Neighboring Oxide Ion and Fragmentation Reactions of 1,3-Chlorohydrins

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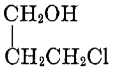
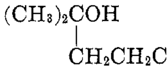
The rates of disappearance of a series of 1,3-chlorohydrins in basic aqueous methanol at various temperatures are reported along with yields of the products. From these data, rate coefficients and the corresponding activation parameters for ring closure, fragmentation, substitution, and elimination are calculated. Fragmentation is observed when the 1,3-chlorohydrin is substituted with a *gem*-dimethyl group so that isobutylene results. In contrast, no fragmentation occurs if the *gem*-dimethyl grouping is moved so that the potential fragmentation products would have these methyl groups at the carbonyl rather than the olefinic fragmentation unit. It is found that the entropy of activation is responsible for the rate of fragmentation of **3** being slightly greater than ring closure, which is consistent with previous reports that these competing reactions are solvent dependent. Rates of ring closure and yields of oxetanes decrease in the order 4-chloro-2-methyl-2-butanol (**2**) > **3** ~ 3-chloro-1-propanol (**1**). Possible reasons for this order are discussed. A comparison of the effect of ring size on the rates of ring closure for a series of ω-hydroxyalkyl chlorides with base is made.

The kinetics of the neighboring oxide ion reactions of 1,2-chlorohydrins [$\mathrm{ND_I}$-($^-$O-3)],[1] to give oxiranes, have been studied extensively.[4,5] Kinetic data for the basic decomposition of other ω-hydroxyalkyl halides, where *n* is greater than 3 in the $\mathrm{ND_I}$-($^-$O-*n*) reaction, are not as prevalent.[4k,n,5a,b,6] We are particularly interested in the $\mathrm{ND_I}$-($^-$O-4) reaction as a model for the neighboring peroxide anion reaction [$\mathrm{ND_I}$-($^-$OO-4)].[7] In the few instances where kinetic data are presented for the $\mathrm{ND_I}$-($^-$O-4) reaction, quantitative product studies are not reported[4k,6b] with one exception.[6d] Quantitative product studies are essential to evaluate the kinetic data, since fragmentation accompanies the $\mathrm{ND_I}$-($^-$O-4) reaction.[4k,5a,6d,8] We now report a systematic kinetic and product study of the basic decomposition of a series of methyl-substituted 1,3-chlorohydrins in aqueous methanol. From these data, kinetic parameters for the $\mathrm{ND_I}$-($^-$O-4), fragmentation, substitution, and elimination reactions are obtained.

Results

Products.—The condensable product yields were determined by gas–liquid chromatography (glc) by the internal standard method.[9] The yields of gaseous products were obtained by standard vacuum line procedures,[10] coupled with mass spectral analyses. Product analyses are reported in Tables I–III for the reaction of 3-chloro-1-propanol (**1**), 4-chloro-2-methyl-2-butanol (**2**), and 3-chloro-2,2-dimethyl-1-propanol (**3**) with base in 40% aqueous methanol. Analyses could be made with excess **3** after 10–20 half-lives; however, under similar conditions with **1** and **2**, the corresponding oxetanes were not stable. Apparently hydrogen chloride is produced from **1** and **2** by a β elimination,


$$\begin{matrix}CH_2OH\\ |\\ CH_2CH_2Cl\end{matrix}$$
1


$$\begin{matrix}(CH_3)_2COH\\ |\\ CH_2CH_2Cl\end{matrix}$$
2

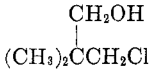
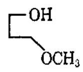
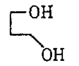

$$\begin{matrix}CH_2OH\\ |\\ (CH_3)_2CCH_2Cl\end{matrix}$$
3

TABLE I

PRODUCTS FROM THE REACTION OF 1[a] WITH SODIUM HYDROXIDE[b] IN 40% AQUEOUS METHANOL

Product	% yield 100°	85°	75°	65°
 **4**	14.6	13.5	13.4	13.0
 **5**	4.65	3.77	2.43	2.49
 **6**	53.5	50.0	49.2	48.2
 **7**	28.5	28.9	25.8	27.2
% product balance	101	96.2	90.8	90.9
% reaction[c]	58.0	61.7	45.7	41.7

[a] $[\mathbf{1}]_0$ = 0.0546 *M*. [b] $[NaOH]_0$ = 0.1063 *M*. [c] Calculated from the difference between the initial and final concentrations of **1**.

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[1] $\mathrm{ND_I}$ refers to "internal nucleophilic displacement"[2] and $^-$O-3 refers to the participating group and the ring size that is developed at the transition state.[3]

[2] W. Hanstein, H. J. Berwin, and T. G. Traylor, *J. Amer. Chem. Soc.*, **92**, 829 (1970).

[3] See R. Heck and S. Winstein, *ibid.*, **79**, 3105 (1957).

[4] (a) W. P. Evans, *Z. Phys. Chem.*, **7**, 335 (1891); (b) L. Smith, *ibid.*, **81**, 339 (1912); **A152**, 153 (1931); (c) H. Nilsson and L. Smith, *ibid.*, **A166**, 136 (1933); (d) L. Smith and B. Platon, *Chem. Ber.*, **61**, 1709 (1928); (e) L. O. Winstrom and J. C. Warner, *J. Amer. Chem. Soc.*, **61**, 1205 (1939); (f) D. Porret, *Helv. Chim. Acta*, **24**, 80E (1941); (g) R. G. Kadesch, *J. Amer. Chem. Soc.*, **68**, 46 (1946); (h) T. Bergkvist, *Svensk Kem. Tidskr.*, **64**, 181 (1952); *Chem. Abstr.*, **46**, 8942*g* (1952), and earlier references cited therein; (i) A. G. Ogston, E. R. Holiday, J. S. L. Philpot, and L. A. Stocken, *Trans. Faraday Soc.*, **44**, 45 (1948); (j) J. E. Stevens, C. L. McCabe, and J. C. Warner, *J. Amer. Chem. Soc.*, **70**, 2449 (1948); (k) G. Forsberg, *Acta Chem. Scand.*, **8**, 135 (1954); (l) P. Ballinger and F. A. Long, *J. Amer. Chem. Soc.*, **81**, 2347 (1959); (m) C. G. Swain, A. D. Ketley, and R. F. W. Bader, *ibid.*, **81**, 2353 (1959); (n) H. W. Heine and W. Siegfried, *ibid.*, **76**, 489 (1954).

