

filtrate yielded 0.3 g. of crude 4-dibenzofurylacetic acid. The crude amide was recrystallized from benzene to yield 1.5 g. (57% yield based on amine) of the pure amide melting at 186–187°.

*Anal.* Calcd. for  $C_{24}H_{21}O_5N$ : N, 3.47. Found: N, 3.71 and 3.72.

**3,4 - Dimethoxy -  $\alpha$  - (4 - dibenzofuroylamino) - acetophenone.**—The reaction between 0.1 g. of 4-dibenzofurancarboxylic acid chloride and 0.1 g. of 3,4-dimethoxy- $\alpha$ -aminoacetophenone hydrochloride was carried out by the same procedure as that just given. The product was recrystallized from ethanol and melted at 178–179°.

*Anal.* Calcd. for  $C_{23}H_{19}O_5N$ : N, 3.71. Found: N, 3.68.

**Acknowledgment.**—The authors are grateful to H. B. Willis for assistance.

### Summary

Experiments are described concerning the preparation and proof of structure of some substituted amines and other derivatives of dibenzofuran. The generalizations on orientation postulated previously have been shown to be adequate for the predominant products which result from polysubstitution of the dibenzofuran nucleus.

AMES, IOWA

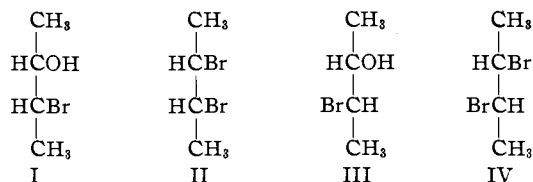
RECEIVED JUNE 26, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 724]

## The Loss of Optical Activity in the Reaction of the Optically Active erythro- and threo-3-Bromo-2-butanols with Hydrobromic Acid

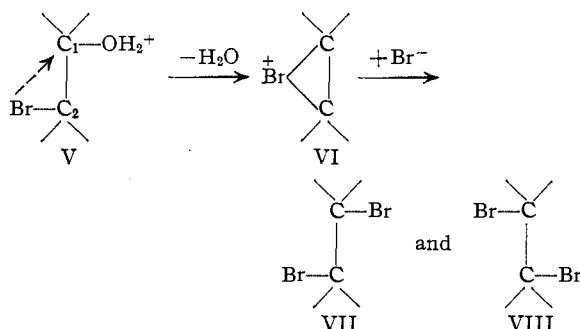
BY S. WINSTEIN<sup>1</sup> AND H. J. LUCAS

Recently it was shown<sup>2</sup> that *dl*-erythro-3-bromo-2-butanol I is converted into *meso*-2,3-dibromobutane II, and *dl*-threo-3-bromo-2-butanol III, is converted into *dl*-2,3-dibromobutane IV, by the action of fuming hydrobromic acid, with complete retention of configuration.<sup>3,4</sup>



In order to account for this unusual behavior, it was assumed that the replacement of the hydroxyl group by the bromine atom took place by a mechanism involving attack by the bromine atom on the adjacent carbon atom of the bromohydrin. This bromine atom, simultaneously with the removal of the  $\text{OH}_2^+$  group V (which is formed from the OH group and a proton), forms a bond with the carbon atom on the face away from the  $\text{OH}_2^+$  group, thus leading to the formation of the positively charged cyclic intermediate, VI,<sup>5</sup> of

Roberts and Kimball<sup>6</sup> which then reacts with bromide ion to produce the two possible dibromides VII and VIII.



On the basis of this mechanism two inversions take place, for the formation of the intermediate, VI, is accompanied by an inversion of carbon atom  $\text{C}_1$ , and the reaction of this with bromide ion is accompanied by a second inversion. If VII is the product,  $\text{C}_1$  is inverted twice, while if VIII is the product  $\text{C}_1$  and  $\text{C}_2$  are each inverted once. This explains the formation of *meso*-2,3-dibromobutane from the *erythro*-bromohydrin, and of *dl*-2,3-dibromobutane from the *threo*-bromohydrin. In fact, each of the active forms of the *threo*-bromohydrin is predicted by this mechanism to give *dl*-2,3-dibromobutane, since VII and VIII would be formed in equal amounts.

