The Experimental Determination of the Conformational Free Energy, Enthalpy, and Entropy Differences for Alkyl Groups in Alkylcyclohexanes by Low Temperature Carbon-13 Magnetic Resonance Spectroscopy

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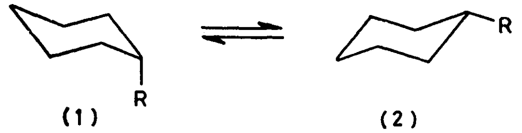
^{13}C N.m.r. studies at low temperatures of solutions in $CFCl_3$–$CDCl_3$ of [*Me*-^{13}C]methylcyclohexane, [α-^{13}C]-isopropylcyclohexane, *cis*-1-ethyl-4-methylcyclohexane, *cis*-1-isopropyl-4-methylcyclohexane, and *cis*-1-ethyl-4-isopropylcyclohexane have yielded conformational enthalpy differences and conformational entropy differences for methyl, ethyl, and isopropyl groups in alkylcyclohexanes. For $-\Delta H°$, the averaged values obtained, in kcal mol^{-1}, were 1.75 (Me), 1.60 (Et), and 1.52 (Pr^i); for $\Delta S°$, the averaged values, in cal mol^{-1} K^{-1}, were −0.03 (Me), 0.64 (Et), and 2.31 (Pr^i). The determined values are in good agreement with those calculated by the Allinger group for the gas phase, using a method based on classical mechanics. As a result of the opposing trends for $-\Delta H°$ and $\Delta S°$ values, the sequence of $-\Delta G°$ values at 300 K, namely Pr^i > Et > Me, is reversed at temperatures below *ca.* 40 K.

THE conformational free energy difference[1,2] for a substituent in a monosubstituted cyclohexane (1) $\rightleftharpoons$ (2) is the standard free energy change ($-\Delta G°$) for the process (1) $\longrightarrow$ (2). Although the $\Delta G°$ values for simple alkyl groups have been determined many times, the methods employed,[3,4] whether thermochemical, spectroscopic, kinetic, or equilibrium, have mostly involved the study of cyclohexanes which contained not only the relevant alkyl group but polar substituents in addition. The derivation of $\Delta G°$ by such methods involves assumptions concerning the possible effects of the additional groups. An exception was the experiment of Anet *et al.*[5] in which methylcyclohexane was studied by low temperature ^{13}C magnetic resonance spectroscopy; however, the accuracy of the derived $-\Delta G°$ value (1.6 kcal mol^{-1}) was limited by spin saturation transfer and by the high noise level of the continuous wave spectrum. Subbotin and Sergeyev,[6] who employed a similar technique, failed to detect signals from the axial conformation of methylcyclohexane at 173 K and set a minimum value for $-\Delta G°$ of 1.8 kcal mol^{-1}. As far as we are aware, the thermodynamic parameters $\Delta G°$, $\Delta H°$, and $\Delta S°$, for the ethyl and isopropyl substituents, have not been determined by a direct analysis of ethylcyclohexane and isopropylcyclohexane. Recent years have witnessed the publication of several papers describing the calculation of the thermodynamic parameters for alkyl groups in alkylcyclohexanes.[7-12] For methylcyclohexane, the calculated values of $-\Delta G°$ display a wide scatter. One of the lowest values reported is 1.03 kcal mol^{-1}, calculated[10] for the molecule at 0 K using a modified Urey–Bradley force field. At the other extreme, a value of 4.3 kcal mol^{-1} was calculated by an *ab initio* self-consistent field method.[9]

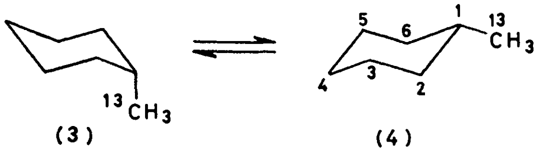
We report here the experimentally derived conformational free energy differences ($-\Delta G°$), conformational enthalpy differences ($-\Delta H°$), and conformational entropy differences ($\Delta S°$) for the substituents methyl, ethyl, and isopropyl. The $-\Delta G°$ values for Me and Pr^i were obtained by studying the low temperature ^{13}C n.m.r. spectra of methylcyclohexane (3) $\rightleftharpoons$ (4) and isopropylcyclohexane (5) $\rightleftharpoons$ (6), each molecule being enriched with ^{13}C at a single carbon atom. A preliminary report on the result for (3) $\rightleftharpoons$ (4) has already appeared.[13] Studies of the low-temperature ^{13}C n.m.r. spectra of *cis*-1-ethyl-4-methylcyclohexane (7) $\rightleftharpoons$ (8) and of *cis*-1-isopropyl-4-methylcyclohexane (9) $\rightleftharpoons$ (10) together with the reasonable assumption of additivity of parameters gave, respectively, a $\Delta G°$ value for Et and a second $\Delta G°$ value for Pr^i. *cis*-1-Ethyl-4-isopropylcyclohexane (11) $\rightleftharpoons$ (12) was also studied so as to afford us a check on the assumption of additivity; however, the difficulty of separating this molecule completely from its *trans*-isomer (13) necessitated that the experiments be carried out on a mixture of isomers.

