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Zwitterion Detection with a Fluorescent Squaramide Cryptand: A Study in Size-Dependent Salt Recognition and Sensing

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Supporting Information

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General information

Unless specifically indicated, all other chemicals and reagents used in this study were purchased from commercial sources and used as received. If necessary purification of products was performed using column chromatography on silica gel (Merck Kieselgel 60, 230-400 mesh) with mixtures of chloroform/methanol. Thin-layer chromatography (TLC) was performed on silica gel plates (Merck Kieselgel 60 F254). ^{1}H and ^{13}C NMR spectra used in the characterization

of products were recorded on Bruker Avance 300 MHz spectrometer. Two-dimensional NMR spectra (ROESY, COSY and HSQC) were recorded on a Bruker Avance III HD 500 MHz. In each case, the spectra were calibrated at the residual solvent resonances. Multiplets were assigned as s (singlet), d (doublet), and m (multiplet). The HRMS data were obtained on a Quattro LC Micromass or Shimadzu LCMS-IT-TOF unit.

Synthetic procedures and chemical details of compounds

Preparation of compound E.

1,8-Diaminoanthracene was obtained from commercially available 1,8-dinitroanthraquinone in two steps according to the procedure described in the literature. [38] To a solution of 1,8-diaminoanthracene (1.0 g, 4.8 mmol) in 40 mL of methanol was added dimethyl squarate (1.36 g, 9.6 mmol). After being stirred for 48 h at room temperature, the reaction mixture was concentrated and purified by silica gel column chromatography (10 % methanol in chloroform) to give compound E as a dark green solid (1.84 g, 4.3 mmol, 90 % yield).

HRMS (ESI): Calculated for $C_{24}H_{17}N_2O_6$, $[M + H]^+$: 429.10811, found:429.10839.

^{1}H NMR (300 MHz, DMSO-d_6, 25°C) δ 11.33 (s, 2H), 9.00 (s, 1H), 8.71 (s, 1 H), 8.07-7.90 (m, 2H), 7.70-7.45 (m, 2H), 7.45-7.30 (m, 2H), 4.34 (s, 6H).

^{13}C NMR (75 MHz, DMSO-d_6, 25°C) δ 189.2, 185.1, 179.2, 171.3, 133.5, 132.1, 127.5, 126.7, 126.2, 126.0, 120.8, 118.2, 61.0.

Preparation of receptor 2.

To a solution of compound E (0.5 g, 2.4 mmol) in 20 mL of methanol was added benzylamine (0.54 mL, 4.8 mmol) and triethylamine (0.726 mL, 9.6 mmol) and the mixture was stirred 24 h at room temperature. The reaction mixture was then centrifuged and the collected solid

material was washed repeatedly with methanol. The obtained dark yellow solid was dried in vacuo to give the receptor **2** (1.16 g, 2.0 mmol, 83 % yield).

HRMS (ESI): Calculated for $C_{36}H_{27}N_4O_4$, $[M + H]^+$:579.20268, found:579.20342.

^{1}H NMR (300 MHz, DMSO-d_6, 25°C) δ 10.16 (s, 2H), 8.89 (s, 1H), 8.69 (s, 1 H), 8.20-7.96 (m, 2H), 7.96-7.80 (m, 2H), 7.60-7.20 (m, 14H), 4.95-4.75 (s, 4H).

^{13}C NMR (75 MHz, DMSO-d_6, 25°C) δ 185.8, 181.4, 169.9, 139.0, 133.7, 132.5, 132.3, 129.2, 128.3, 128.1, 128.0, 127.9, 126.3, 125.0, 124.8, 124.6, 117.7, 117.6, 47.7.

Preparation of receptor 3.

To a stirred solution of the 1,10-Diaza-18-crown-6 (0.8 g, 3.05 mmol), potassium carbonate (1.94 g, 18.3 mmol) and a catalytic amount of potassium iodide (70 mg, 0.42 mmol) in 100 mL of acetonitrile 3-(chloromethyl)benzonitrile (0.92 g, 6.1 mmol) were added. The solution was refluxed overnight under argon. Acetonitrile was removed under a vacuum, and the solid residue was taken up in chloroform and washed with distilled water. The organic phase was dried over $MgSO_4$, and the organic solvent was removed under reduced pressure. The residue was dissolved in a minimal amount of chloroform and loaded on silica gel. The silica gel was eluted with 2% methanol in chloroform. The obtained white-off solid was dried in vacuo to give the receptor **3** (1.29 g, 2.62 mmol, 86 % yield).

HRMS (ESI): Calculated for $C_{28}H_{36}N_4O_4$ Na, $[M + Na]^+$:515.26288, found:515.26371.

^{1}H NMR (300 MHz, DMSO-d_6, 25°C) δ 7.79 (s, 2H), 7.70-7.60 (m, 4H), 7.60-7.40 (m, 2H), 3.70 (s, 4H), 3.60-3.45 (m, 16H), 2.80-2.55 (m, 8H).

^{13}C NMR (75 MHz, DMSO-d_6, 25°C) δ 142.5, 134.0, 133.7, 132.2, 130.9, 129.7, 119.5, 111.5, 70.5, 69.6, 58.5, 54.0.

Preparation of receptor 1.

To a stirred solution of receptor **3** (0.3 g, 0.6 mmol) in anhydrous tetrahydrofuran (7 mL) was added dropwise under an argon atmosphere 1 M suspension of $LiAlH_4$ (4.8 ml, 4.8 mmol) in tetrahydrofuran. The reaction mixture was stirred overnight at room temperature under an argon atmosphere. The reaction was quenched by a minimum amount of aqueous saturated magnesium sulfate solution under a chilling temperature. The slurry mixture was filtered under vacuum and the residue washed with ethyl acetate. The combined filtrates dried over $MgSO_4$ and evaporated in a vacuum. The crude product A was obtained as a pale yellow oil and used in the next step without further purification. A solution of the compound E (0.25 g, 0.58 mmol) in methanol (150 mL) was heated to 70°C, triethylamine (0.484 mL, 3.48 mmol) was added then the compound A (0.29 g, 0.58 mmol) in methanol (20 ml) was added dropwise via syringe pump (at 2 mL/Hr). The mixture was stirred at reflux for 72 h under an argon atmosphere. The resulting crude precipitate was isolated by filtration and finally was then recrystallized from the DMSO/methanol mixture. The obtained dark yellow solid was dried in vacuo to give the desired receptor **1** (0.31g, 0.36 mmol, 62 % yield).

HRMS (ESI): Calculated for $C_{50}H_{52}N_6O_8$ Na, $[M + Na]^+$: 887.37388, found: 887.37392.

^{1}H NMR (300 MHz, DMSO-d_6, 60°C) δ 9.99 (s, 2H), 8.91 (s, 1H), 8.69 (s, 1H), 8.18 (s, 2H), 8.00-7.85 (m, 2H), 7.60-7.40 (m, 2H), 7.40-7.10 (m, 10H), 5.15-4.75 (m, 4H), 3.70 (s, 4H), 3.67-3.30 (m, 16H), 2.80-2.55 (m, 8H).

^{13}C NMR (75 MHz, DMSO-d6, 60°C) δ 185.6, 181.3, 170.3, 165.0, 138.7, 133.8, 132.3, 132.0, 129.0, 128.4, 128.2, 126.3, 126.2, 125.0, 124.8, 124.5, 124.1, 117.5, 70.7, 70.5, 69.7, 59.6, 54.5, 53.9, 47.9.

Preparation of compound N1.

To a stirred solution of the 1-aza-18-crown-6 (0.5 g, 1.90 mmol), potassium carbonate (0,79 g, 5.7 mmol) and a catalytic amount of potassium iodide (70 mg, 0.42 mmol) in 50 mL of acetonitrile 3-(chloromethyl)benzonitrile (0.3 g, 1.90 mmol) were added. The solution was refluxed overnight under argon. Acetonitrile was removed under a vacuum, and the solid residue was taken up in chloroform and washed with distilled water. The organic phase was dried over $MgSO_4$, and the organic solvent was removed under reduced pressure. The residue was dissolved in a minimal amount of chloroform and loaded on silica gel. The silica gel was eluted with 1% methanol in chloroform. The obtained white-off solid was dried in vacuo to give the compound N1 (0.54 g, 1.43 mmol, 75 % yield).

HRMS (ESI): Calculated for $C_{20}H_{30}N_2O_5$ Na, $[M + Na]^+$: 401.20469, found: 401.20432.

^{1}H NMR (300 MHz, DMSO-d_6, 25°C) δ 7.80 (s, 1H), 7.79-7.65 (m, 2H), 7.65-7.45 (m, 1H), 3.70 (s, 2H), 3.69-3.35 (m, 20H), 2.75-2.52 (m, 4H).

^{13}C NMR (125 MHz, DMSO-d_6, 25°C) δ 137.56, 133.50, 133.30, 130.50, 129.45, 118.92, 111.18, 70.01, 69.90, 69.79, 69.56, 61.86, 60.21, 53.34.

Preparation of compound A1.

To a stirred solution of compound N1 (0.5 g, 1.3 mmol) in anhydrous tetrahydrofuran (10 mL) was added dropwise under an argon atmosphere 1M suspension of $LiAlH_4$ (5.2 mL, 5.2 mmol)

in tetrahydrofuran. The reaction mixture was stirred overnight at room temperature under an argon atmosphere. The reaction was quenched by a minimum amount of aqueous saturated magnesium sulfate solution under cooling. The slurry mixture was filtered under vacuum and the residue washed with ethyl acetate. The combined filtrates were dried over $MgSO_4$ and evaporated in a vacuum. The compound A1 was obtained as a pale yellow oil and was used further without purification (0.4 g, 1.04 mmol, 80% yield).

HRMS (ESI): Calculated for $C_{20}H_{34}N_2O_5$ Na, $[M + Na]^+$: 405.48498 found: 405.48485.

^{1}H NMR (300 MHz, DMSO-d_6, 25°C) δ 7.38-7.05 (m, 4H), 3.70 (s, 2H), 3.60 (s, 2H), 3.59-3.40 (m, 22H), 2.75-2.55 (m, 4H).

^{13}C NMR (75 MHz, DMSO-d_6, 25°C) δ 144.48, 139.98, 128.27, 127.70, 126.92, 125.90, 70.58, 70.45, 70.16, 69.66, 61.20, 59.82, 53.86, 46.15.

Preparation of receptor 4.

Compound E1 was synthesized according to the procedure described in the literature.[39] To a solution of the compound E1 (0.275 g, 0.91 mmol) in anhydrous dichloromethane (30 mL), DIPEA (0.32 mL, 1.82 mmol) and the compound A1 (0.35 g, 0.91 mmol) were added. The mixture was stirred at reflux for 48 h under an argon atmosphere. The residue was dissolved in a minimal amount of chloroform and loaded on silica gel. The silica gel was eluted with 10% methanol in chloroform. The obtained yellow oil was dried in vacuo to give the desired receptor **4** (0.31 g, 0.47 mmol, 52 % yield).

HRMS (ESI): Calculated for $C_{38}H_{43}N_3O_7$ Na, $[M + Na]^+$: 676.29932, found: 676.2986.

^{1}H NMR (300 MHz, DMSO-d_6, 60°C) δ 10.00 (s, 1H), 8.81 (s, 1H), 8.64 (s, 1H), 8.49 (s, 1H), 8.25-8.05 (m, 2H), 7.92-7.82 (m, 1H), 7.65-7.20 (m, 8H), 4.89 (s, 2H), 3.75-3.65 (m, 2H), 3.65-3.45 (m, 20H), 2.85-2.60 (m, 4H).

^{13}C NMR (125 MHz, DMSO-d_6, 60°C) δ 185.15, 180.36, 169.58, 164.51, 138.49, 133.27, 131.75, 131.18, 130.94, 128.60, 128.29, 127.86, 126.60, 126.09, 125.95, 125.27, 124.50, 123.95, 121.00, 115.88, 69.94, 69.81, 69.56, 53.21, 47.17.

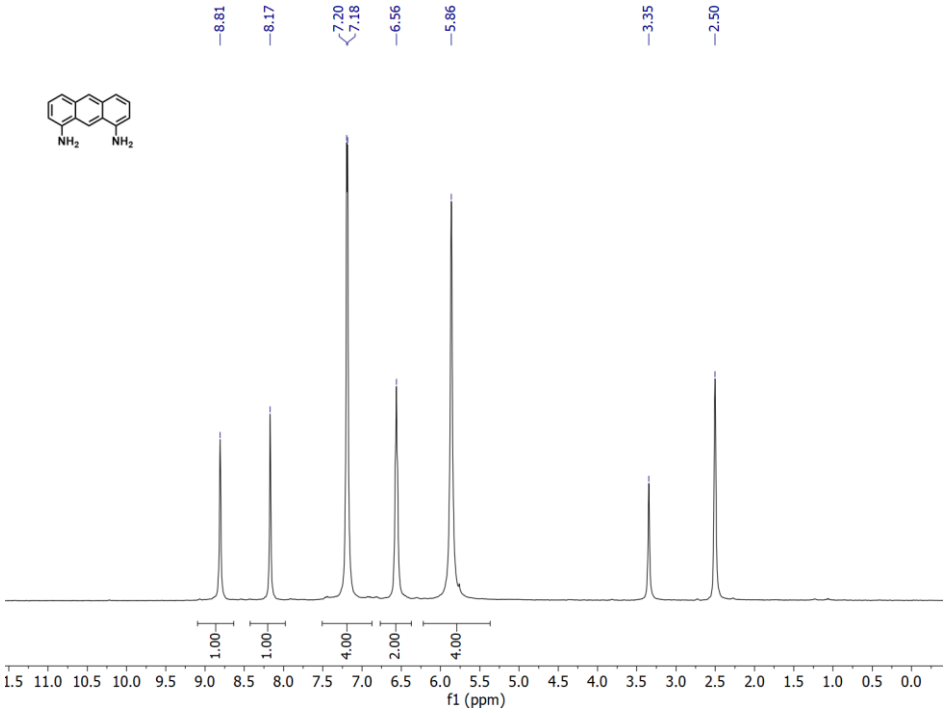

Fig. S1. ^{1}H NMR spectrum of 1,8-diaminoanthracene in DMSO-d_6.

