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Influence of Fluorinated Alcohols on Cyclodextrin : Pyrene Complexation

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Abstract. An investigation of the effect of fluorinated alcohols on complexation between pyrene and β- and γ-cyclodextrin (CD) in aqueous solution is reported. Using fluorescence spectrophotometric analysis, pyrene I/III vibronic band ratios were monitored upon the addition of CD, both in the absence and presence of fluorinated alcohols, as well as in the presence of their nonfluorinated alcohol analogs. The fluorinated alcohols studied were 2,2,2-trifluoroethanol and 2,2,3,3,3-pentafluoro-1-propanol. In aqueous solution, the alcohols were found to have no effect on the pyreneI/III ratio in the absence of CD, but a strong effect when CD was present. For β-CD, the stoichiometry of the CD/pyrene complex was found to be predominantly 2 : 1, whereas for γ-CD it was 1 : 1. Apparent complexation equilibrium constants for the CD/pyrene complexes in the absence and presence of the alcohols were calculated by use of nonlinear regression analysis. Interactions between the alcohols and CDs were also investigated using ^{1}H and ^{19}F NMR techniques.

Key words: Cyclodextrin inclusion, pyrene, fluorinated alcohols, fluorescence, nuclear magnetic resonance.

1. Introduction

Cyclodextrins (CDs) have been found to form inclusion complexes with many different types of guest molecules [1]. Much of the original interest in CDs was sparked by their potential use as enzyme mimics. With the research that followed, further applications of the complexation behavior of CDs have been developed, including drug encapsulation and chromatographic separations.

Pyrene is a widely-used fluorescent probe which has been found to undergo relatively strong complexation with CDs. Various aspects of the complexation of pyrene with both β- and γ-CD have been investigated by many different researchers [2–8]. Pyrene is particularly amenable to CD complexation studies because of the sensitivity of its spectrum to changes in the microenvironment of the molecule. The fluorescence emission spectrum of pyrene has five distinct vibronic bands; the relative intensities of the I and III bands have been used as measures of the polarity of the microenvironment [9, 10]. Upon complexation, the CD cavity provides the guest molecule with a relatively non-polar environment compared to bulk aqueous solution, causing a measurable decrease in the ratio of the intensities of the I and III

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bands. In previous studies, the pyrene I/III band ratio has been successfully used as an indicator of the degree of complexation with CDs [5, 6].

Ternary systems containing CD, guest, and cosolvent have been widely investigated to obtain information on the effects of third components on the CD/guest systems [11–19]. In the systems containing alcohol, the apparent association constants are dramatically enhanced suggesting a strong interaction with the binary system. Nelson *et al.* [18, 19] have reported the formation of strong ternary complexes between CDs and pyrene in the presence of alcohols of different size and polarity. The role of the size and geometry of the alcohol was effectively demonstrated by use of CD/pyrene model complexes [20, 21]. It has been noted that the strength of the ternary complexes is based on the ability of the third component to aid in the shielding of the fluorophor from solution interactions. In some instances, halogenated alcohols have been used in room temperature phosphorescence studies to introduce the heavy atom as a constituent of the third component modifier [22, 23]. The observed increased shielding in the presence of halogenated alcohols together with enhanced formation constants provided a better environment for room temperature phosphorescence to occur. It should be noted, however, that the success of the experiment is dependent upon the selection of a heavy atom (e.g. 2-bromoethanol) which will effectively promote enhanced intersystem crossing. As a result of these initial studies, the present work examines the influence of fluorinated alcohols as part of our continuing investigation of CD/pyrene/cosolvent interactions.

Fluorinated alcohols are also of interest as third components in CD/pyrene complexes because of their slightly larger volume as compared to nonfluorinated alcohols, and because of the effect of the high electronegativity of the fluorine groups [24–26]. In some cases, the inductive effect of the fluorine groups causes the alcohol to be 10^6 times more acidic than its nonfluorinated counterpart [25]. One of the driving forces behind the formation of ternary complexes of CD, pyrene, and alcohol is believed to be hydrogen bonding between the CD and alcohol. The strong electron-withdrawing capabilities of fluorine cause the hydroxyl proton of the alcohol to be a better hydrogen bond donor than the corresponding nonfluorinated alcohol [24].

The effects of 2,2,2-trifluoroethanol (TFE) and 2,2,3,3,3-pentafluoro-1-propanol (PFP) on the stoichiometry and apparent formation constants of the β- and γ-CD/pyrene complexes are investigated through a comparison of changes in the pyrene I/III ratio. Our evaluation of the complexes in terms of a 1 : 1 or 2 : 1 stoichiometry is based on previous studies in this laboratory [4]. The choice of a series of only two fluorinated alcohols was partly dictated by solubility considerations in water; the similarly fluorinated 1-butanol was not sufficiently water-soluble for our studies.

2. Experimental

2.1. Apparatus

Fluorescence emission spectra were acquired with a SPEC Model F2T21I fluorescence spectrophotometer with cooled PMT detection. Excitation and emission bandwidths were 5.2 and 1.7 nm, respectively. Pyrene emission spectra were obtained with an excitation wavelength of 335 nm. Fluorescence measurements were performed at $20 \pm 0.1°C$.

