Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
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Supporting information for :

A versatile strategy for appending a single functional group to a multifunctional host through host-guest covalent-capture

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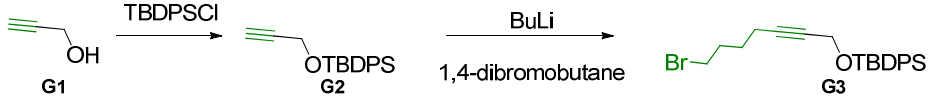
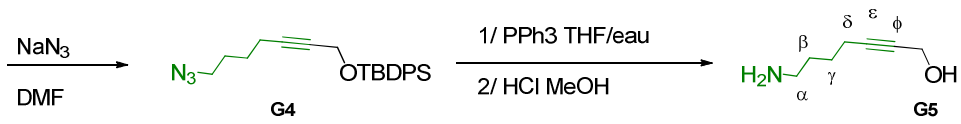
1/ Materials and methods

Solvents and chemicals were of reagent grade and were distilled prior to use. ESI-MS analyses were obtained with a ThermoFinnigen LCQ Advantage spectrometer (ion trap analyzer) using methanol and dichloromethane as solvents. HR-MS analyses were carried out on a Thermo Scientific Exactive spectrometer (Orbitrap analyzer). NMR spectra were recorded on a Brucker ARX250 MHz spectrometer or an Advance 500 spectrometer.

2/ Synthesis of guest G5





G2 was prepared according to a reported procedure.[1]

a) Synthesis of **G3**

A solution of **G2** (4 g, 13.6 mmol) in THF (20mL) and DMPU (10 mL) was cooled down to -78 ° C under argon. Butyllithium (10 mL, 14.9 mmol, 1.6 M in hexanes) was added dropwise and stirred for one hour at -78°C. The mixture was added dropwise under argon to a solution of 1,4-dibromobutane (4.9 mL, 40.8 mmol) in THF (20 mL)at -78°C, and raised overnight to room temperature. Water (10 mL) was added, and the mixture was extracted with diethyl ether (3 x 30 mL). The gathered organic phases were dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography (SiO_2), eluted first with cyclohexane to remove excess 1,4-dibromobutane; then cyclohexane/AcOEt (4:1) to yield **3** as an oil (5.35 g, 92%)

^{1}H NMR ($CDCl_3$, 250 MHz, 300 K): δ (ppm): 1.05 (s, 9H, *t*Bu); 1.59 (m, 2H, γ); 1.91 (m, 2H, β); 2.19 (tt, J_1 =14 Hz, J_2= 4.5 Hz,2H, δ); 3.39 (t, J_1 =14 Hz, 2H, α); 4.31 (t, J_2= 4.5 Hz, 2H, CH_2O); 7.41 (m, 6H, H_{Ph}); 7.71 (m, 4H, H_{Ph}).

b) Synthesis of **G4**

G3 (3.45g, 8 mmol) and sodium azide (1.04 g, 16 mmol) were mixed in 10 mL DMF and stirred at room temperature for 15 hours. The reaction mixture was diluted with water (10 mL) and extracted with Et_2O (4 x 25 mL). The organic extracts were washed with water (4x10 mL), dried over Na_2SO_4, filtered and evaporated to dryness to yield **4** as an oil (2.7 g, 86%).

^{1}H NMR ($CDCl_3$, 250 MHz, 300 K): δ (ppm): 1.06 (s, 9H, *t*Bu); 1.53 (m, 2H, γ); 1.66 (m, 2H, β); 2.19 (tt, J_1 =13.5 Hz, J_2= 4.3 Hz,2H, δ); 3.26 (t, J_1 =13.5 Hz, 2H, α); 4.31 (t, J_2= 4.3 Hz, 2H, CH_2O); 7.40 (m, 6H, H_{Ph}); 7.71 (m, 4H, H_{Ph}).

c) Synthesis of **G5**

G4 (2.66 g, 6.8 mmol) and triphenylphosphine (2.14 g, 8.2 mmol) were stirred at room temperature under argon in a degassed THF/water mixture (18 mL / 2 mL). After 20 hours, HCl 37% was added (1.5 mL) and the mixture was evaporated to dryness. Methanol (20 mL) and HCl 10 % (2.5 mL) were added and stirred for one hour. Diethyl ether was added until complete solubilization and the mixture was overnight at room temperature. After evaporation to dryness, water (10 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL) to remove PPh_3=O. The aqueous phase was made basic with NaOH (pH = 8) and extracted with CH_2Cl_2 (4 x 20 mL). The organic phases were dried over Na_2SO_4 and evaporated to dryness to yield **5** as an oil that solidifies on standing. (0,76 g, 88%)

^{1}H NMR ($CDCl_3$, 250 MHz, 300 K): δ (ppm): 1.55 (m, 4H, γ β); 2.24 (m, ,2H, δ); 2.71 (m, , 2H, α); 4.20 (t, J_2= 4.5 Hz, 2H, CH_2O).

^{13}C NMR ($CDCl_3$, 75 MHz, 300 K): δ (ppm): 18.17 (δ); 25.99 (γ);32.64 (β); 41.58 (α); 50.87 (CH_2O); 79.42 (ϕ); 85.51 (ε).

HRMS: peak of mass 128.10703 corresponds to the formula $C_7H_{14}NO$ in agreement with [**5** + H]$^+$ (mass error: 0.04 mmu; 0.3 ppm).

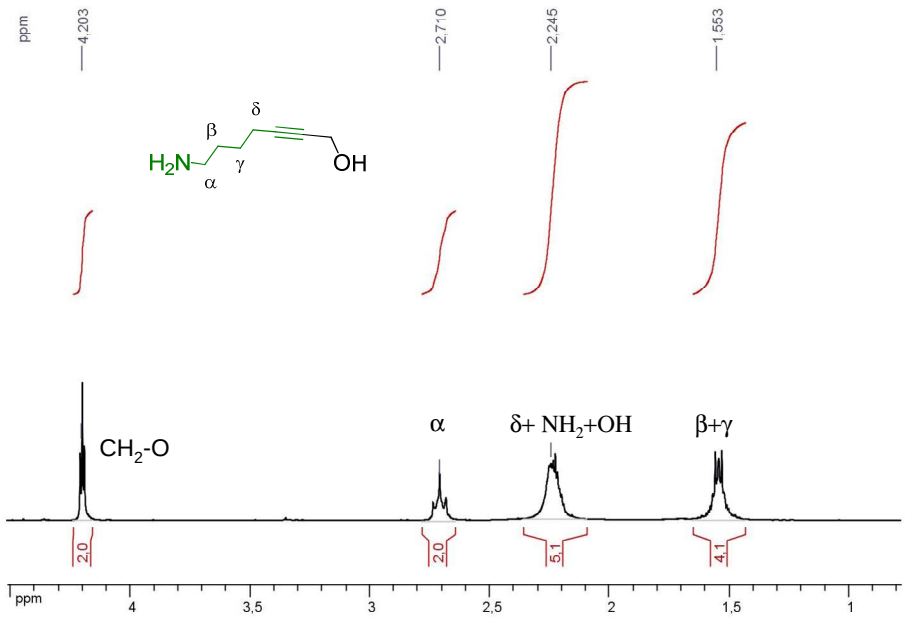


Figure S1. ^{1}H NMR spectrum($CDCl_3$, 250 MHz, 300 K) of **G5.**

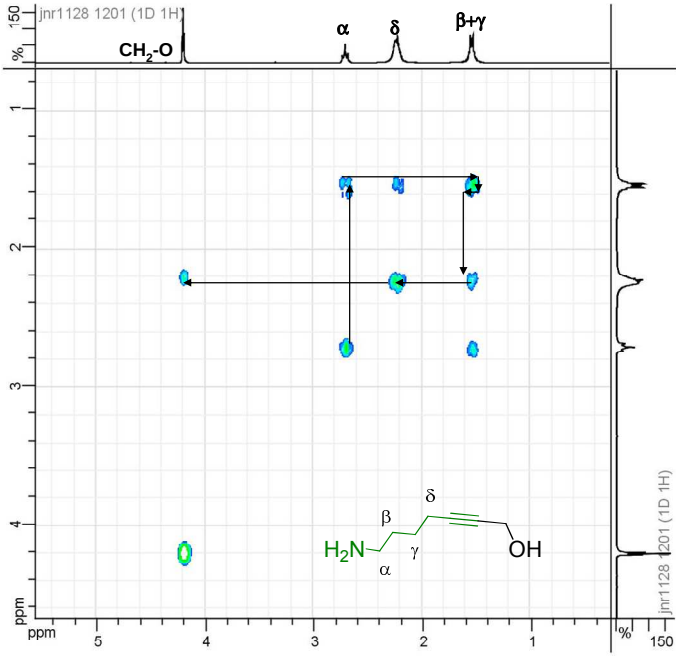


Figure S2. COSY spectrum ($CDCl_3$, 250 MHz, 300 K) of **G5.**

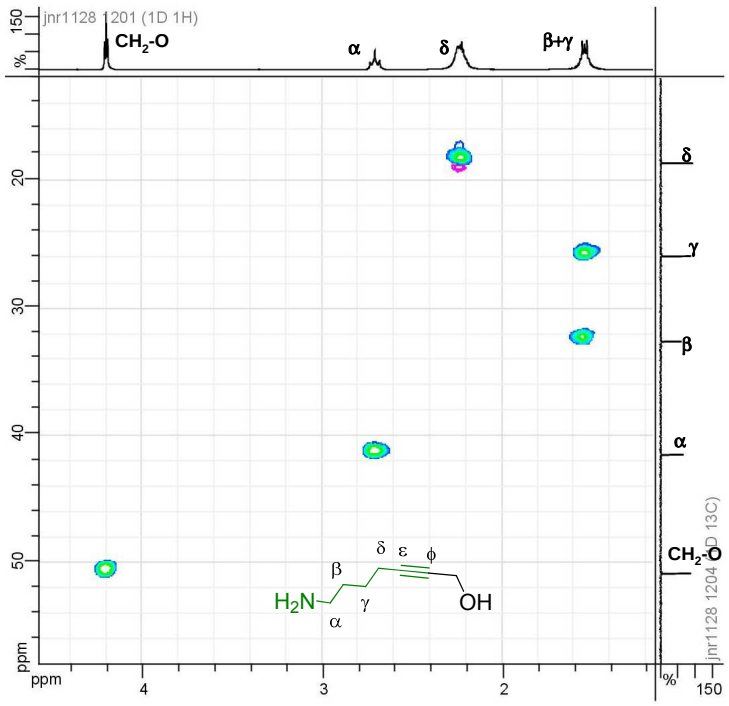


Figure S3. HSQC spectrum ($CDCl_3$, 250 MHz, 300 K) of **G5.**

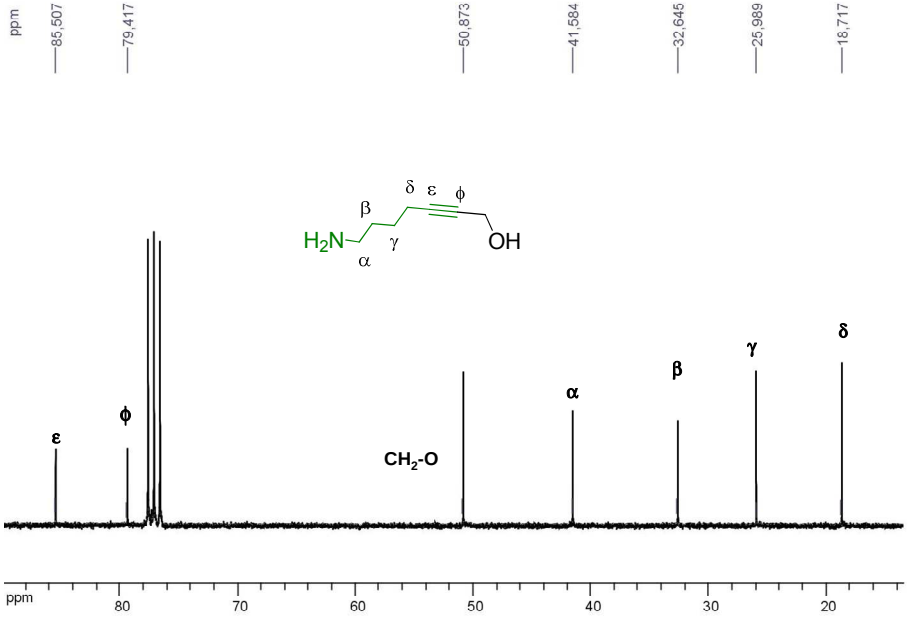
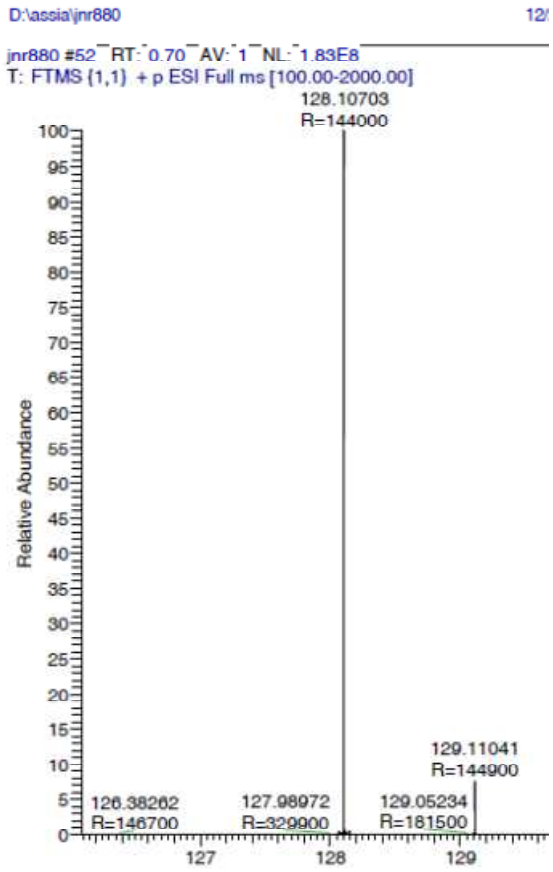


