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Oxetanes. IX. Structural and Solvent Effects in the Reaction of γ-Bromoalcohols with Base[1,2]

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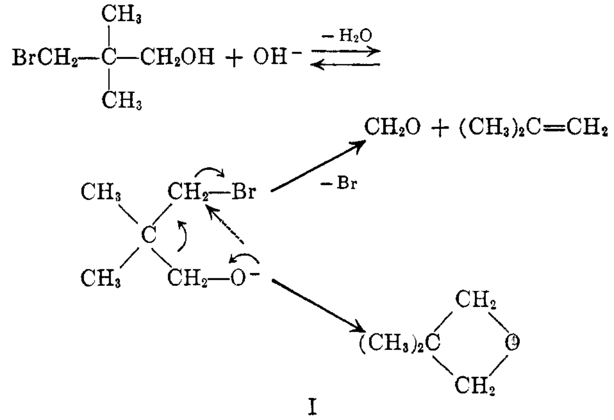
The alkaline decomposition of a series of 3-bromo-1-propanols, having various hydrocarbon substituents on carbon-2, was investigated with respect to influence of C-2 substitution and of the medium on the relative yields of intramolecular substitution and 1,4-elimination products. Elimination is favored by thermodynamic stability of the olefin that can be formed, and it is also favored by a more ionizing media. The results indicate that both the intramolecular substitution process and the 1,4-elimination process have a common intermediate, the γ-bromoalkoxide ion, and that the former process goes by a dissociation mechanism, the latter by a displacement mechanism. Several new oxetanes were prepared in the course of the work.

The yield of 3,3-dimethyloxetane from the reaction of 2,2-dimethyl-3-bromo-1-propanol with alkali is much less than might be expected from a compound which cannot undergo 1,2-elimination of hydrogen bromide as a side reaction. Although this common side reaction in intramolecular Williamson reactions is here blocked, a 1,4-elimination of hydrogen bromide occurs to a considerable extent.[3] This process results in cleavage of a carbon-carbon bond, forming isobutylene and formaldehyde, and may logically be interpreted as due to an inherent instability of the γ-bromoalkoxide ion (I) that is required for the intramolecular Williamson reaction.



I

It is common for alkyl halides to react by substitution and elimination processes simultaneously, but this particular pair of parallel processes seems rather unusual. The substitution process appears to be of the displacement type but is intramolecular and involves the closing of a strained ring. The elimination process is of a type that is not commonly associated with substitution, as it resembles the retrograde aldol condensation, the decomposition of salts of β-bromo acids[3] and similar cleavage reactions.[4,5]

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[1] Previous paper in this series: S. Searles, Jr., and E. F. Lutz, *J. Am. Chem. Soc.*, **81**, 3674 (1959).

[2] Supported in part by research grants from the Graduate School, Northwestern University, and from the National Science Foundation, for which grateful acknowledgment is given. Most of the material is abstracted from the Ph.D. Dissertation of Richard G. Nickerson, Northwestern University, 1955.

[3] S. Searles, Jr., and M. J. Gortatowski, *J. Am. Chem. Soc.*, **75**, 3050 (1953).

[4] S. J. Cristol and W. P. Norris, *J. Am. Chem. Soc.*, **75**, 632, 2645 (1953).

[5] Other examples are the alkaline decomposition of β,β-dimethyl-α-tosyloxy-γ-butyrolactone into β,β-dimethylacrylate ion, formaldehyde, and tosylate ion (H. Bretschneider and H. Hass, *Monatsh.*, **81**, 945 (1950), and the alkaline decomposition of dimethylaminopivalophenone into isobutylene, benzoic acid and trimethylamine (H. R. Synder and J. H. Brewster, *J. Am. Chem. Soc.*, **71**, 1061 (1949)). In each case, the action of base produces an intermediate, bearing a negative charge on oxygen, which can

On account of the importance of this competition in the usual synthesis of oxetanes, a study was made of the effect of solvent and structural changes. The results are also of interest for comparison with the effects of such factors in the ordinary bimolecular substitution and 1,2-elimination competition that has been carefully studied by Hughes, Ingold and co-workers.[6]

For this purpose a series of 3-bromo-1-propanols having various alkyl and/or aryl groups at carbon-2 were prepared in good yield from the corresponding glycols by reaction with hydrobromic acid in acetic acid, the intermediate acetate ester being alcoholized to the bromo alcohol. The bromo alcohols were treated with aqueous potassium hydroxide of two different concentrations under standardized conditions, and the yields of olefins and oxetanes were determined by isolation. Alcoholic base was also used in several instances and aqueous sodium carbonate in one instance. The yield of oxetane provides a measure of the extent of intramolecular substitution occurring, and the yield of olefin was used as a measure of the extent of 1,4-elimination. The results are compiled in Tables I, II, and III. Since duplicate runs were made in most cases, it is felt that the yields recorded are correct within about 3%.

