Tetrahedron Letters No. 25, pp. 2267-2270, 1971. Pergamon Press. Printed in Great Britain.

ON THE ACID-CATALYZED REARRANGEMENT OF β,γ-UNSATURATED KETONES

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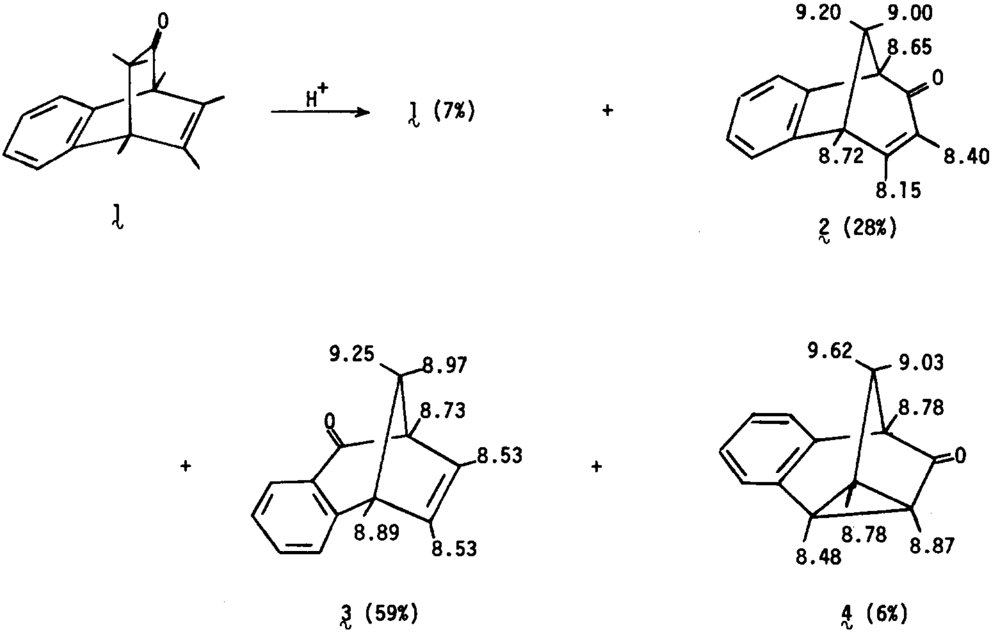
(Received in USA 3 May 1971; received in UK for publication 18 May 1971)

The rearrangement of β,γ-unsaturated ketones in acid has considerable potential for the synthesis of unusual bi- and tricyclic ring systems. In most examples described thus far, however, the double bond is present in the relatively strained cyclobutene ring.[1] We describe here a synthetically useful rearrangement of this type in which the double bond is in a six-membered ring, but is located in a favorable geometry for interaction with the protonated ketone.

Ketone 1[2] is readily accessible from hexamethyl-2,4-cyclohexadienone[3] and benzyne. When 1 was refluxed with trifluoracetic acid for several hours, an equilibrium mixture of 1-4



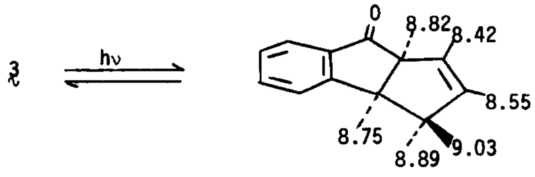
was obtained in the amounts shown. The reaction was clean; no other products were detected by nmr examination of the product mixture or by vpc. The same equilibrium mixture was obtained when each of the rearranged ketones was separately subjected to the isomerization conditions.

Ketones 2 and 3 were α,β-unsaturated ($\nu_{C=O}$ 1667 cm^{-1}) whereas 4 was not ($\nu_{C=O}$ 1720 cm^{-1}). The nmr spectrum of 2 showed two coupled allylic methyl groups (τ 8.15, 8.40; $J \cong 1$ Hz); the low-field methyl was readily exchanged by reflux with NaOMe/MeOD. The remaining methyls were assigned by measuring the slopes of the chemical shifts as a function of the mol ratio of europium shift reagent.[4,5]

Ketone 3, though conjugated, had no exchangeable methyl protons, even after prolonged reflux with NaOMe/MeOD. This fact requires that the carbonyl group be conjugated with the aromatic ring, not the double bond. The allylic methyl groups had, not unexpectedly, identical chemical shifts (τ 8.53) and appeared as a slightly broadened singlet. But when treated with a europium shift reagent, the allylic methyl closer to the carbonyl group had 1.6 x the slope of the other allylic methyl, and as soon as the two peaks separated the homoallylic coupling between them ($J \cong 1$ Hz) became apparent. The remaining peaks were assigned using the shift reagent.[5]

The non-conjugated ketone 4 had no allylic methyl groups, and therefore was tricyclic. The lowest field methyl group (τ 8.48) lies directly in the plane of the aromatic ring, whereas the highest field methyl group (τ 9.62) lies over the aromatic ring. The remaining assignments were made using the shift reagent.[5]

Irradiation of ketone 3 (Pyrex) gave an equilibrium mixture of 3 and its 1,3-acyl shift isomer 5; the equilibrium was approached from both sides, and favors 5 the more polar the solvent. Compound 5 was a five-membered ring conjugated ketone ($\nu_{C=O}$ 1705 cm^{-1}) and had no exchangeable allylic methyl protons. The nmr assignments were made using the shift reagent.



