Visualization of Molecular Length of α,ω-Diamines and Temperature by a Receptor Based on Phenolphthalein and Crown Ether

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Supramolecular chemistry and/or host−guest chemistry based on molecular recognition has become attractive not only for organic chemists but also for researchers in other academic fields, and remarkable progress has recently been made in this area.[1] The recognition of various attributes of guest molecules, such as size,[2] length,[3] and chirality[4] has been studied previously. If the weak signals derived from such molecular interaction could be transformed into visual information, more information could be directly available. Some dyes have the ability to selectively capture metal cations, and thereby undergo a color change,[5] and are used practically as sensors.[6] In addition, color-producing molecules which can differentiate enantiomers have recently been reported.[7] In this paper, we report for the first time visual determination of the chain length of linear diamines using a functional molecule **1**[8] consisting of phenolphthalein (**3**) and two loops of crown ether. Visualization of the "length" of a guest molecule as well as "temperature" is possible using **1**.

Interactions of host compounds (**1** and **2**) and phenolphthalein (**3**) with a terminal diamine **4** ($n = 8$) and nonylamine (**5**) were examined by taking UV−visible spectra in MeOH at 25 °C (Figure 1). While diamine **4** ($n = 8$) developed no color change with **3**, a slight color change was observed with **2**. In contrast, dramatic color change was seen with compound **1**. The change in color depends on the length of the diamine (Figure 2a, b). The color development by **1** and amines was greatest with guest diamines of $n = 8$ and 9. Diamines shorter than 1,5-diaminopentane gave no coloration that could be detected by the naked eye.

The degree of color development by **1** and diamines **4** is quite sensitive to temperature. The absorbance at 571 nm by the complex of **1** and diamine **4** ($n = 9$) decreases with a rise in temperature. The reversibility and reproducibility of this change were confirmed as follows. The temperature of the mixture was gradually increased from 20 to 50 °C over 30 min and then dropped to 20 °C over another 30 min. This temperature profile was repeated more than 10 times while monitoring the UV−visible spectrum at 571 nm (Figure 3). In the ^{1}H NMR spectrum of the complex, the signal of the α-methylene of the diamine at δ 2.47 ppm was broad at 22 °C, but sharpened to a triplet at 60 °C (Supporting Information). These experiments show that the diamine **4** ($n = 9$) dissociates from the host molecule **1** to show free rotation at a higher temperature. Thus, color development due to complex formation reflects changes in temperature.

To better understand the above phenomena, the structure of the colored complex of **1** and diamine **4** ($n = 9$) was investigated in detail. The values of pK_a1′ and pK_a2′ in 50% aqueous methanol at 30 °C were 10.4 and 11.1 for **1**, and 9.6 and 11.3 for **3**.[9] These data suggest that there is no correlation between the coloration of **1** and the difference in pK_a′ values. Tamura and co-workers[10]

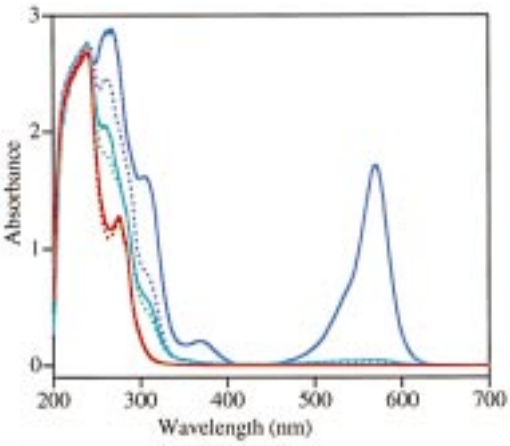

Figure 1. UV−visible spectra of **1** (blue), **2** (green), and **3** (red) with the diamine **4** ($n = 8$) (solid lines) and with nonylamine (**5**) (dotted lines) in MeOH at 25.0 ± 0.1 °C. The concentrations are 2.5×10^{-4} M for the hosts and 2.5×10^{-3} M for the guests.

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(8) For the synthesis of **1** and **2**, see Supporting Information.

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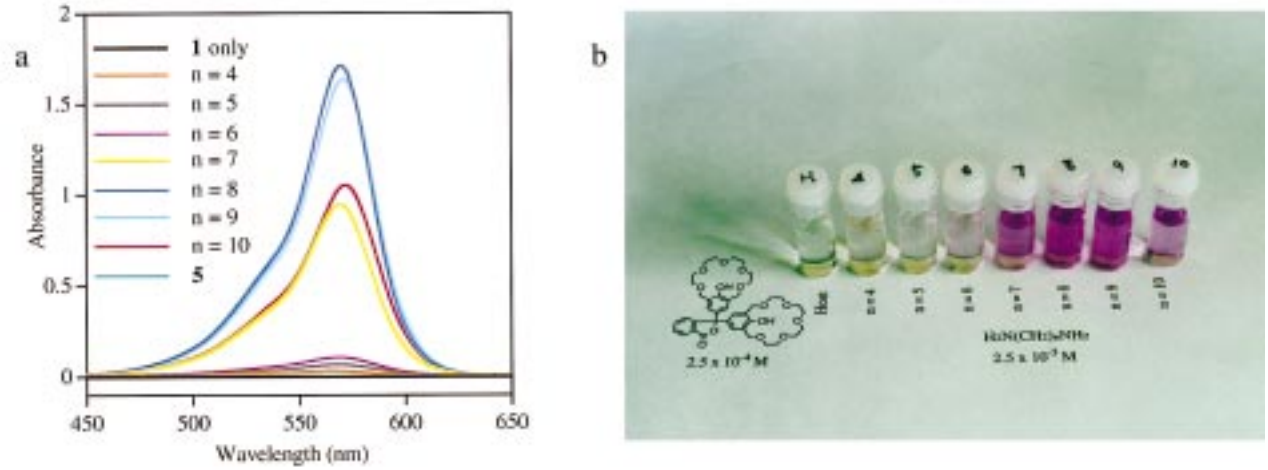

Figure 2. (a) UV−visible spectrum of **1** with the diamines **4** in MeOH. The concentration of **1** was 2.5×10^{-4} M and those of diamines **4** and nonylamine (**5**) were 2.5×10^{-3} and 5.0×10^{-3} M, respectively. (b) Visible difference between diamines **4** ($n = 4-10$).

