SOME STEREOCHEMICAL ASPECTS OF
THE CLAISEN REARRANGEMENT

by

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Typed by Lilah N. Potter
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INTRODUCTION

In the well known ortho-Claisen rearrangement of allyl aryl ethers it has been clearly indicated (23, p. 107; 24, p. 780; 35, p. 2217; 41, p. 1884) that the reaction proceeds through a cyclic transition state. However, very little information has been available on the stereochemistry of this interesting rearrangement especially with reference to the geometry of the transition state. Alexander and Kluiber (1, p. 4306) have found that the rearrangement of optically active $\alpha,\gamma$-dimethylallyl phenyl ether (I) gave optically active 2-($\alpha,\gamma$-dimethylallyl)-phenol (II). Although the configuration of the initial and final states was not established, it was suggested by Hart (17, p. 4304) that the rearrangement proceeds with retention of configuration.

\[\text{I} \quad \rightarrow \quad \text{II}\]
If it is assumed that a modified cyclohexane chair is most reasonable for the transition state, conformational analysis suggests that Hart's ideas should be erroneous. In order, therefore, to gain more intimate knowledge of the transition state the rearrangement of \( \alpha, \gamma \)-dimethylallyl phenyl ether (4-phenoxypent-2-ene) (I) was re-investigated with particular attention focused on the cis- and trans-configuration about the allylic double bond in the starting ether, the phenolic product and the unreacted ether. This ether was well suited for this purpose, and, in addition, information could be obtained on the occurrence of the abnormal Claisen rearrangement proposed by Lauer and co-workers (27, p. 3044; 28, p. 290; 29, p. 3048). According to this proposal 4-phenoxy- pent-2-ene (I) would rearrange to 2-(\( \alpha \)-ethylallyl)-phenol (III) which should no longer show cis-trans isomerism about the allylic double bond.

To establish unequivocally the configuration of the allyl phenyl ether (I) a synthesis had to be devised
which would allow separation of the optical antipodes after the asymmetric carbon atom was produced. Further, any reactions carried out after introduction of the asymmetric center must not involve this center. In this work a synthetic scheme was formulated to meet these requirements.
The Claisen rearrangement is a reaction in which allyl ethers of phenols and enols when heated to elevated temperatures produce C-allyl compounds. The first example of this reaction was discovered by Claisen (hence the name) in 1912 (6, p. 3157). Upon distilling ethyl-O-allylacetoacetate (I) at atmospheric pressure in the presence of ammonium chloride he obtained ethyl-α-C-allylacetoacetate (II).

\[
\begin{align*}
I & : O(CH_2CH=CH_2)CH_3C=CHCOOC_2H_5 \\
II & : O(CH_2CH=CH_2)CH_3C-CH-COOC_2H_5
\end{align*}
\]

Although this reaction produces some interesting results in open chain compounds, it is more important and useful in the aromatic series. In this series it was found that allyl aryl ethers rearrange smoothly in the neighborhood of 200° to ortho-allyl phenols provided that an ortho position is available. One of the earliest examples studied (7, p. 79) was that of the simplest member of the series allyl phenyl ether (III) which rearranged to o-allyl phenol (IV).
Later it was discovered that if both ortho positions are occupied the allylic group migrates to the para position. An example of this reaction was provided by Marvell and co-workers (33, p. 1923) who rearranged α-methylallyl-2,6-dimethylphenyl ether (V) to 2,6-dimethyl-2-(α-methylallyl)-phenol (IV).

The original proposition of a cyclic mechanism was put forth by Claisen and Tietze (8, p. 278). They had observed inversion of the allylic grouping during the course of the reaction, and had explained this by an intermediate cyclic stage in the rearrangement. In their example γ-phenylallyl phenyl ether (VII) rearranged
to 0-(a-phenylallyl)-phenol (VIII).

In 1937 Mumm and Möller (35, p. 2217) gave a much clearer explanation of the cyclic mechanism using the following scheme of representation:

It was easily seen that the γ-carbon atom of the allyl ether (IX) became attached to the ortho position of the benzene nucleus in the allylphenol (XIII) while passing through a cyclic six-membered transition state (X). The inversion observed by Claisen (see above) was neatly
explained.

Since that time much evidence has been presented all of which has indicated that a concerted cyclic mechanism indeed was involved. Some of the first support was that of Hurd and Schmerling (23, p. 107) who heated a mixture of \( \beta \)-phenylallyl phenyl ether (VII) and allyl-\( \beta \)-naphthyl ether (XIII) and obtained no o-allylphenol (IV) indicating that the reaction was intramolecular in that no cross products were formed.

\[
\begin{align*}
\text{VII} & \quad + \quad \text{XIII} \\
\text{O-CH}_2\text{CH=CH}\Phi & \quad \text{OCH}_2\text{CH=CH}_2 \\
\end{align*}
\]

In 1952 Ryan and O'Connor (40, p. 5867) heated allyl phenyl ether (III) in which the \( \alpha \)-carbon was labeled with radioactive carbon. After degradation of
the \( \alpha \)-allylphenol (IV) the activity was found in the carbon atom attached to the benzene nucleus indicating inversion of the allyl group.

\[
\begin{align*}
\text{III} & \quad \rightarrow \quad \text{IV} \\
\text{O-CH}_2\text{CH}^{\bullet}\text{CH} = \text{CH}_2 & \quad \text{OH-CH}_2\text{CH} = \text{CH}_2
\end{align*}
\]

There has been a great deal of kinetic work done on the Claisen rearrangement which has indicated the reaction was unimolecular. In the latest work Goering and Jacobson (14, p. 3277) subjected fifteen allyl and ring substituted ethers to the Claisen conditions. All cases showed first-order kinetics which data further supported the cyclic concerted mechanism.

