methylmagnesium chloride to cyclopentanone gave very low yields of the alcohol (20% or less). The principal product in these reactions was 2-cyclopentylidenecyclopentanone, b.p. 103–118° at 13 mm., oxime[13,14] m.p., 122°, and 2,5-dicyclopentylidenecyclopentanone,[13] m.p. 66–68°. Addition of the ketone to methylmagnesium chloride gave the alcohol in 62% average yield.

Halides were prepared by reactions of anhydrous hydrogen halides with the alcohols and 1,2-dimethylcyclopentene as described elsewhere.[3] Excess hydrogen halide was removed from the reaction mixtures by extraction with cold water and the pentane solution was dried briefly over anhydrous calcium sulfate. No solution was stored for more than an hour before use.

Procedure. The pentane solutions of halides (approximately 0.02 mole in 20–25 cc. of pentane) were diluted to exactly 25 ml. with pentane. Ten-milliliter aliquots were added to 75 ml. absolute alcohol containing $0.1N$ lithium perchlorate. Solvolysis rates were measured using the rapid intermittent titration method.[15] The titrant was a standard $1N$ solution of triethylamine in absolute ethanol. Bromophenol blue was employed as the visual indicator. Solvolysis of the bromides was followed for about 100 min. and the reactions of the chlorides were followed for about 5000 min. As neither initial concentrations nor infinity titers were known with high precision, the rate constants were determined by the method of Guggenheim.[16] Plots of milliequivalents of base added versus time were used to obtain pairs of concentration values at fixed time intervals (25 min. for the bromides and 1000 min. for the chlorides). The values of $\log (C_2-C_1)$ were plotted against t and the rate constants were calculated by multiplication of the slopes of the resulting straight lines by 2.303. While rates sometimes decreased slightly toward the end of a run, the data could never be resolved to give two clearly distinct rates. The values reported in Tables I and II represent maximum rates, as earlier points were used in runs in which the decrease in rate was noticeable.

Acknowledgment. This work was supported by a grant from the Office of Basic Ordnance Research of the United States Army.

AMES, IOWA

---

[13] O. Wallach, *Ber.*, **29**, 2955 (1896).

[14] M. Godchot and F. Taboury, *Bull. soc. chim. France*, [4], **13**, 12 (1913); H. Meerwein, *Ann. Chem.*, **405**, 129 (1914).

[15] J. K. Kochi and G. S. Hammond, *J. Am. Chem. Soc.*, **75**, 3445 (1953).

[16] F. Daniels, J. H. Mathews, J. W. Williams, P. Bender, and R. A. Alberty, *Experimental Physical Chemistry*, McGraw-Hill, New York (1956), p. 134.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

Conformational Analysis. IX. The *Gem*-Dimethyl Effect[1,2]

NORMAN L. ALLINGER AND VERA ZALKOW

Received October 28, 1959

The *gem*-dimethyl effect is quantitatively interpreted for a group of ring closure reactions which lead to substituted cyclohexane systems. The pronounced effect of alkyl substituents in shifting the equilibrium toward the cyclic compound is due in part to an enthalpy effect and in part to an entropy effect. The effect of alkyl groups on the enthalpy of ring closure is interpreted in terms of the change in the number of *gauche* interactions in going from the reactant to the product. The entropy effect, after allowing for the different symmetries of the compounds, is interpreted as being due mainly to the increased height of the barriers to internal rotations in the acyclic compounds upon chain branching.

While the fact that alkyl substitution tends to promote the rate of formation of a cyclic system from its noncyclic analog as well as to increase the concentration of the cyclic material at equilibrium has been recognized for nearly half a century,[3] no convincing explanation of the effect has been forthcoming.[4] Various attempts to explain the phenomenon have been made, and some of these such as the "Thorpe-Ingold effect"[5] and steric hindrance to rotation[4] are probably of importance in certain cases. It is the purpose of this paper to show that certain aspects of the phenomenon have a straightforward thermodynamic basis and are completely general. This general effect, which for historical[4] reasons has been simply called the *gem*-dimethyl effect in this paper, must always be taken into account before the importance of any "special" effects such as the Thorpe-Ingold effect can be ascertained.

