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# STEREOCHEMICAL STUDIES—XXVIII

## CONFORMATIONAL EQUILIBRIA OF 2-$OCH_3$, 2-$OCOCH_3$ AND 2-Br DERIVATIVES OF ω-SUBSTITUTED METHYLENECYCLOHEXANES

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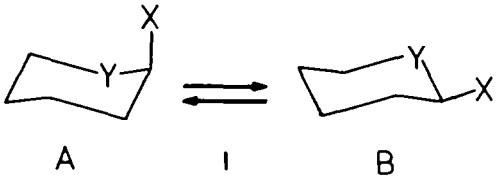
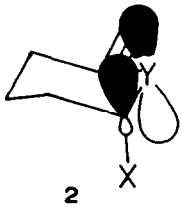
**Abstract**—The conformational equilibria of the titled compounds, **10–13**, have been determined by $^1H$ NMR and analysed in terms of steric ($A^{1,3}$) repulsion, **15**) and electronic effects. The conformational equilibria of OMe and Br derivatives depend on the position and electronic properties of ω-substituent/s, attached to the double bond, which may be rationalized in terms of "anomeric" type of resonance, **9**. In contrast, OAc derivatives are the subject of steric repulsion and the electronic influence of the remote =CHCN and =C(CN)$_2$ groups is negligible.

The mechanisms by which substituents remote from each other interact and thereby change the expected conformation of organic molecules have been investigated. On the other hand, the study of conformational deviations from usually observed behavior, i.e. of "conformational effects",[1] may in principle shed light on the problem of substituent interaction. For instance, one of the basic paradigms of conformational analysis predicts that equatorial orientation of a substituent attached to a 6-membered ring is more favored than an axial one. The best known violation of this rule is the "anomeric effect"[1-4] which manifests the perference of the axial (**1A**) electronegative substituent, X, in tetra-

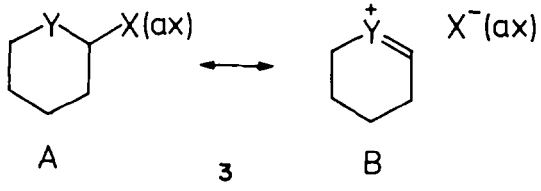



hydropyrane ring systems. The anomeric effect has been studied and successfully reproduced theoretically by quantum chemical methods of various approximations.[3] The conceptualization of these quantum chemical arguments[1-4] suggests that the conditions for the stabilizing interactions invoking back donation from *p*-type oxygen orbital into the orbital of the C–X bond are better in axial conformation, **1A**, which is visualized in formula **2**. The corresponding valence-bond picture[1-4] is depicted

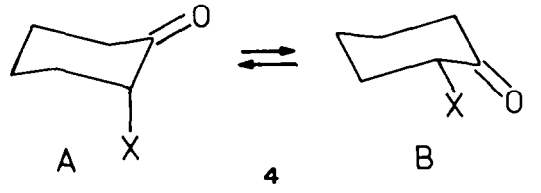



**2**

by the formulas **3**, which include charged resonance form **3B**.[5] This $n \rightarrow \sigma^*$ interaction has now became a widely accepted rubric for interpretation of conformational phenomena.

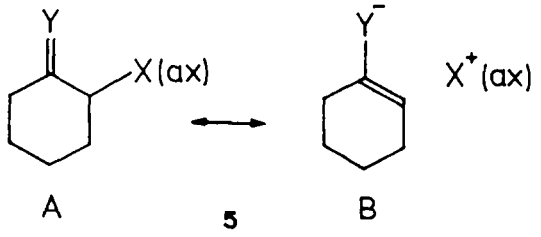



The predominance of axial conformation (**4A**) has been repeatedly observed for the equilibrium of a number of 2-substituted cyclohexanones,[1,8,11-15] **4**. This

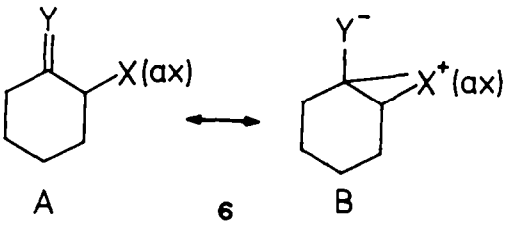



phenomenon has also been explained in terms of the overlap either between $\pi^*$-orbital of C=O group and the $\sigma$-orbital of the C–X bond[11-14] (the *double bond–no bond* representation is shown by formulas **5**, Y=O) or between the *n*-orbital of substituent and $\pi^*$-orbital of C=O bond[15] (the resonance representation is shown by formulas **6**, Y=O).

