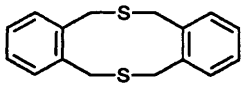
Synthesis and Properties of Some New Ditopic Thiacyclophanes

Lyall R. Hanton* and Harrison Sikanyika
Department of Chemistry, University of Otago, PO Box 56, Dunedin, New Zealand

Intermolecular coupling of 1,2,4,5-tetrakis(bromomethyl)benzene with 1,2-bis(sulfanylmethyl)-benzene (2 equiv.) under high dilution conditions in the presence of NaOH in benzene–ethanol yields the new ditopic thiacyclophanes **3** and **4** in good yield. An X-ray crystal structure of 5*H*,7*H*,10*H*,-12*H*,17*H*,19*H*,22*H*,24*H*-5,11,18,23-tetrathia-8,2;9,20-dimethenodibenzo[*a*,*k*]cycloeicos-20-ene **3** is described.

Although compound **1** was first reported in 1903,[1] it is only recently that this dithiacyclophane[2] and its five isomers[3–5] have been characterized by X-ray crystallography. Solution studies[2,5,6] indicate that these medium-sized cyclic dithioethers or 'mesocycles' exhibit novel and complex conformational processes. In addition, they have been shown[7,8] to be effective ligands for transition metals. For example, **1** and its Se analogue form air-stable complexes with Ag^{I},[7] Cu^{I}[7] and Ru^{II}.[8] Herein are described our preliminary results on the synthesis and properties of the ditopic thiacyclophanes **3** and **4** and the crystal structure of **3**. Unlike **1** and its Se analogue, both of which form mononuclear complexes with transition metals,[7,8] compounds **3** and **4** have the potential to coordinate to two metal centres.[9] They have also been identified as important intermediates in the synthesis of tube-shaped compounds[10] to make novel host systems and artificial channels.



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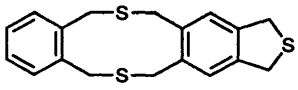

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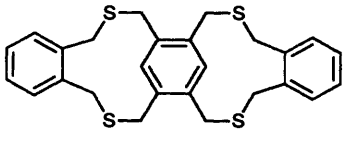

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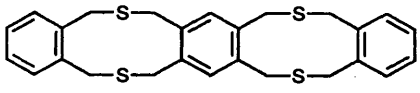

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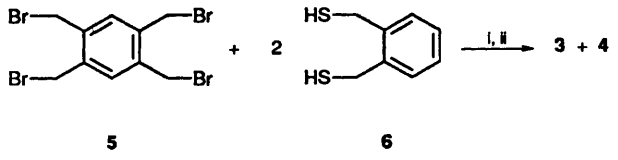
Compounds **3** and **4** are based on tetrafunctionalized durene, which is proving to be an excellent building block for these systems. Coupling 1,2,4,5-tetrakis(bromomethyl)benzene **5** with 1,2-bis(sulfanylmethyl)benzene[11] **6** (2 equiv.) under high dilution conditions in the presence of NaOH in benzene–ethanol afforded a mixture of **3** and **4** (see Scheme 1). The two



5 **6**

Scheme 1 *Reagents:* i, NaOH; ii, benzene–ethanol

isomers were readily separated by column chromatography, eluting with a gradient solvent mixture of hexane–dichloromethane. First to be eluted was **3**, followed by **4**. No other material could be isolated. Both compounds are air-stable white solids. The coupling reaction is sensitive to the reaction conditions and choice of starting materials. If the reaction is carried out under high dilution in the presence of Cs_2CO_3 in DMF at 50–60 °C, yields of **3** and **4** are reduced and the new ring-closed thiacyclophane **2** is formed. If 1,2,4,5-tetrakis-(sulfanylmethyl)benzene and 1,2-bis(bromomethyl)benzene are coupled in ethanol–benzene at room temp. using NaOH, a significant quantity of a disulfide of **2** is isolated.

The crystal structure of **3** (Fig. 1) shows the molecule adopts a stepped *anti-anti* conformation with *exo* S atoms. Interplanar angles between the *ortho* and *meta* rings for the two independent molecules are 13.8 and 16.4°. This contrasts with 2,11-dithia[3.3]orthometacyclophane, which in the solid state adopts a *syn* conformation with *exo* S atoms.[5] This suggests the energy barrier to *anti*/*syn* rearrangement is probably low. The predominant intermolecular interactions in the solid state are between methylene hydrogens, which will have small positive charges, and the π-electrons of aromatic rings and not π–π interactions as might have been expected.[8] Close intermolecular contacts between methylene and aromatic carbons are in the range 3.2–3.7 Å. Close contacts (3.43 Å) are also found between S atoms.

