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Synthesis and guest recognition of molecular cleft consisting of terpyridine–Pt(II) acetylide complexes

Tatsuya Nabeshima *, Yuki Hasegawa, Robert Trokowski, Masaki Yamamura

Graduate School of Pure and Applied Sciences, Tsukuba Research Center for Interdisciplinary Materials Sciences, University of Tsukuba,1-1-1 Tennodai, Tsukuba, Ibaraki 305 8571, Japan

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ABSTRACT

The stable molecular clefts **1** consisting of inert Pt–acetylide moieties and a 1,1′:3′,1″-terphenyl spacer were synthesized. Guest binding behavior of **1a** was examined by ^{1}H NMR spectroscopy to determine the association constants; naphthalene (K_a ~0 M^{-1}) < anthracene (10 M^{-1}) < pyrene (50 M^{-1}) < coronene (640 M^{-1}) in chloroform-*d*/acetonitrile-d_3 (3:1, v/v). **1a** is stable enough to resist disassembly in the presence of anionic species. Thus, **1a** shows a higher affinity to large electron-rich aromatic compounds. In addition, anionic aromatic guests were bound more strongly by **1a** (K_a = 540 M^{-1} for 1-pyrenecarboxylate) due to the electrostatic interactions, π–π interactions, and the stable cleft scaffold.

Molecular clefts and tweezers are employed as a structurally flexible host, which shows selective molecular recognition via hydrogen bonding, π–π interaction, etc.[1] Bosnich and co-workers reported that a metallo-cleft, which has flat terpyridine Pt complexes as a recognition component of the cleft host, captured a planar Pt complex and an aromatic compound in the cleft.[2] However, the synthesis of the host requires laborious multi-step processes because the scaffold of the host is maintained by covalent bonds. In contrast, a metallo-host, whose framework is synthesized via a spontaneous coordination bond formation under mild conditions, is very useful and easy to prepare. In particular, a labile coordination bond has often been used to make a variety of macrocyclic supramolecular systems, such as ionophores, receptors, cages, capsules, etc.[3] Very recently, an acyclic metallo-cleft bearing terpyridine–Pt(II) acetylide unit has been synthesized based on a coordination bond formation strategy.[4] The cleft bound terpyridine–Pt(II) complexes as a guest in a 1:1 stoichiometry. Another cleft-type Pt(II) host, which consists of two Pt(II)–thiolate[5] complex moieties, has a very flexible structure and showed a high affinity to DNA.[6] However, its detailed binding mode is still ambiguous. In these hosts, less labile coordination bonds, Pt(II)–acetylide[7] and Pt(II)–thiolate bonds, can be used to make the acyclic cleft scaffold because the host formation proceeds without any undesired side reactions such as oligomerization, which often takes place in typical macrocyclizations.

We now report the synthesis and binding properties of a stable molecular cleft having inert terpyridine–Pt(II) acetylide moieties and a 1,1′:3′,1″-terphenyl spacer, which should provide a suitable binding space for aromatic planes.[2,4b] In particular, the host showed a high affinity to a large aromatic compound, that is, coronene. Compared to neutral aromatic compounds, the binding strength was enhanced for the anionic aromatic guests due to the electrostatic interactions and the inertness of the Pt–acetylide linkage, which resists ligand exchange by the anions and does not decompose the cleft structure.

The terphenyl spacer **8** was prepared from 3-bromoanisole (**2**) via a seven-step synthesis in a 26% total yield (Scheme 1). The cleft molecules **1a** and **1b** were synthesized by the reaction of **8** with terpyridine platinum complexes **9a** and **9b**[8] in the presence of a catalytic amount of CuI in DMF. The successive addition of $NaBF_4$ gave **1a** and **1b** in 39% and 55% yields, respectively (Scheme 2).[9,10] The identification of the clefts was performed by ^{1}H NMR, ^{13}C NMR, IR spectra, mass spectral techniques, and elemental analysis. The cleft **1b** is only slightly soluble in most solvents except for DMSO, while **1a** is soluble in acetonitrile, DMSO, acetonitrile-chloroform, and aqueous acetonitrile. The higher solubility of **1a** is probably due to the steric hindrance of the *tert*-Bu groups on the terpyridine that inhibits intermolecular π–π stacking.[6b]

^{1}H NMR spectra of **1a** were strongly dependent on the solvents (Fig. 1). As the acetonitrile content in $CDCl_3$–CD_3CN increased, all the signals were more broadened and the protons H1, H4, and H5 on the terpyridine moiety were shifted upfield. The ^{1}H NMR spectra in 1:1 acetonitrile-d_3/D_2O (1:1, v/v) showed an even higher

* Corresponding author. Tel./fax: +81 29 853 4507.
E-mail address: nabesima@chem.tsukuba.ac.jp (T. Nabeshima).