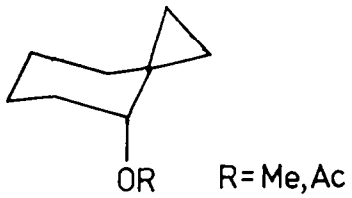
It is of importance, that simple MO consideration (e.g. of type **2** or their equivalents of type **3**, **5** and **6**) can be




used as a guiding force for the search of new model compounds having analogous MO interactions and hence the same conformational behaviour.[1,16] For example, it



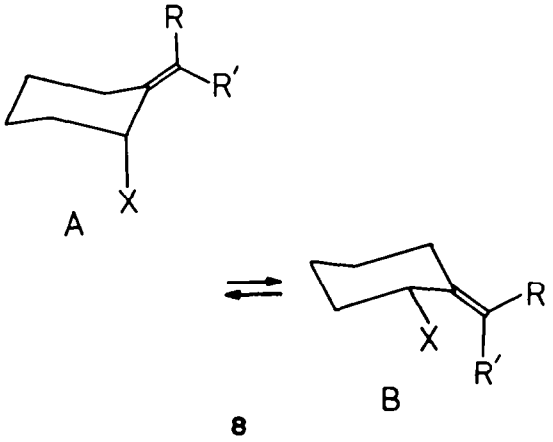

was reported[16] that RO-substituents at $C_4$ in spiro[5, 2]octane derivatives **7** prefer the axial conformation. It




**7**

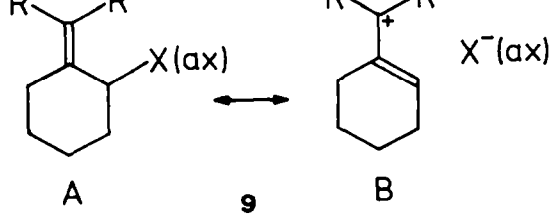
was suggested that an interaction between the electrons of one of the two degenerate orbitals of *e*-type symmetry of the cyclopropane ring and the $\sigma^*$-orbital of the adjacent C-O bond could be responsible, at least in part, for this axial preference.[1]

In an attempt to obtain experimental evidence of the importance of the *double bond–no bond* resonance (of type **3** or **5**) Lessard *et al.*[17,18] and Zefirov *et al.*[19–21] have studied a number of 2-substituted derivatives of methylencyclohexane, **8**. Indeed, this model is sufficiently




**8**

changeable due to the possible variation of three substituents (**8**, X, R and R') and it seems possible that proper substitution of *exo*-double bond can discriminate the two types of resonance, namely **9** (we shall label it as *anomeric resonance* taking into account the distribution of charges in formulas **9B** and **3B**) and **5**(Y=CRR') (or *antianomeric* resonance; *cf* charge distribution for **3B** and **5B**).




Lessard *et al.*[17] have shown that 2-methoxymethylenecyclohexane (**8**, X=OMe, R=R'=H) has preferred axial conformation **8A** (*vide infra*). Moreover, the introduction of OMe group onto the double bond (**8**, X=R=OMe, R'=H) causes further stabilization of the axial conformer, which supports the concept of the resonance of type **9**. The PE-spectra of *p*-butyl derivatives of methoxymethylenecyclohexane with axial and equatorial OMe group are also consistent with the $\pi \rightarrow \sigma^*$ stabilization of type **9**.[22]

However in accordance with this concept the proportion of the axial conformer should increase with increasing of substituent electronegativity (*cf* data[12]). Unexpectedly, it was found[18,20] that the preference for the axial conformer in 2-acetoxymethylenecyclohexane (**8**, X=OAc, R=R'=H) is definitely less than for analogous methoxy derivative. Moreover, low temperature $^1$H NMR data revealed, that the axial conformer is stabilized by enthalpy term only in the case of methoxy (**8**, X=OMe, R=R'=H) compound.[20] This observation is inconsistent with the oversimplified picture of conformational behaviour of the compounds **8** due to the resonance of type **9**. To rationalize these data the hypothesis of operation of the resonance of type **6** (Y=CRR') has been suggested.[19,20] However the general picture needs to be more investigated.

In this paper we have studied the conformational equilibria of 2-methoxy, 2-bromo and 2-acetoxy derivatives of methoxymethylenecyclohexane, containing the CN group/s, attached to the double bond (**8**, R, R'=CN) (preliminary communications see Refs. 19–20). The idea behind this was to try to gain an insight into mechanism/s governing these conformational equilibria.

