Kinetics and Mechanism of the Oxidation of Some Chelating Agents by Perbenzoic Acids

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The kinetics of the *N*-oxidation of ethylenediaminetetra-acetic acid, diethylenetriaminepenta-acetic acid, and ethylenediaminetetramethylenephosphonic acid by substituted perbenzoic acids has been studied. The dependence of the second-order rate constant on the nature of the peracid, pH, the basicity of the nitrogen atom of the chelating agent, and the temperature of the reaction is consistent with a mechanism involving nucleophilic attack of the nitrogen of the chelating agent on the outer peroxidic oxygen of the peracid. The kinetic data is of importance in assessing how added chelators suppress the metal-ion catalysed reactions of peracids.

It is well known that aminocarboxylic acid chelating agents such as ethylenediaminetetra-acetic acid (EDTA) inhibit the metal-ion catalysed decomposition of peracids.[1] Recently it has been shown that methylenephosphonic acid analogues of chelators such as EDTA inhibit the metal-ion catalysed reaction of peracids and hydrogen peroxide in alkaline solution.[2] In a preliminary communication we have reported that EDTA is rapidly oxidised to EDTA *N,N'*-dioxide by peracid.[3] This finding throws open the question of how added chelating agents inhibit the metal catalysed reactions of peracids. One or more of the following modes of action are possible. Firstly, the *N*-oxide of the chelator, formed from its reaction with peracid, may inhibit metal-ion catalysed reactions either by chelating the metal or by scavenging free radical chain propagators, as we observed[3] for the Cu^{II} catalysed oxidation of amaranth by *m*-chloroperbenzoic acid (MCPBA). Secondly, before it is oxidised by the peracid, the chelator may sequester the metal ions and the resulting complex may be stabilised with respect to *N*-oxidation of the ligand.[3] Thirdly, under the particular conditions of an experiment the rate of oxidation of the chelator may simply be slow compared with the reaction of interest. For example, the eventual oxidation of EDTA by hydrogen peroxide prevents this chelator from suppressing the catalytic decomposition of hydrogen peroxide indefinitely.[4]

The present study was carried out to determine the effect of pH and temperature on the rate of oxidation of chelators by substituted perbenzoic acids. The results are consistent with nucleophilic attack of the nitrogen atom of the chelator on the outer peroxidic oxygen of the peracid.

Experimental

Materials.—The disodium salt of EDTA and diethylenetriaminepenta-acetic acid (DTPA) were purchased from BDH and Fluka, respectively. Ethylenediaminetetramethylenephosphonic acid (EDTMP)·H_2O (92:8), was provided by Warwick International Ltd. The following perbenzoic acids contain the parent acid as the only significant impurity and, except for MCPBA (which was purchased from BDH), were provided by Interox Chemicals Ltd: MCPBA, 85%; *p*-NO_2-PBA, 40%; *p*-CH_3-PBA, 40%; *p*-CH_3O-PBA, 40%; *p*-$(CH_3)_3C$-PBA, 94%; *o*-HO_2C-PBA, 75%; and *p*-HO_3S-PBA, 90%. Buffer solutions for the stoicheiometric and kinetic studies were made up in distilled water using the best available grade reagents, giving pH ranges: sodium formate–formic acid, 3.3–3.8; sodium acetate–acetic acid, 4.0–5.9; disodium hydrogen phosphate–sodium dihydrogen phosphate, 5.6–8.3; disodium carbonate–sodium hydrogen carbonate, 8.5–10.6.

Stoicheiometry.—The concentration of MCPBA was determined iodometrically before and after the addition to the peracid solution of a small volume of a solution containing a known amount of the chelating agent.

