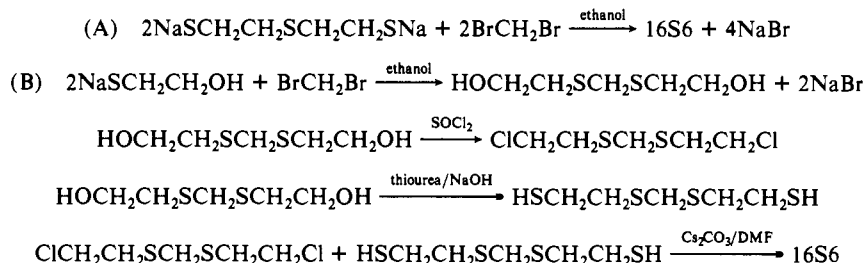Contribution from the Department of Chemistry,
University of Winnipeg, Winnipeg, Manitoba, Canada R3B 2E9

Synthesis and Structural Characterization of the Crown Thioether 1,3,6,9,11,14-Hexathiacyclohexadecane (16S6) and the Copper(I) Complex [Cu(16S6)][ClO₄]

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The crown thioether ligand 1,3,6,9,11,14-hexathiacyclohexadecane (16S6) was prepared by two different synthetic routes (methods A and B):

(A)　$2NaSCH_2CH_2SCH_2CH_2SNa + 2BrCH_2Br \xrightarrow{ethanol} 16S6 + 4NaBr$

(B)　$2NaSCH_2CH_2OH + BrCH_2Br \xrightarrow{ethanol} HOCH_2CH_2SCH_2SCH_2CH_2OH + 2NaBr$

$HOCH_2CH_2SCH_2SCH_2CH_2OH \xrightarrow{SOCl_2} ClCH_2CH_2SCH_2SCH_2CH_2Cl$

$HOCH_2CH_2SCH_2SCH_2CH_2OH \xrightarrow{thiourea/NaOH} HSCH_2CH_2SCH_2SCH_2CH_2SH$

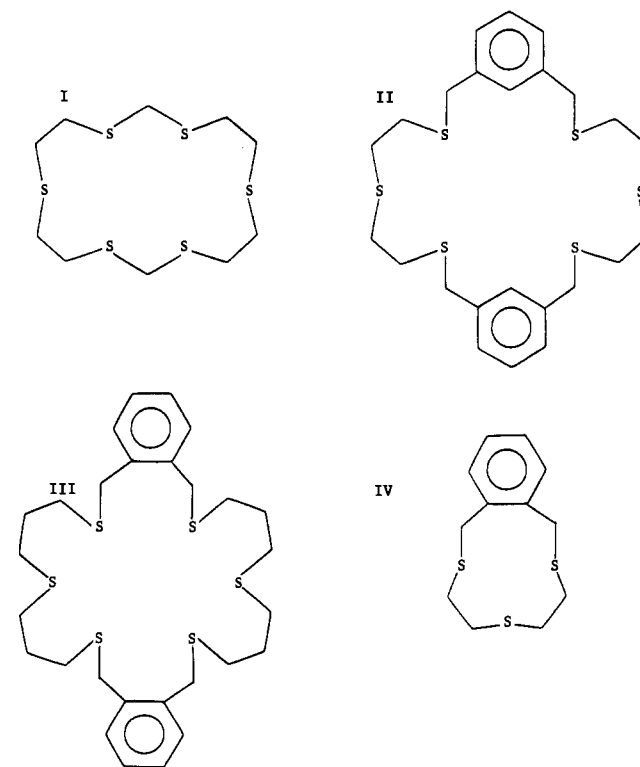$ClCH_2CH_2SCH_2SCH_2CH_2Cl + HSCH_2CH_2SCH_2SCH_2CH_2SH \xrightarrow{Cs_2CO_3/DMF} 16S6$

This compound was identified by ¹H and ¹³C{¹H} NMR spectroscopy, GCMS, and X-ray crystallography. It crystallizes in the space group $P2_1/n$ with $a = 16.386$ (4) Å, $b = 5.322$ (2) Å, $c = 17.986$ (3) Å, $\beta = 107.64$ (3)°, $V = 1494.7$ (9) Å³, and $Z = 4$. The structure was refined to final $R = 2.59\%$ and $R_w = 2.95\%$ for 1663 reflections with $F_o^2 > 3\sigma(F_o^2)$. Four of the S atoms are exodentate and two of the S atoms are endodentate to the 16-membered ring. The Cu(I) complex [Cu(16S6)][ClO₄] was prepared from the reaction of 16S6 with [Cu(CH₃CN)₄][ClO₄] and characterized by ¹H and ¹³C{¹H} NMR spectroscopy and X-ray crystallography. It crystallizes in the space group $P2_12_12_1$ with $a = 8.464$ (5) Å, $b = 18.321$ (9) Å, $c = 12.477$ (6) Å, $V = 1934$ (2) Å³, and $Z = 4$. The structure was refined to $R = 5.15\%$ and $R_w = 5.51\%$ for 1445 reflections with $F_o^2 > 3\sigma(F_o^2)$. The Cu atom is in a tetrahedral environment bonded to four of the six S atoms of 16S6. The remaining two S atoms are oriented toward the Cu atom at nonbonding distances.

Introduction

Although thioethers have moderately low σ-donor and π-acceptor abilities, the bonding analogy between thioether and phosphine ligands suggests that transition-metal complexes utilizing SR₂ donor ligands might mimic or complement those containing PR₃.[1,2]　Indeed, recent studies employing crown thioether ligands[3-43] such as 1,4,7-trithiacyclononane (9S3)[3-20]

Chart I

and 1,4,7,10,13,16-hexathiacyclohexadecane (18S6)[21-31] have shown that these ligands may be capable of producing transi-

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tion-metal complexes with some unique properties. For example, the low-spin states of Co(II)[7,8,10,11,23,29] and Fe(II)[8,17] are stabilized by an S_6 ligand sphere and this environment also stabilizes some unusual oxidation states such as Pd(III),[18] Pt(III),[13] and Rh(I-I).[15,20] Perhaps more importantly, the Rh(I) complex of 1,4,8,11-tetrathiacyclotetradecane (14S4) exemplifies the effect thioether donors may have on complex reactivity. This complex is a strong nucleophile and undergoes oxidative addition with CH_2Cl_2 at room temperature, a result that has been attributed to the low π-acidity of the thioether donors.[41]

While the majority of these crown thioether ligands are ideal for studying the electronic effects of the SR_2 moiety, the nature of their encapsulating coordination modes does not usually allow for coordinative unsaturation and the subsequent type of reactivity observed for [Rh(14S4)]$^+$. We have, therefore, designed and prepared a series of crown thioether ligands that have the potential to bind a metal atom, or atoms, while simultaneously allowing for the interaction of ancillary ligands or substrate molecules (see Chart I for examples).

