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Supplementary information

For

Trimacrocyclic hexasubstituted benzenes for recognition of guanidinium and the anti-cancer and antimicrobial activity

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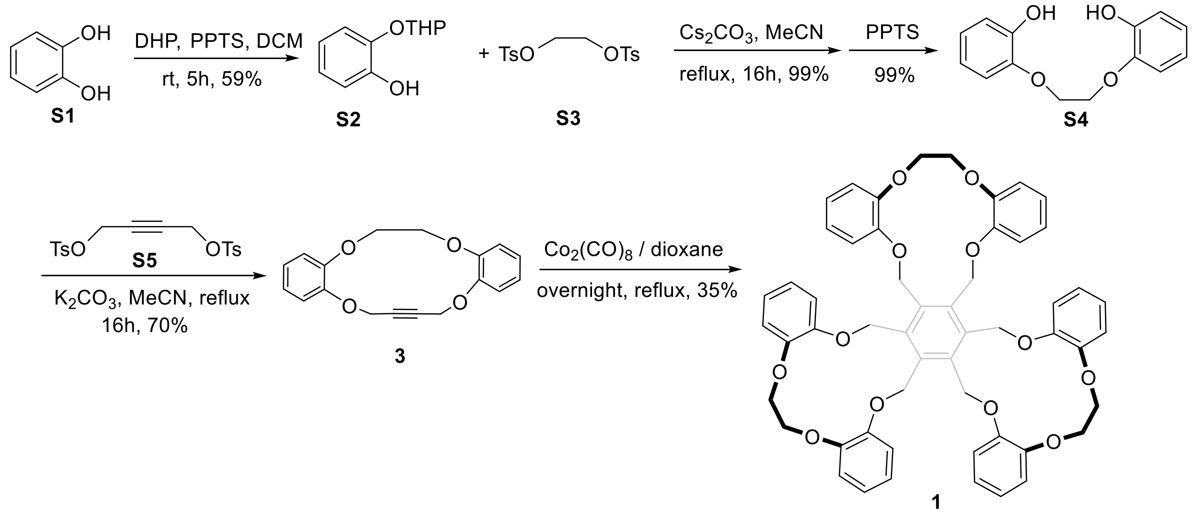
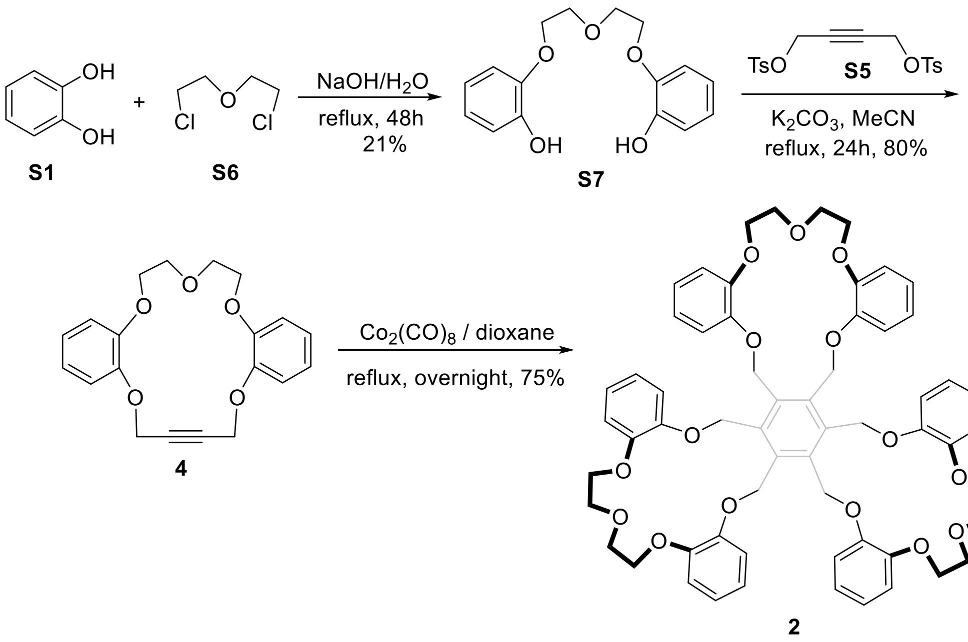
1. General information

All solvents and chemicals used were purchased from Sigma–Aldrich, TCI, Energy–Chemical, or Acros and used without further purification. TLC analyses were carried out using Sorbent Technologies silica gel (200 mesh) sheets. Flash column chromatography was performed on silica gel (300–400 mesh). ^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE 400 spectrometers and the spectroscopic solvents were purchased from Cambridge Isotope Laboratories or Sigma–Aldrich. Residue solvent or tetramethylsilane (TMS) was used as an internal reference. The chemical shifts are expressed in δ (ppm). High–resolution mass spectra (HRMS) were recorded on a Bruker Apex–Q IV FTMS mass spectrometer using ESI (electrospray ionization) employing a mixture of $CHCl_3/CH_3OH$ (9:1, v/v) as the solvent. X–ray crystallographic analyses were carried out on a Brucker D8 Advance diffractometer using a μ–focused Mo Kα radiation source (λ = 0.71073 Å) or a Brucker D8 Venture diffractometer using a μ–focused Cu Kα radiation source (λ = 1.5418 Å) or on a ROD. All theoretical calculations were carried out with the Gaussian 16 suite[1] of programs using the X3LYP density functional.[2] Structural optimization was performed using a 6–31G* basis set while single–point energies were calculated using the 6–31++g** basis set by a SMD model ($CHCl_3$). Complexation energies were corrected for basis set superposition error (BSSE) using the counterpoise correction method.[3-4]

2. Synthesis



Scheme S1. Synthesis of receptor **1**.



Scheme S2. Synthesis of receptor **2**.

Compounds **S1** and **S6** are commercially available.

Synthesis of S2

Catechol **S1** (17.62 g, 0.16 mol) was dissolved in CH_2Cl_2 (90 mL). Pyridinium *p*-toluenesulfonate (PPTS, 534 mg, 2.125 mmol) and dihydropyran (14.65 ml, 0.16 mol) were added and stirred for 5 h until the solution was completely clarified. The resulting mixture was washed with water (3 × 50 mL). The organic layer was then separated and dried over anhydrous Na_2SO_4. Next, the solvent was removed under vacuum. The obtained solid was redissolved in a mixture of petroleum ether and CH_2Cl_2 (50/50, v/v). After filtration through silica gel and removal of solvent, the product was obtained as pale yellow oil. Yield: 18.30 g (59% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, J = 8.0 Hz, 1H), 6.96 (d, J = 4.4 Hz, 2H), 6.86-6.77 (m, 1H), 6.63 (s, 1H), 5.19 (dd, J = 5.3, 2.3 Hz, 1H), 4.03-3.98 (m, 1H), 3.66-3.60 (m, 1H), 2.00-1.85 (m, 3H), 1.72-1.60 (m, 3H).[5]

Synthesis of S3

To a solution of ethylene glycol (1.55 g, 25.0 mmol) in THF (50 mL), 50 mL of NaOH (5.55 g, 138.75 mmol) in water was added. After cooling to 0 °C, to the mixture a solution of *p*-tosyl chloride (10.49 g, 55.0 mmol) in THF (75 mL) was added dropwise over the course of 1 h. The resulting mixture was stirred at 0 °C for 2 h and then extracted with EtOAc. The organic phase was washed with saturated $NaHCO_3$, brine, then dried over anhydrous $MgSO_4$. After filtration, the solvent was removed under reduced pressure to give a white solid (7.4 g, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.67 (m, 4H), 7.33 (d, J = 8.1 Hz, 4H), 4.18 (s, 4H), 2.45 (s, 6H).[6]

Synthesis of S4

Compound **S2** (4.895 g, 25.2 mmol) was dissolved in dry MeCN (60 mL), to which Cs_2CO_3 (9.03 g, 27.72 mmol) was added. The resulting mixture was then heated at reflux for 15 min. To the reaction solution a dry MeCN (60 mL) solution of **S3** (4.445 g, 12 mmol) was added dropwise. The resulting mixture was refluxed for an additional 16 h. The reaction mixture was next cooled to room temperature. The precipitates were filtered off and the filtrate was concentrated under reduced pressure to give the crude product, which was further purified by silica gel column chromatography (petroleum ether / ethyl acetate = 6:1, eluent) to afford a white solid (4.92 g, 99% yield). Then the white solid was dissolved in a mixture of CH_2Cl_2 (40 mL) and MeOH (110 mL), followed by addition of pyridinium *p*-toluenesulfonate (PPTS, 616 mg, 2.45 mmol). The resulting solution was heated at 45 °C for 4h. After removal of the solvent, the residue was redissolved in DCM (40 mL), which was subsequently wash with water (3 × 40 mL). The organic layers were combined and dried over anhydrous Na_2SO_4. After removal of the solids by filtration, the solvent was removed to give the desired product as a white solid (2.90 g, 99% yield). ^1H NMR (400 MHz, DMSO-d_6) δ 8.91 (s, 1H), 6.98 (dd, J = 7.7, 1.5 Hz, 1H), 6.84-6.70 (m, 3H), 4.28 (s, 2H).[5, 7]

S5 was synthesized according to literature procedures.[6, 8]

Synthesis of precursor 3

To a stirred solution of bisphenol **S4** (2.46 g, 10 mmol) in dry MeCN (120 mL), K_2CO_3 (6.91 g, 50 mmol) was added. The reaction mixture was then heated at reflux for 30 min. A dry MeCN (120 mL) solution of 2-butyne-1,4-diol ditosylate **S5** (3.94 g, 10 mmol) was then added to the mixed solution, followed by refluxing for 24 h. After the reaction mixture was cooled to room temperature, the suspension was filtered off and the filtrate was concentrated under reduced pressure to give the crude product, which was further purified by silica gel column chromatography (petroleum ether/ethyl acetate = 6/1, eluent) to afford precursor **3** as a white solid (2.07 g, 70% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.09-7.01 (m, 4H), 6.98-6.89 (m, 4H), 4.72 (s, 4H), 4.44 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 147.9, 124.5, 121.8, 121.4, 113.8, 82.6, 67.4, 62.1. HRMS (ESI) m/z 297.1121 $[M + H]^+$ calcd for $C_{18}H_{17}O_4$, found 297.1118. HRMS (ESI) m/z 319.0941 $[M + Na]^+$ calcd for $C_{18}H_{16}O_4Na$, found 319.0936.

Synthesis of compound 1

To a solution of intermediate **3** (770 mg, 2.6 mmol) in anhydrous dioxane (45 mL) in an oven dried Schlenk flask, $Co_2(CO)_8$ (89 mg, 0.26mmol) was added. The reaction mixture was heated at reflux for 16 h under an N_2 atmosphere. After the reaction was completed (as inferred from TLC monitoring), the filtrate was concentrated and further purified by silica gel column chromatography (dichlormethane/methanol = 50:1, eluent) to afford **1** (270 mg, 35% yield) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, J = 4.2 Hz, 12H), 6.94 (d, J = 7.8 Hz, 6H), 6.84-6.77 (m, 6H), 5.70 (s, 12H), 4.53 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 149.2, 138.8, 124.5, 122.9, 122.3, 114.9, 68.8, 67.2. HRMS (ESI) m/z 911.3038 $[M + Na]^+$ calcd for $C_{54}H_{48}O_{12}Na$, found 911.3022.

Synthesis of S7

To a solution of catechol **S1** (27.53 g, 250.0 mmol) and NaOH (3.44 g, 86 mmol) in water (200 mL) under nitrogen, 2,2'-Dichlorodiethyl ether (6.03 g, 42.2 mmol) was added dropwise over the course of 3 h. The mixture was heated at reflux for 48 h. After the reaction solution was cooled to room temperature, it was extracted with EtOAc (3 × 100 mL). Then the organic phases were combined dried over anhydrous $MgSO_4$. After removal of the solids by filtration, the filtrate was concentrated under reduced pressure. The resulting crude product was subjected to column chromatography over silica gel (petroleum ether /ethyl acetate = 2:1, eluent) to afford **S7** as a white solid (4.29 g, 35% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.88 (s, 2H), 6.92 (dd, J = 7.8, 1.6 Hz, 2H), 6.82-6.68 (m, 6H), 4.13-4.05 (m, 4H), 3.86-3.78 (m, 4H).[8-9]

Synthesis of precursor 4

To a stirred solution of bisphenol **S7** (499 mg, 1.72 mmol) in dry MeCN (20 mL), K_2CO_3 (1.19 g, 8.60 mmol) was added. The reaction mixture was then heated at reflux for 30 min, to which a dry MeCN (20 mL) solution of **S5** (678 mg, 1.72 mmol) was then added, followed by refluxing for 24 h. The reaction mixture was cooled and filtered. The filtrate was concentrated under reduced pressure to give the crude product, which was further purified by silica gel column chromatography (petroleum ether/ethyl acetate = 2:1, eluent) to afford precursor **4** as a white solid (468 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01-6.86 (m, 8H), 4.71 (s, 4H), 4.19 (t, J = 5.2 Hz, 4H), 4.05 (t, J = 5.3 Hz, 4H).[8, 10]

Synthesis of compound 2

To a solution of intermediate **4** (408 mg, 1.2 mmol) in anhydrous dioxane (20 mL) in an oven dried Schlenk flask, $Co_2(CO)_8$ (41 mg, 0.12 mmol) was added. The reaction mixture was heated at reflux for 12 h under N_2 atmosphere. At the conclusion of the reaction (as inferred from TLC monitoring), the filtrate was concentrated and further purified by silica gel column chromatography (dichlormethane/methanol = 20:1, eluent) to afford **2** (306 mg, 75% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99-6.87 (m, 12H), 6.85-6.76 (m, 12H), 5.57 (s, 12H), 4.17-4.05 (m, 12H), 3.83-3.70 (m, 12H). ^{13}C NMR (100 MHz, CDCl3) δ 150.3, 148.6, 138.2, 122.4, 121.0, 118.5, 113.4, 69.5, 67.8, 67.5. HRMS (ESI) m/z 1043.3824 $[M + Na]^+$ calcd for $C_{60}H_{60}O_{15}Na$, found 1043.3810. HRMS (ESI) m/z 1059.3564 $[M + K]^+$ calcd for $C_{60}H_{60}O_{15}K$, found 1059.3551.

3. Host-guest binding studies of 1 and 2

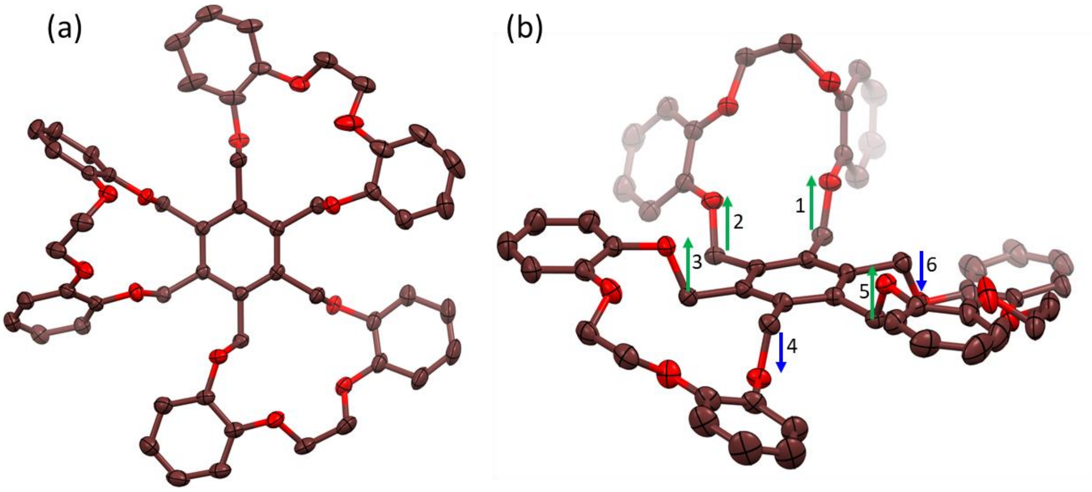


Fig. S1. (a) Top view and (b) side view of the single-crystal structure of compound **1** shown in ellipsoid model. In the solid state, the arms of hexasubstituted benzene core adopts *aaabab* positions above (*a*, green arrows) and below (*b*, blue arrows) the ring. Displacement ellipsoids are scaled to the 50% probability level. All disordered solvent molecules and hydrogen atoms are omitted for clarity.

