[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 1316]

1,2-Dimethylethyleneiodonium Ions as Intermediates in Reactions of the 3-Iodo-2-butanols

BY H. J. LUCAS AND H. K. GARNER

The transitory existence of a cyclic positively charged bromonium[1] ion was demonstrated in the reaction of 3-bromo-2-butanol with hydrobromic acid[2] and has been shown to be involved in the reaction of 3-bromo-2-butanol with phosphorus tribromide,[3] and of 2-bromocyclohexanol with hydrobromic acid or phosphorus tribromide.[4] Similarly a cyclic chloronium ion appears to be involved in the reaction of 3-chloro-2-butanol with thionyl chloride[5] although with some other reagents the cyclic intermediate does not occur. Also it has been shown recently that the concept of a cyclic iodonium ion satisfactorily accounts for the greatly increased reactivity of the hydroxyl group in 2-iodocyclohexanol[6] and of the tosyloxy group in 2-iodocyclohexyl tosylate.[7] In the present study with 3-iodo-2-butanol the stereochemical results observed can be accounted for only on the basis of the corresponding intermediate, 1,2-dimethylethyleneiodonium ion.

TABLE I

PROPERTIES OF THE IODOHYDRINS AND DIHALIDES

Compound	B. p., °C. (cor.)	Mm.	M. p., °C. (cor.)	$n^{25}D$	d^{25}_4	$\alpha^{25}D$ obs.	$[\alpha]^{25}D$	M_D Calcd.	M_D Obs.	M_D Diff.
L(+)-*erythro*-3-Iodo-2-butanol (I)			18.4–18.9	1.5371	1.7753	+50.04	+28.19	35.00	35.19	0.19
(+)-*threo*-3-Iodo-2-butanol (II)	28.8–30.8 43	0.7 2.5		1.5352	1.7692	+ 3.06	+ 1.73	35.00	35.21	0.21
L(+)-*erythro*-2-Bromo-3-iodobutane (from I)	53.0 dec.	6	−9.5 to −9.0	1.5642	2.0362	+ 4.13	+ 2.03	41.24	42.01	0.77
L(+)-*erythro*-2-Chloro-3-iodobutane (from I)	34.8–35.3	5		1.5312	1.7532	+13.98	+ 7.97	38.34	38.57	0.23
DL-*threo*-2-Bromo-3-iodobutane (from II)	29–30	0.9		1.5736	2.0629	+ 0.01		41.24	42.04	0.80
DL-*threo*-2-Chloro-3-iodobutane (from II)	33.2–33.5	4		1.5337	1.7587	+ 0.05		38.34	38.59	0.25

Proof of the transitory existence of a cyclic iodonium ion by stereochemical studies of the active 3-iodo-2-butanols cannot be obtained from a reaction with hydriodic acid, analogous to the effect of hydrobromic acid on 3-bromo-2-butanol,[2] because of the instability of the resulting 2,3-diiodobutanes. However, hydrochloric and hydrobromic acids yield iodohalides of sufficient stability. The interpretation of results is not so simple as in the case of the 2,3-dibromobutanes for it is necessary to establish the configurations of both *erythro* and *threo*-2,3-dihalobutanes, C_4H_8IX. The properties of these and also of the iodohydrins are shown in Table I, and the configurations of the compounds involved in the changes are shown in Fig. 1.

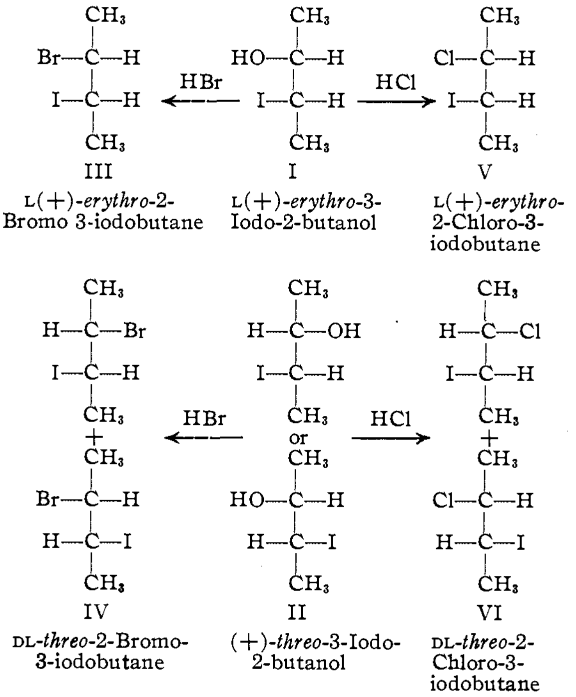


Fig. 1.—Stereochemical results of the reactions of L(+)-*erythro*-3-iodo-2-butanol and (+)-*threo*-3-iodo-2-butanol with hydrochloric and hydrobromic acids.

---

[1] I. Roberts and G. E. Kimball, THIS JOURNAL, **59**, 947 (1937).