## RESULTS

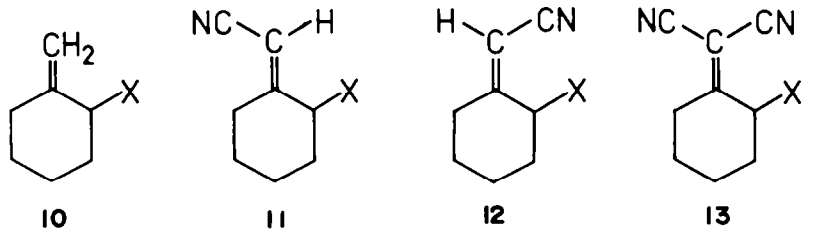
### A. *Synthesis*

The compounds investigated are presented on Chart 1. Bromides **11c–13c** were prepared by NBS bromination of cyclohexylideneacetonitrile and cyclohexylidenemalononitrile respectively. We have not been able to separate the mixture of **11c** and **12c** (2:1) and have used it as it is. Methoxy derivatives **11a–13a** were obtained from corresponding bromides with $AgNO_3$. The mixture of **11a** and **12a** was separated by TLC. The acetates **11b–12b** were prepared from bromides **11c–12c**; the acetates **11b** and **12b** have been also separated by the TLC. Unfortunately we could not prepare bromide **10c** using the reported procedure.[23] Although the properties of the sample resemble those reported,[23] the $^1$H NMR data indicate the rearranged structure **14** ($\delta$ 3.97 ppm (2H, $CH_2Br$) and 5.93 ppm (1H, olefinic proton).

### B. *$^1$H NMR spectra and determination of the position of conformational equilibria* **8**

The $^1$H NMR spectra of the compounds **10–13** support their structures. Geometrical isomers **11** and **12** have been recognized using the following criteria: (a) *syn*-CN group in **12** causes the downfield shift of the H-C-X proton and (b) a functional group X causes the downfield shift of the olefinic proton in *anti*-isomers **11**.

It is safe to accept that compounds **11–13** exist in the chair conformation, **8**.[24] The position of the conformational equilibrium **8A**⇄**8B** can be estimated in terms of the mole fraction, **n**, of the axial conformation **8A** by the widely used Eliel Eq (1) using the bandwidth of $H_X$



10 11 12 13

a X = $OCH_3$ ; b X = $OCOCH_3$ ; c X = Br ; d X = $C_6H_5$

Chart 1.

signal. This signal may be treated as the X part of ABX system and its width is equal to $|J_{AX} + J_{BX}|$.[25] Appropriate $^1$H NMR data are listed in Table 1.

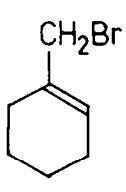
$$W_{obs} = W_{8A} \cdot n + (1 - n) \cdot W_{8B} = n \cdot (J_{ee} + J_{ea}) + (1 - n) \cdot (J_{aa} + J_{ae}). \quad (1)$$

Owing to difficulties connected with the choice of the "standard" coupling constants of the individual conformers, $W_{8A}$ and $W_{8B}$, we have used parameters taken from low temperature NMR data. In particular, we have used the values $W_{8A} = 5.8$ Hz and $W_{8B} = 17.6$ Hz as standard for the series **10** (they have been taken from low temp. NMR spectra of **10a** and **10b** respectively[20]). For the series **11** and **12** the values $W_{8A} = 5.8$ Hz (*vide supra*) and $W_{8B} = 17.7$ Hz (taken from low temp spectrum of **11a**) have been used. Finally, the values $W_{8A} = 4.9$ Hz (taken from low temperature NMR data of 2-chlorocyclohexylidenemalonoitrile (**8**, X=Cl, R=R'=CN)[19]) and $W_{8B} = 17.6$ Hz (*vide supra*) have been used for the series **13**. To reveal the influence of solvent upon the conformational equilibra, **8**, the NMR measurements have been performed in five solvents. Data obtained for conformational equilibria are summarized in Table 2.

## DISCUSSION

The equilibrium between the axial (**8A**) and the equatorial (**8B**) conformers of compounds investigated may provide valuable information on the nature of interactions between fragments if one is able to partition the sum of interactions, affecting conformational equilibria, into the component parts (steric, electrostatic, electronic etc).[1] To reveal the importance of every particular interaction we used the comparison of conformational behaviour of nitriles **11**, **12** and **13** with reference to methylenecyclohexanes **10**.