The present paper will be limited in scope as far as quantitative aspects are concerned to equilibria, and the treatment will be applied quantitatively to six-membered ring systems since these are particularly amenable to study and the necessary data are available.[6] The same considerations will apply, in principle, to compounds of other classes equally well.

Consider the reaction of n-hexane to give cyclohexane and hydrogen in the gas phase at 25°. This reaction can be taken as the reference point,

---

[1] This work was supported by a grant from the Sloan Foundation.

[2] Paper VIII, *J. Am. Chem. Soc.*, in press.

[3] C. K. Ingold, *J. Chem. Soc.*, **119**, 305, 951 (1921).

[4] For a recent summary of the status of the problem, and leading references, see F. G. Bordwell, C. E. Osborne, and R. D. Chapman, *J. Amer. Chem. Soc.*, **81**, 2698 (1959).

[5] R. M. Beesley, C. K. Ingold, and J. F. Thorpe, *J. Chem. Soc.*, **107**, 1080 (1915).

[6] Selected Values of Properties of Hydrocarbons and Related Compounds, American Petroleum Institute Research, Project 44, Carnegie Institute of Technology, Pittsburgh, Pa.

TABLE I

THERMODYNAMIC QUANTITIES FOR THE CYCLIZATION REACTIONS OF SUBSTITUTED HEXANES (H) TO CYCLOHEXANES (C)

Hexane	σ_H	σ_C	Optical Isomers H	Optical Isomers C	—ΔH Calcd.	—ΔH Found	ΔS Calcd.	ΔS Found	—ΔF Calcd.	—ΔF Found
n	2	6	1	1	0.0	0.0	0.0	0.0	0.0	0.0
2-CH_3	1	1	1	1	0.8	0.9	3.4	3.3	1.8	1.9
3-CH_3	1	1	2	1	1.6	1.6	2.0	2.2	2.2	2.2
2,2-$(CH_3)_2$	3	1	1	1	0.0	0.1	6.8	5.7	2.0	1.8
2,3-$(CH_3)_2$[a]	1	2	2	2	1.6	2.4	3.2	4.1	2.6	3.6
2,3-$(CH_3)_2$[b]	1	1	2	2	0.0	0.6	4.6	5.0	1.4	2.0
2,4-$(CH_3)_2$[a]	1	1	2	2	0.8	0.3	4.6	5.0	2.2	1.8
2,4-$(CH_3)_2$[b]	1	1	2	1	2.4	2.3	3.2	3.6	3.4	3.3
2,5-$(CH_3)_2$[a]	2	2	1	1	1.6	1.4	4.6	3.8	3.0	2.6
2,5-$(CH_3)_2$[b]	2	1	1	1	0.0	−0.5	3.2	5.2	1.0	1.1
3,3-$(CH_3)_2$	1	1	1	1	1.6	1.2	4.6	4.1	3.0	2.4
3,4-$(CH_3)_2$[a,c]	2	2	2	2	3.2	2.6	4.6[c]	3.0	4.2	3.6
3,4-$(CH_3)_2$[b,c]	1	1	1	2	0.8	0.8	6.0[c]	3.9	2.2	2.0
2-C_2H_5	1	1	2	2	0.8	0.8	3.4	2.7	1.8	1.6
3-C_2H_5	1	1	1	2	1.6	1.2	4.8	3.5	3.0	2.2

[a] For ring closure to *trans* form. [b] For ring closure to *cis* form. [c] The *dl* closes to give *trans*, and the *meso* to give *cis*. It has been assumed that the open chain material is a 1:1 mixture of the two diastereomers.

and for the reaction we can define ΔF = ΔH = ΔS = O. If now various alkyl groups are substituted on the hexane chain so that various alkylcyclohexanes are obtained upon cyclization, these latter reactions will, relative to the unsubstituted case, generally show negative values for ΔF. The task at hand is to calculate these values of ΔF from elementary principles. It is necessary to calculate ΔH and ΔS separately, and then to find ΔF.

One simplifying assumption is made to facilitate the calculations, which is to consider for each isomer only the form or forms of lowest enthalpy instead of using partition functions. The errors introduced by this approximation are expected to cancel to a large extent when only comparisons between fairly similar compounds are used. The ultimate justification for this approximation is the agreement between the calculated and experimental results.

