

WALDEN INVERSIONS INVOLVING THE ISOMERIC 2,3-BUTANEDIAMINES  
AND RELATED COMPOUNDS

AN EXPERIMENTAL TEST OF KIRKWOOD'S THEORY OF OPTICAL  
ROTATORY POWER

ZERO-POINT VIBRATIONAL CONTRIBUTIONS TO THE OPTICAL ACTIVITY  
OF ISOTOPICALLY ASYMMETRIC MOLECULES

Thesis by  
Wildon Fickett

In Partial Fulfillment of the Requirements  
for the Degree of  
Doctor of Philosophy

California Institute of Technology  
Pasadena, California

1952

## ACKNOWLEDGEMENTS

I am grateful to Professor Howard J. Lucas and to Professor John G. Kirkwood for suggesting most of the research described herein and for their cooperation in encouraging work on both the theoretical and experimental aspects of the problem of absolute configuration. The directing of the experimental work by Professor Lucas and the directing of the theoretical work by Professor Kirkwood are also acknowledged. In addition, acknowledgement should be made of the assistance of Professor Verner Schomaker in working out problems of internal conformation; of Dr. William W. Wood, who was very helpful in connection with many of the theoretical aspects of optical rotation; and of Mr. Robert P. Waldron, who imparted much information concerning the spectroscopic problems involved.



## ABSTRACT

It has been demonstrated that the reaction of ammonia with 1,2-dimethylethyleneimine is attended by a single Walden inversion and that the analogous reaction of ammonia with 2,3-epoxybutane very probably proceeds in the same way. This result and other evidence have been used to assign configurations to the 3-amino-2-butanols and to draw certain conclusions about the courses of the reactions in which they are involved.

Optically active 1,2-dichloropropane has been prepared and its relative configuration determined. Measurements of its optical rotatory power in different solvents and at different temperatures permit an approximate determination of the optical rotations of the two forms of the molecule corresponding to the two lowest potential minima for internal rotation about the 1,2-carbon-carbon bond. These values are compared with the results of a theoretical calculation; the resulting assignment of absolute configuration is consistent with a previous result for 2,3-epoxybutane.

Kirkwood's theory of optical rotation has been modified so as to take into account contributions arising from zero-point vibrational effects. The theory is used to calculate the optical rotations of compounds of the type  $R_1R_2CHD$ . The result for  $\alpha$ -deuteroethylbenzene is found to be comparable in magnitude with an experimental value and consistent in sign with previous assignments of absolute configuration.

# TABLE OF CONTENTS

<u>PART</u>	<u>TITLE</u>	<u>PAGE</u>
I	WALDEN INVERSIONS INVOLVING THE ISOMERIC 2,3-BUTANEDIAMINES AND RELATED COMPOUNDS . . . . .	1
	Outline of the Problem and Preceding Work. . . . .	1
	The Determination of Stereochemical Purity; Resolution of <u>DL</u> -2,3-Butanediamine . . . . .	8
	Preparation of Derivatives. . . . .	9
	Attempted Reduction of <u>L</u> (-)-2,3-Dimethylethyleneimine by Lithium Aluminum Hydride . . . . .	15
	Experimental Procedures . . . . .	16
	References . . . . .	27
II	AN EXPERIMENTAL TEST OF KIRKWOOD'S THEORY OF OPTICAL ROTATORY POWER . . . . .	28
	Kirkwood's Theory of Optical Rotatory Power; the Choice of Compounds for an Experimental Test of the Theory . . . . .	28
	Comparison of Theoretical and Experimental Values for the Optical Rotations of 2,3-Epoxybutane and 1,2-Dichloropropane; The Solvent and Temperature Dependence of the Rotation of 1,2-Dichloropropane . . . . .	45
	The Preparation of <u>L</u> (-)-1,2-Dichloropropane . . . . .	71
	Experimental Procedures . . . . .	90
	References . . . . .	101
III	ZERO-POINT VIBRATIONAL CONTRIBUTIONS TO THE OPTICAL ACTIVITY OF ISOTOPICALLY ASYMMETRIC MOLECULES. . . . .	103
	Modification of Kirkwood's Theory of Optical Rotation to Take into Account Zero-Point Vibrational Effects . . . . .	103
	Application to $\alpha$ -Deuteroethylbenzene and 2-Deuterobutane . . . . .	123
	References . . . . .	132

PART I

WALDEN INVERSIONS INVOLVING THE ISOMERIC  
2,3-BUTANEDIAMINES AND RELATED COMPOUNDS

WALDEN INVERSIONS INVOLVING THE ISOMERIC 2,3-  
BUTANEDIAMINES AND RELATED COMPOUNDS\*

Outline of the Problem and Preceeding Work

The main purpose of this investigation is the location of the Walden inversions involved in the reaction sequences connecting the isomeric 3-amino-2-butanols, 2,3-dimethylethyleneimines, and 2,3-butanediamines. The accomplishment of this objective, together with a comparison of the contributions of the amino and hydroxyl groups to the optical rotatory power of the compounds of the series, is sufficient for the assignment of configuration to all of the diastereoisomers and enantiomorphs involved.

The series of reactions which were carried out is shown in Figures 1 and 2, pages 2 and 3. The configurations of the epoxides and of the compounds preceding them have been determined previously<sup>(2,3)</sup>. All of the remaining configurational relationships (with the exception of the assignment of D and L configurations to the enantiomorphs of active threo-3-amino-2-butanol and of active 2,3-butanediamine) follow unambiguously from the following well-founded assumption: an odd number of Walden inversions accompanies

- - - - -  
Of the work described here the first part was carried out by Dr. F. H. Dickey, the middle part jointly by Dr. Dickey and the author, and the last part by the author alone. Those parts of the work carried out jointly are described in Dr. Dickey's thesis<sup>(1)</sup>, and they are not repeated here except as embodied in the brief general outline of the problem.

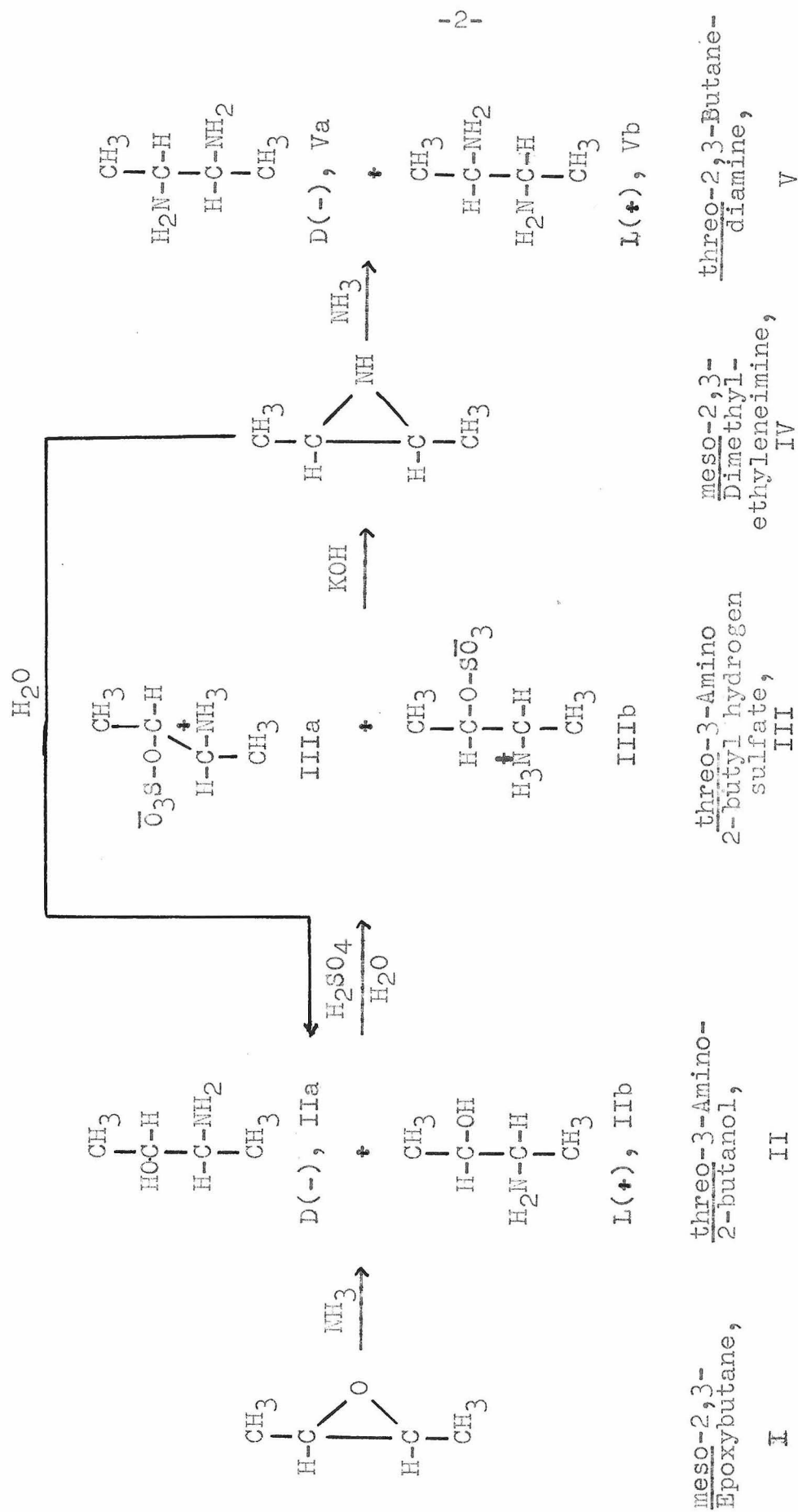


Figure 1. Configurational Relationships of Compounds from meso-2,3-Epoxybutane.

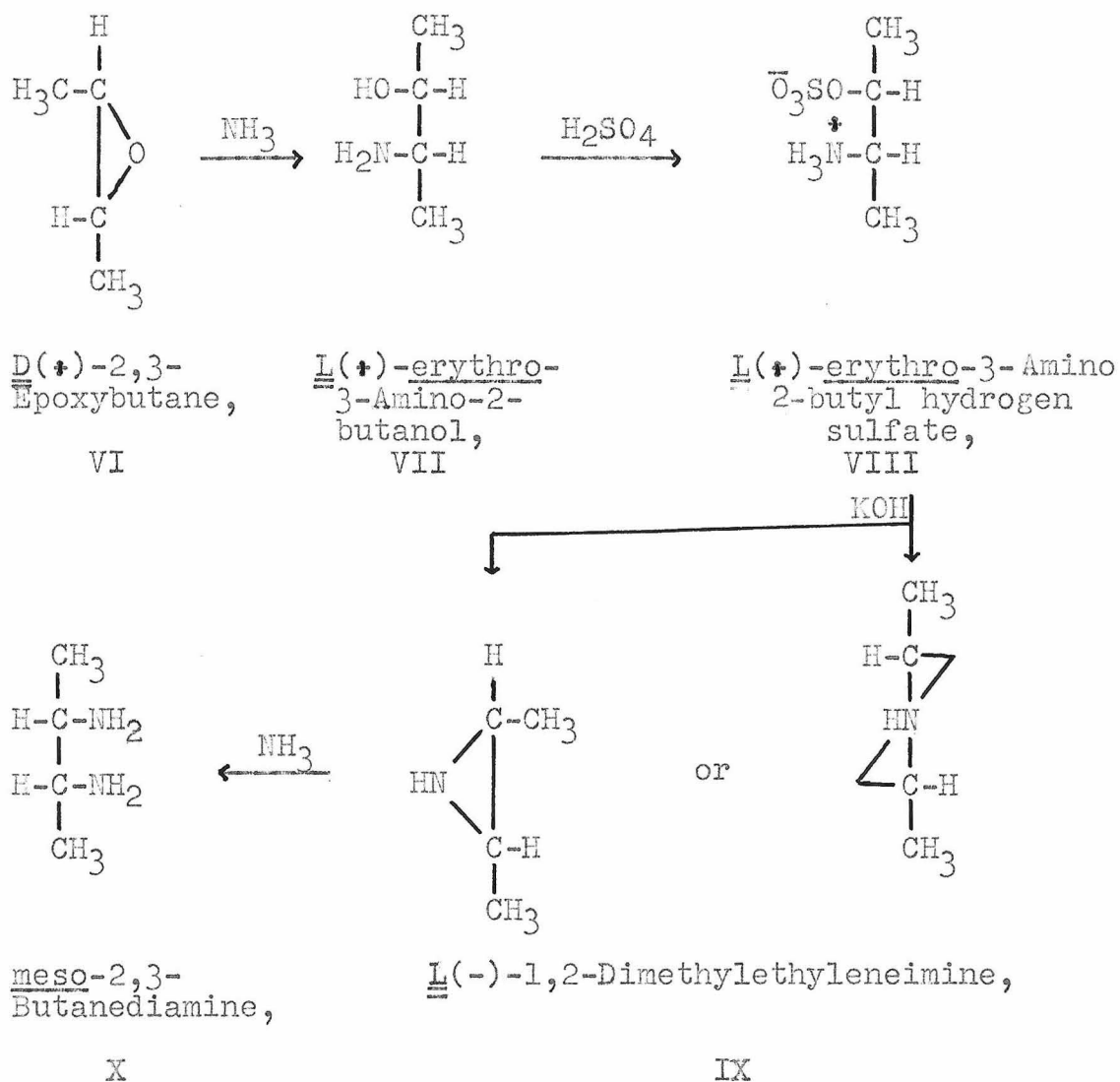


Figure 2. Configurational Relationships of Compounds from D(+)-2,3-Epoxybutane

the opening of the epoxide ring by ammonia. The strongest support for this assumption is probably the recent observation that one inversion accompanies the opening of the epoxide ring of 1,2-epoxycyclohexane with ammonia<sup>(4)</sup>. In addition, it can be said that in the absence of neighboring functional groups epoxide rings are nearly always opened with inversion<sup>(5)</sup>. In view of the general similarity of stereochemical results among different epoxides it is reasonable to suppose that the reaction of 2,3-epoxybutane with ammonia follows the same course. Finally, it was found that the product obtained by reaction of 2,3-epoxybutane with dimethylamine could be made to undergo ring closure by elimination of trimethylamine to produce the same epoxide isomer from which it is prepared<sup>(3)</sup>. Since an odd number of inversions is expected to accompany the ring closure, this result is consistent with the assumption of an odd number of inversions in the ring opening.

If one inversion accompanies the opening of the epoxide ring with ammonia then this reaction should produce DL-threo-3-amino-2-butanol, II, from meso-2,3-epoxybutane, I, and active L-erythro-3-amino-2-butanol, VII, from D-2,3-epoxybutane, VI. Since meso-2,3-dimethylethyleneimine, IV, is formed from the threo-3-amino-2-butanol, II, it follows that one inversion is involved in this transformation. Otherwise, only a single inversion would be involved in the conversion of oxide to imine and the imine from the meso epoxide would then necessarily be DL. In the case of the active oxide

similar considerations apply. If one inversion accompanies the opening of the oxide ring the amino alcohol from the D-oxide will be L-erythro, carbon atom C-3 having been inverted. In the closing to the imine carbon atom C-2 is inverted and the configuration of the imine is thus L, both carbon atoms having been inverted in the course of the reactions. Attempted resolution of the 2,3-butane-diamines obtained by reaction of the imines with ammonia showed that the diamine obtained from the meso imine was DL and that from the active imine was meso. One inversion was thus shown to accompany the opening of the imine ring with ammonia.

Since the opening of the imine ring of meso-2,3-dimethylethyleneimine with water produced an amino alcohol identical with that produced by the reaction of the meso oxide with ammonia, one inversion must accompany this opening of the imine ring. It is perhaps interesting to note that this relationship obtained between the oxide, amino alcohol, and imine allows all of the foregoing discussion to be based on the assumption of inversion in the opening of the imine ring with water rather than upon the assumption of an inversion in the opening of the oxide ring with ammonia. Either assumption follows from the other because of the experimental connection of the imine and oxide to the same amino alcohol isomer. Thus the assumption that one inversion accompanies the opening of the imine ring with water requires an inversion in the opening of the epoxide with ammonia; otherwise, the number of inversions between the meso-oxide and meso-imine would not be correct.



There is, however, less direct evidence for the opening of the imine ring by water with inversion, and it seems preferable to base the argument on the assumption of an odd number of inversions in the oxide-ammonia reaction.

Comparison of the optical rotations of the amino alcohols, imine, and diamine with those of the oxide and glycol leads to the hypothesis that the contributions to the rotation made by the imine and amino groups are somewhat greater in magnitude than those of the epoxy and hydroxyl groups and have the same sign. On the basis of this hypothesis, a completely consistent body of relationships between configurations and the sign and magnitude of rotation for the compounds of the series can be found. The observed rotations of the pure compounds are as follows<sup>(1)</sup>:

(1) an active diamine, Va, Vb, has  $29^{\circ}$ , whereas the glycol has  $13^{\circ}$ ; (2) an active threo- amino alcohol, IIa, IIb, has a rotation of  $17^{\circ}$ , intermediate between those of the glycol and diamine; (3) active erythro-amino alcohol, VII, has  $0.85^{\circ}$  whereas threo has  $17^{\circ}$ ; (4) L-erythro-3-amino-2-butanol has a positive rotation, as does the L-glycol. It can be immediately seen that the hypothesis is consistent with the relationship between imine and oxide, for the configurationally related enantiomorphs have the same sign of rotation and the rotation of the imine is the larger. It is correct with respect to magnitude in the comparison of diamine with glycol, the rotation of the diamine being higher. The configurations

of the diamine enantiomorphs were assigned on the basis of the correctness of the hypothesis with regard to sign. In the case of the amino alcohols, the erythro isomer would be expected to have a very low rotation since the effects of amino and hydroxyl are opposed; the sign of this small rotation should be that corresponding to the configuration about the carbon atom bearing the amino group. These conclusions are borne out by the small positive rotation of the L-erythro isomer. In the threo isomer, on the other hand, the configurations about both carbons are the same, and the rotation would be expected to be of a somewhat larger magnitude than that of the corresponding glycol. This is indeed found to be the case, and the configurations of the threo-amino alcohol enantiomorphs were also assigned on the basis of the correctness of the hypothesis with regard to sign.\*

-----

\* The results of the present investigation suggest that the configurations assigned by Read and Campbell to the isomeric 2-amino-1,2-diphenylethanol are incorrect<sup>(7)</sup>. They assumed no inversion in the opening of the oxide ring and assigned the erythro configuration to the amino alcohol obtained from the meso-oxide. The same compound, termed iso-2-amino-1,2-diphenylethanol, was obtained by Weissberger and Bach<sup>(6)</sup> by reaction of meso-stilbene imine with water. In addition, of the pair of compounds obtained from the cis and trans oxides, that from the trans oxide had the higher melting point. All of the experimental facts here are consistent with our results and on the basis of present knowledge the erythro configuration should be assigned to the product from the trans oxide, 2-amino-1,2-diphenylethanol, m.p. 165°, and the threo configuration to that from the meso oxide, iso-2-amino-1,2-diphenylethanol, m.p. 130°. The correct names for these two compounds are therefore erythro-2-amino-1,2-diphenylethanol and threo-2-amino-1,2-diphenylethanol, respectively.

The Determination of Stereochemical Purity;  
Resolution of DL-2,3-Butanediamine

The stereochemical purity of the compounds involved has been discussed previously<sup>(1)</sup>. Additional evidence of configurational purity was obtained by preparation of the meso imine from the L(+)-threo amino alcohol. The imine so prepared had a rotation of + 0.22°, compared to -103.8° for the optically pure L imine. Since a lack of inversion in the closing of the ring would be expected to produce the levorotatory L imine the slight positive rotation observed should probably be attributed to the presence of a small percentage of the stereoisomeric erythro amino alcohol in the starting material. Although it is possible that the effects of the two influences could partly cancel each other, this result demonstrates fairly conclusively the near absence of both non-inverting ring closure and appreciable amounts of stereochemical impurities.

Partial resolution of the DL diamine on a small scale was carried out during the first part of the work, but the product obtained was not pure. The synthesis of the DL diamine by an improved procedure and its complete resolution are described in the experimental section.

### Preparation of Derivatives

Characterization derivatives of all of the new compounds were prepared. In order to make comparisons of rotations throughout the entire series, acetyl and *p*-toluene sulfonyl derivatives were chosen, as these had already been prepared for the glycols<sup>(2,8)</sup>. In the case of the imines, attempted preparation of the tosyl derivatives in the usual way (tosyl chloride in pyridine) resulted in the formation of 3-chloro-2-*p*-toluenesulfonoxybutanes. Apparently the imine ring had been opened by chloride ion in the course of the preparation. The yields were rather low, but the compounds were readily recrystallized and quite easy to purify. Attempts to prepare the acetyl derivative by direct reaction of the imine with acetic anhydride were unsuccessful. It was learned later that this reaction had been investigated previously and found to lead to no single product. No more acetylations were attempted; the second derivatives chosen for the imines were the 3-chloro-2-benzenesulfonoxybutanes. These proved to have desirable properties similar to the analogous tosyl compounds, but the yields were again low.

The derivatives which were prepared, together with their melting points, optical rotations, and microanalyses, are listed in Tables I and II. The relationships between the optical rotations of analogous nitrogen and oxygen compounds are found to follow the same general pattern as those between the rotations of the compounds themselves. Thus the rotation

TABLE I

Constants of Some 2,3-Disubstituted Butanes

	M.P. OC	B.P.* OC	mm.	$d_4^{25}$	$n_D^{25}$	$\alpha_D^{25}$	$[\alpha]_D^{25}$
3-Amino-2-butanol,							
DL-threo, II <sup>a</sup>	18-20	69-70	20	0.9299	1.4445		
<u>D(-)-threo</u> , II	15-16	70.6-71.3	20	0.9289	1.4450	-15.84°	-17.05°
<u>L(+)-threo</u> , II <sup>a</sup>	7-11			0.9274 <sup>b</sup>	1.4448 <sup>b</sup>	+15.69°	+16.91°
<u>L(+)-erythro</u> , VII	49.2-49.3			0.9378 <sup>b</sup>	1.4488 <sup>b</sup>	+ 0.80°	+ 0.85°
<u>DL-erythro</u> <sup>c</sup>	43.0-44.8	75.0-75.5	20	0.9447 <sup>b</sup>	1.4420 <sup>b</sup>		
2,3-Dimethylethylene- imine,							
meso, IV <sup>d</sup>	-9 to -6	82.5-82.9	747	0.8171	1.4172	+ 0.22°	
<u>L(-)</u> , IX <sup>f</sup>	-26 to -23	74.5-74.8	746	0.7880	1.4070	-80.37°	-102.0°
2,3-Diaminobutane,							
<u>DL</u> , V	-22 to -21	57-58	60	0.8499	1.4408		
<u>L(+)</u> , V <sup>b</sup>		58-59	60		1.4462	+25.18	+29.48
meso, X	-24 to -22	59-60	60	0.8564	1.4420		
2,3-Epoxybutane, meso, I <sup>g</sup>		59.7 <sup>±</sup> .05	742	0.8226	1.3802		
<u>DL</u> , I <sup>g</sup>		53.5 <sup>±</sup> .05	742	0.8010	1.3705		
<u>D(+)</u> , VI <sup>h</sup>		53.5-53.7	745	0.7998	1.3705	+47.23°	+59.05°
2,3-Butanediol,							
<u>DL</u> , I <sup>i</sup>		176.7	742				
<u>D(-)</u> , I <sup>j</sup>	7.6	77.5-177.6	10	0.9869	1.4308	-13.0°	-13.19°
<u>L(+)</u> , I <sup>h</sup>	19.7			0.9872	1.4306		+13.19°
meso, I <sup>i</sup>	34.4	181.7	742	1.0003	1.4367		

Footnotes to Table I

- a) Previous values<sup>(9)</sup>, b.p., 85-105° (185 mm.),  $n_D^{25}$  1.4425.
- b) Supercooled liquid
- c) Previous values<sup>(9)</sup>, b.p., 116-119° (185 mm.),  $n_D^{25}$  1.4445.
- d) Previous values for the trans (?)<sup>(9)</sup>: b.p., 75-76° (185 mm.),  $n_D^{25}$  1.4070,  
 $d_D^{25}$  0.7887, and b.p., 76-77° (185 mm.),  $n_D^{25}$  1.4105.
- e) One product from L(\*)-threo-3-amino-2-butanol
- f) Previous values for the DL<sup>(9)</sup>: b.p., 75-76° (185 mm.),  $n_D^{25}$  1.4074.
- g) S Winstein and H. J. Lucas, J.A.C.S., 61, 2845 (1939).
- h) Ref. 2
- i) Ref. 3
- j) A. C. Neish, Can. J. Research, 238, 10 (1945).

\* All melting points and boiling points are corrected.

