SUPPORTING INFORMATION

Recognition of Primary Amines in Water by a Zinc Funnel Complex Based on Calix[6]arene†

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MATERIALS. Solvents and chemicals were of reagent grade and were used without purification. Calixarene **1** was synthesized according to ref. 1. HRMS were performed at the Institut de Chimie des Substances Naturelles, France. MS (ESI) analyses were obtained with a ThermoFinnigen LCQ Advantage spectrometer using methanol as solvent. NMR spectra were recorded on a Brucker ARX250 MHz spectrometer or an Advance 500 spectrometer. The pD values of the solutions were corrected considering pD = pH_{read} + 0.4 at 25°C. IR spectra were obtained with a Perkin-Elmer Spectrum on FTIR spectrometer equipped with a MIRacleTM single reflection horizontal ATR unit (germanium crystal). The standard deviation σ of each calculated value "g" (*K*, *K'*, pK_{aeff}, ΔH, ΔS) was calculated based on the following formula:

$$\sigma_{n-1} = \sqrt{\frac{\sum_i (g_i - \overline{g})^2}{n-1}} \text{ with: } \overline{g} = \frac{1}{n}\sum_i g_i \text{ where } n \text{ is the number of independent experiments.}$$

Ion-exchange resin

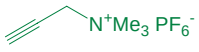
"Dowex 1*2-100 ion-exchange resin", Aldrich: 21,737-9 [60267-37-0]

0.6 equiv./mL ie. 4.8 mequiv./g

"Dowex 1*2-100 ion-exchange resin" (1 g) was treated by 50 mL of a 1M solution of nitric acid. After 15 min stirring (on rotary evaporator without any heating or vacuum), the resin was filtered (fritté n°3) and washed with water until the solution filtered reached neutral pH. This protocol was repeated twice.

1/ SYNTHESIS

Propargyltrimethylammonium hexafluorophosphate



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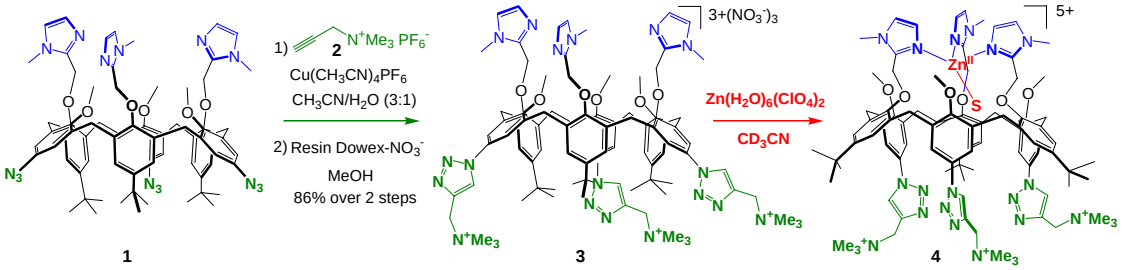
Propargyltrimethylammonium hexafluorophosphate was obtained from the previously described propargyltrimethylammonium bromide,[2] by a simple counter-ion exchange based on the following procedure: a solution of potassium hexafluorophosphate (7.94 g, 43.2 mmol) in water was added to the solid propargyltrimethylammonium bromide (14.4 mmol). The

[1] B. Colasson, M. Save, P. Milko, J. Roithová, D. Schröder and O. Reinaud, *Org. Lett.*, 2007, **9**, 4987.
[2] E. H. Ryu and Y. Zhao, *Org. Lett.*, 2005, **7**, 1035.

mixture was stirred for 30 min. The obtained precipitate was filtered, washed with water and ether to yield compound **2** in 83% yield (2.90 g).

^{1}H NMR (250 MHz, CD_3CN, 300 K): δ (ppm) = 3.11 ($HCCCH_2N^+(C\underline{H}_3)_3$, s, 9H), 3.21 ($\underline{H}CCCH_2N^+(CH_3)_3$, t, *J* = 2.5 Hz, 1H), 4.11 ($HCCC\underline{H}_2N^+(CH_3)_3$, d, *J* = 2.5 Hz, 2H).

*Calixarene **3***



To a solution of $L^{(N_3)_3}$ **1** (65 mg, 0.052 mmol) in CH_3CN/H_2O (3.5 mL/1 mL) were added 4.2 equivalents of propargyl trimethylammonium hexafluorophosphate **2** (53 mg, 0.22 mmol) and 1.5 equivalents of 2,6-lutidine (9 µL, 0.078 mmol). Argon was bubbled through the solution, then 0.6 equivalent of [$Cu(CH_3CN)_4.PF_6$] (11.6 mg, 0.031 mmol) were added. The reaction mixture was refluxed for 64 h. An IR spectrum of one reaction sample revealed the presence of starting material. Argon was bubbled at RT through the reaction mixture. After adding 0.6 equivalent of [$Cu(CH_3CN)_4.PF_6$] (11.6 mg, 0.031 mmol) and 1.5 equivalents of 2,6-lutidine (9 µL, 0.078 mmol), the reaction mixture was refluxed for additional 24 h and monitored by IR (ATR method): the reaction was stopped as soon as the 2100 cm^{-1} band (N_3) fully disappeared.

The mixture was cooled to RT, water (7 mL) and 2 drops of NH_4OH (20% aqueous) were added. The obtained precipitate was collected by filtration and dissolved in acetone/methanol (20 mL/10 mL). 540 mg of ion-exchange resin were added. The mixture was gently stirred at RT mechanically for 15 minutes, then filtered. The resin was rinsed with MeOH. The filtrate was concentrated and yielded, after drying under vacuum, 69 mg of **3** as a tan solid (yield = 86% from **1**).

The IR (ATR) spectra indicated the disappearance of the PF_6^- band at 843 cm^{-1}.

^{1}H NMR (250 MHz, CD_3CN, $Zn(ClO_4)_2.6H_2O$ excess, 300 K): δ (ppm): 1.38 (*t*-Bu, s, 27H), 3.03 (N^+Me_3, s, 27H), 3.63 (OCH_3, s, 9H), 3.72 (NCH_3, s, 9H), 3.63-3.73 ($ArCH_2$, m, 6H), 3.69 ($ArCH_2$, d, *J* = 14 Hz, 6H), 4.58 ($CH_2N^+Me_3$, s, 6H), 5.12 (CH_2Im, br s, 6H), 6.56 (H_{Artria}, s, 6H), 6.95 (H_{Im}, d, *J* = 1.8 Hz, 3H), 7.44 ($H_{Art\text{-}Bu}$, s, 6H), 7.46 (H_{Im}, d, *J* = 1.8 Hz, 3H), 7.87 ($H_{triazole}$, bs, 3H).