Figure S4. ^{13}C NMR ($CDCl_3$, 75 MHz, 300 K) of **G5.**



Elemental composition search on mass 128.11

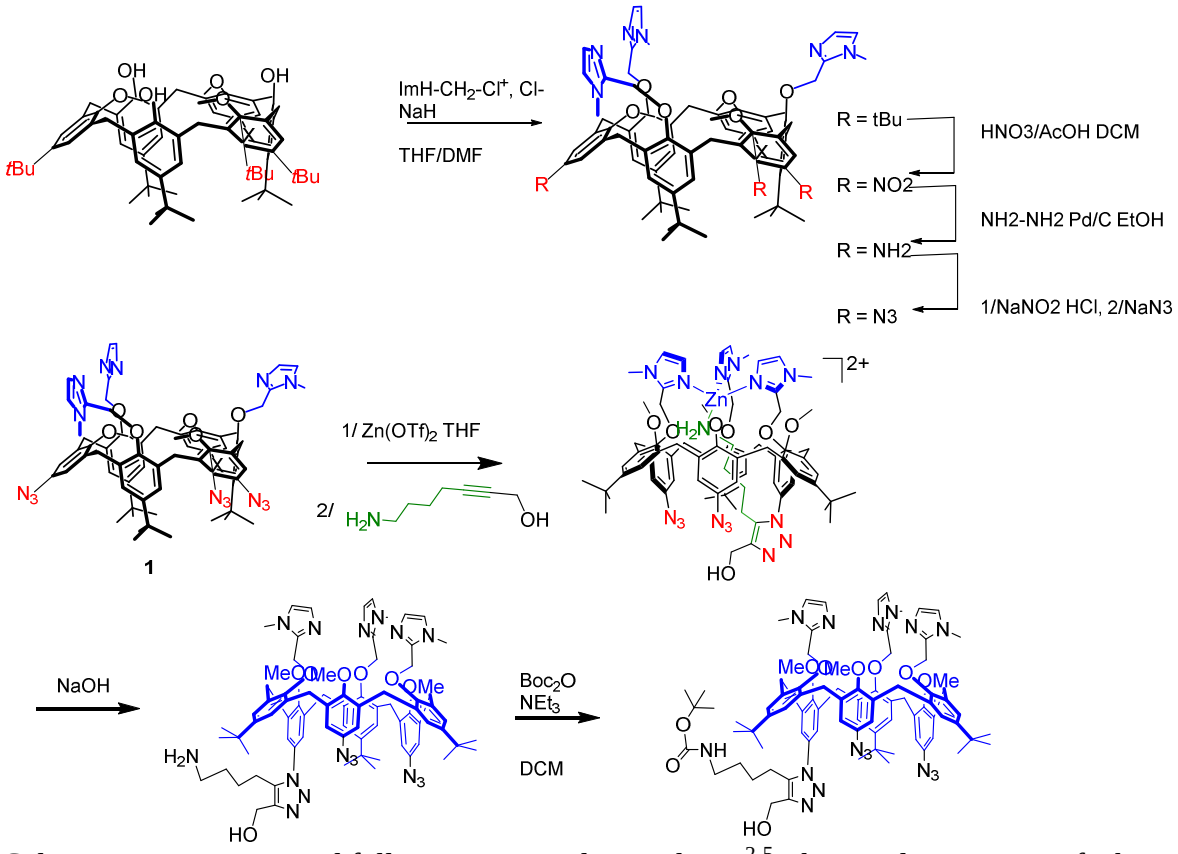
m/z= 123.11-133.11

m/z	Theo. Mass	Delta (mmu)	RDB equiv.	Composition
128.11	128.11	0.04	1.5	$C_7H_{14}ON$
	128.11	1.38	2.0	$C_5H_{12}N_4$
	128.12	-11.19	1.5	$C_6H_{14}N_3$
	128.12	-12.54	1.0	$C_8H_{16}O$
	128.09	12.62	2.0	$C_6H_{12}ON_2$

Figure S5. HRMS spectrum of **G5.** the peak associated to mass 128.10703 corresponds to the formula $C_7H_{14}NO$ in agreement with [**G5** + H]$^+$ (mass error: 0.04 mmu; 0.3 ppm).

3/ Synthesis of calix[6]arene 3

Synthesis of monofunctionalized precursor **3**



Calixarene **1** was prepared following reported procedures.[2-5] The covalent capture of a host-guest is derived from a previously reported methodology.[6,7]

a) Synthesis of [Zn(**2**)](OTf)$_2$ = L_{OH}^{C4NH2} Zn(OTf)$_2$

1 (100 mg, 80 µmol) and Zn(OTf)$_2$ (29 mg, 80 µmol) were mixed in THF (10 mL). The solution was stirred for one hour and evaporated to dryness. The residue was taken up in toluene (12 mL) and 7-hydroxy-hept-5-yn-1-amine (19 mg, 160 µmol) was added. The mixture was stirred under reflux for 5 hours, and then evaporated to dryness. The solid was washed with diethyl ether (2x5 mL), centrifugated, and dried under vacuum. [Zn(**2**)](OTf)$_2$ is obtained as a solid (136 mg, 98%).

Isolation of the ligand **2** (L_{OH}^{C4NH2}):

[Zn(**2**)](OTf)$_2$ (303 mg, 174 µmol) was treated with NaOH 3M in CH_2Cl_2. Organics were extracted with CH_2Cl_2, organic phases washed with water and dried over with Na_2SO_4. After filtration and evaporation, **2** is obtained as a yellow solid (240 mg, 92%). The ligand gives broad ^{1}H NMR signals at room temperature in various solvents. It was thus characterized as its Zn complex [Zn(**2**)](OTf)$_2$.

^{1}H (500 MHz, CD_3CN, 300 K) δ (ppm): -1.07 (m, 2H, β); -0.17 (m, 2H, γ); 0.82 (m, 2H, α); 1.37 (s, 18H, *t*Bu); 1.44 (s, 9H, *t*Bu); 1.61 (t, J = 7.5 Hz, 2H, δ); 2.23 (m, 2H, NH_2); 2.89 (s, 1H, OH) 3.53 (d, J = 15.5 Hz, 2H, CH_2Ar); 3.59 (d, J = 15.5 Hz, 2H, CH_2Ar); 3.60 (s, 6H, OCH_3); 3.72(d, J = 15.5 Hz, 2H, CH_2Ar); 3.79 (s, 3H, OCH_3); 3.80 (s, 6H, NCH_3); 3.84(s, 3H, NCH_3) ; 4.12 (m, 6H, CH_2Ar); 4.40 (s, 2H, CH_2OH); 5.21 (d, J = 15.5 Hz, 2H, CH_2Im); 5.32 (d, J = 15.5 Hz, 2H, CH_2Im); 5.40 (s, 2H, CH_2Im); 6.12 (s 2H, H_{ArTria}); 6.29 (s 4H,

H_{ArN3}); 6.93 (d, J = 1.5 Hz, 1H, H_{ArTria}); 6.95 (d, J = 1.5 Hz, 2H, H_{ArTria}); 7.44 (d, J = 2.7 Hz, 2H, H_{ArtBu}); 7.45 (d, J = 2.7 Hz, 2H, H_{ArtBu}); 7.49 (s 2H, H_{ArtBu}); 7.52 (m, 3H, H_{Im})

^{13}C (500 MHz, CD_3CN, 300 K) δ (ppm): 19.07; 20.73; 24.49; 26.86; 30.15; 30.35; 30.81; 31.17; 31.67; 35.14; 35.30; 40.95; 42.31; 50.87; 56.06; 61.25; 61.70; 65.64; 65.79; 117.75; 117.95; 124.6; 124.99; 125.12; 128.40; 128.47; 130.17; 130.30; 130.48; 132.39; 132.48; 132.54; 133.21; 136.05; 136.10; 136.59; 136.60; 136.72; 144.57; 147.45; 149.38; 149.52; 152.61; 154.94; 155.02; 156.06

ESI-MS (CH_3OH): m/z = 1379.5 (calcd for [L_{OH}^{C4NH2} +H]$^+$: 1379.7)

HRMS: peak at 721.34027 corresponds to the formula $C_{79}H_{94}N_{16}O_7Zn$ in agreement with [L_{OH}^{C4NH2} Zn]$^{2+}$ (mass error: 1.68 mmu; 2.3 ppm).

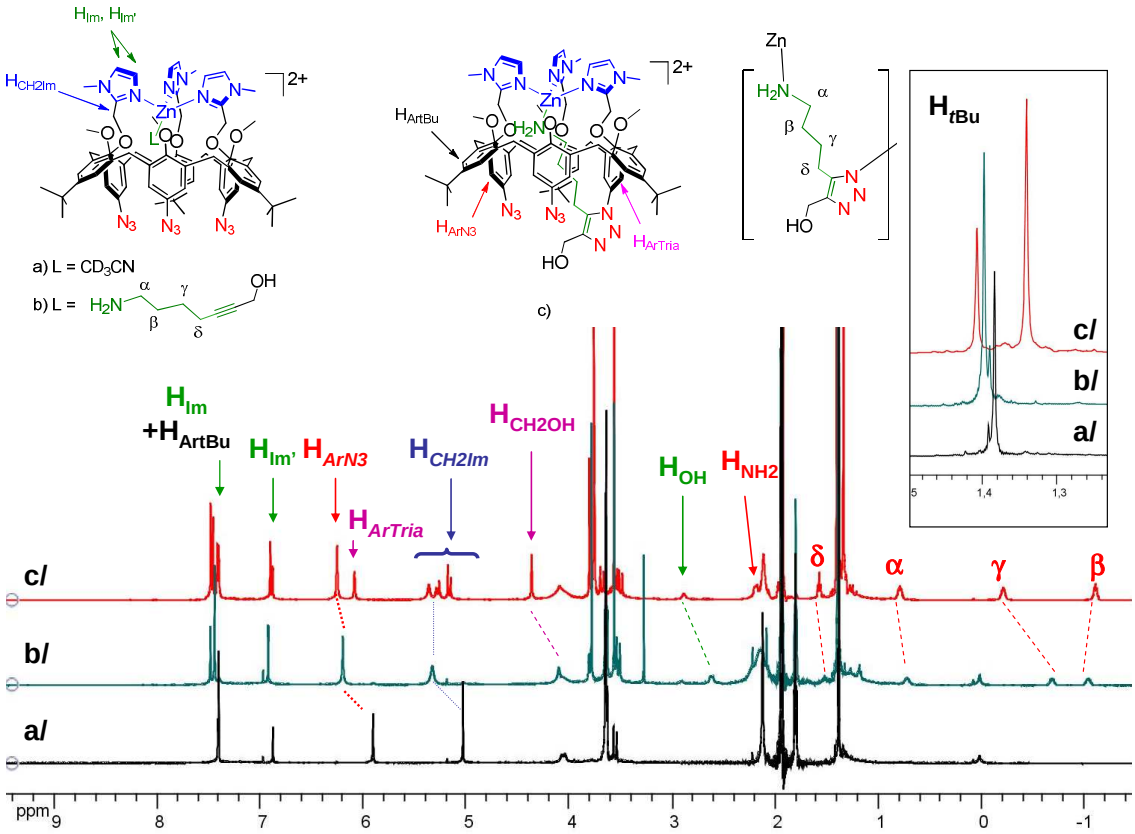


Figure S6. Evolution of the ^{1}H NMR spectra (500 MHz, 300 K, CD_3CN) during the course of the covalent capture of the host-guest adduct. a) [Zn(**1**)(S)]$(ClO_4)_2$, b) [Zn(**1**)$(NH_2(CH_2)_4C{\equiv}C\text{-}CH_2OH)](ClO_4)_2$, c) [Zn(**2**)(S)]$(ClO_4)_2$.