Table II

Di-p-toluenesulfonyl and Dibenzenesulfonyl Derivatives

	M.P. °C (corr.)	$[\alpha]_D^{25}$ in butanone	Carbon, % Calcd. Found	Hydrogen, % Calcd. Found	Nitrogen % Calcd. Found	Sulfur, % Calcd. Found
3-p-Toluenesulfonyl- amido-2-p-toluene- sulfonoxybutane,						
DL-threo	125.7-126.7		54.26	5.85	3.52	16.11
<u>D(+)-threo</u>	140.1-141.0	+42.5°	54.26	5.85	3.52	16.11
DL-erythro	94.5-96.3		54.26	5.85	3.52	16.11
<u>L(-)-erythro</u>	104.2-105.2	-7.14°	54.26	5.85	3.52	16.11
2,3-Di-toluene- sulfonamidobutane,						
DL-threo	179.3-180.7		54.52	6.10	7.07	16.17
<u>L(-)-threo</u>	201.1-202.8	-70.3°	54.52	6.10	7.07	16.17
<u>meso</u>	168.5-169.0		54.52	6.10	7.07	16.17
3-Chloro-2-p- toluene-sulfonyl- amidobutane,						
DL-threo <sup>a</sup>	100.5-101.5		50.47	6.16	5.37	13.55 <sup>c</sup>
<u>L-erythro</u> <sup>b</sup>	96.3-96.7	-23.6°	50.47	6.16	5.37	13.55 <sup>c</sup>
3-Chloro-2-benzene- sulfonamidobutane,						
DL-threo <sup>a</sup>	120.6-121.7		48.48	5.70	5.66	14.51 <sup>c</sup>
<u>L-erythro</u> <sup>b</sup>	54.2-54.8	-24.8°	48.48	5.70	5.66	14.51 <sup>c</sup>
		a) From the <u>meso</u> -imine		b) From the <u>L</u> -imine	c) chlorine,	%

Table III

Diacetyl Derivatives					
	M.P. °C (corr.)	$[\alpha]_D^{25}$ in butanone	Carbon, % Calcd. Found	Hydrogen, % Calcd. Found	Nitrogen % Calcd. Found
3-Acetamide-2-acetoxybutane,					
<u>DL</u> -threo	73.4-	74.4	55.47	8.73	8.09
<u>D</u> (+)-threo	59.3-	60.5	55.47	8.73	8.09
<u>DL</u> -erythro	51.0-	52.4	55.47	8.73	8.09
<u>L</u> (-)-erythro	62.3-	63.3	55.47	8.73	8.09
2,3-Diacetamido- butane,					
<u>DL</u> -threo	178.6-	178.9	55.78	9.37	16.27
<u>L</u> (-)-threo	199.3-	199.7	55.78	9.37	16.27
<u>meso</u> -	277.9-	280.0a	55.78	9.37	16.27

a) Sealed tube



of the tosyl derivative of the active diamine, L-2,3-di-p-toluenesulfonamidobutane, is  $-70.3^{\circ}$  compared to  $+37.2^{\circ}$  for the tosyl derivative of the D-glycol, D-2,3-di-p-toluenesulfonoxybutane<sup>(8)</sup>. The rotation of the ditosyl derivative of D-threo-3-amino-2-butanol, D-threo-3-p-toluenesulfonamido-2-p-toluenesulfonoxybutane, is  $+42.5^{\circ}$ , intermediate between those of the corresponding glycol and diamine derivatives given above. The rotation of the L-erythro-3-p-toluenesulfonamido-2-p-toluenesulfonoxybutane is only  $-7.14^{\circ}$  and is thus considerably smaller in magnitude than that of the threo isomer and of the opposite sign as expected for the erythro isomer.

Similarly, the rotations of the diacetyl derivatives increase in magnitude in the same order: glycol, threo-amino alcohol, and diamine, the values being  $+13.7^{\circ}$ ,  $+35.0^{\circ}$  and  $-56.8^{\circ}$  for D-2,3-acetoxybutane, D-threo-3-acetamido-2-acetoxybutane, and L-2,3-diacetamidobutane, respectively. The single partial inconsistency in this general scheme is the rather high rotation of the acetyl derivative of the erythro amino alcohol. The rotation of the L-derivative,  $-33.0^{\circ}$ , does have the expected negative sign, but it is nearly as large in magnitude as that of the acetyl derivative of the threo isomer.

The unexpectedly high rotation of the acetyl derivative of the erythro amino alcohol is still less in magnitude than that of the threo isomer. Therefore all of the relationships pointed out between the rotations of the derivatives represent confirming evidence of the assigned configurations.

Attempted Reduction of L(-)-2,3-Dimethyl-  
ethyleneimine by Lithium Aluminum Hydride

The recent work of Brewster, Hughes, Ingold, et. al.<sup>(13)</sup> determines the configurational relationships between the carbohydrates and the amino acids. Their paper appeared during the course of the present work, which had as its object the determination of the configuration of s-butyl amine. If this were achieved, essentially the same result would have been accomplished.

Lithium aluminum hydride was chosen as the reducing agent because it has been found to reduce epoxides satisfactorily and the stereochemistry of the reduction is known<sup>(9,10)</sup>. However, the attempted reduction of the imine failed completely under ordinary conditions. Even when the conditions were made quite severe the original imine was still recovered largely unchanged.

Structural comparison of the imine with epoxides indicates a single important difference upon which to base a reasonable explanation of this failure: the presence of the acid hydrogen on the imine ring. This could be expected to react with the lithium aluminum hydride to produce a salt-like compound with positively charged lithium and negatively charged nitrogen. It has been fairly well established that the reduction takes place by negatively charged aluminohydride ions of some sort<sup>(10)</sup>; the presence of the negative charge on the imine nitrogen would undoubtedly lower the reactivity of the compound in the hydride reduction. As is often the

case, quantitative prediction of the result would undoubtedly be quite difficult, but a satisfactory qualitative explanation has been provided.

### Experimental Procedures\*

meso-2,3-Dimethylethyleneimine from L(+)-threo-3-Amino-2-butanol. - A solution of 4.4 g. (0.05 moles) of the amino alcohol was neutralized to a methyl orange end point with a measured volume of 50% aqueous sulfuric acid, and then an equal volume of the acid was added in excess. This solution was evaporated on a steam bath at 15-20 mm. until a solid lump remained (8 hours). The yield in this intermediate step was not determined, since it had been found in previous preparations to be nearly quantitative. To a cooled solution of the solid sulfate in 20 ml. of water was added slowly, with further cooling, a cold solution of 10 g. (0.18 moles) of potassium hydroxide in 10 g. of water. The mixture was then placed in a distilling apparatus and warmed slowly. At about 80° a white precipitate of potassium sulfate appeared. Distillation began at 85° and was continued to 100°. The imine was salted out of the distillate with potassium hydroxide and dried over the same reagent. The crude dry product weighed 2.14 g. and was fractionated in a semi-micro apparatus; the total weight of the distillate was 1.57 g., 48% yield. Other preparations on a larger scale gave much higher yields.

- - - - -  
\* Microanalyses were by A. Elek. Physical data not given here will be found in Tables I and II. All melting points and boiling points are corrected.

The first fraction, b.p. 83.3°-84.2° at 746 mm., 0.46 g., had  $n_D^{25}$  1.4188,  $\alpha_D^{25}$  +0.35° (undiluted); the second, b.p. 84.2-84.4° at 746 mm., 1.11 g., had  $n_D^{25}$  1.4177,  $\alpha_D^{25}$  + 0.16 (undiluted). The average rotation of +0.22° indicates a contamination by active imine to the extent of about 0.2 percent.

DL-2,3-Butanediamine. - The method of preparation was essentially that given by Clapp for similar compounds<sup>(11)</sup>. The reaction vessels were war-surplus stainless steel oxygen bail-out cylinders having a capacity of 320 ml. The imine and ammonium chloride were placed in the cylinder which was then cooled in dry ice and evacuated to a pressure of a few mm. The ammonia was introduced by connecting the reaction cylinder through small copper tubing to an ordinary ammonia tank and keeping the small cylinder in dry ice. About half an hour was required to introduce 100 g. of ammonia into the cylinder. The reaction was carried out with 20.1 g. (0.29 moles) of meso-2,3-dimethylethyleneimine, 1.59 g. (0.06 moles) of ammonium chloride, and approximately 210 g. (12 moles) of ammonia, divided between two cylinders. Heating was at 100° C. for 56 hours. The bombs were cooled and opened. The slightly rust-colored reaction mixture ( in this respect the stainless steel tanks are far superior to the monel metal containers used in the earlier part of the work, which gave very dark reaction mixtures containing much solid material) was poured into a cold flask and allowed to evaporate through a condenser kept at -10° C. to prevent escape of unreacted

imine. The remaining material was distilled rapidly at 60 mm. and then fractionated. About 5 g., 25% yield, of imine, b.p. 83-86°; 2.2 g. of an intermediate fraction; and 8.5 g., 30% yield, of DL-diamine boiling at 58.8-61.8° (all boiling points at 60 mm.) were obtained. The material remaining in the pot, about 2 g., was probably largely polymeric. The yield could probably have been improved slightly by decomposing the solid residue from the first distillation with base.

Resolution of DL-2,3-Butanediamine. - The acid tartrate of the DL-diamine was prepared by adding to a warm solution of 20.47 g. (0.1364 moles) of (+)-tartaric acid in 450 ml. of absolute ethanol and 250 ml. of water 6.0 g. (0.68 moles) of DL-2,3-butanediamine dissolved in 50 ml. of absolute ethanol. After standing overnight the mixture was filtered and the rosette-shaped crystals were dried in vacuum over calcium chloride. The dry weight was 14.80 g. so that the solubility in this solvent (ethanol-water 2:1) was 1.55 g./100 ml. A 5% solution of the solid in water had  $\alpha_D^{25} +0.95^\circ$ . After five recrystallizations from the same solvent, 6.85 g. of material were obtained having a constant solubility of 0.40 g./100 ml. and a rotation  $\alpha_D^{25} +0.89^\circ$  under the same conditions as before. By reworking the mother liquors another 3.0 g. of material having the same solubility was obtained; yield, 9.85 g., 74%.

As a further check on the completeness of resolution of the acid tartrate, 0.02 g. were dissolved in a few drops of

warm water and several pellets of potassium hydroxide were added with external cooling. The diamine separated as an upper layer and was dissolved by adding dry benzene and stirring gently; the aqueous layer was not extracted with the benzene. The benzene solution was filtered and had  $\alpha_D^{25} + 0.82$ ,  $[\alpha]_D^{25} + 28.8^\circ$ . The concentration of diamine (0.0284 g./ml.) was determined by passing dry hydrogen chloride in 1.00 ml. of the benzene solution and weighing the precipitated dihydrochloride (0.0520 g.).

One gram of the acid tartrate salt was then recrystallized from 20 ml. of the same solvent and the same measurement was repeated on the recrystallized material. The solution of the diamine (0.0266 g./ml.) in benzene had  $\alpha_D^{25} + 0.78^\circ$ ,  $[\alpha]_D^{25} + 29.3^\circ$  (weight of dihydrochloride from 1 ml. of solution, 0.0486 g.).

The recovery of the active diamine from the acid tartrate salt was carried out in the same way. The benzene solution was first distilled through a small Vigreux column to remove the benzene-water azeotrope. The last of the benzene was removed at 120 mm. and finally at 60 mm. through a small semi-micro column, and the diamine was distilled through the same column at the latter pressure. From 4 g. of salt were obtained about 0.35 g., 40% yield, of diamine, b.p.  $57-58^\circ$ ,  $n_D^{25}$  1.4462,  $d_4^{25}$  29.48°. The high refractive index may have been due to the presence of some benzene; because of the small amount of material obtained fractionation may not have been quite complete.

The tartrate salt of the other enantiomorph of the diamine, obtained by evaporation of the mother liquors, was decomposed with base. The diamine thus obtained had  $[\alpha]_D^{25} -11.43^\circ$ . Further resolution of this material was attempted by preparation of the acid malate salt (with (+) malic acid). This material was very gummy and only a small portion of it could be induced to crystallize; the attempted resolution of the other enantiomorph was abandoned at this stage.

DL-threo-3-p-Toluenesulfonamido-2-p-toluenesulfonoxybutanes.  
 - To a solution of 0.89 g. (0.10 moles) of DL-threo-3-amino-2-butanol in 6 ml. of pyridine were added slowly, with cooling and shaking, 4.0 g. of p-toluenesulfonyl chloride. After about an hour the solution was filled with crystals of pyridine hydrochloride and was allowed to stand overnight. The solution was neutralized with 10 ml. of 6 M hydrochloric acid, the resulting yellow precipitate removed by filtration, and the aqueous solution extracted with benzene. The DL-threo-3-p-toluenesulfonamido-2-p-toluenesulfonoxybutane was recrystallized from benzene-ligroin, giving after one recrystallization 2.88 g., 72% yield, of nearly white needles. Six recrystallizations were required for constant melting point. The D-threo isomer prepared from D(-)-threo-3-amino-2-butanol had  $[\alpha]_D^{25} +42.5^\circ$  (c = 0.0792,  $\alpha = +3.37^\circ$ , butanone). The L-erythro isomer prepared from L(+)-erythro-3-amino-2-butanol had  $[\alpha]_D^{25} -7.14^\circ$  (c = 0.0560,  $\alpha = -0.40^\circ$ , butanone).

DL-threo-3-Acetamido-2-acetoxybutane. - To a solution of 0.45 g. (0.0050 moles) of DL-threo-3-amino-2-butanol in 1.2 ml. of pyridine were added dropwise, with cooling, 1.53 g. (0.015 moles) of acetic anhydride. After standing overnight the mixture was placed in a vacuum desiccator over sulfuric acid and potassium hydroxide. After about ten days 0.82 g., 94% yield, of dry white needles remained. Constant melting point was reached after two recrystallizations from benzene-ligroin. The D-threo-3-acetamideo-2-acetoxybutane prepared from D(-)-threo-3-amino-2-butanol had  $[\alpha]_D^{25} +35.0^\circ$  (c = 0.0503,  $\alpha$  = 1.76°, butanone). The L-erythro isomer prepared from L(+)-erythro-3-amino-2-butanol had  $[\alpha]_D^{25} -33.0^\circ$  (c = 0.0500,  $\alpha$  = -1.65°, butanone). It was found necessary to carry out the final recrystallizations of both optically active isomers in ethyl ether, preparing the solution at room temperature and cooling in dry ice to effect crystallization.

3-Chloro-2-p-toluenesulfonamidobutanes. - To a cooled solution of 0.35 g. (0.005 moles) of L(-)-2,3-dimethylethyleneimine in 3 ml. of pyridine were added dropwise 1.0 g. (0.005 moles) of p-toluenesulfonyl chloride dissolved in 2 ml. of pyridine. After standing for three days the solution was evaporated in vacuum to 3 ml. and 10 ml. of benzene were added. The two-phase mixture was shaken with 25 ml. of 1 N hydrochloric acid which was then extracted after separation from the aqueous phase with another 10 ml. of benzene. Vacuum evaporation of the dried benzene extracts gave 0.30 g., 21%



yield, of white needles crystallizing in rosette patterns. Three recrystallizations from isopropyl ether were required to reach constant melting point. The D-erythro-3-chloro-2-p-toluenesulfonamidobutane thus obtained had  $[\alpha]_D^{25} -23.6^\circ$  ( $c = 0.0500$ ,  $\alpha = 1.18^\circ$ , butanone). The DL-threo isomer was prepared similarly from meso-2,3-dimethyleneimine.

3-Chloro-2-benzenesulfonamidobutanes. - The reaction was carried out in exactly the same way as for the tosyl derivative except that the reaction mixture was allowed to stand a week before being worked up. The crystals were similar to those of the tosyl derivative but smaller. The yield of D-erythro-3-chloro-2-benzenesulfonamidobutane from L(-)-2,3-dimethylethyleneimine was 0.22 g., 18%,  $[\alpha]_D^{25} -24.8^\circ$  ( $c = 0.0400$ ,  $\alpha = -0.99^\circ$ , butanone). It was found to be too soluble in isopropyl ether and so was recrystallized from heptane. Constant melting point was reached after three recrystallizations. The DL-threo isomer was prepared similarly from meso-2,3-dimethylethyleneimine.

2,3-Di-p-toluenesulfonamidobutanes. - The reaction was carried out as for the amino alcohols, using 0.44 g. (0.0050 moles) of meso-2,3-butanediamine. The original product was quite yellow, but after two recrystallizations from isopropyl ether 0.74 g., 37% yield, of colorless crystals of meso-2,3-di-p-toluenesulfonamidobutane were obtained. Four more recrystallizations were required to reach constant melting point.

The DL isomer was prepared similarly from DL-2,3-butanediamine. The L isomer, prepared from L(+)-2,3-butanediamine, had  $[\alpha]_D^{25}$  -70.3° (c = 0.0298,  $\alpha$  = -2.09°, butanone).

2,3-Diacetamidobutanes. - To a cooled solution of 0.44 g. (0.005 moles) of meso-2,3-butanediamine in 2 ml. of pyridine were added dropwise 1.53 g. (0.015 moles) of acetic anhydride. A white precipitate appeared as the anhydride was added. The whole was placed in a vacuum desiccator over sulfuric acid and potassium hydroxide and the liquid was allowed to evaporate. The resulting white needle-like crystals of meso-2,3-diacetamidobutane weighed 0.86 g., 100% yield. The material was recrystallized from acetone, although the temperature coefficient of solubility was not as high as might be desired. Constant melting point was reached after four recrystallizations. The DL isomer was prepared in the same way from DL-2,3-diacetamidobutane. The L isomer prepared from L(+)-2,3-butanediamine had  $[\alpha]_D^{25}$  -56.8° (c = 0.0095,  $\alpha$  = -0.54°, butanone).

Hydration of meso-2,3-Dimethylethyleneimine and Identification of the Product. - To 50 ml. of 1 N sulfuric acid were added 1.42 g. (0.02 moles) of meso-1,2-dimethylethyleneimine. After twenty days standing at room temperature some imine odor could still be detected. The solution was made basic with 30% sodium hydroxide solution and distilled to dryness. The distillate was then distilled through a semimicro column. A first cut, approximately 0.5 ml., b.p. 90-97°, was probably largely unreacted imine. The remaining material was distilled

to dryness at 80 mm. and the distillate titrated with hydrochloric acid to a methyl red end point. The amount of acid required was 0.00991 moles (9.20 ml. of 1.078 N HCl), indicating approximately 50% yield of amino alcohol. The solution was evaporated almost to dryness, care being taken to avoid excessive heating. The resulting yellow syrup was dried in vacuum over sulfuric acid. This crude hydrochloride was dissolved in about 5 ml. of methanol and a solution of 0.23 g. of sodium in about 5 ml. of methanol was added. The resulting precipitate of sodium chloride was removed by filtration and the solution was then distilled through a semi-micro column. The last fraction, about 0.5 ml., had b.p. ca. 70° at 20 mm. and  $n_D^{25}$  1.4441.

A small amount of this material was converted to the ditosyl derivative, and the derivative was recrystallized three times from benzene-ligroin. It had m.p. 126.1-126.9°, mixed melting point 126.2-127.0° with the ditosyl derivative, m.p. 125.7-126.7°, of DL-threo-3-amino-2-butanol, the ammoniation product of meso-2,3-epoxybutane. The product of the aqueous imine hydrolysis was thus reasonably pure threo isomer. Had any erythro isomer been present it would have been concentrated in the last fraction, since its boiling point is slightly higher.

DL-erythro-3-amino-2-butanol. - The method of preparation was the same as that used by Dickey for L erythro isomer<sup>(1)</sup>.

from 15.5 g. (0.25 moles) of DL-2,3-epoxybutane were obtained 8.40 g., 38% yield, of DL-erythro-3-amino-2-butanol. The product had b.p. 76.0-77.4° at 20 mm., m.p. 43.0-44.8°,  $n_D^{25}$  1.4485,  $d_4^{25}$  0.9447 (supercooled).

L(-)-2,3-Dimethylethyleneimine. - This compound was prepared as described in the experimental section above for the meso imine. From 18 g. (0.127 moles) of L(+)-erythro-3-amino-2-butyl hydrogen sulfate were obtained 7.96 g., 95% yield, of L(-)-2,3-dimethylethyleneimine, b.p. 74.7-75.7° at 746 mm.,  $n_D^{25}$  1.4076,  $[\alpha]_D^{25}$  -103.8° (c = 0.002218,  $\alpha$  = -2.29°, n-heptane).

Attempted Reductions of L(-)-2,3-Dimethylethyleneimine with Lithium Aluminum Hydride. - In a 200 ml. 3-neck flask fitted with a reflux condenser, dropping funnel, and sealed stirrer were placed 40 ml. of dry ether and 2.0 g. (0.50 moles, 100% excess) of lithium aluminum hydride. The condenser was closed with a drying tube filled with calcium chloride and soda lime and the mixture was refluxed with occasional stirring for three hours to effect solution of the hydride. The solution was allowed to come to room temperature and 3.5 g. (0.05 moles) of imine were added from the dropping funnel with vigorous stirring. The addition required about half an hour, since it was accompanied by rapid evolution of hydrogen. The solution was refluxed for three hours after the addition was complete. Then the excess hydride was destroyed by dropwise addition of water with stirring and cooling of the reaction flask in an ice bath. Then excess 20% sulfuric acid was added and the

phases were separated. The aqueous phase was made basic with sodium hydroxide. The resulting gelatinous mixture was distilled until the boiling point reached  $98^{\circ}$ . The product was salted out of the distillate with potassium hydroxide, dried over additional potassium hydroxide, and distilled through a semimicro column. About 2.8 g. of material boiling at  $74-75^{\circ}$  were obtained. It had  $n_D^{25}$  1.4047,  $[\alpha]_D^{25}$   $-103.2^{\circ}$  ( $c = 1.618$ ,  $\alpha = -1.67^{\circ}$ , n-heptane). The appropriate constants for s-butyl amine are b.p.  $63^{\circ}$ ,  $n_D^{16.7}$  1.39051,  $[\alpha]_D^{20}$   $7.4^{\circ}$  (12). A sample of redistilled s-butyl amine (E.K. white label) had  $n_D^{25}$  1.3903. Thus the material recovered was probably mostly imine.

The attempted reduction was repeated under more vigorous conditions. The procedure was the same as before, using 4.9 g. (0.07 moles) of the same imine and 3.8 g. (0.10 moles, 135% excess) of lithium aluminum hydride. The solvent was tetrahydrofuran, and the reaction mixture was refluxed for five hours after addition of the imine. The reaction of water with excess hydride at the conclusion of the reaction was deceptively slow at first and when there was no significant reaction for several minutes following the addition of the first few drops of water another ml. of water was added dropwise. The whole reaction mixture became hot and part of it was blown out of the flask. The remainder was worked up as before except that the water-soluble tetrahydrofuran was removed by fractional distillation before adding base. About 0.2 g. of material were obtained, b.p. approximately  $73^{\circ}$ ,  $n_D^{25}$  1.4060,  $[\alpha]_D^{25}$   $+84.6^{\circ}$  ( $c = 0.0117$ ,  $\alpha = 0.99^{\circ}$ , n-heptane).

REFERENCES

1. F. H. Dickey, Thesis, California Institute of Technology, (1949).
2. H. J. Lucas and H. K. Garner, J. Am. Chem. Soc., 70, 990 (1948).
3. C. E. Wilson and H. J. Lucas, J. Am. Chem. Soc., 58, 2396 (1936).
4. G. E. McCasland, R. K. Clarke, Jr., and H. E. Carter, J. Am. Chem. Soc., 71, 2396 (1936).
5. S. Winstein and R. B. Henderson, "Heterocyclic Compounds", Vol. I, Edited by R. C. Elderfield, New York: John Wiley and Sons, 1950, Chapter I.
6. A. Weissberger and H. Bach, Ber. 64, 1095 (1932).
7. J. Read and I. G. M. Campbell, J. Chem. Soc., 2377 (1930).
8. H. J. Lucas, F. W. Mitchell, and H. K. Garner, J. Am. Chem. Soc., 72, 2143 (1950).
9. P. J. Leroux and H. J. Lucas, J. Am. Chem. Soc., 73, 41 (1951).
10. L. W. Trevoy and W. G. Brown, J. Am. Chem. Soc., 71, 1675 (1949).
11. L. B. Clapp, J. Am. Chem. Soc., 70, 184 (1948).
12. "Handbook of Chemistry and Physics", Edited by C. D. Hodgman, Cleveland, Ohio: Chemical Rubber Publishing Co., 1943.

PART II

AN EXPERIMENTAL TEST OF KIRKWOOD'S THEORY  
OF OPTICAL ROTATORY POWER

AN EXPERIMENTAL TEST OF KIRKWOOD'S THEORY  
OF OPTICAL ROTATORY POWER  
Kirkwood's Theory of Optical Rotatory Power;  
the Choice of Compounds for an Experimental  
Test of the Theory

Kirkwood and Wood have recently applied Kirkwood's theory of optical rotatory power to the calculation of the optical rotation of several organic compounds<sup>(1)</sup>. Before the considerations governing the choice of these compounds and the preparation of one of them are discussed the theory itself will be reviewed briefly.

In many theoretical treatments of the macroscopic physical properties of matter a convenient division of the problem into two parts is made. One part concerns itself with the properties of the molecules themselves such as their polarizability or intermolecular potential energy. The other considers the necessary molecular properties as given, and concerns itself with the expression of the macroscopic properties in terms of molecular parameters. The first part is generally quantum mechanical in character, while the second is often a statistical mechanical theory. The complete theory of optical rotatory power can be divided in this way into a quantum mechanical theory of the effect of radiation on a single molecule and a statistical mechanical theory of the observed optical rotation in terms of molecular parameters.

In order to ascertain the form of the molecular parameters it is appropriate to consider first the microscopic problem, that is, the quantum mechanical calculation of the



electric and magnetic moments induced in a molecule by a varying electromagnetic field. The calculation of the induced moments is formulated as a time-dependent perturbation problem. The unperturbed system is taken to be the molecule in the absence of external fields. The perturbing field is then taken to be that associated with the electromagnetic radiation incident on the molecule. Since the wave length of visible light is of the order of a thousand times molecular dimensions the field is in first approximation the same at all positions in space within the molecule at any given instant of time. In the calculation of optical rotatory power, however, this approximation is not justified, since the expression for the induced moment is found to be independent of the symmetry properties of the molecule. When the space variation of the field over the dimensions of the molecule is taken into account the induced moments are found to exhibit a small dependence on the time derivatives of the field, and the proportionality constant of this dependence is found to have the desired symmetry properties. With suitable simplifications the perturbation treatment gives for the induced moments (after averaging over all spatial orientations of the molecule)<sup>(1,2)</sup>:

$$\vec{\mu} = \alpha \vec{E} + \beta \vec{B} - g \left( \frac{1}{c} \dot{\vec{B}} \right) \quad (1)$$

$$\vec{m} = \mu \vec{B} + \beta \vec{E} + g \left( \frac{1}{c} \dot{\vec{E}} \right)$$

$$g = \frac{c}{4\pi i h} \sum_{n=1}^{\infty} \frac{\vec{m}_{n0} \cdot \vec{\mu}_{0n} - \vec{\mu}_{n0} \cdot \vec{m}_{0n}}{\nu_{n0}^2 - \nu^2}$$

Here  $\vec{\mu}_{on}$  and  $\vec{m}_{no}$  are the matrix elements of the electric and magnetic moment operators with the unperturbed wave functions of the molecule,  $\nu$  is the frequency of the incident radiation, and  $\hbar \nu_{no}$  is the energy of the  $n$ th unperturbed state. The quantity  $\alpha$  is the ordinary polarizability; neither  $\alpha$  nor  $\beta$  makes any contribution to the rotatory power. The electric moment operator  $\vec{\mu}$  is a vector, being given by

$$\vec{\mu} = e \sum_i \vec{r}_i \quad (2)$$

where  $e$  is the electronic charge and  $\vec{r}_i$  is the position vector of electron  $i$  and the sum extends over all electrons of the molecule. The magnetic moment operator  $\vec{m}$  is given by

$$\vec{m} = \frac{e}{2mc} \sum_i \vec{r}_i \times \vec{p}_i \quad (3)$$

where  $m$  is the electron mass and  $\vec{p}_i = -i\hbar \nabla_i$  is the momentum operator for electron  $i$ . The product  $\vec{\mu}_{on} \cdot \vec{m}_{no}$  is therefore essentially a triple vector product and is thus a pseudo-scalar quantity, which changes sign when the coordinate system is reflected. In a system having a plane of symmetry it must therefore be zero. Hence the parameter  $g$  does have the properties required of a quantity measuring optical activity.

