25 ml. of carbon tetrachloride was refluxed for 14 hours. Evaporation of the yellowish solution left a yellow sirup which crystallized upon trituration with methanol. Recrystallization from ethanol gave 50 mg. (50%) of tiny white needles, m.p. 93.5–94.5°. There was no melting point depression on admixture with a sample of the *trans*-hydrocarbon prepared by oxidation of the *trans*-hydrazine VIIb.

Hydrogenation of *cis*-1,2-Diphenylbenzocyclobutene.—A stream of hydrogen was passed for 8 hours at room temperathrough a solution of 200 mg. of *cis*-1,2-diphenylbenzocyclobutene in 50 ml. of ethanol to which 150 mg. of palladium-charcoal catalyst (10%) was added. Filtration and evaporation of the solvent gave, after recrystallization from ethanol, 100 mg. (49.5%) of *o*-dibenzylbenzene as white crystals, m.p. 76.5–78° (lit.[28] m.p. 78°). It had been reported previously by Jensen and Coleman[16] that the *trans* isomer was reduced to *o*-dibenzylbenzene under similar conditions. This was verified by reduction of a sample of the *trans*-hydrocarbon obtained by oxidation of VIIb.

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[28] A. Bistrzycki and B. Brenken, *Helv. Chim. Acta*, **5**, 20 (1922).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY, DETROIT 2, MICH.]

Conformational Analysis. XXVIII. The 3-Alkylketone Effect[1,2]

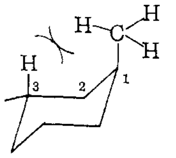
BY NORMAN L. ALLINGER AND LESLIE A. FREIBERG

RECEIVED JANUARY 11, 1962

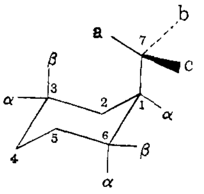
The energy of an axial methyl group relative to an equatorial in the position 3 to a ketone was measured by equilibrating the *cis* and *trans* isomers of 3,5-dimethylcyclohexanone, and the value found was 1.4 kcal./mole. The reduction of energy due to the 3-alkylketone effect was therefore 0.6 kcal./mole. This value is consistent with that predicted by van der Waals interactions.

Robins and Walker, in their study on the stability relationships of the 1,4-dioxophenanthrenes,[3] found their results were most easily interpretable if certain interactions, which had been ignored up until that time, were taken into account. Klyne[4] generalized these interactions as the 2-alkylketone and the 3-alkylketone effects. Recent studies, both theoretical and experimental, have indicated that the 2-alkylketone effect of a methyl group should be and is negligibly small.[5] The present work was aimed at evaluating, both theoretically and experimentally, the 3-alkylketone effect.

The evaluation of the 3-alkylketone effect by Klyne was based on the idea that the energy of the axial methyl group, in other words the energy of a gauche interaction, resulted mainly from the van der Waals repulsion between the hydrogen on the methyl and the axial hydrogens at C-3 and C-5 as indicated. If C-3 is converted to a carbonyl group, then one of these interactions would be eliminated, and the energy of the methyl axial should be reduced to half the value it has on the saturated ring.



It has recently been shown in a number of cases[6] that a semi-quantitative evaluation of the energies involved in such van der Waals interactions can be carried out using the general method developed by Hill.[7] Unfortunately, precise calculations are not now possible because neither the van der Waals functions nor the molecular geometry is known with sufficient accuracy. It is possible to calculate the energy of an axial methyl (relative to an equatorial one) on a cyclohexane ring by this method by summing the interaction energies for each pair of atoms for which the distance differs in the two conformations, and most of the pertinent data are given in Table I.



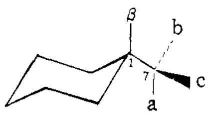


TABLE I

DATA FOR VAN DER WAALS ENERGY CALCULATION[a]

Interaction	Distance, Å.	Times Axial	Times Equatorial	Energy Axial	Energy Equatorial
3βH-aH	1.85	2	0	+1.04	...
3C-7C	2.95	2	0	+ .22	....
7C-3βH	2.60	2	0	− .03	....
3C-aH	2.60	2	0	− .03	....
aH-2αH	2.55	0	2	....	−0.09
3C-1βH	2.70	0	2	....	− .11
7C-2αH	2.70	0	2	....	− .11
1βH-3βH	2.55	0	2	....	− .09
1αH-2αH	2.45	2	0	−0.10	....
7C-3C	3.85	0	2	....	−0.19
7C-3βH	4.2	0	2	....	−0.03
1αH-3C	3.50	2	0	−0.09	....
				+1.01	−0.62

[a] Other data required for the calculations: van der Waals radii; C = 1.70 Å., H = 1.20 Å., ϵ = 42 cal./mole (H–H repulsion); ϵ = 67 cal./mole (C—H repulsion) and ϵ 107 cal./mole (C–C repulsion). These quantities are either those of Hill,[7] or from unpublished work of the authors.