In this paper, we outline the preparation of the crown thioether ligand 16S6 (I in Chart I) and the characterization of this compound by ^{13}C and ^1H NMR spectroscopy, GCMS, and X-ray crystallography. An investigation of the ligand's binding ability is also described, with the Cu(I) ion used as a simple probe for determing the conformational effects of complexation. The complex [Cu(16S6)][ClO$_4$] is characterized by variable-temperature $^{13}C\{^1H\}$ and ^1H NMR spectroscopy and an X-ray structure determination.

Experimental Section

[Cu(CH$_3$CN)$_4$][(ClO$_4$)] was prepared by the literature method.[44] 2-Mercaptoethanol, 3-thiapentane-1,5-dithiol, and dibromomethane were purchased from Aldrich and used as received. Absolute ethanol was purified by distillation from CaH$_2$ under N$_2$. All reactions were conducted under an atmosphere of N$_2$, and solvents were degassed prior to use. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded at 300.1 and 75.4 MHz, respectively, on a Bruker AM300 spectrometer locked to the deuterated solvent. ^1H NMR simulation calculations were performed by using the program LAOCOON. Infrared spectra were recorded on a Perkin-Elmer 781 grating spectrometer. GCMS experiments were routinely performed to monitor reaction progress by using a HP 5970 Series MSD coupled to a HP 5890a gas chromatograph.

Preparation of 3,5-Dithiaheptane-1,7-diol. Na metal (11.64 g, 506 mmol) was dissolved in anhydrous ethanol (500 mL). 2-Mercaptoethanol (39.56 g, 506 mmol) was added and the resulting solution stirred for 1 h. This solution was heated to reflux under N$_2$ and dibromomethane (44.01 g, 253 mmol) in anhydrous ethanol (100 mL) added dropwise over a period of 4 h. The mixture was then refluxed for a further 12 h, during which time a white solid precipitated and the solution slowly changed to orange-brown. The solvent was removed and the residue taken up in diethyl ether (300 mL). The solids were removed by filtration and the solution dried over MgSO$_4$. The diethyl ether was removed in vacuo and the resulting oily residue vacuum distilled (bp 149–152 °C/1 mmHg). Yield: 26.1 g (61%). MS: m/e 168. IR: ν(OH) 3340 cm^{-1} (vs, br). $^{13}C\{^1H\}$ NMR (CDCl$_3$): δ 60.74 (CH$_2$OH), 35.41 (CH$_2$S), 33.99 (SC-H$_2$S). ^1H NMR (CDCl$_3$): δ 3.77 (t, 4 H, CH$_2$O) (^3J = 5.9 Hz), 3.72 (s, 2 H, SCH$_2$S), 2.91 (s, 2 H, OH), 2.83 (t, CH$_2$S, 4 H). Anal. Calcd for C$_5$H$_{12}$O$_2$S$_2$: C, 35.68; H, 7.20; S, 38.11. Found: C, 35.31; H, 7.20; S, 38.14.

Preparation of 3,5-Dithiaheptane-1,7-dithiol. To a suspension of thiourea (6.74 g, 88.6 mmol) in 3,5-dithiaheptane-1,7-diol (7.45 g, 44.3 mmol) under N$_2$ was added HBr (aq, 48%) (22.4 g, 132.9 mmol). The mixture was refluxed for 9 h and then cooled to room temperature. Sodium hydroxide (5.32 g, 132.9 mmol) in H$_2$O (50 mL) was added dropwise, during which time a white solid precipitated. Upon heating, the solid dissolved. This solution was then refluxed for another 9 h, during which time the product separated as an oil. The mixture was cooled to room temperature and extracted with CH$_2$Cl$_2$ (3 × 50 mL). The organic layer was dried over Na$_2$SO$_4$ and filtered. The solvent was removed in vacuo and the oily residue vacuum distilled. The fraction distilling from 120–155 °C (2 mmHg) was collected and redistilled fractionally (bp 135–140 °C/2 mmHg). Yield: 1.4 g (16%). MS: m/e 200. IR: ν(SH) 2540 cm^{-1} (m). $^{13}C\{^1H\}$ NMR (CDCl$_3$): δ 36.06 (CH$_2$S), 34.52 (SCH$_2$S), 24.19 (CH$_2$SH). ^1H NMR (CDCl$_3$): δ 3.71 (s, 2 H, SCH$_2$S), 2.82 (m, 8 H, CH$_2$CH$_2$), 1.71 (t, 2 H, SH). A satisfactory elemental analysis could not be obtained.

Preparation of 1,7-Dichloro-3,5-dithiaheptane. *Extreme Caution! Vesicant.* Thionyl chloride (5.21 g, 40 mmol) was added via syringe to 3,5-dithiaheptane-1,7-diol (3.11 g, 18.5 mmol) dissolved in CH$_2$Cl$_2$ (15 mL) under N$_2$ in a 50-mL Schlenk flask. During the addition, gas was evolved and the solution developed an orange-brown color. The mixture was stirred for 1 h and then the solvent removed in vacuo. CH$_2$Cl$_2$ (10 mL) was added followed by NaHCO$_3$ (aq, saturated) (5 mL) and the mixture stirred vigorously. The two-phase system was then filtered through phase separation paper and the organic layer dried over MgSO$_4$. After filtration and removal of solvent in vacuo, the product was obtained as a pale orange-brown liquid. Due to the dangerous nature of this product no further purification was attempted. However, the material was >97% pure by GCMS. MS: m/e 204. Yield: 2.50 g (66%). $^{13}C\{^1H\}$ (CDCl$_3$): δ 43.24 (CH$_2$Cl), 36.08 (CH$_2$S), 34.11 (SCH$_2$S). ^1H NMR (CDCl$_3$): δ 3.75 (s, 2 H, SCH$_2$S), 3.68 (t, 4 H, CH$_2$Cl) (^2J = 7.9 Hz), 3.00 (t, CH$_2$S, 4 H).

