A solution of sodium hydroxide in ethylene glycol was prepared by mixing an appropriate amount of carbonate-free 40% sodium hydroxide solution with ethylene glycol. The concentration of sodium hydroxide in the solution was determined by titration of weighed aliquots, after diluting 10-fold with distilled water, against standard sulfuric acid using phenolphthalein as indicator.

The hydrolysis of the amide was carried out in a 3-necked flask equipped with a reflux condenser, a thermometer and an inlet for nitrogen gas which was bubbled slowly through the reaction mixture. The outlet of the reflux condenser was led into a known volume of standard sulfuric acid solution which served as an absorption system for ammonia. The reaction flask was heated by a heating mantle and the temperature was controlled by a Thermocap relay.[19]

A weighed amount of a 0.5 molal solution of sodium hydroxide in ethylene glycol was placed in the reaction flask. The temperature of the system was brought rapidly to 190–192°, and a weighed amount of amide ($^1/_{20}$ of the molar concentration of sodium hydroxide in the solution) was introduced.

The condenser and the absorption system was immediately connected to the reaction flask. Ammonia evolved during the course of the reaction was entrained by the stream of nitrogen and absorbed in the standard sulfuric acid solution. After 48 hr. the reaction was stopped and the amount of ammonia from the hydrolysis was estimated by titration of the excess acid against standard sodium hydroxide solution using as indicator screened methylene blue-methyl red. The results are shown in Table I.

Reaction of Hindered Aromatic Amides with Sodium Hydroxide in Ethylene Glycol.—A procedure similar to that described for the hydrolysis of aliphatic amides was employed. After the formation of nitrile was observed in preliminary experiments, the apparatus was modified by replacing the reflux condenser by a distilling condenser. The nitrile formed during the course of the reaction was removed from the reaction mixture by co-distillation with ethylene glycol. The reaction was carried out for 12 hr. during which about 10% of the reaction mixture was distilled. The amount of ammonia evolved was determined by titration. The nitrile was isolated from the distillate.

Mesitonitrile (m.p. 50°, reported[20] m.p. 53°) was purified by sublimation at 40° and 0.1 mm. pressure. The infrared spectrum (chloroform solution) showed an intense band at 4.6 μ (2170 cm.$^{-1}$) due to the nitrile function.[21] In one experiment, an intimate mixture of 0.30 g. of mesitamide and 2.8 g. of powdered sodium hydroxide was heated at 290–310° under 20 mm. pressure for 0.5 hr. Mesitonitrile (m.p. 49°) was obtained in 86% yield.

2,3,5,6-Tetramethylbenzonitrile (m.p. 73–74°, reported[22] m.p. 76–77°) was purified by sublimation at 50° and 0.08 mm. pressure. The infrared spectrum (chloroform solution) showed an intense band at 4.6 μ (2170 cm.$^{-1}$).

2,4,6-Triisopropylbenzonitrile was purified by chromatography of the crude substance in redistilled Skellysolve F (petroleum ether, b.p. 35–55°) over activated alumina. The solvent was removed under reduced pressure at room temperature. The residue was distilled to afford a pure sample of the nitrile, b.p. 264–268° at 740 mm., n^{20}_{D} 1.5089 (lit.[15] n^{20}_{D} 1.5093). Physical properties and the infrared spectrum of this nitrile were identical with those of a sample of the nitrile obtained by the dehydration of 2,4,6-triisopropylbenzamide by means of thionyl chloride in benzene solution. The results are summarized in Table II.

Acidic Hydrolysis of Hindered Aliphatic Nitriles.—A mixture of the nitrile[8] and sulfuric acid of known concentrations was heated at a specific temperature. After a certain period of heating, the reaction mixture was poured into a large excess of ice-water, and the mixture was worked up by the usual method of extraction. The extent of hydrolysis of the nitrile was indicated by the yield of the amide and the amount of recovered nitrile. The conditions and results of these experiments are summarized in Table III.

Conversion of Aliphatic Amides to Acids.—The amides were treated with a mixture of sodium nitrite and sulfuric acid according to procedures described in the literature.[9] The conditions and results are shown in Table IV.

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[19] Niagara Electronic Laboratories, Andover, N. Y. This instrument controlled the supply of electrical power to the heating system. The change of electric capacity necessary for the operation of this type of relay was effected by the movement of the mercury thread in the thermometer to which the relay lead was connected.

[20] R. Scholl and F. Kacer, *Ber.*, **36**, 331 (1903).

[21] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954.

[22] O. Jacobsen, *Ber.*, **22**, 1224 (1889).

COLUMBUS 10, OHIO

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Synthesis and Solvolysis of the 2-Halo-1,4-endoxocyclohexanes[1]

BY JAMES C. MARTIN[2] AND PAUL D. BARTLETT

RECEIVED DECEMBER 17, 1956

A kinetic study of the hydrolysis of *exo*-2-chloro-1,4-endoxocyclohexane has shown it to be less reactive than *exo*-norbornyl chloride by a factor of approximately 2000. Its relative inertness is considered to result from the inductive effect of the oxygen bridge, enhanced by its geometric situation. Solvolysis of *endo*-2-chloro-1,4-endoxocyclohexane was slower than that of its *exo* isomer by a factor of 160 (at 140°). This factor is of the same order of magnitude as the corresponding factor in the solvolysis of norbornyl derivatives suggesting that the anchimeric acceleration of ionization of the *exo*-2 substituent is not greatly affected by substitution of an oxygen bridge for the methylene bridge of the norbornyl derivatives. In every case the solvolysis product was that expected to result from rearrangement, 3-formylcyclopentanol. The structures of these chloro ethers, which were obtained from the photochlorination of 1,4-endoxocyclohexane, were confirmed by dipole moment studies. *exo*-2-Bromo-1,4-endoxocyclohexane, isolated from the N-bromosuccinimide bromination of the parent ether, showed a reactivity 30-fold greater than its chloro analog. An interesting side product (16%) isolated from this bromination reaction was β-bromopropionyl isocyanate.

Introduction

A large amount of work of a quantitative nature has been performed on the solvolytic reactions of the various norbornyl derivatives.[3] In the frame of understanding created by this work we have examined the chemical consequences of the replace-

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[1] Presented before the Organic Division of the American Chemical Society at its Atlantic City Meeting, September, 1956.

[2] National Science Foundation Fellow, 1953–1954.

[3] (a) J. D. Roberts, W. Bennett and R. Armstrong, THIS JOURNAL, **72**, 3329 (1950); (b) J. D. Roberts and W. Bennett, *ibid.*, **76**, 4623 (1954); (c) S. Winstein and D. Trifan, *ibid.*, **71**, 2953 (1949); (d) S. Winstein and D. Trifan, *ibid.*, **74**, 1147, 1154 (1952); (e) S. Winstein, B. Morse, E. Grunwald, H. Jones, J. Corse, D. Trifan and H. Marshall, *ibid.*, **74**, 1127 (1952); (f) S. Winstein, E. Clippinger, A. H. Fainberg and G. C. Robinson, *Chem. and Ind.*, 664 (1954); (g) J. D. Roberts and C. C. Lee, THIS JOURNAL, **73**, 5009 (1951); (h) J. D. Roberts, C. C. Lee and W. H. Saunders, Jr., *ibid.*, **76**, 4501 (1954); (i) P. D. Bartlett and L. H. Knox, *ibid.*, **61**, 3184 (1939); (j) W. von E. Doering and E. F. Schoenewaldt, *ibid.*, **73**, 2333 (1951); (k) S. Winstein, M. Shatavsky, C. Norton and R. B. Woodward, *ibid.*, **77**, 4183 (1955); (l) S. Winstein and M. Shatavsky, *ibid.*, **78**, 592 (1956).

ment of the 1,4-endomethylene bridge of the norbornyl system by the oxygen bridge of the 1,4-endoxocyclohexane system.

Results and Discussion

The photochlorination of 1,4-endoxocyclohexane at −40° led to the isolation of a series of chloro ethers including *exo*-2-chloro-1,4-endoxocyclohexane and *endo*-2-chloro-1,4-endoxocyclohexane. Infrared analysis showed the *exo* isomer to be formed in amount 2.2 times that of the *endo* isomer. None of the α-chloro ether, 1-chloro-1,4-endoxocyclohexane, which would result from bridgehead chlorination, was isolated. This is in accord with previously reported[4] unsuccessful attempts to obtain bridgehead chlorination in other systems.

