## NOTE

The Difference in Free Energy between Equatorial and Axial Isopropyl Groups

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The differences in free energy between equatorial and axial lower alkyl groups are the fundamental quantities on which conformational analysis is based; the values for the methyl and ethyl groups are known to be near -1.8kcal./mol. $^{1-4,7,8,10}$  while those for the isopropyl group are in the wide range of  $-2.5 \sim$  $-3.55^{3,4}$  kcal./mol. or are at least often taken<sup>5</sup> to be considerably greater those of methyl and ethyl. Further, an isopropyl group was often assumed to be almost as big as a t-butyl group<sup>6)</sup>.

Recently, however, Lewin and Winstein<sup>7)</sup> have given a value of ca. -2.3 kcal./mol. for the isopropyl group from the chemical shifts in the NMR of the 1-proton in isomeric 4isopropylcyclohexanols. Allinger and his coworkers<sup>8)</sup> reported a lower value of -2.1 kcal./ mol. from the equilibrium points for the isomerization of *cis*- and *trans*-diisopropylcyclohexanes and of isomeric 4-isopropylcyclohexanecarboxylic acid ethyl esters.

In the present work, the difference in free energy between equatorial and axial isopropyl groups has been determined in the following way. New cis- and trans-4-isopropylcyclohexylcarbinyl p-tosylates have been prepared and acetolyzed, and from the observed rates (k), the difference in free energy  $(\Delta F)$  between the equatorial and axial isomers\* have first been calculated by using the equations<sup>3,9,10</sup>: K =

 $(k_{\rm a}-k)/(k-k_{\rm e})$  and  $\Delta F = -RT \ln K$ , where K is the equilibrium constant between equatorial and axial isomers and  $k_a$  and  $k_e$  are, respectively, the rates for cis- and trans-4-t-butylcyclohexylcarbinyl *p*-tosylates in the same reaction. The calculated values are shown in Table I, along with the relative rates and the mole fractions  $(N_{\rm B})$  of the axial isomers.

Therefore, the difference in free energy  $(\Delta F_{i-Pr})$  between equatorial and axial isopropyl groups may be calculated as follows: The  $\Delta F$  value of +0.32 or 0.42 kcal./mol. for the cis-4-isopropyl compound may be regarded as the sum of an energy needed for moving the tosyloxymethyl group from an equatorial to an axial position (i. e.,  $\Delta F_{\text{Tos}} = -1.7$  at 100 and -1.8kcal./mol. at  $110^{\circ}C^{10}$ ) and an energy needed for moving the isopropyl group from an axial to an equatorial position (i.e.,  $-\Delta F_{i-Pr}$ ), as illustrated by the relationship:  $\Delta F =$  $-\Delta F_{i-Pr} + \Delta F_{Tos}$ ; thus, the  $\Delta F_{i-Pr}$  is -2.02 or -2.22 kcal./mol. The averaged value is -2.1The good agreement of this value kcal./mol. with those obtained by Lewin and Winstein and by Allinger and his co-workers supports the conclusion<sup>8)</sup> that the isopropyl group is essentially the same size as a methyl or ethyl group and is in quite a separate class from the t-butyl group.

On the basis of the above findings, the energy level of the diaxial conformation of the trans-4-isopropyl compound should be 2.1+1.75 kcal./mol. higher than that of its diequatorial conformation. This corresponds to a K value of about 150 and leads to the prediction, borne out experimentally, that the acetolysis rate for trans-4-isopropylcyclohexylcarbinyl *p*-tosylate is identical with  $k_e$  within the range of experimental error.

## Experimental

cis- and trans-4-Isopropylcyclohexylcarbinyl pwere prepared from the corresponding Tosylates known carbinols<sup>11</sup>) in the usual manner<sup>12</sup>), by

<sup>1)</sup> W. G. Dauben and K. S. Pitzer, in M. S. Newman's "Steric Effects in Organic Chemistry", John Wiley & Sons, New York (1956), p. 1.

<sup>2)</sup> N. L. Allinger and S. Hu, J. Am. Chem. Soc., 84, 370 (1962).

