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Conformational Analysis. XVII.¹ The 1,3-Diaxial Methyl-Methyl Interaction²

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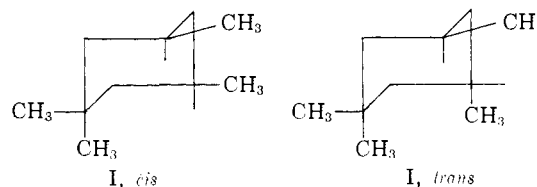
The equilibration of *cis* \rightleftharpoons *trans*-1,1,3,5-tetramethylcyclohexane has been studied over the range 520–631°K. For the reaction $\Delta H_{575} = +3.70$ kcal./mole, $\Delta S_{575} = +1.65$ e.u. (liquid phase). The energy of a 1,3-diaxial dimethyl interaction was found to be 3.7 kcal./mole.

The energies of most of the common groups in the axial position on a simple cyclohexane ring are now known^{3a} and form a basis for quantitative conformational studies. Two quantitative values for interactions between two or more substituents diaxial on the same side of a cyclohexane ring have been previously reported,^{3b,c} and other available examples show qualitatively that such interactions are of rather high energy. The 1,3-diaxial interaction of two bromine atoms in *cis*-2,6-dibromocyclohexanone is, for example, sufficient to cause the bromines to take up the diequatorial conformation,⁴ and the energy of the interaction of two methyl groups axial on the same side of a cyclohexanone ring is so great the ring goes over to a boat form.⁵

The energy of a 1,3-diaxial dimethyl interaction is one of the fundamental interactions of this class which will be useful as a basis for quantitative studies, and it has been commented on occasionally in the literature. It has been stated⁶ that "such an arrangement has been shown on 1,3-dimethylcyclohexane to introduce an energy factor of at least 5.4 kcal./mole." The value 5.4 kcal./mole (6a) was "arbitrarily assigned" to the 1,3-dimethyl-(diaxial)-cyclohexane,⁷ and appears to have no experimental justification. Equally interesting is the 1,3-diaxial interaction found in *cis-syn-cis*-perhydrophenanthrene, for which energies of 4.8 and 8–9 kcal./mole have been estimated by different authors.^{6,8}

In the present paper a direct experimental measurement of the 1,3-diaxial dimethyl energy is described. The actual compound studied was 1,1,3,5-tetramethylcyclohexane (I). The molecule exists in *cis* and *trans* forms which have previously been prepared.⁹ The structures were assigned on the basis of physical properties, and do not seem open to question,¹⁰ and the assignment is confirmed by the present work.

The *cis* isomer in principle exists in two conformations, but one of these has 3 methyl groups axial on the same side of the ring and it is clear the amount of this conformation present will be negligible, even at the high temperatures used in this study. This compound is a *meso* form.



The *trans* isomer of I, on the other hand, exists as a single conformation but it is a *dl*-mixture.

If the enthalpy change for the reaction *cis*-I \rightleftharpoons *trans*-I is established, it is a direct measure of the energy required to move a methyl group from the equatorial to the axial position when another 3-methyl is also present in the axial position, provided that it can be shown that the *trans* isomer has not gone over to a boat form.

A mixture of the stereoisomeric compounds was obtained by the literature procedures and the isomers were separated on a preparative scale by vapor phase chromatography on a silicone column. Equilibrium was approached from both sides at various temperatures over the range 247–358° by heating small samples in sealed tubes with a palladium catalyst.¹¹ A plot of $\ln K$ vs. $1/T$ was made, and was linear. From the slope and intercept of the line which was fit to the data by the method of least squares, the thermodynamic constants for the reaction were found.¹⁰ For the reactions *cis*-(I) \rightleftharpoons *trans*-(I), $\Delta H_{575} = +3.70 \pm 0.2$ kcal./mole, $\Delta S_{575} = +1.65 \pm 0.3$ e.u. (liquid phase).

