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

Optical Rotatory Dispersion Studies. XXVI.[1] α-Haloketones (Part 4).[2] Demonstration of Conformational Mobility in α-Halocyclohexanones[3]

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The preparation of optically active 2-chloro- and 2-bromo-5-methylcyclohexanone is reported. The optical rotatory dispersion curve of 2-chloro-5-methylcyclohexanone in the nonpolar solvent octane exhibited a negative Cotton effect curve which, on the basis of the earlier enunciated "axial α-haloketone rule," is only consistent with a predominance of that chair form in which both the chlorine and methyl substituents are axial. When the dispersion curve was measured in methanol solution, the sign of the Cotton effect was inverted demonstrating the presence of an appreciable amount of the other conformer in which both substituents are now equatorial. The large amplitude changes in the rotatory dispersion curves of 2-bromo-5-methylcyclohexanone in polar and nonpolar solvents are interpreted in a similar fashion.

Our extensive studies[2,5] of the optical rotatory dispersion of halogenated steroid ketones have led to an empirical generalization,[6] which permits the prediction of the sign of the Cotton effect. This offers an important means for determining absolute configurations[6] of cyclohexanones with known conformation, or of establishing the latter if information on the absolute configuration is available. Briefly, this rule states that the sign of the Cotton effect curve[7] of a given six-membered ketone (existing in the chair conformation)[8] is not altered by introduction of equatorial fluorine,[2] chlorine,[5] bromine,[5] or iodine.[2] On the other hand, when axial chlorine or bromine (but not fluorine[5]) is present in the α-position (to the left of observer looking down the O=C axis as indicated by arrow in I), the Cotton effect will be negative, while when it is in the α'-location (to the right of observer as in II), a positive Cotton effect curve will be observed. As noted recently,[2] appropriate application of this rule can also offer valuable information about the preferred existence of a given "free-rotational" isomer as for instance in 17α-halo-20-keto steroids.

The bulk of our earlier work was carried out with polycyclic ketones of rigid conformation and it was clearly desirable to examine the applicability of these empirical generalizations to monocyclic cyclohexanones, which are subject to conforma-

(1) Paper XXV, C. Djerassi, J. Osiecki, and W. Closson, *J. Am. Chem. Soc.*, **81**, 4587 (1959).

(2) Part 3, C. Djerassi, I. Fornaguera, and O. Mancera, *J. Am. Chem. Soc.*, **81**, 2383 (1959).

(3) A preliminary communication concerning part of this work has already been published by C. Djerassi and L. E. Geller, *Tetrahedron*, **3**, 319 (1958).

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

(6) C. Djerassi and W. Klyne, *J. Am. Chem. Soc.*, **79**, 1506 (1957). This has proved to be a specific case of the general "octant rule" for predicting the sign of the Cotton effect of cyclohexanones (see: C. Djerassi, *Rec. Chemical Progress*, **20**, 101 (1959); C. Djerassi, *Optical Rotatory Dispersion: Applications to Organic Chemistry*, Chap. 13, New York, McGraw-Hill, (1960); W. Moffitt, A. Moscowitz, R. B. Woodward, W. Klyne, and C. Djerassi, in preparation.)

(7) For nomenclature and recording of experimental data see C. Djerassi and W. Klyne, *Proc. Chem. Soc.*, 55 (1957).

(8) We have recently found that the rule is also applicable to cyclohexanones existing in the boat conformation; see C. Djerassi, N. Finch, and R. Mauli, *J. Am. Chem. Soc.*, **81**, 4997 (1959).

tional mobility. The most convenient optically active model ketone appeared to be (+)-3-methylcyclohexanone (III), since it is readily available from pulegone[9] and its absolute configuration has been established without any doubt.[9]

The mono-halogenation of 3-methylcyclohexanone (III) is rather complicated, since there are possible two position isomers, each of which can exist as two geometrical (cis or trans relationship of halogen atom to methyl group) isomers and each of these can in turn be accommodated in two nonequivalent chair conformations.[10] Consequently, there are at least eight plausible alternate representations for an α-halo-3-methylcyclohexanone and as will be shown in the sequel, rotatory dispersion offers a powerful tool for the solution of this problem.

