Crown Thioether Chemistry. Synthesis and Structural Investigation of 1,5,9-Trithiacyclododecane (Trithia-12-crown-3) and its Copper(II) Chloride Adduct†

Simon C. Rawle, Gary A. Admans, and Stephen R. Cooper *
Inorganic Chemistry Laboratory and Chemical Crystallography Laboratory, University of Oxford, Oxford OX1 3QR

1,5,9-Trithiacyclododecane (L^1) (trithia-12-crown-3) adopts a square conformation similar to that of cyclododecane, with one sulphur atom at a corner and two in side positions. Reaction with copper(II) chloride yields an adduct, $[Cu(L^1)_2Cl_2]$, that has been characterized by *X*-ray diffraction. Each copper ion occupies a centre of inversion and has idealized octahedral microsymmetry, with thioether groups at distances of 2.447(1) and 3.050(1) Å. The conformation adopted by the macrocycle is virtually identical to that adopted by the free ligand, which suggests that its conformation is determined by intrinsic factors rather than packing forces.

Efficient design of ligands requires grasp of their conformational preferences in order to optimize metal–ligand interaction by minimizing strain in the co-ordinated ligand (*i.e.* to maximize the macrocyclic effect).[1] We have previously extended to crown thioethers[2] the pioneering work of Dale[3] on conformational analysis in crown ethers. This work has shown that in $(\text{–CCE–})_n$ (*i.e.* ethyl-linked) macrocycles with E = O the C–E bonds greatly prefer to adopt *anti* placement (dihedral angle 180°). On the other hand, the C–E bonds show an equally pronounced tendency to adopt *gauche* placement (dihedral angle 60°) if E = S. This contrast derives at least in part from the difference in C–E bond length for E = O and S, and the consequent difference in 1,4-repulsion between terminal methylene groups of (–CCEC–) units.

These conclusions rest upon conformational data derived largely from *X*-ray diffraction studies; consequently, it may be asked to what extent ligand conformations reflect extrinsic factors (*e.g.* packing forces) rather than intrinsic conformational preferences of the ligand. The present work on L^1‡ and its adduct with $CuCl_2$ suggests that, at least in this system, intrinsic factors largely determine the ligand conformation.

Experimental

Dry, degassed solvents were used in all preparations. Tetrahydrofuran was distilled from sodium–benzophenone under nitrogen and dmf was distilled from barium oxide under vacuum. Other reagents were of the highest grade available and were used as received. Elemental analyses were performed by the microanalytical service of the Inorganic Chemistry Laboratory, Oxford.

Table 1. Crystallographic data for trithia-12-crown-3 (L^1) and $[Cu(L^1)_2Cl_2]$

Compound	L^1	$[Cu(L^1)_2Cl_2]$
Formula	$C_9H_{18}S_3$	$C_{18}H_{36}Cl_2CuS_6$
M	222.4	579.3
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/a$ (no. 14)	$C2/c$ (no. 15)
a/Å	7.569(2)	20.213(5)
b/Å	8.241(1)	8.521(5)
c/Å	20.806(2)	16.214(4)
α/°	90	90
β/°	90	116.29(3)
γ/°	116.74(2)	90
U/Å^3	1 159.08	2 503.76
D_c/g cm^{-3}	1.27	1.54
Z	4	4
Radiation, λ/Å	Cu-K_α, 1.5418	Mo-K_α, 0.71069
F(000)	480	1 212
μ/cm^{-1}	52.0	15.8
Crystal size/mm	0.40 × 0.35 × 0.35	0.45 × 0.40 × 0.30
Reflections collected	$\pm h, +k, +l$	$\pm h, +k, +l$
No. of reflections collected	3 300	5 225
Unique data with $F^2 > 3\sigma(F^2)$	1 963	1 770
2θ range/°	2—150	2—54
Final R	0.0342	0.0686
Final R'	0.0520	0.0696
Goodness of fit	0.76	1.00
No. of variables	110	124
Temp.	Ambient	Ambient
Scan rate/° min^{-1}	0.7—3.7	0.7—3.7
Scan mode	ω—2θ	ω—2θ
Max. absorption correction	1.43	2.33
R_{merg}	0.0352	0.0635

* The goodness of fit is defined as $[\Sigma w(|F_o| - |F_c|)^2/(n_o - n_v)]^{\frac{1}{2}}$, where n_o and n_v denote the number of data and variables, respectively.

