Synthesis of a Large Cavity Homoleptic Thioether Cage and its Cobalt(III) Complex

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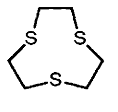
The cobalt(III) complex of the large hexathioether cage (1,9-dimethyl-3,7,11,15,18,22-hexathiabicyclo[7.7.7]tricosane) shows substantially different redox and spectral properties relative to the smaller homologous [6.6.6]icosane.

Although the simple thioethers are rather poor ligands for first row transition metal ions for both steric and electronic reasons[1] (exhibiting weaker σ-donor and π-acceptor properties than the corresponding phosphines), the crown thioethers form much more stable complexes with a wide range of transition metals, and their extensive chemistry has recently been the subject of two comprehensive reviews.[2] The tridentate ligand [9]aneS_3 **1** has received the most attention, with reports of metal complexes covering most of the transition metals.[2] A large number of homoleptic thioether complexes of the type [M([9]aneS_3)$_2$] have been reported, spanning a range of oxidation states, whereas complexes of the S_6 analogue [18]aneS_6 **2**, have been much less extensively studied.[2] Both of these ligands are capable of coordinating with fewer than their total complement of thioether donors, in order to accommodate the steric or geometric constraints of a particular metal or oxidation state. Crown thioethers in which there are trimethylene units linking sulfur atoms (such as the cyclam analogue [14]aneS_4 **3** and [12]aneS_3 **4**) have also been synthesised, and their coordination chemistry has been investigated.[2]

The crystal structure of the free ligand **1** shows that this molecule is already in the endodentate conformation required for facial coordination of the three thioether atoms,[3] whereas the other crystallographically characterized free crown thioethers have some or all of their sulfur atoms in an exodentate conformation,[4,5] requiring a conformational rearrangement (with the accompanying thermodynamic cost) before complexation can take place. Together with the greater conforma-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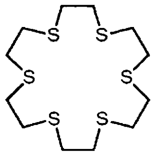
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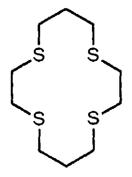
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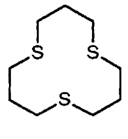
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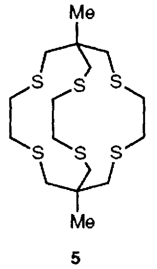
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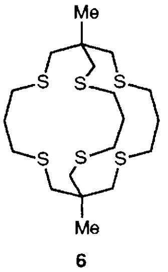
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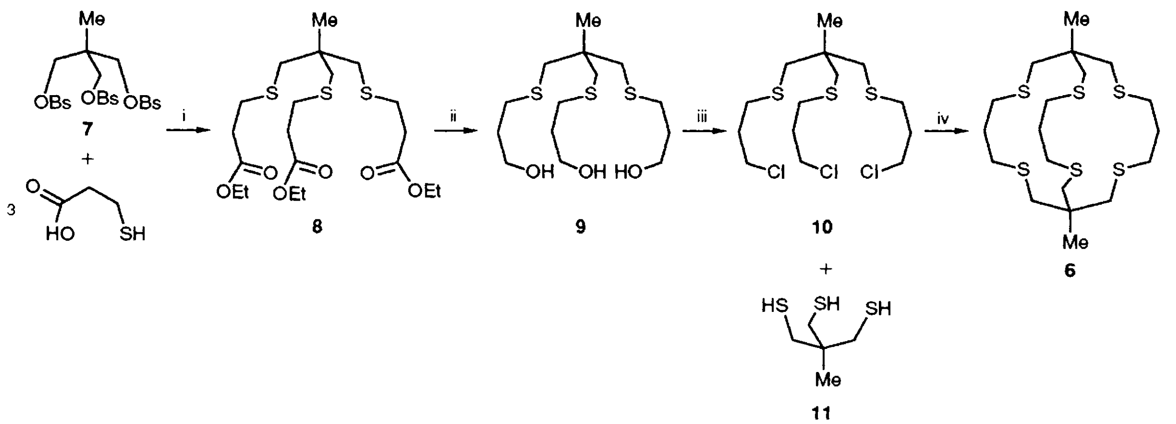

Scheme 1 *Reagents and conditions*: i, (*a*) NaOEt, EtOH; (*b*) HCl, EtOH; ii, $LiAlH_4$, THF; iii, $SOCl_2$, $CHCl_3$; iv, Cs_2CO_3, dimethylformamide, 60 °C, 34 h (OBs = benzene sulfonate)

tional flexibility of the trimethylene unit, this can lead to destabilization of the metal complex. Thus, $[Ni([12]aneS_3)_2]^{2+}$ for example, is hydrolysed immediately by traces of water to yield the free ligand **4** and $[Ni(H_2O)_6]^{2+}$,[6] whereas the corresponding complex of **1** can be recrystallized from boiling water.

