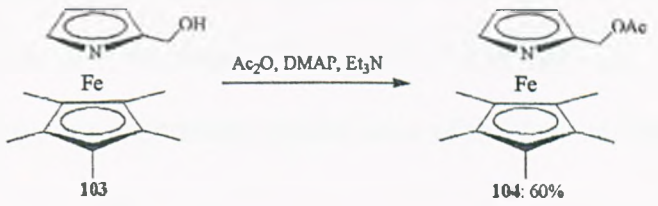

**Figure 34**

Fu's azaferrocenyl alcohol was prepared by the reaction of iron(II) chloride with the consecutive addition of lithium pentamethylcyclopentadienide and a suitably substituted lithiated pyrrole (Equation 53). This gives the desired azaferrocenyl alcohol **103** in 50% yield (lit.[94a] yield 22 – 43%). Fu *et al.* then protect the alcohol **103** as its silyl ether, however, we wish to substitute at this position, so need to transform the alcohol into a leaving group.



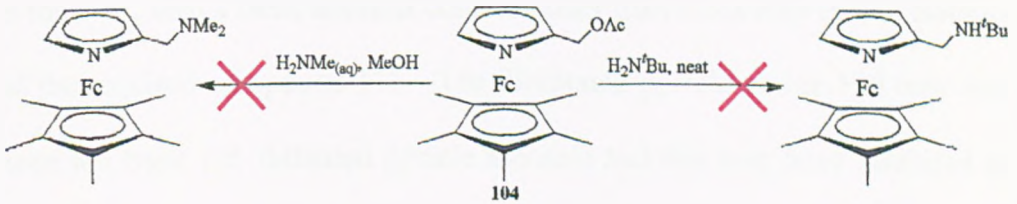

(53)

The leaving group chosen was acetate, since this had previously been used as a leaving group for ferrocenyl α-substitutions.[33] Transformation of the alcohol **103** into an acetate proceeded smoothly to give (±)-2-methyl-(1′,2′,3′,4′,5′-pentamethylazaferrocenyl) acetate **104** in good yield (60%) (Equation 54).




(54)

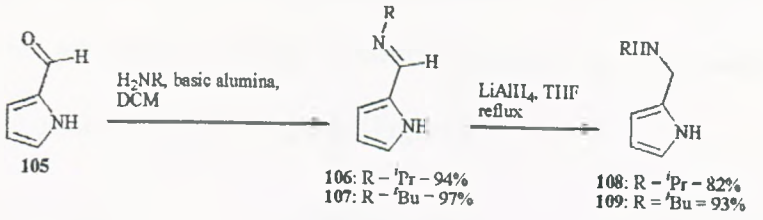
Attempts to displace the acetate with a suitable amine using a procedure analogous to that used during early work on *N,N*-dimethyl-1-ferrocenylethylamine (**15**) failed (Section 6.1.1).[38] Only decomposition products and starting material **104** formed, probably due to sensitivity of **104** to the aqueous reaction conditions. Treatment of the acetate **104** with neat *tert*-butylamine yielded only quantitative recovery of starting material **104** (Scheme 35).




**Scheme 35**

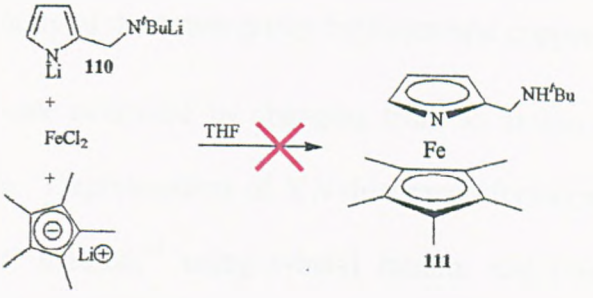
To avoid the substitution step, the preparation of pyrrole amines was investigated, with the view to use these directly in the complexation step. Condensation of pyrrole-2-carboxaldehyde (**105**) with either isopropylamine or

*tert*-butylamine furnished the corresponding imines **106** and **107**, and subsequent reduction with lithium aluminium hydride gave the amines **108** and **109** in excellent overall yields (Scheme 36).




**Scheme 36**

A complexation reaction was then performed using dilithiated *tert*-butylpyrrol-2-ylmethylamine **110** in place of the pyrrole-2-methanol salt (Equation 55). Disappointingly, this experiment yielded none of the desired diamine product.




**(55)**

There are a few possible explanations for this lack of success. The product **111** would be expected to be highly polar, and it is possible that it was formed, but could not be removed from the silica column used for chromatography. If this is the case, then a basic alumina column rather than silica may enable isolation of the required compound **111**. The dilithiated pyrrole amine **110** may have been too basic (cf. dithiated pyrrole alcohol) and this may have inhibited the reaction in some way.

Work on azaferrocenyl bases had to be abandoned at this point due to time constraints, however, there are many interesting areas still to be investigated.

# 7 Conclusions

All investigations into the *ortho*-functionalisation of *N,N*-dimethyl-1-ferrocenylethylamine (**15**) have been unsuccessful. Attempts to develop an electrophilic amination strategy proved fruitless, as did work on the introduction of an *ortho*-alkoxy group (Figure 35).

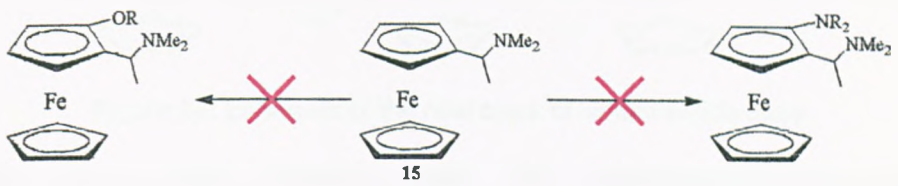
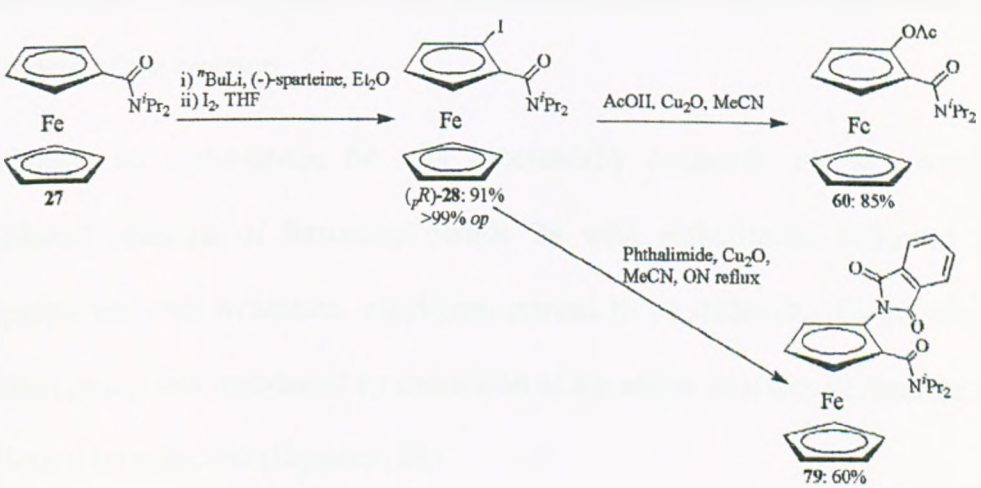



**Figure 35**

The problems encountered in this phase of the investigation were thought to be due to the high affinity of the amine group for boron and copper reagents.

These problems were overcome by changing from an amino *ortho*-directing group to an amide. Deprotonation of *N,N*-diisopropylferrocene carboxamide (**27**), by Snieckus' method,[44] using *n*-butyl lithium and (-)-sparteine (**26**), afforded us high optical purities for the asymmetric introduction of a range of *ortho*-groups.




**Scheme 37**

Iodination of the *ortho*-position gave us a coupling partner for the introduction of both amine and oxygen groups (Scheme 37). These substrates were then elaborated to give a range of *ortho*-methoxy and isopropoxy lithium amide bases, in good overall yield (Figure 36).

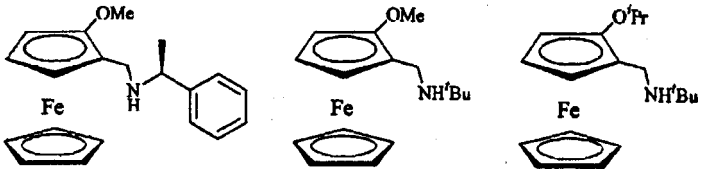



**Figure 36:** Examples of the new class of lithium amide base

These bases were assayed using the deprotonation of 4-*tert*-butylcyclohexanone (**8**), but none gave outstanding results.

A planar chiral base with a non-chelating *ortho*-methyl group **92** was assayed, and this gave almost identical results to its methoxy analogue **67** (Figure 37).

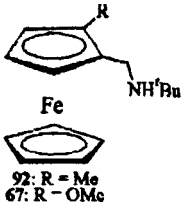
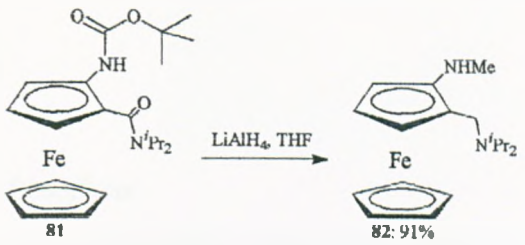



**Figure 37**

This indicates that chelation is not substantially affecting the stereochemical outcome of the reaction.

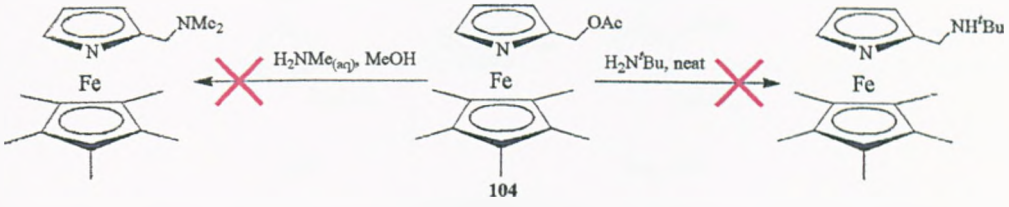
Although an *ortho*-amine **80** was successfully prepared, *via* the copper mediated coupling of ferrocenyl iodide **28** with phthalimide, followed by deprotection with hydrazine, alkylation proved to be difficult. Eventually a methyl group was introduced by protection of the amine as a Boc carbamate **81** followed by reduction (Equation 56).




(56)

Sadly, the resultant amine **82** did not act as a lithium amide base.

Preliminary investigations were carried out into the preparation of azaferrocenyl lithium amide bases. An azaferrocenyl acetate **104** was prepared, but substitution reactions did not work (Scheme 38).




**Scheme 38**

To summarise, a range of planar chiral ferrocenyl bases have been successfully prepared. Sadly, preliminary base assay results have been less than impressive, but there is a large scope for modification of the bases.

# 8 Future Work

## *8.1 Further Assay Reactions*

The bases that have been prepared to date have only been assayed for the deprotonation of conformationally locked prochiral ketones, and therefore, further assays could be carried out for rearrangement of epoxides and $\eta^6$-arene chromium tricarbonyl functionalisation (Figure 38).

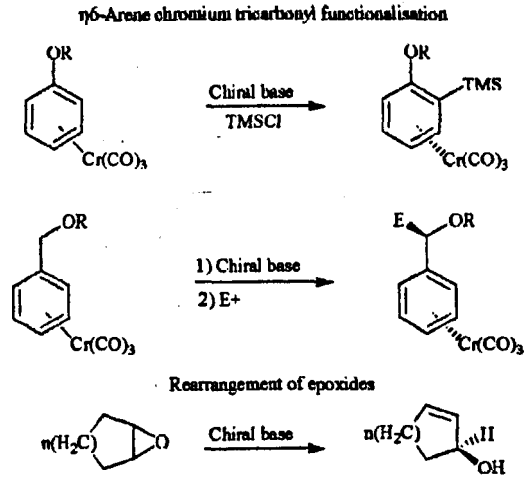
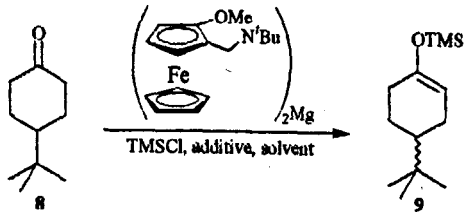



**Figure 38**

It was hoped that our bases would be effective across the range of transformations, but their lack of success in asymmetric ketone deprotonation does not mean that they will prove ineffective for other reactions.

## *8.2 Magnesium Bisamide Bases*

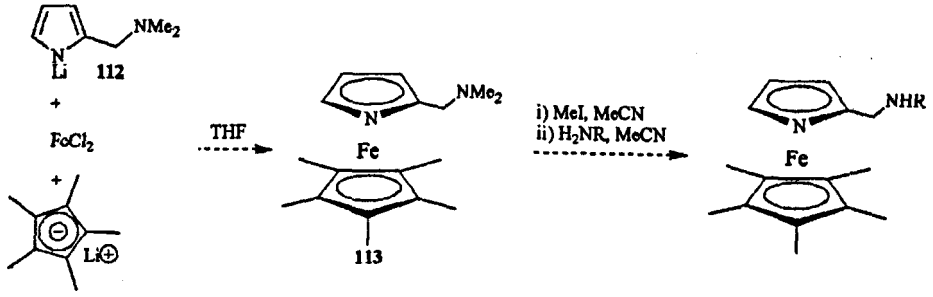
Although an attempt to use one of our bases as its magnesium bisamide was performed, this is undoubtedly an area that requires more investigation (Equation 57), since Kerr *et al.*[11] achieve such good results with a very simple chiral ligand.




(57)

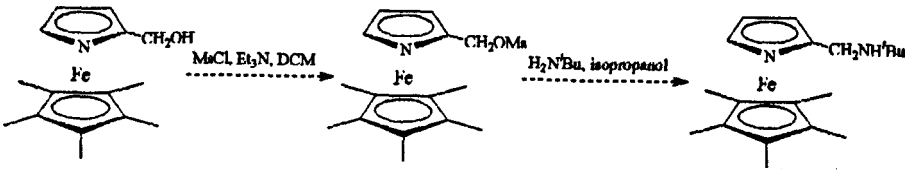
### *8.3 Further Azaferrocene Investigations*

The preliminary work on azaferrocene bases looked promising, but time constraints meant further investigation was not possible. The high basicity of a compound with two lithium amide centres was postulated as a possible reason for the failure of the complexation of the diamine ligand **109**. If this is the case, then the use of a dimethylamine derivative **112** instead of the secondary amine should help. This compound **113** could then be substituted, using methyl iodide and a primary amine, by analogy to earlier work (Scheme 39).



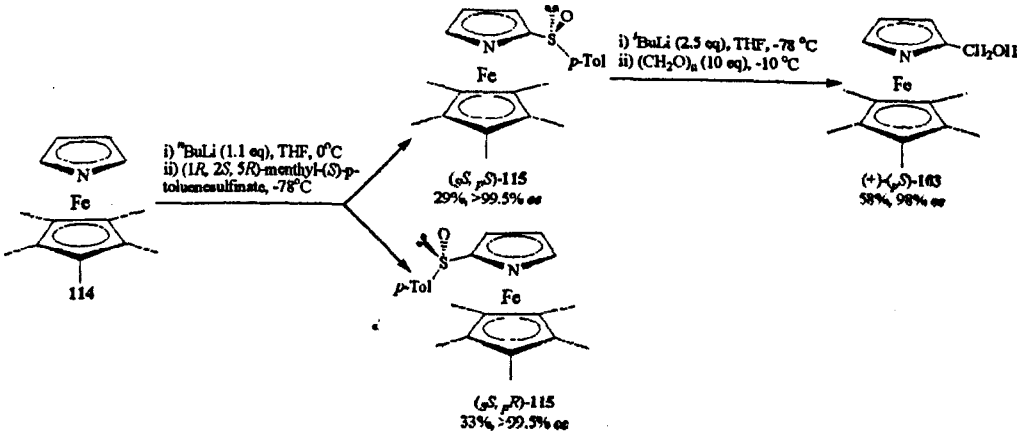

**Scheme 39**

If none of these strategies work, then a different leaving group could be used, instead of the acetate in **104**, to activate the complex towards substitution. Work by Kuehne *et al.*[99] demonstrates that changing from an acetate leaving group to a mesylate group can dramatically increase the yields of ferrocenyl substitution reactions (Scheme 40).




**Scheme 40**

Work by Johannsen *et al.*[100] on enantioselective synthesis of planar chiral azaferrocenes provides us with a route to enantiomerically enriched material (Scheme 41). Treatment of pentamethylazaferrocene **114** with butyl lithium, followed by (*1R, 2S, 5R*)-menthyl-(*S*)-*p*-toluenesulfinate, yields two diastereomeric azaferrocene sulfoxides **115**, which are separable by column chromatography. Treatment of the sulfoxide ($_{S}S$, $_{p}S$)-**115** with butyl lithium gives a planar chiral azaferrocenyl anion, which can be quenched with paraformaldehyde to give the desired alcohol (+)-($_{p}S$)-**103** (Scheme 41).



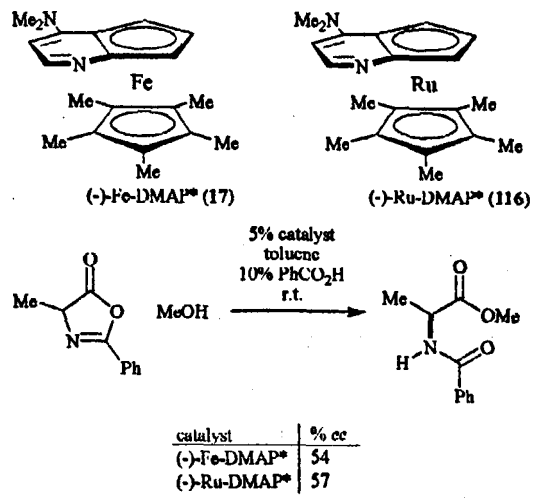

**Scheme 41**

Preparation of the primary alcohol (+)-($_{p}S$)-**103** followed by mesylation and substitution using the procedure by Kuehne *et al.*[98] should then give a homochiral azaferrocene base (Scheme 40).

### *8.4 Ruthenocene and Osmocene Analogues*

The nature of the metallocene metal centre can have a positive effect on the stereochemical outcome of a reaction, as shown by the work of Fu *et al.*[95] and

Togni *et al.*.[101] On moving from a ferrocenyl DMAP analogue **17** to a ruthenocenyl DMAP analogue **116**, Fu *et al.* observe a small increase in the enantiomeric excess for the ring opening of azlactones (dynamic kinetic resolution) (Scheme 42).



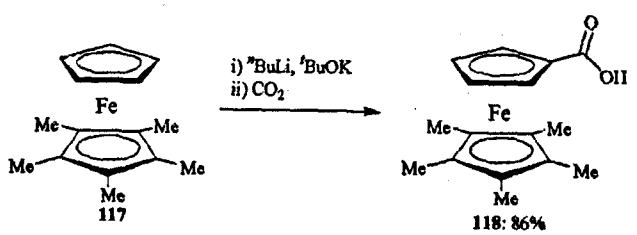

| catalyst | % ee |
|---|---|
| (-)-Fe-DMAP* | 54 |
| (-)-Ru-DMAP* | 57 |

**Scheme 42**

Therefore, it would be interesting to prepare the ruthenocene or osmocene analogues of some of our most successful bases to compare their reactivity.

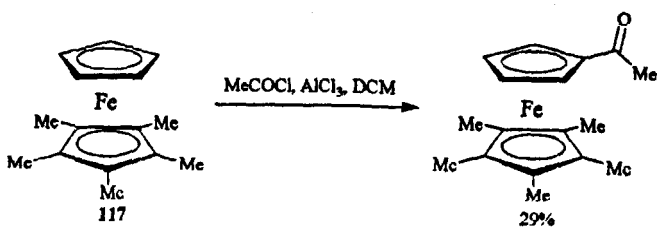
### *8.5 Pentamethylferrocene and Pentaphenylferrocene Analogues*

Finally, it has been shown that changing the nature of the "bottom" cyclopentadienyl ligand can have a positive effect on the stereochemical yield of reactions. Work by Fu *et al.*[16] has shown that changing from Cp* to the more bulky $C_5Ph_5$ ligand increases the selectivity factor for the kinetic resolution of (±)-1-phenylethanol from 1.7 to 10 (see section 5.2.3). Preparation of Cp* analogues of our most successful bases could be carried out using the published synthesis of 1,2,3,4,5-pentamethylferrocene (**117**),[102] followed by the normal procedure. Preparation of 1,2,3,4,5-pentamethylferrocene-1'-carboxylic acid (**118**) has been reported by Bildstein *et al.*[103] (Equation 58)




(58)

Friedel-Crafts acylation of 1,2,3,4,5-pentamethylferrocene (**117**) has been reported by Schwink and Knochel[104] and provides an alternative approach, but proceeds in low yield (Equation 59).




(59)

Despite the low yield, use of 2-chlorobenzoyl chloride as a Friedel-Crafts acylation partner might still provide a viable alternative method of preparing pentamethylferrocene carboxylic acid **118**.

Hopefully, these procedures would also prove to be applicable to the preparation of pentaphenylferrocenyl analogues of the most successful bases.

### *8.6 Conclusions*

Although the preliminary results of base assay reactions have been disappointing, there are many avenues still to be explored. The use of azaferrocenes as bases looks highly promising, and there are many factors which may be varied in order to optimise the results obtained.

# 9 Experimental Procedure

## *9.1 General Experimental Details*

The products of all reactions are assumed to be toxic and harmful.

All glassware was oven dried at 120 °C and flame-dried before use. Unless otherwise stated, all reactions were carried out in stoppered flasks under an atmosphere of $N_2$. Standard Schlenk techniques were used where indicated. Dry box working used an M-Braun Uni Lab Glove Box with an argon atmosphere.

Cooling to 0 °C was effected using an ice-water bath. Cooling to –78 °C was effected using a dry ice-acetone bath.

Commercial reagents were used as supplied, with the following exceptions: $Et_3N$ – freshly distilled from $CaH_2$; diisopropylamine – distilled from KOH; TMEDA, (-)-sparteine and *n*-butylamine – distilled from $CaH_2$; chlorotrimethylsilane – freshly distilled from $CaH_2$ onto polyvinylpyridine; 1,2-diiodoethane – was dissolved in ether and was washed with a 10% solution of sodium thiosulfate, dried ($MgSO_4$) and concentrated *in vacuo*; 4-*tert*-butylcyclohexanone – recrystallised from hexane and stored in a desiccator; methyl iodide – passed through a short column of basic alumina immediately prior to use; isopropylamine and *tert*-butylamine – redistilled grade purchased from Aldrich.

Solutions of *n*-butyl lithium in hexanes and *tert*-butyl lithium in pentane were purchased from either Aldrich or Lancaster, and standardised with *N*-pivaloyl-*o*-toluidine.[105]

Copper phthalimide was prepared according to literature procedures.[59]

The following reaction solvents were pre-dried and distilled immediately prior to use: THF was pre-dried over sodium wire and distilled from potassium/benzophenone under a nitrogen atmosphere; diethyl ether was pre-dried over sodium wire and distilled from sodium/benzophenone under a nitrogen atmosphere; toluene was pre-dried over sodium wire and distilled from sodium; and DCM was distilled from $CaH_2$ powder under a nitrogen atmosphere and was later bought as analytical grade and used as supplied. Anhydrous grade acetonitrile, DMF and acetone were all purchased from Aldrich, and used as supplied.

Thin layer chromatography was carried out using either Polygram® SIL G/$UV_{254}$ 0.25 mm silica gel pre-coated plastic sheets with fluorescent indicator $UV_{254}$ or Polygram® ALOX N/$UV_{254}$ 0.2 mm aluminium oxide pre-coated plastic sheets. The plates were visualised using ultra violet light (254 nm), anisaldehyde or basic $KMnO_4$ solution as appropriate.

Flash column chromatography was carried out using Fluorochem silica gel 60, 35 - 70μ. The liquid phase was freshly distilled hexane or analytical grade 40-60 petroleum ether (petrol) and other eluants were used as supplied.

Gravity column chromatography was carried out using BDH aluminium oxide, Brockmann Grade II – III. This was neutralised by standing in ethyl acetate for 7 days, followed by filtration and washing sequentially with ethanol, water and ethanol before oven drying at 120 °C overnight. The alumina was deactivated to activity grade IV prior to use. This involved shaking the alumina in a bag with 10% w/w of water.

Melting points are uncorrected and were recorded on a Reichert Melting Point Apparatus.

All spectra are reported as seen and coupling constants are uncorrected.

Optical rotations were recorded on a Jasco DIP370 Digital Polarimeter and are reported in deg $cm^2$ $g^{-1}$.

Infrared spectra were recorded on a Perkin-Elmer 1600 FTIR instrument as solutions in chloroform between sodium chloride plates, unless otherwise stated.

Proton NMR spectra were recorded on a Brüker AM 400 or a Brüker AV 400 spectrometer at 400 MHz as dilute solutions in deuterochloroform ($\delta_H$ $CHCl_3$ = 7.27 ppm), containing tetramethylsilane as the internal reference ($\delta_H$ = 0 ppm). Chemical shifts are reported downfield in parts per million (ppm) relative to a solvent standard or tetramethylsilane, and all coupling constants, *J*, are reported in Hertz. The multiplicity of each signal is described by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; w, weak.

Carbon-13 NMR spectra were recorded on a Brüker AM 400 spectrometer at 100 MHz as dilute solutions in deuterochloroform with the chemical shifts reported relative to the solvent standard ($\delta_C$ $CDCl_3$ = 77.1 ppm).

Mass spectra were acquired on VG micromass 70E and AIMS 902 instruments.

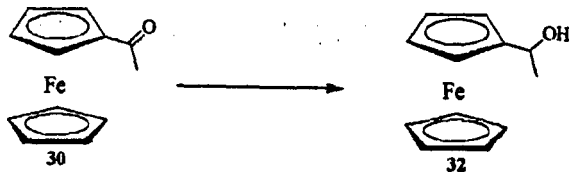
Elemental analyses were acquired on an Exeter Analytical Inc. CE440 Elemental Analyzer.

Single crystal X-ray diffraction was carried out by the X-ray crystallography department at the University of Nottingham using a Brüker SMART 1000 CCD area detector diffractometer.

**Acetylferrocene (30)**[48]

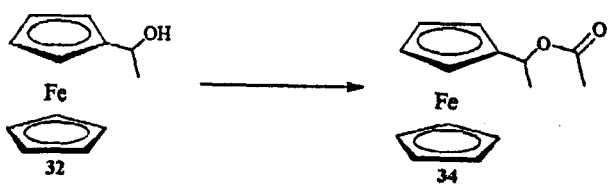

Preparation of acetylferrocene (**30**) followed the literature procedure, with purification being effected by flash column chromatography (silica; 100% hexane to 100% ether to 100% EtOAc), to yield ferrocene (**21**) (2.70 g, 27% recovery) followed by an orange solid which was recrystallised from hexane-ether to yield acetylferrocene (**30**) (8.74 g, 71%) as orange needle-like crystals. mp = 84 – 86 °C (lit.[38] mp = 85 – 86 °C); $R_f$ = 0.39 (30% EtOAc / hexane); IR $\nu_{max}$ 2993 (C-H stretch), 1652 (C=O ferrocenyl ketone), 1455, 1357, 1114, 893 $cm^{-1}$; $^1H$ NMR: δ 2.40 (3H, s, C*H*$_3$), 4.20 (5H, s, C*H* Cp$_{unsubs}$), 4.50 (2H, t, *J* = 2, C*H* Cp$_{subs}$), 4.77 (2H, t, *J* = 2, C*H* Cp$_{subs}$); $^{13}C$ NMR: δ 27.4 (1C, *C*H$_3$), 69.6 (2C, *C*H Cp$_{subs}$), 69.9 (5C, *C*H Cp$_{unsubs}$), 72.4 (2C, *C*H Cp$_{subs}$), 79.0 (1C, *C* Cp$_{subs}$), 202.0 (1C, *C*=O); m/z (ES$^+$): 229 (100%, M$^+$+H). Further elution yielded 1,1'-diacetylferrocene (**31**) (0.15 g, 1%) as a dark brown solid. mp = 124 – 126°C (lit. mp[106] = 124 – 125°C); $R_f$ = 0.09 (30% EtOAc / hexane); IR $\nu_{max}$ 2991 (C-H stretch), 1681 (C=O, ferrocenyl ketone), 1455, 1358, 1116, 1038, 894 $cm^{-1}$; $^1H$ NMR: δ 2.35 (6H, s, C*H*$_3$), 4.51 (4H, t, *J* = 2, C*H* Cp), 4.77 (4H, t, *J* = 2, C*H* Cp); $^{13}C$ NMR: δ 27.7 (2C, *C*H$_3$), 71.0 (4C, *C*H Cp), 73.6 (4C, *C*H Cp), 81.0 (2C, *C* Cp), 201.0 (2C, *C*=O).

