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Specific Cage Effects Provided by Kyuphane on Guest Recognition in Aqueous Media

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The fluorescence of α-PNA placed in Kyuphane was quenched by ketones incorporated into the same host cavity. A metastable 1:2 Kyuphane–pyrene complex initially formed was transformed into a thermodynamically stable 1:1 species as confirmed by fluorescence spectroscopy with attention to the monomer and excimer emission originated from pyrene.

In view of current interest in host–guest chemistry, molecular recognition by various cyclophane derivatives has been examined in aqueous media.[1] Cyclophane hosts, which provide a three-dimensionally extended hydrophobic cavity, have been shown to be much superior in guest recognition capability to macrocycles with a single skeleton that furnishes only a shallow cavity.[2] Such extended internal cavities seem to execute molecular recognition toward various guests through the lock-and-key mechanism. In most cases, however, the internal cavities are not well shielded from an external aqueous medium for efficient host–guest interactions of hydrophobic, electrostatic, and hydrogen-bonding modes. In this context, we now report the unique guest recognition ability of a novel host (**1**), whose internal cavity is considerably shielded from external aqueous media.[3] Host **1**, under the name of Kyuphane,[4] furnishes a relatively rigid and large hydrophobic cavity surrounded by six faces each consisting of a 2,11,20,29-tetraaza[3.3.3.3]paracyclophane ring. The corresponding non-cage host (**2**) has also been used as a reference with which to contrast the specific molecular recognition features of **1**. Compounds **1** and **2** were prepared after procedures reported previously.[4]

We examined quenching of the α-PNA fluorescence by ketones on the basis of Stern-Volmer plots. The lifetime ratios, τ_0/τ, where τ_0 and τ are lifetimes observed in the absence and presence of a quencher, respectively, were independent of quencher concentrations. This indicates that the quenching process takes place exclusively in the host cavity; a static process. Addition of various ketones to aqueous solutions containing Kyuphane and α-PNA resulted in reduction of the fluorescence intensity at 400 nm originated from α-PNA. Since the fluorescence quenching[5] occurs through the static process, the Stern-Volmer constant (K_{SV}) for association of a quencher

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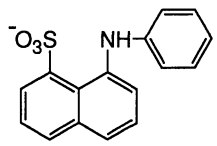
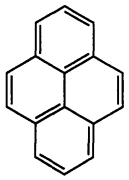
with the Kyuphane–α-PNA complex is given:[6] $I_0/I = I + K_{SV}[Q]$, where I_0 and I are fluorescence intensities in the absence and presence of a quencher, respectively, and [Q] is a quencher con-

