Novel Chiral Ferrocene Imines

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Received 20 October 2000

The synthesis of a series of novel chiral imines based on (*S*)-1-ferrocenylethylamine or (*S*)-1-phenylethylamine and suitably substituted benzaldehydes or ferrocene-1,1′-dicarbaldehyde is described. These chiral imines are designed to be the ligands in transition metal complexes, possible catalysts for various stereoselective reactions.

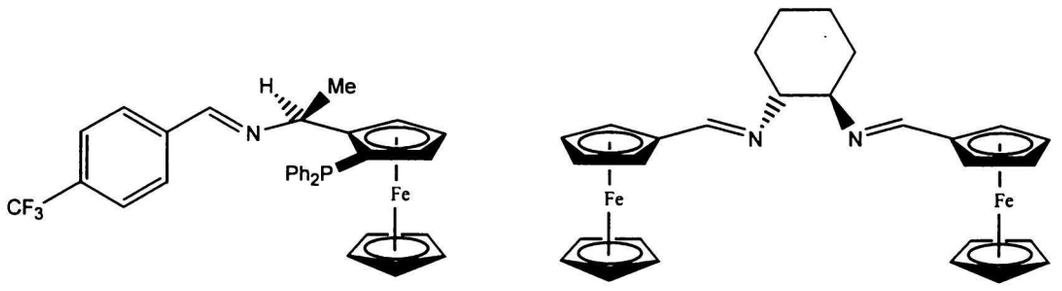
Chiral ferrocene ligands are prominent class of compounds in stereoselective synthesis and their development is very rapid [1]. Especially chiral ferrocenylphosphine [2, 3] ligands are established as very effective ligands in rhodium- or ruthenium-catalyzed stereoselective reductions. The well known (*R, pS*)-BPPFA* developed by *Hayashi* [4] is one of the most successful examples employed in enantioselective rhodium-catalyzed reductions of *N*-acylaminoacrylic acids. On the other hand, chiral ferrocenyloxazolines [5] are very effective ligands in palladium-catalyzed enantioselective allylic substitutions [6] or diethylzinc additions [7]. Surprisingly only chiral ferrocene ligands *I* and *II* (Formula 1), based on imine moiety are so far known [8, 9].

In this work we wish to present the preparation of a new series of chiral ferrocenyl imines based on (*S*)-1-ferrocenylethylamine or (*S*)-1-phenylethylamine and suitably substituted benzaldehydes or ferrocene-1,1′-dicarbaldehyde.

* BPPFA – (*R*)-*N*,*N*-dimethyl-1-[(*S*)-1′,2-bis(diphenylphosphino)ferrocenyl]ethylamine

New chiral ferrocene imines contain, in addition to the imine nitrogen, another donor atom (N, O, S) in a suitable position for complexation of the metal. Synthesis of these chiral ferrocene imines is based on the utilization of the well known (*S*)-*N*,*N*-dimethyl-1-ferrocenylethylamine as starting material [10]. Conversion of amine to the corresponding acetate proceeded with retention of configuration as well as displacement of acetate with ammonia by which (*S*)-1-ferrocenylethylamine was formed (Scheme 1). Reactions of different aromatic aldehydes with this amine in benzene in the presence of molecular sieves resulted in formation of Schiff bases *III*—*VI* (Scheme 1, Formula 2). Crude products were purified by chromatography and crystallization.

Planar chiral ligand *VII* was prepared by reaction of (*S, pR*)-1-(2-diphenylphosphanyl)ferrocenylethylamine [8] with 2-piperidinobenzaldehyde. C_2-symmetric ligands *VIII* and *IX* containing two imine functionalities were prepared by the reaction of ferrocene-1,1′-dicarbaldehyde [11], either with (*S*)-1-ferrocenylethylamine or commercially available (*S*)-1-phenylethylamine.