Preparation of 1,3,6,9,11,14-Hexathiacyclohexadecane (16S6). Method A. 3-Thiapentane-1,5-dithiol (15.9 g, 103 mmol) was added to anhydrous ethanol (250 mL) in which Na metal (4.73 g, 206 mmol) had been dissolved and the resulting solution was stirred for 1 h. Dibromomethane (17.9 g, 103 mmol) was then dissolved in anhydrous ethanol (250 mL) and both solutions simultaneously added dropwise to anhydrous ethanol (500 mL) by using constant-addition funnels. The addition was over a period of 4 h, during which time a white precipitate formed. The mixture was stirred overnight and then filtered. The filtrate was concentrated and the residue extracted with CH$_2$Cl$_2$ (300 mL). The CH$_2$Cl$_2$ fraction was filtered through Celite and the filtrate evaporated, leaving an oily residue. The residue was then dissolved in a minimum amount of CH$_2$Cl$_2$ and added dropwise to boiling ethanol (100 mL). Upon cooling, a white solid was deposited, which was filtered and recrystallized from CHCl$_3$. Yield: 1.44 g (8.4%). **Method B.** Cesium carbonate (3.79 g, 12 mmol) was suspended in DMF (250 mL) under an atmosphere of N$_2$(g). To this mixture was added a solution of 3,5-dithiaheptane-1,7-dithiol (2.12 g, 11 mmol) and 1,7-dichloro-3,5-dithiaheptane (2.17 g, 11 mmol) in DMF (45 mL). The addition was over a period of 6 h with the reaction temperature maintained at 50–55 °C. After the addition period, the mixture was allowed to cool to room temperature and stirred for a further 12 h. The DMF was removed in vacuo and the resulting oily residue and white solid extracted with CH$_2$Cl$_2$. This was filtered and then washed with H$_2$O (2 × 50 mL). The CH$_2$Cl$_2$ solution was dried over MgSO$_4$ and filtered, and the filtrate was taken to dryness. The resulting residue was then treated as in method A. Yield: 2.45 g (62%).

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Table I. Crystallographic Data for 16S6 and [Cu(16S6)][ClO4]

chem formula	$C_{10}H_{20}S_6$	$C_{10}H_{20}ClCuO_4S_6$
fw	332.7	495.7
a, Å	16.386 (4)	8.464 (5)
b, Å	5.322 (2)	18.321 (9)
c, Å	17.986 (3)	12.477 (6)
β, deg	107.64 (3)	
space group	$P2_1/n$	$P2_12_12_1$
V, Å^3	1494.7 (9)	1934 (2)
ρ(calcd), g cm^{-3}	1.48	1.70
Z	4	4
μ, cm^{-1}	8.11	18.25
λ, Å	0.710 69	0.710 69
T, °C	24	24
$R(F_o^2)$, %	2.59	5.15
$R_w(F_o^2)$, %	2.95	5.51

Mp: 92.5–94.5 °C. MS: m/e 332. $^{13}C\{^1H\}$ NMR (CDCl$_3$): δ 36.54 (SCH$_2$S), 32.02 (CH$_2$S), 31.90 (CH$_2$S). ^{1}H NMR (CDCl$_3$): δ 3.80 (s, 4 H, SCH$_2$S) ($^2J = -13.0$ Hz; $^3J = 6.1$ and 9.1 Hz; see Figure 4), 2.91 (m, 16 H, CH$_2$CH$_2$). Anal. Calcd for C$_{10}$H$_{20}$S$_6$: C, 36.10; H, 6.07; S, 57.83. Found: C, 36.05; H, 6.10; S, 58.47.

Preparation of [Cu(16S6)(ClO$_4$)]. *Caution! Perchlorate salts of metal complexes with organic ligands are potentially explosive.* 16S6 (246 mg, 0.74 mmol) was suspended in acetonitrile (3 mL) and dichloromethane added until a clear solution resulted. [Cu(CH$_3$CN)$_4$]-[ClO$_4$] (242 mg, 0.74 mmol) dissolved in acetonitrile (4.5 mL) was added and the mixture warmed to 40 °C. The resulting clear, colorless solution was stirred for 1 h and cooled to room temperature and the solvent removed in vacuo. The remaining white solid was recrystallized from acetonitrile resulting in colorless needles. Yield: 324 mg (88%). IR: ν(ClO) 1090 cm^{-1} (vs, br). $^{13}C\{^1H\}$ NMR (CD$_3$CN): δ 38.91 (SCH$_2$S), 36.00 (CH$_2$), 35.87 (CH$_2$). ^{1}H NMR (CD$_3$CN): δ 3.91 (s, 4 H, SCH$_2$S), 3.06 (s, 16 H, CH$_2$CH$_2$). Anal. Calcd for C$_{10}$H$_{20}$ClCuO$_4$S$_6$: C, 24.23; H, 4.07; S, 38.82. Found: C, 24.37; H, 4.05; S, 37.95.

General X-ray Diffraction Data Collection, Solution, and Refinement. Diffraction experiments were performed on a four-circle Syntex P2$_1$ diffractometer with graphite-monochromatized Mo Kα radiation. The initial orientation matrices were obtained from 15 machine-centered reflections selected from rotation photographs. Partial rotation photographs around each axis were used to determine the crystal system. Ultimately, 30 high-angle reflections were used to obtain the final lattice parameters and orientation matrices. Machine parameters, crystal data, and data collection parameters are summarized in Table I and detailed in Table S-I. The intensities of three standard reflections were recorded every 197 reflections and showed no statistically significant changes over the duration of the data collections. The data were processed by using the SHELX-76 program package on the computing facilities shared with the University of Manitoba. The absorption coefficients were small and ψ-scans recorded showed no significant absorption effects. Thus, no absorption correction was applied to the data. Refinement was carried out by using full-matrix least-squares techniques on F minimizing the function $\sum w(|F_o| - |F_c|)^2$, where $w = 4F_o^2/\sigma^2(F_o^2)$ and F_o and F_c are the observed and calculated structure factors. Atomic scattering factors[45] and anomalous dispersion[46] terms were taken from the usual sources. Fixed H-atom contributions were included with C–H distances of 0.95 Å and thermal parameters equal to 1.1 times the isotropic thermal parameter of the bonded C atoms. No H atoms were refined, but all values were updated as refinement continued.

