salt and the diluted ethanol was extracted with benzene. The residue after distillation of the benzene was refluxed for 2 hr. with a solution containing 2 g. of chromic acid in 30 ml. of acetic acid. By benzene extraction 22.8 mg. of *p*-chlorobenzoic acid and 1.0 g. 2,4′-dichlorobenzil, m.p. 98.8–99.4°, was obtained. The latter did not depress the melting point of the 2,4′-dichlorobenzil previously prepared and the infrared spectra were identical.

Conformational Analysis. XXX. The Cyano Group[1,2]

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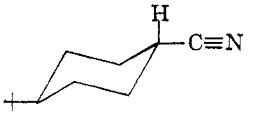
The standard free energy of a cyano group in the axial position on a cyclohexane ring (relative to the equatorial) has been determined by equilibrating the *cis* and *trans* isomers of 4-*t*-butylcyclohexyl cyanide at 66° and the experimental value is 0.25 kcal./mole.

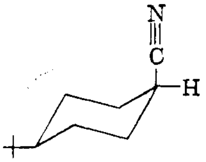
Conformational analysis has been put on an increasingly quantitative basis by the determination of the relative standard free energies of various groups in the axial and equatorial positions on a cyclohexane ring.[3] A group which has not been previously studied in this respect is the cyano group. Information on this group was of particular interest because it could be used to find a radius for carbon which would be suitable for calculations of the van der Waals type.

The experimental method was straightforward, and involved equilibrating the *cis* and *trans* isomers of 4-*t*-butylcyclohexyl cyanide (I). It can safely be assumed that the *t*-butyl group occupies an equatorial position and that the *cis* and *trans* isomers possess the conformations indicated in the figure.[4] The *cis* and *trans* isomers of 4-*t*-butylcyclohexyl cyanide were prepared from the known corresponding acids[5] by conversion of the acid to the acid chloride with thionyl chloride, reaction of the acid chloride with ammonia to give the amide, and dehydration of the latter with thionyl chloride. The nitrile obtained in each case was analyzed by gas phase chromatography on a Tide column, and it was noted that considerable epimerization had occurred and a mixture of the two nitriles was in fact obtained. The *trans* acid, however, led predominantly to one nitrile which was assigned the *trans* structure, while the *cis* acid led predominantly to the other nitrile, which was assigned the *cis* structure. Pure samples of the nitriles were obtained by vapor phase chromatography. When pure, both the *cis* and *trans* isomers proved to be crystalline and melted at 60° and 37°, respectively.

Equilibrium was established in tetrahydrofuran solvent at 66° using potassium *t*-butoxide as catalyst. The equilibrium was approached from both sides, and the mixture obtained in each case contained 59% of the *trans* isomer. The $\Delta F°$ for the cyano group moving from the equatorial to the axial position was thus +0.25 kcal./mole.



It



Ic

As an independent method for carrying out the determination of the conformational energy of the cyano group, the n.m.r. method introduced by Eliel[6] was considered. Compounds Ic and It must show nuclear resonance characteristic respectively of equatorial and axial protons attached to the cyano bearing carbon. The unsubstituted cyclohexyl cyanide must show the corresponding resonance at a field which is between these extremes, and which is a quantitative reflection of the relative concentrations of the axial and equatorial conformers.

Experimentally it was found that Ic showed a signal at 7.09 τ which corresponded in area to one proton and was assigned to the proton at C-1. With compound It, the corresponding proton showed a signal which was in the region of other resonance and could not be identified with certainty. The resonance definitely occurred above $\tau = 7.55$, however. For cyclohexyl cyanide itself, the signal was observed at 7.46 τ. These values indicate that there is at least 20% of axial cyanide in the latter compound, and although a quantitative value cannot be determined from these data, an upper limit for the energy of the cyano group can be set as 0.8 kcal./mole.

A theoretical approach to the energy of the axial cyano group can be made in the following way. Increasing the van der Waals radius in a series of

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[1] Paper XXIX, N. L. Allinger and S. Hu, *J. Org. Chem.*, **26**, 3417 (1962).

[2] This research was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of this fund.

[3] For a recent tabulation of groups for which such determinations have been carried out, together with their free energies, see E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, 1962, p. 236.

