[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Neighboring Groups in Addition. III. The Tertiary OH and O^- Groups in α,α-Dimethylallyl Alcohol[1]

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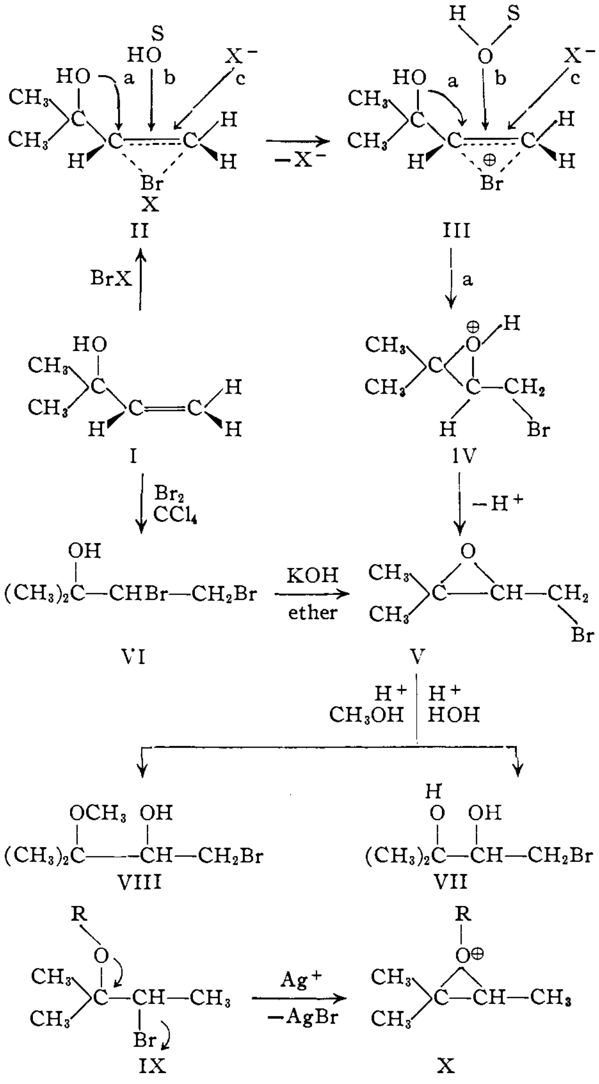
Because of the expected general connection between the incidence of participation of neighboring groups in addition reactions and the magnitude of anchimeric assistance provided by the neighboring group in substitution processes, halogen addition to α,α-dimethylallyl alcohol has been studied. In the case of the tertiary alcohol, in contrast to allyl alcohol, hydroxyl participation begins to play a part, the epoxy-bromide being obtained as one of the products. Under alkaline conditions, conducive to participation of the alkoxide ion group, hypobromite solution, even when free of halide ion, converts the tertiary alcohol essentially completely to epoxy-bromide. The results of a kinetic study of the reaction are consistent with a mechanism involving reaction of the conjugate base of the alcohol with hypobromous acid. The present results and others on participation of functional neighboring groups or carbon substituents in addition reactions are in line with expectations based on driving forces in substitution.

In the previous[2] article it was reported that no participation of the primary hydroxyl group in the process of halogen addition to allyl alcohol was observed under any of the conditions employed. Also, it was pointed out that a general connection can be expected between the incidence of such participation in addition reactions and the magnitude of anchimeric[3] assistance supplied by the neighboring group in substitution processes with similarly constituted structures. On this basis, participation by the tertiary hydroxyl group in the process of bromine addition to α,α-dimethylallyl alcohol I would be more likely than in the case of allyl alcohol, judging by the effect of methyl groups on driving forces due to neighboring group participation.[4] Examples of analogous neighboring group participation in substitution are afforded by the action of silver ion on 2-hydroxy- or 2-methoxy-2-methyl-3-bromobutane[5] (IX, R = H or CH_3), which yields the cyclic oxonium ion X. On the basis of driving forces,[4] participation by O^- in addition reactions should compete with other addition modes even more efficiently than does the OH group. The present article reports an investigation of participation by OH and O^- in the process of bromine addition to α,α-dimethylallyl alcohol I.

Following the previous discussion,[2] OH participation in addition to α,α-dimethylallyl alcohol (I), whether[2] it occurs from intermediate II or the olefin-bromonium ion III, would give rise to the conjugate acid IV of the oxide V. The latter, 1-bromo-2,3-epoxy-3-methylbutane, is a known substance, readily accessible through the addition of bromine in carbon tetrachloride to the tertiary alcohol I and treatment of the dibromide VI with potassium hydroxide. The oxide V is a liquid, but it is opened readily by aqueous acid to the bromo-glycol VII, a crystalline solid, and this reaction was useful for characterizing the oxide V.

For the addition reactions, an attempt was made to avoid the complication introduced by competition of halide ion with solvent or neighboring group in the addition reaction (II or IIIabc), by using N-bromosuccinimide (NBS) as the positive bromine donor or by using bromine with silver oxide to precipitate bromide ion.



The reaction of NBS in methanol with the tertiary alcohol I was relatively slow, but catalysis by acid, sometimes employed in cases of this kind, was avoided in order to preserve any oxide V which might be formed in the reaction. Ap-

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[1] Some of the material of this paper was presented in summary: (a) before the Organic Division of the American Chemical Society at St. Louis, Mo., September, 1948; (b) in Abstracts of Eleventh National Organic Symposium, Madison, Wisconsin, June 21, 1949, p. 65.