TABLE I

Products from 3-Bromo-1-propanols and 15% Potassium Hydroxide

3-Bromo-1-Propanol	Yields, %		Ratio, Oxetane/ Olefin
	Oxetane	Olefin	
2,2-Dimethyl	12	60	0.2
2,2-Diethyl	27	54	0.5
2-Ethyl-2-isopropyl	14	50	0.3
2-Ethyl	23	19[a]	1.2
2-Butyl	21	24	0.9
2-Phenyl	0	26[b]	0.1
2-Methyl-2-phenyl	0	15	0.0
2-Ethyl-2-phenyl	0	47	0.0
2,2-Tetramethylene	8	63	0.13
2,2-Pentamethylene	33	50	0.66

[a] 2-Ethylallyl alcohol, the product of ordinary 1,2-elimination, was isolated in 19% yield. [b] 40% yield of 2-phenyl alcohol also obtained.

TABLE II

Products from 3-Bromo-1-propanols and 50% Potassium Hydroxide

Substituents in 3-Bromo-1-propanol	Yields, %		Ratio, Oxetane/ Olefin
	Oxetane	Olefin	
None	15	0	. .
2,2-Dimethyl	57	33	1.7
2,2-Diethyl	57	9	6.
2-Ethyl-2-isopropyl	47	6	8.
2-Ethyl	25	5[a]	5.
2-Butyl	30	0[b]	. .
2,2-Tetramethylene	48	26	1.8

[a] Also obtained was a 19% yield of 2-ethylallyl alcohol. [b] Also obtained was a 33% yield of 2-butylallyl alcohol.

TABLE III

Products from 3-Bromo-1-propanols and Other Bases

3-Bromo-1-propanol	Yields, %		
	Base	Oxetane	Olefin
2,2-Dimethyl	20% $Na_2CO_3(H_2O)$	10[a]	30[a]
2,2-Dimethyl	6% NaOEt(EtOH)	. . .[b]	18
2,2-Diethyl	6% NaOEt(EtOH)	43	. .[b]
2,2-Pentamethylene[c]	10% KOH(EtOH)	68	. .
2,2-Dibenzyl[d]	5.7% NaOEt(EtOH)	46.7	17

[a] The yields in this particular case are based on amount of bromoalcohol not recovered; 50% of the starting bromoalcohol was recovered from the distillate. [b] The compound indicated was not isolated in a pure state due to the difficulty of separating it from the ethanol by fractional distillation. [c] Experiment performed by Eugene F. Lutz. [d] Experiment performed by Shogo Nukina.

With the 2,2-disubstituted compounds the difference between the sum of these two yields and 100% is largely due to incomplete reaction, for some bromo alcohol was always carried over in the distillation of the products from the reaction mixture. With compounds monosubstituted at carbon-2, some 1,2-elimination, giving allylic alcohols, and bimolecular substitution, giving diols and hydroxyethers, takes place during the alkali treatment, and of course the olefin and epoxide yields are thereby lowered. These processes, however, were not taken further account of, because they would not involve intermediate formation of the γ-bromoalkoxide ion. The ratio of oxetane to olefin then still gives the relative tendencies of the alkoxide ion to undergo cleavage (1,4-elimination) or cyclization (intramolecular substitution).

It is seen that at either base concentration, substituents at carbon-2 favor the 1,4-elimination process over intramolecular substitution in the order:

$$C_6H_5 \gg CH_3 > C_2H_5,\ n\text{-}C_4H_9 > H$$

This order appears to parallel the thermodynamic stability of the olefins formed. Comparing isomeric compounds, we see that there is relatively more tendency to form methylpropene, $\Delta H_f^{25^\circ}$ -3343

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decompose into an olefin, a carbonyl compound, and an easily formed ion or molecule.

