

# $\text{Li}^+ \cdots \pi$ interaction in coronene–azacrown ether system

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**Abstract**—The combination of the coronene ring and azacrown ether generated a new kind of host molecule in which the  $\text{Li}^+$  binding ability originated from the cation–dipole interaction (crown moiety) and the cation– $\pi$  interaction (coronene ring). Introducing a large  $\pi$  face (coronene ring) enhanced cation binding ability of the crown ether. The NMR, the fluorescence spectra, and ab initio calculations strongly indicated the effect of the cation– $\pi$  interaction.

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The cation– $\pi$  interaction has been emphasized in recent chemistry as one of the important interactions in biological systems.<sup>1</sup> During the initial and important studies, the pure cation– $\pi$  interaction was observed under gas phase conditions, in which the reaction free energies of the benzene–alkali cations were estimated.<sup>2</sup>

However, under natural environment, in vivo or in vitro, several interactions, that is, hydrogen bond, electrostatic interaction, van der Waals interaction, etc., simultaneously operate besides the cation– $\pi$ . Moreover, cations are strongly solvated. Thus, it is still ambiguous whether the cation– $\pi$  effectively operates in the environment. Examples of studies of such kind were performed by Gokel et al. who tried to confirm whether aromatic amino acid units (phenylalanine, tyrosine, or tryptophan) act as cation donors.<sup>3</sup>

On the other point of view, we started to study the cation– $\pi$  interaction using large  $\pi$  system. According to the theoretical calculations, a  $\pi$  electron system larger than benzene interacts more strongly with cations than benzene.<sup>4</sup> Therefore, the cation– $\pi$  interaction in solution will be able to be observed using such a large  $\pi$  system.

In a previous report, we investigated the cation– $\pi$  interaction in solution using the pyrene-connected azacrown

ether.<sup>5</sup> Cation complexation of the compound resulted in overlap of the crown moiety and the pyrene ring. Therefore, the pyrene-connected azacrown ether is one of the simplest and most adequate systems used to observe the cation– $\pi$  interaction in solution. Because theoretical calculations of the polyaromatics– $\text{Li}^+$  system stimulated our interest,<sup>4a</sup> the pyrene–azacrown ether was extended to the coronene–azacrown ether system.

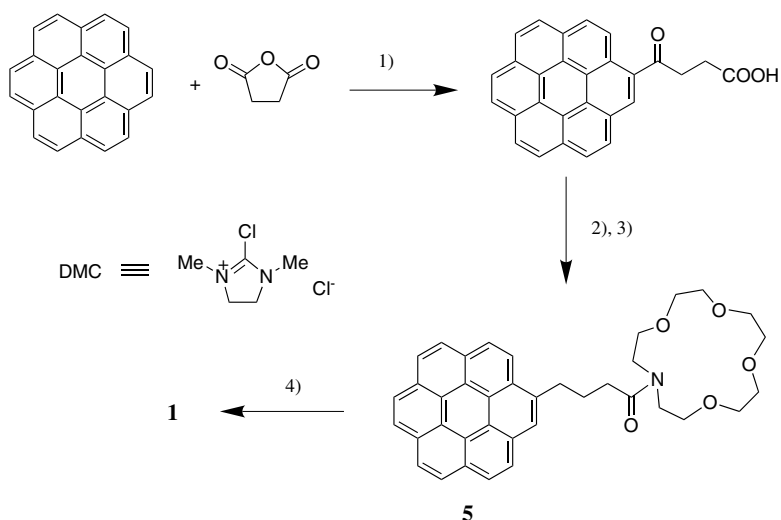
The synthesis of compound **1** was achieved as shown in Scheme 1. The starting 4-coronenyl butyric acid was prepared according to a literature method.<sup>6</sup> A coupling reaction between the 4-coronenyl butyric acid and azacrown-5 ether smoothly proceeded using 2-chloro-1,3-dimethylimidazolium chloride in the presence of triethylamine at room temperature. The resultant amide precursor **5** was reduced to compound **1** by the borane dimethyl sulfide complex. These compounds were fully characterized by the NMR, MS, and HR-MS spectra.

