# Discrete stack of an odd number of polarized aromatic compounds revealing the importance of net vs. local dipoles

**Yoshihiro Yamauchi[a], Michito Yoshizawa[b,c,1], Munetaka Akita[b], and Makoto Fujita[a,1]**

[a]Department of Applied Chemistry, School of Engineering, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan; [b]Chemical Resources Laboratory, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 226-8503, Japan; and [c]Precursory Research for Embryonic Science and Technology, Japan Science and Technology Agency, 4-1-8 Honcho, Kawaguchi, Saitama 332-0012, Japan

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**Three polarized aromatic guest molecules (pyrene-4,5-dione, 1) form a triple-layered stack in the box-shaped cavity of an organic pillared coordination cage in water. The cavity size strictly limits the number of stacked planar guests but does not restrict guest orientation, and thus enables the study of discrete stacks of polarized guests and their preferred conformations. Crystallographic study shows that the guest molecules in the cavity are rotated 120° with respect to each other, canceling the net dipole moment rather than the local dipole moment. The unique conformation of a discrete, triple stack of 1 sharply contrasts to the standard head-to-tail conformation in infinite stacks of 1.**

$\pi$–$\pi$ interactions | aromatic molecule | coordination cage | dipole moment | self-assembly

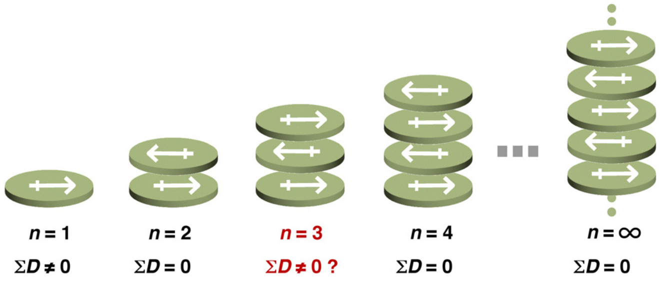

**Fig. 1.** Prediction of the net dipole moment of discretely and infinitely layered polarized molecules.

The large dipole moment (6.1–6.7 D) of pyrene-4,5-dione (**1**) (1–3) induces an infinite, head-to-tail columnar stacking in the crystalline state (4). This alternating stacking motif should also be present in finite stacks and, when an even number of **1** form a stack, the offset stacking will result in a net dipole moment of zero. However, if an odd number of **1** stack in a finite manner, the head-to-tail stacking cannot fully cancel the dipole moments. As for $n = 3$, if the first 2 molecules form an offset pair, then the third molecule should result in a residual overall dipole moment (Fig. 1). The stepwise, alternating stacking of polar aromatic molecules has, however, never been examined because of insufficient methodology to precisely control the number of stacking units. The self-assembled cavity (5–12) of the box-shaped, organic pillared coordination cage **2** (Fig. 2) is capable of containing a predetermined number of aromatic stacks and provides a method to examine the behavior of the head-to-tail stacking of 3 molecules **1**. Accordingly, we examined the self-assembly of an inclusion complex, $\mathbf{2}\supset(\mathbf{1})_3$, and studied the guest orientation. Diffraction study shows the unique way of the highly polarized molecule to cancel the net dipole moments rather than local dipole moments.

## Results and Discussion

The inclusion complex, $\mathbf{2}\supset(\mathbf{1})_3$, was quantitatively formed by self-assembly (13). NMR analyses (1D, COSY, NOESY, and DOSY) confirmed the formation of a single product where ratio of **2** and **1** is 1:3. All of the signals could be assigned (Fig. 3) and were observed at the same diffusion coefficient in DOSY (see SI), indicating a stable host-guest complex on the NMR time scale. Two sets of signals are observed for dione **1** in a 2:1 ratio and both are considerably shifted upfield ($\Delta\delta = -1.13$ to $-2.96$ ppm) as a result of shielding from the nearby $\pi$-systems. The structure of $\mathbf{2}\supset(\mathbf{1})_3$ is stable enough in both aqueous solution and solid states.