Attention was first directed towards the monobromination of (+)-3-methylcyclohexanone (III), since this has been reported[11] to give a crystalline isomer (m.p. 83-85°) in unspecified yield. We have been able to secure the identical product in 21% yield by conducting the bromination in aqueous solution.[12] Kötz and Steinhorst[11b] have assigned the 2-bromo-5-methylcyclohexanone (IV) structure to this isomer since upon dehydrobromination with aniline, it afforded less than 1% of 5-methylcyclohex-2-en-1-one (Va). In view of the well known tendency towards rearrangement in such amine-promoted dehydrohalogenations, a structure proof based on such a poor yield is unacceptable and it was imperative to settle this point by an alternate procedure. For this purpose, we selected the dehydrobromination with 2,4-dinitrophenylhydrazine,[13] which has been shown not to involve any rearrangement[14] even in such cases where bases such as collidine or pyridine produce one. When the reaction was performed in acetic acid solution[14a] there was obtained in good yield the 2,4-dinitrophenylhydrazone of a methylcyclohexenone, which had to possess structure Vb since it exhibited [α]D −219°. The alternate isomer, VII, derived from 2-bromo-3-methylcyclohexanone (VI) is, of course, optically inactive.

By settling the position of the bromine atom, only four representations[10,15] (IV t,e; IV t,a; IV c,a; IV c,e) have to be considered, two of them

possessing a trans (IV t,e; IV t,a) and two a cis (IV c,a; IV c,e) relationship between the bromine atom and the methyl group. Corey[16]—on the basis of a number of model experiments with monobromocyclohexanones—has made the generalization that in the absence of 1,3-diaxial interactions between bromine (or chlorine) and an alkyl group, the halogen atom will assume the axial orientation, since electrostatic repulsion between the halogen atom and the carbonyl group is minimized over that existing in the equatorial isomer. Subsequent dipole moment measurements[17] have shown that this picture cannot hold for solvents of differing polarity and the situation has now been clarified by Allinger and Allinger,[12,18] who have demonstrated that there exists an equilibrium between the two conformational isomers (e.g. IV c,a ⇌ IV c,e). In a nonpolar solvent, this equilibrium lies substantially on the side of the axial conformer (e.g. IV c,a) and thus approximates the picture visualized by Corey,[16] but in polar solvents an appreciable amount of the equatorial conformer (e.g. IV c,e) may be present in solution.

The axial or equatorial character of a halogen atom in an α-halocyclohexanone can be recognized readily by infrared[19] or ultraviolet[20] spectral means. Such spectral measurements have now been conducted on the crystalline 2-bromo-5-methylcyclohexanone (IV) in a variety of solvents and these results, together with the dipole moment studies, are presented in the following paper.[21] The results are in accord with the earlier data obtained with 2-bromocyclohexanone[12] in that the proportion of equatorial isomer is augmented as the polarity of the solvent is increased. It should be noted that the spectral data do not differentiate between the two pairs (IV t,e; IV t,a vs. IV c,a; IV c,e) of conformational isomers and it was thus not possible to assign a cis (IV c,a; IV c,e) or trans (IV t,e; IV t,a) relationship to the bromine and methyl groups.

(+)-3-Methylcyclohexanone (III) exhibits a positive Cotton effect curve[22-24] in all of the sol-

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

(10) We are ignoring in this case the existence of boat representations or intermediate forms.

(11) (a) N. Zelinsky and M. Roschdestwensky, Ber., 35, 2695 (1902); (b) A. Kötz and H. Steinhorst, Ann., 379, 18 (1911).

(12) J. Allinger and N. L. Allinger, Tetrahedron, 2, 64 (1958).

(13) V. R. Mattox and E. C. Kendall, J. Am. Chem. Soc., 70, 882 (1948) and later papers.

(14) (a) C. Djerassi, J. Am. Chem. Soc., 71, 1003 (1949); (b) M. Gates and G. M. K. Hughes, Chem. & Ind. (London), 1506 (1956).

