115. *The Reaction of* 1 : 4-*Dichloro-2* : 3-*epoxybutane with Sodium Methoxide.*

By A. W. Adams, E. G. E. Hawkins, G. F. Oldham, and R. D. Thompson.

The reaction of 1 : 4-dichloro-2 : 3-epoxybutane with sodium methoxide has been shown to provide a complex mixture, including 1 : 3 : 4-trimethoxybutan-2-ol, 3-methoxy-2-methoxymethyloxetan, and *cis*- and *trans*-4-chloro-1-methoxybut-3-en-2-ol. Possible reaction routes are considered.

The reaction of simple epoxides with alkali (or metal alkoxides) normally leads to glycols (or glycol monoethers);[1] epichlorohydrin similarly yields glycerol (or glycerol ethers).[2] A dichloroepoxyalkane, 1 : 2-dichloro-3 : 4-epoxybutane, has been found to provide under alkaline conditions mainly 2-chloro-3 : 4-epoxybut-1-ene by preferential loss of hydrogen chloride, although further reaction with a metal alkoxide brings about opening of the epoxide ring.[3] Studies on the points of initial attack of 1-bromo-2 : 3- and 3-bromo-1 : 2-epoxybutane by sodium methoxide [4] and sodium phenoxide [5] have indicated that variations in the reactant cause some alteration in the mode of attack, so that sometimes the halogen is first replaced and at other times the epoxide ring is first opened. However, a metal alkoxide and the symmetrical 1 : 4-dichloro-2 : 3-epoxybutane could lead to a variety of products, depending on the relative reactivities of the chloro-atoms and the epoxy-group in this molecule. Possible reaction routes (using sodium methoxide) are shown in the diagram.

Route 1 involves initial replacement of chlorine by methoxyl followed either by similar replacement of the second chlorine atom (1a) or by opening of the epoxide ring in one of two directions (1b or 1c). Both routes (1a) and (1b) would lead finally to 1 : 3 : 4-trimethoxybutan-2-ol (IV), whereas route (1c) might be expected to yield either 1 : 3-dimethoxybut-3-en-2-ol (VIII) or 3-methoxy-2-methoxymethyloxetan (IX). Route 2, on the other hand, involves opening of the epoxide ring followed by immediate ring closure to 1-chloro-3 : 4-epoxy-2-methoxybutane (XI) and thence by three possible routes to

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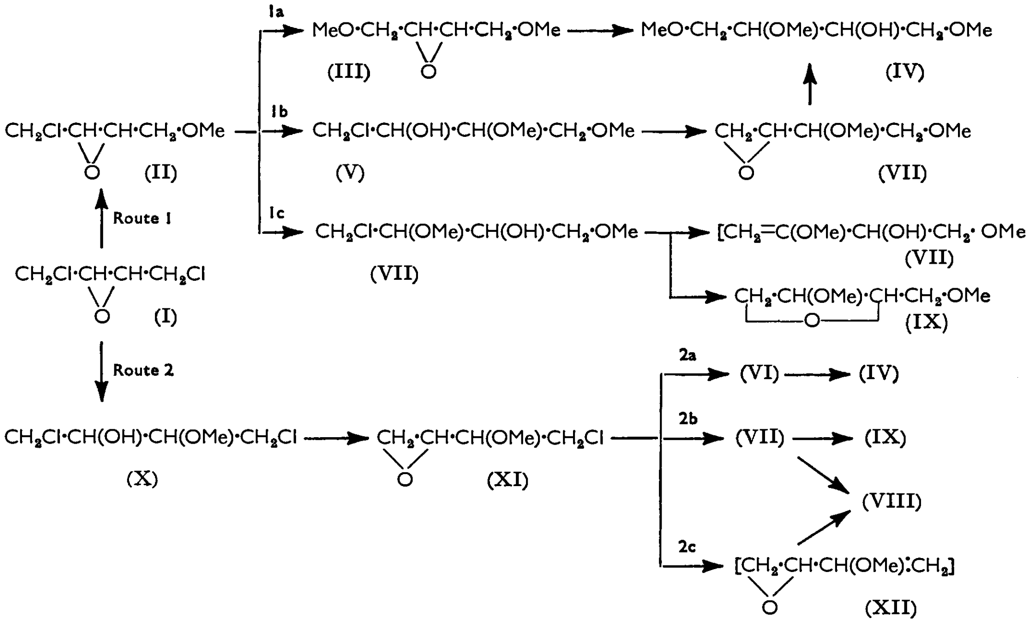
[1] Graham, Millidge, and Young, *J.*, 1954, 2180; Swern, Billen, and Knight, *J. Amer. Chem. Soc.*, 1949, **71**, 1152; Kadesch, *ibid.*, 1946, **68**, 41.

[2] Huntress, " Organic Chlorine Compounds," John Wiley & Sons, New York, 1948, pp. 668—669.

[3] Hawkins, *J.*, 1959, 248.

[4] Waters and VanderWerf, *J. Amer. Chem. Soc.*, 1954, **76**, 709.

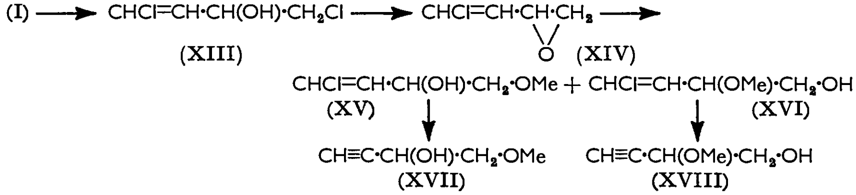
[5] Rowton and Russell, *J. Org. Chem.*, 1958, **23**, 1002.



1 : 3 : 4-trimethoxybutan-2-ol (route 2a), to the oxetan (IX) or unsaturated hydroxy-ether (VIII) (routes 2b, 2c).

Treatment of the dichloroepoxybutane with an excess of sodium methoxide in boiling methanol led to a product with a wide boiling range. Examination of the distillation fractions showed that two of the predicted compounds, *i.e.*, trimethoxybutanol and the oxetan, were major constituents (*ca.* 40% and 16% respectively), but the dimethoxybutenol (VIII) could not be identified.

