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Solvolytic Reactivities of Some 7-Chloronorbornane Derivatives[1]

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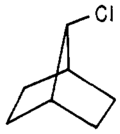
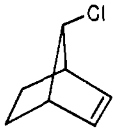
7-Chloronorbornane, a number of saturated 7-chloronorbornane derivatives and *syn*-7-chloronorbornene have been found to possess very unreactive chlorine under conditions where *exo*-norbornyl and cyclopentyl chlorides solvolyze readily. In contrast, *anti*-7-chloronorbornene (like *anti*-7-norbornenyl *p*-toluenesulfonate, Winstein, Woodward and co-workers) is quite reactive and solvolyzes about 55 times more rapidly than *exo*-norbornyl chloride and about 7 times more rapidly than α-methylallyl chloride in 80% ethanol at 100°. The solvolysis of *anti*-7-chloronorbornene is probably facilitated through stabilization of the carbocationic transition state by electron delocalization analogous to that predicted theoretically for the cyclopropenyl cation. First-order molecular orbital and steric strain calculations provide support for this formulation. The very low reactivity of *syn*-7-chloronorbornene and 7-chloronorbornane derivatives may be accounted for on the basis of steric inhibition of hyperconjugation.

syn-7-Chloro-*exo*-norbornyl *p*-toluenesulfonate solvolyzes 1.25 times faster than the *anti*-7-chloro isomer in acetic acid at 78°. Both isomers react only about 1/280 as fast as *exo*-norbornyl *p*-toluenesulfonate at 25°. Substantial participation of a non-classical hydrogen-bridged cationic intermediate ion-pair is proposed to account for the observed "internal return" and solvolysis products. *anti*-7-Chloro-*exo*-norborneol appears to liberate chloride about 5.5 times faster than the *syn*-7-chloro isomer in ethanolic alkali at 85°. Both isomers and the corresponding methyl ethers possess quite unreactive chlorine in the absence of base.

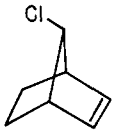
In continuation of earlier work on the solvolytic reactivities of nortricyclyl, dehydronorbornyl and norbornyl halides,[4] an investigation has been made of the reactivities of 7-chloronorbornane (I), *syn*- and *anti*-7-chloronorbornene (II and III), *syn*- and *anti*-7-chloro-*exo*-norbornyl *p*-toluenesulfonates (IV and V), *syn*- and *anti*-7-chloro-*exo*-norborneols (VI and VII) and *syn*- and *anti*-7-chloro-*exo*-norbornyl methyl ethers (VIII and IX). Solvolysis rate constants for I–III and some suitable reference compounds are given in Table I.



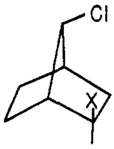
I



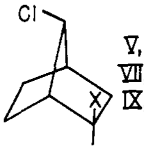
II



III

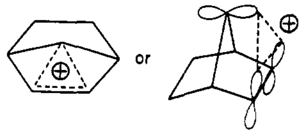


IV, X = TsO-
VI, X = HO-
VIII, X = CH_3O-



V, X = TsO-
VII, X = HO-
IX, X = CH_3O-

As stated in an earlier preliminary report,[5] I and II solvolyze very slowly in aqueous ethanol—at least two, and possibly more, orders of magnitude slower than cyclopentyl chloride. In contrast, III is very reactive as would be anticipated from the discovery by Winstein, Woodward and coworkers[6] of high solvolytic reactivity for *anti*-7-*exo*-5-dibromonorbornene (X) and *anti*-7-norbornenyl *p*-toluenesulfonate (XI). The unusual reactivity of III, X and XI may be ascribed to stabilization of the carbocationic transition state by delocalization of the unsaturation electrons which would be more effective if the leaving group is *anti* with respect to the double bond.[6] Solvolysis of III or XI can be presumed to involve the intermediate cation XII which is inferred from the reaction rates to be relatively stable as carbocations go. Although XII can be described as a "homoallylic" cation,[6,7] we prefer classification as a

