# SUBSTITUTION AND REARRANGEMENT REACTIONS OF ALLYLIC COMPOUNDS[1]

R. H. DeWOLFE

*Department of Physical Science, Santa Barbara College of the University of California, Goleta, California*

AND

W. G. YOUNG

*Department of Chemistry, University of California at Los Angeles, Los Angeles, California*

CONTENTS

## I. INTRODUCTION

Allylic compounds are those organic substances having an ethylenic linkage $\alpha,\beta$ to a carbon atom bearing an electronegative functional group:

$$RR'C{=}CR''''CR''R'''Y$$
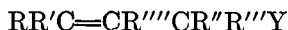
The group Y is usually Cl, Br, I, OH, OR, or OCOR; R, R', R'', R''', and R''''
may be saturated or unsaturated organic radicals, or other functional groups.
It is frequently convenient to apply the term allylic to $\beta,\gamma$-unsaturated organo-
metallic compounds in which Y is an electropositive group such as MgX, Li,
Na, or K.

## A. IMPORTANCE OF ALLYLIC COMPOUNDS

Reactions of allylic compounds are important from both a practical and a
theoretical point of view. The ethylenic bond of the allylic system activates the
functional group, with the result that allylic compounds undergo replacement
reactions much more readily than analogous saturated compounds. For this
reason allylic intermediates are widely used in organic synthesis.

In addition, allylic systems are found in many natural products, such as
alkaloids, steroids, and terpenes. Allylic systems are particularly common among
the terpenes, and allylic substitution reactions are widely used in the synthesis
of essential oils, vitamin A and its analogs, and other unsaturated compounds.

Allylic compounds are of theoretical interest because of their high reactivity
and the ease with which they undergo rearrangement reactions. Migrations of
electronegative substituents from one end of an allylic system to the other are
well known, and rearrangement frequently accompanies allylic replacement re-
actions in these systems.

Reactions of this type were christened "anionotropic rearrangements" by Bur-
ton and Ingold (102), the term anionotropy being used to denote the formal
similarity of these rearrangements to the well-known phenomenon of prototropy.
The interpretation of allylic, or anionotropic, rearrangements in terms of modern
electronic theories was due primarily to Burton and Ingold in England, Prevost
and Kirrman in France, Meisenheimer in Germany, and Winstein and Young in
the United States. These studies have yielded information of value to the whole
field of theoretical organic chemistry.

## B. PREVALENCE OF ALLYLIC REARRANGEMENTS

Allylic rearrangements are reactions of the type:

$$RR'C{=}\overset{\overset{\displaystyle R''''}{|}}{C}{-}CR''R'''X \quad \rightarrow \quad RR'CYC{=}CR''R'''$$
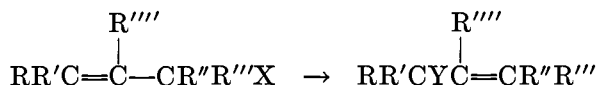
where X and Y may be the same or different functional groups. Such reactions
are quite common among unsymmetrically substituted allylic compounds. This
fact was not generally appreciated prior to 1920. As a result, many reactions of
allylic compounds reported in the early literature were assumed to give only
"normal" (unrearranged) products when actually rearranged products were
formed. Even more recently, many organic chemists have used allylic compounds
as intermediates in syntheses without being aware of the possibility of allylic
rearrangement. The purpose of the present article is to point out which reactions
of allylic compounds are likely to occur with allylic rearrangement and to indi-

cate, where possible, the experimental conditions which are least likely to result in rearrangement.

<div align="center">C. SCOPE OF THE REVIEW</div>

<div align="center">*1. Types of reactions*</div>

The field of allylic chemistry is a very broad one with a voluminous literature. For this reason, it has been necessary to limit the scope of the present article. Reactions of allylic compounds can be divided into three types.

<div align="center">(a) Substitution reactions</div>

Allylic substitution reactions are those reactions of allylic compounds in which one electronegative functional group is replaced by another, with or without allylic rearrangement:

$$RR'C{=}CR''''{-}CR''R'''{-}X \rightarrow RR'C{=}CR''''{-}CR''R'''{-}Y$$

$$+ \; RR'CY{-}CR''''{=}CR''R'''$$
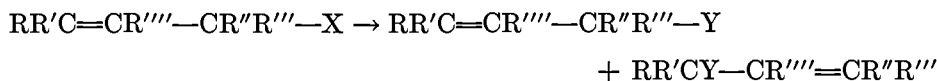
It is this type of reaction with which the present article is primarily concerned.

<div align="center">(b) Isomerization reactions</div>

Allylic isomerization reactions are those reactions in which an electronegative functional group migrates from one end of an allylic system to the other:

$$RR'C{=}CR''''{-}CR''R'''X \rightarrow RR'CX{-}CR''''{=}CR''R'''$$
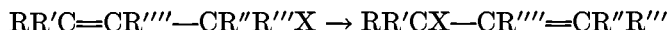
The distinction between this type of reaction and a substitution reaction, while a formal one, has some practical utility. Another type of isomerization reaction is the Claisen rearrangement of allyl aryl ethers and related compounds. Here the functional group, as well as the allylic system, undergoes rearrangement:
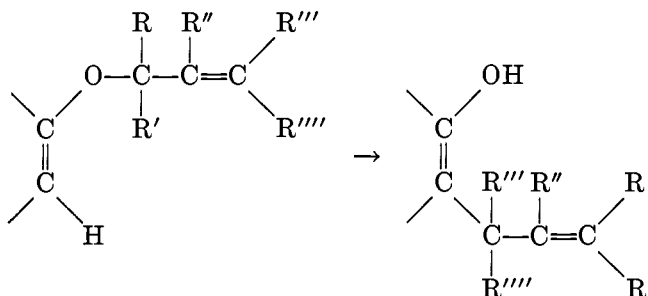


Isomerization reactions of allylic compounds are not discussed in the present article except where they precede, accompany, or follow substitution reactions.

The Claisen rearrangement was reviewed by Tarbell in 1940 (598, 599). Important advances in the elucidation of its mechanism were made more recently (532, 533, 534, 535, 536, 559, 560, 561, 562, 600, 600a).

Isomerization reactions of allylic alcohols, esters, and ethers have been reviewed by Braude (76, 77). Again, recent important advances bearing on the

mechanisms of these reactions have been made. Other types of allylic isomerization reactions are known but less well understood.

### (c) Reactions of allylic organometallic compounds

The reactions and properties of Grignard reagents prepared from allylic halides, and of other allylic organometallic compounds, have been extensively studied by W. G. Young and coworkers.

### 2. Types of allylic compounds discussed

The present article is mainly concerned with reactions of unsymmetrically substituted allylic alcohols, halides, esters, ethers, and amines. Unsymmetrically substituted allylic compounds are those which have different substituents on the $\alpha$- and $\gamma$-carbon atoms of the allylic system:

$$\overset{\displaystyle R''''}{\underset{\gamma \quad \beta \quad \alpha}{RR'C = C - CR''R'''Y}}$$
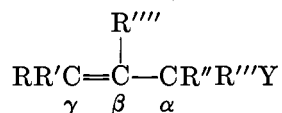
that is, those for which R and R′ are different from R″ and R‴. There are two reasons for concentrating on unsymmetrically substituted compounds. First, allylic rearrangements are observable only in reactions of these compounds, since "rearranged" and "unrearranged" products from a symmetrically substituted allylic compound (e.g., $CH_2\!=\!CHCH_2X$) are indistinguishable unless isotopic labels are used. Consequently, allylic rearrangements present no problem in reactions of symmetrically substituted compounds. Second, most of our knowledge of the mechanisms of allylic substitution reactions has come from studies of unsymmetrical allylic compounds. Symmetrical compounds which are optically active by virtue of asymmetric $\alpha$-carbon atoms also yield valuable information concerning mechanisms of replacement reactions, and a few such optically active allylic compounds are discussed in the present article.

By omitting the simpler symmetrically substituted allylic compounds from consideration, the task of surveying the literature was considerably simplified. For example, the Shell Chemical Company has published a monograph on the chemistry of allyl halides ($CH_2\!=\!CHCH_2X$) which has a bibliography of over seven hundred references (567a).

### 3. Literature coverage

The literature coverage of the present article is critical rather than exhaustive. The early literature is difficult to interpret, simply because much of it appeared before the existence of allylic rearrangements was generally appreciated. For this reason, coverage of the recent literature is as complete as possible, while only the more important papers in the older literature are considered.

Many steroids and alkaloids contain allylic systems in their molecules. It is likely that the considerations which apply to open-chain and simple alicyclic

allylic compounds are also applicable to these more complex molecules. Representative examples of allylic reactions in steroid and alkaloid systems are presented, but an exhaustive survey of the literature on these types of compounds was not made.

## II. Preparation of Allylic Compounds from Non-Allylic Starting Materials

It seems appropriate to begin a discussion of reactions of allylic compounds with a brief survey of some of the reactions by means of which these versatile substances can be prepared. A complete discussion of preparation of allylic compounds from non-allylic starting materials is beyond the scope of the present article. The outline which follows is intended merely to indicate some of the synthetic possibilities and give leading references to the literature.

### A. ADDITION REACTIONS

#### 1. Additions to conjugated dienes

Allylic compounds are formed when hydrogen halides, halogens, and $\alpha$-halo ethers are added to conjugated dienes under a variety of experimental conditions. Owing both to the occurrence of 1,4-addition and to isomerization of the initially formed allylic halides, mixtures of allylic halides are usually obtained from such reactions (167, 189, 200, 327, 329, 425, 435, 501, 504, 508, 517, 571, 613):

$$
\underset{\diagup}{\overset{\diagdown}{C}}=\underset{\diagup}{\overset{\diagdown}{C}}-\overset{|}{C}=\overset{|}{C}\diagup
$$

with reactions:

HX: $\diagdown C = \overset{|}{C}-\overset{|}{C}X-\overset{|}{C}H\diagup + \diagdown CH-\overset{|}{C}=\overset{|}{C}-\overset{|}{C}\diagdown X$

X₂: $\diagdown CX-\overset{|}{C}X-\overset{|}{C}=\overset{|}{C}\diagup + \diagdown CX-\overset{|}{C}=\overset{|}{C}-\overset{|}{C}\diagdown X$

RCHXOR′: $R'OCHR-\overset{|}{C}-\overset{|}{C}=\overset{|}{C}-\overset{|}{C}X +$

$R'OCHR-\overset{|}{C}-\overset{|}{C}X-\overset{|}{C}=\overset{|}{C}\diagup$

Reaction of *tert*-butyl hypochlorite with conjugated dienes in hydroxylic solvents (alcohols and carboxylic acids) yields mixtures of allylic chloro ethers and chloro esters (461, 464):

*tert*-C₄H₉OCl $+ \diagdown C=\overset{|}{C}-\overset{|}{C}=\overset{|}{C}\diagup \xrightarrow{ROH} Cl\overset{|}{C}-\overset{|}{\underset{OR}{C}}-\overset{|}{C}=\overset{|}{C}\diagup +$

$Cl\overset{|}{C}-\overset{|}{C}=\overset{|}{C}-\overset{|}{C}OR$

*2. Addition of organometallic compounds to α,β-unsaturated carbonyl compounds*

One of the most widely used methods of preparing allylic alcohols is the addition of Grignard reagents to α,β-unsaturated carbonyl compounds such as acrolein, crotonaldehyde, and cinnamaldehyde:

$$\diagup\!\!\!\!\diagdown C\!\!=\!\!C\!\!-\!\!\overset{O}{\overset{\|}{C}}\!\!-\quad+\quad RMgX\quad\rightarrow\quad \diagup\!\!\!\!\diagdown C\!\!=\!\!C\!\!-\!\!\overset{OH}{\underset{|}{C}}\!\!-\!\!R$$
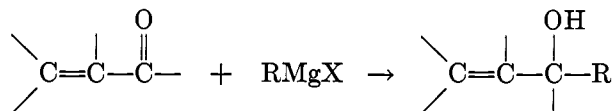
These reactions are carried out using ordinary procedures and usually give normal products.

*3. Addition of vinyl organometallic compounds to carbonyl compounds*

A useful synthesis of allylic alcohols from carbonyl compounds and lithium alkenyls has been developed by Braude and coworkers (79, 80, 81, 82, 83, 83a, 85, 87, 88, 89, 91):

$$\diagup\!\!\!\!\diagdown C\!\!=\!\!C\!\!-\!\!Li\quad+\quad R\overset{O}{\overset{\|}{C}}R'\quad\rightarrow\quad\diagup\!\!\!\!\diagdown C\!\!=\!\!C\!\!-\!\!\overset{OH}{\underset{|}{C}}RR'$$
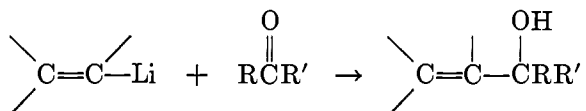
Vinyl Grignard reagents have also been used for the preparation of allylic alcohols from ketones (3, 83a, 699, 700).

*4. Reduction of multiple bonds*

(a) Reduction of α,β-unsaturated carbonyl compounds

There are a number of methods of reducing α,β-unsaturated carbonyl compounds or α,β-unsaturated carboxylic acids and their esters to allylic alcohols:

$$\diagup\!\!\!\!\diagdown C\!\!=\!\!C\!\!-\!\!\overset{O}{\overset{\|}{C}}R\quad\overset{H}{\longrightarrow}\quad\diagup\!\!\!\!\diagdown C\!\!=\!\!C\!\!-\!\!CHOHR$$
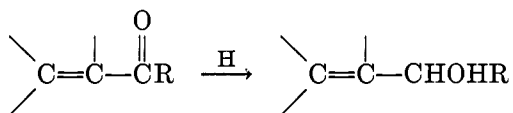
Probably the most satisfactory reducing agent is lithium aluminum hydride (92, 194, 258, 261, 412, 413, 656), although sodium borohydride (413) and aluminum isopropoxide (37, 670) are also used. Reduction with zinc in acetic acid, zinc–copper couples in water, and sodium in ethanol has been used, but frequently gives low yields of the allylic alcohol.

(b) Hydrogenation of propargyl compounds

Acetylenic Grignard reagents react with carbonyl compounds to yield substituted propargyl alcohols. The acetylenic bond of the propargyl alcohol can be partially reduced, yielding an allylic alcohol:

$$RCOR' + R''C\!\equiv\!CMgX \rightarrow RR'\overset{OH}{\underset{|}{C}}C\!\equiv\!CR'' \xrightarrow{2H} RR'\overset{OH}{\underset{|}{C}}CH\!\!=\!\!CHR''$$
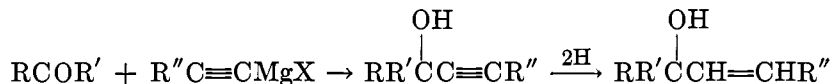
The reduction is usually carried out catalytically, using a catalyst such as palladium on barium sulfate (258). Lithium aluminum hydride has also been used (463). Catalytic reduction yields *cis* alcohols, while hydride reduction yields *trans* alcohols.

## B. ELIMINATION REACTIONS

### 1. Dehydrohalogenation reactions

Treatment of 1,2- and 1,3-dihalides with alkali or quinoline yields mixtures of dehydrohalogenation products which contain allylic compounds (248, 263, 391, 448, 614):

$$XC-CX-CH- \xrightarrow{-HX} XC-C=C$$

$$XC-\underset{H}{C}-CX \xrightarrow{-HX} XC-C=C$$
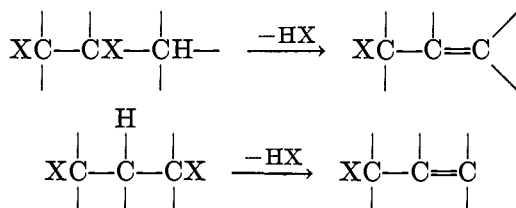
### 2. Dehydration reactions

Treatment of $\alpha$-halo alcohols with phosphorus pentoxide or thionyl chloride often results in formation of allylic halides (472, 345, 417, 497):

$$CX-\underset{OH}{C}-CH \xrightarrow{-H_2O} CX-C=C$$
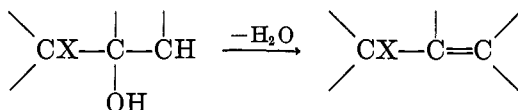
## C. SUBSTITUTION REACTIONS

### 1. Allylic halogenation of olefins

Free-radical halogenation of olefins usually yields mixtures of allylic halides. When *N*-bromosuccinimide is used, allylic bromides are formed (179a):

$$RR'C{=}CR''''CHR''R''' \xrightarrow{N\text{-bromosuccinimide}}$$

$$RR'C{=}CR''''CR''R'''Br \; + \; RR'CBrCR''''{=}CR''R'''$$
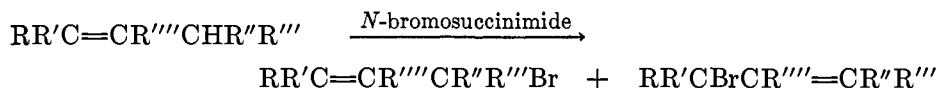
Allylic chlorination of olefins is sometimes feasible (20); chlorine is the usual chlorinating agent.

### 2. Selenium dioxide oxidation of olefins

Oxidation of olefins with selenium dioxide in acetic anhydride forms mixtures of isomeric allylic acetates (138, 639).

$$RR'C{=}\overset{R''''}{C}CHR''R''' \xrightarrow[(CH_3CO)_2O]{SeO_2}$$

$$RR'C{=}\overset{R''''}{C}CR''R'''OCOCH_3 \; + \; RR'C(OCOCH_3)\overset{R''''}{C}{=}CR''R'''$$
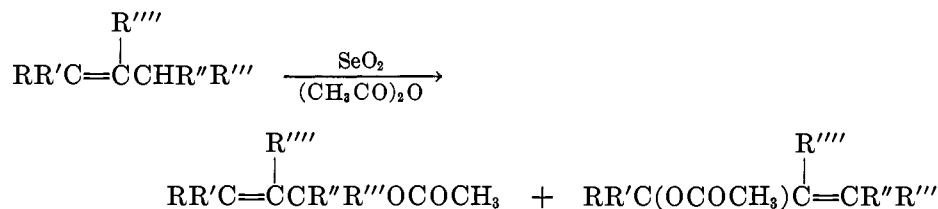
### D. REPLACEMENT OF CARBONYL GROUPS IN $\alpha,\beta$-UNSATURATED CARBONYL COMPOUNDS

#### 1. Conversion to dihalides

$\alpha,\beta$-Unsaturated aldehydes and ketones are converted to $\alpha$-halloallyl halides by treatment with phosphorus pentahalides or oxalyl chloride. The initially formed dihalides frequently isomerize under the conditions of the reaction (9, 12, 128, 338, 564, 581, 586, 590).

$$RR'C{=}CR''COR''' \xrightarrow[\text{or (COCl)}_2]{PX_5} $$

$$RR'C{=}CR''CX_2R''' \ + \ RR'CXCR''{=}CXR'''$$
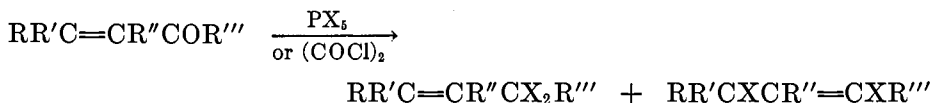
#### 2. Conversion to esters

$\alpha,\beta$-Unsaturated aldehydes are converted to $\alpha$-acetoxyallyl acetates by reaction with acetic anhydride in the presence of an acid catalyst. Acetyl chloride yields $\alpha$-haloallyl acetates (340, 341, 574, 575).

$$RR'C{=}CR''CHO \begin{cases} \xrightarrow{(CH_3CO)_2O} RR'C{=}CR''CH(OCOCH_3)_2 \\ \xrightarrow[CH_3COCl]{} RR'C{=}CR''CHCl(OCOCH_3) \end{cases}$$
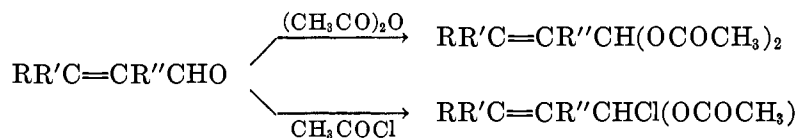
These esters isomerize in the presence of acid catalysts.

#### E. PROTOTROPIC REARRANGEMENTS

Allylic compounds are sometimes formed by prototropic rearrangements of substituted vinyl halides. The following sequence of reactions is illustrative (54, 372, 429):

$$ClCH{=}CRCH_2Cl \xrightarrow{MY} ClCH{=}CRCH_2Y \xrightarrow[X^-]{ROH} XCH_2CH{=}CHY$$
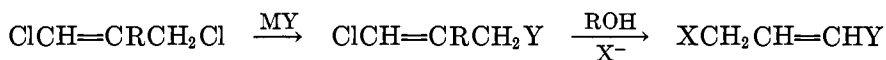
MY may be a metal cyanide or a Grignard reagent (and probably other nucleophilic reagents as well). The allylic chlorine atom formed by the prototropic shift will usually be replaced by the anion of the basic catalyst used to effect the rearrangement.

### III. MECHANISMS OF SUBSTITUTION IN ALLYLIC SYSTEMS

#### A. INTRODUCTION

Nucleophilic replacement reactions of allylic compounds are similar in many respects to analogous reactions of saturated compounds. Many investigators—notably Hughes, Ingold, and their collaborators in England and Bartlett, Winstein and others in this country—have demonstrated that nucleophilic substitution reactions at a saturated carbon atom may be divided into three general types (294, Chapter VII).

One mechanism, designated $S_N2$, is the familiar bimolecular, usually second-

order substitution of an electron donor such as hydroxide ion, alkoxide ion, or acetate ion for a halogen atom or similar substituent, as in equation 1. This replacement involves attack of the nucleophilic reagent at the backside of the

$$Y^- + RX \rightarrow YR + X^- \tag{1}$$
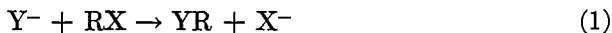
substituted carbon atom, the new bond being formed and the old one broken in a concerted process which results in a Walden inversion.

Another mechanism of substitution, designated as $S_N i$, involves an intramolecular rearrangement to form a product of retained configuration. An illustration of this mechanism is the decomposition of the chlorosulfite ester from an alcohol and thionyl chloride to produce an alkyl chloride and sulfur dioxide:

$$SOCl_2 + ROH \rightarrow ROSOCl \rightarrow RCl + SO_2$$

The third mechanism, called unimolecular nucleophilic substitution, involves electrophilic attack of solvent on the halogen or other substituent group to form an intermediate alkyl carbonium ion or ion-pair, which subsequently reacts rapidly with an electron donor to yield the final product. This mechanism is designated $S_N 1$ and may be represented by the following sequence of reactions:

$$RX \rightarrow R^+X^- \rightarrow R^+ + X^-$$

$$R^+ + YH \rightarrow RY + H^+$$

or

$$R^+ + Y^- \rightarrow RY$$
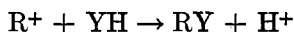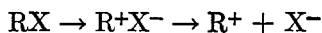
A variation of the $S_N 1$ mechanism involves electrophilic attack of a reagent such as silver ion on a halogen atom to produce the carbonium-ion intermediate.

### B. NORMAL BIMOLECULAR NUCLEOPHILIC DISPLACEMENT, $S_N 2$

Of the several mechanisms of substitution available to allylic compounds, normal bimolecular nucleophilic substitution most closely resembles the corresponding reactions of saturated compounds and bears the same mechanistic designation, $S_N 2$. $S_N 2$ reactions of allylic compounds have two distinguishing features: they are bimolecular (which in most cases is indicated by second-order kinetics) and they give *only* normal substitution products, in which the new functional group is attached to the same carbon atom of the allylic system as the group which it replaced:

$$RCH{=}CHCH_2X + Y^- \rightarrow RCH{=}CHCH_2Y + X^-$$
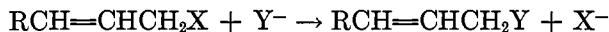
Practically all of the theoretical considerations which apply to $S_N 2$ reactions in saturated systems also apply to $S_N 2$ reactions of allylic compounds. For detailed theoretical background the reader is referred to a specialized treatise (294). The present discussion is limited to a brief survey of various structural and environmental factors which affect the rates of $S_N 2$ reactions of allylic compounds, and an enumeration of several substitution reactions of allylic compounds which appear to involve this mechanism.

*1. Factors influencing rates of $S_N2$ reactions of allylic compounds*

(a) The allylic double bond

Allylic halides are more reactive in $S_N2$ displacements than the corresponding saturated halides. For example, allyl chloride reacts with ethanolic sodium ethoxide 37 times faster than n-propyl chloride at 44.6°C., and γ-methylallyl chloride reacts 95 times faster than n-butyl chloride (629). Similarly, allyl chloride reacts 80 times faster with potassium iodide in acetone than n-propyl chloride (139). The reasons for the high $S_N2$ reactivity of allylic compounds compared to the corresponding saturated compounds are incompletely understood, but may involve a more favorable entropy of activation (629) and a lower energy of activation due to stabilization of the transition state by tautomeric release of electrons from the allylic double bond to the α-carbon atom (279).

$$C=\overset{\curvearrowleft}{C}-\underset{\vdots}{\overset{\overset{Y^{\delta-}}{\vdots}}{C^{\delta+}}}$$
$$\underset{X^{\delta-}}{}$$
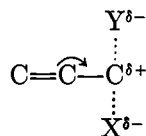
(b) Influence of substituents on the allylic group

Substituents on the allylic system, $\underset{\alpha}{C}=\underset{\beta}{C}-\underset{\gamma}{C}-X$, affect the rates of bimolecular displacement reactions in two ways: by electron release to, or withdrawal from, the site of reaction, and by steric interference with the approach of the nucleophilic reagent. Two bimolecular reactions have been studied for a sufficiently large number of allylic chlorides to permit steric and electronic effects to be evaluated: reaction with potassium iodide in anhydrous acetone and reaction with sodium ethoxide in absolute ethanol. The results of these studies agree well with the limited data available for other $S_N2$ reactions of allylic halides.

Steric retardation of $S_N2$ reactions by substituents on the α-carbon atom is very pronounced and occurs with both electron-releasing and electron-withdrawing substituents. Thus, α-methylallyl chloride and 3,3-dichloropropene are only a small fraction as reactive as allyl chloride in bimolecular substitution reactions (see table 1). When there are two substituents on the α-carbon atom, displacement by the normal $S_N2$ mechanism is usually so hindered that it is not observed. In such cases reaction occurs by either the unimolecular or the abnormal bimolecular mechanism, which will be discussed later.

It is not possible to predict from theoretical considerations how electron withdrawal from, and release to, the substituted carbon atom should affect the rates of $S_N2$ displacements. Electron-releasing substituents could facilitate bimolecular displacements by making it easier for the substituent to separate from the molecule with the pair of bonding electrons, or retard them by hindering the approach of a nucleophilic reagent. Electron-withdrawing substituents, on the other hand, should facilitate approach of the attacking reagent and render more difficult the separation of the leaving group.

The available data show that electron-releasing substituents facilitate bimo-

TABLE 1

*Relative reactivities of monosubstituted allyl chlorides with potassium iodide in acetone at 20°C. and sodium ethoxide in ethanol at 50°C. (11, 243, 244, 250, 251, 259, 349, 458, 576)*

| Substituent | $\alpha$ | | $\beta$ | | $\gamma$ | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | cis | | trans | |
| | KI | C₂H₅ONa | KI | C₂H₅ONa | KI | C₂H₅ONa | KI | C₂H₅ONa |
| Cl............. | ~0.01 | 0.012 | 0.72 | 0.47 | 8.58 | 2.8 | 2.90 | 3.47 |
| Br............. | | | 0.87 | 0.82 | 20 | 5.8 | 1.2 | 2.9 |
| CH₃.......... | 0.023 | 0.06 | 1.58 | 1.03 | 8.35 | 5.14 | 1.56 | 4.43 |
| C₆H₅......... | | | 2.27 | 1.12 | 17.5 | | 11.0 | 6.83 |
| | | | | | | | | (at 44.6°C.) |
| H............. | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |

lecular displacement reactions of allylic halides. This fact can be rationalized by assuming that electron-releasing substituents lower the energy of activation of the displacement reaction by stabilizing II, one of the canonical structures contributing to the transition state of the reaction.
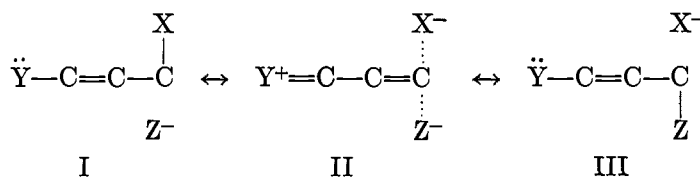


The facilitating effect of electron-releasing groups on bimolecular substitution reactions of allylic halides is in accord with results reported for $S_N2$ reactions of *p*-alkyl-substituted benzyl halides (57). The situation with regard to $S_N2$ reactions of other alkyl halides is complicated by the difficulty encountered in considering separately the steric and electronic effects of substituents on reaction rates. Webb and Young (636) have surveyed the literature on this controversy.

Halogen, aryl, and alkyl substituents on the $\gamma$-carbon atom of allylic chlorides increase the rate of bimolecular reactions with potassium iodide in acetone and with sodium ethoxide in ethanol (table 1). A $\gamma$-phenyl group is particularly effective in facilitating $S_N2$ displacements. It will be noted that a *cis*-$\gamma$-substituted allyl chloride is usually more reactive than its *trans* isomer. The reason for this is not evident.

Substituents on the $\beta$-carbon atom of the allylic system cannot bring into play the conjugative mechanism of electron release and, with the exception of the phenyl group, their effect on $S_N2$ reactivity is in line with their inductive effects; halogens retard bimolecular reactions and methyl and phenyl groups accelerate them. The rate differences are small, as might be expected for purely inductive effects.

Table 2 lists relative reactivity data for a number of di- and trisubstituted allyl chlorides. Most of these data are in line with the conclusions reached for monosubstituted allyl chlorides. Thus, two alkyl groups, two chlorine atoms, or an alkyl group and a chlorine atom on the $\gamma$-carbon atom of the allyl system

TABLE 2

*Relative reactivities of di- and trisubstituted allyl chlorides*

| Compound | Potassium Iodide | C₂H₅ONa | References |
|---|---|---|---|
| (CH₃)₂C=CHCH₂Cl | 28 | ~15 | (249, 629) |
| C₂H₅C(CH₃)=CHCH₂Cl | | ~20 | (636) |
| CH₃CH=C(CH₃)CH₂Cl | 3.8 | 5.5 | (597) |
| CH₃CCl=CHCH₂Cl (α) | 23.3 | 4.8 | (249) |
| CH₃CCl=CHCH₂Cl (β) | 27.8 | 6.16 | (249) |
| CH₃CH=CHCHCl₂ | 2.37 | 3.7 | (597) |
| CH₃CHClCH=CHCl | | 0.23 | (11) |
| CHCl=C(CH₃)CH₂Cl (α) | 32.8 | | (244, 250) |
| CHCl=C(CH₃)CH₂Cl (β) | 8.45 | | (244, 250) |
| CH₃CCl=CClCH₂Cl (cis) | 69 | 5.95 | (248) |
| CH₃CCl=CClCH₂Cl (trans) | 23 | 6.66 | (248) |
| CCl₂=C(CH₃)CH₂Cl | >33 | 7.42 | (244, 250) |
| CH₂=C(CH₃)CCl₂CH₃ | 0.07 | 0.11 | (248) |
| CHCl=CFCH₂Cl (α) | 48 | 3.3 | (254) |
| CHCl=CFCH₂Cl (β) | 4.2 | 2.0 | (254) |
| CH₂=CHCH₂Cl | 1.00 | 1.00 | |

greatly facilitate the $S_N2$ mechanism. Two compounds exhibit unexpectedly high reactivities: the low-boiling isomers of 1,2,3-trichloro-2-butene and 1,3-dichloro-2-fluoropropene are more reactive than the analogous compounds lacking β-halogen substituents, contrary to the expectation that β-halogen substituents deactivate the system.

Vernon (629) recently published the results of a kinetic investigation which are in substantial agreement with conclusions reached by other workers. He found the relative bimolecular reactivities of a series of allyl chlorides with sodium ethoxide in ethanol at 44.6°C. to be: $CH_2$=CHCH₂Cl, 1.00 ($k_2$ = 1.2 × 10⁻²); $CH_2$=C(CH₃)CH₂Cl, 0.89; CH₃CH=CHCH₂Cl, 2.62; CH₃CHClCH=CH₂, 0.049; (CH₃)₃CCH=CHCH₂Cl, 1.96; C₆H₅CH=CHCH₂Cl, 6.83; (CH₃)₂C=CHCH₂Cl, 15.0. It is interesting to note that γ-methylallyl chloride is more reactive than γ-*tert*-butylallyl chloride. Hyperconjugative electron release apparently is an important factor in the activating effect of γ-alkyl substituents. The second γ-methyl group produces a much larger increase in reactivity than the first. Thus, γ-methylallyl chloride is 2.62 times as reactive as allyl chloride, while γ,γ-dimethylallyl chloride is 5.7 times as reactive as γ-methylallyl chloride.

Vernon (629) appears to be the first to demonstrate definitely the occurrence of a bimolecular base-catalyzed elimination reaction (E₂) as a side reaction in the conversion of an allylic chloride to the corresponding ethyl ether with sodium ethoxide in ethanol. He isolated a small amount of butadiene from the products of reaction of α-methylallyl chloride with ethanolic sodium ethoxide. The E₂ reaction of α-methylallyl chloride is faster than the corresponding reaction of *sec*-butyl chloride, probably owing to resonance stabilization of the transition state of the reaction. No elimination product was isolated in the reaction with γ-methylallyl chloride, probably owing to the ease with which it undergoes substitution by mechanism $S_N2$.

Other $S_N2$ reactions for which kinetic data are available have not been extended to as many allylic halides as the reactions with potassium iodide or so-

dium ethoxide, but the results are usually in qualitative agreement with the conclusions reached in the preceding paragraphs. Thus, the $S_N2$ displacement of bromide by radiobromide ion in acetone is 160 times faster with $\gamma$-methylallyl bromide than with $\alpha$-methylallyl bromide (193). The relative rates of $S_N2$ exchange of chloride ion in acetone at 44.6°C. are: $CH_2\!\!=\!\!CHCH_2Cl$, 1.00; $CH_3CH\!\!=\!\!CHCH_2Cl$, 2.52; and $CH_3CHClCH\!\!=\!\!CH_2$, 0.031 (629). The reactivities of substituted allyl chlorides toward bimolecular hydrolysis in 50 per cent ethanol decrease in the order $\gamma$-$CH_3 > \beta$-$CH_3 > \gamma$-Cl > allyl (11, 629). Reactivities of allylic chlorides toward bimolecular hydrolysis in 50 per cent aqueous dioxane decrease in the sequence $\gamma$-Cl > allyl > $\beta$-$CH_3 > \beta$-Cl (352). Prevost (493) reported that $\gamma$-methylallyl chloride reacts about ten times as fast with alcoholic sodium ethoxide, alcoholic pyridine, and alcoholic ammonia as does $\alpha$-methylallyl chloride. $\gamma$-Methylallyl chloride reacts 18 times faster than $\alpha$-methylallyl chloride with sodium ethoxide in ethanol at 99.5°C., and 55 times faster at 25°C. (121, 660). $\gamma$-Methylallyl bromide is about four times as reactive as allyl bromide toward potassium iodide in acetone (308).

### (c) Nature of the displaced group

Quantitative information on the effect of the nature of the displaced group on the rate of $S_N2$ substitutions in allylic systems is very meager. Juvala (308) found that allyl bromide reacts over 800 times faster than allyl chloride with potassium iodide in acetone. Alkyl bromides usually react 30 to 40 times faster than the corresponding chlorides by the $S_N2$ mechanism (294, page 339). One reason for the lack of information regarding allylic compounds is that many of them are too labile for convenient study; they often react so rapidly that kinetic study is difficult, and in addition may isomerize even more rapidly than they undergo substitution. However, constitutional influences of the displaced group in aliphatic and allylic systems are qualitatively quite similar.

### (d) Nucleophilic character of the substituting agent

With a given allylic compound one would expect the rate of bimolecular substitution to increase with increasing nucleophilic character of the reagent. Again, there is a scarcity of quantitative information, but that which is available is in agreement with expectation. 3,3-Dichloropropene, for example, undergoes $S_N2$ substitution by ethoxide and phenoxide ions in ethanol at almost the same rate (phenoxide reacting somewhat faster), while the reaction with thiophenoxide ion, a powerful nucleophilic reagent for carbon, is about 250 times faster (173).

### (e) Effect of changes in medium on rate of bimolecular substitution

Increasing the polarity of the solvent should change the rate of $S_N2$ reactions, the magnitude and direction of the change depending on the disposition of charges in the reactants and in the transition state of the reaction (294, page 347). The rate of bimolecular displacement of halide by anionic reagents should show a small decrease with increasing solvent polarity. The predicted solvent effect is observed in bimolecular displacement reactions of alkyl halides, but

allylic chlorides behave erratically. The rate of hydrolysis of allyl chloride in alkaline aqueous dioxane solutions increases with increasing water content of the solvent (480, 629), contrary to theoretical predictions. The bimolecular reaction of allyl chloride is faster in alkaline aqueous ethanol than in absolute ethanol containing sodium ethoxide. This fact may be of little significance, however, since the nucleophilic reagent changes at the same time the solvent composition changes (629). Addition of nitromethane to the acetone solvent used in chloride-ion exchange reactions of allyl chloride decreased the rate of the reaction, as expected for an increase in solvent polarity, but the retardation was less with allyl chloride than with $n$-propyl chloride (629).

Pourrat and Schmitz (480) found that rates of bimolecular hydrolysis of allyl and methallyl chlorides are greatest in 50 per cent aqueous ethanol, less in 50 per cent aqueous dioxane, and least in 50 per cent acetone. The order of decreasing dielectric constants of these solvents is 50 per cent alcohol > 50 per cent acetone > 50 per cent dioxane. These results are discussed by Kirrman and Saito (352).

Of more importance than the relatively small effect of solvent polarity on rates of bimolecular displacement reactions of allylic compounds is the fact that these compounds are so reactive by the unimolecular mechanism that bimolecular substitution is often unobservable in polar solvents.

The effect of increasing the ionic strength of the reaction medium on the rate of $S_N2$ reactions should parallel the effect of increasing the dielectric constant of the solvent, provided that mass law effects are not involved, since in both cases the polarity of the reaction medium is increased. Schmitz (563) found that the rate of bimolecular hydrolysis of allyl and $\beta$-methylallyl chlorides in aqueous dioxane is decreased by the addition of sodium nitrate or sodium perchlorate to the solution, as predicted by theory.

### 2. Examples of substitution by the $S_N2$ mechanism

The $S_N2$ mechanism undoubtedly operates in many substitution reactions of allylic compounds which have not been investigated kinetically. The normal bimolecular mechanism is probably involved in the great majority of substitution reactions of primary and secondary allylic halides which take place in solvents of low polarity and give only normal products. This has been demonstrated by kinetic experiments for reactions in which hydroxide, alkoxide, phenoxide, thiophenoxide, and halide ions are the nucleophilic reagents, as already discussed.

The exclusive formation of normal substitution products (in which the structure of the allyl group is the same as in the starting material) is usually a reliable indication of substitution by the $S_N2$ mechanism in allylic compounds, since the unimolecular and abnormal bimolecular mechanisms give varying amounts of abnormal product. This criterion must be used with caution, however, since it is easy to overlook small amounts of abnormal product in working up a reaction mixture. In addition, many workers only report the main product of a reaction and neglect to mention whether other products were obtained. It should be pointed out that formation of a mixture of substitution products does not mean

that bimolecular substitution does not occur; it only means that this cannot be the only mechanism operating.

Reactions of primary and secondary allylic halides with alcoholic alkoxide, phenoxide, and thiophenoxide ions proceed by the $S_N2$ mechanism in a great majority of the cases reported. Reactions of primary and secondary allylic halides with amines frequently involve this mechanism, together with varying proportions of substitution by the abnormal bimolecular mechanism, $S_N2'$ (page 771). Hydrolysis of primary allylic halides by aqueous alkali often gives predominantly the normal substitution product. Reactions of allylic halides with a number of anionic reagents—azide, cyanide, halide, thiocyanate, hydride, phthalimide, and the anions derived from active methylene compounds and Grignard reagents—frequently appear to involve normal bimolecular substitution. The $S_N2$ mechanism probably operates in many instances when allylic alcohols are converted to halides via intermediate formation of phosphite, chlorosulfite, or chlorocarbonate esters. These and other possible examples of $S_N2$ replacement reactions are discussed in detail in the section on replacement reactions of allylic compounds.

## C. THE ABNORMAL BIMOLECULAR MECHANISM OF NUCLEOPHILIC SUBSTITUTION

### 1. Introduction

The usual mechanism of bimolecular substitution reactions of allylic compounds involves attack of the nucleophilic reagent at the substituted ($\alpha$) carbon atom of the allylic system. In 1938 Hughes (280) and Winstein (649) independently postulated that a second mechanism of bimolecular nucleophilic substitution should be available to allylic compounds. According to this mechanism, the nucleophilic reagent attacks the unsaturated carbon atom of the allylic system and displaces the substituent on the $\alpha$-carbon atom in a concerted process:

$$Y: + \ C{=}C{-}C{-}X \rightarrow (Y^{\delta-}\cdots C^{\delta+}{=}C{=}C^{\delta+}\cdots X^{\delta-}) \rightarrow Y{-}C{-}C{=}C + X^-$$
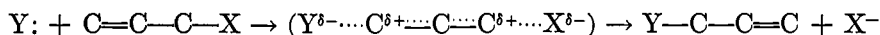
This process is called abnormal bimolecular substitution and is represented by the symbol $S_N2'$.

At least three conditions must be met before a reaction can be classified as an example of abnormal bimolecular substitution:

1. The rate of the reaction must be proportional to the concentration of both the substituting reagent and the compound being substituted (usually this implies second-order kinetics).
2. The reaction must give isolable amounts of abnormal substitution products.
3. It must be demonstrated that neither the starting material nor the normal substitution product undergoes rearrangement under the conditions of the reaction.

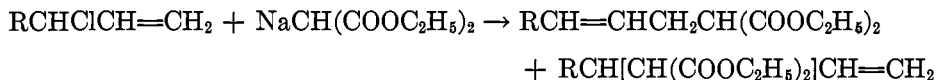Early attempts to establish the existence of the $S_N2'$ mechanism were fruitless. Hughes (279), in 1941, briefly mentioned unpublished work on the reaction of $\alpha$- and $\gamma$-methylallyl chlorides with sodium ethoxide in ethanol in which only normal substitution products were obtained. Roberts, Young, and Winstein (539) in 1942 published the results of an independent investigation of the same and

other reactions, in which it was found that the bimolecular reactions of neither the primary nor the secondary chloride give isolable amounts of abnormal substitution products. In 1948 Catchpole and Hughes (120) described a study of the effect of lithium $p$-nitrobenzoate on the rate of isomerization of $\alpha$-phenylallyl $p$-nitrobenzoate in acetonitrile and acetic anhydride solutions; it was concluded that the small variation in rate of isomerization with salt concentration could be attributed to salt effects, and that the $S_N2'$ mechanism does not operate significantly in this reaction. These workers also published a more detailed account of the reaction of $\alpha$- and $\gamma$-methylallyl chlorides with ethanolic sodium ethoxide, referred to by Hughes in 1941 (279), and concluded that substitution by mechanism $S_N2'$ does not occur under the conditions employed (121).

In 1948 preliminary results of a study of the exchange reaction between $\alpha$-methylallyl bromide and radioactive bromide ion in acetone at 30°C. were described. It was found that the rate of the $S_N2'$ reaction is less than one-hundredth of the rate of $S_N2$ substitution, and the conclusion reached was that abnormal bimolecular substitution is usually not available as a mechanism of allylic rearrangement (166).

As a result of these unsuccessful attempts to detect abnormal bimolecular substitution, Catchpole, Hughes, and Ingold (122) concluded in 1948 that substitution by $S_N2'$ apparently cannot be realized, and that it does not apply in the simplest and most typical cases of allylic rearrangement. They attributed the lack of appearance of $S_N2'$ reactions to shielding of the $\gamma$-carbon atom of the allylic system by the $\pi$-electrons of the double bond.

In 1944 Webb (633) found that $\alpha$-methylallyl chloride undergoes a bimolecular reaction with diethylamine which forms only abnormal product, and in the following year Kepner, Young, and Winstein (326) published the first evidence for the occurrence of an $S_N2'$ reaction. They found that $\alpha$-methylallyl and $\alpha$-ethylallyl chlorides react with sodium malonic ester in ethanol to give 10 and 23 per cent, respectively, of the product which would result from an abnormal bimolecular displacement involving attack on the $\gamma$-carbon atom. Kinetic studies with $\alpha$-ethylallyl chloride showed that the reaction was second order:

$$RCHClCH\!\!=\!\!CH_2 + NaCH(COOC_2H_5)_2 \rightarrow RCH\!\!=\!\!CHCH_2CH(COOC_2H_5)_2$$
$$+ RCH[CH(COOC_2H_5)_2]CH\!\!=\!\!CH_2$$

Dewar (177) questioned the validity of the conclusions reached from these results, maintaining that the observed formation of abnormal substitution product could be due to $O$-alkylation by the anion of the pseudo-acid reagent, followed by Claisen rearrangement of the resulting vinyl ether:

$$RCHClCH\!\!=\!\!CH_2 \quad + \quad Na^+[CH(COOC_2H_5)_2]^- \quad \rightarrow$$

RCHCH=CH₂
   |
   OC=CHCOOC₂H₅ → RCH=CHCH₂CH(COOC₂H₅)₂
   |
   OC₂H₅

I                                        II
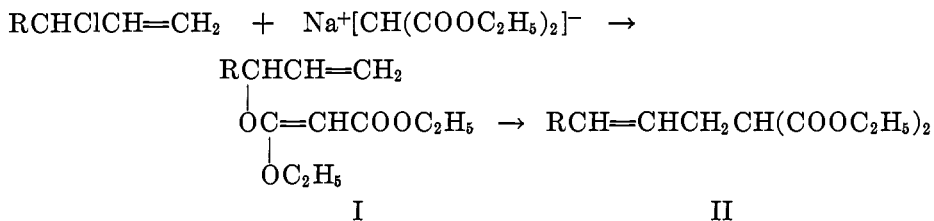
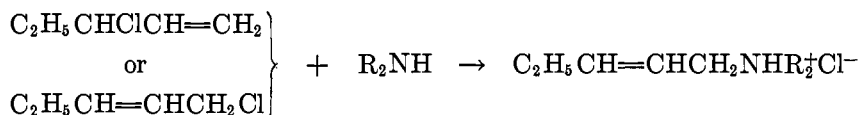However, this process is a rather unlikely explanation of the observed results. As Winstein (648) has pointed out, the postulated intermediate (I) is a ketene acetal, which would be expected to react with the alcohol solvent to give an ortho ester rather than the abnormal product (II). As mentioned elsewhere (page 861), a wide variety of primary allylic halides react with the sodium derivatives of acetoacetic and malonic esters to give high yields of normal $C$-alkylated products; no $O$-alkylated products have been reported from such reactions. Perhaps the most convincing argument against the occurrence of $O$-alkylation in these reactions is based on the fact that a significant amount of abnormal product was obtained when sodium malonic ester was allowed to react with $\alpha$-methylallyl chloride at room temperature. Under these mild conditions it is very unlikely that I would rearrange if it were formed. Simple vinyl allyl ethers undergo thermal isomerization at appreciable rates only when heated above 150°C. (51, 288, 565, 583).

Once the existence of the $S_N2'$ mechanism had been demonstrated, further examples were soon discovered. Young, Webb, and Goering (692) found that $\alpha$-methylallyl chloride undergoes a bimolecular reaction with diethylamine which gives only abnormal product, and demonstrated that the $S_N2'$ mechanism is involved. England and Hughes (193) a short time later published the results of a study of bromide-exchange reactions of $\alpha$- and $\gamma$-methylallyl bromides, in which the rates of substitution by the $S_N2$ and $S_N2'$ mechanisms were determined. More recently, de la Mare and Vernon (168, 172, 173, 174, 175) have published a series of papers on $S_N2'$ reactions of allylic chlorides having sterically hindered $\alpha$-carbon atoms, and Stork and White (588) have described abnormal bimolecular displacement reactions of substituted cyclohexenyl 2,6-dichlorobenzoates. These reactions will be discussed in more detail in the following paragraphs.

### 2. Examples of abnormal bimolecular displacement reactions

### (a) Abnormal reactions of allylic compounds with amines

Meisenheimer and Link (419) appear to have been the first to obtain abnormal products from the reaction of an amine with an allylic halide. They found that $\alpha$-ethylallyl chloride on treatment with diethylamine or methylaniline yielded abnormal products, the same ones obtained from $\gamma$-ethylallyl chloride.

$$\left.\begin{array}{l} C_2H_5\,CHClCH{=}CH_2 \\ \qquad\text{or} \\ C_2H_5\,CH{=}CHCH_2\,Cl \end{array}\right\} \;+\; R_2NH \;\rightarrow\; C_2H_5\,CH{=}CHCH_2NHR_2^+Cl^-$$

More recently, Jones, Lacey, and Smith (303) observed the formation of abnormal products from the reaction of diethylamine with the halides $RC{\equiv}CCH{=}CHCHClCH_3$ ($R = H$ or $n\text{-}C_4H_9$), and Blicke (62) reported that 2-chloro-3-penten-1-ol yields only abnormal product when heated with ethylamine. Only abnormal products are formed by the reaction of 5-alkoxy-3-chloro-1-pentenes with diethylamine and ethylaniline; aniline gave a mixture of normal and abnormal substitution products (506).

In 1949 Kepner, Winstein, and Young (326) speculated that some of these

results might be due to abnormal bimolecular displacement reactions, and in 1951 Young, Webb, and Goering (692) reported the results of an investigation in which they found that both $\alpha$- and $\gamma$-methylallyl chlorides react with diethylamine in benzene solution to give $N,N$-diethyl-$\gamma$-methylallylamine; it was later found that $\alpha$-methylallyl chloride and dimethylamine undergo an analogous abnormal reaction (641). Formation of abnormal product in the diethylamine reaction was not due to rearrangement of $\alpha$-methylallyl chloride prior to substitution or to rearrangement of an initially formed normal substitution product. Kinetic studies showed that the reaction is a bimolecular process in which two moles of diethylamine are consumed for each mole of halide, in accordance with the kinetic equation:

$$d[RNH(C_2H_5)_2{}^+Cl^-]/dt$$
$$= k_2'[(RCl)_0 - (RNH(C_2H_5)_2{}^+Cl^-)][((C_2H_5)_2NH)_0 - 2(RNH(C_2H_5)_2{}^+Cl^-)]$$

The reaction indicated by the kinetics is one in which one mole of diethylamine is consumed in a bimolecular substitution reaction and a second mole is subsequently converted to diethylammonium ion:

(1)  $(C_2H_5)_2NH + CH_2{=}CHCHClCH_3 \rightarrow ((C_2H_5)_2NHCH_2CH{=}CHCH_3)^+Cl^-$

(2)  $((C_2H_5)_2NHCH_2CH{=}CHCH_3)^+Cl^- + (C_2H_5)_2NH$

$$\rightarrow (C_2H_5)_2NCH_2CH{=}CHCH_3 + (C_2H_5)_2NH_2{}^+Cl^-$$
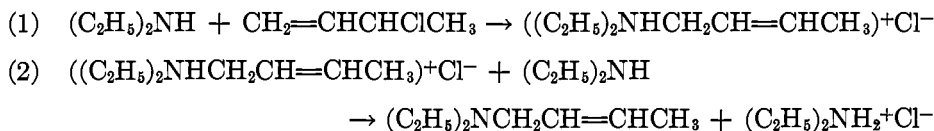
Step 2 could be caused by a combination of the relative basicities of the two amines and the lesser solubility of diethylamine hydrochloride in benzene. Throughout the reaction an amine hydrochloride is precipitated from the benzene solution, and this may be an important factor in shifting the equilibrium of step 2 to the right. The reaction of $\alpha$-methylallyl chloride with triethylamine was also found to yield only abnormal substitution product, but the reaction mechanism could not be assigned in this case since neither the chloride nor the normal substitution product is stable under the conditions of the reaction.

It was suggested by Kepner, Winstein, and Young (326) that the formation of abnormal product in reactions of diethylamine with secondary allylic chlorides might be aided by preliminary hydrogen bonding between the amine and the chlorine atom of the halide:
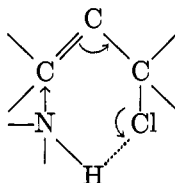


Owing to this possibility of hydrogen bonding, England and Hughes (193) and Ingold (294) choose to classify these reactions not as examples of the $S_N2'$ mechanism but as examples of the $S_Ni'$ mechanism (substitution by intramolecular rearrangement of an intermediate compound). Hydrogen bonding is a rather weak

interaction compared to the covalent bonding usually involved in the intermediate complexes of $S_Ni'$ substitutions, and it would seem to be largely a matter of personal preference whether to consider this cyclic process a modification of the $S_N2'$ mechanism or a borderline case of the $S_Ni'$ mechanism.

Young and Clement (665, 666) have recently shown that preliminary hydrogen bonding is not a necessary condition for the operation of the $S_N2'$ mechanism in reactions of amines with allylic halides. The reaction of trimethylamine with $\alpha$-methylallyl chloride in acetone solution is second order, and between 40°C. and 75°C. yields a mixture of quaternary ammonium salts consisting of 30 per cent trimethyl-$\alpha$-methylallylammonium chloride, 7 per cent cis-trimethyl-$\gamma$-methylallylammonium chloride, and 63 per cent trans-trimethyl-$\gamma$-methylallylammonium chloride. In other words, 70 per cent of abnormal product is formed. It was demonstrated that neither $\alpha$-methylallyl chloride nor the normal substitution product rearranges under the conditions of the experiments—convincing evidence that the abnormal substitution product is formed by abnormal bimolecular substitution.

Even allyl chloride reacts with secondary and tertiary amines by the $S_N2'$ mechanism. By using $C^{14}$-labeled chloride it was possible to demonstrate that the bimolecular reaction with dimethylamine in benzene solution forms 25 per cent of abnormal product, while in the reaction with trimethylamine $S_N2'$ substitution accounts for 7 per cent of the reaction product (641). These results are significant in two respects: They provide further evidence for the facilitation of abnormal substitution by the hydrogen atom of secondary amines, and they show in a striking way the relative unimportance of steric effects in $S_N2'$ reactions of amines. In reactions of amines steric suppression of the normal $S_N2$ reaction by $\alpha$-substituents apparently is not required for the observance of reaction by the $S_N2'$ mechanism.

Amundsen and Brill (7) report that 3-chloro-5-methoxy-1-pentene yields only the abnormal substitution product in reactions with dimethylamine in hexane. The secondary chloride and both of the possible amine reaction products are stable under the conditions of the reactions, and the reaction rate was "approximately second order." The $S_N2'$ mechanism was proposed to explain these results.

Stork and White (588) found that trans-6-alkyl-2-cyclohexenyl 2,6-dichlorobenzoates undergo a bimolecular reaction with piperidine, trans-4-(1-piperidyl)-alkyl-2-cyclohexenes being the only isolable products.
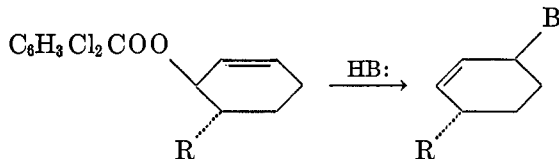


The cis relationship of the entering and departing groups is in agreement with the steric course postulated for the $S_N2'$ mechanism by Young, Webb, and Goering (692).

Morpholine and piperidine give abnormal substitution products in reactions with 3-chloromethylbenzothiophene 1,1-dioxide:
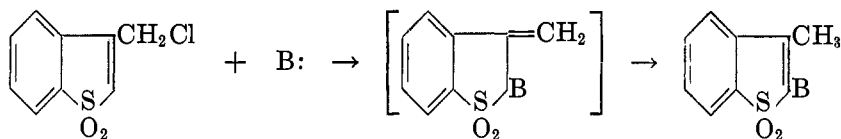


Kinetic and chemical evidence shows that these abnormal reactions are of the $S_N2'$ type (67). This reaction appears to be the only example reported of an $S_N2'$ substitution reaction of a primary $\gamma$-substituted allylic halide.

### (b) Exchange reactions

Substitution reactions in which the entering and leaving groups are the same should provide an ideal tool for establishing the occurrence of abnormal bimolecular substitution. The reason for this is that each act of substitution by the $S_N2$ mechanism gives unchanged starting material, which thus remains available for isomerization by the $S_N2'$ mechanism:



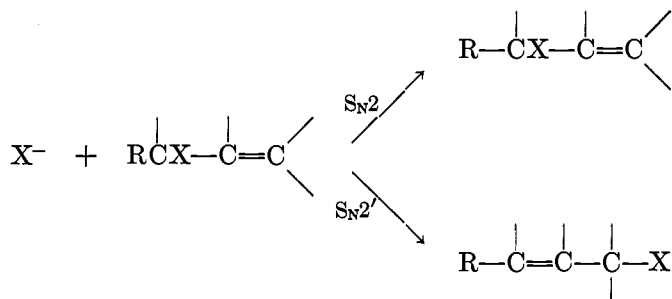The simplest means of demonstrating the operation of the $S_N2'$ mechanism in an exchange reaction is to show that the rate of isomerization of the allylic compound is proportional to the concentration of the common ion, $X^-$. Catchpole and Hughes (120) investigated the effect of lithium $p$-nitrobenzoate on the rate of isomerization of $\alpha$-phenylallyl $p$-nitrobenzoate in acetonitrile and acetic anhydride solutions, and concluded that the observed small increase in rate was probably a salt effect rather than evidence for the operation of the $S_N2'$ mechanism.

de la Mare, England, Fowden, Hughes, and Ingold (166) described an elegant extension of this technique. In addition to determining the rate of isomerization of an allylic compound, they proposed the use of an isotopically labeled substituting agent, which would permit an accurate determination of the rate of exchange by the $S_N2$ mechanism. If no detectable isomerization occurred, it would then be possible to state how many half-lives of mechanism $S_N2$ fail to produce conversion by mechanism $S_N2'$. The practical limit to the severity of this test

TABLE 3

*Kinetic data on the exchange reactions of α- and γ-methylallyl bromides (192)*

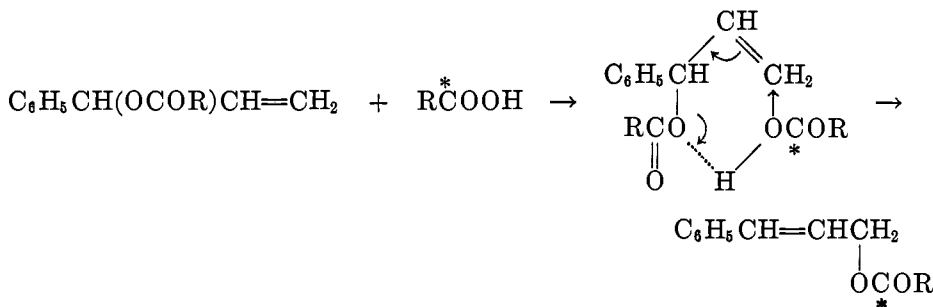| Bromide | Reaction | $10^8 k_2$ (25°C.) | log $A$ | $E_A$ |
|---|---|---|---|---|
| α-Methylallyl .................. | $S_N2$ | 87.4 | 9.06 | 16.5 |
| α-Methylallyl.................. | $S_N2'$ | 14.9 | 9.40 | 19.4 |
| γ-Methylallyl.................. | $S_N2$ | 141,000 | 9.93 | 14.7 |
| γ-Methylallyl.................. | $S_N2'$ | 5 | ⏝9 | ⏝19 |

would be determined by the rate of isomerization by mechanisms $S_N1$ and $S_Ni'$, and, of course, by the rates of all side reactions which destroy the starting material.

In 1951 England and Hughes (192, 193) published the results of an investigation of the exchange reactions of α- and γ-methylallyl bromides with radioactive lithium bromide in acetone solution. The rates of the normal and abnormal substitution reactions appear in table 3. The values labeled $S_N2'$ were calculated on the basis that isomerization of the bromides occurs only by this mechanism under the conditions studied.

The $S_N2'$ reaction of α-methylallyl bromide is only three times faster than that of γ-methylallyl bromide, in contrast to the large steric retardation of the $S_N2$ reaction by a methyl group on the carbon atom being substituted. Actually, the small difference in rates of isomerization of these bromides is a consequence of their similar thermodynamic stabilities, since the relative rates of isomerization (whatever the mechanism involved) must be such that the well-known equilibrium composition of ca. 80 per cent primary bromide and ca. 20 per cent secondary bromide is attained (652). The limitation in this study is that isomerization by mechanism $S_N1$ or $S_Ni'$ is not ruled out. If thermal or lithium-ion-catalyzed isomerization of the bromides were involved, the rates given for $S_N2'$ substitution would not be valid, but could nevertheless be used in estimating a lower limit for the ratio $k_{S_N2}/k_{S_N2'}$. It is not possible rigorously to demonstrate the occurrence of $S_N2'$ substitution in exchange reactions of this type, for which the normal substitution reactions are more rapid than the isomerization reactions; even when the rate of isomerization is directly proportional to the concentration of lithium bromide, it is possible that the reaction involved is lithium-ion-catalyzed isomerization by mechanism $S_N1$ or $S_Ni'$. This possibility might be excluded by demonstrating that the rate of rearrangement is independent of the nature of the cation of the bromide salt.

Braude, Turner, and Waight (90) recently studied the exchange and isomerization reactions of α-phenylallyl p-nitrobenzoate in chlorobenzene solutions of radioactive p-nitrobenzoic acid. At low concentrations of p-nitrobenzoic acid the rate of exchange was much less than the rate of rearrangement to γ-phenylallyl p-nitrobenzoate, but at higher acid concentrations the rate of exchange increased rapidly. The majority of the exchange does not involve rearrangement. The acid-catalyzed rearrangement is bimolecular and may involve attack of the unionized acid at the γ-carbon atom of the allylic system through a cyclic transi-

tion state involving a hydrogen bond:

$$C_6H_5CH(OCOR)CH=CH_2 \ + \ \overset{*}{R}COOH \ \rightarrow \ \underset{O}{\underset{\|}{\underset{RCO}{\overset{C_6H_5CH}{\overset{CH}{\diagdown}}}}} \overset{CH_2}{\underset{OCOR}{\uparrow}} \ \rightarrow$$

$$C_6H_5CH=CHCH_2$$
$$|$$
$$\underset{*}{OCOR}$$

This would be an abnormal bimolecular substitution reaction. However, it is also possible that a preliminary proton transfer occurs, followed by intramolecular rearrangement of the conjugate acid of the ester ($S_Ni'$).

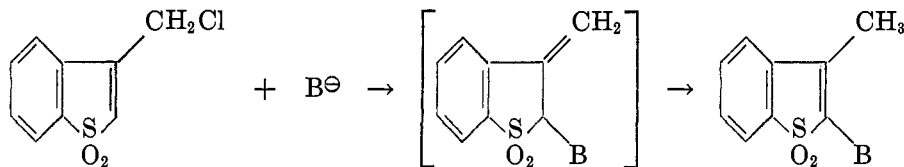### (c) Abnormal substitutions by alkoxide, phenoxide, thiophenoxide, and sulfide ions

The reaction of $\alpha$-methylallyl chloride with sodium ethoxide in ethanol is bimolecular and yields less than 5 per cent abnormal product (121, 175, 279, 539). The corresponding primary chloride, $\gamma$-methylallyl chloride, appears to form only normal substitution products under these conditions. The predominant or exclusive formation of normal products in these reactions does not mean that substitution by mechanism $S_N2'$ does not occur, but only that the rate of normal substitution is so much greater than the rate of abnormal substitution with these simple compounds that abnormal reaction by mechanism $S_N2'$ cannot be detected. $\alpha$-Methylallyl chloride undergoes a second-order reaction with alcoholic sodium thiophenoxide to give a mixture of products containing some $\gamma$-methylallyl phenyl sulfide, but this abnormal product may arise from thermal isomerization of the normal substitution product (142, 175).

Catchpole, Hughes, and Ingold (122) suggested that introduction of suitable substituents into the allylic system might sterically inhibit mechanism $S_N2$ sufficiently to render substitution by the $S_N2'$ mechanism observable. De la Mare and Vernon (168, 172, 173) later published a series of papers utilizing this principle. They found that 3,3-dichloropropene undergoes simultaneous $S_N2$ and $S_N2'$ reactions with alcoholic sodium ethoxide, phenoxide, and thiophenoxide, and that 3,3,3-trichloro-2-methyl-1-propene reacts with alcoholic sodium thiophenoxide and ethoxide predominantly or entirely by the $S_N2'$ mechanism (174, 346, 417). $\alpha,\alpha$-Dimethylallyl chloride also seems to undergo exclusive abnormal bimolecular substitution by alcoholic sodium thiophenoxide (175). The effects of steric and electronic properties of substituents on the allylic system on the extent and rate of $S_N2'$ reactions will be discussed later.

Kland-English and Wilson (356) recently reported that furfuryl chloride undergoes a bimolecular reaction with methanolic sodium methoxide which forms 40 per cent of abnormal product (279).

