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

Reductions with Metal Hydrides. VII. Reduction of Epoxides with Lithium Aluminum Hydride–Aluminum Chloride

BY ERNEST L. ELIEL AND MARK N. RERICK[1]

RECEIVED JULY 28, 1959

Reduction of epichlorohydrin, 3-phenyl-1,2-epoxypropane, 3-phenoxy-1,2-epoxypropane, α- and β-diisobutylene oxide and α-methylstyrene oxide with lithium aluminum hydride (LAH) involves hydride attack at the less substituted position of the oxide. Tetramethylethylene oxide also has been reduced with LAH but tetraphenylethylene oxide was resistant to reduction in boiling ether. Addition of aluminum chloride to the LAH solution brings about complete reversal of the outcome of reduction in the case of α-methylstyrene oxide and α-diisobutylene oxide but little or no reversal in the case of epichlorohydrin, 3-phenyl-1,2-epoxypropane and 3-phenoxy-1,2-epoxypropane. The "reversal" seems to involve a hydride shift to a carbonyl intermediate. β-Diisobutylene oxide similarly undergoes a *t*-butyl shift and is reduced to 2,2,3,3-tetramethylbutanol-1, and tetramethylethylene oxide undergoes a partial methyl shift being reduced to a mixture of pinacolyl alcohol and dimethylisopropylcarbinol. Tetraphenylethylene oxide is again inert under these conditions and cyclohexene oxide is reduced to cyclohexanol.

In a previous publication[2] the reduction of certain epoxides with lithium aluminum hydride (LAH) and with LAH–aluminum chloride in ether was described. The results of this study are summarized in Fig. 1. Reduction with LAH alone involved attack of hydride at the least substituted carbon whereas the "mixed hydride"[3] (LAH–$AlCl_3$) involved, in most cases, reduction at the most highly substituted carbon, formally speaking. Tracer studies indicated, however, that this "reversed reduction" actually involved a hydride shift producing a carbonyl intermediate which was then further reduced to alcohol. The "reversal" occurred readily with isobutylene oxide, trimethylethylene oxide, styrene oxide, 1,1-diphenylethylene oxide and triphenylethylene oxide but only to a minor degree with propylene oxide. It was the objective of the present work to study further reductions of epoxides with LAH in the presence and absence of aluminum chloride so as to determine exactly when "reversal" might or might not be expected to occur. Included in this study were tetrasubstituted ethylene oxides which cannot undergo a hydride shift to give the carbonyl intermediate shown in Fig. 1, but which could conceivably undergo shift of an alkyl group under the influence of the Lewis acid, aluminum chloride, to give, after reduction, carbinols of the type $R_3CCHOHR$.

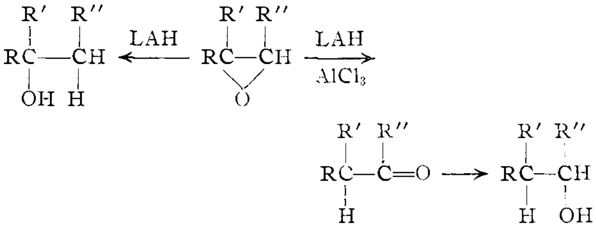


Fig. 1.

Results of the present work and the earlier study[2] are summarized in Tables I and II. Table I lists reductions with LAH alone. The following general conclusions may be drawn: (1) Reduction of epoxides with LAH, if it succeeds at all, involves exclusive or nearly exclusive hydride attack on the less substituted side of the epoxide; cases of epoxide reduction in the literature[4] agree with this conclusion.[5] (2) As the epoxide becomes more highly substituted, the yield of reduction product decreases and unchanged epoxide is recovered, this being the case with trimethylethylene oxide, triphenylethylene oxide, tetramethylethylene oxide and β-diisobutylene oxide (I, Fig. 2). The last-named oxide, surprisingly, does undergo reduction to the extent of 21%, although attack at a neopentyl carbon is involved; in contrast, tetraphenylethylene oxide does not undergo reduction[6] in ether at 35°.

The reduction of epichlorohydrin (Table I) is noteworthy in that it was carried out with a limited amount of LAH using the inverse addition technique (hydride solution added to compound); the main product, under these conditions, is 1-chloro-2-propanol. Previously, epichlorohydrin had been reduced to propanol-2 using an excess of LAH[7]; the present result indicates that attack at the terminal position of the epoxide precedes reduction of the primary chloride.[8]

Table II summarizes the reductions of epoxides with LAH–aluminum chloride. Previous work[2] has indicated that in the case of styrene oxide and isobutylene oxide, this type of reduction involves a hydride shift. It may be presumed, therefore, that a hydride shift such as is shown in Fig. 1 occurs

---

[1] This paper is based on the Ph.D. dissertation of M. N. Rerick.

[2] Paper VI, E. L. Eliel and D. W. Delmonte, THIS JOURNAL, **80**, 1744 (1958).

[3] For a review of reductions with the "mixed hydride" *cf.* M. N. Rerick, "Selective Reductions of Organic Compounds with Complex Metal Hydrides," Metal Hydrides, Inc., 33 Congress Street, Beverly, Mass., 1959. The exact nature of the reagent remains to be elucidated. In the present work, the LAH:$AlCl_3$ ratio was 1:4.

[4] Summarized by (a) N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, N. Y., 1956, pp. 646–673; and (b) V. M. Micovic and M. L. Mihailovic, "Lithium Aluminum Hydride in Organic Chemistry," Belgrade, Yugoslavia, 1955, pp. 68–74.

