Synthesis of Two Novel [2.2]Metacyclophanes, 4,6,12,14-Tetramethyl- and 4,6,12,14-Tetramethoxy-1,2,9,10-tetrathia[2.2]metacyclophane

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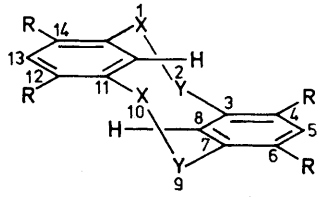
The syntheses of two novel 1,2,9,10-tetrathia[2.2]metacyclophanes are described, and the ^{1}H n.m.r. and mass spectra of the compounds obtained are discussed. These dimers display high stability to electron impact. The ^{1}H n.m.r. spectra show that the intra-annular aryl protons resonate at dramatically lower field with respect to the corresponding protons in [2.2]metacyclophane ($\Delta\delta$ *ca.* 3.6 p.p.m.). Evidence of the ability of the tetramethoxy-derivative to generate clathrates trapping volatile organic solvents is also reported.

SEVERAL reports have appeared concerning the syntheses [1] of [2.2]metacyclophane (1) and its structural analysis by *X*-ray [2] and ^{1}H n.m.r. investigations.[3] Compound (1) has been shown to exist as a step-like molecule with two distorted benzene rings, arranged in two parallel planes. The intra-annular aryl protons resonate at unusually high field (δ 4.29), due either to the diamagnetic ring current effect of the opposing benzene rings, over which these protons are extended, or to the overlap of the π-orbitals in the two rings, associated with strains and distortions of the bonds.[4] In addition, the temperature independence of the methylene resonance pattern of (1) between −80 and +190 °C,[5] indicates that the molecule is frozen in the stepped conformation.

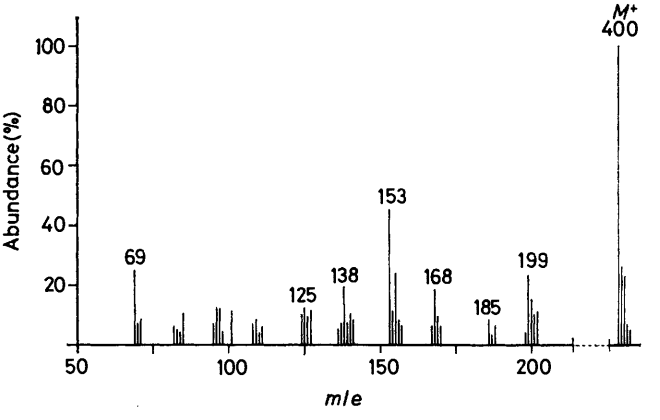
Analogous features have been observed in structurally related [2.2]metacyclophanes.[6] In particular, in 1,10-dithia[2.2]metacyclophane (2),[7] in spite of the increased C(8)–C(16) distance, no temperature dependence of the ^{1}H n.m.r. spectra was detected up to 180 °C, and the intra-annular aryl protons appeared at slightly lower field [δ 4.41 (16-H) and 5.42 (8-H)] with respect to (1).[7]



(1) X = Y = CH_2, R = H
(2) X = S, Y = CH_2, R = H
(3) X = Y = S, R = CH_3
(4) X = Y = S, R = OCH_3

In this report, we describe the synthesis of two related 1,2,9,10-tetrathia[2.2]metacyclophanes. We felt that such compounds, hitherto unreported, could be of use in elucidating the stereochemistry and the unusual ^{1}H n.m.r. absorption patterns of such cyclophanes.

Compounds (3) and (4) were obtained at room temperature by mild oxidation of the appropriate dithioresorcinol derivatives with iodine in benzene, using the high dilution technique. The compounds were characterized by ^{1}H n.m.r. and by mass spectrometry. Dimeric 1,2,9,10-tetrathia[2.2]metacyclophanes display greater stability to electron impact than the tetrameric octathia[2.2.2.2]metacyclophanes.[8] The mass spectrum of compound (4) (Figure) shows the molecular ion at *m/e* 400 as the base peak, and a diagnostically important peak at *m/e* 199 [$(M/2 - 1)^+$], arising from homolytic cleavage of the two S–S bonds. Other abundant fragments present in the spectrum, *m/e* 185, 168, 153, 138, and 125, can be rationalized by the loss of sulphur,



Mass spectrum (70 eV; 200 °C) of compound (4)

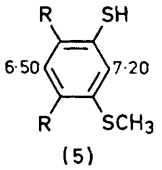
methyl groups, and carbon monoxide from the fragment at *m/e* 200. Analogous features are shown in the mass spectrum of compound (3) (see Experimental section).

The ^{1}H n.m.r. spectrum of compound (4) shows that the aromatic protons resonate as singlets at δ 7.85 and 6.43. In order to assign these signals to the respective protons, two structurally related compounds (5) and (6) were synthesized. Their ^{1}H n.m.r. spectra showed singlets at δ 6.50 and 7.20 for compound (5), and at 6.53 and 7.50 for compound (6).

