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CARBON-13 PULSE FOURIER TRANSFORM NMR

CONFORMATIONAL PREFERENCE OF THE HYDROXYL AND THE ACETOXYL GROUP IN 2-METHYL-2-CYCLOHEXENOL AND ITS ACETATE

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Abstract—^{13}C Fourier transform NMR of *cis* and *trans* 5 - t - butyl - 2 - methyl - 2 - cyclohexenol, 2 - methyl - 2 - cyclohexenol and their acetates has been examined indicating that the pseudo-axial orientation of the hydroxyl and the acetoxyl group at the allylic position is favoured in 2 - methyl - 2 - cyclohexenol and its acetate.

A pseudo-equatorial group in cyclohexene ring which takes half-chair conformation is brought towards an eclipsed relationship with the adjacent vinylic substituent. The pseudo-axial group experiences one pseudo-axial, axial interaction in place of the two axial, axial repulsion in cyclohexane. On both accounts, therefore, a pseudo-axial group will be favoured in a cyclohexene system more than the same group when axial on a saturated ring, and the effect will be enhanced as the size of the adjacent vinylic substituent increases. The orientation of the OH group in allylic cyclohexenol was investigated by Ferrier and Prasad using the equilibrium technique of *cis* and *trans* 5 - t - butyl - 2 - cyclohexenol.[1] They concluded that the allylic OH group favours the pseudo-equatorial orientation by 0·4 kcal/mol. Conversely, Hanaya reported that pseudo-axial orientation of the allylic OH group is favoured in the equilibrium study of epimeric 5 - methyl - and 5 - phenyl - 2 - cyclohexenols.[2]

We examined the ^{13}C pulse Fourier transform NMR spectroscopy of epimeric 5 - t - butyl - 2 - methyl - 2 - cyclohexenols (*cis*-**1** and *trans*-**1**), 2 - methyl - 2 - cyclohexenol (**2**) and their acetates (*cis*-**3** and *trans*-**3** and **4**, respectively) and discussed the quantitative distribution of conformational isomers of **2** and **4**.

4 - t - Butyl - 1 - methylcyclohexene was oxidised by mercuric acetate in acetic acid to form 5 - t - butyl - 2 - methyl - 2 - cyclohexenyl acetate. The gas chromatogram of the resulting mixture showed two main peaks (98%) which corresponded to two epimeric 5 - t - butyl - 2 - methyl - 2 - cyclohexenyl acetates and minor parts (2%). The ratio of two epimeric 5 - t - butyl - 2 - methyl - 2 - cyclohexenyl acetates were 55% of A_{OAc} and 45% of B_{OAc}. These acetates were reduced with LAH to give corresponding cyclohexenols. The steric configuration of two epimeric cyclohexenols (A_{OH} and B_{OH}) and their acetates (A_{OAc} and B_{OAc}) were determined by proton and ^{13}C NMR spectroscopy.

The PMR of A_{OH}, A_{OAc}, B_{OH}, and B_{OAc} are listed in Table 1. The methine proton at the allylic carbinol carbon of A_{OH} resonated at 4·02 ppm and of A_{OAc} did at 5·22 ppm as a doublet. The vicinal coupling constants were approximately 3·5 Hz of both. On the other hand, the methine proton of the allylic carbinol carbon of B_{OH} resonated at 4·12 ppm and of B_{OAc} did at 5·38 ppm as a broad singlet. The width at half heights of these signals was approximately 19 and 14 Hz respectively.

If it is possible to apply the Garbisch model[3] for cyclohexene to the conformation of epimeric **1** and **3**, the following estimation can be established; (i) the dihedral angles between C-6—H_e and C-1—H_e for *trans*-**1** and *trans*-**3** are approximately 86° and C-6—H_a and C-1—H_e are 29°. (ii) The dihedral angles between C-6—H_a and C-1—H_a for *cis*-**1** and *cis*-**3** are approximately 137° and C-6—H_e and C-1—H_a are 22° (Fig 1). Alternatively, if the estimated dihedral angles between allylic protons and homoallylic ones of shikimic acid are applied to these compounds,[4] the dihedral angles between C-6—H_e and C-1—H_e for *trans*-**1** and *trans*-**3** are estimated as 70° and C-6—H_a and C-1—H_e as 50°, whereas

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Table 1. Proton chemical shifts of epimeric 5 - t - butyl - 2 - methyl - 2 - cyclohexenols and their acetates[a]