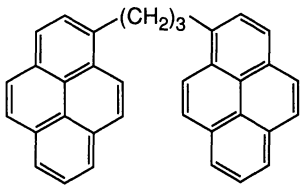
Guest molecules



α-PNA

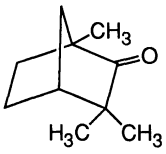


Pyrene

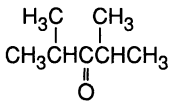


PC_3P

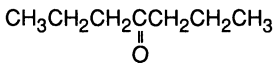
Quencher molecules



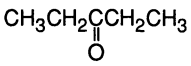
L-(-)-Fenchone



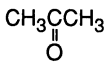
Diisopropyl ketone



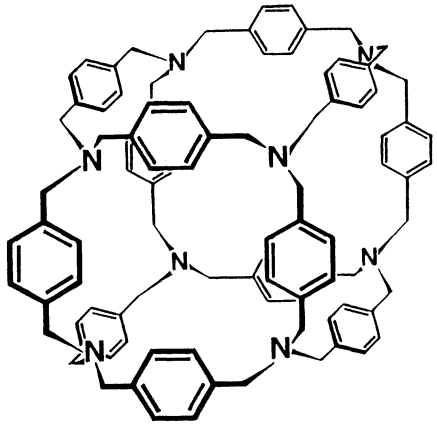
Dipropyl ketone



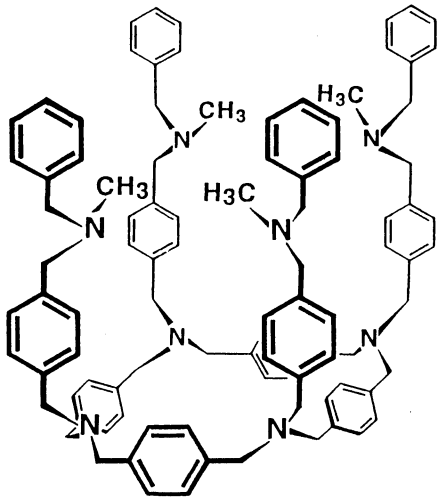
Diethyl ketone



Acetone



1



2

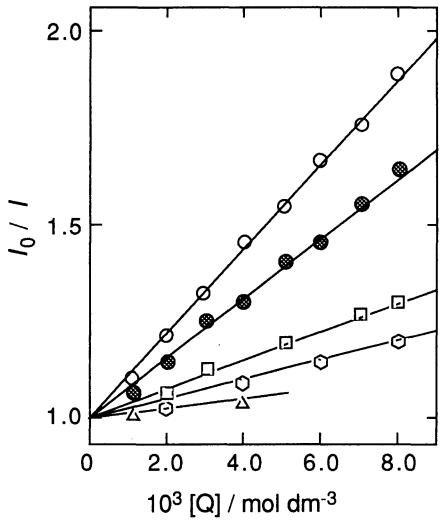


Fig. 1. Stern-Volmer Plots
Quenchers: ○, diethyl ketone; ◉, dipropyl ketone; □, diisopropyl ketone; ⬡, acetone; △, L-(-)-fenchone. Concentrations in mol dm^{-3}; α-PNA, 1.0×10^{-6}; Kyuphane, 1.0×10^{-5}.

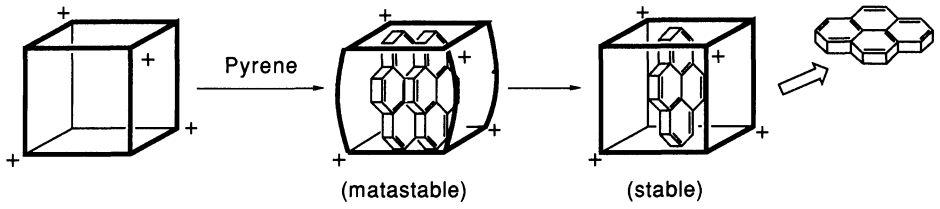
Table 1. Stern-Volmer Constants (K_{SV}) and Formation Constants (K_t) for 1:1:1 Complexes Formed with Kyuphane, α-PNA, and Ketones[a)]

Ketone	K_{SV} / dm^3 mol^{-1}	K_t / dm^6 mol^{-2}
L-(-)-Fenchone	12	1.1×10^6
Diisopropyl ketone	35	3.1×10^6
Dipropyl ketone	83	7.3×10^6
Diethyl ketone	118	1.1×10^7
Acetone	22	1.9×10^6

a) Measured in acetate buffer [0.01 mol dm^{-3}, pH 4.0, μ 0.10 (KCl)] at 30.0 °C.

centration. The K_{SV} value (Table 1 and Fig. 1) is correlated with the formation constant for the 1:1 Kyuphane–α-PNA complex (K_b= 8.8 x 10^4 dm^3 mol^{-1} in aqueous media at 30.0 °C and μ 0.10)[10] and the formation constant for the 1:1:1 Kyuphane–α-PNA–quencher complex, K_t, as follows: $K_t = K_b \times K_{SV}$. The K_{SV} value decreases in the following order with respect to the ketones having various molecular bulkiness: diethyl ketone > dipropyl ketone > diisopropyl ketone > acetone > L-fenchone. This result indicates that diethyl ketone, among various ketones used here, fits most tightly in the residual space of the Kyuphane cavity which is already occupied by α-PNA.

When an aqueous stock solution of Kyuphane was injected into an aqueous acetate buffer (pH 4.0; Kyuphane in the tetracationic state) containing an equimolar amount (1.0 x 10^{-6} mol dm^{-3}) of pyrene, a normal 1:1 complexation took place under ordinary fluorescence-monitoring conditions; the binding constant being 5.6 x 10^3 dm^3 mol^{-1} at 30.0 °C and μ 0.10. In a marked contrast, the excimer emission immediately appeared at 470 nm upon addition of an ethanolic stock solution of pyrene in the aqueous buffer containing an equimolar amount (1.0 x 10^{-6} mol



Scheme 1.

