To show that the fact that part of the nitrile was in the form of the anion did not alter the apparent value of the equilibrium constant, an equilibration experiment was carried out as previously, except that the reaction was not quenched. Instead an aliquot was withdrawn with a hypodermic needle and inserted directly into the gas chromatograph. The same *cis–trans* ratio was obtained as previously.

Description of Vapor Phase Chromatography of Equilibrium Mixture.—The equilibrated mixtures of 4-*t*-butylcyclohexyl cyanide were analyzed using an 8-mm. × 6-ft. glass column packed with Tide at a column temperature of 139°, and a preheater temperature of 168° with a helium flow rate of 105 cc. per minute. The *cis* isomer under these conditions had a retention time of 26 min. and the *trans* isomer had a retention time of 32 min.

N.m.r. Spectra.—These were determined at 56.4 Mc. in dilute solution in carbon tetrachloride using tetramethylsilane as an internal standard.

Acknowledgment.—The authors are indebted to Dr. Norbert Muller and Mr. William Tosch of Purdue University for determining the n.m.r. spectra and for helpful discussion regarding same.

Conformational Analysis. XXXIV. The Phenyl Group[1,2]

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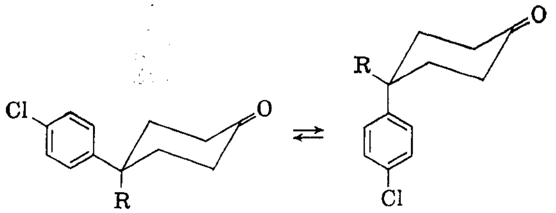
Dipole moment measurements on 4-(*p*-chlorophenyl)cyclohexanone and on 4-methyl-4-(*p*-chlorophenyl)cyclohexanone give the energy of the axial phenyl as 2.0 kcal./mole greater than that of the equatorial.

The important numerical quantities on which the conformational analysis of six-membered rings is based are the energies of various substituents in the axial position, relative to the equatorial.[4] Some time ago, we determined the conformational energy of the phenyl group.[5] The method chosen for the determination was somewhat indirect, but convenient, as the necessary compounds were available from other studies.



Ie. R = H
IIe. R = Me

IIa. R = H
IIa. R = Me

Compound I (4-(*p*-chlorophenyl)cyclohexanone) must exist as an equilibrium mixture of two conformations in which the aryl group is, respectively, equatorial (Ie) and axial (Ia). It was hoped that the energy of the boat form would be sufficiently great as to prevent it from contributing significantly to the properties of the compound. Under these circumstances measurement of the dipole moment of I should establish the position of the equilibrium. From the dipole moments of cyclohexanone (3.06 D.) and *p*-chlorotoluene[1] (1.95 D.) and the known geometry of the cyclohexanone ring,[7] the moments of Ie and Ia were calculated to be 1.89 and 3.14 D., respectively.

Compound I was prepared by a Dieckmann cyclization of the previously described[8] ethyl 4-(*p*-chlorophenyl)pimelate. The experimental moment (1.96 *D*) showed that Ie greatly predominated in the conformational equilibrium, the mole fraction of Ia being only 0.045. At 25° this corresponds to a free energy change of +1.8 kcal./mole when the aryl group goes from equatorial to axial. Unfortunately, because small deviations from ideal geometry are expected, the accuracy of this value left something to be desired. It is felt that from these data the free energy change can safely be said to be greater than 1.4 kcal./mole, but a more exact value cannot be assigned.

To obtain a more accurate measurement of the equilibrium constant by this method, it seemed that instead of balancing the phenyl against the hydrogen, it would be better to balance it against a larger group, and to determine the free energy difference between the phenyl and the other group. In this case the same error in percentage composition would yield a much more accurate value for the free energy. The methyl group was chosen since it has a reasonable size, is simple to treat theoretically, and accurate data concerning it are available.[9]

The synthesis of the desired compound (II)

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(1) Paper XXXIII, N. L. Allinger, S. P. Jindal, and M. A. DaRooge, *J. Org. Chem.*, **27**, 4290 (1962).

(2) This work was supported by a grant from the National Science Foundation.

(3) Predoctoral National Institutes of Health Fellow, Division of Medical Sciences, 1960–1962.

(4) A recent summary of the available data is given by E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., New York, N. Y., 1962, p. 236.

