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Evidence for cyclodextrin dioxiranes. Part 2. Catalytic and enantioselective properties of cyclodextrin dioxiranes formed from keto-derivatised hydroxypropyl–cyclodextrins☆

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Abstract

Following our recent study of the bromine oxidation, at neutral pH, of α-cyclodextrin, β-cyclodextrin, O-methylated β-cyclodextrins and sucrose, which yield ketone and carboxylic acid-containing materials in the oxidation products (M.E. Deary, D.M. Davies, *Carbohydr. Res.*, 309 (1998) 17), we have extended the work to hydroxypropyl-α-cyclodextrin and hydroxypropyl-β-cyclodextrin. ^{13}C NMR analysis confirms the presence of ketone groups (δ 207) in the oxidation products of both of these compounds. The continued ability of the products of these oxidations to complex *p*-nitrophenol demonstrates that ring integrity is maintained. The ketone-containing products are capable of catalysing the peroxomonosulfate (PMS) oxidation of a range of substrates including aryl alkyl sulfoxides, pyridine, 4-bromopyridine, aniline, 4-aminobenzoate, 4-bromoaniline and several amino acids, most probably by the formation of a more reactive cyclodextrin–dioxirane intermediate. A small degree of enantioselectivity is observed in the oxidation of (*R*)-(+)- and (*S*)-(−)-methyl *p*-tolyl sulfoxide by PMS in the presence of the keto derivative of hydroxypropyl-α-cyclodextrin, though not for the β analogue.

Keywords: Cyclodextrin; Hydroxypropyl–cyclodextrin; Bromine oxidation; Ketone; Dioxirane

1. Introduction

There has been a considerable amount of research into the use of cyclodextrins as a basis for artificial enzymes [2]. Cyclodextrins possess a hydrophobic cavity, capable of anchoring hydrophobic parts of molecules, and two hydroxyl rims that can either react with included molecules directly, as in the case of ester cleavage at high pH [3–5] or which can be functionalised, for example by the addition of an imidazole group that can participate in acyl transfer reactions at conditions nearer to those found in living systems [6,7]. Other nucleophiles, including α-nucleophiles such as hydroxylamine and hydrogen peroxide, have also been attached to the primary and secondary hydroxyl rims of cyclodextrin, allowing preassociation to occur between nucleophile and substrates [8].

We have recently produced evidence for the formation of a dioxirane group attached to cyclodextrin. The precursor to the cyclodex-

☆ For Part 1, see Ref. [1].

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trin–dioxirane is a keto-derivatised cyclodextrin, formed from bromine oxidation of secondary hydroxyls at neutral pH [1]; sucrose is similarly transformed [1]. The keto derivatives are capable of catalysing the peroxomonosulfate (PMS) oxidation of a range of substrates in an analogous way to other ketones such as cyclohexanone, which is known to generate a dioxirane upon reaction with PMS [9]. However, in contrast to cyclohexanone there is no regeneration of the keto-cyclodextrin from the cyclodextrin dioxirane. This aspect encouraged us to extend the study to hydroxypropyl cyclodextrins, with the objective of finding more stable keto-cyclodextrins. Hydroxypropyl-α-cyclodextrin and hydroxypropyl-β-cyclodextrin have average degrees of substitution of 0.6, and 1.0 CH_2–$CH(CH_3)OH$ groups per glucose residue, respectively. The substitutions are random and can occur at both the primary and secondary hydroxyls, as well as on the secondary hydroxyl groups of the hydroxypropyls, in which case side chains containing $(CH_2$–$CH(CH_3)O)_nH$ where $n>1$ are possible. Bromine oxidation can, therefore, occur not only at the secondary hydroxyl rim of the cyclodextrin, but also at the secondary alcohols of the hydroxypropyl groups, in which case flexible ketone groups (acetonyls) would be formed. Acetonyls might reasonably be expected to be less susceptible to oxidation (to a carboxylic acid) than β-hydroxyketones, which are the products of bromine oxidation of the native cyclodextrins. We report here on the preparation of keto-derivatives of hydroxypropyl cyclodextrins and their effect on PMS oxidation of a range of substrates including aryl alkyl sulfoxides, pyridine, 4-bromopyridine, aniline, 4-aminobenzoate, 4-bromoaniline and several amino acids.

2. Results and discussion

Bromine reacts with hydroxypropyl-α-cyclodextrin over a period of ca. 30 min at pH 7.6 (results not shown). The subsequent formation of the characteristic absorbance band of the keto-containing product at 285 nm takes approximately 24 h, and in this respect differs little from the previously reported results for the native cyclodextrins [1]. The reaction of bromine under identical conditions with hydroxypropyl-β-cyclodextrin is somewhat slower (results not shown), and this also mirrors the results for the native cyclodextrins, where β-cyclodextrin consumed bromine at a slower rate than α-cyclodextrin. The bromine oxidation products of both hydroxypropyl cyclodextrins can complex *p*-nitrophenol, indicating that ring integrity is largely maintained during bromine oxidation (results not shown).