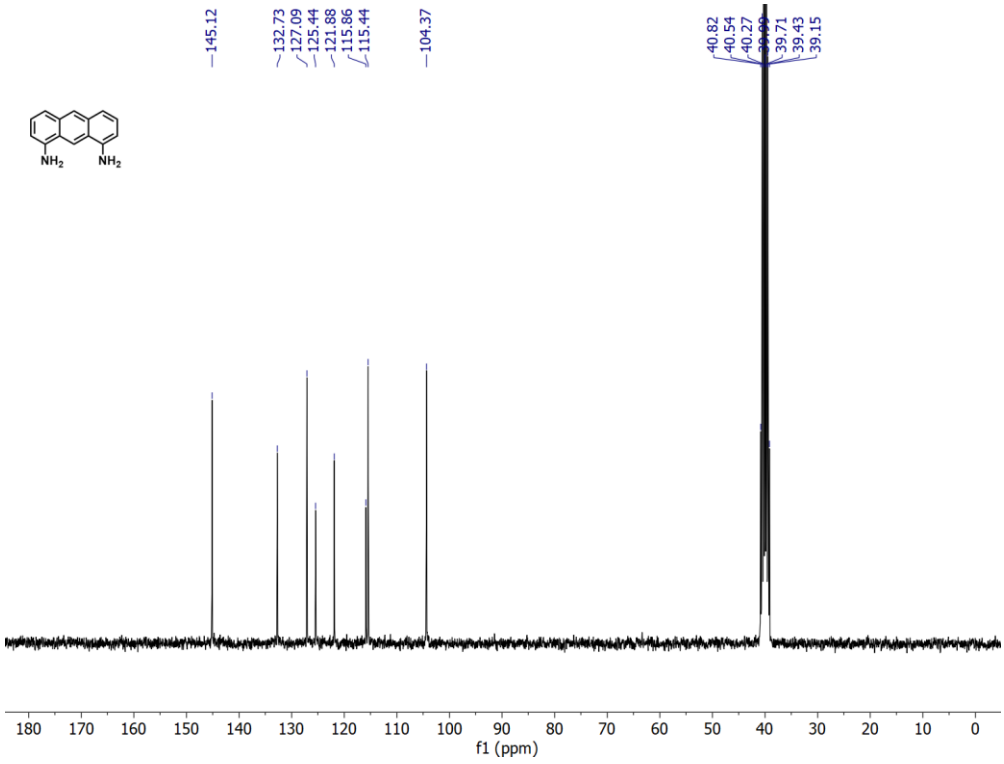

Fig. S2. ^{13}C NMR spectrum of 1,8-diaminoanthracene in DMSO-d_6.

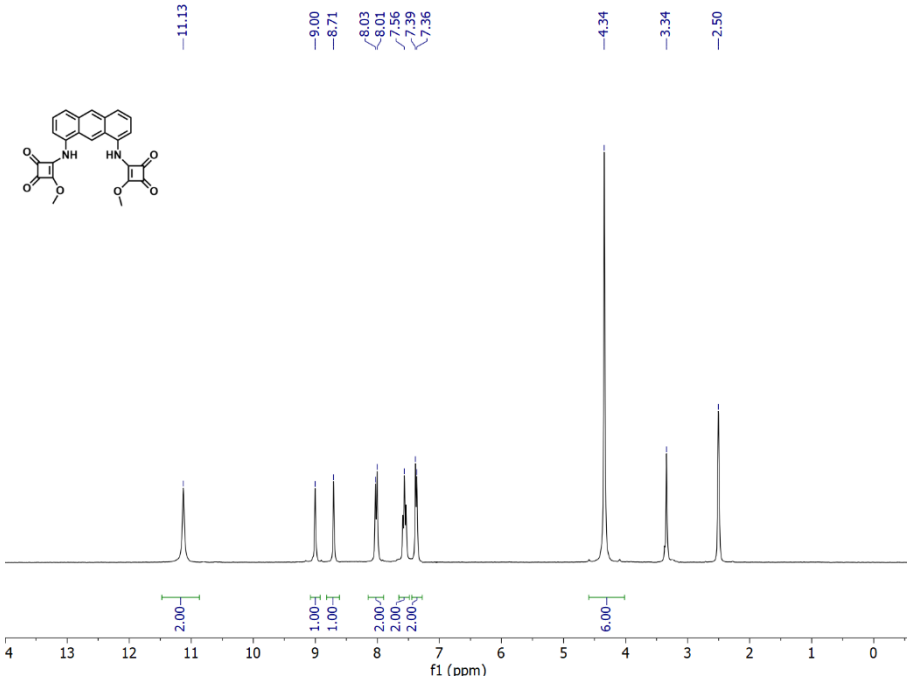

Fig. S3. ^{1}H NMR spectrum of compound E in DMSO-d_6.

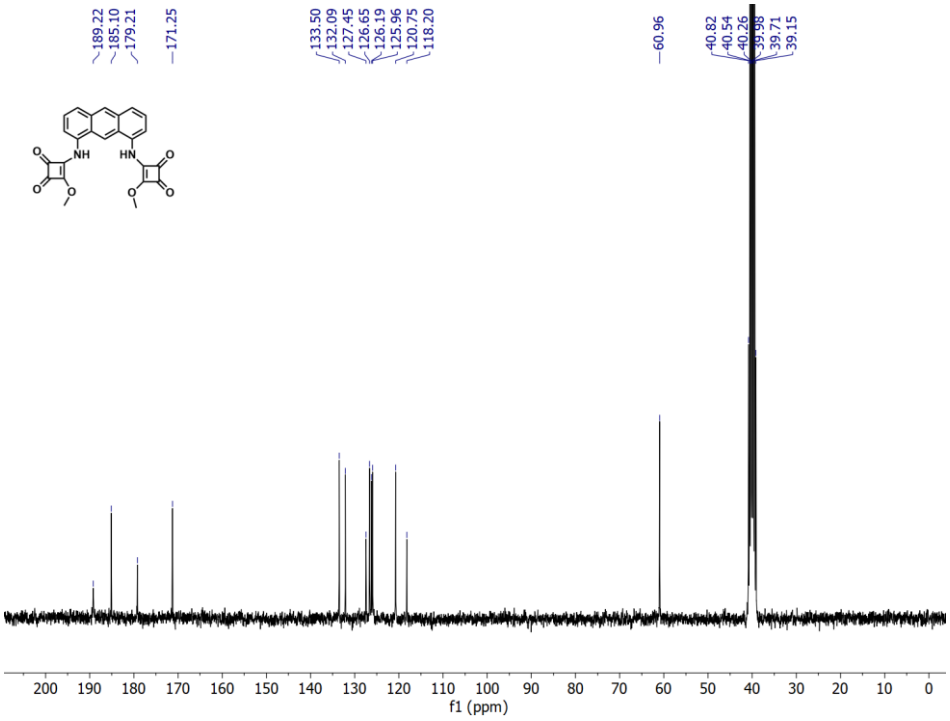

Fig. S4. ^{13}C NMR spectrum of compound E in DMSO-d_6.

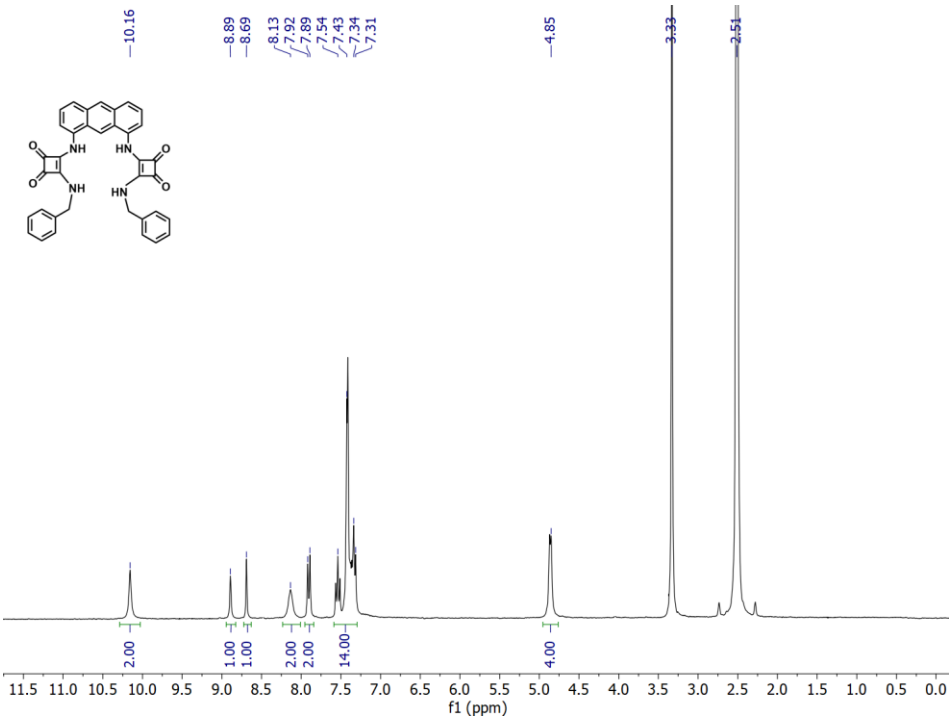

Fig. S5. ^{1}H NMR spectrum of receptor **2** in DMSO-d_6.

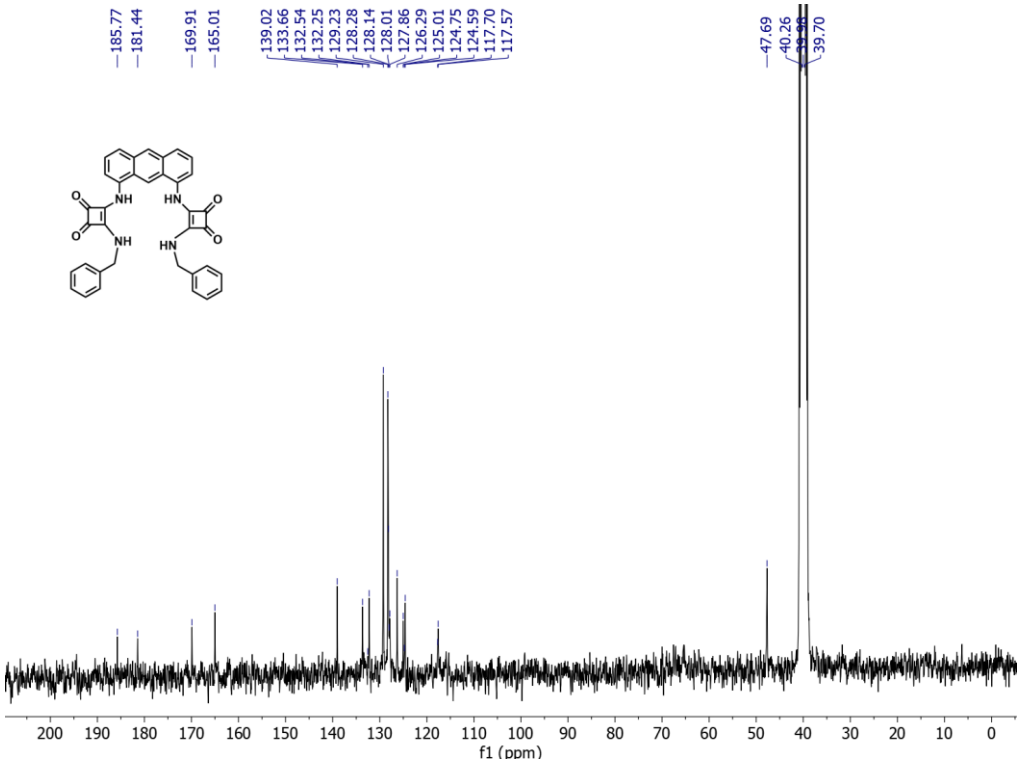

Fig. S6. ^{13}C NMR spectrum of receptor **2** in DMSO-d_6.

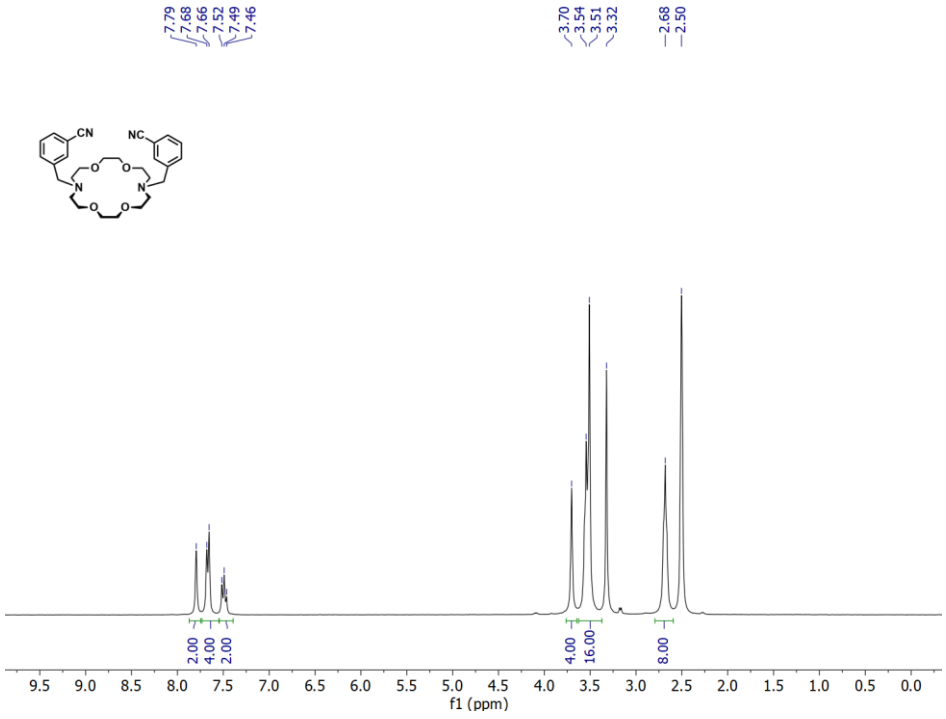

Fig. S7. ^{1}H NMR spectrum of receptor **3** in DMSO-d_6.

