Part I

THE REACTION OF SODIUM AZIDE WITH SOME EPOXIDES

Part II

THE ATTEMPTED SYNTHESIS OF 2-FLUORO-1,4-NAPHTHOQUINONE

by

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Part I

THE REACTION OF SODIUM AZIDE WITH SOME EPOXIDES
Section I

INTRODUCTION and HISTORICAL BACKGROUND
The Nature of the Attack of Epoxides by Bases

The reactions of epoxides with bases is an example of the general class of bimolecular nucleophilic displacement reactions.\(^1\)\(^2\) The two criteria by which a bimolecular nucleophilic displacement reaction may be recognized, bimolecular kinetics and Walden inversion, have been applied to the reaction of bases with epoxides by several investigators.

Although the number of kinetic studies is limited, two excellent investigations have been carried out. Bronsted, Kilpatrick and Kilpatrick\(^3\) allowed potassium iodide to react with ethylene oxide, glycidol, and epichlorohydrin, titrating the liberated hydroxide ion with strong acid to maintain a constant pH. In each case the rate of the reaction was directly proportional to the concentrations of the epoxide and the iodide present. In another series of experiments these investigators reacted epoxides with buffered solutions containing weak acids and their alkali metal salts, and they again found that the rate of reaction was directly proportional to the concentrations of oxide and of anion. In the range of pH 6-9 the rate was independent of hydrogen ion concentration. Ross\(^4\), following the general scheme of Bronsted et. al., reacted various epoxides with thiosulfate ion in 50% aqueous acetone solution, and again he found the rate to be directly proportional to the concentration.
of epoxide and thiosulfate ion. In the case of both of these investigations the hydroxide ion liberated was continuously titrated to prevent any reversal of the reaction. Thus the reaction between epoxides and anions in neutral to faintly basic solutions is shown to proceed with bimolecular kinetics.

The number of examples of Walden inversion resulting from the reaction of epoxides with bases is considerable. Two clearcut cases of inversion have been observed for the reaction of malonate ion on epoxides. Grigsby, Hind, Chanley and Westheimer\textsuperscript{5} obtained trans-cyclopentane-1-ol-2-malonic ester from the reaction of sodiomalonic ester on cyclopentene oxide, and Newman and VanderWerf\textsuperscript{6} obtained trans-cyclohexane-1-ol-2-malonic ester from the reaction of the same anion with cyclohexene oxide. Several investigators have shown that the reactions of amines with epoxides occur with inversion. McCasland, Clarke and Carter\textsuperscript{7} obtained trans-2-aminocyclohexanol from the reaction of cyclohexene oxide with aqueous ammonia, alcoholic ammonia and potassium amide in liquid ammonia, and McCasland and Smith\textsuperscript{8} converted cyclopentene oxide into trans-2-aminocyclopentanol with aqueous ammonia. Weinsein
and Boschan also obtained trans-2-aminocyclohexanol from cyclohexene oxide and aqueous ammonia in the presence of ammonium chloride. Dickey, Fickett and Lucas working with meso and D(+) epoxybutanes showed that inversion occurred upon reaction with aqueous ammonia. From meso-2,3-epoxybutane they obtained a mixture of D and L threo-3-amino-2-butanol (equation I), and from D(+) -2,3-epoxybutane they obtained L(+) -erythro -3-amino-2-butanol (equation II).

Equation I

\[
\begin{align*}
\text{CH}_3 & \quad \text{H} \\
\text{H} & \quad \text{O} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\end{align*}
\]

\[
\text{NH}_3 \rightarrow \begin{align*}
\text{HO} & \quad \text{CH}_3 \\
\text{H} & \quad \text{O} \\
\text{CH}_3 & \quad \text{H} \\
\text{CH}_3 & \\
\text{H}_2 \text{N} & \\
\text{CH}_3 & \\
\end{align*}
\]

Equation II

\[
\begin{align*}
\text{CH}_3 & \quad \text{H} \\
\text{H} & \quad \text{O} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\end{align*}
\]

\[
\text{NH}_3 \rightarrow \begin{align*}
\text{HO} & \quad \text{CH}_3 \\
\text{H} & \quad \text{O} \\
\text{CH}_3 & \quad \text{H} \\
\text{H}_2 \text{N} & \\
\text{CH}_3 & \\
\end{align*}
\]

In the field of carbohydrate chemistry Fest has given numerous examples of inversion in the reactions of sodium methoxide and ammonia with ethylene oxide type anhydro sugars and their derivatives. Trevoy and Brown have given evidence that the reduction products of 1,2-dimethyl-1,2-epoxycyclopentane and 1,2-dimethyl-1,2-epoxycyclohexane with lithium aluminum hydride possess the trans configuration, although they were unable to furnish unequivocal proof. They point out the analogy between the direction of ring opening in the attack of malonate ion, which is
known to react with epoxides via an $S_N^2$ mechanism, and aluminum hydride ion on styrene oxide and butadiene monoxide as evidence that the reduction of epoxides with lithium aluminum hydride proceeds via an $S_N^2$ mechanism. Swern$^{13}$ has presented a consistent set of reactions to explain the relationships between the stereoisomeric 9,10-epoxy, 9-chloro-10-hydroxy- and 9,10-dihydroxystearic acids which involves as one step the base-catalyzed hydrolysis of both stereoisomeric 9,10-epoxystearic acids to the corresponding glycols with inversion, but he has offered no proof of the configurational relationships involved. There thus exist several unequivocal proofs and other strong indications that the reaction of epoxides with bases involves Walden inversion.

Since the reaction of epoxides with bases meets the two established criteria for a bimolecular nucleophilic displacement reaction there can be little doubt that it is of that type.

B. The Direction of Ring Opening of Unsymmetrical Epoxides with Bases

Any attempt to predict \textit{a priori} in which of two possible directions an unsymmetrical epoxide will open when reacted with a base must take into account the steric and electronic effects which are operative when the base approaches the epoxide molecule along the favored
reaction path. The mechanism of the reaction having been established as being of the $S_N^2$ type, the base will approach one or possibly both of the carbon atoms terminating the epoxide ring at the face of the tetrahedron opposite to the carbon oxygen bond. Although it is not possible on the basis of the experimental work thus far completed to arrive at any definite conclusion regarding the relative importance of steric factors and electronic factors in determining the course of the reaction, a consideration of these effects is nonetheless useful, particularly in designing experiments which will ultimately establish the relative importance of each.

The electronic effects may best be elucidated by considering the generalized case of attack on an epoxide by a base and concentrating attention on the resonance structures contributing to the transition state. The following reaction illustrates this generalized reaction:

\[
\begin{align*}
\text{TRANSITION STATE} \\
\text{Structure I of the three contributing transition state structures pictured above represents the base } B \text{ at slightly greater than normal bonding distance from one of the carbon atoms of an epoxide. A consideration of this}
\end{align*}
\]
structure would lead to the prediction that the negatively charged base $B^-\phantom{0}$ would attack the less electron-rich carbon atom since the energy required for it to enter a region of low electron density would be less than that required for it to enter a region of high electron density.

Structure II represents both the base $B^-\phantom{0}$ and the negatively charged oxygen of the epoxide at slightly greater than normal bonding distance from carbon 2, but neither bonded to it. By considering this structure and the corresponding structure for attack at the other carbon atom it can be seen that the tendency of a base $B^-\phantom{0}$ to attack either carbon 1 or carbon 2 will depend upon the relative stability of the two carbonium ion structures.

Structure III represents the base $B\phantom{0}$ attached to carbon 2 with the negatively charged epoxide oxygen at slightly greater than normal bonding distance from it. A consideration of this structure and of the one in which $B\phantom{0}$ is attached to carbon 1 and the negatively charged oxygen atom to carbon 2 shows that the contribution which these structures make to the transition state will be governed by the relative stabilities of the two anions. It is, however, difficult to say whether a structure in which $B\phantom{0}$ is bonded to carbon 1 and the negatively charged oxygen atom to carbon 2 is more stable than the one in which the two groups are reversed.
The steric effects, as the name implies, have to do with the size and position in space of the groups already joined to the carbon atoms terminating the oxygen bridge of the epoxide and with the size of the attacking base. If the size and position in space of the attached groups are such that they will not permit a base of a particular size to approach along the favored reaction path to within bonding distance of carbon 1 or carbon 2 they can prevent reaction at one carbon atom or at both carbon atoms. They may thus force the reaction to go in one of the two possible manners or not at all.

Having thus considered the effects which may be expected to be of importance in determining the direction of ring opening by bases, let us attempt to evaluate the importance of the several factors by examining the experimental results which have been obtained for the reaction of various epoxides with bases.

Propylene oxide has been reacted with a variety of bases of assorted sizes and types, and attack has in all cases been predominantly or exclusively at the terminal carbon atom. Among the bases which have been used are sodium methoxide,$^{15,16}$ sodiomalonic ester,$^{17}$ sodiocyanacetic ester,$^{18}$ sodioacetoacetic ester,$^{19}$ ethylene diamine,$^{20}$ hydrazine,$^{21}$ sodium ethoxide,$^{15}$ sodium alloxide,$^{22,23}$ amines and ammonia,$^{15,24-29}$ and sodium phenoxide.$^{30}$ In view of the factors already considered either or both of
two explanations seem capable of explaining this predominance of terminal attack by bases. It is possible that the steric requirements of the methyl group are so great that even ammonia and methoxide ion are unable to approach the secondary carbon from the rear and thus must attack the primary carbon if reaction is to occur. In view of what we know of the steric requirements of the methyl group and considering the fact that trimethylethylene oxide and 2,3 epoxybutane react with bases in the normal manner this explanation by itself becomes untenable. From electronic considerations it is possible to reason that if structure I makes a much greater contribution to the transition state than structure II attack by a base would be expected to occur at the terminal carbon atom. The following discussion illustrates this point:

\[
\begin{align*}
\text{Structure I} & \\
\text{for attack at carbon 2} & \\
\text{Structure II} & \\
\text{for attack at carbon 1}
\end{align*}
\]

In structure I the electron release of the methyl group resulting from the carbon hydrogen dipoles causes the electron density of carbon 1 to be
higher than that of carbon 2. This favors the attack of the nucleophilic reagent B at carbon 2. Considering structure II first for attack at carbon 1 and then for attack at carbon 2, we conclude that attack at carbon 1 leads to a contributing carbonium ion structure which may be stabilized by resonance to a greater extent than the carbonium ion structure resulting from attack at carbon 2, which would make attack at carbon 1 more probable.

Since there is at present no way of evaluating the relative contributions of structures I and II to the transition state, no conclusion can be drawn as to the validity of this explanation. It seems likely, however, that some factor other than or in addition to steric factors is necessary to account for the exclusive attack by bases on the primary carbon atom of propylene oxide, and the electronic interpretation given above seems reasonable in view of the small amount of importance usually attached to resonance stabilization through structures involving hyperconjugation in $S_{N2}$ displacement reactions.

1,2-Epoxybutane has been attacked by only one base, so that the direction of ring opening by bases in general can not be stated with certainty. de Montmollin and Matile allowed aqueous ammonia to react with this epoxide, and they obtained as a product 1-amino-2-butanol,
the product resulting from terminal attack. The steric and electronic considerations are in this case very similar to those discussed for propylene oxide, and, reasoning by analogy, attack would be expected to occur predominantly if not exclusively at the terminal carbon.

The reactions of 2-methyl-1,2-epoxypropane (isobutylene oxide) with bases have been more or less thoroughly investigated. Thus attack by ammonia,\textsuperscript{32} amines,\textsuperscript{33-36} α-aminoesters\textsuperscript{37,38} and sodioacetoacetic ester\textsuperscript{18} occurs at the terminal carbon atom to yield the tertiary alcohol as shown in the following equation:

\[
\begin{align*}
\text{CH}_3\text{CCH}_2 + \text{B} & \rightarrow \text{CH}_3\text{CCH}_2 \text{OH} + \text{HO}^{-} \\
\text{CH}_3\text{CCH}_2 \text{OH} & \rightarrow \text{CH}_3\text{CCH}_2 + \text{OH}^{-}
\end{align*}
\]

The steric and electronic effects are in this case very similar to those discussed for propylene oxide, the differences being of degree not of kind. Thus a prediction based on steric factors or on structure I of the transition state would favor terminal attack while a prediction based on structure II of the transition state would favor secondary attack. All effects would be more pronounced than in the case of propylene oxide. The transition states for attack of isobutylene oxide by a base are given below.
Again we may state, therefore, that the experimental fact of exclusive terminal attack by bases is caused by two factors operative either independently or in conjunction with one another; namely, the steric factor and the fact that transition state structure I, which probably contributes more significantly in this case than structure II (a structure showing high charge separation), favors terminal attack.

The attack by bases on 2,3-epoxy-2-methylbutane (trimethylethylene oxide) has been carried out only with amines. In all cases only one product was reported, that resulting from attack at the least substituted carbon. The conditions required to bring about the reaction were quite strenuous; for example, with dimethyleamine the reaction required refluxing for three days at 100° and with aniline the reaction required heating in a sealed tube at 160°-180° for 6-8 hours.
2,3-Epoxy-2,3-dimethylbutane has been attacked only by ammonia,\(^{41}\) the conditions required to carry out the reaction being refluxing for 10 hours at 100° with a ten volume excess of 33% ammonia. The reaction failed at 45°.

The results of the attack of bases on these two epoxides indicate two things: first, as observed previously, attack occurs at the least substituted carbon atom; secondly, the reaction becomes more difficult to carry out as the degree of substitution increases. Whether these results are due to steric factors or to the possibility that structure I makes the most important contribution to the transition state is impossible to determine in these cases.

Glycidol has been allowed to react with ammonia,\(^{42-44}\) amines\(^{42,44,45}\) and alloxide ion,\(^{22}\) and in all cases except the last one attack was exclusively terminal. In the case of the reaction of glycidol with alloxide ion, which reportedly gave 75% terminal attack and 25% secondary attack, the methods of identification of the isomers were inadequate, and some of the results therein reported on the basis of these methods have been proved to be erroneous.\(^{23}\)

The reaction of epichlorohydrin with bases is interesting because three different products may be obtained when attack is terminal depending upon whether one, two or three moles of base are used. It is probable that the reaction occurs in the following manner:
Drozdov and Cherntsov\textsuperscript{46} carried out the following sequence of reactions:

\[
\text{Cl}-\text{CH}_2-\text{CH}-\text{CH}_3 + B - \text{Cl} \rightarrow \text{CH}_2-\text{CH}-\text{CH}_3B + \text{Cl}^-
\]

\[
\text{CH}_2-\text{CH}-\text{CH}_3B + B \rightarrow \text{BCH}_2-\text{CH}-\text{CH}_3B \xrightarrow{\text{H}_2\text{O}} \text{B}-\text{CH}_2-\text{CH}-\text{CH}_3B + \text{OH}^-
\]

Gross\textsuperscript{47} carried out the same series using diethylamine instead of methylamine and obtained the same results, indicating that the reaction does indeed proceed in the manner pictured above. Since in many cases a mixture of the three products are obtained regardless of the amount of base used the first reaction need not go to completion before the second and third commence.

Epichlorohydrin has been allowed to react with ammonia,\textsuperscript{48} amines,\textsuperscript{46,49-59} sodium alloxide,\textsuperscript{22} sodium phenoxide,\textsuperscript{30,60-65} sodium mercaptides,\textsuperscript{66-68} sodium bisulfite,\textsuperscript{67} sodioacetoacetic ester,\textsuperscript{69} sodiomalonic ester,\textsuperscript{69} sodium glycolate,\textsuperscript{70} lithium aluminum hydride,\textsuperscript{12} sodium acetylide,\textsuperscript{71} and in all cases the products of the reaction have been those resulting from terminal attack.
by the base to produce one or more of the generalized products pictured below:

\[
\text{Cl} - \text{CH}_2 - \text{CH} - \text{CH}_3 \quad \text{OH} \\
\text{OH} \\
\text{Cl} - \text{CH}_2 - \text{CH} - \text{CH}_3 \quad \text{OH}
\]

The steric effects in glycidol and epichlorohydrin are similar to those of propylene oxide or 1,2- epoxybutane, and apparently are the dominant factors in determining the direction of ring opening of these compounds by bases. The electronic effects operative in these two molecules may again be elucidated by considering structures I and II of the transition state. Structure I for glycidol and epichlorohydrin are shown below.

\[
\begin{align*}
\text{HO} & \quad \text{CH}_2 & \quad \text{CH} - \text{CH}_3 \\
\text{O} & \quad \text{CH}_2 & \quad \text{CH} - \text{CH}_3 \\
\text{Cl} & \quad \text{CH}_2 & \quad \text{CH} - \text{CH}_3
\end{align*}
\]

It may be seen by looking at these structures that in each case carbon 2 is somewhat deficient in electrons due to the dipole forces existing between carbon 1 and the oxygen and chlorine atoms respectively. The extent to which this effect is transmitted to carbon 2 is difficult to estimate, but considering the fact that both the \text{CH}_2\text{OH} group and the \text{CH}_2\text{Cl} group direct an electrophilic reagent to the ortho and para positions in benzene, and, furthermore, that
they activate the benzene ring to electrophilic substitution it is unlikely that the electron density of carbon 2 is decreased appreciably, if indeed it is changed at all by the presence of these groups. It is thus doubtful that structures of type I make a very significant contribution to the respective transition states of these molecules. The amount of resonance stabilization afforded by structures of type II would not be expected to be significantly greater for attack at carbon 2 than for attack at carbon 3. This is shown by a consideration of the following structures of type II first for attack at carbon 2 and then for attack at carbon 3 for glycidol:

\[
\begin{align*}
\text{A} & : \text{HOCH}_2\text{CH}_2\text{CH}_2 \quad \text{B} : \text{HOCH}_2\text{CH}_2\text{CH}_2 \\
\text{B} & \\
\text{HOCH}_2\text{CH}_2\text{CH}_2 & \\
\text{O} & \\
\text{O} & \\
\end{align*}
\]

and for epichlorohydrin:

\[
\begin{align*}
\text{A} & : \text{Cl-CH}_2\text{CH}_2\text{CH}_2 \\
\text{B} & \\
\text{Cl-CH}_2\text{CH}_2\text{CH}_2 & \\
\text{O} & \\
\text{O} & \\
\end{align*}
\]

There is no particularly good reason for favoring B over A and thus structures of type II would be expected to make about an equal contribution to the transition state whether attack was at carbon 2 or at carbon 3. In view of the
above discussion it seems altogether reasonable to assume
that exclusive terminal attack by bases on these two epoxides
is due largely to steric effects.

