

Cocrystallization with a clip-type molecule catcher: a novel method to determine structures of liquid molecules

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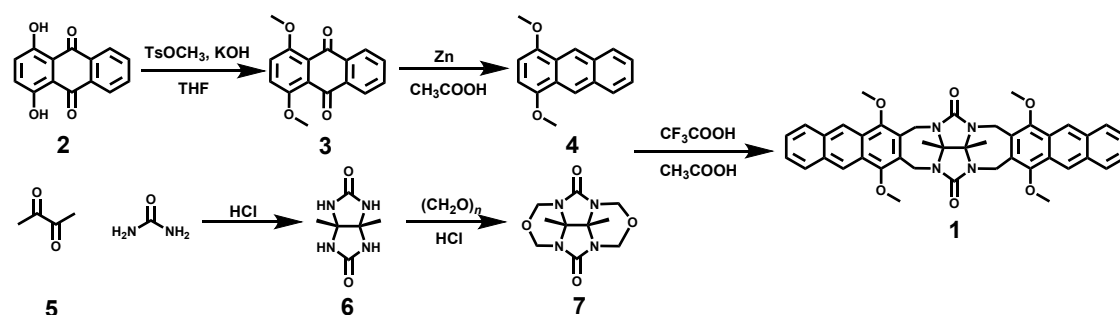
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1. <i>Materials and instrumentations</i>	S2
2. <i>Synthesis and characterization of compounds</i>	S2
3. <i>Crystallographic data for the molecular clip 1</i>	S6
4. <i>Association constant and stoichiometry determination for the complexation between 1 and 4-nitrophenol</i>	S12
5. <i>Crystallographic data for the host–guest complex of 1 and 4-nitrophenol</i>	S13
6. <i>Association constant for the complexation between 1 and TNP</i>	S16
7. <i>Crystallographic data for the host–guest complex of 1 and TNP</i>	S17
8. <i>Crystallographic data for the molecule catcher toward liquid molecules</i>	S19
9. <i>The host–guest complexation between 1 and liquid molecules</i>	S25
10. <i>References</i>	S27

1. Materials and instrumentations

All reagents were commercially available and used as supplied without further purification. Compounds **4** and **7** were prepared according to previous work.^[S1,S2] ¹H NMR, ¹³C NMR and NOESY spectra were recorded with an Agilent 600 MHz DirectDrive2 instrument with use of the deuterated solvent as the lock and the residual solvent or TMS as the internal reference. High-resolution mass spectrometric (HRMS) experiments were performed with a Bruker 7-Tesla FT-ICR mass spectrometer equipped with an electrospray source (Billerica, MA, USA). Single crystal X-ray data sets were obtained on an Oxford Diffraction Xcalibur Atlas Gemini captra instrument.

2. Synthesis and characterizations of compounds



Scheme S1. Synthetic route to molecular clip **1**.

Synthesis of compound 4. 1,4-Dimethoxyanthracene **4** was synthesized according to our previous work.^[S1] The ¹H NMR spectrum of molecule **4** is shown in Figure S1. ¹H NMR (600 MHz, CDCl₃, 298 K) δ (ppm): 8.77 (s, 2 H), 8.02–8.04 (m, 2 H), 7.46–7.48 (m, 2 H), 6.61 (s, 2 H), 4.04 (s, 6 H).

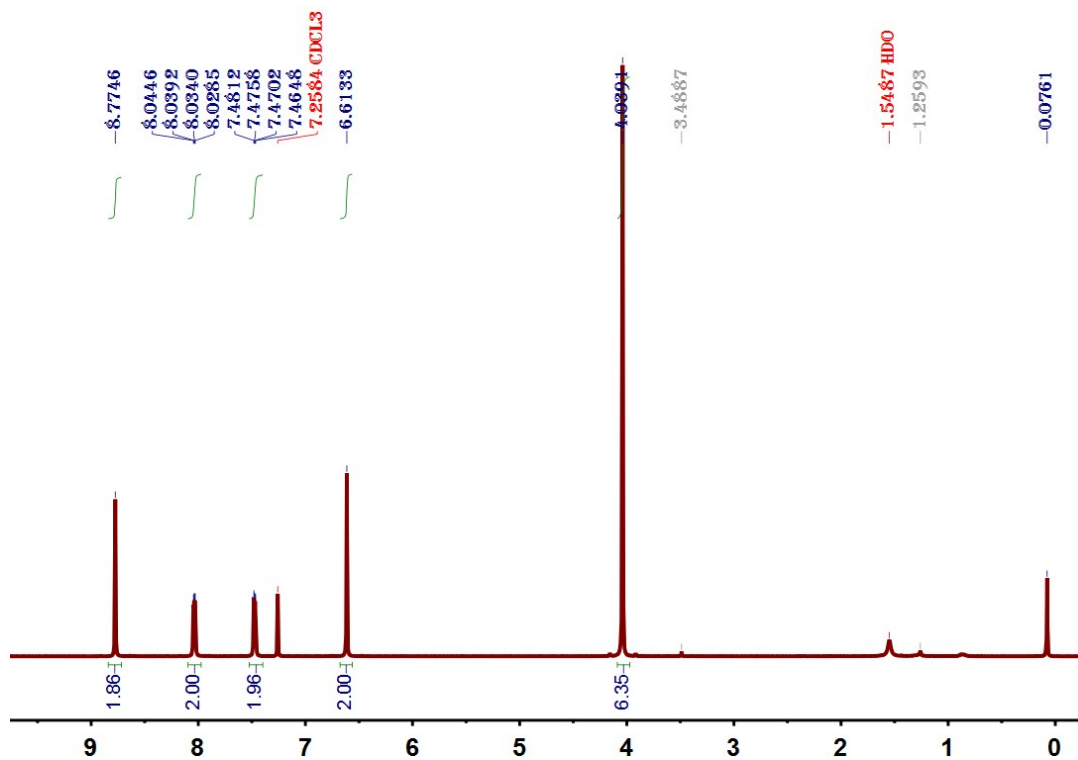


Figure S1 ^1H NMR spectrum (600 MHz, CDCl_3 , 298 K) of **4**.

Synthesis of compound 7. Compound **7** was prepared according to previous work.^[S2] The ^1H NMR spectrum of **7** is shown in Figure S2. ^1H NMR (600 MHz, $\text{DMSO}-d_6$, 298 K) δ (ppm): 5.20–5.21 (d, $J = 12$ Hz, 4 H), 4.98–5.00 (d, $J = 12$ Hz, 4 H), 1.80 (s, 6 H).

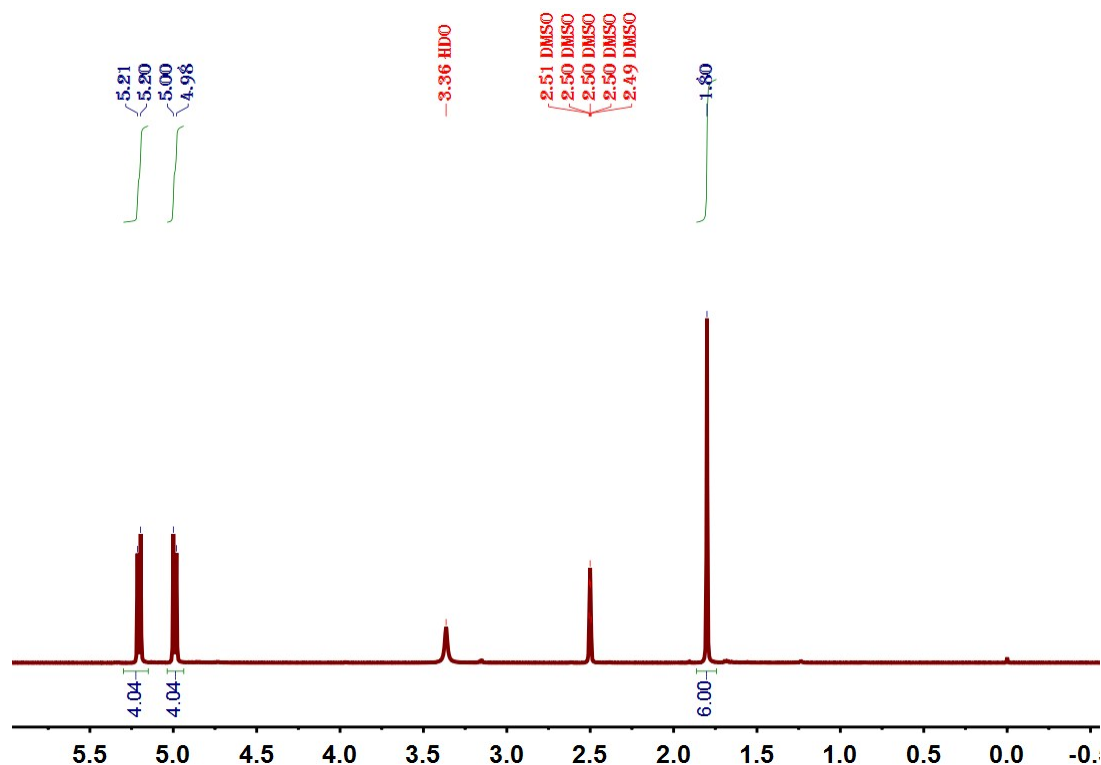


Figure S2 ^1H NMR spectrum (600 MHz, $\text{DMSO-}d_6$, 298 K) of **7**.

Synthesis of molecular clip 1. To a 25 mL round bottom flask, 1,4-dimethoxyanthracene (**4**, 1.00 g, 4.20 mmol), compound **7** (0.51g, 2.00 mmol), 10.0 mL of HOAc and 10.0 mL of CF_3COOH were added. The reaction mixture was stirred at 90 °C for 2 hours. After precipitation by the addition of 100 mL of methyl alcohol, the solid was filtered and purified by column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate ($v : v = 1 : 2$) as the eluent to give 1.14 g (82% yield) of **1** as a pale yellow solid. Mp: over 330 °C. The ^1H NMR spectrum of compound **1** is shown in Figure S3. ^1H NMR (600 MHz, CDCl_3 , 298 K) δ (ppm): 8.50 (s, 4 H), 7.91–7.94 (m, 4 H), 7.39–7.42 (m, 4 H), 5.67–5.70 (d, $J = 18$ Hz, 4 H), 4.12–4.15 (d, $J = 18$ Hz, 4 H), 4.06 (s, 12 H), 1.86 (s, 6 H). The ^{13}C NMR spectrum of **1** is shown in Figure S4. ^{13}C NMR (150 MHz, CDCl_3 , 298 K) δ (ppm): 158.5, 152.7, 134.3, 131.0, 129.3, 128.5, 128.1, 124.8, 65.7, 39.5, 19.8. The HR ESI-MS of **1** is shown in Figure S5: m/z calcd for $[\text{M}+\text{H}^+]$ $\text{C}_{42}\text{H}_{39}\text{O}_6\text{N}_4^+$, 695.2864; Found 695.2843, error 3.0 ppm.

