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

Conformational Analysis. II. The 2-Bromo-4-*t*-butylcyclohexanones[1,2]

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The *cis* and *trans* isomers of 2-bromo-4-*t*-butylcyclohexanone have been prepared and furnish simple flexible molecules in which the bromine substituents are known to have the equatorial and axial conformations, respectively. The spectral properties of each compound are as predicted from rigid steroid systems. For the reaction *cis*-2-bromo-4-*t*-butylcyclohexanone ⇄ *trans*-2-bromo-4-*t*-butylcyclohexanone, the equilibrium constant was found to be 1.7 in dioxane solution and 3.5 in carbon tetrachloride solution by infrared analysis. These values are in agreement with the equilibrium constants between the conformational isomers of 2-bromocyclohexanone deduced earlier.

Introduction

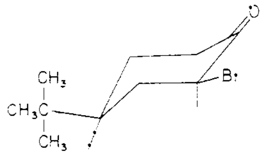
Jones and his co-workers showed[3] that the presence of an equatorial halogen next to a keto group in various steroids always caused a displacement of the carbonyl stretching band in the infrared to higher frequency relative to the parent ketone, whereas the presence of an axial halogen produced no such shift. Corey made a study of simple flexible halocyclohexanones,[4] and concluded that with these compounds the conformation of the halogen also could be established from the infrared spectrum. Cookson[5] showed that the halogen's conformation could similarly be determined from the ultraviolet spectrum since the characteristic R band was shifted to longer wave length by an adjacent axial, but not by an equatorial, halogen.

From both his study of the infrared spectrum of 2-bromocyclohexanone and from theoretical calculations, Corey[4a] concluded that the bromine was principally in the axial position in this compound, but, on the other hand, Kumler and Huitric[6] interpreted their dipole moment measurements as indicating that either the bromine was mainly equatorial, or else that the six-membered ring was not a regular chair. A re-interpretation of these data, together with additional studies, led to the conclusion[2] that all of the known facts were entirely consistent with the existence of an equilibrium between the equatorial and axial conformational isomers of 2-bromocyclohexanone which had an equilibrium constant varying from about 3 in nonpolar solvents to near 1 in dimethyl sulfoxide.

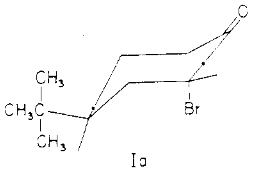
Discussion

The purpose of the present work was twofold. First, it seemed desirable to separate for spectral study two isomers of a simple flexible system in which the halogens were constrained respectively to the axial and equatorial conformation by the presence of only a distant non-polar substituent. Second, the equilibration of these isomers would furnish a test as to the correctness of the earlier conclusions drawn for 2-bromocyclohexanone[2] because here the compounds would be geometric rather than conformational isomers and the point of equilibrium between the axial and equatorial halogen could be established without ambiguity.

The compounds chosen for this work were the *cis*- and *trans*-2-bromo-4-*t*-butylcyclohexanones (I). Winstein and Holness[7] and Eliel and co-workers[8] previously have used the *t*-butyl group as a distant yet compelling agent for determining conformation. Since the bulky *t*-butyl group may be considered to occupy exclusively the equatorial position, to the extent that the compounds are in the chair conformation,[9] *cis*-2-bromo-4-*t*-butylcyclohexanone would have structure Ie (bromine equatorial) while the *trans* isomer would have structure Ia (bromine axial).



Ie



Ia

In so far as was determined previously[7,8] the presence of the *t*-butyl group in the 4-position has no effect on the reactivity of the carbonyl group or its derivatives.[10] It was therefore expected that Ie would be an example of a simple flexible molecule in which the halogen was unambiguously and exclusively equatorial,[9] and the infrared and ultraviolet spectra could be determined for such a system. Isomer Ia would likewise have the characteristics of an axial halogen in these respects. Since such halides can be equilibrated by allowing them to stand in a solvent with hydrobromic acid, the point of equilibrium in solvents of different polarity was to be determined by infrared analysis using the fingerprint region and comparison with the known pure isomers.

Results

Bromination of 4-*t*-butylcyclohexanone (II) afforded a mixture of *cis*- and *trans*-2-bromo-4-*t*-

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[1] Sponsored by the Office of Ordnance Research, U. S. Army.

