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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA]

## The Conformational Preference of the Bromo and Methyl Groups by Infrared Spectral Analysis<sup>1</sup>

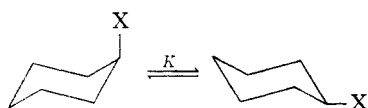
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The preference of the bromo group for an equatorial over an axial position in cyclohexane is  $-0.61$  kcal./mole, and for the methyl group,  $-1.97$  kcal./mole. Evidence is presented indicating that conformational C-Br molecular extinction coefficients are nearly identical for the cyclohexyl and 4-methylcyclohexyl systems. However, the ratio of the equatorial and axial molecular extinction coefficients is  $k_{C-Br(e)}/k_{C-Br(a)} = 1.85$ .

### INTRODUCTION

Conformational analysis is a valuable method in organic chemistry.<sup>2</sup> One of the basic parameters,  $\Delta F_x$ , is an estimate of the relative preference of a functional group for an equatorial over an axial conformation in a six membered ring system. A simple approach for measuring this parameter is to determine the equilibrium constant for the following system:



The  $\Delta F_x$  is then readily calculated from the relationship  $\Delta F_x = -RT \ln K$ .

Techniques for measuring these equilibria include a kinetic method,<sup>3,4</sup> determination of hydroxy acid-lactone equilibria,<sup>5a</sup> epimerization of substituted

cyclohexanols,<sup>5b</sup> NMR spectroscopy,<sup>6</sup> and infrared spectroscopy.<sup>7</sup>

This paper reports the results of an infrared spectral determination of the  $\Delta F$  values for bromine and methyl. Also, the constancy of molar extinction coefficients for substituted and unsubstituted cyclohexane systems is checked.

The infrared stretching frequencies differ for an axial and an equatorial substituent<sup>8</sup>; hence, a direct measure of the equilibrium is available by recording the spectrum of the cyclohexyl-X system. There are two problems associated with this technique. First, the equatorial and axial C-X absorption frequencies must be assigned correctly. Second, the molar extinction coefficients for pure C-X axial and equatorial absorptions must be determined. This can be accomplished by utilizing the corresponding *cis*- and *trans*-4-*t*-butylcyclohexyl compounds and assuming that the molar extinction coefficients are the same as those for the two conformations of the cyclohexyl derivative. In contrast with the kinetic technique, which has been used most

(1) Acknowledgment is made to the donors of The Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(2) (a) W. G. Dauben and K. S. Pitzer, in *Steric Effects in Organic Chemistry*, M. Newman, ed., John Wiley and Sons, Inc., New York, N. Y., 1956, pp. 1-60. (b) D. H. R. Barton and R. C. Cookson, *Quart. Revs.*, **10**, 44 (1956). (c) W. Klyne, *Progress in Stereochemistry*, Vol. I, Butterworths Scientific Publications, London, U.K., 1954, pp. 36-89. (d) E. L. Eliel, *J. Chem. Ed.*, **37**, 126 (1960).

(3) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955).

(4) (a) E. L. Eliel and R. S. Ro, *Chemistry and Industry*, 251 (1956); *J. Am. Chem. Soc.*, **79**, 5995 (1957). (b) E. L. Eliel and C. S. Lukach, *J. Am. Chem. Soc.*, **79**, 5986 (1957).

(5) (a) L. J. Dolby and D. S. Noyce, 136th Meeting of the American Chemical Society, Atlantic City, N. J., 1959, Abstracts of Papers, p. 73p. (b) E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, **82**, 1367 (1960).

(6) E. L. Eliel, *Chem. and Ind.*, 568 (1959).

(7) R. A. Pickering and C. C. Price, *J. Am. Chem. Soc.*, **80**, 4931 (1958).

(8) R. N. Jones and C. Sandorfy, in *Chemical Applications of Spectroscopy*, W. West, ed., Vol. IX of *Technique of Organic Chemistry*, A. Weissberger, Editor in Chief, Interscience Publishers, Inc., New York, N. Y., 1956, pp. 247-580.

