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The Mechanism of Halide Reductions with Lithium Aluminum Hydride. IV. Tracer Studies in the Reduction of Halohydrins[1]

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2-Bromo-1-butanol, 2-chloro-2-methylpropanol and 2-chloro-2-phenylethanol have been reduced to the corresponding alcohols 1-butanol, 2-methyl-1-propanol and 2-phenylethanol with lithium aluminum hydride in ether solution. This strengthens the assumption made in previous papers in this series that the halohydrins are intermediates in the reduction of the corresponding α-haloacids to alcohols. Reduction of the halohydrins is facilitated by the addition of hydroxyl compounds, such as water and alcohols, to the reaction mixture. The reduction products of the above halohydrins with lithium aluminum deuteride have been investigated by mass spectrometry and infrared analysis. 2-Bromo-1-butanol is reduced normally to 1-butanol-2-*d*. 2-Chloro-2-methylpropanol, however, gives 85% 2-methyl-1-propanol-1-*d*, the product of a hydride shift, and only 15% of 2-methyl-1-propanol-2-*d*. With 2-chloro-2-phenylethanol the product is largely (*ca.* 95%) 2-phenylethanol-2-*d* with a small amount of 2-phenylethanol-1-*d*. The results with the aliphatic products have been confirmed by oxidative degradation.

In previous papers in this series[3,4] the reduction of α-chloroacids RR'CClCOOH and their esters with lithium aluminum hydride has been described. Evidence was adduced that the primary reduction product is largely the chlorohydrin RR'CClCH$_2$OH, that further reduction of the chlorohydrin intermediate to the alcohol RR'CHCH$_2$OH takes place considerably more readily than the reduction of simple alkyl chlorides and that the ease of reduction is primary chlorine > secondary chlorine < tertiary chlorine. From this it was concluded that at least two mechanisms are involved in the reduction of chlorohydrins to alcohols, one applying to primary chlorides and the other to tertiary chlorides, and that both of these mechanisms are different from the simple nucleophilic displacement mechanism which accounts for the less ready reduction of alkyl halides to alkanes by means of lithium aluminum hydride.[5] A hydride shift mechanism has been suggested[3,6] to account for the ready reducibility of RR'CClCH$_2$OH presumably *via* RR'CHCHO.

Four objectives of the present work were (1) to confirm the reality of the halohydrin intermediates by reducing them further to alcohols, (2) to prove or disprove the reality of the hydride shift, (3) to propose a comprehensive mechanism for the reduction of the hydroxy-substituted primary alkyl chlorides and (4) to do likewise for the tertiary chlorides. Points 1 and 2 are dealt with below and point 3 in the accompanying paper,[7] while point 4 will be reported on later.[8]

Results

Difficulties were encountered in the initial stages of this work because of the low and poorly reproducible yields of propyl and isobutyl alcohol obtained in the reduction of 2-chloro-1-propanol[7] and 2-chloro-2-methylpropanol, respectively. This was particularly disturbing since α-chloropropionic acid and α-chloroisobutyric acid were reduced to the corresponding alcohols in 44 and 70% yield, respectively.[4] The logical conclusion that the chlorohydrins are *not* intermediates in the reduction of the chloroacids to the alcohols was not acceptable because it had been found[4] that chloroesters are reduced to chlorohydrins with a limited amount of hydride and to alcohols with an excess of hydride. The difficulty was cleared up when it was discovered that the alcohol yield could be improved and made reproducible through addition of water, methanol, *t*-butyl alcohol or ethyl acetate (but not aluminum *t*-butoxide) to the reaction mixture. These addends were chosen so as to simulate the reaction medium which exists in the reduction of a chloroester or chloroacid where alkoxides or oxides of aluminum are formed as primary products in addition to chlorohydrin salts (or complexes). The effect of these addends on the reduction of 2-chloro-2-methylpropanol is shown in Table I, the effect in the reduction of 2-chloro-1-propanol being discussed elsewhere.[7] For reasons not understood the highest yield of isobutyl alcohol obtained in the reduction of the chlorohydrin in the presence of water (41%) is still considerably below that obtained in the reduction of α-chloroisobutyric acid (70%), but there is little doubt that the chlorohydrin (or rather a lithium aluminum salt or complex thereof) is an in-

TABLE I

YIELD OF ISOBUTYL ALCOHOL IN THE REDUCTION OF 2-CHLORO-2-METHYLPROPANOL WITH LITHIUM ALUMINUM HYDRIDE IN THE PRESENCE OF VARIOUS ADDED COMPOUNDS

