A thorough study of the electrocyclic reactions of pyrans 1, 6 and 11 was carried out. The effect of changing solvent polarity on the equilibrium between pyran 1 and its valence isomer was investigated. Change from tetrachloroethylene to pyridine caused an increase in the dienone concentration. However, the rates of interconversion were slightly greater in both directions in pyridine.
The NMR spectra of pyrans 6 and 11 showed reversible changes with heating which could be ascribed to reversible formation of their valence isomers. At 83° the equilibrium constant between pyran 6 and its valence isomer was 0.14 in triethylamine.

A kinetic method was developed and used to determine rates of ring opening for stable pyrans. The basic process is illustrated by the equation:

\[
\text{pyran} \xrightleftharpoons[k_1]{\text{dienone}} \xrightarrow{\text{reducing agent}} \text{alcohol}
\]

If the reducing agent reacts rapidly and is present in sufficient quantity, the overall rate of formation of alcohol will be equal to the rate of conversion of the pyran to its dienone. Rate measurements were made on pyran 1 using LiBH₄ in THF and LiAlH₄ in diethyl ether, and on pyrans 6 and 11 using only LiAlH₄ in ether. The results of these measurements are shown in the table.

<table>
<thead>
<tr>
<th>Pyran</th>
<th>Reducing Agent</th>
<th>Temp (°C)</th>
<th>(k_1 \times 10^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LiBH₄</td>
<td>40</td>
<td>9.4</td>
</tr>
<tr>
<td>1</td>
<td>LiBH₄</td>
<td>15</td>
<td>0.35</td>
</tr>
<tr>
<td>1</td>
<td>LiAlH₄</td>
<td>15</td>
<td>0.30</td>
</tr>
<tr>
<td>6</td>
<td>LiAlH₄</td>
<td>15</td>
<td>0.80</td>
</tr>
<tr>
<td>11</td>
<td>LiAlH₄</td>
<td>15</td>
<td>5.4</td>
</tr>
</tbody>
</table>
The alcohols which were isolated from preparative scale runs had structures which would be expected to result from 1,2 hydride addition to the acyclic valence isomers of pyrans 1, 6 and 11. Only a single isomer was formed in the case of pyran 11 indicating that only one of two possible disrotatory pathways is operating in the ring opening of that compound.
The Kinetics and Stereochemistry of Electrocyclic Ring Cleavage of Some 2H-Pyrans

by

Thomas Carl Chadwick

A THESIS

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The author would like to express his sincere appreciation to Dr. Elliot N. Marvell for his encouragement and for the continuing interest which he has shown in this work. The author would also like to thank his wife, Kristine, for her help in preparing this manuscript.
To Kristine
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</tbody>
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THE KINETICS AND STEREOCHEMISTRY OF 
ELECTROCYCLIC RING CLEAVAGE OF 
SOME 2H-PYRANS 

INTRODUCTION

Due largely to the frenetic activity which is so characteristic of organic chemistry in modern times, there are very few classes of simple monocyclic heterocycles which are largely or completely unknown. 2H-Pyrans, 2H-oxetes and 2H-oxocins belong to this select group of compounds. While there are roughly a score of 2H-pyrans known today, there were only one-half dozen or so simple pyrans known a decade ago. To date, only four clear cut examples of isolable oxetes and no oxocins have been reported in the literature.

2H-Oxete 2H-Pyran 2H-Oxocin

At first glance the lack of knowledge of these compounds is puzzling since the carbocyclic analogues are well known.

It has been suggested that the reason for the scarcity of these compounds lies in their inherent thermodynamic and kinetic instability (77, p. 2). Another possibility is a lack of interest attending this area of chemistry. A brief examination of the literature pertaining to these compounds suggests that the latter explanation is incorrect.
The suggestion has been made, based on the products isolated from attempted syntheses of pyrans and oxetes, that a likely route for decomposition of these heterocyclic compounds is electrocyclic ring cleavage. In this reaction a member of this series containing \( n \) double bonds will give rise to an acyclic product containing one carbonyl group conjugated with a system of \( n \) double bonds. The process is shown below for a 2H-pyran.

\[
\begin{align*}
\text{pyran} & \quad \xrightarrow{\text{reaction}} \quad \text{dienone}
\end{align*}
\]

A very rough thermodynamic calculation (based solely on bond energies) estimates the enthalpy of reaction proceeding from pyran to dienone as \(-8 \text{ Kcal/mole} \) (78, p. 163). This simple estimate does not consider energy terms due to electron delocalization, strain, steric factors or hybridization changes. Since the entropy change favoring the open chain isomer will be small, the free energy difference will also be relatively low. Under appropriate conditions both isomers should be present but it should also be possible to tip this free energy balance by structural changes (i.e., by changes in the energy terms neglected in the simple calculation), to favor one or the other isomer exclusively. It is obvious that for any member of this series of compounds the bond enthalpy difference between the
heterocyclic and acyclic valence isomers is a constant -8 Kcal/mole.

In spite of the apparent importance of electrocyclic reactions to the question of oxete, pyran, and oxocin stability and isolability, there have been very few studies of the electrocyclic ring openings which these compounds apparently undergo. Few efforts have been made to study the stereochemistry of these electrocyclic cleavages or the effect of substituent size at C-2 in any of these heterocyclic compounds on the rate of isomerization.

It was the aim of the present study to review what is known, at present, regarding the occurrence, stereochemistry and rates of electrocyclic reactions in oxetes, pyrans, and oxocins. It was the aim of the experimental portion of this work to study solvent and structural effects on the rates of the dienone-pyran electrocyclic reaction, of solvents on the position of equilibrium and of structural alteration on the stereochemistry of ring opening.
HISTORICAL

Introduction

The thermal and photochemical electrocyclic reactions of cyclobutene, cyclohexadiene, and cyclooctatriene and their derivatives are well known (144, 200).

Comparatively little is known about the corresponding reactions of oxetes, pyrans, and oxocins. Available information has been disguised under a wide variety of topics. In this review we will survey the information available regarding electrocyclic processes in these three types of heterocyclic compounds.

\[ \begin{align*}
4\pi & \leftrightarrow 2\pi + 2\sigma \text{ Processes - The Oxete Rearrangement} \\
\end{align*} \]

The oxete rearrangement provides us with an analogue of the cyclobutene - butadiene interconversion. Although direct observation
of the reaction has been reported only recently, a number of complex
reaction sequences are thought to involve such a rearrangement.
Büchi and coworkers were among the first to postulate the existence
of oxetes as intermediates in reaction sequences (36). They reported
that either benzaldehyde or acetophenone reacts with 5-decyne in the
presence of ultraviolet light (wavelength unspecified) to produce
α,β-unsaturated ketones by way of oxete intermediates.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{O} + \text{n-C}_4\text{H}_9\text{-C≡C-n-C}_4\text{H}_9 & \xrightarrow{h\nu} \text{Product} \\
\text{Product} & \xrightarrow{h\nu (?)} \text{α, β-unsaturated ketone}
\end{align*}
\]

R = CH₃, H

The major product of the reaction had a trans configuration for the
smaller of the two groups of the carbonyl entity and the n-butyl group.

A number of similar reactions have been reported using boron
trifluoride-etherate as a catalyst to effect the cycloaddition of the
acetylenic and carbonyl compounds (29). Vieregge, Bos and Arens
found that acetylenic ethers (ethoxy acetylene, for example) react
smoothly with carbonyl compounds at 0° to form α,β-unsaturated
esters (196).
Acetylenic thioethers were found to behave in a similar manner.

Boonstra and Arens reported that ethylthioethyne and acetone react with a catalytic amount of boron trifluoride to yield \( \beta,\beta \)-dimethylacrylate (23). Later work carried out by Bos and Arens demonstrated that the reaction of thioethers with carbonyl compounds catalyzed by boron trifluoride is a general one (25). Acetaldehyde, cyclopentanone, acetone, 2-butanone, crotonaldehyde, benzaldehyde, aceto-phenone and cyclohexanone, all react with ethynyl or propynyl ethyl thio ethers in yields from 3% to 89%.

Phenylacetylene was found to react with substituted benzaldehydes, chloral or benzophenone under the influence of boron trifluoride etherate (24, 26).

Reinvestigation of the reaction of ethoxyethyne with carbonyl compounds was carried out by Arens and coworkers (197). The reactions were generally run at \(-15^\circ\) to \(0^\circ\) in ether by adding an equivalent of 1-alkynyl ether to an equimolar mixture of boron trifluoride and the carbonyl compound.

Yields of products derived from aliphatic aldehydes were low
due to polymerization, but aliphatic \( \alpha, \beta \)-unsaturated aldehydes, aromatic and heterocyclic aldehydes and aliphatic or aromatic ketones all gave fair to excellent yields. The stereochemistry of the \( \alpha, \beta \)-unsaturated esters were studied for these cases where two isomers were possible. If an unsymmetrical ketone or an aldehyde was used and the groups adjacent to the carbonyl carbon differed greatly in size, then only one isomer was formed. The stereochemical results of this study and a similar one (25) performed on the reaction products of carbonyl compounds and alkyl thioacetylenes, are shown in Table 1.

The mechanisms of all the reactions discussed so far are thought to be similar.

\[
\begin{align*}
R^1 & \quad O \cdots BF_3 + HC\equiv C-XR^3 \\
R^2 & \quad \text{or } C_6H_5
\end{align*}
\]

\[X = O, \quad S\]

\[R^3 = C_2H_5^-, \quad C_3H_7^-\]

In the initial step, the ketone and the acetylenic compound undergo a boron trifluoride catalyzed cycloaddition. The second step is thought to involve a \( 2\pi + 2\sigma \rightarrow 4\pi \) thermal electrocyclic process.

Similar reactions have been reported involving yneamines and carbonyl compounds (67). Ficini and Krief reported the reaction of \( \alpha, \beta \)-unsaturated ketones and yneamines, catalyzed by boron trifluoride
Table 1. Stereochemical results of some oxetene ring cleavage reactions

A compound is said to have the trans configuration if it has the structure

where \( R^2 \) is larger than \( R^1 \).

<table>
<thead>
<tr>
<th>Carbonyl Component</th>
<th>Acetylenic Component</th>
<th>Product %</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{C}_6\text{H}_5\text{CHO} )</td>
<td>( \text{HC}=\text{CO}\text{C}_2\text{H}_5 )</td>
<td>trans 100</td>
</tr>
<tr>
<td>( 4\text{-CH}_3\text{O-C}_6\text{H}_4\text{CHO} )</td>
<td>&quot;</td>
<td>trans 100</td>
</tr>
<tr>
<td>( 4\text{-NO}_2\text{-C}_6\text{H}_4\text{CHO} )</td>
<td>&quot;</td>
<td>trans 100</td>
</tr>
<tr>
<td>( \text{CH}_3\cdot\text{CH=CH-COCHO} )</td>
<td>&quot;</td>
<td>trans 96</td>
</tr>
<tr>
<td>( \text{HC} \rightarrow \text{C} \rightarrow \text{O} )</td>
<td>Methoxypropyne</td>
<td>trans 100</td>
</tr>
<tr>
<td>( \text{i-C}_4\text{H}_9 )</td>
<td>&quot;</td>
<td>cis/trans 37:63</td>
</tr>
<tr>
<td>( \text{C}_2\text{H}_5\text{O-C-CH}_3 )</td>
<td>( \text{HC}=\text{C-OC}_2\text{H}_5 )</td>
<td>&quot; 15:85 GLC</td>
</tr>
<tr>
<td>( \text{C}_6\text{H}_5\text{O-C-CH}_3 )</td>
<td>&quot;</td>
<td>&quot; 17:83 NMR</td>
</tr>
<tr>
<td>( \text{i-C}_4\text{H}_9\text{C-CH}_3 )</td>
<td>( \text{CH}_3\text{C} \rightarrow \text{C-OC}_2\text{H}_5 )</td>
<td>&quot; 45:55</td>
</tr>
<tr>
<td>( \text{i-C}_4\text{H}_9\text{C-CH}_3 )</td>
<td>&quot;</td>
<td>&quot; 29:71</td>
</tr>
</tbody>
</table>

See reference #8

<table>
<thead>
<tr>
<th>Carbonyl Component</th>
<th>Acetylenic Component</th>
<th>Product %</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{CH}_3\text{CHO} )</td>
<td>( \text{CH}_3\text{C} \rightarrow \text{C-SC}_2\text{H}_5 )</td>
<td>trans 100</td>
</tr>
<tr>
<td>( \text{CH}_3\text{CH}_2\text{CH}_2\text{CHO} )</td>
<td>( \text{HC}=\text{C-SC}_2\text{H}_5 )</td>
<td>cis/trans 42:58</td>
</tr>
<tr>
<td>&quot;</td>
<td>( \text{CH}_3\text{C} \rightarrow \text{C-SC}_2\text{H}_5 )</td>
<td>&quot; 45:55</td>
</tr>
<tr>
<td>( \text{C}_6\text{H}_5\text{CHO} )</td>
<td>( \text{HC}=\text{C-SC}_2\text{H}_5 )</td>
<td>trans 100</td>
</tr>
<tr>
<td>&quot;</td>
<td>( \text{CH}_3\text{C} \rightarrow \text{C-SC}_2\text{H}_5 )</td>
<td>trans 100</td>
</tr>
<tr>
<td>( \text{p-NO}_2\text{C}_6\text{H}_4\text{CHO} )</td>
<td>( \text{HC}=\text{C-SC}_2\text{H}_5 )</td>
<td>trans 100</td>
</tr>
<tr>
<td>&quot;</td>
<td>( \text{CH}_3\text{C} \rightarrow \text{C-SC}_2\text{H}_5 )</td>
<td>trans 100</td>
</tr>
<tr>
<td>&quot;</td>
<td>( \text{HC}=\text{C-SC}_2\text{H}_5 )</td>
<td>Exo/Endo 55:45</td>
</tr>
</tbody>
</table>

See reference 25
The products were acrylamides. Kuehne and Scheeran reported the reaction of benzophenone with yneamines to yield both cyclobutenones and products derived from oxetes (123). Delaunois and Ghosez postulated a zwitterionic intermediate which could close to give either an oxete or a cyclobutenone (44).

\[
\begin{align*}
R_1^1 & \quad C=C=O + R-C≡C-N(C_2H_5)_2 & \quad BF_3 & \quad R_1^1 R_2^2 C \quad R_3^3 C=C=N(C_2H_5)_2 \\
C≡C=O & \quad + \quad R-C≡C-N(C_2H_5)_2 & \quad \Delta & \quad R_1^1 R_2^2 C \quad R_3^3 N(C_2H_5)_2
\end{align*}
\]

Fuks and Viehe have investigated the reaction of yneamines with ketones and aldehydes (66). Unlike the similar reactions of alkoxyacetylenes with carbonyl compounds, the yneamine additions only required 1-5 mole percent of boron trifluoride etherate as a catalyst. The stereochemical results are similar to those observed in the alkoxyacetylene reaction (see Table 2). Reaction of N,N-dimethylaminophenylacetylene with benzaldehyde gave a typical result. Only one isomer (cis) was produced. It was demonstrated that this compound and its trans isomer (produced by independent synthesis) did
### Table 2. Stereochemical results of some oxetene ring cleavage reactions.

