Syntheses of Optically Active [8][10]Paracyclophane[1] and Doubly Bridged [2,2]Paracyclophane

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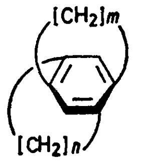
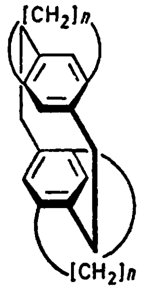
Summary The syntheses of the optically active forms of the [8][10]paracyclophane (**1b**) and the double bridged [2,2]-paracyclophane (**2b**) are reported.

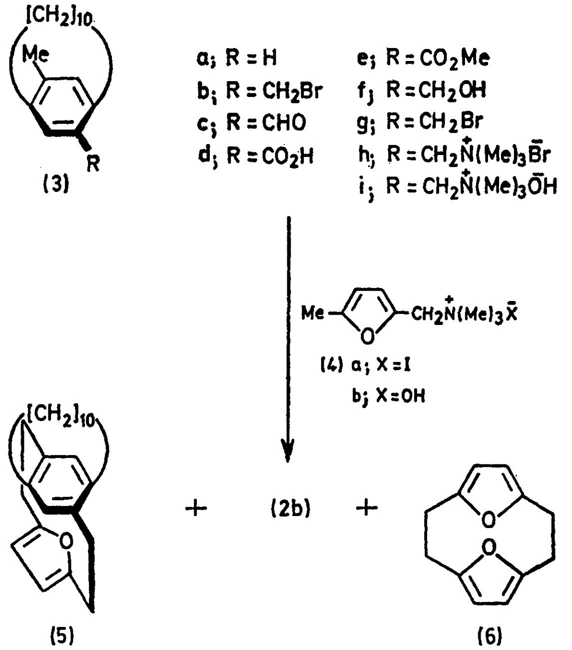
WE have previously reported[2] the preparations of novel classes of paracyclophanes (**1**) and (**2**) with benzene rings flanked from both sides. Compounds (**1a**), (**2a**), and (**2b**) have D_2 symmetry, whereas (**1b**) has C_2 symmetry, and they are all chiral. The optically active forms of (**1b**) and (**2b**) have now been synthesised as shown.



(1) a; $m = n = 8$
b; $m = 8$; $n = 10$



(2) a; $n = 8$
b; $n = 10$



(3)

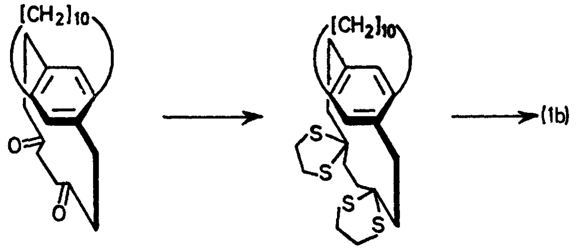
a; R = H
b; R = CH_2Br
c; R = CHO
d; R = CO_2H
e; R = CO_2Me
f; R = CH_2OH
g; R = CH_2Br
h; R = $CH_2\overset{+}{N}(Me)_3\bar{Br}$
i; R = $CH_2\overset{+}{N}(Me)_3\bar{O}H$

(4) a; X = I
b; X = OH

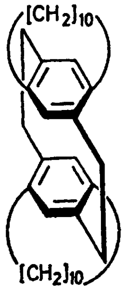
(5) (6)

Bromomethylation[3] of (**3a**)† with formaldehyde, HBr, and phosphoric acid afforded the bromomethyl derivative (**3b**), which was oxidised with sodium propanenitronate[3] in ethanol to give the aldehyde (**3c**). Permanganate oxidation of aldehyde (**3c**) in acetone gave the racemic acid (**3d**), m.p. 168—169°, the brucine salt of which was found to be satisfactory for successful optical resolution. The optically active (**3d**), m.p. 134—135°, $[\alpha]_D^{21}$ $-$ 28° ($CHCl_3$), so obtained was converted into the methyl ester (**3e**) which was then reduced ($LiAlH_4$) to the alcohol (**3f**), b.p. 145—147° at 0·1 mmHg, $[\alpha]_D^{26}$ $+$ 8·1° ($CHCl_3$). This alcohol was treated with PBr_3 to afford the bromide (**3g**) which was converted into the quaternary ammonium salt (**3h**), m.p. 252—254°, $[\alpha]_D^{21}$ $+$ 14·1° ($CHCl_3$).

An equimolar mixture of the quaternary salt (**3h**) and (**4a**)[5] was treated with silver hydroxide to give a mixture of Hofmann bases which was pyrolysed in boiling toluene. The mixture was extracted with n-hexane, and the extract was chromatographed on neutral alumina to give the following fractions: (i) the doubly bridged [2,2]paracyclophane (**2b**), m.p. 219—221°, $[\alpha]_D^{21}$ $+$ 61·3° ($CHCl_3$) (5%); (ii) the benzene–furan 'hybrid' [2,2]paracyclophane (**5**), b.p. 154—156° at 0·01 mmHg, $[\alpha]_D^{22}$ $-$ 21·3° ($CHCl_3$) (10%); (iii) [2,2]furanophane (**6**).



(7) (8)



(9)

The synthetic procedure and the observed optical activity necessitate that the doubly bridged [2,2]paracyclophane (**2b**) has the staggered configuration indicated, and the identity of its i.r. and mass spectra with those of the racemic form previously reported confirms our assumption[6] that this compound has the staggered rather than eclipsed structure (**9**) (the *meso* form).

The furan fragment of the hybrid was modified to an octamethylene bridge as described for the racemic form.[2] (**5**) was treated with 10% sulphuric acid in acetic acid to give the 1,3-diketone (**7**), m.p. 159—160°, $[\alpha]_D^{24}$ $-$ 140·2° ($CHCl_3$), which reacted with ethanedithiol and boron trifluoride to yield the bis-dithioacetal (**8**), m.p. 194—195°, $[\alpha]_D^{24}$ $-$ 60·1° ($CHCl_3$). Compound (**8**) was desulphurised with Raney nickel in boiling ethyl acetate to give ($-$)-[8][10]paracyclophane (**1b**), b.p. 182—183° at 2 mmHg, $[\alpha]_D^{25}$ $-$ 6·3° ($CHCl_3$), the i.r. and mass spectra of which were identical with those of the racemic form.

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† 12-Methyl[10]paracyclophane (**3a**) was prepared by reduction ($LiAlH_4$) of 12-bromomethyl[10]paracyclophane which was obtained by the bromomethylation of [10]paracyclophane.[4]

[1] See D. H. Smith, 'Bridged Aromatic Compounds', Academic Press, New York, 1964, p. 13.
[2] M. Nakazaki, K. Yamamoto, and S. Tanaka, *Tetrahedron Letters*, 1971, 341.
[3] A. T. Blomquist and B. H. Smith, *J. Amer. Chem. Soc.*, 1960, **82**, 2073.
[4] D. J. Cram and H. U. Daeniker, *J. Amer. Chem. Soc.*, 1954, **76**, 2743.
[5] H. E. Weiberg, F. S. Fawcett, W. E. Mochel, and C. W. Theobald, *J. Amer. Chem. Soc.*, 1960, **82**, 1428.
[6] D. T. Longone and H. S. Chow, *J. Amer. Chem. Soc.*, 1964, **86**, 3898.