Firstly, the introduction of an *exo*-cyclic double bond into a 6-membered ring leads to steric repulsion between a *syn*-hydrogen of this double bond and an equatorial substituent at $C_2$(**15**). This interaction, **15**, arising from



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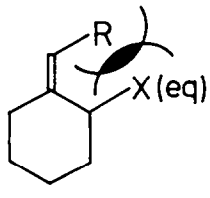

15

substituents at 1 and 3 position of allylic system has been termed $A^{(1,3)}$ strain.[20,26,27] Recently it was demonstrated that $A^{(1,3)}$ strain can force even 2-phenyl (in solution)[20] or 2-butyl (in solid)[27] groups in the cyclohexylidene systems to adopt the axial position. Thus, the operation of repulsive interaction *syn*-CN · · · X for **12** and **13** is

Table 1. $^1$H NMR data for substituted methylenecyclohexanes

| No | $W_{1/2}$ of $H_X$ signal ( δ ,ppm) | | | | |
|---|---|---|---|---|---|
| | $CCl_4$ | $CS_2$ | $C_6D_6$ | $CDCl_3$ | $CD_3CN$ |
| 10a | 8.4(3.52) | 7.9(3.50) | 8.0(3.48) | 8.0(3.62) | 9.1(3.62) |
| 10b | 11.5(5.02) | 12.9(5.13) | 14.6(5.28) | 12.3(5.25) | 14.3(5.18) |
| 10d | 16.7(3.28) | 17.2(3.20) | 17.8(3.23) | 17.2(3.37) | 16.8(3.25) |
| 11a | 14.9(3.63) | 15.3(3.61) | - (3.03) | 15.2(3.64) | 15.4(3.46) |
| 11b | 11.5(5.23) | 11.5(5.50) | - | - | - |
| 11c | 8.1(4.84) | 8.0(4.84) | 8.4(4.17) | 8.7(4.87) | 8.4(5.00) |
| 12a | 6.9(4.28) | 7.0(4.20) | 6.9(4.18) | 7.1(4.29) | 8.0(3.96) |
| 12b | 10.1(5.57) | 10.1(5.67) | 10.7(5.58) | 10.1(5.73) | 11.1(5.70) |
| 12c | 6.1(5.34) | 6.1(5.34) | 6.3(5.14) | 6.6(5.38) | 6.7(5.42) |
| 13a | 7.2(4.30) | 7.3(4.28) | 8.3(3.98) | 7.5(4.22) | 9.1(4.29) |
| 13b | 9.4(5.75) | 9.3(5.52) | 9.5(5.39) | 9.9(5.36) | 10.1(5.60) |
| 13c | 6.2(5.33) | 6.1(5.27) | 6.0(4.91) | 6.2(5.36) | 6.5(5.29) |
| 13d | 7.7(4.38) | 8.1(4.25) | 8.1(4.13) | 7.9(4.67) | 8.4(4.34) |

Table 2. Conformational equilibrium data for substituted methylenecyclohexanes **10–13**

| No | $-\Delta G_{e-a}$ kcal/mol(% of axial conformer) | | | | |
|---|---|---|---|---|---|
| | $CCl_4$ | $CS_2$ | $C_6D_6$ | $CDCl_3$ | $CD_3CN$ |
| 10a | 0.75±0.09(78) | 0.90±0.11(82) | 0.86±0.10(81) | 0.86±0.10(81) | 0.56±0.08(72) |
| 10b | 0.05±0.05(52) | −0.24±0.06(40) | −0.65±0.08(25) | −0.12±0.06(45) | −0.56±0.08(28) |
| 10d | −1.45±0.21( 8) | −2.06±0.32( 3) | −2.72±0.48( 1) | −2.06±0.32( 3) | −1.53±0.22( 7) |
| 11a | −0.72±0.09(23) | −0.86±0.10(19) | - | −0.82±0.10(20) | −0.86±0.10(19) |
| 11b | 0.05±0.05(52) | 0.05±0.05(52) | - | - | - |
| 11c | 0.86±0.10(81) | 0.86±0.10(81) | 0.75±0.09(78) | 0.65±0.08(75) | 0.75±0.09(78) |
| 12a | 1.37±0.18(91) | 1.30±0.18(90) | 1.37±0.18(91) | 1.24±0.15(89) | 0.86±0.10(81) |
| 12b | 0.34±0.07(64) | 0.34±0.07(64) | 0.19±0.06(58) | 0.34±0.07(64) | 0.12±0.06(55) |
| 12c | 2.06±0.32(97) | 2.06±0.32(97) | 1.89±0.29(96) | 1.53±0.22(93) | 1.45±0.21(92) |
| 13a | 0.90±0.11(82) | 0.86±0.10(81) | 0.59±0.08(73) | 0.82±0.10(80) | 0.42±0.07(67) |
| 13b | 0.37±0.07(65) | 0.37±0.07(65) | 0.34±0.07(64) | 0.26±0.07(61) | 0.22±0.06(59) |
| 13c | 1.30±0.17(90) | 1.37±0.18(91) | 1.37±0.18(91) | 1.30±0.17(90) | 1.13±0.13(87) |
| 13d | 0.75±0.09(78) | 0.65±0.08(75) | 0.65±0.08(75) | 0.68±0.08(76) | 0.56±0.08(72) |