The ^{13}C NMR spectrum of a ca. 180 mM solution of the bromine oxidation product of hydroxypropyl-α-cyclodextrin in water at ca. pH 6 (Fig. 1) shows a weak ketone carbonyl carbon resonance at 207.4 ppm. This is in agreement with the ketone carbonyl carbon resonances observed at 207.8 and 206.5 ppm for bromine-oxidised α-cyclodextrin and with literature δ values for ketone carbonyl carbons that result from the bromine oxidation of a range of carbohydrates at neutral pH [8,10]. The resonances for the corresponding ketone hydrates, which are normally expected between 92 and 98 ppm [1] are likely to have been obscured by the resonance of the cyclodextrin anomeric carbon, which appears as a double resonance and which is shifted upfield compared to the native cyclodextrins. It

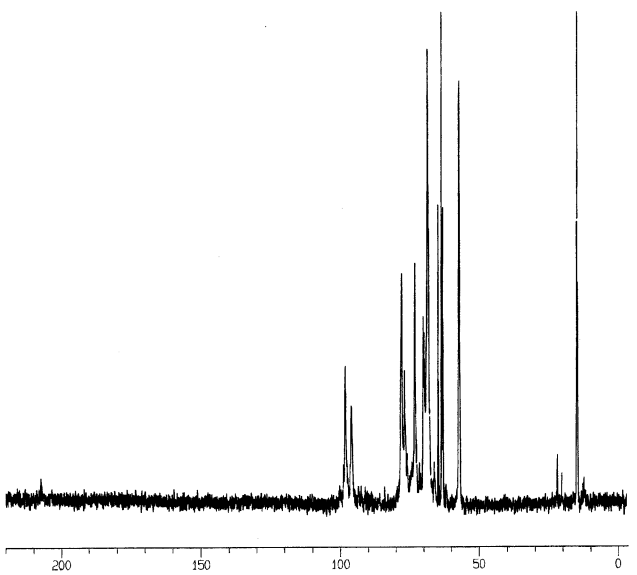
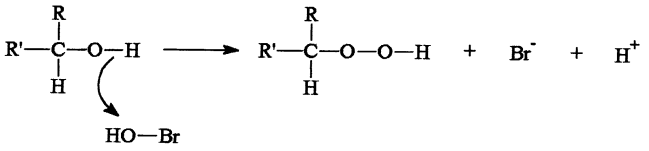
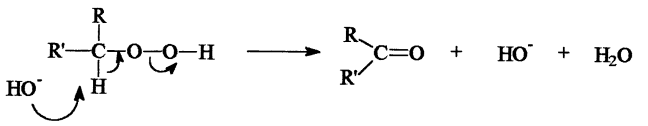


Fig. 1. Fully decoupled ^{13}C NMR spectrum of the bromine oxidation product of hydroxypropyl-α-cyclodextrin in H_2O at 67.8 MHz.



Scheme 1.



Scheme 2. Kornblum–De La Mare-type mechanism.

is also possible that the keto–keto-hydrate equilibrium for these compounds strongly favours the keto form, in which case no keto-hydrate resonance would be expected [10–12]. For hydroxypropyl-β-cyclodextrin, a weak signal is observed at 207.0 ppm (results not shown). Significantly, no carboxylic acid carbonyl resonances were detected under the conditions used to obtain the keto derivatives of these compounds (initial bromine excess of 1.5), indicating that unlike the native cyclodextrins, hydroxypropyl cyclodextrins do not readily oxidise to form carboxylic acid-containing products under these conditions. When the bromine excess over hydroxypropyl-β-cyclodextrin was increased to 6.8, however, a carboxylic acid carbonyl carbon resonance was detected at 167.7 ppm (not shown).

The position of the ketone group is uncertain, since it is possible for bromine oxidation to occur at hydroxyls on either the secondary hydroxyl rim of the cyclodextrin, or on the secondary hydroxyls of the hydroxypropyl substituents. Nevertheless, the presence in Fig. 1 of downfield-shifted methyl carbonyl resonances for the hydroxypropyl group, which occurs at ca. 15 ppm in hydroxypropyl-α-cyclodextrin, is consistent with there being some oxidation of hydroxypropyl hydroxyls.