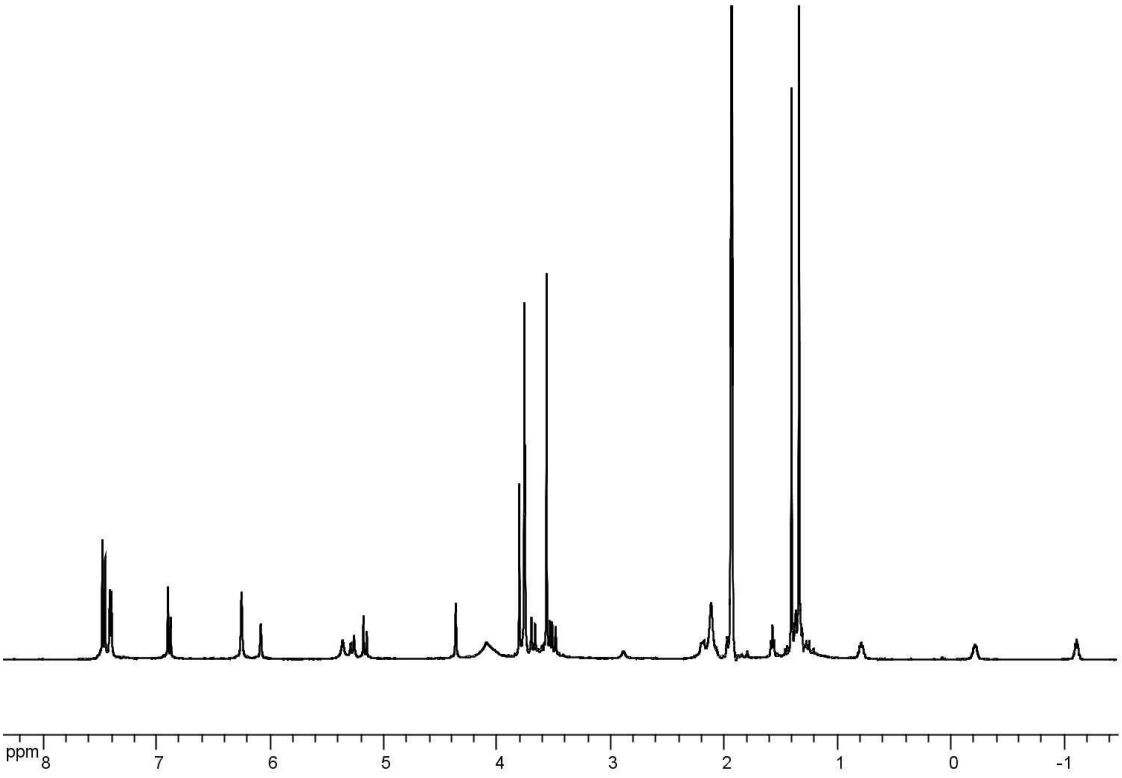


Figure S7. ^{1}H spectrum of L_{OH}^{C4NH2} $Zn(OTf)_2$ (500 MHz, CD_3CN, 300 K)

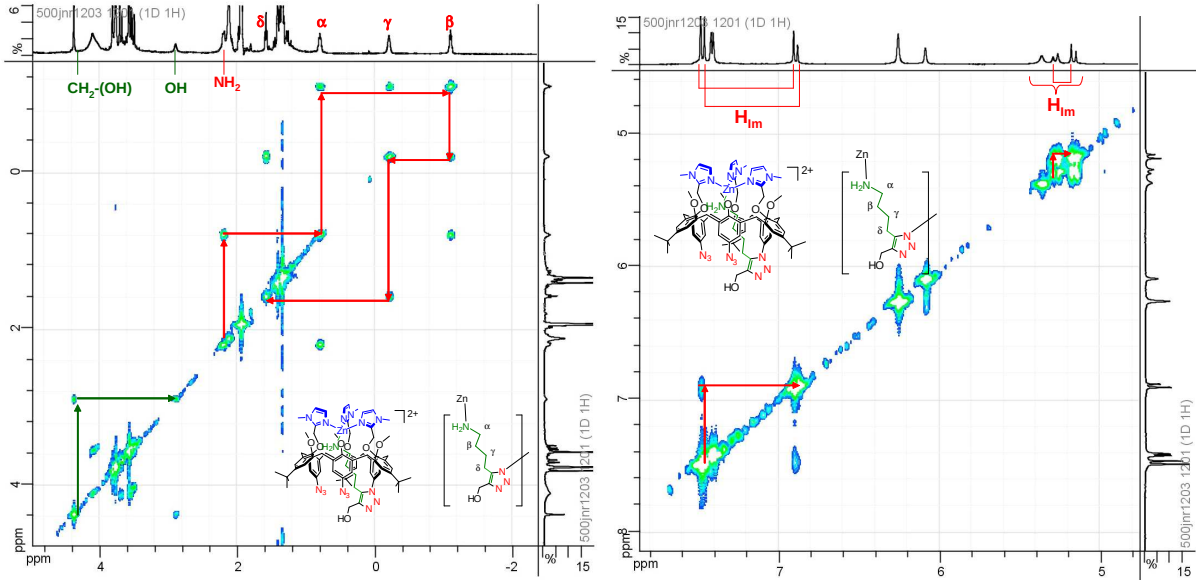


Figure S8. COSY spectrum of L_{OH}^{C4NH2} $Zn(OTf)_2$ (500 MHz, CD_3CN, 300 K)

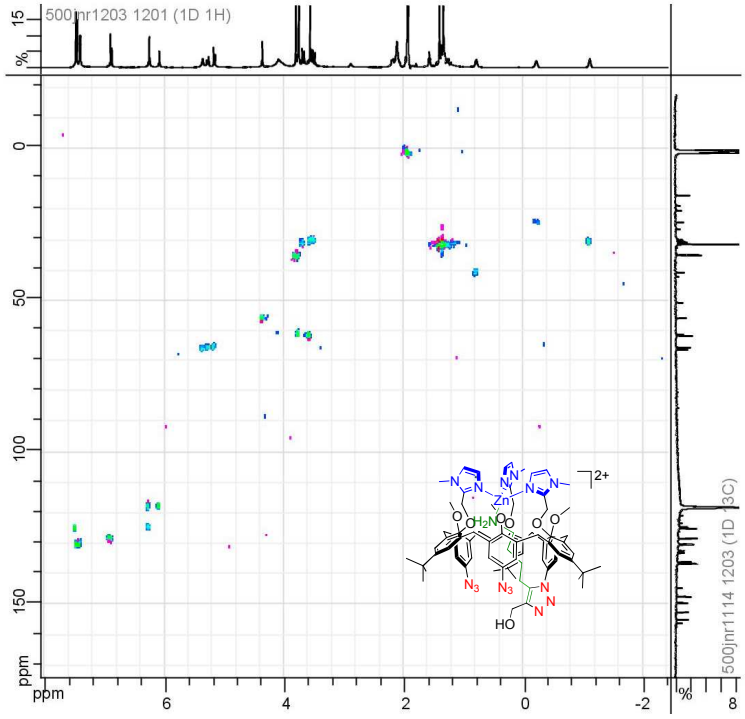


Figure S9. HSQC spectrum of L_{OH}^{C4NH2} $Zn(OTf)_2$ (500 MHz, CD_3CN, 300 K)

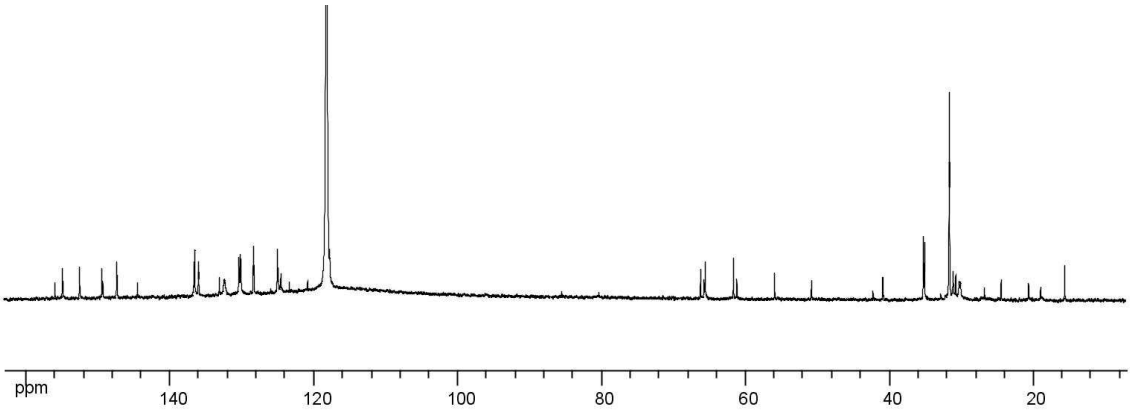


Figure S10. ^{13}C spectrum of L_{OH}^{C4NH2} $Zn(OTf)_2$ (125 MHz, CD_3CN, 300 K)

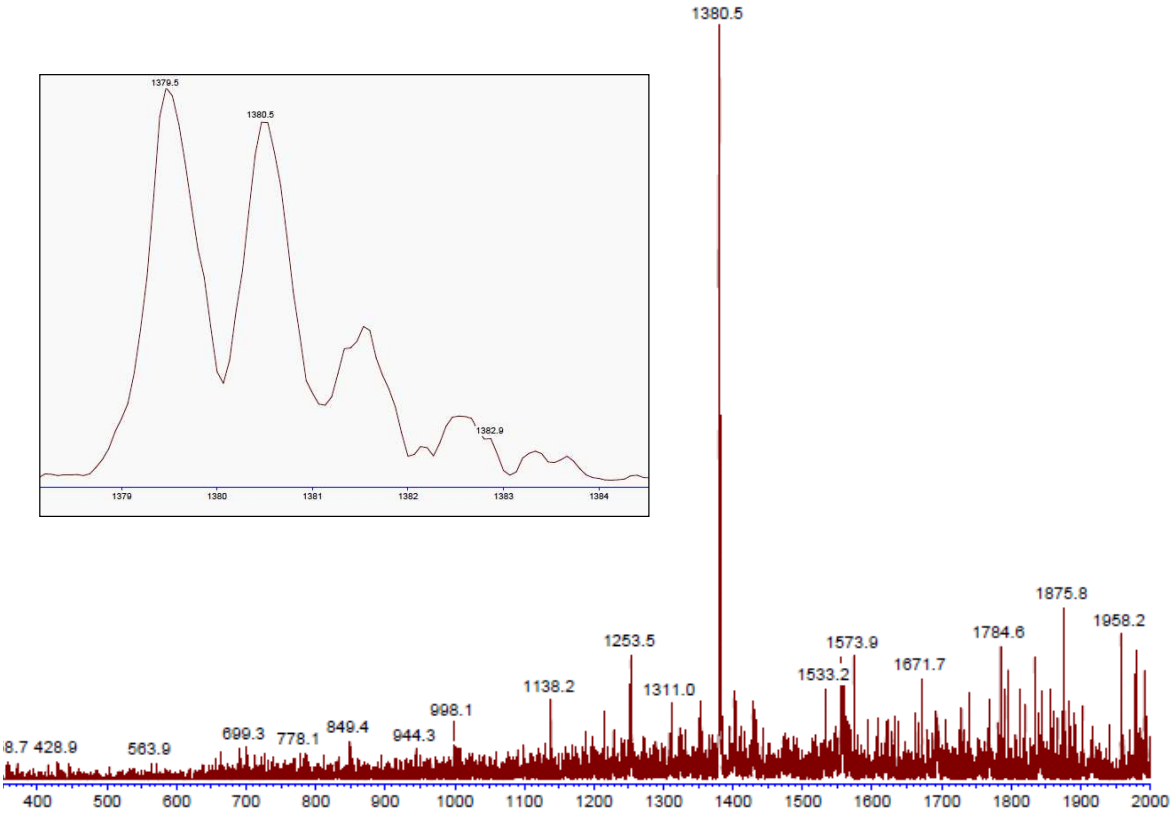


Figure S11. ESI mass spectrum (MeOH) of L_{OH}^{C4NH2}. m/z = 1379.5 ([L_{OH}^{C4NH2} +H]$^{+}$)