Consideration of the form of the moments induced by a plane wave serves to clarify to some extent the details of the rotatory process. As a consequence of one of Maxwell's equations,

$$\nabla \times \vec{E} = -\frac{1}{c} \vec{B} \quad (4)$$

equation (1) for the induced electric moment may be written in the form

$$\vec{\mu} = \alpha \vec{E} + g \nabla \times \vec{E} \quad (5)$$

(The term  $\beta \vec{H}$  has been omitted since it makes no contribution to the rotatory power.) A plane wave at a point  $\underline{r}$ , being propagated in the z-direction and having an amplitude  $E_0$  in the x-direction may be written

$$\vec{E} = E_0 \vec{i} \cos 2\pi \left( \nu t - \frac{\vec{k} \cdot \vec{r}}{\lambda} \right) \quad (6)$$

where  $\nu$  is the frequency and  $\lambda$  is the wavelength;  $\vec{i}$ ,  $\vec{j}$ , and  $\vec{k}$  are unit vectors along the x, y, and z-axes, respectively. Then curl  $\vec{E}$  becomes

$$\nabla \times \vec{E} = \left( \frac{2\pi}{\lambda} \right) E_0 \vec{j} \sin 2\pi \left( \nu t - \frac{\vec{k} \cdot \vec{r}}{\lambda} \right) \quad (7)$$

The induced moment is then

$$\begin{aligned} \vec{\mu} = & \alpha E_0 \vec{i} \cos 2\pi \left( \nu t - \frac{\vec{k} \cdot \vec{r}}{\lambda} \right) \\ & + g \left( \frac{2\pi}{\lambda} \right) E_0 \vec{j} \sin 2\pi \left( \nu t - \frac{\vec{k} \cdot \vec{r}}{\lambda} \right) \end{aligned} \quad (8)$$

which may be written in the form

$$\vec{\mu} = \left( \alpha - \left( \frac{2\pi}{\lambda} \right) |g| \right) E_0 \vec{i} \cos 2\pi \left( \nu t - \frac{\vec{k} \cdot \vec{r}}{\lambda} \right) + E_0 \left( \frac{2\pi}{\lambda} \right) \left[ |g| \vec{i} \cos 2\pi \left( \nu t - \frac{\vec{k} \cdot \vec{r}}{\lambda} \right) + g \vec{j} \sin 2\pi \left( \nu t - \frac{\vec{k} \cdot \vec{r}}{\lambda} \right) \right] \quad (9)$$

The first term is directly proportional to the electric field, while the second has two orthogonal components  $90^\circ$  out of phase, characteristic of circular polarization. This part of the induced moment thus emits a circularly polarized wave whose direction of polarization depends on the sign of  $g$ . The net result is a small difference between the refractive indices for the two circularly polarized components of a plane polarized wave traversing the medium.

The calculation of this difference is the object of the statistical mechanical theory<sup>(1)</sup>. The contributions of the moments induced in all the molecules of the system to the field at a given point in space are averaged over the phase space of the system. The resulting field is taken to be the field used in the calculation of the induced moment of a molecule at the point. Since the molecular velocities are small compared to that of light the fields arising from molecular motions as such are neglected, and the averages are taken over the configuration space of the system. With appropriate assumptions and simplifications the result for the macroscopic polarization has somewhat the same form as equation (5) for the moment induced in a single molecule:

$$\vec{P} = \frac{4\pi\bar{N}\alpha}{3} \frac{n^2+2}{n^2-1} \vec{P} + \frac{8\pi\bar{N}}{n^2+1} \frac{g}{c} \nabla \times \vec{P} \quad (10)$$

where  $\alpha$  is the molecular polarizability,  $\bar{N}$  is the number density, and  $n$  is the refractive index of the medium. The polarization can be described as a plane wave propagated in the z-direction and having the same frequency,  $\nu$ , as the incident radiation. (The statistical mechanical theory shows that this result is correct to within terms of order  $(b/\lambda)^2$ , where  $b$  is the distance from the center of the molecule to the point where  $(\tilde{g}(r)-1)$  no longer makes a significant contribution to the integrals in which it occurs. Here  $\tilde{g}$  is the radial distribution function;  $b$  is then of the order of several molecular diameters, a distance still considerably less than the wavelength of the light used.) When equation (10) is solved for  $\vec{P}$  it is found that

$$P_y/P_x = \pm \tan 2\pi(\nu t - \frac{n\vec{k}\cdot\vec{r}}{\lambda}) \quad (11)$$

and that there are two solutions for  $n$ , depending on the sign chosen here. With the positive sign

$$\vec{P} = P_0 [\vec{i} \cos 2\pi(\nu t - \frac{n_r\vec{k}\cdot\vec{r}}{\lambda}) + \vec{j} \sin 2\pi(\nu t - \frac{n_r\vec{k}\cdot\vec{r}}{\lambda})] \quad (12)$$

and with the negative sign

$$\vec{P} = P_0 [\vec{i} \cos 2\pi(\nu t - \frac{n_l\vec{k}\cdot\vec{r}}{\lambda}) - \vec{j} \sin 2\pi(\nu t - \frac{n_l\vec{k}\cdot\vec{r}}{\lambda})] \quad (13)$$

where  $\underline{n}_l$  and  $\underline{n}_r$ , the two solutions for  $\underline{n}$ , are given in terms of the mean refractive index,  $\underline{n}_0$ , by

$$n_l - n_r = \frac{16\pi^2 g}{\lambda} \frac{n_0^2 + 2}{3} \quad n_0^2 = \frac{1 + 8\pi\bar{N}\alpha/3}{1 - 4\pi\bar{N}\alpha/3} \quad (14)$$

It can be seen that the solutions for  $\vec{P}$  correspond to right and left circularly polarized light and that  $\underline{n}_r$  and  $\underline{n}_l$  are the corresponding refractive indices.

The observed optical rotation is related to the difference in the two refractive indices by the well-known Fresnel formula for the rotation of the plane of polarization per centimeter of path length ( $\lambda$  in centimeters)

$$\phi = \frac{\pi}{\lambda} (n_l - n_r) \quad (15)$$

The final result for the specific rotation  $[\alpha]$  (in degrees/decimeter) is then

$$[\alpha] = 1800 \frac{16\pi^2 N}{\lambda^2 M} \frac{n_0^2 + 2}{3} g \quad (16)$$

where  $\underline{N}$  is Avagadro's number and  $\underline{M}$  is the molecular weight. For the sodium  $\underline{D}$  line this becomes

$$[\alpha]_D = 4.930 \times 10^5 \frac{n_0^2 + 2}{3M} g \quad (17)$$

if  $\underline{g}$ , which has dimensions of length to the fourth power, is computed with the angstrom as the unit of length.

In principle, then, the problem is solved. However, so little is known about molecular wave functions at the present time that direct calculation of the matrix elements is out of the question. Kirkwood's approach to this problem involves a perturbation calculation of appropriate wave functions in terms of certain unperturbed wave functions satisfactory for most molecules and concerning which no specific information is required<sup>(3)</sup>.

His treatment begins by basing the unperturbed wave functions on a division of the molecule into groups. In an organic molecule the groups would be the usual organic substituents: alkyl, halogen, hydroxyl, phenyl, etc. The unperturbed wave function for the molecule is taken to be the product of those for the separate groups. The wave function for each group is taken to be that describing the group when it is unaffected by any external influences; specifically, when it is unaffected by electrostatic fields arising from other groups in the molecule. The perturbing field is then taken to be that representing dipole-dipole electrostatic interactions between pairs of groups, and the wave functions to be used in the calculation of the matrix elements in equation (1) are then obtained by the usual perturbation methods.

Since almost no information concerning the unperturbed wave function was taken into account, and since the perturbing potential involved the electrostatic group interactions, it is perhaps not too surprising that the final result should express  $g$  in terms of the properties of the groups which determine

this interaction, viz., their polarizability tensors and their positions in space relative to each other. The result for  $g$  is (for groups having an optical axis of symmetry);

$$g^0 = \frac{1}{6} \sum_{i < k=1}^N \alpha_i \beta_i \alpha_k \beta_k G_{ik} \vec{R}_{ik} \cdot (\vec{b}_i \times \vec{b}_k)$$

$$\vec{R}_{ik} = \vec{R}_k - \vec{R}_i \quad (18)$$

$$G_{ik} = \vec{b}_i \cdot \underline{T}_{ik} \cdot \vec{b}_k = \frac{1}{R_{ik}^3} \left[ \vec{b}_i \cdot \vec{b}_k - \frac{3}{R_{ik}^2} (\vec{b}_i \cdot \vec{R}_{ik})(\vec{R}_{ik} \cdot \vec{b}_k) \right]$$

The symbol  $g^0$  is used since higher terms involving the intrinsic activity of the groups and the interactions of the magnetic moment of one group with the electric moment of another have been neglected. As previously implied, the sum extends over a set of intrinsically inactive groups into which the molecule is divided for the purpose of calculation. The indices  $\underline{i}$  and  $\underline{k}$  refer to these groups, the requirement  $\underline{i} < \underline{k}$  indicating that to any pair of groups there corresponds one and only one term in the sum. Here  $\vec{R}$  is the vector distance from the center of mass of the molecule to the center of mass of the group,  $\vec{b}$  is the unit vector along the optical symmetry axis of the group, and  $\beta$  is the anisotropy of the polarizability of the group. The quantities  $\alpha$  and  $\beta$  are defined more precisely below.

Since  $\underline{T}_{ik}$  is the electrical dipole-dipole interaction tensor of groups  $\underline{i}$  and  $\underline{k}$ , each term in the sum corresponds to an electrical interaction of this type between one pair of groups. It should also be noted that if the polarizability



of any group is isotropic then all terms containing quantities related to that group vanish since the value of  $\beta$ , the anisotropy of the polarizability, will then be zero. There is another way in which a term can vanish, viz., the vectors composing the triple product  $(\vec{R}_{ik} \cdot \vec{b}_i \times \vec{b}_k)$  can all lie in the same plane. This will be the case if both groups have their optical axes of symmetry along the bonds joining them to the central group, e. g., two halogens bonded to an asymmetric carbon atom. (The polarizability tensor of each halogen would have the C-X bond as a symmetry axis.)

In calculating  $g^0$  for any given molecule it is necessary first of all to decide on an appropriate subdivision of the molecule into groups. The general considerations which guide us here are concerned with the approximations involved in the theory and the necessity of evaluating properly the values of the polarizability anisotropy for the different groups so chosen. The approximate representation of the group interactions as dipole-dipole becomes more valid as the distance between the groups is increased. On the other hand the size and bonding of the groups must be such that the values of  $\beta$  can be obtained from the available experimental data. After the division into groups has been carried out the individual terms in the sum must be evaluated. Inspection of the expression for  $g^0$  reveals that there are four types of quantities required for each group: its mean polarizability  $\alpha$ , its anisotropy ratio  $\beta$ , the direction of its optical symmetry axis  $\vec{b}$ , and its spatial position  $\vec{R}$ .

The quantities  $\alpha$  and  $\beta$  are precisely defined in terms of the polarizability tensor of the group. If  $\vec{b}_i$  is the unit vector in the direction of the optical axis of symmetry of the group then the polarizability tensor may be expressed in the form

$$\alpha_m^{(i)} = \alpha_i \left[ \left( \frac{1}{3} - \beta_i \right) + \beta_i \vec{b}_i \vec{b}_i \right] \quad (19)$$

where

$$\alpha_i = \frac{1}{3} (\alpha_{11}^{(i)} + 2\alpha_{22}^{(i)}) \quad \beta_i = \frac{\alpha_{11}^{(i)} - \alpha_{22}^{(i)}}{\alpha_i} \quad (20)$$

$\alpha_{11}^{(i)}$  and  $\alpha_{22}^{(i)}$  being the components of  $\alpha_m^{(i)}$  parallel and perpendicular to  $\vec{b}_i$ .

The calculation of the mean polarizabilities of the groups from available experimental data presents little difficulty. They are given in terms of the ordinary atomic refractions  $A_s$  by

$$\alpha_i = \frac{3}{4\pi N} \sum_s A_s^{(i)} \quad (21)$$

The determination of the anisotropies of the polarizabilities is somewhat more involved and has received considerable discussion elsewhere (Kirkwood<sup>(3)</sup> has listed values of  $\alpha$  and  $\beta$  for many of the common groups of interest.) It is sufficient to state here that these values are obtained from measurements of the degree of depolarization of scattered light or of the

Kerr effect for appropriate molecules containing the group in question. The direction of the optical symmetry axis, which partially defines the coordinate system in which the polarizability tensor is diagonal, can be determined from the known form and symmetry of the groups.

The determination of the geometry of the molecule may be quite difficult. The rotatory power of the molecule is not particularly sensitive to small changes in the ordinary bond angles and distances, and the usual electron diffraction data provide this information with an accuracy greater than that required by the theory. It can be seen, however, that changes in internal conformation (from free or partially hindered rotation about one or more single bonds in the molecule) may bring about relatively large changes in the relative orientation of the groups and the distances between them. Since the expression for  $g^0$ , equation (18), contains the intergroup distances and vector products which depend markedly on the relative orientations of the groups, the calculated optical rotation is quite sensitive to changes of the usual magnitude in the internal conformation.

If a comparison with experiment is to be made, the compound must be capable of being resolved or of being synthesized in an optically active form. Of the compounds suitable for theoretical calculation, there are a surprisingly small number for which this is feasible. Both the requirements of the theory and difficulties in the techniques of synthetic

chemistry sharply limit the choice of a suitable compound. The limitations of the theory arise largely from the type of data required. As was pointed out above, we are concerned with two general types of molecular properties; the geometry of the molecule and the optical properties of the groups. In order that their optical properties be obtainable from the available data the groups must have an approximate axis of optical symmetry. This is strictly true for only a few groups. Many are treated as approximately cylindrically symmetrical: partially free-rotating methyl is assigned a symmetry axis along the bond joining it to the rest of the molecule; phenyl is considered to have a cylindrical axis of optical symmetry along the geometrical six-fold axis. The choice of groups, then, is first limited to those to which the approximation of cylindrical symmetry can be applied. This choice is further limited by the lack of much accurate datum for the degree of depolarization of scattered light or the Kerr constant, from which the anisotropy ratio  $\beta$  is calculated. The number of groups for which the value of  $\beta$  is known is thus a relatively small one.

The other type of limitation is connected with the difficulty of determining the internal conformation of the molecule. Usually, the situation is such that the internal conformation is described by a continuous angular parameter  $\phi$  which specifies the relative angular positions of the groups at the two ends of the single bond about which free or partially hindered internal rotation can occur. Information

about  $V(\phi)$ , the potential function of internal conformation, can be obtained for the simpler molecules from electron diffraction studies, the variation of the dipole moment with temperature, or Raman and infra-red spectra. For molecules of any complexity there is considerable uncertainty and the potential functions are usually known only qualitatively. When this potential function is known the problem is solved, if the necessary optical data for the groups are available, for then the optical rotation may be calculated as a function of  $\phi$ , and an average taken over all conformations, using  $(e^{-\frac{V(\phi)}{RT}})$  as the weighting function. Uncertainty in the calculated rotation due to lack of knowledge of  $V(\phi)$  arises only when the atoms at both ends of the single bond about which free rotation is possible carry groups which will make contributions to  $g^0$ . (In practice, this means nearly every group but hydrogen; its polarizability and anisotropy are quite small and contributions from its interactions with other groups are usually neglected.)

It can be seen that the complexity of the calculations increases rapidly with the number of groups that must be considered, particularly when the molecule contains more than one single bond about which free or partially hindered rotation is possible. To the increased complexity of the calculations is added the difficulty of obtaining information about the potential of internal conformation, and in practice the application of the theory is limited to relatively simple

compounds, preferably rigid ones. When the theoretical limitation with respect to the complexity of the molecule is applied, the experimental difficulties arise largely from the character of the groups which can be treated by the theory. Such groups as hydroxyl introduce a serious difficulty; although the hydrogen atom itself is considered to make a small contribution, its position determines the direction of the optical symmetry axis of the hydroxyl group and thus markedly affects the calculated value of the rotation. But this type of group offers a convenient reaction site which does not involve the asymmetric center and makes the molecule more easily derivatized for resolution. Such groups as methyl and halogen, more amenable to theoretical treatment, are relatively unreactive and offer no safe "handles" for use in resolution. Moreover, the halogens participate in many reactions as neighboring groups, thus confusing questions of optical purity and configurational assignment.

The nature of the experimental difficulties encountered is illustrated by the case of optically active trans-dichlorocyclopropane. The calculation of its optical rotation would be quite straight-forward, since no question of internal conformation is involved. Presumably, monochlorocyclopropane has a plane of symmetry and is optically inactive; therefore the chlorine-ring interaction must be zero, and in the dichloro compound the entire contribution comes from the chlorine-chlorine interaction. (Perturbations of the ring by the second chlorine are expected to be small, and are neglected.) Thus

this compound would seem to offer a good test of the theory. It has not been prepared, however.\*

Another source of difficulty for the synthetic chemist is the desirability of obtaining the configurational relationships between the compounds for which calculations are made. If this is done it provides a test of the consistency of the theory, by comparing the experimental and theoretical relationships between the signs of rotation of related compounds. Furthermore, it is desirable that the D or L configuration be assigned (Fischer convention), since the result regarding absolute configuration then applies to a large body of compounds already related to each other.

The actual choice of the compounds for which the calculations<sup>(1)</sup> were carried out represents a compromise between the limitations in both directions. The two compounds chosen were 2,3-epoxybutane and 1,2-dichloropropane. The 2,3-epoxybutane had already been prepared and its relative configuration determined. Since it is a rigid molecule no questions of internal conformation arise. The uncertainty in the calculations is due to the lack of knowledge of the optical properties of the carbon and oxygen atoms bound in a three-membered ring of this type. These data were obtained indirectly from the observed

-----  
\* The preparation and determination of configuration of this compound are under consideration by Dr. D. H. Deutsch<sup>(4)</sup> of this laboratory who has proposed a method of synthesis based on active trans-cyclopropane-dicarboxylic acid, which would be resolved and made to undergo a Hunsdiecker reaction to form the dichloride. Its relative configuration might be determined by hydrogenolysis of the ring to give some active 1,2-dichloropropane, whose preparation is described here.

rotation of 1,2-epoxypropane, in which some of the same interactions occur. The choice of 1,2-dichloropropane was made on a different basis. The optically active compound had not been prepared; the preparation had just been started when the calculations for it were completed. With regard to the application of the theory, the two compounds complemented each other nicely. The 2,3-epoxybutane presented no problem in internal conformation, but the theory could not be applied in a straightforward way since some of the optical data were not available. On the other hand, the application of the theory to 1,2-dichloropropane for a given internal conformation (position of rotation about the 1,2-carbon-carbon bond) was quite straightforward and satisfactory; the difficulty lay in the determination of the potential of internal conformation. Interpretation of electron diffraction data and of the variation of the dipole moment with temperature provided sufficient knowledge of the potential function to allow an unambiguous prediction of the rotatory power. Measurement of the variation of the optical rotation with temperature (after the optically active form was obtained) was also found to provide information useful in this connection.



Comparison of Theoretical and Experimental Values for the  
Optical Rotations of 2,3-Epoxybutane and 1,2-Dichloropropane;  
The Solvent and Temperature Dependence of the Rotation of  
1,2-Dichloropropane

In order to provide a proper background for the comparison of the theoretical and experimental results we shall first review briefly the calculation of the optical rotations of both of the compounds considered.\* The methods of determining the polarizability  $\alpha$  and its anisotropy  $\beta$  have been discussed in the previous section. The values used in the calculations described below are given in Table I.

We first apply equations (17) and (18) to the calculation of the optical rotatory power of 2,3-epoxybutane. The spatial model to which the calculations apply, the configurationally related 1,2-epoxypropane, and the corresponding Fischer projection formulas are shown in Fig. 1. We first divide the molecule into groups. We consider it to be composed of three groups: the three-membered ring with its attached hydrogens, and the two methyl groups.\*\*

-----  
\* These calculations, whose description comprises pages 45-60 of this section, were carried out by W. W. Wood<sup>(1)</sup>.

\*\* We do not intend to imply by our terminology that the methyl-ring interaction must contribute only a single term to  $g^0$ . It is more correct and in keeping with the intent of the theory to consider it as being itself the sum of three terms describing the interactions of the methyl group with the two carbons and oxygen of the ring, plus terms describing the interactions of the ring atoms with each other. (The sum of these latter terms describing interactions within the ring is probably small since the ring has a plane of symmetry in the absence of perturbing influences.) Thus the "methyl-ring interaction term" actually comprises a sum of terms and the terminology is adopted for the sake of convenience; the optical properties of carbon and oxygen in such an environment are not sufficiently well known to allow separate calculation of these terms.

TABLE I

Values of the Mean Polarizabilities,  $\alpha$ ,  
and of the Anisotropy Ratios,  $\beta$

Group	$\alpha \cdot 10^{24}(\text{c.c.})^a$	$\beta$
CH <sub>3</sub>	2.25	0.35 <sup>b</sup>
CH <sub>3</sub>		0.31 <sup>c</sup>
Cl	2.35	0.35 <sup>b,d</sup>
CH <sub>2</sub> Cl	4.17	0.34 <sup>b,e</sup>
CH <sub>2</sub> Cl		0.33 <sup>c,e</sup>

a) Landolt-Bornstein, Physikalische-Chemische Tabellen, V. W. II, 985; Eisenlohr, Zeits. f. physik. Chemie 75, 585 (1910), 79, 129 (1912).

b) Values obtained by Cabannes; see Landolt-Bernstein, Physikalisch Chemische Tabellen, 5th ed., Eg. II, p. 88; Eg. III, p. 1204.

c) Average of two values: H. A. Stuart, Hand-und-Jahr-buch der Chemischen Physik, Leipzig, 1939, 10 III, p. 27, and W. M. Breazeale, Phys. Rev. (2) 49, 625 (1936).

d) Stuart, op. cit. p. 27.

e) Assumed to have an approximate axis of symmetry along the C-Cl bond.

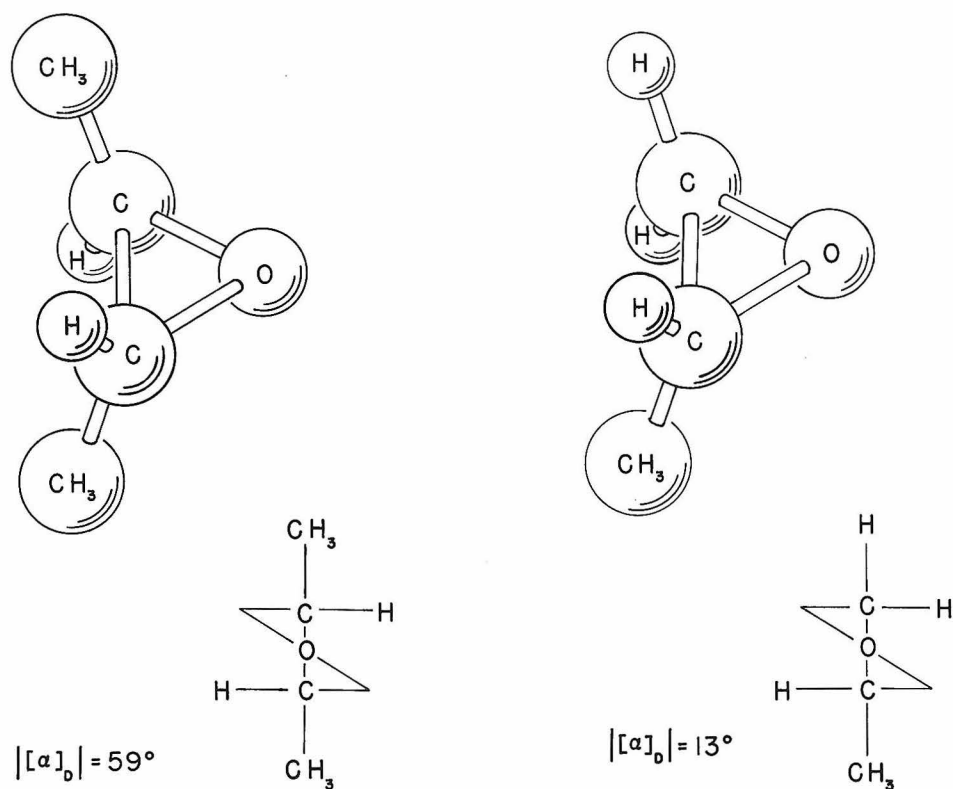


Figure 1. Enantiomorph of 2,3-Epoxybutane to which the Calculations Apply, the Configurationally Related 1,2-Epoxypropane, and the Corresponding Fischer Projection Formulas.

Three pairs can be chosen from these groups and therefore three terms contribute to the rotatory power: two representing the methyl-ring interactions, identical in both magnitude and sign; and one representing the methyl-methyl interaction.

