Synthesis and crystal structure of chiral N-ferrocenylmethyl alkamine imine

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Two chiral ferrocenylimine alcohols have been prepared, [Fe(η^5-(C_5H_5){η^5-C_5H_4CH=NCH(CH_2OH)(CH_2R)}] (R = Ph, **5a**; R = Pr^i, **5b**). Single crystal X-ray diffraction analysis reveals that the molecular structure of compound **5b** is enantiomerically pure.

Keywords: ferrocenylimine alcohols, synthesis, crystal structure, chirality, imine

Enantiomerically pure ferrocenylimine alcohol compounds have found widespread use as chiral ligands or auxiliaries in asymmetric reactions. These compounds are very effective catalysts for a wide range of reactions such as epoxidation, epoxide ring opening, Diels–Alder reactions and aldol reactions.[1-4] In addition, the steric effect of the specific microenvironment created by the ferrocene skeleton structure can modulate the catalytic behaviour of the chiral ferrocenylimine alcohol.

Considerable effort has focused on the design of ferrocenylimine alcohol compounds with potential applications in drug delivery and biomedical engineering. In this paper, we report the synthetic and structural investigation of two novel chiral ferrocenylimine alcohols **5a** and **5b** (Scheme 1).

Experimental

All reactions were carried out under argon and monitored by thin-layer chromatography (TLC). Diethyl ether was dried using Na under reflux. Melting points (uncorrected) were measured with an XT4 melting point apparatus. ^{1}H NMR spectra were recorded on a Varian 300 spectrometer, using $CDCl_3$ as solvent and TMS as the internal standard. Optical rotations were measured on a WZZ-3 polarimeter. Column chromatography was performed on silica gel (200–300 mesh). Formylferrocene was prepared by a literature method[5] (m.p. 122–124 °).

Synthesis of chiral α-amino alcohols

3a: To anhydrous methanol (65 mL) contained in a 250 mL three-neck flask, with stirring and cooling to –10 ° with an ice-salt bath, was slowly added $SOCl_2$ (7.2 mL, 0.099 mol) drop by drop (temperature cannot exceed 0°). When the addition was finished, the mixture was cooled at –5–0 ° for about 1 h. Then L- phenylalanine (8.0 g, 0.076 mol) was added, stirring was continued for 3 h at room temperature, then the mixture was refluxed for 2 h. After cooling, the liquids were removed by vacuum distillation, leaving a white crude solid (yield 83.2%). m.p.157–159 °C, $[\alpha]_D^{20}$ + 37.5 ° (*c* 2.0, C_2H_5OH). [lit. $[\alpha]_D^{27}$ + 38.1 ° (C = 2.0, C_2H_5OH)].[6] The crude material was recrystallised from ethanol–ether giving white needle crystals (11.3 g). Anal. Calcd for $C_{10}H_{14}ClNO_2$: C, 55.69; H, 6.54; N, 6.49. Found: C, 55.48; H, 6.39; N, 6.23%; IR *ν*/cm^{-1}: 3001.85; 2963.72; 2625.84; 1754.61; 1583.69; 1491.30; 1237.23. The crystals were dissolved in water and saturated $NaHCO_3$ solution was added until pH = 8. Then the reaction mixture was extracted with methylene chloride, the organic layer was washed with water, dried over anhydrous magnesium sulfate, then evaporated to afford L-phenylalanine methylester (**2a)** (colourless oil). **2a** was reduced to *L*-phenylalaninol (**3a)** with KBH_4 and $CaCl_2$ as the reducing agent. (Yield: 68.9%). m.p.90–91 °C, $[\alpha]_D^{20}$ –22.5 °C (*c* 1.2, C_2H_5OH); IR *ν*/cm^{-1}: 3380.6(OH); 1569.8(NH_2); 1348.1(CH_2); 1052.3(C–O).

