# Rearrangements of Some Furan and Benzofuran 1,5,-Dienols

David Martin, Julie A. Wurster, Mary J. Boylan,
Robert M. Borzilleri, Gregory T. Engel and Edward J. Walsh*
Department of Chemistry, Allegheny College, Meadville, PA 16335, USA

Abstract: Isomers of 1-(2-furyl)-methyl-3-buten-ols and their benzofuran analogs
were studied for their oxy-Cope and anionic oxy-Cope reactivity.

It has been found that placing a hydroxy group at either the 3 or the 4 position in
a 1,5-diene accelerates the Cope rearrangement of these compounds by as much as a factor
of (1×10^3).[1] These oxy-Cope rearrangements can be seriously jeopardized by the retro-ene
side reaction. The retro-ene can be avoided and the rate for the Cope process accelerated
by as much as 10^{10-17} if the hydroxy group is deprotonated before rearrangement.[2] This
reaction is called an anionic oxy-Cope.
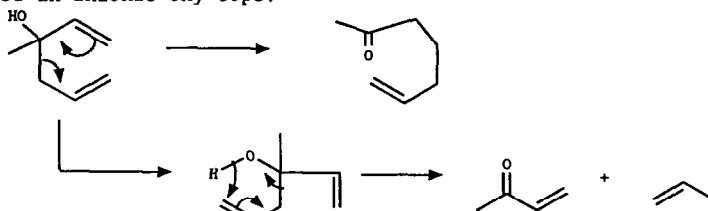
We are interested in the anionic oxy-Cope for those cases where one of the double
bonds in the 1,5-diene is incorporated in an aromatic ring. The reaction has failed when
one of the double bonds is in a benzene ring but has found some success with the naphthyl
nucleus[3a,b], particularly when the molecule is strained.

Jung and Hudspeth[3b] were the first to report a base-catalyzed oxy-Cope rearrangement
in which one of the olefins was part of a furan ring (Eq. 1). Paquette's group has recently
reported the involvement of a
3-substituted furan ring, also
constrained to a bicyclic
system, which participates in
the anionic oxy-Cope rearrange-
ment[4] (Eq.2). This report and
Wilson's excellent review of
the anionic oxy-Cope reaction[5]
have prompted us to report our
findings at this time.
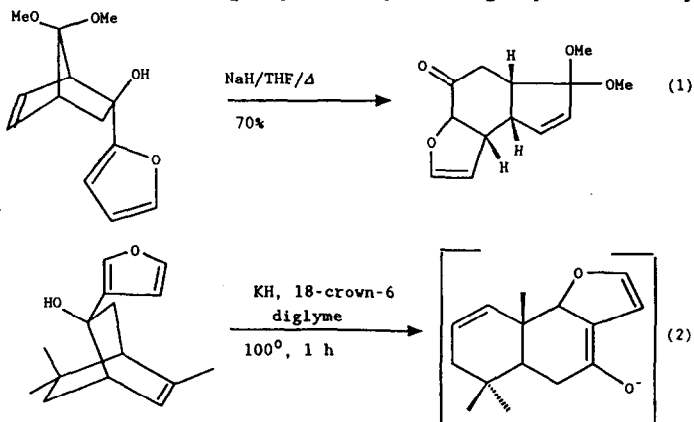
We have been studying the simple furan and benzofuran 1,5-dienol derivatives in terms of their reactivity in the oxy and anionic oxy-Cope reactions. Usually, the conditions we employed for the anionic oxy-Cope reactions of these derivatives included using 2 to 3 equivalents of KH, 1 to 2 equivalents of 18-crown-6 in all THF. The KH was treated with I_2[6] before use.
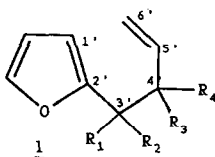
a. $R_1 = OH$, $R_2 = R_3 = R_4 = H$
b. $R_1 = OH$, $R_2 = Me$, $R_3 = R_4 = H$
c. $R_1 = OH$, $R_2 = Me$, $R_3 = H$, $R_4 = Me$
d. $R_1 = R_2 = H$; $R_3 = OH$, $R_4 = Me$

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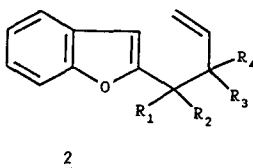
a. $R_1 = OH$, $R_2 = Me$, $R_3 = R_4 = H$
b. $R_1 = OH$, $R_2 = Me$, $R_3 = H$, $R_4 = Me$
c. $R_1 = R_2 = H$; $R_3 = OH$, $R_4 = Me$

2

The 1-Methyl-3-Buten-1-ol System (OH at the 3' position):

Under these conditions we found that **1a** and **b** were recovered unreacted from KH solutions containing added HMPA or 18-crown-6 after anywhere between 2 to 12 h in refluxing THF. The compound **1c** gave a formal [1,3] sigmatropic rearrangement under forcing conditions (72 h in refluxing glyme) but no [3,3] product (Eq. 3). It appears that the

$$(3)$$
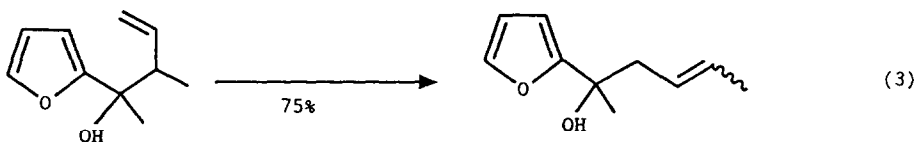
aromaticity of the furan is retarding the [3,3] rearrangement thereby allowing the [1,3] or fragmentation-recombination[7] to occur as the only rearrangement. Therefore, it seemed more likely that an anionic oxy-Cope rearrangement would occur in this system if the aromaticity of the heterocyclic ring could be attenuated. Toward this end we studied the behavior of the benzofuran derivatives, **2**.