A new example which we wish to report here is the alkaline decomposition of 3-dimethylamino-2,2-dimethylpivaldehyde methiodide (in 25% aqueous potassium hydroxide at about 150°) to form trimethylamine (isolated in 15% yield), isobutylene (20%) and presumably formate ion. The Cannizzaro reaction, reported by E. R. Alexander, *J. Am. Chem. Soc.*, **70,** 2592 (1948), occurs simultaneously, but this elimination process had been overlooked in the earlier work. It is, of course, entirely analogous to the case of Synder and Brewster cited above.

(6) (a) E. D. Hughes, C. K. Ingold, and coworkers, *J. Chem. Soc.*, 157 *et seq.* (1946); (b) *J. Chem. Soc.*, 2038, *et seq.* (1948); (c) E. D. Hughes, *Quart. Rev.*, **5,** 245 (1951).

cal./mole,[7] than 1-butene, $\Delta H_f^{25°}$ 280 cal./mole, from the corresponding bromohydrins. Likewise, formation of 2-ethyl-1-butene, $\Delta H_f^{25°}$ -12920 cal./mole,[6] competes with oxetane formation better than that of 1-hexene, $\Delta H_f^{25°}$ -9960 cal./mole.[6] Particularly striking is the effect of the phenyl group on carbon-2, which results in the elimination reaction occurring so easily that no oxetane formation whatever was observed. This may be ascribed to the stabilizing effect of the phenyl group on the double bond.

For a complete analysis, certainly other factors besides the stability of the possible olefin formed should be considered, such as the relative stability of the possible oxetane formed and the Thorpe-Ingold effect of a *gem*-dialkyl grouping at carbon 2, bringing the oxygen atom into closer proximity to carbon-3.[8] The latter may be a cause of the greater ratio of oxetane to olefin from 2,2-diethyl-3-bromo-1-propanol than that from the dimethyl- and the tetramethylene-substituted bromohydrins. Molecular models suggest that the better yield of oxetane from 2,2-pentamethylene-3-bromo-1-propanol, as compared to that from 2,2-tetramethylene-3-bromo-1-propanol, may be due to interaction of the axial hydrogens on the exocyclic methylenes, thereby forcing them into closer proximity. Operating in the same direction, however, would be the probable greater stability of the double bond in methylenecyclopentane, as compared to methylenecyclohexane.[9]

These substituent effects resemble somewhat those affecting the relative yields of substitution and elimination products in ordinary bimolecular reactions of bases with alkyl halides. The latter have been interpreted, however, on the basis of steric retardation of the substitution process by the β-substituent regulating the relative rates of substitution and elimination.[6] Such a steric factor is unlikely in the present case, due to the cyclic transition state that must be involved in the intramolecular substitution process.

A marked solvent effect was observed on the competition between the intramolecular substitution and the 1,4-elimination processes. Comparison of the results from the use of 15% aqueous potassium hydroxide and of alcoholic base show clearly that the elimination is favored by a more ionizing media. Comparison of the results obtained with 15% and with 50% aqueous potassium hydroxide leads to the same conclusion, since the latter must be a poorer ionizing solvent. With most of the water molecules in 50% potassium hydroxide tied up by solvation of potassium and hydroxide ions, the capacity to solvate new ions must be relatively low.[10] The basicity of the medium does not appear to be a major factor, because the oxetane/olefin ratio was not greatly different when the reaction was carried out in 20% aqueous sodium carbonate solution.

This solvent effect is exactly opposite to that observed in the usual reactions of primary alkyl halides with bases, where elimination is favored over substitution by less ionizing (or solvating) media.[6] The solvent effect found in this investigation is in accord with the 1,4-elimination going by a dissociative mechanism and the substitution process by a displacement mechanism. This confirms that the γ-bromoalkoxide ion, such as I, is a discrete intermediate, which can undergo either solvolysis with concurrent rupture of C=C bonds, or cyclization by an internal displacement process.