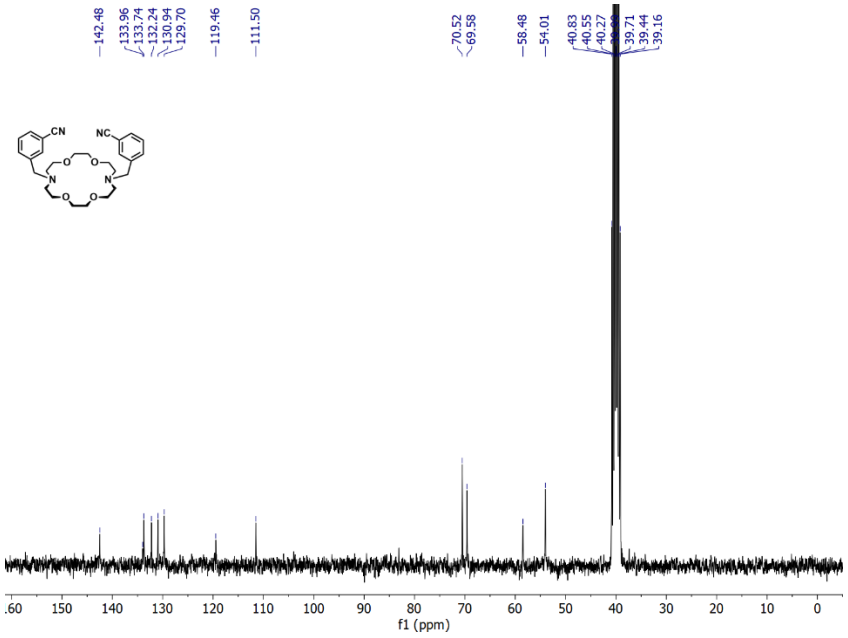

Fig. S8. ^{13}C NMR spectrum of receptor **2** in DMSO-d_6.

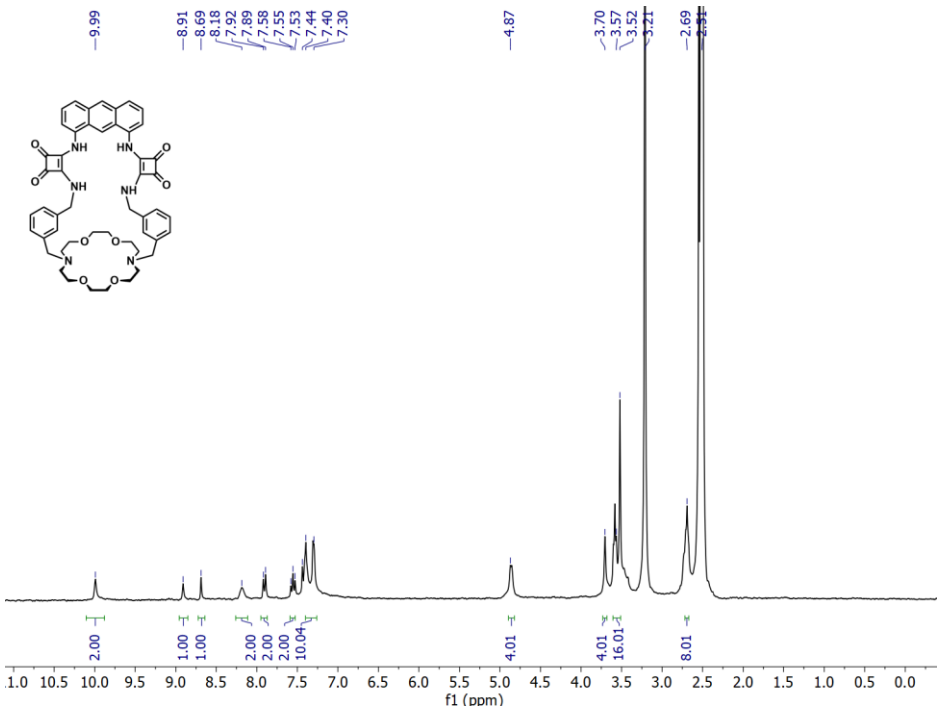

Fig. S9. ^{1}H NMR spectrum of receptor **1** in DMSO-d_6 at a temperature of 60°C.

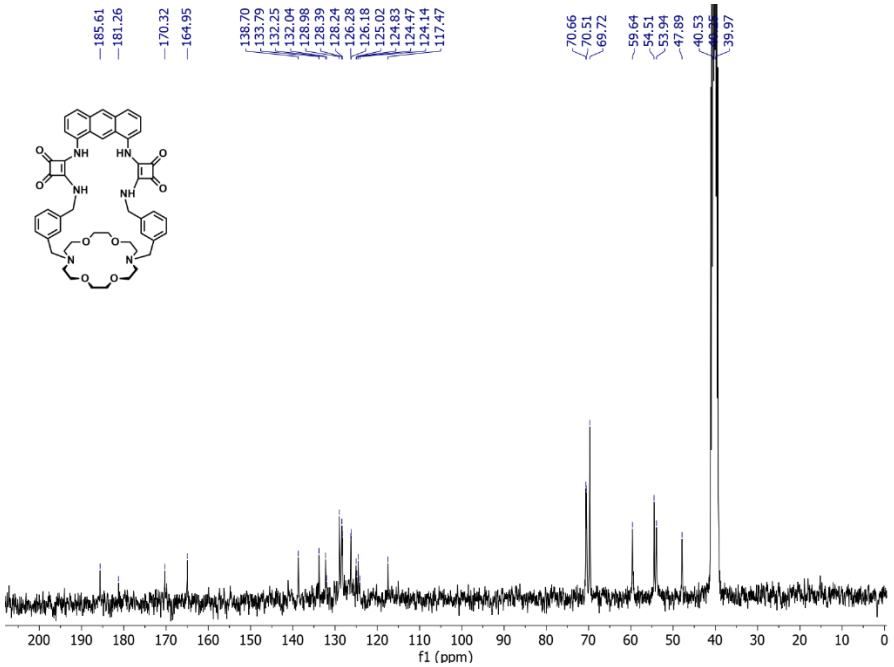

Fig. S10. ^{13}C NMR spectrum of receptor **1** in DMSO-d_6 at a temperature of 60°C.

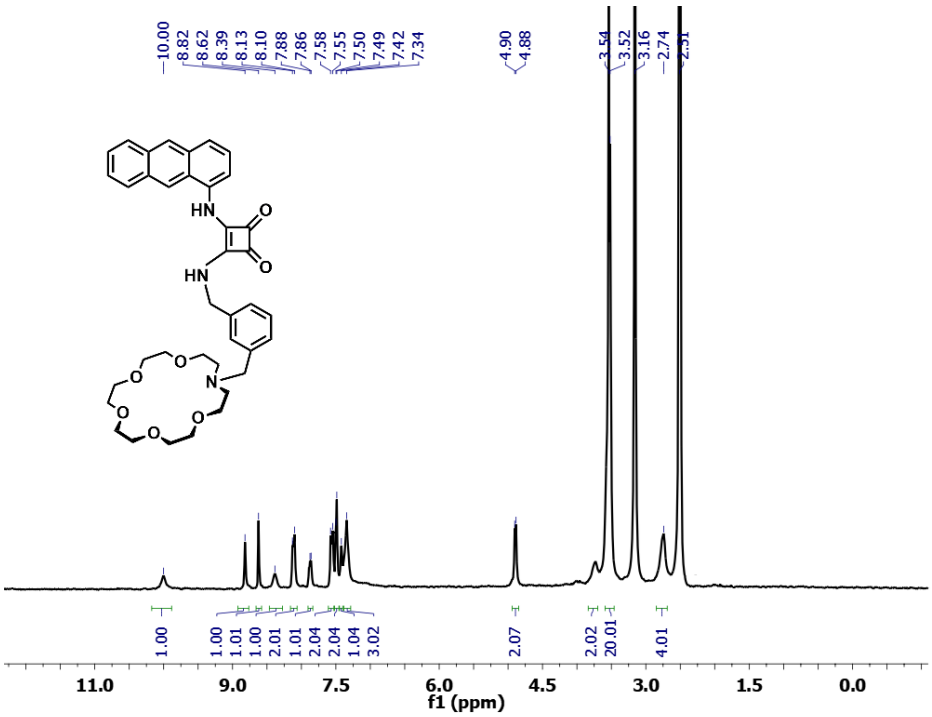

Fig. S11. ^{1}H NMR spectrum of receptor **4** in DMSO-d_6 at a temperature of 60°C.

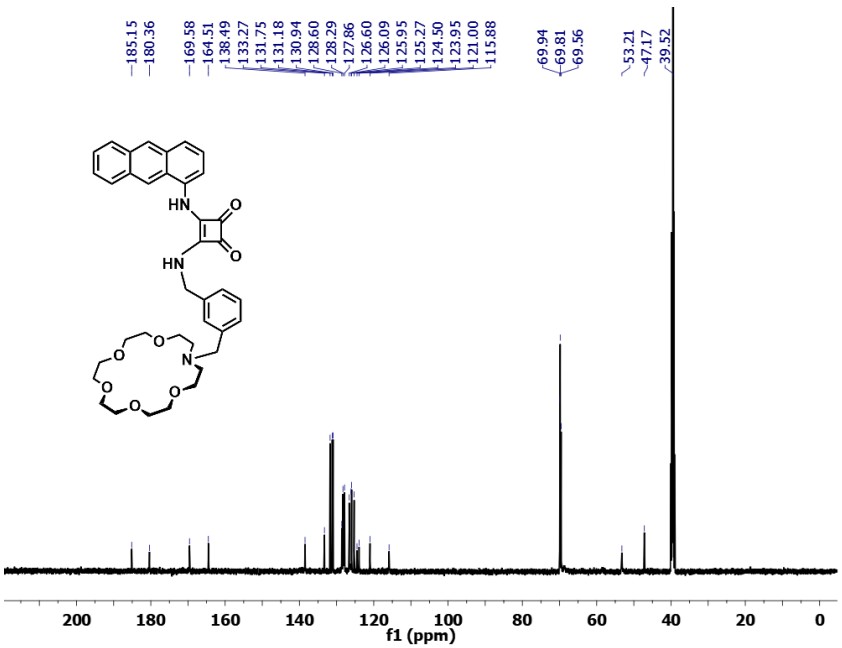

Fig. S12. ^{13}C NMR spectrum of receptor **4** in DMSO-d_6 at a temperature of 60°C.

Crystal data

Single crystal X-ray diffraction of **1×**NaBr. The X-ray measurement of **1×**NaBr was performed at 130.0(5) K on a Bruker D8 Venture PhotonII diffractometer equipped with a TRIUMPH monochromator and a MoKα fine focus sealed tube (λ = 0.71073 Å). A total of 2397 frames were collected with Bruker APEX3 program. [2] The frames were integrated with the Bruker SAINT software package [3] using a narrow-frame algorithm. The integration of the data using a triclinic unit cell yielded a total of 48819 reflections to a maximum θ angle of 25.05° (0.84 Å resolution), of which 8369 were independent (average redundancy 5.833, completeness = 99.9%, Rint = 3.88%, Rsig = 2.92%) and 6920 (82.69%) were greater than 2σ(F2). The final cell constants of a = 9.2134(5) Å, b = 13.8879(8) Å, c = 19.1338(11) Å, α = 90.438(2)°, β = 102.358(2)°, γ = 97.765(2)°, V = 2367.9(2) Å3, are based upon the refinement of the XYZ-centroids of 9906 reflections above 20 σ(I) with 5.176° < 2θ < 50.13°. Data were corrected for absorption effects using the Multi-Scan method. [4] The ratio of minimum to maximum apparent transmission was 0.917. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.762 and 0.966.

The structure was solved and refined using SHELXTL Software Package [5,6] using the space group P"1"¯, with Z = 1 for the formula unit, C104H114Br2N12Na2O17 corresponding to: 2 × C50H52N6O8 + 2 × NaBr + Et_2O. The final anisotropic full-matrix least-squares refinement on

F2 with 663 variables converged at R1 = 3.28%, for the observed data and R2 = 8.66% for all data. The goodness-of-fit was 1.037. The largest peak in the final difference electron density synthesis was 0.480 e-/Å3 and the largest hole was -0.246 e-/Å3 with an RMS deviation of 0.047 e-/Å3. Based on the final model, the calculated density was 1.409 g/cm3 and F(000), 1050 e-. The details concerning the crystal data and structural parameters of 3+NaBr are collected in Table S1.

The crystal contains disordered Et_2O molecule. The solvent is located on the centre of symmetry and occupies two alternative positions with fixed ratio of 0.5:0.5. Br anion coordinated by two squaramide units of the macrocycle is disordered over two positions with refined occupancy ratio yielding 0.946(4):0.054(4). All but one non-hydrogen atom (including those in the disordered Et_2O molecule) were refined anisotropically, low occupancy position of disordered Br- anion was refined isotropically. Most of the hydrogen atoms were placed in calculated positions and refined within the riding model. Four H atoms engaged in hydrogen bonds were freely refined together with their isotropic temperature factors. To preserve reasonable geometry of the disordered solvent molecule number of distance, angle and ADP restraints were used. The temperature factors of all constraint hydrogen atoms were not refined and were set to be 1.2 or 1.5 times larger than Ueq of the corresponding heavy atom. The atomic scattering factors were taken from the International Tables. [7] Molecular graphics were prepared using the program Mercury 2020.3.0. [8] Thermal ellipsoids parameters are presented at a 50% probability level in Figure S13.

Single crystal X-ray diffraction of **1**×CH_3COOH. The X-ray measurement of **1**×CH_3COOH was performed at 130.0(5) K on a Bruker D8 Venture PhotonII diffractometer equipped with a INCOATEC IμS micro-focus source (λ = 1.54178 Å) and a mirror monochromator. A total of 1416 frames were collected with Bruker APEX3 program [1]. The frames were integrated with the Bruker SAINT software package [3] using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 14460 reflections to a maximum θ angle of 36.39° (1.30 Å resolution), of which 2591 were independent (average redundancy 5.581, completeness = 99.7%, Rint = 13.90%, Rsig = 12.15%) and 1544 (59.59%) were greater than 2σ(F2). The final cell constants of a = 17.319(2) Å, b = 12.8227(16) Å, c = 24.862(3) Å, β = 99.564(5)°, V = 5444.5(12) Å3, are based upon the refinement of the XYZ-centroids of 2203 reflections above 20 σ(I) with 7.212° < 2θ < 72.51°. Data were corrected for absorption effects using the Multi-Scan method [4]. The ratio of minimum to maximum apparent transmission

was 0.780. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.793 and 0.993.