It was pointed out that this feature could be used as a test for the mechanism by starting

(1) At present National Research Fellow in Chemistry at Harvard University.

(2) Winstein and Lucas, *THIS JOURNAL*, **61**, 1576 (1939).

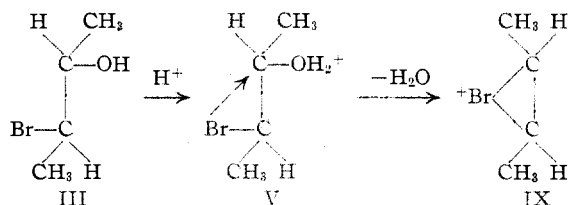
(3) Only one of the two antipodes of the *dl*-compounds is shown.

(4) By retention of configuration in these cases is meant merely that an *erythro*-bromohydrin gives rise to a *meso*-dibromide and a *threo*-bromohydrin to a *dl*-dibromide. Strictly speaking, configuration is not retained.

(5) We propose to call the simplest ion having this structure, ethylenebromonium ion.

(6) Roberts and Kimball, *THIS JOURNAL*, **59**, 947 (1937).

with optically active *threo*-bromohydrin III. The predicted loss in activity in going from an active *threo*-bromohydrin to an inactive dibromide may be better understood perhaps by noting that the cyclic intermediate IX has the internally compensated *cis* configuration, and thus can give rise to only inactive products.



It has now been found that both the *erythro*- and *threo*-bromobutanols in the active form give rise to inactive dibromides. Moreover, optically active acetates of these two bromobutanols also give rise to inactive dibromides. The conversion was carried out with optically active forms of both the *erythro*- and *threo*-bromohydrins so as to make the test of the proposed mechanism free of any doubt that might be cast on it by questioning the assignment of configurations to the 3-bromo-2-butanols or the 2,3-dibromobutanols.

Optically active bromobutanols and acetates were obtained by partial acetylation of the bromohydrins with acetic anhydride in carbon tetrachloride containing brucine, according to the method which Wegler<sup>7</sup> used in other cases. The *dl*-*erythro*-3-bromo-2-butanol gave rise to a (+)-*erythro*-3-bromo-2-butanol and a (-)-*erythro*-3-acetoxy-2-bromobutane, while the *dl*-*threo*-3-bromo-2-butanol gave rise to a (-)-*threo*-3-bromo-2-butanol and a (-)-*threo*-3-acetoxy-2-bromobutane. The resolution to be expected from the method employed is of course quite incomplete.

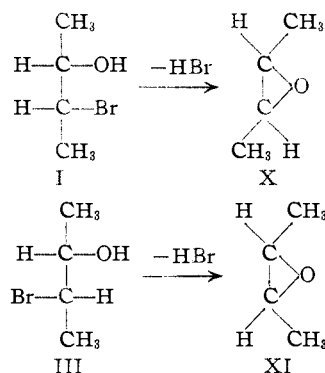
TABLE I  
SUMMARY OF THE OPTICAL ROTATION DATA

Substance	Config.	$\alpha_D$ (1 dcm.)
1 3-Bromo-2-butanol	<i>erythro</i>	+1.91 ± 0.02°
2 2-Acetoxy-3-bromobutane	<i>erythro</i>	-3.01 ± .03
3 2,3-Dibromobutane from 1	<i>meso</i>	0.00 ± .02
4 2,3-Dibromobutane from 2	<i>meso</i>	0.01 ± .02
5 2,3-Epoxybutane from 1	<i>trans</i>	+4.37 ± .01
6 3-Bromo-2-butanol	<i>threo</i>	-1.17 ± .02
7 3-Bromo-2-butanol	<i>threo</i>	-1.04 ± .01
8 2-Acetoxy-3-bromobutane	<i>threo</i>	-0.31 ± .01
9 2,3-Dibromobutane from 6	<i>dl</i>	.00 ± .01
10 2,3-Dibromobutane from 7	<i>dl</i>	.00 ± .02
11 2,3-Dibromobutane from 8	<i>dl</i>	.00 ± .01
12 2,3-Epoxybutane from 7	<i>cis</i>	.01 ± .01