Apparently the π-electrons on oxygen in this intermediate are potentially mobile, like those in the double bond in allylic halides, and can facilitate the release of γ-bromide even when the latter is primary, if the β-carbon bears an alkyl or aryl group. This 1,4-elimination process then appears to be a neat example of the nonconcerted mechanism termed by Ingold "E1cb",[11] and is particularly interesting in view of the observation that 1,4-elimination of hydrogen halide from a four-carbon chain is thought to proceed by a concerted mechanism.[12,13]

Some additional experiments were carried out to investigate the possible generality of the 1,4-elimination process, which can be formulated as $\overset{\curvearrowright}{X—}C—\overset{\curvearrowright}{C}—\overset{\curvearrowright}{C—}Y$. Little olefin formation was observed, however, when 3-dimethylamino-2,2-dimethyl-1-propanol methiodide[14] ($X = OH$, $Y = NMe_3$) or 1,1-methylamino-3-bromo-2,2-dimethylpropane[15] ($X = NHCH_3$, $Y = Br$) were heated with aqueous potassium hydroxide nor when 1,3-di-

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(7) Heats of formation from *Properties of Hydrocarbons*, American Petroleum Institute, Project 44, Table 8p.

(8) R. M. Beesley, C. K. Ingold, and J. F. Thorpe, *J. Chem. Soc.*, **107**, 1080 (1915).

(9) H. C. Brown, J. H. Brewster, and H. Schechter, *J. Am. Chem. Soc.*, **76**, 467 (1954).

(10) An analogy is the observation of G. L. Lucas and L. P. Hammett, *J. Am. Chem. Soc.*, **64**, 1928 (1942), that sodium hydroxide retards the rate of hydrolysis of *tert*-butyl nitrate.

(11) C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, N. Y., 1953, p. 467.

(12) S. J. Cristol, W. Barasch, and C. H. Tiemann, *J. Am. Chem. Soc.*, **77**, 583 (1955); S. J. Cristol, Abstracts of Fourteenth National Organic Chemistry Symposium, ACS, 1955, p. 12.

(13) (a) A related 1,4-elimination process, the cleavage of 3-dialkylamino-1,1-diphenylpropanols to 1,1-diphenylethylene and other products when heated in refluxing acetic anhydride, has been reported by D. W. Adamson, *Nature*, **164**, 500 (1949). It, of course, does not proceed *via* a conjugate base, however. (b) A number of other 1,4-eliminations with cleavage are discussed by C. A. Grob and W. Baumann, *Helv. Chim. Acta*, **38**, 594 (1955).

(14) C. Mannich, F. Lesser, and E. Sieten, *Ber.*, **65**, 378 (1932).

(15) C. Mannich and E. Baumgarten, *Ber.*, **70**, 210 (1937).

TABLE IV

LITHIUM ALUMINUM HYDRIDE REDUCTION[a] OF MALONIC ESTERS

Starting Ester	1,3-Propanediol	Yield, %	B.P. ° (mm.)	
			Obs.	Lit.
Ethyl ethylmalonate[b]	2-Ethyl	71	124–127 (16)	83–86 (1–2)[h]
Ethyl ethylisopropylmalonate[b]	2-Ethyl-2-isopropyl[d]	76	72–74 (0.3)	
Ethyl phenylmalonate[b]	2-Phenyl[e]	36	189 (16)	
Ethyl cyclopropane-1,1-dicarboxylate[b]	2,2-Dimethylene	72	70	
Ethyl cyclobutane-1,1-dicarboxylate[c]	2,2-Trimethylene	76[i]	132–140 (22)	147 (20)[j]
Ethyl cyclopentane-1,1-dicarboxylate[c]	2,2-Tetramethylene[g]	81	M.P. 92–92.5	
Ethyl cyclohexane-1,1-dicarboxylate [c]	2,2-Pentamethylene	68	M.P. 93–98	97–97.5[k]
Ethyl dibenzylmalonate	2,2-Dibenzyl	92	M.P. 82–83[l]	