Each of the isomers exhibits two 8 H singlets for the CH_2 protons in the region 3.14–3.72 ppm. That only two singlets are observed for the aliphatic protons signifies both isomers are conformationally very mobile. Their fluxional behaviour in solution is currently being investigated by variable-temperature NMR studies. Results for **3** indicate that at 223 K the high-field singlet has only broadened slightly but that the low-field singlet is split into a well-resolved AB system $\delta(CDCl_3)$ = 3.91(d) and 3.53(d) ppm (^2J 12.3 Hz). Comparisons of the spectra of compound **3**, 2,11-dithia[3.3]orthometacyclophane and 1,2,4,5-tetrakis(sulfanylmethyl)benzene suggest that it is the *ortho*-substituted methylene protons at the peripheries of **3** that are still conformationally active. By analogy with the conformational analysis of 2,11-dithia[3,3]orthometa cyclophane,[5] models indicate that interconversion of the two *anti* forms with *endo* S atoms allows exchange of these geminal protons. Such exchange requires rotation about the approximately parallel,

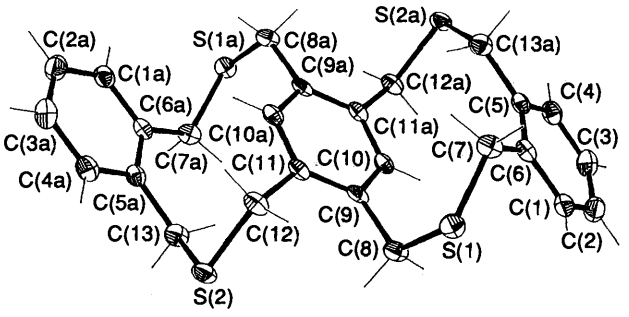


Fig. 1 X-Ray crystal structure of **3** showing 50% probability ellipsoids. Symmetry generated atoms are labelled (a). Selected geometric parameters (Å,°): S(1)–C(7) 1.817(4), S(1)–C(8) 1.837(5), S(2)–C(12) 1.830(4), S(2)–C(13) 1.820(5), C(7)–S(1)–C(8) 103.0(2), C(12)–S(2)–C(13) 102.8(2), C(6)–C(7)–S(1) 117.3(3), C(9)–C(8)–S(1) 112.0(3), C(11)–C(12)–S(2) 112.7(3), C(5a)–C(13)–S(2) 116.6(3).

C(aromatic)–C(*ortho*-CH_2) bonds and S–C(*meta*-CH_2) bonds and not four C–S bonds as suggested.[5] This exchange does not affect the *meta*-substituted methylene protons and only requires a small movement for the *ortho*-substituted ring. Interconversion of the *meta*-substituted methylene protons involves rotation about the remaining bonds. The energy barrier for this process is calculated[12] to be 51.6 ± 0.5 kJ mol^{-1}. The eight protons of the two *o*-xylyl units are observed as two well-separated 4 H multiplets in the regions 7.24–7.30 and 7.59–7.81 ppm. Whereas the two protons of the central aromatic ring of **4** appear as a singlet at 7.83 ppm, the corresponding protons in **3** are observed as a singlet at 5.93 ppm. This shift indicates that the latter protons are shielded by the π-cloud of the appended *o*-xylyl units. Such shielding is only possible in an *anti-anti* conformer with *exo* S atoms[5] as found in the solid state. Hence this *anti-anti* conformation must predominate in solution.

The synthesis of isomeric ditopic thiacyclophanes incorporating *meta*- and *para*-xylyl units is currently in progress.

Experimental

Synthesis of Ditopic Thiacyclophanes **3** *and* **4**.—Solutions were degassed and the reaction carried out under dry N_2. To a solution of NaOH (4.00 g, 100 mmol) in 95% ethanol (1.2 dm^3) at room temp. was added, dropwise with vigorous stirring, a solution of **5** (4.50 g, 10 mmol) and **6** (3.40 g, 20 mmol) in benzene (800 cm^3) over 48 h. After addition was complete the reaction mixture was stirred for a further 10 h, after which time TLC analysis showed two major products. Upon evaporation to dryness, the solution gave a dark residue which was suspended in water (500 cm^3) and CH_2Cl_2 (300 cm^3). The organic layer was separated and the aqueous layer was further extracted with CH_2Cl_2 (3 × 300 cm^3). The organic extracts were combined, washed once with water, dried ($MgSO_4$) and the solvent removed. The crude products were purified by silica gel (230–400 mesh), column chromatography, eluting with hexane–CH_2Cl_2 gradient solvent mixture to yield in the first band, after recrystallization (CH_2Cl_2–hexane) **3** (1.22 g, 26%), m.p. > 298 °C (decomp.); $\delta_H(CDCl_3)$ 3.15 (s, 8 H, $ArCH_2S$), 3.72 (s, 8 H, $ArCH_2S$), 5.93 (s, 2 H, ArH, central ring), 7.24–7.29 (m, 4 H, ArH) and 7.76–7.81 (m, 4 H, ArH); $\delta_C(CDCl_3)$ 29.46 (CH_2S), 31.59 (CH_2S) and 127.64, 129.78, 133.86, 136.44 and 136.57 (5 ArC); *m/z* 466 (M^+) (Found: C, 66.8; H, 5.7; S, 27.5. $C_{26}H_{26}S_4$ requires C, 66.9; H, 5.6; S, 27.5%); and in the second band **4** (1.82 g, 39%), m.p. > 162 °C; $\delta_H(CDCl_3)$ 3.46 (s, 8 H, $ArCH_2S$), 3.49 (s, 8 H, $ArCH_2S$), 7.25–7.30 (m, 4 H, ArH), 7.59–7.64 (m, 4 H, ArH) and 7.83 (s, 2 H, ArH, central ring); $\delta_C(CDCl_3)$ 28.64 (CH_2S), 29.13 (CH_2S) and 128.25, 130.17, 131.84, 137.51 and 137.83 (5 ArC); *m/z* 466 (M^+) (Found: C, 66.6; H, 5.6; S, 27.4%).