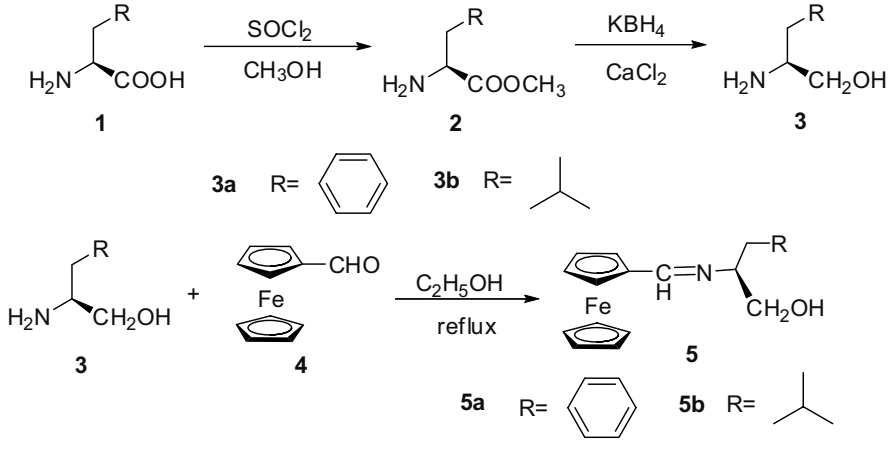
3b: Prepared in similar manner to **3a,** starting with L-leucine. The crude material was recrystallised from ethanol–ether giving white needle crystals of **2b** (9.9 g, 72.1%), m.p. 150–152°C, $[\alpha]_D^{20}$ + 13.2 (*c* 2.0, H_2O). [lit. $[\alpha]_D^{26}$ + 13.4 ° (C = 2.0, H_2O)].[7] Anal. Calcd for $C_7H_{16}ClNO_2$: C, 46.28; H, 8.88; N, 7.71, Found: C, 46.09; H, 8.25; N, 7.73%; IR *ν*/cm^{-1}: 2960.27; 2627.68; 1736.13; 1583.68; 1223.37. **2b** was reduced to L-leucinol (**3b**) with KBH_4 and $CaCl_2$ as the reducing agent. (Yield: 58.6%). m.p.56–58 °C, $[\alpha]_D^{20}$–11.2 °C (*c* 1.3, C_2H_5OH); IR *ν*/cm^{-1}: 3378.5(OH); 1572.8(NH_2); 1346.2(CH_2); 1051.6(C–O).

Synthesis of ferroceneimine alcohols **5**

The title compounds were prepared according to Scheme 1. Formylferrocene (**4**) (5 mmol) was treated in benzene at 80 ° with L-phenylalaninol (L-leucinol) (5 mmol) using modification of reported procedures, giving imines **5a** and **5b** respectively. After evaporation of the solvent, both imines were recrystallised from dichloromethane/petroleum ether giving orange crystals.

5a: 82.6%. m.p. 118–120 °, $[\alpha]_D^{20}$–123.2 (*c* 0.153, CH_2Cl_2). The IR spectrum indicated the presence of the unsubstituted cyclopentadienyl ring (1103.9 and 996.6 cm^{-1}), 1022.0–1147.6 cm^{-1} (single substituted cyclopentadienyl), 486.1 cm^{-1} and 509.9 cm^{-1} (ν_{Fe-C}), 1641.1 cm^{-1}(N=CH); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.94 (s, 1H, N=CH), 7.30–7.21 (m, 5H, ArH), 4.63(s, 1H, OH), 4.45–4.31 (m, 4H, Cp-H), 3.96 (s, 5H, Cp-H), 3.77–3.71 (m, 2H,, CH_2–OH), 3.50–3.46 (m, 1H, N–CH), 2.92–2.86 (m, 2H, Ph-CH_2),

5b: 75.1% m.p. 98–100 °, $[\alpha]_D^{20}$–106.2 (c 0.104, CH_2Cl_2). The IR spectrum indicated the presence of the unsubstituted cyclopentadienyl ring (1100.1 and 996.0 cm^{-1}), 1021.0–1145.6 cm^{-1} (single substituted cyclopentadienyl), 486.5 cm^{-1} and 509.7 cm^{-1}(ν_{Fe-C}), 1636.2 cm^{-1}



Scheme 1 Preparation of chiral ferrocenylimine alcohols.

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(N=CH); ^{1}H NMR (300 MHz, $CDCl_3$, ppm):δ 8.05 (s, 1H, N=CH), 4.75(s, 1H, OH), 4.46–4.30 (m, 4H, Cp-H), 4.17 (s, 5H, Cp-H), 3.75–3.73 (m, 2H,, CH_2–OH), 2.81–2.76 (m, 1H, N–CH), 1.92–1.85, m, 1H, $(CH_3)_2CH$), 0.95–0.98 (d, 3H, J = 7.6 Hz, CH_3), 0.89-0.91 (d, 3H, J = 7.6 Hz, CH_3).

