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Chiral organometallic NADH mimics: Highly stereoselective reductions of ethyl benzoylformate with a 1,4-dihydronicotinoyl fragment attached to the homochiral auxiliary [(η^5-C_5H_5)Fe(CO)(PPh3)] and possessing a homochiral β-hydroxy-carboxamide at C-5.

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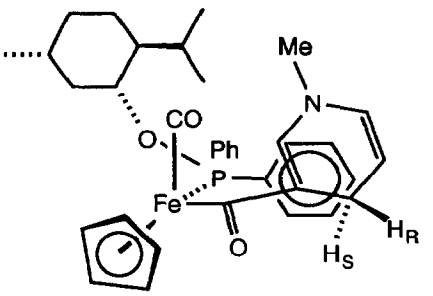
Abstract: A series of homochiral organometallic NADH mimics incorporating the chiral auxiliary [(η5-C_5H_5)Fe(CO)(PPh_3)] at the C-3 carbonyl and a chiral carboxamide at C-5 of a 1,4-dihydronicotinoyl fragment have been prepared. These complexes were shown to stereoselectively reduce ethyl benzoylformate to either (R)- or (S)-ethyl mandelate by a combination of steric and chelation control. For example, complex (R,R)-**12** bearing a carboxamide derived from (R)-(+)-methylbenzylamine afforded (R)-ethyl mandelate in 89% enantiomeric excess. Utilisation of complexes (R,S)-**19a** and (R,R,S)-**22a** bearing chiral β-hydroxy-carboxamides derived from valinol and norephedrine respectively gave the (R)-ethyl mandelate in greater than 97% enantiomeric excess.

Introduction:

The development of compounds which mimic the activity of the coenzyme nicotinamide adenine dinucleotide hydrogenase (NADH) has been actively pursued for the past fifteen years.[1-6] The attractive feature inherent in such enzyme mediated reactions is the high stereoselectivity of hydride transfer and the high rate of catalytic reaction. In the biological system the coenzyme reacts with a substrate in an environment created by the apoenzyme and it is this particular environment which accounts for the stereoselectivity of hydride transfer.[7] In contrast, for the biomimetic system Ohno[4] established that the presence of magnesium (II) ion was essential to achieve any stereocontrol in the asymmetric reduction of ethyl benzoylformate by creating a well-ordered transition state between the substrate and the 1,4-dihydropyridine. It is widely believed that the magnesium (II) ion, through chelation to a suitable polar C-3 substituent on the 1,4-dihydropyridine, orientates and directs the substrate over the reaction centre.[1-6] However, in order to achieve a high degree of stereocontrol it is also essential that only one of the diastereotopic hydrogens at C-4 of the 1,4 dihydropyridine is available for reaction. Two innovative approaches which have addressed this latter requirement involve either the incorporation of a methyl group at C-4,[5] thus obviating the need for discrimination, or the incorporation of a C_2 axis of symmetry[6] within the mimic compound thereby rendering the C-4 hydrogens equivalent.

Recently we reported[8] an alternative approach which relied on selectively blocking one face of the 1,4-dihydronicotinoyl moiety by incorporation of a sterically demanding chiral auxiliary at C-3. The mimic compound (R)-(-)-**1** incorporating the chiral auxiliary [(η^5-C_5H_5)Fe(CO)(PPh_2(O-(*l*)-menthyl))] was prepared and utilised in the asymmetric reduction of ethyl benzoylformate. However, the enantiomeric excess of the corresponding mandelate was moderate (52%) and it was concluded that the steric bulk of the iron auxiliary was preventing efficient chelation of the magnesium (II) ion with both the iron acyl carbonyl at C-3 and the carbonyl of the substrate. It was therefore envisaged that incorporation of a polar functional group at C-5 in our model

compound could provide the chelation necessary for the orientation of the substrate and thus complement the steric control exerted by the chiral iron auxiliary at C-3.



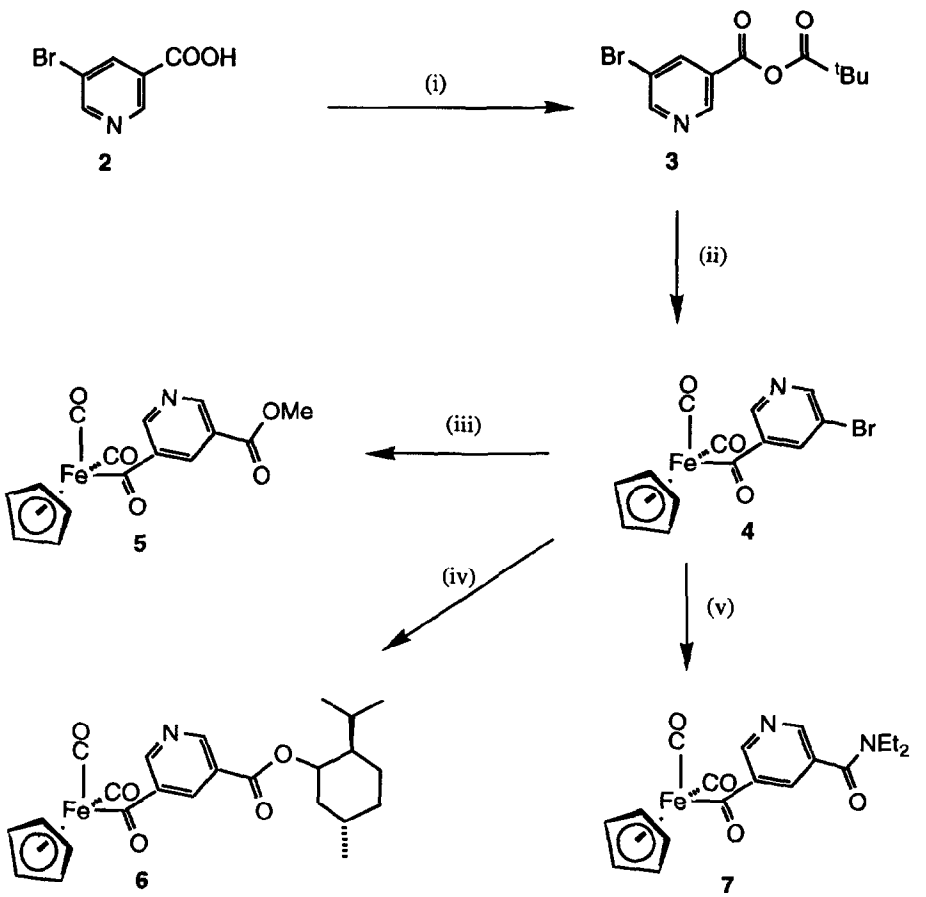
(R)-**1**

The initial objective in this study was to prepare NADH mimics related to (R)-**1**, bearing additionally a carboxamide moiety at C-5, and ascertain their effect on the asymmetric reduction of ethyl benzoylformate. The results of this study, some of which have been previously communicated,[9] are described below.

Results

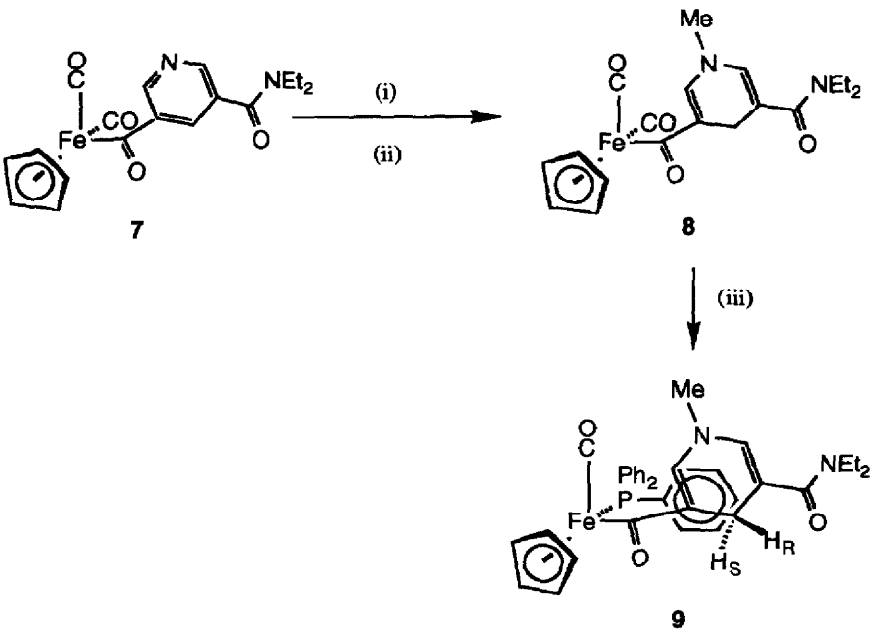
The key intermediate utilised for the synthesis of a variety of compounds described herein was the 5-bromonicotinoyl complex **4** which was readily prepared on a large scale. Treatment of nicotinic acid according to a literature method[10] afforded methyl 5-bromonicotinoate in 88% yield, which on base hydrolysis in a mixture of methanol and water (1:1) gave 5-bromonicotinic acid **2** in 91% yield. The acid **2** in a solution of benzene and triethylamine was treated with pivaloyl chloride and stirred overnight to afford the corresponding mixed anhydride **3** in 96% yield. Treatment of cyclopentadienylirondicarbonyl anion[11] with a solution of the anhydride **3** in tetrahydrofuran at -78°C, followed by warming to room temperature afforded the iron nicotinoyl complex **4** in 89% yield (Scheme 1). It should be noted that the preparation of complex **4** was also investigated using the acid chloride rather than the mixed anhydride **3**, but in this case the yield was substantially lower (*ca.* 55%).

Manipulation of complex **4** allowed us ready access to a variety of functionalised amides and esters by coupling the bromo moiety with an appropriate amine or alcohol utilising a palladium (0)-catalysed carbonylation reaction.[12] In general these reactions were clean and efficient affording the products as pure crystalline solids after column chromatography. For example, the corresponding methyl ester **5** was readily prepared in 89% yield by stirring a solution of **4** in methanol (5 ml) with palladium (II) chloride (0.04 equiv.) and triphenylphosphine (0.08 equiv.) under an atmosphere of carbon monoxide in a Fischer-Porter bottle for 4.5 h at 100°C. When using a chiral secondary alcohol such as (*l*)-menthol the reaction times were longer affording the corresponding ester **6** in 64% yield after 72 h at 100°C. Amides were prepared in an analogous manner, for example, when a solution of **4** in diethylamine (7 ml), palladium (II) chloride (0.04 equiv.) and triphenylphosphine (0.08 equiv.) were stirred under an atmosphere of carbon monoxide for 6 h at 100°C the amide **7** was obtained in 79% yield (Scheme 1).



Scheme 1. *Reagents. (i) ^{t}BuCOCl, NEt_3, benzene, 95%. (ii) $[(\eta^5\text{-}C_5H_5)Fe(CO)_2]^- Na^+$, THF, 89%. (iii) $PdCl_2$, PPh_3, CO, MeOH, NEt_3, 89%.(iv) $PdCl_2$, PPh_3, CO, (l)-menthol, NEt_3, 64%. (v) $PdCl_2$, PPh_3, CO, $HNEt_2$, 79%.*

Since we were interested in preparing NADH mimics with a carboxamide substituent at C-5, compound **7** was converted into the racemic 1,4-dihydronicotinoyl complex **9** *via* the following sequence of steps (Scheme 2). Treatment of compound **7** with iodomethane in dichloromethane afforded, in quantitative yield, the corresponding pyridinium salt, which was reduced with sodium dithionite in a biphasic system (methanol/water/dichloromethane) to give the corresponding 1,4-dihydronicotinoyl derivative **8** in 92% yield. Photolytic ligand exchange of carbon monoxide for triphenylphosphine in a solution of **8** in cyclohexane for 2.5 h afforded the racemic iron complex **9** in an unoptimised yield of 30%. The ^{1}H n.m.r. spectrum (300 MHz) of complex **9** revealed a large difference in the chemical shifts of the diastereotopic hydrogens at C-4 (δ3.07 *vs* δ2.48) suggesting that one face of the 1,4-dihydronicotinoyl moiety is shielded by the triphenylphosphine ligand as illustrated (Scheme 2).[8]



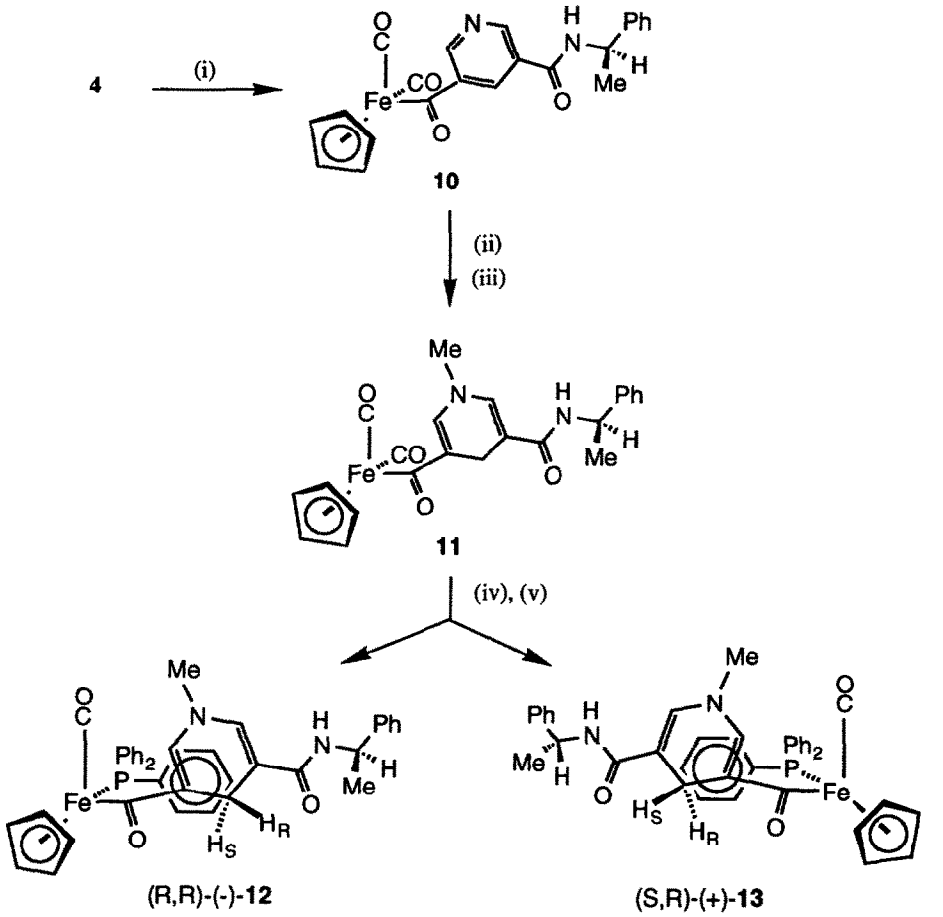
Scheme 2. *Reagents. (i) MeI, CH_2Cl_2, 100%. (ii) $Na_2S_2O_4$, $NaHCO_3$, MeOH, H_2O, 92%. (iii) PPh_3, hv, cyclohexane, 30%.*

When the racemic complex **9** was utilised in the reduction of ethyl benzoylformate under conditions previously reported[8] it was found, as expected, to function as a reasonable reducing agent. Thus after 4 days, g.l.c. analysis of the reaction mixture indicated a 74% conversion to the corresponding mandelate.

Having demonstrated that the racemic 1,4-dihydronicotinoyl complex **9** functions as an efficient reducing agent, the preparation of an analogous homochiral 1,4-dihydronicotinoyl complex was investigated. It was considered that utilisation of a homochiral amine of known absolute configuration in the palladium (II)-catalysed carbonylation reaction, followed by the photolytic exchange with triphenylphosphine would provide a mixture of diastereoisomers which may be separated by either chromatography or crystallisation.

Treatment of a solution of complex **4** in tetrahydrofuran with palladium (II) chloride (0.04 equiv.), triphenylphosphine (0.08 equiv.) and R-(+)-methylbenzylamine[13] (1 equiv.) under an atmosphere of carbon monoxide in a Fischer-Porter bottle for 6 h at 100°C afforded the corresponding homochiral amide **10** $[\alpha]_D^{22}$ +2.7 (c 1.21, CH_2Cl_2) in 87% yield (Scheme 3). Compound **10** upon treatment with iodomethane in dichloromethane afforded, in quantitative yield, the corresponding pyridinium salt, which was reduced with sodium dithionite under standard conditions[1] to give the corresponding 5-substituted 1,4-dihydronicotinoyl complex **11** $[\alpha]_D^{22}$ +2.1 (c 1.57, CH_2Cl_2) in 94% overall yield. Photolytic ligand exchange of carbon monoxide for triphenylphosphine in a cyclohexane/tetrahydrofuran (2:3) solution of **11** afforded a 1:1 mixture of diastereoisomers **12** and **13** which were readily distinguishable by ^1H n.m.r. spectroscopy. It should be noted that the lack of stereoselectivity observed in the photolytic step indicates that the chirality present at the amide side chain is too far removed from the iron centre to have any effect. Separation of the two

diastereoisomers was achieved by careful chromatographic separation on basic alumina to afford homochiral (R,R)-(-)-**12** $[\alpha]_D^{22}$ -547 (c 0.055, CH_2Cl_2) and (S,R)-(+)-**13** $[\alpha]_D^{22}$ +141 (c 0.054, CH_2Cl_2) in 15% and 11% overall yield, respectively (Scheme 3). As in the case of complex **9** the ^1H n.m.r. spectra (300 MHz) of **12** and **13** revealed a significant chemical shift difference in the diastereotopic C-4 hydrogens in each case (δ2.96 *vs* δ2.14 and δ2.97 *vs* δ2.14, respectively), consistent with the triphenylphosphine ligand shielding one face of the 1,4-dihydronicotinoyl moiety as illustrated (Scheme 3).