(60 per cent)  (40 per cent)
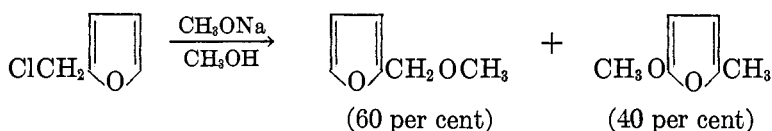
The initially formed abnormal product is assumed to undergo rapid prototropic rearrangement to 2-methoxy-5-methylfuran. This reaction is the only kinetically established example of abnormal bimolecular substitution at the terminal double bond of a conjugated dienic system. 3-Chloromethylbenzothiophene 1,1-dioxide undergoes $S_N2'$ reactions with sodium methoxide and sodium thiophenoxide (67):



A number of reactions which have not been investigated kinetically may be examples of abnormal bimolecular substitutions by alkoxide, sulfide, or phenoxide ions in alcoholic solution. A mixture of normal and abnormal substitution products is obtained from the reaction of 3,3-dichloro-1-propene with sodium ethylmercaptide in ethanol (540). This is probably the result of an $S_N2'$ reaction, since this chloride has been shown to undergo abnormal bimolecular substitution by sodium ethoxide in ethanol (172). $\alpha,\alpha$-Dimethylallyl chloride on treatment with methanolic sodium methoxide yields a mixture of primary and tertiary ethers, as does $\alpha$-methyl-$\alpha$-propylallyl chloride (438, 440, 612). However, these tertiary chlorides should be very reactive by the $S_N1$ mechanism, and it is probable that the observed mixtures of products are the result of unimolecular solvolysis reactions. 1-Carbomethoxy-6-methylphenoxide ion reacts with $\alpha$-ethylallyl chloride in methanol to give a mixture of the normal and abnormal substitution products (536). 5-Alkoxy-3-chloro-1-pentenes upon treatment with alcoholic sodium hydrosulfide yield only abnormal substitution products (510, 515). As the kinetics of these reactions have not been studied, it is not possible to state that the abnormal products were formed by bimolecular reactions.
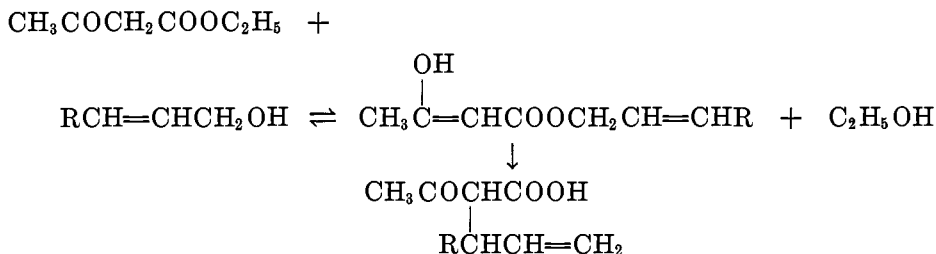
Stork (587) suggests that the reaction of $\alpha$-chlorocodide with methoxide ion and similar displacements are examples of $S_N2'$ reactions forced by steric hindrance to the normal displacements.
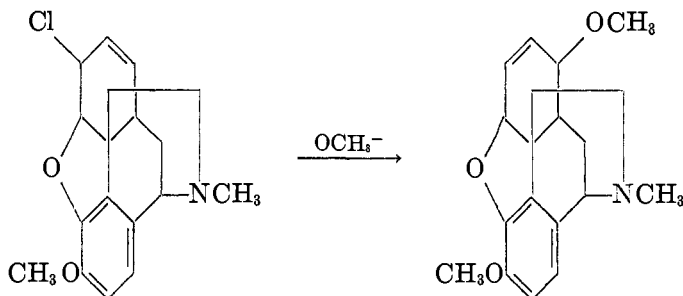
(d) *Abnormal substitutions by anions of pseudo acids*

The only definitely established $S_N2'$ reaction involving anions from active methylene compounds is that of sodium malonic ester with α-ethylallyl chloride (326) (see page 770). Barnard and Bateman (37) also report the formation of the abnormal substitution product in this reaction. Several similar substitutions by anions of acetoacetic ester and malonic ester in ethanol solution give varying amounts of abnormal products, and the strong nucleophilic character of the reagents makes it likely that at least some of these reactions involve the $S_N2'$ mechanism. Only abnormal products are obtained from the reactions of the sodium salts of acetoacetic and malonic esters with 3-chloro-5-methoxy-1-pentene in ethanol solution (503, 510). Barnard and Bateman found that a mixture of linalyl and geranyl chlorides reacts with alcoholic sodium malonic ester to give only geranyldiethyl malonate—a result which they explain by assuming that linalyl chloride (a tertiary allylic chloride) undergoes only abnormal bimolecular substitution. The formation of only abnormal products in bimolecular reactions of tertiary allylic halides is to be expected, owing to steric suppression of $S_N2$ reactions by the alkyl substituents on the α-carbon atom. In spite of this, the formation of γ,γ-dimethylallyl diethyl malonate by the reaction of isoprene hydrobromide with sodium malonic ester has been cited as evidence that the bromide was the primary isomer (582). While this assignment is probably correct, both the primary and the tertiary bromide would be expected to give the same product with sodium malonic ester.

Carroll (115, 116, 117) carried out substitution reactions with several allylic alcohols where the nucleophilic reagent was the acetoacetic ester anion and obtained only rearranged products. Wilson (644) suggested that these reactions might be examples of abnormal bimolecular substitution. It was subsequently shown that a more likely mechanism is ester interchange between acetoacetic ester and the allylic alcohol, followed by a Claisen-type rearrangement of the enol form of the resulting allylic ester (336):

$$CH_3COCH_2COOC_2H_5 \; +$$

$$
\begin{array}{c}
\qquad\qquad\qquad\qquad OH \\
\qquad\qquad\qquad\qquad | \\
RCH{=}CHCH_2OH \; \rightleftharpoons \; CH_3C{=}CHCOOCH_2CH{=}CHR \; + \; C_2H_5OH \\
\qquad\qquad\qquad\qquad\qquad \downarrow \\
\qquad\qquad\qquad\qquad CH_3COCHCOOH \\
\qquad\qquad\qquad\qquad\quad | \\
\qquad\qquad\qquad\qquad RCHCH{=}CH_2
\end{array}
$$

Diene dibromides react with the sodium salts of malonic, acetoacetic, and cyanoacetic esters to give substituted cyclopropane derivatives (332, 333, 334). These reactions probably involve $S_N2$ substitution followed by "intramolecular $S_N2'$" ($S_Ni'$) reactions.

Bergmann in 1937 reported that sodium malonic ester reacts with optically active α,γ-dimethylallyl chloride to form a racemic product (50). He explained this result by means of a mechanism closely resembling the $S_N2'$ mechanism later

proposed by Hughes and Winstein (280, 649). Abnormal bimolecular substitution could not be definitely established, since substitution by mechanisms $S_N2$ and $S_N2'$ gives the same product with this symmetrically substituted allylic chloride. It seems unlikely that the $S_N2'$ mechanism would operate to the exclusion of $S_N2$ in this case; more probably the chloride racemized before it underwent substitution.

### (e) Abnormal bimolecular substitution by thiourea

$\alpha,\alpha$-Dimethylallyl chloride undergoes with thiourea in acetone a second-order reaction which yields only the abnormal substitution product, $\gamma,\gamma$-dimethyl-allylthiuronium chloride (543, 659).

$$(CH_3)_2CClCH{=}CH_2 + S{=}C(NH_2)_2 \rightarrow (CH_3)_2C{=}CHCH_2S{=}C(NH_2)_2{}^+Cl^-$$
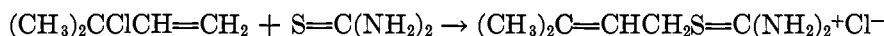
The fact that this reaction gave good second-order kinetics and was less than a tenth as fast as the corresponding reaction of $\gamma,\gamma$-dimethylallyl chloride strongly indicates that abnormal bimolecular substitution occurred. If slow isomerization of the tertiary chloride to its primary isomer followed by rapid substitution of the primary halide were involved, second-order kinetics would not have been observed; and if rapid isomerization of the tertiary halide followed by a slower reaction of the primary halide occurred, $\alpha,\alpha$- and $\gamma,\gamma$-dimethylallyl chlorides would have undergone substitution at the same rate. 3-Chloromethyl-benzothiophene 1,1-dioxide has recently been reported to undergo $S_N2'$ substitution by thiourea (67).

### (f) Other reactions which may involve abnormal bimolecular substitution

A number of nucleophilic displacement reactions of allylic compounds occur under conditions which should lead to bimolecular substitution, yet give rise to varying amounts of abnormal products. Some of these have been postulated to involve the $S_N2'$ mechanism. It would be well to reëmphasize at this point that a careful study of the kinetics and products of a reaction, as well as the ease of isomerization of reactants and products, is required to establish definitely that a reaction is $S_N2'$. Most of the examples discussed in the following paragraphs are based on the formation of abnormal product alone and are therefore purely speculative.

Furfuryl chloride when shaken with aqueous sodium or potassium cyanide
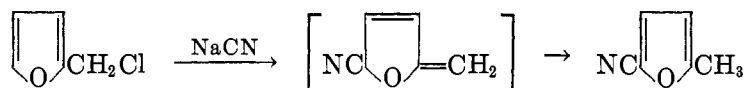


Furfuryl chloride

yields a mixture of nitriles in which the abnormal product predominates (427, 526, 544). Sorbyl chloride undergoes a similar abnormal reaction (528).

$$CH_3CH{=}CHCH{=}CHCH_2Cl \xrightarrow{\text{aq. KCN}} CH_3CH(CN)CH{=}CHCH{=}CH_2$$
Sorbyl chloride
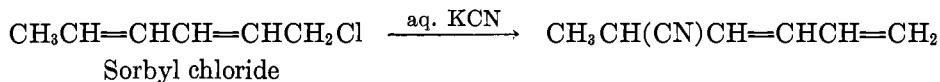
If these reactions proceed through a carbonium-ion intermediate, a significant amount of substitution by hydroxyl rather than cyanide would be expected; however, no hydrolysis is reported. The recent kinetic demonstration of an $S_N2'$ reaction between furfuryl chloride and methanolic sodium methoxide (356) supports the idea that substitution by cyanide may proceed by the $S_N2'$ mechanism. Eliel and Peckham (188) found that furfuryltrimethylammonium iodide forms a small amount of abnormal product when heated with sodium cyanide at 200°C. and suggest that this may be due to an $S_N2'$ reaction:



$$\text{(5\%)} \qquad\qquad \text{(27\%)}$$
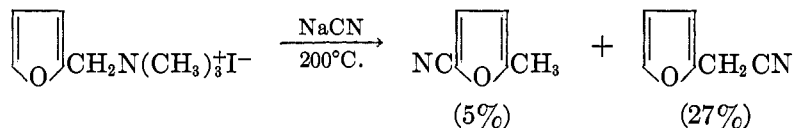
The drastic conditions of the reaction make it difficult to rule out an ionic mechanism in this case.

5-Alkoxy-3-chloro-1-pentenes react with sodium and magnesium dialkyl phosphites in ether or in absence of solvent to give only abnormal products (500, 513).

2,3,3-Trichloro-1-butene is reduced to 2,3-dichloro-2-butene by lithium aluminum hydride (248). Since primary allylic halides undergo reduction without rearrangement with this reagent (page 860), an $S_N2'$ substitution of chloride by hydride seems a reasonable explanation for this reaction.

Phillips reports that $\alpha$- and $\gamma$-methylallyl chlorides react with diazoacetic ester to give mixtures of $\alpha$-halo esters rather than the expected cyclopropane derivatives (474). The formation of products in which the structure of the allylic system has been inverted is postulated to be due to $S_N2'$ attack on the allylic halides by a highly reactive carbethoxy carbene fragment from diazoacetic ester.

$$\text{C}_2\text{H}_5\text{OOCCH:} + \text{CH}_2\text{=CHCHClCH}_3 \rightarrow \text{C}_2\text{H}_5\text{O}_2\text{CCHClCH=CHCH}_3$$

The author stated that a kinetic study of this reaction was in progress.

Formation of 2-$\alpha$-acetoxy-$\Delta^4$-cholesten-3-one in the reaction of 6-$\beta$-bromo-$\Delta^4$-cholesten-3-one with potassium acetate in acetic acid (202) may be due to $S_N2'$ attack of acetate ion on the enol form of the ketone:
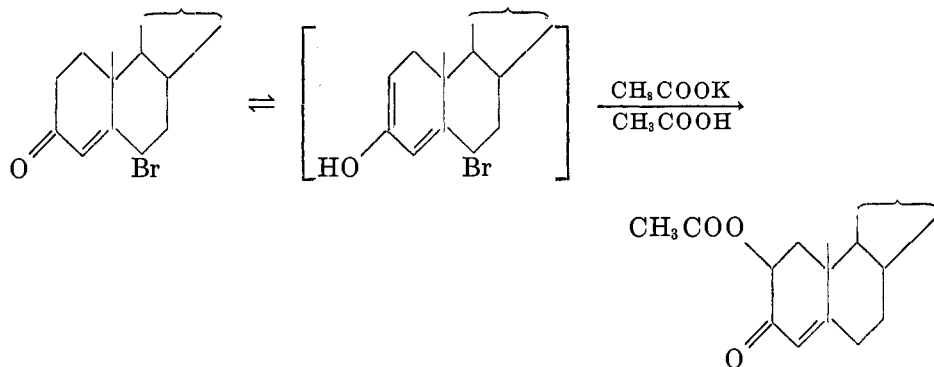
6-Bromotestosterone acetate has been reported to undergo a similar reaction (578).

### 3. Factors influencing the extent and rate of abnormal bimolecular substitution

#### (a) Structure of the allylic system

The most important effect of structure on the $S_N2'$ mechanism operates indirectly. $\alpha$-Substituents on the allylic system sterically retard the normal bimolecular substitution without similarly retarding the abnormal bimolecular substitution. That is, $\alpha$-substituents increase the ratio $(k_{S_N2'}/k_{S_N2})$ of rates of $S_N2'$ to $S_N2$ reaction. With very few exceptions, $S_N2'$ reactions have been observed only with secondary or tertiary allylic compounds having no substituents on the $\gamma$-carbon atom.

Primary allylic halides appear to undergo only normal bimolecular substitution (121, 279, 539, 660). This does not mean that substitution by mechanism $S_N2'$ does not occur, but only that the ratio $k_{S_N2'}/k_{S_N2}$ is very small. The only well-established cases of abnormal bimolecular substitution of simple primary allylic halides are the bromide-exchange experiments of England and Hughes (193) with $\gamma$-methylallyl bromide and the reaction of $C^{14}$-labeled allyl chloride with secondary and tertiary amines (641).

The available data indicate that secondary allylic chlorides of the type $RCHClCH{=}CH_2$ undergo abnormal bimolecular displacements by anionic reagents to only a limited extent (121, 175, 279, 539), while tertiary chlorides of the type $R_2CClCH{=}CH_2$ are substituted almost exclusively by the $S_N2'$ mechanism in bimolecular reactions with any nucleophilic reagent (175, 543, 659). A single $\alpha$-halogen substituent on the allylic system (e.g., $CHCl_2CH{=}CH_2$) is sufficient to cause considerable $S_N2'$ displacement (172, 173), while two $\alpha$-halogen substituents [$CCl_3C(CH_3){=}CH_2$, for example] result in abnormal bimolecular displacement to the exclusion of the normal reaction (171, 174).

If the steric course postulated by Young, Webb, and Goering (666, 692) for $S_N2'$ reactions is correct, this mechanism should be relatively free from steric hindrance by substituents on the $\gamma$-carbon atom. With the exception of the bromide-exchange reaction already mentioned (193), the only $S_N2'$ reactions of $\gamma$-substituted allylic compounds thus far reported involve cyclic allylic compounds (67, 356, 588). It is probable that $\alpha,\alpha,\gamma$-trialkylallylic halides would undergo bimolecular substitution by mechanism $S_N2'$, but establishing this experimentally may be difficult owing to the very high unimolecular reactivity to be expected for such compounds.

The effect of substituents on rates of bimolecular substitution reactions seems to be qualitatively the same for the $S_N2$ and the $S_N2'$ mechanisms. Substituents which can release electrons to the $\alpha$-carbon atom by either the inductive or the mesomeric process increase the rate of reaction by mechanism $S_N2'$. For example, the rate of reaction of $\alpha,\alpha$-dimethylallyl chloride with alcoholic sodium thiophenoxide is at least ten times that of the similar reaction of $\alpha$-methylallyl chloride, and 3,3,3-trichloro-2-methyl-1-propene reacts over twice as fast with this reagent as does 3,3-dichloropropene. The data of de la Mare and
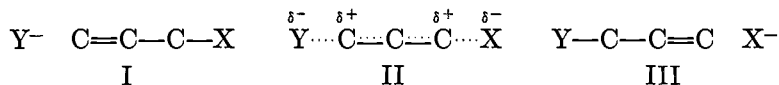
TABLE 4

*Reaction of allylic chlorides with sodium thiophenoxide in ethanol at 25°C.*

($S_N2'$ rates: $k_2 = Be^{-E/RT}$; time in minutes)

| Halide | $k_{S_N2'}$ | $k_{S_N2}$ | $E_{S_N2'}$ | $\log B\ S_N2'$ |
|---|---|---|---|---|
| | | | kcal./mole | |
| $CHCl_2CH{=}CH_2$ ............... | ca. $2.5 \times 10^{-4}$ | ca. $3 \times 10^{-4}$ | 21.2 | 13.34 |
| $CCl_3C(CH_3){=}CH_2$ ............ | $6 \times 10^{-5}$ | | 20.3 | |
| $C(CH_3)_2ClCH{=}CH_2$ ........... | $9 \times 10^{-2}$ | | 19.6 | 13.35 |
| $CH_3CHClCH{=}CH_2$ ............ | $>7 \times 10^{-3}$ | $4.5 \times 10^{-2}$ | | |

Vernon for these reactions are collected in table 4 (172, 174, 175). It appears that $\alpha$-substituents alter the rate of $S_N2'$ reactions mainly by altering the activation energy. The preëxponential term of the Arrhenius equation was practically the same for 3,3-dichloropropene and $\alpha,\alpha$-dimethylallyl chloride; as this term is usually associated with steric effects on the reaction rate, this result is quite reasonable. Additional data on the effect of substituents on $S_N2'$ reactivity are needed to test the validity of these conclusions. The abnormal bimolecular reaction of allyl chloride with dimethylamine in benzene at 60°C. is only 75 per cent as fast as the corresponding reaction of $\alpha$-methylallyl chloride (641).

de la Mare and Vernon (166, 172, 174) postulated that $\alpha$-chlorine substituents should facilitate $S_N2'$ reactions by shifting the $\pi$-electron cloud of the allylic double bond away from the $\gamma$-carbon atom, and could conceivably retard substitution by this mechanism by making more difficult the separation of the leaving group as an anion; similarly, $\alpha$-methyl groups should polarize the double bond in such a way as to retard attack by the nucleophilic reagent at the $\gamma$-carbon, but should also facilitate concerted removal of the allylic substituent (175). On the basis of these inductive effects alone it is clearly impossible to predict the effect of substituents on the rates of abnormal bimolecular displacements.

A more reasonable explanation of substituent effects is to assume, as has been done for unimolecular and normal bimolecular substitution reactions, that substituents which can release electrons to the allylic system by either the inductive or the tautomeric mechanism facilitate abnormal bimolecular substitution by stabilizing the transition state of the reaction. The transition state of an $S_N2'$ reaction is probably best represented by a resonance hybrid of canonical structures I, II, and III; any substituent on the $\alpha$- or $\gamma$-carbon atom which can release electrons to the allylic system will stabilize structure II and thereby lower the activation energy of the reaction. The steric effect of $\gamma$-substituents will, however, strongly predominate over their electronic effect:

$$Y^-\quad C{=}C{-}C{-}X \qquad \overset{\delta^-\quad\ \delta^+}{Y\cdots C} \overset{\delta^+\ \quad\delta^-}{\underset{}{{-}C{-}C\cdots X}} \qquad Y{-}C{-}C{=}C\quad X^-$$
$$\text{I} \qquad\qquad\qquad \text{II} \qquad\qquad\qquad \text{III}$$

The validity of this hypothesis could be checked by studying the rates of abnormal bimolecular displacement reactions of a series of $\alpha,\alpha$-dialkyl-$\beta$-substituted allyl chlorides in which only the $\beta$-substituent is varied from $CH_3$ to Cl. It is to be expected that a $\beta$-halogen substituent would decrease the reaction

rate, while a $\beta$-alkyl group would increase it, since substituents on the $\beta$-carbon atom can only influence the reaction by their inductive effects, assuming steric effects to be negligible. This was found to be the case for $S_N2$ reactions of $\beta$-substituted allyl chlorides (page 765).

### (b) Nature of the reagent

The nature of the nucleophilic reagent affects both the rate of $S_N2'$ reactions and the ratio of normal to abnormal bimolecular substitution, $k_{S_N2}/k_{S_N2'}$. The limited evidence which is available indicates that uncharged nucleophilic reagents such as tertiary amines are less discriminating between the $\alpha$- and $\gamma$-carbon atoms of the allylic system than are anionic nucleophilic reagents. $\alpha$-Methylallyl chloride yields a substantial amount of abnormal product in bimolecular reactions with trimethylamine (665, 666), while reactions with alcoholic ethoxide or thiophenoxide give mainly or entirely normal products (121, 175, 279, 539, 660). Sodium ethyl malonate in ethanol, a reagent in which the negative charge of the anion is shared by three centers, gives an appreciable amount of abnormal product in reactions with $\alpha$-methyl- and $\alpha$-ethylallyl chlorides (326). Even allyl chloride undergoes abnormal bimolecular substitution by trimethylamine in benzene solution, 7 per cent of the abnormal product being formed (641).

The tentative conclusion, then, is that uncharged reagents and anionic reagents in which the charge is dispersed over more than one center yield higher proportions of abnormal products in bimolecular reactions with secondary allylic halides than do ordinary anionic reagents. This question needs to be more fully investigated. Any acceptable explanation for $k_{S_N2}/k_{S_N2'}$ ratios would also have to allow for steric effects due to the bulk of the nucleophilic reagent, an aspect of these reactions which has not been investigated. If the ratio of normal to abnormal reaction is indeed greater for anionic reagents than for uncharged reagents, a reasonable explanation is that an anionic reagent attacking the $\alpha$-carbon atom will facilitate separation of the leaving group more than the same reagent attacking the $\gamma$-carbon atom. An uncharged reagent attacking at either the $\alpha$- or the $\gamma$-carbon atom would not offer this electrostatic assistance to the departure of the leaving group.

de la Mare and Vernon found that in reactions of 3,3-dichloropropene with sodium ethoxide, sodium phenoxide, and sodium thiophenoxide in ethanol, the rate of reaction is much greater with thiophenoxide ion than with the less nucleophilic reagents, but that mixtures having approximately the same proportion of normal and abnormal products are formed with all three reagents (table 5).

TABLE 5

*$S_N2'$ reactions of 3,3-dichloropropene in ethanol at 100°C. (173)*

| Reagent | $OC_2H_5{}^-$ | $OC_6H_5{}^-$ | $SC_6H_5{}^-$ |
|---|---|---|---|
| $(k_{S_N2} + k_{S_N2'})^*$ | 0.036 | 0.030 | 8.73 |
| Per cent Cl released | 70 | 89 | 81 |
| Per cent $S_N2'$ | 60 | 22 | 38 |

* Liters/mole min.

This suggests that, for anionic reagents, the rate of substitution is more sensitive to nucleophilicity of the reagent than is $k_{S_N2}/k_{S_N2'}$.
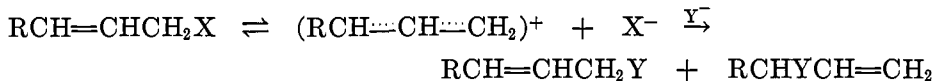
### (c) Solvent composition

3,3-Dichloropropene and 3,3,3-trichloro-2-methyl-1-propene react with sodium thiophenoxide more than twice as fast in 75 per cent aqueous ethanol as in absolute ethanol (171). For the dichloropropene, the rate of the concurrent $S_N2$ reaction is increased by a somewhat larger factor than the rate of the abnormal reaction on going to aqueous ethanol. The direction of this solvent effect is not in agreement with theoretical predictions of the influence of solvent polarity on bimolecular substitutions of this type. The rate of a bimolecular reaction in which charge is dispersed on going to the transition state should decrease slightly as solvent polarity is increased (294, page 347). On the other hand, the reaction of $\alpha$-methylallyl chloride with dimethylamine is about ten times faster in benzene than in cyclohexane, in agreement with the expected large increase in rate with increasing solvent polarity for bimolecular substitutions of this charge type (641).

### D. THE $S_N1$ MECHANISM OF SUBSTITUTION AND REARRANGEMENT

#### 1. Introduction

The unimolecular mechanism of substitution and rearrangement in allylic compounds is similar to the well-known $S_N1$ mechanism of nucleophilic aliphatic substitution (294, page 310), in that its rate-determining step involves heterolytic cleavage of the allylic compound into a carbonium ion and an anion. There is one important difference, however: the carbonium ion formed by an allylic compound is mesomeric and can react with the solvent or other nucleophilic reagent to yield, in the case of unsymmetrically substituted allylic systems, a mixture of isomeric products.

$$RCH\!=\!CHCH_2X \;\rightleftharpoons\; (RCH\!\cdots\!CH\!\cdots\!CH_2)^+ \;+\; X^- \xrightarrow{Y^-}$$
$$RCH\!=\!CHCH_2Y \;+\; RCHYCH\!=\!CH_2$$

If X and Y are different, substitution with partial allylic rearrangement is observed. When they are the same, the result is isomerization. In either case the essential features of the reactions are identical, and both the substitution and the isomerization are examples of mechanism $S_N1$. The ionization step may be aided by electrophilic interaction of solvent molecules or metal ions with the allylic substituent, or may be essentially a thermal dissociation. The leaving group X may or may not become completely free of the carbonium ion. All that is necessary is that heterolytic bond fission occur at least to the point where an ion-pair is formed.

Prevost (487) in 1927 seems to have been the first to propose an ionic mechanism for the rearrangement of certain allylic compounds. In 1928 Burton and Ingold (102) discussed this mechanism in much more detail. They later presented evidence for unimolecular reactions in the rearrangements and substitution

reactions of certain allylic esters (97–101, 295). Prevost (484, 490) and Meisenheimer and Link (419) were partially successful in developing concepts to correlate the experimental facts about replacement reactions involving allylic rearrangement. The satisfactory application of mechanistic theories to the problem of allylic rearrangement is due primarily to Young and coworkers in the United States (539, 674) and to Kenyon, Hughes, and Ingold in England (16, 279, 295).

### 2. Factors influencing reaction rate

Unimolecular reactions of allylic compounds generally exhibit first-order kinetics, and their rates are strongly influenced by the structure of the allylic system and by solvent composition.

### (a) The allylic double bond

Hughes suggested in 1941 (279) that the allylic double bond should greatly facilitate unimolecular displacements by tautomeric electron release, which should aid the departure of the leaving group and stabilize the resulting carbonium ion:

$$C{=}C{-}C{-}X \quad \rightarrow \quad \overset{\delta+}{C}{\cdots}C{\cdots}\overset{\delta+}{C} \quad + \quad X^-$$
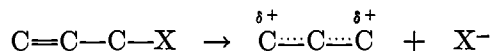
This facilitating effect turned out to be much smaller than expected, presumably owing to an opposing inductive effect. Allyl chloride is solvolyzed in slightly aqueous formic acid only 25 times faster than $n$-propyl chloride (628).

### (b) Structure of the allylic system

It has long been known qualitatively that electron-releasing substituents on either the $\alpha$- or the $\gamma$-carbon atom of the allylic system greatly increase the rates of unimolecular displacement reactions, probably by facilitating the ionization step and by stabilizing the resulting carbonium ion. Andrews and Kepner (11) demonstrated this in 1948 in a study of the rates of hydrolysis of several allylic chlorides in aqueous ethanol, and Webb and Young in 1951 found that $\gamma$-ethyl-$\gamma$-methylallyl chloride reacts with absolute ethanol nearly 100 times faster than crotyl chloride (636). As Webb and Young pointed out, however, it is not safe to draw quantitative conclusions from data obtained in hydroxylic solvents, since bimolecular displacement of chloride by solvent is possible and kinetically undistinguishable from a unimolecular reaction. Vernon overcame this difficulty by solvolyzing a number of allylic chlorides in moist formic acid, a solvent in which the $S_N1$ mechanism is likely to operate exclusively (628). The available kinetic data for the solvolysis of allylic chlorides in ethanol, 50 per cent ethanol, and formic acid containing 0.5 per cent water are collected in table 6. Some of the implications of these data will be discussed in more detail later.

A chlorine substituent on either the $\alpha$- or the $\gamma$-carbon atom of allyl chloride causes a small increase in the rate of formolysis. This would indicate, as already noted for $S_N2$ reactions, that tautomeric electron release is more important than

## TABLE 6

*Relative rates of solvolysis of allylic chlorides (10, 11, 170, 171, 176, 240, 539, 628, 629, 636, 660)*

| Compound | Solvent | | |
|---|---|---|---|
| | Absolute ethanol 25°C. | 50% Aqueous ethanol 25°C. | 99.5% Formic acid 44.6°C. |
| $CH_2=CHCH_2Cl$ | 1.00 (ca. 3 × $10^{-9}$)* | 1.00 (1.59 × $10^{-7}$) | 1.00 (3.6 × $10^{-5}$) |
| $CH_2=C(CH_3)CH_2Cl$ | 1.3 | | 0.5 |
| $CHCl=CHCH_2Cl$ (cis) | ca. 0.6 | 1.00 | 2.1 |
| $CHCl=CHCH_2Cl$ (trans) | ca. 0.6 | 1.01 | 3.09 |
| $CH_2=CHCHCl_2$ | | 1.02 | 65.4 |
| $(CH_3)_3CCH=CHCH_2Cl$ | | | 2260 |
| $(CH_3)_3CCHClCH=CH_2$ | | | 2520 |
| $CH_3CH=CHCH_2Cl$ | 17 | 95 | 3550 |
| $CH_3CHClCH=CH_2$ | 3.0 | 75 | 5670 |
| $C_6H_5CH=CHCH_2Cl$ | 150 | 8800 | |
| $(CH_3)_2C=CHCH_2Cl$ | 2200 | 1.9 × $10^5$ | |
| $(CH_3)_2CClCH=CH_2$ | 6000 | 1.3 × $10^5$ | |
| $C_2H_5C(CH_3)=CHCH_2Cl$ | 1500 | | |
| $C_2H_5C(CH_3)ClCH=CH_2$ | 3300 | | |
| $CH_3CH=CHCHClCH_3$ | 2.2 × $10^4$ | | |
| $C_6H_5CH=CHCHCl_2$ | 3.3 × $10^4$ | | |

* Relative rates in absolute ethanol calculated on the assumption that the rate of ethanolysis of allyl chloride is 3.0 × $10^{-9}$ sec.$^{-1}$

inductive electron withdrawal in determining the effect of halogen substituents on rates of substitution reactions. An alkyl group on either the $\alpha$- or the $\gamma$-carbon atom produces an increase in rate of over 1000-fold, and an alkyl group on the $\alpha$-carbon is slightly more effective than a $\gamma$-alkyl substituent, as would be expected for purely electronic effects. Steric effects are obviously unimportant for these unimolecular reactions. Methyl groups increase the rate of reaction somewhat more than *tert*-butyl groups, probably owing to their greater hyperconjugative electron release. The effect of a second methyl group is similar in magnitude to that of the first; a $\gamma$-phenyl substituent is intermediate in its effect on rate between one and two methyl groups.

Table 1 shows that the rates of solvolysis reactions of allylic chlorides in other solvent systems fall in line with those in formic acid, except for several cases where concerted displacement by solvent may occur. This point will be discussed in some detail later.

Goering, Nevitt, and Silversmith (225) measured the rates of solvolysis of several cyclic allylic chlorides in ethanol at 30°C: *cis*-5-methyl-2-cyclohexenyl chloride, 2.15 × $10^{-5}$ sec.$^{-1}$; *trans*-5-methyl-2-cyclohexenyl chloride, 1.57 × $10^{-5}$; 3-cyclohexenyl chloride, 1.86 × $10^{-5}$; ($\alpha,\gamma$-dimethylallyl chloride, 7.59 × $10^{-5}$); 3-cyclopentenyl chloride, 1.13 × $10^{-2}$. It is interesting to note that 3-cyclopentenyl chloride is 600 times as reactive as cyclohexenyl chloride, and that the cyclohexenyl chlorides are approximately as reactive as acyclic chlorides with two alkyl substituents.

### (c) Nature of the leaving group

No quantitative data on the effect of the nature of the group X in the allylic system C=C—C—X on the rates of unimolecular reactions are available. Quali-

tatively, Ingold and coworkers (102, 295) have shown that for a given allylic system the mobility of the group X in isomerization reactions increases markedly with the stability of $X^-$ as an anion (using as a criterion of stability the strength of the conjugate acid HX). Thus, in the reaction

$$C_6H_5CHXCH=CH_2 \rightarrow C_6H_5CH=CHCH_2X$$
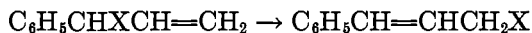
halides isomerize more readily than esters, which in turn rearrange more rapidly than the alcohol.

This argument assumes that the isomerization reactions occur by mechanism $S_N1$. Allylic bromides isomerize much more readily than allylic chlorides; it is to be expected that they would undergo unimolecular substitution at a faster rate than the corresponding chlorides, as is the case with aliphatic bromides (294, page 339).

### (d) Ionizing power of the solvent

As expected for reactions whose rates are determined by ionization, the velocity of unimolecular reactions of allylic compounds is highly dependent upon solvent polarity. Most of the pertinent data refer to solvolysis reactions whose mechanisms are not unambiguously known. Solvolysis of $\alpha,\alpha$- and $\gamma,\gamma$-dimethylallyl chlorides in ethanol and aqueous ethanol is definitely unimolecular, however, and the reaction rates for these compounds show the strong dependence on solvent polarity predicted by theoretical considerations. Solvolysis of these compounds is about 5000 times as fast in 50 per cent aqueous ethanol as in absolute ethanol (see table 6). Solvolysis of $\alpha$- and $\gamma$-methylallyl chlorides shows a somewhat smaller dependence on solvent polarity, presumably owing to nucleophilic interaction between the solvent and substrate in the transition state of the reaction.

### (e) Electrophilic catalysts

Ions such as $Ag^+$, $Fe^{+++}$, and $H^+$ and Lewis acids such as $BF_3$ accelerate many unimolecular substitution and isomerization reactions of allylic compounds, owing to electrophilic interaction with the allylic substituent. Young and coworkers found that conversions of $\alpha$- and $\gamma$-methylallyl chlorides to alcohols and acetate esters proceed much more rapidly in the presence of silver oxide and silver acetate than under ordinary solvolysis conditions and that mixtures of products are formed, as would be expected for unimolecular substitution (539, 660). Oae and VanderWerf (458) studied the reaction of several allylic chlorides with alcoholic silver nitrate. These reactions are first order in both chloride and silver nitrate, and form nitrate esters rather than ethers. For this reason they may not be closely comparable to unimolecular substitutions. Hatch studied the effect of acidic cuprous chloride on the rate of hydrolysis of allylic chlorides and demonstrated that cuprous ion accelerates the reaction (245, 247, 256, 257). A number of investigators have reported that cuprous, zinc, and ferric salts catalyze the isomerization of allylic halides, and it is well established that hydrogen ion and Lewis acids catalyze the rearrangement of allylic alcohols and esters.

### 3. Solvolysis reactions of allylic compounds

Much of our present knowledge of the unimolecular mechanism of substitution in allylic compounds was gained from studies of solvolysis reactions, particularly those of allylic chlorides. For this reason it is well to consider some of the complications which arise in assigning definite mechanisms to these reactions.
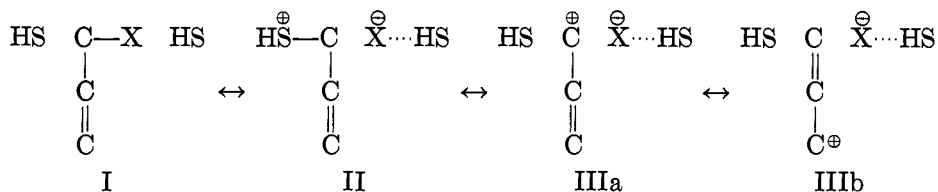
### (a) Possible mechanisms of solvolysis reactions

Solvolysis reactions are nucleophilic substitutions in which the solvent is the nucleophilic reagent. They generally exhibit first-order kinetics, simply because the solvent is present in such large excess that kinetic dependence of rate on solvent concentration is not observable. Substitution by solvent could involve concerted displacement of the allylic substituent by a solvent molecule ($S_N2$) or could be a true unimolecular reaction ($S_N1$). Vernon (629) calls these processes bimolecular and unimolecular solvolysis, respectively.

Winstein, Grunwald, and Jones (651) have suggested that solvolysis reactions have a continuous spectrum of mechanisms of which the classical $S_N1$ and $S_N2$ mechanisms of Hughes and Ingold (41, 221, 279, 281) are special cases. According to this idea, nucleophilic interaction of solvent with the substituted carbon atom and electrophilic interaction between solvent and the leaving group will in general both contribute to the driving force of the reaction. Reactions classified as $S_N2$ are those in which there is covalent interaction between solvent (or other nucleophilic reagent) and the substituted carbon atom in the transition state, while reactions of the $S_N1$ type are those in which such covalent interaction is negligible. As there are, in principle, infinite gradations in the relative contributions of nucleophilic and electrophilic solvation to the driving force of the reaction, there is no sharp dividing line between mechanisms $S_N1$ and $S_N2$.

It is therefore better to assign a single intermediate mechanism to a solvolysis reaction which falls between the mechanistic extremes than to assume that such a reaction involves separate, competing unimolecular and bimolecular processes. The experimental support for this hypothesis is found in the effect of solvent properties on rates of solvolysis reactions. A detailed discussion of this topic is beyond the scope of the present article, but the experimental results can be summarized as follows: If nucleophilic substitution reactions proceed only by mechanisms $S_N1$ and $S_N2$, it is necessary to postulate that for some compounds, such as crotyl chloride, solvolysis reactions in certain solvents proceed by simultaneous unimolecular and bimolecular processes. If this were the case, the reaction should change from a purely bimolecular process in solvents of very low ionizing power and relatively high nucleophilicity to a purely unimolecular process in solvents of similar nucleophilicity but much higher ionizing power. According to the theory of Winstein and Grunwald (240, 651), a plot of log (solvolysis rate) vs. solvent ionizing power should show a distinct curvature or even a break at the region of transition from mechanism $S_N1$ to mechanism $S_N2$ if two separate mechanisms are involved. Actually, very good straight lines are obtained (653), a result which is considered to be evidence that a single mechanism intermediate between $S_N1$ and $S_N2$ is involved.

The transition state for solvolysis reactions of allylic compounds is considered to be a resonance hybrid of the following canonical structures:

$$\text{HS} \quad \overset{\underset{\parallel}{\textstyle C}}{\underset{\underset{C}{\parallel}}{\underset{C}{|}}}\!\!\text{—X} \quad \text{HS} \qquad \text{HS}\!\!-\!\!\overset{\oplus}{\underset{\underset{C}{\parallel}}{\underset{C}{|}}}C \quad \overset{\ominus}{X}\!\cdots\!\text{HS} \qquad \text{HS} \quad \overset{\oplus}{\underset{\underset{C}{\parallel}}{\underset{C}{|}}}C \quad \overset{\ominus}{X}\!\cdots\!\text{HS} \qquad \text{HS} \quad \overset{}{\underset{\underset{C^{\oplus}}{|}}{\underset{C}{\parallel}}}C \quad \overset{\ominus}{X}\!\cdots\!\text{HS}$$

I $\qquad\qquad$ II $\qquad\qquad$ IIIa $\qquad\qquad$ IIIb

If structures I and II adequately represent the transition state, the reaction will be at the nucleophilic extreme of the mechanistic spectrum and can accurately be described as a bimolecular displacement by solvent. This mechanism is to be expected for solvolysis of allylic halides not having activating electron-releasing substituents, particularly in hydroxylic solvents of low ionizing power. The rate of such a reaction will be relatively insensitive to the ionizing power of the solvent, and substitution without allylic rearrangement will be observed.

If structures I, II, and III contribute to the transition state of a solvolysis reaction, its mechanism will be intermediate between a pure bimolecular substitution and a unimolecular substitution. The effect of solvent ionizing power on rate will be greater than for a bimolecular solvolysis, and a mixture of products will be obtained—not, however, the same mixture that would be formed by a free, solvated carbonium ion. The proportion of normal substitution product will be greater than if a free ion were involved.

If the transition state is adequately represented by structures I, IIIa, and IIIb, a true unimolecular substitution is involved. Actually, in this case a solvated carbonium ion or an ion-pair is formed as a discrete intermediate. This is to be expected for highly activated allylic systems such as dialkylallyl chlorides. The reaction will be strongly affected by solvent ionizing power and will give mixtures of products approaching those to be expected from a mesomeric carbonium ion.

(b) Experimental evidence bearing on the mechanism of solvolysis reactions

The available evidence bearing on intimate mechanisms of solvolysis reactions —solvent effects, structural effects, product compositions, and mass law effects— will now be considered.

(1) Solvent effects: The rate of a bimolecular solvolysis reaction will be less dependent on solvent polarity (ionizing power) than will the rate of a unimolecular reaction. The variation of rate with solvent polarity is expressed quantitatively by an equation developed by Winstein and Grunwald (240, 651):

$$\log (k/k_0) = m\mathbf{Y}$$

where $k$ is the rate of solvolysis of a compound in a given solvent, $k_0$ is the rate of solvolysis of the same compound in a standard solvent, and $\mathbf{Y}$ is the ionizing power of the solvent, as measured by the rate of a standard unimolecular reaction in the solvent under consideration. $m$ is a constant which measures the

TABLE 7

*m values for solvolysis of allylic chlorides*

| Compound | Aqueous Ethanol (25°C.) | Aqueous Acetone (25°C.) | Aqueous Formic Acid (44.6°C.) |
|---|---|---|---|
| $CH_2$=CHCH$_2$Cl.................... | 0.455 (50°C.) | | |
| $CH_3$CH=CHCH$_2$Cl................. | 0.655 | 0.904 | 0.81 |
| $CH_3$CHClCH=CH$_2$................. | 0.875 | 0.919 | 1.00 |
| $(CH_3)_2$C=CHCH$_2$Cl.............. | 0.974 | 1.085 | |
| $(CH_3)_2$CClCH=CH$_2$.............. | 0.99 | | |

sensitivity of the reaction to solvent ionizing power. The higher the value of $m$, the greater is the increase in rate of solvolysis with increasing solvent polarity. Usually $m$ has a value of about 0.4 for reactions which definitely belong in the bimolecular category and a value of about 0.9–1.0 for reactions which are definitely unimolecular. Reactions formerly referred to as borderline cases have intermediate values of $m$. Table 7 lists some $m$ values for the solvolysis of several allylic chlorides in aqueous ethanol, aqueous acetone, and aqueous formic acid (653).

Insofar as $m$ values are a reliable criterion of mechanism, these results are in substantial agreement with conclusions arrived at from other evidence. Solvolysis of allyl chloride would seem to be largely bimolecular in aqueous ethanol. Solvolysis of $\alpha,\alpha$- and $\gamma,\gamma$-dimethylallyl chlorides, on the other hand, is clearly unimolecular. The $m$ values for $\alpha$-methylallyl chloride show that its solvolyses are predominantly unimolecular, while those of $\gamma$-methylallyl chloride indicate an intermediate mechanism in aqueous ethanol and a unimolecular mechanism in aqueous acetone and aqueous formic acid.

Vernon (628, 629) has recently published data which support the idea that bimolecular solvolysis reactions are much more sensitive to solvent nucleophilicity than are unimolecular solvolyses, while the unimolecular reactions are much more sensitive to the ionizing power of the solvent. He studied the solvolysis of several allylic chlorides in moist formic acid, 50 per cent aqueous ethanol, and absolute ethanol. Formic acid and 50 per cent ethanol have similar ionizing powers, but 50 per cent ethanol is much more nucleophilic than the acidic solvent. Ethanol and 50 per cent ethanol have similar nucleophilic character but widely different ionizing powers.

The ratio $k_{50\% C_2H_5OH}/k_{HCOOH}$ in table 8 indicates that the rates of unimolecular solvolysis reactions are unaffected by solvent nucleophilicity, as expected. Allyl chloride and 1,3-dichloropropene, whose solvolyses in aqueous ethanol are predominantly bimolecular, react considerably faster with aqueous ethanol than with formic acid, the solvent of lower nucleophilicity. $\alpha$-Methylallyl chloride and 3,3-dichloropropene, whose solvolyses in 50 per cent ethanol are predominantly unimolecular, are solvolyzed somewhat more slowly in aqueous ethanol than in formic acid. Crotyl chloride, whose solvolysis in aqueous ethanol is probably in the transition region of the mechanistic spectrum, is solvolyzed slightly faster in aqueous ethanol than in formic acid.

A comparison of solvolysis rates in 50 per cent ethanol and absolute ethanol

shows the effect of varying solvent polarity while keeping nucleophilicity substantially constant. Allyl chloride, β-methylallyl chloride, and 1,3-dichloropropene, whose solvolyses in aqueous ethanol are probably bimolecular, are fairly insensitive to solvent polarity. For these three compounds the ratio $k_{50\% \text{ C}_2\text{H}_5\text{OH}}/k_{\text{C}_2\text{H}_5\text{OH}}$ is in the range 30–40. This ratio is several thousand for $\alpha,\alpha$- and $\gamma,\gamma$-dimethylallyl chlorides, whose solvolyses are plainly unimolecular. $\alpha$-Methylallyl chloride and cinnamyl chloride have intermediate values, while the value for crotyl chloride is lower still.

Young and Andrews (660) first called attention to the fact that secondary allylic chlorides are solvolyzed somewhat more slowly in aqueous ethanol than the isomeric primary chlorides, contrary to the usual observation that primary chlorides react more slowly by an $S_N1$-type process than secondary chlorides. They explained this result by postulating that the primary chloride (crotyl chloride) reacts in part by a bimolecular process. Similar observations were subsequently made by other workers (11, 121, 628). Roberts, Young, and Winstein (539) later showed that the expected order of reactivity (secondary greater than primary) is indeed observed in the less nucleophilic solvent, acetic acid, and Vernon (628) found the same thing to be true in moist formic acid. $\alpha,\alpha$-Dimethylallyl chloride is more reactive than its primary isomer not only in acetic acid, but also in aqueous ethanol (628, 660). It is fairly well established that a secondary or tertiary allylic compound is more reactive by the unimolecular mechanism than its primary isomer.

Pourrat and Schmitz (480) found that the rate of hydrolysis of allyl chloride in aqueous dioxane increases only twentyfold when the water content increases from 25 per cent to 65 per cent. This strongly suggests a bimolecular reaction in these media.

(2) *Structural effects:* The effect of structure of the allylic system on rates of unimolecular reactions has already been commented upon (see table 6). It is pertinent here to point out that the rate-accelerating effect of electron-releasing substituents is much greater than would be expected for bimolecular solvolysis reactions or solvolysis reactions of intermediate mechanisms. Table 6 illus-

TABLE 8

*Rates of solvolysis of allylic chlorides at 44.6°C. (628, 629)*

Rates in reciprocal seconds; 99.5% HCOOH; 0.5% $H_2O$; 50% aqueous ethanol; absolute ethanol

| Compound | $k_{\text{HCOOH}}$ | $k_{50\% \text{ C}_2\text{H}_5\text{OH}}$ | $k_{\text{C}_2\text{H}_5\text{OH}}$ | $\dfrac{k_{50\% \text{ C}_2\text{H}_5\text{OH}}}{k_{\text{HCOOH}}}$ | $\dfrac{k_{50\% \text{ C}_2\text{H}_5\text{OH}}}{k_{\text{C}_2\text{H}_5\text{OH}}}$ |
|---|---|---|---|---|---|
| $CH_2{=}CHCH_2Cl$ | $3.62 \times 10^{-8}$ | $1.69 \times 10^{-6}$ | $6.3 \times 10^{-8}$ | 47 | 27 |
| $CH_2{=}C(CH_3)CH_2Cl$ | | $2.56 \times 10^{-5}$ | $8.0 \times 10^{-6}$ | | 32 |
| $CHCl{=}CHCH_2Cl$ (*trans*) | $1.45 \times 10^{-7}$ | $1.65 \times 10^{-6}$ | $3.8 \times 10^{-8}$ | 11 | 42 |
| $CH_2{=}CHCHCl_2$ | $2.37 \times 10^{-6}$ | $2.22 \times 10^{-6}$ | | 0.9 | |
| $CH_3CH{=}CHCH_2Cl$ | $1.28 \times 10^{-4}$ | $1.54 \times 10^{-4}$ | $1 \times 10^{-6}$ | 1.2 | 154 |
| $CH_3CHClCH{=}CH_2$ | $2.05 \times 10^{-4}$ | $1.37 \times 10^{-4}$ | $2.10 \times 10^{-7}$ | 0.7 | 650 |
| $C_6H_5CH{=}CHCH_2Cl$ | | $1.29 \times 10^{-2}$ | $8.8 \times 10^{-6}$ | | 1500 |
| $(CH_3)_2C{=}CHCH_2Cl$ | | $2.2 \times 10^{-1}$ | $6.53 \times 10^{-5}$ | | 3400 |
| $(CH_3)_2CClCH{=}CH_2$ | | $9 \times 10^{-1}$ | $1.87 \times 10^{-4}$ | | 4800 |

trates this point: the reactivities of $\alpha$- or $\gamma$-alkyl- or aryl-substituted allylic chlorides with moist formic acid, a solvent in which solvolysis is predominantly or entirely unimolecular even for allyl chloride, are much greater than that of allyl chloride; in aqueous ethanol, however, there is a much smaller spread in relative reactivities, owing to bimolecular interaction between the chlorides and the more nucleophilic solvent.

(3) *Mass law effects:* Ingold (294, page 362) has suggested that addition of an anionic nucleophilic reagent different from the allylic substituent (a non-common ion) should accelerate a bimolecular reaction and have no effect on a unimolecular reaction. This would be strictly true only for solvolysis reactions in which ion-pair formation accompanied by internal return is not involved, and where salt effects are small. Except for these latter complications, the rate-determining step of a unimolecular reaction involves formation of a carbonium ion, whose fate, once it has formed, does not ordinarily enter into the rate equation. The rate-determining step in a bimolecular reaction, however, involves a nucleophilic attack on carbon, and any added reagent which can compete with solvent molecules in this process will accelerate the reaction. This criterion has been applied to the solvolysis of allylic chlorides by studying the effect of added hydroxide or alkoxide ions on the rate of disappearance of chloride. Young and Andrews (660) found that the rate of hydrolysis of crotyl chloride in aqueous ethanol is increased by the addition of sodium hydroxide, while the rate of hydrolysis of $\alpha$-methylallyl chloride is practically independent of hydroxyl-ion concentration. This result was taken to mean that the hydrolysis of the secondary chloride is unimolecular, while that of crotyl chloride is partly bimolecular. This criterion of mechanism has also been applied by de la Mare and Vernon (171, 629), who found that the rates of reaction of allyl chloride, $\beta$-methylallyl chloride, and 1,3-dichloropropene with ethanol and aqueous ethanol are quite sensitive to added alkali, while the solvolyses of $\alpha,\alpha$- and $\gamma,\gamma$-dimethylallyl chlorides are unaffected by added alkali. Solvolyses of cinnamyl and $\alpha$-methylallyl chlorides were only slightly affected by the addition of alkali, while crotyl chloride falls between allyl and $\alpha$-methylallyl chlorides in sensitivity to added base. It was concluded that the alkali-insensitive compounds undergo unimolecular solvolysis and the alkali-sensitive compounds undergo bimolecular solvolysis, a conclusion supported by the data on solvent effects already discussed. The validity of this criterion of mechanism depends on the accuracy of the assumption that hydroxide and alkoxide ions are so much more nucleophilic than solvent molecules that relatively low concentrations of alkali will successfully compete with solvent in bimolecular substitutions. This hypothesis is not definitely proven but it is a reasonable one, since the conclusions inferred from the effect of added alkali on rates of solvolysis are in agreement with those reached from other kinds of evidence.

(4) *Composition of reaction products:* Much can be learned about the mechanisms of allylic solvolysis reactions by studying the products they form. If only normal substitution product is formed, a bimolecular mechanism is clearly implied but not necessarily required. It is conceivable that unimolecular sub-

stitution could give only normal product, but there is no well-established example of this. de la Mare and Vernon (171) found that solvolysis of *trans*-1,3-dichloropropene in aqueous ethanol gives only the normal substitution product, in agreement with other evidence that this reaction is a bimolecular displacement of chloride by solvent. Allyl chloride and β-methylallyl chloride probably undergo bimolecular reaction with solvent in aqueous ethanol, but an investigation of the products from isotopically labeled starting materials would be required to establish this.

The solvolysis of most allylic halides yields mixtures of the normal and abnormal substitution products, and this is usually assumed to be evidence for unimolecular substitution. In the cases where both members of a pair of isomeric halides give identical mixtures of products, it is probable not only that unimolecular substitution is involved but that both isomers react via a common intermediate. This could be either a classical mesomeric carbonium ion or an ion-pair.

Usually, however, the two members of an isomeric pair of allylic derivatives form somewhat different mixtures of solvolysis products under identical reaction conditions. That is, a "product spread" is observed. (In the following discussion, *product spread* is defined as the difference in percentage of primary substitution product contained in the mixtures of solvolysis products formed by the members of a primary–secondary or primary–tertiary pair of allylic isomers under identical reaction conditions.) The existence of a product spread definitely means that both allylic isomers do not react exclusively with formation of the same ionic intermediate, be it a solvated carbonium ion or an ion-pair. *One* of the two isomers (the secondary or tertiary) may have reacted entirely by formation of a carbonium-ion or an ion-pair intermediate, but both of them could not have done so, and neither of them may have done so. In this context, *intermediate* refers to a true chemical entity, as contrasted with *transition state*, which refers to a configuration of atoms of maximum energy through which the system must pass on its way from reactants to products.

One possible explanation for the occurrence of product spreads would be that at least one isomer reacts by simultaneous $S_N1$ and $S_N2$ processes, thus giving rise to a different mixture of products than that formed by $S_N1$ alone. However, reasons have already been given for believing that solvolyses of allylic compounds do not usually involve competing unimolecular and bimolecular reactions.

A discussion of the various factors affecting product compositions and product spreads in allylic solvolysis reactions is seriously hampered by the scarcity of accurate data. Before the advent of quantitative infrared spectrophotometry, the accurate analysis of solvolysis product mixtures required careful, often tedious separations of isomeric ethers, esters, and alcohols by methods which did not cause them to isomerize. Many of the solvolysis reactions reported in the literature were performed with the object of preparing and isolating only one of the possible products, and even in those cases where both products were separated it is usually possible to make only rough estimates as to the composition of the

## TABLE 9

*Products of solvolysis reactions of allylic halides*

| Compound | Conditions | Temperature | Primary Product | Spread | Reference |
|---|---|---|---|---|---|
| | | °C. | per cent | | |
| $CH_3CH=CHCH_2Cl$ | 0.8 $N$ aqueous NaOH | 25 | 60 | 22 | (660) |
| $CH_3CHClCH=CH_2$ | | 25 | 38 | | |
| $CH_3CH=CHCH_2Cl$ | $H_2O-Ag_2O$ | 25 | 45 | 11 | (660) |
| $CH_3CHClCH=CH_2$ | | 25 | 34 | | |
| $CH_3CH=CHCH_2Cl$ | $H_2O-Ag_2O$ | 95 | 39 | 6 | (659a) |
| $CH_3CHClCH=CH_2$ | | | 33 | | |
| $CH_3CH=CHCH_2Cl$ | 0.5 $N$ Na$_2$CO$_3$ | 25 | 55 | 19 | (659a) |
| $CH_3CHClCH=CH_2$ | | | 36 | | |
| $CH_3CH=CHCH_2Cl$ | 50% Aqueous acetone, CaCO$_3$ | 47 | 56 | 13 | (659a) |
| $CH_3CHClCH=CH_2$ | | | 43 | | |
| $CH_3CH=CHCH_2Cl$ | 50% Aqueous acetone, CaCO$_3$ | 25 | 59 | 19 | (659a) |
| $CH_3CHClCH=CH_2$ | | | 40 | | |
| $CH_3CH=CHCH_2Cl$ | 0.5 $N$ Na$_2$CO$_3$ in 45% aqueous ethanol | 25 | 68 | 29 | (660) |
| $CH_3CHClCH=CH_2$ | | | 39 | | |
| $CH_3CH=CHCH_2Cl$ | $C_2H_5OH$ + CaCO$_3$ | 78 | 91 | 38 | (659a) |
| $CH_3CHClCH=CH_2$ | | | 53 | | |
| $CH_3CH=CHCH_2Cl$ | Ethanol | 78 | 92 | 10 | (121) |
| $CH_3CHClCH=CH_2$ | | | 82 | | |
| $CH_3CH=CHCH_2Cl$ | Ethanol, Ag$_2$O | 78 | 70 | 24 | (659a) |
| $CH_3CHClCH=CH_2$ | | | 46 | | |
| $CH_3CH=CHCH_2Cl$ | $CH_3COOAg$ + $CH_3COOH$ | 25 | 60 | 4 | (539) |
| $CH_3CHClCH=CH_2$ | | | 56 | | |
| $CH_3CH=CHCH_2Br$ | 10% Na$_2$CO$_3$ | 100 | 65 | 11 | (659a) |
| $CH_3CHBrCH=CH_2$ | | | 54 | | |
| $C_2H_5CH=CHCH_2Cl$ | $CH_3COOAg$ + $CH_3COOH$ | | 58 | 5 | (419) |
| $C_2H_5CHClCH=CH_2$ | | | 53 | | |
| $C_2H_5CH=CHCH_2Cl$ | Aqueous Na$_2$CO$_3$ | 25 | 45 | 14 | (419) |
| $C_2H_5CHClCH=CH_2$ | | | 31 | | |
| $C_6H_5CH=CHCH_2Cl$ | $CH_3COOAg$ | 50 | 63 | | (419) |
| $C_6H_5CH=CHCH_2Cl$ | $CH_3COOK$ in $CH_3COOH$ | | 67 | | (419) |

TABLE 9—*Continued*

| Compound | Conditions | Temperature | Primary Product | Spread | Reference |
|---|---|---|---|---|---|
| | | °C. | per cent | | |
| C₆H₅CH=CHCH₂Br | AgNO₃ in C₂H₅OH | | 45 | | (419) |
| C₆H₅CH=CHCH₂Br | 70% Aqueous C₂H₅OH, KOH | | 80 | | (419) |
| (CH₃)₂C=CH₂CHCl<br>(CH₃)₂CClCH=CH₂ | C₂H₅OH + CaCO₃ | 25 | 48<br>30 | 18 | (659a) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | 10% Aqueous Na₂CO₃ | 25 | 15<br>15 | 0 | (659a) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | 10% Aqueous NaHCO₃ | | 20<br>0 | | (438) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | CH₃COOK in CH₃COOH | 25–50 | 70<br>45 | 25 | (438) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | HCOONa in HCOOH | 25 | 100 (?)<br>50 | | (446) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | CH₃ONa in CH₃OH | 25–60 | 100<br>33 | 66 | (438) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | H₂O + Ag₂O | 95 | 17<br>16 | 0 | (659a) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | H₂O + Ag₂O | 25 | 15<br>14 | 0 | (659a) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | C₂H₅OH + Ag₂O | 25 | 35<br>20 | 15 | (659a) |
| (CH₃)₂C=CHCH₂Cl | 10% Na₂CO₃ | 95 | 20 | | (659a) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | Ethanol | 60 | 40<br>30 | 10 | (170) |
| (CH₃)₂C=CHCH₂Cl<br>(CH₃)₂CClCH=CH₂ | CH₃COOAg in CH₃COOH | 25 | 55<br>55 | 0 | (659a) |
| (CH₃)₂C=CHCH₂Br | 10% Aqueous Na₂CO₃ | 25 | 0 | | (484) |
| (CH₃)₂C=CHCH₂Br | H₂O + NaOH<br>H₂O + NaHCO₃<br>H₂O + CaCO₃<br>H₂O + Ag₂O | 95 | 19 ± 2 | | (659a) |
| (CH₃)₂C=CHCH₂Br | 63% Aqueous acetone | 25 | 19 | | (659a) |
| (CH₃)₂C=CHCH₂Br | 83% Aqueous acetone | 25 | 23 | | (659a) |
| (CH₃)₂C=CHCH₂Br | 65% Aqueous acetone | 55 | 12 | | (659a) |

TABLE 9—*Concluded*

| Compound | Conditions | Temperature | Primary Product | Spread | Reference |
|---|---|---|---|---|---|
| | | °C. | per cent | | |
| $(CH_3)_2C=CHCH_2Br$ | $H_2O + Ag_2O$ | 0 | 13 | | (659a) |
| $(CH_3)_2C=CHCH_2Br$ | $H_2O + Na_2CO_3$ $H_2O + NaHCO_3$ $H_2O + CaCO_3$ $H_2O + Ag_2O$ | 25 | 14 | | (659a) |
| $(CH_3)_2C=CHCH_2Br$ | $H_2O + NaOH$ | 25 | 18 | | (659a) |
| $(CH_3)_2C=CHCH_2Br$ | $CH_3COOAg + CH_3COOH$ | 25 | 52 | | (659a) |
| $C_2H_5C(CH_3)=CHCH_2Cl$ | $C_2H_5OH + CaCO_3$ | 25 | 49 | | (636) |
| $C_2H_5C(CH_3)=CHCH_2Cl$ $C_2H_5C(CH_3)ClCH=CH_2$ | 10% $Na_2CO_3$ | 25 | 12 12 | 0 | (659a) |
| $C_2H_5C(CH_3)=CHCH_2Cl$ $C_2H_5C(CH_3)ClCH=CH_2$ | $C_2H_5OH + Ag_2O$ | 25 | 39 26 | 13 | (659a) |
| $C_2H_5C(CH_3)=CHCH_2Cl$ $C_2H_5C(CH_3)ClCH=CH_2$ | $H_2O + Ag_2O$ | 25 | 14 12 | 2 | (659a) |
| $C_2H_5C(CH_3)=CHCH_2Cl$ $C_2H_5C(CH_3)ClCH=CH_2$ | $CH_3COOAg + CH_3COOH$ | 25 | 55 54 | 1 | (659a) |
| $C_2H_5C(CH_3)=CHCH_2Cl$ | 10% NaOH | 25 | 19 | | (659a) |
| $C_3H_7C(CH_3)=CHCH_2Cl$ $C_3H_7C(CH_3)ClCH=CH_2$ | $CH_3ONa$ in $CH_3OH$ | 25-50 | 100 75 | 25 (?) | (440) |
| $C_3H_7C(CH_3)=CHCH_2Cl$ $C_3H_7C(CH_3)ClCH=CH_2$ | $CH_3COOK$ in $CH_3COOH$ | 25-50 | 65 50 | 15 (?) | (440) |
| $C_3H_7C(CH_3)=CHCH_2Cl$ $C_3H_7C(CH_3)ClCH=CH_2$ | 10% $NaHCO_3$ | 25-45 | 15 ca. 0 | ca. 15 | (440) |
| $CH_3CH=CHCH=CHCH_2Cl$ $CH_3CHClCH=CHCH=CH_2$ | Aqueous $NaHCO_3$ | 25 | 10 10 | 0 | (443) |
| $CH_3CH=CHCH=CHCH_2Cl$ $CH_3CHClCH=CHCH=CH_2$ | $CH_3COOK$ in $CH_3COOH$ | 45 | 25 15 | 10 | (443) |
| $C_6H_5CH=CHCH=CHCH_2Cl$ | 50% Aqueous dioxane | | 50 | | (442) |
| $(CH_3)_2C=CHCH=CHCH_2Cl$ | $CH_3COOK$ in $CH_3COOH$ | 25 | 80 | | (441) |
| $(CH_3)_2C=CHCH=CHCH_2Cl$ | Aqueous $NaHCO_3$ | 25 | ca. 0 | | (441) |

original mixtures. The bulk of the quantitative data on which the following discussion is based was obtained by W. G. Young and coworkers. The products of solvolysis of a number of allylic halides under various conditions are collected in table 9.

As kinetic and relative reactivity data would lead one to expect, product spreads are greater in solvents of low ionizing power than in those of higher ionizing power but similar nucleophilicity, and greater in hydroxylic solvents than in carboxylic acids. This is true because solvolysis of both allylic isomers will approach the limiting (ionic) mechanism as solvent nucleophilicity is decreased and ionizing power is increased; when both isomers react by the ionic mechanisms, they will, of course, give identical mixtures of products (see table 10 for examples of reactions with zero product spreads). The primary member of an isomeric pair is much more susceptible to nucleophilic interaction with solvent than the secondary or tertiary member, and invariably gives the larger percentage of primary reaction product when product spreads are observed.

Electrophilic catalysts such as silver ion facilitate the formation of carbonium ions, and product spreads are smaller in their presence than in pure solvent. Product spreads for several allylic chlorides in ethanol, water, and acetic acid, with and without silver ion, are given in table 10.

In any given solvent product spreads are greater for primary–secondary isomer pairs than for primary–tertiary pairs. This is not surprising, since kinetic data indicate that reactions of dialkylallylic halides are more nearly unimolecular than those of monoalkylallylic halides. The butenyl chlorides, for example, give product spreads in all solvents studied, while the dimethylallyl and methylethylallyl chlorides give product spreads only in ethanol, the least polar and most nucleophilic of the solvents used.

Allylic solvolysis reactions which are truly unimolecular involve formation of a mesomeric carbonium ion which can react with solvent at either of the two allylic positions to give a mixture of normal and rearranged substitution products. That is, the composition of the product mixture is subject to kinetic rather than thermodynamic control. It is interesting that the thermodynamically less stable product is almost always formed in greater than equilibrium proportion and is frequently the major product of the reaction. At equilibrium the primary member of a pair of allylic isomers will predominate by a factor of about 5 to 1 for a primary–secondary pair or a factor of about 10 to 1 for a primary–tertiary pair. This is probably due to resonance stabilization of the primary isomer by hyper-

TABLE 10

*Product spreads in solvolysis of allylic chlorides under standard conditions*

| System | $C_2H_5OH$ | $C_2H_5OH$ $Ag_2O$ | $H_2O$ | $H_2O$ $Ag_2O$ | $CH_3COOH$ | $CH_3COOAg$ $CH_3COOH$ |
|---|---|---|---|---|---|---|
| [$CH_3CHCHCH_2$]Cl...................... | 38 | 24 | 19 | 11 | | 4 |
| [$C_2H_5CHCHCH_2$]Cl................. | | | 13 | | | |
| [$(CH_3)_2CCHCH_2$]Cl.................. | 18 | 15 | 0 | 0 | 0 | |
| [$C_2H_5C(CH_3)CHCH_2$]Cl............. | 23 | 13 | 0 | 0 | | 0 |

## TABLE 11

*Products from allylic carbonium ions*

| Solvent | $CH_3$, $C_2H_5$, $\overset{H}{\underset{}{C}}$ $C^{\oplus}$ $CH_2$ | $CH_3$, $CH_3$, CH $C^{\oplus}$ $CH_3$ | $CH_3$, H, CH $C^{\oplus}$ $CH_2$ |
|---|---|---|---|
| H$_2$O | 12% P | 15% P | 35% P |
| C$_2$H$_5$OH | 26% P | 25% P | 50% P |
| CH$_3$COOH | 55% P | 55% P | 56% P |

conjugation of $\gamma$-alkyl substituents with the allylic double bond (29). Evidently, hyperconjugation in the transition state of the reaction of the carbonium ion with solvent increases the positive character of the secondary (or tertiary) atom of the allylic system, since the secondary (or tertiary) solvolysis product usually predominates in those reactions where ionic intermediates are clearly involved. Table 11 gives product compositions for reactions of allylic carbonium ions with water, ethanol, and acetic acid. Figures quoted for the primary–tertiary systems are, wherever possible, for reactions under conditions where isomeric chlorides gave zero product spreads. Product compositions in ethanol are those given by the tertiary halides in the presence of silver oxide. The values given for the butenyl carbonium ion are product compositions from silver-ion-catalyzed reactions of the secondary halide. For all three systems the less stable product predominates in ethanol and water, while the two products are formed in approximately equal amounts in acetic acid. The proportion of primary product given by the butenyl carbonium ion in reactions with water and ethanol is considerably greater than that given by the two primary–tertiary systems, in support of the view that hyperconjugation tends to increase the positive character of the most alkylated carbon atom. The percentage of primary product formed in acetic acid appears to be unaffected by structure of the allylic system and is considerably larger than in water or ethanol. This finding is difficult to rationalize. Perhaps in the poorer ionizing solvent the SOH (solvent molecules) have to cluster around a primary bond to give the best solvation, or else the anion of the ion-pair is at the secondary–tertiary end of the allylic system and the SOH (solvent molecules) more at the primary end.