Other approaches to stabilising an S_6 donor set have included the synthesis of a 'supertripodal' thioether ligand[7] and a cryptand containing six thioether and two amine groups.[8] As part of our ongoing studies on cage ligands with varying donor groups [9,10] and cavity sizes[10,11] we have recently reported the synthesis of a novel thioether cage **5** (Me_2S_6sar) together with its cobalt(II) and cobalt(III) complexes, which represent the first fully encapsulated transition metal complexes with a homoleptic thioether donor set.[12] The recognition of the potential of such ligands for the complexation of the later, and larger, transition metals, and the greater steric constraints imposed by an encapsulating ligand when compared with the S_6 macrocyclic species or the facially coordinated S_3 crown thioethers prompted us to explore the synthesis of a thioether cage **6**, which has a larger cavity than the S_6 cage species **5**. In this paper we report the synthesis of this novel larger cavity cage, its isolation and purification as the cobalt(III) complex, together with the properties of the complex, and the subsequent isolation and characterization of the free ligand by demetallation of the reduced cobalt(II) complex.

The synthesis of the thioether cage was based on the method developed for the Me_2S_6sar cage, and involves a caesium carbonate mediated ring closure,[13] of the type used in the synthesis of the crown thioethers, as the key step (Scheme 1).

The tripodal intermediate **9** was prepared by refluxing a solution of **7** with 3-mercaptopropionic acid (3 equiv.) and NaOEt (6 equiv.) in ethanol for 24 h. Workup led to the ethyl ester **8**, which was reduced to the alcohol using $LiAlH_4$ in tetrahydrofuran (THF). The alcohol was converted to the trichloride **10** by treatment with an excess of $SOCl_2$ in chloroform, and the trithiol **11** was prepared by standard literature methods.[14] The coupling was carried out in a similar manner to that described for $[18]aneS_6$.[15] All of the intermediate species were characterized using ^1H and ^{13}C NMR spectroscopy. The NMR spectra of the reaction mixture were complex, which implied that a number of products had been formed. Preliminary TLC studies confirmed this, but no satisfactory separation was achieved for the target cage molecule, which was only present as a minor component of the product mixture. It was reasoned that complexation of the cage by the Co^{II} ion, followed by oxidation would yield a stable cobalt(III) complex, which might be separated from the organic products by solvent extraction, and from other cobalt complexes by ion-exchange chromatography. The crude reaction mixture was therefore dissolved in CH_2Cl_2 and added slowly to a solution of $Co(ClO_4)_2{\cdot}6H_2O$ in nitromethane–methanol (5 : 1). The dichloromethane was then removed under vacuum, and $AgClO_4$ in absolute ethanol was added [1 equiv. based on the cobalt(II) present]. The solvent was removed, the product was dissolved in dilute aqueous HCl, filtered (to remove Ag formed by oxidation of cobalt(II) to cobalt(III) and the excess of Ag^+ as AgCl), and extracted with chloroform. The aqueous phase was chromatographed on Dowex 50W-X2 using HCl as eluant, and the desired product $[(Co(Me_2S_6tricosane]Cl_3)$ was obtained.

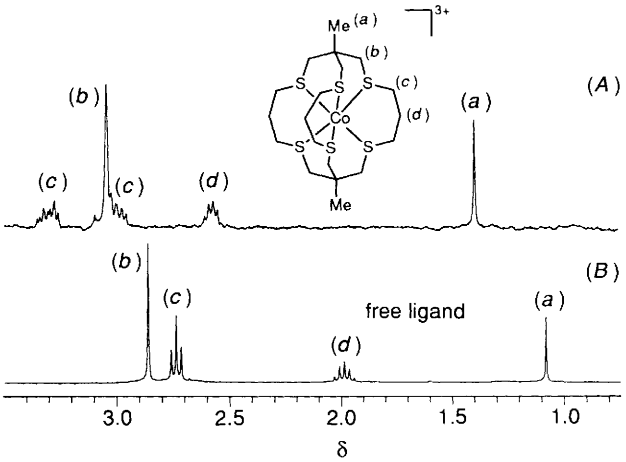

Fig. 1 300 MHz ^1H NMR spectra of (*A*) $[Co(Me_2S_6tricosane)]Cl_3$ in D_2O and (*B*) Me_2S_6tricosane in $CDCl_3$ together with peak assignments

The simplicity of the ^1H NMR spectrum (Fig. 1) and the presence of only five resonances in the ^{13}C NMR† clearly show that the metal is fully encapsulated with octahedral or pseudooctahedral coordination geometry, and that on the NMR timescale the molecule at least averages to D_3 symmetry. In contrast to the ^1H NMR spectrum of $[Co(Me_2S_6sar)]^{3+}$ for which the the 'cap' methylene protons show an AB splitting pattern (implying that the cap is conformationally 'locked', at least on the NMR timescale), the cap methylene protons of $[Co(Me_2S_6tricosane)]^{3+}$ have coalesced into a singlet. However, the trimethylene linkages give rise to a pattern that implies conformational rigidity. Clearly the two protons on the methylene (*c*) in the figure are inequivalent. In contrast to the vast majority of thioether