The calculation of ΔH for the ring closure will be considered first. The experimental values listed in Table I are taken directly from the API tables.[6] The calculated values are arrived at as follows. A given chain structure is considered in the form of minimum enthalpy and the number of *gauche* interactions are counted and substracted from the number of *gauche* interactions in the most stable form of the cyclic reaction product. The result is the increase in *gauche* interactions upon ring closure. The closure of *n*-hexane to cyclohexane requires 6 additional *gauche* interactions. The increase in *gauche* interactions in the substituted case, less this number 6, gives the increase in *gauche* interactions relative to the unsubstituted case. When this increase is multiplied by 0.8 kcal. per *gauche* interaction,[7] the change in enthalpy of ring closure relative to the unsubstituted case is found. These values are listed as the calculated enthalpies in Table I.

Hammond[8] has suggested that the entropy loss upon cyclization is less in the substituted compound than with the corresponding methylene compound since the substituents would restrict the rotation in the acyclic system thereby lowering its entropy.

The entropies of the branched chain hydrocarbons dealt with in the present work have previously been calculated by the statistical method.[9,10] Similar calculations have also been carried out for the methylated cyclohexanes.[11] A simplified approximate expression for calculating the entropy of a branched chain paraffin has also been presented by Pitzer and Scott[12] and is given by Eq. 1 where

$$S = S_n + R\ln 2 + R\ln (I/\sigma_e\sigma_i) - 3.5B \qquad (1)$$

S and S_n are the entropies of the branched and normal isomers, I is the number of optical or other isomers considered, σ_e and σ_i are the symmetry numbers for external and internal rotation respectively, and B is the number of chain branchings. The constant 3.5 is to take care of the branching effects not evaluated in detail and is empirical. Clearly a similar equation can be written for the cyclic compounds. If the ΔS for the ring closure of a substituted hexane (H) to a substituted cyclohexane (C) relative to the parent case of *n*-hexane to cyclohexane is considered, then Eq. 2 may

---

(7) K. S. Pitzer, *Chem. Revs.*, **27**, 39 (1940).

(8) G. S. Hammond, Chapter of *Steric Effects in Organic Chemistry*, edited by M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., 1956, p. 468.

(9) K. S. Pitzer, *J. Chem. Phys.*, **8**, 711 (1940).

(10) K. S. Pitzer and J. E. Kilpatrick, *Chem. Rev.*, **39**, 435 (1946).

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

(12) K. S. Pitzer and D. W. Scott, *J. Am. Chem. Soc.*, **63**, 2419 (1941).

$$\Delta S = R\ln 6 - R\ln 2 + R\ln [I_C/(\sigma_e\sigma_i)_C] - R\ln [I_H/(\sigma_e\sigma_i)_H] + aB \quad (2)$$

be written to describe the entropy of the reaction. The first two terms account for the symmetry present in cyclohexane and *n*-hexane respectively. The constant *a* is to be evaluated empirically. The constant used by Pitzer and Scott (3.5 e.u./branch) contains a contribution from the increased barrier to internal rotation upon branching. The higher rotational barrier leads to a smaller entropy for the branched open-chain structure than for the unbranched one. The cyclic compounds have lost all of their internal rotational entropy (except for the side chains), and consequently the entropy loss upon cyclization is less for the branched structure. Therefore the constant *a* is expected to have a value of less than 3.5. It is found empirically that the best value is 1.2. If Eq. 2 is then rewritten as Eq. 3, the predicted entropies of cyclization for the various compounds can be easily found:

$$S = 2.18 + 1.2B + 1.98 \ln [I_C(\sigma_e\sigma_i)_H/I_H(\sigma_e\sigma_i)_C] \quad (3)$$

The symmetry numbers have the usual meaning, where σ_i applies only to rotation of part of the carbon skeleton, not to the rotation of a methyl. The isomers to be considered in the open-chain compounds are only the actually physically separable ones, not the conformers. For the rings on the other hand, a compound like *cis*-1,2-dimethylcyclohexane is taken to be DL, since it so exists at any instant.[13] The presence of less stable forms, such as axial-methylcyclohexane and boat forms, is ignored as they have a negligible (for present purposes) effect on the free energy.