Hydride,[a] moles	Cpd. added, moles[a]	*i*-BuOH, %	Recovery,[b] %
1.5	None	16	64
0.6	None	10	75
1.0	None	28	30
0.8	None[c]	14	36
1.5	CH$_3$COOC$_2$H$_5$, 1	43	[d]
1.0	*t*-C$_4$H$_9$OH, 1	19	60
1.0	Al(*t*-C$_4$H$_9$O)$_3$, 1	7	40
1.5	H$_2$O, 1	41	18
1.25	H$_2$O, 1	36	27
1.25[e]	H$_2$O, 1	32	32

[a] Per mole chlorohydrin. [b] Of chlorohydrin. [c] In tetrahydrofuran (all other reductions were carried out in ether). [d] No chlorohydrin recovered as such, but 26% isobutyraldehyde in product. [e] Deuteride.

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[1] Presented in part before the 14th International Congress of Pure and Applied Chemistry, Zurich, Switzerland, 1955.

[2] Socony–Mobil Fellow, 1955–1956.

[3] E. L. Eliel and J. P. Freeman, THIS JOURNAL, **74**, 923 (1952).

[4] E. L. Eliel, C. Herrmann and J. T. Traxler, *ibid.*, **78**, 1193 (1956).

[5] L. W. Trevoy and W. G. Brown, *ibid.*, **71**, 1675 (1949).

[6] See also B. Tchoubar, *Bull. soc. chim. France*, 1363 (1955), especially footnote 1, p. 1380.

[7] E. L. Eliel and J. T. Traxler, THIS JOURNAL, **78**, 4049 (1956).

[8] Work in progress with D. Delmonte.

termediate in the reduction of the chloroacid to the alcohol.

The reduction of three representative halohydrins, 2-chloro-2-methylpropanol, 2-chloro-2-phenylethanol and 2-bromo-1-butanol (chosen in preference to the chloro compound because of better yields in the reduction) with lithium aluminum deuteride was then studied. The position of the deuterium in the products was determined by direct mass spectrometric analysis.[9] Thus the principal peaks in the mass spectrum of isobutyl alcohol, $(CH_3)_2CHCH_2OH$, correspond to m/e 31 and 43, due largely to CH_2OH^+ and $(CH_3)_2CH^+$ ions in the spectrometer chamber. In isobutyl-1-*d* alcohol, $(CH_3)_2CHCHDOH$, the corresponding peaks appear at 32 ($CHDOH^+$) and 43, whereas isobutyl-2-*d* alcohol, $(CH_3)_2CDCH_2OH$, has major peaks at 31 and 44 [$(CH_3)_2CD^+$]. Comparison of the mass spectrum of the product of the reduction of 2-chloro-2-methylpropanol with lithium aluminum deuteride with that of isobutyl alcohol indicated that the reduction product was largely but not exclusively isobutyl-1-*d* alcohol. In order to put this conclusion on a quantitative basis, authentic samples of isobutyl-1-*d* and -2-*d* alcohol had to be synthesized. Isobutyl-1-*d* alcohol was obtained by reduction of isobutyraldehyde with lithium aluminum deuteride. Isobutyl-2-*d* alcohol was obtained from isobutyric-α-*d* acid by reduction with lithium aluminum hydride. The acid, in turn, was prepared from dimethylmalonyl chloride by hydrolysis with heavy water, followed by decarboxylation and equilibration with ordinary water.[10] The essential isotopic purity of the deuterated acid was demonstrated by the complete absence of infrared absorption at 8.06 μ, at which wave length ordinary isobutyric acid has an intense absorption band. (The deuterated acid in turn absorbs at 8.42 μ where the hydrogen compound is transparent.) From the mass spectra of isobutyl alcohol and its 1-*d* and 2-*d* analogs, the sensitivity[9] of these spectra at m/e 31, 32 and 44 was computed and from these and the mass spectrum of the reaction product the composition of the latter was calculated in the usual way[9] as being 79.7% $(CH_3)_2CHCHDOH$, 13.8% $(CH_3)_2CDCH_2OH$ and 6.5% $(CH_3)_2CHCH_2OH$. These percentages are probably accurate to about 2–3%. In order to confirm the calculations, a synthetic mixture of approximately the above composition was prepared; its mass spectrum (Table II) agreed satisfactorily with that of the unknown in the essential peaks. Comparison of the infrared spectrum of the isobutyl-*d* alcohol mixture with that of a synthetic mixture of known composition also confirmed the above analysis.