(15) 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.

(16) E. J. Corey, J. Am. Chem. Soc., 75, 2301 (1953); Experientia, 9, 329 (1953).

(17) W. D. Kumler and A. C. Huitric, J. Am. Chem. Soc., 78, 3369 (1956).

(18) N. L. Allinger and J. Allinger, J. Am. Chem. Soc., 80, 5476 (1958).

(19) R. N. Jones, D. A. Ramsay, F. Herling, and K. Dobriner, J. Am. Chem. Soc., 74, 2828 (1952).

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

(21) N. L. Allinger, J. Allinger, L. E. Geller, and C. Djerassi, J. Org. Chem., 25, accompanying paper (1960).

(22) H. S. French and M. Naps, J. Am. Chem. Soc., 58, 2303 (1936).

(23) C. Djerassi, Bull. Soc. Chim. France, 741 (1957).

(24) C. Djerassi and G. W. Krakower, J. Am. Chem. Soc., 81, 237 (1959).

vents examined and application of our earlier generalizations[6] from the steroid series would predict a similar positive Cotton effect for the two equatorial isomers IV t,e and IV c,e,[25] and especially for the axial isomer IV c,a. On the other hand, a strong negative Cotton effect curve would be predicted for the axial conformer IV t,a and such a curve was found experimentally (Fig. 1) for the crystalline
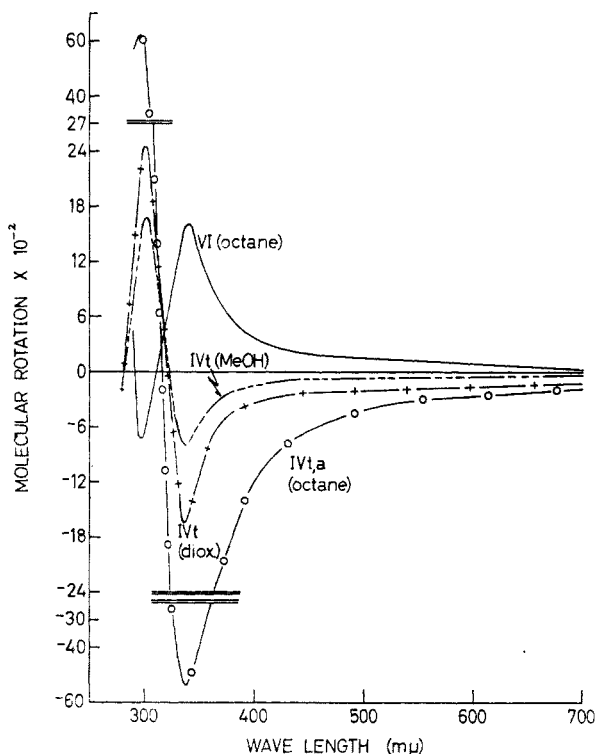

Fig. 1. Optical rotatory dispersion curves of trans-2-bromo-5-methylcyclohexanone (IV t) and 2-bromo-3-methylcyclohexanone (VI)

bromoketone IV. The amplitude of this negative Cotton effect is greatly reduced as the polarity of the solvent is augmented — indicating the presence of increasing amounts of the equatorial conformer IV t,e with its positive Cotton effect. The quantitative aspects of the rotatory dispersion shifts summarized in Fig. 1 and their relationship to the

(25) On the basis of the refinements introduced by the octant rule (see ref. 6) which also considers the contribution of substituents in the position β to the carbonyl group, a negative Cotton effect would also be assumed for the equatorial isomer IV, c,e, since this is now based on a conformation (see ref. 27) different from that existing in our parent ketone III—a situation which did not exist in our steroid reference ketones (ref. 2,5). Nevertheless, we can exclude this possibility, because the corresponding axial isomer IV c,a definitely possesses a strong positive Cotton effect curve (see Fig. 3 in ref. 21) and consequently a shift in sign from the positive to the negative side would be expected in increasing the polarity of the solvent. In actual fact, the reverse shift was observed (see Fig. 1) and this is even more noticeable with the corresponding chloroketone (VIII) (see Fig. 2), where the sign of the Cotton effect was actually inverted—an observation which is only consistent with the pairs IV t,e–IV t,a and VIII t,e–VIII t,a.

spectral and dipole moment studies are discussed in detail in the accompanying communication.[21]

The rotatory dispersion results offer a decisive answer in favor of the trans relationship between the methyl and bromine substituents and this has now been confirmed independently by x-ray studies[26] which show that IV t,a represents the correct expression in the crystal lattice.