**(±)-α-Ferrocenylethanol (32)**[49]




Preparation of (±)-α-ferrocenylethanol (**32**) was in accordance with the published procedure, with purification effected by flash column chromatography (silica; 10% ethyl acetate / hexane to 20% ethyl acetate / hexane) to yield ethylferrocene (**33**) (0.39 g, 8%) as a brown oil. $R_f$ = 0.74 (30% EtOAc / hexane); $^1$H NMR: δ 1.16 (3H, t, *J* = 7.5, C*H*$_3$), 2.33 (2H, q, *J* = 7.5, C*H*$_2$), 4.04 (2H, m, C*H* Cp$_{subs}$), 4.06 (2H, m, C*H* Cp$_{subs}$), 4.10 (5H, s, C*H* Cp$_{unsubs}$) further data was in agreement with that reported in the literature.[107] Further elution yielded an orange solid which was recrystallised from hexane to yield (±)-α-ferrocenylethanol (**32**) (4.84 g, 88%) as orange needle-like crystals. mp = 81 – 82 °C (lit.[49] mp = 78 – 79 °C); $R_f$ = 0.30 (30% EtOAc / hexane); IR $\nu_{max}$ 3601 (O-H stretch), 2974 (C-H stretch), 1373, 1105, 1068, 999, 871 cm$^{-1}$; $^1$H NMR: δ 1.44 (3H, d, *J* = 6.3, C*H*$_3$), 1.87 (1H, s br, O*H*), 4.19 (9H, m, C*H* Cp), 4.55 (1H, q, *J* = 6.3, C*H*(OH)); $^{13}$C NMR: δ 23.8 (1C, *C*H$_3$), 65.0 (1C, *C*H(OH)), 66.2 (2C, *C*H Cp$_{subs}$), 68.0 (2C, *C*H Cp$_{subs}$), 68.4 (5C, *C*H Cp$_{unsubs}$), 95.0 (1C, *C* Cp$_{subs}$); m/z (ES$^+$): 230 (100%, M$^+$).

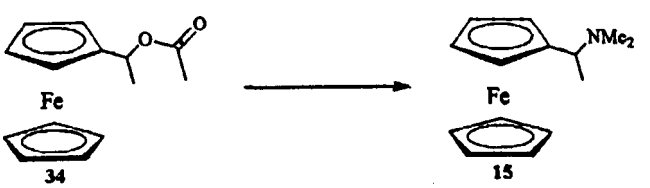
**(±)-α-Ferrocenylethylacetate (34)**




To a stirred solution of (±)-α-ferrocenylethanol (**32**) (4.48 g, 19.5 mmol) in pyridine (15 mL) at 0 °C, was added *N,N*-dimethylaminopyridine (DMAP)

(200 mg, 1.8 mmol), followed by acetic anhydride (4.4 mL, 39 mmol). The reaction mixture was left to stir at r.t. for 16 h then diluted with ether (25 mL) and pyridine removed by washing the mixture with a sat. aq. solution of $CuSO_4$. The organic layer was washed with a sat. solution of $NaHCO_3$, dried ($MgSO_4$) and concentrated *in vacuo* to yield (±)-α-ferrocenylethylacetate (**34**) (4.97 g, 94%) as a yellow-orange solid, which was used without further purification. mp = 71 – 74°C (lit.[38] mp = 70 – 71°C); $R_f$ = 0.38 (50% EtOAc / hexane); IR $\nu_{max}$ 2984 (C-H stretch), 1714 (C=O, ferrocenyl ester), 1369, 1105, 1063, 1000, 946 $cm^{-1}$; $^1H$ NMR: δ 1.56 (3H, d, $J$ = 6.5, $CHCH_3$), 2.03 (3H, s, $C(=O)CH_3$), 4.15 (5H, s, $CH\ Cp_{unsubs}$), 4.22 (2H, s, $CH\ Cp_{subs.}$), 4.27 (2H, s, $CH\ Cp_{subs.}$), 5.84 (1H, q, $J$ = 6.5, $CHCH_3$); $^{13}C$ NMR: δ 20.1 (1C, $CH_3$), 21.0 (1C, $CH_3$), 66.1 (1C, CH), 68.0 (2C, CH $Cp_{subs}$), 68.4 (2C, CH $Cp_{subs}$), 68.8 (5C, CH $Cp_{unsubs}$), 88.0 (1C, C $Cp_{subs}$), 171 (1C, C=O); m/z ($ES^+$): 213 (100%, $M^+$-($OCOCH_3$)).

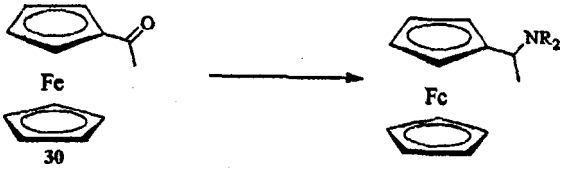
**(±)-*N,N*-Dimethyl-1-ferrocenylethylamine (15)[38]**



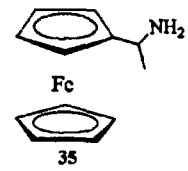
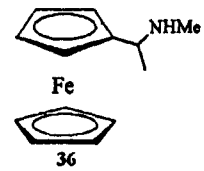
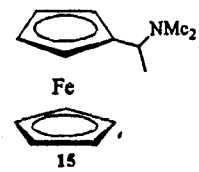

To a stirred suspension of (±)-α-ferrocenylethylacetate (**34**) (3.77 g, 13.9 mmol) in methanol (50 mL) was added dropwise dimethylamine (40 wt. % aqueous, 3.5 mL, 28 mmol). The reaction mixture was left to stir at r.t. for 8 h, then concentrated *in vacuo* and the residue dissolved in phosphoric acid (8.5% wt. solution, 15 mL). This solution was washed with ether (3 × 50 mL), then basified with a sat. aq. solution of $NaHCO_3$ and the basic aqueous phase was extracted with DCM. The DCM phase was dried ($MgSO_4$) and concentrated *in*

*vacuo* to yield (±)-*N,N*-dimethyl-1-ferrocenylethylamine (**15**) (3.03 g, 85%, 80% based on (±)-α-ferrocenylethanol (**32**), lit.[38] yield = 35 – 70% based on α-ferrocenylethanol (**32**)) as a brown oil, which was used without further purification. $R_f$ = 0.18 (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 2963 (C-H stretch), 2507, 1643, 1456, 1371, 1096, 1044, 1000, 957, 903 $cm^{-1}$; $^1H$ NMR: δ 1.44 (3H, d, $J$ = 6.8, $CH(N(CH_3)_2)CH_3$), 2.07 (6H, s, $N(CH_3)_2$), 3.59 (1H, q, $J$ = 6.8, $CH(N(CH_3)_2)CH_3$), 4.10 (9H, m, *CH* Cp); $^{13}C$ NMR: δ 16.1 ($CH(N(CH_3)_2)CH_3$), 40.7 (2C, $N(CH_3)_2$), 58.7 (1C, $CH(N(CH_3)_2)CH_3$), 66.9 (1C, *CH* $Cp_{subs}$), 67.2 (1C, *CH* $Cp_{subs}$), 67.4 (1C, *CH* $Cp_{subs}$), 68.6 (5C, *CH* $Cp_{unsubs}$), 69.4 (1C, *CH* $Cp_{subs}$), 87.3 (1C, *C* $Cp_{subs}$); HRMS ($FAB^+$) $C_{14}H_{19}FeN$ calcd. 257.0867, found 257.0874.

**Preparation of *N,N*-Dialkyl-1-ferrocenylethylamines Using the Bhattacharyya Method[52]**




Acetylferrocene (**30**) (4.56 g, 20.0 mmol) was treated according to the known literature procedure. Products and yields are shown in the table below.

| Entry | Amine hydrochloride | Product | Yield (%) | Lit. Yield (%) |
|---|---|---|---|---|
| 1 | Ammonium chloride |  35 | 40 | 75%[52] |
| 2 | Methylamine hydrochloride |  36 | 48 | - |
| 3 | Dimethylamine hydrochloride |  15 | 29 | - |

**(±)-1-Ferrocenylethylamine (35)**

$^1$H NMR: δ 1.34 (3H, d, $J$ = 6.6, CHC$H_3$), 1.55 (2H, s br, N$H_2$), 3.79 (1H, q, $J$ = 6.6, C$H$CH$_3$) 4.15 (9H, m, C$H$ Cp). Data was in agreement with that reported in the literature.[52]

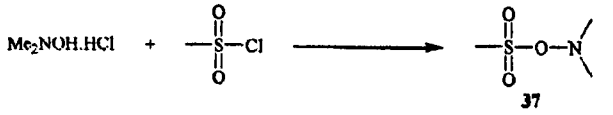
**(±)-*N*-Methyl-1-ferrocenylethylamine (36)**

$^1$H NMR: δ 1.37 (3H, d, $J$ = 6.5, CHC$H_3$), 1.54 (1H, s br, N$H$CH$_3$), 2.40 (3H, s, NHC$H_3$), 3.40 (1H, q, $J$ = 6.5, C$H$CH$_3$) 4.14 (9H, m, C$H$ Cp). Data was in agreement with that reported in the literature.[108]

**(±)-*N,N*-Dimethyl-1-ferrocenylethylamine (15)**

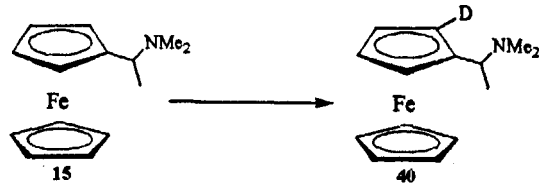
Spectroscopic data in agreement with that reported above.

**_N,N_-Dimethyl-_O_-(methylsulfonyl)hydroxylamine (37)**



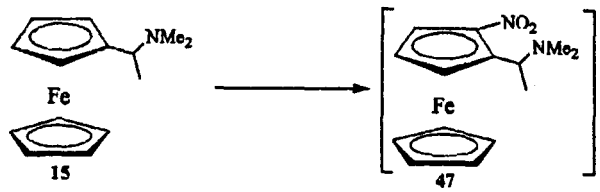

To a suspension of *N,N*-dimethylhydroxylamine hydrochloride (2.39 g, 24.5 mmol) in DCM (20 mL) at −15 °C, was added triethylamine (8.5 mL, 61 mmol). After 10 min, a solution of methane sulfonylchloride (1.7 mL, 22 mmol) in DCM (20 mL) was added dropwise. The reaction was allowed to stir at −15 °C for 3 h and then allowed to warm slowly to r.t. overnight. The reaction mixture was quenched with ice water. The organic and aqueous phases were separated and the aqueous phase was washed with cold DCM (0 °C, 3 × 20 mL). The combined organic phases were then dried ($MgSO_4$) and concentrated *in vacuo* at 0 °C, yielding a pale yellow oil. Addition of a small portion of ether followed by sonication caused precipitation followed by solvation of the solid, leaving an insoluble orange oil. The colourless supernatant liquid was removed and concentrated *in vacuo* to yield *N,N*-dimethyl-*O*-(methylsulfonyl)hydroxylamine (**37**) (982 mg, 32%) as an off-white solid, which was used without further purification. mp = 43 – 48 °C (lit.[53] mp = 33 – 35 °C); $^1$H NMR: δ 2.78 (3H, s, $SO_2CH_3$), 2.86 (6H, s, $N(CH_3)_2$); $^{13}$C NMR: δ 33.1 (1C, $SO_2CH_3$), 37.5 (2C, $N(CH_3)_2$); m/z (EI$^+$): 123 (42%, $M^+$-O), 108 (11%, $M^+$-$CH_3O$), 44 (100%, $M^+$-$CH_3SO_3$).

**(±)-2-Deutero-*N,N*-dimethyl-1-ferrocenylethylamine (40)**[109]




To a solution of (±)-*N,N*-dimethyl-1-ferrocenylethylamine (**15**) (0.10 g, 0.39 mmol) in ether (2.5 mL), at –78 °C, was added dropwise *n*-butyl lithium (0.7 M, 1.2 mL, 0.86 mmol). The reaction was stirred at this temperature for 1 h, before being left to warm to r.t.. The reaction mixture was then cooled to –78 °C and $D_2O$ (2 mL) was added slowly. The reaction mixture was left to warm to r.t. slowly and stirred at r.t. over the weekend. The two phases were separated and the "aqueous" phase was extracted with ether. The combined ether layers were then dried ($MgSO_4$) and concentrated *in vacuo* to yield (±)-2-deutero-*N,N*-dimethyl-1-ferrocenylethylamine (**40**) (94 mg, 93%) as a brown oil. $^1$H NMR: δ 1.44 (3H, d, $J$ = 6.9, $CH(N(CH_3)_2)CH_3$), 2.08 (6H, s, $N(CH_3)_2$), 3.59 (1H, q, $J$ = 6.9, $CH(N(CH_3)_2)CH_3$), 4.11 (8H, m, *CH* Cp); $^{13}$C NMR: δ 16.1 (1C, $CH(N(CH_3)_2)CH_3$), 40.7 (2C, $N(CH_3)_2$), 58.7 (1C, $CH(N(CH_3)_2)CH_3$), 66.9 (1C, *CH* $Cp_{subs}$), 67.2 (1C, *CH* $Cp_{subs}$), 67.3 (1C, *CH* $Cp_{subs}$), 68.6 (5C, *CH* $Cp_{unsubs}$), 69.0 (1C, t w, $^1J_{C\text{-}D}$ = 26, *CD* $Cp_{subs}$), 87.2 (1C, *C* $Cp_{subs}$); HRMS ($FAB^+$) $C_{14}H_{18}DFeN$ calcd. 258.0930, found 258.0935.

**Nitration of (±)-*N,N*-Dimethyl-1-ferrocenylethylamine (15)**




Sample Procedure (corresponds to run 4):

The following reaction was carried out using standard Schlenk techniques. To a solution of (±)-*N,N*-dimethyl-1-ferrocenylethylamine (**15**) (520 mg, 2.0 mmol) in ether (20 mL), in a 500 mL Schlenk flask at –78 °C, was added *tert*-butyl lithium (1.6M, 1.6 mL, 2.6 mmol) dropwise and the reaction mixture was

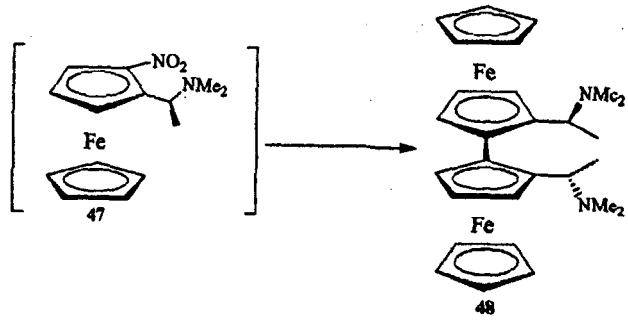
left to stir for 1 h before being allowed to warm to r.t.. The ether was removed *in vacuo* and the residue was dissolved in THF (20 mL). The reaction mixture was then frozen around the walls of the flask, in as thin a layer as possible using a liquid nitrogen bath, then placed under a static vacuum. Dinitrogen tetraoxide (470 mg, 5.1 mmol) was condensed, as a blue solid, into a pre-weighed, evacuated Schlenk flask using an acetone-dry ice bath. The flask was then allowed to warm to r.t. to give a brown gas. A piece of Portex™ tubing fitted with a needle was attached to the flask and used to condense the gas into the reaction vessel. The reaction mixture was then warmed rapidly using a methanol bath and agitated vigorously. The pale brown frozen solution turned a deep red colour. The excess dinitrogen tetraoxide and THF were removed *in vacuo* and the residue was dissolved in DCM. The DCM solution was then filtered, washed with water, dried ($Na_2SO_4$) and concentrated *in vacuo*, yielding red oil (0.48 g).

| Run | Starting material (g) | Equivalents of $N_2O_4$ | Crude product appearance (yield, g) | Comments |
|---|---|---|---|---|
| 1 | 0.50 | 2.5 | Black & insoluble. | - |
| 2 | 0.50 | 3.8 | Black & insoluble. | - |
| 3 | 0.51 | 2.55 | Brown oil (0.18) | Material oxidised before purification was possible |
| 4 | 0.52 | 0.8 | Red oil (0.48) | Flash column chromatography gave some clean product, but $^1$H NMR broad due to oxidation to $Fe^{3+}$, <0.1g obtained |
| 5 | 1.03 | 1.0 | Red oil (unknown) | Oxidation occurred before yield or purification were possible |
| 6 | 1.06 | 1.0 | Red oil (unknown) | Flash column chromatography yielded: A (97 mg) – oxidised; B (58 mg) – oxidised; C (60 mg) – red oil, clean $^1$H and $^{13}$C NMR but oxidised before further data could be collected; D – oxidised. |
| 7 | 1.64 | 0.8 | Red oil (0.8) | Flash column chromatography yielded A (19 mg) – oxidised; B (11 mg) – oxidised; C (162 mg) – red oil, $^1$H NMR as run 4, but already broadened; D (516 mg) – starting material |
| 8 | 1.06 | 1.0 | Red oil (1.04) | Used immediately for hydrogenation reaction |

**Red oil isolated in entry 6 (Mixture of starting material 15 and product 47)**

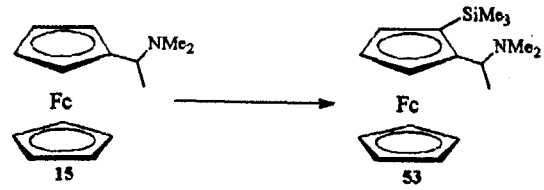
$^1$H NMR: δ 1.45 (d, C*H*$_3$), 1.55 (d, C*H*$_3$), 2.08 (s, N(C*H*$_3$)$_2$), 3.60 (q, C*H*), 4.11 (s, C*H* Cp), 4.48 (m, C*H* Cp$_{subs}$), 4.63 (q, C*H*), 5.25 (s, C*H* Cp$_{subs}$); $^{13}$C NMR: δ 15.5 (*C*H$_3$), 16.1(*C*H$_3$), 40.4 (N(*C*H$_3$)$_2$), 40.7 (N(*C*H$_3$)$_2$), 54.4 (*C*H), 58.7 (*C*H), 66.9 (*C*H Cp$_{subs}$), 67.2 (*C*H Cp$_{subs}$), 67.4 (*C*H Cp$_{subs}$), 68.0 (*C*H Cp$_{subs}$), 68.6 (5C, *C*H p$_{unsubs}$), 69.4 (*C*H Cp$_{subs}$), 70.1 (*C*H Cp$_{subs}$), 72.3 (*C*H Cp$_{subs}$), 87.3 (*C* Cp$_{subs}$), 87.4 (*C* Cp$_{subs}$).

**(±)-2,2'-Bis[1-(*N,N*-dimethylamino)-ethyl]-1,1'-biferrocenyl (48)**



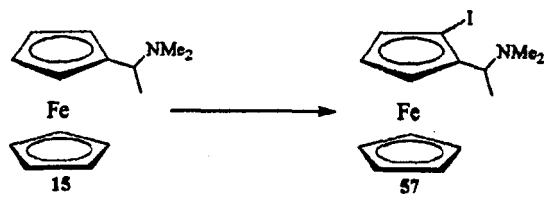

To the crude nitration reaction mixture (1.04 g, theoretically 3.44 mmol of **47**) was added platinum(IV) oxide (99.0 mg, 0.44 mmol) and ethanol (100 mL). The reaction flask was stirred under hydrogen at atmospheric pressure and r.t. for 2 h. The reaction mixture was filtered through Celite™ and concentrated *in vacuo*, yielding 0.87 g of brown oil. Purification by flash column chromatography (silica; 4% DCM / 95% methanol / 1% $Et_3N$ to 50% methanol / 50% $Et_3N$) yielded (±)-*N,N*-dimethyl-1-ferrocenylethylamine (**15**) (0.29 g, 27% recovery) followed by (±)-2,2'-bis[1-(N,N-dimethylamino)-ethyl]-1,1'-biferrocenyl (**48**) (0.33 g, 31%, based on (±)-*N,N*-dimethyl-1-ferrocenylethylamine (**15**)) as a brown-orange solid. mp = 145 – 147 °C; IR $\nu_{max}$ 2933 (C-H stretch), 2775, 1601, 1455, 1366, 1106 $cm^{-1}$; $^1H$ NMR: δ 1.37 (6H, d, $J$ = 6.8, $CH(NMe_2)CH_3$), 1.80 (12H, s, $N(CH_3)_2$), 3.68 (2H, q, $J$ = 6.8, $CH(NMe_2)CH_3$), 4.15 (2H, s, $CH$ $Cp_{subs}$), 4.24 (10H, s, $CH$ $Cp_{unsubs}$), 4.44 (2H, s, $CH$ $Cp_{subs}$); $^{13}C$ NMR: δ 14.5 (2C, $CH(NMe_2)CH_3$), 40.4 (4C, $N(CH_3)_2$), 55.7 (2C, $CH(NMe_2)CH_3$), 65.8 (2C, $CH$ $Cp_{subs}$), 67.0 (2C, $CH$ $Cp_{subs}$), 69.7 (10C, $CH$ $Cp_{unsubs}$), 85.9, 90.4; HRMS ($FAB^+$) $C_{28}H_{37}Fe_2N_2$ calcd. 513.1655, found 513.1651 ($M^+$+H). Anal. calcd. for $C_{28}H_{36}Fe_2N_2$: C, 65.65; H, 7.08; N, 5.47; found: C, 65.16; H, 7.11; N, 5.42%; Single crystal X-ray diffraction data confirms structure (see appendix).

**(±)-2-Trimethylsilyl-*N,N*-dimethyl-1-ferrocenylethylamine (53)**




To a solution of (±)-*N,N*-dimethyl-1-ferrocenylethylamine (**15**) (1.09 g, 4.24 mmol) in ether (40 mL), at –78 °C, was added dropwise *tert*-butyl lithium (1.65 M, 4.0 mL, 6.6 mmol). The reaction was stirred at –78 °C for 1 h, before being left to warm to r.t.. The solvents were removed *in vacuo* and the residue was taken up in THF (30 mL). The reaction mixture was then cooled to –78 °C and a solution of TMS-isocyanate (0.63 g, 5.5 mmol) in THF (10 mL) was added slowly. The reaction mixture was left to warm to r.t. slowly and stirred overnight. The reaction mixture was concentrated in vacuo, and the residue was taken up in 8.5% wt. $H_3PO_4$ (50 mL). The aqueous phase was washed with ether (3 × 20 mL) and then basified with 1M NaOH before being extracted into DCM (3 × 20 mL). The DCM layer was dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography (silica; 50% hexane / 49% EtOAc / 1% $Et_3N$) yielded (±)-2-trimethylsilyl-*N,N*-dimethyl-1-ferrocenylethylamine (**53**) (0.482 g, 36%) as a brown oil. $^1$H NMR: δ 0.23 (9H, s, Si($CH_3$)$_3$), 1.21 (3H, d, $J$ = 6.7, CH(N($CH_3$)$_2$)$CH_3$), 2.03 (6H, s, N($CH_3$)$_2$), 3.80 (1H, q, $J$ = 6.7, $CH$(N($CH_3$)$_2$)$CH_3$), 4.05 (6H, m, $CH$ Cp), 4.23 (1H, t, $J$ = 2.3, $CH$ Cp$_{subs}$), 4.27 (1H, s, $CH$ Cp$_{subs}$). Further data was in agreement with the literature.[33]

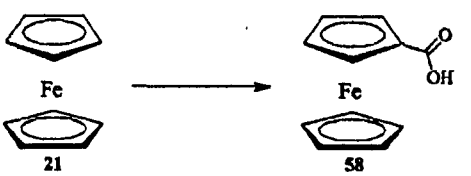
**(±)-2-Iodo-*N,N*-dimethyl-1-ferrocenylethylamine (57)**




To a solution of (±)-*N,N*-dimethyl-1-ferrocenylethylamine (**15**) (2.00 g, 7.78 mmol) in ether (40 mL), at –78 °C, was added dropwise *tert*-butyl lithium (1.32 M, 7.66 mL, 10.1 mmol). The reaction was stirred at –78 °C for 1 h, before being left to warm to r.t.. The reaction mixture was then cooled to –78

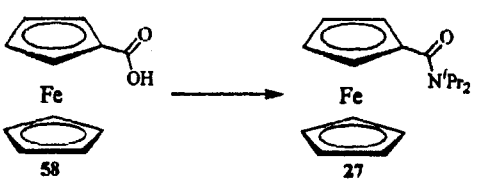
°C and a solution of diiodoethane (2.86 g, 10.1 mmol) in THF (20 mL) was added slowly. The reaction mixture was left to warm to r.t. slowly overnight. The reaction mixture was quenched with water (50 mL). The phases were separated and the organics were washed with a 10% aq. solution of sodium thiosulfate (3 × 50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography (silica; 50% hexane / 49% EtOAc / 1% $Et_3N$) yielded (±)-2-iodo-*N,N*-dimethyl-1-ferrocenylethylamine (**57**) (2.62 g, 88%) as a brown oil. $^1$H NMR: δ 1.50 (3H, d, $J$ = 6.8, $CH(N(CH_3)_2)CH_3$), 2.14 (6H, s, $N(CH_3)_2$), 3.62 (1H, q, $J$ = 6.8, $CH(N(CH_3)_2)CH_3$), 4.12 (5H, s, $CH$ $Cp_{unsubs}$), 4.15 (1H, dd, $J$ = 2.6, 1.3, $CH$ $Cp_{subs}$), 4.24 (1H, t, $J$ = 2.6, $CH$ $Cp_{subs}$), 4.46 (1H, dd, $J$ = 2.4, 1.3, $CH$ $Cp_{subs}$). Further data was in agreement with the literature.[110]

**Ferrocene carboxylic acid (58)**[74]




Ferrocene carboxylic acid (**58**) was obtained according to the literature procedure as a pale brown-orange solid (16.7 g, 73%, lit.[74] yield = 74-83%) mp = 152 °C (dec.) (lit.[74] mp = 214-216 °C (dec.)); $^1$H NMR: δ 4.26 (5H, s, $CH$ $Cp_{unsubs}$), 4.47 (2H, t, $J$ = 2.0, $CH$ $Cp_{subs}$), 4.86 (2H, t, $J$ = 2.0, $CH$ $Cp_{subs}$); Further data was in agreement with the literature.[74]

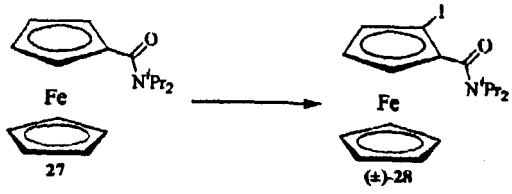
***N,N*-Diisopropylferrocene carboxamide (27)**[44]




Preparation was effected according to the literature procedure, followed by recrystallisation from hexane to yield *N,N*-diisopropylferrocene carboxamide

(**27**) (10.5 g, 76%, lit.[44] yield = 74%) as orange needle-like crystals. mp = 84 – 86 °C (lit.[44] mp = 88 – 91 °C); $^1$H NMR: δ 1.10 – 1.60 (12H, br d, N(CH(C*H*$_3$)$_2$)$_2$), 3.10 – 3.60 (2H, br, N(C*H*(CH$_3$)$_2$)$_2$), 4.23 (5H, s, C*H* Cp$_{unsubs}$), 4.27 (2H, s, C*H* Cp$_{subs}$), 4.56 (2H, s, C*H* Cp$_{subs}$). Further data was in agreement with that reported in the literature.[44]

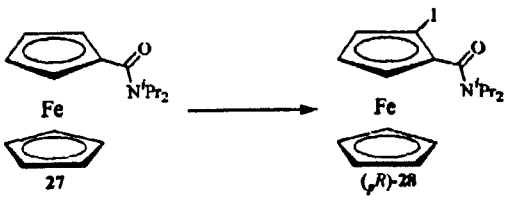
**(±)-*N,N*-Diisopropyl-2-iodoferrocene carboxamide (28)[44]**




To a stirred solution of *n*-butyl lithium (2.2M, 16 mL, 35 mmol), TMEDA (5.3 mL, 35 mmol) and ether (100 mL) at –78 °C was added a solution of *N,N*-diisopropylferrocene carboxamide (**27**) (5.0 g, 16 mmol) in ether (80 mL). The reaction mixture was stirred at –78 °C for 1 h followed by addition of a solution of iodine (12 g, 48 mmol) in THF (120 mL). The reaction mixture was stirred at –78 °C for a further hour before being allowed to warm slowly to r.t.. The reaction mixture was then poured onto a sat. solution of $NH_4Cl$ (300 mL) and the phases were separated. The organic phase was washed successively with a 10% solution of sodium thiosulfate (2 × 200 mL), water (2 × 200 mL) and brine (2 × 200 mL), then dried ($MgSO_4$), and concentrated *in vacuo* to yield a brown solid. Recrystallisation from hexane yielded (±)-*N,N*-diiospropyl-2-iodoferrocene carboxamide, (±)-(**28**) (6.2 g, 89 %, lit.[44] yield = 85%) as brown flat crystals. mp = 131 – 133 °C (lit.[44] mp = 97 – 99 °C); $^1$H NMR: δ 0.99 (3H, d, *J* = 6.0, N(CH(C*H*$_3$)$_2$)$_2$), 1.11 (3H, d, *J* = 6.0, N(CH(C*H*$_3$)$_2$)$_2$), 1.52 (6H, s, N(CH(C*H*$_3$)$_2$)$_2$), 3.30 – 3.50 (1H, br,

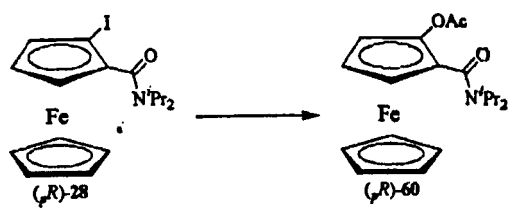
N(C*H*(CH$_3$)$_2$)$_2$), 3.50 – 3.70 (1H, br, N(C*H*(CH$_3$)$_2$)$_2$), 4.18 (1H, t, *J* = 2.4, C*H* Cp$_{subs}$), 4.29 (1H, dd, *J* = 2.4, 1.3, C*H* Cp$_{subs}$), 4.35 (5H, s, C*H* Cp$_{unsubs}$), 4.43 (1H, dd, *J* = 2.4, 1.3, C*H* Cp$_{subs}$). Further data was in agreement with that reported in the literature for the preparation of non-racemic material.[44]

**($_p$*R*)-*N*,*N*-Diisopropyl-2-iodoferrocene carboxamide (28)[44]**




Preparation of ($_p$*R*)-*N*,*N*-diisopropyl-2-iodoferrocene carboxamide ($_p$*R*)-(**28**) (8.96 g, 91%, lit.[44] yield = 85%), as a brown crystalline solid, was effected according to literature procedure.[44] $[\alpha]_D^{25} = +94.6$, ($CHCl_3$, c = 0.992); lit.[44] $[\alpha]_D^{25} = +91.0$, ($CHCl_3$, c = 1.06).

