Self-Assembled Tetrazine Cryptophane for Ion Pairs Recognition and Guest Release by Cage Disassembly

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Supplementary information

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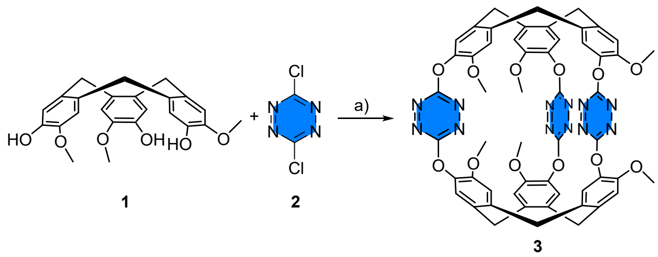
1. Materials and Methods

Starting material and solvents were of commercial grade and were used without further purification. Column chromatography was carried out with Merck 60 A (0.040–0.063 mm) silica gel. TLC was performed with Merck silica gel 60 F254 plates. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance III HD 300 MHz, 400 MHz and 500 MHz spectrometers. Chemical shifts are reported in ppm on the δ scale relative to residual solvent as the internal references. Coupling constants (J) are reported in hertz (Hz). Multiplicities are described with the following standard abbreviations: s =

singlet, d = doublet, t = triplet, m = multiplet. High-resolution mass spectra (HRMS) were performed on a SYNAPT G2 HDMS (Waters) mass spectrometer equipped with atmospheric pressure ionization source (API) pneumatically assisted. Spectra were obtained with TOF analysis. Measurements were realized with two internal standards. Infrared spectra were recorded on a Bruker TENSOR 27 Fourier Transform infrared spectrometer equipped with a single reflection diamond Attenuated Total Reflexion accessory (Bruker A222).

2. Synthesis



Scheme S1. *Synthesis of cryptophane **3**. a) conditions: Et_3N, acetonitrile, 25°C, 3.5h, 15%.*

CTV (-OMe, -OH) 1. This compound was prepared following the literature procedure.[1]

Cryptophane 3.

Under inert condition, CTV (-OMe, -OH) **1** (50 mg, 0.12 mmol) and 3,6-dichlorotetrazine **2** (27 mg, 0.18 mmol) were dissolved in anhydrous acetonitrile (27 mL). 10 minutes later, triethylamine (56 mg, 0.55 mmol) was added and the resulting mixture was stirred at room temperature for 3.5 hours. Saturated aqueous NH_4Cl solution (5 mL) was added to quench the reaction. Aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL) and the combined organic layers were dried over $MgSO_4$ and evaporated under reduce pressure. The crude product was then purified by silica gel column chromatography using CH_2Cl_2 100 % and then CH_2Cl_2/acetone: 90/10 as eluant, to afford **3** as a pink solid (20 mg, 15%). ***R*$_f$** (SiO_2, CH_2Cl_2/acetone: 97/3): 0.35. **Mp**: > 250 °C; **IR** (neat): 2925 (w) C-H vibrations in methoxy functional group, 1665 (w) C=N vibrations, 1510 (m), 1465 (w), 1405 (m), 1385 (s), 1327 (w), 1278 (m), 1207 (w), 1083 (w), 1013 (w). **^{1}H NMR** (400 MHz, $CDCl_3$): 7.07 (s, 6H), 6.80 (s, 6H), 4.77 (d, ^2J = 13.8 Hz, 6H), 3.61 (d, ^2J = 13.8 Hz, 6H), 3.60 (s, 18H). **^{13}C NMR** (100 MHz, $CDCl_3$): 166.4, 149.7, 139.9, 138.1, 131.5, 122.7, 114.3, 56.2, 36.4. **ESI-MS:** $[M+NH_4]^+$ 1068.3 and $[M+CH_3COO]^-$ 1109.3. **HRMS** (ESI-TOF) m/z calc for $C_{54}H_{42}N_{12}O_{12}Na$ $(M+Na)^+$ 1073.2937, found 1073.2938.

3. Titration experiments

A solution of host **3** (1 mM or 0.79 mM in CD_3CN, 600 µL) was titrated in NMR tubes with aliquots of a concentrated solution (24 mM or 19 mM in the same solvent) of guests. For the fast exchange compared to the NMR time scale: The shifts δ of the host's protons signals were measured after each addition and plotted as a function of the guest/host ratio ([G]/[H]). Association constant K_a was obtained by nonlinear least-squares fitting of these plots using bindfit program from Thordarson's group.[2,3] For the slow exchange compared to the NMR time scale: Using the 1:1 equilibrium of host-guest complexation, association constant K_a was determined with the following equations:[4]

$$K_a = \frac{[C]}{([H]_t - [C]) \cdot ([G]_t - [C])}$$

$$[C] = \frac{n}{m+n} \cdot [H]_t$$

Where *C* is complex; *H*, host and *G*, guest. The ratio of *n*/(*m*+*n*) is obtained from the NMR spectral data.

4. Single Crystal X-Ray Diffraction Data

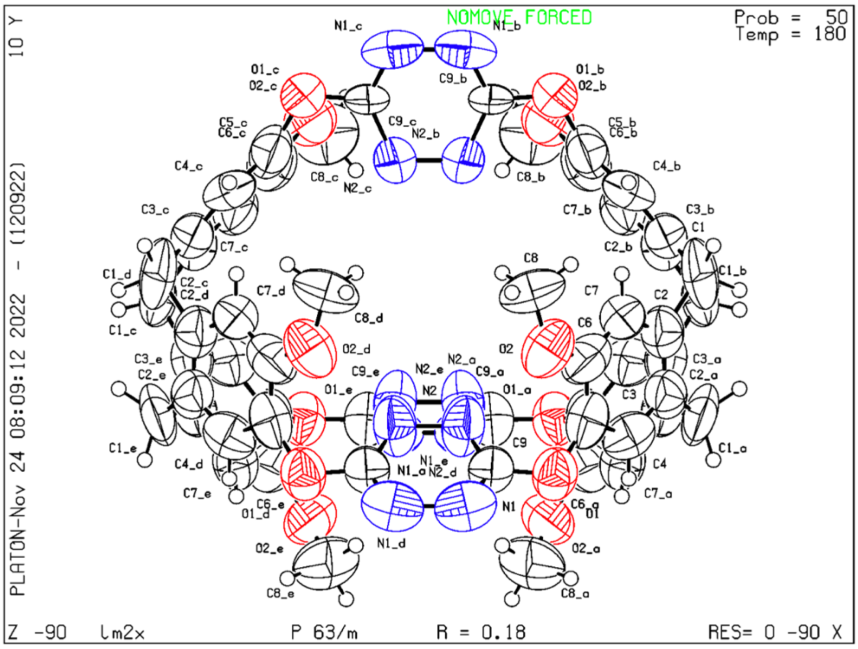


Figure S1. Thermal ellipsoid plot of **3** with the anisotropic displacement parameters drawn at the 50% probability level.

Single crystals of $C_{54}H_{42}N_{12}O_{12}$ were crystallized by slow evaporation of acetonitrile at 4°C from a solution of compound **3**. A suitable crystal was selected and mounted on a SuperNova, Dual, Cu at home/near, AtlasS2 diffractometer. The crystal was kept at 180.00(10) K during data collection. Using Olex2,[5] the structure was solved with the SHELXT[6] structure solution program using Intrinsic Phasing and refined with the SHELX refinement package using Least Squares minimization. The resolution is very average, as the crystals are full of solvent and degrade very quickly. The solvent is not represented in the structure, as it is too disordered to be identified.

