

Synthesis, Structure and Preliminary Complexation Behaviour of Macrocyclic Thioureas and Ureas

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Tricyclic ligands incorporating bis(thiourea) subunits may be prepared from the corresponding monocyclic [18]- and [24]-ring N_4O_2 and N_4O_4 polyaza-compounds and adopt a *trans*-conformation in the free ligand; an unusual trisilver(I) complex is formed with the N_4O_2 -derived ligand with bridging nitrate groups in which the thiourea groups are *cis*-oriented.

Although the urea carbonyl group is an excellent σ -donor for charge-dense cations, and the related thioureas form stable linear 2:1 complexes with soft ions such as gold(I),¹ and silver(I), there have been relatively few reports of their complexation behaviour when incorporated in a macrocyclic ligand. Most effort has been directed towards the synthesis of 'crown-ureides'² incorporating benzimidazolone moieties⁴ or of hemi-spherands including imidazolidinone sub-units.^{2,3} There appear to be no reports of the complexation behaviour of cyclic poly(thioureas). We report a general synthesis of cyclic bis(thioureas), *e.g.* **1** and **4**, linked in this case by polyoxyethylene chains, their conversion to the corresponding bis(ureas), **3** and **6**, the structural characterisation of two of the bis(thioureas) and the structural identification of an oligonuclear silver(I) complex.

The synthetic strategy adopted was to convert 1,4-diaza units (ethylenediamine groups) in a polyaza macrocycle into the desired thiourea units by reaction with carbon disulfide,⁵ subsequently transforming the thiourea group to a urea by

reaction with mercury(II) acetate.⁶ Thus reaction of 1,10-dioxa-4,7,13,16-tetraazacyclooctadecane **7** with carbon disulfide, followed by treatment with HCl (reflux, 14 h) afforded **1** as a colourless solid [m.p. 246–247 °C, $\delta_C(\text{CDCl}_3)$ 182.2 (C=S)] whose ¹H NMR spectrum (CDCl_3 , 293 K) was consistent[†] with the ring being in a single low-energy conformation. The X-ray structure revealed that the ligand

[†] New compounds gave satisfactory microanalytical, mass spectral and NMR (COSY and HETCOR) data in accord with the proposed structures: selected data, **1**: $\delta_H(\text{CDCl}_3)$ 4.64 (4H, ddd, NCH_2CH_2O), 3.94 (4H, m, NCH_2CH_2N), 3.80 (4H, ddd, NCH_2CH_2O), 3.64 (4H, AA'BB', $NCH_2'CH_2'O$), 3.36 (4H, AA'BB', $NCH_2'CH_2'O$), 2.96 (4H, m, $NCH_2'CH_2'N$); $\delta_C(\text{CDCl}_3)$: 182.2 (C=S), 67.8 (CH_2O), 47.4 (NCH_2CH_2O), 47.0 (CH_2N). **4**: $\delta_H(\text{CDCl}_3)$ 3.83 (8H, t, J 10 Hz, NCH_2CH_2O), 3.70 (8H, t, J 10 Hz, NCH_2CH_2O), 3.69 (8H, s, NCH_2CH_2N), 3.61 (8H, s, OCH_2CH_2O); $\delta_C(\text{CDCl}_3)$ 182.6 (C=S), 70.6 (OCH_2CH_2O), 70.4 (NCH_2CH_2O), 48.3 (OCH_2CH_2N), 48.0 (NCH_2CH_2N).

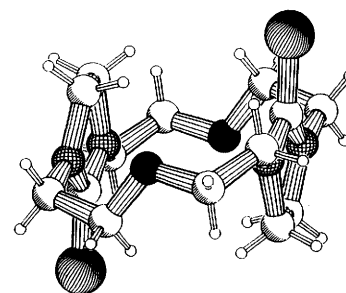
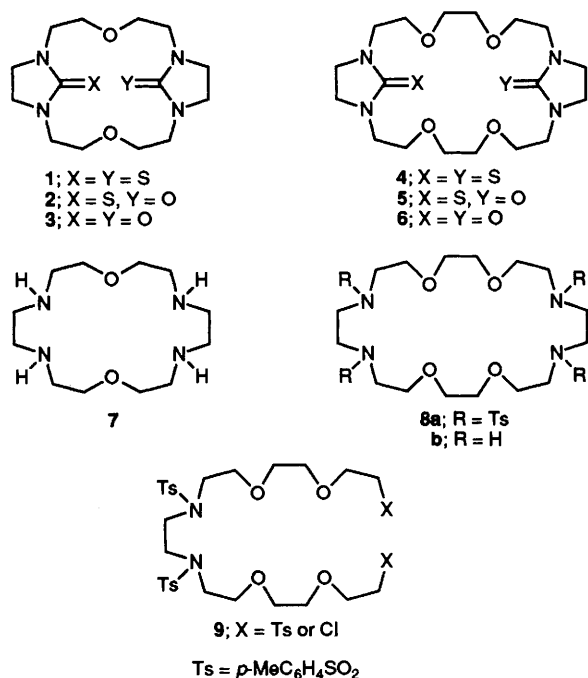