Structure Determination of 16S6. Crystals of 16S6 were grown by slow evaporation of a CHCl$_3$ solution of the compound. Preliminary photography was consistent with a monoclinic crystal system. Observed extinctions were consistent with space group $P2_1/n$. Intensity data ($\pm h, +k, +l$) were collected in one shell (4.5° < 2θ < 45°). A total of 1940 reflections were collected, and 1663 unique reflections with $F_o^2 > 3\sigma(F_o^2)$ were used in the refinement. The six S atom positions were determined by direct methods from the E map with highest figure of merit. The remaining non-hydrogen atoms were located from successive difference Fourier map calculations. In the final cycles of refinement, sulfur and carbon atoms were assigned anisotropic thermal parameters. This resulted in $R = \sum||F_o| - |F_c|/\sum|F_o|| = 0.0259$ and $R_w = (\sum w(|F_o| - |F_c|)^2/\sum w F_o^2)^{1/2} = 0.0295$ at final convergence.

The Δ/σ value for any parameter in the final cycle was less than 0.004. A final difference Fourier map calculation showed no peaks of

Table II. Positional Parameters^a for 16S6

atom	x	y	z
S1	2709 (1)	6907 (1)	3243 (1)
S2	6317 (1)	11464 (1)	5147 (1)
S3	5395 (1)	6094 (1)	3216 (1)
S4	2733 (1)	8562 (1)	8307 (1)
S5	6386 (1)	7959 (1)	10299 (1)
S6	5455 (1)	7970 (1)	8392 (1)
C1	2869 (1)	9367 (5)	3958 (1)
C2	6161 (2)	8486 (5)	4629 (1)
C3	5700 (2)	8933 (5)	3787 (1)
C4	4393 (1)	5402 (4)	3402 (1)
C5	3678 (1)	7146 (5)	2967 (1)
C6	2736 (2)	1450 (5)	8838 (1)
C7	6542 (1)	10479 (5)	9681 (1)
C8	5764 (1)	10799 (5)	8977 (1)
C9	4446 (2)	7273 (5)	8571 (1)
C10	3732 (1)	8867 (5)	8071 (1)

^{a} Multiplied by 10^4.

Table III. Selected Bond Distances and Angles for 16S6

Distances (Å)			
S1–C1	1.798 (2)	S4–C6	1.809 (2)
S1–C5	1.807 (2)	S4–C10	1.819 (2)
S3–C3	1.810 (2)	S6–C8	1.819 (2)
S3–C4	1.810 (2)	S6–C9	1.816 (2)
S2–C2	1.817 (3)	S5–C7	1.808 (2)
C2–C3	1.492 (3)	C7–C8	1.509 (3)
C4–C5	1.514 (3)	C9–C10	1.502 (3)

| Angles (deg)			
C1–S1–C5	101.3 (1)	S3–C3–C2	114.2 (2)
C3–S3–C4	100.1 (1)	S3–C4–C5	112.5 (2)
C6–S4–C10	100.9 (1)	S1–C5–C4	114.9 (2)
C8–S6–C9	100.1 (1)	S5–C7–C8	111.1 (2)
S2–C2–C3	109.3 (2)	S6–C9–C10	111.3 (2)

chemical significance; the largest was 0.25/Å^3 and was associated with the C1 carbon atom. Atomic positional parameters are summarized in Table II, and selected bond distances and angles, in Table III. Anisotropic thermal parameters (Table S-II), hydrogen atom parameters (Table S-III), and values of 10|F_o| and 10|F_c| (Table S-VI) are deposited as supplementary material.

Structure Determination of [Cu(16S6)][(ClO$_4$)]. Crystals of [Cu-(16S6)][ClO$_4$] were obtained by recrystallization from acetonitrile. Preliminary photography was consistent with an orthorhombic crystal system. Observed extinctions were consistent with space group $P2_12_12_1$. Intensity data ($+h, +k, +l$) were collected in one shell (4.5° < 2θ < 45°). A total of 1862 reflections were collected, and 1445 unique reflections with $F_o^2 > 3\sigma(F_o^2)$ were used in the refinement. The Cu atom position was determined by conventional heavy-atom methods, and the remaining non-hydrogen atoms were located from successive difference Fourier map calculations. In the final cycles of refinement, the copper, chlorine, sulfur, and oxygen atoms were assigned anisotropic thermal parameters. The carbon atoms were assigned isotropic thermal parameters. The correct enantiomorph was determined by inversion of the atomic positions and comparison of resulting R and R_w values for the possible enantiomorphs at convergence. This resulted in $R = \sum||F_o| - |F_c|/\sum|F_o|| = 0.0515$ and $R_w = (\sum w(|F_o| - |F_c|)^2/\sum w F_o^2)^{1/2} = 0.0551$ at final convergence for the correct enantiomorph.

The Δ/σ value for any parameter in the final cycle was less than 0.033. A final difference Fourier map calculation showed no peaks of chemical significance; the largest was 0.92 e/Å^3 and was associated with the chlorine atom. Atomic positional parameters are summarized in Table IV, and selected bond distances and angles, in Table V. Thermal parameters (Table S-IV), hydrogen atom parameters (Table S-V), and values of 10|F_o| and 10|F_c| (Table S-VII) are deposited as supplementary material.

Results

Synthesis. The macrocyclic thioether ligand 16S6 can be prepared by two different synthetic routes. The simplest is the reaction described in eq 1, which employs high-dilution techniques.

method A

$$2NaSCH_2CH_2SCH_2CH_2SNa + 2BrCH_2Br \xrightarrow{\text{ethanol}}$$
$$16S6 + 4NaBr \quad (1)$$
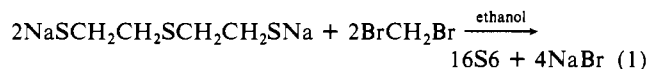
(45) Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*; Kynoch: Birmingham, England, 1974.

(46) (a) Cromer, D. T.; Mann, J. B. *Acta. Crystallogr., Sect. A: Cryst. Phys., Diffr., Theor. Gen. Crystallogr.* **1968**, *A24*, 321; **1968**, *A24*, 390.