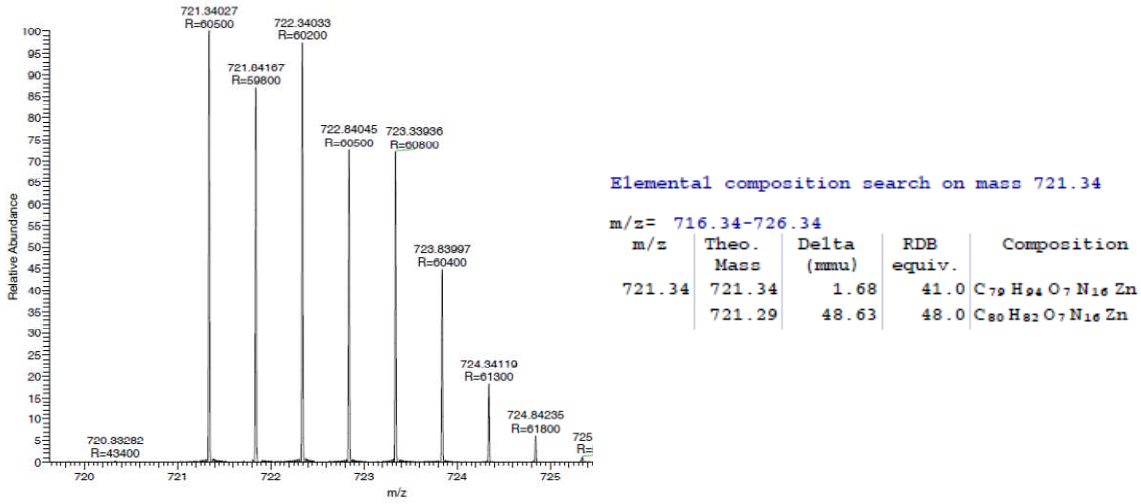


Figure S12. HRMS spectrum of L_{OH}^{C4NH2} Zn(OTf)$_2$**.** the peak associated to mass 721.34027 corresponds to the formula $C_{79}H_{94}N_{16}O_7Zn$ in agreement with [L_{OH}^{C4NH2} Zn]$^{2+}$ (mass error: 1.68 mmu; 2.3 ppm).

b) Synthesis of **3** ($L_{OH}^{C4NHBoc}$)

Ligand **2** (L_{OH}^{C4NH2}) (218 mg, 158 µmol) and NEt3 (22 µL, 158 µmol) were mixed in dry THF (10 mL). The solution was colled to 0°C and Boc_2O (34.5 mg, 158 µmol) in 1 mL of THF

was added dropwise. The temperature was raised to 20°C overnight. The solution was diluted with CH_2Cl_2 (20 mL) and washed with a saturated solution of NH_4Cl was added (5 mL). The aqueous phase (pH around 7) was extracted with 3x20 mL CH_2Cl_2. The organic phases were washed with water, drie dover Na_2SO_4, filtered and evaporated to dryness. The residue was washed with 2x4 mL Et_2O, centrifugated and dried under vacuum to yield a yellowish solid (214 mg, 92%). ^{1}H NMR resonances were broad in various solvents. **3** ($L_{OH}^{C4NHBoc}$) was thus characterized as its mononuclear Zn complex. $L_{OH}^{C4NHBoc}$ Zn(MeCN)$(OTf)_2$:

^{1}H (500 MHz, CD_3CN, 300 K) δ (ppm): 1.27 (m, 4H, β+γ); 1.35 (s, 18H, *t*Bu); 1.38 (s, 9H, *t*Bu); 1.39 (s, 9H, *t*Bu Boc);2.49 (t, J = 7.2 Hz, 2H, δ); 2.86 (m, 2H, α); 3.08 (s, 1H, OH) 3.53 (d, 4H, J = 16 Hz, CH_2Ar); 3.63 (s, 6H, NCH_3); 3.64 (s, 6H, OCH_3);3.65(d, 2H, J = 16 Hz, CH_2Ar); 3.67 (s, 3H, NCH_3); 3.75 (s, 3H, OCH_3); 4.00 - 4.19 (m, 6H, CH_2Ar); 4.48 (d, 2H, J = 4.8 Hz, CH_2OH); 5.05 (s, 4H, CH_2Im); 5.09 (s, 2H, CH_2Im); 5.17 (s, 1H, NHBoc); 5.80 (s, 2H, H_{ArN3}); 5.87 (s, 2H, H_{ArN3}); 6.29 (s 2H, H_{ArTria}); 6.90 (d, 1H, J = 1.6 Hz, H_{Im}); 6.92 (d, 2H, J = 1.6 Hz, H_{Im}); 7.38 (s, 4H, H_{ArtBu}); 7.40 (s, 2H, H_{ArtBu}); 7.43 (m, 3H, H_{Im}).

^{13}C (500 MHz, CD_3CN, 300 K) δ (ppm): 22.46; 26.28; 28.73; 29.84; 31.13; 31.21; 31.68; 31.75; 35.05; 35.21; 40.40; 55.96; 61.03; 61.12; 64.65; 64.71; 79.22; 116.44; 116.72; 120.89; 123.19; 123.45; 124.96: 128.01; 128.11; 129.84; 130.06; 130.15; 132.33; 132.67; 133.45; 136.25; 136.91; 137.09; 145.30; 148.04; 148.08; 148.94; 149.11; 153.96; 155.14; 155.27; 156.36

ESI-MS (CH_3OH): m/z = 1479.5 (calcd for [**3**+H]$^+$: 1479.8); 1501.5 (calcd for [**3**+Na]$^+$: 1501.8)

HRMS peak at 1479.81372 corresponds to the formula $C_{84}H_{103}N_{16}O_9$ in agreement with [**3**+H]$^+$ (mass error: 4.87 mmu; 3.3 ppm).

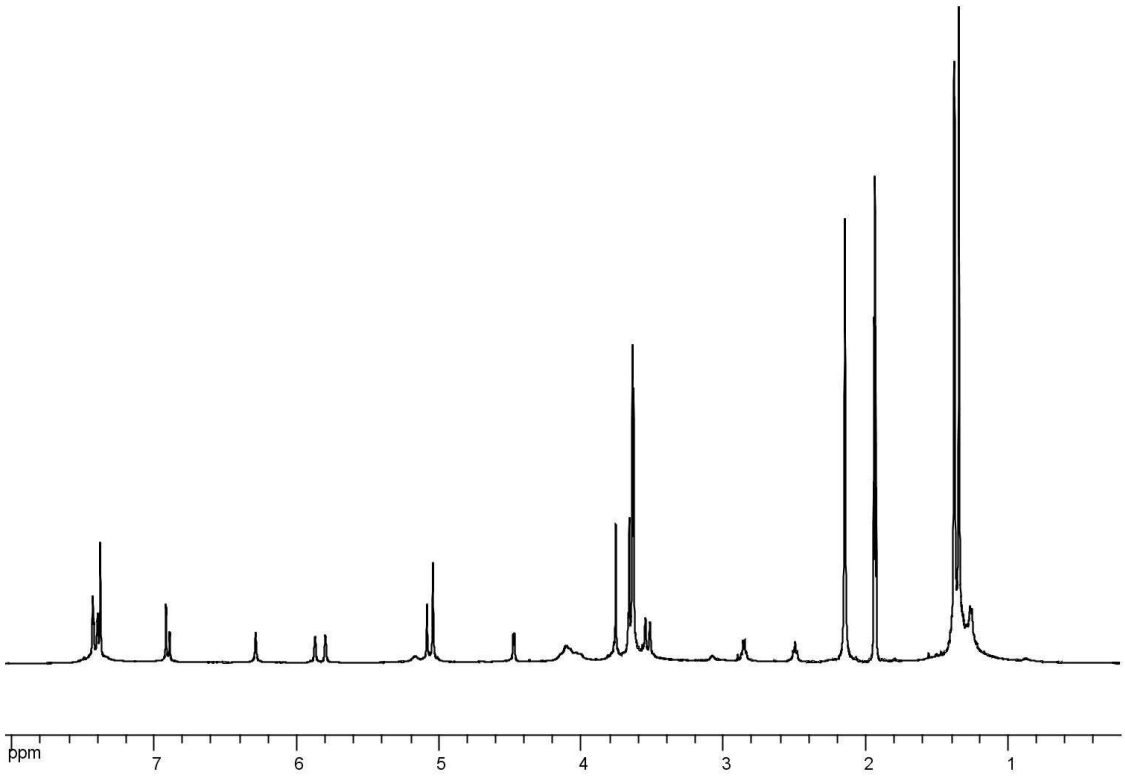


Figure S13. ^{1}H spectrum of [Zn(**3**)(CD_3CN)]$(OTf)_2$ (500 MHz, CD_3CN, 300 K)

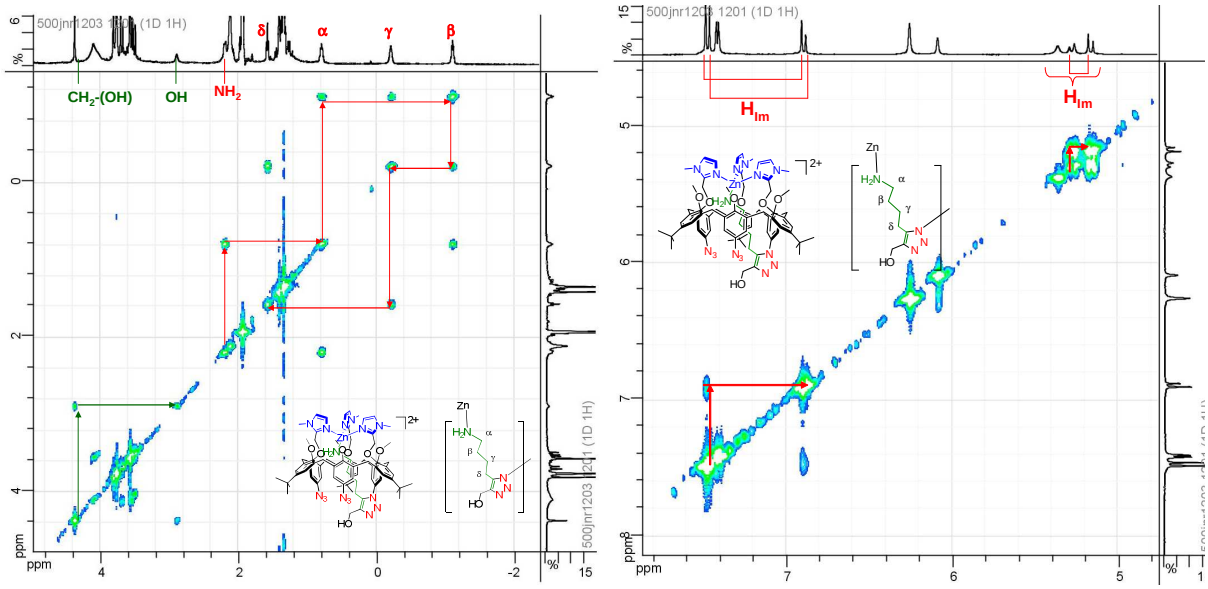


Figure S14. COSY spectrum of [Zn(**3**)(CD_3CN)]$(OTf)_2$ (500 MHz, CD_3CN, 300 K)

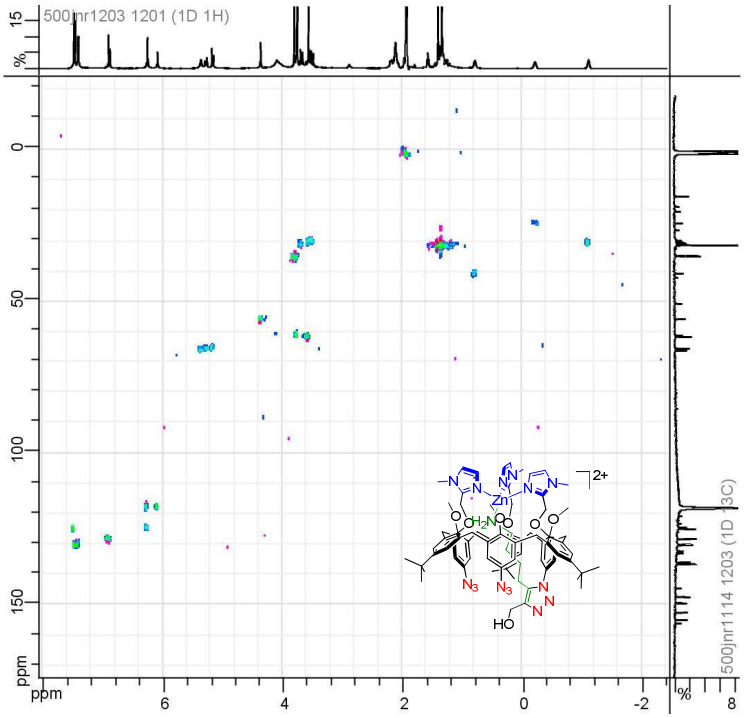


Figure S15. HSQC spectrum of [Zn(**3**)(CD_3CN)]$(OTf)_2$ (500 MHz, CD_3CN, 300 K)