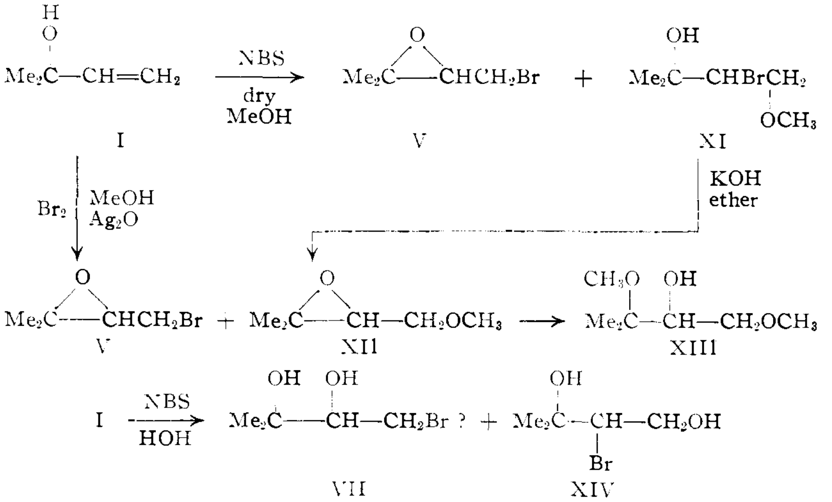
[2] S. Winstein and L. Goodman, THIS JOURNAL, **76**, 4368 (1954).

[3] S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, *ibid.*, **75**, 147 (1953).

[4] S. Winstein and E. Grunwald, *ibid.*, **70**, 828 (1949).

[5] S. Winstein and L. L. Ingraham, *ibid.*, **74**, 1160 (1952).

proximately one-seventh of the reaction did indeed proceed with formation of this oxide V, the predominant product, however, being the product of addition of the elements of methyl hypobromite to the double bond (XI). The distillation fractions consisting mainly of oxide V possessed properties agreeing with those of authentic oxide from dibromide VI, and treatment of these with aqueous acid gave a bromo-glycol, obviously VII. This material behaved as a 1,2-bromohydrin on titration with standard base and as a 1,2-glycol to periodic acid, the equivalent weights being within 1 and 2.5%, respectively, of theoretical; also, no melting point depression was observed on mixing the material with authentic bromo-glycol VII from oxide V which had been prepared from dibromide VI.



The methoxybromo-alcohol XI obtained as the main product of treatment of I with NBS in methanol behaved as a 1,2-bromohydrin to standard base, the equivalent weight being within experimental error of theoretical. The material yielded a 3,5-dinitrobenzoate, but an attempt to prepare a naphthylurethan was unsuccessful. The tertiary alcohol structure XI is assigned to the methoxybromo-alcohol product. The isomer of XI, VIII, 1-bromo-2-hydroxy-3-methoxy-3-methylbutane, which is also a 1,2-bromohydrin, and which could be conceived to arise under the conditions of the addition reaction, through opening of oxide V by methanol, was prepared for contrast. This isomer VIII, prepared by acid-catalyzed opening of oxide V in methanol, titrated as a 1,2-bromohydrin to standard base, yielded a 3,5-dinitrobenzoate different from the one from XI, and it did yield a naphthylurethan.

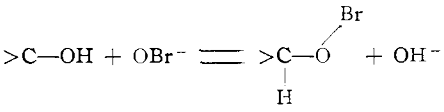
When α,α-dimethylallyl alcohol I was treated in methanol with bromine and silver oxide, the product contained two oxides, the bromo-oxide V and the methoxy-oxide XII. These were substantially separated by distillation. Then the bromo-oxide V was characterized by the acid-catalyzed hydration to the bromo-glycol VII. The methoxy-oxide XII resembled oxide prepared by treatment of the methoxybromohydrin XI with potassium hydroxide. Further, both samples of XII, the one from XI and the one from the addition reaction, gave, on acid-catalyzed opening with methanol, samples of dimethoxy-alcohol XIII which agreed in properties and yielded identical 3,5-dinitrobenzoates.

A control experiment indicated that bromo-oxide V is not converted easily to methoxy-oxide XII by silver oxide in methanol under the conditions of the addition reaction and, therefore, the probable route for formation of XII is by dehydrohalogenation by silver oxide of the initially formed methoxybromo-alcohol XI, which can be isolated as the main product in the absence of silver oxide.

Treatment of α,α-dimethylallyl alcohol I with NBS in water gave, as the main product, a new bromo-glycol XIV, a crystalline solid, but different from VII, the mixture of XIV and VII being liquids. Crystalline XIV titrated as a 1,2-bromohydrin to standard base and failed to react appreciably with periodic acid. When this material was used to seed the main fractions of the crude reaction product from alcohol I and NBS in water, they all crystallized, the predominance of bromo-glycol XIV in the crude product being quite high. However, the crude reaction product probably contained some bromo-glycol VII, since fractions which displayed quite good equivalent weights in base titration gave indications of 4–16% vicinal glycol in periodic acid titration.

Although bromo-oxide V was not detected in the product of treatment of I with NBS in water, it seems likely that some was formed, just as in methanol, but that it was opened to bromo-glycol VII under the reaction conditions since the pH of the NBS suspension in water was found to be 4.2.