Fig. 1 A PLUTON view of the ligand 1 (294 K)

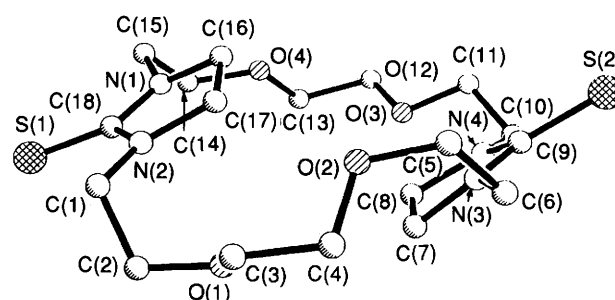
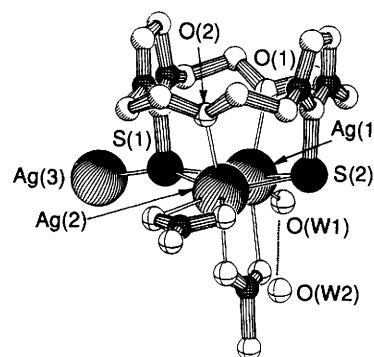


Fig. 2 A view of the ligand 4 (150 K)

possessed a centre of inversion in the crystal, with the two thiourea groups *trans*-disposed (Fig. 1). The homologous macrocycle 4 (m.p. 233–235 °C) was prepared in an analogous manner from 1,4,13,16-tetraoxa-7,10,19,22-tetraazacyclo-tetraicosane 8b, which was in turn prepared from the cyclic tosylamide 8a derived from the acyclic ditosylate or dichloride 9 using standard Richman–Atkins cyclisation conditions [Cs_2CO_3 , dimethylformamide (DMF), (66% or 52%) cyclisation yield]. The structure of 4 (Fig. 2) revealed that the two thiourea rings were again oriented *trans* to one another in this case with the sulfurs directed outside the ring.† Molecular modelling studies suggest that there is a relatively low energy barrier to reorientation of these thiourea groups so that they may be directed inwards as needed to bind, e.g. a gold(i) cation in a *trans*-chelating manner.

Reaction of 1 with silver nitrate (in excess) in methanol led to formation of a crystalline complex with the stoichiometry 1 : 3 (ligand : silver). Crystallographic analysis of this complex revealed that the coordination geometry about each of the three silver cations was quite different (Figs. 3 and 4). The ligand is arranged in a *cis*-configuration such that the two sulfur atoms bridge each of the silver cations [all four Ag–S bond lengths are in the range 2.53(1) to 2.69(1) Å; Ag(1)⋯Ag(2) is 2.90(1) Å]. The ring oxygens O(1) and O(2)

Fig. 3 PLUTON view of the silver complex $[1 \cdot \text{Ag}_3(\text{NO}_3)_3]$ omitting the disordered nitrates and the ring hydrogens for clarity (294 K)

are also bonded to Ag(1) and Ag(2) respectively, Ag(1)–O(1), 2.63(1) Å; Ag(2)–O(2), 2.53(2) Å. The silver cations Ag(1) and Ag(2) are bridged by two oxygens of a nitrate group and a second nitrate group is bound to Ag(2) in a bidentate fashion, Ag(2)–O: 2.43(3) and 2.63(3) Å. The third silver cation Ag(3) is bonded to one of the macrocyclic ring sulfur atoms S(1), with Ag(3)–S(1) 2.57(1) Å. In addition it is bound to two more nitrate groups which are disordered about inversion centres. These nitrates bridge symmetry-related Ag(3) cations such that the two Ag(3)⋯Ag(3) distances are 6.22(1) and 6.34(1) Å.

In contrast, ligand 4 forms a discrete 1 : 1 complex {FABMS (3-nitrobenzyl alcohol): m/z 641, 639 [$M + \text{Ag}^+$]}, with the two thiourea groups presumably able to bind in a *trans*-spanning manner.

