

Supplementary material

Modulation and Binding Properties of Extended Glycoluril Molecular Clips

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1. NMR Titrations of clip 1.

(a) Clip 1 with H₂O.

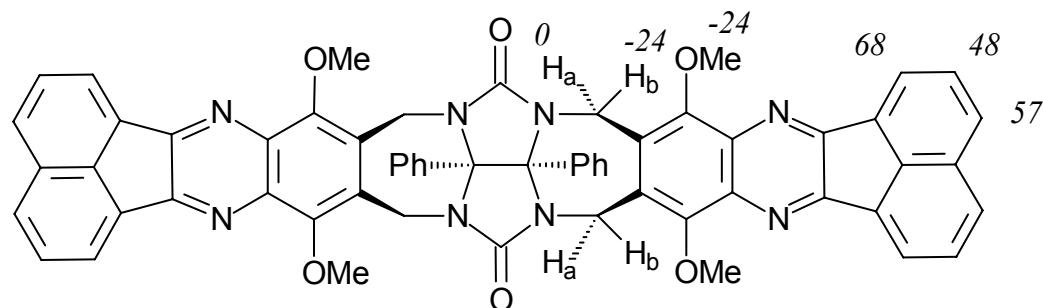


Figure S1: Temperature dependent ¹H NMR chemical shift changes $\Delta\delta$ (ppb) for clip 1 in the presence of water. Numbers correspond to the chemical shift difference $\Delta\delta$ in ppb when the temperature was varied from 25 °C to -55 °C. ($\Delta\delta = \delta_{-55\text{ }^\circ\text{C}} - \delta_{25\text{ }^\circ\text{C}}$).

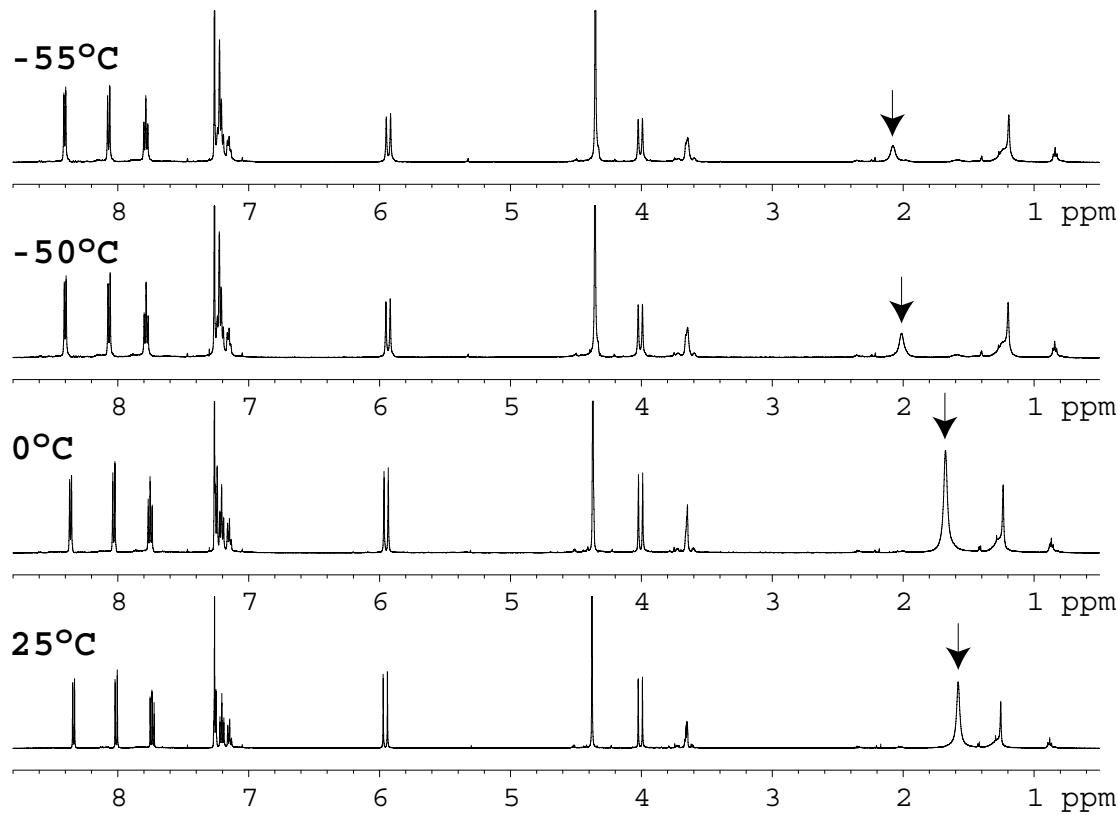


Figure S2: ¹H NMR spectra of clip 1 in the presence of water (500 MHz, CDCl₃ solution) recorded at the indicated temperatures. The arrow indicates the position of the water signal.

(b) Clip 1 with resorcinol.

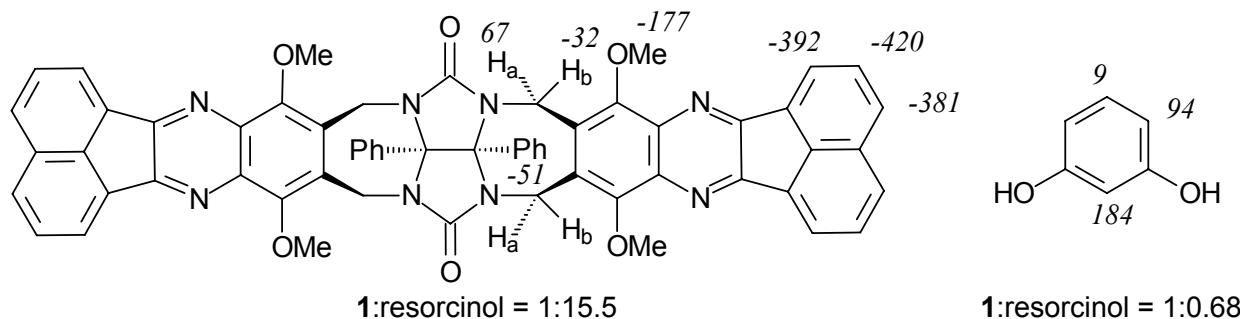


Figure S3: ^1H NMR chemical shift changes $\Delta\delta$ (ppb) for clip **1** and resorcinol. Values for clip **1** correspond to a clip:resorcinol ratio of 1:15.5. Values for resorcinol correspond to a clip>resorcinol ratio of 1:0.68. $\Delta\delta = \delta_{(\mathbf{1}+\text{resorcinol})} - \delta_{\mathbf{1}}$ (or $\delta_{\text{(resorcinol)}}$).

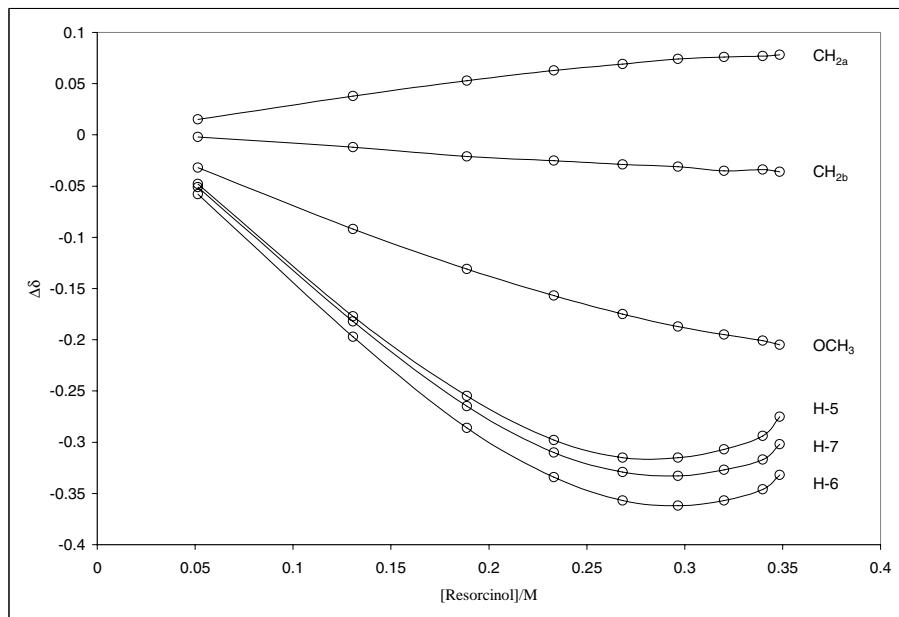


Figure S4: Chemical shift changes vs. resorcinol concentration for selected protons of clip **1** (CDCl_3 solution, 500 MHz, 25°C). [clip **1**] = 0.082 M.

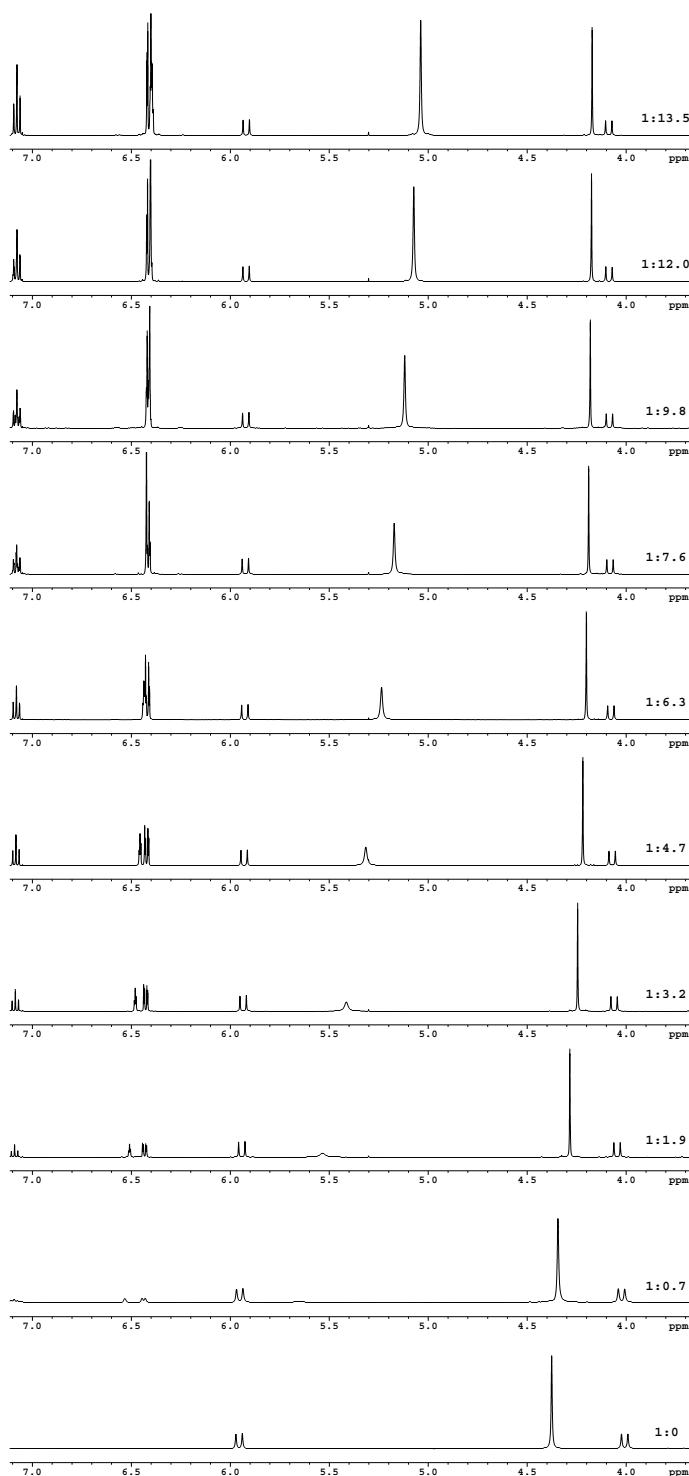


Figure S5: Expansions of ^1H NMR spectra showing resorcinol and aliphatic clip proton signals observed upon titration of a solution of clip **1** with resorcinol (CDCl_3 solution, 500 MHz, 25°C). Molecular ratios of clip **1**:resorcinol are indicated.