[2] (a) S. Winstein and H. J. Lucas, *ibid.*, **61**, 1576 (1939); (b) **61**, 2845 (1939).

[3] S. Winstein, *ibid.*, **64**, 2791 (1942).

[4] S. Winstein, *ibid.*, **64**, 2792 (1942).

[5] H. J. Lucas and C. W. Gould, Jr., *ibid.*, **63**, 2541 (1941).

[6] S. Winstein, E. Grunwald, R. E. Buckles and C. Hanson, *ibid.*, **70**, 816 (1948).

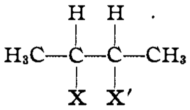
[7] (a) S. Winstein and E. Grunwald, *ibid.*, **68**, 536 (1946); (b) S. Winstein, E. Grunwald and L. L. Ingraham, *ibid.*, **70**, 812 (1948).

Configurations.—There can be little doubt as to the configurations of the 3-iodo-2-butanols, for their method of preparation from the isomeric 2,3-epoxybutanes is closely analogous to the preparation of the isomeric 3-bromo-2-butanols from these same oxides with hydrobromic acid,[2] that of the 3-chloro-2-butanols with hydrochloric acid,[5,8] and that of 3-acetoxy-2-butanol with acetic acid.[9] Therefore, the iodohydrin from *cis*-2,3-epoxybutane is DL-*threo*-3-iodo-2-butanol and the one from D(+)-2,3-epoxybutane is L-*erythro*-3-iodo-2-butanol.[10] The complete configuration of the active *threo* isomer, II, was not established, for it was prepared by partial resolution of the DL form.

Proof of the configurations of the 2,3-dihalobutanes, C_4H_8ClI and C_4H_8BrI, rests upon three kinds of evidence: (1) the relation between their physical properties and the properties of the isomeric forms of 2,3-dichloro- and 2,3-dibromobutane; (2) the magnitude of the optical rotations of the active forms of C_4H_8XI; (3) the stereochemical relationship between these and the 3-iodo-2-butanols. There is agreement among these three methods and each gives the same configuration for an active isomer. Therefore, it is believed that the configurations are well established.

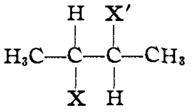
The best evidence for the configuration of the iodohalides, III, IV, V and VI, comes from the physical data which are summarized in Table II. It seems reasonable to assign the *erythro* configuration to the isomer having the lower refractive index and density, for it would be expected to resemble the *meso* form of $C_4H_8Cl_2$ and $C_4H_8Br_2$, while the *threo* form would resemble the DL isomer.

The magnitude of rotation of *erythro* isomers of C_4H_8XX' would be expected to be greatest when X and X' are least alike, and, moreover, the rotation of an *erythro* form would be expected to be lower than that of the isomeric *threo* form, since again an *erythro* resembles a *meso* and a *threo* resembles a DL form. It is noted from Table I that the rotation for L-*erythro*-2-bromo-3-iodobutane, III, is +2.03°, while that of L-*erythro*-2-chloro-3-iodobutane, V, is +7.97°, as would be expected of *erythro* dihalides. The relatively low value for the rotation of L-*erythro*-2-chloro-3-iodobutane shows that it is not the *threo* isomer. The *threo* isomer would be expected to have a rotation between that of active 2,3-dichlorobutane and active 2,3-diiodobutane, and this last would be expected to have the highest value. Although pure active 2,3-dichlorobutane has not yet been obtained, it should have a rotation[11] of about 44°.



$$H_3C{-}\overset{\displaystyle H}{\underset{\displaystyle X}{C}}{-}\overset{\displaystyle H}{\underset{\displaystyle X'}{C}}{-}CH_3$$

erythro



$$H_3C{-}\overset{\displaystyle H}{\underset{\displaystyle X}{C}}{-}\overset{\displaystyle X'}{\underset{\displaystyle H}{C}}{-}CH_3$$

threo

An *erythro*-2,3-C_4H_8IX should result from *erythro*-3-iodo-2-butanol and a *threo*-2,3-C_4H_8IX should result from *threo*-3-iodo-2-butanol by the action of fuming hydrochloric or hydrobromic acid, provided these two iodohydrins react by the same mechanism as the 3-bromo-2-butanols, of which the *erythro* isomer gave *meso*-2,3-dibromobutane and the *threo* isomer gave DL-2,3-dibromobutane.[2a] It is shown later that the mechanisms are alike.

Additional proof of configuration would be the preparation of antipodes of 2,3-C_4H_9BrI. The one from L(+)-*erythro*-3-bromo-2-butanol and hydriodic acid should be the antipode of the one from L(+)-*erythro*-3-iodo-2-butanol and hydrobromic acid. Unfortunately, the only product which could be isolated from the action of phosphorus and iodine or aqueous hydriodic acid on the bromohydrin was inactive 2-iodobutane.

