

THE REACTION BETWEEN  
PROPYLENE OXIDE AND HYDROGEN HALIDES

by

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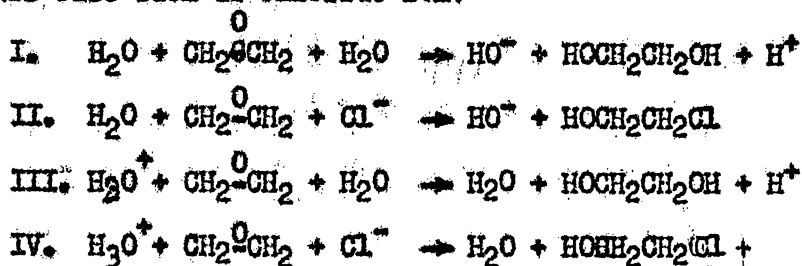
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**SECTION I**

**INTRODUCTION AND HISTORICAL BACKGROUND**

By virtue of their reactivity toward almost any reagent, and the many conditions feasible for their reactions, ethylene oxide and substituted ethylene oxides have provided a fruitful field for the investigations of theoretical organic chemistry.

Bronsted, Kilpatrick, and Kilpatrick (1), in the classical kinetic study in the field demonstrated that, by proper control of experimental conditions, any one of four separate reactions could be isolated in the reaction of ethylene oxide in an aqueous solution of a Lewis base such as chloride ion:



Swain (2) has shown that, in addition to the above reactions, a separate reaction is capable of occurring with each combination of electrophilic and nucleophilic reagents present in the reaction medium. In addition, his correlation of reaction rates makes possible the extrapolation of the available data so that the importance of any specific set of nucleophilic and electrophilic reagents in determining the products can be evaluated.

Other noteworthy investigations of the kinetics of ring opening reactions are the work of Smith (3) and Hansson (4) on the reaction of epoxides with amines, of Ross (5) on the

reactivities of various epoxides toward thiosulfate ion, and of Boyd and Marie (6) on the reactivities of various phenoxide ions toward ethylene and propylene oxides.

Walden inversion in the ring opening of epoxides has been established for lithium aluminum hydride (7), hydrogen chloride, p-toluene-sulfonic acid, water, methanol, malonic ester, and many other reagents (8).

With the elucidation of mechanisms in this field, it is surprising that only recently has sufficient orientation data been obtained to permit even a fragmentary understanding of the fundamental factors which determine the direction of ring opening, although the potential of this field of study is as great as that of the study of orientation in aromatic substitution. Perhaps the reason for the slow progress is to be found in the lack of methods for analysis of mixtures of very similar isomers and in the lack of methods of preparation of the pure isomers without question of rearrangement by neighboring group effects (9) or intermediate formation of the epoxide itself. The use of infrared analysis upon isomeric mixtures has shown itself to be surprisingly applicable, the prime disadvantage being the high cost of equipment and lack of general availability, at least in academic institutions. The recent studies on preparative uses of lithium aluminum hydride (10) have provided an exceptionally useful tool for the preparation of pure isomers of this type, a conclusion substantiated by the present investigation.

In general, the information needed for proper evaluation of

the relative importance of the many factors affecting orientation of ring opening are:

(1) Studies of the effect of substitution of epoxides in cases where steric factors are either eliminated or compensated,

(2) Studies, under similar conditions, of the effect of the strength of the attacking base,

(3) Studies on the effect of the strength of the electrophilic species involved in the reaction, and

(4) Studies of the effect of experimental conditions, particularly solvent and temperature.

Feldstein (11) has investigated the effect of substitution where steric effects may be totally absent in his studies on the reactions of para substituted stilbene oxides with lithium aluminum hydride. When the para substituent was a methyl group, attack of the hydride was slightly greater at the carbon adjacent to the p-methylphenyl group, giving 1-phenyl-2-(p-methylphenyl) ethanol. When the para substituent was chlorine, the direction of attack was reversed and the major product was 1-(p-chlorophenyl)-2-phenylethanol.

Guss (12) has shown that in the reaction of substituted styrene oxides with sodium phenoxide and phenol, the amount of secondary attack increases with a para-methoxy group, and decreases with a nitro group in any position of the ring. Fuchs

(13) has found a similar order in lithium borohydride reduction of substituted styrene oxides.

Smith and Skyle (14) have studied the reactions of hydrochloric and hydrobromic acids with epoxides and found that with hydrochloric

acid the percentage of primary attack of halogen on epichlorohydrin was 100%, on glycidol, 90%, on propylene oxide, 75%, and on isobutylene oxide, 45%. With hydrobromic acid, epichlorohydrin gave 100% primary attack and glycidol 90%, the same ratios as with hydrochloric acid.

Halperin, Donahoe, Kleinberg, and VanderWert (15), in one of the few systematic studies on the effect of the attacking base in which both isomers were obtained, found that 1,2-epoxybutane reacted with hydrochloric, hydrobromic, and hydroiodic acids to give 55, 64, and 81% primary attack of halide, respectively. The results, based on low pressure fractionation of isomers boiling only two to three degrees apart are not to be considered of great accuracy, but it is to be expected that the order is correct. These data are in disagreement with the findings of Smith and Skyle, above, that epichlorohydrin and glycidol give the same composition of isomers with hydrobromic as with hydrochloric acid, but these data are difficult to employ in a comparison of bases, since the amount of secondary attack is very small, and no indication of the precision is given. Both investigations are slightly ambiguous in the sense that it is impossible to tell whether the shift, if it occurs at all, is due to the differences in steric requirements, base strength of the attacking base, or both.

Many good examples of the shift toward secondary attack under acid conditions have been observed, perhaps the most clear of which

are the data of Chitwood and Freure (16) on the direction of ring opening of propylene oxide with methanol. In the presence of sodium methoxide, total primary attack was observed, whereas the uncatalyzed reaction gave 17% secondary attack; with sulfuric acid or boron trifluoride catalysis this amount increased to 40-55%.

Smith (17) found that at  $-10^{\circ}\text{C}$ ., the reaction of epichlorohydrin with hydrochloric acid gave 0.3% of secondary attack. At  $100^{\circ}$ , this was increased to 4%. On the basis of this, and other reactions, he postulated a rule that an increase in temperature will cause an increase in the amount of that isomer which is formed in lowest quantity. Hammett (18) has shown that this is demanded by the absolute reaction rate theory, provided the entropy of activation is essentially the same for both reactions.

Guss (19), in studying the reaction of styrene oxide with phenol and sodium methoxide showed that in phenol as solvent, the amounts of primary attack at 24, 70, 100, 138, and  $190^{\circ}\text{C}$ . were 8, 11, 12, 21, and 34% respectively. This was interpreted as evidence for a unimolecular ring opening, although it shows only that the secondary product is favored by activation energy over the primary product.

In studying the effect of solvent on the same reaction, Guss found that the amount of primary attack increased in the solvent order phenol < water < toluene < nitrobenzene < methanol < ethanol < acetal < dioxane < tetrahydrofuran. These results were interpreted in terms of hydrogen bonding between phenol, or water, and the solvent and epoxide. The assumption is that phenol and water may hydrogen bond

to the epoxide oxygen to aid in ring opening, while the alcohols and ethers compete with the epoxide oxygen for the excess phenol present. It may be noted that, with perhaps the exceptions of nitrobenzene and toluene, the order of secondary attack increases with the "ionizing power" of the solvent (20). The interpretation of these results as indicating a unimolecular ring opening before the attack of the incoming group is unnecessary in the light of Swain's evidence that such reactions may be expected for be termolecular, and may have the same substituent effect as solvolysis reactions even though a concerted mechanism is operative. In the light of the kinetic data on acid catalyzed methanolysis of 3,4-epoxy-1-butene (21), in which the rate of ring opening is dependent upon methanol concentration, such a unimolecular ring opening seems further improbable.

One of the purposes of the present investigation was to show the effects of solvent and temperature on a ring opening which is unquestionably a concerted process. Bronsted, Kilpatrick, and Kilpatrick (1) have shown that the reaction of hydrochloric acid with ethylene oxide, epichlorohydrin, and glycidol is third order, and assumedly the same will be true of propylene oxide. These data are for cases where the attack is almost entirely at the primary carbon (from the data of Smith and Skyle mentioned above) and one might question the conclusion that attack at the secondary carbon will follow the same path. Levene and Watti (22) have shown that acid catalyzed hydrolysis of dextrarotatory propylene oxide

gave a weakly dextrarotatory propylene glycol, corresponding to a net inversion. From the data of Chitwood and Freure (16) on ring opening with methanol under similar conditions, attack at the secondary carbon (leading to inversion) would be expected to be only slightly faster than attack at the primary carbon (leading to retention). What attack actually occurs at the secondary carbon, therefore, must take place with total, or at least very nearly total inversion.

Many attempts at explanation have been offered for observed orientations, some of which are at complete variance with available information. Many other attempts to explain the nature of the results have presented tenable hypotheses which, however, do not go far enough to provide adequate understanding of the picture.

Steric effects have been credited as the major factor in many results (23) and indeed must play an important role, judging from the large predominance of primary attack obtained in almost any series of data. The reaction is far too complex, however, to be explained on the basis of steric factors alone, as is shown by comparison of the substituted styrene oxides or of epichlorohydrin, glycidol, and propylene oxide quoted above, where steric factors should be similar.

Repulsion energies in the attack of the negative base, leading to a preference for attack at the more positive carbon atom have

been proposed as an explanation of orientation (16). This theory would predict that the substitution of an electron withdrawing group as in epichlorohydrin should produce greater secondary attack than in propylene oxide. The reverse is found to be true (14).

Swern, Billen, and Knight (24) have proposed that the predominant factor in determining orientation is the strength of the carbon to oxygen bonds. Thus, epichlorohydrin should be attacked more at the primary carbon, since the electron withdrawal of the substituent should cause the secondary carbon to bond more tightly to the oxygen. Unfortunately, this theory by itself would predict that the strengthening of bonds in epichlorohydrin would lead to a decrease in rate of attack of a base such as chloride ion, as compared to ethylene oxide. The reverse is found to be true (1).

Feldstein (11) has proposed an interesting counterbalance of the relative effects of bond strength and repulsion energy, following the Hinshelwood treatment (25).

Bartlett and Ross (26) have proposed that resonance in the transition state may be the principal factor in determining orientation trends. This in general would lead to the same predictions as the bond strength argument mentioned above, and would have the same weaknesses.

It would seem desirable to consider separately the purely electrostatic effects upon the rate produced by a change in charge of the seat of substitution (25), or by dipole effects of

a substituant (27), and the effects of resonance stabilization of the transition state. This may be shown schematically in Figure I, where the hypothetical intermediate has the nuclear positions of the transition state, but the electronic configuration of the initial state. (Fig. I on separate page.)

The energy of the first step may be calculated from purely electrostatic considerations, assuming that the species involved are point charges and that the dielectric constant of the medium is effectively unity. From the principles of electrostatics (28), the energy of two charges compared to infinite separation is expressed by the product of the two charges divided by the distance between them. For simplification, a proportionality constant which should be used to convert to appropriate units has been omitted. If the unit of charge is taken as the electron, the unit of distance the Angstrom, the energies expressed as kilocalories per mole, the numerical value of the constant is 331.8.

By this method, the energy of the transition state configuration of nuclei, with reference to the initial state, is:

$$(1) \quad E = \frac{e_A e_B}{r_{AB}} - \frac{e_B e_C}{r_{BC}} \left( \frac{r_{BC}}{r_{BC}^0} - 1 \right) + \frac{e_A e_C}{r_{AC}} + W$$

where  $r_{xy}$  is the distance in the transition state between  $x$  and  $y$ ,  $r^0$  is the initial state distance,  $e_i$  is the charge on a species  $i$ .

Figure I Reaction Path

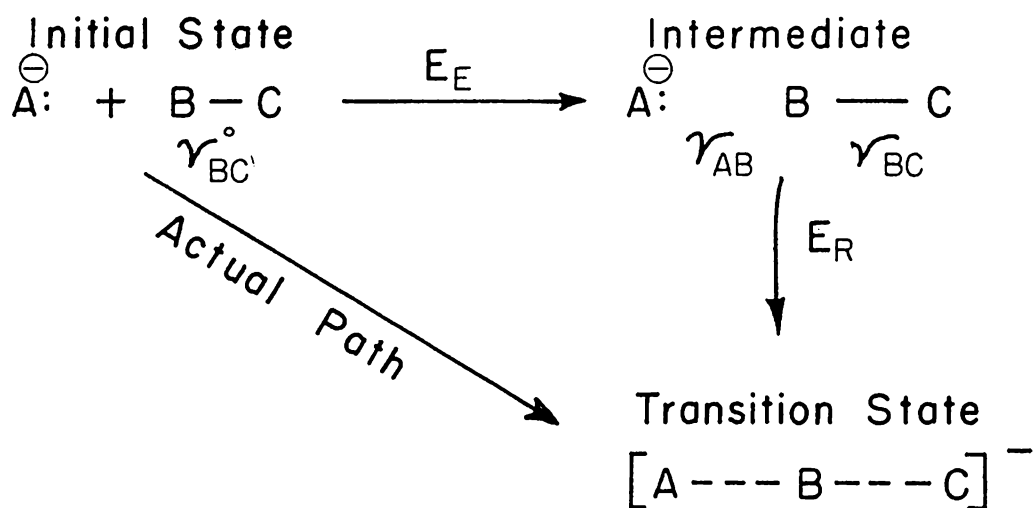
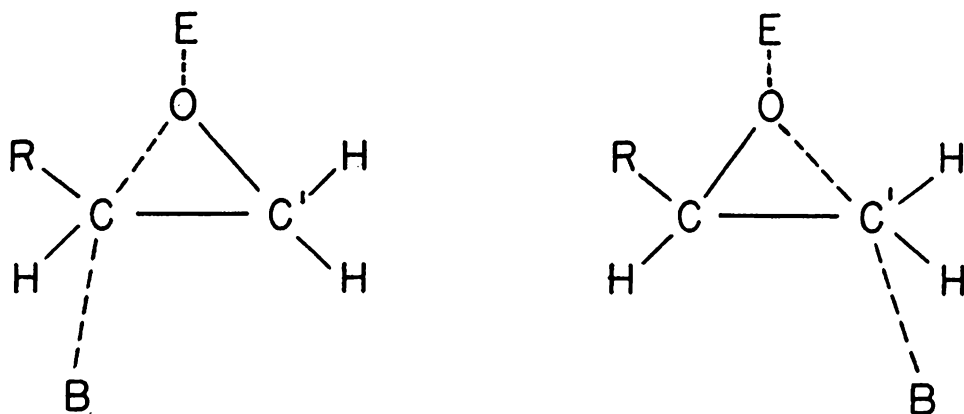


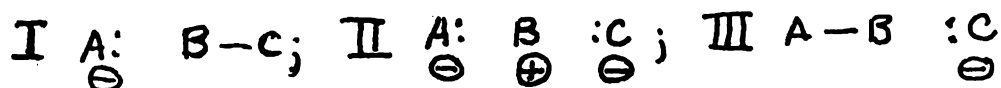
Figure II Epoxide Transition States



and  $W$  is a constant which represents the non-electrostatic energies in the process. If substitution is assumed to affect only the charge on the seat of substitution,  $e_B$ , then the change in activation energy upon substitution will be:

$$(2) \quad \Delta E = \left[ \frac{e_A}{\gamma_{AB}} - \frac{e_C}{\gamma_{BC}} \left( \frac{\gamma_{BC}}{\gamma_{BC}^0} - 1 \right) \right] \delta e_B$$

Having eliminated electrostatic factors of this nature from the electronic energy, the resonance effect of a substituent will depend only upon the stabilization of charge, not upon the energies of the A-B and B-C bonds, to a first approximation. The transition state may be described in general terms as a hybrid of three structures:



where only structure II will be expected to show appreciable stabilization by means of substitution.

In a normal displacement of the  $\text{Sn}_2$  type (29), structure II should have very little contribution to the transition state, since it contains no bonds from carbon to either of the strong bases A and C; and since it shows a high degree of charge separation. One may expect, then, that the influence of electrostatic forces will determine the effect of a substituent, and an electron releasing substituent should decrease the rate of reaction,

as Hinshelwood has predicted from equation (2). This corresponds to a positive value of  $\rho$  in the Hammett equation (18) and will be termed a "positive" substituent effect.