1,2-Epoxy-3-butene has been attacked by several
bases, and the point of attack has ranged from exclusively
terminal to exclusively secondary, although the evidence for
the latter is questionable. Russell and VanderWerf\textsuperscript{72}
report exclusive terminal attack by sodiomalonic ester,
and van Zyl and van Tamelen\textsuperscript{73} report the same results with
substituted sodiomalonic esters. Exclusive terminal attack
has likewise been reported by Long\textsuperscript{74} with amino-alcohols,
Gilman and Fullhart\textsuperscript{75} and Massie\textsuperscript{76} with sodium mercaptides,
Kadesch\textsuperscript{77} with sodium methoxide and Petrov\textsuperscript{78,79} with sodium
alkoxides. The reaction of butadiene monoxide with sodium
methoxide has been reinvestigated by Bartlett and Ross\textsuperscript{80}
who obtained an inseperable mixture of 1-methoxy-3-butene-2-ol
and 2-methoxy-3-butene-1-ol.

\[
\begin{align*}
\text{CH}_2=\text{CH}-\text{CH}_2&+\frac{1}{2}\text{NaOCH}_2\xrightarrow{\text{H}_2\text{O}} \text{CH}_2=\text{CH}-\text{CH}_2 + \text{CH}_2=\text{CH}-\text{CH}_2 \\
\text{OH} \quad \text{OCH}_3 & \quad \text{CH}_3\text{O} \quad \text{OH}
\end{align*}
\]

Although they were unable to separate the two isomers
they proved the presence of each by hydrogenating the
mixture, fractionating the products and making the 3,5-
dinitrobenzoates of each of the two saturated ether alcohols.

Ettlinger\textsuperscript{81} reacted butadiene monoxide with ammonia and
obtained 45% of 1-amino-3-buten-2-ol and 7% of 2-amino-3-buten-1-ol.

\[
\text{CH}_2 = \text{CH} - \text{CH} - \text{CH}_2 \rightarrow \text{CH}_2 = \text{CH} - \text{CH} - \text{CH}_2 + \text{CH}_2 = \text{CH} - \text{CH} - \text{CH}_2
\]

Trevoy and Brown\textsuperscript{12} reduced this epoxide with lithium aluminum hydride and obtained 58% 3-buten-2-ol and 13% 3-buten-1-ol. Swern, Billen and Knight\textsuperscript{22} obtained an unspecified yield of what they designated as 2-alloxy-3-buten-1-ol by reaction of butadiene monoxide with sodium alloxide. In view of the methods which they used to identify their products this result should be reinvestigated.

It may be seen by examining the results which have been obtained that the attack of a base on butadiene monoxide occurs primarily at the terminal carbon, but that in contrast to the other epoxides which have been considered the attack also occurs to some extent at the secondary carbon. A possible explanation of this difference may be found by again considering the steric and electronic effects which might be operative.

The steric effects which are operative in this case are about the same as those which exist in propylene oxide or 1,2-epoxybutane, and they naturally favor terminal attack. The difference then must lie in the different electronic effects which obtain in the two cases.
Structure I of the transition state for the attack of a base on butadiene monoxide may be pictured as follows:

\[
\begin{align*}
\text{CH}_2=\text{CH}-\text{CH}^\cdot\text{CH}_2 \\
\text{B}^\cdot
\end{align*}
\]

Although it is difficult to estimate the magnitude of the electron withdrawing effect of the vinyl group it seems reasonable to assume that the oxide ring being a region of high electron density would displace the electron pair of the double bond away from carbon 2 causing it to be somewhat deficient in electrons. To the extent that this effect is transmitted to carbon 3 it too will become electron deficient and attack at carbon 3 by a base will thus be favored. A consideration of structure II for attack first at carbon 3 and then for attack at carbon 4 also leads to the conclusion that attack at carbon 3 would be favored. Thus looking at structure II for the

\[
\begin{align*}
\text{CH}_2=\text{CH}-\text{CH}^\cdot\text{CH}_2 \\
\text{B}^\cdot
\end{align*}
\]

attack at carbon 3

\[
\begin{align*}
\text{CH}_2=\text{CH}-\text{CH}^\cdot\text{CH}_2 \\
\text{B}
\end{align*}
\]

attack at carbon 4
two cases it can be seen that in the case of attack at carbon 3 stabilization through allylic type resonance can occur while in the case of attack at carbon 4 this is not possible. Resonance of the allylic type would be expected to cause greater stabilization than the resonance involving hyperconjugation which we have previously considered, thereby causing structure II to make a greater contribution to the transition state than it does in the examples previously considered. Since both structure I and structure II favor attack at the secondary carbon and since structure II makes a larger contribution to the transition state than it has in the cases previously considered the question might be asked: Why is the attack by a base not predominantly at the secondary carbon atom rather than predominantly at the primary? In answer to this question it should be pointed out that although allylic resonance causes more stabilization than the hyperconjugative type, in the allyl carbonium ion the two contributing structures are exactly equivalent.

\[ \text{CH}_2=\text{CH}^-\text{CH}_\text{aq} \leftrightarrow \text{CH}_a^-\text{CH}=\text{CH}_2 \]

In the case under consideration the contributing structures are not equivalent and they involve a considerable degree of charge separation. In summary then we must conclude that although the electronic effects favor attack at the secondary carbon the stabilization afforded is not sufficient to overcome the steric effects.
Styrene oxide has been reacted with many bases, and the point of attack by the base has ranged from exclusive primary attack to exclusive secondary attack. Terminal attack has been reported with sodiomalonic ester,\textsuperscript{72} substituted sodiomalonic esters,\textsuperscript{73} sodioacetosacetic ester,\textsuperscript{19} ammonia,\textsuperscript{82} amines,\textsuperscript{20,82,83} sodium mercaptides,\textsuperscript{75,76} and lithium aluminum hydride.\textsuperscript{12,84} Attack at both carbon atoms to produce a mixture of isomers has been reported for attack by sodium methoxide,\textsuperscript{85} sodium phenoxide and phenol,\textsuperscript{86,87} and sodium B-naphtoxide.\textsuperscript{87,88} There have been two reported cases of exclusive secondary attack on styrene oxide itself: namely, by alloxide ion\textsuperscript{22} and by azide ion.\textsuperscript{89} Although the former case is open to question, the latter case certainly is not for the product was isolated in 63-68\% yield and its structure proven beyond doubt.

An examination of the results mentioned above shows that the tendency for secondary attack to occur with styrene oxide is greater than with any of the aliphatic ethylene oxides including butadiene monoxide. To explain this fact we must again consider the steric and electronic effects which might be expected to operate.

The steric effects are not very different from those present in the aliphatic ethylene oxides, and they of course favor terminal attack. The electronic effects are quite different from those met with previously, and undoubtedly play a more important role in determining the
direction of ring opening. An examination of structure I of the transition state gives very little information as to the expected direction of ring opening, because the phenyl group may be either weakly electron donating or weakly electron withdrawing and there is virtually no way to determine which behavior it exhibits in this case. The two possibilities are represented as follows:

\[
\begin{align*}
\text{Structure I} & \\
\text{Structure II} & 
\end{align*}
\]

Reasoning as in the case of butadiene monoxide we might presume that since the oxide ring is a region of high electron density the phenyl group would be likely to exhibit electron withdrawing properties making carbon 1 slightly deficient in electrons and favoring secondary attack.

Structure II is more readily interpreted, and definitely favors secondary attack. Structure II first for attack at carbon 1 and then for attack at carbon 2 is as follows:

\[
\begin{align*}
\text{Structure II} & \\
\text{Structure III} & 
\end{align*}
\]
It may readily be seen by examining these structures that the contributing carbonium ion structure arising from attack by the base at carbon 1 is considerably more stable than the one arising from attack at carbon 2 due to resonance stabilization. Although individually structures B, C, and D do not make as great a contribution to the transition state as structure A because there are two equivalent structures represented by A, they nonetheless add to the stability of the carbonium ion structure. Thus structures of type II lead to the prediction of secondary attack, and would be expected to make a considerable contribution to the transition state. Since attack by a base still occurs largely at the terminal carbon atom it appears that the steric effects are still predominant in most cases. It is possible to ascribe the change from predominant terminal attack with certain bases to predominant secondary attack with others to the steric requirements of the bases themselves, but a consideration of the behavior of ammonia, sodium methoxide and sodium azide indicate that size is not the determining factor. Whether the linearity of the azide ion allows it to meet the steric requirements necessary for attack at carbon 1 is a question which is difficult to resolve, but one which should be kept in mind as a possibility.

In order to determine the importance of the electronic effects in aryl ethylene oxides we might examine the experimental results obtained by attacking the following
three epoxides with a base:

\[
\begin{align*}
O_2N &- \begin{array}{c}
\text{CH-CH}_2 \\
\end{array} \\
\begin{array}{c}
\text{CH-CH}_2 \\
\end{array} &- \begin{array}{c}
\text{CH}_3O \\
\text{CH-CH}_2 \\
\end{array}
\end{align*}
\]

Unfortunately the only data available is for attack by different bases under differing experimental conditions. 4-Nitrostyrene oxide was reacted with sodium phenoxide in aqueous solution,\(^{90}\) yielding two parts secondary alcohol and one part primary alcohol and with sodiomalonic ester, yielding exclusively secondary alcohol; styrene oxide when attacked by sodium phenoxide,\(^{86}\) yielded equal parts of primary and secondary alcohols in dioxane solution and three parts primary alcohol, one part secondary alcohol in aqueous solution; styrene oxide when attacked by ethylamine\(^{82}\) and various other amines yielded exclusively secondary alcohol; 3,4-dimethoxystyrene oxide\(^{92}\) yielded a mixture of primary and secondary alcohols in unspecified amounts when attacked by aqueous methylamine. An examination of these results affords no possibility of separating the several steric and electronic effects which control the reaction, and until standardized experiments are conducted on some series designed to emphasize one of these effects, such as the one above, it will be impossible to do more than speculate as to the relative importance of steric and electronic effects in this type of reaction.
1-Phenyl-1,2-epoxypropane has been reacted with hydrazine,\textsuperscript{93} \textit{N,N}-dimethylhydrazine,\textsuperscript{93} and \textit{N,N}-diethylhydrazine,\textsuperscript{93} and in each case only one product was isolated; namely, that arising from attack at the carbon bearing the phenyl group. This may be illustrated for hydrazine by the following equation:

\[
\text{\begin{array}{c}
\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{
(+)- ephedrine  
(-)- epoxide  
mainly (-)- isoeptedrine

These workers then prepared an epoxide or mixture of epoxides from d,l-isoephedrine and reacted these epoxides with methylamine to yield exclusively pseudoephedrine. This series of reactions may be represented as follows:

\[
\text{d,l-isoephedrine} \quad \rightarrow \quad \begin{array}{c}
\text{isoaffrole oxide} \\
\text{was reacted with dimethylamine,}
\end{array}
\]

and yielded exclusively the product resulting from attack at the carbon atom bearing the phenyl group as shown in the following equation:

\[
\text{The results which have been reported with 1-phenyl-1,2-epoxypropane and its derivatives bring out several interesting facts: first, there is a much greater tendency for attack to occur at the carbon adjacent to the phenyl group than in styrene oxide; secondly, whether attack occurs at carbon 1 or at carbon 2 depends on whether the cis}
\]
or trans epoxide is utilized as a starting material. Although the first fact is evident, the reasoning which leads to the second may need clarification. The (+)-epoxide arising from (-)-ephebrine produces, upon treatment with methylamine, some (-)-ephebrine, resulting from attack at carbon 2, but mainly (+)-isoehebrine, resulting from attack at carbon 1. The (-)-epoxide obtained from (+)-ephebrine gave largely (-)-isoehebrine, the result of attack at carbon 1. Since the two epoxides were prepared from the enantiomorphic ephedrines, the reaction involving inversion at carbon 2, and yielded largely the enantiomorphic isoehebrines, the reaction involving inversion at carbon 1, the epoxides must be enantiomorphs, either cis or trans. On the other hand the epoxides obtained from d,l-isoehebrine, the reaction involving inversion at carbon 1, yielded pseudoephebrine upon treatment with methylamine, the reaction involving inversion at carbon 2. These epoxides must have been diastereoisomers of those obtained from the ephedrines, and, whereas the former were attacked largely at carbon 1, the latter were attacked predominantly if not exclusively at carbon 2.

Any explanation of the direction of ring opening of these epoxides must then take into account the different steric factors involved in attack upon the cis epoxides as compared to those involved in attack upon the trans epoxides. By making models of the cis and trans epoxides it is obvious that the steric factors are different, but because any
models which represent accurately the relative size and bond angles of the atoms are by no means sufficiently flexible to allow the distortion of the bond angles necessary to represent the oxide ring, it is not possible to state with any degree of certainty which of the two carbon atoms would be more easily attacked in the cis epoxide and which in the trans. The steric factors in these molecules thus remain unknown quantities.

A consideration of the electronic factors leads to the following conclusions based on the same type of reasoning involved in the discussion of the previous cases: structure I favors attack at carbon 2, while structure II which would be expected to make a considerable contribution to the transition state, favors attack at carbon 1. The contribution of structure II to the transition state should be even greater for isosaffrole oxide and operative in the same direction as in the parent compound.

In summary it may be stated that electronic effects favor attack at the carbon adjacent to the phenyl group, while the steric effects depend upon the configuration of the epoxide, and are not easily estimated.

Stilbene oxide and its derivatives have been attacked by only one base, lithium aluminum hydride, although the reaction has been attempted with other bases. The unreactivity of these compounds toward attack by a base is almost surely due to steric factors since, as has
previously been pointed out, electronic factors would be favorable to such an attack.

To conclude this discussion of the various factors which are important in determining the direction of ring opening of unsymmetrical epoxides by bases it should be stated that in many if not in all cases considered it is difficult to evaluate the relative importance of the various steric and electronic factors which are operative. Here is a fertile field for investigation, where experiments specifically designed to resolve these factors would be most useful in aiding one to predict a priori the direction of ring opening of as yet uninvestigated epoxides with various bases.

C. The Structure of the Azide Ion and Organic Azides

The structure of the azide ion although it has been the subject of considerable controversy is now rather universally accepted as being both linear and symmetrical. It is perhaps best described as a resonance hybrid receiving approximately equal contributions from the following three structures:

\[
\begin{array}{c}
\equiv N \equiv N \equiv N \leftrightarrow \equiv N = N = \equiv N \leftrightarrow \equiv N \equiv N \equiv N
\end{array}
\]
The evidence supporting this view is derived partially from chemical data but principally from physical data. The parallelism which exists between the physical properties of the alkali cyanates and azides,\textsuperscript{97,98,99} plus the fact that the cyanates and azides are isomorphous indicates that they are in all probability isoelectronic. Inasmuch as the cyanate ion has been shown to be linear, it is likely that the azide ion is likewise linear. X-ray diffraction studies on sodium and potassium azide\textsuperscript{100} and Raman spectra studies on the azide ion in solution\textsuperscript{101} showed the ion to be both linear and symmetrical. The distance between either terminal nitrogen atom and the center one in the ionic sodium and potassium azide crystals is $1.15 \pm 0.02$ A.,\textsuperscript{100,102} while the distance calculated on the basis of equal contributions of the three resonance structures pictured above is 1.15 A. This value also agrees with that measured by spectroscopic investigation.

In view of the considerable evidence supporting the linear, symmetrical structure for the azide ion there can no longer be any doubt that it is the correct one.

