

Stereochemical Relationships of the Isomeric
3 Chloro 2 butanols and the 2,-3-Dichlorobutanes.

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Introductory:

This research was suggested by Prof. H. J. Lucas and Dr. Saul Winstein, who found that when the erythro 3 bromo 2 butanol was treated with fuming hydrobromic acid, the product is the meso 2,-3-dibromobutane, and that in the same manner the threo bromohydrin yielded the dl dibromide.

It was interesting to us to determine whether the corresponding chloride analogs in the same series behave in the same way, i.e., does the erythro 3-chloro-2-butanol react, say with fuming hydrochloric acid to give the meso dichloride? It was found that, unfortunately, the chlorohydrins react with fuming hydrochloric acid to give only traces of dichloride, so that an exact parallel of work on the bromides and bromohydrins has not been possible.

However, the two other most likely possible chlorinating agents, phosphorous pentachloride and thionyl chloride, were used for the conversion of the chlorohydrins to the dichlorides with interesting results.

Method of Attack:

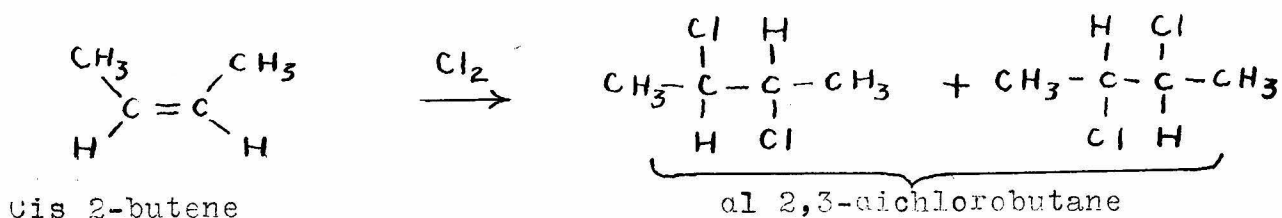
In order to follow the stereomutations which accompanied the various reactions it was necessary first to prepare, characterize and establish the configurations of the isomeric inactive 2,3-dichlorobutanes. The characterization was accomplished by means of physi-

cal properties alone, since the isomers have the same chemical properties.

The next step was to prepare and characterize the isomeric 3-chloro-2 butanols, and from these isomers prepare dichlorides, whose physical properties were then compared with the properties of the pure isomeric dichlorides.

The isomeric 2,3 dichlorobutanes:

The inactive isomers were prepared from the pure 2-butenes:



And:



These formulations assume trans addition of the halogen to the olefinic bond, in accordance with the general rule. That this assumption is correct in this case has been established beyond doubt by another synthesis (see page 7) of a dl dichloride having optical activity.

The chlorinations indicated above presented some experimental difficulty. The apparatus is shown in figure 2. The experimental conditions were: temperatures of -20°C , dim artificial light, slight, continual excess of chlorine over olefin. Yields were

63 and 80 % for the meso and dl dichloride, respectively. Occurring with the simple addition of chlorine to the double bond, there was appreciable substitution resulting in the formation of tri- and tetra-chlorobutanes to the extent of 5-10 %.

The dichlorides were distilled through a 40 cm. Weston² column until the boiling points, refractive indices and dielectric constants were the same after the fourth and fifth redistillations of the materials. The properties of the dichlorides, after the fifth distillation, are given in Table I.

Table I. Physical properties of the inactive dichlorides.

Configuration	meso	dl
parent 2-butene	trans	cis
b.p./80	49.52 ± .03° C.	53.16 ± .03° C.
b.p./746	113.1° C.	117.1° C.
n_D^{25}	1.4386	1.4409
d_4^{25}	1.1024	1.1064
d_4^{25}	8.85 ₂	9.76 ₃
condenser reading ²⁵	163.3	179.5

The condenser reading, from which the dielectric constant was calculated, was measured with the apparatus described previously.³ The liquid was drawn up into a new measuring cell which had a volumetric capacity of 1.2 ml. Since in this cell the condenser plates were in contact with the liquid, the condenser reading was very nearly a linear function of the dielectric constant. The cell was calibrated with air, carbon tetrachloride, benzene, chlorobenzene, ethyl bromide and ethylene dichloride. The constants for these calibrating substances are given elsewhere.³