(7) Wegler, *Ann.*, **506**, 77 (1933).

The optical rotations of these compounds, as well as optical data on the oxides and dibromides, are given in Table I.

To make certain that the optical activity in the case of the (-)-*threo*-bromohydrin was not due largely to the presence of a quite small amount of an optically active *erythro* isomer, which would give optically inactive dibromobutane, some of the active *erythro*- and *threo*-bromohydrins were converted to oxides. One would expect active *erythro*-3-bromo-2-butanol I to yield an active *trans*-2,3-epoxybutane X, and active *threo*-3-bromo-2-butanol III to yield inactive internally compensated *cis*-2,3-epoxybutane XI since one inversion accompanies the formation of the oxide ring.<sup>2</sup>



The active bromobutanols behaved as expected on conversion to oxides. It was found that the *trans* oxide from (+)-*erythro*-3-bromo-2-butanol has a (+) rotation while the *cis* oxide from (-)-*threo*-3-bromo-2-butanol was inactive (Table I). Thus, the active *threo*-bromohydrin was not contaminated with appreciable amounts of an active *erythro*-bromohydrin.

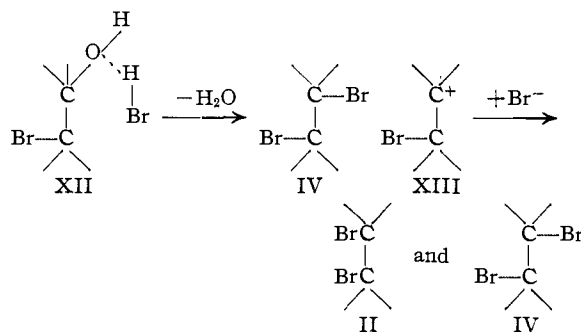
The inactivity of the dibromide from the active *threo*-3-bromo-2-butanol (Table I) hardly can be explained on the basis of a low specific rotation for a *d*- or *l*-2,3-dibromobutane.<sup>8</sup> It seems quite unlikely that the rotation to be expected from (+)- or (-)-2,3-dibromobutane would be smaller than the rotation of (-)-*threo*-3-bromo-2-butanol by a factor of approximately 50 or 100, and thus be within experimental error of zero. Thus it must be that (-)-*threo*-3-bromo-2-butanol gives *dl*-2,3-dibromobutane. This definitely confirms

(8) In many cases, the optical activity of an alcohol is comparable to or less than that of the corresponding halide; see for example, Kenyon, Phillips and Pittman, *J. Chem. Soc.*, 1072 (1935); Levene and Rothen, *J. Biol. Chem.*, **127**, 237 (1939); Hughes, Ingold and Masterman, *J. Chem. Soc.*, 1196 (1937); Hughes, Ingold and Scott, *ibid.*, 1201 (1937); Cowdrey, Hughes and Ingold, *ibid.*, 1208 (1937); Stevens and McNiven, *This Journal*, **61**, 1295 (1939).

the proposed mechanism, which involves the formation of 1,2-dimethylethylenbromonium ion, VI.