As the charge of the attacking base decreases, or as the transition state distances increase due to the attack of a weaker base, equation (2) would predict a shift toward a negative substituent effect, possibly reaching the point of reversal. At the same time, the above factors will tend to increase the contribution of structure II to the transition state, also effecting a shift toward a more negative or less positive substituent effect. In the limit of an  $S_N1$  type (29) reaction, where the attacking base is nonexistent, or only a weak dipole as the theories of Swain (30) would suggest, both factors are operative to produce a negative substituent effect. As the data collected by Swain clearly show, this is in agreement with the observed results.

In applying a similar treatment to ring opening reactions of epoxides, it becomes necessary to consider several changes. The simplifying assumption will be made that resonance stabilization at the primary carbon is negligible. The electrostatic equation becomes considerably more complicated, due to the added presence of an adjacent carbon which also shares inductively, but to a lesser extent, the change in charge produced by substitution. The presence of an electrophilic reagent attacking the epoxide oxygen is more evident (30) and should be included in the equations. One further complication is the modification of bond distances produced

by bending the oxygen to the adjacent carbon, which can have the effect only of decreasing the distance of withdrawal attained in the transition state. The two transition states are shown in Figure II. Following the method given for calculation of energies for normal displacement reactions, again assuming that distances are unaffected by substitution, the difference in energy between the two transition states, the "electrostatic driving force" of orientation will be expressed by the equation:

$$(3) \Delta E - \Delta E' = \left[ \frac{e_B}{r_{Bc}} \left( 1 - \frac{r_{Oc}}{r_{Bc'}} \right) - \frac{e_E}{r_{cE}} \left( 1 - \frac{r_{cE}}{r_{cE'}} \right) - \frac{e_O}{r_{cO}} \left( \frac{r_{cO}}{r_{cO'}} - 1 \right) \right] (\delta e_c - \delta e_{c'})$$

Considering the significance of the terms involved, it may be deduced that the coefficient of  $e_E$  is less than the corresponding term for a simple displacement reaction, and the term  $e_O$  slightly less, due to the "tensing" effect of the unbroken bond to the adjacent carbon. The "repulsion energies" of the attacking base and electrophilic reagent should be relatively less effective compared to the "bond strength" term than for a comparable benzyl halide displacement. In addition, the effect of the substituent as measured in changes in charge will be less, since the quantity involved is the difference in charge between the adjacent and farther carbon. The net result as related to electrostatic energies, then,

should be to decrease the magnitude of any effect and to shift the value slightly toward a more negative substituent effect. The assignment of numerical values of any accuracy to the quantities in these equations seems highly dubious at this time, although certain natural limits may be imposed from considerations of bond distances and the charges that would be available from total ionization of covalent bonds.

The resonance picture remains much the same as for the halide displacement reactions. One may reasonably expect that, due to the weakness of the strained ring bonds, the transition state will more nearly approach the carbonium ion character, which will predict a greater resonance stabilization than for other displacement reactions.

If the above considerations are correct, then the following predictions may be made concerning the effect of substitution on ethylene oxides:

(1) The influence of substitution upon orientation will be shifted toward a negative effect, both by changes in electrostatic considerations, and by increased resonance stabilization of the transition state. Ring opening of styrene oxides with sodium phenolate (12), for example, shows a marked negative substituent effect, although the same reagent would be expected to show a positive substituent effect in a halide displacement.

(2) The effect of substitution upon the rate at the terminal

carbon, where resonance effects are practically nil, should be small, but probably parallel to the effects observed in displacement reactions. This is consistent with the kinetic data mentioned concerning ring opening reactions of epichlorohydrin, glycidol, ethylene oxide, and propylene oxide, if one considers only base catalyzed ring openings, but for the reactions with hydrogen halides, epichlorohydrin becomes proportionately slower as compared to ethylene oxide, since the electron withdrawing power of the substituent decreases the attraction of the oxide for a proton. The effect upon the rate of reaction at the substituted carbon will be more complicated, involving both resonance and electrostatic effects. The rate must, at any rate show a more negative substituent effect than the rate at the primary carbon.

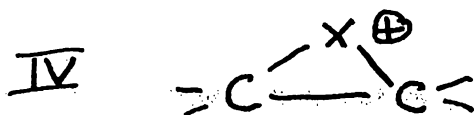
(3) An increase in the base strength or charge of the attacking reagent should decrease the resonance effect, and produce a more positive substituent effect from electrostatic considerations, both of these operating in the same direction. This point has been verified by the present experimental work.

(4) An increase in the strength of the electrophilic reagent, such as in the transition to acid catalysis, should greatly increase the resonance effect by giving the transition state greater carbonium ion character, but should have a small, opposite effect from electrostatic considerations. Winstein and Henderson (8) have pointed out that acid catalyzed reactions generally give a greater amount of secondary attack, and this investigation adds further evidence in this direction.

(5) The effect of solvent will depend upon several factors. The dielectric constant of the medium should play very little, if any role, since the differences between the two alternate transition states correspond essentially to intramolecular differences in distribution of charge. If the solvent acts as either electrophilic or nucleophilic reagent, its main effect should be due to this character. Otherwise, observed differences should be predictable from the effect of solvation on the reacting species. From the diffuse nature of the transition state, it would seem probable that solvation should usually be more important in the initial state. If this is true, greater energy should be required for reaction, and, by the reasoning of Hinshelwood, greater bond distances should be attained in the transition state. In such a case, greater carbonium character and less electrostatic difference between the ring carbons is to be expected, leading to the prediction that a strongly solvating solvent will produce a more negative substituent effect. A comparison of epoxide opening in water and ether with hydrogen halides, and of positive halogen addition to olefins in ether and chloroform presented in the experimental section would seem to bear out this prediction.

An extension of the above discussion may readily be made to predict orientation in reactions involving the addition of positive halogen radicals to a double bond, or to the consumption of a

neighboring group reaction (9). If the positive halogen addition occurs by formation of an open halo-carbonium ion, the effect of structure should be the same as for the addition of hydrogen halides to olefins, and Markovnikoffs rule should hold. If, however, the reaction proceeds through a cyclic "halonium" ion as has been postulated (15), with an intermediate such as IV, followed by attack of



an anion upon this species in a reaction formally analogous to an epoxide ring opening, orientation should be predictable on the basis of the above treatment, with the added generalization that the halogens should show a greater carbonium ion character than the corresponding oxonium compound. Evidence for such a cyclic ion consists of the experimental observation (31) of trans addition in such reactions.

A summary of sixty-four of the more pertinent cases of ring opening reactions of epoxides, where structure proofs are available, and reasonable examination of reaction products have been made (32) reveals no particular contradictions to the above predictions. In the case of positive halogen reactions, very little evidence is available, some of the older work is unreliable, and hence no systematic discussion of previous work may be made at this time. Some of the available data will be presented in the discussion of the experimental results.

## SECTION II

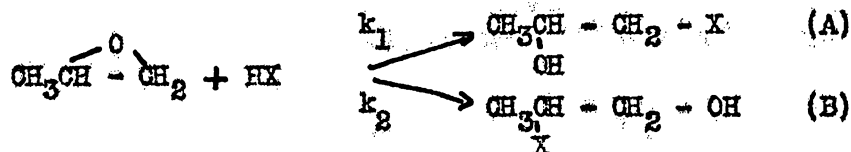
### SUMMARY OF EXPERIMENTAL RESULTS

### A. Preparations and Analyses:

Suitable preparations for each of the six propylene chloro, bromo, and iodohydrins have been described, and the physical properties of these compounds and their 3,5-dinitrobenzoates determined. From the infrared spectra of the compounds, suitable analytical methods have been developed for each pair of isomers.

### B. Ring Opening of Propylene Oxide with Hydrogen Halides:

The reaction of propylene oxide with a hydrogen halide may be expected to give two isomers in proportion to the rate constants for ring opening at either carbon of the epoxide ring, as shown below:



$$(4) \text{ and } (\text{A})/(\text{B}) = k_1/k_2$$

Following the derivation given by Hammett (18), the relationship between the two rates and the entropies and enthalpies of activation is given by the equation:

$$(5) \ln \frac{(\text{A})}{(\text{B})} = \ln \frac{k_1}{k_2} = \frac{\Delta S_1^\ddagger - \Delta S_2^\ddagger}{R} - \frac{\Delta H_1^\ddagger - \Delta H_2^\ddagger}{RT}$$

where  $\Delta S^\ddagger$  is the entropy of activation,  $\Delta H^\ddagger$  the enthalpy of activation,  $R$  the ideal gas constant, and  $T$  the absolute temperature. A plot of the logarithmic ratio of products against reciprocal temperature in the fashion of a vapor pressure plot should enable the determination of the entropy and enthalpy terms,

provided they are relatively constant over the temperature range employed. This has been done for the reactions of hydrogen chloride, bromide, and iodide in water, and for hydrogen chloride and bromide in ether with propylene oxide. The thermodynamic properties so calculated from the least squares lines through the experimental points in Figures III and IV are given in Table I.

TABLE I

Differences in Entropy and Enthalpy of Activation:

Series:	Halide:	Solvent:	$\Delta^2 S,^\ddagger$ cal/mol	$\Delta^2 H,^\ddagger$ kcal/mol
(1)	Cl	Water	-0.85	-0.55
(2)	Br	"	-0.70	-0.85
(3)	I	"	-0.32	-1.12 *
(4)	Cl	Ether	-2.8	-1.54
(5)	Br	"	-2.0	-1.56 *

(\* Data from only two determinations.)

#### C. The Effect of Reaction Conditions:

The reactions of propylene oxide with sodium bromide in an acetate-acetic acid buffer, with ammonium bromide in an ammonium-ammonia buffer, and with magnesium bromide etherate to give mixtures of bromohydrins have been studied. The ratio of isomers is indicated in the column headed "MBr" in Table II, while the corresponding ratio for the reaction with HBr under the same conditions is given for reference. This data has been interpolated between temperatures by means of Figures III and IV.

Figure III

Van't Hoff Plot, Propylene Oxide + HX, Aqueous

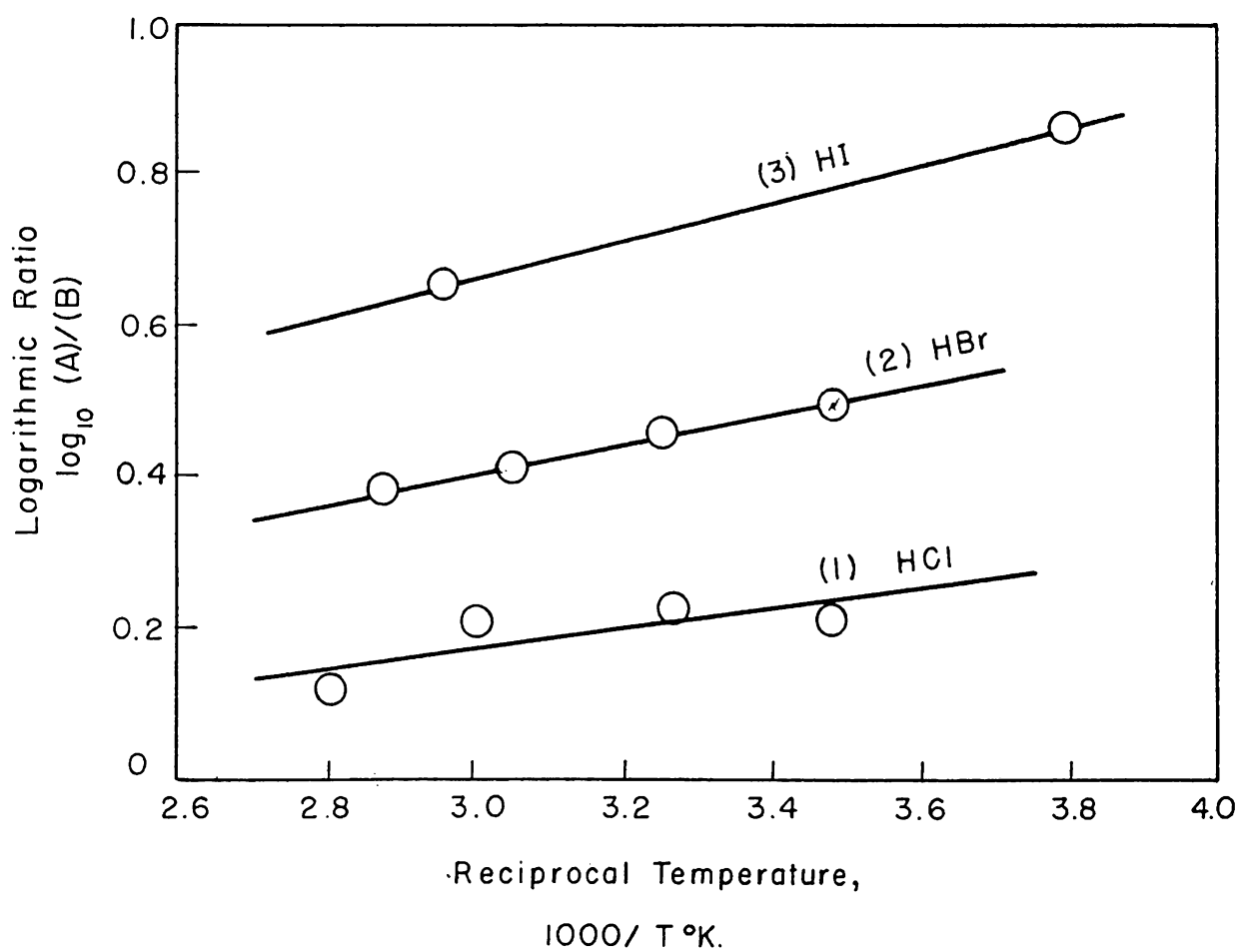


Figure IV

Van't Hoff Plot, Propylene Oxide + HX, Ether

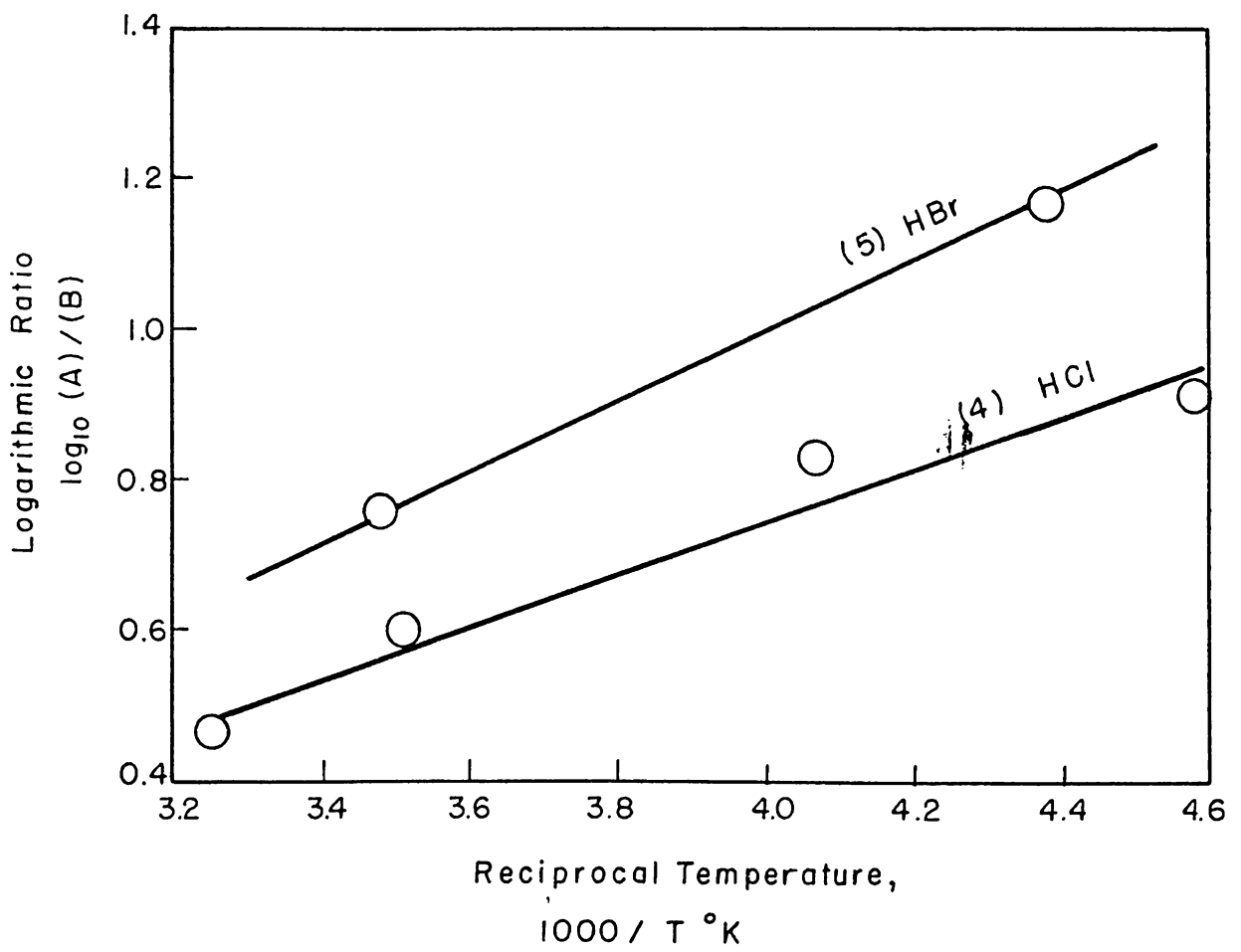


TABLE II

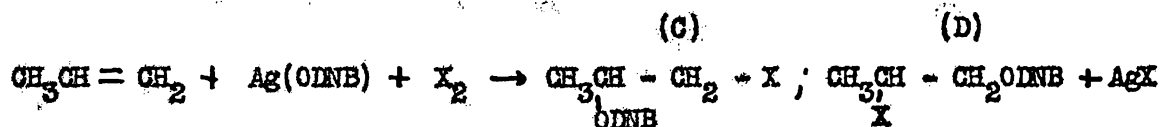
The Effect of Catalysis:

"Catalyst", MBr	(A)/(B), MBr	(A)/(B), HBr
Sodium Bromide	95/5	75/25
Ammonium Bromide	77/23	74/26
Magnesium Bromide etherate	84/16	83/17

As may be seen from the Table, ammonium and magnesium bromides give roughly the same composition of isomers as the corresponding reactions with HBr, while sodium bromide gives a marked shift toward greater primary attack.