<table>
<thead>
<tr>
<th>Carbonyl Component</th>
<th>Acetylenic Component</th>
<th>Product %</th>
</tr>
</thead>
<tbody>
<tr>
<td>C₆H₅CHO</td>
<td>C₆H₅C≡CNCH₃</td>
<td>trans 100</td>
</tr>
<tr>
<td>p-CH₃O-C₆H₅CHO</td>
<td></td>
<td>trans 100</td>
</tr>
<tr>
<td>2,3(CH₃O)₂C₆H₃CHO</td>
<td></td>
<td>trans 100</td>
</tr>
<tr>
<td>2,4(CH₃O)₂C₆H₃CHO</td>
<td></td>
<td>trans 100</td>
</tr>
<tr>
<td>C₆H₅CHO</td>
<td>CH₃C≡CN(C₂H₅)₂</td>
<td>trans 100</td>
</tr>
<tr>
<td>2,4(CH₃O)₂C₆H₃CHO</td>
<td></td>
<td>trans 100</td>
</tr>
<tr>
<td>CH₃(CH₂)₃CHO</td>
<td>C₆H₅C≡C(N(CH₃)₂)</td>
<td>trans 100</td>
</tr>
<tr>
<td>(CH₃)₂NCHO</td>
<td></td>
<td>trans 100</td>
</tr>
<tr>
<td>C₂H₅OCHO</td>
<td></td>
<td>trans 100</td>
</tr>
<tr>
<td>C₂H₅CHO</td>
<td>(CH₃)₂C≡C-N(CH₃)₂</td>
<td>trans 93%</td>
</tr>
<tr>
<td>2,4(CH₃O)₂C₆H₃CH₂CH₂CCH₃</td>
<td>C₆H₅C≡C-N(CH₃)₂</td>
<td>cis/trans 50:50</td>
</tr>
<tr>
<td>C₆H₅CH₃</td>
<td></td>
<td>cis/trans 17:83</td>
</tr>
</tbody>
</table>

*see reference 66*
not isomerize under conditions of the reaction. Equilibration with iodine showed that the cis product was the thermodynamically less stable isomer. The cis adduct must therefore be a result of kinetic control of ring opening of the oxete intermediate.

\[
\begin{align*}
C_6H_5C\equiv C-N(CH_3)_2 + C_6H_5CHO & \xrightarrow{BF_3} \xrightarrow{I_2, \Delta} \text{nitrobenzene} \\
\end{align*}
\]

Photochemical reactions of acetylenes with carbonyl compounds have been reported. The example found by Büchi and coworkers has been mentioned (36). Zimmerman and Kraft have discovered that p-benzoquinone reacts photochemically with diphenylacetylene to form a 1:1 adduct (201). The structure of the adduct and the postulated mechanism of formation are shown below.
The results of Zimmerman and Kraft were confirmed simultaneously by Bryce-Smith, Fray and Gilbert who also verified the structure of the adduct by reduction and identification of the reduced product (32, 201). Bryce-Smith, Gilbert and Johnson have reported a similar reaction between anthraquinone and diphenylacetylene (33).

The oxetes in the reactions shown above are presumed to exist, but they cannot be isolated. Analogous reactions (Paterno-Büchi) are known to occur between olefins and carbonyl compounds (179, 191). The resultant oxetanes are stable and can be isolated.

Photochemical additions of methylthiopropyne and 1-methoxypropyne to carbonyl compounds have been reported (27). The direction of photochemical addition is exactly opposite that of the boron trifluoride catalyzed addition.
The initial step in the sequence is thought to be an \( n \rightarrow \pi^* \) excitation of the non-bonding electron pairs on oxygen followed by spin inversion to form a triplet biradical. The biradical may then add to the acetylenic compound in either of two ways to yield biradicals which then close to give oxetes I and III and finally products II and IV. Evidently when methylthiopropyne is a reactant the biradical which gives rise to oxete I is much more stable than is the biradical which gives rise to oxete III. The reverse situation applies when 1-methoxypropyne is used as the reactant.

There are a few examples known of oxetes which can be isolated and whose thermal electrocyclic reactions can be observed directly. Rupe and Huber claimed the preparation of an oxete (163). Their claim is somewhat surprising considering the reported instability of recently characterized oxetes and their claim of preparation has been disputed (26, p. 848).

The first incontestable preparation of an oxete was reported by Middleton (129). Condensation at room temperature of hexafluoroacetone and ethoxyacetylene without catalyst or solvent gave only \( \beta,\beta\)-bis(trifluoromethyl)acrylate. The same reaction carried out at dry ice temperatures led to a new unstable substance which rearranged slowly at room temperature or very rapidly with the evolution of heat at 70° to form \( \beta,\beta\)-bis(trifluoromethyl)acrylate. NMR and IR data make it clear that the substance which was isolated
Table 3. NMR data for isolable oxetenes.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>δ4.60 (s)</td>
<td>(129)</td>
</tr>
<tr>
<td>δ4.85(s)</td>
<td>(194)</td>
</tr>
<tr>
<td>δ3.23</td>
<td>(97)</td>
</tr>
<tr>
<td>δ1.58 (m, J &lt; 1 Hz)</td>
<td>(63)</td>
</tr>
<tr>
<td>δ1.72 (m, J &lt; 1 Hz)</td>
<td></td>
</tr>
</tbody>
</table>
was indeed an oxete. The rearrangement reaction is that of the oxete undergoing an electrocyclic ring opening.

\[ \text{HC} = \text{C-OC}_2\text{H}_5 \]

Van den Bosch, Bos and Arens have reported a similar reaction between hexachloroacetone and ethoxyacetylene (194). Although the oxete was not isolated in this case, its formation and rearrangement to the acrylate ester was observed by NMR spectroscopy. These two examples are particularly important because they provide further evidence for the intermediacy of oxetes in boron trifluoride catalyzed condensations of alkoxy, thioalkoxy acetylenes, and yneamines with carbonyl compounds.

A stable oxete has been reported as one of the products of photolysis of cyclooctatetraene oxide (97). This oxete shows no tendency to rearrange under the conditions of rearrangement for the previous two examples.

Perhaps the most interesting example of oxete isolation and rearrangement is that of Friedrich and Schuster (63, 64). Irradiation of 3,4-dimethylpent-3-en-2-one through a vycor filter led to the formation of a new substance. Hydrogenation led to an oxetane whose
structure was verified by synthesis.

\[
\text{CH}_3\text{CH}=\text{CH}_2 + \text{H}_2/\text{Pd on CaCO}_3 \xrightarrow{\Delta} \text{CH}_3\text{CH}=\text{CH}_2
\]

Ring opening of the oxete in refluxing pentane had a half-life of approximately 12 hours. Kinetic measurements have shown that the rate of ring opening is not effected by changes in solvent polarity. That observation is consistent with an electrocyclic ring opening attended by little charge separation.

\[
6\pi \rightarrow 4\pi + 2\sigma \text{ Processes - The Pyran Rearrangement}
\]

Examples of electrocyclic processes involving pyrans are more numerous than examples of the closely related oxete rearrangements. Literature evidence through 1965 for thermal electrocyclic pyran reactions has been summarized by Gosink (77), but the reactions considered were only for simple pyrans. Related phenomena such as photochromism and thermochromism of spiropyrans were not considered. An attempt will be made in this section to summarize all the information not considered in Gosink's review relating to electrocyclic pyran reactions, both thermal and photochemical.
Simple Pyrans - Thermal Reactions

Electrocyclic reactions of pyrans are possibly involved in a number of more complex reactions. Some time ago Herzenberg and Gelas postulated such an electrocyclic process as one step in the complicated synthesis of pyridines from ammonia, aldehydes and ketones (73, 90). The first step of a rapid thermal rearrangement of pentaphenyl pentadienoic acid chloride has been interpreted as involving an electrocyclic pyran-forming reaction (11, 50, 51, 145).

Mousseron-Canet and coworkers found that the photochemical rearrangement of trans-β-ionone (37) works for related compounds as well (37, 132). The rearrangement of trans-β-inoic acid may proceed by way of an electrocyclic pyran-forming reaction.
Photolysis of conjugated unsaturated ketones has also been studied by Kluge and Llilya (119). Photolysis of 5-methyl-3, 5-heptadienone was reported to yield 2, 3, 6-trimethyl-2H-pyran. Similarly photolysis of 4, 6-dimethyl-3, 5-heptadienone yielded a mixture of 2, 2, 4, 6-tetramethyl-2H-pyran and 3, 4-dihydro-2, 2, 6-trimethyl-4-methylene-2H-pyran. The 2H-pyrans arise by electrocyclic ring closure of a dienone. An electrocyclic ring closure to a pyran followed by electrocyclic ring opening is used by the authors to explain the facile interconversion of cis, cis-dienones to cis, trans-dienones. Such a process has already been observed to proceed through a pyran intermediate.

Gelin and Gelin discovered that at 180° a thermal equilibrium exists between 2, 3-dihydro-4-pyrones and 1-penten-3, 5-diones (74, 75, 76).

An electrocyclic pyran reaction is probably involved (11).

Hutchinson and Tomlinson isolated a compound from the condensation reaction between mesityl oxide and 4-hydroxycoumarin and assigned it a pyran structure (110).
An electrocyclic reaction must close the initially formed dienone to form the product.

α-Pyrans have been suggested as intermediates in reaction sequences involving the addition of dihalocarbenes to furans and dihydrofurans using quinoline and benzonitrile as solvents (45, 165, 166).

A suggestion that the reaction proceeded through an ionic intermediate (1) was refuted by the study of Sarel and Rivlin (165). They succeeded in isolating a reactive intermediate whose gas chromatographic behavior suggested a pyran structure. Their structural assignment is questionable, however, since the reported UV spectral properties of the intermediate are not consistent with a pyran structure.
DeSelms and Kriebich (45) studied the kinetics of the reaction sequence in benzonitrile and found that rearrangement of the initial adduct of dichlorocarbene and dihydrofuran and not the electrocyclic ring opening was the rate determining step in that solvent.

Maier and Weissler reported the formation of equilibrium mixtures of pyrans and their valence isomers by pyrolysis of cis and trans substituted cyclobutene esters (125).

In the case where R = H an equilibrium between the dienones and the pyran was reported but no concentrations were specified. In the case where R = Me the pyran was present to the extent of 50% at equilibrium and the authors reported that it could be isolated by recrystallization from the reaction mixture.

Roedig and coworkers discovered a rearrangement of chlorinated aldehydes to acid chlorides which they explained by a series
of electrocyclic pyran reactions (150, 151).

\[
\begin{array}{c}
\text{Cl} \quad \text{Cl} \\
\text{Cl} \quad \text{Cl} \\
\text{Cl} \quad \text{Cl} \\
\text{Cl} \quad \text{Cl} \\
\end{array} \xrightarrow{\Delta, 4 \text{ hours}} \begin{array}{c}
\text{CHCl}=\text{CCl}=\text{CCl}=\text{CCl}=\text{COCl} \\
\text{Cl} \quad \text{Cl} \\
\text{Cl} \quad \text{Cl} \\
\text{Cl} \quad \text{Cl} \\
\text{Cl} \quad \text{Cl} \\
\end{array}
\]

2, 3, 4, 5, 5-Pentachloro-2, 4-pentadienal rearranges to 2, 3, 4, 5-tetrachloropentadienoyl chloride in four hours at the reflux temperature of carbon tetrachloride. Experiments with the aldehyde labelled (C\textsuperscript{14}) at C-5 indicate that the oxygen and the chlorine do indeed trade positions. Kinetic experiments gave a value for $\Delta H^\ddagger$ of 22.8 Kcal and for $\Delta S^\ddagger$ a value of -(8 to 11) entropy units (146, 147). The negative entropy of activation is strongly suggestive of a rate determining ring closure. The reaction rate was found to be independent of solvent, and radical initiators and scavengers had no effect on the rate. All of these data are strongly suggestive of a rate determining electrocyclic pyran ring closure.
Note that the mechanism indicated accomplishes transfer of a chlorine either by a concerted shift or by an ionization. It is not known whether either one or both of these pathways is operative (146).

The reaction has been applied to a number of compounds and these are shown in Table 4. Not all compounds which could rearrange in this manner do so. Sometimes cis → trans interconversions are competitive. In at least one case the aldehyde simply failed to react in any fashion after more than 100 hours in refluxing carbon tetrachloride (154).

If chlorinated cis-pentadienals are warmed with Lewis acids such as SbCl$_4$ or SbCl$_5$ (in CS$_2$) or FeCl$_3$ in a mixture of CS$_2$ and ether, pyrylium salts are formed. The pentadienal probably undergoes an electrocyclic ring closure and the resulting pyran loses a chloride ion to form the pyrylium salt (156, 157).

\[
\begin{align*}
R^1 &= \text{Cl, H, C}_6\text{H}_5 \\
R^2 &= \text{H, C}_6\text{H}_5
\end{align*}
\]
Table 4. Rearrangements of polychlorinated dienals.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>[diagram of rearrangement reactions]</td>
<td>150, 151</td>
</tr>
<tr>
<td>[diagram of rearrangement reactions]</td>
<td>153</td>
</tr>
<tr>
<td>[diagram of rearrangement reactions]</td>
<td>149</td>
</tr>
<tr>
<td>[diagram of rearrangement reactions]</td>
<td>152</td>
</tr>
<tr>
<td>[diagram of rearrangement reactions]</td>
<td>155</td>
</tr>
<tr>
<td>[diagram of rearrangement reactions]</td>
<td>148</td>
</tr>
<tr>
<td>[diagram of rearrangement reactions]</td>
<td>148</td>
</tr>
<tr>
<td>[diagram of rearrangement reactions]</td>
<td>148</td>
</tr>
<tr>
<td>[diagram of rearrangement reactions]</td>
<td>147</td>
</tr>
</tbody>
</table>
This result gives an additional reason for thinking that the aldehyde-acid chloride rearrangement may involve an electrocyclic ring closure.

