methylcyclohexanone (VI) as shown below by dehydrobromination with 2,4-dinitrophenylhydrazine. R.D. in *methanol* (c 0.0895): $[\alpha]_{700}$ +18.5°, $[\alpha]_{589}$ +36°, $[\alpha]_{335}$ +634°, $[\alpha]_{290}$ −319°, $[\alpha]_{265}$ +313°. R.D. (Fig. 1) in *octane* (c 0.046): $[\alpha]_{700}$ +126°, $[\alpha]_{589}$ +147°, $[\alpha]_{337.5}$ +832°, $[\alpha]_{295}$ −381°.

Anal. Calcd. for $C_7H_{11}BrO$: C, 43.97; H, 5.76; Br, 41.88; O, 8.38. Found: C, 44.08; H, 5.69; Br, 41.53; O, 8.26.

5-Methylcyclohex-2-en-1-one 2,4-dinitrophenylhydrazone (Vb). To a solution of 300 mg. of *trans*-2-bromo-5-methylcyclohexanone (IV t) in 10 cc. of glacial acetic acid,[14a] which was heated on a hot plate in a current of nitrogen, was added 339 mg. of 2,4-dinitrophenylhydrazine and heating was continued for 10 min. Water was added, the product was extracted with benzene, the latter was concentrated and then filtered through a short column of Fischer activated alumina. The resulting 2,4-dinitrophenylhydrazone was recrystallized from ethanol–ethyl acetate to provide 240 mg. of orange-red crystals, m.p. 143–145°, $[\alpha]_D$ −219° (c 0.06 in chloroform), $\lambda_{max}^{CHCl_3}$ 380 mμ,[30] log ϵ 4.45.

Anal. Calcd. for $C_{13}H_{14}N_4O_4$: C, 53.79; H, 4.86; N, 19.30. Found: C, 54.00; H, 5.03; N, 19.77.

Dehydrobromination of the liquid bromo-3-methylcyclohexanone mixture with 2,4-dinitrophenylhydrazine. The above liquid bromoketone mixture (320 mg.) was dehydrobrominated in acetic acid solution with 365 mg. of 2,4-dinitrophenylhydrazine exactly as described in the preceding experiment. The total 2,4-dinitrophenylhydrazone obtained after filtration through a small column of alumina but *before* recrystallization exhibited m.p. 132–156°, $[\alpha]_D$ −100° (c 0.27 in chloroform) from which a composition of *ca.* 45% IV and 55% VI can be calculated.

This mixture of 2,4-dinitrophenylhydrazones was chromatographed on 20 g. of Fischer activated alumina using hexane-benzene (6:4) as the developing agent and collecting fourteen 50-cc. fractions. The separation was followed by determining the rotation of various eluates and the first six fractions were combined and recrystallized from ethanol-ethyl acetate to provide 5-methylcyclohex-2-en-1-one 2,4-dinitrophenylhydrazone (Vb), m.p. 138–142°, $[\alpha]_D$ −221°. After some intermediate fractions ($[\alpha]_D$ −105°), there appeared optically inactive hydrazone and the last five fractions were combined and recrystallized from ethanol-ethyl acetate to yield 50 mg. of 3-methylcyclohex-2-en-1-one 2,4-dinitrophenylhydrazone (VII), m.p. 178–179.5°, $[\alpha]_D$ ±4° (c 0.144 in chloroform).

Anal. Calcd. for $C_{13}H_{14}N_4O_4$: C, 53.79; H, 4.86; N, 19.30. Found: C, 54.16; H, 5.11; N, 19.36.

trans-2-Chloro-5-methylcyclohexanone (VIII t). A mixture of 16.5 g. of sulfuryl chloride and 16.5 cc. of carbon tetrachloride was added dropwise at room temperature with stirring to 13.73 g. of (+)-3-methylcyclohexanone (III) dissolved in 65 cc. of carbon tetrachloride. No heat was evolved and when addition was completed, the pale yellow solution was washed successively with water, sodium bicarbonate solution, and finally with saturated salt solution. After drying and removing the carbon tetrachloride by careful distillation through a Vigreux column, the residue was fractionally distilled at 12 mm., seven fractions being collected. The residue from the distillation was semisolid and after sublimation at 61°/1.3 mm. furnished 215 mg. of chloroketone. Similarly, storage of the last two distillate fractions (b.p. 91°/12 mm. and 74°/3 mm.) in the ice box provided additional crystalline material and combination of these, followed by sublimation, furnished a total of 1.54 g. of *trans*-2-chloro-5-methylcyclohexanone (VIII t), m.p. 67–69°. The analytical sample was recrystallized from petroleum ether and sublimed, whereupon it exhibited m.p. 68–69°, $[\alpha]_D$ +6.4° (c 0.88 in chloroform). R.D. (Fig. 2) in *methanol* (c 0.096): $[\alpha]_{700}$ +9.3°, $[\alpha]_{589}$ +10°, $[\alpha]_{305}$ +755°, $[\alpha]_{295}$ +354°. R.D. (Fig. 2) in *octane* (c 0.0825): $[\alpha]_{700}$ −41°, $[\alpha]_{589}$ −81° $[\alpha]_{330}$ −1092°, $[\alpha]_{315}$ −191°. R.D. in *carbon tetrachloride* (c 0.051): $[\alpha]_{700}$ −16°, $[\alpha]_{589}$ −20°, $[\alpha]_{332.5}$ −1002°, $[\alpha]_{300}$ +795°.