In the mechanistic scheme outlined by Mumm and Möller (see above) the intermediate postulated was a dienone (XI). That the dienone does exist has been shown in the para-Claisen rearrangement which in its first stages is closely analogous to the ortho-Claisen. Conroy and Firestone (9, p. 2291) first demonstrated the existence of the dienone through the isolation of its Diels-Alder adduct albeit in very small yields. Later, Kalberer and Schmid (24, p. 780) by heating
allyl-2,4,6-trimethyl phenyl ether (XIV) with maleic anhydride (XV) obtained the Diels–Alder adduct (XVI) in 87% yield.

This result adequately proved the presence of the dienone (XVII) in the reaction mixture.
Concerning the geometry of the transition state very little experimental data has been available other than the dubious retention of optical activity observed by Alexander and Kluiber (1, p. 4304) and interpreted by Hart (17, p. 4034). Rhoads and Grecelius (39, p. 5059) have indicated what some of the geometric requirements of the transition state should be by a comparison of activation energies and entropies of $\alpha$-substituted allyl aryl ethers.
A. Synthetic Procedures

In this work the sequences of reactions that were carried out are given in Table 1. Compounds II and III were reported in the literature (20, p. 1221; 38, p. 74), and they were prepared in the manner described.

Replacement of the tosyl group with the phenoxy group in the tosylate ester (III) led to some difficulties. The frequently used procedure employing phenol in aqueous sodium hydroxide solution gave either extremely small yields or polymeric material. Finally, using a method patterned after that of Slotta and Frank (42, p. 684) the desired phenyl ethynyl ether (IV) was prepared in good yield. This method required the use of 95% ethanol, solid potassium hydroxide and phenol plus the discrete use of heat. At all times, both during the heating of the reaction mixture and the distillation of the pure product, the heating bath was kept below 65° to avoid undue polymerization of the compound. Infrared analysis of the ether (IV) showed the presence of a terminal acetylene, an aryl ether, and a monosubstituted benzene nucleus.

Carbonation of the terminal acetylenic group in the aryl ether (IV) was accomplished through the use of
Table 1.

<table>
<thead>
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<th>Reaction</th>
<th>Formula</th>
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<tbody>
<tr>
<td>I</td>
<td>$\text{CH}_3\text{CHO} + \text{HC}≡\text{CH}$</td>
</tr>
<tr>
<td>II</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>III</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>IV</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>V</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>VI</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>VII</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>VIII</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>IX</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>X</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
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<tr>
<td>XI</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>XII</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>XIII</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>XIV</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>XV</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
<tr>
<td>XVI</td>
<td>$\text{CH}_3\text{CH}-\text{C}≡\text{CH}$</td>
</tr>
</tbody>
</table>

**Reactions:**

1. $\text{CH}_3\text{CHO} + \text{HC}≡\text{CH}$
2. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
3. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
4. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
5. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
6. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
7. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
8. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
9. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
10. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
11. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
12. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
13. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
14. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
15. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
16. $\text{CH}_3\text{CH}-\text{C}≡\text{CH}$
the Grignard reagent and solid carbon dioxide (18, p. 505). This resulted in good yields of the \( \alpha,\beta \)-unsaturated acetylenic acid (V) which was characterized through its neutralization equivalent, its \( p \)-phenylphenacyl ester and its infrared spectrum which indicated a disubstituted acetylene and an \( \alpha,\beta \)-unsaturated acid.

Hydrogenation of the acetylenic acid (V) to the cis-olefinic acid (VI) was done at atmospheric pressure over either the Lindlar catalyst (32, p. 450; 37, p. 200) or 2.5% palladium on calcium carbonate. Using the Lindlar catalyst poisoned with a small amount of synthetic quinoline (coal tar quinoline was unsatisfactory) hydrogen uptake stopped at one mole, and excellent yields of the cis-olefinic acid were obtained. However, the catalyst was quite erratic, and at times little or no hydrogen was absorbed. Alternatively, employing the palladium on calcium carbonate catalyst hydrogen uptake was always rapid, but the hydrogenation had to be arbitrarily stopped after one mole hydrogen had been absorbed. The product from the latter hydrogenation was quite impure containing some completely saturated acid. After two fractional crystallizations a 70% yield of the pure cis-olefinic acid (VI) was realized. Characterization of the acid was achieved through determination of its neutralization equivalent, and the preparation
of its p-phenylphenacyl ester. The infrared spectrum showed the presence of a cis-olefin and the absence of a trans-olefin.

Chemical reduction of the cis-olefinic acid (VI) with lithium aluminum hydride (31, p. 3188; 36, p. 2549) led cleanly to high yields of the cis-α,β-unsaturated primary alcohol (VII). This low melting alcohol was difficult to recrystallize, but it was found that petroleum ether fractionated to give a cut that had a boiling range of 38-43° was the most satisfactory solvent for this purpose. The alcohol was characterized by the preparation of its N-α naphthylcarbamate and its infrared spectrum which indicated that there were polymeric associated hydroxyl groups and an unsaturated primary alcohol present.