However, there were other, unexpected, components in the product: the bulk of these was *trans*-4-chloro-1-methoxybut-3-en-2-ol (XV) (*ca.* 19%), with smaller amounts of the corresponding *cis*-isomer and *trans*-4-chloro-2-methoxybut-3-en-1-ol (XVI), and also 1-methoxybut-3-yn-2-ol (XVII) (up to 6%). These compounds presumably arose by a third route, as follows:



The products from this third route were isolated by gas-phase chromatography on a Tween–Celite column at 160°. Infrared spectroscopy showed the presence of hydroxyl and methoxyl in each compound; the relative positions of these groups were found by catalytic hydrogenation (using an alkaline Raney nickel catalyst) to 1-methoxybutan-2-ol (from XV and XVII) or 2-methoxybutan-1-ol (from XVI). The presence of the *trans*-isomers of (XV) and (XVI) was demonstrated by the appearance of a strong band at 938 cm.$^{-1}$ (*trans*-1-halogen-substituted alk-1-ene [6]) in their infrared spectra: the spectra of the corresponding *cis*-isomers were similar in many ways except that the 938 cm.$^{-1}$ band was absent. A band at 3300 cm.$^{-1}$ in the spectrum of (XVII) agreed with the postulated acetylenic

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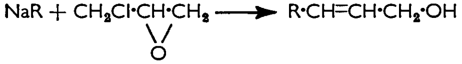
[6] Bellamy, "The Infra Red Spectra of Complex Molecules," Methuen, London, 1958, p. 46.

structure.[7] The epoxide (XIV), not identified amongst the reaction products, was synthesised from 1-chlorobutadiene *via* the bromohydrin. From its spectrum this synthetic epoxide appeared to be largely the *trans*-compound, but reaction with acid methanol yielded *ca.* 70% of *cis*-4-chloro-2-methoxybut-3-en-1-ol (XVI) with *ca.* 30% of the *trans*-isomer, whilst with sodium methoxide it provided a mixture of the two acetylenic compounds (XVII and XVIII), together with *cis*- and *trans*-compounds (XV) and (XVI) [mainly the *cis*- and *trans*-components (XV)]. The products from the synthetic 1-chloro-3 : 4-epoxybut-1-ene and from 1 : 4-dichloro-2 : 3-epoxybutane were compared by means of their physical properties and by mixed m.p.s of their 3 : 5-dinitrobenzoates.

Isomerisation of epoxides to unsaturated alcohols in the presence of acid is known,[8] but there are few references to this rearrangement under alkaline conditions; however, the products of reaction of epichlorohydrin with sodium toluene-*p*-sulphinate,[9] sodium cyanide,[10] and sodium acetylide [11] suggest that a similar mechanism was involved in these cases.



$$\text{NaR} + \text{CH}_2\text{Cl·}\underset{\diagdown\text{O}\diagup}{\text{CH·CH}_2} \longrightarrow \text{R·CH=CH·CH}_2\text{·OH}$$

The acetylenic secondary alcohol (XVII) evidently arose by dehydrochlorination of the compound (XV). A similar (slow) production of methoxybutynols has been noticed on reaction of 3-chloro-1-methoxybut-3-en-2-ol or 3-chloro-2-methoxybut-3-en-1-ol with sodium methoxide.[12]

Other compounds identified in minor amounts in the product included diacetyl, 1-chloro-2 : 3-epoxy-4-methoxybutane (II), and 1 : 2-epoxy-3 : 4-dimethoxybutane (VI).

In order to obtain further information on the intermediate stages of this reaction, 1 : 4-dichloro-2 : 3-epoxybutane was treated with only one mol. of sodium methoxide. The product contained, in addition to much starting material and the compounds obtained when an excess of sodium methoxide was used, a large amount of 4-chloro-1 : 3-dimethoxybutan-2-ol (VII), with some 1-chloro-3 : 4-dimethoxybutan-2-ol (V), 2 : 3-epoxy-1 : 4-dimethoxybutane (III), and possibly a trace of 1-chloro-3 : 4-epoxy-2-methoxybutane (XI).

From the above it is evident that all three routes are involved in the reaction, although the relatively large amount of trimethoxybutanol isolated suggested that route 1 is the preferred one. That the trimethoxybutanol arises mainly by this route was demonstrated by study of the reaction of the intermediate epoxide (II) with sodium methoxide: there were produced trimethoxybutanol (IV; *ca.* 80%), the oxetan (IX; *ca.* 8%), 2 : 3-epoxy-1 : 4-dimethoxybutane (III; 2%), and unchanged epoxide (II; 6%). The small amount of oxetan obtained from (II) evidently arose by route (1c) since 4-chloro-1 : 3-dimethoxybutan-2-ol (VII) under similar conditions gave this compound (IX) almost completely, with less than 10% of the ether (IV). The majority of the oxetan formed in the overall reaction arose *via* route 2; both of the intermediates (X) and (XI) independently gave 75—80% of (IX) and 20—25% of (IV) on treatment with sodium methoxide.

It appears, therefore, that the reaction of 1 : 4-dichloro-2 : 3-epoxybutane with sodium methoxide follows largely the routes (1a), (1b), (2b), and (3) and only slightly routes (1c) and (2b); there is no evidence that route (2c) is involved.

Most of the compounds formulated in the diagram were synthesised as reference materials for spectroscopy and chromatography, starting from 1 : 4-dichloro-2 : 3-epoxybutane and 1 : 2-dichloro-3 : 4-epoxybutane. In these syntheses the direction of ring opening of several epoxides was found to differ from that generally accepted. 1 : 2-Epoxides normally provide secondary alcohols under alkaline, and primary alcohols under

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[7] Ref. 6, p. 58.

[8] Hickinbottom, *J.*, 1948, 1331; Gasson, Graham, Millidge, Robson, Webster, Wild, and Young, *J.*, 1954, 2170.

[9] Culvenor, Davies, and Savige, *J.*, 1949, 2198.

[10] Culvenor, Davies, and Haley, *J.*, 1950, 3123.

[11] Haynes, Heilbron, Jones, and Sondheimer, *J.*, 1947, 1583.

[12] Hawkins, unpublished work.

acid, reaction conditions;[1] however, epichlorohydrin gives mainly secondary alcohols under both sets of conditions (Swern *et al.*[2]), and it seems probable that the way the ring opens depends to some extent on the substituents in the epoxide molecule and on the structure of the reacting alcohol (Swern *et al.*[2]).

