Metal ion complexation by a new, highly sterically hindered, bowl-shaped carboxylate ligand†

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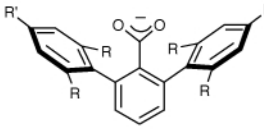
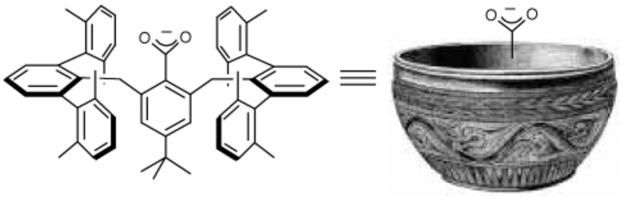
A carboxylate encapsulated by arene groups arranged in a bowl-like shape coordinates to Fe(II), Co(II) and Cu(II) to form mononuclear complexes with atypical structures enforced by the extreme steric demands of the ligand.

Carboxylate groups (from Asp or Glu side chains or C termini) play key roles as supporting ligands in a diverse array of metalloprotein active sites.[1] Such carboxylates are notable for the facility with which they adopt different binding modes,[2] in particular during the catalytic cycles of dioxygen-activating mono- and di-iron enzymes.[3] In efforts to synthesize models of these metalloprotein active sites, we[4] and others[5,6] have begun using sterically bulky carboxylate ligands in order to control coordination geometry, mimic the hydrophobic active site environment, and access coordinatively unsaturated species akin to those implicated during enzymatic catalysis. For example, novel biologically relevant structures and reactivity have been discovered for iron complexes of carboxylates **1**[4] and **2**,[5] which contain arene substituents on the benzoate unit that provide a high degree of hydrophobic 'shielding'. In expectation of even greater encapsulation of metal sites in model complexes, we targeted **3**, a carboxylate derivative of the known irregular 'bowl-shaped' 4-*tert*-butyl-2,6-bis[(2,2″,6,6″-tetramethyl-*m*-terphenyl-2′-yl)methyl]phenyl (Bmt) fragment that was used to isolate various species BmtX (X = Br, SH, SO, SI, SO_2H, AlH_3).[7] Herein we report the successful synthesis and X-ray crystallographic characterization of $BmtCO_2H$ (**3**-H) and Fe(II), Co(II) and Cu(II) complexes of **3**, which adopt atypical structures owing to the extreme steric bulk of the new carboxylate ligand.



1 (R = R' = Me)
2 (R = H, R' = Me)



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The synthesis of $BmtCO_2H$ was achieved by lithiation of BmtBr,‡ addition of CO_2(g), acidification, and then column chromatography. The product was identified using spectroscopic (ESI†) and X-ray diffraction§ data. Treatment of $BmtCO_2H$ with Bu^nLi in thf afforded the lithium carboxylate ($BmtCO_2Li{\cdot}2thf$) that was isolated as an analytically pure solid for use as the starting material for the preparation of metal complexes.

Reaction of $BmtCO_2Li{\cdot}2thf$ (2 equiv.) with MCl_2 in MeOH afforded $[M(BmtCO_2)_2(MeOH)_n]{\cdot}m$MeOH [M = Fe(II), Co(II), $n = m = 4$; M = Cu(II), $n = 2$, $m = 0$]. Use of >2 equiv. of the carboxylate yielded the same products, indicating that only two of these bulky ligands may be accommodated. The X-ray crystal structures§ of the Fe and Cu complexes are shown in Figs. 1 and 2, respectively. The Co structure is isomorphous with that of Fe, so only data for the Fe case is presented. Common to all of the complexes is a *trans* disposition of two