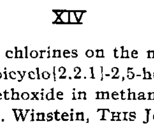


XII

XIII

"bis-homocyclopropenyl" cation to emphasize its relationship to the cyclopropenyl cation (XIII) which is predicted by simple molecular orbital theory to have a very stable π-electron system (calculated delocalization energy = 2.00β).[8] The arrangement of the $2p$-orbitals at C_2, C_3 and C_7 of XII may not appear to be very favorable for effective overlap, but the net stabilization energy (taking into account angle strain) computed by a molecular orbital procedure based on that of Simonetta and Winstein[7] is substantially greater than that predicted for the most favorable open-chain "homoallylic" carbocation.[7]

The calculations of the net stabilization energy of XII relative to the corresponding classical cation XIV were based on a geometrical model for the



XIV

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[1] Presented at the Dallas Meeting of the American Chemical Society, April, 1956.

[2] (a) National Science Foundation Predoctoral Fellow, 1955–1956; (b) U. S. Rubber Co. Predoctoral Fellow, Massachusetts Institute of Technology, 1952–1953.

[3] Gates and Crellin Laboratories, California Institute of Technology.

[4] (a) J. D. Roberts, L. Urbanek and R. Armstrong, THIS JOURNAL, **71**, 3049 (1949); (b) J. D. Roberts, W. Bennett and R. Armstrong, *ibid.*, **72**, 3329 (1950); (c) J. D. Roberts and W. Bennett, *ibid.*, **76**, 4623 (1954).

[5] J. D. Roberts, F. O. Johnson and R. A. Carboni, *ibid.*, **76**, 5692 (1954).

[6] (a) S. Winstein and M. Shatavsky, *ibid.*, **78**, 592 (1956); S. Winstein, M. Shatavsky, C. Norton and R. B. Woodward, *ibid.*, **77**, 4183 (1955). (b) In this connection, it may be noted also that E. T. McBee, J. D. Idol, Jr., and C. W. Roberts, *ibid.*, **77**, 6674 (1955), have reported recently that the chlorines on the methylene bridge in 1,4,5,6,7,7-hexachloro-2-phenylbicyclo[2.2.1]-2,5-heptadiene exhibit unique lability toward sodium methoxide in methanol.

[7] M. Simonetta and S. Winstein, THIS JOURNAL, **76**, 18 (1954).

[8] J. D. Roberts, A. Streitweiser, Jr., and C. M. Regan, *ibid.*, **74**, 4579 (1952).

TABLE I

SOLVOLYSIS RATES OF CHLORIDES IN AQUEOUS ETHANOL

Chloride	Volume % ethanol in solvent	Temp., °C.	k_1, sec.$^{-1}$	Rel. k_1	Reaction,[a] %	Purity, %
α-Methylallyl	80	99.7	1.4×10^{-3}[b]	1	..	....
anti-7-Norbornenyl (III)	80	50.2	$8.7 \pm 0.3 \times 10^{-5}$		67	97 ± 2
	80	61.2	$2.7 \pm 0.2 \times 10^{-4}$	..	73	97 ± 1
	80	99.7	$1.0 \pm 0.5 \times 10^{-2}$[c]	7	..	....
exo-Norbornyl	80	99.7	$1.75 \pm 0.06 \times 10^{-4}$	0.13	63	100
Cyclopentyl	50	99.7	1.9×10^{-4}[d]	1.0	..	....
Cyclohexyl	50	99.7	1.4×10^{-5}[d]	0.07	..	....
anti-7-Norbornenyl (III)	50	24.9	$2.3 \pm 0.2 \times 10^{-4}$	..	57	97 ± 2
	50	50.2	$4.0 \pm 0.1 \times 10^{-3}$	..	89	97 ± 2
	50	99.7	$3.6 \pm 1.4 \times 10^{-1}$[c]	1900	..	....
syn-7-Norbornenyl (II)	50	99.7	$<2 \times 10^{-6}$[e]	<0.01	25[f]	75 ± 2
7-Norbornyl (I)	50	99.7	$<1 \times 10^{-6}$[e]	<0.005	8[f]	77 ± 2
Nortricyclyl	50	99.7	$8.2 \pm 0.5 \times 10^{-4}$	4.3	87	90