1 : 2-Dichloro-3 : 4-epoxybutane with acid methanol gave the secondary alcohol, 3 : 4-dichloro-1-methoxybutan-2-ol; this was proved by conversion of the product into 1-chloro-2 : 3-epoxy-4-methoxybutane by alkali. Similarly, 1 : 2-epoxy-3 : 4-dimethoxybutane (VI) with acid methanol yielded the same 1 : 3 : 4-trimethoxybutan-2-ol as did 2 : 3-epoxy-1 : 4-dimethoxybutane (III); and with hydrogen chloride the epoxide (VI) gave 1-chloro-3 : 4-dimethoxybutan-2-ol (V), one of the products of reaction of 1-chloro-2 : 3-epoxy-4-methoxybutane (II) with acid methanol. 1-Chloro-3 : 4-epoxy-2-methoxybutane (XI) with hydrogen chloride also gave a secondary alcohol, 1 : 4-dichloro-3-methoxybutan-2-ol (X), identical with that obtained by addition of acid methanol to 1 : 4-dichloro-2 : 3-epoxybutane (I). 1-Chloro-3 : 4-epoxy-2-methoxybutane (XI) with acid methanol forms the secondary alcohol, 4-chloro-1 : 3-dimethoxybutan-2-ol (VII); this alcohol, and the original epoxide (XI), react with sodium methoxide to give 2-methoxymethyl-3-methoxyoxetan (IX), demonstrating that both acid and alkaline methanol here open the epoxide ring in the same direction.

However, 2-chloro-3 : 4-epoxybut-1-ene follows the normal pattern, providing the corresponding secondary alcohol with sodium methoxide and the primary alcohol with acid methanol. The reactions of 1-chloro-3 : 4-epoxybut-1-ene with acid methanol and sodium methoxide have already been mentioned.

The 1 : 4-dichloro-2 : 3-epoxybutane used in this work was prepared by oxidation of 1 : 4-dichlorobut-2-ene with performic acid, with use of a shorter reaction time and a smaller quantity of formic acid ($\frac{1}{4}$—$\frac{1}{2}$ mol.) than was used by Owen.[13] Owen reported that he isolated only *meso*-1 : 4-dichlorobutane-2 : 3-diol, m. p. 127°, from this reaction; in our work, however, with a mixture of *cis*- and *trans*-dichlorobutene, both the *meso*- and the (±)-glycol were isolated by fractional crystallisation of the products of hydration of the epoxide. The mixture of *cis*- and *trans*-epoxide was not appreciably separable by distillation.

EXPERIMENTAL

Preparation of 1 : 4-*Dichloro*-2 : 3-*epoxybutane*.—(a) *Using performic acid.* 85% Hydrogen peroxide (32 c.c.) was added, with stirring, during 1 hr. to a mixture of 1 : 4-dichlorobut-2-ene (mixture of *trans* 70% and *cis* 30%; 125 g.) and 98—100% formic acid (23 c.c.) at 60°; stirring at 60° was maintained for a further 2 hr. The product was cooled, added to water (*ca.* 400 c.c.), and extracted with ether. The aqueous phase gave no residue on evaporation, and the ethereal phase on drying, evaporation, and distillation gave fractions: (1) (4·7 g.), b. p. <150°; (2) (49·2 g.), b. p. 150—160°, n_D^{20} 1·4870; (3) (11·8 g.), b. p. 160—180°, n_D^{20} 1·4847; (4) (52·6 g.), b. p. 180—186·5°, n_D^{20} 1·4771; and residue (3·8 g.). Fraction 2 was unchanged dichlorobutene, and fraction 4 was the epoxide.

Redistillation gave the pure *epoxide*, b. p. 187—188°, n_D^{20} 1·4763 (Found: C, 34·15; H, 4·3; Cl, 50·1. $C_4H_6OCl_2$ requires C, 34·0; H, 4·25; Cl, 50·4%). The Nicholet–Poulter and other methods for epoxide determination gave unsatisfactory figures with this compound.

(b) Via *the bromohydrin*. *N*-Bromosuccinimide (19 g.) in water (80 c.c.) was stirred at room temperature with 1 : 4-dichlorobut-2-ene (12·5 g.) in ether (80 c.c.) until all the solid had disappeared ($21\frac{1}{2}$ hr.). The combined ethereal layer and extracts were washed, dried, and distilled to give the *bromohydrin* (16·3 g.), b. p. 70—80°/0·7 mm., n_D^{20} 1·5352 (Found: C, 21·8; H, 3·4; Br, 36·0; Cl, 31·7. $C_4H_5OBrCl_2$ requires C, 21·8; H, 2·2; Br, 36·3; Cl, 32·3%).

A solution of sodium hydroxide (4·2 g.) in water (15 c.c.) was added, during 10 min. at room temperature, to a stirred mixture of the bromohydrin (22 g.) and water (10 c.c.); after stirring had been continued for $1\frac{1}{2}$ hr. the product was worked up to give the epoxide (6·8 g.), b. p. 181—190°, n_D^{20} 1·4810 (Found: Cl, 50·9%), identical spectroscopically with that obtained by oxidation by performic acid.

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[13] Owen, *J.*, 1949, 241.

Hydration of 1 : 4-*Dichloro*-2 : 3-*epoxybutane*.—The epoxide (400 g.) was added gradually to 98—100% formic acid (200 g.); stirring was necessary to prevent local overheating in this exothermic reaction. The mixture was then heated under reflux for a short time, water was added, and boiling continued. Most of the formic acid was removed in steam, and the residual acid and water were evaporated under reduced pressure to leave the semi-solid, crude glycol. Crystallisation from carbon tetrachloride–ethyl acetate gave the *meso*-1 : 4-dichlorobutane-2 : 3-diol (224·6 g.; m. p. 124—126°); recrystallisation from ethyl acetate raised the m. p. to 126—129° (cf. ref. 13) (Found: C, 30·2; H, 5·0; Cl, 44·5. Calc. for $C_4H_8O_2Cl_2$: C, 30·2; H, 5·0; Cl, 44·7%). The diol provided a *bisphenylurethane*, m. p. 222—224° (from acetone) (Found: C, 54·6; H, 4·7; Cl, 17·7; N, 7·1. $C_{18}H_{18}O_4N_2Cl_2$ requires C, 54·4; H, 4·5; Cl, 17·9; N, 7·05%), almost insoluble in benzene.

The mother-liquors were distilled and appropriate cuts crystallised and recrystallised, to give the (±)-glycol (83·0 g.), m. p. 58—60° (Found: C, 30·4; H, 5·1; Cl, 44·5%) [*bisphenylurethane*, m. p. 170—172° (from benzene) (Found: C, 54·6; H, 4·4; Cl, 17·5; N, 7·0%)].