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[1] Paper XXVII, N. L. Allinger and H. M. Blatter, *J. Org. Chem.*, **27**, 1523 (1962).

[2] This work was supported by the U. S. Army Research Office under Grant Number DA-20-018-ORD 22743.

[3] P. A. Robins and J. Walker, *Chemistry & Industry*, 772 (1955); *J. Chem. Soc.*, 1789 (1955); 3960 (1954).

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

[5] N. L. Allinger and H. M. Blatter, *J. Am. Chem. Soc.*, **83**, 994 (1961).

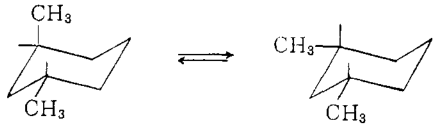
[6] (a) N. L. Allinger, J. Allinger, L. A. Freiberg, R. Czaja and N. A. LeBel, *J. Am. Chem. Soc.*, **82**, 5876 (1960); (b) N. L. Allinger and W. Szkrybalo, *J. Org. Chem.*, **27**, 722 (1962).

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

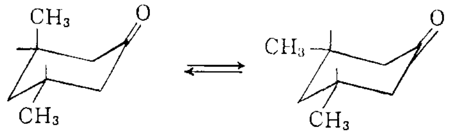
The interactions not specifically listed are assumed to be sufficiently similar in the two conformations as to cancel out. Unfortunately the number of terms involved is large, and the over-all accuracy consequently is low. Certain qualitative features of this calculation are of interest, however; they are: (1) net repulsions tend to destabilize the axial methyl (by 1.01 kcal./mole), but attractions tend to stabilize the equatorial methyl (by 0.62 kcal./mole), and these effects are comparable in magnitude; (2) the net repulsion in the axial case is the sum of a number of repulsions and attractions, the latter being smaller but not negligible; (3) the hydrogen–hydrogen repulsion between the methyl and the 3- and 5-positions accounts for only about two-thirds the observed difference in energy between the axial and equatorial methyls.

A more accurate calculation of the 3-alkylketone effect was then made by considering what change in repulsion resulted when a hydrogen at C-3 was removed; all of the other terms were assumed to stay constant.[8] For the axial conformer, one each of interactions 1 and 3 were removed; for the equatorial conformer, interaction 8 was similarly removed. The energy of the former was thus lowered by 0.54 kcal./mole, that of the latter was increased by 0.05 kcal./mole and the change in repulsion was calculated to be 0.59 kcal./mole. This value represents a theoretical value for the 3-alkylketone effect of a methyl and it might be hoped that it would be good to 0.1 or 0.2 kcal./mole.

For the experimental evaluation of the effect the following two epimerizations were considered:



(1)



(2)

For reaction 1 the enthalpy change was known from heat of combustion measurements[9] and from direct equilibration studies[10] to have the value −1.96 ± 0.10 kcal./mole. This value (rather than the often quoted[11] 1.6-1.8 kcal./mole) properly represents the energy of an axial methyl group. Equilibration measurements for (2) were undertaken to obtain the energy of the axial methyl in this system, and the difference between the values for ΔH° of (1) and (2) are a measure of the 2-alkylketone effect.

For the equilibration study, both the *cis* and *trans* isomers of 3,5-dimethylcyclohexanone were obtained. Heating of either isomer with a palladium-on-carbon catalyst gave a complex mixture of compounds. Separation of this mixture by vapor phase chromatography showed that it contained unsaturated hydrocarbons, *m*-xylene, a mixture of isomeric alcohols, and the desired ketones, and 3,5-dimethylphenol was evident from the infrared spectrum. The alcohols were not readily separable from the ketones by gas phase chromatography, but could be removed (presumably by dehydration) by brief treatment of the equilibrated mixture with concentrated sulfuric acid at room temperature. It was shown that this treatment did not affect the composition of a known mixture of ketones.

The results of the equilibration experiments are given in Table II.