S. Winstein and N. J. Holness, ibid., 77, 5562 (1955).
 D. S. Noyce and L. J. Dolby, J. Org. Chem., 26, 3619 (1961).

<sup>5)</sup> A. R. H. Cole and P. R. Jefferies, J. Chem. Soc., 1956, 4391; W. Takagi and T. Mitsui, J. Org. Chem., 25, 1476 (1960).

<sup>6)</sup> For example, W. Klyne, *Experientia*, 12, 119 (1956);
B. C. Lawes, J. Am. Chem. Soc., 84, 239 (1962).
7) A. H. Lewin and S. Winstein, ibid., 84, 2464 (1962).
8) N. L. Allinger, L. A. Freiberg and Shih-En Hu,

ibid., 84, 2836 (1962).

<sup>\*</sup> These mean those conformational isomers having, respectively, a tosyloxymethyl group in an equatorial or axial position.

<sup>9)</sup> E. L. Eliel and C. A. Lukach, J. Am. Chem. Soc., 79, 5986 (1957).

<sup>10)</sup> N. Mori, This Bulletin, 35, 1755 (1962).

<sup>11)</sup> R. G. Cooke and A. K. Macbeth, J. Chem. Soc., 1936, 1246.

<sup>12)</sup> For example, N. Mori, This Bulletin, 34, 1567 (1961).

4-Substituent	at 99.8 $\pm$ 0.1°C				at 110.0±0.1°C			
	Relative rate	K	$\Delta F$ kcal./mol.	$N_{\rm a} \times 100$	Relative rate	K	$\Delta F$ kcal./mol.	$N_{a} \times 100$
cis-t-Bu	4.23	0.00ª		100	4.36	0.00ª		100
cis-i-Pr	2.96	0.65	+0.32	60	3.12	0.58	+0.42	63
trans-i-Pr	1.00	œ		0.0	1.00	~	-	0.0
trans-t-Bu	1.00	cic <sup>8</sup>		0.0	1.00	∞ <sup>8</sup>		0.0

TABLE	I
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a Assumed

Table II. Acetolysis of *cis*-4-isopropylcyclohexylcarbinyl *p*-tosylate at  $110^{\circ}$ C

Time, sec.	Tosylate, mol./l. 9.68×10 <sup>-3</sup>	$k, sec^{-1}$
7200	8.33	$(2.08) \times 10^{-1}$
12000	7.29	2.35
15600	6.68	2.38
19200	6.08	2.42
22800	5.58	2.41
26400	5.12	2.41
30120	4.56	2.41
	Mean	2.40

treating them with one equivalent proportion of ptoluenesulfonyl chloride in pyridine at  $0\sim5^{\circ}C$  and recrystallizing from aqueous methanol. The cisisomer was obtained as plates melting at  $44.3\sim$  $44.6^{\circ}C$ , and the trans-isomer, as prisms melting at  $54\sim54.5^{\circ}C$ .

Calcd. for  $C_{17}H_{26}O_3S: C, 65.77$ ; H, 8.44. Found : C, 65.69; H. 8.48 for the *cis*-isomer and C, 65.70; H, 8.32% for the trans-isomer.

All reactions and rate measurements were carried out using the same acetic acid without base and TABLE III. SUMMARY OF ACETOLYSIS RATES

Tosylate 10 <sup>3</sup> mol./l.	Temp., °C $(\pm 0.1^{\circ}C)$	$10^{5}k$ , sec <sup>-1</sup>
9.68	99.8	0.860
9.68	110.0	2.40
9.61	99.8	0.285
9.61	110.0	0.767
15.5	99.8	1.23
15.5	110.0	3.35
15.5	99.8	0.290
15.5	110.0	0.768
	Tosylate 10 <sup>8</sup> mol./l. 9.68 9.61 9.61 15.5 15.5 15.5 15.5	Tosylate $10^8$ mol./l.Temp., °C $(\pm 0.1^\circ C)$ 9.6899.89.68110.09.6199.89.61110.015.599.815.5110.015.599.815.5110.015.5110.0

following the same procedure as has been previously reported<sup>18)</sup> to a 30% completion at 99.8°C and to a 40% completion at 110°C. The calculated first order rate constants were steady to 3%. Table II lists the data for a typical run with *cis*-4-isopropylcyclohexylcarbinyl *p*-tosylate. The rate constants are summarized in Table III.

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13) N. Mori, ibid., 33, 1144 (1960).