Anal. Calcd. for $C_7H_{11}ClO$: C, 57.34; H, 7.55; Cl, 24.19; O, 10.92. Found: C, 56.97; H, 7.71; Cl, 23.80; O, 11.07.

The position of the chlorine atom was established by dehydrochlorination with 2,4-dinitrophenylhydrazine exactly as described for the corresponding bromoketone IV t, and afforded orange-red needles of 5-methylcyclohex-2-en-1-one 2,4-dinitrophenylhydrazone (Vb), m.p. 140–142°, $[\alpha]_D$ −211°.

Acknowledgment. We are indebted to the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service, for a research grant (No. CY-2919).

DETROIT, MICH.

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(30) See C. Djerassi and E. Ryan, *J. Am. Chem. Soc.*, **71**, 1000 (1949).

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

Conformational Analysis. VI.[1a] Optical Rotatory Dispersion Studies. XXVII.[1b] Quantitative Studies of an α-Haloketone by the Rotatory Dispersion Method

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The equilibrium between the conformational isomers of *trans*-2-bromo-5-methylcyclohexanone (I t) has been examined in a variety of solvents by measurements of dipole moments, and infrared and ultraviolet spectra. Under all conditions used in this work, the halogen atom was found to be predominantly in the equatorial conformation. A study of the rotatory dispersion curves of I t and of equilibrium mixtures of I c and I t in various solvents shows that such curves can be used in a quantitative manner for the determination of conformational equilibria.

INTRODUCTION

The qualitative usefulness of rotatory dispersion curves in establishing the conformations and absolute configurations of α-haloketones has been well established.[3] A quantitative study of con-

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[1] (a) Paper V, ref. 13; (b) Paper XXVI, ref. 4.

[2] Present address; Department of Chemistry, Stanford University, Stanford, California.

[3] (a) C. Djerassi and W. Klyne, *J. Am. Chem. Soc.*, **79**, 1506 (1957); (b) C. Djerassi and L. E. Geller, *Tetrahedron*, **3**, 319 (1958); (c) C. Djerassi, I. Fornaguera, and O. Mancera, *J. Am. Chem. Soc.*, **81**, 2383 (1959).

formational equilibria by this method is also possible and forms much of the subject of this paper. The approach used is strictly empirical and although the quantitative aspects of the theory of the rotatory dispersion Cotton effect are not yet completely understood, such an understanding is not essential to the present work.

For these studies an α-halocyclohexanone was desired which could be obtained optically active and which would exist as a mixture containing comparable amounts of two conformers. The compound chosen was *trans*-2-bromo-5-methylcyclohexanone (I t), the synthesis of which has been described.[4]

As the methyl group in I t[5] prefers to be equatorial while the bromine atom prefers to be axial, the opposed and nearly balanced forces will cause the compound to exist in solution as a mixture containing both the I t,e and I t,a conformers. The Cotton effect is positive for (+)-3-methylcyclohexanone in which the carbon atom bearing the methyl group is known[6] to have the R[7] configuration. Consequently I t,e and I t,a are expected, from the "axial α-haloketone rule",[3a] to show positive and negative Cotton effects, respectively. The observed Cotton effect curve of I t is then a resultant of two opposing curves, and should be a measure of the point of equilibrium between the two conformers. As an unfavorable electrostatic repulsion exists between the bromine and oxygen atoms, I t,e will become more stable relative to I t,a as the effective dielectric constant of the solvent is increased.[8] Qualitatively then, the observed Cotton effect of I t should become increasingly positive as the solvent becomes increasingly polar, and this is what is found experimentally.

RESULTS AND DISCUSSION

One of the objectives of the present work was to establish the quantitative applicability of rotatory dispersion measurements to conformational problems. The second principal objective was to show that the energy of an α-bromine atom in a cyclohexanone ring, as found from earlier work,[8,9] could be used, together with the known conformational energy of a methyl group (a 3-alkylcyclohexanone[10] in this case), to calculate the equilibrium constant for a simple system such as I t, and the variation of this constant with solvent. The correctness of these calculated equilibrium constants was checked by measurements of the dipole moment, and infrared and ultraviolet spectra, as functions of solvent.[8,11]

The energy of an axial methyl group (3-alkylcyclohexanone) relative to the corresponding equatorial form is 0.80 kcal./mol. The energy of an equatorial bromine atom relative to the axial one (2-bromocyclohexanone) varies with solvent and is assigned the following values from the earlier dipole moment work of Kumler and Huitric[8,9]: 0.45 kcal./mole in heptane, 0.24 kcal./mole in benzene, and 0.02 kcal./mole in dioxane. From these numbers it was possible to calculate the energy[12] of I t,a relative to I t,e. From the relationship $E = -RT \ln K_t$, the equilibrium constants for the conformational change and the percentages of the axial conformer in I t were also calculated and the values are given in Table I.