The bromination of the parent ether, 1,4-endoxocyclohexane, with N-bromosuccinimide yielded *exo*-2-bromo-1,4-endoxocyclohexane.

These monohalo ethers were separated and purified by fractional distillation. The more highly chlorinated ethers resulting from further treatment with chlorine were separated by means of chromatography on alumina. A summary of the pure compounds isolated is presented in Table I.

TABLE I

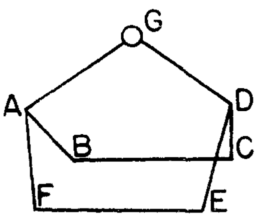
PRODUCTS OF THE HALOGENATION OF 1,4-ENDOXOCYCLOHEXANE

Ether	M.p. or b.p. °C.
endo-2-Chloro-1,4-endoxocyclohexane	68.0 (27)[a]
exo-2-Chloro-1,4-endoxocyclohexane	48.0 (4)[a]
exo-2-Bromo-1,4-endoxocyclohexane	68.2 (2)[a]
Dichloro ether	143.2–144.0
Trichloro ether	154.5–145.8
Tetrachloro ether	77.8–78.8
Hexachloro ether	108.6–109.0
Octachloro ether	158.8–159.4

[a] The value in parentheses refers to pressure (mm.).

The constraint afforded by the bicyclic structure of this series of halo ethers maintains quite constant the angles between the various bonds and, therefore, the angles between the bond moments. This greatly facilitates the interpretation of dipole moment data. If one considers the composite electric moment of the unsubstituted 1,4-endoxocyclohexane to be a vector directed toward the oxygen atom and perpendicular to the plane of carbon atoms 2, 3, 5 and 6, the effect of superposing moments arising from replacement of the various hydrogen atoms by halogen may be computed.

A geometric model for the bicyclic nucleus of this system was derived using vector analytical procedures.[5] The model chosen for these calculations used a value for the C–C bond length of 1.55 Å. and for the C–O bond length, 1.44 Å. The values of the angles in this model were: ∠ FAB = 101°, ∠ ABC = 103°, ∠ AGD = 102° 54′ and ∠ BAG = 101° 14′.



The theoretical dipole moments were calculated as the resultant of the ether dipole moment (the experimental moment of 1,4-endoxocyclohexane, 1.74 *D*) and the C–Cl bond moment (the experimental moment of cyclopentyl chloride, 2.08 *D*)[6].

TABLE II

RESULTS OF DIPOLE MOMENT STUDIES ON THE MONOHALO-1,4-ENDOXOCYCLOHEXANES

Compound	Solvent	Moment, *D* Calcd.	Moment, *D* Found
1,4-Endoxocyclohexane	Benzene	..	1.70
	CCl_4	..	1.78
1-Chloro-1,4-endoxocyclohexane	.....	3.20	..
exo-2-Chloro-1,4-endoxocyclohexane	Benzene	3.17	3.07
	CCl_4	3.17	2.99
endo-2-Chloro-1,4-endoxocyclohexane	Benzene	0.82	1.08
exo-2-Bromo-1,4-endoxocyclohexane	CCl_4	3.17	3.03

These data make it clear that the assignment of structure for *endo*-2-chloro-1,4-endoxocyclohexane is the correct one. The data for the other chloro ether are compatible with either *exo*-2-chloro-1,4-endoxocyclohexane or 1-chloro-1,4-endoxocyclohexane. The isolation of 3-formylcyclopentanol (V) as the solvolysis product from both of the chloro ethers confirmed the assignment of the structure *exo*-2-chloro-1,4-endoxocyclohexane. The structure of the bromo ether was similarly shown to be *exo*-2-bromo-1,4-endoxocyclohexane. The hydroxyaldehyde was formed nearly quantitatively in the solvolyses of all three of these halo ethers. The structure 3-formylcyclopentanol was established by Wolff–Kishner reduction to the known[7] *trans*-3-methylcyclopentanol.

The assigned structures for these halo ethers were found to be compatible with the observed infrared spectra and proton nuclear magnetic resonance (NMR) spectra. The NMR spectra, obtained using a Varian Associates model V-4300B high resolution spectrograph, are schematically summarized in Fig. 1.

The parent ether, 1,4-endoxocyclohexane, shows two resonance peaks, of approximate relative intensities 4 and 1, at positions corresponding to Gutowsky δ-values[8] of approximately −0.43 and −0.10 (the methylene and the bridgehead hydrogens, respectively). No evidence of splitting, from spin-spin interaction, was observed for either of these peaks.

The spectra of the *exo*-2-halo-1,4-endoxocyclohexanes show a total of four main resonance peaks corresponding, presumably (in order of increasingly negative δ-values), to the bridgehead hydrogens (intensity 2), the halomethylene hydrogen (1), the methylene adjacent to halomethylene (2) and the other two methylene groups (4). The positions of these peaks are expressed as δ-values: *exo*-chloride, (−0.10, −0.15, −0.37, −0.43); *exo*-bromide (−0.10, −0.15, −0.35, −0.43). The peak at 0.10 is a poorly resolved doublet, as might be expected from the non-equivalence of the bridgehead hydro-

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(4) See D. E. Applequist and J. D. Roberts, *Chem. Revs.*, **55**, 1065 (1954).

(5) E. J. Corey and R. A. Sneen, THIS JOURNAL, **77**, 2505 (1955).

(6) H. Rogers and J. D. Roberts, *ibid.*, **68**, 843 (1946).

(7) M. Godelot, G. Cauquil and R. Calas, *Bull. soc. chim.*, **6**, 1351 (1939).

(8) L. H. Meyer, A. Saika and H. S. Gutowsky, THIS JOURNAL, **75**, 4567 (1953).

TABLE III

ENTHALPIES AND ENTROPIES OF ACTIVATION FOR SOLVOLYSIS

Compound	Solvent	$\Delta H^{\ddagger}$, kcal.	$\Delta S^{\ddagger}$, e.u.
exo-2-Chloro-1,4-endoxocyclohexane	50% dioxane–H_2O	29.43 ± 0.12	− 7.47 ± 0.29
endo-2-Chloro-1,4-endoxocyclohexane	50% dioxane–H_2O	30.87 ± 0.15	−14.07 ± 0.34
exo-2-Bromo-1,4-endoxocyclohexane	50% dioxane–H_2O	24.6 ± 0.54	−15.00 ± 1.45
exo-2-Norbornyl *p*-bromobenzenesulfonate	Acetic acid	23.3[a]	7.7[a]
endo-2-Norbornyl *p*-bromobenzenesulfonate	Acetic acid	26.0[b]	− 1.5[b]

[a] This value, calculated from the data of Winstein,[3e] was from two runs at temperatures differing by 8.77°. [b] Calculated from the data of Winstein.[3e]

TABLE IV

SOLVOLYSES OF THE 2-HALO-1,4-ENDOXOCYCLOHEXANES

Run	Compound	Concentration halide, mole/l.	Temp., °C.	Reaction followed, %	Added salt	Salt concn., mole/l.	k, sec.$^{-1}$[a]
1	*exo*-Br	0.03967[b]	85.0	58.1			$(8.58 \pm 0.06) \times 10^{-7}$
2	*exo*-Br	.03988[c]	85.0	52.9			$(4.64 \pm .05) \times 10^{-7}$
3	*exo*-Br	.04028[d]	85.0	79.0			$(8.24 \pm .04) \times 10^{-6}$
4	*exo*-Br	.04020[d]	100.7	70.6			$(3.77 \pm .03) \times 10^{-5}$
5	*exo*-Br	.04344[d]	120.0	90.0			$(1.85 \pm .03) \times 10^{-4}$
6	*exo*-Br	.04026[d]	85.0	32.5	KCl	0.10	$(8.41 \pm .04) \times 10^{-6}$
7	*exo*-Br	.04193[d]	85.0	52.8	$NaClO_4$	.10	$(9.07 \pm .03) \times 10^{-6}$
8	*exo*-Cl	.04328[d]	100.7	32.8			$(1.17 \pm .03) \times 10^{-6}$
9	*exo*-Cl	.04069[d]	120.0	64.1			$(8.81 \pm .37) \times 10^{-6}$
10	*exo*-Cl	.04032[d]	140.0	79.1			$(5.66 \pm .04) \times 10^{-5}$
11	*endo*-Cl	.03969[d]	140.0	38.7	NaOAc	0.042	$(3.47 \pm .09) \times 10^{-7}$
12	*endo*-Cl	.03948[d]	160.0	66.4	NOaAc	.041	$(2.08 \pm .02) \times 10^{-6}$
13	*endo*-Cl	.03420[d]	175.0	71.4	NaOAc	.042	$(7.10 \pm .08) \times 10^{-6}$
14	*endo*-Cl	.03961[d]	140.0	84.6			Autocatalytic
15	*endo*-Cl	.03610[d]	140.0	44.2	HCl	.02	Autocatalytic
16	*endo*-Cl	.03312[d]	140.0	19.6	KCl	.02	Autocatalytic