The optical purity of the iodohalides, C_4H_8IX, is believed to be high. The rather narrow melting range of a crude preparation of L(+)-*erythro*-2-bromo-3-iodobutane (III), namely, −9.5 to −9.0°, seems to indicate reasonably good purity. Two preparations of L(+)-*erythro*-2-chloro-3-iodobutane had rotations of +13.98° and +14.02° respectively. The good agreement here would seem to indicate a product of uniform purity, which would hardly be the case if some other optical isomer were being formed.

Table II

Physical Constants of Some 2,3-Dihalobutanes

Compound	Configuration	$n^{25}D$	d^{25}
2,3-Dichlorobutane[5]	*meso*	1.4392	
	DL	1.4410	
2,3-Dibromobutane[9]	*meso*	1.5091	1.7747
	DL	1.5125	1.7836
2-Chloro-3-iodobutane	L-*erythro*	1.5312	1.7532
	DL-*threo*	1.5337	1.7587
2-Bromo-3-iodobutane	L-*erythro*	1.5642	2.0362
	DL-*threo*	1.5736	2.0629

Results and Interpretation.—When L(+)-*erythro*-3-iodo-2-butanol (I), (Fig. 1) reacts with concentrated hydrobromic acid or concentrated hydrochloric acid, the dihalides, III and V, which are obtained possess optical activity. Furthermore, the configuration of the products is the same as that of the starting material, showing that zero or an even number of inversions occurred at each asymmetric carbon atom during the reaction. However, when active *threo*-3-iodo-2-butanol (II), reacts under the same conditions, optical activity is lost, although the products, IV and VI, still have the *threo* configura-

---

[8] H. J. Lucas and H. K. Garner, This Journal, **70**, 990 (1948).

[9] S. Winstein and H. J. Lucas, *ibid.*, **61**, 1581 (1939).

[10] Named as a derivative of 2-butanol, the configuration is determined by the higher numbered asymmetric carbon atom, that is, the one to which the iodine atom is attached.[8]

[11] From L(+)-*erythro*-3-chloro-2-butanol, $\alpha^{25}D$ +0.82°, thionyl chloride plus pyridine gave[5] 2,3-dichlorobutane, $\alpha^{25}D$ −3.80°. Pure L(+)-*erythro*-3-chloro-2-butanol,[8] $\alpha^{25}D$ +9.47° would be expected to give an active dichloride of about −44°.

tion. The number of inversions is therefore even, presumably two. In addition, the reaction must proceed through an internally compensated intermediate, in order for the D isomer of the DL-mixture to be formed from the original L-iodohydrin. These facts are best accounted for by the two mechanisms outlined in Fig. 2 and 3.

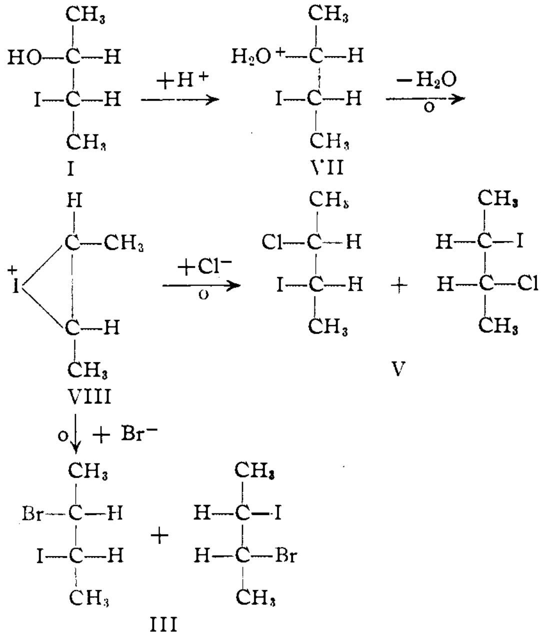


Fig. 2.—The mechanism of the reaction of L(+)-*erythro*-3-iodo-2-butanol with hydrohalic acids.

In Fig. 2, the first step is the addition of a hydrogen ion to the hydroxyl group of the iodohydrin, I, to form the protonated complex, VII. In the second step, the neighboring iodine atom swings in, displaces the water molecule, and closes the three-membered ring to form the cyclic iodonium intermediate, VIII. This is undoubtedly a single process, that is, the closing of the ring occurs simultaneously with the departure of the water molecule. The closing of the ring is accompanied by a single Walden inversion at carbon atom C-2.

The cyclic intermediate presumably is L-*threo*-1,2-dimethylethyleneiodonium ion and possesses optical activity. Therefore, when attack by bromide or chloride ion takes place at either C-2 or C-3, again with inversion (step three) the resulting dihalide is optically active, and, moreover, possesses the same configuration as the iodohydrin. It is evident that if the attacking ion were iodide ion rather than chloride or bromide ion, the di-iodide should have the *meso* configuration and thus be inactive. It is unfortunate that the di-iodide proved to be too unstable to isolate.