A number of examples of electrocyclic pyran reactions are provided by the action of nucleophiles on pyrylium salts. Nucleophiles may attack pyrylium cations to yield either 2H or 4H pyrans. The 4H-pyrans are generally stable and can be isolated but in many instances the initially formed 2H-pyrans are able to react further (11). Balaban has arranged pyrylium salt reactions into three classes (10). Classification depends on the behavior of the 2H-pyran initially formed. Reactions of the first class consist of those which result in the formation of a pyran or its valence isomer only. Class two consists of reactions in which the pyran opens to its valence isomer and the new group (the nucleophile) is incorporated in a new heterocyclic ring. Class three reactions are like those of class two, however a side chain which was originally part of the pyrylium cation is incorporated into the ring of the final product. The three types of reactions are illustrated below.

Class I

![Diagram of Class I reactions](image-url)
The reaction of hydroxyl ion with 2, 4, 6-triphenylpyrylium perchlorate has been investigated by Griot, Royer and Dreux (80).

They claim that such a reaction leads to a mixture of isomers (II and IV) which is pH dependent.
Williams has studied the kinetics for the formation of pseudo bases of 2, 4, 6-trimethyl, 2, 4, 6-triphenyl and 2-methyl-4, 6-diphenyl pyrylium cations (199). The mechanism which he proposes is shown below.

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5 \\
\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5 \\
\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5
\end{align*}
\]

\[
\text{C}_6\text{H}_5 + \text{OH}^- \quad \text{C}_6\text{H}_5 \quad \text{C}_6\text{H}_5
\]

A similar study of the rate of hydrolysis of 2, 6-dimethyl-4-ethoxy and 4-ethoxy pyrylium cations was made by Salvadori and Williams (164). Attack by water (or hydroxide and water) can take place at either the 2 or 4 position leading ultimately to a 4-pyrone or a diketone.

The reactions of hydrazine (7, 8, 35), hydroxylamine (6, 143), ammonia (12), amines (188), amino acids (189), proteins (139), and hydrogen sulfide (11, p. 258), with pyrylium salts have been studied. All of these reactions proceed via class 2 processes. The initially formed pyrans are much less stable than the heterocyclic compounds which finally form.

Use of the nucleophiles listed above usually leads not to pyrans but other heterocycles (class II or III reactions) but if nucleophiles
such as borohydride ion or carbanions derived from aryl and alkyl lithium and Grignard reagents are used, usually only class I processes are observed (11). One major side reaction is attack in the 4 position. Some pyrylium salts react with these carbanionic and hydride donating reagents to yield 4H-pyrans exclusively (47, 49). In some cases 2H-pyran (159) or dihydropyrans derived from 2H-pyrans by allylic rearrangement are isolated (160).

In still other instances only dienones, derived by electrocyclic ring-opening of initially formed pyrans, or mixtures of pyrans and dienones are formed from reactions of pyrylium salts with nucleophiles (43, 48, 49).

Rather unlikely nucleophiles such as acetate ion (57), and iodide ion (9) are thought to react sometimes with pyrylium cations to form pyrans. Such process and subsequent electrocyclic reactions of the unstable pyran intermediate have been used to explain incorporation of deuterium in the 3 position of 2,6-diphenylpyrylium cation catalyzed by acetate ion.

Electrocyclic reactions are thought to accompany the formation of pyrans or dienones during the reaction of Grignard reagents with 2-pyrones. The reaction has been investigated by several workers (11, 77) and has been investigated in detail by Dreux and a number of his coworkers (52, 91, 130, 131, 158, 177, 178).
The proposed mechanism for the formation of pyrans and dienones is shown below:

Pyrans are sometimes isolated but the dienones derived from them are also isolated. The proposed mechanism accounts for this either by electrocyclic ring-closure of the dienone to the pyran or dehydration of a pyranol derived from an intermediate hydroxy ketone. Duperrier and Dreux considered a direct equilibrium between pyrans and dienones to be a distinct possibility and they have discussed the various steric factors which they feel determine whether an initially formed pyran will remain as a pyran or undergo an electrocyclic ring opening (53).
Further evidence for direct interconversion of pyrans into dienones is provided by work done by Royer and Dreux (161, 162). They have demonstrated that pyrans will react with Grignard reagents to produce doubly unsaturated alcohols. The only likely mechanism, based on their work, is shown below.

Simple Pyrans - Photochemical Reactions

While there are numerous examples of either confirmed or assumed electrocyclic reactions occurring in simple pyran ring systems there are very few examples of the corresponding photochemical process which have been reported. Becker and Mickl reported that if flindersine, a pyran, was subjected to ultraviolet irradiation in a rigid medium, a compound whose ultraviolet spectrum was consistent with a dienone structure was produced (18).

Flindersine
In a later investigation Becker and Kolc studied the photochemical behavior of 2-benzyl-2, 4, 6-triphenyl-2H-pyran, the corresponding thiopyran and 2, 4-dimethyl-2, 6-diphenyl-2H-pyran (17). Photolysis of the benzyltriphenyl pyran in a rigid or viscous medium at low temperature produced a yellow substance whose ultraviolet-visible spectrum was consistent with a dienone structure. The original substance was regenerated by heating and the cycle could be repeated several times with little apparent change. The thiopyran reacted similarly. 2, 4-Dimethyl-2, 6-diphenyl-2H-pyran also yielded a dienone but side products were also formed.

$$\begin{array}{c}
\text{R}_1 \text{R}_2 \text{R}_3 \text{R}_4 \\
\text{X}
\end{array}$$

$$\begin{array}{c}
\text{R}_1 \text{R}_2 \text{R}_3 \text{R}_4 \\
\text{X}
\end{array}$$

<table>
<thead>
<tr>
<th>R$^1$</th>
<th>R$^2$</th>
<th>R$^3$</th>
<th>R$^4$</th>
<th>X</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$_6$H$_5$CH$_2$-</td>
<td>C$_6$H$_5$-</td>
<td>C$_6$H$_5$-</td>
<td>C$_6$H$_5$-</td>
<td>O</td>
</tr>
<tr>
<td>&quot;  &quot;  &quot;  &quot;  &quot;</td>
<td>S</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$_6$H$_5$-</td>
<td>CH$_3$-</td>
<td>CH$_3$-</td>
<td>C$_6$H$_5$-</td>
<td>O</td>
</tr>
</tbody>
</table>

**Kinetic Studies**

Although kinetic data are still scarce for these pyran reactions, some have been gathered and some conclusions regarding the nature of electrocyclic transformations can be made.
The kinetic results of Roedig and coworkers have been mentioned but lack of direct observation of dieneone-pyran interconversion renders the data less useful than it could be.

Marvell and coworkers reported the first direct observation of the thermal interconversion of a pyran (1-oxa-2, 5, 5, 9-tetramethyl-1, 5, 6, 7, 8, 10-hexahydronaphthalene) (I) and its valence isomer (II) (77, 127).

\[
\begin{align*}
\text{(I)} & \quad \overset{\Delta}{\rightarrow} \quad \text{(II)} \\
\end{align*}
\]

Büchi and Yang reported that trans-β-ionone yields, upon photolysis, several products. To one of these they assigned the pyran structure (I). No evidence was found to indicate the existence of cis-β-ionone. Marvell and coworkers found that if pyran (I) was heated and a NMR spectrum taken of the warm material several extraneous lines appeared in the normal pyran spectrum. As the temperature increased the lines grew at the expense of pyran absorptions. Upon cooling the spectrum slowly returned to its former state and the process could be repeated several times. These changes were interpreted as being due to a reversible thermal equilibrium between the pyran (I) and cis-β-ionone (II). The
kinetics of the interconversion were measured by heating the pyran (dissolved in $\text{C}_2\text{Cl}_4$) to $120^\circ$ to produce appreciable quantities of its valence isomer. The sample was then thermostatted at the temperature of interest and the reaction was followed by observing changes in the spectrum of the dienone as a function of time. Both rate and equilibrium constants were obtained for the reaction. The reaction has since been studied in several solvents and it has been demonstrated that changing solvent polarity has little effect on either the rate or equilibrium constants (60, 128).

It is interesting to note that there is now one other report of a thermal equilibrium between an $\alpha$-pyran and cis-dienone (118). Photolysis of 5-methyl-3, 5-heptadienone in ether is reported to yield 5-methyl-3, 5-heptadienone and 2, 3, 6-trimethyl-2H-pyran. Evidence has been found which indicates that the pyran is not a single substance but consists of an equilibrium mixture of pyran (87%) and dienone (13%). No kinetic data were presented.

Gosink was able to isolate 2, 4, 6-trimethyl-2H-pyran at low temperatures and spectroscopically follow the kinetics of its isomerization (77). These two preceding cases are somewhat unusual in that the major isomer in either case studied could be isolated (if only for a moment) and the progress of the reaction could be followed by directly observing the disappearance of this unstable isomer. Schiess and coworkers have measured the rates of electrocyclic ring
closure of a number of substituted pentadienals by measuring the rate of cis $\rightarrow$ trans isomerization (169, 170, 171). They have been able to show that the process proceeds through a pyran intermediate. In some cases these intermediates have been trapped as Diels-Alder adducts with tetracyanoethylene. This technique is interesting since it provides a way to measure a reaction involving the formation of a pyran which is usually present in such small concentration that it can not be detected. All of the results of the kinetic studies of pyran electrocyclic reactions which have been studied so far appear in Tables 5A and 5B.

Kinetic studies by Maier and coworkers indicate that thermal pyran ring closure is a non-radical, non-ionic process (146, 147). The non-ionic nature of the process is supported by kinetic results obtained by Chadwick and Flannery (60, 128).

Benzopyrans - Thermal Rearrangements

![Diagram of 2H-pyran and 2H-1-benzopyran (chromene)]

Benzopyrans, unlike the simple 2H-pyrans, are well-known stable substances. This stability could, in part, be attributed to their inability to enter into the electrocyclic reactions which
Table SA. Selected kinetic data for electrocyclic pyran ring closure.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>k x 10^5 (sec^-1)</th>
<th>ΔH° (kcal/mole)</th>
<th>ΔS° (e.u.)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Isooctane</td>
<td>57.8</td>
<td>4.35</td>
<td>22.4 ± 0.2</td>
<td>-10.6 ± 0.5</td>
<td>(170)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>67.3</td>
<td>11.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>77.5</td>
<td>31.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>57.8</td>
<td>4.35</td>
<td>22.4</td>
<td>-11.5</td>
<td>(171)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>67.3</td>
<td>11.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>77.5</td>
<td>15.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>59.0</td>
<td>7.37</td>
<td>21.8</td>
<td>-12.1</td>
<td>(171)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>68.8</td>
<td>18.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>78.0</td>
<td>46.1</td>
<td></td>
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<tr>
<td></td>
<td>Ethylene Chloride</td>
<td>18.0</td>
<td>140</td>
<td>(E_a) 20</td>
<td></td>
<td>(127)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0</td>
<td>15.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.0</td>
<td>35.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>18.0</td>
<td>139</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pyridine</td>
<td>0.0</td>
<td>6.8</td>
<td></td>
<td></td>
<td>this</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18.0</td>
<td>75</td>
<td></td>
<td></td>
<td>work</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>25.0</td>
<td>10 to 30</td>
<td></td>
<td></td>
<td>(60)</td>
</tr>
<tr>
<td></td>
<td>Carbon Tetrachloride</td>
<td>25.0</td>
<td>750</td>
<td>22.8</td>
<td>-8 to -11</td>
<td>(147)</td>
</tr>
<tr>
<td></td>
<td>2-Propanol</td>
<td>25.0</td>
<td>750</td>
<td>11</td>
<td></td>
<td>(60)</td>
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<tr>
<td></td>
<td>Benzene</td>
<td>25.0</td>
<td>950</td>
<td>11</td>
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</tr>
<tr>
<td></td>
<td>Ethanol</td>
<td>25.0</td>
<td>3.76</td>
<td>(E_a) 24.7</td>
<td>9.0</td>
<td>(60)</td>
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<tr>
<td></td>
<td>Acetone</td>
<td>25.0</td>
<td>47.3</td>
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<tr>
<td></td>
<td>Chloroform</td>
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<td>133</td>
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<tr>
<td></td>
<td>Carbon Tetrachloride</td>
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<td>211</td>
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<tr>
<td></td>
<td>Benzene</td>
<td>25.0</td>
<td>1120</td>
<td>16.5</td>
<td>-7.2</td>
<td></td>
</tr>
</tbody>
</table>
Table 5B. Selected kinetic data for electrocyclic pyran ring opening.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>k rate (\times 10^{-5}) (sec(^{-1}))</th>
<th>(E_a) (kcal/mole)</th>
<th>(S \times (e.u.))</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylene Chloride</td>
<td>Ethylene Chloride</td>
<td>18</td>
<td>1.3</td>
<td>27</td>
<td></td>
<td>(127)</td>
</tr>
<tr>
<td>&quot;</td>
<td>Ethylene Chloride</td>
<td>0</td>
<td>0.066</td>
<td></td>
<td></td>
<td>(128)</td>
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<tr>
<td>&quot;</td>
<td>Ethylene Chloride</td>
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<td>0.25</td>
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</tr>
<tr>
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<td>Ethylene Chloride</td>
<td>18</td>
<td>1.31</td>
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</tr>
<tr>
<td>Pyridine</td>
<td>Pyridine</td>
<td>0</td>
<td>0.062</td>
<td></td>
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<td>this work</td>
</tr>
<tr>
<td>&quot;</td>
<td>Pyridine</td>
<td>18</td>
<td>1.30</td>
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<tr>
<td>Tetrahydrofuran</td>
<td>Tetrahydrofuran</td>
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<td>9.1</td>
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</tr>
<tr>
<td>&quot;</td>
<td>Tetrahydrofuran</td>
<td>15</td>
<td>0.35</td>
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<tr>
<td>Diethyl ether</td>
<td>Diethyl ether</td>
<td>15</td>
<td>0.32</td>
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<td>Pentane</td>
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<td>(77)</td>
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<tr>
<td>Diethyl ether</td>
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<td>this work</td>
</tr>
<tr>
<td>&quot;</td>
<td>Diethyl ether</td>
<td>15</td>
<td>5.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethanol</td>
<td>Ethanol</td>
<td>25</td>
<td>0.032</td>
<td>26.8</td>
<td>6.6</td>
<td>(60)</td>
</tr>
<tr>
<td>Acetone</td>
<td>Acetone</td>
<td>25</td>
<td>0.063</td>
<td>25.7</td>
<td>4.4</td>
<td></td>
</tr>
<tr>
<td>Chloroform</td>
<td>Chloroform</td>
<td>25</td>
<td>0.013</td>
<td>23.8</td>
<td>-5.2</td>
<td></td>
</tr>
<tr>
<td>Benzene</td>
<td>Benzene</td>
<td>25</td>
<td>0.046</td>
<td>20.9</td>
<td>-12.5</td>
<td></td>
</tr>
</tbody>
</table>
occur so readily in simple pyrans. The benzopyrans would thus seem to be unlikely candidates for study as far as electrocyclic pyran reactions are concerned. In spite of this, there is a growing body of evidence which would indicate that the same thermal and photochemical reactions which occur in simple pyrans also occur in benzopyrans. Admittedly, the opening of a benzopyran ring occurs infrequently and only at elevated temperatures, but the reverse reaction is thought to occur in a number of reactions.

