The interaction of α-cyclodextrin with aliphatic, aromatic and inorganic peracids, the corresponding parent acids and their respective anions

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Potentiometric or combined potentiometric and spectrophotometric or kinetic techniques have been used to determine stability constants for complexes between α-cyclodextrin and 20 of the title compounds. Linear free energy relationships indicate that 4-substituted benzoic acids, perbenzoic acids and perbenzoates have predominantly the same orientation within the cyclodextrin cavity, with the carboxylic acid, percarboxylic acid and percarboxylate groups located at the narrow (primary hydroxy) end of the cavity. 4-Substituted benzoates orientate in the opposite way with the carboxylate group located at the wide end of the cavity. Alkyl carboxylic acids, percarboxylic acids and their anions show a linear dependence between log stability constant and the number of carbons. They are likely to bind with the functional group at the narrow end of the cavity, although the carboxylate groups will probably be located outside the cavity because of solvation requirements. 2:1 cyclodextrin–guest complexes are observed for several of the compounds studied.

Introduction

Cyclodextrins have proved to be a very attractive molecule for study as is evidenced by the wealth of papers on them.[1] These naturally occurring oligomers, which are considered as being shaped like truncated cones, can have either six (α), seven (β) or eight (γ) α-(1,4) linked glucopyranose units, giving internal cavity diameters (wide end) ranging from 5.2 to 8.3 Å.[2] α-Cyclodextrin forms complexes with a wide range of different substrates, including small organic molecules,[3] substituted benzenes,[4–8] surfactants,[9] noble gases,[10] small anions[11] and several series of alkyl substrates.[12–16]

We have recently proposed a model to predict the strength of inclusion compound formation between 1,4-disubstituted benzenes and α-cyclodextrin.[17] In this model, uncharged guests are orientated within the cavity so that the guest dipole is antiparallel to the host's, with electron-withdrawing substituents, as defined by the Hammett σ-value, located at the narrow end of the cavity. A charged substituent, which will be solvated, is likely to be located at the wide end of the cavity where it can retain significant contact with the bulk solvent. The size and polarisability of the substituent located at the narrow end of the cyclodextrin cavity (termed the X-substituent), as defined by the molar refractivity Rm_x, is also used in our model. This successfully predicted the stability constants of α-cyclodextrin complexes of a series of aryl alkyl sulfides, sulfoxides and sulfones once the width of the sulfur-containing substituent was taken into account.[18] As well as 1:1 complexes, 2:1 host–guest complexes have been widely reported for 1,4-disubstituted benzenes.[4–8,19] For a range of aryl alkyl sulfides we have found large binding constants for the second binding step, with cooperative binding displayed in several instances.[18] We have suggested that substrate promoted dipole–dipole interactions between cyclodextrins are responsible for these large values. The strength of the second binding step has been shown to correlate to K_{11}, the 1:1 stability constant, and Rm_y, the molar refractivity of the substituent protruding from the wide end of the cavity of the first cyclodextrin molecule.[18]

The log stability constants for the 1:1 complexes of cyclodextrin with alkyl substrates, including *m*- and *p*-substituted-alkyl phenols, alkanols, carboxylic acids, carboxylates and esters show a linear dependence of alkyl chain length up to about C-6.[12] 2:1 and higher host–guest complexes have also been reported for carboxylic acids,[16] carboxylates[16] and α-ω dicarboxylic acids[15] when the alkyl chain length exceeds five.

We have described the cyclodextrin complexes of some substituted perbenzoic acids as part of a study of their reaction with iodide[20,21] and have recently extended this work to the corresponding reactions with sulfides, described in the subsequent paper.[22] Using a potentiometric technique, or a combination of potentiometric and kinetic or spectrophotometric techniques we have obtained 20 additional stability constants for 1:1 inclusion complexes between α-cyclodextrin and various aliphatic, aromatic and inorganic peracids and their anions and some of the corresponding parent acids and their anions. Linear free energy relationships have been used to determine the likely orientations of these molecules within the α-cyclodextrin cavity. We also report on the observation of 2:1 cyclodextrin–guest complexes for some of the guest molecules studied. The part of our original study[20] concerned with 4-methylperbenzoic acid was subject to a small but significant systematic error as described in a recent short communication.[23] These results are included in the present paper.