I *II*

Formula 1

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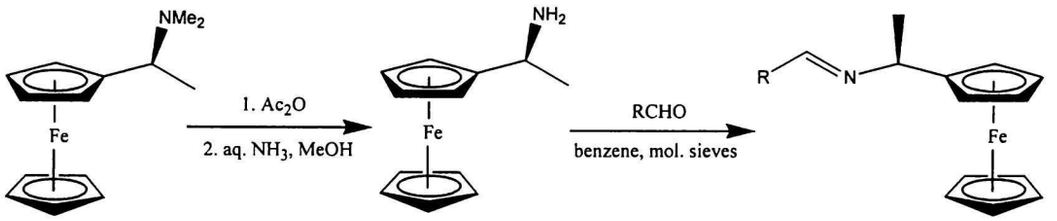
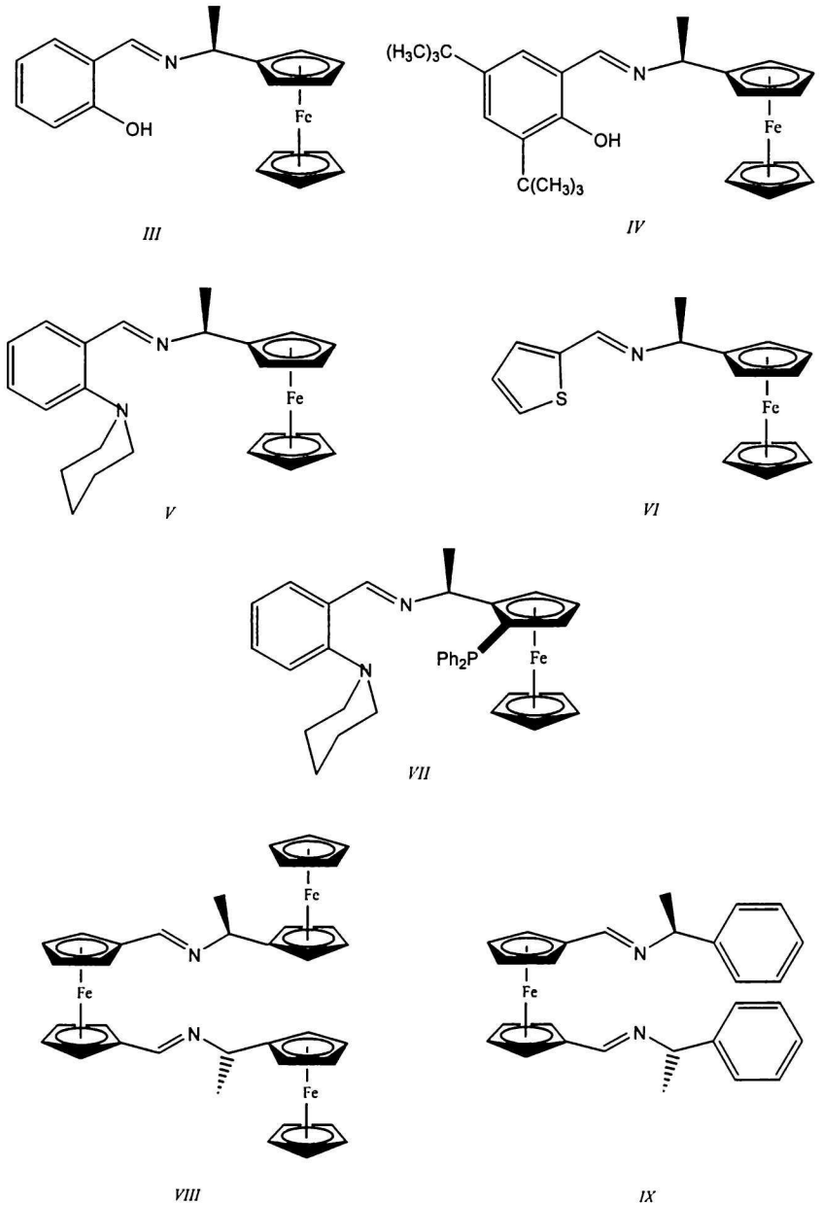


Scheme 1



III *IV* *V* *VI* *VII* *VIII* *IX*

Formula 2

Reactions of (*S*)-1-ferrocenylethylamine with diketones (pentane-2,4-dione and phenanthrenequinone) were also carried out, but were unsuccessful. Despite the fact that TLC and ^{1}H NMR of the crude mixtures proved the formation of new compounds, we were not able to isolate them in a pure state and to give some useful characteristics. Preparation of the corresponding Schiff base from benzene-1,2-dicarbaldehyde

was also unsuccessful – either by using the mentioned methodology, or by several other common procedures*.

The utilization of the prepared aldimines as the ligands for transition metal complexes, possible suitable catalysts in enantioselective cyclopropanations, aziridinations, and allylic substitutions is under investigation.