	A_{OH} (*trans*)	A_{OAc} (*trans*)	B_{OH} (*cis*)	B_{OAc} (*cis*)
⊃—H	5·58 (d)	5·74 (d)	5·47 (b,s)	5·69 (b,s)
—C$\underline{H}$OH	4·02 (d)	—	4·12 (b,s)	—
—C$\underline{H}$OAc	—	5·22 (d)	—	5·38 (b,s)
—OH	2·00 (b,s)	—	2·34 (b,s)	—
—OAc	—	2·05 (s)	—	2·04 (s)
⊃—Me	1·81 (s)	1·68 (s)	1·75 (s)	1·61 (s)
t-Bu-	0·91 (s)	0·85 (s)	0·87 (s)	0·86 (s)
Others	1·40–2·16	1·48–1·88	1·00–2·24	1·00–2·64

[a] All shifts are in part per million down-field from tetramethylsilane. s, singlet; b,s, broad singlet; d, doublet.

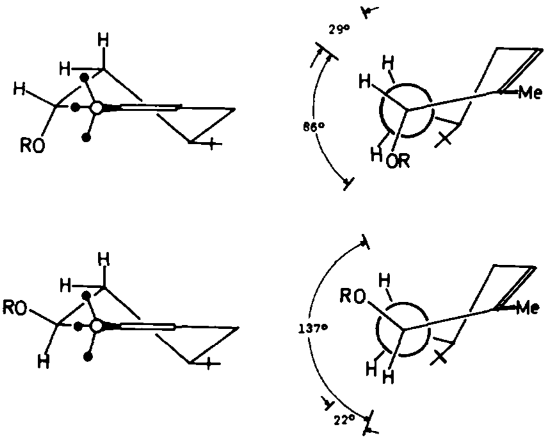


Fig 1.

those between C-6—H_a and C-1—H_a for *cis*-1 and *cis*-3 are estimated as 170° and C-6—H_e and C-1—H_a as 50° (Fig 2). Either way, the coupling constants of allylic proton with homo-allylic ones of *cis*-1 and *cis*-3 would be greater than those of the *trans*.

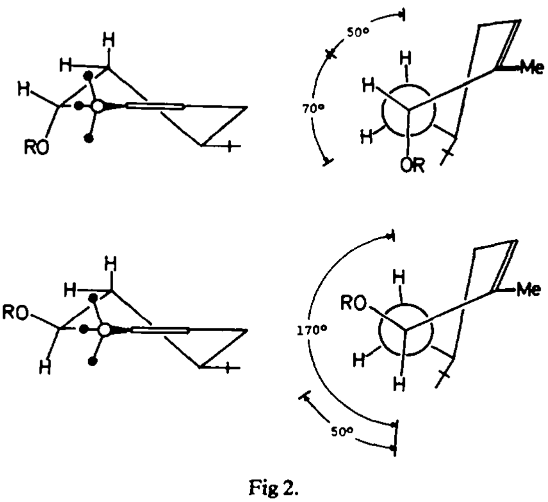


Fig 2.

The natural abundance 25·15 MHz ^{13}C spectra were obtained with pulse Fourier transform NMR using the proton decoupling techniques. The chemical shifts of ^{13}C NMR spectra of A and B are tabulated in Table 2. The individual chemical shifts were assigned to specific carbon atom with an off-resonance proton decoupling technique.

The ^{13}C chemical shifts of cyclohexanols and steroids showed that when the OH group or OAc group takes an axial orientation the signals of the carbinol carbon and C-5 carbon appeared at higher field than the signals when the OH group or OAc group takes an alternative orientation.[5,6]

Taking account of these informations appeared in the proton and ^{13}C NMR spectra with the assumed conformation of the molecule, it is confirmed that the isomer A corresponds to the *trans* isomer whose OH or OAc group takes pseudo-axial orientation and B corresponds to the *cis* whose OH or OAc group takes pseudo-equatorial orientation.

The chemical shifts of the ^{13}C spectra of **2** and **4** are also listed in Table 2. For each pair of isomers (**1** and **3**), a shielding difference of 2·73 ppm is found for the allylic carbinol carbons, the pseudo-axial appearing at the higher field. Assuming these values to be characteristic of the two "fixed" half-chair conformations, estimates of k_e, the conformational equilibrium constant, for the OR group (R = H or Ac) are given by

$$k_e = (\delta_{cis} - \delta)/(\delta - \delta_{trans})$$

where δ is the observed shielding of the mobile system, **2** or **4**. From the chemical shift of allylic carbinol carbon, k_e for **2** is 38·0. The OH group in **2**, therefore, exists in a distribution of 97·4% of pseudo-axial orientation and 2·6% of pseudo-equatorial. Since k_e for **4** is estimated as 8·75, the OAc group in **4** exists in 89·7% of pseudo-axial and 10·3% of pseudo-equatorial. We confirmed that in this system the "allylic strain" of the substituent at