Reaction of 1 : 4-*Dichloro*-2 : 3-*epoxybutane with Sodium Methoxide*.—The products obtained from this reaction were identified by comparison with the synthetic compounds described below by infrared spectra, gas-phase chromatography, m. p. of derivatives, and catalytic hydrogenation. The chromatographic separations were carried out on columns of Tween–Celite at 160° or Apiezon–Celite at 117° with nitrogen carrier gas and a hydrogen-flame detector; Tween 60 is polyoxyethylene sorbitan monostearate, the Apiezon K was a high-vacuum grease from Messrs. Edwards, and the Celite was of 100—120 mesh.

(a) *Using* 2·5 *mols. of sodium methoxide*. (i) The epoxide (176 g.), in methanol (20 c.c.), was heated under reflux with sodium (75·2 g.) in methanol (600 c.c.) for 4 hr.; little change in the sodium methoxide content occurred during the last 2 hr., and *ca*. 80% of the calculated amount (based on chlorine) had then been consumed. The excess of alkali was exactly neutralised with ethereal hydrogen chloride, the product filtered, and the filtrate evaporated and distilled (4 ft., helices-packed column) to give fractions as tabulated.

Fr.	B. p. (13 mm.)	Wt. (g.)	n_D^{20}	Fr.	B. p. (13 mm.)	Wt. (g.)	n_D^{20}
1	58—61°	20·9	1·4256	12	85—88°	3·7	1·4618
2	61—63	5·3	1·4272	13	88—92	4·2	1·4538
3	63—65	5·1	1·4295	14	92—95	4·9	1·4430
4	65—70	4·8	1·4329	15	95—96	6·8	1·4362
5	70—71	6·3	1·4382	16	96—96·5	37·4	1·4319
6	71—75	4·8	1·4471	17	96·5—98	7·3	1·4339
7	75—80	5·0	1·4558	18	98—106	4·5	1·4390
8	80—82	6·4	1·4620	19	106—130	1·7	1·4461
9	82—83	8·4	1·4645	20	130—140	1·2	1·4549
10	83—84	10·1	1·4655	Res.	—	15·1	—
11	84—85	2·7	1·4647				

Infrared spectroscopy showed that the first five fractions consisted largely of 3-methoxy-2-methoxymethyloxetan, but that a carbonyl compound was present in fractions 2—8 (maximum in fr. 6). Fractions 5—17 (maximum in fr. 10) contained an unsaturated compound with a *trans*-1-substituted alk-1-ene system and hydroxyl and methoxyl groups. Above fraction 12 the main constituent appeared to be 1 : 3 : 4-trimethoxybutan-2-ol.

Examination of fractions 4—8 by gas-phase chromatography on a Tween–Celite column at 160° showed that the oxetan content decreased from 55% (fr. 4) to 2% (fr. 7) and that there were also present in fractions 4—7 1-methoxybut-3-yn-2-ol (up to 25% in fr. 5), an unidentified material which yielded diacetyl 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 326—327°, and 1-chloro-2 : 3-epoxy-4-methoxybutane. Fractions 6—8 contained increasing quantities of mixed 4-chloromethoxybut-3-enols (fraction 7 contained 80%, and fraction 8·88%); the *cis*-isomers were separable from the *trans*-isomers on the column used but the secondary alcohols were not separable from the corresponding primary alcohols, and the ratio of these was obtained by catalytic hydrogenation on alkaline Raney nickel. Thus fraction 7 contained 40% of *cis*-isomers (4 parts secondary alcohol : 1 part primary alcohol) and 40% of *trans*-isomers (4·7 parts secondary alcohol : 1 part primary alcohol). The *cis*-isomer, separated chromatographically, provided the 3 : 5-*dinitrobenzoate*, m. p. 68·5—70·5° (Found: Cl, 10·3. $C_{12}H_{11}O_7N_2Cl$ requires Cl, 10·7%), of *cis*-4-chloro-1-methoxybut-3-en-2-ol and the *trans*-isomer similarly gave the 3 : 5-*dinitrobenzoate*, m. p. 75—77° (Found: C, 43·2; H, 3·3; Cl, 10·75; N, 8·4. $C_{12}H_{11}O_7N_2Cl$ requires C, 43·6; H, 3·3; Cl, 10·7; N, 8·5%).

Fraction 10 provided two 3 : 5-dinitrobenzoates. The first, m. p. 75—77°, was identical with that above (*trans*-4-chloro-1-methoxybut-3-en-2-yl), and the second, obtained by fractional crystallisation of the mother-liquors (m. p. 96—98°) (Found: C, 43·3; H, 3·3; Cl, 11·1; N, 8·5%), was trans-4-*chloro*-2-*methoxybut*-3-*enyl* 3 : 5-*dinitrobenzoate*. This fraction also provided an α-*naphthylurethane*, m. p. 78—80° (Found: C, 62·6; H, 5·1; Cl, 11·9; N, 4·6. $C_{16}H_{16}O_3NCl$ requires C, 62·8; H, 5·2; Cl, 11·6; N, 4·6%), probably of the secondary alcohol. Catalytic hydrogenation of this fraction gave mainly 1-methoxybutan-2-ol (3 : 5-dinitrobenzoate, m. p. and mixed m. p. 89—91°) with a small amount of 2-methoxybutan-1-ol (3 : 5-dinitrobenzoate, m. p. and mixed m. p. 60—62°).

Fraction 12 was found to be entirely *trans*-4-chloromethoxybut-3-enols by chromatography (4·4 parts of secondary alcohol : 1 part of primary alcohol, by hydrogenation) and provided the same two 3 : 5-dinitrobenzoates as fraction 10.

Fraction 16 yielded the 3 : 5-*dinitrobenzoate*, m. p. and mixed m. p. 90—91° (Found: C, 47·3; H, 5·45; N, 7·9. $C_{14}H_{18}O_9N_2$ requires C, 46·9; H, 5·0; Cl, 7·8%), of 1 : 3 : 4-trimethoxybutan-2-ol.