At temperatures below 195 K, the ^{13}C n.m.r. spectra of (1) $\rightleftharpoons$ (2) reveal signals due to both conformations, as the rate of exchange is much lower than the frequency difference between structurally identical carbon atoms in the two conformations. An assessment of the equilibrium constant K {= [(2)]/[(1)]} can therefore be made by integration of appropriate signals in the spectrum. The range of temperature over which it was possible to make measurements was 140—195 K. However, in this range the equilibrium constant K for [(1) $\rightleftharpoons$ (2) R = alkyl] is between 150 and 1 500, so that an accurate estimation of the minor conformation presents severe problems. The situation is improved by the use of molecules in which one of the carbon atoms is enriched with carbon-13. However, experiments in which a large dynamic range is to be estimated by pulse Fourier transform n.m.r. are limited by the capability of the computer used to accumulate the data. According to Cooper,[14] the observable dynamic range is generally limited to 2^{d+1} where d is the number of bits in the digitiser of the A/D converter. With a 9-bit digitiser, for example, the limit of dynamic range is 1 024, and if this is exceeded, the minor signal cannot be detected; double precision is clearly of no value in this instance. This general analysis may, however, be unduly pessimistic for ^{13}C spectra, as it is likely that carbon signals below the threshold of digitisation will be carried through along with the noise, and will eventually be observed. The final signal to noise ratio obtained is proportional, *inter alia*, to $(W - d)$, the difference between the word length of the data system (W) and the digitiser resolution.

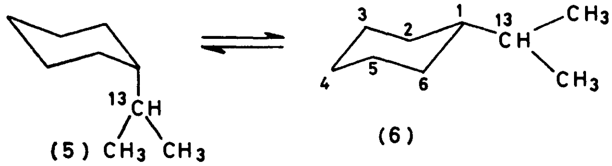
Problems are also encountered in the interpretation of integrals in a multi-pulse ^{1}H-decoupled ^{13}C experiment. However, as indicated previously,[15] if measurements are made below 220 K, the comparison of integrals is meaningful if they refer to carbon atoms carrying the same number of hydrogen atoms, and provided the pulse repetition time is at least 2 s. In the present experiments, comparisons were made between structurally identical carbon atoms in the two conformations, and the pulse repetition time was 4 s.



(1) (2)



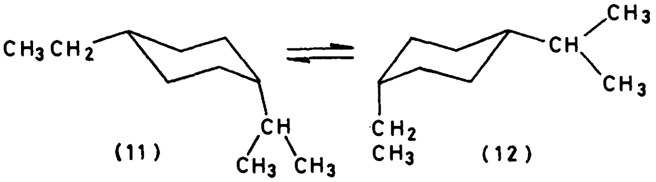
(3) (4)



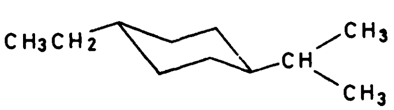
(5) (6)

(7) R = Et (8) R = Et

(9) R = Pr^{i} (10) R = Pr^{i}



(11) (12)



(13)

The disubstituted cyclohexanes required in this study were synthesised from 4-alkylcyclohexanols by sequential procedures of (a) oxidation, (b) conversion of the resulting ketone to a tertiary alcohol by a Grignard reagent, (c) dehydration of the tertiary alcohol, and (d) catalytic hydrogenation of the alkene to a mixture of *cis*- and *trans*-1,4-dialkylcyclohexanes (*cf.* ref. 16). In the majority of cases, a good separation of the isomeric cyclohexanes was obtained by preparative g.l.c. The synthesis of [*Me*-^{13}C]methylcyclohexane (3) $\rightleftharpoons$ (4) utilised cyclohexanone and ^{13}C-enriched methyl iodide in stage (b) above; the synthesis of [α-^{13}C]isopropylcyclohexane (5) $\rightleftharpoons$ (6) utilised [2-^{13}C]acetone and bromocyclohexane in stage (b).

