Pentadentate dinucleating ligands affording bis(μ-carboxylato-*O*,*O′*)diiron(II) complexes

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New pentadentate pyridine- or imidazole-containing ligands showing dinucleating behaviour are reported: ligand L^1 stabilizes a diiron(II) complex in which the bridging carboxylates are linked to the capping moieties of the ligands.

The active sites of the non-haem iron proteins including haemerythrin (Hr),[1] methane monooxygenase (MMO)[2] and the R2 subunit of the ribonucleotide reductase (RRB2)[3] possess carboxylate-bridged diiron centres. The role of these enzymes is to bind dioxygen reversibly,[4] to hydroxylate alkanes catalytically[5] and to catalyse the reduction of ribonucleotides to their corresponding deoxyribonucleotides.[6] It is in their diferrous form that the proteins bind or activate dioxygen at a vacant or labile coordination site. A large number of diiron(III) model compounds involving a variety of multidentate ligands has been described, affording considerable insight into the structural and physical properties of the diferric active sites.[7] More challenging has been the synthesis of diferrous complexes.[8] Polydentate ligands in which the potential bridging groups are linked to the capping moities could afford a dinucleating behaviour and thus stabilize corresponding diiron(II) complexes. Moreover, such a type of ligand is biologically relevant because the carboxylate bridges in these enzymes are part of the protein. Hazell *et al.*[9] have tried this type of approach by using 3-[bis(2-pyridylmethyl)amino]propionate (bpp). Unfortunately, the too flexible carboxylate arm of bpp acts as a monodentate donor in the corresponding diiron(III) compounds.

Here we report the synthesis of three dinucleating pentadentate ligands L^1, L^2 and L^3 (Fig. 1 shows their sodium salts) and the molecular structure and properties of a dinuclear iron(II) complex of L^1. The synthetic strategy leading to the new ligands is shown in Scheme 1. The starting materials 1-methyl-2-imidazolecarbaldehyde (**A**, R^1 = MeIm),[10] 2-aminomethylimidazole (**B**, R^2 = Im)[11] and ethyl 2-bromomethyl benzoate (**D**)[12] were prepared according to literature methods. The reductive amination[13] of the aldehydes (**A**) with the primary amines (**B**) leads to the key intermediates bis(2-pyridylmethyl)amine, (2-pyridylmethyl)[2-(1-methylimidazolyl)methyl]amine and (2-imidazolylmethyl)[2-(1-methylimidazolyl)methyl]amine (**C**) respectively. The polydentate ligands were then obtained as their L^1Na, L^2Na and L^3Na salts through reaction of ethyl 2-bromomethyl benzoate (**D**) with the secondary amines (**C**), followed by the deprotection of the carboxylate group.† Reaction of L^1Na with iron(II) perchlorate hexahydrate under anaerobic conditions in methanol–water leads to a yellow powder of dinuclear complex **1** $\{[Fe_2L^1{}_2(H_2O)_2](ClO_4)_2\}$.‡

Recrystallization of **1** from methanol affords good quality single crystals of complex **1′** with two coordinated methanol molecules instead of water. Structural analysis of **1′**§ shows that the complex is a dinuclear molecule in which two $FeL^1(MeOH)$ units are bridged through the carboxylate groups of the L^1 ligands. An inversion centre is located at the barycentre of the Fe–O(2)–C(14)–O(1′)–Fe′–O(2′)–C(14′)–O(1) polygon. The coordination around the iron centre is a distorted octahedron. Examination of bond lengths and angles (Fig. 2) shows that no pure and simple octahedron distortion can describe the iron environment. In the asymmetric unit of the complex molecule, the iron centre is coordinated to the pentadentate ligand by the N(1) and N(3) pyridine and the N(2) tertiary amine nitrogen, the latter being *trans* to the O(2) carboxylate oxygen. *trans* To the O(1) carboxylate oxygen donor, the O(3) oxygen belonging to a coordinated methanol molecule completes the coordination sphere, affording a labile site on the metal centre. Each carboxylate bridges the two iron centres in the unusual *syn–anti* mode.[14] To our knowledge, $[Fe_2(O_2CMe)_2(tpa)_2](BPh_4)_2$ [tpa = tris(2-pyridylmethyl)amine][8a] is the only other diiron(II) compound having this type of bridging mode and thereby similar structural features. The Fe–O(2) distance [1.99(1) Å], corresponding to the *syn*-bonded oxygen donor is shorter than Fe–O(1) [2.09(1) Å], reflecting the higher basicity of the *syn* lone pair of the carboxylate oxygen. In the present case, this unusual bridging mode[14] can be explained by the fact that the carboxylate group is linked to the capping moiety of the ligand *via* an aromatic ring and thereby is submitted to steric constraints. A consequence of the *syn–anti* bidentate mode is the especially long Fe···Fe′ distance [4.612(3) Å] compared to those found in the more common *syn–syn* carboxylate bridged