[5] For reviews, see (a) B. Capon, *Quart. Rev.*, **18**, 45 (1964); (b) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill, New York, N. Y., 1962, p 110; (c) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," Wiley, New York, N. Y., 1961, p 288.

[6] (a) C. G. Swain, D. A. Kuhn, and R. L. Schowen, *J. Amer. Chem. Soc.*, **87**, 1553 (1965); (b) G. Forsberg, *Nord. Kemikermoede, 9th*, **7**, 170 (1950); *Chem. Abstr.*, **48**, 7405 (1954); (c) H. W. Heine, *J. Amer. Chem. Soc.*, **79**, 6268 (1957); (d) R. B. Clayton, H. B. Henbest, and M. Smith, *J. Chem. Soc.*, 1982 (1957).

[7] (a) W. H. Richardson, J. W. Peters, and W. P. Konopka, *Tetrahedron Lett.*, 5531 (1966); (b) W. H. Richardson, Abstracts, *Int. Symp., Chem. Organischen Peroxide, Berlin, DDR*, 81 (Sept 1967); (c) W. H. Richardson and V. F. Hodge, *Tetrahedron Lett.*, 2271 (1970); (d) R. Curci and J. O. Edwards, "Organic Peroxides," Vol. 1, D. Swern, Ed., Wiley–Interscience, New York, N. Y., 1970, p 256.

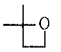
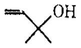
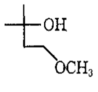
[8] (a) S. Searles, *Chem. Heterocycl. Compounds*, **19**, 983 (1964); (b) H. B. Henbest and B. B. Millward, *J. Chem. Soc.*, 3575 (1960); (c) S. Searles, R. G. Nickerson, and W. K. Witsiepe, *J. Org. Chem.*, **24**, 1839 (1959); (d) G. Adam, *Angew. Chem.*, **79**, 619 (1967); (e) S. Searles and M. J. Gortatowski, *J. Amer. Chem. Soc.*, **75**, 3030 (1953); (f) P. S. Wharton and G. A. Hiegel, *J. Org. Chem.*, **30**, 3254 (1965); (g) P. S. Wharton, *ibid.*, **26**, 4781 (1961); (h) C. H. Issidorides and A. I. Matar, *J. Amer. Chem. Soc.*, **77**, 6382 (1955); (i) E. J. Corey, R. B. Mitra, and H. Uda, *ibid.*, **86**, 485 (1964); (j) R. R. Burford, F. R. Hewgill, and P. R. Jefferies, *J. Chem. Soc.*, 1983 (1957).

[9] S. Dal Nogare and R. S. Juvet, Jr., "Gas-Liquid Chromatography," Interscience, New York, N. Y., 1962, p 256.

[10] (a) K. B. Wiberg, "Laboratory Technique in Organic Chemistry," McGraw-Hill, New York, N. Y., 1960, Chapter 3; (b) R. T. Sanderson, "Vacuum Manipulation of Volatile Compounds," Wiley, New York, N. Y., 1948.

TABLE II

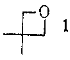
PRODUCTS FROM THE REACTION OF **2**^{a} WITH SODIUM HYDROXIDE^b IN 40% AQUEOUS METHANOL

Product	% yield 100°	85°	75°	65°
 **8**	81.7	82.6	79.1	75.9
 **9**	1.5	1.2	1.8	2.3
 **10**	16.4	14.6	19.4	23.4
% product balance	99.1	98.4	100.3	101.6
% reaction^c	37.8	43.3	40.6	36.0

^{a} $[\mathbf{2}]_0 = 0.0652\ M$. ^{b} $[\mathrm{NaOH}]_0 = 0.1049\ M$. ^{c} Calculated from the difference between the initial and final concentrations of **2**.

TABLE III

PRODUCTS FROM THE REACTION OF **3**^{a} WITH SODIUM HYDROXIDE^b IN 40% AQUEOUS METHANOL

Product	% yield 95°	85°	75°	65°
 **11**	40.0, 39.7	46.4	49.0	54.3, 54.3
 **12**	54.0		54.6	57.2
% product balance	94.0		103.6	111.5
No. of half-lives	10.6, 20.6	10.4	9.9	10.3, 20.3

^{a} $[\mathbf{3}]_0 = 0.194\text{–}0.207\ M$. ^{b} $[\mathrm{NaOH}]_0 = 0.0188\ M$.

which is not possible with **3** after the base is expended and the acid catalyzes the opening of the oxetane ring.[8a,11] For this reason, product analyses from **1** and **2** were conducted with excess base and the reaction was allowed to proceed for about 1 half-life. Yields are based on the amount of **1** and **2** that underwent reaction. Small amounts of the glycol (2-methyl-2,4-butanediol) were detected from the reaction of **2** with base, but quantitative analyses were not pursued. Control experiments with base and the oxetanes **4** and **8**, as well as allyl alcohol (**5**) under conditions which approximated those of the reaction of **1** and **2** with base, showed that these products were stable. The constancy in yield of oxetane **11** with variation in reaction time (Table III) shows that **11** is stable under the reaction conditions. Ethylene would be produced from the basic fragmentation of **1**, but the *maximum* possible yield was 0.2%. Acetone, which would arise from the basic fragmentation of **2**, was not observed.