The finding that the hydroxyl group in α,α-dimethylallyl alcohol I competes to some extent with solvent in the process of halogen addition suggests that under alkaline conditions, where the hydroxyl group is partially converted to the O^- group, such participation should become very predominant. This type of participation may indeed explain the observations of Strauss and Kühnel[6] who obtained a 60% yield of bromo-oxide V from treatment of α,α-dimethylallyl alcohol I with sodium hypobromite solution. This report we have been able to confirm. Although Strauss and Kühnel obtained bromo-oxide from two other unsaturated tertiary alcohols this method is rather limited in scope. With alcohols with α-hydrogen atoms, oxidation is the dominant reaction, probably involving the steps



$$>\underset{\mathrm{H}}{\mathrm{C}}\text{—OH} + \mathrm{OBr}^- \rightleftharpoons >\underset{\mathrm{H}}{\mathrm{C}}\text{—}\overset{\mathrm{Br}}{\mathrm{O}} + \mathrm{OH}^-$$

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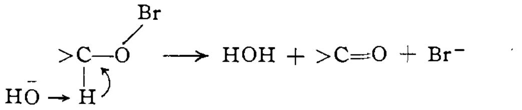
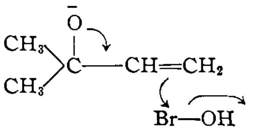
[6] F. Strauss and R. Kühnel, *Ber.*, **66B**, 1834 (1933).



Thus with allyl alcohol, no epibromohydrin was obtained.

As regards the mechanism of the formation of bromo-oxide V from the tertiary alcohol I, Strauss visualized some rearrangement of the hypobromite ester of the alcohol I. Our present-day approach makes it seem more likely to us that bromo-oxide is produced by ring closure involving the O⁻ group at some stage. The first thing to be ruled out is that the oxide is produced by ordinary dehydrohalogenation of the dibromohydrin VI. The latter conceivably could be produced as an intermediate since the hypobromite solutions employed by Strauss and Kühnel contained bromide ion at high concentrations. However, we found bromo-oxide is produced just as well by the action of bromide-free hypobromite on the tertiary alcohol I, eliminating dibromide VI as the precursor.

The most likely course for the formation of bromo-oxide V under these conditions involves the conjugate base of the alcohol I and hypobromous acid as is briefly symbolized in XV.



XV

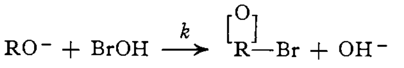
This has the organic substrate reacting in the more highly nucleophilic form represented by the conjugate base, with the O⁻ group now competing very favorably with solvent or halide ion. Also, this representation makes use, not of OBr⁻, as the positive bromine donor, but of the much more electrophilic species, HOBr. Some support for the interpretation involving the conjugate base of alcohol I is derived from the inertness of the methyl ether of I toward sodium hypobromite solutions.

The equilibria governing the concentrations of the alcoholate ion, RO⁻, and the HOBr are shown in equations 1 and 2, the concentration of RO⁻ being proportional to, and the concentration of HOBr being inversely proportional to [OH⁻].

$$\mathrm{ROH + OH^- \overset{K_1}{\rightleftharpoons} RO^- + HOH} \qquad (1)$$

$$\mathrm{OBr^- + HOH \overset{K_2}{\rightleftharpoons} HOBr + OH^-} \qquad (2)$$

On this basis, the rate of a reaction symbolized by XV and expressed in equation 3, should be given by equation 4.



$$\mathrm{RO^- + BrOH \xrightarrow{k} \overset{[O]}{R}{-}Br + OH^-} \qquad (3)$$

$$\begin{aligned} -d(\mathrm{OBr^-})/dt &= k(\mathrm{RO^-})(\mathrm{BrOH}) \\ &= kK_1(\mathrm{ROH})(\mathrm{OH^-})K_2(\mathrm{OBr^-})/(\mathrm{OH^-}) \\ &= k'(\mathrm{ROH})(\mathrm{OBr^-}) \end{aligned} \qquad (4)$$

Thus the reaction should be first order in alcohol I, first order in hypobromite and insensitive to the concentration of alkali. Strauss[6] had commented that the speed of reaction appeared independent of the concentration of alkali provided sufficient alkali was present to prevent decomposition of hypobromite to bromate and bromide. We carried out a brief survey of the kinetics of the reaction, in aqueous solution at 24.90°, which established this point more definitely and also some of the other features of equation 4.

The reaction between alcohol I and hypobromite was followed by titration of the latter with standard arsenite solution. The low solubility of the bromo-oxide V in water necessitated working at low concentrations of this material. The ionic strength was maintained at *ca.* 2.00 *M* with potassium nitrate in all but one run. To minimize the further oxidation of the bromo-oxide V by hypobromite solution, the alcohol I was maintained in ten-to fifteen-fold excess. This effectively maintained the concentration of alcohol, [ROH], constant in any run, so that the integrated form of equation 4 is given by equation 5. Thus a plot of log [OBr⁻] *vs.* time, *t*, should give a straight line; this was found to be the case, a sample plot being shown in Fig. 1. The slopes of the least-squares lines from a number of runs gave values of $k'[\mathrm{ROH}]_{\mathrm{av.}}/2.303$, the corresponding values of k' being given in Table I.

$$\log\,[\mathrm{OBr^-}] = -\frac{k'[\mathrm{ROH}]}{2.303}\,t + C \qquad (5)$$

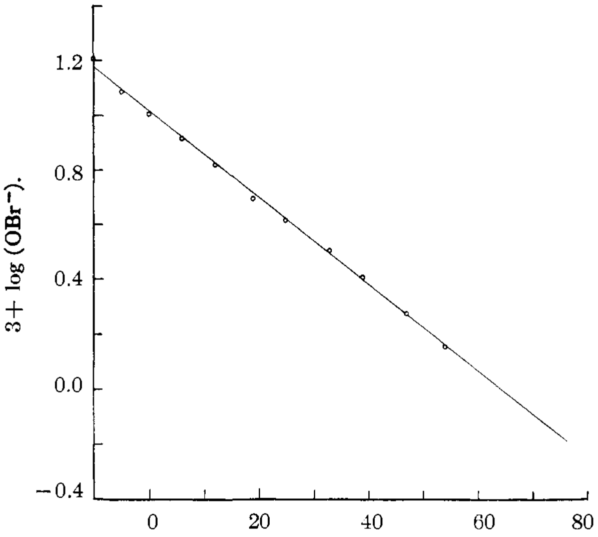


Fig. 1.—Plot of log (OBr⁻) *vs.* time for reaction of α,α-dimethylallyl alcohol with hypobromite solution at 24.90°: (ROH) 0.1151 *M*; (KNO₃) = (OH⁻) 0.99 *M*; (OBr⁻) 0.0162 *N*.

