THE CLAISEN REARRANGEMENT

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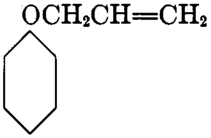
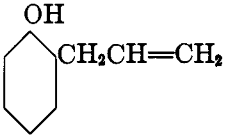
I. INTRODUCTION

It was discovered by Claisen (23) in 1912 that allyl ethers of enols and phenols undergo a smooth rearrangement on heating, yielding the isomeric *C*-allyl compounds. This change, which can be illustrated by the conversion of allyl phenyl ether (I) to 2-allylphenol (II), has been investi-



I
Allyl phenyl ether



II
2-Allylphenol

gated extensively by Claisen and other workers, and a large amount of information about it has been accumulated. The usefulness of the Claisen rearrangement in synthetic work, particularly in the synthesis of natural products, its application as a tool in the study of the bond structures of aromatic compounds, and its intrinsic interest as a molecular rearrangement have combined to stimulate a large amount of research.

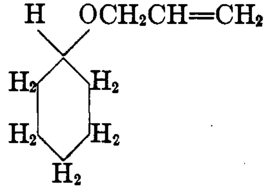
The present review will discuss the general topic of the Claisen rearrangement under three headings: (*1*) the nature and scope of the reaction, including the rearrangement of compounds analogous to allyl ethers but involving elements other than carbon and oxygen; (*2*) applications of the Claisen rearrangement as a tool in organic chemistry; and (*3*) possible mechanisms for the rearrangement.

II. Nature and Scope of the Claisen Rearrangement

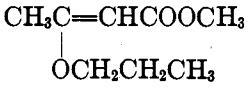
A. GENERAL CONDITIONS OF THE REARRANGEMENT

The types of compounds which undergo the Claisen rearrangement will be discussed in detail in later sections, but the general structural features necessary will be mentioned here.

The group of atoms $C{=}C{-}O{-}CH_2CH{=}CH_2$ must be present, in which the $C{=}C{-}O$ group may belong to an open-chain molecule or to an aromatic ring. The replacement of the hydrogens of the allyl group by alkyl or aryl groups does not, in general, hinder rearrangement, but this point will be discussed later. That the $C{=}C{-}O$ group is necessary is shown by Claisen's demonstration (21, page 97) that allyl cyclohexyl ether does not rearrange when refluxed. The necessity for the double bond in the allyl group is shown by the stability of methyl *O*-propylacetoacetate (23, 34) and *n*-propyl phenyl ether.

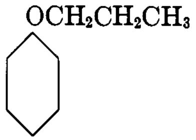


Allyl cyclohexyl ether



$$\underset{\displaystyle OCH_2CH_2CH_3}{CH_3C}{=}CHCOOCH_3$$

Methyl *o*-propylacetoacetate



n-Propyl phenyl ether

The benzyl phenyl ethers, $C_6H_5OCH_2C_6H_5$, contain the necessary atomic grouping, but they do not give the rearrangement under conditions (94, 26) comparable to those effective for the allyl ethers. Rearrangement can be forced under more drastic conditions, however (45, 11), but the product contains a large proportion of the para-compound.

As would be anticipated from the reactivity of allyl compounds in general, unsaturated ethers with the double bond in other than the β-position do not rearrange. Powell and Adams (94) showed that γ-butenyl phenyl ethers of the type $C_6H_5OCH_2CH_2CH{=}CH_2$ could be refluxed for 12 hr. without change, and that vinyl phenyl ether, $C_6H_5OCH{=}CH_2$, gave no rearrangement analogous to that of the allyl ethers. The same authors, and later Hurd and Cohen (49), showed that the double bond in the allyl group cannot be replaced by a triple bond, for the phenyl propargyl ethers, $C_6H_5OCH_2C{\equiv}CH$, do not rearrange on refluxing, although they give some phenol and other decomposition products.

The rearrangement of allyl aryl ethers is a process entirely distinct from the rearrangement of alkyl aryl, vinyl aryl, and benzyl aryl ethers (110); these ethers are usually rearranged in the presence of acidic catalysts and give a mixture of ortho- and para-products, frequently with considerable disubstitution. The allyl aryl ethers require no catalyst, almost invariably give no para rearrangement if an ortho-position is open, and give only traces of disubstitution products.

The following groups containing elements other than carbon and oxygen have been shown to give rearrangements analogous to the Claisen rearrangement (section F):

$CH_2{=}CHCH_2OCH{=}NR$ (109, 90, 16)

$CH_2{=}CHCH_2SC{=}C$ (51)

$CH_2{=}CHCH_2SC{\equiv}N$ (12, 17, 90a)

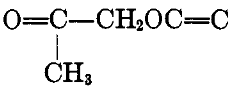
$CH_2{=}CHCH_2{-}C{-}C{=}C$ (31)

It will be noted that the relative positions of the two centers of unsaturation in these systems are the same as in the allyl ethers.

Compounds containing the following systems have been shown not to give a Claisen type of rearrangement on heating:

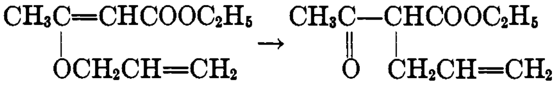
$CH_2{=}CHCH_2N{-}C{=}C$ (20)

$N{\equiv}CCH_2OC{=}C$ (94)



$O{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}CH_2OC{=}C$ (106)

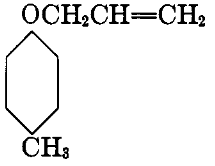
In his initial article (23) Claisen reported that O-allylacetoacetic ester, when distilled with ammonium chloride at atmospheric pressure, yielded the C-allylacetoacetic ester:



$$CH_3\underset{\displaystyle OCH_2CH{=}CH_2}{\underset{|}{C}}{=}CHCOOC_2H_5 \rightarrow CH_3\underset{\displaystyle O}{\underset{\|}{C}}{-}\underset{\displaystyle CH_2CH{=}CH_2}{\underset{|}{C}H}COOC_2H_5$$

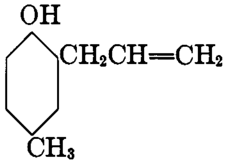
O-Allylacetoacetic ester   *C*-Allylacetoacetic ester

In extending his work to allyl ethers of phenols, Claisen found that the ammonium chloride catalyst was unnecessary and that high yields of the rearranged product were obtained by refluxing the ether for a short time under atmospheric pressure. Thus allyl 4-methylphenyl ether (I) gave an 80 per cent yield of 2-allyl-4-methylphenol (II) when refluxed without solvent for 1 hr. at atmospheric pressure (25, page 43).



I

Allyl 4-methylphenyl ether



II

2-Allyl-4-methylphenol

Since the rearrangement is markedly exothermic, the temperature of the liquid goes up during the reaction. The product of the reaction has a higher boiling point than the starting material, and therefore the progress of the reaction is accompanied by an increase in the boiling point, which ceases when the change is complete.

For simple allyl aryl ethers which have boiling points not too far above 200°C., this simple procedure of refluxing at atmospheric pressure until a constant boiling point is obtained is usually satisfactory. Claisen soon found that better yields were obtained in many cases when the ether was refluxed under diminished pressure, since undesirable side reactions were caused by refluxing at high temperatures (25, page 33). The same result was obtained more conveniently by mixing the ether with a solvent to act as diluent, the solvents most frequently employed being dimethylaniline (b.p. 193°C.) and diethylaniline (b.p. 215°C.). According to Claisen (21, page 72), better yields were obtained with these basic solvents than with indifferent hydrocarbon solvents (*cf.* 30). Recent kinetic studies of the rearrangement (70, 107, 69) have shown that dimethylaniline has only a negligible effect on the rate, and one is inclined to suspect that the superior solvent properties of the anilines are due to the fact that they can be separated from the product so readily by washing with dilute acid. Paraffin oil (21, page 111), tetralin (61), and kerosene (37) have been employed for the rearrangement with satisfactory results.

The reaction mixture in the case of phenols is usually worked up by removing the basic solvent, if present, by dilute mineral acid, taking up the residue in petroleum ether, and extracting with alkali to separate the phenolic product from the neutral by-products and starting material. When the phenols are highly substituted, especially the 2,6-disubstituted ones, their acidity may be so greatly diminished that they are practically insoluble in aqueous alkali; in such cases "Claisen's alkali" (21, page 96), prepared by dissolving 350 g. of potassium hydroxide in 250 cc. of water and diluting to 1 liter with methanol, has proved of great service in isolating weakly acidic phenols (21, 102, 37).

The use of a non-oxidizing atmosphere, such as hydrogen, carbon dioxide, or nitrogen, usually gives a better product (53). In working with 1,5-diallyloxyanthracene, Fieser and Lothrop (39) found that no pure product was obtained when the compound was heated in diethylaniline, but when the rearrangement was carried out in the presence of acetic anhydride and diethylaniline, the rearrangement product was readily isolated in the form of its diacetate. The very sensitive dihydroxy compound formed was protected from decomposition by acetylation to give the stable diacetate.

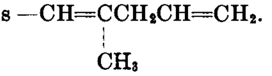
TABLE 1

Rearrangement of straight-chain ethers

COMPOUND*	PRODUCT	REFERENCES
Ethyl *O*-allylacetoacetate	Ethyl *C*-allylacetoacetate	(23, 22, 73)
Ethyl *O*-cinnamylacetoacetate	Ethyl *C*-(α-phenylallyl)acetoacetate	(73, 15)
	Ethyl *C*-cinnamylacetoacetate	(15)
O-Allylacetylacetone	*C*-Allylacetylacetone	(23)
O-Allyloxymethylenecamphor	*C*-Allyloxymethylene camphor	(23)
Allyl vinyl ether	Allylacetaldehyde	(56)
Allyl α-methylvinyl ether	Allylacetone	(56)
Allyl α-phenylvinyl ether	Allylacetophenone	(56)
γ-Ethylallyl vinyl ether	(α-Ethylallyl)acetaldehyde	(57)
	(α, γ-Dimethylallyl)acetaldehyde	(57)
2-Propenyl-4-propyl-6-methoxyphenyl	1,2,4,6-$C_6H_2(OH)(R)(C_3H_7)(OCH_3)$†	(28)
2-Propenyl-4,6-dichlorophenyl	1,2,4,6-$C_6H_2(OH)(R)(Cl)_2$†	(28)
2-Propenyl-4,6-dimethylphenyl	1,2,4,6-$C_6H_2(OH)(R)(CH_3)_2$†	(28)

* In these tables, benzene compounds are named as derivatives of allyl phenyl ether, the words "allyl" and "ether" being omitted, except in the case of substituted allyl groups. Thus "4-methylphenyl" in the table refers to "allyl 4-methylphenyl ether." Ethers derived from polycyclic aromatic hydrocarbons and heterocyclic compounds are named as allyloxy derivatives of the nucleus in question: thus, "2-allyloxynaphthalene" instead of "allyl 2-naphthyl ether."

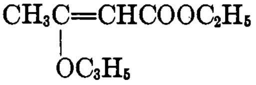
† R equals



$$-CH{=}\underset{\displaystyle CH_3}{\underset{|}{C}}CH_2CH{=}CH_2.$$

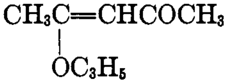
B. REARRANGEMENT OF OPEN-CHAIN COMPOUNDS

In his first report (23, 22), as mentioned before, Claisen stated that ethyl *O*-allylacetoacetate (I) and *O*-allylacetylacetone (II) on distillation with ammonium chloride gave the corresponding *C*-allyl derivatives in good yield (III from I and the corresponding compound from II). The *O*-allyl derivative of oxymethylenecamphor gave a similar rearrangement to the *C*-allyl compound, whose structure was proved by cleavage with alcoholic alkali to *C*-allylcamphor and formic acid:



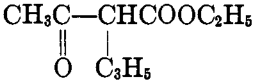
$\underset{\displaystyle OC_3H_5}{CH_3C}{=}CHCOOC_2H_5$

I
Ethyl
O-allylacetoacetate



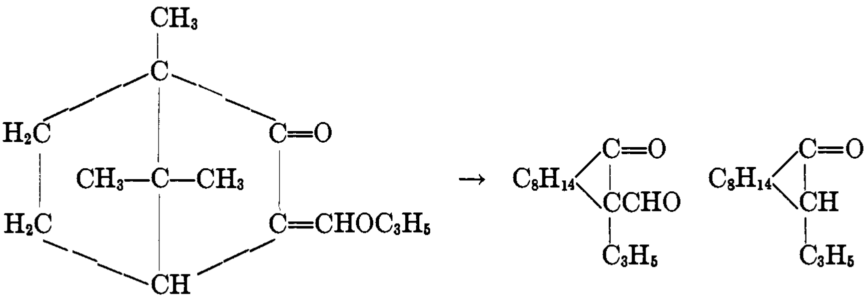
$\underset{\displaystyle OC_3H_5}{CH_3C}{=}CHCOCH_3$

II
O-Allylacetylacetone



$\underset{\displaystyle O}{\overset{\|}{CH_3C}}{-}\underset{\displaystyle C_3H_5}{CH}COOC_2H_5$

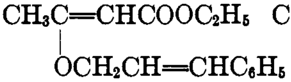
III
Ethyl
C-allylacetoacetate



C-Allylcamphor

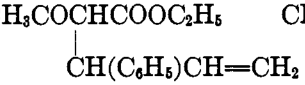
Claisen's paper gave no experimental details of his work with the enol ethers, but this was supplied later by Lauer and Kilburn (73), who showed that there was a slow rearrangement of I at 150–200°C., which was more rapid in the presence of ammonium chloride. The structure of the rearrangment product (III) was proved by comparison, through a solid derivative, with a known sample.

In the rearrangement of ethyl *O*-cinnamylacetoacetate (IV), Lauer and Kilburn (73) observed that the substituted allyl group after migration was attached by the γ-carbon, giving V, instead of being attached by the same carbon which was bonded to the oxygen in the ether. This phenomenon of γ-attachment is called inversion and is of very general occurrence.



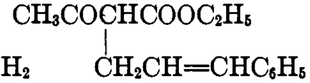
$\underset{\displaystyle OCH_2CH{=}CHC_6H_5}{CH_3C}{=}CHCOOC_2H_5$

IV
Ethyl
O-cinnamylacetoacetate



$CH_3CO\underset{\displaystyle CH(C_6H_5)CH{=}CH_2}{CH}COOC_2H_5$

V

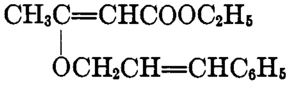


$CH_3CO\underset{\displaystyle CH_2CH{=}CHC_6H_5}{CH}COOC_2H_5$

VI
Ethyl
C-cinnamylacetoacetate

Lauer and Kilburn carried out the rearrangement at 110°C. with ammonium chloride as catalyst and proved the structure of the product by reducing the double bond and forming the pyrazolone, which was identical with the pyrazolone prepared from compounds of known structure.

When ethyl *O*-cinnamylacetoacetate (IV) was heated for 4 hr. at 260°C., Bergmann and Corte (15) found that rearrangement took place without inversion; the product was shown to be VI by hydrolysis and decarboxylation to the ketone. When IV was hydrolyzed with alcoholic alkali, two products were obtained:



$$\begin{array}{l} CH_3C{=}CHCOOC_2H_5 \\ \;| \\ \;OCH_2CH{=}CHC_6H_5 \end{array} \rightarrow CH_2{=}CHCH(C_6H_5)CH_2COOH +$$

IV
Ethyl *O*-cinnamylacetoacetate

β-Phenyl-β-vinylpropionic acid

$$CH_2{=}C(CH_3)OCH_2CH{=}CHC_6H_5$$

Cinnamyl α-methylvinyl ether

One was β-phenyl-β-vinylpropionic acid, which would be formed by rearrangement with inversion to give V, followed by acid cleavage. The second was cinnamyl α-methylvinyl ether, which would be formed by hydrolysis and decarboxylation of the starting material, without rearrangement. This compound is of considerable interest, in view of Hurd and Pollack's work (56) on the rearrangement of allyl vinyl ethers.

