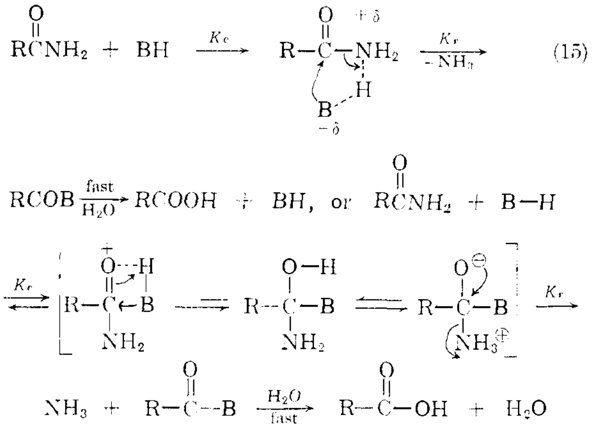
$$BH \overset{K_a}{\rightleftarrows} B^{\ominus} + H^{\oplus}$$

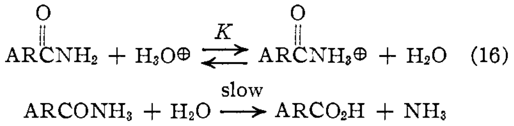
$$H^{\oplus} + RCONH_2 \overset{K_a'}{\rightleftarrows} RCONH_3^{\oplus} \qquad (14)$$

$$B^{\ominus} + RCONH_3^{\oplus} \xrightarrow{k_r} RCOB + BH$$

$$RCOB \xrightarrow[H_2O]{fast} RCOOH + BH$$


(15)

$k_{HPO_4^{\ominus}}$ and $k_{H_3BO_3} = k_{H_2BO_3^{\ominus}}$ for amide hydrolysis (when BH = $H_2PO_4^{\ominus}$ or $HPO_4^{\ominus}$, etc.) can only be explained through mechanism 15. In the preprotonation mechanism of Wyness[16] (14) the concentration of protonated amide is dependent only on the *p*H and K_a' while the value of k_r will depend on K_a (from the Brönsted relationship). One would then predict a large difference in the rates for catalysis by H_2PO_4 (pK_a 6.5) and HPO_4^- (pK_a 11–12). If, on the other hand, the process of proton transfer and nucleophilic attack are concerted (15) then one might expect the observed rates to be insensitive to the pK_a of BH. Thus, if BH were a strong acid the protonation of the amide would be favored but nucleophilic attack of B at the carbonyl group would not. If BH were a weak acid protonation would not be favored but nucleophilic attack by B would. It is reasonable to believe that these two factors would have an equal influence on the over-all rate so that it would be insensitive to the pK_a' of BH but sensitive only to the nature of B (borate or phosphate). This leads to the experimentally verifiable prediction that for a series of acids, as carboxylic acids, the slope of the Brönsted plot, α, (*i.e.*, $\log k_{rate} = \alpha pK_a' + C$) would be almost zero for the catalysis of amide hydrolysis. The finding that the observed over-all rate of amide hydrolysis by mechanism 18 is insensitive to pK_a' of BH relates to the observations of Leisten[27] and Edwards[28] on the electronic effects of substituents on acid-catalyzed benzamide hydrolysis (16). In 16 the ρ-for the preprotonation step is


(16)

$$ARCONH_2 + H_3O^{\oplus} \overset{K}{\rightleftarrows} ARCONH_3^{\oplus} + H_2O \qquad (16)$$

$$ARCONH_3 + H_2O \xrightarrow{slow} ARCO_2H + NH_3$$

+1.40 while that for the rate-determining step is −1.30.[24] The over-all ρ-value is then but 0.1 and the over-all reaction is insensitive to electronic effects. The similarity in 15 and 16 then lies in the inverse importance in basicity and electronic effects in the protonation and nucleophilic attack.

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Conformational Analysis. XXI. The Ethyl Group[1,2]

BY NORMAN L. ALLINGER AND SHIH-EN HU

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The thermodynamic constants of an axial ethyl group, relative to an equatorial, were calculated as follows: $\Delta H°_{298} = +1.71$ kcal./mole, $\Delta S°_{298} = -0.51$ e.u., $\Delta F°_{298} = +1.86$ kcal./mole. Equilibration of the *cis* and *trans* isomers of 1,3-diethylcyclohexane, and of 1,4-diethylcyclohexane, by heating the compounds with a palladium catalyst at elevated temperatures gave $\Delta H°_{554}$ and $\Delta S°_{554}$ for these isomerizations. These quantities were also calculated for the ethyl group from the data and statistical considerations. Theory and experiment agree that the free energy of an axial ethyl group is only slightly greater than the corresponding value for an axial methyl group.

