mine complex. This positive bromine complex is identical with the intermediate usually assumed in connection with halogen addition to olefins,

and chemically is analogous to the oxide–proton complex.

The Reaction Steps in the Conversion of 2,3-Diacetoxybutane to 2,3-Dibromobutane

By S. Winstein and H. J. Lucas

The result obtained by Wilson and Lucas[1] that the reaction of 2,3-diacetoxybutane with fuming aqueous hydrogen bromide to replace the acetoxy groups by bromide gave rise to an odd number of Walden inversions, has led us to examine more closely the mechanism of the transformation and to study the presence or absence of Walden inversion at each of the several steps involved in the transformation.

Ester Splitting.—Splitting of esters by hydrogen bromide is little used except with carbohydrate derivatives.[2] Acetic acid is generally used as a solvent for the splitting of esters by hydrogen bromide.[2,3] Sapper did not use a solvent but studied[4] the splitting reaction with hydrogen bromide dissolved in the ester. He obtained a slow reaction and claimed the reaction to be even slower with aqueous hydrogen bromide. However, Sapper probably mistook an equilibrium effect for a rate effect. It has been our experience in this Laboratory that when aqueous hydrogen bromide gives the halide on reaction with an ester it does so much more rapidly than in acetic acid as solvent, and much more rapidly than reported by Sapper for the reaction without a solvent. In the presence of very high concentrations of hydrogen bromide, acid–alcohol–ester–water equilibria are established[4] quite rapidly so that when the splitting of an ester by hydrogen bromide is carried out in the presence of water, it becomes possible that the mechanism is chiefly one of hydrolysis of the ester to the alcohol and acid, with consequent reaction of the alcohol with hydrogen bromide. This mechanism seems to operate in the case of the diacetoxybutanes.

The Intermediates.—On the above basis, the intermediates in the transformation of 2,3-diace-toxybutane to 2,3-dibromobutane would be 3-acetoxy-2-butanol, 2-acetoxy-3-bromobutane, and 3-bromo-2-butanol. 2,3-Butanediol is ruled out as a possible intermediate because it was shown to undergo rearrangement[1] under the conditions of the experiments.

Isolation experiments in which reaction mixtures were neutralized and organic material extracted disclosed the fact that these formulated intermediates are present. The preparation of the inactive *erythro*- and *threo*-3-bromo-2-butanols and their reaction with hydrogen bromide with retention of configuration are reported elsewhere.[5]
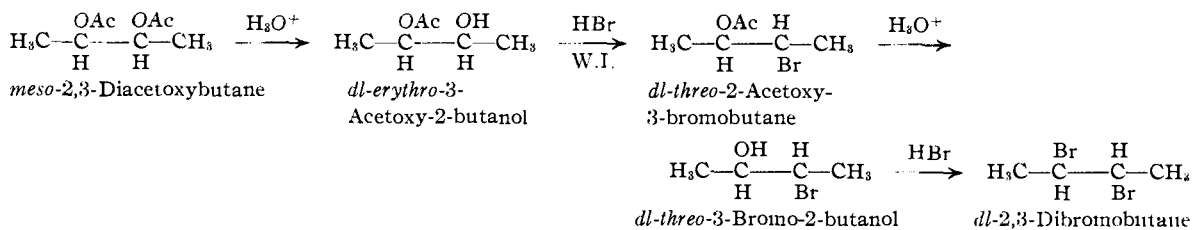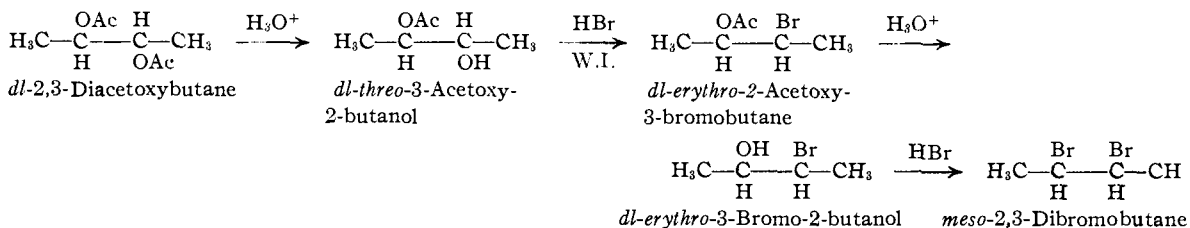
The inactive 2-acetoxy-3-bromobutanes have been prepared by acetylation of the corresponding bromohydrins. One of the 3-acetoxy-2-butanols was prepared from *meso*-2,3-butanediol by acetylation, and from *trans*-2,3-epoxybutane by acetic acid addition, both preparations proving identical.