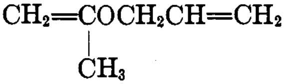
This work by Lauer and Bergmann confirms Claisen's results, and indicates that the inversion of cinnamyl enol ethers depends on the conditions employed.

The simplest compounds containing the C=C—O—C—C=C unit are the vinyl allyl ethers, which have been carefully investigated recently by Hurd and Pollack (56). Vinyl allyl ether itself rearranged cleanly at 255°C. in the gas phase:

$$CH_2{=}CHOCH_2CH{=}CH_2 \rightarrow CH_2{=}CHCH_2CH_2CHO$$

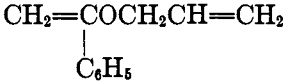
Vinyl allyl ether

No rearrangement took place at 215°C., and the reaction appeared to be about 50 per cent complete at 255°C. α-Methylvinyl allyl ether (VII) and α-phenylvinyl allyl ether (VIII) gave similar reactions,



$$\begin{array}{l} CH_2{=}COCH_2CH{=}CH_2 \\ \qquad | \\ \qquad CH_3 \end{array}$$

VII
α-Methylvinyl allyl ether

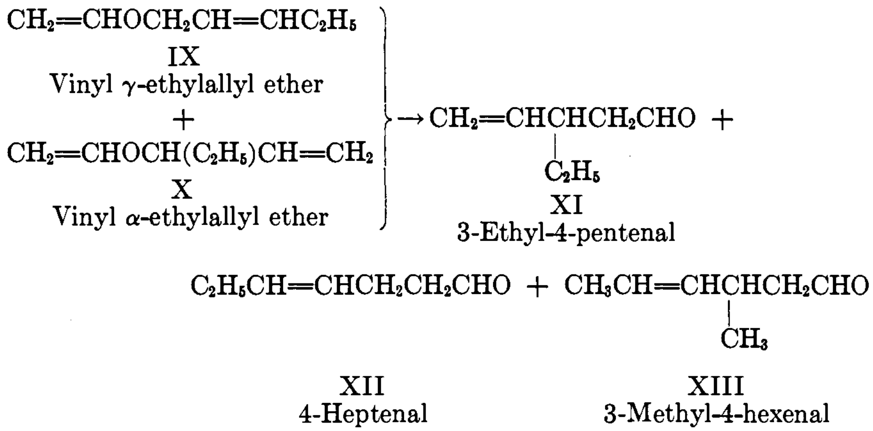


$$\begin{array}{l} CH_2{=}COCH_2CH{=}CH_2 \\ \qquad | \\ \qquad C_6H_5 \end{array}$$

VIII
α-Phenylvinyl allyl ether

the former rearranging practically completely at 255°C. in the gas phase, and the latter after 15 min. refluxing at atmospheric pressure. The rate of rearrangement of these three compounds evidently increases in the order named.

In the rearrangement of a substituted vinyl allyl ether, Hurd and Pollack (57) found that inversion took place.



$CH_2{=}CHOCH_2CH{=}CHC_2H_5$
IX
Vinyl γ-ethylallyl ether
+
$CH_2{=}CHOCH(C_2H_5)CH{=}CH_2$
X
Vinyl α-ethylallyl ether

$$\rightarrow CH_2{=}CH\underset{\displaystyle C_2H_5}{\underset{|}{C}}HCH_2CHO + C_2H_5CH{=}CHCH_2CH_2CHO + CH_3CH{=}CH\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CHO$$

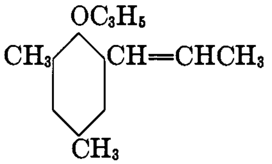
XI
3-Ethyl-4-pentenal

XII
4-Heptenal

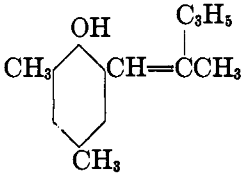
XIII
3-Methyl-4-hexenal

The ether rearranged was a mixture of two allylic isomers, vinyl γ-ethylallyl ether (IX) and vinyl α-ethylallyl ether (X), consisting of 81 per cent of the former and 19 per cent of the latter; the figures are based on an analysis of the mixture of the isomeric bromides, 1-bromo-2-pentene and 3-bromo-1-pentene, from which the ethers were prepared, and the assumption was made that there were no allylic shifts involved in the preparation of the ethers. Rearrangement of the mixture of ethers was carried out at 255°C. in the gas phase, followed by heating in a sealed tube at 220°C. The product was a mixture of three compounds: (*1*) 3-ethyl-4-pentenal (XI, 76 per cent) formed from IX by inversion; (*2*) 4-heptenal (XII, 18 per cent) formed from X by inversion; (*3*) 3-methyl-4-hexenal (XIII, 4 per cent), an example of the anomalous type of rearrangement in which the substituted allyl group is attached by some carbon other than the γ-carbon after migration. Analyses of the mixtures of allylic isomers were carried out by ozonization and determination of the amounts of formic, acetic, and propionic acids formed.

A different type of rearrangement in which the allyl group migrates to an open-chain double bond was reported by Claisen and Tietze (28). They found that allyl phenyl ethers with a propenyl group in one ortho-position and substituents in the other ortho-position and in the para-position could be rearranged to phenols with the allyl group attached to the side chain. Thus, XIV gives XV in 37 per cent yield when refluxed



XIV



XV

under diminished pressure at 177°C. for 7 hr. Two other examples of this type of rearrangement were reported (57), and the reaction is interesting because it is analogous to the rearrangement of allyl phenyl ethers to the para-position of the benzene ring.

C. REARRANGEMENT OF ALLYL ARYL ETHERS TO THE ORTHO-POSITION

The most important case of the Claisen rearrangement is the formation of *o*-allylphenols from allyl aryl ethers. A search of the literature indicates that more than one hundred and fifty examples of this type of reaction are known (table 2), of which approximately one-third involve ethers with substituted allyl groups; the compounds studied involve aromatic and heterocyclic nuclei with a variety of substituents in the nucleus and side chain.

1. *General methods of preparing allyl aryl ethers*

The most general method of preparing allyl aryl ethers is that of Claisen (25, page 29), which consists in refluxing the phenol with allyl bromide and anhydrous potassium carbonate in acetone for several hours; allyl bromide may be replaced advantageously by allyl chloride and sodium iodide (85, 99). The method generally gives very good yields, but is unsatisfactory for weakly acidic phenols, which must be treated with sodium ethoxide in alcohol solution to obtain ether formation. The Claisen method is also unsatisfactory for phenolaldehydes, which condense with acetone in the presence of potassium carbonate. Substituted allyl chlorides and bromides usually can be used successfully (30, 58, 71, 10), although the yields are poorer, owing probably to *C*-alkylation.

The alkylation may be carried out in aqueous acetone with sodium hydroxide and allyl bromide (64), which gives a more rapid reaction and somewhat higher yields. The Williamson synthesis, using sodium ethoxide and allyl bromide in alcohol solution, is also more rapid than the acetone–potassium carbonate method and gives good results (25, 29, 26, 10).

TABLE 2

Rearrangement of allyl aryl ethers to the ortho-position

COMPOUND	PRODUCT	REFERENCES
	1. Benzene derivatives	
Phenyl	$1,2\text{-}C_6H_4(OH)(R)$*	(21, p. 79; 74, 1, 53, 59)
	2-Methyldihydrobenzofuran	(21, p. 79)
	$1,2\text{-}C_6H_4(OH)(CH_2CH(CH_3)OC_6H_4R)$	(59)
2-Methylphenyl	$1,2,6\text{-}C_6H_3(OH)(CH_3)(R)$	(25, p. 56)
3-Methylphenyl	$1,2,3\text{-}C_6H_3(OH)(R)(CH_3)$ $1,3,6\text{-}C_6H_3(OH)(CH_3)(R)$	(25, p. 58)
4-Methylphenyl	$1,2,4\text{-}C_6H_3(OH)(R)(CH_3)$	(25, p. 43; 64, 70)
2-Hydroxymethylphenyl	CH_2O and complete decomposition	(25, p. 106)
2-Allylphenyl	$1,2,6\text{-}C_6H_3(OH)(R)_2$	(21, p. 91)
2,4-Dimethylphenyl	$1,2,4,6\text{-}C_6H_2(OH)(R)(CH_3)_2$	(28, 69)
3,5-Dimethylphenyl	$1,2,3,5\text{-}C_6H_2(OH)(R)(CH_3)_2$	(2)
Mixture of 2-allyl-3-methylphenyl and 2-allyl-5-methylphenyl	$1,3,x,x\text{-}C_6H_2(OH)(CH_3)(R)_2$	(25, p. 58)
2-Allyl-4-methylphenyl	$1,2,4,6\text{-}C_6H_2(OH)(R)(CH_3)(R)$ (?)	(25, p. 45)
2-Propyl-4-methylphenyl	$1,2,4,6\text{-}C_6H_2(OH)(C_3H_7)(CH_3)(R)$	
	$1,2,4\text{-}C_6H_3(OH)(C_3H_7)(CH_3)$	(64)
2,3,5-Trimethylphenyl	$1,2,3,5,6\text{-}C_6H_1(OH)(CH_3)_3(R)$	(101, 99)
5-Allyloxy-6-methylindan	4-Allyl-5-hydroxy-6-methylindan	(79)
4,7-Dimethyl-5-allyloxyindan	4,7-Dimethyl-5-hydroxy-6-allylindan	(79)
4-(β-Carbomethoxyvinyl)phenyl	$1,2,4\text{-}C_6H_3(OH)(R)(CH{=}CHCOOCH_3)$	(86)
4-Chlorophenyl	$1,2,4\text{-}C_6H_3(OH)(R)(Cl)$	(25, p. 37)
2,4-Dichlorophenyl	$1,2,4,6\text{-}C_6H_2(OH)(Cl)_2(R)$	(28, 95)
2-Bromophenyl	$1,2,6\text{-}C_6H_3(OH)(Br)(R)$	(61)

4-Bromophenyl	1,2,4-$C_6H_3(OH)(R)(Br)$	(25, p. 38)
2,4-Dibromophenyl	1,2,4,6-$C_6H_2(OH)(Br)_2(R)$	(61)
3,5-Dibromophenyl	1,2,3,5-$C_6H_2(OH)(R)(Br)_2$	(61)
	2-Methyl-4,6-dibromodihydrobenzofuran	
2-Nitrophenyl	1,2,6-$C_6H_3(OH)(NO_2)(R)$	(25, p. 59)
4-Nitrophenyl	1,2,4-$C_6H_3(OH)(R)(NO_2)$	(25, p. 40)
4-Aminophenyl	1,2,4-$C_6H_3(OH)(R)(NH_2)$	(21, p. 111)
4-Acetaminophenyl	1,2,4-$C_6H_3(OH)(R)(NHCOCH_3)$	(21, p. 107)
2,3,5-Trimethyl-4-formaminophenyl	1,2,3,4,5,6-$C_6(OH)(CH_3)_2(NHCHO)(CH_3)(R)$	(99)
2,3,5-Trimethyl-4-acetaminophenyl	1,2,3,4,5,6-$C_6(OH)(CH_3)_2(NHCOCH_3)(CH_3)(R)$	(99)
2-Allyl-4-acetaminophenyl	1,2,4,6-$C_6H_2(OH)(R)(NHCOCH_3)(R)$	(21, p. 112)
4-(Phenylazo)phenyl	1,2,4-$C_6H_3(OH)(R)(N{=}NC_6H_5)$	(25, p. 42)
2-Hydroxyphenyl	1,2,6-$C_6H_3(OH)_2(R)$	(65, 93, 52)
	1,2,4-$C_6H_3(OH)_2(R)$	
2-Methoxyphenyl	1,2,6-$C_6H_3(OH)(OCH_3)(R)$	(23, 85)
2-Hydroxy-3-allylphenyl	1,2,3,6-$C_6H_2(OH)_2(R)_2$	(52)
2-Methoxy-4-allylphenyl	1,2,4,6-$C_6H_2(OH)(OCH_3)(R)_2$	(25, p. 47)
2-Methoxy-4-propyl	1,2,4,6-$C_6H_2(OH)(OCH_3)(C_3H_7)(R)$	(28)
2-Methoxy-4(γ-hydroxypropyl)phenyl	1,2,4,6-$C_6H_2(OH)(OCH_3)(CH_2CH_2CH_2OH)(R)$	(67)
2-Allyloxyphenyl	Mixture containing 1,2,3,6-$C_6H_2(OH)_2(R)_2$	(65, 52)
3-Hydroxyphenyl	1,3,6-$C_6H_3(OH)_2(R)$	(52, 91)
3-Methoxyphenyl	1,3,6-$C_6H_3(OH)(OCH_3)(R)$	(84)
3-Hydroxy-4-nitrophenyl	1,3,4,6-$C_6H_2(OH)_2(NO_2)(R)$	(6)
3-Allyloxyphenyl	1,3,4,6-$C_6H_2(OH)_2(R)_2$	(52)
3-Allyloxy-4,6-diallylphenyl	1,2,4,5,6-$C_6H_1(OH)(R)_2(OR)(R)$	(52)
4-Methoxyphenyl	1,2,4-$C_6H_3(OH)(R)(OCH_3)$	(84)
4-Benzoyloxyphenyl	1,2,4-$C_6H_3(OH)(R)(OCOC_6H_5)$	(43)
4-Allyloxyphenyl	1,2,3,4-$C_6H_2(OH)(R)_2(OH)$	(37)
	1,2,4,5-$C_6H_2(OH)(R)(OH)(R)$	
2,3-Methylenedioxyphenyl	1,2,3,6-$C_6H_2(OH)(-OCH_2O-)(R)$	(8)
	1,2,3,4-$C_6H_2(OH)(-OCH_2O-)(R)$	(7)
2-Allyloxy-3-methoxyphenyl (?)	1,2,3,x,x-$C_6H_1(OH)_2(OCH_3)(R)_2$	(55)

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* R equals $-CH_2CH{=}CH_2$.