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

[5] H. H. Lau and H. Hart, *ibid.*, **81**, 4897 (1959).

[6] E. L. Eliel, *Chem. Ind.* (London), 568 (1959).

atoms A also leads to increasing the C—A bond length. The van der Waals repulsion of any single atom axial on a cyclohexane ring is always small, regardless of the size of the atom,[7] and in fact the energies of groups are small for such things as —OH and —SH, (and probably —NH_2), where the hydrogens can turn out away from the ring.[8]

The usefulness of approximate van der Waals calculations in conformational analysis has been recently demonstrated,[9,10] and the method of Hill[11] is particularly simple and of wide applicability.[10,12] Since carbon is of special interest, and since its van der Waals radius (or at least the appropriate value to use for this quantity in such a calculation) is not known and is not directly available by Hill's method, it was deemed desirable to derive a satisfactory value for this quantity from the energy of the cyano group.

To apply Hill's method to carbon, both the van der Waals radius and the constant ϵ must be known. Numerical values for the latter were determined for nitrogen, oxygen, and fluorine following the procedure of Hill, and the values were respectively 100, 111, and 108 cal./mole.[13] Since no trend is apparent, the average of these, 107 cal./mole, was selected for carbon for the present work. The van der Waals radius of carbon can be estimated as 1.70 Å. by extrapolation of the values for fluorine, oxygen, and nitrogen.[14,15] These values, together with the distance of the nitrile carbon from the near neighboring atoms as indicated in Table I, gave relative van der Waals energies for the axial and equatorial cyano group of +.34 and −.12 kcal./mole, thus indicating that the axial group is less stable than the equatorial by 0.46 kcal./mole. Since small deformations of bond angles require so little energy, this value would be expected to be slightly larger than that of the actual (deformed molecule). The agreement with experiment is in any case excellent, and the value of 1.70 Å. for the van der Waals radius of carbon is supported.

TABLE I

DISTANCES AND ENERGIES FOR INTERACTIONS OF THE CYANIDE CARBON WITH THE OTHER ATOMS DESIGNATED[a]

	Distance Å.[b]	Energy, kcal./mole
	Axial cyanide	
C-3	2.90	+0.20
Ax H at C-3	2.60	.00
Eq H at C-2	2.65	− .03
	Equatorial cyanide	
Eq H at C-2	2.65	−0.03
Ax H at C-2	2.65	−0.03

[a] Interactions involving the nitrogen, and those involving the cyanide carbon and other atoms not mentioned in Table I are assumed to be quite similar in the two conformers and hence have been neglected. [b] Measured on Dreiding models.

Experimental

***cis* and *trans*-4-*t*-Butylcyclohexanecarboxamides.**—The acids were prepared from 4-*t*-butylbenzoic acid by hydrogenation as described by Lau and Hart,[5] the isomers were separated and converted *via* the acid chlorides to the amides, *cis*, m.p. 158–160° (lit.,[5] m.p. 161°); *trans* (containing some *cis*), m.p. 123–131° (lit.,[5] m.p. 134–135°).

***cis*-4-*t*-Butylcyclohexyl Cyanide (Ic).**—A mixture of 10 g. of *cis*-4-*t*-butylcyclohexane carboxamide and 25 ml. of thionyl chloride was heated under reflux for 5 hr. The excess thionyl chloride was removed in vacuum and distillation furnished the product, b.p. 116–117° (8 mm.), wt. 6.5 g. (72%). Vapor phase chromatographic analysis showed that the product consisted of 52% *cis*- and 48% *trans*-4-*t*-butylcyclohexyl cyanide.

A pure sample of the *cis* isomer was obtained by vapor phase chromatography using a Beckman Megachrom instrument equipped with a General Electric SE-30 silicon rubber column at 146°. This material was crystallized once from pentane at −80°, m.p. 59.5–60°. the purified *cis* isomer was analyzed on a small Tide column and was found to contain 97% *cis*- and 3% *trans*-4-*t*-butylcyclohexyl cyanide.

Anal. Calcd. for $C_{11}H_{19}N$: C, 79.94; H, 11.59; N, 8.48. Found: C, 80.09; H, 11.27; N, 8.50.