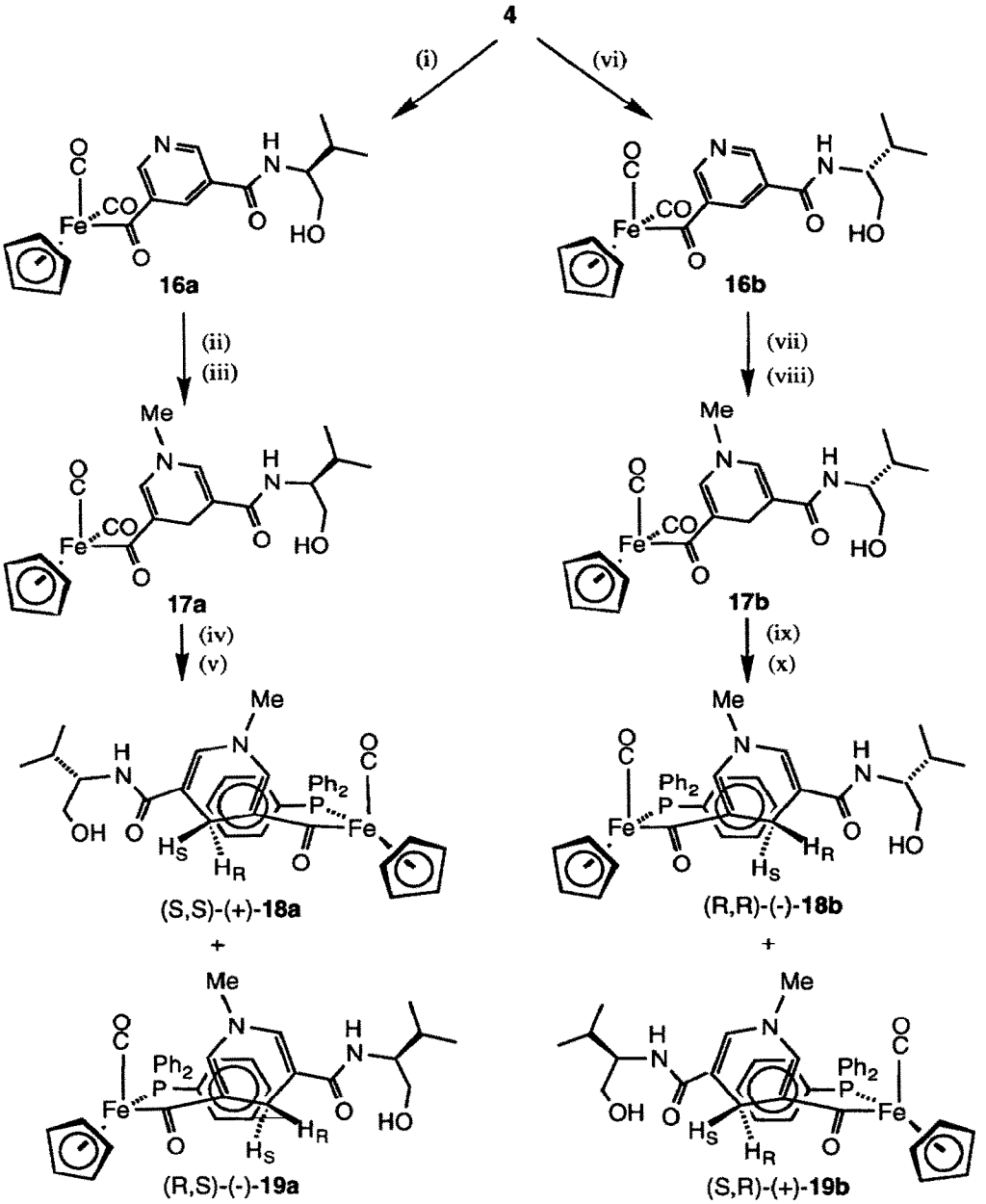


Scheme 3. *Reagents. (i) $PdCl_2$, PPh_3, CO, R-(+)-methylbenzylamine, 87%. (ii) MeI, CH_2Cl_2, 100%. (iii) $Na_2S_2O_4$, $NaHCO_3$, MeOH, H_2O, 94%. (iv) PPh_3, hv, cyclohexane/tetrahydrofuran (1:1). (v) separation, 15% 12 and 11% 13 .*

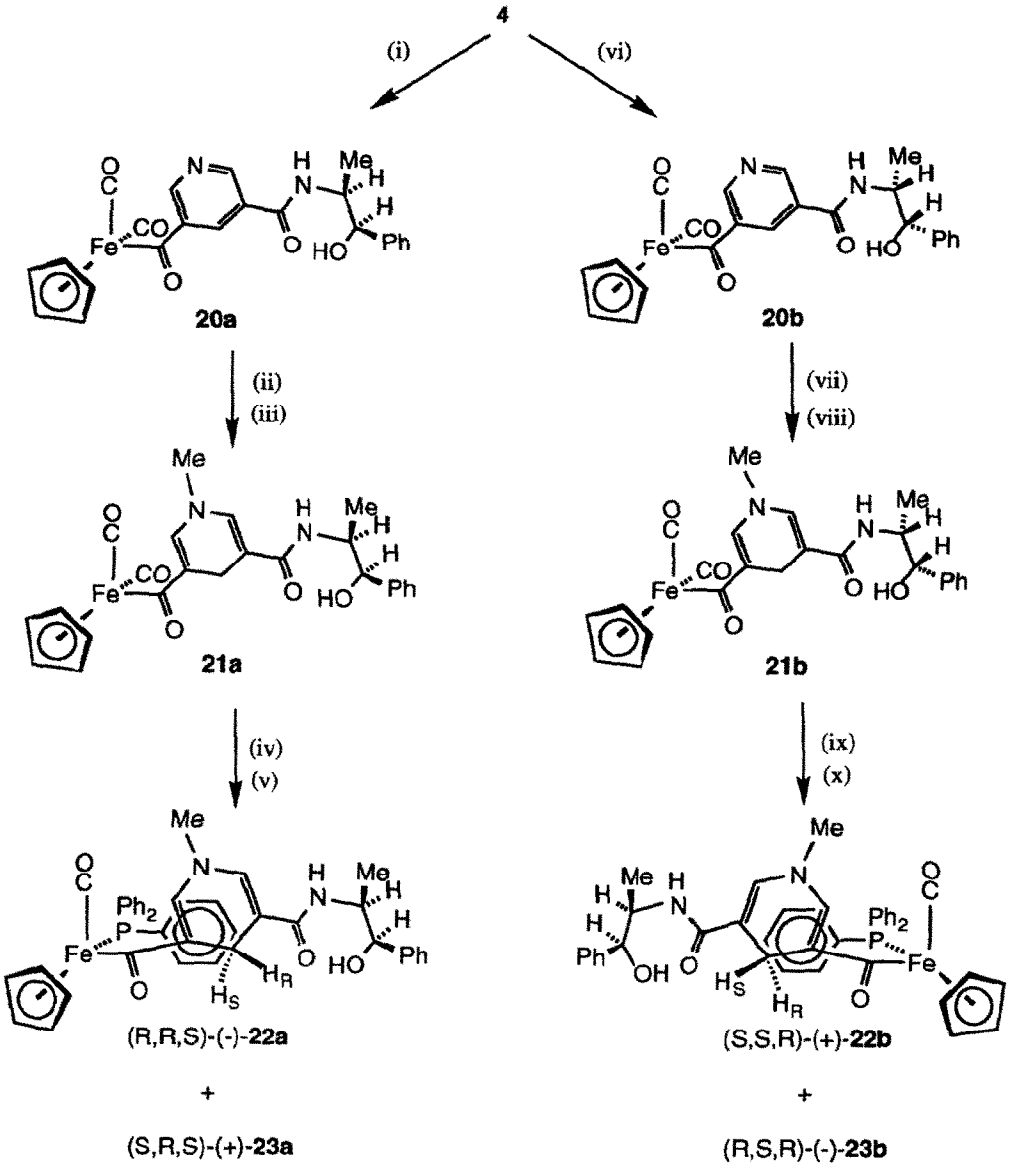
The diastereoisomers **12** and **13** were diastereoisomerically pure within the detection limits of ^1H, ^{13}C and ^{31}P n.m.r. spectroscopy. Furthermore, each diastereoisomer exhibited distinct and discernible R_f values on t.l.c. The absolute configuration at the iron centre was assigned by analogy with the sign of rotation of the iron complex (R)-(-)-**1**.[8] The results of the asymmetric reduction of ethyl benzoylformate to the corresponding mandelates are presented in Table 1.

The β-hydroxy carboxamides derived from valinol were prepared in a manner analogous to that described above. Initially efforts were made to protect the alcohol function but to our advantage it was discovered that protection was unnecessary. However, under the carbonylation conditions the carboxamides were prone to decomposition and as such the reactions were stopped after a few hours, affording, after chromatography, the corresponding products and recovered starting material **4**. Thus, compound **4** in the presence of (S)-(+)-valinol[14] gave the homochiral amide **16a** $[\alpha]_D^{22}$ -18.5 (c 0.054, CH_2Cl_2) in 92% yield,[15] whereas in the presence of (R)-(-)-valinol[14] the homochiral amide **16b** $[\alpha]_D^{22}$ +18.0 (c 0.083, CH_2Cl_2) was obtained in 64% yield.[15] Conversion of compounds **16a** and **16b** (Scheme 4) into the corresponding pyridinium salts, followed by reduction, gave the substituted 1,4-dihydronicotinoyl compounds **17a** $[\alpha]_D^{22}$ -7.2 (c 0.074, CH_2Cl_2) and **17b** $[\alpha]_D^{22}$ +6.9 (c 0.058, CH_2Cl_2) in 94% and 98% overall yield, respectively. Photolytic ligand exchange of carbon monoxide for triphenylphosphine in a tetrahydrofuran/cyclohexane (approx. 1:1) solution of **17a** afforded a 1:1 mixture of diastereoisomers **18a** and **19a**, which were readily distinguishable by ^1H n.m.r. spectroscopy (300 MHz). Similarly, **17b** afforded a 1:1 mixture of diastereoisomers **18b** and **19b**. Separation of the diastereoisomeric mixture **18a** and **19a** was achieved by careful chromatography on basic alumina affording homochiral (S,S)-(+)-**18a** $[\alpha]_D^{22}$ +394 (c 0.055, CH_2Cl_2) and (R,S)-(-)-**19a** $[\alpha]_D^{22}$ -394 (c 0.069, CH_2Cl_2) in 13% and 17% yield, respectively. Likewise chromatographic separation of the diastereoisomeric mixture **18b** and **19b** gave homochiral (R,R)-(-)-**18b** $[\alpha]_D^{22}$ -393 (c 0.043, CH_2Cl_2) and (S,R)-(+)-**19b** $[\alpha]_D^{22}$ +394 (c 0.037, CH_2Cl_2) in 19% and 11% yield, respectively (Scheme 4). The similarity in the magnitude of the specific rotation measured for both of these diastereoisomers is acknowledged and has been checked. The ^1H n.m.r. spectra (300 MHz) of **18** and **19** each revealed a significant chemical shift difference in the diastereotopic C-4 hydrogens (δ3.01 *vs* δ2.14 and δ2.99 *vs* δ2.24, respectively) suggesting that the triphenylphosphine ligand is again shielding one face of the 1,4-dihydronicotinoyl moiety as illustrated (Scheme 4). The diastereoisomers **18** and **19** were diastereoisomerically pure within the detection limits of ^1H, ^{13}C and ^{31}P n.m.r. spectroscopy. Furthermore, each diastereoisomer exhibited distinct and discernible R_f values by t.l.c. The absolute configuration at the iron centre was assigned by analogy with the sign of rotation of the iron complex (R)-**1**.[8] The results of the asymmetric reductions of ethyl benzoylformate to the corresponding mandelates by **18a**, **18b**, **19a** and **19b** are presented in Table 2.

The homochiral complexes **22a** and **22b** (Scheme 5) derived from norephedrine were also prepared by the method described above. Thus compound **4**, in the presence of (1R,2S)-(-)-norephedrine, afforded the homochiral amide **20a** $[\alpha]_D^{22}$ -43 (c 0.10, CH_2Cl_2) in 88% yield,[15] whereas in the presence of (1S,2R)-(+)-norephedrine the homochiral amide **20b** $[\alpha]_D^{22}$ +40 (c 0.09, CH_2Cl_2) was obtained in 61% yield.[15] Conversion of compounds **20a** and **20b** into the corresponding pyridinium salts, followed by reduction, gave the 5-substituted 1,4-dihydronicotinoyl compounds **21a** $[\alpha]_D^{22}$ -23 (c 0.11, CH_2Cl_2) and **21b** $[\alpha]_D^{22}$ +19 (c 0.08, CH_2Cl_2) in 96% and 91% yields, respectively. Photolytic ligand exchange of carbon monoxide for triphenylphosphine in a tetrahydrofuran/cyclohexane (approx. 3:1) solution of **21a** afforded a 1:1 mixture of diastereoisomers **22a** and **23a** which were readily distinguishable by ^1H n.m.r. spectroscopy. Similarly, **20b** afforded a 1:1 mixture of diastereoisomers **22b** and **23b**. Isolation of one of the diastereoisomers was achieved by crystallisation from a solution of dichloromethane/diethyl ether (*ca.* 1:10) at -20°C. Usually after a second crystallisation the diastereoisomeric ratio was greater than 120:1 and in all cases homochiral (R,R,S)-(-)-**22a** $[\alpha]_D^{22}$ -324 (c 0.05, CH_2Cl_2) was obtained in 16% yield after a third crystallisation.



Scheme 4. *Reagents. (i) $PdCl_2$, PPh_3, CO, L-valinol, 100°C, 92%. (ii) MeI, CH_2Cl_2, 100%. (iii) $Na_2S_2O_4$, $NaHCO_3$, H_2O, MeOH, 94%. (iv) PPh_3, hv, tetrahydrofuran/cyclohexane (1:1). (v) separation, 17% (**19a**) and 13% (**18a**). (vi) $PdCl_2$, PPh_3, CO, D-valinol, 100°C, 64%. (vii) MeI, CH_2Cl_2, 100%.(viii) $Na_2S_2O_4$, $NaHCO_3$, H_2O, MeOH, 98%. (ix) PPh_3, hv, tetrahydrofuran /cyclohexane (1.2:1). (x) separation, 11% **19b** and 19% **18b** .*

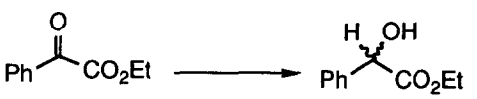


Scheme 5. *Reagents. (i) $PdCl_2$, PPh_3, CO, (1R,2S)-norephedrine, 100°C, 88%. (ii) MeI, CH_2Cl_2, 100%. (iii) $Na_2S_2O_4$, $NaHCO_3$, H_2O, MeOH, 96%. (iv) PPh_3, hv, tetrahydrofuran/cyclohexane (3:1). (v) crystallisation, 16%* **22a** *. (vi) $PdCl_2$, PPh_3, CO, (1S,2R)-norephedrine, 100°C, 61%. (vii) MeI, CH_2Cl_2, 100%. (viii) $Na_2S_2O_4$, $NaHCO_3$, H_2O, MeOH, 91%. (ix) PPh_3, hv, tetrahydro -furan /cyclohexane (3:1). (x) crystallisation, 10%* **22b** *.*

Selective crystallisation of the diastereoisomeric mixture **22b** and **23b** afforded homochiral (S,S,R)-(+)-**22b** $[\alpha]_D^{22}$ +328 (c 0.12, CH_2Cl_2) in 10% yield (Scheme 5). Unfortunately it was not possible to obtain the complexes **23a** and **23b** in a diastereoisomerically pure form. The ^1H n.m.r. spectra (300 MHz) of **22a** and **22b** revealed a significant chemical shift difference in the diastereotopic C-4 hydrogens (δ2.88 *vs* δ2.13) suggesting that the triphenylphosphine ligand is shielding one face of the 1,4-dihydronicotinoyl moiety as illustrated (Scheme 5). The enantiomers **22a** and **22b** were diastereoisomerically pure within the detection limits of ^1H, ^{13}C, and ^{31}P n.m.r. spectroscopy. The absolute configuration at the iron centre was assigned by analogy with the sign of rotation of an iron complex reported earlier.[8] The results of the asymmetric reduction of ethyl benzoylformate to the corresponding mandelates by **21a**, **22a** and **22b** are presented in Table 2.

Discussion

Having established a procedure for the preparation of 1,4-dihydronicotinoyl derivatives **12** and **13** bearing a chiral carboxamide at C-5 derived from (R)-(+)-methylbenzylamine, the utility of these compounds in the asymmetric reduction of ethyl benzoylformate was investigated. The results are summarised in Table 1. As predicted both diastereoisomers **12** and **13** enhance the enantiomeric excess of **15** compared with the earlier mimic compound **1**, presumably because of the additional chelation afforded by the oxygen of the amide carbonyl to the magnesium (II) ion. The significance of the steric control afforded by the chiral iron auxiliary is illustrated by comparing an early NADH mimic compound,[4] similar to **12** but lacking the iron auxiliary, in which (R)-(-)-ethyl mandelate was obtained in only 20% ee. While the incorporation of the C-5 carboxamide enhances the overall stereoselectivity of the reaction, the configuration of the carboxamide moiety does not determine the configuration of the predominant mandelate which is governed by the chirality at the iron centre, even though the iron atom is three bonds removed from the reaction site. That chelation is necessary to ensure high stereoselection is illustrated by a fall in stereoselectivity (80 *vs* 89%) when a 0.75 molar ratio of magnesium (II) perchlorate is used.