Table S1. Crystal data and structure refinement for cryptophane **3.**

Identification code	lm2x
Empirical formula	$C_{54}H_{42}N_{12}O_{12}$
Formula weight	1051

Temperature/K	180.00(10)
Crystal system	hexagonal
Space group	$P6_3/m$
a/Å	14.165(2)
b/Å	14.165(2)
c/Å	20.997(3)
α/°	90
β/°	90
γ/°	120
Volume/Å^3	3648.3(13)
Z	12
ρ_{calc}g/cm^3	0.957
μ/mm^{-1}	0.581
F(000)	1092.0
Crystal size/mm^3	0.24 × 0.08 × 0.06
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.348 to 151.546
Index ranges	-16 ≤ h ≤ 16, -17 ≤ k ≤ 12, -25 ≤ l ≤ 22
Reflections collected	8709
Independent reflections	2521 [R_{int} = 0.0481, R_{sigma} = 0.0507]
Data/restraints/parameters	2521/12/120
Goodness-of-fit on F^2	1.016
Final R indexes [I>=2σ (I)]	R_1 = 0.1751, wR_2 = 0.2949
Final R indexes [all data]	R_1 = 0.2209, wR_2 = 0.3118
Largest diff. peak/hole / e Å^{-3}	0.33/-0.42

Table S2. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for cryptophane **3**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
O1	3527(6)	10242(5)	3753(3)	109(2)
O2	5630(6)	10580(6)	3683(3)	129(2)
N1	3490(6)	10917(5)	2863(4)	122(3)
N2	3624(8)	9303(6)	2839(3)	129(3)
C1	4788(11)	7604(9)	5198(4)	141(5)
C2	4349(10)	8261(9)	4823(5)	108(3)
C3	3279(10)	8054(9)	4857(4)	105(3)
C4	3054(8)	8656(7)	4487(5)	106(3)
C5	3838(10)	9502(10)	4078(5)	120(3)
C6	4891(10)	9695(10)	4064(6)	124(4)
C7	5108(9)	9073(10)	4427(5)	112(3)
C8	6568(8)	10695(10)	3527(6)	154(5)
C9	3560(8)	10196(6)	3118(4)	94(3)

Table S3. Anisotropic Displacement Parameters (Å^2×10^3) for cryptophane **3**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
O1	145(5)	99(4)	92(4)	-2(3)	5(4)	67(4)
O2	132(6)	105(5)	126(5)	4(4)	35(5)	42(4)
N1	117(6)	68(4)	177(9)	-10(4)	7(5)	43(4)
N2	205(9)	114(6)	84(5)	10(4)	16(5)	92(6)
C1	213(13)	121(8)	63(5)	-27(6)	-45(7)	64(8)
C2	132(8)	112(7)	84(6)	-9(5)	-8(5)	63(6)

C3	143(9)	111(7)	82(6)	-8(5)	-7(6)	80(7)
C4	114(7)	79(6)	128(8)	-25(6)	5(6)	50(6)
C5	141(7)	128(7)	84(6)	-18(5)	8(6)	62(6)
C6	111(8)	143(10)	116(8)	-8(7)	25(7)	63(8)
C7	127(7)	140(8)	95(6)	-13(5)	-7(5)	88(6)
C8	98(8)	179(12)	200(13)	2(10)	38(8)	81(8)
C9	149(8)	66(5)	94(6)	1(4)	4(6)	75(5)

Table S4. Bond lengths for cryptophane **3.**

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
O1	C5	1.490(13)	C1	C2	1.566(13)
O1	C9	1.336(9)	C1	C3[2]	1.433(13)
O2	C6	1.412(12)	C2	C3	1.393(14)
O2	C8	1.296(10)	C2	C7	1.391(13)
N1	N1[1]	1.526(16)	C3	C4	1.306(12)
N1	C9	1.201(9)	C4	C5	1.440(13)
N2	N2[1]	1.422(14)	C5	C6	1.376(14)
N2	C9	1.438(10)	C6	C7	1.312(14)

[1]+X,+Y,1/2-Z; [2]+Y-X,1-X,+Z

Table S5. Bond Angles for cryptophane **3.**

Atom	**Atom**	**Atom**	**Angle/˚**	**Atom**	**Atom**	**Atom**	**Angle/˚**
C9	O1	C5	113.1(7)	C3	C4	C5	124.0(11)
C8	O2	C6	120.8(10)	C4	C5	O1	118.8(10)

C9	N1	N1^1	116.5(6)	C6	C5	O1	121.5(11)
N2^1	N2	C9	114.1(4)	C6	C5	C4	119.1(12)
C3^2	C1	C2	115.6(7)	C5	C6	O2	116.0(12)
C3	C2	C1	124.3(11)	C7	C6	O2	127.4(12)
C7	C2	C1	114.8(11)	C7	C6	C5	116.6(12)
C7	C2	C3	120.9(10)	C6	C7	C2	124.0(11)
C2	C3	C1^3	126.6(10)	O1	C9	N2	118.0(7)
C4	C3	C1^3	117.7(11)	N1	C9	O1	112.5(8)
C4	C3	C2	115.3(11)	N1	C9	N2	129.4(9)

^{1}+X,+Y,1/2-Z; ^{2}+Y-X,1-X,+Z; ^{3}1-Y,1+X-Y,+Z

Table S6. Torsion Angles for cryptophane **3.**

A	**B**	**C**	**D**	**Angle/°**	**A**	**B**	**C**	**D**	**Angle/°**
O1	C5	C6	O2	-4.9(15)	C3	C2	C7	C6	0.1(16)
O1	C5	C6	C7	172.1(8)	C3	C4	C5	O1	-171.0(8)
O2	C6	C7	C2	175.5(9)	C3	C4	C5	C6	0.7(15)
N1^1	N1	C9	O1	-178.4(6)	C4	C5	C6	O2	-176.3(8)
N1^1	N1	C9	N2	-1.4(14)	C4	C5	C6	C7	0.7(16)
N2^1	N2	C9	O1	178.3(6)	C5	O1	C9	N1	-168.2(9)
N2^1	N2	C9	N1	1.3(13)	C5	O1	C9	N2	14.3(13)
C1	C2	C3	C1^2	-4.2(16)	C5	C6	C7	C2	-1.1(17)
C1	C2	C3	C4	-177.0(8)	C7	C2	C3	C1^2	173.9(9)
C1	C2	C7	C6	178.5(9)	C7	C2	C3	C4	1.2(15)
C1^2	C3	C4	C5	-175.0(8)	C8	O2	C6	C5	-165.4(11)
C2	C3	C4	C5	-1.6(14)	C8	O2	C6	C7	18.1(17)
C3^3	C1	C2	C3	94.6(13)	C9	O1	C5	C4	-119.4(9)
C3^3	C1	C2	C7	-83.7(12)	C9	O1	C5	C6	69.2(12)

^{1}+X,+Y,1/2-Z; ^{2}1-Y,1+X-Y,+Z; ^{3}+Y-X,1-X,+Z

Table S7. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for cryptophane **3**.

Atom	***x***	***y***	***z***	**U(eq)**
H1A	5547.54	8115.59	5330.2	169
H1B	4348.11	7308.48	5589.6	169
H4	2328.58	8528.71	4487.66	128
H7	5826.84	9184.45	4418.55	134
H8A	6459.37	10116.27	3229.38	231
H8B	6936.91	10647.4	3910.69	231
H8C	7015.52	11406.48	3325	231

Table S8. Solvent masks information for cryptophane **3**.

Number	**X**	**Y**	**Z**	**Volume**	**Electron count**	**Content**
1	-0.261	-0.524	-0.312	1444.3	549.0	?
2	0.333	0.667	0.750	102.4	42.3	?
3	0.667	0.333	0.250	102.4	42.2	?

Crystal structure determination of cryptophane **3**

Crystal Data for $C_9H_7N_2O_2$ (M =175.17 g/mol): hexagonal, space group $P6_3/m$ (no. 176), a = 14.165(2) Å, c = 20.997(3) Å, V = 3648.3(13) Å^3, Z = 12, T = 180.00(10) K, μ(Cu Kα) = 0.581 mm^{-1}, $Dcalc$ = 0.957 g/cm^3, 8709 reflections measured (8.348° ≤ 2Θ ≤ 151.546°), 2521 unique (R_{int} = 0.0481, R_{sigma} = 0.0507) which were used in all calculations. The final R_1 was 0.1751 (I > 2σ(I)) and wR_2 was 0.3118 (all data).

