Electronic Supplementary Information

2,3-Dialkoxynaphthalene-Based Naphthocage

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1. Experimental Section

1.1 General. All the reagents involved in this research were commercially available and used without further purification unless otherwise noted. Solvents were either employed as purchased or dried prior to use by standard laboratory procedures. Thinlayer chromatography (TLC) was carried out on 0.25 mm Yantai silica gel plates (60F-254). Column chromatography was performed on silica gel 60 (Tsingdao 40 -63 nm, 200 – 300 mesh). ¹H, ¹³C, ¹H, ¹H-COSY, and ¹H, ¹H-ROESY NMR spectra were recorded on Bruker Avance-400 or 500 spectrometers. All chemical shifts are reported in *ppm* with residual solvents as the internal standards. The following abbreviations were used for signal multiplicities: s, singlet; d, doublet; t triplet; m, multiplet. Electrospray-ionization time-of-flight high-resolution mass spectrometry (ESI-HRMS) experiments were conducted on an applied Q EXACTIVE mass spectrometry system. Conformers 2-I and 2-II in Fig. 1c were optimized at the semiempirical PM6 level of theory by Spartan'14 (Wavefunction, Inc.) with 4⁺ as a guest. However, the guest was removed to just show the structures of the two conformers. Energy-minimized structures of complexes 3+@1-I, 3+@1-II, 3+@2-I and 3+@2-II calculated by DFT at the wB97XD/6-31G(d) level of theory in CH₂Cl₂. Butyl groups of 1 are shortened to methyl groups for viewing clarity.

1.2 Isothermal Titration Calorimetry (ITC). Titration experiments were carried out in 1,2-dichloroethane/CH₃CN 1 : 1 (v/v) at 25 °C on a Nano ITC LV – 190 μ L (Waters GmbH, TA Instruments, Eschborn, Germany). In a typical experiment, a 190 μ L solution of **2** was placed in the sample cell at a concentration of 0.075 mM, and 50 μ L of a solution of the hexafluorophosphate salt (0.5 mM in the same solvent) was in the injection syringe. The titrations consist of 25 consecutive injections of 1.96 μ L each with a 200 s interval between injections. Heats of dilution, measured by titration of the salt into the sample cell with blank solvent, were subtracted from each data set. All solutions were degassed prior to titration. The data were analysed using the instrumental internal software package and fitted with a 1:1 binding model.



1.3 Synthesis of Naphthocage 2

A solution of compound S1^[1] (700 mg, 2.3 mmol) and compound S2 (676 mg, 1.5 mmol) in dry THF (50 mL) was added dropwise through a syringe pump over 4 h to the mixture of NaH (110 mg, 4.6 mmol) and Cs₂CO₃ (1.5 g, 4.6 mmol) in dry THF (200 mL) at reflux under Argon. The resulting mixture was refluxed for another 60 h. The solvent was removed under reduced pressure. The residue was suspended in H₂O (30 mL), and then extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phases were washed with saturated NaCl and dried over anhydrous Na₂SO₄. The solvent was removed in vacuo to yield the crude product which was purified by column chromatography (SiO₂, PE : EA = $30:1 \sim 15:1$) to give product as a light-yellow liquid, which was then mixed with MeOH (50 mL). The resulting mixture stood for 6 h. The precipitate was collected through filtration and dried to afford 2 as a white solid (150 mg, yield 15%). ¹H NMR (500 MHz, CD₂Cl₂, 298 K) δ [ppm] = 6.86 (dd, J = 6.5, 3.5 Hz, 6H), 6.15 (dd, J = 6.4, 3.3 Hz, 6H), 4.70 (d, J = 7.2 Hz, 24H), 3.68 (t, J = 6.6 Hz, 12H), 2.99 (q, *J* = 7.5 Hz, 12H), 1.76 – 1.70 (m, 12H), 1.19 (t, *J* = 7.5 Hz, 18H), 0.99 (t, J = 7.4 Hz, 18H). ¹³C NMR (126 MHz, CD₂Cl₂, 298 K) δ [ppm] = 149.81, 145.47, 132.78, 130.26, 127.10, 124.91, 123.90, 76.46, 66.30, 62.76, 24.08, 22.88, 17.27,