The composition of the reduction product of 2-bromo-1-butanol was determined similarly, the results being shown in Table III. Comparison of the 31, 43 and 44 peaks indicates the reduction product to be substantially pure butyl-2-*d* alcohol. The reason for the *greater* intensity of the 32 peak in the spectrum of the *authentic* butyl-2-*d* alcohol is not understood, but it certainly cannot be taken to indicate the presence of butyl-1-*d* alcohol in the reduction product. The infrared spectrum of the reduction product was completely identical with that of the authentic butyl-2-*d* alcohol, which in turn is quite different from that of authentic butyl-1-*d* alcohol.[11] The authentic sample of butyl-2-*d* alcohol required in these comparisons was synthesized from propionaldehyde by reduction to propyl-1-*d* alcohol with lithium aluminum deuteride, followed by conversion to propyl-1-*d* bromide by means of phosphorus tribromide in the cold,[12] subsequent formation of a Grignard reagent, carbonation and direct reduction of the acid salt so formed to the alcohol by means of lithium aluminum hydride.[13]

TABLE II

MASS SPECTRAL PATTERNS OF ISOBUTYL ALCOHOL AND DEUTERATED ISOBUTYL ALCOHOLS[a]

m/e	$(CH_3)_2$-$CHCH_2OH$	(CH_3)-$CDCH_2OH$	$(CH_3)_2CH$-$CHDOH$	Synthetic[b] mixture	Reacn. product
31	79.76	54.64	18.66	27.92	28.70
32	1.96	15.74	47.93	42.94	43.15
43	100.00	64.55	100.00	100.00	100.00
44	4.26	100.00	5.84	18.83	19.42

[a] Abbreviated table; for complete data see reference 14.
[b] Composition: 81.5% $(CH_3)_2CHCHDOH$, 13.1% $(CH_3)_2CDCH_2OH$, 5.4% $(CH_3)_2CHCH_2OH$.

TABLE III

MASS SPECTRAL PATTERNS OF BUTYL ALCOHOL AND DEUTERATED BUTYL ALCOHOLS[a]

m/e	CH_3CH_2-CH_2CH_2OH	CH_3CH_2-CH_2CHDOH[11]	CH_3CH_2-$CHDCH_2OH$	Reacn. product
31	100.00	16.56	100.00	100.00
32	1.89	100.00	13.99	8.61
43	61.93	64.82	37:17	36.58
44	5.05	7.88	60.52	59.70

[a] Abbreviated table; for complete data see reference 14.

The composition of the reduction product of 2-chloro-2-phenylethanol was determined indirectly, since authentic 2-phenylethanol-2-*d*, $C_6H_5CHDCH_2OH$, was not available. The deuterated phenethyl alcohol[14] was converted to the tosylate and reduced to deuterated ethylbenzene by means of lithium aluminum hydride. The ethylbenzene was analyzed mass spectrometrically by comparison with authentic samples of ethylbenzene-α-*d*[15] and ethylbenzene-β-*d*. The latter was prepared both by the reduction of phenethyl tosylate with lithium

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[9] H. W. Washburn, "Mass Spectrometry" in W. G. Berl, "Physical Methods in Chemical Analysis," Vol. I, Academic Press, Inc., New York, N. Y., 1950. For application of a similar technique, *cf.* L. Friedman and J. Turkevich, THIS JOURNAL, **74**, 1666, 1669 (1952).

[10] C. C. Price, E. L. Eliel and R. Convery, to be published.

[11] Kindly provided by Dr. Andrew Streitwieser, Jr.

[12] A. T. Shulgin, THIS JOURNAL, **77**, 2338 (1955), reports substantial absence of carbon skeleton rearrangement in a similar reaction. The present study indicates that hydrogen migration does not take place to any appreciable extent either in the reaction of a primary aliphatic alcohol with phosphorus tribromide. D. G. Hill, B. Stewart, S. W. Kantor, W. A. Judge and C. R. Hauser, *ibid.*, **76**, 5129 (1954), report no loss of deuterium when $(C_2H_5)_2CDCH_2OH$ is converted to the corresponding bromide by means of HBr.

[13] A. P. Mathers and M. J. Pro, THIS JOURNAL, **76**, 1182 (1954).

[14] The mass spectral pattern of the phenethyl alcohols (Table IV), ethylbenzenes (Table V), isobutyric acids (Table VI) and *n*-butyric acids (Table VII), as well as the *complete* patterns for the isobutyl (Table II) and *n*-butyl alcohols (Table III) referred to in this paper have been deposited as Document number 4817 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document number and by remitting in advance \$1.25 for photoprints or \$1.25 for 35 mm. microfilm payable to: Chief, Photoduplication Service, Library of Congress.