^{13}C NMR (125 MHz, CD_3CN, $Zn(ClO_4)_2.6H_2O$ excess, 300 K): δ (ppm): 31.5, 32.1, 35.4, 53.7, 53.9, 54.0, 61.4, 61.6, 65.3, 119.6, 125.3, 127.3, 128.5, 13.5, 132.6, 133.7, 137.3, 137.8, 148.3, 149.5, 155.7, 156.6.

IR (ATR): ν (cm^{-1}) = 3454.0 (br), 2959.6, 1641.6, 1479.9, 1339.6 (NO_3^-), 1231.3, 1186.8, 110.0, 1050.5, 1001.5, 976.0, 897.6, 760.1

ESI-MS (MeOH) m/z: 515.6 (calcd for $[M]^{3+}$ 515.6); 386.8 (calcd for $[M+H]^{4+}$ 386.9).

HRMS (TOF ES+) 1607.9234 (calcd for $[M^{3+}+NO_3^-]^{2+}$ 1607.9282.

2/ CHARACTERIZATION IN ORGANIC SOLVENTS

The ^{1}H NMR spectra of compound **3** in organic solvents such as MeCN, DMSO were extremely broad and uninterpretable, even at high T. Such a behavior is typical of calix[6]arenes with three bulky groups at one rim and three other bulky groups at the opposite rim on different aromatic units. This is due to slow conformational motions of the calixarene core on the NMR time scale. As for a closely related calixarene bearing three imidazole and three triazole substituents,[1] coordination to Zn(II) was then used to rigidify the calixarene core and obtain a nice spectrum with sharp resonances. Therefore, full characterisation of ligand **3** has been performed in the presence of Zn(II) as the corresponding tetrahedral dicationic complex depicted above as compound **4**.

When a stoechiometric amount of $[Zn(OH_2)_6](ClO_4)_2$ was added, sharp resonances due to the rigidification of calix[6]arene core upon complexation appeared (Figure S1). The resonances corresponding to the imidazolyl protons are split into two peaks (6.95 and 7.46 ppm), in agreement with zinc complexation. The chemical shift of the OMe groups (3.72 ppm) shows that they point away from the cavity. These observations account for the formation of a monometallic zinc complex **4** with zinc cation being coordinated to the imidazole units and to a solvent molecule (CD_3CN) that is included in the calixarene cavity. When additional amounts of $[Zn(OH_2)_6](ClO_4)_2$ (up to 3 equiv.) were added, no significant changes were

observed. In contrast to the previously reported tris(imidazolyl)calixarenes bearing neutral triazole derivatives at their large rim,[1] no coordination of a second metal center on the triazole units could be detected, even in the presence of a large excess of Zn(II). Indeed, in the case of the ligand **3**, coordination of the triazole units must be hindered by charge repulsion because of the proximity to positively-charged trimethylammonium substituents. Finally, when calixarene **3** in the presence of one equivalent of $Zn(NO_3)_2.6H_2O$ was dissolved in a mixture of deuterated acetonitrile/methanol (4:1, 1.6 mM), addition of water up to 20% v/v could be achieved without affecting the observation of characteristic chemical shifts of the complex by ^1H NMR.

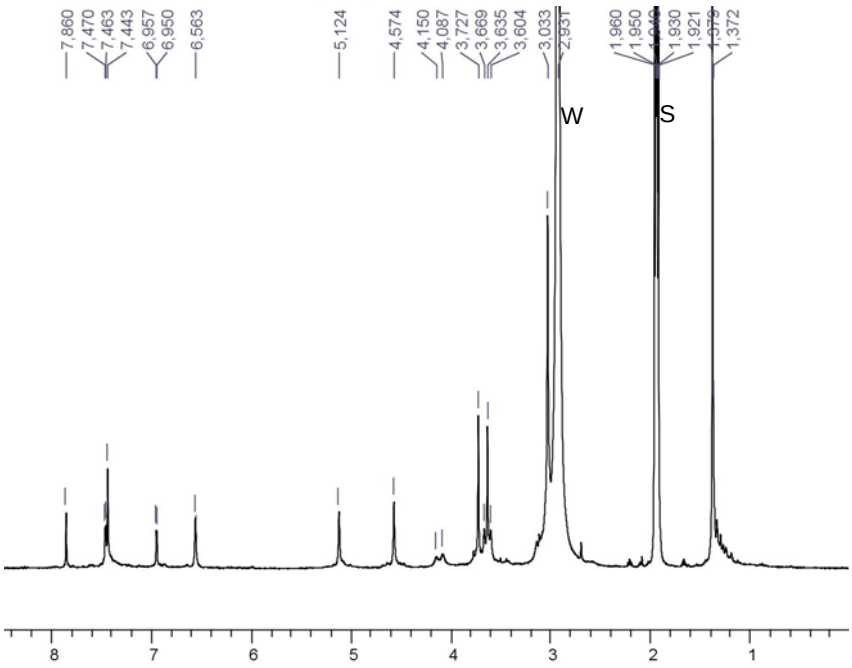


Figure S1: ^1H NMR (250 MHz, CD_3CN, $Zn(ClO_4)_2.6H_2O$ excess, 300 K); w = water, s = solvent.