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

[3] R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952).

[4] (a) E. J. Corey, *ibid.*, **75**, 2301, 3297 (1953); (b) E. J. Corey, T. H. Topie and W. A. Wozniak, *ibid.*, **77,** 5415 (1955); (c) E. J. Corey and H. J. Burke, *ibid.*, **77**, 5418 (1955).

[5] R. C. Cookson, *J. Chem. Soc.*, 282 (1954).

[6] W. D. Kumler and A. C. Huitric, THIS JOURNAL, **78,** 3369 (1956).

[7] S. Winstein and N. J. Holness, *ibid.*, **77,** 5562 (1955).

[8] E. L. Eliel and R. S. Ro, *Chemistry & Industry*, 251 (1956); E. L. Eliel and C. A. Lukach, THIS JOURNAL, **79,** 5986 (1957); E. L. Eliel and R. S. Ro, *ibid.*, **79,** 5992, 5995 (1957).

[9] There is no reason to expect any significant amount of I to be in other than the chair conformation, since the only known cases where such a situation prevails in flexible systems involve either very large steric effects (J. C. Banerji, D. H. R. Barton and R. C. Cookson, *J. Chem. Soc.*, 5041 (1957); R. E. Lyle, *J. Org. Chem.*, **22,** 1280 (1957)) or else a substantial reduction of Pitzer strain for the flexible form as is inherent in 1,4-cyclohexanedione (C. G. LeFevre and R. J. W. LeFevre, *Rev. Pure Appl. Chem.*, **5,** 261 (1955)).

[10] Available information[8] suggests that the *t*-butyl group in the 3-position, perhaps because of an induced deformation (D. H. R. Barton, A. J. Head and P. J. May, *J. Chem. Soc.*, 935 (1957)), may cause some change in reactivity and physical properties.

butylcyclohexanone (I) from which the *cis* isomer Ie was obtained by crystallization, m.p. 67°. Chromatography on silica gel of I, from which the bulk of Ie had been removed by crystallization, employed pentane–chloroform as developing solutions and separated the *trans* isomer Ia cleanly from the *cis* compound. The so-obtained Ia, melting point less than 0°, was shown to contain less than 5% of Ie by comparison of the infrared fingerprint region of the two compounds. The *cis* and *trans* structures were assigned on the basis of the spectral properties discussed below.

Infrared Studies.—The carbonyl infrared absorption maxima of pure Ia and Ie were at 4 and 15 cm.$^{-1}$ higher frequency, respectively, than the parent 4-*t*-butylcyclohexanone (II) in carbon tetrachloride solution. These values are similar in magnitude to those established for pure axial (−3 to +5 cm.$^{-1}$) and equatorial (+13 to +19 cm.$^{-1}$) isomers of steroid systems[3] and to those found for the axial (0 cm.$^{-1}$) and equatorial (+12 cm.$^{-1}$) absorptions of 2-bromocyclohexanone.[2]

In the work with 2-bromocyclohexanone[2] it was necessary to make the assumption that the extinction coefficients of the infrared carbonyl bands of the axial conformer and of the parent ketone were in the same ratio (unity) as the integrated absorption intensities. With compounds Ia and II (4-*t*-butylcyclohexanone) this assumption was demonstrably untrue. In carbon tetrachloride the ratio of the extinction coefficients of Ia to II was 0.77, while for the integrated intensities the ratio was 0.91. The difference between these numbers as well as the difference of the former from unity was well beyond experimental error and was qualitatively clear on inspection of the original spectra. The carbonyl bands of both Ia and Ie had markedly lower extinction coefficients, but greater band widths than II. A synthetic mixture of Ia and Ie afforded only a non-resolved *albeit* noticeably unsymmetrical absorption curve. Since the separation of the carbonyl maxima in wave numbers of Ia and Ie was the same as that for the conformational isomers of 2-bromocyclohexanone, the resolution in the latter but not the former case can be due only to the greater band widths of Ia and Ie. The correctness of the assumption made in the earlier work remains unquestioned.