In Fig. 3, the same steps are involved in the conversion of (+)-*threo*-3-iodo-2-butanol (II), into DL-*threo*-2-bromo-3-iodobutane (IV), or DL-*threo*-2-chloro-3-iodobutane (VI). However, in this case when the ring is closed with one inversion the cyclic iodonium intermediate, X, is the symmetrical *cis*-1,2-dimethylethyleneiodonium ion, and optical activity is lost. Attack by chloride ion can now give rise to two different products, *viz.*, the D- and L-*threo*-2-chloro-3-iodobutanes (VIa) and (VIb), respectively, which are formed in equal amounts. Attack by bromide ion similarly yields both the D- and L-*threo*-2-chloro-3-iodobutanes (IVa) and (IVb). Thus loss of activity in the reaction of active *threo*-3-iodo-2-butanol with hydrohalic acids is strong evidence for the intermediate cyclic ion.

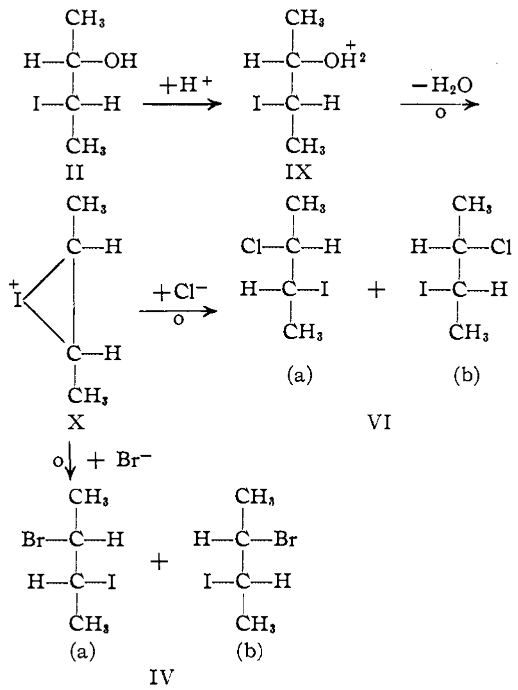


Fig. 3.—The mechanism of the reaction of active *threo*-3-iodo-2-butanol with hydrohalic acids.

Other evidence that the reaction actually goes by the proposed path is provided by the rate. While no quantitative measurements were made, a qualitative comparison with other replacement reactions is possible. It was observed that when either isomer of 3-iodo-2-butanol was mixed with ordinary concentrated hydrochloric or hydrobromic acid, the resulting clear solution suddenly became cloudy after a very short time, 15–60 seconds, and the reaction appeared to be complete in a matter of minutes. Winstein and coworkers[6] have shown that the corresponding 3-bromo-2-butanols, on the other hand, require about three hours with fuming hydrobromic acid for 50% conversion into the dibromides, that the chlorohydrins do not yield any dihalide on standing for twenty-five days with fuming hydrobromic acid, and that 2-butanol is 50% converted into 2-bromobutane in seventy-five minutes by the fuming aqueous acid. The rate sequence, therefore, is: iodohydrin > bromohydrin ≈ unsubstituted alcohol > chlorohydrin. The high reactivity of the iodine compounds is best explained on the basis of a direct participation of the iodine atom in the replacement process.

A simple replacement not involving the neighboring iodine atom could not account for the observed high reactivity of the iodohydrins. As Winstein and co-workers have pointed out[6] physical evidence such as the ionization constants of the aliphatic halogen acids and the dipole moments of the alkyl halides would lead one to expect the effect on the rate to be approximately equal for the various halogens if the rate determining step were the removal of the hydroxy group to form a carbonium ion (S_N1). This argument can be extended to include two other types of replacement reactions, namely, bimolecular displacement (S_N2) and rearrangement of an intermediate with retention of configuration (S_Ni). If the influence of the halogen atom operated mainly through an inductive effect, no great difference would be expected among chlorine, bromine and iodine analogs. The exclusion of any mechanism not involving the iodine atom in a direct way is therefore justified, since the reactivities are not even of the same order of magnitude.

On the other hand, the mechanisms shown in Figs. 2 and 3 are entirely compatible with the rate data. Iodine, because of its greater polarizability, is generally a much better nucleophilic reagent than bromine or chlorine. Therefore, if the closing of the iodonium ring is presumed to be the rate determining step, the sequence of reactivities becomes understandable.

The stereochemical results (Fig. 1) also are inconsistent with any replacement mechanism not involving the iodonium ion. No mechanism which does not involve the neighboring iodine atom can account for loss of optical activity when the *threo*-iodohydrin (II), reacts with the hydrohalic acids, and at the same time explain the retention of activity when the *erythro*-iodohydrin (I), undergoes the same reactions.