(5) An independent value obtained by another method has also been reported (ref. 6) as approximately 2.6 kcal./mole.

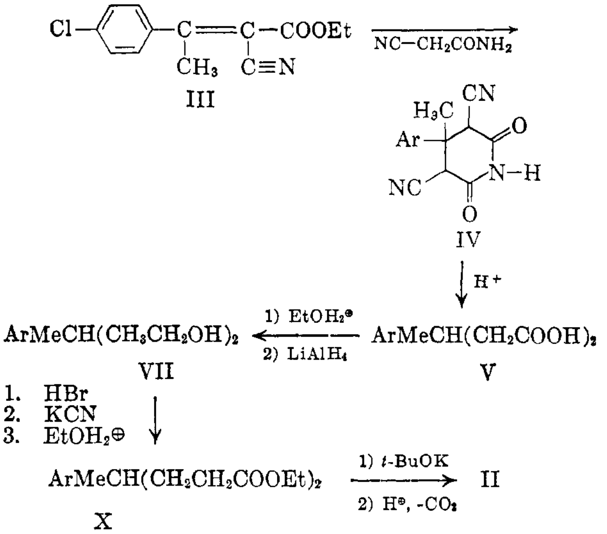
(6) E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, **82**, 1367 (1960).

(7)(a) J. Allinger and N. L. Allinger, *Tetrahedron*, **2**, 64 (1958); (b) E. J. Corey, *J. Am. Chem. Soc.*, **75**, 2301 (1953).

(8) N. L. Allinger and S. Greenberg, *ibid.*, **81**, 5733 (1959).

(9) C. W. Beckett, K. S. Pitzer, and R. Spitzer, *ibid.*, **69** 2488 (1947).

was carried out as outlined on the flow sheet. A Knoevenagel reaction[10] of p-chloroacetophenone with ethyl cyanoacetate gave III, which underwent Michael addition of cyanoacetamide to give the cyclic imide IV.[11] The latter was hydrolyzed[12] to β-methyl-β-(p-chlorophenyl)glutaric acid V, which was esterified (VI), and reduction of the ester gave the diol (VII) which was converted via the bromide (VIII) to the nitrile IX. Esterification of the latter gave diester X, which was cyclized to yield II.



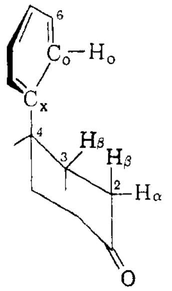
The dipole moment measurements were carried out on II, and an experimental moment of 2.56 D. was obtained. This moment corresponds to a mole fraction of IIa of 0.47, which gives a free energy for the axial phenyl which is 0.06 kcal./mole greater than that of the methyl. The best value for the latter is 1.95 kcal./mole[9], so the energy of the axial phenyl is taken as 2.0 kcal./mole.

TABLE I

VAN DER WAALS REPULSIONS IN AXIAL-4-PHENYLCYCLOHEXANONE[13]

Atom Pair	Distance	α	U/ϵ	ϵ	U
βH_2–C_0	2.40	0.827	3.6	67	0.24
C_x–C_2	2.82	.829	3.6	107	.39
C_0–βH_3	2.45	.845	2.4	67	.16
H_0–βH_3	1.93	.804	6.6	42	.28
					1.07 kcal./mole

A van der Waals calculation[13] was carried out to ascertain the reason for the observed energy difference. The equatorial phenyl shows one conformation (with the carbonyl and phenyl planes perpendicular) in which where are no serious van der Waals repulsions. The axial phenyl on the other hand cannot avoid such repulsions completely, the best arrangement seems to be when the plane of the phenyl is approximately perpendicular to the line connecting C-1 and C-4 which puts a plane of symmetry through C_1, C_4, and C_x. The repulsions on one side of the plane are listed in Table I. The total repulsion energy is twice this total. Any repulsion of less than 0.1 kcal./mole and all attractions (which include the βH_2–H_0, C_2–C_0, C_2–H_0, and C_x–βH_2 interactions) were neglected in the calculation, since they should nearly cancel when the axial and equatorial forms are compared. The calculated enthalpy of the axial phenyl (+2.1 kcal./mole) is in good agreement with the observed free energy (+ 2.0 kcal./mole). Since the phenyl has essentially no rotational freedom in either conformation, the entropies for the two conformations should be similar and the calculations are thus in good agreement with experiment.



