Enol Tautomers of Malonic and Methylmalonic Acids as Intermediates in Nitrosation

Alan Graham and D. Lyn H. Williams*

Chemistry Department, University Science Laboratories, South Road, Durham DH1 3LE, UK

At relatively high acid concentration in the presence of bromide ion catalyst, nitrosation of both malonic and methylmalonic acids involves rate-limiting enolisation of the carboxylic acids.

There continues to be much interest in the chemistry of enols derived from ketones and aldehydes. Studies have focused on the synthesis of stable enols[1] as well as on the measurement of rates of ketonisation and other reactions.[2] In principle other compounds containing the carbonyl group should behave similarly, but not much has been established experimentally. Enol intermediates derived from carboxylic acids (and esters) have occasionally been postulated, but their presence has not been widely demonstrated conclusively. Stable enols derived from ketones have been synthesised by using large substituent groups which stabilise the enol form, and recently this approach has successfully been applied[3] to the synthesis of enols derived from carboxylic acids and esters, using two pentamethylphenyl substituents. Calculations suggest[4] that simple 'acid enols' are much less stable than are those derived from ketones and aldehydes, so it is not surprising that they have not been so clearly identified. More recently the enol of mandelic acid has been generated by flash photolysis methods and measurements of its ketonisation rate and the enolisation rate have enabled the value of 15.4 to be obtained for the pK_E.[5]

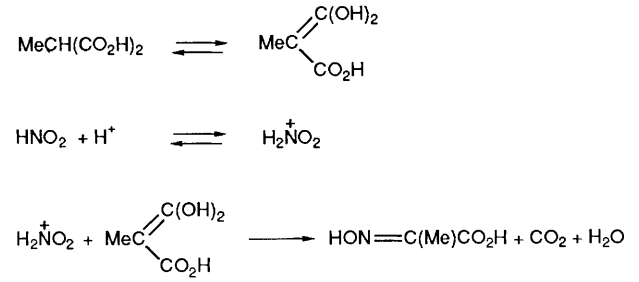
We have examined the kinetics of the nitrosation of malonic (MA) and methylmalonic (MMA) acids using acidified aqueous solutions of nitrous acid. The product from MMA has been characterised[6] as the oxime (see Scheme 1) formed after a decarboxylation reaction. The product from MA is too unstable to be isolated and characterised.[7] At very low acid concentrations (pH *ca.* 1–2) and without added nucleophilic

$$MeCH(CO_2H)_2 \rightleftarrows Me\bar{C}(CO_2H)_2 + H^+$$

$$HNO_2 + H^+ \rightleftarrows H_2\overset{+}{N}O_2$$

$$H_2\overset{+}{N}O_2 + Me\bar{C}(CO_2H)_2 \rightarrow HON{=}C(Me)CO_2H + CO_2 + H_2O$$

Scheme 1



Scheme 2

catalysts (*e.g.* Br$^-$) we find the reaction to be first order in [HNO_2] and [MMA or MA], and within this range there is no acid catalysis. This suggests that reaction occurs *via* an anionic form of the reactant, probably the carbanion as outlined in Scheme 1. At this acidity there is a pronounced catalysis by Br$^-$ as expected when NOBr becomes the effective reagent.

However at higher acidity (greater than *ca.* 0.1 mol dm^{-3}) the reaction becomes acid catalysed (see Fig. 1), suggesting that reaction occurs *via* a different intermediate, which does not arise by an equilibrium proton loss. A likely structure is the enol form of the carboxylic acid (see Scheme 2). The shape of the curve in Fig. 1 is then qualitatively explained by the change of intermediate, from the carbanion at high pH to the enol at low pH. Further evidence for these mechanistic ideas comes from a study of the corresponding Br$^-$ catalysed reactions. In 1.33 mol dm^{-3} $HClO_4$ in the presence of Br$^-$ the reaction gradually loses its first-order dependence on [HNO_2] with increasing [Br$^-$], becoming a fully zero-order process at 0.50 mol dm^{-3} Br$^-$ when there is no Br$^-$ catalysis. At much lower acidities (typically 0.05 mol dm^{-3} $HClO_4$) even in the presence of 0.50 mol dm^{-3} Br$^-$, the reaction remains fully first-order in [HNO_2] and Br$^-$ catalysis occurs. The zero-order reaction is readily interpreted as rate-limiting enolisation which occurs when the rate of nitrosation is much larger than that of ketonisation. Malonic acid behaves in a similar fashion although it is less easy to achieve the fully zero-order behaviour. The intermediate zero–first-order pattern can readily be treated as a mixed-order situation and both rate constants obtained.

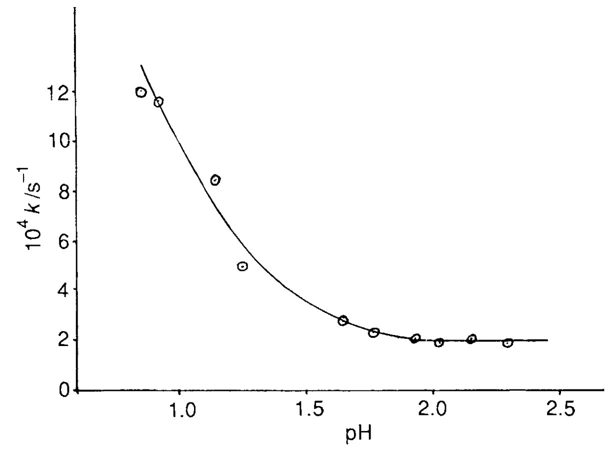


Fig. 1 Dependence of the rate constant for nitrosation of MMA upon pH

As yet we have not established the detailed form of the acid catalysis of enolisation, beyond showing that it exists. We find a value of 8.5×10^{-5} s^{-1} for the first-order rate constant (rate = k[MMA]) for enolisation at 25 °C in 1.33 mol dm^{-3} $HClO_4$. Recently[8] the rate constant for enolisation of MMA has been measured (at one acidity) by monitoring the H-atom exchange with deuterium using ^{1}H NMR. These authors[8] find a value of 5.7×10^{-5} s^{-1} for the reaction in 1 mol dm^{-3} sulphuric acid at 25 ± 2 °C. These two values are probably in reasonable agreement, given the different acidities used. The comparable value for the enolisation of acetone[9] (again from nitrosation reactions) is 5.1×10^{-5} s^{-1} extrapolated to 1.33 mol dm^{-3} $HClO_4$, suggesting that these acid catalysed enolisations are not very structure-dependent in these cases.

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