TABLE 2—*Continued*

COMPOUND	PRODUCT	REFERENCES
1. Benzene derivatives—*Continued*		
2-Allyloxy-3-hydroxyphenyl (?)	1,2,3,x,x-$C_6H_1(OH)_3(R)_2$*	(55)
2-Aldehydophenyl	1,2,6-$C_6H_3(OH)(CHO)(R)$	(25, p. 96)
4-Aldehydophenyl	1,2,4-$C_6H_3(OH)(R)(CHO)$	(25, p. 107)
2-Allyl-4-aldehydophenyl	1,2,4,6-$C_6H_2(OH)(R)(CHO)(R)$	(25, p. 108)
2-Carbethoxyphenyl	1,2,6-$C_6H_3(OH)(COOC_2H_5)(R)$	(23)
	(For methyl ester)	(25, p. 70)
4-Carbethoxyphenyl	1,2,4-$C_6H_3(OH)(R)(COOC_2H_5)$	(25, p. 87; 74)
2-Allyl-4-carbethoxyphenyl	1,2,4,6-$C_6H_2(OH)(R)(COOC_2H_5)(R)$	(25, p. 89)
2-Methoxy-4-aldehydophenyl	1,2,4,6-$C_6H_2(OH)(OCH_3)(CHO)(R)$	(25, p. 116)
3-Hydroxy-4-aldehydophenyl	1,2,3,4-$C_6H_2(OH)(R)(OH)(CHO)$	(6)
3-Methoxy-4-aldehydophenyl	1,3,4,6-$C_6H_2(OH)(OCH_3)(CHO)(R)$	(6)
3-Hydroxy-4-acetylphenyl	1,2,3,4-$C_6H_2(OH)(R)(OH)(COCH_3)$	(5)
3-Methoxy-4-acetylphenyl	1,3,4,6-$C_6H_2(OH)(OCH_3)(COCH_3)(R)$	(5)
2-Allyl-3-hydroxy-4-acetylphenyl	1,2,3,4,6-$C_6H_1(OH)(R)(OH)(COCH_3)(R)$	(5)
3-Methoxy-4-acetyl-6-allylphenyl	1,2,3,4,6-$C_6H_1(OH)(R)(OCH_3)(COCH_3)(R)$	(5)
3-Hydroxy-4-propionylphenyl	1,2,3,4-$C_6H_2(OH)(R)(OH)(COC_2H_5)$	(6)
3-Methoxy-4-propionylphenyl	1,3,4,6-$C_6H_2(OH)(OCH_3)(COC_2H_5)(R)$	(6)
3-Acetyl-4-hydroxyphenyl	1,2,3,4-$C_6H_2(OH)(R)(COCH_3)(OH)$	(6)
3-Acetyl-4-methoxyphenyl	1,2,3,4-$C_6H_2(OH)(R)(COCH_3)(OCH_3)$	(6)
2. Derivatives of polycyclic aromatic hydrocarbons and heterocyclic compounds		
1-Allyloxynaphthalene	1-Hydroxy-2-allylnaphthalene	(25, p. 61)
2-Allyloxynaphthalene	1-Allyl-2-hydroxynaphthalene	(23)
1-Allyl-2-allyloxynaphthalene	Unchanged by long heating	(23)
2-Allyloxy-1,4-naphthoquinone	2-Hydroxy-3-allyl-1,4-naphthoquinone	(35)
4-Allyloxy-1,2-naphthoquinone	2-Hydroxy-3-allyl-1,4-naphthoquinone	(35)
1-Allyloxy-3,7-dimethylnaphthalene	1-Hydroxy-2-allyl-3,7-dimethylnaphthalene	(37)

1-Allyloxy-5-methoxynaphthalene	1-Hydroxy-2-allyl-4-methoxynaphthalene	(46)
1,4-Diallyloxynaphthalene	1,4-Dihydroxy-2,3-diallylnaphthalene (as diacetate)	(37)
1,4-Diallyloxy-5,8-dihydronaphthalene	1,4-Dihydroxy-2,3-diallyl-5,8-dihydronaphthalene	(37)
2,6-Diallyloxynaphthalene	1,5-Diallyl-2,6-dihydroxynaphthalene	(38)
1,5-Diallyl-2,6-diallyloxynaphthalene	Only decomposition	(38)
2-Allyloxy-3-carbomethoxynaphthalene	1-Allyl-2-hydroxy-3-carbomethoxynaphthalene	(13)
4-Allyloxybiphenyl	3-Allyl-4-hydroxybiphenyl	(41)
2-Allyloxybiphenyl	2-Hydroxy-3-allylbiphenyl	(3)
2-Allyloxyphenanthrene	1-Allyl-2-hydroxyphenanthrene	(40)
3-Allyloxyphenanthrene	3-Hydroxy-4-allylphenanthrene	(40)
1-Methyl-7-isopropyl-9-allyloxyphenanthrene	1-Methyl-7-isopropyl-9-hydroxy-10-allylphenanthrene	(40)
1-Allyl-2-allyloxyphenanthrene	Decomposition only	(40)
2,6-Diallyloxyanthracene	1,5-Diallyl-2,6-dihydroxyanthracene (as diacetate)	(39)
1,5-Dimethyl-2,6-diallyloxyanthracene	Decomposition only	(39)
2-Allyloxyfluorene	1-Allyl-2-hydroxyfluorene and the 3-allyl isomer	(78)
1-Allyl-2-allyloxyfluorene and 3-allyl-2-allyloxyfluorene	1,3-Diallyl-2-hydroxyfluorene	(78)
1,2-Dimethyl-3-allyloxyfluorene	1,2-Dimethyl-3-hydroxy-4-allylfluorene	(78)
1,4-Dimethyl-3-allyloxyfluorene	1,4-Dimethyl-2-allyl-4-hydroxyfluorene	(78)
2-Allyloxyfluorenone	1-Allyl-2-hydroxyfluorenone and the 3-allyl isomer	(14)
1,6-Diallyloxydihydropleiadene	Decomposition only	(38)
2-Methyl-4-allyloxyquinoline	2-Methyl-3-allyl-4-hydroxyquinoline	(81)
2-Allyloxydibenzofuran	1-Allyl-2-hydroxydibenzofuran	(42)
4-Methyl-7-allyloxycoumarin	4-Methyl-7-hydroxy-8-allylcoumarin	(5)
2-Methyl-3-methoxy-7-allyloxychromone	2-Methyl-3-methoxy-7-hydroxy-8-allylchromone	(96)
2-Methyl-3-methoxy-7-allyloxy-8-allylchromone	2-Methyl-3-methoxy-6,8-diallyl-7-hydroxychromone	(96)
7-Allyloxyflavone	7-Hydroxy-8-allylflavone	(96)
7-Allyloxy-8-allylflavone	6,8-Diallyl-7-hydroxyflavone	(96)
3-Allyloxy-6-hydroxyfluoran	2-Allylfluorescein	(60)
3,6-Diallyloxyfluoran	2,7-Diallylfluorescein	(60)
Allyl 6-allyloxy-9-phenylfluorone-11-carboxylate	Allyl ester of 2-allylfluorescein	(60)

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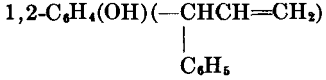
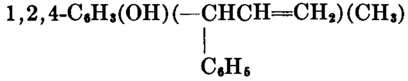
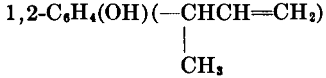
* R equals $—CH_2CH{=}CH_2$.

TABLE 2—*Continued*

COMPOUND	PRODUCT	REFERENCES
3. Rearrangements involving displacement of carbon monoxide and carbon dioxide from the ortho-position R equals $—CH_2CH{=}CH_2$		
2-Aldehydo-6-allylphenyl	$1,2,6\text{-}C_6H_3(OH)(R)_2$ and CO $1,2,4,6\text{-}C_6H_2(OH)(CHO)(R)_2$	(25, p. 102)
2-Aldehydo-4-allyl-6-methoxyphenyl	$1,2,4,6\text{-}C_6H_2(OH)(R)_2(OCH_3)$ and CO	(25, p. 115)
2-Aldehydo-6-methoxyphenyl	$1,2,6\text{-}C_6H_3(OH)(R)(OCH_3)$ $1,2,4,6\text{-}C_6H_2(OH)(R)(CHO)(OCH_3)$ $1,2,4,6\text{-}C_6H_2(OH)(CHO)(R)(OCH_3)$	(25, p. 112)
2-Carboxy-4,6-dichlorophenyl	$1,2,4,6\text{-}C_6H_2(OH)(R)(Cl)_2$	(21, p. 85)
2-Carboxy-6-methylphenyl	$1,2,6\text{-}C_6H_3(OH)(R)(CH_3)$ and CO_2 $1,2,4,6\text{-}C_6H_2(OH)(COOH)(R)(CH_3)$	(25, p. 83)
2-Carboxy-6-allylphenyl	$1,2,6\text{-}C_6H_3(OH)(R)_2$ and CO_2 $1,2,4,6\text{-}C_6H_2(OH)(COOH)(R)_2$	(25, p. 75)
2-Carboxy-4,6-diallylphenyl	$1,2,4,6\text{-}C_6H_2(OH)(R)_3$ and CO_2	(25, p. 79)
2-Carboxy-6-methoxyphenyl	$1,2,6\text{-}C_6H_3(OH)(R)(OCH_3)$ and CO_2 $1,2,4,6\text{-}C_6H_2(OH)(COOH)(R)(OCH_3)$	(21, p. 117)
4. Ethers with monosubstituted allyl groups		
β-Chloroallylphenyl	$1,2\text{-}C_6H_4(OH)(CH_2CCl{=}CH_2)$ 2-Methylbenzofuran	(62)
β-Bromoallyl phenyl	$1,2\text{-}C_6H_4(OH)(CH_2CBr{=}CH_2)$ (?)	(62, 18)
γ-Chloroallyl phenyl	Phenolic compounds	(62)
γ-Chloroallyl 4-methylphenyl	Polymeric products	(62)
γ-Bromoallyl phenyl	$BrCH_2CH{=}CHBr$ and phenol	(62)
α-Ethylallyl phenyl	$1,2\text{-}C_6H_4(OH)(CH_2CH{=}CHC_2H_5)$	(71)
α-Ethylallyl 4-carbethoxyphenyl	$1,2,4\text{-}C_6H_3(OH)(CH_2CH{=}CHC_2H_5)(COOC_2H_5)$	(77)
α-*n*-Propylallyl-4-carbethoxyphenyl	$1,2,4\text{-}C_6H_3(OH)(CH_2CH{=}CHC_3H_7)(COOC_2H_5)$	(75)

The following series of β-methylallyl ethers:†		
Phenyl	$1,2\text{-}C_6H_4(OH)(R)$	(10, 97)
4-Chlorophenyl	$1,2,4\text{-}C_6H_3(OH)(R)(Cl)$	(10)
2-Methylphenyl	$1,2,6\text{-}C_6H_3(OH)(CH_3)(R)$	(10)
3-Methylphenyl	$1,3,6\text{-}C_6H_3(OH)(CH_3)(R)$	(10)
4-Methylphenyl	$1,2,4\text{-}C_6H_3(OH)(R)(CH_3)$	(10)
2-(β-Methylallyl)phenyl	$1,2,6\text{-}C_6H_3(OH)(R)_2$	(10)
2,4-Dimethylphenyl	$1,2,4,6\text{-}C_6H_2(OH)(CH_3)_2(R)$	(10)
2,5-Dimethylphenyl	$1,2,5,6\text{-}C_6H_2(OH)(CH_3)_2(R)$	(10)
3,4-Dimethylphenyl	$1,3,4,6\text{-}C_6H_2(OH)(CH_3)_2(R)$	(10)
2-Isopropyl-5-methylphenyl	$1,2,5,6\text{-}C_6H_2(OH)(CH(CH_3)_2)(CH_3)(R)$	(10)
2-(β-Methylallyl)-4-methylphenyl	$1,2,4,6\text{-}C_6H_2(OH)(R)(CH_3)(R)$	(10)
2-(β-Methylallyl)-5-methylphenyl	$1,2,5,6\text{-}C_6H_2(OH)(R)(CH_3)(R)$	(10)
2-Methoxyphenyl	$1,2,6\text{-}C_6H_3(OH)(OCH_3)(R)$	(10)
3-(β-Methylallyloxy)phenyl	$1,3,4,6\text{-}C_6H_2(OH)_2(R)_2$	(10)
Cinnamyl phenyl	 $1,2\text{-}C_6H_4(OH)(-\underset{\underset{\displaystyle C_6H_5}{\vert}}{C}HCH{=}CH_2)$	(29, 59)
Cinnamyl 4-methylphenyl	 $1,2,4\text{-}C_6H_3(OH)(-\underset{\underset{\displaystyle C_6H_5}{\vert}}{C}HCH{=}CH_2)(CH_3)$	(29)
2-Cinnamyloxy-3-carbomethoxynaphthalene	1-(α-Phenylallyl)-2-hydroxy-3-carbomethoxynaphthalene	(13)
γ-Methylallyl phenyl	 $1,2\text{-}C_6H_4(OH)(-\underset{\underset{\displaystyle CH_3}{\vert}}{C}HCH{=}CH_2)$	(19, 30, 76)
1-(γ-Methylallyloxy)naphthalene	1-Hydroxy-2-(α-methylallyl)naphthalene	(19, 30)
2-(γ-Methylallyloxy)-1,4-naphthoquinone	2-Hydroxy-3-(α-methylallyl)-1,4-naphthoquinone	(36)
4-(γ-Methylallyloxy)-1,2-naphthoquinone	Same compound as above	(36)

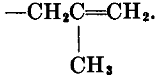
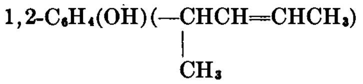
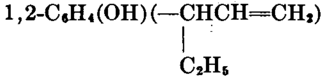
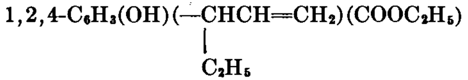
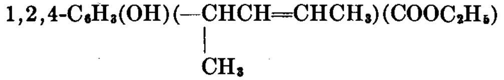
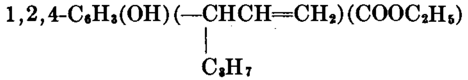
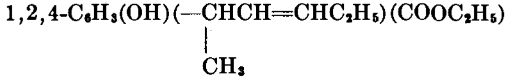
† R equals  $-CH_2\underset{\underset{\displaystyle CH_3}{\vert}}{C}{=}CH_2$.