[a] These first-order rate constants were determined by a least squares treatment of the data. The uncertainties which are indicated are standard deviations. [b] In 80% ethanol (vol.). [c] In 80% ethanol (wt.). [d] In 50% dioxane (wt.).

gens because of the halogen at position 2. The halomethylene hydrogen resonance at −0.15 is strongly split into a triplet, presumably from spin–spin interaction with the protons of the neighboring methylene. The resonance of this neighboring methylene, at −0.37 or −0.35, appears as a doublet, as expected from such an interaction.

The *endo*-chloride shows a similar spectrum with an additional poorly resolved peak, of intensity approximately 1, at −0.32, possibly to be attributed to a transannular interaction of an *endo*-hydrogen at position 6 with the *endo*-chlorine. In addition, there is some evidence of splitting in the methylene peak at −0.43. The positions of the resonance peaks for this compound are (−0.05, −0.12, −0.32, −0.37, −0.43).

Results of kinetic studies on the solvolytic reactions of these ethers are outlined in Tables III and IV. The reactions were followed by acidimetric titration of aliquots.

A direct comparison of the rate constants for the *exo*- and *endo*-2-chloro-1,4-endoxocyclohexanes at 140° in 50% dioxane–water gives a reactivity ratio of 163 for these isomers, the *exo* isomer being the more reactive. Table V gives calculated values for this ratio from the present work, the work of Roberts and the work of Winstein. It can be seen that this ratio is not changed greatly in the 1,4-endoxocyclohexane system from its value in the norbornyl system.

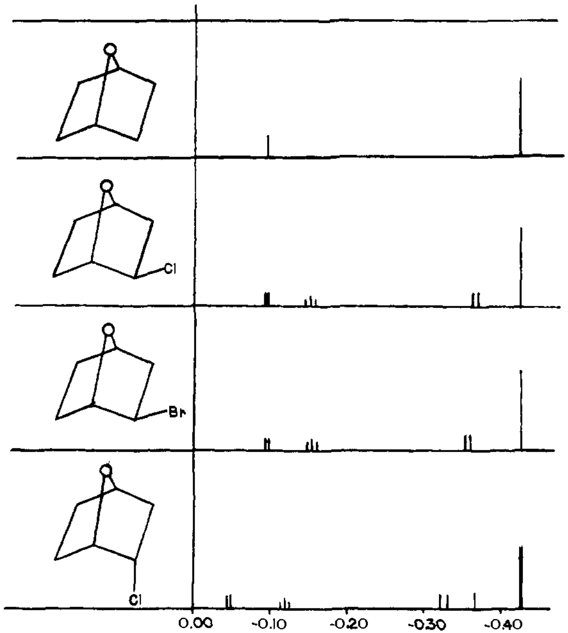


Fig. 1.—Proton nuclear magnetic resonance spectra of 1,4-endoxocyclohexane derivatives.

The calculated value (from ΔH^* and ΔS^*) of the rate constant for the solvolysis of *exo*-2-chloro-1,4-endoxocyclohexane in 50% aqueous dioxane at 85.0° is 1.88×10^{-7} sec.$^{-1}$. The value of the rate constant for the solvolysis of the corresponding bromo ether is decreased by a factor of 9.6 when the solvent is changed from 50% dioxane–water to 80% (by vol.) ethanol–water. Assuming a parallel change in the rate constant for the chloro ether in these two solvents, one calculates a rate constant for the *exo*-chloride at 85.0° in 80% (by vol.) ethanol of 1.96×10^{-8} sec.$^{-1}$. Under these same conditions Roberts^{3b} found a rate constant of 3.89×10^{-5} sec.$^{-1}$ for *exo*-norbornyl chloride.

Comparison of these values for the two bicyclic systems shows the norbornyl chloride to be more reactive than its oxygen-bridged analog by a factor of 2.0×10^3. A similar calculation for the *endo* isomers gives a factor of 6.0×10^3.

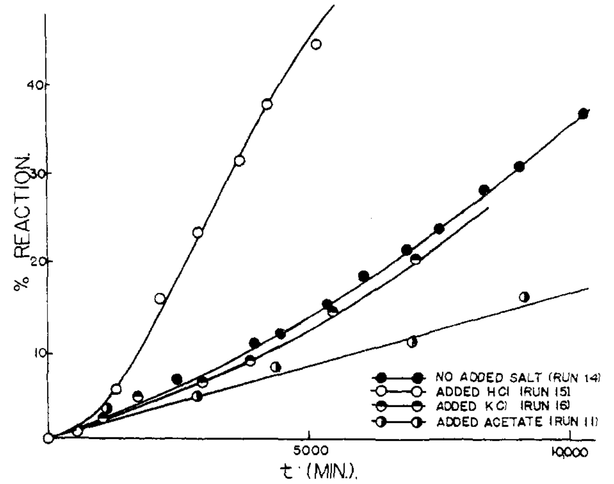
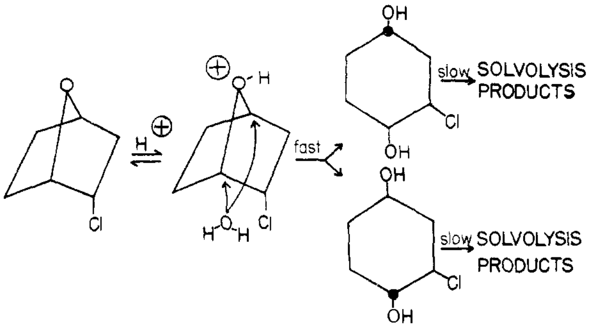


Fig. 2.—Solvolysis of *endo*-2-chloro-1,4-endoxocyclohexane in 50% dioxane–water (by weight) at 140°.

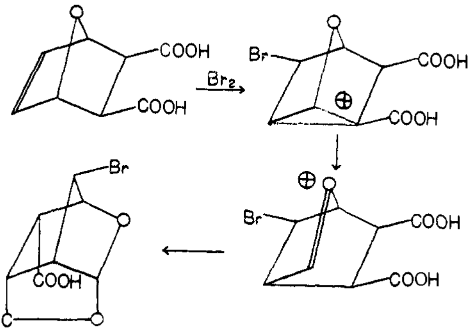
Early kinetic runs on the solvolysis of *endo*-2-chloro-1,4-endoxocyclohexane, with no added salt, proved to be autocatalytic. Several possible mechanisms for this autocatalysis were investigated (see Fig. 2). The possibility that the autocatalytic agent was chloride ion, perhaps operating through an SN2 inversion to give the reactive *exo*-chloride, was ruled out when the rate with added potassium chloride proved to be almost identical to the rate with no added salt. The addition of hydrochloric acid to the reaction mixture gave, after an induction period, an appreciable acceleration of rate. A direct catalysis, by hydrogen ion, of the ionization of the chloride, such as that observed by Bartlett and Pöckel[9] in the isomerization of camphene hydrochloride, was ruled out by the observation of an induction period in this run. When an equivalent amount of sodium acetate was added to the reaction and the rate of solvolysis followed by titrating aliquots for excess acetate, the reaction was found to follow the first-order rate law very closely.