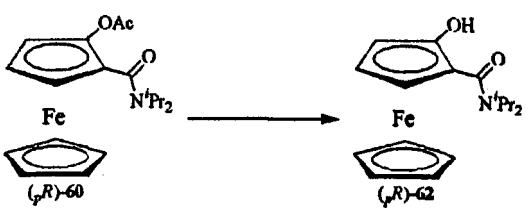
**($_p$*R*)-2-(*N*,*N*-Diisopropylamido)ferrocenylacetate (60)**




To a flask containing copper(I) oxide (694 mg, 4.85 mmol) was added a solution of ($_p$*R*)-*N*,*N*-diisopropyl-2-iodoferrocene carboxamide (($_p$*R*)-**28**) (3.38 g, 7.70 mmol) in acetonitrile (50 mL). Acetic acid (0.53 mL, 9.2 mmol) was added to the reaction mixture and it was warmed to reflux for 2.5 h. The reaction mixture was filtered through a sinter funnel and concentrated *in vacuo*. The residue was dissolved in ether (50 mL) and washed with a sat. aq. solution of $NH_4Cl$ (2 × 50 mL) and brine (2 × 50 mL) then dried ($MgSO_4$), and concentrated *in vacuo* to yield a golden brown oil. Purification by column

chromatography (silica; 10% EtOAc / hexane) yielded a pale brown oil which solidified on standing. Recrystallisation from hexane yielded ($_pR$)-2-(*N,N*-diisopropylamido)ferrocenylacetate (($_pR$)-**60**) (2.44 g, 85%) as golden brown crystals. mp = 94 – 96 °C; $R_f$ = 0.55 (30% EtOAc / hexane); $[\alpha]_D^{25}$ = +107.4 (c = 1.095, $CHCl_3$); IR $\nu_{max}$ 2968 (C-H stretch), 1754 (C=O stretch, ferrocenyl acetate), 1620 (C=O stretch, ferrocenyl amide), 1462, 1370, 1322 $cm^{-1}$; $^1H$ NMR: δ 1.10 (6H, br s, $N(CH(CH_3)_2)_2$), 1.50 (6H, br s, $N(CH(CH_3)_2)_2$), 2.18 (3H, s, $C{=}OCH_3$), 3.39 (1H, br s, $N(CH(CH_3)_2)_2$), 3.98 (1H, t, $J$ = 2.6, *CH* $Cp_{subs}$), 4.10 (2H, dd and br s, $J$ = 2.6, 1.4, *CH* $Cp_{subs}$ and $N(CH(CH_3)_2)_2$), 4.36 (5H, s, *CH* $Cp_{unsubs}$), 4.42 (1H, dd, $J$ = 2.6, 1.4, *CH* $Cp_{subs}$); $^{13}C$ NMR: δ 20.9 (4C, br, $N(CH(CH_3)_2)_2$), 21.2 (1C, $OC{=}OCH_3$), 46.0 (1C, br, $NCH(CH_3)_2$), 50.6 (1C, br, $NCH(CH_3)_2$), 61.0 (1C, *CH* $Cp_{subs}$), 61.9 (1C, *CH* $Cp_{subs}$), 62.8 (1C, *CH* $Cp_{subs}$), 71.3 (5C, *CH* $Cp_{unsubs}$), 79.3 (1C, *CC*=O$N^iPr_2$), 115.2 (1C, *COC*=$OCH_3$), 166.1 (1C, *C*=O), 169.9 (1C, *C*=O); m/z ($FAB^+$) 371 (100%, $M^+$), 329 (30%), 228 (12%); HRMS $C_{19}H_{25}FeNO_3$ calcd. 371.1184, found 371.1159. Anal. calcd. for $C_{19}H_{25}NFeO_3$: C, 61.47; H, 6.79; N, 3.77; found: C, 61.58; H, 6.78; N, 3.58%.

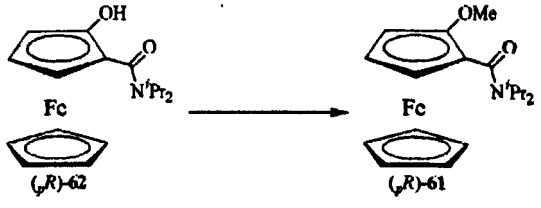
### ($_pR$)-*N,N*-Diisopropyl-2-hydroxyferrocene carboxamide (62)




To a solution of ($_pR$)-2-(*N,N*-diisopropylamido)ferrocenylacetate (($_pR$)-**60**) (8.67 g, 23.3 mmol) in ethanol (230 mL) was added a solution of NaOH (1.4 g, 35 mmol) in water (35 mL). The reaction mixture was stirred at r.t. for 30 min

before being quenched with a sat. aq. solution of $NH_4Cl$ (200 mL). The resultant mixture was extracted with DCM (3 × 100 mL). The organics were washed with water (2 × 100 mL) and brine (2 × 100 mL) then dried ($MgSO_4$). Concentration *in vacuo* gave (*pR*)-*N,N*-diisopropyl-2-hydroxyferrocene carboxamide ((*pR*)-**62**) (6.74 g, 88%) as a dark brown solid, which was used without further purification. mp = 104 – 106 °C; $R_f$ = 0.65 (30% EtOAc / hexane); IR $\nu_{max}$ 3196 (O-H stretch, H-bonded), 2967 (C-H stretch), 1588 (C=O stretch, ferrocenyl amide, H-bonded), 1503, 1345, 1209, 816 $cm^{-1}$; $^1H$ NMR: δ 1.20 – 1.60 (12H, br m, $N(CH(CH_3)_2)_2$), 3.40 – 3.60 (1H, br s, $NCH(CH_3)_2$), 3.93 (1H, t, *J* = 2.8, *CH* $Cp_{subs}$), 4.04 (1H, s, *CH* $Cp_{subs}$), 4.17 (5H, s, *CH* $Cp_{unsubs}$), 4.45 (1H, s, *CH* $Cp_{subs}$), 4.70 – 4.80 (1H, br s, $NCH(CH_3)_2$), 9.68 (1H, s, disappears with $D_2O$ shake, O*H*); $^{13}C$ NMR: δ 21.2 (4C, br, $N(CH(CH_3)_2)_2$), 46.9 (1C, br, $NCH(CH_3)_2$), 49.2 (1C, br, $NCH(CH_3)_2$), 58.0 (1C, *CH* $Cp_{subs}$), 59.6 (1C, *CC*=O$N^iPr_2$), 61.8 (1C, *CH* $Cp_{subs}$), 62.6 (1C, *CH* $Cp_{subs}$), 70.3 (5C, *CH* $Cp_{unsubs}$), 128.8 (1C, *COH*), 174.9 (1C, *CC*=O$N^iPr_2$); m/z (FAB$^+$) 329 (100%, $M^+$), 228 (15%), 200 (13%); HRMS $C_{17}H_{23}FeNO_2$ calcd. 329.1078, found 329.1105. Anal. calcd. for $C_{17}H_{23}NFeO_2$: C, 62.04; H, 7.04; N, 4.26; found: C, 61.92; H, 7.04; N, 4.26%.

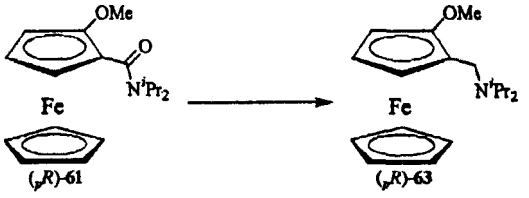
**(*pR*)-*N,N*-Diisopropyl-2-methoxyferrocene carboxamide (61)**




To a slurry of sodium hydride (60 % in mineral oil, 687 mg, 17.1 mmol) in THF (20 mL), at 0 °C, was added a solution of (*pR*)-*N,N*-diisopropyl-2-

hydroxyferrocene carboxamide ((*pR*)-**62**) (3.77 g, 11.5 mmol) in THF (120 mL). The reaction mixture was stirred at 0 °C for 45 min before addition of methyl iodide (1.4 mL, 23 mmol). The reaction mixture was allowed to warm slowly to r.t. overnight. The solvents were removed *in vacuo* and the residue was dissolved in ether (150 mL). The organics were washed with water (3 × 100 mL) and the aqueous phase was back extracted with ether (2 × 50 mL). The combined ether extracts were washed with brine (2 × 150 mL) then dried ($MgSO_4$). Concentration *in vacuo* yielded (*pR*)-*N,N*-diisopropyl-2-methoxyferrocene carboxamide ((*pR*)-**61**) (3.14 g, 80%) as a pale orange solid, which was used without further purification. mp = 132 – 134 °C; $R_f$ = 0.60 (30% EtOAc / hexane); $[\alpha]_D^{25}$ = +210.4 (c = 0.960, $CHCl_3$); IR $\nu_{max}$ 2966 (C-H stretch), 2234, 1616 (C=O stretch, ferrocenyl amide), 1413, 1323, 1257, 1136, 1049, 819 $cm^{-1}$; $^1H$ NMR: δ 1.00 – 1.20 (6H, br d, $N(CH(CH_3)_2)_2$), 1.49 (6H, br s, $N(CH(CH_3)_2)_2$), 3.40 (1H, br s, $N(CH(CH_3)_2)_2$), 3.71 (3H, s, $OCH_3$), 3.84 (1H, t, *J* = 2.5, *CH* $Cp_{subs}$), 4.03 (2H, dd and br s, *J* = 2.5, 1.5, *CH* $Cp_{subs}$ and $N(CH(CH_3)_2)_2$), 4.11 (1H, dd, *J* = 2.6, 1.5, *CH* $Cp_{subs}$), 4.34 (5H, s, *CH* $Cp_{unsubs}$); $^{13}C$ NMR: δ 21.2 (4C, br, $N(CH(CH_3)_2)_2$), 46.1 (1C, br, $NCH(CH_3)_2$), 50.6 (1C, br, $NCH(CH_3)_2$), 52.7 (1C, $OCH_3$), 58.2 (1C, *CH* $Cp_{subs}$), 60.3 (1C, *CH* $Cp_{subs}$), 64.3 (1C, *CH* $Cp_{subs}$), 70.2 (5C, *CH* $Cp_{unsubs}$), 76.3 (1C, *CC*=O$N^iPr_2$), 125.0 (1C, *C*$OCH_3$), 167.1 (1C, *CC*=O$N^iPr_2$); m/z ($FAB^+$) 343 (100%, $M^+$), 243 (6%), 86 (3%); HRMS $C_{18}H_{25}NO_2Fe$ calcd. 343.1235, found 343.1219. Anal. calcd. for $C_{18}H_{25}FeNO_2$: C, 62.99; H, 7.34; N, 4.08; found: C, 62.90; H, 7.18; N, 4.03%.

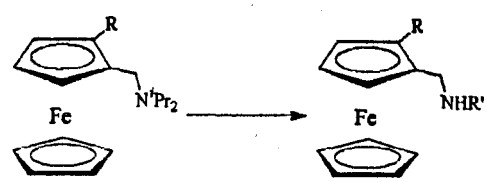
**($_p$*R*)-*N*,*N*-Diisopropyl-(2-methoxyferrocenyl)methylamine (63)**




To a slurry of lithium aluminium hydride (0.995 g, 26.2 mmol) in ether (15 mL) at 0 °C was added a solution of ($_p$*R*)-*N*,*N*-diisopropyl-2-methoxyferrocene carboxamide (($_p$*R*)-**61**) (3.00 g, 8.74 mmol) in ether (65 mL). The reaction mixture was warmed to reflux and stirred overnight. The reaction mixture was then cooled to 0 °C and water (1 mL) was added cautiously, followed by 2M NaOH (1 mL) then a further portion of water (3 mL). The reaction mixture was then stirred for a further 20 min to allow formation of a granular white solid. The reaction mixture was filtered, and the filtrate was washed with ether (10 mL). The ether layer was extracted with a 10 % solution of phosphoric acid (3 × 50 mL). The acidic aqueous layer was basified with 2M NaOH and extracted back into ether (3 × 50 mL), and these ether extracts were then washed with brine (2 × 50 mL), dried ($MgSO_4$), and concentrated *in vacuo* to yield ($_p$*R*)-*N*,*N*-diisopropyl-(2-methoxyferrocenyl)methylamine (($_p$*R*)-**63**) (2.32 g, 81%) as an orange oil, which was used without further purification. $R_f$ = 0.70 (50% EtOAc / 49% hexane / 1% $Et_3N$); $[\alpha]_D^{25} = +182.7$ (c = 1.040, $CHCl_3$); IR $\nu_{max}$ 2964 (C-H stretch), 2820 (O-$CH_3$ stretch), 1492, 1418, 1289, 1204, 1050 (C-O stretch, $COCH_3$) $cm^{-1}$; $^1H$ NMR: δ 0.99 (6H, d, *J* = 6.6, N(CH(C*H*$_3$)$_2$)$_2$), 1.02 (6H, d, *J* = 6.6, N(CH(C*H*$_3$)$_2$)$_2$), 3.04 (2H, septet, *J* = 6.6, N(C*H*(CH$_3$)$_2$)$_2$), 3.44 (1H, d, *J* = 14.3, CpC*H*$_a$H$_b$N$^i$Pr$_2$), 3.58 (1H, d, *J* = 14.3, CpCH$_a$*H*$_b$N$^i$Pr$_2$), 3.66 (3H, s, OC*H*$_3$), 3.71 (1H, t, *J* = 2.6, C*H* Cp$_{subs}$), 3.94 (1H, dd, *J* = 2.5, 1.4, C*H* Cp$_{subs}$), 4.00 (1H, s, C*H* Cp$_{subs}$) 4.12 (5H, s, C*H* Cp$_{unsubs}$);

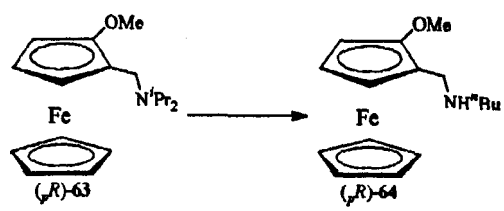
$^{13}C$ NMR: δ 20.5 (2C, $N(CH(CH_3)_2)_2$), 21.5 (2C, $N(CH(CH_3)_2)_2$), 41.1 (1C, $CH_2$), 47.6 (1C, $OCH_3$), 52.3 (1C, *C*H $Cp_{subs}$), 58.0 (2C, *C*H), 59.7 (1C, *C*H $Cp_{subs}$), 65.1 (1C, *C*H, $Cp_{subs}$), 69.0 (5C, *C*H $Cp_{unsubs}$), 77.3 (1C, $CCH_2N^iPr_2$), 126.0 (1C, $COCH_3$); m/z ($FAB^+$) 329 (100%, $M^+$), 229 (62%), 114 (11%); HRMS $C_{18}H_{27}NOFe$ calcd. 329.1442, found 329.1443. Anal. calcd. for $C_{18}H_{27}FeNO$: C, 65.66; H, 8.26; N, 4.25; found: C, 65.68; H, 8.26; N, 4.24%.

**General Procedure for the Quarternisation and Substitution of Pendant Amines**




This procedure is based on that published by Kumada *et al.*.[14] To a solution of tertiary ferrocenylamine (1 eq) in acetonitrile (5 mL $mmol^{-1}$) was added methyl iodide (60 eq). The reaction mixture was stirred at r.t. for 1½ h before the volatiles were removed *in vacuo*. The residue was dissolved in acetonitrile (5 mL $mmol^{-1}$) and a primary amine (30 eq) was added *via* syringe. The reaction mixture was stirred at r.t. overnight before removal of the solvents *in vacuo*. The residue was taken up in DCM and washed with water and brine, then dried ($MgSO_4$), and concentrated *in vacuo*.

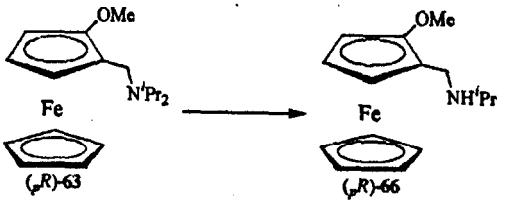
**($_pR$)-*N*-Butyl-(2-methoxyferrocenyl)methylamine (64)**




Preparation of the title compound ($_pR$)-**64**, followed the general procedure and used ($_pR$)-*N*,*N*-diisopropyl-(2-methoxyferrocenyl)methylamine (($_pR$)-**63**) (5.38

g, 16.3 mmol) and *n*-butylamine (48 mL, 490 mmol). Purification by column chromatography (silica; 49% EtOAc / 50% hexane / 1% $Et_3N$) yielded starting material **63** (1.13 g, 21%) followed by ($_pR$)-*N*-butyl-(2-methoxyferrocenyl)methylamine (($_pR$)-**64**) (3.15 g, 64%) as a pale brown oil. $R_f$ = 0.72 (50% EtOAc / 49% hexane / 1% $Et_3N$); $[\alpha]_D^{25}$ = +274.3 (c = 1.125, $CHCl_3$); IR $\nu_{max}$ 3323 (N-H stretch), 3096, 2925 (C-H stretch), 2184, 1495, 1419, 1284, 1049 (C-O stretch, $COCH_3$), 819 $cm^{-1}$; $^1H$ NMR: δ 0.90 (3H, t, *J* = 7.3, $CH_2CH_3$), 1.33 (3H, m, N*H* and $CH_2CH_2CH_3$), 1.46 (2H, m, $CH_2CH_2CH_3$), 2.60 (2H, m, $NHCH_2CH_2$), 3.42 (1H, d, *J* = 13.0, $CpCH_aH_bN^iPr_2$), 3.65 (3H, s, $OCH_3$), 3.74 (1H, t, *J* = 2.6, C*H* $Cp_{subs}$), 3.78 (1H, d, *J* = 13.0, $CpCH_aH_bN^iPr_2$) 3.93 (1H, dd, *J* = 2.6, 1.4, C*H* $Cp_{subs}$), 3.98 (1H, dd, *J* = 2.6, 1.4, C*H* $Cp_{subs}$), 4.13 (5H, s, *CH* $Cp_{unsubs}$); $^{13}C$ NMR: δ 14.2 (1C, $CH_2CH_3$), 20.7 (1C, $CH_2CH_2CH_3$), 32.4 (1C, $CH_2CH_2CH_3$), 46.5 (1C $NHCH_2CH_2$), 49.4 (1C, $CpCH_2NH^nBu$), 52.3 (1C, CH $Cp_{subs}$), 57.6 (1C, $OCH_3$), 59.8 (1C, CH $Cp_{subs}$), 63.9 (1C, CH $Cp_{subs}$), 68.9 (5C, CH $Cp_{unsubs}$), 75.4 (1C, $CCH_2NH^nBu$), 126.3 (1C, $COCH_3$); m/z ($FAB^+$) 301 (34%, $M^+$), 243 (24%), 229 (100%), 73 (44%); HRMS $C_{16}H_{23}FeNO$ calcd. 301.1129, found 301.1139. Anal. calcd. for $C_{16}H_{23}FeNO$: C, 63.76; H, 7.70; N, 4.65; found: C, 63.40; H, 7.59; N, 4.78%.

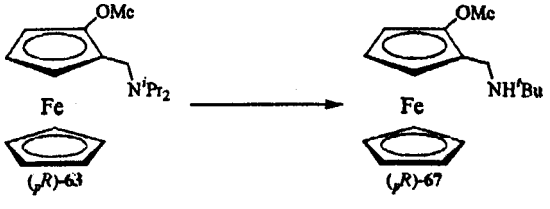
**($_pR$)-*N*-Isopropyl-(2-methoxyferrocenyl)methylamine (66)**




Preparation of the title compound ($_pR$)-**66**, followed the general procedure and used ($_pR$)-*N,N*-diisopropyl-(2-methoxyferrocenyl)methylamine (($_pR$)-**63**) (850

mg, 2.58 mmol) and isopropylamine (6.6 mL, 77 mmol). Purification by column chromatography (silica; 20% EtOAc / 79% hexane / 1% $Et_3N$), yielded starting material ($_pR$)-**63** (0.129 g, 15%) followed by ($_pR$)-*N*-isopropyl-(2-methoxyferrocenyl)-methylamine (($_pR$)-**66**) (0.188 g, 25%) as an orange oil. $R_f$ = 0.22 (50% EtOAc / 49% hexane / 1% $Et_3N$); $[\alpha]_D^{23} = +282.8$ (c = 1.040, $CHCl_3$); IR $\nu_{max}$ 3313 (N-H stretch), 2959 (C-H stretch), 1638, 1382, 1105, 1049, 1000 $cm^{-1}$; $^1H$ NMR: δ 1.05 (3H, d, *J* = 6.2, $NCH(CH_3)_2$), 1.06 (3H, d, *J* = 6.2, $NCH(CH_3)_2$), 1.37 (1H, br s, N*H*), 2.83 (1H, quintet, *J* = 6.2, $NCH(CH_3)_2$), 3.44 (1H, d, *J* = 12.9, $CpCH_aH_bNH^iPr$), 3.65 (3H, s, $OCH_3$), 3.75 (2H, m, $CpCH_aH_bNH^iPr$ and C*H* $Cp_{subs}$), 3.93 (1H, dd, *J* = 2.6, 1.5, C*H* $Cp_{subs}$), 3.98 (1H, dd, *J* = 2.6, 1.5, C*H* $Cp_{subs}$), 4.13 (5H, s, C*H* $Cp_{unsubs}$); $^{13}C$ NMR: δ 22.8 ($NCH(CH_3)_2$), 23.1 ($NCH(CH_3)_2$), 43.9 ($CpCH_2NH^iPr$), 47.9, 52.2, 57.5 ($OCH_3$), 59.7, 63.6, 68.8 (5C, *C*H $Cp_{unsubs}$), 75.4 ($CCH_2NH^iPr$), 126.1 ($COCH_3$); m/z (EI+) 287 (100%, $M^+$), 255 (32%), 229 (24%), 121 (23%); HRMS $C_{15}H_{21}FeNO$ calcd. 287.0973, found 287.0975. Anal. calcd. for $C_{15}H_{21}FeNO$: C, 62.73; H, 7.37; N, 4.88; found: C, 62.45; H, 7.18; N, 4.79%.

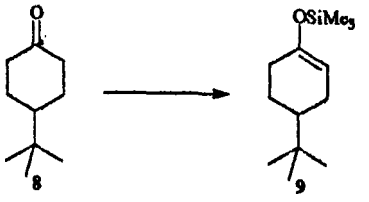
**($_pR$)-*N*-*tert*-Butyl-(2-methoxyferrocenyl)methylamine (67)**




Preparation of the title compound ($_pR$)-**67**, followed the general procedure and used ($_pR$)-*N*,*N*-diisopropyl-(2-methoxyferrocenyl)methylamine (($_pR$)-**63**) (883 mg, 2.68 mmol) and *tert*-butylamine (8.45 mL, 80.5 mmol). Purification by column chromatography (silica; 20% EtOAc / 79% hexane / 1% $Et_3N$), yielded

starting material ($_pR$)-**63** (0.115 g, 13%) followed by ($_pR$)-*N*-*tert*-butyl-(2-methoxyferrocenyl)methylamine (($_pR$)-**67**) (398 mg, 49%) as an orange oil. $R_f$ = 0.22 (50% EtOAc / 49% hexane / 1% $Et_3N$); $[\alpha]_D^{28}$ = +275.3 (c = 0.975, $CHCl_3$); IR $\nu_{max}$ 3307 (N-H stretch), 2961 (C-H stretch), 1490, 1364, 1130, 1104, 1050, 1000 $cm^{-1}$; $^1H$ NMR: δ 1.15 (9H, s, NHC($CH_3$)$_3$), 1.25 (1H, br s, N*H*$^t$Bu), 3.41 (1H, d, *J* = 11.8, CpC$H_a$H$_b$NH$^t$Bu), 3.65 (3H, s, OC$H_3$), 3.67 (1H, d, *J* = 11.8, CpCH$_a$$H_b$NH$^t$Bu), 3.72 (1H, t, *J* = 2.6, C*H* Cp$_{subs}$), 3.96 (2H, m, C*H* Cp$_{subs}$), 4.12 (5H, s, C*H* Cp$_{unsubs}$); $^{13}C$ NMR: δ 29.1 (3C, C($CH_3$)$_3$), 39.4 (CpCH$_2$NH$^t$Bu), 50.6 (*C*(CH$_3$)$_3$), 52.3 (*C*H Cp$_{subs}$), 57.6 (OCH$_3$), 59.7 (CH Cp$_{subs}$), 63.4 (*C*H Cp$_{subs}$), 68.8 (5C, *C*H Cp$_{unsubs}$), 76.3 (CpCH$_2$NH$^t$Bu), 126.0 (*C*OCH$_3$); m/z (FAB$^+$) 301 (100%, M$^+$), 229 (80%), 57 (16%); HRMS $C_{16}H_{23}FeNO$ calcd. 301.1129, found 301.1150. Anal. calcd. for $C_{16}H_{23}FeNO$: *C, 63.76; H, 7.70; N, 4.65; found: C, 63.78; H, 7.58; N, 4.38%.*

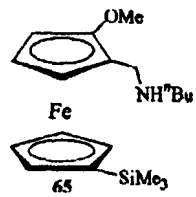
**Preliminary General Procedure for the Deprotonation of 4-*tert*-Butylcyclohexanone (8)**




To a solution of ferrocenyl-base (1.25 eq) in THF (6 mL mmol$^{-1}$) at 0 °C was added TMEDA (1.25 eq), followed by *n*-butyl lithium (1.25 eq). The reaction mixture was stirred for 1 h, then cooled to –78 °C before addition of chlorotrimethylsilane (5.00 eq). The reaction mixture was stirred for 20 min before addition of a solution of 4-*tert*-butylcyclohexanone (**8**) (1.00 eq) in THF (9 mL mmol$^{-1}$). The reaction mixture was stirred at –78 °C for 5 h before addition of a sat. solution of $NaHCO_3$ (10 mL mmol$^{-1}$). The mixture was left to

warm slowly to r.t. and the phases were separated. The organics were washed with $NaHCO_3$ (3 portions) and the combined aqueous layers were back-extracted with ether (3 portions). The combined ether layers were dried ($Na_2SO_4$), and concentrated *in vacuo*. Purification by gravity column chromatography (deactivated alumina; hexane to 20% EtOAc / 80% hexane) yielded 4-*tert*-butyl-1-trimethylsilyloxycyclohex-1-ene (**9**) as a clear, colourless oil. $R_f$ = 0.58 (100% hexane on alumina); IR $\nu_{max}$ 3021, 2957 (C-H stretch, alkane), 2967, 1673 (C=C stretch, alkene), 1364, 1252, 1193, 890, 845 $cm^{-1}$; $^1H$ NMR: δ 0.19 (9H, s, OSi($CH_3$)$_3$), 0.88 (9H, s, C($CH_3$)$_3$), 1.20 – 1.28 (2H, m), 1.79 – 1.84 (2H, m), 1.98 – 2.10 (3H, m), 4.84 – 4.86 (1H, m, C=C*H*); $^{13}C$ NMR: δ 0.43 (OSi($CH_3$)$_3$), 24.5 ($CH_2$), 25.2 ($CH_2$), 27.5 (3C C($CH_3$)$_3$), 31.1 ($CH_2$), 32.2 ($C(CH_3)_3$), 44.1 (*C*H), 104.0 (C=*C*H), 150.4 (*C*=CH). Further elution yielded ferrocenyl amines, which were further purified, as described below.

