Unsymmetrically Tris-bridged [2.2.2]Cyclophanes. Synthesis of [2.2.2](1,2,4)(1,3,5)Cyclophane[1]

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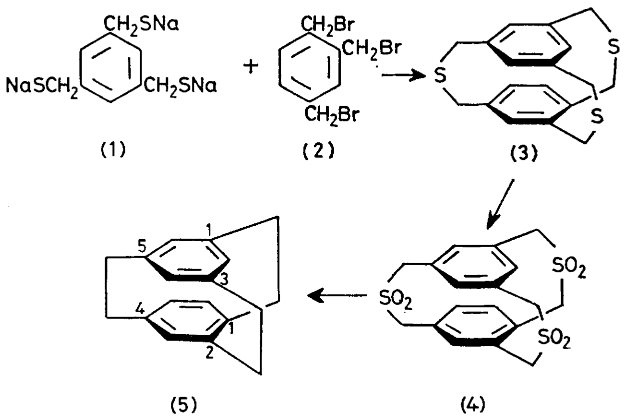
Summary [2.2.2](1,2,4)(1,3,5)Cyclophane (**5**) was synthesized, and its unusually strained and skew structure was supported by its u.v. and n.m.r. spectra.

[2.2.2](1,3,5)CYCLOPHANE[2] (D_{3h} symmetry), [2.2.2](1,2,4)-cyclophane[3] (C_s symmetry), and [2.2.2.2](1,2,4,5)cyclophane[4] (D_{2h} symmetry) so far have been the only representatives of the highly strained cyclophanes which have two benzene rings held together with three or more ethanobridges. One notable feature of these compounds is the strong transannular interaction between their aromatic π-electron clouds as shown by their spectral and chemical properties.

We are interested in the syntheses and absolute configurations of dissymmetrically twisted cyclophanes,[5] and we report the synthesis of [2.2.2](1,2,4)(1,3,5)cyclophane (**5**); a chiral compound (C_1 symmetry) constructed from 1,3,5-trimethylbenzene and 1,2,4-trimethylbenzene units.



1,3,5-Tris(mercaptomethyl)benzene[6] was prepared from 1,3,5-trimethoxycarbonyl benzene and converted into the sodium salt (**1**) which was refluxed in ethanol with 1,2,4-tris(bromomethyl)benzene (**2**)† to afford trithia[3.3.3](1,2,4)(1,3,5)cyclophane (**3**),‡ 40% yield, colourless prisms, m.p. 200—201 °C (from benzene); u.v. λ_{max} (iso-octane) 255 nm (ϵ 5020); n.m.r. ($CDCl_3$) τ 2·79—3·60 (5H, m, ArH), 4·21 (1H, s, ArH), and 5·92—6·91 (12H, m, CH_2).

The trithiacyclophane (**3**) was treated with hydrogen peroxide to furnish the trisulphone (**4**), colourless powder, m.p. >300 °C. Pyrolysis (520 °C, 1 h) of (**4**) according to Staab's procedure,[7] followed by silica gel chromatography and recrystallization from pentane gave [2.2.2](1,2,4)(1,3,5)cyclophane (**5**)§ (6·1% yield), colourless plates, m.p. 87—88 °C; u.v. λ_{max} (iso-octane) 235 (shoulder, ϵ 10,030) and 300 nm (380); n.m.r. ($CDCl_3$) τ 3·20 (1H, d, ArH), 3·18 and 3·40 (2H, AB q, J_{AB} 8 Hz, ArH), 3·68 (1H, t, ArH), 4·12 (1H, d, ArH), 4·96 (1H, t, ArH), and 6·48—8·36 (12H, m, CH_2). The remarkable upfield shift of one aromatic proton to τ 4·96 clearly indicates a skew geometry (C_1 symmetry) of the molecule in which the corresponding atoms of the two benzene rings are not directly opposite each other. This highly strained skew structure shows an unusual u.v. spectrum and a marked tendency to resinify at room temperature.

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† B.p. 64—65 °C, prepared from 1,2,4-trimethoxycarbonylbenzene by $LiAlH_4$ reduction followed by PBr_3 treatment.

‡ The structural formulae (**3**), (**4**), and (**5**) respectively represent one of their possible enantiomers.

§ Satisfactory elemental analysis and mass spectral data have been obtained for all new compounds.

[1] The nomenclature used is that proposed by F. Vögtle and P. Neumann, *Tetrahedron*, 1970, **26**, 5847.
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