Tetrahedron Letters No.21, pp. 1311-1315, 1964. Pergamon Press Ltd.
Printed in Great Britain.

THE PROTONATION OF CONJUGATED ENOL ETHERS.

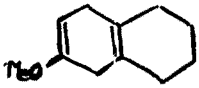
N. A. J. Rogers and A. Sattar

Department of Chemistry, University of Birmingham.

(Received 6 April 1964)

In the course of experiments connected with the synthesis, of various hexalins(1), it was observed in these laboratories that the acid catalysed hydrolysis of the dienol ether (II), under conditions which did not cause equilibration of the products, gave a significant yield of the octalone (VI). Since this seemed to be in opposition to the generally accepted pattern for the protonation of conjugated enols(2), the hydrolysis of the dienol ether (IV) was studied in the same qualitative manner, the results suggesting that in this case, α-protonation was the preferred mode of reaction. The apparent sensitivity of the site of protonation to changes of structure lead us to undertake a more thorough study of this reaction for a range of substituted homo- and heteroannular dienol ethers.

In a recent communication(3) Ringold described the kinetically controlled deuteration of the steroidal dienol ether (IX) which yielded exclusively the 6-β-deutero-4-en-3-one (X). From this result it was concluded that the transition state for the protonation of the conjugated enol and its ethers, unlike that for the protonation of the corresponding enolate ion, closely resembled the product. In the light of this communication, we wish now to present some of our own early results in this field, covering some aspects of the protonation of the ethers (II) and (III).



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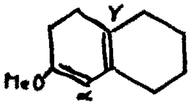

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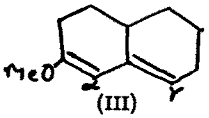

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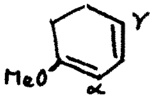

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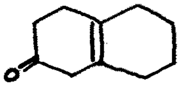

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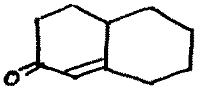

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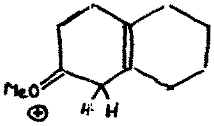
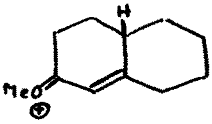
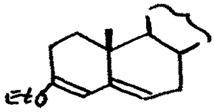


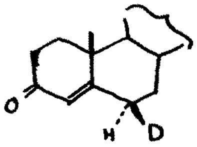
(VII)



(VIII)



(IX)



(X)

The ether (II) was chosen as the first object of study, and was prepared from 6-methoxy tetralin by reduction with lithium in liquid ammonia(4) to give the dienol ether (I) followed by isomerisation with potassamide under carefully controlled conditions(5,6). The product was a mixture of the dienol ethers (I) and (II), and 6-methoxytetralin. The percentage of homoannular conjugated diene in the mixture could be varied over a wide range by slight changes in the reaction conditions, but never exceeded about 75% (as determined by gas-liquid chromatography on polyethylene-glycol-adipate). Further purification of these mixtures was not achieved since chromatography on various grades of alumina, silica gel or Florisil resulted in the complete hydrolysis of the ethers(cf. 7). Preparative gas-liquid chromatography, while apparently separating the components of the mixture, appeared to result in a near quantitative conversion of (II) to 6-methoxytetralin during collection.

Accordingly, the mixtures were used directly in hydrolysis experiments, which were carried out in 1, 2-dimethoxy-ethane containing aqueous acetic acid. (In a typical experiment: 250 mgs. of the dienol ether mixture was dissolved in 2.5 ml. of dimethoxyethane to which was added 2.5 ml. of 50% aqueous acetic acid). The hydrolysis was studied at a number of temperatures between 8° and 45°C., the reaction being followed by taking aliquots at suitable time intervals and quenching by pouring into chilled sodium carbonate solution. The product was isolated under very mild conditions and analysed by gas-liquid chromatography.

At the temperatures studied, we were able to show that no appreciable change in composition of the dienol ether mixture occured during the reaction times involved (up to six hours). Further, under the hydrolysis conditions, no isomerisation of the ketone (V) to the conjugated isomer (VI) occured, and the dienol ether (I) yielded only the non-conjugated ketone (V). From this latter observation, it is clear that under these conditions, the α-protonation of the conjugated diene (II) is irreversible, and if the further reasonable assumption is made, that γ-protonation is also irreversible, then the only reactions to be considered can be represented in the scheme:

$$\begin{tikzcd}
(VI) & (VIII) \arrow[l, "H_2O"'] & (II) \arrow[l, "k_\gamma"'] \arrow[r, "k_\alpha"] & (VII) \arrow[r, "H_2O"] & (V) \\
 & & & (I) \arrow[u] &
\end{tikzcd}$$

Assuming that the reactions of the protonated species (VII) and (VIII) with water are rapid (cf. 8), it follows that the ratio of non-conjugated to conjugated ketone in the product, arising from the dienol ether (II), is equal to the ratio of k_α to k_γ. From the results of our experiments, k_α and k_γ were readily obtained at several temperatures, and hence also the Arrhenius parameters for the α- and γ- protonation reactions. These results will be reported in detail elsewhere.

At all temperatures studied, it was apparent that α- and γ-protonation of (II), under kinetically controlled conditions, are competitive processes. The percentage of α-protonation varied from 40 to 48%. Since these results differed markedly from those obtained by Ringold(3) for the dienol ether (IX) under very similar conditions, we investigated the kinetically controlled hydrolysis of the dienol ether (III), which would appear to be a close model for Ringold's work. In this case however, we could hope to make a complete analysis of the products, a process not readily achieved in the case of the less volatile steroidal compounds. Under standard hydrolysis conditions at 25°, this substance; showed no evidence of α-protonation, although as little as 1% can be detected by our method.

We are continuing our investigation of the effect of structural changes on the mode of reaction of conjugated enols and their ethers with acids and other electrophilic reagents, with particular emphasis on the apparent differences between the reactions of homo- and heteroannular dienol ethers.

Our thanks are due to the Royal Society for a grant towards the purchase of a Pye "Argon" Gas Chromatogram.

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