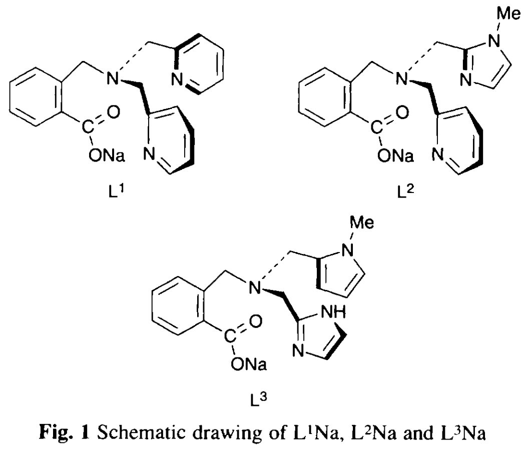
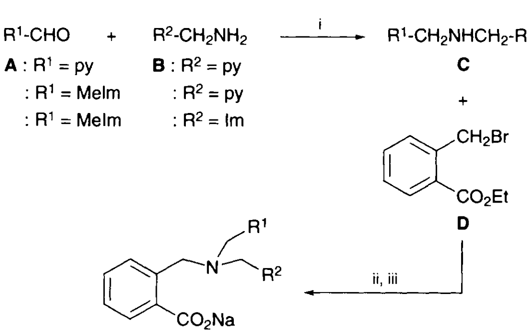


Fig. 1 Schematic drawing of L^1Na, L^2Na and L^3Na



Scheme 1 Synthetic route to the three pentadentate dinucleating ligands. *Reagents and conditions*: i, AcOH–NaBH$_3$CN–MeOH, 48 h, 85–77%; ii, Et$_3$N–THF, 48 h, 48–31%; iii, NaOH–MeOH, 2 h.

complexes (3.05–3.68 Å).[8] The perchlorate anions are inserted between adjacent dimeric molecules in the crystal lattice.

The Mössbauer spectra of **1** recorded at 293, 220, 150 and 80 K consist of a single quadrupole split doublet. They were least-squares fitted with Lorentzian lines. The isomer shift (δ = 1.16 mm s^{-1} relative to metallic iron at 293 K) and quadrupole splitting (ΔE_Q = 3.00 mm s^{-1}) values at 80 K are typical for high-spin iron(II) in a ligand environment with O and N donors. The large ΔE_Q value decreasing slightly from 3.00 (80 K) to 2.83 mm s^{-1} (293 K) indicates that the $^5T_{2g}$ state from O_h symmetry is split by crystal field distortions affording a well isolated ground orbital singlet and indicates a significant axial anisotropy of the ligand field. Comparison with the Mössbauer parameters of the dinuclear iron sites of MMO$_{red}$ (δ = 1.30, ΔE_Q = 3.14 mm s^{-1})[15] and RRB2 (δ = 1.26, ΔE_Q = 3.13 mm s^{-1}),[16] shows that ΔE_Q of **1** is in a good agreement whereas its δ value is significantly smaller, probably due to the N_3O_3 coordination sphere of **1** which is more nitrogen-rich than those of the metalloproteins iron(II) dinuclear centres.

Variable-temperature magnetic susceptibility data were obtained on a polycrystalline powder sample. The temperature dependence of the effective magnetic moment per Fe atom (μ_{eff}/Fe) of **1** decreases from 5.15 μ_B at 300 K to 1.27 μ_B at 2 K, indicating a weak antiferromagnetic coupling of the S = 2 spin system of the two iron(II) species in the dinuclear unit. The experimental data have been fitted[17] to the theoretical magnetic susceptibility calculated by exact diagonalization of the effective spin Hamiltonian taking into account single-ion zero-field splitting (ZFS).[18] The least-squares refinement of the experimental data to the theoretical magnetic susceptibility calculated from this model afforded a very good fit for the parameters $J = -1.7$ cm^{-1}, $D = +3.2$ cm^{-1}, $g_\perp = 2.168$, $g_\parallel = 1.980$ and Par = 3.2%, where Par is the mole percent of a paramagnetic impurity assumed to be a small amount of Fe^{III} species also detected by Mössbauer spectroscopy. The absolute value obtained for D clearly indicates that the magnetic behaviour of **1** is relevant to the case where the single-ion ZFS is of the order of magnitude of the exchange integral and cannot be treated as a perturbation. As for $[Fe_2(O_2CMe)_2(TPA)_2](BPh_4)_2$[8a] ($J \approx 1$ cm^{-1}), a small antiferromagnetic exchange operates through the carboxylate bridges despite the large distance between the two metal centres.