TABLE I  
APPARENT MOLECULAR EXTINCTION COEFFICIENTS ( $k_{C-Br}$ ) AND DERIVED DATA FROM THE INFRARED SPECTRA OF *cis*- AND *trans*-4-METHYLCYCLOHEXYL BROMIDES

Instrument	$k_{C-Br}^a(e)$	$k_{C-Br}^b(a)$	$\frac{k_{C-Br}(e)}{k_{C-Br}(a)}$	Temp.	$K_1$	$\Delta F_1 = \Delta F_{CH_3} - \Delta F_{Br}$ , Kcal./Mole
Baird <sup>c</sup>	102	55.4	1.84	32	9.7	-1.37
Baird <sup>d</sup>	68.9	38.0	1.81	34	10.1	-1.40
Perkin Elmer <sup>e</sup>	74.1	39.0	1.90	27	8.9	-1.30
						av. -1.36 ± 0.04

Data for Cyclohexyl Bromide					
Instrument	Wt. Sample, G.	Calc. Wt. Sample, G.	Temp.	$K_2$	$\Delta F_2 = \Delta F_{Br}$ , Kcal./Mole
Baird <sup>f</sup>	0.2080	0.2011	32	2.8	-0.62
Perkin Elmer <sup>g</sup>	0.1494	0.1420	27	2.7	-0.59
					av. -0.61 ± 0.02

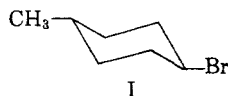
<sup>a</sup> Apparent equatorial C—Br molecular extinction coefficient, from *trans*-isomer. <sup>b</sup> Apparent axial C—Br molecular extinction coefficient, from *cis*-isomer and  $k_{C-Br}(e)$  by difference. <sup>c</sup> A 0.5 mm. cell; concentrations, 0.17M. <sup>d</sup> A 0.1 mm. cell; concentrations, 0.85M. <sup>e</sup> A 0.1 mm. cell; concentrations, 1.11M. <sup>f</sup> A 0.1 mm. cell; concentration, 1.23M. <sup>g</sup> A 0.1 mm. cell; concentration, 0.87M.

extensively, no assumptions are necessary concerning the reaction path, the transition state, or the rate of equilibration of the conformations. The  $\Delta F_{OH}$  has been determined by the infrared technique.<sup>7</sup> However, the result was obtained by measuring the concentration of equatorial OH in cyclohexanol using the equatorial OH absorption of *trans*-4-*t*-butylcyclohexanol and calculating the concentration of axial OH by difference. This was necessitated by the complexity of the axial OH absorption in *cis*-4-*t*-butylcyclohexanol. Hence the validity of the assumption of equal molar extinction coefficients in the substituted and unsubstituted cyclohexanols was not checked.

The necessary pure isomeric bromides were obtained by stereospecific cleavage by bromine of the corresponding organomercury compound.<sup>9</sup> This reaction occurs with retention of configuration in pyridine solution.

#### RESULTS AND DISCUSSION

The results are summarized in Table I. The apparent molar extinction coefficient for an equatorial C—Br was obtained by recording the spectrum of *trans*-4-methylcyclohexyl bromide (I). This compound showed one C—Br stretching absorption. It should exist almost exclusively in the



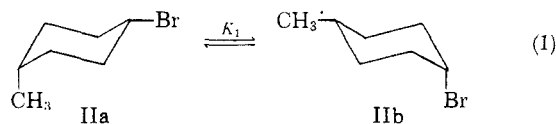
diequatorial conformation; hence the C—Br absorption should be characteristic of an equatorial configuration. The  $k_{C-Br}(e)$  was calculated using the absorbance of the band at 705  $\text{cm}^{-1}$  which has been assigned to the equatorial C—Br stretching frequency<sup>10</sup> and the relationship:

(9) F. R. Jensen and L. H. Gale, *J. Am. Chem. Soc.*, **82**, 145 (1960).

$$k = \frac{\log I_0/I}{cl}$$

where  $\log I_0/I$  is the absorbance,  $c$  is the concentration in moles/liter and  $l$  is the width of the cell in cm. This is an apparent molar extinction coefficient because the width of the cells was not accurately known; however, as the same cell was used in an experiment, this parameter canceled.