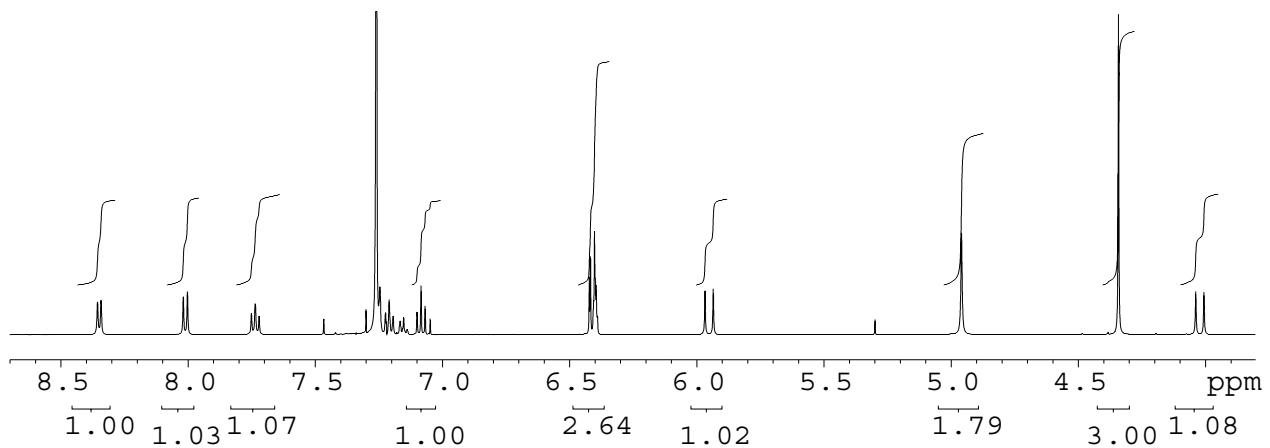
Clip 1 – resorcinol precipitate

Figure S6: ¹H NMR spectrum of collected precipitate obtained from a solution of clip **1** + excess of resorcinol (500 MHz, CDCl₃ solution).

(c) Clip 1 with AgClO₄.

Table S1: ¹H NMR chemical shift changes for clip **1** upon addition of AgClO₄. $\Delta\delta = \delta_{(1+Ag^+)} - \delta_1$. Solvent CDCl₃:CD₃OD 9:1.

1:Ag⁺		H _{2a}	H _{2b}	H ₅	H ₆	H ₇	CH ₃	Ph			
1:0	δ	3.952	5.840	8.251	7.644	7.927	4.244	7.114			
1:0.2	δ	3.954	5.839	8.231	7.630	7.913	4.241	7.120			
	$\Delta\delta$	0.002	0.001	-0.020	-0.014	-0.014	0.003	0.006			
1:0.6	δ	3.958	5.835	8.192	7.601	7.885	4.234	7.121			
	$\Delta\delta$	0.006	-0.010	-0.060	-0.043	-0.042	-0.01	0.007			
1:0.8	δ	3.959	5.835	8.175	7.589	7.873	4.231	7.122			
	$\Delta\delta$	0.007	-0.010	-0.080	-0.055	-0.054	-0.013	0.008			
1:1	δ	3.973	5.830	8.1(br)	7.52(br)	7.82(br)	4.213	7.13			
	$\Delta\delta$	0.021	-0.010	-0.150	-0.124	-0.107	-0.031	0.016			
1:1.2	δ	3.995	5.816	small and broad peaks			4.177(br)	7.15(br)			
	$\Delta\delta$	0.043	-0.020				-0.067	0.036			
1:2	δ	4.018(br)	5.755	No peaks			4.076	7.2			
	$\Delta\delta$	0.066	-0.090				-0.168	0.086			
1:3	δ	-	5.730				4.037	7.21			
	$\Delta\delta$		-0.110				-0.207	0.096			
1:4.4	δ	4.120	5.735				4.010	7.22			
	$\Delta\delta$	0.168	-0.110				-0.234	0.106			
1:7	δ	Very small and broad signals									
1:11	δ	All signals corresponding to 1 disappear									

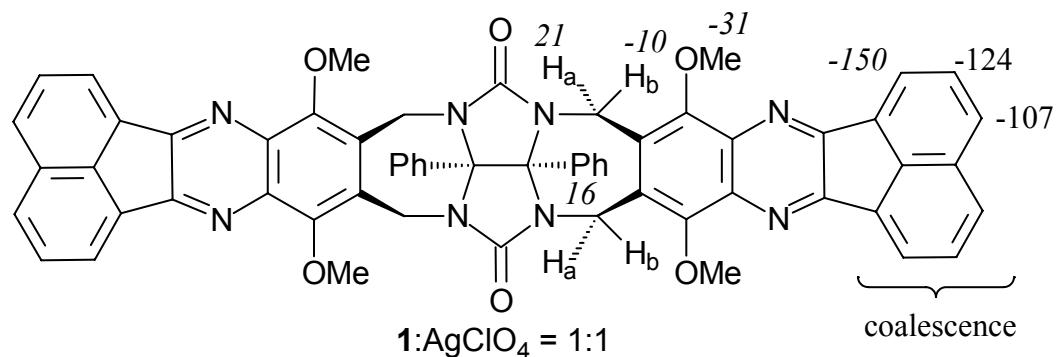


Figure S7: ¹H NMR chemical shift changes $\Delta\delta$ (in ppb) for clip **1** for clip:Ag⁺ ratio of 1:1.

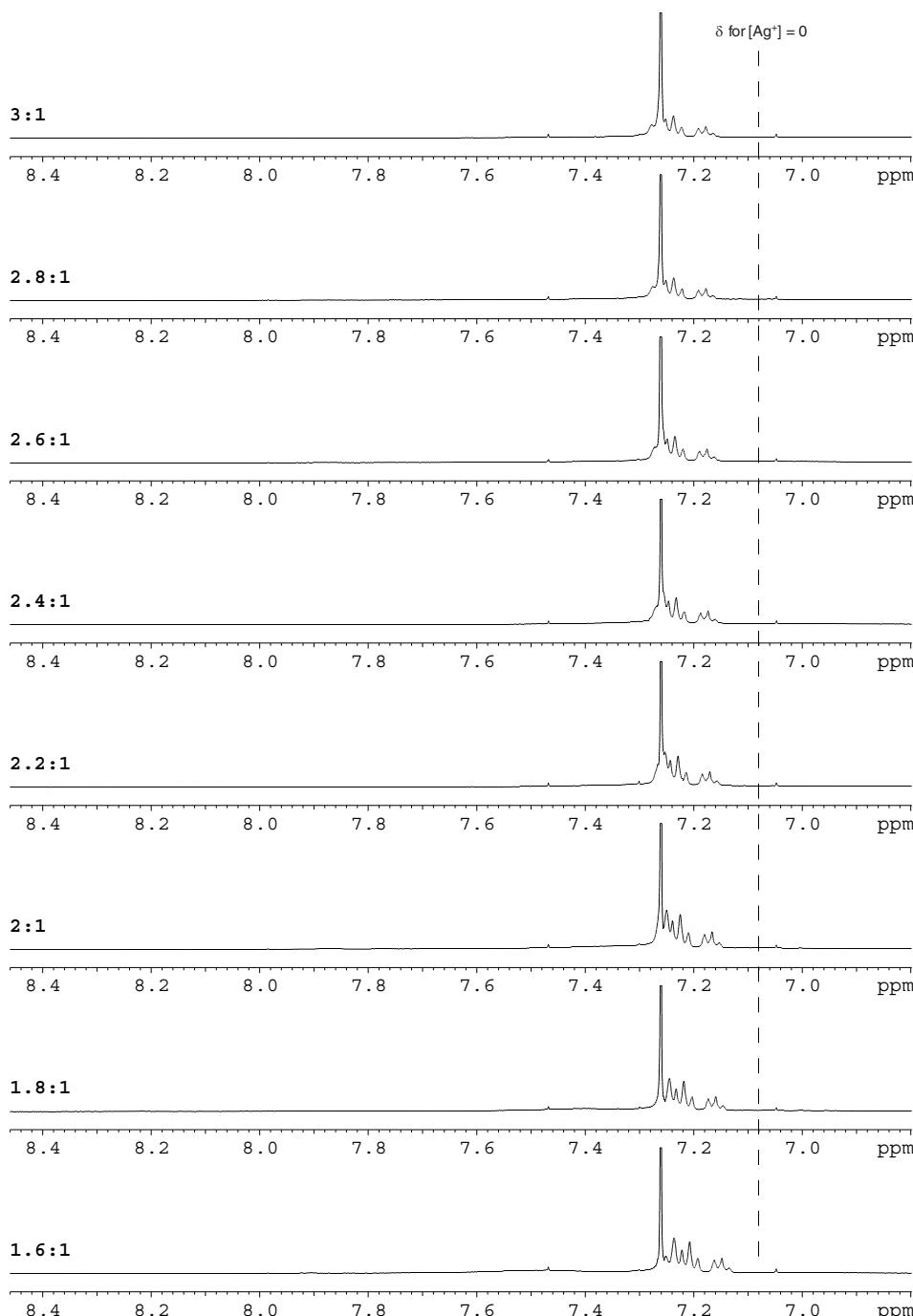


Figure S8: Expansion of aromatic region of ^1H NMR spectra with various Ag^+ : clip 1 ratios (500 MHz, solvent $\text{CDCl}_3:\text{MeOH-d}_4$ 9:1) (continued from **Error! Reference source not found.**). Aliquots of AgClO_4 solution added to clip 1, ratios indicated on left hand side of spectra. The dashed line indicates the δ of *para*-Ph protons in the absence of Ag^+ (continued overleaf).

