PERKIN 2

# Halogenation of malonic acid and malonic acid monoethyl ester. Enolisation pathways and enol reactivity

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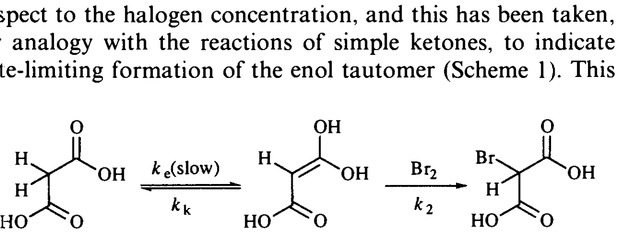
**Reactions of iodine (2 × $10^{-5}$ mol dm$^{-3}$) and bromine (5 × $10^{-5}$ mol dm$^{-3}$) in water with malonic acid (MAL) (in large excess) are first-order in [halogen] and in [MAL] and are independent of acidity in the range 0.02–0.16 mol dm$^{-3}$ H$^+$. These results are consistent only with a rate-limiting reaction between the halogen and the enol form of MAL. Evidence is presented that these reactions occur at the diffusion limit and the results enable a value for $K_E$ (the equilibrium constant for enolisation) of 7.4 × $10^{-9}$ to be deduced. At a much higher bromine concentration (*ca.* 2 × $10^{-3}$ mol dm$^{-3}$) the reaction is zero-order in [$Br_2$], consistent with a rate-limiting enolisation. Values of $k_e$ (the rate constant for enolisation) for MAL and for malonic acid monoethyl ester (EHM) are reasonably similar (4.0 × $10^{-3}$ and 1.1 × $10^{-3}$ s$^{-1}$, respectively) and are about $10^2$ greater than the value for diethyl malonate, supporting a mechanism of enolisation involving internal H$^+$ transfer for both MAL and EHM. Under conditions zero-order in [$Br_2$], the dependence of the observed rate constant upon the total stoichiometric concentration of malonic acid [MAL]$_T$ over the pH range 1.0–4.3 enables the kinetic identification of a reaction pathway involving base catalysis by malonate ion in addition to the solvent promoted reaction which is dominant at lower pH. At higher pH values there is evidence of a third pathway involving malonate ion catalysis of enolisation of the malonate ion.**

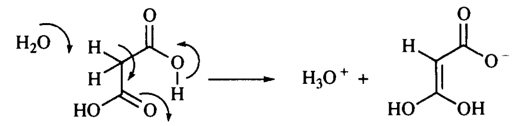
In recent years there has been a renewal of interest in the chemistry of enols,[1] particularly those derived from carboxylic acids, esters and amides.[2] Some of this interest has centred on the synthesis of stable enols, generally using the idea pioneered by Fuson *et al.*[3] for enols derived from simple ketones. This is based on the use of large substituent groups which destabilise the keto form by a reduction of the solvation associated with the polar carbonyl group, and which also can make it more difficult for a base (often the solvent) to remove the C–proton. Relatively stable enols have been identified from desilylation of ketene acetals[4] and by ketene hydration.[5] More recently the enol of a carboxylic acid has been isolated (and its structure established) when complexed to an (ethane-1,2-diamine)–platinum(II) fragment.[6] Other approaches have concentrated on kinetic analysis of such keto–enol systems and have obtained quantitative data on keto–enol equilibrium constants $K_E$ and rate constants for enolisation $k_e$ and ketonisation $k_k$.[7-9] The work of the Kresge group has included an extension of their earlier work to the generation of carboxylic acid enols by flash photolysis procedures.

The halogenation of malonic acid (MAL) was first studied kinetically in 1912[10] and has been examined subsequently.[11-14] Usually, the reaction has been found to be zero-order with respect to the halogen concentration, and this has been taken, by analogy with the reactions of simple ketones, to indicate rate-limiting formation of the enol tautomer (Scheme 1). This requires that the rate of reaction of the enol is much faster than the rate of its ketonisation, $k_2[Br_2] \gg k_k$. A significant finding was that enolisation here is not an acid-catalysed process[13] and it has been suggested that an intramolecular proton transfer takes place [reaction (1)]. Proton loss to the solvent from $-CH_2$ could be a concurrent or a later process.