In preparing the tosylate ester (VIII) of the cis-alcohol (VII) the method of Hahn and Walter (16, p. 1540) was employed. This method uses tosyl chloride and pulverized potassium hydroxide in anhydrous ether. The desired ester was obtained as a low melting solid whose melting point was very near to that of the alcohol. However, a mixture of the two compounds melted below room temperature. The tosyl ester itself proved to be quite unstable as has been reported (12, p. 467) for tosylates
of allyl alcohols. It decomposed at room temperature in a few days; in an Abderhalden apparatus with phosphorous pentoxide at reduced pressure within three hours. The compound was kept for an indefinite period of time over calcium chloride in a freezer. In the infrared spectrum of the ester characteristic peaks were observed for p-toluenesulfonates.

Alkylation (37, p. 198) of the aryl acetylenic ether (IV) by means of lithamide and methyl iodide in liquid ammonia proceeded cleanly to give the disubstituted acetylenic aryl ether (IX). In contrast to the starting material (IV) this ether did not appear to be subject to thermal polymerization. Its infrared spectrum showed the presence of a disubstituted acetylene.

The cis-allyl phenyl ether (X) was prepared from the ether (IX) by hydrogenation at atmospheric pressure over the Lindlar catalyst (32, p. 450; 37, p. 200) poisoned with a small amount of quinoline. Again the hydrogen uptake ceased at slightly more than one mole hydrogen absorbed. However, the catalyst showed no erratic behavior as with the acetylenic acid, and the acetylenic linkage always was reduced smoothly. By chemical reduction with lithium aluminum hydride (43, p. 645) the tosylate ester (VIII) was reduced to the cis-allyl phenyl ether (X) in good yields.
Characterization through infrared analysis indicated the presence of a cis-olefin and the absence of a trans-olefin.

Compounds XII through XIV were reported in the literature (1, p. 4305; 30, p. 706; 1, p. 4305) and were prepared as described therein. The trans-allyl phenyl ether (XIV) was characterized by the presence of trans-olefin band and the absence of a cis-olefin band in the infrared.

The cis- and trans-aryl allyl ethers (X and XIV) were rearranged by heating them as one molar solutions in mesitylene which had been distilled to give a main fraction, b.p. 162-165°. A thermometer placed into the refluxing solutions indicated the internal temperature as 165°. At the end of the various heating periods the solvent was removed at reduced pressure either in a rotatory evaporator or through a Vigreux column. Neither procedure was completely satisfactory because some unreacted ether was lost along with the solvent. After taking up the residual oil in hexane the phenolic material (XV) was isolated by alkaline extraction and the unreacted ether by evaporation of the solvent. These two fractions were subjected to infrared analysis.

Samples of the phenolic material (XV) from the cis- and trans-allyl aryl ethers (X and XIV) were
converted to the methyl ethers (XVI) by the use of dimethyl sulfate in aqueous alkali (21, p. 2168). High yields of the methyl ethers were obtained. Gas chromatographic analysis of these compounds showed only a single peak, an indication of their purity.

B. Theoretical

Table 1 contains the experimental data for the rearrangement under study. The composition of the unreacted ether is taken from standard curves of log $I_o/I$ versus composition and is to be construed only as an estimate. Phenolic composition is also an estimation.

Some interesting new pieces of information can be garnered from Table 1. They are:

1. the trans-ether remains in the trans configuration.
2. the trans-ether gives predominantly trans-phenol with a small but significant amount of cis.
3. the cis-ether is transformed into the trans.
4. the cis-ether gives trans-phenol with a constant, very small amount of cis.
5. the amount of cis-phenol obtained in the rearrangement is definitely and reproducibly less from the cis-ether than from the trans.

There are four explanations for the conversion of
<table>
<thead>
<tr>
<th></th>
<th>cis-4-Phenoxypent-2-ene</th>
<th></th>
<th>trans-4-Phenoxypent-2-ene</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Reacted</td>
<td></td>
<td>% Reacted</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>85</td>
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<td>100</td>
<td>95</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
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</tr>
<tr>
<td></td>
<td>100</td>
<td>25</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>95</td>
</tr>
</tbody>
</table>

**Table 1**
Diagram 1.
the cis-ether into the trans:

1. thermal isomerism
2. return from the dienone intermediate
3. interconversion in the transition state
4. acid catalyzed isomerism (autocatalytic).

The argument for thermal isomerism is weakened considerably by the data of Kistiakowsky and White (25, p. 641; 26, p. 767) who have shown that the cis-trans isomerism of an isolated double bond at 400° occurs at a rate much smaller than the observed rate of reaction of 4-phenoxypent-2-ene.

Curtin and Crawford (11, p. 3157) have shown that the intermediate dienone with a methyl and an allyl groups in the 2-position goes to product 2.7 times faster than it returns to ether. In the present case the 2-position is occupied with a hydrogen atom and an allyl group. The almost infinite increase in mobility of the hydrogen atom over that of the methyl group means that this dienone should go to product at a much greater rate. This then would suggest that cis-trans isomerism is not due to the return from the dienone.

The proposed interconversion of the transition states can be analyzed by the following scheme:
in which cis = cis-ether, tr = trans-ether, k = reaction rate, x = transition state and P = product.