Absolute structural evidence was provided by X-ray analysis of the bright orange crystals of the TMEDA derivative $\mathbf{2}'\supset(\mathbf{1})_3$. The crystal structure confirmed the expected $\mathbf{2}'\supset(\mathbf{1})_3$ structure in which 3 molecules of **1** are stacked (≈3.3 Å) within the cavity of cage **2**′ (Fig. 4).

Unexpectedly, the 3 guest molecules in the cavity are not stacked in a head-to-tail fashion but rather they are twisted by 120° with respect to each other. As a result of the higher ($D_{3h}$) symmetry, the net dipole moment is fully cancelled. No significant interactions are observed between **1** and any species existing outside the cage (e.g., counter ions or water of crystallization). Because negatively charged carbonyl oxygen atoms of **1** and cationic Pd(II) centers of **2** are not in a close proximity, they do not seem to interact. Therefore, the guest orientation is directed neither by crystal packing nor by the host-guest electrostatic interaction but by the polar guests' own nature to find their optimal way of stacking. We believe that the stacking manner of **1** in the cavity of **2** is the most preferable for $n = 3$.

The cancellation of the dipole moments among the 3 guests generates dipole-dipole interaction as an attractive force. It seems that the $(\mathbf{1})_3$ structure is stabilized by the dipole-dipole interaction and thus the $\mathbf{2}\supset(\mathbf{1})_3$ complex is formed efficiently. In fact, we failed to obtain $\mathbf{2}\supset(\mathbf{G})_3$ complexes with nonpolarized aromatic molecules (**G**) such as colonene, pyrene, and perylene, even though the size of the cavity fits that of the layered trimer $(\mathbf{G})_3$ structures. It is well known that the interaction in the donor-donor-donor arrays of electron rich molecules is rather repulsive and they apt to make offset (herringbone-type) stacks (18).

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The authors declare no conflict of interest.

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Data deposition: The atomic coordinates have been deposited in the Cambridge Structural Database, Cambridge Crystallographic Data Centre, Cambridge CB2 1EZ, United Kingdom (CSD reference no. 703950).

[1]To whom correspondence should be addressed. E-mail: yoshizawa.m.ac@m.titech.ac.jp or mfujita@appchem.t.u-tokyo.ac.jp.

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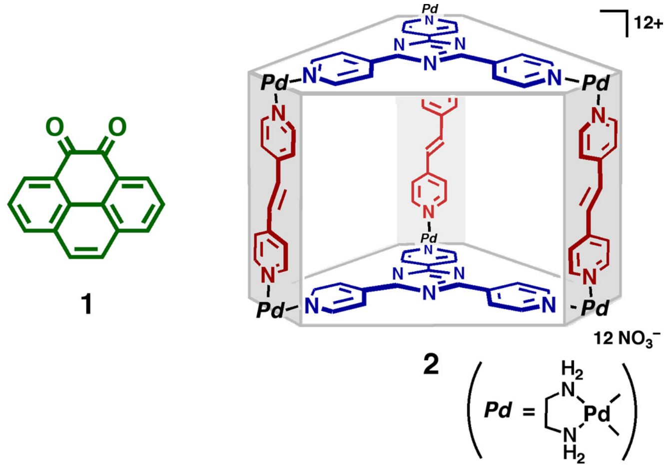


Fig. 2. Chemical structures of pyrene-4,5-dione (**1**) and organic pillared coordination cage **2**.

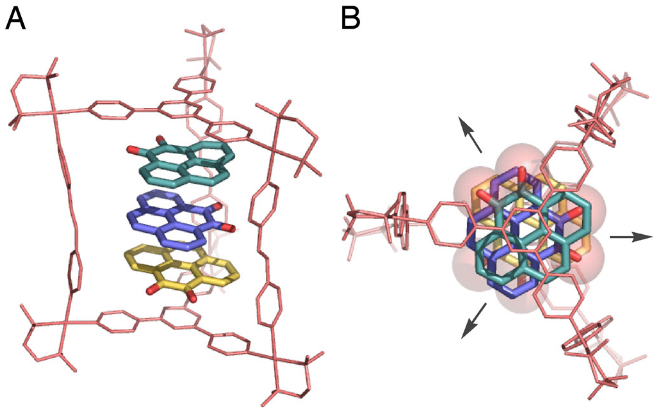


Fig. 4. X-ray crystal structure of $\mathbf{2}'\supset(\mathbf{1})_3$. (*A*) Side view. (*B*) Top view. Solvent molecules ($H_2O$) and counter anions ($NO_3^-$) are omitted for clarity.