**Scheme 1**

Alternatively the reaction may occur without such intramolecular participation since the powerfully electron-withdrawing $CO_2H$ groups make the carbon protons sufficiently acidic to allow the reaction to occur. There are a number of examples in the literature where enolisation (*e.g.* of 1,3-dichloroacetone)[15] is not acid catalysed. This is interpreted as base-catalysed (solvent in this case) ionisation leading to the carbanion↔enolate intermediate.



(1)

Two accounts[12,13] report that when enolisation is rate limiting, the order with respect to [MAL] is > 1, and eqn. (2)

$$\text{Rate} = k_o = k_e[\text{MAL}] + k[\text{MAL}]^2 \qquad (2)$$

was established experimentally,[12] but no mechanistic interpretation was offered. Later[14] it was suggested that this might arise from malonate ion catalysed enolisation.

At much lower iodine concentrations it has been shown[13] that the reaction with malonic acid is first-order in [$I_2$], consistent with a change in the rate-limiting step from enolisation to the halogenation of the enol. This will occur (Scheme 1) when $k_2[I_2] \ll k_k$. There is the possibility of reaction *via* the enol and/or enolate (carbanion). This has been described, for example, in the nitrosation of dimedone[16] and of Meldrum's acid[17] as well as in the halogenation of a number of enols such as those derived from a number of dimedone and tetronic acid derivatives.[18] Kresge and co-workers[9] have drawn attention to the fact that enols from carboxylic acids (or esters) should be more acidic than their counterparts derived from ketones or aldehydes and have estimated that the extra α-OH group should contribute *ca.* 2 p$K_a$ units. It is to be expected therefore that reaction pathways *via* the enolate anion should be more evident for reactions of enols and enolates derived from carboxylic acids and esters. Bell and Yates[19] have quantified that pathway for the halogenation of diethyl malonate.

In this paper we present results of a kinetic study of the

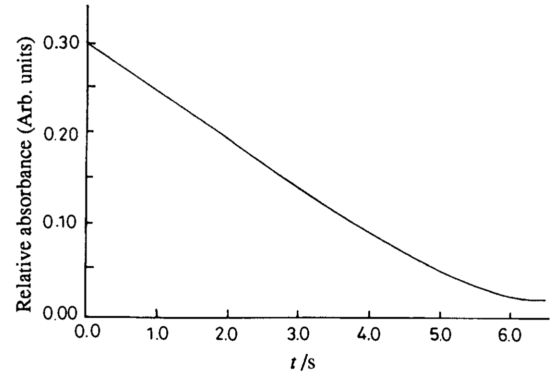


**Fig. 1** Typical zero-order plot for the reaction of bromine ($2 \times 10^{-3}$ mol dm$^{-3}$) with MAL ($5 \times 10^{-2}$ mol dm$^{-3}$) at pH 2.75

**Table 1** Values of $k_o/[\mathrm{MAL}]_T$ for the reaction of MAL with $Br_2$ ($2 \times 10^{-3}$ mol dm$^{-3}$) at pH 1.0

| $[\mathrm{MAL}]_T$/mol dm$^{-3}$ | $(k_o/[\mathrm{MAL}]_T)/10^{-3}$ s$^{-1}$ |
|---|---|
| 0.050 | 3.86 |
| 0.075 | 3.92 |
| 0.100 | 3.96 |
| 0.125 | 4.02 |
| 0.150 | 3.98 |

**Table 2** Values of $k_o$ for the reaction of EHM (0.050 mol dm$^{-3}$) with $Br_2$ ($1.8 \times 10^{-3}$ mol dm$^{-3}$) at different acidities

| $[H^+]$/mol dm$^{-3}$ | $k_o/10^{-5}$ mol dm$^{-3}$ s$^{-1}$ |
|---|---|
| 0.20 | 5.31 |
| 0.40 | 5.15 |
| 0.60 | 6.45 |
| 0.80 | 5.80 |

**Table 3** Values of $k_o/[\mathrm{EHM}]_T$ for the reaction of EHM with $Br_2$ ($2.5 \times 10^{-3}$ mol dm$^{-3}$) at 0.1 mol dm$^{-3}$ $H^+$

| $[\mathrm{EHM}]_T$/mol dm$^{-3}$ | $(k_o/[\mathrm{EHM}]_T)/10^{-4}$ s$^{-1}$ |
|---|---|
| 0.05 | 8.70 |
| 0.10 | 8.78 |
| 0.15 | 8.57 |
| 0.20 | 9.97 |
| 0.25 | 9.76 |

