

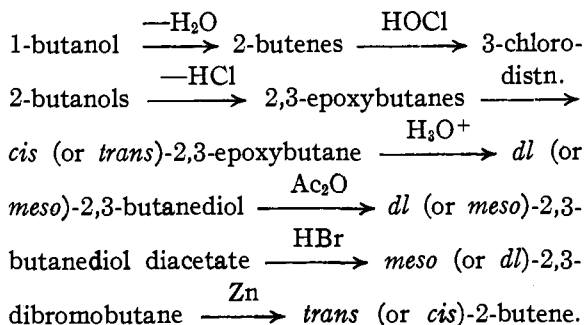
[CONTRIBUTION FROM GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 557]

## Stereochemical Relationships of the Isomeric 2,3-Butanediols and Related Compounds; Evidence of Walden Inversion

BY CHESTER E. WILSON AND HOWARD J. LUCAS

This investigation has been undertaken for the purpose of synthesizing *cis*- and *trans*-2-butene in a pure state and of studying the Walden inversion. Incidentally, the work has constituted an independent confirmation of the observation that the butene produced in the dehydration of 1-butanol in the presence of sulfuric acid is approximately 68% *trans*-2-butene and 32% *cis*-2-butene.<sup>1</sup> The reliability of this result has been questioned,<sup>2</sup> on the basis that the dibromide method of analysis<sup>3</sup> is faulty.<sup>4</sup> This confirmation rests upon the observation that *cis*-2-butene is converted through the chlorohydrin to *cis*-2,3-epoxybutane and that the crude epoxybutane mixture obtained from the crude butene mixture is approximately 65% *trans*-2,3-epoxybutane and 35% *cis*-2,3-epoxybutane, with little or no 1,2-epoxybutane.

**The Method of Synthesis.**—This is outlined below:



The butene mixture from the decomposition of 1-butanol was converted into a mixture of chlorohydrins and this into a mixture of epoxybutanes by hot potassium hydroxide solution. Fractionally distilling the oxides is more satisfactory than distilling the butenes because the former are liquids, whereas the latter are gases, and because the difference in boiling points of the isomeric 2,3-epoxybutanes is 6°, whereas it is 2.7° for the isomeric 2-butenes. Each oxide, contaminated with a small amount of its stereoisomer, was hy-

(1) Young and Lucas, *THIS JOURNAL*, **52**, 1964 (1930). A similar conclusion has been drawn independently by H. B. Hass, who has separated the isomeric 2,3-epoxybutanes and has converted each to a glycol (private communication).

(2) Komarewsky, Johnstone and Yoder, *ibid.*, **56**, 2705 (1934); Pines, *ibid.*, **55**, 3892 (1933).

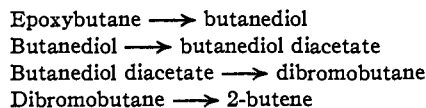
(3) Dillon, Young and Lucas, *ibid.*, **52**, 1953 (1930).

(4) See also Young and Winstein, *ibid.*, **58**, 102 (1936).

drated to a 2,3-butanediol, which could be purified from the small amount of its diastereomer by crystallization. Conversion of the glycol to its diacetate afforded another opportunity for purification, especially in the case of the lower melting (liquid) glycol, for its diacetate is a solid. Each pure diacetate was converted into a pure 2,3-dibromobutane by saturated, aqueous hydrobromic acid. The dibromides are known to yield the isomeric 2-butenes.<sup>5</sup>

A necessary condition of obtaining pure compounds at the different steps is the avoidance of racemization, that is, there must be, at each asymmetric carbon atom, either zero or 100% Walden inversion. Fortunately, under the conditions employed, this condition held. No attempt was made to modify conditions so as to bring about racemization.

**Possibility of Walden Inversions.**—An odd number of Walden inversions are involved, starting with a pure 2-butene and passing, through the changes outlined above, to a pure 2-butene, since *cis*-2-butene is obtained from *trans*-2-butene. Because of the symmetrical structure of the compounds involved, it should be possible to determine whether only one Walden inversion takes place during the following changes:



In order to establish the possibility of Walden inversions, the compounds involved (except the 2-butene) must be prepared with optical activity. An epoxybutane and a diol have been obtained with optical activity, although not in the pure form. The hydration of the epoxybutanes to the butanediols takes place through a Walden inversion, which is 100% in each case.<sup>6</sup> Although