EXPERIMENTAL

Standard procedures have been used for purification and drying of the solvents. NMR spectra were measured on Varian Gemini 2000 (300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR). Tetramethylsilane was used as the internal standard. Melting points were measured on Kofler apparatus. Optical rotations were measured on Perkin—Elmer 241 apparatus. All reactions were carried out under inert atmosphere. (*S*)-*N*,*N*-Dimethyl-1-ferrocenylethylamine was prepared by Ugi's resolution procedure [10]. (*S, pR*)-1-(2-Diphenylphosphanyl)ferrocenylethylamine was prepared according to Hayashi's procedure [8]. 3,5-Di-*tert*-butyl-2-hydroxybenzaldehyde was prepared from 2,4-di-*tert*-butylphenol [12]. 2-Piperidinobenzaldehyde was prepared from 2-fluorobenzaldehyde and piperidine [13]. Ferrocene-1,1′-dicarbaldehyde was prepared by dilithiation of ferrocene and subsequent quenching with dimethylformamide [11].

(*S*)-1-Ferrocenylethyl Acetate

In a tube (*S*)-*N*,*N*-dimethyl-1-ferrocenylethylamine (1.0 g; 3.906 mmol) was dissolved in acetic acid anhydride (3 cm^3) and the tube was sealed and heated to 100 °C for 2.5 h. After cooling, the mixture was poured into ether and extracted three times with sodium carbonate solution and twice with water. Organic layer was dried over Na_2SO_4 and after filtration, the solvent was removed *in vacuo*. The crude product was used without further purification into the next step.

(*S*)-1-Ferrocenylethylamine

The material from the previous reaction was dissolved in methanol (30 cm^3) and concentrated aqueous ammonia solution (20 cm^3) was added. The reaction mixture was heated to reflux for 17 h. Methanol was evaporated and the oily residue was dissolved in 10 % H_3PO_4. The solution was extracted with ether (to remove starting acetate and other side products), aqueous phase was then adjusted to pH = 12 using solid Na_2CO_3 and extracted with ether. Organic layer was washed with brine and dried over Na_2SO_4. After filtration of the desiccant, the solution was concentrated *in vacuo* to give 717 mg (80 %) of orange viscous oil. $[\alpha]$ (20 °C, D, 0.58 g/100 cm^3 $CHCl_3$) = +21.7° (Ref. [14] for (*R*)-amine gives $[\alpha]$ (20 °C, D, 3.3 g/100 cm^3 EtOH) = −22.1°), ^{1}H NMR spectrum ($CDCl_3$), δ: 1.35 (d, 3H, CH_3), 1.55 (br s, 2H, NH_2), 3.80 (q, 1H, CH), 4.10—4.16 (m, 9H, Fc).

* Use of $BF_3.Et_2O$ as Lewis acid, azeotropic distillation in toluene.

Aldimines *III*—*IX*

(*S*)-1-Ferrocenylethylamine (0.263 mmol) and corresponding aldehyde (0.263 mmol) were dissolved in benzene (3 cm^3), molecular sieves were added and the mixture was stirred overnight at 20 °C. Molecular sieves were filtered off and washed with benzene. Solvent was then evaporated *in vacuo* and the residue was purified by crystallization. Some decomposed material was removed mainly in the filtration step. Characterization of pure products is given in Table 1.

(S)-[N-(2-Hydroxybenzylidene)]-1-ferrocenylethylamine (*III*) was recrystallized from ethanol to give orange crystals. ^{1}H NMR spectrum ($CDCl_3$), δ: 1.57 (d, 3H, CH_3, $^3J_{HH}$ = 6.6 Hz), 4.08—4.16 (m, 9H, Fc), 4.29 (q, 1H, CH, $^3J_{HH}$ = 6.6 Hz), 6.90 (t, 1H, Ph), 6.99 (d, 1H, Ph), 7.28—7.32 (m, 2H, Ph), 8.38 (s, 1H, CH=N), 13.78 (s, 1H, OH); ^{13}C NMR spectrum ($CDCl_3$), δ: 23.7 (CH_3), 63.1 (CH), 66.5, 66.8, 67.8, 68.0 ($C_{\alpha,\beta}$ (Cp)), 68.8 (Cp), 92.2 (C_i (Cp)), 117.3, 118.7, 119.0, 131.5, 132.5, 161.6 (Ph), 162.9 (CH=N).