From the data in Table I, it may be seen that the rate constant k' was unaffected by change in the concentration of alcohol I by a factor of *ca.* 2.5. Also, k' was relatively insensitive to the value of the base concentration. The rate constant decreased by 14% when [OH⁻] was increased from 1 to 2 *M*, but this is not a serious deviation. Kinetic measurements in solutions less than 0.75 *M* in hydroxide ion showed deviations from linearity at the beginning of each run, but this effect was not studied further. Possibly it was due to such

TABLE I

RATE CONSTANTS FOR REACTION BETWEEN α,α-DIMETHYLALLYL ALCOHOL WITH HYPOBROMITE AT 24.90°

$[OH^-]$, M	$[KNO_3]$, M	μ	$[OBr^-]$, N	[ROH] (average during run), M	$k'[ROH]_{av.}/2.303$	k', l./(mole, min.)
2.01	0.0	2.01	0.0181	0.1147	0.0136	0.273
2.01	.0	2.01	.0174	.1148	.0137	.275
1.76	.25	2.01	.0161	.1152	.0142	.284
1.76	.25	2.01	.0196	.1143	.0142	.286
1.74	.25	1.99	.0173	.1149	.0140	.281
1.74	.24	1.98	.0179	.1928	.0230	.275
1.74	.25	1.99	.0160	.1933	.0239	.285
1.76	.25	2.01	.0163	.0756	.00983	.299
1.76	.25	2.01	.0139	.0762	.00982	.297
1.50	.50	2.00	.0150	.1154	.0149	.297
1.26	.74	2.00	.0160	.1152	.0149	.298
1.26	.74	2.00	.0170	.1149	.0148	.297
1.25	.74	1.99	.0149	.1155	.0155	.309
0.99	.99	1.98	.0179	.1147	.0159	.319
.99	.99	1.98	.0162	.1151	.0159	.318
.99	.0	0.99	.0217	.1138	.0152	.308
.75	1.24	1.99	.0173	.1149	.0175	.351

factors as decomposition of the hypobromite or formation of appreciable concentrations of hypobromite ester of I at the lower base concentrations.

The participation by the tertiary hydroxyl group of α,α-dimethylallyl alcohol I helps to orient us on the scope of such participation by neighboring groups in addition processes. One can anticipate that the alkoxyl group would similarly participate, giving rise to migrations of alkoxyl akin to such migrations[5] in substitution (by way of intermediates such as X). The observed participation of hydroxyl and the anticipated participation of alkoxyl could probably be made much more predominant by use of a less nucleophilic solvent such as acetic acid which we have used to advantage in connection with participation of the benzamido group.[7]

The superiority of tertiary over primary OH is in line with expectations based on driving forces[4] due to participation in substitution. So is the very complete control of the addition process by participation of the neighboring O^- group in the conjugate base of α,α-dimethylallyl alcohol. Similarly, the effective participation of the benzamido and similar groups is understandable. Relative driving forces in substitution or rearrangement[8,9] help also to correlate cases of participation by neighboring carbon in addition reactions. Thus, for example, such participation does not occur in halogen addition to *t*-butylethylene,[10] but it does occur with bicycloheptene[11] and probably also with 3-phenyl-3-methyl-1-butene.[12]

It is striking how nearly completely non-Markownikow is the direction of addition to α,α-dimethylallyl alcohol except for the part of the reaction involving neighboring hydroxyl participation. This tendency for non-Markownikow addition is much more pronounced than in the case of allyl alcohol.[2] It seems likely that the geometry of the transition state for the reaction involving attack of solvent on carbon (see II and III) is such that repulsion between non-bonded atoms is much smaller for the non-Markownikow than for the Markownikow addition. This situation is similar to that prevailing for addition to Δ^5-cholestene,[13] where the electrophilic reagent appears to approach from the α-side, away from the 10-methyl group, while the nucleophilic reagent completes the predominantly non-Markownikow addition from the β-side, attacking mainly the carbon atom most remote from the 10-methyl group.

Experimental[14]

α,α-Dimethylallyl Alcohol (I).—This alcohol was prepared essentially as described by Webb.[15] Isoprene, 1500 ml. (15 mole), was mixed with 1500 ml. of glacial acetic acid and the solution was cooled in an ice–salt-bath. Gaseous hydrogen chloride, 530 g. (15 mole), was added to the stirred solution and the resulting solution was divided into two parts, each of which was washed with four 400-ml. portions of water. Each washed portion was added to a stirred suspension of 3 l. of water and 400 g. (4 mole) of calcium carbonate and the mixture was stirred at room temperature until the upper layer gave only a faint chloride test with alcoholic silver nitrate solution (*ca.* 14 hours required). The mixture was steam distilled until a clear distillate was obtained. The organic layer was separated from the steam distillate and the aqueous layer was saturated with salt and extracted with three 200-ml. portions of ether, the ether being combined with the organic layer. After drying over potassium carbonate, the ether was distilled using column A and the residue was fractionated using the same column. The fraction boiling at 60–63° (180 mm.), 600 g. (46%), was retained. Before use the product was redistilled and the portion, b.p. 95.4–96.1° (752 mm.), n^{25}_{D} 1.4143 (reported[15] n^{25}_{D} 1.4145), was employed.

