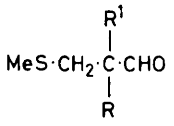
Electrophilic Methylthiomethylation of Enol Ethers and Activated Aromatic Compounds. Application of the Former Reaction to the Synthesis of the Macrocycle, 3,3,7,7,11,11,15,15-Octamethyl-1,9-dithia-5,13-diazacyclohexadecane

By **Robert McCrindle,* Alan J. McAlees,** and **Donald K. Stephenson,** Guelph-Waterloo Centre for Graduate Work in Chemistry, Guelph Campus, Department of Chemistry, University of Guelph, Guelph, Ontario, Canada N1G 2W1

Enol ethers of dialkylacetaldehydes, either as such, or generated *in situ* from the corresponding acetals, undergo ready methylthiomethylation when heated with dimethyl sulphoxide–acetic anhydride (or methylthiomethyl acetate) in the presence of boron trifluoride–diethyl ether. These same reagent combinations can be used to methylthiomethylate certain activated aromatic compounds. The synthetic utility of the former reaction is demonstrated in the synthesis of 2,2,6,6-dimethyl-4-thiaheptanedial (4) which has been converted into 3,3,7,7,11,11,15,15-octamethyl-1,9-dithia-5,13-diazacyclohexadecane (7).

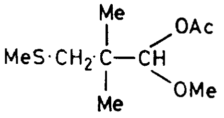
In the course of studies of the complexing properties of polydentate ligands which have quaternary carbon atoms in the backbone, we required an efficient route to 2,2-dialkyl-3-(alkylthio)aldehydes (1). By analogy with the boron trifluoride–diethyl ether catalysed condensation [1] of methylal with ethyl isobutenyl ether to give a 1,1,3-trialkoxy-2,2-dimethylpropane, it was anticipated that methylthiomethyl acetate might react with enol ethers under similar conditions. Since this sulphide can be generated by heating dimethyl sulphoxide with acetic anhydride,[2] a mixture of these and methyl isobutenyl ether was heated in the presence of a catalytic amount of boron trifluoride–diethyl ether whereupon an essentially quantitative (by ^{1}H n.m.r.) conversion into 1-acetoxy-1-methoxy-2,2-dimethyl-3-methylthiopropane (2) was observed. Since (2) undergoes ready hydrolysis to 2,2-dimethyl-3-methylthiopropanal (1a) the general scope of the reaction appeared to warrant exploration.



$\mathrm{MeS{\cdot}CH_2{\cdot}C(R^1)(R){\cdot}CHO}$

(1)

a; R = R^1 = Me
b; R = Et, R^1 = Bu
c; R = R^1 = Et

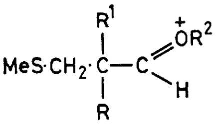


$\mathrm{MeS{\cdot}CH_2{\cdot}C(Me)_2{-}CH(OAc)(OMe)}$

(2)

When a mixture of dimethyl sulphoxide, acetic anhydride, and methyl isobutenyl ether was heated in the absence of boron trifluoride–diethyl ether, ^{1}H n.m.r. spectroscopy indicated the formation of compound (2) in small yield (*ca.* 10%), although virtually all of the dimethyl sulphoxide had been consumed, largely in formation of the Pummerer product, methylthiomethyl acetate.[2] Formation of compound (2) under these conditions suggests that at least one intermediate in the Pummerer rearrangement has some carbocationic character. Addition of the catalyst at this stage, followed by heating, resulted in the disappearance of the methylthiomethyl acetate and the formation of compound (2). The method was extended to include the preparation of the homologous aldehydes (1b) and (1c). In these syntheses, acetals were used in the expectation that the boron trifluoride would catalyse their *in situ* cleavage to vinyl ethers, an extra molar equivalent of acetic anhydride being added to remove the alcohol generated. Indeed, hydrolytic work-up of these reactions, followed by distillation, gave the aldehydes, (1b) and (1c), which were characterised as 2,4-dinitrophenylhydrazones, in yields approaching 50%.

