

# Oxacalixarenes and Oxacyclophanes Containing 1,8-Naphthyridines: A New Class of Molecular Tweezers With Concave-Surface Functionality

## Supplementary Material

Jeffrey L. Katz,\*<sup>a</sup> Bram J. Geller<sup>a</sup> and Peter D. Foster<sup>a</sup>

<sup>a</sup>Department of Chemistry, Colby College, 5754 Mayflower Hill, Waterville, ME 04901, USA, Fax: (207) 859-5760; Tel: (207) 859-5754; Email [jlkatz@colby.edu](mailto:jlkatz@colby.edu)

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## General information

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker Avance 400 spectrometer at ambient temperature. Chemical shifts are reported in ppm versus tetramethylsilane with either tetramethylsilane or the residual solvent resonance used as an internal standard. Infrared spectra were recorded on a PerkinElmer Spectrum One spectrometer. Mass spectra were obtained on an IonSpec HiResMALDI Fourier transform mass spectrometer.

## Synthetic Procedures and Characterization Data

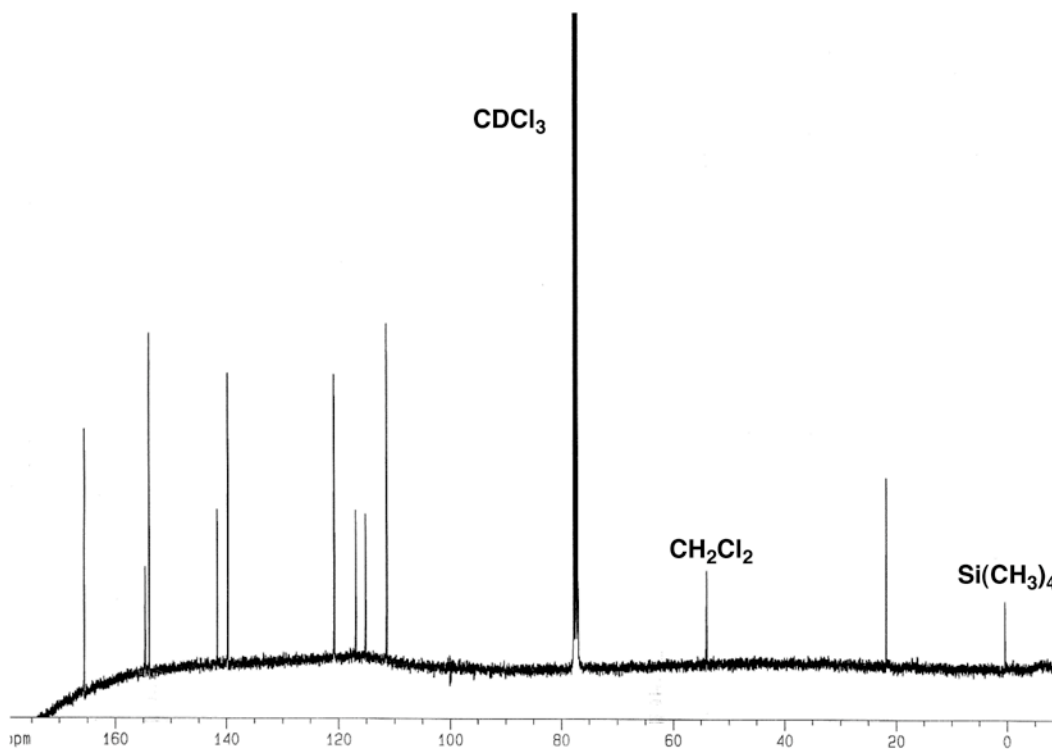
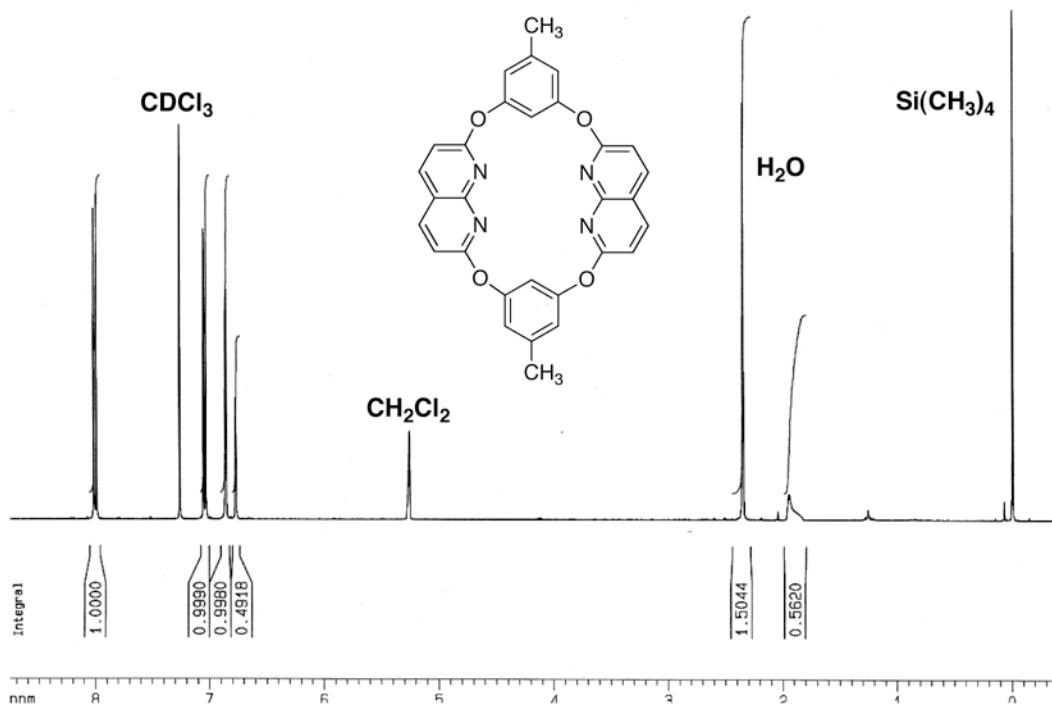
**General Reaction Procedure:** 2,7-Dichloro-1,8-naphthyridine (**1**) (133 mg, 0.67 mmol, 1 equiv), diphenol **3**, **6**, or **7** (0.67 mmol, 1 equiv), and  $\text{Cs}_2\text{CO}_3$  (545 mg, 1.67 mmol, 2.5 equiv) were combined under an argon atmosphere. DMSO (10 mL) was added, and the reaction was heated to 100 °C and stirred vigorously for 18 hr. The reaction mixture was then cooled to room temperature, and purified as described below.