The total entropy changes calculated are included in Table I, and from these values and the calculated enthalpies the calculated free energies are obtained. The corresponding experimental values for all the cyclohexanes for which data are available are also listed for comparison, and the agreement is satisfactory. The calculated and experimental values are found to differ by 1 kcal./mole at most. This is not much more than the maximum deviation expected from the combined probable errors in the heats of combustion (about 0.2 kcal./mole for each compound). It seems likely that the agreement between theory and experiment would be somewhat improved if the statistical entropies were used, if the corresponding enthalpies were calculated from the partition functions, and if correlation energies[14] were taken into account. The authors feel however that agreement between theory and experiment has been shown, and more refined calculations hardly justify the labor involved. A pronounced shift of equilibrium toward the cyclic compound upon substitution is noted in every case, the free energy changes brought about by substitution varying from 1.6 to 4.2 kcal./mole. The entropy and enthalpy effects are of comparable importance and neither can be neglected if a proper interpretation of the effect is to be made. In more general cases where the product is not the highly symmetrical cyclohexane in the unsubstituted ring closure, the entropy effect will be of lesser importance.

The agreement between the calculated and observed free energies summarized in Table I appears to support the suggestion that a fundamental basis for the *gem*-dimethyl effect as it pertains to equilibria is to be found in the considerations outlined above. These considerations apply in principle to other compounds containing heteroatoms and more complicated substituents although additional factors may also become important in such cases.

The rates at which ring closure reactions occur are also known to be accelerated by the presence of alkyl substituents. If an open-chain compound forms a cycle in the rate determining step of a reaction, the arguments presented here for ΔF, ΔH, and ΔS will carry over directly to $\Delta H^‡$, and $\Delta S^‡$ and consequently to $\Delta F^‡$ and to the rate of ring closure. This is because in a reaction in which the ring closure is the rate determining step, the absolute rate theory shows that $\Delta F^‡$ can be considered as determined by an equilibrium between the starting state (open chain) and transition state. The latter has the geometry of the cyclic system except that one bond is somewhat stretched. The *gauche* interactions in the transition state and cycle are very similar and consequently, as far as the *gem*-dimethyl effect is concerned, going from the open chain to the transition state is essentially the same as going from the open chain to the cycle.

Ring closure reactions in which the cyclization does not occur in the rate-determining step need individual consideration, but can be handled in a straightforward way utilizing the ideas developed previously in conjunction with standard methods of kinetics.

A ring-opening reaction is on the contrary quite a different situation. In this case ordinarily either the rate determining step will be the ring opening, or it will precede the ring opening. In either situation the number of *gauche* interactions is the same in the starting and transition states, and the entropy changes are expected to be relatively independent of the presence of alkyl groups unless there is a direct interaction between the alkyl group and the incoming reagent or the solvation shell. The only way the *gem*-dimethyl effect could apply directly in a ring opening would appear to be in a case where the rate-determining step followed an equi-

---

[13] The treatment of "optical isomerism" used in the cyclic systems is the more correct one. The open chains are treated in a simplified manner because of the large number of conformers which would need to be considered. Justification for this approximation has been made.[10,12]

[14] K. S. Pitzer and E. Cataland, *J. Am. Chem. Soc.*, **78**, 4844 (1956).

librium step between cyclic and noncyclic structures.

It seems reasonable that these ideas should apply to other than six-membered rings, and an examination of the equilibrium data for five-membered rings shows a qualitative parallelism.[6] In this case because of the indefinite ring conformation[15] the concept of *gauche* interactions cannot be applied in as straightforward a manner. For larger and smaller rings again the same qualitative results are expected, but quantitative calculations are difficult and detailed experimental data are unavailable. Qualitatively the existence of a *gem*-dimethyl effect on ring closures in small rings is well known, and it has also been observed in the eight-membered ring.[16]

DETROIT 2, MICH.

---

(15) (a) K. S. Pitzer and W. E. Donath, *J. Am. Chem. Soc.*, **81**, 3213 (1959). (b) F. V. Brutcher, Jr., T. Roberts, S. J. Barr, and N. Pearson, *J. Am. Chem. Soc.*, **81**, 4915 (1959).