Product Analysis.—EDTA *N,N'*-dioxide was prepared using hydrogen peroxide following the method of Coeur and Alary.[5] A reaction vessel containing Na_2EDTA (25 g) in water (75 cm^3), NaOH (30%, 25 cm^3), and H_2O_2 (30%, 75 cm^3) was stirred for 24 h at room temperature and the resulting solution was acidified with H_2SO_4 (20 cm^3) to give a white precipitate which was washed with water and then with ethanol. The product of the reaction of EDTA and MCPBA in alkaline solution was obtained using a similar procedure.[3] In a second experiment the reaction of EDTA and MCPBA was carried out at a lower pH by using sodium hydroxide to maintain the pH between 5 and 7.

Kinetic Measurements.—Absorbances were measured using a Hewlett Packard HP 8451A spectrophotometer with a thermostatted cell holder. The reduction of peracid was monitored in the region 240–250 nm at a single wavelength depending on the pH and nature of the peracid. Kinetic runs were carried out under pseudo first-order conditions with the chelating agent in excess. The peracid was dissolved in distilled water to a concentration of about 5×10^{-3} mol dm^{-3}, which was determined iodometrically. A small volume of the peracid solution was micropipetted into the thermostatted spectrophotometer cell which contained a known volume of a solution of the chelating agent dissolved in buffer and the cell contents were mixed. The ionic strength of the buffer was 0.1 mol dm^{-3} unless stated otherwise. A simple program written for the HP 8451A was used to plot ln $(A - A_\infty)$ against time and to calculate the rate constant using linear regression. For each of the sets of conditions used, rate constants were measured for at least five different concentrations of the chelating agent.

Results and Discussion

Stoicheiometry and Product Analysis.—Elemental analyses of the products of the reactions, in alkaline solution, of EDTA and MCPBA (Found: C, 36.0; H, 4.9; N, 8.5%) and H_2O_2 (Found: C, 36.0; H, 5.1; N, 8.6%) are both consistent with EDTA *N,N'*-dioxide·$0.5H_2O$ ($C_{10}H_{16}O_{10}N_2 \cdot 0.5H_2O$ requires C, 36.0; H,

Table 1. Observed second-order rate constants (25 °C) for the reaction of EDTA with substituted perbenzoic acids at pH 5.03 ± 0.03 in acetate buffer, ionic strength 0.1 mol dm^{-3}.

Substituent	pK_a[a]	k/dm^3 mol^{-1} s^{-1}
p-NO$_2$	7.14	46
m-Cl	7.53	17.8
p-SO$_3^-$	7.56	13.1
p-(CH$_3$)$_3$C	7.63[b]	8.7
p-CH$_3$	7.69[b]	7.2
p-CH$_3$O	7.93	7.6
σ-CO$_2^-$	8.08	4.5

[a] From ref. 6 unless stated otherwise. [b] Present work, determined by the method described in ref. 6.

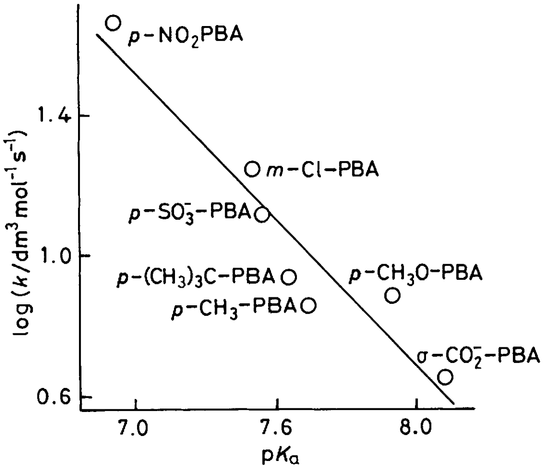

Figure 1. Brønsted-type correlations of log k *vs.* pK_a for the reaction of perbenzoic acids with EDTA.

5.1; N, 8.4%). Both products decompose at 154 °C. The product of the reaction of EDTA and MCPBA at neutral pH is identical with the above products since it has the same decomposition temperature and i.r. spectrum. Coeur and Alary report[5] that the product of the reaction of H_2O_2 and EDTA is EDTA N,N'-dioxide·H_2O, m.p. 182.3 °C. The reason for the discrepancy between our results and those of Coeur and Alary is not known.