[a] Degree of completion of reaction during kinetic experiments. [b] Calculated from data at lower temperatures obtained by C. A. Vernon, *J. Chem. Soc.*, 423 (1954), and W. G. Young and L. J. Andrews, THIS JOURNAL, **66**, 421 (1944), with the aid of the rate–solvent correlations of E. Grunwald and S. Winstein, *ibid.*, **70**, 846 (1948). [c] Calculated from the data at lower temperatures. [d] Calculated from the data of J. D. Roberts and V. C. Chambers, *ibid.*, **73**, 5034 (1951), and unpublished results at 100°. [e] Upper limit for rate after correction for ethanol–hydrochloric acid reaction (see Experimental). [f] Maximum extent of solvolysis after all of nortricyclyl chloride impurity had reacted.

carbon skeleton of XIV derived from an electron diffraction study of bicyclo[2.2.1]heptadiene.[9] In particular, the five-membered ring defined by carbons 1, 2, 3, 4 and 7 of XIV was considered to be identical with the analogous portion of the bicyclo[2.2.1]heptadiene framework. The structural parameters are listed in Table II. With θ_2 and θ_7 as the angles between the line joining the C_2, C_7 nuclei and the *p*-orbital axes at C_2 and C_7, respectively, the overlap integral S_{27} was obtained from eq. 1 where γ is the angle between the *p*-orbital axes at C_2 and C_7 as seen by an observer sighting along the C_2–C_7 internuclear line. If ϕ_{27} is the angle in space between the C_2 and C_7 *p*-orbital axes, cos γ may be computed from eq. 2. The integrals $S_{\sigma\sigma}$ and $S_{\pi\pi}$ were taken from Kopineck's tables[10] on the assumption of an effective nuclear charge of 3.09.[7] The resonance integral β_{27} was evaluated by Mulliken's approximation[7] with S and β for a normal ethylenic bond set equal to 0.28 and −20 kcal./mole, respectively. β_{23} was assigned the normal value. The π-electron energy calculations were made using the simple molecular orbital (LCAO) procedure[7,11] with neglect of overlap in the off-diagonal terms. The electron delocalization energies (*DE*) were computed by subtracting $2(\alpha + \beta)$ from the energy of the lowest electronic configuration.

TABLE II

STRUCTURAL PARAMETERS ASSUMED FOR CATION XIV

Angle	Value	Bond	Length, Å.
C_1–C_2–C_3	109.1°	C_1–C_2	1.522
C_2–C_1–C_7	96.4	C_1–C_4	2.329
C_1–C_7–C_4	96.7	C_1–C_7	1.558
C_6–C_1–C_2	99.3[a] (102.2)	C_2–C_3	1.333
C_6–C_1–C_7	99.3[a] (96.4)	C_2–C_7	2.296

[a] Averaged values.

$$S_{27} = \cos\theta_2 \cos\theta_7 S_{\sigma\sigma} + \sin\theta_2 \sin\theta_7 \cos\gamma S_{\pi\pi} \quad (1)$$

$$\cos\gamma = \frac{\sin^2\theta_2 + \sin^2\theta_7 - 4\sin^2\phi_{27}/2 + (\cos\theta_2 + \cos\theta_7)^2}{2\sin\theta_2 \sin\theta_7} \quad (2)$$

The strain energies (*SE*) were calculated with the aid of eq. 3 and 4, with θ_b as the half-angle of bending from the normal value of 109°28′ for a given bond angle.

$$SE \text{ per angle} = 118 \left[0.996 - \frac{(0.5 + 1.5\cos\theta_b)(0.577 + 2^{1/2}\cos\theta_b)}{4}\right] \quad (3)$$

$$SE \text{ per angle} = 118 \left[1.000 - \frac{(0.5 + 1.5\cos\theta_b)^2}{4}\right] \quad (4)$$

Equation 3 applies to bonds which can be considered to involve carbon sp^2 orbitals on one carbon and sp^3 orbitals on the other carbon.[12] Equation 4 applies to bonds where bond formation may be regarded as a result of overlap of sp^3 orbitals on both atoms.[12] In the calculations of *SE* and *DE*, XII was considered to be distorted solely through changes of the dihedral angle between the C_1–C_2–C_3–C_4 plane and the C_1–C_7–C_4 plane symmetrically with respect to the C_4–C_5–C_6–C_1 plane. *SE* for unperturbed XII was calculated to be 5.2 kcal. considering only the three pairs of angles about the line connecting the C_1–C_4 nuclei. With this value as a zero point, *SE* was calculated for smaller values of R_{27} by taking into account the small decrease in the strain of angles, C_{543}, C_{547}, C_{612} and C_{617} accompanying the larger increase of strain in angles C_{217} and C_{347}. The "net *SE*" and the *DE* data are given in Table III.