Experimental

Materials

Analytical grade reagents were used in all cases. Solutions of α-cyclodextrin (Aldrich) were made up in distilled water and were filtered through a 10 μm sintered-glass funnel prior to use. Perbenzoic acid was prepared by hydrolysing benzoyl peroxide (Aldrich) in 0.1 mol dm^{-3} sodium hydroxide for 3 h and then adjusting to the working pH using sulfuric acid. The solution (*ca.* 13×10^{-3} mol dm^{-3} in peroxide and the parent acid) was standardised iodometrically for the peroxide. The parent acid concentration was calculated spectrophotometrically using molar absorbtivities (232 nm) of 10 810 and 13 260 dm^3 mol^{-1} cm^{-1} for the parent and peracid respectively. The peracid molar absorbtivity was obtained by observing absorbance changes at 232 nm during the decomposition of perbenzoic acid to benzoic acid in distilled water over a period of several days. Peracetic acid (Aldrich) was used after first removing the hydrogen peroxide impurity. This was done by raising the pH of a diluted solution to 10.5 and leaving for 5 min before adjusting to the

working pH.[24] Caro's acid (peroxomonosulfate) in the form of the triple salt $2KHSO_5 \cdot K_2SO_4 \cdot KHSO_4$, was supplied by Aldrich. The other peroxide solutions were prepared by stirring the solid peroxide in distilled water for several hours, filtering through a sintered-glass funnel and then standardising iodometrically. The parent acid concentration in the peroxide solutions was determined by potentiometric titration. Solutions of the pure parent acids were prepared in the same way and standardised by potentiometric titration. 4-*tert*-Butylperbenzoic acid was obtained from Interox Chemicals and contained approximately 10% of the parent acid as the only significant impurity. Nonanoic acid was obtained from Sigma Chemicals. The other parent acids were supplied by Aldrich. Samples of pernonanoic and peroctanoic acids were provided by Warwick International Ltd and contained 10 and 25% of the parent acids as impurities respectively. A solution of methyl 4-nitrophenyl sulfide in distilled water was prepared and standardised using the method described previously for aryl alkyl sulfides.[18]

Potentiometric determinations of binding constants

This method has been widely used to measure binding constants of organic acids,[7,14–16] phenols[6] and amines.[4] Most determinations utilised a modified version of the method of Schwartz *et al.*[25] although determinations for acetic acid used the method of Connors.[7] Schwartz *et al.*[25] observed the direct change in pH upon adding weighed amounts of cyclodextrin to a solution containing partially neutralised substrate. Because peracids have a maximum decomposition rate at the pK_a, the equilibration time necessary to allow full dissolution of the cyclodextrin was an unacceptable delay. Instead, we measured the pH changes upon addition of 2 ml cyclodextrin solution to 4 ml peracid (0.8×10^{-3} to 4×10^{-3} mol dm^{-3} depending on solubility) immediately after the peracid had been half neutralised. The pH change upon addition of water alone was subtracted as the blank. All determinations were made at 25 °C and in 0.05 mol dm^{-3} aqueous $NaNO_3$.

Determinations of binding constants by spectrophotometric titration

The binding constants of 4-*tert*-butylbenzoic acid were determined using this procedure.[18,26] Determinations were carried out on a Hewlett Packard HP8451A diode array spectrophotometer at 25 °C in sulfuric acid solution, pH 1.7.

Kinetics

Binding constants for 4-*tert*-butylperbenzoic acid, peroctanoic and pernonanoic acid were determined by finding best fits to both potentiometric and kinetic data using non-linear regression. The reaction system studied was the oxidation of methyl 4-nitrophenyl sulfide by peracids in the presence of α-cyclodextrin at 25 °C in acetate buffer, pH 4.6 and ionic strength 0.025 mol dm^{-3}. Pseudo-first-order rate constants were determined from non-linear regression of the mono exponential decrease in absorbance at 350 nm (due to the methyl 4-nitrophenyl sulfide), using an Applied Photophysics SX-17MV stopped-flow spectrophotometer. Observed second-order rate constants were obtained from the quotient of the pseudo-first-order rate constant and the peracid concentration. The concentration of methyl 4-nitrophenyl sulfide was 1.6×10^{-5} mol dm^{-3} with the peroxide in at least thirtyfold excess. The cyclodextrin concentration ranged from 0.24×10^{-3} to 38×10^{-3} mol dm^{-3}. Details of the method and data analysis are given in the subsequent paper.[22]

Results

Determination of stability constants from potentiometric titration data

Both 1:1 and 2:1 host:guest complexes are possible for the conjugate acid and the conjugate base forms of the compounds studied in this paper, as defined by eqns. (1) – (4), where AH

$$AH + CD \overset{K_{11a}}{\rightleftharpoons} AH,CD \quad (1)$$

$$AH,CD + CD \overset{K_{12a}}{\rightleftharpoons} AH,(CD)_2 \quad (2)$$

$$A + CD \overset{K_{11b}}{\rightleftharpoons} A,CD \quad (3)$$

$$A,CD + CD \overset{K_{12b}}{\rightleftharpoons} A,(CD)_2 \quad (4)$$

and A are the protonated and anionic forms of the guest molecules. The observed change in the pK_a of the guest species with increasing cyclodextrin concentration is a function of the binding steps, as defined by eqn. (5), although not all of the

$$\Delta pK_a = \log \frac{1 + K_{11a}[CD] + K_{11a}K_{12a}[CD]^2}{1 + K_{11b}[CD] + K_{11b}K_{12b}[CD]^2} \quad (5)$$

complexes are necessarily formed for any particular guest molecule.

