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[7]METACYCLOPHANE AND ITS 13-BROMO DERIVATIVE

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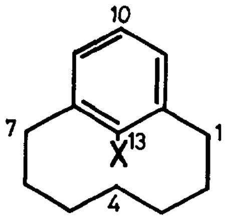
In extention of our studies on [7](2,6)pyridinophanes,[1] the present report deals with the synthesis and properties of [7]metacyclophane (I) and its 13-bromo derivative (II) having the same heptamethylene bridges.[2]

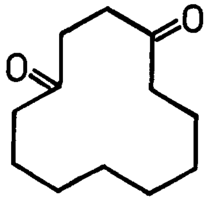
Intramolecular aldol condensation of cyclododecane-1,4-dione[3] (III) with methanolic NaOH gave a bicyclic enone (IV, 87%, b.p. 95°/2 mm, IR 1696, 1646 cm^{-1}, M^+ m/e 178),[4] which was converted to the corresponding allyl alcohol (V, 86%, b.p. 96°/0.1 mm, IR 3320 cm^{-1}, M^+ m/e 180)[4] on lithium aluminium hydride reduction. The treatment of V with CHBr$_3$-t-BuOK[5] afforded 13-bromo[7]metacyclophane (II) in a 32% yield (m.p. 47.5-48.5°, IR 3070, 3055, 1572 cm^{-1}, MS m/e 254, 252 (M^+), 173 (M^+ - Br)).[4] The direct formation of II is ascribed to the spontaneous aromatization of the intermediary dibromocarbene adduct (VI). The lithiation of II with n-butyllithium and the subsequent quenching with water gave [7]metacyclophane (I, b.p. 115°/4 mm, IR 3105, 3061, 3030, 1610, 1590, 1490 cm^{-1}, M^+ m/e 174)[4] in a 70% yield. 13-Deuterio derivative (I_D, IR 2258 cm^{-1} (ν_{C-D}), >0.96d/molecule) was also prepared in a similar way using 99.8% deuterium oxide as a quencher.



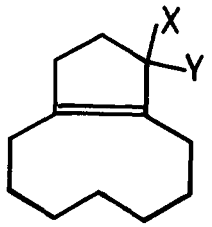
I X=H

I_D X=D

II X=Br

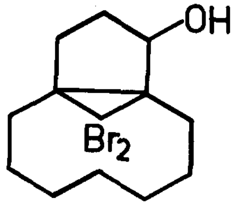


III



IV X,Y=O

V X=H, Y=OH



VI

The PMR spectrum of I is shown in Fig. 1. In contrast to that of m-xylene,[6] the aromatic protons showed a split signal, in which one proton (δ 7.43) was deshielded to a considerable extent (ca. 0.4 ppm). This signal was assigned to the C-13 proton, since it was absent in the PMR of 13-deuterio derivative, I_D (Fig. 1).[7] The down-field shift of the C-13 proton is attributed to the van der Waals effect[8] of the surrounding heptamethylene chain which is exerting a steric compression on the aromatic proton.

The PMR spectrum of the heptamethylene protons consisted of three groups of multiplets at room temperature. The remarkably high-field signal (δ -0.18) is assigned to two protons on C-4, as that of the C-4 protons of [7](2,6)pyridinophane has been observed at δ 0.16. The heptamethylene signals of I were temperature-dependent as shown in Fig. 1. At -73.5°, one of the C-4 protons showed an PMR signal at δ -1.33. The low-field counterpart was possibly concealed behind the multiplets of the other methylenes. These signals of C-4 protons coalesced at -27.6°.

The shielding effect in I is ascribed to the diamagnetic ring current of the benzene ring.[9] An inspection of the molecular models of I indicates that

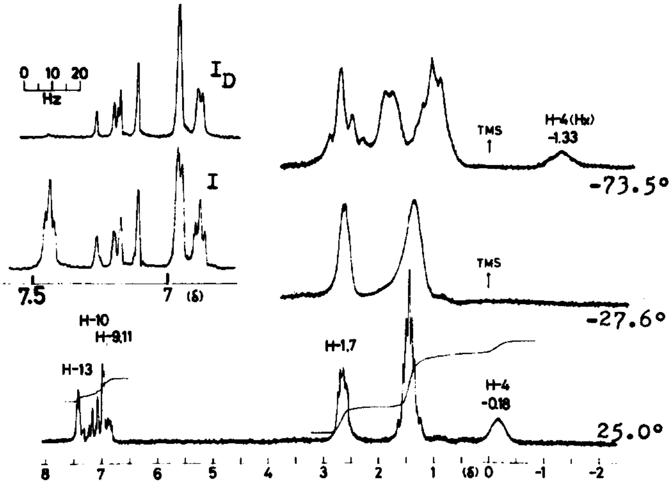
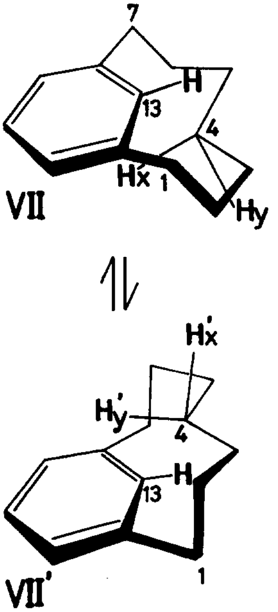


Fig. 1. The PMR Spectra of I at Different Temperatures (60 MHz) and The Aromatic Part of I and I_D (100 MHz, 31°)[10]