(ii) The reaction (i) was carried out on a one-tenth scale; after removal of the solvent the total product was flash-distilled and analysed chromatographically, on both a Tween–Celite column at 160° and an Apiezon–Celite column at 117°. The following approximate analysis was obtained: 3-methoxy-2-methoxymethyloxetan (16%), 1-methoxybut-3-yn-2-ol (6%), 1 : 2-epoxy-3 : 4-dimethoxybutane (1—2%), 1-chloro-2 : 3-epoxy-4-methoxybutane (1·5%), a mixture (3%) of *cis*-4-chloro-1-methoxybut-3-en-2-ol and *cis*-4-chloro-2-methoxybut-3-en-1-ol, a mixture (24%) of *trans*-4-chloro-1-methoxybut-3-en-2-ol (80%) and *trans*-4-chloro-2-methoxybut-3-en-1-ol (20%), 1 : 3 : 4-trimethoxybutan-2-ol (40%), and an unknown compound (7—8%).

(b) *Using* 1 *mol. of sodium methoxide.* (i) 1 : 4-Dichloro-2 : 3-epoxybutane (176 g.) in methanol (20 c.c.) was heated under reflux with a solution of sodium (30 g.) in methanol (300 c.c.) for *ca.* 4½ hr.; nearly all the sodium methoxide reacted. Working up as before finally gave the fractions tabulated.

Fr.	B. p. (13 mm.)	Wt. (g.)	n_D^{20}	Fr.	B. p. (13 mm.)	Wt. (g.)	n_D^{20}
1	60—63°	6·1	1·4281	11	78—80°	7·1	1·4649
2	63—65	2·7	1·4306	12	80—86	5·3	1·4625
3	65—67	4·3	1·4344	13	86—90	1·9	1·4586
4	67—70	4·6	1·4382	14	90—97	4·9	1·4502
5	70—72	7·3	1·4477	15	97—99	3·3	1·4447
6	72—74	8·6	1·4536	16	99—101	5·7	1·4429
7	74—75	20·5	1·4591	17	101—104	19·3	1·4438
8	75—76	14·3	1·4632	18	104—106	13·1	1·4519
9	76	18·7	1·4658	Res.	—	2·7	—
10	76—78	20·7	1·4653				

Infrared spectroscopic examination showed that fractions 1 and 2 were largely the oxetan, which was present up to fraction 5. Fractions 5—12 contained 1-chloro-2 : 3-epoxy-4-methoxybutane and some unchanged dichloroepoxide. The *trans*-unsaturated chloro-compound (938 cm.$^{-1}$ band) appeared in fractions 10—16, and the later fractions were mainly 1 : 3 : 4-trimethoxybutan-2-ol although fractions 15 and 16 probably contained chlorodimethoxybutanols.

Fraction 16 gave the 3 : 5-dinitrobenzoate of 1 : 3 : 4-trimethoxybutan-2-ol, and fraction 18 provided the 3 : 5-*dinitrobenzoate*, m. p. and mixed m. p. 106—108° (Found: C, 43·3; H, 4·5; Cl, 10·0; N, 7·55. $C_{13}H_{15}O_8N_2Cl$ requires C, 43·0; H, 4·1; Cl, 9·8; N, 7·7%), of 4-chloro-1 : 3-dimethoxybutan-2-ol.

(ii) The experiment (i) was repeated on a one-tenth scale, and the solvent-free product flash-distilled and examined chromatographically on Tween–Celite at 160° and Apiezon–Celite at 117°. The following approximate analysis was obtained: 3-methoxy-2-methoxymethyloxetan (11%), 1-methoxybut-3-yn-2-ol (3%), 1 : 2-epoxy-3 : 4-dimethoxybutane (0·4%), a mixture (3%) of 2 : 3-epoxy-1 : 4-dimethoxybutane and 1-chloro-3 : 4-epoxy-2-methoxybutane, 1-chloro-2 : 3-epoxy-4-methoxybutane (14%), unchanged 1 : 4-dichloro-2 : 3-epoxybutane (20%), a mixture (5%) of *cis*-4-chloro-1-methoxybut-3-en-2-ol and *cis*-4-chloro-2-methoxybut-3-en-1-ol, a mixture (14%) of *trans*-4-chloro-1-methoxybut-3-en-2-ol and *trans*-4-chloro-2-methoxybut-3-en-1-ol, 1 : 3 : 4-trimethoxybutan-2-ol (13%), 4-chloro-1 : 3-dimethoxybutan-2-ol (16%), and an unknown component (<1%).

Preparation of Reference Compounds.—1-*Chloro*-3 : 4-*epoxybut*-1-*ene.* (*a*) Preparation.

1-Chlorobutadiene (80 g.) in ether (1000 c.c.) was stirred with *N*-bromosuccinimide (150 g.) in water (1 l.) at room temperature until all the solid had dissolved. The ethereal extracts were evaporated, and the crude bromohydrin, without further purification, was stirred with sodium hydroxide (40 g.) in water (80 c.c.) at *ca.* 30° for 1 hr. The ethereal extract of the product, on distillation, provided the *epoxide* (27·6 g.), b. p. 70—72°/100 mm., 126°/1 atm., n_D^{20} 1·4698 (Found: C, 45·4; H, 5·1; Cl, 34·25%; epoxide equiv., 117. C_4H_5OCl requires C, 45·9; H, 4·8; Cl, 34·0%; epoxide equiv., 104·5).

(*b*) Reaction with acid methanol. The epoxide (7·5 g.) was heated under reflux for 2 hr. with methanol (25 c.c.) containing a trace of sulphuric acid. The solution was cooled, neutralised with solid sodium hydrogen carbonate, filtered, diluted with ether, and washed with water. Distillation gave 4-chloromethoxybut-3-enols (4·2 g.), b. p. 82·5—84·5°/15 mm., n_D^{20} 1·4650, and a residue (1·3 g.). A sample on catalytic hydrogenation yielded entirely 2-methoxybutan-1-ol, and chromatography showed that ratio of *cis* : *trans* was *ca.* 7 : 3. Hence the product consisted of *cis*- (70%) and *trans*-4-chloro-2-methoxybut-3-en-1-ol (30%). The *α-naphthylurethane*, m. p. 77—78·5° (Found: C, 62·7; H, 5·2; Cl, 11·85; N, 4·3. $C_{16}H_{16}O_3NCl$ requires C, 62·8; H, 5·2; Cl, 11·6; N, 4·6%), and 3 : 5-*dinitrobenzoate*, m. p. 90·5—92·5° (Found: C, 43·9; H, 3·65; Cl, 11·2; N, 8·3. $C_{12}H_{11}O_7N_2Cl$ requires C, 43·6; H, 3·3; Cl, 10·7; N, 8·5%), were derivatives of *cis*-4-chloro-2-methoxybut-3-en-1-ol.