The spectrum of *cis*-4-methylcyclohexyl bromide (II) was then recorded. The concentration of the conformation with an equatorial C—Br (IIa) was calculated using the previously calculated

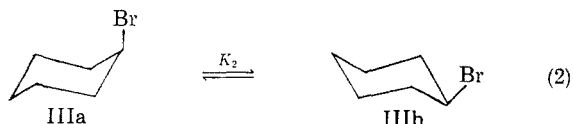


molar extinction coefficient determined from *trans*-4-methylcyclohexyl bromide. The assumption, which can only be justified empirically, was made that the apparent molar extinction coefficient for the equatorial C—Br is the same for the *cis*- and *trans*-isomers. This is a reasonable assumption, as the only change in structure is the configuration in the 4-position. Evidence is given later which supports this view. The concentration of axial C—Br (IIb) was calculated by difference. From these data, the equilibrium constants  $K_1 = \text{IIb}/\text{IIa}$  and  $\Delta F_1 = -RT \ln K_1$  were calculated for the *cis*-isomer. A value of  $-1.36 \pm 0.04$  kcal./mole was calculated for  $\Delta F_1$ , which corresponds to the difference in the  $\Delta F$  values for the methyl and bromo groups. The apparent molar extinction coefficient for an axial C—Br was then calculated using the concentration of the axial conformation (IIb) and the absorbance of the band at 685  $\text{cm}^{-1}$

(10) (a) P. Klaeboe, J. J. Lothe, and K. Lunde, *Acta Chem. Scand.*, **10**, 1465 (1956); **11**, 1677 (1957). (b) D. H. R. Barton, J. E. Page, and C. W. Shoppee, *J. Chem. Soc.*, 331 (1958).

which has been assigned to the axial C—Br stretching frequency.<sup>11</sup> As different cells were used in each of three determinations, the absolute values of the apparent molar extinction coefficients vary; however, the ratios of the apparent molar extinction coefficients  $k_{\text{C-Br}(e)}/k_{\text{C-Br}(a)}$ , are in good agreement.

The spectrum of cyclohexyl bromide (III) was then recorded. The concentration of each conformation could be calculated independently using the previously determined apparent molecular extinction coefficients. The analytical bands in this case



were shifted slightly to lower frequency, the equatorial C—Br absorption occurring at 688  $\text{cm.}^{-1}$  and the axial C—Br at 659  $\text{cm.}^{-1}$ .<sup>11</sup> From these data,  $K_2$  and  $\Delta F$  for bromine were calculated yielding a value of  $\Delta F_{\text{Br}}$  of  $-0.61 \pm 0.02$  kcal./mole. The calculated total concentration of cyclohexyl bromide agreed within 5% of the actual weight (Table II, columns 4 and 5), which indicates that the assumption of equal molar extinction coefficients for the methylcyclohexyl and cyclohexyl systems is probably good; however, the possibility can not be excluded that the coefficients deviate in opposite directions and the apparent check is not real.

The value reported here ( $-610$  cal./mole) for the  $\Delta F_{\text{Br}}$  is listed in Table II along with those reported or calculated from data in the literature. The value of  $\Delta F_{\text{Br}}$  of  $-730$  cal./mole (kinetic method) was determined from the bimolecular substitution and elimination rates of cyclohexyl bromide and *cis*- and *trans*-4-*t*-butylcyclohexyl bromide,<sup>11</sup> and should be reliable. The value of  $\Delta F_{\text{Br}}$  of  $-625$  cal./mole (infrared method) was recalculated from data in various solvents<sup>12</sup> correcting for the ratio of extinction coefficients (1.85) reported in the present study. These authors had made the erroneous assumption that the equatorial and axial coefficients from bromine are the same. Using the average of the reported equilibrium constants obtained making this erroneous assumption leads to a value of  $\Delta F_{\text{Br}} = -1000$  cal./mole. The value of  $\Delta F_{\text{Br}} = -460$  cal./mole (infrared method) was calculated from the ratios of axial and equatorial absorbances obtained in various solvents,<sup>13</sup> using the ratio of molecular extinction coefficients (1.85) reported in the present study. These authors<sup>13</sup> also made a rough estimate of  $\Delta H_{\text{Br}}$  of  $-200$  cal./mole. The last two values of  $\Delta F_{\text{Br}}$  (NMR method) reported in Table

II were obtained assuming the resonance signals of axial and equatorial bromine to occur at the same frequencies in cyclohexyl bromide and the *cis*- and *trans*-4-*t*-butylcyclohexyl bromides. This assumption, to the required precision, can not be justified at the present time on theoretical or empirical grounds, and therefore the values obtained by this method are subject to a considerable uncertainty.