Methyl Ether of α,α-Dimethylallyl Alcohol.—The hydrogen chloride–isoprene addition product was solvolyzed by stirring with a suspension of calcium carbonate in dry methanol. After filtration and dilution with water, the product was isolated by petroleum ether (b.p. 35–50°) extraction. Removal of the solvent through column A and fractionation of the residue from column B gave a 67.3% combined yield of tertiary ether (66.7%) and primary ether (33.3%). A previous preparation yielded 73% of product which was 65% tertiary ether. The tertiary ether had b.p. 79.8–80.2° (749 mm.), $n^{24.5}_{D}$ 1.3957 (reported[16] b.p. 80–83°, n^{20}_{D} 1.3980); the primary ether (2-methyl-4-methoxy-butene-2) had b.p. 104.6–105.2° (749 mm.), $n^{24.5}_{D}$ 1.4138 (reported[16] b.p. 102–105°, n^{20}_{D} 1.4130).

1,2-Dibromo-3-hydroxy-3-methylbutane (VI).—An equimolar quantity of bromine was added to a cold (0°) solution of I in dry carbon tetrachloride. After the customary washing, drying, and distillation of the solvent, an 85% yield of product was collected at 79–84° (3.0–3.8 mm.), $n^{24.5}_{D}$ 1.5264–1.5267 (reported[17] b.p. 94.5° (10 mm.), n^{20}_{D} 1.5290).

1-Bromo-2,3-epoxy-3-methylbutane (V). (a) By Dehydrohalogenation.—An ethereal solution of VI was added to

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(7) S. Winstein, L. Goodman and R. Boschan, THIS JOURNAL, **72**, 2311 (1950).

(8) S. Winstein, *et al.*, *ibid.*, **74**, 1127 (1952).

(9) S. Winstein, *et al.*, *ibid.*, **74**, 1113 (1952).

(10) (a) G. G. Ecke, N. C. Cook and F. C. Whitmore, *ibid.*, **72**, 1511 (1950); (b) H. Marshall, unpublished work.

(11) (a) J. D. Roberts, E. R. Trumbull, Jr., W. Bennett and R. Armstrong, *ibid.*, **72**, 3116 (1950); (b) H. Kwart and L. A. Kaplan, Abstracts of 124th Meeting of the American Chemical Society, Chicago, Ill., Sept. 6–11, 1953, pages 88–90.

(12) R. Korupp, unpublished work.

(13) (a) L. Fieser, *Experientia*, **6**, 312 (1950); (b) D. H. Barton, E. Miller and H. T. Young, *J. Chem. Soc.*, 2598 (1951).

(14) All melting and boiling points are uncorrected. Columns A and B were 12-inch glass center-rod columns rated at 15 and 65 plates, respectively. No ring correction has been included in the calculated molar refractions for epoxy compounds.

(15) I. Webb, Dissertation, U.C.L.A., 1944.

(16) I. N. Nazarov, I. N. Azerbaen and V. N. Rakcheeva, *J. Gen. Chem.* (*U.S.S.R*), **18**, 407 (1948); *C. A.*, **43**, 1136 (1949).

(17) A. A. Petrov, *J. Gen. Chem.* (*U.S.S.R.*), **13**, 741 (1943); *C. A.*, **39**, 695 (1945).

a well-stirred suspension of finely powdered potassium hydroxide (30% excess) in ether. After being refluxed for 4 hours, the mixture was filtered and the residual salts were dissolved in water. The aqueous solution was ether extracted and the extracts added to the original filtrate, the whole of which was dried over potassium carbonate. Distillation through column A gave, after removal of the ether, 83,4% of product, b.p. 71.5–72.0° (50 mm.), $n^{24.5}_{\mathrm{D}}$ 1.4608–1,4610, $d^{24.4}_{4}$ 1.3749, MR_{D} 32.94 (calculated 32.50). A previous preparation gave a 92% yield of product, b.p. 71.8–72,2° (50 mm,), n^{25}_{D} 1,4603 (reported[18] b.p. 48.25° (15 mm.), n^{20}_{D} 1.4642, d^{20} 1.3832 (these latter two figures give MR_{D} 32.94)),

(b) **From the Strauss[6] Reaction.**—The hypobromite solution was prepared by adding 19 ml. (0.37 mole) of bromine slowly, with stirring, to a solution of 135 g. (2.0 moles) of 85% potassium hydroxide in 600 ml. of water maintained at 0°. This solution was allowed to warm to 10° and 28 g. (0,32 mole) of I was rapidly added to the stirred solution. There was no noticeable heat effect. After stirring for an hour the layers were separated and the upper layer was extracted with ether. The extract was combined with the lower layer and the solution was dried over potassium carbonate. Distillation through column A gave, after removal of the ether and a considerable forerun, 3.2 g., b.p. 60–61.5° (30 mm.), n^{25}_{D} 1.4609, and 27.6 g., b.p. 62–62.2° (30 mm.), n^{25}_{D} 1,4633, n^{20}_{D} 1.4656, d^{25} 1.4074, MR_{D} 32.32, the two fractions representing a 58,3% yield. Strauss[6] reported a 60% yield of material, b.p. 50.5–51.5° (15 mm.), $n^{20.1}_{\mathrm{D}}$ 1.4652, d^{20}_{4} 1.3907, MR_{D} 32.81. These constants are noticeably different than for the oxide prepared in (a) and probably indicate contamination by carbon tetrabromide, a substance isolated by Strauss when large excesses of hypobromite were used.