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† ^1H NMR (300 MHz, D_2O) δ (*vs.* internal dioxane at δ 3.74) 1.40 (s, 6H, Me), 2.57 (q, 6H, *J* 6 Hz, $CH_2CH_2CH_2$), 2.96–3.10 (m and overlapping s, 20H, CH_2S), 3.26–3.33 (m, 6H, CH_2S). $^{13}C\{H\}$ NMR (75 MHz, D_2O) δ (*vs.* internal dioxane at δ 67.39) 21.59 ($CH_2CH_2CH_2$), 29.30 (Me), 33.34 ($CH_2CH_2CH_2$), 39.02 (C_qCH_2S), 39.25 (C_q). Electronic spectrum (in water) (λ_{max}/nm): 244, 322 and 494.

complexes it might therefore prove possible to resolve these thioether cage complexes.

The UV–VIS spectrum of the [Co(Me$_2$S$_6$tricosane)]$^{3+}$ chromophore has a similar band pattern to that of the smaller cage homologue, but the effect of the enlarged cavity is seen in the shift of the band maxima to lower energy, reflecting the weaker ligand field exerted by the enlarged cavity. The [Co(Me$_2$S$_6$tricosane)]$^{3+}$ complex band maxima occur at 279, 365 and 522 nm, whereas the corresponding peaks in [Co(Me$_2$S$_6$sar)]$^{3+}$ are at 244, 322 and 494 nm, respectively. The electrochemistry also shows the effect of the different cavity size in the two cage ligands. Cyclic voltammetry of the [Co(Me$_2$S$_6$tricosane)]$^{3+}$ in aqueous solution shows a near-reversible (ΔE_p = 82 mV) cobalt(III)/(II) couple at 400 mV (*vs.* normal hydrogen electrode; Pt or glassy carbon electrode, scan rate 500 mV s^{-1}, T = 295 K, I = 0.2 mol dm^{-3}, KCl), and another quasi-reversible couple at ~−500 mV that has been assigned to the cobalt(II)/(I) couple. The corresponding couples in the [Co(Me$_2$S$_6$sar)]^3 complex occur at 245 and −686 mV, respectively, under these conditions, and they are both reversible.[16] Thus, the 3+/2+ couple is 160 mV more positive for the larger cage complex, and the 2+/1+ couple is 190 mV more positive. These differences arise because it is harder to accommodate the larger 2+ and 1+ ions in the smaller Me$_2$S$_6$sar cavity than in the larger cavity homologue. However, for the larger cavity cobalt complex, the couples were less well defined, and higher scan rates were required implying that [Co(Me$_2$S$_6$tricosane)]$^{2+}$ is less stable in aqueous solution than [Co(Me$_2$S$_6$sar)]$^{2+}$ with respect to dissociation of the metal ion. This is not too surprising in the light of the hydrolytic instability of first row transition metal complexes of [12]aneS$_3$.[6]

Sodium dithionite reduced [Co(Me$_2$S$_6$tricosane)]$^{3+}$ readily in water. The solution rapidly turned pale and Co^{II} was efficiently sequestered by ethylenediaminetetraacetic acid disodium salt. The free Me$_2$S$_6$tricosane was extracted into chloroform, and characterized by ^{1}H (Fig. 1) and ^{13}C NMR and high-resolution mass spectrometry.‡ The five-line ^{13}C NMR spectrum shows the D_3 symmetry or higher, and the splitting pattern of the ^{1}H NMR spectrum shows that the ligand is conformationally labile on the NMR timescale.

The syntheses of transition metal complexes of this new cage together with those of the smaller cavity thioether cage **6** are in progress. The effect of the differing cavity size on the stability and electronic properties of the later transition metal complexes, and especially those of the second and third row elements, constrained in an S$_6$ donor set, is an area of particular interest. In the light of the significant differences between the macrocyclic amines and the amine cage ligands, these thioether cages should add a new dimension to the coordination chemistry of the crown thioethers.

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‡ ^{1}H NMR (300 MHz, CDCl$_3$) δ (*vs.* internal dioxane at δ 3.74) 1.08 (s, 6H, Me), 1.98 (q, 6H, J 6 Hz, CH$_2$CH_2CH$_2$), 2.73 (t, 12H, J 6 Hz, CH$_2$CH_2S), 2.86 (s, 12H, C$_q$CH$_2$S). ^{13}C{H} NMR (75 MHz, CDCl$_3$) δ (*vs.* CDCl$_3$ at δ 77.00), 24.18 (Me), 28.44 (CH$_2$CH$_2$CH$_2$), 31.59 (CH$_2$CH$_2$CH$_2$), 40.88 (C$_q$), 42.25 (C$_q$CH$_2$S). High-resolution MS m/z exact mass calc. for C$_{19}$H$_{36}$S$_6$ 456.1141, found 456.1140.

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