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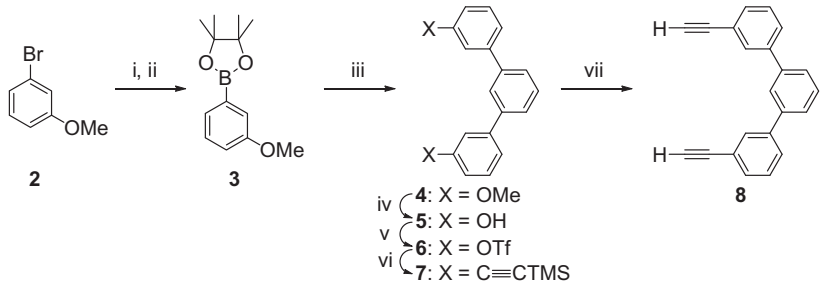
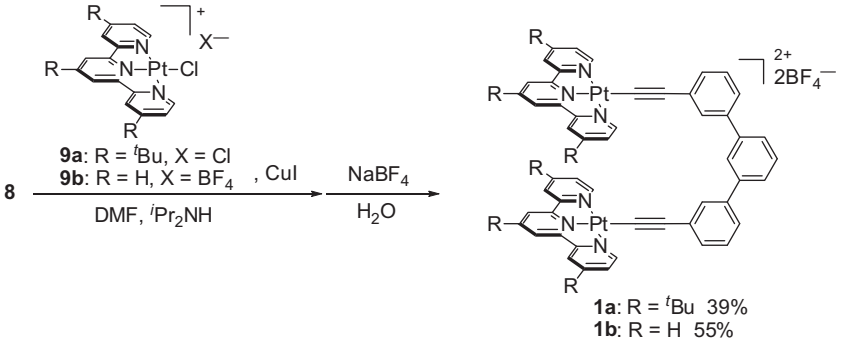


Scheme 1. (i) (a) Mg, THF, toluene, (b) $B(OMe)_3$: 80%; (ii) pinacol, toluene: >99%; (iii) dibromobenzene, $Pd(PPh_3)_4$, K_2CO_3, 1,4-dioxane: 41% (Ref.11); (iv) BBr_3, CH_2Cl_2: 96%; (v) Tf_2O, pyridine: 96%; (vi) trimethylsilylacetylene, $[PdCl_2(PPh_3)_2]$, CuI, $^nBu_4NI$, DMF, Et_3N: 89%; (vii) K_2CO_3, THF, MeOH: 97%.



Scheme 2. Synthesis of clefts **1**.

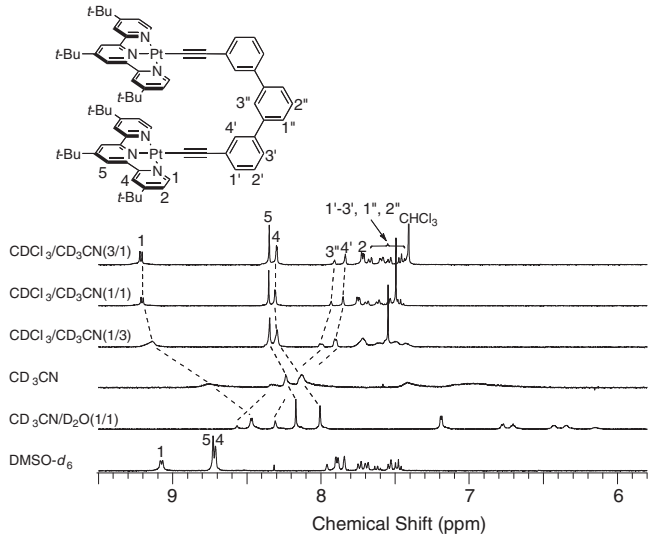


Figure 1. ^1H NMR spectra of **1a** (400 MHz, 25 °C, [**1a**] = 2.0 mM) in various solvents.