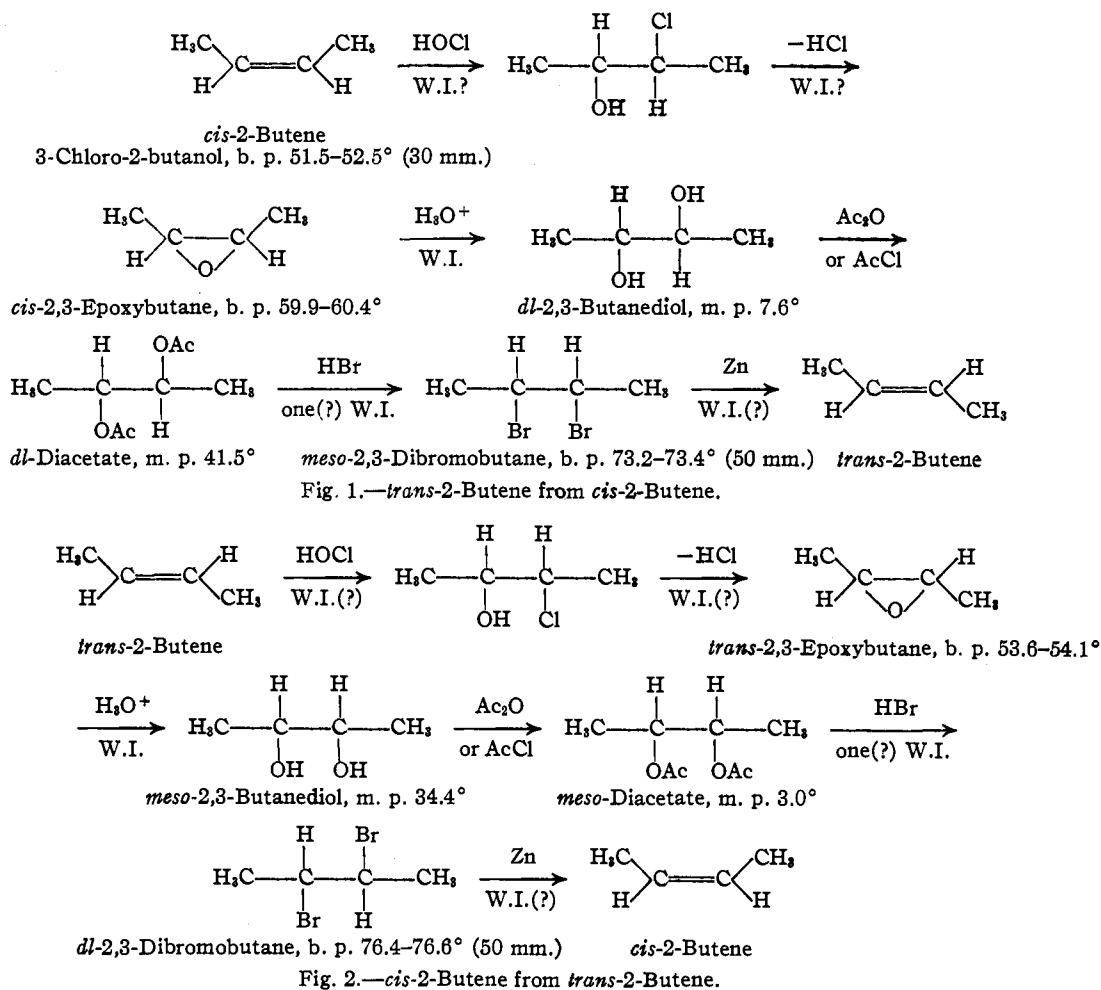
(5) The purity of the dibromides was regarded as proof that pure butenes would result, for it has been shown already, Ref. 1, that a butene and its dibromide are interconvertible. Since this work was started, Kistiakowsky, *et al.*, *ibid.*, **57**, 879 (1935), have obtained these hydrocarbons in a high state of purity.

(6) Walden inversions have been observed in the hydration of epoxy compounds to glycols: Kuhn and Ebel, *Ber.*, **58B**, 919 (1925); Van Loon, Thesis, Delft, 1918; Böeseken, *Rec. trav. chim.*, **47**, 683 (1928).

the hydration of the oxide is the only step for which there is a definite proof of Walden inversion in this work, it is probable that a total of five single inversions are involved in passing from *cis*-2-butene to *trans*-2-butene, as outlined in Fig. 1, in which the stereochemical relationships of the different compounds are shown. Similar stereochemical relationships are outlined in Fig. 2 for the conversion of *trans*-2-butene to *cis*-2-butene. In this case the second compound, the chlorohydrin, has not yet been obtained pure. A Walden inversion is indicated by the letters W. I. In the case of the *dl*-compounds, the configuration of but one of the two possible antipodes is shown.

double bond.<sup>7</sup> If this is true, then an inversion is involved at the second step, that is, during the closing of the oxide ring. At the third step, *i. e.*, the opening of the oxide ring through hydration, a Walden inversion is definitely proved, by establishing the configuration of the oxides and glycols.

**Configurations of the Isomeric 2,3-Epoxybutanes.**—These were established by obtaining one (the lower boiling isomer) with optical activity, although not as a pure isomer. For this purpose the oxide was converted by the usual steps to a corresponding *dl*-3-dimethylamino-2-butanol, *dl*- $\alpha,\beta$ -dimethylcholine iodide and *dl*- $\alpha,$



Although no evidence is available as yet to show that a Walden inversion is involved in the conversion of the butenes to the chlorohydrins, and of these to the oxides, it is reasonable to postulate an inversion at the first step, in conformity with the general rule of *trans* addition to the

$\beta$ -dimethylcholine. The latter was partially resolved with tartaric acid. Distillation of the active base with aqueous sodium hydroxide gave trimethylamine and an *optically active* butene

(7) Michael, *J. prakt. Chem.*, **52**, 344 (1893); Chavanne, *Rev. gen. sci.*, **35**, 229 (1924).

oxide.<sup>8</sup> It was shown further that each *dl*- $\alpha,\beta$ -dimethylcholine gave the pure oxide from which it had been prepared. Therefore the original lower boiling oxide, b. p. 54°, as well as the recovered active oxide, must have the *trans* configuration, and the higher boiling, b. p. 60°, must have the *cis* configuration.