(S)-[N-(2-Hydroxy-3,5-di-tert-butylbenzylidene)]-1-ferrocenylethylamine (*IV*) was recrystallized from ethanol to give yellow crystals. ^{1}H NMR spectrum ($CDCl_3$), δ: 1.32 (s, 9H, tBu), 1.47 (s, 9H, tBu), 1.57 (d, 3H, CH_3, $^3J_{HH}$ = 6.6 Hz), 4.14 (m, 9H, Fc), 4.26 (q, 1H, CH, $^3J_{HH}$ = 6.8 Hz), 7.10 (m, 1H, Ph), 7.39 (m, 1H, Ph), 8.39 (s, 1H, CH=N); ^{13}C NMR spectrum ($CDCl_3$), δ: 23.3 (CH_3), 29.5 (tBu—CH_3), 31.6 (CH_3 (tBu)), 34.2 (C (tBu)), 35.1 (C (tBu)), 62.7 (CH), 66.4, 66.7, 67.6, 67.7 ($C_{\alpha,\beta}$ (Cp)), 68.7 (Cp), 92.3 (C_i (Cp)), 117.9, 126.8, 128.8, 136.8, 139.9, 158.3 (Ph), 163.7 (CH=N).

(S)-[N-(2-Piperidinobenzylidene)]-1-ferrocenylethylamine (*V*) was recrystallized from hexane to give orange-red crystals. ^{1}H NMR spectrum ($CDCl_3$), δ: 1.57 (m, 5H, CH_3, CH_2), 1.73 (m, 4H, CH_2), 2.92 (m, 4H, NCH_2), 4.16 (m, 9H, Fc), 4.38 (q, 1H, CH, $^3J_{HH}$ = 6.5 Hz), 7.04 (m, 2H, Ph), 7.34 (m, 1H, Ph), 7.92 (m, 1H, Ph), 8.60 (s, 1H, CH=N); ^{13}C NMR spectrum ($CDCl_3$), δ: 23.3 (CH_3), 24.2 (CH_2), 26.4 ((CH_2)$_2$), 54.6 (N—(CH_2)$_2$), 64.8 (CH), 66.2, 67.2, 67.4, 67.6 ($C_{\alpha,\beta}$ (Cp)), 68.5 (Cp), 92.9 (C_i (Cp)), 118.4, 122.5, 128.1, 129.8, 130.8, 154.0 (Ph), 157.7 (CH=N).

(S)-[N-(Thiophene-2-methylidene)]-1-ferrocenylethylamine (*VI*) was recrystallized from hexane giving yellow-orange crystals. ^{1}H NMR spectrum ($CDCl_3$), δ: 1.53 (d, 3H, CH_3, $^3J_{HH}$ = 6.6 Hz), 4.15 (m, 9H, Fc), 4.31 (q, 1H, CH, $^3J_{HH}$ = 6.6 Hz), 7.07 (dd, 1H, H_{arom}), 7.30 (d, 1H, H_{arom}), 7.38 (d, 1H, H_{arom}), 8.36 (s, 1H, C=N); ^{13}C NMR spectrum ($CDCl_3$), δ: 22.9

Table 1. Characterization of the Imines *III*—*IX*

Comp.	Formula	M_r	w_i(calc.)/% w_i(found)/%			Yield	M.p.	$[\alpha]^a$
			C	H	N	%	°C	(ρ)
III	$C_{19}H_{19}FeNO$	333.2	68.48 68.75	5.75 5.93	4.20 4.01	95	65—67	+ 103.8° (0.63)
IV	$C_{27}H_{35}FeNO$	445.1	72.79 72.59	7.93 8.11	3.15 3.15	87	107—109	+ 80.4° (0.24)
V	$C_{24}H_{28}FeN_2$	400.3	72.0 71.72	7.05 7.06	7.0 6.89	71	100—102	+ 136° (0.275)
VI	$C_{17}H_{17}FeNS$	323.2	63.17 63.27	5.30 5.29	4.33 4.26	87	74—75	+ 282.9° (0.34)
VII	$C_{36}H_{37}FeN_2P$	584.5	73.97 73.81	6.38 6.48	4.79 4.69	95	223—225	+ 326.7° (0.49)
VIII	$C_{36}H_{36}Fe_3N_2$	664.2	65.09 65.23	5.46 5.43	4.22 4.09	94	177—178	+ 242.6° (0.13)
IX	$C_{28}H_{28}FeN_2$	448.4	75.0 75.17	6.30 6.42	6.25 6.37	72	105—107	−342.3° (0.53)

a) $[\alpha]$(20 °C, D, ρ(g/100 cm^3 $CHCl_3$)).