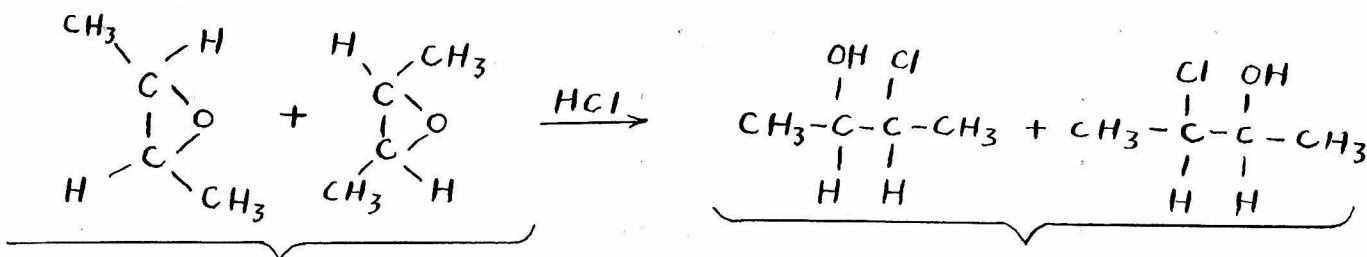
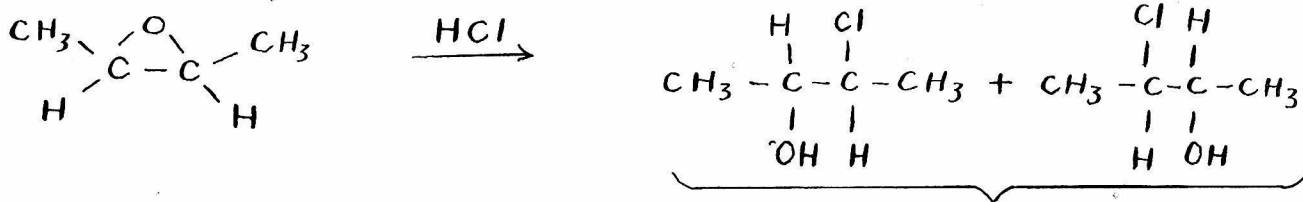
FIGURE 1.
CONDENSER READING OF DICHLORIDE MIXTURES



The condenser readings were enough different to permit analysis of dichloride mixtures by electrical means. Figure 1 is a plot of condenser reading against the weight percent composition of dichloride mixtures.

3 Chloro 2 butanols

These substances were prepared from the fractionated 2,3-epoxybutanes whose properties are recorded:



After 3 distillations through the Weston column, the 3 chloro 2 butanols had the properties given in Table II. The refractive index, boiling point, and condenser reading changed only about 0.1 % from the second distillation to the third, so that the chlorohydrins were quite pure. There was no partial stereo-mutation in going from one pure oxide to its chlorohydrin. This

conclusion is borne out also by the sharp melting points of the 3,5 dinitro benzoates.

Table II. Physical properties of the isomeric 3 chloro 2 butanols.

configuration	erythro	threo
parent oxide	trans	cis
boiling point/80 mm.	58.1° C.	52.0° C.
boiling point/746 mm.	135.4 ° C.	130.8° C.
n_D^{25}	1.4387	1.4387
m.p. of 3,5 dinitro benzoate	91.4 - 92.1 °C	99.9 - 100.6 °C

Action of HCl, HCl + ZnCl₂, PCl₃ and SOCl₂ on the erythro chloro hydrin.

The threo isomer was not used for these experiments because of its scarcity. But we assume that the threo chlorohydrin resembles the erythro form in chemical properties. This reasonable assumption will be tested in the future.

HCl and HCl + ZnCl₂: erythro chlorohydrin was dissolved in 49 % HCl in a sealed ampoule. After two weeks standing at room temperature the only evidence of reaction was a darkening of the solution. No dichloride phase was formed. The HCl.ZnCl₂ reagent, discussed by Lucas,⁴ was tried. Chlorohydrin was dissolved in the reagent; the test tube containing the mixture was sealed and heated at 100° for four hours. An oil phase separated which was composed of β/β'

dichloro dibutyl ether, and a very high boiling material which could not be distilled. A parallel experiment made with the $\text{HCl} \cdot \text{ZnCl}_2$ reagent and n-butanol gave a 70 % yield of n-butyl chloride with almost no side reactions: dibutyl ether was noticeable by odor alone.

Apparently the chlorine atom already present in the chlorohydrin molecule stabilizes the C-O bond to such an extent that it can not be cleaved by hydrochloric acid. It should be noted that Winstein was able to obtain a 94 % replacement of Br for OH in the butylene bromohydrins using HBr. This emphasizes the fundamental differences in chemical properties of bromides and chlorides.

PCl_5 in chloroform: The erythro chlorohydrin was added to a saturated refluxing solution of PCl_5 in chloroform. The dichloride product of the reaction possessed the following properties:

b.p./20 = 50.5°C to 53°C , $n_D^{25} = 1.4401$, condenser reading 171.0.

These values (see Table I and Fig. 1) correspond to a dichloride mixture composed of 47.5 % meso and 52.5 % dl. Racemization, i.e., partial stereomutation, had taken place.

SOCl_2 : The reaction product of the erythro chlorohydrin and SOCl_2 possessed the following properties: b.p./80 $48.5 - 49.0^\circ \text{C}$, condenser reading 161.4, $n_D^{25} = 1.4392$. It was therefore essentially meso dichloride with a persistent impurity of lower dielectric constant and higher refractive index; this impurity was therefore not the dl dichloride. See Table I and figure 1. The reaction therefore took place with either 0 or 2 Walden Inversions.