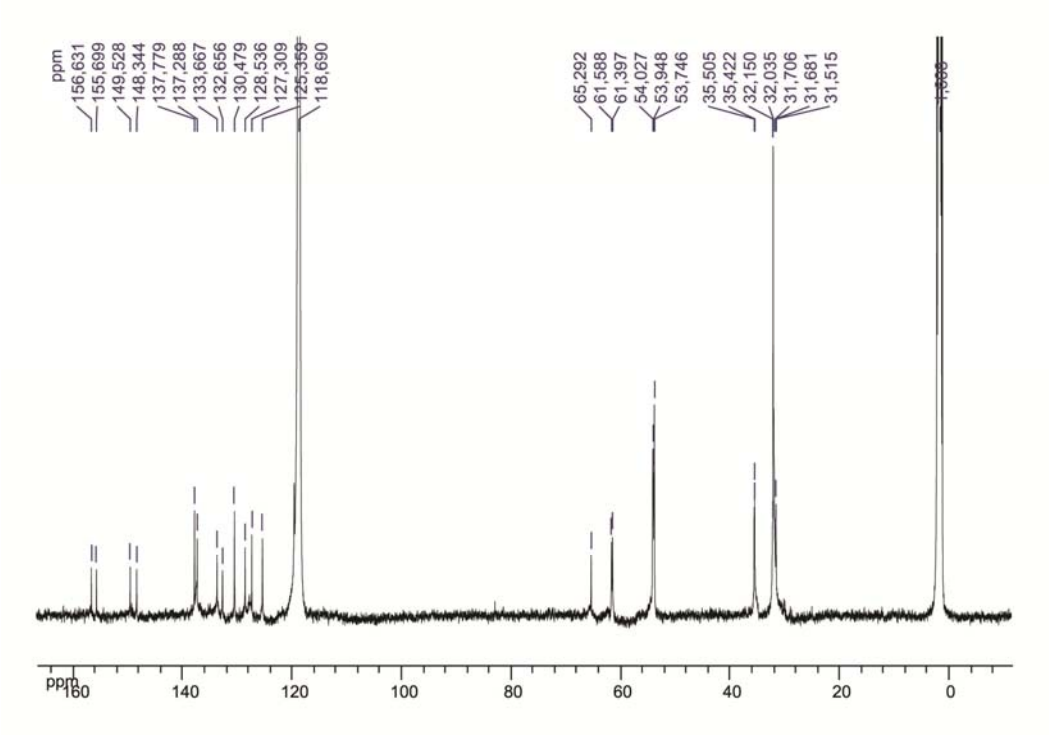


Figure S2: ^{13}C NMR (125 MHz, CD_3CN, $Zn(ClO_4)_2.6H_2O$ excess, 300 K)

3/ GRADUAL ADDITION OF WATER

When the complexation to calixarene **3** was performed with $Zn(NO_3)_2.6H_2O$, a similar signature was obtained, attesting to the formation of the same dicationic complex. The nitrate complex revealed soluble and stable in a mixture of deuterated acetonitrile/methanol (4:1, at 1.6 mM), and addition of water up to 20% v/v did not affect the ^1H NMR signature, thereby attesting to the stability of the complex in such a mixed organic-aqueous medium.

0.729 μmol of ligand **3** and 0.729 μmol of $Zn(NO_3)_2.6H_2O$ were dissolved in 400 μL of CD_3CN and 100 μL of MeOD. ^1H NMR 250 MHz spectra were recorded after each addition of D_2O.

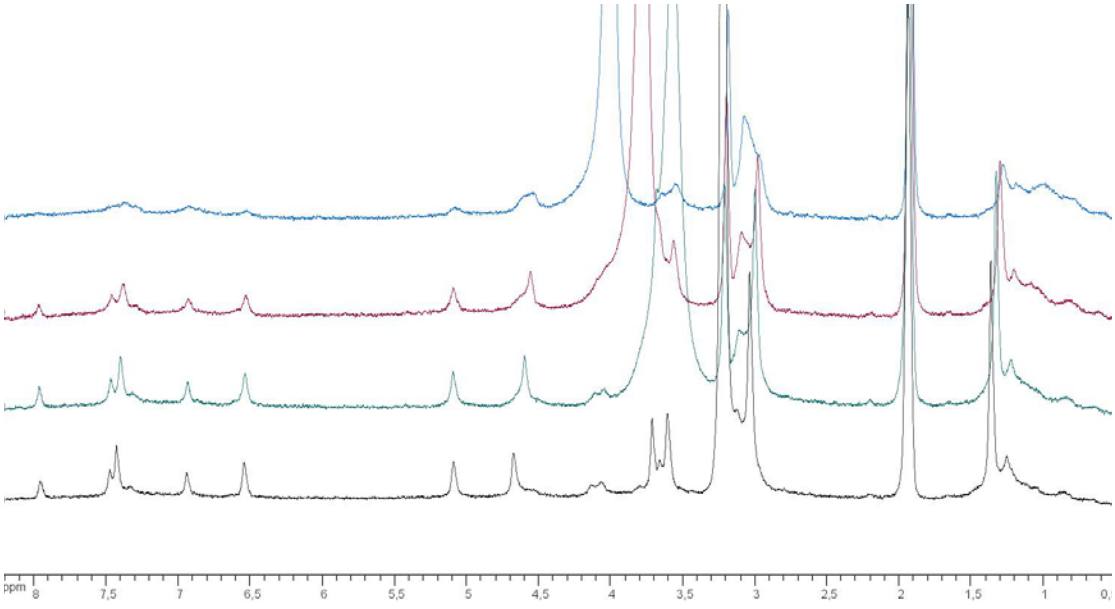
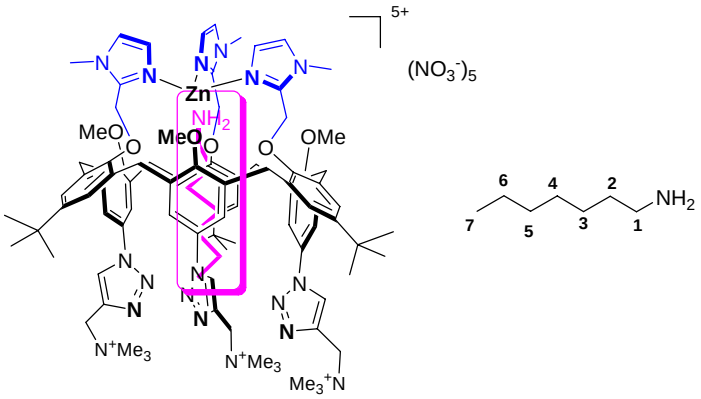


Figure S3: ^{1}H NMR spectrum (250 MHz) of compound **3** from bottom to top 1) after addition of one equivalent of $Zn(NO_3)_2.6H_2O$ in CD_3CN/MeOD (400 µL : 100 µL), 2) after addition of 50 µL of D_2O, 3) after addition of 100 µL of D_2O, 4) after addition of 200 µL of D_2O.