Solvolysis product composition seems to be affected only slightly by temperature changes. Hydrolysis of either $\gamma,\gamma$-dimethylallyl chloride or bromide gives about 5 per cent more primary carbinol at 95°C. than at 25°C. Silver-oxide-catalyzed hydrolysis of the butenyl chlorides yielded product mixtures with an 11 per cent spread at 25°C. and a 6 per cent spread at 95°C. (table 11).

### (c) Ion-pair intermediates

There is some reason to believe that the intermediate formed during unimolecular allylic solvolysis reactions is not always a solvated carbonium ion but may be an ion-pair instead:

$$\begin{array}{c} R \diagdown \\ \phantom{R} {}^{\delta+} \diagup C \diagdown \\ R \diagup C {}^{\delta+} \\ R \diagup \phantom{C} X_{\ominus} \end{array}$$
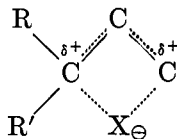
Such an ion-pair could either react with solvent, giving solvolysis product, or undergo "internal return" to the original halide or its allylic isomer.

Young, Winstein, and Goering (694) found that the acetolysis of $\alpha,\alpha$-dimethylallyl chloride is accompanied by simultaneous isomerization to $\gamma,\gamma$-dimethylallyl chloride. Addition of chloride ion to the reaction medium did not affect the rate of this isomerization, thus ruling out the formation of a free carbonium ion followed by simultaneous reaction of this ion with acetic acid and chloride ion. This isomerization reaction does not appear to have a concerted intramolecular mechanism, since such a process would not involve separation of charge and should be essentially independent of solvent. The tertiary chloride does not isomerize rapidly in the liquid state or during solvolysis in ethanol.

The question of whether the ion-pair involved in the isomerization reaction is a transition state or an intermediate of appreciable life has not been settled. However, it is more probable that the ion-pair is a common intermediate in the isomerization and solvolysis reactions:

$$R_t Cl \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} R^{\oplus} Cl^{\ominus} \quad \begin{array}{l} \xrightarrow{k_s} \text{ solvolysis products} \\ \xrightarrow[k_2]{} R_p Cl \end{array}$$
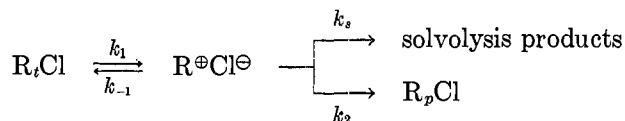
This formulation provides a reasonable explanation for the facts that isomerization of the tertiary chloride does not occur during ethanolysis, and that acetolysis and ethanolysis occur at very nearly the same rates. Unimolecular ethanolysis is usually slower than acetolysis (240). In the nucleophilic solvent ethanol, $k_{-1}$ and $k_2$ are probably negligible compared to $k_s$, so that the observed solvolysis rate is essentially equal to $k_1$. In acetic acid $k_2$ and $k_{-1}$ become important, so that the observed rate of solvolysis is only a fraction of $k_1$. The ionization step represented by $k_1$ is probably faster in acetic acid than in ethanol, as expected.

This conclusion is supported by the recent report of Goering, Nebitt, and Silversmith (225) that in the acetolysis and ethanolysis of optically active cis- and trans-5-methyl-2-cyclohexenyl chlorides the rate of loss of optical activity ($k_1$ in the above scheme) is greater in acetic acid than in ethanol, while the rate of formation of solvolysis products is actually less in acetic acid than in absolute ethanol. For both isomers in either acetic acid or ethanol the rate of racemization is greater than the rate of solvolysis and is unaffected by added chloride ion. These facts, together with the observation that racemized chloride recovered before completion of solvolysis has not undergone cis-trans isomerization, strongly suggests that the solvolysis of these cyclohexenyl chlorides occurs by an ion-pair mechanism similar to that proposed for $\alpha,\alpha$-dimethylallyl chloride.

Intramolecular isomerization was found by de la Mare and Vernon (170) to occur during the solvolysis of $\alpha,\alpha$-dimethylallyl chloride in 75 per cent ethanol, a more ionizing solvent than absolute ethanol. This shows that the isomerization is not uniquely associated with acetolysis, and demonstrates a dependence on solvent polarity which would not be expected for a concerted intramolecular process of the $S_Ni'$ type. They also found that in 75 per cent aqueous ethanol which was 1 molar in LiCl[36], isomerization of $\alpha,\alpha$-dimethylallyl chloride is accompanied by exchange with chloride ion from the solution. Even in this 1 $M$ solution of chloride ion, however, a considerable part of the isomerization was due to an intramolecular chloride shift.

Other evidence for the existence of ion-pair intermediates in unimolecular displacement reactions is furnished by the solvolysis of optically active esters of allyl alcohols. For example, the solvolysis of $\alpha,\gamma$-dimethylallyl hydrogen phthalate in carboxylic acids and alcohols was found to be accompanied by extensive racemization of the recovered unreacted ester (30, 32). Goering and Silversmith recently made a detailed study of the hydrolysis of optically active cis- and trans-5-methyl-2-cyclohexenyl acid phthalates in aqueous acetone (227). They found that in 50–90 per cent aqueous acetone the rate of racemization ($k_1$) is greater than the rate of hydrolysis ($k_s$). $k_1$ and $k_s$ showed a strong dependence on solvent polarity, and the ratio $k_1/k_s$ was nearly independent of temperature and solvent composition. These facts make it appear that a common ionic intermediate is involved in both isomerization and solvolysis.

### (d) Solvolysis reactions of optically active allylic compounds

Kenyon and coworkers have made an extensive investigation of reactions of optically active allylic compounds of the type RCHXCH=CHR'. They found that optically active hydrogen phthalate esters are hydrolyzed in neutral or weakly basic media to alcohols of low optical purity (31, 323). Solvolysis of resolved hydrogen phthalate esters in methanol, ethanol, formic acid, acetic acid, and benzoic acid is accompanied by extensive or complete racemization, and in some cases it was shown that mixtures of products are formed (2, 30, 32, 16, 186, 322). In the solvents of highest ionizing power, such as formic acid, complete racemization was usually observed. In the alcohols, the product was active but of low optical purity. The sign of rotation of the active products showed that inversion of configuration had occurred. It was found that when the products of solvolysis of $\gamma$-methyl-$\alpha$-propylallyl hydrogen phthalate and chloride were hydrogenated, the small residual optical activity completely disappeared (16). This means that the activity must have been due to normal substitution products, since only the normal products lose asymmetry on hydrogenation. Optically active allylic chlorides are also solvolyzed with varying degrees of racemization and rearrangement. Hydrolysis of $\alpha,\gamma$-dimethylallyl chloride was found to exhibit first-order kinetics in 75 per cent aqueous acetone and to give alcohol of low optical purity (17). $\gamma$-Methyl-$\alpha$-propylallyl and $\gamma$-methyl-$\alpha$-ethylallyl chlorides were hydrolyzed with much racemization and formed mixtures of alcohols (2, 16). Acetolysis of $\gamma$-methyl-$\alpha$-propylallyl chloride gave racemic product, and

methanolysis gave an ether of low optical purity whose activity disappeared on hydrogenation (16).

All of these results are most readily accounted for by postulating a unimolecular mechanism for the solvolysis reactions. The allylic systems involved are highly activated by the $\alpha$- and $\gamma$-alkyl groups, and a carbonium-ion intermediate would account for the formation of mixtures of racemic products.

## IV. REPLACEMENT REACTIONS OF ALLYLIC COMPOUNDS

### A. CONVERSION OF ALLYLIC ALCOHOLS TO ALLYLIC HALIDES

#### 1. Introduction

Allylic halides are extremely useful starting materials and intermediates in organic synthesis. They are much more reactive than saturated aliphatic halides, and can be converted by suitable displacement reactions into unsaturated alcohols, ethers, thiols, thioethers, esters, amines, acids, hydrocarbons, and many other types of compounds. The analogous saturated compounds can often be prepared from the allylic derivatives by hydrogenation. In addition, Grignard reagents prepared from allylic halides react smoothly with many carbonyl compounds which react poorly or not at all with saturated Grignard reagents. Since allylic halides are usually prepared from allylic alcohols, it seems appropriate to begin a discussion of replacement reactions of allylic compounds with those reactions by which alcohols are converted to halides.

The reagents most frequently used in preparing allylic halides from the corresponding alcohols are hydrogen halides, phosphorus halides, and thionyl chloride. Some of the reactions involved are stereospecific, while others usually lead to mixtures of isomeric allylic halides. This fact, together with the lability of allylic bromides and tertiary allylic chlorides, resulted in a considerable amount of confusion in the early chemical literature. Before the phenomenon of allylic rearrangement was discovered, an allylic halide was often assumed to be structurally related to the alcohol from which it was prepared. This is quite frequently not the case, and the discovery of allylic rearrangements was primarily due to this fact.

Secondary allylic alcohols are conveniently prepared by condensing Grignard reagents with $\alpha,\beta$-unsaturated carbonyl compounds such as acrolein, and for this reason they are frequently used as starting materials for the preparation of allylic halides. Baudrenghien (46, 47) seems to have been the first to convert vinylalkylcarbinols to halides. He reported that reaction of two of these alcohols with dry hydrogen chloride gave mixtures of isomeric chlorides. The products obtained using hydrogen bromide were obviously mixtures, but were not easily fractionated. Later workers gave conflicting reports. Some (72, 73, 123, 130, 163, 308, 484, 485) claimed that either the secondary alcohols or their primary isomers were converted exclusively to primary bromide by treatment with hydrogen bromide or phosphorus tribomide, while others (236, 285, 286, 287, 623, 681) reported that mixtures of bromides are formed. While it has been realized for over thirty years that formation of allylic halides from secondary alcohols is accom-

panied by rearrangement, there was a period in which it was not known whether the rearrangement was partial or complete, or whether rearrangement occurs during or after the substitution reaction—that is, whether product composition is subject to kinetic or thermodynamic control. The situation was particularly complicated in the case of allylic bromides, owing to the ease with which they isomerize.

The reactions of allylic bromides could not be interpreted correctly until the question of their purity and lability had been settled. For example, reactions reported to give partially rearranged products might actually be normal reactions if the bromides used were mixtures instead of pure products as frequently assumed. The first attempts to determine the composition of the allylic bromides formed by primary and secondary allylic alcohols used physical methods of analysis such as fractional distillation at atmospheric pressure (46, 47) and Raman spectra. Gredy and Piaux (236), who used the latter method, erroneously concluded that the products formed by reaction of crotyl alcohol with hydrogen bromide or $\alpha$-methylallyl alcohol with phosphorus tribromide are identical mixtures of cis- and trans-crotyl and $\alpha$-methylallyl bromides.

Young and Prater (681) were the first to suggest that the problem involves not only the composition of the bromides formed during their preparation but also the extent to which they rearrange during purification. Young and Winstein (652), a short time later, described a procedure whereby $\alpha$- and $\gamma$-methylallyl bromides could be quantitatively separated without appreciable isomerization by means of distillation at reduced pressure. They developed a method of calculating the composition of bromide mixtures from their refractive indexes. Using these techniques, it was possible to study the composition of bromide mixtures formed from various allylic alcohols under different reaction conditions and to determine the equilibrium composition of mixtures of isomeric bromides (652, 673, 674, 678, 683). These results will be discussed shortly.

Allylic chlorides are considerably more stable than the analogous bromides, and primary and secondary chlorides show little tendency to isomerize during ordinary purification procedures. However, very little work has been done to determine the variation in composition of product mixtures obtained using different reaction conditions. Allylic iodides are so reactive and unstable that very few of them have been prepared. It seems unlikely that isomeric allylic iodides would be sufficiently stable to be separated.

## 2. Reaction of allylic alcohols with hydrogen halides

Allylic alcohols react with hydrogen bromide, hydrogen chloride, and hydrogen iodide to form mixtures of isomeric allylic halides. These conversions can be brought about in a number of ways. The allylic alcohol is frequently shaken or stirred with a concentrated aqueous solution of the hydrogen halide, with or without addition of a small amount of concentrated sulfuric acid. A saturated solution of the dry hydrogen halide in glacial acetic acid may also be used. Halide mixtures are frequently prepared by bubbling dry gaseous hydrogen halide into the alcohol, or into a solution of it in ether or dioxane.

TABLE 12

*Composition of butenyl bromides obtained from crotyl and α-methylallyl alcohols and hydrogen bromide under controlled conditions*

| Reaction Conditions | Butenol used | Composition of Bromides | | Differences in Per Cent Primary Bromide from Primary and Secondary Alcohols |
|---|---|---|---|---|
| | | Primary | Secondary | |
| 48% HBr at −15°C................................ | Primary | 86 | 14 | 2.8 |
| | Secondary | 83.2 | 16.8 | |
| 48% HBr + H₂SO₄ at −15°C....................... | Primary | 84 | 16 | 4.2 |
| | Secondary | 79.8 | 20.2 | |
| Saturated HBr at 0°C............................. | Primary | 79 | 21 | 5 |
| | Secondary | 74 | 26 | |
| HBr gas at −20°C................................. | Primary | 83 | 17 | 12 |
| | Secondary | 71 | 29 | |
| Glacial CH₃COOH saturated with HBr gas.......... | Primary | 85.5 | 14.5 | 13.5 |
| | Secondary | 72 | 28 | |

Young, Lane, and Nozaki (673, 674, 678) studied the reaction of α- and γ-methylallyl alcohols with hydrogen bromide under a variety of standardized conditions. They found that under all conditions studied similar but not identical mixtures of primary and secondary bromides are formed by each alcohol, and that these mixtures always contain more secondary bromide than the equilibrium mixtures. Their data are summarized in table 12.

The mechanism of the reaction of allylic alcohols with hydrogen bromide or hydrogen chloride is probably similar to that proposed for unimolecular substitution reactions of allylic halides (page 784). The fact that identical product mixtures are not formed by isomeric alcohols means that all of the reaction product cannot arise from a common intermediate, i.e., from a mesomeric carbonium ion. The experimental results are satisfactorily accounted for by a mechanism in which part of the product arises by a direct displacement of water from the conjugate acid of the alcohol by halide ion while the rest of the product is formed by reaction of a solvated mesomeric allylic carbonium ion with halide ion (674).

$$RCH{=}CHCH_2OH \xrightleftharpoons{H_3O^+} RCH{=}CHCH_2\overset{+}{O}H_2 \xrightleftharpoons[H_2O]{Br^-} RCH{=}CHCH_2Br$$

$$\Big\updownarrow -H_2O \qquad \qquad Br^- \diagup \diagdown -Br^-$$

$$[RCH{\cdots}CH{\cdots}CH_2]^+$$

$$\Big\updownarrow -H_2O \qquad \qquad -Br^- \diagdown \diagup Br^-$$

$$RCHOHCH{=}CH_2 \xrightleftharpoons{H_3O^+} \underset{H_2\overset{+}{O}}{RCHCH{=}CH_2} \xrightleftharpoons[H_2O]{Br^-} RCHBrCH{=}CH_2$$

This mechanism is probably somewhat oversimplified, but should be basically correct. The bimolecular reaction may not be as clear-cut as pictured, since the observed product spreads could also be due to a reaction involving displacement

of water from conjugate acid molecules which are just beginning to form carbonium ions but which have not completely lost their structural identity.

$$
\begin{array}{c}
\text{OH}_2{}^{\delta+} \\
\overset{\displaystyle \nearrow \qquad \searrow}{} \\
\underset{\delta+}{\text{RCH}} \qquad\qquad \overset{}{\underset{\delta+}{\text{CH}_2}} \\
\searrow \qquad \nearrow \\
\text{CH}
\end{array}
$$

If strictly bimolecular displacement by bromide does occur, it is possible that mechanisms $S_N2$ and $S_N2'$ are both operating. The formation of the conjugate acid of the alcohol is very probably the first step of the reaction, but it is not necessary to assume, as Ogg (659) has done, that the oxonium ion is the only intermediate in the reaction of crotyl alcohol with hydrobromic acid.

No systematic study of the reaction of allylic alcohols with hydrogen chloride or hydrochloric acid has been reported. However, it is known that with concentrated hydrochloric acid and dry hydrogen chloride isomeric allylic alcohols give similar but not identical mixtures of allylic chlorides in which the primary isomer predominates. Cuprous chloride was found to catalyze the reaction of allyl alcohol with concentrated hydrochloric acid, even when present in low concentrations (299). The catalyst concentration was too low for an increase in chloride-ion concentration to account for its action, so it seems likely that cuprous ion is the effective reagent. This ion is a potent electrophilic catalyst for many reactions, and it may function in the present case by complexing with the hydroxyl oxygen atom of the alcohol.

It is interesting that reaction of crotyl or $\alpha$-methylallyl alcohols with hydrochloric acid or dry hydrogen chloride gives $\gamma$-methylallyl chloride as the main product (46, 121, 195, 147, 458, 507, 539), while addition of hydrogen chloride to butadiene under a variety of experimental conditions gives mainly the secondary product, $\alpha$-methylallyl chloride (327, 508). Both the addition and the replacement reactions have been postulated to involve formation of an intermediate allylic carbonium ion (167). This is very unlikely, since the two reactions give widely different product mixtures. Addition of hydrogen chloride to butadiene probably involves preliminary formation of a $\pi$-complex, followed by attack of chloride ion at the secondary carbon:

$$
\begin{array}{c}
\text{H} \\
\overset{\displaystyle \nearrow \overset{+}{} \searrow}{} \\
\text{CH}_2{=}\text{CH}-\text{CH}-\text{CH}_2 \\
\uparrow \; - \\
\text{Cl}
\end{array}
$$
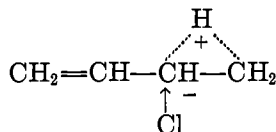
On the other hand, reaction of the alcohols with aqueous hydrochloric acid probably proceeds with formation of a mesomeric carbonium ion which reacts with chloride ion to give mainly $\gamma$-methylallyl chloride.

Table 13 contains a compilation of preparations of unsymmetrically substituted allylic halides from allylic alcohols using hydrogen chloride, hydrogen bromide, and hydrogen iodide or solutions of them in various solvents. It is

believed to be reasonably complete, with the limitation that where a compound has been prepared by the same procedure by several people, the original reference is frequently the only one listed. In the majority of cases the original references do not contain exact data concerning product compositions. Those which do are

TABLE 13

*Conversion of allylic alcohols to allylic halides by hydrogen halides*
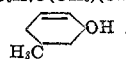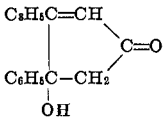
| Alcohol | HCl Reactions | | HBr Reactions | |
|---|---|---|---|---|
| | Conditions† | References | Conditions | References |
| $CHBr=CHCH_2OH$ | I | (251*) | | |
| $CH_2=C=CHCH_2OH$ | I | (113*) | | |
| $CH_3CH=CHCH_2OH$ | I, II | (121, 123, 147, 195, 327, 458, 507, 539) | I, II, III, V | (123, 201, 452, 673, 674, 678) |
| $CH_3CHOHCH=CH_2$ | I, II | (46, 208, 257*, 258*, 539, 507, 385) | I, II, III, V | (46, 130, 208, 230, 300, 673*, 674) |
| $CH_2OHCH=CHCH_2Cl$ | II | (363) | II | (619) |
| $CH_3CCl=CHCH_2OH$ | II | (245) | | |
| $CHCl=C(CH_3)CH_2OH$ | I | (247*, 623*) | | |
| $CH_2=CHCHOHC\equiv CH$ | I | (265*) | | |
| $C_2H_5CH=CHCH_2OH$ | II | (419*) | | |
| $C_2H_5CHOHCH=CH_2$ | II | (47, 381*, 419*, 420*) | II, V | (47, 285, 289, 419, 683) |
| $(CH_3)_2C=CHCH_2OH$ | II | (438*) | | |
| $(CH_3)_2C(OH)CH=CH_2$ | II | (438*) | I | (129) |
| $CH_3CH=CHCHOHC\equiv CH$ | I | (265*) | | |
| $CH_3CH=CHCH=CHCH_2OH$ | IV | (443*) | | |
| $CH_3CHOHCH=CHCH=CH_2$ | IV | (443*) | | |
| $n-C_3H_7CHOHCH=CH_2$ | | | V | (286, 289, 683) |
| $CH_3CH=CHCHOHC_2H_5$ | | | I | (196) |
| $C_2H_5C(CH_3)(OH)CH=CH_2$ | I | (636*) | | |
| $(CH_3)_2C(OH)C(CH_3)=CH_2$ | | | I | (129) |
| $CH_2=CHCHOHCHOHCH=CH_2$ | II | (239) | II | (239) |
| $(CH_3)_2CH=CHCH=CHCH_2OH$ | IV | (441*) | | |
| $(CH_3)_2C(OH)CH=CHCH=CH_2$ | IV | (441) | | |
| $n-C_4H_9CHOHCH=CH_2$ | | | V | (58, 59, 60) |
| $C_3H_7C(CH_3)(OH)CH=CH_2$ | II | (440*) | | |
| ⟨═⟩OH  H₃C | Dry HCl in dioxane | (224) | | |
| $C_2H_5OCH_2CH_2CH=CHCH_2OH$ | II | (507) | | |
| $C_2H_5OCH_2CH_2CHOHCH=CH_2$ | II | (507) | | |
| $(CH_3)_2C(OH)CH=CHC(CH_3)_2OH$ | II | (182, 292) | II | (32, 33) |
| $CH_3CH=CHCHOHC_4H_9$ | I | (197) | I | (197) |
| $CH_3CH=CHCHOHCH_2CH(CH_3)_2$ | I | (197) | I | (197) |
| $C_6H_5CH=CHCH_2OH$ | I, II | (124, 181, 355, 358, 414, 419, 545) | I, II, III | (93, 102, 124, 131, 355, 358, 408, 419, 430) |
| $C_6H_5CHOHCH=CH_2$ | II | (414, 419, 420, 618) | II, III | (156, 355, 419, 430) |
| $CH_3CH=CHCHOHC\equiv CC_4H_9$ | I | (265) | | |
| $C_6H_5CHOHC(CH_3)=CH_2$ | | | I | (585) |
| $m-CH_3C_6H_4CH=CHCH_2OH$ | | | II | (102) |
| $m-CH_3C_6H_4CHOHCH=CH_2$ | | | II | (102) |
| $o-CH_3C_6H_4CHOHCH=CH_2$ | | | I | (156) |
| $C_6H_5CH_2CHOHCH=CH_2$ | | | I | (156) |
| $C_2H_5CH=C(CH_3)CHOHC_4H_9$ | I | (197) | I | (197) |
| $C_2H_5CH=C(CH_3)CHOHCH_2CH(CH_3)_2$ | I | (197) | I | (197) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2OH$ | II | (182) | II | (182) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)(OH)CH=CH_2$ | II | (182, 292) | II | (182, 292) |
| $C_6H_5CH=CHCHCH_2OH$ | IV | (442*) | | |
| $C_6H_5CHOHCH=CHCH=CH_2$ | IV | (442*) | | |
| $C_6H_5CH=CHCHOHC_2H_5$ | II | (420) | | |

TABLE 13—*Concluded*

| Alcohol | HCl Reactions | | HBr Reactions | |
| --- | --- | --- | --- | --- |
| | Conditions† | References | Conditions | References |
| C₆H₅CH₂CH₂CHOHCH=CH₂................ | | | I | (156) |
| C₆H₅CH₂CH₂CH₂CHOHCH=CH₂............ | | | I | (156) |
| C₆H₅CH=CHCHOHC(CH₃)₃................. | I | (460) | | |
| p-ClC₆H₄CH=CHCCl=CHCHOHC₆H₄Cl-p.... | I | (589) | | |

$C_6H_5C≡CH$
$\quad\backslash$
$\quad\quad C=O$ .......................... Alcoholic HCl (105*)
$C_6H_5C—CH_2$
$\quad|$
$\quad OH$

⟨ring⟩—CH₂CHOHC(CH₃)=CHC≡CC₄H₉....... I (153*)

| (C₆H₅)₂C(OH)CH=CHC₃H₅.................. | I | (700*) | | |
| (C₆H₅)₂C=CHCHOHC₆H₅..................... | IV | (699*) | | |
| RC≡CC(CH₃)(OH)CH=CHCl................ | I | (306) | | |

| | HI Reactions | |
| --- | --- | --- |
| | Conditions† | References |
| CH₃CH=CHCH₂OH.......................... | I | (123) |
| C₃H₅CH=CHCH₂OH......................... | I | (419) |
| C₃H₅CHOHCH=CH₂......................... | I | (419) |

† Reaction conditions: I, concentrated HX; II, dry HX; III, HX in CH₃COOH; IV, HX in ethyl ether; V, concentrated HX and H₂SO₄.

marked with an asterisk. The following generalizations can be made about the other cases: The primary isomer, when there is one, predominates in all cases. With α- or γ-phenylallyl alcohols, the γ-phenyl-substituted halide is usually the only product obtained. The products from reactions of primary–tertiary pairs of isomeric alcohols are predominantly primary, and in the case of bromides only the primary halide is isolated.

### 3. Reaction of allylic alcohols with phosphorus halides

Allylic halides may be prepared from allylic alcohols by allowing them to react with phosphorus trihalides or phosphorus pentahalides under a variety of conditions. The yields depend on the particular alcohol, phosphorus halide, and reaction conditions used. The reaction usually gives better yields with phosphorus tribromide than with phosphorus trichloride, and phosphorus tribromide has been extensively used for the preparation of allylic bromides.

In spite of the synthetic value of these reactions, little is known concerning their mechanisms. A few studies have been made in which yields and product compositions are reported, but many workers using these reactions for synthetic purposes have not even reported yields of halides, and very few have reported the proportions of isomeric allylic halides in their reaction products. Any discussion of the mechanisms of these reactions is therefore largely speculative. The

statements which are made in the following paragraphs are based primarily on results of studies of reactions of phosphorus halides with saturated alcohols.

Phosphorus trihalides are non-polar acid halides, and the initial products of their reactions with alcohols are alkyl phosphite esters (53, 209, 213, 360).

$$ROH + PX_3 \rightarrow \begin{cases} P(OR)_3 \\ ROPX_2 + HX \\ (RO)_2PX \end{cases}$$
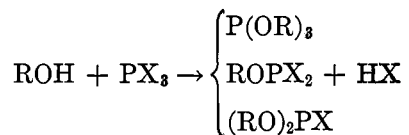
The type of ester formed depends on the relative proportions of phosphorus trihalide and alcohol. In many cases, mixtures of alkyl phosphite and alkyl halophosphite esters are obtained. These esters are stable enough to be isolated in the absence of hydrogen halide. The reactions are usually conducted under conditions such that the hydrogen halide produced by the reaction forming the ester remains in the reaction medium. It can then react with the phosphite esters to form alkyl halides and various phosphorus compounds (53, 209, 213, 507).

(1)  $(RO)_3P + HX \rightarrow (RO)_3PH^+X^- \rightarrow RX + (RO)_2PHO$

(2)  $(RO)_2PX + HX \rightarrow (RO)_2PHX^+X^- \rightarrow RX + (RO)PXHO$

(3)  $ROPX_2 + HX \rightarrow ROPX_2H^+X^- \rightarrow RX + X_2PHO$

(4)  $(RO)_2PHO + HX \rightarrow RX + ROPO(OH)$.
etc.

Reactions 1, 2, and 3 are similar and involve initial formation of a phosphonium halide or possibly an unionized complex of HX and the trialkyl phosphite or alkyl halophosphite ester. Trialkyl phosphites (1) react more readily with HX than dialkyl halophosphites. Reactions of the type depicted in equation 4 are much slower than reactions 1, 2, and 3. The reactions which actually form alkyl halide frequently involve bimolecular displacements of a substituted phosphite anion by halide ion, and the higher nucleophilicity of bromide and iodide ions results in reactions analogous to 2 and 3 occurring more readily with these ions than with chloride ion—hence the higher yields of RX usually obtained in reactions with phosphorus tribromide. The formulation of the product-forming step as a bimolecular displacement by halide ion is supported but not proven by the well-known fact that optically active alcohols were converted to optically active halides of inverted configuration by these reagents (294, page 392).

The above arguments may be extended with only slight modification to re-reactions of allylic alcohols with phosphorus trihalides. The initially formed phosphite esters from primary allylic alcohols are converted by action of HX to a mixture of halides in which the primary isomer predominates, thus indicating an $S_N2$ displacement by halide ion in the product-forming step. Secondary and tertiary allylic alcohols, on the other hand, are converted to mixtures of halides containing a considerable proportion of the primary halide (507, 673). The

phosphite esters of secondary and tertiary allylic alcohols apparently react by a predominantly ionic mechanism.

$$(CH_2\!\!=\!\!CHCHO)_3\overset{+}{P}HX^- \;\rightarrow\; (CH_2\!\!=\!\!CHCHO)_2PHO \;+$$

with subscript R under the CHO groups, then:

$$[CH_2\!\cdots\!CH\!\cdots\!CHR]^+ \;+\; X^-$$
$$\downarrow$$
$$RCH\!\!=\!\!CHCH_2X \;+\; RCHXCH\!\!=\!\!CH_2$$

As expected, the allylic esters are more easily converted to halides by both the $S_N2$ and the $S_N1$ mechanisms than are saturated alkyl phosphite esters. Reaction of allylic alcohols with phosphorus trichloride frequently gives satisfactory yields of allylic chlorides, while reactions of phosphorus trichloride with saturated alcohols, particularly primary alcohols, often give very poor yields of chlorides and much phosphite ester. The yields of allylic bromides obtained in reactions with phosphorus tribromide are usually quite satisfactory.

Reactions of allylic alcohols with phosphorus trihalides are usually carried out in the presence of varying amounts of pyridine. The advantage of having pyridine in the reaction mixture is not clear, since the yields of halides and the composition of the halide mixture do not seem to be markedly influenced by the presence of small amounts of tertiary amines. Indeed, the presence of an excess of pyridine is detrimental. In this case the hydrogen halide is removed from the system as fast as it is formed by the esterification reaction, and the product of the reaction is phosphite ester rather than allylic halide. When Meisenheimer and Link (419) treated $\alpha$-ethylallyl alcohol with phosphorus trichloride in the presence of an excess of pyridine, no pentenyl chloride was obtained. Heating the reaction product (probably phosphite esters) caused it to decompose with evolution of an unsaturated hydrocarbon, while passing a stream of dry hydrogen chloride into it gave a high yield of pentenyl chlorides.

Tertiary amines seem to serve no important purpose in reactions of allylic alcohols with phosphorus trihalides, and their use probably persists more for historical than for practical reasons.

Phosphorus pentahalides have been used to prepare allylic halides from alcohols. The initial step of this reaction probably yields allylic halide and phosphorus oxyhalide; phosphorus oxyhalide can react with more alcohol, but this reaction is much slower than the first step and frequently gives phosphate esters (210).

$$PX_5 + ROH \rightarrow RX + POX_3 + HX$$

Landauer and Rydon (376) recently described a related method of preparing alkyl and allylic halides. Triphenyl phosphite methiodide, prepared from triphenyl phosphite and methyl iodide, reacts with $\alpha$- and $\gamma$-methylallyl alcohols to give the allylic iodides in yields higher than 80 per cent:

$$(C_6H_5O)_3P \;+\; CH_3I \;\rightarrow\; (C_6H_5O)_3\overset{+}{P}CH_3 \;+\; I^-$$
$$ROH \downarrow$$
$$(C_6H_5O)_2PCH_3O \;+\; RI \;+\; C_6H_5OH$$

This reaction probably involves a preliminary alcohol interchange followed by an Arbuzov rearrangement of the resulting allylic ester (14). Allyl chloride, bromide, and iodide were prepared by refluxing allyl alcohol and triphenyl phosphite with benzyl chloride, benzyl bromide, and methyl iodide, respectively. These reactions should be equally applicable to substituted allylic alcohols. When dry hydrogen chloride was passed into a mixture of triphenyl phosphite and allyl or crotyl alcohol, allyl chloride and butenyl chlorides (mostly $\gamma$-methylallyl chloride) were obtained. However, the hydrogen chloride alone should have sufficed to convert the alcohols to halides. Allyl bromide was also prepared by treating allyl alcohol with triphenylphosphite dibromide (134):

$$(C_6H_5O)_3P \;+\; Br_2 \;\rightarrow\; (C_6H_5O)_3PBr_2 \;\xrightarrow{\text{ROH}}$$
$$(C_6H_5O)_2POBr \;+\; RBr \;+\; C_6H_5OH$$
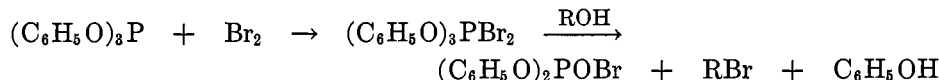
This procedure was not tried with substituted allyl alcohols.

Primary allylic alcohols react with phosphorus trichloride to give mostly the primary chloride with a few per cent of its allylic isomer (64, 243, 248, 257, 258, 380, 425, 507). This result is best explained in terms of an $S_N2$ substitution of chloride for phosphite, as previously mentioned. Unsymmetrically substituted secondary and tertiary allylic alcohols give mixtures containing comparable amounts of the isomeric allylic chlorides (64, 231, 258, 326, 419, 507, 636), indicating that an ionic mechanism is involved in these reactions. The same holds true for reactions with phosphorus tribromide, with one reservation. Unless special precautions are taken, the allylic bromides isomerize to an equilibrum mixture during their isolation and purification, the net result being that most workers report products consisting mostly of primary bromide, regardless of the structure of the alcohol used. Young and Lane (673), using methods which do not cause isomerization of the butenyl bromides, found that $\gamma$-methylallyl alcohol reacts with phosphorus tribromide in the presence of pyridine at low temperatures to form a mixture of bromides consisting of about 95 per cent $\gamma$-methylallyl bromide. $\alpha$-Methylallyl alcohol under these conditions yielded a mixture containing 45 per cent $\gamma$-methylallyl bromide and 55 per cent $\alpha$-methylallyl bromide. It was demonstrated that this mixture is formed in the actual reaction of the secondary alcohol with phosphorus tribromide and is not due to isomerization of $\alpha$-methylallyl bromide during or prior to separation of the reaction products. Allylic alcohols with an aryl substituent or more than one alkyl substituent on the $\alpha$- or $\gamma$-carbon atoms of the allylic system yield bromides which are particularly labile, and bromides obtained from such alcohols are invariably equilibrium mixtures. In the case of aryl-substituted systems the thermodynamic equilibrium is so far in favor of the $\gamma$-aryl allylic bromides that these are the only products obtained.

Phosphorus trichloride is usually used in the preparation of optically active allylic chlorides from resolved asymmetric alcohols. The reaction occurs with inversion of configuration and is usually accompanied by loss in optical purity (5, 50, 64, 257, 394, 667). The formation of active halides of inverted configuration is not necessarily due to operation of the $S_N2$ mechanism in these cases, since the same product could be formed by a unimolecular reaction involving

## TABLE 14

*Conversion of allylic alcohols to allylic halides with phosphorus halides*

| Alcohol | Allylic Chlorides | | Allylic Bromides | |
|---|---|---|---|---|
| | Reaction conditions | References | Reaction conditions | References |
| $CHCl=CHCH_2OH$ | $PCl_3$ | (347*) | | |
| $CHCl=CFCH_2OH$ (cis and trans) | $PCl_3, C_5H_5N$ | (254*) | | |
| $CH_2=C=CHCH_2OH$ | $PCl_3, C_5H_5N$ | (113*) | | |
| $CH_3CH=CHCH_2OH$ (trans) | $PCl_3$ | (507*, 123) | $PBr_3$ | (180) |
| $CH_3CH=CHCH_2OH$ (cis and trans) | $PCl_3, C_5H_5N$ | (64, 257*, 258*) | $PBr_3, C_5H_5N$ | (59, 308, 354, 452, 673*, 678*, 682) |
| $CH_3CHOHCH=CH_2$ | $PCl_3, C_5H_5N$ | (64, 231, 507*) | $PBr_3, C_5H_5N$ | (74, 163, 164, 235, 236, 452, 621, 673*, 678*) |
| $CH_2OHCH=CHCH_2OH$ (cis) | $PCl_3, C_5H_5N$ | (425*) | $PBr_3$ | (496, 619) |
| $CH_2=CHCHOHCH_2OH$ | | | $PBr_3, C_5H_5N$ | (481*) |
| $CH_3CCl=CHCH_2OH$ (cis and trans) | $PCl_3, C_5H_5N$ | (261*) | | |
| $CH_3CCl=CClCH_2OH$ (cis) | $PCl_3, C_5H_5N$ | (248*) | | |
| $CH_2=CHCHOHCOOH$ | | | $PBr_3$ | (524) |
| $CH_2=CHCHOHCOOR$ | | | $PBr_3$ | (350, 522, 524, 525) |
| $CH_2=CHCHOHCN$ | | | $PBr_3$ | (524) |
| $C_2H_5CH=CHCH_2OH$ | $PCl_3, C_5H_5N$ | (233) | | |
| $C_2H_5CHOHCH=CH_2$ | $PCl_3, C_5H_5N$ | (326, 419*) | $PBr_3, C_5H_5N$ | (70, 71, 72, 163, 164, 165, 233, 282, 283, 419, 494, 495) |
| $C_2H_5CHOHCH=CH_2$ | $PCl_5$ | (490) | | |
| $(CH_3)_2C=CHCH_2OH$ | | | $PBr_3, C_5H_5N$ | (65) |
| $(CH_3)_2C(OH)CH=CH_2$ | $PCl_3$ | (375) | $PBr_3$; $PBr_3 +$ $C_6H_5N$; $PBr_3$ in petroleum ether | (19, 312, 553, 557, 570) |
| $CH_3CH=C(CH_3)CH_2OH$ | $PCl_3, C_5H_5N$ | (380) | $PBr_3, C_5H_5N$ | (380) |
| $CH_3CHOHC(CH_3)=CH_2$ | | | $PBr_3, C_5H_5N$ | (380) |
| $HC=CCH=CHCH_2OH$ | | | $PBr_3, PBr_3 +$ $C_5H_5N$ | (125, 268) |
| $HC=CCHOHCH=CH_2$ | | | $PBr_3$ | (125) |
| $CH_3CH=CHCHOHCH_3$ (optically active) | $PCl_3, C_5H_5N$ | (5, 17, 50, 275, 394) | | |
| $HC=CCHOHCH=CHCH_3$ | | | $PBr_3, C_5H_5N$ | (268*) |
| $HC=CC(CH_3)(OH)CH=CH_2$ | | | $PBr_3, PBr_5$ in $(C_2H_5)_2O$ | (108, 277, 278) |
| $CH_2=CHCH_2CHOHCH=CH_2$ | $PCl_3, C_5H_5N$ | (394*) | $PBr_3$ | (366, 367) |
| $n-C_3H_7CHOHCH=CH_2$ | | | $PBr_3, C_5H_5N$ | (71, 72, 163, 164, 237) |
| $(CH_3)_2CHCHOHCH=CH_2$ | | | $PBr_3, C_5H_5N$ | (72, 163, 164) |
| $C_2H_5CHOHCH=CHCH_3$ | $PCl_5$ in $(C_2H_5)_2O$ | (289) | | |
| $C_2H_5CHOHCH=CHCH_3$ | $PCl_3$ in $(C_2H_5)_2O$ | (284) | | |
| $C_2H_5C(CH_3)(OH)CH=CH_2$ | $PCl_3, C_5H_5N$ | (636) | | |
| $CH_2=CHCHOHCHOHCH=CH_2$ | | | $PBr_3$ | (199, 482) |
| $n-C_4H_9CHOHCH=CH_2$ | | | $PBr_3, C_5H_5N$ | (71, 72, 161, 163, 164, 165) |
| $(-)-C_4H_9CHOHCH=CH_2$ | $PCl_5$ in $(C_2H_5)_2O$ | (395*) [(+) RCl] | $PBr_5$ [(+) RBr] in $(C_2H_5)_2O$ | (395) |
| $n-C_3H_7CHOHCH=CHCH_3$ | $PCl_3$ in $(C_2H_5)_2O$ | (284) | | |

TABLE 14—*Continued*
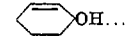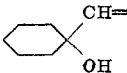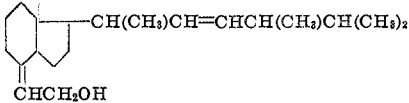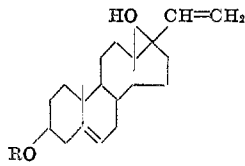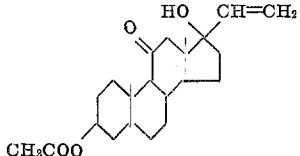
| Alcohol | Allylic Chlorides | | Allylic Bromides | |
|---|---|---|---|---|
| | Reaction conditions | References | Reaction conditions | References |
| $n$-C$_3$H$_7$CHOHCH=CHCH$_3$ | PCl$_5$; PCl$_5$ in (C$_2$H$_5$)$_2$O | (289, 291) | | |
| C$_2$H$_5$C(CH$_3$)(OH)C(CH$_3$)=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (136) |
| ⬡CH$_2$OH | PCl$_5$ in C$_6$H$_6$ | (433) | | |
| ⬡OH H$_3$C | PCl$_3$ in hexane and ether | (224*) | | |
| $n$-C$_5$H$_{11}$CHOHCH=CH$_2$ | | | PBr$_3$; PBr$_3$ + C$_5$H$_5$N | (163, 164, 232, 234, 455) |
| $n$-C$_4$H$_9$CHOHCH=CHCH$_3$ | PCl$_5$ in (C$_2$H$_5$)$_2$O | (289) | | |
| ⬡⟨CH=CH$_2$ / OH | | | PBr$_3$ | (178) |
| CH$_3$CH=CHCH$_2$CH$_2$CHOHC=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (228) |
| CH$_3$OCH$_2$CH=C(CH$_3$)CH=CCH$_2$OH | | | PBr$_3$, C$_5$H$_5$N | (453) |
| C$_6$H$_5$CH=CHCH$_2$OH (*cis*) | PCl$_5$, C$_5$H$_5$N | (243)* | PBr$_3$ in C$_6$H$_6$; PBr$_3$ | (232, 430, 545) |
| C$_6$H$_5$CH=CHCH$_2$OH (*trans*) | PCl$_5$ in C$_6$H$_6$ | (545) | | |
| C$_6$H$_5$CHOHCH=CH$_2$ | | | PBr$_3$ in C$_6$H$_6$; PBr$_3$ | (71, 72, 156, 430, 494) |
| $n$-C$_6$H$_{13}$CHOHCH=CH | | | PBr$_3$, C$_5$H$_5$N | (164) |
| (CH$_3$)$_2$C=CHCH$_2$CH$_2$CHOHCH=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (643) |
| CH$_3$CH$_2$CH=CHCH$_2$CH$_2$CHOHCH=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (282, 552, 596) |
| $n$-C$_7$H$_{15}$CHOHCH=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (158, 160, 164) |
| $o$-(and $p$-)CH$_3$C$_6$H$_4$CHOHCH=CH$_2$ | | | PBr$_3$ | (156) |
| C$_6$H$_5$CH$_2$CHOHCH=CH$_2$ | | | PBr$_3$ | (156) |
| (CH$_3$)$_2$C=CHCH$_2$CH$_2$C(CH$_3$)=CHCH$_2$OH | PCl$_3$ in petroleum ether or C$_6$H$_6$ | (192, 546, 583) | PBr$_3$, C$_5$H$_5$N | (382, 485) |
| (CH$_3$)$_2$C=CHCH$_2$CH$_2$C(CH$_3$)=CHCH$_2$OH | PCl$_3$ in petroleum ether | (546) | | |
| (CH$_3$)$_2$C=CHCH$_2$CH$_2$C(CH$_3$)(OH)CH=CH$_2$ | PCl$_3$; PCl$_3$ in C$_6$H$_6$ or petroleum ether | (182, 394, 475, 476) | PBr$_3$, C$_5$H$_5$N | (389, 579) |
| (CH$_3$)$_2$C=CHCH$_2$CH$_2$C(CH$_3$)(OH)CH=CH$_2$ | PCl$_5$ in CHCl$_3$ | (620) | | |
| (CH$_3$)$_2$C=CHCH$_2$CH$_2$CHOHC(CH$_3$)=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (558) |
| (CH$_3$)$_2$CHCH$_2$CH$_2$CH$_2$CHOHC(CH$_3$)=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (558) |
| (CH$_3$)$_2$CHCH$_2$CH$_2$CH$_2$C(CH$_3$)(OH)CH=CH$_2$ | | | PBr$_3$ in petroleum ether | (320) |
| $n$-C$_8$H$_{17}$CHOHCH=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (164) |
| $n$-C$_6$H$_{13}$CH(CH$_3$)CHOHCH=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (164) |
| (CH$_3$)$_2$C=C(CH$_3$)CH$_2$CH$_2$C(CH$_3$)(OH)CH=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (320) |
| $n$-C$_9$H$_{19}$CHOHCH=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (158, 160, 164) |
| (CH$_3$)$_2$CH(CH$_2$)$_3$CH(CH$_3$)CH$_2$CHOHCH=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (164) |
| $n$-C$_{12}$H$_{25}$CHOHCH=CH$_2$ | | | PBr$_3$, C$_5$H$_5$N | (164) |
| CH$_3$[CH(CH$_3$)CH$_2$CH$_2$CH$_2$]$_2$C(CH$_3$)=CHCH$_2$OH | | | PBr$_3$, C$_5$H$_5$N | (204) |
| CH$_3$[CH(CH$_3$)CH$_2$CH$_2$CH$_2$]$_2$C(CH$_3$)=CHCH$_2$OH | | | PBr$_3$ in petroleum ether | (319) |
| CH$_3$[CH(CH$_3$)CH$_2$CH$_2$CH$_2$]$_2$C(CH$_3$)(OH)CH=CH$_2$ | | | PBr$_3$ | (313) |
| CH$_3$[C(CH$_3$)=CHCH$_2$CH$_2$]$_2$C(CH$_3$)=CHCH$_2$OH | | | PBr$_3$, C$_5$H$_5$N | (314) |

TABLE 14—*Concluded*

| Alcohol | Allylic Chlorides | | Allylic Bromides | |
|---|---|---|---|---|
| | Reaction conditions | References | Reaction conditions | References |
| $CH_3[C(CH_3)=CHCH_2CH_2]_2C(CH_3)(OH)CH=CH_2$... | | | PBr$_3$, C$_5$H$_5$N | (314, 549) |
| $C_8H_{15}CH=CHC(CH_3)(OH)CH=CH_2$............... | | | PBr$_3$ | (229) |
| $C_8H_{17}CH_2CH_2C(CH_3)=CHCH_2OH$................. | | | PBr$_3$ | (229) |
| $C_9H_{17}CH_2CH_2C(CH_3)(OH)CH=CH_2$............... | | | PBr$_3$ | (229) |
| $C_9H_{18}CH_2CH_2C(CH_3)(OH)CH=CH_2$ ............... | PCl$_5$ | (550) | | |
| $C_6H_5CH=CHCHOHCHOHCH=CHC_6H_5$.......... | | | PBr$_3$ | (364) |
| $CH_3[C(CH_3)=CHCH_2CH_2]_3C(CH_3)(OH)CH=CH_2$... | | | PBr$_3$, C$_5$H$_5$N | (547, 549) |
| $CH_3[CH(CH_3)CH_2CH_2CH_2]_3C(CH_3)(OH)CH=CH_2$.. | | | PBr$_3$; PBr$_3$ in petroleum ether | (179, 313) (315) |
| $CH_3[CH(CH_3)CH_2CH_2CH_2]_3C(C_2H_5)(OH)CH=CH_2$. | | | PBr$_3$ in petroleum ether | (319) |
| $CH_3[CH(CH_3)CH_2CH_2CH_2]_3C(C_3H_7)(OH)CH=CH_2$. | | | PBr$_3$ in petroleum ether | (319) |
| "RCH=CHCH$_2$OH".............................. | PCl$_5$ | (488) | | |
| "RCHOHCH=CH$_2$" .............................. | PCl$_5$ | (488) | PBr$_3$, C$_5$H$_5$N | (73, 157, 163) |



| | | | PBr$_3$, C$_5$H$_5$N | (179) |



| | | | PBr$_3$ | (551) |



| | | | PBr$_3$ | (554) |

"unfree" carbonium ions (294, page 393) or ion-pairs. The stereospecificity of phosphorus trichloride reactions is also taken advantage of in the preparation of *cis*-γ-substituted allylic chlorides from the corresponding *cis* alcohols (243, 248, 254, 257, 258, 261, 425, 667).

A number of different procedures have been used in preparing halides by reactions of allylic alcohols with phosphorus trihalides. The phosphorus trihalide may be added slowly to the alcohol or a mixture of the alcohol and pyridine, with or without cooling. Sometimes the alcohol is added to the acid halide, and frequently one or both of the reactants are diluted with an inert solvent such as ether, petroleum ether, or benzene. The reaction mixture can be worked up by extracting it with dilute alkali or bicarbonate solution and distilling the organic material. It is also possible to distill the allylic halides directly from the reaction

mixture and then purify this crude product. No systematic study has been made to determine the optimum conditions for conversion of allylic alcohols to allylic halides by means of phosphorus trihalides.

Reactions in which unsymmetrically substituted allylic alcohols were converted to allylic halides by treatment with halides of phosphorus are collected in table 14. Reaction conditions are not described in detail, but mention is made of use of inert diluents or inclusion of pyridine in the reaction mixtures. An asterisk by the literature reference number indicates that the composition of the allylic halide mixture obtained from the reaction is reported in the original article.

### 4. Reaction of allylic alcohols with thionyl halides

Many reactions of thionyl chloride with allylic alcohols have been carried out under conditions which lead to the formation of mixtures of isomeric allylic chlorides. Recently, the usefulness of this reaction has been greatly increased by the discovery of experimental conditions which lead to pure chlorides of completely preserved allylic structure and certain other conditions which give a chloride of completely rearranged allylic structure (75a, 118, 119, 662).

The possible mechanisms for the reactions of saturated alcohols with thionyl chloride have been clearly defined by Hughes and Ingold (144). They assumed that the first step of such reactions is formation of the chlorosulfinate ester of the alcohol:

$$ROH + SOCl_2 \rightarrow ROSOCl + HCl$$
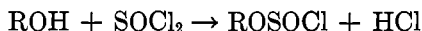
That this assumption is reasonable is indicated by the fact that chlorosulfinates of many primary and secondary alcohols have actually been isolated (211, 212). The chlorosulfinate ester was then assumed to decompose by one or more of three different processes, with the stereochemical results noted:



(1)    $S_N i$; retention

(2)    $S_N 2$; inversion

(3)    $S_N 1$; inversion with racemization
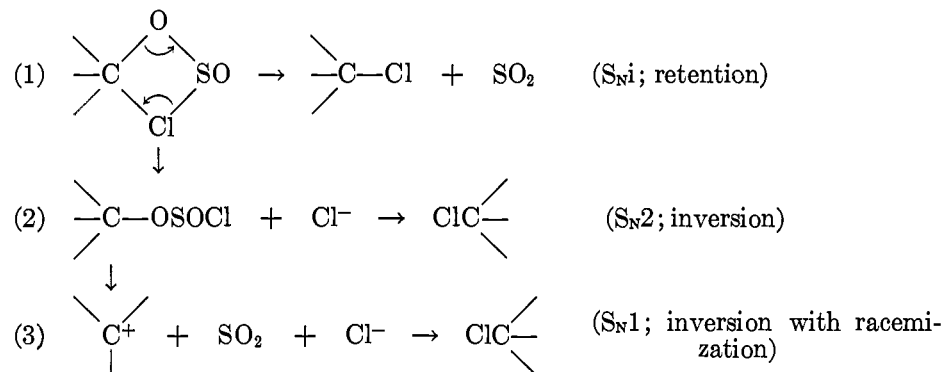
The validity of mechanisms 1, 2, and 3 has been supported by the work of Boozer and Lewis (66, 404) on the kinetics of decomposition of alkyl chlorosulfinates.

This mechanistic picture for saturated systems may be easily extended to include allylic compounds. It may be assumed that allylic chlorosulfinates are intermediates in the reactions of allylic alcohols with thionyl chloride. Allyl

TABLE 15

*Allylic chlorides expected from allylic chlorosulfinates*

| Mechanism | Allylic Structure | Optical Configuration |
|---|---|---|
| $S_N2$ | No rearrangement | Inverted |
| $S_Ni$ | No rearrangement | Retained |
| $S_N1$ | Partial rearrangement | Racemized |
| $S_Ni'$ | Complete rearrangement | Inverted |

chlorosulfinate itself has been isolated, but the instability of substituted allylic chlorosulfinates has made their isolation impossible. The allylic chlorosulfinates may react by any or all of the processes (1, 2, and 3) formulated for the saturated chlorosulfinates. However, in the case of the allylic systems, it is necessary to consider whether or not allylic rearrangement will occur, in addition to the question of whether the configuration of any optically active center will be retained, racemized, or inverted in the course of the various reactions. The results to be expected for each mechanism are summarized in table 15.

An additional mechanism ($S_Ni'$) is uniquely available to allylic systems. In this mechanism, chlorine attacks the $\gamma$-carbon atom of the allylic system with simultaneous shift of the double bond and elimination of sulfur dioxide. It is reasonable to expect that optically active chlorides would be formed from optically active alcohols reacting by the $S_Ni'$ mechanism, since one particular conformation of the transition state may be favored over all others.
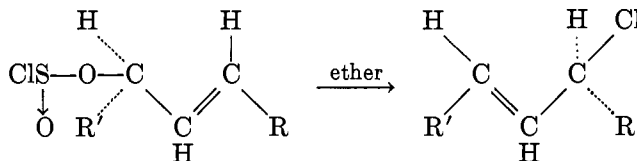


This cyclic process ($S_Ni'$) was first postulated by Roberts, Young, and Winstein (539) to explain the predominance of rearranged chloride obtained from either of the isomerically related allylic alcohols by Meisenheimer and Link (419). Treatment of $\alpha$-ethylallyl alcohol with thionyl chloride in the absence of a solvent or with a small amount of ether as solvent produced a mixture of chlorides containing about 80 per cent $\gamma$-ethylallyl chloride, whereas analogous treatment of $\gamma$-ethylallyl alcohol gave a mixture of chlorides containing approximately 75 per cent of $\alpha$-ethylallyl chloride (419).

Thus, allylic chlorosulfinates may conceivably yield allylic chlorides by at least four different processes (659): $S_N1$, $S_N2$, $S_Ni$, and $S_Ni'$. The most satisfactory procedure for simplifying the study of the thionyl chloride reaction was to eliminate competition by both the $S_N1$ and the $S_N2$ reactions by using a non-polar solvent containing no chloride ion. This should make it possible to compare the relative rates of the $S_Ni$ and $S_Ni'$ reactions. The exclusion of chloride ion was difficult, since hydrogen chloride is generated during the formation of the allylic chlorosulfinates which, in general, decompose too rapidly to permit isolation. Fortunately, this difficulty could be overcome by carrying out the reaction in

TABLE 16

*Reaction of α- and γ-methylallyl alcohols with thionyl chloride under controlled conditions†* (663)

p-ROH = $CH_3CH$=$CHCH_2OH$; s-ROH = $CH_3CHOHCH$=$CH_2$; p-RCl = $CH_3CH$=$CHCH_2Cl$; s-RCl = $CH_3CHClCH$=$CH_2$

| Add | to | Solvent | s-RCl | p-RCl |
|---|---|---|---|---|
| | | | *per cent* | *per cent* |
| p-ROH | SOCl₂ | pentane | 90 | 10 |
| s-ROH | SOCl₂ | pentane | 22 | 78 |
| p-ROH | SOCl₂ + C₅H₅N | ether | 22 | 78 |
| s-ROH | SOCl₂ + C₅H₅N | ether | 43 | 57 |
| SOCl₂ | p-ROH + (C₄H₉)₃N | ether | 0 | 100 |
| SOCl₂ | s-ROH + (C₄H₉)₃N | ether | 69 | 31 |
| p-ROH | SOCl₂ | ether | 99 | 1 |
| s-ROH | SOCl₂ | ether | 0 | 100 |
| p-ROH | SOCl₂ (5.6 M) | ether | 76 | 24 |
| p-ROH | SOCl₂ | SO₂ | 57 | 43 |
| s-ROH | SOCl₂ | SO₂ | 32 | 68 |
| s-ROH $(\alpha_D^{29} = +2.17°)$ | SOCl₂ | SO₂ | 32* *$(\alpha_D^{31} = +1.21°$ = retained + 62% racemized)* | 68 |
| s-ROH $(\alpha_D^{26} = +2.30°)$ | SOCl₂ | SO₂ ((C₆H₅)₃CCl added) | 32* *$(\alpha_D^{25} = +1.40°$ = retained + 59% racemized)* | 68 |
| s-ROH $(\alpha_D^{25} = +2.22°)$ | SOCl₂ | None | 33* *$(\alpha_D^{25} = +1.40°$ = retained + 59% racemized)* | 67 |

† Thionyl chloride concentration 0.7 M except where otherwise noted.

relatively dilute solution (0.5 to 1.0 M) in anhydrous ethyl ether (75a, 118, 662), which forms a hydrogen-bonded non-ionic complex with dry hydrogen chloride (107, 126, 428). Using this ether technique, Young and coworkers (119, 662) were able to convert α- and γ-methylallyl alcohols into the pure chlorides of rearranged allylic structure (see table 16). This proves that the $S_Ni$ mechanism cannot compete with the $S_Ni'$ process in non-polar media. Ether has been used as a solvent for the reactions of thionyl chloride with allylic alcohols by other investigators (20, 37, 419), but in most cases the thionyl chloride concentration was several molar. Consequently, the medium was semipolar in character and more than one mechanism could operate. For example, when the thionyl chloride concentration was 5.6 M, γ-methylallyl alcohol gave a mixture containing 24 per cent of the unrearranged isomer (table 16). The use of the technique of dilute (0.5 to 1.0 M) ether solutions has been extended to *cis-* and *trans-α,γ*-dimethylallyl alcohol (119) and *cis-* and *trans-*5-methyl-2-cyclohexenol (222), both of which give only the rearranged ($S_Ni'$) products under these conditions.

Examples of the stereospecific nature of the reactions included the conversion of (−)-*trans-α,γ*-dimethylallyl alcohol into (−)-*trans-α,γ*-dimethylallyl chloride (119) and (+)-*cis-*5-methyl-2-cyclohexenol into (+)-*cis-*5-methyl-2-cyclohexenyl chloride (222) with almost quantitative retention of optical purity. Although the ether technique has been successful in many cases, it should be pointed out that allylic alcohols having multiple or especially strong activating groups may form chlorosulfinates which tend to react by several mechanisms. This difficulty may be overcome by keeping the thionyl chloride concentration 0.1 M

or less. Under these conditions, even cinnamyl alcohol has been converted quantitatively into α-phenylallyl chloride. These conditions have the disadvantage of a very slow rate of formation of the chlorosulfinate from the alcohol and the handling of large quantities of solvent.

It is not possible to decide from present evidence whether the $S_N i'$ mechanism involves a one-stage concerted process or ionization to an intimate, rigidly oriented carbonium ion–chlorosulfinate ion-pair (119, 361) followed by internal return of the chloride component of the chlorosulfinate anion to give rearranged chloride. The stereochemical consequences of either process would be identical.
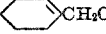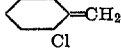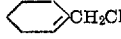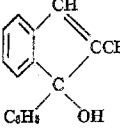
Having established the conditions for isolating the $S_N i'$ mechanism, it remained only to add soluble chloride ion to the ether solution to measure the relative importance of the $S_N i'$ and $S_N 2$ reactions. This was accomplished by carrying out the reaction in the presence of tributylamine, which formed an ether-soluble hydrochloride. With primary alcohols such as γ-methylallyl alcohol, the bimolecular displacement reaction ($S_N 2$) became dominant, and only a chloride of preserved allylic structure was formed (662) (table 16). When only the tributylamine hydrochloride was used, some rearranged chloride was formed. Thus, the reaction is more complicated than it first appears. The chlorosulfinate ester may react to form a quaternary salt with the free amine of the type:
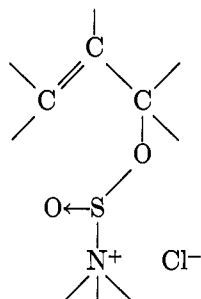


In that portion of the ester which forms the quaternary salt, the $S_N i'$ mechanism is not possible, and only the $S_N 2$ process can occur. In ether containing tributylamine, α-methylallyl alcohol yielded a mixture containing only 68 per cent α-methylallyl chloride (table 16). Steric hindrance at the secondary carbon atom reduced the effectiveness of the $S_N 2$ reaction and allowed the $S_N i'$ mechanism to become competitive. This difficulty has been overcome in converting secondary alcohols into secondary chlorides by preparing the diallyl sulfites. These disulfites reacted with tributylamine hydrochloride by the $S_N 2$ process to give chlorides of completely preserved allylic structure. The use of other amines such as pyridine, which form insoluble hydrochlorides, invariably has led to the production of mixtures of chlorides. This may have been due to ionization ($S_N 1$ reaction) induced by absorption on the surface of the suspended solid salts.

Under ideal conditions for producing dissociated allylic carbonium ions from allylic chlorosulfinates, both allylic isomers should give a common carbonium-ion intermediate which reacts to form the same mixture of allylic chlorides with complete racemization. Since α- and γ-methylallyl alcohols reacted with thionyl

TABLE 17
*Reactions of allylic alcohols with thionyl chloride*

| Alcohol | Reaction Conditions | Product Composition† | References |
|---|---|---|---|
| $CH_2=CH\overset{*}{C}H_2OH$ | $SOCl_2$ to ROH | 51% $\overset{*}{C}H_2=CHCH_2Cl$ <br> 49% $CH_2=CH\overset{*}{C}H_2Cl$ | (457) |
| $CH_3CH=CHCH_2OH$ | $SOCl_2$ to ROH | 46% $CH_3CH=CHCH_2Cl$ <br> 54% $CH_3CHClCH=CH_2$ | (628) |
| $CH_3CH=CHCH_2OH$ | $SOCl_2$ added to ROH in ether | 59% $CH_3CH=CHCH_2Cl$ <br> 41% $CH_3CHClCH=CH_2$ (?) | (37) |
| $CH_2OHCH=CHCH_2OH$ | $SOCl_2$ to ROH + $C_5H_5N$ | N (?) | (8) |
| $CH_2=CHCHOHCN$ | $SOCl_2$ to ROH + $C_5H_5N$ | N | (523, 524, 525) |
| $CH_2OHCH=CHCN$ | | N | (524) |
| $CH_2OHCH=CHCOOH$ | | N | (523, 524) |
| $C_2H_5CH=CHCH_2OH$ | $SOCl_2$ to ROH | 25% $C_2H_5CH=CHCH_2Cl$ <br> 75% $C_2H_5CHClCH=CH_2$ | (419) |
| $C_2H_5CH=CHCH_2OH$ | ROH to $SOCl_2$ | N (?) | (567) |
| $C_2H_5CHOHCH=CH_2$ | $SOCl_2$ to ROH | 80% $C_2H_5CH=CHCH_2Cl$ <br> 20% $C_2H_5CHClCH=CH_2$ | (419) |
| $CH_2=CHCH=CHCH_2OH$ | $SOCl_2$ to ROH | N (?) | (657) |
| $CH_2=CHCHOHCOOCH_3$ | | N (?) | (524, 525) |
| $CH_3CH=CHCHOHC≡CH$ | $SOCl_2$ to ROH + $C_5H_5N$ in ether | R | (265) |
| $CH_3CH=CHCH=CHCH_2OH$ | ROH to $SOCl_2$ + $C_5H_5N$ | N (?) | (527, 528) |
| $(+)-CH_3CH=CHCHOHC_2H_5$ | $SOCl_2$ + quinoline | (−) N (?) | (2) |
| $C_2H_5C(CH_3)(OH)CH=CH_2$ | $SOCl_2$ + $C_5H_5N$ | M | (636) |
| $C_2H_5CHOHC(CH_3)=CH_2$ | $SOCl_2$ + $C_5H_5N$ | N (?) | (96) |
| $CH_2=CHCHOHCOOC_2H_5$ | | N (?) | (522) |
|  $CH_2OH$ | ROH in ether to $SOCl_2$ in ether | 85%  $=CH_2$ (Cl) <br> 15%  $CH_2Cl$ | (20) |
| $CH_3$  OH (*cis* and *trans*) | $SOCl_2$ in ether | R | (224) |
| $CH_3OCH_2CH=C(CH_3)CH=CHCH_2OH$ | $SOCl_2$ + $C_5H_5N$ | N (?) | (453) |
| $C_6H_5CH=CHCH_2OH$ | $SOCl_2$ + $C_5H_5N$ in $CHCl_3$ | N | (217, 243) |
| $C_6H_5CH_2CH=CHCH_2OH$ | $SOCl_2$ | N (?) | (567) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2OH$ | $SOCl_2$ + $C_5H_5N$ in ether | M | (37) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2OH$ | $SOCl_2$ + $C_5H_5N$ | N (?) | (205) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)(OH)CH=CH_2$ | $SOCl_2$ + $C_5H_5N$ | R (?) | (475, 476) |
| $p-C_2H_5OC_6H_4CH_2CH=CHCH_2OH$ | $SOCl_2$ | N (?) | (567) |
| $\alpha-C_{10}H_7CH_2CH=CHCH_2OH$ | $SOCl_2$ | N (?) | (567) |
|  | $SOCl_2$ | R (?) | (104) |
|  | $SOCl_2$ | M | (106) |
|  | $SOCl_2$ | R (?) | (103) |

† M = mixture; R = rearranged product; N = no rearrangement.

chloride in the absence of solvent to give different mixtures of chlorides (see table 16), it was necessary to find a better ionizing medium to isolate the $S_N1$ mechanism from its competitors. Liquid sulfur dioxide should be ideal for this purpose. When optically active $\alpha$-methylallyl alcohol was allowed to react with thionyl chloride in liquid sulfur dioxide, both with and without added chloride ion, the same mixture of chlorides (68 per cent $\gamma$-methylallyl chloride and 32 per cent $\alpha$-methylallyl chloride) was formed. Contrary to expectation, only 60 per cent racemization occurred; the remaining 40 per cent of the $\alpha$-methylallyl chloride was of retained optical configuration (table 16). Comparable experiments carried out in the absence of solvent gave the same results as those found in sulfur dioxide. It would appear that the initially formed ion-pairs could collapse at the secondary carbon atom with retention of optical configuration or dissociate to give racemization plus rearrangement. The primary isomer, $\gamma$-methylallyl alcohol, gave 57 per cent of rearranged product in sulfur dioxide. Thus, it would appear that the $S_N i'$ process was still competing with the $S_N1$ process even in this ideal ionizing medium.