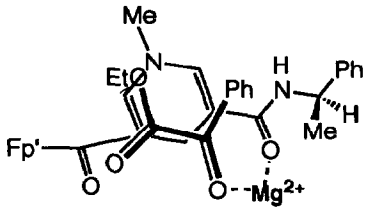
14 **15**

Table 1. Asymmetric reduction of ethyl benzoylformate **14** to ethyl mandelate **15** by compounds **12** and **13**.[a]

Reagent	Time (hours)	Configuration of **15**	Chemical Yield[b] (%)	Enantiomeric Excess[c] (%)
(R,R)-**12**	24	R	68	89 (88)
(S,R)-**13**	24	S	66	77 (78)
(R,R)-**12**[d]	168	R	79	80 (78)

[a]For a general procedure see Experimental. [b]Isolated yield. [c]Based on the ^{19}F and ^1H n.m.r. spectra of the corresponding (R)-α-(trifluoromethyl)methoxyphenylacetate.[16] Figures in brackets are based on the specific rotation of pure **15**; $[\alpha]_D^{20}$ -104 (EtOH) for (R)-(-)-**15**[4]; $[\alpha]_D^{20}$ +94 (c 0.6, EtOH) for (S)-(+)-**15**[4] of 90% e.e. [d]Ratio of reagent to magnesium (II) perchlorate was 1:0.75 in 3 ml of dry acetonitrile

In line with our previous model[8] we anticipate that the chelation of the magnesium (II) ion to both the C-5 carbonyl oxygen of the nicotinoyl derivative and the keto carbonyl oxygen of ethyl benzoylformate will present the *si*-face of the ketone to the C-4 *pro*-(R) hydrogen of (R,R)-**12**, thus producing the mandelate (R)-(-)-**15** as the major enantiomer (Figure 1). Delivery of the *re*-face has been shown by molecular modelling studies to be energetically disfavoured due to steric interactions between the benzoyl-phenyl ring and the iron chiral auxiliary.[8]



Fp' = R-[(η^5-C_5H_5)Fe(CO)(PPh_3)]

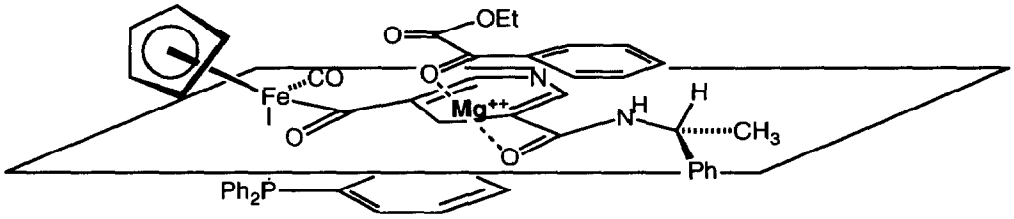


Figure 1: Delivery of the *si*-face of ethyl benzoylformate to the pro-R hydrogen of (R,R)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh_3)]-1-methyl-5-(N–α-methylbenzylcarbamoyl)-1,4-dihydronicotinoyl **12** by chelation.

From the results presented in Table 1 it is evident that, compared to our earlier mimic compound (**1**), the carboxamide side chain at C-5 improves the stereoselectivity of reduction for both diastereoisomers (R,R)-**12** (89% ee) and (S,R)-**13** (77% ee), presumably by providing a better chelation site for the magnesium (II) ion. Although the relative configuration of the methylbenzyl side chain appears, in this instance, to exert a relatively minor influence (± 6%) it does play a role in determining the overall stereoselectivity of reduction with the higher enantiomeric excess of 89% being achieved when the (R)-(+)-methylbenzyl side chain is matched with the (R)-configuration at iron.

We anticipated that a further improvement in stereoselectivity, due to additional chelation, could be achieved by incorporating an alcohol[3,5c] function within the C-5 side chain. For reasons of ready availability and enantiomeric purity the β-hydroxy-amines valinol and norephedrine were chosen for the construction of β-hydroxy-carboxamide side chains. The results of the asymmetric reduction of ethyl benzoylformate to ethyl mandelate **15** by complexes **18a**, **18b**, **19a**, **19b**, **21a**, **22a** and **22b** are summarised in Table 2. As predicted, the incorporation of an appropriate β-hydroxy-carboxamide at C-5 of the 1,4-dihydronicotinoyl complex can enhance the enantiomeric excess of **15** compared with the earlier mimic compound **12**,

presumably because of the additional chelation afforded by the alcohol function of the amide with that of the magnesium ion, e.g. utilising (S,R)-(-)-**19b** afforded (S)-(+)-**15** in 97% ee.

Table 2. Asymmetric reduction of ethyl benzoylformate **14** to ethyl mandelate **15** by compounds **18a, 18b, 19a, 19b, 21a, 22a** and **22b.**[a]

Reagent	Time (hours)	Configuration of **15**	Chemical Yield[b] (%)	Enantiomeric Excess[c] (%)
(S,S)-**18a**	8	S	64	16 (18)
(R,R)-**18b**	21	R	85	15 (16)
(R,S)-**19a**	8	R	82	98 (99)
(S,R)-**19b**	12	S	84	97 (99)
(R,S)-**21a**	20	R	67	55 (54)
(R,R,S)-**22a**	1.5	R	75	98 (98)
(S,S,R)-**22b**	3	S	78	97 (98)

[a]For a general procedure see Experimental. [b]Isolated yield. [c]Based on the ^{19}F and ^{1}H n.m.r. spectra of the corresponding (R)-α-(trifluoromethyl)methoxyphenylacetate.[16] Figures in brackets are based on the specific rotation of pure **15**, $[\alpha]_D^{20}$ -104 (EtOH) for (R)-(-)-**15**[4]; $[\alpha]_D^{20}$ +94 (c 0.6, EtOH), for (S)-(+)-**15**[4] of 90% e.e.

While the presence of the valinol and norephedrine substituted carboxamides in complexes **19** and **22** respectively enhances the stereoselectivity in the reduction of **14**, the configuration of the predominant mandelate produced in the reaction is still governed by the chirality at the iron centre. As such, since the homochiral complexes **19** and **22** are available in both enantiomeric forms the corresponding (R)- and (S)-mandelates are available in high enantiomeric purity. The contribution of the chirality at the iron centre to the stereoselectivity of reaction is illustrated when **14** is reduced by complex **21a**. In the absence of chirality at the iron centre there is a dramatic drop in enantiomeric excess from 98% to 55% presumably resulting from the loss of the sterically demanding triphenylphosphine substituent and hence the high selectivity of the substrate for only one of the C-4 hydrogens. In line with this observation the C-4 hydrogens of **21a** have equivalent chemical shifts by n.m.r. but are separated by 0.75 ppm in complex (R,R,S)-**22a**.

That the reduction of ethyl benzoylformate by (R,R,S)-**22a** does not proceed in the absence of magnesium (II) perchlorate and the solubility of (R,R,S)-**22a** in acetonitrile is dramatically increased in the presence of magnesium (II) perchlorate indicates that the magnesium (II) ion plays a role in the reduction of **14** presumably *via* complexation of the ion to complex (R,R,S)-**22a**. The binding sites and the subsequent arrangement of the complex formed between (R,R,S)-**22a** and magnesium (II) ion is fundamental to the understanding of the stereochemical course of these reductions. As ^{13}C n.m.r. spectroscopy has previously proved to be useful in the recognition of these binding sites,[6,17] the ^{13}C n.m.r. chemical shift values for (R,R,S)-**22a** in acetonitrile-d_3 both in the absence and the presence of one equivalent of magnesium (II) perchlorate were measured. The resonance of the C-5-substituted carbonyl presents a distinctive upfield shift (9.2 ppm) upon addition of the magnesium (II) perchlorate while there is relatively little movement (0.9 ppm) of the resonance attributed to the C-3-substituted carbonyl. This is in contrast with ^{13}C n.m.r. studies of (R)-**1**

with magnesium (II) ion where a significant downfield shift (6.3 ppm) was observed for the C-3-substituted carbonyl.[8b] We see this behaviour as evidence of complexation between the amide carbonyl oxygen of (R,R,S)-**22a** and the magnesium (II) ion.

Chemical shifts of protons in n.m.r. spectra of (R,R,S)-**22a** in the presence of varying amounts of magnesium (II) ion (0-4 equivalents) were recorded with the only significant shift being observed for the olefinic C-6 proton, which showed a downfield shift proportional to the magnesium (II) ion concentration. The addition of Eu(fod)$_3$ (5%) to a solution of (R,R,S)-**22a** in acetonitrile-d_3 showed either a broadening or a shift in the resonance of not only the proton at C-6 but also those protons close to the hydroxy function of the norephedrine substituent. These results are consistent with the proposal that the magnesium (II) ion chelates with both the carbonyl and the alcohol functions of the amide side chain.

Data from i.r. spectroscopy suggests a different situation. Upon addition of up to one equivalent of magnesium (II) perchlorate there is a shift in the absorption corresponding to the stretching vibration of the C-3-substituted carbonyl of (R,R,S)-**22a**. A similar shift was observed for the C-3-substituted carbonyl of complex (R)-**1**.[8b] A shift in the signal assigned to the C-5-substituted carbonyl of (R,R,S)-**22a** was only observed in the presence of two equivalents of magnesium (II) perchlorate. With more than two equivalents of magnesium (II) perchlorate a shift of the absorption frequency of the CO ligand on iron was observed. Contrary to the observation made from ^{13}C n.m.r. data these results would suggest that the first site of chelation of magnesium (II) ion is the C-3 acyl carbonyl rather than the C-5 amide carbonyl. Further investigations into the effect of the magnesium (II) ion concentration on the signal shift in ^{13}C n.m.r. spectra showed no significant shift in the signal corresponding to the C-3 acyl carbonyl when two equivalents of magnesium (II) ion were added to the sample. This inconsistency between i.r. and ^{13}C n.m.r. data was also observed by Ohno and Ushida.[1]

In an attempt to investigate the effect of the concentration of magnesium (II) ion on the rate and the stereoselectivity of the reaction, the reduction of **14** by; (a) (R,R,S)-**22a** in the presence of two equivalents of magnesium (II) and (b) (R,S)-**19a** with one half, two and five equivalents of magnesium (II), was studied (Table 3). Ohno *et al.*[18,19] stated that, in general, reductions of ethyl benzoylformate do not show a reduction in reaction rate with concentrations of magnesium (II) ion greater than one equivalent. However, in this case it is clear that the rates of reaction of (R,S)-**19a** and (R,R,S)-**22a** are slower when more than one equivalent of magnesium (II) ion is added to the reaction mixture. Additional chelation of magnesium ion to **14**, which would create repulsive forces between the positively-charged interacting species and thereby suppress the reduction, was dismissed by Ohno[18] as ethyl benzoylformate has a low ability for complexation with magnesium ion. An excess of magnesium (II) ions may result in additional chelation of the amide carbonyl and hydroxy functions thus changing the geometry of the ternary complex and perhaps hindering approach of the substrate. Alternatively excess magnesium ion may chelate with the oxidised forms of **22a** and **19a** thereby picking up the substrate and rendering it unavailable for reduction. The rate of reduction by (R,S)-**19a** in the presence of 0.5 equivalents of magnesium (II) ion is also decreased since presumably fewer of the (R,S)-**19a** molecules are activated towards reduction.

It should be noted that a decrease in stereoselectivity occurs when **14** is reduced by (R,S)-**19a** in the presence of more than one equivalent of magnesium (II) ion. This observation is consistent with the above proposal, chelation of independent magnesium (II) ions to the amide carbonyl and hydroxy functions of (R,S)-**19a** would distort the complex from the geometry it would usually adopt with one equivalent of magnesium ion. As it is this geometry which is responsible for controlling the stereochemistry of reduction by influencing

the orientation of the substrate, any distortion of the otherwise prevailing chiral environment would be expected to alter the stereoselectivity. Inouye *et al.*[20] observed that the enantiomeric excess of ethyl mandelate decreased with an increase of magnesium (II) ion concentration above one equivalent only when hydroxy groups were present in the amide side chain. The high enantioselectivity observed with up to one equivalent of magnesium (II) ion has been attributed to the formation of a reactive species whereby the 1,4-dihydropyridine and the oxidized form of the 1,4-dihydropyridine are complexed to the same magnesium (II) ion.[20] However, an analogous explanation for the observed enantioselectivity dependence on magnesium (II) ion concentration for (R,S)-**19a** would seem unlikely due to the combined bulk of the iron auxiliary and the valinol derived side chain. Irrespective of the mechanism of reduction it would appear that both the reaction rate and the stereoselectivity in the reduction of **14** are greatest when one equivalent of magnesium (II) ion is used.

Table 3. Asymmetric reduction of ethyl benzoylformate **14** to ethyl mandelate **15** by compounds (R,S)-**19a** and (R,R,S)-**22a**.[a]

Reagent	Mg^{++} equiv.	Time (hours)	Configuration of **15**	Chemical Yield[b] (%)	Enantiomeric Excess[c] (%)
(R,R,S)-**22a**	1	1.5	R	75	98 (98)
	2	20	R	68	99 (99)
(R,S)-**19a**	0.5	48	R	46	97 (96)
	1	8	R	82	98 (99)
	2	22	R	70	94 (94)
	5	70	R	48	91 (93)

[a]For a general procedure see Experimental. [b]Isolated yield. [c]Based on the ^{19}F and ^{1}H n.m.r. spectra of the corresponding (R)-α-(trifluoromethyl)methoxyphenylacetate.[16] Figures in brackets are based on the specific rotation of pure **15**, $[\alpha]_D^{20}$ -104 (EtOH) for (R)-(-)-**15**[4]; $[\alpha]_D^{20}$ +94 (c 0.6, EtOH), for (S)-(+)-**15**[4] of 90% e.e.

In line with our previous model and consistent with ^{13}C n.m.r. data, we anticipate, in the presence of one equivalent of magnesium (II) ion, the formation of a ternary complex involving chelation of magnesium (II) ion to the amide carbonyl oxygen, the amide alcohol function of the dihydronicotinoyl and the ketonic oxygen of ethyl benzoylformate. Consequently when ethyl benzoylformate is reduced by, for example, (R,S)-**19a** the *si*-face of the ketone is presented to the C-4 *pro*-(R) hydrogen thus producing the mandelate (R)-(-)-**15** as the major enantiomer (Figure 2). It is apparent that the additional chelation provided by the alcohol function is crucial in contributing to the very high stereoselectivity of the hydride transfer process. Although intramolecular hydrogen bonding of the alcohol function with the carboxamide carbonyl has not been represented in Figure 2, such interaction may well occur in the transition state.

The conformation of the 1,4-dihydronicotinoyl 'ternary complex' is assumed to be as represented (Figure 2) based on recent evidence suggesting the importance of an out-of-plane orientation of the carbonyl dipole at C-5 *syn* to the departing hydride.[21] The relevance of this *syn* orientation has also been discussed with respect to the stereoselectivity of hydride transfer in biological systems.[7] Attempts were made to investigate the

relative orientation of the C-5 amide carbonyl to the dihydronicotinoyl moiety in **22a** using n.O.e. experiments. While irradiation of the doublet at δ4.99 (NH) in complex **22a** in chloroform-d_1 gave a 7% enhancement of each of the doublets at δ2.88 and δ2.13 (diastereotopic hydrogens at C-4), irradiation of the same signal for **22a** in acetonitrile-d_3 in the presence of one equivalent of magnesium (II) ion gave neither enhancement of the C-4 hydrogens nor enhancement of the C-6 hydrogen. Although these results give no definitive indication about the orientation of the C-5 carbonyl of **22a** in the reaction mixture, if the conformation of the ternary complex was such that the C-5 carbonyl oxygen was orientated away from C-4 the required *syn* orientation to the departing hydride would be impossible to achieve.[7,21] Furthermore, in this orientation chelation of the magnesium (II) ion to both the C-5 carbonyl of the 1,4-dihydronicotinoyl and the ketonic oxygen of the substrate would displace the substrate reactive centre a considerable distance from the C-4 hydrogens. Consequently we propose a transition state geometry with the C-5 carbonyl orientated *syn* to the C-4 departing hydride.

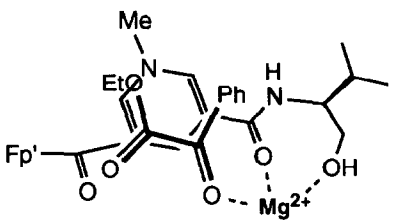
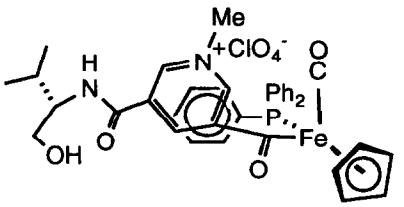


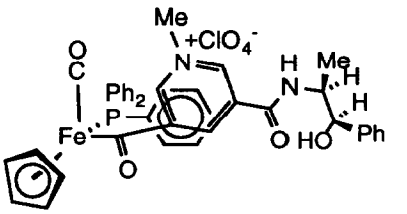
Figure 2: Delivery of the *si*-face of ethyl benzoylformate to the *pro*-(R) hydrogen of (R,S)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh3)]-1-methyl-5-(1-hydroxymethylisopropylcarbamoyl)-1,4-dihydronicotinoyl **19a** by chelation. Fp'=[(η^5-C_5H_5)Fe(CO)(PPh3)].

Of interest in Table 2 is the dramatic effect exerted by the valinol-substituted carboxamide in the diastereoisomeric complexes **18** and **19**, e.g. complex (R,R)-**18b** affords (R)-**15** in 15% ee whereas complex (S,R)-**19b** affords (S)-**15** in 97% ee. It appears that in compound **19b** the high enantiomeric excess of 97% is achieved through a complementary matching of the configurations of the (R)-valinol derived substituent with the (S)-iron auxiliary. In this instance the pairing of matched configurations promotes chelation of the substrate without hindering the face-blocking effect of the iron auxiliary. At first glance it would appear that for (S,R)-**19b** the (R)-configuration of the valinol derived carboxamide and the (S)-configuration of the iron auxiliary should be mismatched due to the large isopropyl substituent appearing to be placed towards the face of the 1,4-dihydronicotinoyl to which the ethyl benzoylformate is expected to approach. However, modelling studies show that when the hydroxyl function chelates with magnesium (II) ion the isopropyl group can lie in a pseudo-equatorial position leaving the upper face of the 1,4-dihydronicotinoyl unblocked and free for reaction. On the other hand for (R,R)-**18b** the (R)-valinol substituted carboxamide is working against the effect of the (R)-iron auxiliary at C-3. Although this mismatching is more difficult to rationalize it is presumed the complex is forced to adopt such a conformation that either chelation of the substrate or selective blocking of one face is ineffective.