The structure was solved and refined using SHELXTL Software Package [5,6] using the space group P21/c, with Z = 4 for the formula unit, C56H63KN8O11 corresponding to C50H52N6O8 + CH_3COOK + H_2O + 2 × MeCN. The final anisotropic full-matrix least-squares refinement on F2 with 376 variables converged at R1 = 9.02%, for the observed data and wR2 = 22.41% for all data. The goodness-of-fit was 1.099. The largest peak in the final difference electron density synthesis was 0.361 e-/Å3 and the largest hole was -0.304 e-/Å3 with an RMS deviation of 0.060 e-/Å3. Based on the final model, the calculated density was 1.297 g/cm3 and F(000), 2248 e-. The details concerning the crystal data and structural parameters of **1**+CH_3COOH are collected in Table S1.

The investigated compound crystallizes very hardly and the crystals are very small, thus it was possible to collect data up to 1.3 Å resolution only. Because of weak scattering power and small number of reflection most atoms in the structure was refined isotropically. Only K ant O atoms were refined anisotropically with restraints for more spherical shape in case of some oxygen atoms. Hydrogen atoms of the methyl group in the acetate anion are disordered over two positions with refined occupancy ratio yielding 0.61(22):0.39(22). Most hydrogen atoms were placed in calculated positions and refined within the riding model. H atoms engaged in hydrogen bonds (N-H, O-H) were refined. To preserve reasonable geometry of H_2O molecule number of distance and angle restraints were used. The temperature factors of hydrogen atoms were not refined and were set to be 1.2 or 1.5 times larger than Ueq of the corresponding heavy atom. The atomic scattering factors were taken from the International Tables. [7] Molecular graphics was prepared using program Mercury 2020.3.0. [8] Thermal ellipsoids parameters are presented at a 50% probability level in Figure S14. The structures are deposited in Cambridge Structural Database under the numbers **CCDC 2323921-2323922** for the **1×NaBr** and **1×CH_3COOK** complexes respectively. The structures can be obtained free of charge from The CCDC via www.ccdc.cam.ac.uk/structures.

Identification code	**1×NaBr**	**1×CH_3COOK**
Formula	$C_{104}H_{114}Br_2N_{12}Na_2O_{17}$ 2 × $C_{50}H_{52}N_6O_8$ + 2 × NaBr + Et_2O	$C_{56}H_{63}KN_8O_{11}$ $C_{50}H_{52}N_6O_8$ + CH_3COOK + H_2O + 2 × MeCN
***M*$_x$/ g mol^{-1}**	702.86	1063.24
***T*/ K**	130.5(5)	130.5(5)

λ/ Å	0.71073	1.54178
Crystal size	0.037 × 0.073 × 0.306 mm	0.005 × 0.012 × 0.172 mm
Crystal habit	yellow needle	yellow needle
Space group	$P\bar{1}$	$P2_1/c$
Unit cell dimensions	a = 9.2134(5) Å b = 13.8879(8) Å c = 19.1338(11) Å α = 90.438(2)° β = 102.358(2)° γ = 97.765(2)°	a = 17.319(2) Å b = 12.8227(16) Å c = 24.862(3) Å β = 99.564(5)°
V/ Å^3, Z	2367.9(2), 1	5444.5(12), 4
D_x/ g cm^{-3}	1.409	1.297
μ/ mm^{-1}	0.941	1.411
F(000)	1050	2248
ϑ_{min}, ϑ_{max}	2.54°, 25.05°	2.59°, 36.39°
Index ranges	-10 ≤ h ≤ 10 -16 ≤ k ≤ 16 -22 ≤ l ≤ 22	-13 ≤ h ≤ 13 -9 ≤ k ≤ 9 -19 ≤ l ≤ 19
Reflections collected/ independent	48819/ 8369 (R_{int} = 0.0388)	14460/ 2591 (R_{int} = 0.1390)
Completeness	99.9%	99.7%
Absorption correction	Multi-Scan	Multi-Scan
T_{max}, T_{min}	0.966, 0.762	0.993, 0.793
Refinement method	Full-matrix LSQ on F^2	Full-matrix LSQ on F^2
Data / restraints / parameters	8369 / 36 / 663	2591 / 21 / 376
GOF on F^2	1.037	1.099
Final R indices	6920 data; I>2σ(I) R1 = 0.0328, wR2 = 0.0803 all data R1 = 0.0448, wR2 = 0.0866	1544 data; I>2σ(I) R1 = 0.0902, wR2 = 0.1938 all data R1 = 0.1547, wR2 = 0.2241
Extinction coefficient	-	0.0008(1)
$\Delta\rho_{max}$, $\Delta\rho_{min}$	0.480 eÅ^{-3}, -0.246 eÅ^{-3}	0.361 eÅ^{-3}, -0.304 eÅ^{-3}

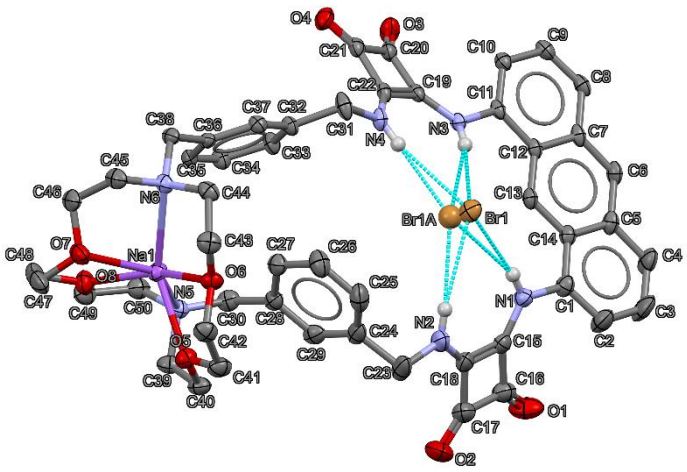

Fig S13. Thermal ellipsoid plot of the **1**×NaBr at 50% probability level together with numbering scheme. Disordered Et_2O molecule and hydrogen atoms omitted for clarity.

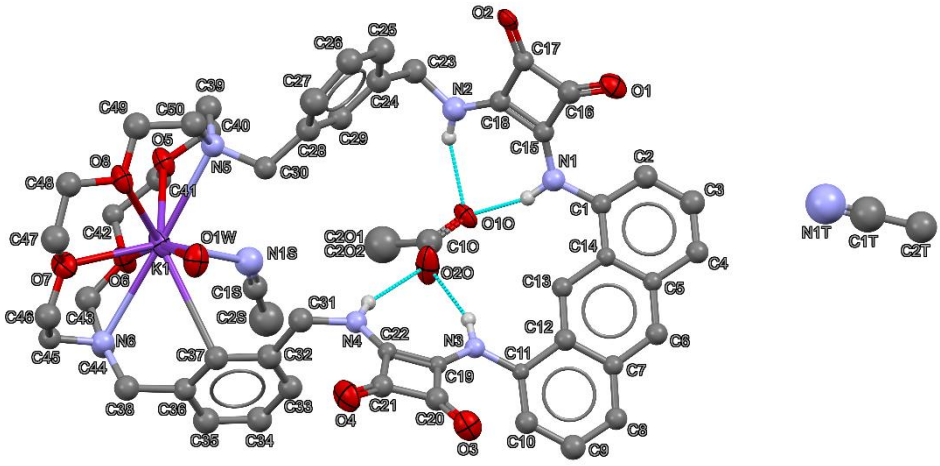

Fig S14. Thermal ellipsoid plot of the **1**×CH_3COOK at 50% probability level together with numbering scheme. Hydrogen atoms were omitted for clarity.

NMR titration experiments

The ^1H NMR titration was conducted at 60°C in DMSO-d_6. In each case, a 500 µL of freshly prepared solution of receptor **1**, **2** or **4** (3.5 mM of **1**; 2.48 mM of **2,** 3.88 mM of **4**) was added to a 5 mm NMR tube. In the case of ion pair titration receptor was firstly pretreated with one or three equivalents of KPF_6, $NaClO_4$ or NH_4PF_6. Then small aliquots of solution of TBACl, containing receptor at constant concentration, were added and a spectrum was acquired after each addition. The resulting titration data were analyzed using BindFit (v0.5) package, available online at http://supramolecular.org (27.11.2023). Each titration was carried out in duplicate. Reported values are calculated as weighted arithmetic mean, where the weights were the errors obtained for each value separately. The given uncertainty of the association constants is the largest of the variance (external or internal).

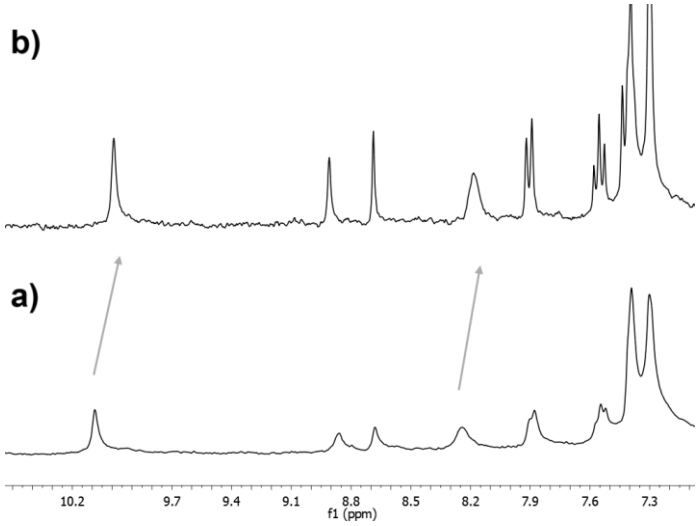

Fig. S15. Partial ^{1}HNMR spectra of receptor **1** (2.0 mM) in DMSO-d_6 recorded (a) at 25°C and (b) at 60°C (signals corresponding to squaramides and phenyl protons).

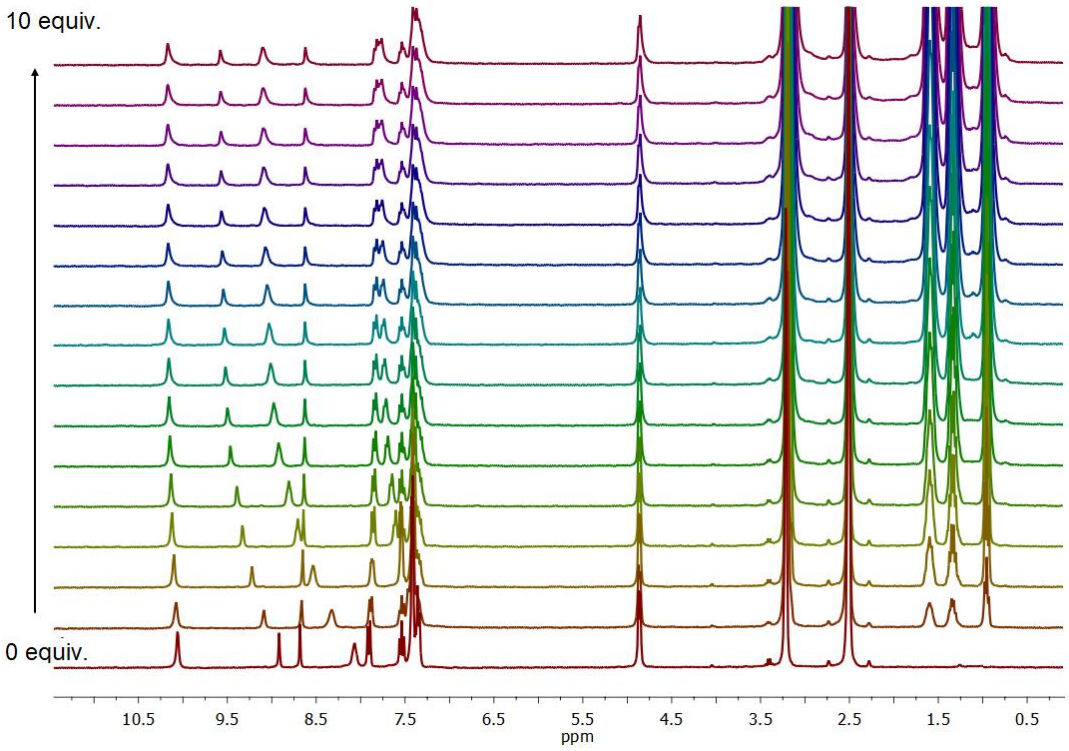

Fig. S16. Typical ^{1}H NMR spectra recorded upon titration of receptor **2** in DMSO-d_6 with TBACl at a temperature of 60°C.

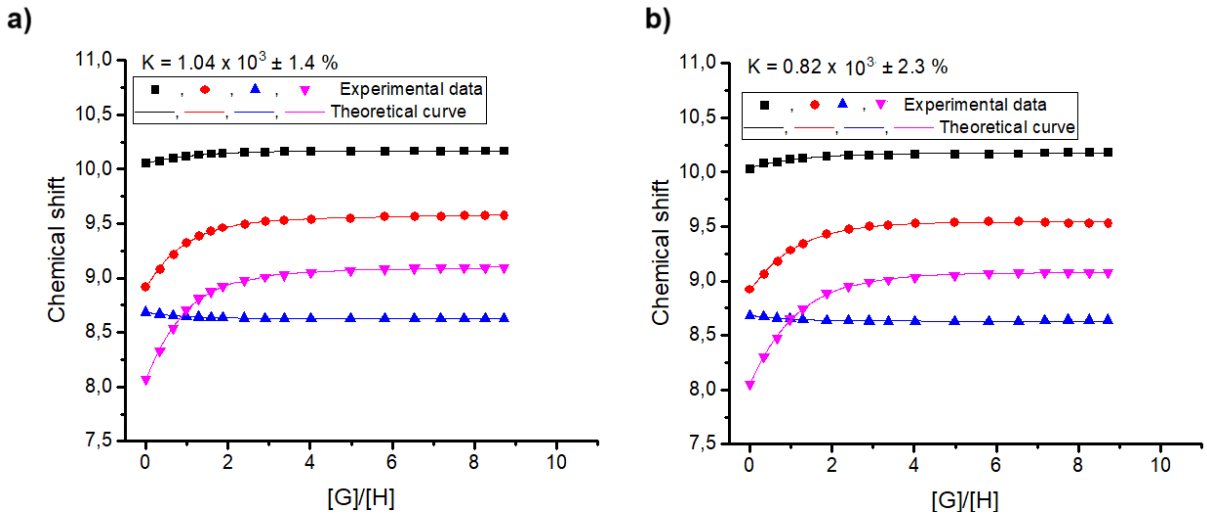

Fig. S17. ^{1}H NMR titration binding isotherms of receptor **2** in DMSO-d_6 upon addition of increasing amounts of TBACl (a) and of TBACl in the presence of 1 equiv. $NaClO_4$ (b).

