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Crystal and molecular structure of protonated (*N*-propyl)-aminomethyl ferrocene, a proton-sensitive redox-responsive fragment

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Abstract

In order to rule out any possible 'chelate' iron–proton interaction which could be responsible for the dramatic changes observed in the Fc^+/Fc redox potential on proton addition in a series of N-substituted aminomethyl ferrocenes (**4a–d**), we report the results of electrochemical titration experiments with strong acids on the free amines in protic and aprotic solvents and the X-ray diffraction structure of (ferrocenylmethyl)propylammonium *p*-toluenesulfonate, [**4aH**][OTs]. Crystals of [**4aH**][OTs] are orthorhombic, space group $P2_12_12_1$, with $a = 11.919(2)$, $b = 21.313(3)$, $c = 8.246(2)$ Å, $Z = 4$. The conformation of the $FcCH_2NH_2C_3H_7{}^+$ cation, which prevents any intramolecular iron–proton interaction, seems imposed by the intermolecular N–H···O hydrogen bonds that the amino H atoms form with oxygen atoms from *p*-toluenesulfonate anions. © 1998 Elsevier Science S.A.

Keywords: Crystal structures; N-substituted aminomethyl complexes; Ferrocene complexes

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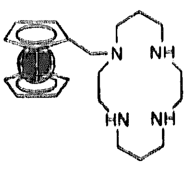
1. Introduction

Ferrocene (Fc), a molecule which undergoes a reversible one-electron oxidation to the stable ferrocenium ion (Fc^+), has frequently been incorporated into multicomponent receptors, with the aim of adding to the system a fragment capable of a redox response upon the complexation of a charged substrate. Among many examples, ferrocene-bearing polyaza [1], polyoxo [2] and polythia [3] macrocyclic and macrobicyclic ligands must be mentioned, in which complexation of metal cations by the macrocyclic component results in an anodic shift of the Fc^+/Fc redox potential. In most cases, the binding component is chosen so that it contains at least one amino group and functionalization leads to systems featuring (N-substituted) aminomethyl ferrocene fragments, as in the representative examples **1**, **2** and **3** (Refs. [1], [2a] and [3], respectively).



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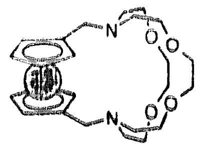

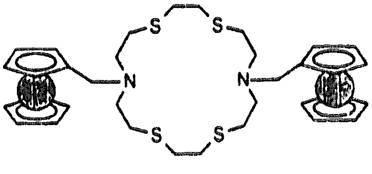

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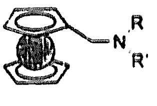

4a R = n-C_3H_7, R' = H
4b R = n-$C_{16}H_{33}$, R' = H
4c R = R' = CH_3
4d R = R' = cyclohexyl

In this kind of system, besides metal cations, another charged species should be able to change dramatically the Fc^+/Fc redox potential, i.e. the proton. Even in non-aqueous solvents, the presence of trace quantities of adventitious water may result in significant protonation of the amino group which bears the $FcCH_2$– function, especially in the case in which the functionalized receptor is used as a sensor and very low concentrations are thus employed. Under this light, we undertook the synthesis and studied the electrochemical behavior in CH_3CN, CH_2Cl_2 and water of a series of N-substituted aminomethyl ferrocenes (**4a–d**), both in their free

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and protonated forms. Moreover, the crystal and molecular structure of [**4aH**][OTs] (OTs = *p*-toluenesulfonate) has been determined, in order to rule out any possible 'chelate' iron–proton interaction which has been suggested to take place in related ferrocene systems [4].

2. Experimental

2.1. Syntheses and materials

4c was obtained from Fluka and used without further purification. **4a**, **4b** and **4d** were prepared by refluxing [$FeCH_2N(CH_3)_3$]I [5] with the stoichiometric quantity of n-propyl amine, n-cetyl amine and dicyclohexyl amine, respectively, in water (**4a**) or water/ethanol mixtures (**4b** and **4d**). Reaction mixtures were evaporated to dryness, treated with 1 M NaOH and extracted with diethyl ether, which, after drying, gave the pure products as oils. By treatment of free $FcCH_2NRR'$ with gaseous HCl in diethyl ether solution the pure, solid ammonium salts of **4a**, **4b** and **4d** were obtained, which gave correct elemental analysis. Pure free bases for DPV experiments were prepared by suspending the ammonium salts in 2 M aqueous NaOH, extracting with ether and evaporating the solid under vacuum after efficient drying.

