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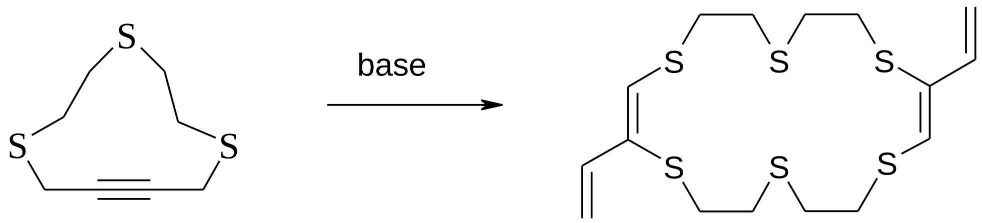


Synthesis of an Alkene Functionalised Thiamacrocycle, 2,11-Divinyl-1,4,7,10,13,16-hexathiacyclooctadeca-2,11-diene

Aaron Berko[a], Peter N. Horton[b], Michael B. Hursthouse,[b] Robert J. Packer[a] and Michael J. Went[a*]

[a] School of Physical Sciences, University of Kent, Canterbury, Kent, CT2 7NR
[b] EPSRC National Crystallography Service, School of Chemistry, University of Southampton, Highfield, Southampton, SO17 1BJ.

Abstract

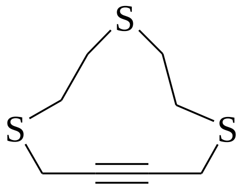
Base-catalysed rearrangement of 1,4,7-trithiacycloundec-9-yne affords 2,11-Divinyl-1,4,7,10,13,16-hexathiacyclooctadeca-2,11-diene characterised by NMR spectroscopy and X-ray crystallography. The eighteen-membered macrocycle has six of the twelve C-S bonds in *anti* configurations.

Keywords: Thioether, Macrocycle, Alkene

During the past 20 years, extensive studies have been undertaken concerning the synthesis and coordination chemistry of cyclic thioethers [1]. Generally it has been observed that this class of ligand forms an extensive range of transition metal complexes, in contrast to crown ethers that bind preferentially to harder Group 1 and 2 cations. In particular 1,4,7,10,13,16-hexathiacyclooctadecane (18S6) and especially 1,4,7-trithiacyclononane (9S3) have been shown to form stable complexes with a large range of metals. Much of the unique coordination chemistry of these two ligands is ascribed to them having, in the case of 9S3, or being easily converted into, in the case of 18S6, an endodentate conformation. However, to date rather limited progress has been made in exploiting the chemistry of their complexes because the ligands are hard to functionalise. Carbon functionalised 9S3 ligands have shown potential as bifunctional chelators for use in radiopharmacy [2] and as ligands for solvent extraction of precious metals [3]. This paper describes a new functionalised 18S6 macrocycle.

1,4,7-trithiacycloundec-9-yne (**1**) can be prepared in high yield by the reaction of 1,4-dichlorobut-2-yne with bis(2-mercaptoethyl)sulfide and KOH under high dilution conditions

[4]. The macrocycle has been previously characterized by X-ray crystallography, NMR and mass spectroscopy [5]. Previous studies of the base-catalysed rearrangement of 1,4,7-trithiacycloundec-9-yne had indicated that the product was 2-vinyl-1,4,7-trithiacyclonon-2-ene (**2**) as indicated by electron impact mass spectroscopy, NMR and elemental analysis [4]. However upon attempting to repeat this reaction[1] it became apparent that another product was also possible. Analysis of the 600 MHz ^{1}H NMR suggested a larger ring as the vicinal coupling constants (J 10.9, J' 5.4 and J 11.2, J' 5.4) indicate an equilibrium mixture dominated by anti S-C-C-S segments which is not consistent with a nine-membered ring [6]. This was confirmed by mass spectroscopy with showed a weak peak at m/z 408 in the EI spectrum and strong peaks at 409 and 426 in the CI spectrum corresponding to M, M+H and M+NH$_3$ respectively. No peak at 204 was observed in the EI corresponding to **2**, however a weak peak was observed in the CI spectrum at 205 corresponding to M+H. In light of these unexpected results the mass spectrum of the starting material **1** was run again and confirmed the presence of exclusively the eleven-membered ring (CI m/z 205 M+H, 222 M+NH$_3$).