\[
\begin{align*}
\text{Thermal ring closure of quinone methides has long been} \\
\text{postulated as a route whereby naturally occurring chromenes were} \\
\text{thought to arise from phenols by oxidation of the phenol to a quinone} \\
\text{methide followed by ring closure to form the benzopyran (141, 190).}
\end{align*}
\]

\[
R = H, \text{ alkyl group}
\]

Campbell, Calzadilla and McCorkindale observed such a reaction during the cyclization of ethylmycophenolate with
dichlorodicyanobenzoquinone (DDQ) (38).

\[ \text{DDQ} \]

The reaction has been used to prepare naturally occurring chromenes such as D, L-cannabichromene, franklinone, alloevodionol, evodionol methyl ether, flemigen C trimethyl ether (39) and flindersine (28).

The preparation of chromenes by the dehydration of phenolic cinnamyl alcohols has been recently reported (133). This reaction could possibly involve dehydration of the phenolic cinnamyl alcohol to form a quinone which would then cyclize to form a chromene.
This scheme also suggests another possibility for the biosynthesis of natural chromenes.

Heaney and Jablonski observed the formation of a chromene as the result of an electrocyclic reaction of a dienone (88). The addition of \( \alpha, \beta \)-unsaturated aldehydes to benzyne leads initially to an oxete and then to the dienone which cyclizes to the pyran.

![Chemical structure]

The reaction is unusual because if it goes by the proposed pathway it involves both \( 4\pi \) and \( 6\pi \) electrocyclic processes in the same reaction sequence.

Thermal rearrangements of o-dienylphenols, propargyl phenolic ethers, and allenic phenolic ethers to form benzopyrans probably involve an electrocyclic pyran formation as the last step in the reaction sequence (83, 84, 86). The rearrangements of phenyl propargyl ethers, observed by Iwai and Ide (110) and Thyagarajan, Balasubramania and Rao (187) are thought to proceed by the
mechanism shown below (95, 202).

Both cis-o-1, 3-pentadienyl phenols and trans-o-1, 3-pentadienyl phenols react to yield 2-ethyl-Δ^3-chromene. Replacement of the phenolic hydrogen with deuterium results in incorporation of deuterium in the product. The trans isomers isomerize only at much higher temperatures than the cis isomers. These reactions are also thought to proceed through quinone-methide intermediates (99).
The cyclization of \(\alpha\)-cis butadienyl phenol has been investigated by Schweizer, Crouse and Dalymple (180). Kinetic investigation of the reaction in various solvents showed that there was a rate increase with decreasing solvent polarity. The reaction has an activation enthalpy of 23 Kcal/mole and an activation entropy of -17 e.u. in DMSO.

![Chemical structure](image)

The recently discovered thermal rearrangement of cyclopropa-(c)chromenes in N, N-diethylaniline to form 2-alkyl-2H-chromenes is a reaction which is similar in nature to those discussed previously (98).

![Chemical structure](image)

All of the previous examples involved only thermal ring closures. One example of thermal ring opening is known, however. If \(\alpha\)-cis-(phenyl-butadienyl)phenol is heated to 200° an equilibrium mixture of the phenol and the corresponding chromene is established (85,
Photochemical electrocyclic reactions of pyrans are well known. Becker and Mickl reported that 2H-benzopyran, 2, 2-di-ethyl-2H-pyran, and a number of other simple benzopyrans formed new colored substances when irradiated in a rigid matrix or viscous solution at low temperature. The ultraviolet absorption spectra of these colored substances were consistent with a dienone structure (18).

The benzopyrans could be regenerated by simply allowing the matrix to warm to room temperature. Becker and Mickl interpreted these
phenomena to mean that an electrocyclic ring cleavage occurred upon photolysis and an electrocyclic ring closure to regenerate the pyran occurred when the matrix was allowed to warm up.

Confirmation of the structures of the colored compounds was obtained by reducing three of them at low temperatures with lithium aluminum hydride in 2-methyltetrahydrofuran. Under the same conditions the benzopyran itself gave no reduction products (121). The structures of the reduced photoproducts indicate that the proposed dienone structure of the photoprodud is correct.

Flannery has obtained kinetic data on the thermal ring closure of 2, 2-diphenyl-5, 6-benzo-2H-benzopyran by first photolyzing it to
obtain the open chain valence isomer and then following its rate of
disappearance by monitoring the ultraviolet-visible absorption
spectrum (60).

**Spiropyran**

Electrocyclic pyran reactions have been implicated in thermal
(42, 135) and photochemical (31, 46, 56) color reactions of spiro-
pyrans.

Spiropyran (I), indolinospiropyran (II), benzothiazolinospiro-
pyran (III), and benzoselenazospiropyran (IV) exhibit either thermal
color reactions (thermochromic reaction) or photochemical color
reactions (photochromic reactions) or both.

In all cases these reactions have been attributed to electrocyclic
rupture of the pyran ring to form highly colored open chain quinones.

Studies carried out by Hirshberg and Fisher (93, 94) have shown that
the thermally and photochemically produced products are identical.

Additional support for the proposed structures of the colored molecules has been given by the previously mentioned work of Kolc and Becker (121).

**Spiropyrans - Thermal Reactions**

Recent studies of pyran thermochromism have been aimed at establishing the nature of the open chain quinone. Although early experiments pointed to the possibility of the quinone actually being a biradical, recent experiments seem to indicate otherwise (60).

That the quinones derived from spiropyrans by thermal electrocyclic cleavage have considerable polar character can be shown by their ability to form salts (3, 21, 137, 173, 174, 176), chelates (175, 186), and their absorption with color change on polar surfaces such as silica gel (14, 15, 55, 113, 135, 198), and zinc oxide (112, 136).

![Chemical structure](image)

Direct observation of the equilibrium between the two valence isomers has usually been followed by ultraviolet-visible spectroscopy
but observation of the electrocyclic interconversion of a pyran and its valence isomer using nuclear magnetic resonance spectroscopy has been reported in one instance (140). Isolation of the colored thermal reaction product(s) has also been reported in one instance (167).

It has become apparent from recent investigations that there are several colored conformers usually present in equilibrium with the pyran. Such a suggestion had been advanced to explain the temperature and solvent dependency of the UV-visible spectra of the colored forms of a number of different pyrans (16, 19, 20, 54, 68, 72, 124, 168).

Spiropyrans - Kinetic Studies of Thermal Reactions

Numerous kinetic studies of the thermal spiropyran-quinone interconversion have been made. Although the ring opening process has been studied, the reverse process is more generally studied. Electronic substituent effects on the rate of thermal decolorization (ring closure) for a series of indolinospiropyrans have been studied by Berman, Fox and Thomson (22). A similar study has been made by Guglielmetti and coworkers on the thermal decolorization of a series of benzothiazolino spiropyrans (81).

Kinetic data on ring closure and opening have been obtained in a variety of different solvent systems, polymers (60, 71, 173) and
even in the solid state (120). All of the kinetic data regarding solvent and substituent effects seem to indicate that there are usually several colored valence isomers in thermal equilibrium with the parent spiro-pyran and also that these colored isomers have considerable ionic character.

**Spiropyrans - Photochemical Reactions**

The primary process in the photochemical reaction of spiropyrans is of the same nature as the thermal process; the pyran ring is cleaved between the oxygen and the adjacent sp\(^3\) hybrid carbon atom. The identity of the products of this reaction and those of the thermal reaction has been discussed (93, 94). No evidence has been found which would implicate radical intermediates in the photochromic reactions of spiropyrans (198). If the photoproduct is irradiated for prolonged periods or if the pyran is subjected to high energy bursts of ultraviolet radiation then irreversibly formed decomposition products are obtained (2, 65, 69).

Recent investigations of photochemical electrocyclic pyran reactions have been designed to determine the nature of the transitions and any intermediates involved in the reactions (5, 192, 193, 198).

It should be mentioned that electrocyclic pyran reactions have their practical aspects too. No fewer than 75 patented devices and
processes, all based on spiropyran photo and thermochromic reactions, appear in the literature (1964 to present). Spiropyrans have found uses in photographic systems (138), lithography (34), safety glasses (195), and even cosmetics (117).

\[ 8\pi \rightarrow 6\pi + 2\sigma - \text{The Oxocin Rearrangement} \]

Any discussion of electrocyclic processes occurring in the 2H-oxocin ring system must be brief since to date, no examples have been reported in the literature. Furthermore, no syntheses of the oxocin half of the reaction pair have been reported.

Paquette and Begland came very close to carrying out a synthesis of 2H-oxocin during the synthesis of a tetrahydrooxocin (142).

Application of the Hoffman reaction to generate 2H-oxocin is a much too obvious possibility to have been ignored by these investigators and
it can only be assumed that the reaction, when tried, looked very unpromising.

In a recent investigation of the gas-phase pyrolysis of 1, 2-epoxy-3, 5-cycloheptadiene no trace of 2H-oxocin or its valence isomer was found (172). These products could be expected to result from such a reaction in the light of a similar reaction which has been investigated for 1, 2-epoxy-3-cyclopentene.

![Reaction Diagram](image)

The matter cannot be considered settled without further investigation because at the temperature of pyrolysis (~400°) the probability of survival of either 2H-oxocin or its valence isomer would be unquestionably low.

One further interesting case is the attempted cyclization of cis, cis-2, 3, 4, 5, 6, 7, 7-heptachloro-2, 4, 6-heptatrienial and the closely related 2, 3-dibromo-4, 5, 6, 7, 7-pentachloro-2, 4, 6-heptatrienial. Both compounds stubbornly resisted $8\sigma \rightarrow 6\pi + 2\sigma$ cyclization, or for that matter, the aldehyde acid chlorid rearrangement ($6\pi \rightarrow 4\pi + 2\sigma$ cyclization) even after 100 hours at the normal boiling
point of carbon tetrachloride (154).

\[
\begin{array}{c}
\text{Cl} & \text{Cl} & \text{Cl} & \text{Cl} \\
\text{Cl} & \text{Cl} & \text{Cl} & \text{Cl} \\
\text{Cl} & \text{Cl} & \text{Cl} & \text{Cl}
\end{array}
\rightarrow \text{no reaction}
\]

\[
\begin{array}{c}
\text{Br} & \text{Br} & \text{Br} & \text{Br} \\
\text{Cl} & \text{Cl} & \text{Cl} & \text{Cl} \\
\text{Cl} & \text{Cl} & \text{Cl} & \text{Cl}
\end{array}
\rightarrow \text{no reaction}
\]
DISCUSSION

Introduction

Although 2H-pyrans have been proposed as reactive intermediates for some time, stable examples of this class of heterocyclic compounds have been known only since the beginning of the last decade. Even now there is some question regarding the identity of compounds to which the pyran structure has been assigned. Also, only a few investigations have been made of the electrocyclic reactions of 2H-pyrans (17, 18, 60, 127, 161, 162, 169, 170, 171). Specific aims of the present investigation were:

1) To examine the effect of increasing solvent polarity on the rates of pyran-dienone interconversion and also on the pyran-dienone equilibrium.

2) To repeat the syntheses and verify the structures of two stable compounds which reportedly possess the 2H-pyran structure.

3) To discover whether traces of valence isomer do indeed exist in equilibrium with the stable pyrans synthesized in part (2).

4) To discover the effect of substituents at C-2 of the pyran ring on the course of the pyran cleavage reaction.
Effect of Increasing Solvent Polarity on Pyran-Dienone Conversion Rates and Equilibrium

Büchi's pyran, 1, was chosen for solvent effect studies since it was the only 2H-pyran which (at that time) was known to be in equilibrium with considerable quantities of its valence isomer at moderate temperatures. Also a usable kinetic method had already been devised in a previous investigation and data had been collected using tetrachloroethylene as a solvent (127).

Synthesis and isolation of the compound were carried out in the manner described by Büchi and Yang (37).

The technique used for measuring pyran-dienone interconversion kinetics consisted of simply heating a solution of the pyran in a suitable solvent to produce an appreciable concentration of the valence isomer, quenching the sample in a dry ice-acetone mixture to fix the concentrations of the two compounds, and then rethermostatting at the temperature of interest and monitoring the disappearance of the dienone by making repetitive NMR scans at known time intervals. The results of kinetic and equilibrium measurements made in pyridine
(dielectric constant, $\varepsilon = 12.3$ at $25^\circ$) (96) and tetrachloroethylene (TCE, $\varepsilon = 2.46$ at $20^\circ$) (134) are presented in Table 6.