SOCl_2 and pyridine: The reaction product of the erythro chlorohydrin was a dichloride, b.p./80 = 53.0 to 53.2° C., $n_D^{25} = 1.4410$, condenser reading 179.2. From figure 1 and Table I it is evident that the dichloride is 98.2 % dl. Reaction was therefore accompanied by one complete Walden Inversion.

Assignment of dichloride configurations:

In the section on the 2,3-dichlorobutanes, the configuration of the high boiling dichloride prepared from the pure cis 2-butene, was assumed to be dl. The dichloride from trans butene was then the meso isomer. The assumption has been confirmed by converting optically active erythro chlorohydrins to dichloride.

Wegler's method,⁵ partial acetylation of the alcohol in the presence of brucine dissolved in chloroform, was used to obtain an erythro chlorohydrin with a rotation (1 dcm) of + 0.82°. The 3 chloro 2 acetoxybutane had a rotation (1 dcm) of -3.37°. The active chlorohydrin, treated with thionyl chloride, gave a dichloride which had a b.p./80 mm, = 49.4 - 49.7°, $n_D^{25} = 1.4385$, condenser reading 164.1, α^{25} (1 dcm) = 0.07°. This chloride was therefore essentially meso, and its small rotation is not significant.

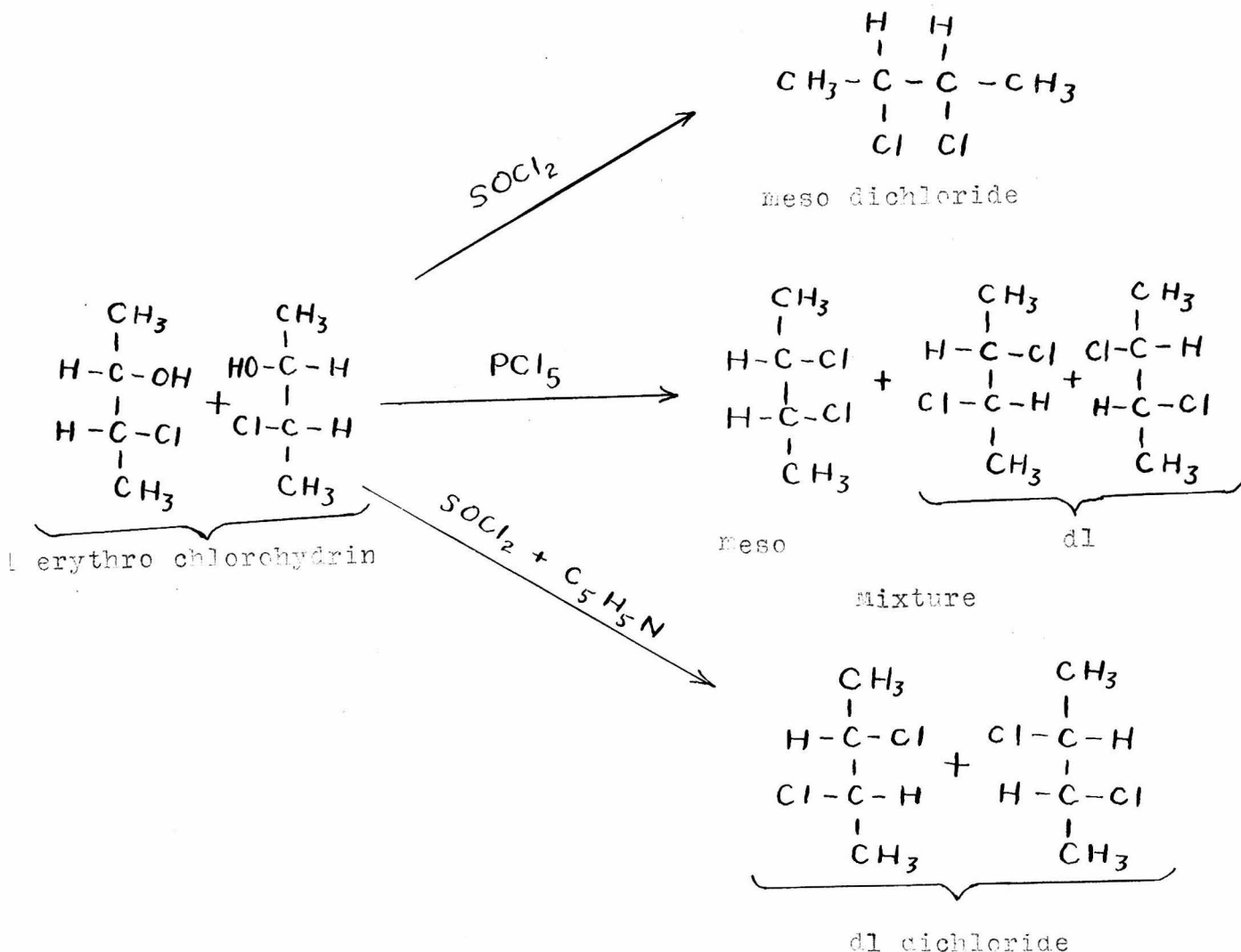
Another sample of the active chlorohydrin was chlorinated with thionyl chloride and pyridine. The redistilled reaction product had b.p./80 = 53.0 - 53.2, $n_D^{25} = 1.4404$, condenser reading 179.4, α^{25} (1 dcm) = 3.80°. This dichloride must be the dl isomer.