Perhaps the most important numerical quantity in the conformational analysis of cyclohexane systems is the value for the energy (actually enthalpy) of a methyl group axial (relative to equatorial) on a cyclohexane ring, 1.6–1.8 kcal./mole. This quantity can be evaluated in many ways; perhaps the earliest and most fundamental evaluation was that made by Beckett, Pitzer and Spitzer,[3] in their fundamental study of the dimethylcyclohexanes.

The corresponding value for the ethyl group has been much less thoroughly studied. The only numerical value for the conformational free energy of this group (2.1 kcal./mole) appears to be that reported by Winstein and Holness.[4] The quantity was determined in a round-about way and was regarded by those authors as only approximate.

In the present work the determination of the enthalpy of the change of an ethyl group from the axial to the equatorial position was determined independently in two separate compounds. The general experimental method is the same as was used earlier to determine $\Delta H°$ and $\Delta S°$ for the isomeriza-

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[1] Paper XX, N. L. Allinger and M. A. DaRooge, *J. Am. Chem. Soc.*, **83**, 4256 (1961).

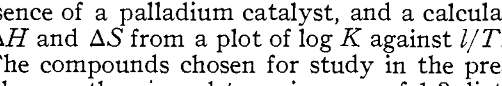
[2] In the discussion part of this paper all temperatures are given in °K. In the experimental part the temperatures are in °C. except where otherwise specified.

[3] C. W. Beckett, K. S. Pitzer and R. Spitzer, *J. Am. Chem. Soc.*, **69**, 977 2488 (1947).

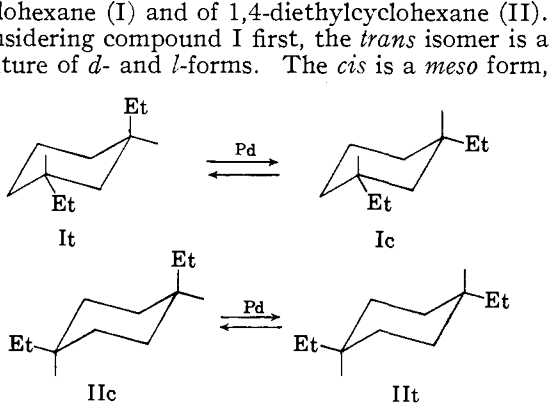
[4] S. Winstein and N. J. Holness, *ibid.*, **77**, 5562 (1955).

tion of a *cis* isomer to a *trans* with the decalins,[5] hydrindanes[6] and others.[7] The method involves the establishment of equilibrium between the *cis* and *trans* isomers at various elevated temperatures in the presence of a palladium catalyst, and a calculation of ΔH and ΔS from a plot of log K against l/T.

The compounds chosen for study in the present work were the *cis* and *trans* isomers of 1,3-diethylcyclohexane (I) and of 1,4-diethylcyclohexane (II). Considering compound I first, the *trans* isomer is a mixture of *d*- and *l*-forms. The *cis* is a *meso* form, and actually is an equilibrium mixture of the diequatorial and diaxial forms. The conformational energy of the latter is not known, but it may be presumed to be at least as large as that of the corresponding dimethyl structure, which is known to be 5.5 kcal./mole.[7] The contribution of the diaxial form of Ic to the physical properties of the system can therefore be neglected in the present approximation. Since boat forms are expected to have energies of over 5 kcal./mole in the systems under discussion, they are also neglected. Because of the high experimental temperatures used in the present study, the neglect of these higher energy structures may introduce small errors.



It Ic

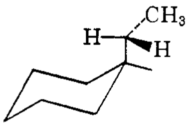


IIc IIt

Theoretical values for the $\Delta H°$ and $\Delta S°$ of the isomerizations were arrived at in the following way. Ethylcyclohexane (III) is assumed to exist exclusively in the chair form. The ethyl group may be equatorial, in which case there are three possible conformations, a *meso* form with $H° = 1.8$ kcal./mole,[8] and a *dl*-pair, each with $H° = 0.9$ kcal./mole. The axial ethyl is a *dl*-pair (IIIa); the theoretically possible *meso* form with the methyl pointing into the ring is of very high energy, and is neglected.

meso *dl*

IIIe



IIIa, *dl*

The various combinations of those possibilities were considered and the total number of forms possible (including *d*- and *l*-forms) was found for both I and II, together with the enthalpy of each. These data are summarized in Table I, and it is seen that *trans*-I contains 12 conformations with energies of 3.6–4.5 kcal./mole, while the *cis* isomer is a mixture of 9 conformations each having an enthalpy from 1.8 to 3.6 kcal./mole. Qualitatively it is clear that the reaction *trans* → *cis*-1,3-diethylcyclohexane will have a negative entropy and a negative enthalpy.