The structure of the organic azides have likewise been the subject of considerable controversy, and the following three formulas have been proposed and each defended by various investigators on the basis of both physical and chemical evidence:
Formula B was proposed before it became known that nitrogen could not be pentavalent, and may now be eliminated as a possibility on that basis. Although structure C is still not universally accepted, it seems certain that it correctly represents these compounds. The evidence for this structure is almost entirely of a physicochemical nature. A comparative study of the densities, vapor pressures and viscosities of phenyl isocyanate and phenyl azide led Carothers\textsuperscript{103} to the conclusion that the two are isosteric, and thus indicate that phenyl azide is not cyclic. The small values of the dipole moments of organic azides, although interpreted by Sutton\textsuperscript{104} as favoring the cyclic formula have been interpreted by a variety of workers\textsuperscript{105,106,107} as favoring the linear arrangement of the three nitrogen atoms. X-ray studies on cyanuric triazole by Sutton\textsuperscript{108} indicate that in this compound the nitrogen atoms of the azide groups lie in a line parallel to the axis of the carbon atom to which they are attached. These results were verified by Mulliken,\textsuperscript{109} Bragg\textsuperscript{110} and Frevel.\textsuperscript{111} The latter investigator also showed that the three nitrogens are linear in methyl azide. Raman spectra studies by Langseth,
Nielsen and Sorensen\textsuperscript{101} indicate that the linear structure for organic azides is the correct one. Electron diffraction studies by Brockway and Pauling\textsuperscript{112} led them to the following values for the interatomic distances and bond angles in methyl azide:

\[
\text{CH}_3 \quad \text{N} \quad \text{A} \quad \text{N} \quad \text{B} \\
\text{N} \quad \text{N} \quad \text{A} \quad \text{N} \\
\text{CH}_3
\]

These values for A and B agree quite satisfactorily with those calculated (1.24 Å and 1.12 Å) on the basis of equal contributions of the following two resonance structures:

\[
\text{CH}_3 \quad \overset{\ominus}{\text{N}} = \overset{\oplus}{\text{N}} = \overset{\ominus}{\text{N}} \quad \overset{\ominus}{\text{N}} - \overset{\oplus}{\text{N}} = \overset{\ominus}{\text{N}} \\
\overset{\ominus}{\text{N}} = \overset{\oplus}{\text{N}} = \overset{\ominus}{\text{N}} = \overset{\ominus}{\text{N}} - \overset{\oplus}{\text{N}} = \overset{\ominus}{\text{N}} \\
\text{CH}_3
\]

From the evidence given above it seems certain that the organic azides have the three nitrogen atoms in a straight line, and may be satisfactorily represented as a hybrid of the two resonance structures I and II

\[
\text{R} - \overset{\ominus}{\text{N}} = \overset{\oplus}{\text{N}} = \overset{\ominus}{\text{N}} = \overset{\ominus}{\text{N}} - \overset{\oplus}{\text{N}} \equiv \overset{\ominus}{\text{N}} \\
\text{I} \\
\text{II}
\]
D. Nature of the Reaction of Sodium Azide
at a Saturated Carbon Atom

There is little evidence to indicate the nature of the reaction of sodium azide at a saturated carbon atom. The only work which might throw any light on the subject is that of Levene and coworkers in which sodium azide was allowed to react with optically active alkyl halides to yield the corresponding alkyl azides. The reaction proceeds according to the following equation in which X represents chlorine, bromine or iodine:

\[
\begin{align*}
\text{CH}_3 & \quad \text{H} - \text{C} - \left(\text{CH}_2\right)^n - X + \text{NaN}_3 \quad \text{CH}_3OH \rightarrow \\
\left(\text{CH}_2\right)^n - \text{CH}_3 & \quad \text{H} - \text{C} - \left(\text{CH}_2\right)^n - \text{N}_3
\end{align*}
\]

These workers showed that when \( n_1 > 0 \) the optically active halides and resulting azides had the same sign of optical rotation and that the values of these rotations differed only slightly. When, however, \( n_1 = 0 \) the sign of the rotation of the resulting azide differed from that of the starting halide, and the change in value (taking into account the sign) was considerable. Assume that the signs of configurationally related halides and azides are the same (or at least, that the change in value is slight) when the halide which is replaced is attached to an asymmetric carbon atom (\( n_1 = 0 \)) as it has been shown
to be when the replaced halide is attached to a nonasymmetric carbon atom. If this assumption is valid, then one can say that if a change in the sign of rotation occurs when \( n = 0 \), Walden inversion has occurred in the process. These workers showed that in every case of the replacement of a halide attached to an asymmetric carbon atom by an azide group, the sign of the optical rotation changed, and furthermore that the value of the rotation, taking into account its sign, was quite different, whereas the absolute value was changed only slightly.

The assumption which was made is of questionable validity inasmuch as the replacement of a group attached to an asymmetric center would be expected to change the rotation of an optically active molecule to a greater extent than the replacement of a group remote from the asymmetric center. Should the assumption be valid and Walden inversion have occurred in this process, however, then the reaction in all probability takes place via an \( S_N^2 \) mechanism, since Walden inversion is one of the most reliable criteria of bimolecular nucleophilic displacement reactions.

In summary it can be said that the mechanism of the reaction of an azide ion at a saturated carbon atom is still in doubt, but probably is of the \( S_N^2 \) type.
E. Objects of This Research

The objects of this research are to determine the following facts:

1. The mechanism of the reaction of sodium azide with epoxides.
2. The nature of the products of the reaction of sodium azide with epoxides.
3. The direction of ring opening of unsymmetrical epoxides with sodium azide.
Section II

Experimental Part
2-Amino-2-phenylethyl Benzoate Hydrochloride

In a pressure tube of approximately 25 ml. capacity were placed 3.8 g. (0.0151 mole), of 2-benzamido-2-phenylethanol (m.p. 152-155), 10 ml. of absolute ethanol and 6.6 ml. of 5N ethanolic hydrogen chloride. The tube was sealed and heated to 100°, at which temperature it was maintained for four hours. After cooling to 0°, during which a solid crystallized out, the tube was opened, and the yellow white solid was collected by suction filtration. It was recrystallized from ethanol to yield 1.6 g. of white crystals, m.p. 194.6-196.6°(dec.), which was subsequently recrystallized from ethanol to yield 1.2 g. of 2-amino-2-phenylethyl benzoate hydrochloride, m.p. 203.2-204.2°, 31.5% of the theoretical yield. Literature value: m.p. 205-205.5°.114

2-Benzamido-2-phenylethanol

In a 500 ml. pressure bottle were placed 1.0 g. (0.00362 mole), of 2-amino-2-phenylethyl benzoate hydrochloride, 50 ml. of absolute alcohol, 0.206 g. (0.00362 mole) of sodium methoxide, and 0.1 g. of platinum oxide. The bottle was placed on the Parr hydrogenation apparatus, and the contents were shaken with hydrogen at a pressure of 40#/in² for 24 hours. The pressure was released, the catalyst was removed by suction filtration, and the alcohol was removed by distillation in vacuo to yield a white solid.
This solid was recrystallized from a mixture of benzene and low boiling Skellysolve to give 0.9 g. of white crystalline 2-benzamido-2-phenylethanol, m.p. 152.2-154.0°, 90% of the theoretical yield. This product did not depress the melting point of an authentic sample of 2-benzamido-2-phenylethanol.

**trans-2-Azidocyclohexanol**

In a 3 l., 2-necked round bottomed flask were placed 81.3 g. (0.83 mole) of cyclohexene oxide and 1300 ml. of dioxane. The solution was heated to reflux temperature and a solution of 68.0 g. (1.15 mole) of sodium azide in 175 ml. of water was added dropwise. The solution was refluxed for 20 hours, at the end of which time it was cooled to room temperature. During the course of the reaction the solution separated into two layers, and these two layers were separated. The lower aqueous layer was washed with two 50 ml. portions of dioxane and then discarded. The dioxane layers were combined, and the dioxane was removed by distillation. The residue was distilled in vacuo to yield 33.0 g. of water-white liquid, b.p. 85-89°/3mm. This liquid was redistilled in vacuo to give 30.4 g. (26.0%) of trans-2-azidocyclohexanol, a clear liquid, b.p. 70-71°/1-2mm., nD²¹ 1.4950, which solidified upon standing.
**trans-2-Aminocyclohexanol**

In a 500 ml. pressure bottle were placed 14.1 g. (0.1 mole) of 2-azidocyclohexanol, 50 ml. of absolute ethanol and 0.1 g. of platinum oxide, and the solution was shaken with hydrogen at a pressure of 45#/in² for 30 hours. The pressure was released, the catalyst was removed by suction filtration, and the alcohol was removed by distillation. The residue was distilled in vacuo to give 9.3 g. (81%) of trans-2-aminocyclohexanol, b.p. 70°/2mm., which solidified to a white, highly hygroscopic solid. Literature value: b.p. 102-107°/9mm, m.p. 68°. A hydrochloride of trans-2-aminocyclohexanol was prepared in an alcohol-ether mixture, m.p. 174-175.2°, which was recrystallized from alcohol-ether to give a white solid, m.p. 175.6-176.4°. Literature value: m.p. 176-177°.

**Anal. Calc'd for C₆H₁₁NO₃:** C, 51.0; H, 7.85; N, 29.8.

**Found:** C, 50.8; H, 7.75; N, 29.5. (Note 1)

---

From the trans-2-aminocyclohexanol obtained above and α-naphthyl isocyanate a urea-urethane was prepared,

---

**Note 1.** All analyses were carried out by the Clark Micro-analytical Laboratory, Urbana, Illinois, unless otherwise stated.
m.p. 258.7-259°.

Anal. Calc'd for C_{28}H_{27}O_{3}N_{3}: C, 74.2; H, 6.00; N, 9.27.

Found: C, 74.3; H, 5.57; N, 9.22.

trans-2-Benzamidocyclohexyl benzoate was prepared from trans-2-aminocyclohexanol and benzoyl chloride in benzene, which upon three subsequent recrystallizations from high boiling Skellysolve, melted at 206.0-207.2°, 207.0-207.6° and 207.4-207.8°, respectively. Literature value: m.p. 215-216°. A mixed m.p. with an authentic sample (Note 2) of m.p. 207.4-207.8° showed no depression.

Anal. Calc'd. for C_{20}H_{21}O_{3}N: C, 74.3; H, 6.55; N, 4.43.

Found: C, 74.3; H, 6.81; N, 4.30.

**trans-2-benzamidocyclohexanol**

In a 100 ml. round-bottomed flask were placed 3.0 g. (0.021 mole) of trans-2-azidocyclohexanol and 50 ml. of benzene. Benzoyl chloride, 3.0 g. (0.021 mole) was added, and the mixture was refluxed for three days. The solution was then cooled, washed with 10 ml. each of 2% sodium carbonate solution, 2% hydrochloric acid and water, and the benzene was removed by distillation. The liquid

---

*Note 2. Authentic samples were furnished by Dr. G. E. McCasland, University of Toronto, Toronto, Canada.*
residue could not be induced to crystallize nor could it be distilled without decomposition. This residue was dissolved in ethanol, 0.1 g. of platinum oxide was added, and the solution was reduced with hydrogen at a pressure of 45#/in². The catalyst was removed by suction filtration, and the alcohol was removed by distillation. Upon the addition of high boiling Skellysolve to the liquid residue, it solidified to yield 2.0 g. of white trans-2-benzamidocyclohexanol, m.p. 167.8-171°. Upon two subsequent recrystallizations from a mixture of ethanol and low boiling Skellysolve, the melting points were 172.2-174° and 172.0-172.8°, respectively. Literature value: m.p. 175-176°. A mixed m.p. with an authentic sample (Note 2) of trans-2-benzamidocyclohexanol melted at 172.2-173.0°.

**Anal. Calc'd. for C₁₃H₁₇O₂N:** C, 71.2; H, 7.82; N, 6.39.  
**Found:** C, 71.0; H, 7.82; N, 6.32.

**trans-2-Aminocyclohexyl Benzoate Hydrochloride**

In a pressure tube were placed 4.7 g. (0.022 mole) of trans-2-benzamidocyclohexanol (m.p. 171.8-172.4°), 15.5 ml. of absolute ethanol and 9.3 ml. of 5N ethanolic hydrogen chloride. The tube was sealed, heated at 100° for 4 hours, and subsequently cooled to 0°. During the cooling process the contents of the tube appeared to solidify. The tube was opened, and a faintly yellow
crystalline precipitate was collected by suction filtration. This material was recrystallized three times from ethanol to yield respectively, 1.0 g. of white crystalline trans-2-aminocyclohexyl benzoate hydrochloride, m.p. 246.8-249.6°; 0.8 g., m.p. 258.5-260.5°; and 0.7 g., m.p. 265-267.0°. Fodor and Kiss give the melting point of trans-2-aminocyclohexyl benzoate hydrochloride as 263°. A mixed melting point with an authentic sample (Note 2) showed no depression.

**trans-2-Benzamidocyclohexanol**

In a 500 ml. pressure bottle were placed 0.633 g. (0.0027 mole) of trans-2-aminocyclohexyl benzoate hydrochloride dissolved in 100 ml. of absolute alcohol, 0.141 g. of 95% sodium methoxide (0.0027 mole) and 0.1 g. of platinum oxide. The bottle was placed on the Parr hydrogenator, and was shaken under a pressure of 45#/in.² for 36 hours. The catalyst was removed by suction filtration, the alcohol was removed by distillation, and to the residue was added 25 ml. of high-boiling Skellysolve. An oil resulted which was induced to crystallize by scratching the sides of the flask. The solid was collected by suction filtration to yield 0.4 g., m.p. 158-164°. Recrystallization from benzene and high-boiling Skellysolve yielded 0.3 g. of white crystalline trans-2-benzamidocyclohexanol,
m.p. 171.6-172.8°, 47.5% of the theoretical yield. A mixed melting point with an authentic sample (Note 2) showed no depression.

**trans-2-Azidocyclopentanol**

In a 1 l. three-necked round bottomed flask equipped with a reflux condenser and an addition funnel were placed 27.8 g. (0.33 mole) of cyclopentene oxide and 650 ml. of dioxane. The solution was heated to reflux temperature and a solution of 27.2 g. (0.42 mole) of sodium azide in 70 ml. of water was added dropwise. The solution was refluxed for 40 hours, during which time two layers appeared, and it was then cooled to room temperature. The two layers were separated, the water layer was washed with two 20 ml. portions of dioxane, and the dioxane layers were combined. The dioxane was removed by distillation, and the residue was distilled in vacuo to yield 17.0 g. of water white trans-2-azidocyclopentanol, b.p. 72-74°/3mm., 40.6% of the theoretical yield. This product decomposed slightly upon standing at room temperature, and was thus redistilled before being submitted for analysis, b.p. 72.5-74°/3mm., nD 1.4878.

**Anal. Calc'd. for C₅H₉ON₃:** C, 47.2; H, 7.13; N, 33.1.

**Found:** C, 47.7; H, 7.29; N, 33.3.
trans-2-Aminocyclopentanol

In a 500 ml. pressure bottle were placed 5.0 g. (0.0394 mole) of trans-2-azidocyclopentanol, 50 ml. of ethanol and 0.1 g. of platinum oxide. The solution was reduced with hydrogen at a pressure of 46.5#/in.\(^2\) for 36 hours. The catalyst was removed by suction filtration, the alcohol was removed by distillation, and the residue was distilled in vacuo to give 2.0 g. of water white trans-2-aminocyclopentanol, b.p. 107-108\(^\circ\)/17mm., \(n_\text{D}^24\) 1.5010, 48.5% of the theoretical yield. Literature value of trans-2-aminocyclopentanol: b.p. 116-119\(^\circ\)/19mm.\(^{116}\)

Anal. Calc'd. for \(C_5H_{11}NO\): C, 59.2; H, 10.9; N, 13.8.
Found: C, 59.3; H, 10.8; N, 13.8.

A hydrochloride of trans-2-aminocyclopentanol was prepared in alcohol and ether, m.p. 186.8-189.0\(^\circ\). Upon recrystallization from alcohol-ether it melted at 191.6-192.8\(^\circ\), and did not depress the melting point of an authentic sample of trans-2-aminocyclopentanol hydrochloride (Note 2). Literature value: m.p. 193-194\(^\circ\).\(^8\)

trans-2-Azidocyclopentyl Benzoate

In a 500 ml. round-bottomed flask equipped with a reflux condenser were placed 25.4 g. (0.2 mole) of trans-2-azidocyclopentanol, 15.8 g. (0.2 mole) of pyridine, and
100 ml. of benzene. Benzoyl chloride, 30.0 g. (0.21 mole) was added, and the mixture was refluxed for 30 minutes. The white precipitate of pyridine hydrochloride was removed by suction filtration, and the benzene was removed by distillation. The residue was distilled in vacuo to yield 29.1 g. of trans-2-azidocyclopentyl benzoate, b.p. 128-130°/< 0.1mm., 63.0% of the theoretical yield.

**Anal. Calc'd. for C_{12}H_{13}O_{2}N_{3}: C, 62.3; H, 5.67; N, 18.2.**

Found: C, 62.5, 62.7; H, 5.56, 5.59; N, 18.3.

**trans-2-Aminocyclopentyl Benzoate**

In a 500 ml. pressure bottle were placed 10 g. (0.043 mole) of trans-2-azidocyclopentyl benzoate, 100 ml. of ethanol, and 0.1 g. of platinum oxide. The solution was reduced with hydrogen at a pressure of 39#/in.² for 36 hours. The catalyst was removed by suction filtration, the alcohol was removed by distillation, and the residue was distilled in vacuo to yield 5.0 g. of trans-2-aminocyclopentyl benzoate, b.p., 106°/0.06mm., 47.7% of the theoretical yield. A hydrochloride was prepared in alcohol and ether, m.p. 193.0-194.0°.

**Anal. Calc'd. for C_{12}H_{16}O_{2}NCl: C, 59.6; H, 6.67.**

Found: C, 59.6; H, 6.47.
2-Azido-3-butanol

In a 2-l. round-bottomed three-necked flask equipped with a reflux condenser and an addition funnel were placed 59.7 g. (0.83 mole) of 2,3-epoxybutane and 650 ml. of dioxane. The solution was heated to reflux, and a solution of 68.0 g. (1.15 mole) of sodium azide was added dropwise. The solution was refluxed for 24 hours, during which time it separated into two layers, and it was then cooled to room temperature. The two layers were separated, the lower aqueous layer was washed with two 50 ml. portions of dioxane and then discarded, and the dioxane layers were combined. The dioxane was removed by distillation, and the residue was distilled in vacuo to yield two fractions:

I b.p. 80-85°/30 mm. 49.0 g.
II b.p. 70-98°/4 mm. 10.5 g.

Both fractions turned orange upon standing, and they were redistilled through a 10" Vigreux column. Fraction I yielded 46.8 g. of water white liquid, b.p. 81-82°/31 mm., \( n_D^{17.5} 1.4560 \) (III), while fraction II gave the following two fractions:

IV b.p. 82-84°/31 mm. 3.3 g. \( n_D^{17.5} 1.4563 \)
V b.p. 52-78°/4 mm. 4.5 g. \( n_D^{17.5} 1.4599 \)

Fractions III and IV were combined (52.5% of the theoretical yield of 2-azido-3-butanol) and submitted for analysis.
2-Amino-3-butanol

In a 500 ml. pressure bottle were placed 8.0 g. of 2-azido-3-butanol, 50 ml. of ethanol, and 0.1 g. of platinum oxide. The solution was reduced with hydrogen at 40#/in². The catalyst was removed by suction filtration, the alcohol was removed by distillation, and the residue was distilled in vacuo to give 5.0 g. of water white liquid, b.p. 158-163°, n_D 1.4466.

Anal. Calc'd. for C₄H₁₂ON: C, 53.9; H, 12.4; N, 15.7.
Found: C, 52.9; H, 11.9; N, 16.1.

A portion of the liquid, 2.0 g., was reduced again in the same manner, the catalyst and alcohol were removed, and the residue was distilled to give 1.5 g. of d,l-threo-2-amino-3-butanol, b.p. 78-79°/33mm.