After 24 h in refluxing THF with 3 equivalents of KH, **2a** was recovered unreacted. The isometer **2b**, on the other hand, rearranged smoothly after 2 h (Eq. 4) and 79% of the [3,3] rearrangement product was isolated. In this case we found that rearrangement occurs with or without 18-crown-6, but we were not able to find conditions that afforded rearomatization of the product.

$$(4)$$
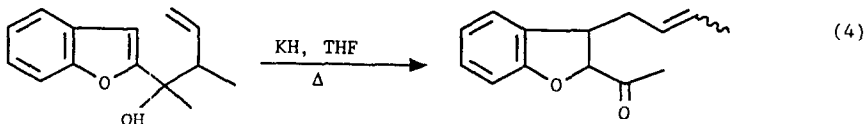
The 2-Methyl-3-Buten-2-ol System (OH at the 4' position):

We were interested in how this unsymmetrical 1,5-dienol system would respond to changing the location of the hydroxy group and were surprised to find that the simple furan derivative **1d** rearranged cleanly to the ketone **3**[8] (Eq. 5) with 2 equivalents of KH and 18-crown-6 in refluxing THF after 1.5 h. The ketone was isolated in 77-81% yields (no

$$ \text{1d} \xrightarrow{\text{KH}} \quad \xrightarrow{[3,3]} \quad \longrightarrow \quad \text{3} \tag{5} $$
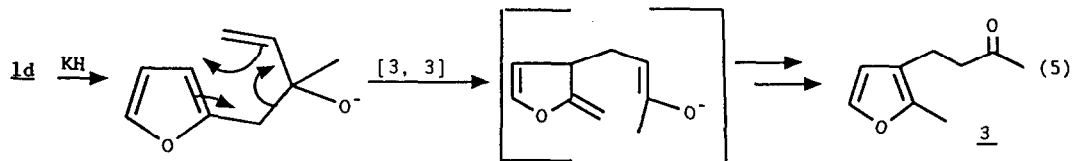
[1,3] product or starting material was observed). If the crown ether is not used, we found that even after 24 h of reflux the recovered alcohol was the major product. *This is, as far as we know, the only example of an anionic oxy-Cope reaction on a simple furan ring.* The reason(s) for the dramatic difference in behavior between the two isomers, **1c** and **1d** is not yet clear to us but is under investigation.

The benzofuran analog of **1d**, **2c**, gave us nothing but the fragmentation product 2-methylbenzofuran (Eq. 6). When the reaction was stirred overnight at ambient temperature, we were able to isolate 94% of this compound, which we assume results from known fragmentation reactions[7] of the alkoxide anion. No attempt was made to isolate the byproduct methyl vinyl ketone, but a polymeric residue was noted on workup.

$$ \xrightarrow[\substack{18\text{-crown-6} \\ 25^\circ}]{\text{KH, THF}} \tag{6} $$
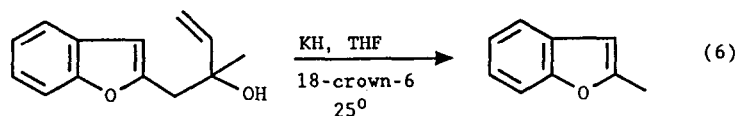
In order to test a non-aromatic analog of **1c**, we prepared the dihydropyranyl derivative **4** and found that, under our conditions, it rearranged smoothly and cleanly in 1 h to give the [3,3] product (isolated in 55% yield) (Eq. 7).

$$ \xrightarrow[18\text{-Crown-6}]{\text{KH, THF}} \tag{7} $$
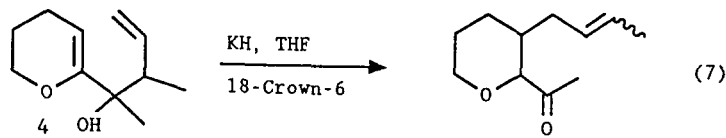
Oxy-Cope Reactions of these Furan and Benzofuran Derivatives:

A flash thermolysis apparatus was used for the oxy-Cope study of these compounds at temperatures between 400 and 500° and pressures of 1 to 1.5 torr.

Compounds **1b** and **c** at 500° gave quantitative yields of the retro-ene product 2-acetylfuran. As expected, **1d** did not give the retro-ene but it also gave no other reaction and was recovered unreacted.

In conclusion, we have found that for both the furan and benzofuran nucleus the location of the hydroxy group in the 1,5-dienol compound is crucial. In the furan case, it is essential that the hydroxy group be at the 4' position while in the benzofuran it must be in the 3' position to afford the [3,3] anionic oxy-Cope rearrangement.

The 3'-hydroxy alcohols were prepared from acetylfuran or acetyl benzofuran and the appropriate Grignard reagent. The 4'-hydroxy isomers were prepared by first lithiating the aromatic nucleus then reacting that anion with propylene oxide.[9] The resulting alcohol was oxidated with $CrO_{3/pyr}$[10] to the ketone which was then reacted with vinyl magnesium bromide.

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8. All new compounds gave ^{1}HNMR and ^{13}CNMR spectra and elemental analyses consistent with their structures. Both **1d** and **3** were also subjected to DEPT experiments that confirmed their structures. The 2,4DNP derivative of **3** was prepared (mp 144-145° from EtOH).

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