An interesting problem is raised by the dielectric constants of the 2,3-dichlorides. The dl isomer has a higher dielectric constant

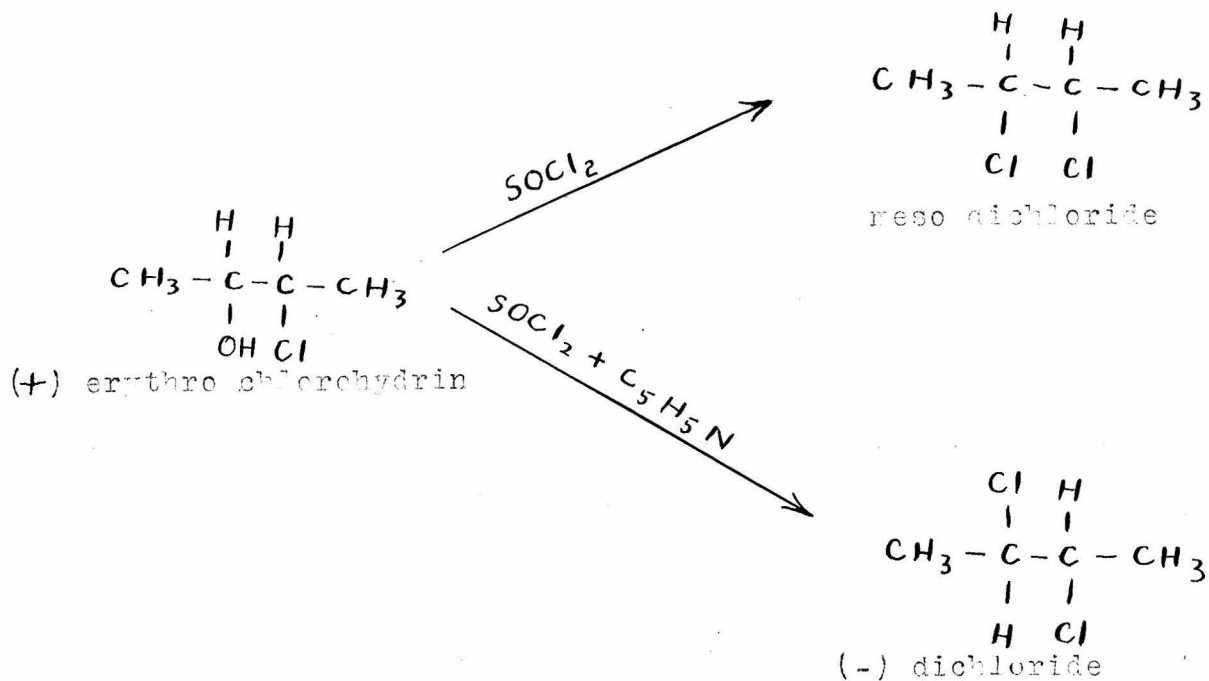
than the meso. For the 2,3, dibromobutanes, it is the meso form that has the higher dielectric constant. Stevenson and Schonaker⁶ found that in the dl and meso dibromides there is restricted rotation about the C₂-C₃ bond and that the bromine atoms lie trans to each other. Now, it seems possible that the chlorine atoms in the dichlorides likewise restrict rotation around the C₂-C₃ bond, but that the chlorines themselves lie cis to each other. This might explain the fact that $\epsilon_{dl} > \epsilon_{meso}$ for the dichlorobutanes.

Discussion.