An investigation of the behaviour of variously substituted enol ethers with methylthiomethyl acetate–boron trifluoride–diethyl ether showed that this reaction is not generally applicable. Thus, none of the desired products was detected in the reactions of ethyl vinyl ether, 3-methoxypent-2-ene ($Z + E$), a mixture of 2-methoxy-3-methylbut-1-ene and -2-ene, 1-methoxycyclohexene, α-methoxy- or β-methoxy-styrene. The failure of this reaction with enol ethers, other than those derived from 2,2-dialkylacetaldehydes, is consistent with the intermediacy ot an alkoxycarbenium ion (3). This ion may initiate polymerisation of the vinyl ether (particularly if unhindered) or it may suffer deprotonation to a new enol ether which can, in turn, undergo polymerisation or further alkylation. Recently reported [3] successful transformations of this type involve Lewis acid-catalysed reactions of chloromethyl methyl sulphide with vinyl silyl ethers.

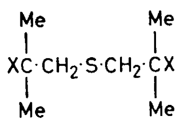


$\mathrm{MeS{\cdot}CH_2{\cdot}C(R^1)(R){-}CH{=}\overset{+}{O}R^2}$

(3)

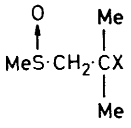
A number of methylthiomethylations and related reactions of aromatic systems have been reported.[4] While many of these involve intramolecular reactions of activated aromatic systems, two report intermolecular Lewis acid-catalysed reactions of chloromethyl methyl sulphide [4e] and of methylthiomethyl acetate.[4f] We have found that the combination, methylthiomethyl acetate–boron trifluoride–diethyl ether, achieves this reaction for certain activated aromatic compounds. Thus, anisole gave mainly *p*-methylthiomethylanisole along with some *p*-methoxybenzyl acetate. A similar (^{1}H n.m.r.) product mixture was obtained by heating anisole with acetic anhydride and dimethyl sulphoxide in the presence of the catalyst. Under the earlier conditions, mesitylene gave a good yield of the monosubstituted product along with some dimesitylmethane. Phenol reacted rapidly to give only viscous polymeric material, while toluene and *NN*-dimethylaniline gave little evidence of reaction. Presumably, in the last case the catalyst is tied up by the amine. Selective methylthiomethylation of thiophen, in the 2 position, was achieved in reactions involving an excess (7 molar equivalents) of thiophen. Alkylation of thiophen usually leads to substantial amounts of substitution at both the 2 and the 3 positions, possibly because 'highly reactive carbonium ions discriminate poorly between α- and β-positions'.[5] Interestingly, α-alkylation tends to predominate [5] in Mannich-type reactions of thiophen. On decreasing the relative amounts of thiophen in the reaction mixture, increasing amounts of polysubstitution occurred. ^{1}H N.m.r. spectra of fractions recovered by preparative t.l.c. are consistent with the presence of the 2,5-di-, 2,3,5-tri-, and 2,3,4,5-tetra-substituted thiophens.

Our successful syntheses of the aldehydes (1a—c) open up routes to a variety of polydentate ligands with quaternary carbon atoms in the backbone since the aldehyde groups offer the possibility of facile synthetic elaboration. However, since dialdehydes of the type (4) would provide even more versatile synthetic intermediates we examined the possibility of adapting the methylthiomethylation reaction of enol ethers for the production of such species. Indeed this has proved possible, and the resulting dialdehyde (4) has been converted into three useful polydentate ligands, namely, the dioxime (5), the diamine (6), and the macrocycle (7).



