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INCLUSION REACTIONS OF SOME PHTHALEIN AND SULPHOPHTHALEIN COMPOUNDS WITH CYCLOMALTO-HEXAOSE AND -HEPTAOSE

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ABSTRACT

Rate and equilibrium constants for the inclusion reactions of cyclomaltohexaose and -heptaose (α- and β-cyclodextrin) with phenolphthalein, *o*-cresolphthalein, Phenol Red, and Cresol Red in aqueous solution have been obtained spectrophotometrically. The structures of the inclusion complexes in solution have been also investigated by ^{1}H- and ^{13}C-n.m.r. spectroscopy. The change in u.v.-visible absorption spectra accompanying the formation of the phenolphthalein–β-cyclodextrin inclusion complex demonstrates that the formation of a lactone ring is induced on inclusion.

INTRODUCTION

Cyclomalto-oligosaccharides (cyclodextrins, CDs) exhibit some of the characteristics of enzyme substrates and drug receptor systems, and give insight into the nature of molecular discrimination and/or molecular recognition in solution.

Static features of CD inclusion complexes such as structure[1] and thermodynamic quantities[2] have been defined, but the driving force for inclusion remains to be explained fully. Hydrogen bonding, van der Waals forces, hydrophobic interaction, the relaxation of the conformational strain in the macrocyclic ring, and the release of the partially hydrogen-bonded water molecules with high energy are involved[3]. The incorporation of functional groups into CDs is one approach to clarifying the role of the various non-bonded interactions involved in inclusion[4].

An understanding of the dynamic aspects is indispensable for clarification of the driving force for inclusion[5]. From this standpoint, we have investigated the relationship between the structures of various types of guest molecules and their inclusion reactions in cyclomaltohexaose (αCD) and cyclomaltoheptaose (βCD). An induced structural interconversion on inclusion has been observed in the phenolphthalein (PP)–βCD system[6]. We now report on the inclusion reaction of PP–CD and related systems, using the temperature-jump method and ^{1}H- and ^{13}C-n.m.r. spectroscopy.

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EXPERIMENTAL

General. — Water was deionised and distilled. Phthalein and sulphophthalein compounds were obtained from Wako. αCD and βCD (Tokyo Kasei) were recrystallised, dried *in vacuo,* and checked for purity by h.p.l.c. with an Erma ERC 7520 RI detector. D_2O (99.9%) and 40% NaOD in D_2O were commercial products. A Hitachi–Horiba pH-meter F7-ss was used to determine pH values. Acid-dissociation constants of the guest molecules were determined spectrophotometrically with a Hitachi recording spectrometer Model 808. The absorption spectra of the acid and the base form of phenolphthalein (PP), *o*-cresolphthalein (CP), Phenol Red (PR), and Cresol Red (CR) at various concentrations of CD showed one set of isosbestic points at constant pH and ionic strength [$I = 0.1$ $mol.dm^{-3}$ (NaCl)]. The formation constants were determined from Hildebrand–Benesi plots. Kinetic measurements were carried out with a Union Giken co-axial-cable temperature-jump apparatus RA-105. The n.m.r. spectra of the inclusion complexes were obtained at room temperature with a JEOL FX-100 or 270 PFT spectrometer. Chemical shifts were given in p.p.m. downfield from the signals for external Me_4Si (^1H) and 1,4-dioxane (^{13}C).

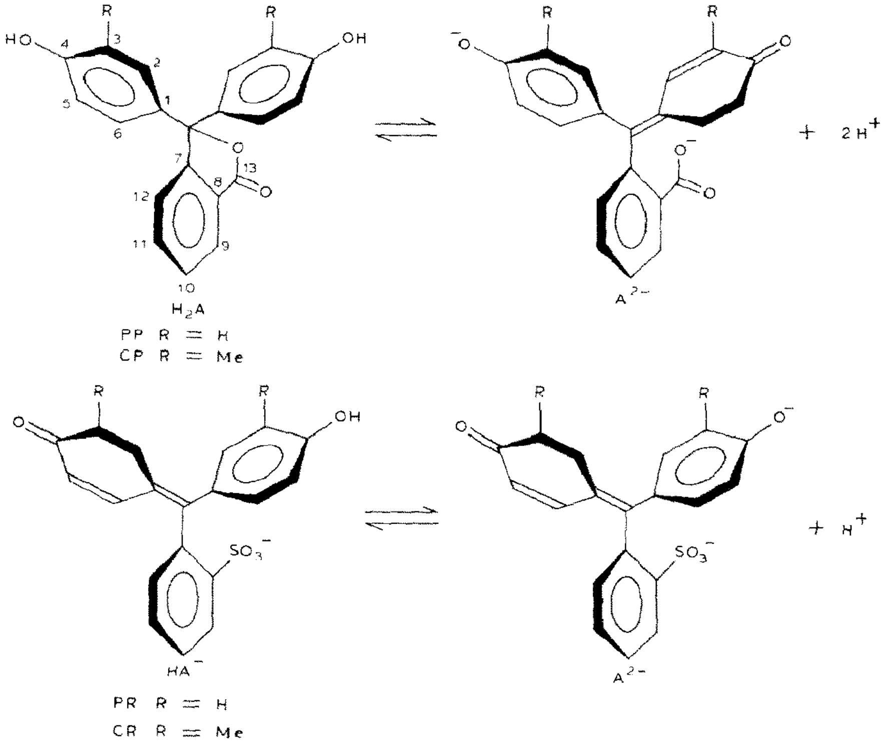


Fig. 1. Acid-dissociation equilibria of phenolphthalein (PP), *o*-cresolphthalein (CP), Phenol Red (PR), and Cresol Red (CR) in aqueous solutions.