#### D. The Addition of Positive Halogen Salts to 1-Propene:

The addition of positive halogen salts of 3,5-dinitrobenzoic acid to 1-propene by the reaction:



where  $\underline{\text{X}}$  is chlorine, bromine, or iodine, and (ODNB) is 3,5-dinitrobenzoate has been studied and the relative amounts of (C) and (D) determined. At dry ice temperatures, only the 1-halo-isopropyl ester, (C), was obtained. At ice temperature, with Bromine, approximately 10% of the isomer, (D), was obtained in ether solution, 25% in chloroform solution. No peroxide effect was observed.

### **SECTION III**

#### **DISCUSSION OF EXPERIMENTAL RESULTS**

### A. Preparations:

The preparations of the pure chlorohydrins and bromohydrins by lithium aluminum hydride reduction of appropriate carbonyl compounds by methods previously described in the literature for analogous preparations has been found to be satisfactory. The preparation of 1-chloro-2-propanol by the method of Dewael (33) was found to be satisfactory, although reported yields could not be duplicated. The preparation of 1-bromo-2-propanol by a similar procedure was found to give poorer yields of a product which was a mixture containing a small amount of the isomeric 2-bromo-1-propanol. If the initial step in the addition of an acid to a double bond is the formation of a carbonium ion, as is generally assumed (29), one might expect that the carbonium ion formed in this case might rearrange to a cyclic bromonium ion:



from which a mixture of isomers would be expected, since the cyclic ion may open in either of two directions. Alternatively, the same cyclic ion might be produced in the hydrolysis of the sulfate ester, which is an intermediate in the reaction, in which case, a neighboring group effect (9) is involved.

The preparation of the iodohydrins by exchange with the corresponding bromohydrins is interesting in that one might expect a neighboring group effect, but none occurs, since the products obtained are

isomerically pure.

The physical properties of the chlorohydrins are in satisfactory agreement with values reported in the literature, except the physical properties reported by Gayler and Waddle (34) for 2-chloro-1-propanol, prepared by chlorination of propyl trichloroacetate. The physical properties of the bromohydrins are in agreement with the limited amount of data available, and the boiling points of the iodohydrins are in agreement with that found by Markownikoff (35) for the product of the reaction of propylene oxide with hydriodic acid.

The melting points of the chlorohydrin 3,5-dinitrobenzoates are in good agreement with those reported by Raimond (36). The melting point of 1-bromo-isopropyl-3,5-dinitrobenzoate found here is higher than that reported by either Bechtle (37) or Huston and Bostwick (38). The work reported in this thesis has shown that preparation by the method used by either of these investigations should lead to a mixture of isomers, and the qualitative observation has been made by this author that separation of isomers by recrystallization from heptane is very slight.

#### B. Analyses:

It is not apparent why the solubility methods of analysis which were investigated failed to give more precise results. Possible explanations might be the presence of varying amounts

of a minor impurity, or esterification of the benzoic acid by the halohydrins. At any rate, the procedure is far more tedious than the rapid and more reliable infrared method developed.

Analytical distillation is at best a poor method if no means of estimating the purity of the fractions is obtained. Considering the closeness of the boiling points of the isomeric halohydrins, it is remarkable that as good agreement as was observed was obtained. Again, the procedure is far more tedious than the infrared method.

#### G. The Reaction Between Propylene Oxide and Hydrogen Halides:

As Hammett points out (18), unless the entropies of activation are essentially the same for two reactions to be compared, it is not strictly correct to compare the enthalpy differences or rate differences in terms of electronic factors. The differences observed here, however, are as small as those cited by him as suitable cases for comparison, for reactions such as benzylation of substituted anilines, hydrolysis of substituted benzyl halides and benzoate esters, and the like. Hammett has also pointed out that variations of entropy with enthalpy of activation are small, if existing at all. In light of these considerations, it is hard to rationalize the magnitudes found for the enthalpy and entropy of activation, although it will be shown that the changes in these terms are what would be expected on the basis of steric considerations

and the theory advanced here.

In each case the entropy difference found is negative. That is, if the enthalpy term were negligible, there would be more attack at the secondary carbon than at the primary. One possible explanation of this, kindly suggested by Dr. W. J. Argersinger, is that, as an incoming group approaches one carbon atom, the oxide oxygen is moving closer to the other side of the ring, and perhaps meets with greater hindrance than is encountered by a group such as a halide ion approaching to transition state distance of the carbon. This "reverse" steric effect might be sufficiently great to produce the negative entropy differences found here, but certainly would be negligible if the attacking base were of much larger size. Another possible explanation might be found in actual differences in heat capacities or vibrational levels, as mentioned by Hammett.

In both aqueous and ether experiments, the entropy difference becomes more nearly positive in progressing from chloride to bromide (to iodide). This is the expected result of increasing the size of the incoming group, which will meet increasingly greater steric hindrance. In ether, the entropy difference is far more negative than in water. This could conceivably be due to hydration and an increase in the size of the halide ions in water, although it may be due rather to whatever the cause that makes the entropy difference negative in each case.

The enthalpy term in each case is also negative, which indicates a favoring of primary attack, rather than the reverse, which is true of entropy. In water, it would appear that there is an increase in the magnitude of this effect in progressing from chloride to bromide to iodide. This is the order of increasing base strength, as measured by the Swain correlation (2), and the order is that expected from decreasing resonance stabilization of a positive charge adjacent to the methyl group by the reasoning given previously. In ether, the difference between chloride and bromide is well within experimental error, although both show a greater effect than in water. This is the result predicted on the basis of resonance energies and solvation energies presented in Section I.

The experimental observation that the order of primary attack increases in progressing from chloride to iodide might be expected to be general. It is in agreement with the observation of Halperin, Donahoe, Kleinberg, and VanderWerf (15) in the reactions of 1,2-epoxybutane, and is the result predicted generally from the theory given.

The observation that a strongly solvating solvent like water gives a greater amount of secondary attack agrees with the finding of Guss (12) in the reaction of styrene oxide with phenolate ion, and again, may reasonably be supposed to be general, at least where the secondary product is that predicted from resonance considerations.

D. The Effect of Halide Salts on the Ring Opening of Propylene Oxide:

Sodium bromide is found to give far greater primary attack in the ring opening of propylene oxide than hydrogen bromide under similar conditions. From the theory of resonance stabilization, this is to be expected, since the acid catalyzed reaction should have far greater carbonium ion character than the reaction in the absence of acid catalyst. It is interesting to note that magnesium and ammonium bromides give practically no shift of this nature. From the ready formation of insoluble complexes between magnesium bromide etherate and any electron donor molecule, it seems reasonable to suppose that a similar coordination occurs here, with the magnesium effectively acting as an acid. The ammonium ion in water may play a similar role, since Swain (30) has shown that the ring opening of epoxides is a case of general acid catalysis.

E. The Addition of Positive Halogen Salts of 3,5-Dinitrobenzoic Acid to 1-Propene:

It has been shown that, in contrast to the data of Halperin et.al., the addition of positive halogen salts of 3,5-dinitrobenzoic acid to propylene under some conditions gives mostly the Markownikoff product, but a small amount of the isomeric compound. If the reaction actually proceeds through a "halonium" ion, analogy with epoxide ring

opening would lead one to expect at least a small amount of primary attack by the incoming anion, which has been verified.

No peroxide effect was observed when the reaction was carried out in a relatively non-polar solvent (chloroform) in the presence of dibenzoyl peroxide. This does not justify the conclusion that no radical reaction could occur in this system, but would suggest that it will not ordinarily be appreciable, and does not account for the reverse product obtained here.

#### F. Miscellaneous Observations:

The unreactivity of 1,2-dichloropropane observed is in agreement with the findings of Petrenko-Kritchenko and Opotskii (39) and of Fickett, Garner, and Lucas (10a).

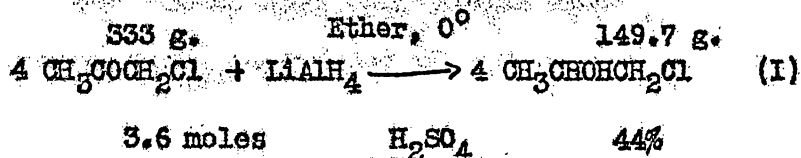
The reduction of epichlorohydrin might perhaps afford as reasonable a synthetic method of obtaining 1-chloro-2-propanol, and, if so, would avoid handling the extremely lachrymatory chloroacetone. The reaction should provide interesting information concerning the relative reactivity of halogens and epoxides to lithium aluminum hydride, and the nature of the reaction.

**SECTION IV**

**EXPERIMENTAL SECTION**

## A. Preparation of Pure Halopropanol Isomers

1-Chloro-2-propanol (I), 2-chloro-1-propanol (II), 1-bromo-2-propanol (III), and 2-bromo-1-propanol (IV) were prepared by lithium aluminum hydride reduction of chloroacetone, chloropropionyl chloride, bromoacetone, and bromopropionyl bromide, respectively, as described in Table III. For example,



The preparation of II by this method has been previously described by Fickett, Garner, and Lucas (10a). The chloroacetone and bromopropionyl bromide were commercial products. Chloropropionyl chloride was obtained from the acid by reaction with thionyl chloride. The bromoacetone used was the crude product boiling at 43-53° at 18 mm., as described in Organic Synthesis (40). Each isomer was redistilled for the determination of physical properties, and it is the boiling point found on redistillation that is reported in the table.

The reduction was carried out in the following manner: A weighed quantity of lithium aluminum hydride was placed in a three-necked flask fitted with a mechanical stirrer, an efficient reflux condenser, and an addition funnel extending nearly to the bottom of the flask. Twenty milliliters of ether per gram of hydride were added through the addition funnel. The solution was refluxed for at least an hour and then cooled

Table III Preparation of Halohydrins by Lithium Aluminum Hydride Reduction

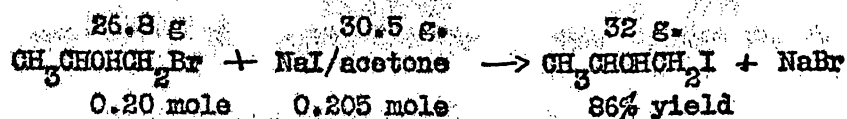
Compound Reduced	Moles	Moles LiAlH <sub>4</sub>	Product	Yield, %	Boiling Point,	Pressure mm. Hg.
Chloroacetone	3.6	1.23	I 1-Chloro-2-propanol	44%	50.6-50.8°	30
$\alpha$ -Chloropropionyl chloride	1.62	1.23	II 2-Chloro-1-propanol	82% (a)	53.0-53.6°	29
Bromoacetone	0.96	0.47	III 1-Bromo-2-propanol	29%	62.0-62.2°	26
$\alpha$ -Bromopropionyl Bromide	1.00	0.59	IV 2-Bromo-1-propanol	84%	62.8-64.0°	23.5-24.0

(a) Fickett, Garner, and Lucas Report 79% yield

in an ice bath, while the indicated quantity of halogen compound was added dropwise over a period of about an hour. The reaction mixture was allowed to stand for half an hour before decomposition of the excess hydride with a small amount of water. Sufficient four normal sulfuric acid was then added to give a separable mixture. The ether layer was decanted, and the aqueous layer was extracted with three equal portions of ether whose total volume was approximately that of the original ether solution. The combined ether layers were dried, first over sodium sulfate, then over magnesium sulfate. The ether was removed on a steam bath, and the remaining liquid was distilled at reduced pressure through a modified Claisen apparatus.

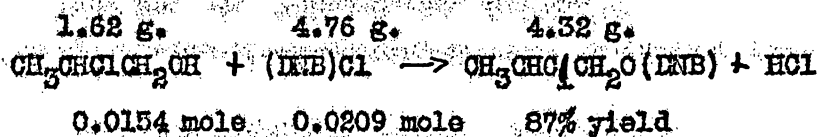
1-Iodo-2-propanol (V) was prepared by the action of sodium iodide in acetone on the corresponding bromohydrin (III) by the following procedure: 26.8 g. (0.20 mole) of bromohydrin, 30.5 g. (0.205 mole) of sodium iodide, and 150 ml. of anhydrous acetone were placed in a flask and allowed to reflux for ten hours. The acetone was removed by evacuation with an aspirator to a pressure of approximately 100 mm. on a water bath at 35°. The halohydrin was taken up in 75 ml. of ether, filtered to remove the precipitated sodium bromide, and the ether removed under reduced pressure, after which the residue was distilled through a modified Claisen apparatus. Approximately 27.5 g. (74% yield) of pure material, b.p. 59-63° at 9 mm., and an

additional 4.5 g. (12%) of less pure fore and end fractions were obtained.



2-Iodo-1-propanol (VI) was prepared from 2-bromo-1-propanol, (IV), by the procedure described above. A forty hour reflux time was allowed for the less reactive secondary halide. The product (25.0 g., 67% yield) boiled at 74-79° at 20 mm. and was slightly colored with free iodine. Redistillation at 9 mm. resulted in further decomposition and was not effective in removal of iodine. The isomeric purity of V, and VI is assumed from the infrared spectra described later (Figures IX and X).

The 3,5-dinitrobenzoates of each of the halohydrins was prepared by heating 0.01-0.015 mole of halohydrin with a slight (5-10%) excess of 3,5-dinitrobenzoyl chloride at 70 to 100° for several hours. For example,



The reaction mixture was taken up in chloroform, washed with sodium carbonate (and with thiosulfate solution in the case of the iodo compounds) solution and the chloroform evaporated under a stream of dry air. The crude material thus obtained was recrystallized

several times from technical heptane which had been shaken with concentrated sulfuric acid, washed with water, and distilled over sodium. The melting points were taken using a thermometer with  $0.2^{\circ}$  divisions which had been calibrated against Bureau of Standards thermometers, and stem corrections have been applied.

The preparation and properties of the dinitrobenzoates are reported in Table IV.

#### B. Determination of Physical Properties.

Density and refractive index were determined using conventional pycnometers and an Abbe refractometer. Temperature for these measurements was maintained by means of a constant temperature bath whose temperature was measured by a Bureau of Standards calibrated thermometer at  $30.05 \pm 0.05^{\circ} \text{C}$ .

Molar refraction was calculated from the above data by the method described in Daniels (41).

Neutralization equivalents were determined by weighing small amounts of halohydrins into glass stoppered bottles, adding a 10% excess of standardized 0.1 normal sodium hydroxide, heating on a steam bath for half an hour, and back titrating the excess base with standard acid, using thymol blue as indicator.

The physical constants of the halohydrins are listed in Table V.