Literature value of d,l-threo-2-amino-3-butanol: b.p. 69-70°/20mm.¹⁰

Anal. Calc'd. for C₄H₁₁ON: C, 53.9; H, 12.4; N, 15.7.
Found: C, 54.0; H, 12.2; N, 15.2.
1-Azido-2-propanol

In a 3 l. three-necked round-bottomed flask equipped with a reflux condenser and an addition funnel were placed 48.2 g. (0.83 mole) of propylene oxide and 650 ml. of dioxane. The solution was heated to reflux, and a solution of 68.0 g. (1.15 moles) of sodium azide in 175 ml. of water was added dropwise. The solution was refluxed for 24 hours, during which time it separated into two layers. The two layers were separated, the lower aqueous layer was washed with two 50 ml. portions of dioxane and then discarded, and the dioxane layers were combined. The dioxane was removed by distillation, and the residue was distilled in vacuo to yield the following two water white fractions:

I b.p. 80-82°/32mm. 45.7 g. \( n_D^{17.5} \) 1.4552
II b.p. 83-109°/32mm. 13.4 g. \( n_D^{17.5} \) 1.4510

Both of these liquids decomposed on standing even in sealed ampules and, therefore, could not be analyzed.

I, 30.0 g., and II, 12.0 g., were mixed together and the mixture was dissolved in 250 ml. of ethanol. Platinum oxide, 0.3 g., was added to the solution, and it was reduced with hydrogen at 45#/ln.² The catalyst was removed by suction filtration, the alcohol was removed by distillation, and the residue was fractionated through a 12' packed column to give the following results:
Ia Forerun 3.0 g.
IIa b.p. 157.7-159° 14.8 g. \( n_D^{16} 1.4515 \)
IIIa Residue 11.0 g.

The residue was distilled without a column to give 4.0 g. of slightly colored distillate IVa, b.p. 158-160°, and a tarry residue of 6.8 g. remained in the flask. A thiourea was prepared from IIa and phenyl isothiocyanate in ethanol, m.p. 106.5-107.5°, but attempts to prepare a solid derivative of IVa were unsuccessful.

1-Amino-2-propanol

1-Azido-2-propanol, 10.1 g. (0.1 mole) of fraction I, was dissolved in 50 ml. of ethanol, 0.1 g. of platinum oxide was added, and the solution was reduced with hydrogen at a pressure of 40#/in.² for 24 hours. The catalyst was removed by suction filtration, the alcohol was removed by distillation, and the residue was distilled in vacuo to give 6.0 g. of a colorless liquid (III), b.p. 157-160°, \( n_D^{17} 1.4507, 80\% \) of the theoretical yield. Literature value: b.p. 159.2-159.5°.\(^{117}\)

Anal. Calc’d for C₃H₉ON: C, 50.0; H, 12.1; N, 18.7.

Found: C, 45.2; H, 10.0; N, 23.5.

The following derivatives were prepared from III:
a picrate (in ether), m.p. 140-143°, which was recrystallized from benzene and chloroform, m.p. 142.0-143.0° (Literature value: m.p. 143-144°\(^{117}\)); a thiourea (from ethanol),
m.p. 106.5-107.5°, which was recrystallized from aqueous ethanol without changing the melting point (literature value: m.p. 107-108°;\textsuperscript{118} and a chloroplatinate (in alcohol), m.p. 194.5-197° which was recrystallized from ethanol, m.p. 194.5-197° (literature value: m.p. 195-200°;\textsuperscript{117}, 205-210°;\textsuperscript{118}).

III, 2.0 g., was dissolved in ethanol, 0.1 g. of platinum oxide was added, and the solution was reduced with hydrogen at a pressure of 40#/in.\textsuperscript{2} The catalyst and ethanol were removed as previously described and the residue was distilled \textit{in vacuo} to give 1.2 g. of 1-amino-2-propanol, b.p. 69°/18mm.

\textit{Anal. Calc'd. for C}_3\text{H}_9\text{ON}: C, 50.0; H, 12.1; N, 18.7.

\textit{Found: C, 48.7; H, 11.7; N, 17.8.}

A sample of 1-amino-2-propanol was obtained from Dow Chemical Co. and the following derivatives were prepared from it: a thiourea, m.p. 106.5-108°, mixed m.p. with the thiourea from III showed no depression; a picrate, m.p. 141.0-142.5°, mixed m.p. with the picrate prepared from III showed no depression.

\textbf{1-Benzamido-2-propanol}

In a 50 ml. round-bottomed flask equipped with a reflux condenser were placed 2.0 g. (0.02 mole) of 1-azido-
2-propanol (fraction I), 3.1 g. (0.022 mole) of benzoyl chloride and 15 ml. of pyridine. The solution was refluxed for 1 hour, and then poured into 45 ml. of water. The two layers were separated, the water layer was washed with benzene, the benzene layer was washed with water, and the benzene layers were combined and dried over magnesium sulfate. The drying agent was removed by suction filtration, the benzene and pyridine were removed by distillation, and the residue was dissolved in 50 ml. of ethanol. The ethanolic solution was placed in a pressure bottle along with 0.1 g. of platinum oxide, and the solution was reduced with hydrogen at a pressure of 40#/in.² The catalyst was removed by suction filtration, the alcohol was removed by distillation, and the residue was distilled in vacuo to yield 2.0 g. of colorless liquid, b.p. 152-155°/<0.1 mm., which partially solidified. This partial solid was recrystallized from a mixture of benzene and high boiling Skellysolve to yield 1.8 g. of white crystalline solid, m.p. 89.6-90.8°. Another recrystallization from the same mixed solvent gave 1.4 g. of 1-benzamido-2-propanol, m.p. 92.2-92.8°. (Literature value: m.p. 92-93°)¹²⁰

Anal. Calc'd for C₁₀H₁₃O₂N: C, 67.0; H, 7.31; N, 7.82.

Found: C, 67.0; H, 7.45; N, 7.88.
1-Azido-2-methyl-2-propanol

In a 3 l. two-necked round-bottomed flask equipped with a reflux condenser and an addition funnel were placed 60.6 g. (0.83 mole) of 1,2-epoxy-2-methylbutane (isobutylene oxide) and 1300 ml. of dioxane. The solution was heated to reflux temperature, and a solution of 68.0 g. (1.15 moles) of sodium azide in 175 ml. of water was added dropwise. The solution was refluxed for 28 hours, during which time it separated into two layers. The two layers were separated, the lower aqueous layer was washed with two 50 ml. portions of dioxane and then discarded, and the dioxane layers were combined. The dioxane was removed by distillation, and the residue was distilled in vacuo to give 31.2 g. of water white liquid, b.p. 41-46°/5mm. This product was redistilled to give the following results:

<table>
<thead>
<tr>
<th></th>
<th>b.p. 75.5-78°/32mm.</th>
<th>25.9 g.</th>
<th>n_2^2 1.4504</th>
<th>26.8% of theory</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>b.p. 79-84°/32mm.</td>
<td>2.2 g.</td>
<td>n_2^2 1.4492</td>
<td></td>
</tr>
<tr>
<td>Residue</td>
<td>3.5 g.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fraction I was submitted for analysis.

Anal. Calc'd for C_4H_9ON_3: C, 41.7; H, 7.88; N, 36.5

Found: C, 41.6; H, 7.95; N, 36.3

1-Amino-2-methyl-2-propanol

In a 500 ml. pressure bottle were placed 8.0 g. (0.0695 mole) of 1-azido-2-methyl-2-propanol, 50 ml. of
ethanol, and 0.1 g. of platinum oxide. The solution was reduced with hydrogen at a pressure of 45#/in.² for 24 hours. The catalyst was removed by suction filtration, the alcohol was removed by distillation, and the residue was distilled in vacuo to yield 3.4 g. of water white 1-amino-2-methyl-2-propanol (IV), b.p. 148.5-151.5°, 57% of the theoretical yield. Literature value: b.p. 150.5-151.5°. 32

**Anal. Calc'd for C₄H₁₁NO:** C, 53.9; H, 12.4; N, 15.7.
Found: C, 53.8; H, 12.4; N, 15.8.

A hydrochloride was prepared from the free base in ether, and was recrystallized from alcohol-ether to give a very hygroscopic white solid, m.p. 74-75°. Literature value for 1-amino-2-methyl-2-propanol hydrochloride m.p. 70-72°. 121 A picrate was prepared from the free base in ether, m.p. 133-134.5° and was recrystallized from benzene and chloroform, m.p. 133-134°. Literature value: m.p. 165-175°. 122

**Anal. Calc'd for C₁₀H₁₄O₈N₄:** C, 37.7; H, 4.33; N, 17.6.
Found: C, 37.7; H, 4.32; N, 17.3.

A thiourea was prepared from the free base in alcohol, m.p. 135.0-136.0°, and was recrystallized from aqueous ethanol without changing its melting point.
Literature value: m.p. 136-137°.122

1-Amino-2-methyl-2-propanol was prepared from isobutylene oxide and ammonia, and the following derivatives were prepared: a thiourea, m.p. 135.5-136.5°; a picrate, m.p. 133.5-134.5°. Mixed melting points of these derivatives with the corresponding derivatives prepared from the free base obtained from reduction of 1-azido-2-methyl-2-propanol showed no depression.

2-Amino-2-methyl-1-propanol was obtained from Commercial Solvents Company, and a thiourea was prepared from the free base, m.p. 127.0-128.5°. A mixed m.p. with the thiourea prepared from IV melted at 111.0-117.0°. A solid picrate could not be prepared from this amine.

1,3-Diazido-2-propanol

In a 3 l. round-bottomed three-necked flask equipped with a reflux condenser and an addition funnel were placed 76.8 g. (0.83 mole) of epichlorohydrin and 650 ml. of dioxane. The solution was heated to reflux temperature, and a solution of 136.0 g. (2.30 moles) of sodium azide in 350 ml. of water was added dropwise. The solution was refluxed for 22 hours, during which time it separated into two layers. The two layers were separated, the lower aqueous layer was washed with two 100 ml. portions of dioxane and then discarded, and the dioxane layers were combined. The dioxane was removed by distillation, and the
residue was distilled in vacuo to yield the following three fractions:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>B.p.</th>
<th>Weight</th>
<th>nD</th>
<th>¹H₂₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>85-87⁰/3mm</td>
<td>56.9 g</td>
<td>17.5</td>
<td>1.5060</td>
</tr>
<tr>
<td>II</td>
<td>87-104⁰/3mm</td>
<td>8.0 g</td>
<td>&quot;</td>
<td>1.5044</td>
</tr>
<tr>
<td>III</td>
<td>106-116⁰/0.6mm</td>
<td>2.0 g</td>
<td>&quot;</td>
<td>1.4935</td>
</tr>
</tbody>
</table>

Residue which decomposed on attempted distillation 10.2 g.

Fraction I was submitted for analysis.

Anal. Calc'd for a diazido compound, C₃H₆O₂N₆:

C, 25.4; H, 4.26; N, 59.1.

Found: C, 25.5; 25.7; H, 3.46, 3.49; N, 59.0.

The sample was submitted to a different analyst (Note 4) for another hydrogen determination.

Found: H, 4.51, 4.33.

Fraction II was dissolved in 100 ml. of ethanol, 0.1 g. of platinum oxide was added, and the solution was reduced with hydrogen at a pressure of 45#/in.² The catalyst was removed by suction filtration, and most of the ethanol was removed by distillation. The residual oil was dissolved in ethanol and an excess of 5N ethanolic hydrogen chloride was added. A gray white precipitate appeared, which was collected by suction filtration and triturated with alcohol, m.p. 181.6⁰ (with decomposition). A mixed m.p. with an authentic sample of 1,3-diamino-2-

Note 4. This analysis was performed by the Oakwold Laboratories, Alexandria, Virginia.
propanol dihydrochloride showed no depression. The yield of 1,3-diamino-2-propanol dihydrochloride based on fraction II (assuming it to be 1,3-diazido-2-propanol) was 50%, 4.6 g. Fractions I and II represent 55% of the theoretical yield of 1,3-diazido-2-propanol.

**1,3-Diamino-2-propanol**

In a 500 ml. pressure bottle were placed 10.0 g. (0.07 mole) of 1,3-diazido-2-propanol (fraction I), 100 ml. of ethanol and 0.2 g. of platinum oxide. The solution was reduced with hydrogen at a pressure of 40#/in.² for 48 hours. The catalyst was removed by suction filtration, the alcohol was removed by distillation and the residue was distilled in vacuo to yield 6.7 g. of water white liquid, b.p. 93-95°/3mm. (V).

**Anal. Calc'd for C₃H₁₀ON₂:** C, 40.0; H, 11.2; N, 31.1.

**Found:** C, 31.3; H, 6.69; N, 47.5.

A dihydrochloride was prepared from a small amount of V with ethanolic hydrogen chloride in ethanol, m.p. 179.2° (with decomposition), which upon trituration with ethanol melted at 182.8° (with decomposition). Literature value for 1,3-diamino-2-propanol dihydrochloride: m.p. 175-177°123 and 184.5°124 A portion of V, 2.6 g., was reduced catalytically in the same manner as before, and the product
was distilled to yield 1.0 g. of colorless liquid.

**Anal. Calc'd. for C₃H₁₀O₂N₂:** C, 40.0; H, 11.2.

**Found:** C, 40.5; H, 11.2.

A dihydrochloride was prepared from the free base in ethanol, m.p. 183.0° (with decomposition), which after trituration with alcohol melted at 183.2° (with decomposition). A picrate was prepared in ether from the free base, m.p. ca. 220° (with decomposition), which upon recrystallization from benzene and chloroform melted at 236-237° (with decomposition). Literature value: m.p. 240-241° (with decomposition). A dihydrochloride was prepared from Eastman Kodak 1,3-diamino-2-propanol with ethanolic hydrogen chloride in ethanol, which, after trituration with ethanol, melted at 183.2° (with decomposition). A mixed melting point with each of the dihydrochlorides of the reduction products of 1,3-diazido-2-propanol showed no depression.

**Reaction of Sodium Azide and Butadiene Monoxide**

In a 2 l. round-bottomed three-necked flask equipped with a reflux condenser and a dropping funnel were placed 58.1 g. (0.83 mole) of butadiene monoxide and 610 ml. of dioxane. The solution was heated to reflux, and a solution of 55.3 g. (0.85 mole) of sodium azide in 150 ml. of water was added dropwise. The solution was refluxed
for 16 hours during which time it separated into two layers. The mixture was then cooled, the two layers were separated and the water layer was washed with 50 ml. of dioxane. The dioxane layers were combined and the dioxane-water azeotrope removed by distillation. (Note 5) When the temperature of the vapor reached 98°, the distillation was discontinued and the solution was allowed to cool. Fractionation of the distillate resulted in the recovery of 6.0 g. of unreacted butadiene monoxide. A dioxane solution of the products remained in the stillpot, and was carried on to the next step.

Reduction of the Reaction Product of Sodium Azide and Butadiene Monoxide with Lithium Aluminum Hydride  (Note 6)

In a 2 l. round-bottomed three-necked flask equipped with a mechanical stirrer, an addition funnel, and a reflux condenser to the top of which was attached a bubble counter, were placed 31.6 g. (0.83 mole) of lithium aluminum hydride and 250 ml. of anhydrous ether. The solution was heated to reflux, and the dioxane solution of the reaction product of sodium azide and butadiene monoxide was added at such a rate as to maintain a moderate rate of reflux.

Note 5.  An attempt to remove all of the dioxane by distillation in a previous run resulted in a violent explosion.

Note 6.  Treatment of the reaction product of sodium azide and butadiene monoxide with hydrogen at 45# / in.\(^2\) in the presence of platinum oxide resulted in incomplete reduction.
The solution was stirred for 1 hour after addition was complete, at which time moist ether was added to destroy the excess lithium aluminum hydride, followed by 50 ml. of water to hydrolyze the salt complex. The solution was then cooled, and the salts were removed by suction filtration. The ether, water, and dioxane were then removed from the filtrate by distillation, and the residue was distilled in vacuo to give the following fractions:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>b.p.</th>
<th>Mass (g)</th>
<th>nD^12.5</th>
<th>b.p.</th>
<th>% of theory</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>81-82°/14 mm</td>
<td>11.6</td>
<td>1.4470</td>
<td>1.4470</td>
<td>18%</td>
</tr>
<tr>
<td>II</td>
<td>83-112°/14 mm</td>
<td>7.5</td>
<td>1.4907</td>
<td>1.4907</td>
<td>11.5%</td>
</tr>
<tr>
<td></td>
<td>(95% b.p. 110-112°)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>96°/4.5 mm</td>
<td>1 c.c.</td>
<td>(yielded 1.3 g. of oxalate)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residue</td>
<td></td>
<td>9.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Small portions of fractions I and II and all of fraction III were separately dissolved in alcohol and each was treated with an alcoholic solution of oxalic acid to give the following oxalates.

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Crude m.p.</th>
<th>1st recryst. m.p.</th>
<th>2nd recryst. m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>141-152°</td>
<td>155.8-157.8°</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>166.8-171.0°</td>
<td>174.4-175.6°</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>170-172°</td>
<td>174.6-175.6°</td>
<td></td>
</tr>
</tbody>
</table>

A mixed m.p. of Ia and an authentic sample of 2-amino-3-butene-1-ol neutral oxalate did not show any depression.

Note 7. Authentic samples of the neutral and acid oxalates of 1-amino-3-butene-2-ol and 2-amino-3-butene-1-ol were supplied by Dr. M. G. Ettlinger, The Rice Institute, Houston, Texas.
Mixed melting points of IIa and IIIa with authentic samples of 1-amino-3-butene-2-ol neutral oxalate$^8_1$ and acid oxalate$^8_1$ (Note 7) and 2-amino-3-butene-1-ol neutral oxalate$^8_1$ and acid oxalate$^8_1$ all showed large depressions.