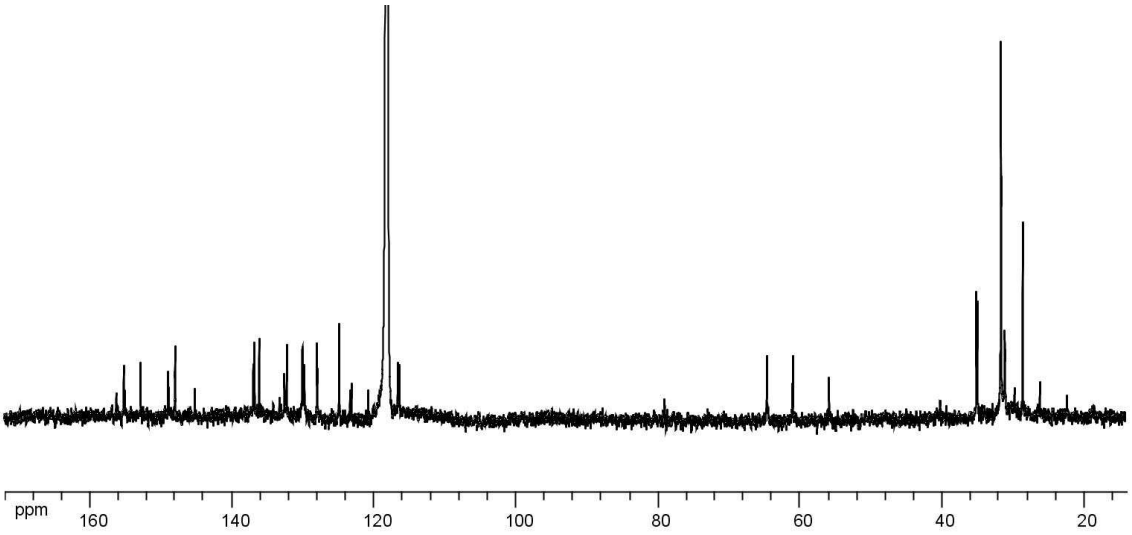


Figure S16. ^{13}C spectrum of $[Zn(\mathbf{3})(CD_3CN)](OTf)_2$ (125 MHz, CD_3CN, 300 K)

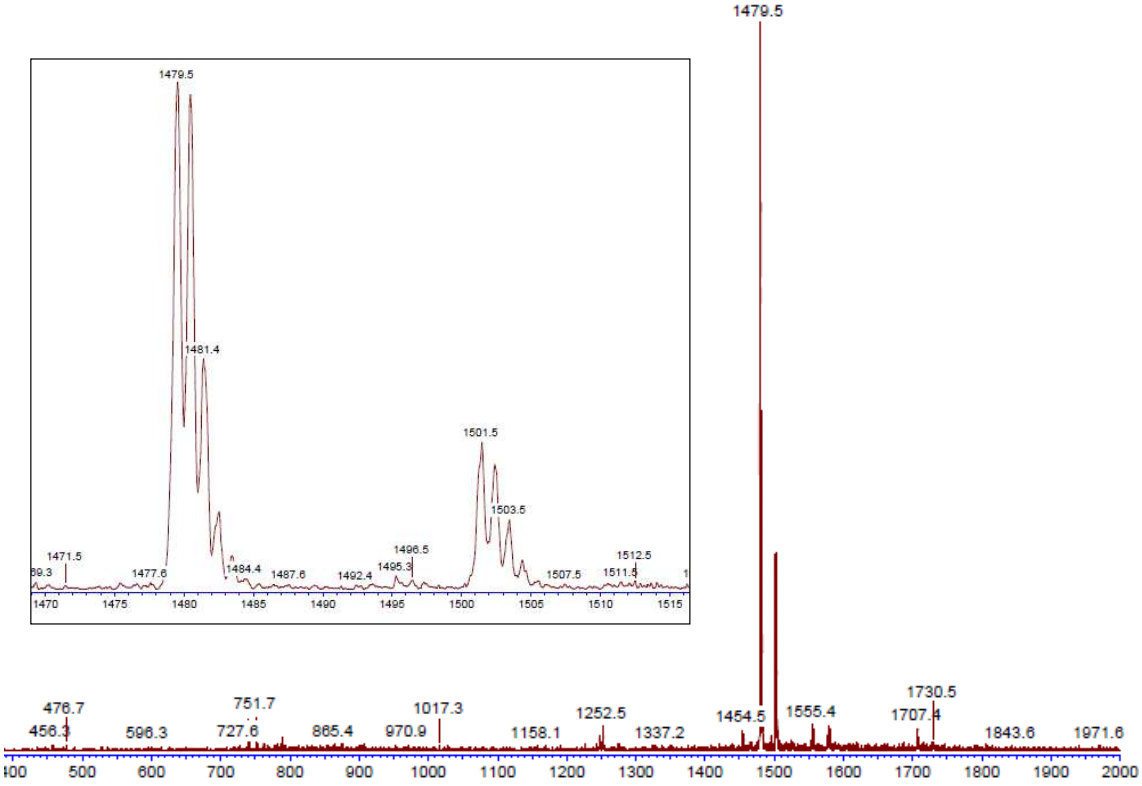
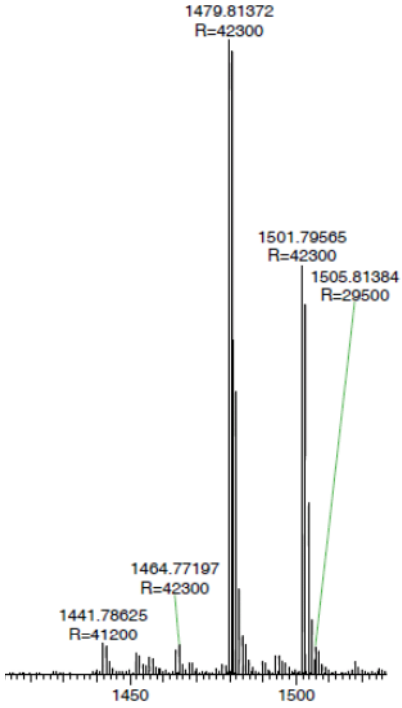


Figure S17. ESI-MS spectrum of **3** (MeOH). m/z = 1479.5 (calcd for $[\mathbf{3}+H]^+$: 1479.8); 1501.5 (calcd for $[\mathbf{3}+Na]^+$: 1501.8)



Elemental composition search on mass 1479.81

m/z= 1474.81-1484.81

m/z	Theo. Mass	Delta (mmu)	RDB equiv.	Composition
1479.81	1479.81	4.87	41.5	$C_{84}H_{103}O_9N_{16}$
	1479.81	6.22	42.0	$C_{82}H_{101}O_8N_{19}$
	1479.82	-6.36	41.5	$C_{83}H_{103}O_8N_{18}$
	1479.80	8.90	37.5	$C_{79}H_{103}O_{11}N_{18}$
	1479.83	-14.91	37.0	$C_{79}H_{105}O_{10}N_{19}$

Figure S18. HRMS spectrum of **3** ($L_{OH}^{C4NHBoc}$)**.** the peak associated to mass 1479.81372 corresponds to the formula $C_{84}H_{103}N_{16}O_9$ in agreement with [$L_{OH}^{C4NHBoc}$ +H]$^+$ (mass error: 4.87 mmu; 3.3 ppm).

4/ Synthesis of building blocks 4 and 5

a) Synthesis of **4** ($L_{Cl}^{C4NHBoc}$)

3($L_{OH}^{C4NHBoc}$) (146 mg, 98 µmol) was dissolved in dry THF (2mL) and dried by solvent evaporation at 80°C under vacuum (repeated twice). The solid was then dissolved in dry CH_2Cl_2 (3 mL) followed by the addition of methanesulfonyl chloride (13 µL, 166 µmol) and cooled under argon to 0 °C. *N*,*N*-diisopropylethylamine (19 µL, 98 µmol) was added dropwise. The ice bath was removed and the solution was stirred overnight at room temperature. The solution was diluted with CH_2Cl_2 (20 mL) and water (5 mL). The pH was raised to 8 with NaOH 3M, and the aqueous phase extracted with CH_2Cl_2 (3x20 mL). The combined organic phases were dried over Na_2SO_4, filtered and evaporated to dryness. The residue was washed with diethylether (2 mL) to yield a yellowish solid (137 mg, 92%). ^{1}H NMR resonances were broad in various solvents. **4** ($L_{Cl}^{C4NHBoc}$)was thus characterized as its mononuclear Zn complex. [Zn(**4**)(CD_3CN)]$(OTf)_2$:

^{1}H (500 MHz, CD_3CN, 300 K) δ (ppm): 1.29 (m, 4H, β+γ); 1.35 (s, 18H, *t*Bu); 1.38 (s, 9H, *t*Bu); 1.39 (s, 9H, *t*Bu Boc);2.53 (t, J = 7.2 Hz, 2H, δ); 2.87 (m, 2H, α); 3.54 (d, 4H, J = 16 Hz, CH_2Ar); 3.63 (s, 6H, NCH_3); 3.64 (s, 6H, OCH_3);3.66 (d, 2H, J = 16 Hz, CH_2Ar); 3.67 (s, 3H, NCH_3); 3.76 (s, 3H, OCH_3); 4.00 - 4.20 (m, 6H, CH_2Ar); 4.64 (d, 2H, J = 4.8 Hz, CH_2Cl); 5.04 (s, 4H, CH_2Im); 5.09 (s, 2H, CH_2Im); 5.13 (s, 1H, NHBoc); 5.80 (s, 2H, H_{ArN3}); 5.88 (s, 2H, H_{ArN3}); 6.29 (s 2H, H_{ArTria}); 6.90 (d, 1H, J = 1.6 Hz, H_{Im}); 6.92 (d, 2H, J = 1.6 Hz, H_{Im}); 7.39 (s, 4H, H_{ArtBu}); 7.41 (s, 2H, H_{ArtBu}); 7.43 (m, 3H, H_{Im}).

^{13}C (500 MHz, CD_3CN, 300 K) δ (ppm): 22.57; 26.06; 28.67; 29.93; 31.13; 31.20; 31.2; 31.68; 31.72; 35.05; 35.22; 37.26; 40.34; 61.04; 61.16; 64.65; 64.70; 79.11; 116.44; 116.70; 120.84; 123.21; 123.40; 124.97; 128.04; 128.12; 129.85; 130.06; 130.19; 132.32; 132.69; 133.01; 136.21; 136.94; 137.10; 148.03; 148.09; 148.93; 149.09; 152.96; 155.14; 155.30; 156.56

ESI-MS (CH_3OH): m/z = 1497.7 (calcd for [**4**+H]$^+$: 1497.7); 749.4 (calcd for [**4**+Na]$^+$: 749.4).

HRMS: peak at mass 1497.78003 corresponds to the formula $C_{84}H_{102}N_{16}O_8Cl$ in agreement with [**4**+H]$^+$ (mass error: 5.07 mmu; 3.4 ppm).

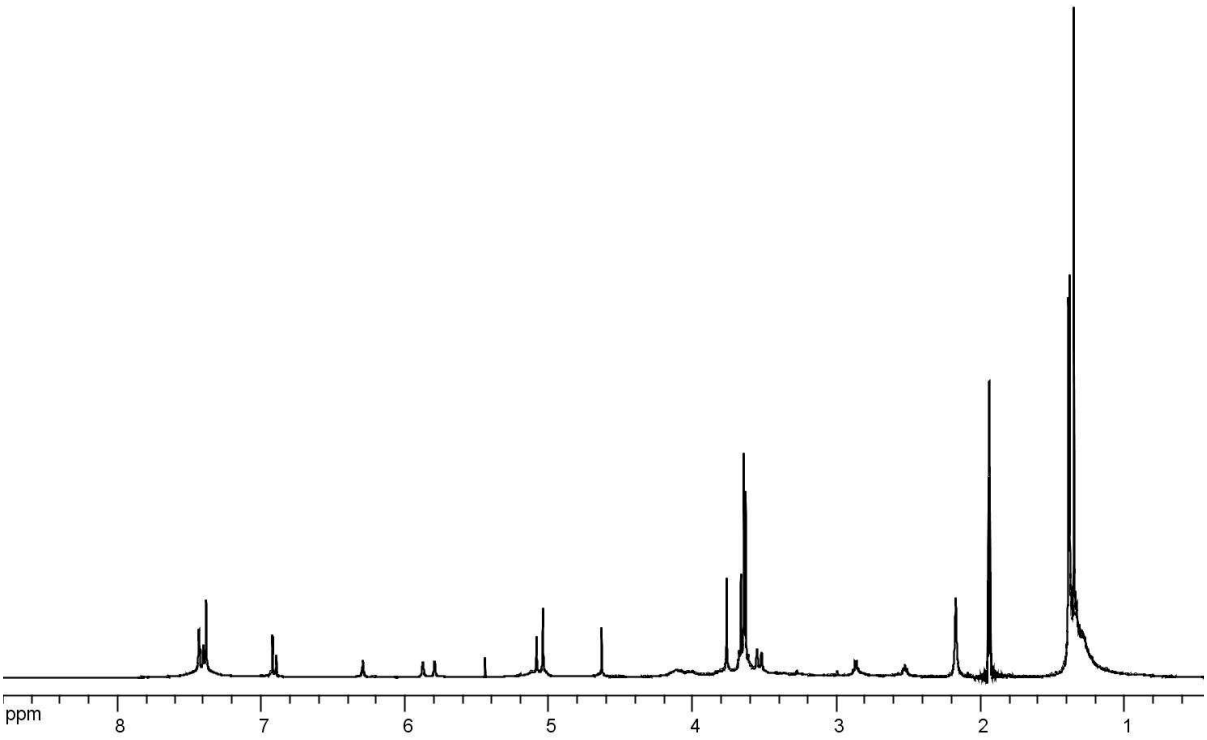


Figure S19. ^{1}H spectrum of [Zn(**4**)(CD_3CN)]$(OTf)_2$ (500 MHz, CD_3CN, 300 K)