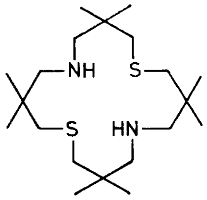
$$\underset{Me}{\overset{Me}{XC}}\cdot CH_2\cdot S\cdot CH_2\cdot\underset{Me}{\overset{Me}{C}}X$$

(4) X = CHO
(5) X = CH·N·OH
(6) X = $CH_2{\cdot}NH_2$
(11) X = CH(OMe)OAc
(12) X = CN



$$Me\overset{O}{\overset{\uparrow}{S}}\cdot CH_2\cdot\underset{Me}{\overset{Me}{C}}X$$

(8) X = CH(OMe)·OAc
(9) X = CH·N·OH
(10) X = CHO



(7)

Oxidation of 1-acetoxy-1-methoxy-2,2-dimethyl-3-methylthiopropane (2) with *m*-chloroperbenzoic acid in methylene chloride afforded the corresponding sulphoxide (8), which was characterized as the oxime (9) of the derived aldehyde (10). The sulphoxide (8) was then heated with acetic anhydride and methyl isobutenyl ether in the presence of boron trifluoride–diethyl ether. The disappearance of (8) and the enol ether was readily monitored by ^{1}H n.m.r. spectroscopy. Hydrolysis of the reaction mixture containing the diacetal (11) afforded a good yield of the dialdehyde (4) which was converted into the crystalline dioxime (5). The known [6] dinitrile (12) and diamine (6) were produced from (5) by successive dehydration, with acetic anhydride, and reduction, with borane in tetrahydrofuran. Reduction, with the same reagent, of the products of condensation of (4) and (6), gave a mixture from which the crystalline macrocycle (7) sublimed on heating *in vacuo*. Reaction of this macrocycle with palladium(II) chloride has given a product which is quite soluble both in chloroform and in water and which on crystallisation from ethanol has analyses consistent with its formulation as $PdCl_2$.(7).H_2O. Its structure is under investigation.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. ^{1}H N.m.r. spectra were recorded with a Varian A-60A or T-60 spectrometer for solutions in [^{2}H]chloroform. Microanalyses were performed by Guelph Chemical Laboratories Limited, Guelph, Ontario. T.l.c. plates were spread with Kieselgel G (Merck).

Starting Materials.—Methylthiomethyl acetate was obtained by the method of Horner and Kaiser.[2] Enol ethers were obtained commercially (β-methoxystyrene, ethyl vinyl ether) or by cracking of acetals as described by House and Kramer [7] (1-methoxycyclohexene) or Newman and Van der Zwan [8] using acetic anhydride instead of succinic anhydride [α-methoxystyrene, a mixture of 3-methoxypent-(*E*)-2-ene and -(Z)-2-ene, a mixture of 2-methoxy-3-methylbut-1-ene and -2-ene; in the preparation of these two mixtures collidine was used in place of pyridine].

1-*Acetoxy*-1-*methoxy*-2,2-*dimethyl*-3-*methylthiopropane* (2).—A mixture of dimethyl sulphoxide (7.8 g, 0.1 mol), acetic anhydride (10.2 g, 0.1 mol) and 1-methoxy-2-methylpropene (8.6 g, 0.1 mol) was heated under reflux in the presence of boron trifluoride–diethyl ether (0.75 cm^3) for 5 h. The reaction mixture was stirred with an excess of cold, aqueous sodium hydrogen carbonate, extracted with ether, and this extract was dried over anhydrous sodium sulphate. Distillation of the dried extract at the water pump gave 1-*acetoxy*-1-*methoxy*-2,2-*dimethyl*-3-*methylthiopropane* (2) (16.8 g, 82%), b.p. 105—106 °C (water pump); δ 1.03 (6 H, s, C-*Me's*), 2.13 (6 H, s, O*Ac* + S-*Me*), 2.58 (2 H, s, S-C*H*$_2$), 3.45 (3 H, s, O-*Me*), and 5.68 (1 H, s, CMe$_2$C*H*) (Found: C, 52.3; H, 8.7; S, 15.75. $C_9H_{18}O_3S$ requires C, 52.36; H, 8.81; S, 15.54%). This compound was hydrolysed by stirring it at ambient temperature for 24 h with aqueous sulphuric acid (2 mol dm^{-3}) to give the known [9] aldehyde (1a) [b.p. 65 °C (water pump); lit.,[9] value 65—75 °C (15 mmHg)].