**Table 4** Values of $k_o/[\mathrm{MAL}]_T$ for the reaction of $Br_2$ ($2.3 \times 10^{-3}$ mol dm$^{-3}$) with MAL at pH 1.40, 1.85, 2.75, 3.30, 3.80 and 4.30

| pH | $[\mathrm{MAL}]_T$/mol dm$^{-3}$ | $k_o/10^{-4}$ mol dm$^{-3}$ s$^{-1}$ | $(k_o/[\mathrm{MAL}]_T)/10^{-3}$ s$^{-1}$ |
|---|---|---|---|
| 1.40 | 0.050 | 2.08 | 4.17 |
| 1.40 | 0.075 | 3.15 | 4.20 |
| 1.40 | 0.100 | 4.25 | 4.25 |
| 1.40 | 0.125 | 5.43 | 4.34 |
| 1.40 | 0.150 | 6.63 | 4.42 |
| 1.85 | 0.050 | 2.25 | 4.50 |
| 1.85 | 0.075 | 3.70 | 4.93 |
| 1.85 | 0.100 | 5.15 | 5.15 |
| 1.85 | 0.125 | 6.81 | 5.44 |
| 1.85 | 0.150 | 8.40 | 5.60 |
| 2.75 | 0.050 | 2.19 | 4.38 |
| 2.75 | 0.100 | 5.50 | 5.50 |
| 2.75 | 0.150 | 11.0 | 7.33 |
| 2.75 | 0.200 | 18.2 | 9.12 |
| 2.75 | 0.250 | 24.0 | 9.60 |
| 3.30 | 0.100 | 4.04 | 4.04 |
| 3.30 | 0.150 | 8.12 | 5.40 |
| 3.30 | 0.175 | 10.29 | 5.88 |
| 3.30 | 0.200 | 13.18 | 6.59 |
| 3.80 | 0.100 | 1.97 | 1.97 |
| 3.80 | 0.150 | 4.10 | 2.72 |
| 3.80 | 0.175 | 7.37 | 3.68 |
| 3.80 | 0.200 | 11.0 | 4.40 |
| 4.30 | 0.100 | 1.06 | 1.06 |
| 4.30 | 0.150 | 2.10 | 1.40 |
| 4.30 | 0.200 | 3.75 | 1.88 |
| 4.30 | 0.250 | 5.84 | 2.34 |

bromination and iodination of malonic acid and its monoethyl ester (EHM) in an attempt to provide evidence for or against the mechanism for enolisation *via* intramolecular hydrogen ion catalysis. Further we hoped to establish the relative importance of reactions *via* the enol and enolate intermediates as well as providing quantitative evidence for the earlier proposal for malonate ion catalysis of enolisation.

## Results and discussion

### Enolisation of MAL and EHM

At relatively high $[Br_2]$ values of 2–3 × $10^{-3}$ mol dm$^{-3}$ and with $[\mathrm{MAL}] > 5 \times 10^{-2}$ mol dm$^{-3}$, we find excellent zero-order plots for over 80% reaction. A typical trace showing the decreasing absorbance due to $Br_2$ is shown in Fig. 1. At higher $[Br_2]$ values we find a departure from zero-order kinetics which we attribute to complications arising from the well known dibromination reaction. Data for reactions at pH 1.0 are given in Table 1. At this pH we expect little interference from a possible malonate ion catalysed pathway (p$K_a$ of malonic acid[20] 2.85) and indeed the reaction is truly first-order in $[\mathrm{MAL}]_T$ as judged by the constancy of $k_o/[\mathrm{MAL}]_T$ over the range of [MAL] used. This yields a value for the enolisation rate constant $k_e$ (where $k_e = k_o/[\mathrm{MAL}]_T$) of $(3.95 \pm 0.06) \times 10^{-3}$ s$^{-1}$. This agrees quite well with literature values of $2.0 \times 10^{-3}$, $2.7 \times 10^{-3}$ and $4.7 \times 10^{-3}$ s$^{-1}$ also obtained from halogenation experiments.[13,14]

We carried out the same experiments with EHM again with $[Br_2]$ *ca.* $2 \times 10^{-3}$ mol dm$^{-3}$ and EHM in a large excess. Good zero-order plots were again obtained up to beyond 80% reaction. The results are presented in Tables 2 and 3. As is evident the rate constant is independent of the acidity in the range 0.2–0.8 mol dm$^{-3}$ $H^+$ and the reaction is first-order in EHM at 0.1 mol dm$^{-3}$ $H^+$. Thus we get two experimental values for $k_e$ of $1.1 \times 10^{-3}$ and $0.92 \times 10^{-3}$ s$^{-1}$, respectively. These values are quite close (within a factor of two) to those reported for MAL particularly when the statistical factor is taken into account. The literature values for $k_e$ for diethyl malonate are about 100 times smaller, typically $2.85 \times 10^{-5}$, $2.4 \times 10^{-5}$ and $2.5 \times 10^{-5}$ s$^{-1}$ obtained from halogenation experiments.[19,21,22]