The hypobromite solution was prepared as before and a solution of 62.9 g. (0.37 mole) of silver nitrate in 100 ml. of water was slowly added to the cold solution, The solution was rapidly filtered, the filtrate allowed to warm to 10°, and 27 g. (0.31 mole) of I was added rapidly; the experiment was completed as described above. The yield of product, b.p. 61–62.5° (30 mm.), n^{25}_{D} 1.4620–1.4626, was 59.5%.

When 32 g. (0.32 mole) of the methyl ether of I was added to the hypobromite solution, there was no apparent reaction, After three hours of stirring at room temperature, the layers were separated and the lower layer extracted with ether, the extract being combined with the upper layer. After drying of the solution and removal of the ether, a 71% recovery of the starting material, b.p. 77–78.7°, $n^{24.5}_{\mathrm{D}}$ 1.3950–1.3955, was realized.

1-Bromo-2,3-dihydroxy-3-methylbutane (VII).—One liter of a 1% sulfuric acid solution, warmed to 55°, was added, with stirring, to 238 g. (1.44 moles) of V (n^{25}_{D} 1.4600–1.4603). The oxide rapidly dissolved when the solution was maintained at 55–60° and after 10 minutes, the solution was neutralized with 8.4 g. of sodium bicarbonate and continuously extracted for 15 hours with chloroform. The chloroform was evaporated in vacuum and the resulting oil was seeded with previously prepared glycol, whereupon it crystallized. The yield of crude product, m.p. 42–45°, was 240 g. (91%). Recrystallized once from a Skellysolve B–benzene mixture, it melted 44–46° (reported[6] 48–49°) and gave an equivalent weight to standard base of 184.8 (theory 183.1). When the oxide from the Strauss reaction was treated similarly a small amount of material failed to dissolve in the acid solution. This was removed and the solution was continuously extracted with ether to give an oil which distilled at 69–70° (1 mm.) and slowly crystallized on standing. The yield was 31%. After two crystallizations from Skellysolve B–benzene it had m.p. 43.5–45°; equivalent weight to standard base, 185.5; molecular weight to periodic acid, 185.5.

Anal. Calcd. for $C_5H_{11}O_2Br$: C, 32.80; H, 6.06. Found: C, 32.84; H, 6.27.

1-Bromo-2-hydroxy-3-methoxy-3-methylbutane (VIII).—A mixture of 31 g. (0.2 mole) of V and 125 ml. of dry methanol was refluxed 2 hours. The methanol was slowly distilled from column A and the residue was fractionated from the same column to give a 91% yield of a product collected in several fractions, b.p. 67–74° (3 mm.), $n^{24.5}_{\mathrm{D}}$ 1.4778–1.4792. A major fraction boiled constantly at 73.0° (3 mm.) and had $n^{24.5}_{\mathrm{D}}$ 1.4778, $d^{24.4}_{4}$ 1.3788, MR_{D} 40.44 (calculated 40.84). The equivalent weight to standard base was 196.2 (theory 197.1). Derivatives were prepared from this fraction, as follows;

The α-naphthylurethan was crystallized several times from Skellysolve F–chloroform and melted at 98–99°. *Anal.* Calcd. for $C_{17}H_{20}O_3NBr$: C, 55.74; H, 5.50. Found: C, 56.67; H, 5.64.

The 3,5-dinitrobenzoate was crystallized several times from Skellysolve F–benzene and melted at 93°. *Anal.* Calcd. for $C_{13}H_{15}O_7N_2Br$: C, 39.91; H, 3.87. Found: C, 40.39; H, 4.00.

The *p*-phenylazobenzoate was prepared and was purified by adsorption on activated alumina and elution with Skellysolve B, The eluate, crystallized from Skellysolve B, melted at 65–66°, *Anal.* Calcd. for $C_{19}H_{21}O_3N_2Br$: C, 56.30; H, 5.22. Found: C, 56.53; H, 5.43.

When V was opened with dry methanol containing a catalytic quantity of benzenesulfonic acid, the reaction mixture being maintained at room temperature and the excess methanol being removed at 160 mm., an 84.6% yield of product, b.p. 71.5–73.4° (5 mm.), $n^{24.5}_{\mathrm{D}}$ 1.4770–1.4776 was obtained. The α-naphthylurethan prepared from the major fraction had m.p. 97.6–99° after four crystallizations. *Anal.* Found: C, 57.23; H, 5.74.

The constant-boiling fractions from the uncatalyzed opening of V were carefully redistilled through column B and a major fraction, b.p. 92.0° (14 mm.), $n^{24.8}_{\mathrm{D}}$ 1.4765, was analyzed.

Anal. Calcd. for $C_6H_{13}O_2Br$: C, 36.56; H, 6.65. Found: C, 36.55; H, 6.77.

The α-napthylurethan prepared from this fraction had m.p. 98–99° and the 3,5-dinitrobenzoate had m.p. 92–92.8° but both derivatives gave high carbon values on analysis. It seems possible that the difficulty of obtaining analytically pure derivatives of VIII is due to displacement of bromine by the neighboring acyl group during preparation and/or purification of the derivative.

