

induced by cooling in Dry Ice, and the solvent was removed with a filter stick. Three recrystallizations of the residual material from ether-pentane yielded 886 mg. (63%) of material which melted at 42.5–43.7°. When mixed with VII, m.p. 54.2–55.0°, the mixture melted at 40.6–46.2°; when mixed with VIII, m.p. 51.0–52.6°, the mixture melted at 43.8–50.0°.

The infrared spectrum of the recovered tosylate was an exact composite of the spectra of VII⁶ and VIII. The absence of bands at 10.55 and 12.00 μ showed that equatorial-bicyclo[3.2.1]octan-2-yl *p*-toluenesulfonate (XVI)⁶ was not present. The equatorial-tosylate XVI is less reactive than VII or VIII and thus if present would survive the conditions of the isolation.

Quantitative infrared analyses were carried out by the method described in the previous paper⁶ with the exception that synthetic mixtures were not analyzed. The bands used for analysis (0.4 *M* solutions in carbon disulfide) were 10.30 μ (VII) and 13.55 μ (VIII). The percentage transmittance at 2.8 μ was arbitrarily set at 100. The results indicated

that the mixture contained 65 \pm 5% VIII and 35 \pm 5% VII.

B. Ethanolysis of axial-Bicyclo[3.2.1]octan-2-yl *p*-Toluenesulfonate (VIII).—A solution of 1.00 g. (0.0036 mole) of VIII, m.p. 51.0–52.6°, in 18 ml. of anhydrous ethanol was heated at 49.03° for 24 hr. (50% reaction). The solution was poured into 100 g. of crushed ice and the resulting mixture was extracted with five 30-ml. portions of ether. The ether extracts were combined, washed with dilute potassium hydroxide solution and water and dried over magnesium sulfate. After removal of the ether the solid residue was recrystallized four times from pentane. This gave 388 mg. (78%) of material which melted at 44.7–45.8°. The infrared spectrum differed from that described in A only in the relative intensities of the peaks. A quantitative infrared analysis indicated that the mixture contained 75 \pm 5% VIII and 25 \pm 5% VII.

A synthetic binary mixture consisting of 70% VIII and 30% VII melted at 42.8–43.8° after one recrystallization from pentane.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY, DETROIT 2, MICH.]

Conformational Analysis. XIV. The Use of the Polarograph for the Determination of the Conformations of the 2-Halocyclohexanones^{1,2}

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The half-wave potentials for the reduction of a number of 2-halocyclohexanones at the dropping mercury electrode have been measured. With systems of relatively fixed conformation, such as the 2-halo-4-*t*-butylcyclohexanones, the epimer with the axial halogen is reduced more easily. A compound such as 2-chlorocyclohexanone, which contains comparable amounts of two conformations, shows the potential characteristic of the more easily reduced (axial) form.

Introduction

The 2-halocyclohexanones have recently been studied in considerable detail by a number of workers, and quite a large amount of information about these compounds has now been accumulated.³ It has been found that the properties of a 2-halocyclohexanone in a more complicated system, such as a steroid, will in general parallel nicely the same properties in a simple system, and methods useful for the determination of conformation in the simple systems can usually be applied to more complicated cases. As it happens the reverse is frequently done also.

In a polyfunctional system it is not always possible to apply criteria such as the location of the carbonyl stretching frequency to determining conformation, since the frequency in question may be obscured by the absorption of other carbonyls in the molecule. Additional methods for

the determination of the axial or equatorial position of a halogen adjacent to a ketone are therefore desirable. It is of particular interest to be able in some way to determine the conformation of a fluorine atom, since the spectral shifts here may be indecisive, chemical methods are difficult to apply, and even the powerful rotatory dispersion method is not generally useful.^{3e}

It is well known that 2-chlorocyclohexanones are polarographically reduced.⁴ It seems likely *a priori* that the reduction potential of such a system will depend on the conformation of the halogen atom. The determination of the reduction potentials of some simple 2-halocyclohexanones was therefore undertaken.

Results and Discussion

The *cis* and *trans* isomers of the 2-halo-4-*t*-butylcyclohexanones (II, X = Br, Cl, F) were available from earlier work. Because of its bulk the *t*-butyl group assumes an equatorial position almost exclusively,⁵ and hence the *cis* isomer has the halogen equatorial (IIe) while in the *trans* isomer it is axial (IIa). These compounds are very nearly conformationally homogeneous,⁶ and

(1) Paper XIII, N. L. Allinger and S. Hu, *J. Am. Chem. Soc.*, **83**, 1664 (1961).