Table IV. Positional Parameters[a] for [Cu(16S6)][ClO$_4$]

atom	x	y	z
Cu	5786 (1)	8716 (1)	6402 (1)
Cl	9897 (3)	11078 (2)	5586 (3)
S1	7668 (3)	8174 (2)	7475 (2)
S2	5212 (5)	6947 (2)	7506 (3)
S3	3175 (3)	8404 (2)	6620 (2)
S4	5419 (3)	9939 (1)	6762 (2)
S5	4566 (4)	9819 (2)	4359 (2)
S6	7107 (3)	8451 (1)	4847 (2)
O1	11279 (18)	10830 (10)	5221 (12)
O2	9995 (18)	11846 (10)	5610 (22)
O3	8859 (28)	11072 (10)	4693 (19)
O4	9069 (31)	10632 (17)	6186 (13)
C1	6750 (15)	7416 (7)	8201 (11)
C2	3418 (17)	7283 (8)	8101 (12)
C3	3079 (17)	8084 (7)	8001 (11)
C4	2360 (14)	9336 (6)	6771 (10)
C5	3451 (13)	9861 (6)	7321 (9)
C6	5033 (12)	10398 (6)	5480 (9)
C7	6498 (16)	9718 (8)	3734 (12)
C8	7738 (14)	9341 (6)	4388 (9)
C9	8945 (15)	8140 (7)	5451 (10)
C10	8618 (17)	7649 (8)	6410 (11)

[a] Multiplied by 10^4.

Table V. Selected Bond Distances and Angles for [Cu(16S6)][ClO$_4$]

Distances (Å)			
Cu–S1	2.305 (3)	S5–C6	1.799 (11)
Cu–S3	2.299 (3)	S5–C7	1.821 (14)
Cu–S4	2.306 (3)	S6–C8	1.808 (12)
Cu–S6	2.291 (3)	S6–C9	1.820 (13)
S1–C1	1.831 (13)	C2–C3	1.501 (19)
S1–C10	1.827 (14)	C4–C5	1.499 (16)
S2–C1	1.785 (13)	C7–C8	1.499 (18)
S2–C2	1.800 (14)	C9–C10	1.522 (18)
S3–C3	1.822 (14)	Cl–O1	1.334 (13)
S3–C4	1.852 (12)	Cl–O2	1.410 (18)
S4–C5	1.811 (11)	Cl–O3	1.418 (16)
S4–C6	1.837 (11)	Cl–O4	1.311 (19)

Nonbonding Distances (Å)			
Cu–S2	3.555 (3)	Cu–S5	3.413 (3)

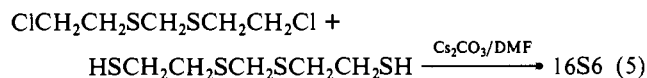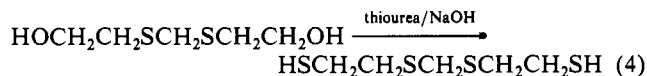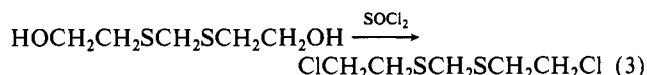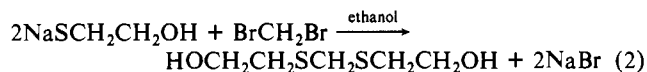| Angles (deg)			
S1–Cu–S3	119.2 (1)	C3–S3–C4	100.6 (6)
S1–Cu–S4	113.5 (1)	S3–C4–C5	114.1 (8)
S3–Cu–S4	95.1 (1)	C4–C5–S4	116.2 (8)
S1–Cu–S6	93.6 (1)	C5–S4–C6	102.0 (5)
S3–Cu–S6	121.1 (1)	S4–C6–S5	116.5 (6)
S4–Cu–S6	115.8 (1)	C6–S5–C7	101.3 (6)
Cu–S1–C1	108.7 (4)	S5–C7–C8	116.3 (9)
Cu–S1–C10	96.2 (5)	C7–C8–S6	112.4 (9)
Cu–S3–C3	103.6 (5)	C8–S6–C9	99.3 (6)
Cu–S3–C4	98.1 (4)	S6–C9–C10	110.8 (9)
Cu–S4–C5	97.0 (4)	C9–C10–S1	109.9 (9)
Cu–S4–C6	107.4 (4)	C10–S1–C1	98.5 (6)
Cu–S6–C8	102.8 (4)	O1–Cl–O2	107.1 (11)
Cu–S6–C9	97.6 (4)	O1–Cl–O3	105.8 (14)
S1–C1–S2	115.8 (8)	O1–Cl–O4	116.9 (18)
C1–S2–C2	104.5 (7)	O2–Cl–O3	93.5 (12)
S2–C2–C3	117.5 (10)	O2–Cl–O4	129.8 (17)
C2–C3–S3	112.6 (10)	O3–Cl–O4	96.5 (12)

Method A is a slight modification of that previously described by Ochrymowycz for the preparation of a series of macrocyclic thioethers.[21] The yields are low, varying from ca. 5 to 10% for any particular attempt, but the desired product can be isolated with minimal manipulation and avoiding chromatography. The reaction sequence to form 16S6 requires the coupling of two intermediate fragments, NaSCH$_2$CH$_2$SCH$_2$CH$_2$SCH$_2$Br, end to end and subsequent cyclization to form the 16-membered ring. The potential problems in this cyclization step are the competition from polymerization and the closure of the intermediate fragment to form the smaller eight-membered ring. Although a lot of polymeric material is formed in this reaction, we observe no evidence for the formation of the smaller ring product. This may
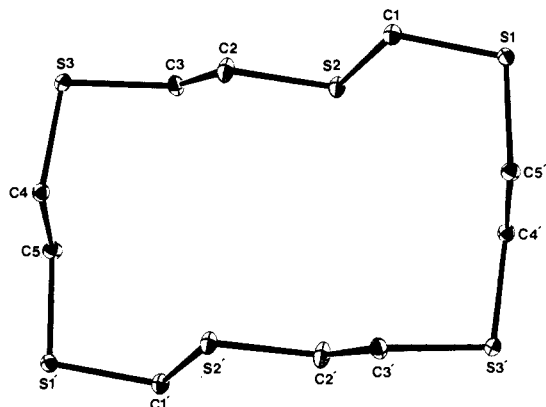
Figure 1. Perspective ORTEP drawing of 16S6, molecule 1, showing the atom-numbering scheme. Thermal ellipsoids of 20% are shown.

be due to the destabilizing effect of incorporating a rigid SCH$_2$S unit in a potentially strained, eight-membered-ring system.