**(±)-*N*-Butyl-(2-methoxy-1'-trimethylsilyl-ferrocenyl)methylamine (65)**

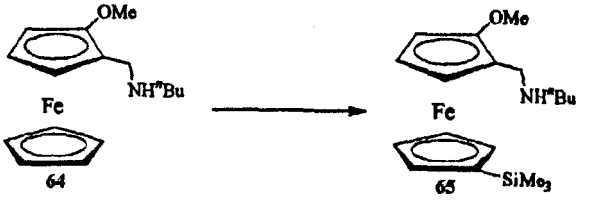



65

Purification of the recovered amine by column chromatography (silica; 25 % EtOAc / 1% $Et_3N$ / 74% hexane) yielded (±)-*N*-Butyl-(2-methoxy-1'-trimethylsilyl-ferrocenyl)methylamine (**65**) (252 mg, 17%) as a yellow oil. $R_f$ = 0.61 (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 3319 (N-H stretch), 2887 (C-H stretch), 2337, 1645, 1456, 1379, 1097, 1050, 900, 867 $cm^{-1}$; $^1H$ NMR: δ 0.21 (9H, s, Si($CH_3$)$_3$), 0.89 (3H, t, *J* = 7.3, $CH_2CH_3$), 1.33 (3H, m,

$CH_2CH_2CH_3$ and NH), 1.45 (2H, m, $CH_2CH_2CH_2$), 2.59 (2H, m, $NHCH_2CH_2$), 3.40 (1H, d, $J$ = 13.0, $CpCH_aH_bNH$), 3.63 (3H, s, $OCH_3$), 3.68 (1H, t, $J$ = 2.6, CH Cp), 3.77 (1H, d, $J$ = 13.0, $CpCH_aH_bNH$), 3.88 (1H, dd, $J$ = 2.6, 1.4, CH Cp), 3.95 (1H, dd, $J$ = 2.6, 1.4, CH Cp), 4.03 (1H, apparent quintet, $J$ = 1.1, CH Cp'), 4.12 (1H, apparent quintet, $J$ = 1.1, CH Cp'), 4.20 (1H, apparent sextet, $J$ = 1.1, CH Cp'), 4.31 (1H, apparent sextet, $J$ = 1.1, CH Cp'); $^{13}$C NMR: δ -0.26 (3C, $Si(CH_3)_3$), 14.1 ($CH_2CH_3$), 20.5 ($CH_2CH_2CH_3$), 32.2 ($CH_2CH_2CH_3$), 46.4 ($NHCH_2CH_2$), 49.2 ($CpCH_2NH$), 52.4 (CH Cp), 57.4 ($OCH_3$), 60.1 (CH Cp), 64.2 (CH Cp), 71.9 ($CSiMe_3$ Cp'), 72.3 (CH Cp'), 72.6 (CH Cp'), 72.7 (CH Cp'), 73.8 (CH Cp'), 74.8 ($CCH_2NHnBu$ Cp), 126.0 (COMe Cp); m/z ($FAB^+$) 373 (100%), 301 (74%), 286 (16%), 73 (73%); HRMS $C_{19}H_{31}FeNOSi$ calcd. 373.1524, found 373.1529. Anal. calcd. for $C_{19}H_{31}FeNOSi$: C, 61.12; H, 8.37; N, 3.75; found: C, 61.20; H, 8.21; N, 3.57%. Followed by (±)-*N*-butyl-(2-methoxyferrocenyl)methylamine (**64**) (760 mg, 62%) with data in agreement with that reported above.

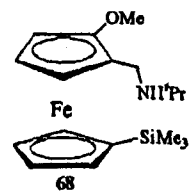
**(±)-*N*-Butyl-(2-methoxy-1'-trimethylsilylferrocenyl)methylamine (65)**




To a solution of (±)-*N*-butyl-(2-methoxyferrocenyl)methylamine (**64**) (700 mg, 2.32 mmol) in THF (35 mL) at 0 °C was added *n*-butyl lithium (2.45M, 2.1 mL, 5.2 mmol). The reaction mixture was stirred for 40 min before being cooled to –78 °C. Chlorotrimethylsilane (1.5 mL, 12 mmol) was added and the reaction mixture was left to stir at –78 °C overnight. A sat. aq. solution of $NaHCO_3$ (20 mL) was added and the reaction mixture was allowed to warm

slowly to r.t.. The phases were separated and the organics were washed with further portions of sat. $NaHCO_3$ solution (3 × 20 mL). The combined aqueous layers were back-extracted with ether (3 × 20 mL) and the combined organics were washed with brine (3 × 25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by column chromatography (silica; 25% EtOAc / 74% hexane / 1% $Et_3N$), yielded a mixture of silylated products (81 mg) and (±)-*N*-butyl-(2-methoxy-1'-trimethylsilylferrocenyl)-methylamine (**65**) (461 mg, 53%) as a yellow oil, with data in agreement with that reported above. Followed by starting material (**64**) (145 mg, 21 %) $R_f$ = 0.72 (50% EtOAc / 49% hexane / 1% $Et_3N$).

**(±)-*N*-Isopropyl-(2-methoxy-1'-trimethylsilylferrocenyl)methylamine (68)**

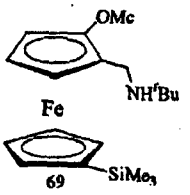



**68**

Purification by column chromatography (silica; 40% EtOAc / 1% $Et_3N$ / 59% hexane) yielded (±)-*N*-isopropyl-(2-methoxy-1'-trimethylsilylferrocenyl)-methylamine (**68**) (40 mg, 18%) as a yellow oil, $R_f$ = 0.30 (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 3310 (N-H stretch), 2930 (C-H stretch, alkane), 1668, 1488, 1462, 1382, 1113, 1050, 901 $cm^{-1}$; $^1H$ NMR: δ 0.22 (9H, s, $Si(CH_3)_3$), 1.04 (3H, d, $J$ = 6.2, $NHCH(CH_3)_2$), 1.05 (3H, d, $J$ = 6.2, $NHCH(CH_3)_2$), 1.26 (1H, br s, N*H*), 2.82 (1H, septet, $J$ = 6.2, $NHCH(CH_3)_2$), 3.42 (1H, d, $J$ = 13.0, $CpCH_aH_bNH$), 3.64 (3H, s, $OCH_3$), 3.68 (1H, t, $J$ = 2.6, C*H* Cp), 3.76 (1H, d, $J$ = 13.0, $CpCH_aH_bNH$), 3.89 (1H, dd, $J$ = 2.5, 1.4, C*H* Cp), 3.96 (1H, dd, $J$ = 2.5, 1.4, C*H* Cp), 4.03 (1H, m, C*H* Cp'), 4.12 (1H, m,

*CH* Cp'), 4.20 (1H, m, *CH* Cp'), 4.32 (1H, m, *CH* Cp'); m/z ($EI^+$) 359 (100%), 327 (31%), 286 (17%), 172 (10%), 73 (10%); HRMS $C_{18}H_{29}FeNOSi$ calcd. 359.1368, found 359.1368. Followed by *N*-isopropyl-(2-methoxyferrocenyl)methylamine (66) (23 mg, 13%) with data in agreement with that reported above.

**(±)-*N*-*tert*-Butyl-(2-methoxy-1'-trimethylsilylferrocenyl)methylamine (69)**

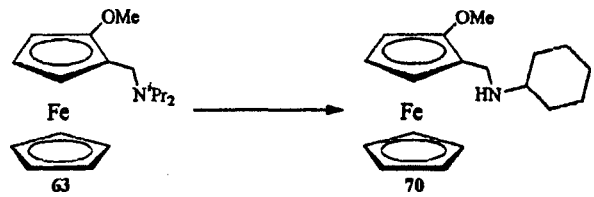


69

Purification of the recovered amine by column chromatography (silica; 40 % EtOAc / 1% $Et_3N$ / 59% hexane) yielded (±)-*N*-*tert*-Butyl-(2-methoxy-1'-trimethylsilylferrocenyl)methylamine (69) (32 mg, 10%) as a yellow oil. $R_f$ = 0.30 (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 3306 (N-H stretch), 2946 (C-H stretch), 2864, 2180, 1418, 1287, 1251, 1130, 1050, 1035, 831 $cm^{-1}$; $^1H$ NMR: δ 0.22 (9H, s, $Si(CH_3)_3$), 1.14 (9H, s, $NHC(CH_3)_3$), 1.20 (1H, br s, N*H*), 3.39 (1H, d, *J* = 12.0, $CpCH_aH_bNH$), 3.64 (3H, s, $OCH_3$), 3.67 (1H, d, *J* = 11.9, $CpCH_aH_bNH$), 3.67 (1H, t, *J* = 2.7, *CH* Cp), 3.92 (1H, dd, *J* = 2.6, 1.4, *CH* Cp), 3.95 (1H, dd, *J* = 2.5, 1.4, *CH* Cp), 4.04 (1H, t, *J* = 1.1, *CH* Cp'), 4.12 (1H, t, *J* = 1.1, *CH* Cp'), 4.21 (1H, apparent sextet, *J* = 1.1, *CH* Cp'), 4.32 (1H, apparent sextet, *J* = 1.1, *CH* Cp'); $^{13}C$ NMR: δ 0.02 (3C, $Si(CH_3)_3$), 29.1 (3C, $C(CH_3)_3$), 39.4 ($CH_2$), 50.6 ($C(CH_3)_3$), 52.6 (*CH* Cp), 57.5 ($OCH_3$), 60.2 (*CH* Cp), 63.8 (*CH* Cp), 71.9 ($CSi(CH_3)_3$), 72.3 (*CH* Cp'), 72.6 (*CH* Cp'), 72.7 (*CH* Cp'), 73.9 (*CH* Cp'), 76.0 ($CCH_2NH^tBu$), 125.9 ($COCH_3$); m/z ($FAB^+$) 373 ($M^+$, 100%), 301 (52%), 147 (16%), 73 (45%), 57 (22%); HRMS $C_{19}H_{31}FeNOSi$ calcd. 373.1524, found 373.1546. Followed by *N*-*tert*-butyl-(2-

methoxyferrocenyl)methylamine (67) (120 mg, 48%) with data in agreement with that reported above.

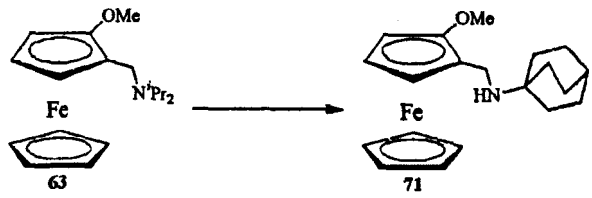
**(±)-*N*-Cyclohexyl-(2-methoxyferrocenyl)methylamine (70)**




Preparation of the title compound **70**, followed the general procedure and used (±)-*N,N*-diisopropyl-(2-methoxyferrocenyl)methylamine (**63**) (500 mg, 1.52 mmol) and cyclohexamine (5.2 mL, 45 mmol). Purification by column chromatography (silica; 30% EtOAc / 69% hexane / 1% $Et_3N$), yielded starting material **63** (81 mg, 16%) followed by (±)-*N*-cyclohexyl-(2-methoxyferrocenyl)methylamine (**70**) (360 mg, 72%) as an orange oil. $R_f$ = 0.50 (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 3306 (N-H stretch), 2841, (C-H stretch), 2662, 2506, 1715, 1643, 1456, 1368, 1350, 1093, 1058, 996, 890 $cm^{-1}$; $^1H$ NMR: δ 1.10 – 1.20 (5H, m, cyclohexyl), 1.27 (1H, br s, N*H*), 1.60 (1H, m, cyclohexyl), 1.72 (2H, m, cyclohexyl), 1.88 (2H, m, cyclohexyl), 2.47 (1H, m, NHC*H*, cyclohexyl), 3.48 (1H, d, $J$ = 12.9, CpC$H_aH_b$NHCy), 3.65 (3H, s, OC$H_3$), 3.74 (1H, t, $J$ = 2.6, C*H* $Cp_{subs}$), 3.78 (1H, d, $J$ = 12.9, CpCH$_a$$H_b$NHCy), 3.93 (1H, dd, $J$ = 2.6, 1.4, C*H* $Cp_{subs}$), 3.98 (1H, dd, $J$ = 2.6, 1.4, C*H* $Cp_{subs}$), 4.13 (5H, s, C*H* $Cp_{unsubs}$); $^{13}C$ NMR: δ 25.06 ($CH_2$, cyclohexyl), 25.10 ($CH_2$, cyclohexyl), 26.2 ($CH_2$, cyclohexyl), 33.4 ($CH_2$, cyclohexyl), 33.6 ($CH_2$, cyclohexyl), 43.3 ($CH_2$NHCy), 52.2 (*C*H, cyclohexyl), 56.2 (*C*H $Cp_{subs}$), 57.5 ($OCH_3$), 59.7 (*C*H $Cp_{subs}$), 63.6 (*C*H $Cp_{subs}$), 68.8 (5C, *C*H $Cp_{unsubs}$), 75.5 (*C*CH$_2$NHCy), 126.1 (*C*OCH$_3$); m/z (FAB$^+$) 327 (100%,

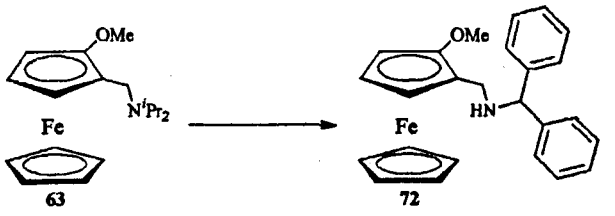
$M^+$), 229 (97%), 73 (11%), 55 (11%); HRMS $C_{18}H_{25}FeNO$ calcd. 327.1286, found 327.1310.

**(±)-*N*-Adamantyl-(2-methoxyferrocenyl)methylamine (71)**



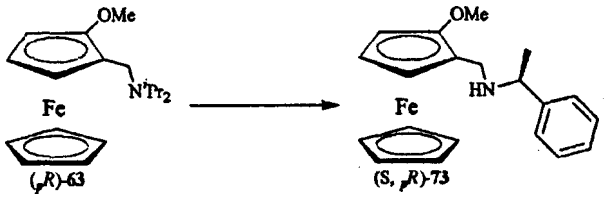

Preparation of the title compound **71**, followed the general procedure and used (±)-*N,N*-diisopropyl-(2-methoxyferrocenyl)methylamine (**63**) (500 mg, 1.52 mmol) and adamantanamine (5.0 g, 33 mmol). Purification by column chromatography (silica; 20% EtOAc / 79% hexane / 1% $Et_3N$), yielded starting material **63** (0.171 g, 34%) followed by (±)-*N*-adamantyl-(2-methoxyferrocenyl)methylamine (**71**) (0.347 g, 65%) as an orange oil. $R_f$ = 0.55 (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 3305 (N-H stretch), 2903, (C-H stretch), 1491, 1450, 1418, 1284, 1104, 1049, 1000, 815, 755 $cm^{-1}$; $^1H$ NMR: δ 1.26 (1H, br s, N*H*), 1.60 (11H, m, adamantyl), 2.08 (2H, s, adamantyl), 3.45 (1H, d, $J$ = 12.0, CpC$H_a$H$_b$NHAd), 3.66 (3H, s, OC$H_3$), 3.69 (1H, d, $J$ = 12.0, CpCH$_a$$H_b$NHAd), 3.72 (1H, t, $J$ = 2.6, C*H* Cp$_{subs}$), 3.96 (1H, br s, C*H* Cp$_{subs}$), 3.97 (1H, br s, C*H* Cp$_{subs}$), 4.13 (5H, s, C*H* Cp$_{unsubs}$); $^{13}C$ NMR: δ 29.8 (*C*H, adamantyl), 36.9 ($CH_2$, adamantyl), 37.3 ($CH_2$, adamantyl), 42.9 ($CH_2$NHAd), 50.7 (*C*, adamantyl), 52.4 (*C*H Cp$_{subs}$), 57.6 ($OCH_3$), 59.7 (*C*H Cp$_{subs}$), 63.4 (*C*H Cp$_{subs}$), 68.8 (5C, *C*H Cp$_{unsubs}$), 76.6 (*C*$CH_2$NHAd), 126.0 (*C*$OCH_3$). Mass spectrum was unsatisfactory.

**(±)-*N*-Diphenylmethyl-(2-methoxyferrocenyl)methylamine (72)**




Preparation of the title compound **72**, followed the general procedure and used (±)-*N,N*-diisopropyl-(2-methoxyferrocenyl)methylamine (**63**) (500 mg, 1.52 mmol) and aminodiphenylmethane (7.9 mL, 46 mmol). The residue was distilled to remove excess aminodiphenylmethane (114 °C / 1 mmHg). Purification by column chromatography (silica; 20% EtOAc / 79% hexane / 1% $Et_3N$), yielded (±)-*N*-diphenylmethyl-(2-methoxyferrocenyl)-methylamine (**72**) (0.468 g, 75%) as an orange oil. $R_f$ = 0.64 (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 3100 (N-H stretch), 2933, (C-H stretch), 2822, 1491, 1453, 1104, 1048 $cm^{-1}$; $^1H$ NMR: δ 1.82 (1H, s, N*H*), 3.36 (1H, d, *J* = 13.2, CpC*H*$_a$H$_b$NHR), 3.62 (3H, s, OC*H*$_3$), 3.74 (1H, t, *J* = 2.6, C*H* Cp$_{subs}$), 3.76 (1H, d, *J* = 13.2, CpCH$_a$*H*$_b$NHR), 3.88 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$), 3.98 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$), 4.08 (5H, s, C*H* Cp$_{unsubs}$), 4.88 (1H, s, C*H*Ph$_2$), 7.19 (2H, m, C*H* Ph), 7.28 (4H, m, C*H* Ph), 7.42 (4H, m, C*H* Ph); $^{13}C$ NMR: δ 44.6 (*C*H$_2$NHCHPh$_2$), 52.4 (*C*H), 57.6 (OCH$_3$), 59.7 (CH), 63.8 (CH), 66.6 (*C*H), 68.8 (5C *C*H Cp$_{unsubs}$), 75.2 (*C*CH$_2$NHCHPh$_2$), 126.1 (*C*OCH$_3$), 126.9 (*C*H Ph), 127.4 (*C*H Ph), 127.5 (*C*H Ph), 128.5 (*C*H Ph), 144.1 (*C* Ph), 144.6 (*C* Ph); m/z (FAB$^+$) 411 (100%, M$^+$), 229 (51%), 167 (23%), 154 (11%), 136 (10%), 69 (12%), 57 (14%), 55 (15%); HRMS $C_{25}H_{25}FeNO$ calcd. 411.1286, found 411.1278. Anal. calcd. for $C_{25}H_{25}FeNO$: C, 73.00; H, 6.13; N, 3.41; found: C, 72.92; H, 6.11; N, 3.58%.

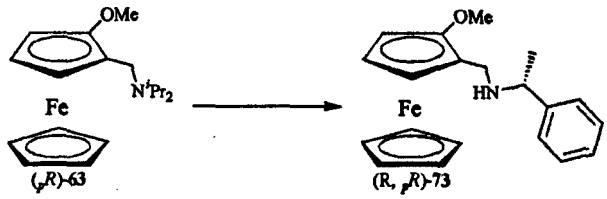
**(*S*, $_p$*R*)-*N*-α-Methylbenzyl-(2-methoxyferrocenyl)methylamine (73)**




Preparation of the title compound ((*S*, $_p$*R*)-**73**), followed the general procedure and used ($_p$*R*)-*N*,*N*-diisopropyl-(2-methoxyferrocenyl)methylamine (($_p$*R*)-**63**) (1.97 g, 5.98 mmol) and (*S*)-(-)-α-methylbenzylamine (23.1 mL, 179 mmol). The residue was distilled to remove excess (*S*)-(-)-α-methylbenzylamine (46 °C / 1 mmHg). Purification by column chromatography (silica; 5% EtOAc / 94% petrol / 1% $Et_3N$), yielded (*S*, $_p$*R*)-*N*-α-methylbenzyl-(2-methoxyferrocenyl)methylamine ((*S*, $_p$*R*)-**73**) (0.525 g, 25%) as an orange oil. $R_f$ = 0.25 (50% EtOAc / 49% petrol / 1% $Et_3N$); $[\alpha]_D^{27}$ = +162.1 (c = 1.018, $CHCl_3$); IR $\nu_{max}$ 2932, (C-H stretch), 1729, 1490, 1452, 1372, 1287, 1104, 1049, 1000 $cm^{-1}$; $^1H$ NMR: δ 1.32 (3H, d, *J* = 6.6, CH(C*H*$_3$)Ph), 1.61 (1H, s, N*H*), 3.28 (1H, d, *J* = 12.8, CpC*H*$_a$H$_b$NHR), 3.62 (3H, s, OC*H*$_3$), 3.64 (1H, d, *J* = 12.8, CpCH$_a$*H*$_b$NHR), 3.71 (1H, t, *J* = 2.7, C*H* Cp$_{subs}$), 3.83 (1H, q, *J* = 6.6, C*H*(CH$_3$)Ph), 3.87 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$), 3.96 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$), 4.06 (5H, s, C*H* Cp$_{unsubs}$), 7.25 (1H, m, C*H* Ph), 7.35 (4H, m, C*H* Ph); $^{13}C$ NMR: δ 24.5 (CH(*C*H$_3$)Ph), 44.4 (*C*H$_2$), 52.2 (*C*H Cp$_{subs}$), 57.4 (O*C*H$_3$), 57.9 (*C*H(CH$_3$)Ph), 59.7 (*C*H Cp$_{subs}$), 63.5 (*C*H Cp$_{subs}$), 68.7 (5C, *C*H Cp$_{unsubs}$), 75.3 (*C*CH$_2$NHR), 126.0 (*C*OCH$_3$), 126.8 (*C*H Ph), 126.8 (*C*H Ph), 128.4 (*C*H Ph), 146.0 (*C* Ph); m/z (FAB$^+$) 349 (82%, M$^+$), 229 (100%), 73 (55%), 55 (57%); HRMS $C_{20}H_{23}FeNO$ calcd. 349.1129, found 349.1118. Anal. calcd. for $C_{20}H_{23}FeNO$: C, 68.78; H, 6.64; N, 4.01; found: C, 68.35; H, 6.51; N, 3.71%. Also isolated, and inseparable by column chromatography,

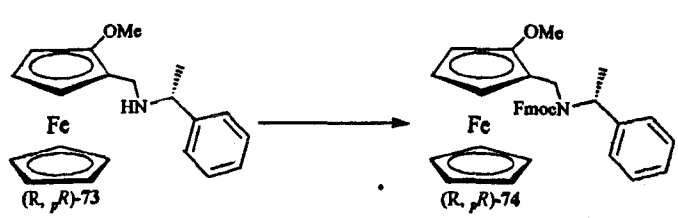
was (*S*, $_p$*R*)-*N*-α-methylbenzyl-(2-methoxyferrocenyl)methylamine ((*S*, $_p$*R*)-**73**) contaminated with about 5% ($_p$*R*)-*N,N*-diisopropyl-(2-methoxyferrocenyl)-methylamine (($_p$*R*)-**63**) (800 mg, 38%).

**(*R*, $_p$*R*)-*N*-α-Methylbenzyl-(2-methoxyferrocenyl)methylamine (73)**




Preparation of the title compound ((*R*, $_p$*R*)-**73**), followed the general procedure and used ($_p$*R*)-*N,N*-diisopropyl-(2-methoxyferrocenyl)methylamine (($_p$*R*)-**63**) (2.03 g, 6.17 mmol) and (*R*)-(+)-α-methylbenzylamine (23.5 mL, 182 mmol). The residue was distilled to remove excess (*R*)-(+)-α-methylbenzylamine (44 – 48 °C / 1 mmHg). Purification by column chromatography (silica; 5% EtOAc / 95% petrol), yielded (*R*, $_p$*R*)-*N*-α-methylbenzyl-(2-methoxyferrocenyl)-methylamine ((*R*, $_p$*R*)-**73**) contaminated with ($_p$*R*)-*N,N*-diisopropyl-(2-methoxyferrocenyl)methylamine (($_p$*R*)-**63**) (about 5% by $^1$H NMR) (1.48 g). Clean product was obtained after Fmoc protection and deprotection, and full data is reported below.

**(*R*, $_p$*R*)-*N*-Fmoc-*N*-α-Methylbenzyl-(2-methoxyferrocenyl)methylamine (74)**

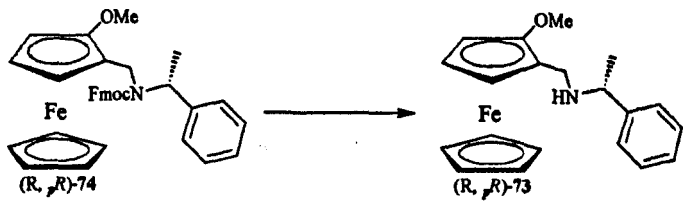



To a solution of 9-fluorenylmethylchloroformate (1.10 g, 4.24 mmol) in ether (80 mL) at 0 °C, was added slowly a solution of (*R*, $_p$*R*)-*N*-α-methylbenzyl-(2-

methoxyferrocenyl)methylamine ((*R*, $_p$*R*)-**73**) (1.48 g, 4.24 mmol) and $Et_3N$ (0.59 mL, 4.24 mmol) in ether (132 mL). The mixture was stirred at 0 °C for 20 min, then warmed to r.t. for 20 min. The mixture was filtered to remove triethylamine hydrochloride. The organics were washed with water (3 × 40 mL), dried ($MgSO_4$) and concentrated *in vacuo* to yield an orange solid. Purification by column chromatography (silica; 5% EtOAc / 95% petrol to 20% EtOAc / 80% petrol), yielded (*R*, $_p$*R*)-*N*-Fmoc-*N*-α-methylbenzyl-(2-methoxyferrocenyl)-methylamine ((*R*, $_p$*R*)-**74**) (1.56 g, 64%) as an orange solid. mp = 135.0 – 136.7 °C; $R_f$ = 0.85 (50% EtOAc / 1% $Et_3N$ / petrol); $[\alpha]_D^{29}$ = +87.3 (c = 0.985, $CHCl_3$); IR $\nu_{max}$ 2938 (C-H stretch), 1682 (C=O stretch, carbamate), 1453, 1323, 1134, 1104, 1050, 999 $cm^{-1}$; $^1$H NMR: δ 1.3 – 1.5 (br s), 3.5 – 4.8 (br m), 5.1 (br s), 5.3 (br s), 7.0 – 7.4 (br m), 7.5 – 7.8 (br m); $^1$H NMR (DMSO @ 90 °C): δ 1.29 (3H, d, *J* = 7.1, CH(C*H*$_3$)Ph), 3.58 (3H, s, OC*H*$_3$), 3.69 (1H, t, *J* = 2.6, C*H* $Cp_{subs}$), 3.72 (1H, br s, C*H* $Cp_{subs}$), 3.79 (1H, d, *J* = 15.2, CpC*H*$_a$H$_b$NFmocR), 4.02 (6H, s, C*H* $Cp_{subs}$ and C*H* $Cp_{unsubs}$), 4.18 (1H, br d, *J* = 15.1, CpCH$_a$*H*$_b$NFmocR), 4.25 (1H, t, *J* = 5.5, Fmoc C*H*), 4.56 (2H, m, Fmoc C*H*$_2$), 4.95 (1H, q, *J* = 7.0, C*H*(CH$_3$)Ph), 7.06 (2H, d, *J* = 7.3), 7.26 (5H, m), 7.42 (2H, t, *J* = 7.4), 7.60 (2H, dd, J = 7.0, 3.4), 7.88 (2H, m); $^{13}$C NMR (DMSO @ 90 °C): δ 17.3 (CH(*C*H$_3$)Ph), 41.1 (CpCH$_2$NFmocR), 47.8 (Fmoc *C*H), 52.4 (*C*H $Cp_{subs}$), 54.7 (*C*H(CH$_3$)Ph), 58.0 (OCH$_3$), 60.6 (*C*H $Cp_{subs}$), 64.5 (*C*H $Cp_{subs}$), 66.3 (Fmoc *C*H$_2$), 69.1 (5C, *C*H $Cp_{unsubs}$), 74.6 (*C*CH$_2$NFmocR), 120.4 (*C*H), 120.5 (*C*H), 125.2 (*C*H), 125.3 (*C*H), 125.7 (*C*OCH$_3$), 127.1 (*C*H), 127.2 (*C*H), 127.4 (*C*H), 127.5 (*C*H), 128.0 (*C*H), 128.5 (*C*H), 141.5 (2C, *C*), 142.1 (*C*), 144.4 (*C*), 144.7 (*C*), 155.9 (*C*=O); m/z (FAB$^+$) 571 (88%, M$^+$), 229 (50%), 154 (100%), 136 (76%), 69 (44%), 57

(48%); HRMS $C_{35}H_{33}FeNO_3$ calcd. 571.1810, found 571.1781. Anal. calcd. for $C_{35}H_{33}FeNO_3$: C, 73.56; H, 5.82; N, 2.45; found: C, 73.54; H, 5.75; N, 2.41%.