**Oxcalix[2]benzene[2]naphthyridine 3:** The reaction mixture was partitioned between EtOAc (80 mL) and 0.1 M HCl (60 mL), separated, and the aqueous layer was extracted twice with EtOAc (30 mL). The combined organics were washed with brine (100 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated *in vacuo*. The product was purified via flash column chromatography through silica (linear gradient 0-3% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to yield 133 mg **3** as a white solid (80%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.00 (d, 4H,  $J = 8.6$  Hz), 7.04 (d, 4H,  $J = 8.6$  Hz), 6.86 (d, 4H,  $J = 1.8$  Hz) 6.77 (t, 2H,  $J = 1.8$  Hz), 2.35 (s, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  165.6, 154.7, 153.9, 141.6, 139.8, 120.7, 116.9, 115.2, 111.4, 21.9; IR (thin film): 2917, 1608, 1590, 1424, 1308, 1221, 1123, 1051, 968, 844, 797, 714  $\text{cm}^{-1}$ ; HRMS [MALDI(+)] with a DHB matrix] calculated for  $(\text{M}+\text{Na})^+$  [ $\text{C}_{30}\text{H}_{20}\text{N}_4\text{O}_4\text{Na}$ ] $^+$ : 523.13768, found: 523.13947. M.P. >533K.

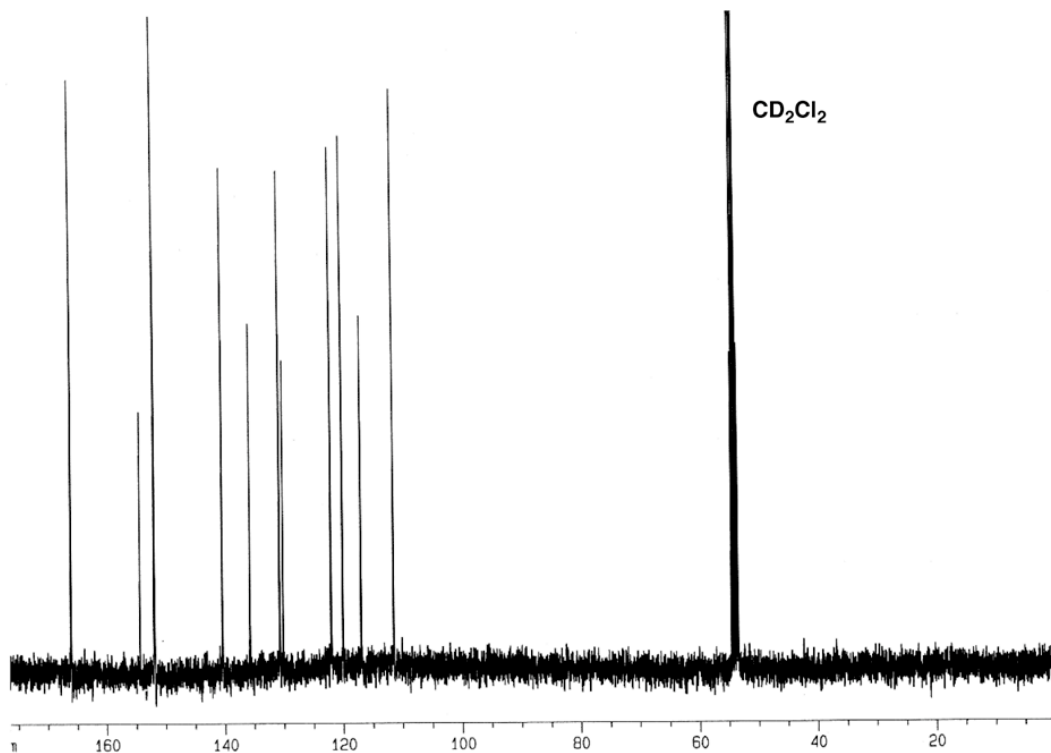
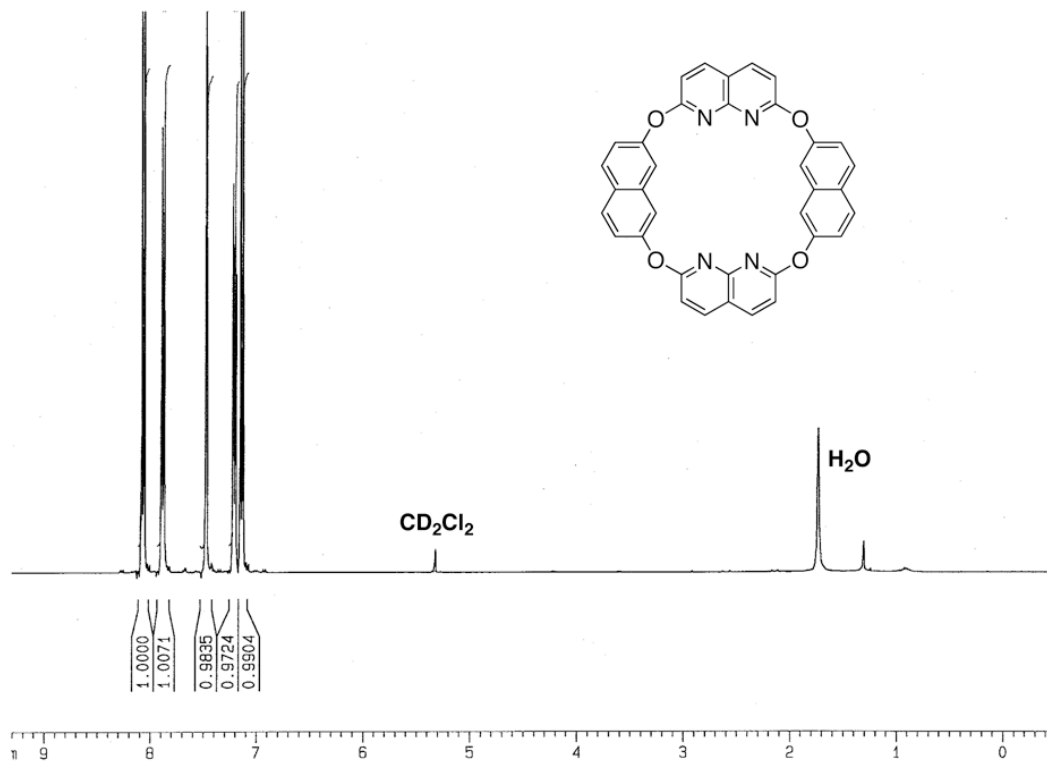
**Oxcalix[2]naphthalene[2]naphthyridine 6:** The reaction mixture was diluted with 20 mL  $\text{H}_2\text{O}$  causing formation of a grey precipitate. The solid was collected by filtration, washed with 10 mL  $\text{H}_2\text{O}$ , dissolved in 1:1  $\text{CH}_2\text{Cl}_2$ :MeOH, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated *in vacuo*. The product was then purified via flash column chromatography through silica (linear gradient 0-3% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to yield 130 mg **6** as a white solid (68%).  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  8.06 (d, 4H,  $J = 8.6$  Hz), 7.88 (d, 4H,  $J = 8.8$  Hz), 7.47 (d, 4H,  $J = 2.1$  Hz) 7.20 (dd, 4H,  $J = 8.8, 2.2$  Hz), 7.13 (d, 4H,  $J = 8.6$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  166.0, 154.2, 151.9, 140.3, 135.7, 130.7, 130.1, 122.0, 120.0, 116.9, 111.5; IR (thin film): 3057, 1728, 1604, 1510, 1495, 1456, 1423, 1370, 1322, 1310, 1250, 1223, 1170, 1125, 962, 896, 855, 838, 797  $\text{cm}^{-1}$ ; HRMS [MALDI(+)] with a DHB matrix] calculated for  $(\text{M}+\text{H})^+$  [ $\text{C}_{36}\text{H}_{21}\text{N}_4\text{O}_4$ ] $^+$ : 573.15573, found: 573.15415. M.P. >533K.