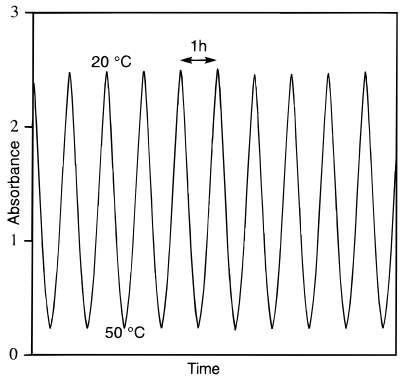

Figure 3. Temperature dependence of the absorbance of **1** (5.0×10^{-4} M) in the presence of **4** ($n = 9$, 1.0×10^{-3} M) at 571 nm in MeOH.

reported that the colored complex of phenolphthalein (**3**) exists in a dianionic form. The colored complex of **1** and diamines is also considered a dianion. A Job plot using UV−visible spectra suggested that the host−guest ratio in the colored complex of **1** and diamine **4** ($n = 9$) was not 1:1, but rather 1:2, 2:3, or some intermediate ratio (Figure S-1, b).[11] These findings, as well as the characteristic red shift, indicate that one molecule of the diamine is bridged between two crown rings and the other serves as a countercation of the carboxylate, derived from ring-opening of the γ-lactone of **1**, in the 1:2 colored complex (complex **a** in Figure 4). An alternative complex **c** (**1**: diamine = 2:3), which may be in equilibrium with complex **a**, is possible, especially when the concentration of the amine is low. To overcome this uncertainty, a new system was designed in which a large excess of *N*-ethylpiperidine exists together with the diamine to act as a countercation for the carboxylate anion. *N*-Ethylpiperidine itself gave no color without a diamine. The Job plot of **1** and diamines **4** ($n = 7-10$) in the presence of *N*-ethylpiperidine clearly showed a 1:1 correlation between them (Figure S-1, a and c−e).[11] Thus, the colored complex consists of **1**, diamine, and *N*-ethylpiperidine

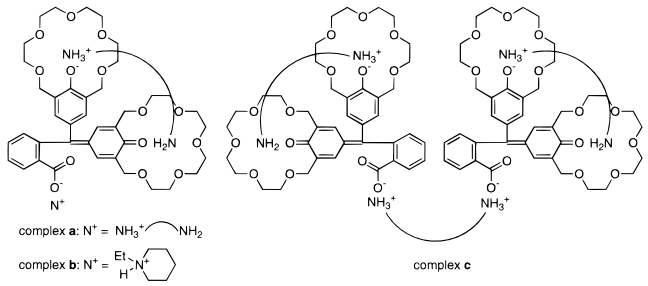

Figure 4. Proposed structures of complexes of **1** with diamine.

Table 1. The Apparent Association Constant (K') of the Complexes of **1** with diamines **4** and Molar Absorption Coefficients (ϵ)

diamine **4**	K' (M^{-1})	ϵ
$n = 7$	910 ± 60	5830 ± 120
$n = 8$	1270 ± 50	8930 ± 100
$n = 9$	2020 ± 100	7940 ± 130
$n = 10$	1370 ± 80	5280 ± 70

in the ratio of 1:1:1 in this system (complex **b** in Figure 4). Molecular mechanics calculations[12] of the complex **a** ($n = 9$ and $n = 5$) show that the match between the length of a guest molecule and the distance between the two crown ether moieties is important for the selectivity. The apparent association constant (K') of the complexes and molar absorption coefficients (ϵ) were determined by UV−visible titration and analyzed by the Rose−Drago method.[13,14] The results listed in Table 1 show that the degree of coloration caused by the interaction between **1** and diamines depends not only on the apparent association constants but also molar absorption coefficients.

In summary, **1** is an interesting host molecule that makes it possible to visualize molecular length on basis of the selective recognition of diamines. In addition, a change in temperature can be followed visually using **1**.

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Supporting Information Available: Experimental details for the preparation of **1** and **2**, variable temperature ^{1}H NMR spectra of the complex of **1** with diamine **4** ($n = 9$) and related spectra, crystal structure of **1**·AcOEt, the optimaized structures of the complex **a** ($n = 9$ and $n = 5$), and Figure S-1 (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) See Supporting Information for Figure S-1.

(12) The MacroModel/MM2 (version 4.5) force field was used. See Supporting Information for the most stable conformations of the complex **a** ($n = 9$) and that of $n = 5$.

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(14) The apparent association constants (K') were determined in the following manner. K= [complex]/[**1**] [diamine **4**] [*N*-ethylpiperidine] where [*N*-ethylpiperidine] ≫ [complex] and [**1**]. Thus, [*N*-ethylpiperidine] can be adequately approximated to constant ∴ $K' = K$[*N*-ethylpiperidine] = [complex]/[**1**] [diamine **4**].