The catalytic effect of hydrochloric acid may be explained by postulating an ether cleavage to yield a chlorohydrin, which solvolyzes at a rate somewhat faster than the chloro ether. In a related case^{3e} the solvolysis of 2-chloro-2-methylpropanol-1 is slower than that of *t*-butyl chloride by a factor of 6.5×10^{-3}. Since *endo*-2-chloro-1,4-endoxocyclohexane is approximately 10^{-4} as reactive as cyclohexyl chloride in solvolytic reactions, we might expect the chlorohydrin from the ether cleavage to be about 60–70 times as reactive as the chloro ether itself. Such a ratio of reactivities could account for the observed behavior.

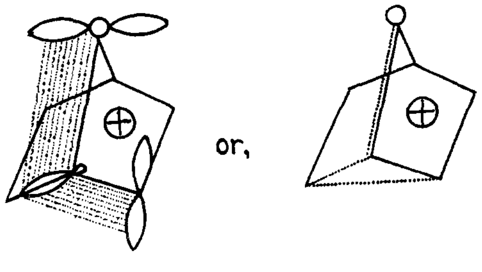


Two different interactions of the unshared electron pairs of the oxygen bridge might be expected to affect the *exo*/*endo* reactivity ratio in these solvolytic reactions.

With regard to the first of these effects, Woodward and Baer[10] postulated an important contribution from the oxonium form of the positively charged intermediate ion as a driving force in the rearrangement which accompanies the addition of bromine to *exo-cis*-3,6-endoxo-Δ^4-tetrahydrophthalic acid.



In the present work we must consider the possible stabilization, by such an oxonium form, of the transition state leading to the positive ion. Any such stabilization involves an interaction between a lone pair orbital of oxygen, the bonding orbital between C_1 and C_6 and the developing p-orbital at C_2, where the leaving group is *exo*.



Since the observed *exo*/*endo* ratio is of the same order of magnitude for the endoxo- and endomethylene series, it is unnecessary to postulate an important contribution of this oxonium form in the transition state. Once the ion is formed, however, slight changes in geometry, perhaps over a very small potential energy barrier, might be expected

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(9) P. D. Bartlett and I. Pöckel, This Journal, **60**, 1585 (1938).

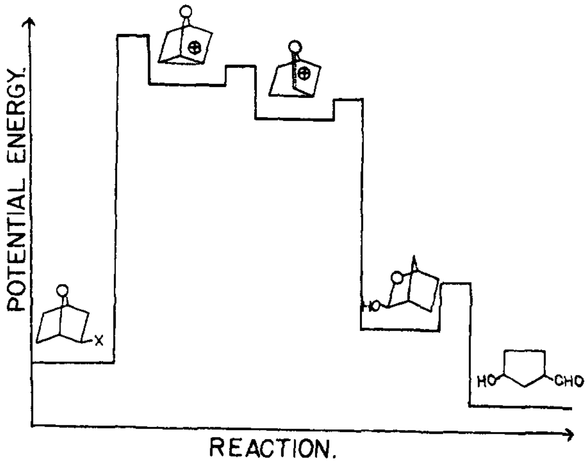
(10) R. B. Woodward and H. Baer, *ibid.*, **70**, 1161 (1948).

TABLE V

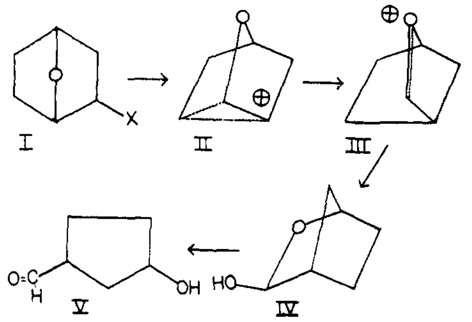
exo/endo REACTIVITY RATIOS IN SOLVOLYTIC REACTIONS

Series of compounds	Temp., °C.	k_{exo}/k_{endo}	k_{endo}, sec.$^{-1}$
Norbornyl chlorides[3b]	85	70	5.6×10^{-7}
Norbornyl brosylates[3f]	25	350	2.5×10^{-7}
	85	275	4.7×10^{-4}
2-Chloro-1,4-endoxocyclohexanes	140	163	3.5×10^{-7}
	85	211	8.9×10^{-10}
	25	318	1.2×10^{-13}

to twist the molecule into a form much more favorable to overlap between oxygen lone pair orbitals and a p-orbital on C_1. The large stabilization so attained would be similar to that in the transition states for the ionizations of α-halo ethers.

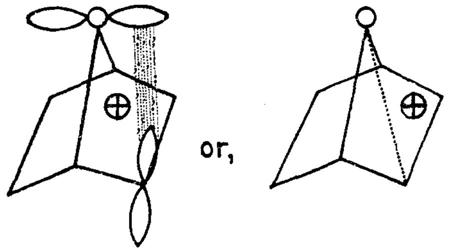


A POSSIBLE POTENTIAL ENERGY SCHEME.



Such a scheme is compatible, but of course not uniquely so, with the observed isolation of rearranged product (as aldehyde) in nearly quantitative yield. It is also compatible with results of experiments designed to intercept the cationic intermediate with azide ion. According to Swain[11] the azide ion is a more active nucleophile than water by a factor of 10^4 to 10^5. In his kinetic treatment of interception experiments using azide ion, Swain considered the alkyl azide to be formed irreversibly where the alkyl group was, for example, triphenylmethyl. In the present work solvolyses with 0.6 *N* added azide (sufficient, using Swain's competition factor, to capture more than 99% of the carbonium ions in competition with water), the product obtained was 3-formylcyclopentanol with less than 3% of an alkyl azide. A possible explanation for this unexpected behavior would involve an attack of azide ion either on II or on III, which is formed very rapidly from II, to give the α-azido ether which is then subject to hydrolysis to 3-formylcyclopentanol.

A second effect to be ascribed to the lone pair electrons might be classified as a homoallylic interaction—a direct interaction between the developing p-orbital at the ionizing center and a lone pair orbital. The situation is superficially similar to that which gave rise to a rate acceleration of 10^{11} in the solvolysis of *anti*-7-dehydronobornyl tosylate.[3k,1] In that system the interaction is between a developing p-orbital at C_7 and the π-electron system of C_2 and C_3. In the present system we might postulate a lesser, but perhaps still substantial, interaction between the developing p-orbital at C_2 and a lone pair orbital on oxygen. The result of such an interaction would be an acceleration of the rate of ionization of an *endo* substituent.



Again, the failure to observe any major difference in the *exo/endo* reactivity ratios for the endoxo and the endomethylene series would seem to rule out any very important contribution from this effect.

It might be argued that the observation of roughly comparable reactivity ratios for the two series of compounds does not, in fact, indicate that these effects are inoperative or of small importance but rather that it represents the result of a fortuitous cancelling of the two effects, which are postulated to affect the *exo/endo* ratio in opposite directions. If such were the case, the reactivity of the entire series of endoxo compounds might be expected to be greater than that observed.

The observed factor of 6×10^3 between the rates of solvolytic reactions of the norbornyl and 1,4-endoxocyclohexyl chlorides is somewhat greater than that to be expected from the consideration of model compounds[12] or that predicted by the dipole interaction calculations of Winstein.[13,14] Winstein concludes that the rate depression in acetolysis reactions to be expected from the purely inductive effect of a neighboring methoxy group is a factor of approximately 100. The observed difference between the solvolysis rates of the endoxo and endomethylene series of compounds is approximately 60 times greater than this.

In the 1,4-endoxo compounds the ether bridge corresponds not only to a β-alkoxy group but also to a γ-alkoxy group relative to substituents at the 2-position. This statement is equivalent to a

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(11) C. G. Swain, C. B. Scott and K. H. Lohmann, THIS JOURNAL, **75**, 136 (1953); C. G. Swain and C. B. Scott, *ibid.*, **75**, 141 (1953).

(12) S. Winstein and E. Grunwald, *ibid.*, **70**, 828 (1948).

(13) S. Winstein, E. Grunwald and L. L. Ingraham, *ibid.*, **70**, 821 (1948).