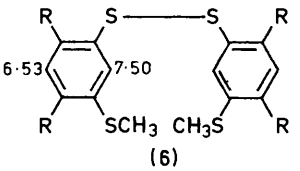
By comparison of these values with those of compound (4), one can attribute, for all three compounds, the high-field signal to the protons between the methoxy groups and the lowfield signal to the protons between the sulphur atoms. Thus, in compound (4) the singlet at

δ 7.85 is assigned to the intra-annular protons. The corresponding intra-annular protons in compound (3) resonate as a singlet at δ 7.88.

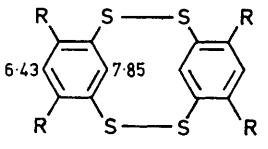
From these data, it emerges that the intra-annular protons in compounds (3) and (4) resonate at dramatically



(5)



(6)



(4)

R = OCH_3

lower fields (*ca.* 3.6 p.p.m.) than the corresponding protons in [2.2]metacyclophane. Inspection of molecular models also reveals that 1,2,9,10-tetrathia[2.2]-metacyclophanes should exist in a stepped conformation, in which the two aryl groups of the molecule are arranged in two parallel planes. In consequence of the larger value of the S–S bond length (2.03 Å),[9] with respect to C–C (1.54 Å) in (1),[2] and C–S (1.82 Å) in (2),[7] compounds (3) and (4) should not suffer such pronounced deformation both of the benzene rings and of the bridging units as in [2.2]metacyclophanes (1) and (2), and therefore the intra-annular protons are expected to resonate at a predictable chemical shift. In fact, considering *only* the deshielding effect produced by the aromatic ring current in the *undistorted molecules*, Bovey calculations[10] yield resonance values in good agreement with the observed ones for the intra-annular protons of compounds (3) and (4).

On the other hand, as previously suggested,[11,12] the magnetic anisotropy of the sulphur atoms might also play a role in the deshielding effect experienced by the intra-annular protons in 1,2,9,10-tetrathia[2.2]metacyclophanes.

The ^1H n.m.r. behaviour dramatically demonstrates the stereochemical differences of 1,2,9,10-tetrathia[2.2]-metacyclophanes compared with [2.2]metacyclophanes.

Another interesting feature of compound (4) is its ability to generate clathrates trapping volatile organic solvents in the crystal structure (see Experimental section). In contrast, cyclophane (3) does not form any inclusion compound with such solvents, and this fact brings to light the key role played by the methoxy groups in the formation of clathrates.

These observations could be of utility considering the potentialities of clathrates both for practical and academic applications.[13]

EXPERIMENTAL

4,6-Dimethyldithioresorcinol,[14] 4,6-dimethoxydithioresorcinol,[14] and 2,4-dimethoxythioanisole[14] were prepared by literature procedures. M.p.s are uncorrected. ^1H N.m.r. spectra were recorded on a Varian A-60 D instrument (Me_4Si as internal standard). Mass spectra were obtained at 70 eV by direct insertion into the source of a JEOL JMS-01SG-2 mass spectrometer (probe temperature 200 °C).

4,6,12,14-Tetramethyl-1,2,9,10-tetrathia[2.2]metacyclophane (3).—4,6-Dimethyldithioresorcinol (1.69 g, 0.01 mol) in benzene (500 ml) and iodine (2.54 g, 0.01 mol) in benzene–alcohol (9 : 1; 500 ml) were added dropwise at the same rate during 10 h to benzene (1 l) with vigorous stirring. The mixture was allowed to stand overnight, then filtered from the precipitate formed,* washed with a dilute solution of thiosulphate, then with water and dried (Na_2SO_4). Removal of benzene *in vacuo* left yellowish crystals of dimer. The crude product recrystallized from ethyl acetate gave pale yellow fibrous *crystals* (21%), m.p. 190—192 °C (Found: C, 57.15; H, 4.3; S, 38.0. $C_{16}H_{16}S_4$ requires C, 57.1; H, 4.8; S, 38.1%); *m/e* 336 (100%, M^+), 303 (16), 288 (9), 270 (18), 199 (13), 167 [$(M/2 - 1)^+$], 135 (27), 91 (26), and 77 (13); δ($CDCl_3$) 7.88 (2 H, s, ArH), 7.01 (2 H, s, ArH), and 2.39 (12 H, s, CH_3).

4,6,12,14-Tetramethoxy-1,2,9,10-tetrathia[2.2]metacyclophane (4).—This compound was synthesized in the same way as (3), from equimolecular amounts of 4,6-dimethoxydithioresorcinol and iodine. Recrystallization of the crude product from dioxan afforded yellowish *crystals* (25%), m.p. 206 °C (decomp.) (Found: C, 47.9; H, 4.1; S, 31.95. $C_{16}H_{16}O_4S_4$ requires C, 48.0; H, 4.0; S, 32.0%); δ($CDCl_3$) 7.85 (2 H, s, ArH), 6.43 (2 H, s, ArH), and 3.87 (12 H, s, OCH_3).

