

Keten Intermediates in the Uncatalysed Alcoholysis of β -Keto-esters and Related Compounds

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Summary Uncatalysed alcoholysis of alkyl acetoacetates and malonates occurs *via* a unimolecular dissociative mechanism involving concerted elimination of alcohol with resultant formation of substituted ketens as reactive intermediates.

observation that propyl acetoacetate and ethyl benzoylacetate underwent exchange of alcohol fragments in heptane solution in the absence of added free alcohol at a rate ($10^5 k_1^1 = 4.9 \text{ s}^{-1}$ at 110°) similar to the rate of reaction of ethyl acetoacetate with propan-1-ol.†

RECENT publication¹ of evidence for an elimination-addition (*E1cB*) mechanism for hydrolysis of certain acetoacetic and malonic esters over a wide range of pH prompts us to publish our results for the uncatalysed alcoholysis of alkyl acetoacetates and malonates in non-aqueous media. These alcoholyses have been studied previously² but an adequate mechanistic interpretation has not yet emerged.

In the present work, initial rates of reaction of ethyl acetoacetate with propan-1-ol in heptane, acetone, and propan-1-ol solutions were used to obtain observed initial first-order rate constants (k_1^1) for first-order disappearance of starting ester.† In heptane solution at 89.6° , $10^5 k_1^1 = 1.6 \pm 0.1 \text{ s}^{-1}$ over a five-fold range of ester concentration and a ten-fold range of alcohol concentration. The variation of k_1^1 with alcohol concentration in acetone solution was somewhat greater (30% over a ten-fold range) but there was no full kinetic order in alcohol. The reaction rate and activation parameters (Table 1) showed only minor variations through the solvent series.

TABLE 1

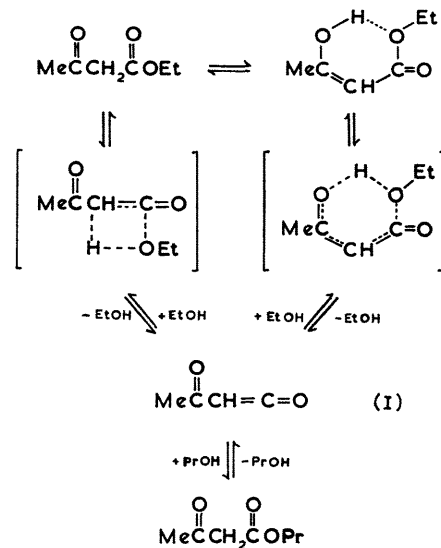
Rate data for reaction of ethyl acetoacetate (0.100M) with propan-1-ol (0.200M where appropriate)

Solvent	Heptane	Acetone	Propan-1-ol
$10^5 k_1^1$ at 110° (s^{-1})	.. 12.0	4.0	5.2
ΔH^\ddagger (kcal mol ⁻¹) ^a	.. 27 ± 2	28 ± 2	25 ± 2
ΔS^\ddagger (e.u.) ^a -7 ± 5	-7 ± 5	-14 ± 5

^a Over the range 90 to 121° . Errors are estimated.

Both the independence of reaction rate on alcohol concentration and the combination of a high enthalpy of activation with a comparatively small negative entropy of activation are inconsistent with a bimolecular displacement mechanism for the reaction. Moreover, the relative ease with which the reaction occurs in hydrocarbon solution and the insensitivity of rate to change of solvent precludes the possibility of a unimolecular heterolytic dissociation mechanism involving significant charge separation in the transition state.

We consider that the results are most readily explained by a mechanism involving rate-determining concerted elimination of alcohol to give acetylketen (I) as a reactive intermediate (Scheme). The present evidence cannot distinguish between direct four-centre elimination from the keto-form of the ester and six-centre elimination *via* the enol form. Such mechanisms receive further support from the



SCHEME

Attempts to detect or trap the acetylketen under the conditions of the exchange reactions have not been successful due, presumably, to the relatively high reactivity of ketens towards alcohols,³ but heating ethyl acetoacetate (b.p. 183°) under slow distillation conditions resulted in fractionation of ethanol from the system, and dehydroacetic acid (i.r., n.m.r., u.v., and m.p. consistent with published data⁴) could be readily isolated from the undistilled material. The formation of dehydroacetic acid can most readily be explained by an *in situ* 4 + 2 cyclodimerisation of (I).

TABLE 2

Rate data for reaction of diethyl malonate (0.100M) with propan-1-ol (0.200M in heptane) in the range 100 – 130°

Solvent	$10^5 (\frac{1}{2} k_1^1)$ at 110° (s^{-1})	ΔH^\ddagger (kcal mol ⁻¹)	ΔS^\ddagger (e.u.)
Heptane	.. 2.1	26 ± 2	-14 ± 5
Propan-1-ol	.. 0.82	28 ± 2	-14 ± 5

Results for the reaction of diethyl malonate with propan-1-ol are summarised in Table 2. For these reactions

† It was established that $>97\%$ of ester disappearing can be accounted for in the formation of n-propyl acetoacetate.

‡ $10^5 k_1^1 = 90 \text{ s}^{-1}$ for reaction of ethyl benzoylacetate with propan-1-ol at 110° in heptane solution.

k_1^1 was derived from the initial rate of formation of ethyl propyl malonate and $\frac{1}{2} k_1^1$ was used for evaluation of activation parameters in order to bring the results statistically in line with those for the monofunctional ester. At 110° in heptane solution k_1^1 decreased by <20% over a five-fold

increase in alcohol concentration. The malonate reaction therefore appears to follow the same mechanism as that suggested for the acetoacetates.

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