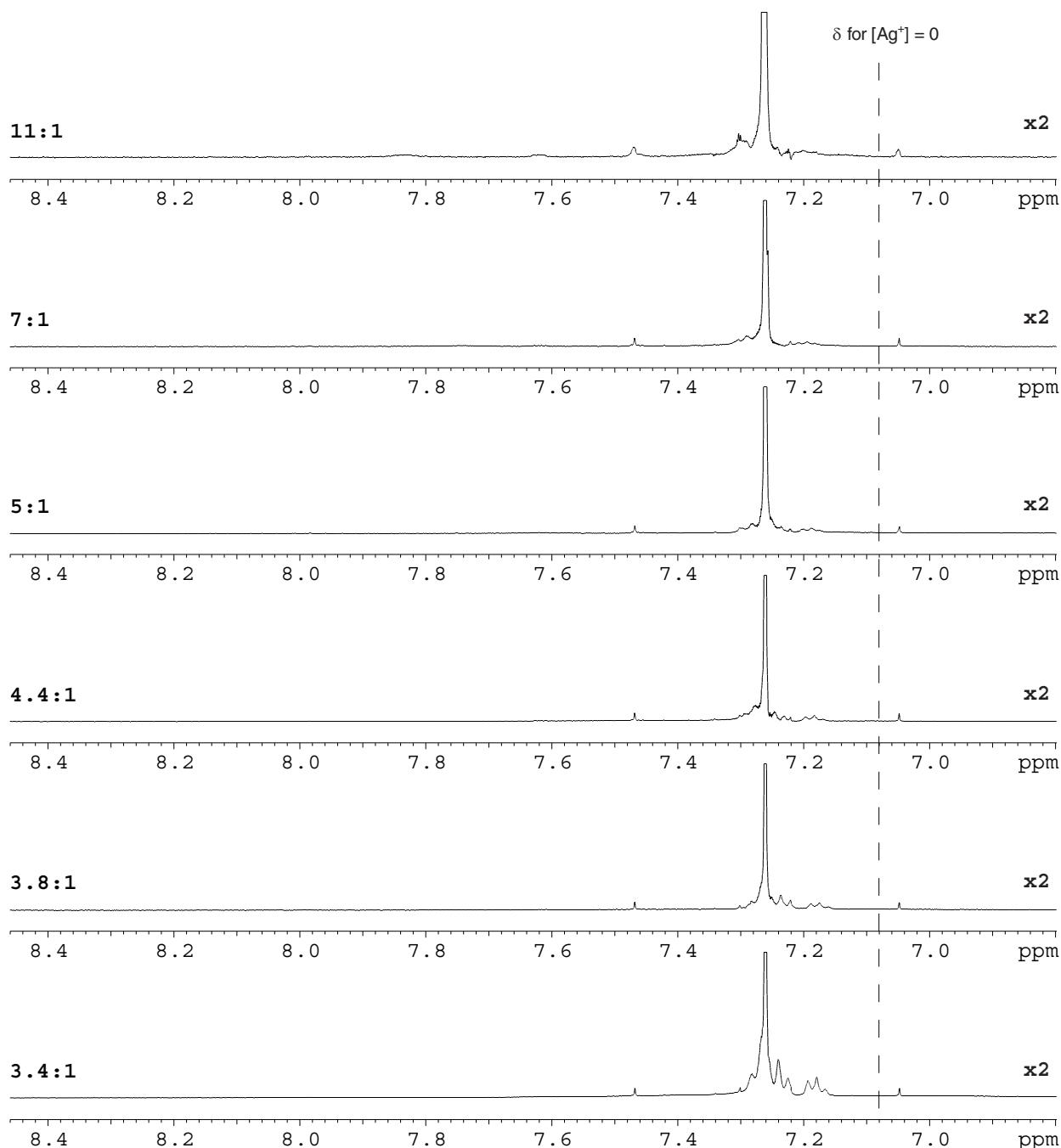


Figure S9: Expansion of aromatic region of ^1H NMR spectra with various Ag^+ : clip 1 ratios (500 MHz, solvent $\text{CDCl}_3:\text{MeOH-d}_4$ 9:1) (continued from previous Figure). Aliquots of AgClO_4 solution added to clip 1, ratios indicated on left hand side of spectra. The vertical scale was increased two times compared to Figures for lower Ag^+ : clip 1 ratios.

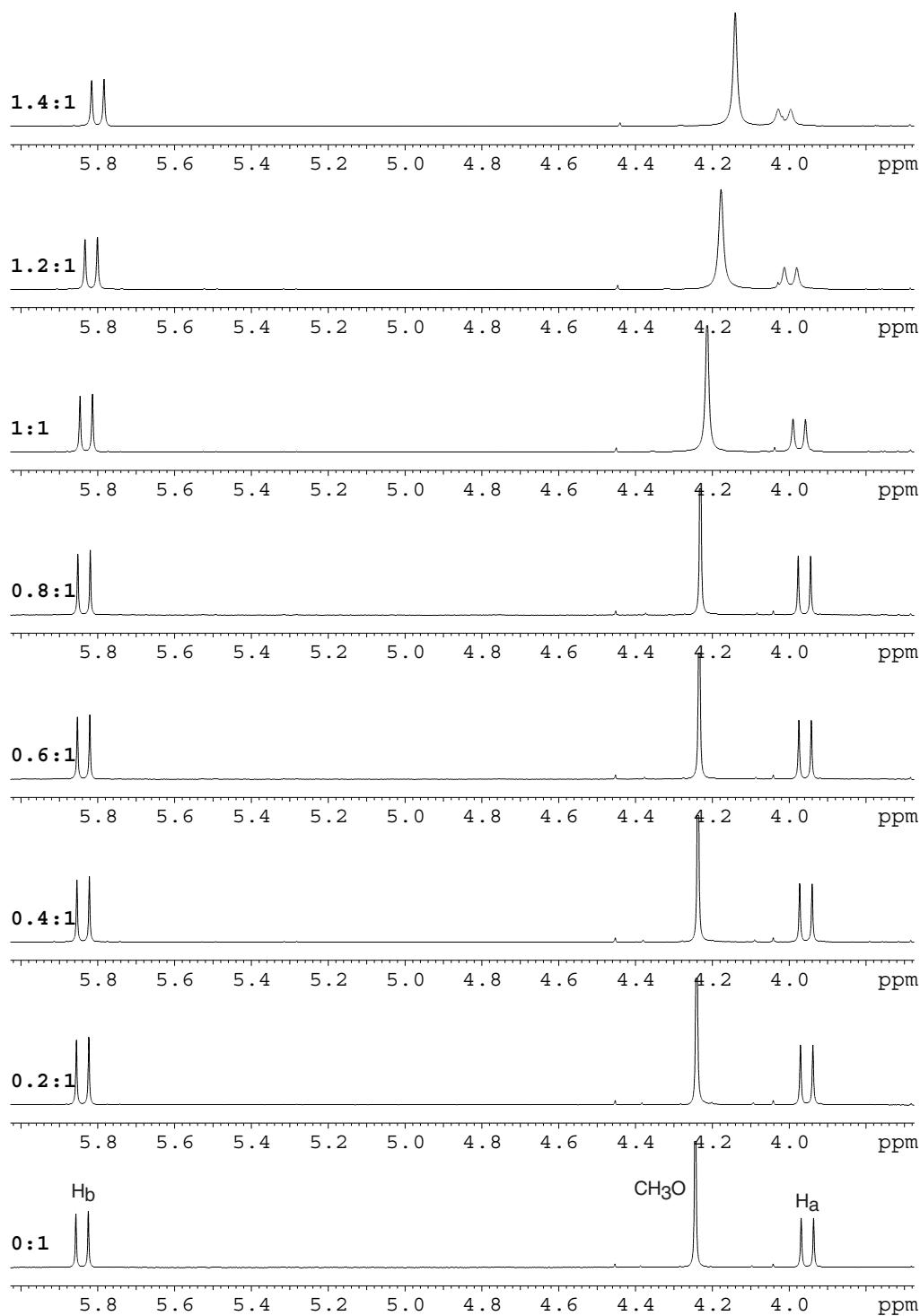


Figure S10: Expansion of aliphatic region of ^1H NMR spectra with various Ag^+ : clip **1** ratios (500 MHz, solvent $\text{CDCl}_3:\text{MeOH-d}_4$ 9:1). Aliquots of AgClO_4 solution added to clip **1**, ratios indicated on left hand side of spectra. Observe the change of chemical shift as well as broadening of the CH_2 proton oriented towards the outside of the cleft and the methoxy protons starting to change beyond the 1:1 ratio (continued overleaf).