TABLE I

CONFORMATIONS OF THE DIETHYLCYCLOHEXANES

1,3-Diethylcyclohexane(I)

	cis			*trans*	
Energy, kcal./mole	1.8	2.7	3.6	3.6	4.5
No. of forms	4	4	1	8	4

1,4-Diethylcyclohexane (II)

	cis		*trans*					
Energy, kcal./mole	3.6	4.5	1.8	1.8	2.7	3.6	5.4	5.4
No. of forms	4	2	1	2	2	1	1	2
Symmetry no.	1	1	1	2	1	2	1	2

Quantitatively, the predicted enthalpies and entropies of isomerization of the 1,3-diethylcyclohexanes were calculated by first calculating for each isomer (at the middle of the temperature range studied experimentally) what the mole fraction of each component would be. Since each conformation was considered separately (a *dl*-pair counting as two conformations), with the usual assumptions concerning the entropies of the internal motions,[8] the equation $\Delta H° = -RT \ln K$ was used. From the mole fractions, since for the 1,3-isomer the symmetry number is one for each conformation, the entropy of isomerization is just the difference in the entropies of mixing of the separate stereoisomers; $S_m° = -R\Sigma N_i \ln N_i$.

These calculations (for 554°K.) gave for the *trans* isomer of 1,3-diethylcyclohexane, $H° = 1.96$ kcal./mole, $S_m^0 = 4.82$ e.u.; and for the *cis* isomer, $H° = 0.32$ kcal./mole, $S_m° = 4.13$ e.u. Hence for the isomerization of *trans*-1,3-diethylcyclohexane $\rightleftarrows$ *cis*-1,3-diethylcyclohexane, $\Delta H°_{554} = -1.64$ kcal./mole, $\Delta S°_{554} = -0.69$ e.u.

The same kind of calculation was carried out for the 1,4-diethylcyclohexanes. The necessary data for obtaining the mole fractions is included in Table I. In this case certain of the conformations have symmetry numbers of 2, and this must be taken into account in obtaining the mole fractions. The value of $H°$ for each conformation was obtained as before, and if $\sigma = 1$, $H° = F°$. For the conformations with $\sigma = 2$, the symmetry contribution to the entropy was $-R \ln 2$, and $F° = H°-TR \ln 2$. The mole fractions were then found using the equation $-\Delta F° = RT \ln K$. From the mole fractions, $H°$ for each stereoisomer was found as described for the 1,3-isomer. $S°$ for each stereoisomer was taken as $R[-\Sigma N_i \ln \sigma + \Sigma N_i \ln N_i]$ where the summations are over all conformations of the stereoisomer concerned. The values calculated for the *cis* isomer were $H° =$

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[5] N. L. Allinger and J. L. Coke, *J. Am. Chem. Soc.*, **81**, 4080 (1959).

[6] N. L. Allinger and J. L. Coke, *ibid.*, **82**, 2553 (1960).

[7] N. L. Allinger and M. A. Miller, *ibid.*, **83**, 2145 (1961), and references given therein.

[8] Throughout this paper, $H°$ is taken relative to a hypothetical form with zero *gauche* interactions.

1.96 kcal./mole, and $S^\circ = 3.45$ e.u. For the *trans* isomer the values were $H^\circ = 0.41$ kcal./mole, $S^\circ = 2.95$ e.u. For the isomerization *cis*-1,4-diethylcyclohexane ⇄ *trans*-1,4-diethylcyclohexane the calculated quantities are $\Delta H^\circ_{554} = -1.56$ kcal./mole, $\Delta S^\circ_{554} = -0.49$ e.u.

The accuracy to which the thermodynamic quantities could be measured in the present work was not as high as desired, due mainly to the fact that the gas phase chromatography column used did not separate the isomers quite completely. There are a number of approximations involved in obtaining the calculated quantities, and these limit the accuracy of the calculations. The agreement between the calculated and found enthalpies and entropies of isomerization is satisfactory, however, and is summarized in Table II.

TABLE II

	trans- ⇄ *cis*-1,3-diethylcyclohexane		*cis*- ⇄ *trans*-1,4-diethylcyclohexane	
	ΔH°_{554}, kcal./mole	ΔS°_{554}, e.u.	ΔH°_{554}	ΔS°_{554}
Calcd.	−1.64	−0.69	−1.56	−0.49
Found	−1.8 ± 0.3	−1.0 ± 0.5	−1.8 ± 0.3	−1.0 ± 0.5

Perhaps a fairer comparison between theory and experiment is to examine the calculated and found values for ΔF° at similar temperatures. This comparison is made in Table III, and the agreement between the calculated and found quantities is surprisingly good.