Kinetic Data.—The overall rates of basic decomposition of **1**, **2**, and **3** were determined by acidometric methods through approximately 3 half-lives. The orders in the 1,3-chlorohydrin and base were established with **3** and the data are given in Table IV. The results indicate first-order dependence on both **3** and base. Kinetic data from which activation parameters were calculated for the overall reaction are given in Table V along with these parameters. The reactions of 1,3-chlorohydrins with base fall into the category of parallel second-order reactions, where the overall rate coefficient (k_2) equals the sum of the second-order rate coefficients for the ND$_\mathrm{I}$ reaction (k_r), fragmentation (k_f), substitution (k_N), and elimination (k_E) (eq 1).[12]

$$k_2 = k_\mathrm{r} + k_\mathrm{f} + k_\mathrm{N} + k_\mathrm{E} = \sum_\mathrm{i} k_\mathrm{i} \tag{1}$$

$$k_\mathrm{i} = k_2 \left(\frac{\%\ \text{yield i}}{100}\right) \tag{2}$$

The individual rate coefficients (k_i) are then calculated, with the aid of eq 2, from data in the preceding tables. The k_i values at various temperatures and their corresponding activation parameters are given in Table VI.

TABLE IV

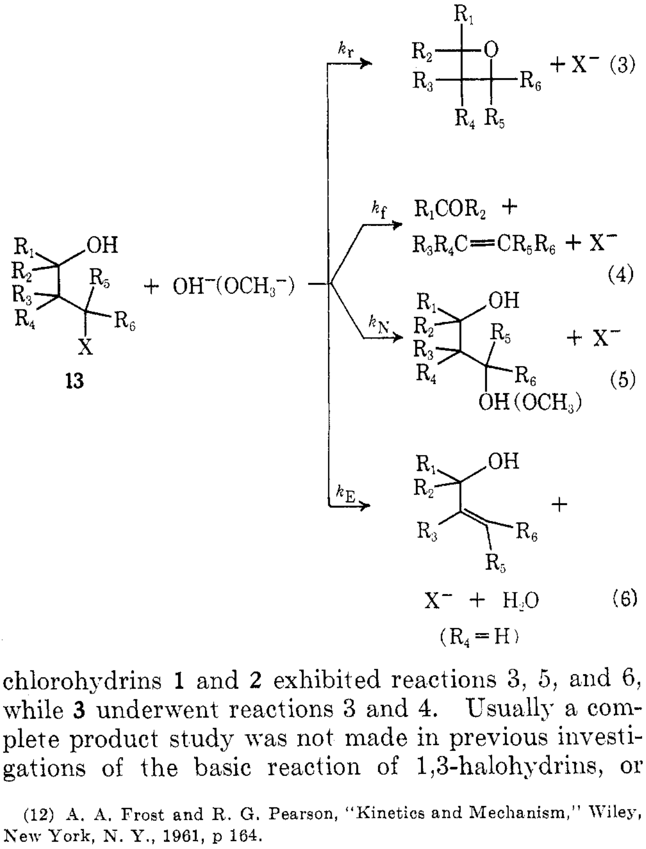
ORDER IN 3-CHLORO-2,2-DIMETHYL-1-PROPANOL (**3**) AND SODIUM HYDROXIDE IN 40% AQUEOUS METHANOL AT 85.00°^{a}

$[\mathbf{3}]_0$, M	$10^2[\mathrm{NaOH}]_0$, M	10^4k_1,^{b} sec^{-1}	10^4k_2,^{c} l. mol^{-1} sec^{-1}
0.1006	0.938	0.365 ± 0.005	3.62 ± 0.05
0.2224	0.938	0.890 ± 0.016	4.01 ± 0.07
0.4012	0.938	1.53 ± 0.02	3.81 ± 0.04
0.6085	0.938	2.10 ± 0.04	3.45 ± 0.06
0.7999	0.938	2.99 ± 0.03	3.74 ± 0.04
1.007	0.938	3.54 ± 0.06	3.51 ± 0.06
			Av 3.69 ± 0.14
1.019	1.88	3.46 ± 0.04	3.53 ± 0.04
1.008	2.81	3.43 ± 0.03	3.40 ± 0.03
1.004	5.63	3.47 ± 0.02	3.46 ± 0.02
1.000	9.38	3.26 ± 0.04	3.26 ± 0.04
			Av 3.43 ± 0.06

^{a} Ionic strength adjusted to 0.499 M with sodium perchlorate. Individual rate coefficients are given with probable error and the calculations were made with the aid of a standard first-order computer program. ^{c} Calculated from $k_2 = k_1/[\mathbf{3}]_0$.

Discussion

The possible reactions of 1,3-halohydrins are generalized in eq 3–6. In the present investigation, 1,3-chlorohydrins **1** and **2** exhibited reactions 3, 5, and 6, while **3** underwent reactions 3 and 4. Usually a complete product study was not made in previous investigations of the basic reaction of 1,3-halohydrins, or



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[11] (a) R. T. Keen, *Anal. Chem.*, **29**, 1041 (1957); (b) H. Rupe and O. Klemm, *Helv. Chim. Acta*, **21**, 1538 (1938); (c) S. Searles, D. G. Hummel, P. O. Throckmorton, and S. Nukina, *J. Amer. Chem. Soc.*, **82**, 2928 (1960).

[12] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," Wiley, New York, N. Y., 1961, p 164.

