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Exciplex Fluorescence in Inclusion Complexes of Naphthalene Derivatives

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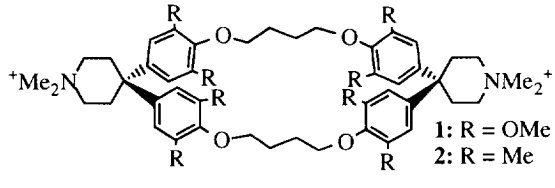
Abstract: Electronic excitation of compounds **3**-**5** complexed within the cavity of cyclophane **1** in aqueous solution produces host-guest exciplexes fluorescing at 420 nm. When cyclophane **2** is employed, the complexed guests fluoresce only as monomers. The ratio of exciplex vs. complexed monomer fluorescence is influenced by steric interactions between the host and complexed guest.

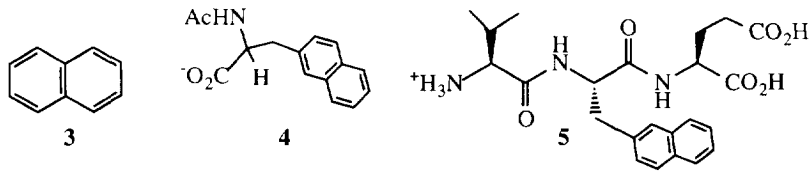
Cyclophanes **1** and **2**, and related macrocycles, have been studied as receptors for aromatic molecules.[1] The resultant supramolecular complexes are stabilized by a combination of π-stacking and edge-to-face dipolar interactions between the guest and the aromatic walls of the cyclophane. Binding is enthalpically driven in



1: R = OMe
2: R = Me

aqueous and in organic media, but is partially counteracted by a large unfavorable entropic term.[2] Reported studies of **1** have centered on complexation of benzene derivatives in aqueous solution[3] and of naphthalene derivatives in organic solvents[4] using ^1H NMR methods. Naphthalene derivatives in aqueous solution have been studied using hosts related to **2**, mainly by fluorescence techniques.[5] In the reported fluorescence studies, fluorescence enhancement of bound guest was observed, resulting from selective excitation of bound guest[5] combined with a decrease in fluorescence quenching by dioxygen.[5,6] No reports have appeared in which binding of aromatic amino acids or peptides has been examined by this class of synthetic receptors.

We report herein initial results of binding studies with hosts **1** and **2** and the guests naphthalene (**3**), (D,L)-N-acetyl β-naphthylalanine (**4**),[7] and the tripeptide **5**[8] which contains (L)-β-naphthylalanine[7] as its central residue. The overall goal in this project is to investigate complexation processes in which interactions external to the cyclophane cavity are involved, such as hydrophobic interactions between the valine and glutamate side chains of **5** and the exterior surface of the cyclophane, as well as ionic forces between guest carboxylates and the quaternary ammonium centers of the host.



3 4 5

For fluorescence titrations with **1**, excitation was feasible only at $\lambda \geq 300$ nm due to strong absorption by **1** at shorter wavelengths. Fortunately, **3** absorbs light to ca. 320 nm, albeit very weakly at $\lambda \geq 300$. A titration of naphthalene (14 μM)[9] with **1** (12.1 μM - 391 μM) in water is shown in Figure 1a, with excitation at 300 nm. A large decrease in fluorescence intensity of **3** was observed as [**1**] increased, exhibiting saturation behavior. Simultaneously, a broad, featureless fluorescence signal centered near 420 nm (F_{420}) appeared, suggesting the involvement of an excited state complex (exciplex).[10] Neither **3** nor **1** fluoresces at this wavelength, although very weak fluorescence for **1** was observed, centered near 390 nm. To our knowledge this represents the first observation of exciplex fluorescence in a host-guest inclusion complex.

A plot of δF_{420} vs. [**1**] at 298K, analyzed by non-linear regression analysis,[11] gave a binding constant of 6.1 kcal mol^{-1} (K_a = 28,000) (Table 1). The same value was calculated by plotting decrease in monomer fluorescence vs. [**1**]. The tremendous reduction of monomer fluorescence under conditions of saturation binding indicates that a large fraction of excited state, complexed naphthalene molecules fluoresce as exciplexes. Exciplex emission from a complex of **1** and **3** was also observed when methanol was used as solvent (data not shown), although binding in this solvent is too weak to allow measurement of K_a by this method. In methanol, λ_{max} shifts to ca. 380 nm, indicative of charge-transfer character in the exciplex.[12]

With guests **4** ([**4**] = 50 μM; [**1**] = 15 μM - 219 μM) and **5** ([**5**] = 50 μM; [**1**] = 22 μM - 652 μM), exciplex fluorescence was observed as well, although fluorescence titrations differed from those recorded for **3**. With **4**, enhancement of both monomer fluorescence and appearance of exciplex fluorescence occurred during the titration (Figure 1b). The exciplex fluorescence was of lower intensity with **4** than with **3** under saturation conditions. Exciplex fluorescence from complexes of **5** was even weaker than with **4**, although monomer fluorescence again decreased with increasing [**1**] (Figure 1c).