^{13}C n.m.r. spectra were recorded, in CFCl$_3$–CDCl$_3$ (9 : 1 v/v) as solvent, for all cyclohexanes, at room temperature and at several temperatures in the range 140—195 K. ^{13}C Chemical shifts for (7) to (13) have already been published;[16] shifts for (3) $\rightleftharpoons$ (4) and (5) $\rightleftharpoons$ (6) are given in Table 1. In the spectrum of (5) $\rightleftharpoons$ (6) at 155 K, the weak signal at δ 24.9 p.p.m. was assigned to the methine carbon of an axial isopropyl group. The shift of δ 24.9 p.p.m. is in excellent agreement with the chemical shifts of signals at δ 25.1 and 25.0 p.p.m. assigned[16] to the methine carbons of axial isopropyl groups in conformations (10) and (11) respectively.

TABLE 1

^{13}C Chemical shifts (p.p.m. downfield from Me$_4$Si) for [*Me*-^{13}C]methylcyclohexane (3) $\rightleftharpoons$ (4) and [α-^{13}C]-isopropylcyclohexane (5) $\rightleftharpoons$ (6) in CFCl$_3$–CDCl$_3$

Conformation	C-1	C-2,6	C-3,5	C-4	CH$_3$	CH-(Pr^{i})	CH$_3$ (Pr^{i})
(3) [a]					17.43		
(4) [a]	33.15 [c]	35.51	26.72 [d]	26.36	23.47		
(5) [b]						33.30	
(6) [b]	44.00 [e]	29.78	26.70 [g]	26.70		25.05	19.85 [f]

[a] At 167 K. [b] At 175 K. [c] Centre of doublet, $'J_{^{13}C,^{13}C}$ 36.0 Hz. [d] Centre of doublet, $^{3}J_{^{13}C,^{13}C}$ 4.3 Hz. [e] Centre of doublet, $^{1}J_{^{13}C,^{13}C}$ 34.8 Hz. [f] Centre of doublet, $^{1}J_{^{13}C,^{13}C}$ 35.4 Hz. [g] Centre of doublet, $^{3}J_{^{13}C,^{13}C}$ 3.0 Hz.

Conformational enthalpy and entropy differences are summarised in Table 2, which also includes the free energy differences calculated for 300 K. As a check on some of the values in Table 2, the conformational enthalpy and entropy differences were determined for *cis*-1-ethyl-4-isopropylcyclohexane (11) $\rightleftharpoons$ (12).

The values thus determined for $\Delta H^{\circ}_{(11)\rightarrow(12)}$ and $\Delta S^{\circ}_{(11)\rightarrow(12)}$ are in reasonable agreement with those obtained by subtraction of the corresponding parameters, listed in Table 2, for the ethyl and isopropyl groups (see Experimental section).

The following comments on Table 2 are appropriate. The established error limits show that more accurate parameters for isopropyl were obtained from the analysis of the equilibrium in *cis*-1-isopropyl-4-methylcyclohexane (9) $\rightleftharpoons$ (10) than from the analysis of [α-^{13}C] isopropylcyclohexane (5) $\rightleftharpoons$ (6). This is because the more evenly balanced equilibrium in (9) $\rightleftharpoons$ (10) is capable of more accurate analysis than the very extreme equilibrium in (5) $\rightleftharpoons$ (6). Where equilibria are extreme, as in (3) $\rightleftharpoons$ (4) and (5) $\rightleftharpoons$ (6), the accuracy in determination of the equilibrium constant K is largely dependent on the signal to noise ratio achieved for the minor signal. In a recent paper, Sergeyev[17] has suggested that the measurement of very large equilibrium constants by the n.m.r. peak area method is futile, because the relative error in the equilibrium constant K shows a nearly linear dependence on K. However, Sergeyev makes the unreasonable assumption that the relative errors in measurement of the areas of both major and minor peaks are the same. In fact, errors in the measurement of the area of the major peak may be neglected because of the high signal to noise ratio for this peak. In the case of [Me-^{13}C]methylcyclohexane, for example, the final signal to noise (peak *height*) ratio at 149 K for the carbon due to Me(equatorial) was *ca.* 10 000. The corresponding ratio for the carbon due to Me(axial) was 30. If we assume an error of 5% in the measurement of the area of the minor signal, the equilibrium constant of 427 may be expressed as 427 ± 21. On the other hand, the formula of Sergeyev leads to a final result in the form $K = 427 \pm 9\,116$. We insist that the measurement, by the n.m.r. peak area method, of high K values, is meaningful provided adequate signal to noise ratios is obtained for the minor signal.