TABLE V

ACTIVATION PARAMETERS FOR THE OVERALL REACTION OF 1,3-CHLOROHYDRINS WITH SODIUM HYDROXIDE IN 40% AQUEOUS METHANOL[a]

1,3-Chlorohydrin	Temp, °C	$10^4 k_2$[b]	E_a[c]	Log A	$\Delta H^\ddagger$[c]	$\Delta S^\ddagger$[d]
1[e]	65.00	1.15 ± 0.01				
	75.00	3.31 ± 0.04				
	85.00	8.27 ± 0.15				
	100.00	32.4 ± 0.9	23.9 ± 0.2	11.5	23.2 ± 0.1	−8.2 ± 0.3
2[f,g]	55.00	1.51 ± 0.06				
	65.00	4.45 ± 0.03				
	75.00	12.2 ± 0.1				
	85.00	31.6 ± 0.2	23.6 ± 0.04	11.9	23.0 ± 0.1	−6.2 ± 0.2
3[g,h]	65.00	0.455 ± 0.004				
	75.00	1.39 ± 0.02				
	85.00	3.69 ± 0.14[i]				
	95.00	10.4 ± 0.3	25.6 ± 0.3	12.2	24.9 ± 0.3	−5.0 ± 0.9

[a] Ionic strength adjusted to 0.499 M with sodium perchlorate. [b] Units in l. mol^{-1} sec^{-1}. Each entry is an average of two measurements. [c] In kcal/mol with probable error. [d] In eu. [e] $[\mathbf{1}]_0$ = 0.120–0.125 M, $[\mathrm{NaOH}]_0$ = 0.0528 M, and k_2 is calculated from a second-order computer program. [f] $[\mathbf{2}]_0$ = 0.317–0.322 M, $[\mathrm{NaOH}]_0$ = 0.02814 M. [g] Second-order rate constant calculated from $k_2 = k_1/[\text{1,3-chlorohydrin}]_0$. [h] $[\mathbf{3}]_0$ = 0.208–0.194 M, $[\mathrm{NaOH}]_0$ = 0.0188 M. [i] Average from $[\mathbf{3}]_0$ = 0.1006–1.007 M, $[\mathrm{NaOH}]_0$ = 0.00938 M, Table IV.

TABLE VI

ACTIVATION PARAMETERS FOR INDIVIDUAL RATE COEFFICIENTS (k_i) IN THE BASIC REACTION OF 1,3-CHLOROHYDRINS IN 40% AQUEOUS METHANOL

1,3-Chlorohydrin	Temp, °C		$10^4 k_i$[a]	E_a[b]	Log A	$\Delta H^\ddagger$[b]	$\Delta S^\ddagger$[c]
		k_r[d]					
1	65.0		0.150				
	75.0		0.444				
	85.0		1.12				
	100.0		4.73	24.6 ± 0.2	11.1	23.9 ± 0.2	−10.2 ± 0.8
		k_{Nm}[e]					
1	65.0		0.554				
	75.0		1.63				
	85.0		4.14				
	100.0		17.3	25. ± 0.2	11.6	23.8 ± 0.2	−7.8 ± 0.7
		k_{Nh}[f]					
1	65.0		0.313				
	75.0		0.854				
	85.0		2.39				
	100.0		9.23	24.3 ± 0.2	11.2	23.6 ± 0.2	−9.6 ± 0.6
		k_E[g]					
1	65.0		0.0286				
	75.0		0.0804				
	85.0		0.312				
	100.0		1.51	28.8 ± 0.7	13.1	28.1 ± 0.7	−1.1 ± 2.5
		k_r[h]					
2	65.0		3.38				
	75.0		9.65				
	85.0		26.1				
	100.0[i]		103	24.5 ± 0.1	12.3	23.7 ± 0.1	−4.4 ± 0.2
		k_{Nm}[j]					
2	65.0		1.04				
	75.0		2.37				
	85.0		4.61				
	100.0[i]		20.6	21.1 ± 1.1	9.63	20.4 ± 1.1	−16.8 ± 3.7
		k_E[k]					
2	65.0		0.102				
	75.0		0.220				
	85.0		0.379				
	100.0[i]		1.89	20.5 ± 1.6	8.21	19.8 ± 1.6	−23.3 ± 5.5
		k_r[l]					
3	65.0		0.247				
	75.0		0.681				
	85.0		1.71				
	95.0		4.15	23.2 ± 0.1	10.4	22.5 ± 0.1	−13.3 ± 0.3
		k_f[m]					
3	65.0		0.260				
	75.0		0.759				
	95.0		5.61	25.3 ± 0.1	11.8	24.6 ± 0.1	−6.9 ± 0.3

[a] Units in l. mol^{-1} sec^{-1}. [b] In kcal/mol with probable error. [c] In eu. For appearance of [d] **4**; [e] **6**; [f] **7**; [g] **5**; [h] **8**. [i] Calculated from an overall rate coefficient which is extrapolated from the 55–85° range to 100°. For appearance of [j] **10**; [k] **9**; [l] **11**; [m] **12**.

product yields were determined by isolation which may be subject to error. The lack of a complete product study by some previous workers was due, in part, to their interest in the basic reaction of 1,3-chlorohydrins solely as a synthetic route to oxetanes.[8a,13] Unfortunately the yield data for oxetanes did not allow one to assign the unreported products to fragmentation, substitution, or elimination products. With the quantitative product study and kinetic data presented here, a more complete evaluation of the relative importance of eq 3–6 can be made.

The fragmentation reaction (eq 4) is of particular interest.[4k,5a,6d,8,14] In a detailed product study of the basic reaction of 2,2-disubstituted 1,3-bromohydrins (**13**, $X = Br$; $R_1 = R_2 = R_5 = R_6 = H$), the yield of the olefinic fragmentation product increased in the order of increasing stability of the olefin.[8c] Product distribution from 1- or 3-substituted 1,3-halohydrins has not been as thoroughly studied. Fragmentation has been reported for 3-substituted 1,3-chlorohydrins (**13**, R_5 = alkyl; $R_1 = R_2 = R_3 = R_4 = R_6 = H$; $X = Cl$),[4k] but not with 1-substituted 1,3-halohydrins.[4k,13a,c] In the latter instances, it cannot be ascertained if fragmentation occurred, but was simply not reported. Fragmentation was reported (55–60% yield) from 1,3-disubstituted hydroxy brosylates (**13**, $R_1 = R_5 = CH_3$; $R_2 = R_3 = R_4 = R_6 = H$; $X = OBs$).[8b] From our data, it is clear that fragmentation occurs only when a substituted olefin can be formed. In principle, fragmentation could be facilitated by 1 substitution of **13**, as in **2**, to generate a more stable carbonyl fragment. Yet no fragmentation was observed with **2**, whereas 2 substitution (as in **3**) does result in fragmentation where a more stable olefin is produced. In changing from 2 to 1 substitution (**3** *vs.* **2**), not only is fragmentation suppressed, but ring-closure (eq 3) and substitution (eq 5) are markedly increased (*cf.* Table VI). The rate of fragmentation of **3** is slightly greater than ring closure; yet $\Delta H^{\ddagger}$ is *greater* for fragmentation (25.3 kcal/mol) than for ring closure (23.2 kcal/mol). Thus, it is $\Delta S^{\ddagger}$ that determines the rate sequence of $k_f \gtrsim k_r$ for **3**. This is consistent with the observation[8c] that fragmentation *vs.* ring closure is solvent dependent. Thus, there appears to be less solvent reorganization for fragmentation of **3** ($\Delta S^{\ddagger} = -6.9$ eu) where there is greater charge dispersion in proceeding to the transition state than in ring closure ($\Delta S^{\ddagger} = -13.3$ eu) with less charge dispersion.