These results suggest that both MAL and EHM have a reaction pathway of lower energy than that for diethyl malonate and give support to the suggestion[13] that intramolecular acid catalysis occurs for the acids. There are literature reports that reveal that enolisation of keto acids is assisted by $H^+$ donation from COOH to the carbonyl oxygen atom in the rate limiting step.[23,24] In one case[24] the enolisation of 2-oxocyclohexanecarboxylic acid is many orders of magnitude faster than is the enolisation of the methyl ester. However it has been argued[25] that COOH assistance is not a feature in the base-catalysed (phosphate) enolisation of EHM.

### Base catalysis by malonate ion

At pH values > *ca.* 2 the enolisation of MAL loses the first-order dependence upon [MAL]. The experimental results are given in Table 4. Henceforth we will use $[\mathrm{MAL}]_T$ to denote the total stoichiometric concentration of malonic acid, [MAL] the concentration of undissociated malonic acid and $[\mathrm{MAL}^-]$ the concentration of the malonate ion. Clearly at the higher pH values the order with respect to $[\mathrm{MAL}]_T$ is greater than one and a possible explanation is base catalysis by $\mathrm{MAL}^-$. If we assume that we now have both pathways (solvent promoted and MAL$^-$ promoted), given by reactions (3) and (4), then the rate equation

$$\mathrm{MAL} \xrightarrow{k_e} \mathrm{ENOL} \qquad (3)$$

$$\mathrm{MAL} + \mathrm{MAL}^- \xrightarrow{k_3} \mathrm{ENOL} \qquad (4)$$

is given by eqn. (5) which can be rearranged to give eqns. (6) and

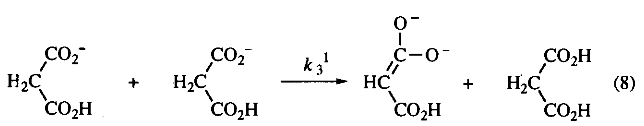
$$\mathrm{Rate} = k_o = k_e[\mathrm{MAL}] + k_3[\mathrm{MAL}][\mathrm{MAL}^-] \qquad (5)$$

$$\mathrm{Rate} = k_o = \frac{k_e[\mathrm{H}^+][\mathrm{MAL}]_\mathrm{T}}{([\mathrm{H}^+] + K_a)} + \frac{k_3K_a[\mathrm{H}^+][\mathrm{MAL}]_\mathrm{T}^2}{([\mathrm{H}^+] + K_a)^2} \qquad (6)$$

(7) by expressing all the concentrations in terms of $[\mathrm{MAL}]_\mathrm{T}$.

$$\frac{k_o}{[\mathrm{MAL}]_\mathrm{T}} = \frac{k_e[\mathrm{H}^+]}{([\mathrm{H}^+] + K_a)} + \frac{k_3K_a[\mathrm{H}^+][\mathrm{MAL}]_\mathrm{T}}{([\mathrm{H}^+] + K_a)^2} \qquad (7)$$

Now $k_o$ is, as before, the measured zero-order rate constant and $K_a$, the first dissociation constant of malonic acid. At each pH, plots of $k_o/[\mathrm{MAL}]_\mathrm{T}$ *vs.* $[\mathrm{MAL}]_\mathrm{T}$ should be linear with a positive slope and intercept. At the higher acid concentrations when $[\mathrm{H}^+] \gg K_a$ (as at pH 1.0) then $k_o = k_e[\mathrm{MAL}]_\mathrm{T}$, as observed. The data from Table 4 have been plotted this way and are shown in Fig. 2. They show that eqn. (7) is reasonably well obeyed. From the intercept of these plots we can evaluate $k_e$. The four values $4.61 \times 10^{-3}$, $5.87 \times 10^{-3}$, $3.07 \times 10^{-3}$ and $4.66 \times 10^{-3}$ s$^{-1}$ [average $(4.5 \pm 0.1) \times 10^{-3}$ s$^{-1}$] are in reasonable agreement with the value obtained at pH 1.0 and the literature values, given the inherent accuracy in the measurements of relatively small intercepts. Similarly values of $k_3$ can be obtained from the slopes of the plots. We obtain values of 0.13, 0.13, 0.13, 0.18 and 0.25 dm$^3$ mol$^{-1}$ s$^{-1}$ for reactions at pH 1.85, 2.75, 3.30, 3.80 and 4.30, respectively. These are constant up to pH *ca.* 3.3 and increase slightly thereafter. This raises the possibility that at the higher pH values, where the concentration of undissociated malonic acid is very small, that enolisation occurs by base (malonate ion) catalysis of the ionised form, the malonate ion [reaction (8)].