There appears to be an increase in both the equilibrium and rate constants in pyridine but the changes are not large. Apparently the equilibrium involves two molecules which are essentially uncharged. Spiropyrans, on the other hand, exhibit rather large changes in the dielectric constants of solvents. Table 7 lists some representative examples found by Flannery for $1',3',3'$-trimethyl-6-nitrospiro(2H-benzopyran-2,2'-indoline). The quinone isomer of the pyran is thought to have considerable ionic character and this idea is supported by the response of the equilibrium constant to increasing solvent polarity (60). Flannery has also confirmed the observations made in this study regarding the Büchi pyran equilibrium and its response to changes in solvent polarity.

Attention was next given to 2, 2, 4, 6-tetramethyl-2H-pyran, 6. This stable compound is reportedly formed as a by-product of the industrial base-catalyzed acetone alcohol synthesis. The compound was prepared as described by Hinnen and Dreux (91). This synthesis produces not only pyran 6 but also an equimolar quantity of 2, 2, 6-trimethyl-4-methylene-2H-pyran, 8. The two isomers could not be separated by distillation but gas chromatographic separation on an Apiezon M column was possible. The spectral properties of the two compounds were exactly as given by Hinnen and Dreux.
Table 6. Equilibrium and rate constants for pyran $\xrightarrow{k_f}^k_r$ dienone reaction.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Temp. (°C)</th>
<th>$K_{eq}$</th>
<th>$k_f \times 10^4$ (sec$^{-1}$)</th>
<th>$k_r \times 10^4$ (sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCE*</td>
<td>0</td>
<td>0.054</td>
<td>0.086</td>
<td>1.58</td>
</tr>
<tr>
<td>Pyridine*</td>
<td>0</td>
<td>0.091</td>
<td>0.322</td>
<td>3.51</td>
</tr>
<tr>
<td>TCE‡</td>
<td>8</td>
<td>0.070</td>
<td>0.25</td>
<td>3.57</td>
</tr>
<tr>
<td>Pyridine*</td>
<td>8</td>
<td>0.14</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>TCE‡</td>
<td>18</td>
<td>0.0943</td>
<td>1.31</td>
<td>13.9</td>
</tr>
<tr>
<td>Pyridine*</td>
<td>18</td>
<td>0.17</td>
<td>1.07</td>
<td>6.21</td>
</tr>
<tr>
<td>TCE‡</td>
<td>54</td>
<td>0.217</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>TCE‡</td>
<td>113</td>
<td>0.658</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

*Marvell, Caple, Gosink, and Zimmer, unpublished results.
*This work

Table 7. Values of equilibrium and rate constants for system Spiropyran $\xrightarrow{k_f}^k_r$ Quinone

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Dielectric Constant</th>
<th>Temp. (°C)</th>
<th>$K_{eq} \times 10^5$</th>
<th>$k_f \times 10^6$ (sec$^{-1}$)</th>
<th>$k_r \times 10^4$ (sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$_6$H$_6$</td>
<td>2.284</td>
<td>25</td>
<td>4.10</td>
<td>4.6</td>
<td>1120</td>
</tr>
<tr>
<td>CHCl$_3$</td>
<td>4.8</td>
<td>25</td>
<td>9.76</td>
<td>1.3</td>
<td>133</td>
</tr>
<tr>
<td>(CH$_3$)$_2$C=O</td>
<td>20.7</td>
<td>25</td>
<td>20.7</td>
<td>6.3</td>
<td>47.3</td>
</tr>
</tbody>
</table>
were no extraneous peaks in the NMR spectrum of 6 taken at about 35° which could be attributed to the valence isomer 7.

Equilibrium studies of pyran 6 were initially tried in tetra-chloroethylene but they failed repeatedly. All attempts to observe an electrocyclic reaction of the pyran were obscured by rapid rearrangement of 6 to 8. The isomerization has been observed by others and is thought to be acid catalyzed (158).

The rearrangement of 6 into 8 proceeds even at room temperature and it was necessary to store freshly prepared 6 at liquid nitrogen temperatures to prevent rearrangement. Careful washing of glassware with aqueous ammonia and the use of pyridine as a solvent eliminated the troublesome rearrangement. With the assistance of the Computer of Average Transients (CAT), several small, reversibly formed peaks in the NMR spectrum at δ1.20 and δ2.06 were detected at elevated temperatures (~80°C). In another experiment NMR spectra taken at ~35°, ~83° and again at 35° using triethylamine as a solvent clearly demonstrate the reversible formation of peaks at δ1.95, δ2.06, δ2.19, δ5.87 and δ6.24. The peaks at δ5.87
and 56.24 are probably the olefinic protons in the dienone. The equilibrium constant, obtained from the integrations of olefinic protons in the pyran and dienone, is 0.14 at 83° in triethylamine.

Variable temperature experiments performed using triethylamine and pyridine as solvents seem to indicate that 2,4-dimethyl-2,6-diphenyl-2H-pyran is also in equilibrium with a small quantity of its valence isomer at elevated temperatures. In triethylamine two small absorptions at 56.64 and 56.88 grow in size with increasing temperature. Comparison of spectra obtained at 30°, 80° and again at 30° indicate that the process is completely reversible. Unfortunately, signals in the methyl region are obscured by solvent absorption lines. Similar spectra obtained in pyridine at 30°, 80°, 100° and again at 30° show that a small absorption at 61.54 grows in size with increasing temperature and then resumes its initial size upon cooling to the initial temperature. The development of some color and the appearance of several extraneous signals in the NMR spectrum after the high temperature run indicate that some
irreversible decomposition accompanies the reversible reaction in pyridine.

Since only small amounts of the dienones are produced even at high temperature, the kinetic method used by Marvell, Caple, Gosink and Zimmer is unadaptable to the present cases. Further attempts to study the kinetics of interconversion of pyrans and dienones by that method were therefore abandoned.

**Kinetic Studies of Electrocyclic Ring Cleavage Reaction**

There are actually two parts to the problem of measuring rates of interconversion of two compounds A and B which are related to one another by reversible first order reactions. In the first case, both compounds A and B can exist in a mixture in appreciable quantities. In the second case, either compound A or compound B is the only compound present to any measurable extent. The methods for obtaining kinetic data in the first case and in the latter case differ markedly.
If measurable amounts of both A and B are present then kinetic measurements are straightforward.

\[
A \xrightarrow{k_f} B \quad \text{where} \quad K_{\text{eq}} = \frac{[B]}{[A]} = \frac{k_f}{k_r}
\]

In the present case the system is diverted from equilibrium at the temperature of interest by heating the mixture and reestablishing thermal equilibrium at that temperature, and the rate of reversion to equilibrium can then be followed spectroscopically. Exact solutions for the case of simple, reversible first order reactions are well known. This technique has been used by Marvell and coworkers to study rates of interconversion of Büchi's pyran and cis-β-ionone. The rate of reversion to equilibrium was followed by NMR spectroscopy.

Techniques which are applicable to the second case will be discussed below. The approach used for rate studies will depend on the reaction of interest. If, for example, A happens to be the predominant isomer and the reverse reaction is of interest (B \rightarrow A), then the only workable approach would be to develop a rapid synthesis of B which would have to be at least ten times faster than the rate of conversion of B to A.

Several techniques are available if the other reaction (A \rightarrow B) is of interest. A procedure which has been refined by Huisgen and
his coworkers appears to have wide applicability in problems involving valence isomerization (100, 101, 102, 103, 104, 105, 106, 108, 109, 122). The success of this method depends on the existence of a reagent 'X' which will react rapidly and selectively with B but not with A.

\[ \begin{align*}
\text{A} & \xrightarrow{k_f} \text{B} + \text{X} \quad \xrightarrow{k_2} \text{Products} \\
\text{k_r} & \\
\end{align*} \]

Under conditions where 'X' is present the rate of formation of product is given by:

\[
\frac{d \left[ \text{Products} \right]}{dt} = k_2 \left[ \text{B} \right] \left[ \text{X} \right]
\]  
(1)

If it is assumed that the steady-state assumption is valid for B, then:

\[
- \frac{d \left[ \text{B} \right]}{dt} = k_2 \left[ \text{B} \right] \left[ \text{X} \right] + k_r \left[ \text{B} \right] - k_f [A] = 0
\]  
(2)

\[
\left[ \text{B} \right] = \frac{k_f [A]}{k_r + k_2 [X]}
\]  
(3)

\[
\frac{d \left[ \text{Products} \right]}{dt} = \frac{k_2 k_f [X]}{k_r + k_2 [X]} \left[ \text{A} \right]
\]  
(4)
If kinetic studies are carried out so that the reaction is pseudo first order in \([A]([X] \gg [A])\) then:

\[
\frac{d[\text{Products}]}{dt} = k_{\text{obs}}[A]
\]  

(5)

If equations (4) and (5) are combined:

\[
k_{\text{obs}} = \frac{k_2k_f[X]}{k_r + k_2[X]}
\]  

(6)

Rearrangement of equation (6) yields equation (7):

\[
k_{\text{obs}} = k_f - \frac{k_r k_{\text{obs}}}{k_2[X]}
\]  

(7)

A plot of \(k_{\text{obs}}\) against \(\frac{k_{\text{obs}}}{[X]}\) should yield a straight line whose intercept equals \(k_f\). In practice it is only necessary to measure the pseudo first-order rate constant of the reaction at various concentrations of \([X]\) and then construct a plot of \(k_{\text{obs}}\) against \(\frac{k_{\text{obs}}}{[X]}\) in order to obtain a value of \(k_f\).

A similar technique, which is nothing more than the limiting case of Huisgen's technique, has been in use for some time. This procedure is best illustrated by a specific example. The rate of enolization of ketones has been studied by measuring the rate of reaction of the ketone with iodine or bromine (79, 87).
The reaction of halogen with the enol is very fast over a wide range of concentrations. This means that the rate of enolization is the rate determining step and the rate of the overall process is equal to the rate of enolization.

**Case Where Dienone is Only Isomer Present at Equilibrium**

Several of the methods described in the previous section have been applied to this case. Gosink investigated the rate of ring opening of 2, 4, 6-trimethyl-2H-pyran by synthesizing the pyran very rapidly from 2, 4, 6-trimethylpyrylium perchlorate and then following its rate of disappearance spectroscopically (77).

Schiess and coworkers have investigated the rate of ring closure of two pentadienals by synthesizing the all-cis dienal and measuring its rate of isomerization to the cis-trans dienal (170, 171). They were able to demonstrate that isomerization proceeded through a pyran by trapping the intermediate as a tetracyanoethylene adduct.
The fact that the pyrans and not the dienones form adducts suggests that Huisgen's technique would also be applicable here.

Case Where Pyran is the Only Isomer Present at Equilibrium

Measurement of the rate of ring closure in this case is possible if a rapid synthesis of the corresponding dienone or dienal could be devised. Photochemical rupture of the pyran ring has been used to synthesize the valence isomer of 2,2-diphenyl-2H-benzopyran. The kinetics of thermal ring closure were then followed by monitoring changes in the UV spectrum of the dienone (60).

Two techniques could be applied to the study of the pyran ring opening reaction. Huisgen's technique was adapted to this purpose during the course of this investigation. The synthesis of an optically active pyran and the monitoring of the rate of loss of optical activity provides another possible approach (126).

Investigation of the Kinetics of Pyran Ring Cleavage

In order to adapt Huisgen's technique to the measurement of the kinetics of pyran ring opening a reagent was needed which would react with dienones but would be inert toward pyrans. Work carried out by Kolc and Becker suggested that lithium aluminum hydride or lithium borohydride might be suitable (121). The recent report of
Royer and Dreux that pyrans react with Grignard reagents to produce alcohols which seem to be derived from the valence isomers of pyrans suggests that Grignard reagents and perhaps lithium alkyls are suitable candidates for this reagent (161, 162). Solubility considerations and the desire to avoid direct reduction of the pyran suggested that lithium borohydride should be used (30). Tetrahydrofuran was used as a solvent.

In order to test the concept of pyran inertness an equimolar mixture of pyran 6 and the methylene pyran 8 were treated with lithium aluminum hydride at room temperature. Analysis of the product mixture by GLC and NMR spectroscopy indicated that no reduction of the methylene pyran 8 occurred whereas the pyran 6 was completely reduced. It appears that within the duration of a kinetic run, direct attack on the pyran ring is unlikely.

The first pyran studied was pyran 1. This pyran was chosen for study because its kinetic behavior had already been studied. Reaction rates were determined by monitoring the disappearance of the 286 nm absorption band. Results of a series of runs at varying LiBH$_4$ concentrations are shown in Table 8. Plots of $k_{obs}$ against [LiBH$_4$] (Figure 1) and $k_{obs}$ against $k_{obs} / [\text{LiBH}_4]$ (Figure 2) were constructed from the data.

At low LiBH$_4$ concentration $k_{obs} = \frac{k_2 k_f}{k_r} [X] = k_2 K_{eq} [X]$. 

Table 8. Rate constants for disappearance of Buechi's pyran in tetrahydrofuran.

<table>
<thead>
<tr>
<th>Temp (C°)</th>
<th>Pyran x 10^4 M</th>
<th>LiBH₄ x 10^4 M</th>
<th>k_{obs} x 10^4 (sec⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>41.0</td>
<td>2.2</td>
<td>2320</td>
<td>9.1</td>
</tr>
<tr>
<td></td>
<td>2.2</td>
<td>480</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>2.2</td>
<td>320</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>2.2</td>
<td>210</td>
<td>5.3</td>
</tr>
<tr>
<td></td>
<td>3.12</td>
<td>1620</td>
<td>9.0</td>
</tr>
<tr>
<td></td>
<td>3.12</td>
<td>1040</td>
<td>8.7</td>
</tr>
<tr>
<td></td>
<td>3.12</td>
<td>455</td>
<td>6.6</td>
</tr>
<tr>
<td></td>
<td>3.12</td>
<td>455</td>
<td>8.9</td>
</tr>
<tr>
<td></td>
<td>3.12</td>
<td>455</td>
<td>8.5</td>
</tr>
<tr>
<td></td>
<td>3.12</td>
<td>170</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>3.12</td>
<td>170</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>3.12</td>
<td>170</td>
<td>4.5</td>
</tr>
<tr>
<td>15.0</td>
<td>2.96</td>
<td>4700</td>
<td>.38</td>
</tr>
<tr>
<td>15.0</td>
<td>2.68</td>
<td>4720</td>
<td>.32</td>
</tr>
</tbody>
</table>
Thus the rate constant which is actually measured is pseudo first order. Plots of $k_{\text{obs}}$ vs. $[X]$ give straight lines. As the concentration of $X$ increases and the reaction of dienone with $X$ becomes faster $k_{\text{obs}}$ approaches the limit of $k_f$. This behavior gives rise to the region or 'plateau' independent of LiBH$_4$ concentration as shown in Figure 1.

