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CARBON-13 PULSE FOURIER TRANSFORM NMR

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

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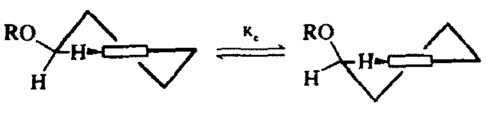
Abstract—^{13}C Fourier transform NMR spectra of *cis* and *trans* 5-t-butyl-2-cyclohexenols, 2-cyclohexenol and their acetates have been examined indicating that the pseudo-axial orientation of the hydroxyl and the acetoxyl group at the allylic position is favoured in 2-cyclohexenol and its acetate.

A pseudo-axial group in a cyclohexene ring which takes a half-chair conformation experiences one pseudo-axial ~ axial interaction in place of two axial ~ axial repulsion in a cyclohexane. On the other hand, a pseudo-equatorial group is eclipsed relationship with the adjacent vinylic substituent. As a consequence, a pseudo-axial group will be favoured in a cyclohexene ring 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. An equilibrium study of *cis* and *trans* 5 - t - butyl - 2 - cyclohexenols were performed by Ferrier and Prasad to investigate the orientational preference of the hydroxyl and the acetoxyl group in allylic cyclohexenol.[1] They concluded that the allylic OH group favours the pseudo-equatorial orientation by 0·4 kcal/mol, while the acetoxyl group of the derived acetate shows no significant orientational preference. On the other hand, Hanaya reported that pseudo-axial orientation of the allylic OH group is favoured by a factor of 2 in comparison with pseudo-equatorial orientation, while the acetoxyl group of derived acetates shows no significant orientational preference in an equilibrium study of epimeric 5-methyl- and 5-phenyl-2-cyclohexenols.[2] The conformational orientation of an allylic hydroxyl and an acetoxyl group still remained obscure.

We examined the ^{13}C pulse Fourier transform NMR spectra of epimeric 5-t-butyl-2-cyclohexenols (*cis*-**1** and *trans*-**1**), 2-cyclohexenol (**2**) and their acetates (*cis*-**3**, *trans*-**3** and **4**, respectively) to attempt to analyse directly the quantitative distribution of conformational isomers of **2** and **4**. The natural abundance 25·15 MHz ^{13}C spectra were obtained using the proton noise decoupling techniques. The ^{13}C chemical shifts of carbinol carbons are listed in Table 1. For each pair of isomers (**1** and **3**), a chemical shift difference of 4·43 ppm was found for the allylic carbinol carbons and that of 4·24 ppm was found for the carbons carrying the acetoxyl group, the carbons carrying the pseudo-axial substituent appearing at a higher field. Assuming these values to be characteristic of the two "fixed" half-chair conformations, the conformational equilibrium constants, K_e, for the OR groups (R=H or Ac) are given by

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



SCHEME 1.

where δ is the observed chemical shift for the mobile systems, **2** and **4**.

No report in the literature has been found concerning the substituent effects of the t-Bu group in a cyclohexene system. No effect of the equatorial Me group on C-3 in cyclohexane ring was observed by Dalling and Grant.[3] Roberts *et al.*, reported that the substituent effects of the t-Bu group which may take exclusively the equatorial orientation in t-butylcyclohexane on C-3 atom is +0·1 ppm.[4] If it is possible to apply the substituent effects of the t-Bu group in cyclohexane to cyclohexene system, K_e for **2** is approximately 5·24 from the chemical shift of the allylic carbinol carbon. The hydroxyl in **2**, therefore, exists in a distribution of 84·0 ± 2·3% of pseudo-axial orientation and 16·0 ± 2·3% of pseudo-equatorial. Since K_e for **4** is estimated as *ca* 2·14, the acetoxyl group in **4** exists in 68·2 ± 2·3% of pseudo-axial and 31·8 ± 2·3% of pseudo-equatorial. The observation that the pseudo-axial OH group is more favoured than the pseudo-axial acetoxyl group compared to the corresponding alternatives in cyclohexene derivatives is parallel to the case of the equilibrium study of 5-methyl- and 5-phenyl-2-cyclohexenols and their acetates.[2]

Table 1. Carbinol carbon chemical shifts of 2-cyclohexenols and their acetates

5-t-Butyl-2-cyclohexenol		2-Cyclohexenol
cis	*trans*	
69·22	64·79	65·40
5-t-Butyl-2-cyclohexenyl acetate		2-Cyclohexenyl acetate
cis	*trans*	
72·07	67·83	69·08

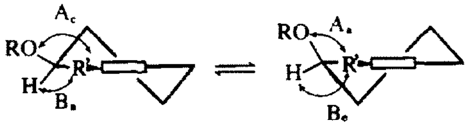
All chemical shifts are expressed in ppm downfield from internal tetramethylisilane. Each chemical shift is estimated to be accurate to ±0·05 ppm.

In a previous paper we found that K_e for 2-methyl-2-cyclohexenol (**5**) is approximately 15·1* and for 2-methyl-2-cyclohexenyl acetate (**6**) is approximately 6·18.*[5] Since the NMR probe temperature was 23°, the tentative estimation from the obtained K_e shows that the OH group in **2** favours the pseudo-axial position by 0·97 ± 0·10 kcal/mol and in **5** by 1·60 ± 0·42 kcal/mol, and the acetoxyl group in **4** also favours the pseudo-axial position by 0·45 ± 0·06 kcal/mol and in **6** by 1·07 ± 0·19 kcal/mol.