A detailed treatment of potentiometric titrations is given in ref. 20, and the data treatment therein was followed in this case. The principal correction is for free cyclodextrin concentration, which is dependent on the concentrations of parent and peracid (if present) and the stability of their respective complexes with cyclodextrin. It is important to note that following the convention recently used by us,[20] the free cyclodextrin concentration is actually calculated as the sum of unbound cyclodextrin and that complexed with (*a*) the nitrate anion in the case of the potentiometric studies, and (*b*) acetic acid in the case of the kinetic studies. Both nitrate[11] and acetic acid (this work and ref. 3) have been shown to complex weakly with cyclodextrin.

Fig. 1 shows the relationship between free cyclodextrin concentration and ΔpK_a for peroxomonosulfate, peracetic acid, acetic acid, nonanoic acid and perbenzoic acid. The lines represent the best fit curves according to eqn. (5) using the values given in Table 1. An absence of any rate enhancement for the reaction between peroxomonosulfate and methyl 4-nitrophenyl sulfide[22] confirms the potentiometric data which suggested that this peroxide does not complex with α-cyclodextrin, or that the stability constant of any such complex is below detectable limits for the methodology that we have employed. The potentiometric titration data for acetic acid (Fig. 1) was best described by eqn. (5) in which K_{11b}, K_{12a} and K_{12b} were all set to zero, yielding a best fit value for K_{11a} of 10.6 dm^3 mol^{-1}, in good agreement with the literature values.[3] Analysis of the potentiometric titration data for nonanoic acid, in which both 1:1 and 2:1 inclusion compounds are expected,[16] is difficult since the

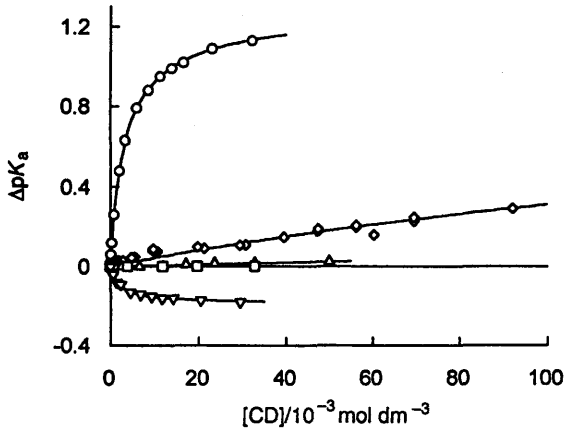


Fig. 1 Effect of α-cyclodextrin on the pK_a of nonanoic acid, circles; acetic acid, diamonds; peracetic acid, triangles; peroxomonosulfate, squares; and perbenzoic acid, inverted triangles

Table 1 Apparent stability constants ($dm^3\ mol^{-1} \pm$ standard deviation) for the α-cyclodextrin complexes of peracids and acids (K_{11a} and K_{12a}) and their anions (K_{11b} and K_{12b})

Compound	K_{11a}	K_{11b}	K_{12a}	K_{12b}
Perbenzoic acid[b]	369 ± 28	569 ± 39	—[a]	—
4-Methylperbenzoic acid[c]	691 ± 35	932 ± 25	10.4 ± 0.9	—
4-*tert*-Butylperbenzoic acid[c]	535 ± 69	857 ± 18	388 ± 79	407 ± 77
Peracetic acid[b]	1.2 ± 0.1	—	—	—
Peroctanoic acid[c]	217 ± 39	570 ± 65	850 ± 339	645 ± 67
Pernonanoic acid[c]	665 ± 196	1614 ± 450	679 ± 70	582 ± 270
Peroxomonosulfate[b]	—	—	—	—
4-*tert*-Butylbenzoic acid[d]	1435 ± 502	64 ± 19	1348 ± 564	522 ± 152
Acetic acid[b]	10.6 ± 0.5	—	—	—
Nonanoic acid[b]	2363 ± 631	1662 ± 720	923 ± 149	68 ± 2

[a] Indicates that the stability constant was not detectable under the conditions employed. [b] Obtained from potentiometric data. [c] Obtained from combined potentiometric and kinetic data. [d] Obtained from combined potentiometric and spectrophotometric data.

values for the calculated parameters are highly dependant on the initial estimates used in the curve fitting analysis. Indeed, unique solutions to eqn. (5) will be impossible to obtain if K_{11a} and K_{11b} or K_{12a} and K_{12b} are very similar. Connors has used a graphical method to overcome this problem[7] and Schwartz has employed a statistical algorithm.[27] In the present work the initial estimates for the four stability constants used in eqn. (5) were interpolated from binding constant data for octanoic and decanoic acid in the literature.[16]

Determination of stability constants from combined potentiometric and kinetic data

For 4-*tert*-butylperbenzoic acid, and the alkyl peracids, peroctanoic acid and pernonanoic acid, 1:1 and 2:1 cyclodextrin–host complexes are observed for both the conjugate acid and base, with the associated analysis problems mentioned above.