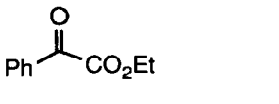
In the reduction of ethyl benzoylformate to ethyl mandelate by a 1,4-dihydronicotinoyl complex the corresponding pyridinium salt is formed which can be isolated upon work-up. For example, utilising (R,S)-**19a** for the reduction affords the corresponding salt (R,S)-**25** (Scheme 6). Similarly, the salts (S,S)-**24** and (R,R,S)-**26** were formed from the oxidation of the 1,4-dihydronicotinoyl complexes (S,S)-**18a** and (R,R,S)-**22a**, respectively. Although the reactions are stoicheiometric the pyridinium salt can be re-reduced with sodium dithionite and crystallised to afford the corresponding homochiral 1,4-dihydronicotinoyl derivatives in 70-80% overall yield.



(S,S)-(-)-**24**



(R,R,S)-(+)-**26**



14

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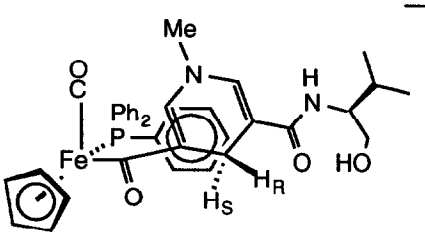
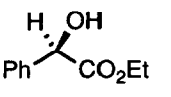


(R,S)-(-)-**19a**

$Mg(ClO_4)_2$, CH_3CN



(R)-(-)-**15**

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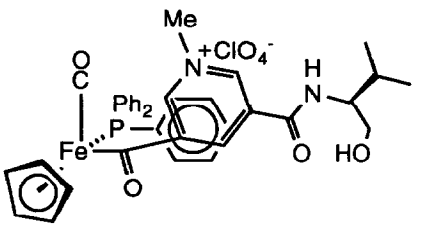

(R,S)-(+)-**25**

Scheme 6

In conclusion we have demonstrated that complexes incorporating two chiral auxiliaries allow high stereoselectivities to be achieved by providing a means of independently introducing both direction and orientation control between an NADH mimic and substrate. Direction control is achieved by the incorporation of a sterically demanding chiral auxiliary at C-3 while orientation control is achieved by incorporating a β-hydroxy-carboxamide at C-5. Diastereoisomeric complexes where the effects of the two chiral auxiliaries are matched and mismatched are formed. Efforts are currently being directed towards determining the range of prochiral substrates amenable to reduction and to rendering these reductions catalytic.

Experimental

With the exception of the n.O.e. experiments ^1H n.m.r. spectra were recorded on a Bruker WH-300 spectrometer at 300.13 MHz and referenced to residual protio solvent with chemical shifts being reported as δ ppm from TMS. N.O.e. experiments were performed on a Bruker AM-500 spectrometer at 500.12 MHz using either $CDCl_3$ or CD_3CN as solvent and internal reference. Unless otherwise stated ^{13}C n.m.r. were recorded on a Bruker AM-250 spectrometer at 62.90 MHz using $CDCl_3$ as a solvent and internal reference and are reported as δ ppm from TMS. ^{13}C N.m.r. spectra obtained from a Varian Gemini 200 spectrometer were recorded at 50.3 MHz. ^{31}P n.m.r. spectra were recorded on a Bruker AM-250 MHz spectrometer at 101.26 MHz using $CDCl_3$ as solvent and are reported as δ ppm from an external reference of triethylphosphate in D_2O. ^2H n.m.r. spectra were recorded on a Bruker AM-250 MHz spectrometer at 38.40 MHz using 1% $CDCl_3$ in $CHCl_3$ as solvent and internal standard. ^{19}F n.m.r. spectra were recorded on a Bruker AM-250 MHz spectrometer at 235.35 MHz using $CDCl_3$ as solvent and are reported as δ ppm from an external reference of $CFCl_3$. I.r. spectra were recorded in deuteriochloroform on a Perkin Elmer 1710 instrument. Mass spectra were recorded on a V.G. micromass ZAB 2F instrument using EI and FD techniques. Accurate mass FAB measurements were recorded on a VGZAB 1F mass spectrometer, voltage scans with 2% PEGMME reference. Optical rotations were measured using a Perkin Elmer 241 polarimeter. Elemental analyses were performed by the Dyson Perrins Laboratory Analytical Service. Gas chromatography was performed utilising a Pye 104 instrument equipped with a 10% w/w Carbowax 20M on Chromosorb W (2 m x 4 mm i.d.) column and flame ionisation detector at an oven temperature of 200°C.

All reactions and purifications were performed under a nitrogen atmosphere using standard vacuum line techniques. Removal of all solvents was carried out under reduced pressure. Dichloromethane was distilled from calcium hydride and hexane refers to that portion of petroleum ether boiling in the range 67-70°C. Acetonitrile was distilled from calcium hydride and then redistilled from phosphorous pentoxide and stored over 4Å molecular sieves. Pyridine was distilled from calcium hydride and stored over sodium hydroxide. Benzene was dried over sodium wire. Tetrahydrofuran was dried over sodium benzophenone ketyl and distilled.

Preparation of 5-bromonicotinic acid **2**- To a vigorously stirred solution of methyl-5-bromonicotinoate (165 g, 0.764 mol) in a mixture of methanol (300 ml) and water (300 ml) was added potassium hydroxide until litmus paper indicated that the solution was basic (pH 10). The black solution was stirred at room temperature for 12 h and acidified with concentrated hydrochloric acid to a pH of approximately 2-3 to give a white precipitate. The slurry was then filtered, washed with water followed by ethanol and dried overnight *in vacuo* to afford the corresponding acid **2** (140.6 g, 91%) as a white solid. Analytically pure **2** was obtained as a white solid by crystallisation from acetic acid; m.p. 174-175°C; (Found: C, 35.42; H, 1.99; N, 7.12; Calc. for $C_6H_4BrNO_2$: C, 35.64; H, 1.98; N, 6.93%); $\nu_{max.}$ (nujol) 3432-3055 and 1675 cm^{-1}; δ_H (d_6-DMSO) 8.99 (1H, d, J 1.5 Hz), 8.88 (1H, d, J 2.0 Hz) and 8.36 (1H, t, J 2.0 Hz, 4-H); δ_C (d_6-DMSO) 166.7 (s, C=O), 155.3 (d, 2-C), 150.2 (d, 6-C), 140.6 (d, 4-C), 130.4 (s, 5-C) and 121.7 (s, 3-C); m/z 201 (M^+-1).

Preparation of tert-butylcarbonyl-5-bromonicotinic acid **3**- To a slurry of the acid **2** (140.6 g 0.699 mol) in dry benzene (1000 ml) was added triethylamine (140 ml, 1.00 mol) and the resulting mixture stirred at room temperature for 1 h. Pivaloyl chloride (100 ml, 4.75 mol) was then added to the inhomogeneous solution and stirred for 16 h. The resulting slurry was then filtered under vacuum, the filtrate washed with benzene (75 ml, x4) and the combined organics concentrated to afford **3** (191 g, 96%) as a grey-white solid. Analytically pure **3** was obtained as a white solid by crystallisation from a mixture of dichloromethane/hexane (1:4); m.p. 172-173°C; (Found: C, 46.21; H, 4.03; N, 4.68. Calc. for $C_{11}H_{12}BrNO_3$: C, 46.15; H, 4.19; N, 4.89 %); $\nu_{max.}$ (CH_2Cl_2) 1810 and 1736 cm^{-1}; δ_H 9.11 (1H, d, J 1.5 Hz), 8.90 (1H, d, J 2.0 Hz), 8.42 (1H, t, J 2.0 Hz, 4-H) and 1.37 (9H, s, $C(CH_3)_3$); δ_C (200 MHz) 172.5 (s, C=O), 159.9 (s, C=O), 155.5 (d, 2-C), 149.0 (d, 6-C), 139.9 (d, 4-C), 126.4 (s, 5-C), 120.7 (s, 3-C), 40.0 (s) and 26.0 (q); m/z 286 (M^+).

Preparation of [(η^5-C_5H_5)Fe(CO)$_2$]-5-bromonicotinoyl **4**- To a stirred solution of cyclopentadienyl-irondicarbonyl anion[8] (226 mmol) in tetrahydrofuran (1200 ml) at -78°C, was added a solution of *tert*-butylcarbonyl-5-bromonicotinic acid **3** (60.0 g, 210 mmol) in tetrahydrofuran (500 ml) over a period of 15 min. The reaction mixture was stirred for 3 h at -78°C and then allowed to warm to room temperature and stirred overnight. The resulting slurry was filtered through Celite under vacuum, washed with dichloromethane (100 ml, x4), and the combined organics concentrated to give a brown solid which was crystallised at -20°C from a mixture of dichloromethane/ethyl acetate (1:1) to afford **4** as yellow needles (68 g, 89%); (Found: C, 43.32; H, 2.10; N, 3.60; Calc. for $C_{13}H_8O_3BrNFe$: C, 43.14; H, 2.23; N, 3.87 %); $\nu_{max.}$ 2030, 1973 and 1620 cm^{-1}; δ_H 8.71 (1H, d, J 1.6 Hz), 8.67 (1H, d, J 2.1 Hz), 7.77 (1H, t, J 2.1 Hz) and 4.96 (5H, s); δ_C (200 MHz) 253.3 (s, C=O), 213.5 (s, C=O), 151.9 (d, 2-C), 146.5 (d, 6-C), 145.6 (s, 3-C), 134.6 (d, 4-C), 121.0 (s, 5-C), 86.4 (d, C_5H_5); m/z 362 (M^+).

Preparation of [(η^5-C_5H_5)Fe(CO)$_2$]-5-(methoxycarbonyl)nicotinoyl **5**- A Fischer-Porter bottle containing a mixture of complex **4** (518.5 mg, 1.43 mmol), palladium(II) chloride (9.2 mg, 4 mol%), triphenylphosphine (27 mg, 8 mol%) and triethylamine (0.27 ml, 1.95 mmol) in methanol (5 ml) was sealed under 4 atmospheres of CO and stirred at 100°C for 4.5 h. Concentration of the black solution followed by column chromatography of the residue in dichloromethane on silica gel (elution with ethyl acetate/hexane, 1:1) afforded compound **5** (437 mg, 89%) as yellow crystals; (Found: C, 52.69; H, 3.21; N, 3.87, Calc. for $C_{15}H_{11}O_5NFe$: C, 52.82; H, 3.25; N, 4.11%); $\nu_{max.}$ (CH_2Cl_2) 2029, 1972, 1729 and 1608 cm^{-1}; δ_H 9.21 (1H, d, J 1.9 Hz), 8.86 (1H, d, J 2.1 Hz), 8.33 (1H, t, J 2.1 Hz, 4-H), 4.98 (5H, s) and 3.99 (3H, s); δ_C 213.2 (s, C=O), 165.3 (s, C=O), 151.5 (d, 2-C), 150.3 (d, 6-C), 144.3 (s, 3-C), 133.8 (d, 4-C), 125.9 (s, 5-C), 86.4 (s, C_5H_5) and 52.2 (s, OMe); m/z 342 (M^++1).

Preparation of [(η^5-C_5H_5)Fe(CO)$_2$]-5-((l)-menthoxycarbonyl)nicotinoyl **6**- A Fischer-Porter bottle containing a mixture of complex **4** (5.0 g, 13.8 mmol), palladium(II) chloride (98 mg, 4 mol%), triphenylphosphine (289 mg, 8 mol%), triethylamine (2.9 ml, 20.7 mmol) and (*l*)-menthol (2.4 g, 15.2 mmol) in tetrahydrofuran (25 ml) was sealed under 5 atmospheres of CO and stirred at 100°C for 72 h. Concentration of the black solution followed by column chromatography of the residue in dichloromethane on silica gel (elution with ethyl acetate/hexane, 1:1) afforded compound **6** (4.10 g, 64%) as a red crystalline solid; $[\alpha]_D^{22}$ -44.6 (c 0.13, CH_2Cl_2); (Found: C, 61.70; H, 5.94; N, 2.87; Calc. for $C_{24}H_{27}O_5NFe$: C, 61.95; H, 5.85; N, 3.01%); $\nu_{max.}$

(CH_2Cl_2) 2032, 1975, 1714 and 1614 cm^{-1}; δ_H 9.21 (1H, d, J 2.0 Hz), 8.87 (1H, d, J 2.0 Hz), 8.33 (1H, t, J 2.0 Hz, 4-H), 4.97 (5H, s, C_5H_5), 4.97 (1H, dt, J 7.2, 4.0 Hz), 2.13 (1H, br d, J 7.5 Hz), 2.02-1.91 (1H, m), 1.81-1.70 (3H, m), 1.65-1.49 (3H, m), 1.22-1.07 (2H, m), 0.96 (3H, d, J 7.2 Hz), 0.94 (3H, d, J 7.2 Hz), 0.80 (3H, d, J 7.5 Hz); δ_C (200 MHz) 253.9 (s, C=O), 213.5 (s, C=O), 164.4 (s, C=O), 151.6 (d, 2-C), 150.5 (d, 6-C), 144.0 (s, 3-C), 133.9 (d, 4-C), 126.3 (s, 5-C), 86.2 (d, C_5H_5), 75.6 (d), 46.9 (d), 40.5 (t), 33.8 (t), 31.1 (d), 26.2 (d), 23.2 (t), 21.7 (q), 20.4 (q), 16.1 (q); m/z 466 (M^++1).

Preparation of [(η^5-C_5H_5)Fe(CO)$_2$]-5-(N, N-diethylcarbamoyl)nicotinoyl **7**- A Fischer-Porter bottle containing a mixture of complex **4** (740 mg, 2.46 mmol), palladium(II) chloride (18 mg, 4 mol%), triphenylphosphine (52 mg, 8 mol%) and diethylamine (7 ml) was sealed under 4 atmospheres of CO and stirred at 100°C for 6 h. Concentration of the black solution followed by column chromatography of the residue in dichloromethane on silica gel (elution with ethyl acetate) afforded compound **7** (740 mg, 79%) as a yellow crystalline solid; (Found: C, 56.58; H, 4.87; N, 7.49; Calc. for $C_{18}H_{18}O_4N_2Fe$: C, 56.57; H, 4.75; N, 7.33%); $\nu_{max.}$ (CH_2Cl_2) 2026, 1971 and 1626 cm^{-1}; δ_H 8.78 (1H, d, J 2.0 Hz), 8.63 (1H, d, J 1.9 Hz), 7.72 (1H, t, J 2.0 Hz), 4.96 (5H, s), 3.68-3.48 (2H, m), 3.37-3.18 (2H, m), 1.27-1.13 (6H, m); δ_C 213.2 (s, C=O), 168.1 (s, C=O), 147.9 (d, 2-C), 144.3 (s, 3-C), 132.7 (s, 5-C), 130.6 (d, 6-C and 4-C), 86.4 (d, C_5H_5), 43.5 (t, CH_2), 39.6 (t, CH_2), 13.8 (q, CH_3) and 12.8 (q, CH_3); m/z 383 (M^++1).

Preparation of [(η^5-C_5H_5)Fe(CO)$_2$]-1-methyl-5-(N, N-diethylcarbamoyl)-1,4-dihydronicotinoyl **8**- To a solution of complex **7** (1.54 g, 4.0 mmol) in dichloromethane (30 ml) was added iodomethane (10 ml) and the solution was gently refluxed for 24 h . Removal of solvent and drying gave the corresponding pyridinium salt (2.06 g, 100%) as a brown amorphous solid; $\nu_{max.}$ 2036, 1978 and 1645 cm^{-1}; δ_H 8.99 (1H, br s), 8.96 (1H, br s), 8.17 (1H, br s 4-H), 5.21 (5H, s, C_5H_5), 4.77 (3H, s, NCH_3), 3.69-3.40 (4H, m, CH_2) and 1.38-1.13 (6H, m, CH_3); δ_C (200 MHz) 251.3 (s, C=O), 212.7 (s, C=O), 163.3 (s, C=O), 146.4 (s, 3-C), 143.5 (d), 143.3 (d), 137.2 (d, 4-C), 136.8 (s, 5-C), 86.9 (d, C_5H_5), 50.0 (q, NCH_3), 44.0 (t), 39.7 (t), 14.1 (q) and 12.3 (q); m/z 397 (M^+ of cation).

The pyridinium salt (2.06 g, 4.04 mmol) was dissolved in a mixture of methanol (20 ml) and dichloromethane (80 ml) and added to a solution of sodium dithionite (85%; 5.45 g, 31.3 mmol) and sodium hydrogen carbonate (3.27 g, 40.0 mmol) in distilled water (60 ml) and stirred vigorously for 5 h in the dark. The organic layer was separated, the aqueous layer washed with dichloromethane (2x30 ml), dried over magnesium sulphate and the combined organics concentrated. Column chromatography over alumina (Grade V) (elution with ethyl acetate/methanol, 9:1) afforded complex **8** (1.47 g, 92%) as a brown viscous oil; $\nu_{max.}$ (CH_2Cl_2) 2018, 1957, 1682 and 1608 cm^{-1}; δ_H (200 MHz) 6.73 (1H, s, CH=C), 6.06 (1H, s, CH=C), 4.86 (5H, s, C_5H_5), 3.37 (4H, q, J 7.5 Hz, $C\underline{H}_2CH_3$), 3.20 (2H, s, CH_2), 3.11 (3H, s, NCH_3) and 1.15 (6H, t, J 7.5 Hz, $CH_2C\underline{H}_3$); δ_C (200 MHz) 239.8 (s, C=O), 215.0 (s, C=O), 170.3 (s, C=O), 147.2 (d, $\underline{C}H$=C), 130.0 (d, $\underline{C}H$=C), 124.0 (s, 3-C), 112.6 (s, 5-C), 85.6 (d, C_5H_5), 40.9 (q, NCH_3), 40.4 (t), 25.4 (t, C-4), and 13.14(q); (Found: m/z 397.0895. $C_{19}H_{22}N_2O_4Fe$ (M^+-1) requires 397.0851).