(*c*) Reaction with sodium methoxide. The epoxide (15·6 g.) was heated under reflux for 6 hr. with sodium methoxide (from 1·5 g. of sodium) in methanol (25 c.c.). After normal working up and distillation there were obtained fractions: (1) (1·7 g.), b. p. 66—70°/14 mm., n_D^{20} 1·4480; (2) (1·4 g.), b. p. 70—72°/14 mm., n_D^{20} 1·4505; (3) (1·7 g.), b. p. 72—75°/14 mm., n_D^{20} 1·4524; (4) (2·7 g.), b. p. 75—80·5°/14 mm., n_D^{20} 1·4600; (5) (3·8 g.), b. p. 80·5—83·5°/14 mm., n_D^{20} 1·4636; and a residue (2·6 g.).

Spectroscopy showed that fractions 1—4 contained acetylenic material in decreasing amounts, and fractions 3—5 contained compounds with a 1-substituted vinyl group (partly *trans*); all fractions contained hydroxyl and methoxyl groups.

A portion of the combined product was chromatographed on a Tween–Celite column at 160° and four fractions were separated: these were examined separately. Fraction (i) consisted of 2-methoxybut-3-yn-1-ol [3 : 5-*dinitrobenzoate*, m. p. 94—95° (Found: C, 48·5; H, 3·5; N, 9·5, 9·6. $C_{12}H_{10}O_7N_2$ requires C, 49·0; H, 3·4; N, 9·5%)], yielding entirely 2-methoxybutan-1-ol on catalytic hydrogenation. Fraction (ii) was 1-methoxybut-3-yn-2-ol [3 : 5-*dinitrobenzoate*, m. p. 54—55·5° (Found: C, 48·9; H, 3·5; N, 9·7, 9·4%)], and gave 1-methoxybutan-2-ol on hydrogenation. Fraction (iii) was a mixture of *cis*-4-chloro-1-methoxybut-3-en-2-ol and *cis*-4-chloro-2-methoxybut-3-en-1-ol (ratio 1·8 : 1 by hydrogenation); it provided the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 90—91·5°, of the primary alcohol, and an impure derivative, m. p. 64—67°, of the secondary alcohol. Fraction (iv) was a mixture of *trans*-4-chloro-1-methoxybut-3-en-2-ol and *trans*-4-chloro-2-methoxybut-3-en-1-ol (ratio 3 : 1 by hydrogenation); only the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 75—76°, of the secondary alcohol was isolated from this fraction.

3 : 4-*Dichloro*-1-*methoxybutan*-2-*ol*. 1 : 2-Dichloro-3 : 4-epoxybutane[3] (150 g.; 70% of low-boiling, 30% of high-boiling isomer) and methanol (250 c.c.) containing sulphuric acid (2 c.c.) were heated under reflux for 24 hr. The excess of methanol was distilled off, and the residue diluted with water and extracted with ether. Distillation gave the *dichloromethoxybutanol* (152·8 g.), b. p. 111—112°/13 mm., n_D^{20} 1·4745 (Found: OMe 18·0. $C_4H_7OCl_2{\cdot}OMe$ requires OMe, 17·9%), chromatographically homogeneous [*phenylurethane*, m. p. 104·5—105·5° (Found: C, 49·3; H, 5·2; Cl, 24·0; N, 4·8. $C_{12}H_{15}O_3NCl_2$ requires C, 49·3; H, 5·1; Cl, 24·3; N, 4·8%)].

1-*Chloro*-2 : 3-*epoxy*-4-*methoxybutane* (II). 3 : 4-Dichloro-1-methoxybutan-2-ol (34·6 g.), suspended in water (25 g.), was stirred at 30—40°, and sodium hydroxide (8 g.) in water (12 g.) added during 5 min.; stirring was continued for 1 hr. Neutralisation, extraction and recovery of the product, and distillation yielded the *epoxide* (II) (22·4 g.), b. p. 76—78°/15 mm., n_D^{20} 1·4460 (Found: C, 43·9; H, 6·7; Cl, 26·3. $C_5H_9O_2Cl$ requires C, 44·0; H, 6·6; Cl, 26·0%).

1-*Chloro*-4-*methoxybutane*-2 : 3-*diol*. 1-Chloro-2 : 3-epoxy-4-methoxybutane (21 g.) and formic acid (10 g.) were heated under reflux for 1 hr., excess of water added, and heating continued for a further hr. Final distillation gave fractions: (1) (2·4 g.), b. p. 110—117°/15 mm., n_D^{20} 1·4734; (2) (2·3 g.), b. p. 117—125°/15 mm., n_D^{20} 1·4732; and (3) (5·2 g.), b. p. 125—130°/15 mm. Fraction 1 contained some unchanged epoxide, but fraction 3 contained the glycol [*bisphenylurethane*, m. p. 182—184° (from benzene, then aqueous alcohol) (Found: C, 58·5; H, 5·6; Cl, 9·3; N, 7·1. $C_{19}H_{21}O_5N_2Cl$ requires C, 58·1; H, 5·35; Cl, 9·05; N, 7·1%)].

1 : 2-*Epoxy*-3 : 4-*dimethoxybutane* (VI). (i) 1-Chloro-2 : 3-epoxy-4-methoxybutane (35 g.) was heated with acid methanol (50 c.c.) for 2½ hr. and worked up normally. Distillation gave a single fraction (36·2 g.), b. p. 104—105·5°/13 mm., n_D^{20} 1·4520, consisting of a mixture of 1-chloro-3 : 4- (V) and 4-chloro-1 : 3-dimethoxybutan-2-ol (VII).

(ii) Sodium hydroxide (9 g.) in water (20 c.c.) was added gradually, with stirring, to the product (35·6 g.) from (i) above, at <30°. After *ca.* 1 hr. the product yielded, on final distillation, fractions (1) (18·0 g.), b. p.[14] 62·5°/13 mm., n_D^{20} 1·4214, (2) (3·1 g.), b. p. 62·5—102·5°/13 mm., n_D^{20} 1·4270, and (3) (4·3 g.), b. p. 102·5°/13 mm., n_D^{20} 1·4478, and a residue. Fraction 1 was the required epoxide (VI) (Found: C, 53·9; H, 9·2%; epoxide equiv., 132·7. Calc. for $C_6H_{12}O_3$: C, 54·5; H, 9·1%; epoxide equiv., 132·0). Fraction 3 was found spectroscopically to consist of 4-chloro-1 : 3-dimethoxybutan-2-ol, prepared also in a different way (see below).