[5] A few exceptions are known. M. Mousseron, R. Jacquier, M. Mousseron-Canet and R. Zagdoun, *Bull. soc. chim. France*, 1042 (1952), claim the reduction of ethylidenecyclohexane oxide to methylcyclohexylcarbinol, but A. Burgstahler, Ph.D. Dissertation, Harvard University, Cambridge, Mass., 1952, indicates the product to be the expected 1-ethylcyclohexanol. The reduction of the 3-hydroxy-5β,6β-epoxycholestanes to 3,5β-dihydroxycholestanes reported by Pl. A. Plattner, *et al.*, *Helv. Chim. Acta*, **32**, 587 (1949), and **37**, 258 (1954), has been explained on conformational grounds.

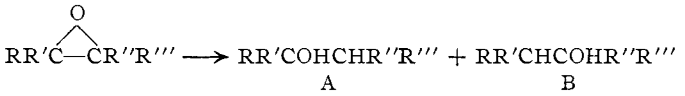
[6] Other cases in which reduction of highly substituted epoxide fails are listed in ref. 4b, p. 74.

[7] L. W. Trevoy and W. G. Brown, THIS JOURNAL, **71**, 1675 (1949).

[8] The preferential reduction of a primary–secondary epoxide over secondary bromide has been observed previously by R. C. Waters and C. A. VanderWerf, THIS JOURNAL, **76**, 709 (1954), but no selectivity was achieved as between a disecondary epoxide and a primary bromide.

TABLE I

PRODUCTS OF REDUCTION OF EPOXIDES WITH LITHIUM ALUMINUM HYDRIDE



$$\mathrm{RR'C(O)CR''R'''} \longrightarrow \underset{A}{\mathrm{RR'COHCHR''R'''}} + \underset{B}{\mathrm{RR'CHCOHR''R'''}}$$

R	R'	R''	R'''	Yield, %	Composition A, %	Composition B, %	Method of anal.[a]
CH_3	H	H	H	60	100	0	M,I[b]
CH_3	CH_3	H	H	26	95–98[c]	2–5[c]	M,I[b]
CH_3	CH_3	CH_3	H	*ca.* 25[d]	100	0	I[b]
CH_3	CH_3	CH_3	CH_3	38[d,e]	100[f]		VPC[g]
$ClCH_2$	H	H	H	65[h]	100	0	VPC[g]
$C_6H_5CH_2$	H	H	H	84	100	0	I[g]
$C_6H_5OCH_2$	H	H	H	*ca.* 85[d]	100	0	I[g]
$(CH_3)_3CCH_2$	CH_3	H	H	84	100	0	I[g]
C_6H_5	CH_3	H	H	80[d,i]	96–97[c]	3–4[c]	VPC[g]
CH_3	CH_3	$(CH_3)_3C$	H	21[d]	100	0	M[g]
C_6H_5	H	H	H	82	90–95[c]	5–10[c]	M,I[b]
C_6H_5	C_6H_5	H	H	92	100	0	I,Is[b]
C_6H_5	C_6H_5	C_6H_5	H	12	100	0	C[b]
C_6H_5	C_6H_5	C_6H_5	C_6H_5	0[j]	.....	...	I,C[g]

[a] M, mass spectrometry; I, infrared spectroscopy; VPC, vapor phase chromatography; Is, isolation; C, elution chromatography. [b] Reference 2. [c] The range given indicates the uncertainty of the analysis. [d] Also recovered epoxide. [e] It has been reported (ref. 23) that the reduction of tetramethylethylene oxide gives 2,3-dimethyl-2-butanol in 82% yield, but the amounts of hydride and epoxide and solvent used are not stated. It was shown elsewhere (ref. 2), that the yield of carbinol obtained in the reduction of triphenylethylene oxide was dependent upon the ratio of hydride to epoxide. [f] Carbinols A and B are identical. No pinacolyl alcohol, possible product of a methyl shift, was detected in the product. [g] This work. [h] Ref. 7 reports 88% 2-propanol with excess LAH. [i] Ref. 22 reports that carbinol A (75% yield) was obtained in refluxing tetrahydrofuran. [j] Epoxide recovered nearly quantitatively.

TABLE II

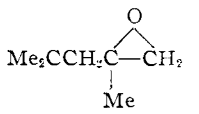
PRODUCTS OF REDUCTION OF EPOXIDES WITH LITHIUM ALUMINUM HYDRIDE AND ALUMINUM CHLORIDE

$$\mathrm{RR'C(O)CR''R'''} \longrightarrow \underset{A}{\mathrm{RR'COHCHR''R'''}} + \underset{B}{\mathrm{RR'R''CCHOHR'''}}$$

R	R'	R''	R'''	Yield, %	Composition A, %	Composition B, %	Method of anal.[a]
CH_3	H	H	H	42	81–84[b]	16–19[b]	M,I[c]
CH_3	CH_3	H	H	55	5–7[b]	93–95[b]	M,I[c]
CH_3	CH_3	H	CH_3	32	0	100	I[c]
CH_3	CH_3	CH_3	CH_3	47[d]	40	60	VPC[e]
$ClCH_2$	H	H	H	21[d,f]	100	0	VPC[e]
$C_6H_5CH_2$	H	H	H	85	90–95[b]	5–10[b]	I[e]
$C_6H_5OCH_2$	H	H	H	81	100	0	I[e]
$(CH_3)_3CCH_2$	CH_3	H	H	78	0	100	VPC,I[e]
C_6H_5	CH_3	H	H	82	0	100	VPC[e]
CH_3	CH_3	$(CH_3)_3C$	H	83	0	77[g]	VPC[e]
C_6H_5	H	H	H	71	2–5[b]	95-98[b]	M,I[c]
C_6H_5	C_6H_5	H	H	89	0	100	I,C[c]
C_6H_5	C_6H_5	H	C_6H_5	91[h]	*ca.* 0	*ca.* 100	Is[c]
C_6H_5	C_6H_5	C_6H_5	C_6H_5	0[i]	......	....	I,C[e]
H[j]	$(CH_2)_2—(CH_2)_2$		H	87	98–100[b,k]	0–2[b]	VPC[e]

