Conformational Changes in Heterocyclic Analogues of Metacyclophane. Interactions between Nonbonded Electron Pairs

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THE metacyclophane molecule (I) has been shown by *X*-ray crystallography[1] to have a nonplanar chair-like conformation† (II) in the crystalline state. The nuclear magnetic resonance (n.m.r.) spectrum of (I) in solution shows[2] an A_2B_2 spectrum for the protons of the methylene groups with vicinal coupling constants that are consistent with the conformation (II). It has recently been shown[3] that the n.m.r. spectrum of (I) is not temperature dependent up to 200° and the resistance of conformation (II) to ring inversion indicated by this result has been further demonstrated[3] by the preparation of the optically active compound (III), which showed no tendency to racemise. To a large extent the high energy barrier to inversion of the conformation (II) results from nonbonded interactions between the hydrogen atoms indicated in (II) in the transition state for ring inversion. It was therefore of interest to study the possibility of ring inversion in heterocyclic analogues of metacyclophane, such as the furan[4] (IV) and pyridine[5] (VI) analogues, in which these hydrogen atoms have been replaced by non-bonding electron pairs.

The n.m.r. spectrum of the furan analogue (IV) shows a singlet signal from the methylene protons in a wide variety of solvents but in hexafluorobenzene solution at 0° these protons give rise to a well-defined A_2B_2 system (see Table). As the temperature of the solution is raised the individual signals of the A_2B_2 spectrum collapse and coalesce to a broad singlet at approximately 63°. Above this temperature the broad line becomes increasingly sharp as the temperature is raised. The observed temperature dependence of the A_2B_2 spectrum is in accord with exchange between the A and B proton environments resulting from rapid inversion of a conformation (V) analogous to the known conformation (II) of metacyclophane. The vicinal coupling constants obtained by analysis of the 0° A_2B_2 spectrum (see Table) are also in accord with this conformation. The collapse of the A_2B_2 system to a singlet is not the result of a decrease in $(\nu_A - \nu_B)$, which may be simulated by the addition of increasing proportions of deuteriochloroform to the hexafluorobenzene solution, since at −10° this gives a series of well-resolved A_2B_2 spectra with the same coupling constants but with decreasing values of $(\nu_A - \nu_B)$. The pyridine analogue of metacyclophane (VI) was also synthesised and its n.m.r. spectrum examined. The methylene protons of (VI) gave an A_2B_2 spectrum at −40° in deuteriochloroform (see Table), which coalesced to a broad singlet at 13·5°. In this case it could easily be recognised that an exchange process was involved since $(\nu_A - \nu_B)$ was large and the temperature dependence of the two principal doublets in the spectrum resembled that

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† The diagram (II) is not intended to be accurate; the crystallographic examination shows considerable boat-like distortion of the benzene rings.

TABLE

N.m.r. results and ring inversion parameters for the metacyclophane and the analogues (IV) *and* (V)

Compound	Solvent	Chemical shifts of methylene protons τ_A and τ_B		Coupling constants[a] (c./sec. ± 0·3) J_{AB}	$J_{AA'}$	$J_{BB'}$	$J_{AB'}$	Coalescence temperature T_c	$\Delta G\ddagger$ (kcal./mole) at 80°	E_a (kcal./mole)	$\log_{10}A$	Ref.
(IV)	C_6F_6	7·19	7·48	−14·0	12·8	3·2	4·5	63°	16·8[b]	—	—	present work
(VI)	$CDCl_3$	6·72	7·45	−12·0	12·6	3·7	4·0	13·5°	14·8[b]	15·3[c]	13·2[c]	present work
(I)	CCl_4	7·01	7·97	−12·0	12·3	3·2	4·0	$\gg$190°	>27[d]	—	—	2, 3

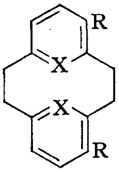
[a] Coupling constants are designated in accord with the labelling of the hydrogens in (II), (V), and (VII).

[b] Based upon the exchange rate, k, at 80° obtained from the approximation $k = \pi(\nu_A - \nu_B)^2/2(W - W_\infty)$.

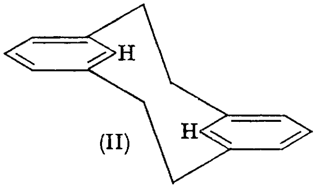
[c] Random errors have not been estimated since the exchange rates were calculated using an approximation.

[d] Based upon the data in reference 3.

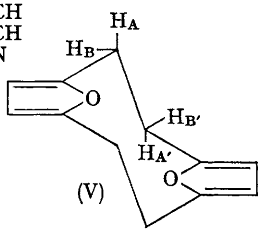
of the doublets of an exchanging AB system. The coupling constants obtained by analysis of the low-temperature A_2B_2 spectrum were again consistent with a chair-like conformation (VII).



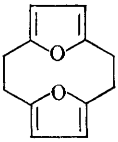
(I) R=H, X=CH
(III) R=Me, X=CH
(VI) R=H, X=N



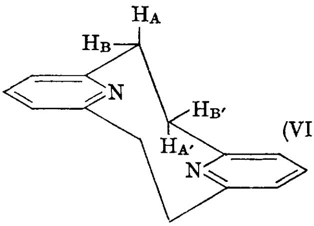
(II)



(V)



(IV)



(VII)

Although the complete analysis of the line shapes of an exchanging A_2B_2 system has not been possible, approximate Arrhenius parameters for the ring inversion of (VII) have been derived from exchange rates, k, calculated by a fast exchange approximation[6] (for k >800 sec.$^{-1}$). This method does not take into account the effects of coupling and uses as the formula for the exchange rate, $k = \pi(\nu_A - \nu_B)^2/2(W - W_\infty)$, where W and W_∞ are the observed line width and the line width for infinitely fast exchange. The A_2B_2 spectrum from (V) is too strongly coupled to permit the use of this approximation to determine Arrhenius parameters but the free energy of activation for the inversion of (V) at 80° (see Table) is based upon the line width of the coalesced singlet since even substantial errors in the rate obtained by this method lead to relatively small errors in $\Delta G\ddagger$. The activation energies for conformational inversion are clearly much lower for (V) and (VII) than for (II) and indicate that in these two cases the transition-state interactions between nonbonded electron pairs are significantly lower than the interaction between similarly located hydrogen atoms. A discussion of the effects of protonation and of possible transition states for these ring inversion processes will be given in the full paper.

These results are of interest in view of recent evidence[7] for the comparative steric effects of hydrogen atoms and nonbonded electron pairs.

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