Electronic Supplementary Information

Aromatically Functionalized Pseudo Crown Ethers with Unusual Solvent Response and Enhanced Binding Properties

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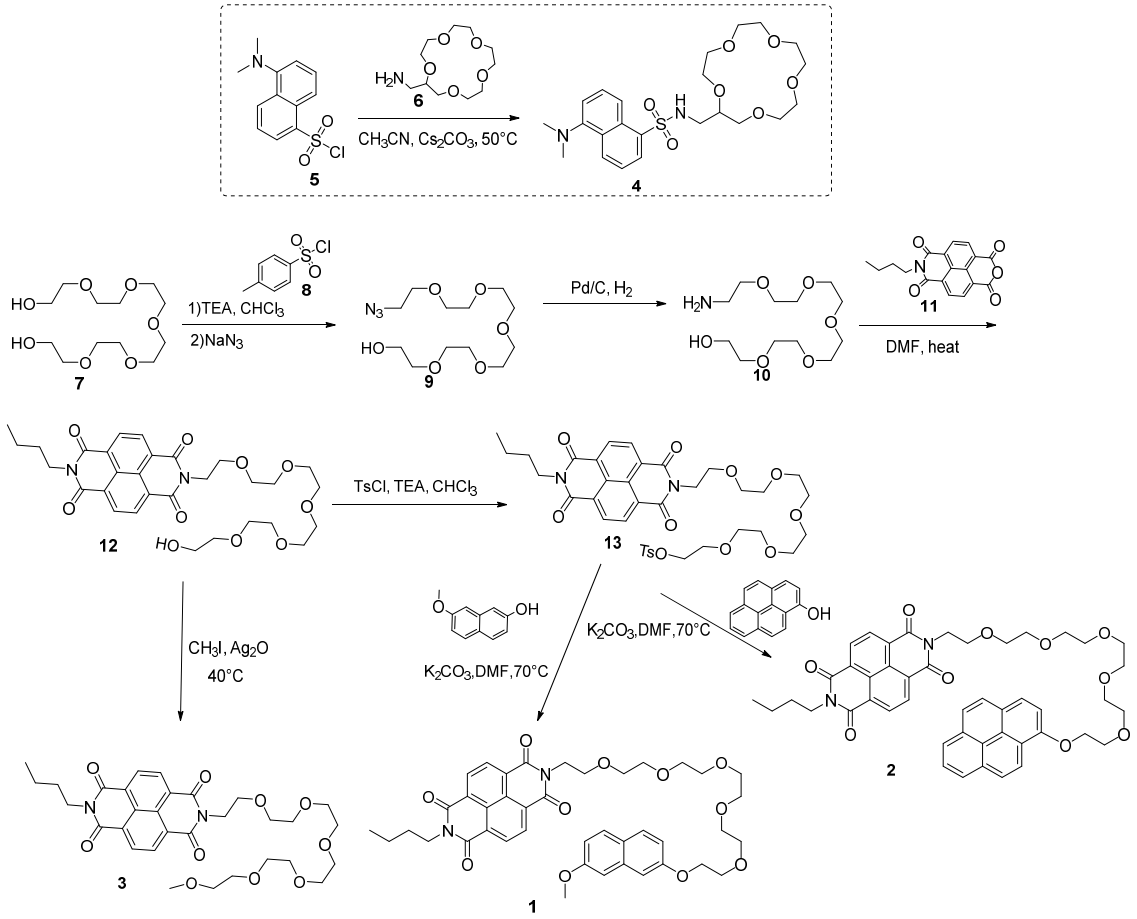
General Method

For spectroscopic purpose, methanol, and dichloromethane (DCM) were of HPLC grade. All other reagents and solvents were of ACS-certified grade or higher, and were used as received from commercial suppliers. Routine ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-400, on a Bruker AV II 600 or on a Varian VXR-400 spectrometer. Variable temperature ^{1}H NMR spectra, nuclear Overhauser effect spectroscopy (NOESY), and diffusion ordered spectroscopy (DOSY) were recorded on a Bruker AV II 600 spectrometer. UV-vis spectra were recorded at ambient temperature on a Cary 100 Bio UV-visible spectrophotometer. Fluorescence spectra were recorded at ambient temperature on a Varian Cary Eclipse Fluorescence spectrophotometer.

Scheme S1



Syntheses

Syntheses of compounds **4**,[1] **9**,[2] **10**,[3] and **11**[4] were previously reported.

Compound 12. Compound **10** (81.4 mg, 0.289 mmol) and compound **11** (98.2 mg, 0.304 mmol) were dissolved in DMF (5 mL). After the reaction mixture was stirred at 120 °C overnight, TLC showed completion of the reaction. The mixture was mixed with water (50

[1] H. Sulowska, W. Wiczk, J. Młodzianowski, M. Przyborowska, T. Ossowski, *Journal of Photochemistry and Photobiology A: Chemistry* **2002**, *150*, 249-255.
[2] M. J. Hynes, J. A. Maurer, *Angewandte Chemie International Edition* **2012**, *51*, 2151-2154.
[3] M. K. Muller, K. Petkau, L. Brunsveld, *Chem. Commun. (Cambridge, U. K.)* **2011**, *47*, 310-312.
[4] S. Zhang, Y. Zhao, *Chemistry – A European Journal* **2011**, *17*, 12444-12451.

mL) and then extracted with ethyl acetate (3 × 30 mL). The organic phase was washed with brine (50 mL), dried with $MgSO_4$, concentrated by rotary evaporation. The residue was purified by flash column chromatography over silica gel with 15:1 dichloromethane/methanol as the eluent to give a brown solid (100 mg, 59%). ^{1}H NMR (600 MHz, $CDCl_3$, δ) 8.76 (s, 4H), 4.46 (t, *J* = 5.8 Hz, 2H), 4.21 (t, *J* = 7.5 Hz, 2H), 3.85 (t, *J* = 5.9 Hz, 2H), 3.73–3.54 (m, 20H), 1.74 (m, 2H), 1.47 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$, δ) 162.9, 162.8, 131.0, 130.9, 126.8, 126.7, 126.6, 77.2, 77.0, 76.8, 72.6, 70.6, 70.6, 70.6, 70.5, 70.5, 70.3, 70.0, 67.8, 61.7, 40.8, 39.6, 30.2, 20.4, 13.8. ESI-MS (*m/z*): $[M+H]^+$ cacld for $C_{30}H_{38}N_2O_{10}$, 587.2599; found, 587.2607.

Compound 13. Compound **12** (41.3 mg, 0.07 mmol), triethylamine (0.1 mL, 0.7 mmol), and 4-dimethylaminopyridine (catalytic amounts) were dissolved in anhydrous dichloromethane (5 mL). The reaction mixture was cooled with an ice bath. After the addition of 4-toluenesulfonyl chloride, the reaction mixture was stirred at room temperature overnight. The mixture was mixed with water (50 mL) and then extracted with dichloromethane (3 × 30 mL). The combined organic phase was washed with brine (50 mL) and dried with $MgSO_4$. After the solvent was removed by rotary evaporation, the crude product was used in the next step without further purification.

Compound 1. Compound **13** (20.4 mg, 0.0275 mmol), 7-methoxy-2-naphthol (9.6 mg, 0.0551mmol), and potassium carbonate (15.2 mg, 0.1102 mmol) was combined in DMF (5 mL). Then the reaction mixture was heated to 70 °C and stirred overnight. After TLC showed completion of the reaction, water (50 mL) was added to the reaction mixture. The mixture was extracted with ethyl acetate (3 × 30 mL), washed with brine (30 mL), and dried with $MgSO_4$. The solvent was removed by rotary evaporation, and the residue was

purified by preparative TLC using 5:1 ethyl acetate/dichloromethane as the developing solvent to give a red powder (8.2 mg, 40%). ^{1}H NMR (600 MHz, $CDCl_3$, δ) 8.73 (s, 4H), 7.57 (d, *J* = 8.5 Hz, 2H), 6.98 (s, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 4.47 (t, *J* = 5.9 Hz, 2H), 4.23 (m, 4H), 3.95 (t, *J* = 4.5 Hz, 2H), 3.91 (s, 3H), 3.87 (t, *J* = 5.9 Hz, 2H), 3.80 (t, *J* = 4.8 Hz, 2H), 3.75–3.59 (m, 14H), 1.78 (m, 2H), 1.50 (m, 2H), 1.03 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$, δ) 162.9, 162.8, 158.0, 157.3, 135.7, 130.9, 130.8, 129.0, 126.6, 126.6, 126.6, 126.4, 124.2, 116.2, 116.0, 106.1, 105.1, 77.2, 77.0, 76.8, 70.9, 70.7, 70.6, 70.6, 70.6, 70.5, 70.1, 69.8, 67.8, 67.4, 55.2, 40.8, 39.6, 30.2, 29.7, 20.4, 13.8. ESI-MS (*m/z*): $[M+Na]^+$ cacld for $C_{41}H_{46}N_2O_{11}$, 765.2994; found, 765.2999.

