The Effect of α-Cyclodextrin on the Oxidation of Formic Acid by Aqueous Bromine: Inhibition Despite Overall Rate Increase

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A strong 1:1 inclusion complex is formed ($K_\alpha = 4690$ dm³ mol⁻¹) between Br_2 and α-cyclodextrin (cd). The reaction kinetics between HCOOH and Br_2(aq) ([H^+] = 0.1 mol dm⁻³) with bromide present in large excess, have been studied potentiometrically both in the presence and absence of cd. It is shown that Br_2 with cd is about half as reactive as aqueous Br_2, and it would appear from the activation parameters that Br_2 should be released from inclusion during the rate-limiting step. However, despite the stabilization of Br_2 by cd, addition of the latter makes the experimental rate constant increase. The reason for this apparent contradiction is that non-reactive tribromide is transformed by cyclodextrin into mildly reactive Br_2cd. The rate constants (25 °C, $I = 0.2$ mol dm⁻³) for the oxidation of $HCOO^-$ by Br_2 and Br_2cd are 27 and 15 dm³ mol⁻¹ s⁻¹, respectively.

Although there is an ever-increasing interest in the physical and chemical properties of inclusion compounds with cyclodextrins, the investigations have mainly centred on large organic compounds.[1] Compared with these, studies of the effect of cyclodextrin on small inorganic entities are relatively scarce.[2] Thus, in the present paper, we report the effect of α-cyclodextrin (cd) on the kinetics of the reduction of aqueous bromine by formic acid. We were interested to see whether that reaction was accelerated or retarded in the presence of cd.

Experimental

The following compounds were used without further purification: cd (Aldrich); bromine, formic acid, and KBr (Merck). cd was exposed to the atmosphere for several days to ensure complete conversion into the hexahydrate before weighing. Fresh stock solutions containing cd were prepared shortly before being used.

The reaction kinetics were studied by a potentiometric method [3,4] with a Servogor 460 BBC Goerz potentiometer using platinum and saturated calomel electrodes. In all experiments HCOOH, H^+ (as HCl), and Br^- (as KBr) were present in a large excess (each 0.1 mol dm⁻³). Temperatures were controlled within ±0.2 °C. That in the presence of cd the reaction reached completion was confirmed by potentiometric measurements using a bromide-specific electrode (in this case no extra Br^- was added, of course). Using the same method the complex formation between cd and bromine was measured using an Ion 85 ion analyser. Emf readings were made after equilibration, typically after 5–10 min of continued magnetic stirring.

Results and Discussion

The oxidation of formic acid by aqueous bromine is reported [3] to proceed *via* the formate anions, [equation (1)]:

$$HCOO^- + Br_2 \xrightarrow{k_1} H^+ + 2Br^- + CO_2 \qquad (1)$$
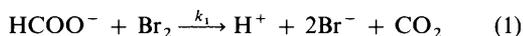
With HCOOH, H^+, and Br^- present in large excess, a pseudo-first-order rate law is obtained:

$$\frac{-2[Br_2]_T}{dt} = k_{obs}[Br_2]_T \qquad (2)$$
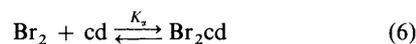
with

$$k_{obs} = \frac{k_1 K_A[HCOOH]_T}{[H^+](1 + K_1[Br^-])} \qquad (3)$$

where $[Br_2]_T$ and $[HCOOH]_T$ are the total concentrations of bromine and formic acid, respectively, K_A is the ionization constant of formic acid (3.6×10^{-4} mol dm⁻³, corrected for $I = 0.2$ mol dm⁻³) and K_1 (17 dm³ mol⁻¹)[4] is the formation constant for tribromide.

$$Br_2 + Br^- \xrightleftharpoons{K_1} Br_3^- \qquad (4)$$
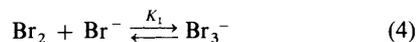
The k_{obs} value of 3.5×10^{-3} s⁻¹ is given by the slope of the plot of emf *vs.* time (Figure 1, top line):

$$k_{obs} = -\left(\frac{2F}{RT}\right)\frac{dE}{dt} \qquad (5)$$

From this, $k_1 = 26.1$ dm³ mol⁻¹ s⁻¹ (lit.,[3] 22 dm³ mol⁻¹ s⁻¹). The addition of increasing amounts of cd changes the kinetic curves as shown in Figure 1. Before analysing these curves, the formation of inclusion compounds with both bromine and formic acid [equations (6) and (7)] was investigated.