Addition of N-Bromosuccinimide (NBS) to I in Dry Methanol.—To a stirred suspension of 89 g. (0.5 mole) of NBS in 350 ml. of dry methanol was added 43.3 g. (0.5 mole) of I. The solution was slowly warmed to 54° from room temperature over a 2-hour period. It was held at 52–54° for 45 minutes, a clear solution resulting. About 220 ml. of methanol was distilled at 150 mm. The residue was filtered from some succinimide and the filtrate was continuously extracted with Skellysolve F (b.p. 35–37°) for 4 hours. After addition of about 80 ml. of methanol, the solution was extracted with fresh Skellysolve F for a further 5 hours. The two extracts were combined, the solvent distilled and the residue distilled from a Claisen flask to give the following fractions: (1) 2.51 g., b.p. 28–45° (50 mm.), $n^{24.5}_{\mathrm{D}}$ 1.4166; (2) 2.79 g., $n^{24.5}_{\mathrm{D}}$ 1.4472; (3) 4.02 g., b.p. 56–63° (8.2 mm.), $n^{24.5}_{\mathrm{D}}$ 1.4582; (4)–(6) 41.35 g., b.p. 62–65° (3.2 mm.), $n^{24.5}_{\mathrm{D}}$ 1.4700–1.4730.

Fraction 1 was quite pure I. Approximately 2 g. more of I was found in the cold trap. Fraction 2, on treatment with 1% sulfuric acid, gave 2.1 g. of an oil which crystallized on seeding with VII. Crystallization from Skellysolve F–benzene gave a product, m.p. 46–48°, which did not depress the melting point of authentic VII. It gave an equivalent weight to standard base of 181.9 and a molecular weight to periodic acid of 179.3 (calculated 183.1). Fraction 3, similarly treated, gave 3.25 g. of an oil which solidified on being seeded with VII and melted at 43–46° after crystallization from Skellysolve F–benzene.

Redistillation of fractions 4–6 through column A showed that essentially all the material boiled within 1° at 5 mm. A major fraction had b.p. 68.1° (5 mm.), $n^{24.5}_{\mathrm{D}}$ 1.4715, $d^{24.4}_{4}$ 1.3562, MR_{D} 40.64 (calculated for XI, 40.84). The equivalent weight to base was 196.1 (calculated for XI, 197.1). The 3,5-dinitrobenzoate melted at 47–50° after several crystallizations from Skellysolve F–benzene.

Anal. Calcd. for $C_{13}H_{15}O_7N_2Br$: C, 39.91; H, 3.87. Found: C, 39.64; H, 4.01.

Attempted preparation of the α-napthylurethan gave a solid which failed to melt below 245° and was presumed to be di-α-napthylurea.

In summary, the yield of XI was about 46% and that of V about 8%, based on unrecovered I.

Reaction of Bromine and I in Methanol Containing Silver Oxide.—Silver oxide (0,5 mole), freshly precipitated and

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[18] A. A. Petrov, *J. Gen. Chem. (U.S.S.R.)*, **15**, 931 (1945): *C. A.*, **40**, 6415 (1946),

thoroughly washed with dry methanol, was added to a solution of 43 g. (0.5 mole) of I in 350 ml. of dry methanol. The well-stirred suspension was cooled to 0° and 80 g. (0.5 mole) of bromine was added during 1.75 hours. The solution was filtered and the precipitate was washed with dry methanol. Distillation at 140 mm. through column A removed most of the methanol. The residue was taken up in ether, a small aqueous layer separated, and the ether was dried. Distillation from a Claisen flask gave, after removal of the ether, the fractions: (1) b.p. 27–50° (25 mm.), lost by accident; (2) 12.60 g., b.p. 50–60° (25 mm.), $n^{24.5}{}_\mathrm{D}$ 1.4208; (3) 4.90 g., b.p. 60–63° (25 mm.), $n^{24.5}{}_\mathrm{D}$ 1.4303; (4) 4.44 g., $n^{24.5}{}_\mathrm{D}$ 1.4534; (5)–(7) 12.74 g., b.p. 61–93° (5 mm.), $n^{24.5}{}_\mathrm{D}$ 1.4590–1.5095. Fractions 5–7 were carefully redistilled but no constant-boiling material could be isolated although the presence of XI was strongly indicated.

Fractions 2–4 were combined and distilled through column A at 30 mm. to give: (1a) 0.80 g., b.p. 47–49.5°, $n^{24.5}{}_\mathrm{D}$ 1.4068; (2a) 5.54 g., b.p. 48.6–49°, $n^{24.5}{}_\mathrm{D}$ 1.4068, $d^{24.4}{}_4$ 0.9172, MR_D 31.16; (3a) 1.37 g., b.p. 49–50°, $n^{24.5}{}_\mathrm{D}$ 1.4090; (4a) 2.40 g., b.p. 50.2–60°, $n^{24.5}{}_\mathrm{D}$ 1.4300; (5a) 4.19 g., b.p. 60–60.8°, $n^{24.5}{}_\mathrm{D}$ 1.4578; (6a) 1.40 g., b.p. 60–94.5°, $n^{24.5}{}_\mathrm{D}$ 1.4565. Fraction 5a, on treatment with 1% sulfuric acid solution, gave 3.2 g. of an oil, of which 2.1 g. solidified. The solid, crystallized from Skellysolve F–benzene, melted at 45–47.5° and did not depress the melting point of authentic VII. Fractions 1a–3a were substantially 1-methoxy-2,3-epoxy-3-methylbutane (XII) (calculated MR_D 30.99), as is demonstrated below.

A sample of XII was prepared by the potassium hydroxide dehydrohalogenation of XI (recovered from the reaction of I and NBS in methanol) dissolved in ether. A 45% yield of product, b.p. 132–133°, $n^{24.5}{}_\mathrm{D}$ 1.4042, $d^{24.4}{}_4$ 0.9088, MR_D 31.29, was collected. These constants should be compared with those of fractions 1a–3a in the preceding paragraph.