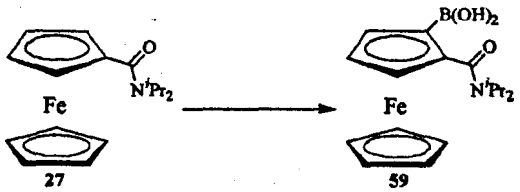
**(*R*, $_p$*R*)-*N*-α-Methylbenzyl-(2-methoxyferrocenyl)methylamine (73)**




To a stirred solution of (*R*, $_p$*R*)-*N*-Fmoc-*N*-α-methylbenzyl-(2-methoxyferrocenyl)methylamine ((*R*, $_p$*R*)-**74**) (927 mg, 1.62 mmol) in DMF (97 mL) was added piperidine (24.3 mL). The reaction mixture was stirred at r.t. for 2 h, then concentrated *in vacuo*. The residue was taken up in DCM (2 × 50 mL) and washed with a sat. solution of $NaHCO_3$ (3 × 50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography (silica; 20% EtOAc / 79% petrol / 1% $Et_3N$), yielded (*R*, $_p$*R*)-*N*-α-methylbenzyl-(2-methoxyferrocenyl)methylamine ((*R*, $_p$*R*)-**73**) (479 mg, 85%) as an orange oil. $R_f$ = 0.24 (50% EtOAc / 49% petrol / 1% $Et_3N$); $[\alpha]_D^{27}$ = +259.0 (c = 1.000, $CHCl_3$); IR $\nu_{max}$ 3316 (N-H stretch), 2930, (C-H stretch), 1643, 1488, 1453, 1373, 1290, 1104, 1049, 1000 $cm^{-1}$; $^1H$ NMR: δ 1.30 (3H, d, *J* = 6.6, CH(C*H*$_3$)Ph), 1.84 (1H, s, N*H*), 3.23 (1H, d, *J* = 13.2, CpC*H*$_a$H$_b$NHR), 3.64 (3H, s, OC*H*$_3$), 3.69 (1H, d, *J* = 13.1, CpCH$_a$*H*$_b$NHR), 3.73 (1H, t, *J* = 2.6, C*H* Cp$_{subs}$), 3.73 (1H, q, *J* = 6.6, C*H*(CH$_3$)Ph), 3.84 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$), 3.97 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$), 4.08 (5H, s, C*H* Cp$_{unsubs}$), 7.25 (1H, m, C*H* Ph), 7.35 (4H, m, C*H* Ph); $^{13}C$ NMR: δ 24.9 (CH(*C*H$_3$)Ph), 44.1 (*C*H$_2$), 52.3 (*C*H Cp$_{subs}$), 57.0 (*C*H(CH$_3$)Ph), 57.6 (OCH$_3$), 59.6 (*C*H Cp$_{subs}$), 64.0 (*C*H Cp$_{subs}$), 68.8 (5C, *C*H Cp$_{unsubs}$), 75.2 (*C*CH$_2$NHR), 126.2 (*C*OCH$_3$),

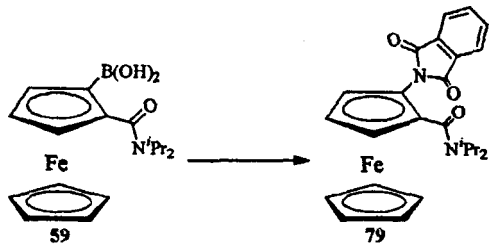
126.8 (*C*H Ph), 126.9 (*C*H Ph), 128.4 (*C*H Ph), 145.7 (*C* Ph); m/z (FAB$^+$) 349 (82%, M$^+$), 229 (100%), 73 (55%), 55 (57%); HRMS $C_{20}H_{23}FeNO$ calcd. 349.1129, found 349.1118. Anal. calcd. for $C_{20}H_{23}FeNO$: C, 68.78; H, 6.64; N, 4.01; found: C, 68.35; H, 6.51; N, 3.71%.

**(±)-2-(*N,N*-Diisopropylamido)ferrocene boronic acid (59)[44]**




To a stirred solution of *n*-butyl lithium (2.3M, 3.05 mL, 7.02 mmol), TMEDA (1.05 mL, 6.96 mmol) and ether (20 mL) at –78 °C was added a solution of *N,N*-diisopropylferrocene carboxamide (**27**) (1.00 g, 3.19 mmol) in ether (20 mL). The reaction mixture was stirred at –78 °C for 1 h followed by addition of trimethylborate (1.05 mL, 9.37 mmol). The reaction mixture was stirred at –78 °C for a further 30 min before being allowed to warm slowly to r.t.. The reaction mixture was then poured onto a sat. solution of $NH_4Cl$(50 mL) and the phases were separated. The organic phase was washed with water (2 × 50 mL) and brine (2 × 50 mL), then dried ($MgSO_4$), and concentrated *in vacuo* to yield a brown solid in a red oil. Crystallisation from hexane yielded (±)-2-(*N,N*-diisopropylamido)-ferrocene boronic acid (**59**) (0.643 g, 56%, lit.[44] yield = 65%) as a brown powdery solid. mp = 148 – 151 °C (lit.[44] mp = 148 – 150 °C); $R_f$ = 0.25 (30% EtOAc / hexane); $^1$H NMR: δ 1.10 – 1.80 (12H, br m, N(CH(C*H*$_3$)$_2$)$_2$), 3.40 – 3.60 (2H, br s, N(C*H*(CH$_3$)$_2$)$_2$), 4.22 (5H, s, C*H* Cp$_{unsubs}$), 4.44 (1H, s, C*H* Cp$_{subs}$), 4.55 (1H, s, C*H* Cp$_{subs}$), 4.66 (1H, s, C*H* Cp$_{subs}$), 7.44 (2H, br s, B(O*H*)$_2$). Further data was in agreement with that reported in the literature for the non-racemic product.[44]

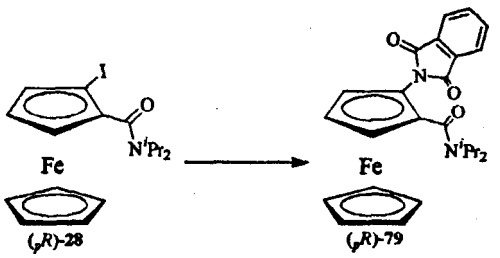
**(±)-2-(*N,N*-Diisopropylamido)ferrocenylphthalimide (79)**




A suspension of (±)-2-(*N,N*-diisopropylamido)ferrocene boronic acid (**59**) (3.80 g, 10.6 mmol) and copper phthalimide (7.57 g, 21.3 mmol) in acetone (100 mL) was warmed to reflux for 2 h then allowed to cool to r.t. overnight. The reaction mixture was concentrated *in vacuo* and the residue was taken up in ethyl acetate. This solution was filtered to remove the copper salts. The organics were washed successively with 10% KOH (2 × 50 mL), water (50 mL), 10% acetic acid (2 × 50 mL), water (50 mL) and brine (2 × 50 mL). The organics were then dried ($MgSO_4$), and concentrated *in vacuo* to yield an orange solid. Purification by column chromatography (silica; 10% EtOAc / hexane) yielded (±)-2-(*N,N*-diisopropylamido)ferrocenylphthalimide (**79**) (960 mg, 20%) as a pale brown solid. mp = 218 – 220 °C; $R_f$ = 0.40 (30% EtOAc / hexane); IR $\nu_{max}$ 1722 (C=O stretch, phthalimide), 1617 (C=O stretch, ferrocenyl amide), 1462, 1372, 1317 $cm^{-1}$; $^1H$ NMR: δ 1.23 (6H, br s, $N(CH(CH_3)_2)_2$), 1.40 (3H, br m, $N(CH(CH_3)_2)_2$), 1.46 (3H, br m, $N(CH(CH_3)_2)_2$), 3.40 (1H, br s, $N(CH(CH_3)_2)_2$), 4.28 (1H, t, *J* = 2.6, *CH* $Cp_{subs}$), 4.39 (6H, s, 5 × *CH* $Cp_{unsubs}$ and *CH* $Cp_{subs}$), 4.52 (1H, dd, *J* = 2.4, 1.4, *CH* $Cp_{subs}$), 4.60 (1H, br s, $N(CH(CH_3)_2)_2$), 7.71 (2H, dd, *J* = 5.4, 3.0, *CH* phthalimide), 7.85 (2H, dd, *J* = 5.4, 3.0, *CH* phthalimide); $^{13}C$ NMR: δ 20.6 (2C, br, $N(CH(CH_3)_2)_2$), 20.8 (1C, br, $N(CH(CH_3)_2)_2$), 21.6 (1C, br, $N(CH(CH_3)_2)_2$), 45.9 (1C, $NCH(CH_3)_2$), 50.5 (1C, $NCH(CH_3)_2$), 64.8 (1C, *CH*

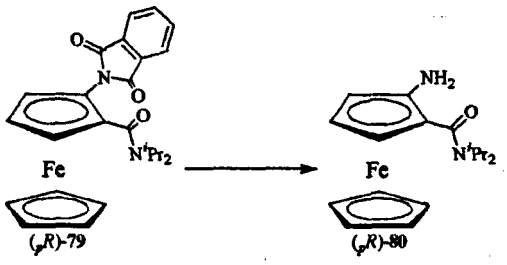
$Cp_{subs}$), 65.0 (1C, *C*H $Cp_{subs}$), 65.2 (1C, *C*H $Cp_{subs}$), 71.8 (5C, *C*H $Cp_{unsubs}$), 80.2 (1C, *C*C=ON$^i$Pr$_2$), 88.8 (1C, *C*N $Cp_{subs}$), 123.2 (2C, *C*H phthalimide), 132.3 (2C, *C* phthalimide), 134.0 (2C *C*H phthalimide), 166.9 (2C, *C*=O phthalimide), 167.2 (1C, CC=ON$^i$Pr$_2$); m/z (EI$^+$) 458 (100%, M$^+$), 330 (10%), 266 (14%), 119 (12%); HRMS $C_{25}H_{20}FeN_2O_3$ calcd. 458.1293, found 458.1288. Anal. calcd. for $C_{25}H_{20}FeN_2O_3$: C, 65.51; H, 5.72; N, 6.11; found: C, 65.41; H, 5.53; N, 6.06%.

**($_p$*R*)-2-(*N*,*N*-Diisopropylamido)ferrocenyl-phthalimide (79)**




A stirred solution of ($_p$*R*)-*N*,*N*-diisopropyl-2-iodoferrocene carboxamide (($_p$*R*)-**28**) (4.94 g, 11.3 mmol), copper(I) oxide (966 mg, 6.75 mmol) and phthalimide (1.99 g, 13.5 mmol) in acetonitrile (68 mL) was warmed to reflux overnight. The reaction mixture was allowed to cool to r.t. and concentrated *in vacuo*. The residue was taken up in EtOAc (70 mL) and filtered to remove the copper salts. The filtrate was washed with 2M NaOH (2 × 50 mL) and brine (2 × 50 mL), then dried ($MgSO_4$) and concentrated in vacuo. Purification by column chromatography (silica; 5% EtOAc / petrol to 20% EtOAc / hexane) yielded ($_p$*R*)-2-(*N*,*N*-diisopropylamido)ferrocenylphthalimide (($_p$*R*)-79) (3.40 g, 66%) as a pale brown solid. Spectroscopic data as racemic material. $[\alpha]_D^{20} = +146.3$ (c = 1.075, $CHCl_3$).

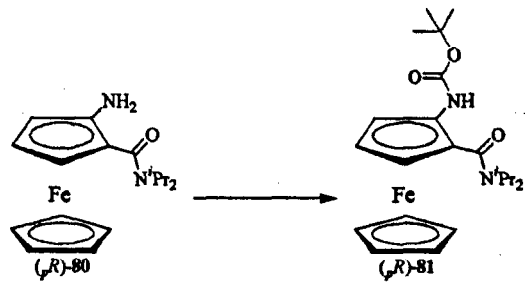
**($_p$*R*)-2-(*N*,*N*-Diisopropylamido)ferrocenylamine (80)**




To a solution of ($_p$*R*)-2-(*N*,*N*-diisopropylamido)ferrocenylphthalimide (($_p$*R*)-**79**) (1.20 g, 2.62 mmol) in ethanol (50 mL) was added hydrazine hydrate (1.3 mL, 26 mmol). The reaction mixture was warmed to reflux for 30 min then allowed to cool to r.t. before being quenched with water (50 mL). The reaction mixture was extracted with ether (3 × 40 mL), then the ether layer was extracted with 15% HCl (3 × 30 mL). The aqueous layer was basified with 2M NaOH and back extracted with ether (3 × 40 mL). The ether layer was then dried ($MgSO_4$), and concentrated *in vacuo* to yield ($_p$*R*)-2-(*N*,*N*-diisopropylamido)ferrocenylamine (($_p$*R*)-**80**) (860 mg, 83%) as a dark brown crystalline solid, which was used without further purification. mp = 125 – 127 °C; $R_f$ = 0.20 (40% EtOAc / hexane); $[\alpha]_D^{25} = -8.82$ (c = 1.032, $CHCl_3$); IR $\nu_{max}$ 3419 and 3326 (N-H stretch), 1581 (C=O stretch, ferrocenyl amide), 1463, 1370, 1336 cm$^{-1}$; $^1$H NMR: δ 1.40 (12H, br s, N(CH(C*H*$_3$)$_2$)$_2$), 3.50 – 4.50 (2H, br s, N(C*H*(CH$_3$)$_2$)$_2$), 3.75 (2H, s, N*H*$_2$), 3.90 (1H, t, *J* = 2.6, C*H* Cp$_{subs}$), 4.08 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$), 4.12 (5H, s, C*H* Cp$_{unsubs}$), 4.17 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$); $^{13}$C NMR: δ 21.3 (br, *C*H$_3$), 21.7 (*C*H$_3$), 45.0 – 50.0 (2C, br, N(*C*H(CH$_3$)$_2$)$_2$), 58.8 (1C, *C*H Cp$_{subs}$), 62.5 (1C, *C*H Cp$_{subs}$), 62.7 (1C, *C*H Cp$_{subs}$), 67.1 (1C, *C*C=ON$^i$Pr$_2$), 70.8 (5C, *C*H Cp$_{unsubs}$), 111.4 (1C, *C*NH$_2$ Cp$_{subs}$), 171.3 (1C, CC=ON$^i$Pr$_2$); m/z (FAB$^+$) 328 (100%, M$^+$), 228 (18%), 200

(8%); HRMS $C_{17}H_{24}FeN_2O$ calcd. 328.1238, found 328.1247. Anal. calcd. for $C_{17}H_{24}FeN_2O$: C, 62.17; H, 7.37; N, 8.54; found: C, 62.25; H, 7.21; N, 8.63%.

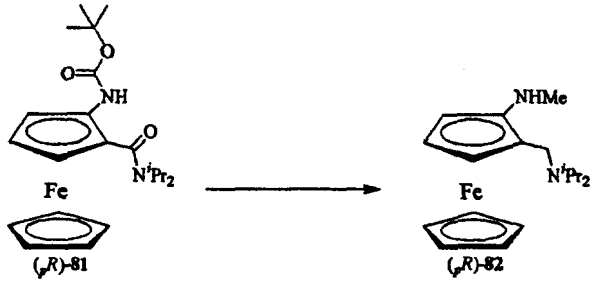
**($_p$*R*)-*N*-Boc-2-(*N'*,*N'*-diisopropylamido)ferrocenylamine (81)**




A mixture of ($_p$*R*)-2-(*N*,*N*-diisopropylamido)ferrocenylamine (($_p$*R*)-**80**) (378 mg, 1.15 mmol), di-*tert*-butyl dicarbonate (329 mg, 1.50 mmol) and DMAP (20 mg, 0.16 mmol) in DCM (4.0 mL) was stirred at r.t. overnight. The reaction mixture was concentrated *in vacuo* and purified by column chromatography (silica; 20% EtOAc / hexane) to yield ($_p$*R*)-*N*-Boc-2-(*N'*,*N'*-diisopropylamido)ferrocenylamine (($_p$*R*)-**81**) (292 mg, 60%) as an orange solid. mp = 132 – 134 °C; $R_f$ = 0.35 (40% EtOAc / hexane); $[\alpha]_D^{24}$ = +505.6 (c = 0.988, $CHCl_3$); IR $\nu_{max}$ 3343 (N-H stretch), 2973 (C-H stretch), 1711 (C=O Boc group), 1595 (C=O ferrocenyl amide), 1454, 1369, 1346, 1315, 1159 $cm^{-1}$; $^1H$ NMR: δ 1.20 – 1.60 (12H, br m, $N(CH(CH_3)_2)_2$), 1.51 (9H, s, $(C=O)OC(CH_3)_3$), 3.20 – 3.80 (1H, br s, $N(CH(CH_3)_2)$, 4.10 (2H, m, *CH* $Cp_{subs}$), 4.17 (5H, s, *CH* $Cp_{unsubs}$), 4.30 – 5.00 (1H, br s, $N(CH(CH_3)_2)$, 5.33 (1H, s, *CH* $Cp_{subs}$), 8.18 (1H, s, *NH*); $^{13}C$ NMR: δ 21.4 ($CH(CH_3)_2$), 28.5 ($C(CH_3)_3$), 49.0 – 51.0 (br, $CH(CH_3)_2$), 62.4 (*CH* $Cp_{subs}$), 63.7 (*CH* $Cp_{subs}$), 64.9 (*CH* $Cp_{subs}$), 66.5, 70.7 (*CH* $Cp_{unsubs}$), 79.7, 100.6, 153.5 (C=O), 171.6 (C=O); m/z ($FAB^+$) 428 (100%, $M^+$), 328 (78%), 228 (19%); HRMS

$C_{22}H_{32}FeN_2O_3$ calcd. 428.1762, found 428.1752. Anal. calcd. for $C_{22}H_{32}FeN_2O_3$: C, 61.69; H, 7.53; N, 6.54; found: C, 61.53; H, 7.51; N, 6.42%.

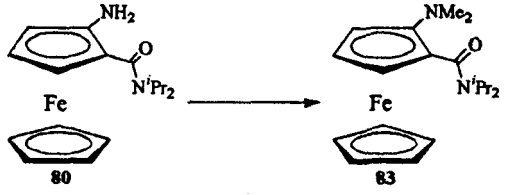
**($_p$*R*)-2-(*N'*-Methylamino)-(*N,N*-diisopropyl)ferrocenylmethylamine (82)**




To a stirred solution of ($_p$*R*)-*N*-Boc-2-(*N',N'*-diisopropylamido)ferrocenylamine (($_p$*R*)-**81**) (1.00 g, 2.33 mmol) in THF (12 mL) was added a solution of $LiAlH_4$ (1M in THF, 9.3 mL, 9.3 mmol). The reaction mixture was warmed to reflux overnight before being allowed to cool to r.t.. Water (0.5 mL) was added very cautiously, followed by 2M NaOH (0.5 mL) and a further portion of water (1.5 mL). The reaction mixture was stirred for a further 30 min, then filtered. The organics were washed with water (3 × 10 mL), then extracted into 1M HCl. The acidic aqueous layer was basified with 2M NaOH then extracted into ether (3 × 10 mL). The ether layer was washed with brine (3 × 10 mL), then dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography (silica; 40% EtOAc / 1% $Et_3N$ / 59% petrol) yielded ($_p$*R*)-2-(*N'*-methylamino)-(*N,N*-diisopropyl)ferrocenylmethylamine (($_p$*R*)-**82**) (697 mg, 91%) as an orange oil. $R_f$ = 0.20 (50% EtOAc / 49% petrol / 1% $Et_3N$); $[\alpha]_D^{26}$ = +344.5 (c = 0.996, $CHCl_3$); IR $\nu_{max}$ 3370 (N-H stretch), 2931 (C-H stretch), 1731, 1364, 1118, 1046, 998 $cm^{-1}$; $^1H$ NMR: δ 0.96 (6H, d, *J* = 6.6, $N(CH(CH_3)_2)_2$), 1.03 (6H, d, *J* = 6.7, $N(CH(CH_3)_2)_2$), 2.73 (3H, d, *J* = 5.8, $NHCH_3$), 3.08 (2H, septet, $N(CH(CH_3)_2)_2$), 3.30 (1H, d, *J* = 5.7, $NHCH_3$), 3.37 (1H, d, *J* = 14.0,

$CH_aH_bN^iPr_2$), 3.74 (2H, s, 2 × C*H* $Cp_{subs}$), 3.76 (1H, d, $J$ = 14.4, $CH_aH_bN^iPr_2$), 3.86 (1H, s, C*H* $Cp_{subs}$), 4.08 (5H, s, C*H* $Cp_{unsubs}$); $^{13}C$ NMR: δ 19.2 ($N(CH(CH_3)_2)_2$), 21.7 ($N(CH(CH_3)_2)_2$), 33.7 ($NHCH_3$), 43.4 ($CH_2$), 46.6 (2C, $N(CH(CH_3)_2)_2$), 52.7 (*C*H $Cp_{subs}$), 60.2 (*C*H $Cp_{subs}$), 65.5 (*C*H $Cp_{subs}$), 68.4 (5C, *C*H $Cp_{unsubs}$), 73.8 ($CCH_2N^iPr_2$), 113.1 ($CNHCH_3$); m/z ($FAB^+$) 328 (100%, $M^+$), 227 (58%), 114 (28%); HRMS $C_{18}H_{28}FeN_2$ calcd. 328.1602, found 328.1619.

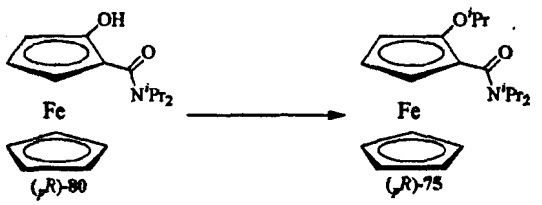
**(±)-*N,N*-Dimethyl-2-(*N',N'*-Diisopropylamido)ferrocenylamine (83)**




To a solution of (±)-2-(*N,N*-diisopropylamido)ferrocenylamine (**80**) (500 mg, 1.52 mmol) in formaldehyde (40% w/v aqueous solution, 1.1 mL, 15 mmol) was added formic acid (98% aqueous solution, 1.2 mL, 30 mmol). The reaction mixture was warmed to reflux for 3 h and turned black. The mixture was allowed to cool to r.t. and diluted with water (5 mL). This solution was basified with 2M NaOH then extracted into ether. The ether layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. Purification by column chromatography (silica; 10% EtOAc / 1% $Et_3N$ / 89% petrol) yielded (±)-*N,N*-dimethyl-2-(*N',N'*-diisopropylamido)ferrocenylamine (**83**) (75 mg, 14%) as a pale brown crystalline solid. mp = 115.9 – 117.2 °C; $R_f$ = 0.68 (40% EtOAc / petrol); IR $\nu_{max}$ 2964 (C-H stretch), 1621 (C=O stretch, ferrocenyl amide), 1456, 1369, 1320, 1039 $cm^{-1}$; $^1H$ NMR: δ 0.93 (3H, d, $J$ = 6.7, $N(CH(CH_3)_2)_2$), 1.08 (3H, d, $J$ = 6.6, $N(CH(CH_3)_2)_2$), 1.45 (3H, d, $J$ = 6.8, $N(CH(CH_3)_2)_2$), 1.48 (3H, d, $J$ = 6.8, $N(CH(CH_3)_2)_2$), 2.59 (6H, s, $N(CH_3)_2$), 3.39 (1H, septet, $J$ =

6.8, N(C*H*(CH$_3$)$_2$)$_2$), 3.80 (1H, septet, *J* = 6.8, N(C*H*(CH$_3$)$_2$)$_2$), 3.82 (1H, dd, *J* = 2.4, 1.6, C*H* Cp$_{subs}$), 3.87 (1H, t, *J* = 2.5, C*H* Cp$_{subs}$), 4.06 (1H, dd, *J* = 2.5, 1.6, C*H* Cp$_{subs}$) 4.42 (5H, s, C*H* Cp$_{unsubs}$); $^{13}$C NMR: δ 19.7 (N(CH(*C*H$_3$)$_2$)$_2$), 20.5 (N(CH(*C*H$_3$)$_2$)$_2$), 20.9 (N(CH(*C*H$_3$)$_2$)$_2$), 21.0 (N(CH(CH$_3$)$_2$)$_2$), 43.6 (2C, N(*C*H$_3$)$_2$), 45.7 (N(*C*H(CH$_3$)$_2$)$_2$), 50.5 (N(*C*H(CH$_3$)$_2$)$_2$), 56.9 (*C*H Cp$_{subs}$), 61.3 (*C*H Cp$_{subs}$), 66.1 (*C*H Cp$_{subs}$), 68.4 (5C, *C*H Cp$_{unsubs}$), 75.9 (*C*C=ON$^i$Pr$_2$), 111.7 (*C*NMe$_2$), 168.4 (CC=ON$^i$Pr$_2$); m/z (FAB$^+$) 356 (100%, M$^+$), 256 (19%), 147 (13%), 73 (53%); HRMS $C_{19}H_{28}FeN_2O$ calcd. 356.1551, found 356.1559. Anal. calcd. for $C_{19}H_{28}FeN_2O$: C, 64.05; H, 7.92; N, 7.86; found: C, 64.20; H, 7.80; N, 7.82%.

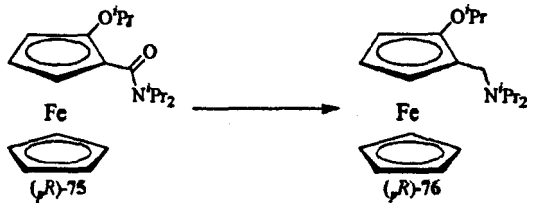
**(*pR*)-*N,N*-Diisopropyl-2-isopropoxyferrocene carboxamide (75)**




To a solution of potassium *tert*-butoxide (710 mg, 6.3 mmol) in THF (5 mL) at 0 °C was added a solution of (*pR*)-*N,N*-diisopropyl-2-hydroxyferrocene carboxamide ((*pR*)-**62**) (1.38 g, 4.22 mmol) in THF (40 mL). The mixture was stirred at 0 °C for 1 h before being allowed to warm to r.t.. Addition of 2-iodopropane (1.7 mL, 17 mmol) caused the mixture to rapidly turn cloudy. The reaction mixture was left to stir at r.t. overnight. The mixture was concentrated *in vacuo* and the residue was partitioned between ether and water. The phases were separated and the organics were washed with water (2 × 20 mL) and brine (2 × 20 mL), dried (MgSO$_4$) and concentrated *in vacuo* to yield (*pR*)-*N,N*-diisopropyl-2-isopropoxyferrocene carboxamide ((*pR*)-**75**) (1.29 g, 82%) as a pale orange solid, which was used without further purification. mp

= 41 - 45 °C; $R_f$ = 0.65 (30% EtOAc / hexane); $[\alpha]_D^{20}$ = +161.0 (c = 1.030, $CHCl_3$); IR $\nu_{max}$ 2969 (C-H stretch), 1633 (C=O stretch, ferrocenyl amide), 1457, 1371, 1321, 1139, 814 $cm^{-1}$; $^1H$ NMR: δ 1.01 (3H, br s, $N(CH(CH_3)_2)_2$), 1.11 (3H, br s, $N(CH(CH_3)_2)_2$), 1.26 (3H, d, $J$ = 6.1, $OCH(CH_3)_2$), 1.37 (3H, d, $J$ = 6.2, $OCH(CH_3)_2$), 1.48 (6H, br s, $N(CH(CH_3)_2)_2$), 3.39 (1H, br s, $N(CH(CH_3)_2)_2$), 3.83 (1H, t, $J$ = 2.6, C*H* $Cp_{subs}$), 3.94 (1H, dd, $J$ = 2.5, 1.4, C*H* $Cp_{subs}$) 3.98 (1H, br s, $N(CH(CH_3)_2)_2$), 4.11 (1H, dd, $J$ = 2.6, 1.4, C*H* $Cp_{subs}$), 4.23 (1H, sep, $J$ = 6.1, $OCH(CH_3)_2$), 4.30 (5H, s, C*H* $Cp_{unsubs}$); $^{13}C$ NMR: δ 20.6 ($CH_3$), 21.2 ($CH_3$), 22.5 ($CH_3$), 22.8 ($CH_3$), 45.8 (CH), 50.3 (CH), 53.6 (CH), 60.2 (CH), 64.0 (CH), 70.3 (5C, CH $Cp_{unsubs}$), 73.7 (CH), 76.8 ($CC{=}ON^iPr_2$), 122.5 ($CO^iPr$), 166.9 (C=O); m/z ($FAB^+$) 371 (100%, $M^+$), 228 (11%); HRMS $C_{20}H_{29}NO_2Fe$ calcd. 371.1548, found 371.1546. Anal. calcd. for $C_{20}H_{29}FeNO_2$: C, 64.70; H, 7.87; N, 3.77; found: C, 64.64; H, 7.83; N, 3.59%.