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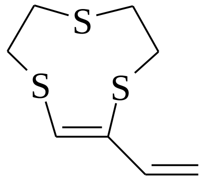

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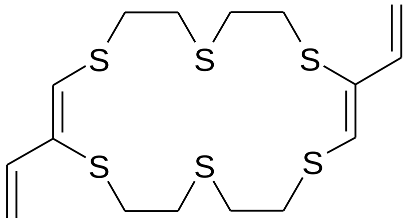

3

The structure of **3** was determined by X-ray crystallography[2] (see figure 1) and confirms the presence of an eighteen-membered ring. The bond lengths and angles are all in the ranges expected thiamacrocycles (see table 1). The molecule has a crystallographically imposed centre of symmetry and hence has a transoid configuration. Interestingly no evidence was found for a second cisoid isomer in the ^{1}H and ^{13}C NMR spectra.

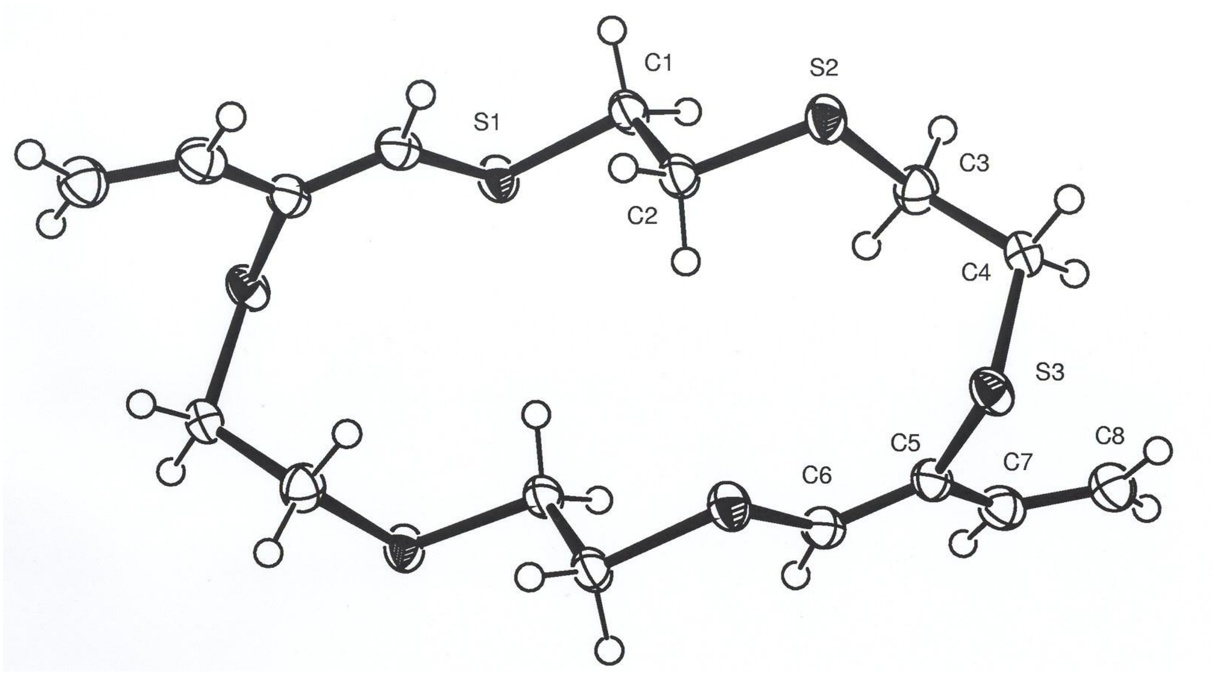

Fig 1 Molecular structure of **3** showing the atom labelling system. Atoms are represented as 50% probability ellipsoids.

Table 1. Bond lengths [Å], angles [°] and torsional angles [°] for **3**.