[15] E. L. Eliel, THIS JOURNAL, **71**, 3970 (1949).

aluminum deuteride and by the reaction of phenethylmagnesium bromide with heavy water. Both reactions gave the same deuterated product, as shown by mass spectrometry, thus indicating the absence of hydrogen shifts in the reduction of the tosylate.[16] However, the material from the Grignard reaction contained 4.8% (by mass spectrometry[14]) of undeuterated ethylbenzene which probably originated in the decomposition of the Grignard product with sulfuric acid The analysis of the ethylbenzene obtained from the deuterated phenethyl alcohol indicated it to be 93% ethylbenzene-α-*d*, 4% ethylbenzene-β-*d* and 3% undeuterated ethylbenzene, thus proving that only 4% of the phenethyl alcohol formed in the reduction of 2-chloro-2-phenylethanol is the β-deuterated material[14] resulting from a hydride shift.

The mass spectral analysis of the composition of the butyl and isobutyl alcohol products was checked by means of oxidative degradation. Deuterium in the 1-position of the alcohol is necessarily lost during oxidation, while deuterium in the 2-position is retained, provided no exchange occurs. The absence of such exchange in permanganate oxidation was proved by oxidizing ordinary isobutyl alcohol in water containing 20% of deuterium oxide; under these conditions the product was isobutyric acid essentially free of α-deuterated material, as evidenced by infrared spectrum.

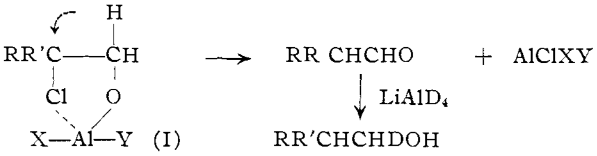
The oxidation product from the isobutyl alcohol–isobutyl-*d* alcohol mixture obtained in the lithium aluminum deuteride reduction described earlier was analyzed by mass spectrometry, infrared spectroscopy (comparison of the infrared spectrum in chloroform solution with that of synthetic mixtures of isobutyric acid and isobutyic-α-*d* acid under identical conditions) and deuterium determination. The accuracy of these analyses is not high, mainly because the oxidation product was obtained in too small amount for extensive purification. Thus the deuterium analysis indicated 24.6 mole % deuterated acid in the mixture, the infrared spectrum was compatible with a deutero-acid content of 25–30% and the mass spectrum[14] indicated 24.4–26.5% deuterated acid.[17] However, clearly none of these analyses are compatible with the presence of only 15% of $(CH_3)_2CDCH_2OH$ in the alcohol mixture, as established by direct mass spectrometry. The discrepancy is due to an isotope effect. Since oxidation of the alcohol was not quantitative and since oxidation of the H–C–OH group is known[18] to be faster than that of D–C–OH, the oxidation product of $(CH_3)_2CDCH_2OH$ is formed in larger proportion than that of $(CH_3)_2CHCHDOH$. The correctness of this interpretation was established by oxidation of a synthetic mixture of 14.4% $(CH_3)_2CDCH_2OH$ and 85.6% $(CH_3)_2CHCHDOH$. The product contained between 20 and 25% $(CH_3)CDCOOH$ as shown by infrared (or 22.1–24.3% by mass spectrometric analysis).[14,17]

The oxidation product of the butyl-*d* alcohol mixture obtained by deuteride reduction was submitted to deuterium analysis and contained only 87.4% of the theoretical 12.5 mole % deuterium. Infrared analysis was not feasible in this case, since butyric acid shows no bands which are not also present in the α-deutero compound. However, mass spectral analysis[14] indicated that the oxidation product contained no light butyric acid, since the 60 and 73 peaks were lower and the 88 peak no higher in this product than in the authentic butyric-α-*d* acid. (Ordinary butyric acid has high peaks at m/e 60 and 73.[19]) The low elementary deuterium analysis of the oxidation product is probably due to the presence of water and other low molecular weight impurities suggested by residuals in the mass spectrum.