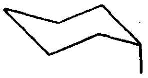
TABLE 2

Conformational enthalpy, entropy, and free energy differences for alkyl groups in alkylcyclohexanes

	$-\Delta H^0$/kcal mol^{-1}		ΔS^0/cal K^{-1} mol^{-1}		$-\Delta G^0_{300}$/ kcal mol^{-1}
Group	Found [a]	Calc.[b]	Found [a]	Calc.[b]	Found [c]
Me [d]	1.75 ± 0.05	1.77	−0.03 ± 0.25	0	1.74
Et [e]	1.60 ± 0.06	1.69	0.64 ± 0.35	0.61	1.79
Pr^i [f]	1.52 ± 0.06	1.40	2.31 ± 0.38	2.18	2.21
Pr^i [g]	1.35 ± 0.49	1.40	4.19 ± 3.04	2.18	2.61

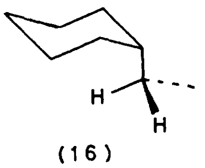
[a] Average of treatments A and B (see Experimental section). [b] Gas phase, ref. 8. [c] From experimental ΔH^0 and ΔS^0 values. [d] From equilibrium in (3) $\rightleftharpoons$ (4). [e] From equilibrium in (7) $\rightleftharpoons$ (8). [f] From equilibrium in (9) $\rightleftharpoons$ (10). [g] From equilibrium in (5) $\rightleftharpoons$ (6).

It is noted from Table 2 that the conformational enthalpy difference ($-\Delta H^\circ$) decreases in magnitude along the series Me, Et, Pr^i, in agreement with Allinger's calculations of 1968,[8] and with a prediction based on classical conformational analysis, *i.e.* on the summation of gauche-butane (g.b.) interactions (*cf.* ref. 18). This latter approach is clearly illustrated by reference to conformations (14)—(24), which are displayed, together, in each case, with the number of g.b. interactions. As is usual in this type of analysis, it is assumed that the repulsive g.b. interactions dominate the overall energetics. Conformations which contain a terminal methyl directed inwards are energetically unfavourable and are not significantly populated: such conformations are not illustrated.

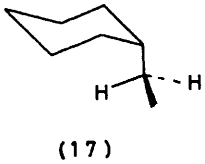


(14)
2 g.b.

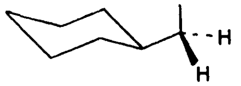
(15)
0 g.b.



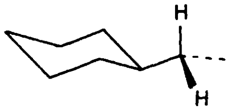
(16)
3 g.b.



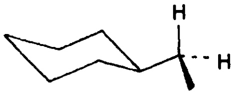
(17)
3 g.b.



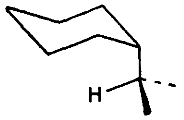
(18)
2 g.b.



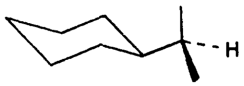
(19)
1 g.b.



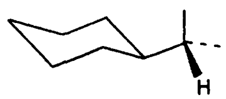
(20)
1 g.b.



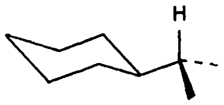
(21)
4 g.b.



(22)
3 g.b.



(23)
3 g.b.



(24)
2 g.b.

There are 2 g.b. interactions in the axial conformation (14) of methylcyclohexane; there are no g.b. interactions in the equatorial conformation (15). Consequently, an enthalpy difference equal to 2 g.b. interactions is expected between the two conformations of methylcyclohexane. The situation is more complicated for ethylcyclohexane. For axial ethylcyclohexane (16) $\rightleftharpoons$ (17) both conformation (16) and its enantiomer (17), suffer 3 g.b. interactions. For equatorial ethylcyclohexane we have to consider the three conformation (18)—(20). Although (19) and its enantiomer (20) each has only 1 g.b. interaction, conformation (18), which makes an appreciable contribution, has 2 g.b. interactions. Thus the overall enthalpy difference between the axial and equatorial conformations of ethylcyclohexane must be *less* than 2 g.b. interactions. For axial isopropylcyclohexane, only (21), with 4 g.b. interactions, will make an appreciable contributions. In equatorial isopropylcyclohexane (22) $\rightleftharpoons$ (23) $\rightleftharpoons$

(24), conformation (24) has 2 g.b. interactions, but now there are two conformations, (22) and its enantiomer (23), each with 3 g.b. interactions. Consequently the enthalpy difference between axial and equatorial isopropylcyclohexane is not only less than 2 g.b. interactions, but almost certainly less than the corresponding difference for ethylcyclohexane.