Of the various methods which have been used for determining conformational composition in systems similar to the one at hand, the dipole moment usually has yielded the most accurate results.[8,9,13] The dipole moment of I t was, therefore, measured in heptane, benzene and dioxane solution. The conformational compositions of I t were calculated from the observed moments in the usual way, and the percentages of axial isomer thus obtained are also included in Table I. The agreement between the conformational equilibrium predicted and that found from the dipole moments is satisfactory, the variation being 0.1–0.2 kcal.

TABLE I

DATA FOR CONFORMATIONAL ISOMERS OF *trans*-2-BROMO-5-METHYLCYCLOHEXANONE (I t)

	Calculated		Per Cent I t,a by Various Methods				
Solvent	$E_{I\ t,a} - E_{I\ t,e}$ Kcal./Mole	K_t	Calcd.	μ	I.R.	U.V.	R.D.
Heptane	0.35	1.82	36	45	39	37	44
Carbon tetrachloride	—	—	—	—	36	36	38
Chloroform	—	—	—	—	32	—	—
Benzene	0.56	2.57	28	29	30	—	—
Dioxane	0.77	3.70	21	19	26	18	20
Ethanol	—	—	—	—	—	16	18
Methanol	—	—	—	—	—	11	17

The high-resolution infrared spectrum of the carbonyl region of I t was obtained in various solvents, and the curves are reproduced in Fig. 1.

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[4] C. Djerassi, L. E. Geller, and E. J. Eisenbraun, *J. Org. Chem.*, preceding paper.

[5] As suggested to us by Dr. W. Klyne, we are using two suffixes: the first denotes configuration (*c* = *cis*, *t* = *trans*), while the second one refers to the orientation of the halogen atom (*e* = equatorial, *a* = axial). The equilibrium mixture of conformers bears only the configurational suffix.

[6] For leading references see E. J. Eisenbraun and S. M. McElvain, *J. Am. Chem. Soc.*, **77,** 3383 (1955).

[7] R. S. Cahn, C. K. Ingold, and V. Prelog, *Exper.*, **12,** 81 (1956).

[8] J. Allinger and N. L. Allinger, *Tetrahedron*, **2,** 64 (1958).

[9] W. D. Kumler and A. C. Huitric, *J. Am. Chem. Soc.*, **78,** 3369 (1956).

[10] W. Klyne, *Exper.*, **12,** 119 (1956).

[11] N. L. Allinger and J. Allinger, *J. Am. Chem. Soc.*, **80,** 5476 (1958).

[12] Energy and free energy are taken to be interchangeable here.

[13] J. Allinger and N. L. Allinger, *J. Am. Chem. Soc.*, **81,** 5736 (1959).

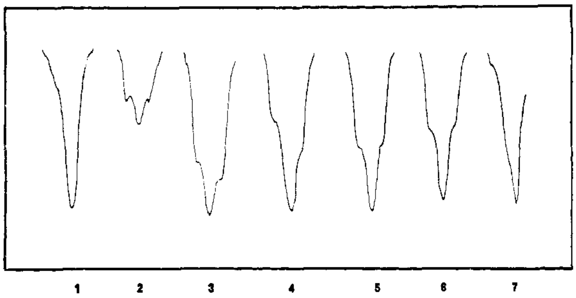

Fig. 1. The infrared carbonyl absorption spectra of I t in various solvents. The numbers correspond to the following solvents: 2, heptane; 3, carbon tetrachloride; 4, chloroform; 5, benzene; 6, dioxane; 7, dimethyl sulfoxide. The band numbered 1 is the parent 3-methylcyclohexanone

Three bands were usually seen. Two of these bands had the approximate relative intensities and showed frequency shifts relative to the unbrominated parent ketone of the proper magnitude (5 cm.$^{-1}$ and 10–25 cm.$^{-1}$) to be assigned to the conformers I t,a and I t,e respectively.[8,11,14] The "extra" band was variable in intensity and was found at a frequency 15 to 30 cm.$^{-1}$ higher than that of the parent ketone. The extra band occurred at 1754 cm.$^{-1}$ (in carbon tetrachloride), and there was present a strong band at 865 cm.$^{-1}$, which suggests that the former is an overtone of the absorption at 865 cm.$^{-1}$, intensified by Fermi resonance. Evidence for a similar situation in the case of 2-bromo-4-cyclopentenone was recently obtained by Yates and Williams.[15] Because of the incomplete resolution of the bands due to the two conformers it was not possible to establish their relative integrated intensities. What could be done easily was to measure the relative apparent extinction coefficients of the two conformers. In this way a rough measure of the ratio of the conformers was found. The approximate conformational composition thus determined is in satisfactory agreement with the calculated values (Table I).

TABLE II

ULTRAVIOLET SPECTRA OF 3-METHYLCYCLOHEXANONE, AND *trans*-2-BROMO-5-METHYLCYCLOHEXANONE

	3-Methylcyclohexanone		*trans*-2-Bromo-5-methylcyclohexanone	
Solvent	λ_{max}	ϵ	λ_{max}	ϵ
Methanol	283	17	292	22
Ethanol	285	18	294	28
Dioxane	287	16	301	30
Carbon tetrachloride	294	14	310	50
Octane	290	14	310	51

The ultraviolet spectra in different solvents were also examined for the bromo compound and for the parent ketone. The data are summarized in Table II.