4/ NMR-CHARACTERIZATION OF THE TERNARY COMPLEX OBTAINED WITH HEPTYLAMINE IN DEUTERATED WATER



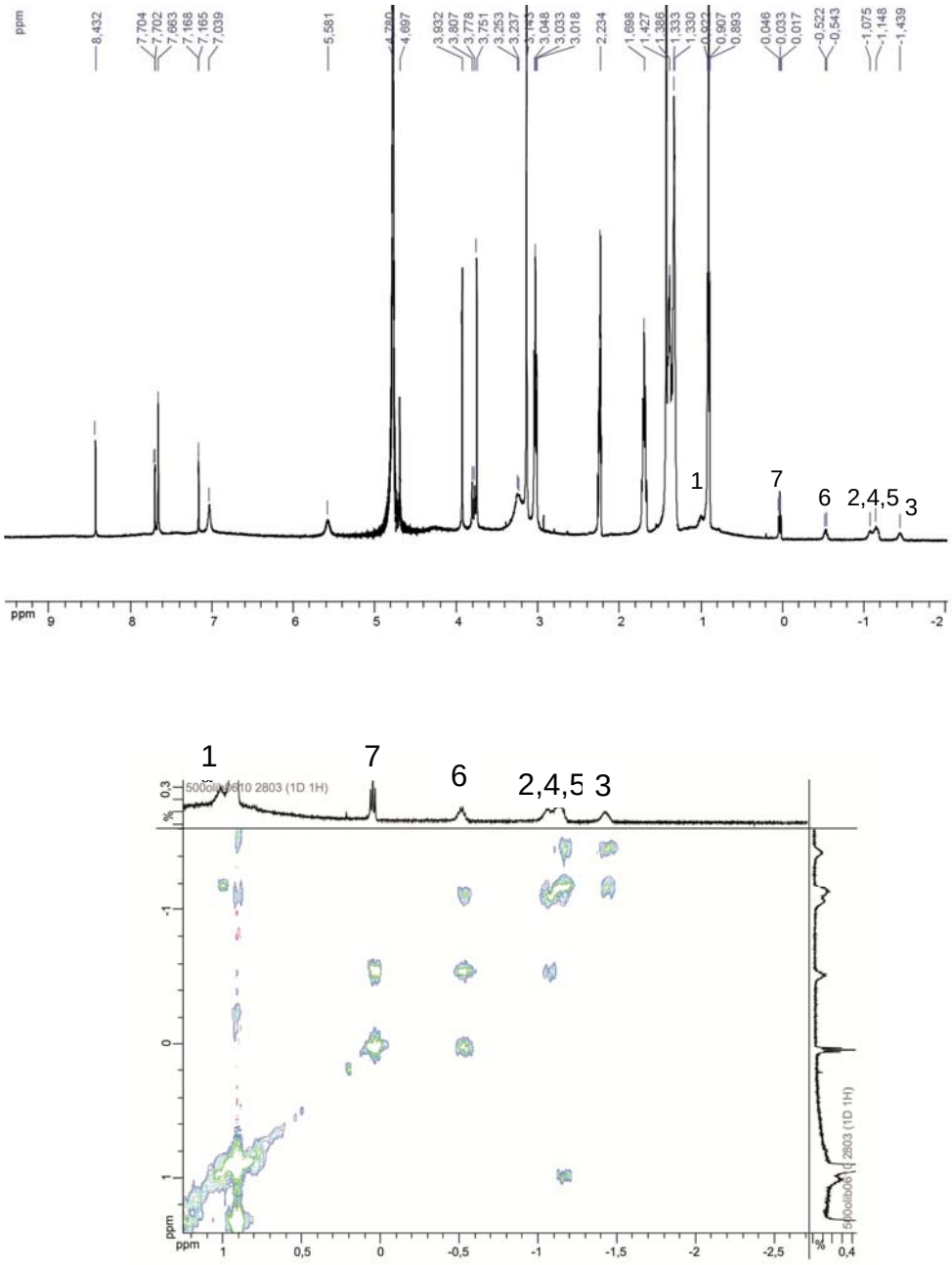


Figure S4: ^{1}H NMR (top) and COSY (bottom) of the ternary complex (D_2O, 500 MHz, 300K, [**3**] = 3.3 mM, in the presence of 3 equiv. $Zn(NO_3)_2.6H_2O$ and 15 equiv. of heptylamine).

^{1}H NMR (500 MHz, D_2O, 300 K): δ (ppm) : -1.43 (CH_2(3) heptylamine *in*, m, 2H), -1.14 (CH_2 (2 and 4) heptylamine *in*, m, 4H), -1.07 (CH_2(5) heptylamine *in*, m, 2H), -0.52 (CH_2(6) heptylamine *in*, m, 2H), 0.04 (CH_3(7) heptylamine *in*, t, *J* = 6.5 Hz, 3H), 0.92 (CH_3(7) heptylamine *out*, t, *J* = 7.5 Hz), 1.01 (CH_2(1) heptylamine *in*, m, 2H), 1.30-1.43 (CH_2(3–6)

heptylamine *out*, m), 1.44 (tBu, s, 27H), 1.71 (CH_2(2) heptylamine *out*, q, *J* = 7.0 Hz), 3.04 (CH_2(1) heptylamine *out*, t, *J* = 8.0 Hz), 3.15 (N^+Me_3, s, 27H), 3.76 (OCH_3, s, 9H), 3.80 ($ArCH_2$, d, *J* = 15 Hz, 6H), 3.94 (NCH_3, s, 9H), 4.71 ($CH_2N^+Me_3$, s, 6H), 5.59 (CH_2Im, br s, 6H), 7.04 (H_{Artria}, s, 6H), 7.17 (H_{Im}, d, *J* = 1.5 Hz, 3H), 7.67 ($H_{Art\text{-}Bu}$, s, 6H), 7.70 (H_{Im}, d, *J* = 1.5 Hz, 3H), 8.43 ($H_{triazole}$, s, 3H).

Proton	*out*	*in*	Δδ
1	3.04	1.01	2.03
2	1.71	-1.14	2.85
3	1.30-1.43	-1.43	2.78
4	1.30-1.43	-1.14	2.49
5	1.30-1.43	-1.07	2.42
6	1.30-1.43	-0.52	1.87
7	0.92	0.04	0.88

5/ pH-DEPENDANCE

Protometric measurements

Solutions containing ligand **3** at a concentration of 10^{-3} mol.L^{-1} were prepared by dissolving the solid compounds in the presence of an excess of nitric acid (10 eq), they are then neutralized by KOH (0.05M).

The ionic strength was kept constant (I = 0.1) by addition of potassium nitrate (Prolabo) of the highest purity (> 99%). The titrating solutions of carbonate-free base KOH 0.05M and nitric acid 0.1 M were prepared from standardized 1 M solutions (Prolabo). All solutions were prepared with glass-distilled, de-ionized water and degassed by argon saturation in order to remove all dissolved CO_2.