**[1<sub>4</sub>]Oxacyclophane 7:** The reaction mixture was diluted with 20 mL  $\text{H}_2\text{O}$  causing formation of a grey precipitate. The solid was collected by filtration, washed with an additional 10 mL  $\text{H}_2\text{O}$ , then dissolved in 1:1  $\text{CH}_2\text{Cl}_2$ :MeOH, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated *in vacuo*. The product was purified via flash column chromatography through silica (linear gradient 0-3% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to yield 86 mg **7** as a white solid (45%).  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  7.78 (dd, 4H,  $J = 6.2, 3.3$ ), 7.72 (s, 4H), 7.66 (d, 4H,  $J = 8.6$  Hz) 7.42 (dd, 4H,  $J = 6.2, 3.3$  Hz), 6.83 (d, 4H,  $J = 8.6$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  164.2, 153.2, 145.0, 139.4, 132.3, 128.1, 126.4, 123.0, 116.5, 110.9; IR (thin film): 3048, 1724, 1604, 1493, 1457, 1424, 1319, 1304, 1245, 1209, 1144, 1119, 886, 837, 793, 739, 711  $\text{cm}^{-1}$ ; HRMS [MALDI(+)] with a DHB matrix] calculated for  $(\text{M}+\text{H})^+$  [ $\text{C}_{36}\text{H}_{21}\text{N}_4\text{O}_4$ ] $^+$ : 573.15573, found: 573.15478. M.P. >533K.

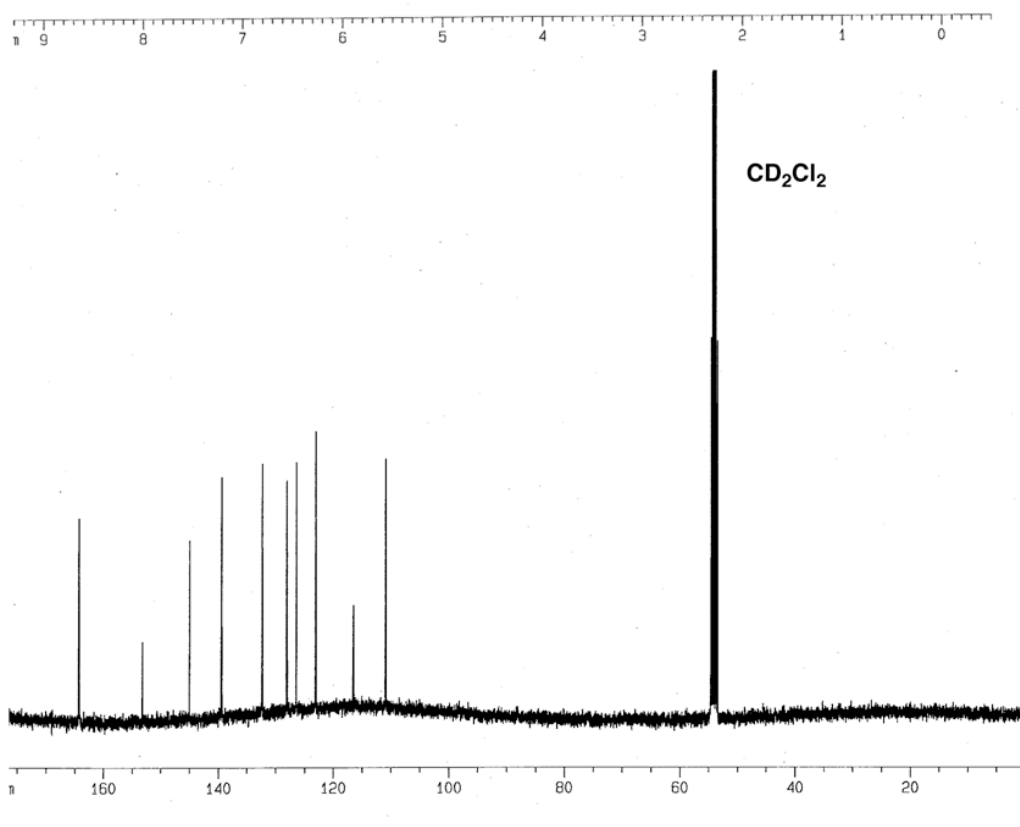
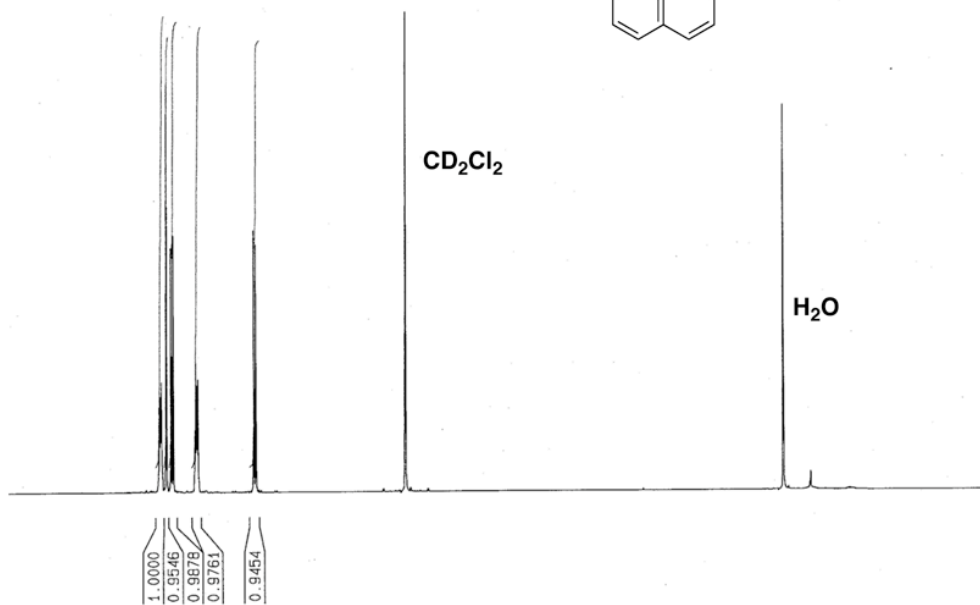
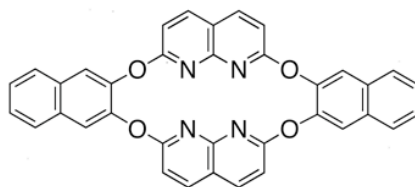
oxacalix[2]benzene[2]naphthyridine 3