It is evident from Table I that the active bromoacetates behave as the bromohydrins do, to give inactive dibromides. This is to be expected since the bromoacetates presumably are converted to the dibromides by way of the bromohydrins.<sup>9</sup> It must be recognized that the butylenbromonium ion can react with water, as well as with bromide ion. The reaction with water, in the case of the *cis* ion, will give rise to *dl*-threo-3-bromo-2-butanol. Here then is a way for the active threo-bromohydrin to become inactive. It is probable, however, that the positive ion reacts practically exclusively with bromide ion in the present reaction medium. This statement is based upon the observations that the corresponding oxide is converted almost quantitatively to bromohydrin,<sup>2</sup> not glycol in concentrated hydrobromic acid, and that in bromine additions to double-bonded compounds, in which bromonium ions<sup>10</sup> are intermediates,<sup>2,6,11</sup> bromide ion competes much better than solvent molecules.

**Other Possible Mechanisms.**—The results obtained show that two other possible mechanisms, which have been proposed for the conversion of monohydric alcohols to bromides, are not operative here. One such mechanism is the internal, cyclic reaction of a bromohydrin-hydrogen bromide complex.<sup>12</sup> This type of reaction which seems to occur in some cases<sup>8</sup> cannot be operative here, otherwise the dibromide IV, resulting from optically active threo-3-bromo-2-butanol XII, would possess optical activity.



(9) Winstein and Lucas, *THIS JOURNAL*, **61**, 1581 (1939).

(10) Pfeiffer and co-workers have isolated and formulated salts which bear a formal resemblance to our bromonium salts, such as  $[(\text{C}_2\text{H}_5)_2\text{NC}_2\text{H}_4]_2\text{CCH}_2\text{Br}^+ \text{ClO}_4^-$  [see Pfeiffer and Wizinger, *Ann.*, **461**, 132 (1928)] and  $[(\text{C}_6\text{H}_5\text{C}_6\text{H}_4)_2\text{CCH}_2\text{Br}]^+ \text{Br}_3^-$  [see Pfeiffer and Schneider, *J. prakt. Chem.*, **120**, 129 (1931)].

(11) (a) Bartlett and Tarbell, *THIS JOURNAL*, **58**, 466 (1936); (b) Read and Williams, *J. Chem. Soc.*, **117**, 359 (1920); (c) Ingold, *Chem. Rev.*, **15**, 225 (1934).

(12) Cowdrey, Hughes, Ingold, Masterman and Scott, *J. Chem. Soc.*, 1252 (1937).

Another such mechanism is the dissociation<sup>12</sup> of the bromohydrin-proton complex, V, to give a halogen substituted carbonium ion XIII, with subsequent reaction of this ion with bromide ion. In the case of both the active *erythro*- and active *threo*-bromohydrins, this would lead to the production of a mixture of the *meso*-dibromide II and an active dibromide IV, unless one postulates that the configuration of the carbonium ion is stabilized in the pyramidal form. If it is possible for the configuration to be so stabilized, then the resulting dibromide from the active *threo*-bromohydrin would possess optical activity. Thus the carbonium ion mechanism, which has been postulated in other cases<sup>12</sup> but which has been the subject of considerable discussion recently,<sup>13</sup> definitely is not operative in the case of these 3-bromo-2-butanols.

While it might turn out to be useful to think that the chief "driving force"<sup>14</sup> of the reaction of formation of the butylenbromonium ion VI is the tendency for the  $-\text{OH}_2^+$  group to be dissociated off as a water molecule, nevertheless we must not regard XIII as an intermediate. The bond between bromine and carbon is formed essentially simultaneously with the dissociation of the  $-\text{OH}_2^+$  group from the rest of the molecule.