A combined potentiometric and kinetic approach was used to elucidate the binding constants of these substrates. Fig. 2 shows the effect of cyclodextrin on (*a*) the observed second-order rate constant, k_{obs}, for the reaction of methyl 4-nitrophenyl sulfide with pernonanoic acid and (*b*) ΔpK_a for pernonanoic acid (the kinetic data are presented in full in the following paper[22]). Best fits were found simultaneously for both potentiometric and kinetic data using global non-linear regression in which the stability constants are common parameters to the two regression equations used [eqns. (5) and (6)]. In eqn. (6),

$$k_{obs} = \frac{k_0 + k_{1obs}[CD] + k_{2obs}[CD]^2}{(1 + K_{s11}[CD] + K_{s11}K_{s12}[CD]^2)} \times 1/(1 + K_{11a}[CD] + K_{11a}K_{12a}[CD]^2) \quad (6)$$

the derivation of which is given in the following paper,[22] K_{11} and K_{12} parameters are stepwise stability constants for the sulfide and peracid, as indicated by the subscript, and k_0, k_{1obs} and k_{2obs} are observed second-, third- and fourth-order rate constants (zero-, first- and second-order in cyclodextrin).

The solid lines in Figs. 2(*a*) and (*b*) are the best fit curves to eqns. (5) and (6) when the assumption is made that 2:1 complexes are formed, whereas the dotted lines are the corresponding fits when the K_{12} parameters are set to zero. A comparison of these curves strongly suggests the presence of 2:1 cyclodextrin–guest complexes. Similar results (not shown) were obtained for peroctanoic acid and 4-*tert*-butylperbenzoic acid. The best fit values, quoted as apparent stability constants in the presence of 0.05 mol dm^{-3} $NaNO_3$, are given in Table 1. It should be noted that the differences in competitive binding by acetate and nitrate for the kinetic and potentiometric data were accounted for in the non-linear regression analysis.

Fig. 3 shows the comparable data for 4-methylperbenzoic acid. In this case the K_{12b} step was either absent or very small and a slightly different procedure was adopted. The value of K_{11a} was calculated from the kinetic data alone and then used as a constant in eqn. (5) to calculate K_{11b} and K_{12a} [omitting the K_{12a} term from eqn. (6) made virtually no difference to the best fit values].

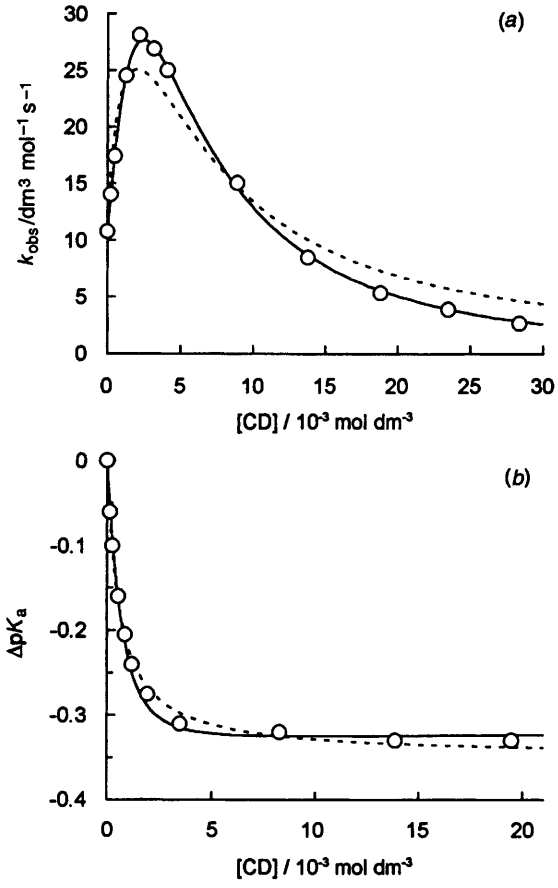


Fig. 2 Effect of α-cyclodextrin on (*a*) the observed second-order rate constant, k_{obs} for the reaction between pernonanoic acid and methyl 4-nitrophenyl sulfide and (*b*) ΔpK_a for pernonanoic acid. The solid lines in (*a*) and (*b*) are best fit curves to eqns. (6) and (5) respectively when the assumption is made that 2:1 host–guest complexes are formed, whereas the dotted lines are the corresponding fits when the K_{12} parameter(s) are set to zero. The reaction between pernonanoic acid (6.78×10^{-4} mol dm^{-3}) and methyl 4-nitrophenyl sulfide (1.6×10^{-5} mol dm^{-3}) was carried out at 25 °C in acetate buffer, pH 4.6, $I = 0.025$ mol dm^{-3}. Potentiometric determinations of stability constants were carried out at 25 °C in 0.05 mol dm^{-3} sodium nitrate using 4.8×10^{-3} mol dm^{-3} pernonanoic acid.