Having defined the number and type of terms in the sum by our division of the molecule into groups we proceed to the actual calculation. Since the molecule is a rigid one no questions of internal conformation arise and the known bond angles and distances<sup>(5)</sup> suffice for the determination of  $\vec{b}_i$ ,  $\vec{b}_k$  and  $\vec{R}_{ik}$  in each term. The values of  $\alpha$  are obtained from Table I. Values of  $\beta$  for the methyl groups are also given in Table I, but no such value is available for the three-membered ring or its component atoms as the necessary experimental data is lacking. Thus we can calculate directly the term representing the methyl-methyl interaction, but not those representing the methyl-ring interactions.

We are thus forced to resort to a quasi-empirical evaluation of these terms. To this end we consider the configurationally related 1,2-epoxypropane molecule, shown in Fig. 1. If we make an analogous division into groups, we arrive at the following result: the methyl group, the three-membered ring together with the two hydrogens chosen so as to correspond to the same group in epoxybutane, and the third hydrogen. Thus we have the following terms to consider: one representing a methyl-ring interaction of the same sign and approximately the same magnitude as in the epoxybutane isomer shown,

one representing a hydrogen-methyl interaction, and one representing a hydrogen-ring interaction. Because of the small polarizability of hydrogen the terms containing it are neglected. (Even if the polarizability of hydrogen were large the hydrogen-methyl interaction would still be zero since the optical symmetry axes and the vector connecting them would lie in the same plane and the triple vector product would vanish. The methyl group is considered free to rotate about the C-C bond and hence has an optical symmetry axis along this bond.) Thus there remains only one term to account for the entire rotatory power of the molecule; this term involves the methyl-ring interaction. Moreover, because of the way in which the groups have been chosen this interaction should be approximately the same as the corresponding methyl-ring interaction in 2,3-epoxybutane. The methyl-ring contribution to the rotatory power of 2,3-epoxybutane is thus equal to the observed specific rotation of the configurationally related 1,2-epoxypropane. Without making an a priori assumption concerning absolute configuration we obtain from the observed specific rotation of 1,2-epoxypropane only the magnitude, and not the sign, of this contribution.

Calculations with equation (18) of the methyl-methyl interaction in the enantiomorph of 2,3-epoxybutane shown in Fig. 1 gives  $+17^\circ$  for this contribution to the rotatory power in a medium of refractive index 1.37, corresponding to the pure liquid. The observed rotation of 1,2-epoxypropane gives

a magnitude of 13 as the quasi-experimental value for the methyl-ring interaction. Remembering that in 2,3-epoxybutane there are two such interactions we obtain  $+17.2 \times (+13) = +43^\circ$  as the predicted specific rotation if we take the positive sign for the methyl-ring interaction, and  $+17.2 \times (-13) = -9^\circ$  if we choose the negative sign. The fact that the enantiomorphs of 2,3-epoxybutane and 1,2-epoxypropane having the same sign of rotation are configurationally related<sup>(6,7)</sup> allows us to reject the latter value, for since the observed rotation of the 2,3-epoxybutane is greater than can be accounted for by the two methyl-ring interactions, the methyl-methyl interaction and methyl-ring interactions must have the same sign. We therefore assign the spatial configurations of Fig. 1 to the dextrorotatory isomers. Since the dextrorotatory isomers have been assigned the D configuration<sup>(6)</sup> the Fischer convention regarding absolute configuration is in agreement with this result. The predicted rotation of  $43^\circ$  is in fair agreement with the observed value of  $59^\circ$ <sup>(6)</sup>.

The theory would be expected to apply most accurately to vapors or dilute solutions in non-polar solvents. Since the experimental results quoted above were those of the pure liquid a possible solvent effect was investigated for 2,3-epoxybutane. No significant change in  $[\alpha]_D^{300\text{OK}} (3/n^2+2)$  was observed for this compound on passing from the pure liquid to a dilute solution in heptane. (A sample having  $[\alpha]_D^{25} +52.4^\circ$  had in heptane solution  $[\alpha]_D^{25} + 53^\circ$  ( $c = 0.00802$ ,  $\alpha = 0.85^\circ$ )). Similar

information for 1,2-epoxypropane is not available, but structural considerations suggest that its behaviour would not differ from that of 2,3-epoxybutane. A related rigid compound, 2,3-iminobutane, has been found to undergo only a slight change in rotation on passing from the pure liquid to a dilute solution in heptane (this thesis, p. 25).

In the calculation of the optical rotatory power of 1,2-dichloropropane we proceed in the same fashion. The molecule is first divided into groups as follows: H, CH<sub>3</sub>, Cl, and CH<sub>2</sub>Cl bonded to the asymmetric carbon atom as the central group. Thus the terms contributing to  $g^0$  correspond to the following interactions: CH<sub>3</sub> with Cl, CH<sub>3</sub> with CH<sub>2</sub>Cl, and Cl with CH<sub>2</sub>Cl. Because of the small polarizability of hydrogen the terms representing its interactions with the other groups have been neglected. Of the three groups listed, CH<sub>3</sub> and Cl are considered to have their optical symmetry axes along the bonds to the central carbon atom, while the polarizability of the CH<sub>2</sub>Cl group is taken to be approximately cylindrically symmetric about the C-Cl bond. As explained above, the contribution from any two groups whose optical symmetry axes lie along their bonds to the central group vanishes because of the vanishing of the triple vector product. Therefore the interaction of CH<sub>3</sub> with Cl makes no contribution and we are left with only two terms in  $g^0$ , those representing the interactions of CH<sub>3</sub> and of Cl with the CH<sub>2</sub>Cl group. In contrast to the case of 2,3-epoxybutane, the experimental data are

sufficiently complete that values of  $\beta$  may be found for all of the groups involved. These are given in Table I. Thus, given the geometry of the molecule, we can calculate the optical rotatory power directly from equations (17) and (18).

However, because of the possibility of rotation about the bond between the asymmetric carbon atom and the  $\text{CH}_2\text{Cl}$  group the geometry of the molecule is not completely defined by present methods of investigation. In Fig. 2 are shown two views of the space model to which the calculations apply and the corresponding Fischer projection formula. The angle  $\phi$ , measuring the internal rotation about the 1,2-carbon-carbon bond is taken to be zero when the chlorine atoms are trans to each other; a positive displacement is defined as one which initially increases the methyl-chlorine distance. Our procedure will be to calculate the rotatory power of the molecule for a series of values of  $\phi$  covering its full range of  $360^\circ$ , and then to obtain an average value of the rotatory power corresponding to that observed experimentally by averaging over all values of  $\phi$  using as the weighting factor  $\exp(-V(\phi)/RT)$  where  $V(\phi)$  is the potential of the internal rotation. We now turn our attention to the problem of performing this averaging and the determination of  $V(\phi)$ . The final results will be given following the discussion of these problems.

Using equations (17) and (18) the optical rotatory power was calculated as a function of the internal conformation.



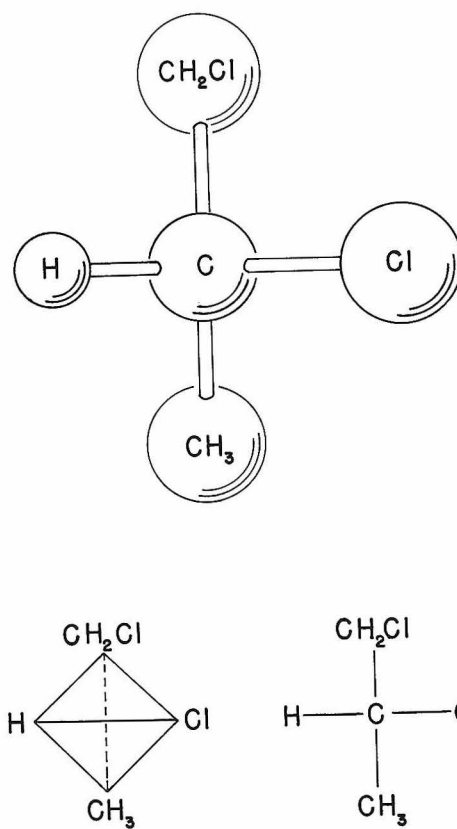


Figure 2. Enantiomorph of 1,2-Dichloropropane to Which the Calculations Apply and the Corresponding Fischer Projection Formula.

TABLE II

The Rotatory Power of 1,2-Dichloropropane as a Function  
of Internal Conformation

$\phi$ degrees	$[\alpha]_D^{300^\circ\text{K.}} \cdot (3/n^2 + 2)$		
	I	II	III
0	+39.9	+47.3	+40.7
20	+29.5	+35.6	+32.2
40	+16.5	+20.1	+14.8
60	+ 1.8	+ 3.2	- 0.7
80	-12.8	-13.9	-16.2
100	-26.7	-30.0	-30.7
120	-38.5	-41.7	-40.7
140	-43.9	-47.9	-45.4
160	-40.1	-45.4	-41.5
180	-26.7	-33.1	-28.5
200	-12.2	-19.0	-13.8
220	- 4.1	-10.3	- 4.6
240	- 1.7	- 5.6	- 0.0
260	+ 0.9	+ 0.1	+ 4.9
280	+ 9.6	+12.1	+14.7
300	+24.9	+29.8	+29.2
320	+39.0	+46.1	+42.1
340	+44.1	+52.6	+46.3

I. Data of Cabannes:  $\beta_{\text{CH}_3} = 0.35$ ,  $\beta_{\text{CH}_2\text{Cl}} = 0.35$ ;

optical center of  $\text{CH}_2\text{Cl}$  group at center of mass.

II. Data of Cabannes; optical center of  $\text{CH}_2\text{Cl}$  group at Cl.

III. Data of Stuart (and Breazeale):  $\beta_{\text{CH}_3} = 0.31$ ,

$\beta_{\text{CH}_2\text{Cl}} = 0.33$ ; optical center of  $\text{CH}_2\text{Cl}$  group at  
center of mass.

(For references see Table I.)

The results are given in Table II where  $[\alpha]_D^{300^\circ K} \cdot (3/n^2 + 2)$  is given as a function of  $\phi$ , the angle describing the internal conformation. The results were approximately the same for values of the chlorine anisotropy ratios from different sources and for two possible choices of the optical center of the  $\text{CH}_2\text{Cl}$  group, indicating the satisfactory stability of the calculations with respect to small changes in the parameters. The bond distances used in the calculation were obtained from covalent radii, and near tetrahedral angles were used. The values later determined by electron diffraction (1) were found to differ so little from these that a repetition of the calculation of the rotatory power did not seem worthwhile.

Having calculated the optical rotatory power in terms of  $\phi$  we now consider the determination of  $V(\phi)$  and its use in properly summing or integrating the contributions of all internal conformations to the optical rotation. Since a reliable theoretical calculation of  $V(\phi)$  seems out of the question at the present time, recourse was had to experiment. There are two principal sources of experimental data: an electron diffraction study carried out largely for this purpose (1), and measurements of the dependence of the observed dipole moment on temperature (8).

An examination of a model for 1,2-dichloropropane shows, in view of the well-established preference for staggered over eclipsed conformations, the presence of three positions at which minima with low enough energies to make significant contributions might be present. These are in the neighborhood of  $\phi = 0^\circ$  (hereafter called trans),  $\phi = +120^\circ$  (hereafter

called skew), and  $\phi = -120^\circ$  (hereafter called staggered cis). Of these the staggered cis represents the most compact structure for the molecule and it was considered sufficiently unstable relative to the other two as to render its population unimportant at temperatures of interest. This conclusion is supported by the work of Thomas and Gwinn on 1,1,2-trichloroethane<sup>(9)</sup>. This assumption is not necessary to our conclusions regarding optical activity; indeed, small amounts of the staggered cis isomer are helpful with regard to certain points. However, the assumption is a convenient one and is believed to be in accord with the physical facts.

The electron diffraction data were unable to distinguish between potentials with one minimum and those with two. Careful examination showed, however, that populations of the skew minimum greater than fifty per cent of the total would be inconsistent with the data. An examination of the model and of data for other molecules provides evidence against such a high figure, and although the estimate is conservatively high, contributions of this magnitude cannot be definitely ruled out on the basis of the electron diffraction data alone.

The importance of determining the relative populations of the two minima to a greater degree of accuracy can be seen from Table II. The contributions to the optical rotatory power of positions in the neighborhood of the two minima are of about the same magnitude but are opposite in sign. If the two are nearly equally populated we cannot expect to obtain an unambiguous prediction of the optical rotation and

hence of the absolute configuration.

The analysis of the dipole moment data carried out by Wood and Schomaker did provide a much more satisfactory basis for the estimation of the skew contributions. Two general types of potential function were used in the analysis and in the calculation of the optical rotation after the characteristic constants of the potentials were determined.

The simplifying assumption was first made that there are only two appreciably contributing minima, viz, the trans and the skew, and that these minima are very narrow and bounded by very steep potential barriers. This assumption thus has the effect of reducing the problem to the consideration of an equilibrium between two isomeric forms of the same molecule, the two isomers being defined by two given values of  $\phi$ , which we call  $\phi_t$  and  $\phi_s$ . If we have these two isomers in equilibrium then the optical rotation of the gaseous mixture is given by

$$\alpha = \frac{\alpha_t + \alpha_s e^{-\Delta F/RT}}{1 + e^{-\Delta F/RT}} \quad (22)$$

$$\Delta F = \Delta E - RT \log \frac{f_s}{f_t}$$

where  $\alpha$  is the observed rotation at absolute temperature  $T$ ;  $\alpha_t$  is the optical rotation of the trans form; and  $\alpha_s$ , that of the skew form. The difference between the free energy of the two forms in the vapor is denoted by  $\Delta F$  and the corresponding difference in internal energy by  $\Delta E$ , while  $f_s$  and  $f_t$

are the vibrational partition functions of the skew and trans forms in their respective minima. Some fitting of the data to more reasonable potential functions with two minima was also carried out. In this case the optical rotation is obtained by numerical evaluation of the integral expression

$$\alpha = \frac{\int_0^{2\pi} \alpha(\phi) e^{-V(\phi)/RT} d\phi}{\int_0^{2\pi} e^{-V(\phi)/RT} d\phi} \quad (23)$$

where  $\alpha(\phi)$  represents the function tabulated in Table II and  $V(\phi)$  is the potential of internal conformation.\*

Some of the results of the analysis, together with values of the vapor rotation calculated using various potential functions, are shown in Tables III and IV. The values of the parameters in the tables indicate approximately the range of variation consistent with the dipole moment and electron diffraction data. A comparison of the two methods was made by calculation of the rotation with equation (22) using the same parameters as those for the calculation of the same quantity with the first potential function of Table IV. The difference between the two values thus calculated is quite small, that from equation (23) being larger by about three degrees. The

\* Pitzer<sup>(10)</sup> has shown that in calculating the classical partition function the effects of the dependence of the vibrational frequencies and the external moments of inertia on the internal angle cancel each other, if the potential energy is free of cross terms between the vibrational coordinates and the internal angle. As a result one may use the simple weighting factor  $\exp(-V(\phi)/RT)$  in calculating classical averages of functions of the internal angle. Further, Gwinn and Pitzer<sup>(11)</sup> showed that for ethylene chloride, where a detailed assignment of the vibrational frequencies of the two isomers is available, that the cancellation holds approximately in the quantum mechanical case. We shall suppose this to be also the case for the closely related propylene chloride.

simplifying assumption of narrow potential wells is thus reasonably satisfactory.

In order to ensure as far as possible that the prediction of absolute configuration on the basis of these results will be unambiguous, the assumed values of the parameters in Table III and the potential barriers in Table IV were chosen so as to afford a conservative estimate of the upper limit of the contribution of the skew form. It is seen that the values obtained for the specific rotation are nevertheless unequivocal with regard to sign and of a satisfactorily large magnitude.

We therefore conclude that the enantiomorph shown in Fig. 2 is dextrorotatory and that its specific rotation in the vapor state is probably between  $+20^\circ$  and  $+30^\circ$ . The vapor value of the rotation was not measured, but reasonable agreement with this range of values was obtained on the basis of the observed rotations in solvents of different dipole moment, discussed in detail in the following section. The Fischer convention assigns the spatial model of Fig. 2 the D configuration; experimentally, the D configuration is assigned to the dextrorotatory isomer (this thesis, p. 71). The Fischer convention is thus again found to be correct, in agreement with the result obtained from 2,3-epoxybutane.

While the above calculation leads approximately to a predicted value for the vapor rotation of 1,2-dichloropropane,

TABLE III<sup>a</sup>

Specific Rotations of 1,2-Dichloropropane Calculated from  
Equation (22)

$\phi_t$	$\phi_g$	$f_s/f_t$	$\Delta E_k$ cal./mole	Fraction of <u>skew</u>	$[\alpha]_D^{300^\circ K.} \cdot (3/n^2 + 2)$
0	$\pm 120^\circ$	1.36	0.96	0.21	$\pm 29^\circ$
0	$\pm 120^\circ$	0.86	0.87	0.17	$\pm 33^\circ$
0	$\pm 90^\circ$	1.26	1.03	0.25	$\pm 30^\circ$
0	$\pm 120^\circ$	0.64	0.82	0.14	$\pm 35^\circ$
0	$\pm 90^\circ$	1.18	0.94	0.20	$\pm 33^\circ$
$\pm 25$	$\pm 120^\circ$	1.41	1.12	0.16	$\pm 19^\circ$

a) Using column II of Table II for  $\alpha(\phi)$ .



TABLE IV<sup>a</sup>

Specific Rotations of 1,2-Dichloropropane Calculated from  
Equation (23) with Different Potential Functions

$V(\phi)$ kcal./mole	Range of $\phi$ degrees	$\Delta E$ kcal./mole	$[\alpha]_D^{300^\circ K. (3/n^2 + 2)}$ degrees
1.			
2.5 (1-cos( $\phi$ ))	-40 - 40	1.1	+26°
2.1	40 - 70		
$\Delta E + 2.5(1-\cos(\phi-120))$	70 - 160		
$\infty$	160 - 320		
2.			
15(1-cos( $\phi-20$ ))	-40 - 50	1.3	+20°
1.6	50 - 60		
$\Delta E + 2.5(1-\cos(\phi-90))$	60 - 140		
$\infty$	140 - 320		
3.			
0.75(1-cos( $\phi$ )) + 0.22(1-cos(3 $\phi$ ))	-30 - 150	(0.96)	+22°
$\infty$	150 - 330		

a) Using column II of Table II for  $\alpha(\phi)$

the values actually observed were for the compound in the pure liquid state and in solutions of the compound in organic solvents. Since there is a difference in energy between the two forms the rotation may be expected to exhibit a temperature dependence. Experimentally, this was found to be the case. In order to make a more direct comparison between theory and experiment a quantitative investigation of these effects was carried out. (The effects of temperature and solvent on optical rotation have been considered previously<sup>(12,13)</sup>.) From the experimental data concerning the temperature dependence it was possible to calculate approximately the free energy difference between the two forms in solution in n-heptane, and also the separate rotatory powers of the trans and skew forms of the molecule; these latter could then be compared directly with the theoretical values.

The variation of the rotatory power of 1,2-dichloropropane in n-heptane with temperature is shown in Table V.\* In order to obtain the values for the separate optical rotatory powers of the skew and trans forms we again assume that the two minima are very narrow so that the problem may be treated as one involving an equilibrium between two isomers.

- - - - -  
\* The rotations in Tables V and VI are for approximately 2-5% solutions. Measurements at lower concentrations showed that the rotation was nearly independent of concentrations in all of the solvents used. The values in Tables V and VI may therefore be taken as those at infinite dilution.

TABLE V

Optical Rotation of L(-)-1,2-Dichloropropane in n-Heptane at  
Different Temperatures

$T^{\circ}\text{K.}$	$\alpha_D^T$ obs. <sup>c</sup>	Concentration <sup>a</sup>	$[\alpha]_D^T$	$n_D^{Tb}$	$[\alpha]_D^T (3/n^2+2)$
298	- 1.113	0.02688	-20.70	0.7652	-15.84
300.7	- 1.094	.02679	-20.42	0.7659	-15.64
303.8	- 1.075	.02669	-19.91	0.7667	-15.21
307.9	- 1.051	.02655	-19.79	0.7678	-15.19
311.1	- 1.020	.02644	-19.29	0.7686	-14.83
315.7	- 1.007	.02628	-19.16	0.7698	-14.75
319.7	- 0.986	.02615	-18.85	0.7708	-14.53
324.6	- 0.964	.02598	-18.55	0.7720	-14.32
330.7	- 0.923	.02577	-17.91	0.7736	-13.86
337.5	- 0.869	.02553	-17.02	0.7754	-13.20
345.7	- 0.838	.02524	-16.60	0.7776	-12.91

a) From coefficients of expansion of n-heptane, I. C. T. 3, 29.

b) From  $dn/dT$  for n-octane, G. Egloff, ed., "Physical Constants of Hydrocarbons", V. I. Reinhold, New York, N. Y., 1939, p. 49.

c) Readings were taken with an ordinary (Winkel-Zeiss) polarimeter to two decimal places. Each value in the table represents an average of at least ten such readings; the last figure was retained in the averaging, although the degree of accuracy is probably not so great as implied by its presence. The probable errors of most of the sets of observations were about 0.007.

The optical rotation of the equilibrium mixture is then given by equation (22), where  $\Delta F$  now refers to the difference in free energy of the two forms under the conditions of observation, viz., in the solvent n-heptane. Equation (22) can be written in the form:

$$\alpha = (\alpha_t - \alpha_s) \left( \frac{1}{1 + e^{-\Delta F/RT}} \right) + \alpha_s \quad (24)$$

The value of  $\Delta F$  is determined from the requirement that the plot of  $\alpha(T)$  against  $(1/(1 + \exp(-\Delta F/RT)))$  be linear, and the values of  $\alpha_t$  and  $\alpha_s$  can be found in terms of the slope and intercept of the line so obtained. This procedure makes evident the relative insensitivity to variations in  $\Delta F$ ; a series of approximate calculations indicated that the width of the range of permissible values was about the same as that resulting from the analysis of the vapor dipole moment data: several hundred cal./mole. A value lying near the middle of the range was chosen,  $\Delta F = 760$  cal./mole. The values of  $\alpha_t$  and  $\alpha_s$  depend somewhat on the value of  $\Delta F$ ; once it is fixed they can be determined within two or three degrees. The values found for  $\alpha_t$  and  $\alpha_s$  were  $+36^\circ$  and  $-56^\circ$ , respectively. These are to be compared with the theoretical values of  $\alpha_t$  and  $\alpha_s$  from Table II (with  $\varnothing = 0^\circ$  and  $\varnothing = +120^\circ$ ),  $+40^\circ$  and  $-39^\circ$ , respectively (to two significant figures).

The observed rotations of the 1,2-dichloropropane in different solvents are shown in Table VI. In order to take into account the effect of the solvent we calculate the lowering of the free energy difference through solvent polarization.

TABLE VI

Optical Rotation of L(-)-1,2-Dichloropropane in Different Solvents

Solvent	Conc.	$\alpha_D^{25}$ observed	$[\alpha]_D^{25}$	$[\alpha]_D^{25} (3/n^2+2)$
pure liquid	1.1512	-6.76	-5.87	-4.33
heptane	.0693	-1.44	-20.8	-15.9
methanol	.0618	-0.20	-3.2	-2.6
dioxane	0.0707	-0.36	-4.5	-3.4

Since the trans form has essentially zero dipole moment we assume that the electrostatic effects of the solvent on its free energy are small. Assuming that non-electrostatic effects are the same for both isomers we may express the free energy difference in solution as

$$\Delta F = \Delta E - \frac{N\mu^2}{r^3} \left( \frac{D-1}{2D+1} \right) \quad (25)$$

where  $\Delta E$  is the difference in internal energy between the two forms in the vapor (as explained previously  $\Delta E$  and  $\Delta F$  for the vapor are equal under the assumption of equal partition functions for the two forms). The second term represents the lowering of the energy of the skew form due to solvent polarization according to the theory of Kirkwood<sup>(14)</sup>. Here  $\mu$  and  $\left(\frac{1}{r^3}\right)$  represent the dipole moment and approximate radius<sup>3</sup> of the skew form,  $D$  is the dielectric constant of the solvent, and  $N$  is Avagadro's number. Since the rotations of the trans and skew forms are about equal in magnitude but opposite in sign, the effect of the solvent should be to decrease the observed rotation by increasing the relative population of the skew form through a decrease in its free energy. This effect should be larger for solvents of high dielectric constant.

Solving equations (24) and (25) for  $\Delta F$  and equating the results we obtain

$$\Delta E - \left( \frac{D-1}{2D+1} \right) (N\mu^2) \left( \frac{1}{r^3} \right) = RT \log \left( \frac{\alpha_s - \alpha}{\alpha_t - \alpha} \right) \quad (26)$$

Here  $\underline{D}$  represents the dielectric constant of the solvent,  $\mu$  is the dipole moment of the skew form and has been obtained from an analysis of the variation of the vapor dipole moment with temperature<sup>(1)</sup>:  $\alpha_s$  and  $\alpha_t$  have been determined above from the temperature dependence of the rotation. The unknowns are taken to be  $\Delta E$  and  $\left(\frac{1}{r^3}\right)$ . The observed rotations in two different solvents of known dielectric constant provides two sets of values for the coefficients and constant term in equation (26). The resulting pair of simultaneous linear equations may be solved for  $\Delta E$  and  $\left(\frac{1}{r^3}\right)$ . Taking the rotations in the solvents n-heptane and methanol (Table VI) and the value 3.1 D. U. for  $\mu$ , corresponding to  $\mu_{\perp} = 1.8$  D. U.<sup>(1)</sup>, we obtain 1050 cal./mole for  $\Delta E$  and 4.5 Å for  $\underline{r}$ . This value of  $\Delta E$  agrees with the approximate value 1000 cal./mole obtained from the dipole moment and electron diffraction data<sup>(1)</sup>. The value of 4.5 Å for  $\underline{r}$  is reasonable in that it is about equal to the distance between a point midway between the centers of the C-Cl bonds and the outer edge of the methyl group when the molecule is in the skew configuration.