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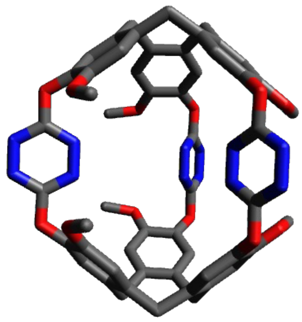
O	-2.257901	12.564117	7.880174
O	0.481610	12.978750	7.733195
N	-2.788380	13.392157	6.011441
N	-1.455454	11.412223	5.961048
C	1.396669	9.328017	10.914241
H	2.110224	9.955597	11.191821
H	0.982867	8.965495	11.736483
C	0.309505	10.133975	10.126853
C	-1.059542	9.880043	10.198243
C	-1.804621	10.618531	9.421354
H	-2.742025	10.462382	9.422740
C	-1.293264	11.656341	8.562577
C	0.061618	11.893099	8.533181
C	0.809530	11.130076	9.295372
H	1.748832	11.266794	9.277629
C	1.728838	13.119824	7.405642
H	1.984849	12.409881	6.780729
H	2.285112	13.061432	8.211276
H	1.858845	13.992614	6.981503
C	-2.178577	12.507688	6.546865
O	-2.669394	4.029792	7.880174
O	-4.398232	6.194961	7.733195
N	-3.121258	3.156363	6.011441
N	-2.073048	5.300679	5.961048
C	-1.694134	8.812792	10.914241
H	-2.594412	9.116959	11.191821
H	-1.173280	8.635690	11.736483
C	-1.848532	7.468302	10.126853
C	-0.944097	6.409638	10.198243
C	-1.211107	5.395136	9.421354
H	-0.607176	4.661395	9.422740

C	-2.365555	5.319080	8.562577
C	-3.248034	6.374063	8.533181
C	-2.961193	7.403285	9.295372
H	-3.549246	8.148386	9.277629
C	-5.144020	7.204556	7.405642
H	-4.657197	7.781239	6.780729
H	-5.371588	7.715499	8.211276
H	-5.964881	6.880750	6.981503
C	-2.660187	4.126703	6.546865
O	4.927295	7.940591	7.880174
O	3.916623	5.360788	7.733195
N	5.909638	7.985980	6.011441
N	3.528502	7.821599	5.961048
C	0.297465	6.393691	10.914241
H	0.484188	5.461944	11.191821
H	0.190413	6.933315	11.736483
C	1.539027	6.932223	10.126853
C	2.003639	8.244819	10.198243
C	3.015729	8.520832	9.421354
H	3.349201	9.410723	9.422740
C	3.658820	7.559079	8.562577
C	3.186417	6.267338	8.533181
C	2.151664	6.001139	9.295372
H	1.800414	5.119320	9.277629
C	3.415181	4.210120	7.405642
H	2.672348	4.343379	6.780729
H	3.086476	3.757569	8.211276
H	4.106037	3.661136	6.981503
C	4.838764	7.900109	6.546865
O	-2.257901	12.564117	2.618326
O	0.481610	12.978750	2.765305
N	-2.788380	13.392157	4.487059

N	-1.455454	11.412223	4.537452
C	1.396669	9.328017	-0.415741
H	2.110224	9.955597	-0.693321
H	0.982867	8.965495	-1.237983
C	0.309505	10.133975	0.371647
C	-1.059542	9.880043	0.300257
C	-1.804621	10.618531	1.077146
H	-2.742025	10.462382	1.075760
C	-1.293264	11.656341	1.935923
C	0.061618	11.893099	1.965319
C	0.809530	11.130076	1.203128
H	1.748832	11.266794	1.220871
C	1.728838	13.119824	3.092858
H	1.984849	12.409881	3.717771
H	2.285112	13.061432	2.287224
H	1.858845	13.992614	3.516997
C	-2.178577	12.507688	3.951635
O	4.927295	7.940591	2.618326
O	3.916623	5.360788	2.765305
N	5.909638	7.985980	4.487059
N	3.528502	7.821599	4.537452
C	0.297465	6.393691	-0.415741
H	0.484188	5.461944	-0.693321
H	0.190413	6.933315	-1.237983
C	1.539027	6.932223	0.371647
C	2.003639	8.244819	0.300257
C	3.015729	8.520832	1.077146
H	3.349201	9.410723	1.075760
C	3.658820	7.559079	1.935923
C	3.186417	6.267338	1.965319
C	2.151664	6.001139	1.203128
H	1.800414	5.119320	1.220871

C	3.415181	4.210120	3.092858
H	2.672348	4.343379	3.717771
H	3.086476	3.757569	2.287224
H	4.106037	3.661136	3.516997
C	4.838764	7.900109	3.951635
O	-2.669394	4.029792	2.618326
O	-4.398232	6.194961	2.765305
N	-3.121258	3.156363	4.487059
N	-2.073048	5.300679	4.537452
C	-1.694134	8.812792	-0.415741
H	-2.594412	9.116959	-0.693321
H	-1.173280	8.635690	-1.237983
C	-1.848532	7.468302	0.371647
C	-0.944097	6.409638	0.300257
C	-1.211107	5.395136	1.077146
H	-0.607176	4.661395	1.075760
C	-2.365555	5.319080	1.935923
C	-3.248034	6.374063	1.965319
C	-2.961193	7.403285	1.203128
H	-3.549246	8.148386	1.220871
C	-5.144020	7.204556	3.092858
H	-4.657197	7.781239	3.717771
H	-5.371588	7.715499	2.287224
H	-5.964881	6.880750	3.516997
C	-2.660187	4.126703	3.951635

5. DFT Calculations



syn configuration of **3**

Figure S2. Geometry optimization of the *syn* cryptophane **3** in the gas phase (PBE0-D3/def2-TZVP).

Calculations within DFT methods were performed with the TURBOMOLE program package.[7] The structures were fully optimized (gas-phase calculations), at the PBE0-D3/def2-TZVP level of theory.[8][9][10][11] The RI approximation was employed, by exploiting the corresponding auxiliary basis sets.[12] Frequency calculations were performed to verify that structures are minima on their potential energy surface.

Optimized structure of *syn*-cryptophane

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Energy = -3639.765740671

O	2.8292254	-3.9075176	-2.5886691
O	-4.7986222	-0.4964223	-2.5886691
C	-0.4583709	1.9215803	-4.8806258
C	-1.4079244	1.0711959	-5.6954282
C	0.9257090	1.7589874	-4.9052150
C	-1.0188280	2.8983429	-4.0541393
C	-1.4349519	-1.3577510	-4.8806258
C	-1.9861823	-0.0778062	-4.9052150
C	1.1416140	3.5506828	-3.2966580
C	1.8933228	-0.5638293	-4.8806258
C	1.0604733	-1.6811812	-4.9052150
C	1.4036232	-2.7782354	-4.1142537

C	-0.2237207	-1.7548962	-5.6954282
C	2.5041745	-2.7640082	-3.2966580
C	3.0194526	-0.5668406	-4.0541393
C	1.6316451	0.6837003	-5.6954282
C	-3.6457885	-0.7866746	-3.2966580
O	1.9693968	4.4039399	-2.5886691
C	1.7042108	2.6046910	-4.1142537
C	-2.0006246	-2.3315024	-4.0541393
C	-3.1078340	0.1735444	-4.1142537
C	1.6314681	0.6840032	5.6957171
N	2.6468853	5.3017454	-0.6488795
C	1.7037130	2.6048641	4.1142371
C	1.4040220	-2.7778908	4.1142371
N	2.6466264	5.3017031	0.6489205
C	3.0194013	-0.5661216	4.0541100
C	-3.6452997	-0.7872331	3.2964043
O	1.9685016	4.4039597	2.5884518
C	-3.1077350	0.1730267	4.1142371
C	1.0607645	-1.6809861	4.9053670
C	-0.2233699	-1.7548945	5.6957171
C	-1.0194249	2.8979390	4.0541100
C	-1.9861589	-0.0781560	4.9053670
C	1.8934132	-0.5634646	4.8807870
C	2.5044137	-2.7633056	3.2964043
C	-1.4080982	1.0708913	5.6957171
O	-4.7981918	-0.4972074	2.5884518
N	1.3408146	3.3317197	0.6530047
C	-1.9999763	-2.3318174	4.0541100
C	-1.4346813	-1.3580116	4.8807870
C	1.1408860	3.5505387	3.2964043
C	0.9253944	1.7591420	4.9053670
C	-0.4587319	1.9214762	4.8807870