The wave length shifts are qualitatively consistent with an increasing amount of equatorial isomer[11,16] with increasing solvent polarity. The magnitude of the extinction coefficient is quantitatively more useful. If the reasonable assumptions are made that the extinction coefficients are 20 and 120 at the maxima for the equatorial and axial conformers respectively,[11] and that the extinction coefficient of the equatorial isomer at the wave length where the axial one has its maximum is 10, the approximate conformational composition can be calculated (see Table I). Again the agreement is very good.

It seems clear then that each of these methods is capable of yielding within the experimental limitations imposed by the particular systems, the conformational composition of such a simple α-bromocyclohexanone.

As is shown in Table I, conformer I t,e always predominates in solution, yet x-ray crystallography has shown that the compound exists in the other conformation, I t,a, in the crystal lattice.[17] Although it is generally recognized[18] that there exists the possibility of a flexible cyclohexane ring having a different preferred conformation in solution from that in the crystal, this is one of the very few cases known where this situation has been demonstrated experimentally.

For a quantitative determination of conformational composition from the rotatory dispersion curves, certain requirements must be satisfied.

One which appears to be met is that it must be experimentally possible to measure the amplitude of the curve to the desired accuracy. Another requirement is that ideal solutions must exist. In the present study, 10^{-3} M concentrations of I t were employed so this condition was probably realized. Finally, the amplitude of the curve $[a]$ for each pure conformer (x and y) must be known, and the peaks and troughs must occur at nearly the same wavelength. If each of these conditions is satisfied, then from the observed amplitude $[a]$[19] and the relationship $[a] = \mathrm{Nx}[a_x] + (1-\mathrm{Nx})[a_y]$, the mole fraction (Nx) of conformer x can be found. The difficulty encountered in the present study arises from the fact that the amplitudes of the molecular rotations of pure I t,a and I t,e cannot be directly determined.

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(14) (a) R. N. Jones, D. A. Ramsay, F. Herling, and K. Dobriner, *J. Am. Chem. Soc.*, **74**, 2828 (1952); (b) E. J. Corey, *J. Am. Chem. Soc.*, **75**, 2301, 3297 (1953).

(15) P. Yates and L. L. Williams, *J. Am. Chem. Soc.*, **80**, 5896 (1958).

(16) R. C. Cookson, *J. Chem. Soc.*, 282 (1954).

(17) Private communication from Dr. R. Pepinsky, Pennsylvania State University.

(18) D. H. R. Barton and R. C. Cookson, *Quart. Rev.*, **10**, 44 (1956).

(19) For basic nomenclature see C. Djerassi and W. Klyne, *J. Chem. Soc. (Proc.)*, 55 (1957). For convenience the symbol $[a]$ will be used to indicate the amplitude of the molecular rotation prefaced usually by a plus or minus sign to indicate the sign of the Cotton effect.

The relationships of the axial haloketone rule[3a] offer a possible solution to this dilemma. When an equatorial halogen is introduced adjacent to a keto group, no essential change in the amplitude of the curve occurs. Introduction of an axial halogen, however, produces a large change in the amplitude, the sign of which is predictable from the absolute configuration of the parent ketone. For I t, it is necessary to make the approximation that the amplitude change from I t,e to I t, a is only negligibly influenced by the conformational change associated with the methyl group and that the major influence on the amplitude is due to the concurrent change of the bromine substituent. The magnitude of this amplitude change might be expected to be relatively constant from one α-haloketone to another. If such were the case, an approximate value for $[\alpha]_{\mathrm{I}\ t,a}$ could be estimated.

Values of $[\alpha]$ for several α-bromo keto steroids in which the bromine substituent is axial and secondary and those of the parent keto steroids are available[20] and the changes ($\Delta[\alpha]$) in the molecular amplitude associated with the introduction of the bromine atom are presented in Table III.

TABLE III

CHANGES IN MOLECULAR AMPLITUDES ON INTRODUCTION OF AXIAL BROMINE

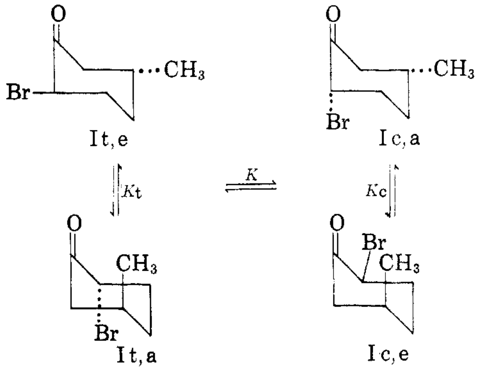
Compound	$\Delta[\alpha]^a$
2α-Bromofriedelin	−15,600°
7α-Bromocholestan-3β,5α-diol-6-one 3-acetate	+19,200°
7α-Bromocholestan-3β,5α-diol-6-one 3,5-diacetate	+24,500°
Methyl 11β-Bromo-3α-acetoxy-12-ketocholanate	−19,600°
6β-Bromo-3β-acetoxycholestan-7-one	+15,700°
12α-Bromo-3β-acetoxyergostan-11-one	−16,100°
3α-Bromoandrostan-2-one-17β-ol propionate	+19,400°

[a] $\Delta[\alpha]$ is the change in molecular amplitude (see ref. 19) which occurs when the axial bromine atom is introduced into the parent ketone.