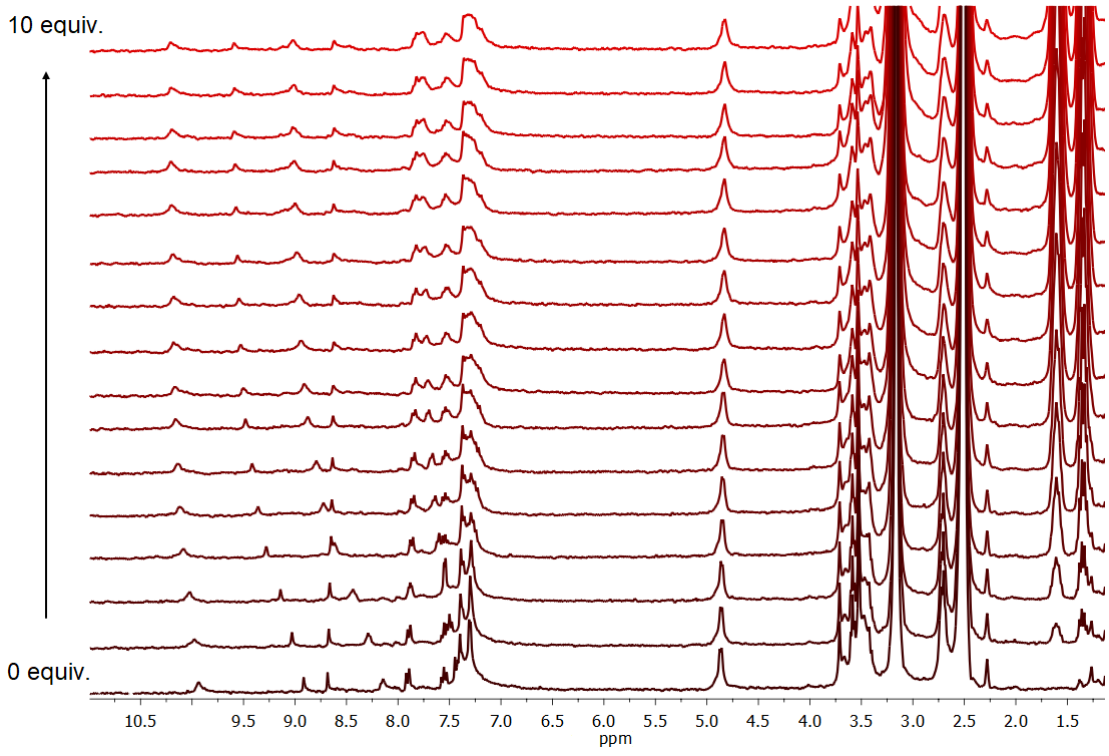

Fig. S18. Typical ^{1}H NMR spectra recorded upon titration of receptor **1** in DMSO-d_6 with TBACl at a temperature of 60°C.

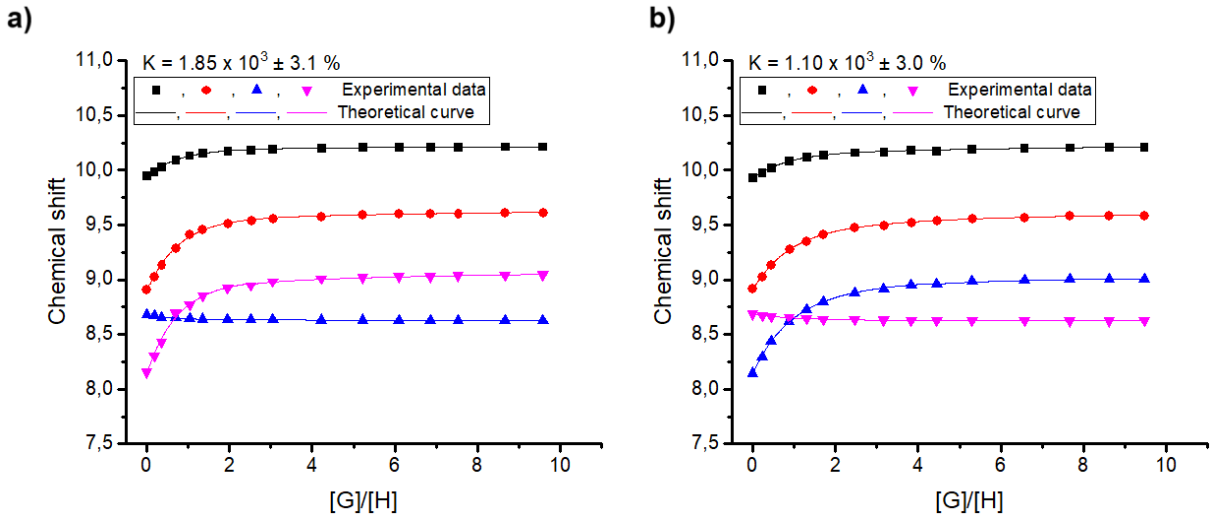

Fig. S19. ^{1}H NMR titration binding isotherms of receptor **1** in DMSO-d_6 upon addition of increasing amounts of TBACl (a) and of TBACl in the presence of 1 equiv. $NaClO_4$ (b).

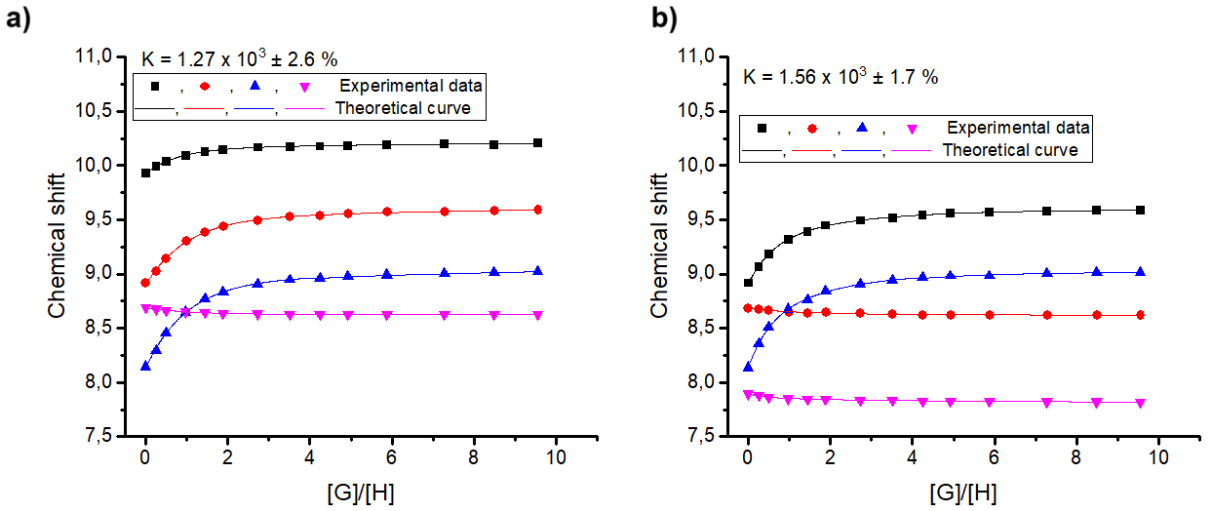

Fig. S20. ^{1}H NMR titration binding isotherms of receptor **1** in DMSO-d_6 upon addition of increasing amounts of TBACl in the presence of 1 equiv. KPF_6 (a) and of TBACl in the presence of 1 equiv. NH_4PF_6 (b).

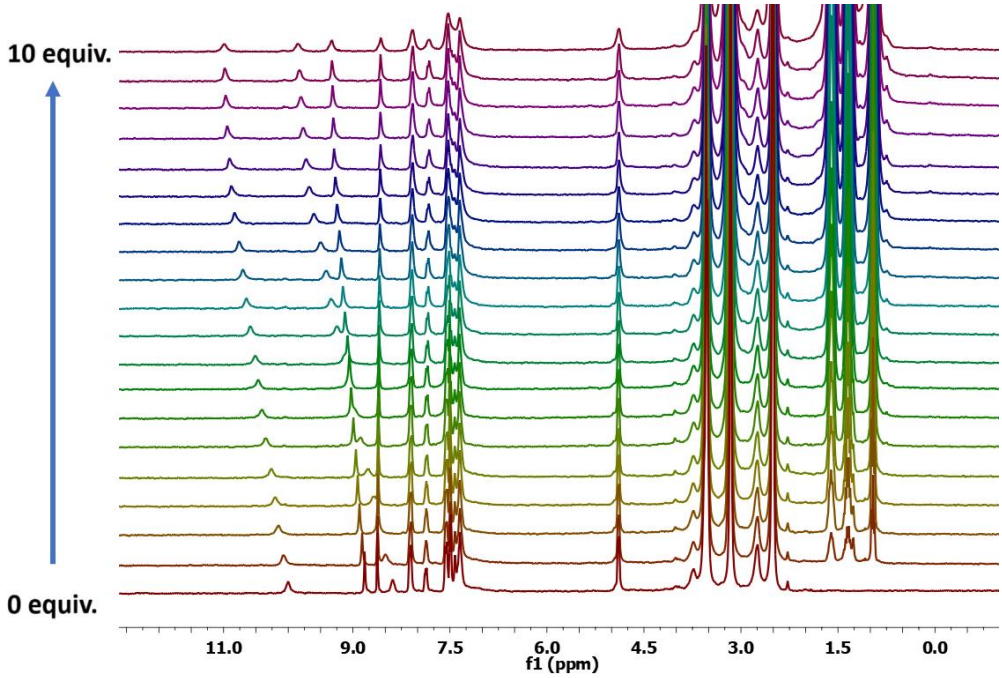

Fig. S21. Typical ^{1}H NMR spectra recorded upon titration of receptor **4** in DMSO-d_6 with TBACl at a temperature of 60°C.

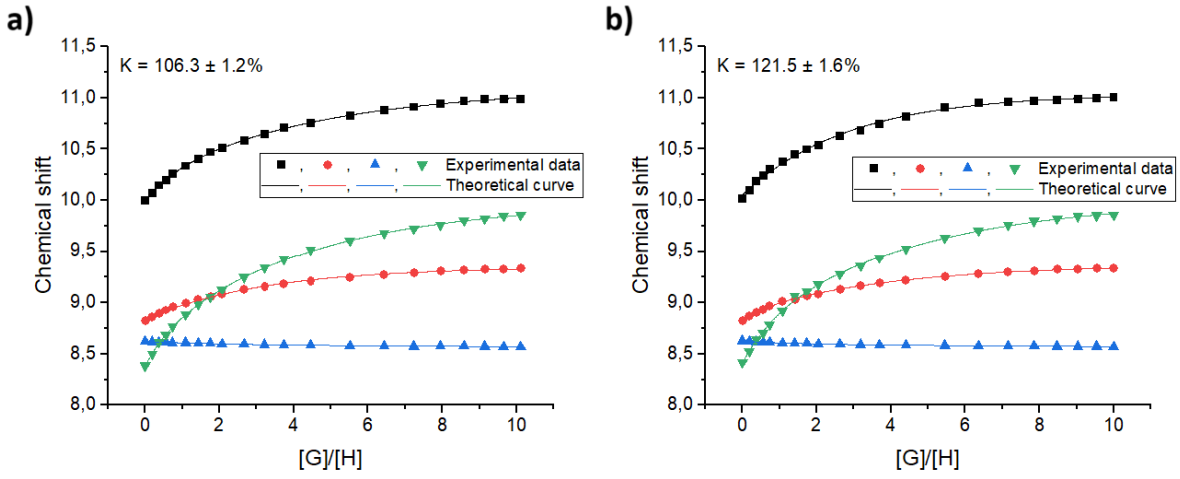

Fig. S22. ^{1}H NMR titration binding isotherms of receptor **4** in DMSO-d_6 upon addition of increasing amounts of TBACl (a) and of TBACl in the presence of 1 equiv. KPF_6 (b).

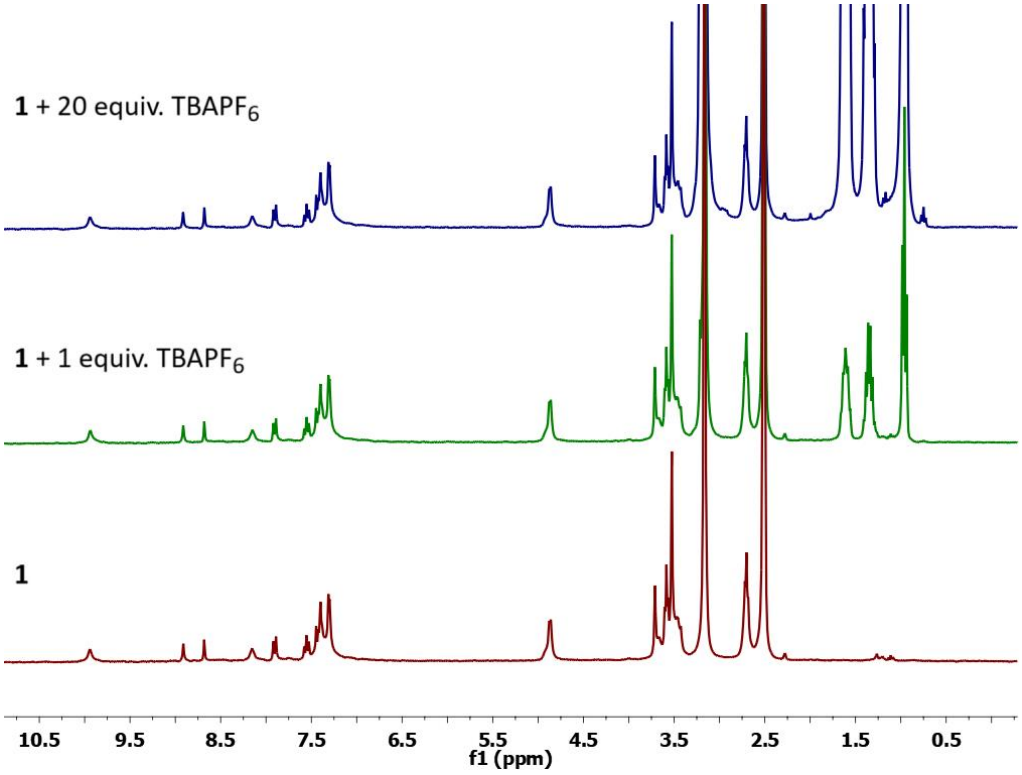

Fig. S23. ^{1}HNMR spectra of receptor **1** (2.0 mM) in DMSO-d_6 (60°C) and (b) after adding 1 or 20 equiv. of $TBAPF_6$.