The UV-visible spectra of $\mathbf{2}\supset(\mathbf{1})_3$, free **1**, and $\mathbf{6}\supset\mathbf{1}$ (where cage **6** is the analogous cage with pyrazine pillars (**6**); 14) were compared (Fig. 5, 6). The carbonyl n-$\pi^*$ transitions of the encapsulated diones in cage $\mathbf{2}\supset(\mathbf{1})_3$ and $\mathbf{6}\supset\mathbf{1}$ are considerably red-shifted ($\Delta\lambda$ = 40 nm) compared with the free **1** because of $\pi$-stacking with the electron deficient triazine panel **4**. Additionally, the spectra of complex $\mathbf{2}\supset(\mathbf{1})_3$ exhibits a strong shoulder at 510 nm (asterisk in Fig. 6) that is not present in the isolated stack $\mathbf{6}\supset\mathbf{1}$. Presumably, this transition is characteristic to the $\pi$-$\pi$ interactions between the diones and a similar band is also found in solid **1** ($\lambda_{\max}$ = 525 nm) (see SI).

In summary, we confirmed that an odd number of polarized aromatic molecules have a unique way of stacking that results in a negligible overall, rather than local, dipole moment. Our results demonstrate that dipole interaction is an important factor in the formation of stable aromatic stacking structures. The pillared cage **2** enables the precise control of stacking units but does not restrict the orientation of the guests, providing opportunities to study the hitherto unexplored properties of discretely stacked aromatic compounds in solution (15–17).

## Materials and Methods

**General.** The $^1$H, $^{13}$C{$^1$H} NMR, and other 2D NMR spectra were recorded on a Bruker DRX-500 (500 MHz) spectrometer. TMS ($CDCl_3$ solution) in a capillary served as external standard ($\delta$ 0 ppm). IR measurements (ATR) were carried out using a DIGILAB Scimitar FTS-2000 instrument. UV-visible spectral data were recorded on a SHIMADZU UV-3150. Melting points were determined with a Yanaco MF-500 V micro melting point apparatus. Diffraction measurements were made using a Bruker APEX CCD diffractometer. Solvents and reagents were purchased from TCI Co., Ltd.; WAKO Pure Chemical Industries, Ltd.; and Sigma–Aldrich. Deuterated $H_2O$ was acquired from Cambridge Isotope Laboratories, Inc. and used as supplied for the complexation reactions and NMR measurements.

**$\mathbf{2}\supset(\mathbf{1})_3$.** A mixture of pillar-like ligand **3** (5.5 mg, 30 $\mu$mol), panel-like ligand **4** (6.3 mg, 20 $\mu$mol), (en)Pd$(NO_3)_2$ (**5**; 17.4 mg, 60 $\mu$mol), and pyrene-4,5-dione (**1**) (7.0 mg, 30 $\mu$mol) in $D_2O$ (1.0 mL) was stirred at 60 °C for 3 h to give clear