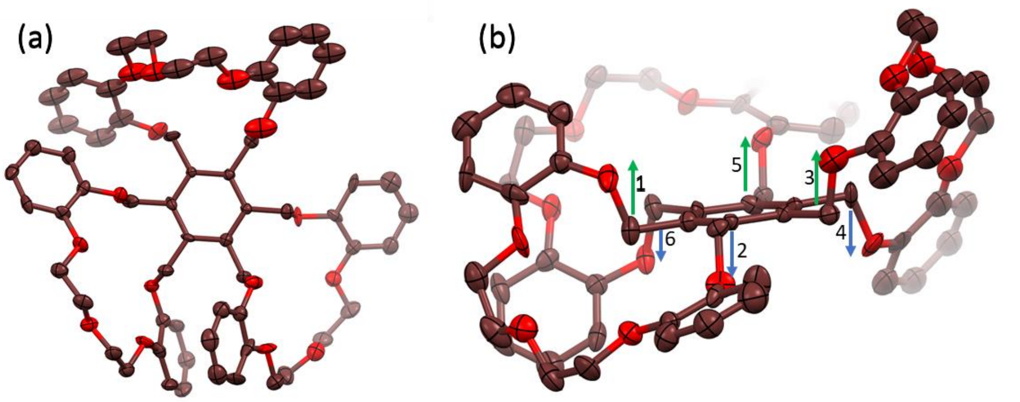


Fig. S2. (a) Top view and (b) side view of the single-crystal structure of compound **2** shown in ellipsoid model form. In the solid state, the arms of hexasubstituted benzene core adopts *alternative ababab* positions above (*a*, green arrows) and below (*b*, blue arrows) the ring. Displacement ellipsoids are scaled to the 50% probability level. All disordered solvent molecules and hydrogen atoms are omitted for clarity.

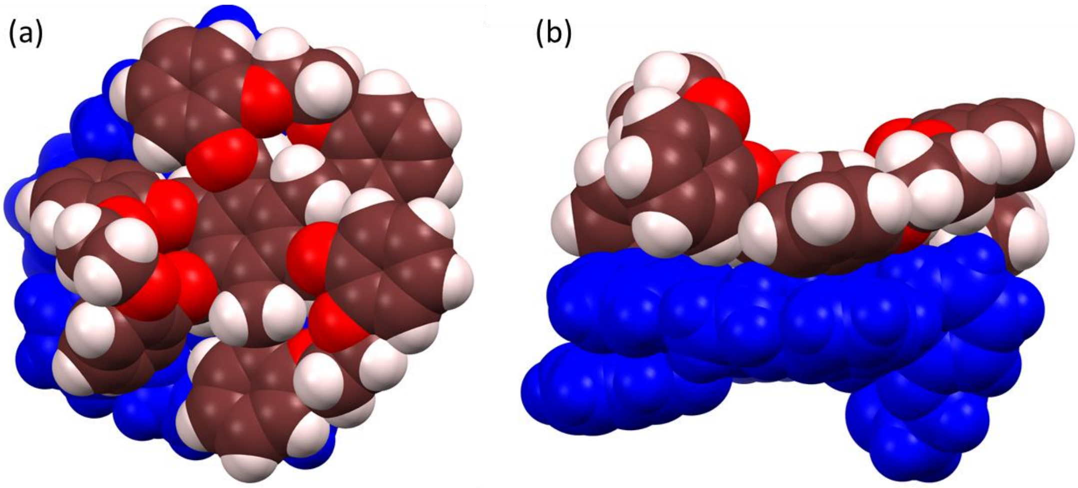


Fig. S3. (a) Top view and (b) front view of dimeric **1**$_2$ shown in ellipsoid form. One molecule of the dimer was shown in blue. Displacement ellipsoids are scaled to the 50% probability level. All disordered solvent molecules and hydrogen atoms are omitted for clarity. No such dimers are seen in the case of compound **2**.

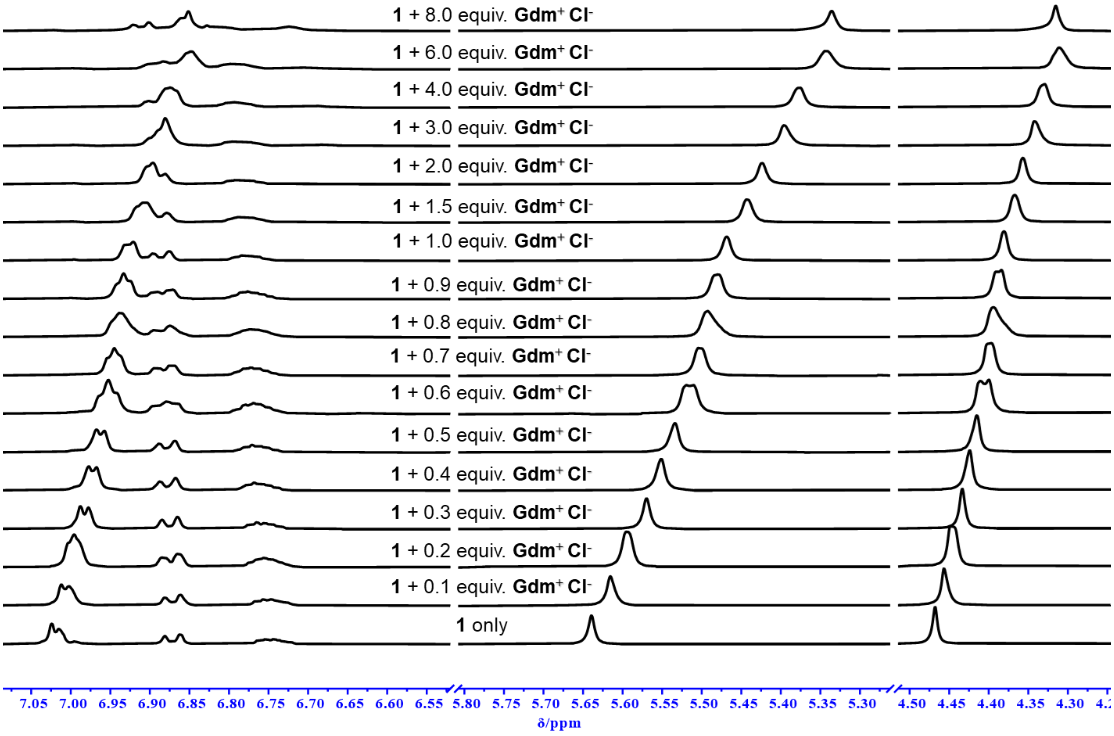


Fig. S4. Selected regions of ^{1}H NMR spectra (CDCl$_3$/CD$_3$OD (9/1, v/v), 298 K) acquired during the titration of **1** with increasing quantities of guanidinium chloride (**Gdm$^+$Cl$^-$**): 0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.5, 2.0, 3.0, 4.0, 6.0, and 8.0 equiv.

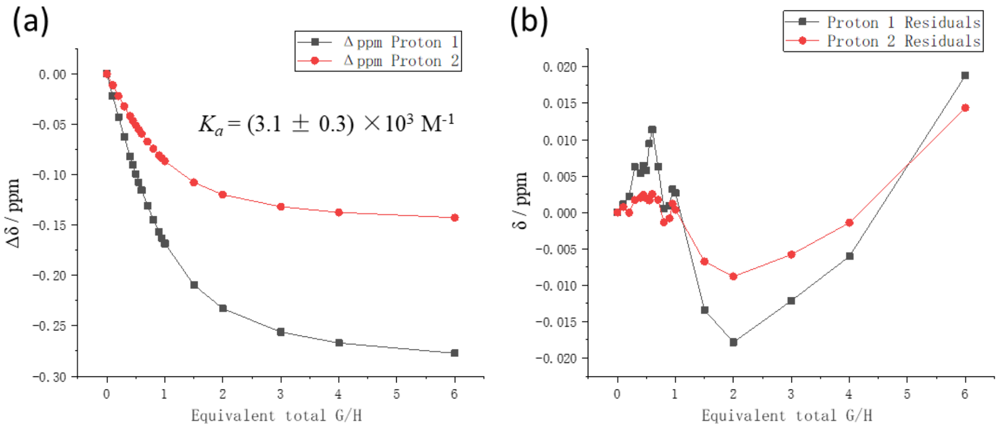


Fig. S5. Nonlinear least-square analysis of the ^{1}H NMR binding data corresponding to the formation of [**1•Gdm**]$^+$ complex. The data were fitted to a 1:1 binding model to give $K_a = (3.1 \pm 0.3) \times 10^3$ M^{-1}. The residual distribution is shown below the binding isotherm. All solid lines were obtained from non-linear curve-fitting to a 1:1 binding model using the www.supramolecular.org web applet.[11]

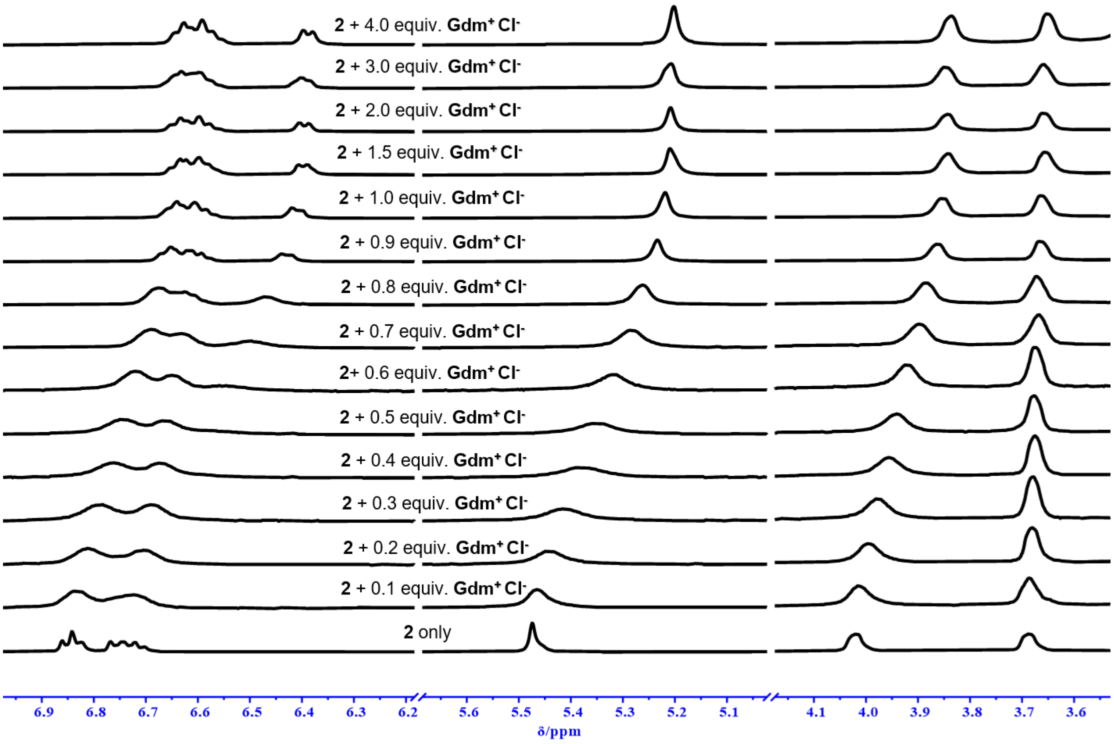


Fig. S6. Selected regions of ^{1}H NMR spectra (CDCl$_3$/CD$_3$OD (9/1, v/v), 298 K) acquired during the titration of **2** with increasing quantities of guanidinium chloride (Gdm$^+$Cl$^-$): 0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.5, 2.0, 3.0 and 4.0 equiv.

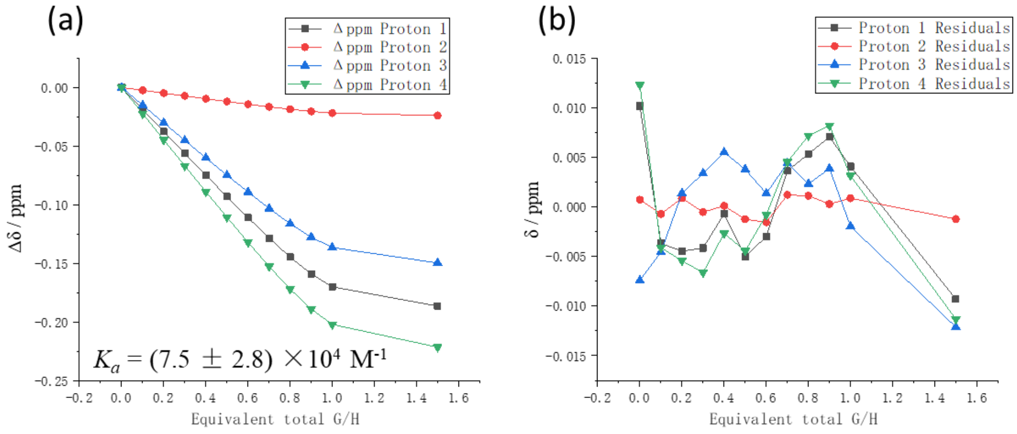


Fig. S7. Nonlinear least-square analysis of the ^{1}H NMR binding data corresponding to the formation of [**2**•Gdm]$^+$ complex. The data were fitted to a 1:1 binding model to give $K_a = (7.5 \pm 2.8) \times 10^4$ M^{-1}. The residual distribution is shown below the binding isotherm. All solid lines were obtained from non-linear curve-fitting to a 1:1 binding model using the www.supramolecular.org web applet.[11]

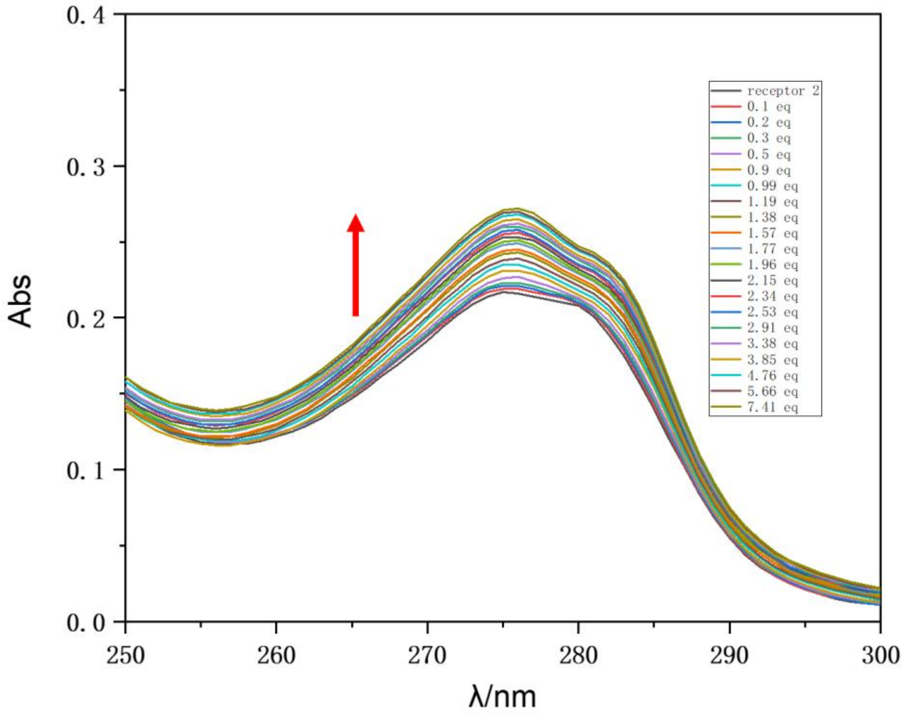
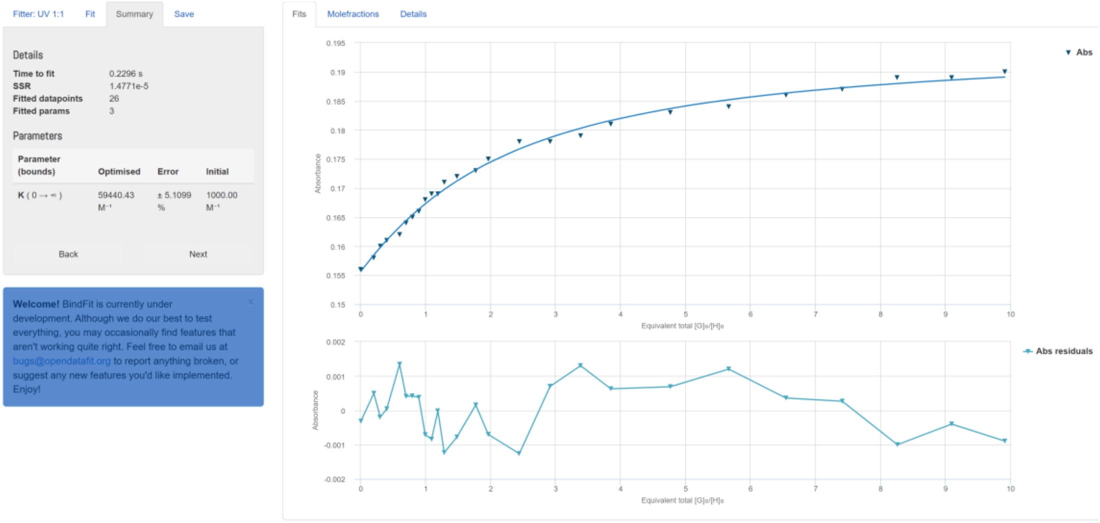


Fig. S8. UV–vis spectroscopic titration of the addition of Guanidinium chloride (0, 0.1, 0.2, 0.3, 0.5, 0.9, 0.99, 1.19, 1.38, 1.57, 1.77, 1.96, 2.15, 2.34, 2.53, 2.91, 3.38, 3.85, 4.76, 5.66, and 7.41, respectively.) to a solution of **2** (1.0×10^{-5} M) in a mixture of $CHCl_3$/MeOH (9:1, v/v).