Since the value for ΔH (3.7 kcal.) corresponds to moving an equatorial methyl to the axial position, it is the energy of interest. Since the energy of the boat form was found to be 5.9 kcal. in a rather analogous system,¹² the amount of boat form present in this case should not be large enough to lead to serious error unless the entropy of the boat form should be rather large. Since the entropy of isomerization is only slightly larger than that anticipated for a chair-chair equilibrium, (1.4 e.u. from the entropy of mixing of the *dl*-isomer), the boat form appears to contribute little, and the conclusion is drawn that the observed ΔH is in fact a good measure of the 1,3-diaxial dimethyl interaction.

(1) Paper XVI, N. L. Allinger and H. M. Blatter, *J. Am. Chem. Soc.*, **83**, 994 (1961).

(2) Sponsored by the Office of Ordnance Research, U. S. Army.

(3) (a) E. L. Eliel, *J. Chem. Ed.*, **37**, 126 (1960); (b) S. J. Angyal and D. J. McHugh, *Chem. and Industry*, 1147 (1956); (c) E. L. Eliel and C. A. Lukach, *J. Am. Chem. Soc.*, **79**, 5986 (1957).

(4) E. J. Corey, *ibid.*, **75**, 3297 (1953).

(5) C. Djerassi, N. Finch, R. C. Cookson and C. W. Bird, *ibid.*, **82**, 5488 (1960); also see D. H. R. Barton, D. A. Lewis and J. F. McGhie, *J. Chem. Soc.*, 2907 (1957).

(6) W. G. Dauben and K. S. Pitzer in M. S. Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 34.

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

(8) W. S. Johnson, *ibid.*, **75**, 1498 (1953).

(9) G. Chiurdoglu and A. Maquestiau, *Bull. soc. chim. Belg.*, **63**, 357 (1954).

(10) N. L. Allinger, *J. Am. Chem. Soc.*, **79**, 3443 (1957).

(11) N. L. Allinger and J. L. Coke, *ibid.*, **81**, 4080 (1959); **82**, 2553 (1960).

(12) N. L. Allinger and L. A. Freiberg, *ibid.*, **82**, 2393 (1960).

It is noted that a value of 3.7 kcal./mole for the methyl-methyl interaction gives a calculated energy difference of 5.5 kcal./mole (one methyl-methyl interaction plus two methyl-hydrogen interactions) between the diequatorial and diaxial forms of *cis*-1,3-dimethylcyclohexane, which is in perfect agreement with the value predicted by Beckett, Pitzer and Spitzer.⁷

When the C-H bonds of each methyl group are staggered relative to the bonds of the carbon atom to which the methyl is bound, keeping normal bond angles and bond lengths, the separation¹³ of one pair of hydrogens is 0.8 Å. The van der Waals repulsion at this distance is enormous (about 200 kcal.¹⁴) and the molecule does not remain in this exact conformational arrangement. If each methyl is rotated through an angle of 25°, the two hydrogens can be moved to a separation of 1.6 Å., but another pair has also come to this same distance, and one hydrogen on each methyl is now 1.75 Å. from the nearby axial hydrogen. The total of these repulsions is 8 kcal. However, the partial eclipsing costs 1.0 kcal. for each methyl, so the total energy of the methyl-methyl interaction is 10 kcal./mole. With this molecule bond angle deformation seems to be rather important. Widening one bond angle in this form (that of the ring carbon between those to which the methyls are attached) to 120° causes the van der Waals repulsion between the two methyls to entirely disappear, and the closest hydrogen on a methyl is 1.8 Å. from the axial ring hydrogen. This repulsion amounts to 1.6 kcal., and the 2.1 kcal. for partial eclipsing¹⁵ plus 2 kcal. for angle deformation¹⁵ gives a total energy of 5.7 kcal. It does not seem unreasonable that the total energy can be further reduced to the observed value by successive adjustment of these and similar quantities.

The value found for the energy of a 1,3-dimethyl interaction cannot be applied to systems

(13) Measured on Dreiding models.

(14) Estimated by the method outlined by N. L. Allinger, J. Allinger, L. A. Freiberg, R. Czaja and N. A. LeBel, *J. Am. Chem. Soc.*, **82**, 5876 (1960).