$$Br_2 + cd \xrightleftharpoons{K_\alpha} Br_2cd \qquad (6)$$

$$HCOOH + cd \xrightleftharpoons{K_\beta} HCOOHcd \qquad (7)$$

The former was derived from the decrease in the reduction potential of mixtures of various concentrations of bromine, with [H^+] and [Br^-] both fixed at 0.1 mol dm⁻³ upon the addition of cd. From equations (4) and (6) the following material-balance equation (8) is derived:

$$[Br_2]^2\{K_\alpha(1 + K_1[Br^-])\} + [Br_2]\{1 + K_1[Br^-] + K_\alpha([cd]_T - [Br_2]_T)\} - [Br_2]_T = 0 \qquad (8)$$

Table 1. Reduction potentials and free bromine concentrations for various total concentrations of α-cyclodextrin and bromine.

$[cd]_T$/mol dm^{-3}	E/V	$[Br_2]_T$/mol dm^{-3}	$[Br_2]^a$/mol dm^{-3}	$[Br_2]^b$/mol dm^{-3}
0	0.795	4.15×10^{-3}	1.60×10^{-3}	
0	0.776	9.96×10^{-4}	3.79×10^{-4}	
0	0.75	1.66×10^{-4}	5.29×10^{-5}	
0	0.73	3.32×10^{-5}	1.16×10^{-5}	
4.08×10^{-3}	0.767	2.49×10^{-3}	1.92×10^{-4}	1.97×10^{-4}
1.36×10^{-2}	0.742	1.66×10^{-3}	2.89×10^{-5}	2.81×10^{-5}
6.78×10^{-3}	0.752	1.66×10^{-3}	6.16×10^{-5}	6.04×10^{-5}
2.71×10^{-3}	0.766	1.66×10^{-3}	1.78×10^{-4}	1.71×10^{-5}
1.36×10^{-3}	0.774	1.66×10^{-3}	3.26×10^{-4}	3.17×10^{-4}
6.78×10^{-4}	0.778	1.66×10^{-3}	4.41×10^{-4}	4.49×10^{-4}
1.35×10^{-4}	0.782	1.66×10^{-3}	5.97×10^{-4}	5.85×10^{-4}
1.35×10^{-4}	0.771	7.95×10^{-4}	2.60×10^{-4}	2.69×10^{-4}

^{a} Calculated from calibration curve: $E = 0.88 + 0.0304 \log [Br_2]$. ^{b} Calculated from equation (8) with $K_\alpha = 4\,690$.

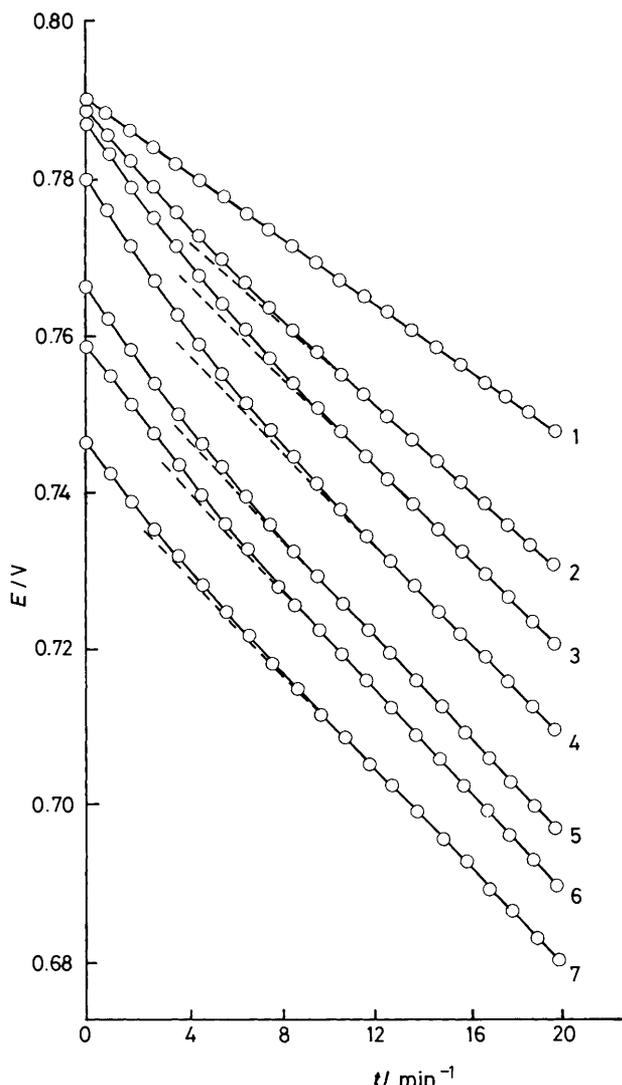**Figure 1.** Measured ($\bigcirc$) and calculated (——) emf values *versus* time for solutions with different concentrations I(mmol dm^{-3}) of cyclodextrin at 25 °C: (1) 0; (2) 0.5; (3) 1; (4) 2.5; (5) 5; (6) 10; (7) 22.5.