TABLE 2—*Continued*

COMPOUND	PRODUCT	REFERENCES
4. Ethers with monosubstituted allyl groups—*Continued*		
γ-Ethylallyl phenyl	 $1,2\text{-}C_6H_4(OH)(-\underset{CH_3}{\underset{\mid}{C}}HCH{=}CHCH_3)$  $1,2\text{-}C_6H_4(OH)(-\underset{C_2H_5}{\underset{\mid}{C}}HCH{=}CH_2)$	(71, 57, 58)
γ-Ethylallyl 2-methylphenyl	$1,2,6\text{-}C_6H_3(OH)(CH_3)(C_5H_9)$	(58)
γ-Ethylallyl 4-carbethoxyphenyl	 $1,2,4\text{-}C_6H_3(OH)(-\underset{C_2H_5}{\underset{\mid}{C}}HCH{=}CH_2)(COOC_2H_5)$  $1,2,4\text{-}C_6H_3(OH)(-\underset{CH_3}{\underset{\mid}{C}}HCH{=}CHCH_3)(COOC_2H_5)$	(77)
3-(γ-Ethylallyloxy)-6-hydroxyfluoran	2-Pentenylfluorescein	(60)
γ-(*n*-Propylallyl)phenyl	$1,2\text{-}C_6H_4(OH)(C_6H_{11})$	(54, 58)
γ-(*n*-Propylallyl) 2-methylphenyl	$1,2,6\text{-}C_6H_3(OH)(CH_3)(C_6H_{11})$	(58)
γ-(*n*-Propylallyl) 4-carbethoxyphenyl	 $1,2,4\text{-}C_6H_3(OH)(-\underset{C_3H_7}{\underset{\mid}{C}}HCH{=}CH_2)(COOC_2H_5)$  $1,2,4\text{-}C_6H_3(OH)(-\underset{CH_3}{\underset{\mid}{C}}HCH{=}CHC_2H_5)(COOC_2H_5)$	(75)
3,6-Di-(γ-*n*-propylallyloxy)fluoran	2,7-Dihexenylfluorescein	(60)
γ-*n*-Butylallyl phenyl	C_6H_5OH and $1,2\text{-}C_6H_4(OH)(C_7H_{13})$	(58)

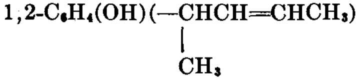
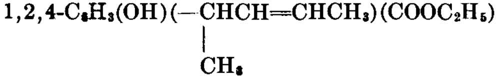
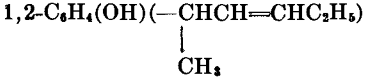
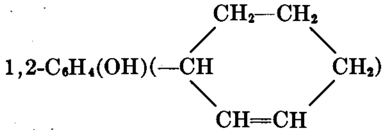
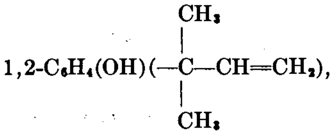
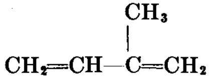
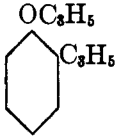
γ-*n*-Butylallyl 2-methylphenyl	$1,2\text{-}C_6H_4(OH)(CH_3)$ and $1,2,6\text{-}C_6H_3(OH)(CH_3)(C_7H_{13})$	(58)
γ-*n*-Propylallyl 2-(γ-*n*-propylallyloxy)-3-hydroxyphenyl (?)	$1,2,3,x,x\text{-}C_6H_1(OH)_3(C_6H_{11})_2$	(55)
γ-*n*-Butylallyl 2-(γ-*n*-butylallyloxy)-3-hydroxyphenyl (?)	$1,2,3,x,x\text{-}C_6H_1(OH)_3(C_7H_{13})_2$	(55)
Geranyl 2-hydroxyphenyl	$1,2,6\text{-}C_6H_3(OH)_2(C_{10}H_{17})$ (?)	(66)
1,4-Difarnesyloxynaphthalene	2,3-Difarnesyl-1,4-naphthohydroquinone (?) (as diacetate)	(80)
	5. Ethers with disubstituted allyl groups	
α,γ-Dimethylallyl phenyl	 $1,2\text{-}C_6H_4(OH)(-\underset{\substack{\mid \\ CH_3}}{C}HCH{=}CHCH_3)$	(24, 50, 71)
α,γ-Dimethylallyl 4-carbethoxyphenyl	1,3-Pentadiene  $1,2,4\text{-}C_6H_3(OH)(-\underset{\substack{\mid \\ CH_3}}{C}HCH{=}CHCH_3)(COOC_2H_5)$  $1,2,4\text{-}C_6H_3(OH)(-\underset{\substack{\mid \\ C_2H_5}}{C}HCH{=}CH_2)(COOC_2H_5)$ (?)	(77)
α,γ-Ethylmethylallyl phenyl	 $1,2\text{-}C_6H_4(OH)(-\underset{\substack{\mid \\ CH_3}}{C}HCH{=}CHC_2H_5)$ C_6H_5OH	(50, 58, 102)
α,γ-Ethylmethylallyl 2-methylphenyl	$1,2\text{-}C_6H_4(OH)(CH_3)$	(58)
α,γ-*n*-Propylmethylallyl phenyl	C_6H_5OH	(58, 63, 50)
α,γ-*n*-Propylmethylallyl 2-methylphenyl	$1,2\text{-}C_6H_4(OH)(CH_3)$	(58)
α,γ-*n*-Butylmethylallyl phenyl	C_6H_5OH	(58)
α,γ-*n*-Butylmethylallyl 2-methylphenyl	$1,2\text{-}C_6H_4(OH)(CH_3)$	(58)

TABLE 2—*Concluded*

COMPOUND	PRODUCT	REFERENCES
5. Ethers with disubstituted allyl groups—*Continued*		
Δ²-Cyclohexenyl phenyl	Phenol, cyclohexadiene, hexahydrodibenzofuran, and 	(32)
γ,γ-Dimethylallyl phenyl	 $1,2\text{-}C_6H_4(OH)(-\overset{CH_3}{\underset{CH_3}{C}}-CH{=}CH_2)$,  C_6H_5OH, and $CH_2{=}CH{-}\overset{CH_3}{C}{=}CH_2$	(29, 30, 24)
α,α,γ,γ-Tetramethylallyl phenyl	C_6H_5OH and $CH_2{=}C(CH_3)CH{=}C(CH_3)_2$	(50)

Allylation of 2-hydroxy-1,4-naphthoquinone has been carried out by treating the silver salt in benzene with allyl bromide (35), which gives some *C*-alkylation as well as *O*-alkylation.

Varying amounts of *C*-alkylation are frequently observed; thus Claisen (21, page 78) found about 1 per cent of allyl *o*-allylphenyl ether (I) during the allylation of phenol by the potassium carbonate–acetone method, and with the more active halides cinnamyl bromide and α,γ-dimethylallyl bromide the proportion of *C*-alkylation was greater (26). Smith, Ungnade, Lauer, and Leekley (102) obtained a complicated mixture of *C*- and *O*-alkylation products by treating phenol with 4-bromo-2-hexene and 4-chloro-2-hexene under the same conditions. Tarbell and Kincaid (107) obtained an appreciable amount of *C*-alkylation in treating 2,6-dimethylphenol with allyl bromide and sodium ethoxide in alcohol. Since, in general, the amount of *C*-alkylation is greatly increased by carrying out the alkylation on the sodium salt of the phenol in benzene (26), this method is unsuitable for the preparation of allyl ethers.

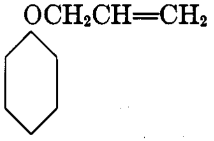


I

Allyl *o*-allylphenyl ether

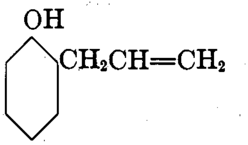
2. Rearrangement of ethers with unsubstituted allyl groups

The simplest allyl aryl ether, allyl phenyl ether (I), rearranges to *o*-allylphenol (II) in practically quantitative yield when heated in an inert atmosphere at 200°C. (21, page 79; 74, 1, 53); a small amount of 2-methyldihydrobenzofuran (III; 21, page 79) is formed concurrently. The



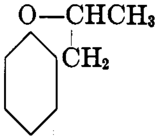
I

Allyl phenyl ether



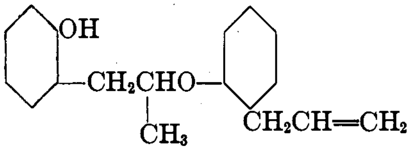
II

o-Allylphenol



III

2-Methyldihydrobenzofuran



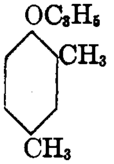
IV

addition of either alkali or acid does not seem to increase the rate of rearrangement, although acid does increase the amount of III; this is not surprising, since *o*-allylphenols are known to be changed to dihydrobenzofurans by acids (29). The rearrangement carried out without using an inert atmosphere gives a lower yield (34 per cent) and considerable amounts of polymeric material, including a dimer which probably has the structure indicated in formula IV (59).

Like nearly all ethers with a free ortho-position, allyl phenyl ether gives no detectable amount of para-product when rearranged (74). The limited number of ethers which give rearrangement to the para-position when the ortho-position is available will be discussed separately (page 525).

The rearrangement of allyl ethers in general gives high yields. Thus allyl 4-methylphenyl ether has been shown to give over 90 per cent of 2-allyl-4-methylphenol when heated in a nitrogen atmosphere for 13 hr. at 200°C. in sealed tubes (70); about 4 per cent of non-volatile material was obtained.

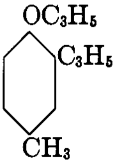
No very significant generalization can be made from the data available about the ease of rearrangement of allyl ethers of aromatic compounds. Although the number of examples is large, the information is almost entirely qualitative. From recent kinetic studies (70, 69) it is known that allyl 2,4-dimethylphenyl ether (V) rearranges about twice as rapidly as the monomethyl compound, allyl 4-methylphenyl ether, the former being completely rearranged by heating for 7 hr. at 193°C. Preliminary work (68) indicates that allyl β-naphthyl ether rearranges approximately twenty times as rapidly as V, the reaction being nearly complete in 25 min. at 174°C. The allyl ethers of 2-phenanthrol (VII) and 3-phenanthrol rearrange at 100°C. (40), which is the lowest temperature recorded for an ether with an unsubstituted allyl group. It seems likely that in numerous cases reported in the literature unnecessarily drastic conditions were employed and that better yields would be obtained at lower temperatures.



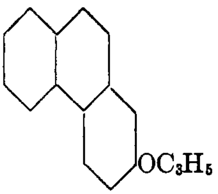
V

Allyl 2,4-dimethylphenyl ether

It appears from work of Claisen (25, pages 45, 58) that ethers with allyl groups in the nucleus, such as allyl 2-allyl-4-methylphenyl ether (VI) and the ethers from the isomeric allyl *m*-cresols, rearrange in poor yield, probably owing to polymerization through the nuclear allyl group.



VI
Allyl 2-allyl-4-methylphenyl ether



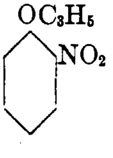
VII
Allyl ether of 2-phenanthrol

The list of allyloxy derivatives of hydrocarbons which have been rearranged (see table 2) includes ethers of benzene, toluene, xylene, allylbenzenes, naphthalene, anthracene, phenanthrene, fluorene, biphenyl, and hydrindene. The use of the Claisen rearrangement in determining bond structures of aromatic hydrocarbons will be discussed later. Among the heterocyclic compounds whose allyl ethers have been rearranged are fluorescein, quinaldine, flavone, chromone, dibenzofuran, and coumarin.

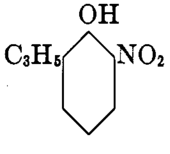
Allyl ethers of a long list of assorted derivatives of aromatic hydrocarbons have been rearranged, the substituents including hydroxyl, methoxyl, methylenedioxy, allyloxy (rearrangement involving migration of two allyl groups), aldehyde, carboxyl (*cf.* also section E for these two groups), acetyl, propionyl, γ-hydroxypropyl, carbethoxyl, β-carbomethoxyvinyl, halogen, nitro, amino, acetamino, and azo (table 2).

It is clear that the rearrangement takes place without regard for the nature of the substituents already present in the ring; there does not seem to be any more difficulty in effecting rearrangement of an ether with meta-directing groups in the ring than in rearranging an ether with the strongly ortho–para-directing hydroxyl or methoxyl groups.

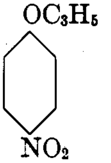
In fact, from the qualitative evidence available, it appears that the rearrangement of allyl 2-nitrophenyl ether (VIII) goes unusually readily, 73 per cent of the rearrangement product IX being obtained by heating for 5 hr. at 180°C. (25, page 59). The allyl 4-nitrophenyl ether (X), however, rearranges much less smoothly, 30 to 40 per cent yields being obtained by refluxing for 1.5 hr. in paraffin oil at 230°C. (25, page 40). The situation



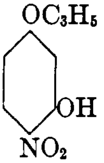
VIII
Allyl 2-nitrophenyl ether



IX



X
Allyl 4-nitrophenyl ether

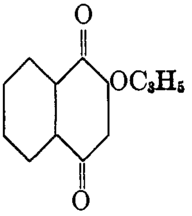


XI
Allyl 3-hydroxy-4-nitrophenyl ether

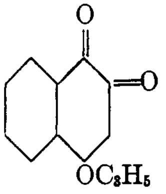
is complicated by the fact that allyl 3-hydroxy-4-nitrophenyl ether (XI) gives only 26 per cent rearrangement after 50 min. heating at 185°C., and 50 per cent of the starting material is recovered (6). On the basis of ordinary experience in aromatic substitution, it would be expected that the compounds VIII and X would rearrange with comparable ease, and that XI would rearrange more rapidly, if the ease of substitution of the nucleus were the decisive factor in the rearrangement.

It is obviously unsafe to draw many conclusions about relative rates of rearrangement from qualitative data on yields under various conditions, but it can be said that there is no correlation evident between the ease of rearrangement of the substituted ethers and the ease with which the same nuclei would react in typical aromatic substitution reactions. As pointed out previously, this may be because unnecessarily high temperatures were used in effecting rearrangements.

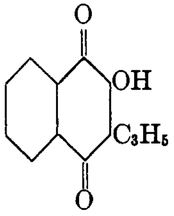
The allyl ethers of the isomeric hydroxynaphthoquinones (XII and XIII) rearrange to give the same compound (XIV) at relatively low temperatures, XII in 10 min. at 135°C. and XIII in a half-hour at 135–145°C. (35). The rapid reaction is probably connected with the fact that the allyl groups are attached to non-aromatic rings.



XII



XIII

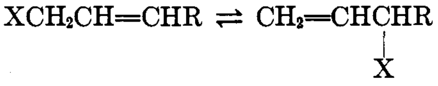


XIV

3. Rearrangement of ethers with substituted allyl groups; the anomalous rearrangement

Allyl ethers with substituents in the allyl group have been investigated in some detail, especially ethers of the types $ArOCH_2CH{=}CHR$ and $ArOCH(R)CH{=}CH_2$, where Ar is some aryl group and R is either alkyl or phenyl.

Work on ethers of this type is complicated by the fact that the halides necessary to prepare them are difficult to obtain pure, because of the ease with which the allylic rearrangement takes place:

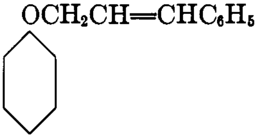


$$XCH_2CH{=}CHR \rightleftharpoons CH_2{=}CH\underset{\substack{|\\ X}}{C}HR$$

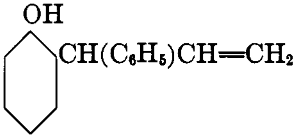
I II

The mobility of this equilibrium was demonstrated first by Winstein and Young (111) for the butenyl bromides (R equals CH_3), and the study was extended by Young and coworkers (112) to the pentenyl, hexenyl, and heptenyl bromides. Probably the alkenyl chlorides do not isomerize as readily as the bromides, but Young's work has demonstrated the necessity of careful proof of structure of compounds derived from halides of the type of I and II, since derivatives of both forms are usually present. Work done on allyl ethers of this type before this fact was realized is therefore open to question.

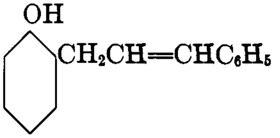
The cinnamyl ethers $ArOCH_2CH{=}CHC_6H_5$ are not open to this objection, since cinnamyl alcohol, $C_6H_5CH{=}CHCH_2OH$, gives only the corresponding bromide, without allylic rearrangement (87). Using cinnamyl phenyl ether (III), Claisen and Tietze (29) first showed that rearrangement to the ortho-position was accompanied by inversion, because the product was different from the product obtained by direct *C*-cinnamylation of phenol. Barring an improbable allylic shift, the latter was *o*-cinnamylphenol (V) and the rearrangement product was IV, which means that the migrating group was attached to the ring by the γ-carbon atom. That IV is actually the sole product of the rearrangement of cinnamyl phenyl ether was proved later by Hurd and Schmerling (59), who ozonized the rearrangement product and showed the presence of formaldehyde and the absence of benzaldehyde.



III
Cinnamyl phenyl ether

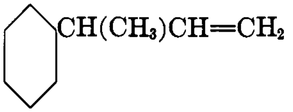


IV



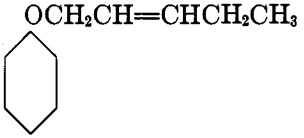
V
o-Cinnamylphenol

Claisen and Tietze (30) showed by the same method that γ-methylallyl phenyl ether, $C_6H_5OCH_2CH{=}CHCH_3$, gave inversion on rearrangement; their crotyl bromide (I; R equals CH_3) evidently contained about 15 per cent of its allylic isomer (111), but that the rearrangement product was principally 2-(α-methylallyl)phenol (VI) was established by Lauer and coworkers (76, 72).