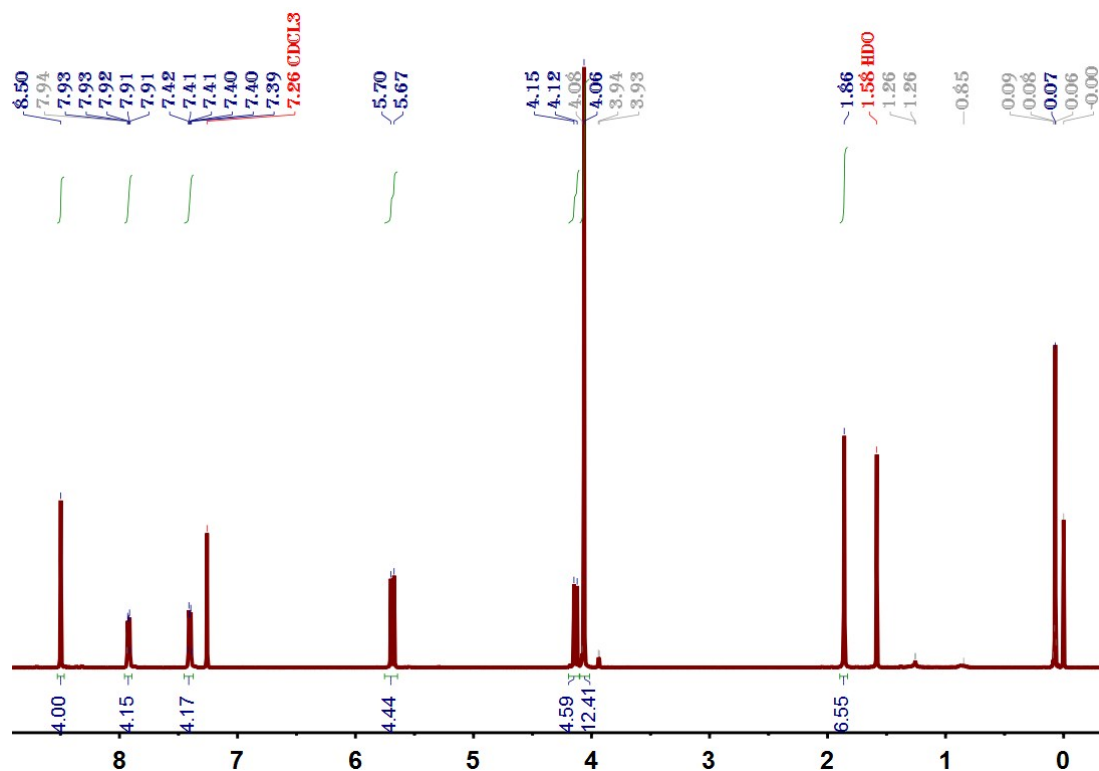


Figure S3 ¹H NMR spectrum (600 MHz, CDCl₃, 298 K) of 1.

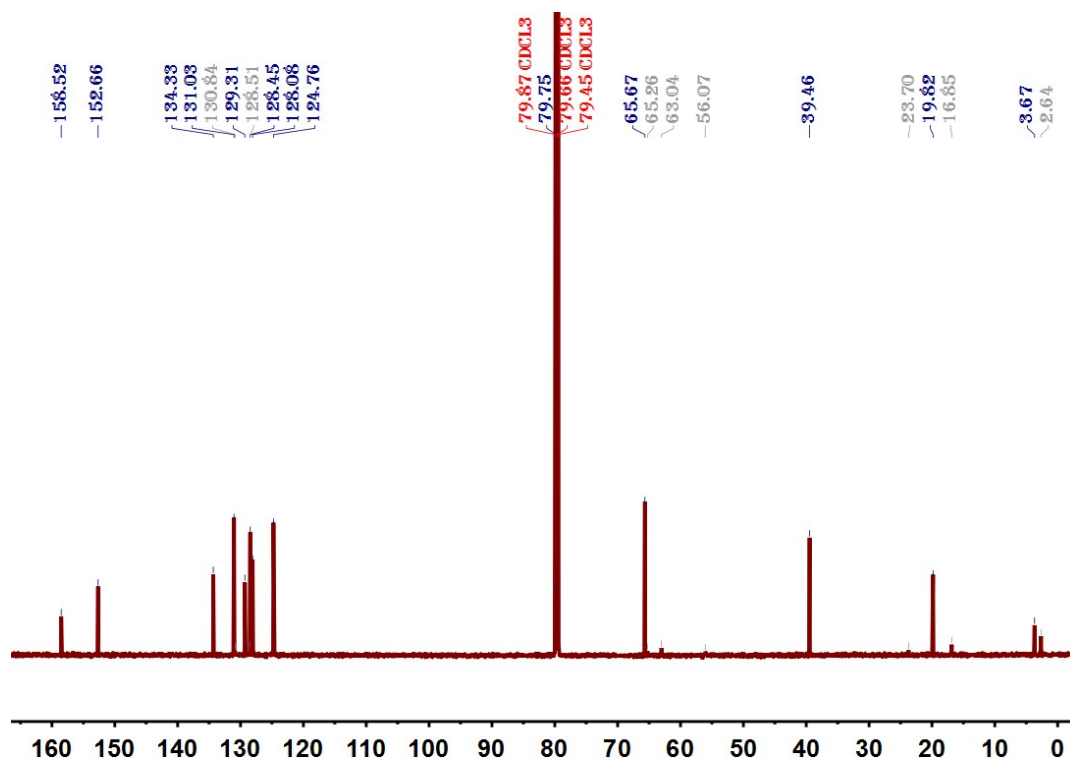


Figure S4 ¹³C NMR spectrum (150 MHz, CDCl₃, 298 K) of 1.

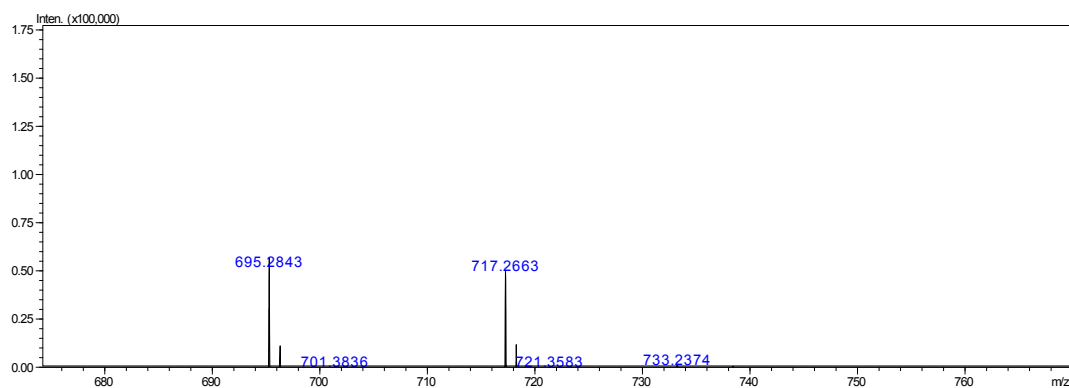


Figure S5 HR ESI-MS spectrum of compound **1** in CHCl₃.

3. Crystallographic Data for the molecular clip **1**

Methods to get single crystals of molecular clip **1** suitable for X-ray analysis:

1•(CH₃CN)

1 (10 mg) was dissolved in acetonitrile to make a hot saturated acetonitrile solution, and the solution was allowed to evaporate slowly at room temperature to afford faint yellow crystals within 6 hours.

1•(CHCl₃)

1 (10 mg) was dissolved in a mixture of chloroform/*n*-hexane (*v* : *v* = 2 : 1), and faint yellow crystals were obtained within 12 hours by slow evaporation.

Table S1. Experimental single crystal X-ray data for **1**•(CH₃CN) and **1**•(CHCl₃)

Formula	1 •(CH ₃ CN)	1 •(CHCl ₃)
Crystallization Solvent	acetonitrile	chloroform/ <i>n</i> -hexane (<i>v</i> : <i>v</i> = 2 : 1)
Collection Temperature	173 K	173 K
Formula	C ₄₈ H ₄₇ N ₇ O ₆	C ₄₃ H ₃₉ Cl ₃ N ₄ O ₆
<i>Mr</i>	817.92	814.13
Crystal Size [mm ³]	0.15 × 0.12 × 0.08	0.15 × 0.1 × 0.08
Crystal System	monoclinic	Triclinic
Space Group	P2 ₁ /n	P-1

a [Å]	14.1397(3)	9.4017(2)
b [Å]	17.9442(4)	11.9309(3)
c [Å]	17.0478(4)	16.8327(4)
α [°]	90	95.0320(10)
β [°]	107.0650(10)	92.8350(10)
γ [°]	90	92.8780(10)
V [Å ³]	4135.02(16)	1875.73(8)
Z	4	2
Dcalcd [g cm ⁻³]	1.314	1.441
μ [mm ⁻¹]	0.458	1.770
F(000)	1728.0	848.0
2θ range [°]	6.234 – 109.85	9.19 – 109.872
Reflections collected	38333	22375
Independent reflections, R_{int}	7729, 0.0406	7014, 0.0421
Data / restraints / parameters	7729 / 0 / 559	7014 / 0 / 511
Final $R1$ values ($I > 2\sigma(I)$)	0.0884	0.0645
Final $R1$ values (all data)	0.0972	0.0683
Goodness-of-fit on F^2	1.000	1.044
Largest difference peak and hole [e.Å ⁻³]	1.52 / -0.99	1.53 / -1.25
CCDC	1960289	1960287