2-*Butyl*-2-*ethyl*-3-*methylthiopropanal* (1b).—A mixture of dimethyl sulphoxide (7.8 g, 0.1 mol), acetic anhydride (20.4 g, 0.2 mol), and 2-ethyl-1,1-dimethoxyhexane [10] (17.4 g, 0.1 mol) was heated in an oil-bath at 100 °C for 5 h with boron trifluoride–diethyl ether (0.75 cm^3). The resulting mixture was stirred with an excess of aqueous sodium hydrogen carbonate and extracted with ether. The ether was evaporated and the residue hydrolysed by stirring it at ambient temperature for 72 h with aqueous sulphuric acid (2 mol dm^{-3}) to give 2-*butyl*-2-*ethyl*-3-*methylthiopropanal* (1b) (8.4 g, 45%), b.p. 112—116 °C (water pump); δ 0.5—2.0 (14 H, complex m, n-C_4H_9 + C_2H_5), 2.13 (3 H, s, S-*Me*), 2.75 (2 H, s, S-CH_2), and 9.25 (1 H, s, C*H*O); it was characterised as the 2,4-*dinitrophenylhydrazone*, m.p. 126—128 °C *ex* dichloromethane–methanol (Found: C, 52.35; H, 6.65; N, 15.25. $C_{16}H_{24}N_4O_4S$ requires C, 52.13; H, 6.58; N, 15.21%).

2,2-*Diethyl*-3-*methylthiopropanal* (1c).—The reaction of 2-ethyl-1,1-dimethoxybutane (14.6 g, 0.1 mol) was carried out as described above except that the reaction product was poured directly into the aqueous sulphuric acid. Distillation of the ether extract from the hydrolysis gave 2,2-*diethyl*-3-*methylthiopropanal* (1c) (7.7 g, 48%), b.p. 87—91 °C (water pump); δ 0.85 (6 H, t, C-*Me*, *J* 7 Hz), 1.67 (4 H, q, Me-CH_2, *J* 7 Hz), 2.15 (3 H, s, S-*Me*), 2.75 (2 H, s, S-CH_2), and 9.60 (1 H, s, C*H*O); it was characterised as the 2,4-*dinitrophenylhydrazone*, m.p. 148—149 °C. *ex* dichloromethane–methanol (Found: C, 49.4; H, 5.95; N, 16.45. $C_{14}H_{20}N_4O_4S$ requires C, 49.36; H, 5.94; N, 16.47%).

Reactions of Other Enol Ethers.—The enol ether (0.1 mol) was heated at 80—120 °C in the presence of boron trifluoride–diethyl ether (0.75 cm^3) with either methylthiomethyl acetate (0.1 mol) or dimethyl sulphoxide–acetic anhydride (0.1 mol each). Monitoring by ^{1}H n.m.r. in all cases showed peaks attributable to the presence of an appreciable amount of methylthiomethyl acetate although all of the enol ether had been consumed. The reaction mixtures were stirred with an excess of cold, aqueous sodium hydrogen carbonate and extracted with ether. Attempted distillation (water pump) of the dried (anhydrous sodium sulphate) extracts gave only small amounts of distillate, which appeared complex (^{1}H n.m.r. and analytical t.l.c.) and were not examined further. In general a considerable amount of non-distillable residue remained in the distillation flask. Similar results were obtained when the enol ethers were added dropwise to the reaction mixture at various temperatures.