In a 500 ml. pressure bottle were placed 6.0 g. (0.069 mole) of 2-amino-3-butene-1-ol (fraction I) dissolved in ethanol and 0.1 g. of platinum oxide. The solution was reduced with hydrogen at a pressure of 45#/in.$^2$ for 24 hours (pressure drop 4.5#/in.$^2$) (Note 8). The catalyst was removed by suction filtration, the alcohol was removed by distillation, and the residue was distilled in vacuo to yield 5.0 g., 81.3% of the theoretical, of colorless 2-amino-1-butanol, b.p. 51-53°/3mm. A picrate, m.p. 104-126°, was prepared in ether; recrystallized from benzene and chloroform it melted at 127.0-129.0°. A picrate, m.p. 127.6-128.8°, was also prepared from Commercial Solvents 2-amino-1-butanol in ether and was recrystallized from benzene and chloroform, m.p. 128.4-129.2°. A mixed m.p. of the two picrates showed no depression.

In a 500 ml. pressure bottle were placed a solution of 4.0 g. of fraction II and 0.1 g. of platinum oxide. The solution was reduced with hydrogen at a pressure

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Note 8. A 9#/in.$^2$ pressure drop at 45#/in.$^2$ corresponds to an uptake of 0.1 mole of hydrogen.
of 45#/in.\(^2\) (pressure drop 4.0#/in.\(^2\)). The catalyst was removed by suction filtration, the alcohol was removed by distillation, and the residue was distilled \textit{in vacuo} to yield 3.0 g. of a colorless liquid, IV, b.p. 94-96\(^\circ\)/9-10 mm., \(n^D_2\) 1.4573. Literature value for 4-amino-1-butanol: b.p. 100\(^\circ\)/15 mm., \(126 n^D_2\) 1.4581,\(^{127}\) 72\% of the theoretical yield. A picrate was prepared in ether, m.p. 77-85\(^\circ\), and was recrystallized from benzene and chloroform, m.p. 86.6-88.6\(^\circ\).

1-Amino-2-butanol was prepared from 1,2-epoxy-butane and 28\% ammonia in 66\% yield, b.p. 70\(^\circ\)/12 mm. Literature value: b.p. 75-77\(^\circ\)/12 mm. A picrate was prepared in ether, m.p. 124.0-125.6\(^\circ\), and was recrystallized from benzene and chloroform, m.p. 124.5-125.6\(^\circ\). A mixed m.p. with the picrate prepared from IV showed a large depression.
Section III

Discussion of Experimental Results
It has been shown in this research that the reaction of styrene oxide with sodium azide described by Conrad\(^\text{89}\) is not an isolated reaction, but rather it is but one example of a general reaction between sodium azide and epoxides. Since the reaction was a new one in organic chemistry, it warranted further investigation. The reaction has been carried out with cyclohexene oxide, cyclopentene oxide, 2,3-epoxybutane, propylene oxide, isobutylene oxide, epichlorohydrin, and butadiene monoxide. The nature of the reaction has been demonstrated, the structure of the products have been proven, and the direction of ring opening of unsymmetrical epoxides with azide ion has been shown.

Since it was obviously impossible to carry out the reaction of sodium azide with all the known epoxides, a few were chosen which were considered to be representative of various types. The choice was made largely on the basis of their usefulness in supplying certain pieces of information. Cyclohexene oxide and cyclopentene oxide were utilized in order to show whether or not inversion occurred, and whether, if the products were cyclic, as it was thought they might be when this work was undertaken, any difference in the nature of the products could be discerned. It was thought that the relatively greater stability of a trans fusion between two six membered
rings over that of a six and a five membered ring might permit the former to exist as a cyclic compound of the oxatriazine type (I) whereas the latter would probably be an open chain compound, II.

![Diagram](image)

It has since been shown that both products were azido-alcohols, so that the question is no longer important from the viewpoint of the structures of the original products, but it is all-important in determining whether or not the corresponding aminobenzoates will rearrange to benzamido-alcohols.

Propylene oxide, isobutylene oxide, and epichlorohydrin were chosen to determine the point at which attack by the azide ion would occur. The latter was also chosen in order to determine whether one or two azide groups would be incorporated into the final product.

Butadiene monoxide was chosen because previous work had shown that, like styrene oxide, it may be attacked by bases at either the primary carbon atom or at both the primary and secondary carbon atoms. Conrad has shown that the azide ion attacks styrene oxide exclusively at the secondary carbon atom, and it was thus of interest to
determine whether the same results would be obtained when sodium azide was allowed to react with butadiene monoxide.

It is felt that a sufficient number and variety of epoxides were utilized in this work to establish the generality of the reaction.

It has been shown by other investigators on the basis of second order kinetics and the occurrence of Walden inversion that the reaction of bases with epoxides is a bimolecular nucleophilic displacement reaction. Although no kinetic studies were carried out in this investigation, the occurrence of Walden inversion was demonstrated for the reaction of cyclohexene oxide and cyclopentene oxide with sodium azide. The fact that Walden inversion did occur indicates very strongly that the azide ion, in common with other bases, reacts with epoxides via an $S_N2$ mechanism.

Conrad$^{89}$, on the basis of benzoylation and reduction studies, provisionally assigned either of the two following structures to the reaction product which he obtained by reacting sodium azide with styrene oxide:

\[ \text{III} \]

\[ \text{IV} \]

He reasoned that benzoylation of III followed by catalytic reduction would produce 2-benzamido-2-phenylethanol, which
he did in fact obtain, whereas, if the same series of reactions were carried out with 2-azido-2-phenylethanol the product obtained would be 2-amino-2-phenylethyl benzoate. The fact that acyl groups are notoriously prone to migrate, 7,8,115,128 however, suggested that an O to N migration of the benzoyl group might have occurred during the hydrogenation. If such a migration could be demonstrated in this particular case, the only serious objection to the azidoalcohol structure for this compound would be eliminated. By treatment of 2-amino-2-phenylethyl benzoate hydrochloride with an equivalent amount of sodium methoxide in ethanolic solution under a hydrogen pressure of 45#/in.² in the presence of platinum oxide it was possible to produce 2-amino-2-phenylethyl benzoate in a medium nearly identical to that in which it possibly existed after reduction of 2-azido-2-phenylethyl benzoate. Under these conditions rearrangement did indeed occur, for the product isolated was 2-benzamido-2-phenylethanol. This fact coupled with the fact that the infrared absorption spectra of Conrad's product showed the two principal absorption bands characteristic of the azide grouping at 4.65-4.7 and 7.9-8.1 microns¹²⁹ indicates very strongly that the correct structure for the reaction product of sodium azide and styrene oxide is 2-azido-2-phenylethanol.
Infra-red Absorption Spectrum of 2-Azido-2-phenylethanol

The same kind of a rearrangement was carried out with trans-2-aminocyclohexyl benzoate to yield trans-2-benzamidocyclohexanol. Since the latter compound was produced by benzoylation and subsequent reduction of the reaction product of cyclohexene oxide and sodium azide, it seemed expedient to show that in this case also this compound could be produced by the reduction of the azido benzoate and subsequent rearrangement.

It is of interest that trans-2-aminocyclopentyl benzoate obtained by the reduction of trans-2-azido-cyclopentyl benzoate does not rearrange to trans-2-benzamidocyclopentanol under the conditions of catalytic hydrogenation, and can be purified by distillation. The O→N rearrangement of 1,2-aminobenzoates has been explained by Fodor and Kiss\textsuperscript{115} and Welsch\textsuperscript{130} as occurring via a cyclic
intermediate as shown in the following scheme:

\[ \text{Intermediate Scheme} \]

In the case of trans-2-aminoclopropentyl benzoate the formation of such an intermediate would involve the trans-fusion of two five-membered rings, and although such a fusion has been reported\(^{13}\), other workers\(^5\) have shown that such a situation is unfavorable, and very rarely achieved. The failure of trans-2-aminoclopropentyl benzoate to undergo rearrangement strengthens the postulation of a cyclic intermediate in the \(0 \to N\) migration of acyl groups. The infrared absorption spectra of the reaction products of cyclohexene oxide and sodium azide and cyclopentene oxide and sodium azide show characteristic absorption regions at 4.8 microns, slightly displaced from the 4.65-4.7 micron range of other azides, and at 7.9 microns, in common with the other azides which have been investigated.
Infra-red Absorption Spectrum of trans-2-Azidocyclohexanol

On the basis of these results, the following structures are assigned to these products and, by analogy, to the products from the reaction of sodium azide with the other epoxides which have been obtained:
It is now possible to present a reaction mechanism which is totally consistent with all the known facts. The facts which must be taken into account are:

- the structure of the azide ion,
- the structure of the organic azides,
- the fact that the rate determining step is a bimolecular displacement reaction involving epoxide and azide ion,
- the structure of the final product and the release of hydroxide ion as the reaction proceeds.

The following reaction scheme, illustrated with cyclohexene oxide and consistent with these facts, represents the probable course of the reaction:

\[
\text{Trans or Backside Attack}
\]

\[
\begin{align*}
\text{Cyclohexene} & + \left[ \text{\(N\equiv N\)} \right] \\
\downarrow & \\
\text{Product} & \\
\end{align*}
\]
The azidoalcohols which have been prepared are moderately stable compounds, although most of them upon standing for considerable periods of time decompose somewhat. Explosions occurred with two of these products; namely, 1,3-diazido-2-propanol, which exploded when an attempt was made to reseal an ampule in which it was contained, and the azidobutenols, which exploded when an attempt was made to remove the last traces of dioxane from the reaction mixture. In general, however, they are quite safe to handle.

The reaction of sodium azide with propylene oxide, isobutylene oxide, and epichlorohydrin produced the products which were expected on the basis of analogy with other base displacement reactions on these epoxides. The only product which could be isolated was that resulting from the attack of the azide ion at the terminal position. Thus propylene oxide gave 1-azido-2-propanol, isobutylene oxide gave 1-azido-2-methyl-2-propanol, and
epichlorohydrin gave 1,3-diazido-2-propanol. Although the yields were not sufficiently high to claim exclusive primary attack, no other products could be isolated, and since there is no reason for assuming that one of the isomers would be destroyed by side reactions any faster than the other, the results obtained certainly indicate that the attack occurred predominantly at the primary carbon atom. Since there are no bona fide cases on record in which basic attack on these epoxides has occurred at any position other than the primary carbon, it is not at all surprising that such is the case with the azide ion.

The case of epichlorohydrin, from which the only product isolated was 1,3-diazido-2-propanol, warrants further discussion inasmuch as there are several other products which might have been predicted on the basis of previous work. It might be expected, for example, that 1-azido-3-chloro-2-propanol and 1-azido-2,3-epoxypropane would have been produced along with 1,3-diazido-2-propanol. Neither of these compounds could be isolated, however, even when the mole ratio of sodium azide to epoxide was less than 2:1. That they were not formed cannot be definitely stated, but if they were they either reacted further or were simply not isolated by the method used.

The case of butadiene monoxide is of particular interest because previous work with this epoxide has shown
that attack by bases occurs largely at the terminal carbon atom, whereas in the case of attack by azide ion the attack occurs largely at the secondary carbon atom. The reaction is also of interest because, in addition to the $S_N2$ reaction which occurs at the secondary carbon atom, another reaction occurs either simultaneously or subsequently which gives rise to a type of product which has not been previously observed in the reaction of bases and butadiene monoxide.

That the attack by azide ion occurs largely at the secondary carbon atom is in line with the attack of azide ion on styrene oxide in which the product of secondary attack was isolated in 63-68% yield, while no product resulting from primary attack could be isolated. From the discussion of the transition states given in the introduction it can be seen that the electronic factors favor secondary attack in both of these cases, and, furthermore, that the resonance stabilization afforded for secondary attack is considerable.

The isolation of 4-amino-1-butanol resulted by reduction of the original reaction mixture with lithium aluminum hydride, fractionation of the products into two fractions, and catalytic reduction of the higher-boiling of these fractions (II). It is altogether probable that II was 4-amino-2-butene-1-ol inasmuch as it produced 4-amino-1-butanol upon reduction with the uptake of only
one mole of hydrogen. (Had the product been 2-hydroxy-3,4-pyrroline or 2-amino-2,5-dihydrofuran reduction to 4-amino-1-butanol, if it occurred at all, would have required two moles of hydrogen.) There are several ways in which 4-amino-2-butene-1-ol could have arisen. The most likely one is via an $S_n^2$ reaction between the azide ion and butadiene monoxide and subsequent reduction of the 4-azido-2-butene-1-ol produced with lithium aluminum hydride. This reaction may be depicted as follows:
The occurrence of an $S_N^2$ reaction, although it has no precedent in the reaction of bases with epoxides, has been frequently observed in the reaction of substituted allylic halides with bases. Thus, Kepner, Weinstein and Young$^{132}$ treated 3-chloro-1-pentene with sodiomalonio ester and obtained 2-pentenyl malonic ester. The reaction was pictured as follows:

\[
\begin{align*}
\text{Cl} & \quad \text{OEt} \\
\text{CH}_3-\text{CH}_2-\text{CH} & \text{CH}-\text{CH}_2 + \text{OEt} & \rightarrow & \text{CH}_3-\text{CH}_2-\text{CH} & \text{CH}-\text{CH}_2-\text{CH} \\
\end{align*}
\]

Young, Webb and Goering$^{133}$ allowed $\alpha$-methylallyl chloride to react with diethylamine and triethylamine, and they obtained N-diethyl-$\alpha$-methylallylamine and $\alpha$-methylallyl-triethylammonium chloride, as pictured below:

\[
\begin{align*}
\text{Et}_2\text{NH} & \rightarrow \text{CH}_3-\text{CH}=\text{CH}-\text{CH}_2-\text{N}(\text{Et})_2 + \text{Et}_3\text{NHCl} \\
\text{Et}_3\text{N} & \rightarrow \text{CH}_3-\text{CH}=\text{CH}-\text{CH}_2-\text{N}(\text{Et})_2 \text{Cl} + \text{Et}_3\text{NCl} \\
\end{align*}
\]

These reactions were found to have second-order kinetics, and in the case of $\alpha$-methylallyl chloride, it was shown that the halide was stable to rearrangement under the conditions of the reaction, thus precluding a rearrangement
previous to the substitution reaction. The reaction of butadiene monoxide with sodium azide to yield 4-azido-2-butene-1-ol probably proceeds in a similar manner.

The other possible ways in which 4-amino-2-butene-1-ol could have arisen involve an allylic rearrangement. Either 1-azido-3-butene-2-ol or 2-azido-3-butene-1-ol could conceivably have undergone an allylic rearrangement to produce 4-azido-2-butene-1-ol, which upon reduction with lithium aluminum hydride would produce 4-amino-2-butene-1-ol. This may be shown as follows:

\[
\begin{align*}
\text{CH}_2=\text{CH}-\text{CH}-\text{CH}_2\text{N}_3 & \rightarrow \text{CH}_2=\text{CH}-\text{CH}-\text{CH}_2\text{N}_3 \leftrightarrow \text{CH}_2=\text{CH}-\text{CH}-\text{CH}_2\text{N}_3 \rightarrow \text{HOCH}_2-\text{CH}=\text{CH}-\text{CH}_2\text{N}_3 \\
\text{OH} & + \text{OH}^\ominus \quad \leftrightarrow \quad \text{OH}^\ominus + \text{CH}^\ominus
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2=\text{CH}-\text{CH}-\text{CH}_2\text{OH} & \rightarrow \text{CH}_2=\text{CH}-\text{CH}-\text{CH}_2\text{OH} \leftrightarrow \text{CH}_2=\text{CH}-\text{CH}-\text{CH}_2\text{OH} \rightarrow \text{NaCH}_2-\text{CH}=\text{CH}-\text{CH}_2\text{OH} \\
\text{N}_3 & + \text{N}_3^\ominus \quad \leftrightarrow \quad \text{N}_3^\ominus + \text{N}_3^\ominus
\end{align*}
\]

Although the reactions just pictured are possibilities, it is very doubtful that they occur in this particular case. Allylic rearrangements are brought about by acid conditions, whereas the reaction between azide ion and butadiene monoxide and the subsequent reduction of the initial reaction products with lithium aluminum hydride took place in a strongly alkaline medium. (The coordination
of Li⁺ with the oxide oxygen could, however, aid allylic rearrangement in the latter reaction.) The reaction of butadiene monoxide with sodium azide may then be summarized by the following equations:

\[
\begin{align*}
\text{CH}_2 - \text{CH} - \text{CH} &= \text{CH}_2 + \text{NaN}_3 \\
\text{CH}_2 - \text{CH} &= \text{CH} - \text{CH}_2
\end{align*}
\]

There are certain general facts which have made themselves apparent in the course of this research. The azide ion is a very strong base toward carbon, and it is not easily displaced once it is attached to carbon. Perhaps because of its linearity, it seems more efficacious than any base as yet utilized in attacking the secondary carbon of epoxides in which the transition state for attack at the secondary carbon atom is considerably stabilized by resonance. The reaction of sodium azide with epoxides suggests itself as a reasonably good method of preparing primary aminomethanol, with no danger of contamination with secondary and tertiary products.
Section IV

Suggestions for Further Work
The following suggestions for further work are offered:

1. A standard series of reactions should be carried out between sodium azide and p-nitrostyrene oxide, styrene oxide and p-methoxystyrene oxide in an attempt to study the effect of electronic factors while keeping the steric factors relatively constant.

2. A standard series of reactions should be carried out between sodium azide and 4-methyl-1,2-epoxy-3-butene, 4,4-dimethyl-1,2-epoxy-3-butene, and butadiene monoxide in an effort to determine the effect of substitution at the 4 position on the yield of the product arising from an $S_N^2$ reaction.
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Part II

THE ATTEMPTED SYNTHESIS OF 2-FLUORO-1,4-NAPHTHOQUINONE
Section I

Introduction
Following the work of Helin\textsuperscript{1} who prepared 2-trifluoromethyl-1,4-naphthoquinone, an analog of Menadione (Vitamin K\textsubscript{3}), as a potential hemorrhagic or antihemorrhagic agent, it was of interest to attempt the preparation of 2-fluoro-1,4-naphthoquinone on the chance that it would show physiological properties either similar to or opposed to Menadione (2-methyl-1,4-naphthoquinone). The basis for anticipating that 2-fluoro-1,4-naphthoquinone might act similarly to Menadione is the principle of isosterism\textsuperscript{2,3} which, stated briefly, holds that molecules or groups possessing the same number of valence electrons have similar properties.