Preparation of Compounds.—*4-Thiaheptane-*1,7-*dithiol.* 3,3′-Thiodipropionic acid (44.7 g, 250 mmol) in dry thf (300 cm^3) was added cautiously with stirring to a 1 mol dm^{-3} solution of BH_3·thf in thf (550 cm^3, 550 mmol) at 0 °C under nitrogen. After addition was complete excess borane was quenched by dropwise addition of water (20 cm^3). The resulting solution was washed twice with concentrated K_2CO_3 solution, dried (Na_2SO_4), and evaporated to yield 37.5 g (100%) of 3,3′-thiodipropanol.

3,3′-Thiodipropanol (25.0 g, 166 mmol), thiourea (28.0 g, 370 mmol), and concentrated HCl (83 cm^3, 1 mol) were refluxed together under nitrogen for 36 h. After cooling, a solution of sodium hydroxide (40 g, 1 mol in 200 cm^3 water) was cautiously added and the resultant mixture refluxed under nitrogen for 2 h. It was then cooled, reacidified to pH 2 with concentrated HCl, and extracted with dichloromethane (3 × 200 cm^3). The organic portions were combined, dried (Na_2SO_4), and

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† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1988, Issue 1, pp. xvii—xx.

‡ Abbreviations used: thf = tetrahydrofuran, dmf = *N,N*-dimethylformamide, L^1 = 1,5,9-trithiacyclododecane (trithia-12-crown-3), L^2 = 1,4,8,11-tetrathiacyclotetradecane, L^3 = 1,4,7,10-tetrathiacyclododecane (tetrathia-12-crown-4), L^4 = 1,4,7-trithiacyclononane, L^5 = 1,4,7,10,13,16-hexathiacyclo-octadecane (hexathia-18-crown-6), and L^6 = 1,5,9,13,17,21-hexathiacyclohexacosane (hexathia-24-crown-6).

Table 2. Atomic co-ordinates for 1,5,9-trithiacyclododecane (L^1)

Atom	*x*	*y*	*z*
S(1)	0.757 7(1)	0.113 58(1)	0.191 95(4)
C(2)	0.996 3(5)	0.171 8(4)	0.156 2(1)
C(3)	1.010 6(5)	0.202 3(4)	0.084 1(1)
C(4)	1.223 1(5)	0.274 4(5)	0.060 4(1)
S(5)	1.386 7(1)	0.502 9(1)	0.087 36(4)
C(6)	1.308 7(4)	0.635 7(4)	0.035 9(1)
C(7)	1.358 5(4)	0.820 3(4)	0.065 4(1)
C(8)	1.244 9(4)	0.810 8(4)	0.126 6(1)
S(9)	0.983 8(1)	0.724 31(9)	0.109 49(3)
C(10)	0.883 4(5)	0.660 3(4)	0.189 4(1)
C(11)	0.882 0(4)	0.484 8(4)	0.212 9(1)
C(12)	0.730 5(4)	0.318 2(4)	0.178 2(1)

Table 3. Bond lengths (Å) and angles (°) for 1,5,9-trithiacyclododecane (L^1)

S(1)–C(2)	1.806(3)	S(1)–C(12)	1.811(3)
S(5)–C(4)	1.816(3)	S(5)–C(6)	1.809(3)
S(9)–C(8)	1.809(3)	S(9)–C(10)	1.805(3)
C(2)–C(3)	1.518(4)	C(3)–C(4)	1.524(5)
C(6)–C(7)	1.522(4)	C(7)–C(8)	1.520(4)
C(10)–C(11)	1.522(4)	C(11)–C(12)	1.518(4)
C(12)–S(1)–C(2)	101.9(1)	C(6)–S(5)–C(4)	100.9(1)
C(10)–S(9)–C(8)	100.1(1)	C(3)–C(2)–S(1)	116.1(2)
C(4)–C(3)–C(2)	111.6(3)	C(3)–C(4)–S(5)	114.3(2)
C(7)–C(6)–S(5)	111.4(2)	C(8)–C(7)–C(6)	114.0(2)
C(7)–C(8)–S(9)	110.3(2)	C(11)–C(10)–S(9)	113.4(2)
C(12)–C(11)–C(10)	112.7(2)	C(11)–C(12)–S(1)	114.3(2)

evaporated to give a yellow oil. Vacuum distillation gave 4-thiaheptane-1,7-dithiol as a colourless mobile liquid, b.p. 80 °C/0.2 × 10^2 Pa. An impurity of low R_f value that codistilled with the dithiol was removed by flash chromatography (SiO_2–CH_2Cl_2).