2.2. Data collection, structure determination and refinement of [4aH][TsO]

The crystallographic data and the most significant experimental details are reported in Table 1. Unit cell parameters were determined from the θ values of 33 $(\theta,\chi,\varphi)_{hkl}$ reflections found in a random search in the $13 < \theta < 18°$ range of the reciprocal lattice. All the measurements were carried out at 295 K using the graphite monochromatized Mo Kα radiation in the $\theta/2\theta$ scanning mode. The intensity of one standard reflection, monitored every 100 reflections, showed no significant fluctuation. The intensities were calculated from profile analysis following Lehmann and Larsen [6] and corrected for Lorentz and polarization effects. No correction for absorption effect was applied. Only the 2282 observed reflections were used in the structure solution and refinements.

The structure was solved by Patterson methods using SHELX86 [7] and then completed by a Fourier ΔF map and refined by the full-matrix least-squares method using SHELX76 [8]. The refinement was carried out first with isotropic and then with anisotropic thermal parameters for the non-hydrogen atoms, except for the carbon atoms of the unsubstituted cyclopentadienyl ring, disordered over two different orientations with site occupancy factors 0.5. Isotropic

Table 1
Experimental data for the X-ray diffraction studies of [**4aH**][OTs]

Formula	$C_{21}H_{27}FeNO_3S$
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Cell parameters at 295 K [a]	
a (Å)	11.919(2)
b (Å)	21.313(3)
c (Å)	8.246(2)
V (Å^3)	2094.7(7)
Z	4
D_{calc} (g cm^{-3})	1.361
$F(000)$	904
Molecular weight	429.356
Linear absorption coefficient (cm^{-1})	8.33
Diffractometer	Siemens AED
Scan type	$\theta/2\theta$
Scan speed (° min^{-1})	3–12
Scan width (°)	$[\theta-0.65]$, $[\theta+0.65+\Delta\lambda\lambda^{-1}\,\mathrm{tg}\,\theta]$
Radiation (Å)	Mo Kα (0.7107)
2θ Range (°)	6–46
Reflections measured	$\pm h$, $+k$, $+l$
Total data measured	3267
Criterion for observed	$I \geq 2\sigma(I)$
Observed data measured	2282
Unique observed data	2085
Agreement between equivalent observed reflections	0.009
No. variables	267
Max. Δ/σ on last cycle	0.07
$R = \Sigma\|\Delta F\|/\Sigma\|F_o\|$	0.043
$R_w = \Sigma w^{1/2}\|\Delta F\|/\Sigma w^{1/2}\|F_o\|$	0.032
$GOF = [\Sigma w^{1/2}\|\Delta F\|^2/(NO-NV)]^{1/2}$	1.063

[a] Unit cell parameters were obtained by least-squares analysis of the setting angles of 33 centered reflections found in a random search on the reciprocal space.

temperature factors for all the atoms involved in the static disorder were assumed.

Since the space group $P2_12_12_1$ leads to a chiral configuration in the structure, one independent final cycle of refinement was carried out using the $-x$, $-y$, $-z$ coordinates. No improvement in the R value was obtained ($R(x,y,z)=0.0428$; $R(-x,-y,-z)=0.0497$). The former model was selected and the reported data refer to this model. All the hydrogen atoms were localized in the ΔF map and refined isotropically, excepting those in the disordered cyclopentadienyl units, which were calculated. The highest remaining peak in the final Fourier ΔF map was equivalent to 0.60 e Å^{-3}. In the final cycles of refinement a weighting scheme $w=k[\sigma(F_o)]^{-2}$ was used; at convergence the k value was 0.7527. The atomic scattering factors, corrected for real and imaginary parts of the non-hydrogen atoms were taken from Cromer and Waber [9]; the values of $\Delta f'$ and $\Delta f''$ were those of Cromer and Ibers [10]. The geometrical calculations were performed by PARST [11]. All the calculations were carried out on a Gould Encore 91 computer of the 'Centro di Studio per la Strutturistica Diffrattometrica del C.N.R.' (Parma, Italy). The final atomic coordinates for the non-hydrogen atoms are reported in Table 2.

