145. *Kinetics of the Bromination of Ethyl Malonate and Methyl Methanetricarboxylate.*

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The rates of bromination of ethyl malonate and methyl methanetricarboxylate have been measured in aqueous solution, bromine concentrations in the range 10^{-5}—10^{-8}M being used. Under these conditions the rate is closely proportional to the bromine concentration, and approximate velocity constants are derived for the reaction of the enols and enolate ions with molecular bromine and tribromide ion.

The halogenation of many carbonyl compounds is believed to take place through the enol or the enolate ion, but since these reactions are usually of zero order with respect to the halogenating agent little is known about the velocity of the halogenation step. In principle this step must become rate-determining if the concentration of halogenating agent is reduced sufficiently, and Bell and Spiro [1] found that the rate of bromination of ethyl malonate became dependent on the bromine concentration in the range 10^{-2}—10^{-4}M. They were able to obtain approximate velocity constants for the bromination of the enol and the enolate ion, and similar information was obtained indirectly for the iodination of ethyl malonate [2] and 2-oxocyclohexanecarboxylate [3] by studying the reverse de-iodination reaction. Recently the measurement of redox potentials has been used to study the fast bromination reactions of anilines,[4] anisoles and phenols,[5] with bromine concentrations in the range 10^{-5}—10^{-8}M. The present paper describes similar measurements for the bromination of ethyl malonate and methyl methanetricarboxylate, special attention being paid to the relative reactivities of molecular bromine and tribromide ion. At these low concentrations the bromination step is almost completely rate-determining, and since only a very small proportion of the ester ($<1\%$) is brominated it is not necessary to allow for the further bromination of ethyl monobromomalonate.

If the ester (RH) is present in large excess and is in equilibrium with very small proportions of the ion R^- and the enol HR, then the rate of disappearance of bromine is given by

$$-\mathrm{d}y/\mathrm{d}t = k_2[\mathrm{Br}_2][\mathrm{R}^-] + k_2'[\mathrm{Br}_3^-][\mathrm{R}^-] + k_3[\mathrm{Br}_2][\mathrm{HR}] + k_3'[\mathrm{Br}_3^-][\mathrm{HR}] \quad . \quad (1)$$

where y is the total bromine concentration $[\mathrm{Br}_2] + [\mathrm{Br}_3^-]$. If the ester concentration is c, the reaction velocity can be represented by a second-order constant $k = -\frac{1}{c}\frac{\mathrm{d}\ln y}{\mathrm{d}t}$, given by:

$$k(1 + K[\mathrm{Br}^-]) = k_2K_a/[\mathrm{H}^+] + k_2'KK_a[\mathrm{Br}^-]/[\mathrm{H}^+] + k_3K_{\mathrm{E}} + k_3'KK_{\mathrm{E}}[\mathrm{Br}^-] \quad (2)$$

where the equilibrium constants are $K = [\mathrm{Br}_3^-]/[\mathrm{Br}_2][\mathrm{Br}^-] = 16$, $K_a = [\mathrm{H}^+][\mathrm{R}^-]/[\mathrm{RH}]$, $K_{\mathrm{E}} = [\mathrm{HR}]/[\mathrm{RH}]$. The constants k_2' and K_a should strictly contain ionic activity coefficients, but their values are not known with sufficient certainty to justify this. It has already been shown [4] that k is related to the change in e.m.f. at 25° by the equation

$$k = -\frac{1}{c}\frac{\mathrm{d}\ln y}{\mathrm{d}t} = -\frac{1}{c}\frac{\mathrm{d}\ln[\mathrm{Br}_2]}{\mathrm{d}t} = -\frac{78{\cdot}2}{c}\cdot\frac{\mathrm{d}E}{\mathrm{d}t} \quad . \quad . \quad . \quad (3)$$

so that the velocity constants k_2, k_2', k_3, and k_3' can in principle be derived from measurements at different acidities and concentrations of bromide ions.

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[1] Bell and Spiro, *J.*, 1953, 429.
[2] Bell and Engel, *J.*, 1957, 247.
[3] Bell and Vogelsong, *J.*, 1958, 243.
[4] Bell and Ramsden, *J.*, 1958, 161.
[5] Bell and Rawlinson, *J.*, 1961, 63.