TABLE III

% *cis* ISOMER AT EQUILIBRIUM

	1,3-Isomer, % (°K).	1,4-Isomer, % (°K.)
Calcd.	75.7 (554)	23.8 (554)
Found	76.6 (548)	22.7 (532)
	75.5 (565)	24.5 (561)

Of wider interest are conformational properties of the ethyl group which can be used in general in organic structures. In an ordinary ethylcyclohexane (with $\sigma = 1$), for the isomerization axial-ethyl ⇄ equatorial-ethyl, the calculated quantities are $\Delta H^\circ_{298} = -1.71$ kcal./mole, $\Delta S^\circ_{298} = +0.51$ e.u. and $\Delta F^\circ_{298} = -1.86$ kcal./mole. Thus at ordinary temperatures the free energy of the axial ethyl is only slightly higher (relative to the equatorial) than the corresponding difference for a methyl group.

Experimental

1,3-Diethylcyclohexane.—1,3-Diethylbenzene was prepared by treatment of benzene with ethyl acetate and aluminum chloride according to Norris and Arthur,[9] and the crude material was purified by sulfonation, crystallization of the barium sulfonate[10] and regeneration of the hydrocarbon, b.p. 181–182° (760 mm.), n^{20}_D 1.4956 (literature,[9] b.p. 181–182° (760 mm.), n^{20}_D 1.4955). Eight grams of pure *m*-diethylbenzene was hydrogenated in 100 ml. of acetic acid with 0.5 g. of platinum oxide. After 4 hours the hydrogenation was complete, the solution was filtered, diluted with water, and the hydrocarbon layer was separated. The hydrocarbon was washed with dilute sodium carbonate solution, then water, and was dried over magnesium sulfate. Distillation gave 7.25 g. of 1,3-diethylcyclohexane, b.p. 172.5°, n^{25}_D 1.4388 (reported[10] b.p. 173.5–174.5°, n^{20}_D 1.4409). Gas phase chromatography using a 10-ft. column of γ-nitropimelonitrile-on-firebrick at 76° showed the synthetic material gave two peaks in the ratio of 78:22 with retention times of 7 and 8 minutes, respectively. These peaks were assigned to the *cis* and *trans* isomers, respectively.[11]

TABLE IV

EQUILIBRATION DATA FOR 1,3-DIETHYLCYCLOHEXANE

Temp., °K.	Equil. time, days	% *cis*
531	14	77.7
548	5	76.6
565	14	75.5
577	8	74.4

EQUILIBRATION DATA FOR 1,4-DIETHYLCYCLOHEXANE

Temp., °K.	Equil. time, hr.	% *trans*
532	72	77.3
561	24	75.5
575	22	75.1
593	8	74.1

1,4-Diethylcyclohexane.—*p*-Ethylacetophenone was prepared by acetylation of ethylbenzene; b.p. 238–239° (760 mm.), n^{25}_D 1.5283 (reported[12] b.p. 90–91° (5 mm.), n^{25}_D 1.5275. Clemmensen reduction[13] yielded diethylbenzene, b.p. 181–182°, n^{25}_D 1.5924 (reported[14] b.p. 182–183° (760 mm.), n^{25}_D 1.4924). The aromatic ring was reduced as described for the 1,3-isomer, and the resulting 1,4-diethylcyclohexane had b.p. 175–176° (746 mm.), n^{25}_D 1.4396 (reported[15] b.p. 174.6–176.4° (746 mm.), n^{20}_D 1.4415). Gas phase chromatography as described for the 1,3-isomer, but with a column temperature of 81°, showed two peaks with areas in the ratio of 20:80 and retention times of 7 and 8 minutes. These peaks were assigned to the *trans* and *cis* isomers, respectively.

Equilibration Studies.—Samples of about 100 mg. of the diethylcyclohexane and 20 mg. of 10% palladium-on-carbon were sealed in small tubes which were heated in a furnace at the desired temperature for a suitable length of time (determined by preliminary experiments) following the general procedure developed earlier.[5,6] Gas phase analysis was carried out at least 3 times on each sample, and the % *cis* varied by ± 0.1% or less for replicate analyses. The data for the equilibration of 1,3-diethylcyclohexane and for 1,4-diethylcyclohexane are summarized in Table IV. In each case a plot of ln K against $1/T$ was made by the method of least squares. The slope and intercept of the line yielded the enthalpy and entropy of isomerization, respectively.

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