where $[cd]_T$ is the total concentration of cd, *i.e.*

$$[cd]_T = [cd]\{1 + K_\alpha[Br_2]\} \qquad (9)$$

Values of $[Br_2]$ derived from the reduction potentials with the aid of a calibration curve (entries 1–4 in Table 1) were fitted

to the solutions of equation (8) with K_α taken as a floating parameter giving $K_\alpha = 4\,690 \pm 40$ dm^3 mol^{-1}. The excellent agreement, seen in Table 1, between the values of the free bromine concentrations calculated from the calibration curve and equation (8) is evidence in favour of the assumptions made, *viz* (i) 1:1 complex formation between bromine and cd and (ii) bromine complexed by cd gives no electrode response.

To evaluate the extent of complex formation between HCOOH and cd [equation (7)] a spectrophotometric method described recently [5] was used which gave $K_\beta = 4.0$ dm^3 mol^{-1} (at 21 °C) which agreed well with the value of 4.12 (at 25 °C) obtained from a pH potentiometric method.[6] Thus, equation (7) can safely be neglected compared with equation (6).

Let us now analyse the kinetic curves displayed in Figure 1. Firstly, the initial reduction potentials ($E_{t=0}$) measured for various values of $[cd]_T$ are those predicted from the treatment above. The non-linear decrease in the potentials with time, becoming linear in the final stages, would indicate that, parallel to the bromine path [equation (1)], the inclusion complex reacts at a similar rate:

$$HCOO^- + Br_2cd \xrightarrow{k_2} H^+ + 2Br^- + CO_2 + cd \qquad (10)$$
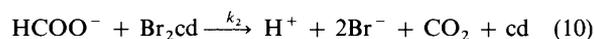
and therefore

$$\frac{d[CO_2]}{dt} = \{k'_1 + k'_2 K_\alpha[cd]\}[Br_2]_T \qquad (11)$$

where $k'_1 = k_1 K_A[HCOOH]_T/[H^+]$ and, similarly, $k'_2 = k_2 K_A[HCOOH]/[H^+]$. The problem now is that the emf does not measure the total bromine concentration, but since the bromide concentration is effectively constant it is a measure of free bromine, $[Br_2]$.

The total bromine concentration at any time is given by

$$[Br_2]_T = [Br_2] + [Br_3^-] + [Br_2cd] \qquad (12)$$

From the material balance:

$$[CO_2] = [Br_2]_0 - [Br_2]_T, \qquad (13)$$

where $[Br_2]_0$ is the initial total concentration of bromine, *i.e.* $[Br_2]_T$ at $t = 0$. It follows that:

$$\frac{d[CO_2]}{dt} = -\frac{d[Br_2]_T}{dt} =$$

$$-\left\{\frac{d[Br_2]}{dt} + \frac{d[Br_3^-]}{dt} + \frac{d[Br_2cd]}{dt}\right\} \qquad (14)$$
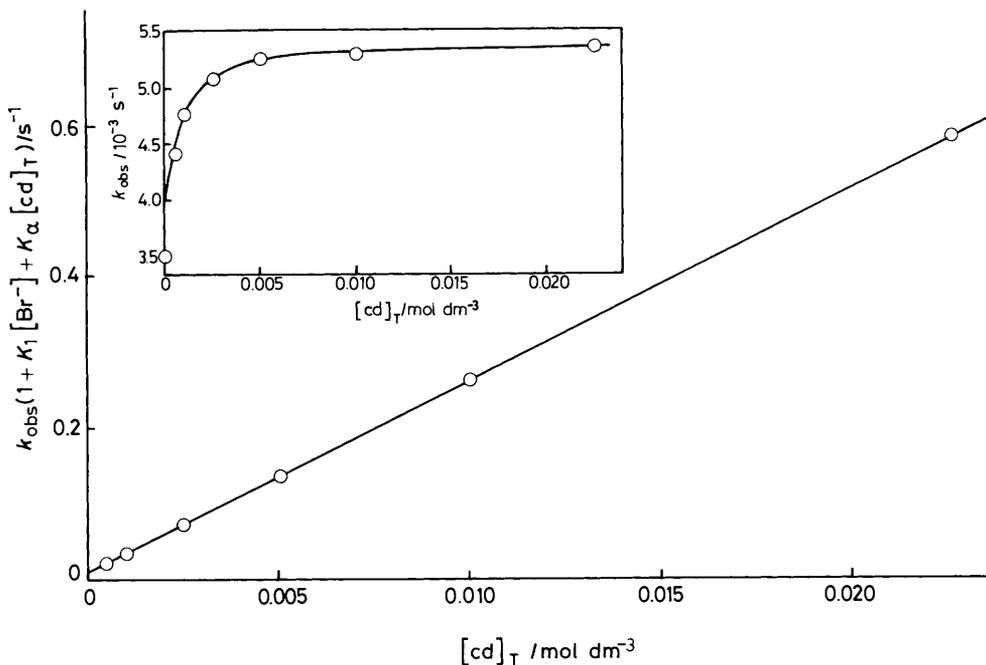
Figure 2. Plot of k_{obs} multiplied by the denominator of equation (16) *versus* the total α-cyclodextrin concentration. The insert shows the variation in k_{obs} with the latter.
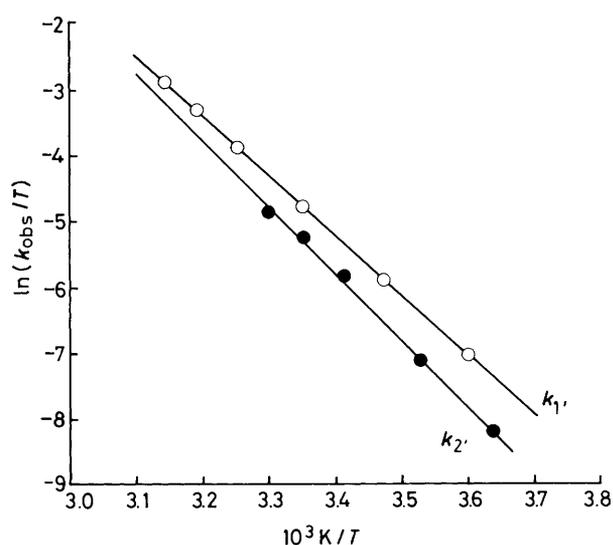

Figure 3. Temperature dependence of experimental rate constants $k'_1 = k_1 K_A$ and $k'_2 = k_2 K_A$.

With this and the material-balance equations (9) and (12), equation (11) can be expressed in terms of the measurable quantity [Br$_2$]:

$$-\frac{d[Br_2]}{dt} =$$

$$\left\{ \frac{k'_1(1 + K_\alpha[Br_2]) + k'_2 K_\alpha[cd]_T}{(1 + K_1[Br^-])(1 + K_\alpha[Br_2]) + K_\alpha[cd]_T/(1 + K_\alpha[Br_2])} \right\}$$
$$[Br_2] \quad (15)$$

In the final stages, when [Br$_2$] becomes sufficiently small, equation (15) approaches a pseudo-first order rate law with the rate constant

$$k_{obs} = \frac{k'_1 + k'_2 K_\alpha[cd]_T}{1 + K_1[Br^-] + K_\alpha[cd]_T} \quad (16)$$

