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2-Naphthol Complexation by β-Cyclodextrin: Influence of Added Short Linear Alcohols

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2-Naphthol (NOH) in its ground state forms a 1:1 complex with β-cyclodextrin (β-CD) both in the absence and presence of linear alcohols. Association constants, K_{app}, were measured using a steady-state fluorescence method. K_{app} decreases linearly with an increasing number of carbon atoms in the chain of the alcohol, n_C, up to $n_C = 5$. We attribute this to a competition between NOH and alcohol for the β-CD cavity. Fluorescence studies confirm the redistribution of NOH from the CD environment to the aqueous phase when alcohols are present. NOH fluorescence is quenched by iodide in all the systems studied. At 2 mM β-CD, alcohols increase the Stern−Volmer constant above the value found in the absence of alcohols. These results suggest that alcohols occupy space within the β-CD cavity with the result that the aqueous NOH concentration is increased. This was further investigated by dynamic fluorescence measurements on the system β-CD:NOH:pentanol. Global biexponential analysis of fluorescence decay data shows that the Stern−Volmer constants correlate inversely with the fraction of NOH complexed by β-CD. By global compartmental analysis of the fluorescence decays, values for the excited-state association and dissociation rate constants were determined. The dissociation rate constant increases from approximately 500 s^{-1} in the absence of pentanol to about 14 000 s^{-1} at a pentanol concentration of 0.1 M. The association rate constant increases from 2.5×10^9 to 5.8×10^9 M^{-1} s^{-1} upon addition of pentanol. The more pronounced increase of the dissociation rate constant leads to an exclusion of complexed NOH into the aqueous bulk phase. As the complexed NOH is shielded against iodide quenching, this explains the increase of the Stern−Volmer constant when an alcohol is added to the aqueous β-CD:NOH system.

1. Introduction

Cyclodextrins (CD) have proven their worth as media for controlling chemical[1−3] and photochemical reactions.[4−6] For example, CD-complexed reagents can exhibit photochemistry which is quite different from that observed in homogeneous solution.[4−6] Reactivity control depends on the cavity of the CD complexing organic reagent molecules ("guest" molecules).[1,4−6] A number of factors influence complexation. Of these it is the "goodness of fit" between host and guest and the hydrophobic effect which are probably most significant.[1] There is interest in manipulating complexation as this is the key to applying CD in fields as diverse as pharmacology,[1] analytical chemistry,[7−9] organic synthesis,[1] and photophysics.[4,5,10−14]

Recently the impact of a third component on CD host:guest binding has attracted attention. Studies of "third-party effects" have examined inter- and intramolecular excimer formation within CD cavities,[15] alteration of quenching of a guest fluorescence probe molecule by use of quenchers that might also be complexed by CD,[16−19] and the variation in chemical behavior with surfactants as the third component.[19−23]

Alcohols have also been studied as "third parties" for a variety of CD:guest systems.[7,24−28] The behavior of CD:guest systems has been probed by both steady-state[7,9,11,12,16−19,21,24−29] and time-resolved fluorescence techniques.[10,13,20,30,31] By far the largest portion of these studies have made use of polyaromatic hydrocarbons (PAHs), such as naphthalene and pyrene derivatives, as guests. PAHs are strongly fluorescent and bind to the CD because of their hydrophobicity.[32] Even so, addition of alcohols increases the strength of binding by formation of ternary CD:PAH:alcohol complexes.[7,24,25,27] Similar results have been found for binding of the more water-soluble α-(naphthyloxy)-acetic acid with γ-CD.[33] From these results a picture of the nature of binding in ternary CD:PAH:alcohol complexes has been emerging. The size and geometry of the alcohol seem to be important factors[7,24] as is its ability to alter the hydrophobicity of the cavity.[25] The presence of the primary and secondary hydroxyl groups of the CD are also essential for formation of ternary alcohol complexes,[25] the stoichiometry of which depends on the specific guest, type of CD, and type of alcohol.[24,25] It should be noted, however, that while this picture is fairly clear for strongly hydrophobic guest molecules, little attention has been paid to more water-soluble guest molecules.

In the present contribution, the influence of added pentanol on the excited-state kinetics of a rather water-soluble naphthalene derivative, 2-naphthol (NOH), complexed with β-cyclodextrin (β-CD) is reported together with the influence of added linear alcohols (methanol to pentanol) on the binding of NOH to β-CD. 1- and 2-substituted naphthalenes are known to form 1:1 complexes with β-CD,[10,34,35] and the formation constant of NOH with aqueous β-CD has been reported to be 590 ± 50 M^{-1}.[35] NOH is a moderately fluorescent naphthalene derivative, and its fluorescence behavior has been extensively studied in the context of excited-state proton transfer.[35−37] In aqueous solution at pH between 2.8 and 9.5, fluorescence from both the protonated (NOH) and deprotonated (NO^-) forms of 2-naphthol can be detected.[36,37] NOH would thus appear to be a promising probe for broadening the understanding of CD:guest:alcohol interactions.

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2. Experimental Section

2-Naphthol (NOH) and β-cyclodextrin (β-CD) from Aldrich were recrystallized twice from water. Alcohols (Aldrich, Merck, Rathburn) were of spectroscopic or HPLC grade and were used without additional purification. Water was conductivity grade (Lab-Ion L2 System or Milli-Q). Sodium iodide (NaI), Merck, was high-purity grade and used as received.

