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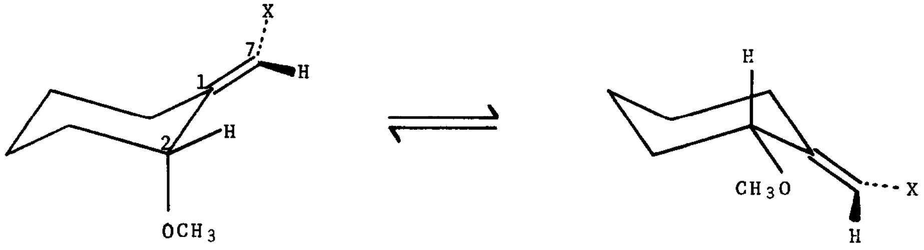
CONFORMATIONAL ANALYSIS OF 7-SUBSTITUTED 2-METHOXY-METHYLENECYCLOHEXANES: EVIDENCE AGAINST $n_O \rightarrow \pi^*$ ORBITAL STABILIZATION OF THE AXIAL CONFORMER

Jean Lessard*, John K. Saunders, and Minh Tan Phan Viet
Département de chimie, Université de Sherbrooke, Sherbrooke
Québec, Canada. J1K 2R1

Summary: Dynamic ^{13}C NMR studies of 7-substituted 2-methoxy-methylenecyclohexanes indicate that the proportion of axial orientation decreases as the 7-substituent becomes less electron donating, the equatorial conformer being largely predominant in the 7-cyano derivative.

We reported earlier[1] that 2-methoxy-methylenecyclohexane (1*a*) exists preferentially in the axial orientation and that this preference is increased upon introducing a methoxy group at position 7 (see 1*b*). These observations



1*a*: X = H; 1*b*: X = OCH_3; 1*c*: X = C_6H_5; 1*d*: X = CN were explained by $\pi\rightarrow\sigma^*_{c-o}$ stabilization of the axial conformer. More recently, we have shown[2] that 2-vinyloxy, 2-phenoxy- , and 2-acetoxymethylenecyclohexanes exist preferentially in the equatorial orientation and pointed out that the difference of conformational preference between a methoxy group and an unsaturated substituent at position 2 cannot be explained by a $\pi\rightarrow\sigma^*_{c-o}$ orbital interaction in the axial conformer. Indeed, the energy of the σ^*_{c-o} orbital should be lower and the stabilization of the axial conformer more important in the case of the unsaturated substituents (and more so for the acetoxy group which shows the smallest axial preference). However this difference could be rationalized in terms of $n_o\rightarrow\pi^*$ stabilization of the axial conformer as suggested for the 2-halo-cyclohexanones[3], since the energy level of the n_o orbital should be lower and the stabilization less important in the case of the unsaturated substituents (and less so for the acetoxy group). In fact, Zefirov and his co-workers[4] have taken the difference of conformational preference between 2-methoxy- and 2-acetoxy-methylenecyclohexane as a proof of $n_o\rightarrow\pi^*$ stabilization of the axial conformer of 2-substituted methylenecyclohexanes. This prompted us to report our results on the conformational properties of 7-substituted 2-methoxy-methylenecyclohexanes which show that such a stabilization cannot be operative.

The conformational equilibria recorded in the Table were determined by dynamic ^{13}C NMR spectroscopy using 3% solutions in CF_2Br_2/CD_2Cl_2 (4:1, v/v) or $CHFCl_2/CD_2Cl_2$ (4:1, v/v). The proportion of axial orientation decreases as the substituent X at position 7 becomes less electron donating and the equatorial conformer largely predominates when X is electron withdrawing. This is shown also by the linewidth of H-2 in the ^1H NMR spectra in CCl_4 solutions. *These results cannot be rationalized in terms of a* $n_o\rightarrow\pi^*$ *stabilization of the axial conformer.* Indeed, the energy level of the π^* orbital should be the lowest in **1*d*** and the highest in **1*b*** with the size of the orbital at C-1 being the smallest in **1*d*** and the largest in **1*b***[5]. Therefore, an $n_o\rightarrow\pi^*$ orbital interaction in the axial conformer should be the strongest in the case of **1*d*** and, if such an interaction was an important factor in determining the conformational properties of 2-substituted methylenexyclohexanes, the proportion of axial orientation should have been the highest for the 7-cyano derivative 1*d* contrary to the experimental results.

The conformational properties of glycenoses and alkenes having the general formula $R\overset{3}{C}H(OR^1)\overset{2}{C}H{=}\overset{1}{C}HX$ (E configuration) have been studied by Tronchet and Xuan[6] and are similar to those of 7-substituted 2-methoxy-methylenecyclohexanes (1): the *cis* conformation in which the alkoxy group eclipses the double bond (corresponding to the equatorial orientation in 1) is particularly favored when X is electron withdrawing by resonance; it becomes less favored or totally unfavored when X is electron donating by resonance. This behavior was explained in terms of a mutual balance between four-electron and two-electron orbital interactions, and by hydrogen bonding between H-1 and OR^1 in the *cis* conformer.

TABLE. Conformational equilibria and linewidth of H-2 in 7-substituted 2-methoxy-methylenecyclohexanes

Substituent	% of axial conformer		Linewidth[c] of H-2 in Hz
	CF_2Br_2/CD_2Cl_2 -113°C[a]	$CHFCl_2/CD_2Cl_2$ -60°C[b]	CCl_4 30°C
CH_3O (1*b*)	>95[d]		5.2
C_6H_5(1*c*)		88[e]	6.7 (7.6)
H (1*a*)	75	63	7.6 (8.4)
CN (1*d*)	12		(14.4)

[a] By careful integration of several spectra. [b] From $\delta m = x\delta eq + (1-x)\delta ax$ where δm is the C-4 chemical shift at -60°C. [c] $\sum J$; values between brackets refer to the linewidth at half height. [d] The equatorial conformer could not be detected (see ref. 1). [e] The C-4 chemical shift of the equatorial conformer could not be determined and $\Delta\delta$(eq-ax) was assumed to be 4.7 ppm.

Obviously, the conformational behavior of the 2-substituted methylene-xyclohexanes reported in this and the previous papers [1,2] cannot be rationalized in terms of a single and unique type of orbital interaction. Electrostatic interactions[1,2] could also contribute to the effects observed and, in the 7-cyano derivative _1d_, hydrogen bonding between H-7 and the methoxy group at C-2 could provide some stabilization of the equatorial conformer.

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