It is seen that $\Delta[\alpha]$ varies somewhat and this can probably be attributed to the different types and numbers of asymmetric centers in each compound. If only very similar systems were compared, a more consistent $\Delta[\alpha]$ would probably be realized. Nevertheless, the rough value for $\Delta[\alpha]$ of 19,000 could be used to obtain the magnitude of the molecular rotation of I t,a and this would allow at least a crude approximation of the conformer composition of I t. A more accurate value for $[\alpha]_{\mathrm{I}\ t,a}$ was available from the dipole measurement of I t in dioxane which estimated 19% of I t,a to be present in this solution. If the value +2690° is taken[21] for $[\alpha]_{\mathrm{I}\ t,e}$ then from the amplitude of the observed Cotton effect curve of I t in dioxane ($[\alpha] = -3{,}940°$) $[\alpha]_{\mathrm{I}\ t,a}$ is calculated to be −32,200°. Employing these amplitudes for I t,a and I t,e along with the measured amplitudes of the Cotton effect curves of I t in various solvents the percent of axial conformer present in the various media was calculated. The results are presented in Table I and the agreement with the values obtained by other methods is good.

Rotatory dispersion measurements thus provide a useful method for the determination of conformational equilibria. The application of this analytical procedure to simple α-halo ketones is limited largely by the necessity of having optically active compounds.

The equilibrium I t $\rightleftarrows$ I c can be readily established by hydrogen bromide treatment of the *trans* isomer (I t). Furthermore, the *cis* isomer (I c) allows the most energetically favorable conformations for each substituent (methyl, equatorial; bromine, axial) and the equilibrium constant K is therefore anticipated to be greater than one in any of the solvents of the present study. As *cis* I, analogous to *trans* I, would exist as a mixture of two conformers, I c,e and I c,a, the proportion of which would be described by a solvent-dependent equilibrium constant K_c, the equilibrium mixture of I t,c would contain four conformers.[22] The equilibrium situation is described as follows. (As a generalized thermodynamic treatment of two isomers, each having two conformers, is straightforward



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[20] C. Djerassi, J. Osiecki, R. Riniker, and B. Riniker, *J. Am. Chem. Soc.*, **80**, 1216 (1958).

[21] Actually the conformational composition of 3-methylcyclohexanone is expected to be the same in any inert solvent. Consequently the amplitude of the Cotton effect curve of this compound should be solvent-independent, and this was found experimentally. It was found that $[\alpha]$ had the value 2690° ± 40° in methanol and octane. Lack of solvent transparency prevented measurement of the complete curve in dioxane, but the observed portion of the curve was identical with the other two, and the same value of $[\alpha]$ is assumed. It has now been found (C. Djerassi, E. Warawa, R. E. Wolff, and E. J. Eisenbraun, *J. Org. Chem.* in press) that introduction of a bromine into the equatorial position at carbon 5 in optically active 3-*t*-butylcyclohexane causes a small change (1220°) in $[\alpha]$. This small change supports the assumption of negligible change made above. If this value is taken into account in calculating the quantities in the R. D. column of Table I, these quantities would be changed by about 3–4% in heptane and carbon tetrachloride and 0–1% in the other solvents. These changes are less than the probable errors in the quantities listed.

[22] The amount of flexible forms is quite small, and is ignored. (See N. L. Allinger, *J. Am. Chem. Soc.*, **81**, 5727 (1959).