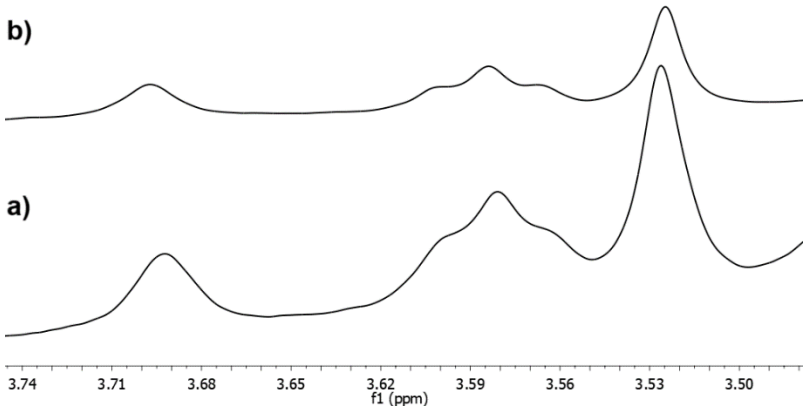

Fig. S24. Partial ^{1}HNMR spectra (a) of receptor **1** (2.0 mM) in DMSO-d_6 (60°C) and (b) upon addition 1 equiv. KPF_6 (signals corresponding to crown ether).

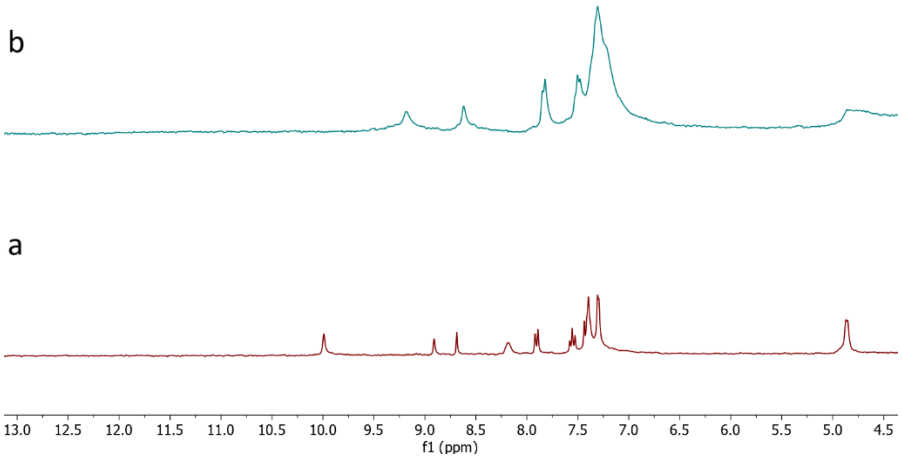

Fig. S25. Partial ^{1}HNMR spectra (a) of receptor **1** (2.0 mM) in DMSO-d_6 (60°C) and (b) after SLE with 5-AVA (signals corresponding to squaramide and aromatic).

The ^{1}H NMR titration was conducted at 298K in CD_3CN. In each case, 500 µL of freshly prepared solution of receptor **1** or **2** (2.0 mM of **1**; 1.7 mM of receptor **2**) was added to a 5 mm NMR tube, then small aliquots of solution of TBACl or $TBACOOCH_3$, containing receptor at constant concentration, were added and a spectrum was acquired after each addition.

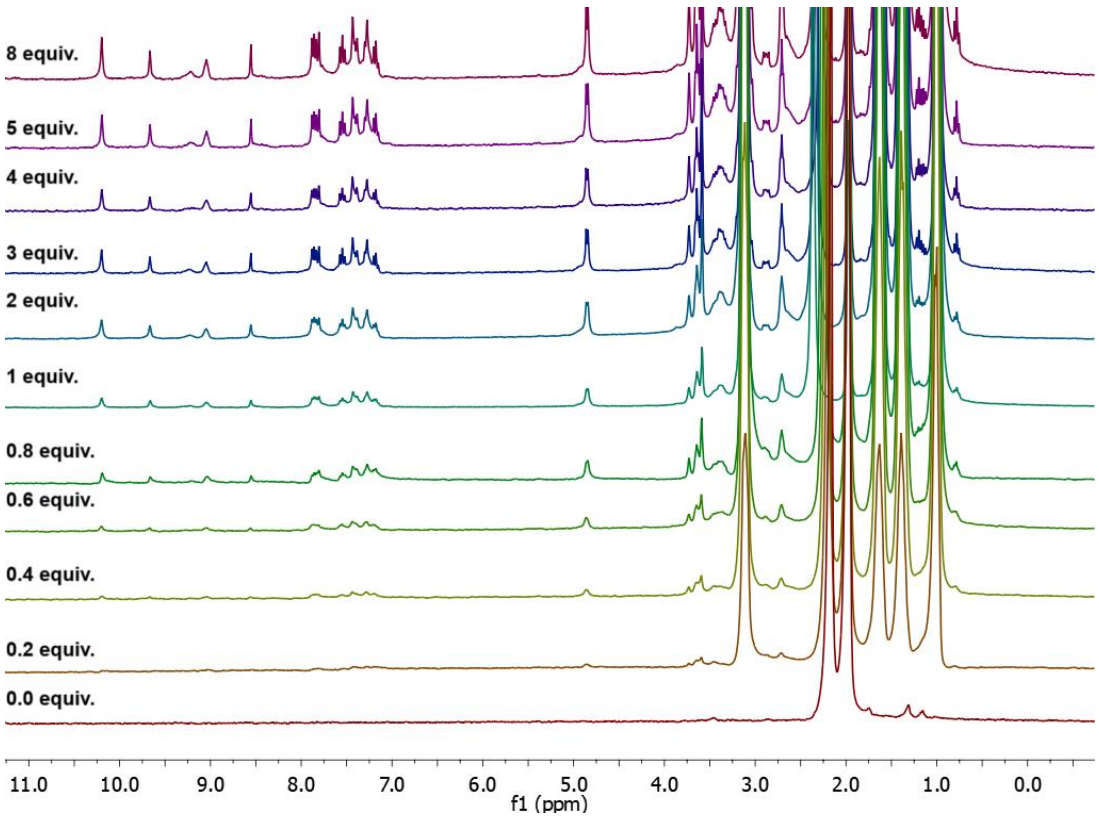

Fig. 26. ^{1}H NMR spectra recorded upon titration of receptor **1** in CD_3CN with TBACl.

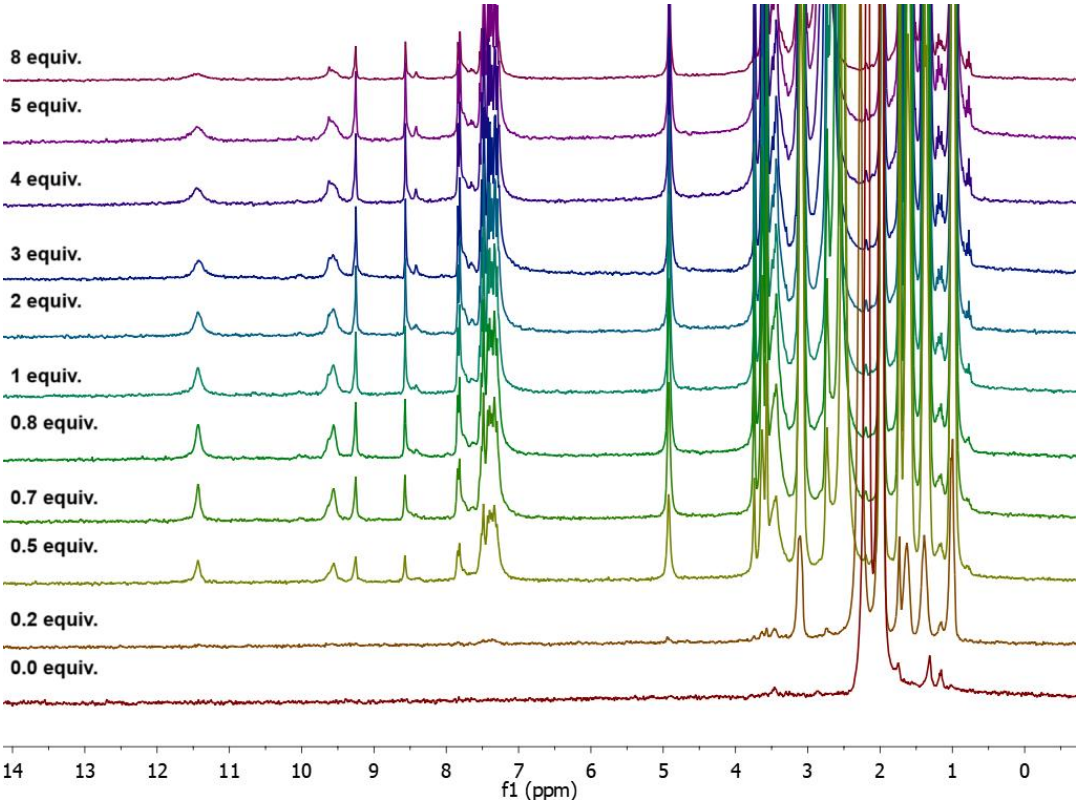

Fig. 27. ^{1}H NMR spectra recorded upon titration of receptor **1** in CD_3CN with $TBACOOCH_3$.

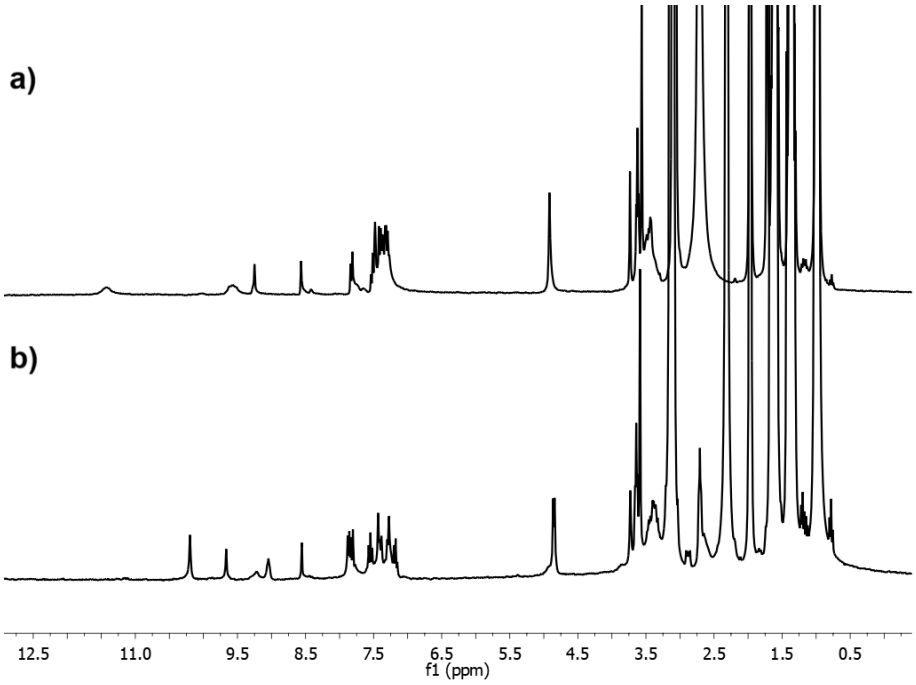

Fig. S28. ^{1}H NMR spectra (a) of receptor **1** after the addition of 3 equiv. $TBACH_3COO$ and (b) after the addition of 3 equiv. TBACl.

2D spectra

Mechanochemical encapsulation

Cryptand **1** (0.01 mmol, 0.01 g) and amino acid (0.05 mmol) were placed in a milling jar (3 mL volume) with 2 agate balls (Ø=4 mm). The milling process using a Specamill™ small grinding lasted for 1 h. The ball-milled sample was dissolved in acetonitrile, and the undissolved residue was filtered using a syringe filter. The filtrate was subjected to NMR analysis.