The bromine oxidation results are consistent with the formation of keto-derivatised hydroxypropyl cyclodextrins via a similar mechanism to that proposed for other cyclodextrins and sucrose [8]. Under the proposed mechanism there is direct attack of a secondary hydroxyl on HOBr, with Br^- then leaving to yield a hydroperoxy cyclodextrin (Scheme 1) that subsequently decomposes via a Kornblum–De La Mare-type reaction to give a ketone (Scheme 2).

The accelerative effect of the keto-derivatised hydroxypropyl-β-cyclodextrin (KHP-β-CD) on *p*-nitrophenol oxidation by PMS is shown in Fig. 2; KHP-α-CD, gives similar results. The levelling off in absorbance at higher KHP-β-CD concentrations is due to the complete consumption of PMS. It is likely that PMS reacts with the keto group to form a dioxirane that subsequently oxidises the *p*-nitrophenol in an analogous way to the keto-derivatives of the native cyclodextrins and other carbohydrates [8].

Data showing the effect of cyclohexanone, KHP-α-CD and KHP-β-CD on the transformation of aryl methyl sulfoxides to the corresponding sulfones is given in Table 1. The accelerative effect is given as the ratio of the initial rate in the presence of ketone compared to that without. Whilst only modest rate enhancements are observed for aryl methyl sulfoxide oxidation, the 3-fold increase seen in the presence of KHP-α-CD, entry 4, for (*S*)-(−)-methyl *p*-tolyl sulfoxide, is superior to the effect observed for the same reaction in the presence of cyclohexanone, entry 2, which has been widely used in the literature for dioxirane generation [13]. The observation of reduced catalytic effects of both KHP-α-CD and KHP-β-CD on the PMS oxidation of 4-bro-

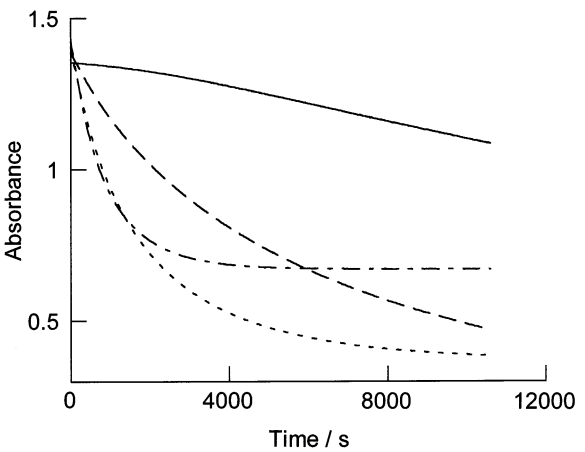


Fig. 2. Absorbance changes at 400 nm for the reaction of 1.0×10^{-4} mol dm^{-3} *p*-nitrophenol and 1.84×10^{-3} mol dm^{-3} PMS in pH 7.6 phosphate buffer, ionic strength 0.2 mol dm^{-3}, 25 °C, solid line and in the presence of: 0.93×10^{-3} mol dm^{-3} KHP-β-CD, dashed line; 3.72×10^{-3} mol dm^{-3} KHP-β-CD, dotted line; and 7.44×10^{-3} mol dm^{-3} KHP-β-CD, dash–dotted line.

Table 1
Effect of cyclohexanone and ketone-containing products of the bromine oxidation of hydroxypropyl-α-cyclodextrin (KHP-α-CD) and hydroxypropyl-β-cyclodextrin (KHP-β-CD), on initial rate for the oxidation of aryl methyl sulfoxides by PMS