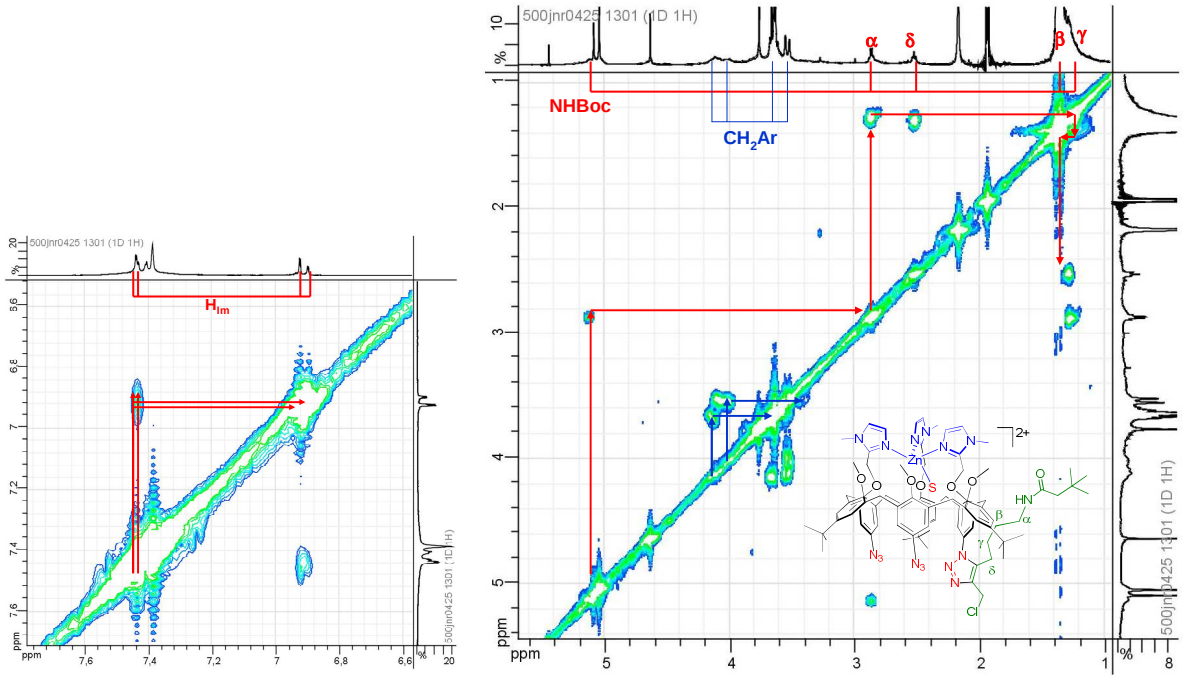


Figure S20. COSY spectrum of [Zn(**4**)(CD$_3$CN)](OTf)$_2$ (500 MHz, CD$_3$CN, 300 K)

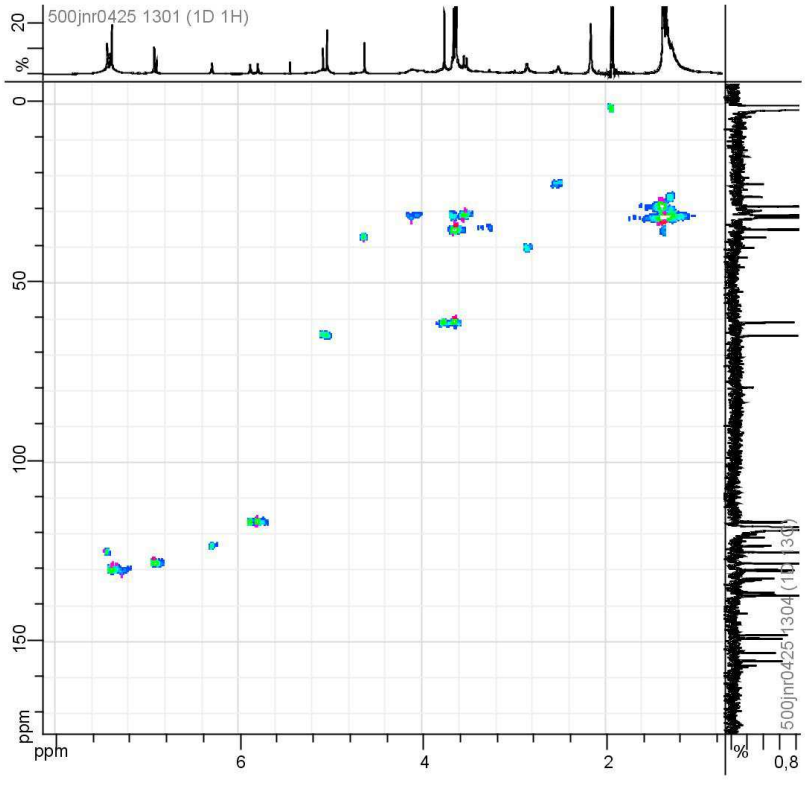


Figure S21. HSQC spectrum of [Zn(**4**)(CD$_3$CN)](OTf)$_2$ (500 MHz, CD$_3$CN, 300 K)

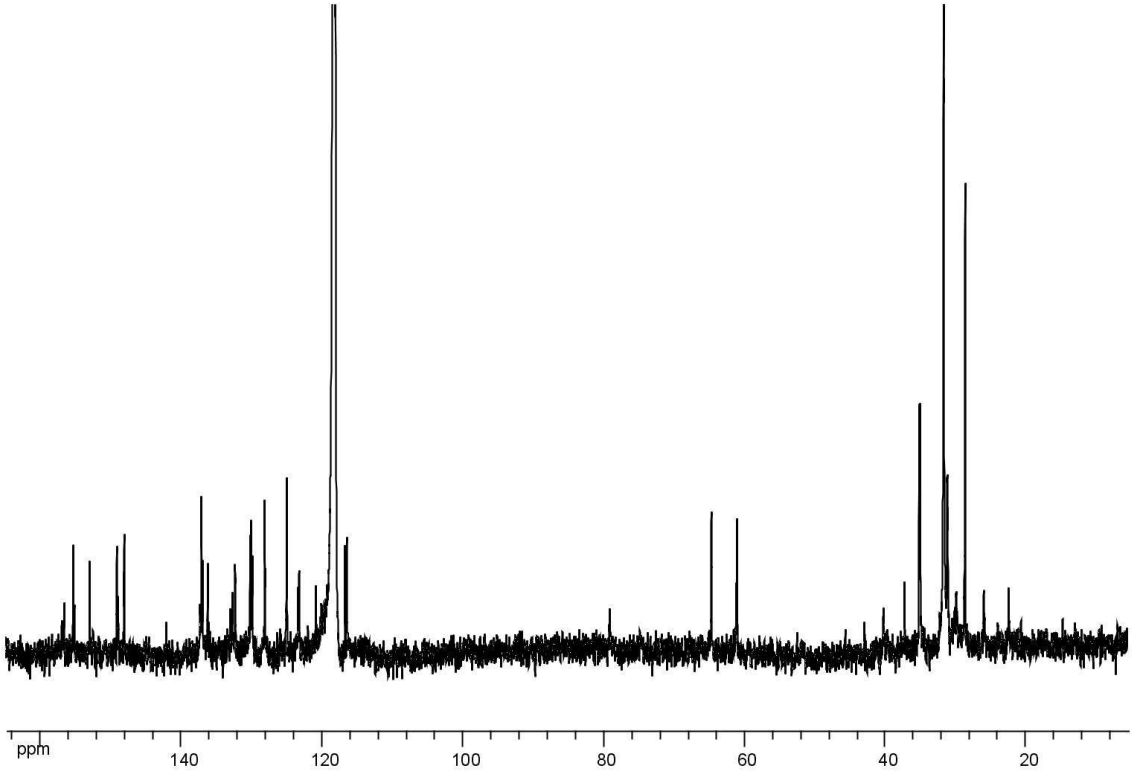


Figure S22. ^{13}C spectrum of [Zn(**4**)(CD_3CN)]$(OTf)_2$ (125 MHz, CD_3CN, 300 K)

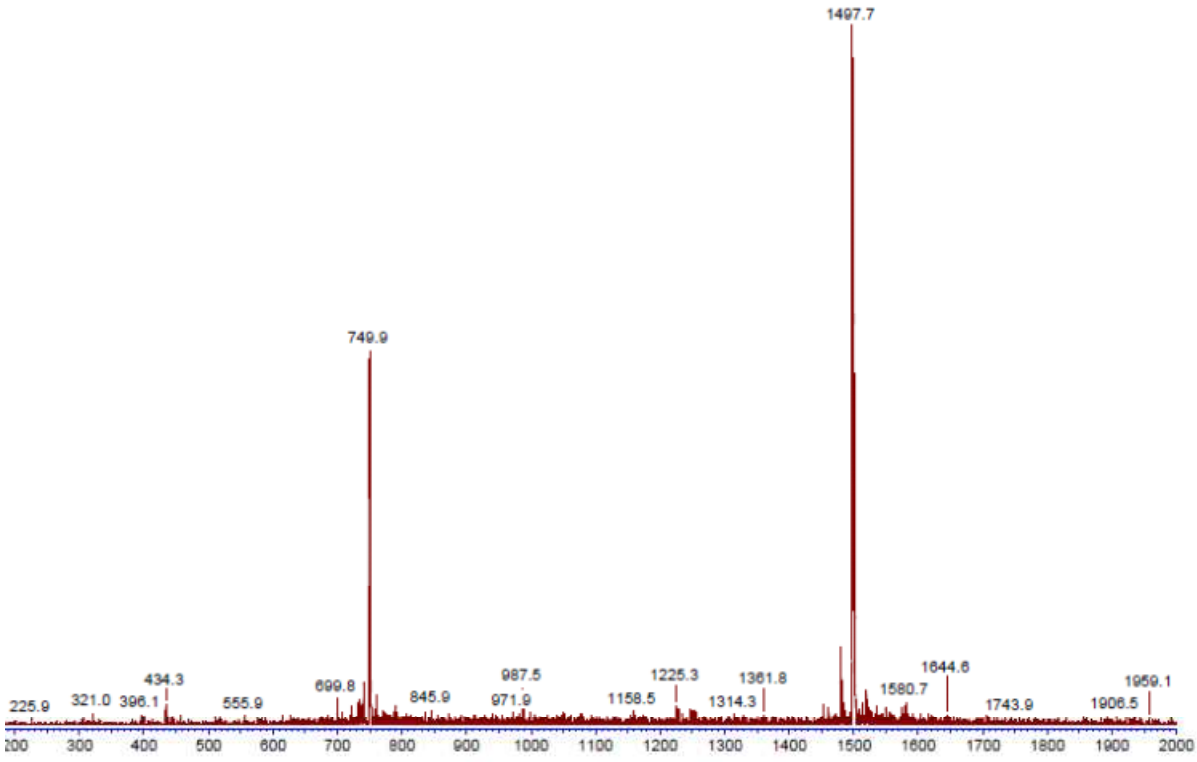
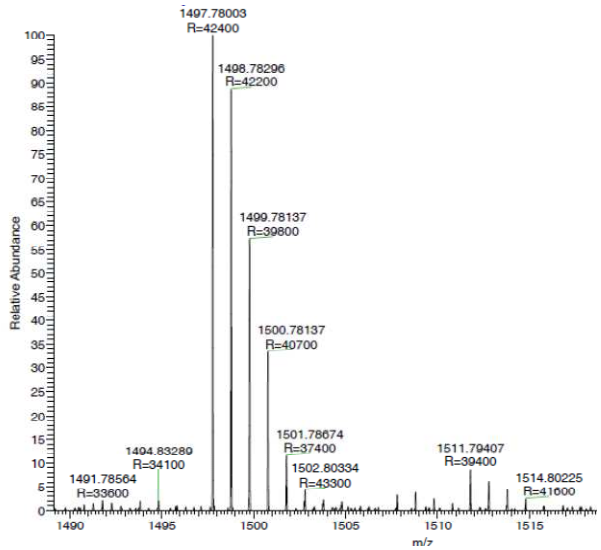


Figure S23. ESI-MS spectrum of **4** ($L_{Cl}^{C4NHBoc}$)(MeOH). m/z = 1497.7 (calcd for [$L_{Cl}^{C4NHBoc}$ +H]$^+$: 1497.7); 749.4 (calcd for [$L_{Cl}^{C4NHBoc}$ +Na]$^+$: 749.4).



