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THE ABSOLUTE CONFIGURATIONS OF [8][8], [8][10]PARACYCLOPHANES AND RELATED PARACYCLOPHANE COMPOUNDS

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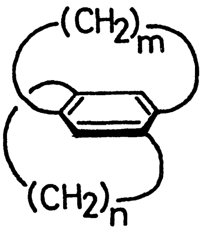
Starting from (+)-[8]paracyclophane-10-carboxylic acid optically active [8][8]paracyclophane was prepared and its absolute configuration was correlated to (S)-(+)-[2.2]paracyclophane-4-carboxylic acid. The absolute configurations of (-)-[8][10]paracyclophane and related optically active paracyclophanes were also discussed.

The preceding papers[1)] in this series reported the preparation of racemic [8][8] and [8][10]paracyclophanes (1)[2)] together with the synthesis of optically active (-)-[8][10]paracyclophane (1b).

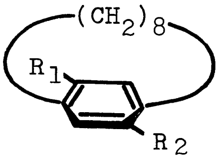
We now wish to report the synthesis of optically active [8][8]paracyclophane (1a) whose absolute configuration can be correlated to (S)-(+)-[2.2]paracyclophane-4-carboxylic acid (21).[3)] This eventually establishes the absolute configurations of other related paracyclophane compounds.