#### C. Infrared Spectra and Analysis:

The spectra of all the compounds described in this thesis have been determined using a Perkin-Elmer Model 21 Infrared

TABLE IV

## Preparation of 3,5-Dinitrobenzoates

Compound Prepared	Alcohol Esterified	Yield, %	Melting Point °C.	Note
VII	I 1-chloro-2-propanol	72	82.8-83.8	(a)
VIII	II 2-chloro-1-propanol	88	77.0-77.9	(b)
IX	III 1-bromo-2-propanol	69	92.4-92.9	(c)
X	IV 2-bromo-1-propanol	66	78.2-79.2	(d)
IX	V 1-iodo-2-propanol	88	80.6-83.8	(e)
X	VI 2-iodo-1-propanol	82	99.4-100.5	(f)

(a) Raimond reports m.p. 83.6-84.7 (36)

(b) Fickett, Garner, and Lucas (10a) report

(c)  $C_{10}H_9N_2O_6Br$ , Calc. % C 36.0, % H 2.70, % N 8.42, % Br 24.0  
Found 36.3, 2.57, 8.55, 23.9

(d)  $C_{10}H_9N_2O_6Br$ , Calc. % C 36.0, % H 2.70, % N 8.42, % Br 24.0  
Found 35.9, 2.59, 8.15, 23.9

(e)  $C_{10}H_9N_2O_6I$ , Calc. % C 31.5, % H 2.36, % N 7.40, % I 33.4  
Found 34.8, 2.25, 7.45, 33.1

(f)  $C_{10}H_9N_2O_6I$ , Calc. % C 31.5, % H 2.36, % N 7.40, % I 33.4  
Found 32.1, 2.27, 7.40, 33.3

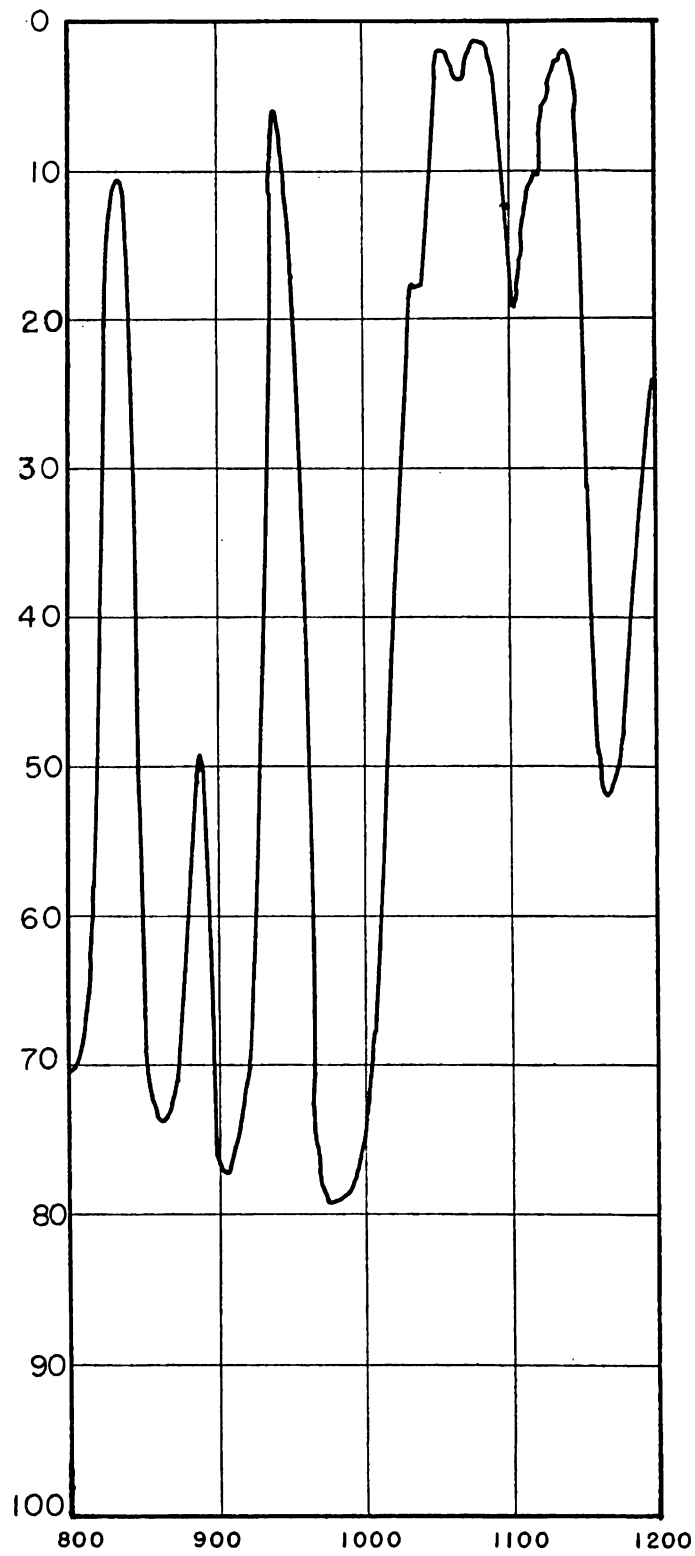
Table V. Physical Properties of Propylene Halohydrins

Compound:	$n_D^{50}$	Density, 50° C.	Molar Found	Refraction Calculated	Neutralization Found	Equivalent Calculated
I 1-Chloro- 2-propanol	1.4352	1.1005	22.43	22.45	94.6	94.54
II 2-Chloro- 1-propanol	1.4355	1.0905	22.56	22.45	94.9	94.54
III 1-Bromo- 2-propanol	1.4762	1.5585	25.17	25.35	138.9	139.0
IV 2-Bromo- 1-propanol	1.4725	1.5551	25.32	25.35	138.9	139.0
V 1-Iodo- 2-propanol	1.5365	1.8999	30.54	30.37	185.2	186.0
VI 2-Iodo- 1-propanol	1.5392	1.8902	30.83	30.37	181.5	186.0

Spectrophotometer. Portions of the spectra are reproduced here as Figures V to XVI. The original spectra have been filed in the catalogue of spectra in room 309 of Bailey Chemical Laboratory. Spectra of the liquid halohydrins were determined on samples of 0.025 mm. thickness in sodium chloride cells, with a similar empty cell as reference. Spectra of the solid dinitrobenzoates were taken from solutions of 150 mg. of dinitrobenzoate per milliliter of chloroform, in 0.05 mm. sodium chloride cells with a similar cell of pure solvent for reference.

Each of the secondary alcohols, I, III, and V, gave a peak in the region of 925 to 940  $\text{cm}^{-1}$ , and each of the primary alcohols, II, IV, and VI, gave a peak in the region of 970 to 985  $\text{cm}^{-1}$ . Preliminary examination of the spectra of known mixtures of isomeric pairs showed that these lines obeyed Beer's Law, except for the very low transmission range, but the data, given as Tables VI, VII, and VIII were calculated in terms of the ratio of the heights of these peaks, measured from the minimum between them. It might be expected that this method of calculation would minimize errors due to faulty adjustment of the machine to zero and one hundred percent transmission, and be less sensitive to impurity, and should certainly be valid for pure binary mixtures. The calibration curves for the three pairs of halohydrins appear as Figures XVII, XVIII, and XIX.

FIGURE V



1 - chloro - 2 - propanol

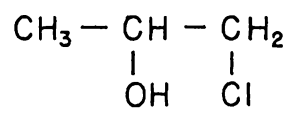
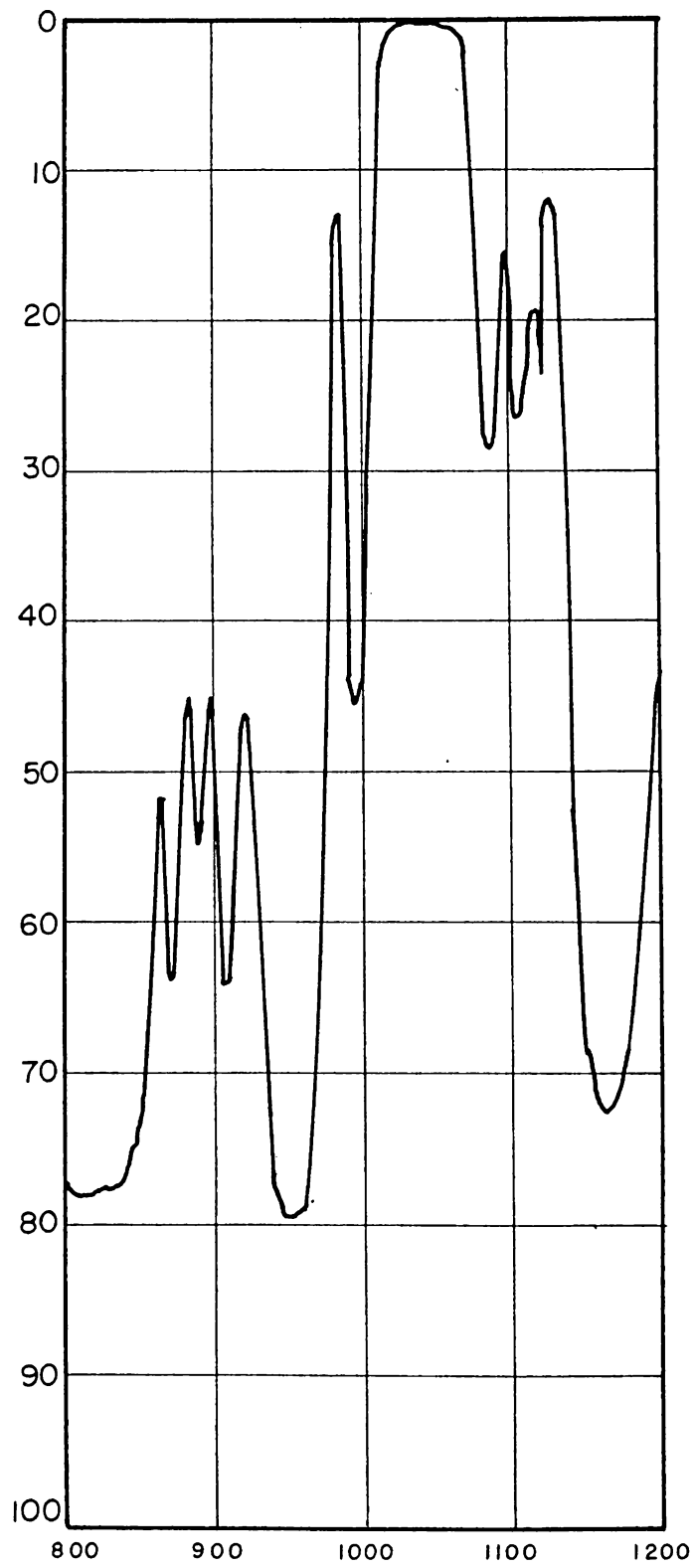


FIGURE VI



2-chloro-propanol

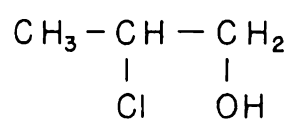
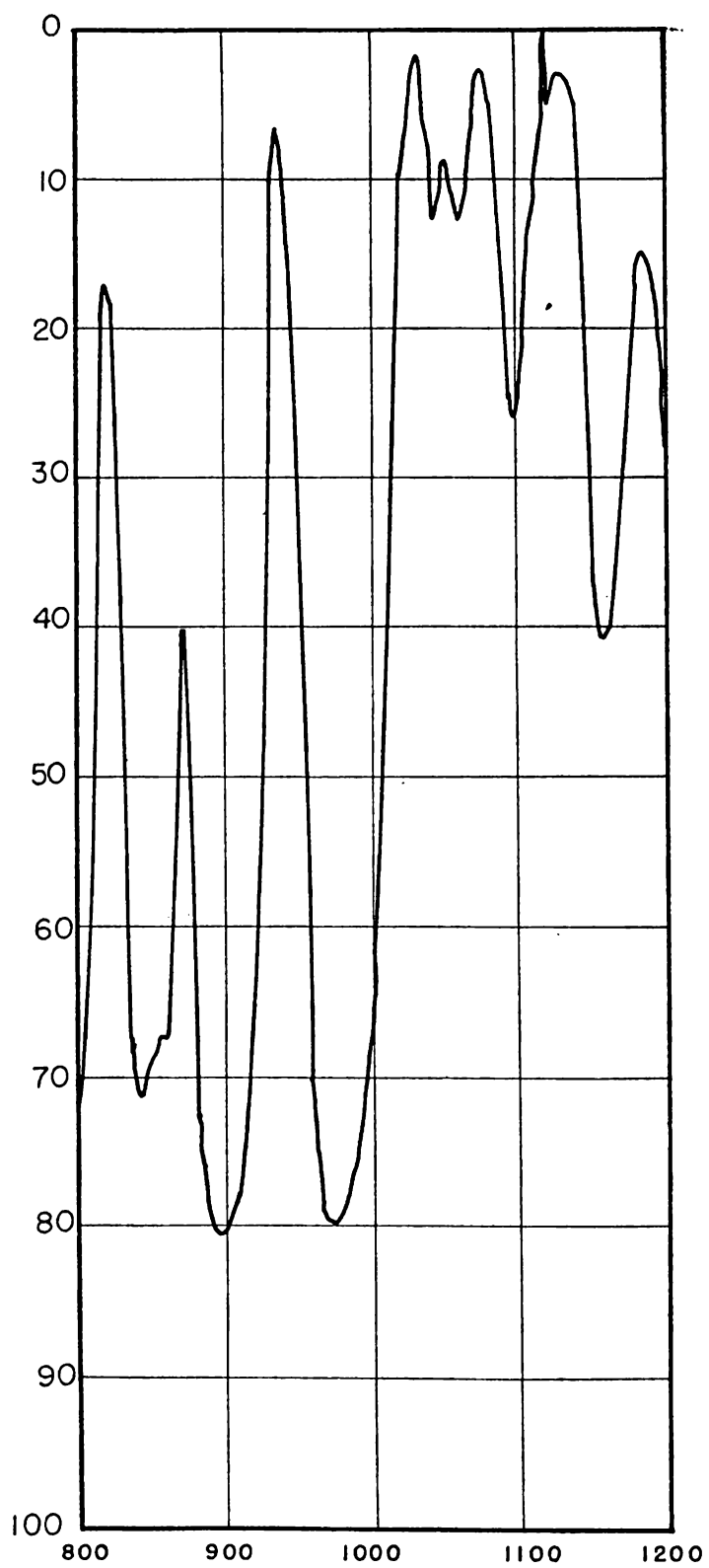