The alternate strategy (method B) requires preparing the larger dithiol and dichloro fragments needed for a one-step formation of 16S6 and then employs the Cs$^+$-mediated cyclization method of Buter and Kellogg for ring closure.[47] This is outlined in eq 2–5.

method B

$$2NaSCH_2CH_2OH + BrCH_2Br \xrightarrow{\text{ethanol}} HOCH_2CH_2SCH_2SCH_2CH_2OH + 2NaBr \quad (2)$$

$$HOCH_2CH_2SCH_2SCH_2CH_2OH \xrightarrow{\text{SOCl}_2} ClCH_2CH_2SCH_2SCH_2CH_2Cl \quad (3)$$

$$HOCH_2CH_2SCH_2SCH_2CH_2OH \xrightarrow{\text{thiourea/NaOH}} HSCH_2CH_2SCH_2SCH_2CH_2SH \quad (4)$$

$$ClCH_2CH_2SCH_2SCH_2CH_2Cl +$$
$$HSCH_2CH_2SCH_2SCH_2CH_2SH \xrightarrow{\text{Cs}_2\text{CO}_3/\text{DMF}} 16S6 \quad (5)$$

The reactions to prepare the diol and dichloro compounds (eq 2 and 3) are clean and give moderately good yields of 61 and 66%, respectively. However, we found the preparation of the dithiol (eq 3) was tedious and the product difficult to clean. A persistent side product was 3-thiapentane-1,5-dithiol, which is presumably formed via the cleavage of a S–C bond at the methylene linkage. This was reflected in a poor yield of 16% for the dithiol. The final cyclization step proceeds smoothly, and the yield for this ring closure reaction is good, 62%. Overall the yield of 16S6 is 4% via method B. Although the final cyclization step is clearly superior to that performed in method A, the final product is obtained in effectively the same quantity. For this reason and due to the time required for method B we recommend method A because of its simplicity. It should be noted, however, that for other large ring thioether macrocycles of this type the formation of the smaller ring compound is heavily favored by using method A and the only practical method of synthesis is that of method B. This is the case for ligands II–IV shown in Chart I.

X-ray Structure of 16S6. The unit cell contains four discrete molecules of 16S6 such that the asymmetric unit contains two independent halves of a molecule, each on a crystallographic center of inversion. Perspective views of the crystallographically independent molecules of 16S6 are shown in Figures 1 and 2. The closest intermolecular nonbonded contact is 2.39 Å between H3B and H10B. Complete listings of interatomic distances and angles are found in Table III. Sulfur–carbon bond distances range from 1.798 (2) to 1.819 (2) Å, and carbon–carbon bond distances range from 1.492 (3) to 1.514 (3) Å. Although the carbon–carbon distances are somewhat shorter than those usually found for

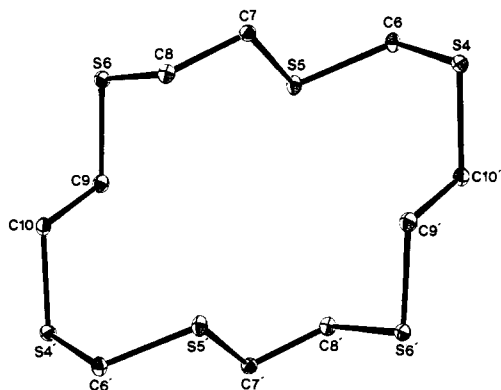(47) Buter, J.; Kellogg, R. M. *J. Org. Chem.* **1981,** 46, 4481–4485.

Figure 2. Perspective ORTEP drawing of 16S6, molecule 2, showing the atom-numbering scheme. Thermal ellipsoids of 20% are shown.

Table VI. Torsional Angles (deg) Associated with 16S6 and [Cu(16S6)][ClO₄]

16S6			
S1–C1–S2–C2	−169.8	S4–C6–S5–C7	64.8
C1–S2–C2–C3	163.7	C6–S5–C7–C8	166.6
S2–C2–C3–S3	173.6	S5–C7–C8–S6	56.4
C2–C3–S3–C4	84.7	C7–C8–S6–C9	112.1
C3–S3–C4–C5	−74.1	C8–S6–C9–C10	−80.3
S3–C4–C5–S1′	170.4	S6–C9–C10–S4	172.6
C4–C5–S1′–C1′	−94.7	C9–C10–S4–C6	−103.6
C5–S1′–C1′–S2′	−72.0	C10–S4–C6–S5	−58.8
[Cu(16S6)][ClO₄]			
S1–C1–S2–C2	102.8	S4–C6–S5–C7	95.2
C1–S2–C2–C3	61.7	C6–S5–C7–C8	63.6
S2–C2–C3–S3	52.8	S5–C7–C8–S6	54.8
C2–C3–S3–C4	−170.2	C7–C8–S6–C9	−173.9
C3–S3–C4–C5	72.2	C8–S6–C9–C10	147.5
S3–C4–C5–S4	53.4	S6–C9–C10–S1	−65.7
C4–C5–S4–C6	−69.6	C9–C10–S1–C1	−158.3
C5–S4–C6–S5	−87.2	C10–S1–C1–S2	−66.9

C(sp³)–C(sp³) bonds, these distances compare well to those found previously for other macrocyclic thioethers.

The conformation of crown thioethers is best described by identifying the torsional angles associated with the ring. These are listed in Table VI for 16S6. The torsional angles favored for crown thioethers have been shown by Cooper to produce –SCH₂CH₂SCH₂CH₂S– "brackets" that resemble a right triangle in projection.[30] These brackets are formed due to the propensity of S–C bonds to favor a gauche placement and C–C bonds to favor an anti placement when part of an –SCH₂CH₂SCH₂CH₂S– string. The result is that almost every crown thioether identified by X-ray diffraction can be described in terms of how these bracket linkages fit together.