The ratio of the extinction coefficients of the carbonyl bands in the infrared of Ie and II was 0.56, and the ratio of the integrated intensities of Ie and II was 0.65 (carbon tetrachloride solution). With polycyclic systems, integrated intensity ratios for axial and equatorial conformations are approximately 1 and 0.75.[3]

Ultraviolet Studies.—The ultraviolet absorption curves of pure Ia, Ie, II and synthetic mixtures of Ia and Ie in the solvents carbon tetrachloride and 95% ethanol were obtained. The ultraviolet properties of each compound were virtually independent of the medium employed for the measurements and were entirely analogous to those reported for the appropriate axial and equatorial α-haloketo steroids.[5] The comparison of the ultraviolet spectral data of 2-bromocyclohexanone (mixture of conformational isomers) and *cis*- and *trans*-2-bromo-4-*t*-butylcyclohexanone (pure conformations) in Table I stresses the similarities and the differences between the compounds which follow logically from the previously given interpretation of the data for 2-bromocyclohexanone. As a result of the greatly enhanced extinction coefficient of Ia relative to Ie, a mixture of isomers in which the equatorial compound predominated slightly would be expected to absorb at a wave length which was not significantly different from that of the pure axial isomer. The λ_{max} values of the synthetic mixtures of pure Ia and Ie clearly substantiate this conclusion. Further, the absorption curves of these synthetic mixtures did not give two peaks but a single peak, similar in appearance to that of the pure axial compound but reduced in intensity and very slightly skewed. Thus the λ_{max} values of 2-bromocyclohexanone can provide no aid in a critical conformational analysis of this compound. On the other hand, although the extinction coefficients of pure Ia and Ie remained virtually identical when the solvent was changed from carbon tetrachloride to 95% ethanol, those of 2-bromocyclohexanone were noticeably influenced by the solvent employed for the measurement. The lower extinction coefficient of this compound in 95% ethanol relative to carbon tetrachloride is entirely consistent with the interpretation that the equilibrium is shifted toward the equatorial isomer in the more polar solvent. Further, if it is assumed that as an approximation the ratio of the extinction coefficients of the axial and equatorial conformational isomers of 2-bromocyclohexanone to cyclohexanone are the same as the ratio of Ia and Ie to II, the percentage of *axial* 2-bromocyclohexanone present in each solvent of the ultraviolet study may be estimated. The values so obtained were 85% axial in carbon tetrachloride and 53% axial in 95% ethanol, in reasonable agreement with the percentages found previously by other methods.[4]

TABLE I

COMPARISON OF THE ULTRAVIOLET SPECTRAL PROPERTIES OF Ia, Ie AND 2-BROMOCYCLOHEXANONE

	Carbon tetrachloride Relative to parent ketone		95% ethanol Relative to parent ketone	
Compound	$\Delta\lambda_{max}$[a]	Δ log ϵ	$\Delta\lambda_{max}$[a]	Δ log ϵ
Ia	+20	0.75	+25	0.78
Ie	− 4	.07	+ 1	.07
Ia + Ie[b]	+18	.51	+23	.51
2-Bromocyclohexanone	+22	.70[c]	+25	.55[c]

[a] Absorption bands of the ketone are broad which precludes accurate determination of the wave lengths of the absorption maxima. [b] Approximately equimolar concentrations of Ia and Ie. [c] The values for these quantities recorded in reference 2 have been found to be incorrect.

Equilibration Studies.—The equilibration of pure Ie to a mixture of Ie and Ia was carried out at room temperature in two solvents of different polar character, carbon tetrachloride and dioxane, employing anhydrous hydrobromic acid as the equilibrating agent. That the equilibrium mixture was attained in each solvent was shown by the fact that the composition was unchanged with longer reaction times. For the dioxane solution, the same equilibrium mixture was approached from both sides. The analyses of these mixtures were done in carbon tetrachloride solution employing the fingerprint region of the infrared spectra of pure Ie, Ia and the equilibrated mixtures, the four most suitable wave lengths being chosen.