The demonstration of structure IV t,a for 2-bromo-5-methylcyclohexanone does not necessarily mean that it represents the initial product of the bromination of (+)-3-methylcyclohexanone (III), since on the basis of earlier work[16] one would anticipate that bromination of the enol of 3-methylcyclohexanone (III) would lead originally to the axial conformer IV c,a, of cis-2-bromo-5-methylcyclohexanone. As demonstrated in the following paper[21] by rotatory dispersion and infrared spectroscopic means, the trans-isomer IV t,a (negative Cotton effect) is readily isomerized to the cis-isomer IV c,a (positive Cotton effect) in carbon tetrachloride solution containing some hydrogen bromide. While the position of this equilibrium lies predominantly on the side of the cis-isomer IV c,a, in carbon tetrachloride solution the isolation of the less favored trans-isomer IV t,a is due to the fact that under the conditions of the bromination (of III) it crystallizes out of solution and thus continuously shifts the equilibrium in the direction ofI V t,a. In carbon tetrachloride solution,[21] no crystallization is observed and IV c,a, is largely obtained.
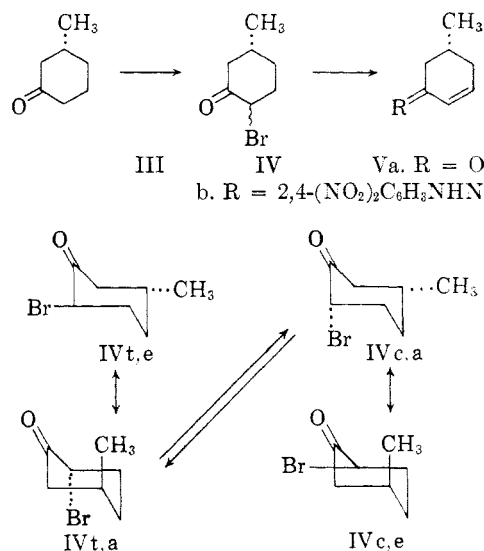

After separation of the crystalline trans-2-bromo-5-methylcyclohexanone isomer (IV t,a), the filtrate was distilled and yielded a liquid isomer of the same analytical composition. Dehydrobromination of this material with 2,4-dinitrophenylhydrazine gave a difficultly separable mixture of the 2,4-

(26) Private communication from Prof. R. Pepinsky, Pennsylvania State University, University Park, Pa.

dinitrophenylhydrazone Vb of 5-methylcyclohex-2-en-1-one and of the 2,4-dinitrophenylhydrazine VII of 3-methylcyclohex-2-en-1-one, thus establishing that the liquid product consists of a mixture of 2-bromo-5-methylcyclohexanone (IV) and 2-bromo-3-methylcyclohexanone (VI). Since the 2,4-dinitrophenylhydrazone Vb has a rotation of ca. −220°, while the isomer VII is optically inactive, a fairly accurate estimate of the quantitative composition of the liquid mixture can be deduced from the optical rotation of the total, crude 2,4-dinitrophenylhydrazone obtained from the liquid; this proved to be 45% IV and 55% VI as an average of several experiments.