TABLE II  
 $\Delta F_{\text{CH}_3}$  AND  $\Delta F_{\text{Br}}$  AXIAL-EQUATORIAL EQUILIBRIUM VALUES OBTAINED BY VARIOUS TECHNIQUES

	Temp.	Solvent	$\Delta F$ , Cal./Mole	Method
$\text{CH}_3^a$	30°	$\text{CS}_2$	$-1970 \pm 60$	IR
$\text{CH}_3^b$			$-1800$	From thermodynamic data
$\text{CH}_3^c$	100°	$\text{H}_2\text{O}$	$-1900$	Hydroxyacid-lactone equilibrium
$\text{CH}_3^d$		ether	$-1500$	Epimerization of 4-methylcyclohexanol
$\text{Br}^e$	30°	$\text{CS}_2$	$-610 \pm 20$	IR
$\text{Br}^f$	25°	$\text{EtOH}$	$-730$	Kinetic
$\text{Br}^g$	25°(?)		$-625$	IR
$\text{Br}^h$	25°(?)		$-460$	IR
$\text{Br}^i$	25°(?)	liquid	$-240$	NMR
$\text{Br}^j$	25°(?)	$\text{CHCl}_3$	$-940$	NMR

<sup>a</sup> This study. <sup>b</sup> C. W. Beckett, K. S. Pitzer, and R. Spitzer, *J. Am. Chem. Soc.*, **69**, 2488 (1947). <sup>c</sup> Ref. 5a. <sup>d</sup> Ref. 5b. <sup>e</sup> Ref. 11. <sup>f</sup> Recalculated from data in various solvents in ref. 12 using the ratio of extinction coefficients reported in the present paper; see text. <sup>g</sup> Calculated from data in various solvents in ref. 13 using the ratio of extinction coefficients reported in the present paper; see text. <sup>h</sup> Ref. 6.

The  $\Delta F_{\text{CH}_3}$  can be calculated by adding the  $\Delta F_{\text{Br}}$  determined from cyclohexyl bromide to  $\Delta F_1$ , which is the difference in the  $\Delta F$  values for the methyl and bromine groups determined from *cis*-4-methylcyclohexyl bromide. This calculation yields a value of  $\Delta F_{\text{CH}_3}$  of  $-1970 \pm 60$  cal./mole. The value obtained by this technique is in reasonable agreement with those given by other methods (Table II).

The precision of the spectral technique is good; however, the accuracy is more difficult to assess. Considering the possible sources of error, the results are believed to be accurate to within 10%, which is probably of comparable accuracy with results of other methods. However, the spectral method has the advantages that it directly measures the concentrations of the conformers.

#### EXPERIMENTAL

**Materials.** The preparation of the *cis*- and *trans*-4-methylcyclohexyl bromides has been described.<sup>9</sup> Because of a slight discoloration of the *cis*-isomer, it was redistilled before using, b.p. 56.0–56.5°/9.0 mm. The cyclohexyl bromide (Eastman Kodak, white label) was redistilled, b.p. 44.0–45.0°/9.5 mm.

**Analysis.** The infrared analyses were made on a Baird Associates, Inc., double beam infrared recording spectro-

(11) E. L. Eliel and R. G. Haber, *J. Am. Chem. Soc.*, **81**, 1249 (1959).

(12) C. G. LeFevre, R. J. W. LeFevre, R. Roper, and R. K. Pierens, *Proc. Chem. Soc.*, 117 (1960).

(13) G. Chiordoglu, L. Kleiner, W. Masschlein, and J. Reisse, *Bull. Soc. Chim. Belges*, **69**, 143 (1960).

photometer using either 0.5 mm. or 0.1 mm. sodium chloride cells. The spectra were recorded at slow speed using a 2X setting of the slit width. The infrared analyses were also made on a Perkin Elmer model 21 spectrophotometer, using sodium chloride optics. Analytical conditions for the runs using a 0.1 mm. sodium chloride cell: slits at 387  $\mu$ , gain 5.5, suppression 0, response 1:1, scattered light filter in. The alkyl bromide samples were quantitatively prepared

by diluting accurately weighed samples to 1 ml. in volumetric flasks with carbon disulfide (Mallinckrodt, analytical reagent). The absorbance of the analytical bands were determined by using the base line technique. In most cases the spectral region being studied was recorded three times and an average absorbance calculated.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