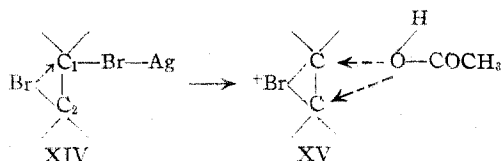
**Other Changes Involving Halonium Ions.**—In addition to the reactions of bromohydrins with acids and of bromine and bromine-donating substances with ethylenic compounds, as discussed previously,<sup>2</sup> there must be other situations in which bromonium ions are intermediates. This would be expected when there is a tendency to remove one group in a molecule in which there is a bromine substituent able to attack the back face of the carbon atom losing the group. Thus, for example, the production of *cis*-1,2-diacetoxycyclohexane from the action of silver acetate on 1,2-dibromocyclohexane in acetic acid does not necessarily indicate that the 1,2-dibromocyclohexane is the *cis* isomer.<sup>15</sup> We prefer the explanation that an odd number of inversions are involved in the transformation to the diacetate and that 1,2-dibromocyclohexane has the *trans* configuration. It seems plausible that the bromonium ion is produced by the action of a silver ion<sup>14,16</sup> simultaneously with the attack by the bromine

(13) (a) Winstein, *THIS JOURNAL*, **61**, 1635 (1939); (b) Bartlett, *ibid.*, **61**, 1630 (1939). See these articles for further references.

(14) Roberts and Hammett, *ibid.*, **59**, 1063 (1937).

(15) Rothstein, *Ann. chim.*, **14**, 461 (1930).

(16) See Hughes, Ingold and Masterman, *J. Chem. Soc.*, 1236 (1937); Cowdrey, Hughes and Ingold, *ibid.*, 1243 (1937).



atom of carbon atom  $C_2$  as shown by XIV and that this ion reacts with solvent as shown by XV. An inversion at the replacement of the second bromine atom by acetate would result in there being three inversions in the whole transformation. It seems plausible that presently the steric course of reactions of dihalides, halohydrins, etc., will be better understood when it is realized to what extent bromonium ions and hitherto unknown compounds of a similar sort play a part.

Besides bromonium ions there may be chloronium and iodonium ions of similar structure.

### Experimental

**Materials.**—The *dl-erythro-3-bromo-2-butanol* was prepared from the pure *trans-2,3-epoxybutane* and the *dl-threo-3-bromo-2-butanol* from both pure *cis-2,3-epoxybutane* or *cis-2-butene* according to directions previously given.<sup>2</sup>

Merck brucine was employed and the acetic anhydride was purified by fractionation.

**Partial Resolution of *erythro-3-Bromo-2-butanol* and Conversion to 2,3-Dibromobutane.**—In 500 ml. of pure carbon tetrachloride was dissolved with heating 50 g. of brucine, then 50 ml. of *dl-erythro-3-bromo-2-butanol* and 22 ml. of acetic anhydride were added in turn and the reaction mixture was refluxed for two hours. After the reaction mixture was cool, it was washed first with dilute hydrochloric acid and then sodium carbonate solution. The mixture was dried over potassium carbonate, most of the carbon tetrachloride was distilled off through a 15-cm. column of glass helices at about 40°, and the residue was fractionated through a 40-cm. Weston<sup>17</sup> column. There was obtained 38 ml. of distillate, 12 ml. being essentially pure bromohydrin, b. p. (13 mm.) 53.1–53.7°,  $n_D^{25}$  1.4762 and 19 ml. being pure acetoxybromobutane, b. p. (13 mm.) 67.0–67.2°,  $n_D^{25}$  1.4488. Intermediate fractions made up the remainder of the material. The rotation  $\alpha_D$  (1 dcim.) of the bromohydrin was 1.91° and of the acetate –3.01°. Half of the bromohydrin sample was converted to oxide as previously described,<sup>2</sup> the oxide exhibiting  $\alpha_D$  (1 dcim.) +4.37°. The oxide and bromohydrin were dissolved in fuming hydrobromic acid, the dibromide b. p. (50 mm.) 73.2°,  $n_D^{25}$  1.5090, possessing  $\alpha_D$  (1 dcim.) 0.00°. The acetate similarly gave rise to dibromide b. p. (50 mm.) 73.2°,  $n_D^{25}$  1.5090 which possessed  $\alpha_D$  (1 dcim.) 0.00°. The intermediate fractions also were converted to dibromide. The combined and redistilled dibromobutane from the bromohydrin and oxide, acetoxybromobutane, and the intermediate fractions, b. p. (50 mm.) 73.3°,  $n_D^{25}$  1.5091 pos-

essed a dielectric constant<sup>2,18</sup> of 6.208. This indicates a few % of *dl*-dibromobutane in the *meso*-dibromide. Some stereomutation from *erythro* to *threo* apparently takes place during the procedure for partial resolution of the bromohydrin.