Compound 2. Compound **13** (130 mg, 0.175 mmol), 1-hydroxypyrene (20 mg, 0.092 mmol), and potassium carbonate (64 mg, 0.46 mmol) was combined in DMF (10 mL). Then the reaction mixture was heated to 70 °C and stirred overnight. After TLC showed completion of the reaction, water (50 mL) was added to the reaction mixture. The mixture was extracted with ethyl acetate (3 × 30 mL), washed with brine (30 mL), and dried with $MgSO_4$. The solvent was removed by rotary evaporation, and the residue was purified by preparative TLC using 5:1 ethyl acetate/dichloromethane as the developing solvent to give a purple powder (68 mg, 94%). ^{1}H NMR (600 MHz, $CDCl_3$, δ) 8.17 (s, 4H), 8.10 (d, *J* = 9.1 Hz, 1H), 7.87 (t, *J* = 6.9 Hz, 2H), 7.82 (t, *J* = 7.3 Hz, 2H), 7.70 (d, *J* = 9.1 Hz, 1H), 7.65 (d, *J* = 8.9 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 4.46 (t, *J* = 4.8 Hz, 2H), 4.39 (t, *J* = 6.0 Hz, 2H), 4.15–4.06 (m, 4H), 3.93–3.79 (m, 6H), 3.75–3.58 (m, 12H), 1.75 (m, 2H), 1.50 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$, δ) 162.6, 162.6, 152.7, 131.2, 131.1, 129.9, 129.8, 127.0, 126.1, 126.0, 125.5, 125.4, 125.4, 125.3, 124.8, 124.8, 124.2, 124.1, 123.9, 121.1, 109.0, 77.2, 77.0, 76.8, 71.2, 70.9, 70.8,

70.6, 70.2, 70.0, 68.6, 68.0, 40.6, 39.5, 30.2, 29.7, 20.4, 13.9. ESI-MS (*m/z*): $[M+Na]^+$ cacld for $C_{46}H_{46}N_2O_{10}$, 809.3045; found, 809.3062.

Compound 3. A mixture of compound **12** (100 mg, 0.17 mmol), methyl iodide (5 mL, 80.32 mmol), and silver oxide (78.8 mg, 0.34 mmol) was stirred at room temperature for three days. After the reaction mixture was concentrated by rotary evaporation, the residue was purified by flash column chromatography over silica gel with 25:1 ethyl acetate/methanol as the eluent to give a deep yellow solid (71.6 mg, 70%). ^{1}H NMR (600 MHz, $CDCl_3$, δ) 8.75 (s, 4H), 4.45 (t, *J* = 5.8 Hz, 2H), 4.20 (t, *J* = 7.6 Hz, 2H), 3.84 (t, *J* = 5.9 Hz, 2H), 3.69 (t, *J* = 4.6 Hz, 2H), 3.66 – 3.52 (m, 18H), 3.37 (s, 3H), 1.73 (m, 2H), 1.46 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$, δ) 162.9, 162.8, 131.0, 130.9, 126.8, 126.7, 126.7, 126.6, 77.2, 77.0, 76.8, 72.0, 70.6, 70.6, 70.5, 70.1, 67.81, 59.0, 40.8, 39.9, 30.2, 20.4, 13.8. ESI-MS (*m/z*): $[M+Na]^+$ cacld for $C_{31}H_{40}N_2O_{10}$, 623.2575; found, 623.2577.

Fluorescence Solvent Study and Data Analysis Method

Stock solution of **1** (4.0 mM), **2** (4.0 mM), and **3** (4.0 mM) in DCM were prepared. For the solvent titration, a typical procedure is as follows. An aliquot of the stock solution was added to 2.00 mL of the appropriate solvent in a quartz cuvette. The sample was gently vortexed for 30 s before the fluorescence spectrum was collected.

Literature method [5] was followed in the two-state curve fitting for the fluorescence data for hosts **1** and **2**:

[5] Y. Zhao, Z. Zhong, *J. Am. Chem. Soc.* **2005**, *127*, 17894-17901.

$$\text{Unfolded} \overset{K_{eq}}{\rightleftharpoons} \text{Folded}$$

According to the two-state model, at any given concentration of the denaturant (i.e., MeOH), only the folded and unfolded conformations are present and their fractions are represented by f_F and f_U. Fraction of the unfolded conformation can be calculated by:

$$K_{eq} = f_F/f_U$$

$$f_F = (I-I_U)/(I_F-I_U)$$

$$f_U = 1-f_F$$

I is the fluorescence intensity at a certain solvent composition. I_U is the intensity at fully unfolded state, and I_F is the state at fully folded state.

The equilibrium constant (K_{eq}) and the free energy (ΔG) for the folding reaction can be calculated using:

$$\Delta G = -RT \ln K_{eq} = -RT \ln(f_F/f_U) = -RT \ln[(1- f_U)/f_U]$$

In the two-state model, the free energies are linearly related to the concentration of denaturant and are assumed to have the same relationship to the $E_T(30)$ values of the solvent:

$$\Delta G = \Delta G_0 + m\, E_T(30)$$

Then we can obtain equations:

$$f_F = 1/(1+1/\exp(-(\Delta G_0 + m\, E_T(30))/RT))$$

$$I = I_U + (I_F-I_U)/(1+1/\exp(-(\Delta G_0 + m\, E_T(30))/RT))$$

A nonlinear least-squares fitting of the experimental data to above equation affords the two-state folding-unfolding curves and f_U.

UV-Vis Titration and Data Analysis Method

Stock solution of **1** (4.0 mM), **2** (4.0 mM) and **3** (4.0 mM) in DCM were prepared. Stock solutions of the guest (LiSCN, NaSCN or KSCN) were prepared in the appropriate solvent mixture, in which titrations would be performed. For the titrations, a typical procedure is as follows. An aliquot of the host stock solution was added to 2.00 mL solvent in a quartz cuvette. The sample was gently vortexed for 30 s before its UV-vis spectrum was recorded. Aliquots of the guest was added and the UV-vis spectrum was recorded after each addition. The titration was continued until saturation was reached and the total volume of the guest solution added was kept below 100 μL. The binding constant was obtained by nonlinear least squares curving fitting of the absorbance data to the 1:1 binding isotherm.[6] Titrations were repeated three times and the reported binding constant was the average with 90% confidence using uncertainty calculation:

$$U = t\frac{1}{\sqrt{n}}\sqrt{\frac{\sum(\overline{K} - K_i)^2}{(n-1)}}$$

in which U is the uncertainty, n is the number of experiments, t is the student t-value, which is 2.92 when n is 3 and 90% confidence for two sides.

[6] H. J. Schneider, A. K. Yatsimirsky, *Principles and methods in supramolecular chemistry*; New York: J. Wiley, **2000**, p 137-146.

Fluorescence Emission Spectroscopy Titration and Data Analysis Method

A stock solution of **4** (2.0 mM) in DCM prepared. Stock solutions of NaSCN were prepared in the appropriate solvent mixture, in which titrations would be performed. For the titrations, a typical procedure is as follows. An aliquot of the host stock solution was added to 2.00 mL solvent in a quartz cuvette. The sample was gently vortexed for 30 s before its fluorescence spectrum was recorded. Aliquots of the guest was added and the fluorescence spectrum was recorded after each addition. The titration was continued until saturation was reached and the total volume of the guest solution added was kept below 100 μL. The binding constant was obtained by nonlinear least squares curving fitting of the fluorescence data to the 1:1 binding isotherm. Titrations were repeated three times and the reported binding constant was the average with 90% confidence.