NMR studies were performed on a General Electric GN 500 NMR spectrometer operating at 500.1 MHz for ^1H and 470.5 MHz for ^{19}F. Spectra were acquired at ambient temperature.

2.2. Materials

Pyrene (99+%), 2,2,3,3,3-pentafluoro-1-propanol (97%), 2,2,2-trifluoroethanol (99+%), 1-propanol (HPLC grade), and the sodium salt of trifluoroacetic acid were purchased from Aldrich and used as received. Cyclohexane (A.C.S. grade) was purchased from Fisher and used as received. Ethanol was purchased from Aaper Alcohol and Chemical Co. (Shelbyville, KY). The β- and γ-CD were obtained from American Maize Products Co. (Hammond, IN) and used without further purification. Fluorescence samples were prepared with deionized water (Continental Water Systems, Atlanta, GA). NMR samples were prepared in D_2O (99.9 atom % D, Aldrich).

2.3. Method

A 5.0×10^{-4} M stock solution of pyrene in cyclohexane was prepared by dissolving 0.010 g of pyrene in 100 mL cyclohexane. A 2.0×10^{-7} M aqueous pyrene solution was then prepared by transferring the appropriate volume of the pyrene stock solution into a clean volumetric flask, evaporating the cyclohexane under a stream of N_2, and redissolving the pyrene in deionized (DI) water. The pyrene/β-CD/alcohol samples were made by adding the appropriate mass of β-CD, 5.0 mL of the aqueous pyrene solution, and the appropriate volume of alcohol to a volumetric flask and diluting to 10.0 mL with DI water. The samples were inverted several times, mixed in an ultrasonic mixer until visual clarity was achieved, and allowed to equilibrate for 22–24 h before analysis. All samples which contained alcohol had a 2.5×10^{-2} M alcohol concentration. Blank samples were also prepared containing all components but pyrene. Analysis was performed by acquiring two emission spectra per sample, averaging the spectra, and subtracting the emission spectrum of the blank sample. The pyrene I/III band ratio was obtained from the averaged, blank-subtracted spectrum by measuring emission intensities at 372 nm (band I) and 383 nm (band III).

In the determination of apparent formation constants, a series of samples containing 1.0×10^{-7} M pyrene, 2.5×10^{-2} M alcohol, and varying CD concentrations was prepared. The β- and γ-CD concentrations ranged from 0–7.0×10^{-3} M and 0–1.2×10^{-2} M, respectively.

Samples for the ^{1}H and ^{19}F NMR studies contained 5.0×10^{-3} M CD and/or 2.5×10^{-2} M alcohol, and were allowed to equilibrate for approximately 20 hours. The chemical shifts in the ^{1}H studies are reported relative to HOD at 4.8 ppm. For the ^{19}F NMR studies, a 2% (w/w) solution of trifluoroacetic acid (TFA), sodium salt in D_2O was used as an external standard.

3. Results and Discussion

3.1. Effect of Alcohol on Pyrene I/III Ratio

In a preliminary fluorescence study, the ideal concentration of PFP for the β-CD/pyrene system was determined by analyzing a series of samples containing a constant concentration of pyrene and β-CD (1.0×10^{-7} M and 5.0×10^{-3} M, respectively), and varying the PFP concentration over the range of 0–0.20 M (Figure 1). The pyrene I/III ratio was found to decrease rapidly from a value of 1.1 without PFP to a value of 0.38 in the presence of 0.020 M PFP. The I/III ratio remained constant at ~0.38 from 0.020 M to 0.20 M PFP. Therefore, 0.025 M PFP was selected as the alcohol concentration at which to study pyrene/CD complexation since it was within the range over which the I/III ratio was at its minimum. This I/III ratio value (0.38) is one of the lowest that this laboratory has ever observed for pyrene in aqueous solution for CD/pyrene/alcohol studies of this type. This value suggests that most of the pyrene is totally complexed and that PFP plays an important role in the enhanced formation of the inclusion complex.

In order to determine whether PFP associated with pyrene in the absence of CD, the I/III ratio was monitored while varying the PFP concentration from 0 to 0.20 M, and no change in the ratio was observed (Figure 1). The same experiment was conducted for TFE from 0 to 0.28 M alcohol, and the I/III ratio remained relatively constant. This in turn suggests that there is no association between the pyrene and either fluorinated alcohol in the absence of CD.

The effects of a fixed concentration (2.5×10^{-2} M) of PFP, TFE, and their corresponding nonfluorinated alcohol analogs on the pyrene emission spectrum were also examined. Figure 2 shows the emission spectrum of 1.0×10^{-7} M pyrene in 5.0×10^{-3} M β-CD in the absence and presence of 2.5×10^{-2} M PFP. The addition of PFP causes a dramatic increase of the band at 383 nm. This is attributed to the transfer of pyrene from the hydrophilic aqueous environment into the hydrophobic β-CD cavity.