(14) E. Grunwald, *ibid.*, **73**, 5458 (1951).

recognition that the orientation of the over-all ether dipole is fixed in such a manner as to increase the effectiveness of its interaction with dipoles at the 2-position.

A somewhat similar situation is discernible in data on the acid dissociation constants of conjugate acids of amines.[15]

Amine	pK_{AH} (25°)
Ethylamine	10.81
β-Methoxyethylamine	9.45
Morpholine	8.70
Piperidine	11.28

The pK_{AH} for ethylamine exceeds that for β-methoxyethylamine by 1.36 units, whereas the difference in the corresponding constants for the two cyclic amines is 2.58.

Another possible explanation for the enhanced inductive effect of the oxygen bridge lies in a consideration of the solubilities of ethers in water. Ferguson[16] has pointed out that the association of liquid water with molecules through hydrogen bonding can apparently be subject to appreciable steric hindrance. The enhanced solubility of cyclic ethers is explained by their greatly reduced steric hindrance to such hydrogen bonding.

An experimental determination of the solubility of 1,4-endoxocyclohexane (10.5 parts per hundred parts water) at 25° showed it to be more soluble than its open-chain analog, diisopropyl ether (0.2 parts per hundred parts water), by a factor of approximately 50.

If this increased solubility may be attributed to increased effectiveness of hydrogen bonding of the ether with water, an individual molecule of the bicyclic ether, in aqueous solution, would be much more likely to be involved in a hydrogen bonded association than an acylic ether. In the rate studies of this work one might expect such hydrogen bonding to deactivate the molecule toward an ionization which would place a positive charge on the bicyclic nucleus.

The most straightforward interpretation of the present results, therefore, would postulate the principal effect of the oxygen bridge on solvolysis rates to be a simple inductive effect. Any resonance effects of this oxygen would seem to be relatively unimportant in the transition states of such reactions.

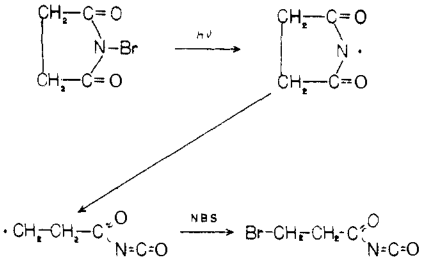
As a side-product in the photochemical bromination of 1,4-endoxocyclohexane with N-bromosuccinimide (NBS), an appreciable yield (*ca.* 15%) of β-bromopropionyl isocyanate was isolated. The material, isolated by distillation at reduced pressure (b.p. 53–56° (2 mm.)), showed an infrared absorption peak at 4.45 μ, an absorption characteristic of organic isocyanates. It reacted vigorously with water to evolve one mole of carbon dioxide and yield crystalline β-bromopropionamide. The identity of the material was further established by comparison of its infrared spectrum and reactivity toward water with that of a sample of β-bromopropionyl isocyanate prepared by the reaction of β-bromopropionyl chloride and silver cyanate.

$$AgCNO + RCOCl \longrightarrow R\overset{\overset{\displaystyle O}{\|}}{C}{-}N{=}C{=}O + AgCl$$

The formation of isocyanate was also observed in the absence of 1,4-endoxocyclohexane when a boiling suspension of NBS in carbon tetrachloride was strongly irradiated. The yield, followed by observation of the infrared absorption at 4.45 μ, was small but definite, reaching a maximum after about 24 hr., then disappearing as heating and irradiation were continued. This is compatible with the observed instability of β-bromopropionyl isocyanate.

The reaction of N-bromosuccinimide to give the isocyanate was found to proceed only under those conditions generally conceded to be favorable to radical mechanisms. For example, the reaction was observed to proceed when a boiling mixture of NBS and carbon tetrachloride was strongly irradiated or when benzoyl peroxide was added to such a boiling mixture in the dark. No isocyanate was observed when the mixture was boiled in the dark with no added source of radicals.

It would therefore seem that the reaction, formally an isomerization of NBS, either proceeds by a radical mechanism or is catalyzed by products of a radical reaction. A possible mechanism would involve initial homolytic cleavage of the N–Br bond of NBS followed by ring opening of the resulting succinimide radical.



Experimental Section

All melting points and boiling points are uncorrected.

The microanalyses were performed by Dr. S. M. Nagy, Massachusetts Institute of Technology; by Dr. H. Manser, Eidg. Techn. Hochschule, Zurich; and by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Chlorination of 1,4-Endoxocyclohexane: Procedure.—The starting material, 1,4-endoxocyclohexane, was prepared after the manner of Fehnel, Goodyear and Berkowitz.[17] It was purified by distillation through a 100-cm., vacuum jacketed column packed with glass helices. The product showed b.p. 119–119.5° (766 mm.), $n^{20}D$ 1.4480; infrared spectrum (letters refer to intensity—strong, medium or weak; wave length in μ): 3.39s, 3.45m, 3.50m, 6.81m, 6.90m, 7.59m, 7.69m, 7.94s, 8.39s, 8.77w, 9.11w, 9.31m, 10.01s, 10.27m, 10.72s, 11.05m, 11.40s, 12.18s, 12.71m, 13.12w.

The chlorinations were carried out in a reaction vessel fitted with a fritted-glass gas dispersion tube. The reaction vessel was immersed in a cooling bath of Dry Ice in acetone in an unsilvered Dewar flask. This permitted the irradiation of the reaction mixture with a sunlamp at a distance of about 4 in. The chlorine was measured by condensing it into a calibrated Pyrex trap and measuring its volume at the boiling point (where its density is 1.56 g./ml.). As the chlorine evaporated it was carried from this trap in a stream of dry nitrogen (Airco Prepurified Nitrogen), through a phosphorus pentoxide drying tower and into the reaction vessel through a gas dispersion tube. Any unreacted chlorine

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(15) R. J. Bruehlman and F. H. Verhoek, THIS JOURNAL, **70**, 1401 (1948).

(16) L. N. Ferguson, *ibid.*, **77**, 5288 (1955).

(17) E. A. Fehnel, S. Goodyear and J. Berkowitz, *ibid.*, **73**, 4978 (1950).

which was carried through the reaction vessel was condensed in a trap at −78°. This chlorine was distilled back into the first trap in the system and recirculated until all of it was used. A loss of chlorine through the final trap became obvious in some of the longer experiments. Each section of this apparatus was suitably protected from suck-back of liquids by interposition of a reversed trap. All of the traps were of approximately 250-ml. capacity. All of the connections in this apparatus were either of Pyrex glass or Tygon tubing. The lamp was a General Electric sunlamp.

The Monochloro Isomers.—In a typical experiment, 1,4-endoxocyclohexane (190 g., 1.94 moles) was placed in a 250-ml. reaction tube in the chlorination system described above and cooled to −22° in a Dry Ice–carbon tetrachloride-bath. To this solution 137 g. (1.94 moles) of chlorine was added slowly, in a stream of nitrogen, through the gas dispersion tube. The mixture was irradiated during this addition by a sunlamp. The chlorine was added in about 1 hr., and the small amount of chlorine from the exit trap was passed again into the reaction vessel. A moderate flow of nitrogen was maintained throughout the reaction to promote stirring and to remove hydrogen chloride formed in the reaction. After 3 hr. all the chlorine was consumed, as indicated by the loss of color. The reaction was allowed to return to room temperature as the stream of nitrogen was continued for 2 hr. more. The crude reaction mixture (260 g.) was then allowed to stand over moist sodium carbonate overnight to destroy any remaining hydrogen chloride. The mixture was then dried over magnesium sulfate and distilled through a 19-plate column at 1 mm. A large fraction distilled at less than 30° (principally the starting ether, 108.0 g.). A second fraction boiling at 30–37° weighed 15.9 g. (6.2%) and consisted principally of *endo*-2-chloro-1,4-endoxocyclohexane. A fraction, b.p. 37–40°, weighing 9.29 g. (3.7%) was a mixture of the two isomers. Another fraction, b.p. 40–43°, weighing 73.0 g. (28.4%) was principally *exo*-2-chloro-1,4-endoxocyclohexane.