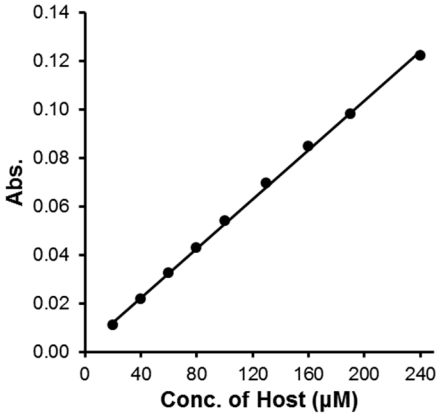


Figure S1. Charge transfer absorbance at 450 nm in MeOH as a function of the concentration of host **1**. A linear relationship was obtained with $R^2 = 0.9972$.

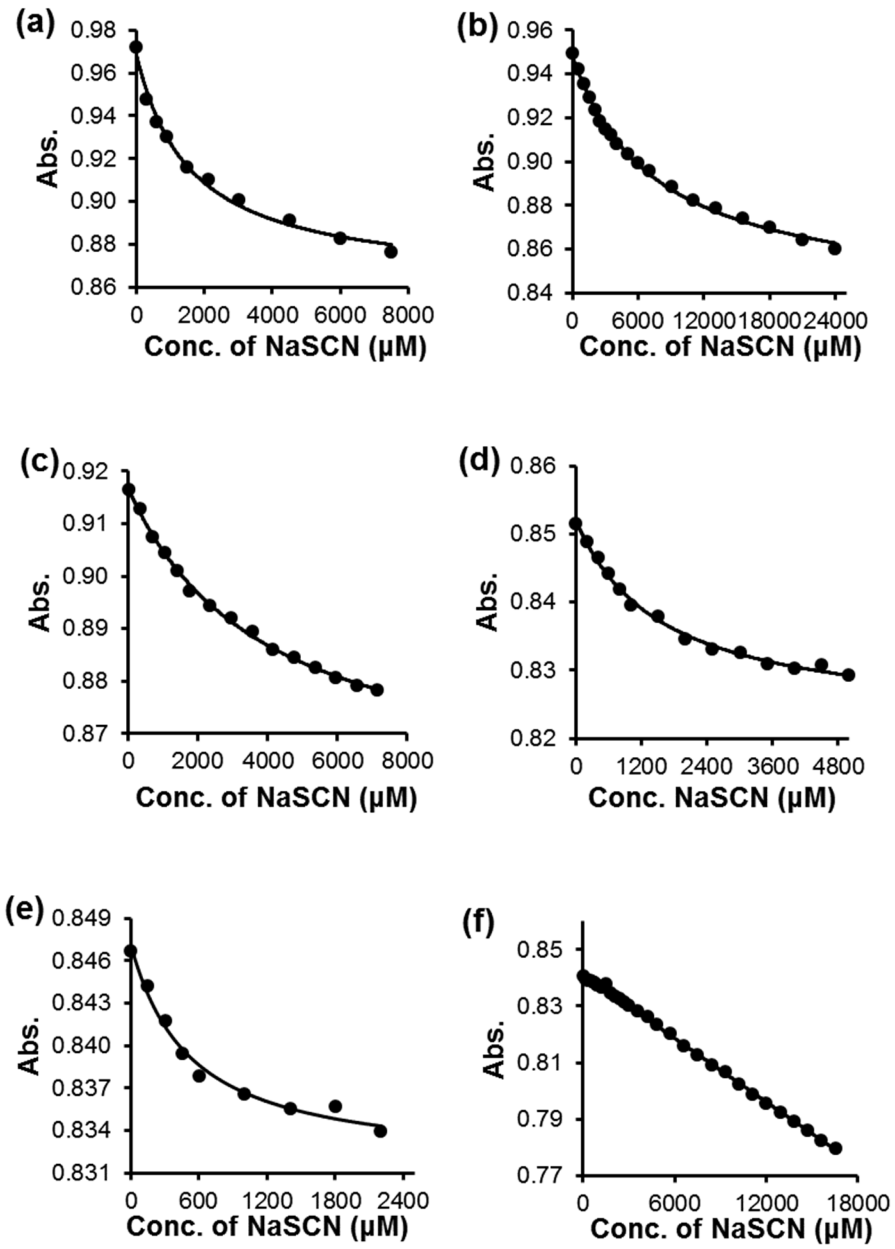


Figure S2. UV-vis titration curves of host **1** by sodium thiocyanate in (a) 4:1 DCM/MeOH (v/v), (b) 3:2 DCM/MeOH (v/v), (c) 2:3 DCM/MeOH (v/v), (d) 1:4 DCM/MeOH (v/v), (e) MeOH, and (f) 9:1 MeOH/H_2O (v/v). [**1**] = 50 μM. The UV absorbance at 358 nm was monitored and the smooth curve was from nonlinear least squares curving fitting to a 1:1 binding isotherm.

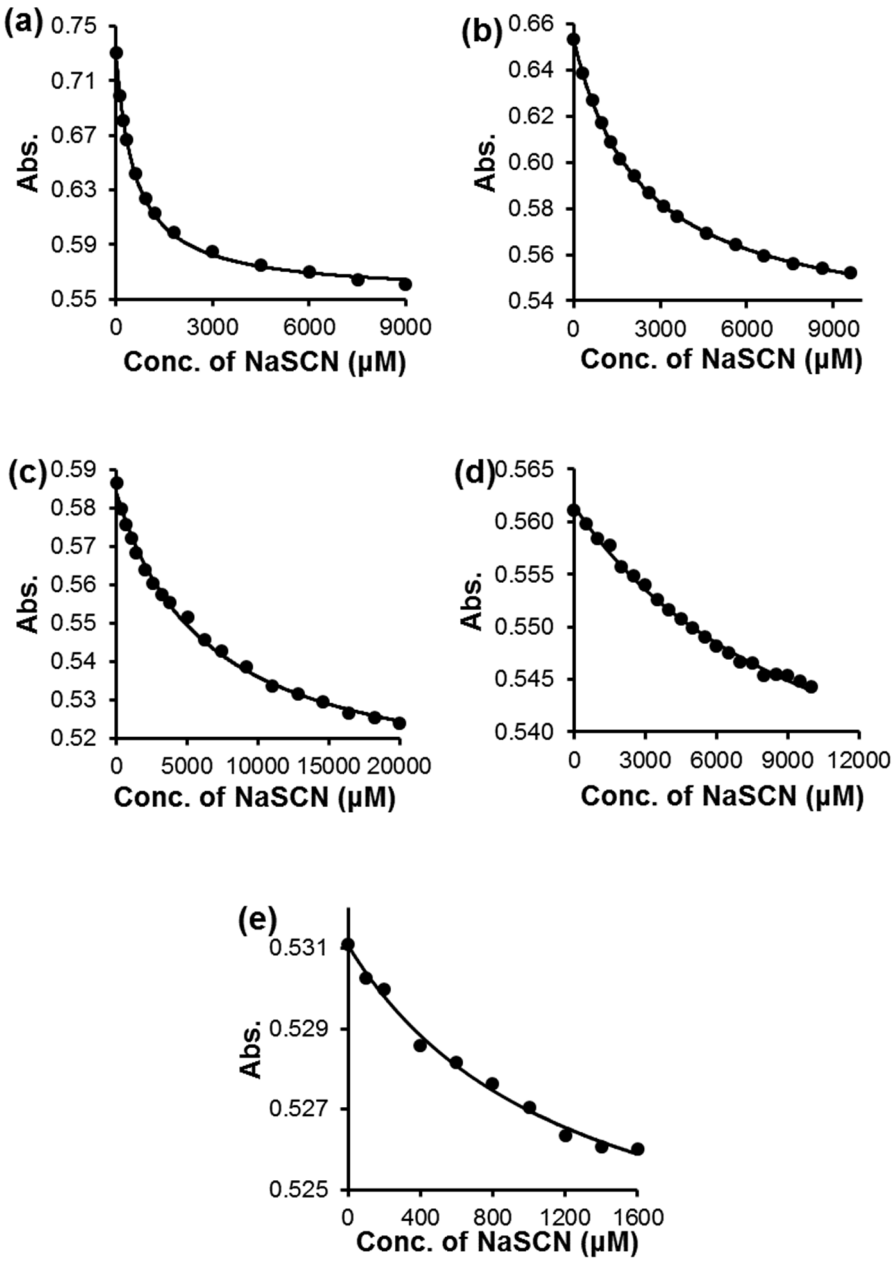


Figure S3. UV-vis titration curves of host **2** by sodium thiocyanate in (a) 4:1 DCM/MeOH (v/v), (b) 3:2 DCM/MeOH (v/v), (c) 2:3 DCM/MeOH (v/v), (d) 1:4 DCM/MeOH (v/v), and (e) MeOH. [**2**] = 20 μM. The UV absorbance at 382 nm was monitored and the smooth curve was from nonlinear least squares curving fitting to a 1:1 binding isotherm.