Entry No.	Ketone or ketone-containing products of bromine oxidation	Substrate (S)	$[S]_o$ (10^{-3} mol dm^{-3})	Buffer (phosphate)	[PMS] (10^{-3} mol dm^{-3})	[Ketone] (10^{-3} mol dm^{-3})	Initial rate (10^{-7} mol dm^{-3} s^{-1})	Acceleration of initial rate
1	cyclohexanone	(*S*)-(−)-methyl *p*-tolyl sulfoxide	0.109	pH 7.8, $I = 0.52$ M	5.13	0.00	2.89 ± 0.08	
						2.00	4.30 ± 0.13	1.49
2		(*S*)-(−)-methyl *p*-tolyl sulfoxide	0.109	pH 7.6, $I = 0.2$M	4.38	0.00	2.20 ± 0.06	
						8.00	7.00 ± 0.19	3.12
3		4-bromophenyl methyl sulfoxide	0.100	pH 7.8, $I = 0.52$ M	5.13	0.00	3.76 ± 0.10	
						2.00	4.67 ± 0.13	1.24
4	KHP-α-CD	(*S*)-(−)-methyl *p*-tolyl sulfoxide	0.109	pH 7.6, $I = 0.2$M	4.38	0.00	2.20 ± 0.06	
						3.23	6.40 ± 0.17	2.91
						6.46	7.14 ± 0.23	3.24
5		(*S*)-(−)-methyl *p*-tolyl sulfoxide	0.109	pH 7.6, $I = 0.2$M	4.44	0.00	1.93 ± 0.04	
						4.84	5.86 ± 0.33	3.03
6		(*R*)-(+)-methyl *p*-tolyl sulfoxide	0.114	pH 7.6, $I = 0.2$M	4.44	0.00	1.92 ± 0.06	
						4.84	4.51 ± 0.04	2.34
7		4-bromophenyl methyl sulfoxide	0.100	pH 7.6, $I = 0.2$M	4.44	0.00	1.87 ± 0.03	
						2.42	2.90 ± 0.06	1.55
						4.84	3.14 ± 0.10	1.68
8	KHP-β-CD	(*S*)-(−)-methyl *p*-tolyl sulfoxide	0.109	pH 7.6, $I = 0.2$M	4.38	0.00	2.05 ± 0.04	
						7.43	5.21 ± 0.09	2.54
9		(*R*)-(+)-methyl *p*-tolyl sulfoxide	0.114	pH 7.6, $I = 0.2$M	4.38	0.00	2.04 ± 0.04	
						7.43	5.08 ± 0.07	2.47
10		4-bromophenyl methyl sulfoxide	0.100	pH 7.6, $I = 0.2$M	4.38	0.00	2.25 ± 0.06	
						3.72	3.57 ± 0.10	1.59
						7.43	4.37 ± 0.10	1.94

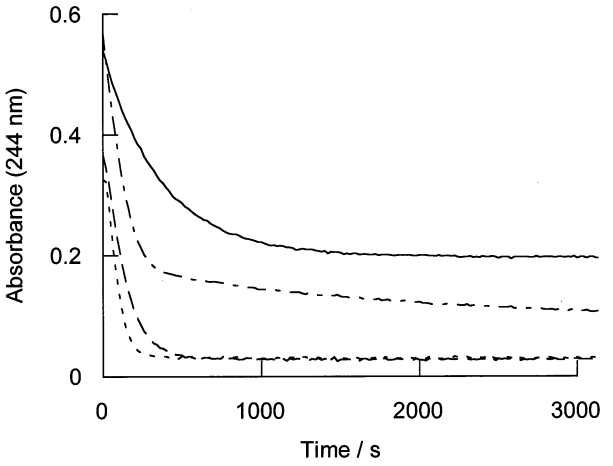


Fig. 3. Effect of KHP-α-CD on the monoperoxosulfate oxidation of (*R*)-(+)- and (*S*)-(−)-enantiomers of methyl *p*-tolyl sulfoxide, dashed and dotted lines, respectively. The solid line shows the reaction with no ketone present and the dash–dotted line shows the effect of cyclohexanone on the oxidation of (*S*)-(−)-methyl *p*-tolyl sulfoxide. The reactions were carried out at 25 °C in pH 7.6 phosphate buffer, $I = 0.2$ mol dm^{-3}; reactant concentrations given in Table 1.

mophenyl methyl sulfoxide compared to either (*R*)-(+) or (*S*)-(−)-methyl *p*-tolyl sulfoxide suggests that, as with the keto derivatives of the native cyclodextrins, the cyclodextrin dioxirane reacts principally with unbound substrates. An increased catalytic effect might have been expected for the stronger binding 4-bromophenyl methyl sulfoxide [14] if the converse were true.

A more significant observation, however, is that of a small degree of enantioselectivity in the oxidation of methyl *p*-tolyl sulfoxide in the presence of KHP-α-CD. There is an approximately 30% increase in initial rate for the (*S*)-(−) form compared to the (*R*)-(+) form of the sulfoxide (entries 5 and 6 in Table 1). Fig. 3 shows the absorbance changes observed during this reaction. This effect was not observed for KHP-β-CD (entries 8 and 9 in Table 1), nor for keto-α-cyclodextrin. Modest enantioselective effects have been reported in studies using cyclodextrins as a resolving agents for enantiomeric mixtures of aryl alkyl sulfoxides [15–17]. Enantioselectivity has also observed for the oxidation of aryl alkyl sulfides by peroxides in the presence of cyclodextrins [18]. In the present case, the observed enantioselectivity may arise through either preferential non-productive binding of the (*R*)-(+) enantiomer, or via a preassociation mechanism involving the cyclodextrin dioxirane and the (*S*)-(−)- enantiomer of methyl *p*-tolyl sulfoxide, in which the sulfoxide is oxidised whilst present in the cyclodextrin cavity.