3. Results

DPV experiments on unprotonated species **4a–d** displayed a reversible, one-electron oxidation wave (to ferrocenium species) in both CH_3CN and CH_2Cl_2 as solvents [1], at potential values similar to those found for plain ferrocene ($E_{1/2}$u in Table 3). Addition of substoichiometric quantities of p-toluenesulfonic acid (TsOH) makes a second wave appear at more positive potentials, which corresponds to the oxidation of the protonated $[FeCH_2NHRR']^+$ species. Remarkably, the current intensity of the new peak increases while that of the less anodic peak decreases with a linear dependance on the equivalents of added acid. In particular, the oxidation peak of $[FeCH_2NHRR']^+$ reaches the maximum current intensity value at 1.0 equivalents of added acid, at which point the signal relative to the free amine disappears (addition of more acid does not change further the electrochemical response).

The potential values at which oxidation of $[FeCH_2NHRR']^+$ takes place are listed in Table 3 ($E_{1/2}$p) and are noticeably higher than the corresponding $E_{1/2}$u values, with ΔE ($E_{1/2}$p $-$ $E_{1/2}$u) values ranging from 140 to 200 mV. This indicates a strong electrostatic interaction between the protonated amino group and the proximate Fe center, making the oxidation of the latter much more difficult than in the free amine (for comparison, Fe oxidation potential increases of 124 and 188 mV in the case of **2**, after complexation with Na^+ and K^+ in CH_3CN solution [2]; complexation of ligand **1** with Ni^{2+} and of ligand **3** with Cu^{2+} leads to potential shifts of +20 and +40 mV, respectively, in CH_3CN solution [1,3]).

Table 2
Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic thermal parameters (Å$^2\times 10^4$) with e.s.d.s in parentheses for the non-hydrogen atoms of [**4aH**][OTs]

Atom	x/a	y/b	z/c	U_{eq} [a]
Fe	5526(1)	6634(0)	5430(1)	588(3)
S(1)	2779(2)	4021(1)	5513(3)	630(8)
O(1)	2619(4)	4484(2)	4211(6)	684(20)
O(2)	2588(4)	4304(2)	7082(6)	801(24)
O(3)	2175(3)	3452(2)	5222(8)	1153(27)
N(1)	2241(3)	5676(2)	5793(7)	458(21)
C(1A)	5974(6)	5737(4)	4843(14)	758(39)
C(2A)	4881(7)	5871(3)	4342(12)	663(33)
C(3A)	4222(4)	6043(3)	5664(10)	475(26)
C(4A)	4916(7)	6015(3)	7059(10)	578(34)
C(5A)	5984(7)	5825(4)	6523(12)	768(40)
C(1B)	6532(14)	7301(7)	4496(30)	483(47)
C(2B)	5640(9)	7287(4)	3636(10)	880(27)
C(3B)	4738(11)	7487(6)	4529(21)	459(43)
C(4B)	5200(14)	7552(8)	6213(25)	472(49)
C(5B)	6301(14)	7429(8)	6117(25)	664(56)
C(1B') [b]	5009(15)	7513(9)	5278(27)	608(57)
C(2B')	5715(19)	7438(8)	6771(21)	778(65)
C(3B')	6817(12)	7258(7)	6026(18)	521(45)
C(4B')	6857(12)	7123(7)	4237(24)	656(58)
C(6)	4598(7)	3263(4)	4812(9)	845(34)
C(7)	5729(7)	3130(4)	4778(10)	858(38)
C(8)	6525(7)	3541(4)	5352(12)	792(37)
C(9)	6114(7)	4100(4)	5983(12)	909(45)
C(10)	4999(6)	4254(3)	6060(10)	727(36)
C(11)	4225(5)	3841(3)	5468(9)	521(24)
C(12)	7771(6)	3379(5)	5320(11)	1173(41)
C(13)	3009(4)	6219(3)	5654(10)	510(27)
C(14)	1040(5)	5863(4)	5671(12)	562(32)
C(15)	275(5)	5324(4)	5878(13)	839(40)
C(16)	−926(5)	5499(5)	5819(17)	1130(50)

[a] Equivalent isotropic U defined as one-third of the trace of the orthogonalized U_{ij} tensor.