Table 17 lists the reported reactions of allylic alcohols with thionyl chloride. Reaction conditions and product compositions are indicated, with the usual limitation that product compositions are those obtained from the work-up procedures and do not necessarily represent the composition of the chloride mixtures actually formed in the substitution reactions. If the experimental conditions might lead to rearrangement or if the results do not agree with those expected as a result of experience in this laboratory, the authors have indicated this with a question mark in the table.

Thionyl bromide is an expensive chemical and seems to have no important advantages over hydrogen bromide or phosphorus tribromide as a reagent for the preparation of allylic bromides from allylic alcohols. It has been used for this purpose in at least one instance, however (206). The procedure used was an indirect one: diallylic sulfites were prepared from the alcohols and thionyl chloride in the presence of pyridine; these were isolated and treated with thionyl bromide and catalytic amounts of pyridine hydrobromide. Mixtures of isomeric allylic bromides were obtained, probably owing to isomerization of the initially formed bromides during distillation. Yields of allylic bromides ranging from 43 to 74 per cent were obtained from alcohols of the type $RCHOHCH=CH_2$ ($R = CH_3$, $C_3H_7$, $C_4H_9$).

### B. OTHER REPLACEMENT REACTIONS OF ALLYLIC ALCOHOLS

#### 1. Conversion of allylic alcohols to esters of carboxylic acids

Allylic alcohols are readily converted to carboxylate esters by direct esterification with carboxylic acids, by reaction with acid anhydrides, and by reaction with acid chlorides. Transesterification reactions have also been used to a limited extent for the preparation of allylic esters.

Certain of the esters, e.g., *p*-nitrobenzoates, are useful primarily as solid derivatives for characterization of the alcohols. Hydrogen phthalate esters of asymmetric allylic alcohols form salts with optically active bases such as brucine

and strychnine, and are frequently employed in the resolution of the alcohols (2, 15, 16, 18, 30, 33, 118, 183, 185, 194, 223, 322, 324, 667). Esterification of tertiary allylic alcohols is frequently accompanied by allylic rearrangement, and provides an indirect method for converting tertiary allylic alcohols into their primary isomers. Many terpene alcohols are allylic (e.g., linalol and geraniol), and their esters are used in the formulation of synthetic flavorings and perfumes. Methods of esterifying linalol, geraniol, and other terpene alcohols have been reviewed recently (388).

### (a) Direct esterification

Esters of allylic alcohols may be prepared by simply heating the alcohol with the appropriate carboxylic acid, with or without a trace of mineral acid as catalyst. When no catalyst is used, primary allylic alcohols and secondary allylic alcohols having no more than one activating alkyl substituent on the $\alpha$- or $\gamma$-carbon atoms of the allylic system usually yield only the esters formed by substitution without allylic rearrangement. Secondary alcohols having an $\alpha$-aryl substituent apparently yield only rearranged esters when esterified with carboxylic acids (322). When $\alpha$- and $\gamma$-methylallyl alcohols are esterified with the strong acid trichloroacetic acid, similar mixtures of isomeric esters are obtained from both alcohols (485). Mixtures of esters are obtained if a mineral acid such as sulfuric acid is used to catalyze the esterification of primary and secondary allylic alcohols (667a). Tertiary allylic alcohols usually give mixtures of esters in which the primary isomer predominates when esterified with carboxylic acids, with or without a trace of mineral acid as catalyst.

Esterification of allylic alcohols could either involve attack of a protonated carboxylic acid molecule or an acylium ion on the alcohol oxygen atom (I), or reaction of an allylic carbonium ion with a carboxylic acid molecule (II):

$$\text{RCOOH} \underset{}{\overset{+\text{H}^+}{\rightleftharpoons}} [\text{RCOOH}_2]^+ \xrightarrow{\text{R'CH=CHCHOHR''}}$$

$$\xrightarrow[-\text{H}^+]{-\text{H}_2\text{O}}$$

$$-\text{H}_2\text{O} \Big\downarrow \qquad\qquad \text{R'CH=CHCHR''OCOR} \quad \text{(I)}$$

$$[\text{RCO}]^+ \xrightarrow{\text{R'CH=CHCHOHR''}} \nearrow -\text{H}^+$$

$$\text{R'CH=CHCH(OH)R''} \underset{}{\overset{+\text{H}^+}{\rightleftharpoons}} \text{R'CH=CHCH(OH}_2)^+\text{R''} \xrightarrow{-\text{H}_2\text{O}}$$

$$[\text{R'CH}\text{---}\text{CH}\text{---}\text{CHR''}]^+$$

$$[\text{R'CH}\text{---}\text{CH}\text{---}\text{CHR''}]^+ \xrightarrow[-\text{H}^+]{+\text{RCOOH}}$$

$$\text{R'CH=CHCH(OCOR)R''} \;+\; \text{R'CH(OCOR)CH=CHR''} \quad \text{(II)}$$
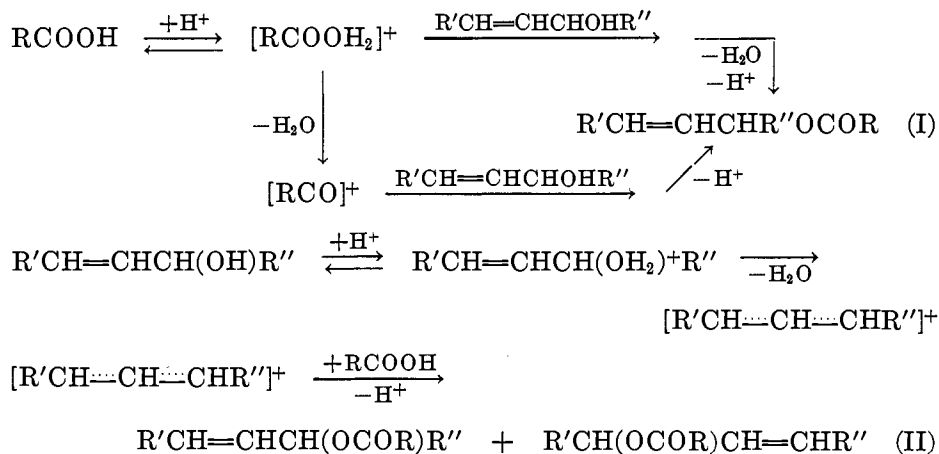
If a cation derived from the carboxylic acid reacts with the alcohol, the carbon–oxygen bond of the alcohol should remain intact, and only normal substitution product would be formed. This is probably what happens in the great majority
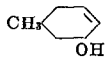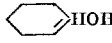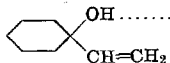
TABLE 18

*Conversion of allylic alcohols to carboxylate esters*

| Alcohol | Reagent and Conditions | Products† | References |
|---|---|---|---|
| CH₂=C=CHCH₂OH | (CH₃CO)₂O + trace of H₂SO₄ | N | (113) |
| CH₃CH=CHCH₂OH | CH₃COOH | N | (123, 452) |
| | p-O₂NC₆H₄COCl + C₅H₅N | N | (452) |
| | (CH₃CO)₂O | N | (123, 236, 452) |
| | CH₃COCl | N | (123) |
| | HCOOH | N | (123) |
| | C₂H₅COOH | N | (123) |
| | (CH₃)₂CHCOOH | N | (123) |
| | (CH₃)₂CHCH₂COOH | N | (123) |
| | (CH₃)₃C₆H₂COCl + C₅H₅N in CHCl₃ | N | (25, 647) |
| | CCl₃COOH | M | (485) |
| | (C₆H₅)₂CHCOCl + C₅H₅N | N | (24) |
| | C₆H₅CH(C₂H₅)COCl + C₅H₅N | N | (24) |
| CH₃CHOHCH=CH₂ | CH₃COOH | N | (235, 485) |
| | CCl₃COOH | M | (99, 485) |
| | (CH₃CO)₂O | N | (46) |
| | (CH₃CO)₂O + trace of H₂SO₄ | M | (46) |
| | p-O₂NC₆H₄COCl + C₅H₅N | N | (98) |
| | C₆H₄C₂O₃ | N | (324) |
| | (CH₃)₃C₆H₂COCl + C₅H₅N in CHCl₃ | N | (25, 647) |
| CH₃CCl=CHCH₂OH | p-O₂NC₆H₄COCl + C₅H₅N (?) | N | (135) |
| | CH₃COCl | N | (471) |
| | 3,5-(O₂N)₂C₆H₃COCl | N | (245) |
| CH₂OHCH=CHCOOH | (CH₃CO)₂O | N | (524, 525) |
| CH₂=CHCHOHCOOH | (CH₃CO)₂O | N | (524) |
| CH₂OHCH=CHCN | (CH₃CO)₂O | N | (524) |
| CH₂=CHCHOHCN | (CH₃CO)₂O | N | (524) |
| CH₂=CHCH=CHCH₂OH | CH₃COCl | N | (657) |
| CH₂=CHCHOHCH=CH₂ | (CH₃CO)₂O | N | (266) |
| C₂H₅CH=CHCH₂OH | 3,5-(O₂N)₂C₆H₃COCl + C₅H₅N (?) | N | (137) |
| | CH₃COCl + C₅H₅N | N | (419) |
| | (CH₃)₃C₆H₂COCl + C₅H₅N in CHCl₃ | N | (25) |

† N = normal product; R = rearranged product; M = mixture of products.

| | | | |
|---|---|---|---|
| $C_2H_5CHOHCH=CH_2$ | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (420) |
| | HCOOH | N | (324) |
| | $(CH_3CO)_2O$ | N | (324) |
| | $C_6H_4C_2O_3$ | N | (324) |
| | $CH_3COCl + C_5H_5N$ | N | (419) |
| | $(CH_3)_2C_6H_2COCl + C_5H_5N$ in $CHCl_3$ | N | (25) |
| $(CH_3)_2C(OH)CH=CH_2$ | $CH_3COOH + $ trace of $H_2SO_4$ | M | (389) |
| | $(CH_3CO)_2O + CH_3COONa$ | M | (450) |
| | $(CH_3CO)_2O$ | M | (691) |
| $(+)\text{-}CH_3CH=CHCHOHCH_3$ | $CH_3COOCOH$ | (−) Formate | (275) |
| | $C_6H_5COCl + C_5H_5N$ | (+) Benzoate | (275) |
| $CH_2=CHCHOHCH_2OCH_3$ | $C_6H_5COCl + C_5H_5N(C_2H_5)_2$ | N | (309) |
| $CH_2=CHCHOHCOOCH_3$ | $(CH_3CO)_2O$ | N | (524) |
| $CH_2=CHCHOHCH_2CN$ | $(CH_3CO)_2O + $ trace of $H_2SO_4$ | N (?) | (655) |
| $CH_2=CHC(OH)(CN)CH_3$ | $(CH_3CO)_2O + CH_3COCl$ | N | (415) |
| $CH_3CH=CHCHOHC=CH$ | $(CH_3CO)_2O + C_5H_5N$ | N | (78) |
| $CH_3CH=CHCHOHCH=CH_2$ | $(CH_3CO)_2O + C_5H_5N$ | N | (266) |
| $CH_3CH=CHCHOHCH=CH_2$ | $(CH_3CO)_2O$ | R | (304, 305) |
| | | (Primary acetate) | |
| $C_3H_7CH=CHCH_2OH$ | $3,5\text{-}(O_2N)_2C_6H_3COCl + C_5H_5N$ (?) | N | (137) |
| $C_3H_7CHOHCH=CH_2$ | $C_6H_4C_2O_3$ | N | (324) |
| $C_2H_5CHOHCH=CHCH_3$ | $(CH_3CO)_2O$ | N (?) | (530, 531) |
| | $CH_3COCl + C_5H_5N$ | N | (2) |
| | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (2) |
| | $C_6H_4C_2O_3 + C_5H_5N$ | N | (2, 32) |
| $C_2H_5C(CH_3)(OH)CH=CH_2$ | $(CH_3CO)_2O$ | M | (691) |
| $CH_3CHOHC(C_2H_5)=CH_2$ | $(CH_3CO)_2O + C_6H_5N$ | N | (416) |
| $(CH_3)_2C(OH)C(CH_3)=CH_2$ | $C_6H_5COCl + C_5H_5N$ | N | (129, 143) |
| $(CH_3)_2C=CHCHOHCH_3$ | $(CH_3CO)_2O + C_6H_5N$ | N | (184) |
| | $C_6H_5COCl + C_5H_5N$ | N | (184) |
| | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ in $C_6H_6$ | N | (424) |
| | $p\text{-}O_2NC_6H_4OCH_2COCl + C_5H_5N$ in $C_6H_6$ | N | (424) |
| | $C_6H_5N=NC_6H_4OCH_2COCl + C_5H_5N$ in $C_6H_6$ | N | (424) |
| | $(CH_3CO)_2O$ | N (?) | (325) |
| | $C_6H_4C_2O_3$ | N (?) | (325) |
| $CH_2=CHCHOHCOOC_2H_5$ | $(CH_3CO)_2O$ | N | (350) |
| $HC≡CCH_2C(CH_3)(OH)CH=CH_2$ | $(CH_3CO)_2O$ | R | (108) |
| $CH_2=CHCH_2CH_2CH=CHCH_2OH$ | $3,5\text{-}(O_2N)_2C_6H_3COCl + C_5H_5N$ (?) | N | (137) |
| $C_4H_9CH=CHCH_2OH$ | $3,5\text{-}(O_2N)_2C_6H_3COCl + C_5H_5N$ (?) | N | (137) |
| $C_4H_9CHOHCH=CH_2$ | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | *N* | (99) |
| | $(CH_3CO)_2O$ | N | (324) |
| | $(C_3H_7CO)_2O$ | N | (324) |
| | $C_6H_5COCl + C_5H_5N$ | N | (324) |
| | HCOOH | N | (324) |
| | $C_6H_4C_2O_3$ | N | (324) |
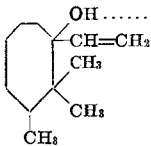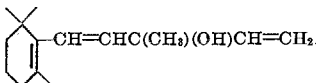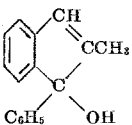
### TABLE 18—*Continued*

| Alcohol | Reagent and Conditions | Products† | References |
|---|---|---|---|
| $(CH_3)_2CHCH_2CHOHCH=CH_2$ | $(CH_3CO)_2O + C_5H_5N$ | N | (38) |
| $(+)-C_3H_7CHOHCH=CHCH_3$ | $(CH_3CO)_2O + C_5H_5N$ | N | (15) |
| | $C_6H_5COCl + C_5H_5N$ | N | (15) |
| | $(CH_3CO)_2O$ | N (?) | (530, 531) |
| | $C_6H_4C_2O_3 + C_5H_5N$ | N | (15, 16) |
| $(CH_3)_2CHCHOHCH=CHCH_3$ | $(CH_3CO)_2O$ | N (?) | (531) |
| $(-)-(CH_3)_2CHCHOHCH=CHCH_3$ | $(CH_3CO)_2O + C_5H_5N$ | N | (39) |
| $C_3H_7C(CH_3)(OH)CH=CH_2$ | $(CH_3CO)_2O + $ trace of $H_2SO_4$ | M | (440) |
| $C_2H_5C(CH_3)(OH)C(CH_3)=CH_2$ | $(CH_3CO)_2O + CH_3COOH$ | M | (136) |
| $CH_3$-⬡-OH (*cis* and *trans*) | $CH_3COCl + C_5H_5N$ | N | (224) |
| | $C_6H_4C_2O_3 + C_5H_5N$ | N | (223) |
| | $p-O_2NC_6H_4COCl + C_5H_5N$ | N | (226) |
| ⬠-CHOHCH_3 | $C_6H_4C_2O_3 + C_5H_5N$ | N | (194) |
| *cis*-$C_5H_{11}CH=CHCH_2OH$ | $(CH_3CO)_2O$ | N | (232, 234) |
| $C_5H_{11}CH=CHCH_2OH$ | $3.5-(O_2N)_2C_6H_3COCl + C_5H_5N$ | N | (137) |
| $(CH_3)_2CHCH_2CH_2CHOHCH=CH_2$ | $(CH_3CO)_2O$ | N | (99) |
| $(CH_3)_2CHCH_2CHOHCH=CHCH_3$ | $(CH_3CO)_2O$ | N (?) | (531) |
| | $(CH_3CO)_2O + C_5H_5N$ | N | (38) |
| $(CH_3)_3CC(CH_3)(OH)CH=CH_2$ | $(CH_3CO)_2O$ or $CH_3COOH$ | R | (406, 405, 658) |
| ⬡-CHOHCH_3 | $C_6H_4C_2O_3 + C_5H_5N$ | N | (194) |
| ⬡(OH)(CH=CH_2) | $(CH_3CO)_2O + CCl_3COOH$ | R-acetate | (178) |
| $CH_3CH=CHCHOHCHOHCH=CHCH_3$ | $(CH_3CO)_2O$ | N, N | (123) |
| $C_6H_5CH=CHCH_2OH$ | $(CH_3CO)_2O$ | N | (232) |
| $C_6H_5CH=CHCH_2OH$ | $CH_3COCl + C_5H_5N$ | N | (419) |
| $C_6H_5CH=CHCH_2OH$ (*cis*) | $(CH_3CO)_2O$ | N | (230) |
| $C_6H_5CHOHCH=CH_2$ | $C_6H_4C_2O_3 + C_5H_5N$ | N | (183, 185) |
| | $(CH_3CO)_2O + C_5H_5N$ | N | (185) |
| | $p-O_2NC_6H_4COCl$ | R | (420) |
| | $CH_3COCl + C_5H_5N$ | N | (419) |
| | $p-O_2NC_6H_4COCl + C_5H_5N$ | N | (102) |
| | $(CH_3CO)_2O$ | R | (102) |

| | | | |
|---|---|---|---|
| $(CH_3)_2CH(CH_2)_3CH=CHCH_2OH$... | $3,5\text{-}(O_2N)_2C_6H_3COCl + C_5H_5N$ (?) | N | (137) |
| $C_6H_{13}CHOHCH=CH_2$... | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (99) |
| $CH_3CHOHC(C_5H_{11})=CH_2$... | $(CH_3CO)_2O + C_5H_5N$ | N | (416) |
| $C_2H_5CH=C(CH_3)CHOHC_3H_7$... | $CH_3COCl + C_5H_5N$ | N | (61) |
| $CH_3CHOHC(C_2H_5)=CHC_3H_7$ | $C_6H_4C_2O_3 + C_5H_5N$ | N | (18) |
| $(C_3H_7)_2C(OH)CH=CH_2$. | $(CH_3CO)_2O$ or $CH_3COOH$ | R | (405, 406, 658) |
| $p\text{-}ClC_6H_4CH=CHCH_2OH$... | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (97) |
| $p\text{-}ClC_3H_4CHOHCH=CH_2$... | $(CH_3CO)_2O$ | R | (97) |
| | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (97) |
| $C_6H_5CH=CHCHOHCH_3$... | $C_6H_4C_2O_3 + C_5H_5N$ | N | (322) |
| | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (322) |
| | $(CH_3CO)_2O$ | N | (98, 322) |
| $C_6H_5CHOHCH=CHCH_3$... | $(CH_3CO)_2O$ | R | (98) |
| | $C_6H_4C_2O_3 + C_5H_5N$ | N | (322) |
| | $(CH_3CO)_2O + C_5H_5N$ (?) | N | (322) |
| | $CH_3COOH$ | R | (322) |
| | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (322) |
| $C_6H_5CH_2CH=CHCH_2OH$... | $3,5\text{-}(O_2N)_2C_6H_3COCl + C_5H_5N$ (?) | N | (137) |
| $m\text{-}CH_3C_6H_4CHOHCH=CH_2$... | $(CH_3CO)_2O$ | R | (97) |
| $p\text{-}CH_3C_6H_4CHOHCH=CH_2$... | $(CH_3CO)_2O$ | R | (102) |
| $m\text{-}CH_3C_6H_4CH=CHCH_2OH$... | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (97) |
| $m\text{-}CH_3C_6H_4CHOHCH=CH_2$... | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (97) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)(OH)CH=CH_2$... | $CH_3COOH$ | M | (584) |
| | $(CH_3CO)_2O$ | R | (34, 56, 691) |
| | $(CH_3CO)_2O\ddagger$ | N | (1) |
| | $(CH_3CO)_2O + H_3PO_4$ | R | (436) |
| | $(CH_3CO)_2O$ | M | (69) |
| | $(CH_3CO)_2O + C_5H_5N$ | N | (691) |
| $C_2H_5CH=C(CH_3)CHOHCH_2CH(CH_3)_2$... | $(CH_3CO)_2O + CH_3COONa$ | N (?) | (60) |
| $(CH_3)_2CH(CH_2)_3C(CH_3)(OH)CH=CH_2$... | $(CH_3CO)_2O$ or $CH_3COOH$ | R | (405, 406, 658) |
| $(-)\text{-}\langle\ \rangle CHOHCH=CHCH_3$... | $(CH_3CO)_2O + C_5H_5N$ | N | (369) |
| $\langle\ \rangle CH_2OH$ (?)... | $C_6H_4C_2O_3$ in $C_5H_5$ | N | (603) |

TABLE 18—*Concluded*

824

R. H. DEWOLFE AND W. G. YOUNG

| Alcohol | Reagent and Conditions | Products† | References |
|---|---|---|---|
| $C_8H_5CHOHCH=CHCH=CH_2$ ............ | $CH_3COOH + CCl_3COOH$ | R (p-acetate) | (696) |
| $C_6H_5CH=CHCHOHC_2H_5$ ............ | $C_6H_4C_2O_3 + C_5H_5N$ | N | (33) |
| | $p\text{-}O_2NC_6H_4COCl + C_5H_5N$ | N | (420) |
| $C_6H_5CHOHCH=CHC_2H_5$ ............ | $C_6H_4C_2O_3 + C_5H_5N$ | N | (33) |
| $2,4\text{-}(CH_3)_2C_6H_3CHOHCH=CH_2$ ............ | $(CH_3CO)_2O$ | R | (99) |
| $(CH_3)_2C=CHCH(CH_3)CH_2C(CH_3)(OH)CH=CH_2$ ............ | $(CH_3CO)_2O + CH_3COOH$ | R | (203, 541) |
| $(CH_3)_2C=C(CH_3)CH_2CH_2C(CH_3)(OH)CH=CH_2$ ............ | $(CH_3CO)_2O + CH_3COOH$ | R | (556) |
| | $(CH_3CO)_2O$ | R | (437) |
| $(CH_3)_2C=CHCH_2CH(CH_3)C(CH_3)(OH)CH=CH_2$ ............ | $(CH_3CO)_2O + CH_3COOH$ | R | (654) |
| $C_2H_5CH=C(CH_3)CHOHCH_2CH_2CH(CH_3)_2$ ............ | $(CH_3CO)_2O + CH_3COONa$ | N (?) | (60) |
| [structure] $C\equiv CC(CH_3)(OH)CH=CH_2$ ............ | $(CH_3CO)_2O$ | R | (423) |
| [structure] OH ............ | $(CH_3CO)_2O + CCl_3COOH$ | R | (555) |
| $\alpha\text{-}C_{10}H_7CHOHCH=CH_2$ ............ | $(CH_3CO)_2O$ | R | (100) |
| $\beta\text{-}C_{10}H_7CHOHCH=CH_2$ ............ | $(CH_3CO)_2O$ | R | (100) |
| $p\text{-}ClC_6H_4CHOHCH=CHC_6H_5$ ............ | $(CH_3CO)_2O$ | M | (102) |
| $CH_3[CH(CH_3)CH_2CH_2CH_2]_2C(CH_3)(OH)CH=CH_2$ ............ | $(CH_3CO)_2O$ | R | (204) |
| [structure] $CH=CHC(CH_3)(OH)CH=CH_2$ ............ | $(CH_3CO)_2O$ | R (p-acetate) | (229) |
| $p\text{-}CH_3C_6H_4CHOHCH=CHC_6H_5$ ............ | $(CH_3CO)_2O$ | M | (102) |
| [structure] ............ | $(CH_3CO)_2O$ | R | (104) |

| | | | |
|---|---|---|---|
| $(CH_3)_2C$ ... C(C$_6$H$_5$)(OH)—CC$_6$H$_5$ ... CO——CH | $(CH_3CO)_2O$ | R | (106) |
| | $CH_3COOH$ | R | (103, 106) |
| (decalin) —OH ... CH$_2$CH$_2$C(CH$_3$)(OH)CH=CH$_2$ | $(CH_3CO)_2O$ | R | (548) |
| CH=CH$_2$ ... —OH (steroid) HO— | $(CH_3CO)_2O + CH_3COOH + CCl_3COOH$ | R | (422) |
| C$_6$H$_5$CH=C ... C(C$_6$H$_5$)(OH)—CC$_6$H$_5$ ... CO——CH | $(CH_3CO)_2O$ | R | (103) |

of the cases reported. The second possibility, in which an allylic carbonium ion (formed by loss of water from the conjugate acid of the alcohol) reacts with the acid, would give rise to a mixture of isomeric esters. It is not possible to state that this mechanism operates in those reactions which yield partially rearranged products, owing to the fact that the allylic esters themselves undergo acid-catalyzed isomerization. Isomerization of initially formed normal products under the influence of acids definitely does occur (see below), and may be the sole factor responsible for formation of allylicly rearranged esters. A thorough study of the relative rates of formation and isomerization of esters under a given set of reaction conditions would be an important step toward solving this problem. It is also possible that the alcohol itself undergoes an acid-catalyzed intramolecular isomerization prior to esterification, but this does not seem likely.

### (b) Esterification with acid anhydrides

Primary, secondary, and tertiary allylic alcohols usually give the esters formed by substitution without allylic rearrangement when allowed to react with anhydrides of carboxylic acids in the presence of one or more equivalents of a tertiary amine such as pyridine. The esterification reaction probably involves attack of the acid anhydride by the alcohol oxygen atom to form the ester and one mole of carboxylic acid. The principal function of the tertiary amine is to neutralize the carboxylic acid as it is formed, thus preventing acid-catalyzed isomerization of the initially formed ester. It is also possible to prevent isomerization of an unstable tertiary allylic acetate by removing the acetic acid formed as a by-product of the esterification by means of azeotropic distillation (1).

Mixtures of products are often obtained when allylic alcohols with two or more activating alkyl substituents are esterified with acid anhydrides in the absence of tertiary amines. Young and Webb (691) found that when linalool, $(CH_3)_2C=CHCH_2CH_2C(CH_3)(OH)CH=CH_2$, is esterified with acetic anhydride in pyridine, linalyl acetate is the only product obtained. When the reaction was carried out without pyridine, only the rearranged ester, geranyl acetate, was obtained. They also observed that linalyl acetate is isomerized to geranyl acetate when allowed to stand at room temperature in acetic acid which was 0.1 $M$ in phosphoric acid. The amount of abnormal product formed when $\alpha,\alpha$-dimethylallyl alcohol and $\alpha$-ethyl-$\alpha$-methylallyl alcohol are esterified with acetic anhydride increases when the reaction time is increased. The tertiary allylic acetates are not rearranged by heating in pure acetic anhydride. All these facts support the view that tertiary acetates are formed when tertiary allylic alcohols react with acetic anhydride, and that these isomerize when heated in the presence of acetic acid. Further evidence that the carbon–oxygen bond of the alcohol remains intact during esterification with acid anhydrides is furnished by the fact that optically active alcohols yield optically active esters of retained configuration and allylic structure (15, 39, 118, 185, 275, 322, 324, 369).

Catalytic amounts of sulfuric acid have frequently been added to the alcohol-acid anhydride reaction mixtures in esterifications of allylic alcohols (see table 18). While this may speed the esterification reaction, it will certainly result in the formation of mixtures of isomeric esters in the great majority of cases.

### (c) Esterification of allylic alcohols by acyl chlorides

Most of the remarks made concerning reactions of allylic alcohols with acid anhydrides apply also to reactions with acyl chlorides. Normal products are usually obtained when the reactions occur in the presence of tertiary amines, and mixtures of isomeric allylic esters are formed when a base is not present. The by-product of these reactions is hydrogen chloride, a much stronger acid than the carboxylic acids formed when acid anhydrides are used. Again, the alcohol oxygen atom makes a nucleophilic attack on the reagent, and any rearranged ester obtained is very probably formed by isomerization of the initially formed normal ester.

Mills (424) reported that labile allylic alcohols undergo dehydration in the presence of pyridinium ion. This resulted in low yields of esters when the alcohols were treated with acyl chlorides in pyridine solution, since pyridine hydrochloride is soluble in pyridine. Improved yields of esters were obtained by carrying the reaction out in pentane or benzene solution; pyridine hydrochloride is not soluble in benzene and therefore precipitates from the reaction mixtures as rapidly as formed.

Optically active allylic alcohols react with acyl chlorides in pyridine solution to yield optically active allylic esters of retained optical configuration and allylic structure (15, 224, 226, 275, 322, 324). This is convincing evidence that the carbon–oxygen bond of the allylic alcohol normally remains intact during such reactions.

### (d) Allylic esters from allylic alcohols by transesterification reactions

A limited number of esters of unsymmetrically substituted allylic alcohols have been prepared by transesterification reactions. When an alkoxide is used to catalyze the reaction, the structure of the allylic moiety is not changed:

$$RCOOR' + R''CH{=}CHCHOHR''' \rightarrow RCOOCHR'''CH{=}CHR'' + R'OH$$
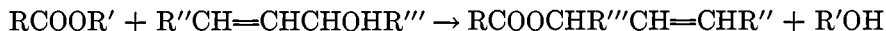
Kimel and Cope (335, 336) added the ethyl ester of the desired acid to the allylic alcohol in which a small quantity of sodium had been dissolved. Crotyl malonate, crotyl benzoylacetate, α-methylallyl malonate, α-methylallylbenzoyl acetate, and cinnamyl cyanoacetate were prepared in this way. Croxall and Van Hook (151) prepared the dicrotyl ester of a substituted succinic acid by a similar procedure.

Acetoacetate esters of a number of allylic alcohols were prepared by adding diketene to solutions of sodium in the alcohols (335).

Table 18 lists reactions of unsymmetrically substituted and optically active allylic alcohols with carboxylic acids, acid anhydrides, and acyl chlorides. Reagents are listed, and reaction conditions indicated.

### 2. Conversion of allylic alcohols to ethers

There are three principal methods of preparing allylic ethers. One of them, the reaction of alkoxides and phenoxides with allylic halides, is discussed elsewhere. Allylic ethers can also be prepared from allylic alcohols, either by converting the alcohol to an alkoxide and allowing this to react with an alkyl halide or alkyl sulfate, or by treating the allylic alcohol with an alcohol in the presence of an

acid catalyst. Allylic ethers have also been prepared by transetherification reactions between vinyl alkyl ethers or acetals and allylic alcohols, but this method has not been widely used.

### (a) Reaction of allylic alkoxides with alkyl halides

Allylic alkoxides react with alkyl halides to produce allyl alkyl ethers. The reaction is probably a bimolecular nucleophilic displacement of halide ion from the alkyl halide by the allylic alkoxide ion and is of particular interest because of its stereospecificity. The carbon–oxygen bond of the alcohol remains intact throughout the synthesis, and no products of allylic rearrangement are obtained.

$$RCH{=}CHCHOHR' \xrightarrow{M}$$

$$RCH{=}CHCH(O^-)R'M^+ \xrightarrow{R''X} RCH{=}CHCH(OR'')R'$$
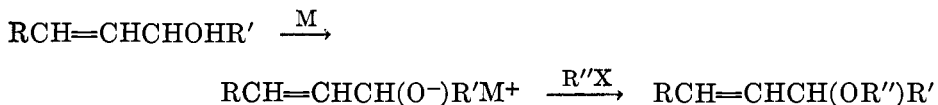
Optically active allylic alcohols are converted to optically active allylic ethers of retained configuration and undiminished optical purity (15, 185, 275, 640).

Allylic alcohols may be converted into the corresponding alkoxides by treatment with an alkali metal or with a strong base such as sodium amide or sodium hydride. Aqueous alkali has also been used for this purpose. Alkyl bromides or iodides are the usual alkylating agents, but methyl sulfate has also been used.

### (b) Acid-catalyzed etherification of allylic alcohols

When an allylic alcohol is added to an excess of a non-allylic alcohol in which an acid catalyst is dissolved, mixtures of allyl alkyl ethers are formed:

$$RCH{=}CHCHOHR' + R''OH \xrightarrow[-H_2O]{+H^+}$$

$$RCH{=}CHCH(OR'')R' + RCH(OR'')CH{=}CHR'$$
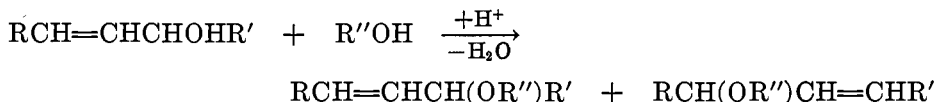
A similar reaction occurs when an acid catalyst is added to an allylic alcohol; all of the possible diallylic ethers are formed (485, 679).

$$RCH{=}CHCHOHR' \xrightarrow[-H_2O]{+H^+} RCH{=}CHCHR'{-}O{-}CHR'CH{=}CHR +$$

$$RCH{=}CHCHR'{-}O{-}CHRCH{=}CHR' +$$

$$R'CH{=}CHCHR{-}O{-}CHRCH{=}CHR'$$
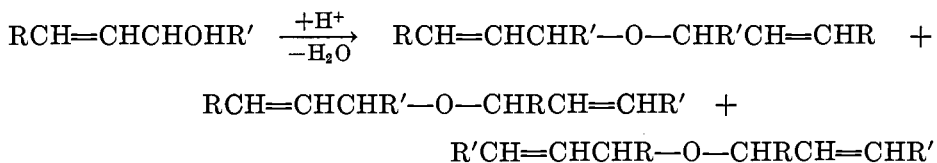
Ease of acid-catalyzed ether formation is greatly increased by alkyl or aryl substituents on the α- and γ-carbon atoms of the allylic system. Optically active allylic alcohols yield ethers which are extensively or completely racemized (30). These observations, together with the fact that allylic rearrangement usually accompanies the etherification reaction, suggest that acid-catalyzed etherification involves an allylic carbonium-ion intermediate. This would be formed by loss of water from the conjugate acid of the alcohol and would react with alcohols to form mixtures of allylic ethers or with water present in the reaction mixture to form a mixture of allylic alcohols:

$RCH$=$CHCHOHR'$

I

$\diagdown$ $H^+$

$I$ + $RCHOHCH$=$CHR'$

$\uparrow H_2O$

$RCH$=$CHCH(OH_2)R'^+$ $\xrightarrow{-H_2O}$ $[RCH \cdots CH \cdots CHR']^+$

II

$\downarrow R''OH$

$RCH(OR'')CH$=$CHR'$ + $RCH$=$CHCH(OR'')R'$
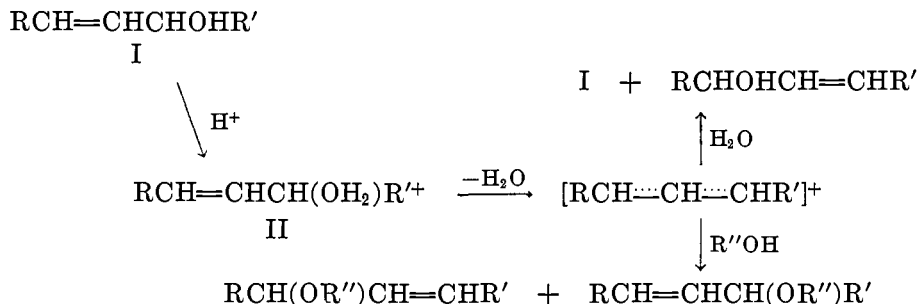
A less likely alternative mechanism would be concerted displacement of water from conjugate acid II by alcohol molecules. This would require that bimolecular displacement by mechanisms $S_N2$ and $S_N2'$ occur at similar rates. The activating effect of $\alpha$- and $\gamma$-substituents is much more easily accounted for in terms of the unimolecular mechanism, although substituent effects have not been established for a bimolecular reaction of this charge type.

The formation of diallylic ethers in which both allylic groups have the re-arranged structure in self-etherification reactions could be due either to isomeriza-tion of the alcohol preceding the etherification reaction, or to isomerization of the initially formed ethers in the presence of the acid catalyst. It is likely that acid-catalyzed isomerizations of allylic ethers are frequently involved. In the self-etherification of $\alpha,\alpha$-dimethylallyl alcohol, low pH favors formation of the thermodynamically most stable primary-primary ether, while higher pH favors formation of the primary-tertiary diallylic ether (388). It also has been shown that either of the isomeric methyl ethers formed from $\alpha,\alpha$-dialkylallyl alcohols and methanol in the presence of sulfuric acid is rearranged to an equilibrium mixture of primary and tertiary ethers on standing in acidic methanol solution (439).

Certain vinyl ethers have been reported to undergo acid- and base-catalyzed transetherification reactions with allylic alcohols (149, 150). The resulting vinyl-allyl ethers can also be prepared from the corresponding acetals:

$$RCH=CHCHOHR' \ + \ \begin{Bmatrix} (C_2H_5O)_2CHCH_2COOC_2H_5 \\ \text{or} \\ C_2H_5OCH=CHCOOC_2H_5 \end{Bmatrix} \longrightarrow$$

$$RCH=CHCHOCH=CHCOOR''$$
$$\vert$$
$$R'$$

$R'' = C_2H_5$ or $RCH$=$CHCHR'$.
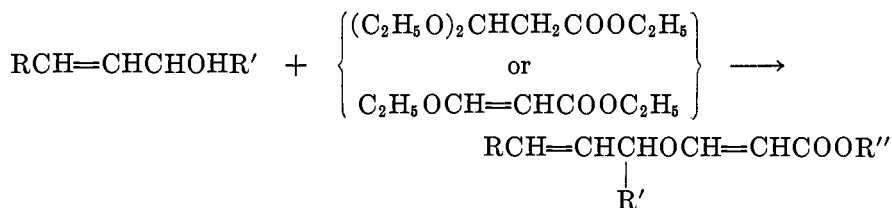
Several reactions have been reported in which ether formation is accompanied by 1,5-shifts of the allylic type. Thus, Ushakov and Kucherov (616, 617) showed that the following rearrangement occurs during the conversion of substituted furyl carbinols into substituted levulinates:

## TABLE 19

*Conversion of allylic alcohols to ethers*

| Alcohol | Reagents and Conditions | Products | References |
|---|---|---|---|
| CH₂CH=CHCH₂OH | Dilute H₂SO₄ | "Dicrotyl ether" | (123) |
| | | ⎧ (CH₃CH=CHCH₂)₂O | |
| | | [CH₃CH(CH=CH₂)]₂O | |
| | Dilute H₂SO₄ | CH₃CH=CHCH₂OCHCH₃ | (679) |
| | | ⎨ │ | |
| | | CH=CH₂ | |
| | | CH₃CHOHCH=CH₂ | |
| | | ⎩ CH₃CH=CHCH₂OH | |
| CH₃CHOHCH=CH₂ | Dilute H₂SO₄ | " | (483, 485, 679) |
| (+)-CH₃CHOHCH=CH₂ | NaH, then CH₃I | (−)-CH₃CH(OCH₃)CH=CH₂ | (640) |
| CH₂=CHCHOHCH=CH₂ | CH₃OH + H₂SO₄ | (CH₂=CH)₂CHOCH₃ | (266) |
| (+)-CH₃CH=CHCHOHCH₃ | K, then CH₃I | (−)-CH₃CH=CHCH(OCH₃)CH₃ | (275) |
| | K, then C₄H₉Br | (−)-CH₃CH=CHCH(OC₄H₉)CH₃ | (275) |
| | CH₃OH + H₂SO₄ | (−)-CH₃CH=CHCH(OCH₃)CH₃ | (30, 275) |
| | n-C₄H₉OH + H₂SO₄ | CH₃CH=CHCH(OC₄H₉)CH₃ (racemic) | (30, 275) |
| (CH₃)₂C(OH)CH=CH₂ | HCl + CuCl | ⎧ [(CH₃)₂CH=CHCH₂]₂O | |
| | | (CH₃)₂CH=CHCH₂OC(CH₃)₂CH=CH₂ | (388) |
| | | ⎩ (CH₃)₂C=CHCH₂OH | |
| | CH₃OH + H₂SO₄ | (CH₃)₂C=CHCH₂OCH₃ | (439) |
| | | (CH₃)₂C(OCH₃)CH=CH₂ | |
| CH₃CH=CHCHOHC≡CH | CH₃OH + H₂SO₄ | CH₃CH(OCH₃)CH=CHC≡CH | (267) |
| | H₂SO₄ | [HC≡CCH=CHCH(CH₃)]₂O | (267) |
| CH₃CH=CHCHOHCH=CH₂ | 10% H₂SO₄ in 60% dioxane | [CH₃CH=CHCH(CH=CH₂)]₂O | (444) |
| | H₃PO₄ | [CH₃CH=CHCH(CH=CH₂)]₂O | (444) |
| CH₂CH=CHCHOHCH=CH₂ | CH₃OH + H₂SO₄ | CH₃CH(OCH₃)CH=CHCH=CH₂ | (304, 305) |
| | C₂H₅OH + H₂SO₄ | CH₃CH(OC₂H₅)CH=CHCH=CH₂ | (266, 304, 305) |
| | CH₂ClCH₂OH + H₂SO₄ | CH₃CH(OC₂H₄Cl)CH=CHCH=CH₂ | (266, 304, 305) |
| C₂H₅C(CH₃)(OH)CH=CH₂ | CH₃OH + H₂SO₄ | ⎧ C₂H₅C(CH₃)(OCH₃)CH=CH₂ | (439) |
| | | ⎩ C₂H₅C(CH₃)=CHCH₂OCH₃ | |
| CH₃OCH₂CH₂CH=CHCH₂OH | CH₃OCH₂CH₂CH=CHCH₂Cl + 50% NaOH | (CH₃OCH₂CH₂CH=CHCH₂)₂O | (510) |
| | CH₃OCH₂CH₂CHClCH=CH₂ + KOH | (CH₃OCH₂CH₂CH=CHCH₂)₂O | (510) |
| n-C₃H₇CHOHCH=CHCH₃ | K, then CH₃I | C₃H₇CH(OCH₃)CH=CHCH₃ | (15) |
| n-C₅H₁₁CH=CHCH₂OH | NaNH₂ in ether, then (CH₃)₂SO₄ | C₅H₁₁CH=CHCH₂OCH₃ | (232) |
| CH₃CH=CHCHOH(n-C₄H₉) | CH₃CH=CHCH(ONa)(n-C₄H₉) + n-C₄H₉X | CH₃CH=CHCH(C₄H₉)OC₄H₉ | (274) |
| CH₃CH=CHCHOH(t-C₄H₉) | CH₃CH=CHCH(ONa)(t-C₄H₉) + t-C₄H₉X | CH₃CH=CHCH(C₄H₉)OC₄H₉ | (274) |

| | | | |
|---|---|---|---|
| ⬡CHOHCH₃ ............................ | H⁺ | (C₈H₁₃)₂O | (194) |
| (CH₃)₂C=CHC(CH₃)(OH)COCH₃ ............... | CH₃OH + H₂SO₄ | (CH₃)₂C(OCH₃)CH=C(CH₃)COCH₃ | (89) |
| | C₂H₅OH + H₂SO₄ | (CH₃)₂C(OC₂H₅)CH=C(CH₃)COCH₃ | (89) |
| (CH₃)₂C(OH)CH=C(CH₃)COCH₃ ............... | C₂H₅OH + H₂SO₄ | (CH₃)₂C(OC₂H₅)CH=C(CH₃)COCH₃ | (89) |
| | CH₃OH + H₂SO₄ | (CH₃)₂C(OCH₃)CH=C(CH₃)COCH₃ | (89) |
| C₆H₅CH=CHCH₂OH ............................ | H₂SO₄ | (C₆H₅CH=CHCH₂)₂O | (419) |
| | NaNH₂ in ether, then (CH₃)₂SO₄ | C₆H₅CH=CHCH₂OCH₃ | (232) |
| | C₂H₅Br + 50% NaOH | C₆H₅CH=CHCH₂OC₂H₅ | (637) |
| | C₆H₅CH=CHCH₂ONa + n-C₄H₉X | C₆H₅CH=CHCH₂OC₄H₉ | (274) |
| | C₆H₅CH=CHCH₂ONa + C₆H₅CH₂CH₂X | C₆H₅CH=CHCH₂OCH₂CH₂C₆H₅ | (274) |
| C₆H₅CHOHCH=CH₂ ............................ | H₂SO₄ | Mostly (C₆H₅CH=CHCH₂)₂O | (419) |
| | Aqueous C₂H₅OH + HCl | { C₆H₅CH=CHCH₂OC₂H₅ ‚ C₆H₅CH=CHCH₂OH | (86) |
| | Na, then CH₃I | C₆H₅CH(OCH₃)CH=CH₂ | (185) |
| | Phthalic anhydride | [C₆H₅CH(CH=CH₂)]₂O ‚ C₆H₅CH=CHCH₂OCOC₆H₄COOH | (311) |
| C₆H₅CHOHCH=CHCH₃ ...................... | Aqueous C₂H₅OH + HCl | C₆H₅CH=CHCH(OC₂H₅)CH₃ ‚ C₆H₅CH=CHCHOHCH₃ | (86) |
| [CH₃CH=CHCHOHC≡]₂ ...................... | C₂H₅OH + H₂SO₄ | [CH₃CH(OC₂H₅)CH=CHC≡]₂ | (267) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)=CHCH₂OH ........ | Na, then C₂H₅Br | (CH₃)₂C=CHCH₂CH₂C(OH₃)=CHCH₂OC₂H₅ | (182) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)(OH)CH=CH₂ ...... | Na, then C₂H₅Br | (CH₃)₂C=CHCH₂CH₂C(CH₃)(OC₂H₅)CH=CH₂ | (182) |
| α-C₁₀H₇CHOHCH=CHCH₃ ................... | 0.1 M HCl in 90% acetone | { C₁₀H₇CHOCH(CH₃)CH=CHC₁₀H₇ \| CH=CHCH₃ ‚ C₁₀H₇CH=CHCHOHCH₃ | (84) |
| C₆H₅CH=CHCHOHCH₂C₆H₅ ................ | C₆H₅CH=CHCH(ONa)CH₂C₆H₅ + n-C₄H₉X | C₆H₅CH=CHCH(CH₂C₆H₅)OC₄H₉ | (274) |
| (C₆H₅)₂C(OH)CH=CHC₆H₅ ...................... | CH₃OH + H₂SO₄ | (C₆H₅)₂C=CHCH(OCH₃)C₆H₅ | (698) |
| | K, then CH₃I | (C₆H₅)₂C(OCH₃)CH=CHC₆H₅ | (700) |
| (C₆H₅)₂C=CHCHOHC₆H₅ ...................... | CH₃OH + H₂SO₄ | (C₆H₅)₂C=CHCH(OCH₃)C₆H₅ | (698, 699) |

C₆H₅CH=C< C(C₆H₅)(OH)—CC₆H₅ / CO————CH >  ............... | Ag₂O + CH₃I | C₆H₅CH=C< C(C₆H₅)(OCH₃)—CC₆H₅ / CO————CH > | (103)

## TABLE 19—*Concluded*

| Alcohol | Reagents and Conditions | Products | References |
|---|---|---|---|
|  | $CH_3OH + H^+$ |  | (359) |
|  | $CH_3OH + H^+$ |  | (359) |

Badger and Pearce (27, 28) found that the acid-catalyzed dehydration of certain 9,10-dihydro-9,10-dihydroxyanthracene derivatives yields rearranged ethers, and proposed the following mechanism to account for their results:
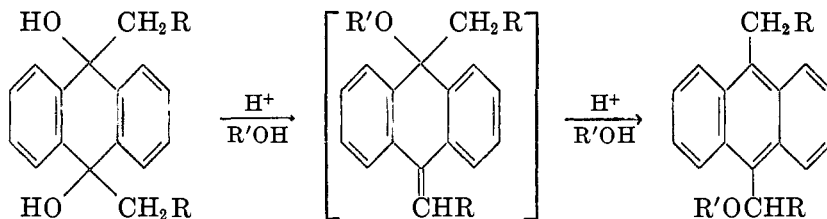


Table 19 lists etherification reactions of unsymmetrically substituted allylic alcohols. Both acid- and base-catalyzed reactions are collected in the table; reagents and reaction conditions are indicated, and the principal products of the reaction are listed in most instances.

### C. REPLACEMENT REACTIONS OF ALLYLIC HALIDES

Owing to the ease with which they can be converted into unsaturated compounds containing almost all of the functional groups of organic chemistry, allylic halides have played an important role in organic synthesis for several decades. The usefulness of unsymmetrically substituted allylic halides is somewhat reduced by the fact that their reactions are frequently accompanied by partial or complete allylic rearrangement.

Much of the earlier literature on reactions of allylic compounds is of questionable value today owing to the failure of early workers to recognize the possibility of allylic rearrangements. A comprehensive survey of the literature on this topic is also handicapped by the fact that mixtures of isomeric halides were often used as starting materials rather than a single halide, as supposed by the investigator. It is difficult to assess the reliability of synthetic experiments performed without an awareness of the possibility of abnormal product formation, especially when this product could arise through use of impure starting materials as well as by allylic rearrangement.

In the pages which follow, the various replacement reactions are discussed both from the standpoint of their synthetic utility and with regard to reaction mechanisms which may be operating.

Knowledge of organic reaction mechanisms in general and mechanisms of allylic rearrangements in particular is sufficiently advanced for a discussion of mechanisms to be desirable. It is hoped that emphasis of reaction mechanisms will enable the practicing chemist to choose reaction conditions which are most likely to lead to the desired product. An awareness of mechanisms should also reduce the number of erroneous reports which appear in the literature even today. Reaction conditions which are certain to give the same products from either of two isomeric halides must be avoided in "structure proofs" of these halides. Time and effort are frequently expended on reactions which give difficultly separable mixtures of products, while the desired compound could be prepared in pure form simply by changing the reaction conditions.

An attempt is made to indicate in the tables which follow the discussions of the various replacement reactions whether normal, rearranged, or mixed substitution products were obtained. The tendency of the synthetic chemist to isolate and purify only the major product of a reaction seriously handicaps this effort. Whenever a single product was reported for a reaction which was carried out under conditions which almost invariably lead to partial allylic rearrangement, a question mark is placed after the product concerned. A question mark after the structural formula of the halide used indicates that there is reasonable doubt as to its purity or structure. Unless special precautions are taken, allylic bromides isomerize rapidly to equilibrium mixtures consisting mostly of the primary isomer, and most early workers erroneously assumed that they were using pure primary bromides rather than equilibrium mixtures. The "primary bromides" listed in the tables usually contained 10–25 per cent of their tertiary or secondary allylic isomers.

### 1. Hydrolysis of allylic halides

Since allylic halides are considerably more reactive than the corresponding saturated halides, they are readily hydrolyzed to allylic alcohols. However, this procedure is of limited usefulness in synthesis because the alcohols themselves are one of the best sources of the halides. A further objection arises from the fact that special care and control must be exercised to prevent formation of mixtures of alcohols and ethers. When mixtures are formed, separation of the isomeric alcohols and ethers is often difficult. In spite of this it is sometimes necessary to prepare allylic alcohols by hydrolysis of the halides, since the particular halide may be readily prepared by allylic halogenation of olefins or by addition of hydrogen halides or halogens to dienes. Even in these cases, better yields of alcohols can often be obtained by converting the halides to acetate esters by bimolecular displacement with acetate ion and saponifying the esters.

Hydrolysis of allylic halides usually occurs by the unimolecular mechanism, as indicated by the formation of mixtures of isomeric alcohols. Alkaline hydrolysis of primary allylic halides having no more than one γ-alkyl or halogen substituent in relatively non-polar solvent mixtures such as aqueous dioxane sometimes yields only normal substitution products. In these cases bimolecular displacement of halide by hydroxyl ion is probably involved. For example, 5-butoxy-1-chloro-2-pentene and its allylic isomer are reported to be hydrolyzed by alkali without rearrangement (509, 516). Young and Andrews (660) found that the composition of the alcohol mixture obtained from hydrolysis of crotyl chloride is sensitive to the presence of alkali in the reaction mixture, evidence for a bimolecular reaction with hydroxyl ion. Second-order kinetics was observed for the alkaline hydrolysis of allyl and methallyl chlorides in 50 per cent aqueous dioxane, acetone, and ethanol (480), and for the hydrolysis of several primary allylic chlorides in alkaline 50 per cent aqueous ethanol (11).

Under ordinary experimental conditions, secondary and tertiary allylic halides, and primary halides having two γ-alkyl or one γ-aryl substituent, are hydrolyzed predominantly or entirely by the unimolecular mechanism. Even primary

halides activated by a single γ-alkyl substituent, such as crotyl chloride, undergo unimolecular hydrolysis to an important extent (660). Pertinent kinetic studies are referred to in the discussion of the unimolecular mechanism of substitution (page 784). The prevalence of unimolecular hydrolysis is the reason why most unsymmetrically substituted halides yield mixtures of hydrolysis products, and why optically active allylic chlorides give racemic hydrolysis products (2, 32, 275).

A variety of experimental conditions have been used for effecting hydrolysis of allylic halides. Usually, for preparative purposes, a mixture of the halide and an aqueous solution of a weak base is agitated until hydrolysis is complete. A strongly alkaline solution (i.e., sodium or potassium hydroxide) is unnecessary and offers no marked advantage except in the hydrolysis of the less reactive primary allylic halides. It is advantageous to keep the reaction medium at least slightly alkaline, however, in order to neutralize the hydrogen halide produced by the hydrolysis reaction. The presence of strong acid in the reaction mixture promotes the side reactions which form ethers, and the accumulation of large amounts of hydrogen halide in the reaction solution results in establishment of an equilibrium between alcohol and halide so that the reaction cannot go to completion. Aqueous bicarbonate solutions are frequently used to neutralize the acid liberated by the reaction, but a suspension of powdered calcium carbonate is more satisfactory. Sodium and potassium hydroxide solutions are also used.

There are a few reports of alcoholic sodium or potassium hydroxide being used for the hydrolysis of allylic halides. Aqueous alcohol, with or without added alkali, has also been used. While aqueous ethanol mixtures make it possible to carry out the reaction in a homogeneous, single-phase system, alcoholysis occurs simultaneously with hydrolysis, resulting in the formation of ethyl ethers as by-products.

Although silver oxide catalyzes the hydrolysis of allylic chlorides, it generally results in the formation of diallylic ethers as well as alcohols. Cuprous chloride also catalyzes the reaction, but its use has been limited mostly to kinetic studies (246, 256, 257) in which the reaction products were not isolated.

Since most allylic halides are only sparingly soluble in water, hydrolysis reactions have usually been carried out in two-phase systems. The existence of two separate phases in the reaction system has the disadvantages of slowing down the hydrolysis reaction and increasing the proportion of ethers formed as by-products. This latter difficulty arises from the relatively high concentration of allylic alcohol present at the water–organic interface during the late stages of the reaction. Since most halides hydrolyze by the unimolecular mechanism, the allylic carbonium ion can react with alcohols to give ethers as well as with water to give alcohols. Reaction rate is increased and by-product formation is decreased if the reaction mixture is efficiently stirred.

The use of mixed solvents such as aqueous dioxane and aqueous acetone would be expected to reduce ether formation, since homogeneous reaction mixtures would be possible. However, the presence of the organic solvent would slow down the reaction and complicate isolation of the reaction products.

Allylic halides may be unstable intermediates in the hydrolysis of certain substituted $\alpha$-halo ketones and vinyl halides. Thus, chloroketone (I) is hydrolyzed by aqueous barium carbonate or silver oxide to rearranged hydroxyketone (II). Presumably, the enol of the chloroketone is an intermediate in the reaction (187):

$$2,6\text{-}(CH_3O)_2C_6H_3CH_2COCH_2Cl \xrightarrow{OH^-}$$

I

$$[ArCH{=}C(OH)CH_2Cl] \rightarrow ArCHOHCOCH_3$$

II
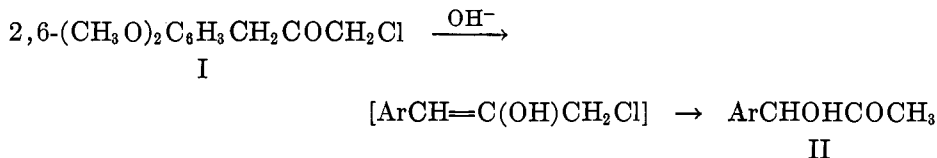
The unsaturated bromo acid (III) is hydrolyzed in alkaline solution to a mixture of acids V and VI. In this case the first step of the reaction is probably a prototropic rearrangement to allylic bromide (IV), which undergoes hydrolysis and rearrangement to the observed products (467, 468).

$$(CH_3)_2C{=}CBrCOOH$$

III

$$\searrow OH^-$$

$$[CH_2{=}C(CH_3)CHBrCOO^-]$$

IV

$$(CH_3)_2CH{=}COCOOH$$

V

$$CH_2OHC(CH_3){=}CHCOOH$$

VI
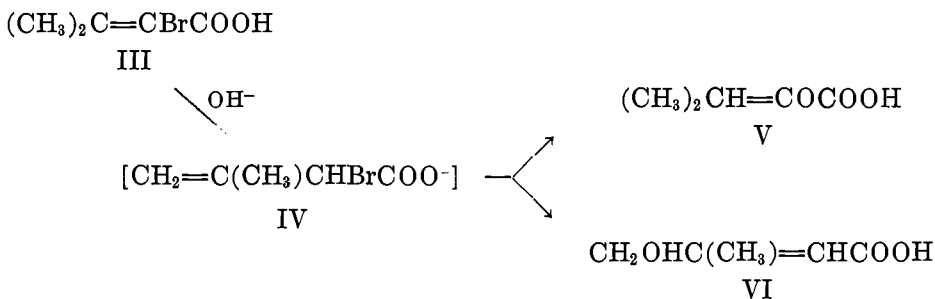
Table 20 lists unsymmetrically substituted and optically active allylic halides which have been hydrolyzed to allylic alcohols. The third column gives product compositions. With regard to product compositions, it should be kept in mind that authors frequently neglect to mention minor components of reaction mixtures, so that mixtures are much more prevalent than indicated by the table.

### 2. Conversion of allylic halides to ethers

#### (a) Reaction with alcohols and alkoxides

Allylic halides are converted to allylic ethers by reaction with alcohols and by treatment with alcoholic alkoxides:

$$R{-}\overset{|}{C}{=}\overset{|}{C}{-}\overset{|}{\underset{|}{C}}{-}X \xrightarrow[\text{or } RO^-]{R'OH} R{-}\overset{|}{C}{=}\overset{|}{C}{-}\overset{|}{\underset{|}{C}}{-}OR' \text{ and/or } R{-}\overset{|}{\underset{|}{C}}(OR')\overset{|}{C}{=}\overset{|}{C}{-}$$
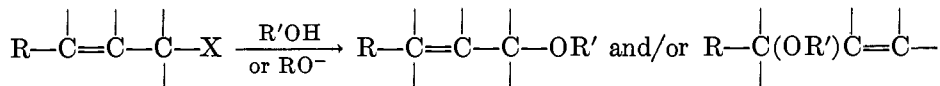
Reactions with alcohols in the absence of alkoxides usually yield mixtures of isomeric ethers, and unimolecular substitution ($S_N1$) is probably involved in the great majority of cases.