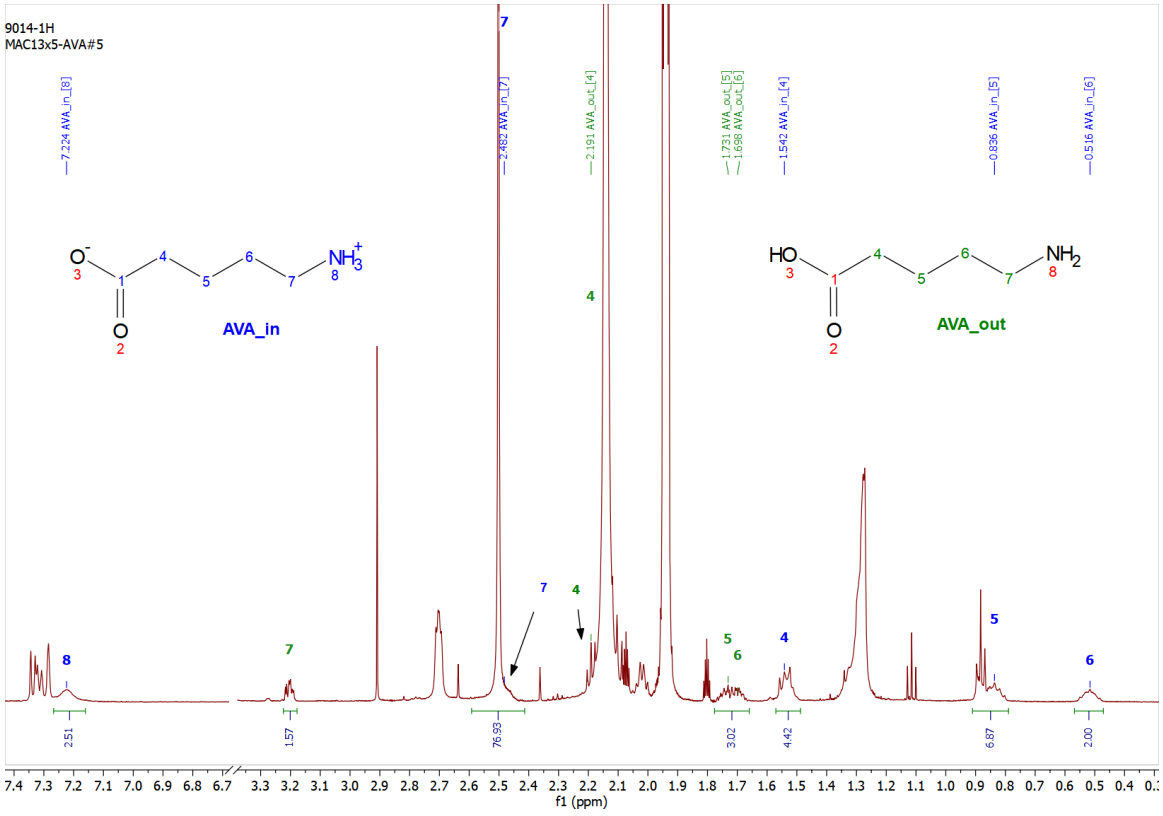

Fig. S29. ^{1}H NMR spectrum of **1**×5-AVA in CD_3CN.

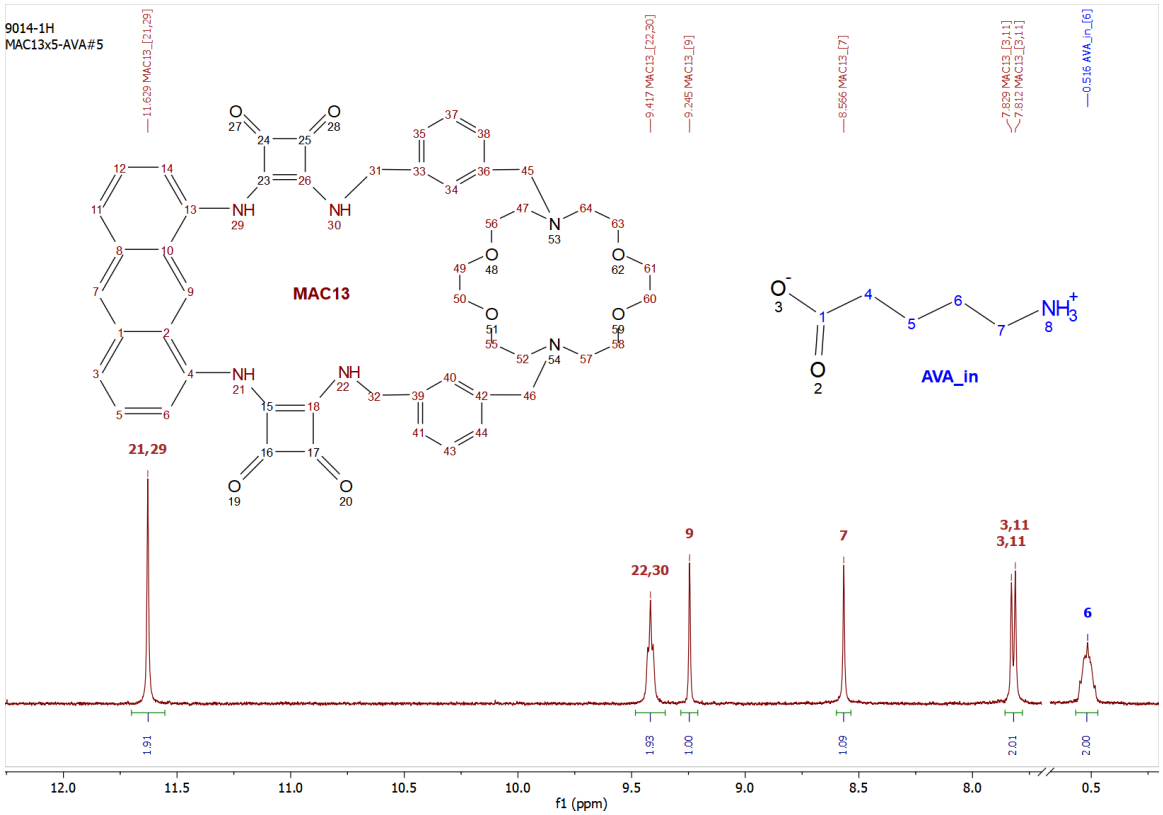

Fig. S30. ^{1}H NMR spectrum of **1**×5-AVA in CD_3CN.

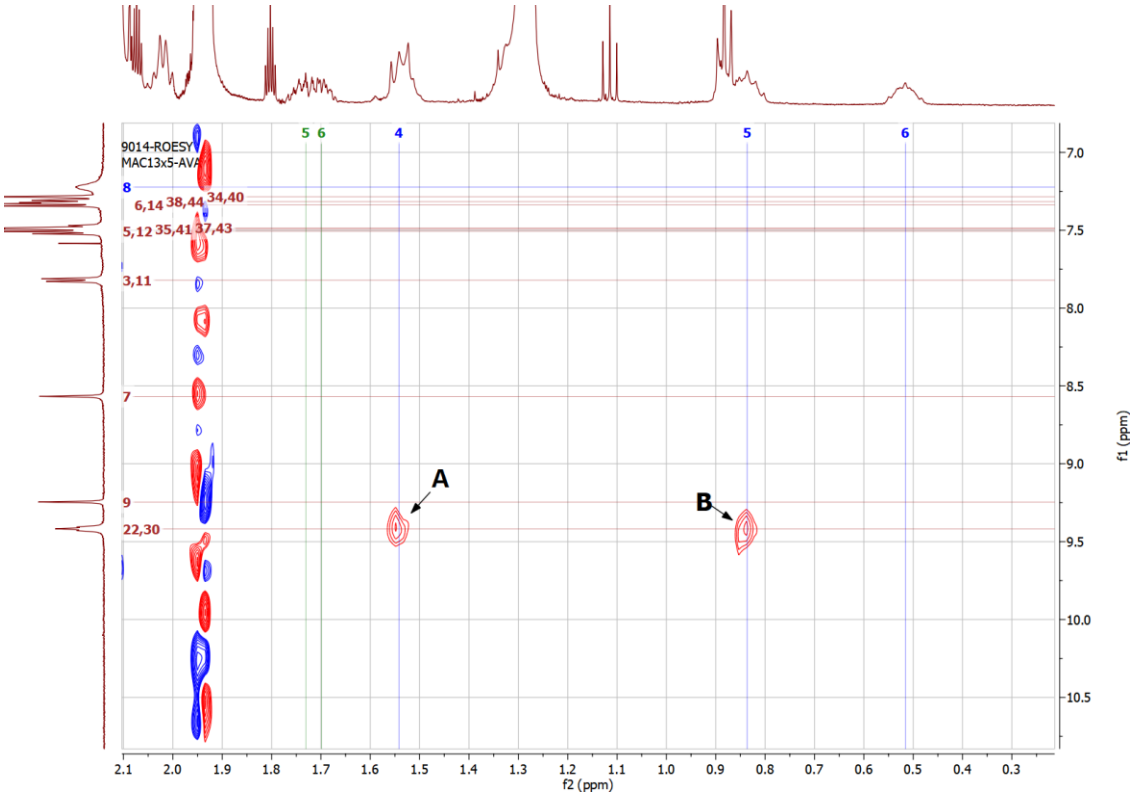

Fig. S31. ROESY NMR spectrum of **1**×5-AVA in CD_3CN.

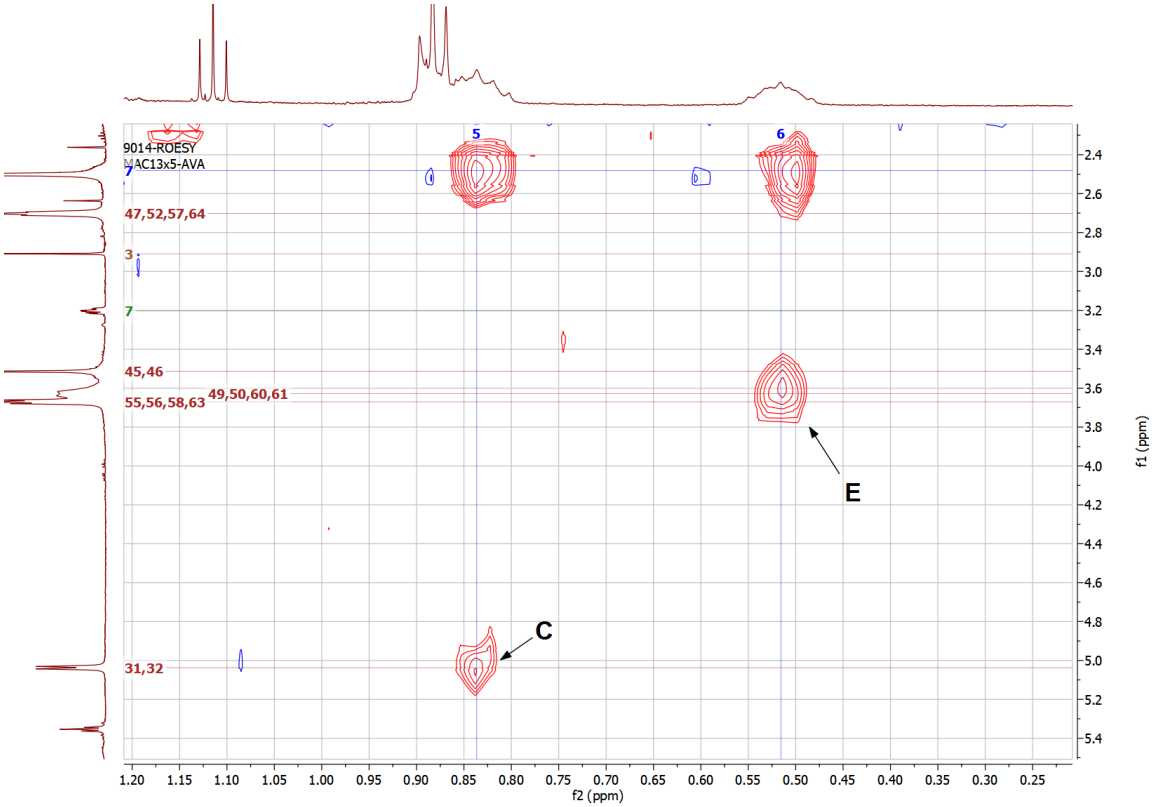

Fig. S32. ROESY NMR spectrum of **1**×5-AVA in CD_3CN.

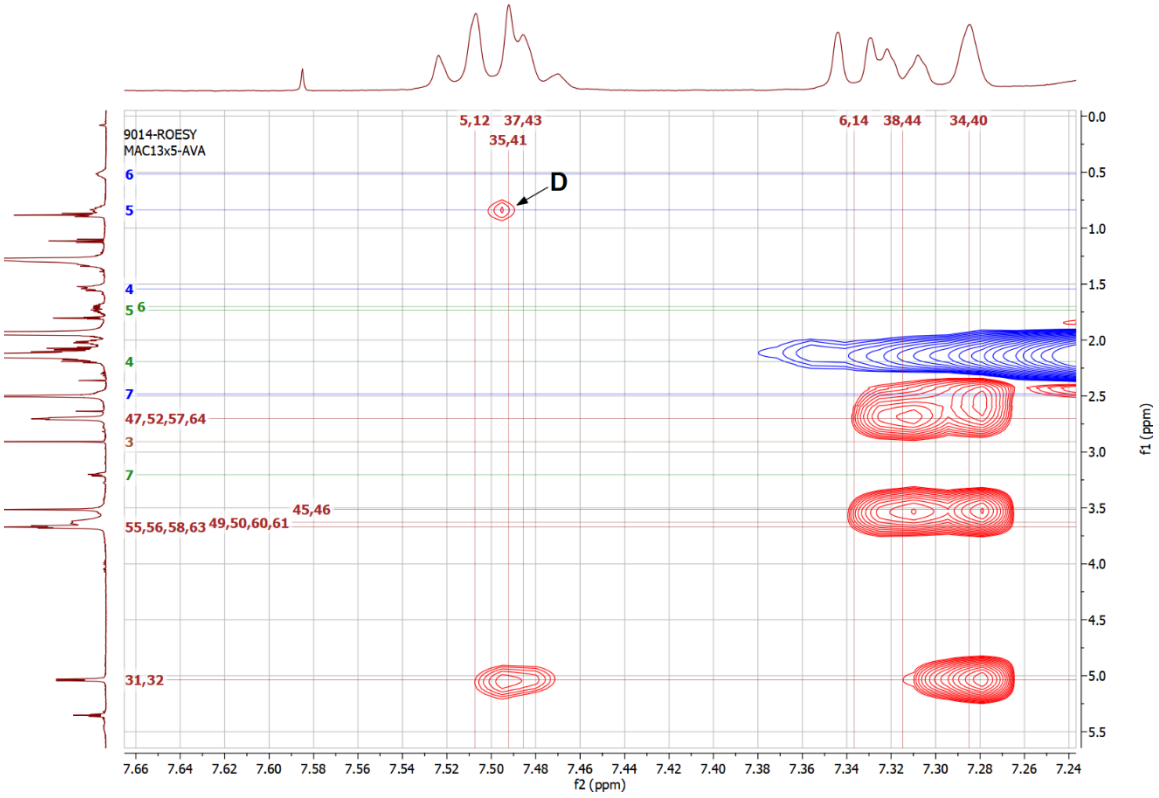

Fig. S33. ROESY NMR spectrum of **1**×5-AVA in CD_3CN.