Incorporation of this pathway into the rate equation contributes another term and the modified form of eqn. (7) is now given by eqn. (9). We have used a non-linear computer

$$\frac{k_o}{[\mathrm{MAL}]_\mathrm{T}} = \frac{k_e[\mathrm{H}^+]}{([\mathrm{H}^+] + K_a)} + \frac{(k_3K_a[\mathrm{H}^+] + k_3{}^1K_a{}^2)[\mathrm{MAL}]_\mathrm{T}}{([\mathrm{H}^+] + K_a)^2} \qquad (9)$$

fitting program to treat the results. Fig. 3 shows the calculated curve for the *slopes* of the $k_o/[\mathrm{MAL}]_\mathrm{T}$ *vs.* $[\mathrm{MAL}]_\mathrm{T}$ plots *vs.* pH using eqn. (7) and a value for $k_3$ of 0.12 dm$^3$ mol$^{-1}$ s$^{-1}$. The points are the experimental points. The fit is quite good except at the higher pH values. If we use the extended form of eqn. (7) *i.e.* eqn. (9), then the fit of the experimental points with the calculated curve is much better, particularly at the higher pH values (Fig. 4). This treatment uses $k_3 = 0.12$ dm$^3$ mol$^{-1}$ s$^{-1}$ and $k_3{}^1 = 5.2 \times 10^{-3}$ dm$^3$ mol$^{-1}$ s$^{-1}$ and provides good quantitative evidence for the third pathway to enolisation at high pH values. The value of $k_3{}^1$ is significantly smaller than $k_3$ reflecting the unfavourable electrostatic repulsion between the two negatively charged reactants. It may also arise from the possible intramolecular H$^+$ catalysis for enolisation of the malonic acid form which is not possible for the malonate ion.

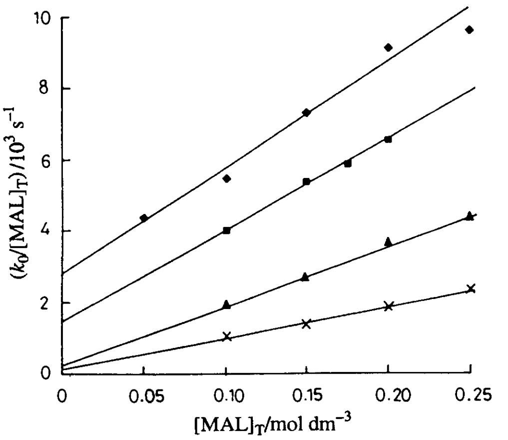


**Fig. 2** Plots of $k_o/[\mathrm{MAL}]_\mathrm{T}$ *vs.* $[\mathrm{MAL}]_\mathrm{T}$ for the bromination of MAL under pseudo-zero-order conditions, ◆ pH 2.75, ■ pH 3.30, ▲ pH 3.80 and × pH 4.30

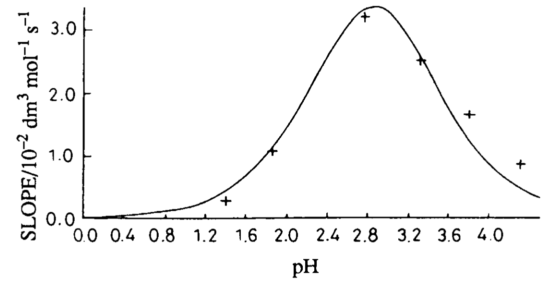


**Fig. 3** Plot of the slopes from Fig. 2 *vs.* pH for the bromination of MAL under pseudo-zero-order conditions. The curve is calculated from eqn. (7).