If the initial bromine concentration is not sufficiently low there will be departures from these simple kinetics in the early part of the reaction, and dE/dt will increase with time. We assume that there is always rapid equilibrium between the enol and its anion, but that the rate of formation of enol and anion from the ester is characterized by a first-order constant k_1 whose value depends on the catalysts present. The usual steady-state assumptions give

$$-dy/dt = kk_1yc/(ky + k_1) \quad . \; . \; . \; . \; . \; . \; . \; . \quad (4)$$

with y still defined by (2), which can be integrated to give

$$t + \frac{y}{k_1c} = -\frac{1}{kc}\ln y + \text{Constant} \quad . \; . \; . \; . \; . \; . \; . \quad (5)$$

Comparing this with (3), we see that the plot of E against t should become linear if the times are corrected by adding y/k_1c: this was in fact the case for ethyl malonate. The values of y were derived from the observed potential, and k_1 from earlier measurements at high bromine concentrations.[1,6]

No correction of this kind was found necessary in the bromination of methyl methanetricarboxylate. Its rate of ionization has not been measured, but its relatively high acidity ($pK = 7{\cdot}86$) suggests $k_1 > 10$ sec.$^{-1}$, which would not have an appreciable effect on the observed rates of bromination. It was not practicable to work with the initial concentration of this ester greatly in excess of the initial bromine concentration, but after the latter had fallen by about one power of ten the concentration of ester remained effectively constant, and the plot of E against t was strictly linear for at least $0{\cdot}06V$ beyond this point. The value of c used in equation (3) was corrected for the ester removed in the early stages of the reaction.

EXPERIMENTAL

Ethyl malonate was repeatedly fractionated under reduced pressure until no further change was produced in the kinetic results. Methyl methanetricarboxylate, m. p. 43°, was prepared as described in "Organic Syntheses"[7] and dried over phosphoric oxide. Inorganic reagents were of "AnalaR" quality, and water was redistilled from potassium permanganate in a glass still.

Kinetic measurements were made by the method previously described.[4,5] The initial concentration of malonic ester was about 4×10^{-3}M in experiments with acetate buffers, and about 4×10^{-2}M in those with acid solutions: in each case the initial bromine concentration was about 4×10^{-5}M. In experiments with methyl methanetricarboxylate the initial ester concentration was about 2×10^{-5}M and that of bromine about 9×10^{-6}M. All measurements were at 25°.

The dissociation constant of methyl methanetricarboxylate was determined in 0·2M-sodium nitrate at 25° by measuring the pH of a half-neutralized M/100-solution with a Cambridge pH-meter. Stable and reproducible readings were obtained, leading to $K_a = 1{\cdot}4 \times 10^{-8}$ at an ionic strength $I = 0{\cdot}2$.

TABLE 1. *Bromination of ethyl malonate.*

(*a*) Acetate buffer, $[HOAc] = [OAc^-] = 1{\cdot}99 \times 10^{-2}$
$[H^+] = 2{\cdot}93 \times 10^{-5}$, ionic strength made up to $I = 0{\cdot}1$ with $NaNO_3$

[NaBr]	0·002	0·01	0·02	0·03	0·04	0·05	0·06	0·07	0·08
k obs.	6·78	6·53	6·88	6·60	6·65	5·48	5·73	5·50	5·40
k calc.	7·12	6·80	6·49	6·27	6·07	5·90	5·78	5·64	5·55

(*b*) 0·0277M-$HClO_4$, ionic strength made up to $I = 0{\cdot}135$ with $NaNO_3$

[NaBr]	0·0142	0·0337	0·0584	0·0829	0·107
k obs.	0·765	0·684	0·558	0·480	0·453
k calc.	0·792	0·663	0·561	0·495	0·447

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[6] Bell, Everett, and Longuet-Higgins, *Proc. Roy. Soc.*, 1949, *A*, **197**, 141.

[7] *Org. Synth.*, 1933, **13**, 100.

The results of the kinetic measurements are given in Tables 1 and 2, in which k is the second-order velocity constant in equations (2)—(5), in l. mole^{-1} sec.$^{-1}$. Each value represents the mean of 3—8 experiments. In the acetate buffer solutions with the lowest bromide concentrations an appreciable proportion of the bromine is present as hypobromous acid. Bell and Spiro[1] suggested, on slender evidence, that hypobromous acid was about half as reactive as molecular bromine. This now seems improbable, and our own results are consonant with a negligible reactivity for hypobromous acid. The velocity constants in Table 1 have been corrected on this assumption: the maximum correction is only a few per cent.

TABLE 2. *Bromination of methyl methanetricarboxylate.*

Perchloric acid solutions, ionic strength made up to $I = 0{\cdot}2$ with $NaNO_3$.