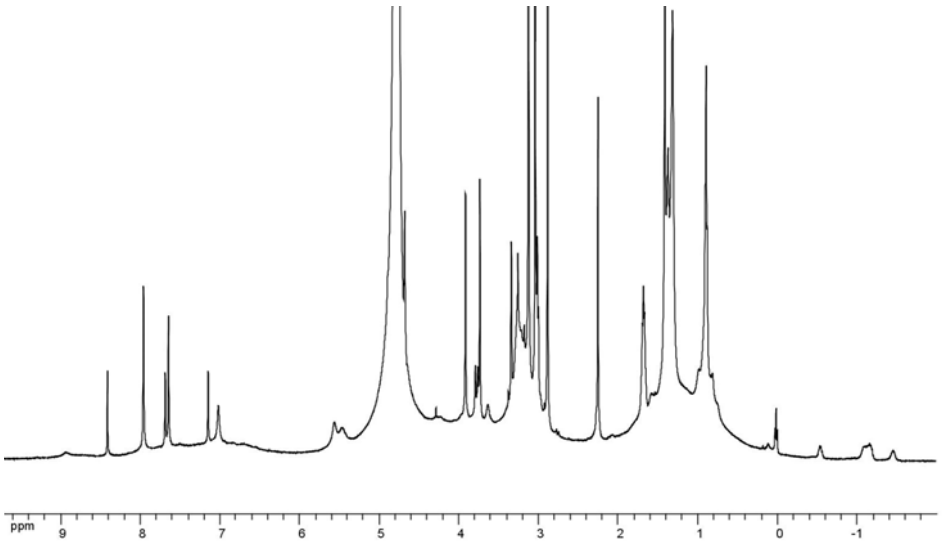
Protometric titrations were carried out with an automatic titrator composed of a microprocessor burette Metrohm Dosimat 665 and a pH-meter Metrohm 713 connected to a computer. The combined type “U” glass electrode used has a very low alkaline error. The titration was fully automated. All measurements were performed within a thermoregulated cell at 25 °C under an argon stream to avoid the dissolution of carbon dioxide. For a classical

titration, a total of 120 to 150 points (volume of titrant, pH) was taken. All equilibrium measurements were carried out in 5.00 mL sample volumes with magnetic stirring. The ionic strength was adjusted to 0.1 with sodium chloride. A HNO_3 solution at exactly 10^{-2} M was used to calibrate the electrode. The electrode slope was checked by titration with a HNO_3 solution, and no correction was necessary in the pH range 2 at 12. The ionic product of water was determined under these conditions (pKw = 13.75) and used in the calculations.
The protonation constants of the ligands were determined from the refinements of neutralisation curves with the general computation program PROTAF.[3]

Optimal pH determination

A solution of calixarene **3** in D_2O ([**3**] = 2.9 mM) in the presence of 1 equiv. of $Zn(NO_3)_2.6H_2O$ and 3 equiv. of heptylamine was prepared and nitric acid was added until pD reaches a starting value of 5.9. Aliquots of a NaOD solution (10.8 mg in 1 mL D_2O) were gradually added to this solution and pD values and ^1H NMR spectra were recorded after each addition. The integration value of one of the encapsulated amine signal in comparison with a reference peak (acetone) was evaluated at different pD by gradual addition of NaOD.

6/ DETERMINATION OF AFFINITY CONSTANT



[3] R. Fournaise, C. Petitfaux, *Talanta*, 1987, **34**, 385.

Figure S5: ^{1}H NMR (500 MHz, D_2O) of calixarene **3** in D_2O ([**3**] = 5.9 mM) with $Zn(NO_3)_2.6H_2O$ (1 equiv.) and heptylamine (1 equiv.) at 300 K, pD = 7.44.

The formation constant K and K'_{pH} of the ternary complex can be defined in the following equilibrium:

$$Zn^{2+} + \mathbf{3}^{3+} + RNH_3^+ + H_2O \rightleftharpoons [Zn(\mathbf{3})(RNH_2)]^{5+} + H_3O^+ \qquad \textbf{(1)}$$

$$K = K_{aeff} = \frac{[[Zn(\mathbf{3})(RNH_2)]^{5+}][H_3O^+]}{[Zn^{2+}][\mathbf{3}^{3+}][RNH_3^+]}$$

and

$$K'_{pH} = \frac{[[Zn(\mathbf{3})(RNH_2)]^{5+}]}{[Zn^{2+}][\mathbf{3}^{3+}][RNH_3^+]}$$

From the above spectrum:

$\rho = [Zn(\mathbf{3})(RNH_2)^{2+}]/ [RNH_2]_{free} = 0.16 \Rightarrow [Zn(\mathbf{3})(RNH_2)^{2+}] = \rho C_0 /(1+\rho) = 0.814$ mM

$\Rightarrow K = Ka_{eff} = 2.25.10^{-4}$ mol^{-1}.L $\Rightarrow pKa_{eff} = 3.7$

and $K'_{7.44} = 6184$ mol^{-2}.L^2

From another experiment:

^{1}H NMR (500 MHz, D_2O) of calixarene **3** in D_2O ([**3**] = 5.9 mM) with $Zn(NO_3)_2.6H_2O$ (1 equiv.) and heptylamine (1.5 equiv.) at 300 K, pD = 7.86.

$\rho = [Zn(\mathbf{3})(RNH_2)^{2+}] / [RNH_2]_{free} = 0.1075 \Rightarrow [Zn(\mathbf{3})(RNH_2)^{2+}] = \rho C_0 /(1+\rho) = 0.859$ mM

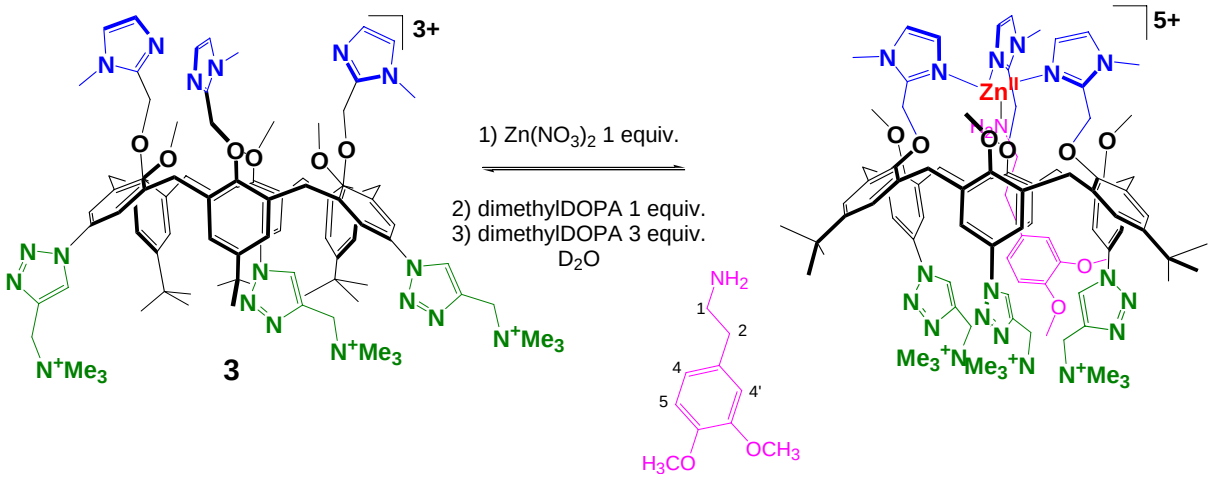
$\Rightarrow K = Ka_{eff} = 5.84.10^{-5}$ mol^{-1}.L $\Rightarrow pKa_{eff} = 4.2$

$K'_{7.86} = 4232$ mol^{-2}.L^2

These calculations were repeated four times, on four different experiments. The obtained average values of pK_{aeff} is 4.0±0.3.