Compound **1** and its complexes ( $\text{Li}^+ \subset \mathbf{1} \cdot \text{ClO}_4^-$ ,  $\text{PF}_6^-$ ,  $\text{Pic}^-$ ,  $\text{Br}^-$ ) were solids but became viscous oils in the presence of very small amounts of solvents. Therefore, a crystallographic analysis could not be done. However, similar to that of the pyrene–azacrown system, the interaction was observed on the basis of their NMR spectra ( $^1\text{H}$ ,  $^{13}\text{C}$ , and  $^7\text{Li}$ ). The solubility of the metal-free compound **1** in  $\text{CD}_3\text{CN}$  was too low to obtain the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra, therefore, the NMR spectral changes were observed in  $\text{CDCl}_3$ . On the other hand, the stability constant determination in  $\text{CH}_3\text{CN}$  could be achieved because the solubility is sufficient to observe the fluorescence spectra in the

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**Scheme 1.** Synthesis of compound **1**. Reagents and conditions: (1)  $\text{AlCl}_3$ ,  $\text{C}_6\text{H}_5\text{NO}_2$ , (2)  $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$ , diethyleneglycol, (3) aza-15-crown-5, DMC,  $\text{Et}_3\text{N}$ , THF, (4)  $\text{Me}_2\text{S}\cdot\text{BH}_3$ , THF.

concentration range around  $10^{-6} \text{ mol dm}^{-3}$ . Also in this experiment, small amounts of  $\text{CHCl}_3$  (<5%) were used as a co-solvent for experimental availability.

In the  $^1\text{H}$  NMR, the signals of the  $-\text{O}-\text{CH}_2\text{CH}_2-\text{O}-$  and  $\text{CH}_2-\text{N}-\text{CH}_2$  protons of the azacrown ether moiety of **1** shifted to higher fields (+0.22–0.34 and +0.25 ppm, respectively), accompanied by complexation with  $\text{Li}^+$ . On the contrary, the  $\text{Ar}-\text{CH}_2-$  and  $(\text{Crown}-\text{N})-\text{CH}_2-$  protons shifted to lower fields (Table 1). In contrast to this phenomenon, the signals of the crown ether protons of *N*-butyl-aza-15-crown-5 (compound **2** in Fig. 1) shifted to a lower field (−0.1 ppm,  $\text{CDCl}_3$ ) by the complexation.<sup>5</sup>

In the  $^{13}\text{C}$  NMR spectra, the carbon signals of the ether moiety,  $-\text{O}-\text{CH}_2\text{CH}_2-\text{O}-$ ,  $-\text{CH}_2-\text{N}(\text{butyl})-\text{CH}_2-$ , and  $(\text{Crown}-\text{N})-\text{CH}_2-$  shifted to higher fields (+2.5–3.4, +2.7, and +5.7 ppm, respectively), by the complexation. On the contrary, the shifts of the aromatic protons and carbon signals were very small. The  $^{13}\text{C}$  signals of  $-\text{OCH}_2\text{CH}_2-\text{O}$  and  $-\text{CH}_2-\text{N}(\text{butyl})-\text{CH}_2-$  of the *N*-butyl-aza-15-crown-5 slightly shifted to higher fields by complexation (+1.65 and +1.31 to +0.36, respectively). In most cases in the crown ethers system, the  $^{13}\text{C}$  signals slightly shift to higher fields upon complexation.<sup>7</sup> However, in the case of  $\text{Li}^+ \subset \mathbf{1}$ , the shifts of the signals are greater than those of the crown ethers. Therefore, the up-field shift of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR signals of  $\text{Li}^+ \subset \mathbf{1}$  can be attributed to the effect of the aromatic ring current.

From these results, similar to the pyrene system (but slightly stronger), the azacrown ether unit was significantly affected by the ring current of the coronene ring after the complexation.