When [tr] is negligible for any time interval \( \Delta t \):

1) rate of product formation =

\[
\frac{k_3 x_{cis} + \frac{k_1 k_4}{k_2 + k_4}}{x_{cis}}
\]

2) rate of tr formation = \( \frac{k_1 k_2}{k_2 + k_4} x_{cis} \)

3) \[
\frac{\Delta P/\Delta t}{\Delta tr/\Delta t} = \frac{k_3 + \frac{k_1 k_4}{k_2 + k_4}}{\frac{k_1 k_2}{k_2 + k_4}} = \frac{k_3 k_2 + k_3 k_4 + k_4 k_4}{k_1 k_2} = \frac{k}{k'}
\]

When [tr] is not negligible:

4) \[
-\frac{dtr}{dt} = \frac{dP_{tr}}{dt}
\]

i.e. [x_{tr}] is small

or \( -dtr = dP_{tr} \)
The above equations (1-5) are valid as long as $x_c \neq 0$.

From an examination of equation 5 it is seen that the ratio of increment in product to increment in trans-ether should increase during the course of the reaction. Using the applicable, if rather limited, data from this investigation Table 2 was constructed. It shows that the above mentioned ratio increases initially but falls off rather markedly near 68% completion. This observation casts doubt on the interconversion of transition states as the sole explanation for the cis-trans isomerism of the ethers.

<table>
<thead>
<tr>
<th>Time, hrs.</th>
<th>g. product</th>
<th>g. cis-ether</th>
<th>g. trans-ether</th>
<th>$\frac{\Delta P/\Delta t}{\Delta \text{tr}/\Delta t}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>---</td>
<td>100</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>66</td>
<td>16</td>
<td>1.1</td>
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<tr>
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<td>33</td>
<td>17</td>
<td>32.0</td>
</tr>
<tr>
<td>20</td>
<td>68</td>
<td>0</td>
<td>32</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Table 2

There remains only the argument that the cis-trans
conversion is an acid catalyzed isomerization. This would necessarily involve autocatalysis by the phenolic product formed during the reaction. Examination of the results in Table 1 show that most isomerization occurs rapidly somewhere between 50% and 68% completion of reaction which could indicate that as the phenol concentration builds up the acid concentration autocatalysis starts and rapidly converts the cis into the trans form. Further substantiation is given by the fact that isomerization of the phenolic product occurs only in a medium of high acidity. However, much more substantial data will be necessary before a clear explanation of the mechanism of the cis-trans-ether isomerism can be elucidated.

Figure 1 shows the transition states available to the trans-ether (I and II) and those available to the cis-ether (III and IV). In I both the large methyl groups occupy the favorable equatorial positions (designated by e,e in diagram 1), and the original double bond between C₂ and C₃ is trans. In the product the double bond between C₁ and C₂ is also trans. The alternate structure (II) for the transition state shows one methyl axial and one equatorial (a,e in diagram 1) which is a less favorable but still a probable conformation. Again the original double bond (C₂-C₃) is trans, but the final
Figure 1.
one \((C_1-C_2)\) is \textit{cis}. Thus \textit{trans}-phenol should be the major product, and this is born out by the experimental evidence.

Structure III shows the favorable conformation for the transition state for the \textit{cis}-ether. Here one methyl is equatorial and one is axial (represented by \(e,a\) in diagram 1). One methyl group is forced to take the less favorable axial position because the original double bond \((C_2-C_3)\) is in the \textit{cis} configuration. The final double bond \((C_1-C_2)\) in the product is \textit{trans}. In IV, the alternate conformation available, both methyl groups occupy the unfavorable axial positions. (See \(a,a\) in diagram 1.) The original double bond \((C_2-C_3)\) is \textit{cis} and the final one \((C_1-C_2)\) is likewise \textit{cis}. Here the \textit{trans}-phenol should be the even more predominant than in the case of the \textit{trans}-ether. Again experimental data bears out this supposition.

Infrared analysis, even with 0.05 millimeter thick samples, showed no evidence of a terminal double bond as is required by the abnormal Claisen rearrangement reported by Lauer and co-workers \(27, \text{p. 3044; } 29, \text{p. 3048}\). These terminal, mono-substituted olefin peaks are found at 990 cm\(^{-1}\) and 910 cm\(^{-1}\) \(3, \text{p. 49}\) and are not obscured by the \textit{trans}-olefin peak at 965 cm\(^{-1}\). Since the terminal
double bond is not observed, it is assumed that the abnormal Claisen reaction is not taking place.
EXPERIMENTAL

But-1-yne-3-ol

This alcohol was prepared in one molar quantities from acetylene and acetaldehyde according to the directions of Campbell, Campbell and Eby (5, p. 2883). It distilled as a water white liquid, b.p. 52-54° (65 mm); \( n^D_{23} 1.4240 \); yield 53%. This compound has been reported to have a boiling point of 46° (50 mm) and \( n^D_{20} 1.4256 \) (20, p. 1221).

But-1-yne-3-yl-p-toluenesulfonate

This ester was prepared from but-1-yne-3-ol in one and one-half molar quantities using a method patterned after that of Reppe et al. (38, p. 74). Optimum conditions require 10% excess p-toluenesulfonyl chloride, 11% excess base and 5 hours stirring time. Under these conditions a 78% yield of light tan crystals was obtained. After two recrystallizations from hexane (b.p. 60-70°), using Norit once, the white crystals melted at 51.5-52.5°. It is reported to melt at 58-60° (38, p. 74).