Since the methyl and fluoride groups are isosteres, 2-fluoro-1,4-naphthoquinone might then be expected to be an active antihemorrhagic. On the other hand the principle of drug antagonism\textsuperscript{4} holds that similarly constituted substances may have apposing actions in the body. This theory is based on the principle that a synthetic and a natural substance of similar composition have opposite physiological actions on the body either because of their competition for active sites or because of the tendency for the synthetic substance to substitute for the natural
metabolite as a building block, coenzyme, or prosthetic
group without being able to be further transformed into a
product utilizable by the body. On the basis of this
theory and, more concretely, on the basis of the fact
that 2-chloro-1,4-naphthoquinone is indeed a hemorrhagic
agent 2-fluoro-1,4-naphthoquinone might also be expected
to be a hemorrhagic.

The synthesis of this compound was undertaken,
and the attempted methods of synthesis are described in
the experimental section.
Section II

Experimental Part
Attempted Synthesis of 2-Fluoro-1,4-Benzquinone

**Route I**

\[
\begin{align*}
\text{C-OC}_2\text{H}_5 + \text{NH}_2 & \xrightarrow{\text{HCl}} \text{C-OC}_2\text{H}_5 \\
\text{NaNO}_2 + \text{NaBF}_4 & \xrightarrow{\Delta} \text{66.5\\%} \text{C-OC}_2\text{H}_5
\end{align*}
\]

**Method A**

\[
\begin{align*}
\text{C-OC}_2\text{H}_5 + \text{NH}_4\text{OH} & \xrightarrow{80\\%} \text{C-OC}_2\text{H}_5 \\
\text{NaOCl} & \xrightarrow{58\\%} \text{NH}_2
\end{align*}
\]

**Method B**

\[
\begin{align*}
\text{C-OC}_2\text{H}_5 & \xrightarrow{(1) \text{NaOH} \ (2) \text{HCl}} \text{C-OC}_2\text{H}_5 \\
\text{H}_2\text{SO}_4 \ (2) \text{NaOH} & \xrightarrow{92\\%} \text{Fuming} \text{HNO}_3 \xrightarrow{56\\%} \text{NH}_2
\end{align*}
\]
2-Carbomethoxybenzenediazonium fluoborate

In a 2 l. stainless steel beaker equipped with an efficient stirrer and a low temperature thermometer and cooled in an ice salt bath were placed a mixture of 275 ml. (3.3 moles) of concentrated hydrochloric acid (sp. gr. 1.18), 300 ml. of water and 35 g. of methyl anthranilate. The mixture was cooled to -5°, and addition of sodium nitrite in the form of moist balls was begun. Additional quantities of methyl anthranilate were added from time to time to maintain an excess of this reagent until a total of 200 g. (1.3 moles) had been introduced. After a total of 90 g. (1.3 moles) of sodium nitrite had been added, stirring was continued for one half hour at which time a solution of 283 g. (2.6 moles) of sodium fluoborate in 400 ml. of water was added all at once. The mixture was stirred for an additional hour, and the precipitate was collected by suction filtration. The precipitate was washed successively with 150 ml. of cold water, 200 ml. of cold alcohol and 200 ml. of cold ether, and was air dried for 24 hours to give 299.3 g. (90% of the theoretical) of 2-carbomethoxybenzenediazonium fluoborate as a white powder.

Methyl-2-fluorobenzoate

In a 1 l. r.b. flask equipped with a condenser set for downward distillation was placed 299.3 g. of
2-carbomethoxybenzenediazonium fluoborate. The powder was heated with a small flame until no more solid remained, and then the melt was heated strongly until no more liquid distilled over. The distillate was diluted with 200 ml. of water, the oil and water layers were separated, and the water layer was extracted with three 200 ml. portions of ether. The ether and oil layers were combined, dried over anhydrous magnesium sulfate, and the ether was removed by distillation. The residue was distilled in vacuo to give 120.3 g. (66.5% of the theoretical) of methyl-2-fluorobenzoate, b.p. 86°/12 mm. Literature value: b.p. 89°/15 mm.¹

2-Fluoroaniline

Method A

2-Fluorobenzamide

In a 2 l. pressure bottle were placed 230.3 g. (1.52 moles) of methyl 2-fluorobenzoate and 1150 ml. of 28% ammonium hydroxide, and the mixture was shaken for six hours. The voluminous mass of white crystals was collected by suction filtration and washed with 200 ml. of water to yield 167 g. (80% of the theoretical) of 2-fluorobenzamide, m.p. 117.0-117.5°. Literature value: m.p. 117.2-117.8°.¹
2-Fluoroaniline

To a solution of sodium hypochlorite at 0°, formed by passing the chlorine generated from 4.2 moles of hydrochloric acid and 82 g. (0.52 mole) of potassium permanganate into 1650 ml. of 10% sodium hydroxide, was added 165 g. (1.25 moles) of 2-fluorobenzamide. The solution was allowed to warm to room temperature and to stand for 24 hours, whereupon it was distilled with steam. The oil and water layers were separated, and the water layer was extracted with three 400 ml. portions of ether. The oil and ether layers were combined, dried over anhydrous sodium sulfate, and the ether was removed by distillation. The residue was distilled in vacuo to yield 77.5 g. (58% of the theoretical) of 2-fluoroaniline, b.p. 62-63°/12mm. Literature value: b.p. 62-63°/12mm.¹

Method B

2-Fluorobenzoic acid

Methyl 2-fluorobenzoate, 357.5 g. (2.32 moles) was hydrolyzed with sodium hydroxide according to the procedure described in Org. Syn., Coll. Vol. I, 391 for the hydrolysis of methyl m-nitrobenzoate. Acidification with hydrochloric acid resulted in the appearance of white crystals of 2-fluorobenzoic acid which were collected by suction filtration, washed with water, and dried at 105° to give 300 g. of white crystals, 92.5% of the theoretical
yield. A small sample of these crystals recrystallized from 1% hydrochloric acid melted at 124-125°. Literature value: m.p. 126.5°.

2-Fluoroaniline

In a 2 l. flask equipped with a mechanical stirrer, a thermometer, a reflux condenser and a solid addition funnel were placed 1050 g. (10.7 moles) of concentrated sulfuric acid and 300 g. (2.14 moles) of 2-fluorobenzoic acid (not recrystallized). The solution was heated to 50° and 150 g. (2.31 moles) of solid sodium azide was added slowly. The solution was maintained at 50-65° for four hours and was allowed to stand overnight at room temperature. The solution was then poured on to ice, and the resulting solution was made basic with sodium hydroxide and subsequently distilled with steam. The oil and water layers were separated, the water layer was extracted with three 200 ml. portions of ether, and the oil and ether layers were combined and dried over anhydrous sodium sulfate. The ether was removed by distillation, and the residue was distilled in vacuo to give 141 g. (59% of the theoretical) of 2-fluoroaniline, b.p. 61-62°/11-12mm.

2-Fluoroacetanilide

In a 1 l. r.b. flask equipped with a reflux condenser was placed a solution of 141 g. (1.27 moles) of
2-fluoroaniline in 500 ml. of benzene. To this solution was added slowly 145 g. (1.4 moles) of acetic anhydride. The benzene and excess acetic anhydride were removed by distillation under vacuum and the solid which remained was recrystallized from ethanol to yield 178 g. (92% of the theoretical) of 2-fluoroacetic anhydride, m.p. 78.0-79.2°C.

Literature value: m.p. 80°C.6

2-Fluoro-4-nitroacetanilide

In a 500 ml. r.b. flask equipped with a reflux condenser and a solid addition funnel was placed 300 ml. of fuming nitric acid (sp. gr. 1.48-1.50) cooled to 0°C. 2-Fluoroacetanilide, 50 g. (0.252 mole) was added at such a rate as to maintain the temperature at 0°C. The solution was allowed to warm to room temperature and was then poured into ice water, whereupon a copious yellow precipitate appeared. The precipitate was collected by suction filtration, washed with 150 ml. of water, and dried in vacuo at 65°C. The yellow solid was then recrystallized from ethanol to yield 36.1 g. (56% of the theoretical) of 2-fluoro-4-nitroacetanilide, m.p. 204.6-206.2°C.


Found: C, 48.7; H, 3.67; N, 13.9.
Diacetyl-2-fluoro-1,4-diaminobenzene

A suspension of 15 g. (0.078 mole) of 2-fluoro-4-nitroacetanilide in 50 ml. of acetic anhydride was placed in a 500 ml. pressure bottle, and 0.2 g. of platinium oxide was added. The bottle was placed on a Parr hydrogenator and the mixture was reduced at an initial pressure of 45#/in.² with an infra red lamp as a source of heat. The hydrogen uptake was 20.5#/in.², 97% of the theoretical. The product was dissolved in 2 l. of methanol, the catalyst was removed by filtration, and some of the solvent was removed from the filtrate by distillation. The methanolic solution was then cooled to yield 10.6 g. (61% of the theoretical) of diacetyl-2-fluoro-1,4-diaminobenzene, m.p. 262-264°. A 2 g. sample was re-crystallized from methanol to yield 1.5 g. of white crystalline material, m.p. 264.5-266°.

Anal. Calc'd. for C₁₀H₁₁O₂N₂F:  C, 57.1; H, 5.27; N, 13.3.
Found: C, 57.2; H, 5.26; N, 13.1.

2-Fluoro-1,4-diaminobenzene dihydrochloride

To a 250 ml. r.b. flask equipped with a mechanical stirrer and a reflux condenser containing 50 ml. of 95% ethanol and 25 ml. of concentrated hydrochloric acid was added 8.6 g. (0.041 mole) of diacetyl-2-fluoro-1,4-diaminobenzene. The mixture was refluxed for two hours
during which time a precipitate appeared. The precipitate was collected by suction filtration, washed with 25 ml. of cold ethanol and dried in a vacuum desiccator to yield 7.3 g. of white solid. Recrystallization from 95% ethanol yielded 4.1 g. (45% of the theoretical) of white solid, m.p. 225.4-226.4°.

Anal. Calc'd for $C_6H_9N_2Cl_2F$: C, 36.2; H, 4.58; Cl, 35.6.
Found: C, 36.7, 36.6; H, 5.16, 5.16; Cl, 35.4.

Before analytical data on this compound had been received an attempt was made to convert it to 2-fluoro-1,4-benzoquinone by liberation of the free base, dissolving it in aqueous sulfuric acid and oxidizing the solution with sodium dichromate. Approximately 0.1 g. of yellow powder which turned black upon standing in a vacuum desiccator for two hours was isolated. No physical properties could be obtained nor could any quinone be obtained by vacuum sublimation.

**Attempted Preparations of 2-Fluoro-1,4-benzoquinone**

The hydrolysis of 15 g. (0.0715 mole) of diacetyl-2-fluoro-1,4-diaminobenzene was attempted with a 38% solution of sulfuric acid at 100°. The suspended solid originally present dissolved and the solution was filtered and cooled to 8°. Benzene (280 ml.) was added and a solution of 26 g. (0.085 mole) of sodium dichromate in
47 ml. of water was added with stirring at such a rate as to maintain the temperature below 10°. After two hours of stirring a partial separation of the benzene and water layers was effected. The benzene layer was dried over Drierite, and the benzene was removed by distillation under reduced pressure. To the residue was added 200 ml. of high boiling Skellysolve, but cooling in an acetone dry ice bath and subsequent removal of the solvent gave only a minute quantity of residue. Hydrolysis under the same conditions and oxidation at 28-30° likewise produced no quinone.

Diacetyl-2-fluoro-1,4-diaminobenzene, 23.0 g. (0.11 mole), was suspended in 235 g. of water, and 20 ml. of concentrated sulfuric acid was added. The mixture was heated under reflux until a clear solution resulted. This was cooled and yielded 20.6 g. of crystalline material (presumably mostly 2-fluoro-1,4-diaminobenzene hydrosulfate, although analysis results later showed that it was not pure), 84% of the theoretical yield.

Anal. Calc'd for C₆H₉O₄N₂FS: C, 32.1; H, 4.05; N, 12.5. Found: C, 32.9, 32.9, 33.2; H, 4.30, 4.18, 4.19; N, 12.3.

This product, 20.5 g (0.092 mole), was dissolved in 165 ml. of water, and a solution of 13.7 g. (0.046 mole) of sodium dichromate dihydrate was added with stirring at 10-20°. The aqueous solution was extracted with ether after 30 minutes, after 1 hour, and after 2 hours. The ether
solutions were combined, the ether was removed by distillation under reduced pressure, and 100 ml. of high boiling Skellysolve was added to the residue. Upon cooling of the solution in a dry ice-acetone bath, 2.5 g. (a crude yield of 22%) of orange-red crystals having a strong quinone odor were collected by suction filtration. A portion of this material was vacuum sublimed and submitted for analysis.

**Anal. Calc'd. for C₆H₃O₂F:**

C, 57.2; H, 2.40.

**Found:**

C, 56.2, 56.0; H, 2.29, 2.17.

Several attempts were then made to produce 2-fluoro-1,4-benzoquinone by oxidation of 2-fluoro-1,4-diaminobenzene hydrosulfate by using other oxidizing agents. All of these attempts were unsuccessful and led to no 2-fluoro-1,4-benzoquinone. Among the agents tried were sodium chlorate plus vanadium pentoxide, (cf. Org. Syn. Coll. Vol. II, 553) manganese dioxide, and hydrogen peroxide.

The oxidation of acetonilide to 1,4-benzoquinone by means of potassium persulfate had been reported\(^7\) and an attempt was made to oxidize 2-fluoroacetonilide to 2-fluoro-1,4-benzoquinone in the same manner, but the starting material was recovered unchanged.
Attempted Synthesis of 2-Fluoro-1,4-Benzoquinone

Route II

\[
\begin{align*}
\text{OC}_2\text{H}_5\text{NH}_2 & \xrightarrow{\text{HCl}} \text{OC}_2\text{H}_5\text{N} = \text{N}^+ \text{BF}_4^- \\
\text{ONH}_2 & \xrightarrow{\text{NaN}_2 \text{O}_2, \text{NaBF}_4} \text{OC}_2\text{H}_5\text{N} = \text{N}^+ \text{BF}_4^- \\
\text{ONH}_2 & \xrightarrow{\Delta} \text{OC}_2\text{H}_5\text{N} = \text{N}^+ \text{BF}_4^- \\
\text{OH} & \xrightarrow{\text{AlCl}_3} \text{OC}_2\text{H}_5\text{N} = \text{N}^+ \text{BF}_4^- \\
\text{OH} & \xrightarrow{\text{H}_2\text{SO}_4, \text{H}_2\text{O}, \text{NaNO}_2} \text{OC}_2\text{H}_5\text{N} = \text{N}^+ \text{BF}_4^- \\
\text{N} = \text{O} & \xrightarrow{\text{Oxidation}} \text{OC}_2\text{H}_5\text{N} = \text{N}^+ \text{BF}_4^- \\
\text{N} = \text{O} & \xrightarrow{\text{Hydrolysis}} \text{OC}_2\text{H}_5\text{N} = \text{N}^+ \text{BF}_4^- \\
\end{align*}
\]
2-Ethoxybenzenediazonium fluoborate

In a 5 l. stainless steel beaker, equipped with a mechanical stirrer and a low temperature thermometer and contained in an ice-salt bath, was placed a mixture of 1200 ml. of concentrated hydrochloric acid (sp. gr. 1.18) and 1400 ml. of water cooled to -5°. To this solution was added 100 g. of o-phenetidine, and the addition of 385 g. (5.5 moles) of sodium nitrite in the form of moist balls was begun. Additional quantities of o-phenetidine were added from time to time until a total of 685 g. (5.0 moles) had been added, always with an excess of the reagent. Stirring was continued for 30 minutes after addition was complete, whereupon a solution of 1200 g. (10.8 moles) of sodium fluoborate in 1400 ml. of water was added all at once. Stirring was continued for an additional hour, after which the precipitate was collected by suction filtration and washed successively with 250 ml. of water, 300 ml. of ethanol and 400 ml. of ether. The precipitate, after being air dried for 20 hours, weighed 1023 g. (86.5% of the theoretical).

2-Fluorophenetole

In two batches, each contained in a 1 l. flask equipped with a condenser set for downward distillation, 1023 g. (4.34 moles) of 2-ethoxybenzenediazonium fluoborate was heated with a small flame until all of the solid had
melted. The melt was then heated strongly until all of the liquid had distilled. After 500 ml. of water had been added to the distillate, the water and oil layers were separated. The water layer was extracted with three 300 ml. portions of ether, the ether layers were combined, the ether was removed by distillation, and the residue was distilled through a Vigreux column to yield 223 g. (37% crude yield) of colorless 2-fluorophenetole, b.p. 150-177°, which was carried on as such to the next step. Literature value: b.p. 167-169°.6

2-Fluorophenol

In a 2 l. r.b. flask equipped with a reflux condenser and a solid addition funnel was placed a solution of 223 g. (1.59 moles) of 2-fluorophenetole in 485 ml. of dry benzene. Then 525.4 g. (3.94 moles) of aluminium chloride was added, and the mixture refluxed on a steam bath for three hours. The mixture was poured on to ice, and after filtration of the solution, the benzene and water layers were separated. The water layer was twice extracted with 200 ml. portions of benzene. The combined benzene layers were extracted with 1500 ml. of 10% sodium hydroxide in three separate portions. The aqueous layer was made acid to litmus with hydrochloric acid, and the oil and water layers were separated. The aqueous solution was extracted with three 300 ml. portions of ether, and the
oil and ether layers were combined. The ethereal solution was dried over Drierite, the ether was removed by distillation, and the residue was distilled to yield 155 g. of liquid, b.p. 80-162°. This liquid was fractionated through a packed column to give four fractions:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>b.p. (°C)</th>
<th>Yield (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>90-148</td>
<td>4</td>
</tr>
<tr>
<td>II</td>
<td>149-153</td>
<td>110</td>
</tr>
<tr>
<td>III</td>
<td>153-155</td>
<td>21.4</td>
</tr>
<tr>
<td>IV</td>
<td>155-158</td>
<td>9.4</td>
</tr>
</tbody>
</table>

77% of the theoretical yield

Literature value: b.p. 151-152°.