The presence of KHP-α-CD and KHP-β-CD also gives rise to significant rate accelerations for the PMS oxidation of pyridine and 4-brompyridine to the corresponding *N*-oxides, as shown in Table 2 and the corresponding plots of absorbance changes in Figs. 4 and 5. Up to 12-fold rate accelerations were observed for pyridine in the presence of KHP-α-CD, entry 3, which on a mole basis is superior to the effect observed with cyclohexanone. KHP-β-CD gives similar accelerations of initial rate to those observed for cyclohexanone. The levelling out observed in Fig. 5 for the KHP-α-CD catalysed oxidation of 4-bromopyridine is due to the complete consumption of PMS during the reaction. This does not occur for the corresponding reaction with pyridine, since the oxidation is complete before the peroxide is consumed. Both acetone and cyclohexanone, through the generation of the corresponding dioxiranes, have been shown to catalyse the PMS oxidation of pyridine to its *N*-oxide [19]. Table 3 compares the relative accelerations produced by cyclohexanone and KHP-α-CD for the oxidations

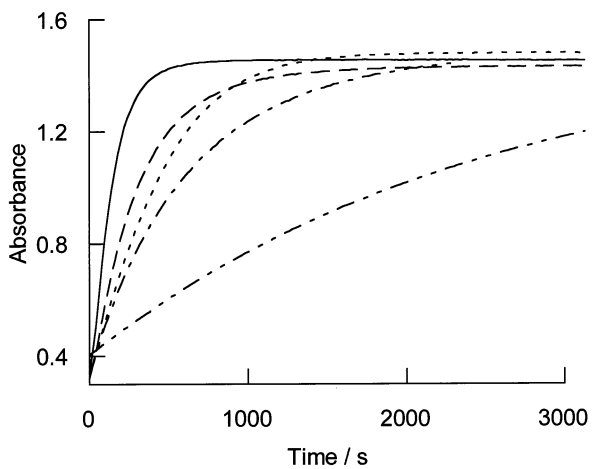


Fig. 4. Absorbance changes at 254 nm for the reaction between 5×10^{-3} mol dm^{-3} PMS and 0.125×10^{-3} mol dm^{-3} pyridine, dash–dot–dotted line; and in the presence of: 5.29×10^{-3} mol dm^{-3} KHP-α-CD, solid line; 1.76×10^{-3} mol dm^{-3} KHP-α-CD, dashed line; 2×10^{-3} mol dm^{-3} cyclohexanone, dotted line; and 1.86×10^{-3} mol dm^{-3} KHP-β-CD, dash–dotted line. Reactions were carried out at 25 °C in pH 7.8 phosphate buffer, ionic strength 0.5 mol dm^{-3}.

Table 2
Effect of cyclohexanone and ketone-containing products of the bromine oxidation of hydroxypropyl-α-cyclodextrin (KHP-α-CD) and hydroxypropyl-β-cyclodextrin (KHP-β-CD), on initial rate for the oxidation of pyridine and 4-bromopyridine by PMS

Entry No.	Ketone or ketone-containing products of bromine oxidation	Substrate (S)	$[S]_o$ (10^{-3} mol dm^{-3})	[PMS] (10^{-3} mol dm^{-3})	[Ketone] (10^{-3} mol dm^{-3})	Initial rate (10^{-8} mol dm^{-3} s^{-1})	Acceleration of initial rate
1	cyclohexanone	pyridine	0.125	5.13	0.00	4.08 ± 0.05	
					2.00	19.74 ± 0.12	4.84
2		4-bromopyridine	0.125	5.13	0.00	1.47 ± 0.08	
					2.00	6.90 ± 0.95	4.67
3	KHP-α-CD	pyridine	0.125	5.13	0.00	4.08 ± 0.05	
					1.76	26.46 ± 0.35	6.49
					5.29	50.41 ± 1.30	11.86
4		4-bromopyridine	0.125	5.13	0.00	1.47 ± 0.08	
					1.76	5.07 ± 0.48	3.43
5	KHP-β-CD	pyridine	0.125	4.42	0.00	4.20 ± 0.05	
					1.86	16.54 ± 0.22	3.94

of pyridine and 4-bromopyridine; the ratio of initial rate acceleration (Py:Br–py) increases markedly on going from cyclohexanone, where no complexation with substrate is possible, to KHP-α-CD, where it is likely. From work that we and others have done, it is reasonable to assume that the presence of a 4-bromo group will give a stronger complex with the cyclodextrin, and that the bromo group is likely to be oriented at the narrow end of the cavity [14]. As with the sulfoxide work reported above, therefore, these results demonstrate non-productive binding and suggest that substrates are oxidised principally in the bulk solution in these systems.