Preparation of [(η^5-C_5H_5)Fe(CO)(PPh_3)]-1-methyl-5-(N, N-diethylcarbamoyl)-1,4-dihydronicotinoyl **9**- A solution of complex **8** (1.47 g, 3.7 mmol) and triphenylphosphine (1.45 g, 5.53 mmol) in a mixture of cyclohexane (100 ml) and tetrahydrofuran (20 ml) was irradiated internally in a quartz immersion apparatus using a Hanovia 125-W medium pressure mercury arc lamp. The reaction was monitored by ^1H n.m.r. spectroscopy (appearance of C_5H_5 signal at δ4.42) and irradiation stopped after 2.5 h. Concentration of the solvent followed by column chromatography of the crude oil on silica gel (elution with ethyl acetate) afforded recovered complex **8** (270 mg, 20%) and further elution with ethyl acetate/methanol (9:1) gave complex **9** (700 mg, 30%) as a red crystalline solid; (Found: C, 68.30; H, 6.05; N, 4.34; Calc. for $C_{36}H_{37}O_3N_2PFe$: C, 68.36; H, 5.89; N, 4.43%); $\nu_{max.}$ (CH_2Cl_2) 1907, 1679 and 1605 cm^{-1}; δ_H 7.49-7.27 (15H, m, Ph), 6.94 (1H, d, J 0.9 Hz, CH=C), 6.07 (1H, d, J 0.9 Hz, CH=C), 4.42 (5H, d, $^3J_{PH}$ 1.1 Hz, C_5H_5), 3.33-3.25 (4H, m, $C\underline{H}_2CH_3$), 3.12 (3H, s, NCH_3), 3.07 (1H, d, J 18.4 Hz, *pro*-(R)-H , 4-H), 2.48 (1H, d, J 18.4 Hz, *pro*-(S)-H, 4-H) and 1.09 (6H, t, J 7.1 Hz, $CH_2C\underline{H}_3$); δ_C 260.8 (d, $^2J_{PC}$ 21 Hz, C=O), 222.8 (d, $^2J_{PC}$ 35.3 Hz, C≡O), 171.0 (s, C=O), 145.1 (s, C=$\underline{C}$H), 136.9 (d, $^1J_{PC}$ 42.5 Hz, Ph C_{ipso}), 133.4 (d, $^2J_{PC}$ 9.5 Hz, Ph, C_{ortho}), 131.3 (s, C=$\underline{C}$H), 129.5 (s, Ph C_{para}), 127.9 (d, $^3J_{PC}$ 9.4 Hz, Ph C_{meta}), 126.1 (d, $^3J_{PC}$ 4.2 Hz, 3-C), 112.0 (s, 5-C), 85.1 (s, C_5H_5), 41.1 (s, NCH_3), 40.8 (s, $\underline{C}H_2CH_3$), 25.8 (s, 4-C) and 13.7 (s, $CH_2\underline{C}H_3$); δ_P 73.15; m/z 632 (M^+).

Preparation of (R)-[(η^5-C_5H_5)Fe(CO)$_2$]-5-(N-α-methylbenzylcarbamoyl)nicotinoyl **10**- A Fischer-Porter bottle containing a mixture of complex **4** (5.0 g, 13.8 mmol), palladium(II) chloride (98 mg, 4 mol%), triphenylphosphine (289 mg, 8 mol%) and (R)-(+)-α-methylbenzylamine (2.34 g, 27.6 mmol) in tetrahydrofuran (18 ml) was sealed under 5 atmospheres of CO and stirred at 100°C for 7.5 h. Concentration of the black solution followed by column chromatography of the residue in dichloromethane on silica gel (elution with ethyl acetate/hexane, 1:1) afforded recovered complex **4** (300 mg, 6%) and further elution with ethyl acetate afforded complex **10** (5.132 g, 86.5%) as a yellow amorphous solid; $[\alpha]_D^{22}$ + 2.7 (c 1.21, CH_2Cl_2); (Found: C, 61.07; H, 4.06; N, 6.95; Calc. for $C_{22}H_{18}O_4N_2Fe$: C, 61.42; H, 4.22, N, 6.51%); $\nu_{max.}$ (CH_2Cl_2) 2032, 1975, 1688 and 1609 cm^{-1}; δ_H 8.99 (1H, d, J 2.0 Hz, 2-H), 8.85 (1H, d, J 2.0 Hz, 6-H), 8.06 (1H, t, J 2.1 Hz, 4-H), 7.41- 7.29 (5H, m, Ph), 6.59 (1H, br d, J 7.2 Hz, NH), 5.32 (1H, quintet, J 7.2 Hz, C$\underline{H}$Me), 4.96 (5H, s, C_5H_5) and 1.63 (3H, d, J 7.2 Hz, $CHC\underline{H}_3$); δ_C (200 MHz) 213.5 (s, C=O), 164.6 (s, C=O), 150.1 (d, 6-C), 149.3 (d, 2-C), 144.3 (s, 3-C), 142.9 (s, 5-C), 131.4 (d, 4-C), 130.1 (s, Ph C_{ipso}), 128.9 (d, Ph), 127.7 (d, Ph), 126.4 (d, Ph), 86.4 (d, C_5H_5), 49.5 (d, $\underline{C}$HMe) and 21.5 (q, $CH\underline{C}H_3$); m/z 431 (M^++1).

Preparation of (R)-[(η^5-C_5H_5)Fe(CO)$_2$]-1-methyl-5-(N-α-methylbenzylcarbamoyl)-1,4-dihydronicotinoyl **11**- To a solution of complex **10** (1.65 g, 3.84 mmol) in dichloromethane (50 ml) was added iodomethane (10 ml) and the solution was gently refluxed for 20 h . Removal of solvent and drying gave the corresponding pyridinium salt (2.19 g, 100%) as a yellow amorphous solid; $\nu_{max.}$ 2213, 1983, 1732, 1671 and 1610 cm^{-1}; δ_H 10.20 (1H, br s), 9.06 (1H, d, J 7.6 Hz, NH), 8.93 (1H, br s), 8.51 (1H, br s), 7.59-7.21 (5H, m, Ph), 5.30 (1H, quintet, J 6.4 Hz, C$\underline{H}CH_3$), 5.08 (5H, s, C_5H_5), 4.57 (3H, s, NCH_3) and 1.77 (3H, d, J 7.1 Hz, $CHC\underline{H}_3$); δ_C (200 MHz) 251.8 (s, C=O), 212.6 (s, C=O), 160.3 (s, C=O), 146.0 (s, 3-C), 143.9 (d), 143.2

(s, 5-C), 142.6 (d), 141.6 (d), 133.9 (s, Ph C_{ipso}), 128.5 (d, Ph), 127.2 (d, Ph), 126.6 (d, Ph), 86.8 (d, C_5H_5), 50.9 (d, $\underline{C}HCH_3$), 49.3 (q, NCH_3) and 22.1 (q, $CH_2\underline{C}H_3$); m/z 445 (M^+ of cation).

The pyridinium salt (2.19 g, 3.84 mmol) was dissolved in a mixture of methanol (20 ml) and dichloromethane (80 ml) and added to a solution of sodium dithionite (85%; 5 g, 28.7 mmol) and sodium hydrogen carbonate (3.0 g, 35.7 mmol) in distilled water (60 ml) and stirred vigorously for 6 h in the dark. The organic layer was separated, the aqueous layer washed with dichloromethane (2x30 ml), dried over magnesium sulphate and the combined organics concentrated affording complex **11** (1.64 g, 94%) as a yellow solid; $[\alpha]_D^{22}$ +2.1 (c 1.57, CH_2Cl_2); δ_H (200 MHz) 7.38-7.16 (5H, m, Ph), 7.01 (1H, s, CH=C), 6.76 (1H, s, CH=C), 5.67 (1H, br d, J 7.5 Hz, NH), 5.20 (1H, quintet, J 7.2 Hz, $C\underline{H}CH_3$), 4.86 (5H, s, C_5H_5), 3.17 (3H, s, NCH_3), 3.12 (2H, s, 4-H) and 1.48 (3H, d, J 7.2 Hz, $CHC\underline{H}_3$); δ_C (200 MHz) 242.3 (s, C=O), 214.9 (s, C≡O), 165.4 (s, C=O), 147.3 (d, $\underline{C}H$=C), 143.4 (s, Ph C_{ipso}), 136.7 (d, $\underline{C}H$=C), 128.5 (d, Ph), 127.1 (d, Ph), 126.5 (s, 3-C), 126.1 (d, Ph), 107.7 (s, 5-C), 85.8 (d, C_5H_5), 48.4 (d, $\underline{C}HCH_3$), 41.3 (q, NCH_3), 23.1 (t, 4-C) and 21.6 (q, $CH\underline{C}H_3$); [Found: m/z 445.0872. $C_{23}H_{22}N_2O_4Fe$ (M^+-1) requires 445.0851].

Preparation of (R,R)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)]-1-methyl-5-(N-α-methylbenzylcarbamoyl)-1,4-dihydronicotinoyl **12** *and (S,R)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)]-1-methyl-5-(N-α-methylbenzylcarbamoyl)-1,4-dihydronicotinoyl* **13**- A solution of complex **11** (3.70g, 8.29 mmol) and triphenylphosphine (3.25 g, 12.43 mmol) in a mixture of cyclohexane (220 ml) and tetrahydrofuran (150 ml) was irradiated internally in a quartz immersion apparatus using a Hanovia 125-W medium pressure mercury arc lamp. The reaction was monitored by ^1H n.m.r. spectroscopy (appearance of C_5H_5 signal at δ4.45) and irradiation stopped after 4 h. Concentration of the solvent followed by column chromatography of the crude oil on alumina (Grade V) (elution with 4% methanol/diethyl ether) afforded a 1:1 mixture of diastereoisomers **12** and **13** (3.6 g, 63 %). Further careful column chromatography on alumina (Grade V) (elution with 4% methanol/diethyl ether) afforded complex **12** (800 mg, 15%), complex **13** (600 mg, 11%) and a mixture of **12** and **13** (600 mg, 11%) as red crystalline solids. Compound **12** exhibited; $[\alpha]_D^{22}$ -547 (c 0.055, CH_2Cl_2); ν_{max} 1911, 1685 and 1581 cm^{-1}; δ_H 7.44-7.23 (20H, m, Ph), 7.03 (1H, s, CH=C), 6.99 (1H, s, CH=C), 5.45 (1H, br d, J 8.1 Hz, NH), 5.24 (1H, quintet, J 7.4 Hz, $C\underline{H}CH_3$), 4.45 (5H, s, C_5H_5), 3.19 (3H, s, NCH_3), 2.96 (1H, d, J 16.7 Hz, *pro*-(R)-H, 4-H), 2.14 (1H, d, J 16.7 Hz, *pro*-(S)-H, 4-H) and 1.44 (3H, d, J 7.0 Hz, $CH\underline{C}H_3$); δ_C 263.1 (d, $^2J_{PC}$ 21.8 Hz, C=O), 222.0 (d, $^2J_{PC}$ 34.9 Hz, C≡O), 165.8 (s, C=O), 145.2 (s, $\underline{C}H$=C), 143.5 (s, 3-C), 137.3 (s, $\underline{C}H$=C), 136.6 (d, $^1J_{PC}$ 42.2 Hz, Ph C_{ipso}), 133.2 (d, $^2J_{PC}$ 8.7 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 128.3 (s, Ph), 127.9 (d, $^3J_{PC}$ 8.9 Hz, Ph C_{meta}), 127.9 (s, Ph C_{ipso}), 126.9 (s, Ph), 126.0 (s, Ph), 106.3 (s, 5-C), 85.1 (s, C_5H_5), 48.2 (s, $\underline{C}HCH_3$), 41.3 (s, NCH_3), 23.1 (s, 4-C) and 21.8 (s, $CH\underline{C}H_3$); δ_P 72.67; [Found: m/z 679.1880. $C_{40}H_{37}N_2O_3FeP$ (M^+-1) requires 679.1813].

Compound **13** exhibited; $[\alpha]_D^{22}$ +141 (c 0.054, CH_2Cl_2); ν_{max} 1910, 1685 and 1582; δ_H 7.45-7.17 (20H, m, Ph), 7.03 (1H, d, CH=C), 5.49 (1H, br d, J 7.9 Hz, NH), 5.21 (1H, quintet, J 7.3 Hz, $C\underline{H}CH_3$), 4.44 (5H, d, $^3J_{PH}$ 0.9 Hz, C_5H_5), 3.20 (3H, s, NCH_3), 2.97 (1H, d, J 16.7 Hz, *pro*-(R)-H, 4-H), 2.14 (1H, d, J 16.7 Hz, *pro*-(S)-H, 4-H) and 1.46 (3H, d, J 7.0 Hz, $CH\underline{C}H_3$); δ_C 263.6 (d, $^2J_{PC}$ 22.0 Hz, C=O), 222.0 (d, $^2J_{PC}$ 33.8 Hz, C≡O), 165.8 (s, C=O), 145.0 (s, $\underline{C}H$=C), 143.7 (s, 3-C), 137.4 (s, $\underline{C}H$=C), 136.6 (d, $^1J_{PC}$ 43.3 Hz, Ph C_{ipso}), 133.2 (d, $^2J_{PC}$ 8.7 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 128.4 (s, Ph), 128.0 (d, $^3J_{PC}$ 8.9 Hz, Ph C_{meta}), 127.9 (s, Ph C_{ipso}), 127.0 (s, Ph), 126.2 (s, Ph), 106.2 (s, 5-C), 85.1 (s, C_5H_5), 48.2 (s,

CHCH$_3$), 41.4 (s, NCH$_3$), 23.1 (s, 4-C) and 21.7 (s, CHCH$_3$); δ_P 72.35; [Found: m/z 679.1750. $C_{40}H_{37}N_2O_3FeP$ (M^+-1) requires 679.1813].

Preparation of (S)-[(η^5-C_5H_5)Fe(CO)$_2$]-5-(1-hydroxymethylisopropylcarbamoyl)nicotinoyl **16a**-A Fischer-Porter bottle containing a mixture of complex **4** (5.0 g, 13.8 mmol), palladium(II) chloride (122 mg, 5 mol%), triphenylphosphine (302 mg, 10 mol%) and *L*-valinol (1.50 g, 14.6 mmol) in tetrahydrofuran (13 ml) was sealed under 5 atmospheres of CO and stirred at 100°C for 2 h. Concentration of the black solution followed by column chromatography of the residue in dichloromethane on silica gel (elution with diethyl ether) afforded recovered complex **4** (1.5 g, 30%) and further elution with a mixture of 10% methanol/diethyl ether afforded complex **16a** (3.4 g, 60%) as a pale yellow amorphous solid; $[\alpha]_D^{22}$ -18.5 (c 0.054, CH_2Cl_2); (Found: C, 55.67; H, 5.03; N, 6.38; Calc. for $C_{19}H_{20}N_2O_5Fe$: C, 55.36; H, 4.89; N, 6.79%); $\nu_{max.}$ 3431, 2037, 1983, 1660 and 1609 cm^{-1}: δ_H 9.02 (1H, d, J 1.5 Hz), 8.83 (1H, d, J 1.8 Hz), 8.07 (1H, t, J 1.8 Hz, 4-H), 6.80 (1H, br d, J 8.3 Hz, NH), 4.97 (5H, s, C_5H_5), 4.08-3.91 (1H, m, CHCH$_2$), 3.77-3.60 (2H, m, CHCH$_2$), 2.99 (1H, br s, 1H, OH, exchange on D_2O), 2.02 (1H, octet, J 6.9 Hz, CHCH$_2$), 1.03 (3H, d, J 6.9 Hz, CH(CH$_3$)$_2$) and 1.01 (3H, d, J 6.9 Hz, CH(CH$_3$)$_2$); δ_C (200 MHz) 255.9 (s, C=O), 213.5 (s, C=O), 165.9 (s, C=O), 149.7 (d), 149.0 (d), 144.2 (s, 3-C), 131.6 (d, 4-C), 130.2 (s, 5-C), 86.4 (d, C_5H_5), 62.5 (t, CH$_2$), 57.6 (d, CHCH$_2$), 29.0 (d, CH(CH$_3$)$_2$), 19.3 (q) and 18.9 (q); m/z 413 (M^++1).

Preparation of (S)-[(η^5-C_5H_5)Fe(CO)$_2$]-1-methyl-5-(1-hydroxymethylisopropylcarbamoyl)-1,4-dihydronicotinoyl **17a**- To a solution of complex **16a** (5.62 g, 13.6 mmol) in dichloromethane (100 ml) was added iodomethane (20 ml) and the solution was gently refluxed for 24 h . Removal of solvent and drying gave the corresponding pyridinium salt (7.54 g, 100%) as a yellow amorphous solid; $\nu_{max.}$ (nujol) 3466, 2029, 1971, 1680 and 1610 cm^{-1}; δ_H (d_6-DMSO) 9.48 (1H, br s), 8.88 (1H, br s), 8.68 (1H, br d, J 7.5 Hz, NH), 8.59 (1H, br s), 5.29 (5H, s, C_5H_5), 4.70 (1H, br t, J 6.1 Hz, OH), 4.45 (3H, s, NCH$_3$), 3.89-3.72 (1H, m, CHCH$_2$), 3.58-3.45 (2H, m, CHCH$_2$), 2.00-1.85 (1H, m, CH(CH$_3$)$_2$), 0.92-0.85 (6H, m, CH)CH$_3$)$_2$); m/z 427 (M^+ of cation).

