

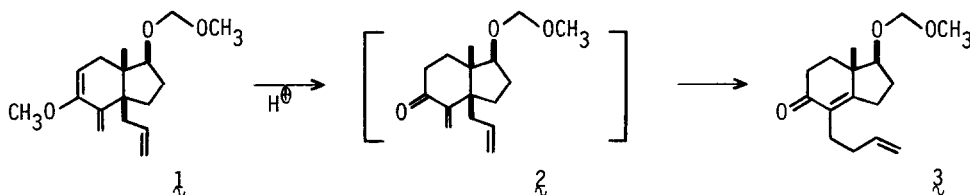
ACID CATALYZED COPE REARRANGEMENTS OF 2-ACYL-1,5-DIENES

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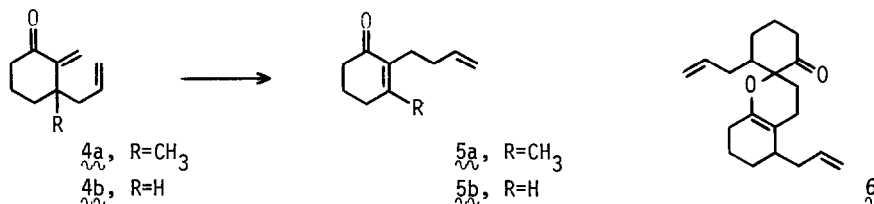
Abstract: The Cope rearrangement of 1,5-dienes bearing acyl substituents in the 2-position of the diene system is strongly accelerated by protic and Lewis acids.

In the course of studies related to the synthesis of tricyclic sesterterpenes, the enol ether **1**, prepared from the known diosphenol,¹ was subjected to mild acid hydrolysis² in order to obtain the unsaturated ketone **2**. However, the only product detected was the enone **3**, a compound derivable from a Cope rearrangement of the desired 1,5-diene **2**. Since Cope rearrangements usually require high temperatures, this result suggests that the rearrangement



of the proposed intermediate **2**, a 2-acyl-1,5-diene is subject to catalysis by acid. We now wish to report that this type of acid catalysis can be generalized to simple 2-acyl-1,5-dienes. The enones **4a** and **4b** have been synthesized³ and their acid-induced and thermal Cope rearrangement to **5a** and **5b** have been studied.

The enone **4a** upon heating in refluxing benzene rearranged ($\tau_{1/2} = 2$ h) to give the known enone **5a**¹⁰ as the sole product.¹¹ Under the same conditions, **4b** rearranged to the known enone **5b**¹² at the same rate. As a minor product, a dimeric compound was isolated and the structure **6** is proposed for this dimer on the basis of spectral data.¹¹



The rearrangements of **4a** and **4b** are greatly accelerated in the presence of a protic or a Lewis acid (see Table 1). The best results are obtained using 1 equivalent of acid.

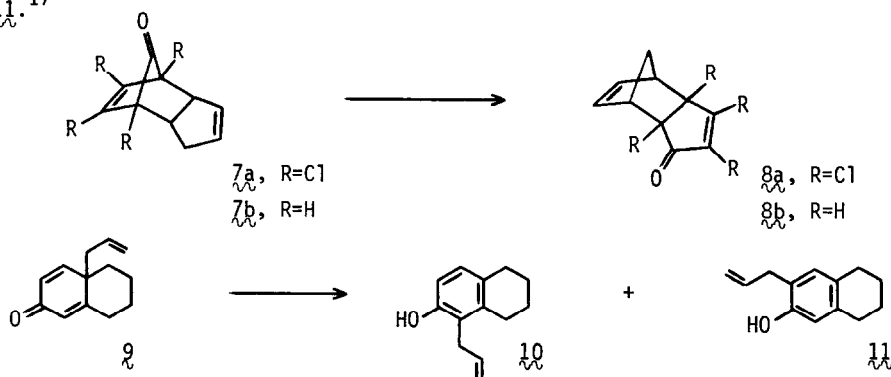
Table 1. Rearrangement of 2-Acyl-1,5-dienes.

Starting Material	Acid	Mol % Acid	Conditions ^a	Products ^b	Isolated Yield
4a	CF ₃ CO ₂ H	100	15 min, CH ₂ Cl ₂	5a(100)	74
4a	CF ₃ CO ₂ H	10	55 h, CH ₂ Cl ₂	5a(75) 4a(25)	83
4a	---	0	68 h, CH ₂ Cl ₂	5a(<10) 4a(>90)	100
4a	BF ₃ ·Et ₂ O	100	10 min, Et ₂ O	5a(85) 4a(15)	73
4b	CF ₃ CO ₂ H	100	90 min, CH ₂ Cl ₂	5b(100)	34
4b	BF ₃ ·Et ₂ O	100	20 min, Et ₂ O	5b(50) ^c	---

^aAll reactions performed at room temperature. ^bPercent in reaction mixture by HNMR. ^cAt least five minor products were formed in addition to 5b (TLC analysis). The crude reaction mixture is unchanged after prolonged treatment with BF₃·Et₂O (up to 8 h).

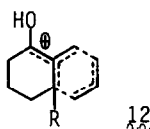
The pure enones 5a and 5b are stable when treated with 1 equivalent of trifluoroacetic acid.¹³ The equilibria of the rearrangements lie entirely on the side of enones 5a and 5b which are expected to be more stable than their isomers 4a and 4b because of the presence of the more highly substituted endocyclic double bond.