(15) N. L. Allinger, *ibid.*, **81**, 5727 (1959).

such as the perhydrophenanthrenes. Certainly, as pointed out by Dauben and Pitzer,⁶ in such a rigid system the deformations which so greatly lowered the energy in the above case cannot readily take place.

Experimental

cis- and *trans*-1,1,3,5-Tetramethylcyclohexane (I).—The hydrocarbons used in the present work were prepared starting from isophorone, which was reduced with hydrogen and a palladium-on-carbon catalyst to 3,3,5-trimethylcyclohexanone. Addition of methyl Grignard gave 1,3,3,5-tetramethylcyclohexanol, which was dehydrated to the olefin with formic acid. Hydrogenation with platinum in acetic acid yielded a mixture of *cis*- and *trans*-1,3,3,5-tetramethylcyclohexane in a 3:2 ratio. The pure isomers were obtained by preparative gas phase chromatography on a column of silicone on firebrick. After redistillation the isomers had the constants: *cis*, b.p. 144.5–145°, n_D^{25} 1.4288, $d_{25.7}$ 0.7811; *trans*, b.p. 148.5–149°, n_D^{25} 1.4342, $d_{25.7}$ 0.7913. The reported⁹ values are: *cis*, b.p. 152.4–152.5°, n_D^{25} 1.4319, d_{25} 0.7813; *trans*, b.p. 156.4–156.5°, n_D^{25} 1.4370, d_{25} 0.7929.

Equilibration of *cis*- and *trans*-1,1,3,5-Tetramethylcyclohexane.—For each run about 100 mg. of a pure isomer of I was sealed in a small tube with about 25 mg. of 10% palladium-on-carbon. Equilibrium was established by heating the tubes at various temperatures for the times specified in Table I. The analysis of the equilibrated mixtures was carried out with a column of γ -nitro- γ -methylpimelonitrile on firebrick at 70°. The area under the curves was measured with a disk chart integrator.

Temp., °C.	Time	K
247	5 days	16.02
284	12 hr.	11.87
297	20 hr.	11.40
324	22 hr.	10.16
358	3.5 hr.	8.33

Each value of *K* in Table I was an average of at least three analyses on the equilibrated sample obtained from the *cis* isomer and three analyses on the equilibrated sample obtained from the *trans* isomer. The average deviation in *K* was about ± 0.25 .

The values for ΔH and ΔS of the reaction were calculated using the values found for *K*, and fitting a straight line to eq. 1 by the least squares method.

$$\ln K = - \left(\frac{1}{T} \right) \left(\frac{\Delta H}{R} \right) + \frac{\Delta S}{R} \quad (1)$$

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Electrophilic Attack of the Aromatic Ring in the Chromic Acid Oxidation of Alkylbenzenes¹

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Ring oxidation is competitive with side-chain oxidation in the chromic acid oxidation of alkylbenzenes under Kuhn-Roth conditions. In the case of *t*-butylbenzene, oxidation proceeds exclusively by way of the ring, the reaction being first-order in hydrocarbon and exhibiting a linear $\log k-H_0$ relationship. Study of a series of methylbenzenes shows that ring oxidation is enhanced by increased substitution, and that the rate is a function of the σ -complex basicity of the hydrocarbon. These results suggest that ring oxidation occurs by electrophilic aromatic substitution.

Introduction

The mechanism of chromic acid oxidation of simpler organic molecules containing functional groups has been the subject of extensive investiga-

tion. An example is the very careful study of the system chromic acid-isopropyl alcohol by Westheimer and co-workers.² More recently, studies of chromic acid oxidation have been directed toward

(1) Presented in part before the Division of Organic Chemistry, 135th Meeting of the American Chemical Society, Boston, Mass., April, 1959.

(2) G. T. E. Graham and F. H. Westheimer, *J. Am. Chem. Soc.*, **80**, 3030 (1958); A. Leo and F. H. Westheimer, *ibid.*, **74**, 4383 (1952); and earlier papers.