2-Bromo-3-methylcyclohexanone (VI) can again exist in four isomeric forms[10,15] (VI t,e; VI t,a; VI c,a; VI c,e) and application of the "axial haloketone rule" as refined by the "octant rule"[6] would predict a positive Cotton effect for the pair VI t,e; VI t,a and a negative one[27] for the pair VI c,a; VI c,e. As shown in Fig. 1, the rotatory dispersion curve of the liquid mixture in octane exhibits a positive Cotton effect and in this solvent of low polarity, the axial conformers (with Cotton effects of increased amplitude as compared to those of the corresponding equatorial conformers) will play the dominant role. As far as the contribution of the 2-bromo-5-methylcyclohexanone (IV) component of the mixture is concerned, the crystalline trans-isomer in the axial orientation IV t,a has been shown above to exhibit a large negative Cotton effect and while a small amount of it may still be present in the liquid mixture due to incomplete crystallization, it must represent a very minor portion in view of the observed positive Cotton effect, which can be attributed largely to conformer IV c,a. No such distinction can be made among the four isomeric representations VI t,e; VI t,a; VI c,a; VI c,e or even the two axial ones (VI t,a and VI c,a) of the 2-methyl-3-bromocyclohexanone (VI) component of the liquid mixture. It will be noted from Fig. 1 that the amplitude of the negative Cotton effect of the crystalline isomer IV in octane is much greater than that of the liquid mixture in the same

solvent. While the pure axial isomer IV t,a would be expected to have the greatest amplitude of any of the eight conformers of IV and VI— the axial bromine atom and the axial methyl group both contributing strongly towards a negative Cotton effect according to the postulates of the "octant rule"[6]— the conformational equilibrium IV t,e ⇌ IV t,a would not be expected[21] to lie as far on the axial side as that of the pair IV c,a ⇌ IV c,e. As long as the "octant rule" is not placed on a quantitative basis by assigning fairly accurate parameters to the contribution of the various substituents, the amplitude differences shown in Fig. 1 between the Cotton effect curves (octane solution) of the pure, crystalline isomer IV t,a and that of the liquid mixture, can be interpreted at the present time equally well in terms of the liquid consisting of ca. 40% of the axial conformer IV c,a of cis-2-bromo-5-methylcyclohexanone (IV c) and 55% of a mixture of any one of the isomers of VI, VI c,a presumably being favored on energetic grounds.[21]
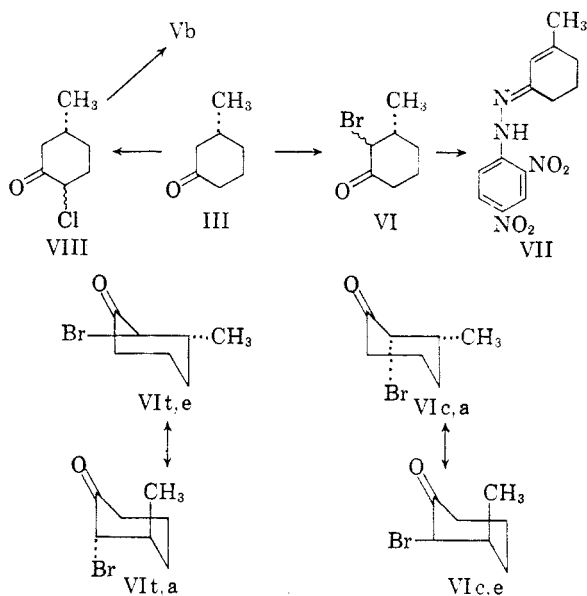
Since chlorination of 3-methylcyclohexanone (III) has also been reported[11b] to produce a crystalline monochloro derivative—presumably 2-chloro-5-methylcyclohexanone (VIII)—we have repeated its preparation using sulfuryl chloride in carbon tetrachloride solution as the chlorinating agent.[28] No attempt was made to develop optimum conditions for the preparation of the crystalline isomer (m.p. 68–69°) which was shown to be 2-chloro-5-methylcyclohexanone (VIII) by dehydrochlorination with 2,4-dinitrophenylhydrazine to the above described 5-methylcyclohex-2-en-1-one 2,4-dinitrophenylhydrazone (Vb) with [α]_D −211°. This substance can exist in four possible representations[10,15] (VIII t,e; VIII t,a; VIII c,a; VIII c,e), the pre-