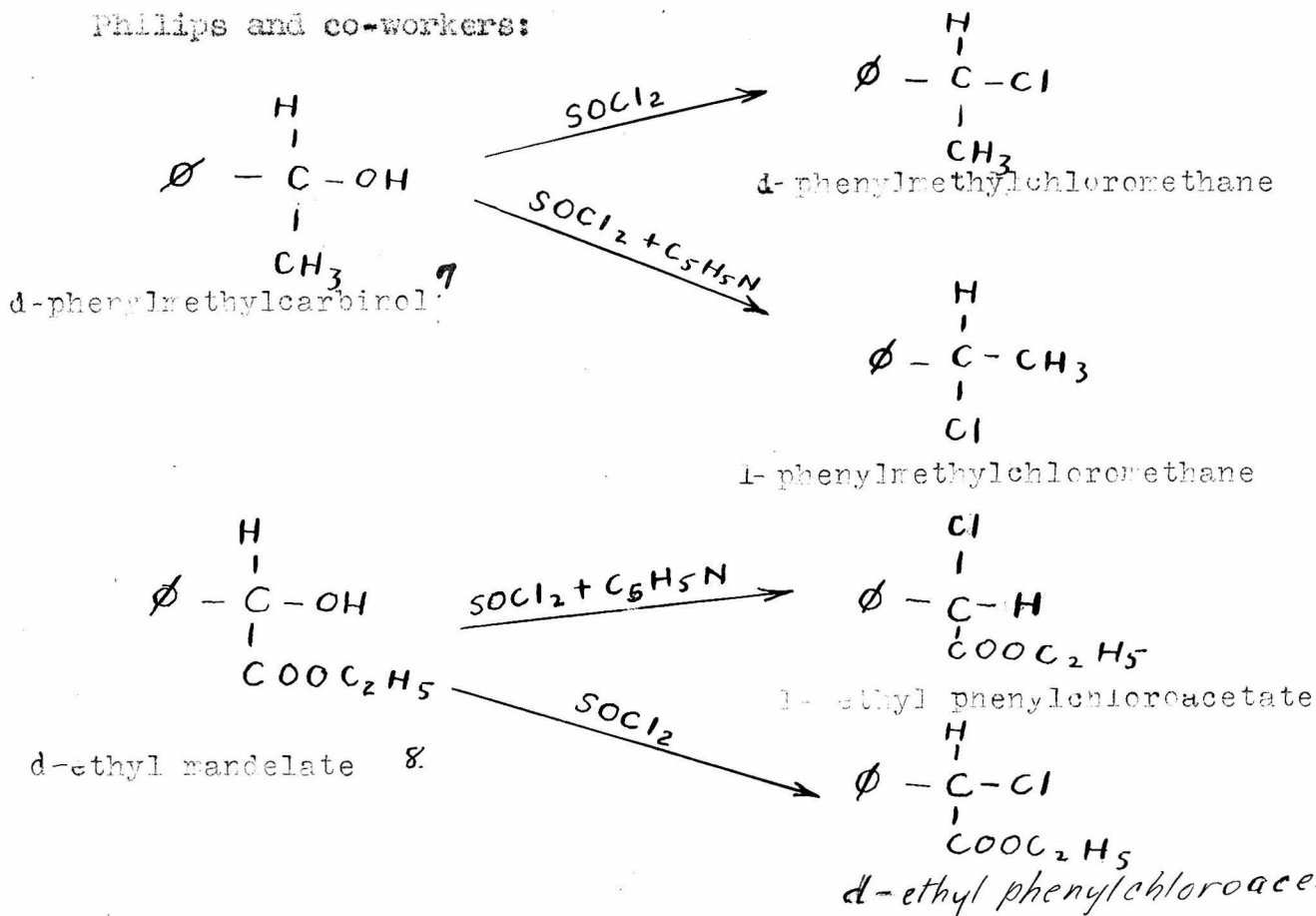
Formulating the steps carried out in the chlorination of the 3 chloro 2 butanols:



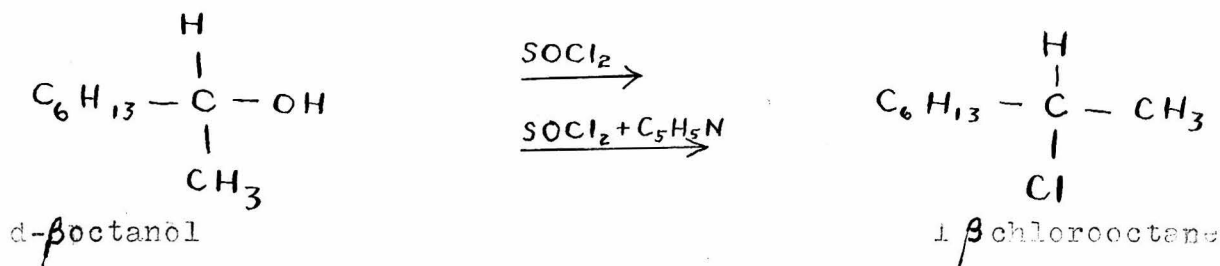
For the experiments with optically active chlorohydrins:



Two parallel cases are noted in the literature by Kenyon, Phillips and co-workers:

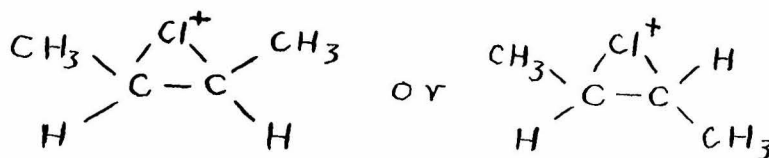


It is interesting to note that β octanol behaves in a different way:⁹



¹⁰
 Kenyon and Phillips suppose that the electron-attracting phenyl group in the phenylmethyl carbinol is responsible for the inversion with SOCl_2 and pyridine, and retention of configuration with SOCl_2 alone. See the reference for details. The chlorohydrins have the electron attracting CH_3CHCl - group attached to the carbinol carbon. For that reason we might expect them to behave analogously to the phenylmethyl carbinols and ethyl mandelates, rather than resemble the β octanol. ef