oxacalix[2]naphthalene[2]naphthyridine 6



[1<sub>4</sub>]oxacyclophane 7



### X-ray Crystallographic Data for 3•2CH<sub>2</sub>Cl<sub>2</sub>

CCDC number	624760
Empirical formula	C <sub>32</sub> H <sub>24</sub> Cl <sub>4</sub> N <sub>4</sub> O <sub>4</sub>
Formula weight	670.35
Temperature	174(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	Pnmm
Unit cell dimensions	$a = 10.6659(9)$ Å $\alpha = 90^\circ$ $b = 16.1506(14)$ Å $\beta = 90^\circ$ $c = 18.2407(16)$ Å $\gamma = 90^\circ$
Volume, Z	3142.2(5) Å <sup>3</sup> , 4
Density (calculated)	1.417 Mg/m <sup>3</sup>
Absorption coefficient	0.421 mm <sup>-1</sup>
F(000)	1376
Crystal size	0.48 x 0.28 x 0.10 mm
$\theta$ range for data collection	1.68 to 28.27°
Limiting indices	$-14 < h < 14, -21 < k < 20, -24 < l < 24$
Reflections collected	26939
Independent reflections	3942 ( $R_{\text{int}} = 0.0973$ )
Completeness to $\theta = 28.27^\circ$	97.8%
Absorption correction	None
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	3942 / 0 / 222
Goodness-of-fit on F <sup>2</sup>	1.054
Final R indices [ $I > 2\sigma(I)$ ]	R1 = 0.0567, wR2 = 0.1586
R indices (all data)	R1 = 0.0675, wR2 = 0.1686
Largest diff. peak and hole	0.748 and -0.295 e-/Å

### Experimental details for 3•2CH<sub>2</sub>Cl<sub>2</sub>

The selected crystal was covered with Paratone-N oil, placed onto the tip of a glass rod drawn out to a fiber, and frozen in the cold stream (-99 °C) provided by a Rigaku/MSX X-stream 2000 low-temperature system. The X-ray intensity data for this colorless plate of C<sub>32</sub>H<sub>24</sub>Cl<sub>4</sub>N<sub>4</sub>O<sub>4</sub> with approximate dimensions 0.48 x 0.28 x 0.10 mm were measured with phi and omega scans at 174 K on a Bruker SMART APEX CCD-based X-ray diffractometer system equipped with a Mo-target X-ray tube ( $\lambda = 0.71073$  Å). The detector was placed at a distance of 5.00 cm from the crystal. A total of 1850 frames were collected (a hemisphere of data) with an exposure time of 30 sec/frame. The frames were integrated with the Bruker SAINT software package using a narrow-frame integration algorithm giving a total of 26939 reflections to a maximum  $2\theta$  angle of 56.5° of which 3942 reflections were independent. The structure was solved (direct methods) and refined using the Bruker SHELXTL version 6.1 Software Package using literature scattering factors (Wilson, A. J. C., Ed. *International Tables for Crystallography*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1992; Vol. C.), and the orthorhombic space group Pnmm, with Z = 4 because of crystallographically imposed mirror symmetry. No absorption correction was applied. The final anisotropic full-matrix least-squares refinement of F<sup>2</sup> converged at R1 = 5.67%, wR2 = 15.86% and a goodness-of-fit of 1.054 for all data. All non-hydrogen atoms were modeled anisotropically. The disordered CH<sub>2</sub>Cl<sub>2</sub> molecule was modeled in two positions using a free variable with a total occupancy of

one. Hydrogen atoms were not added to the  $\text{CH}_2\text{Cl}_2$  molecule. No further modeling was attempted, resulting in the largest peak value of  $0.748 \text{ e-}/\text{A}^3$ . All hydrogen atoms were placed at calculated distances and use a riding model, which means that the positional and thermal parameters are derived from the atom each hydrogen atom is bound to, while maintaining the calculated distance and optimal angles. The largest peak and hole in the final difference map were  $0.748$  and  $-0.295 \text{ e-}/\text{A}^3$ , respectively. The calculated density is  $1.417 \text{ g/cm}^3$  and  $F(000)$  is  $1376 \text{ e-}$ .

### X-ray Crystallographic Data for 6•0.5CH<sub>2</sub>Cl<sub>2</sub>•0.5H<sub>2</sub>O

CCDC number	624761
Empirical formula	C <sub>36.50</sub> H <sub>22</sub> Cl <sub>4</sub> O <sub>4.50</sub>
Formula weight	624.03
Temperature	180(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	$a = 9.6887(8)$ Å $a = 100.3880(10)^\circ$ $b = 13.1957(10)$ Å $b = 107.1250(10)^\circ$ $c = 13.4844(10)$ Å $\gamma = 111.1100(10)^\circ$
Volume, Z	1455.5(2) Å <sup>3</sup> , 2
Density (calculated)	1.424 Mg/m <sup>3</sup>
Absorption coefficient	0.184 mm <sup>-1</sup>
F(000)	644
Crystal size	0.46 x 0.22 x 0.14 mm
$\theta$ range for data collection	1.67 to 28.29°
Limiting indices	$-12 < h < 12$ , $-16 < k < 17$ , $-17 < l < 17$
Reflections collected	13087
Independent reflections	6628 ( $R_{\text{int}} = 0.0512$ )
Completeness to $\theta = 28.29^\circ$	91.7%
Absorption correction	None
Refinement method	Full-matrix least-squares on $F^2$
Data / restraints / parameters	6628 / 0 / 433
Goodness-of-fit on $F^2$	1.157
Final R indices [ $I > 2\sigma(I)$ ]	$R1 = 0.0557$ , $wR2 = 0.1811$
R indices (all data)	$R1 = 0.0698$ , $wR2 = 0.1893$
Largest diff. peak and hole	0.790 and $-0.279$ e-/Å