Dunitz and Schomaker[13] have shown that the strain energy of cyclobutane can be adequately ac-

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[9] Unpublished research by V. Schomaker and W. Hamilton; *cf.* W. C. Hamilton, Ph.D. thesis, California Institute of Technology, 1954.

[10] H. J. Kopineck, *Z. Naturforsch.*, **5A**, 420 (1950).

[11] E. Hückel, *Z. Physik*, **70**, 204 (1931); R. S. Mulliken, *Phys. Rev.*, **41**, 49 (1932); *J. Chem. Phys.*, **3**, 375 (1935); H. Eyring, J. Walter and G. E. Kimball, "Quantum Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1944, Chapter 13.

[12] J. E. Kilpatrick and R. Spitzer, *J. Chem. Phys.*, **14**, 463 (1946).

[13] J. D. Dunitz and V. Schomaker, *J. Chem. Phys.*, **20**, 1703 (1952).

TABLE III

SUMMARY OF CALCULATIONS FOR CATION XII

R_{27}, Å.	θ_2	θ_7	γ	S_{27}	β_{27}/β_{23}	DE, kcal./mole	Net SE, kcal./mole	Net E, kcal./mole
2.296	68°10′	58°55′	17°29′	0.0802	0.3394	7.7	0.0	7.7
2.200	64°44′	53°39′	24°10′	.0994	.4133	10.8	3.2	7.7
2.000	59°10′	44°37′	33°12′	.1454	.5803	18.4	7.9	10.5
1.800	55°9′	37°29′	47°25′	.1852	.7143	25.1	15.6	9.5

TABLE IV

p-TOLUENESULFONATE SOLVOLYSIS RATE CONSTANTS

p-Toluenesulfonate	Solvent	Temp., °C.	k_1, sec.$^{-1}$	Rel. k_1
syn-7-Chloro-*exo*-norbornyl (IV)	AcOH, 0.035 *M* KOAc	78.2	$6.6 \pm 0.2 \times 10^{-5}$	...
		25.0	1×10^{-7a}	2.4
	75% $(CH_3)_2CO$–25% H_2O	55.9	$1.16 \pm 0.02 \times 10^{-5}$	
anti-7-Chloro-*exo*-norbornyl (V)	AcOH, 0.035 *M* KOAc	78.2	$5.2 \pm 0.2 \times 10^{-5}$	..
		25.0	6×10^{-8a}	1.3
	75% $(CH_3)_2CO$–25% H_2O	55.9	$1.07 \pm 0.06 \times 10^{-5}$	
exo-Norbornyl	AcOH, 0.035 *M* KOAc	25.0	2.50×10^{-5b}	512
Cyclohexyl	AcOH	25.0	4.9×10^{-8b}	1.0

[a] Approximate rate constants obtained from less than 10% complete reactions. Reactions at the higher temperatures were run to at least 75% completion. [b] Data from S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan and H. Marshall, THIS JOURNAL, **74**, 1127 (1952).

counted for by considering the sizable repulsions between non-bonded carbons, in addition to the angle bending and torsional strain. In the present case, the non-bonded carbon–carbon distances are rather comparable to those in cyclobutane, but these repulsions have not been considered because of uncertainties in treating partial relief of the C_2–C_7 and C_3–C_7 repulsions. For this reason, the "net *SE*" values must be considered as approximate minima.

The maximum value of the net stabilization energy *E* (10.5 kcal.) approaches that calculated for the allyl cation (16.6 kcal.) and is considerably greater than the value of 7.2 kcal. computed for the homoallylic cation.[6] On this basis, it is not surprising that the first-order solvolysis rate constant for III is approximately 110 times greater than that for *exo*-dehydronorbornyl chloride at 85° in 80% ethanol. It is interesting in this connection that the computed DE for the dehydronorbornyl cation with an unperturbed carbon skeleton is 2.8 kcal. as compared to 7.7 kcal. for unperturbed XII.

