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[3.2]METACYCLOPHANES: SYNTHESIS AND RING INVERSION[1]

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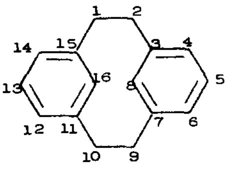
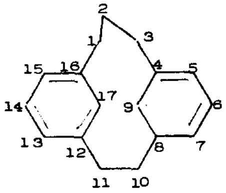
The unusual chemical and physical properties of [2.2]metacyclophanes (I)[2] have prompted us to study derivatives of the next member in this series, [3.2]metacyclophane (II). The specific points of interest are the transannular electronic effects and reactions,[3] the effect of the ring current induced diamagnetic field, the proton magnetic resonance spectrum,[4] and the reactivity[5] and rigidity of the medium-membered ring. We report here the syntheses of 2,2-dicarbethoxy[2.3]metacyclophane and the 1,1,3,3-tetradeutero derivative with an estimate of the ring inversion activation energy.



I



II

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Of the several routes we have examined in the preparation of [3.2]metacyclophanes, the most successful synthesis has been a seven-step scheme starting from m-bromotoluene, with an overall yield of 1% of 2,2-dicarbethoxy[3.2]metacyclophane. 3,3-Bis-(bromomethyl)bibenzyl and diethyl malonate in xylene were slowly added to an excess of sodium hydride in refluxing xylene. Elution chromatography of the crude reaction product afforded an 11% yield of 2,2-dicarbethoxy[3.2]metacyclophane and 16% yield of the corresponding dimer. This appears to be the first example of such a cyclization in the eleven-membered ring series.

Anal. Calcd. for $C_{25}H_{26}O_4$: C, 75.33; H, 7.15; mol. wt., 365. Found: C, 75.54; H, 6.99; mol. wt. (thermoelectric osometer) 360; IR: 5.79 μ; λ_{max}^{EtOH} 269 mμ (log ε 2.59).

The proton magnetic resonance spectrum at 60 mc./sec. (Varian Associates A-60 N.M.R. spectrophotometer using a V-6040 N.M.R. Variable Temperature Controller) taken in carbon tetrachloride solution showed the following features for the diester given in ppm from TMS (internal standard): 7.0, multiplet, 6 protons (aromatic); 4.87, singlet, 2 protons (9,17-protons); 4.28, quartet, 4 protons (ester methylene); 3.04, AB system, 4 protons (1,3-methylene, J = 15 cps, v = 42.4 cps); 2.57, A_2B_2 system, 4 proton (10,11-methylene, v = 49.4 cps); 1.32, triplet, 6 protons (ester methyl). The high field absorption of the two aromatic protons and the close similarity between the A_2B_2 system with that of [2.2]metacyclophane[6] afford evidence for the assigned structure. The 9,17-protons exhibit a diamagnetic shift of 2.1 ppm as compared with the shift of 2.9 ppm of the 8,16-protons of [2.2]metacyclophane.

At 84°, the methylene proton signals begin to broaden and one very large peak results at 112°, which is replaced at higher temperatures by two singlets located at the centers of the previous AB and A_2B_2 systems. This behavior is attributed to the rapid inversion of the 11-membered ring at temperatures above 125°.[7] Since the AB and A_2B_2 systems overlap and obscure the coalescence points, a quantitative estimate of the energy of activation for the ring inversion could not be made.

In order to obtain an estimate of this energy barrier, the 1,1,3,3-tetradeutero derivative of 2,2-dicarbethoxy[3.2]metacyclophane was prepared by reducing 3,3-dicarbomethoxybibenzyl with lithium aluminum deuteride, treating the alcohol with hydrogen bromide, and carrying out the ring-closure as described above. The previous assignments in the proton magnetic resonance spectrum were confirmed by the deuterium derivative; the AB system was absent from an otherwise identical spectrum.

At 84°, the apparent quartet of the A_2B_2 system collapses to two lines, removing an 8 cps splitting. At 112°, these two lines coalesce. The calculated[7] specific rates at these temperatures at 16.7 sec.^{-1} and 110 sec.^{-1}; the free energy of activation is 19.2 kcal./mole and 19.1 kcal./mole, respectively.[8] The approximate experimental activation energy[9] calculated only from these two points is 18.3 ±1.5 kcal./mole.[11] This probable error was determined from sample calculations showing a 10% error for a 1° error in temperature measurement.

An attempt to obtain additional rates in the 120°-150° range using the correlation of line narrowing with rate of inversion[10] is being made. A kinetic study of several 2-monosubstituted [3.2]metacyclophanes, to be reported at a later date, gives similar experimental activation energies.

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[8] Calculated from the transition state theory, with a transmission coefficient of one.

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[11] This calculation of rate is an approximation, since the collapsing system bears little similarity to an AX system. A more accurate method of calculation is given by S. Alexander, J. Chem. Phys., 37, 967 (1962); thus, the present system would be similar to cyclohexane.