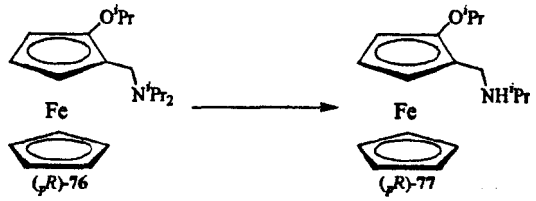
**($_p$*R*)-*N*,*N*-Diisopropyl-(2-isopropoxyferrocenyl)methyl-amine (76)**




To a stirred solution of ($_p$*R*)-*N*,*N*-diisopropyl-2-isopropoxyferrocene carboxamide (($_p$*R*)-**75**) (0.916 g, 2.47 mmol) in ether (12.5 mL) was added a solution of lithium aluminium hydride in THF (1M, 3.70 mL, 3.70 mmol). The reaction mixture was warmed to reflux and stirred overnight. The reaction mixture was cooled to r.t. and water (0.2 mL) was added cautiously, followed by 2M NaOH (0.2 mL) and a further portion of water (0.6 mL). The reaction

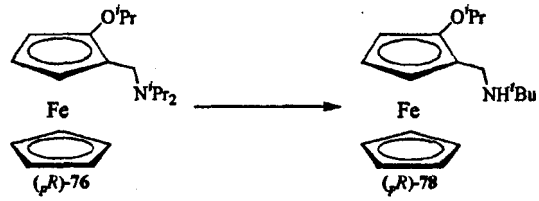
mixture was then stirred for a further 25 min to allow formation of a white solid. The reaction mixture was filtered and the organic phase was washed with water (2 × 5 mL), then extracted into 1M HCl. The acidic aqueous layer was basified with 2M NaOH and extracted back into DCM. The DCM layer was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to yield ($_pR$)-*N,N*-diisopropyl-(2-isopropoxyferrocenyl)methylamine (($_pR$)-**76**) (0.723 g, 82%) as a pale brown oil. $R_f$ = 0.22 (50% EtOAc / 49% hexane / 1% $Et_3N$); $[\alpha]_D^{20}$ = +111.6 (c = 1.145, $CHCl_3$); IR $\nu_{max}$ 2966 (C-H stretch), 1480, 1453, 1381, 1288, 1202, 1139, 1105, 1002, 812 $cm^{-1}$; $^1H$ NMR: δ 0.98 (6H, d, *J* = 6.6, $N(CH(CH_3)_2)_2$), 1.02 (6H, d, *J* = 6.6, $N(CH(CH_3)_2)_2$), 1.22 (3H, d, *J* = 6.1, $OCH(CH_3)_2$), 1.35 (3H, d, *J* = 6.2, $OCH(CH_3)_2$), 3.03 (2H, septet, *J* = 6.6, $N(CH(CH_3)_2)_2$), 3.40 (1H, d, *J* = 14.1, $CpCH_aH_bN^iPr_2$), 3.59 (1H, d, *J* = 14.1, $CpCH_aH_bN^iPr_2$), 3.70 (1H, t, *J* = 2.6, *CH* $Cp_{subs}$), 3.92 (1H, dd, *J* = 2.5, 1.4, *CH* $Cp_{subs}$), 3.96 (1H, dd, *J* = 2.6, 1.4, *CH* $Cp_{subs}$), 4.07 (5H, s, *CH* $Cp_{unsubs}$), 4.15 (1H, sep, *J* = 6.1, $OCH(CH_3)_2$); $^{13}C$ NMR: δ 20.3 (2C, $N(CH(CH_3)_2)_2$), 21.4 (2C, $N(CH(CH_3)_2)_2$), 22.6 ($OCH(CH_3)_2$), 22.8 ($OCH(CH_3)_2$), 40.9 ($CH_2$), 47.3 (CH), 54.4 (CH), 59.7 (CH), 64.7 (CH), 69.2 (5C, CH $Cp_{unsubs}$), 72.9 ($OCH(CH_3)_2$), 76.4 ($CCH_2N^iPr_2$), 124.0 ($CO^iPr$); m/z ($FAB^+$) 357 (100%, $M^+$), 257 (48%), 215 (16%), 114 (11%); HRMS $C_{20}H_{31}NOFe$ calcd. 357.1755, found 357.1757. Anal. calcd. for $C_{20}H_{31}FeNO$: C, 67.23; H, 8.74; N, 3.92; found: C, 66.83; H, 8.58; N, 3.86%.

**($_p$*R*)-*N*-Isopropyl-(2-isopropoxyferrocenyl)methylamine (77)**



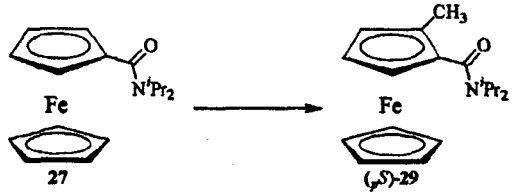

Preparation of the title compound ($_p$*R*)-**77**, followed the general procedure and used ($_p$*R*)-*N,N*-diisopropyl-(2-isopropoxyferrocenyl)-methylamine (($_p$*R*)-**76**) (695 mg, 1.95 mmol) and isopropylamine (5.0 mL, 60 mmol). Purification by column chromatography (silica; 10% EtOAc / 89% hexane / 1% $Et_3N$), yielded ($_p$*R*)-*N,N*-diisopropyl-(2-isopropoxyferrocenyl)methylamine (($_p$*R*)-**76**) (143 mg, 21%) followed by ($_p$*R*)-*N*-isopropyl-(2-isopropoxyferrocenyl)-methylamine (($_p$*R*)-77) (414 mg, 67%) as a pale brown oil. $R_f$ = 0.22 (50% EtOAc / 49% hexane / 1% $Et_3N$); $[\alpha]_D^{27}$ = +195.0 (c = 1.018, $CHCl_3$); IR $\nu_{max}$ 3302 (N-H stretch), 2930 (C-H stretch), 1731, 1456, 1382, 1314, 1116, 1104, 999 cm$^{-1}$; $^1$H NMR: δ 1.05 (6H, t, *J* = 6.3, 2 × C*H*$_3$), 1.24 (3H, d, *J* = 6.1, C*H*$_3$), 1.36 (3H, d, *J* = 6.2, C*H*$_3$), 1.39 (1H, br s, N*H*), 2.83 (1H, septet, *J* = 6.2, NH(C*H*(CH$_3$)$_2$)), 3.44 (1H, d, *J* = 13.1, CpC*H*$_a$H$_b$NH$^i$Pr), 3.73 (1H, t, *J* = 2.6, C*H* Cp$_{subs}$), 3.74 (1H, d, *J* = 13.0, CpCH$_a$*H*$_b$NH$^i$Pr), 3.90 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$), 3.94 (1H, dd, *J* = 2.6, 1.4, C*H* Cp$_{subs}$), 4.09 (5H, s, C*H* Cp$_{unsubs}$), 4.12 (1H, sep, *J* = 6.1, OC*H*(CH$_3$)$_2$); $^{13}$C NMR: δ 22.6 (*C*H$_3$), 22.86 (*C*H$_3$), 22.90 (*C*H$_3$), 23.1 (*C*H$_3$), 43.8 (*C*H$_2$), 47.7 (*C*H), 54.5 (*C*H), 59.8 (*C*H), 63.1 (*C*H), 69.1 (5C, *C*H Cp$_{unsubs}$), 73.4 (O*C*H(CH$_3$)$_2$), 75.4 (*C*CH$_2$NH$^i$Pr), 124.2 (*C*O$^i$Pr); m/z (FAB$^+$) 315 (100%, M$^+$), 257 (39%), 214 (22%), 186 (9%); HRMS $C_{17}H_{25}NOFe$ calcd. 315.1286, found 315.1294.

**($_pR$)-*N*-*tert*-Butyl-(2-isopropoxyferrocenyl)methylamine (78)**



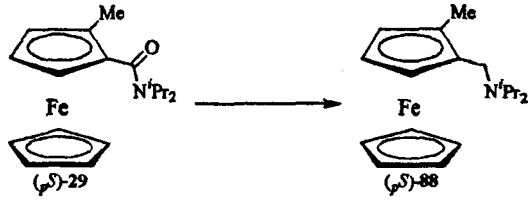

Preparation of the title compound ($_pR$)-**78**, followed the general procedure and used ($_pR$)-*N,N*-diisopropyl-(2-isopropoxyferrocenyl)methylamine (($_pR$)-**76**) (571 mg, 1.60 mmol) and *tert*-butylamine (5.0 mL, 50 mmol). Purification by column chromatography (silica; 20% EtOAc / 79% hexane / 1% $Et_3N$), yielded ($_pR$)-*N,N*-diisopropyl-(2-isopropoxyferrocenyl)methylamine (($_pR$)-**76**) (157 mg, 27%) followed by ($_pR$)-*N*-*tert*-butyl-(2-isopropoxyferrocenyl)methylamine (($_pR$)-**78**) (294 mg, 56%) as a pale brown oil. $R_f$ = 0.22 (50% EtOAc / 49% hexane / 1% $Et_3N$); $[\alpha]_D^{25}$ = +188.6 (c = 1.035, $CHCl_3$); IR $\nu_{max}$ (liquid film) 3320 (N-H stretch), 2969 (C-H stretch), 1454, 1382, 1286, 1230, 1122, 1105, 813 cm$^{-1}$; $^1$H NMR: δ 1.15 (10H, s and br s, C(C*H*$_3$)$_3$ and N*H*), 1.25 (3H, d, *J* = 6.1, OCH(C*H*$_3$)$_2$), 1.35 (3H, d, *J* = 6.2, OCH(C*H*$_3$)$_2$), 3.39 (1H, d, *J* = 11.9, CpC*H*$_a$H$_b$NH$^t$Bu), 3.66 (1H, d, *J* = 11.9, CpCH$_a$*H*$_b$NH$^t$Bu), 3.72 (1H, t, *J* = 2.6, C*H* Cp$_{subs}$), 3.93 (1H, m, C*H* Cp$_{subs}$), 3.95 (1H, dd, *J* = 2.5, 1.3, C*H* Cp$_{subs}$), 4.09 (5H, s, C*H* Cp$_{unsubs}$), 4.14 (1H, m, OC*H*(CH$_3$)$_2$); $^{13}$C NMR: δ 22.7 (OCH(*C*H$_3$)$_2$), 22.8 (OCH(*C*H$_3$)$_2$), 29.1 (C(*C*H$_3$)$_3$), 39.5 (*C*H$_2$), 50.6 (*C*(CH$_3$)$_3$), 54.6 (*C*H), 59.8 (*C*H), 63.0 (*C*H), 69.1 (5C, *C*H Cp$_{unsubs}$), 73.5 (OCH(CH$_3$)$_2$), 76.2 (*C*CH$_2$NH$^t$Bu), 124.0 (*C*O$^i$Pr); m/z (FAB$^+$) 329 (100%, M$^+$), 257 (70%), 214 (40%), 186 (21%), 73 (45%); HRMS $C_{18}H_{27}NOFe$ calcd. 329.1442, found 329.1438.

**($_p$*S*)-*N*,*N*-Diisopropyl-2-methylferrocene carboxamide (29)[44]**




Preparation of ($_p$*S*)-*N*,*N*-diisopropyl-2-methylferrocene carboxamide (($_p$*S*)-**29**) was in accordance with the published procedure, and was followed by recrystallisation from hexane to yield ($_p$*S*)-*N*,*N*-diisopropyl-2-methylferrocene carboxamide (($_p$*S*)-**29**) (6.61 g, 64%, lit.[44] yield = 91%) as an orange crystalline solid. mp = 81 – 82 °C (lit.[44] mp = 80 – 81 °C); $R_f$ = 0.75 (30% EtOAc / hexane); $[\alpha]_D^{27}$ = +29.0, ($CHCl_3$, c = 1.110); lit.[44] $[\alpha]_D^{25}$ = +25.5, ($CHCl_3$, c = 0.97); $^1$H NMR: δ 1.04 (6H, br s, N(CH(C*H*$_3$)$_2$)$_2$), 1.49 (6H, br s, N(CH(C*H*$_3$)$_2$)$_2$), 2.05 (3H, s, C*H*$_3$), 3.40 (1H, br s, N(C*H*(CH$_3$)$_2$)$_2$), 4.00 (1H, br s, N(C*H*(CH$_3$)$_2$)$_2$), 4.01 (1H, t, *J* = 2.4, C*H* Cp$_{subs}$), 4.10 (1H, m, C*H* Cp$_{subs}$), 4.15 (1H, dd, *J* = 2.4, 1.4, C*H* Cp$_{subs}$) 4.22 (5H, s, C*H* Cp$_{unsubs}$). Further data was in agreement with that reported in the literature.[44]

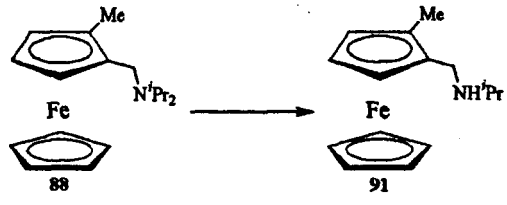
**($_p$*S*)-*N*,*N*-Diisopropyl-(2-methylferrocenyl)methylamine (88)**




To a solution of ($_p$*S*)-*N*,*N*-diisopropyl-2-methylferrocene carboxamide (($_p$*S*)-**29**) (412 mg, 1.26 mmol) in ether (6.3 mL) was added a solution of lithium aluminium hydride in THF (1 M, 1.89 mL, 1.89 mmol). The reaction mixture was warmed to reflux and stirred overnight. The reaction mixture was then allowed to cool to r.t. and water (0.1 mL) was added cautiously, followed by

2M NaOH (0.1 mL) and a further portion of water (0.3 mL). The reaction mixture was then stirred for a further 20 min before filtration. The ether layer was extracted into 1M HCl (3 × 5 mL). The acidic aqueous layer was basified with 2M NaOH and extracted back into DCM, which was washed with brine (2 × 10 mL), dried ($MgSO_4$), and concentrated *in vacuo* to yield ($_pS$)-*N,N*-diisopropyl-(2-methylferrocenyl)methylamine (($_pS$)-**88**) (236 mg, 60%) as an orange oil, which was used without further purification. $R_f$ = 0.72 (50% EtOAc / 49% hexane / 1% $Et_3N$); $[\alpha]_D^{26} = +11.0$ (c = 1.255, $CHCl_3$); IR $\nu_{max}$ 2964 (C-H stretch), 1361, 1201, 1176, 1033 $cm^{-1}$; $^1H$ NMR: δ 0.98 (12H, m, $N(CH(CH_3)_2)_2$), 1.98 (3H, s, $CH_3$), 2.99 (2H, septet, $J$ = 6.6, $N(CH(CH_3)_2)_2$), 3.41 (1H, d, $J$ = 13.6, $CpCH_aH_bN^iPr_2$), 3.52 (1H, d, $J$ = 13.6, $CpCH_aH_bN^iPr_2$), 3.90 (1H, m, C*H* $Cp_{subs}$), 4.00 (6H, s, C*H* $Cp_{subs}$ & 5C*H* $Cp_{unsubs}$), 4.08 (1H, br s, C*H* $Cp_{subs}$); $^{13}C$ NMR: δ 13.7 ($CH_3$), 20.2 (2C, $N(CH(CH_3)_2)_2$), 21.2 (2C, $N(CH(CH_3)_2)_2$), 42.5 ($CH_2$), 46.6 (2C, $N(CH(CH_3)_2)_2$), 64.8 (*C*H $Cp_{subs}$), 69.1 (5C, CH $Cp_{unsubs}$), 69.3 (*C*H $Cp_{subs}$), 70.0 (*C*H, $Cp_{subs}$), 83.8 (*C*), 86.4 (*C*); m/z ($FAB^+$) 313 (55%, $M^+$), 213 (58%), 154 (100%), 136 (79%), 73 (46%); HRMS $C_{18}H_{27}NFe$ calcd. 313.1493, found 313.1507. Anal. calcd. for $C_{18}H_{27}FeN$: C, 69.01; H, 8.69; N, 4.47; found: C, 68.93; H, 8.77; N, 4.51%.

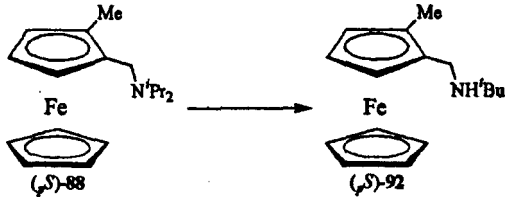
**(±)-*N*-Isopropyl-(2-methylferrocenyl)methylamine (91)**




Preparation of the title compound **91**, followed the general procedure and used (±)-*N,N*-diisopropyl-(2-methylferrocenyl)methylamine (**88**) (200 mg, 0.638

mmol) and isopropylamine (1.6 mL, 19 mmol). Purification by column chromatography (silica; 20% EtOAc / 79% petrol / 1% $Et_3N$), yielded starting material **88** (109 mg, 55%) followed by (±)-*N*-isopropyl-(2-methylferrocenyl)methylamine (**91**) (57 mg, 33%) as an orange oil. $R_f = 0.23$ (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 3311 (N-H stretch), 2919 (C-H stretch), 1463, 1381, 1370, 1104, 1056, 1036, 1000 $cm^{-1}$; $^1H$ NMR: δ 1.07 (3H, d, $J$ = 6.2, NCH($CH_3$)$_2$), 1.08 (3H, d, $J$ = 6.2, NCH($CH_3$)$_2$), 1.40 (1H, br s, N*H*), 1.98 (3H, s, $CH_3$), 2.84 (1H, septet, $J$ = 6.2, NC*H*($CH_3$)$_2$), 3.49 (1H, d, $J$ = 12.9, CpC$H_a$H$_b$NH$^i$Pr), 3.59 (1H, d, $J$ = 12.9, CpCH$_a$$H_b$NH$^i$Pr) 3.96 (1H, t, $J$ = 2.4, C*H* Cp$_{subs}$), 4.02 (5H, s, C*H* Cp$_{unsubs}$), 4.05 (1H, s, C*H* Cp$_{subs}$), 4.12 (1H, dd, $J$ = 2.2, 1.6, C*H* Cp$_{subs}$); $^{13}C$ NMR: δ 13.2 ($CH_3$), 22.8 (NCH($CH_3$)$_2$), 23.2 (NCH($CH_3$)$_2$), 45.1 (CpCH$_2$NH$^i$Pr), 48.3 (NCH($CH_3$)$_2$), 65.5 (*C*H Cp$_{subs}$), 68.0 (*C*H Cp$_{subs}$), 68.9 (5C, *C*H Cp$_{unsubs}$), 69.9 (*C*H Cp$_{subs}$), 83.0 (*C*), 85.8 (*C*); m/z (FAB$^+$) 271 (93%, M$^+$), 213 (100%), 154 (26%), 136 (22%), 95 (19%), 91 (19%); HRMS $C_{15}H_{21}FeN$ calcd. 271.1023, found 271.1016. Anal. calcd. for $C_{15}H_{21}FeN$: C, 66.44; H, 7.81; N, 5.16; found: C, 66.30; H, 7.74; N, 4.68%.

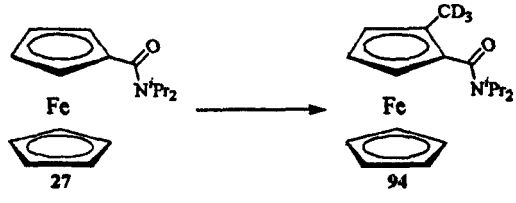
**($_p$*S*)-*N*-*tert*-Butyl-(2-methylferrocenyl)methylamine (92)**




Preparation of the title compound ($_p$*S*)-**92**, followed the general procedure and used ($_p$*S*)-*N,N*-diisopropyl-(2-methylferrocenyl)methylamine (($_p$*S*)-**88**) (0.200 g, 0.638 mmol) and *tert*-butylamine (2.0 mL, 19 mmol). Purification by column chromatography (silica; 20% EtOAc / 79% petrol / 1% $Et_3N$), yielded

starting material ($_pS$)-**88** (110 mg, 55%) followed by ($_pS$)-*N*-*tert*-butyl-(2-methylferrocenyl)methylamine (($_pS$)-**92**) (69 mg, 38%) as an orange oil. $R_f$ = 0.22 (50% EtOAc / 49% hexane / 1% $Et_3N$); $[\alpha]_D^{26} = -6.25$ (c = 1.072, $CHCl_3$); IR $\nu_{max}$ 3309 (N-H stretch), 2909 (C-H stretch), 1461, 1390, 1380, 1363, 1104, 1074, 1036, 999 $cm^{-1}$; $^1H$ NMR: δ 0.82 (1H, br s, N*H*), 1.15 (9H, s, NHC($CH_3$)$_3$), 1.98 (3H, s, $CH_3$), 3.44 (1H, d, $J$ = 11.9, CpC$H_a$H$_b$NH$^t$Bu), 3.51 (1H, d, $J$ = 11.9, CpCH$_a$$H_b$NH$^t$Bu) 3.94 (1H, t, $J$ = 2.4, C*H* Cp$_{subs}$), 4.02 (5H, s, C*H* Cp$_{unsubs}$), 4.03 (1H, m, C*H* Cp$_{subs}$), 4.13 (1H, t, $J$ = 1.8, C*H* Cp$_{subs}$); $^{13}C$ NMR: δ 13.1 ($CH_3$), 29.2 (3C, NHC($CH_3$)$_3$), 40.5 (CpCH$_2$NH$^t$Bu), 50.6 (NHC($CH_3$)$_3$), 65.4 (*C*H Cp$_{subs}$), 68.0 (*C*H Cp$_{subs}$), 69.0 (5C, *C*H Cp$_{unsubs}$), 69.6 (*C*H Cp$_{subs}$), 82.9 (*C*), 86.5 (*C*); m/z (FAB$^+$) 285 (15%, M$^+$), 213 (22%), 109 (23%), 97 (33%), 95 (42%), 85 (27%), 83 (48%), 81 (49%), 69 (78%), 55 (100%); HRMS $C_{16}H_{23}FeN$ calcd. 285.1180, found 285.1156. Anal. calcd. for $C_{16}H_{23}FeN$: C, 67.38; H, 8.13; N, 4.91; found: C, 67.66; H, 8.04; N, 4.71%.

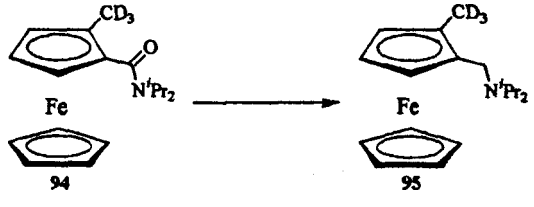
**(±)-*N,N*-Diisopropyl-2-methyl-d$_3$-ferrocene carboxamide (94)**




To a stirred solution of *N,N*-diisopropylferrocene carboxamide (**27**) (5.00 g, 16.0 mmol) in ether (240 mL) was added TMEDA (5.3 mL, 35 mmol). The mixture was cooled to –78 °C before addition of *n*-butyl lithium (2.39 M, 14.7 mL, 35.1 mmol). The mixture was stirred for 1 h before addition of iodomethane-d$_3$ (2.98 mL, 47.9 mmol). The reaction mixture was allowed to warm slowly to r.t. before being quenched with a saturated aq. solution of

$NH_4Cl$ (200 mL). The phases were separated and the organic phase was washed successively with a further portion of $NH_4Cl$ (2 × 100 mL) and brine (2 × 100 mL), then dried ($MgSO_4$), and concentrated *in vacuo* to yield an orange oil. Purification by column chromatography (silica; 10% EtOAc / 90% petrol), yielded (±)-*N,N*-diisopropyl-2-methyl-$d_3$-ferrocene carboxamide (**94**) (4.04 g, 77%) as an orange crystalline solid. mp = 57.3 – 59.1 °C; $R_f$ = 0.73 (30% EtOAc / petrol); IR $\nu_{max}$ 2970 (C-H stretch), 1622 (C=O stretch, ferrocenyl amide), 1460, 1370, 1345, 1315 $cm^{-1}$; $^1H$ NMR: δ 1.05 (6H, br s, $N(CH(CH_3)_2)_2$), 1.51 (6H, br s, $N(CH(CH_3)_2)_2$), 3.40 (1H, br s, $N(CH(CH_3)_2)_2$), 3.95 (1H, br s, $N(CH(CH_3)_2)_2$), 4.01 (1H, t, $J$ = 2.4, CH $Cp_{subs}$), 4.10 (1H, dd, $J$ = 2.3, 1.3, CH $Cp_{subs}$), 4.15 (1H, dd, $J$ = 2.4, 1.3, CH $Cp_{subs}$) 4.22 (5H, s, CH $Cp_{unsubs}$); $^{13}C$ NMR: δ 12.6 (1C, septet, $J$ = 20, $CD_3$), 21.1 (4C, $N(CH(CH_3)_2)_2$), 45.8 ($N(CH(CH_3)_2)_2$), 50.2 ($N(CH(CH_3)_2)_2$), 65.3 (CH $Cp_{subs}$), 66.4 (CH $Cp_{subs}$), 68.7 (CH $Cp_{subs}$), 70.3 (5C, CH $Cp_{unsubs}$), 84.1 (C), 87.2 (C), 168.3 ($C$=O$N^iPr_2$); m/z (FAB$^+$) 330 (100%, $M^+$), 230 (7%); HRMS $C_{18}H_{22}D_3FeNO$ calcd. 330.1474, found 330.1493.

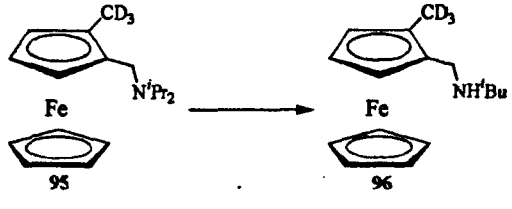
**(±)-*N,N*-Diisopropyl-(2-methyl-$d_3$-ferrocenyl)methylamine (95)**




To a solution of (±)-*N,N*-diisopropyl-2-methyl-$d_3$-ferrocene carboxamide (**94**) (3.00 g, 9.08 mmol) in ether (50 mL) was added a solution of lithium aluminium hydride in THF (1 M, 18.2 mL, 18.2 mmol). The reaction mixture was warmed to reflux and stirred overnight. The reaction mixture was then

allowed to cool to r.t. and water (1 mL) was added cautiously, followed by 2M NaOH (1 mL) and a further portion of water (3 mL). The reaction mixture was then stirred for a further 20 min before filtration. The ether layer was extracted into 1M HCl (3 × 30 mL). The acidic aqueous layer was basified with 2M NaOH and extracted back into DCM (3 × 30 mL). The DCM layer was washed with brine (2 × 30 mL), dried ($MgSO_4$), and concentrated *in vacuo* to yield (±)-*N,N*-diisopropyl-(2-methyl-$d_3$-ferrocenyl)methylamine (**95**) (1.96 g, 68%) as an orange-brown oil, which was used without further purification. $R_f$ = 0.71 (50% EtOAc / 49% petrol / 1% $Et_3N$); IR $\nu_{max}$ 2930 (C-H stretch), 1731, 1461, 1381, 1362, 1104, 999, 882 $cm^{-1}$; $^1H$ NMR: δ 0.97 (6H, d, $J$ = 5.5, $N(CH(CH_3)_2)_2$), 0.98 (6H, d, $J$ = 6.4, $N(CH(CH_3)_2)_2$), 2.99 (2H, septet, $J$ = 6.6, $N(CH(CH_3)_2)_2$), 3.40 (1H, d, $J$ = 13.6, $CpCH_aH_bN^iPr_2$), 3.52 (1H, d, $J$ = 13.6, $CpCH_aH_bN^iPr_2$), 3.90 (1H, s, *CH* $Cp_{subs}$), 4.00 (6H, s, *CH* $Cp_{subs}$ & 5*CH* $Cp_{unsubs}$), 4.08 (1H, s, *CH* $Cp_{subs}$); $^{13}C$ NMR: δ 12.8 (1C, septet, $J$ = 19.2, $CD_3$), 20.2 (2C, $N(CH(CH_3)_2)_2$), 21.3 (2C, $N(CH(CH_3)_2)_2$), 42.5 ($CH_2$), 46.6 (2C, $N(CH(CH_3)_2)_2$), 64.8 (*CH* $Cp_{subs}$), 69.1 (5C, *CH* $Cp_{unsubs}$), 69.3 (*CH* $Cp_{subs}$), 70.0 (*CH*, $Cp_{subs}$), 83.6 (*C*), 86.5 (*C*); m/z ($FAB^+$) 316 (51%, $M^+$), 216 (100%), 69 (45%), 55 (70%); HRMS $C_{18}H_{24}D_3FeN$ calcd. 316.1681, found 316.1689.