beyond doubt. Hence it is reasonable to divide the experimentally observed $\Delta G_{exp}$ values in accordance with Eq (2):

$$\Delta G_{exp} = \Delta G_{ref} + \Delta G_A(1,3) + \Delta G_e \quad (2)$$

where $\Delta G_{ref}$ for 2-substituted methylenecyclohexane **10**; $\Delta G_{A(1,3)}$ is the contribution of $A^{(1,3)}$ strain and $\Delta G_e$ is the other effects. To evaluate the magnitude of $\Delta G_{A(1,3)}$ term one could ignore the change of this repulsion due to the introduction of *anti*-CN group, accepting as a reasonable approximation the same value of the $\Delta G_{A(1,3)}$ terms for the both *anti*-nitriles **11** and reference compounds **10**. Hence, one may evaluate the term $\Delta G_e$, reflecting the electronic influence of the CN group, attached to the double bond. At the simple level of additivity, when one ignores the difference in electronic influence between *syn* and *anti* CN group (in other words, accepting the same $\Delta G_e$ terms for both *syn* and *anti* isomers), the comparison of the equilibria of **11** and **12** shows the steric $A^{(1,3)}$ interaction, of **10** and **12** as the sum of $A^{(1,3)}$ and non-steric influence ($\Delta G_e$) of CN group and of **10** and **11** the single non-steric term $\Delta G_e$. These considerations are visualized on Chart 2.[28]

The comparison of conformational behavior of mononitriles **11**, **12** and dinitriles **13** is also instructive. Indeed, the replacement of either of the hydrogens of the double bond of the nitriles **11** and **12** by CN group to give **13** could be used in the same manner for the evaluation both the $A^{(1,3)}$ strain and non-steric influence of CN group (parameter $\Delta G_e'$). Indeed, the comparison of **12** and **13** reveals the non-steric effect of added CN group against the background of the $A^{(1,3)}$ CN···X strain and non-steric influence of the present *syn*-CN group. These data are also exhibited on Chart 2.

*The magnitude of* $A^{(1,3)}$ *interaction.* Application of additive treatment of type Eq (2) gives the magnitudes of $A^{(1,3)}$ interactions as ~2.1 kcal/mol for CN···Me, ~1.2 kcal/mol for CN···Br and ~0.3 kcal/mol for CN···OAc interactions.[28] Thus, $A^{(1,3)}$ strain destabilizes the equatorial conformation, **8B**, in the case of methoxy derivatives, has intermediate value for bromine substituted ones and has a minimal value for acetoxy compounds. An order or a magnitude of "size" of substituents depends on their position with respect to the rest of the molecular framework.[1,30,31] For example, OH and Br groups have effectively small steric requirements in ordinary cyclohexane systems, but one has to regard them as "large" groups in the 3-*endo*-position of bicyclo[3,3,1]nonanes.[30a,b] Nevertheless such a drastic difference between $A^{(1,3)}$ values for OMe and OAc groups is unexpected. Indeed, the pure steric CN···X interaction may be reasonably modelled by the pairwise contribution values for rotational barriers in derivatives of biphenyl,[31] which are equal to 6.4($OCH_3$), 10.2(Br) and 7.0(OAc) kcal/mol. Evidently the order of these contributions is in striking contrast with our data. One may suppose that $A^{(1,3)}$ repulsion values reflect the effective interaction, where the steric effect co-exists with unavoidable contribution from electrostatic interactions, which are more pronounced in the case of acetoxy derivatives. Some indirect arguments may be presented to support this conclusion. For example, the conformational equilibria of 1, 2-*trans*-dimethoxycyclohexane[32] and 1, 2-*trans*-methoxyacetoxycyclohexane[33] exhibit the presence of ~20% of diaxial conformer. However, the content of the diaxial conformer for 1, 2-*trans*-diacetoxycyclohexane drops down to ~1%.[32] This phenomenon has been explained by dipole-dipole interactions of two *gauche* OAc groups.[32] It seems reasonable to assume the analogous electrostatic attractive interaction, *syn*-CN···OAc, as the possible origin of the sharp decrease in the magnitude of the total $A^{(1,3)}$ strain for this case as compared with *syn*-CN···OMe one.

Now we are able to evaluate the term $\Delta G_e$, which reflects the electronic influence of remote *anti*-CN group on the conformational equilibria (Chart 2).