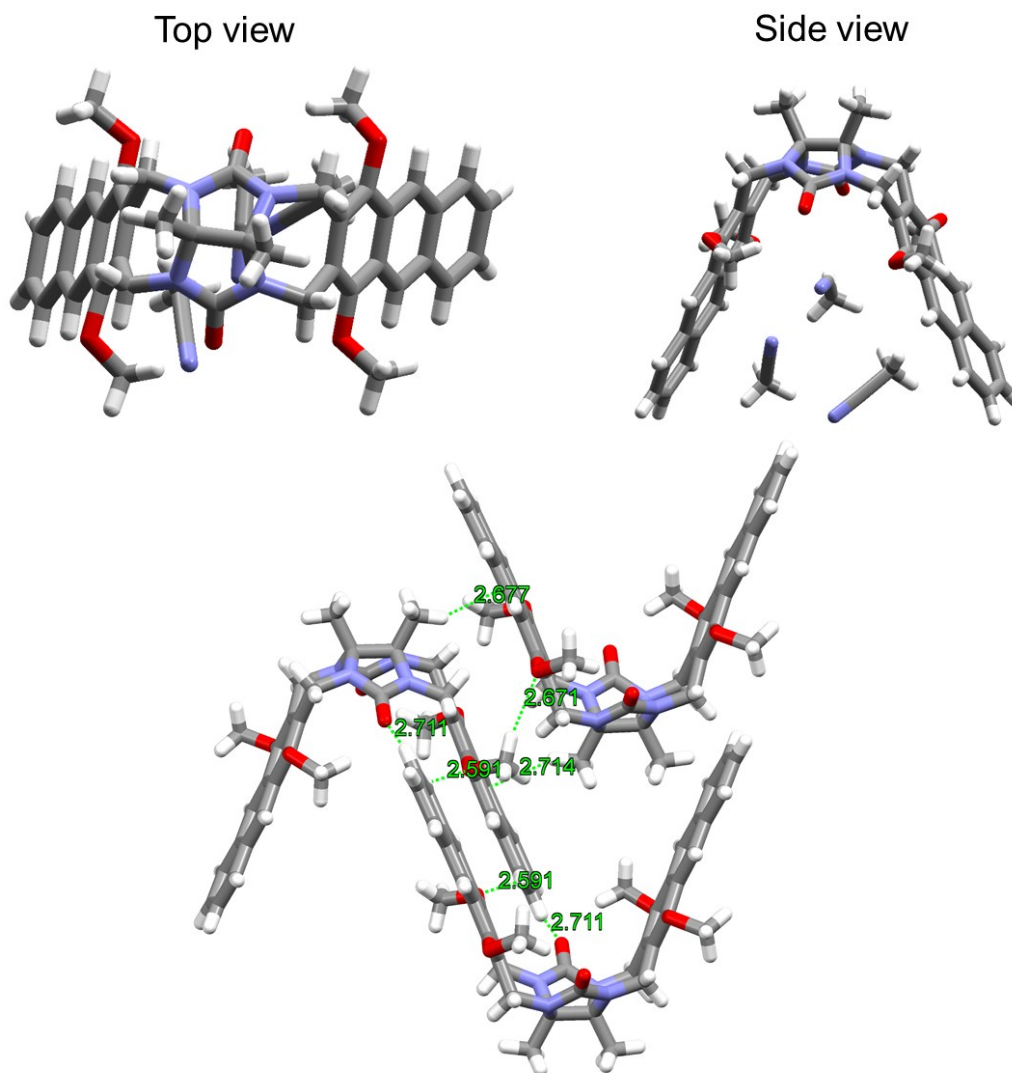
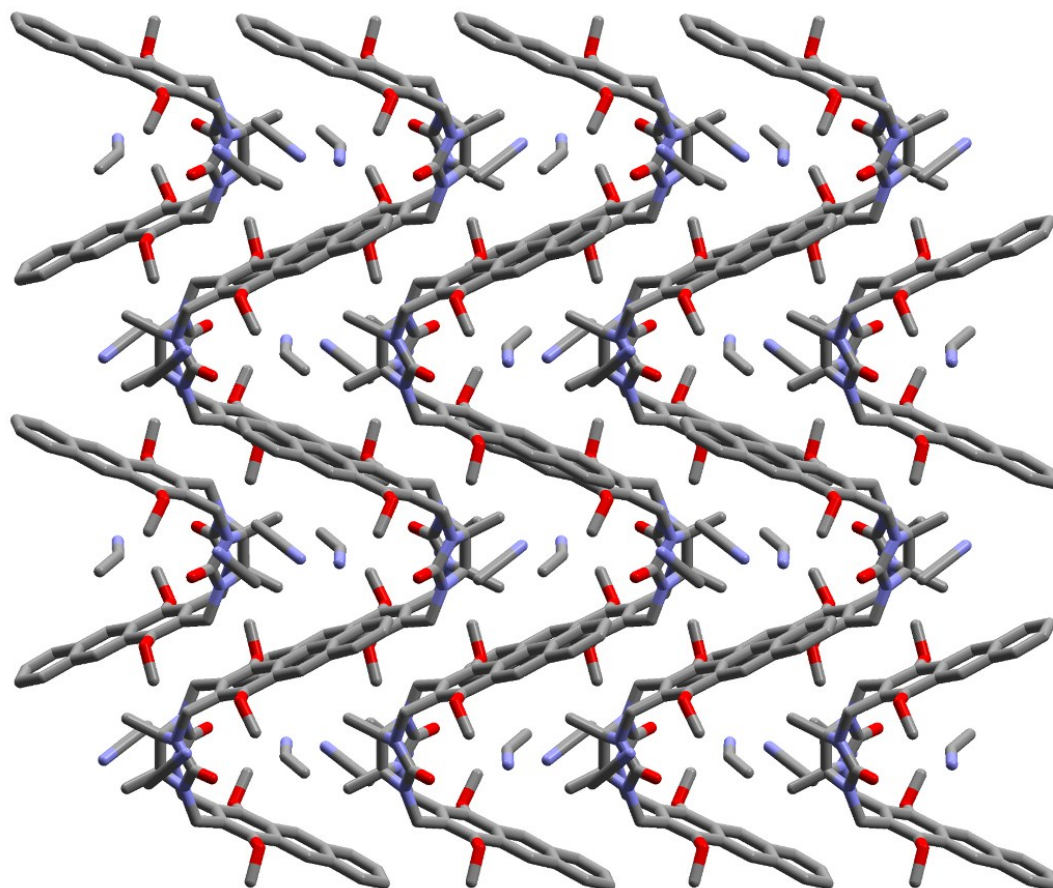


Figure S6 Single crystal structure of **1**•(CH₃CN). C gray, O red, H white, N blue. C–H··· π interactions with H··· π -plane distances of 2.677 and 2.714 Å; H···O distances for C–H···O interactions between two adjacent molecular clips (Å): 2.591, 2.711 and 2.671 Å.



View along a axis

Figure S7 The packing structure of **1•(CH₃CN)**. Hydrogen atoms are omitted for clarity.

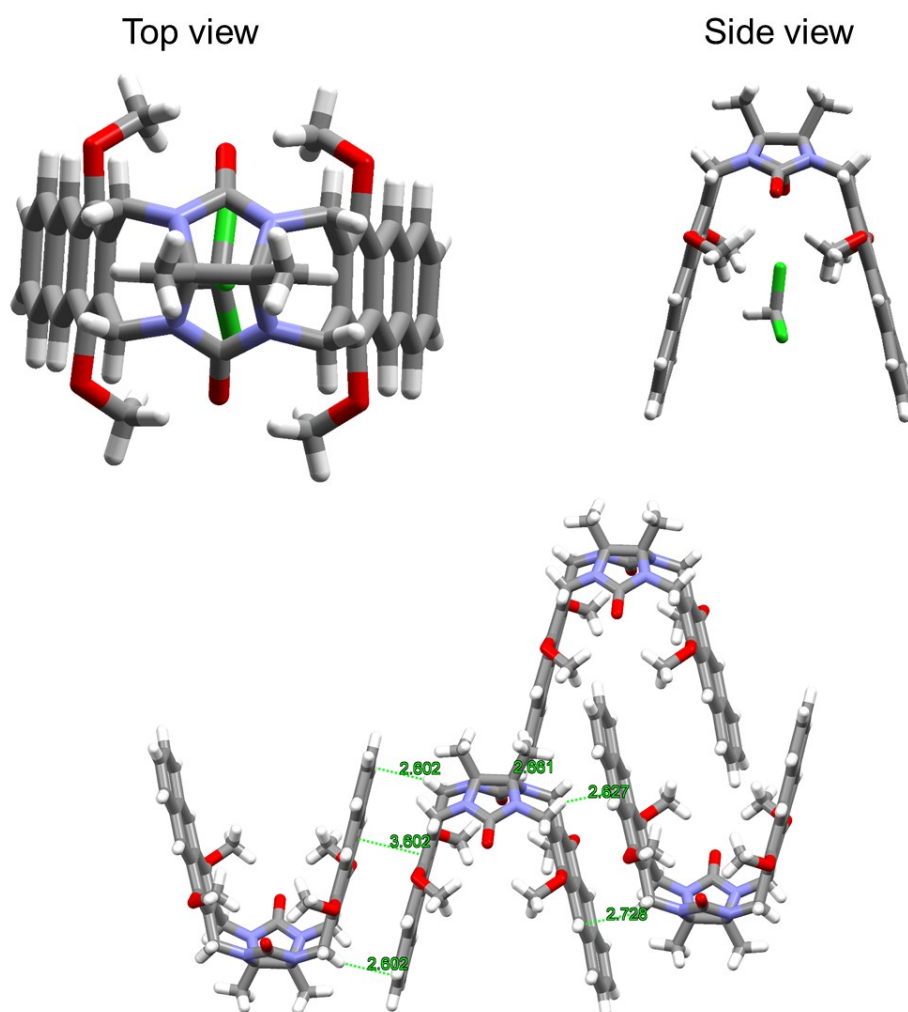
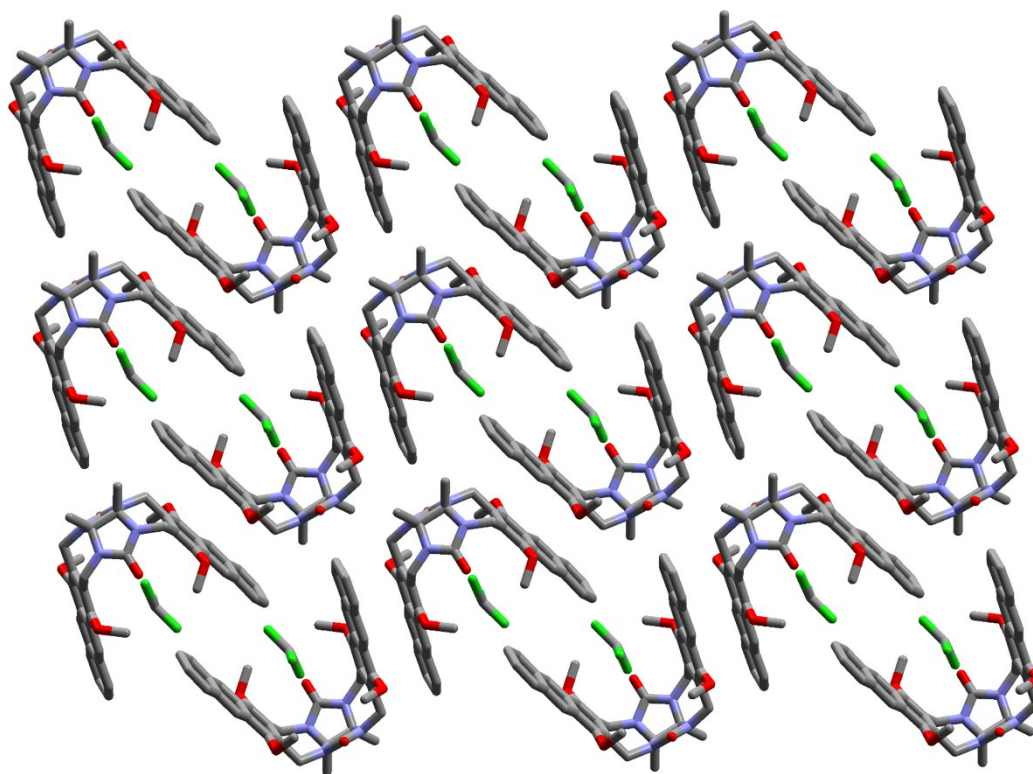


Figure S8 Single crystal structure of **1**•(CHCl₃). C gray, O red, H white, N blue, Cl green. Certain H atoms are omitted for clarity. C–H··· π interactions with H··· π -plane distances of 2.602, 2.728 and 2.627 Å; H···O distance for C–H···O interaction between two adjacent molecular clips (Å): 2.661; Face-to-face π -stacking parameters: centroid-centroid distance (Å): 3.602, ring plane/ring plane inclination (deg): 1.16.