Over the range of pH values used in the kinetic studies the stoicheiometries of the reactions of EDTA, EDTMP, and DTPA are 2:1, 2:1, and 3:1 respectively, which are consistent with the formation of EDTA N,N'-dioxide, EDTMP N,N'-dioxide and DTPA N,N',N''-trioxide.

Kinetics.—The kinetics of the reactions of the peracids and chelating agents were followed using a large excess of the latter, and thus correspond to mono N-oxide formation. Plots of ln $(A - A_\infty)$ against time, which correspond to peracid reduction, were linear for at least three half-lives and the observed pseudo first-order rate constants, k_{obs}, obtained from the slopes of the plots were independent of the initial concentration of the peracid. At any given pH, k_{obs} was directly proportional to the concentration of the chelating agent and independent of the buffer concentration when this was varied keeping the ionic strength constant with $NaNO_3$. The above results lead to the rate law given in equation (1) where $[PH]_T$ and $[Y]_T$ represent the total concentration of peracid and chelating agent respectively and k is the second-order rate constant at any given pH as defined in equation (2).

$$\frac{-d[PH]_T}{dt} = k[PH]_T[Y]_T \qquad (1)$$

$$k = k_{obs}/[Y]_T \qquad (2)$$

Reaction of EDTA and Substituted Perbenzoic Acids.—Table 1 shows the pK_a values of the peracids,[6] and the second-order rate constants, k, for their reactions with EDTA at pH 5, buffer ionic strength 0.1 mol dm^{-3}. Below ionic strength 0.02 mol dm^{-3} a marked positive dependence of k upon the ionic strength is observed (results not shown) for peracids with negatively charged substituents: this is consistent with a reaction involving like-charged species. At higher ionic strength, however, there is virtually no dependence of rate upon ionic strength for any of the peracids and so the electrostatic contribution of charged substituents to the observed substituent effects are negligible.

The reactivity of the peracids varies inversely with pK_a, giving a Brønsted slope of -1.00 ± 0.17 (Figure 1). This slope is typical[7] of reactions which proceed by a nucleophilic displacement on the peroxidic oxygen of the peracid and strongly suggests that EDTA N-oxide formation takes place by nucleophilic attack of a tertiary nitrogen of EDTA on the outer peroxidic oxygen of the protonated form of the peracid.

Reactions of EDTA, DTPA, and EDMTP with MCPBA.—Figure 2 shows the pH dependencies of the second-order rate constants. These are consistent with the mechanism shown in equations (3)–(5) in which the protonated peracid, PH, reacts with various forms of the chelators, H_nY^{n-m}, where m is 4, 5, and 8 respectively for EDTA, DTPA, and EDTMP and n varies from 0–m.

$$PH \underset{}{\overset{K_a}{\rightleftharpoons}} P^- + H^+ \qquad (3)$$

$$H_{1+n}Y^{1+n-m} \overset{K_{n+1}}{\rightleftharpoons} H_nY^{n-m} + H^+ \qquad (4)$$

$$H_nY^{n-m} + PH \xrightarrow{k_n} \text{products} \qquad (5)$$

This mechanism leads to the rate equation shown in equation (6)

$$-\frac{d[PH]_T}{dt} = \sum_{n=0}^{m} k_n[PH][H_nY^{n-m}] \qquad (6)$$

From equations (1) and (6) and the expressions for the equilibrium constants (7) and (8) and the mass conservation equations (9) and (10) the relationship between the second-order rate constant and $[H^+]$ shown in equation (11) is obtained.