Elemental composition search on mass 1497.78

m/z= 1492.78-1502.78

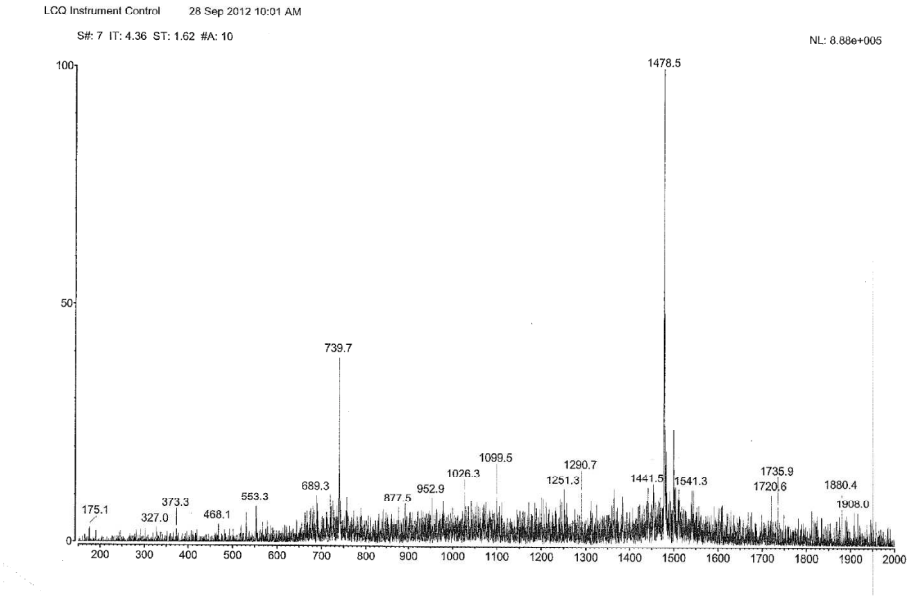
m/z	Theo. Mass	Delta (mmu)	RDB equiv.	Composition
1497.78	1497.77	5.07	41.5	$C_{84}H_{102}O_8N_{16}Cl$
	1497.80	-18.74	41.0	$C_{84}H_{104}O_7N_{17}Cl$
	1497.69	87.74	48.5	$C_{84}H_{90}O_7N_{18}Cl$
	1497.89	-111.49	91.5	$C_{84}O_7N_{17}Cl_4$
	1497.89	-111.49	91.5	$C_{84}O_7N_{17}Cl_4$

Figure S24. HRMS spectrum of **4** ($L_{Cl}^{C4NHBoc}$)**.** the peak associated to mass 1497.78003 corresponds to the formula $C_{84}H_{102}N_{16}O_8Cl$ in agreement with [$L_{Cl}^{C4NHBoc}$ +H]$^+$ (mass error: 5.07 mmu; 3.4 ppm).

b) Synthesis of **5** ($L_{CHO}^{C4NHBoc}$)

3 ($L_{OH}^{C4NHBoc}$) (31 mg, 20 µmol) and IBX (17 mg, 60 µmol) were mixed in dichloroethane (1 mL) and heated to 80°C for 5 hours. The mixture was left to stir at room temperature overnight and centrifuged. The filtrate was diluted in dichloromethane (10 mL), washed with saturated Na_2CO_3 (5 mL), and water (5 mL), dried over Na_2SO_4, filtered and evaporated to dryness. The residue was purified through a very short plug of neutral alumina, eluted with CH_2Cl_2/MeOH 92:8. The collected fractions were evaporated to yield **5** ($L_{CHO}^{C4NHBoc}$) as a yellowish solid (25 mg, 80 %).
^{1}H NMR resonances were broad in various solvents. **5** ($L_{CHO}^{C4NHBoc}$) was thus characterized as its mononuclear Zn complex. [Zn(**5**)(CD_3CN)]$(OTf)_2$:

^{1}H (500 MHz, CD_3CN, 300 K) δ (ppm): 1.29 (m, 4H, β+γ); 1.34 (s, 18H, *t*Bu); 1.38 (s, 9H, *t*Bu); 1.39 (s, 9H, *t*Bu Boc); 2.73 (t, J = 7.2 Hz, 2H, δ); 2.87 (m, 2H, α); 3.54 (d, 4H, J = 16 Hz, CH_2Ar); 3.63 (s, 6H, NCH_3); 3.65 (s, 6H, OCH_3); 3.66 (d, 2H, J = 16 Hz, CH_2Ar); 3.68 (s, 3H, NCH_3); 3.77 (s, 3H, OCH_3); 4.00 - 4.19 (m, 6H, CH_2Ar); 5.05 (s, 4H, CH_2Im); 5.08 (s, 2H, CH_2Im); 5.15 (s, 1H, NHBoc); 5.81 (s, 2H, H_{ArN3}); 5.89 (s, 2H, H_{ArN3}); 6.34 (s 2H, H_{ArTria}); 6.90 (d, 1H, J = 1.6 Hz, H_{Im}); 6.93 (d, 2H, J = 1.6 Hz, H_{Im}); 7.38 (s, 4H, H_{ArtBu}); 7.39 (s, 2H, H_{ArtBu}); 7.43 (m, 3H, H_{Im}); 9.99 (s, 1H, H_{CHO})
^{13}C (500 MHz, CD_3CN, 300 K) δ (ppm): 23.02; 25.99; 28.68; 29.78; 30.36; 31.16; 31.20; 31.60; 31.72; 33.86; 35.06; 35.22; 40.28; 61.08; 61.25; 64.67; 64.78; 79.18; 116.52; 116.74; 120.71; 123.25; 123.58; 125.00; 125.84; 128.08; 128.20; 129.90; 130.09; 130.25; 131.83; 132.37; 132.69; 136.14; 137.00; 137.14; 137.38; 148.03; 148.13; 148.97; 149.17; 153.02; 155.14; 155.28; 156.88; 186.85
ESI-MS (CH_3OH): m/z = 1477.7 (calcd for [**5**+H]$^+$: 1477.79); 739.3 (calcd for [**5**+2H]$^{2+}$: 739.40).
HRMS: peak at mass 1477.79810 corresponds to the formula $C_{84}H_{101}N_{16}O_9$ in agreement with [**5**+H]$^+$ (mass error: 4.90 mmu; 3.3 ppm).



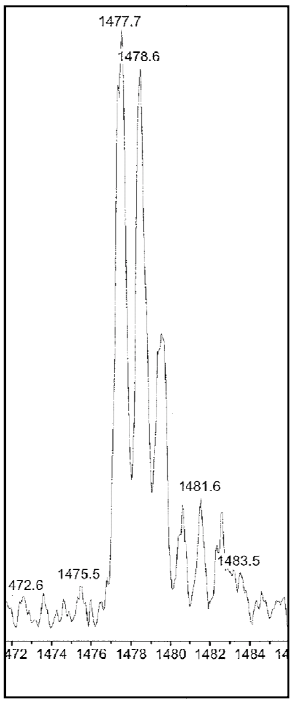
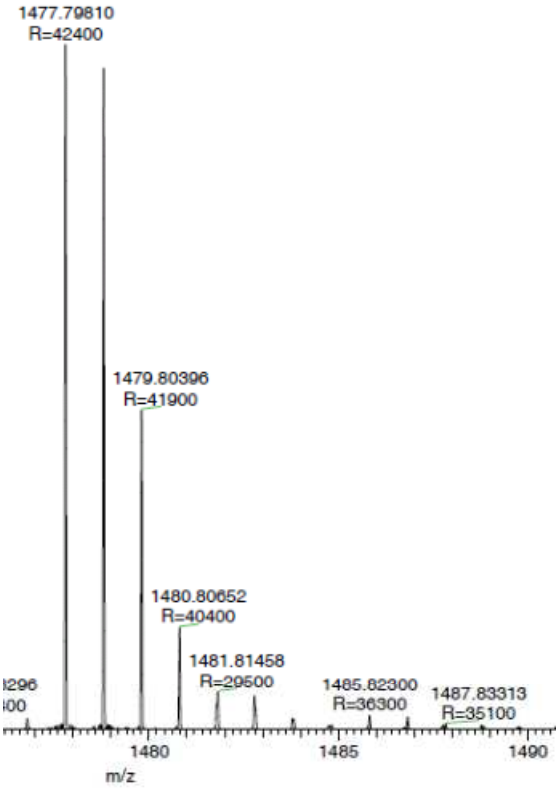


Figure S25. ESI-MS spectrum of **5** ($L_{CHO}^{C4NHBoc}$)(MeOH). m/z = 1477.7 (calcd for [**5**+H]$^{+}$: 1477.79); 739.3 (calcd for [**5**+2H]$^{2+}$: 739.40).



Elemental composition search on mass 1477.80

m/z= 1472.80-1482.80

m/z	Theo. Mass	Delta (mmu)	RDB equiv.	Composition
1477.80	1477.79	4.90	42.5	$C_{84}H_{101}O_9N_{16}$
	1477.80	-6.33	37.0	$C_{84}H_{107}O_{13}N_{11}$
	1477.78	17.48	37.5	$C_{84}H_{105}O_{14}N_{10}$
	1477.82	-18.90	42.0	$C_{84}H_{103}O_8N_{17}$
	1477.77	28.71	43.0	$C_{84}H_{99}O_{10}N_{15}$

Figure S26. HRMS spectrum of **5** ($L_{CHO}^{C4NHBoc}$)**.** **T**he peak associated to mass 1477.79810 corresponds to the formula $C_{84}H_{101}N_{16}O_9$ in agreement with [$L_{CHO}^{C4NHBoc}$ +H]$^+$ (mass error: 4.90 mmu; 3.3 ppm).

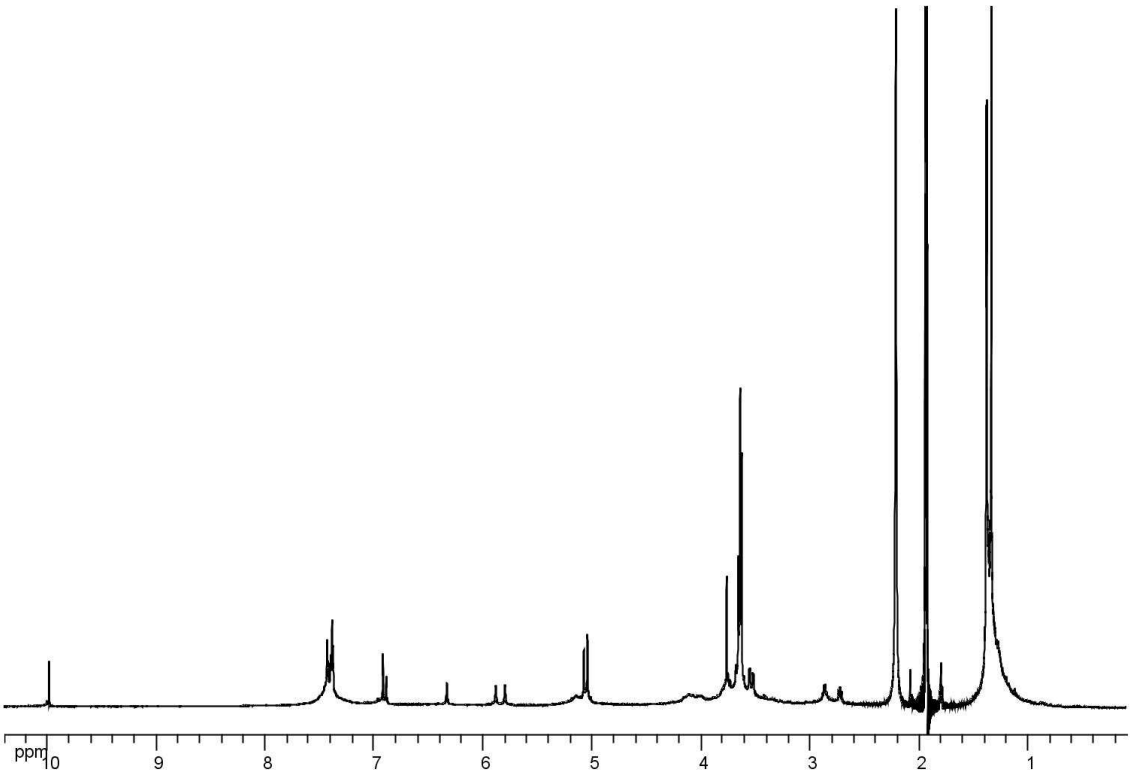


Figure S27. ^{1}H spectrum of [Zn(**5**)(CD_3CN)]$(OTf)_2$ (500 MHz, CD_3CN, 300 K)

