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KETONIC CARBANIONS AS INTRAMOLECULAR NUCLEOPHILES IN KETOESTERS

Keith Bowden * and Mohsen Chehel-Amiran
Chemistry Department
University of Essex, Wivenhoe Park, Colchester, Essex, CO4 3SQ, England.

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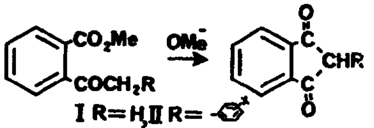
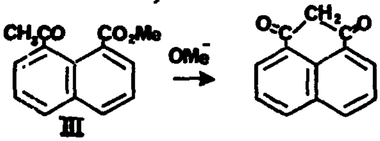
The reactivity of weak carbon acids has attracted much interest;[1] but there are many unexplained features. Our present studies have enabled us to demonstrate and interpret some of these. The process chosen was the methoxide catalysed cyclisation of the acyl esters, methyl 2-acetylbenzoate, I, methyl 2-(substituted phenylacetyl)benzoate, II, and methyl 8-acetyl-1-naphthoate, III, to form 1,3-diones[2,3] as shown below, (i) and (ii). The



(i)



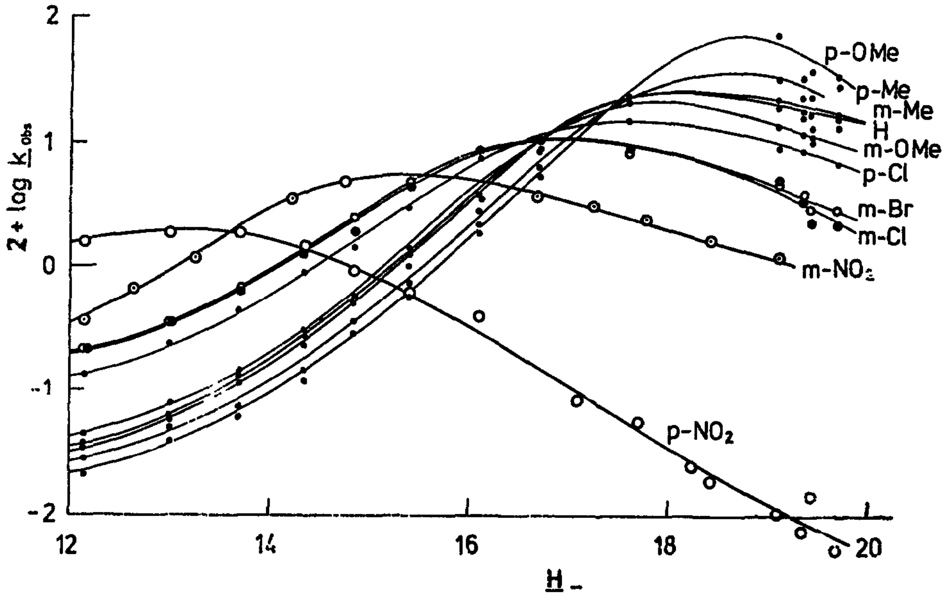
III

(ii)

generalised scheme shown (iii) indicates that a carbon acid HA ionises to form its conjugate carbanion A^-, followed by formation of the product.

$$HA + OMe^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A^- + HOMe \xrightarrow{k_2} \text{Products} \quad ...... \text{(iii)}$$

It has been possible to demonstrate all three variant pathways. As shown in the Figure the substituted phenylacetyl esters (generated from either the normal ester, II, or the pseudo ester or benzylidenephthalide) rearrange in methanolic DMSO containing methoxide with the rates increasing with increasing basicity to reach a maximum, and then decreasing. The sole exception is the p-nitro derivative whose rate decreases with increasing basicity over the whole range. With the exception of the latter the ρ values in methanol and 94 mole% methanolic DMSO are 1.8 and -1.4, respectively. The kinetic isotope effects for the 2-phenylacetyl esters using α,α-dideutero substrates is between 0.8 and 1.0 over the whole range of basicity. The kinetic order in methoxide anion is first order in methanol, but zero in 94 mole % methanolic DMSO. The spectral changes immediately on adding base to the 2-phenylacetyl substrates at high basicities clearly indicate the formation of an anionic species, which also occurs for the p-nitro derivative over the range of basicity. For the 2-phenylacetyl system the evidence indicates that k_{obs} at low basicity is equal to Kk_2 and at high basicity to k_2. Methyl 2-acetylbenzoate, I, and 8-acetyl-1-naphthoate, III, have kinetic isotope effects, using the α,α,α-trideuterio substrates, of 0.7 to 0.9 and 5 to 7, respectively. Both systems have rates of reaction which increase with increasing basicity. The relative rate ratios (uncorrected for benzoate ester tautomeric equilibria) for III/II and I/II are 35 (methanol) and 0.0088 (80 mole % methanolic DMSO), respectively. Thus k_{obs} for the naphthoate ester, III, is equal to k_1 and for the benzoate ester, I, to Kk_2.



Relation between log $\underline{k}_{obs}$ for the Intramolecular Cyclisation of Methyl 2-(substituted phenylacetyl)benzoates with $\underline{H}_-$

The following conclusions can be drawn:-

(i) Stereochemical control of reactivity can be achieved so that the formation of the carbanion is rate-determining and the innate high nucleophilicity of the latter is exposed;

(ii) Substituent effects on the reactivity can be reversed as stabilisation of the carbanion reduced its reactivity as a nucleophile but increases its ease of formation;

(iii) Aprotic/protic solvent effects on reactivity can be reversed depending on whether they increase the ease of formation or decrease the nucleophilicity of the carbanion.

References

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