The overall ring conformation observed for 16S6 can also be described in these terms, but the conformation is slightly different for each of the two independent molecules. Molecule 1 (Figure 1) is easily seen to be the result of two bracket units joined at S1 and S2 by the methylene linkage. The result is a conformation that appears rectangular in projection and has sulfur atoms (S1, S3, S1′, and S3′) at the four corners. This requires four out of six S–C bonds to be gauche and two out of two C–C bonds to be anti. Overall this results in a designation of two S atoms (S2 and S2′) as endodentate and four S atoms (S1, S3, S1′, and S3′) as exodentate to the ring. For molecule 2 (Figure 2), the rectangular shape is somewhat less pronounced as each of the bracket units is distorted on one edge. This is the result of having five out of six S–C bonds with a gauche placement but only one out of two C–C bonds with an anti placement. Molecule 2 is also designated as having two S atoms (S5 and S5′) endodentate and four S atoms (S4, S6, S4′, and S6′) exodentate to the ring. The presence of six gauche placements for molecule 2 versus only four gauche placements for molecule 1 is seen as the major conformational difference. It appears that a slight degree of rotation about the S2–C2 bond in molecule 1 would essentially produce the conformation observed for molecule 2. This conversion would also
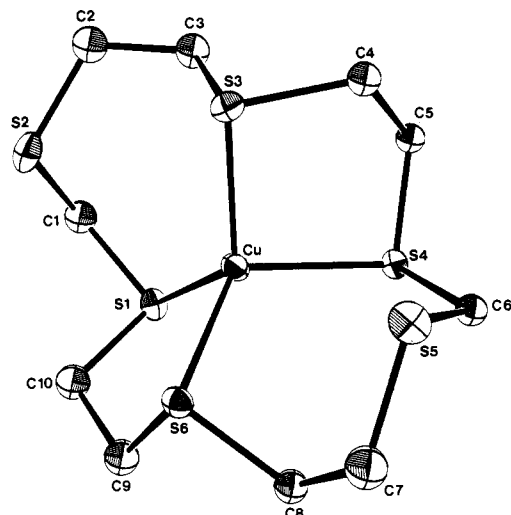

Figure 3. Perspective ORTEP drawing of the [Cu(16S6)]⁺ cation, showing the atom-numbering scheme. Thermal ellipsoids of 20% are shown.

result in changing the anti placements of the S2–C1 and C2–C3 bonds adjacent to this linkage to gauche, as observed for molecule 2. This interconversion process would presumably require little energy, since the energetic difference between the two conformations must be small to allow crystallization in the same unit cell.

X-ray Structure of [Cu(16S6)][ClO₄]. The unit cell contains four [Cu(16S6)]⁺ cations and four [ClO₄]⁻ anions. A perspective view of the cation is shown in Figure 3. The closest cation to anion nonbonded contact is 2.53 Å between O4 and H8A, and the closest approach of the ClO₄ anion to the Cu atom is 4.49 Å for O4. Complete listings of interatomic distances and angles may be found in Table V.

The Cu(I) ion is encapsulated by the 16S6 ligand bonding directly to S1, S3, S4, and S6 at distances of 2.305 (3), 2.299 (3), 2.306 (3), and 2.291 (3) Å, respectively. The remaining two sulfur atoms are directed at the Cu center but are at nonbonding distances of 3.555 (3) Å for S2 and 3.413 (3) Å for S5. The Cu(I) ion is in a tetrahedral environment with S–Cu–S angles ranging from 93.6 (1) and 95.5 (1)° for the five-membered chelate rings to 115.8 (1) and 119.2 (1)° for the seven-membered chelate rings. The average S–Cu–S angle is 110 (11)°. The sulfur–carbon bond distances range from 1.785 (13) to 1.852 (12) Å, and the carbon–carbon bond distances range from 1.499 (16) to 1.522 (18) Å. These ranges are slightly larger than those found for the free ligand, 16S6, but are well within expected limits. The perchlorate anion has expected tetrahedral geometry although the large thermal parameters of the atoms suggest some degree of disorder. In spite of the presumed disorder, the Cl–O distances (range 1.311 (19)–1.418 (18) Å) and the O–Cl–O angles (range 93.5 (12)–129.8 (17)°) are comparable to those in other determinations.[48]

The torsional angles of the 16S6 ligand in [Cu(16S6)]⁺ are useful for a comparison to those observed for the free 16S6 ligand, since they may give some indication of the amount of conformational adjustment required for the ligand to coordinate in a tetrahedral geometry. This is of interest, since the majority of the sulfur atoms in crown thioethers are exodentate and must be converted to endodentate for complexation to be favorable.[2] The torsional angle analysis shows that 8 out of 12 S–C bonds are in gauche placements and 4 out of 4 C–C bonds are in gauche placements. The major change from the free ligand form is the need for C–C bonds to have gauche placements in the bonded conformation. This is simply the result of placing a C–C linkage in the backbone of a metal chelate ring. However, this entirely disrupts the bracket formations favored in the uncomplexed ligand and may restrict the coordinating ability of certain crown thioether ligands.

NMR Spectroscopy. The ¹H and ¹³C{¹H} NMR spectra of the free 16S6 ligand are routine. The only feature of note is the
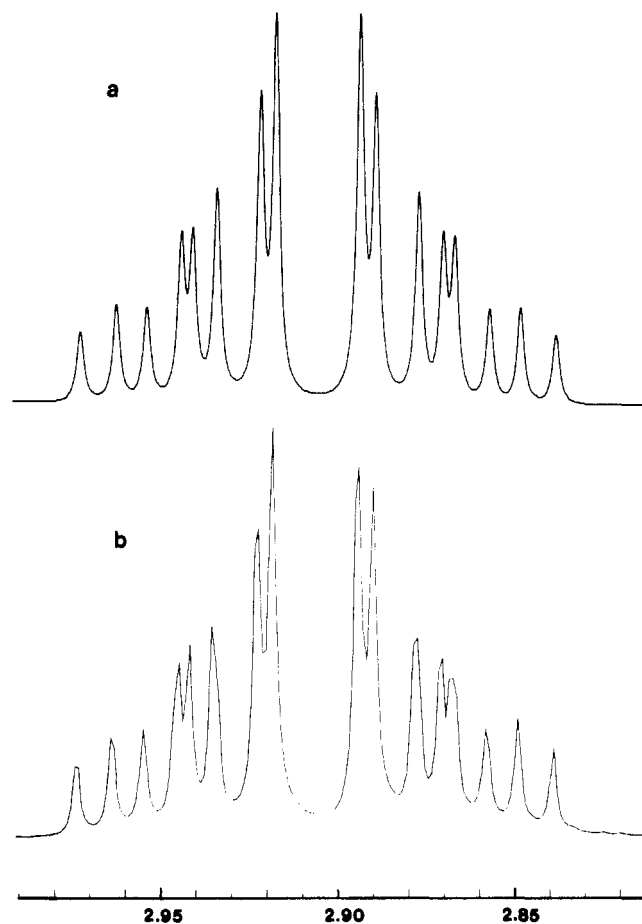
Figure 4. ^1H NMR spectra of the AA'BB' multiplet due to the –SCH$_2$CH$_2$SCH$_2$CH$_2$S– "bracket" portion of the 16S6 ligand: (a) simulated; (b) observed. $^2J = -13.0$ Hz; $^3J = 6.1$ and 9.1 Hz.