1-*Chloro*-3 : 4-*dimethoxybutan*-2-*ol* (V). 1 : 2-Epoxy-3 : 4-dimethoxybutane (VI) (10 g.) was treated, with cooling, with an excess of ethereal hydrogen chloride. Distillation provided 1-*chloro*-3 : 4-*dimethoxybutan*-2-*ol* (V) (10·0 g.), b. p. 101—105·5°/14 mm., n_D^{20} 1·4520 (Found: OMe, 37·2. $C_6H_{13}O_3Cl$ requires 2OMe, 36·8%), chromatographically pure [*phenylurethane*, m. p. 59—60·5° (Found: C, 54·0; H, 6·0; Cl, 12·3; N, 4·9. $C_{13}H_{18}O_4NCl$ requires C, 54·25; H, 6·3; Cl, 12·3; N, 4·9%)].

1 : 4-*Dimethoxybut*-2-*ene*. This was prepared by essentially the method of Reppe *et al.*[15] from 1 : 4-dichlorobut-2-ene (250 g.). The dimethoxybutene (176 g.), b. p. 146°/1 atm., n_D^{20} 1·4214, was found on chromatography to be a mixture of *trans*- and *cis*-isomers (72·5 : 27·5); the dichlorobutene used was a similar mixture (70 : 30).

2 : 3-*Epoxy*-1 : 4-*dimethoxybutane* (III). 1 : 4-Dimethoxybut-2-ene (65 g.) in ether (400 c.c.) and *N*-bromosuccinimide (100 g.) in water (400 c.c.) were stirred together at room temperature until the solid had disappeared (28 hr.). The crude bromohydrin, after extraction with ether and evaporation of the solvent, was stirred at *ca.* 30° for 1½ hr. with sodium hydroxide (24 g.) in water (50 c.c.). Working up gave the *epoxide* (41·9 g.), b. p. 67—70°/13 mm., n_D^{20} 1·4220 (Found: C, 54·35; H, 8·9%; epoxide equiv., 136·3. $C_6H_{12}O_3$ requires C, 54·5; H, 9·1%; epoxide equiv., 132·0).

1 : 3 : 4-*Trimethoxybutan*-2-*ol* (IV). (i) 2 : 3-Epoxy-1 : 4-dimethoxybutane (III) (15 g.) was heated for 2 hr. with methanol (30 c.c.) containing a trace of sulphuric acid. Working up gave the *trimethoxybutanol* (15·0 g.), b. p. 98·5—99·5°/14 mm., n_D^{20} 1·4311 (Found: OMe, 56·3. $C_7H_{16}O_4$ requires 3OMe, 56·7%), chromatographically pure (3 : 5-dinitrobenzoate, m. p. 90—91°).

(ii) 1 : 2-Epoxy-3 : 4-dimethoxybutane (VI) (4·5 g.) was treated as in (i), to give 1 : 3 : 4-trimethoxybutan-2-ol (3·7 g.), b. p. 101°/13 mm., n_D^{20} 1·4311; this had an identical infrared spectrum and gave a similar 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 90·5—91·5°, to the product from the 2 : 3-epoxy-1 : 4-dimethoxybutane, above.

1 : 4-*Dichloro*-3-*methoxybutan*-2-*ol* (X). 1 : 4-Dichloro-2 : 3-epoxybutane (150 g.) and methanol (250 c.c.) containing sulphuric acid (1 c.c.) were heated under reflux overnight. Distillation of the product gave fractions (1) (1·1 g.), b. p. <110·5°/13 mm., (2) (141·8 g.), b. p. 110·5—111°/13 mm., n_D^{20} 1·4760, (3) (13·9 g.), b. p. 111—130°/13 mm., partially solid, and (4) (6·2 g.), b. p. 130—135°/13 mm., solid, and a residue (0·2 g.). Fraction 4, after recrystallisation from ethyl acetate–carbon tetrachloride, had m. p. 126—128°, undepressed on admixture with *meso*-1 : 4-dichlorobutane-2 : 3-diol. Fraction 2 was the *dichloro-methoxybutanol* (Found: C, 34·35; H, 5·9; Cl, 41·3; OH, 9·2. $C_5H_{10}O_2Cl_2$ requires C, 34·7; H, 5·8; Cl, 41·05; OH, 9·8%). By vapour-phase chromatography it was shown to contain two isomers (presumably *erythro* and *threo*) in a ratio of *ca.* 3 : 1. It yielded a *phenylurethane*, m. p. 100—102° (Found: C, 49·1, 49·2; H, 5·1, 5·4; Cl, 24·6, 23·9; N, 4·7, 5·3. $C_{12}H_{15}O_3NCl_2$ requires C, 49·3; H, 5·1; Cl, 24·3; N, 4·8%).

1-*Chloro*-3 : 4-*epoxy*-2-*methoxybutane* (XI). 1 : 4-Dichloro-3-methoxybutan-2-ol (140 g.) was stirred with aqueous sodium hydroxide solution at 30—40° for 2 hr., and on working up gave the *epoxide* (XI) (97·5 g.), b. p. 67—68°/15 mm., n_D^{20} 1·4468 (Found: C, 43·8; H, 6·6; Cl, 25·7; OMe, 23·7%; epoxide equiv., 140·3. $C_5H_9O_2Cl$ requires C, 43·95; H, 6·6; Cl, 26·0; OMe, 22·7%; epoxide equiv., 136·5). On vapour-phase chromatography the epoxide was found to be a mixture of two isomers (*ca.* 2 : 1).

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[14] Blicke and Biel, *J. Amer. Chem. Soc.*, 1954, **76**, 3163.

[15] Reppe *et al.*, *Annalen*, 1955, **596**, 1.

The epoxide (12 g.) was kept in an excess of ethereal hydrogen chloride overnight. Distillation then gave 1 : 4-dichloro-3-methoxybutan-2-ol (14·5 g.), b. p. 106°/11 mm., n_D^{20} 1·4770 (phenylurethane, m. p. and mixed m. p. 102—103°), identical spectroscopically with the precursor of epoxide (XI).