Since alcohols are relatively non-polar solvents and alkoxide ions are strongly nucleophilic reagents, most primary and many secondary allylic halides react with alcoholic alkoxides by the normal bimolecular mechanism, giving only products of normal substitution without allylic rearrangement. Reactions of

## TABLE 20

*Hydrolysis of allylic halides*

| Halide | Reaction Conditions | Product Composition† | References |
|---|---|---|---|
| $CH_2=CHCHCl_2$ | Aqueous $C_2H_5OH$ | R + ethers; M | (169, 171, 348) |
| $CH_2=CHCHCl_2$ | $H_2O + Ag_2O$ | R | (347) |
| $CH_2=CHCHCl_2$ | Aqueous NaOH | R | (563) |
| $CHCl=CHCH_2Cl$ | Aqueous $Na_2CO_3$ | N | (255, 262) |
| $CHCl=CHCH_2Cl$ | $H_2O + Ag_2O$ | N | (347) |
| $CHCl=CHCH_2Cl$ | Aqueous $C_2H_5OH$ | N | (169, 171, 348, 480) |
| $CHBr=CHCH_2Br$ | Aqueous $Na_2CO_3$ | N | (251) |
| $CHCl=CHCH_2I$ | Aqueous KOH | N | (624) |
| $CHCl=CFCH_2Br$ | Aqueous $Na_2CO_3$ | N | (254) |
| $CH_2=C=CHCH_2Cl$ | Aqueous $NaHCO_3$ | N | (113, 626) |
| $CH_2=C=CHCH_2Br$ | Aqueous $NaHCO_3$ | N | (113) |
| $CH_3CH=CHCH_2Cl + CH_3CHClCH=CH_2$ | $H_2O + CaCO_3$ | M | (402) |
| $CH_3CH=CHCH_2Cl$ | $H_2O + Ag_2O$ | M | (660) |
| $CH_3CH=CHCH_2Cl$ | Aqueous $Na_2CO_3$ or NaOH | M | (660) |
| $CH_3CHClCH=CH_2$ | $H_2O + Ag_2O$ | M | (660) |
| $CH_3CHClCH=CH_2$ | Aqueous $Na_2CO_3$ or NaOH | M | (660) |
| $CH_3CCl=CHCH_2Cl$ | Aqueous $Na_2CO_3$ | N | (128, 195, 252, 257, 258, 307) |
| $CH_3CCl=CHCH_2Cl$ | $H_2O + CaCO_3$ | M | (605) |
| $CH_3CCl=CHCH_2Cl$ | Aqueous CuCl + HCl | M | (245, 246) |
| $CH_3CCl=CHCH_2Cl$ | Steam | N | (135) |
| $CH_3CHClCH=CHCl$ | | N | (338) |
| $CHCl=C(CH_3)CH_2Cl$ | Aqueous NaOH | N | (263) |
| $CH_3CH=CClCH_2Cl$ | $H_2O + CaCO_3$ | M | (605) |
| $CH_2ClCH=CHCH_2Cl$ | Aqueous $Na_2CO_3$ | M | (504) |
| $CH_3CCl=CClCH_2Cl$ | Aqueous $Na_2CO_3$ | N | (248) |
| $CH_3CCl_2CCl=CH_2$ | Aqueous $Na_2CO_3$ | R | (248) |
| $CH_2=C(CH_3)CCl_3$ | Aqueous $Na_3PO_4$ | R | (346) |
| $CCl_2=C(CH_3)CH_2Cl$ | Aqueous $Na_3PO_4$ | N | (346) |
| $CH_3CH=CHCH_2Br$ (?) | Aqueous $Na_2CO_3$ | M | (98, 130) |
| $CH_3CCl=CHCH_2Br$ | Aqueous $Na_2CO_3$ | N | (171) |
| $CH_3CH=CHCH_2Br$ (?) | Aqueous NaOH | M | (470) |
| $CH_3CH=CHCH_2Br$ (?) | $H_2O$ | N (?) | (95) |
| $CH_2BrCH=CHCOOH$ | $H_2O + Ag_2O$; aqueous KOH | N | (524) |
| $CH_2BrCH=CHCN$ | $H_2O + Ag_2O$; aqueous KOH | N | (524) |
| $CH_2BrCH=CHCH_2Br$ | Aqueous $Na_2CO_3$; aqueous NaOH | M | (483, 619) |
| $C_2H_5CH=CHCH_2Cl$ | Aqueous NaOH; aqueous $Na_2CO_3$ | M | (419) |
| $C_2H_5CHClCH=CH_2$ | Aqueous NaOH; aqueous $Na_2CO_3$ | M | (419) |
| $CH_3CHClC(CH_3)=CH_2$ | $H_2O + CaCO_3$ | M | (604) |
| $CH_3CH=C(CH_3)CH_2Cl$ | $H_2O + CaCO_3$ | M | (604) |
| $(CH_3)_2C=CHCH_2Cl$ | $H_2O + Ag_2O$ | M | (633) |
| $(CH_3)_2C=CHCH_2Cl$ | Aqueous $Na_2CO_3$; aqueous $NaHCO_3$ | M | (26, 438, 446, 611, 633) |
| $(CH_3)_2CClCH=CH_2$ | Aqueous $Na_2CO_3$; aqueous $NaHCO_3$ | M | (438, 611, 633) |
| $(CH_3)_2CClCH=CH_2$ | $H_2O + Ag_2O$ | M | (68, 438) |
| $(CH_3)_2C=CHCH_2Br$ (?) | Aqueous KOH | R (?) | (129) |
| $(CH_3)_2C=CHCH_2Br$ (?) | Aqueous $Na_2CO_3$, $NaHCO_3$, or NaOH | M | (426, 633) |
| $(CH_3)_2C=CHCH_2Br$ (?) | $H_2O + Ag_2O$; $H_2O + CaCO_3$ | M | (633) |
| $CH_3CHBrCH=CHBr$ (?) | Aqueous $Na_2CO_3$ | M | (98, 491) |

TABLE 20—*Concluded*

| Halide | Reaction Conditions | Product Composition† | References |
|---|---|---|---|
| CH₂BrCH=CHCOOCH₃............................ | H₂O + Ag₂O; aqueous KOH | N | (524, 525) |
| (CH₃)₂C=C(CH₃)CH₂Cl........................... | Aqueous Na₂CO₃ | R (?) | (253) |
| CH₃CH=CHCHClC₂H₅............................ | H₂O + CaCO₃ | M | (2) |
| (−)-CH₃CH=CHCHClCH₃........................ | H₂O + CaCO₃ | Inactive ROH | (32, 275) |
| CH₃CH=CHCH=CHCH₂Cl....................... | Aqueous NaHCO₃ | M | (443) |
| CH₃CHClCH=CHCH=CH₂........................ | Aqueous NaHCO₃ | M | (443) |
| (CH₃)₂C=C(CH₃)CH₂Br (?)...................... | Aqueous KOH | R (?) | (49, 129) |
| Dibromocyclohexene, m.p. 108°C................. | Aqueous NaOH or NaHCO₃ | M | (48) |
| CH₃OCH₂CH₂CH=CHCH₂Cl..................... | Ethanolic KOH | N | (509) |
| CH₃OCH₂CH₂CH=CHCH₂Cl + isomer.......... | Aqueous Na₂CO₃ | M | (191) |
| CH₃OCH₂CH₂CHClCH=CH₂...................... | Ethanolic KOH | N | (509) |
| CH₃CHClCH=CHOCOCH₃ (?)................... | H₂O | R (?) | (580) |
| (CH₃)₂C=CHCH=CHCH₂Cl...................... | Aqueous NaHCO₃ | R (?) | (441) |
| C₃H₇C(CH₃)=CHCH₂Cl.......................... | Aqueous NaHCO₃ | M | (440) |
| C₃H₇C(CH₃)ClCH=CH₂.......................... | Aqueous NaHCO₃ | N (?) | (440) |
| C₂H₅OCH₂CH₂CH=CHCH₂Cl + isomer.......... | Aqueous Na₂CO₃ | M | (191) |
| C₂H₅OCH(CH₃)CH₂CHClCH=CH₂.............. | Aqueous Na₂CO₃ | M | (189) |
| C₂H₅OCH(CH₃)CH₂CHClCH=CH₂ + isomer.... | Aqueous Na₂CO₃ | M | (191) |
| C₆H₅CH=CHCH₂Cl.............................. | Aqueous NaOH or Na₂CO₃ | M | (419) |
| C₆H₅CH=CHCH₂Cl.............................. | Aqueous ethanolic AgNO₃ | M | (182) |
| C₆H₅CHClCH=CH₂.............................. | Aqueous NaOH or Na₂CO₃ | M | (419) |
| C₆H₅CH=CHCHCl₂.............................. | Aqueous ethanol | R | (12) |
| C₄H₉OCH₂CH₂CH=CHCH₂Cl.................... | Ethanolic KOH | N | (516) |
| C₄H₉OCH₂CH₂CH=CHCH₂Cl.................... | Aqueous Na₂CO₃ | M | (189, 191) |
| C₄H₉OCH₂CH₂CHClCH=CH₂.................... | Aqueous Na₂CO₃ | M | (189, 191) |
| C₂H₅CH=CHCH₂Br............................. | H₂O | N (?) | (93) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)ClCH=CH₂ (?).... | H₂O + Ag₂O; ethanolic KOH | N (?) | (620) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)=CHCH₂Cl........ | Aqueous ethanolic AgNO₃ | M | (181) |
| C₄H₉OCH(CH₃)CH₂CH=CHCH₂Cl + isomer.... | Aqueous Na₂CO₃ | M | (191) |
| C₅H₁₁OCH₂CH₂CH=CHCH₂Cl................... | Aqueous Na₂CO₄ | M | (189) |
| (CH₃)₂CHCH₂OCH(CH₃)CH₂CH=CHCH₂Cl + isomer......................................... | Aqueous Na₂CO₃ | M | (191) |
| (CH₂ClCH=CHCH₂CH₂)₂O...................... | | M | (454) |
| C₆H₅CH=C(CH₃)CH₂Br......................... | Aqueous NaOH | N (?) | (585) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)=CHCH₂Br........ | H₂O + Ag₂O | R (?) | (181) |
| C₆H₅CH=CHCH=CHCH₂Cl...................... | Aqueous NaHCO₃ | M | (442) |
| C₆H₅CCl=CHCHBrC₆H₅......................... | | N | (589) |
| C₆H₅CH=CHCCl=CHCHBrC₆H₅................ | | N | (589) |
| C₆H₅CH=CHCCl=CHCHClC₆H₅................ | | N | (589) |
| p-ClC₆H₄CHClCH=CHCH=CHC₆H₄Cl-p....... | | N (?) | (589) |
| C₆H₅CHBrCHBrCH=CHCH=CHC₆H₅......... | H₂O + Ag₂O | R | (364) |
| C(C₆H₅)=CC₆H₅........................ (CH₃)₂C〈 〉 CO——CHCl | Aqueous KOH | N | (106) |

† In this and the tables which follow, M indicates that a mixture of isomeric products was isolated, N means that only the normal substitution product was reported, and R means that only the product formed by allylic rearrangement is reported.

primary and secondary allylic chlorides with sodium ethoxide in ethanol are kinetically second order (11, 121, 244, 246, 248, 257, 539, 576, 597, 636), and only products of normal substitution are formed. Other alkoxides react with primary allylic halides in alcoholic solution to give only primary allyl alkyl ethers

## TABLE 21

*Conversion of allylic halides to alkyl ethers*

| Halide | Reaction Conditions | Products† | References |
|---|---|---|---|
| $CH_2=CHCHCl_2$ | $C_2H_5ONa$ in $C_2H_5OH$ | R (?) M | (168, 172, 347) |
| $CH_2=CHCHCl_2$ | $CH_3ONa$ in $CH_3OH$ | R (?) | (347) |
| $CHCl=CHCH_2Cl$ | $C_2H_5ONa$ in $C_2H_5OH$ | N | (347, 576) |
| $CHCl=CHCH_2Cl$ | $CH_3ONa$ in $CH_3OH$ | N | (347) |
| $CHCl=CHCH_2Cl$ | 50% Aqueous $C_2H_5OH$ | M (+ ROH) | (348, 480) |
| $CH_2=CHCCl_3$ | $CH_3ONa$ in $CH_3OH$ | R | (451) |
| $CCl_3=CHCH_2Cl$ | $CH_3ONa$ in $CH_3OH$ | N | (374, 451) |
| $CCl_2=CHCH_2Cl$ | $C_2H_5ONa$ in $C_2H_5OH$ | N | (374) |
| $CH_3CH=CHCH_2Cl$ | $C_2H_5ONa$ in $C_2H_5OH$ | N | (121, 539, 691) |
| $CH_3CH=CHCH_2Cl$ | 90% $C_2H_5OH$, 10% $H_2O$ + $CaCO_3$ | M | (660) |
| $CH_3CHClCH=CH_2$ | $C_2H_5ONa$ in $C_2H_5OH$ | N | (121, 539) |
| $CH_3CH=CHCH_2Br$ (?) | $NaOR$ + $ROH$ ($R = CH_3$, $C_2H_5$, $C_4H_7$) | N (?) | (123) |
| $CH_3CH=CHCH_2Br$ (?) | $C_2H_5OH$ | M | (390) |
| $CH_2ClCH=CHCH_2Cl$ | $ROH$ + $KOH$ ($R = CH_3$, $C_3H_7$, $C_4H_9$) | N | (504) |
| $CH_2ClCH=CHCH_2Cl$ | $NaOR$ + $ROH$ ($R = C_4H_9$, $C_5H_{11}$, $i$-$C_8H_{17}$, $C_{12}H_{25}$) | N | (155) |
| $CH_3CHClCH=CHCl$ (?) | $KOH$ in $C_2H_5OH$ | N (?) | (321) |
| $CH_3BrCH=CHCH_2Br$ (?) | $KOH$ in $C_2H_5OH$ | N (?) | (482) |
| $CH_3CCl=CHCH_2Br$ | $KOH$ in $ROH$ | N | (471) |
| $CH_2=C(CH_3)CCl_3$ | $C_2H_5ONa$ in $C_2H_5OH$ | R | (174, 346, 417) |
| $CCl_2=C(CH_3)CH_2Cl$ | $C_2H_5ONa$ in $C_2H_5OH$ | N | (345, 346) |
| $HC\equiv CCH=CHCH_2Cl$ | $CH_3OH$ | M | (265) |
| $C_2H_5CH=CHCH_2Cl$ | $KOH$ in $C_2H_5OH$ | N | (419) |
| $C_2H_5CH=CHCH_2Cl$ | $C_2H_5ONa$ in $C_2H_5OH$ | N | (490) |
| $C_2H_5CHClCH=CH_2$ | $C_2H_5ONa$ in $C_2H_5OH$ | M | (490) |
| $(CH_3)_2C=CHCH_2Cl$ | $C_2H_5OH$ | M | (170) |
| $(CH_3)_2C=CHCH_2Cl$ | $NaOR$ in $ROH$ ($R = CH_3$, $C_2H_5$, $C_3H_7$, $i$-$C_3H_7$, $C_4H_9$) | N | (249, 438, 612) |
| $(CH_3)_2CClCH=CH_2$ | $C_2H_5OH$ | M | (170) |
| $(CH_3)_2CClCH=CH_2$ | $CH_3ONa$ in $CH_3OH$ | M | (438, 612) |
| $HC\equiv CCH=CHCH_2Br$ | $CH_3ONa$ in $CH_3OH$ | N | (125) |
| $(CH_3)_2C=CHCHBr$ | $CH_3OH$ | R (?) | (592) |
| $(CH_3)_2C=CHCH_2Br$ | $C_2H_5ONa$ in $C_2H_5OH$ | N | (129) |
| $(CH_3)_2C=CClCH_2Cl$ | $KOH$ in $C_2H_5OH$ | N | (614) |
| $CH_2BrC(CH_3)=CHCH_2Br$ | $RONa$ in $ROH$($R=CH_3, C_2H_5$) | N | (472) |
| $C_2H_5C(CH_3)=CHCH_2Cl$ | $C_2H_5ONa$ in $C_2H_5OH$ | N | (691) |
| $C_2H_5C(CH_3)=CHCH_2Cl$ | $K_2CO_3$ + $C_2H_5OH$ | M | (691) |
| $C_2H_5C(CH_3)ClCH=CH_2$ | $C_2H_5OH$ | M | (633) |
| $CH_3OCH_2CH_2CH=CHCH_2Cl$ | $KOH$ in $ROH$ ($R = CH_3$, $C_2H_5$, $C_3H_7$, $i$-$C_3H_7$, $C_4H_9$) | N | (505, 508, 510, 513) |
| $CH_3OCH_2CH_2CHClCH=CH_2$ | $KOH$ in $ROH$ ($R = CH_3$, $C_2H_5$, $C_3H_7$, $i$-$C_3H_7$, $C_4H_9$) | M | (508, 510) |
| $CH_2ClCH=CHN(CH_3)_3^+Cl^-$ | $C_2H_5ONa$ in $C_2H_5OH$ | R | (296) |
| $HC\equiv CC(CH_3)=CHCH_2Br$ | $CH_3ONa$ in $CH_3OH$ | N | (108, 278) |
| $(CH_3)_2C=C(CH_3)CH_2Br$ | $C_2H_5ONa$ in $C_2H_5OH$ | N | (129) |
| $CH_2=CHCH_2CH=CHCH_2Br$ (?) | $C_2H_5ONa$ in $C_2H_5OH$ | N (?) | (43) |
| $CH_2=CHCH_2CH=CHCH_2Br$ (?) | $KOH$ in $C_2H_5OH$ | N (?) | (316) |
| $CH_2BrCH=CHCH=CHCH_2Br$ | $CH_3ONa$ in $CH_3OH$ | N | (317) |
| $CH_2BrCH=CHCH=CHCH_2Br$ | $NaOH$ in $C_2H_5OH$ | N | (199) |
| Dibromocyclohexene, m.p. 108°C | $NaHCO_3$ in $CH_3OH$ | M | (48) |
| $HC\equiv CCH_2C(CH_3)=CHCH_2Cl$ | $CH_3ONa$ in $CH_3OH$ | N | (277) |
| $C_8H_7C(CH_3)=CHCH_2Cl$ | $CH_3ONa$ in $CH_3OH$ | N | (440) |
| $C_8H_7C(CH_3)ClCH=CH_2$ | $CH_3ONa$ in $CH_3OH$ | M | (440) |
| $CH_3\underset{}{\overset{Cl}{\diagup\!\!\diagdown}}$ (cis and trans) | $C_2H_5OH$ | M | (225) |

TABLE 21—*Concluded*

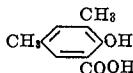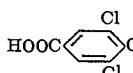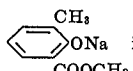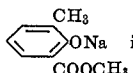| Halide | Reaction Conditions | Products† | References |
|---|---|---|---|
| $C_2H_5OCH(CH_2Cl)CH_2CH=CHCH_2Cl$ | KOH in ROH (R = $CH_3$, $C_2H_5$, $C_4H_9$) | N | (502) |
| $C_6H_5CH=CHCH_2Cl$ | Aqueous ethanolic $AgNO_3$ | M | (181, 419) |
| $C_6H_5CH=CHCH_2Cl$ | NaOH in $C_2H_5OH$ | M | (419) |
| $C_4H_9OCH_2CH_2CH=CHCH_2Cl$ | KOH in ROH | N | (516) |
| $C_4H_9OCH_2CH_2CHClCH=CH_2$ | KOH in ROH | M | (516) |
| $C_6H_5CH=CHCH_2Br$ | $C_2H_5OH$ | M | (124) |
| $C_6H_5CH=CHCH_2Br$ | NaOH in $C_2H_5OH$ | N | (355) |
| $C_6H_5CH=CHCH_2Br$ | $C_4H_9ONa$ in xylene | N | (273) |
| $CH_2ClCH=CHN(C_2H_5)_3{}^+Cl^-$ | $C_2H_5ONa$ in $C_2H_5OH$ | R | (296) |
| $C_6H_5CH=CHCHCl_2$ | $C_2H_5ONa$ in $C_2H_5OH$ | R | (10, 12) |
| $C_6H_5CH=CHCHCl_2$ | $CH_3ONa$ in $CH_3OH$ | R | (590) |
| $C_6H_5CCl=CHCH_2Cl$ | $CH_3OH$ | N | (590) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2Cl$ (?) | $C_2H_5ONa$ in $C_2H_5OH$ | N | (205) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2Br$ (?) | $C_2H_5ONa$ in $C_2H_5OH$ | N | (182) |
| $C_6H_5CH=CH-CH=CHCH_2Cl$ | $CH_3ONa$ in $CH_3OH$ | M | (442) |
| $(C_2H_5)_2C=CHCHClC_2H_5$ | $CH_3ONa$ in $CH_3OH$ | M | (700) |
| $C_6H_5CH=C\begin{smallmatrix}C(C_6H_5)=CC_6H_5\\ \mid\\ CO-\!\!-CHCl\end{smallmatrix}$ | $CH_3OH$ | N | (103) |
| $C_6H_5CH=C\begin{smallmatrix}C(C_6H_5)Cl-CC_6H_5\\ \parallel\\ CO-\!\!-CCl\end{smallmatrix}$ | $CH_3OH$ | N | (103) |
| $C_6H_5CH=CHCCl=CHCHClC_6H_5$ | $CH_3OH$ | N | (589) |
| $C_6H_5CHClCH=CClC_6H_5$ | $CH_3OH$ | N | (589) |
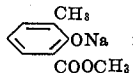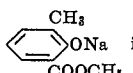
† M indicates that a mixture of isomeric products was isolated, N means that only the normal substitution product was reported, and R means that only the product formed by allylic rearrangement is reported.

(108, 125, 155, 277, 278, 317, 347, 374, 438, 440, 472, 612). Tertiary allylic chlorides are converted to mixtures of isomeric ethers upon treatment with methanolic sodium methoxide (438, 440, 612). This result is probably due to unimolecular substitution. However, in the absence of kinetic data it is not possible to rule out the occurrence of simultaneous normal and abnormal bimolecular substitution ($S_N2$ and $S_N2'$). 3,3-Dichloro-1-propene reacts with ethanolic sodium ethoxide to give a mixture of normal and abnormal substitution products (168, 172), and 3,3,3-trichloro-2-methyl-1-propene yields only the abnormal product, 1,1-dichloro-3-ethoxy-2-methyl-1-propene (174, 346, 417). Both of these reactions have been shown to be examples of abnormal bimolecular substitution (see page 776). Cinnamal chloride ($C_6H_5CH=CHCHCl_2$), on the other hand, undergoes unimolecular solvolysis in ethanolic sodium ethoxide solution (10), a fact which is easily explained on the basis of the facilitating effect of the $\alpha$-chlorine atom and the $\gamma$-phenyl group on unimolecular substitution and their steric hindrance to substitution by mechanisms $S_N2$ and $S_N2'$.

Most primary allylic halides are converted to mixtures of primary allyl alkyl ethers and primary allylic alcohols by treatment with alcoholic sodium or potassium hydroxide (199, 471, 482, 502, 504, 505, 508, 510, 516, 612). These reactions probably involve normal bimolecular substitutions by alkoxide ions.

Cinnamyl chloride has been reported to form a mixture of cinnamyl ethyl ether and phenylvinyl carbinyl ethyl ether when treated with ethanolic sodium or potassium hydroxide (419), and secondary allylic chlorides frequently give mixtures of products with alcoholic potassium hydroxide (508, 510, 516). These

TABLE 22

*Conversion of allylic halides to aryl ethers*

| Halide | Phenol and Reaction Conditions | Reference |
|---|---|---|
| $CCl_2=CHCH_2Cl$ | $p$-$ClC_6H_4OH$ in ethanolic KOH | (374) |
| $CCl_2=CHCH_2Cl$ | $\alpha$-$C_{10}H_7OH$ in ethanolic KOH | (374) |
| $CH_3CH=CHCH_2Cl$ | $p$-$O_2NC_6H_4ONa$ in $C_2H_5OH$ | (676) |
| $CH_3CH=CHCH_2Cl$ | $p$-$NaOOCC_6H_4ONa$ in $C_2H_5OH$ | (385) |
| $CH_3CH=CHCH_2Cl$ | $\underset{COOCH_3}{\overset{CH_3}{\langle \rangle ONa}}$ in $CH_3OH$ | (534) |
| $CH_3CHClCH=CH_2$ | $p$-$NaOOCC_6H_4ONa$ in $C_2H_5OH$ | (385) |
| $CH_3CHClCH=CH_2$ | $\underset{COOCH_3}{\overset{CH_3}{\langle \rangle ONa}}$ in $CH_3OH$† | (534) |
| $CH_3CH=CHCH_2Br$ | $CH_3\underset{COOH}{\overset{CH_3}{\langle \rangle OH}}$ + $CH_3ONa$ in toluene | (456) |
| $CH_3CH=CHCH_2Br$ (?) | $C_6H_5OH$ + $K_2CO_3$ in acetone | (130) |
| $CH_3CH=CHCH_2Br$ | $HOOC\underset{Cl}{\overset{Cl}{\langle \rangle OH}}$ + NaOH in aqueous acetone | (600a) |
| $CH_2ClCH=CHCH_2Cl$ | NaOAr in $C_2H_5OH$ (14 phenols) | (55) |
| $CH_2BrCH=CHCH_2Br$ | $C_6H_5OK$ | (411) |
| $C_2H_5CHClCH=CH_2$ | $\underset{COOCH_3}{\overset{CH_3}{\langle \rangle ONa}}$ in $CH_3OH$† | (536) |
| $C_2H_5CH=CHCH_2Cl$ | $\underset{COOCH_3}{\overset{CH_3}{\langle \rangle ONa}}$ in $CH_3OH$ | (536) |
| $C_2H_5CH=CHCH_2Cl$ | $C_6H_5OH$ + $K_2CO_3$ in acetone | (381) |
| $C_2H_5CH=CHCH_2Cl$ | $p$-$C_2H_5OOCC_6H_4OH$ + $K_2CO_3$ in acetone | (386) |
| $C_2H_5CHClCH=CH_2$ | $C_6H_5OH$ + $K_2CO_3$ in acetone | (381) |
| $C_2H_5CHClCH=CH_2$ | $p$-$C_2H_5OOCC_6H_4OH$ + $K_2CO_3$ in acetone | (386) |
| (−)-$CH_3CHClCH=CHCH_3$‡ | $C_6H_5OH$ or 2,6-$(CH_3)_2C_6H_3OH$ + $K_2CO_3$ in acetone | (5) |
| $(CH_3)_2C=CHCH_2Br$ (?) | $o$-$(CH_3O)C_6H_4ONa$ in $C_2H_5OH$ | (582) |
| $C_3H_7CH=CHCH_2Cl$ | $p$-$C_2H_5OOCC_6H_4OH$ + $K_2CO_3$ in acetone | (383) |
| $C_3H_7CHClCH=CH_2$ | $p$-$C_2H_5OOCC_6H_4OH$ + $K_2CO_3$ in acetone | (383) |
| $C_3H_7CHClCH=CH_2$ | $C_6H_5OH$ + $K_2CO_3$ in acetone | (291) |
| $CH_3OCH_2CH_2CH=CHCH_2Cl$ | $C_6H_5OH$ + $K_2CO_3$ in acetone | (510) |
| $C_5H_9CH=CHCH_2Br$ | $C_6H_5OH$ + $K_2CO_3$ in acetone | (290) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2Br$ (?) | $C_2H_5OOCC_6H_4OH$ + $K_2CO_3$ in acetone | (382) |

† Mixture of ethers formed.

‡ Optically active ethers formed.

results are probably due to operation of an ionic mechanism, since dienes are sometimes among the products.

Table 21 lists allylic halides which have been converted to alkyl allylic ethers by treatment with alcohols or alcoholic alkoxides. The third column of the table indicates the composition of the reaction products, as given in the original article. As pointed out previously, the report of a single product frequently means only that minor constituents of a mixture of products were not isolated in pure form. Cases where this seems particularly likely to have occurred are indicated by a question mark after the product reported.

### (b) Reaction of allylic halides with phenols and phenoxide ions

Phenoxide ions are strongly nucleophilic and generally react with primary and secondary allylic halides in acetone or alcohol solutions to form normal substitution products. Such reactions have been extensively used in preparing allyl aryl ethers, and Tarbell describes the preparation of these ethers in his review of the Claisen rearrangement (598). The most common way of preparing allyl aryl ethers is to heat the allylic halide, the phenol, and anhydrous potassium carbonate in acetone. Sodium and potassium phenoxides in alcohol are also used, and usually give normal products. It has recently been reported, however, that α-ethyl and α-methylallyl chlorides react with the sodium salt of methyl o-cresotinate in methanol solution to give mixtures of normal and abnormal products (534, 536). The kinetics of the reaction was not studied, so it is not possible to decide by what mechanism the abnormal products were formed. Pudovik and Arbuzov prepared an allyl phenyl ether by treating 1-chloro-5-methoxy-2-pentene with aqueous sodium phenoxide (510). The crotyl ether of methyl 3,5-dimethylsalicylate has been prepared by treating crotyl bromide with the anhydrous sodium salt of the phenol in toluene (456).

Table 22 lists reactions of a number of unsymmetrically substituted allylic halides with phenols or their salts. Only normal substitution products were reported, except where otherwise noted.

A number of substituted vinyl halides are converted to allylic ethers by treatment with alcoholic alkoxides or phenoxides. The first step of these reactions is probably a prototropic rearrangement of the vinyl halide into an allylic halide,

TABLE 23

*Conversion of vinyl halides into allylic ethers*

| Halide | Reagent and Conditions | Product | Reference |
|---|---|---|---|
| $CHCl{=}C(CH_3)CH_2CN$ ............... | $C_6H_5ONa$ in $C_2H_5OH$ | $C_6H_5OCH_2C(CH_3){=}CHCN$ | (429) |
| $ArCH_2CH{=}CHCl$ ...................... | Ethanolic KOH | $ArCH{=}CHCH_2OC_2H_5$ | (54) |
| $(CH_3)_2C{=}CBrCOOH$ .................... | Ethanolic $C_2H_5ONa$ | $CH_2{=}C(CH_3)CH(OC_2H_5)COOH$ $+ C_2H_5OCH_2C(CH_3){=}CH{-}COOH$ | (468) |
| $CH_2CH{=}CBrCOOH$ ..................... | Ethanolic $C_2H_5ONa$ | $CH_2{=}CHCH(OC_2H_5)COOH$ | (467) |
| $CH_3OCH_2CH{=}CBrCOOH$ ................ | Methanolic $CH_3ONa$ | $(CH_3O)_2CHCH{=}CHCOOH$ | (469) |
| $(C_6H_5)_2CHCH{=}CClCH{=}CHC_6H_5$ ........ | Methanolic $CH_3ONa$ | $(C_6H_5)_2C{=}CHCH(OCH_3){-}CH{=}CHC_6H_5$ | (591) |

which reacts readily with alkoxide or phenoxide to form the observed products:

$$YCH_2CH{=}CHX \xrightarrow{\ NaOR\ } YCH{=}CHCH_2X \rightarrow YCH{=}CHCH_2OR$$
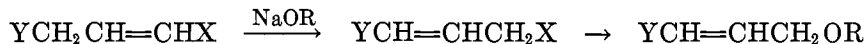
A number of such reactions are listed in table 23.

A somewhat different type of reaction, in which an initial prototropic shift is followed by replacement of a halide atom made allylic by the shift, may explain the conversion of $\alpha$-chloro ketone (I) to rearranged $\alpha$-ethoxy ketone (II) (187):

CH$_3$O

⬡ CH$_2$COCH$_2$Cl $\longrightarrow$

CH$_3$O

I

$$[ArCH{=}\overset{\overset{\textstyle OH}{|}}{C}CH_2Cl] \xrightarrow[C_2H_5OH]{CH_3COOAg} ArCH(OC_2H_5)COCH_3$$

II
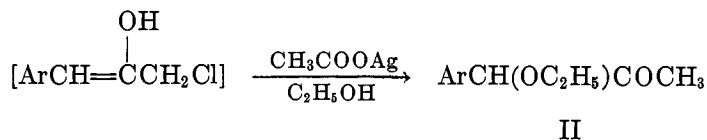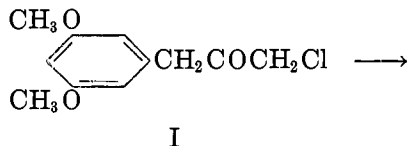
### 3. Conversion of allylic halides to thiols and thioethers

Primary allylic chlorides react with aqueous or alcoholic alkali sulfides to give mixtures of thiols and thioethers in which the structure of the allylic group is unchanged (127, 499, 510, 515). No kinetic studies have been reported, but the strong nucleophilic character of the reagents and the formation of products of normal substitution point to operation of the $S_N2$ mechanism. Thioether formation is apparently due to reaction of the initially formed thiol with unreacted allylic chloride in the alkaline solution (510).

Thiophenoxide and thioalkoxide ions react with primary and secondary allylic chlorides in ethanol solution, giving predominantly or entirely the thioethers which would be formed by $S_N2$ substitution (142, 175, 407, 540). Reactions of $\alpha$-methylallyl chloride, $\alpha,\alpha$-dimethylallyl chloride, and 3,3-dichloro-1-propene with sodium thiophenoxide in ethanol are kinetically second order (173, 175). However, $\alpha,\alpha$-dimethylallyl chloride and 3,3-dichloropropene yield significant amounts of abnormal products, evidence for the occurrence of abnormal bimolecular substitution with these sterically hindered halides.

Table 24 lists reactions of alkali sulfides, mercaptides, and thiophenoxides with unsymemetrically substituted allylic halides.

Perhaps the most satisfactory synthesis of allylic mercaptans from halides is an indirect one. Allylic thiuronium halides (prepared from the halides and thiourea) are hydrolyzed to mercaptans by aqueous alkali (see page 858).

### 4. Conversion of allylic halides to esters

Allylic halides react with carboxylic acids and their salts to form esters of allylic alcohols. This conversion is of considerable synthetic importance, since it

TABLE 24

*Reactions of allylic halides with alkali sulfides, mercaptides, and thiophenoxides*

| Halide | Reagent and Conditions | Products† | References |
|---|---|---|---|
| $CH_2=CHCHCl_2$ .............. | $C_2H_5SNa$ in aqueous ethanol | M | (407) |
| $CH_2=CHCHCl_2$ .............. | $C_6H_5SNa$ in ethanol | M | (171, 173) |
| $CHCl=CHCH_2Cl$ .............. | $Na_2S$ in ethanol | $(CHCl=CHCH_2)_2S$ | (127) |
| $CHCl=CHCH_2Cl$ .............. | $HOC_2H_4SNa$ | N | (127) |
| $CHCl=CHCH_2Cl$ .............. | $CH_3SNa$ | N | (127) |
| $CH_2=CHCCl_3$ .............. | $Na_2S$ in aqueous ethanol | $(CCl_2=CHCH_2)_2S$ | (451) |
| $CH_3CH=CHCH_2Cl$ .............. | $C_4H_9SNa$ in ethanol | N | (407) |
| $CH_3CH=CHCH_2Cl$ .............. | $C_6H_5SNa$ in ethanol | N | (142) |
| $CH_3CHClCH=CH_2$ .............. | $C_4H_9SNa$ in ethanol | N | (407) |
| $CH_3CHClCH=CH_2$ .............. | $C_6H_5SNa$ in ethanol | M ($\sim$95% N) | (175) |
| $CH_3CH=CHCH_2Br$ (?) ......... | NaSH | $(CH_3CH=CHCH_2)_2S$ | (123) |
| $CH_3CCl=CHCH_2Cl$ .............. | $Na_2S$ in water | $(CH_3CCl=CHCH_2)_2S + RSH$ | (499) |
| $CH_2=C(CH_3)CCl_3$ .............. | $C_6H_5SNa$ in ethanol | R | (171) |
| $(CH_3)_2CClCH=CH_2$ .............. | $C_3H_5SNa$ in ethanol | R | (142, 175) |
| $C_2H_5CH=CHCH_2Br$ (?) ......... | $Na_2S$ | M | (159, 165) |
| $CH_3OCH_2CH_2CH=CHCH_2Cl$ ... | NaSH in ethanol | $N(R_2S + RSH)$ | (515) |
| $C_4H_9CH=CHCH_2Br$ (?) ......... | $Na_2S$ | M | (165) |
| $C_2H_5OCH_2CH_2CH=CHCH_2Cl$... | NaSH in ethanol | $N(R_2S + RSH)$ | (515) |
| $C_2H_5OCH_2CH_2CHClCH=CH_2$.. | NaSH in ethanol | $R(R_2S + RSH)$ (?) | (515) |
| $C_4H_9OCH_2CH_2CH=CHCH_2Cl$... | NaSH in ethanol | $N(R_2S + RSH)$ | (515) |

† M indicates that a mixture of isomeric products was isolated. N means that only the normal substitution product was reported, and R means that only the product formed by allylic rearrangement is reported.

provides allylic esters and the derived alcohols from allylic halides, which are frequently prepared from starting materials other than the alcohols. The sequence of transformations secondary (or tertiary) allylic alcohol to primary halide to primary ester to primary alcohol, is a convenient and frequently used method of preparing primary allylic alcohols from the more readily available secondary and tertiary alcohols.

The conversion of an allylic halide into an allylic ester or mixture of esters may be effected in a number of ways. Perhaps the simplest is to solvolyze the halide in the appropriate carboxylic acid. Solvolysis reactions have two drawbacks from the synthetic point of view: they are frequently inconveniently slow, and they almost invariably give mixtures of isomeric allylic esters. Owing to the fact that carboxylic acids are fair ionizing solvents of very low nucleophilicity, most solvolysis reactions in carboxylic acids occur by the $S_N1$ mechanism.

By far the most common way of preparing esters from allylic halides is to allow the halide to react with a salt of the carboxylic acid in some suitable solvent. One widely used procedure is to heat the halide with a solution of the sodium or potassium salt of the acid in the acid itself. These reactions apparently involve simultaneous $S_N1$ and $S_N2$ substitution in many cases. Roberts, Young, and Winstein (539) found in a kinetic investigation that the reaction of crotyl chloride with potassium acetate or diphenylguanidinium acetate in acetic acid involves simultaneous unimolecular and bimolecular substitution. Meisenheimer and Beutter (418) reached the same conclusion in a study of the reaction of cinnamyl chloride with acetic acid solutions of several metal acetates. In general either
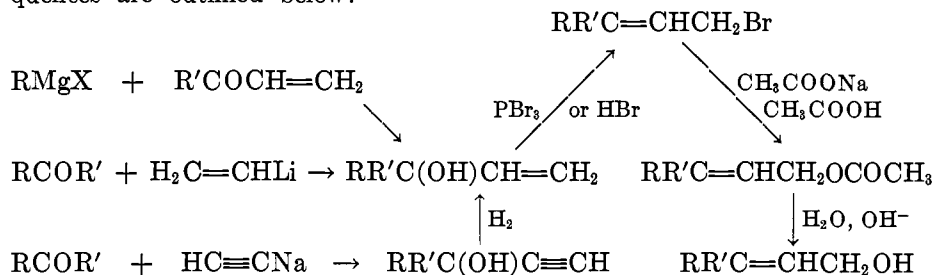
member of a pair of isomeric allylic chlorides yields a mixture of acetate esters when treated with sodium acetate in acetic acid; the primary chloride usually gives predominantly the primary acetate. Highly reactive primary chlorides (e.g., $\gamma,\gamma$-dimethylallyl chloride) and most secondary (539) and tertiary (694) chlorides react mainly by the $S_N1$ mechanism, and for these chlorides the presence of an acetate salt in the reaction mixture has little influence on either reaction rate or product composition. It is not possible to decide from the available evidence whether there is always a bimolecular component to the reactions involving primary chlorides, but the fact that mixtures of esters are obtained makes it probable that there is almost always a unimolecular component, especially since there is no well-authenticated case of an abnormal bimolecular displacement ($S_N2'$) with a primary chloride.

Allylic bromides behave somewhat differently from the related chlorides in reactions with acetate salts in acetic acid. Allylic bromides are so readily isomerized that unless special precautions are taken, an equilibrium mixture containing 80–90 per cent primary bromide and 10–20 per cent secondary (or tertiary) bromide is obtained, regardless of the structure of the starting material and the method of preparation (683). Yet, treatment of these mixtures with sodium or potassium acetate in acetic acid apparently gives only the primary acetate. No kinetic study of the reaction of allylic bromides with acetate ion in acetic acid has yet been reported, but if the numerous claims that only primary acetate is formed are correct, this result can be explained in at least two ways. First, the primary allylic bromide may react with acetate ion in acetic acid only by the $S_N2$ mechanism, while its secondary (or tertiary) isomer rearranges to primary bromide much more rapidly than it reacts with acetate ion or acetic acid. Alternatively, the primary bromide may undergo normal bimolecular substitution and the secondary or tertiary bromide react predominantly or entirely by the abnormal bimolecular mechanism, $S_N2'$. The former explanation seems the more reasonable, since it is well known that secondary and tertiary halides are much less reactive than their primary isomers by the bimolecular mechanism and that isomeric allylic bromides exist in mobile equilibrium (652). However, this explanation should be regarded as only tentative until a careful study of both the kinetics and products of such a reaction has been made.

The above mechanism has two interesting implications. It would appear that while bromides are more reactive than chlorides by both mechanism $S_N1$ and mechanism $S_N2$, the difference in reactivity is greater for bimolecular substitution than for unimolecular substitution. That is, it may be easier to effect normal substitution of an allylic bromide than of the chloride having the same skeletal structure. It also appears that secondary allylic bromides, like tertiary allylic chlorides (694), may undergo isomerization by ionization-internal return in acetic acid solution.

The conversion of secondary and tertiary allylic alcohols to bromides and the acetolysis of these bromides has found wide application in organic synthesis, particularly in the natural products field. Some of the possible synthetic se-

quences are outlined below:

$$RR'C{=}CHCH_2Br$$

$$RMgX \ + \ R'COCH{=}CH_2 \quad\quad\nearrow \quad \searrow CH_3COONa$$

$$PBr_3 \diagup \text{or HBr} \quad\quad CH_3COOH$$

$$RCOR' + H_2C{=}CHLi \rightarrow RR'C(OH)CH{=}CH_2 \quad RR'C{=}CHCH_2OCOCH_3$$

$$\uparrow H_2 \quad\quad\quad \downarrow H_2O, OH^-$$

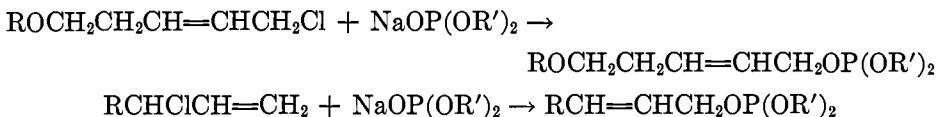$$RCOR' \ + \ HC{\equiv}CNa \ \rightarrow \ RR'C(OH)C{\equiv}CH \quad RR'C{=}CHCH_2OH$$

The reaction of acetate salts with primary and secondary allylic halides in solvents such as acetone, acetic anhydride, and ethanol gives only products of normal substitution. All of these solvents are less polar than acetic acid. For example, crotyl chloride gave only crotyl acetate upon reaction with potassium acetate in acetic anhydride, and $\alpha$-methylallyl acetate was the only product from the reaction of $\alpha$-methylallyl chloride with tetramethylammonium acetate in acetone (539). Goering, Nevitt, and Silversmith (224) found that optically active 5-methyl-2-cyclohexenyl chloride is converted to 5-methyl-2-cyclohexenyl acetate of inverted configuration by treatment with tetramethylammonium acetate in acetone solution. Reactions of other allylic chlorides with potassium acetate in alcohol and acetic anhydride have been reported to yield only normal products (20, 265). Allylic bromides yield primary acetates when allowed to react with sodium acetate in acetic anhydride or potassium acetate in acetone (136, 313, 389, 437, 558).

Allylic esters are also prepared by treating the halides with silver salts of carboxylic acids, using the acid, ether, benzene, or alcohol as solvent. Silver ion is a powerful electrophilic catalyst, and these reactions generally involve ionic intermediates, as indicated by the formation of mixtures of isomeric esters.

Table 25 lists reactions of unsymmetrically substituted allylic halides with carboxylic acids and their salts. For the sake of simplicity most reactions of allylic bromides are recorded in the table as involving the primary bromides; this is the claim usually made in the earlier literature. Actually, allylic bromides almost always consist of mixtures in which the primary isomer predominates.

*Phosphite esters:* Pudovik reports that primary and secondary alkoxychloropentenes, $\alpha$- and $\gamma$-methylallyl chloride, and 1,4-dichloro-2-butene react with sodium dialkylphosphites in ether and benzene solutions to give primary allylic dialkyl phosphites as the only isolable products (500, 504, 513, 514):

$$ROCH_2CH_2CH{=}CHCH_2Cl + NaOP(OR')_2 \rightarrow$$

$$ROCH_2CH_2CH{=}CHCH_2OP(OR')_2$$

$$RCHClCH{=}CH_2 + NaOP(OR')_2 \rightarrow RCH{=}CHCH_2OP(OR')_2$$

### 5. Conversion of allylic halides to amines

Ammonia and amines react with allylic halides to form allylic amines or quaternary ammonium salts. The product obtained depends on the halide, the amine, and the reaction conditions. Primary allylic halides usually yield normal substitution products in reactions with primary, secondary, and tertiary amines,

## TABLE 25

*Conversion of allylic halides to esters of carboxylic acids*

| Halide | Reaction Conditions | Product Composition† | References |
|---|---|---|---|
| $CH_2=CHCHCl_2$ | $CH_3COONa$ in $CH_3COOH$ | R (?) | (347) |
| $CHCl=CHCH_2Cl$ | $CH_3COONa$ in $CH_3COOH$ | N | (347) |
| $CHCl=CHCH_2Cl$ | $CH_2ClCOOAg$ in $(C_2H_5)_2O$ | N (?) | (127) |
| $CH_2=CHCHBr_2$ | | Rearranged p-nitro- benzoate | (351) |
| $CCl_2=CHCH_2Cl$ | $CH_2=CHCOONa$ in $C_2H_5OH$ | N | (373) |
| $CH_2=C=CHCH_2Cl$ | $CH_3COONa$ in $CH_3COOH$ | N | (113) |
| $CH_3CH=CHCH_2Cl$ | $CH_3COOK$ in $CH_3COOH$ | M | (46, 539, 573) |
| $CH_3CH=CHCH_2Cl$ | $CH_3COOAg$ in $CH_3COOH$ | M | (539) |
| $CH_3CH=CHCH_2Cl$ | $CH_3COO^-N(CH_3)_4^+$ in acetone | N | (539) |
| $CH_3CHClCH=CH_2$ | $CH_3COO^-N(CH_3)_4^+$ in acetone | N | (539) |
| $CH_3CHClCH=CH_2$ | $CH_3COOK$ in $CH_3COOH$ | M | (539) |
| $CH_3CHClCH=CH_2$ | $CH_3COOAg$ in $CH_3COOH$ | M | (539) |
| $CH_2=C=CHCH_2Br$ | $CH_3COONa$ in $CH_3COOH$ | N | (113) |
| $CH_3CH=CHCH_2Br$ | $CH_3COOK$ or $CH_3COONa$ in $CH_3COOH$ | N | (46, 208, 236) |
| $CH_3CH=CHCH_2Br$ | $(NO_2)_3C_6H_2COOAg$ | N (?) | (452, 631) |
| $CH_2ClCH=CHCH_2Cl$ | $CH_3COOK$ in $CH_3COOH$ | M | (504) |
| $CH_3CHClCH=CHCl$ | $CH_3COONa$ in $CH_3COOH$ | N | (338) |
| $CH_3CCl=CHCH_2Cl$ | $(NO_2)_3C_6H_2COOAg$ in $C_2H_5OH$ | N (?) | (245) |
| $CH_2=CHCHClCH_2Cl$ | $CH_3COOK$ in $CH_3COOH$ | M | (504) |
| $BrCH_2CH=CHCH_2Br$ | $CH_3COONa$ in $CH_3COOH$ | M | (481, 483, 619) |
| $BrCH_2CH=CHCH_2Br$ | $CH_3COOAg$ in $CH_3COOH$ | M | (238) |
| $CCl_2=C(CH_3)CH_2Cl$ | $CH_3COONa$ in $CH_3COOH$ | N | (345, 346) |
| $CCl_2=C(CH_3)CH_2Cl$ | Reflux in $CH_2=C(OC_2H_5)_2$ | Primary acetate | (370) |
| $CH_2=C(CH_3)CCl_3$ | $CH_3COONa$ in $CH_3COOH$ | R | (346) |
| $CH_2BrCH=CHCOOH$ | $CH_3COONa$ in $CH_3COOH$ | N | (524, 525) |
| $CH_2BrCH=CHCN$ | $CH_3COONa$ in $CH_3COOH$ | N | (524) |
| $C_2H_5CH=CHCH_2Cl$ | $CH_3COOK$ in $CH_3COOH$ | M | (47, 419, 490, 573) |
| $C_2H_5CH=CHCH_2Cl$ | $CH_3COOAg$ in $CH_3COOH$ | M | (419) |
| $C_2H_5CHClCH=CH_2$ | $CH_3COOAg$ in $CH_3COOH$ | M | (419) |
| $C_2H_5CHClCH=CH_2$ | $CH_3COOK$ in $CH_3COOH$ | M | (47, 419, 490, 573) |

## TABLE 25—*Continued*

| Halide | Reaction Conditions | Product Composition† | References |
|---|---|---|---|
| HC≡CCH=CHCH₂Cl................................ | CH₃COOK in CH₃OH | N | (265) |
| CH₂=CHCH=CHCH₂Cl (?)......................... | CH₃COONa in CH₃COOH | Primary acetate | (657) |
| (CH₃)₂C=CHCH₂Cl............................... | CH₃COONa in CH₃COOH | M | (438) |
| (CH₃)₂C=CHCH₂Cl............................... | RCOONa in RCOOH (R = H, C₂H₅, C₃H₇) | M | (446) |
| (CH₃)₂C=CHCH₂Cl............................... | CH₃COOAg in acetone | M | (633) |
| (CH₃)₂CClCH=CH₂............................... | CH₃COOAg in acetone | M | (633) |
| (CH₃)₂CClCH=CH₂............................... | CH₃COONa in CH₃COOH | M | (438) |
| C₂H₅CH=CHCH₂Br............................... | CH₃COONa or CH₃COOK in CH₃COOH | N | (70, 71, 72, 233) |
| (CH₃)₂C=CHCH₂Br.............................. | CH₃COOK in CH₃COOH | N | (384) |
| (CH₃)₂C=CHCH₂Br.............................. | CH₃COOAg in acetone | M | (633) |
| CH₃COOCH=CHCH₂Cl............................ | CH₃COONa in CH₃COOH | R | (339) |
| CH₂BrCH=CHCOOCH₃............................ | CH₃COONa in CH₃COOH | N | (524, 525) |
| CH₃CHBrCH=CHCH₂Br........................... | CH₃COONa in CH₃COOH | M | (486) |
| CH₂BrC(CH₃)=CHCH₂Br.......................... | CH₃COOK in CH₃COOH | N | (568) |
| Dibromocyclopentenes (?)......................... | CH₃COOAg in CH₃COOH | M | (466) |
| Dibromocyclopentenes (?)......................... | CH₃COO⁻N(CH₃)₄⁺ in acetone | M | (466) |
| Dibromocyclopentenes (?)......................... | CH₃COOK in CH₃COOH | M | (63, 466) |
| CH₃CH=CHCH=CHCH₂Cl.......................... | CH₃COOK in CH₃COOH | M | (443) |
| CH₃CH=CHCH=CHCH₂Cl.......................... | C₃H₇COOAg in ether | M | (528) |
| CH₃CHClCH=CHCH=CH₂.......................... | CH₃COOK in CH₃COOH | M | (443) |
| C₃H₇CH=CHCH₂Cl............................... | | M | (573) |
| C₃H₇CHClCH=CH₂............................... | | M | (573) |
| CH₃OCH₂CH₂CH=CHCH₂Cl........................ | CH₃COONa in CH₃COOH | M | (509) |
| CH₃OCH₂CH₂CHClCH=CH₂........................ | CH₃COONa in CH₃COOH | M | (509) |
| CH₂=CHCH₂CH=CHCH₂Br......................... | CH₃COOK in CH₃COOH | N | (16, 23) |
| CH₂=CHCH₂CH=CHCH₂Br (?)...................... | CH₃COOAg in CH₃COOH | N (?) | (366, 367) |
| C₃H₇CH=CHCH₂Br............................... | CH₃COOK in CH₃COOH | N | (71, 72, 237) |
| (CH₃)₂CHCH=CHCH₂Br........................... | CH₃COOK in CH₃COOH | N | (71) |
| CH₂BrCH=CHCOOC₂H₅........................... | CH₃COONa in CH₃COOH | N | (350) |
| CH₂=CHCHBrCOOC₂H₅........................... | CH₃COONa in CH₃COOH | R | (524) |
| CH₃CH=CHCCl=CHCH₂Cl......................... | HCOONa in HCOOH | M | (445) |
| CH₂BrCH=CHCH=CHCH₂Br........................ | CH₃COONa in (CH₃CO)₂O | N | (482) |
| CH₂BrCH=CHCH=CHCH₂Br........................ | CH₃COOAg in CH₃COOH | N (?) | (317) |
| CH₂BrC(CH₃)=C(CH₃)CH₂Br....................... | CH₃COOK in C₂H₅OH | N | (594) |
| CH₃CHBrCH=CHCHBrCH₃......................... | CH₃COONa in CH₃COOH | M | (486) |

TABLE 25—*Continued*
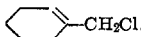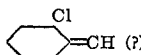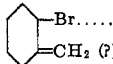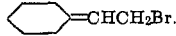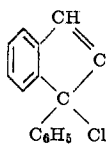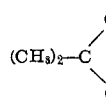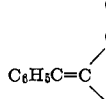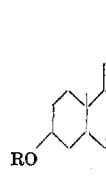
| Halide | Reaction Conditions | Product Composition† | References |
|---|---|---|---|
| Br⟨Cl⟩ (structure) | CH₃COOAg in CH₃COOH | N (?) | (431) |
| (CH₃)₂C=CHCCl=CHCH₂ | CH₃COOK in CH₃COOH | M | (441) |
| C₄H₉CH=CHCH₂Cl | | M | (573) |
| C₄H₉CHClCH=CH₂ | | M | (573) |
| C₃H₇C(CH₃)=CHCH₂Cl | CH₃COONa in CH₃COOH | M | (440) |
| C₃H₇C(CH₃)ClCH=CH₂ | CH₃COONa in CH₃COOH | M | (440) |
| ⟨structure⟩—CH₂Cl | CH₃COOK in (CH₃CO)₂O | N | (20) |
| ⟨Cl structure⟩=CH (?) | CH₃COOAg in CH₃COOH | Primary acetate | (432) |
| CH₃COOCH₂CH=C(CH₃)CH₂Cl | CH₃COOK in CH₃COOH | N | (464) |
| C₄H₉CH=CHCH₂Br | CH₃COOK in CH₃COOH | N | (71, 72) |
| C₂H₅C(CH₃)=C(CH₃)CH₂Br | CH₃COOK in acetone | N | (136) |
| ⟨structure⟩—Br =CH₂ (?) | CH₃COOAg in CH₃COOH | N (?) | (431) |
| CH₃⟨structure⟩Br (?) | CH₃COOAg in CH₃COOH | N (?) | (431) |
| (CH₃)₂C=CHCCl=CHCH₂Cl | HCOONa in HCOOH | N | (445) |
| C₅H₁₁CH=CHCH₂Cl | | M | (573) |
| C₅H₁₁CHClCH=CH₂ | | M | (573) |
| CH₃CH=CHCH₂CH₂CH=CHCH₂Br | C₆H₅COOAg in ether | N (?) | (228) |
| C₅H₁₁CH=CHCH₂Br | CH₃COOK in CH₃COOH | N | (232, 234) |
| ⟨structure⟩=CHCH₂Br | CH₃COOK in CH₃COOH | N | (178) |
| C₆H₅CH=CHCH₂Cl | CH₃COOAg | N (?) | (430, 618) |
| C₆H₅CH=CHCH₂Cl | CH₃COOAg in CH₃COOH | M | (419) |
| C₆H₅CH=CHCH₂Cl | CH₃COOK in CH₃COOH | M | (418, 419) |
| C₄H₉OCH₂CH₂CH=CHCH₂Cl | CH₃COONa in CH₃COOH | M | (189, 518) |
| C₄H₉OCH₂CH₂CH=CHCH₂Cl | CH₃COONa in CH₃CONH₂ | N | (189) |
| C₄H₉OCH₂CH₂CHClCH=CH₂ | CH₃COONa in CH₃COOH | M | (518) |
| C₆H₅CH=CHCH₂Br | CH₃COOK in CH₃COOH | N | (71, 72) |
| C₂H₅CH=CHCH₂CH₂CH=CHCH₂Br | C₆H₅COOAg in ether | N (?) | (282, 552, 596) |
| (CH₃)₂C=CHCH₂CH₂CH=CHCH₂Br | C₃H₅COOAg in ether | N (?) | (643) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)=CHCH₂Cl | CH₃COOK in C₂H₅OH | M | (182, 292) |
| ⟨structure⟩CH₂Cl (?) | CH₃COONa | N | (603) |

TABLE 25—*Concluded*

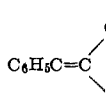| Halide | Reaction Conditions | Product Composition† | References |
|---|---|---|---|
| $(CH_3)_2CHCH_2OCH(CH_3)CH_2CH=CHCH_2Cl$............... | $CH_3COONa$ in $CH_3COOH$ | N | (189) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2Br$................ | $CH_3COOK$ in acetone | N | (389, 558) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2Br$................ | $CH_3COONa$ in $CH_3COOH$ | N | (485) |
| $n\text{-}C_7H_{15}CH=CHCH_2Br$................................... | $CH_3COOK$ in $CH_3COOH$ | N | (158) |
| $(CH_3)_2CH(CH_2)_3CH=C(CH_3)CH_2Br$...................... | $CH_3COOK$ in acetone | N | (558) |
| $CH_3CHClCH=CHC\equiv CCH=CHCHClCH_3$............... | $CH_3COOK$ in $CH_3OH$ | N | (265) |
| $(CH_3)_2C=C(CH_3)CH_2CH_2C(CH_3)=CHCH_2Br$............. | $CH_3COOK$ in acetone | N | (437) |
| $(CH_3)_2C=C(CH_3)CH_2CH_2C(CH_3)=CHCH_2Br$............. | $CH_5COONa$ in $CH_3COOH$ | N | (437) |
| $n\text{-}C_9H_{18}CH=CHCH_2Br$................................... | $CH_3COOK$ in $CH_3COOH$ | N | (158) |
| $C_9H_{16}CH=CHC(CH_3)=CHCH_2Br$........................ | $CH_3COONa$ in $CH_3COOH$ | N | (229) |
| $(CH_3)_2C=CHCH_2CH=C(CH_3)(CH_2)_3C(CH_3)=CHCH_2Br$.. | $CH_3COOK$ in $CH_3COOH$ | N | (549) |
| $CH_3[CH(CH_3)CH_2CH_2CH_2]_3C(CH_3)=CHCH_2Br$........... | $CH_3COOK$ in acetone | N | (313) |
| $CH_3[C(CH_3)=CHCH_2CH_2]_3C(CH_3)=CHCH_2Br$........... | $CH_3COOK$ in $CH_3COOH$ | N | (549) |
| "$RCH=CHCH_2Cl$"....................................... | $CH_3COONa$ in $CH_3COOH$ | N (?) | (488) |
| "$RCH=CHCH_2Cl$"....................................... | $CH_5COONa$ in $CH_3COOH$ | R (?) | (488) |
| "$RCHClCH=CH_2$"....................................... | $CH_3COOK$ in $CH_3COOH$ | N | (73) |



| | CH₃COOAg in CH₃COOH | R | (104) |



| | CH₃COOAg in CH₃COOH | N | (106) |



| | CH₃COOAg in CH₃COOH | N | (103) |



| | CH₃COOAg in CH₃COOH | N | (103) |



| | CH₃COOK in acetone | N | (554) |



| | CH₃COOK in acetone | N | (551) |

† M indicates that a mixture of isomeric products was isolated, N means that only the normal substitution product was reported, and R means that only the product formed by allylic rearrangement is reported.

and these reactions probably occur by the $S_N2$ mechanism. The initial products of reactions of allylic halides with ammonia, primary amines, and secondary amines are amines themselves and can therefore react with the halide; for this reason, di- and triallylated products are sometimes isolated from reaction mixtures.

Secondary allylic halides usually give at least some product in which the structure of the allylic group has been inverted. Secondary amines seem to form rearranged products exclusively in reactions with secondary allylic halides (303, 419, 692). It has been demonstrated that the abnormal substitution products from reactions of diethylamine and trimethylamine with α-methylallyl chloride are formed by bimolecular reactions (665, 666, 692). This is convincing proof that the $S_N2'$ mechanism is involved in these displacements (page 770) and strongly indicates that abnormal bimolecular displacements are responsible for formation of rearranged products in other reactions of amines with secondary halides.

A particularly interesting example of the displacement of allylic halogen atoms by secondary amines is the reaction of the isomeric cyclopentadiene dibromides with dimethylamine. Most workers report obtaining a solid and a liquid dibromide from the addition of bromine to cyclopentadiene. These were long thought to be trans- and cis-3,5-dibromocyclopentene, respectively (602). It has recently been found that the solid dibromide is cis-3,5-dibromocyclopentene (I), while the liquid is a mixture consisting largely of trans-3,4-dibromocyclopentene (II) (241). Cope, Estes, Emery, and Haven (140) found that the solid and liquid dibromides are converted to the same product, trans-1,2-bis(dimethylamino)cyclopentene (III), when allowed to react with dimethylamine in benzene solution. The processes by which this compound could reasonably be formed from I and II are shown below.
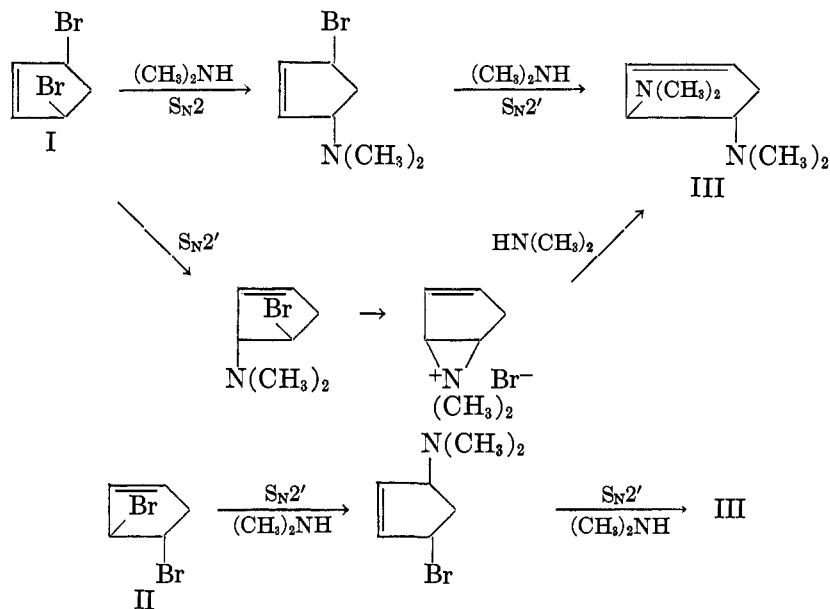
TABLE 26

*Conversion of allylic halides to amines*

| Halide | Amine and Reaction Conditions | Products | References |
|---|---|---|---|
| CHCl=CHCH₂Cl | (C₂H₅)₂NH | CHCl=CHCH₂N(C₂H₅)₂ | (296, 347) |
| CHCl=CHCH₂Cl | (C₂H₅)₃N | CHCl=CHCH₂N(C₂H₅)₃⁺Cl⁻ | (296) |
| CHCl=CHCH₂Cl | NH₃ in C₂H₅OH | (CHCl=CHCH₂)₂NH + (CHCl=CHCH₂)₃N | (127) |
| CH₂=CHCCl₃ | (C₂H₅)₂NH in CH₂OH | (C₂H₅)₂NCH₂CH=CCl₂ | (451) |
| CH₃CH=CHCH₂Cl | (CH₃)₃N | CH₃CH=CHCH₂N(CH₃)₃⁺Cl⁻ | (665, 666) |
| CH₃CH=CHCH₂Cl | C₆H₅NHCH₃ | CH₃CH=CHCH₂N(CH₃)C₆H₅ | (357) |
| CH₃CH=CHCH₂Cl | (C₂H₅)₂NH in C₆H₆ | CH₃CH=CHCH₂N(C₂H₅)₂ | (692) |
| CH₃CH=CHCH₂Cl | (C₂H₅)₃N in C₆H₆ | CH₃CH=CHCH₂H(C₂H₅)₃⁺Cl⁻ | (692) |
| CH₃CHClCH=CH₂ | (C₂H₅)₃N in C₆H₆ | CH₃CH=CHCH₂H(C₂H₅)₃⁺Cl⁻ | (692) |
| CH₃CHClCH=CH₂ | (C₂H₅)₂NH in C₆H₆ | CH₃CH=CHCH₂H(C₂H₅)₂ | (692) |
| CH₃CHClCH=CH₂ | (CH₃)₃N in acetone | CH₃CH[N(CH₃)₃⁺Cl⁻]CH=CH₂ + CH₃CH=CHCH₂N(CH₃)₃⁺Cl⁻ | (665, 666) |
| CH₂=CHCHClCH₂OH | (C₂H₅)₂NH | (C₂H₅)₂NCH₂CH=CHCH₂OH | (62) |
| CH₃CH=CHCH₂Br (?) | (CH₃)₃N | CH₃CH=CHCH₂N(CH₃)₃⁺Br⁻ | (95) |
| CH₃CH=CHCH₂Br (?) | C₆H₅NHCH₃ | CH₃CH=CHCH₂N(CH₃)C₆H₅ | (95) |
| CH₃CCl=CHCH₂Cl | NH₃ (liquid, 100°C.) | RNH₂ + R₂NH + R₃N | (642) |
| CH₃CCl=CHCH₂Cl | C₅H₁₀NH | CH₃CCl=CHCH₂NC₅H₁₀ | (642) |
| CH₃CCl=CHCH₂Cl | CH₃NH₂ | (CH₃CCl=CHCH₂)₂NCH₃ | (608, 642) |
| CH₃CCl=CHCH₂Cl | (CH₃CCl=CHCH₂)₃N | (CH₃CCl=CHCH₂)₄N⁺Cl⁻ | (642) |
| CH₃CCl=CHCH₂Cl | NH₃ | CH₃CCl=CHCH₂NH₂ | (608) |
| CH₃CCl=CHCH₂Cl | (CH₃)₂NH | CH₃CCl=CHCH₂N(CH₃)₂ | (608) |
| CH₃CCl=CHCH₂Cl | (C₂H₅)₂NH | CH₃CCl=CHCH₂N(C₂H₅)₂ | (608) |
| CH₂ClCH=CHCH₂Cl | NH₃ | H₂NCH₂CH=CHCH₂NH₂ | (8) |
| C₂H₅CH=CHCH₂Cl | (CH₃)₂NH | C₂H₅CH=CHCH₂N(CH₃)₂ | (567) |
| C₂H₅CH=CHCH₂Cl | C₆H₅NHCH₃ | C₂H₅CH=CHCH₂N(CH₃)C₆H₅ | (419) |
| C₂H₅CH=CHCH₂Cl | (C₂H₅)₂NH | C₂H₅CH=CHCH₂N(C₂H₅)₂ | (419) |
| C₂H₅CHClCH=CH₂ | (C₂H₅)₂NH | C₂H₅CH=CHCH₂N(C₂H₅)₂ | (419) |
| C₂H₅CHClCH=CH₂ | C₆H₅NHCH₃ | C₂H₅CH=CHCH₂N(CH₃)C₆H₅ | (419) |
| (CH₃)₂C=CHCH₂Cl | C₆H₅NH₂ | (CH₃)₂C=CHCH₂NHC₆H₅ | (446) |
| (CH₃)₂C=CHCH₂Cl | (C₂H₅)₂NH | (CH₃)₂C=CHCH₂N(C₂H₅)₂ | (446) |
| (CH₃)₂C=CHCH₂Cl | C₅H₁₀NH | (CH₃)₂C=CHCH₂NC₅H₁₀ | (446) |
| cis-CHBrCH=CHCHBrCH₂ ‾‾‾‾‾‾ | (CH₃)₂NH in C₆H₆ | trans-CH[N(CH₃)₂]CH[N(CH₃)₂]CH=CHCH₃ ‾‾‾‾‾‾ | (140) |
| trans-CHBrCHBrCH=CHCH₂ ‾‾‾‾ | (CH₃)₂NH in C₆H₆ | trans-CH[N(CH₃)₂]CH[N(CH₃)₂]CH=CHCH₃ ‾‾‾‾‾‾ | (140) |
| CH₃CHClCH=CHC≡CH | NH₃ | CH₃CH(NH₂)CH=CHC≡CH | (303) |

| | | | |
|---|---|---|---|
| CH₃CHClCH=CHC≡CH | C₂H₅NH₂ | CH₃CH(NHC₂H₅)CH=CHC≡CH | (303) |
| CH₃CHClCH=CHC≡CH | C₆H₅NH₂ | CH₃CH(NHC₆H₅)CH=CHC≡CH | (303) |
| CH₃CHClCH=CHC≡CH | (C₂H₅)₂NH | CH₃CH=CHCH[N(C₂H₅)₂]C≡CH | (303) |
| CH₃OCH₂CH₂CH=CHCH₂Cl | R₂NH(R=H, CH₃, C₂H₅) | CH₃OCH₂CH₂CH=CHCH₂NR₂ | (6, 506) |
| CH₃OCH₂CH₂CH=CHCH₂Cl | C₆H₅NHC₂H₅ | CH₃OCH₂CH₂CH=CHCH₂NRR′ | (506) |
| CH₃OCH₂CH₂CH=CHCH₂Cl | C₆H₅NH₂ | CH₃OCH₂CH₂CH=CHCH₂NHC₆H₅ | (506) |
| CH₃OCH₂CH₂CHClCH=CH₂ | (CH₃)₂NH | CH₃OCH₂CH₂CH[N(CH₃)₂]CH=CH₂ (?) | (6) |
| CH₃OCH₂CH₂CHClCH=CH₂ | (C₂H₅)₂NH | CH₃OCH₂CH₂CH=CHCH₂NR₂ | (506) |
| CH₃OCH₂CH₂CHClCH=CH₂ | C₆H₅NHC₂H₅ | CH₃OCH₂CH₂CH=CHCH₂NR₂ | (506) |
| CH₃OCH₂CH₂CHClCH=CH₂ | C₆H₅NH₂ | CH₃OCH₂CH₂CH(NHC₆H₅)CH=CH₂ + CH₃OCH₂CH₂CH=CHCH₂NHC₆H₅ | (506) |
| CH₃OCH₂CH₂CHClCH=CH₂ | (CH₃)₂NH in hexane | CH₃OCH₂CH₂CH=CHCH₂N(CH₃)₂ | (7) |
| (CH₃)₂C=C(CH₃)CH₂Br | C₆H₅NH₂ in ether | C₆H₅N[CH₂C(CH₃)=C(CH₃)₂]₂ | (129) |
| CH₂BrCH=CHCOOC₂H₅ | (C₂H₅)₂NH | (C₂H₅)₂NCH₂CH=CHCOOC₂H₅ | (525) |
| (+)-C₄H₉CHClCH=CH₂ | NH₃ in methanol | (−)-C₄H₉CH(NH₂)CH=CH₂ | (395) |
| C₂H₅OCH₂CH=CHCH₂Cl | C₄H₉NH₂ | C₂H₅OCH₂CH₂CH=CHCH₂NHC₄H₉ | (189, 191) |
| C₂H₅OCH₂CH₂CHClCH=CH₂ | C₄H₉NH₂ | C₂H₅OCH₂CH₂CH(NHC₄H₉)CH=CH₂ | (189) |
| (CH₃)₂CHOCH₂CH₂CH=CHCH₂Cl | (C₂H₅)₂NH | (CH₃)₂CHOCH₂CH₂CH=CHCH₂N(C₂H₅)₂ | (506) |
| (CH₃)₂CHOCH₂CH₂CHClCH=CH₂ | (C₂H₅)₂NH | (CH₃)₂CHOCH₂CH₂CH=CHCH₂N(C₂H₅)₂ | (506) |
| C₆H₅CH=CHCH₂Cl | C₆H₅NHCH₃ | C₆H₅CH=CHCH₂N(CH₃)C₆H₅ | (357) |
| C₆H₅CH=CHCH₂Cl | C₂H₅NH₂ | C₆H₅CH=CHCH₂NHC₂H₅ | (419) |
| C₆H₅CH=CHCH₂Cl | C₆H₅N | C₆H₅CH=CHCH₂NC₅H₅⁺Cl⁻ | (130, 355) |
| C₆H₅CH=CHCH₂Cl | (CH₃)₂NR | C₆H₅CH=CHCH₂N(CH₃)₂R⁺Cl⁻ | (148) |
| CH₂ClCH=CHC≡CC₄H₉ | (C₂H₅)₂NH | (C₂H₅)₂NCH₂CH=CHC≡CC₄H₉ | (303) |
| C₄H₉OCH₂CH₂CH=CHCH₂Cl | C₄H₉NH₂ | C₄H₉OCH₂CH₂CH=CHCH₂NHC₄H₉ | (189) |
| C₄H₉OCH₂CH₂CH=CHCH₂Cl | (C₂H₅)₂N | C₄H₉OCH₂CH₂CH=CHCH₂N(C₂H₅)₂ | (506) |
| C₄H₉OCH₂CH₂CHClCH=CH₂ | (C₂H₅)₂NH | C₄H₉OCH₂CH₂CH=CHCH₂N(C₂H₅)₂ | (506) |
| C₄H₉OCH₂CH₂CHClCH=CH₂ | C₄H₉NH₂ | C₄H₉OCH₂CH₂CH(NHC₄H₉)CH=CH₂ | (189) |
| CH₃CHClCH=CHC≡CC₄H₉ | (C₂H₅)₂NH | CH₃CH=CHCH[N(C₂H₅)₂]C≡CC₄H₉ | (303) |
| (CH₃CHClCH=CHC≡)₂ | (C₂H₅)₂NH | [CH₃CH=CHCH[N(C₂H₅)₂]C≡]₂ | (303) |
| (CH₃CHClCH=CHC≡)₂ | CH₃NH₂, C₂H₅NH₂ | [CH₃CH(NHR)CH=CHC≡]₂ | (303) |
| CH₃CHClCH=CHC≡CC(CH₃)=CHCH₃ | CH₃NH₂, C₂H₅NH₂ | CH₃CH=CHCH[N(C₂H₅)₂]C≡CC(CH₃)=CHCH₃ | (303) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)=CHCH₂Cl | NaNH₂ in liquid NH₃ | (CH₃)₂C=CHCH₂CH₂C(CH₃)=CHCH₂NH₂ | (330) |

It is more likely that the first step in the reaction of I with dimethylamine is an $S_N2$ reaction than an $S_N2'$ reaction, since the only $S_N2'$ reaction which would lead to the observed final product would involve a *trans* relationship between the entering amine molecule and the leaving halide ion. There are theoretical reasons for believing that this steric course is unlikely in reactions of secondary amines with halides.