The pyridinium salt (7.54 g, 13.6 mmol) was dissolved in a mixture of methanol (20 ml) and dichloromethane (100 ml) and added to a solution of sodium dithionite (85%; 7.5 g, 43.1 mmol) and sodium hydrogen carbonate (5.0 g, 59.5 mmol) in distilled water (80 ml) and stirred vigorously for 2 h in the dark. The organic layer was separated, the aqueous layer washed with dichloromethane (2x30 ml), dried over magnesium sulphate and the combined organics concentrated. Drying of the crude product under vacuum afforded complex **17a** (5.4 g, 94%) as a yellow amorphous solid; $[\alpha]_D^{22}$ -7.2 (c 0.074, CH_2Cl_2); $\nu_{max.}$ 2023, 1961, 1687 and 1588 cm^{-1}; (Found: C, 55.84; H, 5.57; N, 6.71; Calc. for $C_{20}H_{24}N_2O_5Fe$: C, 56.09; H, 5.65; N, 6.54%); δ_H 7.01 (1H, s, CH=C), 6.77 (1H, s, CH=C), 5.64 (1H, br d, J 7.1 Hz, NH), 4.87 (5H, s, C_5H_5), 3.88-3.52 (3H, m, CHCH$_2$), 3.48 (1H, br t, J 6.0 Hz, OH, exchange on D_2O), 3.19 (3H, s, NCH$_3$), 3.14 (2H, s, 4-H), 1.91 (1H, octet, J 7.2 Hz, CH(CH$_3$)$_2$), 0.95 (3H, d, J 7.2 Hz, CHCH$_3$)$_2$) and 0.92 (3H, d, J 7.2 Hz, CHCH$_3$)$_2$); δ_C (200 MHz) 242.5 (s, C=O), 214.9 (s, C=O), 167.2 (s, C=O), 147.2 (d, CH=C), 136.7 (d, CH=C), 126.6 (s, 3-C), 107.6 (s, 5-C), 85.7 (d, C_5H_5), 63.3 (t, CH$_2$OH), 56.9 (d, CH(CH$_3$)$_2$), 41.3 (q, NCH$_3$), 28.6 (d, CHCH$_2$), 23.0 (t, 4-C), 19.2 (q) and 18.5 (q); m/z 427 (M^+-1).

Preparation of (S,S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)]-1-methyl-5-(1-hydroxymethylisopropyl carbamoyl)-1,4-dihydronicotinoyl **18a** *and (R,S)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh_3)]-1-methyl-5-(1-hydroxymethylisopropyl-carbamoyl)-1,4-dihydronicotinoyl* **19a**- A solution of complex **17a** (5.4 g, 12.6 mmol) and triphenylphosphine (4.95 g, 16.9 mmol) in a mixture of cyclohexane (270 ml) and tetrahydrofuran (250 ml) was irradiated internally in a quartz immersion apparatus using a Hanovia 125-W medium pressure mercury arc lamp. The reaction was monitored by ^{1}H n.m.r. spectroscopy (appearance of C_5H_5 signal at δ4.46) and irradiation stopped after 7.5 h. Concentration of the solvent followed by column chromatography of the crude oil on alumina (Grade V) (elution with diethyl ether/methanol 4%) afforded a 1:1 mixture of diastereoisomers **18a** and **19a** (4.1 g, 49%). Further careful column chromatography on alumina (Grade V) (elution with diethyl ether/methanol 4%) afforded complex **19a** (1.4 g, 17%), complex **18a** (1.1 g, 13%) and a mixture of **18a** and **19a** (1.5 g, 18%) as red crystalline solids. Compound **19a** exhibited; $[\alpha]_D^{22}$ -394 (c 0.069, CH_2Cl_2); $\nu_{max.}$ 3436, 1911, 1684 and 1580 cm^{-1}; δ_H 7.46-7.27 (15H, m, Ph), 7.06 (1H, s, CH=C), 7.01 (1H, s, CH=C), 5.32 (1H, br d, J 7.5 Hz, NH), 4.46 (5H, d, $^3J_{PH}$ 1.1 Hz, C_5H_5), 3.79-3.55 (3H, m, C<u>H</u>C<u>H</u>$_2$), 3.40 (1H, t, J 5.2 Hz, OH, exchange on D_2O), 3.21 (3H, s, NCH_3), 2.99 (1H, d, J 16.6 Hz, *pro*-(R) H, 4-H), 2.24 (1H, d, J 16.6 Hz, *pro*-(S) H, 4-H), 1.86 (1H, octet, J 6.8 Hz, C<u>H</u>(CH$_3$)$_2$), 0.94 (3H, d, J 6.7 Hz, CH(C<u>H</u>$_3$)$_2$) and 0.94 (3H, d, J 6.7 Hz, CH(C<u>H</u>$_3$)$_2$); δ_C 263.5 (d, $^2J_{PC}$ 22.1 Hz, C=O), 221.9 (d, $^2J_{PC}$ 34.7 Hz, C≡O), 167.8 (s, C=O), 144.6 (s, <u>C</u>H=C), 137.6 (s, <u>C</u>H=C), 136.4 (d, $^1J_{PC}$ 42.3 Hz, Ph C_{ipso}), 133.1 (d, $^2J_{PC}$ 8.7 Hz, Ph C_{ortho}), 129.4 (s, Ph C_{para}), 127.9 (d,$^3J_{PC}$ 9.2 Hz, Ph C_{meta}), 128.0 (s, 3-C), 105.8 (s, 5-C), 85.0 (s, C_5H_5), 64.2 (s, CH_2OH), 57.6 (s, <u>C</u>HCH$_2$), 41.3 (s, NCH_3), 28.8 (s, <u>C</u>H(CH$_3$)$_2$), 23.1 (s, 4-C), 19.3 (s, CH(<u>C</u>H$_3$)$_2$) and 18.9 (s, CH(<u>C</u>H$_3$)$_2$); δ_P 72.48; [Found: m/z 663.2084. $C_{37}H_{39}N_2O_4FeP$ (M^++1) requires 663.2075].

Compound **18a** exhibited; $[\alpha]_D^{22}$ +394 (c 0.055, CH_2Cl_2); $\nu_{max.}$ 3436, 1910, 1684 and 1580 cm^{-1}; δ_H 7.46-7.27 (15H, m, Ph), 7.05 (1H, s, CH=C), 7.00 (1H, s, CH=C), 5.32 (1H, br d, J 7.8 Hz, NH), 4.46 (5H, s, C_5H_5), 3.75-3.70 (2H, m, CHC<u>H</u>$_2$), 3.57-3.54 (1H, m, C<u>H</u>CH$_2$), 3.28 (1H, br t, J 4.9 Hz, OH, exchange on D_2O), 3.21 (3H, s, NCH_3), 3.01 (1H, d, J 16.7 Hz, *pro*-(R) H, 4-H), 2.24 (1H, d, J 16.7 Hz, *pro*-(S) H, 4-H), 1.86 (1H, octet, J 6.8 Hz, C<u>H</u>(CH$_3$)$_2$), 0.96 (3H, d, J 6.7 Hz, CH(C<u>H</u>$_3$)$_2$) and 0.89 (3H, d, J 6.7 Hz, CH(C<u>H</u>$_3$)$_2$); δ_C 263.4 (d, $^2J_{PC}$ 22.0 Hz, C=O), 221.9 (d, $^2J_{PC}$ 34.6 Hz, C≡O), 167.8 (s, C=O), 144.7 (s, <u>C</u>H=C), 137.5 (s, <u>C</u>H=C), 136.5 (d, $^1J_{PC}$ 43.0 Hz, Ph C_{ipso}), 133.8 (d, $^2J_{PC}$ 8.9 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 127.9 (d,$^3J_{PC}$ 9.1 Hz, Ph C_{meta}), 128.1 (s, 3-C), 105.9 (s, 5-C), 85.0 (s, C_5H_5), 64.1 (s, CH_2OH), 57.4 (s, <u>C</u>HCH$_2$), 41.3 (s, NCH_3), 28.8 (s, <u>C</u>H(CH$_3$)$_2$), 23.1 (s, 4-C), 19.5 (s, CH(<u>C</u>H$_3$)$_2$) and 18.8 (s, CH(<u>C</u>H$_3$)$_2$); δ_P 72.51; [Found: m/z 663.2007. $C_{37}H_{39}N_2O_4FeP$ (M^++1) requires 663.2075].

Preparation of (R)-[(η^5-C_5H_5)Fe(CO)$_2$]-5-(1-hydroxymethylisopropylcarbamoyl)nicotinoyl **16b**-Two Fischer-Porter bottles containing in total a mixture of complex **4** (8.0 g, 22.2 mmol), palladium(II) chloride (158 mg, 4 mol%), triphenylphosphine (465 mg, 10 mol%) and *D*-valinol (2.40 g, 23.3 mmol) in tetrahydrofuran (27 ml) were sealed under 8 atmospheres of CO and stirred at 100°C for 2.5 h. The crude reaction mixtures were combined and concentration of the black solution followed by column chromatography of the residue in dichloromethane on silica gel (elution with diethyl ether) afforded recovered complex **4** (2.8 g, 35 %) and further elution with a mixture of diethyl ether/methanol (10%) afforded complex **16b** (3.77 g, 41%) as a pale yellow amorphous solid; $[\alpha]_D^{22}$ +18.0 (c 0.083, CH_2Cl_2); (Found: C, 55.65; H, 4.79; N, 6.48; Calc. for

$C_{19}H_{20}N_2O_5Fe$: C, 55.36; H, 4.89; N, 6.79%); $\nu_{max.}$ 3430, 2032, 1976, 1661 and 1610 cm^{-1}: δ_H 9.02 (1H, d, J 1.5 Hz), 8.80 (1H, d, J 1.8 Hz), 8.07 (1H, t, J 1.8 Hz, 4-H), 7.18 (1H, br d, J 8.3 Hz, NH), 4.97 (5H, s, C_5H_5), 4.07-3.89 (1H, m, C<u>H</u>CH_2), 3.89-3.63 (2H, m, CHC<u>H</u>$_2$), 2.40 (1H, br s, 1H, OH, exchange on D_2O), 2.02 (1H, octet, J 6.9 Hz, C<u>H</u>CH_2), 1.03 (3H, d, J 6.9 Hz, CH(C<u>H</u>$_3$)$_2$) and 1.01 (3H, d, J 6.9 Hz, CH(C<u>H</u>$_3$)$_2$); δ_C (200 MHz) 255.6 (s, C=O), 213.4 (s, C=O), 165.7 (s, C=O), 149.7 (d), 149.0 (d), 144.0 (s, 3-C), 131.9 (d, 4-C), 130.1 (s, 5-C), 86.2 (d, C_5H_5), 62.2 (t, CH_2), 57.4 (d, <u>C</u>HCH_2), 28.8 (d, <u>C</u>H$(CH_3)_2$), 19.1 (q) and 18.8 (q); m/z 413 (M^++1).

Preparation of (R)-[(η^5-C_5H_5)Fe(CO)$_2$]-1-methyl-5-(1-hydroxymethylisopropylcarbamoyl)-1,4-dihydronicotinoyl **17b**- To a solution of complex **16b** (4.14 g, 10.05 mmol) in dichloromethane (80 ml) was added iodomethane (20 ml) and the solution was gently refluxed for 40 h . Removal of solvent and drying gave the corresponding pyridinium salt (5.57 g, 100%) as a yellow amorphous solid; $\nu_{max.}$ (nujol) 3467, 2029, 1971, 1660 and 1610 cm^{-1}; δ_H (DMSO-d_6) 9.39 (1H, br s), 8.88 (1H, br s), 8.69 (1H, br d, J 7.5 Hz, NH), 8.61 (1H, br s), 5.29 (5H, s, C_5H_5), 4.72 (1H, br t, J 6.1 Hz, OH), 4.45 (3H, s, NCH_3), 3.90-3.72 (1H, m, C<u>H</u>CH_2), 3.60-3.45 (2H, m, CHC<u>H</u>$_2$), 2.00-1.85 (1H, m, C<u>H</u>$(CH_3)_2$), 0.92-0.85 (6H, m, CH)C<u>H</u>$_3$)$_2$); m/z 427 (M^+ of cation).

The pyridinium salt (5.57 g, 10.05 mmol) was dissolved in a mixture of methanol (20 ml) and dichloromethane (80 ml) and added to a solution of sodium dithionite (85%; 7.5 g, 43.1 mmol) and sodium hydrogen carbonate (5.0 g, 59.5 mmol) in distilled water (60 ml) and stirred vigorously for 2 h in the dark. The organic layer was separated, the aqueous layer washed with dichloromethane (2x30 ml), dried over magnesium sulphate and the combined organics concentrated. Drying of the crude under vacuum afforded complex **17b** (4.2 g, 98%) as a yellow amorphous solid; $[\alpha]_D^{22}$ +6.9 (c 0.058, CH_2Cl_2); (Found: C, 56.19; H, 5.72; N, 6.49; Calc. for $C_{20}H_{24}N_2O_5Fe$: C, 56.09; H, 5.65; N, 6.54%); $\nu_{max.}$ 3439, 2023, 1961, 1687 and 1588 cm^{-1}; δ_H 7.02 (1H, s, CH=C), 6.77 (1H, s, CH=C), 5.64 (1H, br d, J 7.1 Hz, NH), 4.87 (5H, s, C_5H_5), 3.88-3.53 (3H, m, C<u>H</u>C<u>H</u>$_2$), 3.35 (1H, br t, J 6.0 Hz, OH, exchange on D_2O), 3.19 (3H, s, NCH_3), 3.14 (2H, s, 4-H), 1.91 (1H, octet, J 7.2 Hz, C<u>H</u>$(CH_3)_2$), 0.96 (3H, d, J 7.2 Hz, CHC<u>H</u>$_3$)$_2$) and 0.92 (3H, d, J 7.2 Hz, CHC<u>H</u>$_3$)$_2$); δ_C (200 MHz) 242.4 (s, C=O), 214.8 (s, C=O), 167.1 (s, C=O), 147.1 (d, <u>C</u>H=C), 136.5 (d, <u>C</u>H=C), 126.5 (s, 3-C), 107.8 (s, 5-C), 85.7 (d, C_5H_5), 63.0 (t, CH_2OH), 56.7 (d, <u>C</u>$H(CH_3)_2$), 41.8 (q, NCH_3), 28.5 (d, <u>C</u>HCH_2), 23.0 (t, 4-C), 19.1 (q) and 18.5 (q); m/z 427 (M^+-1).

Preparation of (R,R)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)]-1-methyl-5-(1-hydroxymethylisopropyl carbamoyl)-1,4-dihydronicotinoyl **18b** *and (S,R)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)]-1-methyl-5-(1-hydroxymethylisopropyl-carbamoyl)-1,4-dihydronicotinoyl* **19b**- A solution of complex **17b** (4.2 g, 9.8 mmol) and triphenylphosphine (3.85 g, 14.7 mmol) in a mixture of cyclohexane (270 ml) and tetrahydrofuran (335 ml) were irradiated internally in a quartz immersion apparatus using a Hanovia 125-W medium pressure mercury arc lamp. The reaction was monitored by ^1H n.m.r. spectroscopy (appearance of C_5H_5 signal at δ4.42) and irradiation stopped after 117 h. Concentration of the solvent followed by column chromatography of the crude oil on alumina (Grade V) (elution with diethyl ether/methanol 4%) afforded a 1:1 mixture of diastereoisomers **18b** and **19b** (2.9 g, 45%). Further careful column chromatography on alumina (Grade V) (elution with diethyl ether/methanol 4%) afforded complex **18b** (1.2 g, 18.5%), complex **19b** (0.70 g, 11%) and a mixture of **18b**

and **19b** (0.70 g, 11%) as red crystalline solids. Compound **18b** exhibited; $[\alpha]_D^{22}$ -393 (c 0.043, CH_2Cl_2); $\nu_{max.}$ 3430, 1911, 1684 and 1579 cm^{-1}; δ_H 7.46-7.26 (15H, m, Ph), 7.05 (1H, s, CH=C), 7.01 (1H, s, CH=C), 5.32 (1H, br d, J 7.8 Hz, NH), 4.46 (5H, s, C_5H_5), 3.74-3.67 (2H, m, $CHC\underline{H}_2$), 3.60-3.50 (1H, m, $C\underline{H}CH_2$), 3.33 (1H, br t, J 5.0 Hz, OH, exchange on D_2O), 3.20 (3H, s, NCH_3), 3.01 (1H, d, J 16.7 Hz, *pro*-(R) H, 4-H), 2.24 (1H, d, J 16.7 Hz, *pro*-(S) H, 4-H), 1.87 (1H, octet, J 6.9 Hz, $C\underline{H}(CH_3)_2$), 0.96 (3H, d, J 6.7 Hz, $CH(C\underline{H}_3)_2$) and 0.90 (3H, d, J 6.7 Hz, $CH(C\underline{H}_3)_2$); δ_C 263.4 (d, $^2J_{PC}$ 22.0 Hz, C=O), 222.1 (d, $^2J_{PC}$ 35.1 Hz, C≡O), 168.1 (s, C=O), 144.8 (s, $\underline{C}H$=C), 137.7 (s, $\underline{C}H$=C), 136.7 (d, $^1J_{PC}$ 43.0 Hz, Ph C_{ipso}), 133.3 (d, $^2J_{PC}$ 9.0 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.2 (s, 3-C), 128.0 (d,$^3J_{PC}$ 9.7 Hz, Ph C_{meta}), 106.0 (s, 5-C), 85.2 (s, C_5H_5), 64.7 (s, CH_2OH), 57.8 (s, $\underline{C}HCH_2$), 41.4 (s, NCH_3), 29.0 (s, $\underline{C}H(CH_3)_2$), 23.2 (s, 4-C), 19.6 (s, $CH(\underline{C}H_3)_2$) and 19.0 (s, $CH(\underline{C}H_3)_2$); δ_P 72.51; [Found: m/z 663.2098. $C_{37}H_{39}N_2O_4FeP$ (M^++1) requires 663.2075].