Experimental

4-(p-Chlorophenyl)cyclohexanone (I).—Sodium metal, 2.3 g., was dissolved in 75 ml. of absolute ethanol. The solvent was removed and the residue was heated in an oil bath maintained at 150° under reduced pressure for 1 hr. A solution of 4 g. of ethyl 4-(4-p-chlorophenyl)pimelate in benzene was added and the mixture was heated under reflux and stirred for 36 hr. The benzene was distilled and ether was added. The reaction mixture was decomposed with an aqueous solution of acetic acid and the product was isolated by extraction with ether. The ether was distilled and the residue was hydrolyzed by refluxing in 33% (volume–volume) sulfuric acid. The product was collected by continuous steam distillation in a liquid–liquid extractor (for solvents heavier than water). The distillate was extracted with ether and the combined ether extracts were washed with water. The dried and filtered ether solution was concentrated and the residue was crystallized from ether–pentane to m.p. 67–68°. From 9 g. of ester was obtained 850 mg. of material, m.p. 69–70° (after sublimation).

Anal. Calcd. for $C_{12}H_{13}OCl$: C, 69.06; H, 6.28. Found: C, 69.27; H, 6.57.

The 2,4-dinitrophenylhydrazone had m.p. 168–170° (from ethanol).

Anal. Calcd. for $C_{18}H_{17}N_4O_4Cl$: C, 55.61; H, 4.41. Found: C, 55.37; H, 4.54.

Ethyl (1-p-chlorophenylethylidene)cyanoacetate (III).—According to the described procedure,[8] 154 g. of distilled p-chloroacetophenone, 113 g. of ethyl cyanoacetate, 15.4 g. of ammonium acetate, 48.0 g. of glacial acetic acid, and 200 ml. of dry benzene afforded 135 g., 54% yield, of pale yellow liquid, b.p. 150–160° (1 mm.), $n^{25}D$ 1.5575. A small sample re-distilled for analysis was colorless, $n^{25}D$ 1.5580.

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(10) S. M. McElvain and D. H. Clemens, *Org. Syn.*, **39**, 25 (1959).

(11) S. M. McElvain and D. H. Clemens, *ibid.*, **39**, 52 (1959).

(12) S. M. McElvain and D. H. Clemens, *ibid.*, **39**, 54 (1959).

(13) The method used was that of Hill (ref. 14). The details and numerical data are given in ref. 15.

(14) T. L. Hill, *J. Chem. Phys.*, **16**, 399 (1948).

(15) N. L. Allinger and L. A. Freiberg, *J. Am. Chem. Soc.*, **84**, 2201 (1962).

Anal. Calcd. for $C_{13}H_{12}O_2NCl$: C, 62.54; H, 4.84. Found: C, 62.73; H, 4.99.

β-(*p*-Chlorophenyl)-β-methyl-α,α′-dicyanoglutarimide (IV).—From 103 g. of III, 320 ml. of absolute ethanol, 9.2 g. of sodium metal, and 34.4 g. of α-cyanoacetamide, there was obtained 110 g. (92%) of the imide, as a pale yellow powder. A small amount of this material was crystallized twice from absolute ethanol and the analytical sample obtained had m.p. 225–230°, hard white needles.

Anal. Calcd. for $C_{14}H_{10}ClN_3O_2$: C, 58.44; H, 3.50. Found: C, 58.23; H, 3.72.

2-(*p*-Chlorophenyl)2-methyl-1,3-dicarboxypropane (V).—The Guareschi imide (IV), 110 g., was added to a mixture of 500 ml. of water, 500 g. of concentrated sulfuric acid, and 400 ml. of water, and the mixture was heated under reflux for 4 days. The work-up procedure was as described[12] and after one crystallization from water, there was obtained 70 g. of white needles, m.p. 148.8–151.1° (71% yield). For analysis a small sample of this material was recrystallized from water, m.p. 149.8–151.0°.

Anal. Calcd. for $C_{12}H_{13}ClO_4$: C, 56.15; H, 5.10. Found: C, 56.20; H, 5.14.