View along a axis

Figure S9 The packing structure of **1**•(CHCl₃). Hydrogen atoms are omitted for clarity.

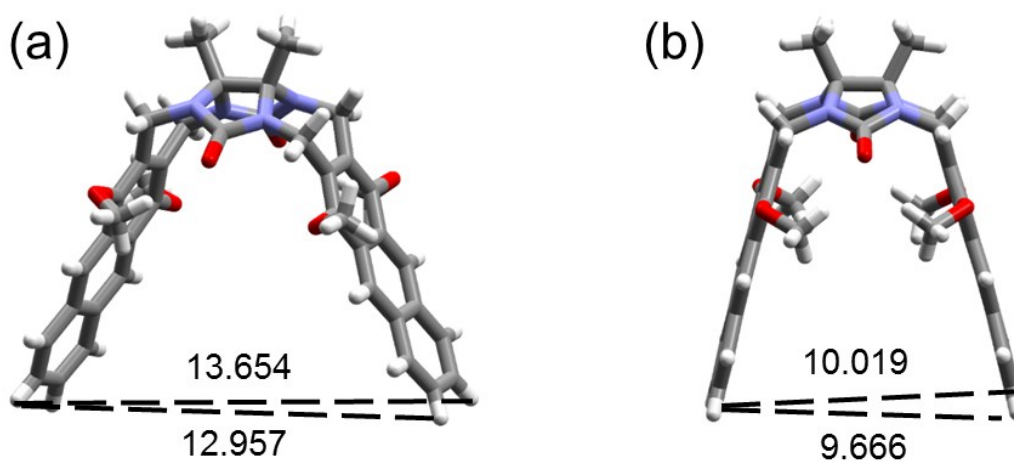


Figure S10 (a) Single crystal structure of **1** based on crystallization in acetonitrile. (b) Single crystal structure of **1** based on crystallization in chloroform/*n*-hexane ($\nu : \nu = 2 : 1$).

4. Association constant and stoichiometry determination for the complexation between **1** and 4-nitrophenol

To determine the association constant and stoichiometry for the complexation between **1** and 4-nitrophenol, ¹H NMR titration was done with solutions which had a constant concentration of the molecular clip (1.00 mM) and varying concentrations of the guest 4-nitrophenol. By a non-linear curve-fitting method, the association constant (K_a) was determined. By a mole ratio plot, 1 : 1 stoichiometry was obtained for the complexation between **1** and 4-nitrophenol.

The non-linear curve-fitting was based on a previous report.^{S3}

$$\Delta\delta = (\Delta\delta_\infty / [H]_0) (0.5[G]_0 + 0.5([H]_0 + 1/K_a) - (0.5 ([G]_0^2 + (2[G]_0 (1/K_a - [H]_0) + (1/K_a + [H]_0)^2)^{0.5})) \dots\dots\dots(S1)$$

where $\Delta\delta$ is the chemical shift change of H_a on the compound **1**, $\Delta\delta_\infty$ is the chemical shift change of H_a when the molecular clip is completely complexed, $[G]_0$ is the initial concentration of the guest 4-nitrophenol, and $[H]_0$ is the fixed initial concentration of the compound **1**.

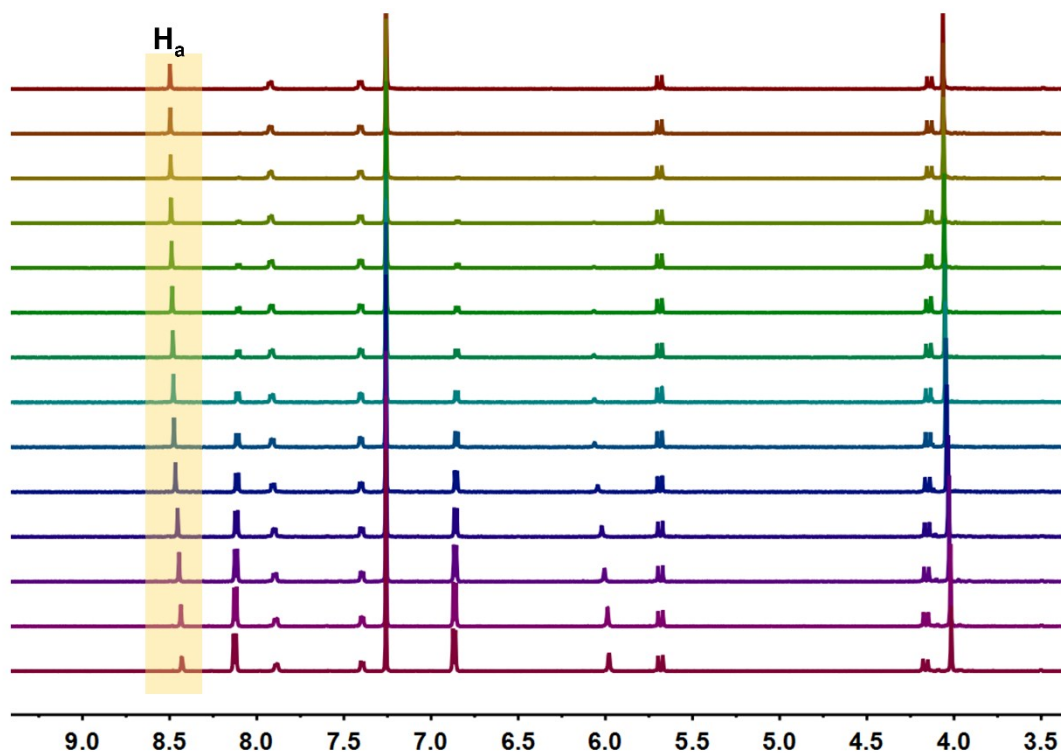


Figure S11 Partial ^1H NMR spectra (600 MHz, CDCl_3 , 298 K) of molecular clip **1** at a concentration of 1.00 mM upon addition of various concentrations of 4-nitrophenol: 0.000 mM, 0.100 mM, 0.200 mM, 0.380 mM, 0.570 mM, 0.820 mM, 1.07 mM, 1.38 mM, 1.67 mM, 2.31 mM, 3.33 mM, 4.11 mM, 5.24 mM, and 6.31 mM from up to bottom.

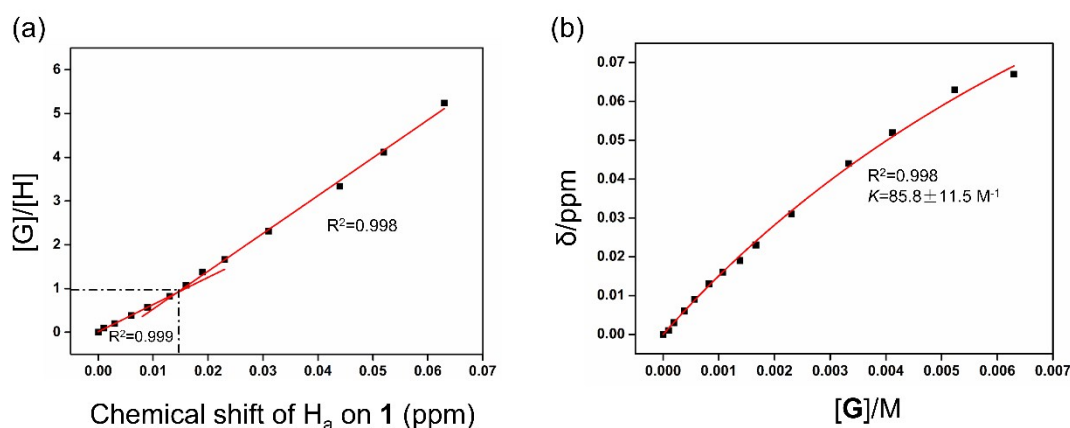


Figure S12 (a) Mole ratio plot for molecular clip **1** and 4-nitrophenol, indicating a 1:1 stoichiometry. (b) The chemical shift changes of H_a on **1** upon addition of 4-nitrophenol. The red solid line was obtained from the non-linear curve-fitting using Eq. S1.

5. Crystallographic data for the host–guest complex of **1** and 4-nitrophenol

Method to get single crystals of the host–guest complex of **1** and 4-nitrophenol:

A mixture of **1** (10 mg) and 4-nitrophenol (5 mg) was dissolved in a mixture of chloroform and hexane ($v : v = 2 : 1$). The solution was allowed to evaporate slowly at room temperature to afford faint yellow single crystals.