Samples for fluorescence analysis were prepared as follows. A stock solution of 0.1 mM NOH in water was prepared. This was used directly, or with an appropriate volume of alcohol added, in homogeneous solution measurements. β-CD samples were prepared by weighing an appropriate mass of β-CD into a 10 mL volumetric flask and diluting it with the 0.1 mM NOH stock. If an alcohol was to be added, the neat alcohol was injected into the β-CD:NOH solution. The injected alcohol volume never exceeded 100 μL in 10 mL. The samples were then stirred overnight. Quencher stock solutions in water were prepared just before use by dissolving an appropriate mass of NaI in water. Quenching experiments were performed by injecting appropriate small aliquots of quencher stock into 2 mL samples of β-CD:NOH:alcohol solutions immediately prior to measurement. Exposure to light was kept to a minimum during all sample preparation and handling. The samples were not buffered.

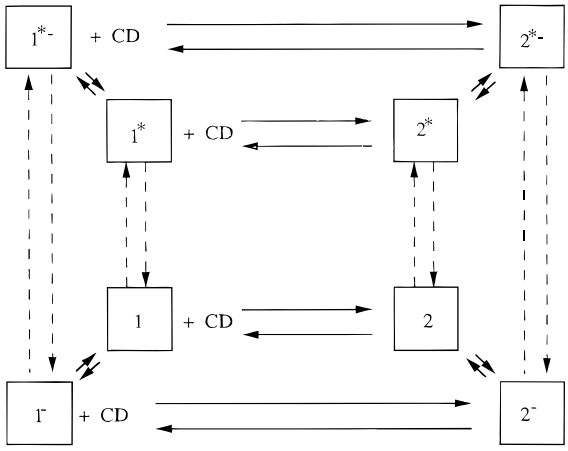
Steady-state fluorescence measurements were carried out at 20 ± 1 °C in a SPEX Instruments FluoroMax instrument (University of Iceland) operating with DataMax 3000 software. Instrument control, data collection, and preliminary data processing were carried out by a PC-486 computer interfaced to the fluorimeter. Samples for fluorescence measurement were contained in homemade 1 × 1 cm^2 Suprasil quartz cuvettes. The spectra were recorded with excitation at 310 nm. At this wavelength the absorption spectra of each combination of NOH and alcohol showed an isosbestic point as the concentration of β-CD was changed. Samples were not degassed as preliminary measurements indicated that this had little influence (<10%) on the observed fluorescence intensity. The band-pass was typically 4.3 nm. The emission spectra were uncorrected. Absorption spectra were recorded with a Perkin-Elmer Lambda 3 UV−vis spectrophotometer and pH values with a Radiometer PHM28 pH meter calibrated with standard buffer solutions. The calculations of the association constants were performed on a Macintosh LC-III within the Kaleidagraph (Abelbeck) framework.

Time-resolved fluorescence measurements were performed (KU Leuven) with the equipment described previously.[38] The excitation wavelength, as obtained by frequency-doubled DCM (4-dicyanomethylene-2-methyl-6-*p*-(dimethylamino)styryl-4*H*-pyrene) emission, was 314 nm, and the emission was monitored at 354 nm. All fluorescence decay curves were observed at the magic angle (54.7°). They contained about 5000 peak counts in 512 channels of the multichannel analyzer, of which about 450 were used in the fittings, starting from the rising edge. The time increment was 48 ps/channel, and the reference compound for deconvolution[39−45] was POPOP (*p*-bis[2-(5-phenyloxazolyl)]benzene, solvent = methanol, decay time = 1.1 ns). All measurements were performed at 18 °C. The fluorescence decay traces were globally analyzed,[46−51] using a general global analysis program[50,51] based on Marquardt's algorithm.[52]

The model used to fit the data was a biexponential decay function including quenching:

$$f(t) = a_1 \exp(-\{k_1 + k_{q1}[Q]\}t) + a_2 \exp(-\{k_2 + k_{q2}[Q]\}t) \quad (1)$$

SCHEME 1: Summary of All Possible Processes Involving NOH and β-CD[a]



[a] 1 is used for the aqueous phase and 2 for the inclusion complex. The deprotonated form, NO^-, is indicated with a minus sign. Full-drawn arrows refer to equilibrium processes, dotted to photophysical processes.

where $f(t)$ denotes the δ-response fluorescence at time t, $a_{1,2}$ are pre-exponential factors, k_i are the first-order decay constants, and k_{qi} are the second-order rate constants of quenching. For samples without β-CD or added quencher, simplified versions of eq 1 were used in the global fittings.

3. Results

3.1. Complex Formation Constants. The β-CD:NOH system is, due to the presence of an acid/base equilibrium and a complexation equilibrium, a complex system with in principle not less than eight different equilibria to be taken into account, see Scheme 1. If all processes were important, it would be more or less impossible to obtain the different rate constants or equilibrium constants from experimental data. Fortunately, it is possible to simplify the system, based on literature data and by a proper choice of pH and emission wavelength.

The two bands observed, Figure 1, are the well-known emissions of the protonated (NOH, emission at 354 nm) and deprotonated (NO^-, emission at 415 nm) forms of 2-naphthol.[4,36,53] In the ground state NOH is a weak acid, pK_a = 9.5, while in the excited state it is a rather strong acid, pK_a* = 2.8.[4,36,53] The equilibrium in the excited state is not completely reached within the excited-state lifetime of NOH (less than 10 ns in water and in β-CD[35]). Emission from the excited states of both NOH and NO^- can then be observed provided the pH is between 2.8 and 9.5. It should also be noted that NOH exhibits emission at 415 nm, while NO^- does not emit at 354 nm.

For the β-CD complexed states, Park et al. have determined the pK_a and the pK_a* to be 9.9 and 3.0,[35] respectively, thus not differing much from the values found in homogeneous aqueous solutions.