[a] One mol. of lithium aluminum hydride was used for 0.75 mol. of ester in ethyl ether. [b] After hydrolysis the reaction mixture was continuously extracted with ethyl ether for 2–3 days to remove the diol. [c] Reaction mixture decomposed with 20% sodium hydroxide, the ether solution being decanted from the solid salts. [d] *Anal.* Calcd. for $C_8H_{18}O_2$: C, 65.71; H, 12.41. Found: C, 65.04; H, 12.21. [e] *Anal.* Calcd. for $C_5H_{10}O_2$: C, 58.80; H, 9.87. Found: C, 59.15; H, 9.75. [g] Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.55; H, 11.11. [h] H. Adkins and H. R. Billica, *J. Am. Chem. Soc.*, **70,** 3121 (1948). [i] By inverse addition; by usual method, yield is about 50% (experiments of E. F. Lutz). [j] N. D. Zelinsky and M. N. Ujedinov, *Ber.*, **46,** 1093 (1913). They reported n_D^{22} 1.4758; the product obtained in our work had n_D^{22} 1.4778. [k] H. J. Backer and H. J. Winter, *Rec. trav. chim.*, **56,** 492 (1937). [l] *Anal.* Calcd. for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.95; H, 8.05.

bromo-2,2-dimethylpropane[16] was heated with alcoholic potassium hydrogen sulfide. (In the last reaction 3 - bromo - 2,2 - dimethyl - 1 - propyl mercaptan (X = SH, Y = Br) is presumably an intermediate.) In the last two cases, intermolecular substitution proceeds with greater ease[15,16] than in the case of the corresponding γ-bromoalcohol. Thus, for the 1,4-elimination process, X should be not very nucleophilic and Y should be easily dissociable.

It is interesting to note that β-substitution is not required for the 1,4-elimination process with γ-halogeno alcohols, if the γ-halogen is not primary. Gaylord and co-workers[17] have shown it to occur when 2-chloro-4-hexanol and 1-phenyl-3-chloro-1-butanol are treated with alkali. These workers postulated that the mechanism for the cleavage process was (1) base-catalyzed hydrolysis of oxetane initially formed, giving a 1,3-diol and (2) base-catalyzed cleavage of the latter to olefin and carbonyl compound. The basis for this postulation was some work by Barbot,[18] but inspection of the latter indicates it to be concerned actually with acid-catalyzed cleavage of 1,3-diols. This mechanism is untenable, as it has been shown[19] that 1,3-diols of the type postulated as formed are cleaved by hot alkali to carbonyl compounds and alcohols, not olefins. Furthermore, base-catalyzed hydrolysis of the substituted oxetanes involved, to form 1,3-diols, required more drastic conditions than required for cleavage of the bromohydrins.

EXPERIMENTAL

The *1,3-diols* were synthesized by lithium aluminum hydride reduction of the corresponding malonic esters,[20] except 2,2-dimethyl-1,3-propanediol, which was a commercial sample. Each was fractionally distilled or crystallized until the b.p. or m.p. agreed with literature values. Preparative data on those diols which are new to the litera-

TABLE V

3-BROMO-1-PROPANOLS

Substituents	Yield, %	B.P., ° (mm.)	n_D (t°)
2-Ethyl	54	60–65 (4)	
2-Butyl	73	105–110 (9)	1.4806 (20)
2-Phenyl[a]	57	90–93 (0.1)	1.5616 (25)
2,2-Dimethyl	84	76–80 (13)[b]	1.4825 (20)
2,2-Diethyl[c]	90	103 (12)	1.4880 (20)
2-Ethyl-2-isopropyl	76	110–120 (1)	1.4910 (20)
2-Ethyl-2-phenyl	78	124–132 (0.5)	1.5628 (27.5)
2,2-Pentamethylene[d]	50	85–87	1.5181 (25)
2,2-Tetramethylene[e]	70	100–105	1.5105 (25)
2,2-Trimethylene	13	75–78	1.5011 (26)
2,2-Dibenzyl[f]	75	183–185 (0.1)	1.5970 (20)