O	2.8296901	-3.9067522	2.5884518
N	-3.5559298	-0.5044604	-0.6534192
N	-3.5557612	-0.5046803	0.6530047
N	-5.9147227	-0.3588059	0.6489205
C	-4.7331467	-0.4736305	-1.2556535
N	-5.9148889	-0.3586028	-0.6488795
C	-4.7328670	-0.4740334	1.2554521
N	3.2680036	-4.9431426	-0.6488795
N	3.2680964	-4.9428972	0.6489205
N	2.2149466	-2.8270394	0.6530047
N	2.2148404	-2.8272954	-0.6534192
N	1.3410894	3.3317557	-0.6534192
C	2.7769585	-3.8617664	1.2554521
C	1.9563973	4.3358405	-1.2556535
C	1.9559085	4.3357998	1.2554521
C	2.7767494	-3.8622100	-1.2556535
H	-0.9186317	0.7128772	-6.6000106
H	-2.2308885	1.7064853	-6.0332501
H	0.7971137	-3.6765768	-4.1251599
H	-1.5662145	-3.3226085	-4.0488781
H	-0.1580540	-1.1519970	-6.6000106
H	-0.3624154	-2.7852488	-6.0332501
H	-3.5827494	1.1473194	4.1252313
H	2.5933039	1.0787635	-6.0332501
H	1.0766856	0.4391197	-6.6000106
H	3.6605706	0.3049227	-4.0488781
H	-2.0943561	3.0176858	-4.0488781
H	2.7854521	2.5286091	-4.1251599
H	1.0764201	0.4393772	6.6001640
H	2.5930284	1.0792042	6.0335859
H	2.7849824	2.5290923	4.1252313
H	-2.0949989	3.0169824	4.0488323

H	0.7977669	-3.6764117	4.1252313
H	3.6602829	0.3058311	4.0488323
H	-0.3618959	-2.7852306	6.0335859
H	-0.1576982	-1.1518958	6.6001640
H	-2.2311325	1.7060263	6.0335859
H	-0.9187219	0.7125186	6.6001640
H	-1.5652840	-3.3228135	4.0488323
H	-3.5825657	1.1479677	-4.1251599
C	-0.2444827	3.7112579	3.2461518
C	-3.0918022	-2.0673572	3.2461518
C	3.3362849	-1.6439007	3.2461518
C	3.3363114	-1.6448229	-3.2464610
C	-0.2436973	3.7117419	-3.2464610
C	-3.0926141	-2.0669190	-3.2464610
O	-3.6829483	-2.9471849	2.4138214
O	-0.7108628	4.6631192	2.4138214
O	4.3938111	-1.7159343	2.4138214
O	4.3940574	-1.7171951	-2.4144434
O	-0.7098942	4.6639629	-2.4144434
O	-3.6841633	-2.9467678	-2.4144434
C	-3.0524537	-4.1895743	-2.2160659
H	-2.0284106	-4.0581756	-1.8503951
H	-3.6428715	-4.7118652	-1.4652844
H	-3.0380137	-4.7853711	-3.1350183
C	5.1545046	-0.5487153	-2.2160659
H	4.5286885	0.2724326	-1.8503951
H	5.9020307	-0.7988867	-1.4652844
H	5.6632598	-0.2383115	-3.1350183
C	-2.1020509	4.7382895	-2.2160659
H	-2.5002778	3.7857429	-1.8503951
H	-2.2591592	5.5107518	-1.4652844
H	-2.6252461	5.0236826	-3.1350183

C	5.1544960	-0.5474900	2.2161441
H	5.9021473	-0.7974217	1.4654362
H	4.5289083	0.2739423	1.8507085
H	5.6630932	-0.2375778	3.1353810
C	-3.0513883	-4.1901795	2.2161441
H	-3.6416610	-4.7126986	1.4654362
H	-2.0272132	-4.0591207	1.8507085
H	-3.0372950	-4.7855937	3.1353810
C	-2.1031077	4.7376695	2.2161441
H	-2.2604862	5.5101203	1.4654362
H	-2.5016951	3.7851785	1.8507085
H	-2.6257982	5.0231714	3.1353810

Optimized structure of [**3**.$Me_4N^+Cl^-$] complex

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Energy= -4314.096939096

O	-3.4002397	-3.4603182	2.7846670
O	5.0284709	-1.4018176	2.1614321
C	1.1284830	1.6381731	4.7321502
C	2.0257521	0.6306287	5.4208138
C	-0.2507524	1.7054948	4.9295001
C	1.7386982	2.5429133	3.8588821
C	1.5828248	-1.7022408	4.4704033
C	2.3691215	-0.5519222	4.5488166
C	-0.3519331	3.6058210	3.4340583
C	-1.6112614	-0.4169044	4.9879344
C	-0.9480759	-1.6279316	4.7948759
C	-1.5764327	-2.6107283	4.0287561
C	0.4031908	-1.9503920	5.3832222
C	-2.8154116	-2.4175907	3.4722143
C	-2.8781026	-0.2329712	4.4272849
C	-1.0258329	0.7296249	5.7832739

C	3.8336659	-1.4737551	2.8647291
O	-1.0856729	4.6466801	2.8799838
C	-0.9653487	2.7136414	4.2764027
C	1.9049044	-2.6937452	3.5423456
C	3.5102649	-0.4766804	3.7497495
C	-1.8318615	1.1498512	-5.4147302
N	-1.6740760	5.7895669	1.0198123
C	-1.5230323	3.0337257	-3.8092248
C	-2.0834076	-2.2975173	-3.7963097
N	-1.7550556	5.8466653	-0.2744515
C	-3.4401056	0.0863336	-3.8468292
C	3.4573076	-1.2304801	-3.5382090
O	-1.4030355	4.8694903	-2.2840211
C	2.9762767	-0.1610551	-4.2497963
C	-1.5904694	-1.2656307	-4.5981407
C	-0.3673474	-1.5471754	-5.4400673
C	1.2111272	2.8288666	-3.8203805
C	1.7198578	-0.1958448	-4.8543912
C	-2.2785515	-0.0523513	-4.6109917
C	-3.2274272	-2.1518971	-3.0521103
C	1.2315874	1.0477281	-5.5556070
O	4.7366491	-1.1799620	-2.9959598
N	-1.0801748	3.5957429	-0.4161424
C	1.4629469	-2.4431333	-4.0126828
C	0.9665792	-1.3676446	-4.7507005
C	-0.7771687	3.8642741	-3.0113522
C	-0.9281526	2.0720300	-4.6311042
C	0.4641505	1.9924757	-4.6548629
O	-3.7176111	-3.2465364	-2.3703078
N	3.8219230	-0.7821763	0.3188634
N	3.7520181	-0.7250947	-0.9837583
N	5.9980238	-1.4099335	-1.1340731

C	4.9436613	-1.2393765	0.8436042
N	6.0682191	-1.4662521	0.1594268
C	4.8059754	-1.1305441	-1.6682817
N	-4.1283127	-4.3502854	0.8479732
N	-4.2097164	-4.2965497	-0.4447157
N	-3.2561847	-2.1436346	-0.4149606
N	-3.1727944	-2.1970887	0.8841632
N	-1.0060350	3.5353662	0.8844543
C	-3.6966015	-3.2188317	-1.0381980
C	-1.2316387	4.6485626	1.5550653
C	-1.3838465	4.7596523	-0.9563309
C	-3.5457557	-3.3214457	1.4603499
H	1.5771520	0.3048269	6.3581445
H	2.9531922	1.1392554	5.6962973
H	-1.0985053	-3.5679967	3.8551240
H	1.2739099	-3.5699450	3.4695985
H	0.5436043	-1.4174144	6.3230939
H	0.4082409	-3.0114023	5.6453088
H	3.6080021	0.7160769	-4.3372004
H	-1.8464184	1.2684632	6.2632887
H	-0.4046632	0.3511882	6.5941218
H	-3.3935438	0.7017626	4.6078005
H	2.8082943	2.4723923	3.7085713
H	-2.0338813	2.8141411	4.4292592
H	-1.3504710	0.8335969	-6.3391279
H	-2.7196414	1.7106357	-5.7173304
H	-2.6011403	3.1463161	-3.7908335
H	2.2901235	2.7465596	-3.8407816
H	-1.5733512	-3.2517058	-3.7318117
H	-3.9782412	1.0248193	-3.8879979
H	-0.4279791	-2.5868618	-5.7705159
H	-0.3951209	-0.9497269	-6.3513516