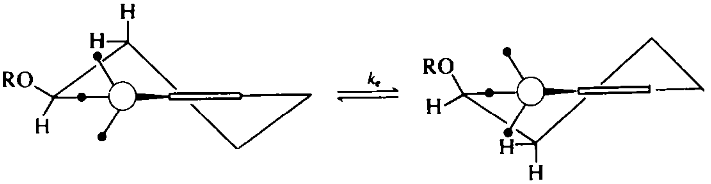
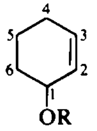


Table 2. ^{13}C chemical shifts of 2 - methyl - 2 - cyclohexenols and their acetates[a]

	5-t-Butyl-2-methyl-2-cyclohexenol A (*trans*)	5-t-Butyl-2-methyl-2-cyclohexenol B (*cis*)	2-Methyl-2-cyclohexenol
C-1	68·80	71·53	68·87
C-2	134·39	136·69	137·67
C-3	125·83	124·13	127·11
C-4	33·13	34·95	32·04
C-5	37·56	43·68	17·85
C-6	27·30	27·12	20·21
$2\text{-}CH_3$	20·93	18·87	25·19
$5\text{-}\underline{C}(CH_3)_3$	31·73	32·09	—
$5\text{-}C(\underline{C}H_3)_3$	27·30	27·12	—
	5-t-Butyl-2-methyl-2-cyclohexenyl acetate		2-Methyl-2-cyclohexenyl acetate
C-1	71·17	73·90	71·45
C-2	130·93	132·93	133·94
C-3	128·50	126·26	129·81
C-4	31·67	32·16	28·80
C-5	38·53	43·14	18·00
C-6	27·18	27·73	20·85
$2\text{-}CH_3$	21·11	21·05	24·19
$5\text{-}\underline{C}(CH_3)_3$	30·40	30·76	—
$5\text{-}C(\underline{C}H_3)_3$	27·18	27·00	—
$1\text{-}\underline{C}OCH_3$	170·36	170·61	173·86
$1\text{-}CO\underline{C}H_3$	20·63	18·63	20·06

[a] All shifts are in part per million down-field from tetramethylsilane.



the allylic position with vicinal Me group at the sp^2 carbon is so large that most of the molecule exists in a conformation with the pseudo-axial OH or the OAc group.

EXPERIMENTAL

NMR spectra. The PMR spectra were obtained with a JNM-PS-100 spectrometer operating at 100 MHz. ^{13}C NMR spectra were obtained with a JNM-PFT-100 system equipped with JNM-PS-100 spectrometer operating at 25·15 MHz. The samples were examined at approximately 10% (w/v) in $CDCl_3$ at 20°.

5 - t - Butyl - 2 - methyl - 2 - cyclohexenols. 4 - t - Butyl - 1-methylcyclohexene, (20 g), which was prepared from 4-t-butylcyclohexanone with MeMgI, followed by heating with $K_2S_2O_7$, was oxidized with 105 g of $Hg(OAc)_2$ in 330 ml of AcOH.[6] After refluxing the mixture for 1 h, the ppt was removed by filtration and the most of AcOH was removed by distillation. The residue was digested in ether which was washed with $NaHCO_3$ aq, followed by brine and dried over Na_2SO_4. The ether was removed by distillation to give an oily product. Distillation afforded 17 g (61%) of epimeric **3**, b.p. 104° (22·5 mm). (Found: C, 74·56; H, 10·41%. $C_{13}H_{22}O_2$ requires: C, 74·24; H, 10·54%). The epimeric mixture was separated with preparative gas chromatography and each fraction was reduced with LAH in ether, *cis*-**1**; b.p. 121–122° (22·5 mm), *trans*-**1**; b.p. 119° (22·5 mm).

The quantitative analysis was performed with the Hitachi K-53 gas chromatograph on a 45 m × 0·25 mm Goley column of PEG 4000 at 120° (*cis*-**3**; long retention time; *trans*-**3**, short retention time). The preparative gas chromatography was performed with Shimadzu 5AP with 6 m PEG 4000 on celite column at 180°.

2 - Methyl - 2 - cyclohexenol. 1 - Methylcyclohexene, 10 g, was oxidized with 67 g of $Hg(OAc)_2$ in 130 ml AcOH. After keeping the mixture at 90–100° for 1 h, the mixture was treated as **3**. Distillation afforded 6 g (38%) of **4**, b.p. 78° (37·5 mm). (Found: C, 70·35; H, 9·02. $C_9H_{14}O_2$ requires: C, 70·10; H, 9·15%). The acetate was reduced with LAH to give 4 g (92%) of **2**, b.p. 86–87° (40 mm).

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