For the equilibrium Ie $\rightleftarrows$ Ia in carbon tetrachloride the experimentally determined equilibrium constant was 3.5. This value corresponds to a free energy change of -0.75 kcal./mole (27°). The equilibrium constant established for the dioxane solution was 1.7 and the calculated change in free energy was -0.32 kcal./mole (29°). The percentages of axial conformational isomer in the equilibrium Ie $\rightleftarrows$ Ia in carbon tetrachloride and dioxane solution are given in Table II and are compared to those values estimated in the earlier study for 2-bromocyclohexanone. The data for the two systems are certainly in reasonable agreement.

TABLE II

PERCENTAGE OF AXIAL CONFORMER AT EQUILIBRIUM

Solvent	2-Bromocyclohexanone	2-Bromo-4-*t*-butylcyclohexanone
Carbon tetrachloride	74%[a]	78%[b]
Dioxane	57%,[a] 51%[c]	63%[b]

Method of analysis: [a] Ratio of the extinction coefficients of the infrared carbonyl absorption maxima of 2-bromocyclohexanone and cyclohexanone.[2] [b] This study, see Experimental for details. [c] Dipole moment studies.[6]

Molecular Weight Determinations.—A mixture of *cis*- and *trans*-2-bromo-4-*t*-butylcyclohexanone (infrared analysis estimated 53% Ie, 47% Ia) had an experimentally determined effective molecular weight 1.2 times greater than the actual molecular weight in cyclohexane solution at a total molal concentration close to that employed for the infrared studies. 4-*t*-Butylcyclohexanone (II) was also slightly complexed in cyclohexane at a similar molal concentration, the ratio of the effective to the actual molecular weight being 1.1. The amount of complexing determined for these compounds in cyclohexane solution was extremely small compared to the corresponding values of 2.7 and 4.8 found[2] for 2-bromocyclohexanone and cyclohexanone, respectively. This difference, and also that found in the infrared spectra, shows that the *t*-butyl group does make some change in the properties of the carbonyl group.

Summary.—The infrared and ultraviolet spectral characteristics established for *cis*- and *trans*-2-bromo-4-*t*-butylcyclohexanone are in agreement with the data obtained from the model polycyclic compounds and for the conformational isomers of 2-bromocyclohexanone. The compositions of the equilibrium mixtures of Ia and Ie in carbon tetrachloride and dioxane solutions provide unequivocal evidence that a significant amount of equatorial bromine is present in simple monocyclic α-halocyclohexanones and that the equilibrium constant for equatorial $\rightleftarrows$ axial is influenced by the particular solvent in which the measurement is made. All the data for *cis*- and *trans*-2-bromo-4-*t*-butylcyclohexanone are entirely consistent with and offer support for the previously proposed interpretation[2] of the 2-bromocyclohexanone system.

Experimental

2-Bromo-4-*t*-butylcyclohexanone (I).—The bromination of 4-*t*-butylcyclohexanone[11] (II) was carried out in aqueous solution on a 0.1-mole scale as previously described[2] for the bromination of cyclohexanone. The crude product was extracted in series with ether and the ether extracts were washed in series twice with water, twice with dilute sodium bicarbonate solution, once with water, and then dried with magnesium sulfate. The ether was evaporated and the pale yellow residue was repeatedly and rapidly Claisen distilled at the lowest possible pressure (about 0.5 mm.) until decomposition was no longer evident (constant pressure was maintained). Three distillations were required and a lower boiling fraction containing starting material was removed each time. There was obtained 6.5 g. of a colorless liquid, b.p. 75°(0.5 mm.), n^{26}D 1.4959. This material plus 1.5 g. of I obtained from another preparation was redistilled through a two-foot column of the Podbielniak type. A small forerun was obtained and then nine fractions were collected having the boiling range 78.5–85° (0.5 mm.); a residue of 0.4 g. remained. Fraction 1, 0.8 g. had n^{27}D 1.4932 and fraction 9 0.6 g. had n^{27}D 1.4946. The infrared carbonyl absorption region for fraction 1 showed a maximum at 1736 cm.$^{-1}$ and an inflection at 1742 cm.$^{-1}$. Fraction 9 had its maximum at 1742 cm.$^{-1}$ with an inflection at 1736 cm.$^{-1}$. The infrared spectra were obtained in carbon tetrachloride solution at similar concentrations of material and the two spectra were run consecutively on the same sheet of paper. Clearly, the low boiling fractions were rich in Ia while the high boiling fractions were rich in Ie. This order is as predicted by the dipole rule.[12] The final yield of I was 5.8 g. (25%) and the compound was a colorless liquid which could be stored at 0° protected from light with no evidence of decomposition. Exposure to light and higher temperatures resulted in facile decomposition.