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Fitted datapoints 26
Fitted params 3

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Welcome! BindFit is currently under development. Although we do our best to test everything, you may occasionally find features that aren't working quite right. Feel free to email us at bugs@opendatafit.org to report anything broken, or suggest any new features you'd like implemented. Enjoy!

Fig. S9. Nonlinear least-square analysis of the UV-Vis binding data (at 275 nm) corresponding to the formation of [**2**•Gdm]$^+$ complex. The data obtained from Fig. S8 were fitted to a 1:1 binding model to give K_a = (5.9 ± 0.3) ×10^4 M^{-1}. The residual distribution is shown below the binding isotherm. All solid lines were obtained from non-linear curve-fitting to a 1:1 binding model using the www.supramolecular.org web applet.[11]

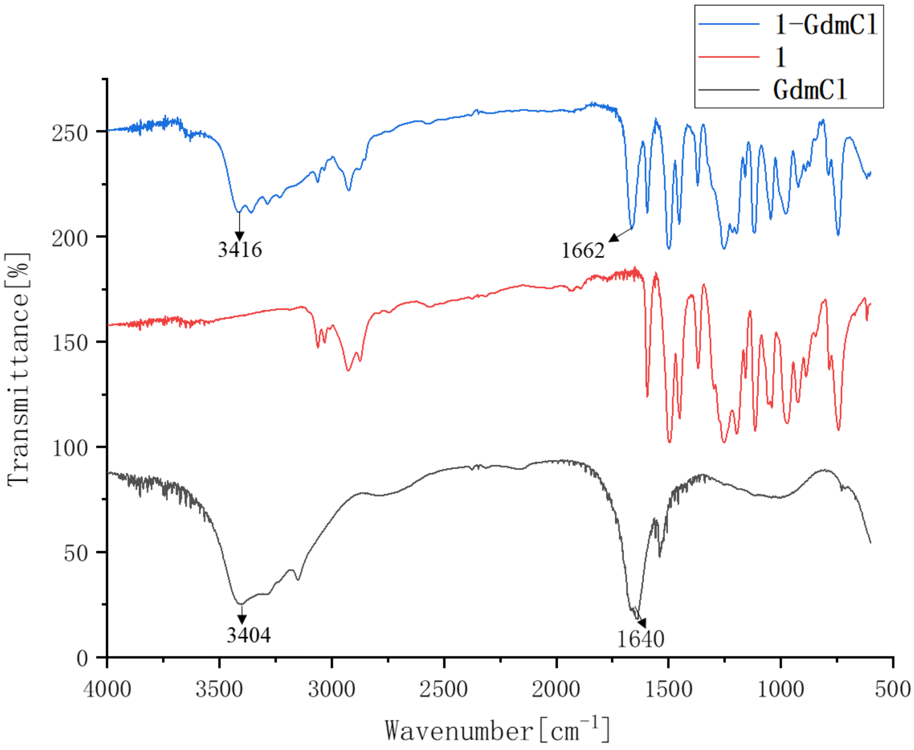


Fig. S10. The infrared spectra (4000-600 cm^{-1}) of **1**·Gdm$^+$Cl$^-$ complex (blue), receptor **1** (red), and Gdm$^+$Cl$^-$ (black) in KBr discs recorded at room temperature. Note: equal-molar **1** and Gdm$^+$Cl$^-$ were mixed in a mixture of CH_3OH and $CHCl_3$ (1:9, v/v) and solvent molecules are removed under reduced pressure to give solid host-guest mixture for IR spectroscopic analysis.

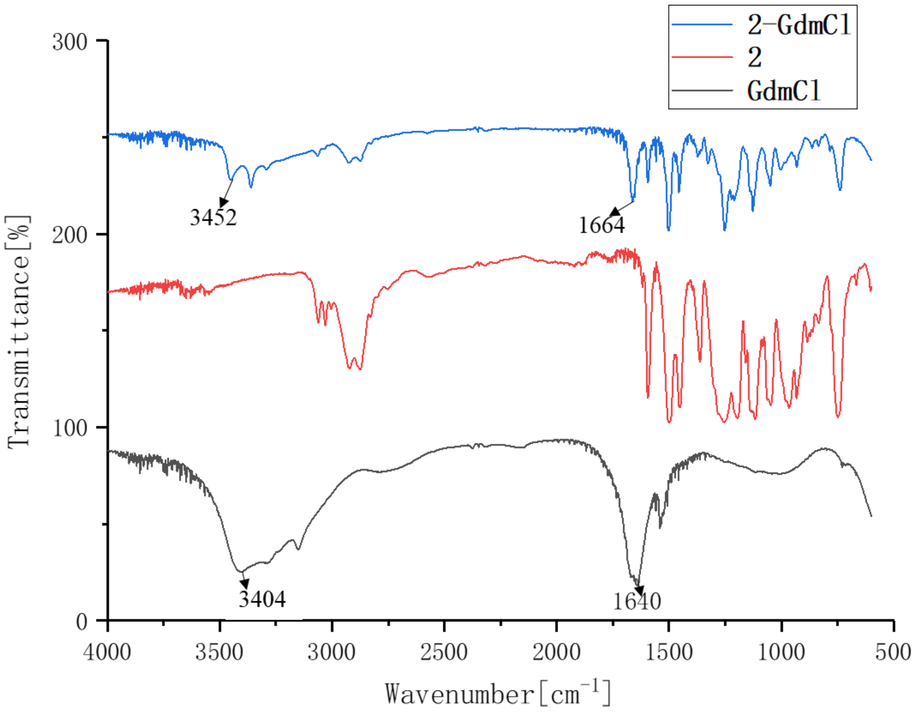


Fig. S11. The infrared spectra (4000-600 cm^{-1}) of **2**·Gdm$^+$Cl$^-$ complex (blue), receptor **2** (red), and Gdm$^+$Cl$^-$ (black) in KBr discs recorded at room temperature. Note: equal-molar **2** and Gdm$^+$Cl$^-$ were mixed in a mixture of CH_3OH and $CHCl_3$ (1:9, v/v) and solvent molecules are removed under reduced pressure to give solid host-guest mixture for IR spectroscopic analysis.

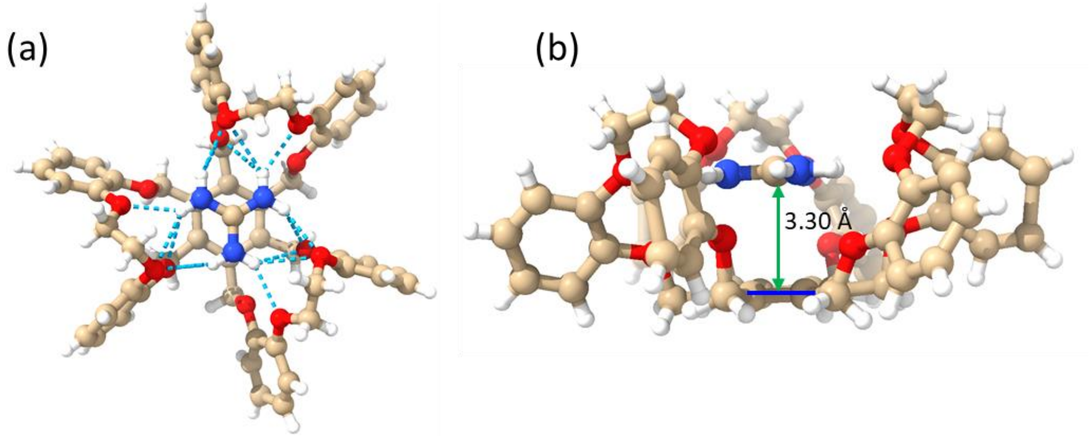


Fig. S12. Single-crystal structure of the Gdm$^+$⊂**1** complex in ball-and-stick model: (a) top view and (b) front view. The solvent molecules and counter anions are removed for clarity. The hydrogen bonds between **1** and guanidinium were indicated by cyan dotted lines.

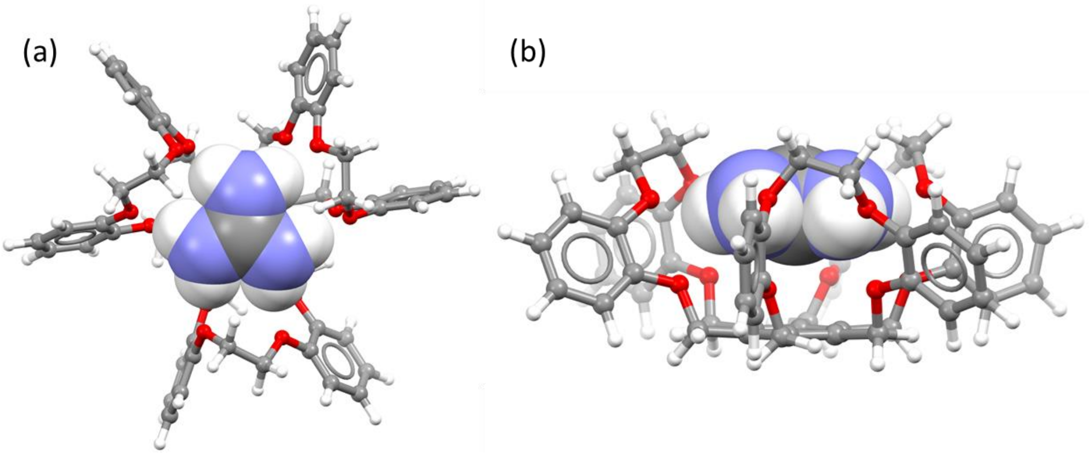


Fig. S13. (a) top view and (b) front view of DFT-optimized structures of Gdm$^+$⊂**1**.

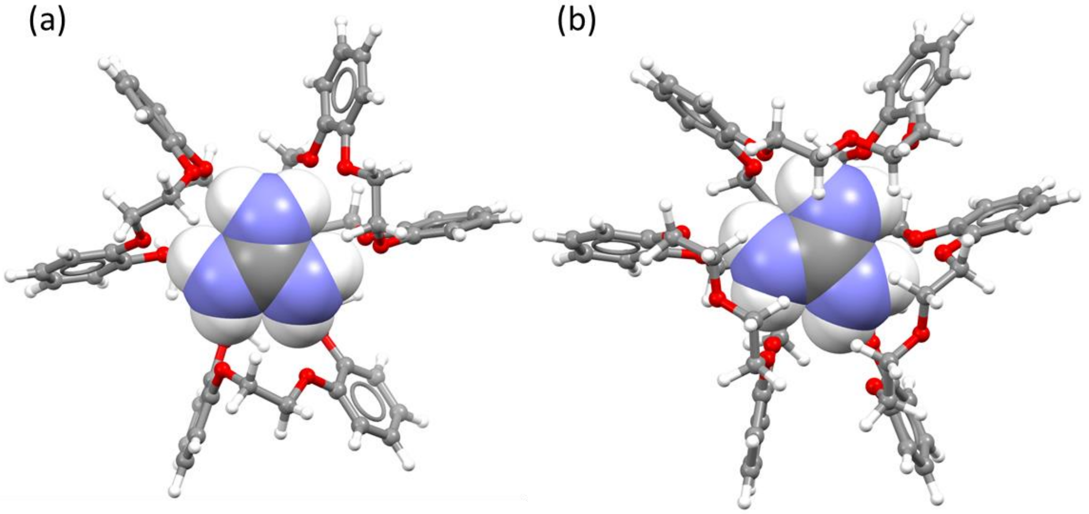


Fig. S14. Top views of DFT-optimized structures of complexes (a) Gdm$^+$⊂**1** and (b) Gdm$^+$⊂**2**.

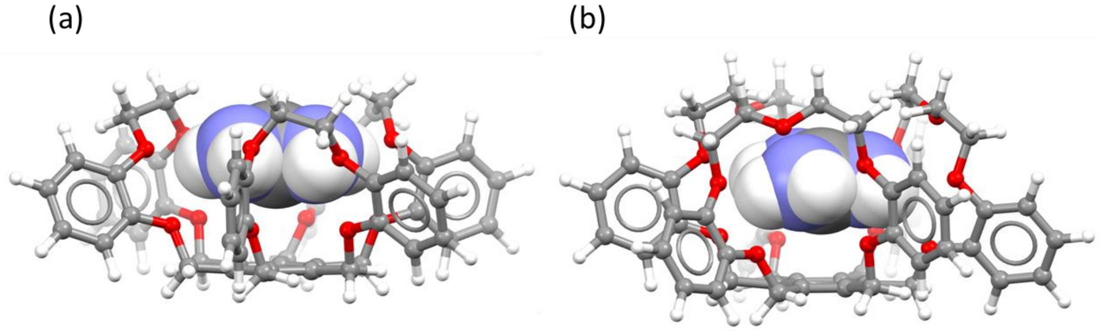


Fig. S15. Front views of DFT-optimized structures of complexes (a) Gdm$^+$⊂**1** and (b) Gdm$^+$⊂**2**.

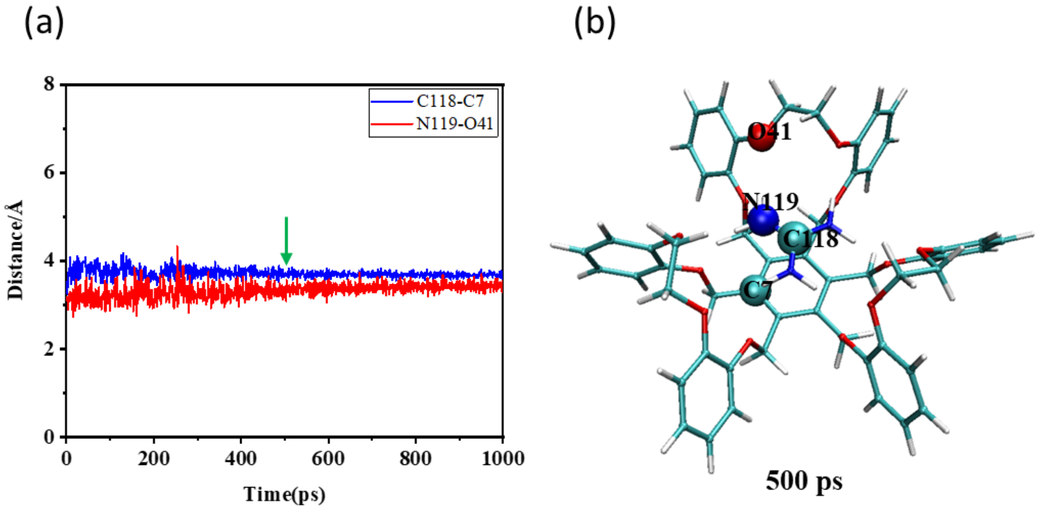


Fig. S16. (a) Time evolution of the distance fluctuations between C118 and C7 (blue line), N119 and O41 (red line) atoms of Gdm$^+$⊂**1** complex during the MD trajectory. (b) The simulated structure at t = 500 ps in (a) on the left indicated by a green arrow. The key elements, e.g. C7, C118, N119, and O41, are labelled in the molecular model in (b). The initial coordinates for MD were extracted from the corresponding single crystal structure.

4. Solid-liquid binding studies with 1 and 2

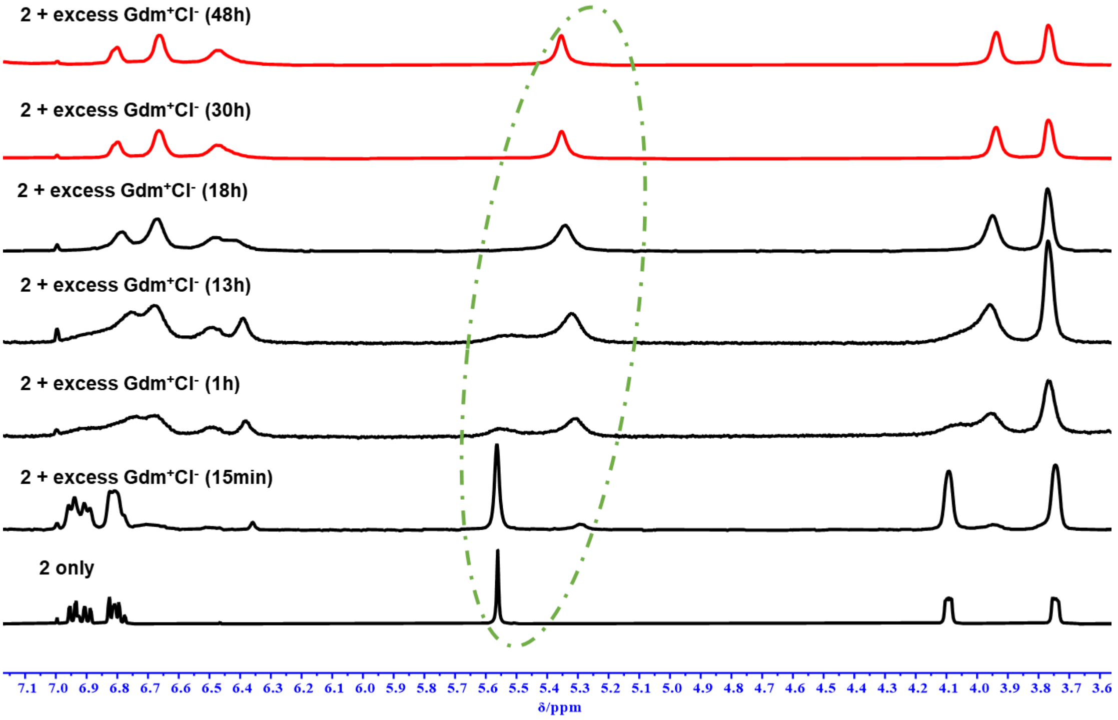


Fig. S17. Selected regions of the ^{1}H NMR spectra ($CDCl_3$, 298 K) of solid-liquid extraction of **2** with excess guanidinium chloride (**Gdm$^+$Cl$^-$**) over time.