[b] B' labels the carbon atoms of the alternative orientation in the disordered cyclopentadienyl ring.

Table 3
DPV measurements

	CH_3CN [a]		CH_2Cl_2 [a]	
	$E_{1/2}$p	$E_{1/2}$u	$E_{1/2}$p	$E_{1/2}$u
4a	186	0	140	0
4b	166	−19	130	−12
4c	210	17	161	0
4d	189	−15	140	−34

[a] DPV measurements carried out in CH_3CN, made 0.1 M with tetrabutyl ammonium perchlorate. Potentials are referred to internal ferrocene standard.

When the water soluble **4a** and **4c** species are taken into consideration, a similar behavior can be found in aqueous

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[1] Solutions were made 0.1 M in tetrabutylammonium perchlorate in both solvents. Concentration of the examined samples were in the 5×10^{-4}–1×10^{-3} M range. Potential values were determined with an internal $[Fe^{II}(phenanthroline)_3]^{2+}$ standard and referred to the Fc^+/Fc couple of plain ferrocene.

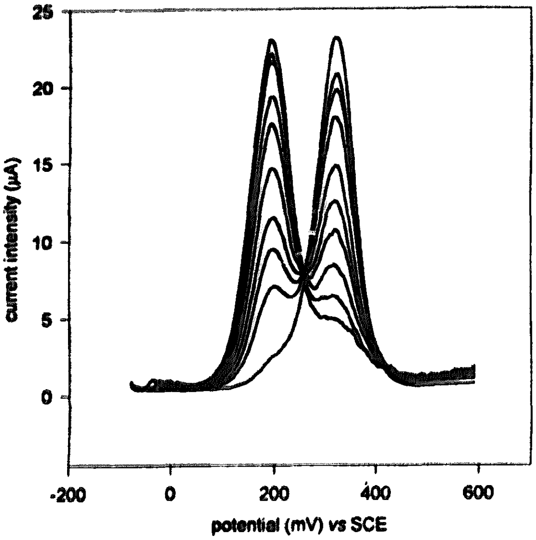

Fig. 1. DPV profiles for unbuffered aqueous solutions containing **4a**, at different pH values. pH ranges from 9.04 (more anodic, single peak curve, corresponding to $[FcCH_2NH_2C_3H_7]^+$) to 13.0 (less anodic, single peak curve, corresponding to the free amine). It is to be noted that in the fifth curve, measured at pH = 10.30, the current intensity is identical for the two peaks.

solutions [2]: titration of the free amine with standard perchloric acid makes a new, more positive wave appear and increase in intensity with decreasing pH, as shown in Fig. 1 ($E_{1/2}$u = 191 and $E_{1/2}$p = 321 mV versus SCE in the case of **4a**; $E_{1/2}$u = 178 and $E_{1/2}$p = 338 mV versus SCE in the case of **4c**). Significantly, 50% of current intensity is found for both signals at a pH = pK_a (pK_a values of 10.25 and 9.58 have been determined for **1a** and **1c** by means of independent potentiometric titration experiments). Finally, it must be mentioned that when DPV experiments are carried out on *buffered* aqueous solutions, what is observed is a *single peak* shifting between the limiting $E_{1/2}$u and $E_{1/2}$p values on changing the pH at which the solution is buffered, in agreement with what has already been described for $Fc(CH_2)_nCOOH$ species [12].