NOH (0.1 mM) in water was found to have a pH of 6.4. At this pH essentially all the aqueous ground-state naphthol is in the protonated NOH form (the ratio $[NO^-]/[NOH]$ is 6×10^{-4} at pH = 6.4 when pK_a = 9.5). This was confirmed by exciting the sample at 360 nm where only the base, NO^-, absorbs. At this excitation wavelength negligible fluorescence was observed between 380 and 520 nm. Thus, the observed NO^- fluorescence upon excitation at 310 nm arises exclusively via dissociation of excited-state NOH (Scheme 1). Adding β-CD up to 10 mM had no influence on the measured pH value, nor had added alcohols. The lack of influence of alcohols on pH is also

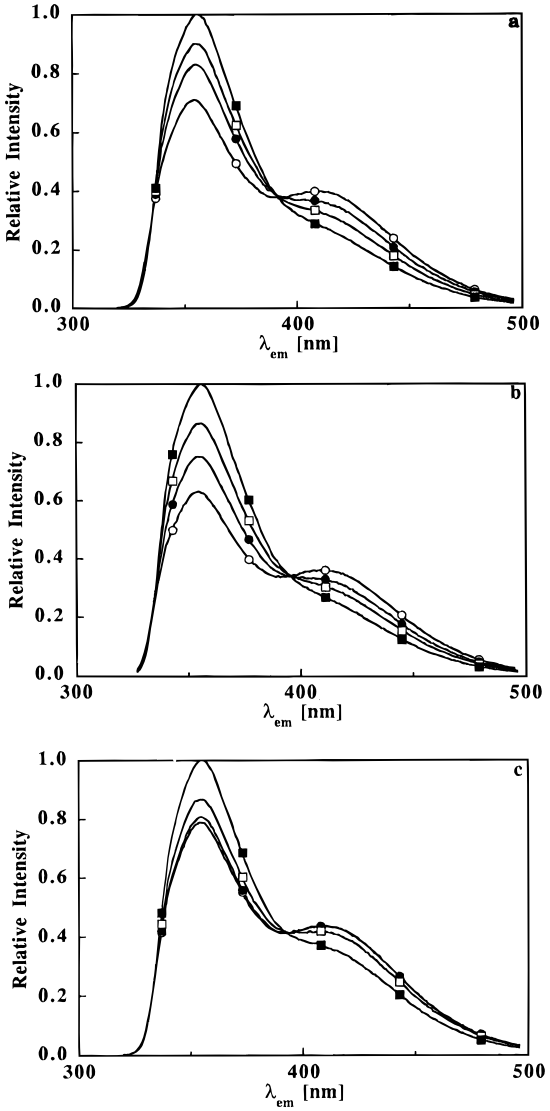


Figure 1. Fluorescence spectra for 0.1 mM 2-naphthol in (a) water, (b) water containing 100 mM methanol, and (c) water containing 92.4 mM pentanol. β-Cyclodextrin concetrations are 0.0 mM (○), 0.7 mM (●), 2 mM (□) and 10 mM (6 mM for pentanol) (■). Excitation at 310 nm. Band-pass 4.3 nm.

illustrated by comparing the value of I_{354}/I_{415} in water (1.81 ± 0.03) with that in water containing 0.1 M methanol (1.78 ± 0.05) or 0.1 M 1-butanol (1.82 ± 0.04). It should also be pointed out that in homogeneous solution the alcohols had minimal influence (<8%) on the intensity of the naphthol fluorescence at 354 nm at an alcohol concentration of 0.2 M.

Van den Bergh et al. have determined the rate constants for the excited-state deprotonation of NOH and protonation of NO^- in aqueous solution: 7.1×10^7 s^{-1} and 5×10^{10} M^{-1} s^{-1}, respectively.[37] At a pH of 6.5, this means that the protonation rate in the excited state is more than 3000 times slower than the deprotonation rate.

All this information allows a significant simplification of Scheme 1. At pH = 6.5 all ground-state naphthol, aqueous or complexed with β-CD, will be in the protonated form. Upon excitation deprotonation will take place due to a significantly lower pK_a in the excited state as compared to the ground state. Reprotonation, however, will not take place, neither for the aqueous phase NOH, nor for β-CD complexed NOH. Upon excitation, only excited-state NOH will be formed initially. Measuring the fluorescence emission at a wavelength where both NOH and NO^- emit would lead to a dual fluorescence, even in homogeneous aqueous solution, due to the deprotonation. If the emission is measured at a wavelength where only one of the excited-state species emits, however, e.g., at 354 nm where only the protonated form exhibits emission, only the decay of this species will be observed. These simplifications transform Scheme 1 into Scheme 2.

SCHEME 2: Simplified Version of Scheme 1 According to the Conditions of the Present System (See Text for Further Details)

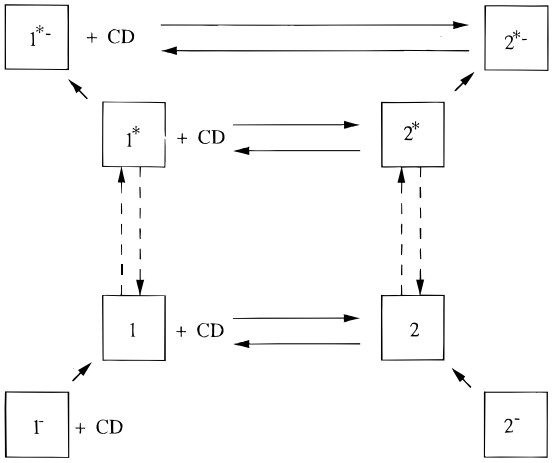


Figure 1 shows a series of fluorescence spectra for 0.1 mM NOH in aqueous solution and in aqueous solution containing 0.1 M methanol or pentanol, at varying concentrations of β-CD. The general shapes of the spectra are the same in each of these systems. In the absence of β-CD, the fluorescence spectrum exhibits two distinct peaks, which are observed at 354 and 415 nm. As the β-CD concentration is increased the peak at 354 nm increases in intensity while that at 415 nm decreases. Comparable sets of fluorescence spectra were obtained for all the systems studied here, i.e., 0.1 mM NOH in aqueous β-CD without alcohol and with 0.1 M methanol, ethanol, propanol, butanol, or pentanol. Attempts were also made to study the influence of hexanol on the β-CD−NOH system. In the presence of 0.1 M hexanol, the NOH fluorescence intensity varied in an unsystematic fashion when the β-CD concentration was altered. No isoemissive point was observed. These observations are probably due to the complete exclusion of NOH from β-CD when hexanol is present. Further examination of the β-CD−NOH−hexanol system was not carried out.