(CH_3), 64.0 (CH), 66.3, 67.2, 67.4, 67.7 ($C_{\alpha,\beta}$ (Cp)), 68.4 (Cp), 92.5 (C_i (Cp)), 127.2, 128.6, 130.0, 143.2 (H_{arom}), 151.8 (CH=N).

(S, pR)-[N-(2-Piperidinobenzylidene)]-1-(2-diphenylphosphanyl)ferrocenylethylamine (*VII*) was recrystallized from acetone to give orange crystals. ^{1}H NMR spectrum ($CDCl_3$), δ: 1.55 (m, 2H, CH_2), 1.66 (d, 3H, CH_3, $^3J_{HH}$ = 6.9 Hz), 1.71 (m, 4H, CH_2), 2.69 (m, 4H, CH_2NCH_2), 3.81 (m, 1H, Fc), 4.03 (s, 5H, Cp), 4.34 (m, 1H, Fc), 4.67 (m, 1H, Fc), 4.85 (m, 1H, CH), 6.69—7.00 (m, 7H, Ph), 7.10 (m, 2H, Ph), 7.36 (m, 3H, Ph), 7.55 (m, 2H, Ph), 8.39 (s, 1H, CH=N); ^{13}C NMR spectrum ($CDCl_3$), δ: 22.4 (CH_3), 24.3 (CH_2), 26.39 ($CH_2(CH_2)_2$), 54.49 ($(CH_2)_2N$), 63.85 (d, CH, $^3J_{PC}$ = 7.5 Hz), 69.24 (d, C—Cp, $^2J_{PC}$ = 4.3 Hz), 69.3 (C—Cp), 69.6 (Cp), 71.4 (d, CCP, $^2J_{PC}$ = 4.8 Hz), 75.7 (d, C—P, $^1J_{PC}$ = 9.4 Hz), 97.5 (d, C_i (Cp), $^2J_{PC}$ = 24.3 Hz), 117.9, 122.0, 127.1, 127.6, 127.6, 127.9, 128.0, 129.0, 130.2, 132.2, 132.4, 135.3, 135.6, 153.8 (Ph), 158.8 (CH=N).

N,N'-Bis[(S)-1-ferrocenylethyl]ferrocene-1,1'-bis-(methylideneamine) (*VIII*) was recrystallized from benzene to give orange crystals. ^{1}H NMR spectrum ($CDCl_3$), δ: 1.54 (d, 6H, CH_3, $^3J_{HH}$ = 6.6 Hz), 4.15—4.23 (m, 20H, Fc + CH), 4.32 (m, 4H, H_β), 4.58 (m, 2H, H_α), 4.60 (m, 2H, $H_{\alpha'}$), 8.04 (s, 2H, CH=N); ^{13}C NMR spectrum ($CDCl_3$), δ: 22.7 (CH_3), 64.1 (CH), 66.4, 67.8, 67.9, 68.0 ($C_{\alpha,\beta}$ (Cp)), 68.8 (Cp), 69.8, 69.9, 71.5, 71.52 ($C_{\alpha,\beta}$ (Cp)), 81.5, 92.6 (C_i (Cp)), 158.1 (CH=N).

N,N'-Bis[(S)-1-phenylethyl]ferrocene-1,1'-bis-(methylideneamine) (*IX*) was recrystallized from hexane to give orange crystals. ^{1}H NMR spectrum ($CDCl_3$), δ: 1.55 (d, 6H, CH_3, $^3J_{HH}$ = 6.6 Hz), 4.27—4.30 (m, 6H, $H_{\beta,\beta'}$), 4.56 (m, 2H, $H_{\alpha'}$), 4.62 (m, 2H, H_β), 7.25 (m, 2H, Ph), 7.32—7.38 (m, 8H, Ph), 8.03 (s, 2H, CH=N); ^{13}C NMR spectrum ($CDCl_3$), δ: 24.9 (CH_3), 69.3 (CH), 69.7, 70.0, 71.3, 71.6 ($C_{\alpha,\beta}$ (Cp)), 81.8 (C_i (Cp)), 126.8, 127.0, 128.7, 145.5 (Ph), 159.1 (CH=N).

Acknowledgements. We are grateful to Professor Štefan Toma and Dr. Battsengel Gotov for valuable discussions. We also thank M. Drapáková for NMR spectra and Dr. K. Gáplovská for elemental analyses. This work was supported by the Slovak Grant Agency for Science, Grant No. 1/7013/20 and Comenius University, Grant No. UK/3760/99.

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