But we prefer to withhold judgment of Kenyon and Phillip's mechanism as being valid in our chlorohydrin-dichloride conversion. It may be that a simpler mechanism can be found. But any mechanism we propose now is premature, until the threo chlorohydrin can be run through the same reactions as described above for the erythro chlorohydrin. In particular, it must be determined whether a cyclic intermediate:



is involved in the reaction

three chlorohydrin $\xrightarrow{\text{SOCl}_2}$ dl dichloride. This should be easily done. If the active dichloride is obtained from an active three 3 chloro 2 butanol, then a cyclic chloronium ion complex is ruled out as an intermediate.

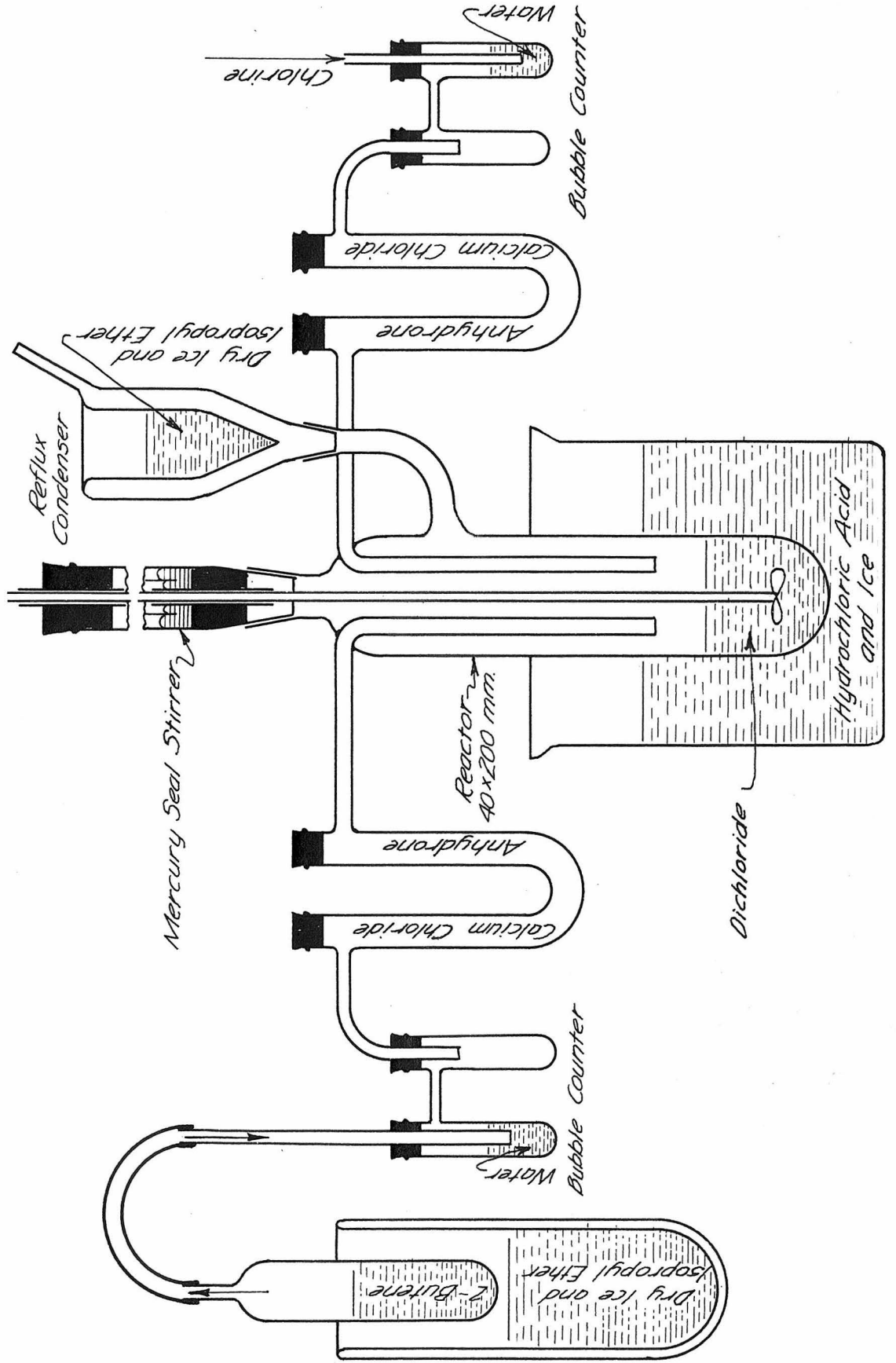
Experimental Part

Cis-2-butene: The substance was prepared from recrystallized meso 2,3-butanediol, m.p. 34.45-34.55° C., according to methods given elsewhere. "