***trans*-4-*t*-Butylcyclohexyl Cyanide (It).**—The *trans* nitrile was obtained from the corresponding amide in the same manner described for a preparation of the *cis* isomer. The compound had b.p. 114–116° (8 mm.), yield 70%. Vapor phase chromatography showed that the material was 90% *trans* and 10% *cis* isomer. A sample of the *trans* isomer was similarly purified by vapor phase chromatography followed by sublimation. Analysis showed the pure material to contain 96% *trans*- and 4% *cis*-4-*t*-butylcyclohexyl cyanide, m.p. 34.5–36.5°.

Anal. Calcd. for $C_{11}H_{19}N$: C, 79.94; H, 11.59; N, 8.48. Found: C, 80.32; H, 11.35; N, 8.61.

Equilibration Experiments.—Potassium metal, 0.12 g., was dissolved in 25 ml. of *t*-butyl alcohol (dried previously by distillation from sodium) under nitrogen, and the excess alcohol was then removed. To the resulting solid potassium *t*-butoxide was added 50 ml. of tetrahydrofuran (dried by distillation from sodium dispersion under nitrogen) containing 5.0 g. of 4-*t*-butylcyclohexyl cyanide (90% *trans* isomer). The solution was heated under reflux (at 66°) for 32 hr., then the equilibration was quenched by pouring the hot solution onto crushed ice. The resulting two-phase solution was saturated with sodium sulfate and extracted with ether. The ether was evaporated and the residue was used directly for the gas phase analysis. A similar experiment was carried out starting with a mixture of *cis* and *trans* nitriles in which the former was present to the extent of 52%. Replicate analyses approaching equilibrium from either side gave values of 59 ± 1% *trans*.

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[7] For example, the energies of axial halogens are as follows (kcal./mole): F, 0.25; Cl, 0.51; 0.48; and I, 0.43 [F. R. Jensen and A. J. Berlin, *Chem. Ind.* (London), 998 (1960)].

[8] The exact value for the hydroxyl group appears subject to variation,[3] but is less than 1 kcal./mole. For the sulfhydryl group, 0.41 kcal./mole has been reported with the axial conformer of lower enthalpy [G. Chiurdoglu, J. Reisse, and M. Vander Stichelen Rogier, *Chem. Ind.* (London), 1874 (1961)]. No quantitative data appear to be available for the amino group.

[9] J. B. Hendrickson, *J. Am. Chem. Soc.*, **83**, 4537 (1961).

[10] N. L. Allinger, J. Allinger, L. A. Freiberg, R. F. Czaja, and N. A. LeBel, *ibid.*, **82**, 5876 (1960).

[11] T. L. Hill, *J. Chem. Phys.*, **16**, 399 (1948).

[12] N. L. Allinger and L. A. Freiberg, *ibid.*, **84**, 2201 (1962).

[13] (a) N. L. Allinger, M. A. DaRooge, and C. L. Neumann, *J. Org. Chem.*, **27**, 1082 (1962). (b) Unpublished calculations by Dr. L. A. Freiberg.

[14] L. Pauling, "The Nature of the Chemical Bond," 3rd ed., Cornell University Press, Ithaca, N. Y., 1960, p. 260.

[15] A slightly larger value, 1.75 Å., was used earlier [N. L. Allinger, M. A. DaRooge, and R. B. Hermann, *J. Am. Chem. Soc.*, **83**, 1974 (1961)] but gives poorer agreement with experiment. Pauling's rule (ref. 14, p. 263) suggests the value 1.60 Å. also has some justification, and the value 1.70 Å. has been accepted as a compromise.

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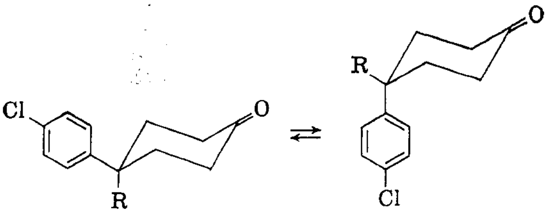
Dipole moment measurements on 4-(*p*-chlorophenyl)cyclohexanone and on 4-methyl-4-(*p*-chlorophenyl)cyclohexanone give the energy of the axial phenyl as 2.0 kcal./mole greater than that of the equatorial.

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).