The rates of ring closure and yields of oxetanes decrease in the order of $\mathbf{2} > \mathbf{3} \sim \mathbf{1}$. On the basis of the Thorpe–Ingold effect,[15] it is expected that the rate of ring closure of **3** should be significantly greater than for **1** due to the *gem*-dimethyl group in **3**, which should decrease the proximity between oxygen and the carbon bearing chlorine.[16] There is then little basis for support of the Thorpe–Ingold hypothesis in these reactions. The reason that the k_r values are in the order $\mathbf{2} > \mathbf{3}$ is found in the $\Delta S^{\ddagger}$ term, since $\Delta H^{\ddagger}$ is greater for **2** (23.7 kcal/mol) than **3** (22.5 kcal/mol). Although the differences in activation parameters between **2** and **3** are reasonably attributed to a change from a tertiary to a primary hydroxy grouping, the interpretation is complicated by the inability to assess the mechanistic details. Isotope studies indicate that the N_{D_I}-($^-$O-3) reaction of ethylene chlorohydrin is a two-step process with an acid–base preequilibrium, while the N_{D_I}-($^-$O-5) reaction of 4-chloro-1-butanol is a concerted process.[6a] The present N_{D_I}-($^-$O-4) reaction occupies an intermediate position between these two studied examples. A larger positive contribution to $\Delta H^{\ddagger}$ from the possible preequilibrium may occur for **3** as compared to **2**, since tertiary alcohols are weaker acids than primary alcohols in protic solvents.[6d] However, a similar ordering of $\Delta H^{\ddagger}$ values for **2** and **3** would also be expected with the concerted reaction. Another possibility exists, namely that a change from a two-step to a concerted mechanism occurs. Indeed, the $\Delta S^{\ddagger}$ value for **2** (−4.4 eu) is considerably more positive than the values for **1** (−10.2 eu) or **3** (−13.3 eu). The $\Delta S^{\ddagger}$ term for the basic aqueous reaction of ethylene chlorohydrin (10 eu) is significantly more positive than the corresponding term for the basic reaction of 4-chloro-1-butanol (−5 eu).[4n] This may suggest that **2**, with a tertiary hydroxyl group, proceeds *via* the two-step mechanism, while **1** and **3**, with primary hydroxyl groups, follow the concerted mechanism.

Capon[5a] previously compared the rates of ring closure for a series of ω-hydroxyalkyl chlorides in aqueous sodium hydroxide at 30°, but 3-chloro-1-propanol (**1**) was missing from the series. Our activation parameters for the ring-closure reaction of **1** allow comparison of an extrapolated value in 40% aqueous methanol with this series. A previous study[4j] of the effect of solvent on the rate of ring closure for the basic reaction of ethylene chlorohydrin showed that the rate was approximately doubled in proceeding from water to 40.9 wt % ethanol at 30°. With this correction, the comparison of ring-closure reactions is given in Table VII. The k_{rel}^{cor}

TABLE VII

EFFECT OF RING SIZE ON THE N_{D_I} REACTION FOR A SERIES OF CHLOROHYDRINS IN AQUEOUS SODIUM HYDROXIDE AT 30°

Chlorohydrin	*n* in N_{D_I}-($^-$O-*n*)	$10^3 k_r$, mol^{-1} sec^{-1}	k_{rel}^{uncor}	$k_{rel}^{cor\,a}$
$Cl(CH_2)_2OH^b$	3	2.16	4300	2000
$Cl(CH_2)_3OH$ (**1**)	4	$5 \times 10^{-4\,c}$	≡1	≡1
$Cl(CH_2)_4OH^b$	5	2.86	5700	$(5700)^d$
$Cl(CH_2)_5OH^b$	6	$10^{-2\,e}$	20	20

[a] Corrected by comparison to the corresponding alcohol where Cl is replaced by CH_3 in each case. [b] From ref 5a, data of Capon and Farazmand, and from ref 4n. [c] Extrapolated value at 30° in 40% aqueous methanol is 9×10^{-4} l. mol^{-1} sec^{-1} and this is corrected to 5×10^{-4} l. mol^{-1} sec^{-1} in H_2O (see text). [d] Uncorrected, since 4-chloro-1-butanol is reported to undergo ring closure by a concerted process.[6a] The k_{rel}^{cor} value, assuming a two-step mechanism, is 4700. [e] Extrapolated.

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[13] (a) C. Moureu and G. Barrett, *Bull. Soc. Chim. Fr.*, **29**, 994 (1921); (b) G. M. Bennett and W. G. Philip, *J. Chem. Soc.*, 1937 (1928); (c) F. Covaert and M. Beyaert, *Naturwetensch. Tijdschr.*, **22**, 78 (1940); (d) R. Lespieau, *Bull. Soc. Chim. Fr.*, **7**, 254 (1940); (e) D. C. Dittmer, W. R. Hertler, and H. Winicov, *J. Amer. Chem. Soc.*, **79**, 4431 (1957).