H	2.0994633	1.5874332	-5.9435208
H	0.6315306	0.7886423	-6.4266091
H	0.8590347	-3.3353314	-3.9103720
H	4.1783430	0.3747091	3.8200153
C	0.6154039	3.7578339	-2.9851980
C	2.6998686	-2.3946784	-3.3855770
C	-3.9403443	-0.9504394	-3.0760558
C	-3.5019370	-1.2177550	3.6781012
C	1.0219194	3.5226849	3.1945113
C	3.0103093	-2.5930589	2.7105037
O	3.2413697	-3.3668398	-2.6418166
O	1.2674134	4.5838018	-2.1394203
O	-5.0744391	-0.9043445	-2.3525167
O	-4.7290267	-1.1235503	3.1365302
O	1.5371089	4.4183487	2.3261465
O	3.3695847	-3.4796343	1.7732736
C	2.4869620	-4.5601067	1.4931440
H	1.5179867	-4.2098088	1.1197340
H	2.9754240	-5.1380057	0.7121963
H	2.3560977	-5.1942154	2.3754063
C	-5.3940875	0.1130055	3.2162691
H	-4.8062370	0.9108926	2.7485546
H	-6.3295186	-0.0111372	2.6739721
H	-5.6152204	0.3866082	4.2538232
C	2.9135146	4.3386867	2.0373123
H	3.1733522	3.3693039	1.5973412
H	3.1167107	5.1299251	1.3183234
H	3.5211585	4.5038188	2.9328159
C	-5.7539802	0.3232401	-2.2671973
H	-6.6004021	0.1554276	-1.6037935
H	-5.1119798	1.1052120	-1.8455622
H	-6.1247632	0.6490147	-3.2453908

C	2.5016484	-4.5717308	-2.4753449
H	3.1339035	-5.2165307	-1.8681197
H	1.5497165	-4.3911311	-1.9618840
H	2.3315920	-5.0523742	-3.4442459
C	2.6716957	4.4875834	-2.0796617
H	2.9933391	5.2232664	-1.3450550
H	2.9903517	3.4887809	-1.7608152
H	3.1306501	4.7220110	-3.0455189
Cl	-0.5224941	-3.9290979	-0.6248608
C	-1.3592067	0.4366173	-0.0985536
H	-1.5968917	0.8446544	0.8820927
H	-1.4761682	1.2079302	-0.8564150
H	-1.9872833	-0.4206942	-0.3255864
C	0.3559855	-0.6433835	-1.4112548
H	0.0647628	0.0464667	-2.2024579
H	1.4241067	-0.8372145	-1.4643635
H	-0.1952997	-1.5836833	-1.4708832
C	0.2836027	-0.9777033	1.0021428
H	1.3440474	-1.2182445	1.0251949
H	-0.0122561	-0.5124700	1.9419410
H	-0.2930487	-1.8812211	0.7963459
C	0.9542247	1.1621341	0.0974941
H	0.6919351	1.6488009	1.0347021
H	1.9794190	0.8017475	0.1273723
H	0.8084099	1.8568103	-0.7274732
N	0.0588227	-0.0018579	-0.0999103

Optimized structure of [**3**.Me_4N^+] complex

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Energy= -3853.827660633

O	-4.2602836	-0.9507990	3.4324685
O	4.3592256	-0.9272323	3.4527134

C	1.1472749	3.6201117	3.4026682
C	1.7243150	2.9951096	4.6548604
C	-0.1857094	4.0137730	3.2875491
C	2.0154545	3.8160929	2.3248566
C	0.8165688	0.6267860	4.9956372
C	1.8299360	1.4919071	4.5807601
C	0.2742012	4.8437174	1.0644603
C	-1.9792277	2.4627711	4.1203592
C	-1.6284823	1.2595733	4.7332692
C	-2.4071401	0.1312556	4.4672740
C	-0.4529752	1.1036473	5.6676545
C	-3.4719030	0.1772918	3.6041838
C	-3.0675555	2.4960741	3.2441070
C	-1.2300381	3.7580667	4.3470032
C	3.1497844	-0.4150055	3.8982012
O	-0.1457575	5.5564169	-0.0488722
C	-0.5907055	4.6463340	2.1098274
C	0.9770613	-0.7503196	4.8191312
C	2.9991085	0.9396293	4.0530806
C	-1.1885254	-1.5513490	-5.5415254
N	-0.3548705	5.6410376	-2.2959633
C	-0.5611101	0.8064221	-5.0412013
C	-2.3785704	-3.6585007	-2.5925300
N	-0.3502471	5.0295077	-3.4348894
C	-3.0387735	-1.3358104	-3.8938608
C	3.1724998	-3.4706684	-1.7858144
O	-0.1274247	3.1102560	-4.6042845
C	3.0277813	-2.8506226	-3.0008665
C	-1.5941214	-3.2546376	-3.6748839
C	-0.4134262	-4.1159809	-4.0533341
C	2.0433399	0.1778885	-4.4502100
C	1.8639776	-2.9882724	-3.7605612

C	-1.9445172	-2.0806531	-4.3420827
C	-3.4490670	-2.9173865	-2.1619601
C	1.7645898	-2.2190429	-5.0547493
O	4.3771149	-3.3790906	-1.1044900
N	-0.2790052	2.9522729	-2.3288389
C	1.0044650	-4.4302866	-2.0302873
C	0.8501129	-3.8158616	-3.2760713
C	0.2974370	1.7899870	-4.6224558
C	-0.1505928	-0.5232864	-5.1617532
C	1.1816256	-0.8320331	-4.8878768
O	-4.2428050	-3.3998644	-1.1319771
N	3.3647083	-1.2395964	1.4214863
N	3.3692243	-1.8593939	0.2693117
N	5.4573061	-2.8133947	0.7990503
C	4.3643115	-1.4834231	2.2434610
N	5.4528488	-2.2004527	1.9382748
C	4.3730191	-2.6764263	0.0259011
N	-5.1076116	-2.5346541	2.0724931
N	-5.1032538	-3.1451889	0.9345990
N	-3.2633831	-1.8463036	0.2335825
N	-3.2678408	-1.2265047	1.3887788
N	-0.2835880	3.5717968	-1.1749191
C	-4.1960181	-2.7532518	0.0286877
C	-0.2362263	4.8879739	-1.1949749
C	-0.2272732	3.6961667	-3.4145997
C	-4.2045389	-1.5602299	2.2522209
H	1.1494810	3.2989361	5.5281035
H	2.7263344	3.4042194	4.8047939
H	-2.1942024	-0.8123784	4.9568070
H	0.1890872	-1.4118298	5.1554620
H	-0.2653485	2.0321229	6.2045137
H	-0.7214318	0.3717844	6.4334345

H	3.8587115	-2.2596817	-3.3694346
H	-1.9513554	4.5782659	4.3293777
H	-0.7880937	3.7741356	5.3417646
H	-3.3366156	3.4394494	2.7869699
H	3.0487932	3.5112647	2.4299764
H	-1.6061137	5.0102039	2.0017892
H	-0.7394949	-2.3698828	-6.1014264
H	-1.9066549	-1.0860910	-6.2206712
H	-1.5757434	1.0939792	-5.2921669
H	3.0762009	-0.0744223	-4.2470823
H	-2.1655172	-4.5865283	-2.0741000
H	-3.3075747	-0.4350109	-4.4302153
H	-0.6801141	-5.1594242	-3.8685453
H	-0.2186622	-4.0497794	-5.1225891
H	2.7692283	-2.1144935	-5.4715318
H	1.1967854	-2.7807446	-5.7945234
H	0.2162506	-5.0790712	-1.6705769
H	3.8295411	1.5765591	3.7698924
C	1.6213195	1.4873608	-4.2941008
C	2.1452369	-4.2593259	-1.2624416
C	-3.7969644	-1.7260882	-2.8021571
C	-3.8196132	1.3674732	2.9616630
C	1.5991389	4.4074863	1.1441527
C	2.1234349	-1.2910754	4.2591894
O	2.3612695	-4.7940586	-0.0457683
O	2.3799590	2.5107143	-3.8564719
O	-4.8489281	-1.0588033	-2.2960751
O	-4.8654197	1.3097771	2.1184647
O	2.3642522	4.6102200	0.0543193
O	2.3458393	-2.5996286	4.0329923
C	1.3593291	-3.5225149	4.4399544
H	0.4139282	-3.3539420	3.9121311