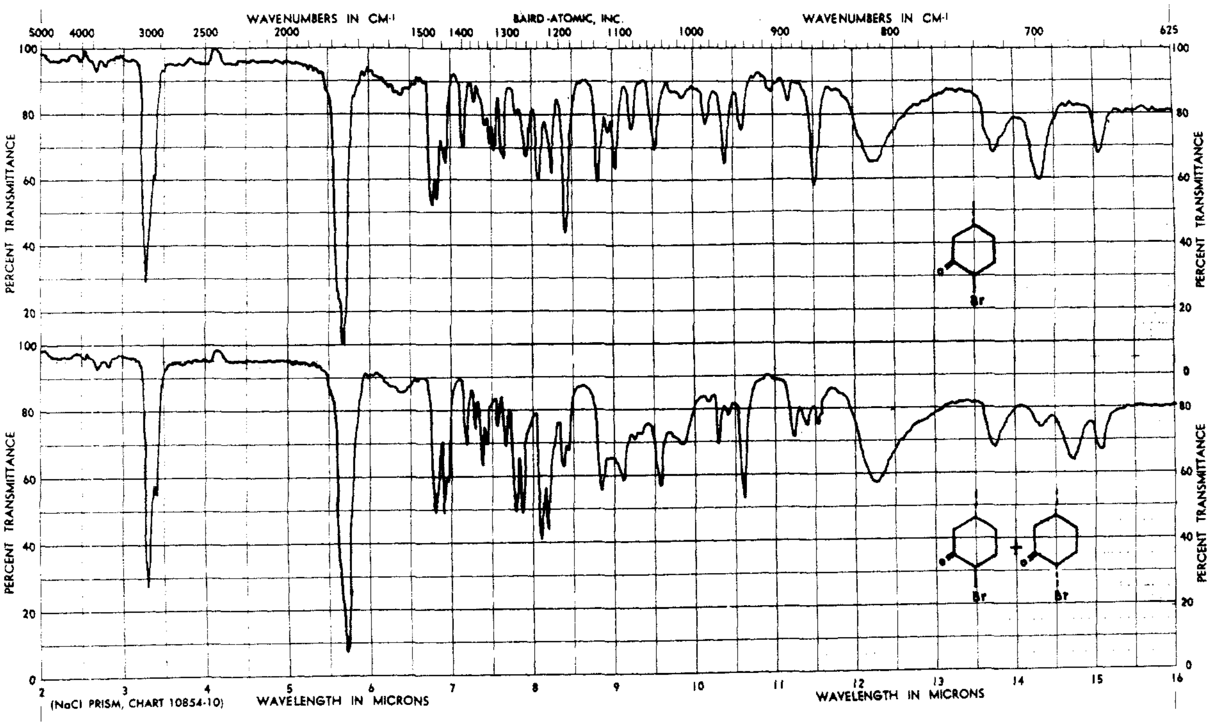

Fig. 2. Infrared absorption spectra of *trans*-2-bromo-5-methylcyclohexanone (It) and of hydrogen bromide catalyzed equilibrium mixture of It ⇄ Ic in carbon tetrachloride solution

but laborious, the equilibrium relationships have been found using the method of Eliel and Ro.[23])

The symmetry number is one for each conformer, and it is assumed that there is no entropy effect due to restricted rotation of the methyl group in any conformation.[24] If K is designated as the equilibrium constant for the isomerization *trans* I ⇄ *cis* I, the relationships between the equilibrium constants are:

(1) By definition:

$$K = \frac{\text{I c,a} + \text{I c,e}}{\text{I t,a} + \text{I t,e}},\ K_c = \frac{\text{I c,e}}{\text{I c,a}},\ K_t = \frac{\text{I t,e}}{\text{I t,a}}$$

Substituting:

$$K = \frac{\text{I c,a} + K_c\,\text{I c,a}}{\text{I t,a} + K_t\,\text{I t,a}}$$

(2) Therefore:

$$K = \frac{\text{I c,a}}{\text{I t,a}} \times \frac{1 + K_c}{1 + K_t}$$

The quantity $\frac{\text{I c,a}}{\text{I t,a}}$ is the equilibrium constant for the conformational change axial 3-methyl→equatorial 3-methylcyclohexanone and as such has the value 3.86 and is solvent-independent. K_c is solvent-dependent and the same type of theoretical treatment employed to obtain K_t gave calculated values for K_c of 0.121, 0.172, 0.251[25] in heptane, benzene and dioxane, respectively. The theoretical values of K_t in benzene and dioxane (Table I) were employed but since a value of K_t = 1.27 for heptane solution was available from rotatory dispersion and dipole moment data, this experimental number was used in that case. The calculated values for K are 1.92 (heptane), 1.29 (benzene) and 1.10 (dioxane); in other words, 38%, 44%, and 49% of I t are predicted to be present at equilibrium in the respective solvents. Pure I t was treated with dry hydrogen bromide in both carbon tetrachloride and benzene solution and the infrared spectrum of each acid-freed solution was obtained and compared with that of the pure *trans* isomer (I t) in each solvent. The amount of I t in an equilibrated sample was estimated using the available strong bands (see Fig. 2) and assuming that I c did not absorb at these wave lengths. The percentage of *trans* isomer calculated from various bands was as follows: carbon tetrachloride 17.1% (14.3μ), 18.2% (11.55μ), 24.4% (8.43μ); benzene 22.8% (11.55μ), 29.4% (10.40μ), 42.8% (8.48μ), 48% (7.59μ).

The data are only fair but appear to indicate 20 ± 4% of the *trans* form (I t) in carbon tetrachloride and 35 ± 10% in benzene solution. Within the sizeable limits of experimental error, the calculated and found values agree for the solution in benzene but not in carbon tetrachloride. The possibility exists that a complex between the ke-

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[23] E. L. Eliel and R. S. Ro, *J. Am. Chem. Soc.*, **79**, 5992 (1957).

[24] Such was the case with the 1,3- and 1,4-dimethylcyclohexanones (C. W. Beckett, K. S. Pitzer, and R. Spitzer, *J. Am. Chem. Soc.*, **69**, 977, 2488 (1947).

[25] These equilibrium constants give values for $E_{I\ c,e} - E_{I\ c,a}$ of +1.25, +1.04 and +0.82 kcal./mole in heptane, benzene and dioxane, respectively.

tone and hydrogen bromide is formed in carbon tetrachloride, the existence of which would be expected to influence strongly the position of conformer and isomer equilibria. Such a complex was looked for in an earlier similar case, but no evidence for its existence could be found.[11] It was shown that the hydrogen bromide treatment of I t did not cause any rearrangement to 2-bromo-3-methylcyclohexanone by preparing the 2,4-dinitrophenylhydrazone of the equilibrated mixture (which yielded only 5-methylcyclohex-2-en-1-one 2,4-dinitrophenylhydrazone), and by measuring the rotatory dispersion curve of the mixture. The presence of rearranged bromide would have led to a diminution in amplitude which was not observed.