**Partial Resolution of *threo-3-Bromo-2-butanol* and Conversion to 2,3-Dibromobutane.**—From the treatment of 44 ml. of *threo-3-bromo-2-butanol* with 44 g. of brucine and 22 ml. of acetic anhydride in 440 ml. of carbon tetrachloride as described above in the case of the *erythro*-bromohydrin and subsequent washing, drying and distillation was obtained 39 ml. of distillate, 8 ml. being quite pure bromohydrin, b. p. (13 mm.) 50.0–50.8°,  $n_D^{25}$  1.4757, 13 ml. being quite pure acetoxybromobutane, b. p. (13 mm.) 69.6°,  $n_D^{25}$  1.4491, the rest of the material consisting of intermediate fractions. The bromohydrin exhibited  $\alpha_D$  (1 dcim.) –1.17° while the acetoxybromobutane possessed  $\alpha_D$  (1 dcim.) –0.31°. The bromohydrin, acetoxybromobutane and the combined intermediate fractions were converted to dibromobutanes in the usual way. The dibromobutane b. p. (50 mm.) 76.1° from the bromohydrin exhibited  $\alpha_D$  (1 dcim.) 0.00°, that from the intermediate fractions, b. p. (50 mm.) 76.0° possessed  $\alpha_D$  (1 dcim.) 0.00°, and the dibromide b. p. (50 mm.) 76.2° from the bromohydrin acetate yielded  $\alpha_D$  (1 dcim.) 0.00°. The combined and redistilled dibromobutane b. p. (50 mm.) 75.9–76.2°,  $n_D^{25}$  1.5121, possessed a dielectric constant of 5.797. Here, too, a little stereomutation must have been involved in the procedure for the partial resolution of the bromohydrin.

When 46 ml. of *threo-3-bromo-2-butanol* was partially resolved with the aid of 46 g. of brucine, 20 ml. of acetic anhydride and 500 ml. of carbon tetrachloride and distillation was carried out, 10 ml. of bromohydrin fraction b. p. (13 mm.) 50.2–50.7°,  $n_D^{25}$  1.4749,  $\alpha_D$  (1 dcim.) –1.04° was obtained. Three ml. of this bromohydrin yielded an oxide having  $\alpha_D$  (1 dcim.) 0.01°. The remainder of the bromohydrin yielded a dibromide, b. p. (50 mm.) 76.3°,  $n_D^{25}$  1.5121, which showed  $\alpha_D$  (1 dcim.) 0.00°.

In Table I the indicated possible errors in the optical rotations are the sum of the mean deviations for a set of readings on the zero point and a set of readings on the substance in question. For the readings a Zeiss 0.01° instrument and a small capacity 1-dcm. tube were employed.

### Summary

There is complete loss of optical activity when active *erythro*- or *threo-3-bromo-2-butanol* is converted to 2,3-dibromobutane. This confirms the mechanism previously proposed in connection with the conversion of *dl-erythro*- and *dl-threo-3-bromo-2-butanol* to *meso*- and *dl-2,3-dibromobutane*, respectively. The mechanism consists of the production of a butylenebromonium ion, and the subsequent reaction of this ion with bromide ion, two inversions occurring in the transformation. Other possible mechanisms for the transformation of bromohydrin to dibromide are discussed and rejected.

RECEIVED AUGUST 9, 1939

(17) Weston, *Ind. Eng. Chem., Anal. Ed.*, **5**, 179 (1933).

(18) Winstein and Wood, unpublished work.