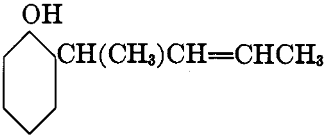


VI
2-(α-Methylallyl)phenol

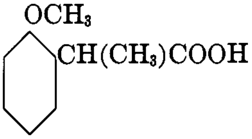
Rearrangement of many substituted allyl ethers has shown that in no case in rearrangement to the ortho-position is the substituted allyl group attached to the nucleus after rearrangement by the same carbon which was attached to the oxygen (*cf.* footnote, page 534); usually the attachment is by the γ-carbon atom (inversion), as shown by Claisen. The first example of anomalous rearrangement—attachment by other than the γ-carbon atom—was observed by Lauer and Filbert (71), who showed that rearrangement of γ-ethylallyl phenyl ether (VII) gave 2-(α,γ-dimethylallyl)phenol (VIII), whose structure was proved by ozonization to acetaldehyde and synthesis of the degradation product X (72). The formation of VIII shows that the allyl group is attached by the δ(or β)-carbon atom rather than the γ-carbon atom. When the allylic isomer of VII, α-ethylallyl phenyl ether (XI), was studied, the sole product obtained was 2-(γ-ethylallyl)phenol (XII), whose structure was proved by ozonization to propionaldehyde.



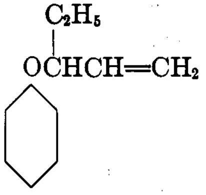
VII
γ-Ethylallyl phenyl ether



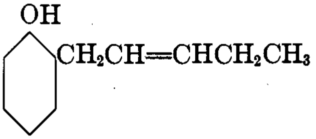
VIII
2-(α, γ-Dimethylallyl)phenol



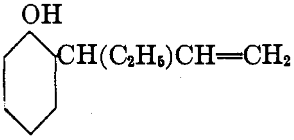
X



XI
α-Ethylallyl phenyl ether



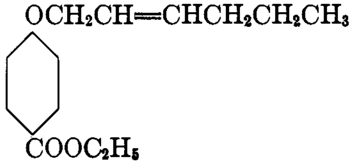
XII
2-(γ-Ethylallyl)phenol



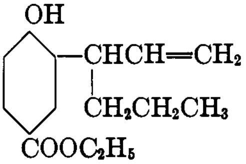
XIII
2-(α-Ethylallyl)phenol

This work was confirmed and extended by Hurd and Pollack (57), who showed that γ-ethylallyl phenyl ether (VII) yielded the normal product 2-(α-ethylallyl)phenol (XIII) in addition to the anomalous product VIII. From a mixture of 90 per cent of VII and 10 per cent of its allylic isomer (XI), they obtained 56 per cent of the normal product (XIII) and 42 per cent of the anomalous product (VIII).

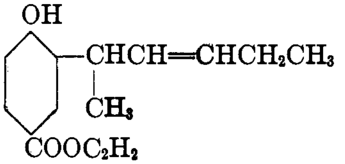
The question has been carefully investigated by Lauer and coworkers in recent papers (75, 77), using substituted allyl ethers of ethyl 4-hydroxybenzoate; this series is particularly well suited for such studies, because the 4-allyloxybenzoic acids are solids and the purity of the allylic isomers, such as XIV and XVII, can be assured by crystallization. Rearrangement of the γ-propylallyl ether (XIV) yielded the normal product (XV) and the anomalous product (XVI), the latter predominating by a ratio of two to one; the α-propylallyl ether (XVII) gave only the normal product (XVIII). The α-ethylallyl and γ-ethylallyl ethers in this series gave results similar to these (77); the former gave only the normal product and the latter gave both the normal and the anomalous products.



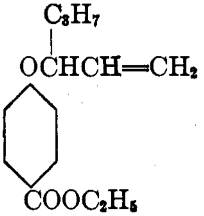
XIV



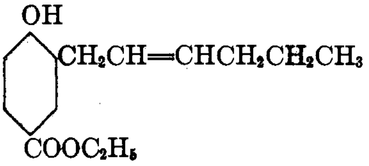
XV



XVI

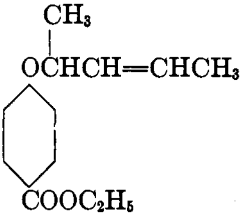


XVII

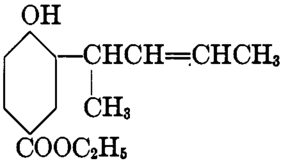


XVIII

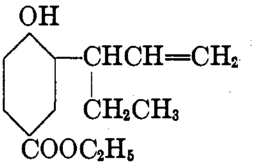
It is noteworthy that in the three cases investigated only the γ-substituted allyl ethers give the anomalous product, which in the ethyl series is formed by attachment through the δ(or β)-carbon, and in the propyl series by attachment through the ϵ(or β)-carbon. The α-substituted allyl ethers, however, give only the normal product. The only exception to this is α,γ-dimethylallyl 4-carbethoxyphenyl ether (XIX), which yields



XIX
α, γ-Dimethylallyl
4-carbethoxyphenyl ether



XX



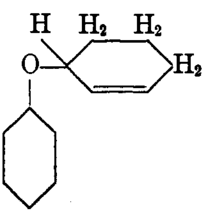
XXI

$CH_2{=}CHCH{=}CHCH_3$

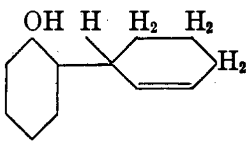
XXII
1, 3-Pentadiene

the expected product XX, but a few per cent of XXI is also formed, because formaldehyde is found in the ozonization product. The main product is 1,3-pentadiene (XXII), formed in 59 per cent yield by a cleavage of the carbon–oxygen link during rearrangement (77).

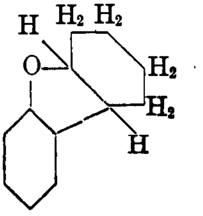
This cleavage of allyl ethers, with formation of a diene and a phenol, has been observed frequently (58, 54, 59, 50), and the tendency evidently increases with increasing substitution on the allyl group. Cornforth, Hughes, and Lions (32) found that cyclohexenyl phenyl ether on heating gave phenol and cyclohexadiene in 50 to 60 per cent yield, with 5 per cent of the rearrangement product XXIV and 15 per cent of hexahydrodibenzofuran formed from XXIV by ring closure. It would be of considerable interest to know if this reaction goes with inversion.



XXIII
Cyclohexenyl phenyl
ether

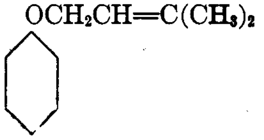


XXIV



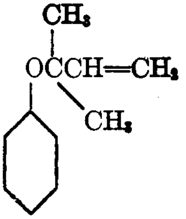
XXV
Hexahydrodibenzofuran

Claisen reported (24, 30), without giving experimental details, that γ,γ-dimethylallyl phenyl ether (XXVI) on pyrolysis gave phenol and isoprene, but that when heated with sodium carbonate it gave rearrangement. The structure of the ether was shown by reduction to isoamyl phenyl ether, and statements in the literature (48, 50) attributing a study of α,α-dimethylallyl phenyl ether (XXVII) to Claisen in this connection are erroneous. A more highly substituted allyl ether, $\alpha,\alpha,\gamma,\gamma$-tetramethylallyl phenyl ether (XXVIII), was shown by Hurd and Cohen (50) to give only the cleavage reaction, 33 per cent of hexadiene being obtained after 1 hr. at 160–170°C.



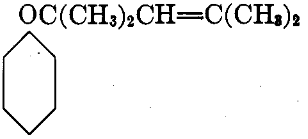
XXVI

γ, γ-Dimethylallyl phenyl ether



XXVII

α, α-Dimethylallyl phenyl ether



XXVIII

α, α, γ, γ-Tetramethylallyl phenyl ether

The small amount of information available indicates that introduction of alkyl groups in the α- or γ-position of the allyl group increases the rate of rearrangement. Smith and coworkers (102) found that α-ethyl-γ-methylallyl phenyl ether rearranged to the extent of 9.6 per cent in 24 hr. at 120°C. Fom this it seems likely that better yields would be obtained in general, if rearrangements were carried out at temperatures well below 200°C.

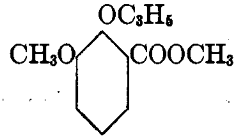
The β-methylallyl ethers are readily prepared from β-methylallyl chloride and phenols by standard methods (10, 97), but they present few points of interest. It has been found that β-methylallyl 4-methylphenyl ether rearranges at practically the same rate as the unsubstituted allyl 4-methylphenyl ether (69), and that the β-methyl group does not have the same complicating effect on the reaction as the α- or γ-methyl group.

Allyl aryl ethers with halogens in the allyl group rearrange very poorly; v. Braun, Kuhn, and Weismantel (18) found that β-bromoallyl phenyl ether gave 30 per cent of its rearrangement product, $2\text{-}HOC_6H_4CH_2CBr{=}CH_2$, after heating in decalin at 215°C. for 1.5 hr. Fifty per cent was recovered unchanged and 20 per cent decomposed. Hurd and Webb (62) could not repeat this result, obtaining only intractable phenolic resins. They did obtain 24 per cent of the rearrangement product from the corresponding chloro compound after heating for 2 hr. at 216–223°C. From the γ-halogen ethers, such as $C_6H_5OCH_2CH{=}CHCl$, Hurd and Webb got no rearrangement product, but only decomposition and formation of phenol.

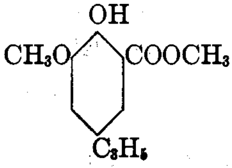
D. REARRANGEMENT OF ALLYL ARYL ETHERS TO THE PARA-POSITION

If both ortho-positions of an allyl aryl ether are blocked, the allyl group migrates to the para-position on heating in the usual manner (25, *passim*). The number of examples of this type of reaction is not large (table 3), but the rearrangement gives as good yields and goes as readily as the rearrangement to the ortho-position. Most of the compounds studied are derivatives of salicylic acid, with the other position ortho to the hydroxyl group occupied either by a methyl group (*o*-cresotic acid) or by a methoxyl group, but a few examples have two alkyl groups or two hydroxyl groups in the ortho-positions.

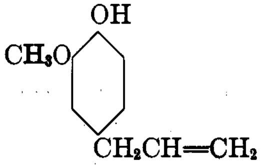
As an example of the facility of para rearrangement may be quoted the case of allyl 2-carbomethoxy-6-methoxyphenyl ether (I), which gave the rearrangement product II in almost quantitative yield on refluxing under diminished pressure for 45 min. (b.p. 201–212°C.) (21, page 118). The product was easily transformed, by hydrolysis and decarboxylation, into eugenol (III).



I
Allyl 2-carbomethoxy-6-methoxyphenyl ether

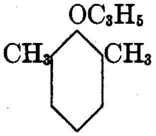


II

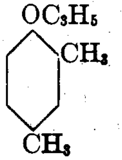


III
Eugenol

From the only pair which has been investigated quantitatively (107, 69), allyl 2,6-dimethylphenyl ether (IV) and allyl 2,4-dimethylphenyl



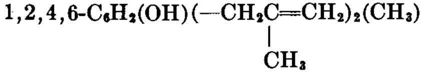
IV
Allyl 2,6-dimethylphenyl ether



V
Allyl 2,4-dimethylphenyl ether

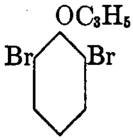
TABLE 3

Rearrangement to the para-position

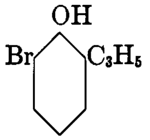
COMPOUND	PRODUCT	REFERENCES
1. Ethers with unsubstituted allyl groups; R equals $—CH_2CH{=}CH_2$. See also the section on rearrangement with displacement in table 2		
2,6-Dibromophenyl	1,2,6-$C_6H_3(OH)(R)(Br)$ 1,2,4,6-$C_6H_2(OH)(Br)(R)(Br)$	(62, 95)
2-Bromo-6-methylphenyl	1,2,6-$C_6H_3(OH)(Br)(CH_3)$ 1,2,4,6-$C_6H_2(OH)(Br)(R)(CH_3)$	(62)
2,6-Dimethylphenyl	1,2,4,6-$C_6H_2(OH)(CH_3)(R)(CH_3)$	(107)
2,6-Diallylphenyl	1,2,4,6-$C_6H_2(OH)(R)_3$	(21, p. 96)
2-Allyl-6-methoxyphenyl	1,2,4,6-$C_6H_2(OH)(R)_2(OCH_3)$	(25, p. 55)
2-Allyloxy-3,6-diallylphenyl	1,2,3,4,5,6-$C_6(OH)_2(R)_4$	(52)
2-Hydroxy-6-methoxyphenyl (?)	1,2,4,6-$C_6H_2(OH)_2(R)(OCH_3)$	(108)
2,6-Dimethoxyphenyl	1,2,4,6-$C_6H_2(OH)(OCH_3)(R)(OCH_3)$	(83, 44)
2,3-Dimethoxy-6-hydroxyphenyl	1,2,3,4,6-$C_6H_1(OH)(OCH_3)_2(R)(OH)$	(4)
2-Carbomethoxy-6-methylphenyl	1,2,4,6-$C_6H_2(OH)(COOCH_3)(R)(CH_3)$	(25, p. 83)
2-Carbomethoxy-6-allylphenyl	1,2,4,6-$C_6H_2(OH)(COOCH_3)(R)_2$	(25, p. 77)
2-Carbomethoxy-6-methoxyphenyl	1,2,4,6-$C_6H_2(OH)(COOCH_3)(R)(OCH_3)$	(21, p. 118)
2. Ethers with substituted allyl groups		
α-Ethylallyl 2-carbomethoxy-6-methylphenyl	1,2,4,6-$C_6H_2(OH)(COOCH_3)(—CH_2CH{=}CHC_2H_5)(CH_3)$	(89)
β-Methylallyl 2-(β-methylallyl)-6-methylphenyl	 1,2,4,6-$C_6H_2(OH)(—CH_2\underset{\underset{CH_3}{\mid}}{C}{=}CH_2)_2(CH_3)$	(10)
Cinnamyl 2-carbomethoxy-6-methylphenyl	1,2,4,6-$C_6H_2(OH)(COOCH_3)(—CH_2CH{=}CHC_6H_5)(CH_3)$	(90)
γ-Methylallyl 2-carbomethoxy-6-methylphenyl	1,2,4,6-$C_6H_2(OH)(COOCH_3)(—CH_2CH{=}CHCH_3)(CH_3)$	(90)
γ-Ethylallyl 2-carbomethoxy-6-methylphenyl	1,2,4,6-$C_6H_2(OH)(COOCH_3)(—CH_2CH{=}CHC_2H_5)(CH_3)$	(89)
γ,γ-Dimethylallyl 2-methoxyphenyl	1,2,4-$C_6H_3(OH)(OCH_3)(—CH_2CH{=}C(CH_3)_2)$	(105)
Imperatorin	Alloimperatorin (see p. 527 for formulas)	(103, 104)
3. Rearrangements involving displacement		
2,6-Diallyl-4-aldehydophenyl	1,2,4,6-$C_6H_2(OH)(R)_3$ and CO	(25, p. 108)
2-Methoxy-4-aldehydo-6-allylphenyl	1,2,4,6-$C_6H_2(OH)(R)_2(OCH_3)$ and CO	(25, p. 118)
2,6-Diallyl-4-carboxyphenyl	1,2,4,6-$C_6H_2(OH)(R)_3$ and CO_2	(25, p. 91)
2,6-Dimethoxy-4-carbomethoxyphenyl	1,2,4,6-$C_6H_2(OH)(OCH_3)(R)(OCH_3)$ and CO_2	(44)

ether (V), it can be concluded that rearrangement to the para-position is not greatly different in rate from that to the ortho-position. The rearrangement of IV actually takes place a little more rapidly (about three and a half times) than rearrangement of V, and the rearrangement product from IV can be isolated in yields exceeding 90 per cent after heating for 7 hr. in sealed tubes at 172°C.