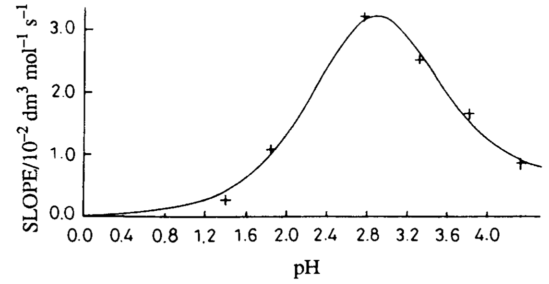


**Fig. 4** Plot of the slopes from Fig. 2 *vs.* pH for the bromination of MAL under pseudo-zero-order conditions. The curve is calculated from eqn. (9).

It is difficult to use a wide pH range to examine base catalysis because of the interference by the malonate ion and also the conversion of malonic acid to malonate beyond pH *ca.* 3. We have tested the catalytic activity of the chloroacetate ion (A$^-$). Plots of $k_o$ *vs.* [A$^-$] at four pH values, 2.05, 2.25, 2.74 and 3.52, were linear with a positive slope and intercept. The kinetic analysis again included catalysis by A$^-$ of enolisation of both malonic acid and malonate ion (rate constants $k_{\mathrm{A}^-}$ and $k_{\mathrm{A}^-}{}^1$, respectively) and a value of $k_{\mathrm{A}^-}$ of $0.09 \pm 0.01$ dm$^3$ mol$^{-1}$ s$^{-1}$ was obtained. This is quite close to the value obtained for malonate ion catalysis which is to be expected given the closeness of the p$K_a$ values of the two acids (2.86 and 2.85). Unfortunately the inherent inaccuracy of the treatment did not allow a sensible value of $k_{\mathrm{A}^-}{}^1$ to be obtained.

Catalysis by the anion also occurs in the enolisation of malonic acid monoethyl ester (EHM). The experimental results giving the variation in $k_o$ (the zero-order rate constant) with $[\mathrm{EHM}]_\mathrm{T}$ at six different pH values are given in Table 5. The

**Table 5** Values of $k_o/[EHM]_T$ for the reaction of $Br_2$ ($2.5 \times 10^{-3}$ mol dm$^{-3}$) with EHM at pH 2.00, 2.50, 3.20, 3.65, 3.90 and 4.65

| pH | $[EHM]_T$/mol dm$^{-3}$ | $k_o/10^{-4}$ mol dm$^{-3}$ s$^{-1}$ | $(k_o/[EHM]_T)/10^{-3}$ s$^{-1}$ |
|---|---|---|---|
| 2.00 | 0.078 | 0.73 | 0.94 |
| 2.00 | 0.111 | 1.14 | 1.03 |
| 2.00 | 0.162 | 1.75 | 1.08 |
| 2.00 | 0.193 | 2.23 | 1.16 |
| 2.50 | 0.051 | 0.50 | 0.96 |
| 2.50 | 0.076 | 0.82 | 1.08 |
| 2.50 | 0.113 | 1.52 | 1.35 |
| 2.50 | 0.152 | 2.45 | 1.61 |
| 2.50 | 0.199 | 3.61 | 1.81 |
| 2.50 | 0.227 | 4.44 | 1.96 |
| 3.20 | 0.076 | 1.35 | 1.77 |
| 3.20 | 0.114 | 2.49 | 2.18 |
| 3.20 | 0.151 | 3.88 | 2.57 |
| 3.20 | 0.183 | 5.36 | 2.93 |
| 3.20 | 0.223 | 7.66 | 3.43 |
| 3.65 | 0.056 | 0.48 | 0.86 |
| 3.65 | 0.093 | 1.06 | 1.14 |
| 3.65 | 0.121 | 2.04 | 1.69 |
| 3.65 | 0.171 | 4.11 | 2.40 |
| 3.65 | 0.200 | 5.63 | 2.82 |
| 3.90 | 0.050 | 0.27 | 0.55 |
| 3.90 | 0.100 | 1.09 | 1.09 |
| 3.90 | 0.150 | 2.35 | 1.57 |
| 3.90 | 0.200 | 4.02 | 2.01 |
| 3.90 | 0.250 | 6.31 | 2.55 |
| 4.65 | 0.050 | 0.12 | 0.25 |
| 4.65 | 0.100 | 0.39 | 0.39 |
| 4.65 | 0.150 | 0.75 | 0.50 |
| 4.65 | 0.200 | 1.22 | 0.61 |
| 4.65 | 0.250 | 1.87 | 0.75 |