Allylic amines having primary amino groups are not conveniently prepared by direct reaction of the halides with ammonia, since mixtures of products are usually obtained. Pure amines of this type are usually prepared by treating the halides with potassium phthalimide, a thiocyanate salt, hexamethylenetetramine, or an alkali azide. The resulting phthalimido, isothiocyano, hexamino, or azido derivatives are then reduced or hydrolyzed to the desired amine. These reactions are discussed elsewhere.

Reactions of allylic halides with amines may be carried out in a solvent such as benzene, acetone, alcohol, or petroleum ether. Usually the reactants are simply mixed together.

Table 26 lists reactions of unsymmetrically substituted allylic halides with ammonia and amines.

### 6. Conversion of allylic halides to nitriles

Allylic halides react with cyanide ion to form $\alpha,\beta$-unsaturated nitriles:

$$\begin{array}{c} \diagdown \\ \diagup \end{array} C{=}\overset{|}{C}{-}\overset{|}{C}{-}X \ + \ CN^- \ \rightarrow \ \begin{array}{c} \diagdown \\ \diagup \end{array} C{=}\overset{|}{C}{-}\overset{|}{C}{-}CN \ + \ X^-$$
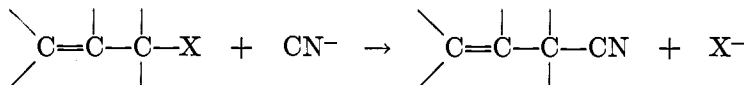
Sodium cyanide, potassium cyanide, cuprous cyanide, and hydrogen cyanide have been used as sources of cyanide ion. Cuprous cyanide is the most frequently used reagent for this conversion. Its effectiveness is probably due in part to the fact that cuprous ion is a good electrophilic catalyst and promotes unimolecular displacement reactions of halides.

The reactions are usually carried out by heating the allylic halide with a slight excess of the cyanide salt. However, water, alcohol, benzene, and acetonitrile have been used as solvents or diluents for one or both of the reactants.

Primary halides give mainly or entirely normal substitution products in reactions with cyanides. The kinetics of such a reaction has not been investigated, but bimolecular substitution ($S_N2$) is a reasonable mechanism for the reactions using sodium and potassium cyanide as the source of cyanide ion. It has been reported that the nucleophilicity of $CN^-$ toward carbon is greater than that of $OH^-$ (264). In the few cases where products of reaction of allylic halides with cuprous cyanide have been carefully examined, however, they were found to consist of mixtures of isomeric nitriles in which the product of substitution at the primary atom of the allylic system predominated (161, 165, 307). Lane, Fentress, and Sherwood (377) found that $\alpha$- and $\gamma$-methylallyl chlorides yield identical mixtures of nitriles in reactions with cuprous cyanide. The interpretation of this result is complicated by the fact that the chlorides isomerize under the conditions of the substitution reaction, but it seems likely that the $S_N1$-type mechanism is involved in reactions with cuprous cyanide.

TABLE 27

*Conversion of allylic halides to nitriles*

| Halide | Reaction Conditions | Product | References |
|---|---|---|---|
| CHCl=CHCH₂Cl | Cu₂⁺⁺ + HCN | CHCl=CHCH₂CN | (372) |
| CH₂=CHCCl₃ | Cu₂(CN)₂ | CCl₂=CHCH₂CN | (451) |
| CCl₂=CHCH₂Cl | Cu₂(CN)₂ | CCl₂=CHCH₂CN | (451) |
| CH₃CH=CHCH₂Cl | Cu₂(CN)₂ | CH₃CH=CHCH₂CN (mostly) + CH₃CH(CN)CH=CH₂ | (377) |
| CH₃CHClCH=CH₂ | Cu₂(CN)₂ | CH₃CH=CHCH₂CN (mostly) + CH₃CH(CN)CH=CH₂ | (377) |
| CH₃CH=CHCH₂Br | Aqueous KCN | CH₃CH=CHCH₂CN | (526) |
| CH₃CH=CHCH₂Br | Cu₂(CN)₂ | CH₃CH=CHCH₂CN (?) | (157, 163, 164) |
| CH₃CH=CClCH₂Cl (?) | HCN + Cu₂X₂ | NCCH₂CH=CHCH₂CN | (302) |
| CHCl=C(CH₃)CH₂Cl | Cu₂(CN)₂ | CHCl=C(CH₃)CH₂CN | (429) |
| CH₂ClCH=CHCH₂Cl | Cu₂(CN)₂ + aqueous HX | NCCH₂CH=CHCH₂CN | (371) |
| CH₂ClCH=CHCH₂Cl | NaCN in aqueous C₂H₅OH | NCCH₂CH=CHCH₂CN | (627) |
| CH₂ClCH=CHCH₂Cl | NaCN + CH₃CN, Cu₂Cl₂ | NCCH₂CH=CHCH₂CN | (293) |
| CH₂ClCH=CHCH₂Cl | HCN + CaCO₃ + CuBr₂ | CH₂ClCH=CHCH₂CN | (498) |
| CH₂ClCH=CHCH₂Cl | HCN + Cu₂(CN)₂ + CaCO₃ + H₂O | NCCH₂CH=CHCH₂CN | (198) |
| CH₂ClCH=CHCH₂Cl | NaCN + Cu + HCl + H₂O | NCCH₂CH=CHCH₂CN | (635) |
| CH₂BrCH=CHCH₂Br | Cu₂(CN)₂ + xylene | NCCH₂CH=CHCH₂CN | (697) |
| (CH₃)₂C=CHCH₂Cl | Cu₂(CN)₂ in C₆H₆ | (CH₃)₂C=CHCH₂CN | (610) |
| (CH₃)₂C=CHCH₂Cl | Aqueous KCN | (CH₃)₂C=CHCH₂CN | (446) |
| (CH₃)₂CClCH=CH₂ | Cu₂(CN)₂ in C₆H₅ | (CH₃)₂C=CHCH₂CN | (610) |
| C₂H₅CH=CHCH₂Br | Cu₂(CN)₂ or aqueous NaCN | C₂H₅CH=CHCH₂CN | (163, 164, 165, 167) |
| (CH₃)₂C=CHCH₂Br | Aqueous KCN | (CH₃)₂C=CHCH₂CN | (526) |
| CH₃CH=CHCH=CHCH₂Cl | Aqueous KCN | CH₃CH=CHCH=CHCH₂CN | (528) |
| C₃H₇CH=CHCH₂Br | Cu₂(CN)₂ | RCH(CN)CH=CH₂ + RCH=CHCH₂CN | (157, 163, 164) |
| (CH₃)₂CHCH=CHCH₂Br | Cu₂(CN)₂ | RCH(CN)CH=CH₂ + RCH=CHCH₂CN | (157, 163, 164) |
| C₄H₉CH=CHCH₂Br | Cu₂(CN)₂ | RCH(CN)CH=CH₂ + RCH=CHCH₂CN | (162, 163, 164, 165, 167) |
| C₄H₉CH=CHCH₂Br | Aqueous NaCN | RCH(CN)CH=CH₂ + RCH=CHCH₂CN | (165) |
| C₅H₁₁CH=CHCH₂Br | Cu₂(CN)₂ | RCH(CN)CH=CH₂ + RCH=CHCH₂CN | (157, 163, 164) |
| C₆H₁₃CH=CHCH₂Br | Cu₂(CN)₂ | RCH(CN)CH=CH₂ + RCH=CHCH₂CN | (157, 163, 164) |
| C₇H₁₅CH=CHCH₂Br | Cu₂(CN)₂ | RCH(CN)CH=CH₂ + RCH=CHCH₂CN | (157, 159, 163, 164) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)=CHCH₂Cl | Cu₂(CN)₂ | (CH₃)₂C=CHCH₂CH₂C(CH₃)C=CHCH₂CN | (37) |
| (CH₂ClCH=CHCH₂CH₂)₂O | | (NCCH₂CH=CHCH₂CH₂)₂O | (454) |
| C₈H₁₇CH=CHCH₂Br | Cu₂(CN)₂ | RCH=CHCH₂CN + RCH(CN)CH=CH₂ | (157, 163, 164) |
| C₉H₁₉CH=CHCH₂Br | Cu₂(CN)₂ | RCH=CHCH₂CN + RCH(CN)CH=CH₂ | (157, 159, 163, 164) |
| C₁₂H₂₅CH=CHCH₂Br | Cu₂(CN)₂ | RCH=CHCH₂CN + RCH(CN)CH=CH₂ | (157, 163, 164) |

Reactions of cyanides with allylic halides obtained by addition of halogen to conjugated dienes give dinitriles, which can be hydrolyzed to dicarboxylic acids. The frequency with which such reactions are reported in the patent literature is due to the potential or actual value of the dinitriles and derived compounds as precursors of monomers for the manufacture of synthetic polymers.

It seems more profitable to view the products of reactions of allylic halides with cyanides as unsaturated nitriles rather than as allylic cyanides, since no reactions have been reported in which the cyanide radical is displaced to give back an allylic compound.

Table 27 lists reactions of unsymmetrically substituted allylic halides with cyanides. The allylic bromides referred to were probably equilibrium mixtures rather than primary bromides as claimed. All reactions using $Cu_2(CN)_2$ probably gave mixtures of isomeric nitriles rather than only the product of primary substitution sometimes claimed.

### 7. Reaction of allylic halides with thiocyanate ion

Sodium, potassium, and ammonium thiocyanates react with allylic halides in alcoholic solution to form allylic thiocyanates. Primary and secondary halides appear to react exclusively by the $S_N2$ mechanism:

$$RCH{=}CHCHXR' \xrightarrow{\ SCN^-\ } RCH{=}CHCH(SCN)R'$$
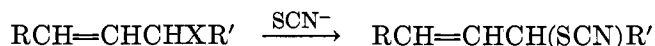
This reaction is of interest because it affords an unambiguous synthetic route to allylic amines with primary amino groups. Most allylic thiocyanates undergo intramolecular rearrangement on heating to isothiocyanates in which the structure of the allylic system has been inverted. The isothiocyanates are converted to allylic amines by treatment with strong mineral acid.

$$\underset{\underset{N{\equiv}CS}{|}}{RCH{=}CHCHR'} \xrightarrow{\ heat\ } \underset{\underset{N{=}C{=}S}{|}}{RCHCH{=}CHR'} \xrightarrow{\ H^+,\ H_2O\ } \underset{\underset{NH_2}{|}}{RCHCH{=}CHR'}$$
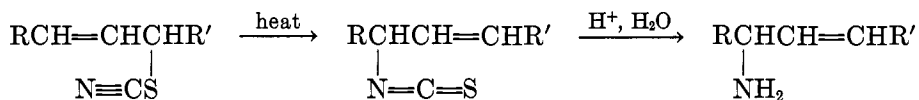
This sequence of reactions provides a route to $\alpha$-substituted allylic primary amines, compounds which are otherwise difficult to prepare. The hydrolysis

TABLE 28

*Reactions of allylic halides with thiocyanate ion*

| Halide | Reaction Conditions | References |
|---|---|---|
| CHCl=CHCH$_2$Cl | KSCN in ethanol | (127) |
| CH$_3$CH=CHCH$_2$Cl | KSCN or NH$_4$SCN in ethanol | (362) |
| CH$_3$CH=CHCH$_2$Cl | NH$_4$SCN in acetone | (692, 666) |
| CH$_3$CH=CHCH$_2$Br | NH$_4$SCN in ethanol | (95, 434, 630) |
| CH$_3$CCl=CHCH$_2$Cl | NH$_4$SCN in ethanol | (499) |
| CH$_3$CCl=CHCH$_2$Br | NH$_4$SCN in methanol | (471) |
| C$_2$H$_5$CH=CHCH$_2$Br | NH$_4$SCN in ethanol | (123) |
| (CH$_3$)$_2$C=CHCH$_2$Br | KSCN in ethanol | (592) |
| CH$_2$=C(CH$_3$)CHClC$_2$H$_5$ (?) | NaSCN in methanol | (96) |
| CH$_3$OCH$_2$CH$_2$CH=CHCH$_2$Cl | NH$_4$SCN in ethanol | (189, 190) |
| CH$_3$OCH$_2$CH$_2$CHClCH=CH$_2$ | NH$_4$SCN in ethanol | (189, 190) |
| C$_4$H$_9$OCH$_2$CH$_2$CH=CHCH$_2$Cl | NH$_4$SCN in ethanol | (189, 190) |
| C$_4$H$_9$OCH$_2$CH$_2$CHClCH=CH$_2$ | NH$_4$SCN in ethanol | (189, 190) |

of the isothiocyanate requires drastic conditions, however, and frequently gives low yields of amine.

$\alpha$-Methylallyl isothiocyanate is smoothly reduced by lithium aluminum hydride to $N$-methyl-$\alpha$-methylallylamine (666).

Table 28 lists reactions of unsymmetrically substituted allylic halides with thiocyanate ion. No thiocyanates of rearranged allylic structure were reported for any of the reactions listed.

### 8. Reactions of allylic halides with potassium phthalimide

Normal substitution products are obtained from reactions of primary and secondary allylic halides with potassium phthalimide (Gabriel's phthalimide synthesis). The reaction has been carried out by simply heating the reactants together, and also using methanol or dimethylformamide as a solvent. Hydrolysis of the resulting $N$-allylphthalimides yields allylic primary amines:
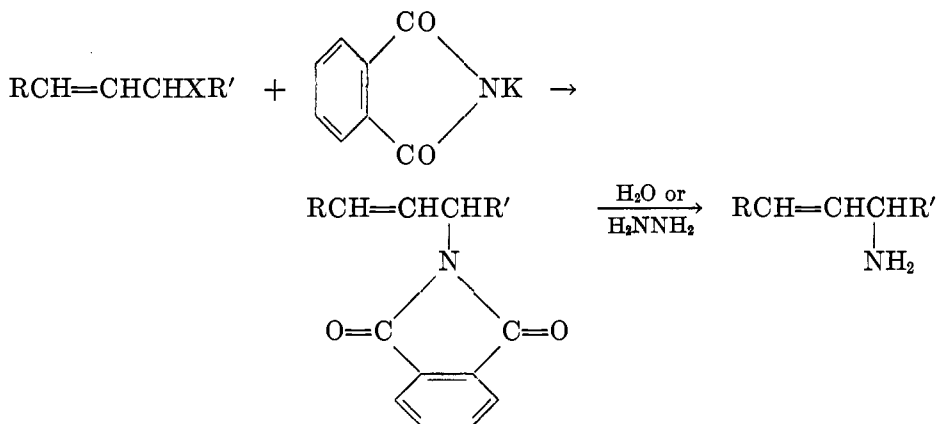


Hydrazine is a superior reagent for converting the phthalimides to amines. The Gabriel synthesis usually gives excellent yields of amines from primary allylic halides, low yields of amines from secondary halides, and poor or negligible yields of amines from tertiary halides. $\alpha,\alpha$-Dimethylallyl chloride, upon treatment with potassium phthalimide, gave a very low yield of $N$-($\gamma,\gamma$-dimethylallyl) phthalimide, much phthalimide and unsaturated hydrocarbon (presumably isoprene), but no $N$-($\alpha,\alpha$-dimethylallyl)phthalimide (569).

TABLE 29

*Reactions of allylic halides with potassium phthalimide*

| Halide | Reaction Conditions | References |
|---|---|---|
| CH₃CH=CHCH₂Cl (*cis* and *trans*) | C₈H₄O₂NK in (CH₃)₂NCHO | (152, 195, 353, 537, 690) |
| CH₃CHClCH=CH₂ | C₈H₄O₂NK in (CH₃)₂ NCHO | (152, 195, 537, 690) |
| CH₃CH=CHCH₂Br | | (354) |
| CH₂ClCH=CHCH₂Cl | C₈H₄O₂NK + K₂CO₃ | (8) |
| CH₂BrCH=CHCH₂Br | C₈H₄O₂NK in CH₃OH | (379) |
| C₂H₅CH=CHCH₂Cl | C₈H₄O₂NK | (419) |
| C₂H₅CHClCH=CH₂ | C₈H₄O₂NK | (419) |
| (CH₃)₂C=CHCH₂Cl | C₈H₄O₂NK | (690) |

Reactions of unsymmetrically substituted allylic halides with potassium phthalimide are listed in table 29.

### 9. Reaction of allylic halides with thiourea: preparation of thiols

Primary allylic halides react with thiourea in ethanol solution to form thiuronium halide salts, which are hydrolyzed to thiols by aqueous alkali.

$$RR'C{=}CHCH_2X \; + \; SC(NH_2)_2 \; \rightarrow$$

$$RR'C{=}CHCH_2S(NH_2)_2{}^+X^- \; \xrightarrow{\text{H}_2\text{O, OH}^-} \; RR'C{=}CHCH_2SH$$
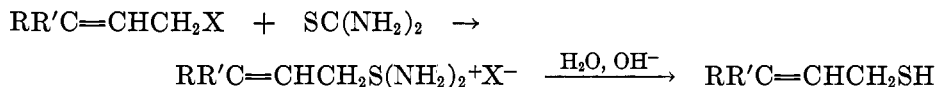
This reaction has been carried out using cis- and trans-γ-methylallyl bromides (59), γ-phenylallyl bromide, β,γ-diphenylallyl bromide (410), and 1,3-dichloro-2-butene (499). The kinetics of reactions of butenyl and pentenyl halides with thiourea in acetone solution has been studied (543). The reactions of α- and γ-methylallyl chlorides and γ,γ-dimethylallyl chloride were second order and gave normal substitution products. The reaction of α,α-dimethylallyl chloride with thiourea in acetone is second order also, but rearranged products are formed, probably owing to operation of the $S_N2'$ mechanism.

### 10. Reaction of allylic halides with hexamethylenetetramine: conversion of halides to aldehydes and primary amines

The Sommelet (577) aldehyde synthesis is applicable to primary allylic halides. Delaby (156, 158, 159, 160) found that reactions of a number of allylic bromides with hexamethylenetetramine yield quaternary salts which are hydrolyzed in neutral aqueous solution to α,β-unsaturated aldehydes:

$$RCH{=}CHCH_2Br \; + \; (CH_2)_6N_4 \; \rightarrow$$

$$RCH{=}CHCH_2\overset{+}{N}N_3(CH_2)_6Cl^- \; \xrightarrow{\text{H}_2\text{O}} \; RCH{=}CHCHO$$
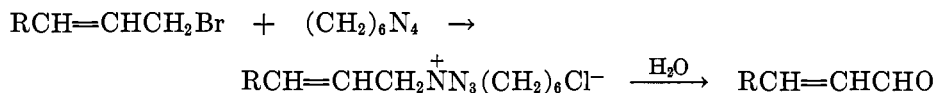
The mechanism of this interesting reaction has recently been reinvestigated (13).

If the quaternary salts are hydrolyzed in acidic rather than neutral solution, primary amines result. Supniewski (592) prepared γ,γ-dimethylallylamine from the bromide by this method.

### 11. Reaction of allylic chlorides with azide ion

Primary and secondary allylic chlorides appear to undergo normal bimolecular substitution by azide ion in aqueous ethanol and aqueous methanol, although the general applicability of the reaction has not been tested. Thus, geranyl chloride, $(CH_3)_2C{=}CHCH_2CH_2C(CH_3){=}CHCH_2Cl$, reacts with sodium azide in aqueous methanol or ethanol to form geranyl azide, which can be reduced to geranylamine (205, 593). (−)-α-Butylallyl azide is formed in the reaction of (+)-α-butylallyl chloride with aqueous ethanolic sodium azide (395).

### 12. Reaction of allylic halides with halide ions: non-isomeric exchange reactions

Allylic chlorides undergo bimolecular displacement reactions with potassium iodide in acetone. The kinetics of this reaction has been studied for a number of

chlorides by Hatch and coworkers (table 1), who do not report isolating the allylic iodides formed by the reaction. It is probable that primary and secondary chlorides react by the $S_N2$ mechanism, although $S_N2'$ reactions are not unlikely for sterically hindered chlorides. The iodides, even if isolated, would probably be too labile to permit conclusions to be reached concerning initial product compositions. England and Hughes (192, 193) have shown, by both kinetic measurements and product analyses, that the reactions of $\alpha$- and $\gamma$-methylallyl bromides with radioactive bromide ion in acetone solution involve mainly $S_N2$ substitution. $(-)$-$\alpha$-Butylallyl bromide reacts with lithium chloride in methanol to give $(+)$-$\alpha$-butylallyl chloride of low optical purity (395). The optical purity of the starting material was not known.

Allylic chlorides may be converted to bromides and iodides by treatment with sodium or calcium bromide, or calcium or potassium iodide. These reactions have been carried out simply by warming the allylic chloride with the halide salt, although this procedure frequently gives rearranged product. Reactions with potassium iodide are usually performed in acetone solution.

Henne and coworkers (272) have found that polyhalogenated olefins having allylic trichloromethyl groups react smoothly with antimony trifluoride to give olefins with trifluoromethyl groups:

$$CX_2{=}CXCCl_3 \xrightarrow{SbF_3} CX_2{=}CXCF_3$$
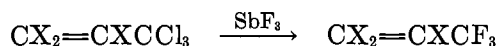
It is not necessary to use a salt of pentavalent antimony as a catalyst, as is required for non-allylic replacements. All three of the allylic chlorine atoms of the trichloromethyl group are replaced, instead of only two as is the case with non-allylic trichloromethyl groups. This reaction appears to be general, but in certain cases is accompanied by allylic rearrangement (271). It is stated that halogen substitution at the $\gamma$-carbon atom of the polyhalide is a necessary condition for the exchange reactions. 1,1,2,3,3-Pentachloropropene reacts with antimony pentafluoride to give 1,2-dichloro-3,3,3-trifluoropropene, a product of substitution with allylic rearrangement.

Table 30 lists some reactions of unsymmetrically substituted allylic chlorides and bromides with chloride, bromide, and iodide ions.

TABLE 30

*Non-isomeric halide-exchange reactions of allylic halides*

| Halide | Reaction Conditions | Products | References |
|---|---|---|---|
| $CH_2{=}CHCHCl_2$ | $CaI_2$ or KI | $CHCl{=}CHCH_2I$ | (624, 625) |
| $CHCl{=}CHCH_2Cl$ | $CaBr_2$ or NaBr in water | $CHCl{=}CHCH_2Br$ | (40, 347) |
| $CHCl{=}CHCH_2Cl$ | $CaI_2$ | $CHCl{=}CHCH_2I$ | (347) |
| $CH_2{=}CHCHClCOOH$ | $CaBr_2$ | $CH_2BrCH{=}CHCOOH$ | (524) |
| $CH_2{=}CHCHClCN$ | $CaBr_2$ | $CH_2BrCH{=}CHCN$ | (524) |
| $CH_2ClCH{=}CHCH_2Cl$ | Aqueous NaBr | $CH_2BrCH{=}CHCH_2Br$ | (40) |
| $CCl_2{=}C(CH_3)CH_2Cl$ | $CaI_2$ | $CCl_2{=}C(CH_3)CH_2I$ | (346) |
| $CH_3CHClC(CH_3){=}CH_2$ | $CaBr_2$ | $CH_3CH{=}C(CH_3)CH_2Br$ | (380) |
| $CH_2{=}CHCHClCOOCH_3$ | $CaBr_2$ | $CH_2BrCH{=}CHCOOCH_3$ | (522, 524, 529) |
| $(-)$-$C_4H_9CHBrCH{=}CH_2$ | LiCl in methanol | $(+)$-$C_4H_9CHClCH{=}CH_2$ | (395) |
| $CH_2IC(CH_3){=}CHCH_2OOCCH_3$ | KI in acetone | $CH_2IC(CH_3){=}CHCH_2OCOCH_3$ | (461) |
| $CH_2ClC(CH_3){=}CHCH_2OOCCH_3$ | $CaBr_2$ in acetone | $CH_2BrC(CH_3){=}CHCH_2OCOCH_3$ | (461) |

*13. Replacement of halide by hydrogen: reaction of allylic halides with lithium aluminum hydride*

Primary allylic halides react with lithium aluminum hydride in ether solution to give products which would be formed by normal bimolecular replacement of halogen by hydrogen. Trevoy and Brown (607) suggest that such reactions involve nucleophilic displacement of halide ions by complex hydride ions, and report that *trans*-1,4-dibromo-2-butene is reduced to *trans*-2-butene. Similarly, *cis*- and *trans*-1,4-dichloro-2-butenes are reduced to *cis*- and *trans*-2-butene, respectively (425). Lithium aluminum hydride reduction of *trans*-γ-methylallyl chloride yields *trans*-2-butene, while reduction of the *cis* chloride gives *cis*-2-butene (566).

Reduction of allylic halides by lithium aluminum hydride has been used in assigning structures to the halides. Thus, *cis*- and *trans*-1-chloropropene were obtained from the low- and high-boiling isomers of 1,3-dichloropropene, a result which indicates that the low-boiling isomer had the *cis* configuration and the high-boiling isomer the *trans* configuration (260). 1-Bromo-3-chloropropene, 1,3-dichloro-2-fluoropropene, and 1,2,3-trichloro-2-butene all react with lithium aluminum hydride to form the expected reduction products (248, 251, 254).

The reaction of 2,3,3-trichloro-1-butene with lithium aluminum hydride gives 2,3-dichloro-2-butene (248). This reaction may well be an abnormal bimolecular displacement of halide by hydride.

The α- and γ-methylallyl bromides are reduced to mixtures of butenes by treatment with a number of metals in ethanol or aqueous ethanol, and by treatment with magnesium in ether followed by hydrolysis of the resulting Grignard reagent (668, 671, 675, 681, 683, 695). While reactions of this type should be generally applicable as methods of reducing allylic halides to olefins, they are fundamentally different from the hydride reductions discussed above in that organometallic compounds are formed as intermediates.

*14. Miscellaneous replacement reactions of allylic halides*

There are a number of replacement reactions of allylic halides which have been reported for only one or two halides. Several of these less common reactions are described in the paragraphs which follow.

Treatment of γ,γ-dimethylallyl bromide with a mixture of potassium hydroxide and calcium cyanamide in methanol was claimed to form $[(CH_3)_2C \!\!=\!\! CHCH_2]_2NCN$ (592).

Oae and VanderWerf found that 1,3- and 3,3-dichloropropene both react with 1 *M* silver nitrate in ethanol to form 3-chloro-2-propenyl nitrate (458). Formation of ethyl ethers would be expected to accompany nitrate ester formation.

Sodium ethyl xanthate in ethanol reacts with 5-alkoxy-1-chloro-2-pentenes to form xanthate esters of the type $ROCH_2CH_2CH \!\!=\!\! CHCH_2SCSOC_2H_5$. The isomeric secondary chlorides gave low yields of the same esters (521). Similar results were obtained using sodium butyl xanthate in butanol.

It was recently reported that allylic hydroperoxides are formed from allylic

bromides and potassium hydroxide–hydrogen peroxide in aqueous methanol (276). Two examples were cited, but no experimental details were given.

Diazoacetic ester reacts with allylic halides in the presence of copper powder to form unsaturated $\alpha$-halo esters. Phillips (474) found that $\alpha$- and $\gamma$-methylallyl chlorides yield mixtures of isomeric ethyl $\alpha$-chloropentenoates in this reaction; he attributed the formation of abnormal products to an abnormal bimolecular displacement of chloride by carbethoxycarbene, followed by reaction of the carbonium ion and chloride ion thus formed:

$$C_2H_5OOCCH: +\ CH_2{=}CHCHXR \rightarrow [C_2H_5OOC\overset{+}{C}HCH_2CH{=}CHR]Cl^- \rightarrow$$
$$C_2H_5OOCCHXCH_2CH{=}CHR$$
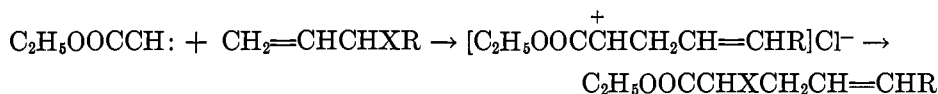
Both 1,3- and 3,3-dichloropropene undergo similar reactions.

In the presence of aluminum chloride or hydrogen fluoride, chlorides having allylic trichloromethyl groups and their allylic isomers alkylate aromatic rings (447, 448, 497):

$$CH_2{=}C(CH_3)CCl_3\ +\ C_6H_5OCH_3 \xrightarrow{\text{HF}} p\text{-}CH_3OC_6H_4CH_2C(CH_3){=}CCl_2$$

$$\left.\begin{array}{l} CH_2{=}CClCCl_3 \\ \quad\text{or} \\ CCl_2{=}CClCH_2Cl \end{array}\right\}\ +\ C_6H_6 \xrightarrow{\text{AlCl}_3}\ C_6H_5CH_2CCl{=}CCl_2$$

$$\left.\begin{array}{l} CH_2{=}CHCCl_3 \\ \quad\text{or} \\ CCl_2{=}CHCH_2Cl \end{array}\right\}\ +\ C_6H_6 \xrightarrow{\text{AlCl}_3}\ C_6H_5CH_2CH{=}CCl_2$$
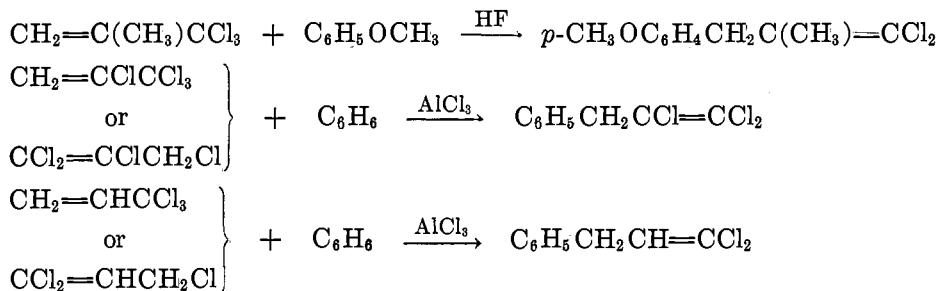
These reactions probably involve electrophilic substitution of the benzene ring by mesomeric allylic carbonium ions.

### 15. Reactions of allylic halides with organometallic compounds

Reagents with potential or actual negatively charged carbon atoms are alkylated by allylic halides. Grignard reagents and alkali metal salts of active methylene compounds are the two most important classes of carbanionic reagents; their reactions with allylic halides lead to compounds such as unsaturated esters, keto esters, or cyano esters in the case of active methylene compounds, and to unsaturated hydrocarbons in the case of Grignard reagents.

#### (a) Reactions of halides with salts of active methylene compounds

The reaction of active methylene compounds with allylic halides occurs much more readily than analogous reactions with alkyl halides and has been widely used as a method of lengthening carbon chains, particularly in the field of the chemistry of natural products. These alkylations are usually carried out by dissolving the active methylene compound (e.g., ethyl malonate, ethyl acetoacetate, ethyl cyanoacetate) in ethanolic sodium ethoxide, adding the allylic halide to the solution, and then heating the mixture or allowing it to stand at room temperature until reaction is complete.

Under these conditions primary allylic halides give only normal alkylation products:

$$R'R''CH^-Na^+ \;+\; RCH{=}CHCH_2X \;\rightarrow\; RCH{=}CHCH_2\underset{\diagdown R''}{\overset{\diagup R'}{C}H} \;+\; NaX$$
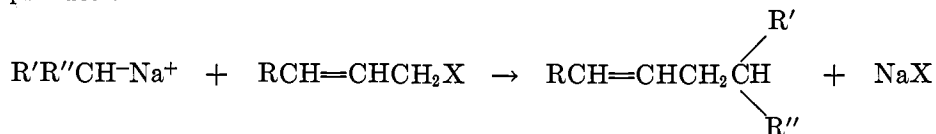
It seems quite likely, in view of the strong nucleophilic character of the substituting agents, the low polarity of the solvent, and the fact that normal products are formed, that primary halides react by the $S_N2$ mechanism.

Secondary allylic halides give varying amounts of abnormal substitution products with these reagents:

$$R'R''CH^-Na^+ + RCHXCH{=}CH_2$$

$$\rightarrow RCH(CHR'R'')CH{=}CH_2 + RCH{=}CHCH_2CHR'R''$$
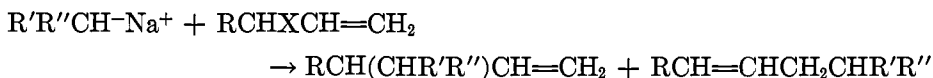
Kepner, Winstein, and Young (326) found that the reaction of sodium diethylmalonate with $\alpha$-ethylallyl chloride in ethanol is strictly bimolecular but gives 23 per cent of abnormal substitution product. This result is best interpreted as being due to simultaneous $S_N2$ and $S_N2'$ substitution (see page 770). 3,3,3-Trichloro-1-propene, a highly hindered allylic chloride, gives only the product of abnormal substitution with sodio diethylmalonate (451).

So-called "primary" allylic bromides, which are usually equilibrium mixtures containing 10–30 per cent secondary (or tertiary) bromide, react with sodium derivatives of active methylene compounds to form only products of substitution at the primary carbon atom of the allylic system. This result could be due to rapid isomerization of the secondary or tertiary bromide to the primary isomer, followed by normal substitution of the primary bromide, or to abnormal bimolecular substitution of the secondary or tertiary isomer, or to a combination of these processes.

Kierstead, Linstead and Weedon (332, 333, 334) found that vinylcyclopropane derivatives are formed in reactions of diene dibromides with malonic, acetoacetic, and cyanoacetic esters. The first step of these reactions is probably an $S_N2$ displacement of bromide by the anion of the active methylene compound. This apparently is followed by an intramolecular displacement of the remaining bromine atom by mechanism $S_Ni'$.

Table 31 lists reactions of unsymmetrically substituted allylic halides with salts of active methylene compounds.

(b) Reactions of allylic halides with non-allylic Grignard reagents

Grignard reagents react with allylic halides to form olefins:

$$RCH{=}CHCHXR' + R''MgX$$

$$\rightarrow RCH{=}CHCHR'R'' + RR''CHCH{=}CHR' + MgX_2$$

Although this reaction is of considerable importance in the synthesis of hydrocarbons, its mechanism is not fully understood. It might seem at first glance

TABLE 31

*Reaction of allylic halides with active methylene compounds*

| Halide | Reagent | ¡Products† | References |
|---|---|---|---|
| CH₂=CHCCl₃ | NaCH(COOC₂H₅)₂ | Abnormal only | (451) |
| CCl₂=CHCH₂Cl | NaCH(COOC₂H₅)₂ | N | (451) |
| CH₃CH=CHCH₂Cl | NaCH(COOC₂H₅)₂ | N | (37, 326) |
| CH₃CH=CHCH₂Cl | NaC(NO₂)(COOC₂H₅)₂ | N | (75) |
| CH₃CHClCH=CH₂ | NaCH(COOC₂H₅)₂ | M | (37, 326) |
| CH₃CH=CHCH₂Br | NaCH(COOC₂H₅)₂ | N | (37, 141) |
| CH₃CH=CHCH₂Br | C₂H₅CNa (CONH / CO \ CONH) | N | (180) |
| CH₃CHBrCH=CH₂ | C₂H₅CNa (CONH / CO \ CONH) | M | (180) |
| CH₃CHBrCH=CH₂ | NaC(C₂H₅)(COOC₂H₅)₂ | M | (180) |
| CH₃CCl=CHCH₂Cl | NaCH(COOC₂H₅)₂ | N | (601) |
| CH₃CCl=CHCH₂Cl | NaCH(COCH₃)(COOC₂H₅) | N | (642) |
| C₂H₅CH=CHCH₂Cl | NaCH(COOC₂H₅)₂ | N | (326) |
| C₂H₅CHClCH=CH₂ | NaCH(COOC₂H₅)₂ | N | (326) |
| (+)-CH₃CH=CHCHClCH₃ | NaCH(COOC₂H₅)₂ | Racemic product | (50) |
| C₂H₅CH=CHCH₂Br | NaCH(COOC₂H₅)₂ | N | (283) |
| CH₃CH=C(CH₃)CH₂Br | NaCH(COCH₃)(COOC₂H₅) | N | (380) |
| (CH₃)₂C=CHCH₂Br | NaCH(COCH₃)(COOC₂H₅) | N | (557) |
| (CH₃)₂C=CHCH₂Br | NaC[CH(CH₃)₂](COOC₂H₅)₂ | N | (570) |
| Dibromocyclopentene | NaCH(COCH₃)(COOC₂H₅) | ? | (529) |
| CH₃OCH₂CH₂CH=CHCH₂Cl | NaCH(COCH₃)(COOC₂H₅) | N | (503, 511) |
| CH₃OCH₂CH₂CH=CHCH₂Cl | NaCH(COOC₂H₅)₂ | N | (511) |
| CH₃OCH₂CH₂CHClCH=CH₂ | NaCH(COOC₂H₅)₂ | M | (511) |
| CH₃OCH₂CH₂CHClCH=CH₂ | NaCH(COCH₃)(COOC₂H₅) | M | (503, 511) |
| Cl (ring) Br | NaCH(COOC₂H₅)₂ | N | (431) |
| C₆H₅CH=CHCH₂Cl | NaCH(COOC₂H₅)₂ | N | (37) |
| C₆H₅CH=CHCH₂Br | NaC(COOC₂H₅)₃ | N | (409) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)=CHCH₂Cl | NaCH(COOC₂H₅)₂ | N | (37, 205) |
| (CH₃)₂C=CHCH₂CH₂C(CH₃)=CHCH₂Cl | NaCH(COCH₃)(COOC₂H₅) | N | (205, 546) |
| C₁₁H₁₉C(CH₃)=CHCH₂Br | NaCH(COCH₃)(COOC₂H₅) | N | (204, 549) |
| C₁₁H₁₇C(CH₃)=CHCH₂Cl | NaCH(COCH₃)(COOC₂H₅) | N | (550) |
| C₁₁H₁₇C(CH₃)=CHCH₂Br | NaCH(COCH₃)(COOC₂H₅) | N | (229) |

† M indicates that a mixture of isomeric products was isolated; N means that only the normal substitution product was reported.
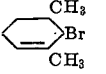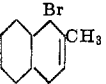
that the halogen atom of the allylic halide is displaced by a carbanion from the Grignard reagent. There are two reasons why this simple explanation is probably incorrect: first, Grignard reagents are not appreciably dissociated into R⁻ and MgX⁺ in ether solution; and second, carbanions would be expected to react with primary allylic halides and perhaps even secondary allylic halides to form

normal substitution products exclusively, especially in a solvent of low polarity like diethyl ether. Actually, mixtures of isomeric olefins are almost invariably formed in these reactions. Either member of a primary–secondary pair of isomeric allylic chlorides or bromides gives a similar mixture of unsaturated hydrocarbons when allowed to react with a Grignard reagent; the product of coupling at the primary carbon atom of the allylic system usually predominates.

The fact that isomeric halides yield similar mixtures of coupling products is strong evidence for an ionic reaction of the $S_N1$ type. It appears that mesomeric allylic carbonium ions are formed as intermediates during reactions of allylic halides with Grignard reagents. Ether is not a sufficiently polar solvent to cause most allylic halides to dissociate, and it is necessary to postulate that formation of the carbonium-ion intermediate is made possible by a weakening of the C—X bond of the halide by preliminary coordination with the Grignard reagent or magnesium halide. In other words, the magnesium compounds act as electrophilic catalysts for the coupling reaction. It is unlikely that "free" carbonium ions are produced; ion-pairs are probably formed in which the allylic cation is sufficiently free to lose its structural identity (647). The differences, although small, in product compositions from coupling reactions of isomeric halides mean that in most cases a true common intermediate (free carbonium ion) is not involved. It is also possible that allylic halides rearrange to an equilibrium mixture under the influence of Grignard reagent and/or magnesium halide at a rate greater than that of the coupling reaction. If this were true, similar mixtures of coupling products would be formed from isomeric halides, whatever the mechanism of the coupling reaction.

These coupling reactions are even more complex than indicated in the preceding paragraphs. Kirrman, Prevost, and others (328, 337, 343, 479, 492, 520) have observed that when allylic halides are coupled with non-allylic Grignard reagents, varying amounts of dienic hydrocarbons resulting from the coupling of two allylic fragments are formed in addition to the expected coupling products. In one case (492) Prevost also found alkyl halide and reduction products derived from the allylic halide. Prevost (492) and Kirrman (342) postulated that these complex mixtures of products are formed due to exchange of functional groups between the allylic halide and the Grignard reagent. The allylic Grignard reagent thus formed would react with allylic halide to give the dienic products or with water (during working up of the reaction mixture) to give the olefins expected from reduction of the allylic halide and its isomer.

$$RCH{=}CHCH_3 \ + \ RCH_2CH{=}CH_2$$

$$\uparrow \ \bigg| H_2O$$

$$RCH{=}CHCH_2X \ + \ R'MgX \ \rightarrow \ R(CH{=}CHCH_2)MgX \ + \ R'X$$

$$\diagup RCH{=}CHCH_2X$$

$$(RCH{=}CHCH_2)_2 \ + \ \underset{CH_2CH=CH_2R}{RCHCH{=}CH_2} \ + \ \underset{RCHCH=CH_2}{RCHCH{=}CH_2}$$

## TABLE 32
*Coupling of allylic halides with non-allylic Grignard reagents*

| Halide | RMgX | Product Composition | References |
|---|---|---|---|
| $CH_2=CHCHCl_2$ | $C_2H_5MgBr$ | A | (347) |
| $CH_2=CHCHCl_2$ | $CH_3MgBr$ | | |
| | $(CH_3)_2CHMgBr$ | N + A | (343, 344, 479) |
| | $C_4H_9MgBr$ | | |
| | $C_3H_7MgBr$ | | |
| $CHCl=CHCH_2Cl$ | $C_2H_5MgBr$ | N | (94) |
| $CHCl=CHCH_2Cl$ | $CH_3MgBr$ | | |
| | $(CH_3)_2CHMgBr$ | N + A | (479) |
| | $C_4H_9MgBr$ | | |
| $CHCl=CHCH_2Cl$ | $n\text{-}C_3H_7MgBr$ | N + A | (343, 344) |
| $CHCl=CHCH_2Cl$ | ArMgX | N | (54) |
| $CHBr=CHCH_2Br$ | $CH_3MgBr$ | | |
| | $C_3H_7MgBr$ | N + A | (337) |
| | $C_2H_5MgBr$ | | |
| $CHBr=CHCH_2Br$ | $C_2H_5MgBr$ | N | (94, 337) |
| $CH_2=CHCCl_3$ | $C_4H_9MgBr$ | A | (451) |
| $CCl_2=CHCH_2Cl$ | $C_4H_9MgBr$ | N | (451) |
| $CHBr=CBrCH_2Br$ | $C_2H_5MgBr$ | $C_2H_5CH_2C\equiv CH$ | (301) |
| $CH_2=C=CHCH_2Cl$ | $CH_3MgCl$ | | |
| | $CH_3MgI$ | | |
| | $C_4H_9MgBr$ | Mostly A | (112, 113, 114) |
| | $C_6H_5MgBr$ | | |
| | $C_6H_5CH_2MgCl$ | | |
| | $C_7H_{15}MgBr$ | | |
| $CH_3CH=CHCH_2Cl$ | $C_4H_9MgCl$ | 85% N; 15% A | (132) |
| $CH_3CH=CHCH_2Cl$ | $C_6H_5MgBr$ | 77% N; 23% A | (647) |
| $CH_3CHClCH=CH_2$ | $C_6H_5MgBr$ | 72% A, 28% N | (647) |
| $CH_3CH=CHCH_2Cl$ + $CH_3CHClCH=CH_2$ | $C_4H_9MgBr$ | ~90% $CH_3CH=CHCH_2C_4H_9$ ~10% $CH_3CH(C_4H_9)$- $CH=CH_2$ | (270) |
| $CH_3CH=CHCH_2Br$ | $C_6H_5MgBr$ | N | (387, 473) |
| $CH_3CH=CHCH_2Br$ (?) | $C_2H_5MgBr$ | N + A | (621, 622) |
| $CH_3CHBrCH=CH_2$ | $C_6H_5CH_2CH_2MgBr$ | N | (387) |
| $CH_3CH=CHCH_2Br$ + $CH_3CHBrCH=CH_2$ | $CH_2CH_2CH_2CH_2CHMgCl$ | $CH_3CHRCH=CH_2$ (mostly) + $CH_3CH=CHCH_2R$ | (477) |
| $CH_2ClCH=CHCH_2Cl$ | $C_6H_7MgBr$ | | |
| | $C_4H_9MgBr$ | N, N + butadiene | (298, 399) |
| | $CH_3MgBr$ | | |
| $CH_2ClCHClCH=CH_2$ | $CH_3MgBr$ | $CH_3CH_2CH=CHCH_2CH_3$ | (399) |
| $CH_2BrCH=CHCH_2Br$ | $CH_3MgBr$ | $CH_3CH_2CH=CHCH_2CH_3$ | (399) |
| $CH_2BrCH=CHCH_2Br$ | $C_5H_9MgBr$ | N + A | (282) |
| $CH_2BrCH=CHCH_2Br$ | $C_2H_5MgBr$ | | |
| | $C_6H_5CH_2MgCl$ | N, N + butadiene | (619) |
| $CCl_2=C(CH_3)CH_2Cl$ | $CH_3MgBr$ | N + A | (346) |
| $C_2H_5CH=CHCH_2Br$ (?) | $C_2H_5MgBr$ | ~20% N; ~80% A | (489) |
| $C_2H_5CH=CHCH_2Br$ (?) | $C_2H_5MgBr$ | | |
| | $C_6H_5MgBr$ | N + A | (494) |
| $(CH_3)_2C=CHCH_2Br$ (?) | $C_2H_5MgBr$ | N | (129, 582) |
| Dichlorocyclopentenes | $CH_5MgBr$ | | |
| | $C_2H_5MgBr$ | N + A | (401) |
| | $C_3H_7MgBr$ | | |
| Dibromocyclopentenes | $C_2H_5MgBr$ | | |
| | $C_8H_{17}MgBr$ | N + A | (35) |
| $(CH_3)_2C=C(CH_3)CH_2Cl$ | "RMgX" | N + A | (396) |
| $(CH_3)_2CClC(CH_3)=CH_2$ | "RMgX" | N + A | (396) |
| $(CH_3)_2CClCH=CHCH_3$ | $C_2H_5MgBr$ | 61% N; 39% A | (397) |
| $CH_3OCH_2CH=C(CH_3)CH_2Cl$ | $C_{11}H_{17}C(OMgBr)(CH_3)C\equiv CMgBr$ | N | (462) |
| $CH_3OCH_2CH_2CH=CHCH_2Cl$ | $C_6H_5MgBr$ | ~70% N; ~30% A | (512) |

TABLE 32—*Concluded*

| Halide | RMgX | Product Composition | References |
|---|---|---|---|
| $CH_3OCH_2CH_2CH=CHCH_2Cl$...... | $C_6H_5CH_2MgBr$ | | |
| | $C_2H_5MgBr$ | $\sim 65\%$ N | (519) |
| | $C_4H_9MgBr$ | $\sim 35\%$ A | |
| $CH_3OCH_2CH_2CHClCH=CH_2$....... | $C_3H_5MgBr$ | $\sim 40\%$ N, $\sim 60\%$ A | (512) |
| $CH_3OCH_2CH_2CHClCH=CH_2$....... | $C_6H_5CH_2MgBr$ | | |
| | $C_2H_5MgBr$ | $\sim 65\%$ A | (519) |
| | $C_4H_9MgBr$ | $\sim 35\%$ N | |
| $(CH_3)_2C=C(CH_3)CH_2Br$ (?)........ | "$RMgX$" | N + A | (396) |
| $(CH_3)_2C=C(CH_3)CH_2Br$ (?)........ | $C_6H_5MgBr$ | N | (129) |
| $(CH_3)_2CBrCH=CHCH_3$ (?)......... | $C_2H_5MgBr$ | 61% N; 39% A | (397) |
| $CH_2ClC(CH_3)=C(CH_3)CH_2Cl$...... | $CH_3MgBr$ | Mostly N,N | (400) |
| ![Br/Cl cyclohexene structure] Br............................ Cl | $C_3H_7MgBr$ $CH_3MgBr$ | N | (431) |
| $CH_2BrCH=CHCH=CHCH_2Br$ (?). | $C_2H_5MgBr$ | A, A | (492, 495) |
| $(CH_3)_2CHCH=C(CH_3)CH_2Cl$...... | $C_{10}H_7MgBr$ | N | (473) |
| $C_2H_5OCH_2CH_2CH=CHCH_2Cl$...... | $C_2H_5MgBr$ | | |
| | $C_4H_9MgBr$ | N | (520) |
| $C_2H_5OCH_2CH_2CHClCH=CH_2$...... | $C_2H_5MgBr$ | | |
| | $C_4H_9MgBr$ | A | (520) |
| $CH_3$ ⟨structure⟩ $Br$ (?)............... | $CH_3MgBr$ | N | (431) |
| $C_5H_{11}CH=CHCH_2Br$ (83%)<br>+<br>$C_5H_{11}CHBrCH=CH_2$ (17%) | $CH_3MgI$ | { 80% $C_5H_{11}CH=CHC_2H_5$<br>20% $C_5H_{11}CH(CH_3)CH=CH_2$ | (42) |
| $CH_3$<br>⟨structure⟩ $Br$ (?)....................<br>$CH_3$ | $CH_3MgBr$ | N | (431) |
| $C_6H_5CH=CHCH_2Cl$............... | $CH_3MgBr$ | N + A | (328, 494) |
| $C_4H_9OCH_2CH_2CH=CHCH_2Cl$...... | $C_4H_9MgBr$ | | |
| | $C_6H_5MgBr$ | N | (520) |
| $C_4H_9OCH_2CH_2CHClCH=CH_2$...... | $C_4H_9MgBr$ | | |
| | $C_6H_5MgBr$ | A | (520) |
| $C_6H_5CH=CHCH_2Br$............... | $C_2H_5MgBr$ | $\sim 70\%$ N; $\sim 30\%$ A | (403, 492) |
| Br<br>⟨structure⟩ CH₃<br>(?)................. | $CH_3MgBr$ | N | (431) |
| $C_6H_5CHClCH=CClC_6H_5$........... | $C_3H_5MgBr$ | N | (591) |
| $C_6H_5CHClCH=CClCH=CHC_6H_5$.. | $C_3H_5MgBr$ | N | (591) |
| $(C_6H_5)_2C=CHCHClC_6H_5$........... | $C_3H_5MgBr$ | N | (591) |
| $(C_6H_5)_2C=C(C_6H_5)CH_2Br$.......... | $C_3H_5MgBr$ | N | (52) |

The exchange reaction would also account for the appearance of alkyl halide among the products. Kharasch and Reinmuth (331, page 1063) state that functional exchange between Grignard reagents and organic halides is a relatively rare reaction, and that when it does occur it probably takes place through a free-radical mechanism.

Table 32 lists coupling reactions of unsymmetrically substituted allylic halides with non-allylic Grignard reagents. In the "product" column, N refers to the

product of normal coupling without rearrangement of the allylic system, and A refers to the abnormal coupling product, in which the structure of the allylic system has been inverted. Percentages, where given, refer only to compositions of products of coupling of the allylic halide with the non-allylic Grignard reagent. Many workers report only one coupling product, in spite of the fact that mixtures of products were found in all cases studied with sufficient care. In these instances the reported product is probably merely the principal one rather than the only one formed. As mentioned before, some investigators have claimed to use primary allylic bromides when equilibrium mixtures of allylic isomers were actually used. Where there seems to be reasonable doubt as to the purity of the halide used, a question mark is placed after the structure appearing in the literature.

### (c) Reaction of allylic halides with allylic Grignard reagents

Under suitable conditions allylic halides react with magnesium metal to form mixtures of dienic hydrocarbons:

$$RCH=CHCHXR' \xrightarrow{Mg}$$

$$
\begin{array}{ccccc}
RCH=CHCHR' & & RCH=CHCHR' & & R'CH=CHCHR \\
| & + & | & + & | \\
RCH=CHCHR' & & R'CH=CHCHR & & R'CH=CHCHR \\
I & & II & & III
\end{array}
$$
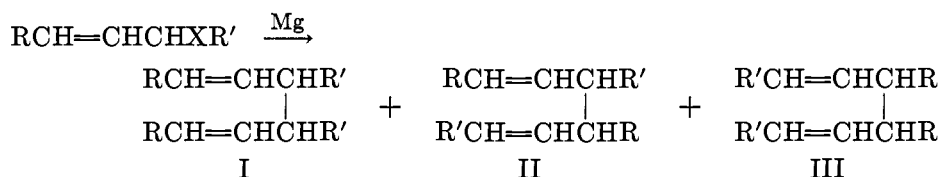
The coupling reaction may be carried out with or without ether as a solvent and has been used as a synthesis of unsaturated hydrocarbons, particularly by Henne, Cope, and Koch and their associates (269, 270, 358, 403). Coupling products are also frequently obtained as by-products in the preparation of allylic Grignard reagents. In general, either member of a primary–secondary pair of isomeric chlorides or bromides gives a mixture of dienes in which the hydrocarbon having a primary allylic residue coupled to a secondary one (II: R' = H) predominates.

It is possible that in some cases at least part of the coupling product is formed by a free-radical reaction of the Wurtz type. In most cases, however, coupling probably involves formation of an allylic Grignard reagent and reaction of this with remaining allylic halide. Rupe and Burgin (545) claimed that part of the product of coupling cinnamyl chloride by magnesium was formed by addition of one molecule of the cinnamyl Grignard reagent across the double bond of another molecule of the reagent. This assumption was not supported by a careful reinvestigation of the reaction (214, 216, 358), and it is doubtful that additions of this type occur.

The comments on mechanism made in the preceding discussion of reactions of allylic halides with non-allylic Grignard reagents are applicable here, except that the situation is more complex. It is possible for rearrangement to occur during formation of the allylic Grignard reagent as well as during its reaction with the allylic halide. In addition, isomerization of the allylic halide and functional

exchange between the halide and the Grignard reagent may conceivably precede or accompany the coupling reaction.

Young, Roberts, and Wax (688) appear to be the only workers who have thoroughly studied the reaction of separately prepared allylic Grignard reagents with allylic halides. They found that α- and γ-methylallyl bromides give different mixtures of dienes in reactions with butenylmagnesium bromide, while α- and γ-methylallyl chlorides form similar mixtures of coupling products in which 3-methyl-1,5-heptadiene predominates. (The same Grignard reagent, whose structure and reactions are discussed elsewhere (page 873), is formed from either α- or γ-methylallyl bromide; for the sake of simplicity this reagent is called butenylmagnesium bromide.) Their results are summarized in table 33.

The fact that 3-methyl-1,5-hexadiene was the major product when allyl chloride was coupled with butenylmagnesium bromide, while 2,6-heptadiene was the principal product of reaction of allylmagnesium chloride with either α- or γ-methylallyl chloride, indicates that the butenyl Grignard reagent tends to furnish α-methylallyl groups, while both α- and γ-methylallyl chlorides tend to furnish γ-methylallyl groups to the coupling products.

The complex results obtained with allylic bromides are not understood. The fact that bromides should undergo Wurtz coupling and functional exchange more readily than chlorides may be responsible.

Table 34 lists self-coupling reactions of allylic halides under the influence of magnesium metal. In coupling reactions of halides of the type $RR'C{=}CHCH_2X$ and $RR'CXCH{=}CH_2$, three products may be formed: $(RR'C{=}CHCH_2)_2$, $RR'C{=}CHCH_2CRR'CH{=}CH_2$, and $(CH_2{=}CHCRR')_2$. These are designated in the table as primary-primary (pp), primary-tertiary (pt), and tertiary-tertiary (tt) coupling products (or pp, ps, and ss if R' = H). When there is reasonable doubt as to the structure or purity of the halide used, a question mark is placed after the structure appearing in the literature.

(d) Coupling of allylic halides with organometallic compounds other than
Grignard reagents

Several reactions of organosodium and organolithium compounds with allylic halides have been reported. In liquid ammonia solution the sodium salt of allylbenzene reacts with α- and γ-methylallyl chlorides to give mixtures of hydrocarbons in which the structure of the α- or γ-methylallyl group is completely retained (403, 672):

$$C_6H_5(CHCHCH_2)^-Na^+ \ + \ CH_3CH{=}CHCH_2Cl \ \rightarrow \ C_6H_5CHCH{=}CH_2$$
$$\underset{\displaystyle CH_2CH{=}CHCH_3}{\big|}$$

$$+$$

$$CH_3CHClCH{=}CH_2 \qquad\qquad +$$
$$\downarrow \qquad\qquad\qquad C_6H_5CH{=}CHCH_2CH_2CH{=}CHCH_3$$

$$\underset{\displaystyle CH_3CCH{=}CH_2}{\overset{\displaystyle C_6H_5CHCH{=}CH_2}{\big|}} \ + \ C_6H_5CH{=}CHCH_2CH(CH_3)CH{=}CH_2$$
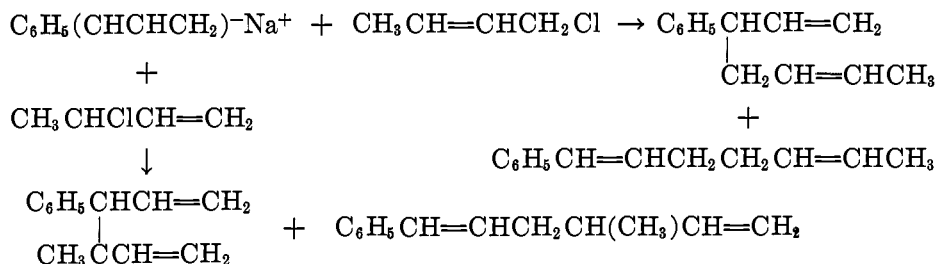
TABLE 33

*Products from the coupling of butenyl halides with butenylmagnesium bromide*

| Halide | 2,6-Octadiene<br>CH₃CH=CHCH₂CH₂CH=CHCH₃ | 3-Methyl-1,5-heptadiene<br>CH₃CH=CHCH₂CH(CH₃)CH=CH₂ | 3,4-Dimethyl-1,5-hexadiene<br>CH₃ CH₃<br>CH₂=CHCH—CHCH=CH₂ |
|---|---|---|---|
| | *per cent* | *per cent* | *per cent* |
| CH₃CH=CHCH₂Br............... | 10 | 88 | 2 |
| CH₃CHBrCH=CH₂............... | 50 | 35 | 15 |
| CH₃CH=CHCH₂Cl............... | 12 | 82 | 6 |
| CH₃CHClCH=CH₂............... | 3 | 86 | 11 |

### TABLE 34
*Products of coupling allylic halides by magnesium*

| Halide | Conditions | Products Reported | References |
|---|---|---|---|
| $CH_3CH=CHCH_2Cl$ | $Mg + (C_2H_5)_2O$ | Trace pp<br>92.5% ps<br>7.5% ss | (270) |
| $CH_3CHClCH=CH_2$ | $Mg + (C_2H_5)_2O$ | 4.5% pp<br>85% ps<br>10.5% ss | (270) |
| $CH_3CH=CHCH_2Br$ (?) | $Mg + (C_2H_5)_2O$ | pp + ps | (95) |
| $CH_3CH=CHCH_2Br$ (87%) | $Mg + (C_2H_5)_2O$ | 50% pp | (392, 393) |
| $CH_3CHBrCH=CH_2$ (13%) | | 50% ps<br>Trace ss | |
| $(CH_3)_2C=CHCH_2Cl + (CH_3)_2CClCH=CH_2$ | $Mg + (C_2H_5)_2O$ | pp + pt | (582) |
| $C_2H_5CH=CHCH_2Br$ (?) | $Mg + (C_2H_5)_2O$ | 29% pp<br>65% ps<br>6% ss | (495) |
| $CH_3CH=CHCH=CHCH_2Cl$ | $Mg + (C_2H_5)_2O$ | ps + ss | (527) |
| $(CH_3)_2CHCHClC(CH_3)=CH_2$ | $Mg + (C_2H_5)_2O$ | ps | (473) |
| $C_4H_9CH=CHCH_2Br$ (?) | $Mg + (C_2H_5)_2O$ | Mixture | (161) |
| $C_5H_{11}CH=CHCH_2Br$ (mostly) | $Mg + (C_2H_5)_2O$ | ps (mostly) | (42) |
| $C_5H_{11}CHBrCH=CH_2$ | | | |
| $C_3H_5CH=CHCH_2Cl$ | $Mg + (C_2H_5)_2O$ | 20% pp<br>75% ps<br>5% ss | (358) |
| $C_6H_5CH=CHCH_2Cl$ | | pp + ps | (216, 545) |
| $C_6H_5CH=CHCH_2Br$ | $Mg + (C_2H_5)_2O$ | 10% pp<br>89% ps<br>1% ss | (358) |
| $C_6H_5CH=CHCH_2Br$ | $Mg + (C_2H_5)_2O$ | pp + ss | (93, 216, 408) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2Cl$ (90%) | Mg or Mg + $(C_2H_5)_2O$ | ~ 65% pt | (36) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)ClCH=CH_2$ | | ~ 35% pp | |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2Br$ (~ 90%) | $Mg + (C_2H_5)_2O$ | ? | (45) |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)BrCH=CH_2$ (~ 10%) | | | |
| $(CH_3)_2C=CHCH_2CH_2C(CH_3)=CHCH_2Br$ (?) | $Mg + (C_2H_5)_2O$ | Mixture | (579) |
| $C_{16}H_{17}CH_2C(CH_3)=CHCH_2Br$ | | pp (?) | (314) |

The fact that no products involving rearrangement of the carbon skeleton of the allylic halides are formed means that these reactions are normal bimolecular displacements ($S_N2$) of chloride by the mesomeric carbanion from sodium allylbenzene. Mechanisms $S_N1$ and $S_N2'$ apparently do not operate to an appreciable extent when liquid ammonia is used as the reaction medium.

In contrast to the stereospecific displacements observed in liquid ammonia, sodium allylbenzene, phenylsodium, and ethylsodium react with $\alpha$- and $\gamma$-methylallyl chlorides in pentane to form nearly identical mixtures of hydrocarbons:

$$RNa + \begin{cases} CH_3CH=CHCH_2Cl \\ \qquad \text{or} \\ CH_3CHClCH=CH_2 \end{cases} \rightarrow \underset{\text{I}}{RCH_2CH=CHCH_3} + \underset{\text{II}}{RCH(CH_3)CH=CH_2}$$

Either of the butenyl chlorides yields predominantly the product of coupling at the primary carbon atom of the allylic system (I).

The sodium salt of allylbenzene reacted with butenyl chlorides in pentane to form 82 per cent I and 18 per cent II from γ-methylallyl chloride and 76 per cent I and 24 per cent II from α-methylallyl chloride (677). Mixtures of similar composition were obtained with α- and γ-methylallyl bromides. Phenylsodium gave a mixture of 90–95 per cent γ-methylallylbenzene and 5–10 per cent α-methylallylbenzene when allowed to react with either α- or γ-methylallyl chloride (146). The only isolable product from the reaction of α- or γ-methylallyl chloride with ethylsodium in pentane was 2-hexane (609).