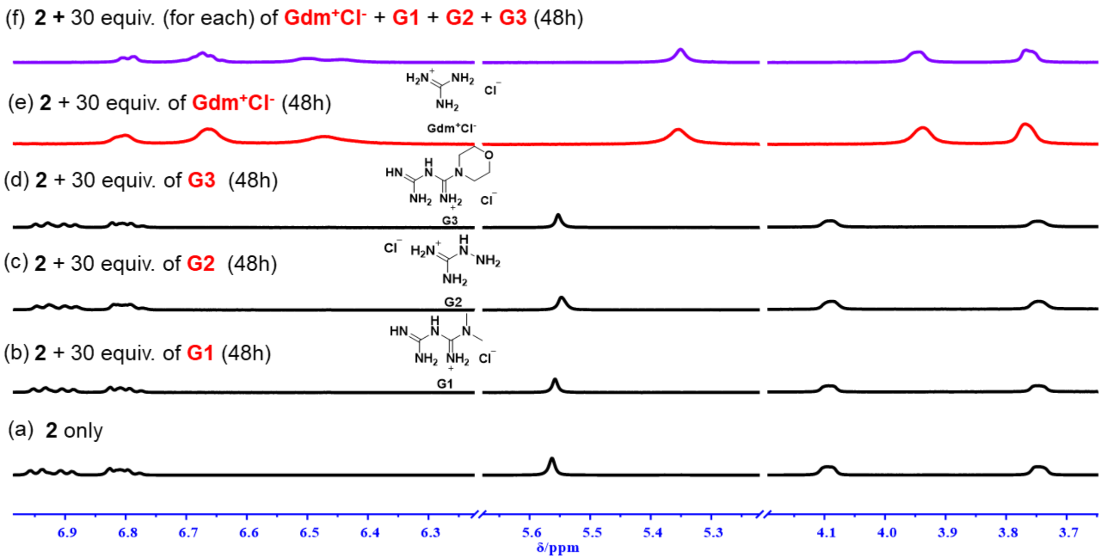


Fig. S18. Selected regions of the ^{1}H NMR spectra (CDCl$_3$, 298 K) of solid-liquid extraction of **2** (1.0 mM) (a) without or with 30 equiv. of (b) G1; (c) G2; (d) G3, (e) guanidinium chloride (Gdm$^+$Cl$^-$), and equal-molar (30 equiv. for each) 1,1-dimethylbiguanide hydrochloride (**G1**), aminoguanidine hydrochloride (**G2**) and moroxydine hydrochloride (**G3**), and guanidinium chloride (Gdm$^+$Cl$^-$). All spectra were recorded after allowing the solid phase and the organic phase to equilibrate for 48 h.

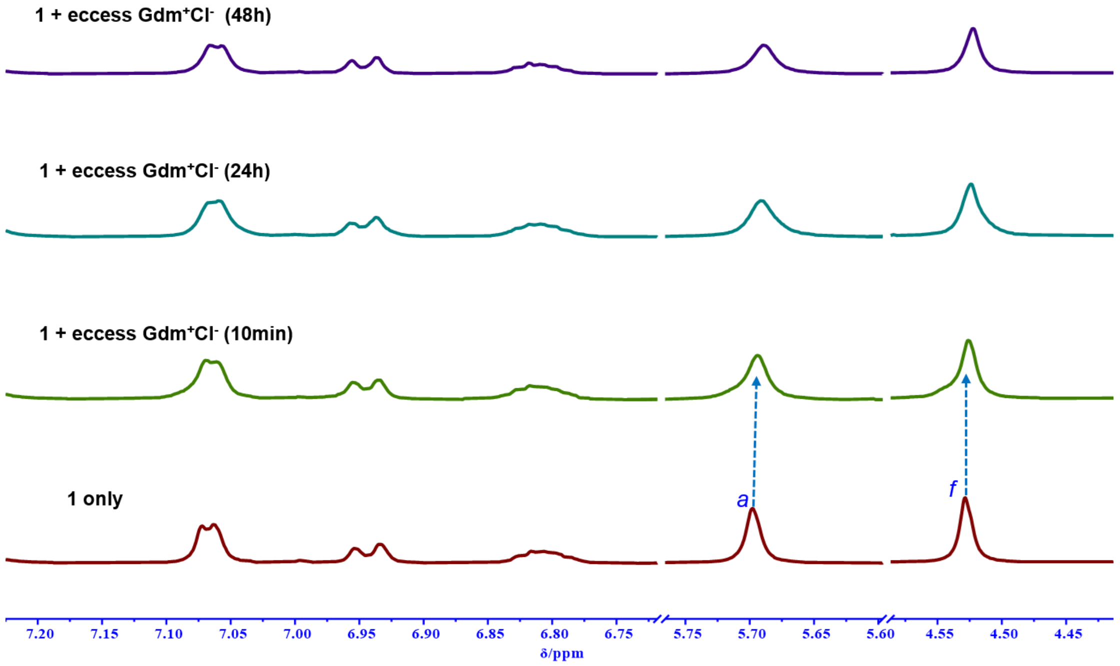


Fig. S19. Selected regions of the ^{1}H NMR spectra (CDCl$_3$, 298 K) of solid-liquid extraction of **1** with excess guanidinium chloride (**Gdm$^+$Cl$^-$**) at 10 min, 24 h, 48 h, respectively.

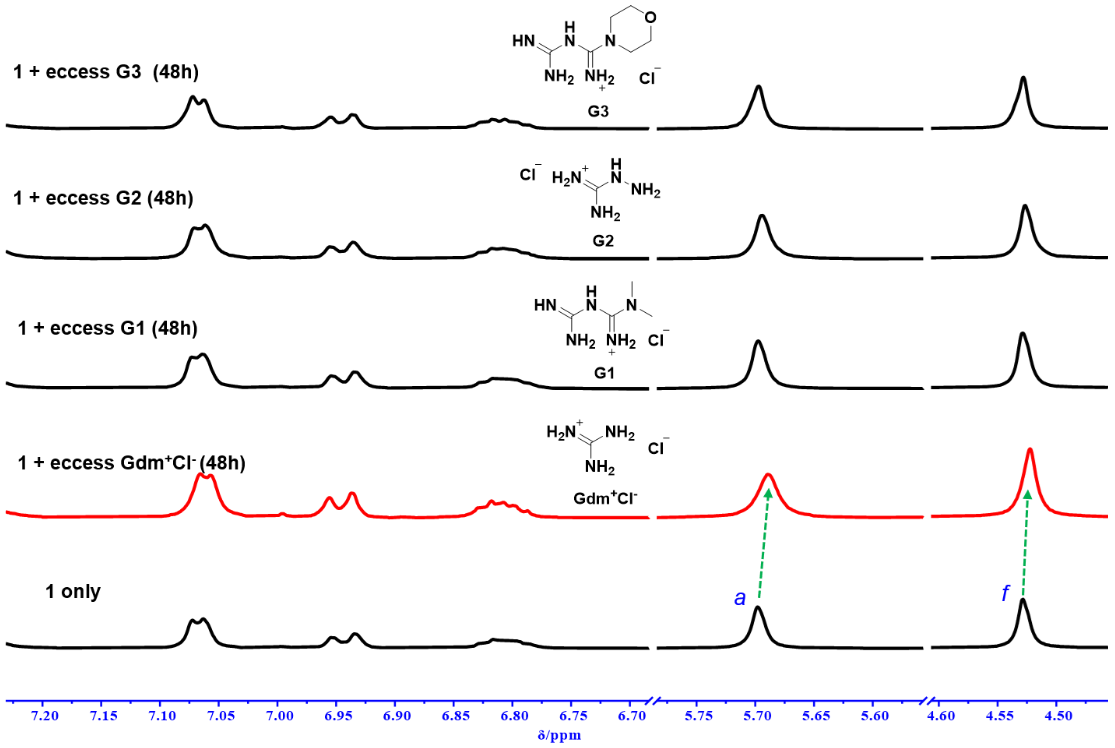


Fig. S20. Selected regions of the ^{1}H NMR spectra (in $CDCl_3$, 298 K) of solid-liquid extraction of **1** (1 mM) recorded in the absence or presence of excess guanidinium chloride (**Gdm^+Cl^-**), 1,1-dimethylbiguanide hydrochloride (**G1**), aminoguanidine hydrochloride (**G2**) and moroxydine hydrochloride (**G3**), respectively.

5. Biological studies with 2

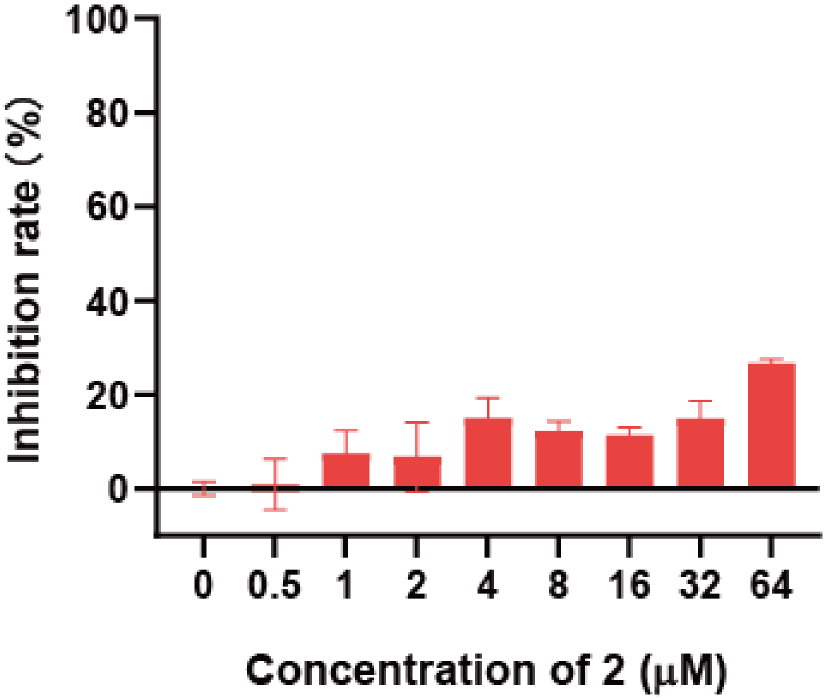


Fig. S21. Cell growth inhibition of Hela cells by different concentrations of receptor **2**.

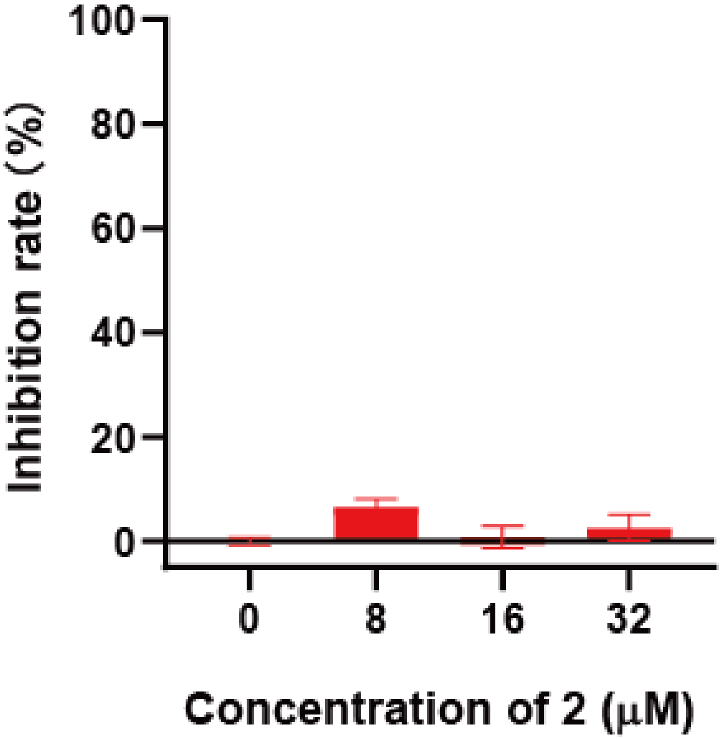


Fig. S22. Cell growth inhibition of *B. subtilis* cells by different concentrations of **2**.

6. X-ray experimental details

X-ray experimental for receptor 1

Single crystals of receptor **1** were obtained as colorless plates via the slow evaporation of a $CHCl_3/CH_3OH$ solution of receptor **1**. A suitable crystal was selected and the data were collected on a Brucker D8 QUEST diffractometer using a μ–focused Mo Kα radiation source (λ = 0.71073 Å). The crystal was kept at 273.15 K during data collection. Using Olex2,[12] the structure was solved with the ShelXT[13] structure solution program using Direct Methods and refined with the ShelXL[14] refinement package using Least Squares minimization. Some free solvent molecules were hard to be accurately determined because of their badly disordered structures, and the PLATON Squeeze program was further used.[15] Owing to the extinction effects, a few reflections were omitted in the course of the least-squares refinements. Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are in the CIF file. CCDC deposition number: 2131662.

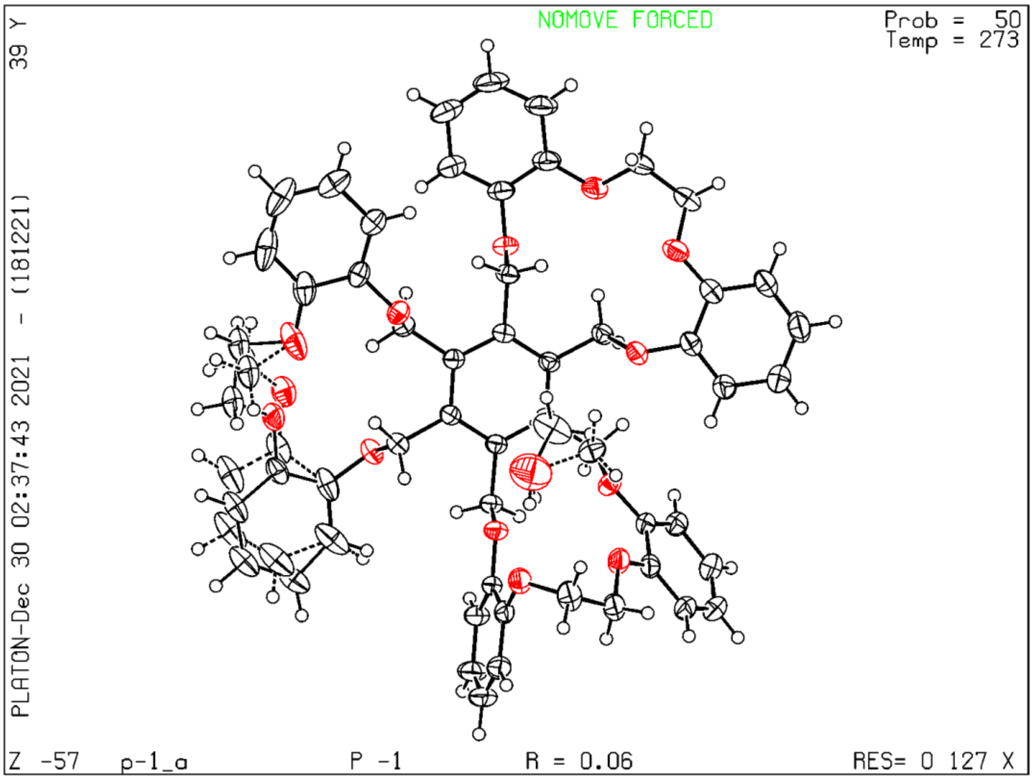


Fig. S23. View of receptor **1**. Displacement ellipsoids are scaled to the 50% probability level.

Table S1 Crystal data and structure refinement for receptor 1.