Using the value of  $\Delta E$  obtained in this way and the values of  $\alpha_s$  and  $\alpha_t$  obtained from the temperature dependence of the rotation a quasi-experimental value for the vapor rotation can be calculated with the use of equation (22). The value obtained in this way for the vapor rotation is +23° for the D-isomer. (The L-isomer was the one actually used for the measurements.) This is to be compared with the theoretical values of Table III and Table IV, obtained from the theoretically calculated dependence of the rotation on the internal

angle and the potential functions obtained from the dipole moment and electron diffraction data<sup>(1)</sup>. The numerical agreement is seen to be satisfactory.

Another approximate check on the theory is the calculation of the rotation of the pure liquid 1,2-dichloropropane making use of its known dielectric constant and the radius of the molecule obtained above, together with equations (22) and (25). The value thus calculated is  $+4.3^\circ$ , and is to be compared with the experimental value of  $+4.6^\circ$ .

The low observed rotation in dioxane appears at first glance to be inconsistent with this general picture, since the dielectric constant of dioxane is about the same as that of heptane. However, the strong quadrupole moment of dioxane, which could markedly effect the trans-skew equilibrium of the 1,2-dichloropropane, does not contribute to the dielectric constant of the material.

Discussion. - Comparison of the theoretical and experimental results indicates that, in general, the numerical agreement is satisfactory considering the approximations involved throughout. Probably the most valid comparison, in the sense of offering the best test of the theory, is that between the theoretical and experimental values for the separate optical rotatory powers of the trans and skew forms of 1,2-dichloropropane. It should be noted here that the theoretical values depend somewhat on the positions chosen for the skew and trans minima. Indeed, a displacement of the trans minimum of about  $5^\circ$  in the direction of positive  $\phi$  would bring the theoretical and experimental values of  $\alpha_t$  into



coincidence. A displacement of this magnitude was considered likely on the basis of the electron diffraction results.

We have assigned the absolute configuration of Fig. 2 to the dextrorotatory isomer of 1,2-dichloropropane. This was done without any experimental data concerning the optically active forms of the molecule, using only the calculated dependence of the rotatory power on conformation (Table II) and the information about the potential of internal conformation obtained from the electron diffraction and dipole moment measurements.

As stated above, it has been possible to obtain experimentally the configurational relationship between the two compounds for which calculations were made. It was found that the enantiomorphs of 2,3-epoxybutane and 1,2-dichloropropane of like sign were configurationally related. (Levorotatory 1,2-dichloropropane was prepared from dextrorotatory 2,3-epoxybutane by a series of reactions involving a single Walden inversion at the asymmetric center.) Since the theory assigns positive rotations to the configurationally related isomers of Fig. 1 and Fig. 2 it is found to be internally consistent in its predictions for these two different molecules and confidence in it is considerably strengthened.

It was shown above that there is semiquantitative agreement between the experimental and calculated temperature dependence of the rotation. Using only the direction of this effect, however, it is possible to make an assignment of absolute configuration which requires less knowledge of the potential of

internal conformation then when the dependence of the rotation on temperature is not known. The following assumptions are sufficient for this assignment: 1) the energy of the skew form is greater than that of the trans form and these are the two principal contributing isomers, 2) the effect of temperature is due largely to an increase in the population of the skew form, 3) the calculated sign of rotation of the trans isomer is correct. It is observed that an increase in temperature, which increases the population of the skew form, produces a decrease in the magnitude of the rotation. It follows that if the observed rotation is positive the rotation of the skew form is algebraically less than that of the trans form, and that the total contribution to the rotation from molecules in the skew form is less than that of those in the trans form. Therefore the sign of rotation of the system is the same as that of the trans form and the correct calculation of this sign alone permits an assignment of absolute configuration.

The Preparation of L(-)-1,2-Dichloropropane

If a significant comparison is to be made between experimental and theoretical results it is desirable that the compounds considered be optically pure. This is not absolutely necessary; it is sufficient that the degree of optical purity be known, provided that the optical purity is such that the observed rotation of the product is high enough for accurate observation. This ~~requirement~~ requirement is perhaps more limiting than might be supposed, inasmuch as it is desirable to know the optical rotation of a dilute solution of the product in an inert solvent. Another consideration is the assignment of relative configuration, that is, the configurational assignment to the D or L series according to the Fischer convention. This is important in the problem of absolute configuration, and also in testing the consistency of the theory by comparing the predicted relationships between the signs of rotation of configurationally related compounds with those observed.

The determination of the relative configuration of 1,2-dichloropropane by working with the optically active material itself would be difficult. Even with the present very extensive knowledge of the participation of neighboring groups in replacement reactions, relatively little is known about the reactions of adjacent halogens. Several possible approaches might be attempted: hydrolysis of one or both chlorines to obtain an active glycol or chlorohydrin; reaction with silver in acetic acid, where the steric course of the reaction might be predicted; or reaction with ammonia to form a chloramine

or diamine. But the stereochemical course of any reaction which might be carried out is subject to considerable uncertainty because of the lack of experimental knowledge of the reacting system, particularly the possible participation of the adjacent chlorine as a neighboring group.

Finding a suitable reaction would probably require a large number of trial experiments. This approach was, in fact, attempted to a limited extent. Hydrolysis of the compound under different conditions was attempted but the only products obtained in appreciable amounts were unsaturated materials, probably chloropropenes. It was decided, therefore, to choose a synthetic method which would establish the configuration.

The steps in the preparation of the optically active 1,2-dichloropropane are shown in Figure 3. The relationship of 2,3-epoxybutane to the general preparative and configurational scheme is included, so that the entire reaction sequence relating these two compounds is shown. The steps in the synthesis are as follows: 1) the preparation of  $\underline{\underline{L}}(+)^a$  erythro-3-chloro-2-butanol from  $\underline{\underline{L}}(-)$ -2,3-butanediol through its diacetyl derivative<sup>(6)</sup>, 2) oxidation of this chlorohydrin to  $\underline{\underline{L}}(+)$ - $\alpha$ -chloropropionic acid with nitric acid, 3) conversion of the acid to its acid chloride in an exchange reaction with benzoyl chloride, 4) reduction of the acid chloride with lithium aluminum hydride to  $\underline{\underline{L}}(+)$ -2-chloro-1-propanol, and 5) reaction of the propylene chlorohydrin with thionyl chloride in pyridine to give  $\underline{\underline{L}}(-)$ -1,2-dichloropropane. The physical constants of the compounds

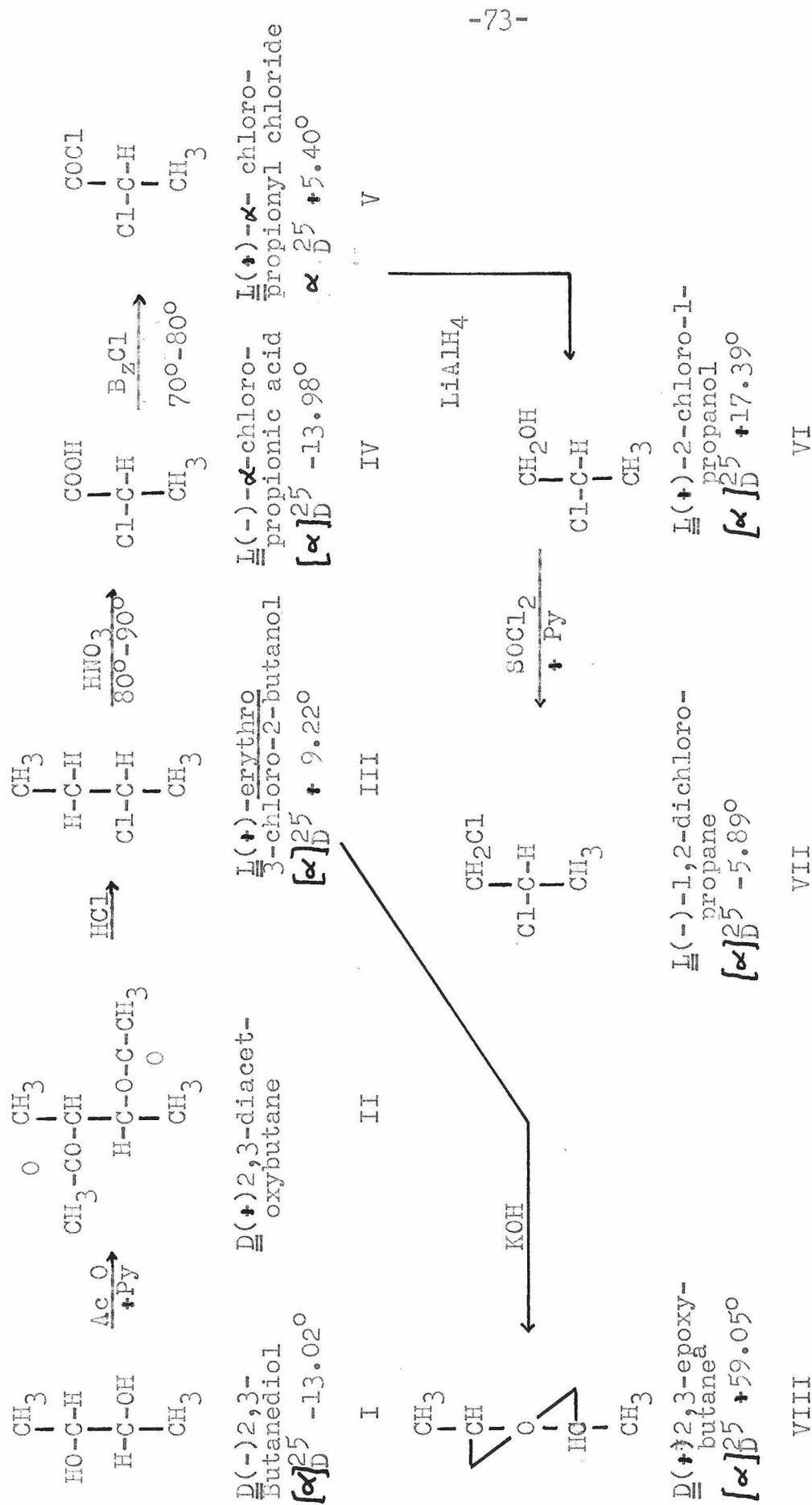


Figure 3. Steps in the Conversion of L(+)-erythro-3-Chloro-2-butanol to L(-)-1,2-Dichloropropane

a) The oxide having this rotation was obtained from a chlorohydrin having  $[\alpha]_D^{25} +9.47^\circ$  (16).

prepared and shown in Table VII. The reactions shown in Fig. 4 were carried out to check the configurational assignment and optical purity of the L(+)-2-chloro-1-propanol and will be discussed below. The method of synthesis thus relates the configuration of 1,2-dichloropropane to those of 1,2-propanediol and 2,3-butanediol, which have been previously established<sup>(7,15)</sup>.

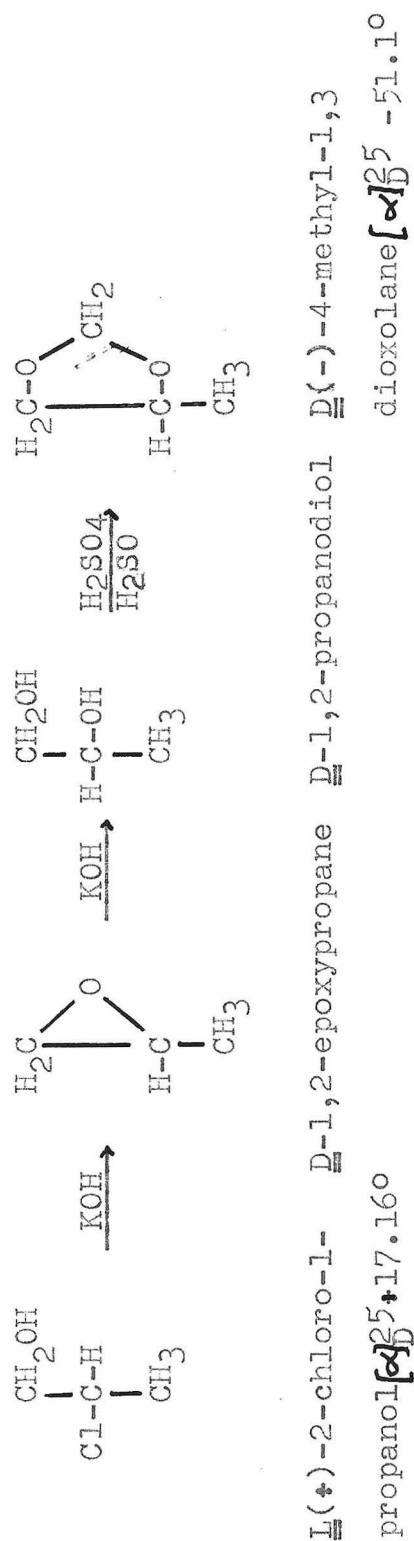
It can be seen that the asymmetric center is involved directly in only a single reaction, the conversion of L(+)-2,3-diacetoxybutane to L(+)-erythro-3-chloro-2-butanol. This reaction has been shown to proceed with complete Walden inversion<sup>(6)</sup>; in addition, the configuration of the  $\alpha$ -chloropropionic acid obtained from this chlorohydrin has been fairly well established independently<sup>(16)</sup>. Thus, barring possible complications such as the participation of the chlorine atom on the asymmetric carbon atom or racemization due to side reactions the final product will be optically pure L(-)-1,2-dichloropropane. Both of these undesirable possibilities can be eliminated on the basis of theoretical and experimental evidence.

The possibility of racemization in all of the steps but the last was completely eliminated by the conversion of the L(+)-erythro-2-chloro-1-propanol to nearly optically pure D(-)-4-methyl-1,3-dioxolane (Fig. 4). Comparison of the observed rotation of the L(+)-erythro-3-chloro-2-butanol prepared here,  $[\alpha]_D^{25} +9.22^\circ$ , with that of the optically pure

TABLE VII Physical Constants

	Yield %	B.P. °C	Pressure mm. Hg.	$n_D^{25}$	$d_4^{25}$	$\alpha_D^{25}$ obs. undil. $[\alpha]_D^{25}$
<u>L</u> (+)-erythro-3-Chloro-2-butanol <sup>a</sup>	53	55.9-56.1	30	1.4392		+8.69 +9.22
<u>L</u> (-)- $\alpha$ -Chloropropionic acid	41	80.7-80.9 <sup>b</sup>	10	1.4335		-17.56 -13.98
<u>L</u> (+)- $\alpha$ -Chloropropionyl chloride	72	69.1-70.1	200	1.4369		+ 5.40 <sup>c</sup> + 4.3
<u>L</u> (+)-2-Chloro-1-propanol	67	70.3-70.5	75	1.4365	1.1025	+19.17 +17.39
<u>L</u> (-)-1,2-Dichloro-propane	25	96.0-96.1	747	1.4368	1.1478	- 6.76 - 5.89
<u>L</u> (-)-2,3-Dichloro-butane <sup>d</sup>	22	53.2-53.3	80	1.4406	1.1048	-28.43 -25.66
<u>DL</u> -1-Chloro-2-propanol <sup>e</sup>	80	64.5	75	1.4366	1.1075	
<u>DL</u> -1-Chloro-2-propanol <sup>f,g</sup>	ca.66	64.7	75	1.4368		
<u>DL</u> -2-Chloro-1-propanol <sup>f,g</sup>	ca.24	70.3	75	1.4367		
<u>DL</u> -2-Chloro-1-propanol <sup>i</sup>	23	70.3	75	1.4360	1.1020	
<u>DL</u> -1,2-Dichloropropane <sup>j</sup>		96.3-96.4	747	1.4368	1.1478	

a) Previous values<sup>4</sup>: b.p. 56.0° (30 mm),  $n_D^{25}$  1.4397,  $[\alpha]_D^{25}$  +9.47°. b) Constants of a redistilled part; b.p. of main portion, 67.0-69.5° (5 mm). c) Previous values (9):  $\alpha$  5780 +5.20,  $[\alpha]_D^{25}$  5780 +4.10. d) Previous values (6): b.p. (80 mm): meso, 49.52°, DL 53.16°,  $n_D^{25}$  1.4386; DL 1.4409,  $d_4^{25}$  meso, 1.1025; DL, 1.1063. e) From allyl chloride. f) From propylene oxide and hydrochloric acid. g) Previous values (8): b.p., 62° (52 mm),  $n_D^{25}$  1.4387,  $d_4^{25}$  1.1120. h) Previous values (8): b.p., 62° (52 mm),  $n_D^{25}$  1.4390,  $d_4^{25}$  1.1092. i) Purified through the 3,5-dinitrobenzoate. j) Previous values: b.p., 96.20°,  $n_D^{25}$  1.43639;  $d_4^{25}$  1.14929. R. R. Dreisbach and R. A. Martin, Ind. Eng. Chem., Anal. Ed., 41, 2875 (1929); b.p., 96.40° O. A. Nelson and H. D. Young, THIS JOURNAL, 55, 2429 (1933).



VI

IX

X

XI

Figure 4. Proof of the Optical Purity of  $\text{L}(+)\text{-2-chloro-1-propanol}$



material<sup>(6)</sup>,  $[\alpha]_D^{25} +9.47^\circ$ , indicates that the 3-chloro-2-butanol prepared here had an optical purity of about 97.5% (the slight optical impurity of this chlorohydrin may have arisen from two sources. The D(-)-2,3-butanediol was from a different source than that used by Lucas and Garner<sup>(16)</sup>. Their glycol had a rotation of  $[\alpha]_D^{25} -13.17^\circ$ , while that used here had  $[\alpha]_D^{25} -13.02^\circ$ , so that its optical purity was 99.0%. The other 1½% lost in the conversion to L(+)-erythro-3-chloro-2-butanol probably arose from the longer time taken for the reaction of the D(+)-2,3-diacetoxybutane with HCl in order to improve the yield). Comparison of the observed rotation of the formal,  $\alpha_D^{25} -50.06^\circ$ , obtained from L(+)-2-chloro-1-propanol, with that of the optically pure material<sup>(10)</sup>,  $\alpha_D^{25} -51.33^\circ$ , shows that the formal obtained here had an optical purity of about 97.4%. Thus no appreciable racemization has occurred at any of the steps leading from L(+)-erythro-3-chloro-2-butanol to L(+)-2-chloro-1-propanol and on to the D(-)-4-methyl-1,2-dioxolane.

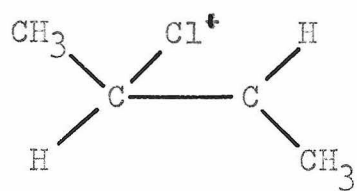
The relative configuration of the L(+)-2-chloro-1-propanol follows from consideration of the configuration of the formal obtained from it. This formal has the D-configuration; since this is the same as that of the original 2,3-butanediol an even number of Walden inversions occurred in the reaction sequence. Although the intermediate products were not isolated, the hydrolysis of the chlorohydrin almost certainly proceeds through the steps shown in Fig. 4. Formation of the

oxide takes place with inversion at the secondary carbon atom, so that the oxide formed has the D configuration. The ring opening of the oxide has been shown to occur exclusively at the primary carbon atom in basic solution<sup>(18)</sup>; the glycol formed thus still has the D configuration. The formal has been assigned the same configuration as the glycol from which it is prepared;<sup>(10)</sup> therefore it, too, has the D configuration. Thus the two known inversions in the entire reaction sequence satisfy the even number requirement, and are placed before and after the L(+)-2-chloro-1-propanol in the reaction sequence so that its configuration is confirmed as opposite to that of the original 2,3-butanediol, thus L.

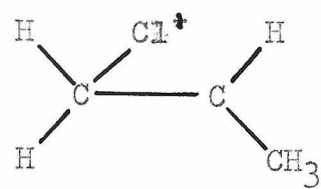
There remains for consideration, then, only the final step in the preparation of the active 1,2-dichloropropane -- the reaction of the L(+)-2-chloro-1-propanol with thionyl chloride in pyridine. Here there are two possible complicating factors. Racemization could take place through attack by chloride ion in the solution on either the active chlorohydrin or the active dichloride. Appreciable attack on the dichloride itself seems unlikely since it partially separates from the reaction mixture as it is formed. The possibility of appreciable attack is ruled out by the work of Lucas and Gould<sup>(19)</sup> on the analogous 2,3-disubstituted butanes. They studied the reactions of the isomeric 3-chloro-2-butanols with various halogenating agents, identifying the products, meso and DL 2,3-dichlorobutane, by means of physical constants, including the dielectric constant. They found that thionyl chloride in pyridine

produced pure meso-2,3-dichlorobutane from threo-3-chloro-2-butanol and pure DL-2,3-dichlorobutane from erythro-3-chloro-2-butanol. Since the products were stereochemically pure, no appreciable racemization occurred.

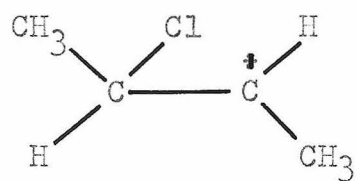
A more serious difficulty is the possibility of participation by the chlorine atom attached to the secondary carbon atom in the chlorination reaction occurring at the primary carbon atom. This introduces the possibility not only of partial racemization but also of inversion, so that the sign of rotation of the final product could be changed. This inversion is possible since the participation would take place through a cyclic chloronium ion, shown together with its resonance forms in Fig. 5, and attack could take place at either carbon atom. Since no inversion would occur in its formation, attack on the primary carbon atom of this ion by chlorine would lead to retention of configuration; attack on the secondary carbon atom, to inversion. If the primary attack were to predominate, partial racemization (in proportion to the amount of secondary attack) would be the result; if the secondary attack were to be more rapid, the result would be partial inversion. (As used here this term indicates a product whose sign is opposite to that of the product expected if no inversion or racemization occurred, but whose optical purity is less than 100%). Before the evidence against the formation of such a cyclic ion is considered, it should be pointed out that if it did form, it



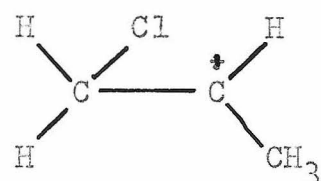
Ia



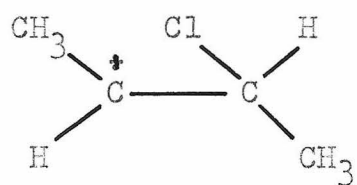
Ib



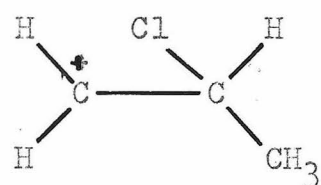
IIa



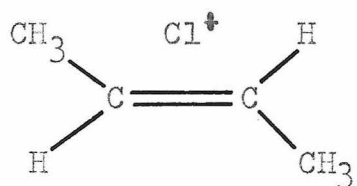
IIb



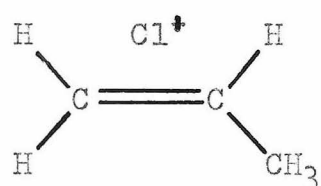
IIIa



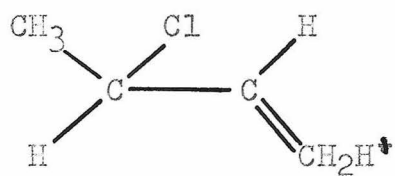
IIIb



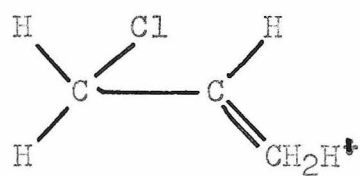
IVa



IVb



Va



Vb

Figure 5. Hyperconjugation in the Resonance Stabilization of the Chloronium ions.

would be expected to react in a manner similar to the conjugate acid of 1,2-epoxypropane<sup>(20)</sup>, whose ring opening by negative ions proceeds with a ratio of attacks on the primary and secondary carbon atoms of about three to one. If analagous reasoning could be applied to the chloronium ion, then the formation of the 1,2-dichloropropane would proceed with partial retention of configuration, the optical purity of the product being about 50%.

That the cyclic chloronium ion did not form is indicated by the work of Lucas and Gould<sup>(19)</sup> referred to above. The configurational relationships of the starting materials and products unambiguously requires an odd number of inversions in the reaction. This would not be the case if the cyclic chloronium ion were involved, for there would then be two inversions: one in its formation and one in its opening by chloride ion. Hence its formation is definitely excluded in this case.

Confirmation of this conclusion was obtained by the conversion of partially active erythro-3-chloro-2-butanol to partially active 2,3-dichlorobutane<sup>(19)</sup>. Loss of optical activity would have been the result if the cyclic intermediate were involved, for it possesses a plane of symmetry. At the time this investigation was carried out optically active 2,3-butanediol was not available and the partially active chlorohydrins were obtained by partial resolution with brucine. Their optical purity was only a few per cent. Since the optically pure erythro-3-chloro-2-butanol is now

available through the active 2,3-butanediol, the above reaction was repeated with the optically pure material; the previous result was confirmed. The optically active 2,3-dichlorobutane obtained had physical properties agreeing fairly well with the previous values for the DL compound. On the basis of the known lack of formation of the cyclic ion in the work described above, it was decided to carry out the chlorination of L(+)-2-chloro-1-propanol with the same reagent and under exactly the same conditions, so that a theoretical comparison of the two systems could be made directly without serious question as to differences in reaction environment.

Of the possible resonance forms of the chloronium ions corresponding to the butylene and propylene chlorohydrins (Fig.5), the forms Ia and Ib, having the largest number of covalent bonds, would be expected to be the largest contributors. The presence of a methyl group on either of the carbon atoms of the cycle should tend to stabilize the resonance structures having a positive charge or a double bond on the carbon adjacent to the methyl group through the operation of hyperconjugation Va and Vb. The positive charge is effectively distributed throughout the methyl group and the energy of the structure is lowered. Let us now compare the effects in the butylene and propylene systems. In the butylene system the energies of all three of the less contributing forms IIa, IIIa, and IVa are lowered since the hyperconjugation effect operates in each. In the case of IVa both methyl

groups contribute to the lowering, producing in effect a triply conjugated system. Obviously, the energies of IIa and IIIa are lowered in equal amounts. In the propylene system, on the other hand, the methyl cannot operate effectively in IIIb, and only one methyl is operating in IVb, so that the total stabilizing effect of the single methyl here is considerably less than that of the two methyls in the butylene system. Thus the propylene chloronium ion should be less stable than the butylene chloronium ion. Under the same conditions of reaction, then, its formation should be less likely, and since it has been shown that the butylene chloronium ion does not form under these conditions it follows that none of the less stable propylene chloronium ion was formed, and that the asymmetric center was not involved in the reaction. Therefore the final product has the same configuration as the L(+)-2-chloro-1-propanol from which it was prepared and is therefore optically pure L(-)-1,2-dichloropropane.