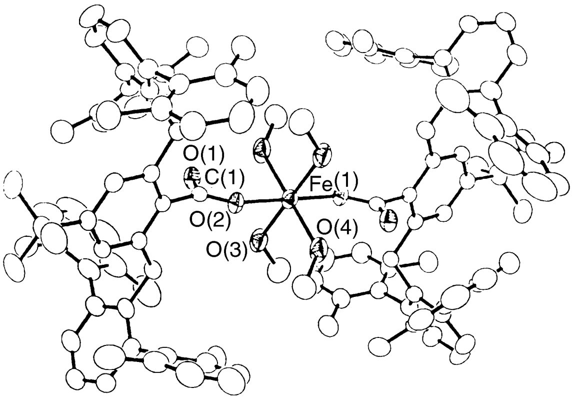

Fig. 1 Representation of the X-ray crystal structure of $[Fe(BmtCO_2)_2(MeOH)_4]{\cdot}4MeOH$ as 50% thermal ellipsoids, with H atoms and the solvent molecules omitted for clarity. Selected bond distances (Å) and angles (°): Fe(1)–O(2) 2.125(18), Fe(1)–O(3) 2.162(2), Fe(1)–O(4) 2.091(2), Fe(1)···O(1) 3.225(2); O(4)–Fe(1)–O(2) 89.69(8), O(4)–Fe(1)–O(3) 90.86(10), O(2)–Fe(1)–O(3) 89.30(8).

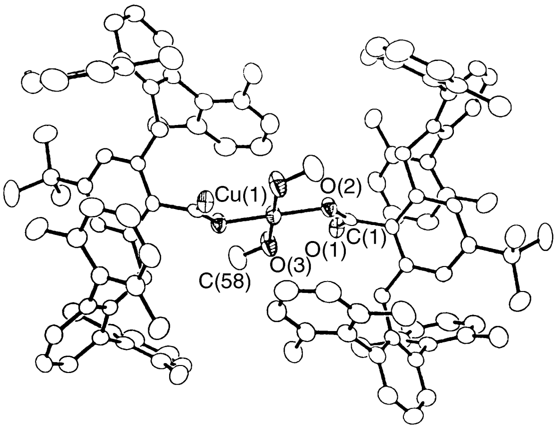

Fig. 2 Representation of the X-ray crystal structure of $[Cu(BmtCO_2)_2(MeOH)_2]$ as 50% thermal ellipsoids, with H atoms omitted for clarity. Selected bond distances (Å) and angles (°): Cu(1)–O(2) 1.893(2), Cu(1)–O(3) 1.950(2), Cu(1)···O(1) 3.245; O(2)–Cu(1)–O(3) 91.70(9), O(2)–Cu(1)–O(3a) 88.30(9).

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† Electronic supplementary information (ESI) available: detailed procedures for the syntheses of BmtBr, $BmtCO_2H$ and $BmtCO_2Li$ as well as characterization data for all new compounds. See http://www.rsc.org/suppdata/cc/b0/b006647h/

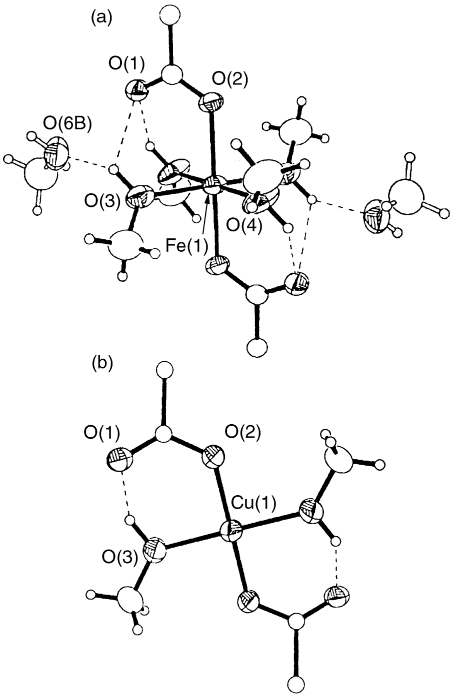

Fig. 3 Coordination spheres of (a) $[Fe(BmtCO_2)_2(MeOH)_4]\cdot 4MeOH$ (showing two of the MeOH solvent molecules; the other two are highly disordered) and (b) $[Cu(BmtCO_2)_2(MeOH)_2]$, with hydrogen bonding interactions indicated by dashed lines. Relevant interatomic distances (Å): (a) O(1)···O(4a) 2.582(3), O(1)···O(3) 3.199(3), O(3)···O(6b) 2.718(7), (b) O(1)···O(3) 2.511(3) Å.

$BmtCO_2^-$ ligands that coordinate in a *syn* monodentate fashion. The noncoordinating carboxylate oxygen atoms participate in hydrogen bonding with the bound MeOH ligands (Fig. 3). Additional hydrogen bonding occurs in the Fe and Co complexes involving included solvent MeOH molecules. Similar intramolecular hydrogen bonding patterns have been seen in other Fe(II)[8] and Cu(II)[9] carboxylate complexes and have been suggested to play a role in stabilizing their structures.