Compound **19b** exhibited; $[\alpha]_D^{22}$ +394 (c 0.037, CH_2Cl_2); $\nu_{max.}$ 3430, 1911, 1684 and 1579 cm^{-1}; δ_H 7.46-7.27 (15H, m, Ph), 7.05 (1H, s, CH=C), 7.01 (1H, s, CH=C), 5.32 (1H, br d, J 7.5 Hz, NH), 4.46 (5H, d, $^3J_{PH}$ 1.1 Hz, C_5H_5), 3.74-3.57 (3H, m, $C\underline{H}C\underline{H}_2$), 3.41(1H, br t, J 5.2 Hz, OH, exchange on D_2O), 3.21 (3H, s, NCH_3), 2.99 (1H, d, J 16.6 Hz, *pro*-(R) H, 4-H), 2.24 (1H, d, J 16.6 Hz, *pro*-(S) H, 4-H), 1.86 (1H, octet, J 6.8 Hz, $C\underline{H}(CH_3)_2$), 0.94 (3H, d, J 6.7 Hz, $CH(C\underline{H}_3)_2$) and 0.89 (3H, d, J 6.7 Hz, $CH(C\underline{H}_3)_2$); δ_C 263.8 (d, $^2J_{PC}$ 21.9 Hz, C=O), 222.0 (d, $^2J_{PC}$ 34.4 Hz, C≡O), 168.1 (s, C=O), 144.8 (s, $\underline{C}H$=C), 137.8 (s, $\underline{C}H$=C), 136.5 (d, $^1J_{PC}$ 43.4 Hz, Ph C_{ipso}), 133.2 (d, $^2J_{PC}$ 8.1 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d,$^3J_{PC}$ 9.5 Hz, Ph C_{meta}), 128.1 (s, 3-C), 105.8 (s, 5-C), 85.1 (s, C_5H_5), 64.6 (s, CH_2OH), 57.9 (s, $\underline{C}HCH_2$), 41.4 (s, NCH_3), 28.9 (s, $\underline{C}H(CH_3)_2$), 23.1 (s, 4-C), 19.4 (s, $CH(\underline{C}H_3)_2$) and 19.0 (s, $CH(\underline{C}H_3)_2$); δ_P 72.52; [Found: m/z 663.2029. $C_{37}H_{39}N_2O_4FeP$ (M^++1) requires 663.2075].

Preparation of (R,S)-[(η^5-C_5H_5)Fe(CO)$_2$]-5-(1-hydroxybenzyl-2-methylcarbamoyl)nicotinoyl **20a**-A Fischer-Porter bottle containing a mixture of complex **4** (3.08 g, 8.5 mmol), palladium(II) chloride (60 mg, 5 mol%), triphenylphosphine (178 mg, 10 mol%) and (1R, 2S)-(-)-norephedrine (1.41 g, 9.3 mmol) in tetrahydrofuran (16 ml) was sealed under 5 atmospheres of CO and stirred at 95°C for 4 h. Concentration of the black solution followed by column chromatography of the residue in dichloromethane on silica gel (elution with diethyl ether) afforded recovered complex **4** (1.15 g, 32%) and further elution with a mixture of diethyl ether/methanol (5%) afforded complex **20a** (2.15 g, 55%) as a pale yellow amorphous solid; $[\alpha]_D^{22}$ -43.0 (c 0.10, CH_2Cl_2); (Found: C, 59.98; H, 4.59; N, 6.08; Calc. for $C_{23}H_{20}N_2O_5Fe$: C, 60.02; H, 4.38; N, 6.09%); $\nu_{max.}$ 3435, 2032, 1975, 1656 and 1610 cm^{-1}; δ_H 8.92 (1H, d, J 1.5 Hz), 8.75 (1H, d, J 1.9 Hz), 8.05 (1H, t, J 1.8 Hz, 4-H), 7.42-7.25 (5H, m, Ph), 6.72 (1H, br d, J 8.3 Hz, NH), 5.02 (1H, m, $C\underline{H}OH$), 4.94 (5H, s, C_5H_5), 4.54-4.48 (1H, m, $C\underline{H}Me$), 4.03 (1H, br s, $CHO\underline{H}$, exchange on D_2O) and 1.12 (3H, d, J 6.9 Hz, $CHC\underline{H}_3$); δ_C (200 MHz) 255.4 (s, C=O), 213.4 (s, C≡O), 165.2 (s, C=O), 149.6 (d), 148.8 (d), 144.2 (s, 3-C), 141.3 (s, 5-C), 131.8 (d, 4-C), 130.0 (s, Ph C_{ipso}), 128.2 (d, Ph), 127.4 (d, Ph), 126.1 (d, Ph), 86.2 (d, C_5H_5), 75.8 (d), 51.4 (d) and 13.3 (q); m/z 461 (M^++1).

Preparation of (R,S)-[(η^5-C_5H_5)Fe(CO)$_2$]-1-methyl-5-(1-hydroxybenzyl-2-methylcarbamoyl)-1,4-dihydronicotinoyl **21a**- To a solution of complex **20a** (5.4 g, 11.6 mmol) in dichloromethane (80 ml) was added iodomethane (20 ml) and the solution was gently refluxed for 38 hours. Removal of solvent and drying gave

the corresponding pyridinium salt (7.0 g, 100%) as a yellow amorphous solid; $\nu_{max.}$ (nujol) 3433, 2019, 1963, 1684 and 1586 cm^{-1}; δ_H (acetone-d_6) 9.96 (1H, br s, 4-H), 8.95 (1H, br s), 8.84 (1H, br d, J 8.3 Hz, NH), 7.52-7.15 (5H, m, Ph), 5.30 (5H, s, C_5H_5), 5.15-5.05 (1H, m, C<u>H</u>OH), 4.70 (3H, s, NCH_3), 4.66 (1H, d, J 4.1 Hz, OH), 4.46-4.25 (1H, m, C<u>H</u>CH_3), and 1.16 (3H, d, J 7.0 Hz, CHC<u>H</u>$_3$); m/z 475 (M^+ of cation).

The pyridinium salt (7.0 g, 11.6 mmol) was dissolved in a mixture of methanol (20 ml) and dichloromethane (100 ml) and added to a solution of sodium dithionite (85%; 7.5 g, 43.1 mmol) and sodium hydrogen carbonate (5.0 g, 59.5 mmol) in distilled water (80 ml) and stirred vigorously for 2 h in the dark. The organic layer was separated, the aqueous layer washed with dichloromethane (2x30 ml), dried over magnesium sulphate and the combined organics concentrated. Drying of the crude under vacuum afforded complex **21a** (5.3 g, 96%) as a yellow amorphous solid; $[\alpha]_D^{22}$ -23 (c 0.11, CH_2Cl_2); (Found: C, 60.33; H, 5.06; N, 5.61; Calc. for $C_{24}H_{24}O_5N_2Fe$: C, 60.50; H, 5.04; N, 5.88%); $\nu_{max.}$ 3437, 2022, 1961, 1686 and 1587 cm^{-1}; δ_H 7.35-7.24 (5H, m, Ph), 7.05 (s, C<u>H</u>=C), 6.75 (s,C<u>H</u>=C), 5.44 (1H, br d, 1H, J 7.7 Hz, NH), 4.85 (5H, s, C_5H_5), 4.83-4.82 (1H, m, C<u>H</u>OH), 4.61 (1H, d, J 4.3 Hz, OH), 4.50-4.39 (1H, m, C<u>H</u>CH_3), 3.19 (3H, s, NCH_3), 3.00 (2H, s, 4-H) and 1.00 (3H, d, J 7.0 Hz, CHC<u>H</u>$_3$); δ_C (200 MHz) 242.7 (s, C=O), 214.8 (s, C≡O), 167.2 (s, C=O), 147.2 (d, C=<u>C</u>H), 141.0 (s, 3-C), 137.1 (d, C=<u>C</u>H), 128.0 (d, Ph), 127.2 (s, Ph), 126.8 (d, Ph), 126.3 (d, Ph), 107.3 (s, 5-C), 85.8 (d, C_5H_5), 51.1 (d), 41.3 (q), 22.9 (t) and 14.3 (q); m/z 475 (M^+-1).

Preparation of (R,R,S)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)]-1-methyl-5-(1-hydroxybenzyl-2-methylcarbamoyl)-1,4-dihydronicotinoyl **22a**- A solution of complex **21a** (5.1 g, 10.1 mmol) and triphenylphosphine (4.2 g, 16.1 mmol) in a mixture of cyclohexane (20 ml) and tetrahydrofuran (100 ml) was irradiated internally in a quartz immersion apparatus using a Hanovia 125-W medium pressure mercury arc lamp. The reaction was monitored by ^1H n.m.r. spectroscopy (appearance of C_5H_5 signal at δ4.42) and irradiation stopped after 8.5 h. Concentration of the solvent followed by column chromatography of the crude on alumina (Grade V) (elution with diethyl ether/methanol 4%) afforded a 1:1 mixture of diastereoisomers **22a** and **23a** (4.0 g, 56%). Crystallisation of the crude from a solution of dichloromethane and diethyl ether (ca. 1:5) at -20°C gave complex **22a** as the major diastereoisomer in a ratio of 12:1. A second crystallisation under the same conditions afforded the diasteromers in a ratio of 120:1. Finally, after a third crystallisation the other diastereoisomer could not be detected by n.m.r. spectroscopy (300 MHz) thus affording **22a** (1.2 g 16%) as an orange solid; $[\alpha]_D^{22}$ -324 (c 0.05, CH_2Cl_2); (Found: C, 68.23; H, 5.53; N, 3.89; Calc. for $C_{41}H_{39}O_4N_2PFe$: C, 68.29; H, 5.49; N, 3.94%); $\nu_{max.}$ 3434, 1911, 1683 and 1572 cm^{-1}; δ_H 7.44-7.23 (20H, m, Ph), 7.12 (1H, s, CH=C), 7.01 (1H, s, CH=C), 5.26 (1H, d, J 4.4 Hz, OH, exchange on D_2O), 4.99 (1H, br d, J 7.0 Hz, NH), 4.77 (1H, dd, J 4.4, 2.2, Hz, C<u>H</u>OH), 4.46 (1H, dq, J 7.0, 2.2 Hz, C<u>H</u>CH_3), 4.42 (5H, s, C_5H_5), 3.23 (3H, s, NCH_3), 2.88 (1H, d, J 16.8 Hz, *pro*-(R) H, 4-H), 2.13 (1H, d, J 16.8 Hz, *pro*-(S) H, 4-H), and 1.02 (3H, d, J 7.0 Hz, CHC<u>H</u>$_3$); In a n.O.e. experiment (500 MHz) of **22a** in $CDCl_3$ irradiation of the singlet at δ4.42 (C_5H_5) gave a 5% enhancement of the singlet at δ7.12 (2-H). Similarly, irradiation of the singlet at δ7.12 (2-H) gave a 5% enhancement of the singlet at δ4.42 (C_5H_5). Irradiation of the doublet at δ4.99 (NH) gave a 7% enhancement of the doublets at δ2.88 and δ2.13 (diastereotopic hydrogens at C-4) and a 4% enhancement of the doublet at δ1.02 (CHC<u>H</u>$_3$) Irradiation of the singlet at δ3.23 (NCH_3) gave a 14% enhancement of the two singlets at δ7.12 (2-H) and δ7.01 (6-H). In a n.O.e. experiment (500 MHz) of **22a**, in CD_3CN in the presence

of one equivalent of magnesium (II) ion, irradiation (50L) of the doublet at δ4.99 (NH) after 88,000 scans gave no observed enhancements.; δ_C 263.5 (d, $^2J_{PC}$ 21.7 Hz, C=O), 221.9 (d, $^2J_{PC}$ 34.2 Hz, C≡O), 168.2 (s, C=O), 144.8 (s, CH=C), 140.7 (s, 3-C), 138.0 (s, CH=C), 136.5 (d, $^1J_{PC}$ 43.0 Hz, Ph C_{ipso}), 133.1 (d, $^2J_{PC}$ 9.0 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 127.9 (d,$^3J_{PC}$ 10.1 Hz, Ph C_{meta}), 127.8 (s, Ph, C_{ipso}), 127.7 (s, Ph), 127.0 (s, Ph), 126.6 (s, Ph), 105.3 (s, 5-C), 85.0 (s, C_5H_5), 77.5 (s, CHOH), 51.5 (s, $CHCH_3$), 41.3 (s, NCH_3), 23.0 (s, 4-C) and 15.7 (s, $CHCH_3$); δ_P 72.75; m/z 709 (M^+-1).

Preparation of (S,R)-[(η^5-C_5H_5)Fe(CO)$_2$]-5-(1-hydroxybenzyl-2-methylcarbamoyl)nicotinoyl **20b**-Two Fischer-Porter bottles each containing a mixture of complex **4** (5.00 g, 13.8 mmol), palladium(II) chloride (98 mg, 5 mol%), triphenylphosphine (289 mg, 10 mol%) and (1S, 2R)-(+)-norephedrine (2.2 g, 14.5 mmol) in tetrahydrofuran (15 ml) were sealed under 4 atmospheres of CO and stirred at 100°C for 3 h. Concentration of the black solution followed by column chromatography of the residue in dichloromethane on silica gel (elution with diethyl ether) afforded recovered complex **4** (2.7 g, 27%) and further elution with a mixture of diethyl ether/methanol (5%) afforded complex **20b** (5.7g, 45%) as a pale yellow amorphous solid; $[\alpha]_D^{22}$ +40.0 (c 0.09, CH_2Cl_2); (Found: C, 59.98; H, 4.59; N, 6.08; Calc. for $C_{23}H_{20}N_2O_5Fe$: C, 60.02; H, 4.38; N, 6.09%); $\nu_{max.}$ 3435, 2032, 1975, 1656 and 1610 cm^{-1}; δ_H 8.92 (1H, d, J 1.5 Hz), 8.75 (1H, d, J 1.9 Hz), 8.05 (1H, t, J 1.8 Hz, 4-H), 7.42-7.25 (5H, m, Ph), 6.87 (1H, br d, J 8.3 Hz, NH), 5.02 (1H, m, CHOH), 4.94 (5H, s, C_5H_5), 4.54-4.48 (1H, m, CHMe), 4.03 (1H, br s, CHOH, exchange on D_2O) and 1.12 (3H, d, J 6.9 Hz, $CHCH_3$); δ_C (200 MHz) 255.5 (s, C=O), 213.4 (s, C=O), 165.4 (s, C=O), 149.3 (d), 148.8 (d), 144.2 (s, 3-C), 141.3 (s, 5-C), 131.6 (d, 4-C), 130.0 (s, Ph C_{ipso}), 128.3 (d, Ph), 127.7 (d, Ph), 126.3 (d, Ph), 86.2 (d, C_5H_5), 75.2 (d), 51.7 (d) and 13.3 (q); m/z 461 (M^++1).

Preparation of (S,R)-(η^5-C_5H_5)Fe(CO)$_2$]-1-methyl-5-(1-hydroxybenzyl-2-methylcarbamoyl)-1,4-dihydronicotinoyl **21b**- To a solution of complex **20b** (5.3 g, 11.5 mmol) in dichloromethane (80 ml) was added iodomethane (20 ml) and the solution was gently refluxed for 44 h . Removal of solvent and drying gave the corresponding pyridinium salt (6.9 g, 100%) as a yellow amorphous solid; $\nu_{max.}$ (nujol) 3433, 2019, 1963, 1684 and 1586 cm^{-1}; δ_H (acetone-d_6) 9.96 (1H, br s, 4-H), 8.95 (1H, br s), 8.84 (1H, br d, J 8.3 Hz, NH), 7.52-7.15 (5H, m, Ph), 5.30 (5H, s, C_5H_5), 5.15-5.05 (1H, m, CHOH), 4.70 (3H, s, NCH_3), 4.66 (1H, d, J 4.1 Hz, OH), 4.46-4.25 (1H, m, $CHCH_3$), and 1.16 (3H, d, J 7.0 Hz, $CHCH_3$); m/z 475 (M^+ of cation).
The pyridinium salt (6.9 g, 11.5 mmol) was dissolved in a mixture of methanol (50 ml) and dichloromethane (150 ml) and added to a solution of sodium dithionite (85%; 7.5 g, 43.1 mmol) and sodium hydrogen carbonate (5.0 g, 59.5 mmol) in distilled water (80 ml) and stirred vigorously for 3 h in the dark. The organic layer was separated, the aqueous layer washed with dichloromethane (2x30 ml), dried over magnesium sulphate and the combined organics concentrated. Drying of the crude product under vacuum afforded complex **21b** (5.0 g, 91%) as a yellow amorphous solid; $[\alpha]_D^{22}$ +19 (c 0.08, CH_2Cl_2); (Found: C, 60.41; H, 5.20; N, 5.69; Calc. for $C_{24}H_{24}O_5N_2Fe$: C, 60.50; H, 5.04; N, 5.88%); $\nu_{max.}$ 3438, 2022, 1960, 1686 and 1587 cm^{-1}; δ_H 7.35-7.24 (5H, m, Ph), 7.05 (s, CH=C), 6.75 (s, CH=C), 5.44 (1H, br d, 1H, J 7.7 Hz, NH), 4.85 (5H, s, C_5H_5), 4.83-4.82 (1H, m, CHOH), 4.61 (1H, d, J 4.3 Hz, OH), 4.50- 4.39 (1H, m, $CHCH_3$), 3.19 (3H, s, NCH_3), 3.00 (2H, s, 4-H) and 1.00 (3H, d, J 7.0 Hz, $CHCH_3$); δ_C (200 MHz) 242.4 (s, C=O), 214.9 (s, C=0), 167.2 (s, C=O), 147.1 (d, C=CH), 141.1 (s, 3-C), 136.9 (d, C=CH), 128.1 (d, Ph), 127.4 (s, Ph),

126.6 (d, Ph), 126.4 (d, Ph), 107.4 (s, 5-C), 85.8 (d, C_5H_5), 77.3 (d), 51.5 (d), 41.3 (q), 23.0 (t) and 14.4(q); m/z 475 (M^+-1).