[a] M, mass spectrometry; I, infrared spectroscopy; VPC, vapor phase chromatography; Is, isolation; C, elution chromatography. [b] The range given indicates the uncertainty of the analysis. [c] Reference 2. [d] Also recovered epoxide. [e] This work. [f] Also obtained 1,3-dichloro-2-propanol (41% yield). [g] The product also contained 2,4,4-trimethylpentanol-3 (15%) and 2,4,4-trimethylpent-1-en-3-ol (8%). [h] Allyl bromide used rather than aluminum chloride (ref. 2). [i] Recovered 91% of the epoxide. [j] Cyclohexene oxide. [k] It is assumed that cyclohexanol (A) is the result of direct reduction rather than hydrogen (R''') migration.

whenever the mixed reagent seemingly opens the epoxide in the opposite direction as pure LAH. Evidently the shift occurs readily in the case of primary–tertiary epoxides, such as isobutylene oxide, α-diisobutylene oxide (II) and α-methylstyrene oxide, secondary–tertiary oxides, such as trimethylethylene oxide and triphenylethylene oxide, and the phenyl-substituted primary–secondary epoxide, styrene oxide. Little or no hydride shift is found with other primary–secondary epoxides,



II

such as propylene oxide, epichlorohydrin,[9] 3-phenyl-1,2-epoxypropane and 3-phenoxy-1,2-epoxypropane. The latter three epoxides, which have electron-withdrawing substituents attached to the secondary carbon, discouraging the development of carbonium ion character at this center, are particularly resistant to rearrangement. Another possible explanation for the formation of secondary (rather than primary) alcohols from the above-mentioned primary–secondary epoxides is that these epoxides do in fact rearrange prior to reduction, but that such rearrangement yields ketones rather than aldehydes. Thus, it is known[10] that 3-phenyl-1,2-epoxypropane is rearranged to phenylacetone, $C_6H_5CH_2COCH_3$, by zinc chloride and further reduction of phenylacetone would yield benzylmethylcarbinol, the actual product of the reduction of the epoxide with mixed hydride. However, this reaction path was excluded when it was found that 3-phenyl-1,2-epoxypropane does not give phenylacetone when treated with ethereal aluminum chloride under the conditions of the reduction with mixed hydride; the major product of this reaction is 1-chloro-3-phenyl-2-propanol.

Since chlorohydrins may be formed in the reaction of primary–secondary epoxides with LAH–$AlCl_3$ by attack of chloride at the primary carbon,[9] the question arose as to whether such chlorohydrins might be intermediates in the reduction of the epoxides to secondary alcohols especially since chlorohydrins with primary chlorine are known to be reduced to alcohols by LAH.[11] However, it was shown in the present work that 1-chloro-3-phenyl-2-propanol, $C_6H_5CH_2CHOHCH_2Cl$, is *not* extensively reduced to 1-phenyl-2-propanol, $C_6H_5CH_2CHOHCH_3$, by LAH–$AlCl_3$, and that therefore the chlorohydrin is not an intermediate in the reduction of benzylethylene oxide to 1-phenyl-2-propanol. This conclusion is in agreement with the observation[12] that LAH–$AlCl_3$ reduces 3-bromopropionic acid and its derivatives only as far as 3-bromo-1-propanol (whereas LAH alone effects reduction largely to 1-propanol).

$$RCH(O)CH_2 \xrightarrow{AlCl_3} RCHOHCH_2Cl \xrightarrow{LAH} RCHOHCH_3$$

The result with β-diisobutylene oxide (I) is particularly noteworthy. This epoxide might have been expected to undergo a hydride shift to *t*-butyl isopropyl ketone (V) which should then have been reduced to *t*-butylisopropylcarbinol (VI). Instead, the major portion of the oxide underwent a *t*-butyl shift followed by reduction to give 2,2,3,3-tetramethylbutanol-1 (IV) (Fig. 2), along with minor amounts of VI and *t*-butylisopropenylcarbinol (VIII). It was believed at first that IV might be the product of thermodynamic control in case the expected product V underwent reduction only very slowly and were reversibly rearranged to III under the influence of the Lewis acid aluminum chloride, III then being rapidly and irreversibly reduced to IV. However, this interpretation is incorrect, for treatment of the oxide I with aluminum chloride alone also produced the aldehyde III in good yield.

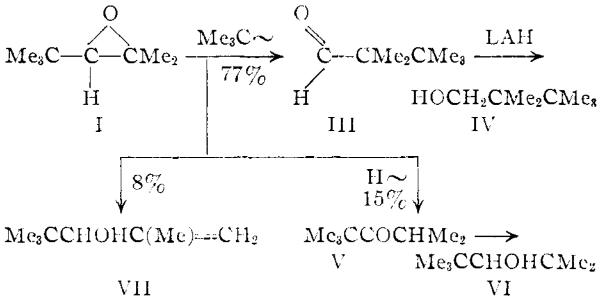


Fig. 2.

Examples of *t*-butyl shifts are relatively rare, but such shifts have been observed in the rearrangement of 2,3,4,4-tetramethylpentane-2,3-diol[13] and di-*t*-butyl ketone[14] to 3,3,4,4-tetramethylpentanone-2. Recent work on the Baeyer–Villiger reaction[15] has, in fact, shown that the *t*-butyl group has a remarkably high migratory aptitude in rearrangement toward electron-deficient centers. The present work seems to indicate that, under appropriate circumstances, *t*-butyl may migrate in preference to hydrogen.

Two other results shown in Table II were surprising, namely, the failure of tetraphenylethylene oxide to undergo any reaction with the mixed reagent, and the fact that tetramethylethylene oxide underwent predominantly direct reduction (even though such direct reduction is slow; *cf.* Table I) along with a minor amount of rearrangement. The alkyl (phenyl or methyl) shifts in these tetrasubstituted epoxides are evidently quite sluggish.