2,4-Dimethoxy-5-methylthiobenzenesulphonyl Chloride.—2,4-Dimethoxythioanisole (9.2 g, 0.05 mol) and pyridine–sulphur trioxide adduct[15] (7.95 g, 0.05 mol) were heated in an autoclave at 120 °C for 24 h. After cooling, the mixture was poured into a saturated aqueous solution of K_2CO_3. The resulting cake was collected on a filter, and washed twice with concentrated K_2CO_3, then with alcohol and ethyl ether. The crude potassium 2,4-dimethoxy-5-methylthiobenzenesulphonate, dried at 110 °C, was pulverized and treated under reflux with $POCl_3$ (30 g) for 2 h. The excess of $POCl_3$ was decomposed on crushed ice and the solid sulphonyl chloride was collected on a filter. The product was dissolved in $CHCl_3$, dried ($CaCl_3$), and recovered by evaporating the solvent under reduced pressure. The crude product recrystallized from toluene as yellow *crystals* (38%), m.p. 128—130 °C (decomp.) (Found: C, 38.35; H, 3.85; Cl, 12.65; S, 22.6. $C_9H_{11}ClO_4S_2$ requires C, 38.2; H, 3.9; Cl, 12.55; S, 22.65%); *m/e* 282 (100%), 267 (5), 245 (5), 231 (2), 203 (5), 199 (14), 184 (6), 168 (25), 153 (27), 138 (15), 125 (12), 108 (28), and 95 (15); δ($CDCl_3$) 7.82 (1 H, s, ArH), 6.64 (1 H, s, ArH), 4.10 (3 H, s, OCH_3), 4.06 (3 H, s, OCH_3), and 2.49 (3 H, s, SCH_3).

2,4-Dimethoxy-(5-methylthio)thiophenol.—To a well stirred mixture of 2,4-dimethoxy-5-methylthiobenzenesulphonyl chloride (2.82 g, 0.01 mol) and zinc dust (12 g) in benzene (40 ml), cooled in an ice-bath, 37% HCl (25 ml) was added dropwise. When addition was complete, the mixture was

* We have some evidence that less soluble cyclic tetramers and/or trimers are also formed in this reaction. Isolation and identification of these macrocyclic compounds will be reported.

warmed (60 °C) for 30 min, and then distilled. The product was extracted with benzene, washed with water, and dried (Na_2SO_4). Removal *in vacuo* of the solvent left light yellow crystals of the desired *thiol* (55%), m.p. 51 °C (from methanol) (Found: C, 49.8; H, 5.65; S, 29.55. $C_9H_{12}O_2S_2$ requires C, 49.95; H, 5.6; S, 29.65%); *m/e* 216 (100%), 201 (46), 173 (8), 168 (9), 155 (6), 140 (4), 124 (4), and 108 (4); δ($CDCl_3$) 7.20 (1 H, s, ArH), 6.50 (1 H, s, ArH), 3.93 (6 H, s, OCH_3), 3.63 (1 H, s, SH), and 2.40 (3 H, s, SCH_3).

Bis-(2,4-dimethoxy-5-methylthiophenyl) Disulphide (6).—Compound (5) (0.54 g, 2.5 mmol) was dissolved in dimethyl sulphoxide [16] (2 ml) and heated at 80—90 °C with stirring for 4 h. After decolourizing with charcoal, the solution, cooled at room temperature, was poured into brine (20 ml) and left for some time. The precipitated disulphide was collected by filtration, washed several times with water, and dried. Recrystallization from ethanol afforded yellow *crystals* (85%), m.p. 120—122 °C (Found: C, 50.35; H, 5.1; S, 29.65. $C_{18}H_{22}O_4S_4$ requires C, 50.2; H, 5.15; S, 29.8%); *m/e* 430 (100%), 399 (9), 215 (66), 201 (13), 185 (3), 169 (50), 154 (20), 140 (13), 127 (4), and 108 (3); δ($CDCl_3$) 7.50 (2 H, s, ArH), 6.53 (2 H, s, ArH), 3.99 (6 H, s, OCH_3), 3.91 (6 H, s, OCH_3), and 2.40 (6 H, s, SCH_3).

Clathrate Formation.—In order to test the ability of our cyclophanes to form inclusion compounds with organic solvents, compounds (3) and (4) were recrystallized from acetone, nitroethane, acetonitrile, benzene, chloroform, dioxan, ethyl acetate, dimethylformamide, and dimethyl sulphoxide. The recrystallized material was then filtered off, washed several times with n-pentane, and dried at room temperature. Through ^1H n.m.r. analyses of the recrystallized materials, compound (3) was not found to include any solvent at all, whereas compound (4) included one mol. equiv. of chloroform, dioxan, ethyl acetate, dimethylformamide, and dimethyl sulphoxide, respectively. The guest solvent however was released when the specimens were dried under high vacuum (10^{-7} mmHg) at room temperatures (*ca.* 30 °C).

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