$$K = \frac{[P^-][H^+]}{[PH]} \qquad (7)$$

$$K_{n+1} = \frac{[H_nY^{n-m}][H^+]}{[H_{1+n}Y^{1+n-m}]} \qquad (8)$$

$$[PH]_T = [PH] + [P^-] \qquad (9)$$

$$[Y]_T = \sum_{n=0}^{m} [H_nY^{n-m}] \qquad (10)$$

$$k = \frac{(k_m[H^+]^m + k_{m-1}K_m[H^+]^{m-1} + k_{m-2}K_mK_{m-1}[H^+]^{m-2} + \cdots + k_0K_mK_{m-1}\cdots K_1)[H^+]}{([H^+]^m + K_m[H^+]^{m-1} + K_mK_{m-1}[H^+]^{m-2} + \cdots + K_mK_{m-1}\cdots K_1)([H^+] + K_a)} \qquad (11)$$

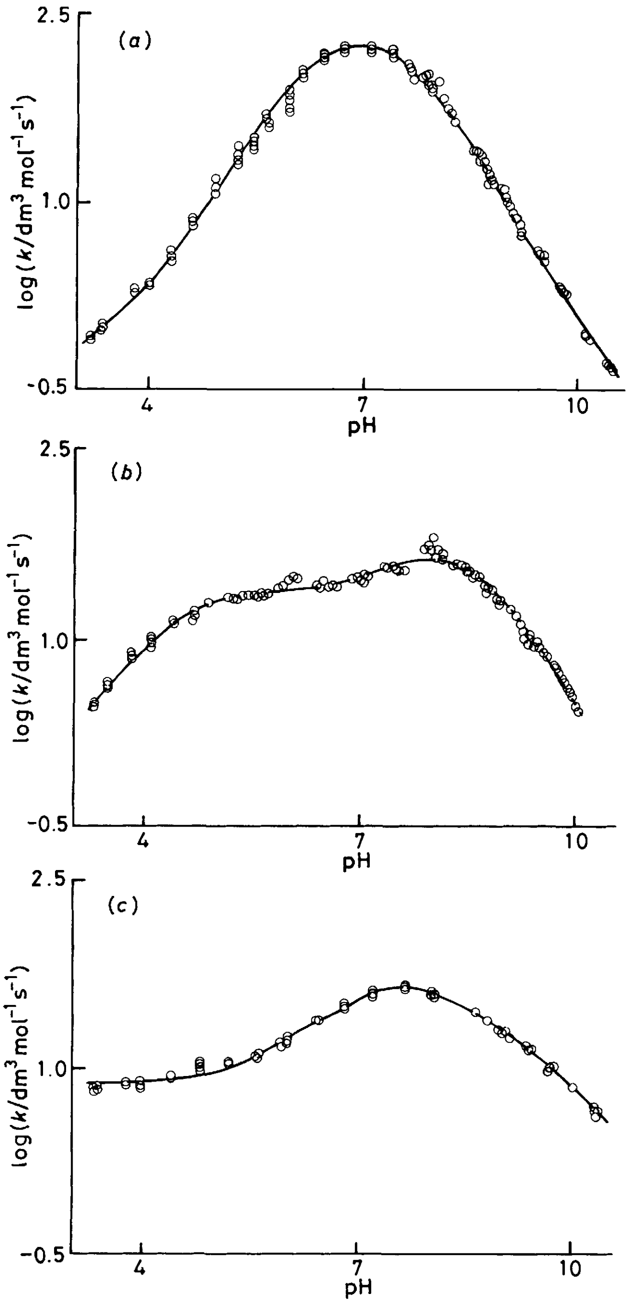

Figure 2. Dependence upon pH of the observed second-order rate constants (25 °C) for the reactions of (*a*) EDTA, (*b*) DTPA, and (*c*) EDTMP, with MCPBA in buffers of ionic strength 0.1 mol dm^{-3}. The curves represent the pH dependencies calculated using equation (11) with the best-fit values of the rate constants k_n defined in equation (5).