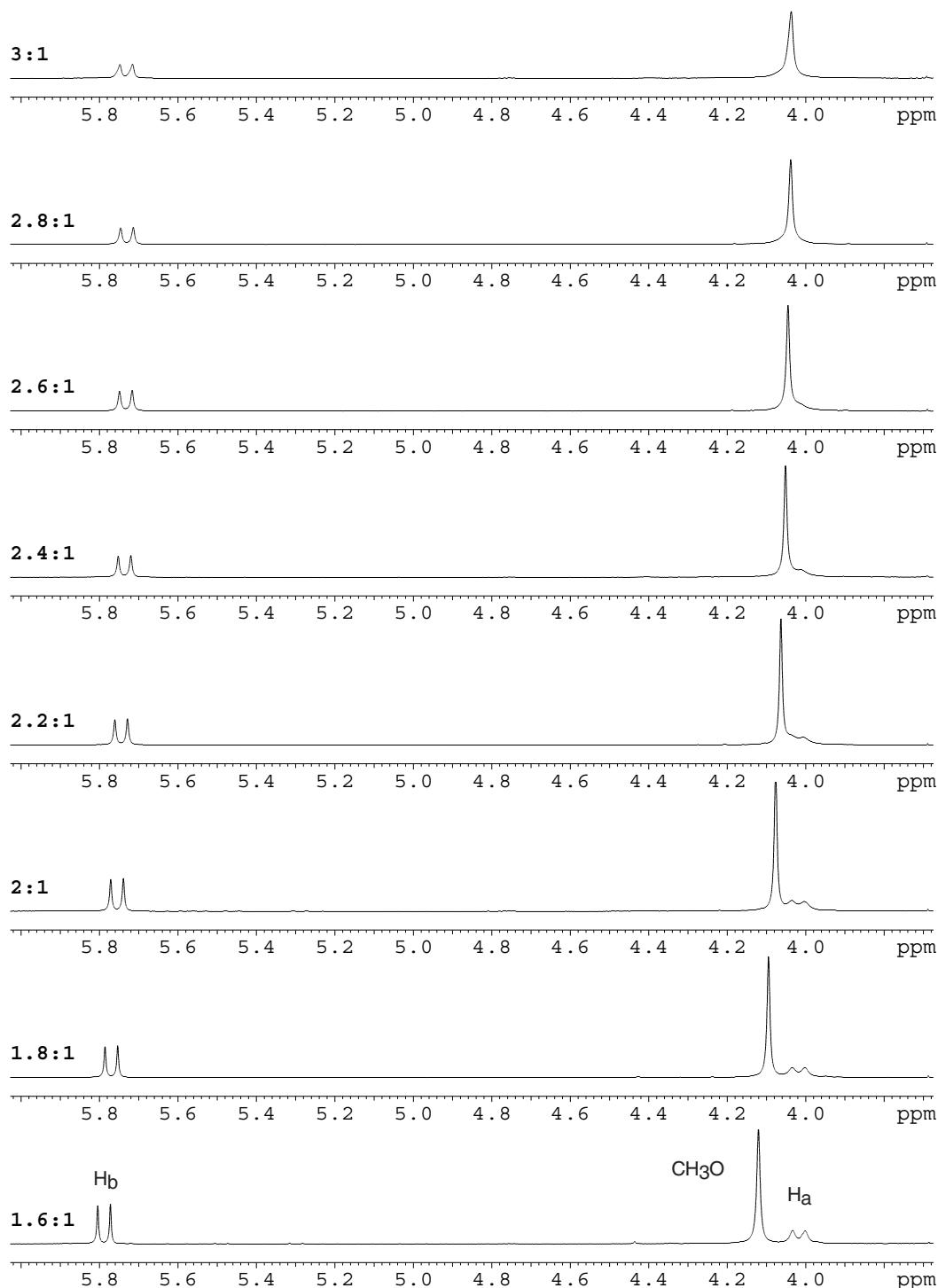


Figure S11: Expansion of the aliphatic region of ¹H NMR spectra with variable Ag⁺: clip 1 ratios (500 MHz, solvent CDCl₃:MeOH-d₄ 9:1) (continued from previous Figure). Aliquots of AgClO₄ solution added to clip 1, ratios indicated on left hand side of spectra. Observe the change of chemical shift as well as broadening of the CH₂ proton oriented outside of the cleft (H_a) and the methoxy protons starting to change beyond the 1:1 ratio (continued overleaf).

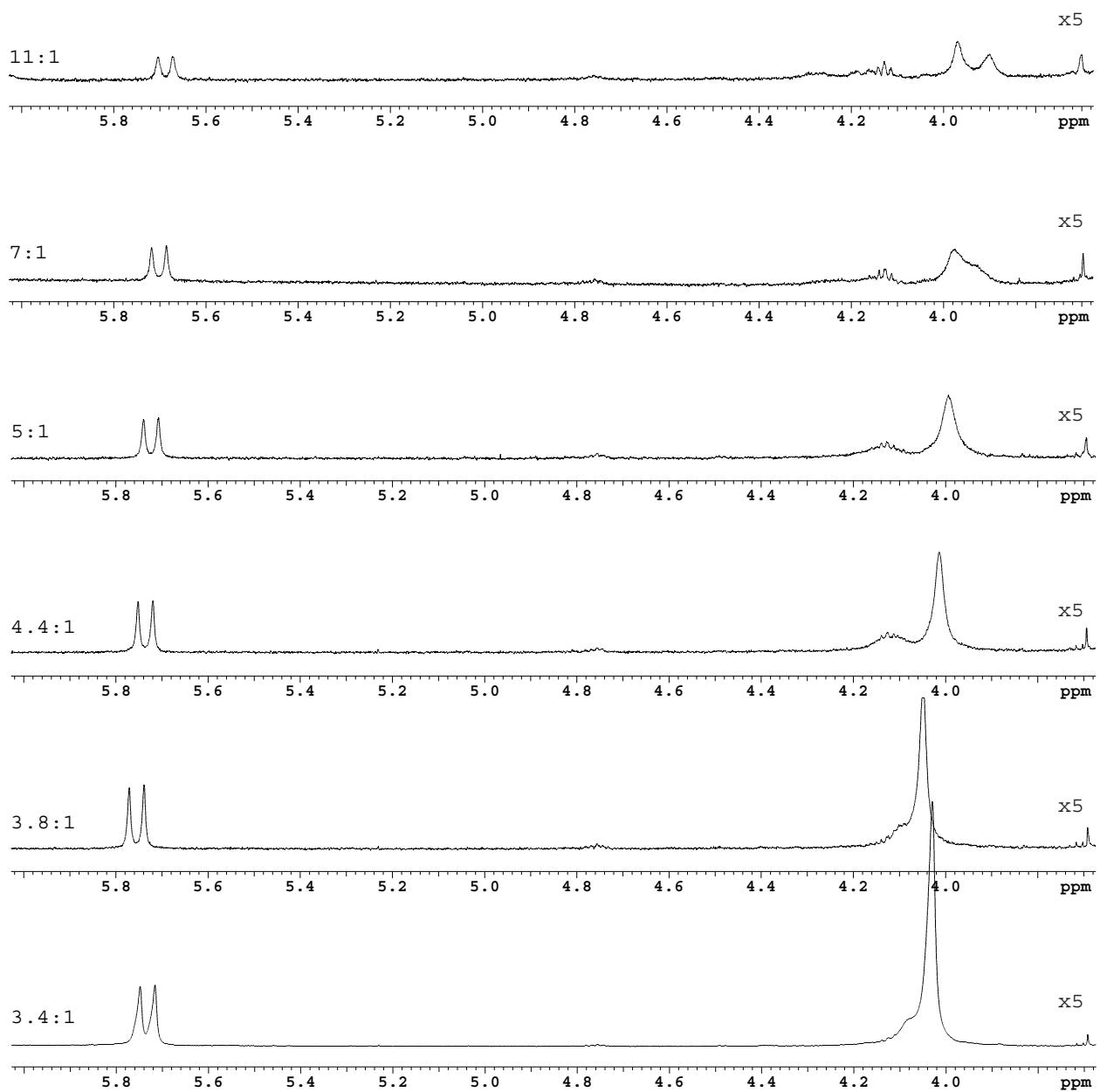
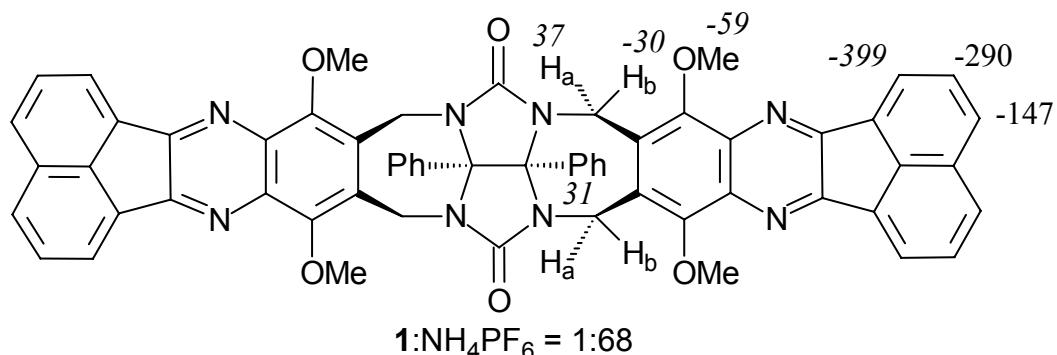


Figure S12: Expansion of the aliphatic region of ¹H NMR spectra with variable Ag^+ : clip **1** ratios (500 MHz, solvent $\text{CDCl}_3:\text{MeOH-d}_4$ 9:1) (continued from previous Figure). Aliquots of AgClO_4 solution added to clip **1**, ratios indicated on left hand side of spectra.

(d) Clip 1 with NH_4PF_6 Figure S13: ^1H NMR chemical shift changes $\Delta\delta$ (in ppb) for clip **1** for clip: NH_4^+ ratio of 1:68.Table S2: ^1H NMR chemical shift changes for clip **1** upon addition of NH_4PF_6 . $\Delta\delta = \delta_{(\mathbf{1}+\text{Ag}^+)} - \delta_{\mathbf{1}}$. Solvent $\text{CDCl}_3:\text{CD}_3\text{OD}$ 7:3.

$1:\text{NH}_4^+$		H_5	H_6	H_7	Ph
1:0	δ	8.141	7.540	7.831	7.059
1:1.1	δ	8.106	7.513	7.818	7.062
	$\Delta\delta$	-0.035	-0.027	-0.013	0.003
1:2.3	δ	8.062	7.481	7.801	7.065
	$\Delta\delta$	-0.079	-0.059	-0.030	0.006
1:3.4	δ	8.016	7.446	7.783	7.069
	$\Delta\delta$	-0.125	-0.094	-0.048	0.010
1:5.1	δ	7.991	7.427	7.774	7.070
	$\Delta\delta$	-0.150	-0.113	-0.057	0.011
1:6.8	δ	7.960	7.404	7.762	7.073
	$\Delta\delta$	-0.181	-0.136	-0.069	0.014
1:8.5	δ	7.922	7.377	7.748	7.075
	$\Delta\delta$	-0.219	-0.163	-0.083	0.016
1:10.8	δ	7.901	7.361	7.741	7.077
	$\Delta\delta$	-0.240	-0.179	-0.090	0.018
1:13.7	δ	7.879	7.346	7.732	7.078
	$\Delta\delta$	-0.262	-0.194	-0.099	0.019
1:17.1	δ	7.853	7.326	7.722	7.081
	$\Delta\delta$	-0.288	-0.214	-0.109	0.022
1:22.8	δ	7.810	7.295	7.707	7.084
	$\Delta\delta$	-0.331	-0.245	-0.124	0.025
1:28.5	δ	7.798	7.286	7.702	7.085
	$\Delta\delta$	-0.343	-0.254	-0.129	0.026
1:34.2	δ	7.778	7.272	7.695	7.086
	$\Delta\delta$	-0.363	-0.268	-0.136	0.027
1:39.9	δ	7.766	7.260	7.691	7.088
	$\Delta\delta$	-0.375	-0.280	-0.140	0.029
1:51.3	δ	7.753	7.260	7.686	7.089
	$\Delta\delta$	-0.388	-0.280	-0.145	0.030
1:68.3	δ	7.742	7.250	7.684	7.090
	$\Delta\delta$	-0.399	-0.290	-0.147	0.031