Despite structural differences with RRB2, in particular the bridging mode of the carboxylate groups and the Fe···Fe′ distance, **1** is the first example in which the two carboxylate bridges are part of the L^1 pentadentate ligands, similarly to the case of the aspartate or glutamate residues in dinuclear iron enzymes. Another interesting feature of **1** is the presence of labile coordination sites occupied by solvent molecules and thus available for dioxygen or substrate binding without breaking down the dinuclear core of the molecule.

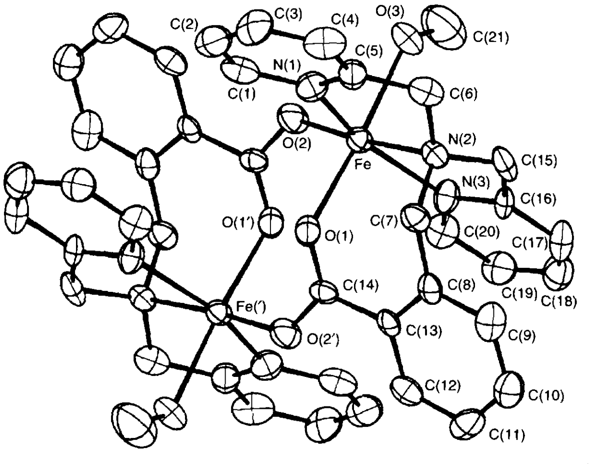


Fig. 2 Molecular structure of the diiron(II) complex **1′** $\{[Fe_2L^1{}_2(MeOH)_2](ClO_4)_2\}$. Hydrogen atoms and perchlorate anions are omitted for clarity. Selected interatomic distances (Å) and angles (°): Fe–N(1) 2.14(1), Fe–N(2) 2.25(1), Fe–N(3) 2.16(1), Fe–O(1) 2.09(1), Fe–O(2) 1.99(1), Fe–O(3) 2.21(1), Fe···Fe′ 4.612(3), N(2)–Fe–O(1) 89.1(3), N(2)–Fe–O(2) 175.4(4), N(2)–Fe–O(3) 89.9(3), N(2)–Fe–N(1) 75.2(3), N(2)–Fe–N(3) 76.5(3), O(1)–Fe–O(2) 94.5(3), O(1)–Fe–O(3) 173.4(3), O(1)–Fe–N(1) 88.0(4), O(1)–Fe–N(3) 94.4(3), O(2)–Fe–O(3) 86.1(3), O(2)–Fe–N(1) 102.0(4), O(2)–Fe–N(3) 106.1(3), O(3)–Fe–N(1) 85.4(3), O(3)–Fe–N(3) 91.7(3), N(1)–Fe–N(3) 151.6(4).

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Footnotes

† *Selected data* for L^{1}Na: ^{1}H NMR (200 MHz, D_2O, 25 °C δ: 8.08 (d, 2 H, py-*H*), 7.44 (t, 2 H, py-*H*), 7.33–7.09 (m, 6 H, Ar-*H*, py-*H*), 6.98 (dd, 2 H, py-*H*), 3.65 (s, 2 H, Ar-C*H*$_2$), 3.43 (s, 2 H, py-C*H*$_2$). FAB-MS, *m*/*z* (rel. intensity) 332 (*M* − Na, 100), 687 (2*M* − Na, 12).

‡ *Selected data* for **1**: yield: 73%. Satisfactory C, H, N, Fe and Cl elemental analyses were obtained ES-MS, *m*/*z* 388.3 ($[Fe^{II}{}_2L^1{}_2]^{2+}$, 100), 875.7 $\{[Fe^{II}{}_2L^1{}_2](ClO_4)^+$, < 1}. IR (CsBr pellets) ν_{CO_2}/cm^{-1}: 1565, 1395. UV (DMF) λ/nm: 270, 332, 414.