Figure 3a shows the effect of varying concentrations of β-CD on the pyrene I/III ratio in the absence of alcohol and in the presence of 2.5×10^{-2} M ethanol and 2.5×10^{-2} M TFE. The values indicated are the mean of three individual

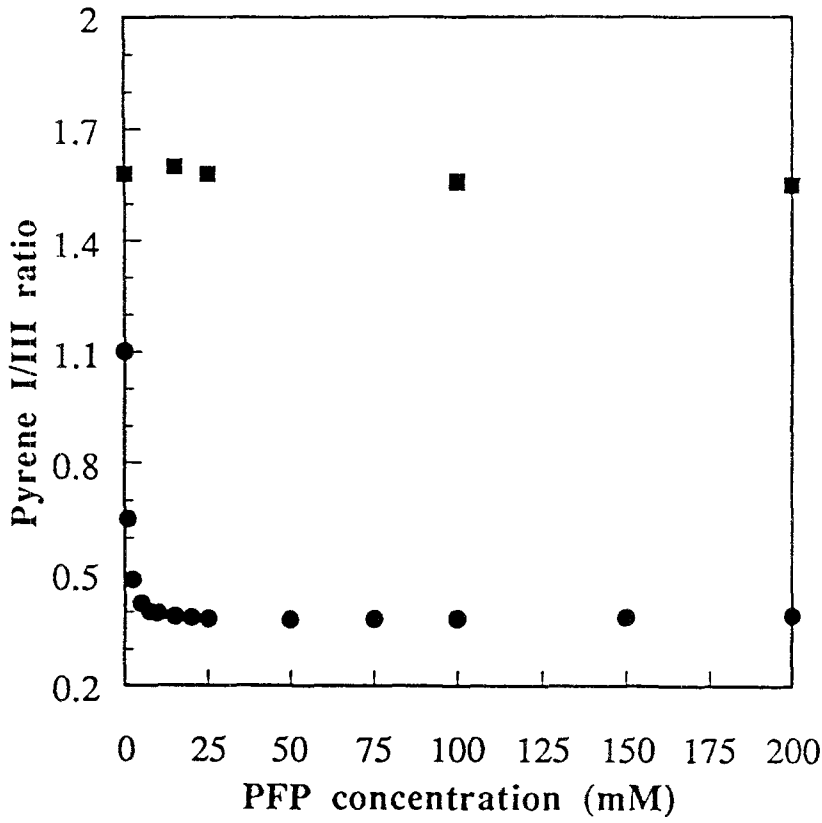

Fig. 1. Pyrene I/III band ratio as a function of 2,2,3,3,3-pentafluoro-1-propanol concentration, with (•) and without (■) 5 mM β-CD. [pyrene] = 1.0×10^{-7} M; emission monitored at 372 nm (band I) and 383 nm (band III).

determinations from three separate experiments, with the error bars indicating the standard deviation about the mean. Both the fluorinated and nonfluorinated ethanols cause a lower I/III ratio than in the absence of alcohol. The bulkier TFE alcohol appears to have a more pronounced influence on the slope of the curve than does ethanol. This change in the slope is accompanied by a lower minimum I/III ratio of 0.61, reached at 5.0×10^{-3} M β-CD. However, in the presence of ethanol, the I/III ratio is approximately 0.90 at 5.0×10^{-3} M β-CD and is still decreasing at 7.0×10^{-3} M β-CD. Likewise, 1-propanol and PFP, as shown in Figure 3b, both have a strong effect on providing a more nonpolar microenvironment around pyrene, hence a lower I/III ratio. There is less of a difference in the changes caused by the fluorinated and nonfluorinated propanols than with the ethanols. Both of the propanols cause a relatively large drop in I/III ratio at relatively low β-CD concentrations. However, the lower I/III ratio with PFP indicates a more nonpolar environment for pyrene in the presence of that alcohol. It could therefore