The exaltations of the molecular refractions of the iodohydrins and dihalides, given in the last column of Table I are of interest, since increases in the refractivity are not usually observed for any of the structural features present in the compounds. That the effect is real and not due to impurities is shown by the excellent agreement in the observed values for each pair of isomers. The exaltation appears to be due to the position of the substituents on adjacent carbon atoms, the greatest effect appearing in the bromoiodo compounds where the largest interaction would be expected. The dibromobutanes also show slightly increased molar refractivity; calculated for *meso* and DL, 36.20; observed, *meso*, 36.34; DL, 36.36.

The reaction used for the partial resolution of the *threo*-iodohydrin was studied in order to determine the nature of the products. When dibromoalkanes are partially resolved by reaction with brucine,[12] the reaction product is a quaternary salt of the alkaloid. The solid obtained from the reaction of the iodohydrin with brucine, however, contained considerable quantities of brucine hydroiodide in addition to the quaternary iodide. Since brucine is a base, it is suggested that dehydrohalogenation to the oxide plays a part in the resolution, as well as the alkylation of the brucine nitrogen. The partial resolution is due to the difference in the rates with which the antipodal iodohydrins undergo these two reactions.

Experimental[13]

meso-**2,3-Butanediol.**—The *meso*-glycol (Lucidol) was obtained free of other isomers by the method described elsewhere[14]; m. p., 33.9–34.3 (cor.).

D(+)-**2,3-Epoxybutane.**—The active oxide was a part of that prepared earlier[15] from D(−)-2,3-butanediol through the steps: D(−)-2,3-butanediol → D(+)-2,3-diacetoxybutane → L(+)-*erythro*-3-chloro-2-butanol → D(+)-2,3-epoxybutane. The physical constants were: b. p. 53.5–53.7° (cor.): $n^{25}{}_D$ 1.3705; $d^{25}{}_4$,0.7998; $[\alpha]^{25}{}_D$, +59.05°.

cis-**2,3-Epoxybutane.**—This was prepared in 71% yield from the *meso*-glycol in the same manner as the active oxide[5]; *meso*-2,3-butanediol → *meso*-2,3-diacetoxybutane → DL-*threo*-3-chloro-2-butanol → *cis*-2,3-epoxybutane. Physical constants checked earlier ones[2a]: b. p., 59.7–60.0° (cor.); $n^{25}{}_D$ 1.3802.

L(+)-*erythro*-**3-Iodo-2-butanol.**—To 0.15 mole (10.8 g.) of D(+)-2,3-epoxybutane in a 200-ml. three-necked flask fitted with a sealed stirrer, dropping funnel, reflux condenser, and thermometer, and cooled to about −10° with an ice and hydrochloric acid bath was added dropwise with vigorous stirring 0.15 mole (35 g., Merck Reagent, 55% aqueous) of hydriodic acid. The rate was adjusted so that the temperature of the reaction mixture remained below 0°. About 40 minutes were required. Stirring was continued for about 10 minutes after the addition was complete, and then the cold mixture was brought to neutrality with 3 *f* potassium carbonate solution. The weight of the light yellow organic phase was 28.0 g. (93%). This was washed to water-whiteness with 5 ml. of dilute sodium thiosulfate solution, and then was washed twice with 10-ml. portions of water and quickly dried with anhydrous potassium carbonate. Final drying was accomplished in a vacuum desiccator over calcium chloride at 8 mm. pressure. The purified product weighed 22.0 g. (75%), and had the following constants: m. p., 18.4–18.9° (cor.); $n^{25}{}_D$ 1.5371; $d^{25}{}_4$ 1.7753; $\alpha^{25}{}_D$ +50.04°; $[\alpha]^{25}{}_D$, +28.19° (pure liquid).

The material was analyzed for iodine by the Volhard method. The sample (200–300 mg.) was weighed out from a weighing pipet into a 100-ml. Kjeldahl flask containing about 1 g. of potassium hydroxide dissolved in 5 ml. of water. The mixture was digested for 20 minutes at 100°, diluted to 50 ml. with water, neutralized with nitric acid, and transferred to a 200-ml. Erlenmeyer. Then 5 ml. of chloride-free 6 *N* nitric acid, 2 ml. of 1 *N* ferric nitrate solution, and 25.00 ml. of standard 0.1 *N* silver nitrate solution were added in order, and the sample was back-titrated with standard 0.1 *N* potassium thiocyanate.

---

[12] H. J. Lucas and C. W. Gould, Jr., THIS JOURNAL, **64**, 601 (1942).

[13] Analyses, except for halogen in the iodohydrins and brucine salts, by G. Oppenheimer and G. A. Swinehart.

[14] H. J. Lucas, F. W. Mitchell, Jr. and H. K. Garner, *ibid.*, **72**, 2138 (1950).

[15] H. J. Lucas and H. K. Garner, *ibid.*, **70**, 990 (1948).

Anal. Calcd. for C_4H_9OI: I, 63.45. Found: I, 63.45.

DL-*erythro*-**3-Iodo-2-butanol.**—The inactive *erythro*-iodohydrin was prepared in the same way as the active isomer and in 80% yield from a sample of pure DL-*trans*-oxide.[16] The physical constants and iodine content were not determined until after the product had been partially resolved (see below).