VII

VII'

such an extreme conformation as VII is most plausible energetically and that, in VII, one proton (H_x) on C-4 is forced close to the π-cloud of the benzene ring. Above room temperature (up to 95°), the heptamethylene bridge appears to be flipping up and down and its protons show average PMR signals. The energy barrier ($\Delta G^{\ddagger}_c$) for the conformational change (VII $\rightleftarrows$ VII') of I was estimated to be 11.5 kcal/mole (at T_c -27.6°),[11] which is larger than that of [7](2,6)pyridinophane ($\Delta G^{\ddagger}_c$ 9.0 kcal/mole, T_c -75.5°).[1] This fact indicated undoubtedly that the lone pair of pyridine nitrogen is sterically less bulky than the aromatic C-H bond.[12] Moreover, 2,6-dithia[7]metacyclophane[13] had the smaller $\Delta G^{\ddagger}_c$ value (10.2 kcal/mole, T_c -50° at 100 MHz) than I. The flexibility introduced by incorporating two sulphur atoms may be ascribed to the fact that C-S bonds are longer than C-C bonds and C-S-C bending requires less energy than C-C-C bending.

The heptamethylene chain of 13-bromo derivative (II) seems to be fixed rigidly even at room temperature as shown by the PMR spectrum (Fig. 2). The signal of <u>one</u> proton on C-4 appeared at δ -1.86. An extreme conformer similar to VII, but more crowded, would explain this unexpectedly high value. The signal of the benzylic methylenes appeared as an AB part of ABCD-type signal, of which parameters were calculated by first-order approximation as follows: ν_A δ 3.37, ν_B δ 2.68, J_{AB} 13.0, $J_{BC} = J_{BD}$ 4.5, J_{AD} 10.5, J_{AC} 4.6 Hz.

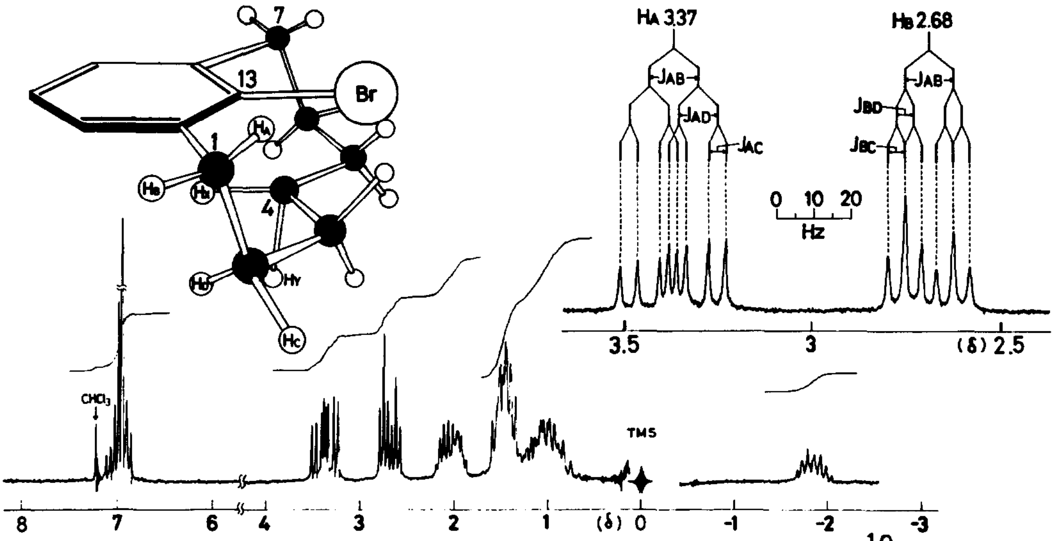


Fig. 2. PMR Spectrum of II (in $CDCl_3$ at 31°, 100 MHz).[10]

Footnotes and References

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4. All the new compounds gave correct analyses.
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7. The other aromatic protons of I_D exhibited a typical AB_2-type signal: ν_A δ 7.17, ν_B 6.92, J_{AB} 7.7 Hz. For the corresponding signal of *m*-xylene-2*d* (ν_A δ 7.03, ν_B 6.86, J_{AB} 7.7 Hz in CCl_4), see R. R. Fraser, *Can. J. Chem.*, **38**, 2226 (1960). See also D. J. Wilson, V. Boekelheide and R. W. Griffin, Jr., *J. Am. Chem. Soc.*, **82**, 6302 (1960); R. Flammang, H. P. Figeys and R. H. Martin, *Tetrahedron*, **24**, 1171 (1968).
8. For example, see L. M. Jackman and S. Sternhell, "*Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*," 2nd Ed., Pergamon Press, London (1969), p. 71.
9. Ref. 8, p. 95.
10. All the PMR spectra were obtained on a JEOL C-60-H and a Varian HA 100 spectrometer in $CDCl_3$ using an internal TMS standard.
11. $k_c = \pi\Delta\nu/\sqrt{2}$, $\Delta G^{\ddagger}_c = 2.303\,RT_c\,(10.319 - \log k_c + \log T_c)$. See G. Binsch, in "*Topics in Stereochemistry*," ed. by E. L. Eliel and N. L. Allinger, Vol. 3, Interscience Publisher, New York (1968), p. 97.
12. cf. N. L. Allinger, *et al.*, *Tetrahedron Letters*, 3345 (1964).
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