The changes in the spectrum of the NOH system as the β-CD concentration was increased in the absence of added alcohols reflect relocation of some ground-state 2-naphthol from the aqueous phase into the interior of the β-CD cavity. The fluorescence quantum yield of NOH increases by a factor of 1.4 upon complexation by β-CD, while the quantum yield for the deprotonated form remains unchanged.[10]

It is well established that naphthalenes substituted in the 2-position fit comfortably within the β-CD cavity, yielding a 1:1 complex.[1,35] For β-CD:NOH the expected structure has been described.[1,35] Figure 2 shows how the intensity at 354 nm increases as a function of β-CD in the absence and presence of added methanol. One can make use of this intensity increase to determine the association constant of ground-state NOH with the β-CD cavity. For a 1:1 complex the association process

$$\text{NOH} + \beta\text{-CD} \rightleftharpoons \beta\text{-CD:NOH} \qquad (2)$$

has the association constant defined by

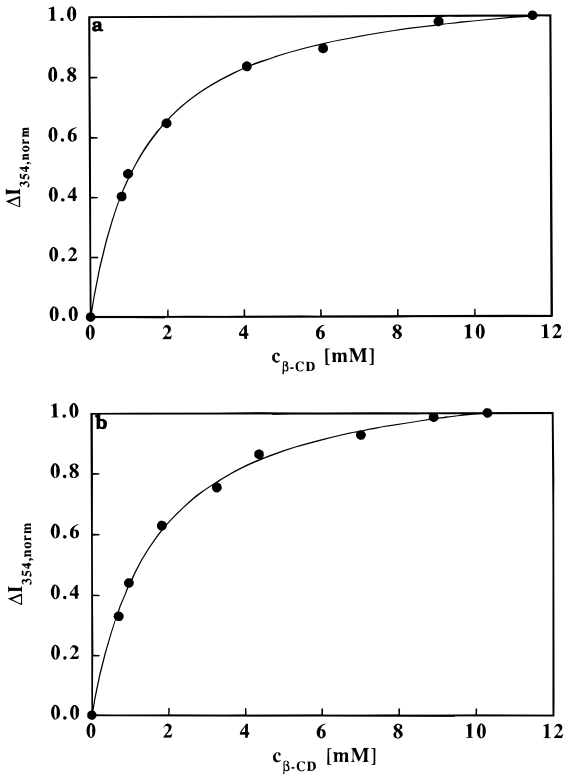


Figure 2. Binding isotherm for 0.1 mM 2-naphthol with β-cyclodextrin. Solvents are (a) water and (b) water containing 100 mM methanol. The lines are nonlinear fits of the data by eq 8.

$$K_1 = \frac{[\beta\text{-CD:NOH}]}{[\text{NOH}][\beta\text{-CD}]} \tag{3}$$

In systems containing alcohol the following two equlibria must also be considered:

$$\text{ROH} + \beta\text{-CD} \rightleftharpoons \beta\text{-CD:ROH} \tag{4}$$

$$\text{ROH} + \beta\text{-CD:NOH} \rightleftharpoons \beta\text{-CD:NOH:ROH} \tag{5}$$

We can combine these two equilibria with that of eq 2 into the general process

$$\text{NOH} + \beta\text{-CD} + \text{ROH} \rightleftharpoons (\text{NOH})_{\text{bound}} \tag{6}$$

for which we can write an apparent association constant

$$K_{\text{app}} = \frac{[\text{NOH}]_{\text{bound}}}{[\text{NOH}][\beta\text{-CD}]} \tag{7}$$

The treatment for extracting the value of K_{app} from the binding isotherm data has been described previously.[28,54] Essentially the binding isotherm data are fit by the model

$$\Delta I = K_{\text{app}} \frac{\Delta i[\text{NOH}]_0[\beta\text{-CD}]}{1 + K_{\text{app}}[\beta\text{-CD}]} \tag{8}$$

The emission intensities at 354 nm were treated according to this equation. ΔI refers to the difference between the fluorescence intensity at [β-CD] and that in the absence of β-CD. $[\text{NOH}]_0$ was held constant in all measurements at 0.1 mM, and Δi reflects the maximum value of ΔI. Figure 2 shows nonlinear regression fits of eq 8 to the binding isotherm data for the aqueous system. Similar plots were obtained for the other systems examined. The calculated K_{app} values obtained are shown in Table 1. It should be noted that there were also systematic changes in the 2-naphthol absorption spectrum as the β-CD concentration was varied. These changes can in principle be used to determine K_{app} as well. They were small, however, compared to the changes in the fluorescence spectrum, and therefore, K_{app} values based on absorption would be subject to larger errors.

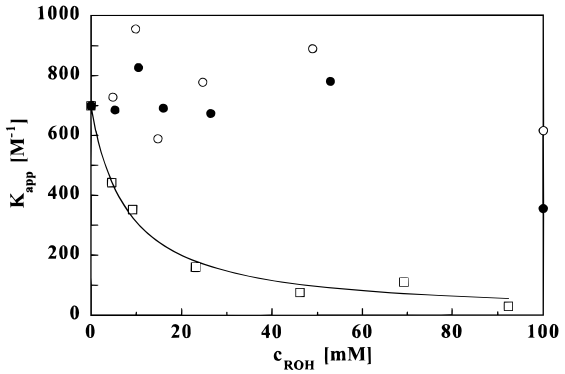


Figure 3. Variation of K_{app} as a function of alcohol concentration for (○) methanol, (●) propanol, and (□) pentanol.