3-Phenoxybut-1-yne

In a 500 ml 3-necked round-bottom flask equipped with a condenser, mechanical stirrer and stopper was
placed a solution of 37.6 g (0.40 mole) of phenol and 26.4 g (0.40 mole) of potassium hydroxide (85%) in 150 ml of 95% ethanol. The solution was stirred mechanically and 74 g (0.33 mole) of the recrystallized tosyl ester of but-1-yn-3-ol was added over a period of forty minutes. During the addition potassium p-toluenesulfonate began to precipitate. The stirring was continued for one hour at room temperature and then for three hours in a water bath maintained at 60-65°. After the reaction mixture had been cooled, 100 ml of ether was added followed by 400 ml of cold water. The increase in volume made it necessary to transfer the mixture to a one liter beaker. Upon separation of the ether layer the aqueous layer was extracted twice with ether. The combined ether layers were extracted three times with 5% aqueous sodium hydroxide solution, washed three times with cold water and dried over anhydrous magnesium sulfate. The ether was removed on a warm water bath; however, after the volume reached 100 ml, the bath was removed and the last of the ether was evaporated at a reduced pressure at room temperature. The product distilled as a water white liquid, b.p. 40-41° (0.60 mm); n\textsuperscript{20}D 1.5191. The yield was 28 g (58%).

**Anal.** Calc. for C\textsubscript{10}H\textsubscript{10}O\textsubscript{1}: C, 82.15%; H, 6.90%.

**Found:** C, 82.23%; H, 7.07%.
4-Phenoxypent-2-ynoic Acid

In a 200 ml 3-necked round-bottom flask equipped with a dropping funnel, a reflux condenser with calcium chloride drying tube and a stopper was placed an ice cold ethereal solution containing 0.1 mole of ethyl magnesium bromide. To this solution was added dropwise a solution of 14.6 g (0.1 mole) of 3-phenoxybut-1-yne in 30 ml of dry ether. The resulting solution was refluxed eight hours and then poured onto a large excess of solid carbon dioxide in a beaker. After placing the beaker in a one liter autoclave additional dry ice was added to bring the total to about 600 g. The autoclave was sealed and allowed to remain at room temperature for one day. Upon release of the excess pressure the sticky Grignard complex was covered with ether, cooled in ice and hydrolyzed with ice-cold 15% sulfuric acid. The ether layer was extracted three times with saturated sodium bicarbonate solution; the combined bicarbonate layers were washed twice with ether, cooled in ice and after addition of 50 ml of ether acidified with ice-cold 15% sulfuric acid. The aqueous layer was extracted twice with ether, and the combined ether fractions were washed twice with water and dried over anhydrous magnesium sulfate. Upon removal of the ether at reduced pressure the residue solidified to
a light tan, waxy solid. The yield was 11.8 g (62%). After three recrystallizations from hexane (b.p. 60-70°), using Norit once, the acid was obtained as white needles, m.p. 82.6-83.6°.

**Anal:** Calc. for $C_{11}H_{10}O_3$: C, 69.47%; H, 5.30%

Found: C, 69.70%; H, 5.51%

Neutralization Equivalent: Calc. 190

Found 189

Ultraviolet: $\lambda_{max}$ 224 µm; $\varepsilon = 6,430$

The $p$-phenylphenacyl ester was prepared according to standard procedures (34, p. 185). After three recrystallizations from 95% ethanol the melting point was 99.5-100.2°.

**Anal:** Calc. for $C_{25}H_{20}O_4$: C, 78.11%; H, 5.24%

Found: C, 77.80%; H, 5.11%

**cis-4-Phenoxypent-2-enoic Acid**

A) Lindlar Catalyst.

This compound was prepared by quantitative hydrogenation at atmospheric pressure of 4-phenoxypent-2-ynoic acid over the Lindlar catalyst. In a typical hydrogenation (10, p. 3512) 0.95 g (0.005 mole) of 4-phenoxypent-2-ynoic acid was dissolved in 8 ml of reagent grade ethyl acetate containing 20% of the compound
weight of the Lindlar catalyst and 3% of the compound weight of quinoline (synthetic). At the end of forty-five minutes 104% of the theoretical amount of hydrogen was absorbed, and no further uptake was observed. The catalyst was removed by filtration and the quinoline by washing with dilute hydrochloric acid. After drying over anhydrous magnesium sulfate the solvent was evaporated at reduced pressure leaving 0.86 g (90%) of light yellow solid. After two recrystallizations from hexane (b.p. 60-70°), using Norit once, the white needles melted at 112-113°.

B) Palladium on Calcium Carbonate.

Alternatively, the acetylenic acid was reduced over a palladium (2.5%) on calcium carbonate catalyst in ethyl acetate. The reduction required 20% of the compound weight of catalyst and was stopped at one mole hydrogen uptake. A 70% yield of acid was obtained after two recrystallizations from hexane (60-70°).

Anal: Calc. for \( C_{11}H_{12}O_3 \); C, 68.74%; H, 6.30%.

Found: C, 68.91%; H, 6.51%.

Neutralization Equivalent: Calc. 192

Found 192

Ultraviolet: \( \lambda_{\text{max}} \) 217 mu; \( \varepsilon = 11,060 \)
The p-phenylphenacyl ester was prepared according to standard procedures (34, p. 185). After four recrystallizations from 95% ethanol the melting point was 95.5-96.8°.

Anal: Calc. for C_{25}H_{22}O_4: C, 77.70%; H, 5.70%.
Found: C, 77.86%; H, 5.98%.