Literature values[8,9] of K_{n+1} and of K_a for MCPBA[6] are substituted into equation (11) and the best-fit values of k_n, shown in Table 2, are obtained using non-linear least squares[10] to fit log k to the logarithm of the right hand side of equation (11)

The reactivity of the chelator anions, k_n, varies systematically with basicity. A Brønsted slope of 0.26 ± 0.07 (Figure 3) is obtained, after statistical adjustment, for the reaction of anions containing one or more free-base nitrogens. This slope is consistent[7] with the proposed mechanism, which involves nucleophilic attack of a tertiary nitrogen of the chelator on the outer peroxidic oxygen of the peracid. A similar Brønsted slope of 0.33 can be calculated from published[11] kinetic data on the Caro's acid oxidation of dimethylanilines.

Table 2. Calculated[a] second-order rate constants (dm^{-3} mol^{-1} s^{-1}, 25 °C) for the reactions of the anions of EDTA, DTPA, and EDTMP with MCPBA.

	EDTA		DTPA		EDTMP	
n	pK_{n+1}	k_n	pK_{n+1}	k_n	pK_{n+1}	k_n
0	10.34	544	10.56	1 120	10.60	6 230
1	6.24	256	8.69	871	9.22	1 300
2	2.75	0.94	4.37	23.9	7.43	122
3	2.07	0	2.87	2.7	6.63	20
4	—	—	1.94	0	6.18	30
5	—	—	—	—	5.05	7.7

[a] The tabulated pK values are taken from refs. 8 and 9.

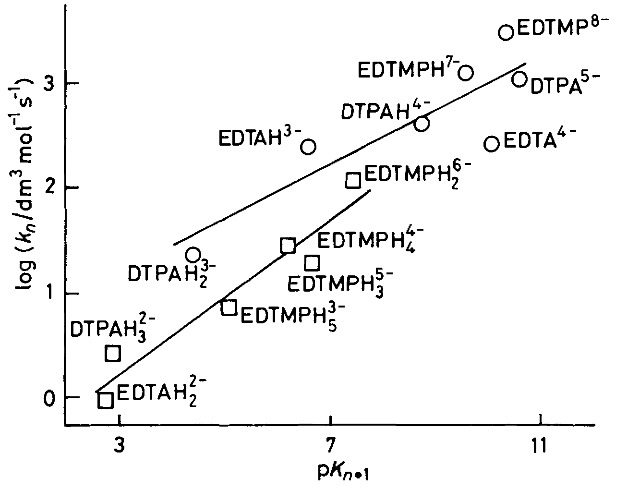

Figure 3. Brønsted-type correlations of log k_n *vs.* pK_{n+1} for the reactions of the anions of EDTA, DTPA, and EDTMP with MCPBA; ○: statistically adjusted values for reactions involving chelator anions containing one or more free-base nitrogens; □: unadjusted data.

It is initially, perhaps, surprising that the more protonated forms of the chelators react with MCPBA since it is well known that the nitrogen atoms of aminocarboxylates are more basic than the oxygen atoms and that, for example, $EDTAH_2^{2-}$ exists in solution predominantly as a zwitterionic doubly nitrogen-protonated species which is not a nucleophile. N.m.r. studies to determine the distributions of protons among the various sites on the ligands, however, indicate microscopic equilibria and that, for example, the extent of protonation of the nitrogen atoms of $EDTAH_2^{2-}$ is 96 ± 2%.[12] Hence there is a significant concentration of free-base nitrogen which can attack the electrophilic outer peroxidic oxygen of the peracid. The correlation between the rate constant and overall basicity of the ligand for the more protonated chelator anions is shown in Figure 3. The Brønsted slope, 0.37 ± 0.05 may, at least in part, reflect a relationship between the basicity of the most basic oxygen anion and the proportion of reactive free-base nitrogen.