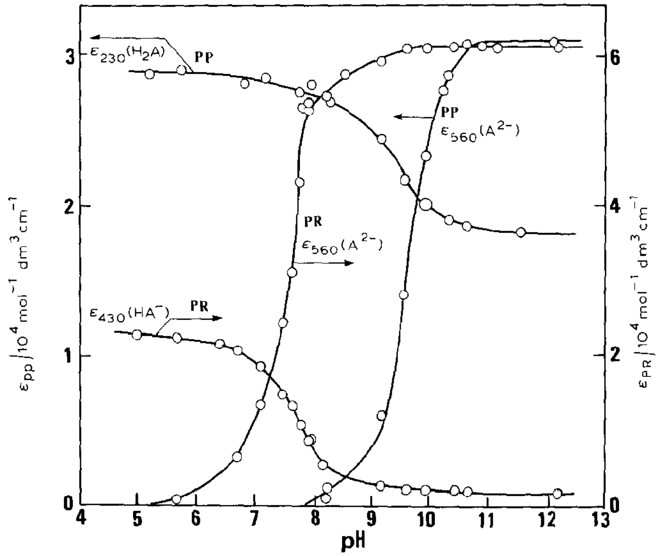


Fig. 2. Dependence of the apparent molar extinction coefficients (ε) of the acid form and the base form of PP and PR on the pH of the solution.

RESULTS AND DISCUSSION

The acid-dissociation equilibria are shown in Fig. 1. The changes in the apparent molar extinction coefficients, ε_{H_2A,HA^-} for the acid form (H_2A for PP and HA^- for PR) and $\varepsilon_{A^{2-}}$ for the base form (A^{2-}) of PP and PR, are shown in Fig. 2.

The acid-dissociation constants, K_a, of such monobasic acids as PR are determined easily using equation *1*,

$$C_t/\Delta A = 1/\Delta\varepsilon + [H^+]/(\Delta\varepsilon \cdot K_a), \qquad 1$$

where C_t and $[H^+]$ denote the total concentration of the guest and the equilibrium concentration of the proton, and ΔA and $\Delta\varepsilon$ the changes in absorbance and the molar extinction coefficient, respectively. A plot of $C_t/\Delta A$ *vs.* $[H^+]$ was linear, thus giving a pK_a value of 7.76 for PR. However, for PP, the plot contained two phases and was curved appreciably. An empirical relationship between $C_t/\Delta A$ and $[H^+]$ can be expressed as equation *2*.

$$C_t/\Delta A = a + b[H^+] + c[H^+]^2 \qquad 2$$

If the acid dissociation of PP takes place in two steps.

$$H_2A \overset{K_{a1}}{\rightleftharpoons} HA^- + H^+ \overset{K_{a2}}{\rightleftharpoons} A^{2-} + 2H^+. \qquad 3$$

The change in absorbance is expressed as

$$\Delta A = C_t \times \frac{\varepsilon_{H_2A}[H^+]^2 + \varepsilon_{HA^-}K_{a1}[H^+] + \varepsilon_{A^{2-}}K_{a1}K_{a2}}{K_{a1}K_{a2} + K_{a1}[H^+] + [H^+]^2}, \qquad 4$$

where the values of ε_{H_2A} and ε_{HA^-} are assumed to be 0 at λ_{max} 560 nm, and the value of $\varepsilon_{A^{2-}}$ is obtained experimentally to be 3.1×10^4 $mol^{-1}.dm^3.cm^{-1}$ at λ_{max} 560 nm. The values of pKa1, pK_{a2}, and $\varepsilon_{A^{2-}}$ of PP were shown to be 9.22, 9.51, and 3.21×10^4 $mol^{-1}.dm^3.cm^{-1}$, respectively, by curve fitting using the damping Gauss–Newton method {final SS = Σ [ΔA (obs) − ΔA (calc)]^2 = 1.734×10^{-4}}. The apparent pK_a value calculated as 9.37 (pK_{a1} + pK_{a2})/2 coincides well with the values evaluated from the inflection point of the plot in Fig. 2 [pK_a (apparent) = 9.34 at λ 230 nm and 9.61 at λ 560 nm]. The pK_a values thus obtained in other systems are summarised in Table I.

The formation of 1:1 inclusion complexes of PP, PR, CP, and CR with CD is confirmed by the presence of isosbestic points in the u.v.-visible spectral change. Fig. 3 shows the spectral change of PR on addition of an excess of βCD (the changes in other concentrations are omitted for clarity). The equilibrium for the inclusion reaction in the acid region is expressed as

$$HA^- + \beta CD \underset{K_d'}{\rightleftharpoons} HA^-\text{–}\beta CD \qquad 5$$

and that in the alkaline region as

$$A^{2-} + \beta CD \underset{K_d}{\rightleftharpoons} A^{2-}\text{–}\beta CD, \qquad 6$$

TABLE I

DISSOCIATION CONSTANTS OF THE INCLUSION COMPLEXES OF PHTHALEIN AND SULPHOPHTHALEIN COMPOUNDS WITH CDS

Guest	pK_a	αCD $K_d(K_d')$ ($mol.dm^{-3}$)	βCD $K_d(K_d')$ ($mol.dm^{-3}$)
PP(H_2A)	9.85	[a]	2.73×10^{-5}
PP(A^{2-})		1.86×10^{-3}	7.18×10^{-5}
PR(HA^-)	7.76	2.39×10^{-3}	1.30×10^{-3}
PR(A^{2-})		1.85×10^{-1}	4.35×10^{-3}
CP(H_2A)	9.93	N.I.[b]	4.59×10^{-3}
CP(A^{2-})		N.I.	1.56×10^{-3}
CR(HA^-)	8.25	N.I.	[a]
CR(A^{2-})		N.I.	[a]

[a] The spectral change is very small. [b] No inclusion.