[a] *Anal.* Calcd. for $C_9H_{11}OBr$: C, 50.25; H, 5.15. Found: C, 50.50; H, 5.25. [b] A. Franke and H. Hinterberger, *Monatash.*, **43,** 655 (1953) report b.p. 73–74° (10 mm.). [c] *Anal.* Calcd. for $C_6H_{15}OBr$: C, 43.08; H, 7.75. Found: C, 43.80; H, 8.10. The allophanate, prepared by passing cyanic acid gas into the bromoalcohol, was obtained as white leaflets, m.p. 110–110.5°, from alcohol. *Anal.* Calcd. for $C_9H_{17}O_3N_2Br$: N, 9.96. Found: N, 9.91. [d] *Anal.* Calcd. for $C_8H_{15}OBr$: C, 46.61; H, 7.34. Found: C, 44.53; H, 7.27. [e] Calcd. for $C_7H_{13}OBr$: C, 43.54; H, 6.79. Found: C, 44.51; H, 7.27. [f] *Anal.* Calcd. for $C_{17}H_{19}OBr$: C, 63.9; H, 6.0. Found: C, 65.0; H, 6.6. This bromohydrin was prepared by alcoholysis of its acetate, which was isolated in this case, and the yield is based on the pure acetate started with. The acetate was isolated by simply removing the solvent under vacuum after the reaction of the diol with hydrogen bromide had proceeded under reflux for 3 hr., giving a tan crystalline residue which was recrystallized from ethanol to give white needles, m.p. 109°. *Anal.* Calcd. for $C_{19}H_{21}O_2Br$: C, 63.16; H, 5.86. Found: C, 63.42; H, 5.79.

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(16) H. J. Backer and K. J. Keuning, *Rec. trav. chim.*, **53,** 808 (1934).

(17) N. G. Gaylord, J. H. Crowdle, W. A. Himmler, and H. J. Pepe, *J. Am. Chem. Soc.*, **76,** 59 (1954).

(18) A. Barbot, *Bull. soc. chim.*, (5), **2,** 1438 (1935).

(19) S. Searles, E. L. Ives, and S. Nukino, *J. Org. Chem.*, **24,** 1770 (1959), and Abstracts, 127th Meeting of ACS, Cincinnati, Ohio, April, 1955, p. 24N; K. C. Brannock and G. R. Lappin, *J. Am. Chem. Soc.*, **77,** 6052 (1955).

(20) R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, 69, 1197 (1947).

TABLE VI

OLEFINIC PRODUCTS[a]

Compound	B.P., °		n_D (t°)	
	Obs.	Lit.	Obs.	Lit.
Methylpropene[b]	−6 to 0	−6.9		
1-Butene	−4 to 0	−6.3		
2-Ethyl-1-butene[c]	65–70	66.5	1.3918 (20)	1.396 (20)
1-Hexene	60–68	67		
3-Methyl-2-ethyl-1-butene	91–93	88–90	1.4028 (27)	1.407 (25)
Styrene	140–149	146		
α-Methylstyrene	83–90 (40 mm.)	68–69 (27 mm.)[d]	1.5248 (18)	1.5334 (20)
α-Ethylstyrene	179–180	181[e]	1.5329 (25)	1.5264 (25)[e]
Methylenecyclohexane	100–110	106[f]	1.4466 (26)	1.4491 (20)[f]
Methylenecyclopentane	76–81	78–81[g]	1.4325 (26)	1.4335 (19)[g]
2-Methylene-1-butanol	130–135	133[h]		
2-Phenyl-2-propen-1-ol	120–130 (60 mm.)	115 (10 mm.)[i]		
2-Benzyl-3-phenylpropene[j]	95 (0.5 mm.)		1.5851 (20)	

[a] Except when otherwise noted, literature values are taken from F. D. Rossini, *Selected Values of Properties of Hydrocarbons and Related Compounds*, Am. Pet. Inst. Proj. 44, Petrol. Res. Lab., Carnegie Inst. of Technology, Pittsburgh, Pa. [b] The 2,4-dinitrobenzenesulfenyl chloride adduct had m.p. 86–87°, in agreement with the value reported by N. Kharasch and C. M. Buess, *J. Am. Chem. Soc.*, **71**, 2724 (1949). [c] The 2,4-dinitrobenzenesulfonyl chloride adduct was crystallized from dilute alcohol and has m.p. 86–87°. To our knowledge, this derivative has not been reported previously. *Anal.* Calcd. for $C_{12}H_{12}ClN_2O_4S$: C, 45.21; H, 4.74. Found: C, 45.66; H, 4.87. [d] M. Tiffeneau, *Ann. Chim.* [8], **10**, 157 (1907). [e] C. G. Overberger and D. Tanner, *J. Am. Chem. Soc.*, **77**, 369 (1955). [f] O. Wallach, *Ann.*, **359**, 249 (1908). [g] O. Wallach, *Ann.*, **347**, 325 (1906). [h] V. I. Lyubomilov and A. P. Terentev, *J. Gen. Chem.* (*U.S.S.R.*), **21**, 1479 (1951). [i] J. M. Butler, U.S. Patent **2,537,622** (Jan. 9, 1951); *Chem. Abstr.*, **45**, 5723 (1951). [j] *Anal.* Calcd. for $C_{16}H_{16}$: C, 92.26; H, 7.74. Found: C, 92.01; H, 8.02.