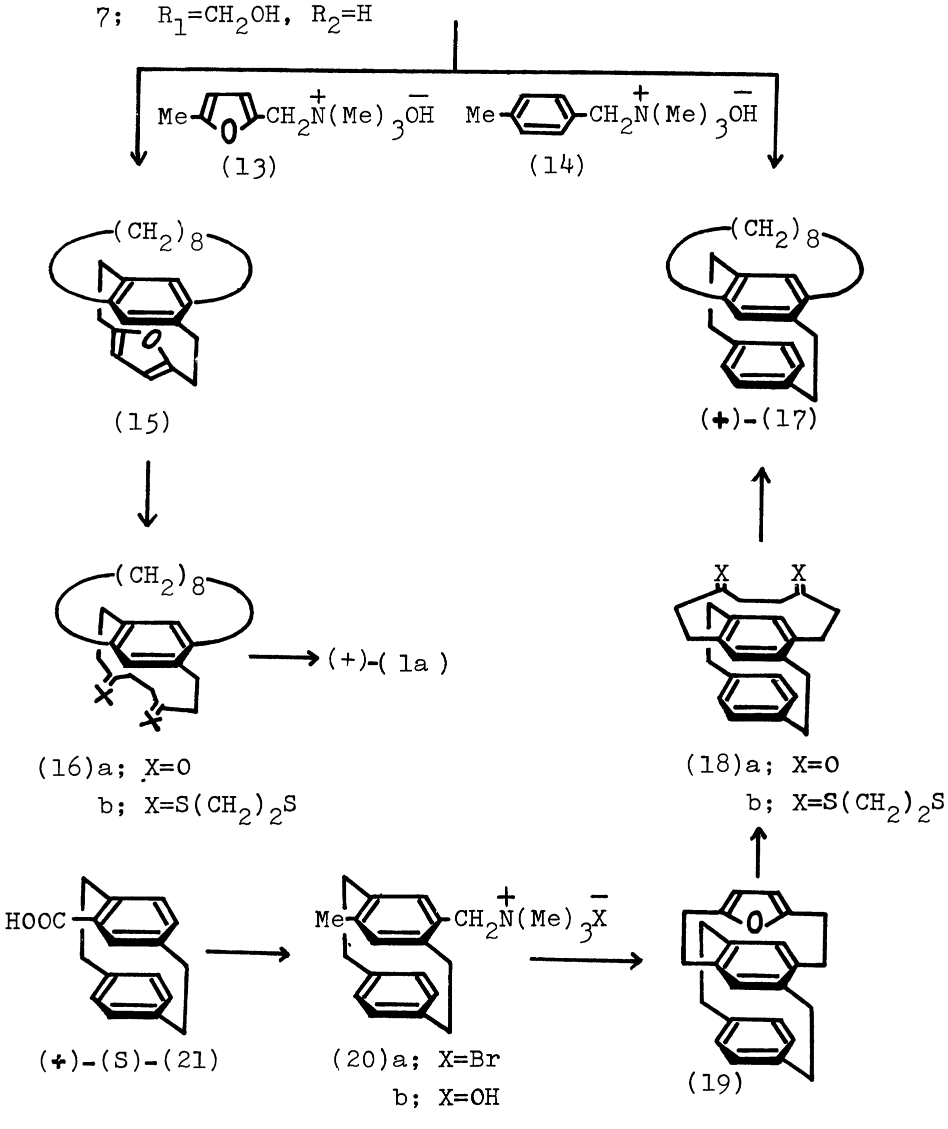
(1)a; m = n = 8
b; m=8 n=10

The bromomethyl compound (3) prepared from [8]paracyclophane (2)[4)] was treated with sodium salt of 2-nitropropane [5)] in ethanol to give the aldehyde (4) which was further oxidized with potassium permanganate in acetone to the (±)-carboxylic acid (5), m.p. 152~153°C. Optical resolution via (+)-1-α-naphthylethylamine salt afforded the (+)-acid (5), m.p. 139~140°C, $[\alpha]_D^{25}$ +18°, the methyl ester (6) of which was reduced ($LiAlH_4$) to the alcohol (7). Conversion to the bromide (8) with PBr_3 followed by reduction with $LiAlH_4$ afforded (+)-10-methyl[8]paracyclophane (9), b.p. 142~143°C/0.1mmHg, $[\alpha]_D^{19}$ +4.6°, which was bromomethylated to the bromide (10).

Construction of the second [8]bridge was carried out via benzene-furan "hybrid"[2.2]paracyclophane (15) provided by pyrolysis (in boiling toluene) of a mixture of the furan quarternary base (13)[6)] and the ammonium base (12) from the bromide (10). After purification by chromatography, the oily product (15) (9%) was directly hydrolyzed with 10% sulfuric acid in acetic acid. In order to complete the synthesis there remained the requirement of removing the carbonyl groups from the 1,4-diketone (16a), and this was accomplished by desulfurization of the compound (16b) with Raney nickel affording optically active [8][8]paracyclophane (1a), b.p. 148~150°C/1.0mmHg, $[\alpha]_D^{20}$ +5.4°.



2; R_1=H, R_2=H
3; R_1=CH_2Br, R_2=H
4; R_1=CHO, R_2=H
5; R_1=CO_2H, R_2=H
6; R_1=CO_2Me, R_2=H
7; R_1=CH_2OH, R_2=H
8; R_1=CH_2Br, R_2=H
9; R_1=Me, R_2=H
10; R_1=Me, R_2=CH_2Br
11; R_1=Me, R_2=$CH_2\overset{+}{N}(Me)_3\overset{-}{Br}$
12; R_1=Me, R_2=$CH_2\overset{+}{N}(Me)_3\overset{-}{OH}$



The [8]bridged [2.2]paracyclophane (17) was selected as our key intermediate which correlates (+)-[8][8]paracyclophane (1a) to (S)-(+)-[2.2]paracyclophane carboxylic acid (21) with known absolute configuration.

When the same optically active starting material, [8]paracyclophane ammonium base (12), was mixed with the p-tolylammonium base (14) and pyrolyzed, the desired (+)-[8]bridged [2.2]paracyclophane (17), m.p. 138~139°C, $[\alpha]_D^{20}$ +14.2°, was obtained in a 5% yield from the reaction mixture.

This dextrorotatory compound could also be drived from (S)-(+)-[2.2]paracyclophane carboxylic acid (21) by the following sequence of conversions. The [2.2]paracyclophane ammonium base (20) accessible from (S)-(+)-(21)[7] was coupled with the furan ammonium base (13) to give rise to the triple-layered paracyclophane (19) (6%), m.p. 111~112°C, $[\alpha]_D^{20}$ +137°.