In regard to configurations, that of the *meso*-2,3-butanediol is known[1] and those of the inactive 3-bromo-2-butanols are discussed elsewhere.[5] Since no inversion can occur in the acetylation of these compounds, the configurations of 3-acetoxy-2-butanol (monoacetate of the glycol) and of the inactive 2-acetoxy-3-bromobutanes (acetates of the bromohydrins), are also known. Since the monoacetate from the *meso* glycol and the monoacetate from the known[1,6] *trans*-2,3-epoxybutane give the same 2,3-dibromobutane (Table I), a Walden inversion is proved in the opening of an oxide ring by acetic acid.

The synthesized predicted intermediates, in contrast to the 2,3-butanediols, reacted smoothly with aqueous fuming hydrobromic acid to give essentially quantitative yields of 2,3-dibromobutanes. The qualitative rates of dibromide formation are in such order as to make reasonable the formulation of these substances as intermediates.

(1) Wilson and Lucas, This Journal, **58**, 2396 (1936).

(2) E. Fischer, *Ber.*, **44**, 1899 (1911).

(3) (a) Perkin and Simonsen, *J. Chem. Soc.*, 855 (1905); (b) Tronow and Ssibgatullin, *Ber.*, **62**, 2850 (1929).

(4) Sapper, *Ann.*, **211**, 178 (1882).

(5) Winstein and Lucas, This Journal, **61**, 1576 (1939).

(6) Brockway and Cross, *ibid.*, **59**, 1147 (1937).

OAc OAc   OAc OH   OAc H   OAc H
H₃C—C——C—CH₃ $\xrightarrow{H_3O^+}$ H₃C—C——C—CH₃ $\xrightarrow[\text{W.I.}]{HBr}$ H₃C—C——C—CH₃ $\xrightarrow{H_3O^+}$
H   H   H   H   H   Br

meso-2,3-Diacetoxybutane   *dl-erythro*-3-Acetoxy-2-butanol   *dl-threo*-2-Acetoxy-3-bromobutane

OH H   Br H
H₃C—C——C—CH₃ $\xrightarrow{HBr}$ H₃C—C——C—CH₃
H   Br   H   Br

dl-threo-3-Bromo-2-butanol   *dl*-2,3-Dibromobutane

Fig. 1.—*dl*-2,3-Dibromobutane from *meso*-2,3-diacetoxybutane.

OAc H   OAc H   OAc Br
H₃C—C——C—CH₃ $\xrightarrow{H_3O^+}$ H₃C—C——C—CH₃ $\xrightarrow[\text{W.I.}]{HBr}$ H₃C—C——C—CH₃ $\xrightarrow{H_3O^+}$
H   OAc   H   OH   H   H

dl-2,3-Diacetoxybutane   *dl-threo*-3-Acetoxy-2-butanol   *dl-erythro*-2-Acetoxy-3-bromobutane

OH Br   Br Br
H₃C—C——C—CH₃ $\xrightarrow{HBr}$ H₃C—C——C—CH
H   H   H   H

dl-erythro-3-Bromo-2-butanol   *meso*-2,3-Dibromobutane

Fig. 2.—*meso*-2,3-Dibromobutane from *dl*-2,3-diacetoxybutane.

It is interesting that none of the intermediates undergo the pinacol rearrangement, and that, starting with diacetate, the relative rates of the reactions concerned are such that the produced monoacetate does not give rise to much glycol and thus rearrangement. In fact, a good yield of dibromobutane can be obtained by using glycol, acetic acid and fuming hydrobromic acid, esterification of the glycol being rapid and complete enough to prevent pinacol rearrangement of the glycol.

The Reaction Steps.—Since the postulated intermediates have been isolated, and the synthesized intermediates give quantitative yields of dibromobutanes at the proper relative rates, it therefore would appear that the several steps in the transformation of 2,3-diacetoxybutane to 2,3-dibromobutane by hydrobromic acid are: (a) hydrolysis to remove one acetyl group; (b) replacement of the free hydroxyl group by bromide; (c) hydrolysis to remove the second acetyl group; and (d) replacement of the second hydroxyl group by bromide.