Reaction with Anisole.—A mixture of anisole (14.5 g, 0.13 mol), methylthiomethyl acetate (16.0 g, 0.13 mol), and boron trifluoride–diethyl ether (0.75 cm^3) was heated at 100 °C for 3 h. Work-up involved stirring with an excess of aqueous sodium hydroxide (2 mol dm^{-3}), extraction into ether, and distillation (water pump) of the dried extract. This gave fractions, b.p. 40—42 °C (4.8 g) and 130—150 °C (9.2 g) and a substantial residue in the distillation flask. Preparative t.l.c. (toluene) of a portion (520 mg) of the higher boiling fraction gave (^{1}H n.m.r. and mass spectroscopy) *p*-methylthiomethylanisole [11] (402 mg) [contaminated with a minor amount (<10%) of what appeared to be (^{1}H n.m.r.) the *ortho*-isomer] and *p*-methoxybenzyl acetate (107 mg). The lower-boiling fraction, which contained anisole and bis(methylthio)methane (^{1}H n.m.r.), gave more *p*-methylthiomethylanisole on heating with a few drops of boron trifluoride–diethyl ether at 100 °C.

Reaction with Mesitylene.—Reaction of mesitylene (12.0 g, 0.1 mol) with methylthiomethyl acetate (12.0 g, 0.1 mol) and work-up, as described above for anisole, gave 2,4,6-trimethyl-(methylthiomethyl)benzene [4e] (11.9 g, 66%), b.p. 128—131 °C [water-pump; lit.,[4e] value 90—91 °C (1 mmHg)]. Trituration of the distillation residue with acetone gave slightly impure (^{1}H n.m.r.), crystalline dimesitylmethane [12] (800 mg), m.p. 128—134 °C after recrystallisation from toluene–ethanol followed by sublimation (lit.,[12] value 129—130 °C).

Reaction with Phenol.—No perceptible reaction occurred (^{1}H n.m.r.) when a mixture of phenol (1.88 g, 0.02 mol), methylthiomethyl acetate (2.40 g, 0.02 mol), and boron trifluoride–diethyl ether (5 drops) was kept at ambient temperature for 20 h. At 120 °C the methylthiomethyl acetate was consumed in less than 1 h with the formation of a syrup (probably a phenol–formaldehyde polymer) that would not dissolve in deuteriochloroform.

Attempted Reaction with NN-*Dimethylaniline*.—No perceptible reaction occurred (^{1}H n.m.r.) when a mixture of *NN*-dimethylaniline (5 cm^3), methylthiomethyl acetate (0.6 g), and boron trifluoride–diethyl ether (5 drops) was heated at 100 °C for four days.

Reaction with Thiophen.—A mixture of thiophen (11.8 g, 0.14 mol), methylthiomethyl acetate (2.4 g, 0.02 mol), and boron trifluoride–diethyl ether (4 drops) was heated to 80 °C for 50 min by which time the acetate had been consumed (^{1}H n.m.r.). Work-up as before and distillation gave 2-methylthiomethylthiophen [13] (1.4 g, 49%), b.p. 104—106 °C [water pump; lit.,[13] value 101—103 °C (15 mmHg)]. When the reaction was repeated using thiophen (1.7 g, 0.02 mol) and methylthiomethyl acetate (4.8 g, 0.04 mol) at 80 °C for 90 min a mixture of products was formed. Preparative t.l.c. (benzene–hexane; 1 : 3) of this material gave, in order of increasing polarity, 2-methylthiomethylthiophen (13% of plated material), 2,5-*bis*(*methylthiomethyl*)*thiophen* [26%, δ 2.0 (6 H, s, S-*Me*'s), 3.8 (4 H, s, S-CH_2's), and 6.7 (2 H, s, aromatic *H*'s); M^+ 204.0097 (calc. 204.0101)], and a more-polar fraction (31%). The last was rechromatographed (benzene–hexane; 1 : 1) and gave 2,3,5-tris(methylthiomethyl)thiophen [δ 2.05 (3 H, s, S-*Me*), 2.09 (3 H, s, S-*Me*), 2.12 (3 H, s, S-*Me*), 3.65 (2 H, s, S-CH_2), 3.83 (2 H, s, S-CH_2), 3.86 (2 H, s, S-CH_2), 6.88 (1 H, s, aromatic)], and 2,3,4,5-tetrakis(methylthiomethyl)thiophen [δ 2.10 (6 H, s, S-*Me*'s), 2.13 (6 H, s, S-*Me*'s), 3.83 (4 H, s, S-CH_2's), and 3.88 (4 H, s, S-CH_2's)].