Three other preparations on the same scale were performed and the yields and refractive indices of I were approximately the same. Two preparations were carried out employing ether as solvent for the reaction.[13] The yields were 25–30% and the physical properties of I were similar to those described above.

***cis*-2-Bromo-4-*t*-butylcyclohexanone** (Ie).—Fractionally distilled compound I, 1.8 g. n^{28}D 1.4978, was dissolved in 5 ml. of pentane with gentle warming, and the solution was cooled to 0°. There was obtained 1.2 g. of white needles, m.p. 54–64°. Two recrystallizations from pentane at 25° afforded 0.5 g. of white needles, m.p. 67–68.2°. A second crop, 0.2 g., having m.p. 67.2–68.2° was obtained from the filtrates.

Anal. Calcd. for $C_{10}H_{17}BrO$: C, 51.47; H, 7.35. Found: C, 51.66, 51.25; H, 7.31, 7.23.

Crystallization from pentane of I purified only by simple distillation afforded a solid having m.p. 64–68° with a cloudy melt. Repeated crystallizations from a variety of solvents did not improve the melting range; the contaminant most probably was a dibromo-4-*t*-butylcyclohexanone.

***trans*-2-Bromo-4-*t*-butylcyclohexanone** (Ia).—A sample of I from fractional distillation, 3.0 g., n^{26}D 1.4955, was dissolved in pure pentane and the solution was placed on a chromatographic column of 90 g. of silica gel (Davison Chemical Corp., mesh size 100–200) which had been made up in and washed with 500 ml. of pure pentane. A heat effect at the top of the column was noted. The chromatogram was developed first with 1 l. of pure pentane, second with 500 ml. of 5% chloroform in pentane, and then with 20% chloroform in pentane. A trace of material was present in the third 500-ml. fraction and 200-ml. fractions were collected hence; the solvent was removed *in vacuo* at 30°. Fraction 4 contained 0.18 g. of a yellow oil; fractions 5, 6, 7 had 0.34, 0.27 and 0.24 g., respectively, of colorless oil; fractions 8 and 9 each contained less than 0.10 g. of material. The remaining material was eluted from the column with pure chloroform, and there was obtained 1.4 g. of an oil which promptly solidified. Crystallization of this material from pentane afforded pure Ie.

The fractions 5–7, 0.85 g., were combined with 0.44 g. of material obtained in a similar manner and the sample was rechromatographed on 50 g. of silica gel employing the above-

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(11) Kindly given to us by the Dow Chemical Co.

(12) N. L. Allinger, THIS JOURNAL, **79**, 3443 (1957).

(13) E. J. Corey, *ibid.*, **76**, 175 (1954).

described pattern of preparation and development of the chromatographic column. There was obtained from the 20% chloroform-pentane elution, six consecutive 200-ml. fractions containing no material. Fraction 7 had *ca.* 0.06 g. of yellow oil, fractions 8–12 each contained *ca.* 0.1 g. of colorless oil, and fractions 13–15 contained material in decreasing amounts.

Fractions 8–12 were combined and dissolved in a small amount of dry benzene, and this solvent was removed *in vacuo* at 35° at a final pressure of 1 mm. There was obtained 0.35 g. of a colorless oil. Approximately one-half of this material was Claisen distilled as rapidly as possible at 0.5 mm., bath temperature 110°, and gave a colorless liquid, $n^{27}D$ 1.4942. The sample readily solidified at temperatures below 0°.

Anal. Calcd. for $C_{10}H_{17}BrO$: C, 51.47: H, 7.35. Found: C, 51.45; H, 7.31.

The infrared spectra of the undistilled and distilled samples were superimposable which showed that rapid distillation led to no epimerization. Further quantitative comparison of the infrared absorption bands in the 8–12 μ region (carbon tetrachloride solution) of the distilled sample with pure Ie showed the Ia isomer contained less than 5% of Ie.