A few other examples of catalyzed Cope rearrangements have been reported.¹⁴ The rearrangements of the 3-acyl-1,5-dienes 7a and 7b to 8a and 8b were reported to be greatly accelerated by sulfuric acid and Lewis acids.¹⁵ In both cases, the equilibrium lies entirely on the side of the conjugated enone and the relief of strain in the methano-bridge in going from a sp²- to a sp³-center may provide an additional driving force.¹⁶ In a separate study, the 1-acyl-1,5-diene 9 has been reported to undergo a rapid acid catalyzed rearrangement to 10 and 11.¹⁷



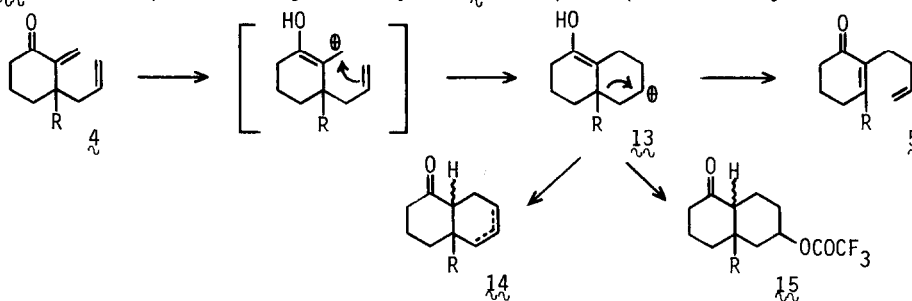
The present study shows that acid catalyzed rearrangement of acyl-1,5-dienes is a general phenomenon and not dependent upon the position of the substituent. Two different

mechanisms have been suggested to rationalize the acid-induced rate enhancement in these dienes. First, it is possible that these rearrangements are concerted and a conjugated carbonium ion $\overset{\ominus}{\text{C}}$ (from the protonation of the carbonyl group) as a substituent on the 1,5-diene system can facilitate the rearrangement by conjugation and stabilization of the six delocalized electrons of the Cope reaction transition state. This concept has been utilized



by Breslow¹⁸ to rationalize the facile solvolytic Cope rearrangements and it is supported by the fact that the conjugated carbonium ion can be in the 1-, 2-, or 3-position of a 1,5-diene system undergoing the Cope rearrangement.

Second, a stepwise carbocationic cyclization-induced rearrangement mechanism^{14,19} is also possible. The protonation of the enone **4** followed by cyclization to the bicyclic intermediate **13** and subsequent cleavage could yield **5**. In principle, the bicyclic intermediate

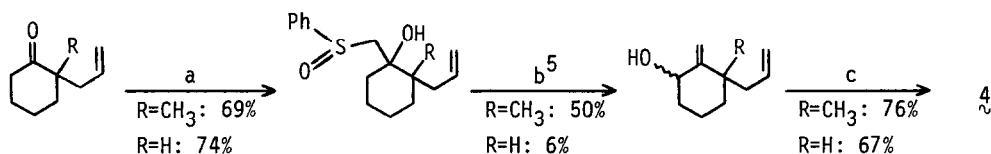


13 also could lead either to the octalone **14** (by deprotonation) or to the ester **15** (by quenching with trifluoroacetate). While the rearrangement of **4a** and **4b** clearly give a single pure product, such is not the case with the $\text{BF}_3 \cdot \text{Et}_2\text{O}$ induced rearrangement of **4b**. More experiments are needed to gain further information as to the mechanism of these acid-catalyzed Cope rearrangements of 1-, 2-, or 3-acyl-1,5-dienes.

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References and Notes

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2. The following conditions were used: 5M HCl-THF, 1:1, 0°C, 20 min or mercuric acetate in 3N formic acid, 1:1, 20°C, 3.5 days. The enol ether was stable for 12 h at 60°C.
3. All new compounds gave satisfactory NMR, IR and elemental analysis. The enones **4a** (R=CH₃) and **4b** (R=H) were prepared from 2-allyl-2-methylcyclohexanone⁴ and 2-allylcyclohexanone respectively, as follows:



^a $\text{C}_6\text{H}_5\text{S}(\text{O})\text{CH}_2\text{Li}$, THF, -70° to 20°C . ^b $(\text{CH}_3)_3\text{COK}$, $(\text{CH}_3)_3\text{COH}$, 20°C , 5 days. ^c CrO_3 , 2 pyridine, CH_2Cl_2 , 30 min, 20°C .

4a: NMR (250 MHz, CDCl_3) δ 1.13 (s,3), 1.55-1.80 (m,2), 1.83-1.97 (m,2), 2.12-2.25 (m,2), 2.33-2.56 (m,2), 5.04 (dm,1,J=17), 5.08 (dm,1,J=10), 5.16 (d,1,J=1.5), 5.72 (ddt,1, J=17,10,7), 5.78 (d,1,J=1.5); IR (neat) 3100, 2960, 1690 cm^{-1} .

4b: NMR (250 MHz, CDCl_3) δ 1.5-2.7 (m,9), 5.0-5.1 (m,2), 5.15 (s,1), 5.76 (m,1), 5.84 (s,1); IR (neat) 3100, 2960, 1690 cm^{-1} .

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The spectra properties for **6** are: IR (film) 3100, 1720, 1640 cm^{-1} ; NMR (250 MHz, CHCl_3) δ 1.3-2.3 (m,22), 4.9-5.1 (m,2), 5.55-5.85 (m,1) ppm; mass spectrum (70 eV) m/e 300 (parent) 259 (base, loss of allyl group).
12. We wish to thank Professor W. S. Johnson for communicating to us the properties of this compound which had been prepared in his laboratory by R. Wightman.
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