(27) The octant rule (ref. 6) predicts a positive Cotton effect for 3-methylcyclohexanone in conformation (i) but a strongly negative one for the alternate conformation (ii). In the conformer VI t,a, the strongly positive contribution (ref. 6) of the axial bromine atom will offset the negative contribution of the axial methyl group (corresponding to ii) and the compound will exhibit a positive Cotton effect, although its amplitude is bound to be reduced over that of IV c,a. On the other hand in VI c,e, the equatorial bromine atom is not expected to make a large contribution and the negative Cotton effect of the substance should be due largely to the axial methyl group.
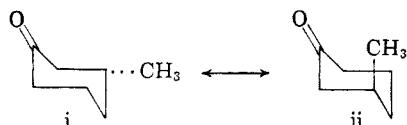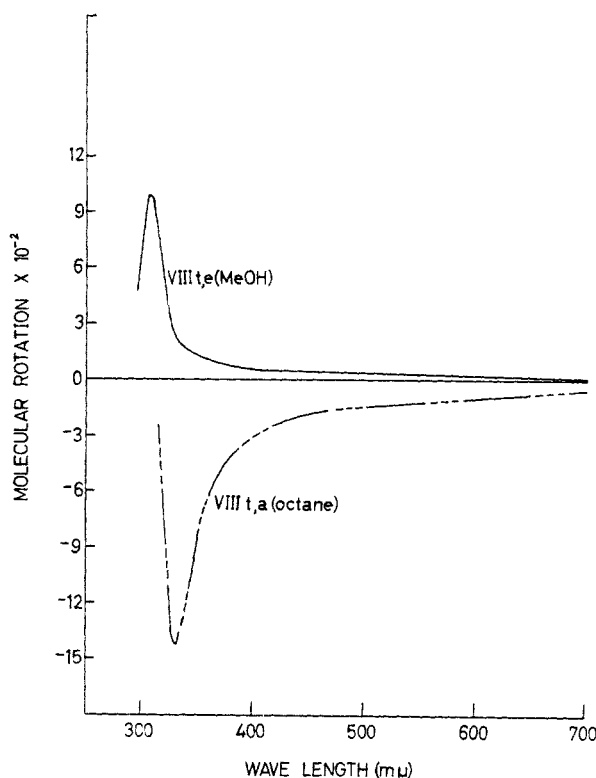
Fig. 2. Optical rotatory dispersion curves of *trans*-2-chloro-5-methylcyclohexanone (VIII *t*) in octane and in methanol

dicted signs of their Cotton effects paralleling those of the corresponding 2-bromo-5-methyl analogs (IV). In this instance, an assignment could be made rapidly and decisively by rotatory dispersion measurements. As reproduced in Fig. 2, the chloroketone exhibited a negative Cotton effect in the nonpolar solvent octane, which is only consistent with the presence of an appreciable amount of the axial conformer VIII *t,a* of *trans*-2-chloro-5-methylcyclohexanone. In the polar solvent methanol, where an increased proportion of the corresponding equatorial conformer VIII *t,e* (predicted[6] to have a positive Cotton effect) is to be expected,[12] there was not observed just a diminution in amplitude (see Fig. 1 for IV *t,a* $\rightleftarrows$ IV *t,e*), but actually a reversal in sign. This striking inversion of the Cotton effect curve upon altering the dielectric constant of the medium is only compatible with the conformational change VIII *t,a* $\rightleftarrows$ VIII *t,e*, since the alternate *cis* pair (VIII *c,e* $\rightleftarrows$ VIII *c,a*) would have exhibited exactly the opposite sign. The unlikely alternate explanation that *trans*-2-chloro-5-methylcyclohexanone (VIII *t*) is isomerized in methanol solution to *cis*-2-chloro-5-methylcyclohexanone (VIII *c*) which would then be responsible for the observed positive Cotton effect (Fig. 2) in methanol solution, was excluded by the following experiment.

A sample of *trans*-2-chloro-5-methylcyclohexanone (VIII *t*), exhibiting a negative Cotton effect curve in octane solution, was dissolved in methanol

solution and kept at room temperature for forty-five minutes. The solvent was then removed under reduced pressure and the rotatory dispersion run immediately in octane solution, starting at 330 mμ. Essentially the same negative Cotton effect curve was obtained as is reproduced in Fig. 2.