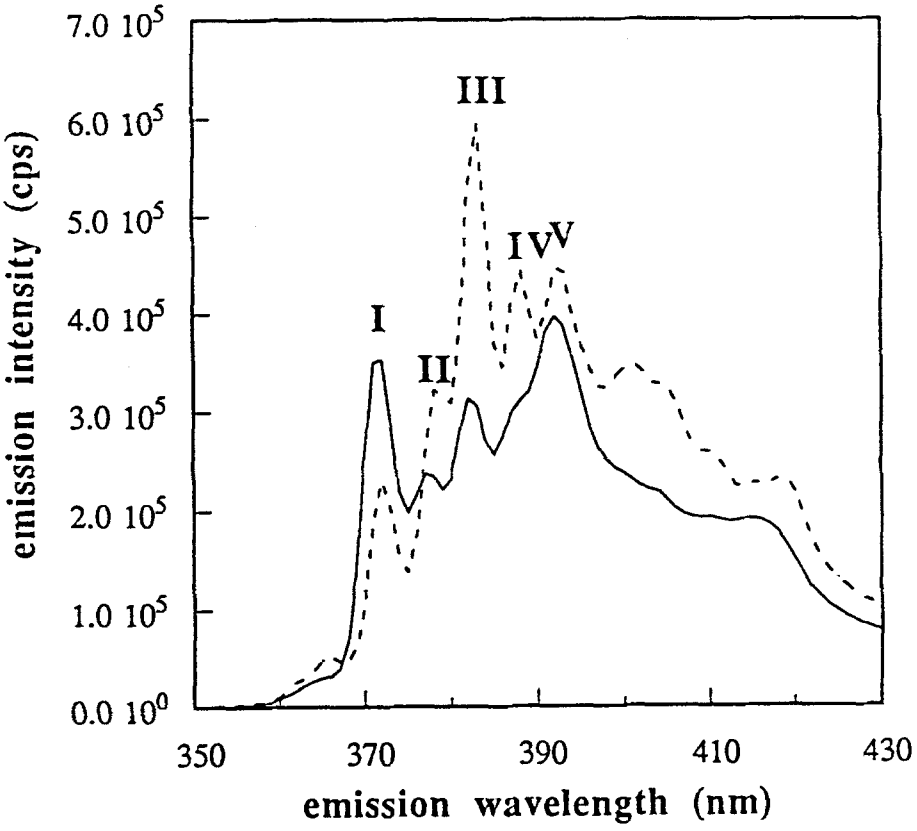

Fig. 2. Fluorescence emission spectra of 1.0×10^{-7} pyrene in the presence of 5 mM β-CD with (- - - -) and without (——) 2.5×10^{-2} M 2,2,3,3,3-pentafluoro-1-propanol. Excitation wavelength of 335 nm. Numbers I–V indicate characteristic five-band emission pattern.

be inferred that more nonpolar alcohols (propanols) appear to lead to stronger β-CD/pyrene/alcohol inclusion complexes.

The effect of the alcohol is decreased greatly in the pyrene/γ-CD system, as seen in Figures 4a and 4b. In fact, within the experimental error (standard deviation of three determinations) of the pyrene I/III ratio, the only alcohol of the four studied which is able to decrease the ratio significantly is PFP. The interior cavity of γ-CD is large and forms a 1 : 1 CD/pyrene complex. The alcohols can co-include with pyrene inside the CD cavity or remain positioned on either side of the openings of the CD cavity. Due to the small sizes of the ethanols and propanols compared to the cavity size, these alcohols are not as effective space regulators for γ-CD as for β-CD. Consequently, the alcohols are not strongly effective in minimizing the pyrene's interactions with the aqueous environment.

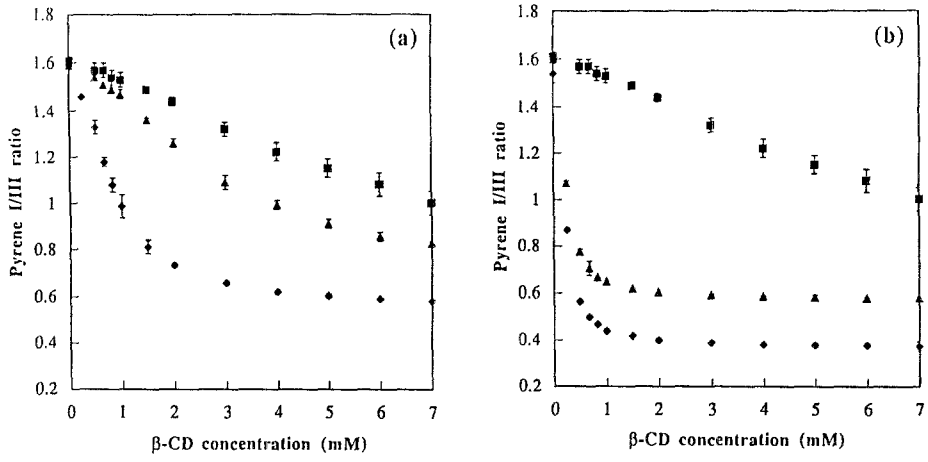

Fig. 3. Effect of (a) ethanol and 2,2,2-trifluoroethanol and (b) 1-propanol and 2,2,3,3,3-pentafluoropropanol on the pyrene I/III vibronic band ratio in the presence of β-CD. Alcohol concentration in all cases is 2.5×10^{-2} M; [pyrene] = 1.0×10^{-7} M.