10.96. HRMS (ESI): m/z calcd for $[M+NH_4]^+ C_{84}H_{112}NO_{12}^+$, 1326.8179; found 1326.8168 (error = - 0.8 ppm).



 1 H NMR spectrum (500 MHz, CD₂Cl₂, 298 K) of **2**



ESI-TOF mass spectrum of 2



 $^1\text{H}, ^1\text{H}\text{-}\text{COSY}$ NMR spectrum (500 MHz, CD₂Cl₂, 6.0 mM, 298 K) of 2



 $^1\text{H}, ^1\text{H}\text{-}\text{ROESY}$ NMR spectrum (500 MHz, CD₂Cl₂, 6.0 mM, 298 K) of 2

2. ¹H NMR Spectra of the Complexes



Fig. S1 ¹H NMR spectra (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 2.0 mM, 298 K) of (a) guest **3-PF**₆, (c) **2**, and (b) their equimolar mixture. Six major signals were detected in the aromatic regions. In addition, some minor signals were detected as well. This suggests that two conformers **2-I** and **2-II** coexist in the mixture with conformer **2-II** as the predominant conformer. The signal of the guest shift upfield and is split into two signals, supporting the above conclusion. The ratios to the two peaks give rise to the ratios of two conformers. Thus, the ratios of two conformers **2-I** and **2-II** are calculated to be 12% and 88%, respectively.



Fig. S2 ¹H NMR spectra (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 2.0 mM, 298 K) of (a) Guest **4-PF**₆, (c) **2**, and (b) their equimolar mixture. Similarly, the ratios of two conformers **2-I** and **2-II** are calculated to be 22% and 78%, respectively.



Fig. S3 ¹H NMR spectra (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 2.0 mM, 298 K) of (a) Guest **5-PF**₆, (c) **2** and (b) their equimolar mixture. Similarly, the ratios of two conformers **2-I** and **2-II** are calculated to be 7% and 93%, respectively.



Fig. S4 ¹H NMR spectra (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 2.0 mM, 298 K) of (a) Guest **6-PF**₆, (c) **2** and (b) their equimolar mixture. Similarly, the ratios of two conformers **2-I** and **2-II** are calculated to be 9% and 91%, respectively.



Fig. S5 ¹H NMR spectra (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 2.0 mM, 298 K) of (a) Guest 7-PF₆, (c) 2 and (b) their equimolar mixture. Similarly, the ratios of two conformers 2-I and 2-II are calculated to be 5% and 95%, respectively.

3. Mass Spectra of the Complexes



Fig. S6 ESI mass spectrum of $3-PF_6@2$. The result indicates $3-PF_6$ and 2 form a 1:1 complex.



Fig. S7 ESI mass spectrum of $4-PF_6@2$. The result indicates $4-PF_6$ and 2 form a 1:1 complex.



Fig. S8 ESI mass spectrum of 5-PF₆@2. The result indicates 5-PF₆ and 2 form a 1:1

complex.



Fig. S9 ESI mass spectrum of $6-PF_6@2$. The result indicates $6-PF_6$ and 2 form a 1:1 complex.



Fig. S10 ESI mass spectrum of **7-PF**₆@**2**. The result indicates **7-PF**₆ and **2** form a 1:1 complex.

4. Binding Constants Determined by ITC



Fig. S11 Titration plots (heat rate versus time and heat versus guest/host ratio) obtained from ITC experiments of **2** with **3**-PF₆ in the 1:1 mixture of 1,2-dichloroethane and CH_3CN .



Fig. S12 Titration plots (heat rate versus time and heat versus guest/host ratio) obtained from ITC experiments of 2 with 4-PF_6 in the 1:1 mixture of 1,2-dichloroethane and CH₃CN.



Fig. S13 Titration plots (heat rate versus time and heat versus guest/host ratio) obtained from ITC experiments of 2 with $5-PF_6$ in the 1:1 mixture of 1,2-dichloroethane and CH₃CN.



Fig. S14 Titration plots (heat rate versus time and heat versus guest/host ratio) obtained from ITC experiments of **2** with 6-PF₆ in the 1:1 mixture of 1,2-dichloroethane and CH₃CN.



Fig. S15 Titration plots (heat rate versus time and heat versus guest/host ratio) obtained from ITC experiments of 2 with $7\text{-}PF_6$ in the 1:1 mixture of 1,2-dichloroethane and CH₃CN.