2-Fluoro-4-nitrosophenol

In a 1 l. r.b. flask equipped with a mechanical stirrer, a thermometer and an addition funnel were placed 581 ml. of water, 33.4 ml. of concentrated sulfuric acid, 223 g. of sodium sulfate and 50 g. (0.44 mole) of crude 2-fluorophenol. The mixture was cooled to 0° and a saturated solution of 40.1 g. (0.53 mole) of sodium nitrite was added dropwise, while the temperature was maintained at -5°. Stirring was continued for two hours after addition was complete, and the brown precipitate which formed was collected by suction filtration, washed with ice water, and dried in a vacuum desiccator for several days to yield 60.4 g. (94% of the theoretical) of 2-fluoro-4-nitrosophenol, m.p. 127.6-129.6°. Literature value: m.p. 129-129.6°. Attempts to crystallize the brown powder from a variety of solvents were unsuccessful.
Synthesis of 2-Fluoro-1,4-Benzoquinone

Route III

\[
\begin{align*}
\text{OH} & \xrightarrow{\text{C}_6\text{H}_5\text{N}_2\text{Cl}} \xrightarrow{65\%} \text{OH} \\
\text{F} & \xrightarrow{\text{From } m\text{-fluorophenol}} \text{N} = \text{N} \\
\text{N} & \xrightarrow{46\%} \text{OH} \\
\text{F} & \xrightarrow{\text{H}_2\text{SO}_4, \text{H}_2\text{O}} \text{NH}_2 \\
\end{align*}
\]
Attempts to oxidize this substance to 2-fluorobenzoquinone with 30% hydrogen peroxide or with ferric chloride or to hydrolyze it (consider its tautomeric form 2-fluoro-1,4-benzoquinone monooxime) in either acid or basic solution were completely unsuccessful.

**3-Fluoro-4-benzeneazophenol**

In a 4 l. beaker equipped with a mechanical stirrer and a low temperature thermometer and surrounded by an ice-salt bath, were placed 95.8 g. (0.855 mole) of m-fluorophenol and 560 ml. of 10% sodium hydroxide. The mixture was stirred until solution was complete, and a solution of benzene diazonium chloride (prepared from 79.5 g. (0.855 mole) of aniline, 92.5 g. of ice, 252 ml. of concentrated hydrochloric acid (sp. gr. 1.16) and 61.5 g. of sodium nitrite) was added through an addition funnel, whose tip extended below the surface of the liquid, at such a rate as to maintain the temperature below 0°. The solution was stirred for 30 minutes after addition was complete and was allowed to stand for two additional hours at 0°. The dark brown precipitate was collected by suction filtration and was washed with 200 ml. of water.

**3-Fluoro-4-aminophenol**

The precipitate of 3-fluoro-4-benzeneazophenol was dissolved in 1845 ml. of 10% sodium hydroxide, and the solution was filtered but yielded no insoluble material.
The filtrate was transferred to a 4 l. beaker equipped with a mechanical stirrer and a thermometer, and 338.3 g. (1.94 moles) of sodium hydrosulfite was added all at once. Stirring at room temperature produced no reaction, so the temperature was raised to 80° and maintained there for one hour with intermittent stirring. A small layer of oil, presumably aniline, collected on the surface, but the solution retained its original deep red color. An additional 100 g. of sodium hydrosulfite was added, whereupon the aniline layer immediately increased in volume, and the solution became noticeably lighter in color. Heating at 80° was continued for an additional 30 minutes, the solution was nearly neutralized until just alkaline to litmus with hydrochloric acid, and was then steam distilled. The oil in the distillate was identified as aniline. The aqueous solution was reduced to half its volume and was cooled in an ice bath, whereupon a red solid, 73.7 g., settled out and was collected by suction filtration. Upon cooling the filtrate further an additional 13.6 g. of red solid was collected, m.p. 137.6-139.6°. The two crops were combined and recrystallized from water to yield 70.3 g. (65% of the theoretical based on m-fluorophenol) of 3-fluoro-4-aminophenol, m.p. 137-138°. Literature value: m.p. 139°.9. Oxidation of a small portion of this product with ferric chloride yielded no 2-fluoro-1,4-benzoquinone.
2-Fluoro-1,4-benzoquinone

To 4400 ml. of 20% sulfuric acid contained in a 5 l. r.b. flask equipped with a thermometer and a mechanical stirrer and maintained at 0° by an ice-salt bath was added 55 g. (0.433 mole) of 3-fluoro-4-aminophenol. A solution of 121 g. (0.405 mole) of sodium dichromate dihydrate was added with stirring at such a rate as to maintain the temperature below 10°. Stirring was continued for 2½ hours after which time 2.0 g. of red material having a strong quinone odor was collected by suction filtration. The aqueous solution was twice extracted with a total of 750 ml. of ether and then returned to the beaker. An additional 10 g. of sodium dichromate dihydrate was added, and stirring was continued for 45 minutes when the aqueous solution was again extracted with a total of 750 ml. of ether. The ether layers were combined, dried over anhydrous magnesium sulfate and the ether was removed by distillation to leave a red crystalline residue. The residue was re-crystallized from high boiling Skellysolve to give 25.0 g. (46% of the theoretical) of yellow crystals of 2-fluoro-benzoquinone, m.p. 75-76°. Literature value: m.p. 80°.9

Attempted synthesis of 2-fluoro-1,4-naphthoquinone

Method I

In a 25 ml. Erlenmeyer flask was placed a solution of 2.0 g. (0.0159 mole) of 2-fluoro-1,4-benzoquinone in 8 ml.
of glacial acetic acid. The contents of the flask were cooled to 0°, and 1.1 g. (0.0197 mole) of butadiene was added. The flask was stoppered, the stopper was wired on, and the flask was placed in a pan of running water for 72 hours with occasional shaking. The solution was then filtered through a layer of acetic acid-washed charcoal, transferred to a 100 ml. flask, and treated at 50° with a solution of 4.65 g. of sodium dichromate in 10 ml. of water at 50° and 0.25 ml. of concentrated sulfuric acid. The temperature rose to 60° and was subsequently maintained at 65° for 1½ hours. To this solution, cooled to room temperature, 10 g. of ice and 10 ml. of water were added. A small amount of a gray powder was collected by filtration and washed with water. None of this solid was sublimable nor would it dissolve in common solvents. It melted above 300° and was assumed to be polymeric material from the butadiene. (cf. L. F. Feiser, J. Am. Chem. Soc. 70, 3168 (1948), Procedure B.)

Method II

In a 200 ml. r.b. flask equipped with a reflux condenser was placed a solution of 5 g. (0.033 mole) of 2-fluoronaphthalene in 75 ml. of glacial acetic acid and the solution was heated to 50°. After the addition of 15 ml. of Superoxol (30% hydrogen peroxide), the solution was
Attempted Conversion of 2-Fluoro-1,4-Benzochinone to 2-Fluoro-1,4-naphthoquinone

\[
\begin{array}{c}
\text{Oxidation or Dehydrogenation} \\
\text{SnCl}_2 \text{ HCl}
\end{array}
\]

0% 82% 71%
heated to $80^\circ$ and was maintained at that temperature for ten hours. The acetic acid was then removed by distillation under reduced pressure, and the residue was steam distilled. A somewhat yellow solid which steam distilled over was extracted with benzene, the benzene was removed by distillation, and the residue was recrystallized from high boiling Skellysolve to yield 2.0 g. of white solid which was identical with the starting material. The same reaction at $100^\circ$ gave the same results. \(\text{cf. R. T. Arnold and R. Larson, J. Org. Chem. 5, 250 (1940)}\)

2-Fluoro-5,8-dihydro-1,4-naphthohydroquinone (?)

This compound was prepared by the method described in the following patent: I. G. Farbenind. A-G, Fr. 677,296, June 25, 1929. In a combustion tube cooled to $-60^\circ$ were placed 0.6 g. of 2-fluorobenzoquinone and 0.4 g. of butadiene. The tube was sealed, placed in a small steel bomb, and heated at $55^\circ$ for one hour, at $80^\circ$ for another hour. It was then cooled in an ice-salt bath and opened. The white solid which resulted was recrystallized from high boiling Skellysolve to give 0.7 g. (82% of the theoretical) of white fluffy needles, m.p. 71.6-72.0°.

**Anal. Calc'd. for $C_{10}H_9O_2F$:**  C, 66.6; H, 5.03.

**Found:**  C, 66.6; H, 4.92.
Whether this compound was 2-fluoro-5,8-dihydro-1,4-naphthohydroquinone or 2-fluoro-5,8,9,10-tetrahydro-1,4-naphthoquinone was never established. It was soluble in sodium carbonate, but could be isomerized by the method of L. F. Feiser, J. Am. Chem. Soc. 70, 3167 (1948) to another white crystalline compound which was also soluble in sodium carbonate.

Isomerization of 2-fluoro-5,8-dihydro-1,4-naphthohydroquinone (?)

A solution of 1.2 g. of 2-fluoro-5,8-dihydro-1,4-naphthoquinone in 4 ml. of glacial acetic acid was heated to 100° in a 25 ml. Erlenmeyer flask. Then 0.1 g. of stannous chloride, 0.7 ml. of concentrated hydrochloric acid, and 3.4 ml. of distilled water were added, and the solution was held at 100° for 15 minutes. Upon cooling the solution, white needles appeared which were collected by suction filtration, washed with water, and dried in a vacuum desiccator to yield 0.85 g. (71% of the theoretical) of an isomer, m.p. 154.0-155.4°. An attempt to oxidize this product, utilizing the method of Feiser (Procedure C) given in the article already cited, led to a minute amount of dark brown very high melting solid from which no material could be obtained by vacuum sublimation.
Attempts to oxidize 2-fluoro-5,8-dihydro-1,4-naphtoquinone

Many attempts were made to convert the Diels Alder addition compound of 2-fluorobenzoquinone and butadiene into the desired 2-fluoro-1,4-naphtoquinone. None were successful.

Among the methods tried were oxidation with sodium dichromate and sulfuric acid, described by L. F. Feiser, J. Am. Chem. Soc. 70, 3168 (1948), with air in strong alkaline solution (C. F. H. Allen and A. Bell, Org. Syn. 22, 37), dehydrogenation with palladium charcoal in boiling xylene as described by E. G. Horning and M. G. Horning, J. Am. Chem. Soc. 69, 1359 (1947), and dehydrogenation with sulfur in boiling xylene.

Attempted synthesis of 1-methoxy-2-nitronaphthalene

In a 3 l. 3-necked r.b. flask equipped with a mechanical stirrer, a low temperature thermometer, and an addition funnel and surrounded by an ice salt bath were placed 474 g. (3.0 moles) of methyl α-naphthyl ether, 474 g. (4.65 moles) of acetic anhydride and 948 g. (15.8 moles) of glacial acetic acid. Acetyl nitrite at 0° was added dropwise to the solution at -5° at such a rate as to maintain the temperature below 2° until a total of 211 g. (3.35 moles) had been added. (The acetyl nitrate was prepared from 100% nitric acid and acetic anhydride,
The solution was stirred in the cold for twenty hours after addition was complete, whereupon it was poured on to ice. The oily red-brown precipitate was collected by suction filtration and washed with water. Attempts to crystallize the oily precipitate from common solvents were unsuccessful, and the mixture was thus reduced by suspending 0.1-mole batches in 50 ml. of alcohol containing 0.1 g. of platinum oxide, and reducing at \( \frac{45}{170} \) hydrogen pressure. The solutions were filtered, and the alcoholic solutions were treated with dry hydrogen chloride to give a gray-white solid soluble in water, presumably an amine hydrochloride. From 293.1 g. of the nitrated mixture, 185.8 g. of the crude amine hydrochloride, m.p. 252-266°, was obtained. Recrystallization of 77.2 g. of the hydrochloride yielded 50 g. of recrystallized gray white fluffy needles, m.p. 255.5-257.5°. Recrystallization of 5 g. of this material yielded 4.0 g. of white fluffy needles, m.p. 260-261°.

**Anal. Calc'd. for C\(_{11}\)H\(_{12}\)ONCl: C, 63.0; H, 5.77; Cl, 16.9.**

**Found: C, 62.7; H, 5.73; N, 16.9.**

A 75 g. portion of the crude hydrochloride was dissolved in water, the solution was made basic with sodium hydroxide, and the water and oil layers were separated. The aqueous layer was extracted with three 200-ml. portions of
ether, the oil and ether layers were combined and dried over solid sodium hydroxide, and the ether was removed by distillation. The residue was distilled in vacuo to yield 28.5 g. of slightly colored liquid, b.p. 130-132°/2-3mm. An acetyl derivative was prepared from 1.0 g. of the distillate; 1.2 g. of white solid, m.p. 184.8-185.2°, corresponding to the 1-methoxy-4-acetaminonaphthalene was obtained. Literature value: m.p. 180-181°. An attempt was made to replace the amino group by a fluorine atom utilizing the Schiemann reaction, but no fluoborate could be isolated.

**Nitration of Methyl α-Naphthyl Ether**

Diacetyl ortho-nitric acid was prepared by the method of Pictet and Genequand as follows: glacial acetic acid and fuming nitric acid (sp. gr. 1.49-1.50) were mixed in molar ratios, and the resulting liquid was distilled, the higher boiling fraction (b.p. 123-124°) being collected.

In a 100 ml. round-bottomed flask equipped with a reflux condenser and a dropping funnel were placed 15.8 g. (0.1 mole) of methyl α-naphthyl ether and 25 ml. of acetic anhydride. Diacetyl ortho-nitric acid (18.3 g., 0.1 mole, calculated as C₄H₉O₇N) was added to the solution at 0° at such a rate as to maintain the temperature at 0-2°. The mixture was stirred for 30 minutes after addition was complete, and it was then poured into a beaker containing
water and ice. An oil separated which solidified when the sides of the beaker were scratched. The yellow solid was collected by suction filtration, washed with water, and recrystallized from ethanol to yield 10.2 g. of yellow solid (50% of the theoretical), m.p. 79-80°. The literature m.p. of 1-methoxy-2-nitronaphthalene is 80°,\textsuperscript{13} of 1-methoxy-4-nitronaphthalene 85-86°.\textsuperscript{14} The yellow solid was shown to be 1-methoxy-4-nitronaphthalene by catalytic reduction in ethanolic solution and preparation of the hydrochloride and acetyl derivatives of the resulting amine. The acetyl derivative melted at 180.5-181.5°. The literature value for the m.p. of 2-acetamino-1-methoxy-naphthalene is 132°,\textsuperscript{14} for that of 4-acetamino-1-methoxy-naphthalene 180-181°.\textsuperscript{10}

**Nitration of α-Naphthol**

In a 100 ml. round-bottomed flask were placed 14.4 g. (0.1 mole) of α-naphthol and 25 ml. of acetic anhydride. To this solution at 0° was added 18.1 g. (0.1 mole) of diacetylorthonitric acid at such a rate as to maintain the temperature below 3°. The mixture was stirred for 30 minutes at 0°, and was then poured into a beaker containing ice and water. The dark yellow solid which formed was collected by suction filtration and washed with water. The solid was extracted with 2% sodium
carbonate solution until no more material dissolved, and it was then discarded. The combined extracts upon acidification yielded 8.0 g. of a dirty yellow solid. This solid was collected by suction filtration and a small portion of it melted at 90-112°. The bulk of the solid was steam distilled, and 0.4 g. of a yellow solid appeared in the distillate. This solid was collected by suction filtration, m.p. 126.6-128.0°. The literature m.p. of 2-nitro-1-naphthol is 128°.15 The contents of the still pot upon cooling yielded 7.0 g. of red-black solid, which was collected by suction filtration. Recrystallization of a 1 g. portion of this material yielded 0.5 g. of a yellow solid, m.p. 162.0-163.2°, presumably 4-nitro-1-naphthol. The literature m.p. of 4-nitro-1-naphthol is 164°.16

**Attempted Preparation of 2-Nitro-1-naphthol**

In a 500 ml. round-bottomed 2-necked flask equipped with a reflux condenser and an addition funnel was placed a solution of 60.0 g. (0.414 mole) of α-naphthol in 150 ml. of acetic anhydride. The solution was cooled to -10°, and a cold solution of acetyl nitrate (Note 1) in

---

**Note 1:** The acetyl nitrate was prepared as follows: nitrogen pentoxide was prepared as described in Inorg. Syn. III, p. 78, McGraw Hill Book Company, Inc., New York, 1950, by the dehydration of nitric acid with phosphorous pentoxide. The 22.4 g. of nitrogen pentoxide prepared in this manner was dissolved in 60 g. of acetic anhydride at 0°, as described by
acetic anhydride was added at such a rate as to maintain the temperature below -5°. The solution was stirred for 30 minutes after addition was complete and was then allowed to warm to room temperature. The solution was poured into a beaker containing ice and water at which time a heavy insoluble layer settled to the bottom. The upper aqueous layer was decanted and extracted with three 200 ml. fractions of benzene. The oil and benzene layers were combined, and the benzene was removed by distillation. The residue was steam distilled; 0.3 g. of greenish yellow solid came over. This was collected by suction filtration and at that time turned to an orange black sticky solid from which no crystalline material could be recovered through an attempt to crystallize it from alcohol. The contents of the still pot were cooled and the coal-black solid (73.0 g.) which was contained therein was collected by suction filtration and air-dried. No crystalline material could be recovered from this brittle tarry residue.

**Attempted Synthesis of 2-Nitro-1-naphthol**

In a 3 l. round-bottomed 2-necked flask equipped with a mechanical stirrer and a reflux condenser were

C. Weygand, Organic Preparations, p. 283. Inter-
sience Publishers Inc., New York, 1945. The method described should give a solution of 0.414 mole of acetyl nitrate in excess acetic anhydride.
placed 300 g. (2.1 moles) of α-naphthylamine, 270 ml. of acetic anhydride, and 2 l. of glacial acetic acid. The mixture was heated to reflux in order to effect solution and then cooled to 20°. Fuming nitric acid (125 ml. of sp. gr. 1.50) was added to the solution at such a rate as to maintain the temperature at 20-25°. The solution was then allowed to stand at room temperature for 48 hours, but no precipitate settled out (cf. G. N. Burkhardt and H. Wood, J. Chem. Soc. 1929, 143). Upon the addition of 2 l. of water to the solution a dark oil which changed to a red semisolid after stirring, separated. This semisolid was collected by suction filtration, air-dried, triturated with alcohol and again air dried to yield 317.3 g. of orange red solid with no definitely observable melting point. This presumably was a mixture of 1-acetamino-2-nitronaphthalene and 1-acetamino-4-nitronaphthalene.

