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CONFORMATIONAL EQUILIBRIA FOR 2-SUBSTITUTED CYCLOHEXYLIDENEMALONONITRILES

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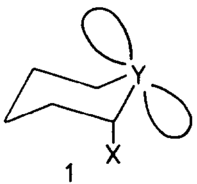
Summary - The conformational effect of predominance for the axial conformer (5A) has been observed for the title compounds and is discussed in terms of steric and orbital interactions.

Recently it has been demonstrated that the anomeric effect [1,2] (predominance of axial conformation for the systems of type 1) can be imitated by the substitution of heteroatom Y by other groups having p-orbitals (e.g. systems 2 [3] and 3 [4]).The phenomenologically analogous effect (see Ref.2) for ketone systems of type 4 has been studied in detail [5].

It seemed attractive to imitate the carbonyl group by substituting for oxygen, a double-bonded carbon atom linked to electronegative substituents and to investigate the possibility of the existence of a conformational effect leading to axial preference in these systems.The 2-substituted cyclohexylidenemalononitriles 5 are good models for that purpose.

Here we report a ^{1}H NMR study of the conformational equilibria of 6-11 which provide the evidence for the conformational effect discussed.Bromide 9 was obtained by NBS bromination of cyclohexylidenemalononitrile;compounds 6, 7 and 11 were synthesized by the condensation of the corresponding ketones with malononitrile [6].Compounds 8 and 10 were obtained as described elsewhere[7].

The ^{1}H NMR spectra of 6-11 were recorded at 30° in five solvents (9 mol%, T-60 Varian).Widths at half-height for the H_x signal were employed to calculate the amount of conformer 5A,using the Eliel eqn: $W_{1/2}^{obs}=nW_{1/2}^{5A}+(1-n)W_{1/2}^{5B}$. The standard values $W_{1/2}^{5A}$= 4.9 Hz and $W_{1/2}^{5B}$= 17.6 Hz were taken from low temperature ^{1}H NMR spectra of 2-Cl-cyclohexylidenemalononitrile 8 and 2-OAc-methyl-



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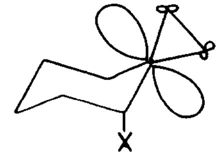

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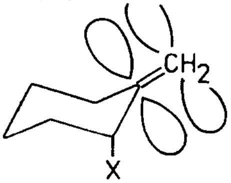

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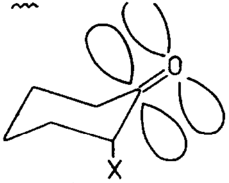

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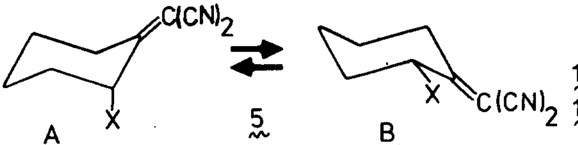

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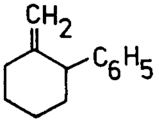
6 X = OCH_3
7 X = F
8 X = Cl
9 X = Br
10 X = $COOCH_3$
11 X = C_6H_6



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idenecyclohexane 3 (HX-90 Bruker,-90°,CS_2) [8].The calculated percentage of axial conformation in 6-11 is listed in the Table.

Table. Conformational equilibria data for 6-11.

Comp.	X	b.p.(mm Hg)	% conformation 5A (± 3% *)				
			CCl_4	CS_2	C_6H_6	$CDCl_3$	CD_3CN
6	OCH_3	115-116°(7)	82	81	73	80	67
7	F	142-144°(14)	62	59	47	55	30
8	Cl	140-142°(5)	92	93	95	91	86
9	Br	156-157°(5)	90	91	91	90	88
10	$COOCH_3$	≠	89	82	78	80	74
11	C_6H_5	m.p. 66-67°	78	75	75	76	72

* the error depends only on pure NMR measurements (uncertainties in width etc) [8];

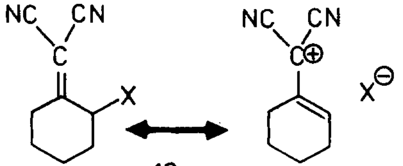
≠ purified by thin layer chromatography (silica gel,cyclohexane - AcOEt)

The results demonstrate the conformational effect of preference of axial conformation 5A in all the compounds investigated.Even the 2-phenyl substituent though possessing quite a large A-value,has the axial orientation in 11. In contrast,the content of equatorial conformer for 2-phenylmethylenecyclohexane (12) is equal to 92% (CCl_4).The observed phenomenon may be understood in terms of two principal types of interactions: (a) a steric repulsion between the syn CN group and the X substituent in the 2-position, and (b) orbital interactions.