Determination of stability constants from combined potentiometric and spectrophotometric data

Fig. 4 shows the effect of cyclodextrin concentration on the spectrum of 4-*tert*-butylbenzoic acid. The insets show the best

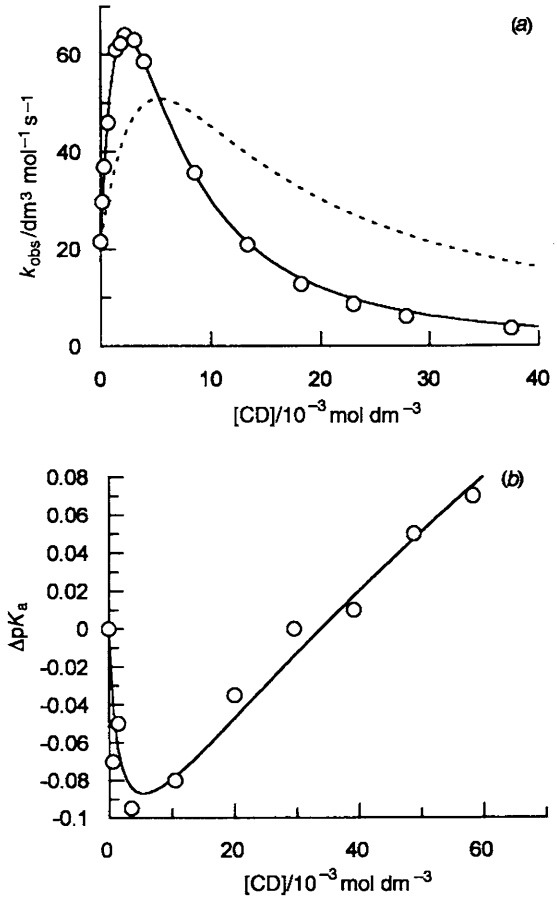


Fig. 3 Effect of α-cyclodextrin on (*a*) the observed second-order rate constant, k_{obs}, for the reaction between 4-methyl perbenzoic acid and methyl 4-nitrophenyl sulfide and (*b*) ΔpK_a for 4-methyl perbenzoic acid. Experimental and fitted curves as in Fig. 2.

fit to a form of eqn. (3) from ref. 18, which describes the spectral changes upon formation of 1:1 and 2:1 cyclodextrin–guest complexes. It is clear from the absorbance changes at 236 nm that there are two binding steps. These give stability constants of 1434 ± 502 and 1348 ± 564 dm^3 mol^{-1} for K_{11a} and K_{12a} respectively. An estimate of the stability constants for the conjugate base was then made from the potentiometric titration data by fixing the values of K_{11a} and K_{12a} in eqn. (5) to those determined by spectrophotometric titration, after adjusting these values to apparent stability constants in 0.05 mol dm^{-3} $NaNO_3$.[20] The resulting best fit curve is shown in an inset to Fig. 4.

Discussion

Peroxomonosulfate

This does not show any appreciable binding with α-cyclodextrin, either for the acid form, or its conjugate base, both of which are charged. Charged groups or molecules, presumably because of unfavourable desolvation energies, do not tend to form strong inclusion complexes.[28] The result for peroxomonosulfate is, therefore, not surprising. On the other hand, large, polarisable, charged molecules, such as tribromide form very stable inclusion compounds with α-cyclodextrin.[29]

1:1 Complexes of benzoic and perbenzoic acids and their anions

The results of our previous study showed that only 1:1 binding is observed for a range of substituted benzoic and perbenzoic acids, and their anions, over the cyclodextrin concentration range studied.[20] In the present study we have also found this to be the case for perbenzoic acid, Fig. 1 and best fit values in Table 1. However, since our previous study we have found that for 4-methylperbenzoic acid, a small systematic error in the original determination of ΔpK_a values led to a situation where the potentiometric data were interpreted as the result of the formation of a weak 1:1 complex between cyclodextrin and the protonated form, only, of the peracid ($K_{11a} = 5.8 \pm 2.2$ dm^3 mol^{-1}).[23] That this is not the case can be seen from Fig. 3. The conjugate acid and base forms of 4-methylperbenzoic acid form 1:1 complexes of similar strength, with the anion binding slightly more strongly, hence the small initial decrease in pH. At higher cyclodextrin concentrations ΔpK_a begins to rise slowly and this is due to the conjugate acid forming a weakly binding 2:1 host–guest complex. Kinetic evidence has been used to confirm these findings for 4-methylperbenzoic acid.[23] 2:1 complexes are also observed for both conjugate acid and base forms of 4-*tert*-butylperbenzoic acid and 4-*tert*-butylbenzoic acid and these are discussed in the next section.