**(±)-*N-tert*-Butyl-(2-methyl-$d_3$-ferrocenyl)methylamine (96)**

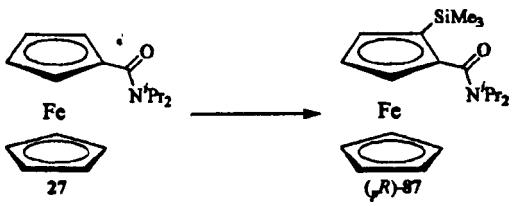



95 96

Preparation of the title compound **96**, followed the general procedure and used (±)-*N,N*-diisopropyl-(2-methyl-$d_3$-ferrocenyl)methylamine (**95**) (1.50 g, 4.74

mmol) and *tert*-butylamine (15.0 mL, 142 mmol). Purification by column chromatography (silica; 5% EtOAc / 94% petrol / 1% $Et_3N$ to 30% EtOAc / 69% petrol / 1% $Et_3N$), yielded starting material **95** (1.03 g, 69%) followed by (±)-*N*-*tert*-butyl-(2-methyl-$d_3$-ferrocenyl)methylamine (**96**) (213 mg, 16%) as an orange oil. $R_f$ = 0.22 (50% EtOAc / 49% petrol / 1% $Et_3N$); IR $\nu_{max}$ 3308 (N-H stretch), 2963 (C-H stretch), 1462, 1390, 1363, 1104, 1000 $cm^{-1}$; $^1H$ NMR: δ 0.95 (1H, br s, N*H*), 1.18 (9H, s, NHC($CH_3$)$_3$), 3.46 (1H, d, $J$ = 11.8, Cp$CH_aH_b$NH$^t$Bu), 3.53 (1H, d, $J$ = 11.8, CpC$H_a$$H_b$NH$^t$Bu) 3.96 (1H, t, $J$ = 2.4, C*H* Cp$_{subs}$), 4.03 (5H, s, C*H* Cp$_{unsubs}$), 4.05 (1H, m, C*H* Cp$_{subs}$), 4.16 (1H, dd, $J$ = 2.0, 1.5, C*H* Cp$_{subs}$); $^{13}C$ NMR: δ 12.3 (1C, septet, $J_{C\text{-}D}$ = 19, $CD_3$), 29.1 (3C, NHC($CH_3$)$_3$), 40.4 (Cp$CH_2$NH$^t$Bu), 50.5 (NH$C$($CH_3$)$_3$), 65.4 (*C*H Cp$_{subs}$), 67.9 (*C*H Cp$_{subs}$), 68.9 (5C, *C*H Cp$_{unsubs}$), 69.5 (*C*H Cp$_{subs}$), 82.7 (*C*), 86.4 (*C*); m/z (FAB$^+$) 288 (91%, M$^+$), 216 (100%), 147 (11%), 73 (37%), 57 (43%); HRMS $C_{16}H_{20}D_3FeN$ calcd. 288.1368, found 288.1368.

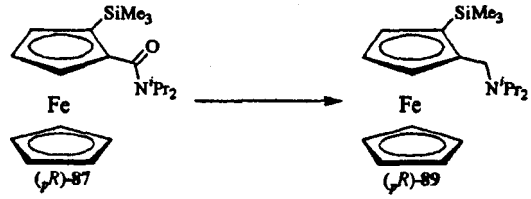
**(*p*R)-*N*,*N*-Diisopropyl-2-trimethylsilylferrocene carboxamide (87)[44]**




Preparation of the title compound (*p*R)-**87** was carried out in accordance with the published procedure, followed by recrystallisation from hexane to yield (*p*R)-*N*,*N*-diisopropyl-2-trimethylsilylferrocene carboxamide ((*p*R)-**87**) (2.46 g, 66%, lit.[44] yield = 96%) as a brown crystalline solid. mp = 97.4 – 99.3 °C (lit.[44] mp = 102 – 104 °C); $[\alpha]_D^{27}$ = +25.1, ($CHCl_3$, c = 1.000); lit.[44] $[\alpha]_D^{25}$ = +20.2, ($CHCl_3$, c = 0.97); $^1H$ NMR: δ 0.28 (9H, s, Si($CH_3$)$_3$), 0.9 – 1.6

(12H, br d, $N(CH(CH_3)_2)_2$), 3.2 – 3.6 (1H, br s, $N(CH(CH_3)_2)_2$), 3.8 – 4.2 (1H, br s, $N(CH(CH_3)_2)_2$), 4.13 (1H, dd, $J$ = 2.3, 1.2, *CH* $Cp_{subs}$) 4.27 (5H, s, *CH* $Cp_{unsubs}$) 4.30 (1H, t, $J$ = 2.3, *CH* $Cp_{subs}$), 4.34 (1H, dd, $J$ = 2.3, 1.2, *CH* $Cp_{subs}$). Further data was in agreement with that reported in the literature.[44]

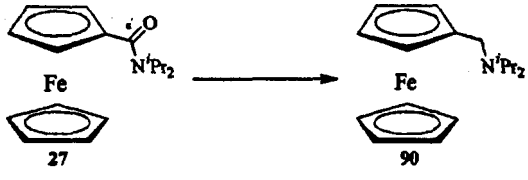
**($_p$*R*)-*N,N*-Diisopropyl-(2-trimethylsilylferrocenyl)-methylamine (89)**




To a stirred slurry of $LiAlH_4$ (812 mg, 21.4 mmol) in THF (20 mL) was added a solution of ($_p$*R*)-*N,N*-diisopropyl-2-trimethylsilylferrocene carboxamide (($_p$*R*)-**87**) (2.75 g, 7.14 mmol) in THF (55 mL). The reaction mixture was warmed to reflux and stirred for 4 days. The reaction mixture was then allowed to cool to r.t. and water (0.8 mL) was added cautiously, followed by 2M NaOH (0.8 mL) and a further portion of water (2.4 mL). The reaction mixture was then stirred for a further 20 min before filtration. The organics were washed with water (3 × 30 mL) and extracted into 1M HCl (3 × 30 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to yield ($_p$*R*)-*N,N*-diisopropyl-2-trimethylsilylferrocene carboxamide (($_p$*R*)-**87**) (0.891 g, 32%). The acidic aqueous layer was basified with 2M NaOH and extracted back into ether (3 × 30 mL). The organics were washed with brine (2 × 30 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by column chromatography (silica; 5% EtOAc / petrol to 1% $Et_3N$ / 10% EtOAc / petrol) yielded ($_p$*R*)-*N,N*-diisopropyl-(2-trimethylsilylferrocenyl)methylamine (($_p$*R*)-**89**) (628 mg, 24%) as an orange oil. $R_f$ = 0.30 (50% EtOAc / 49% petrol / 1%

$Et_3N$); $[\alpha]_D^{24} = -75.5$, ($CHCl_3$, c = 0.954); IR $\nu_{max}$ 2963 (C-H stretch), 1461, 1362, 1105, 1000, 865, 839 $cm^{-1}$; $^1H$ NMR: δ 0.30 (9H, s, $Si(CH_3)_3$), 0.97 (6H, d, $J$ = 6.6, $N(CH(CH_3)_2)_2$), 0.98 (6H, d, $J$ = 6.6, $N(CH(CH_3)_2)_2$), 3.00 (2H, septet, $J$ = 6.6, $N(CH(CH_3)_2)_2$), 3.37 (1H, d, $J$ = 14.0, $CpCH_aH_bN^iPr_2$), 3.59 (1H, d, $J$ = 14.0, $CpCH_aH_bN^iPr_2$), 4.00 (1H, dd, $J$ = 2.3, 1.4, $CH$ $Cp_{subs}$), 4.07 (5H, s, $5CH$ $Cp_{unsubs}$), 4.19 (1H, t, $J$ = 2.3, $CH$ $Cp_{subs}$), 4.47 (1H, t, $J$ = 1.7, $CH$ $Cp_{subs}$); $^{13}C$ NMR: δ 0.81 ($Si(CH_3)_3$), 20.6 (2C, $N(CH(CH_3)_2)_2$), 21.0 (2C, $N(CH(CH_3)_2)_2$), 44.9 ($CH_2$), 47.0 (CH), 68.8 (5C, CH $Cp_{unsubs}$), 68.9 (CH), 70.6 (C), 73.8 (CH), 93.9 (C); m/z ($FAB^+$) 371 (13%, $M^+$), 271 (100%), 73 (18%), 57 (14%), 55 (18%); HRMS $C_{20}H_{33}FeNSi$ calcd. 371.1732, found 371.1723. Anal. calcd. for $C_{20}H_{33}FeNSi$: C, 64.68; H, 8.96; N, 3.77; found: C, 64.63; H, 8.83; N, 3.81%. Followed by *N,N*-diisopropylferrocenylmethylamine (**90**) (0.397 g, 19%) as a brown oil with spectroscopic data consistent with that reported below.

**_N,N_-Diisopropylferrocenylmethylamine (90)**

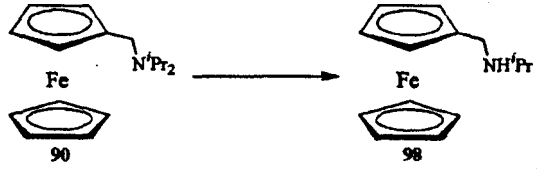



27 90

To a slurry of lithium aluminium hydride (1.45 g, 38.3 mmol) in ether (20 mL) was added a solution of *N,N*-diisopropylferrocene carboxamide (**27**) (4.10 g, 13.1 mmol) in ether (100 mL). The reaction mixture was warmed to reflux and stirred overnight. The reaction mixture was allowed to cool to r.t. and water (1.5 mL) was added cautiously, followed by 2M NaOH (1.5 mL) and a further portion of water (4.5 mL). The reaction mixture was then stirred for a further 30 min to allow formation of a granular white solid. The reaction mixture was

filtered and the organics were washed with water (2 × 25 mL). The ether layer was extracted into 1M HCl and the acidic aqueous layer was basified with 2M NaOH and extracted back into ether (3 × 50 mL). The ether layer was then washed with brine (2 × 50 mL), dried ($MgSO_4$), and concentrated *in vacuo* to yield *N,N*-diisopropyl-ferrocenylmethylamine (**90**) (3.15 g, 80%) as an orange oil, which was used without further purification. $R_f$ = 0.29 (30% EtOAc / 70% hexane); $^1$H NMR: δ 1.00 (12H, d, *J* = 6.6, N(CH(C*H*$_3$)$_2$)$_2$), 3.04 (2H, septet, *J* = 6.6, N(C*H*(CH$_3$)$_2$)$_2$), 3.44 (2H, s, CpC*H*$_2$N$^i$Pr$_2$), 4.04 (2H, t, *J* = 1.8, C*H* Cp$_{subs}$), 4.09 (5H, s, C*H* Cp$_{unsubs}$), 4.19 (2H, t, *J* = 1.8, C*H* Cp$_{subs}$). Further data was in agreement with that reported in the literature.[43]

**N-Isopropylferrocenylmethylamine (98)**




Preparation of the title compound **98**, followed the general procedure and used *N,N*-diisopropylferrocenylmethylamine (**90**) (1.50 g, 5.01 mmol) and isopropylamine (12.8 mL, 150 mmol). Purification by column chromatography (silica; 10% EtOAc / 89% hexane / 1% $Et_3N$), yielded *N,N*-diisopropylferrocenyl-methylamine (**90**) (0.190 g, 13% recovery) followed by *N*-isopropylferrocenylmethylamine (**98**) (863 mg, 67%) as an orange oil. $R_f$ = 0.21 (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 3310 (N-H stretch), 2910 (C-H stretch), 1644 – 1766 (broad), 1464, 1382, 1370, 1105, 1059, 1000 cm$^{-1}$; $^1$H NMR: δ 1.00 (6H, d, *J* = 6.3, NHCH(C*H*$_3$)$_2$), 1.20 (1H, br s, N*H*), 2.78 (1H, septet, *J* = 6.2, NHC*H*(CH$_3$)$_2$), 3.42 (2H, s, CpC*H*$_2$NH$^i$Pr), 4.01 (2H, t, *J* = 1.8, C*H* Cp$_{subs}$), 4.04 (5H, s, C*H* Cp$_{unsubs}$), 4.11 (2H, t, *J* = 1.8, C*H* Cp$_{subs}$); $^{13}$C

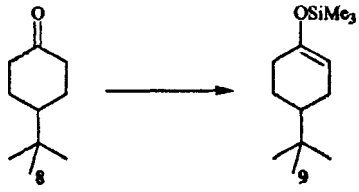
NMR: δ 22.9 (2C, NHCH($CH_3$)$_2$), 46.5 ($CH_2$), 48.1 (NH$CH$($CH_3$)$_2$), 67.6 (2C, *C*H Cp$_{subs}$), 68.2 (2C, *C*H Cp$_{subs}$), 68.3 (5C, *C*H Cp$_{unsubs}$), 87.4 ($CCH_2$NH$^t$Pr); m/z (FAB$^+$) 257 (100%, M$^+$), 199 (98%), 147 (24%), 73 (62%), 69 (47%); HRMS $C_{14}H_{19}FeN$ calcd. 257.0867, found 257.0870. Anal. calcd. for $C_{14}H_{19}FeN$: C, 65.39; H, 7.45; N, 5.45; found: C, 65.89; H, 7.50; N, 5.00%.

**_N-tert_-Butylferrocenylmethylamine (99)**


90 99

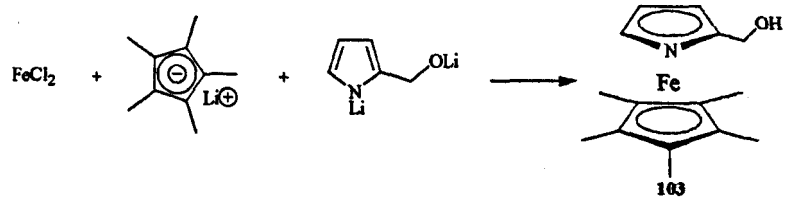
Preparation of the title compound 99, followed the general procedure and used *N,N*-diisopropylferrocenylmethylamine (90) (1.00 g, 3.34 mmol) and *tert*-butylamine (10.5 mL, 100 mmol). Purification by column chromatography (silica; 20% EtOAc / 79% hexane / 1% $Et_3N$), yielded *N,N*-diisopropylferrocenylmethylamine (90) (60 mg, 6% recovery) followed by *N-tert*-butylferrocenylmethylamine (99) (0.493 g, 54%) as an orange solid. mp = 61.5 – 63.0 °C, (lit.[111] mp = 60 – 62 °C); $R_f$ = 0.22 (50% EtOAc / 49% hexane / 1% $Et_3N$); IR $\nu_{max}$ 3321 (N-H stretch), 2963 (C-H stretch), 1644 – 1729 (broad), 1390, 1363, 1104, 1000 cm$^{-1}$; $^1$H NMR: δ 1.00 (1H, br s, N*H*), 1.15 (9H, s, NHC($CH_3$)$_3$), 3.44 (2H, s, Cp$CH_2$NH$^t$Bu), 4.08 (2H, t, *J* = 1.8, C*H* Cp$_{subs}$), 4.12 (5H, s, C*H* Cp$_{unsubs}$), 4.20 (2H, t, *J* = 1.8, C*H* Cp$_{subs}$); $^{13}$C NMR: δ 29.2 (3C, NHC($CH_3$)$_3$), 42.0 ($CH_2$), 50.6 (NH*C*($CH_3$)$_3$), 67.7 (2C, *C*H Cp$_{subs}$), 68.2 (2C, *C*H Cp$_{subs}$), 68.4 (5C, *C*H Cp$_{unsubs}$), 88.4 ($CCH_2$NH$^t$Bu); m/z (FAB$^+$) 271 (71%, M$^+$), 199 (100%), 73 (51%); HRMS $C_{15}H_{21}FeN$ calcd. 271.1023, found 271.1017. Anal. calcd. for $C_{15}H_{21}FeN$: C, 66.44; H, 7.81; N, 5.16; found: C, 66.25; H, 7.77; N, 5.07%.

**Optimised General Procedure for the Deprotonation of 4-*tert*-Butylcyclohexanone (8)**



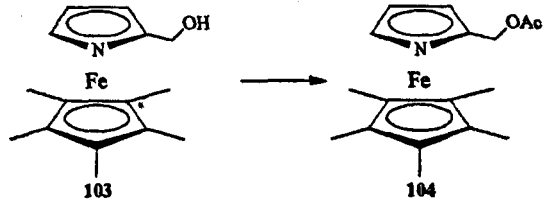

To a stirred solution of ferrocenyl base (1.25 eq) in THF (5 mL $mmol^{-1}$) at 0 °C was added sequentially TMEDA (1.25 eq) and *n*-butyl lithium (1.25 eq). The reaction mixture was cooled to –78 °C before addition of freshly distilled chlorotrimethylsilane (5.00 eq), followed by a solution of 4-*tert*-butylcyclohexanone (**8**) (1.00 eq) in THF (10 mL $mmol^{-1}$). The reaction mixture was stirred at –78 °C for 2 h before addition of $Et_3N$ (2 mL $mmol^{-1}$) and a sat. solution of $NaHCO_3$ (10 mL $mmol^{-1}$). The mixture was left to warm slowly to r.t. and the phases were separated. The organics were washed with $NaHCO_3$ (3 portions) and the combined aqueous layers were back-extracted with ether (3 portions). The combined ether layers were dried ($MgSO_4$), and concentrated *in vacuo*. Purification by column chromatography (silica; 10% $Et_2O$ / 90% petrol to 20% EtOAc / 1% $Et_3N$ / 79% petrol) yielded 4-*tert*-butyl-1-trimethylsilyloxycyclohex-1-ene (**9**) as a clear, colourless oil. $R_f$ = 0.58 (100% hexane on alumina); further data in agreement with that reported above, followed by recovered ferrocenyl base. For full results of base assays, see Results and Discussion sections 6.2.7 and 6.2.9.

**(±)-2-Hydroxymethyl-1',2',3',4',5'-pentamethylazaferrocene (103)[15]**




Preparation of the title compound **103** was carried out according to the published procedure[15] to yield (±)-2-hydroxymethyl-1',2',3',4',5'-pentamethylazaferrocene (**103**) (0.599 g, 50%; lit.[15] yield = 22 – 43%) as an orange-brown solid. $R_f$ = 0.45 (1% methanol / 99% acetone); IR $\nu_{max}$ 3185 (O-H stretch), 2909 (C-H stretch), 1729, 1454, 1382, 1058, 1024, 995 $cm^{-1}$; $^1H$ NMR: δ 1.90 (15H, s, $CH_3$ Cp*), 4.13 (1H, s), 4.14 (1H, s), 4.31 (1H, br s), 4.55 (2H, m, $CH_2$), 4.86 (1H, s); $^{13}C$ NMR: δ 10.9 (5C, $CH_3$ Cp*), 59.8, 72.7, 76.0, 81.2, 91.6, 104.3; m/z ($FAB^+$) 287 (63%, $M^+$), 269 (100%), 190 (19%) 152 (15%), 133 (20%); HRMS $C_{15}H_{21}FeNO$ calcd. 287.0973, found 287.0975.

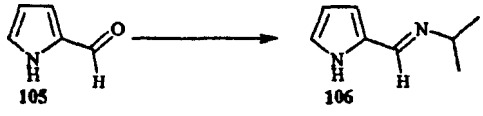
**(±)-2-methyl-(1',2',3',4',5'-pentamethylazaferrocenyl) acetate (104)**




To a solution of (±)-2-hydroxymethyl-1',2',3',4',5'-pentamethylazaferrocene (**103**) (0.200 g, 0.700 mmol) and DMAP (9.0 mg, 0.07 mmol) in DCM (3.5 mL) was added triethylamine (0.3 mL, 2 mmol) followed by acetic anhydride (79 μL, 0.84 mmol). The reaction mixture was stirred at r.t. for 1 h, then washed successively with a saturated solution of $NaHCO_3$ (3 × 5 mL) and brine (3 × 5 mL), dried ($MgSO_4$) and concentrated *in vacuo* to yield an orange-brown oil. Purification by column chromatography (silica; 50% EtOAc / 50%

petrol) yielded (±)-2-methyl-(1',2',3',4',5'-pentamethylazaferrocenyl) acetate (**104**) (138 mg, 60%) as an orange solid. $R_f$ = 0.88 (1% methanol / 99% acetone); IR $\nu_{max}$ 2951 (C-H stretch), 2910 (C-H stretch), 1732 (C=O stretch, ester), 1453, 1373, 1023 $cm^{-1}$; $^1H$ NMR: δ 1.90 (15H, s, C*H*$_3$ Cp*), 2.02 (3H, s, (C=O)C*H*$_3$), 4.18 (1H, d, *J* = 2.1, C*H*), 4.22 (1H, d, *J* = 1.8, C*H*), 4.85 (1H, d, *J* = 12.0, C$H_a$H$_b$OAc), 4.96 (1H, s, C*H*), 5.28 (1H, d, J = 12.0, CH$_a$$H_b$OAc); $^{13}C$ NMR: δ 10.9 (5C, *C*H$_3$ Cp*), 21.0 ((C=O)*C*H$_3$), 62.8 (*C*H$_2$), 74.2 (*C*H), 76.5 (*C*H), 81.4 (5C, *C* Cp*), 93.0 (*C*H), 98.9 (*C*CH$_2$OAc), 170.9 (*C*=O); m/z (FAB$^+$) 330 (26%, M$^+$+H), 329 (22%), 270 (52%) 250 (100%), 176 (25%), 136 (27%), 73 (53%); HRMS $C_{17}H_{23}FeNO_2$ calcd. 328.1078, found 329.1069.

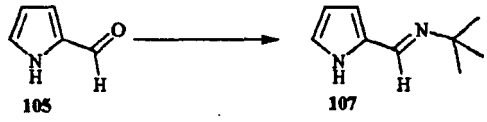
**Isopropyl-[1-(1*H*-pyrrol-2-yl)methylidene]amine (106)**[111]




To a slurry of pyrrole-2-carboxaldehyde (**105**) (670 mg, 7.04 mmol) and basic alumina (3.52 g) in DCM (35.2 mL) was added isopropylamine (3.00 mL, 35.2 mmol). The reaction mixture was stirred at r.t. overnight before being filtered and concentrated *in vacuo* to yield isopropyl-[1-(1*H*-pyrrol-2-yl)methylidene]amine (**106**) (898 mg, 94%) as a colourless oil. IR $\nu_{max}$ 3460 (N-H stretch), 3196, 3084, 2933 (C-H stretch), 2850 (C-H stretch), 2567, 1725, 1616 (C=N stretch), 1418, 1312, 1288, 1219, 1140, 1033 $cm^{-1}$; $^1H$ NMR: δ 1.19 (6H, d, *J* = 6.3, CH(C*H*$_3$)$_2$), 3.46 (1H, septet, *J* = 6.4, C*H*(CH$_3$)$_2$), 6.20 (1H, dd *J* = 3.4, 2.6, C*H*), 6.45 (1H, dd, *J* = 3.5, 1.4, C*H*), 6.81 (1H, t, *J* = 1.7, C*H*), 8.10 (1H, s, CC*H*N$^i$Pr), 10.2 (1H, br s, N*H*); $^{13}C$ NMR: δ 24.4 (2C, CH(*C*H$_3$)$_2$), 60.9 (*C*H(CH$_3$)$_2$), 109.4 (*C*H), 113.7 (*C*H), 121.6 (*C*H), 130.5

(*C*CHN$^i$Pr), 149.4 (CCHN$^i$Pr); m/z (EI$^+$) 136 (96%, M$^+$), 121 (100%, M$^+$-CH$_3$), 94 (55%), 83 (45%), 68 (26%), 58 (40%); HRMS $C_8H_{12}N_2$ calcd. 136.1001, found 136.1002.

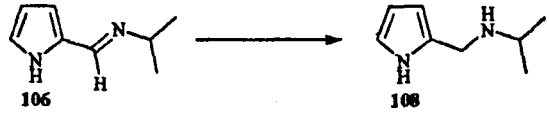
**_tert_-Butyl-[1-(1*H*-pyrrol-2-yl)-methylidene]amine (107)[112]**



105 107

To a stirred slurry of pyrrole-2-carboxaldehyde (**105**) (500 mg, 5.26 mmol) and basic alumina (2.6 g) in DCM (26 mL) was added tert-butylamine (2.8 mL, 26.3 mmol). The reaction mixture was stirred at r.t. overnight, then filtered and concentrated *in vacuo* to yield *tert*-butyl-[1-(1*H*-pyrrol-2-yl)-methylidene]amine (**107**) (770 mg, 97%) as a pale yellow solid. IR $\nu_{max}$ 3456 (N-H stretch), 2963 (C-H stretch), 2565, 1731, 1624 (C=N stretch), 1423, 1207, 1032 cm$^{-1}$; $^1$H NMR: δ 1.24 (9H, s, C(C*H*$_3$)$_3$), 6.21 (1H, dd, *J* = 3.5, 2.7, C*H*), 6.45 (1H, dd, *J* = 3.5, 1.5, C*H*), 6.82 (1H, m, C*H*), 8.09 (1H, s, C*H*N$^t$Bu), 9.35 (1H, br s, N*H*); $^{13}$C NMR: δ 29.9 (3C, C(*C*H$_3$)$_3$), 56.7 (*C*(CH$_3$)$_3$), 109.5 (*C*H), 113.3 (*C*H), 121.2 (*C*H), 131.2 (*C*CHN$^t$Bu), 146.4 (CCHN$^t$Bu); m/z (EI$^+$) 150 (100%, M$^+$), 135 (97%, M$^+$-CH$_3$), 94 (48%), 85 (68%), 57 (45%); HRMS $C_9H_{14}N_2$ calcd. 150.1157, found 150.1169.

**Isopropylpyrrol-2-ylmethylamine(108)[112]**

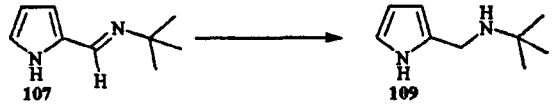


106 108

To a stirred solution of isopropyl-[1-(1*H*-pyrrol-2-yl)methylidene]amine (**106**) (803 mg, 5.90 mmol) in THF (30 mL) was added LiAlH$_4$ (1M in THF, 8.81 mL, 8.81 mmol). The mixture was warmed to reflux overnight before being

allowed to cool to r.t.. Water (0.5 mL) was added cautiously followed by 2M NaOH (0.5 mL) and water (1.5 mL). The mixture was left to stir for 25 min before being filtered to remove the inorganic precipitate. The organics were dried ($MgSO_4$) and concentrated *in vacuo* to yield isopropylpyrrol-2-ylmethylamine (**108**) (669 mg, 82%) as a clear, pale yellow oil. IR $\nu_{max}$ 3466 (N-H stretch), 2961 (C-H stretch), 2846 (C-H stretch), 2236, 1573, 1433, 1338, 1125, 1057, 1027, 817 $cm^{-1}$; $^1H$ NMR: δ 1.08 (6H, d, $J$ = 6.3, $CH(CH_3)_2$), 1.66 (1H, br s, N*H*$^i$Pr), 2.85 (1H, septet, $J$ = 6.3, C*H*$(CH_3)_2$), 3.78 (2H, s, $CH_2$), 6.01 (1H, m, C*H*), 6.11 (1H, dd, $J$ = 5.8, 2.7, C*H*), 6.69 (1H, td, $J$ = 2.6, 1.6, C*H*), 9.15 (1H, br s, N*H*); $^{13}C$ NMR: δ 22.9 (2C, $CH(CH_3)_2$), 44.4 ($CH_2$), 48.6 ($CH(CH_3)_2$), 106.0 (*C*H), 107.9 (*C*H), 117.2 (*C*H), 130.9 ($CCH_2NH^iPr$); m/z (EI$^+$) 138 (18%, $M^+$), 80 (100%), 58 (30%), 51 (13%); HRMS $C_8H_{14}N_2$ calcd. 138.1157, found 138.1159.