Cyclohexene oxide, previously reduced to cyclohexanol with LAH alone,[7] was reduced with the mixed hydride in the hope of obtaining cyclopentylcarbinol, in view of the fact that reaction of this expoxide with phenylmagnesium bromide is reported[16] to give phenylcyclopentylcarbinol. However, the only product of reduction was cyclohexanol. It is not known whether this product was formed by direct reduction of the epoxide or *via* prior rearrangement to cyclohexanone; this information could be obtained by carrying out the reduction with lithium aluminum deuteride–$AlCl_3$.

Some of the rearrangements of epoxides postulated to occur during reduction with LAH–$AlCl_3$ are at variance with rearrangements reported elsewhere in the literature. For example, if the scheme shown in Fig. 1 operates, triphenylethylene oxide must rearrange nearly quantitatively to phenyl

---

[9] The large amount of 1,3-dichloropropanol obtained from epichlorohydrin is a result of the inverse addition technique. Since LAH is in deficit, attack of $AlCl_3$ on the epoxide competes successfully with hydride reduction. Halide attack by the mixed hydride has previously been found with propylene oxide which gives some 1-chloro-2 propanol (ref. 2). It is analogous to the well-known formation of halohydrins from epoxide by magnesium halide which occurs when epoxides are treated with Grignard reagents; *cf.* M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, Chapter XIV.

(10) J. Levy and L. Sfiras, *Compt. rend.*, **184**, 1335 (1927).

(11) E. L. Eliel and J. T. Traxler, This Journal, **78**, 4049 (1956).

(12) R. F. Nystrom, *ibid.*, **77**, 2544 (1955); **81**, 610 (1959).

(13) M. Stiles and R. P. Mayer, *ibid.*, **81**, 1497 (1959).

(14) S. Barton and C. R. Porter, *J. Chem. Soc.*, 2483 (1956).

(15) M. F. Hawthorne, W. D. Emmons and K. S. McCallum, This Journal, **80**, 6393 (1958).

(16) V. M. Micovic and A. Stojiljkovic, *Compt. rend.*, **236**, 2080 (1953).

benzhydryl ketone (by a hydride shift), since reduction with the "mixed reagent" gives phenylbenzhydrylcarbinol in over 90% yield. It has been reported, however,[17] that with boron trifluoride etherate triphenylethylene oxide gives triphenylacetaldehyde (phenyl shift) in 69% yield. Also the scheme shown in Fig. 2 requires a *t*-butyl shift to occur in the reduction of β-diisobutylene oxide (I) with the mixed hydride, whereas previous work[18] indicates that I rearranges mainly to *t*-butyl isopropyl ketone (V) containing but a little tetramethylbutyraldehyde (III) in the presence of alumina at 270–290°. Moreover, tetraphenylethylene oxide, which is unaffected by mixed hydride, does rearrange to benzopinacolone under the influence of mineral acid.[19] These facts confirm what already has been found elsewhere,[20] namely, that even where kinetic control is clearly operative, the products of pinacol rearrangements may depend on reaction conditions. We hope to investigate this point further.

Experimental

All melting and boiling points are uncorrected; infrared spectra recorded by Mr. Rolland S. Ro and Mr. Richard F. Love on a Baird model 4-55 instrument. Mass spectra were recorded by Mr. George Young and Mr. Peter Grillo on a Consolidated 21–103A instrument. Elementary analysis by Midwest Microlab, Indianapolis, Ind.

Epoxides.—Epichlorohydrin, α- and β-diisobutylene oxide, 3-phenyl-1,2-epoxypropane, 3-phenoxy-1,2-epoxypropane and cyclohexene oxide were commercial materials and were purified by distillation before use.

α-Methylstyrene oxide was prepared by the method described for the preparation of styrene oxide.[21] Fifty-nine grams (0.50 mole) of α-methylstyrene was added to 89.0 g. (0.50 mole) of N-bromosuccinimide and 200 ml. of water and the mixture stirred for one hour. The bromohydrin layer was taken up in ether and the aqueous layer extracted with ether. The crude bromohydrin obtained by concentration of the ether solution was added dropwise to 80.0 g. of sodium hydroxide in 300 ml. of water. The mixture was stirred for one hour at 60°, the epoxide taken up in ether and the ethereal solution dried over anhydrous potassium carbonate. Distillation gave 46.8 g. (78% yield) of α-methylstyrene oxide, b.p. 62° (2.3 mm.), $n^{20}\text{D}$ 1.5218 (lit.[22] b.p. 84–85° (14 mm.), $n^{20}\text{D}$ 1.5205).

Tetramethylethylene oxide was prepared according to a series of reactions suggested previously[23] without experimental details. Dimethylisopropylcarbinol, prepared from methyl isopropyl ketone and methylmagnesium iodide, was dehydrated by a variation of a previously described procedure.[24] Seventy-seven grams of dimethylisopropylcarbinol (containing traces of olefin due to thermal dehydration during distillation) was added to 400 g. of anhydrous oxalic acid,[25] and the mixture heated at reflux (63°) for 8 hours. The condenser was replaced with a distilling head and olefins collected at 748 mm. and finally under slight vacuum (180 mm.). The distillate was washed with ice-water, 5% sodium carbonate solution and ice-water. The material was dried over anhydrous calcium chloride and fractionally distilled to give 26.3 g. (19.4% yield from methyl isopropyl ketone) of 2,3-dimethyl-2-butene, b.p. 71.0–72.3° (745 mm.), $n^{20}\text{D}$ 1.4120 (lit.[23] b.p. 72.6–73.4°, $n^{20}\text{D}$ 1.4120). 2,3-Dimethyl-1-butene, 9.97 g. (7.3% yield), b.p. 55–57°, $n^{20}\text{D}$ 1.3906–1.3923 (lit.[23] 54–55.8°, $n^{20}\text{D}$ 1.3902), also was obtained. Diagnostic bands of 2,3-dimethyl-1-butene at 6.05 and 8.05 μ were absent in the infrared spectrum of the 2,3-dimethyl-2-butene. Perbenzoic acid was prepared by the method of Braun,[26] extracted into ether, dried over anhydrous sodium sulfate and titrated iodometrically. The ethereal solution (345 ml.) containing 19.4 g. (0.14 mole) of perbenzoic acid was cooled to 0° and 11.0 g. (0.13 mole) of 2,3-dimethyl-2-butene was added over a half-hour period at such a rate that the temperature did not rise above 3°. After the reaction mixture had been allowed to stand at 0° for 12 hours, a peracid determination showed that 95% of the olefin had reacted. The ethereal solution was washed with 10% sodium hydroxide, water and portions of dilute ferrous sulfate solution until no further color change was observed in the aqueous layer. The above process was repeated using 21.4 g. (0.155 mole) of perbenzoic acid and 13.4 g. (0.16 mole) of 2,3-dimethyl-2-butene. The combined solutions from both epoxidations were dried over anhydrous potassium carbonate, concentrated and the crude oil fractionally distilled to give 13.6 g. (47% yield) of tetramethylethylene oxide, b.p. 90–90.5° (741 mm.), $n^{20}\text{D}$ 1.4010 (lit.[23] b.p. 90–93°, $n^{20}\text{D}$ 1.3986).