upfield shift of the protons except for H4′ and H3″ inside the cleft than in acetonitrile-d_3. The upfield shift of signals assigned to the terpyridine units strongly suggested that **1a** was aggregated in a self-recognition way by π–π stacking in the polar medium.[12] Under these conditions, the terphenyl unit of a host is captured in the terpyridine-based cleft cavity of another host. The significant concentration and temperature effects of the NMR signals are also indicative of the self-recognition (see Supplementary data, Fig. S2); upfield shifts were observed at higher concentrations, revealing that the chemical shift changes are based on the self-assembly.[13] VT-NMR studies showed a downfield shift at higher temperatures due to the disassembly (Fig. S5). This self-recognition property means a high binding ability of **1a** toward the Pt(II) complex. In chloroform-rich solvents (3:1 or 1:1 $CDCl_3$–CD_3CN), the solvent effect of the signals is almost negligible. This result suggests that self-recognition is considered not to occur in such a less polar solvent. In order to neglect the contribution of the self-recognition for analyzing the guest recognition, a less polar solvent, chloroform-*d*/acetonitrile-d_3 (3:1, v/v), was employed for the guest binding studies because the cleft **1a** exists in the monomeric form.[14]

The NMR titration experiments were carried out for different aromatic guests in chloroform-*d*/acetonitrile-d_3 (3:1, v/v). In the presence of 3.9 equiv of coronene, large upfield shifts of H1 ($\Delta\delta$ – 0.76 ppm), H4 ($\Delta\delta$ – 0.57 ppm), and H5 ($\Delta\delta$ – 0.68 ppm) were observed (Fig. 2). In addition, the signals of coronene were shifted upfield by 0.12 ppm. These spectral changes are similar to those of the self-recognition described above, indicating that the recognition of the aromatic guests took place inside the cleft cavity. This guest recognition mode by the cleft in the case of coronene was supported by the ^1H–^1H NOESY spectrum of a mixture of **1a**

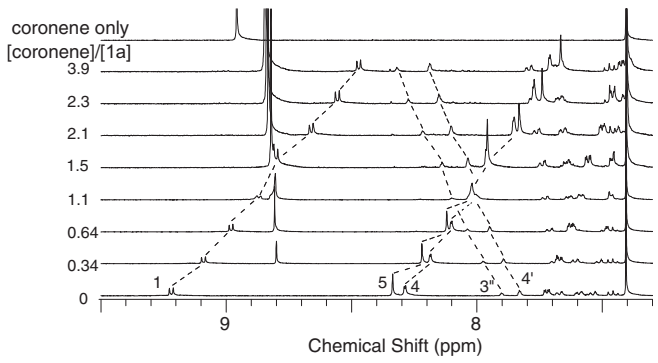


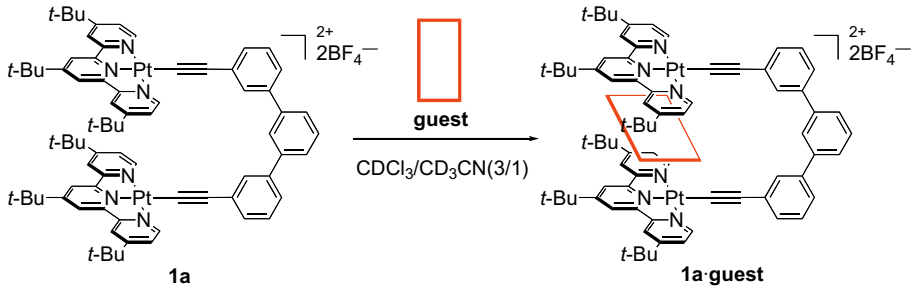
Figure 2. ^1H NMR spectra upon titration of **1a** with coronene (400 MHz, 3:1 $CDCl_3$/CD_3CN (v/v), 25 °C, [**1a**] = 2.0 mM).