The results outlined in this paper illustrate once more the wide applicability of rotatory dispersion measurements to a variety of organic chemical problems.[23] Further work is in progress in this laboratory with optically active cyclohexanones, especially those in which conformational mobility is inhibited by suitably situated bulky substituents.
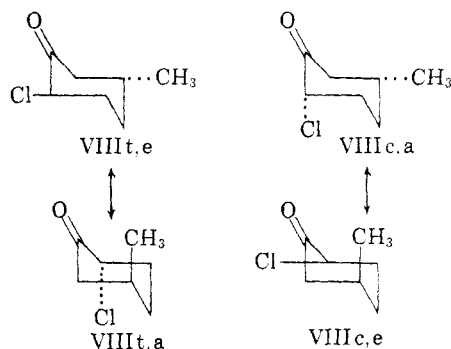
EXPERIMENTAL[29]

Bromination of (+)-*3-methylcyclohexanone* (III). Bromine (11.79 g.) was added dropwise over a 2-hr. period to a vigorously stirred biphasic system consisting of 25 cc. of water and 8.25 g. of (+)-3-methylcyclohexanone (III) prepared[9] from pulegone. The reaction flask was cooled with tap water to prevent the temperature rising above 20° and the mixture was stirred for an additional 3 hr. at which time both layers were colorless. Extraction with ether, washing of the organic phase with water, drying over anhydrous sodium sulfate and evaporation left 12.38 g. of a pale yellow oil. Freezing in a Dry Ice–acetone bath and filtration of the various crops (followed each time by washing with pentane, evaporation of the solvent and repeated freezing) gave a total of 3.2 g. of *trans*-2-bromo-5-methylcyclohexanone (IV *t, a*). Recrystallization from petroleum ether or sublimation at 28° and 0.05 mm. gave the colorless bromoketone, m.p. 83.5–84°, $[\alpha]_D$ −64.4° (*c* 1.06 in toluene); lit.,[11a] m.p. 83–85°, $[\alpha]_D$ −47.9° (in toluene). R.D. (Fig. 1) in *methanol* (*c* 0.117): $[\alpha]_{700}$ −26°, $[\alpha]_{589}$ −32°, $[\alpha]_{337.5}$ −423°, $[\alpha]_{305}$ +1200°, $[\alpha]_{270}$ −670°. R.D. (Fig. 1) in *dioxane* (*c* 0.0686): $[\alpha]_{700}$ −66°, $[\alpha]_{589}$ −67°, $[\alpha]_{335}$ −862°, $[\alpha]_{300}$ +1285°, $[\alpha]_{280}$ −58°. R.D. (Fig. 1) in *octane* (*c* 0.133): $[\alpha]_{700}$ −96°, $[\alpha]_{589}$ −140°, $[\alpha]_{337.5}$ −2820°, $[\alpha]_{295}$ +3730°. R.D. in *carbon tetrachloride* (*c* 0.0475): $[\alpha]_{700}$ −84°, $[\alpha]_{589}$ −150°, $[\alpha]_{335}$ −2630°, $[\alpha]_{320}$ −1055°.

Anal. Calcd. for $C_7H_{11}BrO$: C, 43.97; H, 5.76; Br, 41.88; O, 8.38. Found: C, 44.03; H, 6.05; Br, 41.76; O, 8.58.

After removal of the crystalline bromoketone IV, *t, a* by freezing, 3.3 g. of the liquid residue was fractionated with a Podbielniak column. The portion (2.01 g.) boiling at 71–74°/3.6 mm. was redistilled to yield 1.9 g. of colorless liquid, b.p. 72°/3.6 mm. representing a mixture of *ca.* 45% of 2-bromo-5-methylcyclohexanone (IV) and 55% of 2-bromo-3-

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°.

DETROIT, MICH.

(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 ab-

solute configurations of α-haloketones has been well established.[3] A quantitative study of con-

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