TABLE VII

OXETANE PRODUCTS

Oxetane	B.P., °	n_D (t°)	Empirical Formula	% C		% H	
				Calcd.	Found	Calcd.	Found
3-Ethyl	98.5–99		$C_5H_{10}O$	69.72	70.02	11.70	11.45
3-Butyl	85–85 (85)	1.4180	$C_7H_{14}O$	73.63	72.49[b]	12.36	12.15
3,3-Dimethyl	76–77[a]	1.3907					
3,3-Diethyl	138–140	1.4230	$C_7H_{14}O$	73.63	73.72	12.36	12.46
3-Ethyl-3-isopropyl	155–157	1.4312 (27)	$C_8H_{16}O$	74.94	73.69[b]	12.58	12.59
3,3-Pentamethylene	173 or 69–70 (20)	1.4584 (25)	$C_8H_{14}O$	76.14	75.73	11.18	11.27
3,3-Tetramethylene	149–150	1.4539	$C_7H_{12}O$	74.95	75.27	10.78	10.85
3,3-Dibenzyl	135 (1)	1.5759	$C_{17}H_{18}O$	85.67	86.83	7.61	7.98

[a] S. Searles and M. J. Gortatowski, *J. Am. Chem. Soc.*, **75**, 3030 (1953) reported b.p. 77–79°. [b] Oxetane analyses tend to run low (probably due to the great ease of peroxide formation in air) as observed by G. M. Bennett and W. G. Philip, *J. Chem. Soc.*, 1938 (1928); D. E. Applequist and J. D. Roberts, *J. Am. Chem. Soc.*, **78**, 4012 (1956); S. Searles, K. A. Pollart, and E. F. Lutz, *J. Am. Chem. Soc.*, **79**, 948 (1957).

ture or which have not been prepared by this method previously, are listed in Table IV.

The *3-bromo-1-propanols* were obtained by acetylating the corresponding 1,3-diols and cleaving the latter with hydrogen bromide to 3-bromo-1-propyl acetates, which then were subjected to ethanolysis. The general procedure[21] was as follows: To a refluxing solution of 1 mole of the diol and 200 ml. of glacial acetic acid, previously heated under reflux with 5 ml. of 48% hydrobromic acid for 20 min., a solution of 1.1 moles of dry hydrogen bromide in 400 ml. of acetic acid was added dropwise over a period of 8–10 hr. After refluxing an additional 8–10 hr., the acetic acid was removed by distillation under reduced pressure. To the undistilled residue was added 350 ml. of absolute alcohol and 3 ml. of 48% hydrobromic acid, and the ethyl acetate–ethanol azeotrope was removed by distillation through a fractionating column until the odor of ethyl acetate was no longer apparent in the distillate. More alcohol and hydrobromic acid were added if necessary. The bromopropanol was isolated by vacuum distillation and was purified by repeated fractional distillation. It was usually not possible to get good analyses on these products, due to their tendency to darken and decompose somewhat on standing even a few days. Preparative data is given in Table V. 2,2-Dimethylene-1,3-propanediol gave only tars.

The reaction of the 3-bromo-1-propanols with base was carried out by a standard procedure, illustrated by the following case: To 120 ml. of 15% potassium hydroxide solution in water, heated to 95° by an oil bath and stirred, was added 30 g. of 2,2-diethyl-3-bromo-1-propanol over a period of 1 hr. Distillate was carried off through a condenser into a trap cooled with solid carbon dioxide. With continued stirring, the temperature was maintained at 100° for an additional hour. Water that distilled over was replaced. Most of the products were collected by this time, but to drive over the last, the temperature was finally raised to 150–180°. The two layers of distillate were separated and the organic materials in the water layer salted out with potassium carbonate.

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(21) A modification of the method of M. Beyaert and M. Hansens, *Natuurk. Tidschr.* (*Ghent*), **22**, 249 (1940) for conversion of pentaerythritol to 2,2-bis(bromomethyl)-1,3-propanediol.