1,5,9-*Trithiacyclododecane* (L^1).—This was prepared by the cyclization of 4-thiaheptane-1,7-dithiol with 1,3-dibromopropane in the presence of Cs_2CO_3.[4] 4-Thiaheptane-1,7-dithiol (9.1 g, 50 mmol) and 1,3-dibromopropane (10.1 g, 50 mmol) were dissolved in dmf (150 cm^3) under nitrogen. The resulting solution was added dropwise under nitrogen over 72 h to a suspension of caesium carbonate (9.8 g, 30 mmol) in dmf (100 cm^3) at 70 °C. After addition was complete the dmf was removed by vacuum distillation; the residue was slurried with dichloromethane (200 cm^3), filtered through Celite, and chromatographed (SiO_2–CH_2Cl_2) to yield L^1 (5.5 g, 50%) as the first fraction. Large colourless prisms suitable for *X*-ray diffraction were obtained by recrystallization from ethyl acetate–pentane. R_f = 0.77, m.p. 97—98 °C, *m/e* 222 (Found: C, 48.55; H, 7.85. Calc. for $C_9H_{18}S_3$: C, 48.60; H, 8.15%). ^1H N.m.r. ($CDCl_3$, $SiMe_4$ reference): δ 1.88 (p, 6 H), 2.70 (t, 12 H), J = 6.5 Hz.[5]

$[Cu(L^1)_2Cl_2]$. Addition of a solution of L^1 (0.89 g, 4.0 mmol) in thf (10 cm^3) to a saturated solution of anhydrous copper(II) chloride (0.27 g, 2.0 mmol) in thf produced a green solution from which the product precipitated as red-brown air-stable crystals. *X*-Ray diffraction quality crystals could be obtained by recrystallization from dmf (Found: C, 37.25; H, 6.55; Cl, 12.25; Cu, 10.60. Calc. for $C_{18}H_{36}Cl_2CuS_6$: C, 37.35; H, 6.20; Cl, 12.30; Cu, 11.00%).

Crystal Structure Determinations.—In both structure determinations a crystal was centred on an Enraf-Nonius CAD4 diffractometer and the unit cell determined by the least-squares fitting of 25 high-angle reflections obtained from a search routine. Important details of data collection and refinement of the structure appear in Table 1. Three standard reflections that were monitored every hour during data collection showed negligible decay (< 2%).

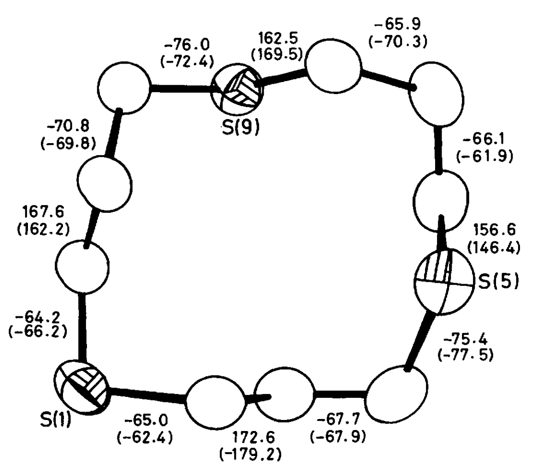

Figure 1. ORTEP drawing of L^1 showing thermal ellipsoids at the 50% probability level (hydrogen atoms are omitted for clarity). Numbering of unique atoms follows I.U.P.A.C. convention, *i.e.* atoms are numbered sequentially around ring [S(1), C(2), *etc.*]. Torsional angles of the free ligand and its $CuCl_2$ adduct (in parentheses) are also shown

Calculations were performed on a VAX 11/750 computer with use of the CRYSTALS[6] suite of crystallographic programs. Scattering factors were taken from the usual source.[7] In both cases anisotropic thermal parameters were used for all non-hydrogen atoms. Fourier difference maps revealed approximately half of the H atoms, but all were included in calculated positions with isotropic thermal parameters (U_{iso} = 0.08 Å^2).

L^1. The systematic absences (*hk*0, *h* odd; 00*l*, *l* odd) uniquely defined the space group as $P2_1/a$. The structure was solved by direct methods (MULTAN)[8] and refined by full-matrix least-squares methods. Co-ordinates of non-hydrogen atoms are presented in Table 2 and important distances and angles are collected in Table 3. The highest peak in the final difference map was 0.4 e Å^{-3}.