Trans 2-butene: The dl 2,-3-,diacetoxy butane, m.p. 41.9 - 42.1, was used as a starting material. The methods have been previously described. "

dl 2,-3-dichlorobutane: The apparatus used is shown in Fig. 2. The reactor was maintained at about -20°C by immersing it in a ice-hydrochloric acid bath which was kept well agitated by adding to the bath small lumps of "dry ice". The cis 2-butene was distilled out of the ampoule at the left in to the reactor at a rate of 5 bubbles/second in the bubble indicator tube. At the same time, chlorine gas (99.5 % pure) was passed through the bubble counter at the right at 6-7 bubbles/second, into the reactor. The dichlorine reaction product acts as a common solvent for the olefin and halogen. Reaction takes place in the liquid phase which should be kept slightly greenish in color due to excess chlorine. The dry ice condenser is necessary to reflux butene and chlorine. The mercury-sealed stirrer prevented local "hot-spots" in the reactor.

FIGURE 2.
APPARATUS FOR DIRECT CHLORINATION OF 2-BUTENE



It was found that best yields of 2,-3-dichloride depend upon low reactor temperatures, absence of strong light, and continual excess of chlorine.

Cis 2-butene, 11.2 g. was reacted in two hours to give 22.1 g. of crude dichloride which was washed repeatedly with 1.0 f K_2CO_3 solution until neutral to litmus, dried over K_2CO_3 and distilled through a Weston column. 92 % of the washed, dried reaction product distilled from 52.5 to 54.5 at 80 mm. pressure. Yield of distilled chloride was 80.0 % based on butene used. The dichloride was redistilled until the b.p., refractive index, and condenser reading did not change after the fourth and fifth distillations.

Meso 2,-3-dichlorobutane: 8.75 g. of trans 2-butene yielded 12.1 g of distilled meso dichloride, b.p. 49.0 to 50.5° C at 80 mm. Yield 63 %. This was likewise subjected to five distillations in all. The boiling point, refractive index and condenser reading did not change from the fourth to the fifth distillation.

The experimental procedure is the same as that given above for the preparation of the dl dichloride.

dl erythro 3 chloro 2 butanol: Two mols, 144 g., of purified trans 2,3 epoxybutane was added dropwise to 250 ml. (3 mols) of C.P. Concentrated Hydrochloric acid. The acid was kept well agitated by an air stirrer. The temperature of the reaction mixture was never allowed to exceed 5° C. This was accomplished by immersing the reaction flask in an ice-hydrochloric acid bath.

The addition of oxide was complete in two hours. The mixture was then allowed to stir for 40 minutes more.

The acid solution of chlorohydrin was poured over solid K_2CO_3 , giving a paste and an oil. The oil was separated; the paste was filtered. The solid was washed with isopropyl ether and the filtrate was extracted with 3 successive portions, 40 ml. each, of isopropyl ether. The oil phase and ether extracts were combined, dried by shaking with K_2CO_3 .

The ether solution was fractionated through a 60 cm. column of glass helices, and total reflux distillation head. 181 g. of chlorohydrin was collected at 55.9 to 56.1 at 30 mm. pressure. Yield 82.5 % of theory.

For determination of physical properties, 20 g. of this chlorohydrin was redistilled twice through the Weston column. The boiling points and refractive indices were the same after the first and second redistillations.

dl three 3 chloro 2 butanol: This chlorohydrin was prepared by the method above from 18 g. (0.25 mol) of pure cis 2,3-epoxybutane. Yield 20.8 g, 77 % of chlorohydrin b.p. 51.6 to 52.1 at 30 mm. This material was redistilled three times through the Weston column. The boiling points and refractive indices did not change from the second to the third redistillation.

Partial Resolution of dl erythro 3 chloro 2 butanol:

86 g (0.79 mol) of chlorohydrin was added to a solution of 79 g.

of Merck brucine and 37.2 ml (0.39 mol) of freshly distilled acetic anhydride in 200 ml. of U.S.P. chloroform. The mixture warmed up spontaneously to 50° C. The mixture was kept at that temperature for five hours.

The chloroform solution was cooled, washed ^{with} 5 successive portions, 125 ml. each, of 6 N. HCl, until a small test portion of the acid washings showed only traces of brucine. These washings were combined, extracted with 2 portions, 150 ml. each, of isopropyl ether to recover any chlorohydrin.

The chloroform and ether solutions were combined, washed with a small amount of water, and dried by shaking with K_2CO_3 .

The chlorohydrin was isolated in the manner described above for the distillation of this material.

The recovery of unacetylated chlorohydrin was 34.8 g., 81 %. The active erythro 3 chloro 2 acetoxybutane amounted to 45 g, b.p. 70-73 ° C. at 30 mm. Rotations were taken upon a half-shadow Lippich polarimeter, with the liquid in a 1 dcm. 1.5 ml. capacity tube. The readings were good within $\pm 0.01^\circ$. α_D^{25} (1 dcm) of chlorohydrin + 0.82 °, α_D^{25} (1 dcm) of acetate -3.37°.