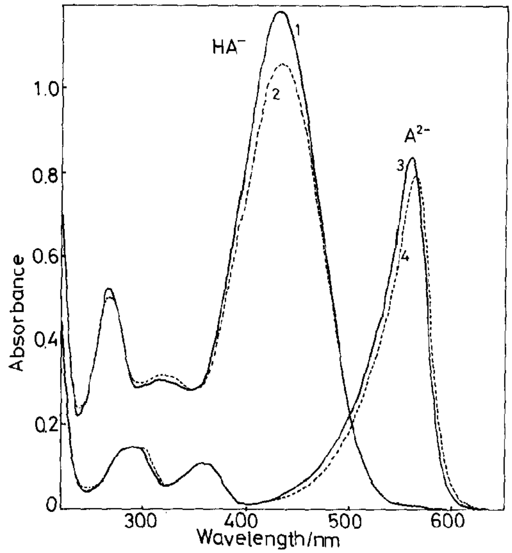


Fig. 3. Absorption spectra of the acid (HA^-) and base (A^{2-}) forms of PR (——) and the PR–βCD complex (----): [HA^-] 5.05×10^{-5}, [A^{2-}] 1.35×10^{-5}; [βCD] 0 (1), 5.43×10^{-3} (2), 0 (3), and 5.43×10^{-3} (4) mol.dm^{-3}.

where K_d = [HA^-][βCD]/HA^-–βCD] and K_d' = [A^{2-}][βCD]/[A^{2-}–βCD]. The decreases in molar extinction coefficients and the red shift, particularly in the A^{2-}–βCD system, are observed as shown in Fig. 3. These changes become much smaller in the αCD system due to the smaller size of the cavity. Furthermore, in the CR–βCD system, the spectral change is too small to determine the dissociation constant and no inclusion was observed in the CR–αCD system. The presence of the Me substituent in the phenol moiety of CR markedly decreases the stability of the CR–CD inclusion complexes.

On the other hand, a marked spectral change was observed in the systems between βCD and the base forms (A^{2-}) of PP and CP. Fig. 4 shows the u.v.-visible spectra of the base form (A^{2-}) with αCD and βCD.

The absorption peaks due to the A^{2-} species of PP disappeared completely in the presence of an excess of βCD even in the alkaline region. In the CP(A^{2-})–βCD system, this spectral change is small owing to the steric hindrance by the Me substituent as observed in the CR(H_2A^-, A^{2-})–βCD systems. Such marked changes in the absorption spectra were not observed in H_2A(PP)–βCD, H_2A(PP)–αCD, and A^{2-}(PP)–αCD systems, and also in sulphophthalein–αCD and –βCD systems. Fig. 5 shows the dependency of the spectra of A^{2-} of PP on [βCD], and the presence of the isosbestic point at 270 nm [*cf.* 240 nm in the acid dissociation equilibrium of PP (equation *3*)]. The peaks at 375 and 560 nm due to the A^{2-} species are suppressed completely and that at ~290 nm is decreased. New peaks at 237(s) and 250 nm (s, sh) are observed which are quite different from the peak at 232(s) due to the H_2A species of PP. The molar extinction coefficients (ε) at the

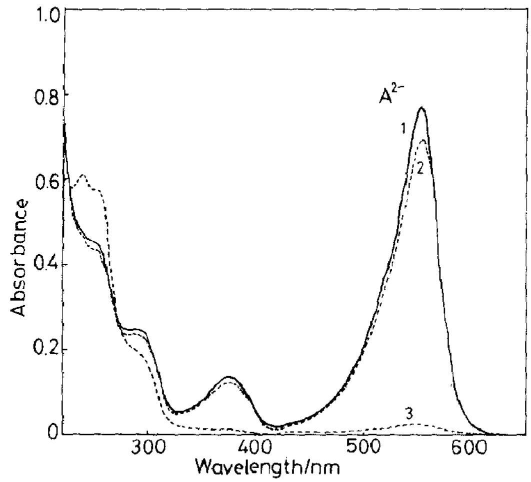


Fig. 4. Absorption spectra of the base form (A^{2-}) of PP (1), PP(A^{2-})-αCD (2), and PP(A^{2-})-βCD (3): [A^{2-}] 2.99×10^{-5}; [αCD] 0 (1), 7.54×10^{-3} (2); [βCD] 5.43×10^{-3} (3) mol.dm^{-3}.

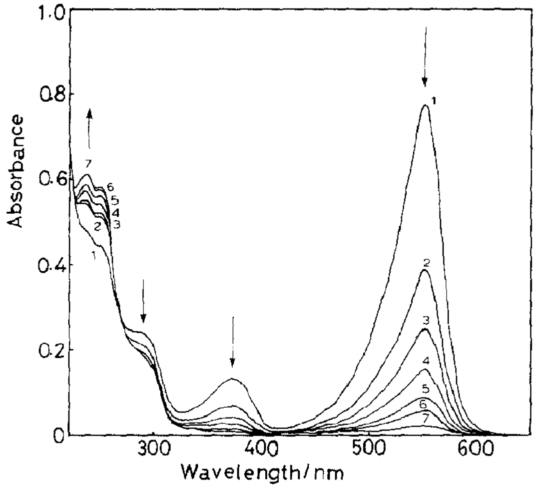


Fig. 5. Changes in absorption spectra of the A^{2-} species of PP upon addition of a large excess of βCD at pH 10.75, I = 0.1 mol.dm^{-3}, and 25°: [βCD] 0 (1), 7.60×10^{-5} (2), 1.52×10^{-4} (3), 3.26×10^{-4} (4), 6.52×10^{-4} (5), 1.09×10^{-3} (6), 5.43×10^{-3} (7) mol.dm^{-3}.

wavelength of 237(s), 250(s, sh), and 290 nm (w) for the A^{2-}(PP)-βCD complex are 2.04×10^4, 1.94×10^4, and 6.15×10^3 mol^{-1}.dm^3.cm^{-1}, respectively, and those of 232(s), 275(w), and 283 nm (w, sh) for the H_2A species of PP 2.52×10^4, 3.34×10^3, and 3.01×10^3 mol^{-1}.dm^3.cm^{-1}, respectively.