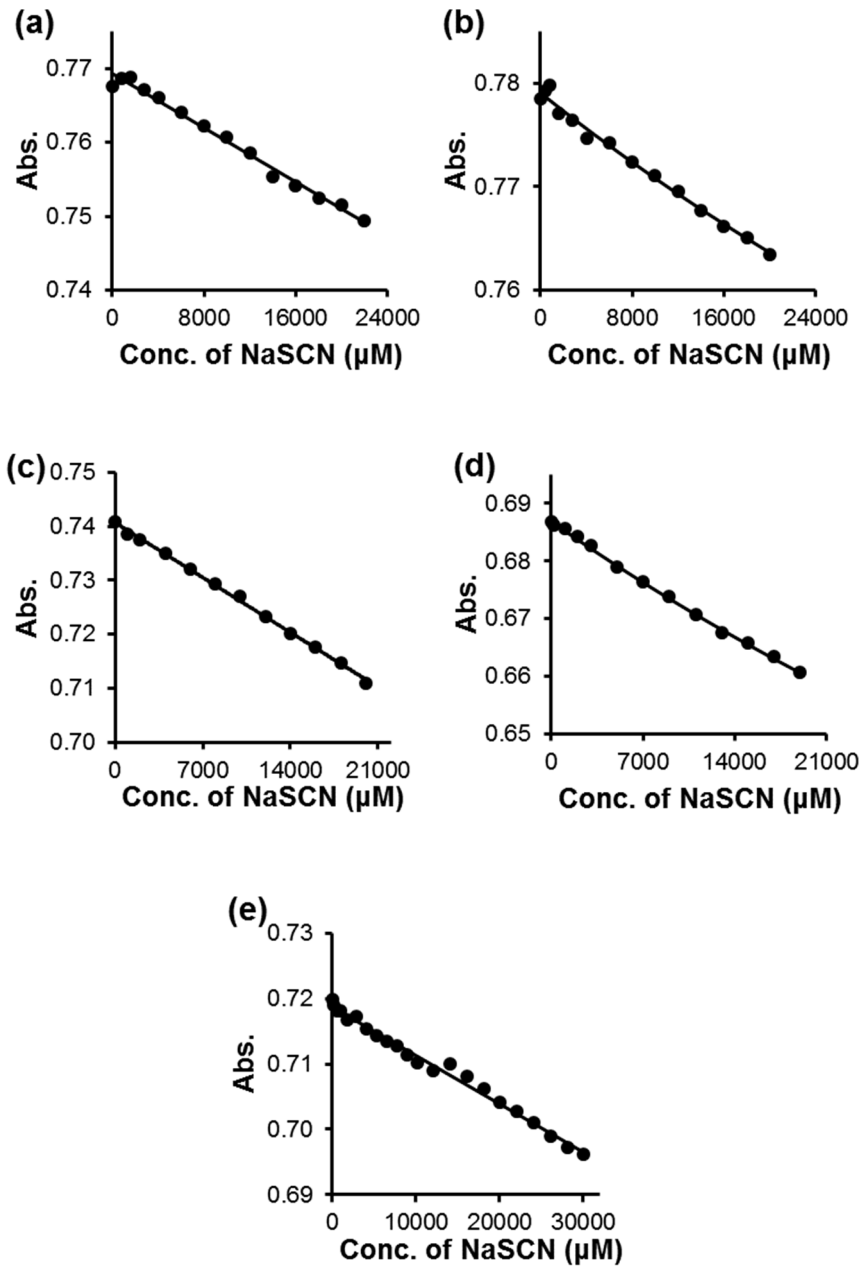


Figure S4. UV-vis titration curves of host **3** (40 μM) by sodium thiocyanate in (a) 4:1 DCM/MeOH (v/v), (b) 3:2 DCM/MeOH (v/v), (c) 2:3 DCM/MeOH (v/v), (d) 1:4 DCM/MeOH (v/v), and (e) MeOH. [**3**] = 40 μM. The UV absorbance at 358 nm was monitored and the smooth curve was from nonlinear least squares curving fitting to a 1:1 binding isotherm.

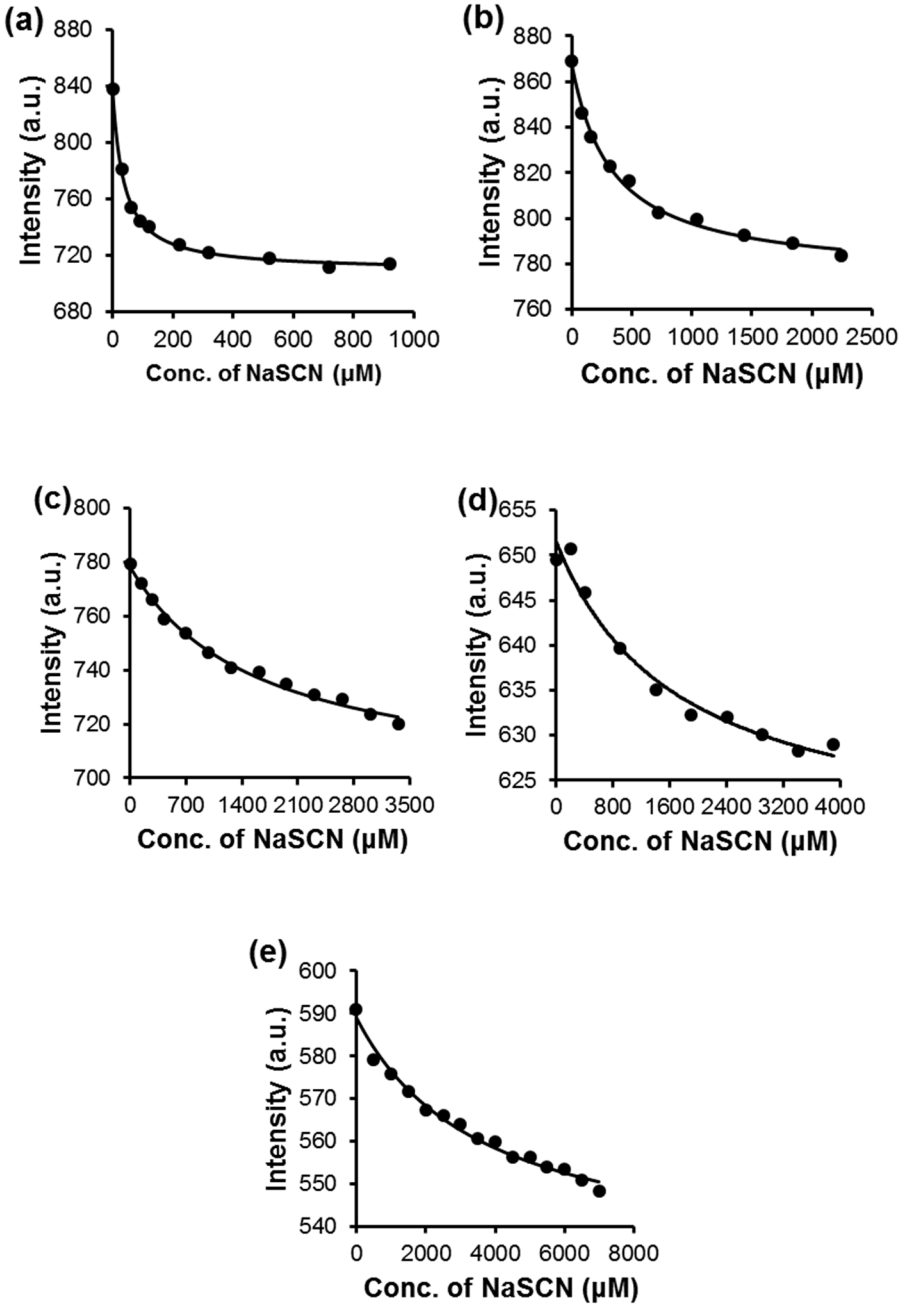


Figure S5. Fluorescence titration curves of host **4** by sodium thiocyanate in (a) 4:1 DCM/MeOH (v/v), (b) 3:2 DCM/MeOH (v/v), (c) 2:3 DCM/MeOH (v/v), (d) 1:4 DCM/MeOH (v/v), and (e) MeOH. [**4**] = 2.0 μM. The maximum emission intensity was

monitored and the smooth curve was from nonlinear least squares curving fitting to a 1:1 binding isotherm.