**Configurations of the Isomeric 2,3-Butane-diols.**—These have been established by three independent observations, as follows: (a) when the optically active oxide is hydrated, the inactivity of the resulting glycol, which is the higher melting isomer, shows that it is the internally compensated form; (b) when the lower melting glycol is partially esterified by *d*-camphor sulfonic acid, the optical activity developed in the unesterified glycol shows that this is the *dl*-glycol; (c) when the higher boiling, *cis*-oxide undergoes hydration in the presence of either *d*-camphor sulfonic acid or *d*-tartaric acid, the optical activity possessed by the resulting, lower melting glycol shows that it is the *dl*-glycol. These results confirm those of Böeseken and Cohen,<sup>9</sup> who resolved the acid sulfate of the liquid glycol by means of brucine. An independent confirmation of their results seemed desirable because of the possibility that a Walden inversion may have taken place in their work, and also because it is sometimes assumed that the solid glycol is the *dl*-isomer since it is produced by bacterial fermentation, and possesses some optical activity.<sup>9,10</sup>

**A Walden Inversion.**—The hydration of the optically active, *viz.*, the *trans* oxide, to the inactive, *viz.*, the *meso* glycol, proves that a complete Walden inversion, *i. e.*, a *trans* opening of the oxide ring, takes place. If there were no inversion, *i. e.*, if there were *cis* opening of the ring, the resulting glycol should possess optical activity, since an optically active glycol would be present. The optical activity could disappear only by conversion to the *meso* form through racemization at one carbon atom or to its antipode through racemization at both asymmetric carbon atoms. Racemization, even at one carbon atom, was never observed during the hydration of the inactive oxides, for a pure *dl*- or *meso*-glycol was obtained.

**Other Possible Inversions.**—Inspection of Figs. 1 and 2 shows that either zero or an even

(8) See Rabe and Halbensleben, *Ber.*, **48**, 2622 (1910); Read and Campbell, *J. Chem. Soc.*, 2377 (1930).

(9) Böeseken and Cohen, *Rec. trav. chim.*, **47**, 839 (1928).

(10) Harden and Walpole, *Proc. Roy. Soc. (London)*, **77B**, 399 (1906). The optical activity is due to contamination by an active form.

number of inversions are involved between the glycols and the final butenes. It is hardly likely that an inversion accompanies the formation of the diacetate, since the C-O bonds are not altered. It is probable that an inversion accompanies the conversion of each butene to its dibromide, and *vice versa*,<sup>1</sup> in line with similar changes<sup>7</sup>. If this is the case, then only one Walden inversion is involved in the formation of the dibromides from the diacetates. This would constitute an unusual and unexpected type of Walden inversion.<sup>11</sup> It is planned to investigate this possibility by attempting to prepare an optically active diacetate and dibromide.

It seems probable, therefore, that five Walden inversions in all are associated with the changes shown in each of Figs. 1 and 2. Of these, the first two are not susceptible of direct proof by the stereochemical method, whereas the last three are. A Walden inversion has been shown to accompany the third step; the fourth and fifth steps require further study.

This research has been aided by a grant from Dr. George Piness, of Los Angeles, whose financial aid is gratefully acknowledged. For the advice and assistance of his colleague, Dr. Gordon A. Alles, the authors desire to express their appreciation and thanks.

### Experimental

**Preparation of 2-Butene.**—The 2-butene,<sup>1</sup> obtained by heating a mixture of 444 g. (6.0 moles) of 1-butanol,<sup>12</sup> 400 ml. of water, and 600 ml. of concd. sulfuric acid, and purified by passing through a sodium hydroxide solution, sulfuric acid, 50–55% by wt., and a drying tower, is condensed, at –15 to –20°, in previously weighed ampoules; yield 130–180 g. (38–48%).

**Preparation of 3-Chloro-2-butene.**—In a 2-liter three-necked flask provided with a mercury-sealed stirrer, a delivery tube and a reflux condenser cooled by carbon dioxide and alcohol,<sup>13</sup> is placed 400–500 g. of a mixture of water and ice, and 295 g. of H. T. H.<sup>14</sup> (1.34 moles of calcium hypochlorite). The flask is cooled by a freezing bath at –10 to –15° and 150 g. (2.68 moles) of liquid butene is poured into the flask through the delivery tube from the weighed

(11) A similar change in configuration has been observed in the case of the 4,5-octanediols and corresponding dibromooctanes by Young, Jasaitis and Levanas, who will publish their results soon.