**cis-4-Phenoxypent-2-ene-1-ol**

In a 200 ml 3-necked round-bottom flask equipped with a stopper, a condenser and a dropping funnel, the latter two equipped with calcium chloride drying tubes, was placed 0.50 g (0.013 mole) of lithium aluminum hydride covered with 40 ml of dry ether. The mixture was refluxed and stirred with a magnetic stirrer for two hours. After cooling the mixture to room temperature a solution of 2.0 g (0.010 mole) of *cis*-4-phenoxypent-2-enoic acid in 40 ml of dry ether was added at such a rate as to maintain gentle reflux. This addition required twenty-five minutes. The mixture was stirred forty minutes at room temperature, and at the end of this period 4 ml of water was added cautiously. After an additional ten minutes of stirring, the mixture became creamy white and was acidified with 20 ml of 8% sulfuric acid. A clear mixture resulted in ten minutes. The ether
layer was separated and the aqueous layer was extracted once with 15 ml of ether. The combined ether extracts were washed with three 30 ml portions of 5% aqueous sodium hydroxide solution followed by three 50 ml portions of water. Upon drying the ethereal solution over anhydrous magnesium sulfate the solvent was evaporated leaving a white solid residue which weighed 3.27 g (88.5%). After two recrystallizations from petroleum ether (b.p. 38-43°) the white needles melted at 41.8-42.8°.

**Anal:** Calc. for C_{11}H_{14}O_{2}: C, 74.12; H, 7.92%. Found: C, 73.86%; H, 7.81%.

The N-α-naphthylcarbamate was prepared according to standard procedures (34, p. 196). After two recrystallizations from hexane (b.p. 60-70°) the fine, white needles melted at 77-78°.

**Anal:** Calc. for C_{22}H_{20}N_{1}O_{3}: C, 76.06%; H, 6.09%. Found: C, 76.16%; H, 6.26%.

**cis-4-Phenoxypent-2-ene-1-yl-p-toluenesulfonate**

In a 100 ml round-bottom flask was placed a solution of 2.19 g (0.0123 mole) of cis-4-phenoxypent-2-ene-1-ol and 2.35 g (0.0123 mole) of p-toluenesulfonyl chloride in 20 ml of dry ether. A condenser carrying a
calcium chloride drying tube was attached, and the solution was cooled to \(-5^\circ\) in an ice-salt bath while being stirred with a magnetic stirrer. At this point 2.18 g (0.033 mole) of pulverized potassium hydroxide (85\%) was added in portions over a period of fifteen minutes. The resulting mixture was stirred four hours and maintained between \(-1^\circ\) and \(4^\circ\). At the end of this time a filtered sample of the reaction mixture gave a negative odor test for tosyl chloride and a negative copper wire flame test for chloride. Enough water was added to dissolve the solid material, and the ether layer was separated. The aqueous layer was extracted once with 10 ml of ether, and the combined ether extracts were washed with three 30 ml portions of water and dried over anhydrous magnesium sulfate. After evaporation of the solvent the light tan residue weighed 3.70 g (90.5\%).

After three recrystallizations from petroleum ether (b.p. 38-43\°) the white needles melted at 41.3-42.3\°.

**Anal:** Calc. for \(\text{C}_{18}\text{H}_{20}\text{O}_{4}\text{S}_{1}\): C, 65.04\%; H, 6.06\%.

Found: C, 64.81\%; H, 6.15\%.

This compound was quite unstable and had to be stored in a freezer in a desiccator containing calcium chloride. It decomposed at room temperature in a few days to a red-brown oil. In a vacuum over phosphorous pentoxide at room temperature it decomposed in three hours.
4-Phenoxypent-2-ynyl

To 500 ml of liquid ammonia in a one liter 3-necked round-bottom flask equipped with a mechanical stirrer, a dropping funnel and a stopper carrying a soda-lime tube, was added 0.06 g of hydrated ferric nitrate, and the resulting solution was stirred for five minutes. At this point 0.06 g of lithium metal cut into very small pieces was added. After five minutes of stirring the mixture was black. Then 1.4 g (0.2 mole) of metallic lithium was added in small pieces, and the mixture was stirred until it turned gray (twenty minutes). A solution of 29.2 g (0.2 mole) of 3-phenoxybut-1-ynyl in 40 ml of dry ether was added dropwise over a period of twenty minutes while the reaction vessel was cooled in a dry ice-acetone bath. Stirring was continued with cooling for three hours and without cooling for one-half hour. After re-cooling the reaction mixture, 35 g (0.25 mole) of methyl iodide dissolved in 30 ml of dry ether was added dropwise over a period of twenty minutes, and the mixture was stirred seven hours with cooling and one hour without cooling. To the brown mixture was added 10 g. of ammonium chloride, and the stirring was continued for one-half hour. The ammonia was allowed to evaporate overnight through the cellophane covered necks of the
flask. After covering the residue with 100 ml of ether 400 ml of cold water was added to effect solution of the precipitate. The ether layer was separated, and the aqueous layer was extracted with two 50 ml portions of ether. The combined ether extracts were washed with six 50 ml portions of 3N sulfuric acid, six 50 ml portions of 5% aqueous sodium hydroxide solution and three 100 ml portions of water. After drying the ethereal solution over anhydrous magnesium sulfate the solvent was removed at reduced pressure, and the light yellow residue was distilled through a short Vigreux column. The main fraction was a water white liquid, b.p. 59.5-60° (0.65 mm), weighing 23.7 g (74%); n^20 D 1.5254. It gave a negative silver nitrate test.

