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Novel synthesis and crystal structure of *Rac-N,N*-dimethyl-1-ferrocenylethylamine hydrochloride

Yu-Mei Zhang[a,b], Zhi-Ming Zhou[a]* and Cong-Xuan Yu[a]

[a]*School of Chemical Engineering & the Environment, Beijing Institute of Technology, Beijing, 100081,China*

[b]*College of Sciences, Hebei University of Science and Technology, Shijiazhuang,050016, China*

The title compound *N, N*-dimethyl-1-ferrocenylethylaminehydrochloride $[Fe(C_5H_5)(C_5H_4CHCH_3N^+H(CH_3)_2)Cl^-]$ was synthesised by esterification of the corresponding alcohol, followed by substitution with $HN(CH_3)_2$ and by extracting HCl from CH_2Cl_2 probably associated with Fe in the substrate molecule. Its structure was first elucidated by X-ray analysis. By analysis of the crystal structure of, it is proposed that diastereoselective *ortho*-deprotonation directed by Ugi's amine may be ascribed to the different hindrance exerted by methyl group at chiral C.

Keywords: synthesis, crystal structure, *N*,*N*-dimethyl-1-ferrocenylethylamine hydrochloride

Ferrocenes with planar chirality are of increasing importance in the synthesis of chiral ligands used in asymmetric catalysis and being building blocks in asymmetric synthesis.[1-3] To prepare ferrocenes with planar chirality, so far the most important method is adopting Ugi's method by diastereoselective *ortho*-lithiation of optically resolved (*S*)-(-)-*N*,*N*-dimethyl-1-ferrocenylethylamine **1** and subsequent reaction with an appropriate electrophile.[4-5] In the course of exploring diferrocenes with planar chirality, we discovered a novel preparation of *rac*-*N*,*N*-dimethyl-1-ferrocenylethylamine hydrochloride **2** (Scheme 1). To the best of our knowledge, the crystal structure of the title compound has not been reported yet.

We present here the crystal structure of *rac*-*N*,*N*-dimethyl-1-ferrocenylethylamine hydrochloride **2** and its novel preparation, from which it may be allowed to a better understanding of diastereoselective *ortho*-deprotonation of the two prochiral protons to Ugi's amine.

Experimental

General procedure

All starting materials were of analytical grade. Elemental analyses (C, H, N) were performed on a Perkin-Elmer 240C elemental analyzer. IR spectra were obtained from KBr pellet with a FT-IR 170SX (Nicolet) spectrometer in the range of 400–4000cm^{-1} with KBr. ^{1}H NMR spectra in deuterium chloroform were recorded on a Varian EM-360 spectrometer, TMS as the internal standard. Melting point was measured with a XT_4 melting point apparatus. The reaction is shown in Schemes 1 and 2.

Preparation of N,N-dimethyl-1-ferrocenylethylamine hydrochloride: 1-Ferrocenylethanol was prepared according to methods listed in the literature,[6] m.p.73–74 °C. A solution of 1-ferrocenylethanol (4.60 g, 20 mmol) and acetic anhydride (8 ml) in pyridine (20 ml) was stirred at room temperature for 24 h, concentrated *in vacuo*. The yellow solid residue was redissolved in methanol, then dimethylamine (10 ml 33% water solution) was added. After being heated for 1 h, the reaction mixture was extracted with methylene chloride, the organic layer was washed with water and dried over anhydrous magnesium sulfate, and evaporated to afford a red oil, then ether was added until no further precipitate was formed, and a yellow solid was given after filtration. Recrystallised from ethanol gave orange single crystals suitable for *X*-ray analysis. Yield 20.4% (1.20 g). M.p. 169–171 °C (decomp.).

Calc. for $C_{14}H_{20}FeN$ Cl, 57.2; H, 6.8; N, 4.7. Anal. Found: C, 57.2; H, 6.8; N, 4.7. 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}($\upsilon_{Fe\text{-}C}$). ^{1}H NMR ($CDCl_3$)δ_H: 1.194 (3H, $CHCH_3$), 3.115 and 3.021 (6H, NCH_3), 3.762 (1H, $C_5H_5FeC_5H_4CH$), 4.183 and 4.297 (9H, $C_5H_5FeC_5H_4$), 11.872 (1H, N^+–H).

The ether liquor was concentrated to afford a red oil *N,N-dimethyl-1-ferrocenylethylamine* **1,** Yield 65.2%(3.35g).