$[Cu(L^1)_2Cl_2]$. The systematic absences were consistent with space groups *Cc* or *C*2/*c*. The additional special condition (*hkl*, *l* = odd weak but not absent) corresponding to approximate C doubling indicated that the Cu atom was at the origin and hence on a centre of symmetry. A Patterson map showed the positions of the S and Cl atoms; the remaining non-hydrogen atoms were found by difference syntheses and refined by full-matrix least-squares techniques. Table 4 shows the co-ordinates of the non-hydrogen atoms and Table 5 includes important distances and angles. The highest peak in the final difference map was 1.4 e Å^{-3}, and located near Cu.

Results

1,5,9-Trithiacyclododecane (trithia-12-crown-3) (Figure 1) crystallizes in a conformation that in projection appears square, with two S atoms in side positions and the remaining one in a corner. This square conformation closely resembles that adopted by both the parent hydrocarbon, cyclododecane,[9] and the related crown thioether tetrathia-12-crown-4 (L^3)[4,10] (in which all four S atoms occupy corner positions). Four of the six C–S bonds and four of the six C–C bonds occur in *gauche* placement; torsional angles are summarized in Figure 1.

Table 4. Atomic co-ordinates for $[Cu(L^1)_2Cl_2]$

Atom	*x*	*y*	*z*
Cu	0.0000	0.0000	0.0000
S(1)	0.143 9(1)	0.037 9(1)	0.174 9(1)
S(5)	0.073 1(1)	0.107 6(1)	0.426 7(1)
S(9)	0.176 7(1)	0.494 0(1)	0.359 5(1)
C(2)	0.111 5(2)	−0.006 6(5)	0.260 1(3)
C(3)	0.170 1(2)	0.000 9(5)	0.359 6(3)
C(4)	0.137 9(2)	−0.040 6(4)	0.426 1(2)
C(6)	0.136 6(2)	0.259 2(4)	0.496 7(2)
C(7)	0.106 5(2)	0.422 6(4)	0.467 2(3)
C(8)	0.091 4(2)	0.468 4(5)	0.369 6(3)
C(10)	0.140 9(2)	0.508 4(4)	0.236 0(3)
C(11)	0.112 8(2)	0.353 0(5)	0.185 8(3)
C(12)	0.174 4(2)	0.238 2(5)	0.202 4(3)
Cl	−0.000 4(1)	0.232 4(1)	−0.060 0(1)

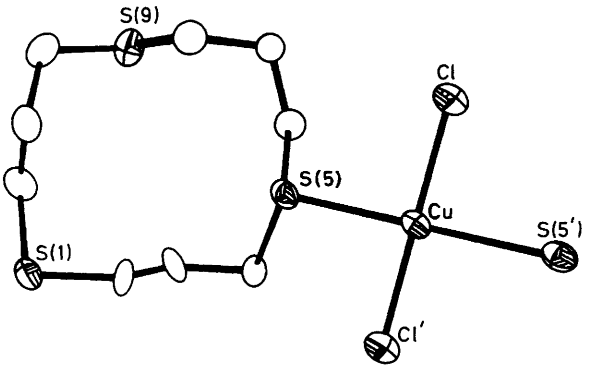

Figure 2. ORTEP drawing of $[Cu(L^1)_2Cl_2]$ showing thermal ellipsoids at the 50% probability level (hydrogen atoms are omitted for clarity). Atomic numbering as in Figure 1

Reaction of L^1 with copper(II) chloride yields $[Cu(L^1)_2Cl_2]$, in which only one sulphur [S(5)] co-ordinates directly to the copper ion; halide ions co-ordinate in preference to the other thioether groups (Figure 2). This behaviour contrasts with $[Cu(L^5)][OC_6H_2(NO_2)_3\text{-}2,4,6]_2$[11] and $[Cu(L^4)_2][BF_4]_2$,[12] in both of which hexakis(thioether) co-ordination occurs. Several workers[13,14] have previously pointed out the critical role of the anion in determining the mode of co-ordination of thioether ligands. The centrosymmetric co-ordination sphere of the Cu ion comprises S(5) atoms from each of two ligands and two chloride ions, at distances of 2.447(1) and 2.205(1) Å, respectively.[15–17] In addition, each Cu interacts weakly with S(1) [3.050(1) Å] of a neighbouring unit to yield a quasi-octahedral co-ordination sphere with a severe tetragonal elongation (Figure 3). Distances and valency angles within the macrocycle are all normal, as are the angles about the co-ordinating thioethers.