DL-*threo*-**3-Iodo-2-butanol.**—This was prepared in 74% yield from the *cis*-oxide in the same manner as the *erythro*-iodohydrins. Final drying and purification was accomplished in this case, however, by distillation; b. p., 43.0° (2.5 mm.). The other physical constants and the iodine content were not determined until after partial resolution (see below).

L(+)-*erythro*-**3-Bromo-2-butanol.**—To 0.20 mole of hydrobromic acid (34 g., J. T. Baker, C. P. 48% aqueous) in a 200-ml. three-necked flask fitted with a mechanical stirrer and thermometer and cooled to $-15°$ with an ice-hydrochloric acid bath, was added 0.10 mole (7.2 g.) of D(+)-2,3-epoxybutane slowly with a dropper at such a rate as to keep the temperature below $-10°$. About twenty minutes were required. When the addition was complete, stirring was continued for about five minutes, and then the mixture was poured into a suspension of 10 g. of sodium bicarbonate in 40 ml. of water and ice. The aqueous phase, after separation, was washed three times with 20-ml. portions of ethyl ether. The bromohydrin and extracts were combined and dried with anhydrous potassium carbonate, and the ether was removed by distillation at atmospheric pressure. Two fractionations of the remaining material at reduced pressure gave 11.2 g. (73%) of pure bromohydrin; b. p. 49.0° (10 mm.), n^{25}D + 1.4758, d^{25}_4 1.4466, α^{25}D 20.15°, $[\alpha]^{25}$D + 13.93°, *M*D calcd. 29.96, found 29.83. Three cuts were taken in the second distillation; the refractive index and boiling point of all three were identical. A second preparation gave 11.3 g. (74%) of bromohydrin with b. p. 49.0° (10 mm.), n^{25}D 1.4757, α^{25}D + 20.14°, in good agreement with the values given above.

Previous values[2a] for DL-*erythro*-3-bromo-2-butanol are: n^{25}D 1.4767, d^{25}_4 1.4474. These are significantly higher than those found above for the active bromohydrin. However, the earlier preparation was carried out at a higher temperature (5°, using DL-*trans* oxide), and it is possible that the product was contaminated with a trace of dibromide. There is considerable evidence, outlined above, that the material obtained in the present work was quite free of other compounds.

Partial Resolution of the DL-**Iodohydrins:** DL-*threo*-**3-Iodo-2-butanol.**—To 0.100 mole (40.0 g.) of brucine dissolved in 200 ml. of chloroform was added 0.369 mole (73.8 g.) of DL-*threo*-3-iodo-2-butanol. After standing at room temperature for 20 hours, the chloroform was pumped off with an aspirator. The oil which remained was shaken with 400 ml. of 30–60° petroleum ether until the excess iodohydrin was extracted and the brucine salts solidified. The solid was removed by suction filtration and washed twice with petroleum ether (weight, 53 g.), filtrate and washings were combined, and the petroleum ether was pumped off with an aspirator at room temperature. The product which remained was distilled at reduced pressure to give 36.0 g. of iodohydrin: b. p. 28.8–30.8° (0.7 mm.) (cor.), n^{25}D 1.5352, d^{25}_4 1.7692, α^{25}D + 3.06°. An analysis for iodine was carried out as described above.

Anal. Calcd. for C_4H_9OI: I, 63.45. Found: I, 63.69.

A portion of this iodohydrin (10 g., 0.05 mole) was converted into the oxide with concentrated base in the usual manner; b. p. 59.6–60.5° (cor.), n^{25}D 1.3796, α^{25}D $-0.11°$. These constants show that the oxide contained about 6% of the DL-*trans* isomer, and 0.2% of the L isomer. The *threo*-iodohydrin, therefore, contained about 6% of the *erythro* isomer, but only a negligible portion of the rotation was due to this impurity. Some stereomutation to the diastereomer apparently took place during the brucine treatment.

Two other methods were tried for the partial resolution of the *threo*-iodohydrin: (a) Selective adsorption on a suspension of brucine in 30–60° petroleum ether, in which the alkaloid is only slightly soluble. This method was used previously for the resolution of *threo*-3-chloro-2-butanol.[5] (b) Selective acetylation of the iodohydrin with acetic anhydride in the presence of brucine.[5,17] The results obtained with the iodohydrins by either of these methods were in general less satisfactory than by the direct reaction with brucine described above. Method (a) gave a rotation of only $-0.21°$. Method (b) involves the separation of the iodohydrin from the iodoacetate, which proved to be difficult; rotations ranging from $+0.92°$ to $-0.43°$ were obtained, depending on the degree of purification attained.