The relationship between the inclusion process of A^{2-}-species of PP by βCD and the proton-dissociation equilibria of PP in equation *3* is now considered. Fig. 6 shows the Kolthoff diagram for the proton dissociation of PP[7]. The univalent anion of PP (**3**) is colourless, but its general form is often believed to be **7**. Structure **2** is

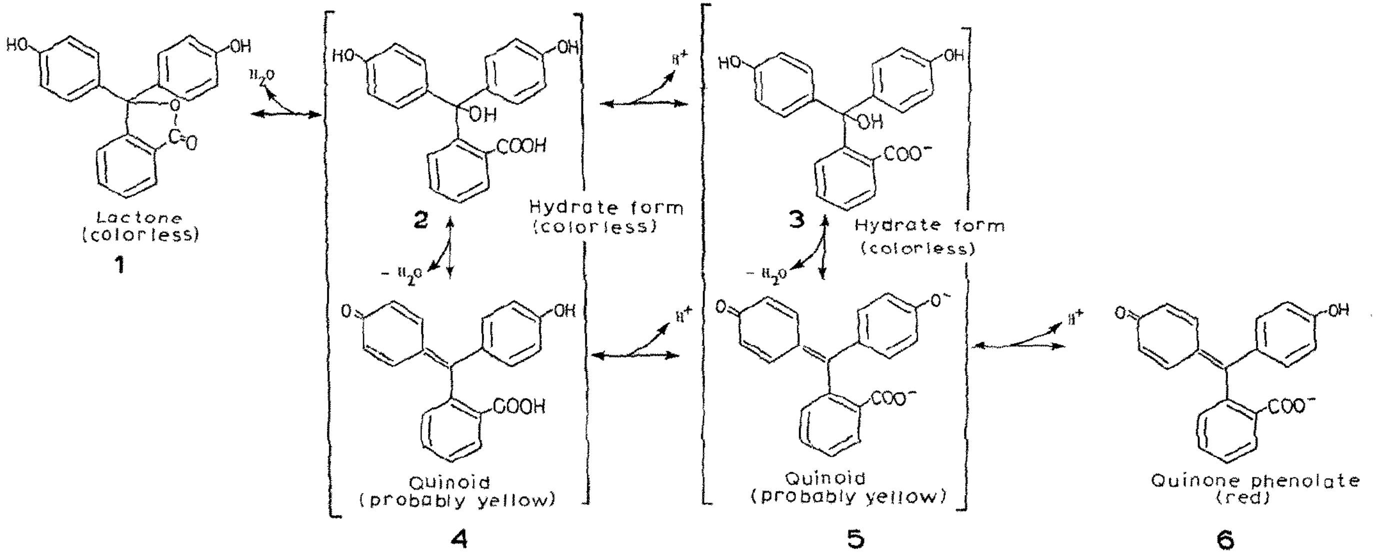
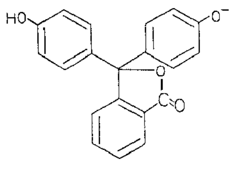


Fig. 6. Kolthoff diagram for the acid-dissociation equilibria (**1** → **6**) of phenolphthalein. The species denoted in square brackets have not been detected spectrophotometrically.



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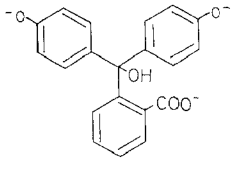

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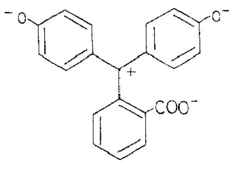


9

an ordinary carboxylic acid. Such acids as benzoic acid have dissociation constants of the order of magnitude 10^{-5} or larger. In an aqueous solution of PP, the concentration of the lactone form **1** is ~10,000 times greater than that of the acid **2**[8]. Furthermore, the concentration of the quinoid forms **4** and **5** must be exceedingly small compared with that of **1** because the solution is colourless[7]. Addition of HO^- displaces the equilibrium of **2** and **3** through **5** to the quinone carboxylate **6**. The equilibrium relationships for PP are represented by the following expressions (the decolourising action of an excess of alkali can be explained only by assuming that little **3** is converted into **8**):

$$\mathbf{1} \rightleftharpoons \mathbf{3} + H^+ \ (K_{a1} = 1.15 \times 10^{-9}) \tag{7}$$

$$\mathbf{3} \rightleftharpoons \mathbf{6} + H^+ \ (K_{a2} = 2.8 \times 10^{-10}) \tag{8}$$

The proton-dissociation processes which control the colour change of PP and other phthaleins are complex. The coloured ion of PP would be **9**, which contains a carbonium ion[7]. Therefore, marked decolourisation of the A^{2-} species of PP by inclusion into βCD coupled with the proton dissociation (Fig. 6) is extremely complex. The disappearance of the absorption peaks characteristic of the A^{2-} species of PP demonstrates that, in the cavity of βCD, **6** is converted into **1, 2, 3**, or **7**. The spectral properties (λ_{max} *etc.*) of the βCD inclusion complex of A^{2-}(PP) are quite different from those of the H_2A species of PP as mentioned above, although, in solution, it is colourless. On the basis of spectrophotometric data, it is proposed that the structure of PP included in the βCD cavity is **3** (or **7**). Further study is required before a choice can be made.