The dibromobutanes which were obtained from the synthesized intermediates proved to be pure and the identification of some of them is indicated in Table I. Inspection of Table I and a consideration of previous results[1,5] show that a monoacetate gives the same dibromide as a corresponding diacetate, and that a 2-acetoxy-3-bromobutane gives the same dibromobutane as the parent bromohydrin. Thus, in the transformation of 2,3-diacetoxybutane to 2,3-dibromobutane, inversions do not occur at the hydrolysis steps. Since it has been decided already[5] that conversion of the bromohy-

TABLE I

THE IDENTIFICATION OF THE 2,3-DIBROMOBUTANES

Source	B. p.₆₀	n^{25}D	K_2	ε
dl-erythro-3-Bromo-2-acetoxybutane	73.3	1.5091	0.0550	
trans-2,3-Epoxybutane	73.2	1.5091	.0551	
dl-threo-3-Bromo-2-acetoxybutane	76.5	1.5125	.0298	
dl-erythro-3-Acetoxy-2-butanol from *meso* glycol	76.4	1.5125		5.768
dl-erythro-3-Acetoxy-2-butanol from *trans* oxide	76.3	1.5125		5.764
Previously described				
Pure *meso*-2,3-dibromobutane	73.3[1]	1.5092[7]	.0544[7]	6.245[8]
Pure *dl*-2,3-dibromobutane	76.4[1]	1.5125[7]	.0297[7]	5.758[8]

drins to dibromides occurs with retention of configuration, the only inversion in the whole transformation is in the reaction of the 3-acetoxy-2-butanol with hydrogen bromide. At this step, there is a clean-cut inversion. Figures 1 and 2 symbolize these facts. In these figures, in which only one of the two possible stereoisomers of *dl* mixtures is shown, W. I. denotes a Walden inversion.

The Walden Inversion.—The clean-cut inversion in the reaction of *erythro*-3-acetoxy-2-butanol with hydrogen bromide to give *threo*-2-acetoxy-3-bromobutane deserves some consideration in view of the considerable racemization accompanying the reaction in the case of an ordinary monohydric alcohol.[9] Apparently the presence of the electron-attracting group and the ionizing

(7) Dillon, Young and Lucas, THIS JOURNAL, 52, 1953 (1930).

(8) Winstein and Wood, unpublished work.

(9) (a) Cowdrey, Hughes, Ingold, Masterman and Scott, *J. Chem. Soc.*, 1252 (1937); (b) Winstein and Lucas, unpublished work.

solvent favor a clean-cut bimolecular exchange (with inversion) of bromide ion for the —+OH₂ group (formed from —OH and a proton). This is shown in formula I. Possibly the monoacetate is

I   II

III
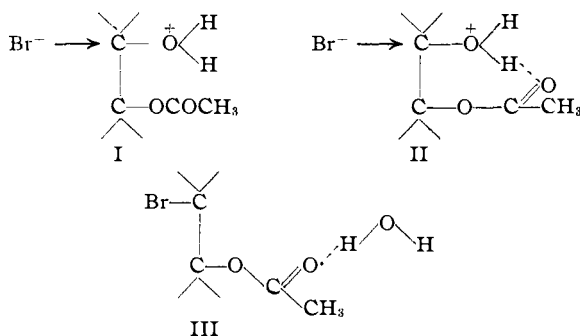
chelated and it is this chelate compound (II) (perhaps carrying more than one proton) which reacts with bromide ion to give acetoxybromobutane hydrogen-bonded to a water molecule (III).

The Reaction in Acetic Acid.—The situation with regard to the reaction between 2,3-diacetoxybutane and hydrogen bromide in acetic acid is not so clear as in the case of aqueous hydrogen bromide. The formation of a mixture of *dl* and *meso*-2,3-dibromobutanes resembles the behavior of a monohydric alcohol with hydrogen bromide rather than the behavior of the diacetate in aqueous solution. Starting with an impure diacetate which with aqueous hydrogen bromide yields a dibromide which is 89% *dl* and 11% *meso*, hydrogen bromide in acetic acid gives a product which is 56% *dl* and 44% *meso*. Whether this is the result of competition between more than one mechanism or whether racemization of the diacetate or intermediate 2-acetoxy-3-bromobutane takes place is not yet known. That it is not due to racemization of the final dibromobutane is indicated by the failure of hydrogen bromide in acetic acid to stereoisomerize *dl*-2,3-dibromobutane. If stereomutation takes place it must then be racemization of the 2-acetoxy-3-bromobutane by bromide ion or racemization of this compound or diacetate or both, due to exchange in strong acid solution of acetate between acetic acid and the substances in question.