Activation Parameters.—The temperature dependence of the reaction between EDTA and substituted perbenzoic acids was measured at five temperatures between 20 and 40 °C at pH *ca.* 5.0. At this pH the predominant species are the protonated peracid, PH, and $EDTAH_2^{2-}$. The predominant reaction is that of $EDTAH^{3-}$.

$$EDTAH_2^{2-} \overset{K_2}{\rightleftharpoons} EDTAH^{3-} + H^+ \qquad (12)$$

$$EDTAH^{3-} + PH \xrightarrow{k_1} \text{products} \qquad (13)$$

Table 3. Activation parameters for the reaction of chelators and substituted perbenzoic acids.

Peracid substituent	Chelator	$\Delta H^\ddagger$/ kJ mol^{-1}	$\Delta S^\ddagger$/ J mol^{-1} K^{-1}
p-NO$_2$	EDTAH^{3-}	29.5 ± 3.6	−92 ± 12
m-Cl	EDTAH^{3-}	20.4 ± 2.9	−130 ± 9
p-SO$_3^-$	EDTAH^{3-}	29.5 ± 3.0	−102 ± 10
p-(CH$_3$)$_3$C	EDTAH^{3-}	29.2 ± 3.0	−107 ± 10
p-CH$_3$	EDTAH^{3-}	33.5 ± 3.5	−94 ± 12
p-CH$_3$O	EDTAH^{3-}	28.5 ± 5.3	−111 ± 17
σ-CO$_2^-$	EDTAH^{3-}	34.7 ± 4.4	−94 ± 15
m-Cl	DTPAH$_2^{3-}$	30.2 ± 1.0	−117 ± 3

Table 4. Lifetimes (25 °C) of the chelators in the presence of MCPBA at pH 4, 7, and 10. Lifetimes defined here as five half-lives, in minutes, are calculated from the kinetic data of Figure 2 for a concentration of MCPBA of 1×10^{-3} mol dm^{-3}.

	Chelator		
pH	EDTA	EDTMP	DTPA
4	28	10	7
7	0.5	1.8	1.8
10	56	10	23

The following equation for the temperature dependence of the second-order rate constant, k measured at pH *ca.* 5.0 can be derived from equations (12) and (13).

$$\ln\left(\frac{k[\mathrm{H}^+]}{K_2(T)\cdot T}\right) = \ln\frac{k_B}{h} + \frac{\Delta S_1^\ddagger}{R} - \frac{\Delta H_1^\ddagger}{RT} \qquad (14)$$

Values of $K_2(T)$ were interpolated from published values[13] using the method described by Robinson and Stokes.[14] The values of $\Delta S^\ddagger$, and $\Delta H^\ddagger$ obtained by linear regression of the left hand side of equation (14) against T^{-1} are shown in Table 3. The values of $\Delta H_2^\ddagger$ and $\Delta S_2^\ddagger$ obtained for the reaction of DTPAH$_2^{3-}$ and MCPBA, using a similar procedure and published[13] values of $K_3(T)$, are also shown in Table 3. The activation parameters lie within the range expected for nucleophilic attack on the outer peroxidic oxygen of the peracid and are, in fact, very close to the values $\Delta H^\ddagger$ 28.4 kJ mol^{-1} and $\Delta S^\ddagger$ −109 J mol^{-1} K^{-1} obtained[15] for the reaction of perbenzoic acid and iodide in aqueous solution.

Conclusions

The experimental results strongly support a mechanism which involves nucleophilic attack of the nitrogen atom of the chelating agents on the outer peroxidic oxygen of the peracid to form a chelate *N*-oxide.

The kinetic data is of importance in assessing how added chelators suppress the metal-ion catalysed reactions of peracids. For example, we have found that EDTMP, but not EDTA, inhibits the reaction of H$_2$O$_2$ and MCPBA at pH 10 (results not shown). Table 4 is a comparison of the lifetimes of the chelators in the presence of peracid and shows that added EDTMP does not suppress the reaction of H$_2$O$_2$ and MCPBA simply by virtue of its inertness towards oxidation because, in fact, at pH 10 it is less inert than is EDTA with respect to oxidation by the peracid.

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