More sensitive measurements of these equilibria were made by means of the rotatory dispersion curves. The rotatory dispersion curve of I t in carbon tetrachloride is shown in Fig. 3. Also shown is the curve obtained from the hydrogen bromide catalyzed equilibrium mixture I t ⇄ I c, the difference between the curves being noteworthy. Analysis of the isomer composition proceeded as follows:

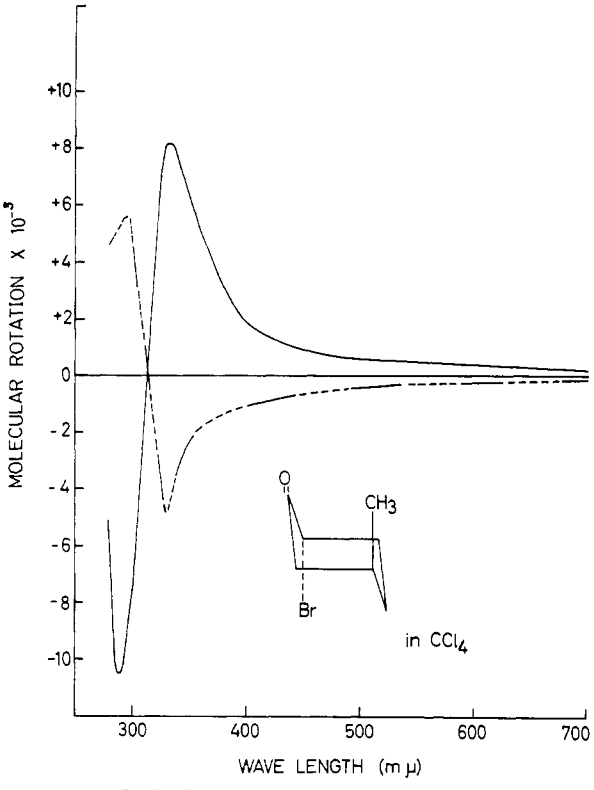

Fig. 3. Optical rotatory dispersion curves of *trans*-2-bromo-5-methylcyclohexanone (I t) and of hydrogen bromide catalyzed equilibrium mixture of I t ⇄ I c in carbon tetrachloride solution

The amplitudes assigned to conformers I t,e and I c,e were the same as for the parent ketone, +2690°, while to I t,a and I c,a there were assigned the value −32,200° and +32,200°, respectively. Knowing the value of [α] for each conformer and the equilibrium constants involved, the molecular amplitudes for I t and I c were calculated to be −12,500° and +29,000° in heptane solution. Using these parameters as reasonable approximations for carbon tetrachloride (on the basis of the similarity of the value of [α] of I t in both heptane and carbon tetrachloride), the observed value of [α] = +18,360° for the equilibrated mixture in that solvent indicated that the mixture contained 21% of I t. This value is in excellent agreement with that obtained (20%) by infrared analysis.

EXPERIMENTAL[26]

trans-2-Bromo-5-methylcyclohexanone (I t). The synthesis of this optically active ketone, m.p. 83.5–84°, was described earlier.[4] The infrared carbonyl spectra were obtained with a Beckmann IR-4 instrument with a scanning time of 0.02 μ/min. The data are summarized in Table I and the absorption spectra are reproduced in Fig. 1. The ultraviolet spectra were obtained with a Beckmann Spectrophotometer, model DU, with a Spectracord attachment. More or less fine structure appeared in the n → π* band. The constants λ_{max} and ε are given (Table II) for a smoothed curve in which the fine structure is averaged out. The rotatory dispersion measurements were performed as described else-

TABLE IV

Dipole Moment Data for *trans*-2-Bromo-5-methylcyclohexanone (I t)

N_2	d_{12}	ϵ_{12}
	Solvent—Heptane	
0.0078106	0.683786	1.9896
0.0054452	0.682235	1.9659
0.0042453	0.681418	1.9535
0.0029712	0.680599	1.9407
0.0015456	0.679620	1.9261
0.0000000	0.678579	1.9114
α = 10.1385	β = 0.66671	$P_{2\infty}$ = 325.47 cc.
ϵ_1 = 1.9105	d_1 = 0.678593	μ = 3.74 D
	Solvent—Benzene	
N_2	d_{12}	ϵ_{12}
0.0057103	0.877178	2.3962
0.0035907	0.875366	2.3490
0.0027275	0.874776	2.3296
0.0013474	0.873630	2.3007
0.0011227	0.873395	2.2966
0.0003330	0.872782	2.2775
0.0000000	0.872482	2.2716
α = 21.814	β = 0.81726	$P_{2\infty}$ = 361.38 cc.
ϵ_1 = 2.2710	d_1 = 0.872498	μ = 3.96 D
	Solvent—Dioxane	
N_2	d_{12}	ϵ_{12}
0.0061965	1.030456	2.3479
0.0035127	1.028849	2.3279
0.0026912	1.028432	2.2653
0.0018567	1.027908	2.2450
0.0010017	1.027420	2.2245
0.0000000	1.026777	2.2024
α = 23.583	β = 0.59111	$P_{2\infty}$ = 382.96 cc.
ϵ_1 = 2.2017	d_1 = 0.973497	μ = 4.09 D

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(26) Pure samples of heptane and octane were used interchangeably as solvents in this work.

where.[27] The values of $[\alpha]$ in various solvents are as follows[4]: methanol, −3,100°; ethanol, −3,700°; dioxane, −4,100°; carbon tetrachloride, −10,440°; octane, −12,500°.