FIGURE VII



1 - bromo - 2 - propanol

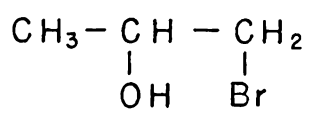
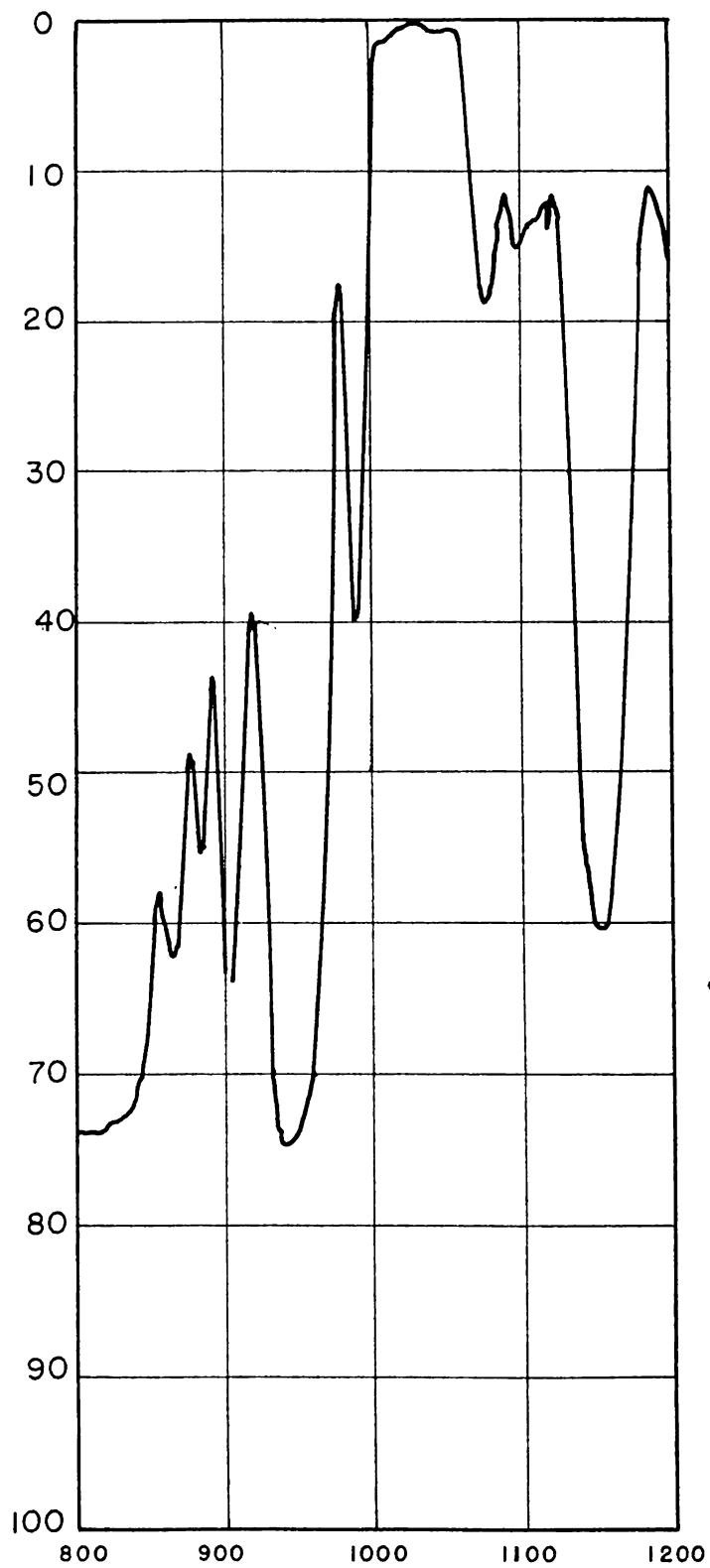


FIGURE VIII



2 - bromo - 1 - propanol

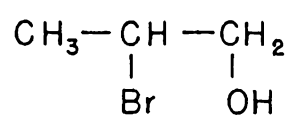
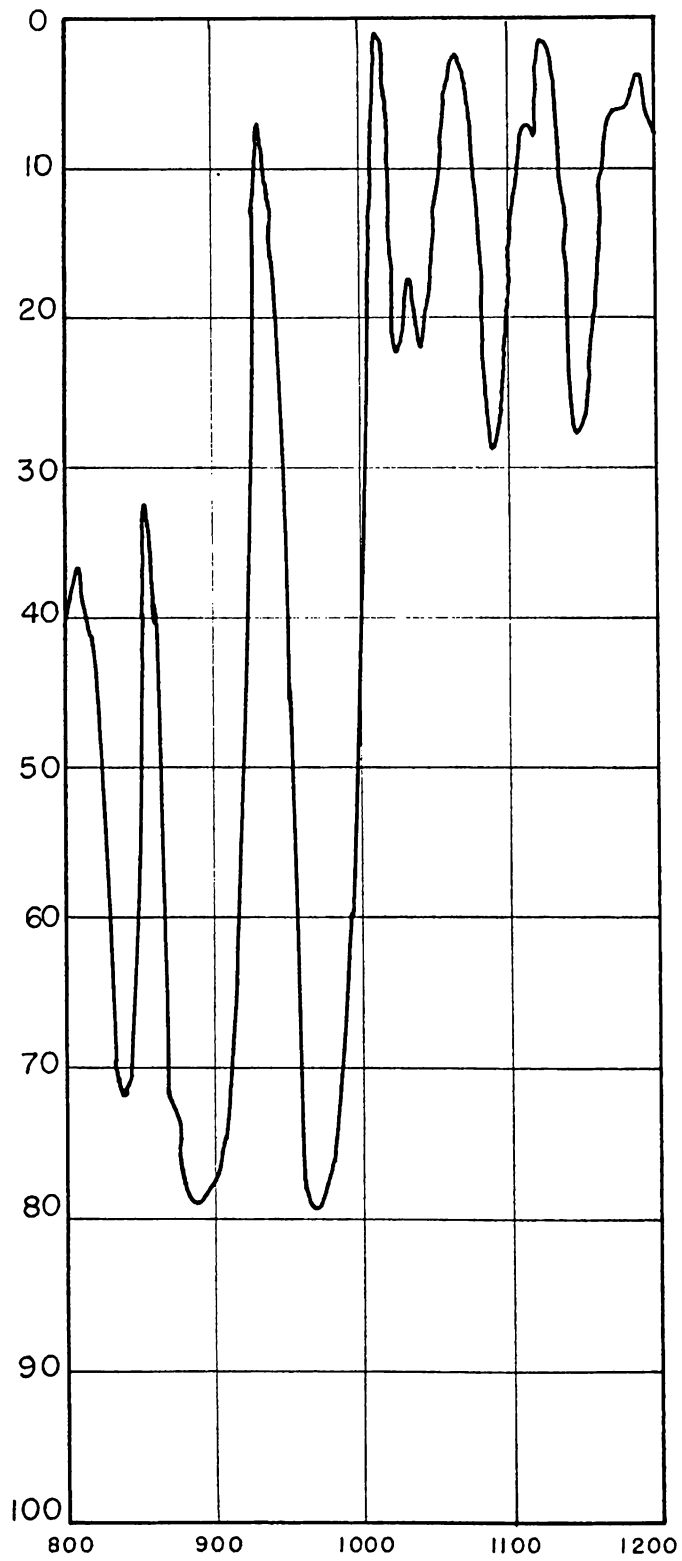
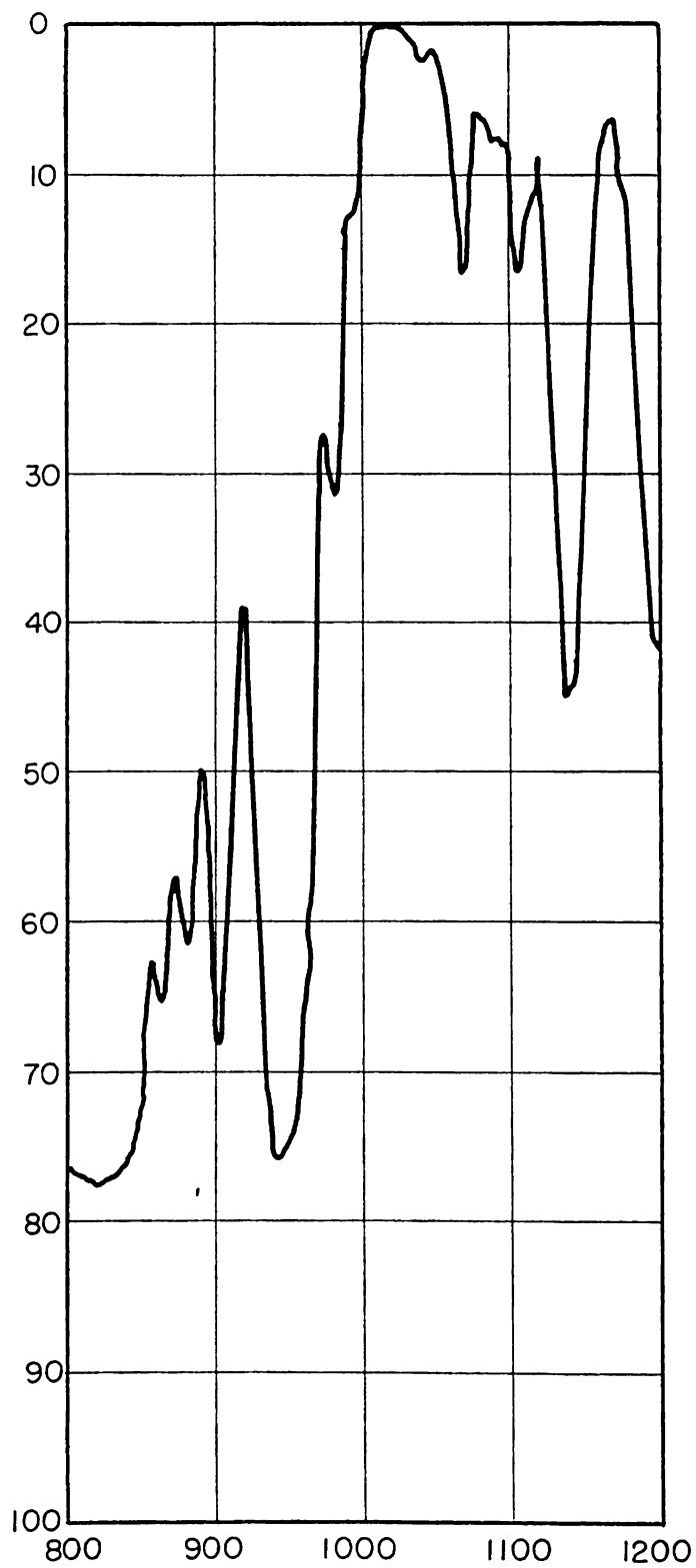


FIGURE IX



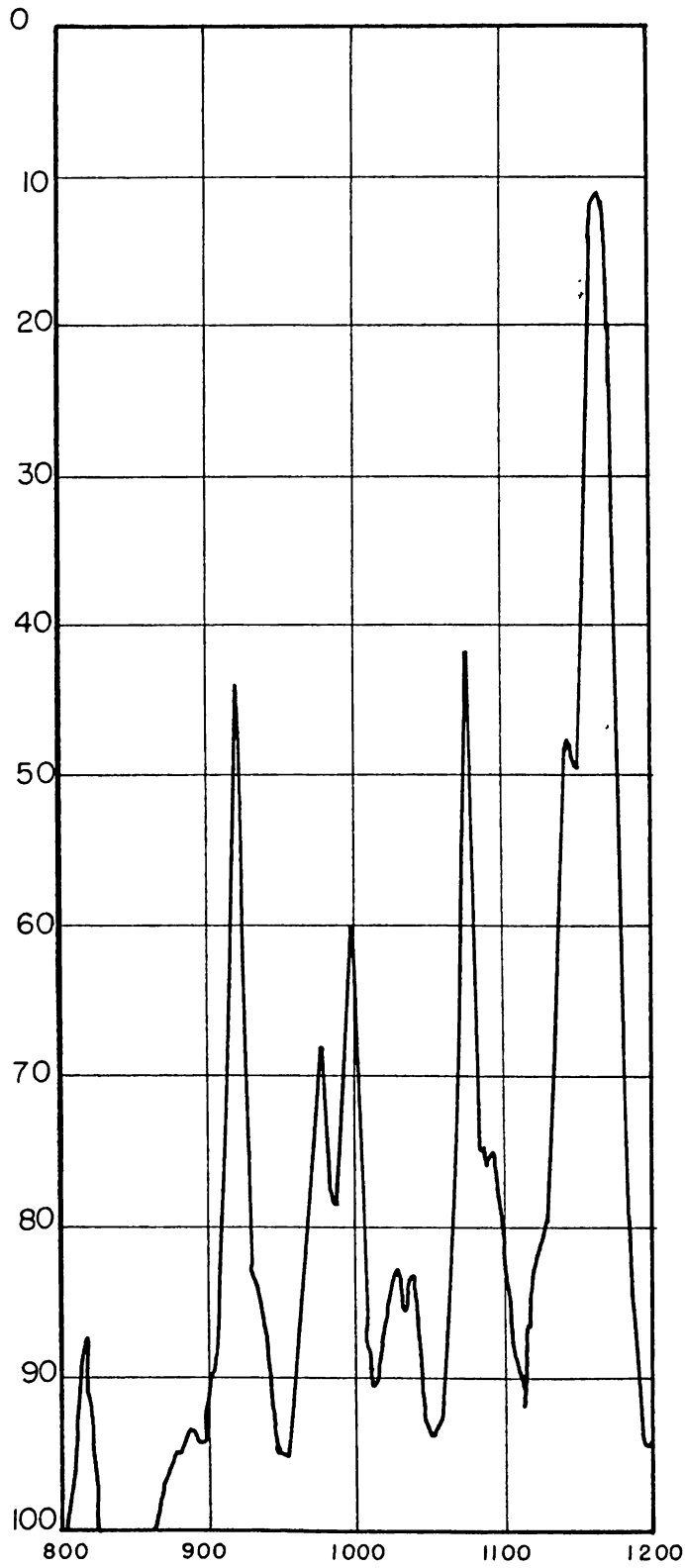
1- iodo - 2 - propanol

FIGURE X



2-iodo-1-propanol

FIGURE XI



1 - chloro - isopropyl  
3,5 - dinitrobenzoate

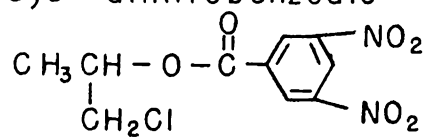
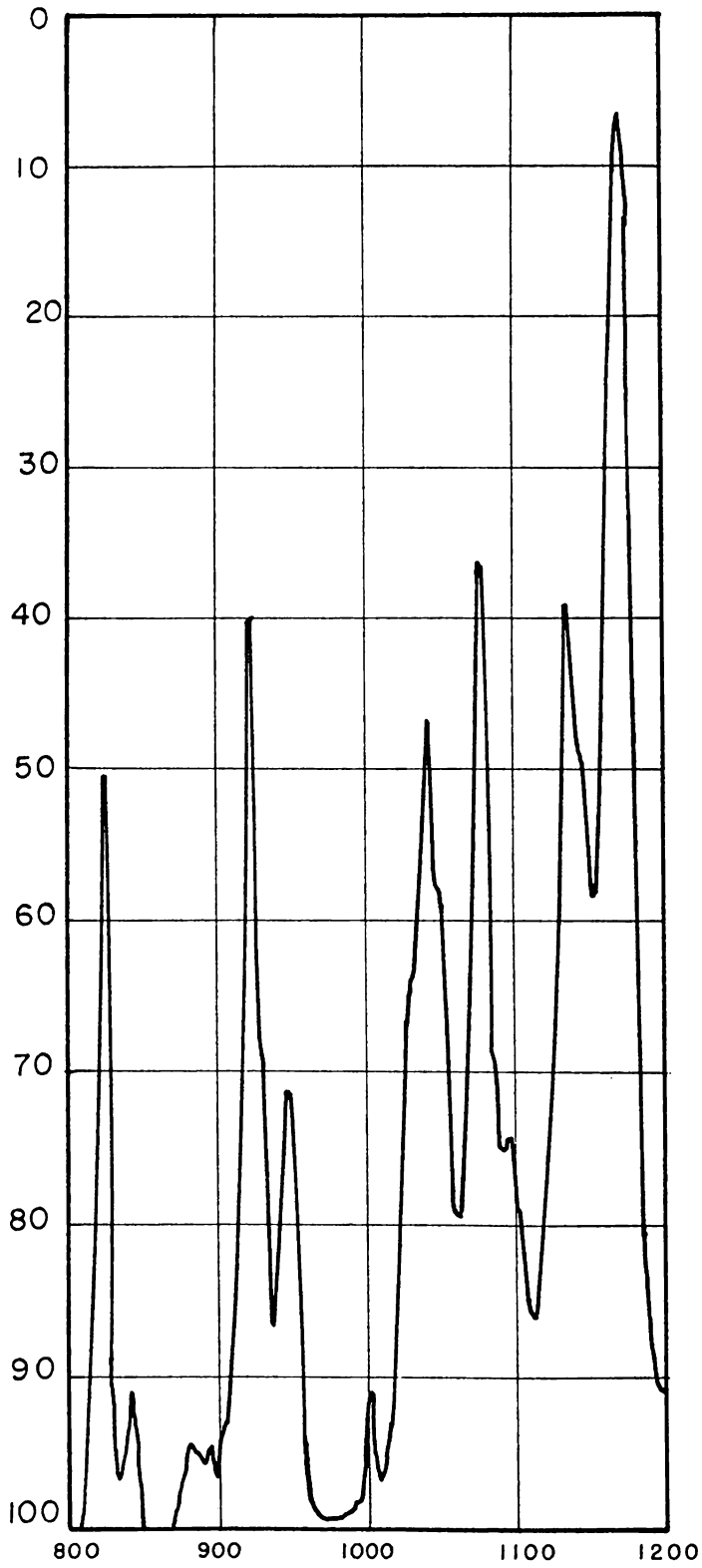