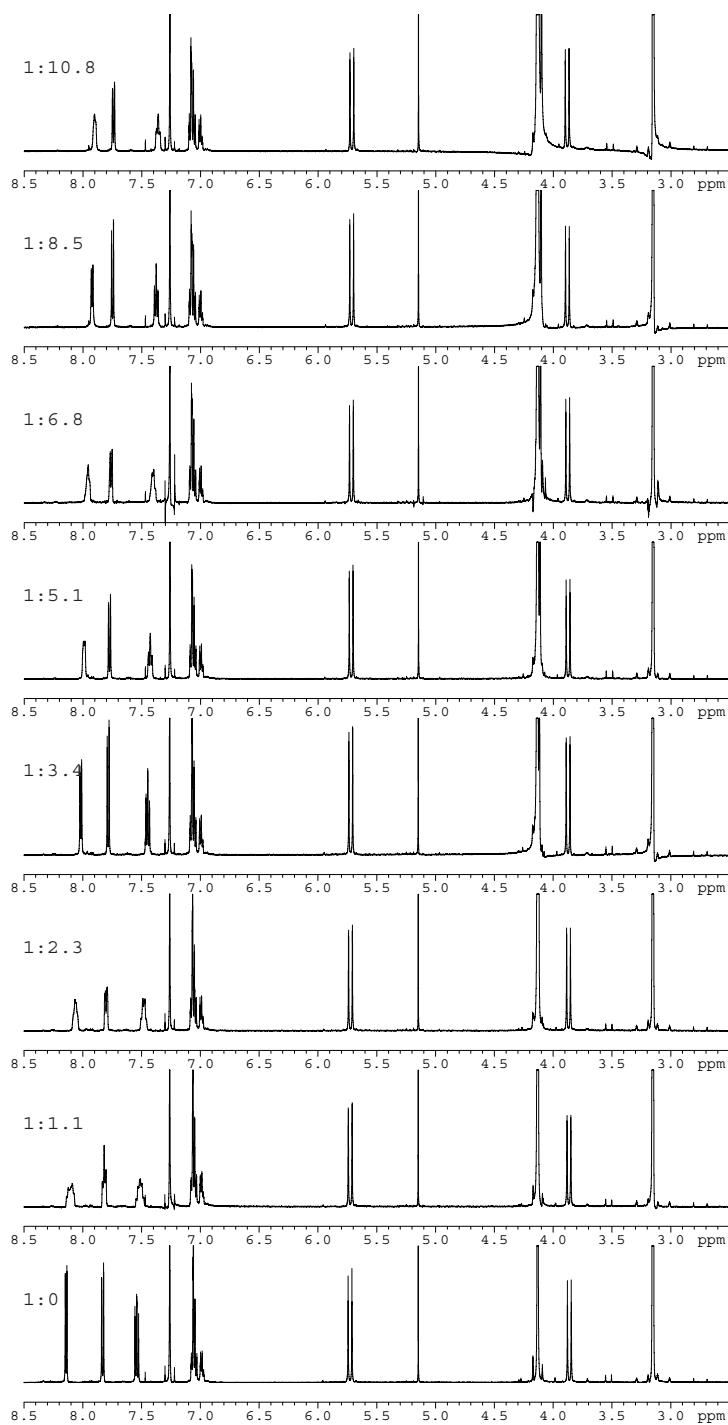


Figure S14: ¹H NMR spectra with various clip 1:NH₄⁺ ratios (500 MHz, solvent CDCl₃:MeOH-d₄ 7:3). Aliquots of NH₄PF₆ solution added to clip 1, ratios indicated on left hand side of spectra (continued overleaf).

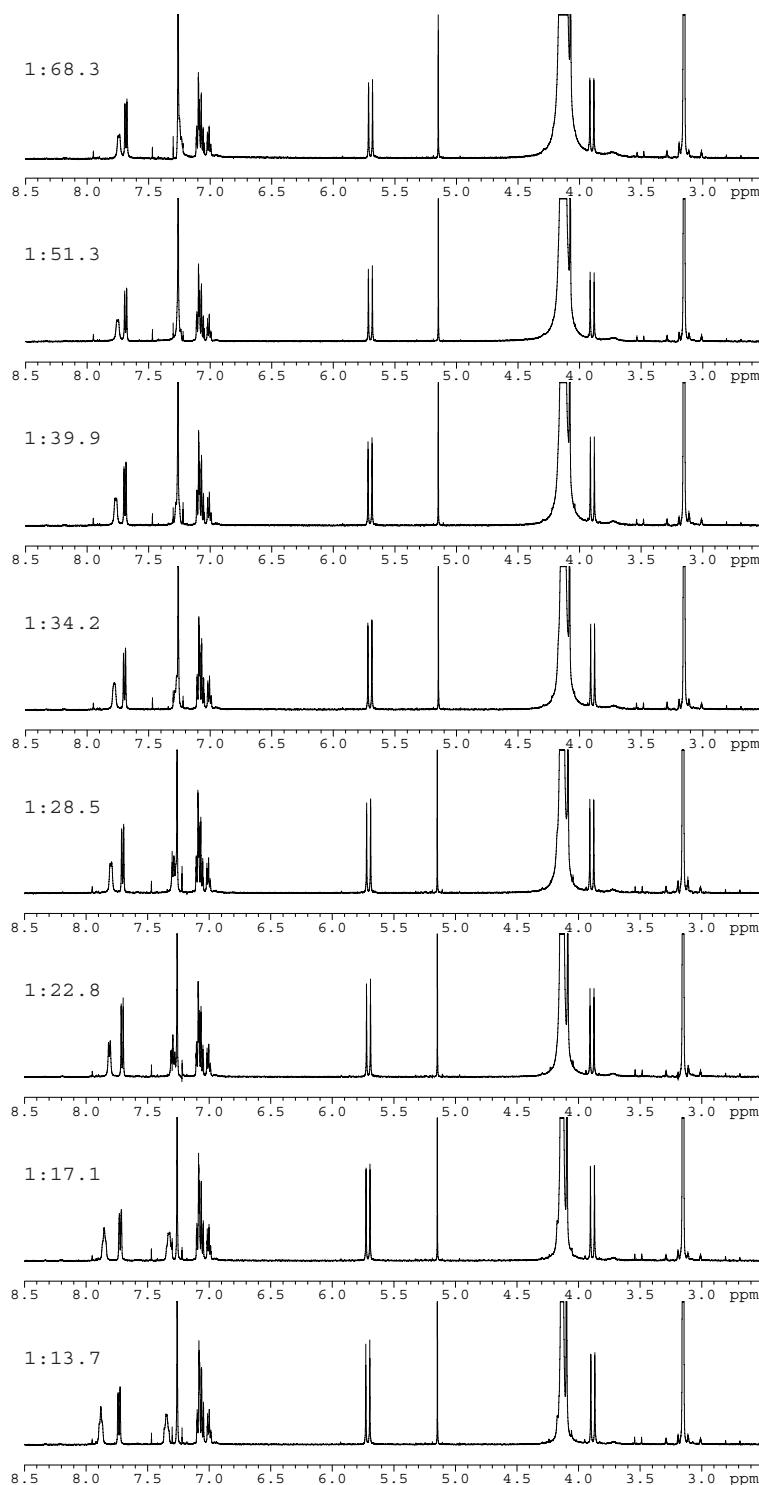


Figure S15: ^1H NMR spectra with various clip 1: NH_4^+ ratios (500 MHz, solvent $\text{CDCl}_3:\text{MeOH-d}_4$ 7:3) (continued from previous Figure). Aliquots of NH_4PF_6 solution added to clip 1, ratios indicated on left hand side of spectra.

Table S3: Survey of guests with clip 1. Chemical shift differences in ppm. Guests are added in more than 10-fold excess to 1 in the same solvent. For signal numbering, see DOI: 10.1039/b715208f. $\Delta\delta = \delta_{(1+guest)} - \delta_1$.

Guest, solvent, pK _a ^a	¹ H NMR shift effects observed for clip 1 on addition of guest					
	H-5	H-6	H-7	Ph	CH ₂	OCH ₃
TFA (added to 1 in CDCl ₃ solution)	To lower shifts at close to 1:1, to higher shifts at excess TFA			0.2 0.15	-0.15 0.15	-0.2
Aq. ammonia (CDCl ₃) not very miscible	All signals to lower chemical shifts					
Hydroxylamine hydrochloride (CDCl ₃ +CD ₃ OD) low solubility pK _a 5.97	-0.054	-0.044	-0.028	0.003	-0.006 0.003	-0.01
Methoxylamine hydrochloride (CDCl ₃ +CD ₃ OD) pK _a 3.9 in 3:2 dioxane-water	-0.036	-0.026	-0.018	0.002	-0.017 0.002	-0.02
o-benzyl hydroxylamine hydrochloride (CDCl ₃ +CD ₃ OD)	-0.021	-0.007	-0.006	0.007	-0.01 0.005	-0.04
Aniline hydrochloride (CDCl ₃ +CD ₃ OD) pK _a 4.19	-0.025	-0.01	-0.009	0.004	-0.015 0.005	-0.024
Benzylamine hydrochloride (CDCl ₃ +CD ₃ OD) pK _a 9.34	-0.01	-0.005	-0.003	0.001	-0.008 0.001	-0.01
9-aminofluorene-HCl CDCl ₃ +CD ₃ OD 3:1) soluble	-0.074	-0.022	-0.01	0.01	-0.012 0.009	-0.027
DL-Cysteine hydrochloride (CDCl ₃ +CD ₃ OD) very low solubility	-0.02	-0.011	-0.008	0.003	-0.019 0.001	-0.018
Guanidine-HCl (CDCl ₃ +CD ₃ OD 3:1) soluble pK _a 13.71	-0.1	-0.076	-0.05	0.005	-0.023 0.012	-0.021
4-guanidinobenzoic acid-4-nitrophenol ester-HCl (CDCl ₃ +CD ₃ OD 3:1) low solubility	-0.026	-0.013	-0.009	0.002	-0.009 0.001	-0.01
L-phenylalanine methylester-HCl (CDCl ₃ +CD ₃ OD 3:1) soluble	All signals move to lower chemical shifts					
L-alanine ethylester-HCl (CDCl ₃ +CD ₃ OD 2:1) soluble	All signals move to lower chemical shifts					
L-Serine ethylester-HCl CDCl ₃ +CD ₃ OD 2:1) soluble	All signals move to lower chemical shifts					
Diethylamine hydrochloride (CDCl ₃)	All signals move to lower chemical shifts					
Dimethylamine hydrochloride (CDCl ₃) pK _a 15.6 in MeCN	All signals move to lower chemical shifts					
1-amidinopyrazole-HCl (CDCl ₃ +CD ₃ OD 3:1) soluble	All signals move to lower chemical shifts					
Pyridine hydrochloride (CDCl ₃) pK _a 5.21	All signals move to lower chemical shifts					
Tetrabutylammonium bromide (CDCl ₃)	All signals move to lower chemical shifts					
Tetraethylammonium bromide (CDCl ₃)	All signals move to lower chemical shifts					
Tetramethylammonium bromide (CDCl ₃ +CD ₃ OD) low solubility	All signals move to lower chemical shifts					
Tetramethylammonium chloride (CDCl ₃ +CD ₃ OD) low solubility	All signals move to lower chemical shifts					

(e) Clip 1 with Trifluoroacetic acid (TFA).