Mononuclear bis(carboxylato) iron(II) complexes possessing *trans* carboxylates are rare,[4a,c,10] and $[Fe(BmtCO_2)_2(MeOH)_4]$ is a unique example with an all-oxygen donor set. The O_{carb}–Fe–O_{carb} angle of 180° presumably results from the tendency of the $BmtCO_2^-$ ligands to position themselves as far apart as possible. This angle in the other two known bis(carboxylato) iron(II) complexes with *trans* monodentate carboxylate groups deviates significantly from linearity [168.5(2) and 154.74(8)°].[4a,c,10] The small space remaining in the equatorial plane of the octahedral $BmtCO_2^-$ complex is ideal for accommodation of small donors such as MeOH.

A Cu(II) complex possessing the same donor set as $[Cu(BmtCO_2)_2(MeOH)_2]$ has been reported,[9a] but in this complex of a functionalized benzoate ('furosemide') there are additional weak axial interactions between the Cu(II) center and the carboxylate oxygen atoms from adjacent molecules [Cu–O 2.720(4) Å]. In the $BmtCO_2^-$ compound, no other potential donor ligand is within bonding distance to the square-planar Cu(II) center due to blocking of the apical site by the carboxylate xylyl groups. The mononuclear structure of the complex contrasts with the familiar dinuclear paddlewheel[11] or other common topologies in which carboxylates bridge between multiple Cu(II) centers.[12] The discrete structure of $[Cu(BmtCO_2)_2(MeOH)_2]$ is also unusual insofar as many Cu(II) carboxylate complexes which exist as monomers in solution form intermolecular hydrogen bonded extended structures in the solid state.[13]

In conclusion, we have developed a synthesis of the carboxylate **3** in which the ligating unit is encapsulated in an irregular 'molecular bowl'. The extreme steric demands of the ligand have been illustrated through characterization of the monomeric Fe(II), Co(II) and Cu(II) complexes comprising two molecules of **3** coordinated *trans* in a *syn* monodentate mode. Further studies will explore the potential for the use of **3** and the complexes described herein for accessing unusual structures pertinent to nonheme, carboxylate rich metalloprotein active sites.

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Notes and references

‡ The precursor BmtBr was synthesized *via* the method described in ref. 7(*e*), but improvements were made that allowed the product to be isolated in higher yield (70% *vs*. 32%). For detailed procedures for the syntheses of BmtBr, $BmtCO_2H$ and $BmtCO_2Li$, see ESI.†

§ *Crystal data* for $BmtCO_2H$ (**3**-H): $C_{171}H_{174}O_6$, M = 2325.10, triclinic, space group $P\bar{1}$, a = 13.2288(7), b = 21.7697(11), c = 26.0770(13) Å, α = 76.040 (1), β = 82.286(1), γ = 84.717(1)°, V = 7208(1) Å^3, T = 173(2) K, Z = 2, μ(Mo-Kα) = 0.062 mm^{-1}, 63 469 reflections measured, 32 161 unique (R_{int} = 0.027) which were used in all calculations. The final $wR(F^2)$ was 0.1298 (all data), $R1$ = 0.0541. For $[Fe(BmtCO_2)_2(MeOH)_4]\cdot 4MeOH$: $C_{122}H_{146}O_{12}Fe$, M = 1860.24, monoclinic, space group $P2_1/n$, a = 21.1152(13), b = 13.3988(9), c = 21.1719(13) Å, β = 115.0900(10)°, V = 5424.7(6) Å^3, T = 173(2) K, Z = 2, μ(Mo-Kα) = 0.198 mm^{-1}, 27 850 reflections measured, 9562 unique (R_{int} = 0.0481) which were used in all calculations. The final $wR(F^2)$ was 0.1772 (all data), $R1$ = 0.0558. For $[Cu(BmtCO_2)_2(MeOH)_2]$: $C_{116}H_{122}O_6Cu$, M = 1675.68, monoclinic, space group $P2_1/n$, a = 15.2154(7), b = 11.1085(5), c = 27.7956(12) Å, β = 97.9700(10)°, V = 4652.6(4) Å^3, T = 173(2), Z = 2, μ(Mo-Kα) = 0.292 mm^{-1}, 23 238 reflections measured, 8203 unique (R_{int}) = 0.0439) which were used in all calculations. The final $wR(F^2)$ was 0.1795 (all data), $R1$ = 0.0598. CCDC 182/1859. See http://www.rsc.org/suppdata/cc/b0/b006647h/ for crystallographic files in .cif format.