Infrared Studies.—The infrared spectra were obtained employing a Baird double beam infrared spectrophotometer, AB model. For the quantitative comparison of two compounds the two solutions of nearly identical concentration in carbon tetrachloride were recorded consecutively on the same sheet of paper. The data are presented in Table III.

TABLE III

THE CARBONYL ABSORPTIONS OF Ia, Ie AND II IN CARBON TETRACHLORIDE SOLUTION

Compound	Molarity	λ_{max},[a] cm.$^{-1}$	ϵ[b]
Ia	0.154	1724	336
II	.149	1720	438
Ie	.128	1748	240
II	.130	1733	428
Ia	.498	1724	[c]
Ie	.482	1737[d]	
I[e]	.576	1739[f]	[c]
Ie	.503	1748	

[a] Although these absolute values could not be exactly reproduced from day to day, the difference between the wave lengths of the absorption maxima of any two compounds whose spectra were recorded consecutively was constant to within 2 cm.$^{-1}$ throughout the investigation. [b] 0.1-mm. cell length but only useful as relative units. [c] Optical density may not be read accurately with these concentrations, transmittance being *ca.* 10%. [d] Another comparison of these compounds at similar concentrations afforded Ia 1727 cm.$^{-1}$ and Ie 1738 cm.$^{-1}$. [e] Synthetic mixture, 60% Ia, 40% Ie. [f] Slight inflection at 1748 cm.$^{-1}$.

The wave length of the infrared carbonyl absorption maximum of I was influenced by the isomer composition of the mixture. For example, the carbonyl absorption of an arbitrary sample of I had its predominant absorption maximum at 1731 cm.$^{-1}$, and the curve had a slight hump on the high frequency side at 1736 cm.$^{-1}$. A new mixture was prepared by addition of a nearly equivalent amount of pure Ie to the original I. The carbonyl absorption curve of this second sample, richer in Ie than the first, had its main absorption maximum at 1739 cm.$^{-1}$ and the dissymmetry appeared on the low frequency side at 1731 cm.$^{-1}$. The two spectra were obtained consecutively in carbon tetrachloride solution at nearly identical molar concentrations.

Using the above-described carbonyl absorption curves of Ia and II, the data were replotted in units of ϵ as a function of wave length on larger paper. These curves were cut out, the same base line being assigned to Ia and II, and weighed. The ratio of the integrated carbonyl intensities of Ia to II was 0.91. In a similar manner the ratio of the integrated intensities of Ie and II was found to be 0.65. These ratios were not particularly dependent on the exact base line assigned as long as the same line was taken for both curves.

Ultraviolet Studies.—The spectra were obtained employing a Beckman spectrophotometer with Spectracord attachment. Beer's law was obeyed for the synthetic mixtures. The data are given in Table IV.

TABLE IV

ULTRAVIOLET ABSORPTION DATA OF Ia, Ie AND II

Compound	λ_{max}, mμ	ϵ
Solvent, carbon tetrachloride		
Ia	315	130
Ie	291	27
Iae[a]	313	75
II	295	23
Solvent, 95% ethanol		
Ia	310	128
Ie	286	25
Iae[b]	308	69
II	285	21

[a] Synthetic mixture, 1.22×10^{-3} *M* Ia and 1.19×10^{-3} *M* Ie. [b] Synthetic mixture, 1.26×10^{-3} *M* Ia and 1.38×10^{-3} *M* Ie.

Employing the measured extinction coefficients of 2-bromocyclohexanone, cyclohexanone and the estimated (see below) extinction coefficients of the pure axial and equatorial conformers of 2-bromocyclohexanone in each solvent, the amounts of *axial* 2-bromocyclohexanone in carbon tetrachloride and 95% ethanol were estimated to be 85 and 53%, respectively. The data are given in Table V.