Crystal Data for the Thiacyclophane **3**.—$C_{26}H_{26}S_4$, M = 466.71, triclinic, space group $P\bar{1}$, a = 9.975(2), b = 10.818(2), c = 11.659(2) Å, α = 76.65(1), β = 82.52(1), γ = 64.46(1)°, V = 1103.8(4) $Å^3$, Z = 2, D_c = 1.404 g cm^{-3}, μ(Mo-Kα) = 4.43 cm^{-1}, $F(000)$ = 492, T = 130 K.

A Nicolet P3 diffractometer with graphite-monochromated Mo-Kα radiation was used to collect data in the range $2° < \theta < 25°$. 4104 Reflections were collected of which 2589 were unique [$I > 2\sigma(I)$]. The structure was solved using direct methods SHELXS-86[13] and refined anisotropically by full-matrix least squares on F^2 using SHELXL-92 (Gamma test version).[13] At convergence for 271 parameters R_1 = 0.0552, wR_2 = 0.1146 and goodness-of-fit on F^2 = 1.058. The structure consists of two crystallographically independent 'half molecules' in the asymmetric unit. The centre of each moiety sits on a crystallographic centre of inversion which generates the complete molecule. The molecules are essentially identical. Tables of fractional atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.*

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* For details of the CCDC Deposition Scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1994, Issue 1.

References

1 W. Authenrieth and A. Bruning, *Ber.*, 1903, **36**, 183.
2 T. Okajima, Z.-H. Wang and Y. Fukazawa, *Tetrahedron Lett.*, 1989, **30**, 1551; L. R. Hanton and T. Kemmitt, unpublished X-ray structure of **1**, 1989; J. J. H. Edema, H. Thijs Stock, J. Buter, R. M. Kellogg, W. J. J. Smeets and A. L. Speak, *Tetrahedron*, 1993, **49**, 4355.
3 R. H. Mitchell, W. Anker and G. W. Bushnell, *Can. J. Chem.*, 1979, **57**, 3080.
4 T. L. Chan, C. D. Poon and T. C. W. Mak, *Acta Crystallogr., Sect. C.*, 1986, **42**, 897.
5 G. J. Bodwell, L. Ernst, H. Hopf, P. G. Jones, J. P. McNally and D. Schomburg, *Chem. Ber.*, 1990, **123**, 2381.
6 Y.-H. Lai and M. Nakamura, *J. Org. Chem.*, 1988, **53**, 2360; Y.-H. Lai, *J. Chem. Soc., Perkin Trans. 2*, 1989, 643; G. Bodwell, L. Ernst, H. Hopf and P. G. Jones, *Tetrahedron Lett.*, 1989, **30**, 6005.
7 R. E. Edie, M.Sc. Thesis, University of Otago, 1994.
8 L. R. Hanton and T. Kemmitt, *J. Chem. Soc., Chem. Commun.*, 1991, 700; L. R. Hanton and T. Kemmitt, *Inorg. Chem.*, 1993, **32**, 3648.
9 S. J. Loeb and G. K. H. Shimizu, *J. Chem. Soc., Chem. Commun.*, 1991, 1119; S. J. Loeb and G. K. H. Shimizu, *Inorg. Chem.*, 1993, **32**, 1001.
10 F. Vögtle, A. Schröder and D. Karbach, *Angew. Chem.*, 1991, **30**, 575; A. Schröder, D. Karbach, R. Güther and F. Vögtle, *Chem. Ber.*, 1992, **125**, 1881.
11 U. Luning, C. Wangnick, K. Peters and H. G. von Schnering, *Chem. Ber.*, 1991, **124**, 397.
12 S. Gladstone, K. J. Laidler and H. Erying, *The Theory of Rate Processes*, McGraw Hill, New York, 1941.
13 SHELXS-86, Program for the Solution of Crystal Structures from Diffraction Data, G. M. Sheldrick, University of Göttingen, Germany, 1986; SHELXL-93, Program for the Refinement of Crystal Structures, G. M. Sheldrick, University of Göttingen, Germany, 1993.

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