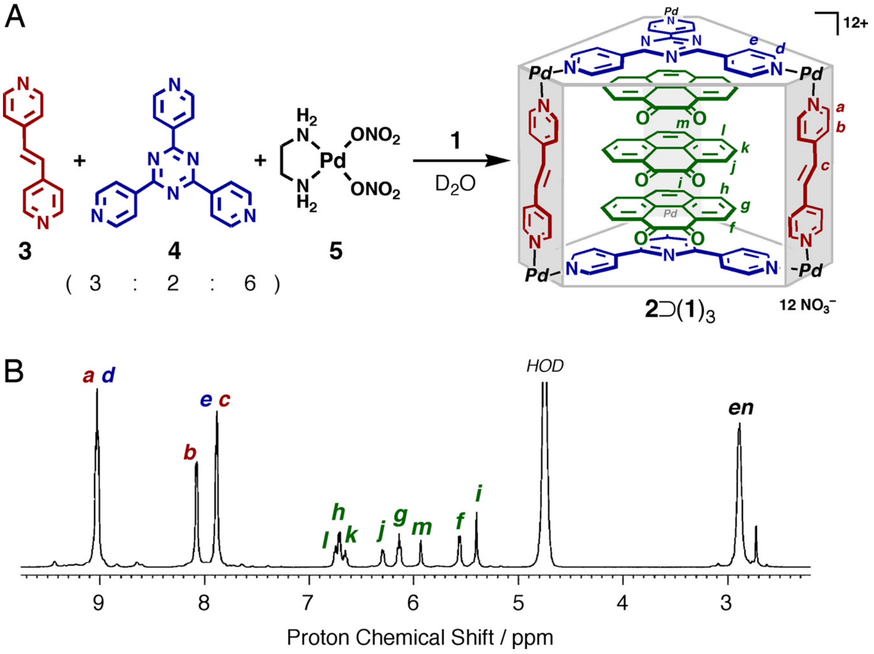
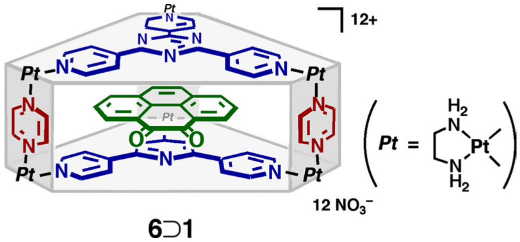


Fig. 3. Synthesis and characterization of complex $\mathbf{2}(\mathbf{1})_3$. (*A*) Schematic representation of a self-assembly of $2\supset(1)_3$. (*B*) $^1$H NMR spectrum (500 MHz, 300 K) of triple-stacked $\mathbf{2}\supset(\mathbf{1})_3$ complex in $D_2O$.



**6⊃1**

**Fig. 5.** Chemical structure of **6**⊃**1**.

orange solution. $^1$H NMR analysis of the solution revealed the formation of **2**⊃(**1**)$_3$ quantitatively. After filtration of the resulted orange solution, the resulting solution was dried by vacuum freeze-drying equipment. **2**⊃(**1**)$_3$ was isolated as an orange powder (32.8 mg, 91% yield). $^1$H NMR (500 MHz, $D_2O$, 27 °C):$\delta$ 9.02 (d, $J$ = 6.5 Hz, 12H), 9.01 (d, $J$ = 6.5 Hz, 12H), 8.06 (d, $J$ = 6.5 Hz, 12H), 7.87 (d, $J$ = 6.5 Hz, 12H), 7.86 (s, 6H), 6.74 (d, $J$ = 7.5 Hz, 2H), 6.70 (d, $J$ = 7.5 Hz, 4H), 6.64 (d, $J$ = 6.5 Hz, 2H), 6.28 (d, $J$ = 6.5 Hz, 2H), 6.13 (t, $J$ = 7.5 Hz, 4H), 5.92 (s, 2H), 5.55 (d, $J$ = 7.0 Hz, 4H), 5.39 (s, 4H), 2.87 (br, 24H); $^{13}$C{$^1$H} NMR (125 MHz, $D_2O$, TMS):$\delta$ 177.2 ($C_q$), 176.6 ($C_q$), 167.9 ($C_q$), 152.2 (CH), 151.7 (CH), 147.5 ($C_q$), 143.6 ($C_q$), 136.4 (CH), 136.0(CH), 132.4 (CH), 129.6 ($C_q$), 129.3 ($C_q$), 128.7 (CH), 128.7 (CH), 127.7 (CH), 127.2 (CH), 126.0 ($C_q$), 126.0 (CH), 125.7 (CH), 124.7 (CH), 124.7 (CH), 124.6 ($C_q$), 46.8 ($CH_2$); DOSY ($m^2$/s): log$D$ = −9.85; IR (ATR, $cm^{-1}$): 3410(br), 3200(br), 3080(br), 1670, 1614, 1519, 1383, 1061, 831, 804; m.p.: ≈230 °C (decomposed); elemental analysis calculated for $C_{132}H_{126}N_{42}O_{42}Pd_6{\cdot}20(H_2O)$: C, 39.92; H, 4.21; N, 14.81. Found: C, 39.76; H, 4.02; N, 15.00.