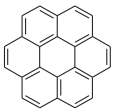
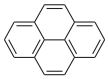
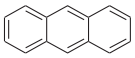
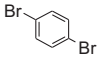
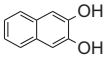
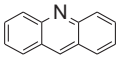
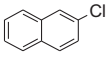
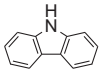
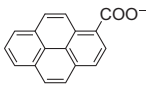
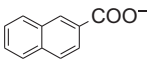
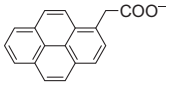
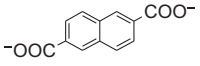
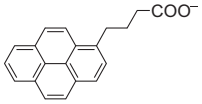
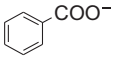
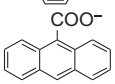
and coronene, in which the cross-correlation peaks between the protons of **1a** (H1, H4, H5, and H4′) and that of coronene appeared.

A Job plot for the complexation of **1a** and coronene clearly showed the 1:1 association (Fig. S8). The binding constants (K_a) of the cleft **1a** with the aromatic guests were determined by a non-linear least-squares analysis of the chemical shift change in H1. The K_a values are summarized in Table 1. As the size of the aromatic guest planes becomes larger, the binding constants increased in the order of naphthalene ($K_a \sim 0\ M^{-1}$) < anthracene ($10\ M^{-1}$) < pyrene ($50\ M^{-1}$) < coronene ($640\ M^{-1}$). This order is probably reflected by the strength of the π–π stacking interaction between the cleft and guest. The K_a value for naphthalene-2,3-diol is slightly higher than that of naphthalene. The cleft **1a** showed no binding ability for the halogenated aromatic guests.[15] This selectivity can be explained in terms of the interactions between the electron-rich guest and the electron-deficient terpyridine Pt units. Among the heterocyclic compounds, the affinity to carbazole is higher than those of acridine and TTF.

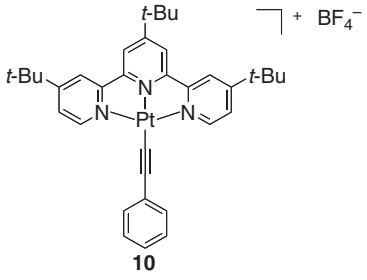
The binding affinity to anionic aromatic guests was also examined because the cationic terpyridine–Pt acetylide complexes showed electrostatic interactions with anionic polyelectrolytes.[16,17] Noteworthy is the fact that the K_a values for the aromatic carboxylates ($K_a = 540\ M^{-1}$ for 1-pyrenecarboxylate and $80\ M^{-1}$ for 9-anthracenecarboxylate) are much higher than those of the corresponding hydrocarbons ($K_a = 50\ M^{-1}$ for pyrene and $10\ M^{-1}$ for anthracene). The drastic enhancement of the affinity is due to the electrostatic interactions between the cationic cleft and the anionic guests. In contrast, our preliminary experiment indicated that the corresponding pyridine-coordinated host molecule was disassembled by the addition of the carboxylate. The pyridine-platinum

Table 1
The binding constants of cleft **1a** with aromatic guests



Guest	K_a (M^{-1})[a]	Guest	K_a (M^{-1})[a]
	640 ± 90		—[b]
	50 ± 5		—[b]
	10 ± 1		—[b]
	—[b]		—[b]
	20 ± 4		—[b]
	—[b]		4 ± 1
	—[b]		50 ± 0.3
	540 ± 60		—[b]
	220 ± 20		—[b]
	78 ± 1		—[b]
	80 ± 5		

[a] Determined by ^1H NMR spectroscopic titration (400 MHz, 3:1 $CDCl_3/CD_3CN$ (v/v), 25 °C, [**1a**] = 2.0 mM).
[b] Too low to be determined.



Scheme 3.

bond is labile enough to be cleaved by the carboxylate anion. However, the acetylide-based Pt cleft is stable enough even in the presence of the anionic guests because of inertness of the acetylide–platinum bonds. Binding studies with three aromatic carboxylates bearing a pyrene unit showed an apparent selectivity for 1-pyrenecarboxylate (K_a = 540 M^{-1}). The affinity to 1-pyreneacetate (K_a = 220 M^{-1}) is higher than 1-pyrenebutyrate (K_a = 78 M^{-1}). This result suggested that the short distance between the aromatic core and carboxylate moiety increases the electrostatic interactions. For compound **10**,[16] a much lower binding constant (K_a = 40 M^{-1}) for 1-pyreneacetate was obtained, when compared to that in the cleft **1a** (Scheme 3). Thus, the two terpyridine Pt units of **1a** play an important role for the stronger binding.