Discussion

The reduction of the secondary halides 2-bromo-1-butanol and 2-chloro-2-phenylethanol to the corresponding alcohols with lithium aluminum hydride proceeds largely or entirely *without* a hydride shift, *i.e.*, by direct displacement of the halogen by hydride. The detailed mechanism of this reduction is discussed in the accompanying paper.[7]

Among halohydrins with tertiary halogen, only 2-chloro-2-methylpropanol could be studied, since the attempted isolation of 2-chloro-2-phenylpropanol[3] and of 2-chloro-2,2-diphenylethanol[20] was unsuccessful. In the case studied, the reduction proceeded with hydride shift to the extent of 85% (adjusted for undeuterated isobutyl alcohol in the product). This is consistent with the mechanism previously postulated.[3] The shift may involve preliminary coördination of aluminum with halogen



Aluminum complexes similar to I (with alkoxide instead of chloride) have been reported recently,[21] and cyclic intermediates involving aluminum have been postulated in other reactions.[22] The analogy of the above hydride shift with the alkyl shifts observed in the reaction of halohydrins with Grignard reagents[23] has been pointed out previously,[3,6,24] and it is of interest that a shift very similar to the above has been observed[25] in the reaction of ethyl α-chloroisobutyrate, $(CH_3)_2CClCOOEt$, with methylmagnesium bromide which gives rise to 2,3,3-trimethylbutanol-2, $(CH_3)_3CCOH(CH_3)_2$. In the

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(16) Skeletal rearrangement in similar reactions have been reported by D. J. Cram, THIS JOURNAL, **74**, 2149, 2152 (1952).

(17) The smaller figure is based on the 43–44 peaks. The larger, based on the 88–89 peaks, is probably more accurate, since residuals in the spectrum indicated low molecular weight contaminants.

(18) F. H. Westheimer and N. Nicolaides, THIS JOURNAL, **71**, 25 (1949).

(19) It is not entirely impossible that both the comparison sample and the oxidation product contained some light acid. The upper limit of such contamination, on the unlikely assumption that *all* of the 60 peak is due to light material, is 11% for the oxidation product and 16% for the comparison sample.

(20) Unpublished results with J. T. Traxler.

(21) G. Bähr and G. E. Müller, *Ber.*, **88**, 251 (1955).

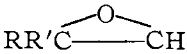
(22) *E.g.*, F. A. Hochstein and W. G. Brown, THIS JOURNAL, **70**, 3484 (1948); A. Dornow, G. Winter and W. Vissening, *Ber.*, **87**, 629 (1954); A. Dornow and M. Gellrich, *Ann.*, **594**, 177 (1955).

(23) For recent references see H. O. House, THIS JOURNAL, **77**, 3070, 5083 (1955).

(24) Other points of similarity between Grignard reagents and lithium aluminum hydride have been pointed out by P. Karrer, *Bull. soc. chim. France*, 907 (1950).

(25) L. Henry, *Rec. trav. chim.*, **26**, 84 (1907).

intermediate I, the aluminum must act as a Lewis acid. This may explain why the addition of water or alcohol to the reaction mixture increases the ease of reduction, for it tends to change X and Y in the intermediate I from hydrogen to the more electron-withdrawing —OR or ═O.

It has been stated previously[3] that epoxides  $RR'C\overset{O}{\frown}CH_2$ are not intermediates in the reduction of halohydrins $RR'CClCH_2OH$ to alcohols $RR'CHCH_2OH$, since the epoxides are reduced to the isomeric alcohols $RR'COHCH_3$.[3,5] However, it has now been found[8] that the direction of opening of the epoxide ring may be partially or completely reversed when the reduction with lithium aluminum hydride is carried out in the presence of aluminum halides. This reopens the possibility of epoxide intermediates.[26] Perhaps such intermediates are responsible for the minor path involved in the reduction of 2-chloro-2-methylpropanol to isobutyl-2-*d* alcohol (15%) and in that part of the reduction of 2-chloro-2-phenylpropanol which proceeds with retention of configuration or with racemization, rather than with the inversion to be expected in the hydride shift.[3] Further work[8] is required to clear up this point.

Experimental

General.—Lithium aluminum hydride reductions were performed by the standard procedure[27] except where otherwise noted. Solutions were decomposed with water followed by 10% sulfuric acid and, in the case of all aliphatic compounds, were subjected to continuous ether extractions for at least 45 hr. The ether solutions (dried over potassium carbonate) were concentrated through a Vigreux column and the products distilled through a small Vigreux column, a jacketted helix-packed column 17 mm. in diameter, 27 cm. long or a jacketted unpacked column 7 mm. in diameter, 64 cm. long. Infrared analyses were carried out by Mr. Rolland Ro and the authors on a Baird double beam instrument and by Mr. Ray Penland on a Perkin-Elmer double beam model 21 instrument. Mass spectrometric analyses were carried out by Mr. George Young[28] on a Consolidated Engineering Type 21-103A instrument.