There exists a marked difference in electronic interaction of the CN group with OMe group as compared with OAc group. Indeed, the replacement of the H atom of the double bond in 2-methoxymethylenecyclohexane by a CN group (**10a**→**11a**) leads to preference for the equatorial conformation, the term $\Delta G_e$ being equal ~1.5 kcal/mol. The introduction of the second CN group in going from **12a** to **13a** also leads to an increase of the equatorial form, the term $\Delta G_e'$ being equal 0.47 kcal/mol. In contrast, the conformational behaviour of the acetoxy derivatives is insensitive to the electronic effect of CN substitution (both $\Delta G_e$ and $\Delta G_e' \sim 0$).

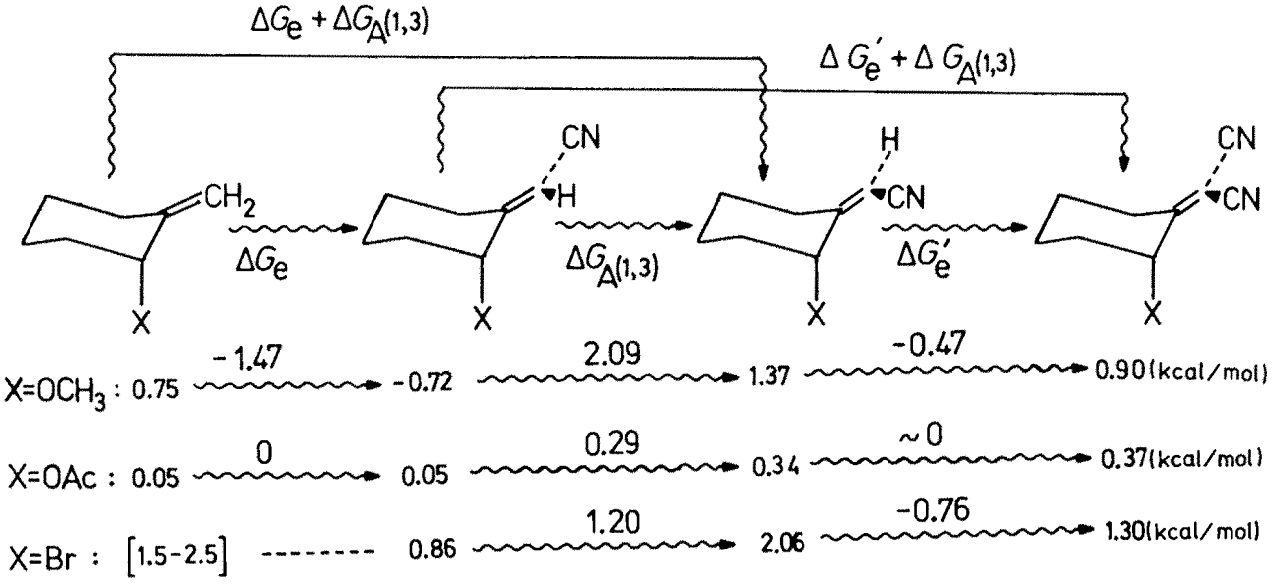
ΔGe + ΔGA(1,3)
Δ Ge' + Δ GA(1,3)
CH2
CN
H
CN
H
CN
CN
ΔGe
ΔGA(1,3)
ΔGe'
X
X
X
X
X=OCH3 : 0.75
-1.47
-0.72
2.09
1.37
-0.47
0.90(kcal/mol)
X=OAc : 0.05
0
0.05
0.29
0.34
~0
0.37(kcal/mol)
X=Br : [1.5-2.5]
0.86
1.20
2.06
-0.76
1.30(kcal/mol)

Chart 2.

*Conformational behaviour of* OAc *vs* OMe *derivatives.* Steric requirements for these substituents in ordinary cyclohexane systems are similar and "the best" A-values are equal 0.6 kcal/mol for both.[14] For the typical anomeric systems of type **1** the preference for axial conformation, **1A**, is usually more prounounced for OAc group as compared with OMe group[2,6,17] (see also Ref. 16). In contrast, the increased content of axial form, **4A**, for the 2-substituted ketones, **4**, has been observed for the methoxy derivative, while the 2-acetoxycyclohexanone exists preferentially in the equatorial conformation, **4B**.[12-14] This difference is explained by the "antianomeric" resonances of type **5** or **6**. The room temperature data about conformational equilibria of the methoxy (**10a**, ~75% of axial form) and acetoxy (**10b**, ~45% of axial form)[17-20] derivatives of methylenecyclohexane mask the situation and only low temperature measurements have revealed that enthalpies of these equilibria have different signs.[18,20] (stabilization of axial form for OMe and of equatorial form for OAc derivatives respectively). This difference has been interpreted as the indication of operation of the resonance of type **6** for both **10a** and **10b**.[20]