Fig. 6 shows the accelerative effect of KHP-α-CD, KHP-β-CD, cyclohexanone and the keto-derivative of sucrose on the oxidation of aniline to nitrobenzene by PMS. Similar trends have been obtained for 4-aminobenzoate and 4-bromoaniline (not shown). The plots show two obvious phases, with the initial phase being relatively unaffected by the addition of ketones (inset) or by pH over the range 6–8 (not shown). In the second phase of the reaction, with the exception of sucrose, there are significant rate enhancements in the presence of the ketones, especially so with KHP-α-CD. The oxidation of aromatic amines to the corresponding nitro compounds by both peracids and dioxiranes has been thoroughly characterised in the literature [9,20].

Both KHP-α-CD and KHP-β-CD can also accelerate the oxidation of amino acids, with the best example being for L-glutamic acid, shown in Fig. 7. Cyclohexanone and KHP-β-CD marginally accelerate the reaction, whereas there are large effects for KHP-α-CD, the keto-sucrose derivative (not shown) and, interestingly, the ketone derived from dimethyl-β-cyclodextrin, which only shows minimal accelerative effects on the rate of aryl alkyl sulfoxide oxidation [8]. The fact that the keto sucrose performs almost as well as KHP-α-CD shows that the effect is unlikely to be due to a preassociation of amino acid and dioxirane moiety in the cyclodextrin cavity. No enantioselectivity is observed, with the reaction of the D and L isomers being accelerated equally. For L-aspartic acid, which has one CH_2 less than glutamic acid and which also exists in the zwitterionic form under these

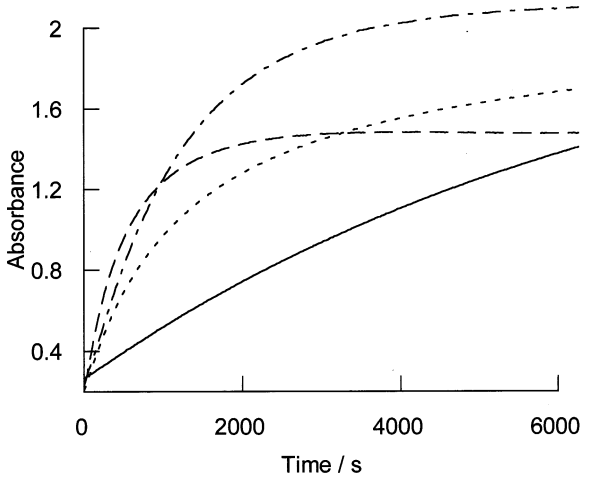


Fig. 5. Absorbance changes at 264 nm for the reaction between 5×10^{-3} mol dm^{-3} PMS and 0.125×10^{-3} mol dm^{-3} 4-bromopyridine in pH 7.8 phosphate buffer, ionic strength 0.5 mol dm^{-3}, 25 °C, solid line; and in the presence of: 5.29×10^{-3} mol dm^{-3} KHP-α-CD, dashed line; 1.76×10^{-3} mol dm^{-3} KHP-α-CD, dotted line; and 2×10^{-3} mol dm^{-3} cyclohexanone, dash–dotted line.

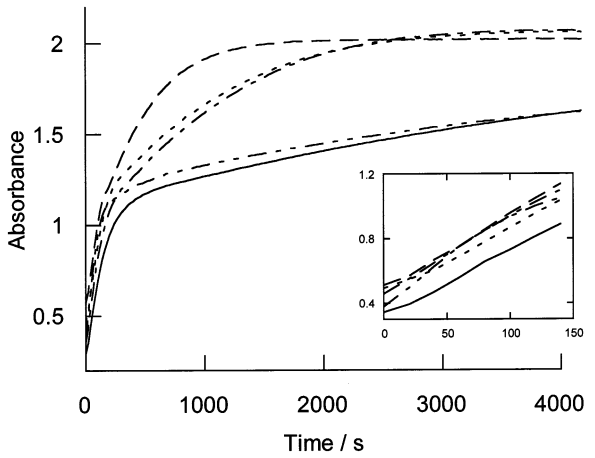


Fig. 6. Absorbance changes at 268 nm for the reaction of 0.25×10^{-3} mol dm^{-3} aniline with 4.6×10^{-3} mol dm^{-3} PMS in pH 7.8 phosphate buffer, ionic strength 0.5 mol dm^{-3}, 25 °C, solid line; and in the presence of 1.5×10^{-3} mol dm^{-3} of cyclohexanone, dash–dotted line, and 1.5×10^{-3} mol dm^{-3} of the keto-derivative of sucrose, dash–dot–dotted line; 1.5×10^{-3} mol dm^{-3} KHP-α-CD, dashed line; and 1.5×10^{-3} mol dm^{-3} KHP-β-CD, dotted line. The inset shows the same data over the first 150 s.

reaction conditions, there was no reaction with PMS, either in the presence or absence of the keto derivatives. It is possible that in the case of glutamic acid there is involvement of the terminal carboxylate group in an intramolecular catalytic mechanism, whereas with L-aspartic acid the shorter chain length may preclude this. Of the other amino acids studied with this system, no reaction was observed for glycine, whereas modest accelerations were observed for all keto-derivatives in the oxidation of L-tryptophan (results not shown). It is likely that these oxidations proceed via oxidative decarboxylation to yield aldehydes or carboxylic acids, as has been reported in literature studies of amino acid oxidation using the PMS/acetone system [21].