Hydrolysis of 1 [$\text{Hg}(\text{OAc})_2 \cdot \text{CH}_2\text{Cl}_2$; then $\text{K}_2\text{CO}_3 \cdot \text{H}_2\text{O}$] yielded the bis(urea) 3, in 42% yield, and the intermediate monothiourea, 2, could also be isolated [m.p. 164–165 °C; $\delta_{\text{C}}(\text{CDCl}_3)$ 180.9 (C=S), 165.4 (C=O)]. Similarly 4 was converted into 6, although, in this case, 5 could not be isolated. Preliminary cation binding studies using FAB mass spectroscopy⁸ (glycerol) show that 3 binds Na^+ selectively amongst univalent cations ($\text{Na}^+ > \text{K}^+ > \text{Li}^+ > \text{Rb}^+ \approx \text{Cs}^+ > \text{NH}_4^+$) and magnesium preferentially ($\text{Mg}^{2+} > \text{Ba}^{2+} > \text{Ca}^{2+}$

† Atomic coordinates, bond lengths and angles, and thermal parameters for 1, 4 and $[1 \cdot \text{Ag}_3(\text{NO}_3)_3]$ have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1. Copies of the structure factor listings are also available from the authors.

Crystal data: 1, ($\text{C}_{14}\text{H}_{24}\text{N}_4\text{O}_2\text{S}_2$): $M = 344.5$, triclinic, $P\bar{1}$, $a = 6.9554(4)$, $b = 7.8297(11)$, $c = 8.1242(13)$ Å; $\alpha = 79.27(1)$, $\beta = 75.50(1)$, $\gamma = 84.37(1)^\circ$; $U = 420.2$ Å³, $Z = 1$, $F(000) = 184$, Mo-K α , $\mu = 1.9$ cm⁻¹, $D_c = 1.36$ g cm⁻³; 1826 reflections measured, 1268 with $I \geq 3\sigma(I)$ used; $R = 0.031$, $R_w = 0.044$.

$[1 \cdot \text{Ag}_3(\text{NO}_3)_3]$: $M = 854.1$, monoclinic, $P2_1/n$, $a = 10.703(4)$, $b = 15.577(4)$, $c = 16.294(3)$ Å, $\beta = 91.62(2)^\circ$; $U = 2715$ Å³, $Z = 4$, $F(000) = 1672$, Mo-K α , $\mu = 23.3$ cm⁻¹, $D_c = 2.09$ g cm⁻³; 2690 reflections measured, 1934 used with $I \geq 2\sigma(I)$ (75% decay in 18 h); $R = 0.126$, $R_w = 0.140$. Data were corrected to allow for crystal decay.

4; ($\text{C}_{18}\text{H}_{32}\text{N}_4\text{O}_4\text{S}_2$): $M = 432.6$, orthorhombic, $Pbca$, $a = 22.531(4)$, $b = 21.502(3)$, $c = 8.961(2)$ Å; $U = 4341(1)$ Å³; $Z = 8$, $F(000) = 1856$, Mo-K α , $\mu = 0.276$ mm⁻¹, $D_c = 1.324$ g cm⁻³; 5043 reflections, 2622 with $I \geq 2\sigma(I)$ used; $R = 0.044$, $R_w = 0.039$.

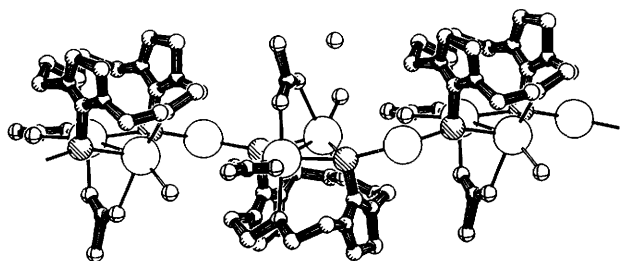


Fig. 4 PLUTON view of the silver complex $[1 \cdot Ag_3(NO_3)_3]$ showing the linking of the units by $Ag(3)$

$\gg Zn^{2+}$ and Cd^{2+} ; although an L_2Ba^{2+} complex was also observed) amongst divalent ions. The hexadentate ligand **6** exhibited a similar selectivity pattern ($Na^+ > Li^+ \gg K^+ \approx Rb^+ \approx Cs^+$; $Mg^{2+} > Ca^{2+} \approx Ba^{2+}$).

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