The signal amplitudes sufficient to determine the rate constants for inclusion were obtained only for the PP(A^{2-})–βCD and the CP(A^{2-})–βCD systems. The kinetic data were obtained under pseudo-first-order conditions using a large excess of βCD. The rate of inclusion was followed at λ_{max} of the inclusion complex. The inclusion reaction of A^{2-} of PP with βCD is

$$A^{2-} + \beta CD \underset{k_-}{\overset{k_+}{\rightleftharpoons}} HA^-\text{–}\beta CD \tag{9}$$

TABLE II

RATE CONSTANTS FOR THE INCLUSION REACTIONS OF PHTHALEIN COMPOUNDS WITH βCD

Guest molecule	$k_+ (mol^{-1}.dm^3.s^{-1})$	$k_- (s^{-1})$
PP(A^{2-})	7.5×10^6	1.5×10^3
CP(A^{2-})	1.1×10^7	5.0×10^4

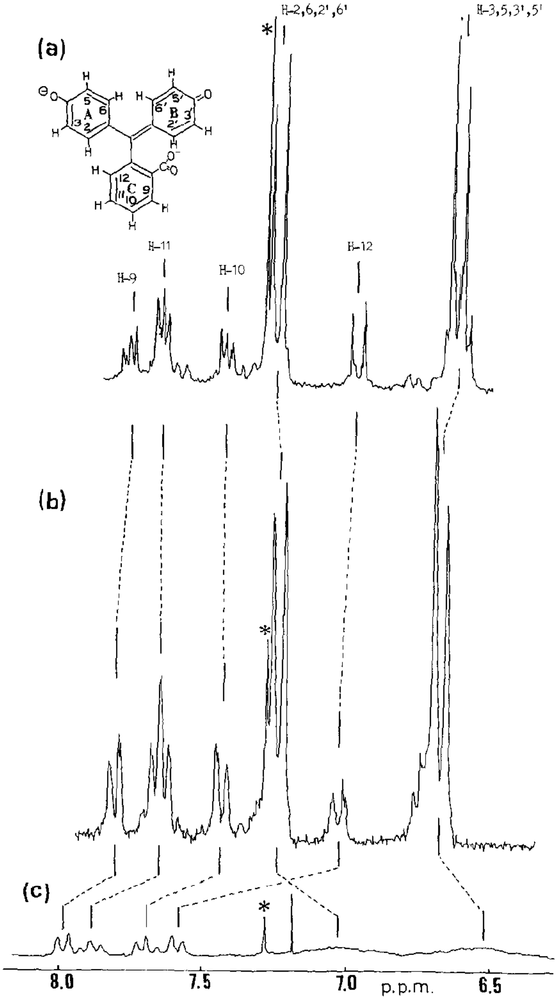


Fig. 7. ^{1}H-N.m.r. spectra of PP in the absence and the presence of αCD and βCD in D_2O (pD 11.5): (a) 5.95 mg of PP in 0.4 mL of D_2O, (b) 5.3 mg of PP and 20.60 mg of αCD in 0.4 mL of D_2O, (c) 5.45 mg of PP and 15.4 mg of βCD in 0.4 mL of D_2O. No change in chemical shift of each resonance was observed at pD 13.56.

The observed relaxation time, τ, for the inclusion reaction (equation *9*) can be expressed as

$$\tau^{-1} = k_+[\beta\text{CD}] + k_- \qquad 10$$

The plot of equation *10* was linear with a slope k_+ and an intercept k_-. The values of the rate constants, k_+ and k_-, are summarised in Table II. The formation rate constant, k_+, was almost the same order of magnitude for the PP–βCD and CP–βCD systems. The destabilisation effects reflected in the value of K_d (Table I) due to the steric hindrance of the Me substituent are also reflected clearly in the value of the dissociation rate constant. For the CP–βCD system, k_- is about thirty times larger than that for the PP–βCD system. The value of k_+ would not correspond to the one for the simple inclusion process with βCD, but to the one for the structural interconversion process from A^{2-} to HA^- accompanying the ring closure to form a lactone ring.

Fig. 7 shows the ^{1}H-n.m.r. spectra of the base form, A^{2-}, of PP in the absence and the presence of αCD and βCD in D_2O (pD 11.32). The assignments shown in Fig. 7a are based on coupling constants, peak heights, substituents effect of OH and COOH, and the additivity rule. Since π-electron conjugations in A^{2-} of PP spread over the rings A (phenol) and B (quinoid) through the central carbon atom, the ^{1}H-n.m.r. spectra show the equivalence between these rings. In the αCD system (Fig. 7b), the resonances of H-10 and H-11 in ring C, and H-2,6 and H-2′,6′ in rings A and B, show almost no shift. A slight downfield shift is observed for the