Exactly what is occurring in coupling reactions of allylic chlorides with organosodium compounds in pentane is obscured by the heterogeneous nature of the reaction. The organosodium compounds are insoluble in pentane. In the case of the reactions with phenylsodium and ethylsodium, the solid organosodium salts were intimately mixed with the sodium chloride formed as a by-product in their preparation. The composition of the hydrocarbon products strongly indicates an ionic mechanism for these reactions. The electrophilic sodium atoms on the surface of the organosodium–sodium chloride aggregates presumably coordinate with the chlorine atoms of the allylic chloride, thus weakening the carbon–chlorine bond and resulting in formation of an allylic carbonium ion. This carbonium ion could coordinate with a carbanion or a chloride ion at the solid–liquid interface to give hydrocarbons or a mixture of isomeric allylic chlorides. Cristol (146) has suggested that reactions of the carbonium ion with $C_6H_5^-$ and $Cl^-$ proceed at similar rates, since recovered unreacted chloride in one experiment was found to have been partially isomerized. It also seems possible that isomerization of the chlorides by ion-pair formation and internal return could accompany or precede the coupling reaction.

Cristol, Overhults, and Meek (147) found that when either α- or γ-methylallyl chloride reacts with phenyllithium or n-butyllithium in diethyl ether, nearly identical mixtures of products are obtained in which coupling has occurred predominantly at the primary carbon atom of the allylic system. γ-Methylallylbenzene or 2-octene comprised more than 90 per cent of the coupling products in the two cases. These results were interpreted in terms of a carbonium-ion mechanism similar to that proposed by Wilson, Roberts, and Young (647) for analogous Grignard coupling reactions.

Ruber (542) treated α-methyl-γ-phenylallyl bromide with dimethylzinc. The only product reported was 3-methyl-1-phenyl-1-butene.

### (e) Coupling of allylic halides by metals other than magnesium

Dienes may be prepared by coupling allylic halides under the influence of a number of metals other than magnesium. γ-Butylallyl bromide is coupled by sodium in ether to give mostly 5,9-tetradecadiene, the primary-primary coupling product (161). In contrast, magnesium gave a mixture of hydrocarbons which probably contained much primary-secondary coupling product. The terpene hydrocarbon squalene has been prepared by coupling farnesyl bromide,

$$CH_3[C(CH_3)=CHCH_2CH_2]_2C(CH_3)=CHCH_2Br$$

with sodium and potassium (314). 1,4-Dibromo-2-butene was converted into a mixture of hydrocarbons consisting mainly of 2,6-octadiene by treatment with sodium in ether (572). Presumably the initial product is dibromoöctadiene; how this is reduced to the hydrocarbon is not made clear. These reactions are probably of the Wurtz type, in which initially formed free radicals dimerize to form the dienes. The limited information available indicates that coupling by sodium and potassium give better yields of unbranched dienes than does coupling by magnesium.

A reaction of a different type occurs when allylic halides are treated with sodium amide in liquid ammonia. Conjugated trienes are usually formed (330). The first step here is probably abstraction of an allylic hydrogen atom from one molecule of allylic halide to give a carbanion which displaces halide from another molecule of the halide. This forms a halodiene which undergoes dehydrohalogenation to a triene.

Cinnamyl chloride is coupled by iron powder suspended in water to give a mixture of hydrocarbons from which 1,6-diphenyl-1,5-hexadiene was isolated (109). Mixtures of isomeric methoxychloropentenes ($CH_3OCH_2CH_2CH=CHCH_2Cl$ and $CH_3OCH_2CH_2CHClCH=CH_2$) are coupled by iron suspended in ethanol or acetonitrile, mixtures of dimethoxydecadienes being formed (615). Small amounts of copper, nickel, cobalt, and mercury, as well as salts of these metals, served as activators for the coupling reaction.

One of the earliest allylic coupling reactions on record is that of Charon (123), who treated "crotyl bromide" (the equilibrium mixture of allylic isomers) with zinc in aqueous ethanol to obtain butenes plus "dicrotyl" of unstated composition.

Young, Lane, Loshokoff, and Winstein (675) studied the coupling and reduction reactions of butenyl bromides with various metals in 80 per cent ethanol. They observed extensive formation of coupling products by magensium, sodium, iron, manganese, tin, copper, silver, cadmium, and nickel but did not fractionate the diene mixtures.

### (f) Coupling of allylic halides by nickel carbonyl

Allylic chlorides react with nickel tetracarbonyl in a Wurtz-type reaction, producing excellent yields of diene hydrocarbons. With unsymmetrically substituted halides either allylic isomer gives essentially the same mixture of hydrocarbons:

$$\begin{bmatrix} 2RCH=CHCH_2Cl \\ \text{or} \\ 2RCHClCH=CH_2 \end{bmatrix} + Ni(CO)_4 \rightarrow RCH=CHCH_2CH_2CH=CHR +$$

$$I$$

$$RCH=CHCH_2CHRCH=CH_2 +$$

$$II$$

$$NiCl_2 + 4CO\uparrow$$
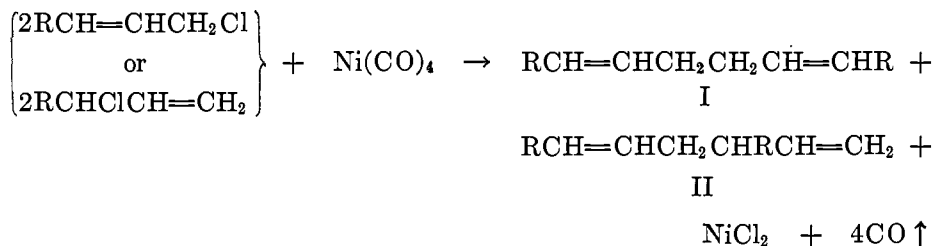
Our knowledge of this reaction is mainly due to Webb (632, 634), who applied it to $\alpha$- and $\gamma$-methylallyl chlorides, $\alpha,\alpha$- and $\gamma,\gamma$-dimethylallyl chlorides, and isomeric methoxychloropentenes. In each case, the product of primary-primary coupling (I) was the main constituent of the diene mixture, a fact which makes this reaction a useful adjunct to coupling by magnesium, which gives mainly primary-secondary products of the type II.

Coupling occurs in methanol and ether but not in petroleum ether. When the reaction was carried out in methanol, no products from reaction with solvent were found. This is evidence for a radical mechanism and against a carbonium-ion or carbanion mechanism. When coupling of $\alpha$-methylallyl chloride was stopped after 25 per cent reaction, the recovered chloride had been isomerized to $\gamma$-methylallyl chloride to the extent of only 20 per cent. Rearrangement of the halide thus appears to be slower than the coupling reaction.

$$ClCH_2CH(OC_2H_5)CH=CHCH_2Cl \text{ (595) and } ClCH_2CH=CHCH_2CN \text{ (498)}$$

have also been coupled by nickel carbonyl in methanol. In both cases the primary-primary coupling product was the principal one formed.

### 16. Allylic Grignard reagents and their reactions

No discussion of reactions of allylic halides would be complete without at least a brief discussion of the preparation and reactions of allylic Grignard reagents. The problem of the structure of allylic Grignard reagents is a complex one, as is the question of the mechanisms of their reactions with carbonyl compounds, active hydrogen compounds, and other substances. The present treatment is intended merely to describe briefly the preparation of allylic Grignard reagents and a few of their more important reactions.

### (a) Preparation

Owing to the ease with which they are coupled by magnesium, allylic halides frequently give poor yields of Grignard reagents under conditions which afford satisfactory yields of alkylmagnesium halides from saturated halides. The side reactions which lead to formation of coupling products can be virtually eliminated by use of large excesses of magnesium metal and by keeping the concentration of unreacted halide very low (215, 218, 219, 220, 661, 675, 682). This requires slow addition of a dilute solution of the allylic halide in ether to a large excess of magnesium stirred vigorously with a large amount of ether. Essentially quantitative yields of the allylic Grignard reagent are possible (675), but in practice a compromise must usually be made in which smaller, more conveniently handled quantities of magnesium and solvent are used at the cost of a somewhat lower yield of Grignard reagent. Under a given set of reaction conditions, higher yields of Grignard reagent are obtained using ethyl ether than using $n$-propyl ether, isopropyl ether, or $n$-butyl ether (675).

### (b) Structure of allylic Grignard reagents

Both members of a pair of isomeric allylic halides form Grignard reagents which are chemically indistinguishable, and it is quite likely that isomeric halides

yield the same Grignard reagent. Young and coworkers (378, 538, 645, 646, 668, 684, 686, 687, 688, 695) made an extensive study of the chemical properties of the Grignard reagent from α- and γ-methylallyl halides and concluded that this reagent is best formulated as γ-methylallylmagnesium halide (686).

Owing to the fact that allylic rearrangements can occur during both the preparation and subsequent reactions of allylic Grignard reagents, it is doubtful that their chemical properties alone can furnish conclusive evidence concerning their structure. A study of their physical properties might prove more fruitful, but is rendered difficult by the experimental problems encountered in preparing and handling pure samples of organomagnesium halides. The ultraviolet absorption spectrum of the Grignard reagent from cinnamyl bromide was recently determined and is qualitatively that of a compound having a styrene chromophore ($C_6H_5CH=CH-$) (669), good evidence that the Grignard reagent consists of cinnamylmagnesium bromide and, possibly, dicinnamylmagnesium. This is particularly significant in view of the fact that the cinnamyl Grignard reagent is similar in its chemical properties to the butenyl Grignard reagent and other unsymmetrically substituted allylic Grignard reagents. It seems quite likely that Grignard reagents prepared from halides of the type $RR'C=CHCH_2X$ or $RR'CXCH=CH_2$ exist mainly or entirely as $RR'C=CHCH_2MgX$.

(c) Reactions of allylic Grignard reagents with active hydrogen compounds

Allylic Grignard reagents react with proton donors to form mixtures of olefins:

$$RCH=CHCH_2MgX \xrightarrow{HY} RCH=RHCH_3 \ (cis \ and \ trans) \ + \ RCH_2CH=CH_2$$

Young and coworkers have studied the conversion of butenyl and cinnamyl Grignard reagents into olefin mixtures under a variety of conditions. They found that the composition of the butene mixture obtained by hydrolyzing butenyl Grignard reagents with aqueous acid is independent of the allylic halide used to prepare the Grignard reagent (668, 681, 695). Reagents prepared from α- and γ-methylallyl chlorides and α- and γ-methylallyl bromides gave approximately the same mixture of butenes, which consisted of about 57 per cent 1-butene, 27 per cent cis-2-butene, and 16 per cent trans-2-butene. Dibutenylmagnesium, prepared by dioxane precipitation of butenylmagnesium bromide from the Grignard reagent, gave a somewhat different hydrocarbon mixture from that obtained with the original Grignard reagent (683). The composition of the butene mixture varies with the solvent in which the Grignard reagent is dissolved at the time of hydrolysis and with the nature of the active hydrogen compound used (645). Cleavage of the Grignard reagent with phenylacetylene gave a mixture containing 93 per cent 1-butene (686). Similar results were obtained with cinnamylmagnesium chloride. Hydrolysis by aqueous acid gave 73 per cent allylbenzene and 27 per cent propenylbenzene (661), while cleavage with phenylacetylene yielded only allylbenzene (110).

(d) Reaction of allylic Grignard reagents with carbonyl compounds

Grignard reagents prepared from either member of a primary-secondary pair of isomeric allylic halides react with aldehydes, ketones, esters, carbon dioxide,

and phenyl isocyanate to give mainly or exclusively the product of addition at the secondary carbon atom of the allylic system:

$$R(CHCHCH_2)MgX + R'COR'' \rightarrow \begin{matrix} RCHCH=CH_2 \\ | \\ R'C(OH)R'' \end{matrix}$$

The butenyl Grignard reagent has been thoroughly studied in reactions of this type. Reaction with carbon dioxide (378, 538) or phenyl isocyanate (687) gives $CH_3CH(COOH)CH=CH_2$, while reactions with aldehydes and ketones usually give $\alpha$-methylallyl carbinols (298, 365, 366, 538, 646, 684, 685, 686). There are two interesting and important features of these carbonyl addition reactions. First, the butenyl Grignard reagent gives excellent yields of carbinols in reactions with highly hindered ketones such as diisopropyl ketone, acetomesitylene, isobutyrylmesitylene, dimesityl ketone, isopropyl tert-butyl ketone, and di-tert-butyl ketone (646). These ketones react poorly or not at all with non-allylic Grignard reagents. And second, the butenyl Grignard reagent adds smoothly to hindered methyl ketones such as acetomesitylene, which are extensively enolized by other Grignard reagents (685). The successful addition of butenyl Grignard reagent to hindered and easily enolizable ketones is evidence for the existence of a special cyclic mechanism for addition reactions of allylic Grignard reagents which is not available to non-allylic reagents. Only with the very highly hindered di-tert-butyl ketone did extensive addition take place at the primary carbon atom of the allylic system (646). With ethyl formate, the butenyl Grignard reagent gave di-$\alpha$-methylallyl carbinol (687). It gave almost no 1,4-addition products with phenyl vinyl ketone and tert-butyl cinnamate, although saturated and aryl Grignard reagents add almost exclusively in the 1,4-manner to these compounds (687).

The preceding observations concerning carbonyl addition reactions of butenyl Grignard reagents are applicable to a number of other allylic Grignard reagents. For example, the Grignard reagents from cinnamyl chloride and bromide react with carbon dioxide, aldehydes, and phenyl isocyanate to give products in which addition has taken place at the secondary carbon atom of the allylic system (214, 215, 217, 242, 366). Since spectroscopic evidence indicates the Grignard reagents have the structure $C_6H_5CH=CHCH_2MgX$ (669), the cyclic addition mechanism proposed for butenyl Grignard reagents (687) must be operating here also.
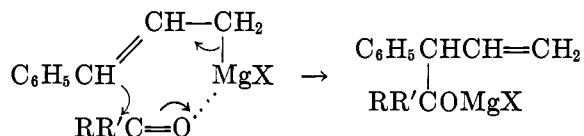


Carbonation of the Grignard reagents from biallyl bromide (mainly $CH_2=CHCH_2CH=CHCH_2Br$) (43, 44) and octenyl bromide (mainly $C_5H_{11}CH=CHCH_2Br$) (42) gave only the secondary adducts, as did carbonation of the Grignard reagent from sorbyl chloride (527). The Grignard reagent from pentadienyl chloride condensed with pentadienal to give $CH_2=CHCH(CH=CH_2)CHOHCH=CHCH=CH_2$ as the only carbinol product (657). The product of

reaction of the Grignard reagent from biallyl bromide with acetophenone was the secondary adduct (318).

There are a few reports of addition occurring at the primary carbon atom of the allylic system. $(CH_3)_2C$=$CHCH_2COOH$ was stated to be the product of carbonation of the Grignard reagent from isoprene hydrobromide (probably mainly $\gamma,\gamma$-dimethylallyl bromide) (582). However, later work showed that this Grignard reagent, and the analogous pentenylmagnesium chloride, yield only the tertiary adduct $[(CH_3)_2C(COOH)CH$=$CH_2]$ on reaction with carbon dioxide (208a, 372a, 543a). Methyl isopropyl ketone, diethyl ketone, and diisopropyl ketone also yielded tertiary adducts (208a). Barnard and Bateman obtained only isohomogeranic acid, $(CH_3)_2C$=$CHCH_2CH_2C(CH_3)(COOH)CH$=$CH_2$ from carbonation of the Grignard reagent of a similar $\gamma,\gamma$-disubstituted halide, geranyl chloride (36). Addition of the Grignard reagent from $\alpha$-isopropyl-$\beta$-methylallyl chloride to diisopropyl ketone gave mostly the primary adduct, but steric hindrance is probably important in this case (478). Grignard reagents of the alicyclic allylic halides I, II, and III have been reported to yield only primary addition products in reactions with carbonyl compounds (179, 403, 606).



I                              II                              III
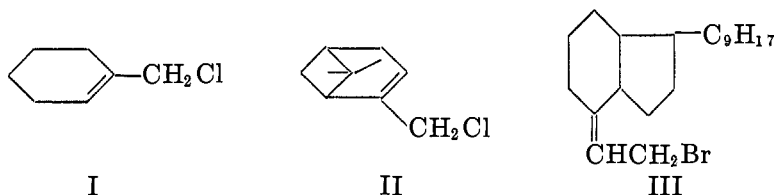
### (e) Other reactions of allylic Grignard reagents

Two other reactions of allylic Grignard reagents are worth mentioning. Young and Roberts (687) prepared the acetal of 2-methyl-3-butenal by treating triethyl orthoformate with butenylmagnesium bromide. The acetal was formed in 84 per cent yield; reactions of this type should prove to be general. Coleman and Forrester (133) obtained a low yield of cinnamylamine from the reaction of the cinnamyl Grignard reagent with chloroamine.

### D. REPLACEMENT REACTIONS OF ALLYLIC ETHERS

Alkoxyl groups are much less easily displaced by nucleophilic reagents than are most of the functional groups thus far discussed, and relatively few replacement reactions of unsymmetrically substituted allylic ethers have been reported. However, allylic ethers are considerably more labile than their saturated analogs, and allylic ethers having two or more activating alkyl or aryl substituents on the $\alpha$- and $\gamma$-carbon atoms of the allylic system undergo substitution reactions fairly readily, especially in the presence of acid catalysts.

### 1. Hydrolysis of α-phenyl-γ-chloroallyl ethers

$\alpha$-Phenyl-$\gamma$-chloroallyl ethers hydrolyze with simultaneous rearrangement to give cinnamaldehyde (10, 590).

$$C_6H_5CH(OR)CH$$=$$CHCl + H_2O \rightarrow C_6H_5CH$$=$$CHCHO + ROH + HCl$$
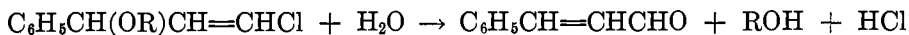
## 2. Conversion of allyl ethers to allyl halides

Allylic ethers having two or more activating aromatic substituents are converted into allylic chlorides by aqueous or anhydrous hydrogen chloride, or by phosphorus pentachloride (589, 591, 700). Rambaud (525) reported that 2-methoxy-3-butenoic acid is converted to the corresponding chloride by dilute hydrochloric acid.

$$CH_2=CHCH(OCH_3)COOH + HCl \rightarrow CH_2=CHCHClCOOH + CH_3OH$$
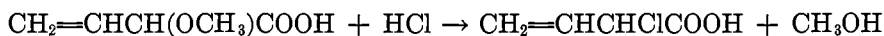
Less reactive ethers require more vigorous reaction conditions. Thus, cinnamyl methyl ether is converted to cinnamyl bromide by hydrogen bromide in sulfuric acid (232) and diallyl, dimethallyl, and dicrotyl ethers are converted to allylic halides by treatment with dry hydrogen chloride or hydrogen bromide under pressure in the presence of cuprous salts (111). These conditions cleaving ethers would bring about rearrangement of the reaction product. Consequently, little can be said about the true nature of the reactions.

## 3. Cleavage of allylic ethers by Grignard reagents

Allylic ethers are cleaved by Grignard reagents, unsaturated hydrocarbons and magnesium alkoxides being the principal reaction products (273, 274, 411, 421, 591).
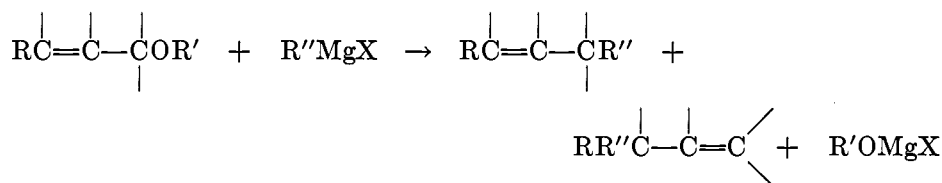


When crotyl o-methoxyphenyl ether was cleaved by phenylmagnesium bromide, a 56 per cent yield of hydrocarbons consisting of 30 per cent α-methylallylbenzene and 70 per cent γ-methylallyl benzene was obtained (421). The abnormal coupling product may be formed through a cyclic mechanism of the following type:
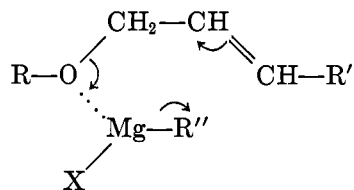


Similar abnormal cleavage reactions have been reported by Hill, Haynes, Simmons, and Hill (273, 274), who also isolated only normal products in a number of reactions of allylic ethers with Grignard reagents. They found that octylmagnesium bromide has a greater tendency to yield abnormal products in cleavage reactions with unsymmetrically substituted allylic ethers than does ethyl-, phenyl-, or benzylmagnesium bromide.

### E. REPLACEMENT REACTIONS OF ALLYLIC ESTERS

#### 1. Conversion of esters to alcohols

Hydrolysis of allylic esters is an important method of preparing allylic alcohols. The esters may be prepared without rearrangement from allylic halides, which frequently are obtained by substitution or addition reactions of non-allylic compounds. In addition, primary allylic esters may be prepared from secondary and tertiary allylic alcohols, either by direct esterification or indirectly via the corresponding bromides. This fact is used to advantage in converting secondary and tertiary allylic alcohols to their primary isomers.

Allylic esters are hydrolyzed by nearly all of the mechanisms known to be involved in carboxylate ester hydrolysis. (For detailed consideration of reaction mechanisms, see the excellent discussion in Ingold's recent book (294).) Which mechanism operates in a particular case depends on a number of factors: the structure of the allylic portion of the ester; the structure of the acyl group; the composition of the reaction medium; and the presence, and concentration, of acid and base catalysts.

#### (a) Saponification of allylic esters

A fact of great importance from the synthetic point of view is that practically all allylic esters can be caused to undergo bimolecular base-catalyzed hydrolysis with acyl–oxygen fission ($B_{AC}2$ in the Ingold classification system):

$$RCOOCHR'CH{=}CHR'' + OH^- \rightleftharpoons RCO^-(OH)OCHR'CH{=}CHR''$$

$$RCO^-(OH)OCHR'CH{=}CHR'' \rightleftharpoons RCOOH + R''CH{=}CHCHR'O^-$$

$$RCOOH + R''CH{=}CHCHR'O^- \rightleftharpoons RCOO^- + R''CHCH{=}CHR'OH$$
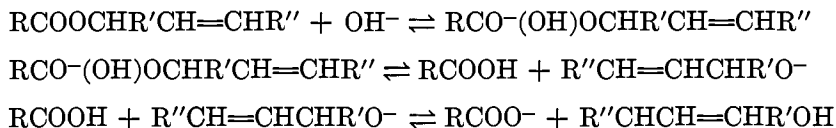
The principal feature of this mechanism of hydrolysis is that the product-forming step involves acyl–oxygen fission. The carbon–oxygen bond at the $\alpha$-carbon atom of the allylic system remains intact throughout the reaction, so that the structure of the allylic group and the configuration of the $\alpha$-carbon atom are completely retained.

The conditions which favor this reaction and minimize other possible modes of hydrolysis are high alkali concentration and low solvent polarity. The hydroxyl-ion concentration required to effect saponification without allylic rearrangement depends primarily on the structure of the allylic part of the ester. Esters with no more than one $\alpha$- or $\gamma$-alkyl substituent are saponified without rearrangement by dilute alkali. Thus, $\alpha$-methylallyl acetate yielded only $\alpha$-methylallyl alcohol when hydrolyzed in 0.5 N sodium hydroxide (297). Several $\gamma$-alkylallyl acetates have been reported to form only $\gamma$-alkylallylic alcohols when hydrolyzed by aqueous sodium carbonate (72) or barium hydroxide (232, 233, 481). Certain disubstituted allylic esters hydrolyze without allylic rearrangement in weakly alkaline solution. The acetate of 4-hexen-1-yn-3-ol undergoes normal hydrolysis in 0.1 M potassium hydroxide (78), and the related 3-acetoxy-1,4-hexadiene is saponified to 1,4-hexadien-3-ol by potassium carbonate in methanol (266).

Esters of allylic alcohols having two or more $\alpha$- and/or $\gamma$-alkyl or -aryl substitu-

ents usually undergo unimolecular hydrolysis in neutral or weakly alkaline media. This mode of reaction is accompanied by allylic rearrangement; in the case of esters which are optically active by virtue of an asymmetric $\alpha$-carbon atom, racemization is also observed. However, even the most labile esters appear to undergo base-catalyzed hydrolysis with acyl–oxygen fission if sufficiently concentrated alkali is used in the saponification. Thus, Kenyon, Partridge, and Phillips (323) found that hydrolysis of the resolved hydrogen phthalate ester of $\alpha$-methyl-$\gamma$-phenylallyl alcohol in aqueous potassium carbonate yielded racemic alcohol, while saponification of the ester by 5 $N$ aqueous sodium hydroxide gave an optically active (though slightly racemized) product. Resolved $\alpha,\gamma$-dialkyl-allyl hydrogen phthalates are saponified with almost complete retention of configuration by concentrated aqueous sodium hydroxide (2, 31, 33, 38, 185, 222, 322, 323, 324, 369, 394, 395), excellent evidence that mechanism $B_{AC}2$ is the principal one operating. The less concentrated the alkali used, however, the greater is the extent of racemization accompanying the saponification (31).

Since saponification of allylic esters with concentrated alkali almost invariably effects hydrolysis without allylic rearrangement, there is little to be gained by tabulating data from the literature on these reactions. There are a few modifications of the reaction which should be mentioned, however. Methanolic or ethanolic sodium or potassium hydroxide is a superior reagent for saponification of esters. Their use makes it possible to carry out saponifications in homogeneous solution, and the lower polarity of alcohols compared to water also minimizes the possibility of labile esters reacting by the $S_N1$ mechanism. Alcoholic alkoxides have also been used for the saponification of allylic esters. Since the alkoxide ion attacks the carboxyl carbon atom, the products of the reaction are the methyl or ethyl ester of the carboxylic acid and the allylic alcohol. The alkoxide is not consumed in the reaction, and only catalytic quantities need be used (466). With the exception of hydrogen phthalates, most allylic esters are no more than sparingly soluble in aqueous alkali. Addition of a suitable detergent to the aqueous suspension emulsifies the ester and increases rate of saponification (222).

### (b) Unimolecular hydrolysis of allylic esters in neutral solutions

Most carboxylic esters are hydrolyzed with fission of the acyl–oxygen bond. If the acyl group is highly electron-attracting, or if the alkyl group is strongly electron-releasing, an ester may undergo uncatalyzed unimolecular solvolysis with alkyl–oxygen fission. Allylic esters having two or more activating $\alpha$- and $\gamma$-substituents on the allylic group satisfy the second condition. Indeed, hydrogen phthalate esters of $\alpha,\gamma$-dialkylallylic alcohols were the first esters recognized to undergo hydrolysis with alkyl–oxygen fission (275).

Hydrolysis of esters by this mechanism actually involves unimolecular nucleophilic substitution:

$$\text{RCOOCHR'CH}{=}\text{CHR''} \rightarrow \text{RCOO}^- + [\text{R'CH}{-}{-}\text{CH}{-}{-}\text{CHR''}]^+$$

$$[\text{R'CH}{-}{-}\text{CH}{-}{-}\text{CHR''}]^+ \xrightarrow{\text{H}_2\text{O}} \text{R'CHOHCH}{=}\text{CHR''} +$$

$$\text{R'CH}{=}\text{CHCHOHR''}$$
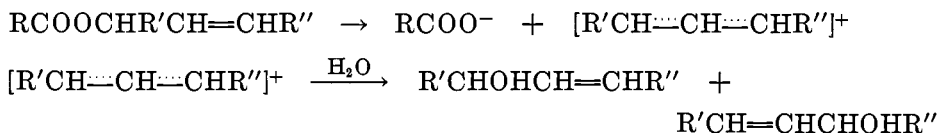
The principal features of this mode of hydrolysis are as follows: (1) hydrolysis by this mechanism is unimolecular and occurs in neutral solution (226, 227); (2) optically active esters yield racemic alcohols (154, 226, 227); (3) hydrolysis is accompanied by allylic rearrangement, (4) ester recovered after partial hydrolysis of optically active esters is partially racemized (154, 226, 227).

While solvolytic hydrolysis of allylic esters is of considerable interest from a theoretical point of view, the fact that this mode of hydrolysis is accompanied by allylic rearrangement and racemization limits its usefulness in synthetic work. As indicated above, bimolecular hydrolysis with acyl–oxygen fission can usually be made to predominate over the unimolecular reaction by using concentrated alcoholic alkali.

Reactions involving alkyl–oxygen heterolysis of carboxylic esters have recently been reviewed by Davies and Kenyon (154).

### (c) Acid-catalyzed hydrolysis of allylic esters

The most common mechanism of acid-catalyzed ester hydrolysis is that which involves acyl–oxygen fission. This appears to be true of allylic as well as ordinary esters. Since the alkyl–oxygen bond remains intact, rearrangement of the allylic radical is not involved in the hydrolysis reaction:

$$RCOOCHR'CH{=}CHR'' + H^+ \underset{}{\overset{H^+}{\rightleftharpoons}} R\overset{\overset{\displaystyle O}{\|}}{C}{-}O{-}CHR'CH{=}CHR''$$

$$R\overset{\overset{\displaystyle O}{\|}}{C}{-}O{-}CHR'CH{=}CHR'' + H_2O \overset{H^+}{\rightarrow} R\overset{\overset{\displaystyle O}{\|}}{C}{-}OH_2^+ + HOCHR'CH{=}CHR''$$
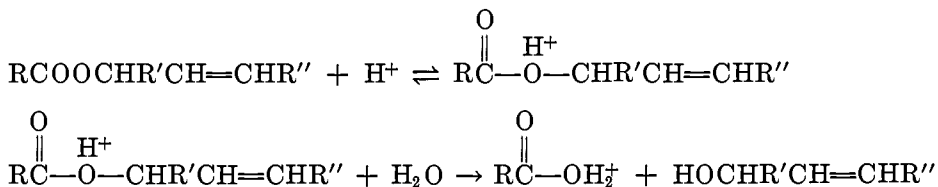
However, it is possible for the initially formed alcohol to undergo rearrangement in the presence of the acid catalyst. This fact frequently makes it difficult to decide whether acyl–oxygen or alkyl–oxygen fission is involved in those reactions which yield rearranged alcohols, unless it can be shown that hydrolysis of the ester is faster than isomerization of the resulting alcohol.

Allylic esters activated by no more than one alkyl group on the $\alpha$- or $\gamma$-carbon atom of the allylic system undergo acid-catalyzed hydrolysis with acyl–oxygen fission and yield alcohols which are sufficiently stable to be isolated before they isomerize. Thus, hydrolysis of $\alpha$- and $\gamma$-methylallyl acetates in dilute acid solution yields only the unrearranged alcohols (297, 485). Apparently, an $\alpha$-ethynyl substituent exerts a smaller activating influence on the allylic portion of the ester than an $\alpha$-alkyl or aryl substituent. Braude (78) studied the acid-catalyzed hydrolysis of $CH_3CH{=}CHCH(OCOCH_3)C{\equiv}CH$, and suggests that the reaction involves acyl–oxygen fission. Only the rearranged, conjugated alcohol $(CH_3CHOHCH{=}CHC{\equiv}CH)$ was isolated; however, it was found that the rate of isomerization of the allylic system (determined spetrophotometrically) is independent of the rate of hydrolysis of the ester and in fact was slower than ester hydrolysis at temperatures below 60°C. The unconjugated alcohol rearranged at a rate comparable to the rate of hydrolysis of the ester under the experimental conditions used.

Goering and Silversmith (226) recently studied the neutral and acid-catalyzed hydrolysis of optically active *cis*- and *trans*-5-methyl-2-cyclohexenyl *p*-nitrobenzoates in aqueous acetone. The interesting observation was made that whereas the optically active esters racemize more rapidly than they hydrolyze in *neutral* solutions, the rate of loss of optical activity in acid solutions exactly equals the rate of hydrolysis. Both the neutral and the acid-catalyzed reactions must involve alkyl–oxygen fission, since racemization accompanies hydrolysis. Heterolysis of a non-protonated ester molecule presumably yields an ion-pair which can react with water or recombine to form racemic ester. In the acid-catalyzed reaction, however, heterolysis of the conjugate acid of the ester yields a mesomeric allylic carbonium ion and an uncharged carboxylic acid molecule. Apparently this heterolysis is effectively irreversible; if it were not, rate of loss of optical activity would necessarily be greater than the rate of hydrolysis. These changes may be pictured as follows:
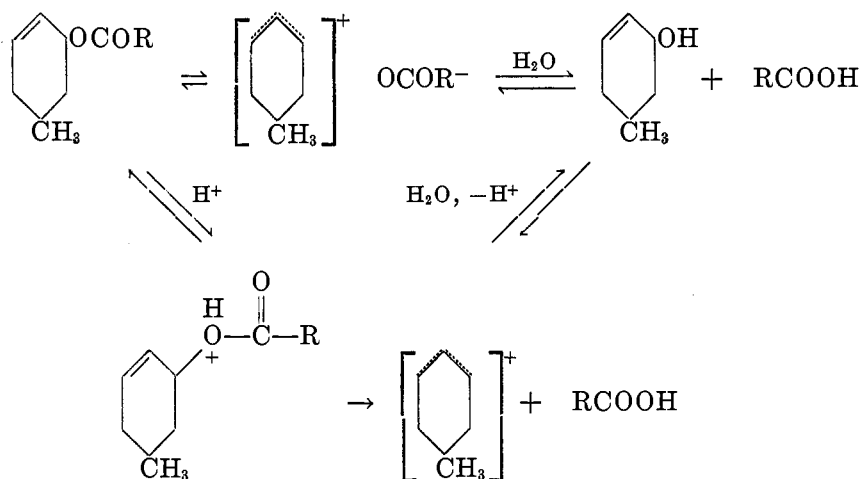


Further evidence that alkyl–oxygen fission is involved in the acid-catalyzed hydrolysis of the 5-methyl-2-cyclohexenyl *p*-nitrobenzoates is furnished by the fact that the allylic esters are hydrolyzed much more rapidly in acidic solution than is cyclohexyl *p*-nitrobenzoate, an ester which very probably is hydrolyzed with acyl–oxygen fission. If the allylic ester underwent acyl–oxygen fission, its rate of hydrolysis should be similar to that of the cyclohexyl derivative. The hydrolysis of *cis*- and *trans*-5-methyl-2-cyclohexenyl *p*-nitrobenzoates appears to be the only well-established case of acid-catalyzed hydrolysis of allylic esters with alkyl–oxygen fission.

### (d) Lithium aluminum hydride reduction of allylic esters

Lithium aluminum hydride reduction of allylic esters yields allylic alcohols (194, 224):

$$\text{RCOOCR'C}=\text{CR''} \xrightarrow{\text{LiAlH}_4} \xrightarrow{\text{H}_2\text{O}} \text{RCH}_2\text{OH} + \text{HOCR'C}=\text{CR''}$$
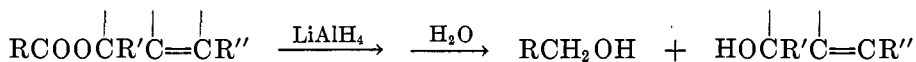
The bond between the oxygen atom and the $\alpha$-carbon atom of the allylic system is not cleaved, and the reaction can be carried out under conditions unlikely to cause rearrangement of the allylic alcohol. In addition, the reduction is carried out in ether, a relatively non-polar solvent. This method would seem to be particularly useful when applied to esters which undergo unimolecular hydrolysis (with alkyl–oxygen fission) during ordinary saponification procedures.

### 2. Reaction of allylic esters with Grignard reagents

Reaction of allylic esters with Grignard reagents may either proceed normally, giving tertiary alcohols derived from the carboxyl group and allylic alcohols, or abnormally, by cleavage of the ester and coupling of the allylic radical with the Grignard reagent:

$$RCOOC-C=CR' \xrightarrow{R''MgX} \begin{array}{l} \rightarrow RR''_2COH + R'C=C-COH \\ \\ \hookrightarrow RCOOMgX + R''C-C=CR' \end{array}$$
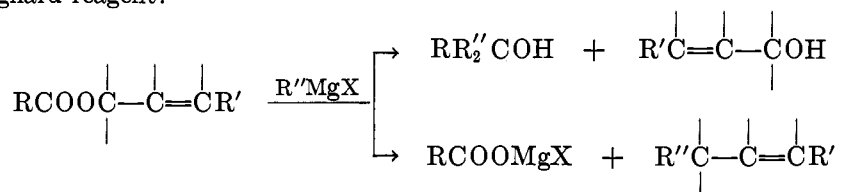
The normal reaction predominates when neither the carboxyl group nor the Grignard reagent is sterically hindered (21, 108). The coupling reaction can be made to predominate by using esters of hindered carboxylic acids such as mesitoic acid (22, 25, 647), triphenylacetic acid, 2,2-diphenylpropionic acid, 2-methyl-2-benzylbutyric acid, or 2,3-dimethylnaphthoic acid (21). Extensive coupling also occurs when an allylic ester of a non-hindered carboxylic acid is allowed to react with a sterically hindered Grignard reagent such as mesitylmagnesium bromide (23, 449, 450).

Arnold and Liggett (22) found that reaction of crotyl mesitoate with phenylmagnesium bromide gives crotylbenzene as the only coupling product. Arnold and Searles (25) later carried out a similar reaction with $\alpha$-methylallyl mesitoate, and again obtained crotylbenzene as the only isolable coupling product. Wilson, Roberts, and Young (647) verified the claim that crotyl mesitoate forms only crotylbenzene in reactions with phenylmagnesium bromide, but found that $\alpha$-methylallyl mesitoate yields a mixture of hydrocarbons consisting of 77 per cent crotylbenzene and 23 per cent $\alpha$-methylallyl benzene. A hydrocarbon mixture of similar composition was obtained from the reaction of $\alpha$-methylallyl chloride with phenylmagnesium bromide.

These facts are best accounted for by assuming that crotyl mesitoate reacts with Grignard reagents by a concerted mechanism involving a cyclic transition state (22),
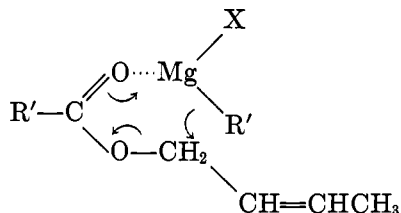
while $\alpha$-methylallyl mesitoate reacts via an ionic mechanism involving an allylic carbonium ion or ion-pair (647).

$\gamma,\gamma$-Dimethylallylmesitylene is apparently the major product of the reaction of either $\alpha,\alpha$-dimethylallyl acetate or $\gamma,\gamma$-dimethylallyl acetate with mesitylmagnesium bromide (449, 450). That the tendency of these disubstituted esters to yield carbonium ions may be more important to the occurrence of coupling reactions than is steric hindrance in the Grignard reagent is indicated by the fact that $\alpha,\alpha$-dimethylallyl acetate underwent both coupling and addition in reactions with ethylmagnesium bromide and phenylmagnesium bromide (449).

### 3. Conversion of esters to ethers

Allylic esters having two activating alkyl or aryl substituents on the allylic system undergo unimolecular solvolysis with alkyl–oxygen fission in methanol or ethanol, as indicated by the formation of mixtures of allylic ethers (2, 30, 32, 185, 266, 322):

$$RCOOCHR'CH{=}CHR'' \xrightarrow{R'''OH}$$

$$RCOOH \;+\; R'''OCHR'CH{=}CHR'' \;+\; R'''OCHR''CH{=}CHR'$$
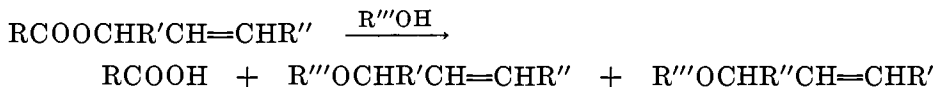
Optically active allylic esters give extensively or completely racemized ethers.

### 4. Conversion of esters to halides

Allylic vicinal diacetates react with dry hydrogen chloride to form $\gamma$-acetoxy-allylic chlorides (339, 341):

$$CH_3CH{=}CHCH(OCOCH_3)_2 \xrightarrow{HCl} CH_3CHClCH{=}CHOCOCH_3$$

$$CH_2{=}CHCH(OCOCH_3)_2 \xrightarrow{HCl} CH_2ClCH{=}CHOCOCH_3$$
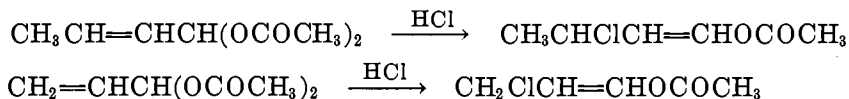
Nystrom and Leak (457) converted allyl alcohol-1-$C^{14}$ to allyl bromide-1-$C^{14}$ by first preparing the tosylate and treating this with sodium bromide "in a suitable solvent."

$$CH_2{=}CH\overset{*}{C}H_2OTs \xrightarrow{NaBr} CH_2{=}CH\overset{*}{C}H_2Br$$
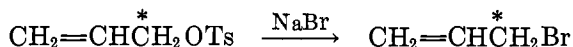
This method might prove to be generally applicable as a stereospecific synthesis of the less labile allylic bromides.

#### F. DEAMINATION REACTIONS OF ALLYLIC AMINES

Most reactions of allylic amines—alkylation, acylation, conversion to isothiocyanates—do not involve fission of the carbon–nitrogen bond, and hence are not accompanied by allylic rearrangement. Such reactions are strictly comparable to similar reactions of non-allylic amines and will not be discussed here.

Deamination by aqueous nitrous acid is one of the very few reactions of allylic amines which result in complete replacement of the amino nitrogen atom (58, 207, 419, 537). The question of the detailed mechanism of this reaction is an interesting one. Deamination of aliphatic primary amines is generally agreed to proceed via a carbonium-ion intermediate:

$$R_3CNH_2 \xrightarrow{HONO} R_3CN_2^+ \xrightarrow{-N_2} R_3C^+ \xrightarrow{R'OH, -H^+} R_3COR'$$
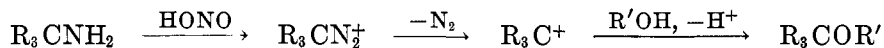
TABLE 35

*Product compositions from the silver-ion-catalyzed solvolysis of allylic halides and deamination of the corresponding allylic amines (690)*

| Solvent | H₂O | | | | CH₃COOH | | | | C₂H₅OH | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Y | Cl | | NH₂ | | Cl | | NH₂ | | Cl | | NH₂ | |
| Product composition / Starting compound | Primary | Secondary or tertiary | Primary | Secondary or tertiary | Primary | Secondary or tertiary | Primary | Secondary or tertiary | Primary | Secondary or tertiary | Primary | Secondary or tertiary |
| | per cent | per cent | per cent | per cent | per cent | per cent | per cent | per cent | per cent | per cent | per cent | per cent |
| CH₃CH=CHCH₂Y...... | 45 | 55 | 47* | 53* | 60 | 40 | 79 | 21 | 70 | 30 | | |
| CH₃CHYCH=CH₂...... | 34 | 66 | 31* | 69* | 56 | 44 | 33 | 67 | 46 | 54 | 50 | 50 |
| (CH₃)₂C=CHCH₂Y..... | 15 | 85 | 16 | 84 | 54 | 46 | 78 | 22 | 35 | 65 | 35 | 65 |
| (CH₂)₂CY—CH=CH₂... | 14 | 86 | 14 | 86 | 55 | 45 | 60 | 40 | 20 | 80 | 55 | 45 |

* Reference 537.

It seemed likely that this would be equally true in the case of allylic primary amines. If loss of nitrogen from an allylic diazonium ion involved less nucleophilic participation by solvent molecules than solvolysis of the corresponding halides, deamination reactions would be a useful tool for studying reactions of "free" mesomeric allylic carbonium ions.

The deaminations of $\alpha$- and $\gamma$-methylallylamines and $\alpha,\alpha$- and $\gamma,\gamma$-dimethylallylamines in water, ethanol, and acetic acid have been thoroughly studied (537, 569). In water the deamination of a given allylic amine and the silver-ion-catalyzed hydrolysis of the corresponding chloride produce essentially the same mixture of alcohols; this fact indicates that both reactions involve exclusive formation of the same carbonium ion. The deamination reactions in acetic acid give significantly larger proportions of products of unrearranged allylic structure than do silver-ion-catalyzed solvolyses of the corresponding allylic chlorides (see table 35), thus indicating that not all of the deamination product is formed from a carbonium ion. However, the fact that mixtures of products are formed when either member of a pair of isomeric allylic primary amines is diazotized indicates that part of the reaction in acetic acid proceeds through a carbonium-ion intermediate.

There are at least four possible mechanisms which could compete with carbonium-ion formation and give rise to unexpectedly large proportions of unrearranged products in allylic deamination reactions in acetic acid. One such possibility is the non-rearranging reaction of the diazo compound formed by loss of a proton from the $\alpha$-carbon atom of the diazonium ion:

$$\text{C=C—CHN}_2^+ \underset{}{\overset{-H^+}{\rightleftharpoons}} \text{C=C—CN}_2 \xrightarrow{ROH} \text{C=C—CHOR} + N_2$$

$$\downarrow -N_2$$

$$\left[ \text{C}\cdots\text{C}\cdots\text{C} \overset{H^+}{} \right] \xrightarrow{ROH} \text{C=C—CHOR} + \text{C(OR)C=CH}$$
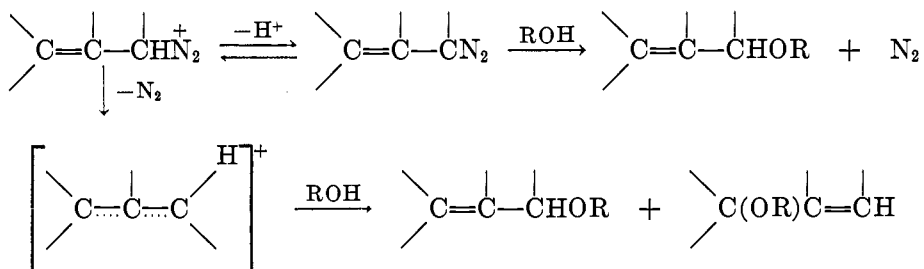
Curtin and Gerber (152) found that the isomeric diazobutenes give only esters of unrearranged allylic structure when allowed to react with 3,5-dinitrobenzoic acid in ether. Mixtures of alcohols and ethers were obtained on acid-catalyzed hydrolysis and ethanolysis of the diazobutenes, but this could be due to the reverse of the reaction by means of which the diazo compounds are postulated to be formed from diazonium ions. The diazonium ion–diazo compound interconversion can now be ruled out in the case of deamination of $\alpha$- and $\gamma$-methylallylamines in acetic acid. Young and Semenow (589) carried out deamination reactions of these amines in deuteroacetic acid ($CH_3COOD$) and obtained mixtures of esters containing no detectable amount of deuterium. Formation of an acetate ester from a diazo compound would require incorporation of deuterium from the acetic acid into the allylic system.

A second possible non-rearranging mechanism is as follows: If an allylic diazonium ion loses nitrogen so readily that participation by the $\pi$-electrons of the allylic double bond is not required to assist in its expulsion, an allylic carbonium ion might form while the molecule is in a conformation which does not permit the electrons of the double bond to enter into conjugation with the positively charged $\alpha$-carbon atom. In this event, the carbonium ion might react with the solvent to form normal substitution product before the positive charge could distribute itself between the $\alpha$- and $\gamma$-carbon atoms of the allylic system. While such a process seems rather unlikely [since preliminary experiments indicate that the rate of the non-rearranging reaction is specifically sensitive to acetate ion concentration (589)], it cannot be ruled out on the basis of available evidence.

The third possible non-rearranging path involves nucleophilic interaction between the solvent or its conjugate base and the $\alpha$-carbon atom of the diazonium ion. That is, reaction of the diazonium ion with the solvent may not be in the limiting ($S_N1$) category as supposed, but may be toward the nucleophilic end of the mechanistic spectrum ($S_N2$).

Finally, the diazonium ion may react with acetate in a non-rearranging cyclic ($S_Ni$) process.

## V. REFERENCES

(1) AESCHBACH, M. E.: U.S. patent 2,423,545 (1947); Chem. Abstracts **42**, 3773 (1948).
(2) AIRS, R. S., BALFE, M. P., AND KENYON, J.: J. Chem. Soc. **1942**, 19.
(3) AKUJOSHI, S., AND OKUNO, K.: J. Chem. Soc. Japan, Pure Chem. Sect. **74**, 467 (1953); Chem. Abstracts **48**, 11294 (1954).
(4) ALEXANDER, E. R.: *Principles of Ionic Organic Reactions*, p. 91. John Wiley and Sons, Inc., New York (1950).
(5) ALEXANDER, E. R., AND KLUIBER, R. W.: J. Am. Chem. Soc. **73**, 4304 (1951).
(6) AMUNDSEN, L. H., AND BRILL, W. F.: J. Am. Chem. Soc. **73**, 1834 (1951).
(7) AMUNDSEN, L. H., AND BRILL, W. F.: Abstracts of Papers Presented at the 119th Meeting of the American Chemical Society, New York City, September, 1951, p. 58M.
(8) AMUNDSEN, L. H., MAYER, R. H., PITTS, L. S., AND MALENTACCHI, L. A.: J. Am. Chem. Soc. **73**, 2118 (1951).

(9) ANDREWS, L. J.: J. Am. Chem. Soc. **68**, 2584 (1946).

(10) ANDREWS, L. J.: J. Am. Chem. Soc. **69**, 3062 (1947).

(11) ANDREWS, L. J., AND KEPNER, R. E.: J. Am. Chem. Soc. **70**, 3456 (1948).

(12) ANDREWS, L. J., AND LINDEN, S. L.: J. Am. Chem. Soc. **69**, 2091 (1947).

(13) ANGYAL, S. J., PENMAN, D. R., AND WARWICH, P. G.: J. Chem. Soc. **1953**, 1742.

(14) ARBUZOV, B. A.: J. Russ. Phys. Chem. Soc. **38**, 687 (1906).

(15) ARCUS, C. L., AND KENYON, J.: J. Chem. Soc. **1938**, 312.

(16) ARCUS, C. L., AND KENYON, J.: J. Chem. Soc. **1938**, 1912.

(17) ARCUS, C. L., AND SMITH, J. W.: J. Chem. Soc. **1939**, 1749.

(18) ARCUS, C. L., AND SMYTH, D. G.: J. Chem. Soc. **1955**, 34.

(19) ARENS, J. F., AND DORP, D. A. VAN: Rec. trav. chim. **67**, 973 (1948).

(20) ARNOLD, R. T., AND LEE, W. W.: J. Am. Chem. Soc. **75**, 5396 (1953).

(21) ARNOLD, R. T., AND LIGGETT, R. W.: J. Am. Chem. Soc. **64**, 2875 (1942).

(22) ARNOLD, R. T., AND LIGGETT, R. W.: J. Am. Chem. Soc. **67**, 337 (1945).

(23) ARNOLD, R. T., LIGGETT, R. W., AND SEARLES, S.: J. Am. Chem. Soc. **70**, 3938 (1948).

(24) ARNOLD, R. T., AND SEARLES, S.: J. Am. Chem. Soc. **71**, 1150 (1949).

(25) ARNOLD, R. T., AND SEARLES, S.: J. Am. Chem. Soc. **71**, 2021 (1949).

(26) ASCHAN, O.: Ber. **51**, 1303 (1918).

(27) BADGER, G. M., AND PEARCE, R. S.: J. Chem. Soc. **1950**, 2311.

(28) BADGER, G. M., AND PEARCE, R. S.: J. Chem. Soc. **1950**, 2314.

(29) BAKER, J. W.: *Hyperconjugation*, p. 67. Oxford University Press, Amen House, London (1952).

(30) BALFE, M. P., HILLS, H. W., KENYON, J., PHILLIPS, H., AND PLATT, B.: J. Chem. Soc. **1942**, 556.

(31) BALFE, M. P., AND KENYON, J.: Nature **148**, 196 (1941).

(32) BALFE, M. P., AND KENYON, J.: Trans. Faraday Soc. **37**, 721 (1941).

(33) BALFE, M. P., KENYON, J., AND WADDAN, D. Y.: J. Chem. Soc. **1954**, 1366.

(34) BARBIER, C.: Compt. rend. **116**, 1200 (1893).

(35) BARBIER, G. W., AND ENGLISH, J.: J. Am. Chem. Soc. **73**, 746 (1951).

(36) BARNARD, D., AND BATEMAN, L.: J. Chem. Soc. **1950**, 932.

(37) BARNARD, D., AND BATEMAN, L.: J. Chem. Soc. **1950**, 926.

(38) BARTLETT, P. D., KUNA, M., AND LEVENE, P. A.: J. Biol. Chem. **118**, 503 (1937).

(39) BARTLETT, P. D., KUNA, M., AND LEVENE, P. A.: J. Biol. Chem. **118**, 513 (1937).

(40) BATAAFSCHE PETROLEUM MAATSCHAPPIJ: British patent 672,757 (1952); Chem. Abstracts **47**, 8087 (1953).

(41) BATEMAN, L. C., CHURCH, M. G., HUGHES, E. D., INGOLD, C. K., AND TAHER, N. A.: J. Chem. Soc. **1940**, 979.

(42) BATEMAN, L., AND CUNEEN, J. I.: J. Chem. Soc. **1950**, 941.

(43) BATEMAN, L., CUNEEN, J. I., FABIAN, J. M., AND KOCH, H. P.: J. Chem. Soc. **1950**, 936.

(44) BATEMAN, L., CUNEEN, J. I., AND KOCH, H. P.: Nature **164**, 242 (1949).

(45) BATEMAN, L., CUNEEN, J. I., AND KOCH, H. P.: J. Chem. Soc. **1950**, 3045.

(46) BAUDRENGHIEN, J.: Bull. soc. chim. Belg. **31**, 160 (1922).

(47) BAUDRENGHIEN, J.: Bull. soc. chim. Belg. **32**, 337 (1923).

(48) BEDOS, P., AND RUYER, A.: Compt. rend. **204**, 1350 (1937).

(49) BERGMANN, A. G.: J. Russ. Phys. Chem. Soc. **52**, 37 (1920); Chem. Abstracts **17**, 1420 (1921).

(50) BERGMANN, E.: Helv. Chim. Acta **20**, 590 (1937).

(51) BERGMANN, E., AND CORTE, H.: J. Chem. Soc. **1935**, 1363.

(52) BERGMANN, E., AND WEISS: Ber. **64**, 1485 (1931).

(53) BERLAK, M. C., AND GERRARD, W.: J. Chem. Soc. **1949**, 2309.

(54) BERT, L.: Compt. rend. **180**, 1504 (1925).

(55) BERT, L.: Compt. rend. **192**, 1563 (1931).

(56) BERTRAM, J., AND GILDEMEISTER, E.: J. prakt. Chem. **49**, 185 (1894).

(57) BEVAN, C. W. L., HUGHES, E. D., AND INGOLD, C. K.: Nature **171**, 301 (1953).
(58) BILLITER, O.: Helv. Chim. Acta **8**, 337 (1925).
(59) BIRCH, S. F., AND McALLAN, D. T.: J. Chem. Soc. **1951**, 2257.
(60) BJELOUSS, E.: Ber. **43**, 2330 (1910).
(61) BJELOUSS, E.: Ber. **45**, 625 (1912).
(62) BLICKE, F. F.: U.S. patent 2,533,085 (1950); Chem. Abstracts **45**, 2499 (1951).
(63) BLOMQUIST, A. T., AND MAYES, W. G.: J. Org. Chem. **10**, 134 (1945).
(64) BOHME, H., AND SIERING, O.: Ber. **71**, 2372 (1938).
(65) BOLLETER, A., EITER, K., AND SCHMID, H.: Helv. Chim. Acta **34**, 186 (1951).
(66) BOOZER, C. E., AND LEWIS, E. S.: J. Am. Chem. Soc. **75**, 3182 (1953).
(67) BORDWELL, F. G., AND WEINSTOCK, J.: Abstracts of Papers Presented before the Division of Organic Chemistry at the 124th Meeting of the American Chemical Society, Chicago, Illinois, September, 1953, p. 60-O.
(68) BOUCHARDAT, G.: Compt. rend. **89**, 1117 (1879).
(69) BOUCHARDAT, G.: Compt. rend. **116**, 1253 (1893).
(70) BOUIS, M.: Compt. rend. **182**, 788 (1926).
(71) BOUIS, M.: Ann. chim. [10] **9**, 402 (1928).
(72) BOUIS, M.: Bull. soc. chim. [4] **41**, 1160 (1927).
(73) BOUIS, M.: Compt. rend. **183**, 133 (1926).
(74) BOURGUEL, M., AND PIAUX, L.: Bull. soc. chim. [4] **51**, 1041 (1932).
(75) BOYD, R. N., AND KELLY, R. J.: J. Am. Chem. Soc. **74**, 4600 (1952).
(75a) BRANDON, D. B.: Ph.D. Thesis, University of California at Los Angeles, 1950.
(76) BRAUDE, E. A.: Quart. Rev. **4**, 404 (1950).
(77) BRAUDE, E. A.: Ann. Repts. on Progress Chem. (Chem. Soc. London) **46**, 125 (1949).
(78) BRAUDE, E. A.: J. Chem. Soc. **1948**, 794.
(79) BRAUDE, E. A., BRUNN, T., WEEDON, B. C. L., AND WOODS, R. J.: J. Chem. Soc. **1952**, 1414.
(80) BRAUDE, E. A., BRUNN, T., WEEDON, B. C. L., AND WOODS, R. J.: J. Chem. Soc. **1952**, 1418.
(81) BRAUDE, E. A., AND COLES, J. A.: J. Chem. Soc. **1950**, 2014.
(82) BRAUDE, E. A., AND COLES, J. A.: J. Chem. Soc. **1952**, 1425.
(83) BRAUDE, E. A., COLES, J. A., AND TIMMONS, C. J.: Nature **166**, 58 (1950).
(84) BRAUDE, E. A., FAWCETT, J. S., AND NEWMAN, D. D. E.: J. Chem. Soc. **1950**, 793.
(85) BRAUDE, E. A., AND FORBES, W. F.: J. Chem. Soc. **1951**, 1755.
(86) BRAUDE, E. A., JONES, E. R. H., AND STERN, E. S.: J. Chem. Soc. **1946**, 396.
(87) BRAUDE, E. A., AND TIMMONS, C. J.: J. Chem. Soc. **1950**, 2000.
(88) BRAUDE, E. A., AND TIMMONS, C. J.: J. Chem. Soc. **1950**, 2007.
(89) BRAUDE, E. A., AND TIMMONS, C. J.: J. Chem. Soc. **1953**, 3131.
(90) BRAUDE, E. A., TURNER, D. W., AND WAIGHT, E. S.: Nature **173**, 863 (1954).
(91) BRAUDE, E. A., AND WHEELER, O. H.: J. Chem. Soc. **1955**, 320.
(92) BRAUDE, E. A., AND WHEELER, O. H.: J. Chem. Soc. **1955**, 329.
(93) BRAUN, J. VON, AND KOHLER, Z.: Ber. **51**, 79 (1918).
(94) BRAUN, J. VON, AND KUHN, M.: Ber. **58**, 2168 (1925).
(95) BRAUN, J. VON, AND SCHIRMACHER, W.: Ber. **56**, 538 (1923).
(96) BRUSON, H. A., AND ESTES, J. W.: J. Am. Chem. Soc. **59**, 2011 (1937).
(97) BURTON, H.: J. Chem. Soc. **1928**, 1650.
(98) BURTON, H.: J. Chem. Soc. **1929**, 455.
(99) BURTON, H.: J. Chem. Soc. **1930**, 248.
(100) BURTON, H.: J. Chem. Soc. **1931**, 759.
(101) BURTON, H.: J. Chem. Soc. **1934**, 1268.
(102) BURTON, H., AND INGOLD, C. K.: J. Chem. Soc. **1928**, 904.
(103) BURTON, H., AND SHOPPEE, C. W.: J. Chem. Soc. **1934**, 197.
(104) BURTON, H., AND SHOPPEE, C. W.: J. Chem. Soc. **1935**, 1156.
(105) BURTON, H., AND SHOPPEE, C. W.: J. Chem. Soc. **1939**, 1409.

(106) Burton, H., Shoppee, C. W., and Wilson, C. L.: J. Chem. Soc. **1933**, 721.
(107) Bushwell, A. M., Rodebush, W. H., and Roy, M. F.: J. Am. Chem. Soc. **60.** 2528 (1938).
(108) Businger, A.: U.S. patent 2,529,482 (1950); Chem. Abstracts **45**, 2966 (1951).
(109) Buu-Hoi, Ng. P., and Hoan, Ng.: J. Org. Chem. **14**, 1023 (1949).
(110) Campbell, T. W., and Young, W. G.: J. Am. Chem. Soc. **69**, 688 (1947).
(111) Carlson, G. J.: U.S. patent 2,494,034 (1950); Chem. Abstracts **44**, 3004 (1950).
(112) Carothers, W. H.: U.S. patent 2,072,867 (1937); Chem Abstracts **31**, 3335 (1937).
(113) Carothers, W. H., and Berchet, G. J.: J. Am. Chem. Soc. **55**, 2807 (1933).
(114) Carothers, W. H., and Berchet, G. J.: J. Am. Chem. Soc. **55**, 2813 (1933).
(115) Carroll, M. F.: J. Chem. Soc. **1940**, 704.
(116) Carroll, M. F.: J. Chem. Soc. **1940**, 1266.
(117) Carroll, M. F.: J. Chem. Soc. **1941**, 507.
(118) Caserio, F.: Ph.D. Thesis, University of California at Los Angeles, 1954.
(119) Caserio, F., Dennis, G. E., DeWolfe, R. H., and Young, W. G.: J. Am. Chem. Soc. **77**, 4182 (1955).
(120) Catchpole, A. G., and Hughes, E. D.: J. Chem. Soc. **1948**, 1.
(121) Catchpole, A. G., and Hughes, E. D.: J. Chem. Soc. **1948**, 4.
(122) Catchpole, A. G., Hughes, E. D., and Ingold, C. K.: J. Chem. Soc. **1948**, 8.
(123) Charon, E.: Ann. chim. [7] **17**, 197 (1899).
(124) Charon, E.: Bull. soc. chim. [4] **7**, 86 (1910).
(125) Cheeseman, G. W. H., Heilbron, I., Jones, E. R. H., Sondheimer, F., and Weedon, B. C. L.: J. Chem. Soc. **1949**, 1516.
(126) Chesterman, D. R.: J. Chem. Soc. **1935**, 906.
(127) Childs, A. F., Plant, S. G. P., Tompsett, A. L. L., and Weeks, G. A.: J. Chem. Soc. **1948**, 2180.
(128) Churbakov, A. N.: Zhur. Obshcheǐ Khim. **10**, 977 (1940).
(129) Claisen, L., Kremers, F., Roth, F., and Tietze, E.: J. prakt. Chem. **105**, 65 (1922).
(130) Claisen, L., and Tietze, E.: Ber. **59**, 2344 (1926).
(131) Clarke, H. T.: J. Chem. Soc. **1910**, 416.
(132) Cleveland, F. F.: J. Chem. Phys. **11**, 1 (1943).
(133) Coleman, G. H., and Forrester, R. A.: J. Am. Chem. Soc. **58**, 27 (1936).
(134) Coe, D. G., Landauer, S. R., and Rydon, H. N.: J. Chem. Soc. **1954**, 2281.
(135) Collins, A. M.: U.S. patent 2,192,299 (1940); Chem. Abstracts **34**, 4392 (1940).
(136) Colonge, J. and Dreux, J.: Compt. rend. **236**, 1791 (1953).
(137) Colonge, J., and Poilane, G.: Compt. rend. **238**, 1821 (1954).
(138) Colonge, J., and Reymermier, M.: Compt. rend. **237**, 226 (1953).
(139) Conant, J. B., Kirner, N. R., and Hussey, R. E.: J. Am. Chem. Soc. **47**, 488 (1925).
(140) Cope, A. C., Estes, L. L., Emery, J. R., and Haven, A. C.: J. Am. Chem. Soc. **73**, 1199 (1951).
(141) Cope, A. C., Hoffman, C. M., and Hardy, E. M.: J. Am. Chem. Soc. **83**, 1852 (1941).
(142) Cope, A. C., Morrison, D. E., and Field, L.: J. Am. Chem. Soc. **72**, 59 (1950).
(143) Courtot, A.: Bull. soc. chim. [3] **35**, 969 (1906).
(144) Cowdry, W. A., Hughes, E. D., Ingold, C. K., Masterman, S., and Scott, A. D.: J. Chem. Soc. **1937**, 1252.
(145) Cram, D. J.: J. Am. Chem. Soc. **75**, 332 (1953).
(146) Cristol, S. J., and Overhults, W. C.: J. Am. Chem. Soc. **73**, 2932 (1951).
(147) Cristol, S. J., Overhults, W. C., and Meek, J. S.: J. Am. Chem. Soc. **73**, 813 (1951).
(148) Crossley, F. S.: U.S. patent, 2,609,392 (1952); Chem. Abstracts **49**, 2497 (1955).
(149) Croxall, W. J., and Fegley, M. F.: U.S. patent 2,526,007 (1950); Chem. Abstracts **45**, 1160 (1951).
(150) Croxall, W. J., and Van Hook, J. O.: J. Am. Chem. Soc. **72**, 803 (1950).
(151) Croxall, W. J., and Van Hook, J. O.: U.S. patent 2,541,957 (1951); Chem. Abstracts **45**, 7140 (1951).