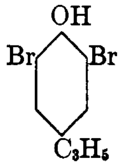
Rearrangement to the para-position goes poorly with two allyl groups or with bromine atoms in the ortho-positions; allyl 2,6-diallylphenyl ether gives a 50 per cent yield of 2,4,6-triallylphenol on refluxing with diethylaniline at 225–248°C. for a half-hour (21, page 96). Allyl 2,6-dibromophenyl ether (VI) was found by Hurd and Webb (62; *cf.* 95) to give a mixture of phenols (VII and VIII), the latter the expected product and the former a result of a displacement of the bromine by the allyl group. Allyl 2-bromo-6-methylphenyl ether also gives a poor yield of rearrangement product.



VI
Allyl 2,6-dibromophenyl ether

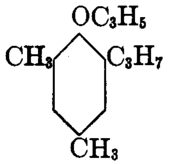


VII

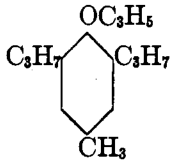


VIII

If both of the ortho-positions and the para-position of an allyl phenyl ether are blocked by groups other than carboxyl or aldehyde, a complex decomposition reaction occurs on heating, but there is no migration of the allyl group to the meta-position. The carboxyl or aldehyde group if present is eliminated as carbon monoxide or carbon dioxide (section E), but with ester groups instead of free carboxyl, complete decomposition results (25, pages 79, 90). Thus Claisen and Tietze (28) found that allyl 2-propyl-4,6-dimethylphenyl ether (IX) yielded, on heating at 200–250°C.



IX
Allyl 2-propyl-4,6-dimethylphenyl ether



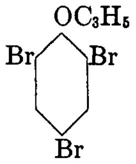
X

$(CH_2{=}CHCH_2)_2$

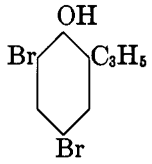
XI
Diallyl

for 15 min., some of the corresponding phenol, a gas (thought to be allene), and diallyl (XI). Recent work by Hurd and Yarnall (64) on an analogous compound (X) confirmed the formation of the phenol and diallyl, but showed that the gas evolved was propene.

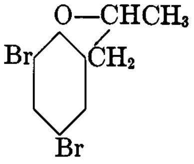
Hurd and Webb (62) obtained a mixture of phenolic and neutral products from allyl 2,4-dibromo-6-methylphenyl ether; allyl 2,4,6-tribromophenyl ether (XII) gave a 68 per cent yield of the *o*-allylphenol (XIII) and a small amount of the corresponding dihydrobenzofuran (XIV).



XII
Allyl 2,4,6-tribromophenyl ether

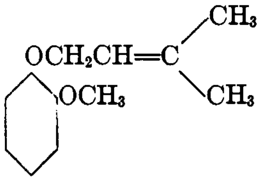


XIII

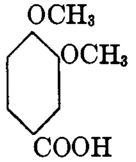


XIV

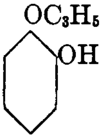
A few exceptional cases are known in which there is some migration of the allyl group to the para-position when there is also an open ortho-position. The first instance was found by Staudinger, Kreis, and Schilt (105), who rearranged γ,γ-dimethylallyl 2-methoxyphenyl ether (XV) and obtained, on methylation and oxidation, a small amount of veratric acid (XVI), showing that at least part of the product was the result of para rearrangement. Kawai (65) found that allyl 2-hydroxyphenyl ether (XVII) at 180–190°C. gave a mixture of products resulting from ortho and para rearrangement, whose structure was proved by methylation and



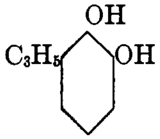
XV
γ,γ-Dimethylallyl 2-methoxyphenyl ether



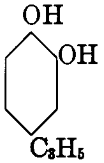
XVI
Veratric acid



XVII
Allyl 2-hydroxyphenyl ether

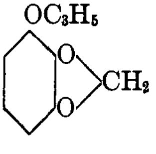


XVIII

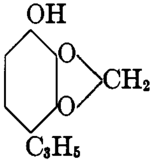


XIX

oxidation to the corresponding dimethoxybenzoic acids; the 1,2,4-compound (XIX) is regarded as a product of para rearrangement rather than meta, since the latter has never been observed. Perkin and Trikojus (93) showed that XVIII and XIX are formed in the ratio of five to four. Baker, Penfold, and Simonsen (7) have reported recently that allyl 2,3-methylenedioxyphenyl ether (XX) gives a mixture containing about 20 per cent of the para-isomer (XXI), whose structure was proved by methylation and oxidation to the substituted benzoic acid. It is noteworthy that each of these compounds giving the para and ortho rearrangement simultaneously is a polyhydroxy compound; perhaps the greater reactivity of the aromatic nucleus is the cause of the para migration. Other instances in which the migrating group goes to the para-position instead of displacing a carboxyl or aldehyde group from the ortho-position are discussed in section E.

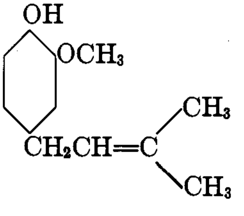


XX
Allyl 2,3-methylenedioxyphenyl ether

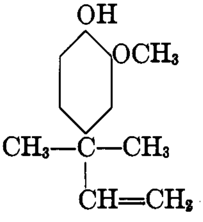


XXI

Some information on the question of inversion of a substituted allyl group on migration to the para-position can be obtained from Staudinger's work, quoted above. The rearrangement product of XV must have been the one formed without inversion (XXII); the isomeric compound (XXIII) would not yield veratric acid (XVI) on methylation and oxidation, since, as Smith and Prichard have shown (100), side chains such as the one in XXIII cannot be oxidized to carboxyl groups by permanganate. The possibility is not excluded that the product was a mixture of XXII and XXIII, but the positive evidence shows that XXII was present.

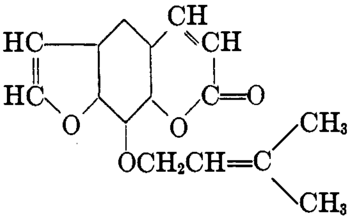


XXII

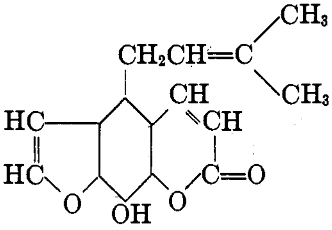


XXIII

More clear-cut evidence on this point was furnished by Späth (104, 103), by showing that imperatorin (XXIV) was changed in 90 per cent

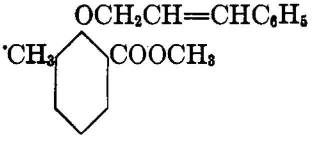


XXIV
Imperatorin

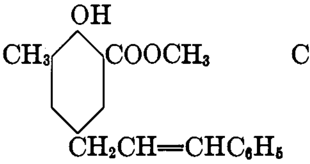


XXV
Alloimperatorin

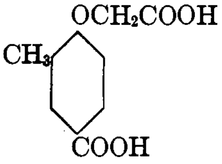
yield on heating for a few minutes at 200°C. to alloimperatorin (XXV); both substances yielded acetone on oxidation with chromic acid, and therefore contained the γ,γ-dimethylallyl group, which had rearranged without inversion. Mumm and Möller (90) observed that rearrangement of cinnamyl 2-carbomethoxy-6-methylphenyl ether (XXVI) also took place without inversion; proof that the rearrangement product had the



XXVI
Cinnamyl 2-carbomethoxy-6-methylphenyl ether



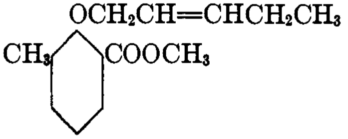
XXVII



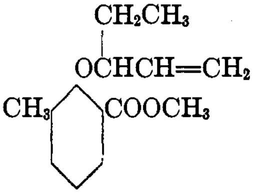
XXVIII

structure XXVII was obtained by removal of the ester group by hydrolysis and decarboxylation, and oxidation of the resulting phenol as the aryloxyacetic acid derivative. The products were 3-methyl-4-hydroxybenzoic acid, as the aryloxyacetic acid derivative (XXVIII), and benzoic acid, showing that there was a cinnamyl side chain in XXVII. A similar result was obtained with the γ-methylallyl ether of the same phenol; rearrangement was not accompanied by inversion.

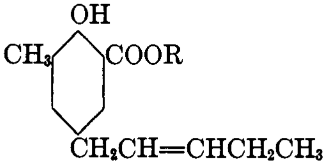
Mumm and coworkers (89) studied a pair of isomeric ethers, γ-ethylallyl 2-carbomethoxy-6-methylphenyl ether (XXIX) and the corresponding α-ethylallyl ether (XXX). It is probable that each of the ethers contained an appreciable amount of the other, because of the difficulty of obtaining



XXIX
γ-Ethylallyl 2-carbomethoxy-
6-methylphenyl ether

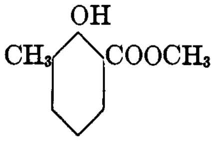


XXX
α-Ethylallyl 2-carbomethoxy-
6-methylphenyl ether

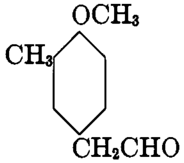


XXXI

the isomeric 1-chloro-2-pentene and 3-chloro-1-pentene pure (57, 77), but the two ethers differed enough in their chemical behavior to show that they were actually different compounds. Both on heating in diethylaniline gave the same product XXXI (R equals CH_3), together with appreciable amounts of *o*-cresotic ester (XXXII), the identity of the two samples of rearrangement product obtained being proved by a mixed melting point of the acid (XXXI; R equals H) obtained from them by hydrolysis.



XXXII
Methyl *o*-cresotate



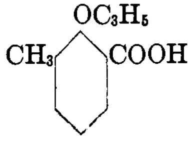
XXXIII

The α-ethylallyl ether (XXX) rearranged during hydrolysis with alcoholic alkali to XXXI (R equals H), but the isomeric ether (XXXIX) did not rearrange under the same conditions; both ethers were cleaved to *o*-cresotic ester by one mole of hydrogen with palladium catalyst.

The structure of the rearrangement product (XXXI) was proved by decarboxylation, methylation, and ozonization to the aldehyde XXXIII, which was analyzed as the semicarbazone. From this work it appears that inversion takes place in the para rearrangement when an α-substituted allyl ether is rearranged, and that there is no evidence for the anomalous rearrangement in the para series. The difference in ease of rearrangement of the two ethers is striking; the α-substituted ether rearranges on standing for some time, as well as in alcoholic alkali,—conditions under which the γ-substituted ether is unaffected.

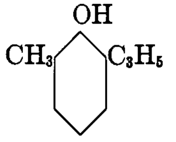
E. REARRANGEMENT OF ALLYL ARYL ETHERS INVOLVING THE DISPLACEMENT OF CARBOXYL AND ALDEHYDE GROUPS

One aspect of the rearrangement which has not been studied since Claisen's pioneer work is the reaction in which a carboxyl or aldehyde group in the ortho- or para-position is displaced from the molecule by the migrating allyl group. The allyl ether of *o*-cresotic acid (I) is an example; it starts to evolve carbon dioxide at 100°C., and gives a mixture of 80 per cent of the displacement product (II) and 20 per cent of the para-product (III) (25, page 83). If the para-position is blocked, the reaction gives practically quantitative yields; with the allyl ether of diallylsalicylic acid (IV) (25, page 79) evolution of carbon dioxide starts at 100°C. and a quantitative yield of 2,4,6-triallylphenol is obtained. The reaction goes just as well with the dichloro compound corresponding to IV.

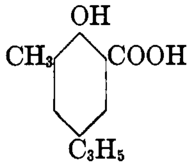


I

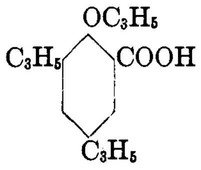
Allyl ether of *o*-cresotic acid



II

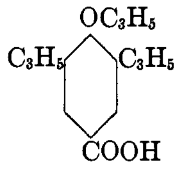


III

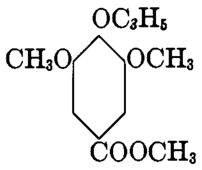


IV

Allyl ether of diallylsalicylic acid



V



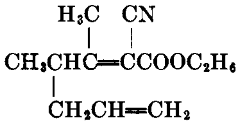
VI

Allyl 2,6-dimethoxy-4-carbomethoxyphenyl ether

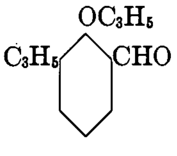
A carboxyl group in the para-position is eliminated with equal facility. Compound V (25, page 90) evolves 99 per cent of the theoretical amount of carbon dioxide, the evolution starting at 150°C. A particularly interesting example is allyl 2,6-dimethoxy-4-carbomethoxyphenyl ether (VI) (44), which is hydrolyzed and rearranged with loss of the carboxyl group by refluxing with aqueous alkali for 10 hr.; the product, 2,6-dimethoxy-4-allylphenol, is obtained in 95 per cent yield.

TABLE 4

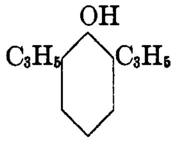
Rearrangement involving elements other than carbon and oxygen

SUBSTANCE	PRODUCT	REFERENCES
Allyl *N*-phenylbenzimino ether	*N*-Allylbenzanilide	(90)
α-Methylallyl *N*-phenylbenzimino ether	*N*-(γ-Methylallyl)benzanilide	(90)
γ-Methylallyl *N*-phenylbenzimino ether	*N*-(α-Methylallyl)benzanilide	(90)
2-Allyloxyquinoline	*N*-Allyl-2-quinolone	(109)
2,6-Diallyloxy-7-methylpurine	1,3-Diallyl-7-methylxanthine	(16)
2,6-Di-(α,γ-ethylmethylallyloxy)-7-methylpurine	1,3-Di-(α,γ-methylethylallyl)-7-methylxanthine	(16)
Allyl phenyl sulfide	1,2-$C_6H_4(SH)(CH_2CH{=}CH_2)$	(51)
Allyl 4-methylphenyl sulfide	1,2,4-$C_6H_3(SH)(CH_2CH{=}CH_2)(CH_3)$	(51)
Allyl thiocyanate	Allyl isothiocyanate	(17)
Cinnamyl thiocyanate	Cinnamyl isothiocyanate	(12)
γ-Methylallyl thiocyanate	α-Methylallyl isothiocyanate	(90a)
α-Ethylallyl thiocyanate	γ-Ethylallyl isothiocyanate (?)	(90a)
γ-Ethylallyl thiocyanate	α-Ethylallyl isothiocyanate (?)	(90a)
Ethyl (1-methylpropenyl)allylcyanoacetate	 $\underset{CH_2CH{=}CH_2}{CH_3CH}\overset{H_3C}{C}{=}\overset{CN}{C}COOC_2H_5$	(31)

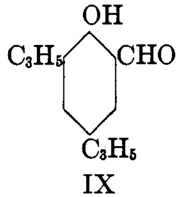
The displacement reaction with aldehyde derivatives is entirely analogous, although a slightly higher temperature seems to be necessary to evolve carbon monoxide. The allyl ether of allylsalicylaldehyde (VII) starts to give off carbon monoxide at 180°C. and gives 72 per cent of the theoretical amount, yielding a mixture of the displacement product (VIII) and the para product (IX) in the ratio of three to one (25, page 102).