The two isomers are easily differentiated and their separation followed by their distinctive C–Cl stretching frequencies in the infrared. The *endo* isomer absorbs at 14.25 μ and the *exo* isomer at 14.5 μ. Since the unsubstituted ether is transparent to radiation in the wave length region 14–16 μ and each of the two monochloro isomers has a well-defined absorption peak in a different part of this region, it was possible to estimate the proportion of these isomers formed in the reaction more accurately by infrared analysis.

The two absorption maxima were shown to obey Beer's law in carbon tetrachloride solution. The extinction coefficient for the 14.25 μ peak of the *endo* isomer was found to be larger than that for the 14.50 μ peak of the *exo* isomer by a factor of 2.1. The analysis was run on the crude product of a chlorination reaction in which the ether was used in sixfold excess to minimize the amount of polychlorination. By comparison of the two (nearly equal) peaks representing the two monochloro ethers, the *exo* isomer was found to be present in quantity 2.2 times as great as the *endo* isomer.

The two monochloro isomers were purified by redistillation. The *endo* isomer boiled at 68° (27 mm.), $n^{25}\text{D}$ 1.4780, d_{25} 1.1833; Infrared spectrum (wave length in μ): 3.39s, 3.46w, 3.54w, 6.84m, 6.93m, 7.56w, 7.62m, 7.69m, 7.91m, 8.03s, 8.33w, 8.45s, 8.71m, 9.04m, 9.33w, 9.65m, 10.05s, 10.57s, 10.93w, 11.55m, 12.06m, 12.39s, 12.75s, 13.11s, 14.25s.

Anal. Calcd. for C_6H_9OCl: C, 54.32; H, 6.84; Cl, 26.74. Found: C, 54.51; H, 6.81; Cl, 27.4 (Stepanov determination).

The *exo* isomer boiled at 48.0° (4 mm.), $n^{25}\text{D}$ 1.4847, d_{25} 1.1927; infrared spectrum (wave length in μ): 3.39s, 3.52m, 6.84m, 6.95m, 7.61w, 7.75m, 7.81m, 7.91m, 7.97m, 8.04m, 8.24m, 8.33m, 8.40s, 8.70w, 8.86m, 9.30m, 9.55s, 9.76m, 10.00s, 10.18m, 10.63s, 10.95m, 11.03m, 11.29s, 11.84m, 12.25s, 12.53m, 13.03m, 14.50m.

Anal. Calcd. for C_6H_9OCl: C, 54.32; H, 6.84; Cl, 26.74. Found: C, 54.08; H, 6.62; Cl, 27.0 (Stepanov determination).

Dichloro-1,4-endoxocyclohexane.—*exo*-2-Chloro-1,4-endoxocyclohexane (10 g., 0.075 mole) in a small reaction tube equipped with a gas dispersion tube was placed in a chlorination train similar to the one described above except that smaller traps were used in order to reduce the volume of the system. The ether was treated with one equivalent of chlorine (5.4 g., 3.4 ml.) at −22°, with irradiation. After reaction was complete (1 hr.), the reaction was warmed to 30° with nitrogen scrubbing for 2 hr. The 11.32 g. of material yielded 2.4 g. (19%) of crystalline material on cooling in a refrigerator, which, after several recrystallizations from benzene and carbon tetrachloride gave small white needles m.p. 143.2–144.0°; infrared spectrum (wave length in μ): 3.32m, 3.38m, 6.90m, 6.95m, 7.59m, 7.80w, 7.90m, 8.05m, 8.16m, 8.27m, 8.40m, 8.55w, 9.80s, 9.95s, 10.20w, 10.55m, 10.85m, 11.03s, 11.40s, 12.42m, 12.51m, 14.02w, 14.81w.

Anal. Calcd. for $C_6H_8OCl_2$: C, 43.10; H, 4.85; Cl, 42.46. Found: C, 43.07, 42.79; H, 4.65, 4.98; Cl, 43.02, 42.28.

More Highly Chlorinated Ethers.—These ethers were formed from the treatment of pure 1,4-endoxocyclohexane with chlorine as described above. Adding more equivalents of chlorine over longer periods of time, it was necessary to raise the temperature of the reaction slowly to prevent formation of solid material. The various crude reaction mixtures were separated by chromatography into crystalline components which were further purified by recrystallization.

A trichloro ether crystallized from benzene as small white needles, m.p. 154.5–154.8°; infrared spectrum (wave length in μ): 3.35w, 6.95w, 7.02m, 7.58m, 7.80w, 7.91m. 8.06m, 8.13m, 8.25m. 8.38m, 8.63m, 9.50w, 9.95s, 10.18m, 10.30w, 10.60m, 10.82m, 11.11s, 11.42s, 12.45s, 14.22m, 14.90m.

Anal. Calcd. for $C_6H_9OCl_3$: C, 35.74; H, 3.50; Cl, 52.75. Found: C, 35.54; H, 3.28; Cl, 52.02.

A tetrachloro ether gave, from pentane solution, chunky rhomboidal crystals, m.p. 77.8–78.8° (softens 77.0°); infrared spectrum (wave length in μ): 3.42w, 6.99m, 7.63w, 7.98m, 8.10m, 8.50m, 8.57m, 8.98m, 9.36m, 9.90m, 10.00m, 10.21s, 10.31m, 10.46m, 10.99m, 12.47s, 13.48m.

Anal. Calcd. for $C_6H_6OCl_4$: C, 30.55; H, 2.57; Cl, 60.12. Found: C, 30.58; H, 2.69; Cl, 60.28.

A hexachloro ether was obtained as white prisms, m.p. 106.8–107.3°, from pentane; infrared spectrum (wave length in μ): 3.30w, 7.73m, 8.08m, 8.23m, 9.67m, 9.74m, 10.25s, 10.55m, 10.69s, 10.90s, 11.62s, 11.73s, 12.76m, 12.90s, 13.43w.

Anal. Calcd. for $C_6H_4OCl_6$: C, 23.65; H, 1.32; Cl, 69.80. Found: C, 23.83; H, 1.49; Cl, 68.78.

An octachloro-1,4-endoxocyclohexane was recrystallized from ligroin to yield long stave-like crystals, m.p. 158.4–159°; infrared spectrum (wave length in μ): 3.28w, 8.25m, 9.57w, 9.90m, 10.28s, 10.66s, 10.74m, 11.06w, 11.58s, 11.96m.

Anal. Calcd. for $C_6H_2OCl_8$: C, 19.28; H, 0.54; Cl, 75.90. Found: C, 19.30; H, 0.61; Cl, 75.83.

Bromination of 1,4-Endoxocyclohexane.—N-Bromosuccinimide (greater than 99% purity) from Arapahoe Chemicals, Inc., was freshly recrystallized from water before use in these experiments. The substitution of NBS from another source (Fisher Scientific Co.) made no apparent difference in the course of the reaction. Merck Reagent carbon tetrachloride was used as solvent.

In a typical experiment 1,4-endoxocyclohexane (196.0 g., 2.0 mole) was dissolved in 500 ml. of carbon tetrachloride in a 1-l. flask fitted with a reflux condenser and a calcium chloride drying tube. NBS (178 g., 1.0 mole) was added to this solution and the suspension heated to boiling while irradiating with a sunlamp. After about 2 hr. the mixture became homogeneous. The heating and irradiation were continued for 5 hr. altogether, and the resulting deep-red solution was cooled overnight in a refrigerator at 0°. The crystals of succinimide (42.0 g., 42.5%) which were deposited during this time were removed by filtration. The solvent and excess 1,4-endoxocyclohexane were removed by distillation at water-pump pressure. The liquid residue was then fractionally distilled through a 50-cm., vacuum-jacketed column packed with glass helices. The following fractions were taken:

Fraction	B.p., °C. (2 mm.)	Weight, g.
I	53.0–56.0	21.40
II	56.0–62.0	7.63
III	62.0–68.0	7.77
IV	68.0–68.5	20.85
V	68.5–75.0	22.30

The various fractions were examined by infrared spectroscopy. The fore-run contained carbon tetrachloride and recovered 1,4-endoxocyclohexane. No part of the fore-run showed an absorption near 4.5 μ which could be attributed to an isocyanate.