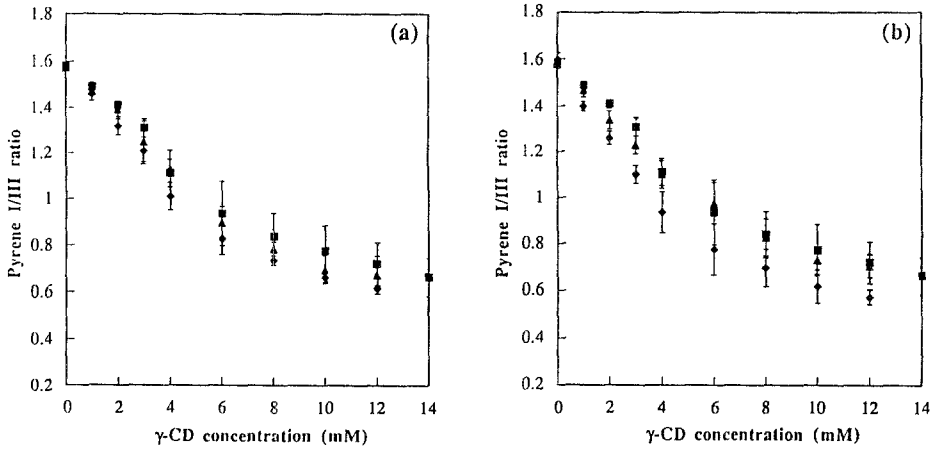

Fig. 4. Effect of (a) ethanol and 2,2,2-trifluoroethanol and (b) 1-propanol and 2,2,3,3,3-pentafluoropropanol on the pyrene I/III vibronic band ratio in the presence of γ-CD. Alcohol concentration in all cases is 2.5×10^{-2} M; [pyrene] = 1.0×10^{-7} M.

3.2. Determination of Complexation Constants

Several studies of the stoichiometry of the pyrene/CD complex have reported conflicting results. In studies in which the pyrene concentration is maintained well below its aqueous solubility, a 1 : 1 γ-CD/pyrene complex is usually observed, whereas both 1 : 1 and 2 : 1 β-CD/pyrene complexes have been observed. This laboratory has reported the existence of a 2 : 1 β-CD/pyrene complex, and this study corroborates those results.

As described previously by Muñoz de la Peña *et al.* [4], equilibrium for the 1 : 1 association of pyrene and CD is given by

$$\mathrm{P} + \mathrm{CD} \rightleftharpoons \mathrm{P(CD)} \tag{1}$$

$$K_1 = \frac{[\mathrm{P(CD)}]}{[\mathrm{P}]\,[\mathrm{CD}]} \tag{2}$$

where [P(CD)] is the equilibrium concentration of the complex and K_1 is the overall equilibrium constant. The following equation can be used to calculate K_1:

$$\frac{1}{R_0 - R} = \frac{1}{K_1(T_0 - R_1)\,[\mathrm{CD}]_0} + \frac{1}{R_0 - R_1} \tag{3}$$

where R_0, R_1, are the pyrene I/III ratio in water and in the CD complex, respectively, and R is the measured I/III value at a given CD concentration [27]. For a 1 : 1 complex, a plot of $1/(R_0 - R)$ vs. $1/[\mathrm{CD}]_0$ will give a straight line of slope $1/K_1(R_0 - R_1)$ and y-intercept of $1/(R_0 - R_1)$.

Similarly, for the 2 : 1 complexation equilibrium,

$$\mathrm{P} + 2(\mathrm{CD}) \rightleftharpoons \mathrm{P(CD)_2} \tag{4}$$

$$K_2 = \frac{[\mathrm{P(CD)_2}]}{[\mathrm{P}]\,[\mathrm{CD}]^2}\,. \tag{5}$$

The following equation applies to the relationship between the pyrene I/III ratio and K_2:

$$\frac{1}{R_0 - R} = \frac{1}{K_2(R_0 - R_2)\,[\mathrm{CD}]_0^2} + \frac{1}{R_0 - R_2} \tag{6}$$

where K_2 is the overall equilibrium constant and R_2 is the pyrene I/III ratio in the 2 : 1 complex. Once again, K_2 can be determined from the straight line obtained from plotting $1/(R_0 - R)$ vs. $1/[\mathrm{CD}]_0^2$.

Figure 5 shows the same set of data plotted with Equations (3) and (6). The fact that an upward concave curve was obtained with Equation (3) and a straight line with Equation (6) suggests that the stoichiometry of the β-CD/pyrene complex is 2 : 1. Similar experiments with γ-CD suggested a 1 : 1 γ-CD/pyrene complex. Even though Equations (3) and (6) proved useful in determining complex stoichiometry, these equations place unequal emphasis on data points from the lowest CD concentrations (the data points with the highest x-ordinate values in Figure 5). Small variations in the I/III ratios of these data points can cause a large variation in the calculated K_1 and K_2 values. Therefore, for the calculations of K_1 and K_2, Equations (3) and (6) were modified to Eadie–Hofstee type Equations (7) and (8), shown below [28, 29]:

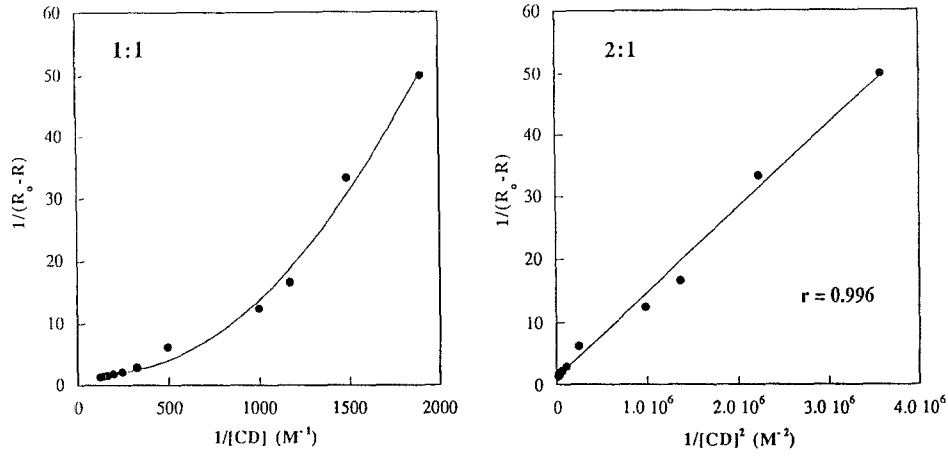

Fig. 5. Benesi–Hildebrand-type double reciprocal plots for the determination of a 1 : 1 or a 2 : 1 pyrene/β-CD complex in the absence of alcohol. [pyrene] = 1.0×10^{-7} M.

$$\frac{[\mathrm{CD}]_0}{R_0 - R} = \frac{1}{R_0 - R_1}([\mathrm{CD}]_0) + \frac{1}{K_1(R_0 - R_1)} \tag{7}$$

$$\frac{[\mathrm{CD}]_0^2}{R_0 - R} = \frac{1}{R_0 - R_2}([\mathrm{CD}]_0^2) + \frac{1}{K_2(R_0 - R_2)} \cdot \tag{8}$$

These linearization equations were used to calculate the values of K_1 and K_2 which were used as estimates in the nonlinear regression analysis (NLR).

The apparent complexation equilibrium constants as determined by NLR for β-CD and pyrene are summarized in Table I. The K_{complex} values shown are the mean of three determinations, which were made independently. In the comparison of the effects of fluorinated and nonfluorinated ethanols, both are observed to increase the equilibrium constant for the formation of the pyrene/β-CD complex. The presence of 2.5×10^{-2} M ethanol increases the equilibrium constant from 6.76×10^4 M^{-2} in the absence of alcohol to 1.52×10^5 M^{-2}, approximately doubling the constant. The TFE, however, increases the constant to 1.47×10^6 M^{-2}, a much larger increase than caused by nonfluorinated ethanol. A similar but greater effect is observed in the propanol series. The 1-propanol increases the K_{complex} value to 1.75×10^7 M^{-2}, indicating a strong interaction between the alcohol and the pyrene/CD complex. The PFP causes a slightly greater increase in complexation, with an equilibrium constant of 2.27×10^7 M^{-2}.

None of the alcohols – fluorinated or nonfluorinated – has a significant effect on the complexation constant of pyrene and γ-CD. As shown in Table II, the K_{complex} values for all five systems are equal, within standard deviation. This result is consistent with the fact that the addition of alcohol to the pyrene/γ-CD solutions, as shown in Figures 3a and 3b, did not significantly lower the pyrene I/III ratio.

TABLE I. Apparent equilibrium constants for complexation of pyrene and β-CD in the presence of various alkyl and fluorinated alcohols[a].

	$K^b \pm$ standard deviation (M^{-2})
no alcohol	$6.76 (\pm 0.38) \times 10^4$
ethanol	$1.52 (\pm 0.16) \times 10^5$
TFE	$1.47 (\pm 0.08) \times 10^6$
1-propanol	$1.75 (\pm 0.10) \times 10^7$
PFP	$2.27 (\pm 0.21) \times 10^7$

[a] Calculated by nonlinear regression.
[b] Values are the mean of three determinations.

TABLE II. Apparent equilibrium constants for complexation of pyrene and γ-CD in the presence of various alkyl and fluorinated alcohols[a].

	$K^b \pm$ standard deviation (M^{-1})
no alcohol	186 ± 131
ethanol	141 ± 53
TFE	178 ± 66
1-propanol	143 ± 67
PFP	189 ± 55

[a] Calculated by nonlinear regression.
[b] Values are the mean of three determinations.

Apparently, the volume of the γ-CD cavity is too large for any of the alcohols to effectively act as a spacer to increase complexation between pyrene and γ-CD.

3.3. NMR Studies of CD/Alcohol Interactions

Nuclear magnetic resonance spectroscopy is a useful technique in the investigation of CD/alcohol interactions in solution. The interaction is assessed by comparing the NMR spectrum of cyclodextrin in the absence and presence of the associated alcohol. Figure 6a shows the ^1H NMR spectrum of β-CD in D_2O. The spectrum is comprised of five different kinds of proton signals: H-1 (doublet at δ 5.08 ppm), H-2 (two doublets at δ 3.66 ppm), H-3 (triplet at δ 3.94 ppm), H-4 (triplet at δ 3.60