TABLE II

EQUILIBRATION DATA FOR THE REACTION *trans*- ⇄ *cis*-3,5-DIMETHYLCYCLOHEXANONE AT 493 ± 10°K.

Starting isomer	Equilibration time, hr.	Workup method	K
cis	10	B	1.68
cis	10	A	1.84
cis	38	B	2.17
cis	38	A	2.02
trans	10	A	2.28
trans	10	B	1.86

For reaction 2, the experimental data gave $\Delta F^0_{493} = -0.67 \pm 0.15$ kcal./mole, and taking $\Delta S^0 = -1.4$ e.u., $\Delta H^\circ_{493} = -1.36$ kcal./mole. This value for ΔH° is smaller than that found for the corresponding hydrocarbon case (1) (−1.96 kcal./mole) by 0.6 kcal./mole. Thus theory and experiment agree that the 3-alkylketone effect is real, though somewhat smaller than suggested by Klyne.

The effects of the presence of boat forms in the compounds investigated has been neglected because of the lack of any method to take them into account. At the high temperature used for the equilibration, the free energy of the *trans* isomer in the chair form might not be much more favorable than that of a boat form, depending on the magnitude of the entropy effect. If a considerable amount of boat form is present, the result would be to stabilize the *trans* isomer relative to the *cis*. Hence the enthalpy difference between the isomers may be somewhat greater than 1.36 kcal./mole, and a value of 0.6 kcal./mole for the 3-alkylketone effect is therefore perhaps best regarded as an upper limit.

Experimental

***trans*-3,5-Dimethylcyclohexanone** was available from earlier work.[12]

***cis*-3,5-Dimethylcyclohexanone** was prepared from 3,5-dimethylphenol by catalytic reduction followed by oxidation, as described earlier,[12] and was fractionally distilled through a 60-cm. Podbielniak column; b.p. 74.5-74.8° (20 mm.), $n^{25}\mathrm{D}$ 1.4405 (reported[12] b.p. 57-59° (6 mm.), n^{25} 1.4404).

Equilibration Studies.—The ketones were equilibrated by heating 150–250-mg. samples, sealed in 8-mm. Pyrex tubes, in the presence of 10–15 mg. of 10% palladium-on-charcoal. The temperature during equilibration was maintained at 220 ± 10°. Samples were quenched by quickly removing them from the heating apparatus and cooling to room temperature within 1 minute.

Equilibrated samples were analyzed by one of two methods. In the first method (A), samples for gas chromatographic analysis were taken directly from the sealed tubes

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[8] This seems to be a good approximation, although the change in bond angle at the carbonyl leads to a small change in geometry.

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

[10] S. Hu, unpublished work.

[11] *E.g.*, 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. 18.

[12] N. L. Allinger, *J. Am. Chem. Soc.*, **81**, 232 (1959).

after they were opened. In the second method (B), samples were prepared by treating the equilibrated mixtures for 30 seconds with 5 ml. of cold concentrated sulfuric acid and then pouring the solution into 25 ml. of water. The samples for vapor phase chromatography were isolated by extracting with ether, washing the extracts with water, drying with anhydrous sodium sulfate, and evaporating the ether. This treatment had the effect of removing alcohols which complicated the analysis. There was no systematic difference in analyses between methods A and B.

Initial experiments with the isomers of 3,5-dimethylcyclohexanone indicated that a good separation could be obtained on a column containing 25% by wt. of the cyanoalkylation product of glycerin on firebrick. However, two of the three isomeric alcohols (prepared for comparison purpose by lithium aluminum hydride reduction of a mixture of *cis*- and *trans*-ketones) had retention times identical to those of the isomeric ketones. Making use of the ability of Tide to separate ketone–alcohol mixtures, a dual column was constructed which contained both stationary phases so that it would separate not only ketone and alcohol but also their isomers. Analysis of a mixture of isomeric ketones and alcohols on Tide alone showed only three peaks, while on the composite column five peaks were observed. The separation while good, was not, however, perfect.

The column used for analysis, a 180 cm. × 7 mm. Pyrex tube bent in a U, contained two different packing materials. The first half of the column contained 40–60 mesh Tide. The second half contained 60–80 mesh firebrick supporting 25% by weight of tris-β-cyanoethyl glyceryl ether as the liquid partitioner. The column was operated at 110° and at an inlet pressure of 8 p.s.i. of helium. The results of equilibration experiments are reported in Table II.