Identification code	receptor **1**
Empirical formula	$C_{55}H_{52}O_{13}$
Formula weight	920.96
Temperature/K	273.15
Crystal system	triclinic
Space group	P-1
a/Å	13.419(2)
b/Å	13.595(4)
c/Å	14.559(3)
α /°	94.620(6)
β /°	105.872(4)
γ /°	95.372(6)
Volume/Å3	2527.9(10)
Z	2
ρ calcg/cm3	1.210
μ /mm-1	0.086
F(000)	972.0
Crystal size/mm3	0.074 × 0.066 × 0.042
Radiation	MoKα (λ = 0.71073 Å)
2Θ range for data collection/°	4.438 to 56.684
Index ranges	-17 ⩽ h ⩽ 17, -15 ⩽ k ⩽ 18, -19 ⩽ 1 ⩽ 19
Reflections collected	28212
Independent reflections	12494 [Rint = 0.0586, Rsigma = 0.0769]
Data/restraints/parameters	12494/130/692
Goodness-of-fit on F2	1.067
Final R indexes [I>=2σ (I)]	R1 = 0.0644, wR2 = 0.1790
Final R indexes [all data]	R1 = 0.0753, wR2 = 0.1901
Largest diff. peak/hole / e Å-3	0.79/-0.56
CCDC number	2131662

X-ray experimental for receptor 2

Single crystals of receptor **2** were obtained as colorless plates via the slow evaporation of a $CHCl_3$/CH_3OH solution of receptor **2**. A suitable crystal was selected and the data were collected on a Bruker D8 QUEST diffractometer using a μ–focused Mo Kα radiation source (λ = 0.71073 Å). The crystal was kept at 273.15 K during data collection. Using Olex2,[12] the structure was solved with the ShelXT[13] structure solution program using Direct Methods and refined with the ShelXL[14] refinement package using Least Squares minimization. Some free solvent molecules were hard to be accurately determined because of their badly disordered structures, and the PLATON Squeeze program was further used.[15] Owing to the extinction effects, a few reflections were omitted in the course of the least-squares refinements. Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are in the CIF file. CCDC deposition number: 2131666.

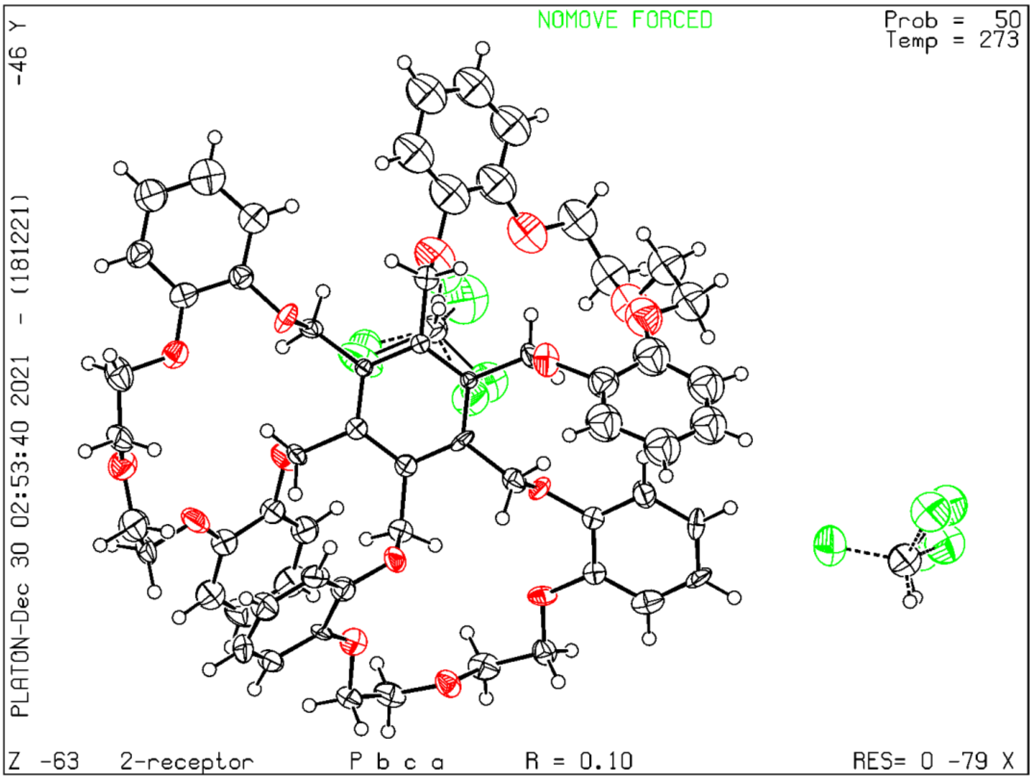


Fig. S24. View of receptor **2**. Displacement ellipsoids are scaled to the 50% probability level.

Table S2 Crystal data and structure refinement for receptor 2.

Identification code	receptor **2**
Empirical formula	$C_{62}H_{62}Cl_6O_{15}$
Formula weight	1259.81
Temperature/K	273.15
Crystal system	orthorhombic
Space group	Pbca
a/Å	18.537(8)
b/Å	17.518(9)
c/Å	36.815(18)
α /°	90
β /°	90
γ /°	90
Volume/Å3	11955(10)
Z	8
ρ calcg/cm3	1.400
μ /mm-1	0.355
F(000)	5248.0
Crystal size/mm3	0.696 × 0.471 × 0.083
Radiation	MoKα (λ = 0.71073 Å)
2Θ range for data collection/°	4.426 to 33.084
Index ranges	-14 ⩽ h ⩽ 14, -14 ⩽ k ⩽ 14, -29 ⩽ l ⩽ 29
Reflections collected	43069
Independent reflections	3154 [Rint = 0.0940, Rsigma = 0.0507]
Data/restraints/parameters	3154/334/803
Goodness-of-fit on F2	1.078
Final R indexes [I>=2σ (I)]	R1 = 0.0976, wR2 = 0.2212
Final R indexes [all data]	R1 = 0.1087, wR2 = 0.2317
Largest diff. peak/hole / e Å-3	0.81/-0.66
CCDC number	2131666

X-ray experimental for the complex 1-GdmCl

Single crystals of receptor **1**-GdmCl were obtained as colorless plates via the slow evaporation of a $CHCl_3/CH_3OH$ solution of receptor **1** in the presence of excess guanidinium chloride. A suitable crystal was selected and the data were collected on a Bruker D8 Venture diffractometer using a *μ*–focused Cu Kα radiation source (λ = 1.5418 Å) or on a ROD. The crystal was kept at 100 K during data collection. Using Olex2,[12] the structure was solved with the ShelXT[13] structure solution program using Direct Methods and refined with the ShelXL[14] refinement package using Least Squares minimization. Some free solvent molecules and the counter ions were hard to be accurately determined because of their badly disordered structures, and the PLATON Squeeze program was further used.[15] Owing to the extinction effects, a few reflections were omitted in the course of the least-squares refinements. Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are in the CIF file. CCDC deposition number: 2131667.

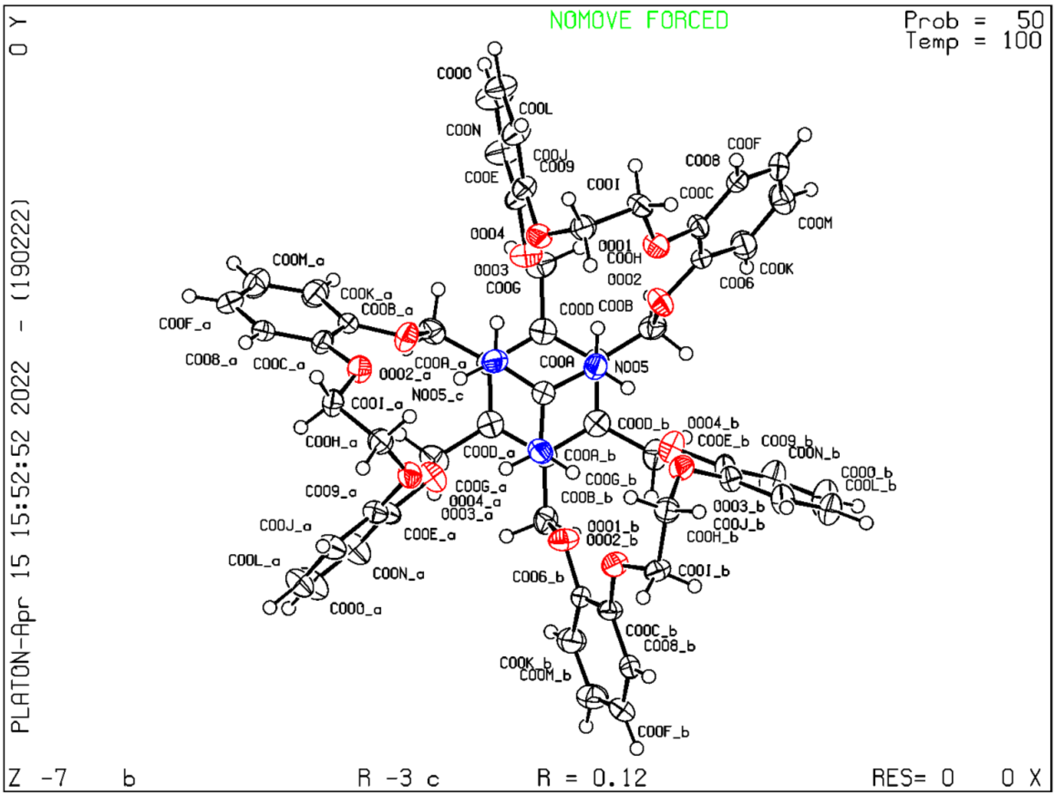
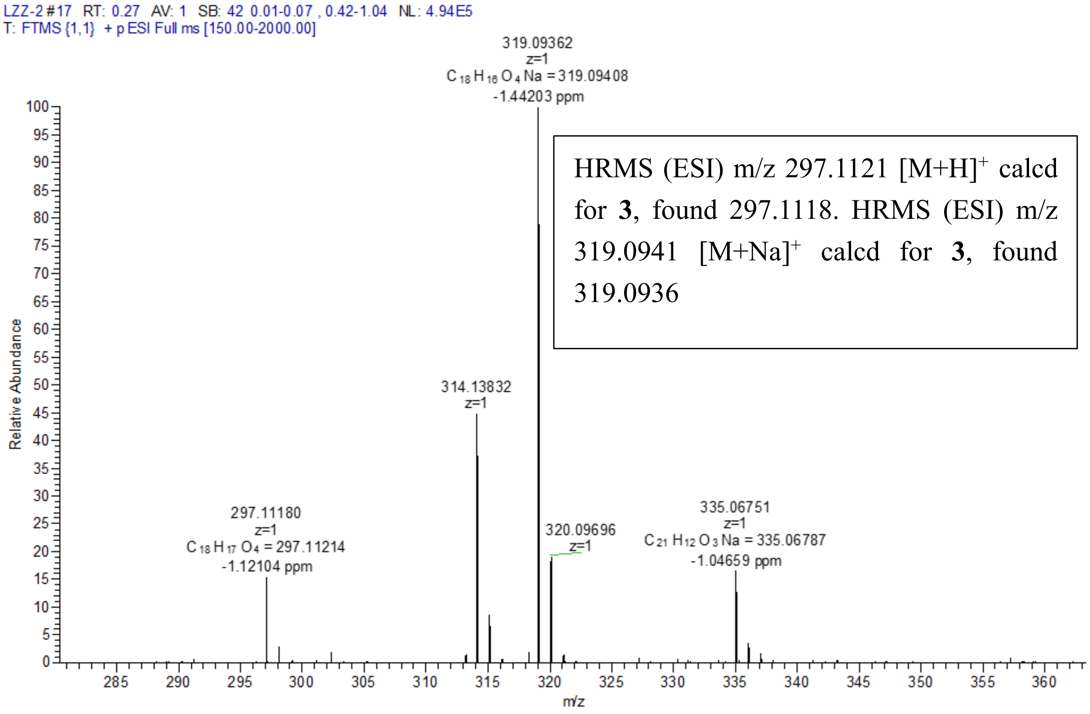


Fig. S25. View of complex **1**-GdmCl.

Table S3 Crystal data and structure refinement for ready.

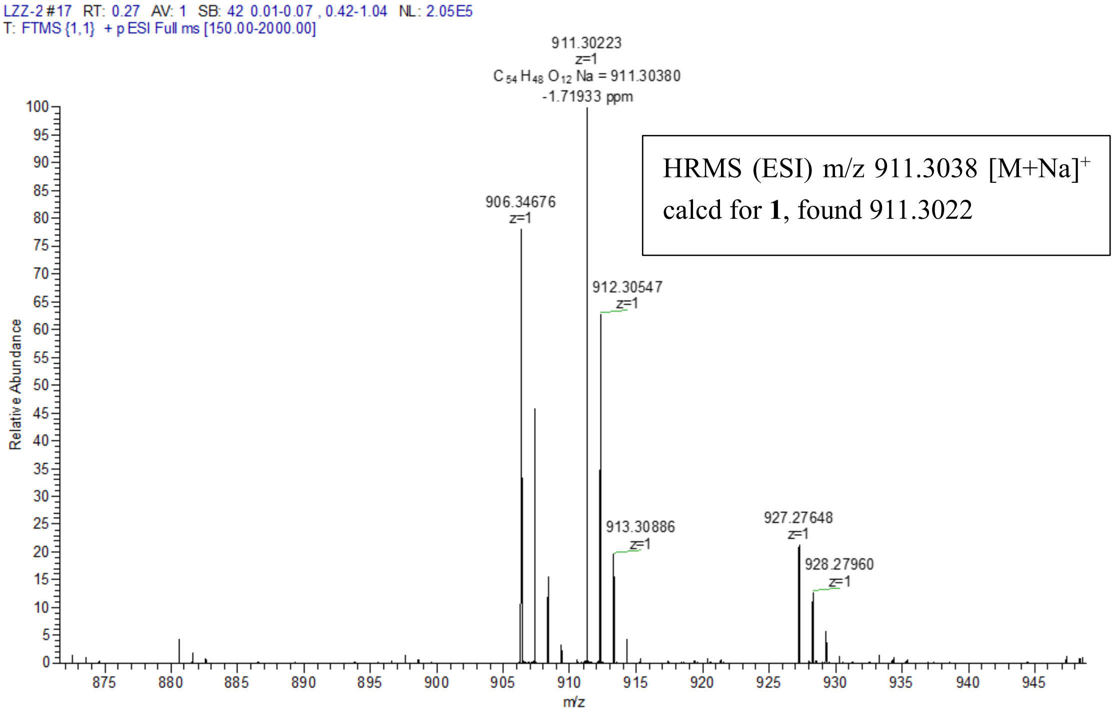
Identification code	**1**-GdmCl
Empirical formula	$C_{55}H_{54}N_3O_{12}$
Formula weight	949.01
Temperature/K	100.0
Crystal system	trigonal
Space group	R-3c
a/Å	16.2429(7)
b/Å	16.2429(7)
c/Å	85.208(6)
α/°	90
β/°	90
γ/°	120
Volume/Å^3	19469(2)
Z	12
ρ_{calc}g/cm^3	0.971
μ/mm^{-1}	0.564
F(000)	6012.0
Crystal size/mm^3	0.065 × 0.052 × 0.041
Radiation	CuKα (λ = 1.54178 Å)
2Θ range for data collection/°	6.224 to 130.528
Index ranges	$-18 \le h \le 19$, $-19 \le k \le 11$, $-99 \le l \le 98$
Reflections collected	20857
Independent reflections	3623 [R_{int} = 0.0608, R_{sigma} = 0.0450]
Data/restraints/parameters	3623/0/211
Goodness-of-fit on F^2	1.048
Final R indexes [I>=2σ (I)]	R_1 = 0.1221, wR_2 = 0.3292
Final R indexes [all data]	R_1 = 0.1266, wR_2 = 0.3343
Largest diff. peak/hole / e Å^{-3}	0.57/-0.41

7. HRMS spectra and NMR spectra



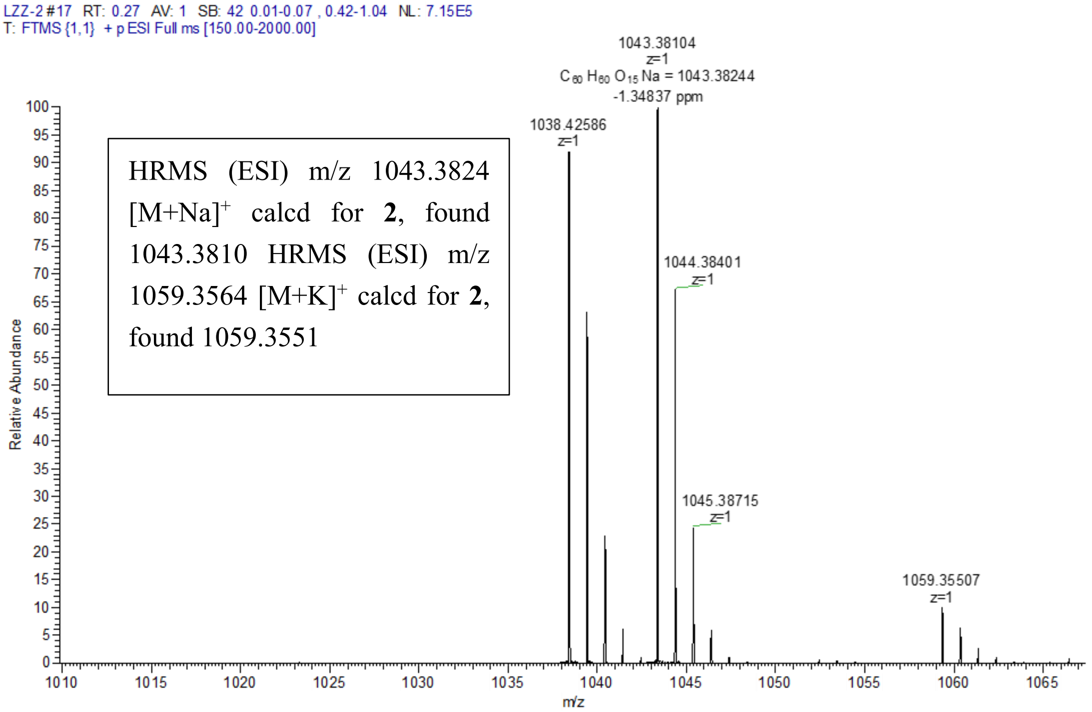
HRMS (ESI) m/z 297.1121 [M+H]$^+$ calcd for **3**, found 297.1118. HRMS (ESI) m/z 319.0941 [M+Na]$^+$ calcd for **3**, found 319.0936

Fig. S26. HRMS spectrum of compound **3**.