2-Bromo-1-butanol.—Ethyl α-bromo-*n*-butyrate (97.5 g., 0.5 mole) in ether solution was reduced by the addition of 250 ml. (0.25 mole) of 1 *M* lithium aluminum hydride solution. Fractionation of the product through a helix packed column gave 54.5 g. (71%) of 2-bromo-1-butanol, b.p. 81–82° (33 mm.), n^{20}D 1.4758; lit.[29] b.p. 65–66° (13 mm.), n^{20}D 1.4802. The 3,5-dinitrobenzoate melted at 70°, lit.[29] 68.2–69.4°.

Reduction of 2-Bromo-1-butanol.—The reduction of 15.3 g. (0.1 mole) of 2-bromo-1-butanol was effected by means of 2.5 g. (0.06 mole) of lithium aluminum deuteride and 0.63 g. (0.07 mole) of finely ground lithium deuteride in ethereal slurry. After 10 hours reflux the reaction mixture was worked up and the product fractionally distilled through an unpacked column to give 3.70 g. (49.2%) of deuterated butyl alcohol, b.p. 54–55° (44–46 mm.), n^{20}D 1.3977 (mass spectrum,[14] Table III, last column), as well as 3.76 g. (24.6%) of recovered 2-bromo-1-butanol, b.p. 88–89° (44 mm.), n^{20}D 1.4761.

Reduction of 2-Chloro-2-methylpropanol.—The reduction of 10.85 g. (0.1 mole) of 2-chloro-2-methylpropanol,[4] b.p. 62° (55 mm.), m.p. 28.5°, n^{20}D 1.4366 (free of carbonyl absorption in the infrared) was effected by means of 5.24 g. (0.125 mole) of lithium aluminum deuteride ethereal slurry to which had been added 1.8 g. (0.1 mole) of water. After a 6-hr. reflux period the reaction mixture was worked up and the product fractionated through an unpacked column to give 2.40 g. (32.4%) of deuterated isobutyl alcohol, b.p. 50–52° (60 mm.), n^{20}D 1.3965 (mass spectrum,[14] Table II, last column), in addition to 3.41 g. (31.8%) of recovered 2-chloro-2-methyl-propanol, b.p. 65–66° (60 mm.), n^{20}D 1.4351. The results of reductions of 2-chloro-2-methylpropanol with lithium aluminum hydride under various conditions are recorded in Table I.

Reduction of 2-Chloro-2-phenylethanol.—Reduction of 8.8 g. (0.056 mole) of 2-chloro-2-phenylethanol,[4] b.p. 76–77° (0.7 mm.), n^{20}D 1.5519 (free of carbonyl in the infrared) was effected by means of 2.46 g. (0.063 mole) of lithium aluminum deuteride in ethereal slurry to which had been added 1.0 g. (0.055 mole) of water. After a 7-hr. reflux period the product, isolated in the usual way, was distilled through a small Vigreux column to give the following fractions: (1) 2.76 g., b.p. 59–62° (0.7 mm.), n^{20}D 1.5330; (2) 1.31 g., b.p. 62–66° (0.7 mm.), n^{20}D 1.5340; (3) 1.40 g., b.p. 66–80° (0.8 mm.), n^{20}D 1.5367. Fractions 1 and 2 considered as deuterated phenethyl alcohol represent a 58% yield (mass spectrum,[14] Table IV, last column). Fraction 3 is considered as deuterated phenethyl alcohol contaminated with 2-chloro-2-phenylethanol (as evidenced by its infrared spectrum).

A similar reduction with lithium aluminum hydride gave phenethyl alcohol boiling at 58–61° (0.7 mm.), n^{20}D 1.5312, in 70–72% yield while the same reaction in the absence of water gave material boiling at 60–65° (0.7 mm.), n^{20}D 1.5307–1.5317, in only 47% yield.

Isobutyl-1-*d* Alcohol.—Reduction of 7.21 g. (0.1 mole) of isobutyraldehyde by 1.16 g. (0.028 mole) of lithium aluminum deuteride in ethereal slurry gave 5.31 g. (70.8%) of isobutyl-1-*d* alcohol, b.p. 59–59.5° (90 mm.), n^{20}D 1.3960, free of carbonyl absorption in the infrared (mass spectrum,[14] Table II).

Isobutyl-2-*d* Alcohol.—Isobutyl-2-*d* alcohol was prepared by reduction of 6.72 g. (0.075 mole) of isobutyric-2-*d* acid[10] with 62 ml. (0.062 mole) of 1 *M* ethereal lithium aluminum hydride solution. After a 2-hr. reflux period the reaction mixture was worked up to give 4.25 g. (75%) of isobutyl-2-*d* alcohol, b.p. 105–106.5°, n^{20}D 1.3903 (mass spectrum,[14] Table II).