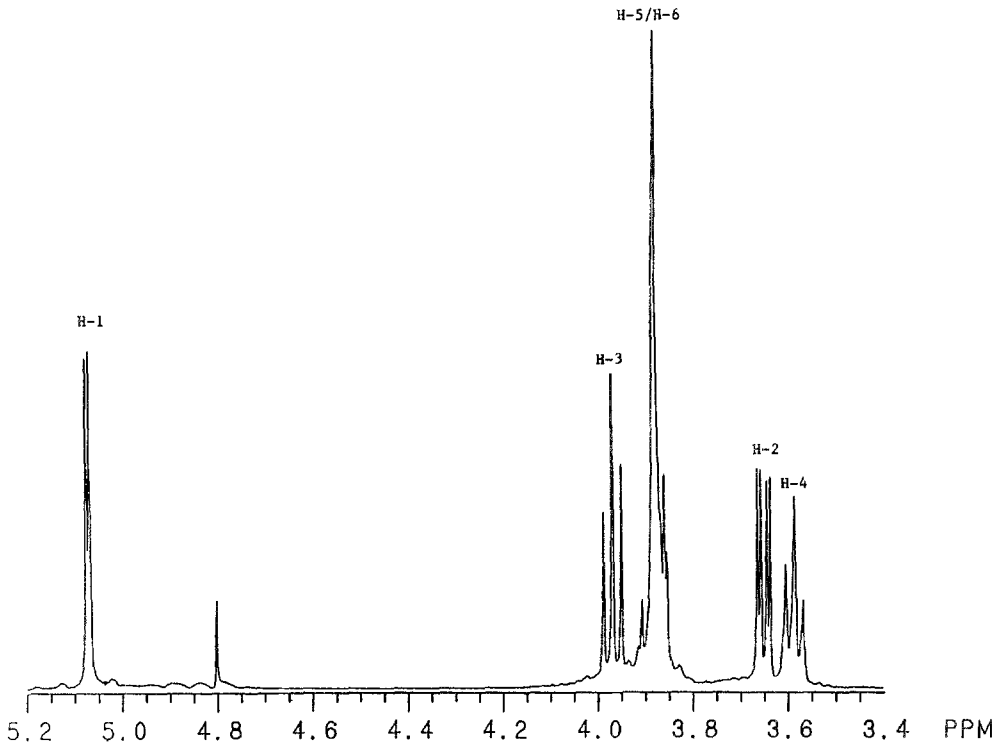

Fig. 6. (a) ^{1}H NMR spectrum of β-CD alone in D_2O.

ppm), and H-5 and H-6 (unresolved peaks at δ 3.86–3.93 ppm). This spectrum has been assigned previously [30]. Upon addition of PFP, a slight change in the chemical shifts of β-CD protons is observed. PFP gives a 0.05 ppm upfield shift of the H-3 signal. In addition, new previously unobserved signals in the spectrum of pure β-CD appear around δ 3.81 ppm, apparently due to the H-5 proton signals shifting upfield from the broad overlapping H-5/H-6 resonances (Figure 6b). The H-3 and H-5 protons are located in the interior of the CD cavity. The shifts are consistent with the finding of Demarco and Thakkar [31] who reported significant changes in the chemical shifts of the H-3 and H-5 protons of CD upon inclusion of a guest molecule. Such shifts were rationalized in terms of the strong shielding of the interior protons upon inclusion of aromatic substrates inside the CD cavity.

The ^{1}H NMR approach to the determination of complexation behavior allows for the estimation of the sites of interaction between CDs and the guest molecules [30]. The H-3 and H-5 proton signals shift upfield upon addition of PFP. In contrast, no effect is observed on the H-1, H-2, and H-4 protons which are located on the outside of the CD molecule. This suggests that there is no association between the alcohol and the exterior of the CD molecule. The addition of the smaller fluorinated alcohol (TFE) has no effective influence on the chemical shifts of β-CD. In addition,