(12) 2-Butanol was not used because it might possibly be contaminated by 2-methyl-2-butanol.

(13) The condenser is made of two large concentric glass tubes in the shape of a Dewar flask, except that there are two small tubes leading into the annular space, *viz.*, a vertical tube at the bottom, up which the warm gas rises and a horizontal tube near the top, out of which the uncondensed gas passes. A mixture of solid carbon dioxide and alcohol is placed in the inner tube.

(14) H. T. H., 65% available chlorine, manufactured by the Mathieson Alkali Works, is a mixture of calcium hypochlorite and sodium chloride.

ampoule. The tube is then replaced by a dropping funnel and 175 ml. (2.9 moles) of glacial acetic acid is slowly run in during vigorous agitation and good cooling. The time is two to three hours, unless one does not object to excessive refluxing.

Nitric acid is added to break the emulsion, the chlorohydrin is separated and the aqueous phase is extracted with three 100-ml. portions of isopropyl ether. After adding a small amount of water to the combined chlorohydrin-ether extracts, the contained acid is neutralized by the addition of potassium carbonate, in small portions. A part of the dissolved water is removed by the addition of calcium chloride and the mixture is then fractionally distilled under reduced pressure. After dichlorobutane, b. p. 50–60° at 80 mm., 30–40° at 30 mm., has been removed, the mixture of the two *dl*-chlorohydrins distils at 50–60° under a pressure of 30 mm.;<sup>15</sup> yield, 160 g. (55%).

Some attempt was made to separate the mixture of chlorohydrins by fractional distillation, but when it was found that the oxides could be separated more easily, the purification of the chlorohydrins was abandoned. Later, when a good supply of *cis*-2-butene was available, its chlorohydrin was prepared and the properties determined as follows: b. p. 51.5–52.5° (30 mm.);  $d_4^{20}$ , 1.0626;  $n_D^{20}$ , 1.4403.

**Preparation of 2,3-Epoxybutane.**—In a 2-liter three-necked flask provided with a mercury-sealed stirrer, a bent tube leading to a condenser, a dropping funnel, and a thermometer extending nearly to the bottom of the flask, 1000 g. (16–17 moles) of technical potassium hydroxide flakes (or pellets) is dissolved in 500 ml. of water, with stirring. With the solution at a temperature of 90°, 400 g. (3.72 moles) of 3-chloro-2-butanol is slowly added during vigorous agitation, over a period of about two hours. A slow current of air drawn through the apparatus at the end will carry over some additional oxide. The liquid is dried by anhydrous potassium carbonate (calcium chloride must not be used, as it forms an addition product with the higher boiling oxide), filtered and distilled. The 50–60° fraction is collected;<sup>16</sup> yield 235 g. (87–90%).

**The Isomeric 2,3-Epoxybutanes.**—A quantity of 1700 g. of the mixed epoxybutanes was subjected to three fractional distillations through a 2-meter column filled with glass rings and under total reflux, using a high reflux ratio, and making cuts at 0.5° intervals. Bromobenzene was added to the last fraction, as a still base. The distillation curves are shown in Fig. 3. The over-all recovery at the end of the third distillation was 90%. No 1,2-epoxybutane could be isolated. The physical properties of the isomeric oxides are given in Table I.

TABLE I  
PROPERTIES OF THE ISOMERIC 2,3-EPOXYBUTANES

	<i>trans</i>	<i>cis</i>
B. p., ° C., 747 mm.	53.6–54.1	59.9–60.4
Sp. gr., 20/20	0.8053	0.8272
Refractive index, $n_D^{20}$	1.3736	1.3826
Molar refraction, $M_D$	20.45	20.34
M. p., ° C.	–85 (?)	–80 (?)
Weight recovered, g.	661	280
Estimated purity, %	96	90

(15) Fourneau and Puyal, *Bull. soc. chim.*, **31**, 424 (1922), reported 138–140° as the boiling point of the chlorohydrin.

(16) Fourneau and Puyal<sup>15</sup> report 56° as the boiling point.

The specific gravities were determined with a 10-ml. pycnometer; the refractive indices with an Abbé refractometer; and the melting points, which are approximate only, with a pentane thermometer immersed in a small test-tube of the material cooled with liquid air in a Dewar flask. The tube was raised or lowered until crystals surrounded the lower half of the thermometer bulb, and the reading was taken after it had remained constant over a period of time while there was no appreciable melting or freezing. The purity of each oxide was estimated from the melting point of the crude glycol obtained when the oxide was hydrated.

Later, after the pure chlorohydrin had been prepared from pure *cis*-2-butene, pure *cis*-2,3-epoxybutane was prepared in 75% yield. Because of the relatively small amount, *viz.*, 10.7 g., the yield was low and the constants were not as satisfactory as those in Table I; b. p. 58.4–61.3°;  $n_D^{20}$  1.3822.