VII
Allyl ether of
allylsalicylaldehyde

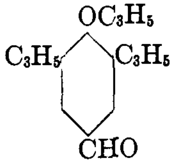


VIII



IX

The allyl ether of 3,5-diallyl-4-hydroxybenzaldehyde (X) starts to lose carbon monoxide at 170°C., giving 74 per cent of the theoretical amount,

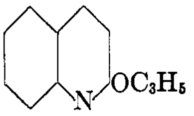


X
Allyl ether of 3,5-diallyl-4-hydroxybenzaldehyde

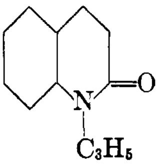
and gives a 51 per cent yield of 2,4,6-triallylphenol (25, page 108).

F. REARRANGEMENT OF COMPOUNDS STRUCTURALLY ANALOGOUS TO THE ALLYL ARYL ETHERS

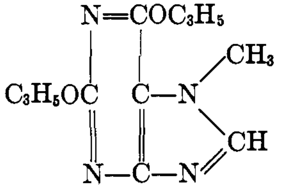
Several classes of allyl ethers are known in which the grouping C=C—C—O—C=N is involved. The first example was reported by Tschitschibabin and Jeletzsky (109), who found that 2-allyloxyquinoline (I) rearranged to *N*-allyl-2-quinolone (II) on distillation at 325°C. Bergmann and Heimhold (16) reported a similar migration from oxygen to nitrogen with 2,6-allyloxy-7-methylpurine (III), and, from a study of the α-methyl-γ-ethylallyl derivative, concluded that rearrangement was accompanied by inversion.



I
2-Allyloxyquinoline

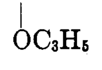


II
N-Allyl-2-quinolone



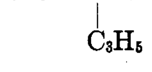
III
2,6-Allyloxy-7-methylpurine

Mumm and Möller (90) showed that allyl *N*-phenylbenzimino ether (IV) rearranged quantitatively in 3 hr. at 210–215°C. to *N*-allylbenzanilide (V). Rearrangement of the γ-methyl-substituted ether (VI) gave inversion,



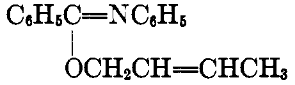
$$\underset{\displaystyle OC_3H_5}{C_6H_5C{=}NC_6H_5}$$

IV
Allyl *N*-phenylbenzimino ether



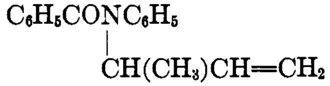
$$\underset{\displaystyle C_3H_5}{C_6H_5CONC_6N_5}$$

V
N-Allylbenzanilide



$$\begin{array}{l}C_6H_5C{=}NC_6H_5\\ \quad|\\ \quad OCH_2CH{=}CHCH_3\end{array}$$

VI



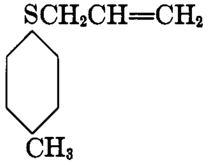
$$\begin{array}{l}C_6H_5CONC_6H_5\\ \qquad\quad|\\ \qquad\quad CH(CH_3)CH{=}CH_2\end{array}$$

VII

N-(α-Methylallyl)benzanilide

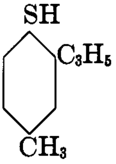
yielding *N*-(α-methylallyl)benzanilide (VII), whose structure was proved by catalytic hydrogenation and hydrolysis to *sec*-butylaniline. The α-methylallyl ether, isomeric with VI, also gave inversion, yielding *N*-(γ-methylallyl)benzanilide. The system C=C—C—O—C=N is thus similar to that in the allyl aryl ethers in its behavior.

Hurd and Greengard (51) have shown that allyl phenyl sulfides, containing the system C=C—C—S—C=C, give a rearrangement similar to that of their oxygen analogs, although it goes much more slowly. Thus, allyl 4-methylphenyl sulfide (VIII) on refluxing for 4 hr. at 228-264°C. gives a 27 per cent yield of the rearrangement product IX, and 45 per cent



VIII

Allyl 4-methylphenyl sulfide

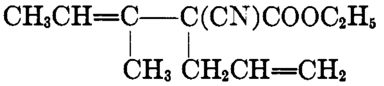


IX

of the starting material is recovered unchanged. The analogous oxygen ether rearranges much more rapidly (*cf.* page 15).

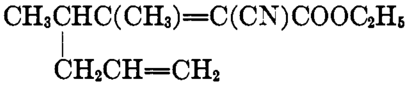
The system C=C—C—S—C≡N is contained in allyl thiocyanate, which, as is well known, rearranges very rapidly on distillation to allyl isothiocyanate, $CH_2{=}CHCH_2NCS$ (17). Even methyl thiocyanate, CH_3SCN, reacts similarly on heating at 180°C. (47), so that the system R—S—C≡N is very much more mobile than R—O—C=C. Bergmann (12) has shown that in the rearrangement of cinnamyl thiocyanate, $C_6H_5CH{=}CHCH_2SCN$, there is no inversion, the product being $C_6H_5CH{=}CHCH_2NCS$. Mumm and Richter (90a) have found, however, that γ-methylallyl thiocyanate, $CH_3CH{=}CHCH_2SCN$, rearranges with inversion to give α-methylallyl isothiocyanate, $CH_2{=}CHCH(CH_3)NCS$.

A very interesting rearrangement involving the carbon system $C{=}C{-}C{-}\overset{*}{C}{-}C{=}C$ (the carbon corresponding to the ether oxygen is starred) has been reported recently by Cope and Hardy (31). Ethyl (1-methylpropenyl)allylcyanoacetate (X), when heated for 4 hr. at 150–160°C. or for 20 min. at 260°C., rearranged completely to XI, the



$$CH_3CH{=}\underset{CH_3}{C}{-}\underset{CH_2CH{=}CH_2}{C}(CN)COOC_2H_5$$

X
Ethyl (1-methylpropenyl)-
allylcyanoacetate



$$CH_3\underset{CH_2CH{=}CH_2}{C}HC(CH_3){=}C(CN)COOC_2H_5$$

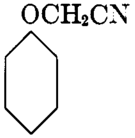
XI

reaction involving a shift of the allyl group to the γ-carbon in the chain, and a shift of the double bond to a position of conjugation with the cyano and carbethoxyl groups. The esters with saturated alkyl groups instead of the allyl group do not rearrange.

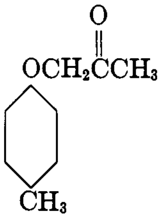
In all of the other rearrangements of the Claisen type, the key atom is either oxygen or sulfur, which have unshared pairs of electrons to participate in or initiate electronic shifts; in this case the carbon has no unshared pairs and the rearrangement must be ascribed to the tendency of X to go into the much more stable conjugated form (XI).

The allylanilines, which contain the system C═C—C—N—C═C, have been studied by Carnahan and Hurd (20). *N*-Allylaniline gives a small amount of aniline when heated at 275°C. for 12 hr., and at higher temperatures propene is evolved; *N*,*N*-diallylaniline gives propene, aniline, and *N*-allylaniline. *N*-Allylacetanilide and *N*-allyltosylanilide give only complex decomposition products.

The grouping N≡C—C—O—C═C is present in phenoxyacetonitrile (XII), but the compound is stable toward long refluxing; the corresponding derivative of *p*-cresol is less stable but no rearrangement product is isolated (94). *p*-Cresoxyacetone, which contains the system O═C—C—O—C═C, gives no rearrangement product on refluxing (106).



XII
Phenoxyacetonitrile



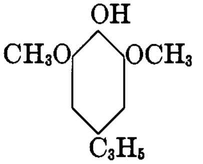
XIII

From the foregoing work and from section A it appears that the system present in the allyl ethers, C═C—C—O—C═C, can be altered by substitution of certain other elements in the —O—C═C part, but that any change in the skeleton of the allyl part, either by substitution of other elements or by changing the position of the double bond, makes rearrangement impossible.

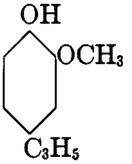
III. Applications of the Claisen Rearrangement

A. APPLICATIONS IN SYNTHETIC WORK

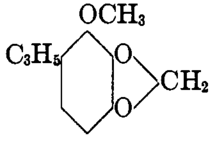
The Claisen rearrangement is a useful reaction in synthetic work, because it provides an easy way of introducing allyl groups into a wide variety of phenolic compounds. Many naturally occurring allylphenols have been synthesized by this method, such as elemicin (I) (83, 44), eugenol (II) (21, page 118), croweacin (III) (7), and dill apiole (IV) (4). Fieser, Campbell, and Fry have used the Claisen rearrangement recently (37) to obtain diallylnaphthoquinones as model substances for vitamin K studies. The substituted allyl side chains occurring in natural compounds, such as farnesyl and phytyl, cannot be introduced by the Claisen rearrangement, because inversion gives a branched chain.[1]



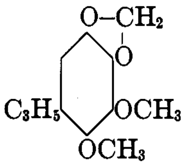
I
Elemicin



II
Eugenol



III
Croweacin



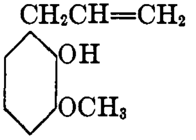
IV
Dill apiole

The allylphenols are also useful as intermediates, since they can be transformed into several other classes of compounds. The allyl side chain can, of course, be reduced catalytically, giving propylphenols; Bartz, Miller, and Adams (10) prepared a series of isobutylphenols for bactericidal tests by the rearrangement and reduction of substituted β-methylallyl phenyl ethers.

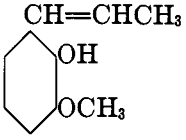
---

[1] Very recently Makino and Morii (111) have reported in a preliminary note that the difarnesyl ether of 1,4-naphthohydroquinone rearranges to give 2,3-difarnesyl-1,4-naphthohydroquinone (isolated as the diacetate). The structure of the rearrangement product was not proved, so that this work cannot be considered to conflict with the statement on page 518 that substituted allyl ethers after rearrangement are never attached by the same carbon which was attached to oxygen.

On heating with concentrated aqueous alkali, the allyl group in allylphenols is isomerized to a propenyl group; thus 2-methoxy-6-allylphenol (V) is isomerized to the propenyl compound (VI) by heating one part of V with two parts of powdered potassium hydroxide and one of water for 1 hr. at 170°C. (25, page 52). This isomerization of the allyl group never seems to take place under the conditions of the rearrangement of the allyl aryl ethers. Propenyl compounds are oxidized by mercuric acetate, and allyl compounds are not, hence this is a useful test reagent for distinguishing allyl- and propenyl-phenols (9); γ,γ-dialkylallyl compounds, however, are oxidized by it (24), so that it must be applied with caution in such cases.

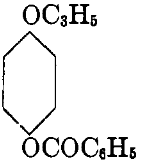


V
2-Methoxy-6-allylphenol

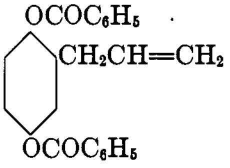


VI
2-Methoxy-6-propenylphenol

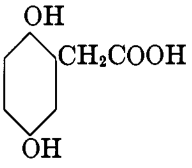
The allylphenols can be oxidized, and in certain cases this is a useful method of preparing substituted phenylacetaldehydes (44, 98, 85) or phenylacetic acids. For example, homogentisic acid (IX), otherwise obtained only with great difficulty, can be made from hydroquinone in 26 per cent yield by rearrangement of the benzoate of hydroquinone monoallyl ether (VII), followed by ozonolysis (as the dibenzoate, VIII) and hydrolysis to IX (43). The propenylphenols obtained by isomerization can also be ozonized to hydroxyaldehydes (67, 85), but these can usually be obtained more readily by other methods.



VII
Benzoate of hydroquinone allyl ether

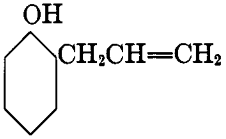


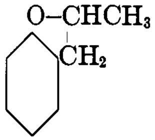
VIII

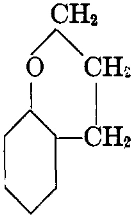


IX
Homogentisic acid

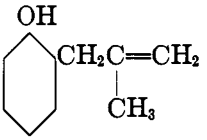
When heated with acid catalysts, such as pyridine hydrochloride (25, page 26), hydrobromic acid-acetic acid, or formic acid (30), *o*-allylphenols are isomerized to 2-methyldihydrobenzofurans (X → XI). By treating the acetate of the allylphenol with hydrogen bromide and a peroxide, the

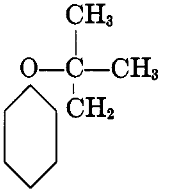

X
o-Allylphenol

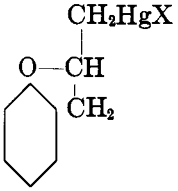

XI


XII

isomeric chroman (XII) can be obtained (53). The dihydrobenzofuran is frequently found as a by-product in the Claisen rearrangement and is evidently formed by isomerization of the *o*-allylphenol by heat (10); the tendency for ring closure is increased by alkyl groups on the double bond. Thus Bartz, Miller, and Adams (10) found that 2-(β-methylallyl)phenol (XIII) isomerized to the dihydrobenzofuran (XIV) on heating or even on standing with anhydrous magnesium sulfate in petroleum ether solution.


XIII
2-(β-Methylallyl)phenol


XIV

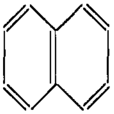

XV

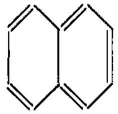
Treatment of *o*-allylphenols with mercuric salts gives derivatives of mercuridihydrobenzofurans of type XV (86). Bromination of *o*-allylphenols gives a mixture of bromomethyldihydrobenzofurans (1).

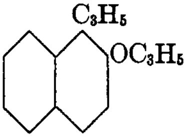
B. DETERMINATION OF BOND STRUCTURES IN AROMATIC COMPOUNDS

It is obvious (section A) that the ether oxygen of an allyl ether must be attached to a double bond for rearrangement to take place. This fact has been utilized by Fieser and coworkers to determine the bond structures of aromatic compounds.

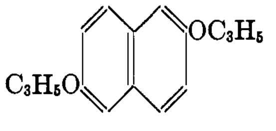
As an example naphthalene may be cited (38). Two Kekulé structures may be written for naphthalene and its derivatives, I and II; if it is possible to obtain reaction products derived from structure II, a substituted allyl


I

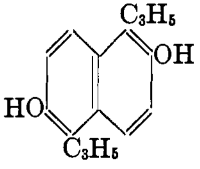

II


III

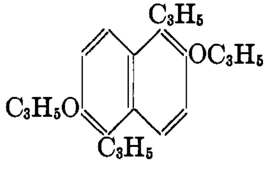
naphthyl ether such as III should rearrange by means of the 2,3-double bond, to give 1,3-diallyl-2-naphthol. Actually, as Claisen (23) showed, III is unchanged by long heating, and hence must be unable to react as structure II. Similarly, 2,6-diallyloxynaphthalene (IV) rearranges to V in 85 per cent yield on heating to 190°C. for a few minutes, but the diether (VI) from V does not rearrange in 5 min. at 200°C., and decomposes on longer heating, giving no alkali-soluble material (38). These facts indicate that naphthalene derivatives react as if they had double bonds in the 1,2- and 5,6-positions, and no double bonds in the 2,3- and 6,7-positions; the reactions show that the symmetrical formula (I) is satisfactory for expressing the chemical behavior of naphthalene compounds. This is usually expressed by saying that the double bonds are fixed.