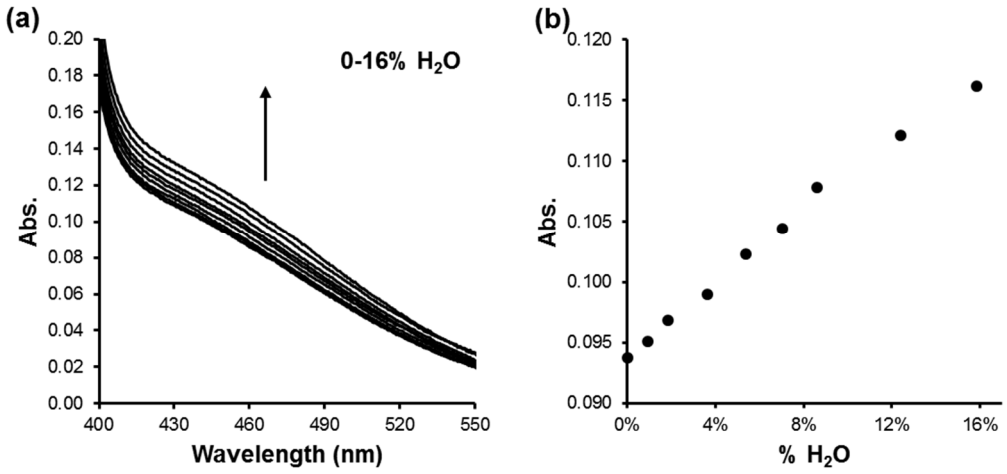


Figure S6. (a) UV-Vis spectra of host **1** with 0–16% H_2O. [**1**] = 180 μM in methanol. (b) Absorbance at 450 nm as a function of H_2O volume percentage.

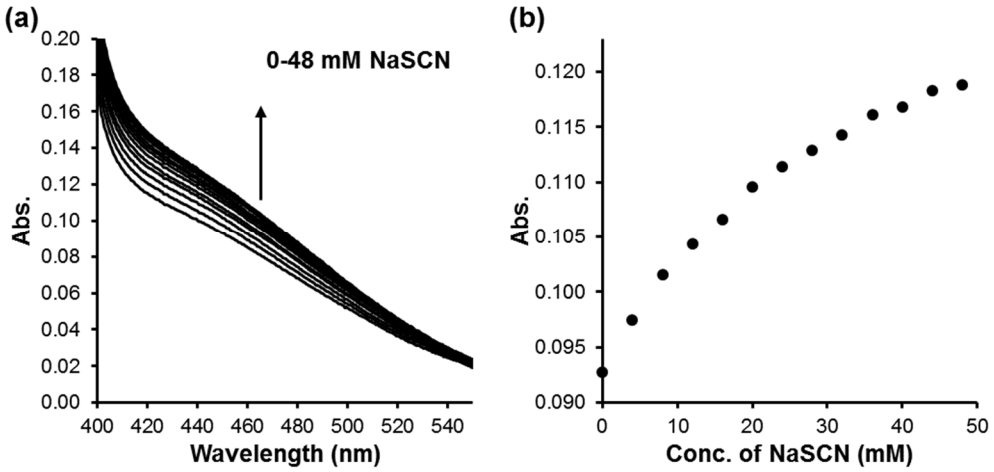


Figure S7. (a) UV-Vis spectra of host **1** with 0-48 mM sodium thiocyanate. [**1**] = 180 μM

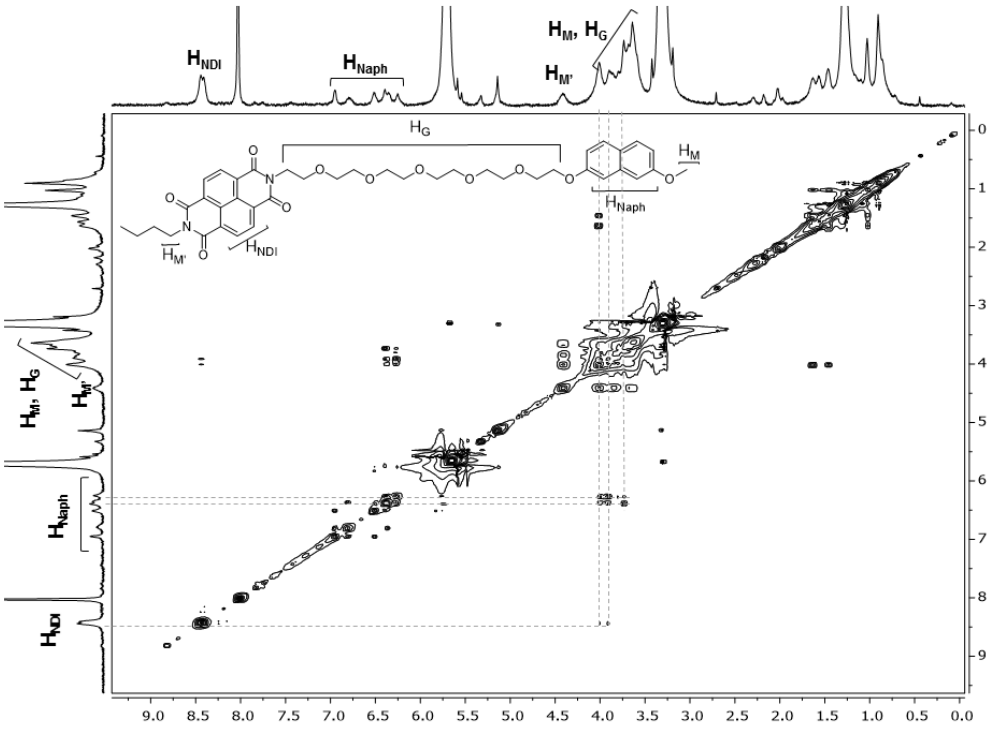


Figure S8. NOESY spectrum of 1 mM host **1** in CD_3OD (with 7% $CDCl_3$ to improve solubility) at 213 K.

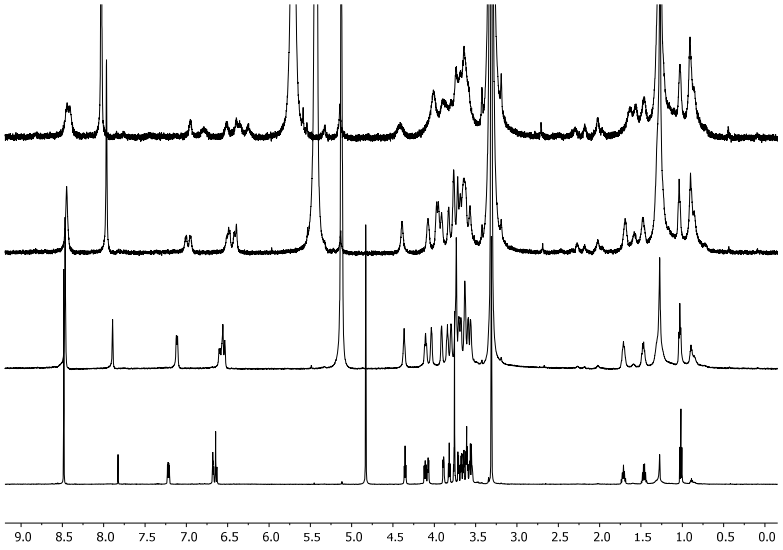


Figure S9. NMR spectra of 1 mM host **1** in CD_3OD (with 7% $CDCl_3$ to improve solubility) at different temperatures. Temperature from bottom to top was 298 K, 273 K, 243 K, and 213 K.