HRMS (ESI) m/z 911.3038 [M+Na]$^+$ calcd for **1**, found 911.3022

Fig. S27. HRMS spectrum of compound **1**.



HRMS (ESI) m/z 1043.3824 [M+Na]$^+$ calcd for **2**, found 1043.3810 HRMS (ESI) m/z 1059.3564 [M+K]$^+$ calcd for **2**, found 1059.3551

Fig. S28. HRMS spectrum of compound **2**.

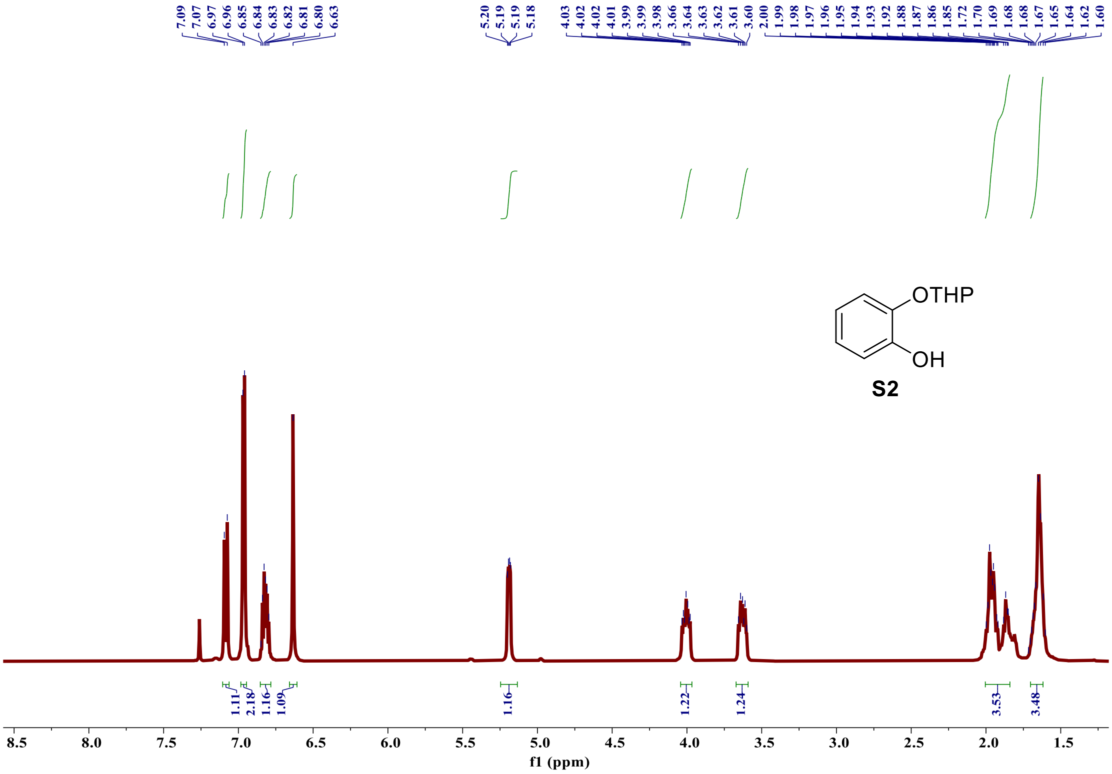


Fig. S29. ^{1}H NMR spectrum of **S2** recorded in $CDCl_3$

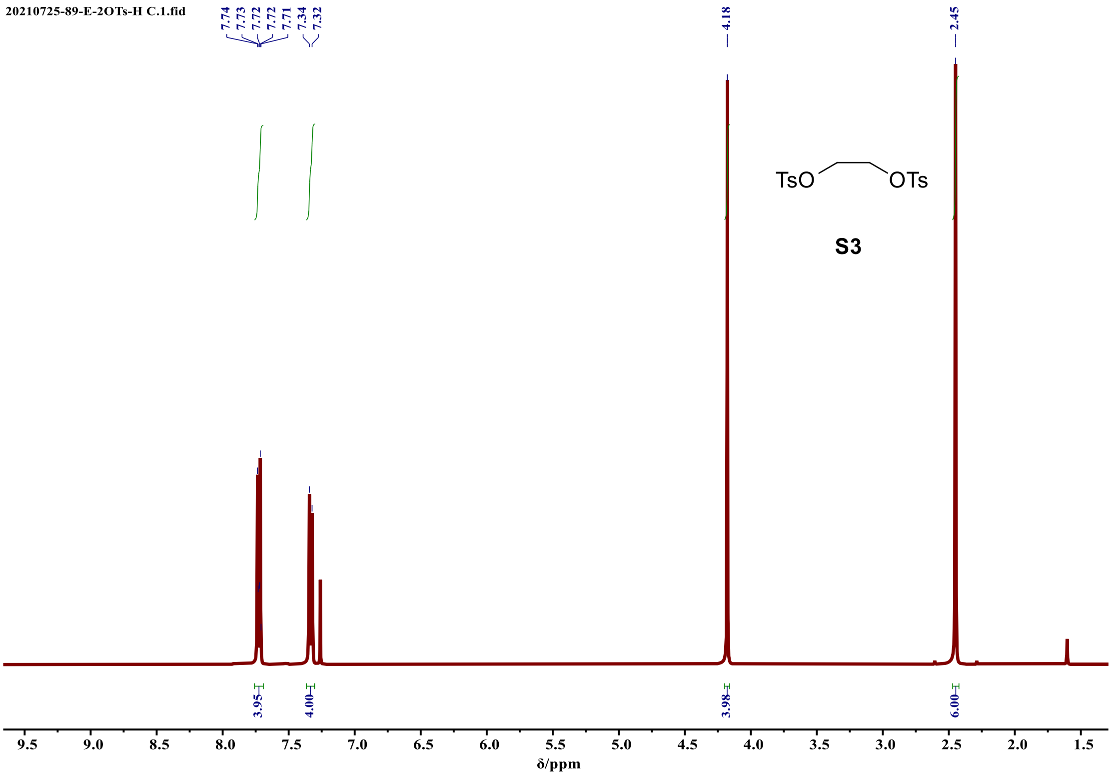


Fig. S30. ^{1}H NMR spectrum of **S3** recorded in CDCl$_3$

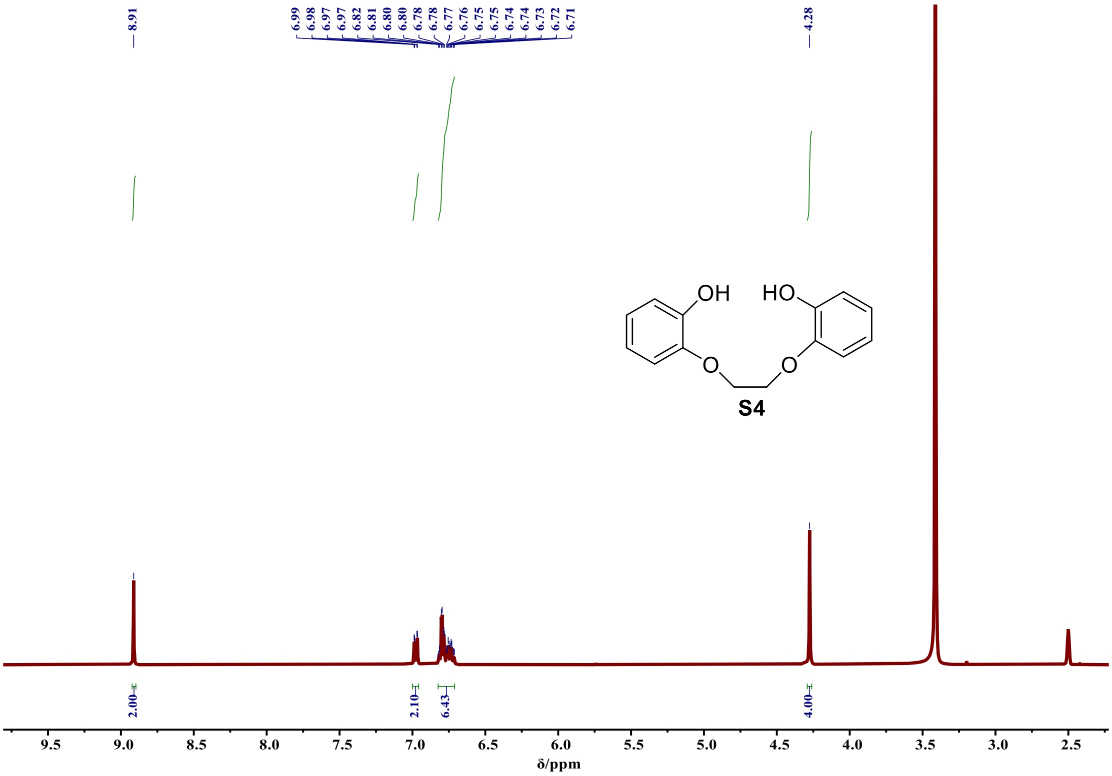


Fig. S31. ^{1}H NMR spectrum of **S4** recorded in DMSO-d_6

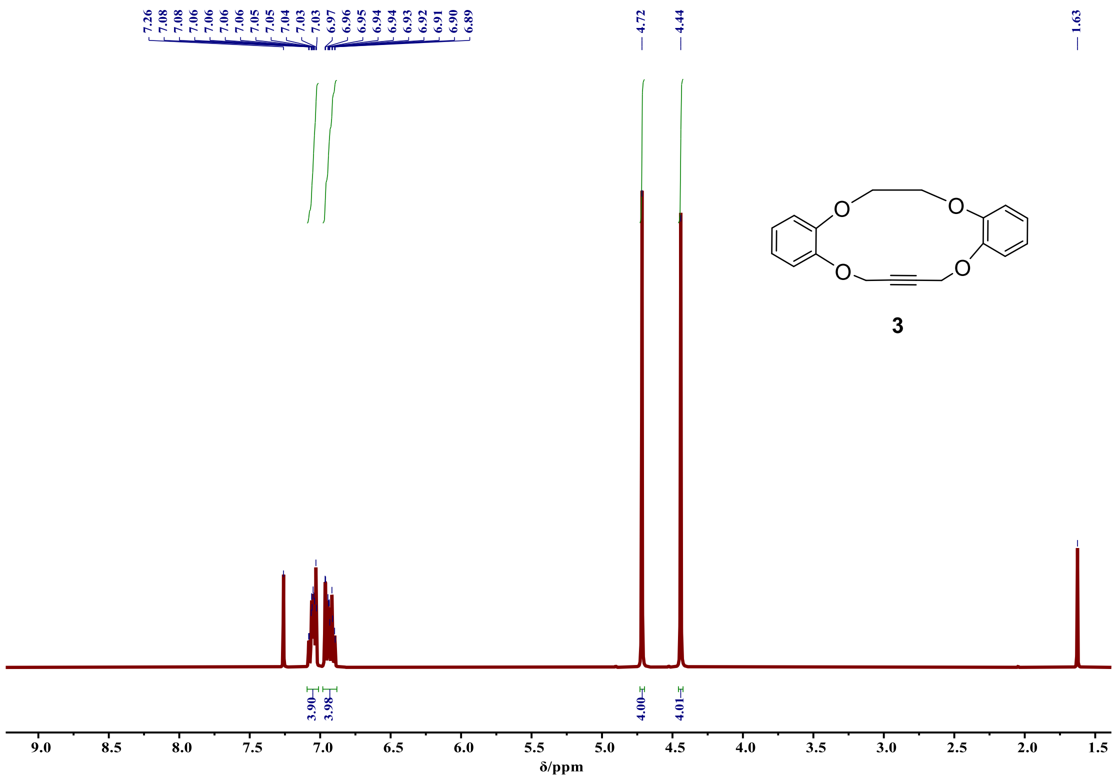


Fig. S32. ^{1}H NMR spectrum of **3** recorded in $CDCl_3$

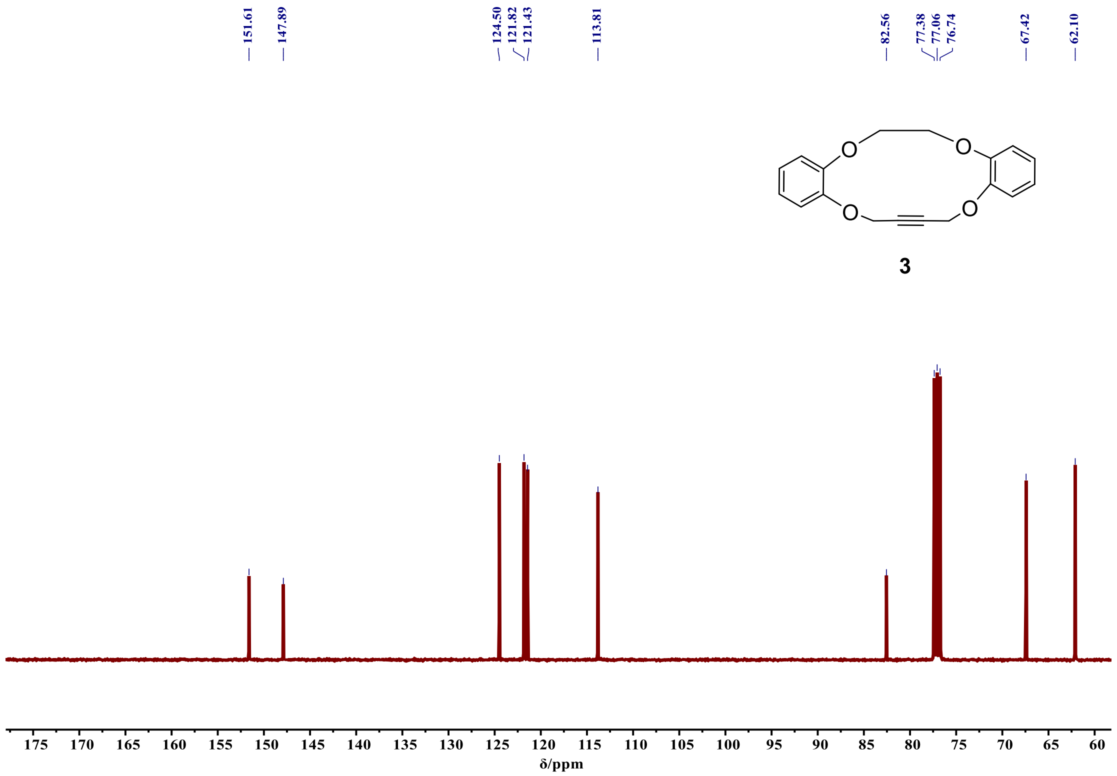


Fig. S33. ^{13}C NMR spectrum of **3** recorded in $CDCl_3$