Experimental

3-Bromo-2-butanols.—The *erythro-* and *threo-*3-bromo-2-butanols were prepared from pure 2,3-epoxybutanes as described elsewhere.[5]

Preparation of 2 - Acetoxy - 3 - bromobutanes.—The *erythro-* and *threo-*2-acetoxy-3-bromobutanes are prepared from the corresponding bromohydrins: 40.5 ml. (0.428

mole) of pure acetic anhydride is added to 54.5 g. (0.356 mole) of pure bromohydrin in several portions over a period of about twenty to thirty minutes. The mixture warms up of its own accord and smooth reaction takes place. After an hour's standing, the mixture is distilled at reduced pressure through a 15-cm. column of glass helices, the yield averaging 62.5 g. (90%) of product possessing a one or two degrees boiling range. Redistillation through a 40-cm. Weston[10] column yielded constant-boiling materials. The properties of the 2-acetoxy-3-bromobutanes are given in Table II.

TABLE II
PROPERTIES OF MATERIALS

Substance	B. p. °C.	Mm.	$n^{25}D$	d^{25}_4	M_D	M_D (calcd.)
dl-erythro-2-Acetoxy-3-bromobutane	67.2	13	1.4489	1.3327	39.24	39.33
dl-threo-2-Acetoxy-3-bromobutane	70.1	13	1.4490	1.3320	39.27	39.33
dl-erythro-3-Acetoxy-2-butanol	79.2	10	1.4215	1.0142	33.06	33.09

Preparation of *erythro*-**3-Acetoxy-2-butanol from Butanediol.**—To 34.6 g. (0.384 mole) of *meso*-2,3-butanediol, m. p. 34.0°, obtained by recrystallization[5] of Lucidol butylene glycol is added 39.3 g. (0.384 mole) of pure redistilled acetic anhydride and 2 small drops of concentrated sulfuric acid. The mixture warms up in a few minutes and is cooled under running water. After one hour's standing, the mixture is distilled at reduced pressure through a 15-cm. column of glass helices; yield 41.0 g. (81%); b. p. (10 mm.) 74.5-75.5°. This material is completely soluble in a small amount of water in contrast to the diacetoxybutane or mixtures of diacetate and glycol and possesses a saponification equivalent determined with potassium hydroxide in diethylene glycol[11] of 131; theoretical is 132.

erythro-**3-Acetoxy-2-butanol from the Oxide.**—43.2 g. (0.60 mole) of pure *trans*-2,3-epoxybutane[5] and 72 g. (1.20 moles) of glacial acetic acid were mixed and allowed to stand at room temperature for several weeks. Distillation through the Weston column yielded 41 g. (52%) of product, b. p. (10 mm.) 79.2°. Other properties are listed in Table II. The saponification equivalent of this material was 131, theoretical 132.

meso-**2,3-Diacetoxybutane.**—This substance was obtained from *meso*-2,3-butanediol, m. p. 34.0°, by the method of Wilson and Lucas.[1]

Conversions to 2,3-Dibromobutanes with Fuming Hydrobromic Acid.—Fifteen hundredths mole of 2,3-diacetoxybutane, 3-acetoxy-2-butanol, 2-acetoxy-3-bromobutane, 3-bromo-2-butanol or 2,3-epoxybutane, which was once thought to be an intermediate in the diacetate–dibromide conversion, are dissolved in cold saturated hydrobromic acid prepared from 130 g. of 48% hydrobromic acid and hydrogen bromide gas at 0° in an ampoule. The ampoule is sealed and left at room temperature. When the dibromide layer does not increase for a time, the dibromide is isolated as previously described.[1,5] The yield averages 93% from the above-mentioned substances and the product is essentially constant boiling when distilled through the Weston column. The identification of the products not

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

(11) Redemann and Lucas, *Ind. Eng. Chem., Anal. Ed.*, **9**, 521 (1937).

identified before is shown in Table I where K_2, the second-order reaction rate constant[7] for the reaction of the dibromobutane with potassium iodide in methanol at 74.93°, or ϵ, the dielectric constant, is shown along with b. p. and n_D. For comparison, the properties of pure 2,3-dibromobutanes are given.

The relative rates of dibromobutane formation from each of the substances can be estimated roughly by the time elapsed before the solution of the substance in fuming hydrobromic acid becomes quite cloudy due to dibromide separation, or by the time necessary for the dibromide layer to cease increasing. The approximate time elapsed before definite cloudiness was in each case approximately as follows: 2,3-diacetoxybutane, one and one-half to two hours; 3-acetoxy-2-butanol, one hour; 2-acetoxy-3-bromobutane or 2,3-epoxybutane, thirty minutes; 3-bromo-2-butanol, fifteen minutes. The time necessary for the dibromide layer to cease increasing varied from three days in the case of the diacetate to nine hours in the case of the bromohydrins.