The low reactivities of I and II are even more striking than the high reactivity of III. Both of these substances are very substantially less reactive than cyclopentyl chloride. At least three factors may be regarded as attributing to the low reactivity. First, there may be some steric hindrance to solvation of the 7-norbornyl cation by repulsions involving C_5 and C_6 and their associated hydrogens. Second, an increase in steric strain may be expected to be associated with the change in hybridization at C_7 during carbocation formation. Finally, and probably most important, would be steric inhibition of *hydrogen* hyperconjugative stabilization[4b,5] of the cation which, though possible for the cyclopentyl cation, is suggested by Bredt's rule to be prohibited for a 7-norbornyl cation. Such loss of hyperconjugative stabilization should be comparable at least to the effect produced by substitution of a single α-methyl group at the carbinyl carbon of an alkyl halide and could result in a decrease of 10^4–10^5 in alcoholysis rate.[14]

Solvolysis rate constants for the *syn*- and *anti*-7-chloro-*exo*-norbornyl *p*-toluenesulfonates IV and V in acetic acid and 75% aqueous acetone are summarized in Table IV. Infrared analysis of the acetolysis products of IV and V indicated that each gave almost the same mixture of *syn*- and *anti*-7-chloro-*exo*-norbornyl acetates. Lithium aluminum hydride reduction of either acetate mixture gave an approximately equimolal mixture of chlorohydrins VI and VII as shown by comparison of the infrared spectra of the reduction products with each other and with synthetic mixtures of the two chlorohydrins. In other experiments, it was found that, although the *p*-toluenesulfonate esters were not significantly interconverted during the first 10% of acetolysis, after 70% acetolysis the unsolvolyzed esters were 20–25% isomerized.

The isomerization and acetolysis product mixtures suggest a reaction path involving a "tight" ion-pair intermediate (XV) which could lead to some isomerized *p*-toluenesulfonate *via* "internal return."[15] Dissociation of XV to a hydrogen-bridged cation[16] (XVI) could then lead to an approximately equimolal mixture of the *syn*- and *anti*-7-chloro-*exo*-norbornyl acetates. Since XVI would be a common intermediate, each *p*-toluenesulfonate would lead to the same mixture of acetates. The apparently inconsequential formation of Wagner–Meerwein rearrangement products like 3-chloro-*exo*-norbornyl acetates in these and similar[5] reactions can be rationalized on the basis that the attack by solvent on intermediates like XVI

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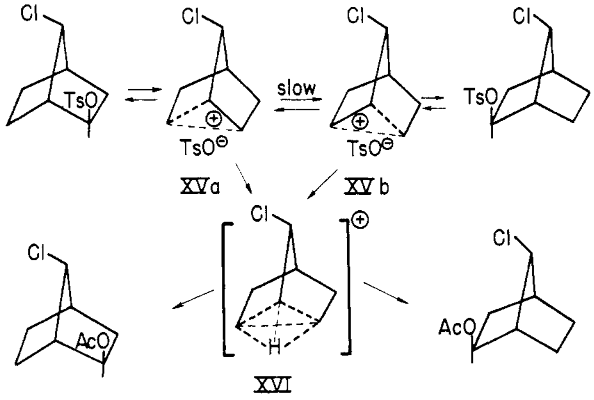
[14] L. C. Bateman, K. A. Cooper, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 925 (1940); E. Grunwald and S. Winstein, THIS JOURNAL, **70**, 841 (1948); S. Winstein, E. Grunwald and H. W. Jones, *ibid.*, **73**, 2700 (1951).

[15] (a) S. Winstein and D. Trifan, *ibid.*, **74**, 1154 (1952); (b) S. Winstein and K. C. Schreiber, *ibid.*, **74**, 2165 (1952).

[16] J. D. Roberts, C. C. Lee and W. H. Saunders, Jr., *ibid.*, **76**, 4501 (1954).

would occur preferentially at the 2- and 6-positions since the 1-positions would have but slight cationic character because of the proximity of the adjacent carbon–chlorine dipole at C_7.