The points plotted in Figure 2 give the expected linear correlation but the points become quite scattered at low LiBH$_4$ concentrations. Reference to Figure 1 shows that the scatter accompanies points below or near the border of the 'plateau' region. This 'plateau' region is reached at very low concentrations of LiBH$_4$ and the measurement of these low concentrations is accompanied by considerable uncertainty. At low LiBH$_4$ concentrations even a small variation in concentration causes a large variation in rate. Since the plot made in Figure 2 is one of a relation between $k_{\text{obs}}$ and $k_{\text{obs}}/[\text{LiBH}_4]$ and since both variables are quite uncertain at low concentrations of LiBH$_4$, considerable scatter of points results.

The intercept at $k_{\text{obs}}/[\text{LiBH}_4]$ equal to zero gives a value for $k_f$ of $9.4 \times 10^{-4}$ sec$^{-1}$ for the ring opening reaction of Böchi's pyran.$^1$ The intercept value compares very favorably with the value of $k$ obtained by direct measurement at high LiBH$_4$ concentration ($k_{\text{obs}} = 9.1 \times 10^{-4}$ sec$^{-1}$; [LiBH$_4$] = 0.232 M). A value at 40° calculated from the data of Marvell et al.$^,$ is $3.55 \times 10^{-4}$ sec$^{-1}$.
Figure 1. Plot of $k_{obs}$ vs. LiBH$_4$ concentration.
Figure 2. Plot of $k_{\text{obs}}$ vs. $\frac{k_{\text{obs}}}{[\text{LiBH}_4]} \times 10^2 \text{ M}^{-1} \text{ sec}^{-1}$ (equation (7), p. 58).
The first rate constant was determined in tetrahydrofuran while the latter was determined in tetrachloroethylene.

In order to minimize the possibility of attack on the pyran ring itself and in order to make a more direct comparison to NMR rates, kinetics were run at 15°. Rate measurements made at about 0.47M LiBH₄ concentrations yielded an average value of \( k = (0.35 \pm 0.03) \times 10^{-4} \text{sec}^{-1} \). Since it had been found that runs made at high concentrations of LiBH₄ yield values which are essentially identical with those found by plotting \( k_{\text{obs}} \) against \( k_{\text{obs}}/[\text{LiBH}_4] \) it was decided to use very concentrated LiBH₄ solutions in order to avoid the necessity of making a plot.

Kinetic Studies Using LiAlH₄ as the Reducing Agent

It could be expected that since LiAlH₄ is much more reactive than is LiBH₄ toward carbonyl compounds that even relatively low concentrations of LiAlH₄ would still make the reduction step quite fast and therefore make ring cleavage the slow step of the sequence (30). This was confirmed by a series of runs at 15° which yielded a rate constant of \( k_f = (0.30 \pm 0.03) \times 10^{-4} \text{sec}^{-1} \). A second series of runs were made in the dark at the same temperature. The reaction progress was followed by GLC analysis. These runs yielded a value for \( k_f = (0.35 \pm 0.020) \times 10^{-4} \text{sec}^{-1} \). The three series of runs yielded values of \( k_f \) which are the same within experimental error.
Both 2, 2, 4, 6-tetramethyl-2H-pyran and 2, 4-dimethyl-2, 6-diphenyl-2H-pyran were studied using the technique described above. The results of these studies are shown in Table 9 and the results for the three pyrans in the various solvents used in this study are shown in Table 10. Typical first order plots for pyrans 1, 6 and 11 are gathered in Appendix 1.

Isolation of Lithium Aluminum Hydride Reduction Products

Pyrans 1, 6, and 11 were reduced with large excesses of lithium aluminum hydride (LAH) under the conditions employed for the kinetic runs. The reaction time necessary in each case to obtain 99% reduction was calculated using the first order rate constants which were determined from kinetic runs. Each pyran reacted cleanly to give only one product. This information was obtained for the reduction products of 1 and 6 by GLC and in the case of 11 by comparison of the NMR spectra of crude and purified (TLC) reaction products. No evidence of conjugate addition (1, 4, or 1, 6) of hydride to any of the dienones was obtained.

Reduction of pyran 1 afforded only cis-β-ionol 2. The NMR spectrum was in complete accord with the assigned structure but one unexpected feature was noted. The geminal methyl groups on the cyclohexene ring appear as two separate singlets instead of the
Table 9. Rate constants for disappearance of pyrans 1, 6 and 11 in ether.

Rate constants for Disappearance of Büchi Pyran for Diethyl Ether

<table>
<thead>
<tr>
<th>Temp (°C)</th>
<th>Pyran x $10^{-4}$ M</th>
<th>LiAlH$_4$ x $10^{-4}$ M</th>
<th>$k_{obs} x 10^{-4}$ (sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.0</td>
<td>3.2</td>
<td>570</td>
<td>0.25</td>
</tr>
<tr>
<td>15.0</td>
<td>3.5</td>
<td>560</td>
<td>0.33</td>
</tr>
<tr>
<td>15.0</td>
<td>4.1</td>
<td>550</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Kinetics monitored by GLC

<table>
<thead>
<tr>
<th>Temp (°C)</th>
<th>Pyran x $10^{-4}$ M</th>
<th>LiAlH$_4$ x $10^{-4}$ M</th>
<th>$k_{obs} x 10^{-4}$ (sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.0</td>
<td>125</td>
<td>3840</td>
<td>0.33</td>
</tr>
<tr>
<td>15.0</td>
<td>145</td>
<td>3840</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Rate Constants for Disappearance of 2, 2, 4, 6-Tetramethyl-2H-Pyran in Ether

<table>
<thead>
<tr>
<th>Temp (°C)</th>
<th>Pyran x $10^{-4}$ M</th>
<th>LiAlH$_4$ x $10^{-4}$ M</th>
<th>$k_{obs} x 10^{-4}$ (sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.5</td>
<td>1.13</td>
<td>1340</td>
<td>3.77</td>
</tr>
<tr>
<td>14.6</td>
<td>1.37</td>
<td>1300</td>
<td>1.68</td>
</tr>
<tr>
<td>14.6</td>
<td>1.74</td>
<td>1310</td>
<td>1.55</td>
</tr>
</tbody>
</table>

Rate Constants for Disappearance of 2, 4-Dimethyl-2, 6-Diphenyl-2H-Pyran in Ether

<table>
<thead>
<tr>
<th>Temp (°C)</th>
<th>Pyran x $10^{-4}$ M</th>
<th>LiAlH$_4$ x $10^{-4}$ M</th>
<th>$k_{obs} x 10^{-4}$ (sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.6</td>
<td>.80</td>
<td>1600</td>
<td>5.3</td>
</tr>
<tr>
<td>14.6</td>
<td>1.2</td>
<td>1500</td>
<td>5.4</td>
</tr>
</tbody>
</table>
Table 10. Summary of kinetic data for pyrans 1, 6 and 11.

<table>
<thead>
<tr>
<th>Pyran</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>$k \text{ (sec}^{-1} \times 10^{4})$</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Pyran 6" /></td>
<td>$C_2Cl_4$</td>
<td>15.0</td>
<td>0.91±</td>
</tr>
<tr>
<td></td>
<td>pyridine</td>
<td>15.0</td>
<td>0.89*</td>
</tr>
<tr>
<td></td>
<td>ether</td>
<td>15.0</td>
<td>0.30 ± 0.030</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.35 ± 0.020</td>
</tr>
<tr>
<td></td>
<td>tetrahydrofuran</td>
<td>15.0</td>
<td>0.35 ± 0.030</td>
</tr>
<tr>
<td><img src="image" alt="Pyran 11" /></td>
<td>diethyl ether</td>
<td>14.6</td>
<td>0.80 ± 0.035*</td>
</tr>
<tr>
<td><img src="image" alt="Pyran 1" /></td>
<td>diethyl ether</td>
<td>14.6</td>
<td>5.35 ± 0.050</td>
</tr>
</tbody>
</table>

* Calculated values
* Corrected for statistical factor
single sharp line that is observed in trans-β-ionol. Two reasons could be suggested for this. Inspection of a Framework Molecular Model shows that neither of the possible conformations which would allow coplanarity of the diene system are very favorable for steric reasons.

This would suggest that the molecule might adopt a conformation with the diene system non-coplanar which would position the side chain over the cyclohexene ring.
This could conceivably bring the asymmetric center close enough to the methyl groups to make them diastereotopic. Alternatively the side chain could rotate from one side of the cyclohexene ring to the other slowly enough to make the magnetic environments of the two methyls decidedly different.

To test these theories variable temperature NMR experiments were carried out by Cole in an effort to raise the rate of equilibration of the two methyl groups to a point where the separate methyl resonance lines would coalesce (40). Even at 173° in either C₂Cl₄ or diphenyl ether the lines remained separate and sharp. Either the barrier to rotation for the side chain is quite high or the nonequivalence of the methyl groups is due solely to the proximity of the asymmetric center. Attempts by Cole, using low temperature TLC, to isolate diastereomers which would result by restricted rotation of the side chain failed (40).

The presence of the cis double bond is indicated by a coupling constant of 12 Hz between Hₐ and Hₐ (as opposed to 15 Hz for the
coupling constant between corresponding protons in the trans isomer).

The ultraviolet spectrum shows a single maximum at 219 nm ($\varepsilon = 3,400$). This value is much lower than the calculated maximum of 234 nm. The hypsochromic shift is undoubtedly due to the deviation of the diene chromophore from coplanarity. Such effects have been discussed by Duperrier and Dreux (53) and by Kluge and Lillya (118) for similar cis dienones. The small extinction coefficient is characteristic of noncoplanar conjugated systems.

Reduction of pyran 6 yielded a single isomer as shown by its NMR spectrum and GLC behavior. Purification was carried out by gas chromatography using a Carbowax 20 m column. The purification procedure presented a problem since successive separations created an acidic impurity on the column which tended to cause elimination of water from the alcohol and creation of olefins. This was corrected by treating the column with triethylamine prior to each collection run.

The hydrogen and methyl on the double bond between C-2 and C-3 are probably cis in view of the 1.25 Hz allylic coupling. The
ultraviolet maximum indicates that the chromophore is not coplanar and this is also supported by the small extinction coefficient.

The reduction of 2, 4-dimethyl-2, 6-diphenyl-2H-pyran 11 presents an interesting problem. Because of the two allowed modes of ring opening isomeric dienones could result. These dienones would then give rise upon reduction to two isomeric alcohols (actually four if the generation of a center of asymmetry is considered).

Both spectral data and thin layer chromatographic behavior indicate that only one isomer is formed. Thin layer chromatography on basic alumina using benzene as the developing solvent gave two spots. One had an $R_f$ value of 0.7 and was in all likelihood a
hydrocarbon formed from the alcohol. The majority (judging by the spot size and density) of the material had an $R_f$ value of 0.2 and proved to be an alcohol. The infrared spectrum and carbon-hydrogen analysis for material eluted from this spot were consistent with the assigned structure.

The NMR spectra of the crude reaction mixture and the purified product were almost identical. Spin decoupling experiments verified

\[ \begin{align*}
5.19 & \quad 1.73 \\
5.47 & \quad \text{H} \\
\text{C}_6\text{H}_5 & \quad \text{OH} \\
& \quad \text{CH}_3 \\
& \quad \text{H} \quad \text{CH}_3 \\
& \quad \text{J} = 2\text{Hz} \\
& \quad 1.91 \\
& \quad \text{C}_6\text{H}_5
\end{align*} \]

6.23 (Calc'd 6.32)  

UV$_{\text{max}}$ 253 nm ($\epsilon$ = 12,300)

the assigned structure. An allylic coupling constant of 2 Hz suggested a cis arrangement for the phenyl and hydrogen on the terminal double bond. This structural assignment is further supported by calculating the expected chemical shift for the vinylic proton on C-4 using as a base value the chemical shift for the corresponding proton in alcohol 10 (115). A cis arrangement for the phenyl and vinylic proton gives a calculated chemical shift of 66.32 which is in much better agreement with the observed 66.23 than the chemical shift which would result for a trans arrangement (65.88). From the UV data it appears that the diene system is twisted from coplanarity.
Since alcohol 10 contains a chromophore which resembles that of trans-1-phenyl-1,3-butadiene (280 nm), it would be expected to have a similar absorption maximum but the absorption maximum at 253 nm is much closer to the maximum for trans-2-phenyl-2-butene (244 nm) (92, 183). It appears that the terminal α-methyl styryl grouping alone is acting as a chromophore.

It cannot be decided from the product composition, whether product formation is thermodynamically or kinetically controlled, since product equilibration experiments were not performed. The alcohol is produced under the same conditions used for kinetic runs which showed no dependence on hydride ion concentration. Under such conditions, the Huisgen treatment indicates that back reactions leading to equilibration of initially formed dienones are quite impossible. Clearly the product must result from kinetic control.

It could be argued that two alcohols actually are formed and these equilibrate upon hydrolysis. This seems unlikely since neutral or slightly basic conditions were used for hydrolysis. Somewhat more acidic conditions would be necessary for equilibration of initially formed alcohols. For example, Cram and Sahyn have found that equilibration of cis and trans 2-phenyl-2-butene is rapid in glacial acetic acid containing 0.10-0.90 M p-toluenesulfonic acid only above 50° (41).
Confirmation of Pyran Structures for Compounds 1, 6 and 11

Isolation and characterization of the products produced during the kinetic studies of pyran ring cleavage have provided further confirmation of the pyran structure for compounds 1, 6, and 11. All the spectral data for the three pyrans studied are in complete accord with the assigned structures. All show good elemental analyses. The lack of rapid reactivity toward lithium aluminum hydride further confirms the structures. Trans-β-ionone, for example, reacts almost explosively under conditions where Büchi’s pyran is almost inert. The other two pyrans behave in a similar manner. The structures of the reduction products are easily assigned from the spectral data and the elemental analyses are consistent with the assigned structures. The compounds obtained from the reduction reactions are precisely the ones which would be expected to arise from the respective pyrans.