The OH group in cyclohexane shows a conformational free energy of 0·7 kcal/mol[6]. At the allylic position, exocyclic bonds are pseudo-axial and pseudo-equatorial, and the substituent on the former experiences one pseudo-axial ~ axial interaction in place of the two axial ~ axial interaction on cyclohexane. Consequently, the 1,3-diaxial interaction of the hydroxyl at the allylic position with the hydrogen should be 0·35 kcal/mol or less. If the value, 0·35 kcal/mol is employed, the allylic strain energy of the OH group is estimated to be 1·32 ± 0·10 kcal/mol in **2**. In this system the allylic strain is simply defined as the difference in the torsional angle strain of a vinylic hydrogen with a pseudo-equatorial OH group and with a pseudo-axial hydrogen, and that of the vinylic hydrogen with the pseudo-axial OH group and with the pseudo-equatorial hydrogen. The allylic strain is otherwise represented as $(A_e + B_a) - (A_a + B_e)$, as shown in Scheme 2.

Similarly, the allylic strain energy in **5** is estimated to be 1·95 ± 0·42 kcal/mol.

Since A value for the acetoxyl group in cyclohexane is also 0·7 kcal/mol, the allylic strain energy of the acetoxyl group in **4** is estimated to be 0·80 ± 0·06 kcal/mol and that in **6** to be 1·42 ± 0·19 kcal/mol. These estimations indicate that by replacing the vinylic hydrogen with the Me group the torsional angle strain with the adjacent allylic



(R = H or Ac)

SCHEME 2.

A_a; Interaction between pseudo-axial OR and vinylic R'
A_e; Interaction between pseudo-equatorial OR and vinylic R'
B_a; Interaction between pseudo-axial H and vinylic R'
B_e; Interaction between pseudo-equatorial H and vinylic R'

OH group increases by *ca* 0·63 kcal/mol and that with the allylic acetoxy group by *ca* 0·62 kcal/mol.

We confirmed from this study that in this system the "allylic strain" is so large that, even the hydrogen is on the adjacent vinylic C atom, the allylic hydroxyl and the acetoxyl group take preferably the pseudo-axial orientation.

EXPERIMENTAL

NMR spectra. The ^{13}C FT NMR spectra were obtained at 25·15 MHz on a JNM-MH-100 instrument equipped with a JNM-MFT-100 Fourier transform accessory. The instrument was controlled with a JEC-6 spectrum computer. Spectra were run using $CDCl_3$ solutions, the deuterium signal of which provided a field-frequency lock. The sample concentrations were 30% (w/v). Measurement conditions were as follows; pulse width, 27·5 μsec (*ca* 45°); repetition time, 2 sec; spectral width, 6·25 kHz; data points, 8192; acquisition time, 0·655 sec. Noise modulated proton decoupling was carried out at a nominal power level of 20 Watts.

Materials

5-t-Butyl-2-cyclohexenol(**1**) *and its acetate*(**3**). *trans*-**1** was prepared with the method reported by Ferrier and Prasad.[7] N-Bromosuccinimide (38·5 g) and benzoyl peroxide (0·2 g) were added to a soln of 4-t-butylcyclohexene (27 g) in CCl_4 (130 ml). After the exothermic reaction was over, the mixture was heated for 30 min, cooled, and filtered and the solvent was removed. The crude bromides were hydrolysed in H_2O and acetone (27%, 690 ml) containing Na_2CO_3 (45 g) by heating them under reflux for 3 hr with vigorous stirring. The precipitated salts were filtered off from the cooled mixture; the acetone was removed by evaporation from the filtrate and the product was extracted with ether. Distillation afforded 20 g of alcohol mixture (yield, 66%), b.p. 95–110°/27·5 mm. GLC showed the presence of 23% *cis*- and 77% *trans*-**1**. The acetates **3** (b.p. 115–125°/27·5 mm) which was prepared with Ac_2O in pyridine were roughly separated with preparative GLC. The crude *trans*-**1** (18 g, b.p. 80–83°/1·0 mm, 92% purity by GLC) which was obtained by the hydrolysis of corresponding acetate in alcoholic alkali soln was esterified with *p*-nitrobenzoyl chloride (25 g). The fractional recrystallisation from EtOH gave pure *trans* ester (20 g, yield 57%, m.p. 95–97°). The *trans* ester was hydrolysed to give *trans*-**1** (7 g, yield 79%, b.p. 83°/1·0 mm), which was acetylated with Ac_2O in pyridine to give *trans*-**3** (b.p. 129–131°/45 mm). *trans*-**1** (7 g) was oxidised on activated MnO_2 (15 g) in hexane (50 ml) and

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*These are corrected values by taking into account the substituent effects of the t-butyl group. The hydroxyl group in **5** exists in a distribution of 93·8 ± 3·7% of pseudo-axial orientation and 6·2 ± 3·7% of pseudo-equatorial. The acetoxyl group in **6** exists in 86·1 ± 3·6% of pseudo-axial and 13·9 ± 3·6% of pseudo-equatorial.

the 5 - t - butyl - 2 - cyclohexenone obtained was reduced with LAH in diethyl ether at −15° to give *cis*-**1** (5 g, yield 72%, b.p. 129–131°/20 mm)[7]. GLC showed the presence of 3% *trans*-**1**. Acetylation of *cis*-**1** gave *cis*-**3** (b.p. 126–129°/35 mm).

2-*Cyclohexenol* (**2**) *and its acetate* (**4**). **2** was obtained by the LAH reduction of 2-cyclohexenone[8] in diethyl ether, b.p. 83°/47·5 mm. **2** was treated with Ac_2O in pyridine to give **4** (b.p. 82–83°/47·5 mm), (Found: C, 68·80; H, 8·55. $C_8H_{12}O_2$ requires: C, 68·54; H, 8·63%).

These compounds were checked by GLC and IR and PMR spectra.

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