DL-*erythro*-**3-Iodo-2-butanol.**—This was resolved by reaction with brucine in chloroform solution in exactly the same manner as the *threo* isomer, b. p., 34.3–34.9° (0.9 mm.), n^{25}D 1.5377, α^{25}D $-3.42°$, iodine, calcd. 63.45%, found, 63.77%. Since the pure D(+)-*erythro*-3-iodo-2-butanol had a rotation α^{25}D +50.04°, the amount of resolution attained in this case was 6.8%.

A portion of the resolved *erythro*-iodohydrin, on treatment with base, gave an oxide with b. p. 53.5–54.0° (cor.), n^{25}D 1.3707, α^{25}D -3.16. These constants indicate the presence of 2% of the *threo*-iodohydrin as an impurity in the resolved product. Stereomutation of one iodohydrin to the diastereomer in the presence of brucine appears to take place to a measurable extent under the conditions used for the resolution.

Composition of the Brucine Salts from the Resolutions.—The brucine salt from the resolution of the *erythro*-iodohydrin was recrystallized three times from water, and dried over phosphorus pentoxide at 0.4 mm. pressure at room temperature. Analysis for iodine: calcd. for brucine·HI, 24.3%; found, 24.1%.

The salt from the resolution of the *threo*-iodohydrin was recrystallized three times from water and dried as above. Iodine analysis: found, 22.3%; calcd. for brucine·HI, 24.3%; calcd. for brucine·C_4H_9OI, 21.4%. This value indicated that the material was a mixture of brucine hydroiodide, and the quaternary salt of brucine and the iodohydrin. A fractional crystallization from water yielded two crops: (a) Iodine analysis: found, 21.9%; calcd. for brucine·C_4H_9OI, 21.4%; (b) iodine analysis: found, 24.1% calcd. for brucine·HI, 24.3%.

L(+)-*erythro*-**2-Chloro-3-iodobutane.**—To 0.05 mole (10.0 g.) of L(+)-3-iodo-2-butanol in a 125-ml. Erlenmeyer flask was added, at room temperature, 0.3 mole of concentrated hydrochloric acid (25 ml., J. T. Baker C. P., 37%). The resulting clear solution suddenly turned cloudy after about a minute, and a second phase separated out. The mixture was stirred mechanically for another hour, transferred to a separatory funnel, and the organic phase, which had turned brown from liberated iodine, was drawn off; weight, 9.4 g. (86%). The material was washed with 10 ml. of dilute potassium carbonate solution to remove hydrochloric acid, and then with dilute sodium thiosulfate solution until water-white. Two washings with 10-ml. portions of water followed by drying with anhydrous calcium chloride and distillation at reduced pressure yielded 6.9 g. (63%) of colorless product, b. p. 34.8–35.3° (5 mm.), n^{25}D 1.5313, d^{25}_4 1.7532, α^{25}D + 13.98°, $[\alpha]^{25}$D + 7.97°.

Anal. Calcd. for C_4H_8ClI: C, 21.99; H, 3.67; AgX, 173.1. Found: C, 21.78; H, 3.76; AgX, 170.4.

A second preparation, on a much smaller scale, gave a product with n^{25}D 1.5318, α^{25}D + 14.02°. The material was not distilled in this case, but the agreement in physical properties of the two preparations was nevertheless satisfactory.

L(+)-*erythro*-**2-Bromo-3-iodobutane.**—This material was prepared in 66% yield from the active *erythro*-iodohydrin (0.043 mole, 8.7 g.) and 48% aqueous hydrobromic

---

[16] This is a part of the oxide described previously.[2a] It had been prepared by H. Sargent: b. p. 53.5°, n^{25}D 1.3705, d^{25}_4 0.8010.

[17] S. Winstein and H. J. Lucas, THIS JOURNAL, **63**, 2541 (1941).

acid (0.2 mole, 34 g.) in a similar manner to the chloroiodo compound. The reaction was started at 0°, and about two minutes were required for the appearance of the first cloudiness. Attempted distillation of the product at 6 mm. pressure (b. p., 53.0°) led to decomposition, so this step in the purification was omitted. The physical properties of the dihalide were: m. p. −9.5 to −9.0°, $n^{25}D$ 1.5642, $d^{25}{}_4$ 2.0362, $\alpha^{25}D$ + 4.13°, $[\alpha]^{25}D$ + 2.03°.

Anal. Calcd. for C_4H_8BrI: C, 18.27; H, 3.05; AgX, 160.7. Found: C, 19.32; H, 3.52; AgX, 161.3.

***meso*-2,3-Di-iodobutane.**—To 1 g. of the active iodohydrin cooled to 0°, was added 5 ml. of 55% aqueous hydriodic acid, also cooled to 0°. The mixture rapidly turned dark with iodine, and heavy oil began to separate out. However, even near the ice temperature, rapid decomposition set in and the oil layer appeared to boil vigorously due to gas evolution. The products were apparently butene, identified by odor, and iodine. No product could be isolated for the measurement of physical properties.