H	1.7455198	-4.5074999	4.1863512
H	1.1868813	-3.4716602	5.5192288
C	-5.2601348	2.4975777	1.4662975
H	-4.4562414	2.8886310	0.8330586
H	-6.1132696	2.2312522	0.8460291
H	-5.5641932	3.2643280	2.1852642
C	3.7267341	4.2519616	0.1234538
H	3.8483975	3.1744712	0.2822442
H	4.1600761	4.5284157	-0.8354099
H	4.2423403	4.7967478	0.9200107
C	-5.2444530	0.1383818	-2.9304153
H	-6.1035892	0.5049689	-2.3727554
H	-4.4442387	0.8859751	-2.9014984
H	-5.5398074	-0.0400884	-3.9687965
C	1.3736265	-5.6462535	0.4916298
H	1.7543052	-5.9784220	1.4551580
H	0.4256376	-5.1159602	0.6367285
H	1.2078952	-6.5179330	-0.1485696
C	3.7421737	2.2607211	-3.5892571
H	4.1702924	3.2145872	-3.2884592
H	3.8628360	1.5340912	-2.7777902
H	4.2635272	1.8992322	-4.4807121
C	-0.6797272	-0.2306332	-1.2682706
H	-1.6476912	-0.6697201	-1.0341549
H	-0.7813156	0.7221367	-1.7842468
H	-0.1038466	-0.9200937	-1.8855361
C	1.3912021	0.5847148	-0.3066796
H	1.2322378	1.5328127	-0.8139955
H	1.9324482	0.7280027	0.6262086
H	1.9379556	-0.1097736	-0.9411517
C	0.2332952	-1.3075465	0.7015813
H	0.7874068	-1.1399453	1.6229834

H	-0.7554828	-1.7079570	0.9108684
H	0.7953362	-1.9787721	0.0552463
C	-0.6877799	0.9261364	0.8927434
H	-1.6554669	0.4845382	1.1235351
H	-0.1171794	1.0599074	1.8117224
H	-0.7902211	1.8831897	0.3849963
N	0.0635159	-0.0060429	0.0044061

Finally, the structure of the [**3**.NMe_4Cl] complex was optimized and a Non-Covalent Interaction analysis was performed with the NCIPlot tool, Figure S3b.[13] The plot shows the interactions between the $(Me_4N)^+$ moiety and either the CTV units (both north and south) or the tetrazine rings. Those contribute to the stability of the encapsulated cation. The analysis reveals as well an interaction between the Cl^- anion and the tetrazine unit, which can be denoted as an anion-π interaction. Thus, the presence of the tetrazine contributes to stabilize the whole ion-pair complex.

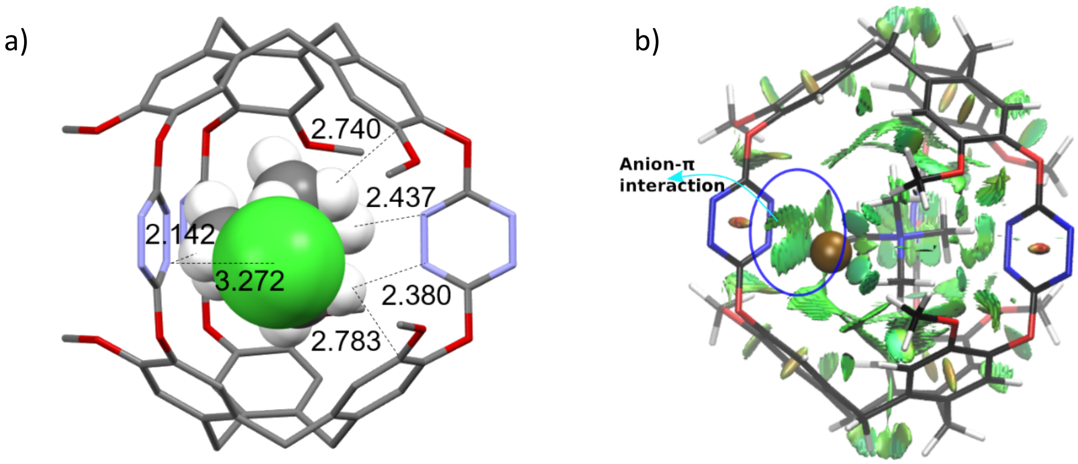

Figure S3. *a) Selected distances between host and guests of the [**3**.NMe_4Cl] complex and b) Non-Covalent Interaction plot of the [**3**.NMe_4Cl] complex.*

6. Supplementary Figures

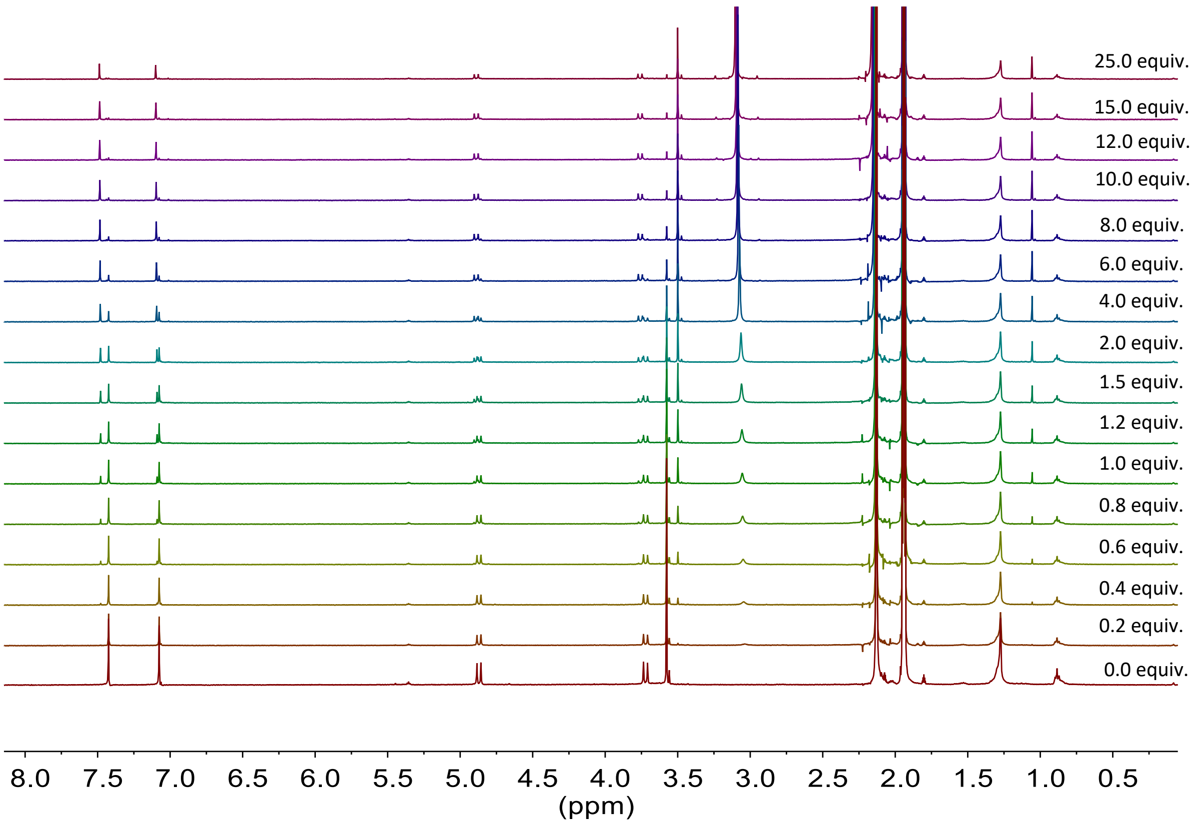

Figure S4. ^{1}H NMR titration (500 MHz, CD_3CN, 298K) of cryptophane **3** (0.79mM) with tetramethylammonium chloride (19 mM).