Table S4: ^1H NMR chemical shift changes for clip **1** upon addition of TFA. $\Delta\delta = \delta_{(\mathbf{1}+\text{TFA})} - \delta_{\mathbf{1}}$. Solvent CDCl_3 . 1.1 μmol clip **1** in 0.7 mL CDCl_3 , 1.35 mmol TFA in 0.4 mL CDCl_3 .

ratio TFA:clip 1	$\Delta\delta\text{-H5}$	$\Delta\delta\text{-H7}$	$\Delta\delta\text{-H6}$	$\Delta\delta\text{-CH-2}_b$	$\Delta\delta\text{-OCH}_3$	$\Delta\delta\text{-CH-2}_a$
15.3	-0.158	-0.046	-0.106	-0.045	-0.134	0.092
21.5	-0.171	-0.046	-0.115	-0.051	-0.155	0.111
30.7	-0.15	-0.024	-0.102	-0.06	-0.175	0.134
46.0	-0.081	0.023	-0.057	-0.067	-0.186	0.152
61.4		0.058	-0.023	-0.071	-0.189	
92.0	0.095	0.14	0.06	-0.079	-0.19	0.176
153.4	0.233	0.249	0.162	-0.089	-0.19	
245.5	0.286	0.296	0.198	-0.094	-0.195	0.214
398.9	0.313	0.335	0.226	-0.102	-0.203	0.236
552.3	0.317	0.343	0.231	-0.103	-0.205	0.243
705.7	0.323	0.353	0.237	-0.108	-0.212	0.255

2. NMR Titrations of clip 2.

$$\Delta\delta = \delta_{(2+\text{guest})} - \delta_2.$$

(a) Clip 2 with resorcinol.

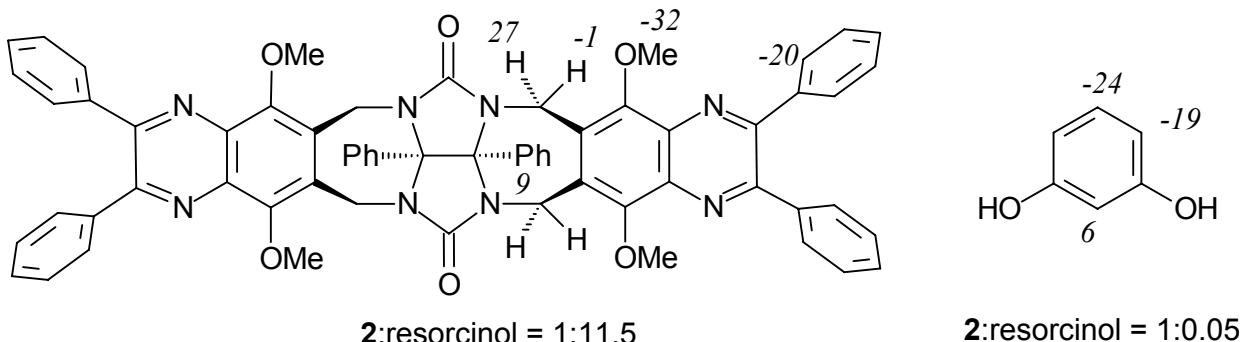


Figure S16: ^1H NMR chemical shift changes $\Delta\delta$ (in ppb) for clip 2 with resorcinol.

(b) Clip 2 with AgClO_4 .

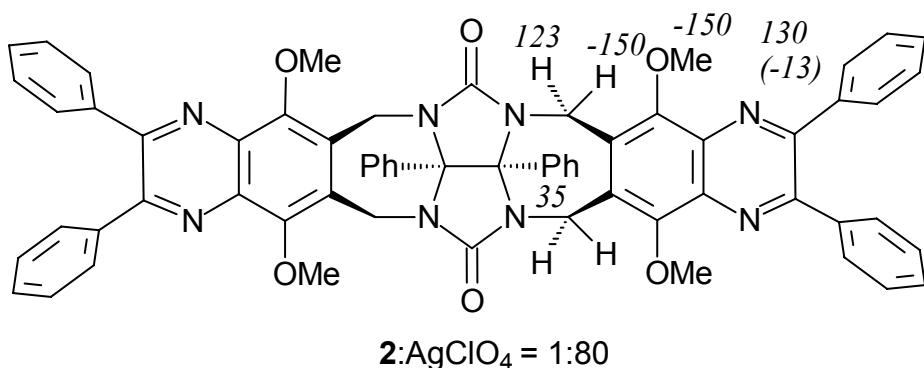


Figure S17: ^1H NMR chemical shift changes $\Delta\delta$ (in ppb) for clip 2 with Ag^+ .

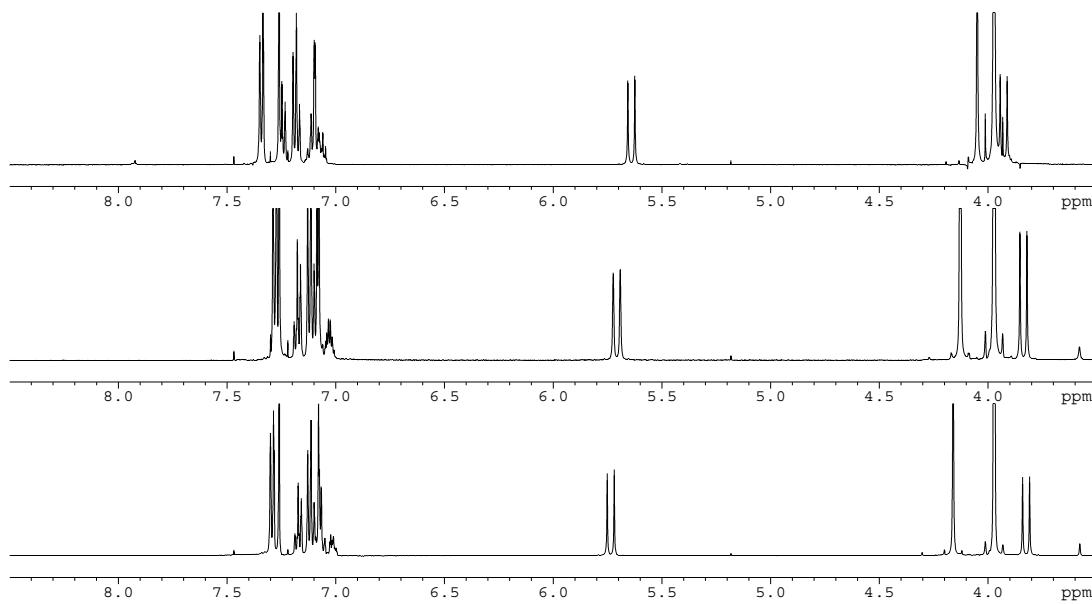
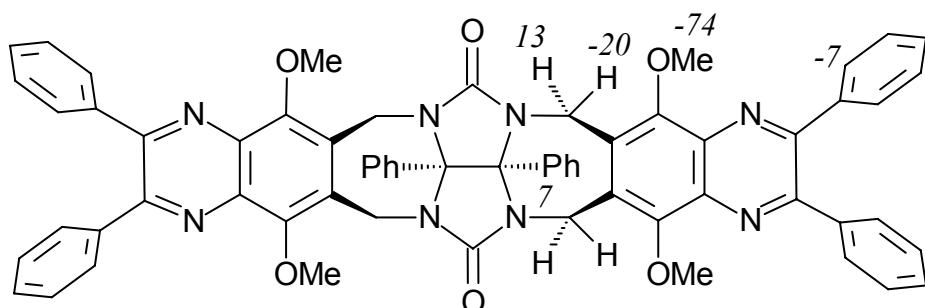
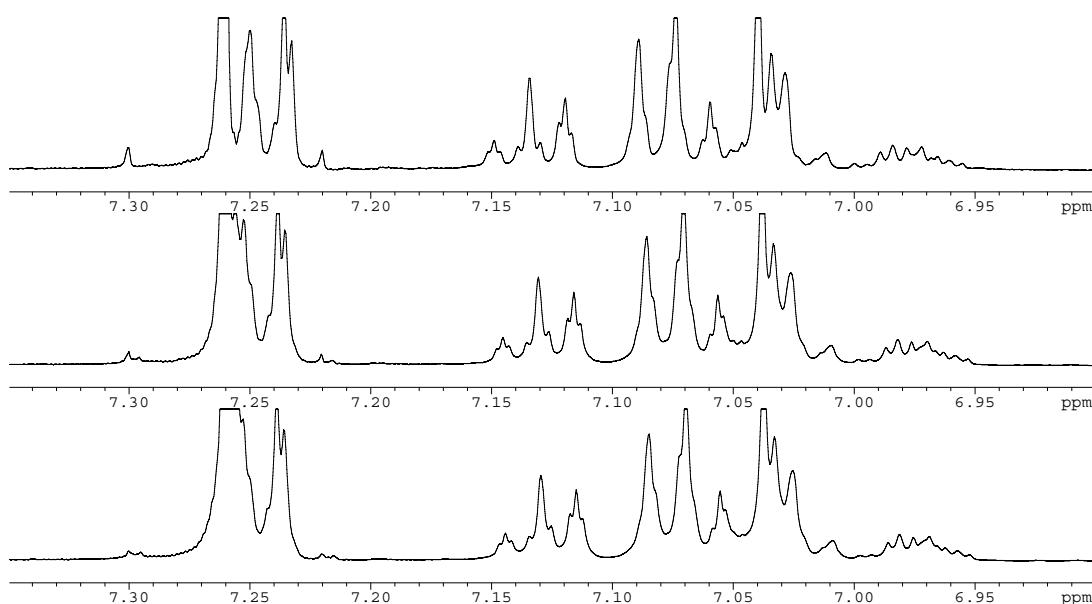


Figure S18: ^1H NMR spectrum of Clip **2** upon addition of AgClO_4 , bottom to top: a) 1:0; b) 1:1; c) 1:20 equivalents.