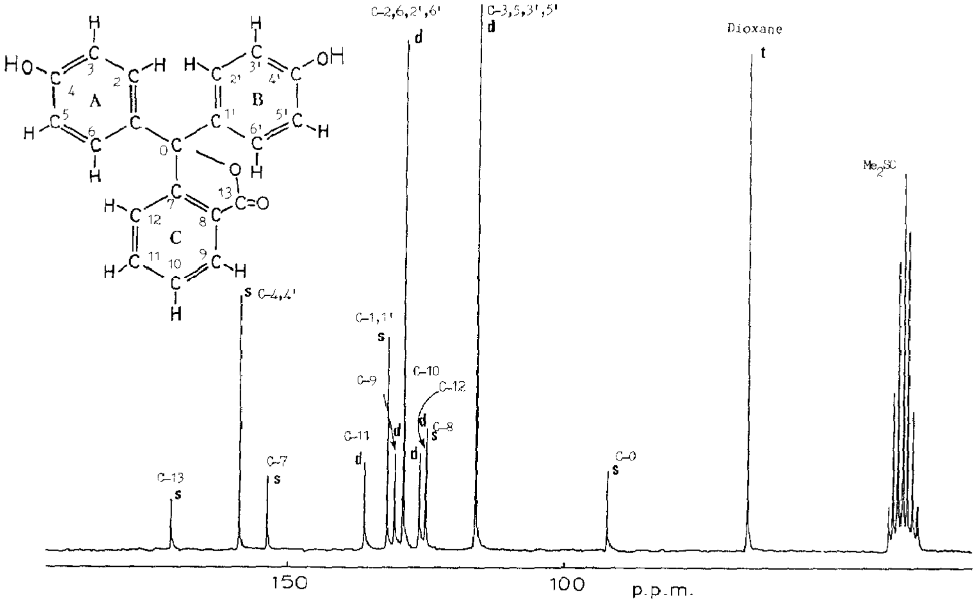
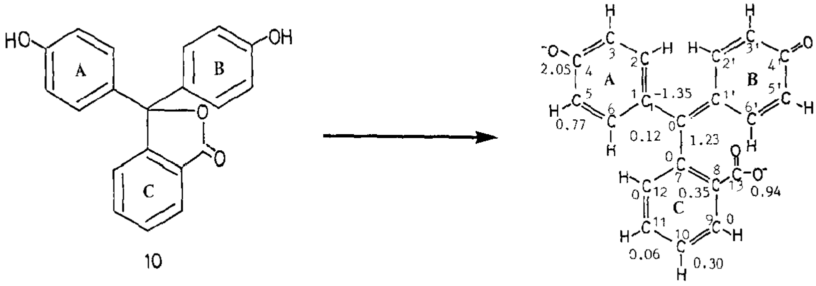


Fig. 8. ^{13}C-N.m.r. spectrum of the H_2A species of PP (20 mg in 0.4 mL of PP in D_2O–Me_2SO).



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resonances of H-3,5, H-3′,5′, H-9, and H-12. The larger downfield shifts of H-3,5 and H-3′,5′ suggest that αCD interacts preferentially with the phenol and/or the quinoid moieties of PP. The dramatic changes in the ^{1}H-n.m.r. spectra were observed in the βCD system (Fig. 7c). The remarkable broadening and the upfield shifts observed in the resonances of the phenol (quinoid) protons, H-2,6 and H-3,5 (H-2′,6′ and H-3′,5′), suggest that βCD also interacts regioselectively with the phenol and/or the quinoid moiety. On the other hand, the downfield shifts of the resonances of H-9/12 in the ring C resemble those observed in the protonation reaction, **6** → **7**. This fact suggests that the preferential binding of the phenol moiety of the A^{2-} of PP with βCD causes protonation and subsequent lactonisation.

Fig. 8 shows the ^{13}C-n.m.r. spectra of the H_2A species of PP in Me_2SO–D_2O. The assignments of 12 peaks in Fig. 8 were based on the proton coupling, the substituent effects, the additivity rule, and the proton off-resonance irradiation. The observed chemical shifts for the carbon atoms in rings A–C coincide well with the theoretical values. On addition of a slight excess of NaOD to the H_2A solution, the signals for the central carbon C-0 and C-1,4,5 in rings A and B, the carboxylate carbon C-13, and C-8,9 in ring C are shifted appreciably downfield or upfield (C-1 only), whereas those for C-7 and C-10/12 in ring C are shifted little (formulae **10** and **11**), suggesting that deprotonation and structural change (**10** → **11** + 2 H^+) occur at the same time.

Fig. 9 shows the ^{13}C-n.m.r. spectra of the base form, A^{2-}, of PP in the absence and the presence of αCD and βCD in D_2O (pD = 11.32). The formation of the inclusion complex leads to an appreciable downfield shift in the resonance of C-1,13 and an upfield shift in those of C-2/6 (2′/6′). The upfield shift of the resonance of C-4 is large, suggesting that protonation participates in formation of the inclusion complex. The large upfield shift of the resonance of C-0 demonstrates that lactonisation is involved in the formation of the inclusion complex. The chemical shifts of the resonances of C-7,9,11,12 in ring C change little. Remarkable broadening of the resonances of C-2,3,5,6 (C-2′,3′,5′,6′) was observed (peaks marked ● in Figs. 9b and 9c). The equivalence between rings A and B in the ^{1}H-n.m.r. spectra was not observed in the ^{13}C-n.m.r. spectra. A more detailed ^{13}C-n.m.r. study will be reported elsewhere[9]. The values of upfield shifts for the ^{13}C

