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THE CONFORMATIONAL EQUILIBRIA OF 4,4a,5,6-TETRAHYDRO-1<u>H</u>,3<u>H</u>-[1,3]OXAZINO [3,4-<u>a</u>]QUINOLINE, 3,4,11,11a-TETRAHYDRO-1<u>H</u>,6<u>H</u>-[1,3]OXAZINO[3,4-<u>b</u>]ISOQUINOLINE AND 1,6,7,11b-TETRAHYDRO-2<u>H</u>,4<u>H</u>-[1,3]OXAZINO[4,3-<u>a</u>]ISOQUINOLINE

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The geminal coupling constant (-8.0 Hz) for the N-CH_2-O protons in hexahydro-1*H*,3*H*-pyrido [1,2-*c*][1,3]oxazine (I)[1] when compared with the corresponding n.m.r. parameter in *cis*-8,12a, 12b-*H*-perhydrobenzo[*e*]pyrido[1,2-*c*][1,3]oxazine[2] (conformationally biased[3] in the *trans*-*syn*-*cis* conformation II; J = -7.2 Hz) and in 3-oxa-1-azabicyclo[3,3,1]nonane[4] (locked in conformation III; J = -10.5 Hz) suggests the existence in solution at ambient temperature of a *cis* ⇄ *trans* conformational equilibrium for this compound in which the *trans*-fused ring conformation IV predominates. Distortion of ring A by the insertion of a double bond at the 6,7; 7,8 or 8,9 position in I might be expected to produce changes in the position of this equilibrium and in order to investigate such an effect compounds VI, VII and VIII were synthesised and their spectral characteristics determined (Table).

The similar values of the chemical shifts and coupling constants for the C4 methylene protons in VI and the C1 methylene protons in I suggests a similar position of conformational equilibrium for the two compounds. The predominance of the *trans*-fused ring conformation in the equilibrium mixture of VI is confirmed by the presence of strong Bohlmann bands[5] (H6ax and H11a *trans* and axial to the nitrogen lone pair) in its i.r. spectrum.

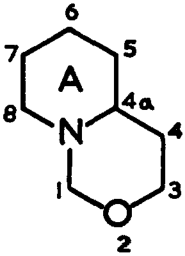
The large chemical shift difference (1.21 p.p.m.) between the C1 methylene protons in VII strongly suggests[6,7] the predominance of the *trans*-fused ring conformation for this compound. The geminal coupling constant of -10.2 Hz (2.3 Hz more negative than the corresponding J in VI) is consistent with this since a decrease in J of similar magnitude is observed[8] for the C1 methylene protons in the *trans*-fused octahydro-3*H*-pyrido[1,2-*c*]pyrimidine system when a N2-methyl group is replaced by N-phenyl. Thus the rather negative J observed for VII is a result of interaction of the nitrogen lone pair with the aromatic ring which reduces the lone pair-C4 methylene overlap with a consequent decrease in J[9]. Since in some related systems axial C-H bonds α to N-phenyl have been found[10] not to give rise to Bohlmann bands the weak absorption in the 2800-2600 cm^{-1} region of the i.r. spectrum of VII is not inconsistent with the trans-fused ring conformation, which in any case possesses one less axial N-CH bond than does VI.

In contrast to VI and VII which exist predominantly in the trans-fused ring conformation the spectral data for VIII demonstrates its existence in the predominantly cis-fused ring conformation IX. The J_{gem} of -10.2 Hz for the C4 methylene group is comparable to that found in a cis-fused hexahydro-1H,3H-pyrido[1,2-c] [1,3]oxazine[1] in which the nitrogen lone pair bisects the H-H internuclear axis as it does in IX and in III. Additional evidence for this stereochemistry is provided by the value of the chemical shift difference (0.19 p.p.m.) between the C4 protons[1], the low field absorption (δ 3.91) of the angular 11b proton[11] and the lack of strong bands between 2800-2700 cm^{-1} in the i.r. spectrum. In all three compounds (VI - VIII) vicinal coupling constant data is completely in accord with the predominance of the proposed conformations.

TABLE[12]

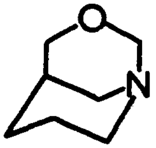
Compound	N.m.r. spectra			I.r. spectra
	Chemical shifts (δ)		Coupling constants (Hz)	2800-2700 cm^{-1} region
	$N-CH_2-O$ protons			
I	4.35	3.53	-8.0	Strong bands
II	4.36	3.40	-7.2	Strong bands
VI	4.48	3.58	-8.2	Strong bands
VII	5.38	4.17	-10.5	Weak bands
VIII	4.51	4.32	-10.2	Weak bands

Thus in systems VI-VIII a consideration of the "rabbit-ear" effect[13] and the difference in non-bonded interactions between the respective cis- and trans-fused conformations does not account for the observed changes in the nature of the preferred ring fusion with the position of fusion of the aromatic ring. A different effect must therefore be operating in these systems which most probably arises from the differing strains in the various structures

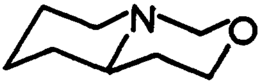


I

II



III



IV

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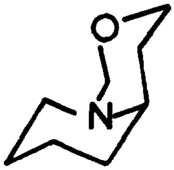
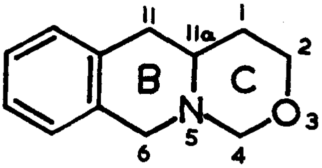
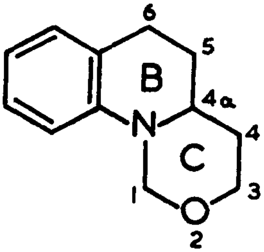


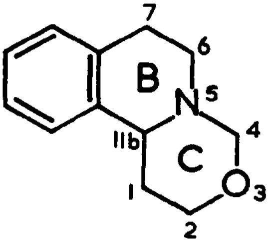
V



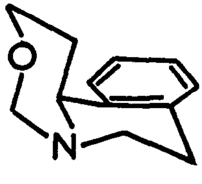
VI



VII



VIII



IX

caused by the necessary utilization in some conformations of pseudoaxial and pseudoequatorial bonds to effect the B:C ring fusion.

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