Effect of Substituents on the Stereochemical Course and Rate of Pyran Cleavage

The evidence for the production of only one of two possible isomeric alcohols from pyran 11 has been discussed. There are several similar cases reported in the literature. Gosink, during his kinetic study of the ring cleavage of 2, 4, 6-trimethyl-2H-pyran,
Table 11. Stereochemical results of some pyran ring cleavage reactions.

<table>
<thead>
<tr>
<th>Pyran</th>
<th>Metal Hydride or Grignard Reagent</th>
<th>Product</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Pyran 16" /></td>
<td>none</td>
<td><img src="image" alt="Product 16" /></td>
<td>77</td>
</tr>
<tr>
<td><img src="image" alt="Pyran 11" /></td>
<td>LiAlH₄</td>
<td><img src="image" alt="Product 11" /></td>
<td>This work</td>
</tr>
<tr>
<td><img src="image" alt="Pyran 18" /></td>
<td>CH₃MgI</td>
<td><img src="image" alt="Product 18" /></td>
<td>82, 83</td>
</tr>
<tr>
<td><img src="image" alt="Pyran 20" /></td>
<td>CH₃MgI</td>
<td><img src="image" alt="Product 20" /></td>
<td>82, 83</td>
</tr>
</tbody>
</table>
reported the formation of only one of two possible isomers. Royer and Dreux have recently published a study of the reaction of pyrans with Grignard reagents to produce alcohols (161). The reaction appears to proceed in the same manner as the hydride reductions. Two pyrans, each of them unsymmetrically substituted, produced only one of two possible isomeric alcohols. The reactants and the products of these reactions are shown in Table 11.

In each of the reactions shown in Table 11 the larger of the two substituents attached to C-2 of the pyran occupies, in the product, a position on the terminal carbon of the pentadienone system which is trans to the remainder of the main carbon chain. It should be recalled that the formation of alcohol 15 from pyran 11 was kinetically controlled. Similar control is undoubtedly involved in the formation of alcohols 19 and 21 from pyrans 18 and 20. No evidence of reversibility was noted in the formation of 17 from 16 so 17 was also probably formed in a kinetically controlled manner.

The kinetically controlled, stereospecific formation of the four products in Table 11 can be explained by suggesting that the initial electrocyclic pyran ring cleavage is a concerted, ground state process. At the transition state the C-O bond is only partially broken.
The smaller of the two groups attached to C-2 must turn inward to minimize non-bonded interactions with one of the two lone pairs of electrons on the oxygen which is simultaneously turning inward. Note that although the process is shown as a disrotatory process it could just as well have been represented as a conrotatory process. The outcome would have been exactly the same in that case. Similar arguments have been advanced to explain the stereochemical consequences of electrocyclic reactions of oxetes and cyclobutenones (13). (Also see Tables 1 and 2 of this work.)

In view of the previous argument it would be expected that in the case where S=H, pyran ring cleavage would be faster than if S=methyl. This is indeed exactly what is observed. Gosink measured the rate constant for ring opening of pyran 16 as $7 \times 10^{-3}$ sec$^{-1}$ at $21^\circ$ (77). Lowering the temperature to $15^\circ$ would perhaps halve the rate ($k = 3.5 \times 10^{-3}$ sec$^{-1}$ at $15^\circ$) but certainly would do no more than that. The corresponding rate constant for isomerization of pyran 6 was $0.80 \times 10^{-4}$ sec$^{-1}$ at $15^\circ$. The ratio of the two rate constants ($\frac{k_{16}}{k_6} = 43$) compares quite favorably with the rate ratio of similarly substituted cyclobutenes undergoing electrocyclic ring cleavage (61, 62).
With regard to kinetic measurements it should be noted that pyran 11 isomerizes 6.7 times faster than 6. This rate enhancement can be explained by assuming that in the transition state C-2 has acquired some positive character. Delocalization of charge by the neighboring phenyl group could explain the observed rate enhancement.
Charge separation in the transition state is consistent with the small kinetic solvent effect observed for Büchi's pyran in pyridine.
CONCLUSIONS

The structures of pyrans 6 and 11 were verified by the reduction products which were isolated. The alcohols which were isolated could only have come from the acyclic valence isomers of 2H-pyran.

The electrocyclic cleavage reaction was common not only to Büchi's pyran, but to stable pyrans 6 and 11 as well. Small quantities of the acyclic valence isomers of both 6 and 11 were observed at high temperature.

The electrocyclic cleavage reaction of pyrans appears to be a concerted process. The reaction rate of pyran 1 is a little affected by changes in solvent polarity. The rates of reaction in both light and dark are the same. The kinetically controlled stereospecificity of the reaction would also argue for a concerted ground state process. The effect of substituent size on the kinetics of ring opening is consistent with the argument that ring opening is a concerted ground state process.

The kinetic technique which has been developed during the course of this study should find general application in the study of electrocyclic ring openings of stable pyrans and perhaps other heterocyclic compounds of this series.
EXPERIMENTAL

Equilibrium Studies

These studies were carried out using the variable temperature probe of the Varian A-60 nuclear magnetic spectrometer. The desired temperature was selected, and the actual probe temperature was determined from the temperature dependent difference of the chemical shifts of methanol protons. The sample under investigation was thermally equilibrated for at least one-half hour before the spectrum and integration were recorded.

Kinetic Studies Using NMR Spectroscopy as the Analytical Probe

These kinetic studies were carried out using the method of Marvell, Caple, Gosink and Zimmer (127). Pyridine, which was used as a solvent instead of tetrachloroethylene, was obtained from a freshly opened bottle of reagent grade material.

Kinetic Studies Using Metal Hydrides

Reagent Preparation

Anhydrous Diethyl Ether. Commercial U.S.P. ether was dried over anhydrous calcium chloride overnight. The ether was decanted
and filtered into a flask. About 1 g/liter of sodium ribbon was pressed directly into the ether and the ether was allowed to stand overnight. If all of the sodium was consumed the process was repeated. The ether was then distilled from sodium and stored over sodium ribbon until needed. Just prior to use, the ether was mixed with and then distilled from lithium aluminum hydride. Ether prepared in this manner was used in all syntheses and kinetic experiments.

**Anhydrous Tetrahydrofuran.** Reagent grade tetrahydrofuran was first checked for peroxides. If excessive amounts were found they were first destroyed by treatment with cuprous chloride, followed by distillation (89). Drying of the THF was accomplished by distillation from lithium aluminum hydride in a dry nitrogen atmosphere.

**Lithium Aluminum Hydride Solutions.** Standard solutions of lithium aluminum hydride in ether were prepared by refluxing, in an inert atmosphere, commercial lithium aluminum hydride (Ventron) with anhydrous ether. After several hours, refluxing was discontinued, the suspension was poured quickly into a modified clean, dry gas washing bottle (see Figure 9), the cylinder was purged with nitrogen, and the fines were allowed to settle. The clear solution which resulted was forced from the gas washing bottle, when needed, with dry nitrogen gas. The solution was standardized by the
iodometric procedure of Felkin (58). Solutions of varying concentrations were prepared by dilution of concentrated solutions.

**Lithium Borohydride Solutions.** These solutions were prepared from commercial lithium borohydride (Ventron) and anhydrous tetrahydrofuran. Solutions were prepared in a dry box by dissolving a weighed quantity of lithium borohydride in tetrahydrofuran and filtering the resulting solution through a sintered glass filter. The clear solutions were standardized before use by hydrolyzing an aliquot of the solution and titrating the liberated base with standard hydrochloric acid (70).

**Procedure**

**Method A.** Kinetic runs were made in the thermostatted cell compartment of a Cary 25 spectrophotometer. The temperature inside the cell was maintained within ±0.1°C and was checked just prior to each run with a calorimeter thermometer immersed in an oil filled cell.

A standard solution of the pyran was prepared by weighing out a quantity of pyran and dissolving it in a known volume of anhydrous ether.

In a typical experiment a silica cell was filled in a glove bag with a known volume of standardized metal hydride solution. The cell was immediately capped with a serum stopple which was wired
in place. The solution was then clarified, if necessary, by centrifugation, and was then thermally equilibrated. After thermal equilibration was completed a measured volume of pyran stock solution was injected through the stopple with a 250 ul syringe. The cell was shaken to mix the contents, clarified again by centrifugation and placed in the cell compartment. The reaction was followed by monitoring the disappearance of the pyran absorption band in the UV.

**Method B.** Measured volumes of pyran and lithium aluminum hydride stock solutions were thermally equilibrated and then mixed thoroughly in a sealed reaction vessel which was also thermostatted. Aliquots were withdrawn at intervals, mixed with a known volume of durene ether standard, and were then quenched by the dropwise addition of water to the reaction mixture. The ether layer was decanted from the precipitated aluminum salts and these salts were then extracted several times with ether. The extracts were combined and evaporated to a total volume of about two milliliters. The mixture was then chromatographed to determine the relative concentrations of durene, pyran, and reduction product (alcohol) [Varian Aerograph 204 Gas Chromatograph equipped with Leeds and Northrup recorder and disc integrator; 1/8" x 7' Carbowax 20 M column (5% on 60/80 mesh Firebrick)]. Both the logarithms of the \( \frac{\text{pyran}}{\text{Durene}} \) ratio and the \( \frac{\text{pyran}}{\text{pyran alcohol}} \) ratio (fraction of pyran remaining) were plotted as functions of time. Plots of the latter type were superior.
Using this method excellent agreement was obtained with results obtained using method A.

2, 5, 5, 9-Tetramethyl-oxa-1, 5, 6, 7, 8, 9-hexahydronaphthalene (Büchi's Pyran-1)

This compound was prepared by a procedure similar to that used by Büchi and Yang (37). Two solutions, one containing 40.0 g (0.208 moles) of β-ionone (Aldrich) in 1000 ml of 100% benzene-free ethanol, and the other containing 43.8 g (0.228 moles) of β-ionone in 1016 ml of ethanol, were separately irradiated for 48 hours in a quartz apparatus with a Hanovia mercury lamp (#679A36). These solutions were then combined, the ethanol was removed, and the residue was distilled through a spinning band column. All low boiling fractions, b.p. 40° -60° C (0.05 mm) were saved, recombined and redistilled. The second distillation yielded 4.6 g (5.5%) of the pure pyran: b.p. 53-54° (0.3 mm); [lit. b.p. 70° (1.0 mm)]; uv max (diethyl ether) 287 nm; [lit. uv max (95% C₂H₅OH) 286 nm (ε 7250)]; nmr (CCl₄) δ1.06 (s, 3), 1.10 (s, 3), 1.30 (s, 3), 1.68 (s, 3), 1.3-2.0 (m, 6), 4.88 (d, 1, J = 6 Hz), 5.56 (d, 1, J = 6 Hz).

Several other fractions (9.5 g, 12%) contained major amounts of the desired pyran, but were still slightly contaminated.
A 1.6678 g sample of Büchi's pyran was added quickly to about 20 ml of 2M lithium aluminum hydride in ether. The reaction flask was purged with dry nitrogen, sealed, and held at 16°C for three days. The reaction mixture was worked up by first destroying excess lithium aluminum hydride by cautious dropwise addition of water. After the violent reaction had subsided, 2M sodium hydroxide solution was added dropwise to obtain the aluminum salts as a granular precipitate. The ether layer was decanted from the precipitate, and the solid was extracted several times with dry ether. The ether extracts were combined, dried (MgSO₄), filtered and the ether was evaporated to yield 1.2873 g (78%) of the crude alcohol. The compound was shown to be almost entirely (95%) cis-β-ionol by gas chromatography. A 15' x 3/8" column of Carbowax 20M (20% w/w on 30-50-mesh firebrick) was used for both analytical work and also to collect spectral and analytical samples: uv max (95% C₂H₅OH) 219 nm (ε 3.4 x 10³); ir (neat) 2.98 μ (-OH), 3.34 μ (C-H on cis C=C), 3.37 μ, 3.42 μ, 3.49 μ (C-H on saturated carbon), 5.86 μ, 6.13 μ (diene), 8.35 μ, 8.60 μ (geminal methyls), 13.35 μ (C-H on cis C=C); nmr (CCL₄) δ 0.90 (s, 3), 0.95 (s, 3), 1.09 (d, 3, J = 6 Hz), 1.53 (s, 3), 1.35-2.30 (m, 7), 4.13 (d of d, 1, J = 10 Hz, J = 6 Hz), 5.39 (d of d, 1, J = 12 Hz, J = 10 Hz), 5.73 (d, 1, J=12 Hz).
Anal. Calculated for $\text{C}_{13}\text{H}_{22}\text{O}$: C, 80.35; H, 11.41

Found: C, 80.29; H, 11.24

4-(2, 6, 6-Trimethyl-1-cyclohexenyl)-trans-3-buten-2-ol

This compound was prepared by the method of Inhoffen and Bohlmann (111). A 1.04050 g (5.4 mmole) portion of $\beta$-ionone was added dropwise to about 50 ml of ice cold 2M lithium aluminum hydride in diethyl ether. The reaction was quite rapid as evidenced by the rapid evolution of heat by the mixture. Work-up was carried out using the procedure described for the preparation of 2. About 1.0 g of oily product was obtained: ir (neat) 3.00$\mu$ (-OH), 3.32$\mu$ (C-H on trans C=C), 3.38, 3.42, 3.49$\mu$ (C-H on saturated carbon), 6.12$\mu$ (diene), 8.36, 8.58$\mu$ (geminal methyls), 10.35$\mu$ (C-H on trans C=C); nmr (CCl$_4$), 60.97 (s, 6), 1.25 (d, 3, $J = 6$ Hz), 1.54 (s, 3), 1.40–2.13 (several broad peaks, 6), 3.92 (s, 1), 4.21 (m, 1 $J = 15$ Hz, $J = 6$ Hz), 5.28 (d of d, 1, $J = 15$ cps, $J = 6$ Hz), 5.94 (d, 1, $J = 15$ Hz); uv max (C$_2$H$_5$OH) 234 nm (e 4800); [lit. uv max 234 nm (e 5099)] (116).