Finally, although a 'chelate' direct interaction of the protonated amino group with the iron center (i.e. $Fe\cdots H{-}N^{\oplus}(RR'){-}CH_2{-}$) could be put forward on the basis of what is reported for a related ferrocene derivative [4] (an effect which could be responsible for the unusually high ΔE values found in this work), this hypothesis can be ruled out in the case of protonated **4a–d**. Quaternarization of **1c** with CH_3I leads in fact to $[FcCH_2N(CH_3)_3]^+$, which is oxidized to ferrocenium species at 241 and 178 mV versus plain ferrocene in CH_3CN and CH_2Cl_2, respectively, displaying ΔE values with respect to free **1c** even higher than in the case of protonation.

Moreover, the X-ray diffraction structure of protonated **4a** definitely rules out metal–proton interactions. The configuration of the (ferrocenylmethyl)propylammonium cation obtained from the crystallographic study of [**4aH**][OTs] is displayed in Fig. 2. The most relevant geometrical parameters are reported in Tables 4 and 5.

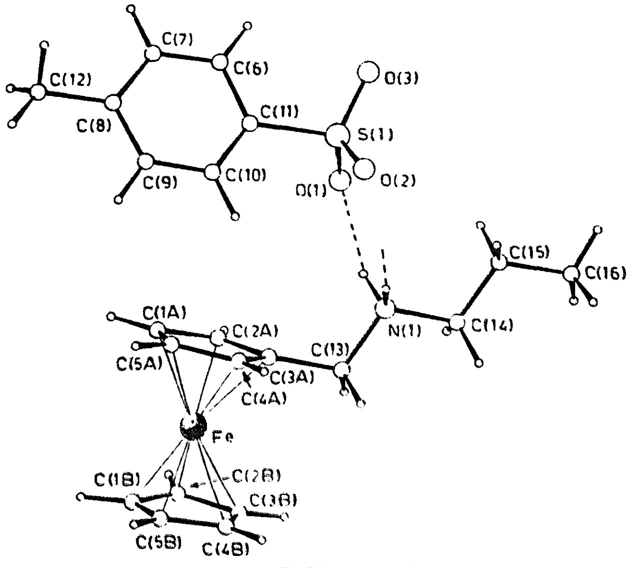

Fig. 2. A perspective view of the $FcCH_2NH_2C_3H_7^+$ cation and of the OTs^- anion in [**4aH**][OTs] with the atom numbering scheme.

The $FcCH_2NH_2C_3H_7^+$ cation shows a pseudo C_s symmetry (the mean least-squares plane through the non-hydrogen atoms of the side chain roughly bisects the C(1A)–C(5A) bond) with the two amino H atoms pointing away from the Fc moiety. The appended chain orientation, which prevents any 'chelate' iron–proton interaction, seems imposed by the two N–H···O hydrogen bonds that the amino H atoms of the cation form with the O(1) oxygen atoms from two symmetrically related *p*-toluenesulfonate anions.

In the Fc moiety the unsubstituted Cp unit is disordered between two different orientations: [C(1B)C(2B)C3B)-C(4B)C(5B)], shown in Fig. 2, and [C(1B')C(2B)-C(2B')C(3B')C(4B')], with the C(2B) atom in common. The Cp(A) and the Cp(B') rings are approximately parallel and eclipsed, whereas the Cp(A) and the Cp(B) rings, which form a dihedral angle of 6.1(5)°, are out of the eclipsed orientation by a mean angle of 16.9(9)°. The low barrier for rotation in metallocene derivatives has been already pointed out [13].

The Fe–C(Cp) distances in the substituted Cp ring (from 2.010(6) to 2.043(9) Å) are quite comparable with the values observed in other Fc derivatives, while a larger range is observed in the Fe–C(Cp) distances of the two disordered Cp rings (1.98(2)–2.18(1) Å).

The distances between the metal center and the centroids of the substituted and unsubstituted Cp rings show no significant differences (1.631(8) versus 1.648(9) (av.) Å) so the introduction of the (methyl)propylammonium substituent at one Cp ring seems to exert a negligible effect upon the bonding to the metal.

The comparison of the structure of the present cation with that of the related (*N*-dimethyl-ethyl)-aminomethyl ferrocene [14] shows a shortening of the C–N bond length in the

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[2] Solutions were made 0.1 M in $NaClO_4$. Samples concentrations were 1×10^{-3} M.