When Lucidol butylene glycol, m. p. 27°, α_D (1-dm. tube) +0.64° is converted to diacetate, α_D (1-dm. tube) -0.71° and this converted to dibromobutane as above described, the dibromobutane possesses a K_2 value of 0.0326 and α_D (1 dm. tube) 0.00°. The melting point of the original glycol corresponds[1] to a composition of 90% *meso* and 10% d plus l while the K_2 value of the dibromide corresponds to 89% dl and 11% *meso*. Thus an odd number of Walden inversions are involved in the transformation. Optically active diacetate is converted to inactive *meso*-2,3-dibromobutane.

When 13.5 g. (0.15 mole) of mixed 2,3-butanediol and 10.5 g. (0.175 mole) of acetic acid are treated with fuming hydrobromic acid as above an 89% yield of dibromobutane is obtained after three days. Considerable darkening of the reaction mixture takes place under these conditions.

Isolation of Intermediates.—52.2 g. (0.30 mole) of *meso*-2,3-diacetoxybutane was left in fuming hydrobromic acid at room temperature for four hours, then the reaction mixture was diluted and neutralized with sodium bicarbonate and extracted with seven 200-ml. portions of isopropyl ether. The ether extract was dried over sodium sulfate and distilled through the Weston column after most of the ether was removed in a preliminary distillation. A 70% recovery of material was obtained, the distillation indicating the presence of materials boiling at 13 mm. at 45° (dibromobutane), 50.5° (*threo*-3-bromo-2-butanol), 70.6° (*threo*-2-acetoxy-3-bromobutane) and 85.5° (3-acetoxy-2-butanol). The first three materials present in comparable amounts, made up approximately half the recovered product. The material of b. p. (13 mm.) 85.5° was easy to obtain pure by the fractionation. It possessed a saponifica-tion equivalent of 131 (theoretical for monoacetate of 2,3-butanediol is 132) and was completely soluble in a small volume of water. Thus, no diacetate remained after four hours in the reaction mixture, but was completely converted to monoacetate and successive products.

Conversions to Dibromobutanes in Acetic Acid.—When 43.0 g. (0.247 mole) of the diacetate of Lucidol glycol and 231.5 g. of 40% hydrogen bromide in acetic acid (1.15 moles hydrogen bromide) are heated in a sealed bomb at 100° for ten hours, a 93% yield of dibromobutane, b. p. (50 mm.) 75–76°, is isolated by dilution with water, separating, washing and drying the dibromobutane layer. Similarly, after two hours at 100°, dibromobutane in 77% yield can be fractionated from unreacted and not fully reacted materials which are precipitated with the dibromide on dilution with water. After three weeks at room temperature a 35% yield is obtained. The K_2 values of these dibromobutane samples were 0.0412, 0.0392, and 0.0425, respectively. The average of these corresponds to a composition of 56% dl and 44% *meso*. This is to be compared with 89% dl and 11% *meso* which is the composition of the dibromobutane obtained by using aqueous fuming hydrobromic acid.

That hydrogen bromide in acetic acid causes no stereomutation of *dl*-2,3-dibromobutane under the conditions of the above experiments was shown by heating pure *dl*-2,3-dibromobutane, $K_2 = 0.0298$ in 26% hydrogen bromide, in acetic acid for six hours at 100° and recovering a dibromide having $K_2 = 0.0298$.

Summary

When *meso*-2,3-diacetoxybutane is converted into *dl*-2,3-dibromobutane by fuming hydrobromic acid, the intermediate products are *erythro*-3-acetoxy-2-butanol, *threo*-2-acetoxy-3-bromobutane and *threo*-3-bromo-2-butanol. The acetoxybutanol is converted into the acetoxybromobutane with complete inversion of configuration, unaccompanied by racemization. Similarly, *dl*-2,3-diacetoxybutane is converted into *meso*-2,3-dibromobutane through analogous intermediates.

Acetic acid converts *trans*-2,3-epoxybutane into *erythro*-3-acetoxy-2-butanol, also with complete inversion of configuration.

When acetic acid is the solvent, *meso*-2,3-diacetoxybutane and hydrogen bromide yield a mixture of *dl*- and *meso*-2,3-dibromobutanes.