5. Variable-Temp ¹H NMR Experiments of Host



Fig. S16 Variable-temperature ¹H NMR spectra (400 MHz, CD_2Cl_2) of **2**. With decreasing the temperatures, the naphthalene protons 1 and 2 (in red dashed box) in the aromatic region of the spectra are broadened and finally disappear into the baseline at -60 °C. This suggests that the barrier for the naphthalene flipping in **2** is very low.

ML 2'+2+2"+2 -1 - 0 1 Ø9 2 8 3 Ø **6**7 4 - 5 a-N-6 7 2'+2+2"+2 11"1 o ø 0 8 L٩ . 8 . 7 . 2 9 6 5 4 3 1 0 -1

6. 2D NMR Spectra of the Complexes

Fig. S17 ¹H, ¹H-COSY NMR spectrum (500 MHz, CD₂Cl₂:CD₃CN=1:1, 6.0 mM, 298 K) of **3-PF**₆@2.



Fig. S18 ¹H,¹H-ROESY NMR spectrum (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 6.0 mM, 298 K) of **3-PF**₆@**2**. The assignment of the NMR peaks in Fig. 2a is according to this ROESY NMR spectrum.



Fig. S19 ¹H, ¹H-COSY NMR spectrum (500 MHz, CD₂Cl₂:CD₃CN=1:1, 6.0 mM, 298 K) of **4-PF**₆@2.



Fig. S20 ¹H,¹H-ROESY NMR spectrum (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 6.0 mM, 298 K) of **4-PF**₆@**2**. The assignment of the NMR peaks in Fig. 2b is according to this ROESY NMR spectrum.



Fig. S21 ¹H,¹H-COSY NMR spectrum (500 MHz, CD₂Cl₂:CD₃CN=1:1, 6.0 mM, 298 K) of **5-PF**₆@2.



Fig. S22 ¹H,¹H-ROESY NMR spectrum (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 6.0 mM, 298 K) of **5-PF**₆@2. The assignment of the NMR peaks in Fig. 2c is according to this ROESY NMR spectrum.



Fig. S23 ¹H,¹H-COSY NMR spectrum (500 MHz, CD₂Cl₂:CD₃CN=1:1, 6.0 mM, 298 K) of **6-PF**₆@2.



Fig. S24 ¹H,¹H-ROESY NMR spectrum (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 6.0 mM, 298 K) of **6-PF**₆@2. The assignment of the NMR peaks in Fig. 2d is according to this ROESY NMR spectrum.



Fig. S25 ¹H,¹H-COSY NMR spectrum (500 MHz, CD₂Cl₂:CD₃CN=1:1, 6.0 mM, 298 K) of **7-PF**₆@2.



Fig. S26 ¹H,¹H-ROESY NMR spectrum (500 MHz, $CD_2Cl_2:CD_3CN=1:1$, 6.0 mM, 298 K) of 7-PF₆@2. The assignment of the NMR peaks in Fig. 2e is according to this ROESY NMR spectrum.

7. Calculation of Packing Coefficient

The cavity volumes of hosts and the solvent excluded volume of guest (SEV, *Fig.* S27) were calculated using rbcavity program in rDock software based on the energyminimized structures in Fig. 4 (maintext).² The probe radius was set to 1 Å. To minimize the influence of molecular orientation on calculated volume, the final data were obtained by averaging over multiple orientations for each molecule, i.e. rotating the molecule by three axes every 30 degrees in the range of 0 to 180 degree. To be consistent with the cavity volume calculation of the host, the guest molecule was first enclosed by a dummy carbon nanotube (*Fig. S28*) to form a closed cavity, and the guest volume was calculated by subtracting the cavity volume of the complex from the cavity volume of the dummy nanotube. However, the error bar is slightly larger than the calculated cavity volume due to error propagation. The calculated cavity volumes of host molecules are shown in mesh (*Fig. S29-S32*).

Table S1. The cavity volume of host (Å³), solvent excluded volume (Å³) of guest, and derived packing coefficient.

guest volume (Å ³)	109.38±14.83			
conformer	1-I	1-II	2-I	2-II
cavity volume (Å ³)	228.28±9.17	251.86±9.85	233.87±8.75	200.72±8.27
packing coefficient	0.48±0.07	0.43±0.06	0.47±0.07	0.54±0.08



Fig. S27 Difference between van der Waals volume (vWV) and solvent excluded volume (SEV). Since there are some corner spaces that cannot be accessed by the probe, SEV is larger than vWV. The probe radius used in this work is 1 Å.