2-(*p*-Chlorophenyl)-2-methyl-1,3-dicarbethoxypropane (VI).—The crude wet acid V was dissolved in a mixture of 2 ml. of concentrated sulfuric acid, 150 ml. of benzene, and 42 g. of absolute ethanol, and the reaction flask was equipped with a water separator. Reflux was maintained overnight, after which time no more water was being produced. An additional 20 ml. of absolute ethanol was added to the reaction mixture and refluxing was continued for 1 hr. No further water was formed during this time. Approximately 50 ml. of solvent was distilled from the reaction and the cooled mixture was diluted with ether. The organic solution was washed twice with water, once with dilute sodium bicarbonate solution, once with water, dried with magnesium sulfate, and then the solvent was removed. The residue was distilled, and after a small forerun, b.p. 120–169° (1.5 mm.), the diester distilled as a colorless liquid, wt. 79 g. (93%), b.p. 169–171° (1.5 mm.), $n^{25}D$ 1.5039.

Anal. Calcd. for $C_{16}H_{21}ClO_4$: C, 61.44; H, 6.77. Found: C, 61.26; H, 6.80.

3-(*p*-Chlorophenyl)-3-methyl-1,5-dihydroxypentane (VII).–The diester VII, 78 g., in 200 ml. of anhydrous ether was added dropwise to a stirred slurry of 14 g. of lithium aluminum hydride and 800 ml. of anhydrous ether during 1 hr. The mixture was stirred at reflux for 1 hr., then cooled to 25° and treated in turn with ethyl acetate, water, and concentrated hydrochloric acid. The two clear phases were separated and the ether solution was washed with water, dilute sodium bicarbonate solution, and water, dried with magnesium sulfate, and the solvent was removed. The residue was distilled and after a 1-g. forerun, b.p. 150–180° (1.5 mm.), the diol which solidified in the receiving flask was obtained, 49.3 g. (69%), b.p. 180–184° (1.5 mm.). The material was crystallized once from acetone at −20° to give dense white needles, m.p. 102–103°.

Anal. Calcd. for $C_{12}H_{17}ClO_2$: C, 63.01; H, 7.49. Found: C, 63.25; H, 7 64.

3-(*p*-Chlorphenyl)3-methyl-1,5-dibromopentane (VIII).—This compound was prepared from 23 g. of diol (VII), 19 g. of phosphorus tribromide, 2.5 g. of Karl Fischer reagent grade pyridine, and 100 ml. of anhydrous benzene employing a standard procedure,[16] the total reaction time being 120 hr. at 25°. The product, a pale yellow liquid after distillation, b.p. 152° (0.5 mm.) $n^{25}D$ 1.5798, was obtained in 79% yield. A small portion of this material was dissolved in methylene chloride and the organic solution was washed with water, dilute hydrochloric acid, water, and then dried over calcium chloride. The solvent was removed and the residue was distilled at reduced pressure. $n^{25}D$ 1.5798.

Anal. Calcd. for $C_{12}H_{15}ClBr_2$: C, 40.64; H, 4.26. Found: C, 40.71; H, 4.30.

3-(*p*-Chlorophenyl)-3-methyl-1,5-dicyanopentane (IX).—The dibromide (VIII) 32.9 g., was treated with 24.6 g. of potassium cyanide in 120 ml. of 95% ethanol at reflux temperature with stirring for a total of 50 hr. according to the usual procedure.[17] Work-up afforded the crude product which was distilled. After 2.0 g. of forerun, b.p. 160–198° (0.7 mm.), $n^{25}D$ 1.5386, there was obtained 19.7 g. (86%) of a clear, viscous, colorless liquid, b.p. 198–200° (0.7 mm.), $n^{25}D$ 1.5420.

Anal. Calcd. for $C_{14}H_{15}ClN_2$: C, 68.15; H, 6.35. Found: C, 67.81; H, 6.19.

3-(*p*-Chlorophenyl)-3-methyl-1,5-dicarboxypentane.—A mixture of dinitrile IX, 1 g., 1.37 g. of potassium hydroxide, 15 ml. of 95% ethanol, and 5 ml. of water was refluxed for 24 hr. The solution was cooled and then acidified to Congo Red paper with concentrated hydrochloric acid. The white precipitate was collected and washed well with water. The solid was dissolved in 100 ml. of boiling water. The diacid crystallized upon cooling, 0.9 g. (79%) of white needles, m.p. 146.6–147.8°.

Anal. Calcd. for $C_{14}H_{17}ClO_4$: C, 59.03; H, 6.01. Found: C, 59.02; H, 6.08.