7/ AMINE RECEPTOR

DimethylDOPA



Ligand **3** (2 mg, 1.3 µmol) was dissolved in D_2O (400 µL). To this solution were added $Zn(NO_3)_2.6H_2O$ (1.3 µmol, 29 µL of a solution containing 6.5 mg of $Zn(NO_3)_2.6H_2O$ in 500 µL D_2O) and dimethylDOPA (3.9 µmol, 25.5 µL of a solution containing 5.5 mg of dimethylDOPA in 200 µL MeOD).

The ^1H NMR spectrum in D_2O of the ternary complex observed in the presence of dimethyldopamine is presented in Figure S6. As observed with heptylamine, it displays characteristic resonances of a dicationic C_3 symmetric complex where the zinc ion is coordinated to the three imidazole groups and to the amine substrate. Addition of only 1 equiv. of dimethylDOPA was enough to detect the NMR signature of the ternary complex. Further addition of dimethyldopamine led to an increase in ternary complex formation. In the absence of buffer and with C = 2.5 mM of calixarene **3** and Zn(II), the maximal amount of ternary complex was observed when 3 equivalents of dimethyldopamine were added. Under these conditions, around 60% of calixarene was effective as amine-receptor.

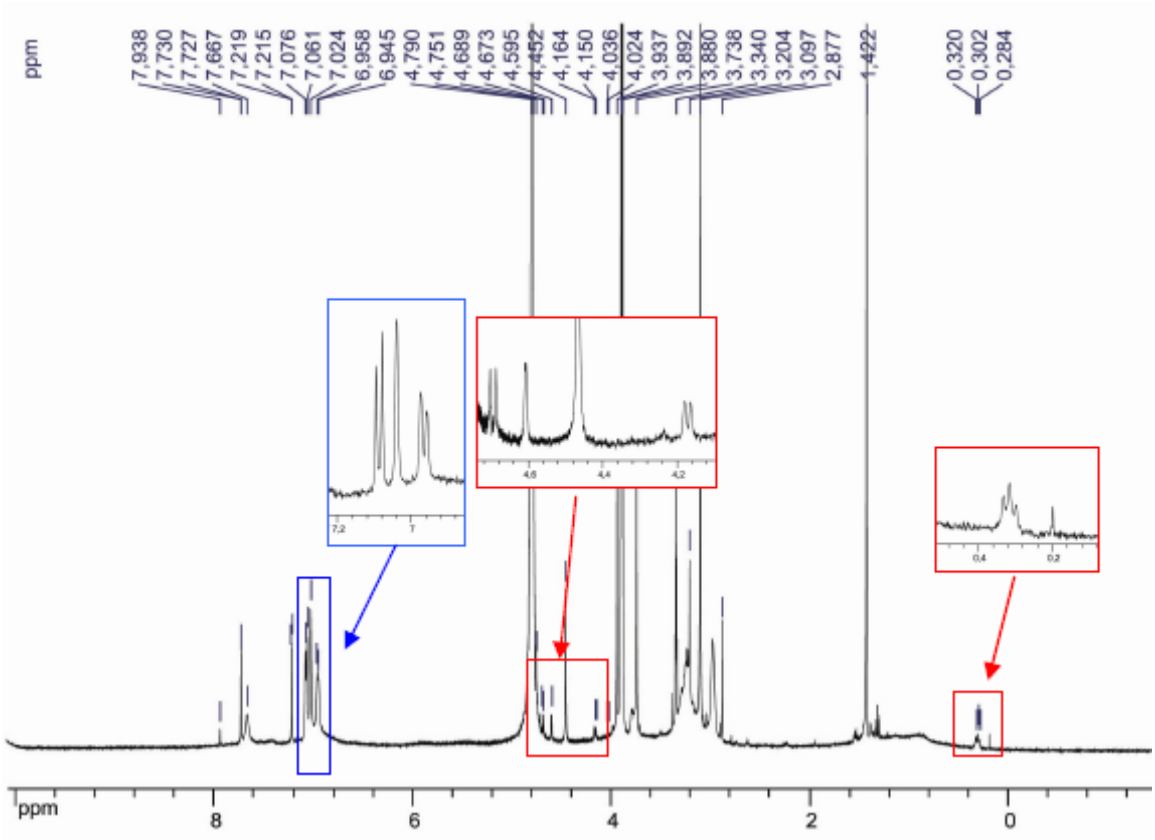


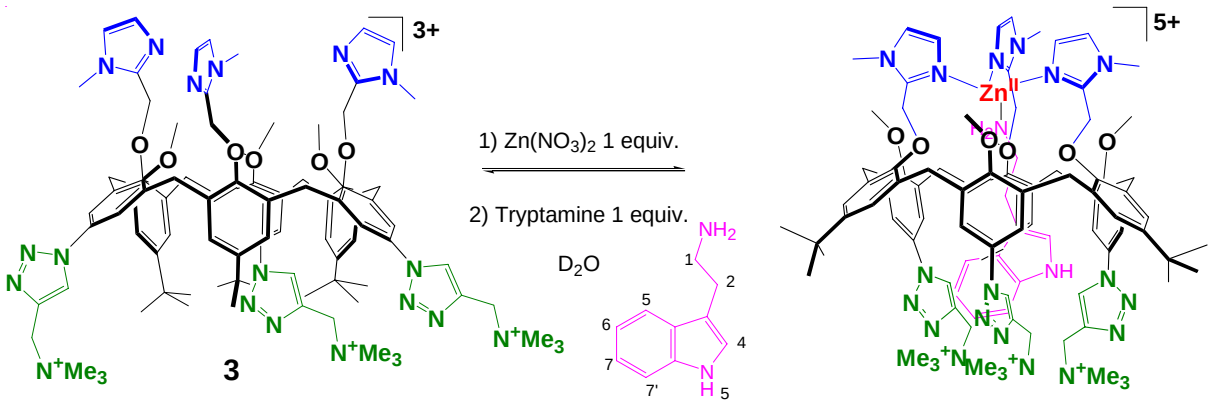
Figure S6: ^{1}H NMR (500 MHz, D_2O, 300 K) of ligand **3** (C = 3.25 mM) with one equivalent of $Zn(NO_3)_2.6H_2O$ and 3 equivalents of dimethylDOPA (blue-framed signals: dimethylDOPA *out*, red-framed signals: dimethylDOPA *in*)