### *tert*-Butylpyrrol-2-ylmethylamine (109)[113]




To a solution of *tert*-butyl-[1-(1*H*-pyrrol-2-yl)-methylidene]amine (**107**) (780 mg, 5.19 mmol) in THF (26 mL) was added a solution of lithium aluminium hydride (1M in THF, 7.78 mL, 7.78 mmol). The reaction mixture was warmed to reflux overnight, then allowed to cool before addition of water (0.3 mL), followed by 2M NaOH (0.3 mL) and a final portion of water (0.9 mL). The mixture was allowed to stir for 20 min before filtration. The filtrate was concentrated *in vacuo* to yield *tert*-butylpyrrol-2-ylmethylamine (**109**) (0.738 g, 93%) as a white crystalline solid. mp = 54.9 – 55.8 °C; IR $\nu_{max}$ 3466 (N-H stretch), 3100, 2947 (C-H stretch), 2868 (C-H stretch), 2236, 1571, 1434, 1230,

1206, 1073, 1026, 818 $cm^{-1}$; $^1H$ NMR: δ 1.14 (9H, s, $C(CH_3)_3$), 1.40 (1H, br s, $NH^tBu$), 3.76 (2H, s, $CH_2$), 6.00 (1H, m, CH), 6.10 (1H, dd, $J$ = 5.8, 2.8, CH), 6.68 (1H, m, CH), 9.25 (1H, br s, NH); $^{13}C$ NMR: δ 29.0 (3C, $C(CH_3)_3$), 39.9 ($CH_2$), 50.6 ($C(CH_3)_3$), 105.4 (CH), 108.0 (CH), 117.0 (CH), 131.4 ($CCH_2NH^tBu$); m/z (EI+) 152 (17%, $M^+$), 137 (10%, $M^+$-$CH_3$), 121 (10%), 79 (68%), 58 (100%); HRMS $C_9H_{16}N_2$ calcd. 152.1314, found 152.1307.

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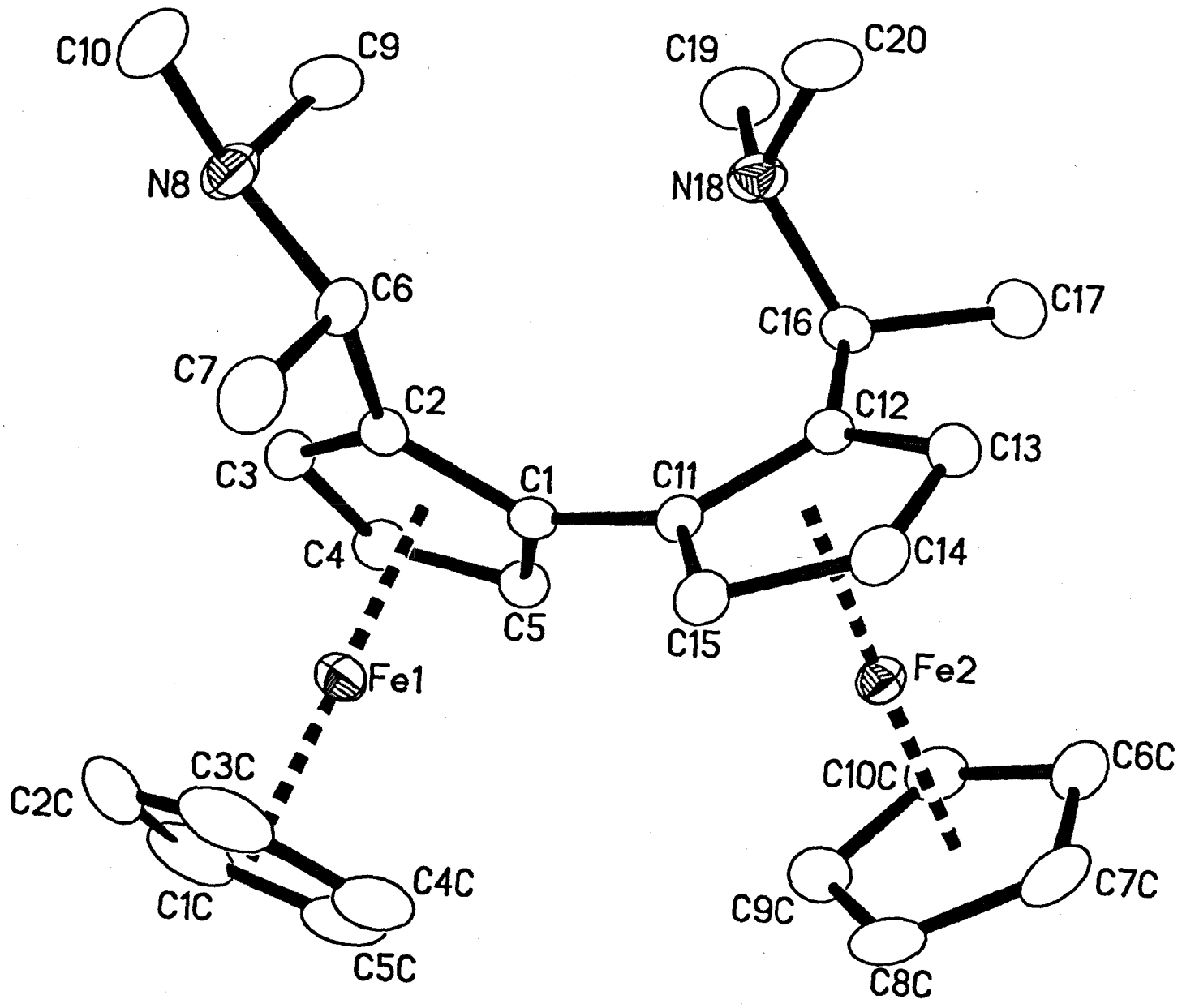
C10
C9
N8
C6
C7
C2
C3
C1
C4
C5
Fe1
C3C
C2C
C1C
C4C
C5C
C19
C20
N18
C16
C17
C12
C13
C11
C14
C15
Fe2
C10C
C6C
C9C
C7C
C8C

Table 1. Crystal data and structure refinement for FCDMAM at 150(2)K.

| | |
|---|---|
| Empirical formula | C28 H36 Fe2 N2 |
| Formula weight | 512.29 |
| Crystal description | orange-brown block |
| Crystal size | 0.50 x 0.46 x 0.35 mm |
| Crystal system | Triclinic |
| Space group | P-1 |
| Unit cell dimensions | a = 10.517(4) A alpha = 104.199(4) deg.<br>b = 10.678(4) A beta = 100.115(4) deg.<br>c = 12.532(5) A gamma = 112.747(3) deg. |
| Volume | 1199.3(9) A^3 |
| Reflections for cell refinement | 901 |
| Range in theta | 2.20 to 28.45 deg. |
| Z | 2 |
| Density (calculated) | 1.419 Mg/m^3 |
| Absorption coefficient | 1.228 mm^-1 |
| F(000) | 540 |
| Diffractometer type | Bruker SMART CCD area detector |
| Wavelength | 0.71073 A |
| Scan type | omega |
| Reflections collected | 10242 |
| Theta range for data collection | 1.76 to 28.81 deg. |
| Index ranges | -13<=h<=14, -13<=k<=13, -16<=l<=16 |
| Independent reflections | 5358 [R(int) = 0.0202] |
| Observed reflections | 4515 [I>2sigma(I)] |
| Absorption correction | Semi-empirical from equivalents<br>(Tmin = 0.539, Tmax = 0.680) |
| Decay correction | none |
| Structure solution by | direct and difference Fourier methods |
| Hydrogen atom location | geometrically placed, Me from deltaF |
| Hydrogen atom treatment | riding model, Me rigid rotating group |
| Data / restraints / parameters | 5358/0/295 (least-squares on F^2) |
| Final R indices [I>2sigma(I)] | R1 = 0.0261, wR2 = 0.0637 |
| Final R indices (all data) | R1 = 0.0353, wR2 = 0.0694 |

| | |
|---|---|
| Goodness-of-fit on F^2 | 1.037 |
| Final maximum delta/sigma | 0.001 |

Weighting scheme
calc w=1/[\s^2^(Fo^2^)+(0.0332P)^2^+0.5667P] where P=(Fo^2^+2Fc^2^)/3

| | |
|---|---|
| Largest diff. peak and hole | 0.339 and -0.319 e.A^-3 |

Table 2. Atomic coordinates ( x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for FCDMAM. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| Fe1 | 9730(1) | 2845(1) | 1885(1) | 18(1) |
| Fe2 | 5867(1) | 2173(1) | 3181(1) | 16(1) |
| C1C | 10913(3) | 4387(2) | 1301(2) | 42(1) |
| C2C | 11812(2) | 4366(2) | 2273(2) | 46(1) |
| C3C | 11273(2) | 4666(2) | 3212(2) | 40(1) |
| C4C | 10051(2) | 4867(2) | 2825(2) | 35(1) |
| C5C | 9832(2) | 4701(2) | 1651(2) | 37(1) |
| C6C | 3917(2) | 2174(2) | 2623(2) | 26(1) |
| C7C | 4863(2) | 3440(2) | 3588(2) | 29(1) |
| C8C | 6118(2) | 4200(2) | 3300(2) | 29(1) |
| C9C | 5953(2) | 3411(2) | 2153(2) | 27(1) |
| C10C | 4588(2) | 2155(2) | 1731(2) | 24(1) |
| C1 | 8075(2) | 1235(2) | 2149(1) | 16(1) |
| C2 | 9310(2) | 959(2) | 2273(1) | 17(1) |
| C3 | 9682(2) | 875(2) | 1226(1) | 19(1) |
| C4 | 8665(2) | 1052(2) | 443(1) | 20(1) |
| C5 | 7670(2) | 1277(2) | 1011(1) | 18(1) |
| C6 | 9959(2) | 593(2) | 3261(1) | 19(1) |
| C7 | 11106(2) | 1938(2) | 4260(2) | 26(1) |
| N8 | 10536(2) | -422(2) | 2806(1) | 23(1) |
| C9 | 9356(2) | -1812(2) | 2024(2) | 32(1) |
| C10 | 11347(2) | -692(2) | 3721(2) | 33(1) |
| C11 | 7289(2) | 1305(2) | 3010(1) | 16(1) |
| C12 | 5888(2) | 200(2) | 2879(1) | 16(1) |
| C13 | 5529(2) | 613(2) | 3914(1) | 19(1) |
| C14 | 6690(2) | 1950(2) | 4683(1) | 20(1) |
| C15 | 7778(2) | 2381(2) | 4127(1) | 18(1) |
| C16 | 5056(2) | -1205(2) | 1885(1) | 19(1) |
| C17 | 3431(2) | -1890(2) | 1743(2) | 26(1) |
| N18 | 5765(2) | -2138(2) | 2013(1) | 22(1) |
| C19 | 5238(2) | -3405(2) | 982(2) | 36(1) |
| C20 | 5705(2) | -2558(2) | 3029(2) | 30(1) |

Table 3. Bond lengths [A], angles [deg] for FCDMAM.

| | |
|---|---|
| Fe1-C1 | 2.0643(17) |
| Fe1-C2 | 2.0869(18) |
| Fe1-C3 | 2.0396(18) |
| Fe1-C4 | 2.0291(18) |
| Fe1-C5 | 2.0393(17) |
| Fe1-C1C | 2.030(2) |
| Fe1-C2C | 2.039(2) |
| Fe1-C3C | 2.051(2) |
| Fe1-C4C | 2.052(2) |
| Fe1-C5C | 2.039(2) |
| Fe2-C11 | 2.0562(17) |
| Fe2-C12 | 2.0565(18) |
| Fe2-C13 | 2.0383(17) |
| Fe2-C14 | 2.0382(18) |
| Fe2-C15 | 2.0451(18) |
| Fe2-C6C | 2.0481(19) |
| Fe2-C7C | 2.0404(18) |
| Fe2-C8C | 2.0403(19) |
| Fe2-C9C | 2.0490(19) |
| Fe2-C10C | 2.0531(18) |
| C1C-C5C | 1.413(3) |
| C1C-C2C | 1.416(3) |
| C2C-C3C | 1.412(3) |
| C3C-C4C | 1.407(3) |
| C4C-C5C | 1.403(3) |
| C6C-C7C | 1.420(3) |
| C6C-C10C | 1.423(3) |
| C7C-C8C | 1.419(3) |
| C8C-C9C | 1.417(3) |
| C9C-C10C | 1.427(3) |
| C1-C2 | 1.430(2) |
| C1-C5 | 1.432(2) |
| C1-C11 | 1.475(2) |
| C2-C3 | 1.425(2) |
| C2-C6 | 1.517(2) |
| C3-C4 | 1.422(2) |
| C4-C5 | 1.426(2) |
| C6-N8 | 1.482(2) |
| C6-C7 | 1.527(2) |
| N8-C10 | 1.461(2) |
| N8-C9 | 1.463(2) |
| C11-C15 | 1.430(2) |
| C11-C12 | 1.437(2) |
| C12-C13 | 1.429(2) |
| C12-C16 | 1.501(2) |
| C13-C14 | 1.422(2) |
| C14-C15 | 1.427(2) |
| C16-N18 | 1.478(2) |
| C16-C17 | 1.533(2) |
| N18-C20 | 1.454(2) |
| N18-C19 | 1.455(2) |
| | |
| C4-Fe1-C1C | 103.38(9) |
| C4-Fe1-C2C | 125.10(9) |
| C1C-Fe1-C2C | 40.72(10) |
| C4-Fe1-C5 | 41.02(7) |
| C1C-Fe1-C5 | 124.82(9) |
| C2C-Fe1-C5 | 163.00(9) |
| C4-Fe1-C5C | 114.72(8) |
| C1C-Fe1-C5C | 40.62(10) |

| | |
|---|---|
| C2C-Fe1-C5C | 68.11(9) |
| C5-Fe1-C5C | 106.46(8) |
| C4-Fe1-C3 | 40.91(7) |
| C1C-Fe1-C3 | 115.01(8) |
| C2C-Fe1-C3 | 107.01(8) |
| C5-Fe1-C3 | 68.68(7) |
| C5C-Fe1-C3 | 148.47(8) |
| C4-Fe1-C3C | 164.83(9) |
| C1C-Fe1-C3C | 68.01(10) |
| C2C-Fe1-C3C | 40.41(10) |
| C5-Fe1-C3C | 154.13(9) |
| C5C-Fe1-C3C | 67.50(9) |
| C3-Fe1-C3C | 129.94(8) |
| C4-Fe1-C4C | 149.95(8) |
| C1C-Fe1-C4C | 68.03(9) |
| C2C-Fe1-C4C | 67.95(9) |
| C5-Fe1-C4C | 119.03(8) |
| C5C-Fe1-C4C | 40.10(9) |
| C3-Fe1-C4C | 169.07(8) |
| C3C-Fe1-C4C | 40.11(9) |
| C4-Fe1-C1 | 68.79(7) |
| C1C-Fe1-C1 | 164.64(9) |
| C2C-Fe1-C1 | 154.49(9) |
| C5-Fe1-C1 | 40.83(6) |
| C5C-Fe1-C1 | 129.29(8) |
| C3-Fe1-C1 | 68.32(7) |
| C3C-Fe1-C1 | 122.47(8) |
| C4C-Fe1-C1 | 111.75(8) |
| C4-Fe1-C2 | 68.33(7) |
| C1C-Fe1-C2 | 150.66(9) |
| C2C-Fe1-C2 | 119.93(8) |
| C5-Fe1-C2 | 68.17(7) |
| C5C-Fe1-C2 | 168.66(8) |
| C3-Fe1-C2 | 40.38(7) |
| C3C-Fe1-C2 | 112.67(8) |
| C4C-Fe1-C2 | 132.73(8) |
| C1-Fe1-C2 | 40.29(6) |
| C14-Fe2-C13 | 40.83(7) |
| C14-Fe2-C8C | 115.73(7) |
| C13-Fe2-C8C | 148.74(8) |
| C14-Fe2-C7C | 106.01(8) |
| C13-Fe2-C7C | 115.61(8) |
| C8C-Fe2-C7C | 40.70(8) |
| C14-Fe2-C15 | 40.91(6) |
| C13-Fe2-C15 | 68.71(7) |
| C8C-Fe2-C15 | 107.59(7) |
| C7C-Fe2-C15 | 127.80(7) |
| C14-Fe2-C6C | 127.38(7) |
| C13-Fe2-C6C | 107.17(7) |
| C8C-Fe2-C6C | 68.52(8) |
| C7C-Fe2-C6C | 40.64(8) |
| C15-Fe2-C6C | 165.94(7) |
| C14-Fe2-C9C | 149.92(7) |
| C13-Fe2-C9C | 168.87(7) |
| C8C-Fe2-C9C | 40.55(8) |
| C7C-Fe2-C9C | 68.30(8) |
| C15-Fe2-C9C | 118.00(7) |
| C6C-Fe2-C9C | 68.48(7) |
| C14-Fe2-C10C | 166.67(7) |
| C13-Fe2-C10C | 129.50(7) |
| C8C-Fe2-C10C | 68.36(7) |
| C7C-Fe2-C10C | 68.24(8) |
| C15-Fe2-C10C | 151.99(7) |
| C6C-Fe2-C10C | 40.61(7) |

| | |
|---|---|
| C9C-Fe2-C10C | 40.72(7) |
| C14-Fe2-C11 | 68.84(7) |
| C13-Fe2-C11 | 68.75(7) |
| C8C-Fe2-C11 | 129.77(7) |
| C7C-Fe2-C11 | 167.16(7) |
| C15-Fe2-C11 | 40.82(6) |
| C6C-Fe2-C11 | 151.68(7) |
| C9C-Fe2-C11 | 109.88(7) |
| C10C-Fe2-C11 | 119.30(7) |
| C14-Fe2-C12 | 68.81(7) |
| C13-Fe2-C12 | 40.83(7) |
| C8C-Fe2-C12 | 169.02(7) |
| C7C-Fe2-C12 | 149.67(7) |
| C15-Fe2-C12 | 68.76(6) |
| C6C-Fe2-C12 | 117.54(7) |
| C9C-Fe2-C12 | 131.04(7) |
| C10C-Fe2-C12 | 109.66(7) |
| C11-Fe2-C12 | 40.90(6) |
| C5C-C1C-C2C | 107.7(2) |
| C5C-C1C-Fe1 | 70.04(12) |
| C2C-C1C-Fe1 | 69.97(12) |
| C3C-C2C-C1C | 107.6(2) |
| C3C-C2C-Fe1 | 70.25(12) |
| C1C-C2C-Fe1 | 69.31(12) |
| C4C-C3C-C2C | 108.4(2) |
| C4C-C3C-Fe1 | 70.01(11) |
| C2C-C3C-Fe1 | 69.34(12) |
| C5C-C4C-C3C | 107.9(2) |
| C5C-C4C-Fe1 | 69.45(11) |
| C3C-C4C-Fe1 | 69.88(11) |
| C4C-C5C-C1C | 108.4(2) |
| C4C-C5C-Fe1 | 70.45(11) |
| C1C-C5C-Fe1 | 69.34(11) |
| C7C-C6C-C10C | 107.73(17) |
| C7C-C6C-Fe2 | 69.39(10) |
| C10C-C6C-Fe2 | 69.88(10) |
| C8C-C7C-C6C | 108.34(17) |
| C8C-C7C-Fe2 | 69.65(11) |
| C6C-C7C-Fe2 | 69.97(10) |
| C9C-C8C-C7C | 108.07(17) |
| C9C-C8C-Fe2 | 70.05(10) |
| C7C-C8C-Fe2 | 69.65(10) |
| C8C-C9C-C10C | 107.90(17) |
| C8C-C9C-Fe2 | 69.39(11) |
| C10C-C9C-Fe2 | 69.80(10) |
| C6C-C10C-C9C | 107.96(17) |
| C6C-C10C-Fe2 | 69.51(10) |
| C9C-C10C-Fe2 | 69.49(10) |
| C2-C1-C5 | 107.84(14) |
| C2-C1-C11 | 124.96(14) |
| C5-C1-C11 | 126.91(14) |
| C2-C1-Fe1 | 70.71(9) |
| C5-C1-Fe1 | 68.64(9) |
| C11-C1-Fe1 | 130.96(11) |
| C3-C2-C1 | 107.65(14) |
| C3-C2-C6 | 125.88(15) |
| C1-C2-C6 | 125.86(14) |
| C3-C2-Fe1 | 68.02(9) |
| C1-C2-Fe1 | 69.01(9) |
| C6-C2-Fe1 | 135.27(11) |
| C4-C3-C2 | 108.60(15) |
| C4-C3-Fe1 | 69.15(9) |
| C2-C3-Fe1 | 71.59(9) |
| C3-C4-C5 | 107.81(15) |

| | |
|---|---|
| C3-C4-Fe1 | 69.94(10) |
| C5-C4-Fe1 | 69.87(10) |
| C4-C5-C1 | 108.07(14) |
| C4-C5-Fe1 | 69.11(10) |
| C1-C5-Fe1 | 70.52(9) |
| N8-C6-C2 | 108.66(13) |
| N8-C6-C7 | 112.02(14) |
| C2-C6-C7 | 112.51(14) |
| C10-N8-C9 | 107.93(15) |
| C10-N8-C6 | 112.53(14) |
| C9-N8-C6 | 110.37(14) |
| C15-C11-C12 | 107.76(14) |
| C15-C11-C1 | 128.01(14) |
| C12-C11-C1 | 124.11(14) |
| C15-C11-Fe2 | 69.17(9) |
| C12-C11-Fe2 | 69.56(9) |
| C1-C11-Fe2 | 129.77(11) |
| C13-C12-C11 | 107.57(14) |
| C13-C12-C16 | 126.90(15) |
| C11-C12-C16 | 125.17(14) |
| C13-C12-Fe2 | 68.90(9) |
| C11-C12-Fe2 | 69.54(9) |
| C16-C12-Fe2 | 132.26(11) |
| C14-C13-C12 | 108.54(15) |
| C14-C13-Fe2 | 69.58(10) |
| C12-C13-Fe2 | 70.27(9) |
| C13-C14-C15 | 107.96(14) |
| C13-C14-Fe2 | 69.59(10) |
| C15-C14-Fe2 | 69.80(10) |
| C14-C15-C11 | 108.18(14) |
| C14-C15-Fe2 | 69.29(10) |
| C11-C15-Fe2 | 70.01(9) |
| N18-C16-C12 | 107.83(13) |
| N18-C16-C17 | 115.23(14) |
| C12-C16-C17 | 112.62(14) |
| C20-N18-C19 | 110.50(15) |
| C20-N18-C16 | 113.99(14) |
| C19-N18-C16 | 112.61(15) |

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for FCDMAM. The anisotropic displacement factor exponent takes the form: -2 pi^2 [ h^2 a*^2 U11 + ... + 2 h k a* b* U12 ]

| | U11 | U22 | U33 | U23 | U13 | U12 |
|---|---|---|---|---|---|---|
| Fe1 | 17(1) | 15(1) | 20(1) | 6(1) | 5(1) | 5(1) |
| Fe2 | 15(1) | 16(1) | 19(1) | 6(1) | 4(1) | 9(1) |
| C1C | 54(1) | 23(1) | 45(1) | 17(1) | 27(1) | 5(1) |
| C2C | 22(1) | 23(1) | 82(2) | 16(1) | 17(1) | 2(1) |
| C3C | 39(1) | 18(1) | 37(1) | 6(1) | -7(1) | -2(1) |
| C4C | 41(1) | 15(1) | 43(1) | 5(1) | 14(1) | 8(1) |
| C5C | 41(1) | 18(1) | 45(1) | 15(1) | 1(1) | 8(1) |
| C6C | 21(1) | 29(1) | 35(1) | 13(1) | 8(1) | 16(1) |
| C7C | 32(1) | 30(1) | 34(1) | 8(1) | 9(1) | 24(1) |
| C8C | 29(1) | 17(1) | 39(1) | 9(1) | 1(1) | 13(1) |
| C9C | 26(1) | 27(1) | 33(1) | 18(1) | 8(1) | 15(1) |
| C10C | 24(1) | 25(1) | 26(1) | 11(1) | 3(1) | 14(1) |
| C1 | 16(1) | 11(1) | 18(1) | 4(1) | 4(1) | 5(1) |
| C2 | 15(1) | 14(1) | 19(1) | 5(1) | 4(1) | 5(1) |
| C3 | 18(1) | 19(1) | 21(1) | 6(1) | 7(1) | 9(1) |
| C4 | 23(1) | 20(1) | 17(1) | 6(1) | 6(1) | 10(1) |
| C5 | 17(1) | 16(1) | 19(1) | 6(1) | 3(1) | 6(1) |
| C6 | 18(1) | 24(1) | 21(1) | 10(1) | 7(1) | 12(1) |
| C7 | 24(1) | 33(1) | 20(1) | 6(1) | 2(1) | 14(1) |
| N8 | 23(1) | 28(1) | 26(1) | 13(1) | 9(1) | 17(1) |
| C9 | 37(1) | 23(1) | 41(1) | 12(1) | 12(1) | 17(1) |
| C10 | 35(1) | 49(1) | 36(1) | 26(1) | 16(1) | 32(1) |
| C11 | 15(1) | 16(1) | 17(1) | 6(1) | 4(1) | 8(1) |
| C12 | 16(1) | 16(1) | 19(1) | 9(1) | 5(1) | 8(1) |
| C13 | 19(1) | 21(1) | 20(1) | 10(1) | 8(1) | 10(1) |
| C14 | 23(1) | 23(1) | 18(1) | 7(1) | 6(1) | 13(1) |
| C15 | 17(1) | 18(1) | 19(1) | 5(1) | 3(1) | 9(1) |
| C16 | 19(1) | 16(1) | 19(1) | 8(1) | 5(1) | 7(1) |
| C17 | 18(1) | 22(1) | 30(1) | 8(1) | 1(1) | 5(1) |
| N18 | 24(1) | 15(1) | 25(1) | 4(1) | 6(1) | 9(1) |
| C19 | 47(1) | 24(1) | 32(1) | 2(1) | 9(1) | 17(1) |
| C20 | 36(1) | 24(1) | 30(1) | 11(1) | 4(1) | 17(1) |

Table 5. Hydrogen coordinates ( x 10^4) and isotropic displacement parameters (A^2 x 10^3) for FCDMAM.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H1C | 11031 | 4225 | 512 | 51 |
| H2C | 12676 | 4181 | 2294 | 55 |
| H3C | 11684 | 4714 | 4012 | 47 |
| H4C | 9443 | 5085 | 3301 | 42 |
| H5C | 9041 | 4787 | 1148 | 45 |
| H6C | 2952 | 1428 | 2579 | 31 |
| H7C | 4680 | 3742 | 4344 | 35 |
| H8C | 6970 | 5130 | 3815 | 35 |
| H9C | 6668 | 3684 | 1719 | 32 |
| H10C | 4180 | 1390 | 949 | 29 |
| H3 | 10512 | 707 | 1066 | 23 |
| H4 | 8646 | 1017 | -365 | 24 |
| H5 | 6834 | 1437 | 674 | 22 |
| H6 | 9161 | 80 | 3561 | 23 |
| H7A | 11423 | 1654 | 4905 | 39 |
| H7B | 10695 | 2600 | 4510 | 39 |
| H7D | 11935 | 2422 | 4004 | 39 |
| H9A | 9757 | -2435 | 1666 | 48 |
| H9B | 8766 | -1654 | 1422 | 48 |
| H9C | 8752 | -2279 | 2460 | 48 |
| H10A | 10754 | -993 | 4218 | 49 |
| H10B | 12235 | 194 | 4182 | 49 |
| H10D | 11597 | -1460 | 3376 | 49 |
| H13 | 4613 | 57 | 4070 | 22 |
| H14 | 6734 | 2495 | 5472 | 24 |
| H15 | 8716 | 3285 | 4458 | 22 |
| H16 | 5170 | -981 | 1168 | 22 |
| H17A | 2917 | -2707 | 1013 | 39 |
| H17B | 3074 | -1167 | 1739 | 39 |
| H17C | 3262 | -2232 | 2387 | 39 |
| H19A | 5822 | -3921 | 1073 | 54 |
| H19B | 5313 | -3101 | 310 | 54 |
| H19C | 4225 | -4047 | 871 | 54 |
| H20A | 4701 | -3196 | 2945 | 45 |
| H20B | 6080 | -1692 | 3716 | 45 |
| H20C | 6294 | -3070 | 3110 | 45 |