(2) This research was supported in part by a grant from the Atomic Energy Commission and in part by a grant from the Alfred P. Sloan Foundation.

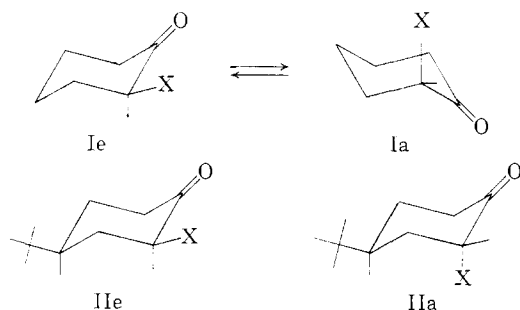
(3) For references to the 2-chlorocyclohexanones see (a) N. L. Allinger, J. Allinger, L. A. Freiberg, R. F. Czaja and N. A. LeBel, *J. Am. Chem. Soc.*, **82**, 5876 (1960). For the 2-bromocyclohexanones see (b) N. L. Allinger, J. Allinger and N. A. LeBel, *ibid.*, **82**, 2926 (1960); (c) N. L. Allinger, J. Allinger, L. E. Geller and C. Djerassi, *J. Org. Chem.*, **25**, 6 (1960). For the 2-fluorocyclohexanones see (d) H. M. Kissman, A. M. Small and M. J. Weiss, *J. Am. Chem. Soc.*, **82**, 2312 (1960). For a brief general review of the physical properties of 2-halocyclohexanones see (e) C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p. 115.

(4) P. J. Elving and R. E. Van Atta, *J. Electrochem. Soc.*, **103**, 676 (1956).

(5) (a) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955); (b) E. L. Eliel and R. S. Ro, *ibid.*, **79**, 5992, 5995 (1957); E. L. Eliel and C. A. Lukach, *ibid.*, **79**, 5986 (1957).

(6) Actually calculations have indicated the presence of about 1% of a boat form in such systems: N. L. Allinger, *ibid.*, **81**, 5727 (1959).

a reduction potential of a *cis* isomer should be the reduction potential characteristic of the equatorial halogen, and the corresponding potential for the *trans* isomer should be characteristic of the axial halogen.



The results are summarized in Table I. The half-wave potentials ($E_{1/2}$) are independent of concentration over the range from 0.18 to 3.79 millimolar for the 2-fluorocyclohexanone and from 0.548 to 2.91 millimolar for the chloro analogs. High concentrations produce maxima near the half-wave values in the case of the chloro compounds; thus no $E_{1/2}$ values are tabulated for concentrations of greater than 3.0 millimolar. This phenomenon was not observed for the fluoro compounds at any concentration used.

TABLE I

POLAROGRAPHIC REDUCTION DATA^a

Compound, cyclohexanone	Concn., mM	I_d , μ a., sec. ^{1/2} / mM. mg. ^{3/2}	$E_{1/2}$, vs. Hg, v.	RT/ anF, v.
2-Chloro-	0.984	0.642	-1.390	0.19
	2.91	.600	-1.400	
<i>cis</i> -2-Chloro-4- <i>t</i> -butyl-	0.598	.516	-1.565	.16
	1.76	.498	-1.573	
	2.88	.520	-1.573	
<i>trans</i> -2-Chloro-4- <i>t</i> -butyl-	0.548	.525	-1.420	.23
	1.61	.502	-1.435	
	2.89	.487	-1.448	
<i>trans</i> -2-Chloro-5-methyl-	0.827	.645	-1.455	.18
	2-Fluoro-	0.790	.685	
<i>cis</i> -2-Fluoro-4- <i>t</i> -butyl-	2.32	.610	-2.008	.14
	3.79	.590	-1.992	
	0.520	.594	-2.076	
<i>trans</i> -2-Fluoro-4- <i>t</i> -butyl-	1.54	.525	-2.080	.12
	2.50	.540	-2.080	
	0.180	1.70 ^b	-1.846	
	0.357	1.36 ^b	-1.856	
	1.05	1.06 ^b	-1.846	.18

^a Obtained with 0.1 *M* tetrabutylammonium bromide in dimethylformamide solvent. ^b Residual current = 0.132 μ a.

A high residual current was found for the tetrabutylammonium bromide-dimethylformamide-electrolyte solvent, even after careful purification. In order to reduce the error in determining values for i_d this requires that at least 0.5 millimolar solutions of the compounds be used. This precaution was observed in all cases except that of

the *trans*-2-fluoro-4-*t*-butylcyclohexanone, where limited availability of this compound precluded many experiments in the desired concentration range.