TABLE 1: Apparant Association Constants, K_{app}, Determined by Eq 8 for the Formation of the 1:1 Complex between 2-Naphthol and Aqueous β-Cyclodextrin in the Presence of Different Linear Alcohols

	[ROH] (mM)	K_{app} (M^{-1})
water	0	699
methanol	4.8	729
	9.9	956
	14.8	859
	24.7	778
	49	890
	100	616
ethanol	100	458
propanol	5.3	686
	10.5	827
	16	692
	26.5	674
	53	781
	100	356
butanol	100	235
pentanol	4.6	442
	9.2	352
	23.1	160
	46.2	76
	92.4	30

The K_{app} values can be used to obtain the binding constants of the alcohols to β-CD if they are estimated at different alcohol concentrations. In principle three equilibria must be considered, each described by its own equilibrium constant: K_1 (eq 2), K_2 (eq 4), and K_3 (eq 5). The relation between K_{app} and these three equilibrum constants is given by[28]

$$K_{\text{app}} = \frac{K_1 + K_2K_3[\text{ROH}]}{1 + K_2[\text{ROH}]} \tag{9}$$

K_1 is the equilibrium constant for binding of NOH to β-CD in the absence of alcohols and can be determined independently. We prefer, however, to use it as a variable which provides an internal check of the reliability of the fit.

Figure 3 shows K_{app} values for the β-CD−NOH system as a function of the concentration of methanol, propanol, and pentanol. The pentanol data were fitted by eq 9 as well as with a simplified version which does not include the possibility of reaction 5. Both models yielded excellent fits. The results are presented in Table 2. As the K_{app} values for methanol and

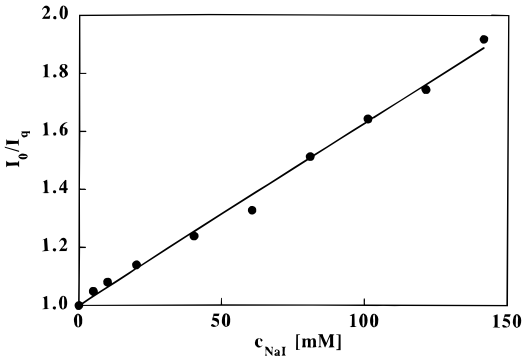


Figure 4. Stern−Volmer plot for iodide quenching of 2-naphthol fluorescence in water containing 6.5 mM β-cyclodextrin.

TABLE 2: Equilibrium Constants for the β-CD−NOH−Pentanol System Estimated by Fitting the Pentanol Data of Figure 3 by the Model of Eq 9

model	K_1 (M^{-1})	K_2 (M^{-1})	K_3 (M^{-1})	r^2
ternary	698 ± 15	106 ± 11	−45 ± 18	0.999
binary	704 ± 24	130 ± 14		0.996

TABLE 3: Stern−Volmer Constants, K_{SV}, for the Quenching of NOH Fluorescence at 354 nm by NaI in Aqueous Solution and in the Presence of Pentanol (Excitation at 310 nm; [NOH] = 0.1 mM)

[β-CD] (mM)		K_{SV}[a] (M^{-1})	fraction of NOH complexed with β-CD[b]
0.0	0	23.0 ± 0.7	0
0.5	0	20.0 ± 0.3	0.3
1.0	0	17.5 ± 0.2	0.4
2.0	0	11.5 ± 0.8	0.6
6.5	0	10.9 ± 0.7	0.8
11	0	11.6 ± 1.1	1.0
0	92.4 mM pentanol	23.9 ± 0.2	0
0.5	92.4 mM pentanol	22.3 ± 0.1	0.04
1.0	92.4 mM pentanol	21.5 ± 0.3	0.08
2.0	92.4 mM pentanol	21.2 ± 1.5	0.1
6.5	92.4 mM pentanol	12.2 ± 1.1	0.3

[a] K_{SV} values are averages of two or three determinations. [b] Calculated from apparent association constant values (Table 1).

propanol showed no significant variation with alcohol concentration, no attempt was made to fit these models to them (vide infra).

3.2. Quenching Studies. To further investigate the influence of alcohols on β-CD:NOH complexation a series of fluorescence quenching experiments were carried out. Iodide salts are often used to quench singlet excited states.[4,55] In the present case NaI was used to quench the fluorescence of NOH in a series of aqueous β-CD:NOH:pentanol systems. The samples were excited at 310 nm, and the emission was monitored at 354 nm. In each system linear Stern−Volmer plots were obtained (Figure 4). The resulting Stern−Volmer constants are presented in Table 3. The K_{SV} values in water and in 11 mM β-CD agree with values reported by Yorozu et al.[56]

The β-CD:NOH:pentanol systems were also investigated using dynamic fluorescence quenching. Figure 5 shows the fluorescence decay of NOH in the presence of β-CD, with and without added pentanol and at several different NaI concentrations. The fluorescence decay was monoexponential for an aqueous NOH solution and biexponential in all systems containing β-CD, corroborating the simplifications made in Scheme 1 to obtain Scheme 2. The biexponential decays consist of a shorter decay time (τ_S) and a longer decay time (τ_L). These fluorescence decay curves were analyzed globally as outlined above (eq 1). The first-order fluorescence decay constants ($k_1 = 1/\tau_S$; $k_2 = 1/\tau_L$) and the second-order constants of quenching for the processes in the bulk aqueous phase ($k_{q1} = k_{q,aq}$) and the β-CD environment ($k_{q2} = k_{q,CD}$) were thus obtained. The numerical results of the global fittings are presented in Table 4.