Tetraphenylethylene Oxide from 1,1,2,2-Tetraphenylethanol.[27]—Anhydrous ammonia (400 ml.) was placed in a one-liter flask equipped with a stirrer, addition funnel and acetone–Dry Ice condenser capped with soda-lime. A crystal of pulverized ferric nitrate was added to the ammonia. Small pieces of potassium metal (8.6 g., 0.22 g. atom) were added over a period of one hour and the Dry Ice condenser replaced with a water-cooled condenser. A solution of 33.65 g. (0.20 mole) of diphenylmethane in 400 ml. of sodium-dried ether was added over a period of one hour. Excess ammonia was removed over a 6-hour period by stirring and the mixture boiled for 2 hours on a steam-bath. A solution of 36.44 g. (0.20 mole) of benzophenone in 100 ml. of sodium-dried ether was added. Magnesium bromide etherate was prepared by adding 35.16 g. (0.22 g. atom) of bromine to 5.35 g. (0.22 g. atom) of magnesium and 100 ml. of ether at room temperature,[28] and added to the reaction mixture. After boiling on a steam-bath for 1.5 hours, water and dilute hydrochloric acid were added. The precipitate was filtered and washed with copious amounts of water to remove magnesium bromide. The ether layer in the filtrate was separated and concentrated and the resulting crystals washed with ether to remove the red coloration and combined with the above solid. The crude material was dissolved in hot dioxane, decolorized with animal charcoal, and the solution diluted with water. On standing, there was obtained 42.0 g. (70% yield) of 1,1,2,2-tetraphenylethanol, m.p. 242–242.5° (lit.[29] m.p. 244°). Its infrared spectrum was identical with that of an authentic sample, kindly supplied by Professor David Y. Curtin, University of Illinois; m.p. 243–243.5°, mixed melting point 242–243.5°.

Thirty-five grams (0.098 mole) of 1,1,2,2-tetraphenylethanol suspended in 1400 ml. of dry carbon tetrachloride was stirred with 40.3 g. (0.224 mole) of N-bromosuccinimide and 1.75 g. of benzoyl peroxide for one hour and then boiled under reflux for an additional hour. Sufficient sodium bisulfite solution was added to remove the bromine coloration and the carbon tetrachloride layer was washed with water and dried over anhydrous potassium carbonate. The dried solution was concentrated to *ca.* 200 ml. and 200 ml. of ethanol added. The crystals formed were washed with ethanol to give 27.0 g. of material, m.p. 195–205°. Recrystallization from chloroform and petroleum ether gave 10.6 g. (31% yield) of tetraphenylethylene oxide, m.p. 206–

---

[17] A. C. Cope, P. A. Trumbull and E. R. Trumbull, THIS JOURNAL, **80**, 2844 (1958).

[18] E. J. Gasson, A. K. Graham, A. F. Milledge, I. K. M. Robson, W. Webster, A. M. Wild and D. P. Young, *J. Chem. Soc.*, 2170 (1954). The same authors, as well as W. J. Hickinbottom, *ibid.*, 1331 (1948), also treated the epoxide I with sulfuric acid in the liquid phase (water or acetic acid solvent), but this resulted in little rearrangement, the major products being 2,4,4-trimethylpentane-2,3-diol or its monoacetate and 2,4,4-trimethylpent-1-en-3-ol (VII).

[19] H. J. Gebhart and K. H. Adams, THIS JOURNAL, **76**, 3925 (1954).

[20] *E.g.*, R. E. Lyle and G. G. Lyle, *ibid.*, **74**, 4059 (1952); G. G. Lyle, R. A. Covey and R. E. Lyle, *ibid.*, **76**, 2713 (1954); B. M. Benjamin and C. J. Collins, *ibid.*, **78**, 4329 (1956).

[21] C. O. Guss and R. Rosenthal, *ibid.*, **77**, 2549 (1955).

[22] E. L. Eliel and J. P. Freeman, *ibid.*, **74**, 923 (1952).

[23] W. J. Hickinbottom and D. R. Hogg, *J. Chem. Soc.*, 4200 (1954).

[24] I. Schurman and C. E. Boord, THIS JOURNAL, **55**, 4930 (1933).

[25] E. Bowden, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 424.

[26] G. Braun, *ibid.*, p. 431.

[27] After this paper was written, the synthesis of tetraphenylethanol by a related method was described by P. J. Hamrick and C. R. Hauser, THIS JOURNAL, **81**, 2096 (1959).

[28] C. G. Swain and H. B. Boyles, *ibid.*, **73**, 870 (1951).

[29] A. Banchetti, *Gazz. chim. ital.*, **72**, 74 (1942).