A separate experiment was run on *trans*-2-chloro-4-*t*-butylcyclohexanone to determine the dependence of the diffusion current on mercury height. An experimental ratio of 1.35 was found for an increase from 26.6 to 42.6 cm. This is to be compared with a ratio of 1.00 for kinetic control, 1.27 for diffusion control and 1.60 for absorption control of the reduction process on the plateau of the wave. It was found that the axial epimer was reduced more easily in each case; for the chloro compounds the *trans* isomer (IIa, X = Cl) shows an average half-wave potential of -1.43 volts, while the value for the *cis* isomer (IIe, X = Cl) is -1.57 volts. For the corresponding fluoro compounds the values are -1.86 and -2.08 volts. The bromo compounds were reduced so close to the potential of the reference electrode under these conditions that the half-wave potentials were too irreproducible to allow differentiation.

These limited data obtained show that the thermodynamically stable equatorial halogen requires a greater potential for reduction than does its epimer.⁷

When a flexible molecule such as 2-chlorocyclohexanone (I) is reduced, since the energy barrier between the equatorial and axial conformers (Ie and Ia, respectively) is small, it is expected that only the potential for the most easily reduced form will be observed. This is true because there are comparable amounts of the two isomers present and their interconversion is very rapid compared to the rate of reduction. Since the *cis*-chloro compound (IIe, X = Cl) must contain at least a small amount of axial chlorine (with the ring in the boat form), and yet it does not show the reduction potential characteristic of axial chlorine, the tentative interpretation that the ratio of axial chlorine to equatorial chlorine present is so small that the reduction potential must be raised past that normally required to reduce axial halogen to near that required for equatorial halogen before the bulk of the material is reduced. If this interpretation is correct, compounds which contain intermediate ratios of axial to equatorial halide might be expected to show intermediate behavior.

In dioxane solution it is known that 2-fluorocyclohexanone⁸ and *trans*-2-chloro-5-methylcyclohexanone⁹ each contain less than 15% of the axial conformer, and this percentage may be expected to be substantially less in the highly polar solutions used for this work. The prediction can therefore be made that while 2-chlorocyclohexanone should show a reduction potential near that of the *trans* epimer IIa, 2-fluorocyclohexanone and *trans*-2-chloro-5-methylcyclohexanone might well show

(7) M. D. Yudis and P. Kabasakalian have reached this conclusion from an independent study carried out with steroidal α -haloketones. The authors are indebted to Dr. Yudis and Dr. Kabasakalian for informing them of this work prior to publication.

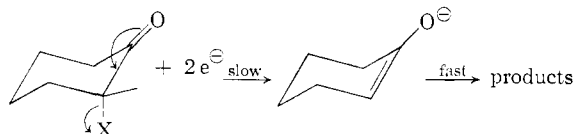
(8) Unpublished work by Dr. H. Blatter.

(9) Unpublished work by Dr. J. Allinger; see C. Djerassi, L. E. Geller and E. J. Eisenbraun, *J. Org. Chem.*, **25**, 1 (1960).

intermediate potentials. Table I shows this is what is in fact found.

Tentative generalizations may be drawn from the limited available data. For truly rigid systems such as the B and C rings in a steroid, it seems likely that given both epimers of an α -haloketone it will be possible to determine which is which by this method, at least when the halogen is chlorine or fluorine. Whether or not it will be possible to determine the conformation when only one epimer is available will depend on the variation of the reduction potentials from one compound to another and more data must be accumulated before this question can be answered. For flexible systems the information that can be obtained depends on the amount of axial conformer present. If this is very small, less than perhaps 1%, the potential will be similar to that of a pure equatorial isomer. The potential will change with an increasing proportion of axial conformer, and it will be similar to that of the pure axial conformer when the latter reaches perhaps 10–20% of the total.

The obvious mechanistic interpretation of the observed results can be made by elaborating the scheme proposed by Elving and Van Atta⁴ to take into account the expected preferred *transoid* nature of such an elimination reaction, and it would be predicted that a lower half-wave potential should be observed for the axial conformer, as was



found. In view of the nature of the polarographic reduction of α -bromo esters,¹⁰ however, these suggestions must be regarded as only tentative.

The values of the slope of plots of E vs. $\log ((i_d - i)/i)$ are given in Table I under the heading $RT/\alpha nF$. If it is assumed that the electrode process consumes two electrons per α -halocyclohexanone, it is readily seen that the reduction is very irreversible. Interpretation of these values will be left to a future paper.