In general it is not possible to assign any decay time to a specific physical state of the system, as all observed decay rates will depend on all physical processes of the excited state.[13,57−59] Analysis of the fluorescence decay from an aqueous NOH solution, without β-CD, yields the decay rate to be associated with that fraction of NOH which is in the aqueous phase. The two observed decay times of the systems with β-CD present, however, cannot be associated with the aqueous or compartmentalized NOH, but are composite constants, including also the rates of deprotonation and the rates of the possible exclusion of NOH into the bulk from the β-CD cavity.

The value of the second-order rate constant for iodide quenching of NOH is reduced in the presence of β-CD. Such protective effects of cyclodextrins have been noted previously.[14,21,24,25,60] It is worthwhile to note that the aqueous phase NOH also appears to be quenched less efficiently when β-CD is present. This effect is most pronounced at higher β-CD concentrations and may reflect an association of iodide with the cyclodextrin cavity.[61] If NOH and I^- were mutually present in the β-CD cavity, this would lead to static quenching. As no sign of static quenching was detected in the steady-state fluorescence quenching experiments (see Figure 4), together with the fact that the association constant of I^- to β-CD is very small (18 M^{-1}),[61] we assume that only an insignificant amount of the iodide quencher is complexed. Therefore, no corrections of the quencher concentration were done for the evaluation of the time-resolved fluorescence quenching measurements.

3.3. Compartmental Analysis. From Table 4 it can be seen that the decay times change with the β-CD concentration. For a system like the present, it is then natural to apply compartmental analysis to the data. This method has been extensively described in the literature[13,37,57,59,62−65] and has proved its usefulness for the determination of excited-state rate constants in real systems.[66,67]

For a compartmental analysis, Scheme 2 can be rewritten as Scheme 3. In Scheme 3 the rate constants of deactivation from the excited states, k_{01} and k_{02}, are introduced as well as the rate constants for interconversion from the aqueous phase to the complexed state, k_{21}, the exclusion rate constant, k_{12}, and the two rate constants of quenching, k_{q1} and k_{q2}. From the discussions on Schemes 1 and 2, it follows that k_{01} and k_{02} will be composite rate constants also including the deprotonation of the excited state and the possible relaxation of NO^- in the aqueous phase and in the β-CD complex. This deactivation, however, can in this special case be treated as a pseudo nonradiative relaxation, even though NO^- does fluoresce, as at the monitoring wavelength only the protonated NOH emits and no reprotonation occurs in the excited state. Compartmental analysis allows the direct determination of the rate constants of interest.

For an intermolecular two-state system with an added fluorescence quencher, it has been shown that full identifiability is achieved if one of the rate constants of Scheme 3 is known a priori.[63] One requirement is that the decay times vary with the reactant concentration.[13] To obtain identifiability, the decay rate k_{01} as determined from aqueous NOH was used as an a priori known parameter. The presence of 0.1 M pentanol did not alter this decay time to a significant extent.

The results of the compartmental analysis are presented in Table 5. All fits showed good statistical parameters.