### Experimental details for 6•0.5CH<sub>2</sub>Cl<sub>2</sub>•0.5H<sub>2</sub>O

The selected crystal was covered with Paratone-N oil, placed onto the tip of a glass rod drawn out to a fiber, and frozen in the cold stream ( $-93^\circ\text{C}$ ) provided by a Rigaku/MSX X-stream 2000 low-temperature system. The X-ray intensity data for this colorless rectangular prism of C<sub>36.50</sub>H<sub>22</sub>Cl<sub>4</sub>O<sub>4.50</sub> with approximate dimensions 0.46 x 0.22 x 0.14 mm were measured with phi and omega scans at 180 K on a Bruker SMART APEX CCD-based X-ray diffractometer system equipped with a Mo-target X-ray tube ( $\lambda = 0.71073$  Å). The detector was placed at a distance of 5.00 cm from the crystal. A total of 1850 frames were collected (a hemisphere of data) with an exposure time of 30 sec/frame. The frames were integrated with the Bruker SAINT software package using a narrow-frame integration algorithm giving a total of 13087 reflections to a maximum  $2\theta$  angle of  $56.6^\circ$  of which 6628 reflections were independent. The structure was solved (direct methods) and refined using the Bruker SHELXTL version 6.1 Software Package using literature scattering factors (Wilson, A. J. C., Ed. *International Tables for Crystallography*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1992; Vol. C.), and the triclinic space group P-1, with  $Z = 2$ . No absorption correction was applied. The final anisotropic full-matrix least-squares refinement of  $F^2$  converged at  $R1 = 5.57\%$ ,  $wR2 = 18.11\%$  and a goodness-of-fit of 1.157 for all data. All non-hydrogen atoms were modeled anisotropically. The solvated CH<sub>2</sub>Cl<sub>2</sub> molecule occupied a special position, and was refined without added hydrogen atoms. Disorder for this CH<sub>2</sub>Cl<sub>2</sub> molecule was not modeled. The disordered water molecule was refined with an occupancy of 0.5. Hydrogen atoms were also not added to the disordered water molecule. All other hydrogen atoms were placed at calculated distances and use a



riding model, which means that the positional and thermal parameters are derived from the atom each hydrogen atom is bound to, while maintaining the calculated distance and optimal angles. The largest peak and hole in the final difference map were 0.790 and  $-0.279 \text{ e-}/\text{A}^3$ , respectively. The calculated density is  $1.424 \text{ g/cm}^3$  and  $F(000)$  is 644 e-.

### X-ray Crystallographic Data for 7•2CH<sub>3</sub>CN

CCDC number	624762
Empirical formula	C <sub>40</sub> H <sub>26</sub> N <sub>6</sub> O <sub>4</sub>
Formula weight	654.67
Temperature	178(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	$a = 19.4444(15)$ Å $a = 90^\circ$ $b = 9.3321(7)$ Å $b = 118.0490(10)^\circ$ $c = 20.5331(16)$ Å $\gamma = 90^\circ$
Volume, Z	3288.3(4) Å <sup>3</sup> , 4
Density (calculated)	1.322 Mg/m <sup>3</sup>
Absorption coefficient	0.088 mm <sup>-1</sup>
F(000)	1360
Crystal size	0.36 x 0.24 x 0.15 mm
$\theta$ range for data collection	1.19 to 28.30°
Limiting indices	$-25 < h < 25, -12 < k < 12, -26 < l < 27$
Reflections collected	28816
Independent reflections	7790 ( $R_{\text{int}} = 0.0685$ )
Completeness to $\theta = 28.30^\circ$	95.4%
Absorption correction	None
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	7790 / 0 / 453
Goodness-of-fit on F <sup>2</sup>	0.924
Final R indices [ $I > 2\sigma(I)$ ]	R1 = 0.0534, wR2 = 0.1343
R indices (all data)	R1 = 0.0957, wR2 = 0.1564
Largest diff. peak and hole	0.484 and -0.221 e-/Å

### Experimental details for 7•2CH<sub>3</sub>CN

The selected crystal was covered with Paratone-N oil, placed onto the tip of a glass rod drawn out to a fiber, and frozen in the cold stream (-95 °C) provided by a Rigaku/MSX X-stream 2000 low-temperature system. The X-ray intensity data for this colorless hexagonal prism of C<sub>40</sub>H<sub>26</sub>N<sub>6</sub>O<sub>4</sub> with approximate dimensions 0.36 x 0.24 x 0.15 mm were measured with phi and omega scans at 178 K on a Bruker SMART APEX CCD-based X-ray diffractometer system equipped with a Mo-target X-ray tube ( $\lambda = 0.71073$  Å). The detector was placed at a distance of 5.00 cm from the crystal. A total of 1850 frames were collected (a hemisphere of data) with an exposure time of 30 sec/frame. The frames were integrated with the Bruker SAINT software package using a narrow-frame integration algorithm giving a total of 28816 reflections to a maximum  $2\theta$  angle of 56.6° of which 7790 reflections were independent. The structure was solved (direct methods) and refined using the Bruker SHELXTL version 6.1 Software Package using literature scattering factors (Wilson, A. J. C., Ed. *International Tables for Crystallography*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1992; Vol. C.), and the monoclinic space group P2(1)/n, with Z = 4. No absorption correction was applied. The final anisotropic full-matrix least-squares refinement of F<sup>2</sup> converged at R1 = 5.34%, wR2 = 13.43% and a goodness-of-fit of 0.924 for all data. All non-hydrogen atoms were modeled anisotropically. Hydrogen atoms were placed at calculated distances and use a riding model, which means that the positional and thermal parameters are derived from the atom each hydrogen

atom is bound to, while maintaining the calculated distance and optimal angles. The largest peak and hole in the final difference map were 0.484 and  $-0.221 \text{ e-}/\text{A}^3$ , respectively. The calculated density is  $1.322 \text{ g/cm}^3$  and  $F(000)$  is 1360 e-.