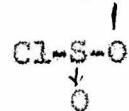
Conversion of chlorohydrin to dichloride with PCl_5 :

21.7 g. (0.2 mol) of dl erythro chlorohydrin was added dropwise to a refluxing solution of 160 g (0.78 mol) of C.P. PCl_5 in 400 ml. of U.S.P. chloroform. The addition took 35 minutes. Then the mixture was refluxed for two hours more, cooled and filtered to remove the excess solid PCl_5 which crystallized out. The filtrate - evaporated to 125 ml. by slowly distilling off the chloroform through

an efficient column, then cooled, and more PCl_5 filtered off. More solvent was removed by distillation, and then the boiler residue was poured onto 150 g. of ice and stirred vigorously with an air stirrer for an hour. During this time small portions of solid K_2CO_3 were added until the oil phase was neutral to litmus. The chloroform-dichloride phase was washed, dried over K_2CO_3 , then fractionated through the Weston column. 11.1 g. of dichloride was collected b.p. 51.7 to 53.0 at 80 mm, yield 43.7 %. Material was redistilled b.p. 53.5 - 53.0 at 80 mm. $n_D^{25} = 1.4401$. Condenser reading 171.0

Conversion of Chlorohydrin to dichloride with SOCl_2 :

32.7 g. (0.3 mol) of dl erythro 3 chloro 2 butanol was added dropwise to 53.5 (0.45 mol) of refluxing thionyl chloride b.p. 74.5 - 75.0°C. (uncorrected), The addition took 30 minutes. Solution was refluxed for three hours, then heated on a steam bath for another three hours, to complete the decomposition of the $\text{CH}_3\text{-CHCl-CHCH}_3$



formed as the first step in the reaction.

When no more sulfur dioxide was noticeable the mixture was poured onto 100 g. of ice, neutralized with solid K_2CO_3 , washed, dried and distilled through the Weston column. 6.1 grams of dichloride was collected between 48.0 and 50.0° C. at 80 mm. Yield 16 %. The dichloride was redistilled twice, b.p. 49.0 - 49.5 at 80 mm, $n_D^{25} = 1.4392$, condenser reading 161.4.

When 21.7 g. (0.2 mol) of the active erythro chlorohydrin, $\alpha_{dm} = + 0.82^\circ$, was converted by the method above to dichloride, the redistilled product, 3.96 g. had the following properties:

b.p. 49.4 - 49.7 at 80 mm, $n_D^{25} = 1.4325$, condenser reading 164.0, $\alpha^{25}(1 \text{ cm}) = 0.08^\circ$, Dichloride yield in this experiment was 15.7 %.

Conversion of Chlorohydrin to dichloride with SOCl_2 and pyridine.

32.7 g. (0.3 mol) of the dl erythro chlorohydrin was dissolved in 53 g. (0.67 mol) of Merck reagent pyridine b.p. 115.5 to 116° C. To this solution was added dropwise 59 g (0.5 mol) of thionyl chloride. The reaction mixture was kept well agitated with mechanical stirring to break up the solid mass of pyridine hydrochloride as fast as it formed. Stirring was continued for 20 minutes after the addition was complete. The mixture was placed upon a steam bath and heated for 3 hours. After standing overnight, the oil phase was separated. The pyridine phase was diluted with water, extracted twice with isopropyl ether,

The oil phase and ether extracts were combined, washed 4 times with 6 N. HCl to remove any pyridine, washed with water, dried with K_2CO_3 and distilled. 33.8 g. of dichloride was collected, b.p. 52.9-53.4 at 80 mm. Yield 63 %. After two redistillations this dichloride had the properties, b.p. 53.0 to 53.2 ° C at 80 mm, $n_D^{25} = 1.4410$, condenser reading 179.2.

When 10.8 g. (0.1 mol) of the active erythro chlorohydrin, $\alpha_{1 \text{ cm}}^{25} = + 0.82^\circ$, was converted to dichloride by the method above, the dichloride had b.p. 52.9 - 53.2 at 80 mm, $n_D^{25} = 1.4403$, condenser reading 179.4, $\alpha^{25}(1 \text{ cm}) = 3.80^\circ$. Dichloride yield here was 43.2 %.

Acknowledgments:

I am grateful to Drs. Wood and Dickinson for valuable assistance in making the dielectric constant measurements.

It is a pleasure to express my thanks to Prof. H. J. Lucas without whose constructive criticisms and suggestions this work could not have been carried out.

Summary:

The stereochemical relationships of the 3 chloro 2 butanols and the 2,3 dichlorobutanes have been studied. Chlorination of the chlorohydrin with thionyl chloride proceeds with zero or two Walden inversion; chlorination with thionyl chloride and pyridine involves one Walden Inversion; PCl_5 as a halogenating agent gives mixtures of dichlorides; and hydrochloric acid does not react with the chlorohydrins to give dichloride.

The properties of the 2,3 dichlorides and 3 chloro 2 butanols are reported for the first time.

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