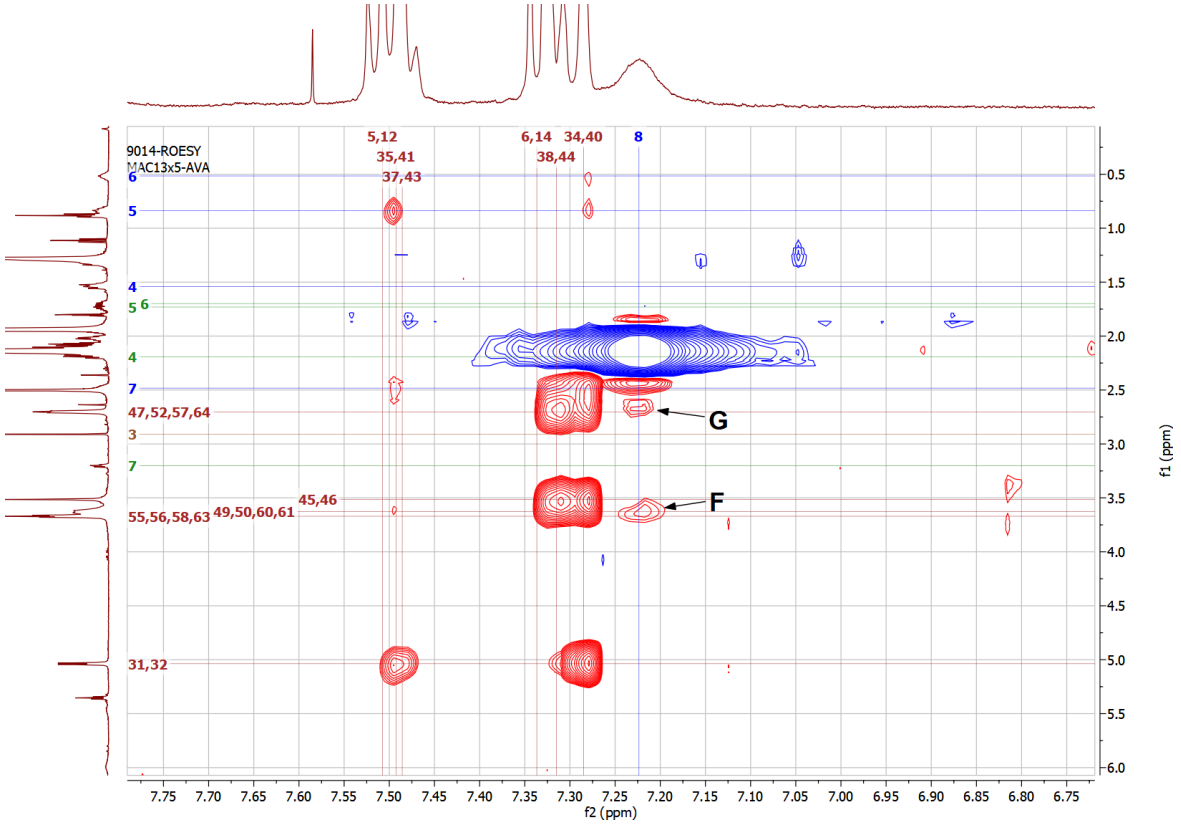

Fig. S34. ROESY NMR spectrum of **1**×5-AVA in CD_3CN.

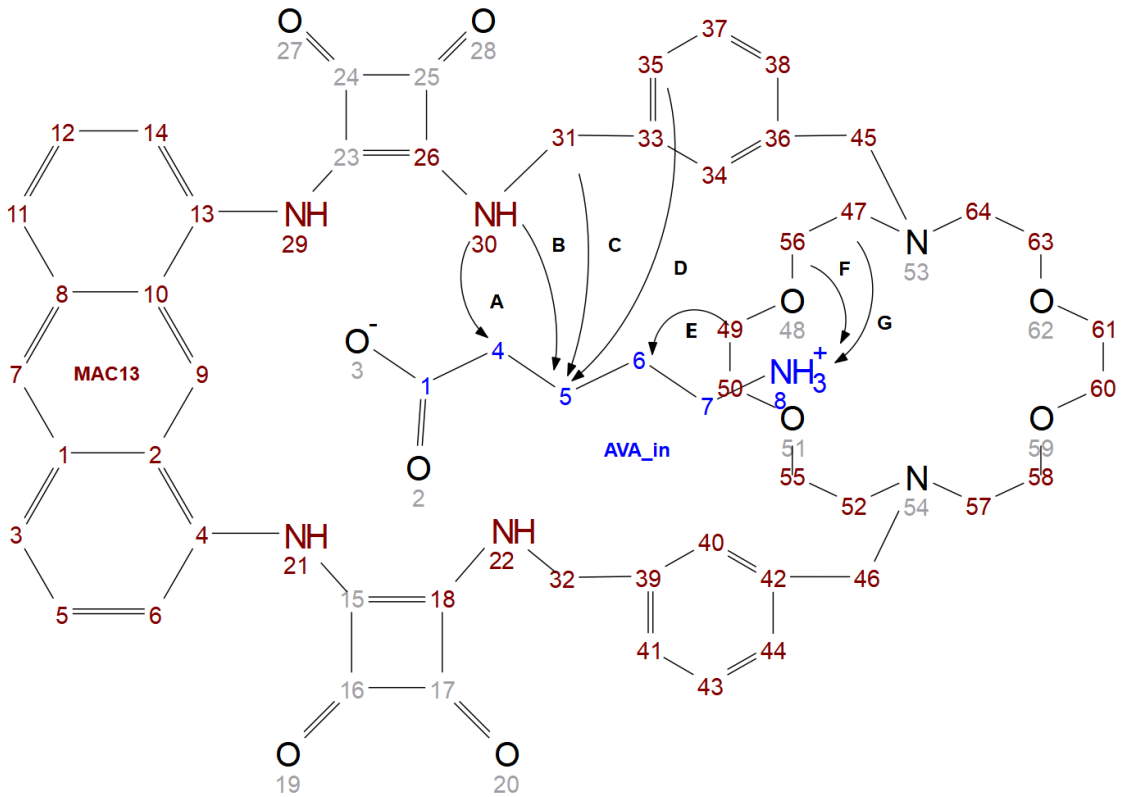

Fig. S35. Interaction scheme of cryptand **1** with the 5-AVA molecule.

Fluorescence experiments

To the solution of receptor **1** or **2** (c = 1.0-2.0 × 10^{-6} M) in CH_3CN were added aliquots of TBAX solution containing the appropriate receptor at the same concentration as in the cuvette. Successive scans were performed measuring fluorescence (λ_{ex}= 418 nm). Fluorescence emission spectra were measured on a Hitachi F-7100 Fluorescence Spectrophotometer at 298K.

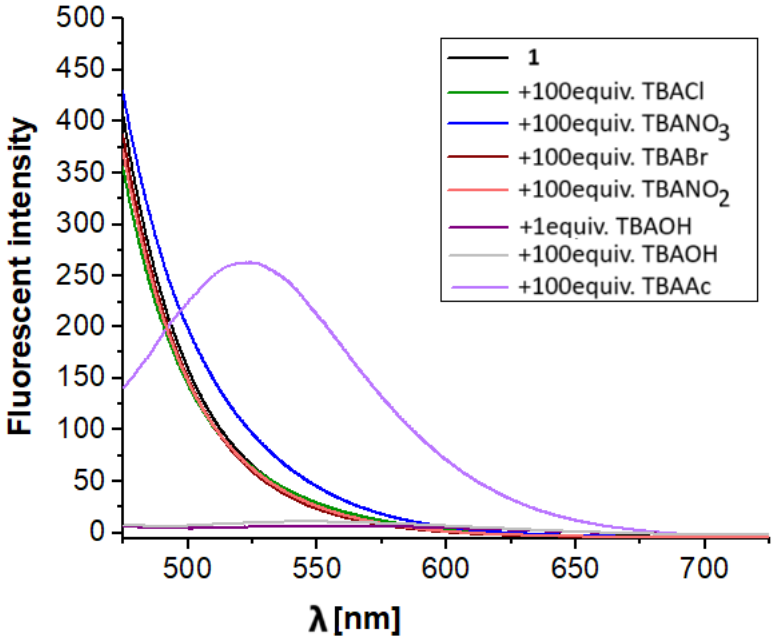

Fig. S36. Emission spectra of receptor **1** (1.0 × 10^{-6} M) and upon addition of TBA salts (excitation at 418 nm) in CH_3CN.

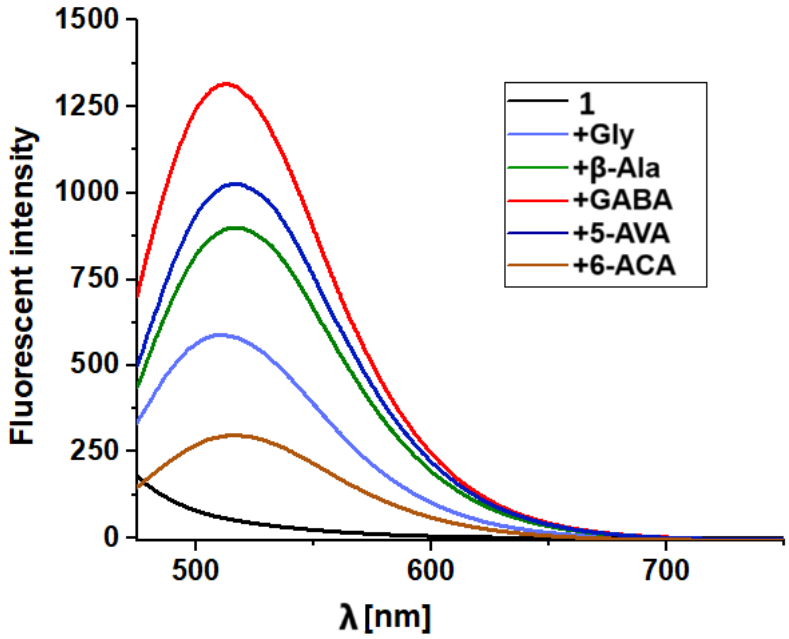

Fig. S37. Emission spectra of sensor **1** (1.0×10^{-6} M) and after amino acid solid-liquid extraction (excitation at 418 nm) in CH_3CN.

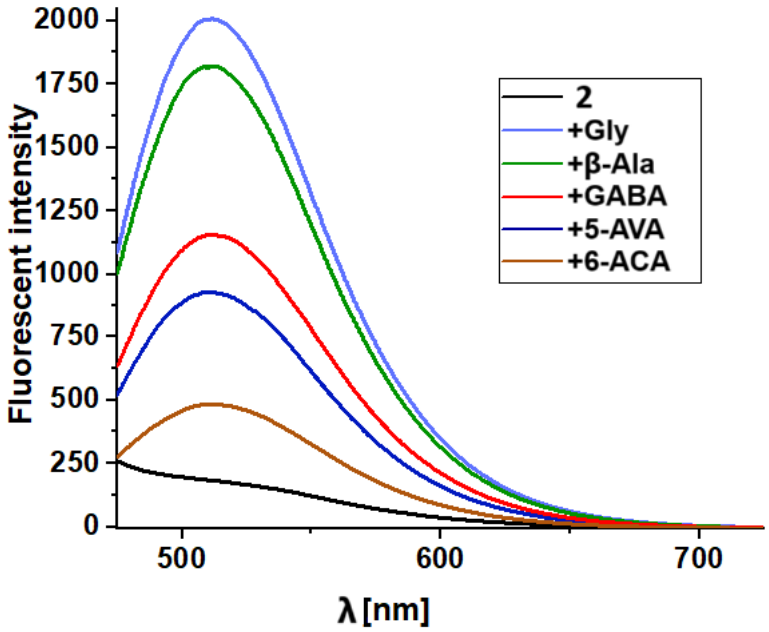

Fig. S38. Emission spectra of receptor **2** (1.5×10^{-6} M) and after amino acid solid-liquid extraction (excitation at 418 nm) in CH_3CN.

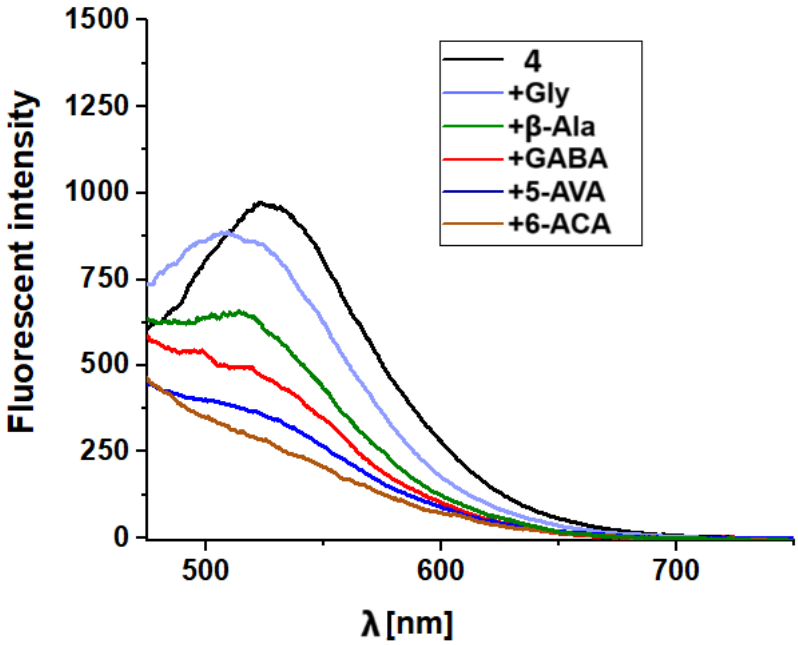

Fig. S39. Emission spectra of receptor **4** (1.0×10^{-6} M) and after amino acid solid-liquid extraction (excitation at 418 nm) in CH_3CN.

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