Little is known about the type of activated complex preceding the formation of a cyclic chloronium ion. It seems very likely, however, that the formation of the activated complex would place some positive charge at the carbon atom adjacent to the one to which the chlorine was originally attached, so that the hyperconjugative effect of the methyl group on the activated complexes would be expected to be similar to the effect on the chloronium ions themselves.

Before the experimental confirmation of the optical purity of the L(+)-2-chloro-1-propanol was obtained the result was predicted from consideration of the reactions involved. The optical purity of the  $\alpha$ -chloropropionic acid was thought to be high because the observed rotation corresponds roughly to that previously recorded at a different wavelength.\* This observed rotation is somewhat higher than that of  $\alpha$ -chloropropionic acid obtained previously from the same source, using sodium hypobromite as the oxidizing agent. The acid thus obtained had  $[\alpha]_D^{25} -14.2^\circ$ . The preparation of  $\alpha$ -chloropropionyl chloride from  $\alpha$ -chloropropionic acid and thionyl chloride has been reported to give an optically pure product, but so far as is known no syntheses of simple optically active acid chlorides have been reported with benzoyl chloride, which gives higher yields with  $\alpha$ -halo-acids<sup>(21)</sup>. It was found in parallel experiments with partially active material that benzoyl chloride and thionyl chloride gave nearly the same result with regard to optical purity of the product, with the benzoyl chloride slightly superior. In view of the known tendency of  $\alpha$ -bromopropionic acid to racemize<sup>(22)</sup>, it might be thought that some racemization of the active  $\alpha$ -chloropropionic acid might take place at the elevated temperature of the reaction. It has been shown, however, that active chloropropionyl chloride is optically

\* It may be of interest that this is apparently the first time that the rotation of optically pure  $\alpha$ -chloropropionic acid has been measured with sodium light. Freudenberg, Kuhn, and Bumann<sup>(23)</sup> found for L- $\alpha$ -chloropropionic acid  $[\alpha]_D^{25} = -19.30^\circ$ . If the rotatory dispersion of chloropropionic acid were the same as that of  $\alpha$ -bromopropionic acid this would correspond to  $[\alpha]_D^{25} -18.5$ .



stable under conditions which racemize  $\alpha$ -bromopropionyl bromide(24).

The lithium aluminum hydride reduction was a source of considerable uncertainty in planning the reaction sequence. Comparatively little is known about the mechanism of the reaction or the nature of the reacting species in the mixture. There appeared to be several undesirable possibilities. Since the ether solution of the lithium aluminum hydride constitutes a highly basic medium and the addition of water after the reaction to destroy excess hydride results in a strongly basic aqueous solution there was a possibility of epoxide formation from the chlorohydrin formed in the reaction. In addition chloride ion or lithium chloride ion-pairs might racemize either the  $\alpha$ -chloropropionyl chloride or the 2-chloro-1-propanol by direct attack. In order to minimize these possibilities the reaction was carried out at 0° C. and the time was kept as short as possible: 20 minutes for addition of the acid chloride, 15 minutes for stirring, and 5 minutes for acidification. Direct racemization seemed unlikely since the reaction seemed to take place immediately with the formation of a white precipitate, probably the lithium or aluminum alcoholate of the desired product. If some oxide were formed it might do no harm other than to lower the yield of desired product. However, it might react with chloride ion present to form a mixture of 2-chloro-1-propanol and 1-chloro-2-propanol with the latter predominating. It was hoped that

the short reaction time would minimize this possibility also. Any oxide formed would have the D-configuration, since one inversion accompanies its formation from the 2-chloro-1-propanol. The 2-chloro-1-propanol formed by the opening of the oxide ring at the secondary carbon atom would thus have the L configuration and would be identical with the desired product. The predominating isomeric 1-chloro-2-propanol would have the D-configuration since no inversion accompanies its formation from the oxide, the attack being at the primary carbon atom. If any of this product were formed it would still be expected to form the desired L(-)-1,2-dichloropropane in the final step since chlorination at the secondary carbon atom would be expected to proceed with inversion. However, there is evidence that 1-chloro-2-propanol was not formed to any appreciable extent, because no lower-boiling fraction corresponding to it was encountered during careful fractional distillation of 2-chloro-1-propanol, the product of the reaction. Also, the physical properties checked closely with those of DL-2-chloro-1-propanol. Moreover, two separate preparations had closely agreeing rotations, viz.,  $\alpha_D^{25} +19.17^\circ$  and  $+18.92^\circ$ .

A more detailed discussion of some of the reactions may be of interest from the synthetic standpoint. A considerable number of small scale experiments were carried out with the nitric acid oxidation of butylene chlorohydrin in order to obtain a workable synthetic procedure. The optimum temperature was not determined exactly, but a catalyst was found to be

unnecessary and the reaction proceeded smoothly in the neighborhood of 85-90° C. The reaction apparently had an induction period of several minutes characteristic of most nitric acid oxidations; if too much chlorohydrin was added at the start to the hot nitric acid the reaction became violent after a few minutes. (The reverse order of addition was not tried.) Once the reaction was properly started, however, the temperature could be maintained in the proper range by regulating the rate of addition of the chlorohydrin, with perhaps occasional gentle cooling. Even so, the reaction is probably slow or has several stages. In order to avoid the appearance of green coloration and substances of intermediate boiling point in the final crude product it was necessary to maintain the reacting temperature for about half an hour after all the chlorohydrin had been added. It was found convenient to separate the water-soluble chloropropionic acid by salting out with sodium sulfate, which also reduced the acidity of the solution, followed by ether extraction. If the final heating time was cut short the oxidation reaction would sometimes start again after stripping off the ether and starting the distillation of the final product. It was also found necessary to provide a constant gentle stirring of the reaction mixture in order to prevent violent bumping from supersaturation of the reaction mixture by the nitrogen oxides formed in the reaction. The yield was improved by operating under an efficient reflux condenser to prevent the stream of nitrogen dioxide from

carrying away product. The method appears to be a practical one for the preparation of optically active  $\alpha$ -chloropropionic acid, since no resolution is required. The yield is much better than that of the hypobromite method, the figures being forty-one percent and sixteen percent, respectively. In addition, the nitric acid oxidation gives an optically pure product, whereas the product of the hypobromite oxidation has an optical purity of about eighty-two percent. The nitric acid oxidation is also simpler to perform.

It might be supposed that reduction of the  $\alpha$ -chloropropionic acid directly with lithium aluminum hydride would be a practical procedure. In a recent study of the reduction of chloroacetic acids with this reagent, however, it was reported that while chloroacetic acid itself gave only thirteen percent yield, the methyl ester gave thirty-seven percent, and the acid chloride gave sixty-two percent. In the present work reduction of both  $\alpha$ -chloropropionic acid and  $\alpha$ -chloropropionyl chloride were attempted. The yields with the acid, using two slightly different procedures, were about twelve and fifteen percent. With the acid chloride however, the yields were about sixty-five percent. Since the acid chloride could be made from the acid in yields of seventy to eighty percent the latter method was chosen. The preparation of the acid chloride offered a great deal of difficulty at first. Many modifications of the thionyl chloride method were tried, including a more recent one involving reaction in an ether solution<sup>(25)</sup>. But the yield never exceeded

about thirty per cent. When carefully purified thionyl chloride was used, the yield was only about eleven percent. The benzoyl chloride method, on the other hand, was found to give much higher yields, depending rather strongly on the ratio of benzoyl chloride to  $\alpha$ -chloropropionic acid.

One preparation of optically active 2-chloro-1-propanol has been reported previously<sup>(26)</sup>. Hydrogen chloride was added to allyl amine to form the chloroamine, which was resolved as the tartrate salt. Treatment of the active 2-chloro-1-amino-propane with nitrous acid gave a product which was thought to be 2-chloro-1-propanol. The observed rotation of the product was only  $+9.26^\circ$ . It seems likely that the nitrous acid reaction was accompanied by some rearrangement. It was later reported by Smith and Platon<sup>(27)</sup>, who repeated the experimental work, that the product was a mixture of nearly equal parts of 2-chloro-1-propanol and 1-chloro-2-propanol.

The optical purity of L(-)-1,2-dichloropropane is believed to be reasonably high, probably about 95%. If it were assumed to be 97% optically pure, on the basis that no racemization took place at the last step,  $\alpha_D^{25}$  would be  $-6.07^\circ$ . Attempts to obtain oxide directly from dichloride were unsuccessful; consequently it was not possible to confirm the optical purity of the final product.

Optically active 2,3-butanediol, the starting point for these researches, was kindly supplied by Dr. C. A. Ledingham, Director, and Drs. A. C. Neish and J. A. Wheat, of the National Research Council of Canada. The author wishes to express his thanks for this courtesy.

Experimental Procedures \*

L(+)-erythro-3-Chloro-2-butanol.- This compound was prepared as previously described<sup>(6)</sup> from redistilled D(-)-2,3-butanediol ( $\alpha_D^{25}$  -12.83°). From 360 g. (4.0 moles) of active glycol were obtained 218 g. (53% overall yield) of chlorohydrin,  $[\alpha]_D^{25}$  +9.07. Redistillation of a portion at 30 mm. gave b.p. 55.9-56.1°,  $n_D^{25}$  1.4392,  $[\alpha]_D^{25}$  +9.22°. In addition, after fractionally distilling the higher boiling material through a 60-cm. column filled with glass helices, there were obtained 78.9 g., 15% yield, of 3-chloro-2-acetoxybutane, b.p. 69.5-69.9° (30 mm), and 18.1 g. of an intermediate fraction.

L(-)- $\alpha$ -Chloropropionic Acid.- This was prepared in several batches, in order to maintain more precise control over the reaction. A typical run is described. In a three-necked 500-ml. flask fitted with reflux condenser, dropping funnel, and stirrer were placed 60-ml. (1.3 moles) of concentrated nitric acid and 15 ml. of water. The nitric acid solution was heated to 85°, a few crystals of sodium nitrite were added, and 32.4 g. (30.4 ml., 0.30 moles) of L(-)-erythro-3-chloro-2-butanol were added with slow stirring. At the start only a

\* Microanalyses were by A. Elek. The individual steps in the preparation of 1,2-dichloropropane were worked out using inactive materials. Then a complete preliminary run starting with  $\alpha$ -chloropropionic acid having 6% activity was carried out before working with the optically pure material. In general the rotations of the optically pure compounds were found to be in agreement with those predicted on the basis of these preliminary experiments.

few drops were added until the reaction had started, as evidenced by the evolution of nitrogen dioxide. The addition was then begun, very slowly at first and then more rapidly as the reaction progressed. It was found that the desirable temperature range, 85-90°, could be maintained with slight cooling if addition of the chlorohydrin was at a rate of about 1 ml. per minute. Toward the last the reaction slowed and it was necessary to add the chlorohydrin more rapidly to maintain the temperature. The addition required about twenty minutes. The mixture was kept at about 85° for twenty minutes after the addition.\* Anhydrous sodium sulfate was added slowly, with stirring, to the cooled reaction mixture until some solid remained. This served a double purpose in reducing acidity and salting out the crude product, which separated as a light green upper layer. The phases were separated, and the aqueous phase was extracted twice with ether. The ether extracts were combined with the crude product and dried over magnesium sulfate. The material from the separate runs was combined and distilled in one batch. From a total of 130 g. (1.20 moles) of chlorohydrin

- - - - -  
\* Separate experiments showed that ~~ox~~chloropropionic acid was reasonably stable toward hot nitric acid of this concentration containing nitrogen oxides. Longer heating after the addition, to complete the oxidation of intermediate products, might be desirable.

were obtained 53.0 g. (41% yield) of  $\alpha$ -chloropropionic acid, b.p. 67.0-69.5° (5 mm.). This material may have been slightly impure but was found to give a pure acid chloride and was used directly. About five ml. were refractionated through a small Vigreux column of ten theoretical plates. The main fraction had b.p. 80.7-80.9° (10 mm.),  $n_D^{25}$  1.4335,  $\alpha_D^{25}$  -17.56°,  $[\alpha]_D^{25}$  -13.98°.

I(+)- $\alpha$ -Chloropropionyl Chloride. - A number of modifications of the thionyl chloride method were attempted, but the yield could not be made to exceed about 35%. Carefully purified thionyl chloride<sup>(28)</sup> was found to give lower yields. A partially active acid, 4.54 g. of inactive acid plus 1.4 g. of active acid,  $\alpha_D^{25}$  -2.95°, equivalent to 6.0 g. (0.055 moles)  $\alpha$ -chloropropionic acid  $\alpha_D^{25}$  -0.72° (calc.), 4.1% active, was refluxed 45 minutes with 10 ml. (16.5 g., 0.14 moles) of purified thionyl chloride. Distillation gave 1.9 g., 29% yield, b.p. 98-99°,  $\alpha_D^{25}$  +0.20°, 3.7% active on basis that the acid chloride,  $\alpha_D^{25}$  +5.40°, is optically pure.

Benzoyl chloride gave yields of 70-80% in an exchange reaction and was thus much superior. The preparation was carried out as described<sup>(21)</sup>, using 158 g. (1.13 moles) of benzoyl chloride for 48.3 g. (0.45 moles) of  $\alpha$ -chloropropionic acid. The material obtained by direct distillation from the reaction mixture boiled at 60-65° (180 mm.) and was redistilled; weight, 37.4 g., 72% yield, b.p. 69.1-70.1° (200 mm.),  $n_D^{25}$  1.4369,  $\alpha_D^{25}$  +5.40°,  $[\alpha]_D^{25}$  +4.3°.



A partially active acid, 53.4 g. (0.49 moles),  $\alpha_D^{25} -1.13^\circ$  (6.4% active) was converted to the acid chloride by the benzoyl chloride method, yield, 50.7 g., 82%, b.p. 68.8-70.0° (195 mm.),  $n_D^{25} 1.4369$ ,  $\alpha_D^{25} +0.38^\circ$ , 7.0% active on the basis that the acid chloride,  $\alpha_D^{25} +5.40$ , is optically pure. The exchange reaction would seem, on the basis of the approximate results with partially active materials, to give better optical results than does thionyl chloride.

L(+)-2-Chloro-1-propanol.- The procedure used was adapted from that previously described for the reduction of chloroacetic acids<sup>(29)</sup>. In a three-necked 500-ml. flask fitted with reflux condenser, stirrer, and dropping funnel were placed 3.42 g. (0.90 moles, 20% excess) of lithium aluminum hydride and 125 ml. of dry ether. The mixture was refluxed for three hours to effect solution. In the dropping funnel were placed 18.8 g. (0.15 moles) of  $\alpha$ -chloropropionyl chloride. When a few drops of the acid chloride were added to the ether solution with vigorous stirring a white precipitate appeared. The reaction mixture was then cooled to 0° for the remainder of the addition, which was completed in twenty minutes. The mixture was stirred for 15 minutes, and then a few ml. of water were added carefully but as rapidly as consistent with the avoidance of a violent reaction. This was followed, again rapidly, with an excess of 10% sulfuric acid.\* The upper phase was separated and the aqueous portion extracted

\* The operations were carried out rapidly to minimize the possibility of oxide formation.

twice with isopropyl ether. The extracts were combined with the crude chlorohydrin and dried over magnesium sulfate, and finally with drierite. Distillation through the small Vigreux column of ten theoretical plates gave 9.58 g., 67% yield, of 2-chloro-1-propanol, b.p. 70.3-70.5°,  $n_D^{25}$  1.4365,  $d_4^{25}$  1.1025,  $\alpha_D^{25}$  +19.17°,  $[\alpha]_D^{25}$  +17.39°. The smallness of the fore-run, approximately 0.4 g., b.p. 69.9-70.3°,  $n_D^{25}$  1.4345, indicated the absence of any appreciable amount of the isomeric 1-chloro-2-propanol. A second preparation from 18.4 g. of acid chloride gave 10.24 g., 72% yield, of chlorohydrin,  $\alpha_D^{25}$  +18.92°,  $[\alpha]_D^{25}$  +17.16°.

I(-)-1,2-Dichloropropane. - The procedure used was that described for 2,3-dichlorobutane(19). The thionyl chloride had been carefully purified(28). The pyridine was Merck reagent grade, freshly distilled. In a 200-ml. three-necked flask fitted with reflux condenser, dropping funnel, and stirrer were placed 9.45 g. (8.5 ml., 0.10 moles) of I(+)-2-chloro-1-propanol and 17.5 g. (0.22 moles) of pyridine. From the dropping funnel were added with vigorous stirring 19.6 g. (11.6 ml., 0.20 moles) of thionyl chloride over a period of about forty minutes. During the addition the flask was kept in a water bath at room temperature. The stirring was continued for twenty minutes after the addition. The flask was then placed on a steam bath for two hours, during which time the volume of the upper dichloride layer increased and the lower layer became quite dark. The flask was then allowed to cool to room temperature, and the upper light yellow layer was poured off. The lower black layer was diluted with about

half its volume of water and extracted twice with ether. It was found necessary to extract small portions at a time with large volumes of ether to avoid emulsion formation. The ether extracts were combined with the crude product, and extracted four times with 6 N hydrochloric acid, twice with water, and dried over potassium carbonate. Distillation was made through the small Vigreux column; weight, 4.52 g., 25% yield. The main fraction had b.p. 96.0-96.1° (747 mm.)  $n_D^{25}$  1.4368,  $d_4^{25}$  1.1478,  $\alpha_D^{25}$  -6.76°,  $[\alpha]_D^{25}$  -5.87°.

L(-)-2,3-Dichlorobutane. - This was prepared as previously described<sup>(19)</sup>. From 11.85 g. (0.10 moles) of L(+)-erythro-3-chloro-2-butanol were obtained 2.74 g., 21.7% yield, of dichloride, b.p. 53.2-53.3° (80 mm.),  $n_D^{25}$  1.4406,  $d_4^{25}$  1.1047,  $\alpha_D^{25}$  -28.43°,  $[\alpha]_D^{25}$  -25.65°. The physical constants check closely those of DL-3-chloro-2-butanol, not those of the meso isomer<sup>(19)</sup>.

1-Chloro-2-propanol by Hydration of Allyl Chloride\* - The method of preparation followed that of Dewael<sup>(30)</sup>. From 336 g. (4.4 moles) of allyl chloride were obtained 334 g., 80.5% yield, of 1-chloro-2-propanol. The product was fractionated twice through a 110-cm. column filled with glass helices. The final main fraction had b.p. 64.5° (75 mm.),  $n_D^{25}$  1.4366,  $d_4^{25}$  1.1075.

2-Chloro-1-propanol and 1-Chloro-2-propanol from Propylene Oxide and Hydrochloric Acid. - The method of preparation was essentially that used previously for the butylene

\* The preparation and separation of the inactive propylene chlorohydrins were performed by Dr. H. K. Garner.

chlorohydrins<sup>(19)</sup>. From 290 g. (5.0 moles) of propylene oxide were obtained 421.5 g., 89.7% yield, of mixed chlorohydrins. Two distillations through a 110-cm. column filled with glass helices gave small fractions of the relatively pure isomers, having constant boiling points when refractionated through the small Vigreux column. The lower-boiling fraction, 1-chloro-2-propanol, b.p. 64.7° (75 mm.), had  $n_D^{25}$  1.4368; the higher boiling fraction, 2-chloro-1-propanol, b.p. 70.3° (75 mm.), had  $n_D^{25}$  1.4367.

3,5-Dinitrobenzoate of 2-Chloro-1-propanol. - In a 500-ml. flask were mixed 138 g. (0.60 moles) of freshly prepared 3,5-dinitrobenzoyl chloride and 57.5 g. (0.61 moles) of 2-chloro-1-propanol (several of the higher boiling fractions from the above separation). The reaction mixture was heated gradually to about 120° over a period of about 45 minutes, then to 140° for another 10 minutes. The mixture was cooled and poured into 500 ml. of dilute potassium carbonate solution, stirred until the mass solidified, collected by suction filtration and washed; weight 167 g. (96% yield), m.p. 67-73°. Three recrystallizations from ethanol gave 100 g., m.p. 78.0-78.3°.

Anal. Calcd. for  $C_{10}H_9O_6N_2Cl$ : C, 41.59; H, 3.14; N, 9.70; Cl, 12.30.

Found: C, 41.66; H, 3.19; N, 9.77; Cl, 12.30.

Recovery of 2-Chloro-1-propanol from the Ester. - In a 1-liter flask fitted with reflux condenser with a dry-ice trap at the condenser outlet were placed 400 ml. (445 g., 4.2 moles)

of diethylene glycol and 50 g. (0.25 moles) of p-toluene-sulfonic acid. The system was evacuated to 3 mm. and the mixture was refluxed to remove water. To the cooled mixture were then added 100 g. (0.35 moles) of the 3,5-dinitrobenzoate ester. When 55 g. of liquid had been collected in the trap the material coming over was apparently largely dioxane, although it gave a positive chlorine test. Calcium chloride was added and the mixture was extracted with ether. The ether extracts were dried with calcium chloride and fractionated. The first fraction, 17.2 g., had b.p. 40-68° at 75 mm. The final fraction, 14.1 g., had b.p. 70.4-70.5° at 75 mm.,  $n_D^{25}$  1.4363. The final and intermediate fractions were then refractionated, giving 13.5 g., 38% yield on the recovery from the ester and 23% yield for the over-all purification starting with the high-boiling fractions from the mixture. The main fraction, b.p. 70.3°, had  $n_D^{25}$  1.4360,  $d_4^{25}$  1.1020.

Optical Purity of L(+)-2-Chloro-1-propanol. - This was converted to the formal of D(-)-1,2-propanediol, without isolation of any intermediates (Fig. 4). Action of base would almost certainly produce first D(+)-1,2-epoxypropane, which would then hydrate (without loss of optical activity if the solution remains basic) to D(-)-1,2-propanediol<sup>(18)</sup>. The formal can be prepared directly from this dilute solution of glycol according to the method of Lucas, Mitchell, and Scully<sup>(17)</sup>.

To a solution of 7.8 g. (0.14 moles) of sodium hydroxide in 300 ml. of water were added 6.6 g. (0.07 moles) of the chloropropanol,  $\alpha_D^{25} +17.16^\circ$ . The solution was sealed in an ampoule and kept at about  $50^\circ$  for forty-eight hours. The ampoule was opened and the solution was neutralized and made approximately 0.05 f. in sulfuric acid. Then 4.5 g. of para-formaldehyde (0.15 moles as formaldehyde) were added. The solution was refluxed under a 60-cm. column filled with glass helices so that the formal could be removed as it was formed. About six hours of refluxing with intermittent takeoff of the formal were required to complete the reaction. The collected formal was dried over potassium carbonate and redistilled; yield 1.8 g., 33%, b.p.  $84-85^\circ$  (745 mm.),  $n_D^{25} 1.3971$ ,  $\alpha_D^{25} -50.06^\circ$ ,  $[\alpha]_D^{25} -51.1^\circ$ . The same formal previously obtained from optically pure 1,2-propanediol<sup>(9)</sup> had b.p.  $84.2^\circ$  (745 mm.),  $n_D^{25} 1.3971$ ,  $\alpha_D^{25} -51.33^\circ$ ,  $[\alpha]_D^{25} -52.4^\circ$ . The optical purity of the present product was thus about 97.4%. Since the optical purity of the original chlorohydrin was estimated to be 97.5%, it is evident that there is no loss of optical activity in the conversion of IV to VI, Fig. 3, or of VI to XI, Fig. 4. The results of Fig. 4 have a parallel in the butane series, for in the steps  $\underline{\underline{D}}(-)\text{-}2,3\text{-butanediol} \longrightarrow \text{butanediol-formal} \longrightarrow \underline{\underline{D}}(-)\text{-}2,3\text{-butanediol}$  the recovered diol has 99.9% of the activity of the initial diol<sup>(31)</sup>.

Assuming that the hydrolysis of the chlorohydrin and oxide are complete, the yield of formal is less than that previously reported<sup>(17)</sup>. Experiments with inactive material

indicated that yields of about 70% could be obtained with much less refluxing of the reaction mixture if the hydrolysis and conversion to formal were carried out in more concentrated solutions.

Attempted Hydrolysis of 1,2-Dichloropropane. - The hydrolysis was attempted under different conditions. Basic hydrolysis was used, since the basic hydrolysis of the epoxide has been found to give 1,2-propanediol of higher optical purity than acid hydrolysis<sup>(18)</sup>. In a typical run 2 g. (0.02 moles) of 1,2-dichloropropane, 2 g. (0.06 moles) of potassium hydroxide and 50 ml. of water were sealed in an ampoule. After three days at 50° the ampoule was cooled and opened. There was considerable pressure within; the issuing inflammable gas had an olefinic odor. The recovery of the glycol was attempted through its formal<sup>(17)</sup>. The solution was made acid and the methanol removed by fractionation. Water was added to make the volume about 50 ml., the solution was made 0.05 f. in sulfuric acid, and 1 g. of paraformaldehyde (0.04 moles of formaldehyde) was added to convert any glycol to the corresponding formal. Fractionation of the resulting solution through a 60-cm. column filled with glass helices, however, failed to give any material boiling lower than 99°. The boiling point of the formal is 84°. The hydrolysis was repeated several times, using about the same concentrations of base and dichloride, with water alone, aqueous dioxane and aqueous methanol as solvents and with heating periods up to ten days,

and temperatures as high as 80°. In no case was any formal obtained. Analogous results have been reported by Goudet and Schenker<sup>(32)</sup> with alcoholic potassium hydroxide, the products being largely chloropropenes. The glycol has been obtained from the dichloride at higher temperatures and pressures<sup>(33)</sup>, but hydrolysis under such drastic conditions would be quite likely to result in racemization.