208° (lit.[30] m.p. 208°), as white needles.[31] A second crop of yellow prisms, m.p. 200–208°, weighing 9.9 g. was obtained from the mother liquor. Chromatography on alumina showed this second crop to contain *ca.* 40% tetraphenylethylene oxide and the analytical yield of epoxide is undoubtedly higher than reported above. Attempts to identify a fraction, m.p. 195–215°, obtained by chromatography were unsuccessful.

Reductions with lithium aluminum hydride alone (Table I) were carried out by means of hydride slurry in sodium-dried ether, using 0.275–0.313 mole of hydride per mole of epoxide.[32] Reaction mixtures were decomposed with water and sulfuric acid, except in the case of epichlorohydrin, α-methylstyrene oxide and the tetrasubstituted epoxides where sodium potassium tartrate solutions were used in lieu of sulfuric acid. Products were isolated in general by simple extraction with ether. The reduction of epichlorohydrin was carried out by the inverse addition of standard ethereal hydride solution and the products were isolated by continuous ether extraction.

Reductions with lithium aluminum hydride and aluminum chloride (Table II) were carried out as previously reported,[2] except that reaction mixtures from reduction of epichlorohydrin, α-methylstyrene oxide, cyclohexene oxide and the tetrasubstituted epoxides were decomposed with water and sodium potassium tartrate solution and products were isolated by simple extraction with ether. The reduction of epichlorohydrin was carried out by the inverse addition of the mixed hydride and the products isolated by continuous ether extraction.

Isomerization of β-Diisobutylene Oxide (I) with Aluminum Chloride.—A solution of 15.5 g. (0.116 mole) of anhydrous aluminum chloride in 50 ml. of sodium-dried ether was prepared at ice-bath temperature. A solution of 12.0 g. (0.094 mole) of I in 50 ml. of sodium-dried ether was added at room temperature and the mixture refluxed for 2.5 hours. Water was added, the aqueous layer extracted with ether and the combined ether layers dried over anhydrous potassium carbonate. Concentration of the ethereal solution gave 12.0 g. (100% return) of halogen-free semi-solid, which was stored under a nitrogen atmosphere. A preliminary experiment indicated that the product was easily oxidized to a carboxylic acid, m.p. 197–198° (lit.[33] reports m.p. 197–198° for 2,2,3,3-tetramethylbutanoic acid). The infrared spectrum of the isomerization product showed bands at 2.91 (very weak), 3.70 (medium) and 5.8-6.0 μ (strong). The product gave a 2,4-dinitrophenylhydrazone (62.4% yield), m.p. 141–161°, unchanged by elution chromatography on alumina. The combined eluted fractions were recrystallized from absolute ethanol to give orange needles, m.p. 164–165°. Addition of water to the mother liquor gave yellow needles, m.p. 162–164°, undepressed by admixture of the orange material. The literature[34] reports m.p. 163–164° for 2,2,3,3-tetramethylbutyraldehyde (III) 2,4-dinitrophenylhydrazone. The melting point of both crops of the 2,4-dinitrophenylhydrazone was depressed by admixture of an authentic sample of 2,4,4-trimethylpentanone-3 (V) 2,4-dinitrophenylhydrazone, m.p. 163–164° (lit.[34] m.p. 163–164°). 2,2,3,3-Tetramethylbutyraldehyde was characterized further by reduction of the crude isomerization product with lithium aluminum hydride in the usual manner. A portion of the semi-solid product of this reduction was chromatographed on alumina and gave two fractions: (a) liquid, b.p. 95–100° (17 mm.), $n^{20}\mathrm{D}$ 1.4512; (b) semi-solid, m.p. 138–148° raised to 149–150° after recrystallization from petroleum ether (lit.[35] reports m.p. 149–150° for 2,2,3,3-tetramethylbutanol-1). The infrared spectrum of fraction a showed no bands at 2.8–3 or 5.8–6 μ. The mass spectral pattern of (a) showed *m/e* values up to and including 257 (dimer[36] of diisobutylene oxide, mol. wt. 256). Fraction b gave a 3,5-dinitrobenzoate, m.p. 92–94° (lit.[35] reports m.p. 88–90° for 2,2,3,3-tetramethylbutyl 3,5-dinitrobenzoate).

The crude reduction product was analyzed by mass spectrometry as an acetone solution using *m/e* values of 73, 87, 112, 157: 2,2,3,3-tetramethylbutanol-1, 94.7%; 2,4,4-trimethylpentanol-3, 4.4%; dimer, 0.9%; 2,4,4-trimethylpent-1-en-3-ol, absent. Vapor phase chromatography (*vide infra*) gave this analysis: 2,2,3,3-tetramethylbutanol-1, 91.2%; 2,4,4-trimethylpentanol-3, 6.4%; dimer 2.4%; 2,4,4-trimethylpent-1-en-3-ol, absent.

Reaction of 3-Phenyl-1,2-epoxypropane with Aluminum Chloride.—To a solution of 20.0 g. (0.15 mole) of anhydrous aluminum chloride in 75 ml. of sodium-dried ether was added a solution of 20.1 g. (0.15 mole) of 3-phenyl-1,2-epoxypropane in 75 ml. of sodium-dried ether. After completion of the addition, the mixture was allowed to stand for a 6-hour period and hydrolyzed with water and sulfuric acid. The aqueous layer was extracted with ether and the combined ether layers dried over anhydrous sodium sulfate. Distillation gave three fractions, b.p. 107–200° (2.0–4.8 mm.), 1.5260–1.5534. All fractions gave a positive test for halogen and a negative test for glycol. The infrared spectra of the fractions were similar to each other and to that of an authentic sample of 1-chloro-3-phenyl-2-propanol, b.p. 113° (2 mm.), $n^{20}\mathrm{D}$ 1.5441 (lit.[37] b.p. 125–127° (11–12 mm.), $n^{20}\mathrm{D}$ 1.5426), but contained a band at 8.5–9.2 μ not present in the authentic spectrum. Diagnostic bands of 3-phenyl-1,2-epoxypropane at 10.4 and 11.8 μ as well as carbonyl absorption bands (5.8–6 μ) were absent. Each of the fractions formed a *p*-nitrobenzoate ester, m.p. 72–74°, not depressed by admixture of an authentic sample of 1-chloro-3-phenyl-2-propyl *p*-nitrobenzoate, m.p. 72–74°. An analytical sample of the authentic ester melted at 73–74°.