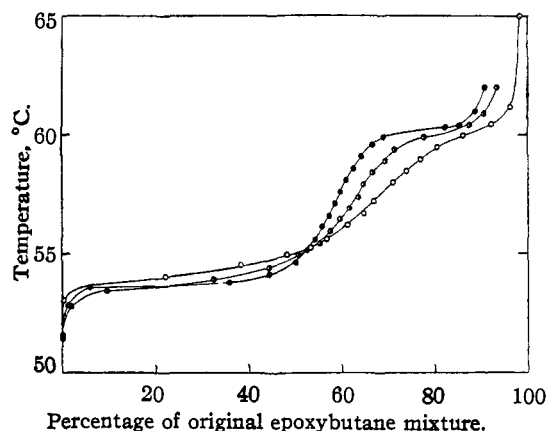


Fig. 3.—Fractionation of epoxybutanes: —○—○—, first distillation; —□—□—, second distillation; —●—●—, third distillation.

#### Optically Active 2,3-Epoxybutane

**Preparation of *dl*-3-Dimethylamino-2-butanols.**—In a pressure bottle are placed 30 g. (0.417 mole) of crude 2,3-epoxybutane (*cis* and *trans* mixture) and 75 ml. of approximately 30% (6.1 normal) aqueous dimethylamine solution (0.457 mole). The bottle is placed in a water-bath which is slowly brought to boiling and kept at this temperature for about one hour. After cooling, several batches are united, nearly saturated with potassium carbonate and extracted three times with ether. The ether extracts, after drying with powdered potassium hydroxide, are fractionated under a pressure of 30 mm. through a 2-meter column with total reflux, yielding 33% of product distilling at 53.7–54.7°, 47% at 72.0–72.3°, total recovery, including intermediate fractions, 86%. At 743 mm. the two main fractions distilled at 141.0–142.0° and 152.5–153.5°, respectively.<sup>17</sup> These dimethylamino alcohols were also prepared from the pure oxides, but since these amino alcohols are more easily purified than the oxides, it is preferable to proceed as described above.

Since the *cis* oxide yielded the lower boiling and the *trans*

(17) Fourneau and Puyal<sup>15</sup> report the boiling point of 3-dimethylamino-2-butanol as 53° under 18 mm., and 145° under ordinary pressure.

oxide the higher boiling dimethylamino alcohol, it is possible to assign a provisional configuration to each of these *dl*-amino alcohols, assuming that a Walden inversion takes place here, as it does when the oxides are hydrated. In conformity with the nomenclature adopted for the  $\alpha,\beta$ -dihydroxybutyric acids<sup>18</sup> the amino alcohol corresponding to the *dl* glycol is called the *threo* and the one corresponding to the *meso* glycol is called the *erythro* amino alcohol (Fig. 4).

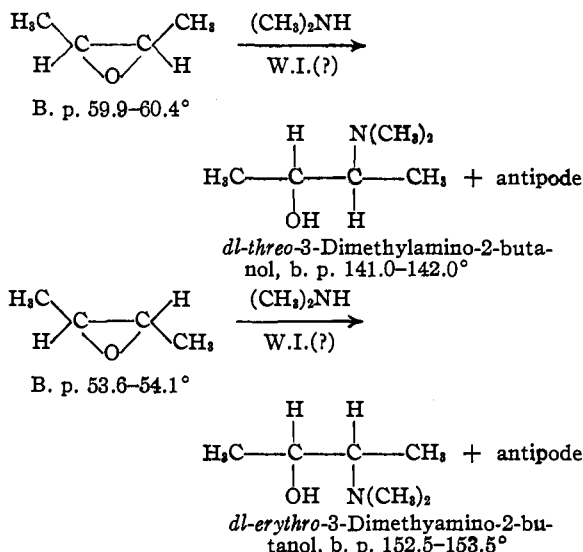


Fig. 4.—Configurations of the *dl*-3-dimethylamino-2-butanols.

**Preparation of *dl*- $\alpha,\beta$ -Dimethylcholine Iodides.**—A solution of 29.5 g. (0.252 mole) of a pure *dl*-3-dimethylamino-2-butanol in 150 ml. of absolute ether is added to a similar solution of 36 g. (0.254 mole) of methyl iodide. A cloudiness develops at once. The higher boiling alcohol reacts much more rapidly than the lower boiling isomer and it is necessary to cool the solution of the former. After standing for several days at room temperature the solid is filtered off and dried. Yields are 93 and 84%, respectively. Iodine,<sup>19</sup> found, 43.8%; calculated for  $\text{C}_7\text{H}_{18}\text{ONI}$ , 49.0%.

**Regeneration of 2,3-Epoxybutanes from *dl*- $\alpha,\beta$ -Dimethylcholine Iodides.**—An aqueous solution of the choline, obtained by adding 9 g. (an excess) of silver oxide to 20 g. of a pure iodide in 20 ml. of water and filtering out the silver iodide, is distilled through a well-cooled condenser. On saturating the aqueous distillate with potassium carbonate, a lighter phase of trimethylamine and epoxybutane separates. This is dried with solid potassium carbonate and fractionally distilled. The yield of oxide is 2.4 g. (43%). The iodide prepared from the lower boiling dimethylamino alcohol yielded an oxide, b. p. 56.0-58.3°, the glycol from which melted at about 4°, while the one from the higher boiling alcohol yielded an oxide, b. p. 51.3-53.8°, whose glycol melted at 28°. This shows that the original oxide was regenerated in each case.