**Anal:** Calc. for C_{11}H_{12}O_1: C, 82.48%; H, 7.55%.
Found: C, 82.56%; H, 7.56%.

**cis-4-Phenoxypent-2-ene**

This compound was prepared by the following two procedures:

A) Catalytic Hydrogenation.

This method used as the starting material 4-phenoxypent-2-ynel. In a typical hydrogenation 5.12 g (0.032 mole) of 4-phenoxypent-2-ynel was dissolved in
10 ml reagent grade ethyl acetate containing 10% of the compound weight of Lindlar (13, p. 541) catalyst and 2% of the compound weight of quinoline (synthetic). At the end of three and one-quarter hours 104% of the theoretical amount of hydrogen had been absorbed, and the hydrogen uptake had almost stopped. The catalyst was removed by filtration, and the quinoline by washing with dilute hydrochloric acid. After drying over anhydrous magnesium sulfate the solvent was removed at reduced pressure to give 4.86 g (95%) of yellowish oil. This oil was distilled through a short Vigreux column to give as the main fraction a water white liquid, b.p. 45° (0.6 mm); n\textsuperscript{20}D 1.5102. The yield was 4.35 g (85%).

B) Chemical Reduction.

This method used as the starting material cis-4-phenoxypent-2-ene-1-yl-p-toluene sulfonate.

In a 200 ml 3-necked round-bottom flask equipped with a stopper, a dropping funnel and a condenser carrying a calcium chloride drying tube, was placed 0.43 g (0.011 mole) of lithium aluminum hydride covered with 40 ml of dry ether. The mixture was refluxed and stirred with a magnetic stirrer for two hours. After cooling to room temperature a solution of 2.32 g (0.007 mole) of cis-4-phenoxypent-2-ene-1-yl-p-toluene sulfonate in 40 ml
of dry ether was added dropwise over a period of twenty minutes. The resulting mixture was stirred three-quarters of an hour at room temperature followed by the cautious addition of 5 ml of water. In fifteen minutes the mixture was a creamy white and was acidified with 30 ml of 8% sulfuric acid. After ten minutes stirring the mixture became clear, and the ether layer was separated. The aqueous layer was extracted with 15 ml of ether, and the combined ether extracts were washed with three 30 ml portions of 5% aqueous sodium hydroxide solution followed by four 50 ml portions of water. The ethereal solution was dried over anhydrous magnesium sulfate, and the solvent was removed by evaporation. The residual oil was taken up in 5 ml of petroleum ether (b.p. 38-43°) and placed in the freezer overnight to precipitate any unreacted tosyl ester. A small amount of white solid was collected on the filter, and the solvent was removed at reduced pressure. Distillation of the residue gave a fraction, b.p. 43-45° (0.6 mm), weighing 0.91 g (80.4%) of a clear liquid; n20D 1.5097.

**Anal:** Calc. for C₁₁H₁₄O₁: C, 81.44%; H, 8.70%.

**Found:** C, 81.55%; H, 8.58%.

**trans-Pent-2-ene-4-ol**

This alcohol was prepared according to the
directions of Alexander and Kluiber (1, p. 4305). It was distilled as a water white liquid, b.p. 64-66° (64 mm); \( n^{20}D \) 1.4280. Yield 57%. This compound has been reported to have a boiling point of 116-121° (760 mm) and \( n^{20}D \) 1.4280 (1, p. 4305).

**trans-4-Chloropent-2-ene**

This halide was prepared according to the directions of Levene and Haller (30, p. 706). It was distilled as a water white liquid, b.p. 31-34° (54 mm); \( n^{20}D \) 1.5330. Yield 85%. This compound is reported to boil at 19-25° (20 mm) with \( n^{20}D \) 1.5337 (1, p. 4305).

**trans-4-Phenoxypent-2-ene**

This ether was prepared according to the directions of Alexander and Kluiber (1, p. 4305). It was purified by distillation, b.p. 48-48.5° (0.4 mm); \( n^{20}D \) 1.5101; yield 28%. It has been reported to have a boiling point of 72° (0.8 mm); \( n^{20}D \) 1.5110 (1, p. 4305).

**Rearrangement of cis-4-Phenoxypent-2-ene**

One molar solutions of cis-4-phenoxypent-2-ene in mesitylene (b.p. 162-165°) were refluxed in a nitrogen atmosphere for various lengths of time. The solvent was
removed at reduced pressure; the residual oil was taken up in 30 ml of hexane (b.p. 60-70°) and extracted with four 10 ml portions of 10% aqueous sodium hydroxide solution. The alkaline extracts were washed with 15 ml of hexane and acidified with cold 6N hydrochloric acid. After three extractions with 15 ml portions of hexane the combined extracts were dried over anhydrous magnesium sulfate, the solvent removed by evaporation and the phenol distilled, b.p. 68-70° (0.3 mm); \( n^{20\circ}D 1.5315 \).

The hexane solution containing the unreacted ether was washed with water and dried over anhydrous magnesium sulfate. Evaporation of the solvent left an almost colorless oil. The oil was distilled, b.p. 40-45° (0.5 mm); \( n^{20\circ}D 1.5090 \).