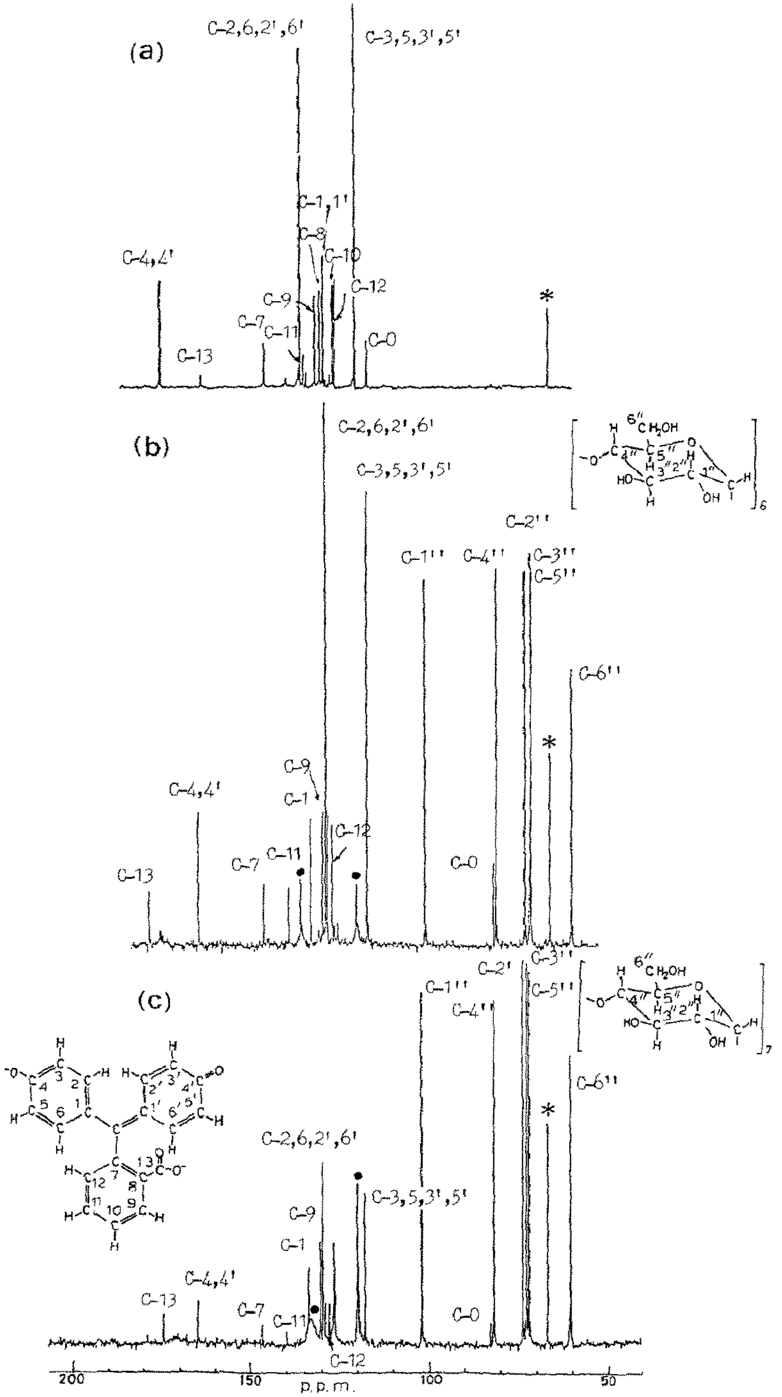
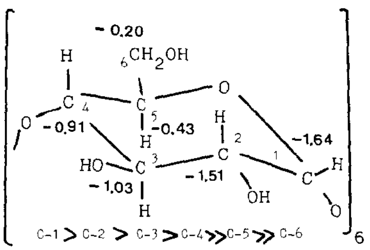
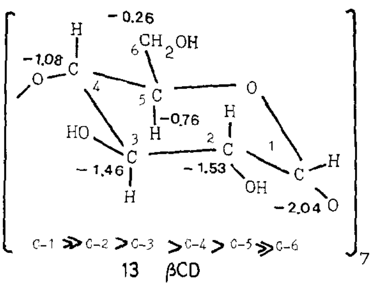


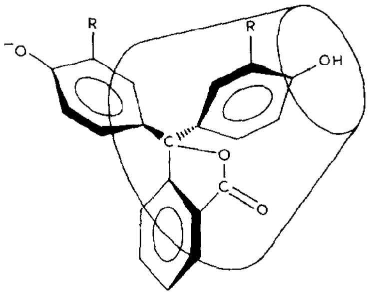
Fig. 9. ^{13}C-N.m.r. spectra of PP in the absence (a) and the presence of αCD (b) and βCD (c) in D_2O (pD 11.5).



12 αCD



13 βCD



14

resonances of αCD and βCD in the presence of PP(A^{2-}) are shown in **12** and **13**. This order has been observed with smaller guest molecules such as *p*-nitrophenol[10]. The order of upfield shifts clearly indicates that the inclusion into the cavity of the CD takes place at the side of the secondary hydroxyl group. The structure **14** is proposed for the PP(A^{2-})-βCD inclusion complex in solution on the basis of the u.v.-visible, ^{1}H-, and ^{13}C-n.m.r. spectral data, and CPK molecular models.

The phenol moiety (ring A) of PP preferentially enters into the cavity of βCD. This inclusion induces the protonation at ring A and lactonisation (**6** → **7**). X-Ray crystallographic study and MM2 calculations on the inclusion are now in progress.

REFERENCES

1 P. C. Manor and W. Saenger, *J. Am. Chem. Soc.*, 96 (1974) 3630–3639; W. Saenger, N. Noltemeyer, P. C. Manor, B. Hinerty, and B. Klar, *Bioorg. Chem.*, 5 (1976) 187–195; K. Lindner and W. Saenger, *Angew. Chem. Int. Ed. Engl.*, 17 (1978) 694–695; K. Linder and W. Saenger, *Biochem. Biophys. Res. Commun.*, 92 (1980) 933–938; K. Harata, *Bull. Chem. Soc. Jpn.*, 55 (1982) 1367–1371; C. Betzel, W. Saenger, B. E. Hingerty, and G. M. Brown, *J. Am. Chem. Soc.*, 106 (1984) 7545–7557; K. Harata, *Chem. Lett.*, (1984) 641–644, 1641–1644; W. Saenger, *Isr. J. Chem.*, 25 (1985) 43–50; K. Harata, K. Uekama, M. Otagiri, F. Hirayama, and Y. Ohtani, *Bull. Chem. Soc. Jpn.*, 58 (1985) 1234–1238; D. R. Alston, A. M. Z. Slawin, J. F. Stoddart, and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, (1985) 1602–1604; V. Zabel, W. Saenger, and S. A. Mason, *J. Am. Chem. Soc.*, 108 (1986) 3664–3673; S. Kamitori, K. Hirotsu, and T. Higuchi, *ibid.*, 109 (1987) 2409–2414; S. Kamitori, K. Hirotsu, T. Higuchi, K. Fujita, H. Yamamura, T. Imoto, and I. Tabushi, *J. Chem. Soc., Perkin Trans. 2*, (1987) 7–14; J. A. Hamilton and L. Chen, *J. Am. Chem. Soc.*, 110 (1988) 4379–4391; 5833–5841; K. Harata, *Bull. Chem. Soc. Jpn.*, 61 (1988) 1939–1944.