FIGURE XII



2-chloro-propyl  
3,5-dinitrobenzoate

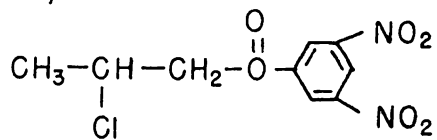
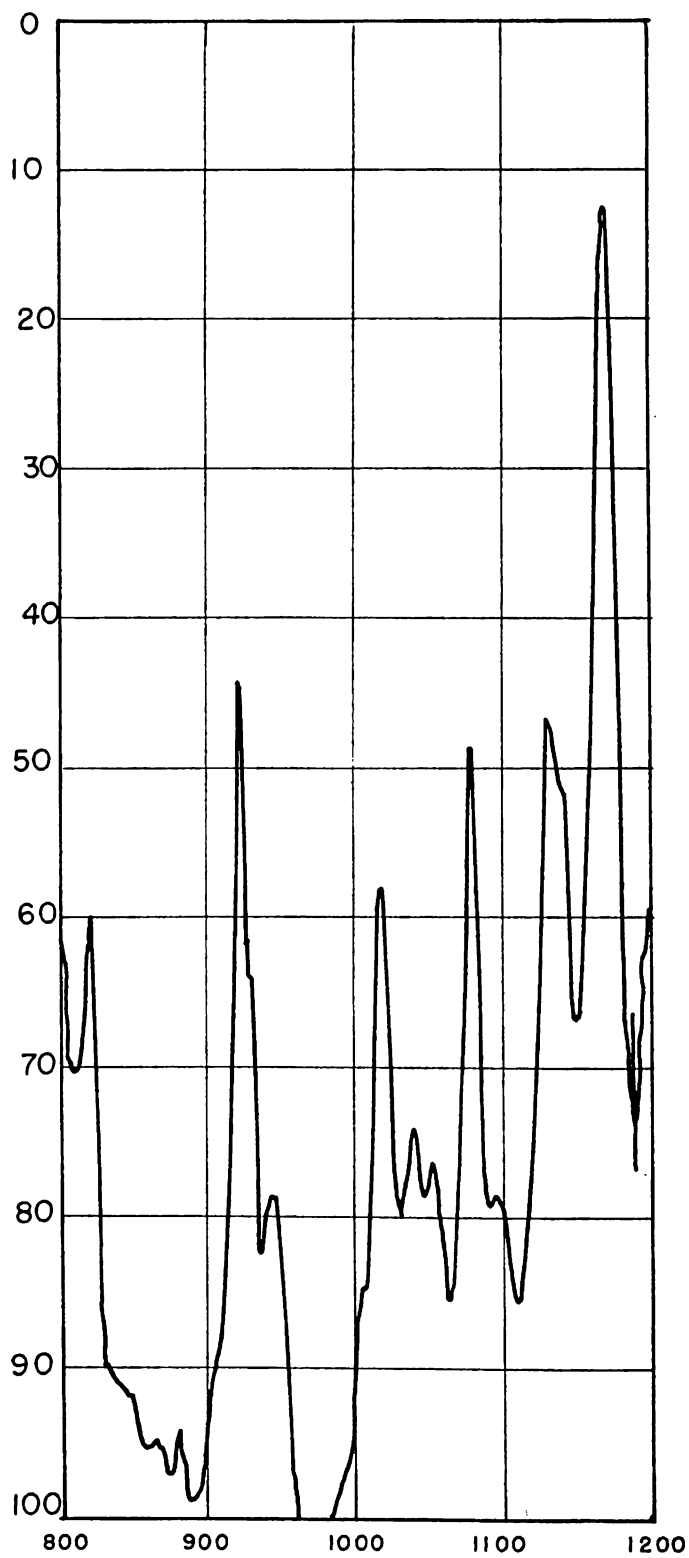


FIGURE XIII



l-bromo-isopropyl  
3,5-dinitrobenzoate

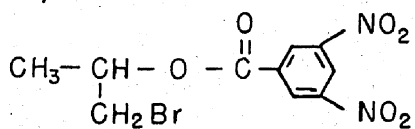
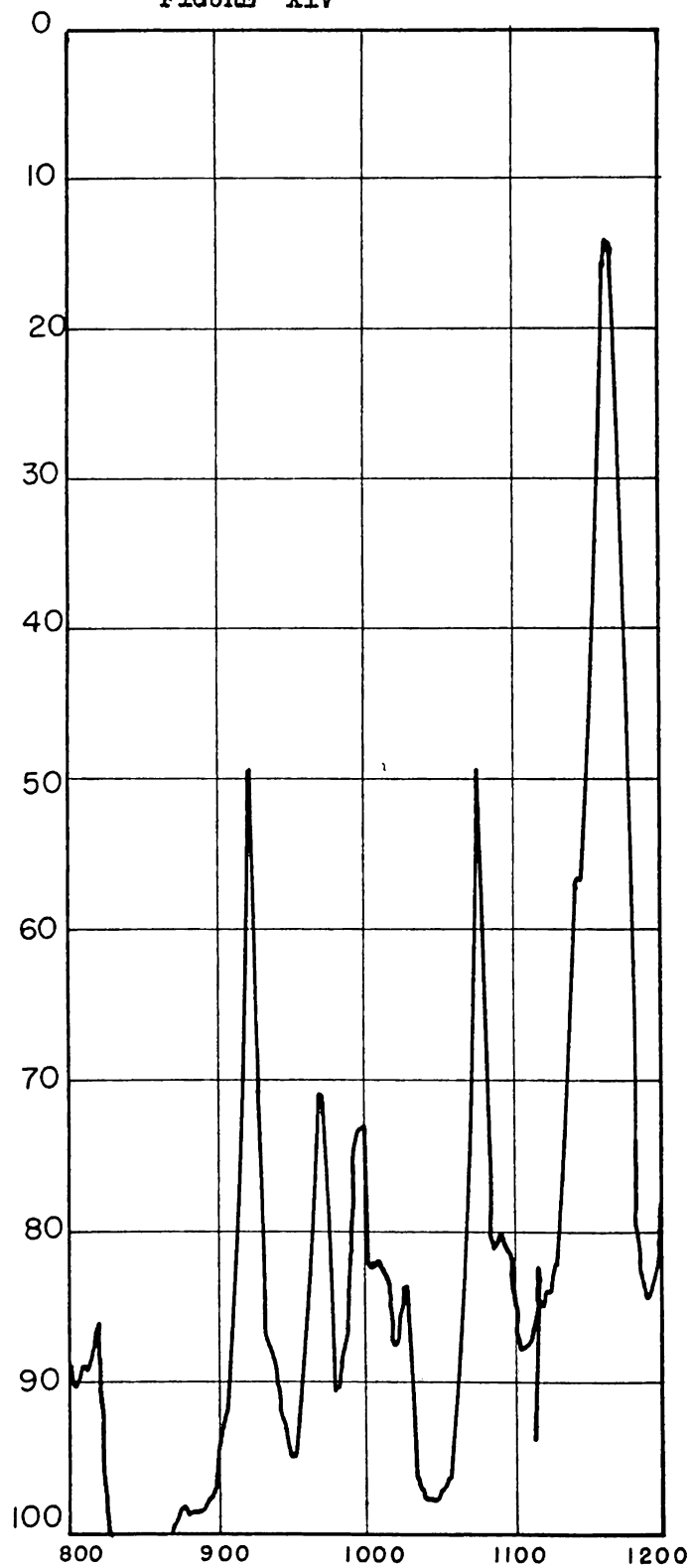


FIGURE XIV



2-bromo-propyl  
3,5-dinitrobenzoate

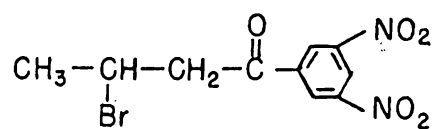
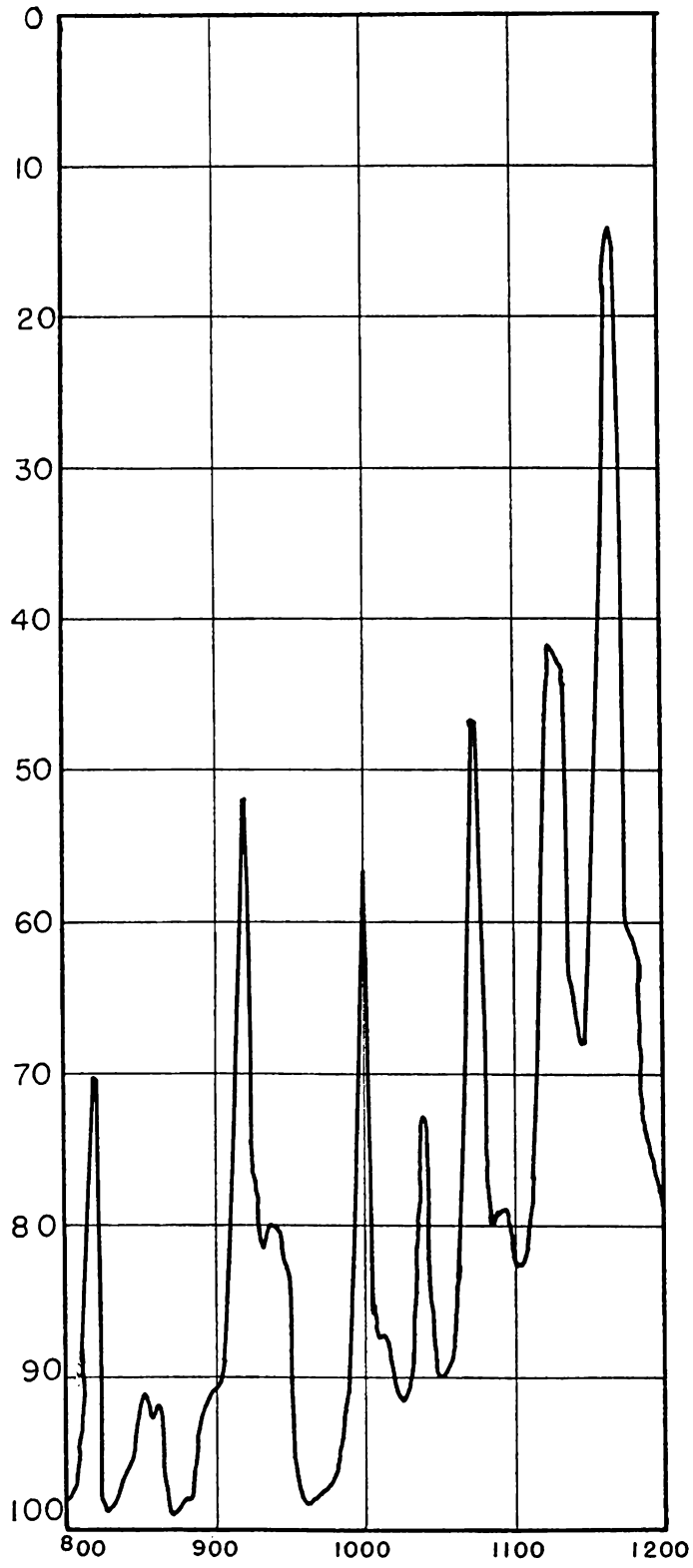
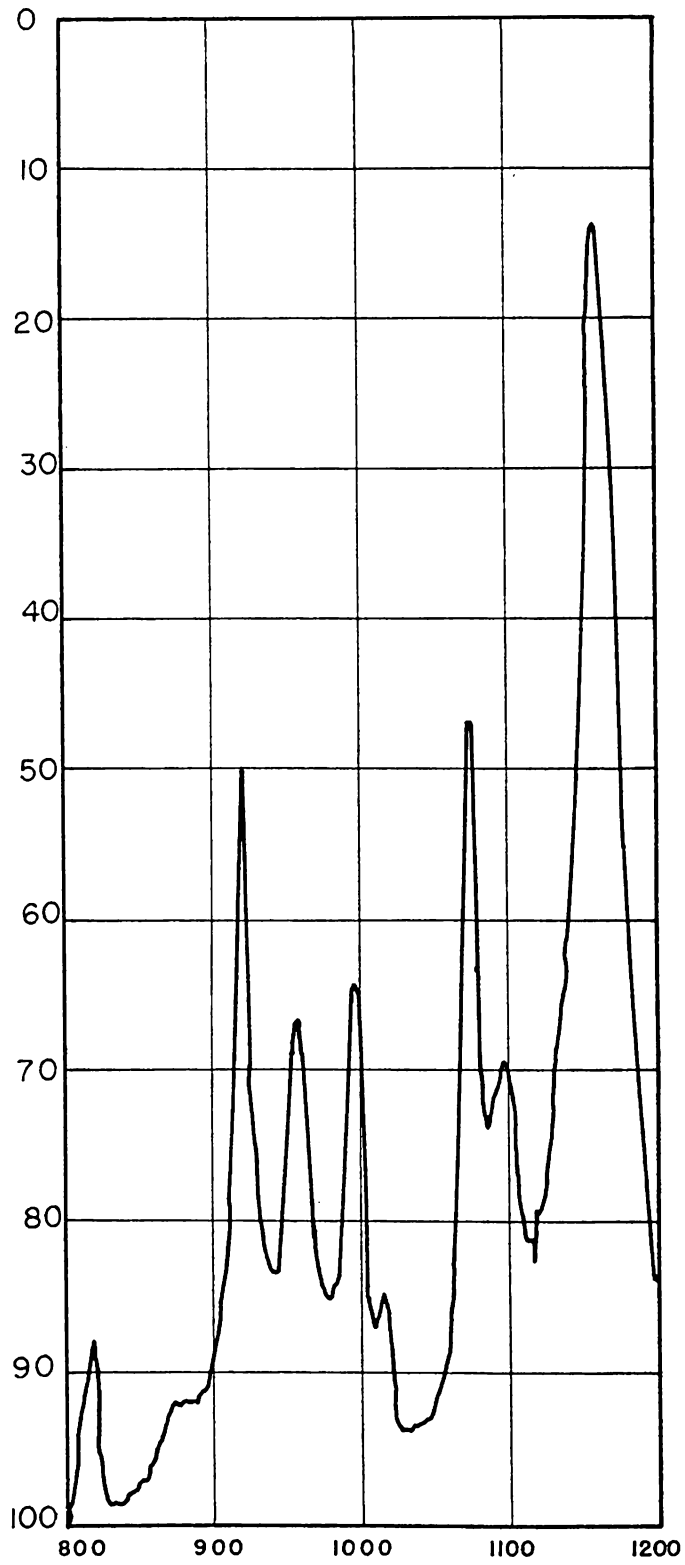


FIGURE XV



l-iodo-isopropyl  
3,5 dinitro benzoate

FIGURE XVI



2-iodo-propyl  
3,5 dinitrobenzoate

TABLE VI

Calibration Data for Infrared Analysis of Chlorohydrins

% I	% II	A Height, 981 $\text{cm}^{-1}$	B Height, 938 $\text{cm}^{-1}$	B/A	A/B
100	0	0.0	73.4	-	0.0
87.5	12.5	8.6	64.6	-	0.148
74.7	25.3	20.8	60.5	-	0.345
61.6	38.4	31.6	56.7	1.59	0.558
49.9	50.1	38.5	51.2	1.33	0.755
38.8	61.2	44.3	45.1	0.915	1.098
25.6	74.4	53.7	33.5	0.620	1.608
12.6	87.4	57.8	21.5	0.368	2.09
0.0	100.0	65.2	2.2	0.03	-

TABLE VII

## Calibration Data for Infrared Analysis of Bromohydrins

% III	% IV	A Height, 977 $\text{cm}^{-1}$	B Height, 937 $\text{cm}^{-1}$	A/B	B/A
100	0.0	0.1	59.5	0.002	-
89.5	10.5	4.4	63.5	0.069	-
81.4	18.6	9.8	58.9	0.166	-
68.9	31.1	17.4	55.5	0.314	3.19
61.5	38.5	21.6	53.0	0.407	2.45
50.0	50.0	29.0	49.2	0.589	1.700
41.6	58.4	32.4	41.8	0.775	1.290
20.4	79.6	40.9	25.3	1.615	0.619
0.0	100.0	55.7	0.8	-	0.015

TABLE VIII

Calibration Data for Infrared Analysis of Iodohydrins

% V	% VI	A Height, 981 $\text{cm}^{-1}$	B Height, 931 $\text{cm}^{-1}$	A/B
100	0.0	—	—	0.00
95.0	5.0	0.8	68.8	0.0116
90.1	9.9	2.5	64.7	0.0386
79.8	20.2	6.3	60.5	0.107
63.5	36.5	15.3	55.0	0.278
50.0	50.0	19.8	45.6	0.434
0.0	100.0	—	—	—

Figure I Calibration Curves for Infrared Analysis of 1-chloro-2-propanol + 2-chloro-1-propanol.