The *syn*-7-chloro-*exo*-norbornyl *p*-toluenesulfonate (IV) is slightly more reactive in solvolysis than the *anti*-isomer V. This is reasonable on electrostatic grounds since the carbon–chlorine dipole of IV would be more favorably disposed toward development of the carbon–*p*-toluenesulfonate dipole in the transition state than would be the case for the *anti*-isomer V. It might also be argued that relief of steric strain[17] could enhance the rate of ionization of IV relative to V.

The *syn*- and *anti*-7-chloro-*exo*-norbornyl ethers (VIII and IX) were found to possess very unreactive chlorine atoms. No reaction was observed in 80% aqueous ethanol at 85° in 24 hours in the presence or absence of dilute sodium hydroxide. Similarly, the chlorohydrins VI and VII were unreactive in 80% aqueous ethanol at 80° but did react in the presence of dilute sodium hydroxide. The *syn*-chlorohydrin appeared to react only about 5.5 times more slowly than the *anti*-isomer. Since the chlorohydrins are unreactive in the absence of base and the chloro ethers are unreactive in the presence of base, it is probable that the hydroxide ion-induced solvolysis of VI and VII involves the corresponding alkoxide ions. Since the difference between the *syn*- and the *anti*-isomers is only a factor of 5.5, it appears possible that direct oxygen participation in the rate-determining step is not very important and the loss of chloride ion is facilitated from the alkoxide ion by the electrical effect of the negative oxygen. A somewhat similar effect has been noted in the solvolysis of halogen in a situtation where direct participation of negative oxygen is sterically unfavorable.[18]

Acknowledgment.—We are indebted to Professor V. Schomaker for helpful discussions with respect to the quantum mechanical calculations.

Experimental

Preparations of *syn*- and *anti*-7-chloro-*exo*-norborneol (VI and VII) *syn*- and *anti*-7-chloronorbornene (II and III) and 7-chloronorbornane (I) have been described previously.[5] Quantitative hydrogenation indicated II and III to have 75 ± 2% and 97 ± 2%, respectively, of the theoretical unsaturation. Compound I prepared by hydrogenation of II contained 23 ± 2% of a much more reactive chloride as judged by its solvolytic behavior. In each case, the infrared spectra indicated the impurity to be nortricyclyl chloride.[5]

syn-**7-Chloro-*exo*-norbornyl *p*-toluenesulfonate (IV)** was prepared in 77% yield from *syn*-7-chloro-*exo*-norborneol by the procedure of Tipson[19] and after crystallizations from ether and ether–pentane yielded colorless rosettes, m.p. 51–52°.

Anal. Calcd. for $C_{14}H_{17}O_3SCl$: C, 55.90; H, 5.70; Cl, 11.79. Found: C, 55.66; H, 5.83; Cl, 11.68.

anti-**7-Chloro-*exo*-norbornyl *p*-toluenesulfonate (V)** was similarly prepared in 53% yield, m.p. 64.0–65.4°.

Anal. Calcd. for $C_{14}H_{17}O_3SCl$: C, 55.90; H, 5.70; Cl, 11.79. Found: C, 55.93; H, 5.69; Cl, 11.72.

syn-**7-Chloro-*exo*-norbornyl Methyl Ether (VIII).**—Sodium hydride (0.80 g., 0.033 mole) was slowly added to a solution of 5.0 g. (0.305 mole) of chlorohydrin VI in 25 ml. of absolute ether. The mixture was stirred at room temperature for 6 hours, a slight excess of methyl iodide was added and the whole stirred and heated occasionally for 12 hours. The sodium iodide was removed by filtration and the ether distilled at atmospheric pressure. Fractionation of the residual oil through a semi-micro column[20] afforded 4.1 g. (75%) of VIII, b.p. 83–87° (13 mm.), n^{25}_{D} 1.4890.

Anal. Calcd. for $C_8H_{13}OCl$: C, 59.81; H, 8.15; Cl, 22.07. Found: C, 59.28; H, 7.99; Cl, 21.51.

anti-**7-Chloro-*exo*-norbornyl methyl ether (IX)** was similarly prepared from chlorohydrin VII and had b.p. 75–80° (12 mm.), n^{25}_{D} 1.4900.

Anal. Calcd. for $C_8H_{13}OCl$: C, 59.81; H, 8.15. Found: C, 60.02; H, 8.09.