^{1}H NMR ($CDCl_3$)δ_H: 1.201 (3H, $CHCH_3$), 3.124 and 3.201 (6H, NCH_3), 3.760 (1H, $C_5H_5FeC_5H_4CH$),4.183 and 4.297 (9H, $C_5H_5FeC_5H_4$)

X-ray structure determination

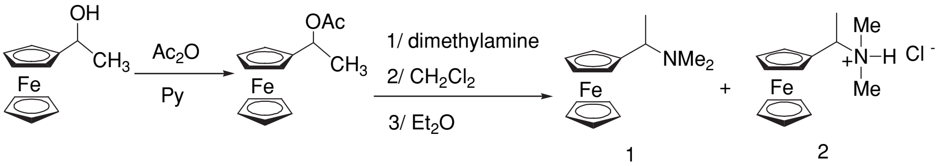
Crystal data: $C_{14}H_{20}FeN$ Cl, M*r* = 293.61, orthorhombic, P2(1)/c, a = 16.460(3) Å, b = 13.639(3) Å, c = 12.104(2) Å, V = 2709.0(9) Å^3, D_x = 1.440 g cm^{-3}, Z = 8, T = 293(2)K. The single crystals were obtained by evaporating the solvent, ethanol. An orange block crystal with approximate dimensions of 0.599 mm × 0.517 mm × 0.229 mm was mounted on a Rigarku Raxis Rapid IP diffractometer equipped with a graphite monochromator for data collection. The determination of unit cell parameters and data collections were performed at 293(2) K, using graphite monochromated MoKα(λ= 0.71073 A) radiation. A total of 6142 independent reflections were measured in the range of $1.24 \leq \theta \leq 27.47°$ with an oscillation method. All data were corrected using the SADABS method. The structure was solved by direct methods using SHELXL-97 program, and refined by full-matrix least-squares on F^2.[7] All non–hydrogen atoms were refined anisotropically, and hydrogen atoms were added according to theoretical modes. The final cycle of refinement gave R = 0.0340, wR = 0.0773 (w $=1/[\sigma^2(F_0{}^2)+(0.0386P)^2]$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 Center and allocated the deposition number CCDC-228143.

Hydrogen-bonding geometries are listed in Table 1. The molecular structure and packing arrangement in the unit cell of the title compound are shown in Figs 1 and 2, respectively.

Table 1 Hydrogen-bonding geometry [Å, deg].

D–H...A	d(D–H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(10B)...Cl(1)	0.910	2.150	3.036	164.0
N(2)-H(20B)...Cl(2)	0.910	2.119	3.014	167.6

Symmetry transformations used to generate equivalent atoms: #1 x,-y+3/2,z+1/2 #2 -x+1,y+1/2,-z+5/2



Scheme 1

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* Correspondent. E-mail: zhangym@bit.edu.cn

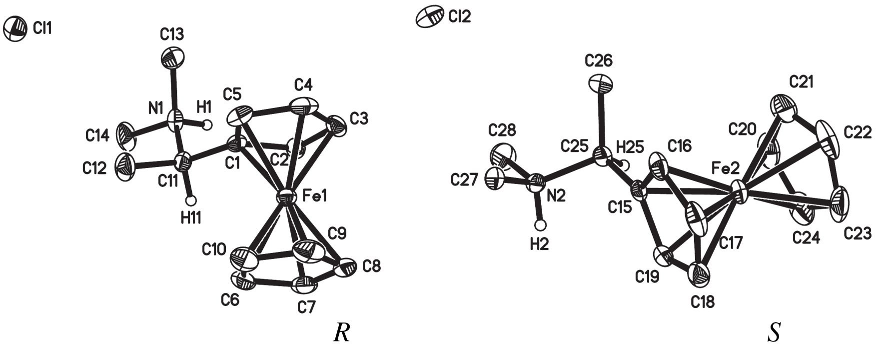


Fig. 1 ORTEP drawing of the R and S molecules coexist in the crystal. H atoms have been omitted for clarity except the H atoms on the chair carbon. Thermal ellipsoids are drawn at 50% probability level.

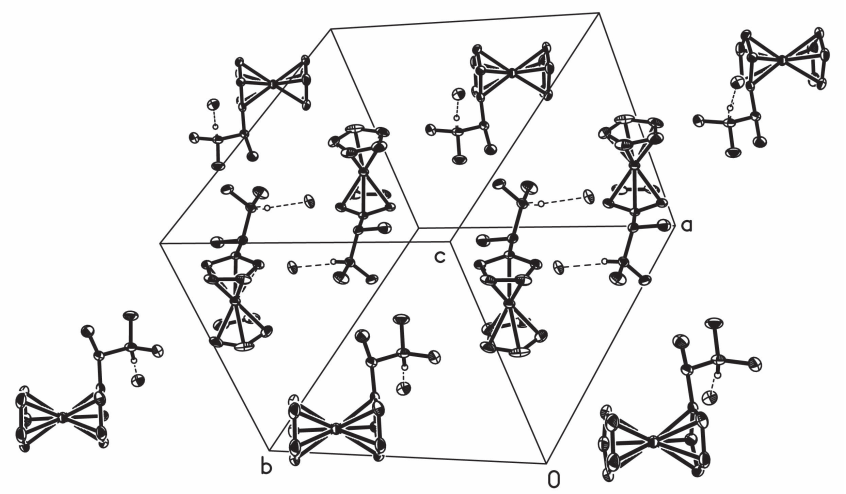


Fig. 2 Three-dimensional molecular-packing diagram of the title complex.