4-*Chloro*-1 : 3-*dimethoxybutan*-2-*ol* (VII). 1-Chloro-3 : 4-epoxy-2-methoxybutane (XI) (25 g.) was added gradually to boiling methanol (50 c.c.) containing sulphuric acid (5 drops); after the exothermic reaction had subsided heating was continued for 3 hr. The product was worked up, to give chromatographically pure *chlorodimethoxybutanol* (VII) (24·0 g.), b. p. 100·5—102·5°/13 mm., n_D^{20} 1·4512 (Found: OMe, 36·3. $C_6H_{13}O_3Cl$ requires 2OMe, 36·8%) {*phenylurethane*, m. p. 82—84° [from light petroleum (b. p. 60—80°)] (Found: C, 54·5; H, 6·0; Cl, 12·15; N, 4·9. $C_{13}H_{18}O_4NCl$ requires C, 54·3; H, 6·3; Cl, 12·3; N, 4·9%); 3 : 5-dinitrobenzoate, m. p. 107—109° (from methanol)}.

3-*Methoxy*-2-*methoxymethyloxetan* (IX). 4-Chloro-1 : 3-dimethoxybutan-2-ol (14 g.) was heated under reflux with sodium methoxide (from 2 g. of sodium) in methanol (40 c.c.) for 8½ hr. After working up, the *oxetan* (6·6 g.), b. p. 58—59°/13 mm., n_D^{20} 1·4233 (Found: C, 54·5; H, 9·05; OMe, 47·3. $C_6H_{12}O_3$ requires C, 54·5; H, 9·1; 2OMe, 47·0%), was obtained, as well as some unchanged chlorodimethoxybutanol and a little trimethoxybutanol. The infrared spectrum of the oxetan showed the OMe group, and absence of unsaturation and OH groups; it had a band at 972 cm.$^{-1}$ due to the oxetan ring.[16]

Heating the oxetan (5 g.) with acid methanol (15 c.c.) gave only 1 : 3 : 4-trimethoxybutan-2-ol (4·0 g.), b. p. 94—95°/13 mm., n_D^{20} 1·4313, identified by its spectrum and 3 : 5-dinitrobenzoate.

When the oxetan (10 g.) was heated under reflux for 6 hr. with sodium methoxide solution no reaction occurred and the oxetan (8·0 g.) was recovered.

1-*Methoxybutan*-2-*ol*. This was obtained by heating 1 : 2-epoxybutane (6 g.) with sodium methoxide. The methoxybutanol (4·5 g.), b. p. 133—135°, n_D^{20} 1·4100, provided a 3 : 5-dinitrobenzoate,[17] m. p. 91·5—94° (from methanol) (Found: C, 48·65; H, 4·9; N, 9·5. Calc. for $C_{12}H_{14}O_7N_2$: C, 48·3; H, 4·7; N, 9·4%).

2-*Methoxybutan*-1-*ol*. This was similarly prepared by heating 1 : 2-epoxybutane with acid methanol. In addition to the 3 : 5-dinitrobenzoate,[17] m. p. 62—64° (from ethanol–light petroleum) (Found: C, 48·8; H, 4·7; N, 9·55%), of 2-methoxybutan-1-ol, there was also isolated the derivative of the 1-methoxybutan-2-ol from the lowest-boiling fraction of the product.

Reaction of Intermediates with Sodium Methoxide.—1-*Chloro*-2 : 3-*epoxy*-4-*methoxybutane* (II). The epoxide (II) (13·6 g.) and sodium methoxide solution (50 c.c. containing 2·88 g. of sodium) were heated at 65—70° for 3½ hr. Distillation of the product gave fractions (1) (1·4 g.), b. p. 67—74°/13 mm., n_D^{20} 1·4310, (2) (1·6 g.), b. p. 74—91·5°/13 mm., n_D^{20} 1·4361, (3) (1·6 g.), b. p. 91·5—95°/13 mm., n_D^{20} 1·4351, (4) (5·9 g.), b. p. 95—97°/13 mm., n_D^{20} 1·4338, (5) (3·1 g.), b. p. 97—98°/13 mm., n_D^{20} 1·4351, and (6) (0·5 g.), b. p. 98—100°/13 mm., n_D^{20} 1·4380, and a residue (0·3 g.). Infrared spectroscopy showed that fraction 1 contained starting material (30%) and oxetan (IX) with possibly some 2 : 3-epoxy-1 : 4-dimethoxybutane (III); fraction 2 had starting material (*ca.* 20%) and some oxetan, but mainly 1 : 3 : 4-trimethoxybutan-2-ol; fractions 3—6 were all trimethoxybutanol.

2 : 3-*Epoxy*-1 : 4-*dimethoxybutane* (III). The epoxide (III) (12 g.) was heated on the bath overnight with an excess of sodium methoxide solution. There was finally obtained 1 : 3 : 4-trimethoxybutan-2-ol (8·5 g.), b. p. 95—96°/13 mm., n_D^{20} 1·4311, identified by its spectrum and 3 : 5-dinitrobenzoate.

1 : 4-*Dichloro*-3-*methoxybutan*-2-*ol* (X). Sodium methoxide (from 3·5 g. of sodium in 50 c.c. of methanol) was added, at 20° with stirring, to 1 : 4-dichloro-3-methoxybutan-2-ol (10 g.) in methanol (10 c.c.), during 10 min. After a further ½ hour's stirring at room temperature the mixture was heated to 65—70° for 5 hr. Normal working up gave fractions (1) (4·4 g.), b. p. 57·5—59°/13 mm., n_D^{20} 1·4238, (2) (0·7 g.), b. p. 59—65°/13 mm., n_D^{20} 1·4251, and (3) (2·0 g.), b. p. 92·5—100°/13 mm., n_D^{20} 1·4423, and a residue (0·3 g.). The infrared spectra showed that fractions 1 and 2 were mainly the oxetan (IX), and fraction 3 mainly trimethoxybutanol (IV).

1-*Chloro*-3 : 4-*epoxy*-2-*methoxybutane* (XI). The epoxide (17 g.), when treated with an excess of sodium methoxide as above, gave finally fractions (1) (2·0 g.), b. p. <58°/15 mm., and (2)

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[16] Ref. 6, p. 119.

[17] Bartlett and Ross, *J. Amer. Chem. Soc.*, 1948, **70**, 926.

(8·5 g.), b. p. 58—58·5°/13 mm., n_D^{20} 1·4229, and a residue (0·7 g.). Fraction 2 (Found: OMe, 47·0. Calc. for $C_6H_{12}O_3$: OMe, 47·0%) consisted of the oxetan (IX); this was confirmed by its infrared spectrum.

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