(c) Clip 2 with NH_4PF_6 .Figure S19: ^1H NMR chemical shift changes $\Delta\delta$ (in ppb) for clip **2** with NH_4^+ .Figure S20: ^1H NMR spectrum of Clip **2** upon addition of NH_4PF_6 : a) 1:0; b) 1:1.3; c) 1:9.6 equivalents

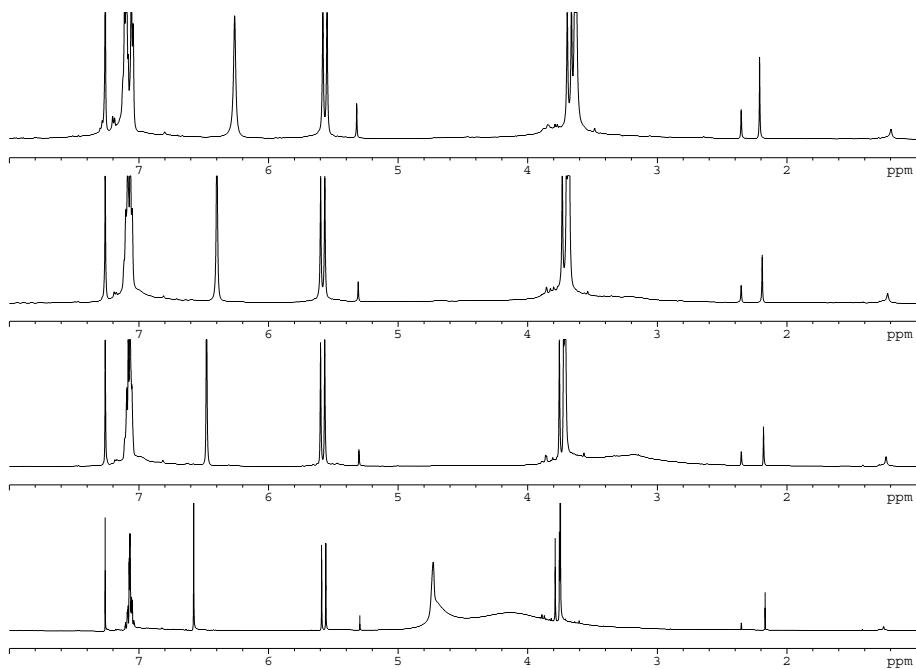
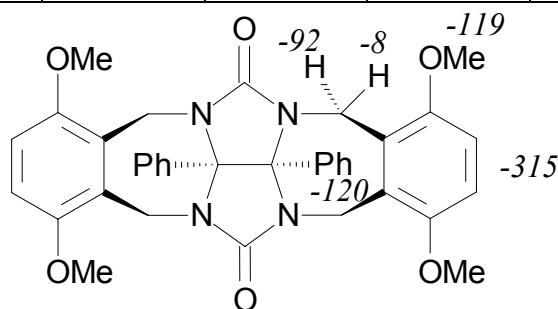
3. NMR Titrations of clip 3.**(a) Clip 3 with H₂O.**

Figure S21: Temperature dependent ^1H NMR chemical shift changes $\Delta\delta$ (ppb) for clip 3 in the presence of water. (a) at 25 °C; (b) 0 °C; (c) -20 °C; (d) -55 °C.

Table S5: Chemical shift changes for protons of clip **3** in variable temperature study in the presence of water. $\Delta\delta = \delta_{-55^\circ\text{C}} - \delta_{25^\circ\text{C}}$.

Clip 3 :H ₂ O	25 °C	5 °C	0 °C	-20 °C	-55 °C	
	δ	δ	δ	δ	δ	$\Delta\delta$
H _a	3.770	3.744	3.734	3.716	3.678	-0.092
H _b	5.572	5.581	5.581	5.582	5.564	-0.008
H ₁	6.577	6.496	6.478	6.389	6.262	-0.315
CH ₃	3.749	3.719	3.712	3.683	3.630	-0.119

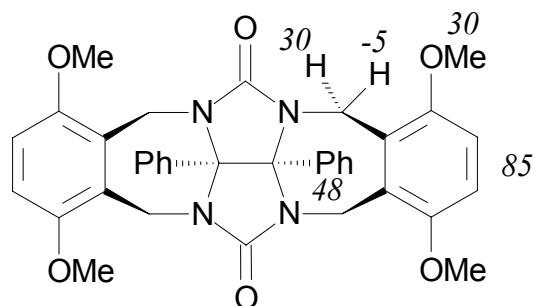


3:water, $\Delta\delta = \delta_{-55^\circ\text{C}} - \delta_{25^\circ\text{C}}$

Figure S22: Temperature dependent ¹H NMR chemical shift changes $\Delta\delta$ (ppb) for clip **3** in the presence of water. Numbers correspond to the chemical shift difference upon changing the temperature from 25 °C to -55 °C. ($\Delta\delta = \delta_{-55^\circ\text{C}} - \delta_{25^\circ\text{C}}$.)

(c) Clip 3 with AgClO₄.Table S6: ¹H NMR chemical shift changes for clip 3 upon addition of AgClO₄. $\Delta\delta = \delta_{(3+\text{Ag}^+)} - \delta_3$.

Clip 3:Ag	1:0	1:excess	
	δ	δ	$\Delta\delta$
H _a	3.660	3.690	0.030
H _b	5.440	5.435	-0.005
H _l	6.581	6.666	0.085
CH ₃	3.646	3.676	0.030
Ph	6.972	7.020	0.048

**3:AgClO₄**Figure S23: ¹H NMR chemical shift changes $\Delta\delta$ (in ppb) for clip 3:Ag⁺ ratio of > 1:80.

4. Overview charts – Chemical shift changes

(a) Clips with resorcinol

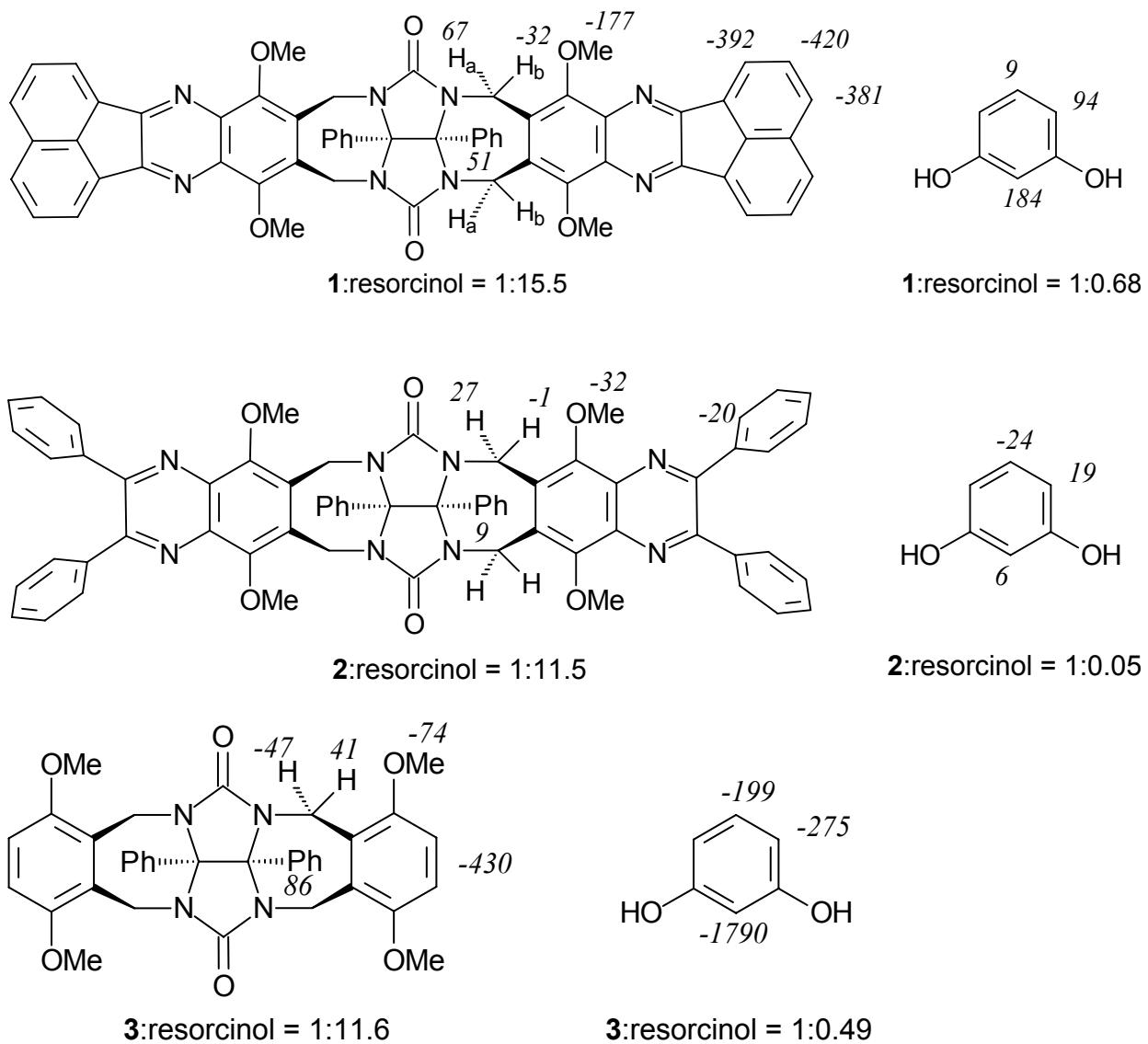


Figure S24: ^1H NMR chemical shift changes for clips **1** – **3** upon addition of resorcinol.