Equilibration experiments. A 1.0-g. sample of *trans*-2-bromo-5-methylcyclohexanone (I t)[4] was dissolved in a solution prepared from 0.32 g. of anhydrous hydrogen bromide and 40 ml. of carbon tetrachloride. The mixture was allowed to stand at room temperature for 2 hr., after which time it was washed with water, dilute sodium bicarbonate solution and water. After drying, the infrared spectrum was obtained directly on the solution.

A similar isomerization was carried out in benzene solution. To show the absence of bromine migration under these conditions, 97 mg. of the bromoketone I t was dissolved in 1 ml. of carbon tetrachloride which had been saturated with dry hydrogen bromide. The solution was allowed to stand overnight at room temperature, after which time 108 mg. of 2,4-dinitrophenylhydrazine in 5 ml. of acetic acid was added. The solution was warmed under nitrogen for 10 min. and was diluted with benzene. After washing with water, the benzene concentrate was poured through a column of Fisher alumina. The benzene was removed from the eluate by distillation and the crude solid residue had $[\alpha]^{25}_{D}$ −200° (chloroform; c, 0.369). The pure 2,4-dinitrophenylhydrazone[4] of 5-methylcyclohex-2-en-1-one has $[\alpha]^{25}_{D}$ −219° (chloroform; c, 0.06).

Dipole moments. The apparatus used for the dielectric constant measurements has been described.[28] The benzene and heptane solvents were purified by refluxing reagent grade solvents with sodium followed by distillation from sodium. The dioxane was purified according to Fieser.[29] The dielectric constant and density were measured with solutions of various mole fractions as indicated in Table IV. The calculations were made following the general procedure of Halverstadt and Kumler[30] as described earlier.[31] The molar refractivity was calculated from standard values[32] of atomic refractivities and had the value 65.929 c.c. Atomic polarization was neglected. Experimental error is about 0.02 D.

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[27] C. Djerassi, E. W. Foltz, and A. E. Lippman, *J. Am. Chem. Soc.*, **77**, 4354 (1955); C. Djerassi "Optical Rotatory Dispersion: Applications to Organic Chemistry," New York, McGraw-Hill, Chapter 3.

[28] M. T. Rogers, *J. Am. Chem. Soc.*, **77**, 3681 (1955).

[29] L. F. Fieser "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 368.

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

[31] N. L. Allinger, *J. Am. Chem. Soc.*, **79**, 3443 (1957).

[32] J. A. Leermakers and A. Weissberger, in H. Gilman "Organic Chemistry", Vol. II, Second Edition, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 1751.

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT OF THE WESTVACO CHLOR-ALKALI DIVISION AND THE CENTRAL RESEARCH LABORATORY OF THE FOOD MACHINERY AND CHEMICAL CORP.]

α-Oximino Ketones. IV. The "Normal" and "Abnormal" Beckmann Rearrangements[1]

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The Beckmann rearrangement of α-oximino ketones possessing the *anti* configuration, whether brought about by acid chlorides like phosphorus pentachloride or thionyl chloride, by strong acids like sulfuric or trifluoroacetic, or by acylating agent and base, has been shown to proceed "abnormally", that is by cleavage to a nitrile and a carboxylic acid. If an amide product is obtained, it is always that which arises from hydrolysis of the nitrile initially formed. It is proposed that the term "second order" be retained to describe this type of Beckmann rearrangement, which is characterized by shift of an electron pair only.

It was observed a long time ago that α-oximino ketones possessing the *anti* or α-configuration behaved differently from simple ketoximes when treated with an acylating agent and base, in that they were cleaved to a carboxylic acid and a nitrile instead of giving the normal amide product of the Beckmann rearrangement.[2-4] This cleavage reaction has been called a Beckmann rearrangement of the second order[2,4] or an "abnormal" rearrangement. In contrast, it is generally stated or implied that rearrangement of α-oximino ketones with acids or acid chlorides such as phosphorus pentachloride proceeds "normally," that is, through an amide intermediate.[3,5,6] It was postulated originally that the rearrangement of α-oximino ketones in polyphosphoric acid proceeded *via* the "normal" route,[7] but more recent studies have shown that actually the "abnormal" or second order route is

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[1] A preliminary account of this work has been presented in *J. Org. Chem.*, **24**, 580 (1959).

[2] A. Werner and A. Piguet, *Ber.*, **37**, 4295 (1904).

[3] A. H. Blatt, *Chem. Revs.*, **12**, 215 (1933).

[4] A. H. Blatt and R. P. Barnes, *J. Am. Chem. Soc.*, **56**, 1148 (1934).

[5] N. V. Sidgwick, *The Organic Chemistry of Nitrogen*, (revised and rewritten by T. W. J. Taylor and W. Baker), Oxford University Press, 1942, p. 182.

[6] V. Migrdichian, *Org. Syntheses*, **Vol. 1**, 376 (1957).

[7] E. C. Horning, V. L. Stromberg, and H. A. Lloyd, *J. Am. Chem. Soc.*, **74**, 5153 (1952).