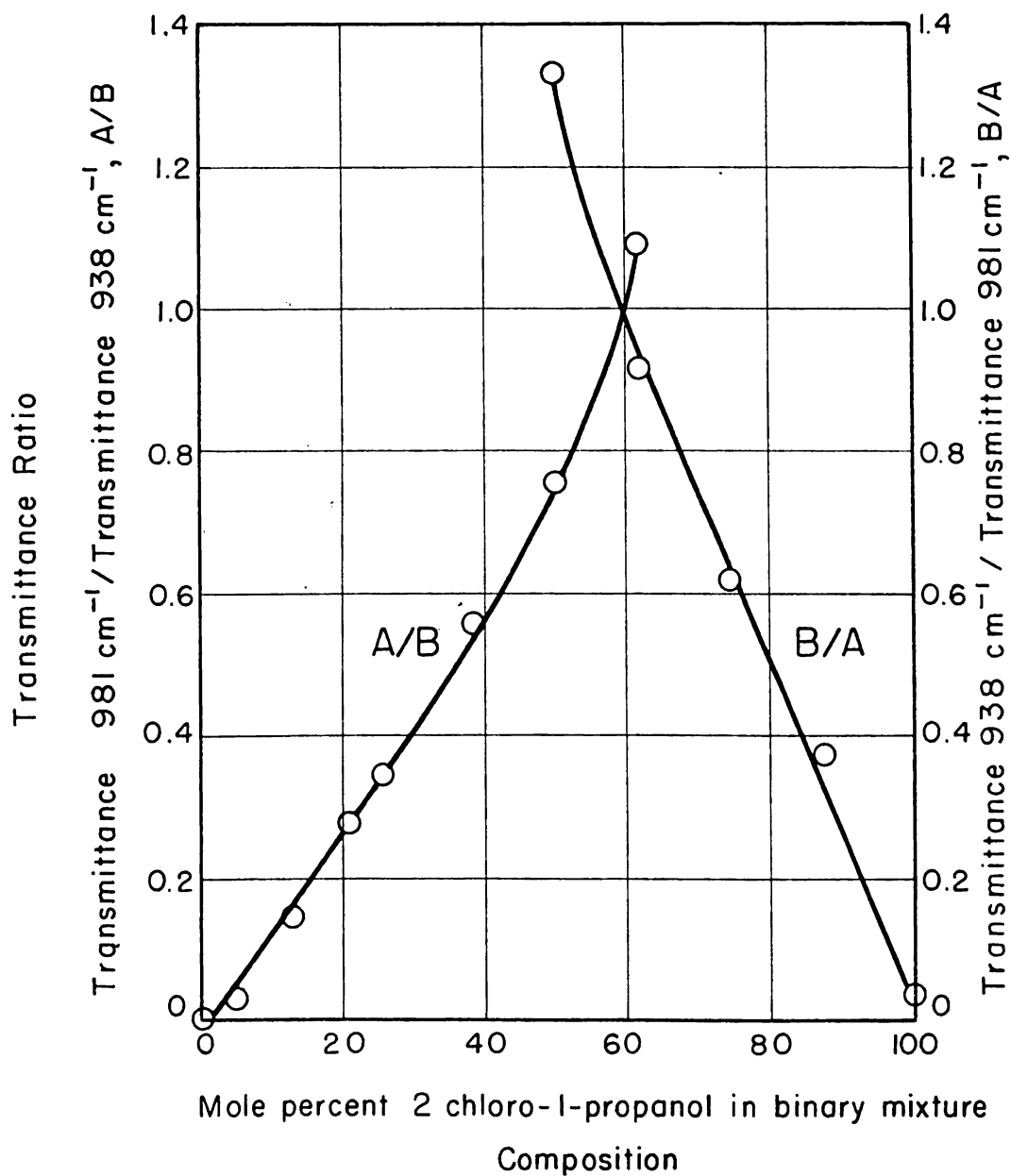


Figure II Calibration Curves for Infrared Analysis  
of 1-Bromo-2-propanol + 2-Bromo-1-propanol

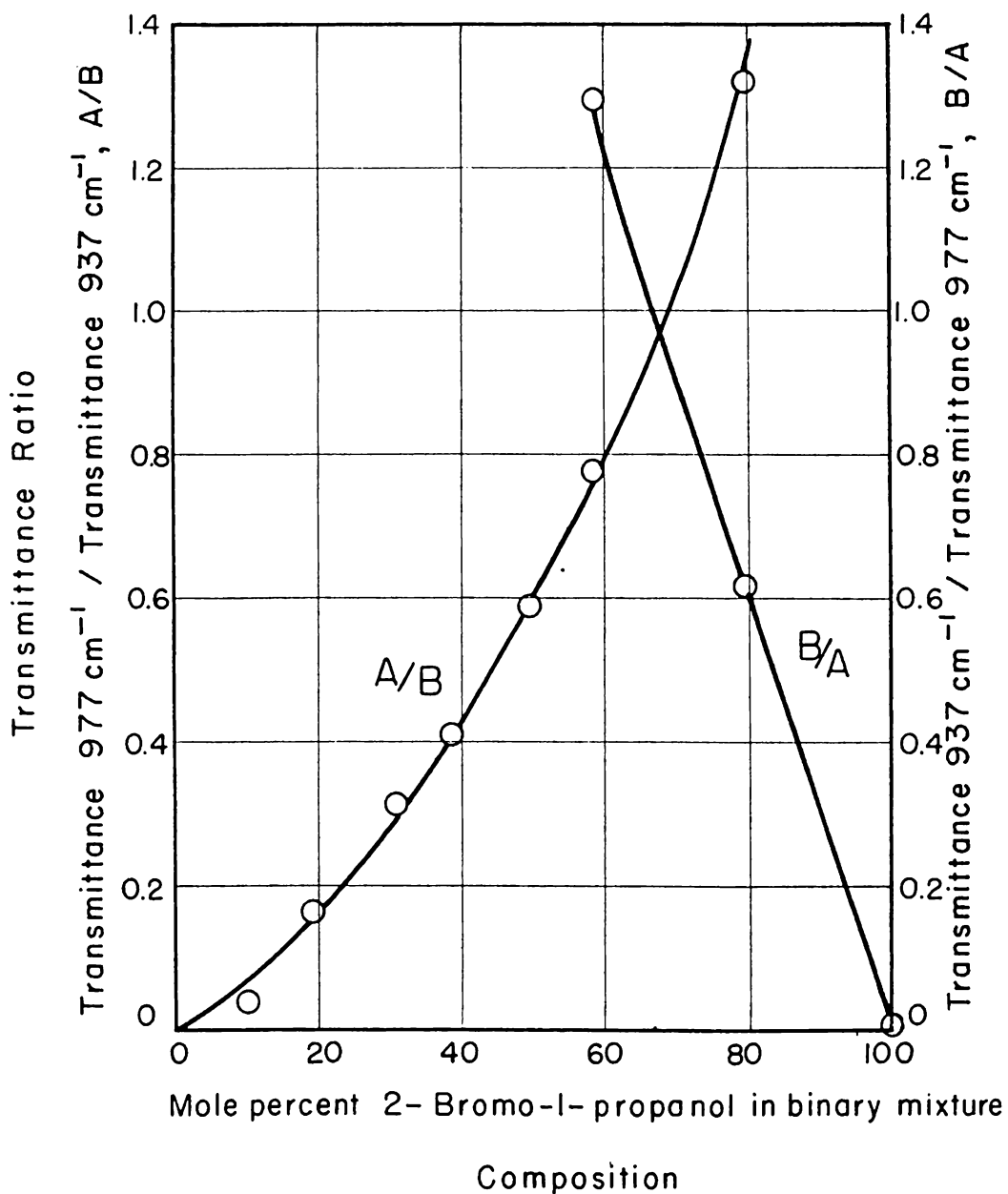
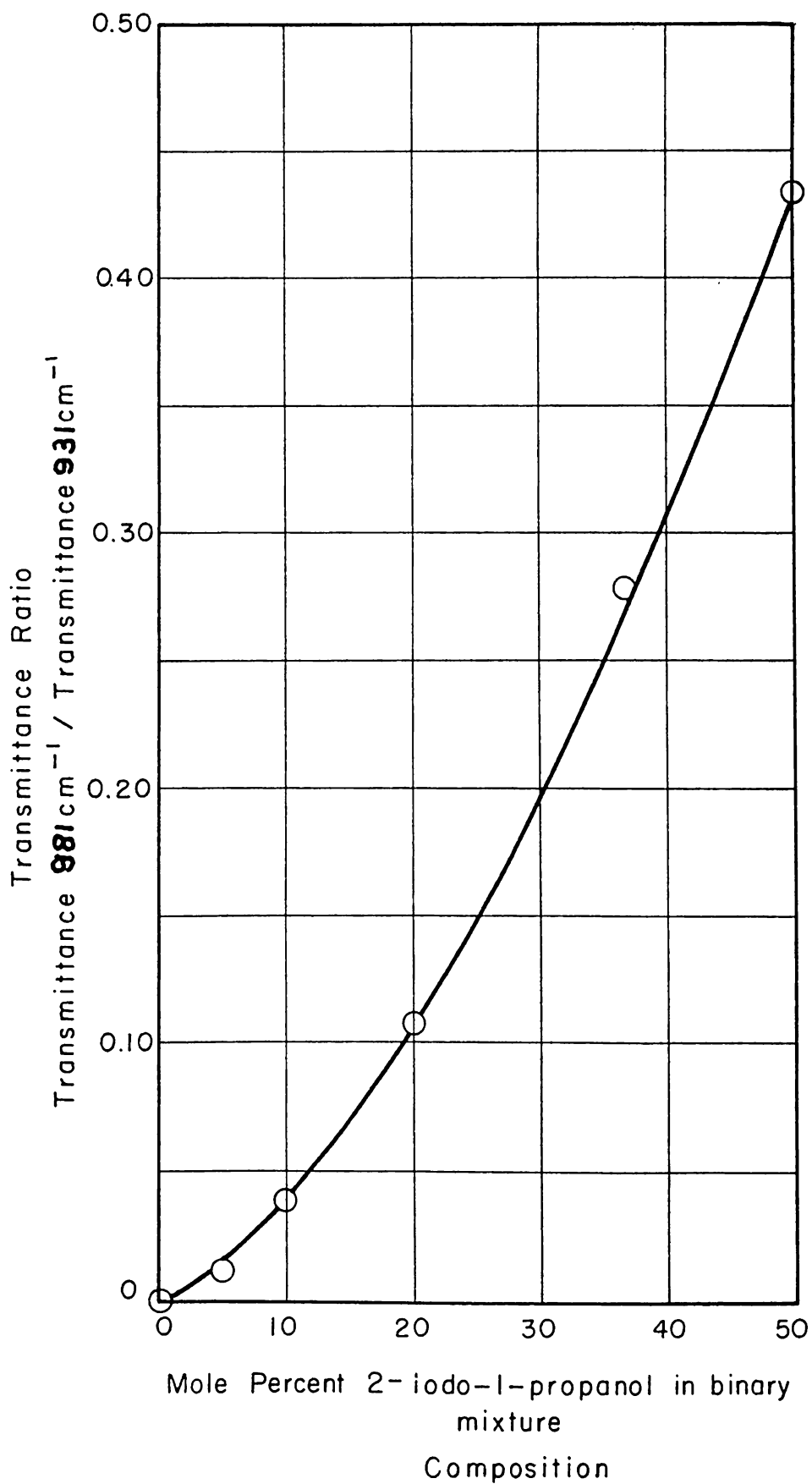


Figure III Calibration Curves for Infrared Analysis of 1-iodo-2-propanol and 2-iodo-1-propanol



As a check on the analytical method, several experimental mixtures of chlorohydrins which had been analysed were diluted with a measured amount of II, so as to bring the composition to approximately 50%, and the composition redetermined. The results, in Table IX below, are an indication of the accuracy of the method.

TABLE IX

## Confirmatory Analysis of Propylene Chlorohydrins

Original Mixture % II found	Synthetic Mixture % II found	calculated	Error %
25.5	48.3	50.1	1.3
19.7	50.2	48.3	1.9
11.0	48.6	49.9	1.3
Average:			<u>1.5</u>

Analysis of mixtures of dinitrobenzoates to be obtained from positive halogen addition reactions were performed in a semiquantitative fashion. The chloro and iodo products showed no trace of a peak given by the corresponding primary ester, and hence were assumed to contain none. The bromopropyl dinitrobenzoates were analyzed by visual comparison of the height of the peak at  $972\text{ cm}^{-1}$  with spectra of synthetic mixtures of 0, 25, 50, 75, and 100% composition of the two esters. The accuracy is very low on these analyses, probably of the order of 10%, although the order is unmistakable from the curves.

#### D. Ring Opening Reactions of Propylene Oxide:

Propylene oxide was allowed to react with hydrogen chloride, hydrogen bromide, or hydrogen iodide under a variety of conditions and the halohydrins so obtained were analyzed by the infrared procedure to determine the isomeric composition. The reaction conditions were:

(a) Fifty milliliters (0.715 mole) of propylene oxide was added to a solution prepared from 56 g. (1 mole) of sodium chloride, 200 ml. of concentrated hydrochloric acid, and 200 ml. of water, held at a specified temperature. The reaction mixture was cooled, extracted with four 100 ml. portions of ether which were combined, dried over sodium sulfate, then over magnesium sulfate, heated on a steam bath to remove ether, and distilled through a forty inch Vigreux column.

(b) Fifty milliliters of propylene oxide and hydrogen chloride were added simultaneously to 400 ml. of ether held at a specified temperature and containing a small amount of thymol blue. The relative rates of addition were adjusted so that the solution was near the yellow-to-red color change of the indicator (pH 2-3 in water). The solution was connected to an aspirator to remove the excess hydrogen chloride added at the end of the reaction, and also the solvent, and the mixture was distilled as in (a).

(c) Fifty milliliters of propylene oxide and anhydrous

hydrogen bromide were allowed to react as in (b). The excess hydrogen bromide and ether were removed on a steam bath rather than under aspiration, and the resulting bromohydrin contained difficultly separable impurities, probably the dibromide.

(d) Fifty milliliters of propylene oxide was added slowly to 125 ml. of concentrated hydrobromic acid at a specified temperature. The reaction mixture was then saturated with sodium chloride and extracted with three 100-ml. portions of ether, and the bromohydrin isolated as in (a).

(e) Twenty-nine grams (0.50 mole) of propylene oxide was added slowly to a solution of 100 ml. of concentrated hydroiodic acid and 100 ml. of water, at a specified temperature. The reaction mixture was saturated with sodium chloride, extracted with three 50-ml. portions of ether, which were combined and dried over sodium and magnesium sulfates, heated on a steam bath to remove the ether, and distilled through a modified Claisen apparatus at reduced pressure.

(f) To a solution of 145 g. (1.5 moles) of ammonium bromide, 50.0 ml (0.715 moles) of propylene oxide, and a trace of methyl orange in 300 ml. of water, concentrated aqueous hydrobromic acid was added at such a rate as to maintain the solution at the indicator change. The product was isolated as in (a).

(g) To the two phase mixture resulting from the reaction between 15 g. (0.615 mole) of magnesium turnings and 80 g. (0.50 mole) of bromine in 400 ml. of dry ether was added

10.0 ml. (1.0 mole) of propylene oxide. The precipitate was filtered, pressed dry, and hydrolyzed with 500 ml. of two normal sulfuric acid. The reaction mixture was worked up as in (a).

(h) Exactly 400 g. of sodium bromide, 50.0 ml. of propylene oxide, and two drops of thymol blue indicator were dissolved in 600 ml. of water. Aqueous acetic acid (40%) was added at such a rate as to keep the solution at the color change (pH 8 in water) of the indicator. The product was isolated as in (a).

The results of the analyses of these products are given in Table X.

To test the possibilities that a change in composition might occur by further reaction of one isomer under the reaction conditions or by distillation, or that isomerization of one compound to the other might occur, the following experiments were performed:

(1) Commercial propylene chlorohydrin (Eastman Kodak, infrared analysis, 75% I) was distilled through the Vigreux column used in isolation of halohydrins from epoxide reactions. An 85% recovery of pure chlorohydrins was found to have a composition of 76% I.