The present study reveals that for methoxy derivatives, **a**, may be well rationalized only using the "anomeric" type of resonance, **9**, which produces a positive charge at *exo*-olefinic C atom. Taking into account the destabilization of this resonance by adjacent CN group/s, one should expect a destabilization of the axial conformation by electron withdrawing substituent/s, which has been in fact experimentally observed. Moreover, an introduction of the *anti*-OMe group (i.e. **8**, X=R=OMe, R'=H) should lead to the opposite effect, which has been also experimentally found.[17]

The conformational behaviour of bromide series, **c**, could also be rationalized, because the comparison of **12c** and **13c** reveals the clear destabilizing effect ($\Delta G_e$' ~0.8 kcal/mol, Chart 2). Unfortunately we could not prepare the reference bromide **10c**; extrapolation of the obtained data permits to evaluate roughly $\Delta G_e$ value to be ~1.5–2.5 kcal/mol, and hence, the strong preference for the axial conformation **8A** (R=R'=H, X=Br). Moreover, it seems quite reasonable that such preference due to the interaction of the Br atom and the double bond is responsible for rapid allylic rearrangement of bromide **10c** into bromide **14**.

Concerning the conformational behaviour of acetoxy derivatives, **b**, if the resonance of type **9** is inherent in the system of 2-substituted methylenecyclohexane it has to be progressively increased along with increasing the ability of the substituent to leave as an anion. Thus, the "anomeric" resonance of type **9** should be a more manifest in AcO as compared with MeO groups. The experimental data contradict this assumption; they ward against a simple extrapolation of pictures of MO interactions over a wide range of substituents without experimental justification. On the other hand, more experimental work concerning the conformational behaviour of the analogous model compounds will provide data of substituent interactions and their influence on the conformational equilibria.

## EXPERIMENTAL

$^1$H NMR spectra were recordered on a Varian T-60 and XL-100 spectrometers. Low temperature $^1$H NMR spectra (−100°, $CS_2$, ~9 wt%) were run on a Bruker HX-90E spectrometer and a JEOL JNH-MH-100 spectrometer. Chemical shifts are reported in ppm ($\delta$) using TMS as an internal standard. Satisfactory analytical data were obtained for all new compounds (±0.3% for C; ±0.3% for H; ±0.4% for N and halogenes).

*2-Methoxymethylenecyclohexane* (**10a**). To a stirred amalgamated Mg (prepared beforehand by stirring 9g(0.39 mol) of Mg turnings and 16 ml of Hg in 100 ml anhyd ether under argon for 6 hr) a soln of 15.8 ml (1.95 mol) of $CH_2I_2$ and 23 g (0.18 mol) 2-methoxycyclohexanone in 40 ml anhyd ether was added dropwise over a period 1 hr at room temp. The suspension was stirred an additional 0.5 hr and refluxed 2 hr, cooled, the ppt was filtered off and washed thoroughly by small portions of ether. Combined ether extracts were washed with water and dried over $Na_2SO_4$. Removal of the solvent and destillation yielded 7.9 g (35%) of **10a**, b.p. 47–55° (30 torr) which was purified by chromatography (silica gel, $CHCl_3$) and redistilled, b.p. 64–66° (45 torr), $n_D^{21}$ 1.4533 (lit.[17], b.p. 66° (25 torr)); $^1$H NMR ($CCl_4$): 3.13 (s, 3H), 3.52 (m, 1H), 4.74 (narrow m, 2H).

*2-Acetoxymethylenecyclohexane* (**10b**). This was obtained using AcCl acylation of methylenecyclohexane-2-ol[15]; b.p. 75–76° (13 torr), $n_D^{17}$ 1.4608; $^1$H NMR ($CCl_4$): 1.92 (s, 3H), 4.64 (narrow m, 2H), 5.06 (m, 1H).

*2-Phenylmethylenecyclohexane* (**10d**). To a stirred suspension of methyltriphenylphosphonium bromide (9 g, 25 mmol) in 100 ml ether at 0° ($N_2$), 48 ml of 0.48 N (23 mmol) ether soln of PhLi was added dropwise. The suspension was stirred 1.5 hr and then a soln of 4.04 g (23 mmol) of 2-phenylcyclohexanone in 20 ml ether was added over a period of 1 hr. It was gently heated under reflux for an additional 4 hr, cooled, and the usual work up gave 3.6 g of crude **10d**, which was distilled, b.p. 124–125° (10 torr), $n_D^{20}$ 1.5480, $^1$H NMR ($CCl_4$): 3.28 (m, 1H), 4.11 and 4.69 (2H), 7.13 (m, 5H).