Preparation of (S,S,R)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)]-1-methyl-5-(1-hydroxybenzyl-2-methylcarbamoyl)-1,4-dihydronicotinoyl **22b**- A solution of complex **21b** (4.8 g, 10.1 mmol) and triphenylphosphine (4.0 g, 15.1 mmol) in a mixture of cyclohexane (100 ml) and tetrahydrofuran (300 ml) was irradiated internally in a quartz immersion apparatus using a Hanovia 125-W medium pressure mercury arc lamp. The reaction was monitored by ^1H n.m.r. spectroscopy (appearance of C_5H_5 signal at δ4.42) and irradiation stopped after 16 h. Concentration of the solvent followed by column chromatography of the crude on alumina (Grade V) (elution with diethyl ether/methanol 4%) afforded a 1:1 mixture of diastereoisomers **22b** and **23b** (2.1 g, 29%). Crystallisation of the crude in a solution of dichloromethane and diethyl ether (ca. 1:10) at -20°C gave complex **22b** as the major diastereoisomer in a ratio of 22:1. After a second crystallisation under the same conditions the other diastereoisomer could not be detected by n.m.r. spectroscopy thus affording **22b** (700 mg, 10%) as an orange solid; $[\alpha]_D^{22}$ +328 (c 0.12, CH_2Cl_2); (Found: C, 68.39; H, 5.53; N, 3.68; Calc. for $C_{41}H_{39}O_4N_2PFe$: C, 68.29; H, 5.49; N, 3.94%); $\nu_{max.}$ 3434, 1911, 1683 and 1572 cm^{-1}; δ_H 7.44-7.24 (20H, m, Ph), 7.12 (1H, s, CH=C), 7.02 (1H, s, CH=C), 5.30 (1H, d, J 4.4 Hz, OH, exchange on D_2O), 4.99 (1H, br d, J 7.0 Hz, NH), 4.77 (1H, dd, J 4.4, 2.2, Hz, C<u>H</u>OH), 4.46 (1H, dq, J 7.0, 2.2 Hz, C<u>H</u>CH_3), 4.42 (5H, s, C_5H_5), 3.24 (3H, s, NCH_3), 2.88 (1H, d, J 16.8 Hz, *pro*-(R) H, 4-H), 2.13 (1H, d, J 16.8 Hz, *pro*-(S) H, 4-H), and 1.02 (3H. d. J 7.0 Hz. $CHCH_3$); δ_C 263.3 (d. $^2J_{PC}$ 21.7 Hz. C=O). 222.1 (d. $^2J_{PC}$ 34.2 Hz. C≡O). 168.5 (s. C=O), 144.9 (s, <u>C</u>H=C), 140.7 (s, 3-C), 138.2 (s, <u>C</u>H=C), 136.6 (d, $^1J_{PC}$ 43.0 Hz, Ph C_{ipso}), 133.3 (d, $^2J_{PC}$ 9.0 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d,$^3J_{PC}$ 10.1 Hz, Ph C_{meta}), 127.9 (s, Ph), 127.8 (s, Ph, C_{ipso}), 127.3 (s, Ph), 126.8 (s, Ph), 105.4 (s, 5-C), 85.2 (s, C_5H_5), 78.0 (s, <u>C</u>HOH), 51.6 (s, <u>C</u>HCH_3), 41.5 (s, NCH_3), 23.0 (s, 4-C) and 16.0 (s, CH<u>C</u>H_3); δ_P 72.74; m/z 711 (M^++1).

General procedure for the asymmetric reduction of ethyl benzoylformate by NADH mimics.- To a flame-dried Schlenk tube containing ethyl benzoylformate (0.21 mmol) was added the 1,4-dihydronicotinoyl complex (0.21 mmol), magnesium (II) perchlorate (0.21 mmol) and 0.6 ml of dry acetonitrile. The reaction mixture was stirred under nitrogen in the dark at 20°C for up to 24 h and then quenched with one drop of water and the solvent removed *in vacuo* . The crude solid was taken up in dichloromethane, chromatographed on silica gel (elution with 10% diethyl ether/hexane) and distilled to afford pure ethyl mandelate **15**. The purity of the mandelate **15** was determined by gas chromatography and ^1H n.m.r. spectroscopy. The specific rotation was measured (±2%).

To a solution of (R)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride[16] in dry pyridine (2 ml) was added a solution of the ethyl mandelate in dichloromethane (3 ml) at room temperature and the reaction mixture was stirred for 2-3 h. The reaction was quenched with water (0.2 ml) and the organics washed with water (2x5 ml) and dried over magnesium sulphate. Filtration and removal of solvent gave the crude derivative which was analysed by ^{19}F n.m.r. spectroscopy (±1%).

*Asymmetric reduction of ethyl benzoylformate by complex (R,R)-(-)-***12**.- A solution of ethyl benzoylformate (33 mg, 0.19 mmol), complex **12** (133 mg, 0.19 mmol) and magnesium (II) perchlorate (44.5 mg, 0.19 mmol) in dry acetonitrile (0.6 ml) was stirred for 24 h. Workup afforded R-(-)-ethyl mandelate (24 mg, 68%); $[\alpha]_D^{20}$ -91.8 (c 0.17, EtOH), 88% ee; δ_F -73.6 (R,R) and -73.9 (S,R) in a relative proportion of 95:6, 89% ee.

*Asymmetric reduction of ethyl benzoylformate by complex (R,R)-(-)-***12**.- A solution of ethyl benzoylformate (31 mg, 0.17 mmol), complex **12** (130 mg, 0.19 mmol) and magnesium (II) perchlorate (32 mg, 0.14 mmol) in dry acetonitrile (3.0 ml) was stirred for 168 h. Workup afforded R-(-)-ethyl mandelate (24.7 mg, 79%); $[\alpha]_D^{20}$ -81.0 (c 0.12, EtOH), 78% ee; δ_F -73.6 (R,R) and -73.9 (S,R) in a proportion of 90:10, 80% ee.

*Asymmetric reduction of ethyl benzoylformate by complex (S,R)-(+)-***13**.- A solution of ethyl benzoylformate (19.6 mg, 0.11 mmol), complex **13** (79 mg, 0.11 mmol) and magnesium (II) perchlorate (27 mg, 0.11 mmol) in dry acetonitrile (0.6 ml) was stirred for 24 h. Work-up afforded S-(+)-ethyl mandelate (13 mg, 66%); $[\alpha]_D^{20}$ +81.8 (c 0.10, EtOH), 78% ee; δ_F -73.6 (R,R) and -73.9 (S,R) in a relative proportion of 11:89, 77% ee.

*Asymmetric reduction of ethyl benzoylformate by complex (R,R)-(-)-***18b**.- A solution of ethyl benzoylformate (24.6 mg, 0.14 mmol), complex **18b** (96 mg, 0.14 mmol) and magnesium (II) perchlorate (33 mg, 0.14 mmol) in dry acetonitrile (0.6 ml) was stirred for 21 h. Work-up afforded R-(-)-ethyl mandelate (21.2 mg, 85%); $[\alpha]_D^{20}$ -16.5 (c 0.21, EtOH), 16% ee; δ_F -73.6 (R,R) and -73.9 (S,R) in a relative proportion of 57.5:42.5, 15% ee.

*Asymmetric reduction of ethyl benzoylformate by complex (S,S)-(+)-***18a** *and preparation of (S,S)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh_3)]-1-methyl-5-(1-hydroxymethylisopropylcarbamoyl)nicotinoyl perchlorate* **24**.- A solution of ethyl benzoylformate (24.6 mg, 0.14 mmol), complex **18a** (96 mg, 0.14 mmol) and magnesium (II) perchlorate (33 mg, 0.14 mmol) in dry acetonitrile (0.6 ml) was stirred for 8 h. Work-up afforded S-(+)-ethyl mandelate (21.2 mg, 85%); $[\alpha]_D^{20}$ +16.5 (c 0.25, EtOH), 16% ee; δ_F -73.6 (R,R) and -73.9 (S,R) in a relative proportion of 41:59, 18% ee.

The crude solid remaining at the top of the column was separated from the silica gel by dissolving the residue in a mixture of methanol and acetone followed by filtration. Removal of the solvent and crystallisation of the crude from a mixture of ethanol and dichloromethane (*ca.* 3:1) afforded the corresponding pyridinium salt **24** (78 mg, 60%) as a yellow solid; $[\alpha]_D^{20}$ -212 (c 0.049, CH_2Cl_2); $\nu_{max.}$ 3438, 2022, 1960, 1686 and 1587 cm^{-1}; δ_H 9.09 (1H, s, 6-H), 8.52 (1H, s, 4-H), 7.63 (1H, br d, J 8.7 Hz, NH), 7.49-7.37 (15H, m, Ph), 6.96 (1H, s, 2-H), 4.71 (5H, d, C_5H_5), 4.25 (3H, s, NCH_3), 4.02-3.92 (2H, m, $C\underline{H}_2OH$), 3.87-3.79 (1H, m, $C\underline{H}CH_2$), 3.05-3.95 (1H, m, OH, exchange on D_2O), 2.08-1.97 (1H, m, $C\underline{H}(CH_3)_2$), 1.00 (3H, d, J 6.7 Hz, $CH(C\underline{H}_3)_2$) and 0.99 (3H, d, J 6.7 Hz, $CH(C\underline{H}_3)_2$); δ_C (DMSO-d_6) 272.1 (d, $^2J_{PC}$ 21.8 Hz, C=O), 220.5 (d, $^2J_{PC}$ 30.7 Hz, C=O), 162.1 (s, C=O), 147.9 (s, 3-C), 144.6 (s), 143.7 (s), 137.7 (s), 135.2 (d, $^1J_{PC}$ 44.5 Hz, Ph C_{ipso}), 134.0 (s, 6-C), 133.3 (d, $^2J_{PC}$ 9.0 Hz, Ph C_{ortho}), 131.1 (s, Ph C_{para}), 129.1 (d,$^3J_{PC}$ 9.4 Hz, Ph C_{meta}), 86.6 (s, C_5H_5), 61.5 (s, $\underline{C}H_2OH$), 58.1 (s, $\underline{C}HCH_2$), 48.7 (s, NCH_3), 29.1 (s, $\underline{C}H(CH_3)_2$), 20.0

(s, $CH(\underline{C}H_3)_2$) and 19.1 (s, $CH(\underline{C}H_3)_2$); δ_P 72.83; [Found: m/z 661.1961. $C_{37}H_{38}N_2O_4FeP$ (M^+) requires 661.1919].

*Asymmetric reduction of ethyl benzoylformate by complex (S,R)-(+)-***19b** .- A solution of ethyl benzoylformate (28.1 mg, 0.16 mmol), complex **19b** (110 mg, 0.16 mmol) and magnesium (II) perchlorate (38 mg, 0.16 mmol) in dry acetonitrile (0.6 ml) was stirred for 20 h. Work-up afforded S-(+)-ethyl mandelate (23.8 mg, 84%); $[\alpha]_D^{20}$ +103 (c 0.25, EtOH), 99% ee; δ_F -73.6 (R,R) and -73.9 (S,R) in a relative proportion of 1.5:98.5, 97% ee.

*Asymmetric reduction of ethyl benzoylformate by complex (R,S)-(-)-***19a** *and preparation of (R,S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)]-1-methyl-5-(1-hydroxymethylisopropylcarbamoyl)nicotinoyl perchlorate* **25**.- A solution of ethyl benzoylformate (29.1 mg, 0.16 mmol), complex **19a** (113 mg, 0.17 mmol) and magnesium (II) perchlorate (39 mg, 0.17 mmol) in dry acetonitrile (0.6 ml) was stirred for 8 h. Work-up afforded R-(-)-ethyl mandelate (24 mg, 82%); $[\alpha]_D^{20}$ -102 (c 0.17, EtOH), 98% ee; δ_F -73.6 (R,R) and -73.9 (S,R) in a relative proportion of 98.7:1.3, 97.5% ee. (Reductions using 0.5 equivalent (19 mg), 2 equivalents (78 mg) and 5 equivalents (195 mg) of magnesium (II) perchlorate were carried out in a similar manner.)

The crude solid remaining at the top of the column was separated from the silica gel by dissolving the residue in a mixture of methanol and acetone followed by filtration. Removal of the solvent and crystallisation of the crude from a mixture of ethanol and dichloromethane (*ca.* 3:1) afforded the corresponding pyridinium salt **25** (78 mg, 60%) as a red solid; $[\alpha]_D^{20}$ +207 (c 0.047, CH_2Cl_2); $\nu_{max.}$ 3438, 2022, 1960, 1686 and 1587 cm^{-1}; δ_H 9.04 (1H, s, 6-H), 8.47 (1H, s, 4-H), 7.73 (1H, br d, J 8.9 Hz, NH), 7.43-7.36 (15H, m, Ph), 7.07 (1H, s, 2-H), 4.75 (5H, d, $^3J_{PH}$ 1.1 Hz, C_5H_5), 4.18 (3H, s, NCH_3), 4.08-3.96 (1H, m), 3.87-3.71(2H, m), 3.53-3.51(1H, m, OH, exchange on D_2O), 2.05-1.96 (1H, m, $C\underline{H}(CH_3)_2$), 1.00 (3H, d, J 6.7 Hz, $CH(C\underline{H}_3)_2$) and 0.99 (3H, d, J 6.7 Hz, $CH(C\underline{H}_3)_2$); δ_C 272.2 (d, $^2J_{PC}$ 27.2 Hz, C=O), 219.7 (d, $^2J_{PC}$ 29.7 Hz, C=O), 162.5 (s, C=O), 147.6 (s, 3-C), 143.2 (s), 141.0 (s), 140.4 (s), 135.3 (s, 5-C), 134.3 (d, $^1J_{PC}$ 40.7 Hz, Ph C_{ipso}), 133.2 (d, $^2J_{PC}$ 8.8 Hz, Ph C_{ortho}), 130.4 (s, Ph C_{para}), 128.5 (d,$^3J_{PC}$ 9.5 Hz, Ph C_{meta}), 86.3 (s, C_5H_5), 63.0 (s, $\underline{C}H_2OH$), 58.8 (s, $\underline{C}HCH_2$), 48.7 (s, NCH_3), 29.2 (s, $\underline{C}H(CH_3)_2$), 19.5 (s, $CH(\underline{C}H_3)_2$) and 19.1 (s, $CH(\underline{C}H_3)_2$); δ_P 66.68; [Found: m/z 661.1967. $C_{34}H_{38}N_2O_4FeP$ (M^+) requires 661.1919].

*Asymmetric reduction of ethyl benzoylformate by complex (R,R,S)-(-)-***22a** *and preparation of (R,R,S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)]-1-methyl-5-(1-hydroxybenzyl-2-methylcarbamoyl)-1,4-dihydronicotinoyl perchlorate* (**26**).- A solution of ethyl benzoylformate (31 mg, 0.18 mmol), complex **22a** (130 mg, 0.18 mmol) and magnesium (II) perchlorate (41 mg, 0.18 mmol) in dry acetonitrile (0.6 ml) was stirred for 1.5 h. Workup afforded R-(-)-ethyl mandelate (23.5 mg, 75%); $[\alpha]_D^{20}$ -102 (c 0.17, EtOH), 98% ee; δ_F -73.6 (R,R) and -73.9 (S,R) in a relative proportion of 98.9:1.1, 97.8% ee. (The reduction of ethyl benzoylformate using 2 equivalents (82 mg) of magnesium perchlorate was carried out in a similar manner.)

The crude solid remaining at the top of the column was separated from the silica gel by dissolving the residue in a mixture of methanol and acetone followed by filtration. Removal of the solvent and crystallisation of the

crude product from a mixture of ethanol and dichloromethane (*ca.* 3:1) afforded the corresponding pyridinium salt **26** (103 mg, 70%) as a yellow solid; $[\alpha]_D^{21}$ +274 (c 0.04, CH_2Cl_2); $\nu_{max.}$ 3438, 2022, 1960, 1686 and 1587 cm^{-1}; δ_H (CD_2Cl_2) 9.03 (1H, br s, 6-H), 8.57 (1H, br s, 4-H), 7.76 (1H, br d, J 7.4 Hz, NH), 7.66-7.25 (20 H, m, Ph), 6.95 (1H, br s, 2-H), 5.04 (1H, br s, OH), 4.74 (5H, s, C_5H_5), 4.72 (1H, m, C<u>H</u>OH), 4.41-4.32 (1H, m, C<u>H</u>CH_3), 4.21 (3H, s, NCH_3), and 1.13 (3H, d, J 6.4 Hz, CHC<u>H</u>$_3$); δ_C (CD_2Cl_2) 271.7 (d, $^2J_{PC}$ 27.5 Hz, C=O), 220.2 (d, $^2J_{PC}$ 28.7 Hz, C=O), 161.1 (s, C=O), 147.8 (s, 3-C), 142.6 (s), 142.0 (s), 140.8 (s), 135.8 (s, 5-C), 135.2 (d, $^1J_{PC}$ 18.5 Hz, Ph C_{ipso}), 133.8 (d, $^2J_{PC}$ 9.5 Hz, Ph C_{ortho}), 130.9 (s, Ph C_{para}), 128.9 (d, $^3J_{PC}$ 9.5 Hz, Ph C_{meta}), 128.7 (s, C_{ipso}), 128.6 (s, Ph), 127.6 (s, Ph), 126.5 (s, Ph), 86.7 (s, C_5H_5), 75.3 (s, <u>C</u>HOH), 49.0 (s, NCH_3), 44.8 (s, <u>C</u>HCH_3), and 13.0 (s, CH<u>C</u>H$_3$); δ_P 66.49; [Found: m/z 709.1959. $C_{41}H_{38}N_2O_4FeP$ (M^+) requires 709.1918].

*Asymmetric reduction of ethyl benzoylformate by complex (S,S,R)-(+)-***22b**.- A solution of ethyl benzoylformate (27.9 mg, 0.16 mmol), complex **22b** (118 mg, 0.16 mmol) and magnesium (II) perchlorate (38 mg, 0.16 mmol) in dry acetonitrile (0.6 ml) was stirred for 3 h. Work-up afforded S-(+)-ethyl mandelate (21.9 mg, 78%); $[\alpha]_D^{20}$ +102 (c 0.17, EtOH), 98% ee; δ_F -73.6 (R,R) and -73.9 (S,R) in a relative proportion of 98.5:1.5, 97% ee.

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