(152) CURTIN, D. Y., AND GERBER, S. M.: J. Am. Chem. Soc. **74**, 4052 (1952).
(153) CYMERMAN, J., HEILBRON, I., JONES, E. R. H., AND LACEY, R. N.: J. Chem. Soc. **1946**, 500.
(154) DAVIES, A. B., AND KENYON, J.: Quart. Rev. **9**, 203 (1955).
(155) DEEBEL, G. F.: U.S. patent 2,555,270 (1951); Chem. Abstracts **45**, 9556 (1951).
(156) DELABY, R.: Compt. rend. **194**, 1248 (1932).
(157) DELABY, R.: Compt. rend. **203**, 1521 (1936).
(158) DELABY, R.: Bull. soc. chim. [5] **3**, 2375 (1936).
(159) DELABY, R., AND BELLER, A.: Bull. soc. chim. [4] **53**, 367 (1933).
(160) DELABY, R., AND GUILLOT-ALLEGRE, S.: Bull. soc. chim. [4] **53**, 301 (1933).
(161) DELABY, R., AND HUBERT, J.: Bull. soc. chim. [5] **10**, 573 (1943).
(162) DELABY, R., AND HUBERT, J.: Bull. soc. chim. [5] **10**, 576 (1943).
(163) DELABY, R., AND LECOMPTE, J.: Bull. soc. chim. [5] **4**, 749 (1937).
(164) DELABY, R., AND LECOMPTE, J.: Bull. soc. chim. [5] **4**, 738 (1937).
(165) DELABY, R., PIAUX, L., AND GUILLEMONAT, A.: Compt. rend. **205**, 609 (1937).
(166) DE LA MARE, P. B. D., ENGLAND, B. D., FOWDEN, L., HUGHES, E. D., AND INGOLD, C. K.: J. chim. phys. **45**, 236 (1948).
(167) DE LA MARE, P. B. D., HUGHES, E. D., AND INGOLD, C. K.: J. Chem. Soc. **1948**, 17.
(168) DE LA MARE, P. B. D., HUGHES, E. D., AND VERNON, C. A.: Nature **169**, 672 (1952).
(169) DE LA MARE, P. B. D., AND VERNON, C. A.: Research **6**, 56-S (1953).
(170) DE LA MARE, P. B. D., AND VERNON, C. A.: J. Chem. Soc. **1954**, 2504.
(171) DE LA MARE, P. B. D., AND VERNON, C. A.: J. Chem. Soc. **1954**, 3679.
(172) DE LA MARE, P. B. D., AND VERNON, C. A.: J. Chem. Soc. **1952**, 3325.
(173) DE LA MARE, P. B. D., AND VERNON, C. A.: J. Chem. Soc. **1952**, 3331.
(174) DE LA MARE, P. B. D., AND VERNON, C. A.: J. Chem. Soc. **1952**, 3628.
(175) DE LA MARE, P. B. D., AND VERNON, C. A.: J. Chem. Soc. **1953**, 3555.
(176) DENNIS, G. E., AND YOUNG, W. G.: Unpublished work.
(177) DEWAR, M. J. S.: Bull. soc. chim. [5] **18**, C 43 (1951).
(178) DIMROTH, K.: Ber. **71**, 1333 (1938).
(179) DIMROTH, K., AND STOCKSTROM, E.: Ber. **75**, 1263 (1942).
(179a) DJERASSI, C.: Chem. Revs. **43**, 271 (1948).
(180) DORAN, W. J., AND SCHONLE, H. A.: J. Am. Chem. Soc. **60**, 2880 (1938).
(181) DUPONT, J., AND LABAUNE, L.: Wiss. ind. ber. R. Bertrand **1**, 38; Chem. Abstracts **5**, 1398 (1911).
(182) DUPONT, J., AND LABAUNE, L.: Wiss. ind. ber. R. Bertrand **1**, 42; Chem. Abstracts **5**, 1437 (1911).
(183) DUVEEN, D.: Compt. rend. **206**, 1185 (1938).
(184) DUVEEN, D. I., AND KENYON, J.: J. Chem. Soc. **1936**, 1451.
(185) DUVEEN, D. I., AND KENYON, J.: J. Chem. Soc. **1939**, 1697.
(186) DUVEEN, D. I., AND KENYON, J.: Bull. soc. chim. [5] **5**, 704 (1938).
(187) EASTHAM, A. M., FISHER, H. E., KULKA, M., AND HIBBERT, H.: J. Am. Chem. Soc. **66**, 26 (1944).
(188) ELIEL, E. L., AND PECKHAM, P. E.: J. Am. Chem. Soc. **72**, 1209 (1950).
(189) EMERSON, W. S., DEEBEL, G. F., AND LONGLEY, R. I.: J. Org. Chem. **14**, 696 (1949).
(190) EMERSON, W. S., AND LONGLEY, R. I.: U.S. patent 2,577,409 (1951); Chem. Abstracts **46**, 7586 (1952).
(191) EMERSON, W. S., AND LONGLEY, R. I.: U.S. patent 2,624,753 (1953); Chem. Abstracts **47**, 11235 (1953).
(192) ENGLAND, B. D.: J. Chem. Soc. **1955**, 1615.
(193) ENGLAND, B. D., AND HUGHES, E. D.: Nature **168**, 1002 (1951).
(194) ENGLISH, J., AND LAMBERTI, V.: J. Am. Chem. Soc. **74**, 1909 (1952).
(195) ETTLINGER, M. G., AND HODGKINS, J. E.: J. Am. Chem. Soc. **77**, 1831 (1955).
(196) FARBENINDUSTRIE A.-G.: German patent 513,364 (1930); Chem. Abstracts **25**, 1261 (1931).

(197) FARBENINDUSTRIE A.-G.: German patent 512,232 (1930); Chem. Abstracts **26**, 4611 (1932).
(198) FARLOW, M. W.: U.S. 2,518,608 (1950); Chem. Abstracts **45,** 639 (1951).
(199) FARMER, E. H., DAS LAROIA, B., SWITZ, T. M., AND THORPE, J. F.: J. Chem. Soc. **1927**, 2937.
(200) FARMER, E. H., AND MARSHALL, F. C. B.: J. Chem. Soc. **1931**, 129.
(201) FIESER, L. F.: J. Am. Chem. Soc. **49**, 875 (1927).
(202) FIESER, L. F., AND ROMERO, M. A.: J. Am. Chem. Soc. **75**, 4716 (1953).
(203) FIRMINICH AND CIE: Swiss patent 262,269 (1949); Chem. Abstracts **45**, 5189 (1951).
(204) FISCHER, F. G., AND LOWENBERG, K.: Ann. **475**, 183 (1929).
(205) FORSTER, M. O., AND CARDWELL, D.: J. Chem. Soc. **1913**, 1338.
(206) FRAZER, M. J., GERRARD, W., MACHELL, G., AND SHEPHERD, B. D.: Chemistry & Industry **1954,** 931.
(207) GALAND, E.: Bull. soc. chim. Belg. **39**, 529 (1930).
(208) GANGULY, S. N.: J. Indian Chem. Soc. **13**, 580 (1936).
(208a) GARNER, B. L.: Ph.D. Thesis, University of California at Los Angeles, 1952.
(209) GERRARD, W.: J. Chem. Soc. **1945**, 848.
(210) GERRARD, W.: J. Chem. Soc. **1946**, 741.
(211) GERRARD, W., NECHVATAL, A., AND WILSON, B. M.: J. Chem. Soc. **1950**, 2089.
(212) GERRARD, W., NECHVATAL, A., AND WILSON, B. M.: J. Chem. Soc. **1949**, 3326.
(213) GERRARD, W., AND RICHMOND, M. J.: J. Chem. Soc. **1945**, 853.
(214) GILMAN, H., AND HARRIS, S. A.: J. Am. Chem. Soc. **49**, 1825 (1927).
(215) GILMAN, H., AND HARRIS, S. A.: J. Am. Chem. Soc. **53**, 3541 (1931).
(216) GILMAN, H., AND HARRIS, S. A.: J. Am. Chem. Soc. **54**, 2072 (1932).
(217) GILMAN, H., AND HARRIS, S. A.: Rec. trav. chim. **50**, 1052 (1931).
(218) GILMAN, H., AND KIRBY, J. E.: J. Am. Chem. Soc. **51**, 3475 (1929).
(219) GILMAN, H., AND McGLUMPHY: Bull. soc. chim. [4] **43**, 1322 (1928).
(220) GILMAN, H., AND ZOELLNER, E. A.: J. Am. Chem. Soc. **52**, 3984 (1930).
(221) GLEAVE, J. L., HUGHES, E. D., AND INGOLD, C. K.: J. Chem. Soc. **1935**, 236.
(222) GOERING, H. L., AND BLANCHARD, J. P.: J. Am. Chem. Soc. **76**, 5405 (1954).
(223) GOERING, H. L., BLANCHARD, J. P., AND SILVERSMITH, E.: J. Am. Chem. Soc. **76,** 5409 (1954).
(224) GOERING, H. L., NEVITT, T. D., AND SILVERSMITH, E. F.: J. Am. Chem. Soc. **77,** 4042 (1955).
(225) GOERING, H. L., NEVITT, T. D., AND SILVERSMITH, E. F.: J. Am. Chem. Soc. **77**, 5026 (1955).
(226) GOERING, H. L., AND SILVERSMITH, E. F.: J. Am. Chem. Soc. **77**, 6249 (1955).
(227) GOERING, H. L., AND SILVERSMITH, E. F.: J. Am. Chem. Soc. **77**, 1129 (1955).
(228) GOETHALS, G.: Bull. soc. chim. Belg. **46**, 409 (1937).
(229) GOULD, R. G., AND THOMPSON, A. F.: J. Am. Chem. Soc. **57**, 340 (1935).
(230) GREDY, B.: Compt. rend. **202**, 664 (1936).
(231) GREDY, B.: Bull. soc. chim. [5] **2**, 1029 (1935).
(232) GREDY, B.: Bull. soc. chim. [5] **3**, 1093 (1936).
(233) GREDY, B.: Bull. soc. chim. [5] **4**, 415 (1937).
(234) GREDY, B.: Compt. rend. **202**, 322 (1936).
(235) GREDY, B., AND PIAUX, L.: Compt. rend. **198**, 1235 (1934).
(236) GREDY, B., AND PIAUX, L.: Bull. soc. chim. [5] **1**, 1481 (1934).
(237) GREDY, B., AND VAN RISSEGHEM, H.: Bull. soc. chim. Belg. **45**, 177 (1936).
(238) GRINER, G.: Compt. rend. **116**, 723 (1893).
(239) GRINER, G.: Ann. chim. [6] **26**, 380 (1892).
(240) GRUNWALD, E., AND WINSTEIN, S.: J. Am. Chem. Soc. **70**, 841 (1948).
(241) HALL, H., YOUNG, W. G., AND WINSTEIN, S.: J. Am. Chem. Soc. **78**, in press (1956).
(242) HARRIS, S. A.: Iowa State Coll. J. Sci. **6**, 425 (1932); Chem. Abstracts **27**, 279 (1933).
(243) HATCH, L. F., AND ALEXANDER, H. E.: J. Am. Chem. Soc. **72**, 5643 (1950).

(244) HATCH, L. F., AND ALEXANDER, H. E.: J. Am. Chem. Soc. **71**, 1037 (1949).
(245) HATCH, L. F., AND BALLIN, S. G.: J. Am. Chem. Soc. **71**, 1039 (1949).
(246) HATCH, L. F., AND BALLIN, S. G.: J. Am. Chem. Soc. **71**, 1041 (1949).
(247) HATCH, L. F., BROWN, A. N., AND BAILEY, H. P.: J. Am. Chem. Soc. **72**, 3198 (1950).
(248) HATCH, L. F., AND D'AMICO, J. J.: J. Am. Chem. Soc. **73**, 4393 (1951).
(249) HATCH, L. F., AND GERHARDT, L. S.: J. Am. Chem. Soc. **71**, 1679 (1949).
(250) HATCH, L. F., GORDON, L. B., AND RUSS, J. J.: J. Am. Chem. Soc. **70**, 1093 (1948).
(251) HATCH, L. F., AND HARWELL, K. E.: J. Am. Chem. Soc. **75**, 6002 (1953).
(252) HATCH, L. F., AND HUDSON, P. S.: J. Am. Chem. Soc. **72**, 2505 (1950).
(253) HATCH, L. F., AND JOURNEAY, G. E.: J. Am. Chem. Soc. **75**, 3712 (1953).
(254) HATCH, L. F., AND McDONALD, D. W.: J. Am. Chem. Soc. **74**, 2911 (1952).
(255) HATCH, L. F., AND MOORE, A. C.: J. Am. Chem. Soc. **66**, 285 (1944).
(256) HATCH, L. F., MORGAN, L. O., AND TWEEDIE, V. L.: J. Am. Chem. Soc. **74**, 1826 (1952).
(257) HATCH, L. F., AND NESBITT, S. S.: J. Am. Chem. Soc. **73**, 358 (1951).
(258) HATCH, L. F., AND NESBITT, S. S.: J. Am. Chem. Soc. **72**, 727 (1950).
(259) HATCH, L. F., AND PATTON, T. L.: J. Am. Chem. Soc. **76**, 2705 (1954).
(260) HATCH, L. F., AND PERRY, R. H.: J. Am. Chem. Soc. **71**, 3262 (1949).
(261) HATCH, L. F., AND PERRY, R. H.: J. Am. Chem. Soc. **77**, 1136 (1955).
(262) HATCH, L. F., AND ROBERTS, G. B.: J. Am. Chem. Soc. **68**, 1196 (1946).
(263) HATCH, L. F., RUSS, J. J., AND GORDON, L. B.: J. Am. Chem. Soc. **69**, 2614 (1947).
(264) HAWTHORNE, M. F., HAMMOND, G. S., AND GRAYBILL, B. M.: J. Am. Chem. Soc. **77**, 486 (1955).
(265) HEILBRON, I. M., JONES, E. R. H., LACEY, R. N., McCOMBIE, J. T., AND RAFAEL, R.: J. Chem. Soc. **1945**, 77.
(266) HEILBRON, I. M., JONES, E. R. H., McCOMBIE, J. T., AND WEEDON, B. C. L.: J. Chem. Soc. **1945**, 88.
(267) HEILBRON, I. M., JONES, E. R. H., AND WEEDON, B. C. L.: J. Chem. Soc. **1945**, 81.
(268) HENBEST, H. B., JONES, E. R. H., AND WALLS, I. M. S.: J. Chem. Soc. **1950**, 3646.
(269) HENNE, A. L., AND CHANAN, H. H.: J. Am. Chem. Soc. **66**, 392 (1944).
(270) HENNE, A. L., CHANAN, H., AND TURK, A.: J. Am. Chem. Soc. **63**, 3474 (1941).
(271) HENNE, A. L., AND NEWBY, T. H.: J. Am. Chem. Soc. **70**, 130 (1948).
(272) HENNE, A. L., WHALEY, A. M., AND STEVENSON, J. K.: J. Am. Chem. Soc. **63**, 3478 (1941).
(273) HILL, C. M., HAYNES, L., SIMMONS, D. E., AND HILL, M. E.: J. Am. Chem. Soc. **75**, 5408 (1953).
(274) HILL, C. M., SIMMONS, D. E., AND HILL, M. E.: J. Am. Chem. Soc. **77**, 3889 (1955).
(275) HILLS, H. W. J., KENYON, J., AND PHILLIPS, H.: J. Chem. Soc. **1936**, 576.
(276) HOFFMAN, J.: Abstracts of Papers Presented before the Division of Organic Chemistry at the 127th Meeting of the American Chemical Society, Cincinnati, Ohio, April, 1955, p. 26N.
(277) HOFFMANN-LAROCHE AND Co.: British patent 619,898 (1949); Chem. Abstracts **43**, 9082 (1949).
(278) HOFFMANN-LAROCHE AND Co.: Swiss patent 257,577 (1949); Chem. Abstracts **44**, 288 (1950).
(279) HUGHES, E. D.: Trans. Faraday Soc. **37**, 606 (1941).
(280) HUGHES, E. D.: Trans. Faraday Soc. **34**, 185 (1938).
(281) HUGHES, E. D., AND INGOLD, C. K.: J. Chem. Soc. **1935**, 244.
(282) HUNSDIECKER, H.: Chem. Ber. **80**, 137 (1947).
(283) HUNSDIECKER, H.: Ber. **75**, 460 (1942).
(284) HURD, C. D., AND COHEN, F. L.: J. Am. Chem. Soc. **53**, 1917 (1931).
(285) HURD, C. D., AND McNAMEE, R. W.: J. Am. Chem. Soc. **59**, 104 (1937).
(286) HURD, C. D., AND PARRISH, C. I.: J. Am. Chem. Soc. **57**, 1731 (1935).
(287) HURD, C. D., AND POLLACK, M. A.: J. Org. Chem. **3**, 565 (1939).
(288) HURD, C. D., AND POLLACK, M. A.: J. Am. Chem. Soc. **60**, 1905 (1938).

(289) HURD, C. D., AND PUTERBAUGH, M. P.: J. Org. Chem. **2**, 381 (1937).
(290) HURD, C. D., AND SCHMERLING, L.: J. Am. Chem. Soc. **59**, 107 (1937).
(291) HURD, C. D., AND WILLIAMS, J. W.: J. Am. Chem. Soc. **58**, 2636 (1936).
  I. G. FARBENINDUSTRIE A-G: See references 196 and 197.
(292) IKEDA, T., AND IKEDA, S.: J. Am. Chem. Soc. **58**, 80 (1937).
(293) IMPERIAL CHEMICAL INDUSTRIES, LTD.: British patent 647,420 (1950); Chem. Abstracts **45**, 7139 (1951).
(294) INGOLD, C. K.: *Structure and Mechanism in Organic Chemistry*. Cornell University Press, Ithaca, New York (1953).
(295) INGOLD, C. K.: Ann. Repts. on Progress Chem. (Chem. Soc. London) **25**, 127 (1928).
(296) INGOLD, C. K., AND ROTHSTEIN, E.: J. Chem. Soc. **1929**, 8.
(297) INGOLD, E. H., AND INGOLD, C. K.: J. Chem. Soc. **1932**, 756.
(298) INHOFFEN, H. H., BOHLMANN, F., AND REINFELD, E.: Chem. Ber. **82**, 313 (1949).
(299) JACQUES, J.: Bull. soc. chim. [5] **12**, 843 (1945).
(300) JOHNSON, J. R., AND JOHNSON, O. H.: J. Am. Chem. Soc. **62**, 2615 (1940).
(301) JOHNSON, J. R., AND McEWIN, W. L.: J. Am. Chem. Soc. **48**, 474 (1926).
(302) JOHNSON, J. R., AND WHITMAN, G. M.: U.S. patent 2,477,617 (1949); Chem. Abstracts **44**, 4023 (1950).
(303) JONES, E. R. H., LACEY, R. N., AND SMITH, P.: J. Chem. Soc. **1946**, 940.
(304) JONES, E. R. H., AND McCOMBIE, J. T.: U.S. patent 2,429,411 (1947); Chem. Abstracts **42**, 1920 (1948).
(305) JONES, E. R. H., AND McCOMBIE, J. T.: British patent 571,777 (1945); Chem. Abstracts **41**, 4507 (1947).
(306) JONES, E. R. H., AND WEEDON, B. C. L.: J. Chem. Soc. **1946**, 937.
(307) JULIA, M.: Compt. rend. **234**, 2615 (1952).
(308) JUVALA, A.: Ber. **63**, 1989 (1930).
(309) KADESCH, R. G.: J. Am. Chem. Soc. **68**, 41 (1946).
(310) KADESCH, R. G.: J. Am. Chem. Soc. **68**, 46 (1946).
(311) KAMAI, G.: Zhur. Obshcheĭ Khim. **1**, 460 (1931).
(312) KARRER, P., ESCHER, R., AND RENTSCHLER, H.: Helv. Chim. Acta **22**, 1287 (1939).
(313) KARRER, P., GEIGER, A., RENTSCHLER, H., ZBLINDEN, E., AND KUGLER, A.: Helv. Chim. Acta **26**, 1741 (1943).
(314) KARRER, P., AND HELFENSTEIN, A.: Helv. Chim. Acta **14**, 78 (1931).
(315) KARRER, P., AND RINGIER, B. H.: Helv. Chim. Acta **22**, 610 (1939).
(316) KARRER, P., AND RINGLI, W.: Helv. Chim. Acta **30**, 863 (1947).
(317) KARRER, P., AND RINGLI, W.: Helv. Chim. Acta **30**, 1771 (1947).
(318) KARRER, P., AND SCHNEIDER, P.: Helv. Chim. Acta **31**, 395 (1948).
(319) KARRER, P., AND STAHELN, M.: Helv. Chim. Acta **28**, 438 (1945).
(320) KARRER, P., AND YAP, K. S.: Helv. Chim. Acta **23**, 581 (1940).
(321) KEKULÉ, A.: Ann. **162**, 98 (1872).
(322) KENYON, J., PARTRIDGE, S. M., AND PHILLIPS, H.: J. Chem. Soc. **1937**, 207.
(323) KENYON, J., PARTRIDGE, S. M., AND PHILLIPS, H.: J. Chem. Soc. **1936**, 85.
(324) KENYON, J., AND SNELLGROVE, D. R.: J. Chem. Soc. **1925**, 1169.
(325) KENYON, J., AND YOUNG, D. P.: J. Chem. Soc. **1940**, 1547.
(326) KEPNER, R. E., WINSTEIN, S., AND YOUNG, W. G.: J. Am. Chem. Soc. **71**, 115 (1949).
(327) KHARASCH, M. S., KRITCHEVSKY, J., AND MAYO, F. R.: J. Org. Chem. **2**, 489 (1937).
(328) KHARASCH, M. S., LAMBERT, F. L., AND URRY, W. H.: J. Org. Chem. **10**, 298 (1945).
(329) KHARASCH, M. S., MARGOLIS, E. T., AND MAYO, F. R.: J. Org. Chem. **1**, 393 (1936).
(330) KHARASCH, M. S., NUDENBERG, W., AND FIELD, E. K.: J. Am. Chem. Soc. **66**, 1276 (1944).
(331) KHARASCH, M. S., AND REINMUTH, O.: *Grignard Reactions of Non-metallic Substances*, p. 1063. Prentice-Hall, Inc., New York (1954).
(332) KIERSTEAD, R. W., LINSTEAD, R. P., AND WEEDON, B. C. L.: J. Chem. Soc. **1953**, 1803.

(333) KIERSTEAD, R. W., LINSTEAD, R. P., AND WEEDON, B. C. L.: J. Chem. Soc. **1953**, 1799.
(334) KIERSTEAD, R. W., LINSTEAD, R. P., AND WEEDON, B. C. L.: J. Chem. Soc. **1952**, 3610.
(335) KIMEL, W., AND COPE, A. C.: J. Am. Chem. Soc. **66**, 1613 (1944).
(336) KIMEL, W., AND COPE, A. C.: J. Am. Chem. Soc. **65**, 1992 (1943).
(337) KIRRMAN, A.: Compt. rend. **182**, 1629 (1926).
(338) KIRRMAN, A.: Compt. rend. **199**, 1228 (134).
(339) KIRRMAN, A.: Bull. soc. chim. [5] **4**, 502 (1937).
(340) KIRRMAN, A.: Bull. soc. chim. [5] **5**, 256 (1938).
(341) KIRRMAN, A.: Bull. soc. chim. [5] **5**, 915 (1938).
(342) KIRRMAN, A.: Bull. soc. chim. [5] **18**, C 9 (1951).
(343) KIRRMAN, A., AND GRARD, J.: Bull. soc. chim. [4] **47**, 834 (1930).
(344) KIRRMAN, A., AND GRARD, J.: Compt. rend. **190**, 876 (1930).
(345) KIRRMAN, A., AND JACOB, R.: Compt. rend. **203**, 1528 (1936).
(346) KIRRMAN, A., AND JACOB, R.: Bull. soc. chim. [5] **7**, 586 (1940).
(347) KIRRMAN, A., PACAUD, AND DOSQUE, H.: Bull. soc. chim. [5] **1**, 860 (1934).
(348) KIRRMAN, A., AND POURRAT, H.: Bull. soc. chim. [5] **15**, 745 (1948).
(349) KIRRMAN, A., POURRAT, H., SCHMITZ, R., AND SAITO, E.: Bull. soc. chim. [5] **19**, 502 (1952).
(350) KIRRMAN, A., AND RAMBAUD, R.: Compt. rend. **194**, 1168 (1932).
(351) KIRRMAN, A., AND RENN, P.: Compt. rend. **202**, 1934 (1936).
(352) KIRRMAN, A., AND SAITO, E.: Bull. soc. chim. [5] **19**, 515 (1952).
(353) KJAER, A., AND RUBENSTEIN, K.: Acta Chem. Scand. **8**, 1335 (1954).
(354) KJAER, A., RUBINSTEIN, K., AND JENSEN, K. A.: Acta Chem. Scand. **7**, 518 (1953).
(355) KLAGES, A., AND KLENK, K.: Ber. **39**, 2552 (1906).
(356) KLAND-ENGLISH, M. J., AND WILSON, C. L.: Abstracts of Papers Presented at the 119th Meeting of the American Chemical Society, New York City, April, 1951, p. 48 M.
(357) KLEINSCHMIDT, R. F., AND COPE, A. C.: J. Am. Chem. Soc. **66**, 1929 (1944).
(358) KOCH, H. P.: J. Chem. Soc. **1948**, 1111.
(359) KOELSCH, C. F.: J. Am. Chem. Soc. **56**, 1337 (1934).
(360) KOSOLOPOFF, G. M.: *Organic Phosphorus Compounds*, Chap. 8. John Wiley and Sons, Inc., New York (1950).
(361) KOSOWER, E.: Ph. D. Thesis, University of California at Los Angeles, 1952, p. 7.
(362) KRUEGER, J., AND SCHWARCZ, M.: J. Am. Chem. Soc. **63**, 2512 (1941).
(363) KRZIKALLA, H., AND WOLDAN, E.: German patent 857,369 (1952); Chem. Abstracts **47**, 11,219 (1953).
(364) KUHN, R., AND WINTERSTEIN, A.: Helv. Chim. Acta **11**, 123 (1937).
(365) KUIN-HOUO, O.: Compt. rend. **208**, 528 (1939).
(366) KUIN-HOUO, O.: Ann. chim. [11] **13**, 175 (1940).
(367) KUIN-HOUO, O.: Compt. rend. **208**, 40 (1939).
(368) KULKA, K.: Am. Perfumer **51**, 141 (1948); Chem. Abstracts **42**, 5417 (1948).
(369) KUNA, M., AND LEVENE, P. A.: J. Biol. Chem. **118**, 315 (1937).
(370) KUNDIGER, D. G., AND RICHARDSON, E. E.: J. Am. Chem. Soc. **77**, 2897 (1955).
(371) KURTZ, P.: German patent 848,809 (1952); Chem. Abstracts **47**, 5425 (1953).
(372) KURTZ, P., AND SCHWARCZ, H.: German patent 825,255 (1951); Chem. Abstracts **47**, 3333 (1953).
(372a) KWART, H., AND MILLER, R. K.: J. Am. Chem. Soc. **76**, 5403 (1954).
(373) LADD, E. C.: U. S. patent 2,594,184 (1952); Chem. Abstracts **47**, 1183 (1953).
(374) LADD, E. C., AND HARVEY, M. P.: U. S. patent 2,594,935 (1952); Chem. Abstracts **47**, 142 (1953).
(375) LAFORGUE, A.: Compt. rend. **228**, 352 (1948).
(376) LANDAUER, S. R., AND RYDON, H. N.: J. Chem. Soc. **1953**, 2224.

(377) LANE, J. F., FENTRESS, J., AND SHERWOOD, L. T.: J. Am. Chem. Soc. **66**, 545 (1944).
(378) LANE, J. F., ROBERTS, J. D., AND YOUNG, W. G.: J. Am. Chem. Soc. **66**, 543 (1944).
(379) LANGENBECK, W., WOLTERSDORF, W., AND BLACKNITZKY, R.: Ber. **72**, 671 (1939).
(380) LAUCHENAUER, A., AND SCHINZ, H.: Helv. Chim. Acta **34**, 1514 (1951).
(381) LAUER, W. M., AND FILBERT, W. F.: J. Am. Chem. Soc. **58**, 1388 (1936).
(382) LAUER, W. M., AND LABRIOLA, R.: J. Am. Chem. Soc. **67**, 1254 (1945).
(383) LAUER, W. M., AND LEEKLEY, R. M.: J. Am. Chem. Soc. **61**, 3043 (1939).
(384) LAUER, W. M., AND LOCKWOOD, R. G.: J. Am. Chem. Soc. **76**, 3974 (1954).
(385) LAUER, W. M., AND SANDERS, P. A.: J. Am. Chem. Soc. **65**, 198 (1943).
(386) LAUER, W. M., AND UNGNADE, H. E.: J. Am. Chem. Soc. **61**, 3047 (1939).
(387) LAWRENCE, J. W., AND SHELTON, J. R.: Ind. Eng. Chem. **42**, 136 (1950).
(388) LEBEDEVA, A. I., AND ALMASHI, L. F.: Zhur. Obshcheĭ Khim. **23**, 994 (1953).
(389) LENNARTZ, T.: Ber. **76**, 831 (1943).
(390) LEPINGLE, M.: Bull. soc. chim. [4] **39**, 864 (1926).
(391) LESPIEAU, R.: Bull. soc. chim. [4] **29**, 528 (1921).
(392) LESPIEAU, R., AND HEITZMANN, P.: Compt. rend. **200**, 1077 (1935).
(393) LESPIEAU, R., AND HEITZMANN, P.: Bull. soc. chim. [5] **3**, 273 (1936).
(394) LEVENE, P. A., AND HALLER, H. L.: J. Biol. Chem. **83**, 185 (1929).
(395) LEVENE, P. A., ROTHEN, A., AND KUNA, M.: J. Biol. Chem. **120**, 777 (1937).
(396) LEVINA, R. Y., FAINZILBERG, A. A., AND ITENBERG, R. V.: Doklady Akad. Nauk S.S.S.R. **75**, 39 (1950); Chem. Abstracts **45**, 4637 (1951).
(397) LEVINA, R. Y., FAINZILBERG, A. A., AND TRESCHOVA, E. G.: Zhur. Obshcheĭ Khim. **22**, 430 (1952).
(398) LEVINA, R. Y., AND SKVARCHENKO, V. R.: Vestnik Moskov. Univ. **6**, No. 5, Ser. Fiz.-Mat. i Estestven. Nauk No. **3**, 1958 (1951); Chem. Abstracts **46**, 3941 (1952).
(399) LEVINA, R. Y., SKVARCHENKO, V. R., KAGAN, Y. B., AND TRESCHOVA, E. G.: Zhur. Obshcheĭ Khim. **19**, 62 (1949).
(400) LEVINA, R. Y., SKVARCHENKO, V. R., OKUNEVICH, A. S., AND TRESCHOVA, E. G.: Zhur. Obshcheĭ Khim. **23**, 725 (1953).
(401) LEVINA, R. Y., TANTSYREVA, T. I., AND TRESCHOVA, E. G.: Zhur. Obshcheĭ Khim. **23**, 729 (1953).
(402) LEVINE, I. E., AND TOLAND, W. G.: U. S. patent 2,464,244 (1949); Chem. Abstracts **43**, 4287 (1949).
(403) LEVY, H., AND COPE, A. C.: J. Am. Chem. Soc. **66**, 1684 (1948).
(404) LEWIS, E. S., AND BOOZER, C. E.: J. Am. Chem. Soc. **74**, 308 (1952).
(405) LOCQUIN, R., AND WOUSENG, S.: Compt. rend. **174**, 1551 (1922).
(406) LOCQUIN, R., AND WOUSENG, S.: Compt. rend. **174**, 1711 (1922).
(407) LONGFIELD, J., JONES, R., AND SIVERTZ, C.: Can. J. Research **28B**, 373 (1950).
(408) LORA-TOMAYO, M., MARTIN-PANIZO, F., AND OSSORIO, R. P.: J. Chem. Soc. **1950**, 1418.
(409) LORA-TOMAYO, M., AND OSSORIO, R. P.: Anal. fís. y quím. (Madrid) **44B**, 981 (1948).
(410) LUTTRINGHAUS, A., KONIG, H. B., AND BOTTCHER, B.: Ann. **560**, 201 (1947).
(411) LUTTRINGHAUS, A., SAAF, G. VON, AND HAUSCHILD, K.: Ber. **71**, 1673 (1938).
(412) LUTZ, R. E., AND RINKER, E. H.: J. Am. Chem. Soc. **77**, 366 (1955).
(413) LUTZ, R. E., AND WEISS, J. O.: J. Am. Chem. Soc. **77**, 1814 (1955).
(414) MARTIN, H., AND TRINK, N. Q.: Compt. rend. **228**, 688 (1949).
(415) MARVEL, C. S., AND BRACE, N. O.: J. Am. Chem. Soc. **70**, 1775 (1948).
(416) MARVEL, C. S., AND WILLIAMS, J. L. R.: J. Am. Chem. Soc. **70**, 3842 (1948).
(417) McELVAIN, S. M., AND STEVENS, C. L.: J. Am. Chem. Soc. **69**, 2667 (1947).
(418) MEISENHEIMER, J., AND BEUTTER, G.: Ann. **508**, 58 (1933).
(419) MEISENHEIMER, J., AND LINK, J.: Ann. **479**, 211 (1930).
(420) MEISENHEIMER, J., AND SCHMIDT, W.: Ann. **475**, 157 (1929).
(421) MELTZNER, R. I., AND KING, J. A.: J. Am. Chem. Soc. **75**, 1355 (1953).
(422) MIESCHER, K., AND SCHOLZ, C.: Helv. Chim. Acta **22**, 120 (1939).

(423) Milas, N. A., Grossi, F. X., Penner, S. E., and Kahn, S.: J. Am. Chem. Soc. **70,** 1292 (1948).

(424) Mills, J. A.: J. Chem. Soc. **1951,** 2332.

(425) Mislow, K., and Hellman, H. M.: J. Am. Chem. Soc. **73,** 244 (1951).

(426) Mokiewski, W.: J. Russ. Phys. Chem. Soc. **32,** 207 (1899); Chem. Zentr. **1900, II,** 331.

(427) Moldenhauer, O., Trautmann, G., and Pfluger, R.: Ann. **583,** 61 (1953).

(428) Mounajed, T.: Compt. rend. **197,** 44 (1933).

(429) Mooradian, A., and Cloke, J. B.: J. Am. Chem. Soc. **68,** 785 (1946).

(430) Moureu, C., and Gallagher, P.: Bull. soc. chim. [4] **29,** 1009 (1921).

(431) Mousseron, M., and Jacquier, R.: Bull. soc. chim. [5] **18,** 106 (1951).

(432) Mousseron, M., Julien, P., and Winternitz, F.: Bull. soc. chim. [5] **15,** 878 (1948).

(433) Mousseron, M., and Phuoc-Du, Ng.: Bull. soc. chim. [5] **15,** 91 (1948).

(434) Mumm, O., and Richter, H.: Ber. **73,** 843 (1940).

(435) Muskat, I. E., and Northrup, H. E.: J. Am. Chem. Soc. **52,** 4043 (1930).

(436) Nametkin, S. S., and Fedoseeva, A. I.: Sintezy Dushistykl Veshchestv., Sbornik Statei **1939,** 257; Chem. Abstracts **36,** 3777 (1942).

(437) Naves, Y. R., Grampoloff, A. V., and Bachmann, P.: Helv. Chim. Acta **30,** 1599 (1947).

(438) Nazarov, I. N., and Azerbaev, I. N.: Zhur. Obshcheĭ Khim. **18,** 414 (1948).

(439) Nazarov, I. N., Azerbaev, I. N., and Rakcheeva, V. N.: Zhur. Obshcheĭ Khim. **18,** 407 (1948).

(440) Nazarov, I. N., Azerbaev, I. N., and Rakcheeva, V. N.: Zhur. Obshcheĭ Khim. **18,** 656 (1948).

(441) Nazarov, I. N., and Fisher, L. B.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1948,** 311; Chem. Abstracts **43,** 112 (1949).

(442) Nazarov, I. N., and Fisher, L. B.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1948,** 436; Chem. Abstracts **43,** 2576 (1949).

(443) Nazarov, I. N., and Fisher, L. B.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1948,** 427; Chem. Abstracts **43,** 112 (1949).

(444) Nazarov, I. N., and Kakhniashvili, A. I.: Sbornik Statei Obshcheĭ Khim. **2,** 919 (1954); Chem. Abstracts **49,** 6848 (1955).

(445) Nazarov, I. N., Kakhniashvili, A. I., and Ryabchenko, V. F.: Sbornik Statei Obshcheĭ Khim. **2,** 913 (1954); Chem. Abstracts **49,** 6847 (1955).

(446) Nazarov, I. N., Rakcheeva, V. N., and Schmonina, L. I.: Zhur. Obshcheĭ Khim. **22,** 611 (1952).

(447) Nesmeyanov, A. N., Freidlina, R. K., and Firstov, V. I.: Doklady Akad. Nauk S.S.S.R. **78,** 717 (1951); Chem. Abstracts **46,** 1957 (1952).

(448) Nesmeyanov, A. N., Freidlina, R. K., and Firstov, A. K.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1951,** 505; Chem. Abstracts **46,** 7034 (1952).

(449) Nesmayanov, A. N., Freidlina, R. K., and Kotchetkov, A. K.: Izvest. Akad. Nauk. S.S.S.R., Otdel, Khim. Nauk **1951,** 273; Chem. Abstracts **46,** 882 (1952).

(450) Nesmeyanov, A. N., Freidlina, R. K., and Kotchetkov, A. K.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1949,** 623; Chem. Abstracts **44,** 3920 (1950).

(451) Nesmeyanov, A. N., Zakharkin, L. I., Kost, V. N., and Freidlina, R. K.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1954,** 258.

(452) Newman, L. W. J., and Rydon, H. N.: J. Chem. Soc. **1936,** 261.

(453) Newman, M. S.: U. S. patent 2,555,599 (1951); Chem. Abstracts **46,** 522 (1952).

(454) Niederhauser, W. D.: U. S. patent 2,653,173 (1953); Chem. Abstracts **48,** 8812 (1954).

(455) Noller, C. R., and Girvin, M. D.: J. Am. Chem. Soc. **59,** 606 (1937).

(456) Nummy, W. R., and Tarbell, D. S.: J. Am. Chem. Soc. **73,** 1500 (1951).

(457) Nystrom, R. F., and Leak, J. C.: J. Am. Chem. Soc. **75,** 3039 (1953).

(458) Oae, S., and Vanderwerf, C. A.: J. Am. Chem. Soc. **75,** 2724 (1953).

(459) Ogg, R. A.: J. Am. Chem. Soc. **61,** 1946 (1939).

(460) OGLOBIN, K. A.: Uchenye Zapiski Leningrad. Gosudarst. Univ., Ser. Khim. Nauk **1940**, No. 5 (54), 258; Chem. Abstracts **37**, 5706 (1943).
(461) OROSHNIK, W.: U. S. patent 2,511,870 (1950); Chem. Abstracts **44**, 9475 (1950).
(462) OROSHNIK, W.: J. Am. Chem. Soc. **67**, 1627 (1945).
(463) OROSHNIK, W., KARMAS, G., AND MEBANE, A. D.: J. Am. Chem. Soc. **74**, 3807 (1952).
(464) OROSHNIK, W., AND MALLORY, R. A.: J. Am. Chem. Soc. **72**, 4608 (1950).
(465) ORTHO PHARMACEUTICAL CORPORATION: British patent 630,865 (1949); Chem. Abstracts **44**, 4036 (1950).
(466) OWEN, L. N., AND SMITH, P. N.: J. Chem. Soc. **1952**, 4035.
(467) OWEN, L. N., AND SULTANBAWA, M. U. S.: J. Chem. Soc. **1949**, 3089.
(468) OWEN, L. N., AND SULTANBAWA, M. U. S.: Nature **163**, 997 (1949).
(469) OWEN, L. N., AND SULTANBAWA, M. U. S.: J. Chem. Soc. **1949**, 3105.
(470) PETROV, A. A.: Zhur. Obshcheĭ Khim. **11**, 713 (1941).
(471) PETROV, A. A.: Zhur. Obshcheĭ Khim. **10**, 1418 (1940).
(472) PETROV, A. A.: Zhur. Obshcheĭ Khim. **13**, 741 (1943).
(473) PETROV, A. D., AND PONOMARENKO, V. A.: Doklady Akad. Nauk S.S.S.R. **74**, 739 (1950); Chem. Abstracts **46**, 87 (1952).
(474) PHILLIPS, D. D.: J. Am. Chem. Soc. **76**, 5385 (1954).
(475) PIGULEVSKIĬ, G. V.: Izvest. Akad. Nauk S.S.S.R., Ser. Fiz. **14**, 401 (1950); Chem. Abstracts **45**, 3246 (1951).
(476) PIGULEVSKIĬ, G. V., AND TROYAN, G. B.: Doklady Akad. Nauk S.S.S.R. **72**, 519 (1950); Chem. Abstracts **45**, 540 (1951).
(477) PLATE, A. F., AND STERLIGOV, O. D.: Zhur. Obshcheĭ Khim. **14**, 955 (1944).
(478) PONOMARENKO, V. A., AND TOLKACHEVA, T. Y.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1953**, 1017; Chem. Abstracts **49**, 2298 (1955).
(479) POURRAT, H.: Compt. rend. **228**, 1031 (1949).
(480) POURRAT, H., AND SCHMITZ, R.: Bull. soc. chim. [5] **19**, 505 (1952).
(481) PREVOST, C.: Compt. rend. **183**, 1292 (1926).
(482) PREVOST, C.: Compt. rend. **184**, 458 (1927).
(483) PREVOST, C.: Compt. rend. **186**, 1209 (1928).
(484) PREVOST, C.: Ann. chim. [10] **10**, 113 (1928).
(485) PREVOST, C.: Ann. chim. [10] **10**, 147 (1928).
(486) PREVOST, C.: Ann. chim. [10] **10**, 351 (1928).
(487) PREVOST, C.: Compt. rend. **185**, 133 (1927).
(488) PREVOST, C.: Compt. rend. **185**, 1283 (1927).
(489) PREVOST, C.: Compt. rend. **187**, 946 (1928).
(490) PREVOST, C.: Compt. rend. **187**, 1052 (1928).
(491) PREVOST, C.: Bull. soc. chim. [4] **43**, 996 (1928).
(492) PREVOST, C.: Bull. soc. chim. [4] **49**, 1372 (1931).
(493) PREVOST, C.: Compt. rend. **214**, 357 (1942).
(494) PREVOST, C., AND DAUJAT, J.: Bull. soc. chim. [4] **47**, 588 (1930).
(495) PREVOST, C., AND RICHARD, G.: Bull. soc. chim. [4] **49**, 1368 (1931).
(496) PREVOST, C., AND VALETTE, A.: Compt. rend. **222**, 326 (1946).
(497) PRICE, C. C., AND MARSHALL, H. D.: J. Org. Chem. **8**, 532 (1943).
(498) PRICHARD, W. W., AND WHITMAN, G. W.: U. S. patent 2,524,833 (1950) Chem. Abstracts **45**, 1618.
(499) PROCHAZKA, J., AND WICHTERLE, O.: Collection Czechoslav. Chem. Communs. **14**, 156 (1949).
(500) PUDOVIK, A. N.: Zhur. Obshcheĭ Khim. **22**, 109 (1952).
(501) PUDOVIK, A. N.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1948**, 321; Chem. Abstracts **43**, 130 (1949).
(502) PUDOVIK, A. N.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1948**, 529; Chem. Abstracts **43**, 2158 (1949).
(503) PUDOVIK, A. N.: Zhur. Obshcheĭ Khim. **19**, 1034 (1949).

(504) Pudovik, A. N.: Zhur. Obshcheĭ Khim. **19**, 1179 (1949).
(505) Pudovik, A. N.: Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk **1949**, 83; Chem. Abstracts **43**, 5737 (1949).
(506) Pudovik, A. N.: Zhur. Obshcheĭ Khim. **21**, 1642 (1951).
(507) Pudovik, A. N.: Doklady Akad. Nauk S.S.S.R. **84**, 519 (1952); Chem. Abstracts **47**, 3226 (1953).
(508) Pudovik, A. N.: Zhur. Obshcheĭ Khim. **22,** 773 (1952).
(509) Pudovik, A. N., and Arbuzov, B. A.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1946**, 541; Chem. Abstracts **42**, 6312 (1948).
(510) Pudovik, A. N., and Arbuzov, B. A.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1947**, 377; Chem. Abstracts **42**, 1556 (1948).
(511) Pudovik, A. N., and Arbuzov, B. A.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1947**, 501; Chem. Abstracts **42**, 1887 (1948).
(512) Pudovik, A. N., and Arbuzov, B. A.: Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1948**, 246; Chem. Abstracts **42**, 4973 (1948).
(513) Pudovik, A. N., and Arbuzov, B. A.: Invest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk **1949**, 522; Chem. Abstracts **44**, 1893 (1950).
(514) Pudovik, A. N., and Frolova, M. M.: Zhur. Obshcheĭ Khim. **22**, 2052 (1952).
(515) Pudovik, A. N., and Kudryavtseva, N. N.: Zhur. Obshcheĭ Khim. **20**, 848 (1950).
(516) Pudovik, A. N., and Nikitina, V. I.: Zhur. Obshcheĭ Khim. **19,** 75 (1949).
(517) Pudovik, A. N., and Nikitina, V. I.: Zhur. Obshcheĭ Khim. **19,** 279 (1949).
(518) Pudovik, A. N., and Nikitina, V. I.: Zhur. Obshcheĭ Khim. **22,** 1377 (1952).
(519) Pudovik, A. N., and Nikitina, V. I.: Zhur. Obshcheĭ Khim. **22,** 1553 (1952).
(520) Pudovik, A. N., and Vinokurova, G. M.: Zhur. Obshcheĭ Khim. **19,** 1882 (1949).
(521) Pudovik, A. N., and Zotikova, S. V.: Zhur. Obshcheĭ Khim. **22,** 1559 (1952).
(522) Rambaud, R.: Compt. rend. **195,** 389 (1932).
(523) Rambaud, R.: Compt. rend. **197,** 767 (1933).
(524) Rambaud, R.: Bull. soc. chim. [5] **1,** 1206 (1934).
(525) Rambaud, R.: Bull. soc. chim. [5] **1,** 1317 (1934).
(526) Reichstein, T.: Ber. **63,** 749 (1930).
(527) Reichstein, T., and Trivelli, G.: Helv. Chim. Acta **16,** 968 (1933).
(528) Reichstein, T., and Trivelli, G.: Helv. Chim. Acta **15,** 254 (1932).
(529) Reid, E. B., and Yost, J. F.: J. Am. Chem. Soc. **72,** 1807 (1950).
(530) Reif, J.: Ber. **39,** 1603 (1906).
(531) Reif, J.: Ber. **41,** 2739 (1908).
(532) Rhoads, S. J., and Crecelius, R. L.: J. Am. Chem. Soc. **77,** 5183 (1955).
(533) Rhoads, S. J., and Crecelius, R. L.: J. Am. Chem. Soc. **77,** 5060 (1955).
(534) Rhoads, S. J., and Crecelius, R. L.: J. Am. Chem. Soc. **77,** 5057· (1955).
(535) Rhoads, S. J., Raulins, R., and Reynolds, R. D.: J. Am. Chem. Soc. **75,** 2531 (1953).
(536) Rhoads, S. J., Raulins, R., and Reynolds, R. D.: J. Am. Chem. Soc. **76,** 3456 (1954).
(537) Roberts, J. D., and Mazur, R. H.: J. Am. Chem. Soc. **73,** 2509 (1951).
(538) Roberts, J. D., and Young, W. G.: J. Am. Chem. Soc. **67,** 148 (1945).
(539) Roberts, J. D., Young, W. G., and Winstein, S.: J. Am. Chem. Soc. **64,** 2157 (1942).
(540) Rothstein, E.: J. Chem. Soc. **1940,** 1550.
(541) Rouve, A., and Stoll, M.: Helv. Chim. Acta **30,** 2216 (1947).
(542) Ruber, R. N.: Ber. **44,** 2974 (1911).
(543) Rule, J. M.: Ph.D. Thesis, University of California at Los Angeles, 1949.
(543a) Rule, J. M.: Senior Thesis, University of California at Los Angeles, 1944.
(544) Runde, M. M., Scott, E. W., and Johnson, J. R.: J. Am. Chem. Soc. **52,** 1284 (1930).
(545) Rupe, H., and Burgin, J.: Ber. **43,** 172 (1910).
(546) Ruzicka, L.: Helv. Chim. Acta **6,** 492 (1923).
(547) Ruzicka, L., and Castro, L.: Helv. Chim. Acta **28,** 590 (1945).
(548) Ruzicka, L., Engel, L. L., and Fisher, W. F.: Helv. Chim. Acta **21,** 364 (1938).
(549) Ruzicka, L., and Firmenich, G.: Helv. Chim. Acta **22,** 392 (1939).

(550) RUZICKA, L., AND FISHER, W.: Helv. Chim. Acta **17**, 633 (1934).
(551) RUZICKA, L., AND MULLER, P.: Helv. Chim. Acta **22**, 416 (1939).
(552) RUZICKA, L., AND SCHINZ, H.: Helv. Chim. Acta **17**, 1602 (1934).
(553) SAMOKHVALOV, G. I., MIROPOLSKAYA, M. A., VAKULOVA, L. A., AND PREOBRAZHEN-
       SKIĬ, N. A.: Doklady Akad. Nauk S.S.S.R. **84**, 1179 (1952); Chem. Abstracts **47**,
       3277 (1953).
(554) SARETT, L. H.: J. Biol. Chem. **162**, 601 (1946).
(555) SCHAPPI, G., AND SEIDEL, C. F.: Helv. Chim. Acta **30**, 2199 (1947).
(556) SCHINZ, H., RUZICKA, L., SEIDEL, C. F., AND TAVEL, C.: Helv. Chim. Acta **30**, 1810
       (1947).
(557) SCHINZ, H., AND SCHAPPI, G.: Helv. Chim. Acta **30**, 1483 (1947).
(558) SCHINZ, H., AND SIMON, H. L.: Helv. Chim. Acta **28**, 774 (1945).
(559) SCHMID, K., HAEGELE, W., AND SCHMID, H.: Experientia **9**, 414 (1953).
(560) SCHMID, K., AND SCHMID, H.: Helv. Chim. Acta **36**, 687 (1953).
(561) SCHMID, H., AND SCHMID, K.: Helv. Chim. Acta **36**, 489 (1953).
(562) SCHMID, H., AND SCHMID, K.: Helv. Chim. Acta **35**, 1879 (1952).
(563) SCHMITZ, R.: Bull. soc. chim. [5] **19**, 509 (1952).
(564) SCHONBERG, A., AND ISMAEL, A. F. A.: J. Chem. Soc. **1942**, 585.
(565) SCHULER, F. W., AND MURPHY, G. W.: J. Am. Chem. Soc. **72**, 3155 (1950).
(566) SEIL, C., AND YOUNG, W. G.: Unpublished work.
(567) SEMEINIK, F., AND JENKINS, G. L.: J. Am. Pharm. Soc. **37**, 118 (1948).
(567a) SHELL CHEMICAL CORPORATION: Technical Publication SC: 49-8 (1949).
(568) SHEPARD, A. F., AND JOHNSON, J. R.: J. Am. Chem. Soc. **54**, 4385 (1932).
(569) SHIH, C.-H.: Ph.D. Thesis, University of California at Los Angeles, 1955.
(570) SIMON, H. L., KAUFFMAN, A., AND SCHINZ, H.: Helv. Chim. Acta **29**, 1133 (1946).
(571) SLOBODIN, Y. M.: Zhur. Obshcheĭ Khim. **24**, 444 (1954).
(572) SLOBODIN, Y. M., AND VINOKUROVA, N. M.: Zhur. Obshcheĭ Khim. **22**, 105 (1952).
(573) SMETS, G.: Trav. lab. chim. gen., Univ. Louvain **1942-47** (1947); Acad. roy. Belg.,
       Classe sci., Mém. **21**, 3 (1947); Chem. Abstracts **44**, 8315 (1950).
(574) SMITH, C. W., AND NORTON, D. G.: U. S. patent 2,575,896 (1951); Chem. Abstracts
       **46**, 6144 (1952).
(575) SMITH, C. W., NORTON, D. G., AND BALLARD, S. A.: J. Am. Chem. Soc. **73**, 5282 (1951).
(576) SMITH, H. A., AND KING, W. H.: J. Am. Chem. Soc. **72**, 95 (1950).
(577) SOMMELET, M.: Compt. rend. **157**, 852 (1913).
(578) SONDHEIMER, F., KAUFMAN, S., MARTINEZ, H., AND ROSENKRANZ, G.: J. Am. Chem.
       Soc. **75**, 4712 (1953).
(579) SORENSEN, N. A., GILLEBO, T., HOLTERMAN, H., AND SORENSEN, J. S.: Acta Chem.
       Scand. **5**, 757 (1951).
(580) SPATH, E., AND SCHMID, H.: Ber. **73**, 243 (1940).
(581) STAUDINGER, H.: Ber. **42**, 3966 (1909).
(582) STAUDINGER, H., KREIS, W., AND SCHILT, W.: Helv. Chim. Acta **5**, 743 (1922).
(583) STEIN, L., AND MURPHY, G. W.: J. Am. Chem. Soc. **74**, 1041 (1952).
(584) STEPHAN, K.: J. prakt. Chem. **58**, 111 (1898).
(585) STEVENS, P. G., ALLENBY, O. C. W., AND DuBOIS, A. S.: J. Am. Chem. Soc. **62**, 1424
       (1940).
(586) STITZ, F.: Osterr. Chem.-Ztg. **48**, 186 (1947); Chem. Abstracts **44**, 7226 (1950).
(587) STORK, G.: In *The Alkaloids*, edited by R. H. F. Manske and H. L. Holmes, Vol. II,
       pp. 176, 180, 185. Academic Press, Inc., New York (1951).
(588) STORK, G., AND WHITE, W. N.: J. Am. Chem. Soc. **75**, 4119 (1953).
(589) STRAUS, F.: Ann. **393**, 235 (1912).
(590) STRAUS, F., AND BERKOW, A.: Ann. **401**, 121 (1913).
(591) STRAUS, F., AND EHRENSTEIN, M.: Ann. **442**, 93 (1925).
(592) SUPNIEWSKI, J.: Chem. Zentr. **1928**, I, 2076.
(593) SUTTON, D. A.: J. Chem. Soc. **1944**, 306.

(594) SWEETING, O. J., AND JOHNSON, J. R.: J. Am. Chem. Soc. **68**, 1057 (1946).
(595) TABET, G. E.: U. S. patent 2,570,887 (1951); Chem. Abstracts **46**, 3071 (1952).
(596) TAKEI, S., ONO, M., KUROIWA, Y., TAKAHATA, T., AND SIMA, T.: J. Agr. Chem. Soc. Japan **14**, 717 (1938); Chem. Abstracts **33**, 2558 (1939).
(597) TAMELE, M., OTT, C. J., MARPLE, K. E., AND HEARNE, G.: Ind. Eng. Chem. **33**, 115 (1941).
(598) TARBELL, D. S.: Chem. Revs. **27**, 495 (1940).
(599) TARBELL, D. S.: *Organic Reactions*, Vol. II, p. 1. John Wiley and Sons, Inc., New York (1944).
(600) TARBELL, D. S., AND WILSON, J. W.: J. Am. Chem. Soc. **64**, 607 (1942).
(600a) TARBELL, D. S., AND WILSON, J. W.: J. Am. Chem. Soc. **64**, 1066 (1942).
(601) TATEVOSYAN, G. T., AND TUTERYAN, M. T.: Zhur. Priklad. Khim. **20**, 287 (1947).
(602) THIELE, J.: Ann. **314**, 296 (1901).
(603) TISHCHENKO, D.: Zhur. Obshcheĭ Khim. **23**, 1002 (1953).
(604) TISHCHENKO, D.: Zhur. Obshcheĭ Khim. **6**, 1549 (1936).
(605) TISHCHENKO, D.: Zhur. Obshcheĭ Khim. **7**, 658 (1937).
(606) TISHCHENKO, D., AND KISSEL, K.: Zhur. Obshcheĭ Khim. **22**, 1857 (1952).
(607) TREVOY, L. W., AND BROWN, W. G.: J. Am. Chem. Soc. **71**, 1675 (1949).
(608) TSUDA, K., AND YOSHIDA, N.: J. Pharm. Soc. Japan **68**, 98 (1948).
(609) ULRICH, S. E., AND LANE, J. F.: J. Am. Chem. Soc. **72**, 5130 (1950).
(610) ULTEE, A. J.: Rec. trav. chim. **68**, 495 (1949).
(611) ULTEE, A. J.: Rec. trav. chim. **68**, 483 (1949).
(612) ULTEE, A. J.: Rec. trav. chim. **68**, 352 (1949).
(613) ULTEE, A. J.: J. Chem. Soc. **1948**, 530.
(614) ULTEE, A. J.: Rec. trav. chim. **68**, 125 (1949).
(615) URBAN, R. S.: U. S. patent 2,658,922 (1953); Chem. Abstracts **49**, 5511 (1955).
(616) USHAKOV, M. I., AND KUCHEROV, V. F.: Zhur. Obshcheĭ Khim. **14**, 1080 (1944).
(617) USHAKOV, M. I., AND KUCHEROV, V. F.: Zhur. Obshcheĭ Khim. **14**, 1073 (1944).
(618) VALEUR, A., AND LUCE, E.: Bull. soc. chim. [4] **27**, 611 (1920).
(619) VALETTE, A.: Ann. chim. [12] **3**, 644 (1948).
(620) VANIN, I. I., AND CHERNOYAROVA, A. A.: Zhur. Obshcheĭ Khim. **7**, 885 (1937).
(621) VAN RISSEGHEM, H.: Bull. soc. chim. Belg. **39**, 349 (1930).
(622) VAN RISSEGHEM, H.: Bull. soc. chim. Belg. **47**, 47 (1938).
(623) VAN RISSEGHEM, H., AND GREDY, B.: Compt. rend. **202**, 489 (1936).
(624) VAN ROMBURGH, P.: Bull. soc. chim. [2] **41**, 189 (1884).
(625) VAN ROMBURGH, P.: Rec. trav. chim. **1**, 233 (1882).
(626) VAN ROMBURGH, P.: Bull. soc. chim. [2] **36**, 549 (1881).
(627) VARDANYAN, S. A.: Zhur. Priklad. Khim. **25**, 1322 (1952); Chem. Abstracts **47**, 11,132 (1953).
(628) VERNON, C. A.: J. Chem. Soc. **1954**, 423.
(629) VERNON, C. A.: J. Chem. Soc. **1954**, 4462.
(630) VLADIMIROVA, M. G., AND PETROV, A. A.: Zhur. Obshcheĭ Khim. **16**, 2141 (1946).
(631) VOIGT, R.: J. prakt. Chem. **151**, 307 (1938).
(632) WEBB, I. D.: U. S. patent 2,654,787 (1953); Chem. Abstracts **48**, 10048 (1954).
(633) WEBB, I. D.: Ph.D. Thesis, University of California at Los Angeles, 1944.
(634) WEBB, I. D., AND BORCHERT, G. T.: J. Am. Chem. Soc. **73**, 2654 (1951).
(635) WEBB, I. D., AND TABET, G. E.: U. S. patent 2,477,672 (1949); Chem. Abstracts **44**, 1131 (1950).
(636) WEBB, I. D., AND YOUNG, W. G.: J. Am. Chem. Soc. **73**, 777 (1951).
(637) WERNER, E. G. G.: Rec. trav. chim. **67**, 442 (1948).
(638) WHALEY, A. M., AND DAVIS, H. W.: J. Am. Chem. Soc. **70**, 1026 (1948).
(639) WHEELER, O. H.: Chemistry & Industry **1954**, 1020.
(640) WIBERG, K. B.: J. Am. Chem. Soc. **74**, 3891 (1952).
(641) WILK, I. J.: Ph.D. Thesis, University of California at Los Angeles, 1954.

(642) WICHTERLE, O., AND HUDLICKY, M.: Collection Czechoslav. Chem. Communs. **12,** 101 (1947).
(643) WILLIMANN, L., AND SCHINZ, H.: Helv. Chim. Acta **35,** 2401 (1952).
(644) WILSON, C. L.: Trans. Faraday Soc. **37,** 603 (1941).
(645) WILSON, K. W., ROBERTS, J. D., AND YOUNG, W. G.: J. Am. Chem. Soc. **72,** 215 (1950).
(646) WILSON, K. W., ROBERTS, J. D., AND YOUNG, W. G.: J. Am. Chem. Soc. **72,** 218 (1950).
(647) WILSON, K. W., ROBERTS, J. D., AND YOUNG, W. G.: J. Am. Chem. Soc. **71,** 2019 (1949).
(648) WINSTEIN, S.: Bull. soc. chim. [5] **18,** C 41 (1951).
(649) WINSTEIN, S.: Dissertation, California Institute of Technology, 1938.
(650) WINSTEIN, S., AND GRUNWALD, E.: J. Am. Chem. Soc. **70,** 828 (1948).
(651) WINSTEIN, S., GRUNWALD, E., AND JONES, H. W.: J. Am. Chem. Soc. **73,** 2700 (1951).
(652) WINSTEIN, S., AND YOUNG, W. G.: J. Am. Chem. Soc. **58,** 104 (1936).
(653) WINSTEIN, S., YOUNG, W. G., GOERING, H. L., JONES, H. W., AND FAINBERG, A. H.: Unpublished data.
(654) WINTER, M., SCHINZ, H., AND STOLL, M.: Helv. Chim. Acta **30,** 2213 (1947).
(655) WISE, P. L.: U. S. patent 2,473,486 (1949); Chem. Abstracts **43,** 7953 (1949).
(656) WOODS, G. F., BOLGIANO, N. C., AND DUGGAN, D. E.: J. Am. Chem. Soc. **77,** 1800 (1955).
(657) WOODS, G. F., AND LEDERLE, H. F.: J. Am. Chem. Soc. **73,** 2245 (1951).
(658) WOUSENG, S.: Ann. chim. [10] **1,** 342 (1924).
(659) YOUNG, W. G.: Abstracts of the 12th National Organic Chemistry Symposium of the American Chemical Society, 1951, pp. 23–6.
(659a) YOUNG, W. G.: Unpublished data.
(660) YOUNG, W. G., AND ANDREWS, L. J.: J. Am. Chem. Soc. **66,** 421 (1944).
(661) YOUNG, W. G., BALLOU, G., AND NOZAKI, K.: J. Am. Chem. Soc. **61,** 12 (1939).
(662) YOUNG, W. G., CASERIO, F., AND BRANDON, D.: Science **117,** 473 (1953).
(663) YOUNG, W. G., CASERIO, F., AND BRANDON, D.: J. Am. Chem. Soc. **78,** in press (1956).
(664) YOUNG, W. G., CASERIO, F., AND DENNIS, G. E.: Unpublished data.
(665) YOUNG, W. G., AND CLEMENT, R.: Science **115,** 488 (1952).
(666) YOUNG, W. G., CLEMENT, R. A., AND SHIH, C.-H.: J. Am. Chem. Soc. **77,** 3061 (1955).
(667) YOUNG, W. G., AND DENNIS, G. E.: Unpublished data.
(668) YOUNG, W. G., AND EISNER, M.: J. Am. Chem. Soc. **63,** 2113 (1941).
(669) YOUNG, W. G., HAGMANN, D., AND DEWOLFE, R. H.: Unpublished data.
(670) YOUNG, W. G., HARTUNG, W. H., AND CROSSLEY, F. S.: J. Am. Chem. Soc. **58,** 100 (1936).
(671) YOUNG, W. G., KAUFMAN, N., LOSHOKOFF, A., AND PRESSMAN, D.: J. Am. Chem. Soc. **60,** 900 (1938).
(672) YOUNG, W. G., KOSMIN, M., MIXER, R. Y., AND CAMPBELL, T. W.: J. Am. Chem. Soc. **74,** 608 (1952).
(673) YOUNG, W. G., AND LANE, J. F.: J. Am. Chem. Soc. **59,** 2051 (1937).
(674) YOUNG, W. G., AND LANE, J. F.: J. Am. Chem. Soc. **60,** 847 (1938).
(675) YOUNG, W. G., LANE, J. F., LOSHOKOFF, A., AND WINSTEIN, S.: J. Am. Chem. Soc. **59,** 2441 (1937).
(676) YOUNG, W. G., McKINNIS, A. C., WEBB, I. D., AND ROBERTS, J. D.: J. Am. Chem. Soc. **68,** 293 (1946).
(676a) YOUNG, W. G., AND McMILLAN, W. G.: Unpublished data.
(677) YOUNG, W. G., AND MIXER, R. Y.: J. Am. Chem. Soc. **78,** in press (1956).
(678) YOUNG, W. G., AND NOZAKI, K.: J. Am. Chem. Soc. **62,** 311 (1940).
(679) YOUNG, W. G., NOZAKI, K., AND WARNER, R.: J. Am. Chem. Soc. **61,** 2564 (1939).
(680) YOUNG, W. G., AND POKRAS, H.: J. Org. Chem. **7,** 233 (1942).
(681) YOUNG, W. G., AND PRATER, A. N.: J. Am. Chem. Soc. **54,** 404 (1932).
(682) YOUNG, W. G., PRATER, A. N., AND WINSTEIN, S.: J. Am. Chem. Soc. **55,** 4908 (1933).
(683) YOUNG, W. G., RICHARDS, L., AND AZORLOSA, J.: J. Am. Chem. Soc. **61,** 3070 (1939).
(684) YOUNG, W. G., AND ROBERTS, J. D.: J. Am. Chem. Soc. **67,** 319 (1945).

(685) YOUNG, W. G., AND ROBERTS, J. D.: J. Am. Chem. Soc. **66,** 2131 (1944).

(686) YOUNG, W. G., AND ROBERTS, J. D.: J. Am. Chem. Soc. **68,** 1472 (1946).

(687) YOUNG, W. G., AND ROBERTS, J. D.: J. Am. Chem. Soc. **68,** 649 (1946).

(688) YOUNG, W. G., ROBERTS, J. D., AND WAX, H.: J. Am. Chem. Soc. **67,** 841 (1945).

(689) YOUNG, W. G., AND SEMENOW, D.: Unpublished data.

(690) YOUNG, W. G., AND SHIH, C.-H.: Unpublished data.

(691) YOUNG, W. G., AND WEBB, I. D.: J. Am. Chem. Soc. **73,** 780 (1951).

(692) YOUNG, W. G., WEBB, I. D., AND GOERING, H. L.: J. Am. Chem. Soc. **73,** 1076 (1951).

(693) YOUNG, W. G., AND WINSTEIN, S.: J. Am. Chem. Soc. **58,** 441 (1936).

(694) YOUNG, W. G., WINSTEIN, S., AND GOERING, H. L.: J. Am. Chem. Soc. **73,** 1958 (1951).

(695) YOUNG, W. G., WINSTEIN, S., AND PRATER, A. N.: J. Am. Chem. Soc. **58,** 289 (1936).

(696) ZALKIND, Y. S., AND KULIKOV, A. I.: Zhur. Obshcheĭ Khim. **15,** 643 (1945).

(697) ZELLNER, C. N.: U. S. patent 2,448,755 (1948); Chem. Abstracts **42,** 9156 (1948).

(698) ZIEGLER, K.: Ber. **58,** 359 (1925).

(699) ZIEGLER, K., GRABBE, H., AND ULRICH, F.: Ber. **57,** 1983 (1924).

(700) ZIEGLER, K., RICHTER, K., AND SCHNELL, B.: Ann. **443,** 161 (1925).