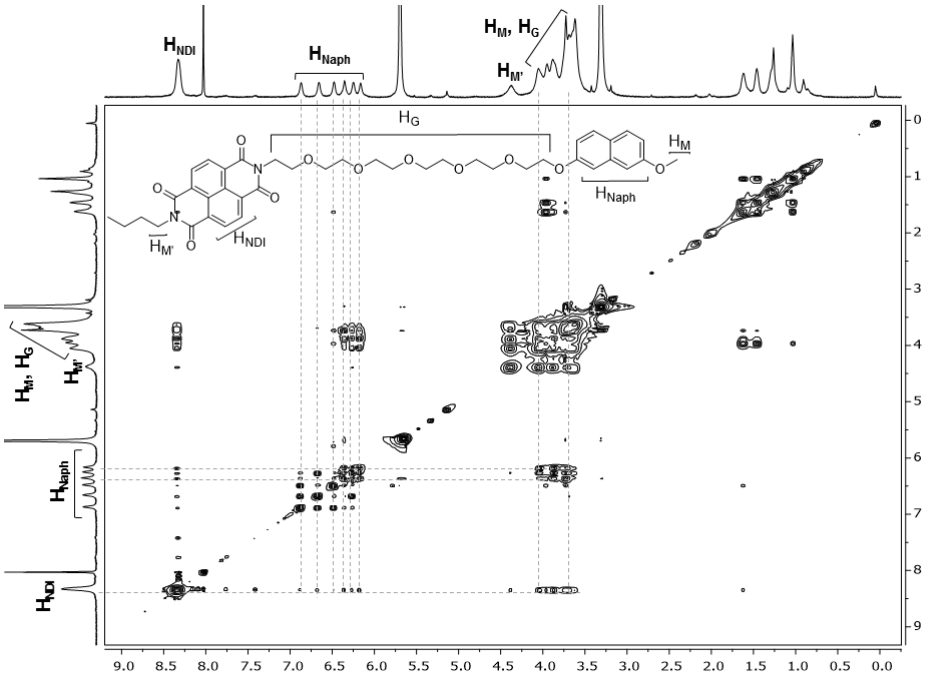


Figure S10. NOESY spectrum of 1 mM host **1** with 8 mM sodium thiocyanate in CD_3OD (with 7% $CDCl_3$ to improve solubility) at 213 K.

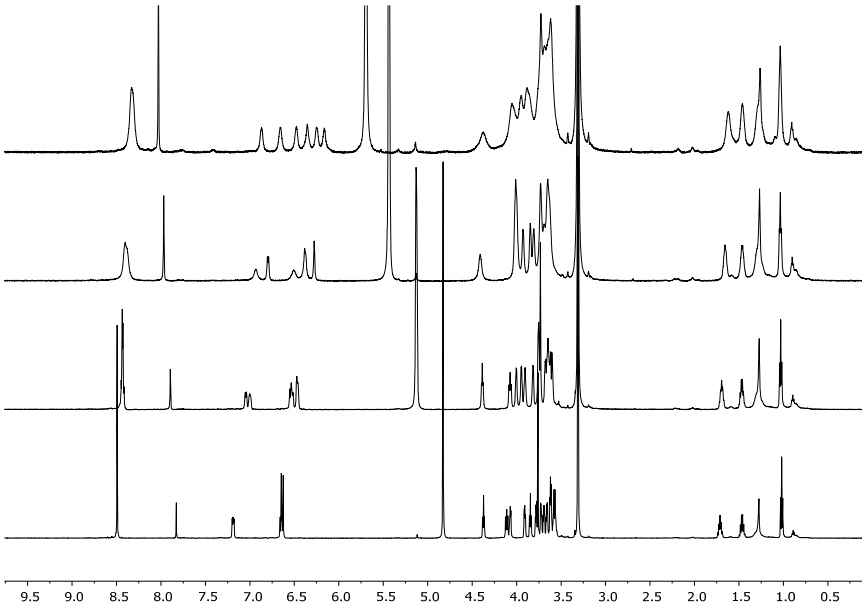


Figure S11. NMR spectra of 1 mM host **1** with 8 mM sodium thiocyanate in CD_3OD (with 7% $CDCl_3$ to improve solubility) at different temperatures. Temperature from bottom to top was 298 K, 273 K, 243 K, and 213 K.

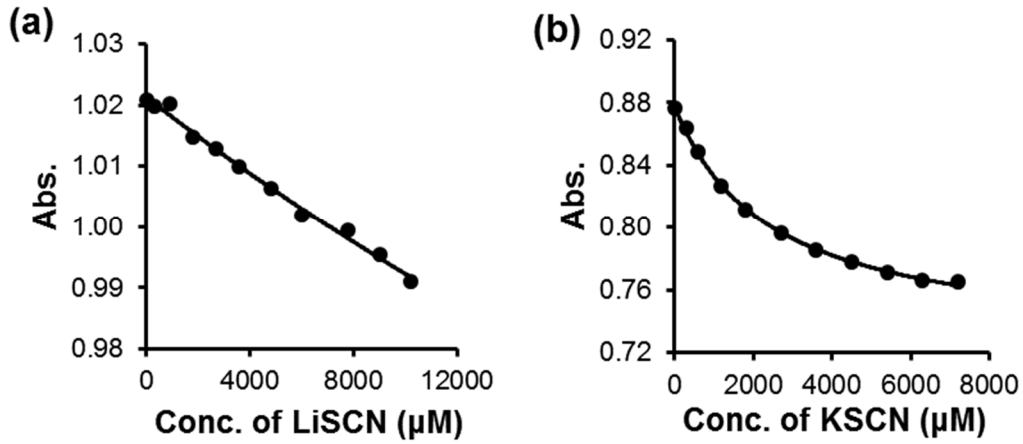


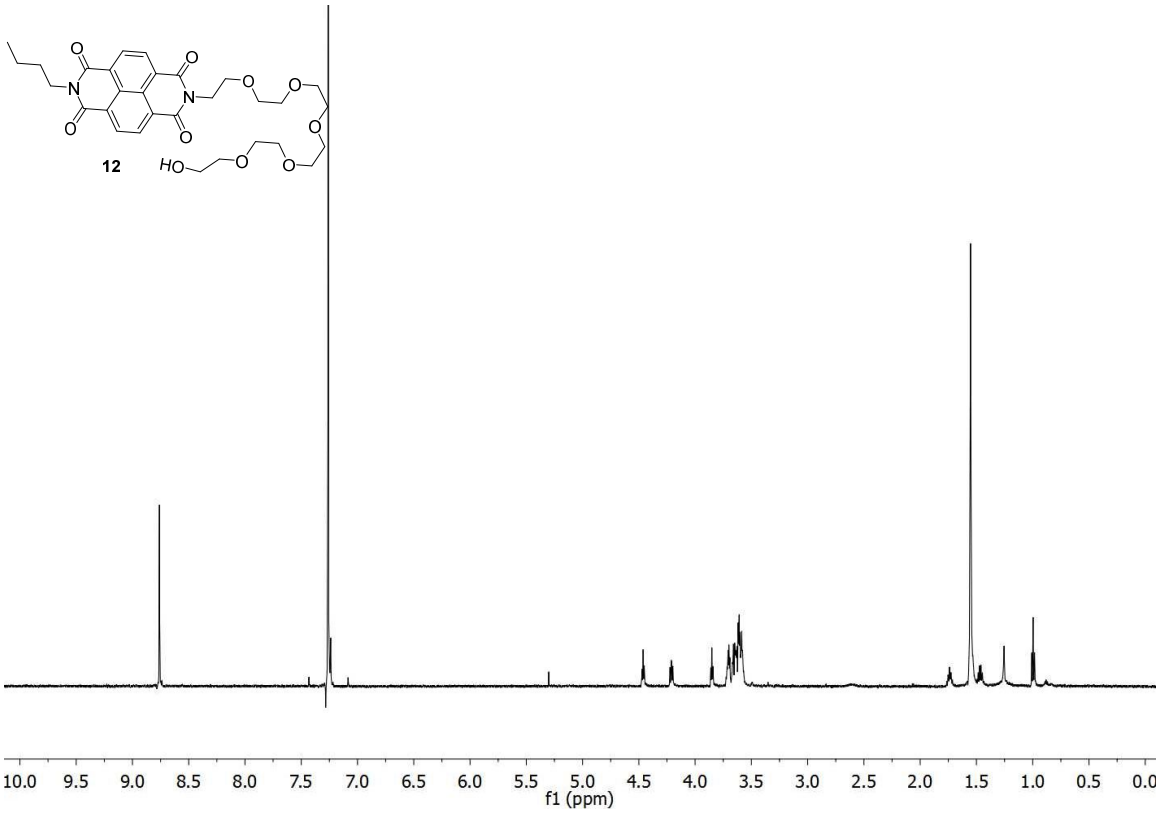
Figure S12. UV-vis titration curves of host **1** by (a) lithium thiocyanate and (b) potassium thiocyanate in methanol. [**1**] = 40 μM. The UV absorbance at 358 nm was monitored and the smooth curve was from nonlinear least squares curving fitting to a 1:1 binding isotherm.