Therefore, it is considered that the crown moiety overlapped on the  $\pi$  plane by the  $\text{Li}^+$  complexation. For further confirmation of this assumption, the  $^7\text{Li}$  NMR spectra were observed. The  $^7\text{Li}$  signal of the  $\text{Li}^+ \subset \mathbf{1}$  appeared at −1.41 ppm ( $\text{CD}_3\text{CN}$ ,  $1.0 \text{ mol dm}^{-3}$   $\text{LiCl}$  in  $\text{D}_2\text{O}$  as the external standard), while the signal of the  $\text{Li}^+ \subset \text{N-butyl-aza-15-crown-5}$  appeared at −0.75 ppm. The higher field shift of the  $^7\text{Li}$  signal ( $\Delta\delta = 0.66 \text{ ppm}$ ) in  $\text{Li}^+ \subset \mathbf{1}$  apparently indicates that the  $\text{Li}^+$  cation locates above the coronene ring. In the previously reported pyrene–azacrown system, the  $^7\text{Li}$  signal of the complex appeared at −0.97 ppm. Therefore, the  $^7\text{Li}$  signal of the  $\text{Li}^+ \subset \mathbf{1}$  appeared at 0.44 ppm higher than that of the pyrene analog.

More evidence of the overlap of the crown moiety and coronene ring was proved by observation of the differential NOE spectra of the  $\text{Li}^+ \subset \mathbf{1}$ . Irradiation of the crown  $-\text{CH}_2-\text{O}$  and  $-\text{CH}_2-\text{N}(\text{butyl})-\text{CH}_2-$  resulted in the apparent enhancement of the proton signals of the coronene ring. Such NOE was not observed in the case of the  $\text{Li}^+$ -free ligand **1** (described in detail below).

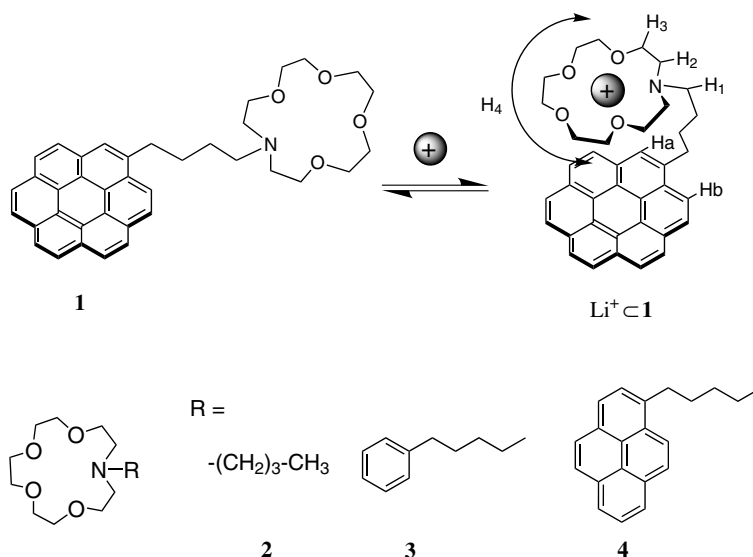
Similar to the NMR spectral changes, the fluorescent property of **1** was changed by the complexation. In the fluorescence titration experiments, the fluorescence

**Table 1.** Chemical shifts ( $^1\text{H}$  and  $^{13}\text{C}$ ) of crown moiety of **1** ( $\delta$ , ppm,  $\text{CDCl}_3$ , 25 °C)

		$-\text{CH}_2-\text{N}-\text{CH}_2-$	$(\text{Crown}-\text{N})-\text{CH}_2-$	$-\text{O}-\text{CH}_2\text{CH}_2-\text{O}-$	$\text{Ar}-\text{CH}_2-$
$^1\text{H}$	A	2.69 (t)	3.25 (t)	3.56, 3.54, 3.52, 3.50	2.54
	B	2.44 (t)	3.48 (t)	3.34, 3.22	2.61
$^{13}\text{C}$	A	54.6	56.8	70.8, 70.2, 69.9	33.7
	B	51.9	51.1	68.3, 67.5, 67.4, 66.5	33.5

A: Cation-free, B: after complexation with  $\text{LiClO}_4$ .

t: Triplet,  $[\mathbf{1}] = 1.2 \times 10^{-2} \text{ mol dm}^{-3}$ .