$[H^+]$	$[Br^-]$	k (obs.)	k (calc.)
0·00985	0·00554	7240	7370
	0·0499	5970	6120
	0·0998	5410	5600
	0·148	5210	5320
	0·188	5100	5170
0·0148	0·00554	5000	5000
	0·0696	3890	3970
	0·124	3720	3620
	0·183	3520	3480
0·0197	0·00553	3860	3810
	0·0696	2900	3030
	0·124	2790	2790
	0·178	2710	2650
0·0296	0·00554	2800	2640
	0·0499	2190	2180
	0·0998	2020	1970
	0·168	1850	1910
0·0493	0·00554	1720	1710
	0·0499	1400	1400
	0·0998	1220	1240
	0·148	1150	1160
0·0985	0·00554	1030	1000
	0·0252	938	955
	0·0499	811	798
	0·0745	782	740
	0·0893	770	712
	0·0998	753	708
0·148	0·00553	767	765
	0·0204	655	688
	0·0351	603	637
	0·0998	571	538

DISCUSSION

The values of k (calc.) for ethyl malonate in Table 1 are obtained from equation (2) with $K = 16{\cdot}0$, $k_2K_a = 2{\cdot}13 \times 10^{-4}$, $k_2'K_a = 1{\cdot}25 \times 10^{-4}$, $k_3K_E = 0{\cdot}93$, $k_3'K_E = 0{\cdot}154$. These values imply that bromination takes place predominantly through the enol at pH 2, and through the enolate ion at pH 5. There are no direct determinations of K_a or K_E for ethyl malonate, but if we use $K_a = 5 \times 10^{-14}$, $K_E = 10^{-5}$, as estimated by Bell and Spiro,[1] this gives $k_2 = 4{\cdot}3 \times 10^9$, $k_2' = 2{\cdot}5 \times 10^9$, $k_3 = 9{\cdot}3 \times 10^4$, $k_3' = 1{\cdot}5 \times 10^4$, all in l. mole^{-1} sec.$^{-1}$. These values are all of the same order of magnitude as those given by Bell and Spiro,[1] but only the first shows close agreement. The present values are to be preferred, since measurements were made at lower bromine concentrations, and no correction was necessary for the introduction of a second bromine atom.

The values of k (calc.) for methyl methanetricarboxylate correspond to $K = 16{\cdot}0$, $k_2K_a = 72{\cdot}0$, $k_2'K_a = 42{\cdot}3$, $k_3K_E = 320$, $k_3'K_E = 50$. For this substance a large proportion of the bromination takes place through the enolate ion even in 0·15M-perchloric acid, and the rate constants for the enol are not known very accurately. Our own measurements give $K_a = 1{\cdot}4 \times 10^{-8}$, whence $k_2 = 5{\cdot}2 \times 10^9$, $k_2' = 3{\cdot}0 \times 10^9$. K_E has not been measured in aqueous solution, but the pure ester contains 1·2% of enol.[8] This will certainly be reduced in aqueous solution, and we have assumed $K_E = 5 \times 10^{-3}$, giving $k_3 = 6 \times 10^4$, $k_3' = 1 \times 10^4$.

The velocity constants for bromination of the enolate anions are of the same order of magnitude as those found indirectly for the iodination of similar species,[2,3] and also directly for the bromination of phenoxide ions:[5] they are close to the maximum value expected for reactions in aqueous solution having zero energy of activation.[9,10] The corresponding velocity constants for the enols are lower by about four powers of ten, and again resemble

[8] Conant and Thompson, *J. Amer. Chem. Soc.*, 1932, **54**, 4039.
[9] Onsager, *J. Chem. Phys.*, 1934, **2**, 599.
[10] Debye, *Trans. Electrochem. Soc.*, 1942, **82**, 265.

those found for the iodination of enols and the bromination of phenols. It is noteworthy, however, that the relative reactivities of bromine and tribromide ion differ considerably in the two series.* In the present work $k(Br_3^-)/k(Br_2)$ was 0·6 for both enolate ions and 0·17 for both enols. On the other hand $k(Br_3^-)$ was only a few per cent of $k(Br_2)$ for the most reactive phenoxide ions, and could not be detected for phenol molecules or anisoles,[5] although the velocity constants for bromine resemble those in the present paper. As pointed out by Stock and Brown [11] and by Shatenshtein,[12] the selectivity of an organic molecule towards different reagents will decrease as the reactivity of the molecule increases, but it is clear that this principle can only be applied to a series of very similar molecules.

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* These relative reactivities are independent of the uncertainties in the absolute values arising from uncertainties in K_a and K_E.

[11] Stock and Brown, *J. Amer. Chem. Soc.*, 1959, **81**, 3233, and earlier papers.

[12] Shatenshtein, *Zhur. fiz. Khim.*, 1960, **34**, 594.