DL-*threo*-2-Chloro-3-iodobutane.—This was prepared in a crude yield of 92% from (+)-*threo*-3-iodo-2-butanol (0.03 mole, 10.0 g.) $\alpha^{25}D$ + 3.06°, and concentrated hydrochloric acid (0.3 mole, 25 ml. of J. T. Baker C. P. 37%) in the same manner as the corresponding *erythro* compound. The first cloudiness appeared after thirty seconds. Distillation of the product gave 7.9 g. (73%) of the pure dihalide, b. p. 33.2–33.5° (4 mm.), $n^{25}D$ 1.5337, $d^{25}{}_4$ 1.7587, $\alpha^{25}D$ + 0.05°.

Anal. Calcd. for C_4H_8ClI: C, 21.99; H, 3.67; AgX, 173.1. Found: C, 22.45; H, 3.75; AgX, 167.1.

A second sample of iodohydrin, $\alpha^{25}D$ + 0.92°, gave a chloroiodobutane with b. p. 45.6–46.4° (8 mm.), $n^{25}D$ 1.5338, $\alpha^{25}D$ 0.00°, in good agreement with the values given above.

DL-*threo*-2-Bromo-3-iodobutane.—This material was prepared in 84% crude yield from the active *threo*-iodohydrin (0.05 mole, 10 g., $\alpha^{25}D$ +3.06°) and aqueous hydrobromic acid (0.3 mole, 35 ml., J. T. Baker C. P., 48%) in the same way as the other dihalides. The first cloudiness appeared in about 15 seconds. Distillation of the product gave 7.2 g. (55%) of colorless material with b. p. 29–30° (0.9 mm.), $n^{25}D$ 1.5736, $d^{25}{}_4$ 2.0629, $\alpha^{25}D$ + 0.01°.

Anal. Calcd. for C_4H_8BrI: C, 18.27; H, 3.05; AgX, 160.7. Found: C, 18.72; H, 3.18; AgX, 163.6.

The Reaction of L(+)-*erythro*-3-Bromo-2-butanol with Hydriodic Acid.—To 0.047 mole (7.25 g.) of the active bromohydrin in an ampoule was added 25 ml. of aqueous 57% hydriodic acid. The solution was cooled to 0°, and gaseous HI, prepared by dropping the aqueous acid onto phosphorus pentoxide, was passed in until 26 g. had been taken up. The ampoule was sealed and allowed to stand overnight at room temperature. The ampoule was then opened, and the contents (rather dark with iodine) were poured onto an equivalent amount of sodium bicarbonate and ice. The oil layer was separated, washed to water-whiteness with sodium thiosulfate solution, and dried with calcium chloride; weight, 6.4 g. The material had $n^{25}D$ 1.4965, b. p. 110–111° (Emich), $\alpha^{25}D$ 0.00°. These constants indicate that the product was inactive 2-iodobutane.

The Reaction of L(+)-*erythro*-3-Bromo-2-butanol with Phosphorus Triiodide.—To 0.03 mole (4.5 g.) of the active bromohydrin in a 25-ml. erlenmeyer flask was added 0.03 mole (0.9 g.) of red phosphorus and 0.03 mole (3.8 g.) of iodine. The mixture warmed somewhat, and was cooled as necessary to keep the temperature at 25–30°. After standing overnight, the mixture was shaken with concentrated hydrochloric acid to remove any remaining bromohydrin, then with dilute sodium bicarbonate solution to neutralize, and finally with sodium thiosulfate solution to remove iodine. After drying with calcium chloride, the colorless oil had $n^{25}D$ 1.4823. Distillation at reduced pressure yielded no 2-bromo-3-iodobutane, and it therefore seems probable that the main product here also was 2-iodobutane.

Summary

When concentrated hydrochloric or hydrobromic acid reacts with L(+)-*erythro*-3-iodo-2-butanol, the formation of L(+)-*erythro*-2,3-C_4H_8IX shows that either zero or two inversions are involved, but the formation of DL-*threo*-2,3-C_4H_8IX from active *threo*-3-iodo-2-butanol shows that two inversions are involved in these reactions.

The stereochemical changes indicate that the iodine atom of each iodohydrin participates in the reaction by the formation of an intermediate, cyclic ion, 1,2-dimethylethyleneiodonium ion, and that this then reacts with chloride or bromide ion to give the final product. From the *erythro*-iodohydrin the intermediate has the *trans* structure, and from the *threo*-iodohydrin it has the *cis* structure. This explains why optical activity is retained in the first case and lost in the second.

The formation of the cyclic intermediate also accounts for the greater reactivity of the iodohydrins in comparison to bromohydrins, because an iodine atom participates more readily than a bromine atom, owing to its greater polarizability.

Configurations have been assigned to 3-iodo-2-butanols, 2-chloro-3-iodobutanes and 2-bromo-3-iodobutanes.

A single Walden inversion accompanies the opening of the ring of 2,3-epoxybutane with hydriodic acid.

PASADENA, CALIFORNIA

RECEIVED AUGUST 8, 1949