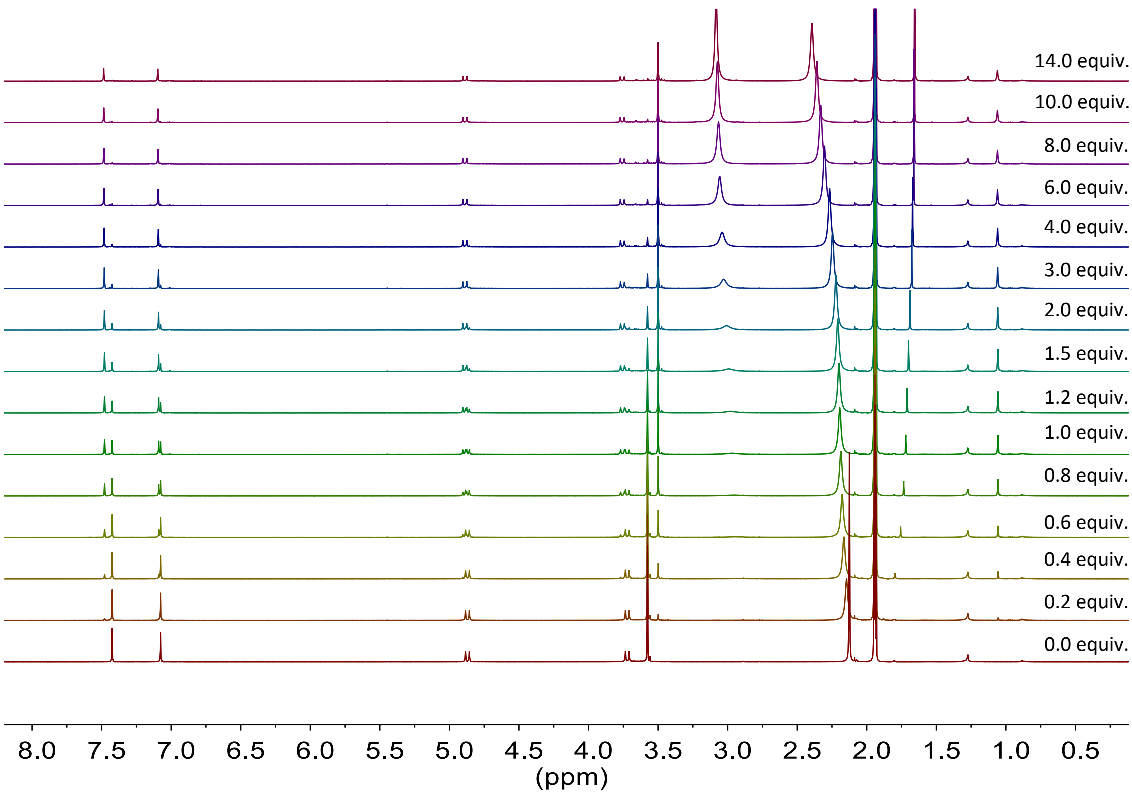

Figure S5. ^{1}H NMR titration (500 MHz, CD_3CN, 298K) of cryptophane **3** (1 mM) with tetramethylammonium acetate (24 mM).

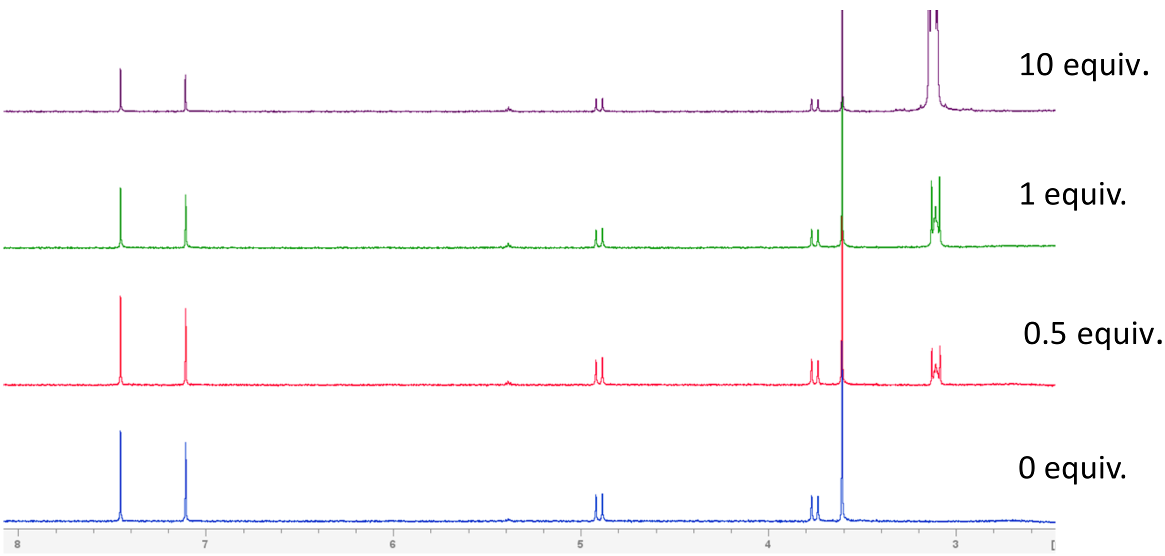

Figure S6. ^{1}H NMR titration (500 MHz, CD_3CN, 298K) of cryptophane **3** (1mM) with tetrabutylammonium chloride (24 mM).

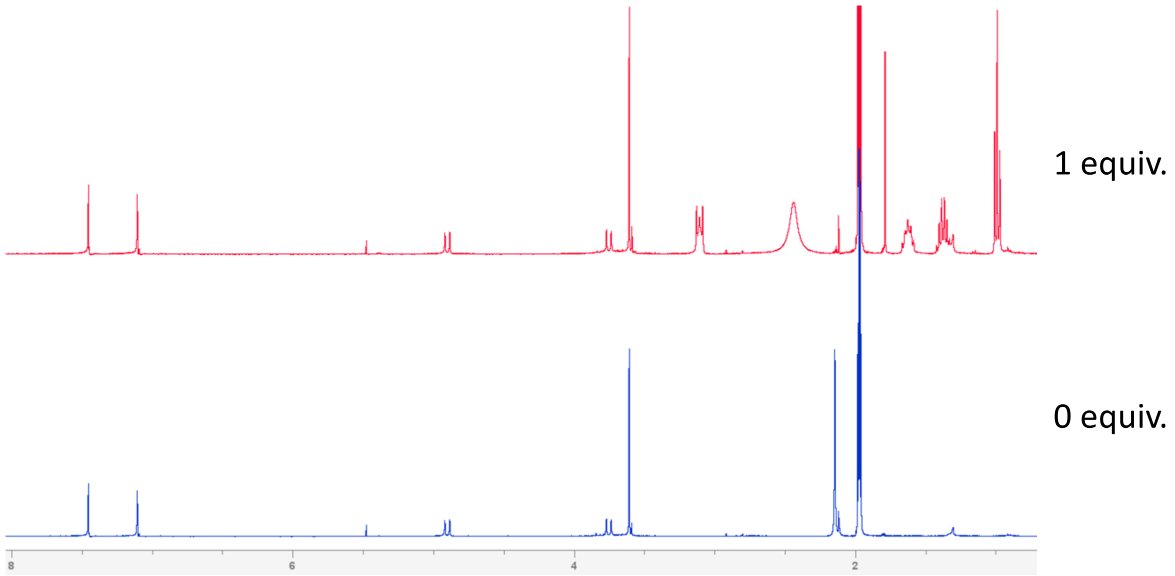

Figure S7. [1]H NMR titration (500 MHz, CD_3CN, 298K) of cryptophane **3** (1 mM) with tetrabutylammonium acetate (24 mM).