1-*Acetoxy*-1-*methoxy*-2,2-*dimethyl*-3-*methylsulphinylpropane* (8).—A solution of *m*-chloroperbenzoic acid (85%, 43.0 g, 0.20 mol) in dichloromethane (500 cm^3) was added dropwise to a solution of (2) (41.2 g, 0.20 mol) in dichloromethane (100 cm^3) with ice cooling. On completion of addition (4 h), the reaction mixture was stirred overnight at room temperature. The mixture was neutralised with aqueous sodium hydrogen carbonate and the dichloromethane layer separated, dried (anhydrous sodium sulphate), filtered, and evaporated to give the oily sulphoxide (8) (54.5 g) which was characterised as the *oxime* (9), m.p. 116—120 °C, *ex.* hexane–ethanol, δ 1.27 (3 H, s, C-*Me*), 1.32 (3 H, s, C-*Me*), 2.60 (3 H, s, S-*Me*), 2.90 (2 H, s, S-CH_2), 7.27 (1 H, s, N=CH), and *ca.* 8 (1 H, br s, N-O*H*) (Found: C, 44.35; H, 8.25; N, 8.9. $C_6H_{13}NO_2S$ requires C, 44.15; H, 8.05; N, 8.6%).

2,2,6,6-*Tetramethyl*-4-*thiaheptanedial* (4).—The crude sulphoxide (8) (54.5 g) was heated to *ca.* 100 °C for 50 min with methyl isobutenyl ether (18.1 g, 0.21 mol), acetic anhydride (20.4 g, 0.20 mol), and boron trifluoride–diethyl ether

(0.75 cm^3) after which the ^{1}H n.m.r. spectrum revealed complete consumption of the enol ether. Dilute sulphuric acid (200 cm^3, 1 mol dm^{-3}) was added to the mixture which was then stirred vigorously at room temperature for 2 days. It was then neutralised with sodium hydrogencarbonate, extracted with diethyl ether (3×100 cm^3), dried (anhydrous sodium sulphate), filtered, and evaporated to give crude dialdehyde (4) (35.8 g), δ 1.20 (12 H, s, C-*Me*), 2.67 (4 H, s, S-CH_2), and 9.42 (2 H, s, C*H*O), which on Kugelrohr distillation (60—80 °C, 5×10^{-3} Torr) gave a purer sample (14.8 g).

The dialdehyde was characterised as the dioxime (5), which was prepared as follows. The crude dialdehyde (20.2 g) was heated with hydroxylamine hydrochloride (13.9 g, 0.20 mol) and sodium acetate trihydrate (27.2 g, 0.20 mol) in methanol–water (1 : 1, 150 cm^3) under gentle reflux for 2 h and then stirred overnight at room temperature. The solvent was evaporated, and water was added to the residue. Extraction with diethyl ether (2×100 cm^3), drying, filtration, and evaporation of the solvent gave the crude dioxime (21.4 g). A small sample of this material was subjected to preparative thin-layer chromatography (2% methanol–dichloromethane) and then crystallisation from diethyl ether–pentane to give pure *dioxime* (5), m.p. 65—66 °C, δ, 1.20 (12 H, s, C-*Me*), 2.63 (4 H, s, S-CH_2), 7.30 (2 H, s, N=C*H*), and *ca.* 8 (2 H, br s, O*H*) (Found: C,51.95; H, 8.75; N, 12.35. $C_{10}H_{20}N_2O_2S$ requires C, 51.7; H, 8.7; N, 12.05%).