Discussion

The most interesting aspect of the present structures is the lack of change in ligand conformation upon complexation, as evidenced by comparison of the torsional angles (Figure 1). A similar parallel was reported previously by De Simone and Glick,[18] who found that co-ordination of $NbCl_5$ to L^2 does not substantially affect the conformation assumed by the thioether ligand. Instead the ligand retains the rectangular exodentate conformation of free L^2 [19] and bridges two $NbCl_5$ units. Since at least for these two ligands even complexation fails to perturb their conformations significantly, it would appear likely that the conformations of the free ligands primarily reflect intrinsic conformational preferences rather than, *e.g.* crystal-packing forces. Therefore, these observations encourage attempts to understand the conformational preferences of such ligands as studied by *X*-ray diffraction.

Table 5. Selected bond lengths (Å) and angles (°) for $[Cu(L^1)_2Cl_2]$

Cu–S(5′)	2.447 4(9)	Cu–Cl	2.205 4(8)
Cu–S(1)	3.050 4(6)		
S(1)–C(2)	1.812(4)	S(1)–C(12)	1.802(4)
S(5)–C(4)	1.822(4)	S(5)–C(6)	1.821(4)
S(9)–C(8)	1.817(4)	S(9)–C(10)	1.806(5)
C(2)–C(3)	1.523(5)	C(3)–C(4)	1.528(5)
C(6)–C(7)	1.510(5)	C(7)–C(8)	1.525(6)
C(10)–C(11)	1.526(6)	C(11)–C(12)	1.510(6)
S(1)–Cu–Cl	97.49(3)	S(1)–Cu–S(5′)	92.33(3)
S(5′)–Cu–Cl	89.61(3)		

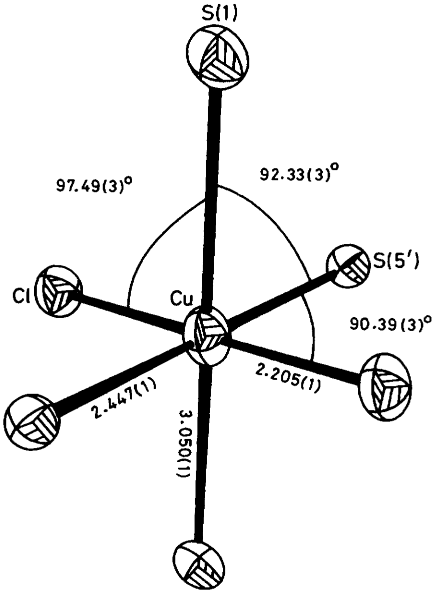

Figure 3. Co-ordination sphere of the Cu^{II} ion in $[Cu(L^1)_2Cl_2]$ showing unique bond distances (Å) and angles (°). Note that S(1) and S(5′) come from different macrocycles

In addition to the lack of conformational change upon complexation, the conformation of L^1 itself also presents unexpected features. Previous studies on ethyl-linked macrocycles have shown a strong preference for *gauche* placements at C–S bonds,[2] but this generalization does not hold for propyl-linked ligands such as L^1. Thus in both free L^1 and $[Cu(L^1)_2Cl_2]$ two of the six C–S bonds adopt *anti* placement rather than *gauche*; similarly, in both $[Ru(L^1)_2][BF_4]_2$* and $[Ni(L^6)][BF_4]_2$[4,20] half of the 12 C–S bonds assume *anti* placement. Examination of models of L^1 suggests that energetically unacceptable H–H repulsions accompany conformations with only *gauche* C–S bonds.

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* In $[Ru(L^1)_2][BF_4]_2$ both ligands assume an endodentate conformation with the three sulphur atoms occupying trigonal faces of the octahedral co-ordination sphere of Ru^{II} (S. C. Rawle, T. J. Sewell, and S. R. Cooper, *Inorg. Chem.*, in the press). This bonding mode is adopted in the absence of anions that compete for co-ordination sites at the metal centre.

Conclusions

The conformational preference of L^1 is pronounced; it is retained even upon co-ordination to $CuCl_2$. This suggests that the conformation of the free ligand may largely reflect an intrinsic energy minimum rather than crystal-packing forces.

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