Table S2. Experimental single crystal X-ray data for **1**⊂4-nitrophenol

Formula	1 ⊂4-nitrophenol
Crystallization Solvent	chloroform
Collection Temperature	173 K

Formula	C ₄₉ H ₄₄ Cl ₃ N ₅ O ₉
<i>Mr</i>	953.24
Crystal Size [mm]	0.1 × 0.03 × 0.02
Crystal System	triclinic
Space Group	P-1
<i>a</i> [Å]	10.3707(5)
<i>b</i> [Å]	12.8735(7)
<i>c</i> [Å]	17.6390(9)
α [°]	71.233(3)
β [°]	81.025(4)
γ [°]	80.639(3)
<i>V</i> [Å ³]	2186.5(2)
<i>Z</i>	2
<i>D</i> _{calcd} [g cm ⁻³]	1.448
μ [mm ⁻¹]	1.614
F(000)	992.0
2 θ range [°]	6.354 – 110.14
Reflections collected	31289
Independent reflections, <i>R</i> _{int}	8221, 0.0634
Data / restraints / parameters	8221 / 0 / 603
Final <i>R</i> ₁ values (<i>I</i> > 2 σ (<i>I</i>))	0.1144
Final <i>R</i> ₁ values (all data)	0.1514
Goodness-of-fit on <i>F</i> ²	1.310
Largest difference peak and hole [e.Å ⁻³]	1.96 / -1.31
CCDC	1960290

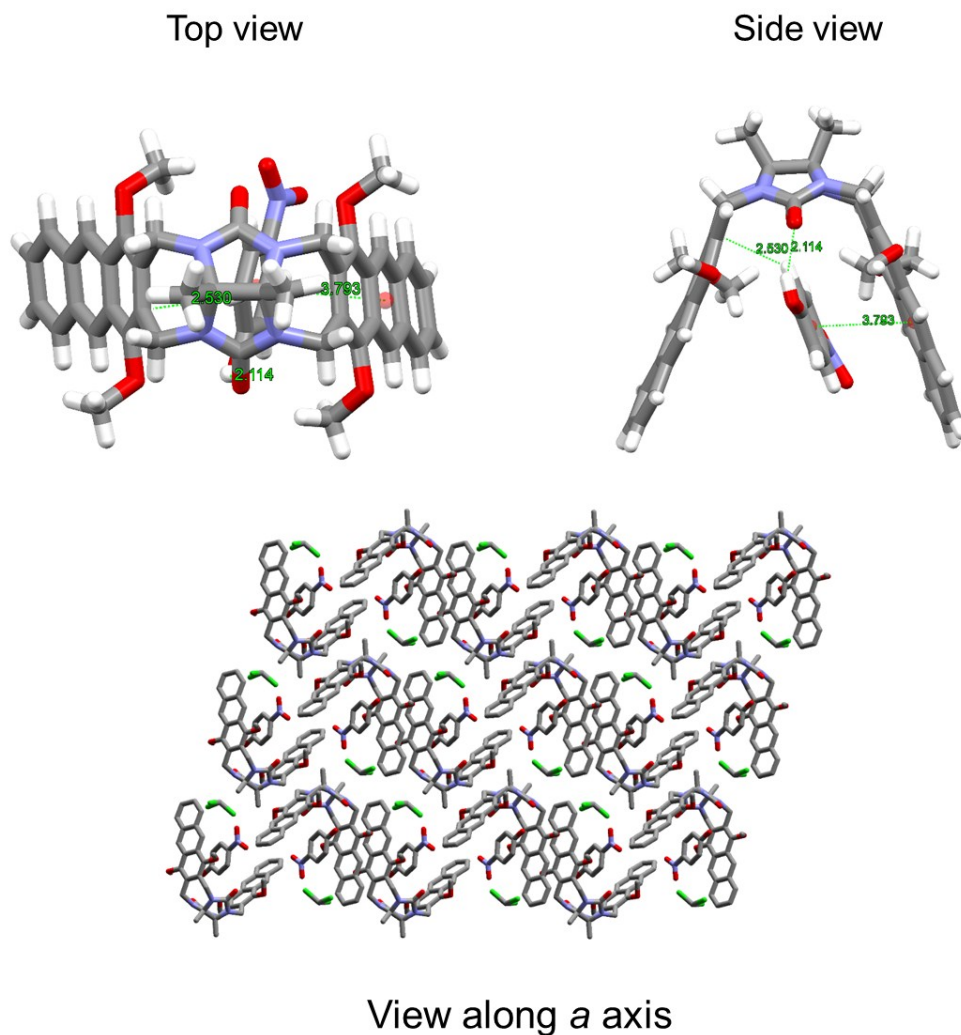


Figure S13 Single crystal structure of **1□4-nitrophenol**. C gray, O red, H white, N blue, Cl green. Certain H atoms are omitted for clarity. C–H··· π interaction with H··· π -plane distance of 2.530 Å; H···O distance for the C–H···O interaction between the hydrogen atom on the phenolic hydroxyl group of 4-nitrophenol and the carbonyl oxygen atom on the spacer (Å): 2.114; Face-to-face π -stacking parameters: centroid-centroid distance (Å): 3.793, ring plane/ring plane inclination (deg): 15.35.

6. Association constant for the complexation between **1** and TNP

To determine the association constant and stoichiometry for the complexation between **1** and TNP, ^1H NMR titration was done with solutions which had a constant concentration of the molecular clip (1.00 mM) and varying concentrations of the guest 4-nitrophenol.

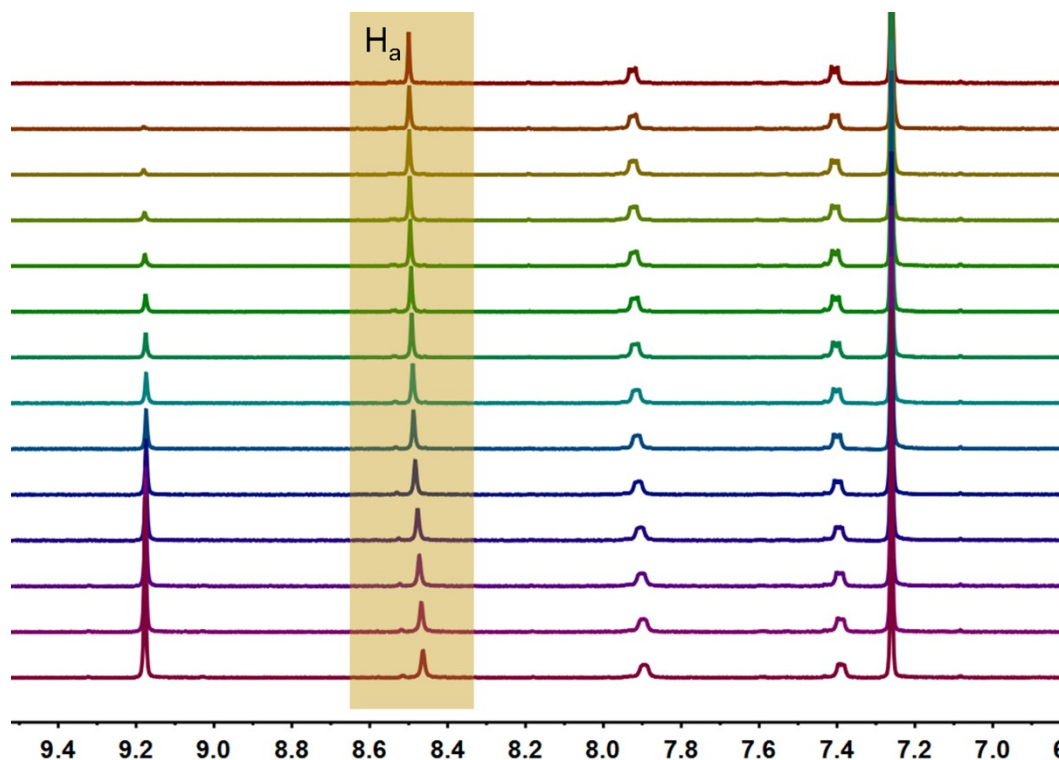


Figure S14 Partial ^1H NMR spectra (600 MHz, CDCl_3 , 298 K) of molecular clip **1** at a concentration of 1.00 mM upon addition of various concentrations of TNP: 0.00 mM, 0.10 mM, 0.20 mM, 0.38 mM, 0.57 mM, 0.82 mM, 1.07 mM, 1.38 mM, 1.67 mM, 2.31 mM, 3.33 mM, 4.11 mM, 5.24 mM, and 6.31 mM from up to bottom.

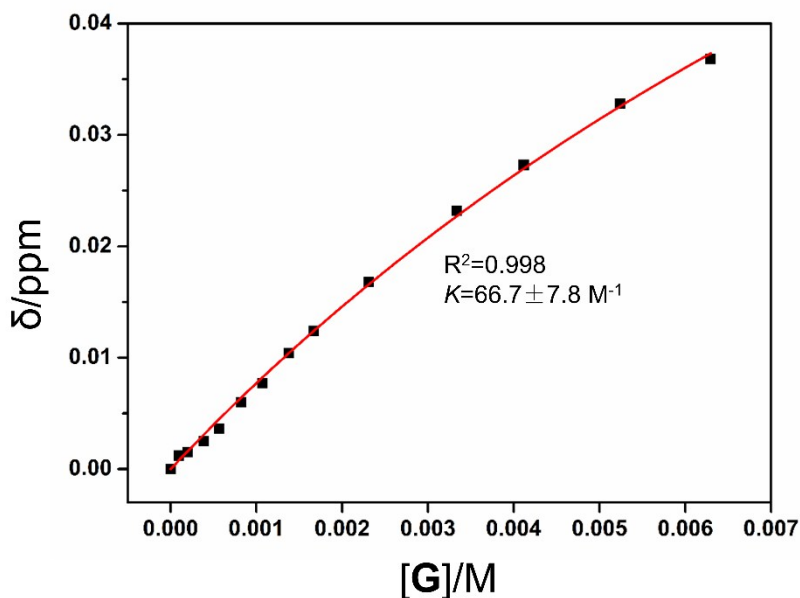


Figure S15 The chemical shift changes of H_a on **1** upon addition of TNP. The red solid line was obtained from the non-linear curve-fitting using Eq. S1.

7. Crystallographic data for the host–guest complex of **1** and TNP

Method to get single crystals of the host–guest complex of **1** and TNP:

A mixture of **1** (10 mg) and TNP (5 mg) was dissolved in a mixture of chloroform and hexane ($v : v = 2 : 1$). The solution was allowed to evaporate slowly at room temperature to afford reddish black single crystals.