## Three Membered Rings. II. The Stereochemistry of Formation of Some 1,1,2,2-Tetrasubstituted Cyclopropanes

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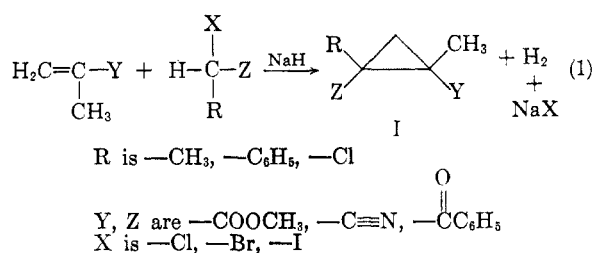
A number of 1,1,2,2-tetrasubstituted cyclopropanes have been formed by the reaction of  $\alpha$ -halo esters, nitriles, or ketones with methyl methacrylate or methacrylonitrile in the presence of sodium hydride. In all cases, the predominant or exclusive product isomer is that in which the activating groups, ester, nitrile, or carbonyl, are *cis* to each other. The effect of several variables on the yields and *cis-trans* isomer ratios has been determined.

The formation of 1,2-cyclopropanedicarboxylic acid esters by reaction of  $\alpha$ -haloesters with  $\alpha,\beta$ -unsaturated esters in the presence of a base has been described.<sup>1</sup> Some extensions and additional examples of this reaction have been reported.<sup>2-7</sup>

The present report gives a more detailed examination of certain aspects of the general problem. This study has been limited to the relatively simple cases in which the cyclopropane product is substituted at only two ring carbons. As a result, only one pair of *cis-trans* isomers is possible in each case. Further, the examples have been picked so that no hydrogens are present *alpha* to the activating groups. Consequently, base catalyzed equilibration of the isomers is not possible, and whatever *cis-trans* isomer ratio is formed in the ring closure reaction is frozen.<sup>8</sup>

Specifically, this study involved three inter-related purposes. The first was to determine how yields of cyclopropane products varied as some of the reaction variables were changed. The second was to observe how the isomer ratios varied with these same changes. Finally, it was of interest to determine if substituents other than methyl, and activating groups other than esters, the groups used in the initial investigation,<sup>1</sup> could be incorporated into

the reaction. The systems actually used may be summarized in the general reaction:



Not all combinations were examined; the results of those that were observed are given in Table I.

*Variables affecting yields.* A change in the reaction temperature from about 25° to 115° had essentially no effect on the yield (Runs 1 and 2, 5 and 6). A pronounced effect on the yield was observed, however, when the halogen, X of reaction 1, was changed from chlorine to bromine to iodine (Runs 2-4, 6-7). Similar variations have been noted previously,<sup>1,2,5</sup> but not all were quite so marked. In comparable cases the chloro compound gives the best results and is strongly preferred. Some systems may give acceptable yields with the bromo derivatives.<sup>4</sup> The iodo compounds

(8) The *cis-trans* isomer ratio has been reported to vary with the base used (ref. 3,5). Unfortunately, all but one of the examples have a hydrogen *alpha* to an ester group. No evidence was presented that the isomers are stable under the reaction conditions, and in two cases (ref. 3) it was shown that warming the reaction product with strong base could cause a complete inversion of the isomer ratio, 95% *cis* to 95% *trans*. The one example with no  $\alpha$ -hydrogens was run with only one base. Consequently, although these variations in isomer ratio with base used are valid for the reactions studied, it is not clear that they represent the isomer ratios produced during the ring closure reaction; the observed ratios may arise by base catalyzed partial isomerization subsequent to ring closure.

(1) L. L. McCoy, *J. Am. Chem. Soc.*, **80**, 6568 (1958).

(2) R. Fraisse and R. Jacquier, *Bull. soc. chim. France*, 986 (1957).

(3) M. Mousseron and R. Fraisse, *Compt. rend.*, **248**, 887 (1959).

(4) M. Mousseron, R. Fraisse, R. Jacquier, and G. Bonavent, *Compt. rend.*, **248**, 1465 (1959).

(5) M. Mousseron, R. Fraisse, R. Jacquier, and G. Bonavent, *Compt. rend.*, **248**, 2840 (1959).

(6) D. T. Warner, *J. Org. Chem.*, **24**, 1536 (1959).

(7) S. Wawzonek and C. E. Morreal, *J. Am. Chem. Soc.*, **82**, 439 (1960); O. Widman, *Ber.*, **51**, 533, 907 (1918).