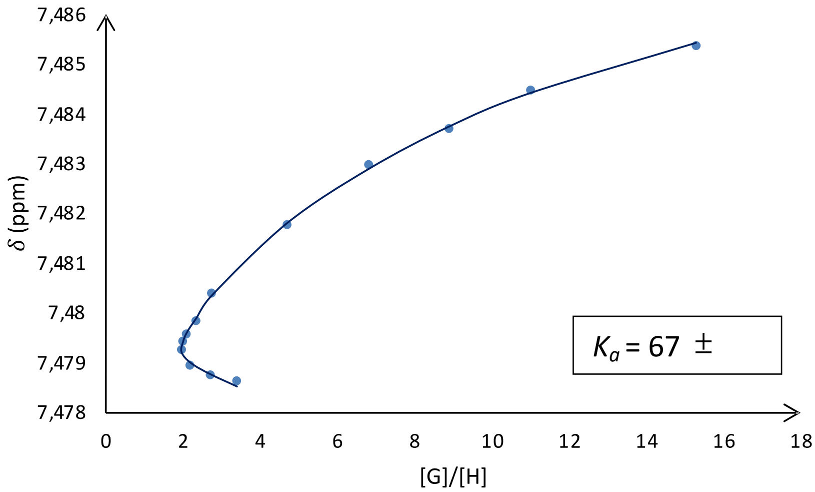

Figure S8. Titration curve of host **3** (1 mM, CD_3CN) with tetramethylammonium acetate (24 mM, CD_3CN). The chemical induced shifts δ of host's proton at 7.48 ppm was measured and plotted as a function of the ratio [G]/[H] (dots). Curve was fitted with the bindfit program (line) assuming a 1:1 stoichiometry.

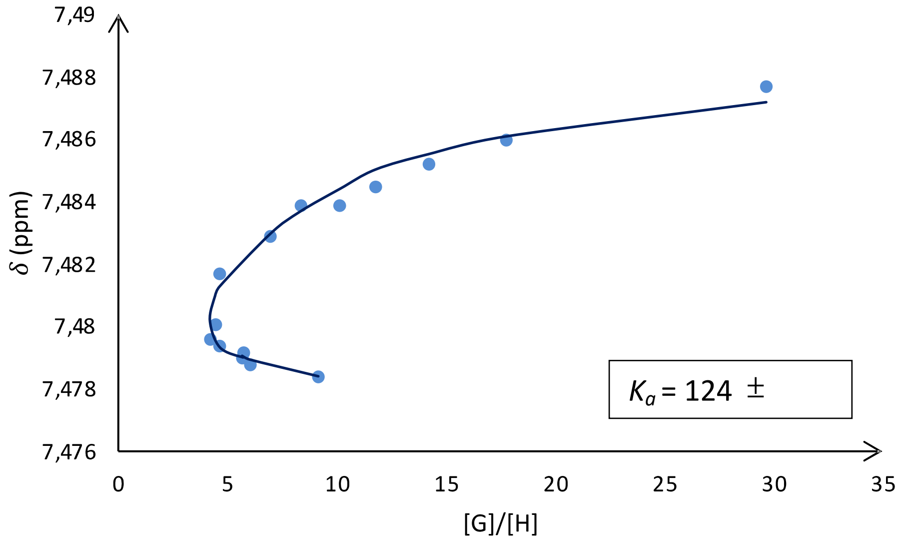

Figure S9. Titration curve of host **3** (0,79 mM, CD_3CN) with tetramethylammonium chloride (19 mM, CD_3CN). The chemical induced shifts δ of host's proton at 7.47 ppm was measured and plotted as a function of the ratio [G]/[H] (dots). Curve was fitted with the bindfit program (line) assuming a 1:1 stoichiometry.

7. NMR spectra of compound **3**

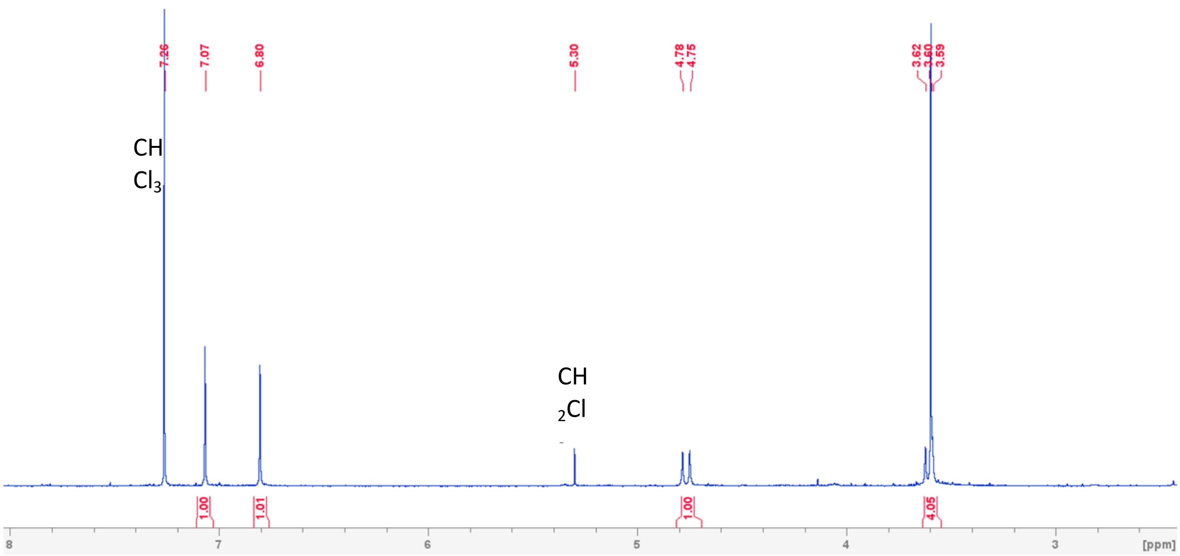

Figure S10. ^1H NMR spectrum (400 MHz, $CDCl_3$, 298K) of cryptophane **3**.

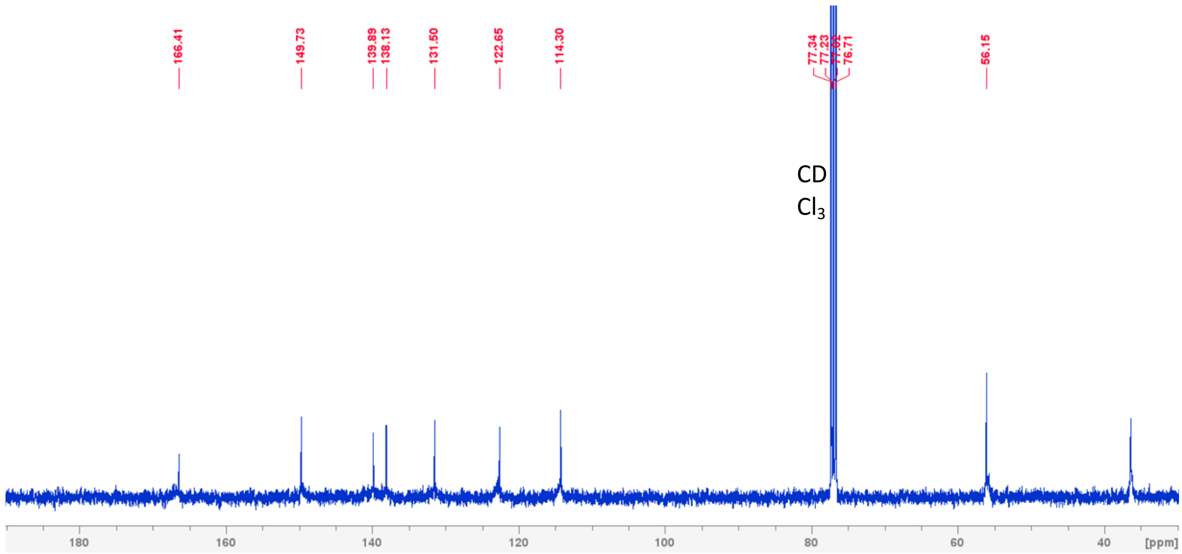

Figure S11. ^{13}C NMR spectrum (400 MHz, $CDCl_3$, 298K) of cryptophane **3**.

8. References

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