When XII, prepared by dehydrohalogenation, was refluxed with dry methanol containing a catalytic quantity of benzenesulfonic acid, there was isolated an 81% yield of a product, b.p. 76–83° (20 mm.), $n^{24.5}{}_\mathrm{D}$ 1.4283–1.4288. A central fraction had $d^{24.4}{}_4$ 0.9764 and MR_D 39.11. A 3,5-dinitrobenzoate, prepared from this fraction in essentially quantitative yield, had m.p. 91.5–92.8° after several crystallizations from Skellysolve F–benzene. When fractions 1a and 2a from the addition reaction were similarly refluxed with dry methanol, a 75% yield of product, b.p. 76–83.2° (20 mm.), $n^{24.5}{}_\mathrm{D}$ 1.4286–1.4295, was isolated. A central fraction had $d^{24.4}{}_4$ 0.9792 and MR_D 39.01 (calculated MR_D for XIII, 39.34). A 3,5-dinitrobenzoate, prepared in excellent yield and crystallized as above, melted at 91.8–93° and did not depress the melting point of the above-described derivative.

Anal. Calcd. for $C_{14}H_{18}O_8N_2$: C, 49.12; H, 5.30. Found: C, 49.13; H, 5.58.

To test the stability of V to the conditions of the experiment, 16.4 g. (0.1 mole) of V ($n^{24.5}{}_\mathrm{D}$ 1.4608–1.4610) was added to a suspension of 23.2 g. (0.1 mole) of dry silver oxide in 80 ml. of dry methanol. The mixture was stirred for 2 hours at 0° and then filtered. The methanol was largely removed by distillation at 170 mm. and the residue was distilled through column A to give a 71% recovery of V, b.p. 64–66.9° (40 mm.), $n^{24.5}{}_\mathrm{D}$ 1.4585–1.4599. On the basis of refractive index less than 5% of the distillate could be XII.

Addition of N-Bromosuccinimide to I in Water.—To a stirred suspension of 89 g. (0.5 mole) of NBS in 300 ml. of water (*p*H 4.2) was slowly added 43 g. (0.5 mole) of I, the temperature being maintained below 30°. The solid dissolved after about 40 minutes of stirring and the solution was continuously extracted for 12 hours with ether. A further 18-hour ether extraction gave additional product. The first extract was dried over potassium carbonate and the ether was distilled from column A. The residue was distilled from a Claisen flask at 0.3 mm. to give the following fractions: (1)–(2) 3.69 g., b.p. 37.5–74°, $n^{24.5}{}_\mathrm{D}$ 1.4750–1.5029; (3) 11.80 g., b.p. 74–76°, $n^{24.5}{}_\mathrm{D}$ 1.5009; (4) 27.25 g., b.p. 76–78°, $n^{24.5}{}_\mathrm{D}$ 1.4981; (5) 7.00 g., b.p. 78–80°, $n^{24.5}{}_\mathrm{D}$ 1.5004; (6)–(7) 7.23 g., b.p. 80–100°, $n^{24.5}{}_\mathrm{D}$ 1.5003–1.4950. Including the material from the second extraction and, on the basis of the equivalent weights of the fractions to base, the yield of mixed glycols was estimated to be 74%. Fractions 3, 4 and 5 gave equivalent weights to base of 184.6, 182.8 and 182.9, respectively (calculated for VII or XIV, 183.1). Fractions 3, 4 and 5 were shown to contain 16.2, 5.4 and 5.9% of a 1,2-glycol, presumably VII, by periodic acid titration. All the fractions, except 1 and 2, partially crystallized when seeded with previously prepared XIV. Crystallization of the solid material of fraction 4 from Skellysolve B–benzene gave a hygroscopic white solid, m.p. 34–36°, which had an equivalent weight to base of 182 and appeared to contain about 4% of VII in the periodic acid determination.

A previous reaction of NBS and I in water had given two high-boiling, viscous liquid fractions which partially crystallized after standing in the refrigerator for several months. The isolated solid, crystallized several times from Skellysolve B–benzene, melted at 35.5–37.5°. When mixed with an equal weight of VII a liquid resulted at room temperature. The solid had an equivalent weight of 181.7 to standard base and consumed no periodic acid within the accuracy of that determination.

Anal. Calcd. for $C_5H_{11}O_2Br$: C, 32.80; H, 6.06. Found: C, 32.84; H, 6.25.

All these results are in agreement with the structure XIV. This material is very hygroscopic and discolors and partially liquefies even when kept in a sealed container in a desiccator.

Procedure for the Kinetic Runs.—The proper weights of potassium hydroxide and potassium nitrate (when necessary) were dissolved in water and the solution was diluted to 250 ml. After titrating an aliquot with standard acid, the solution was transferred to a reaction vessel equipped with a stirrer, maintained in the thermostat at 24.90 ± 0.05°. The proper quantity (*ca.* 12 drops) of purified bromine was added to the stirred solution and, after 0.5 hour, an aliquot of this hypobromite solution was pipetted into an excess of standard sodium arsenite solution containing an excess of sodium bicarbonate. After standing for 5 minutes the solution was acidified to the point of carbon dioxide ebullition with 2 *N* acetic acid and the excess arsenite was titrated with standard iodine solution using starch indicator.[19,20] At a given time, a known volume of I was added to the stirred hypobromite solution, and thereafter aliquots were withdrawn, pipetted into excess arsenite solution, and titrated as above. It was determined that the hypobromite solution did not change in titer more than 0.2% during the time required for a run and that the presence of I in the solutions had no effect on the titrations with the iodine solution.

LOS ANGELES, CALIFORNIA

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[20] R. M. Chapin, THIS JOURNAL, **56**, 2211 (1934).