X-ray crystal-structure analysis of **5b**

Crystals suitable for X-ray structure determination were obtained from the filtration by slow evaporation of the solvent. *Crystal data:* $C_{16}H_{20}FeNO$, M*r* = 298.18, Monoclinic, C2, *a* = 24.124(5) Å, *b* = 8.9923(18) Å, *c* = 6.6417(13)Å, *V* = 1433.6(5) Å^3, D_x = 1.381 g cm^{-3}, *Z* = 4, *T* = 113(2)K. Absolute structure parameter is –0.010(19). Slow evaporation of the compound **5b** in petroleum ether and ethyl acetate yielded single crystals suitable for X-ray analysis. An orange block crystal with approximate dimensions of 0.16 × 0.12 × 0.06 mm was mounted on a Bruker Smart 1000 CCD diffractometer equipped with graphite monochromator data collection. The determination of unit cell parameters and data collection were performed at 113(2) K, using graphite monochromated MoKα (λ = 0.71073 A) radiation. A total of 29018 reflections with 3727 independent ones with *R*int = 0.0384 were measured in the range of 2.42≤θ≤24.98 ° by an oscillation method. All data were corrected using the SADABS method. The structure was solved by direct methods using the SHELXL-97 program and refined by full-matrix least-squares on F^2.[8] All non–hydrogen atoms were refined anisotropically, and hydrogen atoms were added according to theoretical modes. The final cycle of refinement gave R = 0.0335, wR = 0.0707 (The weighting scheme was w = 1/[s^2(F_0^2) + (0.0202P)^2] where $P = (F_0^2 + 2F_c^2)/3$). The final refinement was performed by full matrix least-squares methods with anisotropic thermal parameters for non-hydrogen atoms on F^2. Molecular graphics were drawn with the program package XP. Full crystallographic details have been deposited with the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC-741091. Further details of the structure analyses are given in Table 1, selected bond lengths and angles are in Tables 2 and 3.

Results and discussion

The title compounds, ferrocenylimine alcohols **5a and 5b,** have been synthesised. **5b** was characterised by X-ray diffraction, its molecular structure is shown in Fig. 1. The compounds were characterised by IR and ^{1}H NMR elemental analysis. The spectroscopic data of the complexes are found to be identical with expected structures. In the ^{1}H NMR spectra of the product, the hydrogen atoms of the unsubstituted Cp moiety appear as a sharp singlet. The imine function of the compounds was registered as strong signals at about 1636 and 1641 cm^{-1} in the IR-spectra, as well as at about 7.94 and 8.05 ppm in the ^{1}H NMR spectra.

Table 1 Crystallographic data and structure refinement summary

CCDC deposit no.	741091
Empirical formula	$C_{16}H_{20}FeNO$,
Formula weight	298.18
Temoerature(K)	113(2)
Wavelength (Mo Ka) (A°)	0.71073
Crystal system	Monoclinic
Space group	*C2*
Unit cell dimensions	
a (Å)	24.124(5)
b (Å)	8.9923(18)
c (Å)	6.6417(13)
Volume(Å ^{3})	1433.6(5)
Z	4
Crystal size	0.16 × 0.12 × 0.06
Calculated density Mg m^{-2}	1.381
Absorption coefficient, mm^{-1}	1.043
F(000)	628
Reflections collected/unique	5225/2476 [R(int) = 0.0384]
Completeness to theta = 24.98	99.7%
Data/restraints/parameters	2476/1/172
Limiting indices	–27< = *h*< = 28, –10< = *k*< = 10, –6< = *l*< = 7
Goodness of fit on F2	1.159
Final R indices [I>2 sigma(I)]	R1 = 0.0335, wR2 = 0.0707
R indices (all data)	R1 = 0.0396, wR2 = 0.0721
Absolute structure parameter	–0.010(19)
Largest diff. peak and hole/e.A-^{3}	0.428 and -0.428

Table 2 Selected bond lengths (Å) for compound **5b**

Bond length/Å		Bond length/Å	
Fe(1)–C(10)	2.025(4)	C(10)–C(11)	1.454(5)
Fe(1)–C(9)	2.056(5)	C(13)–C(14)	1.525(4)
Fe(1)–C(8)	2.058(4)	C(12)–C(16)	1.525(4)
Fe(1)–C(7)	2.047(3)	C(12)–C(13)	1.535(4)
Fe(1)–C(6)	2.041(4)	C(13)–C(15)	1.530(5)
Fe(1)–C(5)	2.050(4)	C(9)–C(10)	1.439(4)
Fe(1)–C(4)	2.043(3)	C(2)–C(3)	1.407(7)
Fe(1)–C(3)	2.035(4)	C(4)–C(5)	1.438(8)
Fe(1)–C(2)	2.040(4)	C(6)–C(7)	1.409(5)
Fe(1)–C(1)	2.041(4)	C(7)–C(8)	1.425(5)
O(1)–C(16)	1.430(4)	C(8)–C(9)	1.419(6)
N(1)–C(11)	1.269(4)	N(1)–C(12)	1.481(4)

Single crystal X-ray diffraction analysis reveals that the molecular structure of **5b** is essentially as expected and confirms the formulation of the compound (shown in Fig. 1). This compound is enantiomerically pure and crystallises in the monoclinic C2 space group.