AA'BB' pattern observed for the SCH$_2$CH$_2$S chain in the ^1H NMR spectrum (Figure 4). This may be related to retention of the –SCH$_2$CH$_2$SCH$_2$CH$_2$S– bracket in solution. The torsional angles estimated[49] from calculated coupling constants are comparable to those observed in the solid-state structure and consistent with an *anti* conformation for S–C–C–S. We have obtained similar ^1H NMR spectral results for other rigid crown thioethers in which the –SCH$_2$CH$_2$SCH$_2$CH$_2$S– bracket has been identified in the solid state.

The [Cu(16S6)]$^+$ cation shows only three singlet resonances in the $^{13}C\{^1H\}$ and two in the ^1H NMR spectra. Since the solid-state conformation of the ligand contains five different CH$_2$ groups, some type of fluxional process must be occurring in solution. Variable-temperature $^{13}C\{^1H\}$ and ^1H NMR spectra showed increased broadening with a decrease in temperature, but the low-temperature limit could not be attained. The solid-state conformation of the ligand in [Cu(16S6)]$^+$ shows that the two nonbonded S atoms (S2, S4) are oriented toward the metal center. A fluxional process in which these nonbonded S atoms exchange with the corresponding S atoms (S1 and S3) of the SCH$_2$S group would seem likely. This could account for the equivalence of the CH$_2$ groups in solution, since this would interchange bonded and nonbonded S atoms of the SCH$_2$S group. The process should be

facile, since the ligand conformation in the tetrahedral complex provides a conformation that already orients the nonbonded S atoms toward the metal center.

Discussion

The 16S6 crown thioether ligand was originally designed as one of a number of potentially ditopic ligands (see Chart I, structures II and III, for other examples). The intent is to create a series of ligands containing two compartmentalized S$_3$ binding sites. By using either –SCH$_2$CH$_2$SCH$_2$CH$_2$S– or –SCH$_2$CH$_2$CH$_2$SCH$_2$CH$_2$CH$_2$S– "chelating strings" separated by rigid organic "spacing units" such as –CH$_2$ (16S6), *o*-CH$_2$C$_6$H$_4$CH$_2$– (III), and *m*-CH$_2$C$_6$H$_4$CH$_2$– (II), it should be possible to create ligands that are incapable of "wrapping around" a metal atom. This would then favor the coordination of *two* separate metal centers rather than the S$_6$ homoleptic environment favored by ligands such as 18S6. We have prepared a variety of these S$_6$ ligands and found that they behave as ditopic ligands and favor binuclear coordination almost exclusively. However, the coordination of 16S6 with Cu(I) described herein appears to be anomalous.

A possible explanation for this may be found from examination of the Cu(I) complexes formed by other crown thioether ligands, 18S6, 15S5, and 14S4. The mononuclear complexes [Cu-(18S6)][BF$_4$], [Cu(15S5)][ClO$_4$], and [Cu(14S4)][ClO$_4$] and the dinuclear complex [Cu$_2$(CH$_3$CN)$_2$(18S6)][ClO$_4$]$_2$ have been structurally characterized.[24,25,36,40] In [Cu(18S6)][BF$_4$] and [Cu(15S5)][ClO$_4$] the thioether ligand coordinates the Cu(I) ion via four S atoms from one continuous section (–SCH$_2$CH$_2$SC-H$_2$CH$_2$SCH$_2$CH$_2$S–) of the macrocyclic ligand in a severely distorted tetrahedral geometry, leaving the remaining S atoms uncoordinated. In the complex [Cu(14S4)][ClO$_4$], three S atoms are coordinated from one macrocycle in a similar manner, with the fourth site occupied by the fourth S atom from a neighboring complex, to give a distorted tetrahedral geometry in a polymeric form. In the dicopper complex, the six S donor sites are coordinated to two (Cu–CH$_3$CN)$^+$ fragments in identical tetrahedral geometries. The two copper atoms are bonded to opposite sides of the macrocyclic ligand in an *in–out* conformation. In the description of the solid-state structure of [Cu$_2$(CH$_3$CN)$_2$-(18S6)][ClO$_4$]$_2$, it was noted that there was a close intramolecular contact between two S atoms (3.64 Å), one from each coordination site, through the center of the complex. It is possible that this interaction would be severe in a similar [Cu$_2$(CH$_3$CN)$_2$(16S6)]$^{2+}$ complex, since only a methylene group would separate the two coordination sites. This potential destabilization of the dinuclear complex and the ability of the 16S6 ligand to form a homoleptic thioether complex using four S atoms from the same macrocyclic ligand, without appreciable distortion from tetrahedral geometry, are seen as the reasons for the stability of this coordination mode relative to those observed for 18S6, 15S5, and 14S4. Although the crown thioether 16S6 was designed to act as a binucleating ligand and therefore *not* wrap around a metal ion, it appears to be ideally suited for encapsulating and providing a homoleptic coordination sphere of tetrahedral coordination.

(48) Cowie, M.; Loeb, S. J. *Organometallics* **1985**, *4*, 852–857 (and references therein).
(49) Jackman, L. M.; Sternhell, S. In *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Barton, D.H. R., Doering, W., Eds.; Pergamon: Oxford, England, 1969; 280–301.