Reaction Rate Measurements.—The solvolysis rates of the *p*-toluenesulfonate esters were determined as described by Winstein and co-workers.[21] The reactions at 25° were quenched by dilution of the samples with an equal volume of petroleum ether.[15a] The chlorohydrins and chloro ethers VI–IX were heated in sealed tubes containing 80% aqueous ethanol in the presence or absence of sodium hydroxide. No reaction occurred with any of the compounds at 85° in the absence of sodium hydroxide. The chloro ethers VIII and IX did not appear to react significantly in the presence of 0.035 *N* sodium hydroxide. However, the chlorohydrins VI and VII reacted with 0.035 *N* sodium hydroxide in 80% aqueous ethanol at 85° with pseudo unimolecular rate constants of $5.0 \pm 0.3 \times 10^{-6}$ and $2.8 \pm 0.3 \times 10^{-5}$ sec.$^{-1}$, respectively.

The chloride solvolysis rates shown in Table III were determined with the aid of a potentiometric method employing a glass electrode for measurement of the hydrochloric acid liberated in the reaction. This technique was helpful because many of the compounds were only available in small quantities and it was desirable to use rather dilute halide solutions. Except for III in 50% ethanol, the solvolyses were carried out in sealed ampoules, zero time being taken as the time of immersion in the constant temperature bath. At appropriate intervals, samples were cooled to 25° and in the 80% ethanol experiments, the increase in acidity during the reactions was followed by pipetting samples into a vessel equipped with a glass electrode and connected by a 1 *M* potassium chloride–2.4% agar bridge to a vessel containing 1 *M* potassium chloride and a standard calomel electrode. The e.m.f. between the glass and calomel electrodes was measured with a Beckman model G *p*H meter. The salt bridge and the 1 *M* potassium chloride solution were eliminated in measurements with the 50% ethanol solutions. The apparatus was calibrated using ten or more solutions of known hydrochloric acid concentrations in the appropriate solvent compositions. Compound III reacted so rapidly in 50% ethanol that the increase of acidity could be measured continuously at 25° with the glass electrode. Zero time was taken as the time of mixing. In view of the

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[17] (a) H. C. Brown, *Science*, **103**, 385 (1946); (b) H. C. Brown and R. S. Fletcher, THIS JOURNAL, **71**, 1845 (1949).

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limited accuracy of the potentiometric method, the best visual fit was made to first-order plots and standard deviations were calculated from the deviations of the experimental points from the lines.

With the very slowly reacting chlorides, complications were introduced by the reaction of the liberated hydrochloric acid with the ethanolic medium, particularly in the later stages. This was particularly true with *syn*-7-chloronorbornene (II) and 7-chloronorbornane (I) which gave complicated rate curves in consequence of the substantial contamination with nortricyclyl chloride, the reaction between ethanol and hydrochloric acid and the very low reactivities of the chlorides themselves. Figure 1 shows a typical plot of $-\log (a - x)$ against time. The steep initial slope results from a relatively rapid initial liberation of hydrochloric acid by the contaminating nortricyclyl chloride. When the concentration of nortricyclyl chloride becomes small, the hydrochloric acid concentration passes through a maximum because the rate of reaction of the acid with ethanol is faster than the solvolysis of II. With approximate reaction rates obtained for hydrochloric acid with ethanol under the experimental conditions at three separate initial acid concentrations comparable to those calculated to be present at the maximum in Fig. 1, it was possible to make a rough empirical correction of the rate data and obtain upper limits for the rate constants of II. A similar procedure was followed for I.

Products from the Solvolyses of *syn*- and *anti*-7-Chloro-*exo*-norbornyl *p*-Toluenesulfonates (IV and V) in Acetic Acid.—Two 25-ml. aliquots of a 0.0322 *M* solution of *syn*-7-chloro-*exo*-norbornyl *p*-toluenesulfonate (IV) in dry acetic acid containing 0.0308 *M* potassium acetate were heated at 78.2° for 45 minutes and 6 hours, respectively. Titration with perchloric acid showed that acetolysis had occurred in the two solutions to the extent of 10 and 70%, respectively. The reaction mixtures were diluted with water, neutralized with sodium carbonate and extracted with ether. The ether extracts were dried over sodium sulfate, evaporated to dryness and the chloronorbornyl acetates removed by trituration with cold pentane. The infrared spectra of the residues showed only IV to be present in the material from the 45-min. reaction while that from the 6-hour reaction showed both IV and V to be present, approximately in the ratio of 4:1.