Isodehydroacetic Acid (4, 6-dimethyl coumalic acid)

This compound was prepared by the procedure of Wiley and Smith (182). The reaction was run on a scale which was as small as
1/10 the size described in the literature with good results. In a full size preparation a 650 g (5 mole) portion of ethylacetoacetate (Eastman, practical) was added to 900 ml of ice cold, well stirred concentrated sulfuric acid (Dupont, reagent). The mixture was allowed to sit at room temperature for seven days after which time it was poured onto 2 kg of ice. After filtering to remove the precipitated acid, the aqueous residue was extracted with three 1.5 liter portions of ether and the precipitated acid was dissolved in the ether extracts. The acid was removed from the ether layer by extraction with several 100 ml portions of 5% sodium carbonate solution. These extracts were combined and acidified to precipitate the acid which was then recrystallized from acidified (HCl) water. Yields ranged from 11 to 20%: m.p. 153° -155° C [lit. m.p. 154° -155° C] ir (KBr pellet) 3.08μ (-OH), 5.84, 5.92μ (C=O).

4, 6-Dimethylcoumalin 5

This compound was prepared using the procedure of Wiley and Smith (177). In a typical run, 50 g (0.30 mole) of isodehydroacetic acid and 2 g of precipitated copper powder were mixed intimately and placed in a round bottom, 100 ml flask equipped with an air condenser. A sand bath, situated on a hotplate and equipped with a shielded thermometer, was used to heat the flask to 235° -250° for two hours. The tarry residue was then placed in a vacuum
sublimator and sublimed to yield 30.2 g (82%) of 4, 6-dimethyl-coumalin. After further purification by vacuum distillation the material had a melting point of 47° -49° [lit. m.p. 51°]; ir (KBr pellet), 5.80, 6.02 μ (C=O).

**2, 2, 4, 6-Tetramethyl-2H-pyran**

This compound was prepared by the method of Hinnen and Dreux (91). 12.33 g of magnesium turnings (Matheson, Coleman and Bell, Grignard Reagent Grade), 26 ml of methyl iodide (Matheson, Coleman and Bell), and 166 ml of anhydrous ether were used to prepare a solution of Grignard reagent (.51 mole). The Grignard reagent was cooled on an ice bath and an ether solution of 7.15 g (57.7 mole) of 4, 6-dimethyl coumalin was added dropwise with stirring. After addition was complete, the reaction mixture was hydrolyzed cautiously by dropwise addition of water. Only enough water was added to precipitate the magnesium salts as a pasty, white mass. The ether layer was decanted from the salts which were then extracted with several portions of ether. All ether solutions were combined and dried (MgSO₄). After drying, the ether was removed on a rotovap and the residual oil (6.73 g) was vacuum distilled. The colorless liquid product (1.7 g, 21.4%) b.p. 36.5° -38.5° (10 mm), proved to be a 1:1 mixture of 2, 2, 4, 6-tetramethyl-2H-pyran and 4-methylene-2, 2, 6-trimethyl-2H-pyran. Final separation
of the two pyrans in the mixture was achieved by gas chromatography on a 1/4" x 3 meter Apiezon M (10% on Chromosorb W 60/80 mesh) column. With a flow rate of 120 ml/min and a column temperature of 85° the retention time of 6 was 15 min. All glass collectors used for collecting the pyran were washed in ammonia water and dried in a 130° oven just prior to use. Collected samples of the pyran 6 were stored at liquid nitrogen temperatures until used.

nmr (CCl₄) δ 1.26 (s, 6), 1.63 (d, 3, J = 2 Hz), 1.73 (s, 3), 4.70 (m, 2).

3, 4-Dihydro-2, 2, 6-trimethyl-4-methylene-2H-pyran

This material was synthesized along with 2, 2, 4, 6-tetramethyl-2H-pyran. The compound was separated from its isomer by gas chromatography. Under GLC conditions used for the separation of 6 this compound had a retention time of eighteen minutes: nmr (CCl₄) δ 1.22 (s, 6), 1.78 (s, 3), 2.18 (m, 2), 4.35 (m, 1), 4.56 (m, 1), 5.14 (m, 1). All multiplets were poorly resolved making it impossible to obtain coupling constants.

2, 4, 6-Trimethylpyrylium perchlorate

This compound was prepared by the procedure of Hafner and Kaiser (82). The reaction was run on a scale which was two-fifths
of that described in the literature. The product (82.9 g, 45%) was moistened with ether and stored in the refrigerator until used. No attempt was made to recrystallize the product since it is reported in the literature that explosions sometimes result during such attempts.

2, 2, 4, 6-Tetramethyl-2H-pyran from the pyrylium salt 6 (161)

Methyl magnesium iodide (0.2 moles) was prepared in ether from 4.87 g of magnesium turnings, 31.2 g of methyl iodide and 130 ml of anhydrous ether. The solution was stored under nitrogen until used.

A 41.1 g (0.185 mole) quantity of 2, 4, 6-trimethylpyrylium perchlorate was placed in a round bottom, three necked flask equipped with condenser, tru-bore stirrer and addition funnel. The salt was covered with anhydrous ether (120 ml) and the air in the apparatus was replaced with nitrogen. The salt-ether mixture was cooled on an ice bath and stirred vigorously while the previously prepared Grignard reagent was added dropwise. The addition of the Grignard reagent was completed in one hour and stirring was continued for an additional hour. The mixture was then hydrolyzed and the magnesium salts precipitated by the addition of 10 ml of 0.25N sodium hydroxide solution. The ether was decanted from the precipitate and the precipitate was extracted with ether three times. All ether solutions were
combined, dried ($\text{MgSO}_4$) and the ether was removed by distillation. The residue was distilled under vacuum to yield 1.39 g (54%) of pyran mixture: b.p. 35° (15 mm). The two pyrans were separated by gas chromatography using conditions described previously.

4, 6-Dimethyl-3, 5-heptadien-2-ol

**Method A**

A mixture of 97.4 mg (.70 mole) of 2, 2, 4, 6-tetramethyl-2H-pyran and anhydrous diethyl ether was added to 25 ml of 0.2M lithium aluminum hydride in ether. The mixture was kept under nitrogen in a 50 ml round bottom flask for 24 hours at a temperature of 16°. The reaction mixture was then worked up by a method similar to that used in the preparation of 2. The alcohol was purified by gas chromatography (triethylamine was added to the mixture to prevent decomposition on the column). A 1/8" x 7' Carbowax column (5% Carbowax 20M on a base washed firebrick- 40/60 mesh) was used for the chromatographic purification. The alcohol was shown to be the only major product of the reaction.

**Method B**

20 ml of 0.51 M lithium aluminum hydride in ether and 355.1 mg of pyran mixture (6 and 8 present in equal amounts) were mixed
thoroughly and allowed to stand for five hours at 17°. The mixture was worked up using the procedure of method A to yield about 0.4 g of a mixture of 8 and 10. The mixture was separated and collected on the column described in method A: uv max (95% C2H5OH) 219 nm (ε 6.47 x 10^3); ir (neat) 2.98μ (-OH), 3.31μ (C-H on C=C), 3.37, 3.42μ (C-H on saturated carbon), 6.10μ (diene), 8.40, 8.52μ (geminal dimethyl); nmr (CCl4) δl.10 (d, 3, J = 6.25 Hz), 1.62 (d, 3, J = 1.25 Hz), 1.71 (d, 3, J = 1.0 Hz), 1.76 (d, 3, J = 1.50 Hz), 3.68 variable (s, 1), 4.24 (m, 1, J = 6.25 Hz, J = 8.75 Hz), 5.22 (d of q, 1, J = 8.75 Hz, J = 1.25 Hz), 5.69 (s, 1); mass spectrum - m/e 140.

Anal. Calculated for C9H16O: C, 77.09; H, 11.50
Found: C, 76.94; H, 11.43

2, 6-Diphenyl-2, 4-dimethyl-2H-pyran 11

This compound was prepared according to the method of Roullier, Gaignaire and Dreux (158). The Grignard reagent was prepared from 80 ml of anhydrous ether, 2.7 g of magnesium turnings, and 17.3 g of bromobenzene (Matheson, Coleman and Bell) and was stored under nitrogen until used. The Grignard reagent was placed in a three necked flask equipped with tru-bore stirrer, addition funnel and nitrogen supply and cooled on a dry ice-acetone bath to -78°. The Grignard reagent precipitated upon cooling. 4, 6-Dimethyl-coumalin (3.89 g, 31.4 mmole) in ether was added dropwise
to the slurry of Grignard reagent with vigorous stirring. Stirring was continued while the mixture was allowed to warm to 0° without removal of the dry ice bath. A 10 ml volume of distilled water was added to hydrolyze the reaction mixture, the ether layer was decanted, and the lumpy precipitate of magnesium salts was extracted three times with 25 ml portions of ether. The ether layers were combined, washed with 40 ml of 5% NaHCO₃ solution and dried (Na₂SO₄). The solvent was removed by distillation and the residue was distilled through a Hickman distillation apparatus (1 x 10⁻³ mm Hg) and recrystallized from methanol to yield 163 mg (1.97%) of light yellow crystals: m.p. 81° -82° [lit. m.p. 84°]; uv max (C₂H₅OH) 317 nm (ε 10, 500), 254 nm (ε 9, 840), 227 nm (ε 12, 270); [lit. uv max (C₂H₅OH) 323 nm (ε 8830), 250 nm (ε 7470), 227 nm (ε 7500)].

1, 5-Diphenyl-3-methyl-2, 4-hexadien-1-ol 15

This compound was prepared by essentially the same procedure as the one used to prepare compounds 2 and 10. A 390.2 mg (1.46 mmole) portion of pyran 11 and 20 ml of 0.132 M lithium aluminum hydride in ether were mixed thoroughly in a 50 ml round bottom flask. The flask was purged with dry nitrogen, stoppered and allowed to stand for five hours before work-up. Spectral and analytical samples were prepared, after the usual work-up, by thick-layer
chromatography using 2 mm x 20 mm x 20 mm preparative plates made with Woelm PF$_{254}$ alumina. These plates were activated at 110°C for three hours before use. Benzene, to which a trace of triethylamine had been added, was used as the eluant. Two developments in this solvent cleanly separated the reaction mixture into two bands ($R_f \approx 0.2$ and $R_f \approx 0.8$). The lower band proved to be the alcohol. This band was removed from the alumina by boiling the alumina and adsorbed alcohol in diethyl ether. Evaporation of the ether and prolonged evacuation of the sample at room temperature yielded a purified sample of the alcohol: UV max ($95\%$ C$_2$H$_5$OH) 253 nm ($\varepsilon 1.23 \times 10^4$); ir (neat) 2.98 μ (-OH), 3.36 μ (aromatic C-H stretch), 3.43 μ (aliphatic C-H stretch), 6.08 μ (diene), 6.30, 6.40, 6.73, 6.96 μ (C=C bond stretching in phenyl groups); 13.27, 14.46 μ (C-H bending on monosubstituted benzene ring); nmr (CCl$_4$) δ 1.73 (s, 3), 1.91 (s, 3), 4.28 (s, 1), 5.19 (d, 1, $J = 9$ Hz) 5.47 (d, 1, $J = 9$ Hz), 6.23 (s, 1), 7.18 (m, 10).

Anal. Calculated for C$_{19}$H$_{20}$O: C, 86.32; H, 7.63
Found: C, 86.17; H, 7.75

Silylation of 1, 5-Diphenyl-3-methyl-2,4-hexadien-1-ol (184)

The alcohol (36 mg, 0.136 mmoles), prepared and purified as described above, was mixed with a vial (3 ml) of Sil-Prep, a commercially available silylating reagent consisting of pyridine, NH$_4$Cl,
(CH₃)₃SiCl, and [(CH₃)₃Si]₂-NH. The mixture was stoppered, mixed thoroughly and allowed to stand for 15 hours. The silylation reaction mixture was chromatographed on an SE-30 column (5% on 60/80 mesh Chromosorb W; 1/8" x 3') using a flow rate of 16 sec/10 ml and a column temperature of 170° C. Under these conditions the silyl derivative had a retention time of approximately 20 min. A mass spectrum showed a parent ion peak at m/e 336.
BIBLIOGRAPHY


40. C. Cole, Oregon State University, Unpublished information.


85. H. -J. Hansen, and H. Schmid, *Chimia*, 24, 89 (1970); see footnote 38, this work.


APPENDIX
Figure 3. Plot of logarithm of fraction of remaining pyran (I) vs. time in THF at 40°.

\[ [\text{LiBH}_4] = 0.23 \text{ M}, \quad [\text{pyran}] = 2.2 \times 10^{-4} \text{ M}. \]
Figure 4. Plot of logarithm of fraction of remaining pyran (1) vs. time in THF at 15°.
[LiBH₄] = 0.47 M, [pyran] = 2.7 x 10⁻⁴ M.
Figure 5. Plot of logarithm of fraction of remaining pyran (1) vs. time in diethyl ether at 15°. [LiAlH₄] = 0.056 M, [pyran] = 3.3 × 10⁻⁴ M.
Figure 6. Plot of logarithm of fraction of remaining pyran (1) determined by GLC vs. time at 15°. \([\text{LiAlH}_4]\) = 0.38 M, [pyran] = 1.45 \times 10^{-2} \text{ M.}
Figure 7. Plot of logarithm of fraction of remaining pyran (5) vs. time at 15°.
[LiAlH₄] = 0.13 M, [pyran] = 1.7 x 10⁻⁴ M.
Figure 8. Plot of logarithm of fraction of remaining pyran (11) vs. time at 15°.

\[ \frac{A_T - A_0}{A_0} \] vs. \( T \) (sec x 10^{-2})

\[ [\text{LiAlH}_4] = 0.15 \text{ M}, \text{[pyran]} = 1.2 \times 10^{-4} \text{ M}. \]
Figure 9. Modified gas washing bottle (x 1/2) used for clarification and dispensing of LiAlH₄ solutions.