The operation of steric repulsive interaction,CN···X,is beyond doubt.Empirically it has been deduced that molecules containing an exocyclic double bond would,with appropriate substitution,have internal non-bonded repulsion [9]. This type of interaction arising from substituents at 1 and 3 position of allylic system has been termed $A^{(1,3)}$strain [9a].Recently it was demonstrated unequivocally that $A^{(1,3)}$ strain can be sufficiently large to force even a 2-tert-butyl group in the cyclohexilidene system to adopt the axial position[9b]. The example of 11 with an axial phenyl group,shown in this work,is likewise impressive (cf. conformational behaviour of 11 and 12).

However some features cannot be explained solely in terms of steric interactions.For example the distinct dependence of the position of some of the conformational equilibria on the solvent polarity (especially for 7) seems to indicate the operation of orbital interactions [10]. The solvent dependence of equilibria (see Table) is analogous to those observed in typical "anomeric" systems [1]. Moreover, these data also seem to demonstrate the "benzene effect" [2b,11] because, in this solvent, the equatorial conformation 5B is slightly more stailized in comparison with CCl_4 and even $CDCl_3$.

For the 2-substituted cyclohexanones two types of principal orbital interactions have been suggested: (1) interaction of occupied $\pi_{C=O}$ and antibonding σ^*_{C-X} orbitals [5] (cf. the PMO interpretation of the anomeric effect [2,12]) and (2) interaction of the n_X orbital with antibonding $\pi^*_{C=O}$ orbital [13]. Both of these interactions are greatly diminished for equatorially oriented substituents. Analogous types of interaction might be considered for compounds of types 3 [4] and 5 (with change of $\pi_{C=O}$ and $\pi^*_{C=O}$ orbitals for $\pi_{C=C}$ and $\pi^*_{C=C}$, respectively). Formulas 13 and 14 represent these interactions in terms of resonance theory.



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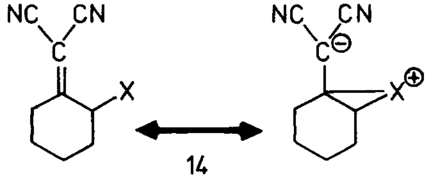

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We believe, that for the nitriles 5 the second type of orbital interaction occurs [14]. The order of increasing percentages of axial conformations for the halogen compounds, $F \ll Cl \sim Br$, is consistent with the order of steric as well as both types of orbital interactions. However, the small but evidently pronounced dependence of the percentage of axial conformation on solvent for 10 and 11 is especially remarkable, because it is difficult to accept the operation of the $\pi \rightarrow \sigma^*$ type of interaction (13) for these compounds. In contrast, the second type of interaction (14) could reasonably occur in these systems. In the case of 11 this involves the perturbation of the one of the highest occupied aromatic π-orbitals by the antibonding $\pi^*_{C=C}$ orbital (the extreme representation is one corresponding to a σ-complex) and this problem is worthy of special consideration [15].

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10. The change of position of conformational equilibria with change of solvent polarity can,in principle,be explained by stabilization of the more polar conformer by the more polar solvent.However this seems unacceptable for the case discussed because of: (i) the small expected difference of dipole moments between conformers 5A and 5B (the double bond approximately bisects the angle between axial and equatorial orientations) and (ii) in some cases,a small overall group moment (for example in 11).
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14. We agree with the referee's comment that other factors or in some instances the alternative $\pi \rightarrow \sigma^*$ interaction are not ruled out.Mentioning for compounds 5 only the operation of $n \rightarrow \pi^*$ interaction we want to stress that its contribution dominates other factors which govern the conformational behaviour of these compounds.
15. Of course,the usual PMO arguments concerning,for instance,the relative magnitude of the coefficients of the AO's in $\pi_{C=C}$ and $\pi^*_{C=C}$ on doubly bonded carbon atoms and the charge polarization in 13 as compared with 14 are in agreement with the point of view discussed.

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