The data in Table 2 shows that there is an *increase* in the conformational entropy difference $\Delta S°$ along the series Me, Et, Pr^i. Such an increase may be correlated roughly with an increase in the number of energetically allowable arrangements for the equatorial conformation, compared with the number for the axial conformation, in proceeding along the series.

The trends in $-\Delta H°$ and $\Delta S°$ run in opposite senses along the series Me, Et, Pr^i. The consequences for $\Delta G°$ are obvious yet interesting. At a very low temperature, say 40 K, the $\Delta G°$ values for the alkyl groups are dominated by the enthalpy term $\Delta H°$, and the preference for the equatorial orientation follows the order Me > Et > Pr^i. On the other hand, at temperatures around room temperature, the $\Delta G°$ values are dominated by the entropy term $T\Delta S°$, ensuring that the preference for an equatorial orientation follows the order Pr^i > Et > Me. In the case of *cis*-1-ethyl-4-methylcyclohexane (7) $\rightleftharpoons$ (8), conformation (8) with ethyl *axial*, was proved by spectral analysis to be the major conformation within the temperature range (140—195 K) used in the ^{13}C n.m.r. study. The temperature at which $\Delta G°_{Me}$ equals $\Delta G°_{Et}$ is approximately 218 K, obtained from the intercept ($\ln K = 0$) of the plot of $\ln K$ against T^{-1}. Above this temperature, the ethyl group has the numerically larger $\Delta G°$; below this temperature the methyl group has the numerically larger $\Delta G°$. The corresponding temperature at which $\Delta G°_{Me}$ equals $\Delta G°_{Pr^i}$ is 99 K.

EXPERIMENTAL

General.—General details for the determination of ^{13}C spectra at low temperatures have been given earlier.[15] ^1H N.m.r. spectra were obtained at 100 MHz with a JEOL JNM-MH-100 instrument.

Analytical g.l.c. used a Pye 104 series instrument. Preparative g.l.c. employed an Aerograph Autoprep. model A-700 with katharometer detector. Most mass spectra were recorded on a A.E.I. M.S. 902 instrument. A few spectra were recorded with a VG70-70F instrument. The intensity of the molecular ion is expressed as a percentage of the base peak.

Synthesis of Cyclohexanes.—The general method of synthesizing *cis*- and *trans*-1,4-dialkylcyclohexanes has been described earlier.[16]

[Me^{13}C]*Methylcyclohexane* (3) $\rightleftharpoons$ (4). Cyclohexanone (1.340 0 g) was allowed to react in ether with the Grignard reagent prepared from [^{13}C]iodomethane (2.000 g, 91.0 ^{13}C atom %) and magnesium turnings (0.337 0 g). Crude [*Me*-^{13}C]-1-methylcyclohexanol (2.073 6 g), obtained as a pale yellow oil containing some ether, was then heated with 4-methylbenzenesulphonic acid (0.180 g) to give [*Me*-^{13}C]-1-methylcyclohexene (0.875 8 g, 66% based on cyclohexanone). Hydrogenation of the alkene (neat) over PtO_2-(0.091 8 g) during 10 h caused the uptake of 230 cm^3 hydrogen (theoretical, 202 cm^3). [*Me*-^{13}C]Methylcyclohexane (0.647 2 g, 73%) was isolated as a mobile oil (>99% pure by g.l.c.). Impurities identified by g.l.c. were [*Me*-^{13}C]-1-methylcyclohexene (<0.5%) and cyclohexanone (<0.5%). The column used was a 5 ft × $\frac{1}{4}$ in stainless steel tube packed with 100—120 mesh, siliconised Diatomite C containing 10% of silicone gum rubber E-30 (methyl type). Mass spectroscopy gave M^+ 99.112 5 (47%) ($^{12}C_6{}^{13}C_1H_{14}$ requires *M*, 99.112 9).

The ^1H n.m.r. spectrum ($CDCl_3$) showed a doublet of doublets (separations 124 and 6 Hz), centred on δ 0.85 ($^{13}CH_3$) and a doublet (separation 6 Hz), centred on δ 0.85 ($^{12}CH_3$).