Fraction I was essentially pure β-bromopropionyl isocyanate. Fraction II contained a small amount of higher boiling material but was mostly the isocyanate. These first two fractions constitute a yield of 16.3% of β-bromopropionyl isocyanate. Redistillation gave a colorless liquid, b.p. 54.0–55.0° (2 mm.), which had a sharp, characteristic odor and was mildly lachrymatory. A small sample of this material was distilled into a tube and sealed off under high vacuum. It began to acquire a yellow color after one day at room temperature and after two weeks was an extremely viscous, semi-solid material of deep orange color.

Fraction IV was essentially pure *exo*-2-bromo-1,4-endoxocyclohexane (11.8%). The distillation was discontinued during the collection of fraction V when a rapid decomposition occurred in the pot leaving a black tar and evolving much hydrogen bromide.

Reaction of the Isocyanate with Water.—To β-bromopropionyl isocyanate (0.50 g., 0.0028 mole) from the reaction described above, tetrahydrofuran containing 10% water was added dropwise until no further gas evolution was observed on adding another drop of the water solution. The evolved gas was carried in a stream of nitrogen through a trap containing aqueous barium hydroxide. The precipitated barium carbonate was filtered, washed with 100 ml. of water and dried at 100° (0.56 g., 1.13 moles per mole of isocyanate). The tetrahydrofuran and excess water were removed from the reaction mixture by distillation at reduced pressure leaving 0.40 g. of a white crystalline material, m.p. 109.5–111.7°. After two recrystallizations from benzene, the material melted 115.6–116.3°. This was mixed with authentic β-bromopropionamide (m.p. 115.3–116.3°) prepared from β-bromopropionyl chloride and ammonia[18] to give a mixed m.p. 115.3–116.3°.

β-Bromopropionyl Isocyanate from Silver Cyanate.—The method used is a rather general one for the preparation of acyl isocyanates.[19] In a 300-ml. round-bottomed flask fitted with a reflux condenser, addition funnel and calcium chloride drying tube, silver cyanate (Eastman Kodak Co., white label grade, 45.0 g., 0.30 mole) was suspended with magnetic stirring in 100 ml. of dry ether. To this suspension was added, over a 2-hr. period, 34.4 g. (0.20 mole) of β-bromopropionyl chloride in 50 ml. of dry ether. The suspension was then heated to boiling with continued stirring for 6 hr. The silver salts were then filtered from the solution, washed with ether and the washings combined with the reaction mixture. Solvent was removed at reduced pressure and the remaining liquid distilled through a 30-cm. Vigreux column at *ca.* 2 mm. The fraction boiling in the range 52–56° (4.4 g., 12%) exhibited an infrared spectrum identical with that of a sample of the isocyanate from the NBS reaction described above. Infrared spectrum (wave length in μ): 3.43w, 4.45s, 5.77s, 7.19m, 7.50w, 7.95w, 8.25w, 8.50m, 8.72m, 9.87m, 9.77m, 9.95m, 15.20m.

Anal. Calcd. for $C_4H_4O_2NBr$: C, 26.00; H, 2.27. Found: C, 26.35; H, 2.70.

This material also reacted vigorously with water to produce β-bromopropionamide.

N-Bromosuccinimide in Carbon Tetrachloride.—Observation of the very intense absorption of β-bromopropionyl isocyanate at 4.45 μ was used to follow its formation from NBS under a variety of conditions. In these experiments NBS (5.0 g.) was suspended in 50 ml. of carbon tetrachloride in a flask fitted with a reflux condenser and protected from atmospheric moisture by a calcium chloride drying tube. During the reaction 1-ml. aliquots were withdrawn at intervals of 6–8 hr. and examined for absorption at 4.45 μ. In parallel experiments, all conducted at the boiling point of carbon tetrachloride, the mixture was in one case irradiated with a sunlamp, shielded from all light in another case and, in a third case, protected from light after adding 0.10 g. of benzoyl peroxide. After 24 hr. spectra of the crude reaction mixtures taken in sodium chloride cells 0.016 in. in thickness against reference cells containing pure carbon tetrachloride showed 63% absorption at 4.45 μ for the irradiated reaction and 85% for the reaction with added benzoyl peroxide. The mixture which was heated in the dark with no added catalyst showed no absorption in this region even after 36 hr. Further heating of the two reaction mixtures which showed absorption at 4.45 μ brought about diminution and eventual loss of this absorption.

***exo*-2-Bromo-1,4-endoxocyclohexane.**—Material from fraction IV of the distillation of the NBS bromination reaction was redistilled (b.p. 68.0–68.2° (2 mm.), n^{25}D 1.5176, d_{25} 1.5410).

Anal. Calcd. for C_6H_9Br: C, 40.7; H, 5.12. Found: C, 40.88; H, 4.89.

This bromo ether (4.4866 g., 0.02534 mole) was dissolved in 20 ml. of 95% ethanol containing 4.748 g. (0.0279 mole) of silver nitrate. The mixture was then allowed to stand in a dark place at room temperature for 24 hr. The precipitated silver bromide was filtered, washed, dried at 95° and weighed (4.7477 g., 0.02528 mole). This corresponds to 45.03% Br in the sample; calcd. for C_6H_9Br, 45.14% Br.

Method of Determining Dielectric Constants.—The heterodyne beat frequency method[20] was used to determine the dielectric constants, at 25.0°, of dilute solutions of the materials being studied, in carbon tetrachloride or benzene. The apparatus used in these determinations is fully described by Osthoff.[21] It consists, in essence, of a fixed frequency crystal oscillator, at 100 kc., coupled with a vacuum-tube oscillator circuit containing the measurement cell and a calibrated precision variable condenser. The frequency of the latter circuit can be very accurately adjusted, by means of the precision condenser, until the beat frequency between the two circuits is zero.

Measurements of Densities.—Densities were measured to an accuracy estimated at one part in 20,000 by means of a single stem pycnometer of 20-ml. volume.

Treatment of Data.—The calculations of the molar polarization at infinite dilution were made by the method of Hedestrand[22] using the convenient notation of Bender, Flowers and Goering.[23] The dipole moments were then calculated from the Debye equation.[20]

Solvolysis of the 2-Halo-1,4-endoxocyclohexanes: Solvents.—Dioxane was purified by the procedure of Hess and Frahm.[24] After this treatment it was distilled through a 100-cm. column packed with glass helices (b.p. 100.6–100.8°). It was then stored under nitrogen in a dark place and used in not more than two weeks.

Absolute ethanol (2 l.) was added to 20 g. of sodium metal and the resulting solution boiled for two days to destroy aldehydes. The ethanol was then distilled and stored under nitrogen until used.

Distilled water from the laboratory source was redistilled from potassium permanganate and stored under nitrogen.

The solvent mixtures used in this work were made up by weighing the required amounts of the pure solvents. The solvent mixture which was made up to volume percentage specifications was weighed out in proportions calculated from the densities of the pure solvents at 25°.

Procedure for the *exo* Isomers.—The kinetic runs were followed by titrating samples individually sealed in glass tubes. These tubes were made by sealing one end of a 12 in. length of 12 mm. Pyrex tubing. Just before use they were carefully flushed with nitrogen and tightly stoppered with a plug of glass wool.

The solutions for kinetic analysis were made up by weighing the halo ether and the added salt into a 250-ml. volumetric flask and making the solution up to volume with the solvent being studied.

A hypodermic needle was used to introduce 16-ml. portions of the solution through the glass wool plugs into the freshly prepared glass tubes. The tubes were then quickly sealed off about 1.5–2 in. above the surface of the liquid, placed in a woven-wire basket and lowered into the constant temperature bath, maintained constant to within ±0.01°.

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[18] C. Hamilton and C. Simpson, THIS JOURNAL, **51**, 3159 (1929).

[19] A. T. Hill and W. M. Degnan, U. S. Patent 2,379,486 (1945).

[20] See C. P. Smyth in A. Weissberger, "Physical Methods of Organic Chemistry," Vol. I. 2nd Ed., Part II. Interscience Publishers Inc., New York, N. Y., 1949, pp. 1611, *et seq.*

[21] R. C. Osthoff, Ph.D. Thesis, Harvard University, 1951. We thank Professor E. G. Rochow for the loan of this apparatus.

[22] G. Hedestrand, *Z. physik. Chem.*, **B2**, 428 (1929).