[14] For a general review, see C. A. Grab and P. W. Schiess, *Angew. Chem., Int. Ed. Engl.*, **6**, 1 (1967).

[15] (a) R. M. Beesley, C. K. Ingold, and J. F. Thorpe, *J. Chem. Soc.*, **107**, 1080 (1915). (b) See ref 8c for a discussion of the Thorpe–Ingold effect in basic decomposition of 1,3-halohydrins.

[16] The Thorpe–Ingold effect is a potential energy factor and the rate (or $\Delta G^{\ddagger}$) argument presumes that potential energy is represented by $\Delta G^{\ddagger}$. See (a) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, p 665; (b) C. D. Ritchie and W. F. Sager, "Progress in Physical Organic Chemistry," S. G. Cohen, A. Streitwieser, Jr., and R. W. Taft, Jr., Ed., Vol. 2, Interscience, New York, N. Y., 1964, p 378.

values are obtained by assuming a two-step mechanism and correcting the equilibrium constant associated with alkoxide ion formation for polar effects. For each ω-hydroxyalkyl chloride, a new equilibrium constant is calculated, where chlorine is replaced by methyl, with the aid of the Taft equation[17] and Ballinger and Long's value of $\rho^* = 1.42$[18] for the pK_a of alcohols. Although a change from a two-step to a concerted mechanism may occur in the series,[6a] the trend in the $k_{\text{rel}}^{\text{cor}}$ may not be greatly altered. Thus, the magnitude of the neighboring group reaction with ethylene chlorohydrin is not simply due to the increased acidity of the hydroxy group, which results from the proximity of the electronegative chlorine atom.[5a] With regard to the relative rate of ring closure/substitution for the reference compound **1**, Table VI may be consulted. Substitution is favored over ring closure, and the relative value is $k_r/k_N = 0.179$ (= $0.444 \times 10^{-4}/2.48 \times 10^{-4}$) at 75°, where $k_N = k_{N_m} + k_{N_h}$.

Experimental Section[19]

Materials.—The aqueous methanol solvent was prepared as volume/volume per cent at 25° or by weight corresponding to the volumes. Methanol (ACS, reagent) was purified by refluxing over magnesium turnings with a catalytic amount of iodine followed by distillation.[20] Anhydrous sodium perchlorate was prepared from the hydrated salt by drying under vacuum at 110° for 48 hr. Oxetane (**4**) (Aldrich) was distilled from potassium hydroxide pellets and the heart-cut was collected (bp 47–48°, lit.[13e] 47–48°). 3-Chloro-1-propanol (**1**) [Matheson Coleman and Bell (MCB)] was distilled and a heart-cut was collected: bp 159.0–159.5° (lit.[21] 165°); ir (CCl_4) 3630, 3330, 2960–2882 cm^{-1}. Nmr (CCl_4) follows: CCH_2C, 1.97, 5, 2.0; $ClCH_2$ and $HOCH_2$, 3.71, m, 4.1; OH, 4.26, s, 1.1. 1,3-Propanediol (**7**) was fractionally distilled on an annular Teflor spinning-band column (Nester and Faust Co.): heart-cut bp 98–99° (6 mm) (lit.[22a] 214°); $n^{23.5}$D 1.4390 (lit.[22b] n^{20}D 1.4389). Allyl alcohol (MCB) was distilled, heart-cut bp 97–98° (lit.[23] 97.2°). 2-Methyl-3-buten-2-ol (Aldrich) was used without further purification.

4-Chloro-2-methyl-2-butanol (2).—The preparation was the same as that reported previously.[13b] The chlorohydrin was obtained in 72% yield from ethyl 3-chloropropionate (Aldrich) and methylmagnesium iodide, bp 66–67° (14 mm) [lit.[13b] 72° (13 mm)]. The ir (CCl_4) showed the following significant absorptions: 3612, 3485, 2880–2972 cm^{-1}. The nmr (CCl_4) consisted of the following absorptions: $(CH_3)_2$, 1.20, s, 5.8; CH_2CH_2Cl, 1.89, t (J = 8 cps), 1.7; CH_2CH_2Cl, 3.57, t (J = 8 cps), 2.0; and OH, 2.48, s, 1.0. Glc shows only one significant component (>99.9% pure). The molecular ion (M) of **2** was not observed in the mass spectrum, but the following significant fragments were detected and they are given with relative abundance: (M − CH_3) m/e 109, 107 (7.90%/23.6% = 0.33); (M − CH_2CH_2Cl) 59 (100%).

3-Chloro-2,2-dimethyl-1-propanol (3).—The method of preparation of **3** was adapted from a procedure for the preparation of pentaerythrityl trichloride.[24] To 25.8 g (0.248 mol) of 2,2-dimethyl-1,3-propanediol (MCB, practical grade) and 17.8 g (0.225 mol) of pyridine, 26.8 g (0.226 mol) of thionyl chloride was added as quickly as possible commensurate with the exothermic reaction. The reaction mixture was allowed to reflux for 135 min and then allowed to stand overnight at room temperature. Ether (200 ml) was added and the organic phase was washed with 6 N hydrochloric acid and then dried over magnesium sulfate. Rotary evaporation of the ether gave 28.68 g of a dark oil which was distilled. The forerun [0.63 g, bp 24–83° (30 mm)] was discarded and the heart-cut [18.62 g, bp 83–86° (30 mm), 86% **3** by glc, 58% yield based on thionyl chloride] was collected. Fractional distillation improved the purity of **3**, but column chromatography proved to be the most successful method to obtain high purity **3** in quantity. Chromatography was carried out on alumina (Merck acid washed, dried 1.5 hr at 110° in a vacuum oven) with a ratio of 8.5 g of alumina/1.0 g of crude **3**. The column was progressively eluted with n-hexane, benzene, and then 85% benzene–15% methanol. Glc analyses showed that essentially pure (99.9% minimum) fractions of **3** were obtained after the initial n-hexane elution. The combined fractions of **3**, after removal of solvent, were distilled through a 4 in. Vigreux column to give a low melting white solid (mp ~30°), bp 87° (35 mm). A 70% recovery of **3** was realized by this method. The ir (CS_2) of **3** showed the following absorptions: OH, 3620 and 3365 cm^{-1}; CH, 2960, 2872 cm^{-1}; CCl, 721 cm^{-1}. The nmr (CS_2) spectrum of **3** showed $(CH_3)_2$, 1.01, s, 6; CH_2Cl and CH_2OH, 3.46, two singlets partially resolved, 4; OH, 3.82, s (broad), 1.1.