[α-^{13}C]*Isopropylcyclohexane* (5) $\rightleftharpoons$ (6). [2-^{13}C]Propanone (0.50 g; 92.2 ^{13}C atom %) was allowed to react in ether with the Grignard reagent from bromocyclohexane (1.553 6 g) and magnesium turnings (0.239 9 g). The normal method of working up gave crude [2-^{13}C]-2-cyclohexylpropan-2-ol (1.311 6 g, >100%), contaminated with bromocyclohexane (g.l.c.). The alcohol (1.311 0 g) was dehydrated by distillation with 4-methylbenzenesulphonic acid (0.136 0 g), giving [α-^{13}C]-1-isopropylcyclohexene (0.666 6 g, 58%) as an oil, contaminated with bromocyclohexane. Mass spectroscopy gave M^+ 125.127 3 (15%) ($^{12}C_8{}^{13}C_1H_{16}$ requires *M*, 125.128 6). The above alkene (0.666 6 g) was hydrogenated, without solvent over PtO_2 (0.255 21) during 6.5 h, when 133 cm^3 H_2 was absorbed (theoretical 120 cm^3). The product (0.475 0 g), recovered by pipette, consisted of [α-^{13}C]isopropylcyclohexane and bromocyclohexane. Preparative g.l.c. gave pure [α-^{13}C]isopropylcyclohexane (0.147 3 g) as an oil. The column used was a 5 ft × $\frac{1}{4}$ in glass column packed with 80—100 mesh Chromosorb W coated with 30% of Apiezon L. Mass spectroscopy gave M^+ 127.142 9 (8%) ($^{12}C_8{}^{13}C_1H_{18}$ requires *M*, 127.144 2).

Determination of Thermodynamic Parameters.—The JEOL variable temperature controller was calibrated frequently against a chromel–alumel thermocouple; temperatures are estimated to be accurate to ±2 K. Free induction decays were sampled over 2 500 Hz using 8 K data points. The pulse width was 4 μs (30° tip angle) and the pulse repetition time was 4 s. The line-broadening factor applied to the F.I.Ds varied between zero (most cases) and 0.4, depending on the signal to noise ratio obtained at the temperature of the experiment.

Equilibrium constants (*K*) were determined at various temperatures by careful measurement of the relative areas of well separated signals due to structurally identical carbon atoms in the two conformations. For *cis*-1,4-disubstituted cyclohexanes it was possible to use at least two pairs of signals, the final result being averaged. Spectra were expanded to 0.11, 0.22, or 0.275 p.p.m. cm^{-1} prior to measurements which employed both instrumental integration and hand planimetry. In hand planimetry, measurements were repeated five times and, again, the results were averaged. The data were treated in two ways. (A) Plots were made of $\ln K$ against T^{-1}, and the best straight line was drawn by eye. Since $\ln K = -\Delta H°/RT + \Delta S°/R$, the slope gives $\Delta H°$ and the intercept gives $\Delta S°$. Errors were obtained by consideration of the possible extremes for the straight line. (B) The Numerical Algorithms Group Library routine GO2CAF was used to fit the data to a line of general form (1) where $y = \ln K$ and $x = T^{-1}$. The

$$Y = a + bx \qquad (1)$$

programme gave values for the intercept *a* and slope *b* of the fitted line, together with standard errors in the two parameters. The errors in the averaged $\Delta H°$ and $\Delta S°$ values of Table 2 are the *worst* errors occurring in the treatments (A) and (B).

(a) [Me-^{13}C]*Methylcyclohexane* (3) $\rightleftharpoons$ (4).

Equilibrium constant K = [(4)]/](3,]

T/K	149	160	167	172
T^{-1}/K^{-1}	0.006 711	0.006 250	0.005 990	0.005 814
K *	426.7	222.5	183.0	164.2
ln$K$	6.056	5.405	5.211	5.101

* Based on relative areas of enriched methyl carbon.

Treatment (A) gave $\Delta H°_{\text{Me}} = \Delta H°_{(3)\rightarrow(4)} = -1.74 \pm 0.05$ kcal mol^{-1}, $\Delta S°_{\text{Me}} = \Delta S°_{(3)\rightarrow(4)} = 0.00 \pm 0.25$ cal mol^{-1} K^{-1}. Treatment (B) gave $\Delta H°_{\text{Me}} = \Delta H°_{(3)\rightarrow(4)} = -1.75 \pm 0.04$ kcal mol^{-1}, $\Delta S°_{\text{Me}} = \Delta S°_{(3)\rightarrow(4)} = -0.05 \pm 0.21$ cal mol^{-1} K^{-1}.