There is good evidence from both NMR[3,30] and crystallographic[31] studies that the carboxylic acid group in benzoic acids is located at the narrow end of the cavity in complexes with α-cyclodextrin. This is not unexpected considering the strongly electron-withdrawing nature of the carboxylic acid group and the fact that dipole–dipole interactions are likely to play a major role in determining the orientation of disubstituted benzenes.[17] Evidence for the orientation of 4-substituted perbenzoic acids, perbenzoates and benzoates comes from the effect on log K_{11a} and K_{11b} of the Hammett σ_p value of the substituents, Fig. 5. The stability constants for 4-substituted perbenzoic acids and perbenzoate anions follow the same trend as the benzoic acids, with increasingly electron-withdrawing substituents destabilising the complex. Following the reasoning of Connors for 4-substituted benzoic acid and benzoate anions,[7] we can infer that both the percarboxylic acid and the percarboxylate moiety are also located at the narrow end of the cavity. The electron withdrawing *p*-substituents destabilise these cyclodextrin complexes by decreasing the favourable dipole–dipole interaction with the positive dipole of the cyclodextrin molecule. Extending the reasoning to the benzoate anions leads to the conclusion that the carboxylate group is located at the wide end of the cavity as Connors has suggested.[7]

Fig. 5 also shows that α-cyclodextrin complexes of benzoic acids are more stable than the corresponding complexes of perbenzoic acids, although because of the more negative Hammett *p*-value for the latter (−0.97 compared to −0.34 for 4-substituted benzoic acids) one might expect similar stability constants for the most highly electron-donating substituents. The low dependence of stability constants for benzoic acids on the electron-withdrawing nature of the substituent group compared to other series' of disubstituted benzenes is possibly a manifestation of increased complex stability due to hydrogen bonding interactions with the primary hydroxy groups of the cyclodextrin. If hydrogen bonding is important then one would expect such interactions between cyclodextrin and the less acidic percarboxylic acid group to be markedly different, thus being one possible reason for the difference in stability of the cyclodextrin complexes with the two moieties. Other reasons include (*a*) the possibility that the benzene ring is slightly displaced from its optimal position within the cavity by the extra length of the percarboxylic acid group compared to the carboxylic acid and (*b*) differences in the electron withdrawing natures of the carboxylic and percarboxylic groups, although this is not quantifiable since no σ_p value, as far as we are aware, has been determined for this substituent.

For the benzoate and perbenzoate anions the linear free energy relationships suggest the latter bind with the percarboxylate group located at the narrow end of the cyclodextrin cavity whilst the former has the carboxylate group located at the wide

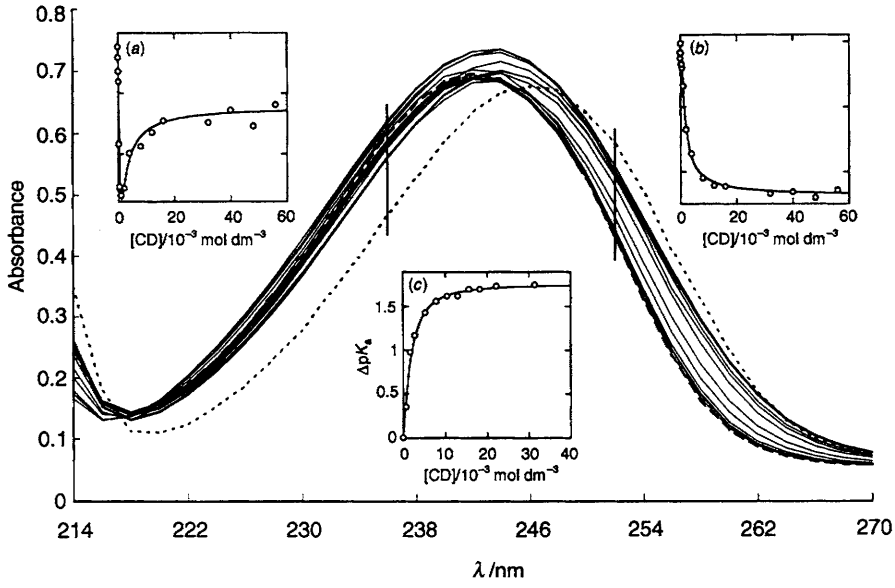


Fig. 4 Effect of α-cyclodextrin concentration on the spectrum of 4-*tert*-butylbenzoic acid (5×10^{-5} mol dm^{-3}) at 25 °C in sulfuric acid solution, pH 1.7. The dotted and dashed lines are, respectively, the calculated spectra of the 1:1 and 2:1 cyclodextrin–guest complexes. Insets (*a*) and (*b*) are examples of the best fits obtained at 236 and 252 nm respectively. Inset (*c*) shows the best fit to the potentiometric data using eqn. (5), in which K_{11a} and K_{12a} were determined by spectrophotometric titration.