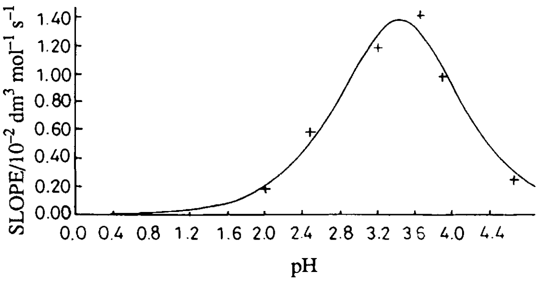


**Fig. 5** Plot of the slopes of the $k_o/[EHM]_T$ *vs.* $[EHM]_T$ plots *vs.* pH for the bromination of EHM under pseudo-zero-order conditions. The curve is calculated from eqn. (10).

same treatment as was used earlier for MAL led to the plot of the slopes of $k_o/[EHM]_T$ *vs.* $[EHM]_T$ [eqn. (10)] *vs.* the pH

$$\text{Slope} = \frac{k_3K_a[H^+]}{([H^+] + K_a)^2} \qquad (10)$$

given in Fig. 5. Again the solid line is that calculated from the non-linear computer fitting program and the experimental points are as shown. This fit is obtained for values of $k_3$ of $(5.4 \pm 0.2) \times 10^{-2}$ dm$^3$ mol$^{-1}$ s$^{-1}$ and of $K_a$ $(3.7 \pm 0.4) \times 10^{-4}$ mol dm$^{-3}$. This gives a p$K_a$ value for EHM of 3.43 which compares well with the literature value[26] of 3.35. The $k_3$ values of MAL and EHM are very similar, particularly when the statistical factor is taken into account.

There is no evidence at the higher pH values of any enolisation *via* the anion form of EHM. This may be due to the significantly higher p$K_a$ value for EHM or possibly because there is no possibility of any intramolecular $H^+$ catalysis for the EHM anion.

**Table 6** First-order rate constants ($k_1$) for the reaction of bromine ($5 \times 10^{-5}$ mol dm$^{-3}$) with MAL at constant ionic strength 0.16 mol dm$^{-3}$

| $[MAL]_T$/mol dm$^{-3}$ | $[H^+]$/mol dm$^{-3}$ | $k_1$/s$^{-1}$ |
|---|---|---|
| 0.0125 | 0.160 | 0.41 |
| 0.025 | 0.160 | 0.85 |
| 0.0375 | 0.160 | 1.20 |
| 0.050 | 0.160 | 1.69 |
| 0.050 | 0.120 | 1.65 |
| 0.050 | 0.080 | 1.72 |
| 0.050 | 0.040 | 1.78 |
| 0.100 | 0.080 | 3.50 |
| 0.150 | 0.080 | 5.67 |

**Table 7** First-order rate constants ($k_1$) for the reaction of iodine ($2 \times 10^{-5}$ mol dm$^{-3}$) with MAL at constant ionic strength 0.16 mol dm$^{-3}$

| $[MAL]_T$/mol dm$^{-3}$ | $[H^+]$/mol dm$^{-3}$ | $k_1$/s$^{-1}$ |
|---|---|---|
| 0.006 25 | 0.160 | 0.18 |
| 0.012 5 | 0.160 | 0.43 |
| 0.025 | 0.160 | 0.82 |
| 0.037 5 | 0.160 | 1.12 |
| 0.050 | 0.160 | 1.53 |
| 0.050 | 0.120 | 1.26 |
| 0.050 | 0.080 | 1.56 |
| 0.050 | 0.040 | 1.57 |
| 0.050 | 0.020 | 1.65 |