(b) [α-^{13}C]*Isopropylcyclohexane* (5) $\rightleftharpoons$ (6).

Equilibrium constant K =[(6)]/[(5)]

T/K	149	155	162	169	175
T^{-1}/K^{-1}	0.006 711	0.006 452	0.006 173	0.005 917	0.005714
K *	723	617	629	561	323
ln$K$	6.584	6.425	6.444	6.329	5.778

* Based on relative areas of enriched α-carbon.

Treatment (A) gave $\Delta H°_{\text{Pr}^{\text{i}}} = \Delta H°_{(5)\rightarrow(6)} = -1.40 \pm 0.19$ kcal mol^{-1}, $\Delta S°_{\text{Pr}^{\text{i}}} = \Delta S°_{(5)\rightarrow(6)} = +3.9 \pm 1.2$ cal. mol^{-1} K^{-1}. Treatment (B) gave $\Delta H°_{\text{Pr}^{\text{i}}} = \Delta H_{(5)\rightarrow(6)} = -1.30 \pm 0.49$ kcal mol^{-1}, $\Delta S°_{\text{Pr}^{\text{i}}} = \Delta S°_{(5)\rightarrow(6)} = +4.5 \pm 3.0$ cal mol^{-1} K^{-1}.

(c) cis-1-*Ethyl*-4-*methylcyclohexane* (7) $\rightleftharpoons$ (8).

Equilibrium constant K = [(8)]/[(7)]

T/K	141	150	160	166	167	177
T^{-1}/K^{-1}	0.007 09	0.006 66	0.006 25	0.006 02	0.005 99	0.005 66
K*	1.226	1.157	1.207	1.135	1.133	1.095
ln$K$	0.2037	0.1458	0.1881	0.1266	0.1248	0.0908

* Based on areas of C-4 and CH_2 of Et.

Treatment (A) (plot) gave $\Delta H°_{(7)\rightarrow(8)} = -0.170 \pm 0.03$ kcal mol^{-1}, $\Delta S°_{(7)\rightarrow(8)} = -0.78 \pm 0.20$ cal mol^{-1} K^{-1}. Treatment (B) (curve-fit) gave $\Delta H°_{(7)\rightarrow(8)} = -0.13 \pm 0.05$ kcal mol^{-1}, $\Delta S°_{(7)\rightarrow(8)} = -0.55 \pm 0.28$ cal mol^{-1} K^{-1}.

Taking into account the experimental values for $\Delta H°_{\text{Me}}$ and $\Delta S°_{\text{Me}}$ from (a), we deduce that $\Delta H°_{\text{Et}} = -1.57 \pm 0.06$ (plot) or -1.62 ± 0.06 kcal mol^{-1} (curve-fit) and $\Delta S°_{\text{Et}} = 0.78 \pm 0.30$ (plot) or 0.50 ± 0.35 cal mol^{-1} K^{-1} (curve-fit).

(d) cis-1-*Isopropyl*-4-*methylcyclohexane* (9) $\rightleftharpoons$ (10).

Equilibrium constant K = [(9)]/[(10)]

T/K	141	147	154	160	171	181	186	192
T^{-1}/K^{-1}	0.00709	0.00680	0.00649	0.00625	0.00585	0.00553	0.005 38	0.005 21
K *	1.376	1.541	1.580	1.474	1.535	1.633	1.769	1.776
ln$K$	0.3192	0.4325	0.4574	0.3879	0.4285	0.4904	0.5705	0.5744

* Based on areas of C-4 and CH_3 of Pr$^{\text{i}}$.

Treatment (A) gave $\Delta H_{(10)\rightarrow(9)} = 0.25 \pm 0.04$ kcal mol^{-1}, $\Delta S°_{(10)\rightarrow(9)} = 2.46 \pm 0.26$ cal mol^{-1} K^{-1}. Treatment (B) gave $\Delta H°_{(10)\rightarrow(9)} = 0.21 \pm 0.05$ kcal mol^{-1}, $\Delta S°_{(10)\rightarrow(9)} = 2.21 \pm 0.32$ cal mol^{-1} K^{-1}.