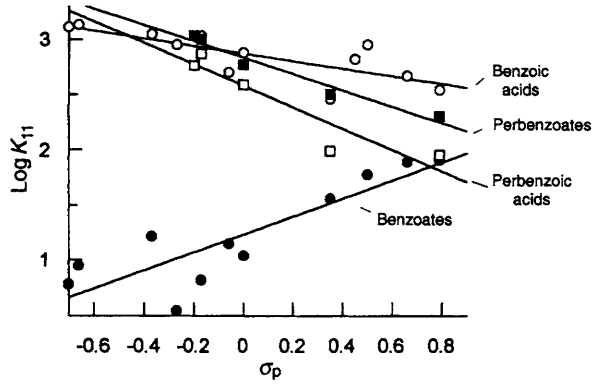


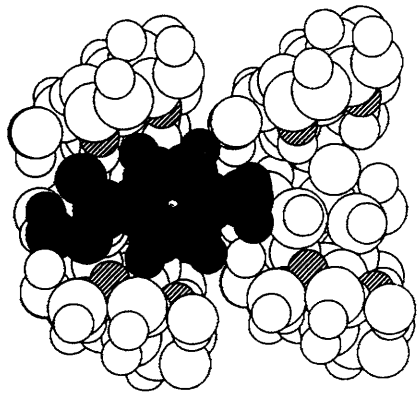
Fig. 5 Effect of electron-withdrawing or -donating 4-substituent groups on log K_{11}. The lines are best fits to linear least squares. Benzoic acid and benzoate data taken from refs. 7 and 20; 4-substituted perbenzoic acid and perbenzoate data from this work and from ref. 20.

end of the cavity. In the case of the percarboxylate group, the additional oxygen atom may allow the charged outer peroxide oxygen to protrude from the cyclodextrin cavity. This results in a favourable charge–dipole interaction with the positive end of the cyclodextrin cavity and allows for partial solvation of the outer peroxidic oxygen. The series formed by substituted benzoates show considerably reduced stability compared to perbenzoates and perbenzoic and benzoic acids, probably, as we have suggested,[17] because charge–dipole repulsion with the negative end of the cyclodextrin dipole (wide end) causes the carboxylate group to be located at some distance from the secondary hydroxy rim, thus pulling the benzene ring from its optimal configuration in the cavity. NMR evidence suggests that the benzene ring in benzoate does not penetrate the cavity as far as benzoic acid (a much smaller down-field shift for the H-5 protons of the cyclodextrin for benzoate compared to benbzoic acid).[30] It is significant that in our model of host–guest binding[17] the molar refractivity of the substituent located at the narrow end of the cyclodextrin cavity was not a significant parameter for carboxylates; this observation is also explained by the carboxylate group being located well outside the cavity.

2:1 Complexes of benzoic and perbenzoic acids and their anions

Although 2:1 complex formation was apparent from the ΔpK_a data for 4-methylperbenzoic acid (Fig. 3) spectrophotometric titration data for 4-*tert*-butylbenzoic acid (Fig. 4) and combined potentiometric and kinetic data for 4-*tert*-butylperbenzoic acid (not shown), we cannot definitely state that it is not occurring for the other peracids and parent acids, even with the aid of the kinetic data for the peracids, especially if the stability constant for the second step is small. Spectrophotometric titration at multiple wavelengths offers a more sensitive technique for elucidating the number of binding steps, as demonstrated by Fig. 4. Results for 4-nitrobenzoic acid, not shown, indicated that only a 1:1 complex was present at cyclodextrin concentrations up to 0.05 mol dm^{-3} cyclodextrin. For most peracid solutions, however, the significant concentration of the parent acid makes this type of analysis unsuitable since parent and peracids have similar spectra.