Modification of the furan moiety of this triple-layered compound to give the (+)-[8]bridged [2.2]paracyclophane (17), m.p. 135~136°C, $[\alpha]_D^{20}$ +33.2°, followed the procedure which was already described for the conversion (15) ⟶ (1a).

These correlations enable us to assign S configuration to (+)-[8]paracyclophane carboxylic acid (5), which eventually leads to S configuration for (+)-[8][8]paracyclophane (1a).

Comparision of the CD spectra (Fig.1) of (S)-(+)-[8][8]paracyclophane (1a) and that of (-)-[8][10]paracyclophane (1b) provides convincing evidence that these two compounds have opposite configurations. Since (R)-(-)-[8][10]paracyclophane (1b) was prepared starting from the (-)-methylcarboxylic acid (22), the latter must have R configuration, and this conclusion is also supported by the CD data (Fig.2) which further indicates R configuration to (-)-[10]paracyclophane carboxylic acid (22) and its related compounds.

It appears to be appropriate to mention that Schlögl[8] recently suggested the opposite configurations to [m][n]paracyclophanes based mainly on the analyses of their CD spectra.

Fig.1

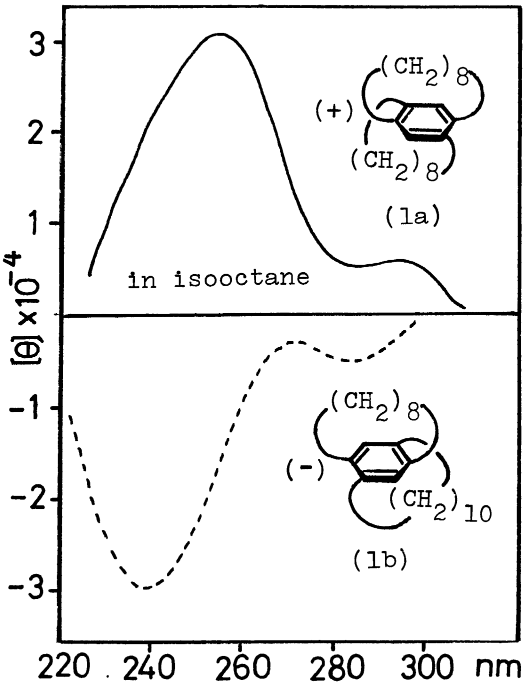
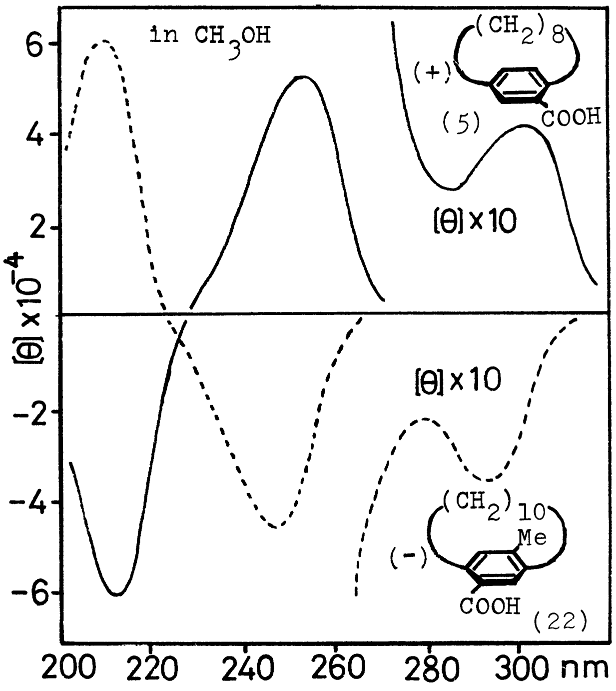


Fig.2



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