Anal. Calcd for $C_5H_{11}OCl$: C, 48.99; H, 9.05; Cl, 28.91. Found: C, 48.62; H, 8.72; Cl, 28.78.

3-Methoxy-1-propanol (6).—A previously reported method[25] was used to prepare **6** in 44% yield. The product, obtained by fractional distillation on an annular spinning-band column, bp 144–145° (lit.[25] 148–149°), gave an ir (CCl_4) spectrum with absorptions at 3630 and 3475 cm^{-1}. The nmr ($CDCl_3$) spectrum showed the following: $CH_2CH_2CH_2$, 1.87, sextuplet (J = 6 cps), 2.0; OH, 2.83, s, 1.35; OCH_3, 3.36, s, 2.95; CH_2OCH_3, 3.66, triplet (J = 6 cps), 2.0; CH_2OH, 3.73, triplet (J = 6 cps), 2.0.

2,2-Dimethyloxethane (8).[26]—The method of Bennett and Philip[13b] was used to prepare **8** in quantitative yield, bp 70–71° (lit.[13b] 71°) from **2** and sodium hydroxide pellets. The nmr (CCl_4) spectrum showed $(CH_3)_2$, 1.27, s, 6.0; 3-CH_2, 2.26, triplet (J = 8 cps), 2.0; and 4-CH_2, 4.25, triplet (J = 8 cps), 2.0.

4-Methoxy-2-methyl-2-butanol (10).—A mixture of 2.45 g (20.0 mmol) of **2**, 1.19 g (22.0 mmol) of sodium methoxide (MCB), and 8 ml of anhydrous methanol was allowed to reflux for 20 hr under anhydrous conditions. The mixture was then filtered, the precipitate of sodium chloride was washed with anhydrous ether, and the filtrate was distilled. The forerun was discarded and a cut was collected at 147–148° (lit.[28] 144°), which corresponded to 0.469 g of **10** (20% yield). The nmr (CCl_4) spectrum of **10** showed $(CH_3)_2$, 1.17, s, 5.9; $CH_2CH_2OCH_3$, 1.68, triplet (J = 6 cps), 2.0; OH, 2.93, s, 1.1; OCH_3, 3.30, s, 2.9; and $CH_2CH_2OCH_3$, 3.54, triplet (J = 6 cps), 1.9.

3,3-Dimethyloxethane (11).[26]—A previously reported method[29] was used to prepare **11** in 4% yield from 2,2-dimethyl-1,3-propanediol (MCB, practial grade) and concentrated sulfuric acid, bp 78–80° (lit.[29] 79.2–80.3°). Glc analysis indicated that the product was 96% pure. The nmr (CCl_4) spectrum gave the following absorptions: $(CH_3)_2$, 1.18, s, 6.0 and CH_2, 4.16, s, 4.0.

Product Analysis.—Condensable products were analyzed by glc using the internal standard method[9] with comparison to a known mixture of the components and the internal standard. Low boiling products from **1** and base were analyzed with a 5 ft × $^1/_8$ in. Porapak Q column at 110° (flow 25 ml/min) and the high boiling components were analyzed on the same column at 165° with *tert*-butyl alcohol as the internal standard. Products from **2** and base were analyzed on a 10 ft × $^1/_8$ in. 15% DIDP on Variport column at 80° (flow 25 ml/min). A 20 ft × $^1/_8$ in. 20% XF-1150 on firebrick column at 86° (flow 15 ml/min) was

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[17] Reference 16a, Chapter 13.

[18] P. Ballinger and F. A. Long, *J. Amer. Chem. Soc.*, **82**, 795 (1960).

[19] All melting points are corrected and boiling points are uncorrected. Nuclear magnetic resonance (nmr) spectra were obtained with a Varian A-60 spectrometer. Chemical shifts are expressed in parts per million (ppm) relative to the internal tetramethylsilane standard as 0 ppm (δ scale). The nmr absorptions are given as ppm, coupling, relative area. Infrared (ir) spectra were determined with a Perkin-Elmer 621 or 337 spectrometer and mass spectra were obtained with a Hitachi RMU-6E instrument. Gas-liquid chromatography (glc) analyses were performed on Varian-Aerograph 1520 and Hy-Fi III instruments. Elemental analyses were performed by C. F. Geiger, Ontario, Calif., or by R. Steed of these laboratories.

[20] L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath, Boston, Mass., 1941, p 359.

[21] C. W. Gayler and H. M. Waddle, *J. Amer. Chem. Soc.*, **63**, 3359 (1941).

[22] (a) H. J. Bernstein, *ibid.*, **74**, 2674 (1952); (b) A. F. Gallagher and H. Hibbert, *ibid.*, **58**, 813 (1936).

[23] M. A. Dolliver, T. L. Gresham, G. B. Kistiakowsky, E. A. Smith, and W. E. Vaughan, *ibid.*, **60**, 440 (1938).

[24] A. Mooradian and J. B. Cloke, *ibid.*, **67**, 942 (1945).

[25] L. I. Smith and J. A. Sprung, *ibid.*, **65**, 1276 (1943).

[26] The numbering system of oxetanes is not uniform. The "Ring Index" system is used here, where oxygen is given the number one.[27]

[27] A. M. Patterson, L. T. Capell, and D. F. Walker, "The Ring Index," American Chemical Society Publication, 1960, p 6.