Results and discussion

Amine **1** was obtained by esterification of the corresponding alcohol, followed by substitution with dimethylamine in methanol, accompanied by N,N-dimethyl-1-ferrocenylethylamine **1** and its HCl salt **2**. The single crystal structure of the title compound was comfirmed by X-ray diffraction (shown in Fig. 1). By heating **1** directly in CH_2Cl_2 (to remove CH_2Cl_2), salt **1** was formed when the ether was added, indicating that the HCl in the salt **1** was extracted from CH_2Cl_2 during the process, which may be associated with Fe in the molecule of the substrate.

It can be seen from Fig. 1 that the title molecule of the complex consists of two enantiomer cations $[Fe(C_5H_5)(C_5H_4CHCH_3N^+H(CH_3)_2)]$, and two isolated Cl^- counter anions in the crystal cell. The bond lengths of Fe–C1 and Fe–C15 (involving the substituted C atom) are 2.018(2) Å and 2.024(2) Å, approximately 0.02 Å shorter than the other nine Fe–C bond lengths [2.033–2.048 Å, 2.030–2.064 Å, respectively]. The distances from the Fe atom to the centres of the cyclopentadiene rings in the crystal structure of ferrocene are between 1.646 and 1.661 Å, with a mean value of 1.653 Å.[8-9] In the *(R)*- enantiomer, the cyclopentadienyl C–C bond-length are 1.402(3)–1.427(3)Å, 1.410(4)–1.415(3) Å for the $\eta^5(C_5H_4)$ and $\eta^5(C_5H_5)$ rings, in the *(S)*-enantiomer, the corresponding values are 1.408(4)–1.427(3) Å and 1.378(4)–1.425(4) Å. The Fe atoms are almost at the centre of the two cyclopentadienyl rings, with the Fe(1)–*Cg*(1) and Fe(1)–*Cg*(2) distances are 1.6386 Å and 1.6475 Å, Fe(2)–*Cg*(1) and Fe(2)–*Cg*(2) distances are 1.6480 Å and 1.6538 Å, where *Cg*(1) and *Cg*(2) are the centroids of the $\eta^5(C_5H_4)$ and $\eta^5(C_5H_4)$ rings. Interestingly the two cyclopentadienyl rings are not parallel, the two cyclopentadienyl rings deviate from an eclipsed geometry in **2**, as evidenced by the interplanar angles of 2.5° and 4.0° between the $\eta^5(C_5H_4)$ and $\eta^5(C_5H_4)$ rings.

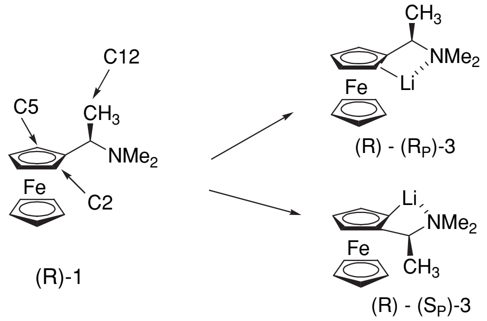
The C1–C11 and C15–C25 bond length are 1.495(3) and 1.498(5) Å, in good agreement with values reported for other ferrocene derivatives,[10] which is shorter than the common distance of the C–C single bond (1.540 Å).[11]

In addition, Fig. 2 illustrates the molecular packing arrangement in the unit cell. From Fig. 2, it can be found that in two classical approximately linear N–H–Cl hydrogen bonds, the N–H–Cl hydrogen bond length is very short and has an Cl–H distance of only 2.119 Å and 2.150 Å (shown in Table 1), shorter than other reported 2.25 Å [12] and 2.28 Å [13] distances.

The crystal structure obtained provided valuable information, which is helpful to understand the mechanism of the stereoselectivity of the chiral ferrocenylamine towards electrophilic reagents.[14] The reason why *(R)–(R$_P$)*-3 is the predominant product could be explained according to the steric hindrance of the α-ferrocenyl methyl group to the *ortho-* C atom of the substituted Cp ring. Taking *(R)*-1 as example, as shown in Table 2 by calculation**,** the distance between C2 and C12 (methyl group) (3.883 Å) is larger than that of C5 and C12 (3.021 Å), indicating that the steric hindrance for C2 is less than that of C5. In addition, assuming the amino nitrogen directs lithiation by prior coordination, metalation preferentially occurs *via* the conformation of *(R)–(R$_P$)*-3 where the N atom is closer to the C2 position than to the C5 position (the distance between N1 and C2 is 3.179 Å and that of N1 and C5 is 3.549 Å) (shown in Table 2). It seems that these two factors may lead to the high diastereoselectivity for the formation of *(R)–(R$_P$)*-3 by lithiation of Ugi's amine.

Table 2 Distance (Å) of two atoms

R				S			
Atom	Distance	Atom	Distance	Atom	Distance	Atom	Distance
N1 and C2	3.179	C2 and C12	3.883	N2 and C16	3.538	C16 and C26	3.028
N1 and C5	3.549	C5 and C12	3.021	N2 and C19	3.221	C19 and C26	3.867



Scheme 2

Worthy of mention is that the point of view above is different from the explanation for such a mechanism by Ugi. In that case he proposed that the selectivity comes from the strong repulsive interaction of the C-methyl and the unsubstituted Cp ring of the ferrocene system, actually no evidence for this proposal has been found by now.[5]

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