The Fe–C contact lengths range from 2.035 (4) to 2.050(4) Å (C1–C5) and from 2.041(3) to 2.058(3) Å (C6–C9) in the molecule. The Fe–C10 contact length is 2.025 (4) Å. Fe atoms are almost at the centre of the two cyclopentadienyl rings, with the Fe(1)–Cg(1) and Fe(1)–Cg(2) distances 1.6585 Å, 1.6405 Å, where Cg(1)and Cg(2) are the centroids of the η5(C_5H_5) and η5(C_5H_4) rings. The iron atoms are slightly closer to the plane of the unsubstituted rings. The two cyclopentadienyl rings are not parallel, the two cyclopentadienyl rings deviate from an eclipsed geometry in compound **5b**, as evidenced

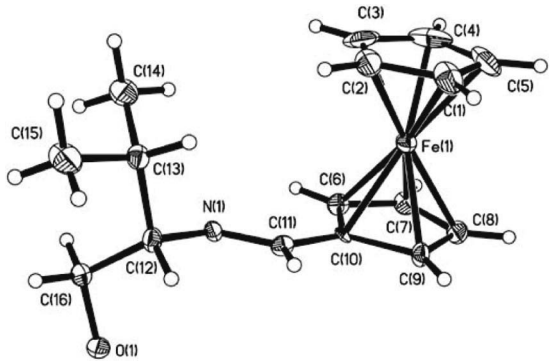

Fig. 1 ORTEP drawing of the structure of **5b**. Thermal ellipsoids are drawn at 50% probability level.

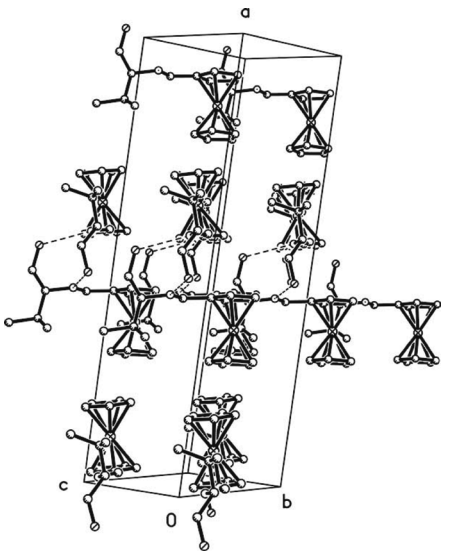

Fig. 2 Three-dimensional molecular-packing diagram of compound **5b**.

Table 3 Selected bond angles and torsion angles (°) for compound **5b**

Bond angle/°		Bond angle/°	
C(10)–Fe(1)–C(6)	41.12(16)	C(5)–C(1)–C(2)	107.4(2)
C(4)–Fe(1)–C(6)	122.04(18)	N(1)–C(12)–C(16)	107.5(3)
C(6)–Fe(1)–C(1)	158.70(14)	N(1)–C(12)–C(13)	109.2(3)
C(9)–C(10)–C(11)	123.9(4)	C(15)–C(13)–C(12)	111.6(3)
N(1)–C(11)–C(10)	123.3(3)	O(1)–C(16)–C(12)	112.2(3)
C(12)–N(1)–C(11)–C(10)	–175.6(3)	C(9)–C(10)–C(11)–N(1)	–176.5(4)
C(11)–N(1)–C(12)–C(16)	–141.6(3)	C(6)–C(10)–C(11)–N(1)	5.8(6)

by the interplanar angles of 5.1° respectively between the $\eta^5(C_5H_4)$ and $\eta^5(C_5H_5)$ rings. The C(10)–C(11) bond length is 1.454(5) Å, in good agreement with values reported for other ferrocenylimine derivatives,[9] which are shorter than the common distance of the C-C single bond 1.540Å.[10] The angles C(9)–C(10)–C(11) = N, and C(6)–C(10)–C(11)–N(1) are –176.5(4) and 5.8(6)° respectively**;** this is in keeping with the suggestion that some delocalisation of electron density is found over the N=C–Cp fragment, indicating that there is conjugation between the C=N unit and the cyclopentadienyl ring. The chiral centre C_{12} substituents are in the *R*-configuration. The packing diagram (Fig. 2) shows that there are intermolecular hydrogen bonds O1–H1…O1 in the unit cell.

CCDC 741091 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data\ request/cif, by e-mailing data\ request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: + 44 (0) 1223-336033.

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