C1-C2	1.519(3)	C1-S1	1.826(2)	C2-S2	1.814(2)	C3-C4	1.523(3)
C3-S2	1.819(2)	C4-S3	1.822(2)	C5-C6	1.355(3)	C5-C7	1.459(3)
C5-S3	1.778(2)	C6-S1	1.737(2)	C7-C8	1.324(3)		

C2-C1-S1	112.85(16)	C1-C2-S2	112.06(15)	C4-C3-S2	112.39(16)
C3-C4-S3	115.00(16)	C6-C5-C7	120.8(2)	C6-C5-S3	118.19(18)
C7-C5-S3	120.70(17)	C5-C6-S1	124.42(18)	C8-C7-C5	127.0(2)
C6-S1-C1	100.39(11)	C2-S2-C3	101.26(11)	C-S3-C4	102.39(11)

S1-C1-C2-S2	172.30(12)	S2-C3-C4-S3	70.5(2)	S3-C5-C6-S1	2.4(3)
C6-C5-C7-C8	-166.2(2)	C2-C1-S1-C6	68.27(19)	C1-C2-S2-C3	-78.60(19)
C4-C3-S2-C2	-128.61(17)	C6-C5-S3-C4	-124.49(19)	C3-C4-S3-C5	66.21(19)
C5-C6-S1-C1	-169.3(2)				

The structures has significant conformation differences compared with 18S6 [7] and 2,3:11,12-dibenzo-1,4,7,10,13,16-hexathiacyclo-octadecane (benzo-18S6) [8].

In 18S6 all the C-S bonds are *gauche* and two of the six sulfurs are endodentate while in benzo-18S6 all the sulfur atoms are exodentate and four of the twelve C-S bonds show *anti* configuration. In **3** ten of the twelve C-S bonds show *gauche* configurations. Compared with benzo-18S6 the thioether group in **3** with the greatest conformational freedom (S2) adopts a gauche and an anti configuration, while the equivalent thioether in benzo-18S6 adopts two anti configurations.

Further studies will explore the synthesis of **3** in more detail, as well as its coordination chemistry and addition reactions of the alkenes.

Footnotes

*Corresponding author. Tel.: +44-1227-823-540; fax: +44-1227-827-558
Email address: m.j.went@kent.ac.uk (M.J. Went).

[1] *Synthesis of L.* 1,4,7-trithiacycloundec-9-yne (0.8 g, 3.9 mmol) was added to a solution of potassium butoxide (0.05 g, 0.45 mmol) in DMSO (25 ml). The mixture was stirred for 24 hours in a water bath keeping the temperature below 30 ^{o}C. Distilled water (25 ml) was added to the resulting brown solution and the organic product extracted into toluene (3 x 30 ml) and then combined and dried with $MgSO_4$. The toluene was then removed by rotary evaporation and the residue recrystallised from dichloromethane (5 ml)/ light petroleum (80 ml) at -25 ^{o}C overnight. Yield 0.07 g, 9%; Microanalysis: Found C, 45.9; H, 5.8; $C_{16}H_{24}S_5$ requires C, 47.0; H 5.9%; ^{1}H NMR (CD_2Cl_2) 6.703 (s, 1H, H_5), 6.435 (dd, 1H, H_6, *J* 10.6, 16.6), 5.570 (ddd, 1H, H_7, *J* 0.5, 1.3, 16.6), 5.081 (ddd, 1H, H_8, *J* 0.6, 1.3, 10.3), 2.946, 2.671 (AA'BB', 4H, *J* 10.9, *J'* 5.4, J_{gem} -13.3, -13.0), 2.928, 2.774 (CCDD', 4H, *J* 11.2, *J'* 5.4, J_{gem} -10.7, -10.7), IR spectrum (KBr disk) 3090(m), 2928(s), 2857(w), 2365(w), 1609(s), 1425(s), 706(m) cm^{-1}. MS CI (NH_3) 409(M+H), 426 (M+NH_3)

[2] *Crystal Structure Determination of* ***3.*** $C_{16}H_{24}S_6$, M = 408.71, Monoclinic, a = 12.6983(3) Å, b = 8.1795(2) Å, c = 10.1079(2) Å, β = 111.9210(10)°, U = 973.96(4) Å^3, T = 120(2) K, space group $P2_1/c$, Z = 2, μ(Mo-K_a) = 0.696 mm^{-1}**,** 18252 reflections measured, 2232 unique (R_{int} = 0.0823) which were used in all calculations. Final R_1 = 0.0387, wR_2 = 0.0890 [$F^2 > 2\sigma(F^2)$], R_1 = 0.0507, wR_2 = 0.0966 (all data).

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Supporting Information Available: Crystallographic data (excluding structure factors) for the structure in this paper, has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC262661. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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