The guest recognition was also confirmed by UV–vis and emission spectroscopy (Fig. S19 and S20). The cleft **1a** showed an absorption band in the 400–500 nm region, which was originally attributed to the charge transfer (CT) excitation from an occupied orbital of the Pt–acetylide bond to an unoccupied orbital delocalized on terpyridine.[18] The CT band decreased in the presence of 1-pyrenecarboxylate, while the UV–vis spectra of **10** showed almost no change by the addition of the same guest. A degassed solution of **1a** showed an emission (ca. 600 nm) with a 3.7% quantum yield. The emission is attributed to phosphorescence because the emission intensity was lowered in an aerated solution. The emission intensity decreased upon the addition of 1-pyrenecarboxylate. These spectroscopic results again suggested the host–guest complexation.

We synthesized stable molecular clefts **1** consisting of inert Pt–acetylide bonds. **1a** captured large electron-rich aromatic compounds. Interestingly, the anionic aromatic guests were bound more strongly by **1a** due to the electrostatic interactions, π–π interactions, and the stable cleft scaffold. We are currently investigating larger supramolecular architectures based on the stable Pt–acetylide bonds.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.08.116.

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10. *Compound* **1a**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.43 (s, 36H), 1.53 (s, 18H), 7.48 (dd, J = 7.5 Hz, J = 7.5 Hz, 2H), 7.54 (d, J = 7.5 Hz, 2H), 7.62 (t, J = 7.5 Hz, 1H), 7.69 (d, J = 7.5 Hz, 2H), 7.74 (d, J = 7.5 Hz, 2H), 7.84 (s, 2H), 7.89 (d, J = 5.8 Hz, 4H), 7.96 (s, 1H), 8.71 (s, 4H), 8.73 (s, 4H), 9.07 (d, J = 5.8 Hz, 4H, ^{195}Pt satellites were not observed due to broadening.); ^{13}C NMR (100 MHz, CD_3CN) 28.9 (CH_3), 29.2 (CH_3), 35.5 (C), 36.5 (C), 97.9 (C), 102.7 (C), 120.6 (CH), 122.4 (CH), 123.3 (CH), 124.2 (CH), 124.5 (CH), 124.8 (CH), 127.0 (C), 128.1 (CH), 128.6 (CH), 129.7 (CH), 129.9 (CH), 138.6 (C), 138.9 (C), 153.1 (CH), 153.2 (C), 157.7 (C), 165.7 (C), 166.7 (C); IR (KBr) ν 2116 cm^{-1} (C≡C); ESI–MS m/z 734.30 $[M-2BF_4]^{2+}$; Anal. Calcd for $C_{76}H_{82}N_6B_2F_8Pt_2{\cdot}H_2O = C_{76}H_{84}N_6B_2F_8OPt_2$: C, 54.95; H, 5.10; N, 5.06. Found: C, 54.60; H, 5.12; N, 4.98. *Compound* **1b**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.46 (d, J = 7.4 Hz, 2H), 7.50–7.53 (m, 6H), 7.72 (t, J = 7.7 Hz, 1H), 7.76 (d, J = 7.4 Hz, 2H), 7.85 (d, J = 8.6 Hz, 2H), 8.11–8.13 (m, 6H), 8.24 (s, 1H), 8.29 (d, J = 8.3 Hz, 4H), 8.40 (br s, 4H), 8.47 (t, J = 7.8 Hz, 1H), 8.55(d, J = 7.8 Hz, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 98.3 (C), 102.6 (C), 124.7 (CH), 124.8 (CH), 125.5 (CH), 125.6 (CH), 126.2 (CH), 127.1 (C), 129.0 (CH), 129.5 (CH), 129.9 (CH), 130.0 (CH), 130.7 (CH), 139.7 (C), 139.9 (C), 141.8 (CH), 142.1 (CH), 152.9 (C), 153.3 (CH), 157.7 (C); ESI–MS m/z 566.06 $[M-2BF_4]^{2+}$.
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13. Based on a monomer-dimer equilibrium model, the dimerization constant, $K_{dim} = [(\mathbf{1a})_2]/[\mathbf{1a}]^2$, was determined to be 758 M^{-1} (Fig. S3).
14. No self-recognition of **1a** in chloroform-d/acetonitrile-d_3 (3:1, v/v) was clarified by the variable-concentration NMR spectra (Fig. S4).
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