**Resolution of *dl*-erythro- $\alpha,\beta$ -Dimethylcholine.**—To 128 g. (0.497 mole) of dimethylcholine iodide prepared from

*dl*-erythro-3-dimethylamino-2-butanol dissolved in 350 ml. of absolute alcohol is added an excess of silver oxide which has been washed with alcohol. The mixture is agitated until the solution fails to give a precipitate with silver nitrate in dilute nitric acid and the solid is filtered out. To the solution is added 76.5 g. (0.510 mole) of *d*, tartaric acid. The resulting bitartrate, at first an oil, is recrystallized many times from absolute alcohol. The specific rotation of the first fraction was  $[\alpha]_{\text{H}_2\text{O}} +17.9^\circ$ , and of the final fraction,  $+19.1^\circ$ , after nine crystallizations. Although this final product was probably contaminated with some of its stereoisomer, it was used for preparing an oxide having optical activity.

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{21}\text{O}_7\text{N}$ : N, 5.24. Found:<sup>19</sup> N, 5.11.

**Optically Active 2,3-Epoxybutane.**—The pyrolysis of cholines, by the method of Rabe and Halbensleben and of Read and Campbell,<sup>8</sup> was applied to the  $\alpha,\beta$ -dimethylcholine obtained from the tartrate of higher rotation, without, however, isolating the choline. To a solution of 14 g. (0.05 mole) of  $\alpha,\beta$ -dimethylcholine bitartrate,  $[\alpha]_{\text{H}_2\text{O}} +18.8^\circ$ , from the lower boiling oxide, in water, made neutral to phenolphthalein with dilute sodium hydroxide, was added an aqueous solution of 19 g. (0.112 mole) of silver nitrate. After filtering off the silver tartrate, the specific rotation,  $[\alpha]_{\text{H}_2\text{O}}$ , of dimethylcholine nitrate, was  $+3.0^\circ$ . The volume was reduced to 15 ml. by evaporation under reduced pressure, 5 g. of sodium hydroxide was added and the solution was distilled at atmospheric pressure. The aqueous distillate, 12-14 ml., was diluted to 18 ml. Its observed rotation,  $\alpha$ , was  $-1.40^\circ$  in a 2-dm. tube. Assuming a 50% yield of oxide, as in other experiments, the specific rotation  $[\alpha]_{\text{H}_2\text{O}}$  of the oxide is approximately  $-7^\circ$ . The distillate obtained by the same procedure from unresolved *dl*-erythro- $\alpha,\beta$ -dimethylcholine *d*-tartrate had zero rotation. The active oxide was not isolated, but was hydrated to a glycol.

#### The 2,3-Butanediols and the 2,3-Dibromobutanes

**Preparation of the Inactive 2,3-Butanediols.**—The 2,3-epoxybutanes hydrate readily to the corresponding glycols, in the presence of a strong acid. The best acid to use is perchloric acid<sup>20</sup> and the weight ratio of water to oxide should not be much below 3, otherwise undesirable by-products, probably ethers, result. To a mixture of 300 ml. of water and 90 g. (1.25 mole) of 2,3-epoxybutane is added 6 drops of 60% perchloric acid and the mixture is cooled under the tap from time to time so that the stopper will not be forced from the flask. After five or ten minutes the undissolved oxide goes into solution. The solution is neutralized at the end of an hour and then fractionally distilled at reduced pressure, the pressure being decreased gradually so that the temperature of the liquid does not rise above 100°. The water fractions are used for hydrating subsequent batches of the same oxide; yield 101-107 g. (90-95%).

The glycols are purified by crystallization from dry isopropyl ether.<sup>21</sup> The *meso* glycol, m. p. 34.4°, is but mode-

(20) Brönsted, Kilpatrick and Kilpatrick, *ibid.*, **51**, 428 (1929).

(21) Drying is easily accomplished by distillation through an efficient fractionating column and discarding the fraction distilling below 67°.

(18) Braun, *THIS JOURNAL*, **51**, 228 (1929).

(19) Analysis by D. Pressman.

rately soluble and a good recovery is obtained when the solution is cooled from about 27 to 0°. Four crystallizations give a very pure product. The *dl*-glycol, m. p. 7.6°, is very soluble and the solution must be cooled to temperatures approaching that of solid carbon dioxide. Five or six crystallizations are necessary.

**Properties of the 2,3-Butanediols.**—Some physical properties of the inactive glycols and derivatives are shown in Table II. The melting point of each crude glycol shows that the purity of the *meso* isomer was about 96%, and of the *dl* isomer about 90% (from Fig. 5), assuming that no water was present. Since water was present, the purity was actually higher than indicated by the above figures.