3-(*p*-Chlorophenyl)-3-methyl-1,5-dicarboethoxypentane (X).—A solution of 182 ml. of 95% ethanol, 70 ml. of concentrated sulfuric acid, and 19.7 g. of dinitrile IX was heated under reflux for 45 hr.[18] The then two-phase solution was cooled and poured into a separatory funnel containing 500 ml. of ice and water. The product was extracted with ether and the ether solutions were washed with water, sodium bicarbonate solution, water, and then dried with magnesium sulfate. The ether was removed and the residue was distilled. After 2.7 g. of forerun, b.p. 140–166° (0.5 mm.), $n^{25}D$ 1.5028, the diester distilled as a clear colorless liquid, b.p. 166° (0.5 mm.), $n^{25}D$ 1.5071, 17.6 g. (71% yield).

Anal. Calcd. for $C_{18}H_{25}ClO_4$: C, 63.51; H, 7.39. Found: C, 63.65; H, 7.22.

TABLE II. DIPOLE MOMENT DATA

Benzene Solution, 25°

N_2	d_{12}	ϵ_{12}
4-(*p*-Chlorophenyl)cyclohexanone—M_R 56.92		
0.00000000	0.873587	2.2744
.00037568	.873851	2.2767
.00069521	.874038	2.2785
.00141633	.874447	2.2826
.00193994	.874791	2.2854
.00262107	.875215	2.2894
$\alpha = 5.670$	$\epsilon_1 = 2.2745$	$d_1 = 0.87360$
$\beta = 0.614$	$P_{2\infty} = 135.7$	$\mu = 1.96 \pm 0.02$ D.
4-(*p*-Chlorophenyl)-4-methylcyclohexanone—M_R 61.58		
0.00000000	0.873631	2.2739
.00084014	.874209	2.2822
.00137553	.874555	2.2872
.00179444	.874767	2.2910
.00228860	.875107	2.2956
$\alpha = 9.461$	$\epsilon_1 = 2.2741$	$d_1 = 0.87365$
$\beta = 0.639$	$P_{2\infty} = 195.4$	$\mu = 2.56 \pm 0.02$ D.
Cyclohexanone[28]—M_R 27.70		
0.00000000	0.873591	2.2726
.00333014	.873774	2.3160
.00515503	.873963	2.3386
.00729705	.874177	2.3663
$\alpha = 12.811$	$\epsilon_1 = 2.2728$	$d_1 = 0.87355$
$\beta = 0.083$	$P_{2\infty} = 219.18$	$\mu = 3.06 \pm 0.03$ D.

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(16) L. H. Smith, "Organic Syntheses," Coll. Vol. III, J. Wiley & Sons, Inc., New York, N. Y., 1955, p. 793.

(17) J. Cason and H. Rapoport, "Laboratory Text in Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1962, p. 380.

(18) N. L. Allinger and V. B. Zalkow, *J. Am. Chem. Soc.*, **83**, 1144 (1961).

4-(*p*-Chlorophenyl)-4-methylcyclohexanone (II).—To a stirred and refluxing solution prepared from 0.76 g. of potassium metal and 100 ml. of dry *t*-butyl alcohol was added 3.0 g. of diester X during 5 min. Refluxing was continued for 19 hr., then the reaction mixture was cooled to 30°, 20 ml. of water was added, and the alcohol was removed maintaining a bath temperature of 60°. The residue was hydrolyzed with 100 ml. of 33% sulfuric acid (by volume), and the product was isolated as described for the preparation of I. The crude product was dissolved in ether and the ether solution was washed twice with water before drying with magnesium sulfate. The ether was removed and distillation of the crude material at 0.8 mm., with a bath temperature 165° gave 1 g. of product which was crystallized from pure pentane at −20°. There was obtained after two crystallizations 0.67 g. of white needles, m.p. 37.9–38.9°. A second crop of 0.05 g., m.p. 37.8–38.7° was obtained from the filtrates, total yield 37%.

Anal. Calcd. for $C_{13}H_{15}ClO$: C, 70.10; H, 6.79. Found: C, 70.05; H, 6.94.

Dipole Moments.—The dipole moments of the various ketones were run at 25°, in benzene solution, and the data are given in Table II. The dipole moment apparatus has been described previously.[19] The moments were calculated by essentially the method of Halverstadt and Kumler,[20] utilizing an IBM 650 computer programmed as described earlier.[21] The molar refractivities were obtained from tables,[22] and atomic polarization was neglected.