Fig. S28 Dummy carbon nanotube built to enclose the guest molecule.



Fig. S29 The cavity volumes of 1-I shown from different sides (blue grid).



Fig. S30 The cavity volumes of 1-II shown from different sides (blue grid).



Fig. S31 The cavity volumes of 2-I shown from different sides (blue grid).



Fig. S32 The cavity volumes of 2-II shown from different sides (blue grid).

8. X-Ray Single Crystallography

Suitable single crystals of $4-PF_6(a)2$ for structural determination were obtained by slow vapour diffusion of the 1:1 mixture of 2 with 4-PF_6 in a 10:1 mixture of EtOAc/MeCN, vapour diffused with a four-fold excess (v/v) of pentane. The reflections were collected with Agilent Super-Nova (Cu) X-ray source and mirror monochromatized Cu-K α (λ = 1.54184 Å) radiation at 120 K. Program CrysAlisPro³ was used for the data collection and reduction. The intensities were corrected for absorption using analytical face index absorption correction method⁴ for all the data. All calculations were performed by full-matrix least-squares methods on F² by using the SHELX program^{5,6}. The asymmetric cell contained one molecule of $C_{84}H_{108}O_{12}$, one molecule of $[C_8H_{20}N][PF_6]$, and some other unknown solvates. Most of the alkyl and alkoxy substituents were found to be disordered over two positions and were modelled accordingly using appropriate restraints (DFIX, DANG, SIMU, RIGU), and in one instance, the EADP constraint. No sensible disordered model could be formulated for the unknown solvates which would match the observed electron density, so the computer program SQUEEZE⁷ within PLATON was used to account for the electron density in this region of the unit cell. The program identified solvent accessible voids totalling 989.4 $Å^3$ and 250.2 electrons per unit cell were recovered. The formula weight, density etc. listed below do not include any correction for the missing solvate.

Crystal data for **4-PF₆@2**: $C_{84}H_{108}O_{12} \cdot [C_8H_{20}N][PF_6]$ (M = 1584.92 g/mol): monoclinic, space group $P2_1/c$, a = 15.7124(6) Å, b = 35.8329(17) Å, c = 16.5563(7)Å, $\beta = 90.796(4)^\circ$, V = 9320.6(7) Å³, Z = 4, T = 120 K, μ (CuK α) = 0.82 mm⁻¹, Dcalc = 1.129 g/cm³, 58798 reflections measured (2.9° $\leq 2 \theta \leq 74.5^\circ$), 18892 unique (R_{int} = 0.079) which were used in all calculations. The final refinement gave R₁ = 0.176 (I > 2 σ (I)), $wR_2 = 0.493$, and S = 1.67. Crystal data of 4-PF₆@2 has been deposited in the Cambridge Crystallographic Data Centre (CCDC 1971100).

PLAT084_ALERT_3_A

Problem: High wR2 Value (i.e. > 0.25)0.49 Report

Response: The crystals were all very weakly diffracting, even with extremely prolonged exposure times using Cu radiation, making it difficult to collect the high angle reflections. This is routinely observed for supramolecular structures, especially if they are comprised of predominantly light atoms, and as a consequence, the quality of the data is lower than would be ideal. However, the identity of the structure was clearly established without issue.

PLAT082_ALERT_2_B

Problem: High R1 Value 0.18 Report

Response: The crystals were all very weakly diffracting, even with extremely prolonged exposure times using Cu radiation, making it difficult to collect the high angle reflections. This is routinely observed for supramolecular structures, especially if they are comprised of predominantly light atoms, and as a consequence, the quality of the data is lower than would be ideal. However, the identity of the structure was clearly established without issue.

PLAT098_ALERT_3_B

Problem: Low Bond Precision on C-C Bonds 0.01019 Ang.

Response: The crystals were all very weakly diffracting, even with extremely prolonged exposure times using Cu radiation, making it difficult to collect the high angle reflections. This is routinely observed for supramolecular structures, especially if they are comprised of predominantly light atoms, and as a consequence, the quality of the data is lower than would be ideal, which had a detrimental effect on the average bond precision values. However, the identity of the structure was clearly established without issue.

9. References

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