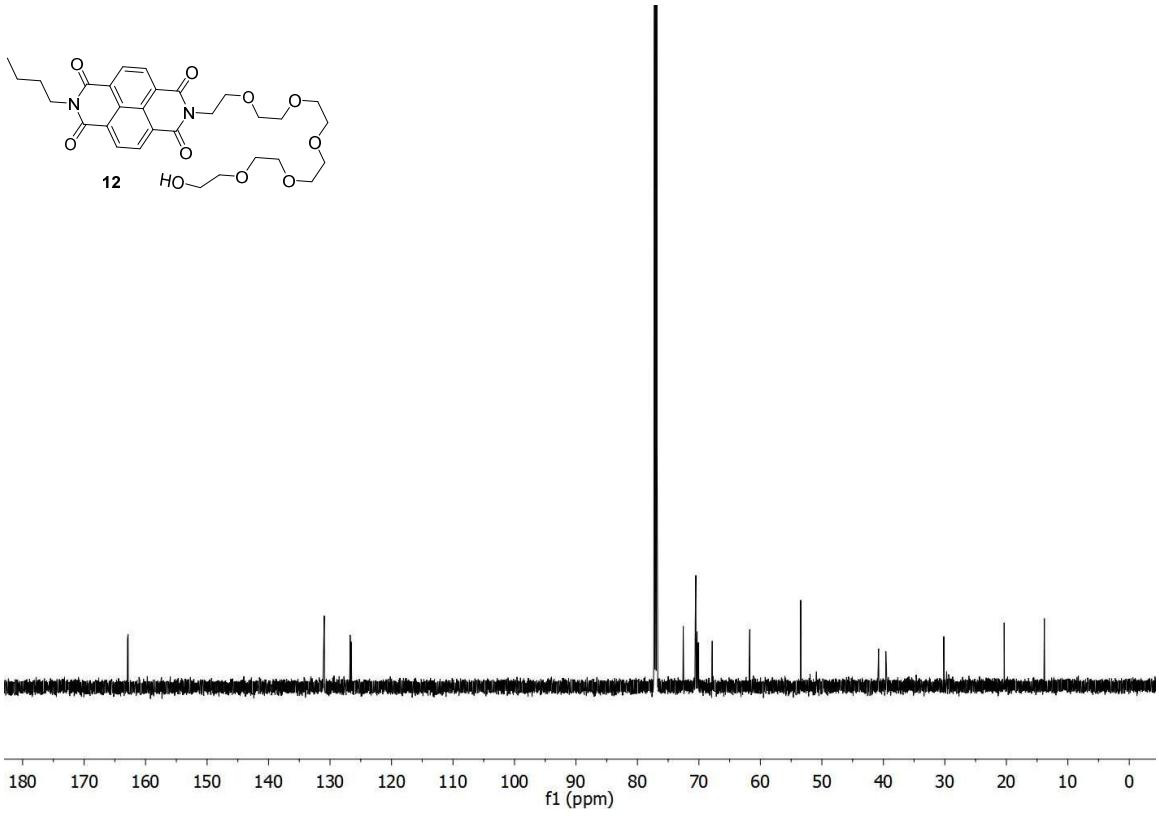
Table S1. Binding constants of hosts **1**–**4** in different solvents. All binding constants were averages of three titrations with 90% confidence.

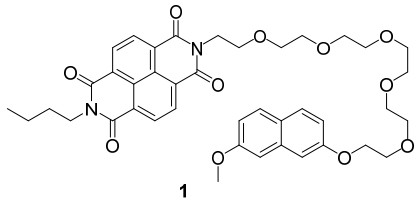
Entry	Host	Solvent(s)	K_a (10^2 M^{-1})
1	**1**	DCM/MeOH 4/1 (v/v)	6.5 ± 1.0
2	**1**	DCM/MeOH 3/2 (v/v)	1.4 ± 0.2
3	**1**	DCM/MeOH 2/3 (v/v)	2.8 ± 0.4
4	**1**	DCM/MeOH 1/4 (v/v)	5.8 ± 1.2
5	**1**	MeOH	16 ± 9
6[a]	**1**	MeOH/H_2O 9/1 (v/v)	-
7	**2**	DCM/MeOH 4/1 (v/v)	17 ± 2
8	**2**	DCM/MeOH 3/2 (v/v)	4.2 ± 0.1
9	**2**	DCM/MeOH 2/3 (v/v)	1.5 ± 0.2
10	**2**	DCM/MeOH 1/4 (v/v)	1.0 ± 0.4
11	**2**	MeOH	5.1 ± 4.6
12[a]	**3**	DCM/MeOH 4/1 (v/v)	-
13[a]	**3**	DCM/MeOH 3/2 (v/v)	-
14[a]	**3**	DCM/MeOH 2/3 (v/v)	-
15[a]	**3**	DCM/MeOH 1/4 (v/v)	-
16[a]	**3**	MeOH	-
17[b]	**4**	DCM/MeOH 4/1 (v/v)	300 ± 40
18[b]	**4**	DCM/MeOH 3/2 (v/v)	31 ± 17
19[b]	**4**	DCM/MeOH 2/3 (v/v)	7.2 ± 2.9
20[b]	**4**	DCM/MeOH 1/4 (v/v)	5.7 ± 2.9
21[b]	**4**	MeOH	2.0 ± 1.2
22[b]	**4**	MeOH/H_2O 9/1 (v/v)	1.8 ± 0.8
23[a][c]	**1**	MeOH	-
24[d]	**1**	MeOH	4.22 ± 0.04

[a] Saturation could not be reached even with high concentrations of guest. Binding was weak. [b] The binding constants were determined by fluorescence titration. [c] The guest was lithium thiocyanate. [d] The guest was potassium thiocyanate.

^{1}H and ^{13}C NMR spectra







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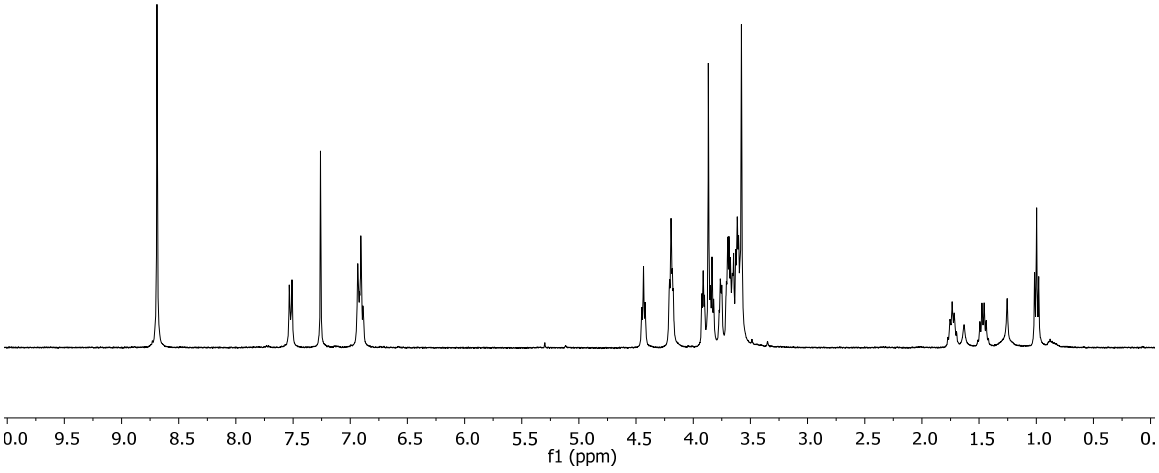
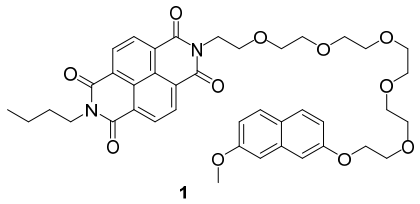
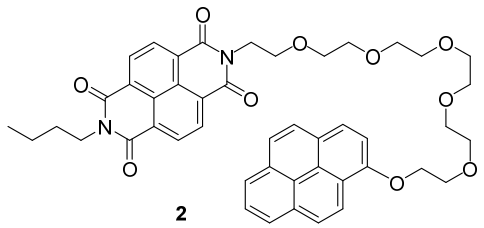