REFERENCES

1. W. W. Wood, Ph. D. Thesis, California Institute of Technology, 1951.
2. L. Rosenfeld, Zeits. f. Physik, 52, 161 (1928).
3. J. G. Kirkwood, J. Chem. Phys., 5, 479 (1937).
4. D. H. Deutsch, private communication.
5. L. A. Brockway and P. C. Cross, J. Am. Chem. Soc., 58, 2407 (1936); ibid, 59, 1147 (1937).
6. H. J. Lucas and H. K. Garner, J. Am. Chem. Soc., 70, 990 (1948).
7. P. A. Levene and A. Walti, J. Biol. Chem., 68, 415 (1926).
8. R. A. Oriani and C. P. Smyth, J. Chem. Phys., 17, 1174 (1949).
9. J. R. Thomas and W. D. Gwinn, J. Am. Chem. Soc., 71, 2785 (1949).
10. K. S. Pitzer, J. Chem. Phys., 14, 239 (1946).
11. W. D. Gwinn and K. S. Pitzer, J. Chem. Phys., 16, 303 (1948).
12. C. O. Beckman and K. Cohen, J. Chem. Phys., 4, 784 (1936).
13. W. J. Kauzmann, J. E. Walter, and H. Eyring, Chem. Rev., 26, 373 (1940).
14. J. G. Kirkwood, J. Chem. Phys., 2, 351 (1934).
15. S. A. Morell and A. H. Auernheimer, J. Am. Chem. Soc., 66, 792 (1944).
16. Ref. 6 and other references given there; A. Fregda, "The Svedberg", Almquist and Wiksells, Upsala, 1944, p. 261.
17. H. J. Lucas, F. W. Mitchell, and C. N. Scully, J. Am. Chem. Soc., 72, 5491 (1950).
18. P. A. Levene and A. Walti, J. Biol. Chem., 73, 269 (1931).
19. H. J. Lucas and C. W. Gould, Jr., J. Am. Chem. Soc., 63, 2541 (1941).

20. G. Forsberg and L. Smith, Acta Chem. Scand., 1, 577 (1947) ; H. Nilsson and L. Smith, Z. Physik. Chem., 166A, 136 (1933).
21. H. C. Brown, J. Am. Chem. Soc., 60, 1325 (1938).
22. K. Freudenberg, "Stereochemie", F. Deuticke, Leipzig, 1933, p. 854.
23. K. Freudenberg, W. Kuhn and I. Bumann, Ber., 63, 2380 (1930).
24. P. Walden, Ber., 28, 1292 (1895).
25. Professor Donald P. Cram (University of California), private communication.
26. E. Abderhalden and E. Bickwald, Ber., 51, 1312 (1918).
27. L. Smith and B. Platon, Ber., 55, 3143 (1922).
28. "Organic Syntheses", Coll. Vol. II, John Wiley and Sons, Inc., New York, N.Y., 1944, p. 570.
29. C. R. Sroog, C. M. Chih, F. A. Short, and H. M. Woodburn, J. Am. Chem. Soc., 71, 1710 (1949).
30. A. Dewael, Bull. Soc. Chim. Belg., 39, 87 (1930).
31. H. K. Garner and H. J. Lucas, J. Am. Chem. Soc., 72, 5497 (1950).
32. H. Goudet and F. Schenker, Helv. Chim. Acta., 10, 132 (1927).
33. A. L. Klebanskii and I. M. Dolgopolskii, J. Applied Chem. (U.S.S.R), 7, 1181 (1934); C. A., 29, 5814 (1935).

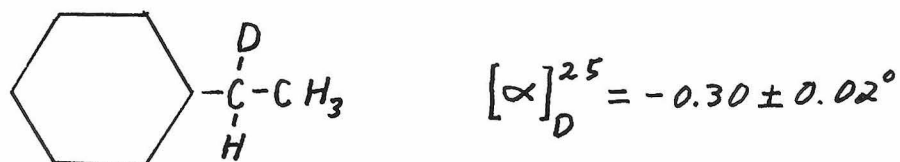
PART III

ZERO-POINT VIBRATIONAL CONTRIBUTIONS TO THE OPTICAL ACTIVITY  
OF ISOTOPICALLY ASYMMETRIC MOLECULES

ZERO-POINT VIBRATIONAL CONTRIBUTIONS TO THE OPTICAL ACTIVITY  
OF ISOTOPICALLY ASYMMETRIC MOLECULES

Modification of Kirkwood's Theory of Optical Rotation  
to Take into Account Zero-Point Vibrational Effects

The long-standing question among organic chemists concerning the possibility of finding optical activity in a molecule whose asymmetry is due only to the presence of different isotopes of the same atom has recently been answered in the affirmative. The compounds prepared were as follows:  $\alpha$ -deuteroethylbenzene<sup>(1)</sup>,



by the reduction of optically active  $\alpha$ -chloroethylbenzene with lithium aluminum deuteride and lithium deuteride; 2,3-dideutero-trans-menthane<sup>(2)</sup>,



by the reduction of active trans-p-menthene with deuterium; and 2-deutero-trans-p-menthane<sup>(3)</sup>,



by the reduction of l-methyl p-toluenesulfonate with lithium aluminum deuteride. The observed rotations are quite small, but are larger than could reasonably be ascribed to observational errors or to optically active impurities. Since the compounds were all hydrocarbons they could be subjected to fairly vigorous treatment to ensure the removal of such impurities. In the case of  $\alpha$ -deuteroethylbenzene, the compound was acetylated by a Friedel-Crafts reaction. The resulting ketone and its carefully purified oxime were found to have small but definite rotations. The existence of the phenomenon is thus fairly well established.

The optical activity of these compounds probably arises largely from the difference in the optical properties of hydrogen and deuterium (or perhaps more properly, of the C-H and C-D bonds). This difference is evident in the differences between the observed polarizabilities of corresponding hydrogen and deuterium compounds<sup>(4)</sup>. The difference in polarizability can be accounted for on the basis of the difference between the vibrational eigenfunctions of hydrogen and deuterium, owing to the difference in mass of the two nuclei. The electronic wave functions of the two are undoubtedly the same to a very high order of approximation, as is therefore the variation of the polarizability with interatomic distance. But the hydrogen nucleus, being lighter, is "spread out" more in its potential by its zero-point vibrational energy. In general, this "spreading", combined with the variation of the polarizability with interatomic

distance, will produce a difference in the observed polarizabilities of pairs of isotopically differentiated molecules.

In the case of non-rigid compounds such as  $\alpha$ -deuteroethylbenzene another effect could operate; the potential of internal conformation could be asymmetric because of the difference in the hindering of internal rotation by hydrogen and deuterium. An asymmetric potential function would, of course, result in an average asymmetric conformation. There is no experimental evidence that this occurs to an appreciable extent, however, and such an effect would almost certainly be exceedingly small. It was considered to be negligible in the present work.

The problem of determining the zero-point vibrational contributions to optical rotation will be treated by modifying Kirkwood's original theory so as to take into account explicitly the fact that the quantities of interest must actually be expectation values over the vibrational ground state of the entire molecule. It will be assumed that the electronic and nuclear motions are separable and that vibrational states above the ground state are not sufficiently populated to make a significant contribution. The application of this general treatment to isotopic substitution will express the optical rotation in terms of the difference between the ground state vibrational eigenfunctions of isotopically differentiated groups. The theory will then be specialized to the simple case of the substitution of hydrogen for deuterium.

The starting point of the modification is taken as Kirkwood's equation (32) for  $g^0$ , before averaging over all spatial configurations of the molecule:

$$g^0 = - \sum_{i \neq k=1}^N ([\vec{a}_3 \cdot \alpha^{(i)} \cdot \vec{T}_{ik} \cdot \alpha^{(k)} \cdot \vec{a}_2][\vec{R}_k \cdot \vec{a}_1])_{av} \quad (1)$$

where  $\vec{a}_1$ ,  $\vec{a}_2$ , and  $\vec{a}_3$  are three vectors defining a coordinate system fixed in space, and the symbol ( ) av. indicates that the quantity within the parenthesis is to be averaged over all spatial orientations of the molecule. The remaining symbols have the same significance as before (equation (18) of part II). This expression is then to be averaged over the ground state vibrational wave functions of the molecule:

$$\langle g^0 \rangle = \int \psi_{v_0}^* g^0 \psi_{v_0} d\tau \quad (2)$$

In order to evaluate the integral it is first assumed that terms higher than quadratic in the vibrational potential function can be neglected so that the wave function can be expressed as a product of wave functions corresponding to the n classical normal modes of vibration characteristic of the same potential function:

$$\psi_{v_0} = \prod_{h=1} \psi(\zeta_h) \quad (3)$$

where the  $s_h$  are the normal coordinates. Equation (1) for  $g^0$  is then expanded about the equilibrium position in normal coordinates:

$$g^0 = (g^0)_0 + \sum_h \left( \frac{\partial g^0}{\partial s_h} \right)_0 s_h + \frac{1}{2} \sum_{h,j} \left( \frac{\partial^2 g^0}{\partial s_h \partial s_j} \right)_0 s_h s_j + \dots \quad (4)$$

In the interest of reducing the number of terms to be written down it is assumed that the only non-negligible terms represent the interaction of a group whose polarizability depends appreciably on the vibrational coordinates with one whose polarizability is nearly independent of the vibration. This assumption actually involves no loss of generality, for the additional terms could be readily written down if needed. For the actual applications of interest it will be seen later that terms of this type are the only ones which need be considered. Then to terms of second order the expression for  $g^0$  becomes

$$\begin{aligned} g^0 = & (g^0)_0 + \sum_{i \neq k=1}^N \left[ \left( \vec{a}_3 \cdot \underline{\alpha}^{(i)} \cdot \underline{T}_{ik} \cdot \underline{\alpha}^{(k)} \vec{a}_2 \right) \left( \left\{ \sum_h \left( \frac{\partial \bar{R}_k}{\partial s_h} \right)_0 s_h \right\} \cdot \vec{a}_1 \right) \right. \\ & + \left( \vec{R}_k \cdot \vec{a}_1 \right) \left( \vec{a}_3 \cdot \underline{\alpha}^{(i)} \cdot \left[ \left\{ \sum_h \left( \frac{\partial \underline{T}_{ik}}{\partial s_h} \right)_0 s_h \right\} \cdot \underline{\alpha}^{(k)} + \underline{T}_{ik} \cdot \left\{ \sum_h \left( \frac{\partial \underline{\alpha}^{(k)}}{\partial s_h} \right)_0 s_h \right\} \right] \cdot \vec{a}_2 \right) \\ & + \left( \vec{R}_k \cdot \vec{a}_1 \right) \left( \vec{a}_3 \cdot \underline{\alpha}^{(i)} \cdot \left\{ \sum_h \left( \frac{\partial \underline{T}_{ik}}{\partial s_h} \right)_0 s_h \right\} \cdot \left\{ \sum_j \left( \frac{\partial \underline{\alpha}^{(k)}}{\partial s_j} \right)_0 s_j \right\} \cdot \vec{a}_2 \right) \\ & \left. + \left( \left\{ \sum_h \left( \frac{\partial \bar{R}_k}{\partial s_h} \right)_0 s_h \right\} \cdot \vec{a}_1 \right) \left( \vec{a}_3 \cdot \underline{\alpha}^{(i)} \cdot \left[ \left\{ \sum_h \left( \frac{\partial \underline{T}_{ik}}{\partial s_h} \right)_0 s_h \right\} \cdot \underline{\alpha}^{(k)} + \underline{T}_{ik} \cdot \left\{ \sum_j \left( \frac{\partial \underline{\alpha}^{(k)}}{\partial s_j} \right)_0 s_j \right\} \right] \cdot \vec{a}_2 \right) + \dots \right] \quad (5) \end{aligned}$$



The remaining second order terms are exactly similar in form to the two first order terms with  $\sum_h \left( \frac{\partial A}{\partial s_h} \right)_0 s_h$  replaced by  $\sum_{h,j} \left( \frac{\partial^2 A}{\partial s_h \partial s_j} \right)_0 s_h s_j$ , where A represents  $\vec{R}_k$ ,  $\alpha^{(k)}$ , or  $T_{ik}$ . The spatial averaging is still to be performed but is not indicated explicitly. It can be seen that these terms are analagous to a term of  $g^0$  as given by equation (1) with  $T_{ik}$ ,  $\alpha^{(k)}$ , or  $\vec{R}_k$  replaced by certain vector or tensor sums. Therefore the result of the averaging process will be the same as the result for the original  $g^0$ , except that one or more of the quantities  $T_{ik}$ ,  $\alpha^{(k)}$ , or  $\vec{R}_k$  will be replaced by the corresponding sums of normal coordinate derivatives. The result of the averaging process applied to all of the zero order terms in the expansion is just the original equation for  $g^0$ , with the position vectors and polarizabilities being those for the molecule with the nuclei in their equilibrium positions. The result of the averaging process is, then, for a single terms in equation (1) for  $g^0$

$$\begin{aligned}
 & \alpha_i \beta_i \alpha_k \beta_k G_{ik} \left\{ \sum_h \left( \frac{\partial \vec{R}_{ik}}{\partial s_h} \right)_0 s_h \right\} \cdot (\vec{b}_i \times \vec{b}_k) \\
 & + \alpha_i \beta_i \left\{ \sum_h \alpha_h^{(k)} \beta_h^{(k)} s_h \right\} G_{ik} \vec{R}_{ik} \cdot (\vec{b}_i \times \vec{b}_k) \\
 & + \alpha_i \beta_i \alpha_k \beta_k G'_{ik} \vec{R}_{ik} \cdot (\vec{b}_i \times \vec{b}_k) \\
 & + \alpha_i \beta_i \left\{ \sum_h \alpha_h^{(k)} \beta_h^{(k)} s_h \right\} G'_{ik} \vec{R}_{ik} \cdot (\vec{b}_i \times \vec{b}_k)
 \end{aligned} \tag{6}$$

$$+ \alpha_i \beta_i \left\{ \sum_h \alpha_h'^{(k)} \beta_h'^{(k)} s_h \right\} G_{ik}' \left\{ \sum_h \left( \frac{\partial \vec{R}_{ik}}{\partial s_h} \right)_0 s_h \right\} \cdot (\vec{b}_i \times \vec{b}_k')$$

$$+ \alpha_i \beta_i \alpha_k \beta_k G_{ik}' \left\{ \sum_h \left( \frac{\partial \vec{R}_{ik}}{\partial s_h} \right)_0 s_h \right\} \cdot (\vec{b}_i \times \vec{b}_k)$$

$$3 \alpha_h'^{(k)} = \left( \frac{\partial \alpha_{11}^{(k)}}{\partial s_h} \right)_0 + 2 \left( \frac{\partial \alpha_{22}^{(k)}}{\partial s_h} \right)_0 \quad \alpha_h'^{(k)} \beta_h'^{(k)} = \left( \frac{\partial \alpha_{11}^{(k)}}{\partial s_h} \right)_0 - \left( \frac{\partial \alpha_{22}^{(k)}}{\partial s_h} \right)_0$$

$$G_{ik}' = \vec{b}_i \cdot \left\{ \sum_h \left( \frac{\partial \vec{R}_{ik}}{\partial s_h} \right)_0 s_h \right\} \cdot \vec{b}_k$$

where the zero order term has not been written down. The vector  $b_k'$  defines the symmetry axis of the derived tensor. When this expression is substituted into equation (2) the result is that  $s_h$  is replaced by  $(s_h)_{00}$  and  $s_h s_j$  by  $(s_h s_j)_{00}$  where

$$(s_h)_{00} = \int \psi^*(s_h) s_h \psi(s_h) d\tau \quad (7)$$

since

$$\int \psi_h^*(s_h) \psi_j(s_j) d\tau = \delta_{hj} \quad (8)$$

because of the orthonormality of the wave functions composing the products. (The matrix elements  $(s_h)_{00}$  are of course zero for the harmonic potential function assumed but are written down here in order to indicate the form which the expression will take when anharmonicity is considered.)

The coordinate derivatives of the geometrical quantities can be calculated explicitly if the normal coordinates of the molecule are known. Since  $\vec{R}_k$  is the vector distance of the center of mass of group  $k$  from the center of mass of the molecule it can be expressed in terms of the masses and displacements of the atoms of the group:

$$\vec{R}_k = \vec{R}_k^0 + \sum_{\mu=1}^3 \sum_{l=1}^{N_k} m_l x_{l\mu} \vec{e}_\mu \left( \sum_{l=1}^{N_k} m_l \right)^{-1} \quad (9)$$

where  $N_k$  is the number of atoms in group  $k$ ,  $m_l$  is the mass of atom  $l$  of the group,  $x_{l\mu}$  is the displacement of atom  $l$  in the direction of one of the three mutually orthogonal unit vectors  $\vec{e}_\mu$ , and  $\vec{R}_k^0$  is the equilibrium value of  $\vec{R}_k$ . The displacements of the atoms during any vibration of the molecule can be expressed as a superposition of the normal coordinates

$$x_{l\mu} = \sum_{h=1}^n a_h^{(l\mu)} s_h \quad (10)$$

so that

$$\vec{R}_k = \vec{R}_k^0 + \sum_{h=1}^n s_h \vec{s}_h^0 \quad \vec{s}_h^0 = \sum_{\mu=1}^3 \sum_{l=1}^{N_k} m_l a_h^{(l\mu)} \vec{e}_\mu \left( \sum_{l=1}^{N_k} m_l \right)^{-1} \quad (11)$$

It is now convenient to neglect the change of the vector  $\vec{R}_k$  with the vibrational coordinates in comparison with that of  $\vec{R}_k^0$ , in order to simplify the computation of the derivatives

of  $\vec{R}_{ik}$  and  $\vec{T}_{ik}$ . This is analagous to the earlier assumption that  $\alpha^{(i)}$  was nearly independent of the vibration. Again there is no real loss of generality, for the extra terms are of the same form as those found explicitly and could be readily written down if needed. As before, it will be found that this assumption is justified for the compounds of interest. The desired derivatives are obtained after a certain amount of algebraic computation, which will not be reproduced in detail here. It is found that

$$\left(\frac{\partial \vec{R}_{ik}}{\partial s_h}\right)_o \approx \left(\frac{\partial \vec{R}_k}{\partial s_h}\right)_o = \vec{s}_h^o \quad \frac{\partial R_{ik}}{\partial s_h} = \frac{\vec{R}_{ik} \cdot \vec{s}_h^o}{R_{ik}} \quad (12)$$

so that finally

$$\begin{aligned} \left(\frac{\partial \vec{T}_{ik}}{\partial s_h}\right)_o = & \frac{3}{R_{ik}^5} \left( [\vec{R}_{ik} \cdot \vec{s}_h^o] \left[ -\frac{1}{R_{ik}} + 5 \frac{\vec{R}_{ik} \cdot \vec{R}_{ik}}{R_{ik}^2} \right] \right. \\ & \left. - [\vec{s}_h^o \cdot \vec{R}_{ik} + \vec{R}_{ik} \cdot \vec{s}_h^o] \right) \end{aligned} \quad (13)$$

The second derivative of the interaction tensor was also computed, but will not be written down because of its length.

The quantities  $\alpha_h^{(k)}$  and  $\beta_h^{(k)}$  always occur as the product

$$\alpha_h^{(k)} \beta_h^{(k)} \quad (14)$$

which is the anisotropy of the derived polarizability tensor of the bond. This quantity is not capable of direct determination, however, and in practice  $\alpha'$  and  $\beta'$  must be evaluated

separately. The quantity  $\alpha'$  is most readily evaluated from the differences in refractive indices of pairs of isotopically differentiated molecules or from the ratio of infra-red and Raman intensities for a single type of molecule<sup>(4)</sup>. The quantity  $\beta'$  for an entire molecule is related to the degree of depolarization of the corresponding Raman line in exactly the same way that the quantity  $\beta$  of the original theory is related to the degree of depolarization of ordinary (Rayleigh) scattered light<sup>(5)</sup>, viz.,

$$\beta'_h = \frac{45 \rho_h}{6-7 \rho_h} \quad (15)$$

where  $\rho_h$  is the degree of depolarization of the Raman line corresponding to the normal vibration h. The value of  $\beta'_h$  as determined in this way relates to the entire molecule; in order to obtain a value characteristic of the group in question it is necessary to choose a molecule in which there are no unusual resonance or electrical effects, and a normal vibration which consists mainly of the motion of the group in question.

The specialization of the theory to the case of the substitution of deuterium for hydrogen effects a considerable simplification. Because of the large difference in mass between these atoms and the others composing the compounds to be treated only a small number of normal modes result in appreciable deformation of the C-H and C-D bonds.

These normal modes will be taken to correspond to C-H (and C-D) stretching and bending. The first order matrix elements of the normal coordinates in equation (6) are of course zero. But it is known that the potential of C-H stretching contains a fairly large cubic term. Of course, if this is to be taken into account the above analysis of the vibration into normal coordinates is not strictly valid. But because of the large mass difference between hydrogen and deuterium and the other atoms of the molecule the normal coordinate analysis is still useful in giving the approximate form of the vibration. In this case a correct procedure would be to calculate the wave functions for the anharmonic potential by a perturbation method, taking as zero-order wave functions those corresponding to the normal coordinates of the harmonic potential. Actually, the normal coordinate for C-H stretching is approximated as the harmonic vibration of H against a larger mass, and the resulting harmonic oscillator wave functions are used as the zero-order functions in the perturbation calculations<sup>(6)</sup>.

Since there is a relatively large cubic term in the C-H stretching potential function the first order terms in the expression for  $g^0$  will probably be important. For C-H bending, on the other hand, the potential function should be nearly symmetric in the absence of concentrations of charge on other atoms close to the hydrogen atom. Hence no terms of odd power should make an appreciable contribution to the

potential function. In the absence of any experimental knowledge concerning the anharmonicity of this type of vibration the terms of odd power in the potential function were taken to be small and first order terms in  $g^0$  corresponding to C-H bending were neglected.

In the specialization of the theory to the case of compounds of the type  $R_1R_2CHD$  with the approximations described above the vectors  $s$  become just the unit vectors in the direction of elongation of the C-H and C-D bonds and are thus equal to  $\vec{b}_H$  and  $\vec{b}_D$  (H and D are here used as group subscripts denoting hydrogen and deuterium). The first, fourth, and fifth terms in equation (6) are then zero since two of the vectors comprising the triple cross product are the same and we then have

$$\begin{aligned} \langle g^0 \rangle = \frac{1}{6} \sum_i & \left[ (\alpha_i \beta_i \alpha'_H \beta'_H G_{iH} + \alpha'_i \beta_i \alpha_H \beta_H G'_{iH}) (\vec{R}_{iH} \cdot \vec{b}_i \times \vec{b}_H) (r_H)_{00} \right. \\ & + (\alpha_i \beta_i \alpha'_D \beta'_D G_{iD} + \alpha'_i \beta_i \alpha_D \beta_D G'_{iD}) (\vec{R}_{iD} \cdot \vec{b}_i \times \vec{b}_D) (r_D)_{00} \\ & + (\alpha_i \beta_i \alpha'_H \beta'_H G'_{iH} R_{iH} \cdot \vec{b}_i \times \vec{b}_H) (r_H^2)_{00} \\ & \left. + (\alpha_i \beta_i \alpha'_D \beta'_D G_{iD} R_{iD} \cdot \vec{b}_i \times \vec{b}_D) (r_D^2)_{00} \right] \end{aligned} \quad (16)$$

where  $\underline{r}$  represents the elongation of the bond from the equilibrium value.

The terms containing second derivatives of the polarizability tensor and of the dipole interaction tensor have been neglected. Since C-H stretching overtones are very difficult to observe in Raman spectra there is probably little hope of evaluating the second derivatives of the polarizability. It seems probable that they are small, however. The type of treatment which neglects such second order quantities is common in spectroscopy and useful semi-quantitative results are often obtained. Actually the second derivative of the polarizability is implicitly taken into account to some extent by the method of evaluating the first derivative, since the observed effect is considered to be accounted for entirely by the first derivative. The terms containing the second derivatives of the interaction tensor and the ordinary  $\alpha$  and  $\beta$  can be expected to be small; the analagous first order term was calculated for  $\alpha$ -deuteroethylbenzene and found to be quite small. The cross term containing derivatives of both the polarizability and the interaction tensor is found to be important. The corresponding cross term for the bending vibration is neglected since the first derivative of the polarizability with respect to this motion is probably small.

The values of  $(r)_{00}$  and  $(r^2)_{00}$  were those for an anharmonic (cubic) oscillator<sup>(5)</sup>. The value of the anharmonicity constant was that given by Dennison<sup>(7)</sup>. Values of for C-H have been calculated by R. P. Bell<sup>(4)</sup> from the observed



differences in refractive index between corresponding hydrogen and deuterium compounds. Using Dennison's spectroscopically determined value for the anharmonicity to obtain the value of  $(r)_{00}$  for hydrogen and deuterium they took the value of the derivative to be given by

$$\frac{\alpha_H - \alpha_D}{(r_H)_{00} - (r_D)_{00}} \quad (17)$$

where  $\alpha_H - \alpha_D$  represents the difference in polarizability of a pair of corresponding hydrogen and deuterium compounds. Since  $\alpha_H$  was found to be greater than  $\alpha_D$  in every case, and since  $(r)_{00}$  is greater for hydrogen than for deuterium the derivative is positive. The analysis was carried out for  $H_2-D_2$ ,  $HCl-DCl$ ,  $HBr-DBr$ , and  $CH_4-CD_4$ . Reasonably consistent results were obtained, the values for this series of compounds being between 1 and 2  $\text{\AA}^2$ . The value of  $\alpha'$  used for the calculation of rotation was that found from  $CH_4-CD_4$ , 1.9  $\text{\AA}^2$ . for one C-H (or C-D) bond.