Taking into account the experimental values for $\Delta H°_{\text{Me}}$ and $\Delta S°_{\text{Me}}$ from (a), we deduce that $\Delta H°_{\text{Pr}^{\text{i}}} = -1.49 \pm 0.06$ (plot) or -1.54 ± 0.06 kcal mol^{-1} (curve-fit) and $\Delta S°_{\text{Pr}^{\text{i}}} = 2.46 \pm 0.36$ (plot) or 2.16 ± 0.38 cal mol^{-1} K^{-1} (curve-fit).

(e) cis-1-*Ethyl*-4-*isopropylcyclohexane* (11) $\rightleftharpoons$ (12).

Equilibrium constant K = [(12)]/[(11)]

T/K	148	153	157	161	167	172	177
T^{-1}/K^{-1}	0.006 773	0.006 530	0.006 363	0.006 205	0.005 983	0.005 809	0.005 653
K *	1.8919	1.9471	1.9113	1.9686	2.1814	2.0998	2.0631
ln$K$	0.6377	0.6663	0.6477	0.6773	0.7800	0.7419	0.7242

* Based on areas of C-2 and -6, CH_3 of Pr$^{\text{i}}$, and CH_3 of Et.

Treatment (A) gave $\Delta H°_{(11)\rightarrow(12)} = 0.18 \pm 0.05$ kcal mol^{-1}, $\Delta S°_{(11)\rightarrow(12)} = 2.48 \pm 0.25$ cal mol^{-1} K^{-1}. Treatment (B) gave $\Delta H°_{(11)\rightarrow(12)} = 0.18 \pm 0.04$ kcal mol^{-1}, $\Delta S°_{(11)\rightarrow(12)} = 2.49 \pm 0.23$ cal mol^{-1} K^{-1}. The averaged values for $\Delta H°_{(11)\rightarrow(12)}$ (0.18) and for $\Delta S°_{(11)\rightarrow(12)}$ (2.48) may be compared with the following values *calculated* by subtraction of the corresponding experimental values for Et and Pr$^{\text{i}}$ in Table 2: $\Delta H°_{(11)\rightarrow(12)}$ (Calc.) = 0.08 kcal mol^{-1}, $\Delta S°_{(11)\rightarrow(12)}$ (Calc.) = 1.67 cal mol^{-1} K^{-1}.

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REFERENCES

[1] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, ' Conformational Analysis,' Interscience, New York, 1965.

[2] J. A. Hirsch, *Topics Stereochem.*, 1967, **1**, 199.

[3] E. L. Eliel and T. J. Brett, *J. Amer. Chem. Soc.*, 1965, **87**, 5039 and references therein.

[4] F. R. Jensen and C. H. Bushweller, *Adv. Alicyclic Chem.*, 1971, **3**, 140.

[5] F. A. L. Anet, C. N. Bradley, and G. W. Buchanan, *J. Amer. Chem. Soc.*, 1971, **93**, 258.

[6] O. A. Subbotin and N. M. Sergeyev, *J.C.S. Chem. Comm.*, 1976, 141.

[7] N. L. Allinger, M. A. Miller, F. A. Van Catledge, and J. A. Hirsch, *J. Amer. Chem. Soc.*, 1967, **89**, 4345.

[8] N. L. Allinger, J. A. Hirsch, M. A. Miller, I. J. Tyminski, and F. A. Van Catledge, *J. Amer. Chem. Soc.*, 1968, **90**, 1199.

[9] J. E. Eilers and A. Liberles, *J. Amer. Chem. Soc.*, 1975, **97**, 4183.

[10] S. Fitzwater and L. S. Bartell, *J. Amer. Chem. Soc.*, 1976, **98**, 5107.

[11] D. Cremer, J. S. Brinkley, and J. A. Pople, *J. Amer. Chem. Soc.*, 1976, **98**, 6836.

[12] E. Osawa, J. B. Collins, and P. v. R. Schleyer, *Tetrahedron*, 1977, **33**, 2667.

[13] H. Booth and J. R. Everett, *J.C.S. Chem. Comm.*, 1976, 279.

[14] J. W. Cooper in *Topics Carbon*-13 *N.M.R.*, 1976, **2**, 391.

[15] H. Booth and M. L. Jozefowicz, *J.C.S. Perkin II*, 1976, 895.

[16] H. Booth, J. R. Everett, and R. A. Fleming, *Org. Magnetic Resonance*, 1979, **12**, 63.

[17] N. M. Sergeyev, *Org. Magnetic Resonance*, 1978, **11**, 127.

[18] B. J. Armitage, G. W. Kenner, and M. J. T. Robinson, *Tetrahedron*, 1964, **20**, 747.