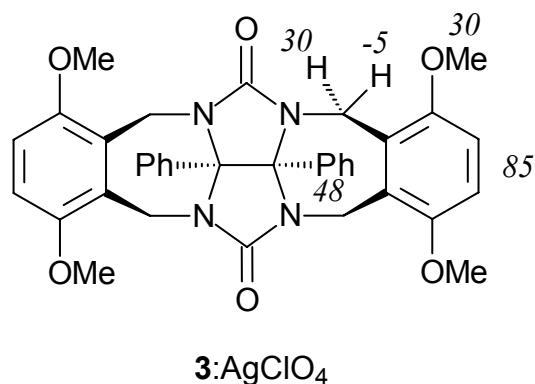
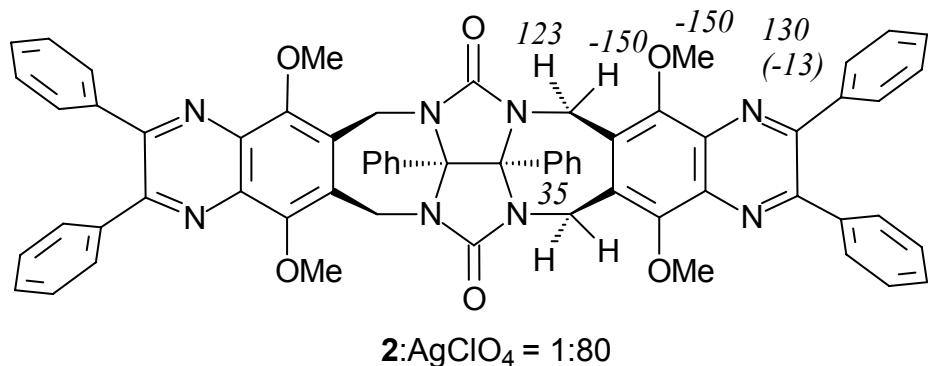
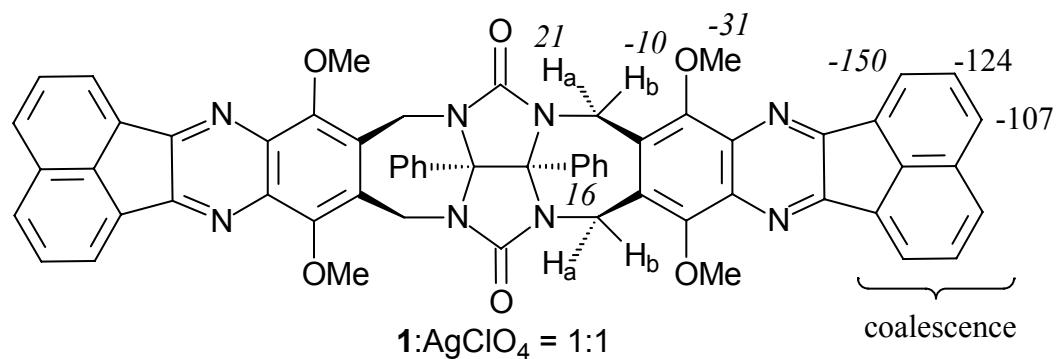
(b) Clips with AgClO₄

Figure S25: ¹H NMR chemical shift differences observed for clips **1** - **3** on addition of AgClO₄.

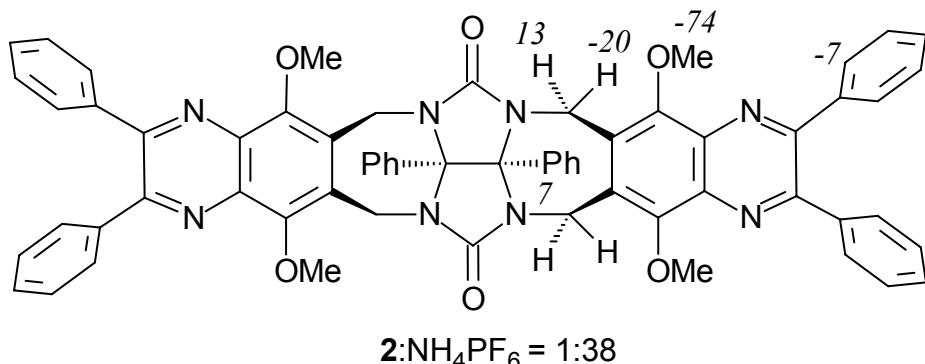
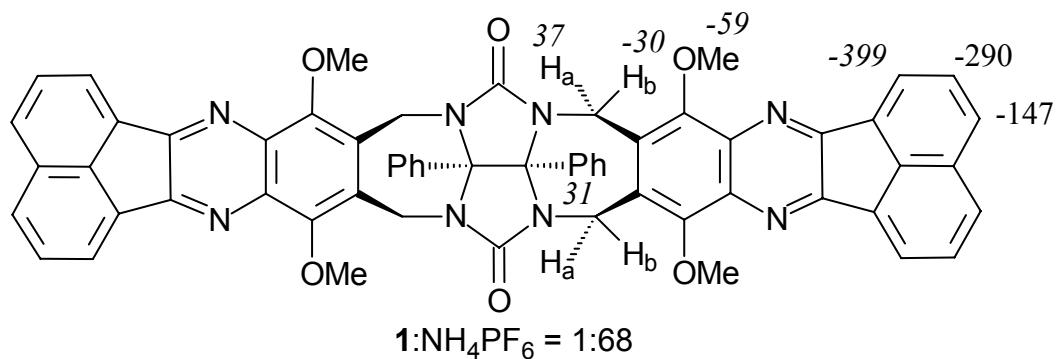
(c) Clips with NH_4PF_6 

Figure S26: ^1H NMR chemical shift differences observed for clips **1** and **2** on addition of NH_4PF_6 .

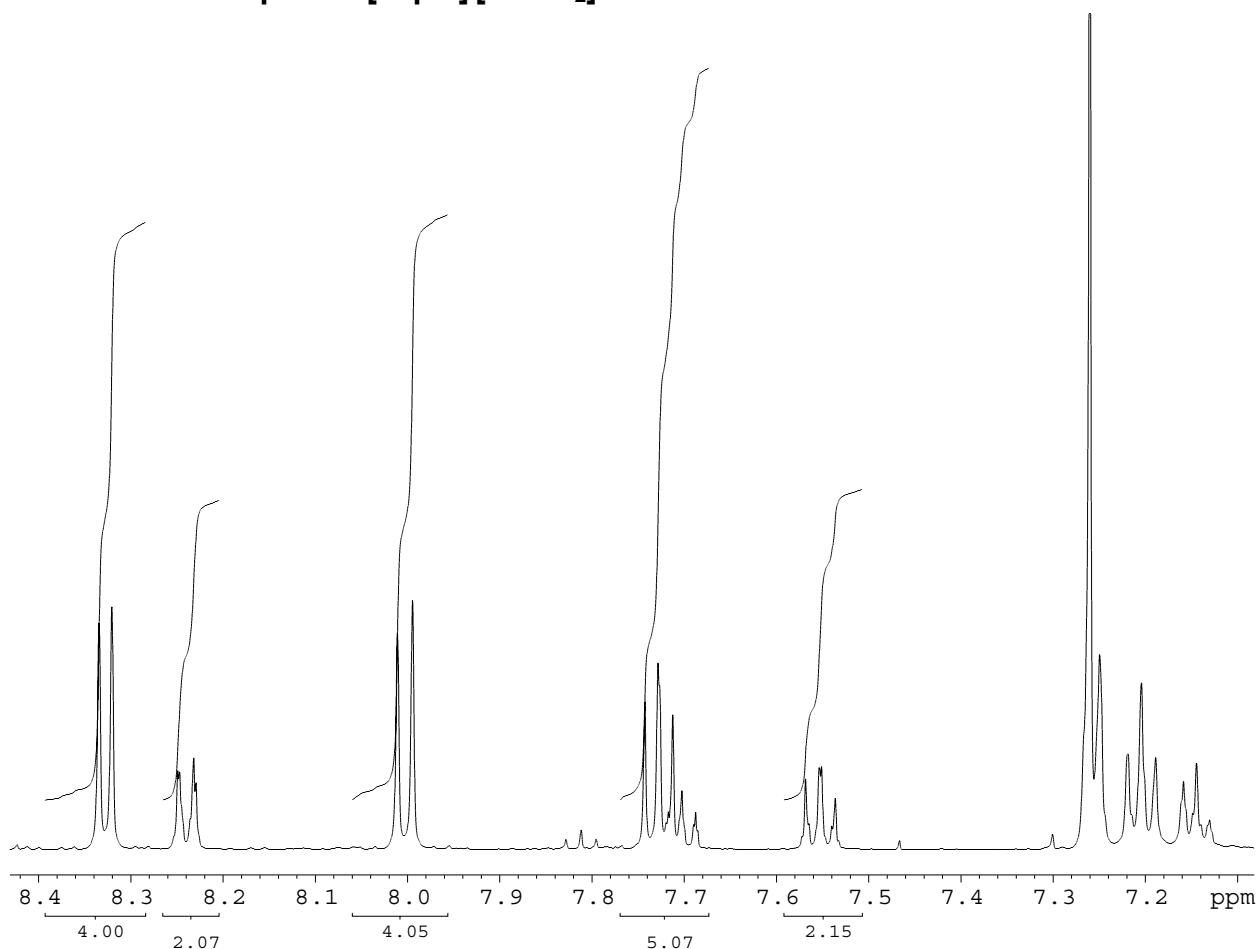
6. Inclusion compound [clip 1]·[PhNO₂]

Figure S27: Expansion from ¹H NMR spectrum obtained from solid residue after evaporation of clip 1 solution in PhNO₂ (500 MHz, CDCl₃ solution, 25°C, d1 = 40s). Clip 1 signals: 8.33 (H-5), 8.00 (H-7), 7.73 (H-6), PhNO₂ signals: 8.24 (*ortho*), 7.70 (*meta*), 7.55 (*para*).

7. Clip wall distances

Measured at outer center acenaphthene carbon

Distance was fixed at the indicated value, followed by energy minimization (Titan, AM1).

Table S7: Relative heat of formation for clip **1** vs. wall distance d_r (Å).

distance d_r, Å	Relative heat of formation, kJ/mol
3.619	35.35
3.869	28.72
4.119	24.41
4.369	21.53
4.869	18.09
5.869	12.61
6.869	8.33
7.869	4.93
8.869	2.39
9.369	1.45
9.869	0.74
10.369	0.26
10.869	0.01
11.369	0.00
11.869	0.23
12.369	0.72
12.869	1.46
13.869	3.76
14.869	7.24
15.869	11.98
16.869	18.23

8. Hydrogen bond parameters for clip 1·NH₄PF₆ crystal structure

Table S8: Hydrogen bonds for clip 1·NH₄PF₆ [Å and °]. Atom numbers refer to the CIF file.

D-H...A	d(D-H)	d(H...A)	d(D...A)	Angle (DHA)
N1F-H1F...O5				
0.933(19)		2.01(2)		
2.887(2)		155(2)		
N1F-H1F...F6i				
0.933(19)		2.64(2)		
3.246(3)		124(2)		
N1F-H3F...N7ii				
0.899(19)		2.24(2)		
3.091(2)		157(2)		
N1F-H3F...O6ii				
0.899(19)		2.32(2)		
2.963(2)		128(2)		

Symmetry transformations used to generate equivalent atoms:

(i): x+1,y,z (ii): -x+2,-y,-z