Identical experiments starting with *anti*-7-chloro-*exo*-norbornyl *p*-toluenesulfonate (V) showed no significant rearrangement after 10% reaction and afforded about a 1:5 mixture of IV and V after 70% acetolysis.

A solution of 2.0 g. (0.0066 mole) of the sulfonate ester IV and 1.0 g. (0.010 mole) of potassium acetate in 50 ml. of dry acetic acid was heated for 24 hours at 100°. The mixture was cooled, the acetic acid neutralized with aqueous sodium carbonate solution and the products extracted with ether. The ether extract was dried over sodium sulfate, the ether evaporated and the residue distilled through a semimicro column. A mixture of chloronorbornyl acetates (0.81 g.) was obtained, b.p. 70–80° (4 mm.), n^{25}_{D} 1.4808.

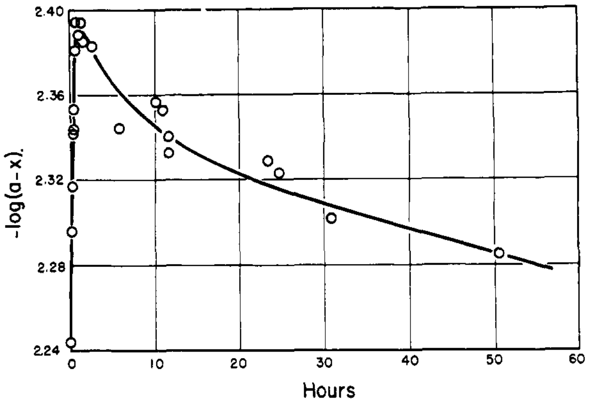

Fig. 1.—Solvolysis rate curve for *syn*-7-chloronorbornene in 50% ethanol at 99.7°.

Anal. Calcd. for $C_9H_{13}O_2Cl$: C, 57.29; H, 6.94; Cl, 18.80. Found: C, 57.57; H, 6.92; Cl, 18.47.

Sulfonate ester V was carried through the same procedure and afforded 0.82 g. of chloronorbornyl acetate mixture, b.p. 80–88° (4–5 mm.), n^{25}_{D} 1.4811.

Anal. Calcd. for $C_9H_{13}O_2Cl$: C, 57.29; H, 6.94; Cl, 18.80. Found: C, 57.31; H, 6.82; Cl, 18.75.

Infrared spectra of the two chloronorbornyl acetate mixtures from IV and V were very similar. Lithium aluminum hydride reduction of each chloronorbornyl acetate mixture yielded mixtures of colorless, waxy solids which were purified by short-path distillation at 128° (4 mm.). Comparison of the infrared spectra of the reduction products with those of synthetic mixtures of chlorohydrins VI and VII revealed that each was approximately a 1:1 mixture of the two chloronorborneols.

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Radiation Induced Oxidation of Cholesterol[1]

BY WILLIAM G. DAUBEN AND PIERRE H. PAYOT[2]

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When C^{14}-labeled cholesterol is stored in the presence of air, it is oxidized on and about the 5,6-double bond and, in the main, the epimeric 7-hydroxy, the 7-keto and the 5α,6β-dihydroxy derivatives are formed. Such an oxidation reaction requires both radiation and oxygen since unlabeled cholesterol in air or C^{14}-labeled cholesterol *in vacuo* are stable.

In 1953,[3] attention was drawn to the fact that certain C^{14}-labeled organic compounds underwent self-induced radiation damage and, subsequently,[4] this reaction has been studied in detail. At that time it also was reported that Chaikoff and his co-workers, in the Department of Physiology of the University of California, had found that C^{14}-labeled cholesterol possessing a specific activity of ~6.5 μc./mg. underwent decomposition over a period of approximately 18 months to the extent of 40%. The extremely large amount of transformation of this important sterol was unexpected and it was of importance to identify the products formed and to evaluate the role of the radiation in the transformation process.

The first samples of C^{14}-cholesterol investigated had been stored in a screw-cap vial and had been exposed to the atmosphere at frequent inter-

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