(16) Unpublished work of S. Greenberg and S. Hu.

[CONTRIBUTION NO. 114 FROM THE INSTITUTO DE QUIMICA DE LA UNIVERSIDAD NACIONAL AUTONOMA DE MEXICO]

Intensities of Carbonyl Bands in the Infrared Spectra of Substituted Cycloalkanones

RAÚL CETINA AND JOSÉ L. MATEOS

Received September 28, 1959

The molecular extinction coefficient and the integrated absorption areas (A) of the carbonyl group of some alicyclic and aliphatic ketones were measured, and the results, discussed in terms of polar and steric effects, show that the nature of the substituent and the steric environment of the ketone affect the intensity of the carbonyl absorption band.

The stretching vibation of the carbonyl group that occurs in the 1600–1900 cm.$^{-1}$ region has been thoroughly studied.[1] Recently, quantitative studies of the infrared bands have been a subject of attention, and several attempts have been made to correlate the integrated absorption area (A), with molecular structure.[2,3] The work of Jones *et al.* in the steroid field is especially noteworthy.[2] They found that the intensity of the carbonyl band in a five membered ring such as the C-17 position of the steroid molecule (2.69 units) is greater than that of a six membered ring ketone (2.2–2.5 units). The A of an aliphatic ketone, such as a 20-keto steroid, is smaller (1.79 units) while the introduction of a bromine atom in the α-position of the carbonyl lowers the value considerably, *i.e.* 2.55 units for a 3-keto steroid and 1.89 units for a 2-bromo-3-keto steroid. These correlations, and finding that the integrated absorption area is an additive quantity, are very useful for characterizing the type and number of carbonyl groups present in the molecule.

Richards[3] showed that the intensity of the absorption band is related to the nature of the carbonyl group and its value increases in the following order: aldehyde, ketone, acid, chloride, ester, acid, amide.

Brown,[4] studying the intensity of the nitrile band of benzonitriles in various solvents found that the intensity of the band is solvent dependent, and that A increases when the electron release ability of the substituent is increased, *i.e.* in carbon tetrachloride, *p*-methylbenzonitrile has an A of 0.28 units and *p*-chlorobenzonitrile, only 0.20 units.

EXPERIMENTAL

The spectra were recorded on a Perkin Elmer 21 model spectrophotometer equipped with a sodium chloride prism. In order to make 1 μ cover 40 cm. two number 45 gears were installed in the A and C positions.[5]

The solutions were approximately 0.02–0.03 molar (in 10 ml. carbon tetrachloride) depending on the band intensity. A cell 0.049 cm. thick was used. This was measured by the interference fringe method and with a microscope, focusing the upper and lower windows in the inner part and measuring the difference. By using a cell of this width the error in nonuniformity and changes in the width is believed to be less than 1%.

All the measurements were made under the same experimental conditions in order to get the minimum possible error.

The absorption curves were measured over a frequency range of 100 cm.$^{-1}$ on each side of the maximum with a slit opening of 49 μ. The enlargement of the scale allows one to measure $\Delta\nu$ 1/2 in a very accurate way.

The integrated absorption areas were calculated by the direct integration method by means of the equation[6]:

$$\mathrm{A} = \frac{K}{cl} \log_{10} \frac{I_0}{I} \Delta\nu\ 1/2 \qquad (1)$$

---

(1) For leading references see R. N. Jones and C. Sandorfy, Chapter IV in *Chemical Applications of Spectroscopy*, Technique of Organic Chemistry, Vol. IX. Interscience Publishers, Inc., New York, 1956.

(2) R. N. Jones, D. A. Ramsay, D. S. Keir, and K. Dobriner, *J. Am. Chem. Soc.*, **74**, 80 (1952).

(3) R. E. Richards and W. R. Burton, *Trans. Faraday Soc.*, **45**, 874 (1949).

(4) T. L. Brown, *J. Am. Chem. Soc.*, **80**, 794 (1958).

(5) For a more complete description see the Perkin Elmer manual.

(6) D. A. Ramsay, *J. Am. Chem. Soc.*, **74**, 72 (1952).