TABLE II  
PROPERTIES OF THE INACTIVE 2,3-BUTANEDIOLS

Glycol, configuration	<i>meso</i>	<i>dl</i>
Oxide from which obtained	<i>trans</i>	<i>cis</i>
Glycol, b. p., ° C., 742 mm.	181.7	176.7
Glycol, b. p., ° C., 16 mm.	89	86
Glycol, m. p., ° C.	34.4	7.6
Glycol, m. p., ° C., crude	31.8	3.0
Diacetate, m. p., ° C.	2.5-3.0	41.0-41.5
Diacetate, b. p., ° C., 5.5 mm.	66	70
Dibenzoate, m. p., ° C.	75.5-76.2	53.0-54.0
Di- <i>p</i> -bromobenzoate, <sup>a</sup> m. p., ° C.	139.0-139.8	205-209

<sup>a</sup> Analysis<sup>19</sup> of the di-*p*-bromobenzoates for bromine by the Carius method gave: *meso* ester, 36.5%; *dl*-ester, 34.2%; calculated for C<sub>18</sub>H<sub>16</sub>O<sub>4</sub>Br<sub>2</sub>, 35.1%.

The esters were prepared by the use of a large excess of the corresponding acid chloride in the presence of either pyridine or dimethylaniline. The yields were above 100% on the basis of monoesters. The liquid diacetate was crystallized from isopropyl ether by cooling with solid carbon dioxide. The lower melting dibenzoate cannot be obtained crystalline unless the glycol is quite pure. It is surprising that the higher melting glycol yields a lower melting diacetate and di-*p*-bromobenzoate, but a higher melting dibenzoate.

For larger scale preparation of the diacetates, the following procedure gave good results: to a mixture of 117 g. (1.15 moles) of acetic anhydride and 45 g. (0.50 mole) of the glycol is added a drop of concd. sulfuric acid. It is necessary to cool the flask after a short time. After standing a day the mixture is fractionally distilled under reduced pressure. When this is 5.5 mm., the *meso* diacetate distils at about 66° and the *dl* at about 70°; yield 78-83 g. (90-95%). A given glycol yields the same diacetate, whether prepared with acetyl chloride in the presence of a tertiary amine or with acetic anhydride, as above. The *dl*-diacetate is easily purified by crystallization from petroleum ether. It is more convenient to purify this diacetate than to attempt to purify the corresponding glycol. Harden and Walpole<sup>10</sup> give 181-183° as the boiling point, and 28° as the melting point of their glycol, obtained by bacterial fermentation. Böeseken and Cohen<sup>9</sup> report a boiling point of 177-180° and a melting point of 25° for a similar product. Ciamician and Silber<sup>22</sup> report that one dibenzoate melts at 77° and that the other is a liquid.

(22) Ciamician and Silber. *Ber.*, **44**, 1280 (1911).

**Melting Point Curve.**—The effect of mixing each inactive glycol with a small amount of the other is shown in Fig. 5. The readings were obtained by slowly warming, in a stoppered test-tube provided with a calibrated thermometer, a partially solidified mixture of the two glycols. The glycols are very hygroscopic and must be protected from the moisture of the air. When water is added, the curve obtained with the *meso* glycol, on a molal basis, is almost identical with the one shown.

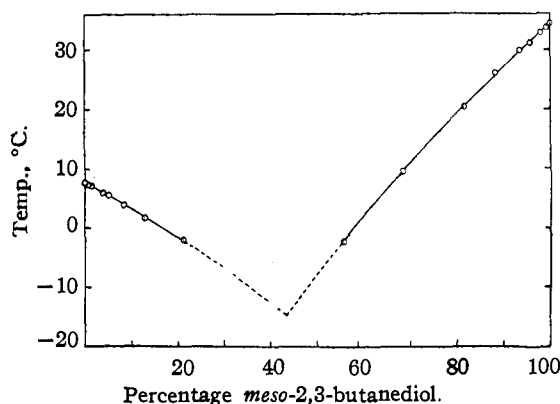


Fig. 5.—Melting point curve of the inactive 2,3-butanediols.

**Configurations of the 2,3-Butanediols; Hydration of the Active Oxide.**—The aqueous distillate obtained from the decomposition of the partially resolved dimethylcholine (page 2400) contained trimethylamine and an optically active 2,3-epoxybutane. It was carefully acidified with 60% perchloric acid and the solution was allowed to stand for a day. The solution was cooled, freed from trimethylammonium perchlorate by filtration, and was then found to have zero rotation. The resulting solid glycol was therefore the internally compensated form. If it were not, then it should possess optical activity. **Partial Resolution of the Liquid Glycol.** A mixture of 11.1 g. (0.123 mole) of the liquid glycol and 13.8 g. (0.059 mole) of *d*-camphorsulfonic acid was placed in a small flask in an oven at 65°, and left there for three weeks. The unreacted glycol was then distilled out of the mixture under a pressure of 3 mm. The 2.9 g. of recovered glycol was dissolved in 18 ml. of water; the solution had an observed rotation of +0.13 ± 0.02°. When the solid glycol was similarly treated, the product had zero rotation. **Asymmetric Hydration of *cis*-2,3-Epoxybutane (Higher Boiling).** When 10 g. (0.139 mole) of the *cis* oxide was added to a solution of 5 g. of *d*-camphorsulfonic acid in 25 ml. of water, heat developed at once. The observed rotation of the resulting glycol, 9.5 g. (0.105 mole) in a 1-dm. tube, was +0.06°, and of 11 g. of glycol, from another experiment, was +0.13° in a 2-dm. tube. The glycol was a liquid. The *trans* oxide, under the same treatment, yielded a solid glycol of zero rotation. Likewise, when the *cis* oxide was hydrated in the presence of *d*-tartaric acid, and the tartrate ion was removed as insoluble silver tartrate before distillation, the observed rotation of the resulting liquid glycol was -0.05°; the solid glycol from the *trans* oxide had zero rotation.