1 R. H. Holm, P. Kennepohl and E. I. Solomon, *Chem. Rev.*, 1996, **96**, 2239.

2 R. L. Rardin, W. B. Tolman and S. J. Lippard, *New J. Chem.*, 1991, **15**, 417.

3 A. L. Feig and S. J. Lippard, *Chem. Rev.*, 1994, **94**, 759; L. Que, Jr., in *Bionorganic Catalysis*, ed. J. Reedijk and E. Bouman, Marcel Dekker, Inc., 1999; B. J. Wallar and J. D. Lipscomb, *Chem. Rev.*, 1996, **96**, 2625.

4 J. R. Hagadorn, L. Que, Jr. and W. B. Tolman, *J. Am. Chem. Soc.*, 1998, **120**, 13 531; (*b*) J. R. Hagadorn, L. Que, Jr., W. B. Tolman, I. Prisecaru and E. Münck, *J. Am. Chem. Soc.*, 1999, **121**, 9760; (*c*) J. R. Hagadorn, L. Que, Jr. and W. B. Tolman, *Inorg. Chem.*, 2001, **40**, in press.

5 D. Lee and S. J. Lippard, *J. Am. Chem. Soc.*, 1998, **120**, 12 153; (*b*) D. Lee, J. D. Bois, D. Petasis, M. P. Hendrich, C. Kres, B. H. Huynh and S. J. Lippard, *J. Am. Chem. Soc.*, 1999, **121**, 9893; (*c*) D. Lee, C. Krebs, B. H. Huynh, M. P. Hendrich and S. J. Lippard, *J. Am. Chem. Soc.*, 2000, **122**, 5000.

6 S. C. Payne and K. S. Hagen, *J. Am. Chem. Soc.*, 2000, **122**, 6399.

7 K. Goto, J. Kobayashi and R. Okazaki, *Organometallics*, 1999, **18**, 1357; (*b*) K. Goto, M. Holler and R. Okazaki, *Chem. Commun.*, 1998, 1915; (*c*) K. Goto, M. Holler and R. Okazaki, *J. Am. Chem. Soc.*, 1997, **119**, 1460; (*d*) K. Goto and R. Okazaki, *Liebigs Ann./Recueil*, 1997, 2393; (*e*) K. Goto, M. Holler and R. Okazaki, *Tetrahedron Lett.*, 1996, **37**, 3141.

8 S. Herold and S. J. Lippard, *J. Am. Chem. Soc.*, 1997, **119**, 145; M. M. Morelock, M. L. Good, L. M. Trefonas, R. Majeste and D. G. Karraker, *Inorg. Chem.*, 1982, **21**, 3044.

9 For examples, see: (*a*) P. Bontchev, H. Kadum, G. Gochev, B. Evtimova, J. Macicek and C. Nachev, *Polyhedron*, 1992, **11**, 1973; (*b*) H. Muhonen, *Acta Crystallogr., Sect. C*, 1983, **39**, 536.

10 B. Singh, J. R. Long, G. C. Papaefthymiou and P. Stavropoulos, *J. Am. Chem. Soc.*, 1996, **118**, 5824; B. Singh, J. R. Long, F. F. deBiani, D. Gatteschi and P. Stavropoulos, *J. Am. Chem. Soc.*, 1997, **119**, 7030.

11 R. J. Doedens, *Prog. Inorg. Chem.*, 1975, **19**, 173; M. Melnik, *Coord. Chem. Rev.*, 1982, **42**, 259.

12 G. Psomas, C. P. Raptopoulou, L. Iordanidis, C. Dendrinou-Samara, V. Tangoulis and D. P. Kessissoglou, *Inorg. Chem.*, 2000, **39**, 3042 and references cited therein.

13 For example, see: H. Muhonen, *Acta Crystallogr., Sect. C*, 1983, **39**, 536; C. K. Prout, R. A. Armstrong, J. R. Carruthers, J. G. Forrest, P. Murray-Rust and J. C. Rossotti, *J. Chem. Soc. A*, 1968, 2791; C. K. Prout, M. J. Barrow and F. J. C. Rossotti, *J. Chem. Soc. A*, 1971, 3326.