IV
2,6-Diallyloxynaphthalene

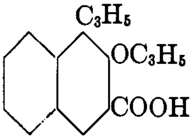


V



VI

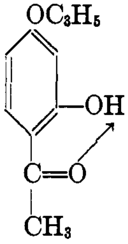
It would be interesting to see whether the compound VII would give the displacement reaction to form 1,3-diallyl-2-naphthol, since the displacement reaction goes at much lower temperatures than the ordinary rearrangement.



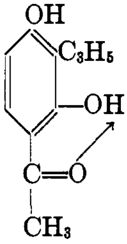
VII

Several aromatic hydrocarbons have been studied by the Claisen rearrangement to determine the bond structures, among them naphthalene (38, 13), anthracene (39), phenanthrene (40), hydrindene (79), fluorene (78), and other compounds, such as chromone (96), flavone (96), and fluorenone (14).

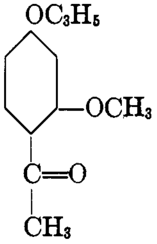
An interesting application of the Claisen rearrangement showing the effect of chelation on the fixation of bonds in benzene derivatives has been developed by Baker and Lothian (5,6). Several lines of evidence indicate that a chelate ring, such as that in VIII, contains a double bond; that this arrangement of the bonds actually determines the reactions of the compound is shown by the formation of IX in 85 per cent yield by rearranging VIII at 210°C. If instead of VIII, its methyl ether X, which cannot form



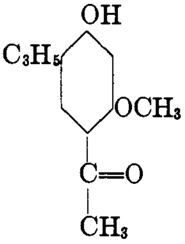
VIII



IX



X



XI

a chelate ring, is rearranged, the allyl group migrates to the other free ortho-position, giving XI. The latter is the usual position for substitution in resorcinol compounds, but the stability of the chelate ring in VIII is such that fixation of the double bonds occurs, and the tendency for formation of the symmetrical product XI is overcome.

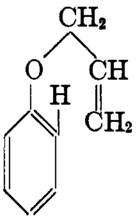
Similar reactions are observed with compounds analogous to VIII and IX, but having aldehyde and propionyl groups instead of acetyl groups.

IV. The Mechanism of the Rearrangement

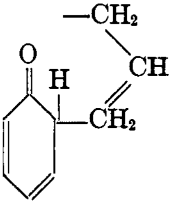
A. MECHANISM OF THE REARRANGEMENT TO THE ORTHO-POSITION

In addition to the facts mentioned so far, any mechanism for the rearrangement must be in harmony with the kinetics of the reaction. Kincaid and Tarbell (70), in a study of the rearrangement of allyl 4-methylphenyl ether, found that the reaction was strictly first order over a fivefold change of concentration in diphenyl ether solution, and that the initial rate in the pure liquid was the same as the rate in solution. The rate of reaction was not appreciably affected by adding 10 per cent of dimethylaniline or 1 per cent of acetic acid, and therefore the rearrangement does not go by a mechanism which requires catalysis by acids or bases. These results support the conclusion of Hurd and Schmerling (59), from experiments on mixtures, that the rearrangement is intramolecular.

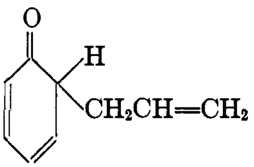
In the paper reporting the first instance of inversion, Claisen and Tietze (29) suggested the first mechanism for the rearrangement. Their idea was that the γ-carbon atom of the allyl group came into close contact with



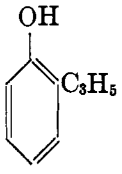
I



II



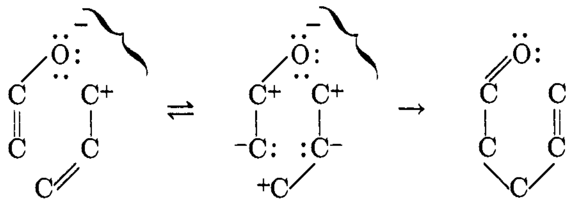
III



IV

the ortho-carbon atom of the nucleus (I); the carbon–oxygen bond broke, the aromatic nucleus assumed the *o*-quinonoid form (II), and simultaneously the allyl group attached itself to the nucleus by the free bond, the double bond in the allyl group shifting. These processes, all occurring practically simultaneously, gave III, which immediately enolized to give IV.

This mechanism is primarily a description of the rearrangement, and is a satisfactory picture. Later writers have restated Claisen's description in electronic terms (90, 89, 33), the clearest account being given by Hurd and Pollack (57). According to them, the system C═C—C—O—C═C goes through the changes indicated below; the carbon–oxygen link is



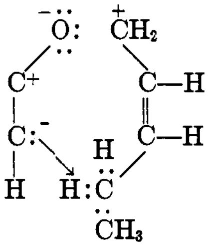
V VI VII

broken, with the pair of electrons going to the oxygen, while the allyl group undergoes a redistribution of electrons and attaches itself to the nucleus by the γ-carbon atom. The last step is the enolization to the phenolic form. It would be expected that there would be considerable resonance energy in the activated complex VI, which would reduce the energy necessary to break the carbon–oxygen bond and therefore the activation energy necessary for the reaction.

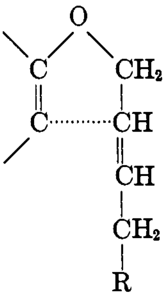
This cylic mechanism agrees with most of the facts known about the simple rearrangement. The first-order reaction kinetics are consistent with the idea that the rate-determining step is the change of VI to VII, and the subsequent enolization of VII must take place very rapidly, since the rate of rearrangement is not affected by dimethylaniline. The invariable occurrence of inversion in the ortho rearrangement is a necessary result of the cyclic form of the activated complex. The displacement of carbon dioxide by the allyl group in allyl 2-carboxyphenyl ethers (page 529) can be correlated with the ease of decarboxylation of β-keto acids by assuming the existence during rearrangement of a β-keto acid analogous to III, which undergoes decarboxylation immediately (21, page 74). This idea is not very satisfactory for explaining the displacement of carbon monoxide from allyloxy aldehydes, however, since β-keto aldehydes do not lose carbon monoxide readily (27).

The failure of the allylanilines to rearrange may be due to the fact that nitrogen has a smaller tendency than oxygen to become a negative ion, and the process of partial ionization cannot take place. On this basis one would expect that allyl phenyl sulfides should rearrange more rapidly than the oxygen compounds, since sulfur is more negative than oxygen, but it is reported that they rearrange much more slowly (51). The failure of propargyl ethers, such as $C_6H_5OCH_2C{\equiv}CH$, to rearrange may be caused by the fact that the $—C—C{\equiv}C$ group must be linear and hence cannot form the cyclic activated complex. The same would be true of $C_6H_5OCH_2C{\equiv}N$.

The mechanism given above fails to explain the course of the anomalous rearrangement in which the migrating group is attached by some carbon other than the γ-carbon. Hurd and Pollack (57) suggested that the γ-ethylallyl phenyl ether is probably a mixture of *cis-* and *trans*-forms, and that in the *cis*-form the δ-carbon is near the ortho-carbon; the activated complex would then be a seven-membered ring (VIII), which by a shift of two hydrogens and formation of a carbon–carbon bond would give the observed product. This extension of the cyclic mechanism has two draw-



VIII

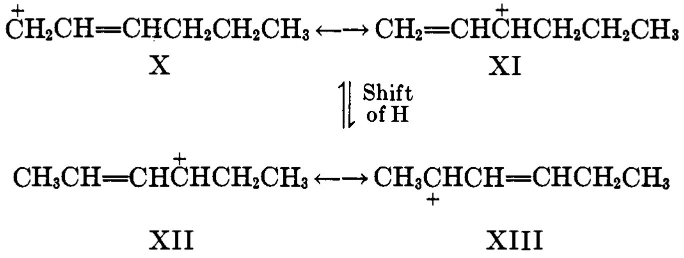


IX

backs: (*1*) If extended to the γ-propylallyl ethers, it requires an eight-membered ring analogous to VIII in the activated complex, which is sterically very unlikely. The formation of such a complex would take place so infrequently in comparison to the formation of the normal complex of type VI that only the normal product would be found, instead of a mixture. (*2*) A complex of type VIII would lack the stabilization by resonance which is present in VI, and the activation energy for a reaction going through VIII would be much greater than for one going through VI.

The anomalous rearrangement can be explained formally by an activated complex (IX) in which the β-carbon atom is concerned in the bond formation with the ortho-carbon. This structure also would have less resonance energy than VI and would require a shift of two hydrogens and of the double bond to give the products obtained.

The anomalous rearrangement has been attributed to a dissociation process in which the substituted allyl group splits off as an ion or radical, which might then undergo the following processes (89):



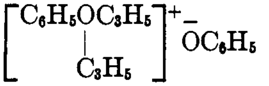
$$\begin{array}{ccc} \overset{+}{C}H_2CH{=}CHCH_2CH_2CH_3 & \longleftrightarrow & CH_2{=}CH\overset{+}{C}HCH_2CH_2CH_3 \\ \text{X} & & \text{XI} \\ & \Big\Updownarrow \text{ Shift of H} & \\ CH_3CH{=}CH\overset{+}{C}HCH_2CH_3 & \longleftrightarrow & CH_3\underset{+}{C}HCH{=}CHCH_2CH_3 \\ \text{XII} & & \text{XIII} \end{array}$$

The observed products are derived from XI and XIII, and no products are found corresponding to the other resonance forms, X and XII.

In the migration of the ethylallyl group to the para-position, only the compound derived from X is formed from both α-ethylallyl and the γ-ethylallyl ethers (page 527). The para rearrangement certainly involves a dissociation (section B), and if the ortho rearrangement went by a dissociation process also, the ethylallyl group should isomerize to the same structure in both cases while in the ion or radical form. That the ethylallyl group gives products derived from XI and XIII in the ortho rearrangement, and from X in the para, is a serious objection against the dissociation mechanism for the ortho rearrangement.

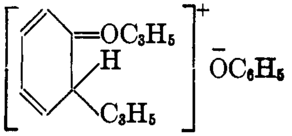
It is certainly significant, in considering the mechanism of the anomalous rearrangement, that α-substituted allyl ethers, such as $ArOCH(CH_2CH_3)CH{=}CH_2$ give only the normal product. This may be due to the fact that the carbon–oxygen bond in these ethers is much more readily broken than that in the γ-substituted compounds. It is well known that secondary ethers are much more readily cleaved by acids than primary ethers (82), and the α-substituent in the allyl ethers may favor the formation of the activated complex VI by promoting electron displacements toward the oxygen. The rearrangement would thus take place at a lower temperature than that of the γ-substituted ethers, and the complicated changes which result in the anomalous products in the latter case would be avoided. The evidence, which is scanty, indicates that α-substituted allyl ethers do rearrange more rapidly than the γ-substituted compounds (102, 89).

The oxonium mechanism of Niederl and Storch (92; *cf.* 57), which was suggested to explain the rearrangements of alkyl phenyl ethers by acidic catalysts and extended to include the Claisen rearrangement, postulates formation of an oxonium salt (XIV). This salt then rearranges through an *o*-quinonoid structure (XV), which breaks up to give the *o*-allylphenol and one molecule of ether. Hurd and Pollack (57) have pointed out two serious arguments against this theory: it does not explain inversion, and it predicts the formation of some allyl 2-allylphenyl ether by decomposition of XV to yield this product and phenol. This is not observed. The mechanism would also require second-order kinetics, which are not found, and the addition of a base like dimethylaniline to the reaction mixture should stop rearrangement completely, since the allyl phenyl ether would form an ammonium salt with the dimethylaniline in preference to an oxonium salt with the very weakly basic ether. Actually, the rate is unaffected by adding as much as 10 per cent of dimethylaniline.



$$\left[\begin{matrix}C_6H_5OC_3H_5\\ |\\ C_3H_5\end{matrix}\right]^{+}\overset{-}{O}C_6H_5$$

XIV



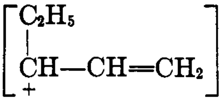
XV

From this discussion, it is evident that no single scheme is compatible with all of the facts known about the rearrangement to the ortho-position; the cyclic mechanism is the most satisfactory, but is reconciled with difficulty with the anomalous rearrangement. The dissociation mechanism is entirely unsatisfactory.

B. MECHANISM OF THE REARRANGEMENT TO THE PARA-POSITION

The kinetics of the rearrangement to the para-position are very similar to those for the ortho-position (107); the reaction is first order both in solution and in the pure liquid, and the rate is not affected markedly by dimethylaniline or acetic acid, although the para rearrangement must involve a dissociation of the allyl group, either as an ion or radical, followed by a substitution reaction in the para-position. This follows both from consideration of the spatial factors and from the fact that inversion in the para rearrangement is the exception. Inspection of models shows that the formation of a cylic intermediate is very improbable, because the distances are too great and because of the distortion of the bond angles of the atoms which would be required (107).

Mumm's work on the para rearrangement of α- and γ-substituted allyl ethers (page 527) is further strong support for the idea that para rearrangement involves dissociation. The α-ethylallyl group



$$\left[\begin{array}{l} C_2H_5 \\ | \\ \underset{+}{C}H{-}CH{=}CH_2 \end{array}\right]$$

after dissociation isomerizes to the form

$$\left[C_2H_5CH{=}CH\underset{+}{C}H_2\right]$$

before attaching itself to the para-position; the γ-ethylallyl group, being already in this form, which is evidently the more stable of the two, gives the same rearrangement product. The fact that the two isomeric ethers give the same product is evidence that they pass through a common intermediate state.

The allyl group obviously may dissociate as a positive ion or as a free radical; serious objections can be raised to both. Against the ionic intermediate is the observation of Mumm (89) that rearrangement can take place on heating in alcoholic alkali; if a positive allyl ion were present, it should combine with an hydroxyl ion to give allyl alcohol.

If radicals were the intermediate stage, one would expect that they would react with the solvent or dimerize to an appreciable extent, so that lower yields of rearrangement product would be obtained. Thus Hickinbottom (45) finds that benzyl phenyl ether heated in quinoline at 250°C. gives benzylquinolines, hydroxyphenylquinolines, and toluene, which indicates that dissociation of the ether into radicals occurs. There is no evidence for the formation of similar products from the Claisen rearrangement.

Hurd and Pollack (57) have suggested that rearrangement to the para-position goes by two steps,—first a shift of the allyl group with inversion to the ortho-position, as described for the ortho rearrangement, followed by another shift with inversion to the para-position. The two inversions would give the result of no inversion, which is contrary to the results of Mumm mentioned above. It seems likely, however, that, as this mechanism suggests, the dissociated allyl group, whether ion or radical, does not get out of the sphere of influence of the other fragment and that recombination of the two takes place more rapidly than other possible reactions.

It is clear that no single mechanism can explain all of the facts observed in the rearrangement of allyl ethers, and that there are many phases of the process that are imperfectly understood.

The author is indebted to Dr. J. F. Kincaid and Dr. T. L. Cairns for many helpful discussions and suggestions.

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[2] The topic of the Claisen rearrangement has been summarized by Hurd on pages 214–225 of *The Pyrolysis of Carbon Compounds* (The Chemical Catalog Company, Inc., New York (1929)). A brief resumé by Watson has appeared recently in the *Annual Reports of the Chemical Society* for 1939, pages 205–7.

Because of the unusual length of two of Claisen's papers (21, 25), they are quoted with the page number of the reference following the reference number.

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