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CONFORMATIONAL DATA FROM THE CHEMICAL SHIFTS OF METHINE PROTONS IN DEUTERATED CYCLOHEXYL DERIVATIVES *

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Recently Jensen and Beck have published data to show that a t-butyl group in the 4-position of a cyclohexyl derivative has an appreciable effect on the chemical shift of the 1-proton (1). This information is important in the calculation of conformational free energy differences based on the chemical shifts of the unsubstituted cyclohexyl derivative compared with that of the t-butyl compound. Our work on deuterated substrates supports the conclusions of Jensen and Beck and offers similar data for several compounds which they did not study. The use of partially deuterated compounds like those in our study offers the advantage that bands are sharper and chemical shifts can thus be measured easily (2).

The data in this work is for several cyclohexyl and 4-t-butylcyclohexyl esters containing four deuterium atoms in the α-positions. Chemical shifts were measured at 60 MHz from a sideband of TMS which had been carefully positioned using a frequency counter. Deuterium decoupling was used in all experiments to further sharpen the observed lines (e.g. see Fig. 1).

Direct measurements of the conformational equilibrium constants were also made at low temperature by comparison of peak areas. Integration of the peaks was accomplished with both an electronic integrator and by weighing tracings of the peaks. In general, good agreement was obtained between the two methods although there was some discrepancy in the case of cyclohexyl-$\underline{d}_4$ acetate.

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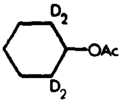
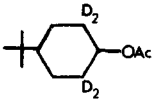
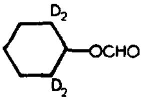
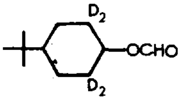
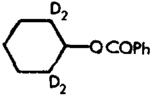
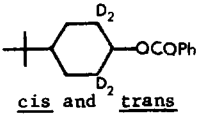
Table I

NMR Data at 60 MHz for β-Deuterated Cyclohexyl and 4-t-Butylcyclohexyl Esters (a)

Compound	Temp. (± 1°C)	Chemical Shifts(b) (± 0.1 Hz)	
	RT	273.9	
	-77	Coalescence	
	-102	262.1	286.5
	-108	261.6	286.1
 cis and trans	RT	266.4 trans	289.9 cis
	-102	260.9	284.4
	RT	285.0	
	-71	Coalescence	
	-102	274.5	299.3
 cis and trans	RT	276.3 trans	300.5 cis
	-102	272.4	296.4
	RT	292.0	
	-74	Coalescence	
	-99	279.7	304.1
 cis and trans	RT	282.5 trans	306.4 cis
	-105	(c)	300.5
	-109	(c)	300.0

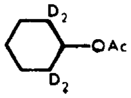
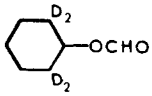
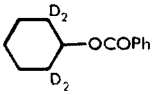
(a) All samples are 6-8% weight-to-volume in carbon disulfide with 5% added TMS. Spectra were taken with deuterium decoupling on a Varian HR-60 modified by the addition of an internal field-frequency lock (4).

(b) Taken from the average of 8-12 determinations.

(c) At low temperatures trans-t-butylcyclohexyl-d_4 benzoate precipitated out of solution so that only an equatorial ring proton could be observed.

Table II

Conformational Data for Cyclohexyl Esters

Compound	Temp. (±5 °C)	Equilibrium Constant(a)	Free Energy Difference (kcal/mole)
	RT	2.87±.06	.62±.02
	-106	6.8±.7(b)	.63±.06
	RT	2.68±.05	.58±.02
	-106	4.3±.2	.48±.03
	RT	2.75±.1(c)	.60±.03
	-106	4.6±.2	.51±.03

(a) Given as number of moles of equatorial ester divided by number of moles axial ester. The values at low temperature are an average of the data obtained by 10 to 12 electronic integrations of the peak areas and weighings of tracings of a comparable number of peaks. The room temperature data was obtained from the chemical shifts of the cyclohexyl esters and the *t*-butylcyclohexyl esters corrected for their differences at low temperature.

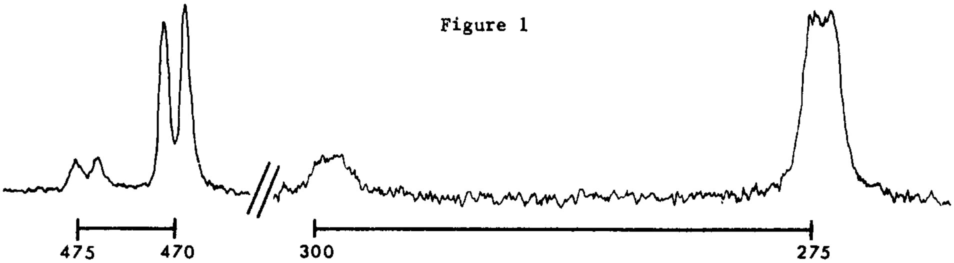
(b) The large error in this case was a result of a difference in the data obtained by electronic integration and weighing of peak tracings.

(c) The adjustment needed in the calculation for the equatorial proton of *trans*-*t*-butylcyclohexyl-d_4 benzoate at room temperature was estimated by analogy with the other compounds.

Examination of the data measured as described above and summarized in Table I shows that there is a difference of 1 to 3 Hz between the absorptions of the methine proton in the partially deuterated cyclohexyl and 4-*t*-butylcyclohexyl esters at low temperature. Assuming that these chemical shift differences do not change with temperature (although the absolute magnitudes of the chemical shifts vary considerably), we can make adjustments to the absorptions of the 4-*t*-butyl esters at room temperature to calculate the theoretical chemical shifts of the cyclohexyl esters undergoing no averaging as has been done already by Jensen and Beck (1). From these values we can then calculate the conformational equilibrium constants of the cyclohexyl esters as shown in Table II.

Although Jensen and Beck have generally studied different compounds, it is possible to compare their results for the acetate esters. Their values of the chemical shifts are uniformly about 3 Hz higher when corrected to 60 MHz but the room temperature free energy differences are in good agreement and also fit an earlier value obtained from coupling constants (3). The chemical shifts at low temperature for the deuterated cyclohexyl acetate and formate have been obtained at 40 MHz by previous workers (2c), but the data reported are in poor agreement with the present work.

Figure 1



Portions of the nmr spectrum (60MHz) of cyclohexyl-d_4-formate at -102°. Chemical shifts are Hz downfield from TMS. The bands at 274.5 and 299.3 Hz are due to the methine protons while the doublets at 469.9 and 474.4 Hz are from the formyl protons. The coupling constant between methine protons and the formyl protons is about 0.9 Hz in both conformers. The bands of the methine protons are broadened by long-range coupling to ring methylene protons.

References

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