Table 4
Relevant bond distances (Å) and angles (°) for [4aH][OTs]

Fe–C(1A)	2.043(9)	C(4A)–C(5A)	1.407(12)
Fe–C(2A)	2.010(8)	C(5A)–C(1A)	1.398(15)
Fe–C(3A)	2.010(6)	C(1B)–C(2B)	1.28(2)
Fe–C(4A)	2.018(8)	C(2B)–C(3B)	1.37(2)
Fe–C(5A)	2.021(9)	C(3B)–C(4B)	1.50(3)
Fe–C(1B)	2.02(2)	C(4B)–C(5B)	1.34(2)
Fe–C(2B)	2.04(1)	C(1B)–C(5B)	1.39(3)
Fe–C(3B)	2.18(1)	C(2B)–C(1B')	1.62(3)
Fe–C(4B)	2.10(2)	C(1B')–C(2B')	1.50(3)
Fe–C(5B)	2.01(2)	C(2B')–C(3B')	1.50(3)
Fe–C(1B')	1.98(2)	C(3B')–C(4B')	1.50(2)
Fe–C(2B')	2.05(2)	C(4B')–C(2B)	1.57(2)
Fe–C(3B')	2.09(1)	C(3A)–C(13)	1.494(7)
Fe–C(4B')	2.14(2)	N(1)–C(13)	1.480(7)
C(1A)–C(2A)	1.396(11)	N(1)–C(14)	1.489(7)
C(2A)–C(3A)	1.393(12)	C(14)–C(15)	1.477(11)
C(3A)–C(4A)	1.418(11)	C(15)–C(16)	1.480(9)
C(2A)–C(1A)–C(5A)	105.9(8)	C(1B')–C(2B')-C(3B')	101(2)
C(1A)–C(2A)–C(3A)	110.4(7)	C(2B')–C(3B')–C(4B')	119(1)
C(2A)–C(3A)–C(4A)	107.2(7)	C(3B')–C(4B')–C(2B)	104(1)
C(3A)–C(4A)–C(5A)	106.6(7)	C(4B'–C(2B)–C(1B')	103(1)
C(4A)–C(5A)–C(1A)	110.0(8)	C(2A)–C(3A)–C(13)	127.4(5)
C(2B)–C(1B)–C(5B)	112(2)	C(4A)–C(3A)–C(13)	125.4(5)
C(1B)–C(2B)–C(3B)	110(1)	C(13)–N(1)–C(14)	112.3(4)
C(2B)–C(3B)–C(4B)	104(1)	C(3A)–C(13)–N(1)	113.7(4)
C(3B)–C(4B)–C(5B)	107(1)	N(1)–C(14)–C(15)	112.2(5)
C(1B)–C(5B)–C(4B)	107(2)	C(14)–C(15)–C(16)	113.4(5)
C(2B)–C(1B')–C(2B')	113(2)		

Table 5
Relevant intermolecular hydrogen bonds [a]

N(1)···O(1)	2.891(6)	H(1N)···O(1)	1.96(1)	N(1)–H(1N)–O(71)	147(1)
N(1)···O(1')	2.844(8)	H(2N)···O(1')	1.90(1)	N(1)–H(2N)–O(1')	149(1)

[a] Symmetry code: ' 1/2 − x, 1 − y, 1/2 + z.

$FeCH_2N$ moiety (1.480(7) versus 1.527(3) Å). It seems reasonable to attribute this to the smaller steric demand of the two H atoms of the protonated amino group with respect to the corresponding methyl groups in the (*N*-trialkyl)-aminomethyl ferrocene cation [14].

The bond distance and angles in the OTs anion are as expected. However it is worth noting the high thermal motion which affects the OTs anion oxygen atoms that are not involved in hydrogen bonds.

4. Supplementary material

A list of the thermal parameters for the non non-hydrogen atoms (Table SI), a list of the atomic coordinates of the hydrogen atoms (Table SII), and a full list of the bond distances and angles (Table SIII) are available from the authors on request.

Acknowledgements

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