TABLE V

ULTRAVIOLET ANALYSIS OF 2-BROMOCYCLOHEXANONE

Compound	Carbon tetra-chloride ϵ_{max}	95% ethanol ϵ_{max}
Axial 2-bromocyclohexanone	119[a]	120[a]
2-Bromocyclohexanone	106[b]	75[b]
Equatorial 2-bromocyclohexanone	26[c]	23[c]
Cyclohexanone	21[b]	20[b]

[a] Calculated with the assumption that it is equal to $\epsilon_{III} \cdot \epsilon_{Ia}/\epsilon_{II}$ (where III refers to cyclohexanone) in the same solvent. [b] Experimental value. [c] Calculated with the assumption it is equal to $\epsilon_{III}\epsilon_{Ie}/\epsilon_{II}$ (where III refers to cyclohexanone) in the same solvent.

Molecular Weight Determinations.—The molecular weights of 4-*t*-butylcyclohexanone (II) and 2-bromo-4-*t*-butylcyclohexanone (I) in cyclohexane were determined in the manner described,[2] employing concentrations closely identical to those of the infrared studies. The ketone II, actual molecular weight of 153.2, had an experimentally determined molecular weight of 164.1 at 0.154 molal concentration. The molecular weight of I in a 0.163 molal solution was 277.0, the actual molecular weight being 233.2 g./mole. Infrared analysis (see later for method) of this sample of I in carbon tetrachloride solution estimated the composition of the mixture as 47% Ia and 53% Ie. As a standard *n*-heptane was employed and the experimental molecular weight (100.9) was virtually identical with the actual value (100.2) at 0.156 molal concentration.

Equilibration Studies. Carbon Tetrachloride Solution.—Pure *cis*-2-bromo-4-*t*-butylcyclohexanone (Ie), 0.2 g., was dissolved in 5 ml. of 0.1 *M* anhydrous hydrobromic acid in carbon tetrachloride and the homogeneous solution was allowed to stand at room temperature (27°) for 1.5 hours. The reaction mixture was poured to a separatory funnel containing 20 ml. of ice-water and was extracted with 60 ml. of pure pentane. The organic phase was washed once with water, twice with cold dilute sodium bicarbonate solution, once with water, dried with sodium sulfate and the solvent was removed *in vacuo* at 30°. The slightly cloudy colorless residue was rapidly Claisen distilled (0.5 mm.), some residue remained, and the distillate was immediately submitted to infrared analysis. In a second equilibration experiment the reaction time was extended to 4.5 hours.

The analyses for the percentage compositions of the mixtures were carried out by comparison of the infrared spectra of approximately 0.5 *M* carbon tetrachloride solutions of pure Ia, pure Ie and the equilibrated samples. The spectra of pure Ie and the mixture were obtained consecutively on the

TABLE VI

INFRARED ANALYSES OF THE EQUILIBRIUM MIXTURES Iae

Wave length, μ	Carbon tetrachloride solution						Dioxane solution								
	Optical densities						Optical densities								
	Ia	Ie[a]	Iae[a,b]	Ia	Ie[d]	Iae[d,e]	Ia	Ie[g]	Iae[g,h]	Ia	Ie[j]	Iae[j,k]	Ia	Ie[m]	Iae[m,n]
10.61	0.182	0.029	0.148	0.182	0.027	0.137	0.182	0.038	0.141	0.182	0.023	0.140	0.182	0.039	0.144
10.34	.032	.110	.051	.032	.116	.048	.032	.118	.076	.032	.103	.062	.032	.117	.073
9.35	.031	.128	.058	.031	.135	.052	.031	.137	.087	.031	.119	.070	.031	.143	.078
8.46	.303	.078	.274	.303	.080	.247	.303	.080	.230	.303	.068	.235	.303	.077	.235
	Estimated percentage compositions														
	77% Ia, 23% Ie[c]			79% Ia, 21% Ie[f]			57% Ia, 43% Ie[i]			63% Ia, 37% Ie[l]			62% Ia, 38% Ie[o]		