^{1}H NMR (500 MHz, D_2O, 300 K): δ (ppm): 0.30 (CH_2(2) dimethylDOPA *in*, t, *J* = 9 Hz, 2H), 1.42 (tBu and CH_2(1) dimethylDOPA *in*, br s, 29H), 2.88 (OCH_3 dimethylDOPA *in*, 6H), 2.97 (br s, CH_2(2) dimethylDOPA *out*), 3.10 (N^+Me_3, s, 27H), 3.20 (OCH_3 dimethylDOPA *in*), 3.30 (CH_2(1) dimethylDOPA *out*, br s), 3.74 (OCH_3, 9H), 3.88 (OCH_3 dimethylDOPA *out*), 3.94 (NCH_3, s, 9H), 4.15 (H(5) dimethylDOPA *in*, d, *J* = 8.0 Hz, 1H), 4.45 ($CH_2N^+Me_3$, s, 6H), 4.59 (H(4') dimethylDOPA *in*, s, 1H), 4.68 (H(4) dimethylDOPA *in*, d, *J* = 8.0 Hz, 1H), 6.95 (H(5) dimethylDOPA *out*, d, *J* = 8.0 Hz), 7.02 (H(4 ') dimethylDOPA *out*, s), 7.07 (d, H(4) dimethylDOPA *out*, *J* = 8.0 Hz), 7.22 (H_{Im}, d, *J* = 1.5 Hz, 3H), 7.67 ($H_{Art\text{-}Bu}$, br s, 6H), 7.73 (H_{Im}, d, *J* = 1.5 Hz, 3H), 7.94 ($H_{triazole}$, s, 3H).

Proton	*out*	*in*	Δδ
1	3.30	1.42	1.88
2	2.97	0.30	2.67
4’	7.02	4.59	2.43
4	7.07	4.68	2.39
5	6.95	4.15	2.80
OCH_3	3.88	3.20 and 2.88	0.68 and 1.01

Tryptamine

Ligand **3** (1 μmol) was dissolved in D_2O (350 μL). To this solution were added $Zn(NO_3)_2.6H_2O$ (1 μmol) and tryptamine (1 μmol, 6.5 μL of a solution containing 7.2 mg of tryptamine in 300 μL MeOD).



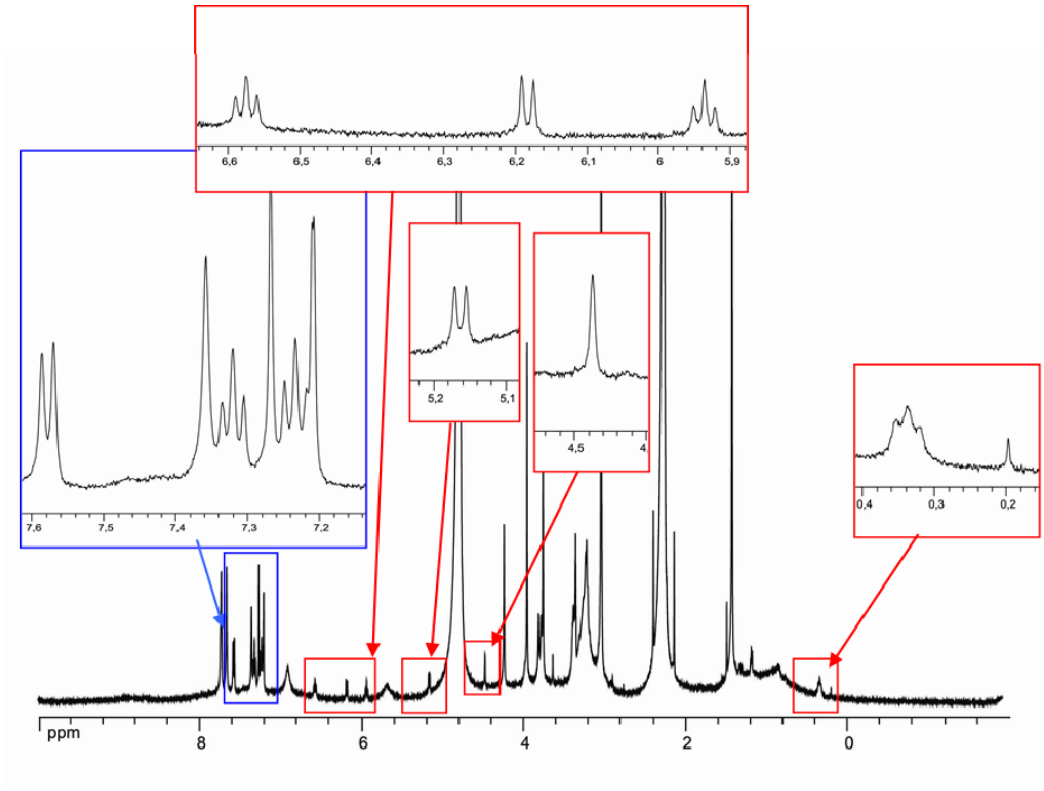


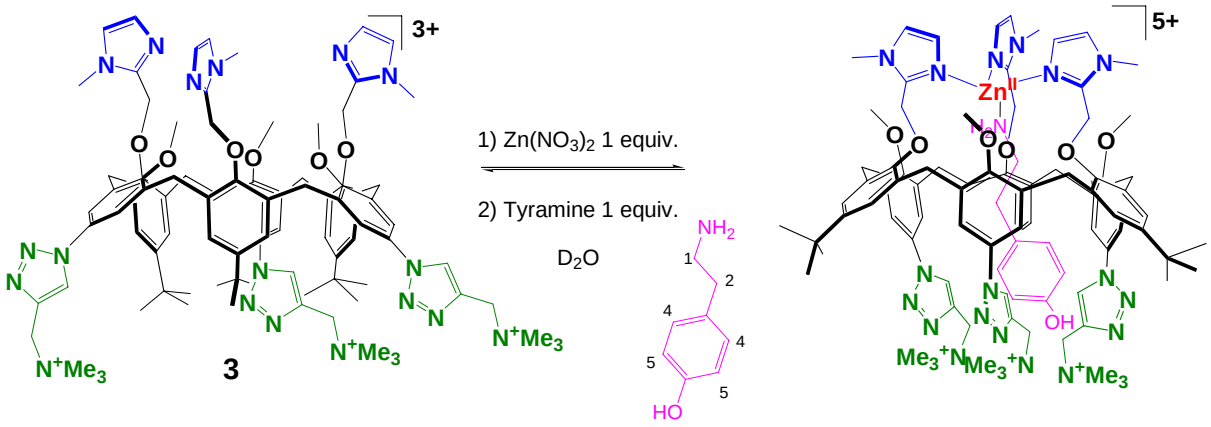
Figure S7: ^{1}H NMR (500 MHz, D_2O, 300 K) of ligand **3** (C = 2.85 mM) with $Zn(NO_3)_2.6H_2O$ (1 equiv.) and tryptamine (1 equiv.) (blue-framed signals: tryptamine *out*, red-framed signals: tryptamine *in*).