Butyl-2-*d* Alcohol and Butyric-2-*d* Acid.—Propionaldehyde (14.5 g., 0.25 mole) was reduced with 2.85 g. (0.068 mole) of lithium aluminum deuteride in ethereal slurry to give 10.6 g. (69.3%) of propyl-1-*d* alcohol, b.p. 51.5–52.0° (100 mm.), n^{20}D 1.3845.

Propyl-1-*d* bromide (10.73 g., 54.7%, b.p. 70°, n^{20}D 1.4288) was prepared from 9.69 g. (0.158 mole) of propyl-1-*d* alcohol and 15.71 g. (0.058 mole) of phosphorus tribromide.[30]

Propyl-1-*d* bromide (10 g., 0.081 mole) was converted to the corresponding Grignard reagent by means of 1.96 g. (0.081 mole) of magnesium shavings in the usual way. The Grignard reagent was poured onto 35 g. of crushed Dry Ice yielding 17 g. of the magnesium bromide salt of butyric-2-*d* acid. A portion (10.2 g.) was reduced directly[13] with 48 ml. (0.048 mole) of 1 *M* lithium aluminum hydride ethereal solution giving 1.74 g. (0.023 mole, 47%) of butyl-2-*d* alcohol, b.p. 61.5° (66 mm.), n^{20}D 1.3980 (mass spectrum,[14] Table III).

The remaining salt (6.8 g.) was hydrolyzed with dilute hydrochloric acid to give 1.42 g. (0.0159 mole, 49%) of butyric-2-*d* acid.

Phenethyl Alcohol-1-*d*.[14]—Phenylacetaldehyde (6.0 g., 0.05 mole) was reduced with 0.63 g. (0.015 mole) of lithium aluminum deuteride in ethereal slurry in the usual manner. There was obtained 4.96 g. (81%) of phenethyl alcohol-1-*d*, b.p. 55–57° (0.7 mm.), n^{20}D 1.5315 (mass spectrum,[14] Table IV).

Ethylbenzene-β-*d*. (A) From (2-Bromoethyl)-benzene.—Phenethyl bromide (18.5 g., 0.1 mole) was converted to its Grignard reagent by 2.5 g. (0.1 mole) of magnesium shavings in the usual way.[31] To this was added 3 g. (0.15 mole) of deuterium oxide, and the reaction mixture was allowed to

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(26) Epoxides do not seem to be intermediate in the rearrangement of halohydrins to carbonyl compounds by alkylmagnesium bromide, reference 23 and D. Y. Curtin and E. K. Meislich, This Journal, **74**, 5905 (1952).

(27) R. F. Nystrom and W. G. Brown, *ibid.*, **69**, 1197 (1947); *cf.* W. G. Brown in R. Adams, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, Chapter 10.

(28) We wish to express our gratitude to Mr. Young for his help in the interpretation of the mass spectra.

(29) B. I. Halperin, H. B. Donahoe, J. Kleinberg and C. A. VanderWerf, *J. Org. Chem.*, **17**, 625 (1952).

(30) C. R. Noller and R. Dinsmore, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 358.

(31) P. M. Dean and W. I. Wolf, This Journal, **58**, 332 (1936).

stand overnight. The salt formed was dissolved with dilute sulfuric acid, the ether layer was dried and concentrated and the residue distilled through an unpacked column to give 6.79 g. (63.5%) of ethylbenzene-*β-d*, b.p. 57–58° (50 mm.), n^{20}D 1.4960 (mass spectrum,[14] Table V).

(B) **From the Tosylate of Phenethyl Alcohol.**—Phenethyl alcohol (12.2 g., 0.1 mole) was converted to its tosylate with 19 g. (0.1 mole) of *p*-toluenesulfonyl chloride.[32] The product, m.p. 38–40°, lit.[32] m.p. 39–40°, weighed 19.5 g. (70.5%).

The tosylate (11.06 g., 0.04 mole) was reduced with 1.84 g. (0.044 mole) of lithium aluminum deuteride in ethereal slurry in the usual way[33] and upon distillation through an unpacked column gave 2.67 g. (69%) of ethylbenzene-*β-d*, b.p. 59.0° (55 mm.), n^{20}D 1.4952 (mass spectrum,[14] Table V).