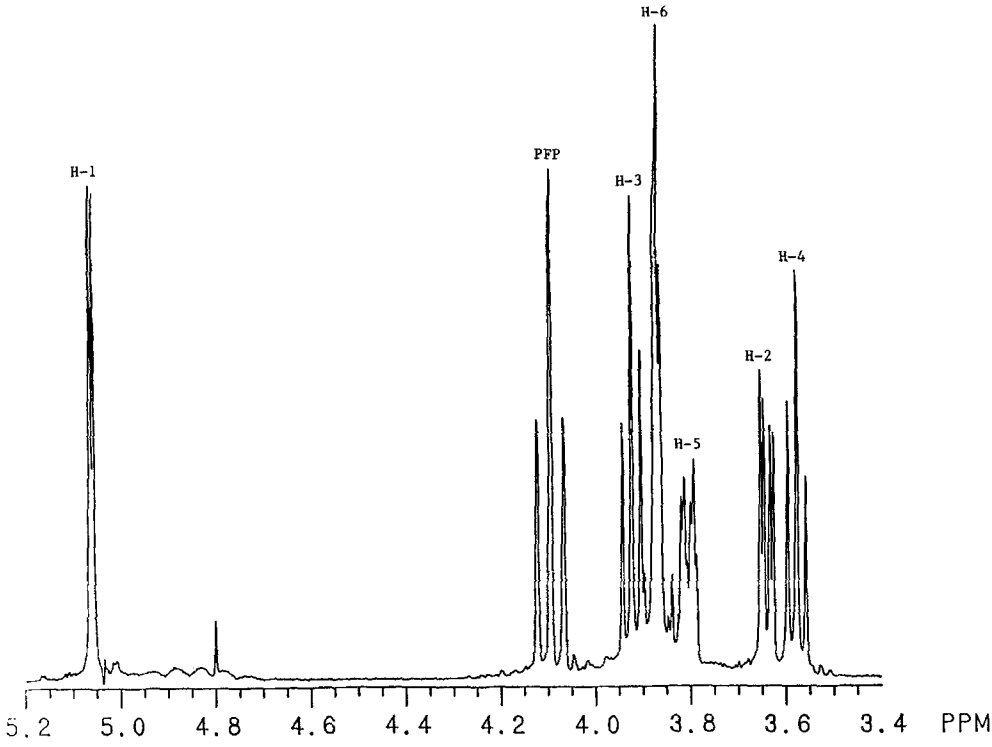

Fig. 6. (b) ^{1}H NMR spectrum of β-CD in D_2O in the presence of 25 mM 2,2,3,3,3-pentafluoro-1-propanol.

neither PFP nor TFE has an effect on the chemical shifts of the γ-CD protons. The ability of NMR to distinguish specific sites of the molecule makes this technique valuable in defining the mode of interaction between CD and the alcohol. The ^{1}H NMR study allows for the detection of distinct spectral perturbations of the H-3 and H-5 signals of β-CD resulting from intracavity inclusion.

It is well established that the chemical shifts of ^{19}F NMR signals are significantly influenced by changes in molecular environment [32–34]. In seeking to understand the mode of interaction between the fluorinated alcohol and the β-CD/pyrene system, ^{19}F NMR experiments were conducted. In the studies presented here, samples were prepared which contained the alcohol in D_2O ([alcohol] $= 2.5 \times 10^{-2}$ M) in the presence and absence of CD ([CD] $= 5.0 \times 10^{-3}$ M). It should be emphasized that an external standard (TFA) was used instead of an internal standard, due to the tendency of the standard to complex with CDs. The ^{1}H decoupled ^{19}F NMR spectrum of PFP in aqueous solution consists of two resonances at δ −50.10 and δ −7.96 ppm. Upon addition of β-CD, no significant change of the fluorine chemical shifts was observed. This is an unexpected result since the fluorescence and ^{1}H NMR experiments indicated considerable interaction between PFP and β-CD.

In order to explain this anomaly, it should be added that pyrene forms a 2 : 1 β-CD/pyrene complex [4]. In the 2 : 1 CD/pyrene complex, there exists residual void cavities on either side of the complex which are amenable to other guest molecules of appropriate size. The CF_3 groups most likely fill the open-end spaces of the β-CD/pyrene complex, protecting the pyrene from the bulk aqueous environment. These assumptions are corroborated by the increase in formation constants in the presence of fluorinated alcohols compared to that in pure water and in the presence of nonfluorinated alcohols (see Determination of Complexation Constants). The ^{19}F NMR experiments were conducted using the same concentrations of β-CD (5.0×10^{-3} M) and PFP (2.5×10^{-2} M) as those employed in the fluorescence studies. Judging from the large excess of PFP, the majority of the alcohol is still in considerable contact with the bulk aqueous environment; hence, no induced chemical shift changes of PFP fluorine atoms due to the presence of β-CD are observed. The ^{19}F NMR chemical shift is assumed to be the weighted average of the CF_3 groups associated with the interior of the CD cavity and those located outside the CD cavity. If the latter is the dominant factor, the observed shift of the fluorine chemical shift upon addition of CD will be small. Therefore, the combination of a partially hydrated CD cavity and a large excess of uncomplexed alcohol appears to result in no observable changes in the ^{19}F chemical shifts upon complexation. Similarly, no fluorine chemical shift change was observed for TFE, which has a single resonance at δ -1.22 ppm. The addition of γ-CD causes no significant change in the fluorine chemical shifts of PFP or TFE.

4. Conclusions

Fluorescence studies indicate that fluorinated alcohols provide a significantly more hydrophobic environment for the pyrene in the pyrene/β-CD complex than do their nonfluorinated analogs. In the presence of PFP, the pyrene I/III ratio in the β-CD complex is 0.38, an extremely low value. In addition, these alcohols cause an increase in the apparent equilibrium constant for the formation of the complex. In the presence of γ-CD, the alcohols have no significant effect on the microenvironment of the pyrene or the apparent equilibrium constant. These results from fluorescence studies suggest that the fluorinated alcohol acts as an effective spacer in the complex, aiding in the exclusion of water molecules from the CD cavity. With the larger cavity of γ-CD, the alcohols are less effective due to unfavorable size-compatibility. The ^1H NMR studies indicate interactions between PFP and the β-CD cavity, with no detected interactions on the exterior of the CD. It was not possible to detect the complexed alcohol by ^{19}F NMR techniques, most likely due to an excess of uncomplexed alcohol in solution and/or partial hydration of the complexed alcohol.

Acknowledgements

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