[a] The optical densities recorded for Ie and Iae are corrected values which correspond to the molar concentration of the Ia solution (0.517 M); actual concentrations were 0.472 M Ie and 0.466 M Iae. [b] Sample obtained from pure Ie after 1.5-hour reaction time. [c] Normalized from actual calculated values, 83% Ia, 25% Ie. [d] The optical densities recorded for Ie and Iae are corrected values which correspond to the molar concentration of the Ia solution (0.517 M); the actual concentrations were 0.476 M Ie and 0.463 M Iae. [e] Sample obtained from pure Ie after 4.5-hour reaction time. [f] Normalized from actual calculated values 74% Ia, 20% Ie. [g] Optical densities recorded for Ie and Iae are corrected values which correspond to the molar concentration of the Ia solution (0.517 M); the actual concentrations were 0.477 M Ie and 0.502 M Iae. [h] Sample obtained from pure Ie after 2.5-hour reaction time. [i] Normalized from actual calculated values of 70% Ia, 52% Ie. [j] Optical densities recorded for Ie and Iae are corrected values which correspond to the molar concentration of the Ia solution (0.517 M); the actual concentrations were 0.456 M Ie and 0.451 M Iae. [k] Sample obtained from pure Ie after 5.0-hour reaction time. [l] Normalized from actual calculated values of 73% Ia, 43% Ie. [m] Optical densities recorded for Ie and Iae are corrected values which correspond to the molar concentrations of the Ia solution (0.517 M), the actual concentrations were 0.480 M Ie and 0.482 M Iae. [n] Sample obtained from a mixture having the estimated composition (infrared analysis) of 67% Ia, 33% Ie after 15-hour reaction time. A longer reaction time (20 hours) afforded a mixture of 63% Ia and 37% Ie. [o] Normalized from actual calculated values of 72% Ia, 45% Ie.

same sheet of paper. The spectrum of Ia that was used for the analyses was obtained earlier and it was not repeated for these equilibration analyses due to the difficulties involved in securing and storing this isomer. A spectrum of pure Ie recorded consecutively with this sample of Ia was identical with the spectra of Ie recorded for each analysis. Employing the four most suitable wave lengths (Table VI), two sets of simultaneous equations were obtained whose solutions provided estimates of the percentage compositions of the equilibrium mixtures. Because of the difficulty of maintaining accurately known concentrations of I in small volumes of volatile solvent the ratio of Ia to Ie, in other words normalized percentages, were used. The accuracy of the method was checked by preparing a mixture of Ia and Ie which was 39% Ie by weight. The infrared analysis showed 36% Ie. Table VI lists the wave lengths employed for the analyses and the optical densities obtained for each pure isomer and for the two equilibrated samples.

The estimated percentage composition of the two equilibrated mixtures (78% Ia, 22% Ie) established that the equilibrium constant for Ie ⇄ Ia in carbon tetrachloride solution with 0.1 M anhydrous hydrobromic acid was 3.5 and the free energy change (at 27°) was -0.75 kcal./mole.

To show that the point of equilibrium was not shifted by the formation of a complex between the ketone and the hydrobromic acid, another experiment was carried out.[14] Pure ketone Ie, 0.11 g., was dissolved in 1 ml. of 0.025 M anhydrous hydrobromic acid carbon tetrachloride solution. Aliquots of the solution were analyzed directly after standing for 4, 20, 44 and 68 hours, and these analyses showed 79, 78, 79 and 75% Ia, respectively.

Equilibration Studies. Dioxane Solution.—Equilibrium mixtures of Ia and Ie were established in 0.1 M anhydrous hydrobromic acid–dioxane solution from pure Ie and from a mixture of Ia and Ie having the composition 67% Ia, 33% Ie. The experimental procedure and the analyses of the various samples were performed as described above and the three most informative sets of data are recorded in Table VI.

The percentage composition of the equilibrated mixtures (63% Ia, 37% Ie) established that the equilibrium constant for Ie ⇄ Ia in 0.1 M anhydrous hydrobromic acid–dioxane solution was 1.7 and the free energy change was -0.32 kcal./mole (29°).

The following control experiments established that no detectable amount of further equilibration was incurred by the described work-up procedure. A sample of I having the composition 62% Ie, 38% Ia by infrared analysis was submitted to the isolation and purification procedure. The recovered material was analyzed and found to be 60% Ie and 40% Ia. Further, a sample of I (60% Ie, 40% Ia) was dissolved in sufficient 0.1 M hydrobromic acid–carbon tetrachloride to give a 10% solution. Direct analysis of the reaction solution was performed after 2 hours and the composition was 73% Ia, 27% Ie. Analysis after 6 hours and 26 hours each indicated the composition of 77% Ia and 23% Ie.

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