The k_{obs} values given by the slopes of the linear part of the curves in Figure 1 increase with increasing [cd]$_T$ towards a limiting value, in accord with equation (16) (inset of Figure 1). Furthermore, a plot of k_{obs} $(1 + K_1[Br^-] + K_\alpha[cd]_T)$ *versus* [cd]$_T$ is linear with slope $= k'_2 K_\alpha = 25.2$ dm^3 mol^{-1} s^{-1} (and hence $k'_2 = 5.37 \times 10^{-3}$ s^{-1}), and a small intercept $k'_1 = 9.86 \times 10^{-3}$ s^{-1} (Figure 2), which is similar to that obtained with no cd added. Theoretical curves calculated from equation (15) using these values fit the observed kinetic curves of Figure 1 very well, thus confirming the present analysis.

From k'_1 or k'_2 the true rate constants for reactions (1) and (10) are calculated to be $k_1 = 27.3$ dm^3 mol^{-1} s^{-1} and $k_2 = 14.9$ dm^3 mol^{-1} s^{-1}, respectively. Hence aqueous bromine is about twice as reactive as the inclusion compound. Nevertheless, the experimental rate constant increases in the presence of cd. This can be explained by the fact that cd transforms inactive Br$_3^-$ into rather active Br$_2$cd. (It may easily be shown that in a solution 0.1 mol dm^{-3} in Br$^-$ and 3 mmol dm^{-3} in Br$_2$, ca. 63% of the bromine is present as tribromide ion.)

It is instructive to consider the lower reactivity of the Br$_2$cd compound in terms of the activation parameters. For this reason we made a temperature-dependence study of k_{obs} under two particular conditions, (i) without cd added, where $k_{obs} = k'_1 = k_1 K_A$ and (ii) in the high [cd]$_T$ region, where $k_{obs} = k'_2 = k_2 K_A$. The (least-square) Eyring lines are displayed in Figure 3.

The activation parameters include the ionization of formic acid [equations (17) and (18)].

$$\Delta H^{\ddagger}_{obs} = \Delta H^{\ominus} + \Delta H^{\ddagger} \quad (17)$$

$$\Delta S^{\ddagger}_{obs} = \Delta S^{\ominus} + \Delta S^{\ddagger} \quad (18)$$

Since $\Delta H^{\ominus}$, the standard enthalpy change for the ionization of formic acid, may be ca. 0,[3] $\Delta S^{\ominus} \approx -70$ J K^{-1} mol^{-1}, from K_A. Therefore the actual activation entropy for the redox step might

Table 2. Activation parameters for the title reaction with and without α-cyclodextrin.

Reaction	$\Delta H^{\ddagger}_{obs}/kJ\ mol^{-1}$	$\Delta S^{\ddagger}_{obs}/J\ mol^{-1}\ K^{-1}$
HCOOH + Br$_2$	72.4	+155.4
HCOOH + Br$_2$cd	78.2	+170.7

be well over $+200\ J\ K^{-1}\ mol^{-1}$ and this should be attributable to the production of carbon dioxide. Of primary interest here, however, are the values of $\Delta\Delta H \approx 6\ kJ\ mol^{-1}$ and $\Delta\Delta S \approx 15\ J\ mol^{-1}\ K^{-1}$ on substitution of Br$_2$ reactant by Br$_2$cd. It would appear that in the activation of the inclusion compound bromine will be displaced since this process requires energy but gains entropy due to the increase in internal motion.

Some additional experiments have been performed which are briefly summarized as follows. (a) The addition of soluble starch, instead of cd, to the HCOOH/Br$_2$ reaction also causes a decrease in the emf, but instead of the behaviour in Figure 1, parallel $E\ vs.\ t$ lines are obtained. It may thus be concluded that Br$_2$ also forms an inclusion complex with starch which is virtually inactive. (b) The addition of β-cd, instead of cd, exerts only small effects on the $E - t$ plots. Either bromine is loosely bound to β-cd or else it has a potential similar to that of bromine. The difference between cd and β-cd lies in the size of

the cavity within the molecule. The diameter of the hole in the former is about 5 Å and in the latter about 6.2 Å.[1] (c) Finally, the effect of α-cd on the Fe^{2+}/Br$_2$ reaction is similar to that of HCOOH/Br$_2$, pointing towards the same kind of reaction mechanism.

Acknowledgements

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