The combined organic layers, weighing 12.4 g., were dried over potassium carbonate and distilled to give 7 g. (55%) of 2-ethyl-1-butene, b.p. 65–70°, and 4.5 g. (26%) of 3,3-diethyloxetane, b.p. 135–140°. The identity of the products in each case was established by means of the properties given in Tables VI and VII and their infrared spectra.

The reactions with alcoholic base were carried out at about 20° lower temperature except for the final baking.

No products were isolated from the reaction of base with 2,2-trimethylene-3-bromo-1-propanol.

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Stereochemistry of the Cycloheptane Ring. Synthesis and Deamination of *cis* and *trans*-2-Aminocycloheptanol

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Cis and *trans*-2-aminocycloheptanol have been prepared by the route: cycloheptene oxide → *trans*-2-aminocycloheptanol → *trans*-2-(*p*-nitrobenzoylamino)cycloheptanol → *cis*-2-*p*-nitrophenyl-4,5-cycloheptanoöxazoline → *cis*-2-aminocycloheptanol. Deamination of the *trans* isomer with nitrous acid gives cyclohexylmethanal, whereas the *cis* isomer affords a mixture of cyclohexylmethanal and cycloheptanone. These results are compared with those obtained from *cis*- and *trans*-2-aminocyclohexanol and are interpreted in terms of the rate of reaction versus the rate of conformational change.

Although a great deal of work has been done on the steric relationships of cyclohexane compounds,[1] comparatively little systematic work has been done on the steric effects operative in seven membered ring systems. Several isolated aspects of the stereochemistry of cycloheptanes have been discussed recently, and a few earlier workers attempted a systematic study of the stereochemistry of medium sized rings.

Ayres and Raphael[2] have recently prepared *trans*-cycloheptane 1,2-dicarboxylic acid, and found that this compound readily forms a *trans* fused cyclic anhydride, in contrast to the behavior of *trans*-cyclohexane-1,2-dicarboxylic acid. The ease of formation of a *trans* anhydride may be explained on the basis that the cycloheptane ring is considerably more flexible than that of cyclohexane. The greater flexibility of the seven-membered ring may also be invoked to explain the formation from both *cis* and *trans* cycloheptane-1,2-diol of a cyclic ketal, under the same conditions, and to rationalize the observation that both *cis* and *trans*-1,2-cycloheptanediol increase the conductivity of boric acid solutions, while neither of the cyclohexane-1,2-diols will do so.[3]

We felt that the application to cycloheptane compounds of a reaction, the steric requirements of which are well defined, would shed additional light on the preferred conformation of cycloheptane derivatives. Such a reaction appeared to be the deamination of *cis* and *trans*-2-aminocycloheptanol. The steric requirements of the reaction of amino alcohols with nitrous acid has been studied thoroughly,[4] and the reaction has been applied to, and its steric implications interpreted for *cis* and *trans*-2-aminocyclohexanol.[5]

Trans-2-aminocycloheptanol (I) was prepared by the reaction of aqueous ammonia with cycloheptene oxide.[6] Of the possible synthetic routes available for the preparation of *cis*-2-aminocycloheptanol, that which appeared best was the general method employed for the conversion of *trans*-2-aminocyclohexanol to the *cis*-isomer.[7]

Trans-2-aminocycloheptanol was converted smoothly to *trans*-2-(*p*-nitrobenzoylamino)cycloheptanol (II), by the action of *p*-nitrobenzoyl chloride and aqueous base. Treatment of this amide with thionyl chloride afforded *cis*-2-*p*-nitrophenyl-4,5-cycloheptanoöxazoline (III). Prolonged boiling of (III) with aqueous hydrochloric acid yielded *cis*-2-aminocycloheptanol (IV) which with *p*-nitrobenzoyl chloride and base gave *cis*-2-(*p*-nitrobenzoylamino)cycloheptanol (V).

Trans-2-aminocycloheptanol was deaminated with sodium nitrite in acetic acid to afford as the only isolable product hexahydrobenzaldehyde (VI), identical in all respects to a sample prepared from cyclohexylmagnesium bromide and triethyl orthoformate.[8] The infrared spectrum of the crude de-

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