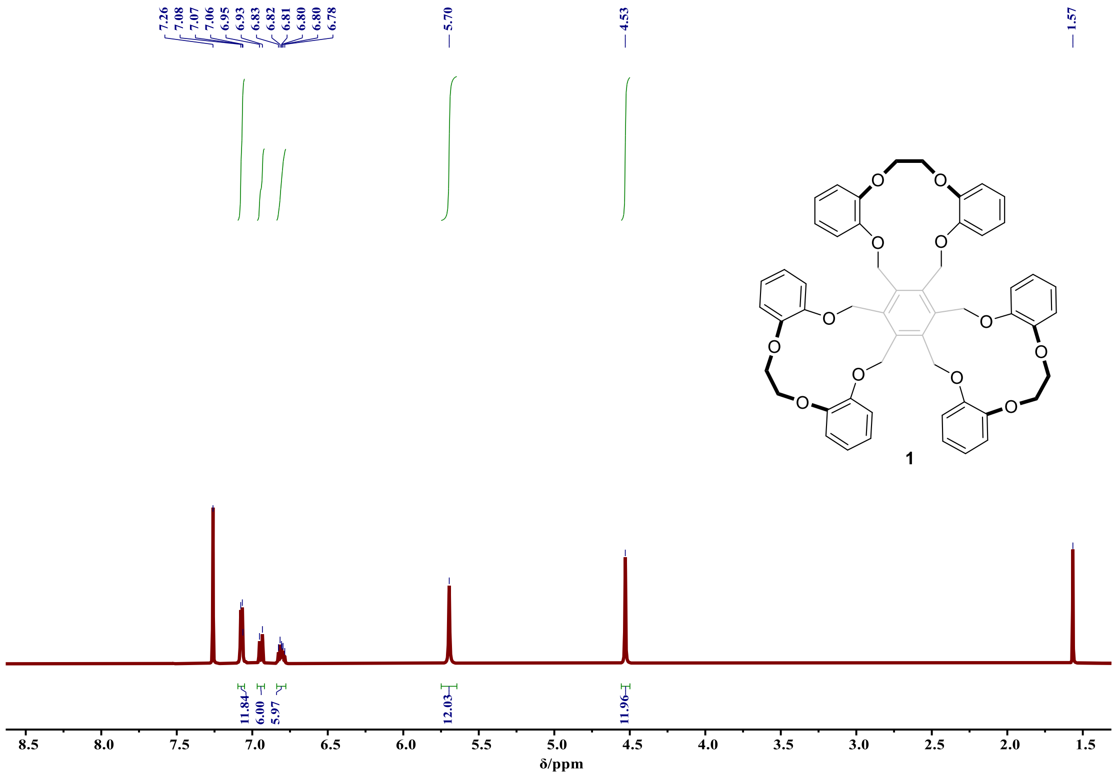


Fig. S34. ^{1}H NMR spectrum of **1** recorded in CDCl$_3$

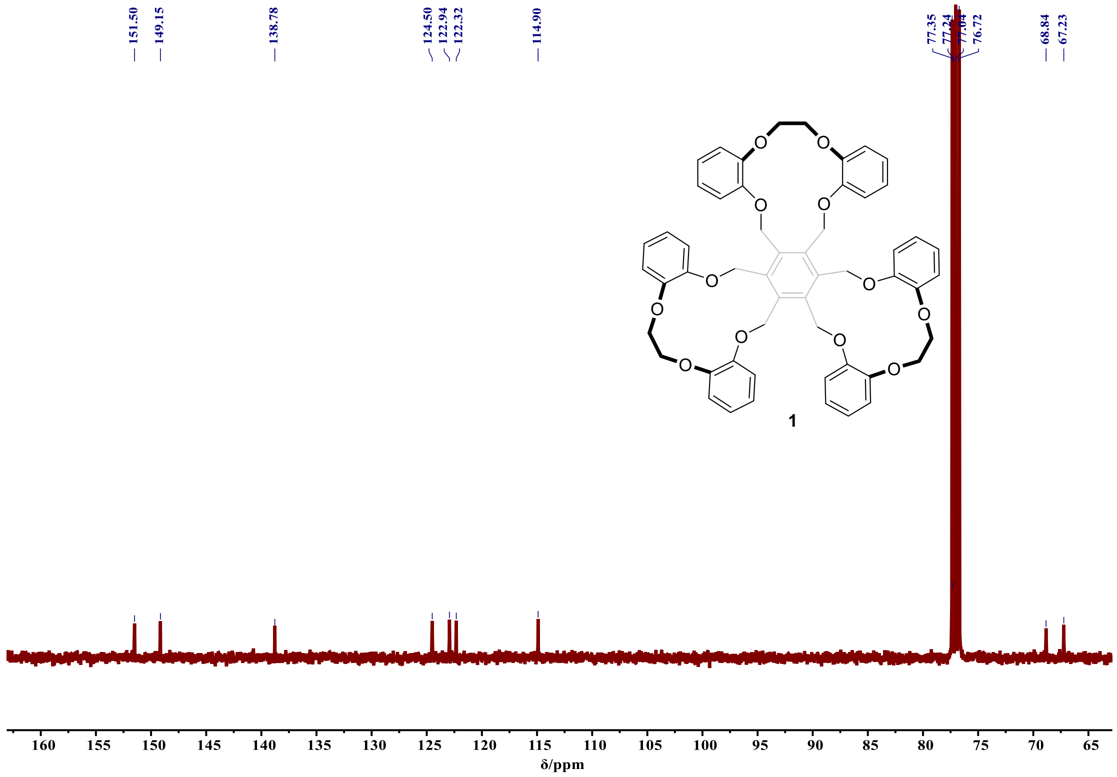


Fig. S35. ^{13}C NMR spectrum of **1** recorded in CDCl$_3$

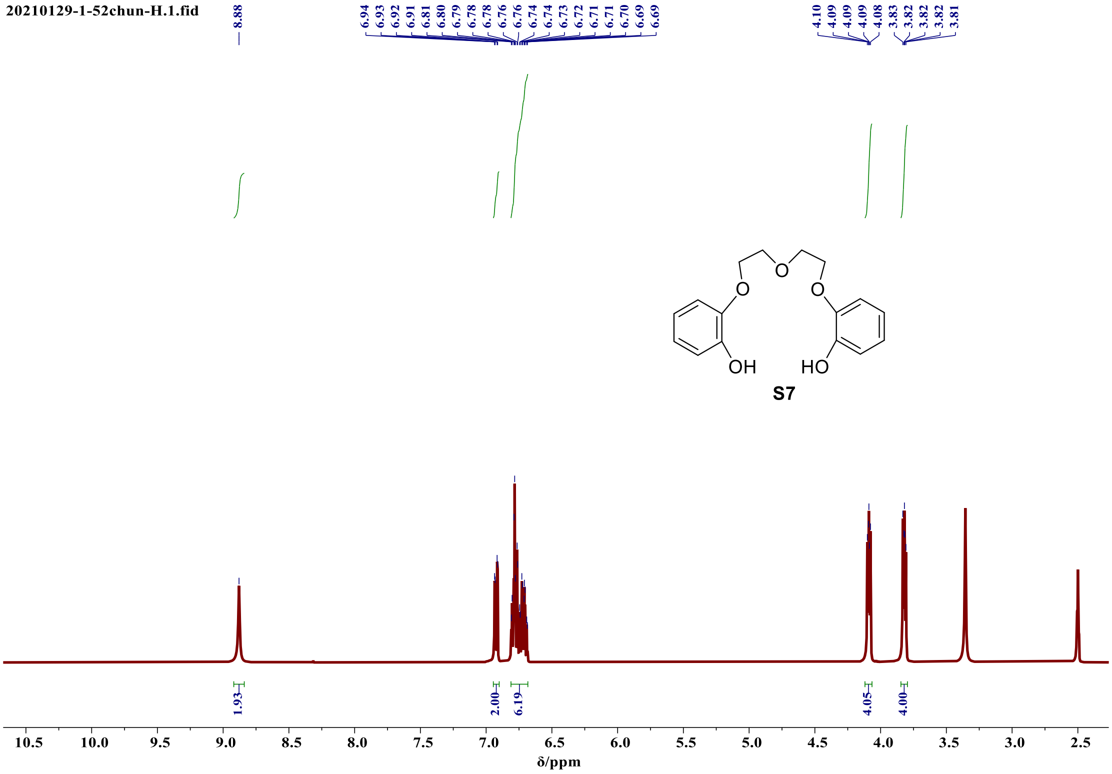


Fig. S36. ^{1}H NMR spectrum of **S7** recorded in DMSO-*d*$_6$

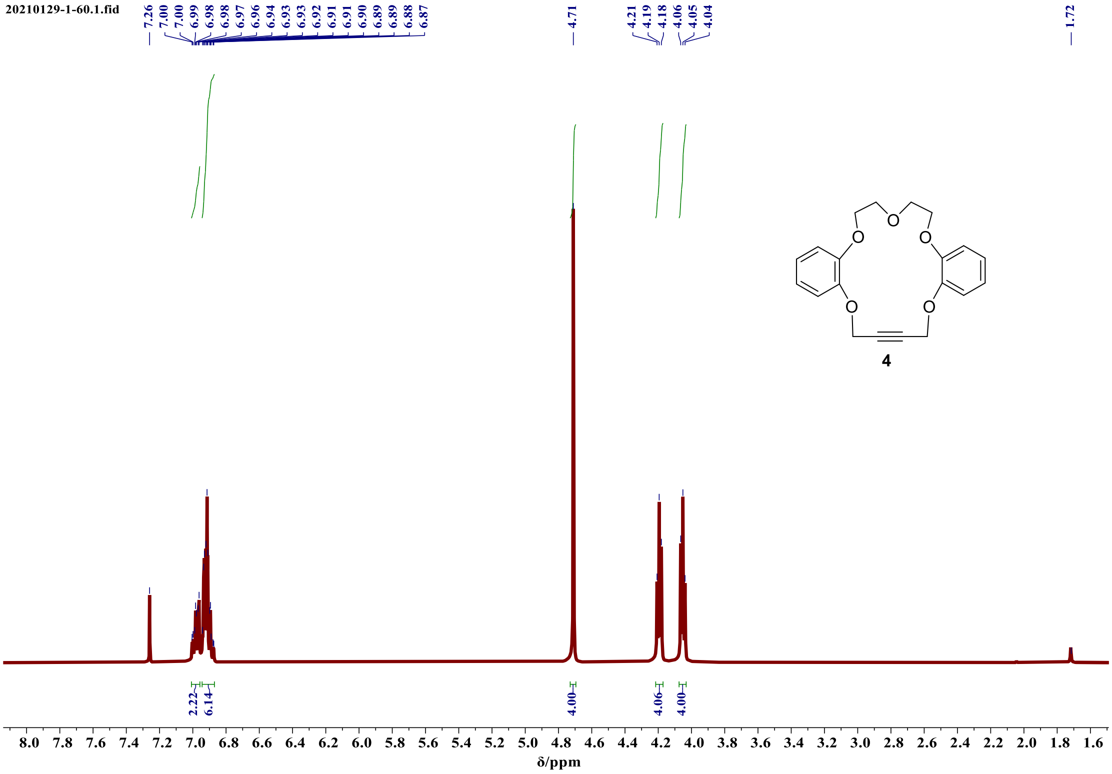


Fig. S37. ^{1}H NMR spectrum of **4** recorded in CDCl$_3$

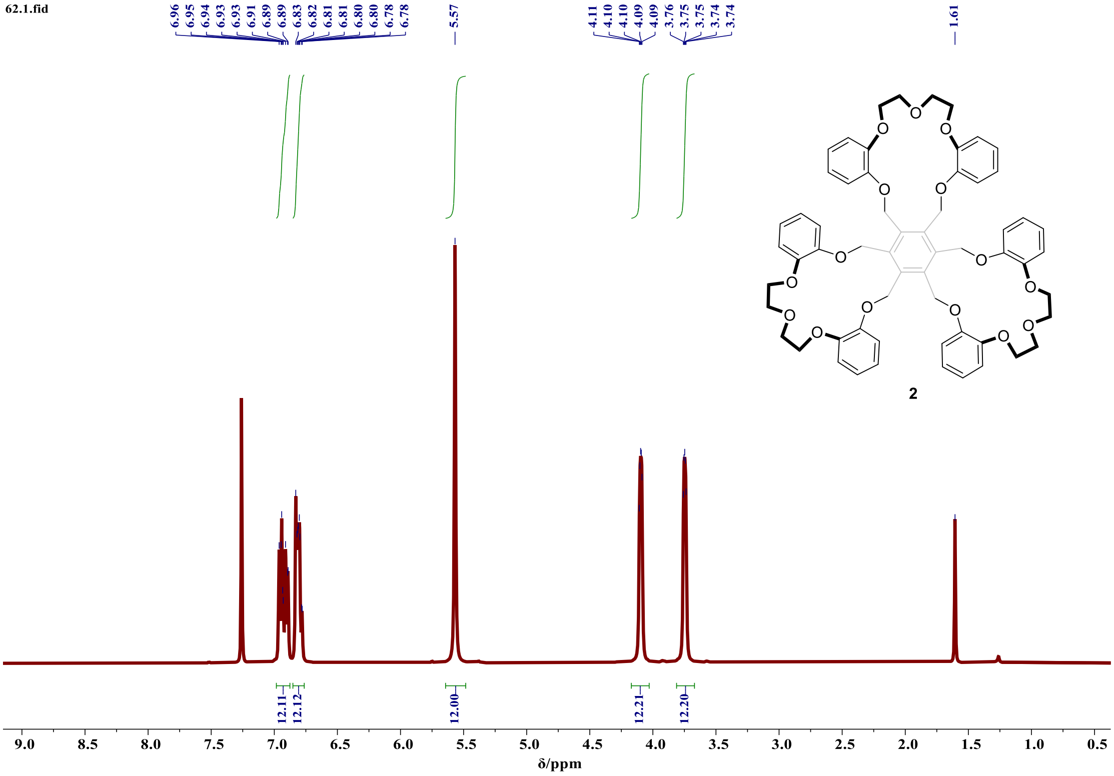


Fig. S38. ^{1}H NMR spectrum of **2** recorded in $CDCl_3$

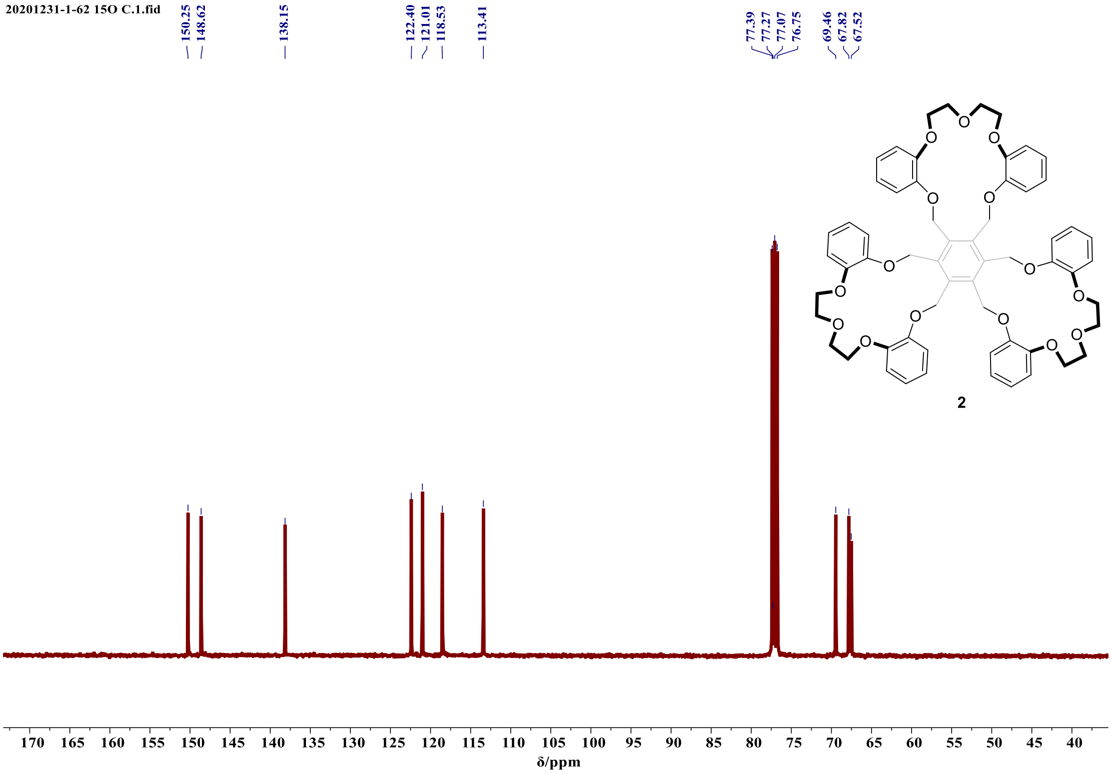


Fig. S39. ^{13}C NMR spectrum of **2** recorded in $CDCl_3$

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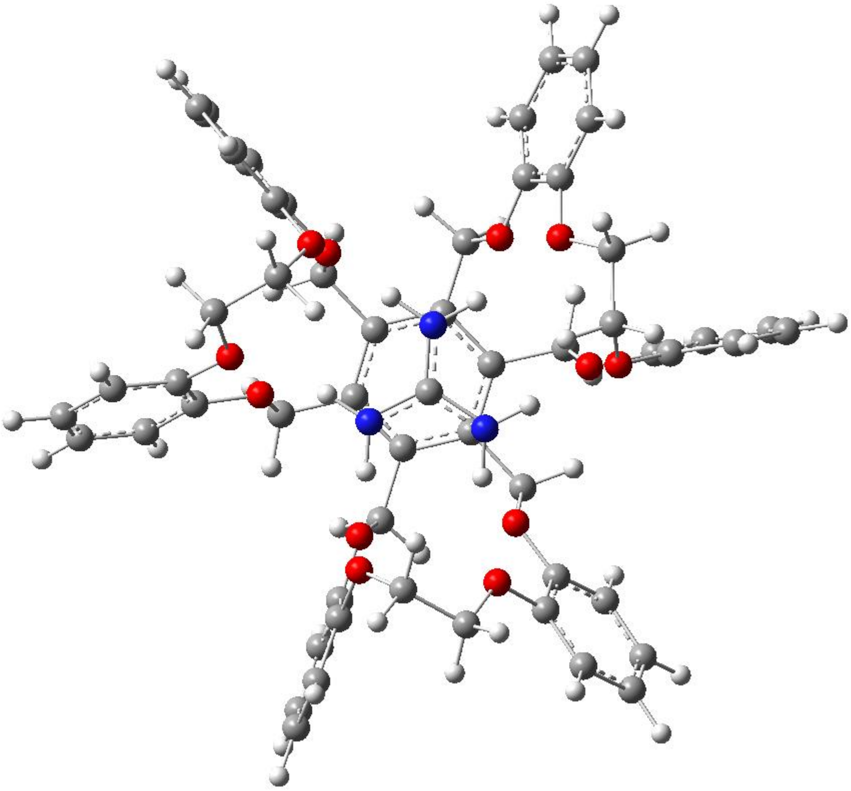
9. Energies and geometrical coordinates of the optimized models in the gas phase