2 E. A. Lewis and L. D. Hansen, *J. Chem. Soc., Perkin Trans. 2,* (1973) 2081–2085; M. Otagiri, T. Miyaji, K. Uekama, and K. Ikeda, *Chem. Pharm. Bull.*, 24 (1976) 1146–1154; R. I. Gelb, L. M. Schwartz, R. F. Johnson, and D. A. Laufer, *J. Am. Chem. Soc.*, 101 (1979) 1869–1874; R. I. Gelb, L. M. Schwartz, N. Cardelion, H. S. Fuheman, R. F. Johnson, and D. A. Laufer, *ibid.*, 103 (1981) 1750–1757; W. C. Chromwell, K. Bystron, and M. R. Eftink, *J. Phys. Chem.*, 89 (1985) 326–332; S. Takagi, T. Kimura, and M. Maeda, *Thermochim. Acta,* 88 (1985) 247–254.

3 K. Harata, *Bull. Chem. Soc. Jpn.*, 49 (1976) 2066–2072; R. J. Bergeron, M. A. Channing, G. J. Gilbeily, and D. M. Pillor, *J. Am. Chem. Soc.*, 99 (1977) 5146–5151; I. Tabushi, Y. Kiyosuke, T. Sugimoto, and K. Yamamura, *ibid.*, 100 (1978) 916–919; Y. Matsui, *Bull. Chem. Soc. Jpn.*, 55 (1982) 1246–1249; Y. Matsui, T. Nishioka, and T. Fujita, *Top. Curr. Chem.*, 128 (1985) 61–89; M. Prabhakaran and S. C. Harvey, *Biopolymers,* 26 (1987) 1087–1096; J. E. H. Koehler, W. Saenger, and W. F. van Gunsterer, *Eur. Biophys. J.*, 15 (1987) 197–210, 211–224.

4 D. W. Griffiths and M. L. Bender, *Adv. Catal.*, 23 (1973) 209–261; I. Tabushi, K. Shimokawa, H. Shirakata, and K. Fujita, *J. Am. Chem. Soc.*, 98 (1976) 7855–7856; J. Emert and R. Breslow, *ibid.*, 97 (1975) 670–672; R. Breslow, *Acc. Chem. Res.*, 13 (1980) 170–177; I. Tabushi, *ibid.*, 15 (1982) 66–72; C. Sirlin, *Bull. Soc. Chim. Fr.*, (1984) 5–40.

5 F. Cramer, W. Saenger, and H.-Ch. Spatz, *J. Am. Chem. Soc.*, 89 (1967) 14–20; J. P. Behr and J.-M. Lehn, *ibid.*, 98 (1976) 1743–1747; R. P. Rohrbach, L. J. Rodrigues, E. M. Eyring, and J. F. Wojcik, *J. Phys. Chem.*, 81 (1977) 944–948; R. J. Bergeron and M. A. Channing, *J. Am. Chem. Soc.*, 101 (1979) 2511–2516; N. Yoshida and M. Fujimoto, *Chem. Lett.*, (1980) 231–234, 1377–1380; N. Yoshida and M. Fujimoto, *Bull. Chem. Soc. Jpn.*, 55 (1982) 1039–1045; N. J. Turro, T. Okubo, and C.-J. Chung, *J. Am. Chem. Soc.*, 104 (1982) 1789–1794; N. Yoshida, A. Seiyama, and M. Fujimoto, *Chem. Lett.*, (1984) 703–706; A. Hersey and B. H. Robinson, *J. Chem. Soc., Faraday Trans. 1,* 80 (1984) 2039–2052; R. J. Klark, J. H. Coates, and S. F. Lincoln, *Carbohydr. Res.*, 127 (1984) 181–191; A. Seiyama, N. Yoshida, and M. Fujimoto, *J. Inclusion Phenom.*, 2 (1984) 765–773; N. Yoshida, A. Seiyama, and M. Fujimoto, *ibid.*, 2 (1984) 573–581; N. Yoshida and M. Fujimoto, *J. Chem. Res.*, (1985) 224–225; A. Seiyama, N. Yoshida, and M. Fujimoto, *Chem. Lett.*, (1985) 1013–1016; A. Örstan and J. F. Wojcik, *Carbohydr. Res.*, 143 (1985) 43–50; N. Yoshida and M. Fujimoto, *J. Phys. Chem.*, 91 (1987) 6691–6695; H. Monzen, N. Yoshida, and M. Fujimoto, *Chem. Lett.*, (1988) 1129–1132; N. Yoshida, H. Monzen, and M. Fujimoto, *ibid.*, (1988) 1971–1974.

6 N. Ise, T. Okubo, and M. Kuroda, *Annu. Meet. Soc. High Polym., Japan, 23rd,* 1974, 5A12; N. Yoshida, T. Shirai, and M. Fujimoto, *Annu. Meet. Coord. Chem., Japan, 34th,* 1984, 3C06; K. Taguchi, *J. Am. Chem. Soc.*, 108 (1986) 2705–2709.

7 I. M. Kolthoff and C. Rosenbaum, *Acid-Base Indicators,* Macmillan, New York, 1937.

8 I. M. Kolthoff, *J. Phys. Chem.*, 35 (1931) 1433–1447.

9 N. Yoshida and M. Fujimoto, *J. Chem. Soc., Perkin Trans. 2,* (1989).

10 R. Bergeron and M. A. Channing, *Bioorg. Chem.*, 5 (1976) 437–439.