## Determination Of Association Constants By <sup>1</sup>H NMR Titration

NMR titrations were performed at 25°C by treating known concentrations of host **6** or **7** in 9:1 CH<sub>2</sub>Cl<sub>2</sub>:CD<sub>2</sub>Cl<sub>2</sub> with aliquots of guest **12** in 9:1 CH<sub>2</sub>Cl<sub>2</sub>:CD<sub>2</sub>Cl<sub>2</sub> and monitoring the chemical shift changes in <sup>1</sup>H resonances. Host-guest complexation and guest monomer-dimer equilibrium are competitive in this determination. The guest dissociation constant (K<sub>d</sub>) was determined separately (see below). Assuming a 1:1 host:guest-monomer complex, the equilibrium guest-monomer concentration [G] in each titration experiment was obtained by iterative solution of the expression:

$$\frac{2[G]^2}{K_d} + [G] - \frac{[H_0]}{(K_a[G] + 1)} - ([G_0] - [H_0]) = 0$$

The complexation-induced species-averaged host chemical shift was then predicted as δ<sub>calc</sub> = (1-χ<sub>HG</sub>) δ<sub>H</sub> + (χ<sub>HG</sub>)( δ<sub>HG</sub>) where the mole fraction of host-guest complex (χ<sub>HG</sub>) is given by:

$$\chi_{HG} = \frac{K_a[G]}{1 + K_a[G]}$$

K<sub>a</sub> and δ<sub>HG</sub> were then determined by non-linear least squares fit (Solver, Microsoft Excel) of the predicted chemical shifts to the titration experiment. Standard deviations were calculated with Solver Aid.<sup>1</sup>

For a 1:1 host:guest-dimer complex the corresponding expressions to be similarly solved and fit are:

$$\frac{2[G]^2}{K_d} + [G] - \frac{[H_0]}{(1 + \frac{K_a}{K_d}[G]^2)} - ([G_0] - 2[H_0]) = 0$$

$$[G_2] = \frac{[G]^2}{K_d}$$

The complexation-induced species-averaged host chemical shift was predicted as δ<sub>calc</sub> = (1-χ<sub>HG<sub>2</sub></sub>) δ<sub>H</sub> + (χ<sub>HG<sub>2</sub></sub>)( δ<sub>HG<sub>2</sub></sub>) where the mole fraction of host-guest complex (χ<sub>HG<sub>2</sub></sub>) is given by:

$$\chi_{HG_2} = \frac{K_a[G_2]}{1 + K_a[G_2]}$$

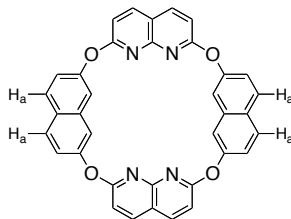
During the experiments, the <sup>1</sup>H NMR resonances of **6** and **7** were also found to vary slightly depending on the amount of residual water present. The specific <sup>1</sup>H resonances on hosts **6** or **7** chosen to determine association constants were not significantly affected by the amount of residual water. No attempt was made to dry the solvents used for the NMR titrations.

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<sup>1</sup> (a) de Levie, R. *Advanced Excel For Scientific Data Analysis*, Oxford University Press, Oxford, 2004. (b) de Levie, R. *J. Chem. Ed.* **1999**, 76, 1594-1598. (c) Fielding, L. *Tetrahedron*, **2000**, 56, 6151-6170.

### Titration experiment between host **6** and salicylic acid (**12**)

The association constant was determined from the chemical shift change of H<sub>a</sub> (below) on host **6**.

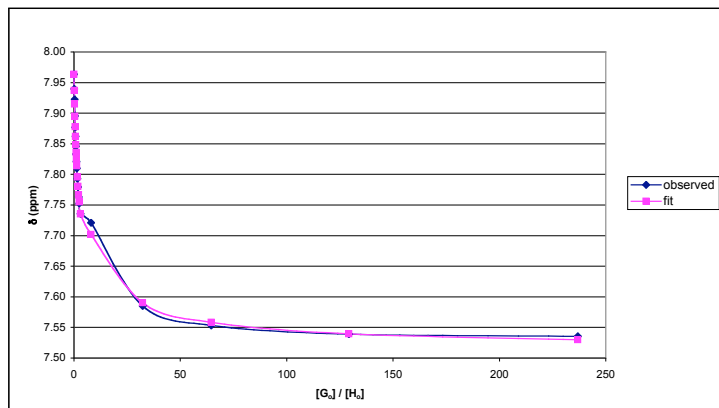


**6**

[H <sub>0</sub> ] (mol/l)	[G <sub>0</sub> ] (mol/l)	[G <sub>0</sub> ]/[H <sub>0</sub> ]	δ <sub>obs</sub> (ppm)	δ <sub>calc</sub> (ppm)
6.46 X 10 <sup>-3</sup>	0.000	0.000	7.9635	7.9635
6.32 X 10 <sup>-3</sup>	9.11 X 10 <sup>-4</sup>	0.144	7.9399	7.9373
6.19 X 10 <sup>-3</sup>	1.78 X 10 <sup>-3</sup>	0.288	7.9223	7.9148
6.06 X 10 <sup>-3</sup>	2.62 X 10 <sup>-3</sup>	0.432	7.8958	7.8951
5.93 X 10 <sup>-3</sup>	3.42 X 10 <sup>-3</sup>	0.576	7.8768	7.8777
5.82 X 10 <sup>-3</sup>	4.19 X 10 <sup>-3</sup>	0.720	7.8621	7.8622
5.70 X 10 <sup>-3</sup>	4.93 X 10 <sup>-3</sup>	0.865	7.8457	7.8483
5.59 X 10 <sup>-3</sup>	5.64 X 10 <sup>-3</sup>	1.01	7.8332	7.8358
5.49 X 10 <sup>-3</sup>	6.32 X 10 <sup>-3</sup>	1.15	7.8208	7.8245
5.39 X 10 <sup>-3</sup>	6.98 X 10 <sup>-3</sup>	1.30	7.8100	7.8141
5.19 X 10 <sup>-3</sup>	8.23 X 10 <sup>-3</sup>	1.58	7.7931	7.7958
5.01 X 10 <sup>-3</sup>	9.39 X 10 <sup>-3</sup>	1.87	7.7794	7.7802
4.85 X 10 <sup>-3</sup>	1.05 X 10 <sup>-2</sup>	2.16	7.7634	7.7667
4.69 X 10 <sup>-3</sup>	1.15 X 10 <sup>-2</sup>	2.45	7.7525	7.7549
4.41 X 10 <sup>-3</sup>	1.33 X 10 <sup>-2</sup>	3.03	7.7356	7.7352
2.04 X 10 <sup>-3</sup>	1.64 X 10 <sup>-2</sup>	8.08	7.7210	7.7016
1.12 X 10 <sup>-3</sup>	3.62 X 10 <sup>-2</sup>	32.3	7.5850	7.5903
7.00 X 10 <sup>-4</sup>	4.52 X 10 <sup>-2</sup>	64.6	7.5535	7.5585
4.00 X 10 <sup>-4</sup>	5.17 X 10 <sup>-2</sup>	129	7.5389	7.5396
2.33 X 10 <sup>-4</sup>	5.53 X 10 <sup>-2</sup>	237	7.5357	7.5302