### First-order halogenation

Often it is possible to change the rate-limiting step from that of enolisation to reaction of the enol (Scheme 1) when $k_2[Br_2] \ll k_k$, by reducing the concentration of the halogen. This approach was developed by Toullec and co-workers[27] in reactions of enols derived from ketones. We have found that both with bromine ($5 \times 10^{-5}$ mol dm$^{-3}$) and iodine ($2 \times 10^{-5}$ mol dm$^{-3}$) the reactions with malonic acid (in large excess) are fully first-order in halogen. Results of the kinetic experiments are shown in Tables 6 (for bromination) and 7 (for iodination) showing the dependence on $[MAL]_T$ and $[H^+]$. For both halogens reaction is clearly first-order in $[MAL]_T$ and is independent of the acidity over the range studied. This demonstrates that reaction proceeds totally *via* the enol form of MAL with no measureable contribution from halogenation of the enolate. We have attempted to estimate the p$K_a$ of the enol to see if this is a reasonable result, and have used the approach developed by Kresge and co-workers,[9] taking the p$K_a$ of the enol of acetaldehyde (10.50[28]) and then estimating the effects of substituents, in this case 1-OH and 2-$CO_2H$ groups. It has been argued that a 1-OH group adds approximately two units to the acidity and we have estimated (based on the effects of 1-CN and 2-Ph and interpolating *via* $\sigma$ values for a 2-$CO_2H$ group) that a 2-$CO_2H$ group is worth *ca.* 4 p$K_a$ units. This leaves us with a crude estimate for the p$K_a$ of the enol from malonic acid of *ca.* 4–5, so it is not surprising that we do not see any contribution from the halogenation of the enolate over the acidity range studied (0.02–0.16 mol dm$^{-3}$).

If reaction occurs by the rate-limiting reaction of the halogen with the enol, then the measured first-order rate constant $k_1$ is given by $k_2K_E[MAL]_T$. We obtain $k_2K_E$ values for bromination of 35 and 34 dm$^3$ mol$^{-1}$ s$^{-1}$ from the $[MAL]_T$ dependence and values over a $[H^+]$ range and similarly 30 and 30 dm$^3$ mol$^{-1}$ s$^{-1}$ for iodination. These values are very similar implying strongly that halogenation of this enol occurs at or near to the diffusion limit. Earlier a value of $k_2K_E$ for the reaction of nitrosyl chloride was determined[14] as 46 dm$^3$ mol$^{-1}$ s$^{-1}$, again reasonably close to the halogenation values. Taking an average of these values and assuming[27] the diffusion limit of $5 \times 10^9$ dm$^3$ mol$^{-1}$ s$^{-1}$ we obtain a value for $K_E$ of $(7.4 \pm 0.9) \times 10^{-9}$. Similar results for the reaction of iodine with EHM yielded a value of $K_E$ for EHM of $(1.5 \pm 0.1) \times 10^{-9}$ again assuming that iodination occurs at the diffusion limit. There are no reliable literature values of $K_E$ for diethyl malonate for comparison purposes although an estimate of $2 \times 10^{-11}$ has been made from nitrosation kinetics.[29] It is to be expected that the values of $K_E$ for malonic acid and its half ester would be significantly larger than that for diethyl malonate because of the possibility of stabilisation of their enol forms by H-bonding. This clearly must have an enormous effect on $K_E$ since comparison with an estimate for $K_E$ for acetic acid[30] reveals that introduction of the second carboxylic group increases $K_E$ by a massive factor of *ca.* $10.^{13}$

Relatively few $K_E$ values have been determined for carboxylic acid enols so a proper structural comparison with our findings is not yet possible. However, values have been obtained for the enols derived from indene-1-carboxylic acid[31] (p$K_E$ 7.26), indene-3-carboxylic acid[31] (p$K_E$ 9.60), cyclopentadien-1-yl carboxylic acid[32] (p$K_E$ 6.7) and α-cyano-α-phenylacetic acid[9] (p$K_E$ 7.22), which are all of comparable magnitude to our values of p$K_E$ 8.13 and 8.84 obtained for MAL and EHM. Similarly values of $k_k$, the rate constant for ketonisation of the enols from MAL and EHM computed from $K_E$ and $k_e$ values, are also roughly comparable to those obtained by Kresge and coworkers.

## Experimental

Both MAL and EHM were commercial samples. The halogenation products are well known. Acid solutions were prepared using standard solutions of perchloric acid. At lower acidities the pH was maintained using the malonic acid–malonate as the buffer. In some of the experiments constant ionic strength was maintained using sodium perchlorate. Kinetic measurements were carried out either by conventional UV spectrophotometry or by stopped-flow spectrophotometry noting the disappearance of the absorbance due to $Br_2$ at 395 nm ($\varepsilon$ 128 dm$^3$ mol$^{-1}$ cm$^{-1}$) or $I_2$ at 459 nm ($\varepsilon$ 697 dm$^3$ mol$^{-1}$ cm$^{-1}$). The appropriate first- or zero-order rate constants were computed using standard software packages. Generally rate constants were reproducible to within $\pm 3\%$ (standard errors are quoted) but for the reactions at low halogen concentration where the absorbance changes are necessarily small, a computer averaging program was used on approximately 10 kinetic experiments to reduce the noise level.

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