^{1}H NMR (500 MHz, D_2O, 300 K): δ (ppm) : 0.34 (CH_2 (2) tryptamine *in*, t, *J* = 8.0 Hz, 2H), 1.42 (tBu and CH_2 (1) tryptamine *in*, s, 29H), 3.03 (N^+Me_3, s, 27H), 3.22 (CH_2(2) tryptamine *out*, br s), 3.38 (CH_2(1) tryptamine *out*, br s), 3.76 (OCH_3, s, 9H), 3.79 (CH_2Ar, d, *J* = 16 Hz, 6H), 3.95 (NCH_3, s, 9H), 4.24 ($CH_2N^+Me_3$, s, 6H), 4.47 (H (4) tryptamine *in*, s, 1H), 5.16 (H (5) tryptamine *in*, d, *J* = 7.5 Hz, 1H), 5.69 (CH_2Im, br s, 6H), 5.94 (H (6) tryptamine *in*, t, *J* = 7.5 Hz, 1H), 6.18 (H (7') tryptamine *in*, d, *J* = 8.0 Hz, 1H), 6.57 (H (7) tryptamine *in*, t, *J* = 7.0 Hz, 1H), 6.91 ($H_{ArTriaz}$, br s, 6H), 7.20 (H_{Im}, d, *J* = 1.5 Hz, 3H), 7.23 (H (6) tryptamine *out*, t, *J* = 7.0 Hz), 7.27 (s, H Triazole, 3H), 7.32 (H (7) tryptamine *out*, t, *J* = 7.5 Hz), 7.35 (H (4) tryptamine *out*, s), 7.58 (H(5) tryptamine *out*, d, *J* = 7.5 Hz), 7.67 ($H_{Art\text{-}Bu}$, s, 6H), 7.73 (H_{Im} and H (7') tryptamine *out*, d).

Proton	*out*	*in*	Δδ
1	3.38	1.42	1.96

2	3.22	0.34	2.88
4	7.35	4.47	2.88
5	7.58	5.16	2.42
6	7.23	5.94	1.29
7	7.32	6.57	0.75
7'	7.73	6.18	1.55

Tyramine



Ligand **3** (1 μmol) was dissolved in D_2O (400 μL, C = 2.5 mM). To this solution were added $Zn(NO_3)_2.6H_2O$ (1 μmol) and chlorhydrate salt of tyramine (1 μmol, 10.8 μL of a solution containing 2.7 mg of chlorhydrate salt of tyramine in 320 μL D_2O). pD value of the solution was recorded and reached 7.94.

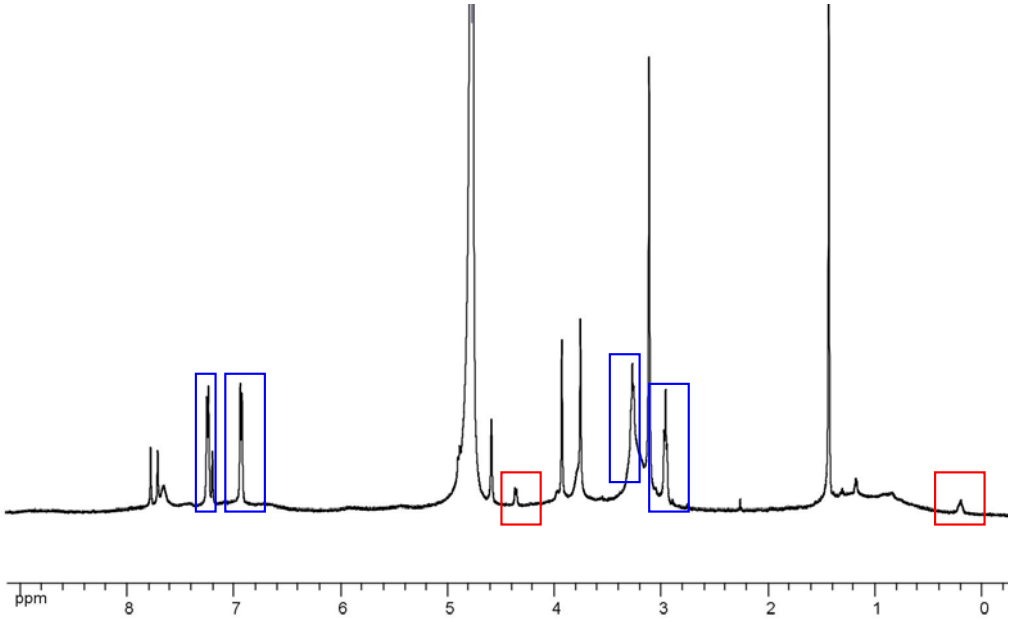


Figure S8: ^{1}H NMR (500 MHz, D_2O, 300 K) of ligand **3** (C = 2.5 mM) with $Zn(NO_3)_2.6H_2O$ (1 equiv.) and chlorhydrate salt of tyramine (1 equiv.) (blue-framed signals: tyramine *out*, red-framed signals: tyramine *in*).

^{1}H NMR (500 MHz, D_2O, 300 K): δ (ppm): 0.21 (CH_2(2) tyramine *in*, m, 2H), 1.45 (tBu and CH_2(1) tyramine *in*, s, 29H), 2.98 (CH_2(2) tyramine *out*, t, *J* = 7.0 Hz), 3.13 (N^+Me_3, s, 27H), 3.28 (CH_2(1) tyramine *out*, m), 3.77 (OCH_3, s, 9H), 3.80 (CH_2Ar, br s, 6H), 3.95 (NCH_3, s, 9H), 4.38 (H(5) tyramine *in*, d, *J* = 7.5 Hz, 2H), 4.60 ($CH_2N^+Me_3$, s, 6H), 4.91 (H(4) tyramine *in*, d, *J* = 7.5 Hz, 2H), 6.95 (H(5) tyramine *out*, d, *J* = 8.0 Hz), 7.22 (H_{Im}, br s, 3H), 7.26 (H(4) tyramine *out*, d, *J* = 8.0 Hz), 7.69 ($H_{Ar\text{-}Bu}$, br s, 6H), 7.73 (H_{Im}, s, 3H), 7.80 (s, 3H, $H_{Triazole}$).

Proton	*out*	*in*	Δδ
1	3.28	1.45	1.83
2	2.98	0.21	2.77
4	7.26	4.91	2.35
5	6.95	4.38	2.57