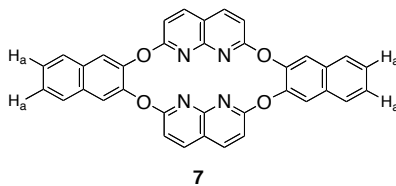
δ<sub>HG</sub> (ppm)  
7.090 ± 0.050

K<sub>a</sub> (M<sup>-1</sup>)  
44.8 ± 2.5



### Titration experiment between host 7 and salicylic acid (12)

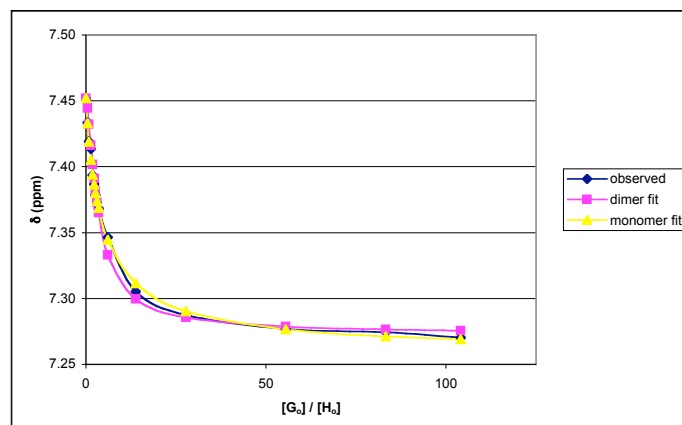
The association constant was determined from the chemical shift change of H<sub>a</sub> (below) on host 7.



[H <sub>o</sub> ] (mol/l)	[G <sub>o</sub> ] (mol/l)	[G <sub>o</sub> ]/[H <sub>o</sub> ]	δ <sub>obs</sub> (ppm)	Monomer-12	Dimer-12
				δ <sub>calc</sub> (ppm)	δ <sub>calc</sub> (ppm)
6.52 X 10 <sup>-3</sup>	0.000	0.000	7.4520	7.4520	7.4520
6.24 X 10 <sup>-3</sup>	2.57 X 10 <sup>-3</sup>	0.411	7.4336	7.4330	7.4444
5.99 X 10 <sup>-3</sup>	4.92 X 10 <sup>-3</sup>	0.822	7.4193	7.4188	7.4322
5.70 X 10 <sup>-3</sup>	7.61 X 10 <sup>-3</sup>	1.34	7.4137	7.4050	7.4164
5.43 X 10 <sup>-3</sup>	1.01 X 10 <sup>-2</sup>	1.85	7.3937	7.3939	7.4017
5.24 X 10 <sup>-3</sup>	1.18 X 10 <sup>-2</sup>	2.26	7.3866	7.3863	7.3911
5.06 X 10 <sup>-3</sup>	1.35 X 10 <sup>-2</sup>	2.67	7.3787	7.3797	7.3815
4.89 X 10 <sup>-3</sup>	1.51 X 10 <sup>-2</sup>	3.08	7.3728	7.3738	7.3729
4.73 X 10 <sup>-3</sup>	1.65 X 10 <sup>-2</sup>	3.49	7.3682	7.3685	7.3653
3.94 X 10 <sup>-3</sup>	2.39 X 10 <sup>-2</sup>	6.06	7.3464	7.3446	7.3330
2.61 X 10 <sup>-3</sup>	3.62 X 10 <sup>-2</sup>	13.9	7.3054	7.3113	7.2997
1.63 X 10 <sup>-3</sup>	4.52 X 10 <sup>-2</sup>	27.7	7.2875	7.2903	7.2857
9.31 X 10 <sup>-4</sup>	5.17 X 10 <sup>-2</sup>	55.5	7.2768	7.2765	7.2789
6.52 X 10 <sup>-4</sup>	5.43 X 10 <sup>-2</sup>	83.2	7.2744	7.2713	7.2766
5.32 X 10 <sup>-4</sup>	5.54 X 10 <sup>-2</sup>	104	7.2703	7.2691	7.2757

δ <sub>HG</sub> (ppm)	δ <sub>HG<sub>2</sub></sub> (ppm)
3.0 ± 4.3	7.2405 ± .0088

K <sub>a</sub> (M <sup>-1</sup> )	K <sub>a</sub> (M <sup>-1</sup> )
1.9 ± 1.9	306 ± 43



### Dilution titration experiment of salicylic acid (12)

NMR dilutions of guest **12** in 9:1 CH<sub>2</sub>Cl<sub>2</sub>:CD<sub>2</sub>Cl<sub>2</sub> were performed to determine the dimer dissociation constant (K<sub>d</sub>) of **12** (G<sub>2</sub> ⇌ 2G) by monitoring its phenolic <sup>1</sup>H chemical shift change. The equilibrium monomer concentration [G] was obtained at each dilution by solution of the quadratic expression:

$$K_d = \frac{2[G]^2}{[G_0] - [G]}$$

The chemical shift of the dimer/monomer mixture was then predicted as  $\delta_{\text{calc}} = (1 - \chi_{G_2})(\delta_G) + (\chi_{G_2})(\delta_{G_2})$  where the mole fraction of dimer ( $\chi_{G_2}$ ) is given by:

$$\chi_{G_2} = \frac{[G_0] - [G]}{[G_0] + [G]}$$

K<sub>d</sub>, δ<sub>G</sub> and δ<sub>G<sub>2</sub></sub> were then determined by non-linear least squares fit of the predicted chemical shifts to the dilution experiments.