Table S3. Experimental single crystal X-ray data for the complex of **1** and TNP

Formula	1 □TNP
Crystallization Solvent	chloroform
Collection Temperature	173 K
Formula	C ₄₉ H ₄₂ Cl ₁₃ N ₇ O ₁₃
<i>Mr</i>	1043.24
Crystal Size [mm]	0.08 × 0.06 × 0.05
Crystal System	monoclinic
Space Group	P2 ₁ /c

a [Å]	9.2666(5)
b [Å]	26.6723(14)
c [Å]	18.5536(9)
α [°]	90
β [°]	101.541(2)
γ [°]	90
V [Å ³]	4493.0(4)
Z	4
Dcalcd [g cm ⁻³]	1.542
μ [mm ⁻¹]	1.659
F(000)	2160.0
2θ range [°]	7.152 – 110.086
Reflections collected	8322
Independent reflections	8322
Data / restraints / parameters	8322 / 0 / 657
Final $R1$ values ($I > 2\sigma(I)$)	0.0626
Final $R1$ values (all data)	0.0739
Goodness-of-fit on $F2$	1.022
Largest difference peak and hole [e.Å ⁻³]	0.75 / -0.65
CCDC	1960292

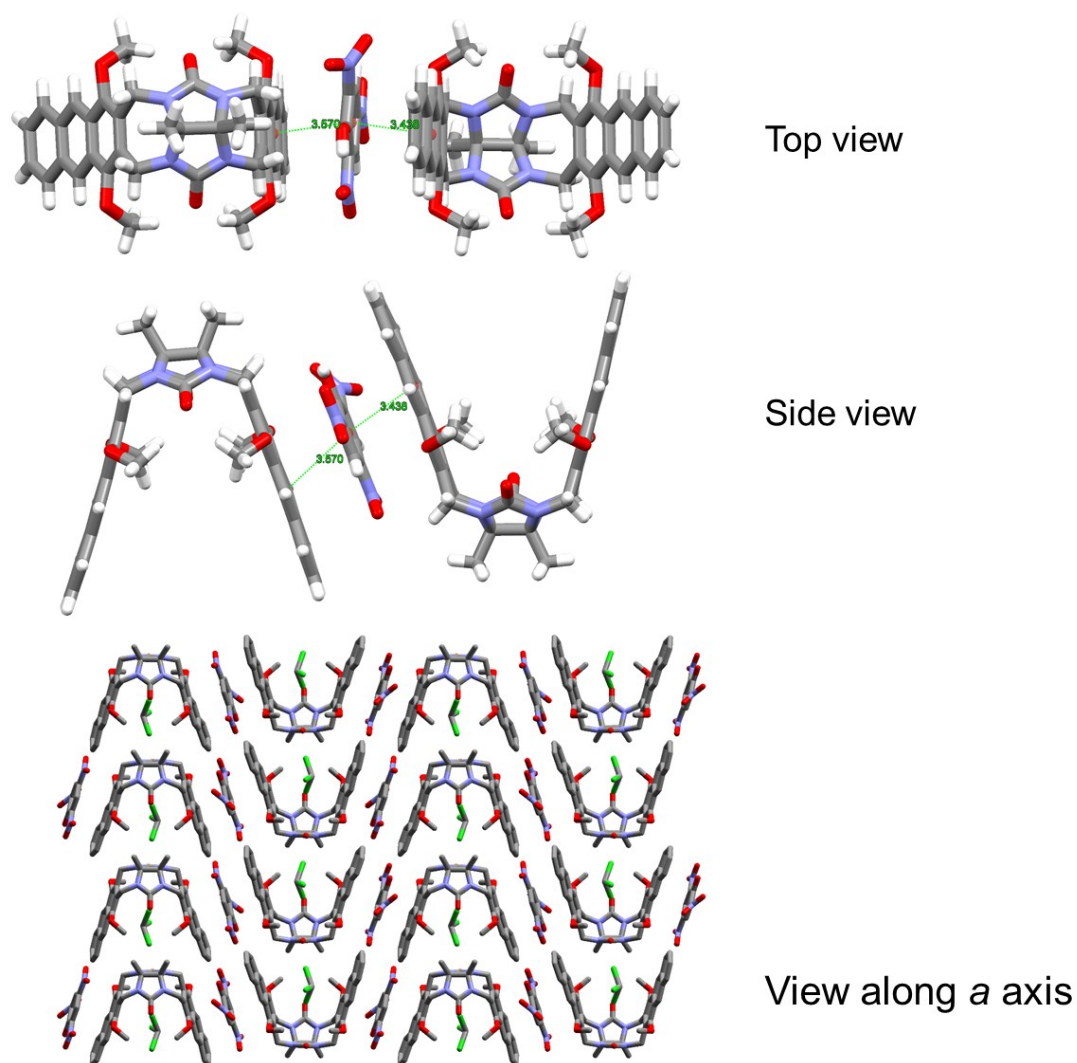
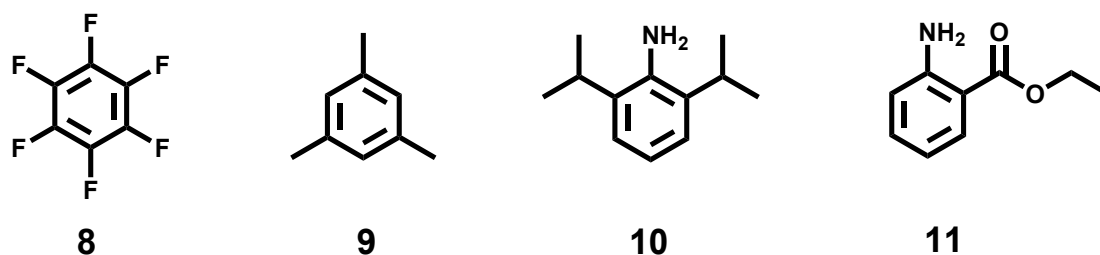


Figure S16 Single crystal structure of the complex of **1** and TNP. C gray, O red, H white, N blue, Cl green. Certain H atoms are omitted for clarity. The anthracene ring and TNP are connected by strong charge-transfer interactions, and the distances between anthracene ring and TNP are 3.570 and 3.438 Å.

8. Crystallographic data for the molecule catcher toward liquid molecules

Methods to get single crystals of the complex of molecular clip **1** and selected liquid molecules fitted to X-ray analysis:

A mixture of **1** (10 mg) and a selected liquid molecule (10 mg) was dissolved in CHCl_3 (0.8 mL), and solution was allowed to evaporate slowly at room temperature. Crystals formed within 24 hours.



Scheme 2 The chemical structure of selected liquid molecules.

Table S3. Experimental single crystal X-ray data for **1•8** and **1•9**

Formula	1•8	1•9
Crystallization Solvent	chloroform	chloroform
Collection Temperature	173 K	173 K
Formula	C ₄₈ H ₃₈ F ₆ N ₄ O ₆	C ₅₁ H ₅₀ N ₄ O ₆
<i>Mr</i>	880.82	814.95
Crystal Size [mm]	0.1 × 0.08 × 0.05	0.12 × 0.08 × 0.06
Crystal System	monoclinic	Triclinic
Space Group	C2/c	P-1
<i>a</i> [Å]	16.0417(3)	10.2940(4)
<i>b</i> [Å]	18.6338(3)	13.4087(5)
<i>c</i> [Å]	13.7075(2)	16.3447(7)
α [°]	90	81.024(2)
β [°]	99.4420(10)	80.676(2)
γ [°]	90	69.255(2)
<i>V</i> [Å ³]	4041.90(12)	2069.98(15)
<i>Z</i>	4	2
D _{calcd} [g cm ⁻³]	1.447	1.308
μ [mm ⁻¹]	0.624	0.443
F(000)	1824.0	864.0
2 θ range [°]	6.376 – 109.934	8.044 – 109.972
Reflections collected	21172	20300
Independent reflections, <i>R</i> _{int}	3806, 0.0359	7603, 0.0604

Data / restraints / parameters	3806 / 0 /292	7603 / 0 /559
Final $R1$ values ($I > 2\sigma(I)$)	0.0520	0.0616
Final $R1$ values (all data)	0.0614	0.0771
Goodness-of-fit on $F2$	1.056	1.070
Largest difference peak and hole [$e \cdot \text{\AA}^{-3}$]	0.30 / -0.35	0.48 / -0.34
CCDC	1960293	1960288

Table S4. Experimental single crystal X-ray data for **1•10** and **1•11**

Formula	1•10	1•11
Crystallization Solvent	chloroform	chloroform
Collection Temperature	173K	173 K
Formula	C59.5H57N6O6	C51H49N5O8
M_r	952.11	859.95
Crystal Size [mm]	0.08 × 0.06 × 0.02	0.05 × 0.03 × 0.02
Crystal System	triclinic	Triclinic
Space Group	P-1	P-1
a [Å]	10.4161(2)	10.6881(3)
b [Å]	14.2726(3)	14.5217(4)
c [Å]	18.0403(4)	16.4855(5)
α [°]	106.7040(10)	111.189(2)
β [°]	91.8020(10)	91.323(2)
γ [°]	100.7610(10)	101.864(2)
V [Å ³]	2513.27(9)	2321.42(12)
Z	2	2
D _{calcd} [g cm ⁻³]	1.258	1.230
μ [mm ⁻¹]	0.422	0.438
F(000)	1008.0	908.0
2θ range [°]	6.136 – 109.752	5.834 – 109.94

Reflections collected	22734	28109
Independent reflections, <i>Rint</i>	9191, 0.0411	8695, 0.0543
Data / restraints / parameters	9191 / 318 / 773	8695 / 0 / 585
Final <i>R</i> 1 values ($I > 2\sigma(I)$)	0.0751	0.0652
Final <i>R</i> 1 values (all data)	0.1015	0.0957
Goodness-of-fit on <i>F</i> 2	1.061	1.055
Largest difference peak and hole [e.Å ⁻³]	0.94 / -0.37	0.29 / -0.32
CCDC	1960291	1960294