0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)



1

00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



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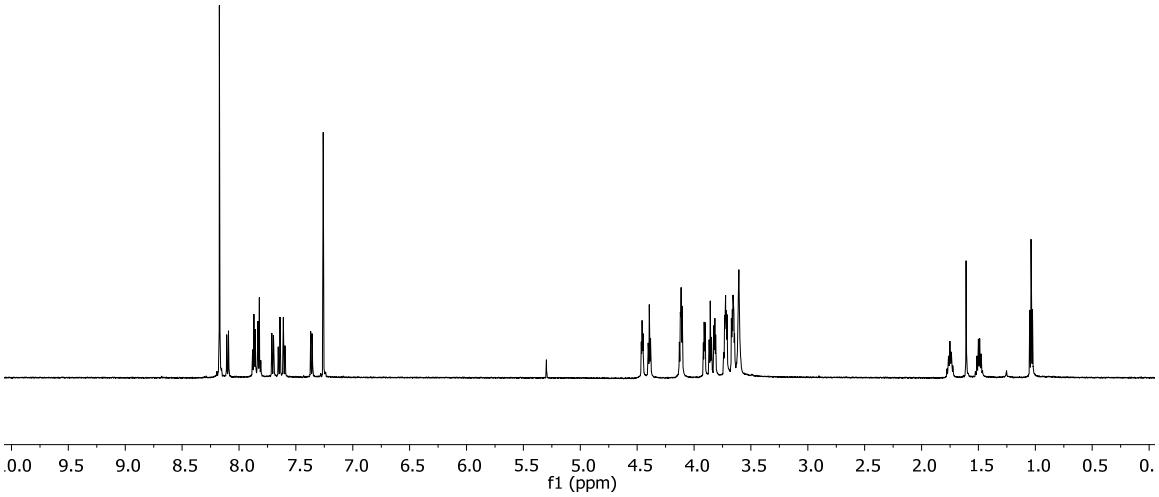

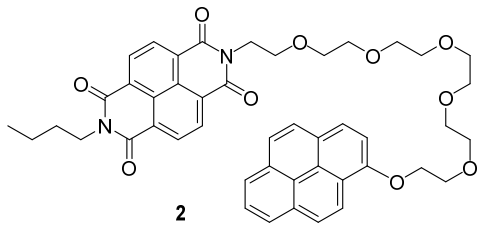

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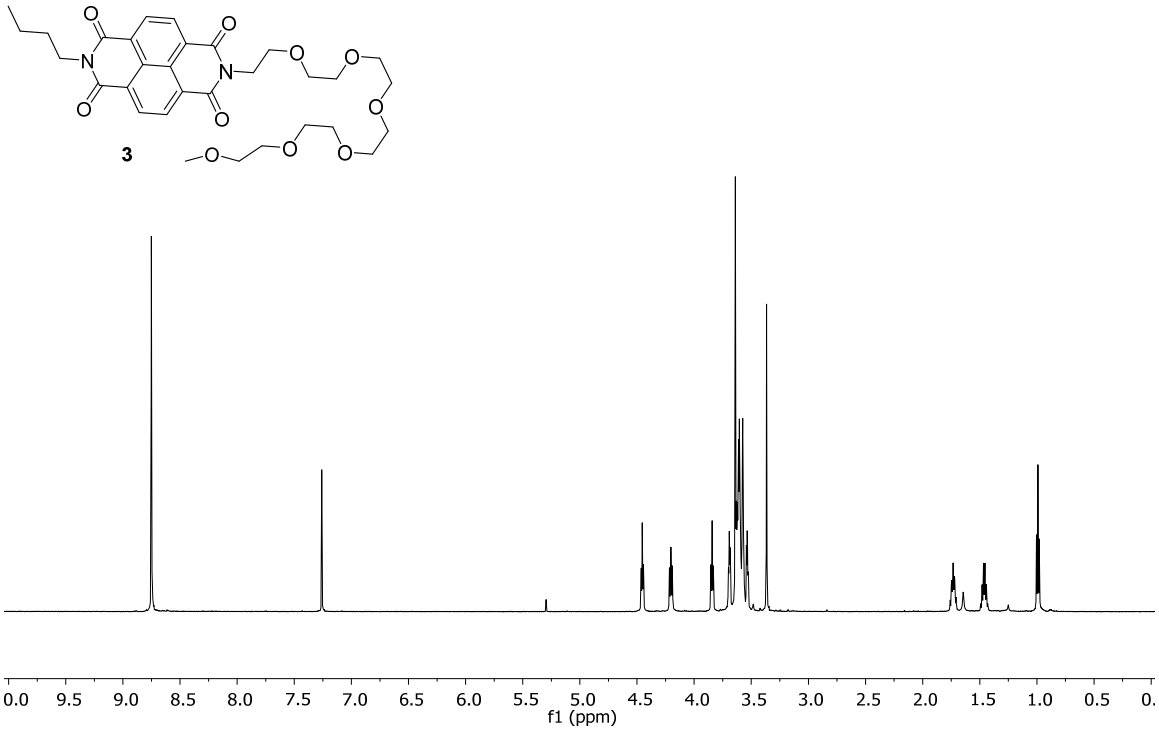
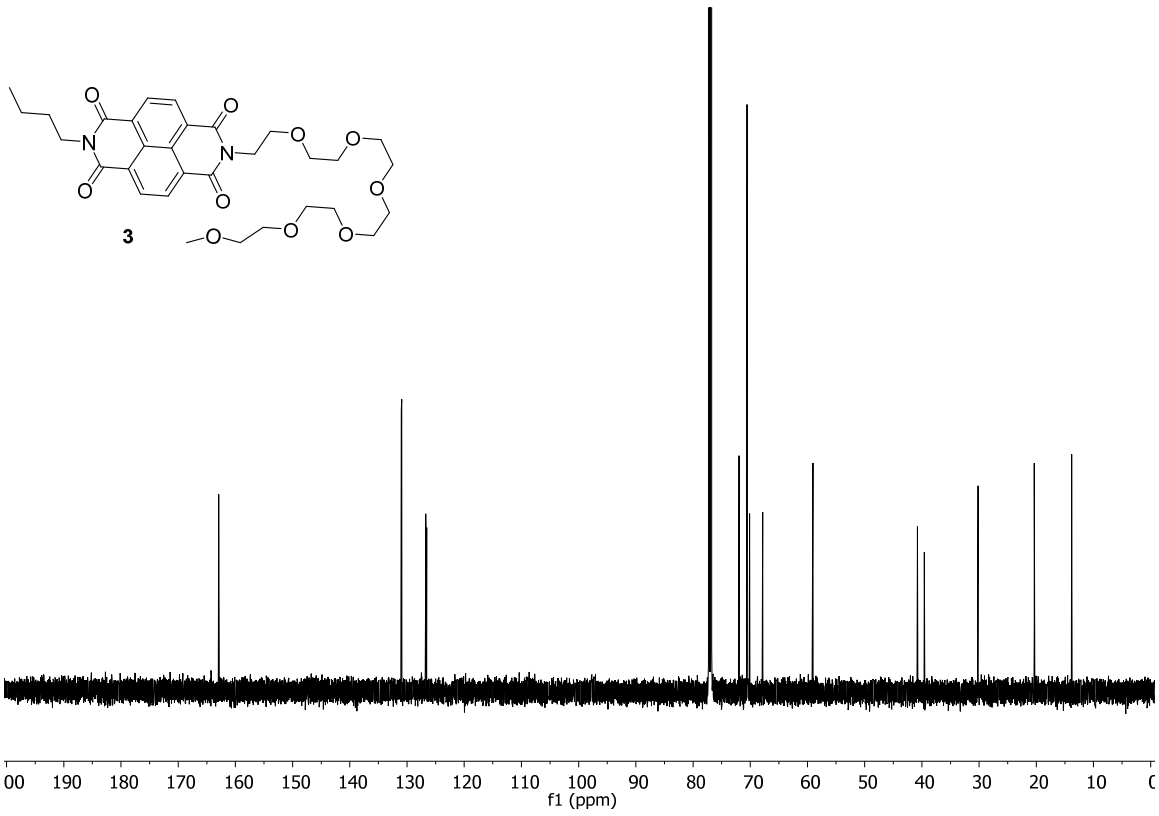

3
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)


3
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)