[23] P. Bender, D. Flowers and H. Goering, THIS JOURNAL, **77**, 3463 (1955).

[24] K. Hess and H. Frahm, *Ber.*, **71B**, 2627 (1938).

At the desired intervals of time samples were withdrawn from the bath, quickly cooled in ice-water and then allowed to come to room temperature. Samples of 15 ml. were then accurately measured out, diluted with 45 ml. of distilled water and titrated with 0.1013 *N* aqueous sodium hydroxide. All titrations were performed using a Beckman Autotitrator with a 5-ml. microburet.

Procedure for Solvolysis of the *endo* Isomer.—The same procedure was used with *endo*-2-chloro-1,4-endoxocyclohexane as with the *exo* isomer with the exception that an amount of sodium acetate approximately equivalent to the halo ether was weighed into the sample. The reaction was then followed by titrating the excess sodium acetate in the aliquots to an end-point at *p*H 3.6 with 0.121 *N* hydrochloric acid.

Treatment of Data.—The first-order rate constants were obtained by a least squares treatment of the data as outlined by Youden.[25] The uncertainties are expressed as standard deviations. The values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were calculated from the absolute rate equation with the uncertainties again expressed as standard deviations.

Product Studies.—*exo*-2-Bromo-1,4-endoxocyclohexane (17.7 g., 0.10 mole) was dissolved in 250 ml. of 50% dioxane-water in a 300-ml. flask equipped with openings for an amber-glass electrode, a calomel electrode, a reflux condenser and the addition tip from the Beckman Autotitrator. The mixture was magnetically stirred with a Teflon-covered bar. It was brought to the boiling point by an electric heating mantle and maintained at *p*H 6.5–7.5 by the Autotitrator for 2000 min. This required 14.55 ml. of 4.89 *N* sodium hydroxide solution (71% reaction).

The solvent was removed by distillation at water-pump pressure leaving a paste of organic matter and sodium bromide. To this was added 50 ml. of dioxane to dissolve the organic matter, and the inorganic bromide was removed by filtration. The filtrate was then made up to 200 ml. with 50% dioxane–water. Aliquots of 20 ml. were taken for analytical tests.

Using this procedure outlined by Wilds,[26] aldehyde was estimated by titration of the hydrochloric acid released by oximation with hydroxylamine hydrochloride. Two aliquots gave values for aldehyde equivalent to 81.1% and 80.2% of the solvolyzed material.

Other aliquots were used to prepare the 2,4-dinitrophenylhydrazone and the *bis*-dimedone condensation product by the directions of Shriner and Fuson.[27]

The solution in which the 2,4-dinitrophenylhydrazone was formed was diluted with 200 ml. of water to make the precipitation complete and then filtered through a sintered-glass crucible. The derivative was washed with 20 ml. of 0.1 *N* hydrochloric acid, then 200 ml. of water, dried at 100° and weighed. After repeated recrystallization from benzene–pentane mixtures, this derivative gave m.p. 118.6–119.8°. The same derivative was isolated from the sealed tube solvolysis of the *endo*- and *exo*-chlorides; infrared spectrum (wave length in μ): 3.41s, 3.52m, 6.85m, 6.92m, 6.98m, 7.60w, 7.68w, 7.79m, 7.94m, 8.17m, 8.40s, 8.75m, 8.89m, 9.60m, 9.80m, 9.98s, 10.21m, 10.41w, 10.68s, 11.00w, 11.10w, 11.35s, 11.90m, 15.15w, 15.39w.

Anal. Calcd. for $C_{12}H_{14}O_5N_4$: C, 48.98; H, 4.80; N, 19.04. Found: C, 49.15; H, 4.59; N, 18.74.

The dimedone derivative was recrystallized from benzene–pentane mixtures to a constant melting point of 163.3–164.2°; infrared spectrum (wave length in μ): 2.79m, 2.95m, 3.42s, 3.70m, 5.80s, 6.97m, 7.25m, 7.50m, 8.10m, 8.55m, 9.30m, 9.89s, 10.53m.

Anal. Calcd. for $C_{22}H_{32}O_5$: C, 70.18; H, 8.56. Found: C, 70.47; H, 8.61.

Runs protected from oxygen by the use of the sealed tube technique showed substantially higher yields of aldehyde. In these experiments two tubes from a kinetic run were opened simultaneously. One 15-ml. aliquot was titrated directly. The other was mixed with 15 ml. of 0.5 *N* hydroxylamine hydrochloride solution, allowed to stand overnight, then titrated to the same *p*H as shown by a parallel blank run. The difference in the two titers represents aldehyde present.

In run 1, in 80% (by vol.) ethanol at 85.0°, such duplicate points were taken at 5212, 12470 and 16820 min. The percentage of aldehyde in the solvolysis product at each of these points was determined by the above outlined method. These percentages were found to be 100.8, 98.2 and 103.2%, respectively, at these three times.

In a special run at 120.0°, the *exo*-chloride, in 50% dioxane, was shown to yield 97.3 and 99.6% aldehyde at 653 and 1213 min.

The solvolysis product of the *endo*-chloride was analyzed at 160°, using points of run 12, in 50% dioxane with added sodium acetate. In these analyses the customary 15-ml. aliquot was diluted with 30 ml. of water and titrated with standard acid to *p*H 3.4 to learn the extent of solvolysis. The 15 ml. of 0.5 *N* hydroxylamine hydrochloride was added and the solution allowed to stand at room temperature overnight. It was then titrated back to *p*H 3.4 with standard base. At 2245 min. this method indicated 91.7% of the solvolysis product to be aldehyde and at 5110 min., 85.4%. (In these runs at the higher temperature a considerable darkening of the solution was observed in samples withdrawn after about 3000 min.)

Identification of 3-Formylcyclopentanol.—A sample (1.5 g.) of the crude product from a solvolysis of *exo*-2-bromo-1,4-endoxocyclohexane in boiling 50% dioxane was dissolved in 10 ml. of hydrazine (Eastman Kodak Co., 95%) and heated on a steam-bath for 24 hr. The solution was then concentrated to 4–5 ml. by distilling excess hydrazine at reduced pressure. This solution was added to an ethanolic solution of sodium ethoxide prepared by dissolving 1.0 g. of sodium in 10 ml. of absolute ethanol. The solution was sealed in a Carius tube and heated at 190–200° for 36 hr. The resulting solution was acidified with concd. hydrochloric acid and distilled. After removal of the ethanol two colorless liquid phases co-distilled at 55° (60 mm.). The non-aqueous phase was taken up in ether and dried over magnesium sulfate. Removal of the solvent left a colorless oil (0.3 g.), n^{28}_{D} 1.4446; *trans*-3-methylcyclopentanol,[7] n^{28}_{D} 1.4450. To this was added 0.24 g. of phenyl isocyanate, the mixture heated on a steam-bath for 10 min. and then diluted with 30 ml. of pentane. On chilling the material the phenylurethan (0.26 g.) was deposited from the solution as white needles (after recrystallization from pentane, m.p. 81.4–82.0°; phenylurethan derivative of *trans*-3-methylcyclopentanol,[7] m.p. 82°).

Solvolysis with Added Azide.—*exo*-2-Bromo-1,4-endoxocyclohexane (15.0 g., 0.0847 mole) was dissolved in a solution of 250 ml. of 50% dioxane containing 20 g. of sodium azide (0.308 mole, 1.23 molar). The solution was treated as in the previously described product studies, being boiled for 1600 min. at *p*H 6.0–7.0. Removal of the solvent and inorganic bromide left 8.45 g. of a viscous oil which showed an infrared spectrum nearly identical with that of 3-formylcyclopentanol with an added absorption peak of medium intensity at 4.74 μ. Chromatography on alumina of 1.60 g. of the crude product gave 29 mg. of an oil (eluted with 100% ether) which showed a very intense absorption at 4.74 μ. This was dissolved in 5 ml. of methanol and 10 mg. of platinum oxide added. The suspension was stirred under one atm. of hydrogen for 12 hr. The supernatant liquid was then saturated with hydrogen chloride and the crystalline amine hydrochloride (18 mg.) collected and dried, m.p. *ca.* 240°.

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