**X-Ray Crystal Data of 2′⊃(1)$_3$.** $C_{156}H_{174}N_{38}O_{65.5}Pd_6$, $M_r$ = 4259.74, crystal dimensions 0.15 × 0.15 × 0.05 mm$^3$, monoclinic space group $P2_1/c$, $a$ = 28.563 (4) Å, $b$ = 16.085 (2) Å, $c$ = 41.635 (5) Å, $\beta$ = 94.598 (3)°, $V$ = 19067 (4) Å $^3$, $Z$ = 4, $\rho_{calcd}$ = 1.487 g·cm$^{-3}$, $F$- (000) = 8704, radiation, $\lambda$(MoK$\alpha$) = 0.71073 Å, $T$ = 80 (2)K, reflections collected/unique 141967/47437 ($R_{int}$ = 0.1607). The structure was solved by direct methods (SHELXL-97) and refined by full-matrix least-squares methods on $F^2$ with 2584 parameters. $R_1$ = 0.1246 ($I > 2\sigma(I)$), $wR_2$ = 0.4073, GOF 0.966; max/min residual density 4.611/−1.703 eÅ$^{-3}$.

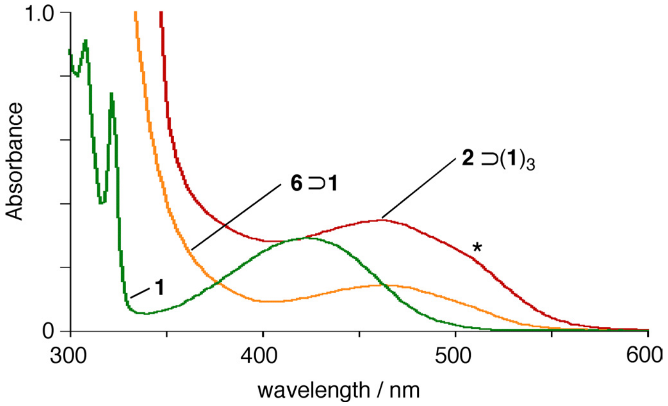


**Fig. 6.** UV-visible spectra (room temperature, 1.0 mM) of **2**⊃(**1**)$_3$, **6**⊃**1** in $H_2O$ and of **1** in $CH_3CN$.

**6⊃1.** Powder of **1** (4.6 mg; 20 $\mu$mol, 2 eq. per **6**) was added to a $D_2O$ solution (1.0 mL) of cage **6** (31 mg; 10 $\mu$mol) and the suspended mixture was stirred at 60 °C for 30 min. After filtration of the resulted orange solution, the $^1$H NMR spectrum revealed the quantitative formation of **6**⊃**1**complex. The solution was evaporated and dried by vacuum freeze-drying equipment to give a orange powder of **6**⊃**1** complex (3.1 mg; 9.2 $\mu$mol) in 92% yield. $^1$H NMR (500 MHz, $D_2O$, 27 °C): 9.59 (s, 12H), 9.08 (d, $J$ = 5.5 Hz, 12H), 8.14 (br, 12H), 7.53 (d, $J$ = 7.5 Hz, 2H), 7.86 (t, $J$ = 7.5 Hz, 2H), 6.30 (s, 2H), 6.20 (d, $J$ = 7.5 Hz, 2H), 2.89 (d, $J$ = 5.5 Hz, 12H), 2.84 (d, $J$ = 5.5 Hz, 12H); $^{13}$C{$^1$H} NMR (125 MHz, $D_2O$, TMS):$\delta$ 177.9 ($C_q$), 167.8 ($C_q$), 153.5 (CH), 151.3 (CH), 144.3 ($C_q$), 135.9 (CH), 131.1 (CH), 130.1 ($C_q$), 128.9 (CH), 127.8 ($C_q$), 127.4 (CH), 125.6 (CH), 47.7 ($CH_2$); DOSY ($m^2$/s): log$D$ = −9.80; IR (ATR, $cm^{-1}$): 3420(br), 3040(br), 1512, 1383, 823, 816, 722, 705; m.p.: ≈230 °C (decomposed).

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