**Preparation of the Isomeric 2,3-Dibromobutanes.**—When attempts were made to prepare these from the glycols by the usual methods, *i. e.*, concentrated hydrobromic acid, concentrated hydrobromic acid and zinc bromide, phosphorus tribromide or phosphorus pentabromide, the mixtures became dark colored and only very small yields of the dibromides were obtained. Moreover, the products were mixtures. A pinacol rearrangement was responsible for the low yields. This was established by isolating methyl ethyl ketone from the reaction mixture. The dibromides can be prepared in good yield by the action of hydrobromic acid upon the diacetates.

Saturated aqueous hydrobromic acid is prepared by saturating the constant boiling acid with dry hydrogen bromide (from tetralin and bromine). In 200 ml. of this solution is dissolved 52 g. (0.3 mole) of a diacetate and the mixture is allowed to stand at room temperature for three or four days. In a short time the solution becomes cloudy and after some time a layer of dibromobutane rises to the top. This is separated, washed with water, aqueous sodium carbonate and water and then dried with calcium chloride; yield of crude dibromide, 61 g., 94%. When fractionated through a 40-cm. Weston column<sup>23</sup> with total reflux, about 50 g. distils within a range of 0.2°.

**Properties of the Dibromides.**—The properties of the dibromides, shown in Table III, are practically identical with the properties of the dibromobutanes obtained by a wholly different synthetic method.<sup>24</sup> The configurations of the butenes, assumed in a previous paper, are now known

TABLE III

## PROPERTIES OF THE INACTIVE 2,3-DIBROMOBUTANES

Dibromide configuration	<i>dl</i>	<i>meso</i>
Diacetate from which obtained	<i>meso</i>	<i>dl</i>
Dibromide, b. p., ° C., 50 mm.	73.2–73.4	76.4–76.6
Dibromide, sp. gr., $d^{20}_4$	1.7783	1.7922
Dibromide, $n^{25}_D$	1.5098	1.5120
Dibromide, $k^a$	0.0541	0.0285

<sup>a</sup> Specific reaction rate constant with KI; see ref. 3; the authors are indebted to Mr. Saul Winstein for these values.

(23) Weston, *Ind. Eng. Chem., Anal. Ed.*, **3**, 177 (1931).

(24) Young, Dillon and Lucas, *THIS JOURNAL*, **51**, 2528 (1929). Their butenes boiled (when corrected to 760 mm.) at the same temperatures as the butenes prepared by Kistiakowsky, *et al.*<sup>5</sup>

to be the correct ones, for they have been settled by Brockway and Cross<sup>25</sup> through electron diffraction studies.

The dibromobutanes shown in Table III are reassigned the configurations previously given them. These configurations still appear to be the correct ones, in the absence of new evidence, on the usual assumption that one Walden inversion takes place when bromine adds to a pure 2-butene.<sup>1,17</sup>

## Summary

*trans*-2-Butene has been obtained from *cis*-2-butene through a series of changes, as follows: *cis*-2-butene  $\rightarrow$  3-chloro-2-butanol  $\rightarrow$  *cis*-2,3-epoxybutane  $\rightarrow$  *dl*-2,3-butanediol  $\rightarrow$  *dl*-butanediol diacetate  $\rightarrow$  *meso*-2,3-dibromobutane  $\rightarrow$  *trans*-2-butene. Through a similar series of changes, *cis*-2-butene has been obtained from *trans*-2-butene.

The lower boiling 2,3-epoxybutane has been shown to have the *trans*, and the higher boiling to have the *cis* configuration. The liquid 2,3-butanediol has the *dl* and the solid the *meso* configuration.

It has been shown that a Walden inversion is involved in the formation of the *dl*-glycol from the *cis* oxide and of the *meso* glycol from the *trans* oxide. It is believed that five inversions are involved when either of the 2-butenes is converted into its stereoisomer, as outlined above.

The inactive 2,3-butanediols undergo a pinacol rearrangement in contact with concentrated hydrobromic acid.

The butene mixture resulting from the decomposition of 1-butanol by hot sulfuric acid (60 by volume) is approximately 35% *cis*-2-butene and 65% *trans*-2-butene.

PASADENA, CALIF.

RECEIVED AUGUST 10, 1936

(25) Brockway and Cross, *ibid.*, **58**, 2407 (1936). The melting points, by Kistiakowsky, *et al.*, ref. 5, lead to the same conclusion.