(2) A sample of commercial chlorohydrin (50.0 g.) was substituted for epoxide in procedure (a) above. A 50% recovery of chlorohydrins containing 75% I was obtained.

TABLE VIII RING OPENING REACTIONS OF PROPYLENE OXIDE

Reagent	Solvent procedure	Temp. °C.	Yield %	n <sub>D</sub> <sup>30</sup>	Neutralization Equivalent *	Products		Percent A	Percent B
						A	B		
HCl	Ether (b)	-55	95	1.4350	94.5	I	II	89	11
	"	-27	89	1.4350	95.0	I	II	87	13
	"	12	87	1.4349	95.9	I	II	80	20
	"	35	85	1.4352	95.5	I	II	74	26
	Water(a)	15	40	1.4352	94.9	I	II	62	38
	"	33	64	1.4350	94.8	I	II	63	37
	"	60	64	1.4352	95.0	I	II	62	38
	"	83	54	1.4352	94.5	I	II	57	43
	Acetone(b)	10	87	1.4350	94.8	I	II	84	16
HBr	Ether(c)	-45	98	1.4830	≠	III	IV	92	8
	"	15	100	1.4816	≠	III	IV	85	15
	Water(d)	15	77	1.4772	138.4	III	IV	76	24
	"	35	84	1.4767	138.4	III	IV	74	26
	"	55	77	1.4765	139.0	III	IV	72	28
	"	75	76	1.4765	139.7	III	IV	71	29
MgBr <sub>2</sub>	Ether(g)	35	60	1.4764	139.3	III	IV	84	16
NH <sub>4</sub> Br	Water(f)	30	71	1.4756	—	III	IV	77	23
NaBr	Water(h)	22	43	1.4754	139.2	III	IV	95	5
HI	Water(e)	-10	75	*	*	V	VI	88	12
HI	"	65	75	≠	≠	V	VI	82	18

\* Calculated, C<sub>3</sub>H<sub>7</sub>OCl, 94.5; C<sub>3</sub>H<sub>7</sub>OBr, 139.0; C<sub>3</sub>H<sub>7</sub>OI, 186.0

≠ Impure products (C<sub>3</sub>H<sub>6</sub>Br<sub>2</sub> or iodine)

(3) A mixture of commercial chlorohydrin, 103 g. of sodium bromide, and 0.1 g. sodium iodide were heated on a steam bath for two hours without solvent. The solution was filtered and distilled as before. An 86% recovery of chlorohydrins with a composition of 76% I was made.

(4) Fifty grams of commercial chlorohydrin was heated with 1.0 g. of potassium hydrogen sulfate at 80° for 47 hours. Direct distillation gave 50.0 g. of chlorohydrin with a composition of 76% I.

(5) Seventy-six grams of bromohydrin having a composition of 83.5% III was substituted for epoxide in procedure (c). There was obtained 81.0 g. of product ("106 % yield") which appeared to be contaminated, probably with dibromide, analyzing for 81.5% III.

On the basis of these experiments, it seems safe to assume that the products obtained represent the true composition of products formed by the reactions involved.

#### E. Addition of Positive Halogen Salts of 3,5-Dinitrobenzoic Acid to 1-Propene:

(a) To a slurry of 16.0 g. (0.050 mole) of silver 3,5-dinitrobenzoate in 200 ml. of anhydrous ether, 5.0 ml. (0.1 mole) of chlorine was added while the mixture was cooled in a mush of chloroform and dry ice. After a 10 minute shaking period, commercial propylene was bubbled in until the odor of chlorine disappeared. The reaction mixture was allowed to warm to room temperature, filtered, and the

ether evaporated in a stream of air. The resulting solid was taken up in a minimum of chloroform (in which dinitrobenzoic acid is quite insoluble) and again evaporated to dryness. There was obtained 2.36 g. (16.4% yield) of crude material which showed no trace of the primary ester, VIII, on infrared analysis. This crude material was recrystallized from heptane to yield a product melting at 65.8-73.5° C. Mixture with an authentic sample of VII, gave a melting point of 71.5-74.9° C.

(b) Experiment (a) was repeated using three ml. of bromine (0.06 mole) in place of the chlorine. The crude material from evaporation of chloroform weighed 1.97 g. (12% yield). Again, no trace of the primary ester, X, was found from infrared analysis. Recrystallization from heptane gave a product melting at 73.8-76.8° C. Mixed melting point with IX was 72.5-77.4° C.

(c) Experiment (a) was repeated, using three ml. of bromine and cooling the mixture in an ice bath, rather than the dry ice and chloroform cooling mixture. The 2.8 g. of crude product (17% yield) showed, on infrared analysis, a peak at 972  $\text{cm}^{-1}$  half as high (from the base line) as that in a mixture of 25% X and 75% IX. After recrystallization from heptane, the composition of the dinitrobenzoate appeared unchanged, and the product melted at 57.9-61.6° C. Mixture with IX gave a melting point of 62.6-72.7° C. With X, a mixed melting point of 52.2-60.5 was obtained.

(d) Experiment (c) was repeated using one-half the quantity of each reactant and replacing the ether by 100 ml. of chloroform. There was obtained 4.48 g. (54% yield) of crude material in which the spectrum appeared identical with that of the 25% mixture of X in IX. Recrystallization resulted in no apparent change in isomer composition, giving a product melting at 59.3-81.4° C. The mixed melting point with IX was 59.5-86.2° C, and X was 59.5-63.6° C.

(e) Experiment (c) was repeated with 200 ml. of chloroform substituted for ether and a solution of 0.1 g. of benzoyl peroxide in 25 ml. chloroform added to the slurry just previous to the addition of the propylene. A total of 5.91 g. (36% yield) of crude material, which by infrared analysis appeared to have exactly the same composition as (d) was obtained. The melting point after recrystallization was 59.3-82.2° C. Mixture with IX gave a melting point of 59.5-87.1°, and with X gave a melting point of 59.5-64.5° C.

(f) Experiment (a) was repeated using 0.025 mole of silver salt and of iodine. The product obtained (5.13 g., 54% yield) appeared on the basis of its infrared spectrum to contain no XII. The melting point after recrystallization was 69.5-75.0°, and the mixed melting point with XI was 68.0-77.0° C.

#### Fl Miscellaneous Experiments:

1-Chloro-2-propanol (I) was prepared by the method of Dewael (33), by the sulfuric acid catalyzed hydration of allyl chloride. Varying amounts of product were obtained, with competing formation of

tars. No trace of the isomeric II could be detected.

1-Bromo-2-propanol (III) was prepared by the same method in 11% yield. Infrared analysis of the product, which had been allowed to stand for several months, indicated that it was a mixture containing 91% III and 9% of the isomer, IV.

An attempt was made to prepare I by lithium aluminum hydride reduction of epichlorohydrin. Small amounts of impure chlorohydrin were obtained, but the reaction mixture was too complex to warrant further investigation as a preparative procedure.

1,2-Dichloropropane was heated in a sealed tube with silver 3,5-dinitrobenzoate for varying periods of time, but all attempts to isolate any halohydrin ester were unsuccessful. Similar results were obtained with the sodium salt.

1,2-Dichloropropane was heated to 40-60° for over a month with 0.1 normal base containing a small amount of sodium iodide, but no decrease in the amount of insoluble dihalide was noted.

#### G. Unsuccessful Analytical Methods:

To a solution of 5.00 ml. of chlorohydrin in 10.00 ml. of water was added a sufficient quantity of benzoic acid (about two grams) to saturate the solution. Under these conditions, two liquid layers were formed in addition to the remaining solid benzoic acid. After equilibrating the mixture for about half an hour in the constant temperature bath, a sample of the water-rich upper layer was removed, weighed, and titrated in the cold with 0.1 normal base to the first

end point with thymol blue indicator. The solubility of benzoic acid in this phase seemed to vary considerably, and an attempt was made to devise an analytical method in this way. In Table XI are given the determinations used for calibration, and in Table XII are given some analyses which were later checked by the infrared method:

TABLE XI

## Calibration of Solubility Analysis Method

% I	% II	Weight % $C_6H_5COOH$
100	0	2.58
75	25	2.21
50	50	1.97
25	25	1.76
0	100	1.51

TABLE XII

## Check of Solubility Analysis

Wt. % $C_6H_5COOH$	Composition, Soly. % I	Composition, True % I
3.19	100	100 (a)
2.69	108	89 (b)
2.67	105	87 (a)
2.33	84	83 (b)
2.29	81	75 (b)
1.79	29	75 (b)
1.51	"-25"	63 (a)

- (a) True composition determined by synthesis from pure isomers.  
 (b) True composition determined by infrared analysis.

This method was abandoned, due to the erratic results obtained, and the development of the superior infrared method, ~~method~~.

Analytical distillation was attempted in order to determine the composition of mixtures of isomers. Dry hydrogen chloride gas was passed into 470 g. (8.10 moles) of propylene oxide until no further gain in weight occurred. The reaction temperature varied from 30 to 50° C., and the total gain in weight was 256 gms. (7.2 moles, as HCl). Preliminary distillation directly from the reaction vessel gave 570 g. (75% yield) of crude chlorohydrins, which were distilled through a jacketed fractionation column four feet in length and packed with glass helices. At a pressure of  $607 \pm 3$  mm., the distillation data plotted in Figure XX, and in differential form in Figure XXI, was obtained. Calculation of percentages of isomers indicated that the chlorohydrins so obtained contained 63% I, 37% II, which is not unreasonable, in view of the more accurate work by infrared analysis. Redistillation of the center fraction of the lower boiling material yielded a product which later infrared analysis indicated contained 5-7% of II. Under these conditions, it seems unwise to expect the results of distillation data to be very reliable.

Figure XX

Distillation Curve, Propylene Chlorohydrins

Pressure =  $607 \pm 3$  mm. Hg

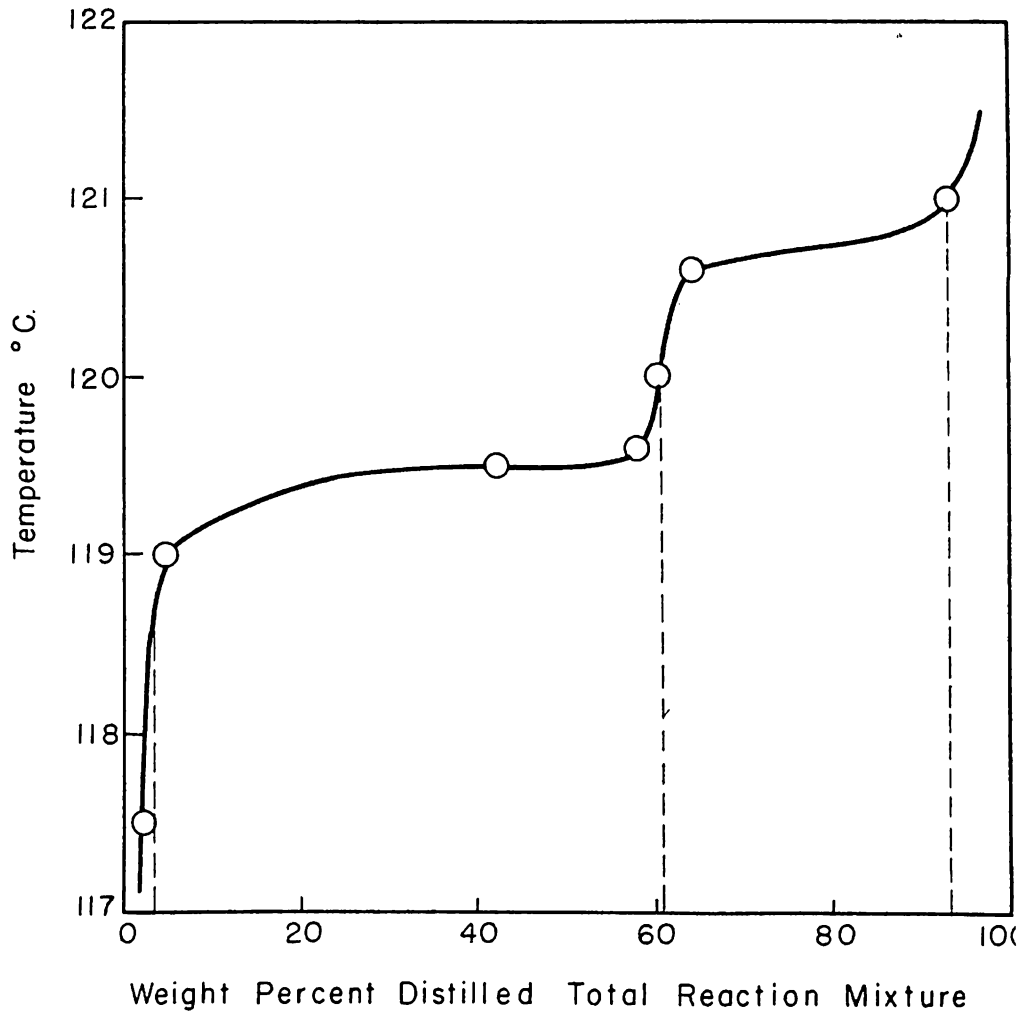
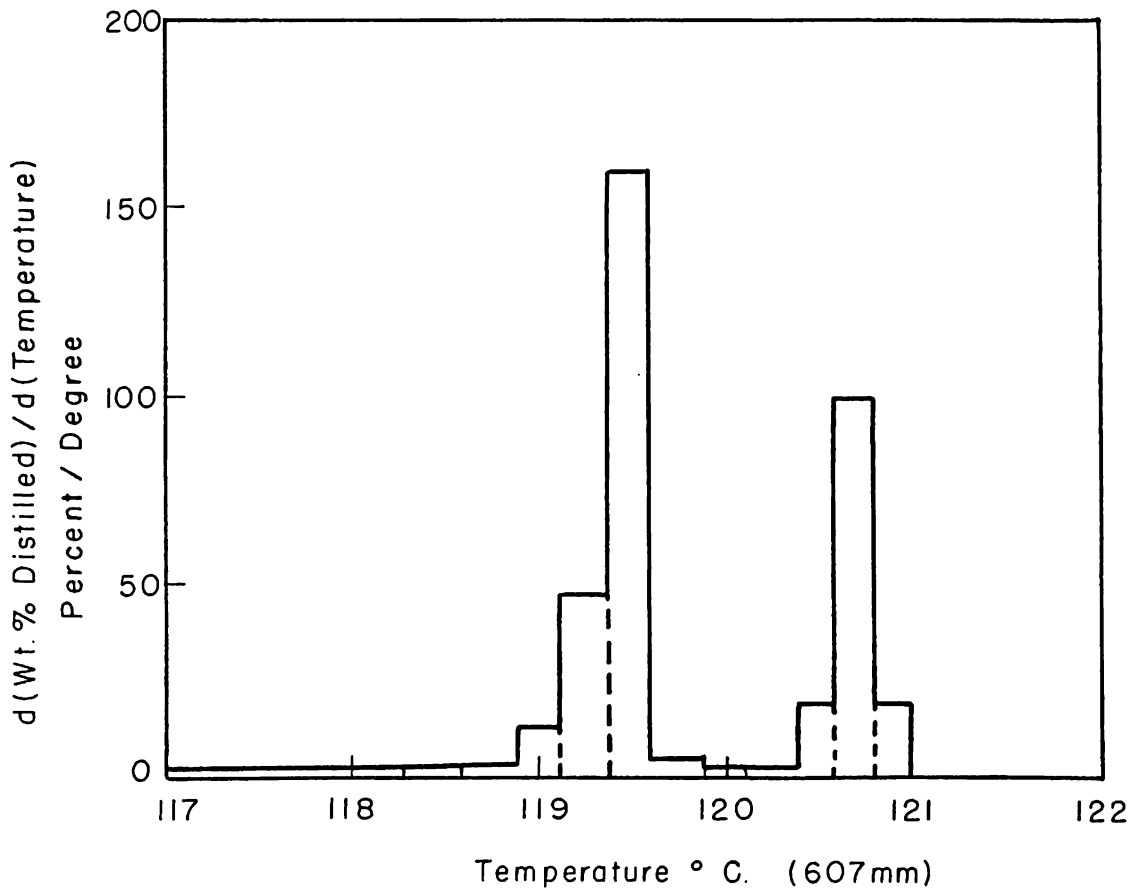


Figure XXI

Differential Curve, Propylene Chlorohydrins

Data from Figure XX



**SECTION V**

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