Experimental

Many of the compounds required for this work, specifically 2-chlorocyclohexanone,^{3a} the *cis*- and *trans*-2-chloro-4-*t*-butylcyclohexanones,^{3a} *trans*-2-chloro-5-methylcyclohexanone,⁹ 2-bromocyclohexanone,^{3b} and *cis*- and *trans*-2-bromo-4-*t*-butylcyclohexanones,^{3b} have been described previously. The fluoroketones were prepared by Dr. H. Blatter in these laboratories.⁸

Capillary Characteristics.—All polarographic reductions except a, b and that of the *trans*-2-fluoro-4-*t*-butylcyclo-

hexanone were run with a capillary of the following characteristics measured with an open circuit: $m = 8.20$ mg./sec., $t = 7.6$ sec., at a mercury height of 40.0 cm. The latter experiments were done with a capillary of the following characteristics measured with an open circuit: $m = 7.57$ mg./sec., $t = 7.3$ sec., at a mercury height of 26.8 cm.

Reagents.—Matheson Coleman and Bell dimethylformamide was used as the reaction solvent except where otherwise specified and was purified according to the procedure of Wawzonek.¹¹

Eastman Kodak Co. white label tetrabutylammonium bromide was purified by the procedure of Silverman.¹² Eastman Kodak Co. white label tetramethylammonium chloride was stored overnight in a vacuum desiccator and used without further purification.

Reference Electrode.—Polarographically used mercury was washed at capillary drop size through a 10% nitric acid column, washed twice with distilled water and once with acetone, then air-dried. A pool of mercury was delivered from a capillary to the bottom of the polarographic cell where contact was made with a platinum probe.

Instruments.—A Sargent model XXI polarograph was used for all polarograms. A Leeds and Northrup model student potentiometer was used for all potential calibrations. The precision was ± 5 millivolts. An Industrial Instruments Inc., model RC16B, conductivity bridge was used for measurement of cell resistance. Tenth molar tetrabutylammonium bromide-dimethylformamide solution has a resistance of 500 ohms.

Cells.—All experiments except a and b were run in a thermostated cylindrical cell 10 cm. high with an inside diameter of 2.4 cm. Experiments a and b were run in a standard polarographic H-cell without thermostating at $25.0 \pm 0.5^\circ$. All other experiments were run at $24.7 \pm 0.1^\circ$. A 3-hole stopper in the top of the cell accommodated a nitrogen capillary bubbler (which could be withdrawn from solution in order to pass nitrogen over the solution while the polarograms were run), a platinum probe with which contact was made to the mercury pool and the D.M.E.'s capillary.

Experiments a and b were run in order to determine whether or not the reduction is independent of the solvent, and to fix the reference potentials relative to the saturated calomel electrode. For a, reduction of 4.34 mM 2-chlorocyclohexanone with 0.1 *N* tetramethylammonium chloride in water gave a value for I of 1.13 $\mu\text{a. sec.}^{1/2}/\text{mM. mg.}^{1/2}$ a value for $E_{1/2}$ of -0.970 v. vs. saturated calomel electrode and a value for $RT/\alpha nF$ of 0.23 v. In b, 1.01 mM IIe with 0.1 *N* tetrabutylammonium bromide in dimethylformamide gave a value for I of 0.43 $\mu\text{a. sec.}^{1/2}/\text{mM. mg.}^{1/2}$ a value for $E_{1/2}$ of -2.00 v. vs. saturated calomel electrode and a value for $RT/\alpha nF$ of 0.13 v. Comparison of the two values for the *cis*-2-chloro-4-*t*-butylcyclohexanone system, neglecting liquid junction potentials, readily fixes the mercury pool-0.1 *M* tetrabutylammonium bromide electrode as being 0.43 v. more negative than the saturated calomel electrode. The addition of 25% water to experiment b did not result in a shift in the half-wave potential; however, a second wave appeared at about -2.3 v., presumably due to water. A comparison of the two values for 2-chlorocyclohexanone results in the aqueous reduction occurring more easily by 0.43 v., in agreement with earlier work.⁴ If the correction for the difference in reference potentials is included, we find that the α -chloroketone is reduced more easily in aqueous media by some 0.86 v. Thus water cannot be thought of as an inert solvent in these reductions.

(10) P. J. Elving, I. Rosenthal and A. J. Martin, *THIS JOURNAL*, **77**, 5218 (1955); I. Rosenthal, J. R. Hayes, A. J. Martin and P. J. Elving, *ibid.*, **80**, 3050 (1958).

(11) S. Wawzonek and A. Gundersen, *J. Electrochem. Soc.*, **107**, 537 (1960).

(12) L. Silverman, *Anal. Chem.*, **31**, 1672 (1959).