**Figure 1.** Cation- $\pi$  interaction of coronene-connected crown ether **1** and structures of related compounds.

**Table 2.** Stability constants of  $\text{Li}^+$  complex of **1** and related compounds

	$\log K_s$
Compound <b>1</b>	4.9 <sup>a</sup>
<i>N</i> -Butyl-aza-15-C-5 <b>2</b>	3.1 <sup>b</sup>
Compound <b>3</b>	3.2 <sup>b</sup>
Pyrene-azacrown <b>4</b>	5.4 <sup>a</sup>

<sup>a</sup> Fluorescence titration in  $\text{CH}_3\text{CN}$ .

<sup>b</sup> NMR titration in  $\text{CD}_3\text{CN}$ .

intensity of compound **1** increased as the concentrations of the  $\text{Li}^+$  cation increased similar to the pyrene-aza-crown system.<sup>5</sup> Non-linear least square treatments<sup>8</sup> of the experimental results afforded the stability constant of  $\text{Li}^+ \subset \mathbf{1}$  (Table 2). The constant,  $\log K_s$ , was compared to those of the related compounds. Apparently, according to the stability constants, the coronene ring enhanced the complexation ability of the azacrown ring. This result should be unequivocally attributed to the cation- $\pi$  interaction.

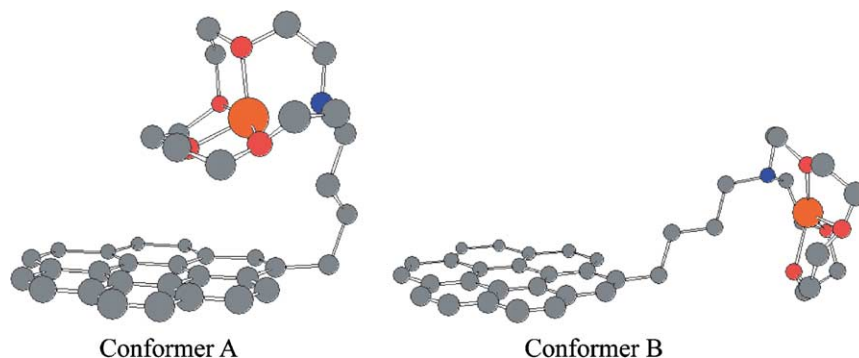
In the case of the cation complexation of compound **3**, *N*-(4-phenylbutyl)-aza-15-crown-5, the proton signals of the crown moiety shifted to lower fields in its  $^1\text{H}$  NMR spectra similar to that of compound **2**, *N*-butyl-aza-15-crown-5. This low field shift is in sharp contrast to the pyrene-crown or coronene-crown system. Moreover, the complexation constant of compound **3** ( $\log K_s = 3.2$ ) is almost the same as that of compound **2** ( $\log K_s = 3.1$ ). From these results, the contribution of the  $\pi$  electron accompanied by cation complexation is considered to be small in the case of compound **3** possessing one benzene ring. On the contrary, larger  $\pi$  system is effective enough to interact with the  $\text{Li}^+ \subset$  crown moiety though both are separated by a butyl group.

Because crystallographic analyses of compound **1** and its  $\text{Li}^+$  complexes were impossible, further information

was obtained by using ab initio calculations with the 3-21G\* basis set of possible conformers, which were pre-optimized by the PM3 calculations. As a result, conformer A is 4.8 kcal mol<sup>-1</sup> stable than conformer B (Fig. 2). In the more stable conformer A, the crown moiety is placed above the periphery of the coronene ring and the results support the experimental data.