During the evaporation of the mesitylene at reduced pressure only negligible amounts of phenolic material were lost in the solvent as indicated by an exhaustive alkaline extraction of the condensed mesitylene. However, unreacted ether distilled with the mesitylene as indicated by an infrared analysis of the condensed solvent. Because of this loss of ether the percent reaction was based on the weight of isolated phenolic product.
Rearrangement of trans-4-Phenoxypent-2-ene

This rearrangement was carried out as described under the cis-ether. The phenolic residue was distilled at 64-65° (0.2 mm); n^{20\text{D}} 1.5333. The unreacted ether was also distilled, b.p. 45-50° (0.4 mm); n^{20\text{D}} 1.5091.

Infrared Analysis of cis- and trans-Ether Mixtures

The infrared analyses were made with a Perkin-Elmer Model 21 infrared spectrophotometer equipped with a sodium chloride prism. All determinations were made with a sodium chloride cell with a 0.025 millimeter spacer. The spectrum was run from 1100 cm\(^{-1}\) to 650 cm\(^{-1}\) using a resolution of 927, pen speed 1000, gain 6, response 1, speed 5 and suppression 5. The percent trans-4-phenoxy pent-2-ene was based on the peak occurring at 965 cm\(^{-1}\) (3, p. 45) and the percent cis-4-phenoxy pent-2-ene on the peak at 718 cm\(^{-1}\) (3, p. 48).

Table 1 contains the data used in establishing the standard curves.

Table 2 contains the experimental data for the unreacted cis- and trans-ethers.
Table 1

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<th>Solution Composition</th>
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<td></td>
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Table 2

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<th>trans-4-Phenoxyopent-2-ene</th>
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<td>68</td>
<td>cis</td>
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<tr>
<td></td>
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</table>
Methylation of the Phenolic Product from cis-4-Phenoxypent-2-ene

To a solution of 1.62 g (0.01 mole) of the phenolic product in 5 ml (0.0125 mole) of cold, aqueous 10% sodium hydroxide solution in a 50 ml round-bottom flask was added 1.2 ml (1.6 g; 0.0127 mole) of dimethyl sulfate. The mixture was stirred with a magnetic stirrer for one-half hour at room temperature and then warmed slowly to reflux, refluxed for one-half hour, 5 ml of 10% sodium hydroxide solution added and the solution refluxed for one-half hour more. After cooling the basic solution to room temperature it was extracted with three 20 ml portions of hexane (b.p. 60-70°). The combined hexane extracts were washed with three 30 ml portions of water and dried over anhydrous magnesium sulfate. Upon evaporation of the solvent there remained a colorless oil, b.p. 126-128° (30 mm); \( \rho^{20D} = 1.5192 \); yield 1.47 g (83.5%).

Methylation of the Phenolic Product from trans-4-Phenoxypent-2-ene

This product was methylated in exactly the same manner as the above phenolic material. Upon distillation it gave a water white liquid, b.p. 130-132° (30 mm); \( \rho^{20D} = 1.5181 \); yield 1.41 g (80.1%).
Investigation of Thermal *cis-trans* Isomerism

The following materials were heated eight hours in sealed tubes at 165-175°:

1) phenol from *cis*-ether -- contained about 5% *cis*-isomer.
2) phenol from *trans*-ether -- contained about 15% *cis*-isomer.
3) methyl ether of phenol in 1.

These results were obtained:

1) *cis*-isomer increased to about 15%.
2) composition did not change.
3) composition did not change.

Below are listed the two materials that were refluxed in mesitylene, b.p. 162-125°, for eight hours:

1) phenol from *cis*-ether -- contained about 5% *cis*-isomer.
2) methyl ether of phenol in 1.

These results were observed:

1) composition did not change.
2) composition did not change.
<table>
<thead>
<tr>
<th>Compound</th>
<th>Peaks (cm(^{-1}))</th>
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Table 3. Infrared Data
(2, p. 1876-1878)
(3, p. 34, 58, 65, 115, 162, 364)
SUMMARY

In order to examine the geometry of the transition state involved in the Claisen rearrangement trans-4-phenoxypent-2-ene (I) and cis-4-phenoxypent-2-ene (II) have been subjected to the Claisen conditions in refluxing mesitylene. The geometry about the allylic double in the phenolic product (III) and the unreacted ether has been investigated by infrared analysis.

It was found that I gave a product (III) in which the configuration about the double bond was higher in trans content than the product (III) from II, but that the trans isomer was predominant in both. This was
explained by an examination of the transition states available to both ethers. For the trans-ether a di-equatorial conformation and an axial equatorial conformation were available. The former was more favorable and led to trans-product; the latter to cis-product. In the case of the cis-ether an equatorial-axial conformation and a diaxial conformation were available. Again the more favorable former one led to trans-product; the latter to cis-product. Since the diaxial conformation for the transition state of the cis-ether is much less favorable than the axial-equatorial one for the trans-ether, there should be less cis-phenol from the cis-ether. This was observed as mentioned above.

Conversion of the cis-ether into the trans-isomer during the reaction was suggested to be due to neither thermal isomerism nor return from a dienone intermediate. Further, the limited data available suggested that the conversion was not due entirely to an interconversion of transition states, but probably also involved an acid catalyzed isomerism (autocatalytic).

No evidence could be found for the presence of phenolic products resulting from the abnormal Claisen rearrangement. It must be presumed that this reaction was not operative in this investigation.
A synthetic scheme was devised which would allow for the separation of optical isomers during the synthesis of the cis-ether (II). This separation would come after the introduction of the asymmetric carbon atom which would not be subjected to further reaction.
BIBLIOGRAPHY