3. Experimental

Preparation of keto-derivatives of hydroxypropyl cyclodextrins.—Bromine oxidations of hydroxypropyl-α- and hydroxypropyl-β-cyclodextrin (Aldrich), the subsequent bromide removal via ion exchange and the ^{13}C NMR analysis of the products were carried out as described previously [8]. A bromine excess of 1.5 over the hydroxypropyl cyclodextrins was used in the preparation of the keto-hydroxypropyl cyclodextrins that were used to accelerate PMS oxidations of various substrates. A bromine excess of 6.8 over hydroxypropyl-β-cyclodextrin was used for one preparation, though this compound was not used in the studies involving PMS. At all bromine ratios only one elution peak was observed on pass-

Table 3
Comparison of the relative accelerations of initial rate for the PMS oxidation of pyridine (Py) and 4-bromopyridine (4-Br-py) in the presence of cyclohexanone and the bromine oxidation product of hydroxypropyl-α-cyclodextrin (KHP-α-CD)[a]

Ketone or ketone-containing products of bromine oxidation	[Ketone] (10^{-3} mol dm^{-3})	Acceleration of initial rate for 4-substituted pyridines		Ratio of acceleration
		Py	4-Br–py	Py: 4-Br–py
Cyclohexanone (entries 1 and 2 in Table 2)	2	4.84	4.67	1.04
KHP-α-CD (entries 3 and 4 in Table 2)	1.76	6.49	3.43	1.89

[a] Conditions given under the appropriate entries in Table 2.

ing the reaction mixture through an ion-exchange resin to remove bromide. All reagents were of analytical grade and were obtained from Aldrich.

Kinetics.—Spectral data and kinetic runs were obtained using a Pharmacia Biotech Ultraspec 2000 Spectrophotometer with thermostatted multiple cell holder. The reactions were carried out in phosphate buffer at either pH 7.6 or pH 7.8 and at ionic strengths of either 0.2 or 0.5 mol dm^{-3}. The high ionic strength reflected the large amount of acidity produced as a result of the reactions, particularly in the presence of the cyclodextrin-ketones, where very often all of the peroxide was consumed during the course of the reaction. Peroxide concentrations were routinely monitored at the end of runs by the addition of 0.5 ml each of 10 g/L potassium iodide and 0.5 N sulfuric acid solutions. The spectrum over the range 200–500 nm was then measured and the peroxide concentration calculated from the absorbance at an appropriate wavelength, having previously conducted a calibration. The aryl alkyl sulfoxide oxidations and subsequent data treatment to give the initial rates were carried out as described recently [8]. Similar methodologies were applied to the PMS oxidation of pyridine, 4-bromo pyridine, aniline, 4-bromoaniline, and 4-aminobenzoate, L-aspartic acid L-glutamic acid, glycine and L-tryptophan, though no kinetic analysis was attempted for the PMS oxidations of either the substituted anilines or the amino acids. UV–vis analysis of the product spectra, both in the presence and absence of ketones, confirmed that pyridine and 4-bromo pyridine were oxidised to the corresponding *N*-oxides [22] and that the substituted anilines were oxidised to the corresponding nitro compounds (comparison made with solutions of the nitro compounds). In the latter case, the formation and loss of the nitroso band at 700–750 nm was also observed. Experimental details are given in the Tables and associated Figures.