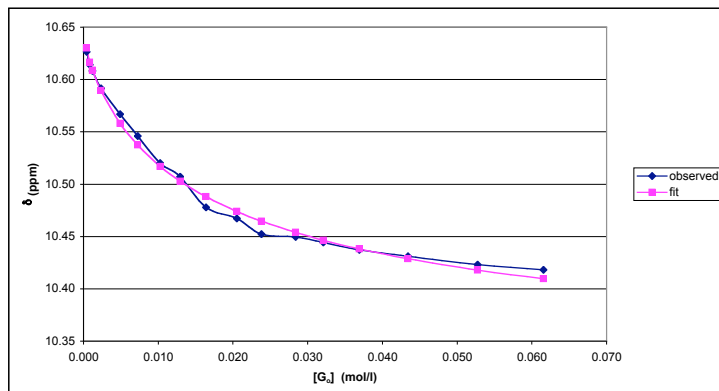
[G <sub>0</sub> ] M/L	δ <sub>obs</sub> (ppm)	δ <sub>calc</sub> (ppm)
4.075 X 10 <sup>-4</sup>	10.6265	10.6300
8.097 X 10 <sup>-4</sup>	10.6142	10.6166
1.207 X 10 <sup>-3</sup>	10.6083	10.6088
2.367 X 10 <sup>-3</sup>	10.5914	10.5894
4.908 X 10 <sup>-3</sup>	10.5667	10.5581
7.240 X 10 <sup>-3</sup>	10.5459	10.5373
1.026 X 10 <sup>-2</sup>	10.5200	10.5170
1.296 X 10 <sup>-2</sup>	10.5073	10.5027
1.641 X 10 <sup>-2</sup>	10.4777	10.4880
2.051 X 10 <sup>-2</sup>	10.4673	10.4740
2.382 X 10 <sup>-2</sup>	10.4522	10.4647
2.840 X 10 <sup>-2</sup>	10.4497	10.4539
3.211 X 10 <sup>-2</sup>	10.4442	10.4465
3.692 X 10 <sup>-2</sup>	10.4374	10.4382
4.344 X 10 <sup>-2</sup>	10.4311	10.4288
5.275 X 10 <sup>-2</sup>	10.4233	10.4179
6.154 X 10 <sup>-2</sup>	10.4181	10.4095

δ <sub>G<sub>2</sub></sub> (ppm) 10.270 ± .016
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δ <sub>G</sub> (ppm) 10.6349 ± .0051
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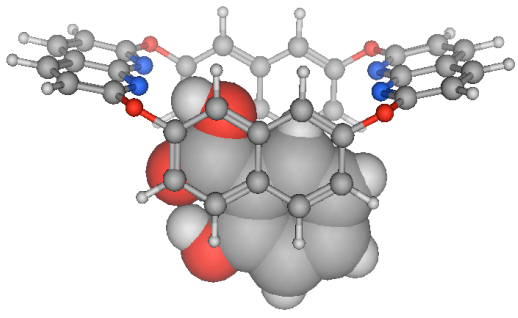
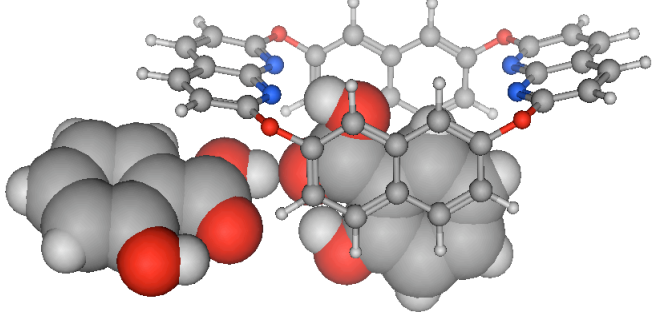
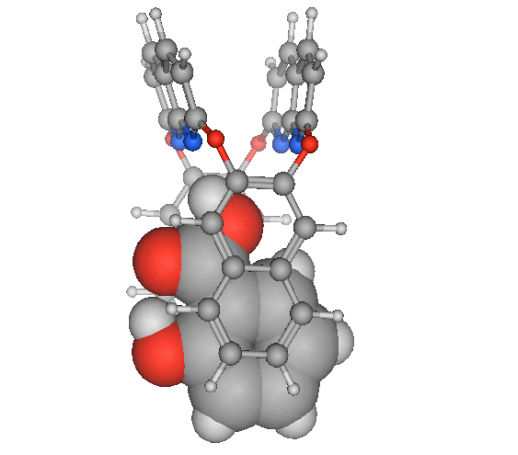
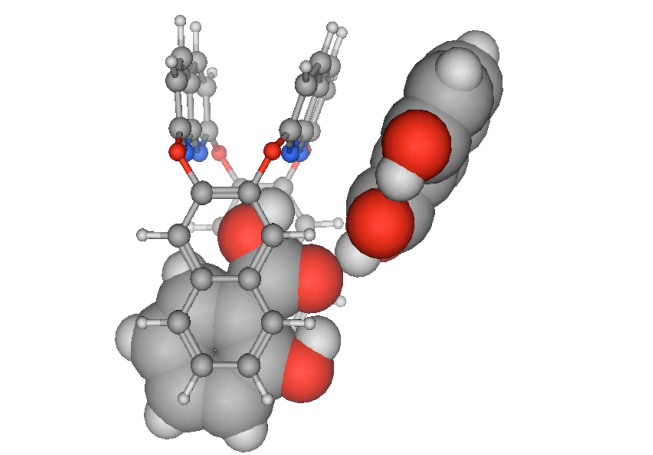
K <sub>d</sub> (M) 0.0290 ± .0047
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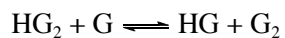


## Molecular Modeling of the 6-12 and 7-12 Host-Guest Complexes

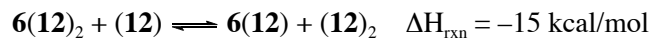
Binding geometries and steric energies were calculated in the Molecular Operating Environment (MOE) using the MMFF force field. Solvation energies were obtained using the Born solvation model with a dielectric constant of 9.1 to simulate  $\text{CH}_2\text{Cl}_2$ . Calculated total energies are the sum of the steric and solvation energies.

 <p><b>host 6-monomer 12</b></p> <p><b>Total Energy: + 86.0 kcal/mol</b></p>	 <p><b>host 6-dimer 12</b></p> <p><b>Total Energy: + 76.8 kcal/mol (dimer)</b></p>
 <p><b>host 7-monomer 12</b></p> <p><b>Total Energy: + 95.4 kcal/mol (monomer)</b></p>	 <p><b>host 7-dimer 12</b></p> <p><b>Total Energy: + 86.4 kcal/mol (dimer)</b></p>
<p><b>Salicylic Acid Monomer:</b></p> <p><b>Total Energy: +1.1 kcal/mol</b></p>	<p><b>Salicylic Acid Dimer:</b></p> <p><b>Total Energy: -4.7 kcal/mol</b></p>

Preferred host-guest binding stoichiometry was estimated from the relationship:

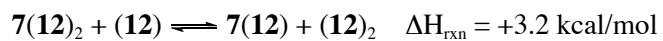


for each host, leading to the predicted energetics for host **6**:



(host **6** – monomer-**12** complex favored)

And for host **7**:



(host **7** – dimer-**12** complex favored)