Structure: Gdm$^{+}\subset$**1**



Cartesian coordinates

Symbol	X	Y	Z
C	0.00310900	-0.00019700	1.33381200
N	0.49578000	-1.24487500	1.36880600
H	1.49429900	-1.39296900	1.23189000
H	-0.10453100	-2.03065400	1.13386700
N	-1.32080400	0.19539300	1.37319700
H	-1.94930200	-0.59572800	1.24268600
H	-1.70301800	1.10853000	1.14269000
N	0.83488500	1.04863400	1.37245600
H	0.46372000	1.98796700	1.23892500
H	1.81548700	0.92215700	1.13648700
C	0.20916800	-1.39293400	-2.22749000
O	-3.18360600	-2.10491300	1.73786500
O	-1.06336400	-3.91248300	1.45207900
C	-5.80903300	-3.90291600	-0.95632800
H	-6.47285100	-4.36720600	-1.67865900

C	-0.59114600	-4.97070500	0.71337700
C	-1.09971200	-0.87602400	-2.23368900
C	-4.07718900	-2.72090700	0.88369400
C	-3.86582400	-2.53381100	-0.49702800
C	-2.29506700	-1.80576400	-2.16433600
H	-2.03211900	-2.84056800	-2.39055900
H	-3.06011500	-1.50047700	-2.88803300
C	-0.08905300	-7.30121900	0.31069800
H	-0.10989200	-8.33202100	0.64912600
C	0.41438700	-2.89376600	-2.13200400
H	-0.11934800	-3.41733300	-2.93712000
H	1.46662100	-3.17001300	-2.20564600
C	0.47808600	-5.64445100	-1.35601800
H	0.90060100	-5.40410300	-2.32478800
O	-2.80925500	-1.72951600	-0.83260800
C	-2.67924400	-2.85426400	2.84713100
H	-3.46350000	-3.04162200	3.59142100
H	-1.93452500	-2.19525600	3.30059000
C	-6.02990900	-4.06577200	0.40676100
H	-6.87071700	-4.65224500	0.76249900
C	0.45394600	-6.97653200	-0.92475000
H	0.86261800	-7.75071300	-1.56614700
O	-0.09435400	-3.30866500	-0.86555600
C	-5.16244800	-3.47016200	1.32663300
H	-5.33265500	-3.59032100	2.39192100
C	-4.73218400	-3.13547900	-1.40982500
H	-4.57439900	-3.01528600	-2.47558600
C	-0.61061600	-6.29565700	1.13354800
H	-1.02364800	-6.55238700	2.10274300
C	-0.04584400	-4.64072800	-0.54671300
C	-2.04420600	-4.17787900	2.44800600
H	-1.59278200	-4.63126800	3.34183000
H	-2.79297400	-4.87100100	2.04840300
C	-1.30629500	0.51523400	-2.22886800
O	-0.24010800	3.80787100	1.73744300
O	-2.86207600	2.86803900	1.45479400
C	-0.48998300	6.98091300	-0.95591400

H	-0.56122300	7.78795200	-1.67812100
C	-4.01252300	2.98872900	0.71265600
C	-0.20414500	1.39026700	-2.23403900
C	-0.32905600	4.88989400	0.88390900
C	-0.26650500	4.61430900	-0.49677700
C	-0.41218100	2.89025900	-2.16495700
H	-1.43965700	3.17937300	-2.39255100
H	0.23539100	3.40057400	-2.88776800
C	-6.28171300	3.71784700	0.30645500
H	-7.16549500	4.24921600	0.64422400
C	-2.70869900	1.08796500	-2.13483000
H	-2.89360300	1.81360500	-2.93882600
H	-3.47412100	0.31522800	-2.21179600
C	-5.12453300	2.40486900	-1.36129400
H	-5.12465300	1.92190100	-2.33161500
O	-0.09121400	3.29802600	-0.83280900
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H	-0.91051200	4.51820600	3.59160800
H	-0.93659800	2.77067000	3.30229100
C	-0.52707800	7.25273200	0.40715800
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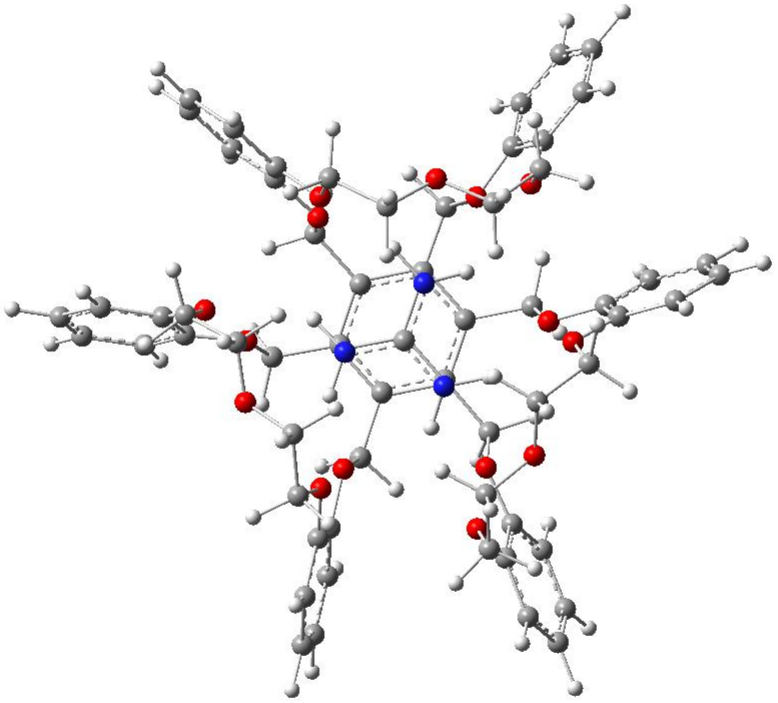
H	-7.14098900	3.12343800	-1.57467900
O	-2.81608200	1.73334100	-0.86722400
C	-0.44336100	6.20372300	1.32691900
H	-0.46736100	6.41095000	2.39213300
C	-0.35580400	5.66541100	-1.40941600
H	-0.32537100	5.46915100	-2.47513200
C	-5.15219900	3.66531400	1.13201000
H	-5.17100300	4.14800400	2.10284700
C	-3.99525100	2.35522200	-0.54922100
C	-2.60377400	3.85071900	2.45097300
H	-3.22061400	3.68371600	3.34531600
H	-2.83375700	4.84510900	2.05226500
C	1.10400700	0.87362100	-2.22809600
O	3.42197300	-1.70084200	1.73819700
O	3.92029200	1.03807500	1.45271500

C	6.29610200	-3.06555200	-0.95646000
H	7.03080800	-3.40626500	-1.67901900
C	4.59974800	1.97650700	0.71369600
C	1.31078000	-0.51841500	-2.23294600
C	4.40409100	-2.16245300	0.88419800
C	4.13408000	-2.07786900	-0.49640000
C	2.71374400	-1.08851800	-2.16373000
H	3.47808000	-0.34311400	-2.39005700
H	2.83186400	-1.90363100	-2.88754300
C	6.36438800	3.57935400	0.31092400
H	7.26610100	4.07897500	0.64975700
C	2.30097100	1.80203100	-2.13342800
H	3.02138600	1.60098400	-2.93830300
H	2.01384300	2.85127400	-2.20815400
C	4.64894100	3.23623000	-1.35752600
H	4.23048500	3.47956900	-2.32731800
O	2.90610300	-1.57211900	-0.83211200
C	3.81444300	-0.88973300	2.84901900
H	4.37001300	-1.47415100	3.59334300
H	2.86955800	-0.57850600	3.30154700
C	6.55031000	-3.17005700	0.40651500
H	7.48164900	-3.59863800	0.76202700
C	5.81276700	3.88419100	-0.92575600
H	6.27839600	4.62504300	-1.56770000
O	2.91458000	1.57038800	-0.86671200
C	5.59959800	-2.71962100	1.32668000
H	5.79098700	-2.80313800	2.39186500
C	5.08925200	-2.52467500	-1.40944500
H	4.90388400	-2.45234000	-2.47509400
C	5.75508800	2.62498600	1.13446400
H	6.18299300	2.39812500	2.10463800
C	4.04222900	2.28080800	-0.54752800
C	4.63955100	0.32561600	2.45242600
H	4.79999300	0.94501100	3.34622800
H	5.61732300	0.02776900	2.05741600

Structure: Gdm$^+$⊂**2**



Cartesian coordinates

Symbol	X	Y	Z
C	-0.00142200	-0.00044600	0.73326500
N	1.33682800	-0.01114600	0.77088200
H	1.84628700	0.86585100	0.70760700
H	1.85262000	-0.83577300	0.48340600
N	-0.67985100	-1.15401000	0.77264900
H	-0.17572000	-2.03416700	0.71077900
H	-1.65244700	-1.18804900	0.48729900
N	-0.66121600	1.16389900	0.77270300
H	-1.67566000	1.16726800	0.71256600
H	-0.20546600	2.02327500	0.48580400
C	1.40725200	-0.00107900	-2.57510200
O	1.18871800	-3.51826100	1.51209100
O	4.17387000	-1.54248500	0.90321000
C	3.62610200	-5.84282000	-0.95395300
H	4.24575800	-6.43139300	-1.62261800
C	5.12107100	-1.52471300	-0.08396200
C	0.69938600	-1.22193600	-2.56637500
C	2.00964200	-4.31258600	0.74552900

C	2.07930900	-4.00372900	-0.63257200
C	1.45639800	-2.52621200	-2.41865000
H	2.51316800	-2.40736200	-2.65596800
H	1.06357500	-3.30884500	-3.07709700
C	7.32576000	-1.92679800	-1.00449300
H	8.33294100	-2.31034300	-0.87680200
C	2.92414000	-0.03318400	-2.60707900
H	3.25062500	-0.66381700	-3.44425500
H	3.35939700	0.95546700	-2.76408900
C	5.63116000	-0.87331900	-2.36472700
H	5.34727900	-0.41378400	-3.30410700
O	1.32223100	-2.93542400	-1.05014100
C	0.91117600	-3.96166900	2.84179900
H	0.61502500	-5.01691100	2.82796000
C	3.56581800	-6.14020000	0.39875600
H	4.13795700	-6.96586300	0.80945900
C	6.93808700	-1.35056300	-2.20546400
H	7.63992800	-1.26502900	-3.02880200
O	3.40378100	-0.56838400	-1.37770100
C	2.75753100	-5.37491600	1.24742000
H	2.71797800	-5.62011200	2.30179300
C	2.88329200	-4.77416700	-1.46828800
H	2.93755200	-4.55632000	-2.52795200
C	6.41633900	-2.01467400	0.05560900
H	6.72237400	-2.47546400	0.98806100
C	4.71669500	-0.97087500	-1.31919500
C	4.61571800	-1.60193800	2.25722200
H	5.60283700	-1.13752700	2.35347100
H	4.67931000	-2.64650100	2.59077200
C	-0.70430400	-1.21935700	-2.57489700
O	-3.64212700	0.73152900	1.51198000
O	-3.42355200	-2.84361400	0.90317400
C	-6.87407800	-0.21338100	-0.95522000
H	-7.69372000	-0.45473400	-1.62412900
C	-3.88141100	-3.67310700	-0.08403200
C	-1.40765900	0.00408700	-2.56589000
C	-4.74037400	0.41868500	0.74490200

C	-4.50755500	0.20387100	-0.63311100
C	-2.91571800	0.00109900	-2.41816700
H	-3.34114900	-0.97376100	-2.65404600
H	-3.39652900	0.73163400	-3.07811100
C	-5.33247800	-5.38094000	-1.00461900
H	-6.16853800	-6.06105000	-0.87704700
C	-1.49034900	-2.51719500	-2.60661500
H	-2.19949900	-2.48520000	-3.44401600
H	-0.85136500	-3.38825300	-2.76300600
C	-3.57205400	-4.44109000	-2.36452600
H	-3.03190500	-4.42540800	-3.30378300
O	-3.20354400	0.32437000	-1.05028800
C	-3.88736600	1.19355700	2.84159600
H	-4.65227800	1.97851400	2.82753300
C	-7.10162800	-0.01235000	0.39748800
H	-8.10295500	-0.09390300	0.80788600
C	-4.63919100	-5.33384700	-2.20539600
H	-4.91607200	-5.98445800	-3.02869800
O	-2.19385300	-2.66490400	-1.37731700
C	-6.03462300	0.30368900	1.24641800
H	-6.22717500	0.46063900	2.30078100
C	-5.57695300	-0.10590400	-1.46916200
H	-5.41530100	-0.26201600	-2.52877600
C	-4.95385700	-4.54931900	0.05535500
H	-5.50617900	-4.58347100	0.98767700
C	-3.19921400	-3.60034500	-1.31900100
C	-3.69612400	-3.19715300	2.25707400
H	-3.78753900	-4.28427700	2.35277300
H	-4.63272600	-2.73015800	2.59040700
C	-0.70344700	1.21838400	-2.57486400
O	2.45346700	2.78858600	1.51168200
O	-0.74904600	4.38511000	0.90281900
C	3.25005700	6.06016600	-0.95545600
H	3.45054200	6.89071200	-1.62441800
C	-1.23918500	5.19637000	-0.08406200
C	0.70780900	1.21586700	-2.56584000
C	2.73146800	3.89626600	0.74488300

C	2.42906000	3.80187500	-0.63312200
C	1.45916500	2.52347500	-2.41818400
H	0.82776000	3.37922900	-2.65509200
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C	-1.99204600	7.30712300	-1.00452000
H	-2.16241100	8.37133700	-0.87707200
C	-1.43445000	2.54795200	-2.60672700
H	-1.05128200	3.14665800	-3.44330300
H	-2.50813400	2.43035900	-2.76447700
C	-2.06017200	5.31244100	-2.36411400
H	-2.31758800	4.83673100	-3.30307400
O	1.88213300	2.61193900	-1.05001400
C	2.97506200	2.77026800	2.84177000
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H	3.96781000	7.06503900	0.80746800
C	-2.29883600	6.68314500	-2.20505800
H	-2.72404500	7.24836400	-3.02817000
O	-1.21194800	3.23044500	-1.37689600
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H	3.51088200	5.16330500	2.30065300
C	2.69492200	4.88283700	-1.46930000
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C	-1.46106000	6.56333000	0.05534800
H	-1.21370200	7.05874100	0.98747400
C	-1.51830200	4.56904400	-1.31872700
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H	-1.81314700	5.42169700	2.35268800
H	-0.04452600	5.37461300	2.58976800
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H	-4.24290800	0.36536000	3.47008400
H	1.80593400	-3.85441800	3.47042200
C	3.62695400	-0.83355300	3.11000200
H	2.60917200	-1.22259600	2.95779500
H	3.89229100	-0.96165000	4.17289900
C	-0.21924600	-3.13596500	3.41915700
H	-0.30837600	-3.37108700	4.49327400

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H	-1.78761800	1.02819800	3.32607300
C	-1.09035300	3.55806300	3.11005300
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H	-1.11259500	3.85244200	4.17276800
C	2.82432400	1.37846900	3.41869100
H	3.07214100	1.41857200	4.49292000
H	1.78309000	1.03317200	3.32430900
O	3.70410200	0.52360600	2.72600400
O	-1.39954400	-3.47052200	2.72651600
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