The free energy change, calculated from the data in Table II for the reaction *trans* ⇄ *cis*-3,5-dimethylcyclohexanone, was $\Delta F^\circ_{493} = -0.67 \pm 0.15$ kcal./mole. Recognizing that the *trans* isomer is a *dl*-mixture and the *cis* isomer is a *meso* form ($\Delta S = -1.4$ e.u.), a value of $\Delta H_{493} = -1.36 \pm 0.18$ kcal./mole was calculated. From available data[9,10] for the reaction *trans*-1,3-dimethylcyclohexane ⇄ *cis*-1,3-dimethylcyclohexane, $\Delta H = -1.96 \pm 0.1$ kcal./mole, and the difference in enthalpy for these reactions can be calculated as $(-1.36 \pm 0.18) - (-1.96 \pm 0.1 = 0.60 \pm 0.28)$ kcal./mole. Thus when a keto group replaces a methylene group on a cyclohexane ring, an axial methyl group on the 3-carbon becomes more favorable by 0.6 kcal./mole.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF BOSTON UNIVERSITY, BOSTON 15, MASS.]

Oxymercuration of D-Glucal and Its 3,4,6-Triacetate

BY PHILIP T. MANOLOPOULOS, MORTON MEDNICK AND NORMAN N. LICHTIN

RECEIVED DECEMBER 28, 1961

Crystalline products obtained on addition of methanolic mercuric acetate to D-glucal and to its 3,4,6-triacetate have been shown with the aid of brominolysis and iodide-catalyzed deoxymercuration to be methyl 2-acetoxymercuri-2-deoxy-β-D-mannoside and methyl 2-acetoxymercuri-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucoside, respectively. Oxymercuration thus yields a *cis* product with D-glucal and a *trans* product with its triacetate. These assignments and related brominolysis data support previously assigned configurations of Fischer's two methyl-2-deoxy-2-bromo-β-D-hexosides. Mechanistic speculations are presented. A small number of related alkoxymercuration products are described.

Results

Relationship between Addition Products.—The reactions of glucal and its 3,4,6-triacetate with methanolic mercuric acetate yield stable crystalline products, which, on the basis of evidence presented below, have been identified, respectively, as methyl 2-acetoxymercuri-2-deoxy-β-D-mannoside (I) and methyl 2-acetoxymercuri-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucoside (III). These appear to be the first reported examples of oxymercuration of glycals. Transformations which establish that III is not the 3,4,6-triacetate of I are summarized in Fig. 1.

Compound I is prepared most efficiently without isolation of glucal; the same product is, however, obtained on treating crystalline glucal with methanolic mercuric acetate. Attempted acetylation of I by acetic anhydride and sodium acetate proceeds with formation of metallic mercury and formation of a solid product, Y, which is not sufficiently soluble in common solvents to permit recrystallization. This product has not yet been identified. However, the fact that its infrared spectrum is devoid of ionic acetate absorption bands (687, 1317, 1607 cm.$^{-1}$) suggests that it may be a dialkyl mercury or a mixture of isomeric compounds of this type. A product with identical infrared spectrum is obtained on subjecting III to the same acetylating conditions. Attempted deacetylation of III by methanolysis catalyzed by sodium methoxide did not yield a pure product even though compound I could be recovered unchanged after exposure to the same conditions. Attempted purification by repeated reprecipitation from diethyl ether of the product of methanolysis of III did not yield a pure substance. Ionic acetate absorption at 687 and 1317 virtually disappeared during this process (but absorption at 1607 did not). Compound III was identified as the triacetate of an isomer of I by comparison of II with V and of I with VI (Fig. 1). The reaction of I with KCl provided only a poor yield of II because of difficulties in freeing the latter of potassium acetate (reaction with NaCl was not attempted), but there is no reason to suspect that I → II involved more than replacement of acetate by chloride. In addition, the infrared spectra of I and II differ largely by the ionic acetate absorption. Similarly III → IV can involve only replacement of ionic acetate by more tightly bound chloride. The reaction of III with aqueous sodium bromide also provides a virtually quantitative yield of D-glucal triacetate·HgBr·OCH_3, the infrared spectrum of which is almost identical with that of IV. Base-catalyzed methanolysis of IV at room temperature to form V does not displace chlorine from mercury and is very unlikely to cause any change other than removal of acetyl groups with retention of configuration at C-3 and C-5. Although II and V have almost the same melting points, the melting point of their mixture is depressed. Their infrared spectra are strikingly different. Among other differences,

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(1) *Cf.* Abstracts of the 138th Meeting of the American Chemical Society, New York, N. Y., Sept., 1960, p. 36-P for a preliminary report.