The NMR experimental results (chemical shifts and differential NOE) coincided with the optimized structures obtained by ab initio calculations of  $\text{Li}^+ \subset \mathbf{1}$  (Fig. 2 and pdb files of the optimized structures in the Supplementary materials should be referred to). In the differential NOE experiments, irradiation of  $\text{H}_1$  proton (Fig. 1) did not enhance coronene proton signals. On the other hand, irradiation of  $\text{H}_3$  enhanced only  $\text{H}_a$  proton signal of coronene ring (singlet, 7.8 ppm in  $\text{CD}_3\text{CN}$ ). Similarly, irradiation of  $\text{H}_2$  enhanced  $\text{H}_a$  and another proton signal of coronene ring (probably  $\text{H}_b$ ). Irradiation of  $\text{H}_4$  resulted in medium enhancement of aromatic signals. Because crown moiety of the optimized structure inclined over the aromatic ring at peripheral position and it is flexible, equatorial protons of  $\text{H}_2$  and  $\text{H}_3$  can be approached to the  $\text{H}_a$  and other partial aromatic protons. Therefore, enhancement of the  $\text{H}_a$  by the irradiation of  $\text{H}_2$  and  $\text{H}_3$  is quite reasonable.

According to the results of the ab initio calculations, the crown protons of  $\text{Li}^+ \subset \mathbf{1}$  are closer to the aromatic ring than those of  $\text{Li}^+ \subset \mathbf{4}$ , and this is coincided with the fact that the crown signals of  $\text{Li}^+ \subset \mathbf{1}$  shifted to higher fields ( $\sim 0.34$  ppm) than those of  $\text{Li}^+ \subset \mathbf{4}$  ( $\sim 0.13$  ppm). Furthermore, the distance between  $\text{Li}^+$  ion and aromatic ring of  $\text{Li}^+ \subset \mathbf{1}$  is about 4.7 Å, but that of the  $\text{Li}^+ \subset \mathbf{4}$  is 5.4 Å. Therefore, the larger high-field shift of the signal of  $^7\text{Li}$  in  $\text{Li}^+ \subset \mathbf{1}$  than that of  $\text{Li}^+ \subset \mathbf{4}$  corresponds to the distance of two components, the crown moiety and the aromatic ring. However this proximity does not correspond to the larger stability of the complex. The



**Figure 2.** Optimized structures of  $\text{Li}^+ \subset \mathbf{1}$  (conformer A and B) obtained by using ab initio calculations.

stability constant of  $\text{Li}^+ \subset \mathbf{1}$  is about half that of the pyrene system, but the reason is still unclear.

In conclusion, using a molecule of simple design, we could obtain positive results suggesting that the cation– $\pi$  interaction is strong enough even in the solution state.

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#### Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.tetlet.2005.09.112](https://doi.org/10.1016/j.tetlet.2005.09.112).

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- The experimental data were processed using the following equation with the computer software Kaleida Graph<sup>TR</sup>.  $\Delta\delta_{\text{obs}} = \Delta\delta/2K[\text{G}]_0[1+K[\text{H}]_0+K[\text{G}]_0 - \{(1+K[\text{H}]_0+K[\text{G}]_0)^2 - 4K^2[\text{H}]_0[\text{G}]_0\}^{1/2}]$ , where  $K$  is the association constant, and  $[\text{H}]_0$  and  $[\text{G}]_0$  are the initial concentrations of the host and guest, respectively. In the fluorescence titration experiments, concentration of **1** was kept at  $[\mathbf{1}] = 1.26 \times 10^{-5} \text{ mol dm}^{-3}$  and  $[\text{LiClO}_4]$  was varied from 0.00 to  $1.25 \times 10^{-3} \text{ mol dm}^{-3}$  ( $\text{CH}_3\text{CN}$ ). In the NMR titration methods (compounds **2** and **3**), the ligands concentrations were kept at  $[\text{L}] = 1.88 \times 10^{-3} \text{ mol dm}^{-3}$  and  $[\text{LiClO}_4]$  was varied from 0.00 to  $5.65 \times 10^{-2} \text{ mol dm}^{-3}$  ( $\text{CD}_3\text{CN}$ ). The measurements were carried out at 25 °C.