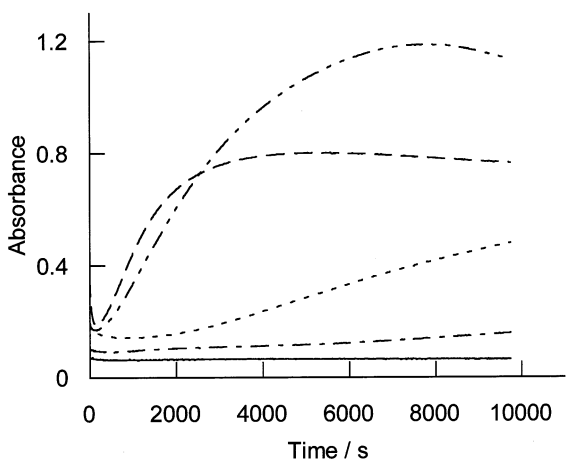


Fig. 7. Absorbance changes at 258 nm for the reaction between 0.25×10^{-3} mol dm^{-3} L-glutamic acid and 4.6×10^{-3} mol dm^{-3} PMS in pH 7.8 phosphate buffer, $I = 0.5$ mol dm^{-3}, 25 °C, solid line; and in the presence of: 1.5×10^{-3} mol dm^{-3} cyclohexanone dash–dotted line; 1.5×10^{-3} mol dm^{-3} of the keto-derivative of 2,6-di-*O*-methyl-β-cyclodextrin, dash–dot–dotted line; 1.5×10^{-3} mol dm^{-3} KHP-α-CD, dashed line; and 1.5×10^{-3} mol dm^{-3} KHP-β-CD, dotted line.

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References

[1] M.E. Deary, D.M. Davies, *Carbohydr. Res.*, 309 (1998) 17.
[2] For a recent review see: R.W. Breslow, S.D. Dong, *Chem. Rev.*, 98 (1998) 1997 and references therein.
[3] D.M. Davies, M.E. Deary, *J. Chem. Soc., Perkin Trans. 2*, (1999) 1027.
[4] R.L. VanEtten, J.F. Sebastian, G.A. Clowes, M.L. Bender, *J. Am. Chem. Soc.*, 89 (1967) 3242.
[5] O.S. Tee, C. Mazza, X. Du, *J. Org. Chem.*, 55 (1990) 3603.
[6] K.R. Rao, T.N. Srinivasan, N. Bhanumathi, P.B. Sattur, *J. Chem. Soc., Chem. Commun.*, (1990) 10.
[7] F. Cramer, G. Mackensen, *Angew. Chem., Int. Ed. Engl.*, 5 (1966) 601.
[8] K.A. Martin, M.A. Mortellaro, R.W. Sweger, L.E. Fikes, D.T. Winn, S. Clary, M.P. Johnson, A.W. Czarnik, *J. Am. Chem. Soc.*, 117 (1995) 10443.
[9] For reviews of dioxirane chemistry see: (a) W.A. Adam, R. Curci, J.O. Edwards, *Acc. Chem. Res.*, 22 (1989) 205. (b) R.W. Murray, *Chem. Rev.* 89 (1989) 1187.
[10] O. Larm, K. Larsson, E. Scholander, B. Meyer, J. Thiem, *Carbohydr. Res.*, 91 (1981) 13.
[11] M.A. Mortellaro, S. Hong, D.T. Winn, A.W. Czarnik, *Bioorg. Med. Chem. Lett.*, 4 (1994) 2041.
[12] H. Xu, P.J. Wentworth, N.W. Howell, J.A. Joens, *Spectrochim. Acta.*, 49 (1993) 1171.
[13] J.O. Edwards, R.H. Pater, R. Curci, F. Di Furia, *Photochem. Photobiol.*, 30 (1979) 63.
[14] D.M. Davies, M.E. Deary, *J. Chem. Soc., Perkin Trans. 2*, (1995) 1287.

[15] F. Cramer, W. Dietsche, *Chem. Ber.*, 92 (1959) 378.
[16] W.L. Hinze, T.E. Rieh, D.W. Armstrong, W. DeMond, A. Alak, T. Ward, *Anal. Chem.*, 57 (1985) 237.
[17] (a) M. Mikolajczyk, J. Drabowicz, *J. Am. Chem. Soc.*, 100 (1978) 2510. (b) M. Mikolajczyk, J. Drabowicz, F. Cramer, *J. Chem. Soc., Chem. Commun.*, (1971) 317.
[18] A. Czarnik, *J. Org. Chem.*, 49 (1984) 924. See also: R. Fornasier, P. Scrimin, P. Tecilla, U. Tonellato, *Phosphorus Sulfur*, 35 (1988) 211.
[19] A.R. Gallopo, J.O. Edwards, *J. Org. Chem.*, 46 (1981) 1684.
[20] K.M. Ibene-Rasa, J.O. Edwards, *J. Am. Chem. Soc.*, 84 (1962) 763.
[21] V.M. Paradkar, T.B. Latham, D.M. Demko, *Synlett*, (1995) 1059.
[22] (a) For 4-bromopyridine *N*-oxide: J.P. Phillips, H. Feuer, B.S. Thyagarajan (Eds.), *Organic Electronic Spectral Data*, Vol. 8, Interscience, New York, 1966. (b) For pryridine *N*-oxide: J.P. Phillips, D. Bates, H. Feuer, B.S. Thyagarajan (Eds.), *Organic Electronic Spectral Data*, Vol. 15, Interscience, New York, 1973.