Anal. Calcd. for $C_{16}H_{14}ClNO_4$: C, 60.07; H, 4.45; Cl, 11.10; N, 4.38. Found: C, 60.20; H, 4.51; Cl, 11.19; N, 4.34.

The *p*-nitrobenzoate ester of the chlorohydrin also was obtained by reaction of 3-phenyl-1,2-epoxypropane with *p*-nitrobenzoyl chloride.

Mixed Hydride Reduction of 1-Chloro-3-phenyl-2-propanol.—Anhydrous aluminum chloride (8.92 g., 0.067 mole) was dissolved in 50 ml. of sodium-dried ether at ice-bath temperature. Standardized 1.05 *M* ethereal lithium aluminum hydride (50 ml., 0.0525 mole) was added at ice-bath temperature. A white precipitate in the mixed hydride failed to dissolve after stirring for one hour. A solution of 17.0 g. (0.10 mole) of 1-chloro-3-phenyl-2-propanol in ether was added and the mixture was boiled for 2.5 hours. After hydrolysis with water and sulfuric acid the aqueous layer was extracted with ether and the ether layers dried over anhydrous potassium carbonate. Distillation gave two fractions: (a) 7.03 g., b.p. 90–103° (1.2 mm.), $n^{20}\mathrm{D}$ 1.5388; (b) 6.42 g., b.p. 103–105° (1.2 mm.), $n^{20}\mathrm{D}$ 1.5435. The infrared spectrum of fraction a was similar to that of 1-chloro-3-phenyl-2-propanol, but contained a band characteristic of 1-phenyl-2-propanol at 10.7 μ. The infrared spectrum of fraction b was identical with the starting chlorohydrin.

Reaction of β-Diisobutylene Oxide (I) and 3,5-Dinitrobenzoyl Chloride. A Preparation of 2,4,4-Trimethylpent-1-en-3-ol.—Ten grams (0.082 mole) of I and 20.0 g. (0.086 mole) of 3,5-dinitrobenzoyl chloride were dissolved in 150 ml. of dry pyridine and heated on a steam-bath for two hours. The solution was poured into 250 ml. of 10% hydrochloric acid and ice. The crystals were filtered, washed with water, dilute sodium hydroxide and water, and recrystallized three times from ethyl acetate and petroleum ether to give 4.65 g. (17% yield) of the 3,5-dinitrobenzoate of 2,4,4-trimethylpent-1-en-3-ol, m.p. 120–121° (lit.[18] m.p. 120–121°). The ester (2.32 g., 0.0069 mole) was dissolved in 25 ml. of methanol and 25 ml. of 20% aqueous potassium hydroxide solution and boiled for a 4-hour period. The reaction mixture was extracted with ether and the extracts dried over anhydrous potassium carbonate. Distillation gave 0.51 g. (58% yield) of 2,4,4-trimethylpent-1-en-3-ol, b.p. 151° (748 mm.), $n^{20}\mathrm{D}$ 1.4416 (lit.[36] b.p. 153–154° (760 mm.), $n^{20}\mathrm{D}$ 1.4376).

---

(30) A. Banchetti, *Gazz. chim. ital.*, **71**, 685 (1941).

(31) We are indebted to Professor K. H. Adams, St. Louis University, for an exchange of information regarding the preparation of tetraphenylethylene oxide from the carbinol and NBS which was independently discovered in his laboratory and ours.

(32) It was found that the use of the slurry rather than of a standard ethereal solution of hydride did not affect the yield nor the ratio of products obtained in the reduction of styrene oxide.

(33) K. L. Loening, A. B. Garrett and M. S. Newman, THIS JOURNAL, **74**, 3929 (1952).

(34) A. Byers and W. J. Hickinbottom, *J. Chem. Soc.*, 284 (1948).

(35) F. C. Whitmore, R. E. Marker and L. Plambeck, THIS JOURNAL, **63**, 1626 (1941).

(36) W. J. Hickinbottom, *J. Chem. Soc.*, 1331 (1948), also has isolated trace amounts of a dimer from the reaction of epoxide I and sulfuric acid (*cf.* ref. 18).

(37) H. Gilman, B. Hofferth and J. B. Honeycutt, THIS JOURNAL, **74**, 1594 (1952).

The product gave negative tests for halogen and a positive test for olefinic unsaturation with tetranitromethane. Its infrared spectrum showed a band at 6.1 μ and the absence of bands at 5.8–6.0 μ.

Analysis of Products.—Preliminary qualitative analysis of all products was made by comparison of infrared spectra with spectra of authentic samples. When the physical constants and the spectrum of the product indicated a pure compound had been obtained, a characteristic derivative generally was prepared and compared with an authentic sample. Authentic samples of the carbinols listed as products in Tables I and II were commercial materials except: 3,3-dimethyl-2-butanol by the LAH reduction[38] of pinacolone[39]; 1-chloro-2-propanol by the LAH reduction[40] of chloroacetone,[41] 3-phenoxy-1-propanol by the reaction of sodium phenoxide with trimethylene chlorohydrin,[42] 1-phenoxy-2-propanol by LAH reduction of 1-phenoxy-2-propanone, 2,4,4-trimethylpentanol-3 by the reaction of isobutyraldehyde and *t*-butylmagnesium chloride,[43] and cyclopentylcarbinol by the LAH reduction of cyclopentanecarboxyaldehyde.[44] Samples of 2,4,4-trimethylpentanol-1, 2,4,4-trimethylpentanol-2 and 2,2,3,3-tetramethylbutanol-1 were not readily available and these products were characterized through suitable derivatives.