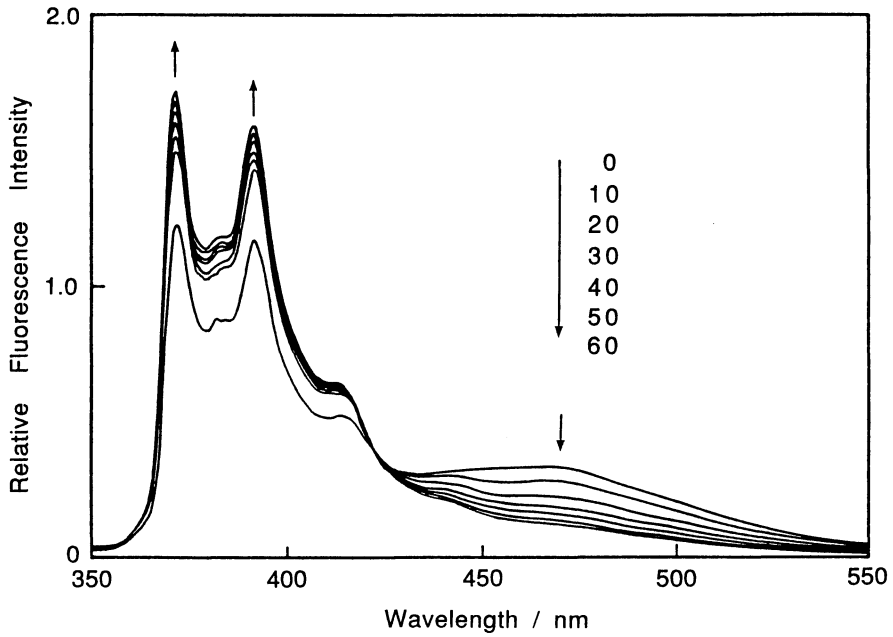


Fig. 2. Fluorescence spectral change for pyrene injected as an ethanolic stock solution into an aqueous buffer containing Kyuphane at 30.0 °C; 2.0 μL of a stock solution of Kyuphane (1.0 x 10^{-3} mol dm^{-3}) in 1.0 mol dm^{-3} HCl–methanol (1:1 v/v) was added to 2.0 mL of an aqueous acetate buffer (1.0 x 10^{-3} mol dm^{-3}, μ 0.10 with KCl), and then 2.0 μL of an ethanolic stock of pyrene (1.0 x 10^{-3} mol dm^{-3}) was added to the resulting solution to observe fluorescene change. Numerals refer to incubation time in min after addition of pyrene.

dm^{-3}) of Kyuphane. The excimer emission then gradually faded and completely disappeared after about 1 h along with enhancement of the monomer emission (Fig. 2). The time-dependent host–guest interaction in the latter case must come from formation of a transient and metastable 1:2 host–guest complex, followed by liberation of one guest molecule from the host cavity (Scheme 1). An analogous time-dependent fluorescence change was not observed when pyrene was added to non-cage host **2**. To examine the state of affair, the complexation of Kyuphane with a covalently bound pyrene dimer, 1,3-di(1-pyrenyl)propane (PC_3P), was studied similarly. In a mixed medium composed of aqueous acetate buffer (0.01 mol dm^{-3}, μ 0.10 with KCl, pH 4.0) and ethanol at a 1:1 volume ratio, PC_3P upon excitation formed an intramolecular excimer at a very low concentration (1.0×10^{-7} mol dm^{-3}) in a manner similar to that reported by Diederich et al.[7] Upon addition of Kyuphane, the excimer emission faded with concomitant enhancement of the monomer emission arising from one of the two pyrenyl moieties. When the concentration of Kyuphane reached 7.3×10^{-6} mol dm^{-3}, the excimer emission completely disappeared and only fluorescence from the single pyrenyl moiety was observed. On the other hand, an attempt to quench the PC_3P excimer emission with **2** was failed even in the presence of a large excess of the host (2.0×10^{-5} mol dm^{-3}). The results indicate that Kyuphane captures one of the two covalently bound aromatic groups to inhibit the intramolecular pyrene-to-pyrene interaction, while non-cage host **2** includes the whole molecule of PC_3P due to the flexible structure of the host.

In conclusion, the constrained but somewhat flexible hydrophobic internal cavity provided by Kyuphane exhibits size-sensitive binding behavior toward ketones after incorporation of α-PNA and a unique time-dependent complexation with pyrene as well.

References

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