Monodeuterated Ethylbenzene from Monodeuterated Phenethyl Alcohol.—Monodeuterated phenethyl alcohol (3.98 g., 0.032 mole) obtained from the lithium aluminum deuteride reduction of 2-chloro-2-phenylethanol was converted to the tosylate (9.4 g., m.p. 35–45°) by 6.15 g. (0.032 mole) of *p*-toluenesulfonyl chloride.[32] The entire product was then reduced with 35 ml. (0.038 mole) of 1.1 *M* lithium aluminum hydride ethereal solution.[33] Distillation of the product through an unpacked column gave 0.36 g. (10.4%) of monodeuterated ethylbenzene, b.p. 59° (55 mm.), n^{20}D 1.4960 (mass spectrum,[14] Table V, last column).

Oxidation of Alcohols.—Monodeuterated isobutyl alcohol (0.75 g., 0.01 mole) was oxidized by a solution of 3.8 g. of potassium permanganate, 0.3 g. of sodium hydroxide and 75 ml. of water, upon standing at room temperature for 2 days. After filtration of the reaction mixture, extraction of the manganese dioxide with hot water, concentration and acidification of the combined filtrate and water extracts and continuous ether extraction of the resulting solution, 0.27 g. (30%) of isobutyric acid (partially deuterated) was obtained by distillation through a Craig column. The mass spectrum of this compound is recorded in Table VI.[14]

Anal.: D, found, 3.08 atom %.

In a similar manner, 0.75 g. (0.01 mole) of a synthetic mixture of 85.6% isobutyl-1-*d* alcohol and 14.4% isobutyl-2-*d* alcohol was oxidized to give 0.18 g. (20%) of isobutyl acid (partially deuterated, mass spectrum[14] in Table VI), and 1.0 g. (0.013 mole) of monodeuterated *n*-butyl alcohol was oxidized to give 0.29 g. (24%) of monodeuterated *n*-butyric acid. The mass spectrum of this compound is recorded in Table VII.[14]

Anal. Calcd. for $C_4H_7DO_2$: atom % D, 12.5. Found: D, 10.92.

Similar oxidations of isobutyl alcohol in water containing 20% deuterium oxide gave isobutyric acid identical in infrared spectrum with an authentic sample (no band at 8.42 μ).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

The Mechanism of Halide Reductions with Lithium Aluminum Hydride. V. Reduction of β-, γ-, δ- and ε-Chloroacids and the Corresponding Chlorohydrins

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The reductions of α- and β-chloroacids containing primary, secondary and tertiary halogen to halohydrins and alcohols by means of lithium aluminum hydride are compared. While the primary and secondary halides are reduced to a similar extent in the α- and β-series, the reduction of tertiary halogen in the α-series is much more facile than the reduction of tertiary halogen in the β-series. This is in agreement with the previously proposed hydride shift mechanism for the reduction of 1,2-chlorohydrins containing tertiary halogen. Reduction of haloacids $Cl(CH_2)_nCOOH$ (n = 1–5) and the corresponding halohydrins $Cl(CH_2)_nCH_2OH$ has been studied as a function of n. Reduction of the chlorine function proceeds quite readily when n = 1 or 2 but not when n = 4 or 5. The result is interpreted in terms of a cyclic transition state for the reduction of chlorohydrins with primary halogen.

In the accompanying paper[2] it was shown that the mechanism of reduction of the secondary bromide 2-bromo-1-butanol is different from the major path of the reduction of the tertiary chloride 2-chloro-2-methylpropanol. Reduction of the tertiary halide with lithium aluminum deuteride involves in the main a hydride shift while that of the secondary halide involves direct displacement of halogen by deuterium. Nevertheless, the rather facile reduction[2,3] of 1,2-chloro- as well as bromohydrins with primary or secondary halogen cannot be a simple SN2 process, since ordinary primary and secondary chlorides (including chloroethers in which inductive effects are similar as in chlorohydrins) are not readily reduced with lithium aluminum hydride in ether. Thus it seemed of interest to study a series of 1,3-, 1,4-, 1,5- and 1,6-chlorohydrins and the corresponding chloroacids in order to determine whether these compounds display the same high reducibility as 1,2-chlorohydrins and if not, where the transition comes from the ready reducibility of the 1,2-compounds to the resistance to reduction of the simple halides. The results for the chlorohydrins (primary chloride) are shown in Table I. Since the first member of the series, ethylene chlorohydrin, was not studied, data for the secondary chlorides 2-chloro-1-propanol and 3-chloro-1-butanol are also included, as are some simple halides for purposes of comparison. Table II shows corresponding data for a series of primary chloroacids. Primary, secondary and tertiary α- and β-chloroacids are compared in Table III.

The data in Table III indicate that in comparing

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[1] Taken from the Ph.D. dissertation of J. T. Traxler.

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[3] E. L. Eliel, C. Herrmann and J. T. Traxler, *ibid.*, **78**, 1193 (1956).