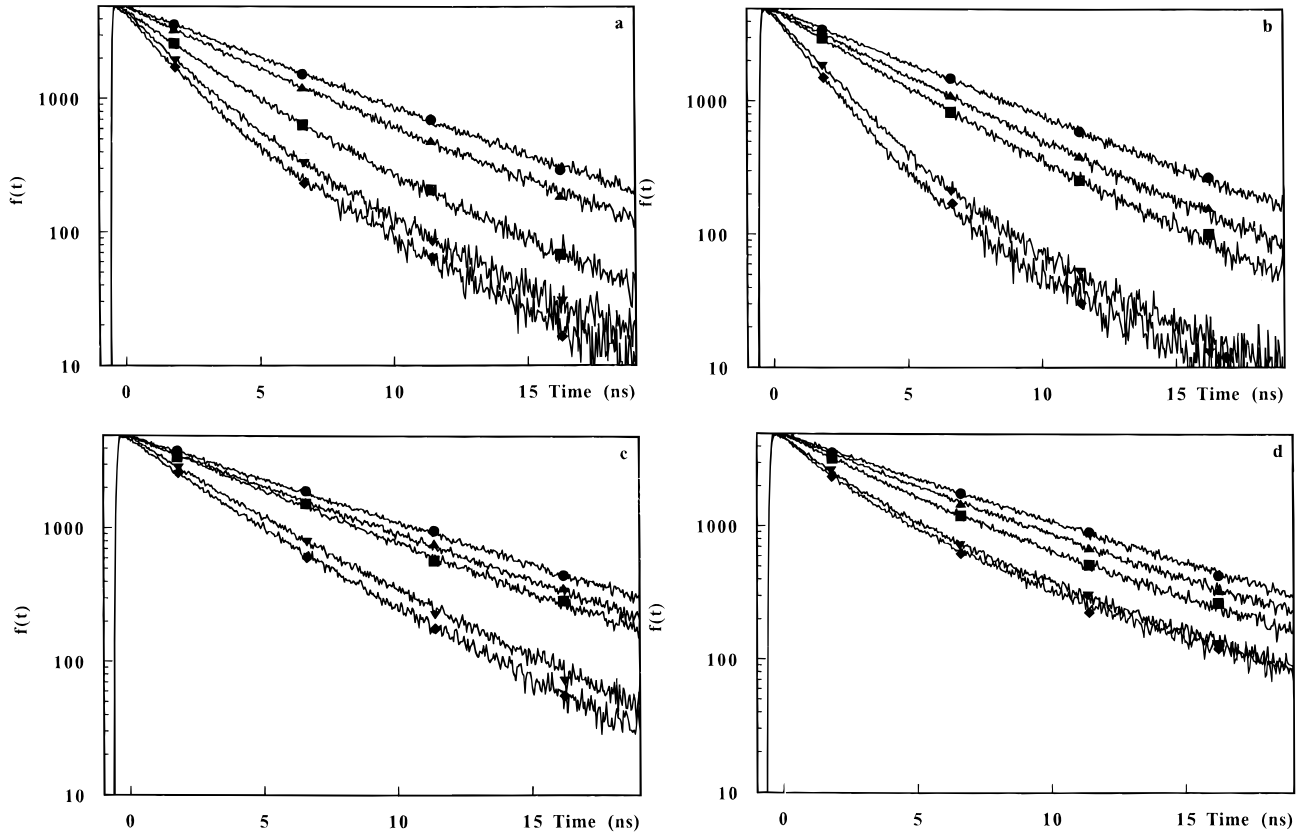


Figure 5. Fluorescence decays from NOH forming inclusion complexes with β-CD with and without added pentanol. **(a)** 0.5 mM β-CD. 0 mM NaI (●), 11 mM NaI (▲), 68 mM NaI (■), 76 mM NaI (▼), and 102 mM NaI (◆). **(b)** 0.5 mM β-CD and 0.1 M pentanol. 0 mM NaI (●), 11 mM NaI (▲), 25 mM NaI (■), 74 mM NaI (▼), and 99 mM NaI (◆). **(c)** 6.5 mM β-CD. 0 mM NaI (●), 11 mM NaI (▲), 25 mM NaI (■), 76 mM NaI (▼), and 101 mM NaI (◆). **(d)** 6.5 mM β-CD and 0.1 M pentanol. 0 mM NaI (●), 12 mM NaI (▲), 45 mM NaI (■), 79 mM NaI (▼), and 106 mM NaI (◆).

TABLE 4: First-Order Decay Times of NOH Fluorescence (τ) and Second-Order Rate Constants for NaI Quenching of NOH Fluorescence (k_q) in Various Environments as Determined by Global Biexponential Analysis According to Eq 1[a]

c_β-CD (mM)	[PentOH] (mM)	τ_S (ns)	$k_{q,aq}$ (10^9 M^{-1} s^{-1})	τ_L (ns)	$k_{q,CD}$ (10^9 M^{-1} s^{-1})	$\chi_\nu^{2\,b}$
0.0	0	5.3	4.4			1.12
0.5	0	4.2	4.0	6.8	1.0	1.01
2.0	0	5.2	3.2	9.6	1.3	1.11
6.5	0	4.6	2.6	7.6	1.1	1.00
0	92.4	5.3	4.5			1.09
0.5	92.4	4.7	4.4	6.2	0.6	1.10
2.0	92.4	4.5	3.7	7.0	0.5	1.04
6.5	92.4	4.4	2.6	7.7	0.3	1.06

[a] Total $c_{NOH} = 0.1$ mM. τ_S Refers to the shorter decay time and τ_L to the longer. See text for further explanations. [b] Reduced global χ^2.

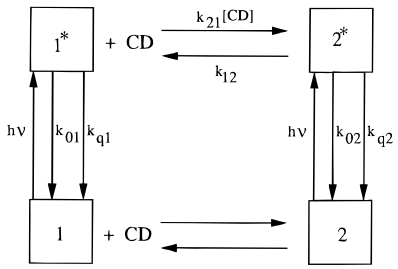
4. Discussion

It has been proposed that alcohols generally increase the binding of polyaromatic hydrocarbons (PAHs) to cyclodextrin cavities.[7,24,25,68] The enhancement in binding of PAHs when an alcohol is present is attributed to increased hydrophobicity of the CD cavity and formation of ternary CD:PAH:alcohol complexes. The strength of ternary complexes depends on the size and shape of the alcohol with larger and branched or cyclic alcohols yielding stronger complexes.[7,24] Formation of hydrogen bonds between the alcohol and the primary and secondary hydroxyl groups of the CD also plays a role.[25,69]

The present results show that a 1:1 complex forms between NOH and β-CD both in the presence and absence of linear alcohols. A 1:1 model fits the binding isotherm data excellently both in the absence and presence of alcohols. In addition, a detailed fluorescence study has shown that the emission spectrum of the 2:1 α-CD:NOH complex closely resembles that observed for NOH in pure alcohols.[35] No such spectral features were observed in the present systems. This establishes that in the present systems only 1:1 complexes are formed between β-CD and NOH.

Alcohols are known to be complexed by cyclodextrin cavities[1,25] and short linear alcohols form 1:1 complexes.[1] In contrast to reports[7,24,25,27] on other types of guest molecules, it is found that the apparent equilibrium constants (Table 1) for association of ground-state 2-naphthol with β-CD decrease in the presence of linear alcohols and that the decrease is in direct

SCHEME 3: Schematic Picture of an Intermolecular Bicompartmental System with Added Quencher[a]



[a] Ground-state species 1 and 2 form a reversible equilibrium described by the inclusion complex formation constant *K*. Excitation by light creates the excited-state species 1* and 2*, which can decay by fluorescence, internal conversion, and intersystem crossing and via other nonradiative pathways with composite rate constants k_{01} and k_{02}, respectively. The second-order rate constant describing the transformation 1* + β-CD → 2* is represented by k_{21}, whereas k_{12} characterizes the first-order dissociation 2* → 1* + β-CD.