[28] F. Straus and W. Thiel, *Justus Liebigs Ann. Chem.*, **525**, 151 (1936).

[29] L. F. Schmoyer and L. C. Case, *Nature*, **183**, 389 (1959).

used to analyze the products from the reaction of **3** with base. The internal standard for the product analyses, resulting from **2** and **3**, was *n*-butyl alcohol.

Kinetic Method.—Sealed ampoules of the reaction mixture were periodically removed from a thermostated oil bath, quenched in ice–water, warmed to room temperature, shaken, and opened, and a 1.00-ml aliquot was transferred to a 125-ml erlenmeyer flask under a nitrogen atmosphere. The aliquots were titrated to the phenolphthalein end point with standardized hydrochloric acid. The data were processed with standard computer programs.

Registry No.—**2**, 1985-88-2; **3**, 13401-56-4; **6**, 1589-49-7; **8**, 6245-99-4; **10**, 27557-84-2; **11**, 6921-35-3.

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Mass Spectral Fragmentation of Spiro Ketones and Olefins[1]

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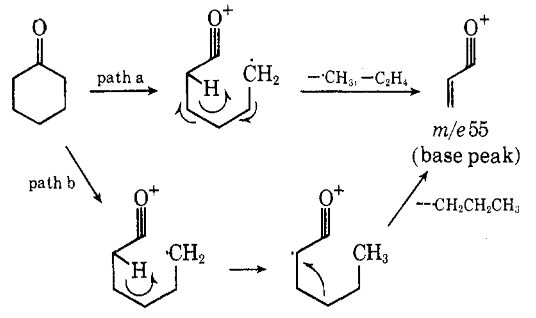
The mass spectra of spiro ketones with varying ring size have been recorded. An unusual fragmentation resulting in the loss of an olefinic radical in a hydrogen-transfer mechanism was observed to be an important decomposition pathway. Deuterium labeling determined the site of the fragmentation to be the nonketone ring. However, in several cases the preferred path of fragmentation was loss of the ketone ring. High-resolution data (Table I) defined the exact composition of the principal fragment peaks. The mass spectra of seven spiro olefins were investigated, and their fragmentation behavior was interpreted in terms of the loss of a series of alkyl radicals correlated with ring size.

Spiro Ketones.—The mass spectra of spiro ketones are found to exhibit a behavior unlike that of simple cycloalkyl ketones such as cyclohexanone or cyclopentanone.[2] The mass spectrum of cyclohexanone, for example, contains significant peaks arising from α cleavage followed by further fragmentation. In particular, the base peak at *m/e* 55 (M − 43) for cyclohexanone arises *via* one or both of the pathways shown in Scheme I. A related scheme can be written for cyclopentanone in which the base peak is also *m/e* 55 (M − 29). It might therefore be expected that a similar mode of fragmentation should occur for the spiro ketones which contain a cyclohexanone or a cyclopentanone ring. However, the prominent M − 43 ion (*m/e* 55) from cyclohexanone is extremely weak (*m/e* 123) in the mass spectrum of spiro[5.5]undecan-1-one (**1**) (Figure 1), whereas the M − 55 (*m/e* 111, $C_7H_{11}O$) peak, which is very small in cyclohexanone, is the base peak. Similarly, in the mass spectrum of spiro[4.5]decan-6-one (**2**) (Figure 2) *m/e* 111 ($C_7H_{11}O$) again appears as one of the two significant peaks (70% of the base peak at *m/e* 67, C_5H_7) but now corresponds to the loss of 41 amu. (See Table I.)

SCHEME I



In order of establish the structure parameters required for the formation of the intense *m/e* 111 peak, two spiro ketones containing five-membered carbonyl-bearing rings were prepared and analyzed. The mass spectrum of spiro[4.5]decan-1-one (**3**) (Figure 3) exhibits an intense peak (70% of the base peak) corresponding to M − 55 (*m/e* 97, C_6H_9O), and spiro[4.4]nonan-1-one (**4**) (Figure 4) also shows a major peak (50% of the base peak) at *m/e* 97 (C_6H_9O), which corresponds to the loss of 41 amu. The origin of the neutral fragment from the *saturated ring* is consistent with a mass shift of 14 amu (*m/e* 97 going to *m/e* 111) when the carbonyl-bearing ring is increased from five (**3** or **4**) to six carbons (**1** or **2**). Moreover, this correlation is also consistent with the observation that the neutral fragment is 41 amu when the *saturated* ring is five-membered, but 55 amu when the saturated ring is six-membered.

To define more precisely the mechanism and ions involved, the α hydrogens of **2** and **4** were exchanged for deuterium by repeated equilibration with D_2O in the presence of base. In the mass spectra of 7,7-dideuteriospiro[4.5]decan-6-one (**5**) (Figure 5) and 2,2-dideuteriospiro[4.4]nonan-1-one (**6**) (Figure 6), *m/e* 111 and *m/e* 97 are shifted completely to *m/e* 113 and *m/e* 99, respectively. We conclude therefore that the neutral fragments under discussion in the foregoing come entirely from the saturated ring and presumably by similar mechanisms.

One pathway, which is consistent with the data above, for the decomposition leading to the *m/e* 97 or *m/e* 111 peaks is postulated in Scheme II. Thus, the molecular ion undergoes β cleavage at the spiro junction followed by transfer of a δ hydrogen[3] to the carbonyl and C–C bond cleavage with loss of an allylic radical ($m = 1$) or a homoallylic radical ($m = 2$). An alternative mechanism might be written in which the spiro carbon carries the positive charge and abstracts the hydrogen.

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[1] We are indebted to the National Science Foundation for financial aid (Grants No. GP-9533 and GP-7193).

[2] For leading references, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, Chapter 3.

[3] S. D. Sample, D. A. Lightner, O. Buchardt, and C. Djerassi, *J. Org. Chem.*, **32**, 997 (1967).