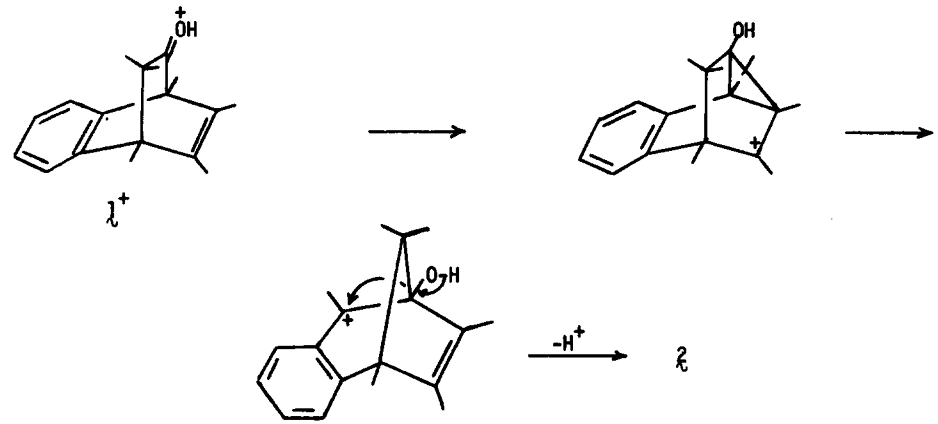
5

The photochemical behavior of ketones 2 and 3 supports the structural assignment, but will be described in detail in a separate paper.

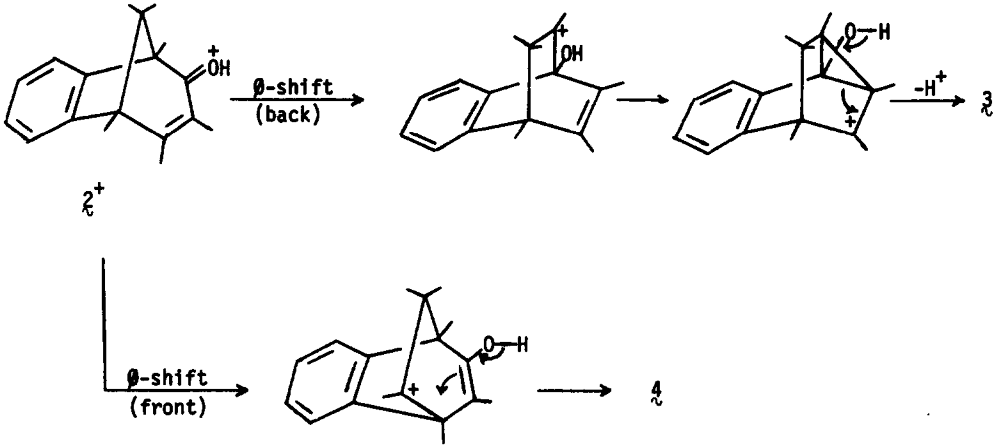
When ketone 1 was allowed to stand at room temperature with CF_3CO_2H it was converted mainly to 2 which only more slowly produced 3.[6]

A possible mechanism for the isomerizations which explains the formation of 2 before 3 is shown in the schemes. In the absence of any mechanistic information and to clarify the presentation the ions are drawn as classical.

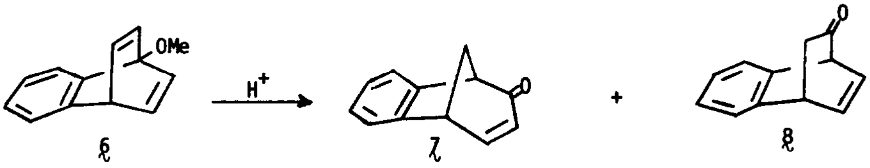
Scheme 1



Scheme 2



Since the same equilibrium mixture was obtained from all four ketones, the steps must be reversible. One can also enter the system at other points. For example the closely related rearrangement of 6 → 7 + 8, and analogs, was recently reported.[7]



Since many 2,2,2-bicyclooctadienones (such as **1**) are readily accessible through Diels-Alder additions to conjugated dienones, these reactions may prove generally useful synthetically. We are exploring the reaction scope and mechanism.

Acknowledgement. We are indebted to the National Science Foundation and the National Institutes of Health for their generous support.

References

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5. The mass spectrum and microanalytical data were consistent with the assigned structure.
6. In these preliminary experiments, followed by nmr, the concentration of **4** was too low to observe accurately.
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