TABLE 5: Results from the Compartmental Analysis Performed on the NOH Fluorescence Decay Data with Added Quencher in the Absence and Presence (0.1 M) of Pentanol[a]

k_{01} (10^8 s^{-1})	k_{21} (10^9 M^{-1} s^{-1})	k_{q1} (10^9 M^{-1} s^{-1})	k_{02} (10^8 s^{-1})	k_{12} (s^{-1})	k_{q2} (10^9 M^{-1} s^{-1})	$\chi_\nu^{2\,b}$
Without Added Pentanol						
1.88[c]	2.5 ± 0.8	3.3 ± 0.1	1.29 ± 0.02	522 ± 37	1.2 ± 0.1	1.12
With Added Pentanol, c_{PentOH} = 92.4 mM						
1.88[c]	5.8 ± 0.5	4.0 ± 0.1	1.30 ± 0.10	14027 ± 1500	0.52 ± 0.02	1.11

[a] See Scheme 3 for the definitions of the rate constants. k_{01} was held constant at the value obtained from an aqueous NOH solution without β-CD, $k_{01} = 1.88 \times 10^8$ s^{-1} (τ_{01} = 5.3 ns, Table 4). [b] Reduced global χ^2. [c] Held constant in the fittings.

proportion to the alcohol chain length. We propose a competition between NOH and the alcohol for the β-CD cavity to explain these observations. The excess alcohol either displaces the NOH into the aqueous phase or prevents aqueous NOH from being complexed. This would lead to a reduction in the quantum yield of fluorescence from the protonated form of the naphthol and a lower measured association constant. A correlation with alcohol size would also be expected. All the alcohols examined here bind to the β-CD cavity, and their binding constants increase monotonically with increasing chain length.[70] Thus, increased displacement of NOH would be reasonable for the longer alcohols used.

The influence of the alcohol chain length on the value of K_{app} is informative in this context. For methanol and propanol no significant variation in K_{app} is observed up to alcohol concentrations of about 50 mM (Figure 3). At 100 mM alcohol a slight decrease is found for propanol while K_{app} remains essentially unchanged for methanol. In contrast, the pentanol concentration has a very pronounced effect on K_{app}. As seen in Table 2, the pentanol results can be well fit by a model involving two or three equilibria. The latter model involves formation of ternary β-CD:NOH:ROH complexes. This model leads, however, to the nonphysical situation of generating an equilibrium constant with a negative value. The model involving two equilibria (reactions 2 and 4) yields more reasonable equilibrium constant values. We thus propose that the interactions in the β-CD−naphthol−alcohol systems do not result in formation of ternary complexes.

It should be pointed out that the value of K_2 determined in the present study is roughly twice that reported in the literature.[70] This likely reflects the different assumptions and approximations made in the evaluation of K_2 in the present work and in the earlier report.

The strength of the binding of methanol, propanol, and pentanol to the β-CD cavity increases with increaseing chain length. Literature values for the binding constants for these alcohols are 0.32, 3.7, and 63 M^{-1}, respectively.[70] If no ternary complexes are being formed, K_{app} should be directly related to the amount of β-CD not forming an inclusion complex with the alcohol. This amount of the total β-CD is thus avaiable for complexation of NOH and can be expressed as $[\beta\text{-CD}]_{available} = [1/(1 + K_2[ROH])][\beta\text{-CD}]_{tot}$. Using this approach we estimate that even at the highest methanol concentration tested only about 3% of the β-CD cavities contain methanol. That is, 97% of the total β-CD is available to complex the naphthol. For propanol, the amount of β-CD containing alcohol becomes significant only above 50 mM propanol. At 100 mM, for example, 27% of the β-CD cavities are associated with an alcohol. For pentanol, on the other hand, 24% of the total β-CD contain an alcohol at just 5 mM added pentanol. The values of K_{app} obtained at this pentanol concentration and in the presence of 100 mM propanol are essentially equal (Figure 3). Evidently the presence of an alcohol in the β-CD cage prevents complexation of NOH, at least for propanol and longer chain linear alcohols.

To try and strengthen the proposition that alcohols cause redistribution of NOH into the aqueous phase, the quenching experiments summarized in Tables 3−5 were carried out. β-CD alone reduces the Stern−Volmer constant for iodide quenching of NOH fluorescence (Table 3). Compartmental analysis (Tables 4 and 5) shows that the quenching of complexed NOH by iodide is much less efficient than the quenching of the bulk phase dissolved probe. This is as expected for a situation where the cyclodextrin cavity acts as a shield against contact between NOH and the quencher. If alcohols are in fact displacing NOH from the β-CD cavity into the aqueous phase, this should then be reflected by more efficient quenching in solutions containing both β-CD and alcohol. In the absence and presence of pentanol the K_{SV} values correlate rather well with the fraction of total NOH bound to the β-CD cavity as estimated from the association constants. As the degree of binding increases, K_{SV} becomes smaller. Once 30−40% of the NOH is bound K_{SV} reaches a minimum value close to 12 M^{-1}. This trend in K_{SV} with extent of complexation is attributed to a marked decrease in the rate constant for quenching of complexed NOH relative to uncomplexed. These observations confirm that the alcohols increase the aqueous concentration of NOH.

From the compartmental analysis (Table 5), it can be seen that the main reason for the change in distribution of NOH between the aqueous bulk and the β-CD cavity upon addition of alcohol is a change in the relative magnitude of k_{21} and k_{12} (Scheme 3). Addition of pentanol to the aqueous β-CD:NOH system causes the exit rate constant, k_{12}, to increase. Similar results have been reported in other systems.[28] This increase in the exit rate constant leads to a much less efficient inclusion of the probe in the cyclodextrin cavity with subsequent change in the distribution. A situation is therefore visualized in which alcohols are complexed by the β-CD cavity, making complexation of NOH relatively unfavorable. The effect is stronger for longer chain alcohols which are more strongly complexed[70] and which fill more of the cavity space.

It would appear, then, that displacement of naphthalene derivatives from β-CD cavities by linear alkyl chains may be a general feature of the interaction of such "third parties" with β-CD:naphthalene complexes.

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