§ *Crystal data* for **1′**: $C_{42}H_{44}Cl_2Fe_2N_6O_{14}$, triclinic, space group $P\bar{1}$, a = 8.830(6), b = 11.72(1), c = 12.725(9) Å, α = 116.49(6), β = 99.96(5), γ = 91.16(6) °, U = 1152(2) Å^3, M_w = 519.7, Z = 2, D_c = 1.49 g cm^{-3}, μ(Mo-Kα) = 8.1 cm^{-1}, T = 293 K. Of 1838 data collected (Enraf-Nonius CAD-4), Mo-Kα radiation (0.7107 Å), $3 < 2\theta < 44$ °, 1458 were used $[I > 3\sigma(I)]$. The structure was solved by direct methods and refined by full-matrix least-squares (SHELXS 86[19] and CRYSTALS[20]). All non-hydrogen atoms belonging to the cationic complex molecule were refined anisotropically. The perchlorate anion, very disordered, was treated as a rigid group with restraints and refined isotropically. Hydrogen atoms were treated as idealized contributions. R = 0.081 and R_w = 0.087, with S = 1.1 and 259 variables. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

References

1 M. A. Holmes, I. Le Tong, S. Turley, L. C. Sieker and R. E. Stenkamp, *J. Mol. Biol.*, 1991, **218**, 583.
2 A. C. Rosenzweig, C. A. Frederick, S. J. Lippard and P. Nordlund, *Nature*, 1993, **232**, 123.
3 P. Nordlund, B.-M. Sjöberg and H. Eklund, *Nature*, 1990, **345**, 593.
4 P. C. Wilkins and R. G. Wilkins, *Coord. Chem. Rev.*, 1987, **79**, 195.
5 J. Green and H. Dalton, *J. Biol. Chem.*, 1989, **264**, 17698.
6 B.-M. Sjöberg and A. Graslund, *Adv. Inorg. Biochem.*, 1983, **5**, 87; J. Stubbe, *J. Biol. Chem.*, 1990, **265**, 5329.
7 See for example: J. B. Vincent, G. L. Olivier-Lilley and B. A. Averill, *Chem. Rev.*, 1990, **90**, 1447; L. Que, Jr., in *Bioinorganic Catalysis*, ed. J. Reedjik, Marcel Dekker, NewYork, 1993, p. 347.
8 (*a*) S. Ménage, Y. Zang, M. P. Hendrich and L. Que, Jr., *J. Am. Chem. Soc.*, 1992, **114**, 7786; (*b*) S. Herold, L. E. Pence and S. J. Lippard, *J. Am. Chem. Soc.*, 1995, **117**, 6134 and references cited therein; (*c*) D. Coucouvanis, R. A. Reynolds III and W. B. Dunham, *J. Am. Chem. Soc.*, 1995, **117**, 7570.
9 A. Hazell, K. B. Jensen, C. J. McKenzie and H. Toftlund, *J. Chem. Soc., Dalton Trans.*, 1993, 3249.
10 K. J. Oberhausen, J. F. Richardson, R. M. Buchanan and W. Pierce, *Polyhedron*, 1989, **8**, 659.
11 L. A. M. Bastiaansen and E. F. Godefroi, *J. Org. Chem.*, 1978, **43**, 1603.
12 F. Vögtle and A. H. Effler, *Chem. Ber.*, 1969, **102**, 3071.
13 A. Schepartz and R. Breslow, *J. Am. Chem. Soc.*, 1987, **109**, 1814.
14 R. L. Rardin, W. B. Tolman and S. J. Lippard, *New J. Chem.*, 1991, **15**, 417.
15 J. G. DeWitt, J. G. Bensten, A. C. Rosenzweig, B. Hedman, J. Green, S. Pilkington, G. C. Papaefthimiou, H. Dalton, K. O. Hodgson and S. J. Lippard, *J. Am. Chem. Soc.*, 1991, **113**, 9219.
16 J. B. Lynch, C. Juarez-Garcia, E. Münck and L. Que, Jr., *J. Biol. Chem.*, 1989, **264**, 8091.
17 J. Chandler, Program 66, Quantum Chemistry Program Exchange, Indiana University, 1973.
18 P. Garge, R. Chikate, S. Padhye, J. M. Savariault, P. De Loth and J. P. Tuchagues, *Inorg. Chem.*, 1990, **29**, 3315.
19 G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 1990, **46**, 467.
20 D. J. Watkin, J. R. Carruthers and P. W. Betteridge, CRYSTALS, Advanced Crystallographic Program System, Oxford University, 1988.

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