In a 500 ml. 3-necked round-bottomed flask were placed 30 g. of the orange-red solid and 90 ml. of ethanol. Heating to reflux effected solution, and 60 ml. of a solution of 30% potassium hydroxide was then added drop-wise, followed by 100 ml. of water. The solution was distilled until 70 ml. of distillate had been collected, 100 ml. of water was added to the distilling flask, and the distillation was continued until the odor of ammonia could no longer be detected in the distillate (about 3 hours).
The solution was then cooled to room temperature, whereupon a dark red solid precipitated. This solid was collected by suction filtration, washed with two 25 ml. portions of 5% potassium hydroxide, and dried in a vacuum desiccator to yield 21.6 g. of a dark red solid. The filtrate was acidified and steam distilled, but yielded no steam-distillable material. A small amount of black solid which could not be induced to yield any crystalline material remained in the stillpot. The 21.6 g. of red solid was dissolved in water, filtered, and the filtrate was extracted with three 100 ml. portions of ether. The aqueous layer was then acidified, whereupon a slightly dirty yellow precipitate appeared. Collected by suction filtration, this yielded 16.5 g. of dirty yellow solid, m.p. 102-134°. This solid was steam distilled, but yielded only a trace of steam-volatile material, m.p. 124.4-126.2°. The literature value for the m.p. of 2-nitro-1-naphthol is 128°.13 The contents of the stillpot were cooled to room temperature, and the 15 g. of orange-black solid which was collected by suction filtration was partially dissolved in hot water. The solution was filtered hot, and, upon cooling, 10.2 g. of nearly colorless crystals, m.p. 162.4-163.7, precipitated and were collected by suction filtration. The literature value for the m.p. of 4-nitro-1-naphthol is 164°.13 The material which did not dissolve
in hot water presumably was 2,4-dinitro-1-naphthol and/or some tarry decomposition products.

**Attempted Preparation of 2-Fluoro-1-nitronaphthalene**

In a 250 ml. stainless steel beaker were placed 70 ml. of 50% sulfuric acid and 10 g. (0.053 mole) of 2-amino-1-nitronaphthalene. The mixture was heated to 80° on a steam bath in an attempt to effect solution. Part of the amine dissolved, and the solution was cooled to -5° while 4.0 g. (0.058 mole) of sodium nitrite was added in the form of moist balls. To the cold solution (solution was not complete) was added a solution of 10.8 g. (0.1 mole) of sodium fluoborate in 20 ml. of water with vigorous stirring. After stirring had been continued for 20 minutes, the yellow solid was collected by suction filtration, washed successively with 5 ml. of water, 10 ml. of alcohol and 10 ml. of ether, and air-dried overnight. A sample decomposed at 98°. The bulk of the solid was added slowly through a thistle tube to a refluxing solution of toluene. The solution was refluxed for 30 minutes after addition was complete, and the toluene solution was filtered while hot to remove a considerable amount of tar formed during the decomposition. After drying of the solution over magnesium sulfate, the toluene was removed by distillation, and the residue was distilled
in vacuo to yield the following two fractions:

- I b.p. 93-95°/3mm. 0.5 g. yellow liquid
- II b.p. 113-115°/2.5mm 0.5 g. greenish orange solid

Fraction I was submitted for analysis.

**Anal. Calc'd. for C_{10}H_6O_2NF:** C, 62.9; H, 3.14.

**Found:** C, 82.3; H, 5.94.

**Anal. Calc'd. for C_{10}H_7F:** C, 82.2; H, 4.80.

Although the hydrogen analysis is off, it appears as though at least part of the material corresponds to 2-fluoronaphthalene. The reaction was unsuccessful because apparently a nitro group in the α position of β-naphthylamine is easily lost or replaced when an attempt is made to diazotize the amine. (cf. H. Willstaedt and G. Scheiber, Ber. 67B, 466 (1934)) These workers obtained a 33% yield of 1-chloro-2-fluoronaphthalene when they carried out a Schiemann reaction on the same compound. They used hydrochloric acid instead of sulfuric acid as a medium for carrying out the diazotization.

**Attempted Synthesis of 2-Nitroso-1-naphthol**

In a 1 l. round-bottomed flask equipped with a mechanical stirrer was placed a solution of 25.0 g. (0.175 mole) of α-naphthol in 7.0 g. (0.175 mole) of sodium hydroxide and 300 ml. of water. The solution was cooled to 0°, and 12.5 g. (0.175 mole) of sodium nitrite was added.
The stirrer was started, and 55 g. (0.23 mole) of concentrated sulfuric acid was added at such a rate as to maintain the temperature at or below 0°. The periodic addition of ice to the reaction mixture aided in maintaining this temperature. Stirring in the cold was continued for 1 hour after addition was complete, during which time a brown solid precipitated out. The solid was collected by suction filtration, washed with cold water, and air-dried to yield 19.4 g. of a brown powder. A portion of this material, 2.0 g., was crystallized from aqueous alcohol to yield 1.6 g. of yellow needles, m.p. 190.0-192.2°. Recrystallization of this material from aqueous alcohol yielded 1.4 g. of yellow needles, m.p. 192.8-193.6°. The literature m.p. of 4-nitroso-1-naphthol is 193-194°17, of 2-nitroso-1-naphthol, 162-164°.18

**Attempted Reduction of 2,4-Dinitro-1-naphthol**

**with Ammonium Sulfide**

In a 1 l. three-necked round-bottomed flask equipped with a gas inlet tube and a gas outlet tube, were placed 23.4 g. (0.1 mole) of 2,4-dinitro-1-naphthol, 50 ml. of ethanol, and 40 ml. of 28% ammonium hydroxide. Hydrogen sulfide was introduced into the flask until a total of 10.2 g. (0.294 mole) had been taken up. The solution was heated to reflux, 50 ml. of water was added, and the mixture was filtered while hot to give a precipitate (A) and a
filtrate. The filtrate was made slightly acidic whereupon a dark yellow solid precipitated. This was collected by suction filtration (ppt. B). The alcohol was removed from the filtrate by distillation; no identifiable product could be isolated from the very small amount of solid residue which remained. Precipitate A was washed with hot water until no more material dissolved and was then discarded. The washings were acidified, whereupon a dirty yellow solid precipitated and was collected by suction filtration (ppt. C). Precipitates B and C were combined, washed with 5% hydrochloric acid, and air dried. The washings were carefully neutralized with ammonia, but they yielded no precipitate, and no ether soluble material was obtained upon ether extraction. After air drying the combined precipitates B and C weighed 19.6 g., and a sample melted at 131.2-131.6°. A mixed m.p. with the original 2,4-dinitro-1-naphthol (m.p. 133-136°) showed no depression. Recovery of the starting material amounted to 83.7%.

Attempted Schiemann Reaction with 2-Amino-1,4-naphthoquinone

In a stainless steel beaker were placed 5.0 g. (0.029 mole) of 2-amino-1,4-naphthoquinone, 6.3 ml. of water, and 6.1 ml. of concentrated hydrochloric acid.
Although solution did not take place, the contents of the beaker were cooled to -5°, and 2.0 g. (0.029 mole) of sodium nitrite was added in the form of moist balls, while the temperature was maintained below 2°. Foaming occurred to such an extent that it was difficult to add the sodium nitrite to the solution. After addition was complete the mixture was stirred for 10 minutes, and a solution of 6.4 g. of sodium fluoborate in 9 ml. of water was subsequently added. The mixture was stirred for 15 minutes and a muddy brown solid was then collected by suction filtration, washed successively with 5 ml. of water, 5 ml. of ethanol, and 10 ml. of ether, and air dried overnight. This solid, 2.0 g., was insoluble in water and did not contain fluorine. It was never identified.

A diazotization of 5.0 g. of 2-amino-1,4-naphthoquinone was attempted using a large excess of 20% sulfuric acid instead of hydrochloric acid, and again no diazonium fluoborate could be isolated.

Attempted Diazotization of 2-Amino-1,4-naphthoquinone in Anhydrous Hydrogen Fluoride

In a monel-metal round-bottomed 2-necked flask equipped with a copper condenser and a copper outlet tube was placed 20.0 g. (0.1155 mole) of 2-amino-1,4-naphtho-
quinone. Anhydrous hydrogen fluoride was introduced through the ice-packed condenser at such a rate that it condensed into the ice-surrounded flask. A total of 46.2 g. (2.31 moles) of hydrogen fluoride was thus added. The outlet tube was replaced with a rubber stopper, and 8.0 g. (0.136 mole) of sodium nitrite was added slowly. The reaction mixture was held at 0° overnight, and it was then warmed to 80° by a water bath and held at that temperature until no more gas was evolved. The condenser was then removed, and the hydrogen fluoride was allowed to evaporate. The residue was steam distilled. Extraction of the colorless distillate with benzene and subsequent evaporation of the benzene yielded no residue. The contents of the still pot were cooled, and the black solid therein contained was collected by suction filtration. This black amorphous solid, 17.5 g., burned and melted in the range 260-300°. An attempt was made to crystallize a portion of this material from ethanol by dissolving it in ethanol, treating the ethanolic solution with charcoal, filtering and cooling the filtrate. A black solid coated the sides of the flask which when dried melted in the same range as the original solid. The alcohol was removed in portions, but when each successive solution was cooled the only material which could be obtained was a coating of black, amorphous, high-melting material, presumably polymeric.
in nature. The distillate from which the original solid was removed by filtration was extracted with benzene, and the benzene was removed from the organic layer by distillation. Only a trace of black residue remained. This material was similar in properties to the solid already obtained, and it could not be crystallized.
Section III

Discussion of Experimental Results
The lack of success in preparing 2-fluoro-1,4-naphthoquinone via any of the synthetic schemes utilized is difficult to explain inasmuch as compounds very similar to the one desired have been prepared by similar methods and have shown a reasonable degree of stability. Thus 2-amino-1,4-naphthoquinone, 2-methyl-1,4-naphthoquinone and other alkyl naphthoquinones, and 2-chloro-1,4-naphthoquinone, have all been prepared in large quantities. The fact that the usual methods for introducing various groups into an aromatic nucleus are not applicable to the introduction of fluorine, however, makes this a somewhat specialized case. The two reactions which have been widely utilized for the introduction of fluorine into an aromatic nucleus; namely, the Schiemann reaction and diazotization in anhydrous hydrogen fluoride, have never been successfully carried out with amino derivatives of naphthoquinones, naphthohydroquinones, naphthols, or nitronaphthalenes. Since these classes of compounds are the most logical starting materials for the synthesis of the desired compound, a synthesis starting with the intact naphthalene nucleus is rendered more difficult. It was for this reason that the first attempts to synthesize 2-fluoro-1,4-naphthoquinone were based on the initial synthesis of 2-fluoro-1,4-benzoquinone in the hope that this intermediate could be converted via the Diels-Alder reaction and subsequent oxidation to the desired naphthoquinone.
One point should be stressed in connection with the synthesis of 2-fluoro-1,4-benzoquinone; namely, that although the oxidation of diamines is commonly given as a satisfactory method of preparing quinones it is most difficult to find exact information on the conditions necessary for this transformation. It is unfortunate that this method is often described as being about as effective in producing quinones as the oxidation of aminophenols or hydroquinones, for it is very doubtful that such is the case. In this particular research a relatively long synthesis was employed to prepare 2-fluoro-1,4-diamino-benzene only to lead to the discovery that the oxidation of this compound did not produce the desired quinone, whereas the oxidation of 4-amino-3-fluorophenol readily produced the desired 2-fluoro-1,4-benzoquinone.

Once the proper conditions were found the conversion of the 2-fluoro-1,4-benzoquinone to its Diels-Alder adduct was easily achieved, but the oxidation or dehydrogenation of this adduct to 2-fluoro-1,4-naphthoquinone could not be carried out. It is very doubtful that the oxidation of this adduct is intrinsically much more difficult than the oxidation of other Diels-Alder adducts which have been converted to the corresponding quinones by the methods employed. It is rather more probable that the desired quinone is itself unstable under the conditions employed, and is destroyed before it can be isolated. The
fact that in no case was the starting adduct recovered unchanged lends credence to this postulation. The reason for the decreased stability of 2-fluoro-1,4-naphthoquinone as compared to 2-chloro-1,4-naphthoquinone is not easily explained. 2-Fluoro-1,4-naphthoquinone may be looked upon as a vinylog of an acid fluoride. Considering it in this light it might be supposed that it would be easily hydrolyzed. This argument breaks down, however, when one considers that 2-chloro-1,4-naphthoquinone is by the same token the vinylog of an acid chloride, and that acid chlorides are more easily hydrolyzed than acid fluorides. This argument is also refuted by the fact that hydrolysis would yield 2-hydroxy-1,4-naphthoquinone, which should have been recovered from the reaction mixture. The fact is that no material having the properties of a quinone or oxidizable to a quinone could be isolated. Bradlow\textsuperscript{19}, in his work with 2-halopyridinium halides, has shown that the 2-fluoro compound is more easily hydrolyzed in acid solution than the 2-chloro compound. These compounds have the feature in common with the 2-halonaphthoquinones that a strong electron withdrawing group adjacent to the halogen-bearing carbon atom is present. Again, however, the failure to isolate 2-fluoro-1,4-naphthoquinone cannot be attributed solely to hydrolysis, because no 2-hydroxy-1,4-naphthoquinone could be isolated. Another possibility is that the desired compound was destroyed by further oxidation. It is
difficult to predict whether the presence of a fluorine group in a quinone would make it more or less subject to oxidation. 2-Chloro-1,4-naphthoquinone is a stronger oxidizing agent than the unsubstituted quinone due to the inductive pull which the chlorine exerts on the ring electrons. Fluorine, however, although it exerts a similar inductive pull on electrons also has a remarkable tendency to donate electrons to an aromatic ring through resonance, a property shown to only a very limited extent by chlorine. This latter effect would tend to make 2-fluoro-1,4-naphthoquinone a weaker oxidizing agent, and thus a more easily oxidizable compound. Since there is no way of evaluating the relative importance of the inductive effect and what we shall call the resonance effect in this particular case, it is impossible to predict whether or not destruction of 2-fluoro-1,4-naphthoquinone by oxidation is a likely prospect or not. Whatever the reason, no 2-fluoro-1,4-naphthoquinone could be isolated as an oxidation product of the Diels-Alder adduct (either before or after rearrangement) of butadiene and 2-fluoro-1,4-benzoquinone.

Since, for reasons unknown, the desired compound could not be produced from the Diels-Alder adduct of 2-fluoro-1,4-benzoquinone and butadiene, it was decided to attempt to synthesize it from substances which contained the naphthalene nucleus. From the results in the benzene
series it was decided that if one key intermediate could be made there was a reasonably good chance that it could be converted into the desired compound. This intermediate was 2-fluoro-1-naphthol. If this compound could be made, either of the following two entirely reasonable paths should lead to 2-fluoro-1,4-naphthoquinone:

All attempts to prepare this intermediate failed. Nitration of \( \alpha \)-naphthol, of methyl \( \alpha \)-naphthyl ether and of 1-acetaminonaphthalene gave only the corresponding \( 4 \)-nitro compound. Nitrosation of \( \alpha \)-naphthol likewise led to the \( 4 \)-substituted naphthol. In each of these cases the electrophilic reagent showed a marked preference for the \( \alpha \) position to the near exclusion of the \( \beta \) position. Nitration of 2-fluoronaphthalene was reported in the literature\(^{20}\) to give a mixture of mono and dinitro fluoronaphthalenes from which attempts to isolate
2-fluoro-1-nitronaphthalene was unsuccessful. Diazotization of 1-nitro-2-naphthylamine was unsuccessful in producing 2-fluoro-1-nitronaphthalene.

When attempts to produce 2-fluoro-1-naphthol failed, miscellaneous methods were employed in an attempt to prepare the desired compound.

The reduction of 2,4-dinitonaphthol with ammonium sulfide resulted in the recovery of the starting material. No other work was done along this line because Hodgson and Smith\textsuperscript{13} had reported that the preferential reduction of this compound yielded 2-nitro-4-amino-1-naphthol instead of the desired 2-amino-4-nitro-1-naphthol when stannous chloride was used as a reducing agent.

The attempted diazotization of 2-amino-1,4-naphthoquinone failed to yield the desired compound either by the Schiemann method or by diazotization in anhydrous hydrogen fluoride. As has been mentioned, there are no reported cases of such compounds being successfully diazotized by either method, but since only one step was involved, an attempt to carry out the reaction in this case seemed warranted.

Other schemes were envisioned, but they were discarded for various reasons. The diazotization of 2-amino-1-naphthylsulfonic acid and subsequent replacement of the sulfonic acid group by a hydroxyl group was considered as
a possible method of preparing 2-fluoro-1-naphthol, but the lack of success in the diazotization of 2-amino-1-nitronaphthalene plus the probability of replacement of the fluorine atom when the sulfonic acid was converted to the naphthol caused the idea to be abandoned. An exchange reaction between antimony pentafluoride and 2-chloro-1,4-naphthoquinone was considered, but the much greater rate of replacement of fluorine than chlorine by other anions in nucleophilic displacement reactions did not augur well for the success of such a scheme.
Section IV

Suggestions for Further Work
The following suggestion for further work is offered:

1. Nitration of α-tetralone in the presence of ultraviolet light would probably produce 2-nitro-1-tetralone. If this compound could be aromatized to 2-nitro-1-naphthol, conversion to the ether, reduction to the amine, and replacement of the amino group with fluorine by one of the standard methods would produce a compound which quite possibly could be converted into 2-fluoro-1,4-naphthoquinone.
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