The evaluation of  $\beta'$  from equation (15) requires the degree of depolarization of a Raman line corresponding to a normal vibration involving largely C-H stretching. The development of facilities for accurate depolarization measurements is comparatively recent, however, and there are relatively few data for appropriate molecules. Of the data available, probably the most suitable are those for the symmetrical vibration of highest frequency for chloroform. A comparatively

large number of measurements of the degree of depolarization of this line have been carried out by different investigators. These results have been collected and tabulated, together with their own value, by Zeitlow, Cleveland, and Meister.<sup>(23)</sup> The values lie between 0.2 and 0.38, the latter being that of the authors. The single value observed for the corresponding vibration of deuteriochloroform,  $\rho = 0.26$ , by the same investigators seems to indicate that any contribution coming from the slight motion of the chlorine atoms probably tends to reduce the total value. The difference between their values of 0.26 for deuteriochloroform and 0.38 for chloroform can hardly be accounted for on the basis of the difference in contributions to the depolarizations from C-Cl motions, for the depolarizations for both of the C-Cl modes in both molecules are less than that for the C-H stretching mode and it seems unlikely that the values of  $\alpha'$  for either of the C-Cl modes are particularly large. (Since  $\beta'$  is the derivative of the anisotropy ratio for the bond polarizability divided by  $\alpha'$  a low value of  $\beta'$  can result from either a small anisotropy derivative or a large value of  $\alpha'$ .) In fact for the C-Cl bond has been determined from the ratio of Raman and Rayleigh intensities for carbon tetrachloride<sup>(8)</sup> and it is only slightly less than the corresponding quantity for C-H. In order to determine approximately the contributions from C-Cl stretching to the depolarization factor for the C-H stretching vibration of  $\text{CHCl}_3$  a normal coordinate analysis

for an equivalent linear triatomic molecule was carried out. It was found that the ratio of C-H to C-Cl stretching in the normal mode of highest frequency was approximately 30:1, while the corresponding ratio for C-D and C-Cl was about 12:1. Because these ratios are so high any differences between the values of  $\beta'$  for the C-H bond of chloroform and those for C-H bonds in, say, saturated hydrocarbons should probably be attributed to the distorting effect of the C-Cl<sub>3</sub> dipole moment on the C-H bond.

The symmetrical CH<sub>3</sub> stretching mode of ethane would perhaps be the most satisfactory source of data for the determination of  $\beta'$  since there are no ordinary resonance effects or unusual electrical influences present. The small C-C stretching would be expected to contribute very little to the result. Unfortunately only qualitative data are available for this molecule. Even if the data were available, one inherent difficulty might remain: the modification of the form of this vibration through Fermi resonance with the first overtone of one of the methyl deformation vibrations. The exact extent and form of the effect of this resonance on the symmetrical vibration might be difficult to ascertain. The deuteromethanes constitute another promising source for the desired information but the necessary data are apparently lacking.

The value of  $\beta'$  finally chosen for use in the calculations was that obtained from the C-H stretching vibration of chloroform. The value of 0.3 was chosen as representative

for the depolarization factor; this gives for  $\beta'$  the value 1.9. Although the value of  $\beta'$  for hydrogen can be expected to be only approximately relevant for C-H, it is perhaps worth mentioning that the observed value for  $\rho$ , 0.14, gives a value for  $\beta'$  of 1.2<sup>(4,9,10)</sup>.

It is also important to determine the sign of  $\beta'$ . Its sign will be positive or negative depending on the relative signs and magnitudes of the derivatives of the polarizabilities parallel and perpendicular to the bond direction. Intuitively, it seems that the change in the direction of the bond is probably greater, and this result is borne out by quantum mechanical calculations<sup>(11,12,13)</sup>.

The sign of  $\beta'$  can be fairly well established from the magnitudes of  $\alpha'$  and  $\beta'$  and the known positive sign of  $\alpha'$ . The expression for  $\beta'$

$$\beta' = \frac{\alpha'_{11} - \alpha'_{22}}{\alpha'} = 3 \frac{\alpha'_{11} - \alpha'_{22}}{\alpha'_{11} + 2\alpha'_{22}} \quad (18)$$

$\alpha'_{nn} = \left( \frac{\partial \alpha_{nn}}{\partial s_n} \right)_0$

can be solved for  $\alpha'_{11}/\alpha'_{22}$ . The result is

$$\alpha'_{11}/\alpha'_{22} = 3.4\beta' = 6.5 \quad (19)$$

Thus the absolute value of  $\alpha'_{11}$  is more than twice as large as the absolute value of  $\alpha'_{22}$ , although the value of 6.5 for the ratio seems somewhat high. But since  $3\alpha'$  is equal to

$\alpha'_{11} + 2\alpha'_{22}$ , and its sign is known to be positive, it follows that  $\alpha'_{11}$  must be positive and thus, on the basis of

this analysis,  $\beta'$  must also be positive.

It might be thought that a classical treatment of the Silberstein type could shed some light on this question.

If we assume two polarizable structures, then for the moments induced in each,  $\vec{P}_1$  and  $\vec{P}_2$

$$\begin{aligned}\vec{P}_1 &= \alpha_1 (\vec{E} + \Lambda_{12} \cdot \vec{P}_2) \\ \vec{P}_2 &= \alpha_2 (\vec{E} + \Lambda_{21} \cdot \vec{P}_1)\end{aligned}$$

$$\Lambda_{12} = \left\{ -\frac{1}{\epsilon} + 3 \frac{\vec{R}_{12} \cdot \vec{R}_{12}}{R_{12}^3} \right\} \frac{1}{R_{12}^3} \quad (20)$$

where  $\alpha_1$  and  $\alpha_2$  are the polarizabilities of the two structures. If  $\vec{E}$ , the external field, is taken in the direction of the line joining the centers of the structures then it is found that the polarizability of the entire structure for this case is

$$\alpha_{11} = \frac{\alpha_1 + \alpha_2 + \frac{4\alpha_1\alpha_2}{R^3}}{1 - 4\frac{\alpha_1\alpha_2}{R^6}} \quad (21)$$

If  $\vec{E}$  is taken perpendicular to the line joining the two the resulting polarizability for this case is

$$\alpha_{\perp} = \frac{\alpha_1 + \alpha_2 - \frac{2\alpha_1\alpha_2}{R^3}}{1 - \frac{\alpha_1\alpha_2}{R^6}} \quad (22)$$

This type of treatment can be expected to be valid only if  $\alpha_1\alpha_2 \ll R^6$ . Approximate derivatives with respect to R can be obtained by expanding the denominators in powers of  $\frac{\alpha_1\alpha_2}{R^6}$

, multiplying by the numerators, and taking derivatives of the resulting series term by term. When this is done the resulting derivatives become

$$\frac{\partial \alpha_{11}}{\partial R} = -12 \frac{\alpha_1 \alpha_2}{R^4} - 24 \frac{(\alpha_1 + \alpha_2) \alpha_1 \alpha_2}{R^7} + \dots$$

$$\frac{\partial \alpha_{12}}{\partial R} = +6 \frac{\alpha_1 \alpha_2}{R^4} - 6 \frac{(\alpha_1 + \alpha_2) \alpha_1 \alpha_2}{R^7}$$
(23)

Thus a large positive value for  $\beta'$  is predicted from this simple classical treatment. The model is hardly appropriate for a bond to hydrogen, for the bond itself is the principal polarizable structure. The result is, in fact, in contradiction to the observed positive sign of  $\alpha'$ . Thus this simple classical model is inadequate here.

This entire treatment of optical rotation due to zero-point vibrations is admittedly a very approximate one. The sign of  $\beta'$  is of course not known with certainty; in the calculations the positive sign was chosen on the basis of the above discussion. Another source of possible error is the attempt to apply the original theory to a bonded hydrogen atom as a polarizable structure. In the original treatment the groups were considered to contain a fairly large number of electrons and one of the bond electrons was arbitrarily assigned to the central group and the other to the substituent group. In the case of C-H where the only electrons are the bond

electrons themselves it is probably more appropriate to consider the bond itself as the polarizable structure. This difficulty is probably not a serious one, since some experimental information about the optical properties of the bond is available. There is some question here as to whether the optical center of the group in this case is close to the center of mass. It may be that  $R_H$  should extend to a point midway between the carbon and hydrogen atoms. However, in performing the calculations the formal structure of the theory was retained and  $R_H$  was taken to be the same in length and direction as the C-H bond.

Application to  $\alpha$ -Deuteroethylbenzene and 2-Deuterobutane

The enantiomorph of  $\alpha$ -deuteroethylbenzene to which the calculations apply and the corresponding Fischer projection formula are shown in Figure 1. The values of bond distances were obtained from covalent radii and the asymmetric carbon atom was assumed tetrahedral. The values used for  $\alpha'$  and  $\beta'$  were those described in the previous section. It was found that the first order terms containing these quantities made the principal contribution to the calculated rotation although the second order terms containing  $\alpha'$ ,  $\beta'$ , and  $\gamma'$  could not be neglected. The problem of determining the actual rotation is similar to that for the previously treated 1,2-dichloropropane. Since internal rotation can take place about the C-C<sub>6</sub>H<sub>5</sub> bond, the optical rotation was first calculated as a function of the internal angle  $\phi$  describing the conformation. The angle  $\phi$  is taken to be zero when the C-C-CH<sub>3</sub> plane is perpendicular to the plane of the ring, and positive for a counterclockwise rotation of the phenyl group with respect to the remainder of the molecule (that is, looking along the C-C<sub>6</sub>H<sub>5</sub> bond from the direction of the ring). The optical rotation was found to be given by

$$[\alpha]_D \left( \frac{3}{n^2+2} \right) = -2.1 \left( \sin \left( 2\phi - \frac{2\pi}{3} \right) + \frac{1}{2} \sqrt{2} \sin \left( 2\phi + \frac{2\pi}{3} \right) \right)^{24}$$

The potential function  $V(\phi)$  governing the internal conformation was assumed to have a plane of symmetry coincident with



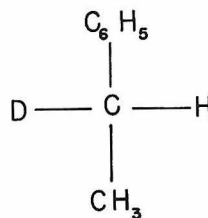
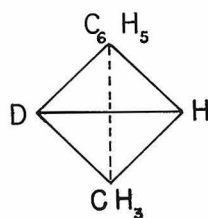
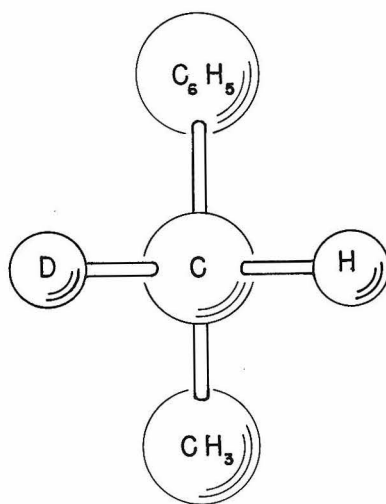


Figure 1. The Space Model of  $\alpha$ -Deuteroethylbenzene to which the Calculations Apply and its Fischer Projection Formula.

the plane of symmetry corresponding to that of ethylbenzene. If this is the case, a small amount of algebraic manipulation shows that a part of equation (24) makes no contribution to the optical rotation. For the part which does not average to zero it is found that

$$[\alpha]_D (3/n^2+2) = +\frac{2.1}{2} \left(1 - \frac{\sqrt{2}}{2}\right) \left(\sin(2\phi + \frac{2\pi}{3}) + \sin(-2\phi + \frac{2\pi}{3})\right) \quad (25)$$

$$= +0.53 \cos(2\phi)$$

Apparently no direct experimental studies of the potential of internal conformation in ethylbenzene have been carried out. However, from the work of Pitzer and coworkers on nitromethane,<sup>(14)</sup> propane<sup>(15,16)</sup>, and the xylenes<sup>(17)</sup> it is possible to make a reasonable estimate of the situation. The available evidence on the height of the six-fold barrier for a methyl group attached to a planar structure such as a nitro group or benzene ring indicates that there may be no hindering in either case, but that barriers as high as 1000 cal./mole are not excluded. Pitzer's rather detailed consideration of the interactions between the two methyl groups in o-xylene has led to the somewhat tentative conclusion that consistency with the thermodynamic data is best obtained by assigning independent potential functions to the two o-methyl groups with barrier heights of about 2000 cal./mole. By comparison of these configurations with those

occurring in ethylbenzene an approximate potential function for the latter can be obtained.

To simplify the problem, it was first assumed that there is no six-fold potential, and that all of the potential energy arises from interactions between the hydrogens of the terminal methyl group and those of the ring. It was also assumed at first that the terminal C-C bond was fixed in the staggered position. In this case the angle  $\phi$  could take on values of approximately 30-35 degrees on either side of the plane corresponding to the plane of symmetry of ethylbenzene before the hydrogen atoms of the methyl group and those of the ring approached closely enough to give rise to a repulsion energy of about 2000 cal./mole on the basis of Pitzer's results for o-xylene. If an attempt is made to increase this range by changing the orientation about the terminal C-C bond it is found that positions close to the eclipsed position for this bond must be taken before appreciable gain is made in increasing the range of  $\phi$ . Since the potential function for the rotation of the terminal C-C bond is probably close to that of ethane, with barrier heights of 3000 cal./mole, the eclipsed position is unlikely. The introduction of a six-fold potential into the problem would make few changes, for two of its maxima coincide with the two positions of the ethyl group in the plane of the ring, and the other four are in approximately the same angular positions as those corresponding to close approach of the hydrogens of the phenyl and methyl groups.

On the basis of these results it was decided to use the following simplified potential function in the calculation of the optical rotation:

$$\begin{aligned} V(\phi) &= 0 \text{ for } -30^\circ \leq \phi \leq +30^\circ \\ &= \infty \text{ otherwise} \end{aligned} \quad (26)$$

on one side of the ring; the potential function with the methyl group on the opposite side would, of course, be exactly similar. Since a sinusoidal function would have its minima corresponding to the centers of ranges of zero potential and would vary little over the allowed range this seems a satisfactory approximation in this respect. Also since the hindering is probably essentially a result of van der Waal's repulsion the potential function describing the interaction of the ring and methyl hydrogens probably rises rather sharply as they approach. The square well potential function is thus a fairly reasonable approximation.

The optical rotation calculated with this potential function for the enantiomorph of  $\alpha$ -deuteroethylbenzene shown in Fig. 1 is

$$[\alpha]_D (3/n^2+2) = +0.27^\circ$$

$$[\alpha]_D = +0.41^\circ$$

The latter value was calculated for a medium of refractive index 1.50, corresponding to the pure liquid. The experimental value for the enantiomorph prepared by the lithium

aluminum deuteride-lithiumdeuteride reduction of L(-) phenylmethylcarbonyl chloride was  $[\alpha]_D^{25} = -0.30^\circ$  for the pure liquid. The configurational relationship between the phenylmethylcarbonyl chloride and phenylmethyl carbinol is well known<sup>(18)</sup>, and phenyl methyl carbinol has been related to lactic acid through methylcyclohexyl carbinol by Levene and coworkers<sup>(19,20)</sup>. If the deuteride reduction of the chloride is accompanied by inversion, as is probably the case, then the (-)  $\alpha$ -deuteroethylbenzene prepared in this way from L(-) phenylmethyl carbonyl chloride has the D configuration, corresponding to the mirror image of the spatial configuration of Fig. 1. Thus if the reduction is actually accompanied by inversion the result is in agreement with the Fischer convention regarding absolute configuration, and is consistent with the findings for 1,2-dichloropropane and 2,3-epoxybutane.

Optically active 2-deuterobutane has not been prepared. However, its preparation should not be particularly difficult and on the basis of previous work it is expected that an optically pure product of known relative configuration could be obtained (see Proposition no. 1, this thesis). Therefore it seemed worthwhile to perform the calculation in order to obtain an indication of the order of magnitude of the rotation. Because of the simplicity of the compound, the absence of any appreciable resonance or anomalous electrical effects, and because of the relatively accurate knowledge of the potential of internal conformation it is probably one of the most satisfactory non-rigid compounds

for the application of the theory.

The enantiomorph to which the calculations apply is shown in Figure 2. The internal angle  $\phi$  was taken to be zero when the methyl groups are trans to each other; a positive displacement from zero is taken to be that which decreases the D-CH<sub>3</sub> distance. As in the case of 1,2-dichloropropane the optical rotation was not found to be a simple function of the internal angle. The molecule can be considered to have three minima: the lower, at  $\phi = 0^\circ$ , corresponding to maximum extension of the carbon chain (hereafter called "straight") and the two higher and energetically equivalent minima at  $\phi = 120^\circ$  and  $\phi = -120^\circ$  (hereafter called "bent"). The potential barriers between the equilibrium positions are high(21). The analysis was therefore carried out in terms of an equilibrium mixture of three isomers corresponding to the three minima. As can be seen from the figure, for  $\phi = \pm 120^\circ$  the vectors  $b_i$  and  $b_k$  for the hydrogen methyl interaction lie in the same plane and hence the corresponding term in  $g^0$  is zero. The relative orientation of the C-D group and the ethyl group in this position can be obtained by a reflection of their relative orientation for  $\phi = 0^\circ$  in the CHCH<sub>3</sub> plane containing the number 1 and 2 carbon atoms. Therefore the term representing the interaction of C-D with CH<sub>3</sub> for  $\phi = \pm 120^\circ$  is equal in magnitude and opposite in sign to that for  $\phi = 0^\circ$ . For

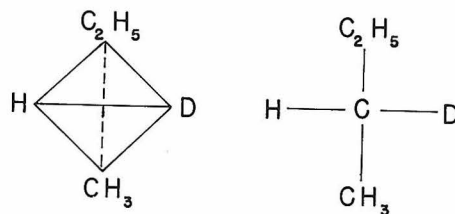
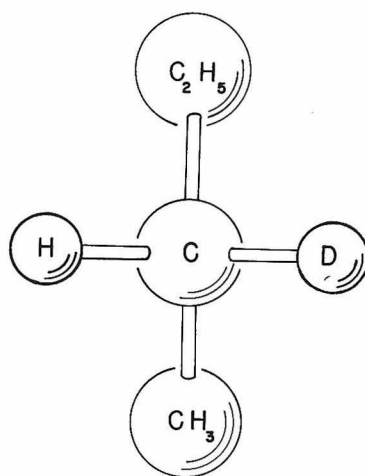


Figure 2. The Space Model of 2-Deuterobutane to which the Calculations Apply, and its Fischer Projection Formula.

$\phi = -120^\circ$  the opposite is true; the interaction of C-D with  $\text{CH}_3$  is zero while the C-H interaction with  $\text{CH}_3$  has the same magnitude as for  $\phi = 0^\circ$  but has the opposite sign. The rotation of a pair of molecules consisting of the two bent forms is therefore equal in magnitude but opposite in sign to that of one molecule in the straight form. With neglect of the entropy difference between a single straight molecule and a single bent one, the observed rotation is then given approximately by

$$\alpha = \frac{\alpha_{st}(1 - e^{-\Delta H/RT})}{1 + 2e^{-\Delta H/RT}} \quad (27)$$

where  $\Delta H$  is the enthalpy difference between the bent and straight forms and  $\alpha_{st}$  is the rotation of the straight form.

The value of  $\Delta H$  has been determined fairly accurately from the temperature dependence of the infra-red spectrum; the value found is 770 cal./mole<sup>(22)</sup>. The final results of the calculation, for the isomer of 2-deuterobutane shown in Fig. 2 are as follows:

$$[\alpha]_D^{25} / (3/n^2 + 2) = +0.88^\circ$$

$$[\alpha]_D^{25} = +1.06^\circ$$

where the final value has been calculated for a medium of refractive index, 1.33, corresponding to the pure liquid.



REFERENCES

1. E. S. Eliel, J. Am. Chem. Soc., 71, 3970 (1949).
2. E. R. Alexander and A. G. Pinkus, J. Am. Chem. Soc., 71, 1786 (1949).
3. E. R. Alexander, J. Am. Chem. Soc., 72, 3796 (1950).
4. R. P. Bell, Trans. Faraday Soc., 38, 936 (1942).
5. G. Herzberg, "Infrared and Raman Spectra of Polyatomic Molecules", New York: D. Van Nostrand, 1947, p. 248.
6. R. P. Bell and E. A. Guggenheim, Trans. Faraday Soc., 32, 1013 (1936).
7. D. H. Dennison, Rev. Mod. Phys. 12, 175 (1940).
8. J. Y. Chien and P. Bender, J. Chem. Phys., 15, 382 (1947).
9. J. Cabannes, Compt. Rend., 206, 88 (1938).
10. S. Bhagavantam, Indian J. Phys., 7, 107 (1932).
11. H. W. Adamov, Doklady Akad. Nauk. S.S.S.R., 62, 461 (1948); C. A. 43, 1264 (1949).
12. J. O. Hirschfelder, J. Chem. Phys. 3, 555 (1935).
13. J. G. Kirkwood, Phys. Zeits. 33, 257 (1932).
14. K. S. Pitzer and W. D. Gwinn, J. Am. Chem. Soc., 63, 3313 (1941).
15. K. S. Pitzer, J. Chem. Phys., 12, 310 (1944).
16. K. S. Pitzer, J. Am. Chem. Soc., 70, 2140 (1948).
17. K. S. Pitzer and D. W. Scott, J. Am. Chem. Soc., 65, 803 (1943).
18. W. A. Cowdry, E. D. Hughes, C. K. Ingold, S. Masterman, and A. D. Scott, J. Chem. Soc., 1937, 1260 (1937).
19. P. A. Levene and S. H. Harris, J. Biol. Chem. 113, 55 (1936).
20. P. A. Levene and P. G. Stevens, J. Biol. Chem. 89, 471 (1930).
21. K. S. Pitzer, J. Chem. Phys. 5, 473 (1937).
22. G. J. Szasz, H. Sheppard, and D. H. Rank, J. Chem. Phys. 16, 705 (1948).

### Propositions

1. Optically active 2-deuterobutane of known configuration might be prepared by lithium aluminum deuteride reduction of active 2,3-epoxybutane, followed by oxidation of the hydroxyl group to a ketone and Clemmensen reduction, or halogenation followed by hydrogenation. The optical rotation of this compound has been calculated to be  $[\alpha]_D^{25} \approx 1^\circ$ .  
Cf. part III of this thesis.
2. The use of optically active deuterio compounds would open a large field of undetermined reaction mechanisms to attack by the optical activity method. For example:
  - a. The character of aliphatic hydride reductions could be determined by reducing active 2-chlorobutane of known configuration with lithium aluminum deuteride and comparing the sign of rotation of the resulting 2-deuterobutane with that obtained from 2,3-epoxybutane.
  - b. The possible mechanisms for reaction of thionyl chloride with primary alcohols might be distinguished; since a primary carbon atom cannot be asymmetric other than by substitution of deuterium for hydrogen the optical activity method has not so far been applied to this problem.
3. Since the molecular orbital pictures proposed by Walsh for cyclopropane and spiropentane contain  $\pi$ -orbitals the quenching cross sections of these compounds for the resonance radiation of metallic atoms should be high on this basis. This is not the case for cyclopropane. The determination of the quenching cross sections of spiropentane and of the ability of both compounds to complex metallic ions in solution would be of interest in this connection.
  - (1) A. D. Walsh, Trans. Faraday Soc. 45, 179 (1949)
  - (2) W. R. Steacie and D. J. LeRoy, J. Chem. Phys. 11, 164 (1943)
4. Wheland and Dewar have proposed different mechanisms for the rearrangement of aromatic allyl ethers (Claisen rearrangement). A decision between these mechanisms might be made by performing the rearrangement with such ethers having  $C^{14}$  at either end of the allyl group.
  - (1) G. W. Wheland, "Advanced Organic Chemistry" (Wiley, New York, 1949), p. 544
  - (2) M. J. S. Dewar "The Electronic Theory of Organic Chemistry" (Oxford, London, 1949), p. 229

5. It should be possible to prepare active threo-3-amino-2-butanol of known configuration from available active erythro-3-amino-2-butanol through the use of benzamido as a neighboring group by treatment with  $\text{SOCl}_2$ , followed by hydrolysis. A method previously suggested for this preparation was tested experimentally and found to be unsuccessful.
  - (1) G. E. McCasland and D. A. Smith, J. Am. Chem. Soc. 72, 2190 (1950)
  - (2) F. H. Dickey, Thesis, California Institute of Technology, 1949; proposition #5
6. Whether halogens or methyls occupy the bridge positions in methyl aluminum dihalide dimers can probably be determined from relatively gross symmetry considerations if their infra-red and Raman spectra are obtained. If the methyls are found to be in the bridge positions, the frequencies and depolarization factors of the C-H lines may give information about the type of C-H and bridge bonds.
7. Kirkwood's first order theory of optical rotation predicts a zero optical rotation for 1,1-chlorobromoethane. A single enantiomorph of this compound might be prepared from active  $\alpha$ -chloropropionic acid by a Hunsdiecker reaction. The perhaps more interesting compounds, fluoro-chlorobromomethane and chlorobromiodomethane, might be prepared from the corresponding active acids in the same way.
8. In previous treatments of the partition functions of rigid molecules with attached tops interaction between the tops—"gearwheeling"—has been neglected. However, the wave equation for identical symmetric tops attached at arbitrary angles to a fixed frame and having a sinusoidal interaction potential is separable, giving products of Mathieu functions and exponentials as solutions; this suggests that at least an approximate treatment of this type of contribution to the partition function could be carried out.
9. In several quantum statistical mechanical derivations the thermodynamic properties of the system are assumed independent of the shape of the containing vessel. The limits of validity of this assumption could be tested in a simple way by writing down the exact partition functions for, say, a cube and a sphere, and comparing the limiting forms of the functions involved. The dif-

ferences would certainly be expected to be small when the particles have wavelengths considerably larger than molecular dimensions. A difference in the limit of validity might appear between Bose and Fermi particles at high densities.

10. A recent study of photoreactivation and apparent reversal of mutations in bacteria by visible light has apparently not considered a possible correlation with the established possibility of producing mutations by prior irradiation of the growth medium and the possible role of peroxides in the mutation process. A further investigation cognizant of these possibilities might prove profitable.
  - (1) A. Kelner, Scientific American, May, 1951; J. Bacteriology 58, 511 (1949)
  - (2) W. S. Stone, O. Wyss, and P. Haas, Proc. Nat. Acad. Sci. 33, 59 (1947)
  - (3) F. H. Dickey, thesis, California Institute of Technology, 1949
11. A computer for performing mappings of functions in the complex plane with visual display of the initial and transformed curves might have sufficient constructional simplicity to be useful for rapid semiquantitative engineering work and possible for educational purposes.