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CYCLOTETRAVERATRYLENE, A CONFORMATIONALLY MOBILE STRUCTURE

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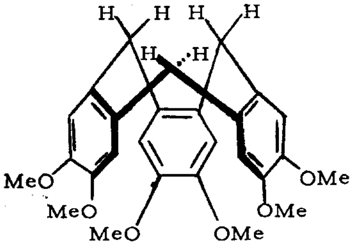
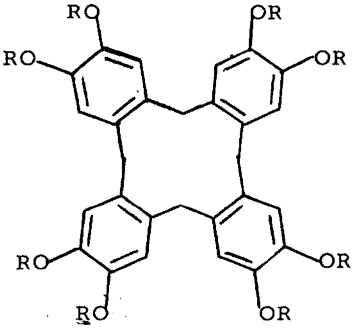
Chloromethylation of veratrole or acid catalyzed dehydration of 3,4-dimethoxybenzyl alcohol has been shown to give cyclotriveratrylene (I) as the major product.[1,2] NMR evidence is suggestive of a "crown" conformation for I, in which the methylene carbons form the truncated apex of a three-sided pyramidal structure.[2-4] The invariance of the NMR spectrum over a wide range of temperature indicates that inversion and rotation are prohibited in such a conformation,[4] and this has been elegantly confirmed by successful resolution of a cyclotriveratrylene derivative into stable optical antipodes.[5,6]

We now find that conditions which lead to I also afford the novel homolog II, and we wish to present evidence supporting a flexible structure for the latter, which, however, can readily be frozen into a single conformation. A solution of 3,4-dimethoxybenzyl alcohol in glacial acetic acid containing a few drops of concd. sulfuric acid, when warmed at 90° for 15 minutes, gave a mixture of I (68%) and II (16%), in addition to a small amount of material of higher molecular weight. Treatment of veratrole in 70% sulfuric acid with aqueous formaldehyde at 0° also afforded I and II in approximately the same proportions. Cyclotetraveratrylene (II) can be separated from I by fractional crystallization from a benzene-chloroform mixture followed by recrystallization from chloroform, m.p. 319-322°, and its composition is established as $C_{36}H_{40}O_8$ by elemental analysis and mass spectrometry. The mass spectrum shows a molecular ion at m/e

600.2732 (calc. m/e 600.2723) and strong peaks at m/e 449, 299, and 151, corresponding to fragmentation to trimer, dimer, and monomer units respectively.



I



II, R = CH_3
III, R = H
IV, R = $COCH_3$

Inspection of molecular models indicates that II should possess a more flexible structure than I, with the possibility of pseudorotation about the methylene carbons. Consecutive rotations about each methylene group would result in the interchange of all intra- and extra-annular methylene protons. In agreement with this hypothesis, the NMR spectrum of II, at room temperature and above, shows only three peaks in the ratio 1:3:1 corresponding to (equivalent) aromatic, methoxyl, and methylene protons respectively. As the temperature is lowered (Fig. 1), signals due to aromatic and

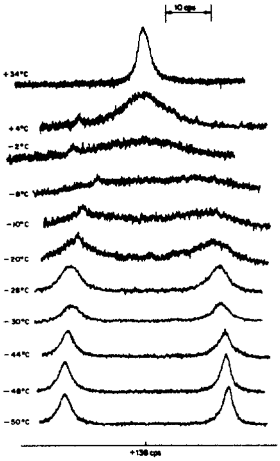
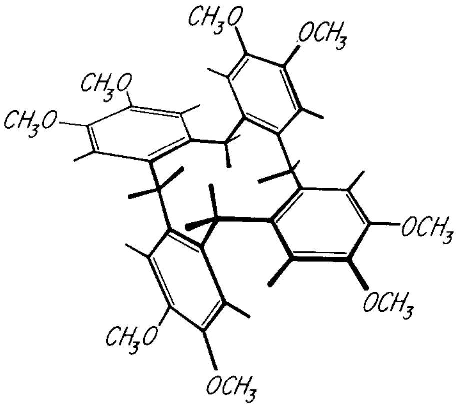
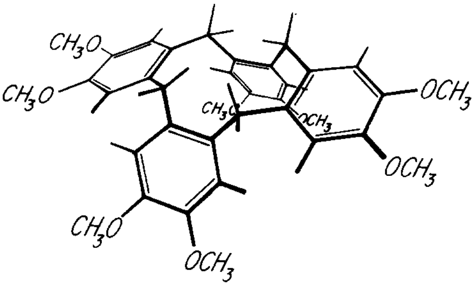


Fig. 1. Aromatic protons of cyclotetraveratrylene (chemical shifts are relative to the aldehyde proton of acetaldehyde).

methoxyl protons broaden until each is split into two well-defined singlets of equal area ($\nu_0\delta$ for aromatic and methoxyl protons is 36.3 and 23.1 cps respectively). Methylene protons now appear as an AB pattern ($J = 16$ cps, $\nu_0\delta = 35.6$ cps), part of which is obscured by the methoxyl resonances. The low temperature spectrum requires a structural symmetry which can be met by either a "chair" conformation (IIa) or a conformation such as IIb ("saddle"). The fully symmetrical (C_{4v}) "crown," analogous to I, is ruled out in the present case, and the steric compression of π-orbitals arising from opposing faces of aromatic rings in IIb argues against this being the thermodynamically favored conformation. Activation parameters for the pseudorotation process were calculated over the temperature range 225-319^0 K (coalescence occurs at ~265^0 K), using the higher field line of the aromatic pair under conditions of slow exchange. Corrected line-widths were obtained and were used to calculate lifetimes (τ) from a plot of line width vs. $\tau\Delta\omega$ for a collapsing doublet. Application of the Eyring formulation gave $\Delta H^{\ddagger}_{265} = 10.4 \pm 0.2$ kcal. mole, $\Delta F^{\ddagger}_{265} = 13.2 \pm 0.3$ kcal. mole^{-1}, and $\Delta S^{\ddagger} = -10.6 \pm 1.8$ cal. deg.$^{-1}$ mole^{-1}.



II a



II b

Treatment of II with boron tribromide in chloroform gave the octahydroxy compound III which yielded the octaacetate IV with acetic anhydride and pyridine. The temperature dependent NMR signals due to the aromatic protons of III indicate that this molecule undergoes conformational changes analogous to those of II. These substances appear to be the first known derivatives of the sym-cyclododecatetraene system, and it is expected that their chemistry, contrasted with that of cyclotriveratrylene (I) and its derivatives, will reflect differences in conformational rigidity of the two ring systems. This and other aspects of cycloveratrylene chemistry are under study.

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3. A. Goldup, A. B. Morrison, and G. W. Smith, J. Chem. Soc., 3864 (1965).
4. B. Miller and B. D. Gesner, Tetrahedron Letters, 3351 (1965).
5. A. Lüttringhaus and K. C. Peters, Angew. Chem. Internatl. Edn., 5, 593 (1966).
6. The monoketone derived from I apparently possesses a more flexible conformation. An interesting consequence of this is the isolation of two conformationally isomeric alcohols (α- and β-cyclotriveratrylenols) upon reduction of the ketone (see N. K. Anand, R. C. Cookson, B. Halton, and I. D. R. Stevens, J. Am. Chem. Soc., 88, 370 (1966)).