2,2,6,6-*Tetramethyl*-4-*thiaheptanedinitrile* (12).—The crude dioxime was treated with acetic anhydride (20.4 g) at 20 °C, whereupon an exothermic reaction occurred. The mixture was then heated to 80 °C for 1 h, after which time ^{1}H n.m.r. revealed complete consumption of the dioxime. The acetic acid was evaporated at the water pump and the crude dinitrile distilled under reduced pressure (1 Torr) to give an impure fraction (b.p. 120—135 °C; 10.7 g) which was crystallised from toluene–hexane to give the pure dinitrile [6.7 g, 30% overall from (2)], m.p. 67—68 °C (lit.,[6] m.p. 66 °C), δ 1.48 (12 H, s, C-*Me*) and 2.92 (4 H, s, S-CH_2).

2,2,6,6-*Tetramethyl*-4-*thia*-1,7-*heptanediamine* (6).—A solution of borane in tetrahydrofuran (1 mol dm^{-3}, 150 cm^3) was added in one portion to an ice-cooled solution of (12) (10.6 g, 0.054 mol) in tetrahydrofuran (50 cm^3) under nitrogen. The solution was allowed to come to room temperature and was then stirred overnight; methanol and then water were added to decompose the excess of borane. The resulting mixture was hydrolysed in dilute hydrochloric acid (1 mol dm^{-3}, 250 cm^3) for 2 days at room temperature and then evaporated to small bulk on the rotary evaporator. Treatment with sodium hydroxide (5 mol dm^{-3}) and extraction into diethyl ether yielded the known [6] diamine (6) (9.9 g, 89.9%), δ 0.97 (12 H, s, C-*Me*), 1.35 (4 H, br s, NH_2), and 2.52 and 2.56 (8 H, overlapping singlets, S-CH_2 and N-CH$_2$). Addition of hydrochloric acid (6 mol dm^{-3}; 100 cm^3) and evaporation gave the dihydrochloride which was taken up in hot absolute ethanol from which it precipitated as a granular solid on cooling.

3,3,7,7,11,11,15,15-*Octamethyl*-1,9-*dithia*-5,13-*diazacyclohexadecane* (7).—To a mixture of the dihydrochloride of (6) (0.277 g, 1 mmol) and anhydrous sodium carbonate (1.1 g) in dichloromethane (30 cm^3) was added a solution of the dialdehyde (4) (0.210 g, 1.05 mmol) in the same solvent (5 cm^3). This mixture was stirred for 2 days at room temperature, filtered, and the solvent evaporated. The residue was dissolved in tetrahydrofuran and treated with borane in tetrahydrofuran (1 mol dm^{-3}; 5 cm^3) at ice-bath temperature under nitrogen. This solution was allowed to come to room temperature and stirred overnight. The excess borane was then decomposed with methanol and water, the solvent evaporated and dilute hydrochloric acid added (1 mol dm^{-3}; 100 cm^3). After being stirred for 2 days, the mixture was neutralized with aqueous sodium hydroxide and the product recovered by extraction with diethyl ether. The crude *macrocycle* (7) was sublimed (Kugelrohr, 90—115 °C, 5×10^{-3} Torr; 0.179 g, 47.3%). An analytical sample was crystallised from methanol–diethyl ether and had m.p. 110—114 °C, δ 0.95 (24 H, s, C-*Me*), 2.34 and 2.50 (both 8 H, s, S-CH_2 and N-CH_2) (Found: C,63.8; H, 11.15; N, 7.6. $C_{20}H_{42}N_2S_2$ requires C, 64.1; H, 11.3; N, 7.5%).

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