For 4-methylperbenzoic acid the second binding step, Table 1, is small by comparison with aryl alkyl sulfides,[18] in which the SCH_3 group has a much higher molar refractivity, but is nevertheless significant. Since only a small part of the peracid is likely to penetrate the second cyclodextrin molecule (structure **1**), this is consistent with our idea of substrate promoted dipole–dipole interactions between cyclodextrins as the driving force behind



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2:1 complex of α-cyclodextrin with 4-methyl perbenzoic acid (H-5 and H-3 protons shown cross-hatched)

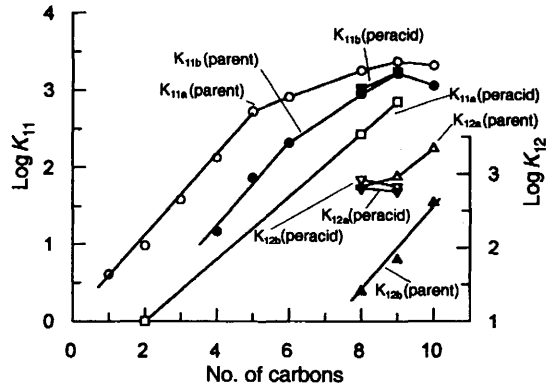

Fig. 6 Dependence of log stability constant on number of carbons for 1:1, left-hand scale, and 2:1, right-hand scale, offset, inclusion compounds of α-cyclodextrin with aliphatic percarboxylic acids and percarboxylates and their respective parent compounds at 25 °C. Lines are guides for the eye. Carboxylic acid and carboxylate data from refs. 16 and 33 (acetic acid, nonanoic acid and nonanoate, this work). Percarboxylic acid and percarboxylate data, this work.

2:1 host–guest complexation.[18] For 4-*tert*-butylbenzoic acid and 4-*tert*-butylperbenzoic acid, the penetrating *tert*-butyl group obviously has a much higher molar refractivity than the methyl (19.62 compared to 5.65[32]) and, consequently the strength of the second binding step approaches that of the first. 2:1 Binding is also observed for the corresponding anions and, in the case of 4-*tert*-butylbenzoate, there is significant cooperative binding of the second cyclodextrin molecule.

Aliphatic percarboxylic acids, their parent acids and their anions

The relationship between alkyl chain length and the log of the 1:1 and 2:1 (where present) stability constants for aliphatic percarboxylic acids, their parent acids and their anions is plotted in Fig. 6 for both the present data, Table 1, and that from the literature.[16,33] Fig. 6 shows that for the 1:1 complexes of the carboxylic acids, log K_{11a}(parent) levels out at a value of about 3.4. The corresponding complexes of the carboxylate anions are less stable with the values of log K_{11b}(parent) displaced by just over one carbon unit to the right, although a similar plateau value is reached. The stability of the 1:1 complexes of the percarboxylate anions are similar to those of the corresponding carboxylate anions whilst the log K_{11a}(peracid) values are displaced by two or three carbon units to the right of log K_{11a}(parent), and the plateau value is not attained for the former. ^{13}C NMR studies of acetic and formic acid complexes of cyclodextrin show that the acids are located at the narrow end of the cavity.[3] The increasing stability with increasing chain length is related to the packing of the chain in the cyclodextrin cavity.[16,33] Hence, we suggest that the pattern of K_{11} values shown in Fig. 6 reflects, to some extent, the degree of protrusion of the acidic or anionic groups out of the narrow end of the cavity. The similarity of K_{11b} values for the carboxylates and percarboxylates reflects a similar orientation of these molecules in the cavity. This is in direct contrast to the situation with the benzoates and perbenzoates where the additional oxygen atom of the latter allows the negatively charged terminal oxygen to protrude out of the narrow end of the cavity but steric hindrance involving the benzene ring[34] prevents the COO^- moiety taking up the same orientation. The greater stability of the α-cyclodextrin complexes of carboxylic acids compared to percarboxylic acids mirrors the situation with benzoic acids and perbenzoic acids and can be explained similarly, in terms of more favourable hydrogen bonding of the parent acids. Likewise, the greater stability of the percarboxylate anions compared with the percarboxylic acids can be interpreted in terms of anion–dipole interactions with the positive (narrow) end of the cyclodextrin dipole.

The plateau in the values of log K_{11} for the 1:1 complexes at the higher chain lengths is due to complete filling of the cavity. Further increases in chain length result in the protrusion of the chain out of the cavity. Eventually there is sufficient alkyl chain length to penetrate a second cyclodextrin molecule and 2:1 complexation ensues. Thus, provided there is little repositioning of the guest with respect to the first cyclodextrin when the second cyclodextrin binds, then the K_{12} values will relate to the degree of protrusion of the acidic or anionic groups out of the narrow end of the cavity in a similar way to the K_{11} values. Fig. 6 shows that the log K_{12a} and K_{12b} values for the peracid and its anion seem to have reached their plateau (note that the log K_{12} scale is offset in Fig. 6) and are therefore not useful for discriminating between modes of binding. The log K_{12b}(parent) values are less than the log K_{12a}(parent) and this confirms the conclusion drawn from the 1:1 stability constants that the carboxylate anion is displaced out of the cyclodextrin cavity compared to the carboxylic acid.

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