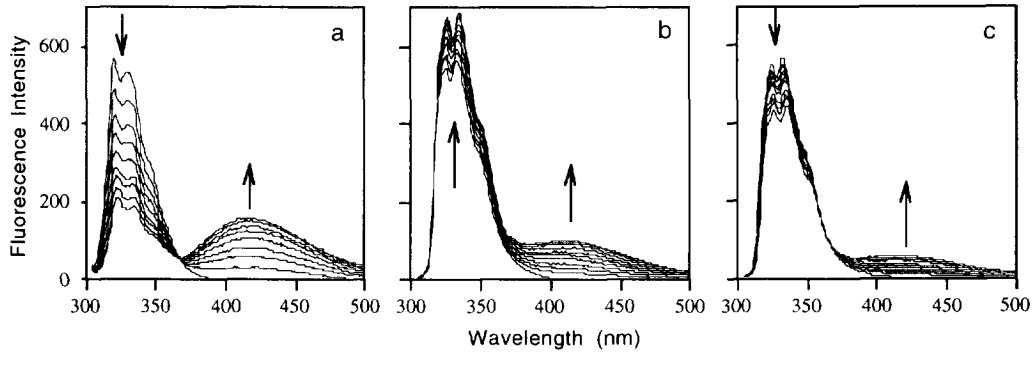


Figure 1. Fluorescence titrations of **3** (a), **4** (b), and **5** (c) with cyclophane **1** at 298 K. In each titration guest concentration remains constant and the cyclophane concentration is varied. See text for details.

Interestingly, complexes of **3**, **4** and **5** with host **2** exhibited only monomer fluorescence (data not shown). A full titration was not possible due to aggregation of host **2** above 20 μM concentration.[1] Fluorescence intensity in this case nearly doubled for each guest as [**2**] was increased, consistent with previously reported fluorescence titrations with a related cyclophane.[5]

Thermodynamic parameters for binding of guests **3-5** with cyclophane **1** are shown in Table 1. ΔH° and ΔS° for **4** and **5** have been determined by van't Hoff analysis of data recorded between 293 and 313 K. Limited solubility of **3** in water[9] led to uncertainty in concentration determination, and thus ΔG° reported for this guest must be regarded as an approximation. As expected,[2] binding is enthalpically favored and entropically disfavored for the other two guests.

Table 1. Thermodynamic Parameters for Complexation of Guests **3-5** by Cyclophane **1** at 298K

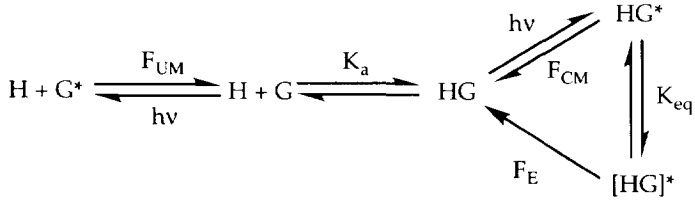
Guest	K_a (L mol^{-1})	$-\Delta G^\circ$ (kcal mol^{-1})	$-\Delta H^\circ$ (kcal mol^{-1})	$T\Delta S^\circ$ (kcal mol^{-1})	F_{CM}/F_E[a]
3	28,000[b]	6.1[b]	-	-	1.1
4[c]	71,000	6.6	13.1	-6.5	7.0
5	14,780	5.7	12.6	-6.9	7.2

a) Ratio of complexed monomer fluorescence to exciplex fluorescence at saturation

b) Approximate value; see reference 9. Other K_a's are accurate to ± 10%

c) 10 mM potassium phosphate buffer, pH 6.8. All other titrations were done in water.

As saturation binding is approached (high ratio of H/G), most guest molecules are complexed within a host cavity. Upon electronic excitation of a complexed guest, three processes can occur (eq. 1): 1) complexed monomer fluorescence (F_{CM}); 2) association of the excited naphthalene with the aromatic walls of the host to form an exciplex which subsequently fluoresces (F_E); and 3) non-radiative decay. Excited state complexed monomer (HG*) and the exciplex ([HG*]) are related by K_{eq} in eq. I (K_{eq} = ([HG*])/(HG*), which is proportional to F_E/F_{CM}). For **3**, K_{eq} is large. For titrations of all three guests with **1** performed at higher temperatures, the ratio F_E/F_{CM} decreases, consistent with an expected decrease in K_{eq}.



(I)

The absence of exciplex formation in **2** derives primarily from the greater steric bulk of the methyl substituents in **2** vs. the methoxy groups in **1**,[13] similar to effects previously reported for excimers of substituted benzenes.[14] Close approach of the π-system of the guest to the aromatic walls of the host, required for efficient exciplex formation, is not attainable with **2** (K_{eq} equals zero). A similar effect may operate in complexes of **4** and **5** due to the presence of substituents on the naphthalene β-position. Different modes of binding may also be important. The various factors which contribute to exciplex fluorescence in **1** is the subject of ongoing efforts, as is the study of biologically relevant fluorescent species such as indoles and phenols.

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