*2-Bromocyclohexylideneacetonitriles* (**11c** and **12c**). These compounds were obtained from $\alpha$-cyanomethylenecyclohexane[36] by NBS bromination (82% crude yield) and purified by TLC on silica gel (EtOAc–hexane, 1/5), b.p. 116–119° (1 torr). The sample contains the mixture of *E*- and *Z*-isomers (2:1). $^1$H NMR spectra ($CCl_4$): *E*-isomer (**11c**) 4.82 (m, 1H, CHBr), 5.44 (narrow m, 1H, =CHCN); *Z*-isomer (**12c**) 5.14 (d, 1H, J = 2.0 Hz, =CHCN), 5.34 (m, 1H, CHBr).

*2-Methoxycyclohexylideneacetonitriles* (**11a** and **12a**). To a stirred 2-bromocyclohexylideneacetonitrile (4.8 g, 24 mmol; mixture of *E* and *Z* isomers) with $N_2$, 100 ml of dry MeOH and 12.2 g $AgNO_3$ was added. The mixture was stirred under reflux for 10 hr, cooled and poured on ice. The mixture was extracted with ether and usual workup gave 1.9 g of mixture **11a** and **12a**, b.p. 132–133° (1 torr). The individual isomers were obtained by preparative TLC (silica gel, hexane–ether, 3/2). $^1$H NMR of *E*-isomer, **11a** ($CCl_4$): 3.24 (s, 3H), 4.26 (m, 1H), 5.02 (m, 1H). $^1$H NMR of *Z*-isomer, **12a** ($CCl_4$): 3.30 (s, 3H), 4.96 (m, 1H), 5.25 (d, 1H, J = 1.8 Hz).

*2-Acetoxycyclohexylideneacetonitriles* (**11a** and **12b**). To a mixture of anhyd AcOAg (8.35 g, 50 mmol) and 100 ml glacial AcOH heated under reflux, a soln of 2-bromocyclohexylideneacetonitrile (5.0 g, 25 mmol, mixture of *E* and *Z* isomers) in AcOH was added dropwise. The mixture was stirred (argon) for 15 hr, cooled, filtered, poured into ice water and extracted with $CHCl_3$. The usual work up and chromatography (preparative TLC, silica gel, hexane–ether, 3/1) gave 500 mg of *E*-isomer and 300 mg of *Z*-isomer. $^1$H NMR spectrum of *E*-isomer, **11b** ($CCl_4$): 2.07 (s, 3H), 5.23 (m, 1H), 5.28 (s, 1H); $^1$H NMR spectrum of *Z*-isomer, **12b** ($CCl_4$): 2.08 (s, 3H), 5.28 (s, 1H), 5.57 (m, 1H).

*Cyclohexylidenemalononitriles* (**13**)—*general procedure.* A mixture of 0.03 mol of 2-substituted cyclohexanone, 2.2 g (34 mmol) malononitrile, 1 g anhydrous ammonium acetate, 3 ml AcOH in benzene (argon) was refluxed with removal of water by azeotropic distillation. After separation of the theoretical amount of water the mixture was cooled, washed with water, $NaHCO_3$ and water again. The organic phase was dried over $Na_2SO_4$, the solvent was removed *in vacuo* and the residue was either distilled *in vacuo* or recrystallized.

*2-Methoxycyclohexylidenemalononitrile* (**13a**) was obtained in 65% yield, b.p. 115–116° (7 torr), $n_D^{16}$ 1.5050; $^1$H NMR ($CCl_4$): 3.23 (s, 3H), 4.30 (m, 1H).

*2-Acetoxycyclohexylidenemalononitrile* (**13b**). Instead of $NH_4OAc$ the same amount of $\beta$-alanine was used, yield 85%. The

compound was purified by chromatography (silica gel, hexane-ether, 1/3), $n_D^{19}$ 1.5026; $^1$H NMR ($CCl_4$): 2.16 (s, 3H), 5.75 (m, 1H).

*2-Phenylcyclohexylidenemalononitrile* (**13d**), Yield 60%, m.p. 67° (with dec., from hexane). $^1$H NMR ($CCl_4$): 4.38 (m, 1H), 7.23 (narrow m, 5H).

*2-Bromocyclohexylidenemalononitrile* (**13c**). To a soln of cyclohexylidenemalononitrile (10.5 g, 73 mmol) in dry $CCl_4$(50 ml), NBS (12.5 g, 70 mmol) and benzoyl peroxide (0.4 g) were added (argon) and the mixture was refluxed for 3.5 hr. The work up including the chromatography (TLC, silica gel, benzene) and redistillation give 20% yield of **13c**, b.p. 156–157° (5 torr), $n_D^{17}$ 1.5561; $^1$H NMR ($CCl_4$): 5.33 (m, 1H).

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