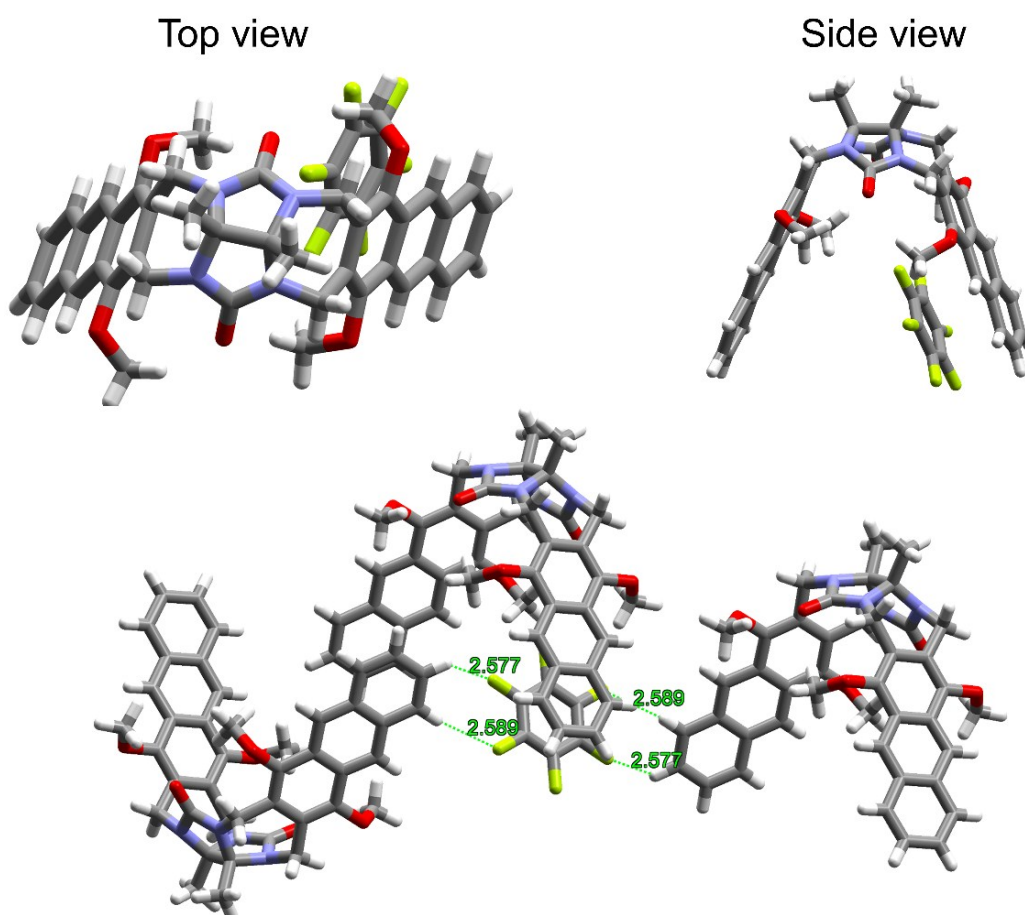


Figure S17 Single crystal structure of **1•8**. C gray, O red, H white, N blue, F yellow. Certain H atoms are omitted for clarity. H \cdots F distances for the C–H \cdots F interactions between the fluorine atoms on **8** and the hydrogen atoms on the anthracene groups (Å): 2.577, 2.589.

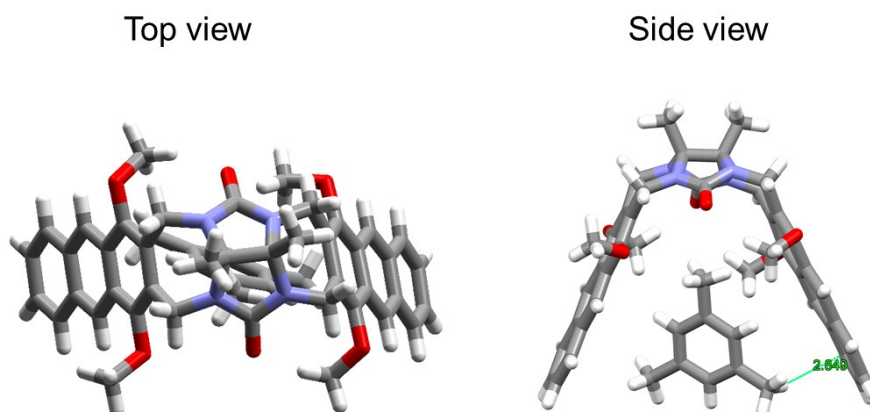


Figure S18 Single crystal structure of **1•9**. C gray, O red, H white, N blue. C–H··· π interaction with H··· π -plane distance of 2.849 Å.

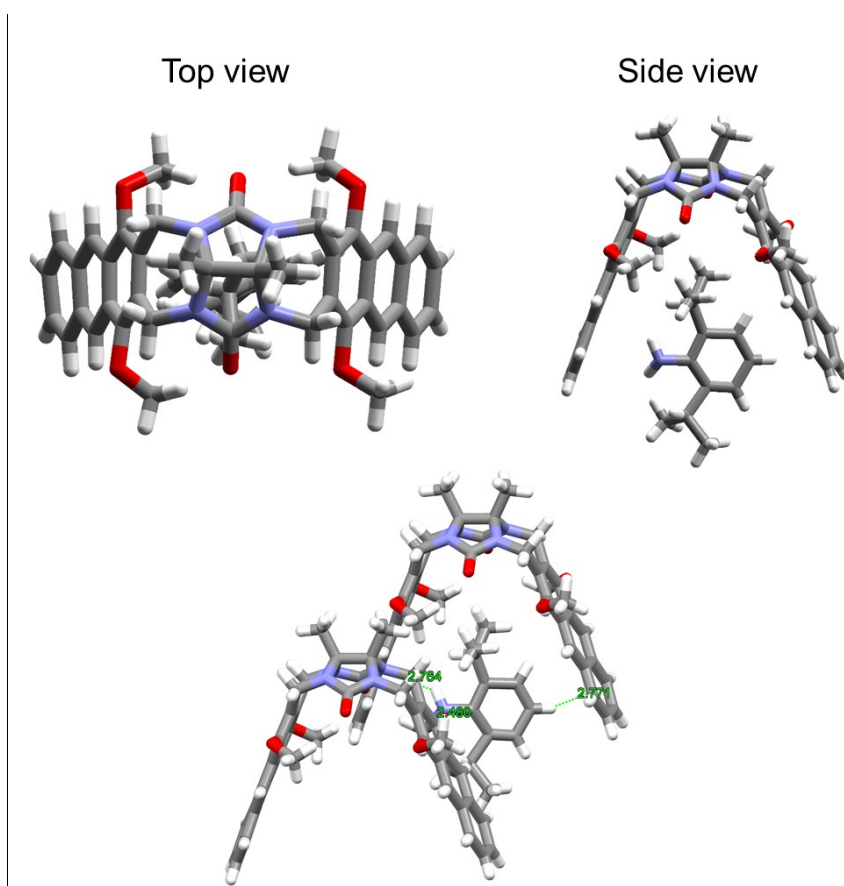


Figure S19 Single crystal structure of **1•10**. C gray, O red, H white, N blue. C–H··· π interaction with H··· π -plane distance of 2.771 Å; N–H··· π interaction with H··· π -plane distance of 2.764 Å; H···N distance for the C–H···N interaction between the hydrogen atom on a methoxy group of molecular clip **1** and a nitrogen atom on amidogen of **10** (Å): 2.480.

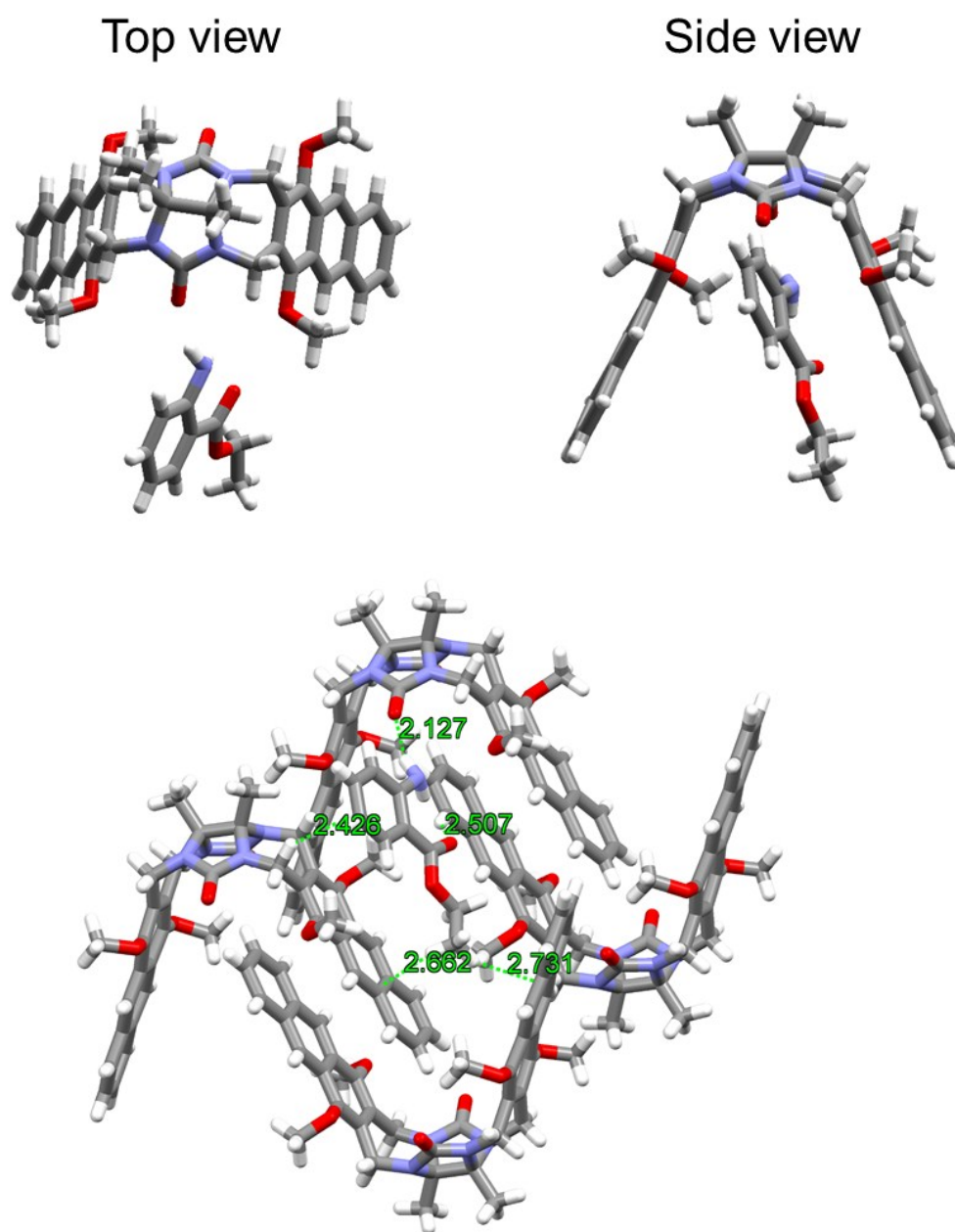


Figure S20 Single crystal structure of **1•11**. C gray, O red, H white, N blue. C–H··· π interaction with H··· π -plane distance of 2.426, 2.662, 2.731 Å; H···O distance for the C–H···O interaction between an oxygen atom on **11** and a hydrogen atom on the anthracene group (Å): 2.507; H···O distance for the N–H···O interaction between an oxygen atom on the spacer and a hydrogen atom on **11** (Å): 2.127.