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[19] N. L. Allinger, H. M. Blatter, M. A. DaRooge, and L. A. Freiberg, *J. Org. Chem.*, **26**, 2550 (1961).

[20] I. F. Halverstadt and W. D. Kumler, *J. Am. Chem. Soc.*, **64**, 2988 (1942).

[21] N. L. Allinger and J. Allinger, *J. Org. Chem.*, **24**, 1613 (1959).

[22] A. I. Vogel, W. T. Cresswell, G. J. Jeffrey, and J. Leicester, *Chem. Ind.* (London), 358 (1950).

[23] A recent value reported for this compound under identical conditions is 3.08 D; see H. H. Günthard and T. Gaumann, *Helv. chim. Acta*, **34**, 39 (1951).

The Conformational Preference of the Cyano Group[1]

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The conformational preference of the cyano group has been determined by the base-catalyzed equilibration of 4-*t*-butylcyclohexanecarbonitrile. At 25° in *t*-butyl alcohol solvent, the equatorial cyano group is favored with $\Delta F = -0.15$ kcal./mole. The temperature dependence of the equilibrium indicates that this small free energy difference is due largely to a positive entropy term, $\Delta S = 0.7 \pm 0.3$, ($\Delta H = 0.04 \pm 0.1$ kcal./mole) for the axial–equatorial interconversion.

Determinations of equatorial–axial conformational preferences in cyclohexane derivatives have provided valuable information regarding the nature of steric interactions in organic molecules.[3] The free energy difference (the Winstein *A* value)[4] does not always parallel the covalent radius of the substituent. A low temperature n.m.r. study[5] of the cyclohexyl halides, for example, has shown that the *A* values follow the order Cl > Br > I > F. It was suggested[5] that the conformational preference of a substituent depends on a combination of bond length, radius of the electron cloud, and the polarizability of this cloud. Such an explanation can account for the order observed with the halides, and also the small *A* value of the bromomercuri group.[6]

The question of electron density and polarizability also arises in substituted cyclohexanones. It has been assumed that the π-cloud of a carbonyl group can be neglected in the calculation of steric interactions,[7,8] giving rise to the "3-alkyl ketone effect." From the position of equilibrium for the geometrical isomers menthone and isomenthone, however, it has been estimated that the π-cloud of the carbonyl group is sterically comparable to an axial hydrogen.[9]

Important substituents for which the conformational preferences are unknown are those in which the group attached to the cyclohexane ring bears a triple bond. Included in this class are the substituents $-\text{C}{\equiv}\text{N}$, $-\overset{+}{\text{N}}{\equiv}\text{N}$, $-\overset{+}{\text{N}}{\equiv}\overset{-}{\text{C}}$, and $-\text{C}{\equiv}\text{C}-\text{R}$. If, in these cases, the π-cloud is of appreciable size, rather large *A*-values for these groups are not unreasonable. For example, as an approximation, the N_2^+ group has been regarded as sterically equivalent to the methyl group.[10]

Preliminary low temperature n.m.r. studies of cyclohexanecarbonitrile[11] indicated a small conformational preference for the cyano group. However, the signals were not sufficiently separated to obtain an accurate value. An alternate method, using the bulky *t*-butyl group with its large equato-

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[1] (a) Supported in part by the National Science Foundation; (b) This work was originally submitted for publication elsewhere, at which time it was learned that Prof. N. L. Allinger had similar work accepted for publication in *J. Org. Chem.* We wish to express our appreciation to Prof. Allinger for delaying publication of his work so that the two papers could appear simultaneously.

[2] Present address: University of California at Santa Barbara, Goleta, Calif.

[3] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 236.

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

[5] A. J. Berlin and F. R. Jensen, *Chem. Ind.* (London), 998 (1960).

[6] F. R. Jensen and L. H. Gale, *J. Am. Chem. Soc.*, **81**, 6337 (1959).

[7] W. Klyne, *Experientia*, **12**, 119 (1956).

[8] N. L. Allinger and L. A. Freiberg, *J. Am. Chem. Soc.*, **84**, 2201 (1962).

[9] B. Rickborn, *ibid.*, **84**, 2414 (1962).

[10] A. Streitwieser, Jr., and W. D. Schaeffer, *ibid.*, **79**, 2888 (1957). The *A*-value for methyl is 1.97 kcal./mole, ref. 13.

[11] Unpublished results of Mr. A. J. Berlin.