When a mixture was obtained, the product was analyzed quantitatively by mass spectrometry[45] or by vapor phase chromatography. The vapor phase chromatographic analysis was carried out on a Wilkens Aerograph instrument in conjunction with a Brown Electronik recorder. Helium was used as the carrier gas maintained at 8 p.s.i. at flow rates of 60–100 ml. per minute. Components were identified by comparison of their retention times with the retention times of authentic samples. When necessary components were collected and identified by infrared spectroscopy. Areas under the peaks were measured with a planimeter and the mole ratio of components calculated from area ratios. Authentic mixtures were analyzed in all cases to verify the assumption that peak areas were proportional to mole ratios. Table III gives the epoxide reduced and the substrate and temperature used for an efficient separation of the products obtained as shown in Tables I and II.

TABLE III

CONDITIONS FOR VAPOR PHASE CHROMATOGRAPHIC ANALYSES

Products from	Substrate	T, °C.
Tetramethylethylene oxide	Ucon-polar	88–89
Epichlorohydrin	Tide detergent	100–105
α-Methylstyrene oxide	Tide detergent	17
α-Diisobutylene oxide	Ucon-polar	129
β-Diisobutylene oxide	Ucon-polar	129
Cyclohexene oxide	Ucon-polar	139

Acknowledgment.—This work is a contribution from the Radiation Project of the University of Notre Dame, supported, in part, under Atomic Energy Commission contract AT(11-1)-38 and Navy loan equipment contract Nonr-06900. We are indebted to Professor V. J. Traynelis and Dr. Zoltan Welvart for helpful suggestions. The vapor phase chromatographic equipment for this investigation was acquired under National Science Foundation Grant G-4058.

NOTRE DAME, IND.

---

(38) *Cf.* A. A. Bothner-By, THIS JOURNAL, **73**, 846 (1951).

(39) G. A. Hill and E. W. Flosdorf, ref. 25, p. 462.

(40) C. A. Stewart and C. A. VanderWerf, THIS JOURNAL, **76**, 1259 (1954).

(41) E. R. Buchanan and H. Sargent, *ibid.*, **67**, 400 (1945).

(42) S. G. Powell, *ibid.*, **45**, 2708 (1923).

(43) F. C. Whitmore and A. L. Houk, *ibid.*, **54**, 3714 (1932).

(44) A generous sample was supplied by Professor George F. Hennion, University of Notre Dame.

(45) *Cf.* E. L. Eliel, T. J. Prosser and G. W. Young, *J. Chem. Ed.*, **34**, 72 (1957), and literature there cited.

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

Reduction with Metal Hydrides. VIII. Reductions of Ketones and Epimerization of Alcohols with Lithium Aluminum Hydride–Aluminum Chloride[1,2]

BY ERNEST L. ELIEL AND MARK N. RERICK

RECEIVED JULY 28, 1959

Whereas lithium aluminum hydride (LAH) reduced 4-*t*-butylcyclohexanone to a mixture of 90% *trans*-4-*t*-butylcyclohexanol (I) and 10% *cis*-4-*t*-butylcyclohexanol (II), LAH–$AlCl_3$ (1:4 ratio) yields 80% *trans*- and 20% *cis*-alcohol under kinetically controlled conditions. Addition of excess ketone or acetone at the end of the reaction leads to thermodynamic control of the reaction products with conversion of the alcohol mixture to one containing over 99% of the *trans* isomer in less than fifteen minutes. The fast reaction and overwhelming preponderance of the *trans* isomer is ascribed to the nature of the species equilibrated which are bulky aluminum complexes, not readily accommodated in the axial position of the cyclohexane ring. The equilibration procedure has been utilized to determine the conformational equilibrium values for methyl and phenyl groups. The conformational free energy differences (A-values) are 1.5 ± 0.1 kcal./mole for methyl and *ca.* 2.6 kcal./mole for phenyl.

There have been several recent papers[3] indicating that the reducing action of LAH–$AlCl_3$ combinations differs from that of LAH alone. For example, in our own laboratories we have observed that epoxides may be reduced in a different way by LAH–$AlCl_3$ than by LAH alone[2,4] and that acetals, unaffected by LAH, are reduced to ethers by the "mixed reagent."[5] Wheeler and Mateos[6] have reported that cholestanone, reduced to a mixture of 88% 3-β-hydroxycholestane (equatorial OH) and 12% 3-α-hydroxycholestane (axial OH) by LAH, gives exclusively the beta (equatorial) isomer with the mixed reagent. The need for substantial quantities of *trans*-4-*t*-butylcyclohexanol (I, equatorial hydroxyl) in other work prompted us to try to apply this reduction to the commercially available 4-*t*-butylcyclohexanone.

---

(1) Presented in part at the San Francisco National Meeting, Am. Chem. Soc., April 14, 1958.

(2) Paper VII, E. L. Eliel and M. N. Rerick, THIS JOURNAL, **82**, 1362 (1960).

(3) For a summary, see M. N. Rerick, "Selective Reductions of Organic Compounds with Complex Metal Hydrides," Metal Hydrides, Inc., Beverly, Mass., 1959.

(4) E. L. Eliel and D. W. Delmonte, THIS JOURNAL, **80**, 1744 (1958).

(5) E. L. Eliel and M. N. Rerick, *J. Org. Chem.*, **23**, 1088 (1958). See also E. L. Eliel and V. G. Badding, THIS JOURNAL, **81**, 6087 (1959).

(6) O. H. Wheeler and J. L. Mateos, *Chemistry & Industry*, 395 (1957); *Can. J. Chem.*, **36**, 1431 (1958).