9. The host-guest complexation between **1** and selected liquid molecules

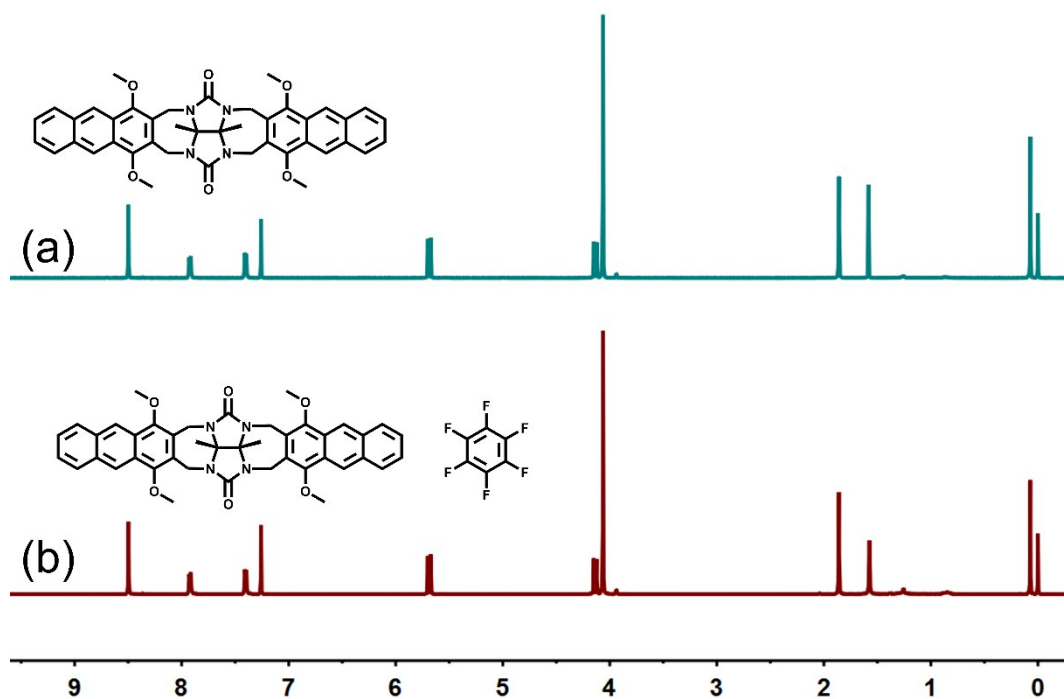


Figure S21 Partial ¹H NMR spectra (600 MHz, 298 K) in CDCl₃: (a) 5.00 mM **1**; (b) 5.00 mM **1** and 5.00 mM **8**.

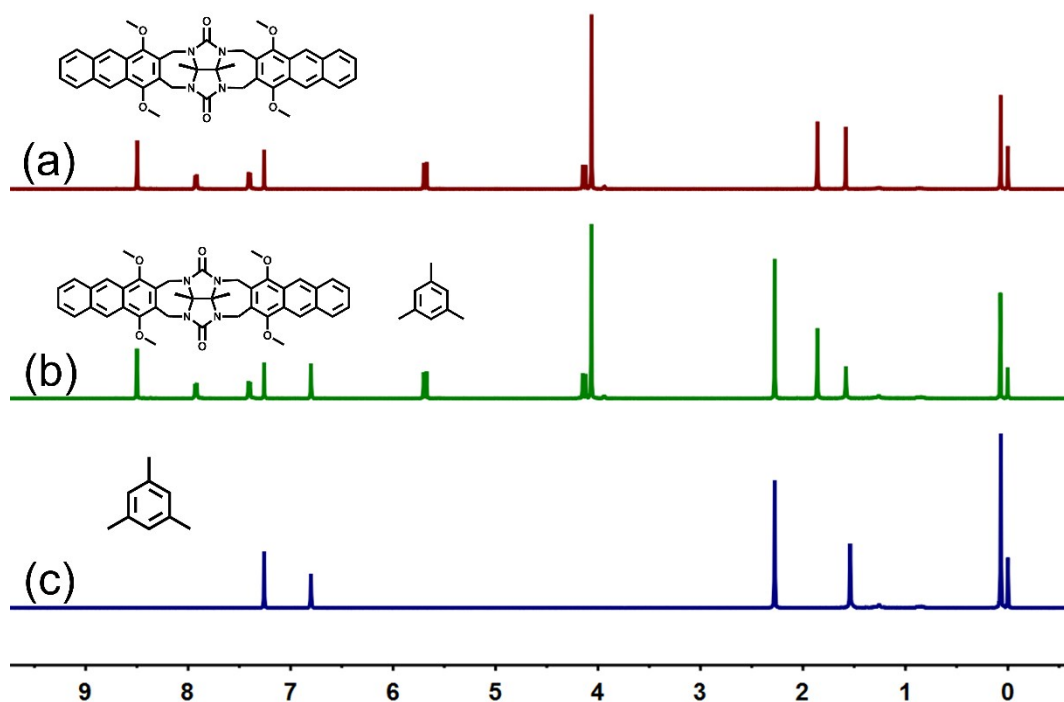


Figure S22 Partial ¹H NMR spectra (600 MHz, 298 K) in CDCl₃: (a) 5.00 mM **1**; (b) 5.00 mM **1** and 5.00 mM **9**; (c) 5.00 mM **9**.

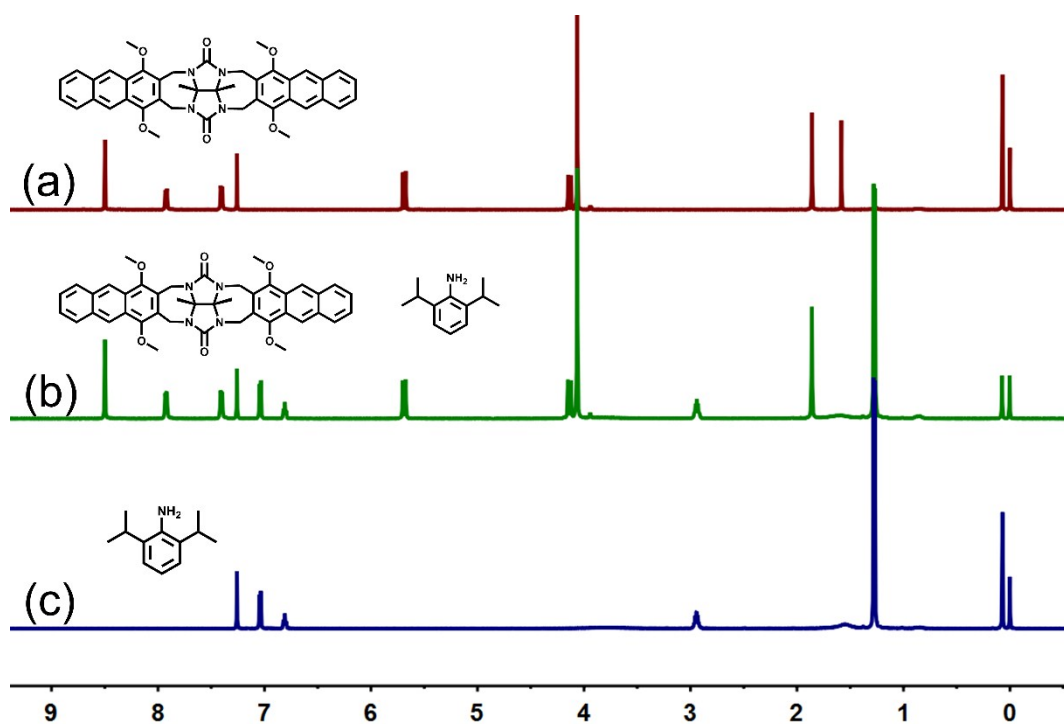


Figure S23 Partial ^1H NMR spectra (600 MHz, 298 K) in CDCl_3 : (a) 5.00 mM **1**; (b) 5.00 mM **1** and 5.00 mM **10**; (c) 5.00 mM **10**.

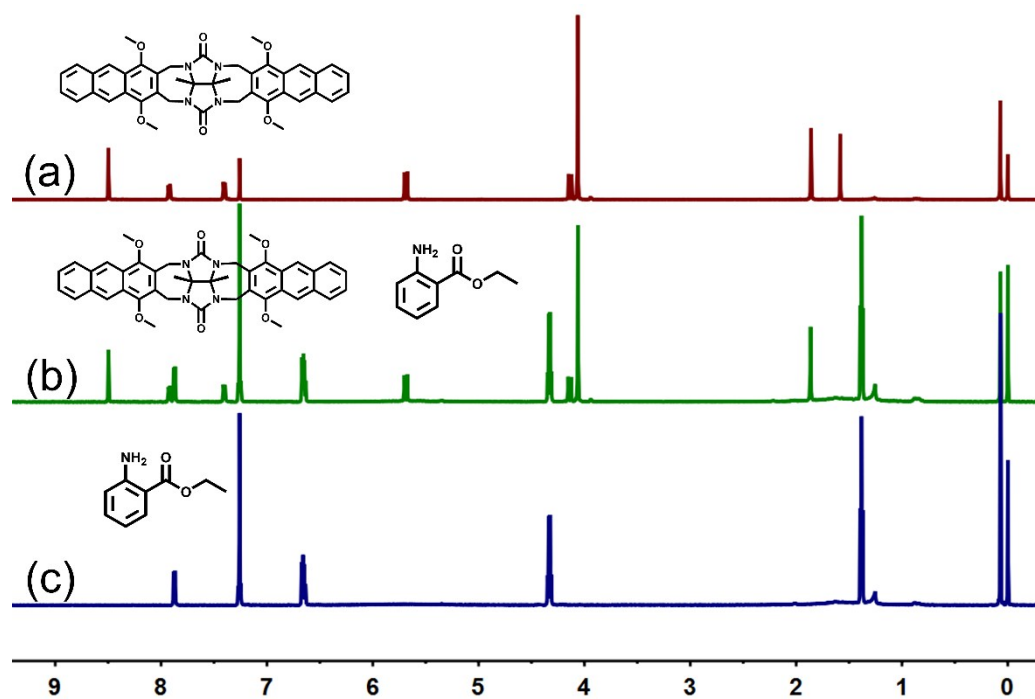


Figure S24 Partial ^1H NMR spectra (600 MHz, 298 K) in CDCl_3 : (a) 5.00 mM **1**; (b) 5.00 mM **1** and 5.00 mM **11**; (c) 5.00 mM **11**.

10. References

- S1. B. Shi, Z. Li, Y. Liu, L. Shangguan, H. Zhu, H. Ju. *Tetrahedron Lett.* **2018**, *59*, 3477–3480.
- S2. D. Ma, G. Hettiarachchi, D. Nguyen, B. Zhang, J. B. Wittenberg, P. Y. Zavalij, V. Briken, L. Isaacs. *Nature Chem.* **2012**, *4*, 503–510.
- S3. P. R. Ashton, R. Ballardini, V. Balzani, M. Bělohradský, M. T. Gandolfi, D. Philp, L. Prodi, F. M. Raymo, M. V. Reddington, N. Spencer, J. F. Stoddart, M. Venturi, D. J. Williams. *J. Am. Chem. Soc.* **1996**, *118*, 4931–4951.