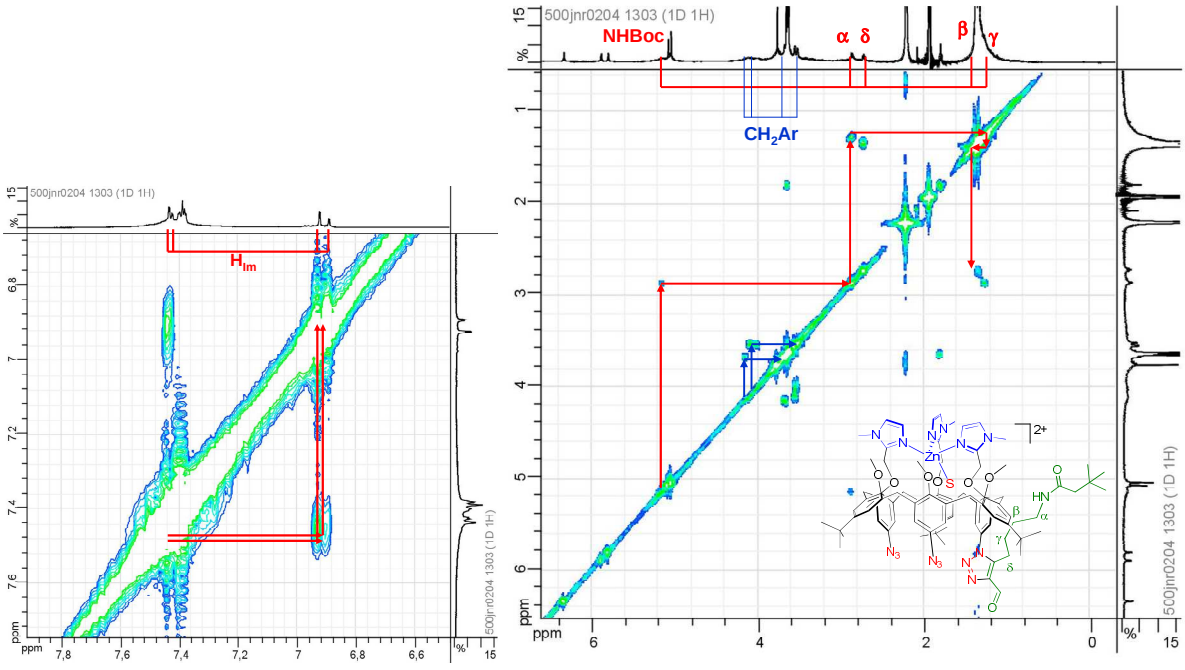


Figure S28. COSY spectrum of [Zn(**5**)(CD_3CN)]$(OTf)_2$ (500 MHz, CD_3CN, 300 K)

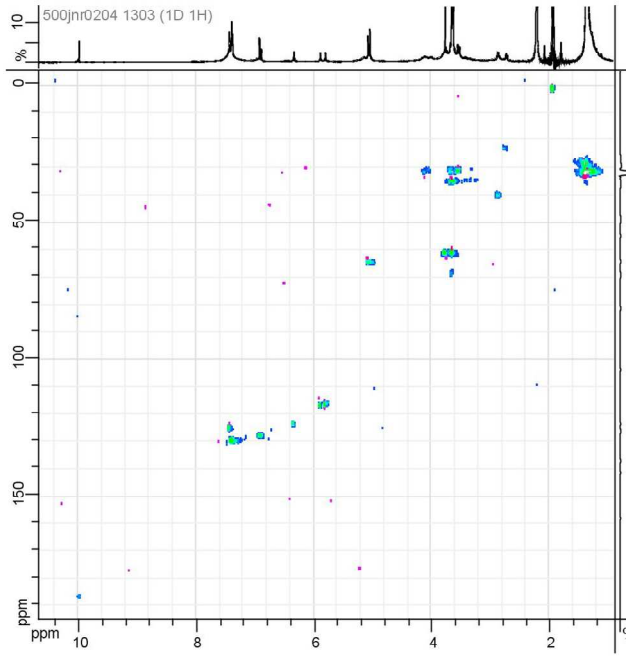


Figure S29. HSQC spectrum of [Zn(**5**)(CD_3CN)]$(OTf)_2$ (500 MHz, CD_3CN, 300 K)

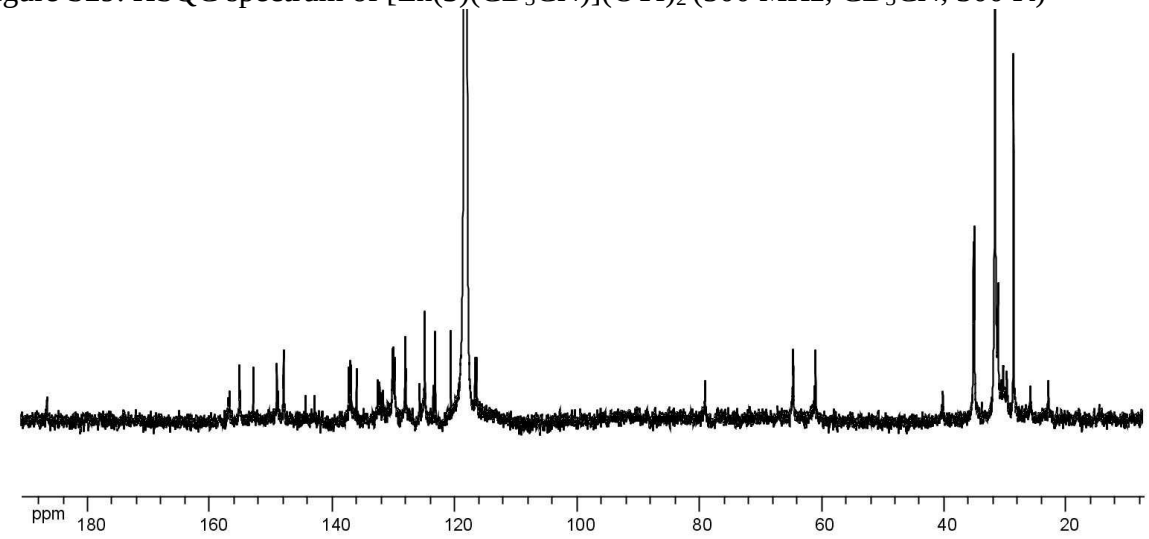


Figure S30. ^{13}C spectrum of [Zn(**5**)(CD_3CN)]$(OTf)_2$ (125 MHz, CD_3CN, 300 K)

5/ Post-functionalization reactions

a) Synthesis of **6**

3 ($L_{OH}^{C4NHBoc}$) (27.5 mg, 18.6 µmol), ferrocene carboxylic acid (4.7 mg, 20.4 µmol) EDC.HCl (10.6 mg, 55.5 µmol) and DMAP (2.5 mg, 20.4 µmol) were mixed in dry CH_2Cl_2 (1 mL) were stirred for 48 hours at room temperature under argon atmosphere. The mixture was diluted with CH_2Cl_2 (15 mL), water (3 mL) and 5 drops of concentrated NH_4OH.The organic phase was washed with water (2 x 3 mL), dried over Na_2SO_4, filtered and evaporated. The residue was washed with a solution of pentane/diethyl ether (4 mL/0.5 mL) to yield an tan solid (26.8 mg, 85%). **6** was characterized by NMR as its mononuclear Zn complex [Zn(**6**)(CD_3CN)]$(OTf)_2$.

^{1}H (250 MHz, CD_3CN, 300 K). δ (ppm): 1.26-1.31 (m, 4H, β+γ); 1.33 (s, 18H, *t*Bu); 1.38 (s, 9H, *t*Bu); 1.39 (s, 9H, *t*Bu Boc);2.61 (t, J = 7.2 Hz, 2H, δ); 2.89 (m, 2H, α); 3.53 (d, 4H, J = 16 Hz, CH_2Ar); 3.63 (s, 6H, NCH_3); 3.64 (s, 6H, OCH_3);3.66 (d, 2H, J = 16 Hz, CH_2Ar); 3.66 (s, 3H, NCH_3); 3.76 (s, 3H, OCH_3); 4.00 - 4.15 (m, 6H, CH_2Ar);4.09 (s, 5H, Fc); 4.39 (t, 2H, J = 2 Hz, Fc); 4.68 (t, 2H, J = 2 Hz, Fc); 5.04 (s, 4H, CH_2Im); 5.08 (s, 2H, CH_2Im); 5.17 (s, 2H, CH_2-OCO-Fc) ; 5.22 (br, 1H, NHBoc); 5.79 (s, 2H, H_{ArN3}); 5.87 (s, 2H, H_{ArN3}); 6.32 (s 2H, H_{ArTria}); 6.88 (d, 1H, J = 1.6 Hz, H_{Im}); 6.91 (d, 2H, J = 1.6 Hz, H_{Im}); 7.38 (m, 6H, H_{ArtBu}); 7.42 (d, 1H, J = 1.6 Hz, H_{Im}) ; 7.43 (d, 1H, J = 1.6 Hz, H_{Im}).
^{13}C (500 MHz, CD_3CN, 300 K) δ (ppm): 22.53; 26.25; 28.71; 29.91; 31.15; 31.19; 31.21; 31.68; 31.75; 35.05; 35.21; 40.18; 57.56; 61.02; 61.15; 64.63; 64.66; 70.64; 70.90; 71.73; 72.45; 79.15; 116.44; 116.70; 118.59; 120.89; 123.16; 123.44; 124.93; 124.95; 128.01; 128.07; 129.81; 130.05; 130.16; 132.26; 132.31; 132.67; 133.21; 136.19; 136.93; 137.04; 137.82; 141.04; 148.03; 148.08; 148.97; 149.10; 152.92; 155.14; 155.27; 156.50; 171.86
ESI-MS 6 (MeOH). m/z = 1692.80 (calcd for [**6**+H]$^+$: 1692.80); 846.90 (calcd for [**6**+2H]$^{2+}$: 846.89).
HRMS: at mass 1691.8017 corresponds to the formula $C_{95}H_{111}N_{16}O_{10}Fe$ in agreement with [**6**+H]$^+$ (mass error: 0.3 ppm).

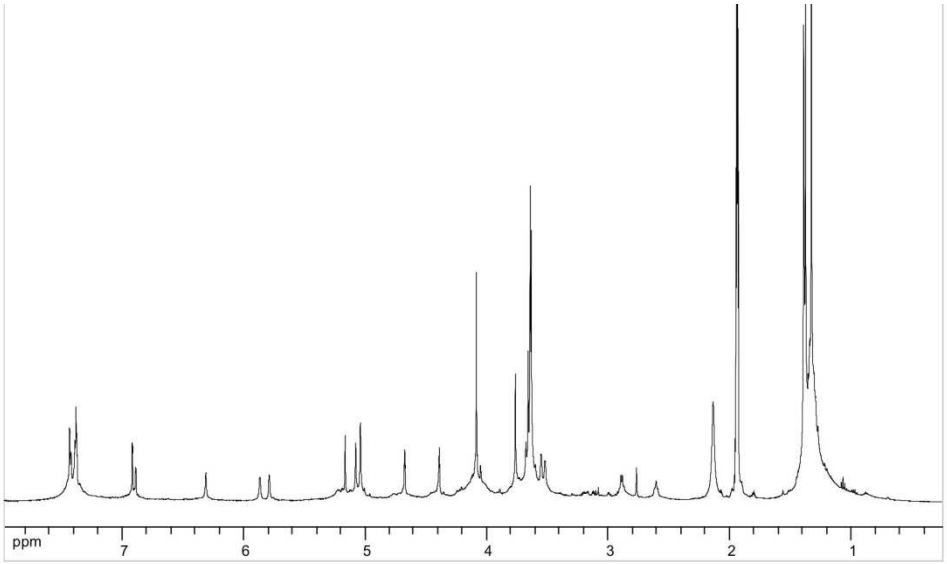


Figure S31. ^{1}H NMR spectrum (500 MHz, CD_3CN, 300 K) of [Zn(**6**)(CD_3CN)]$(OTf)_2$.

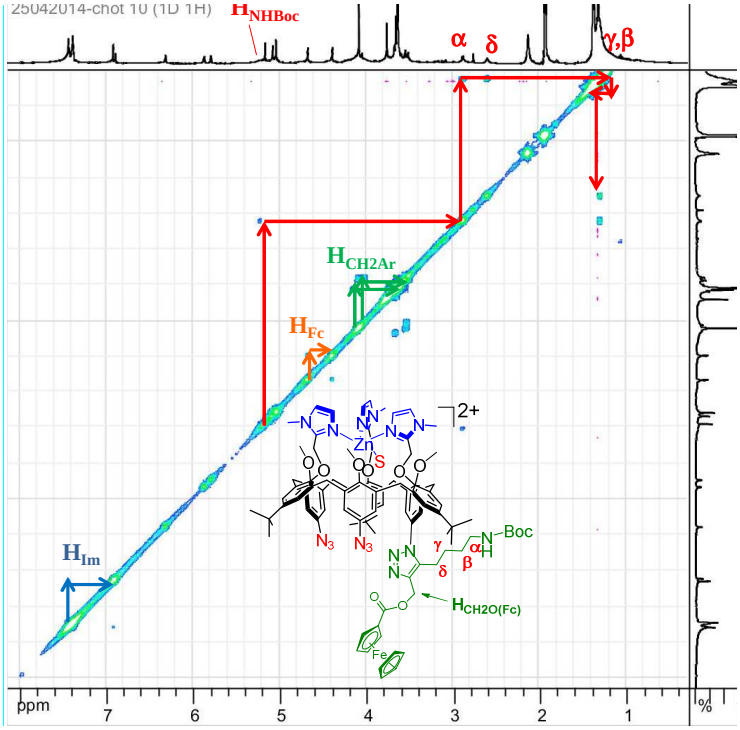


Figure S32. COSY spectrum (500 MHz, CD_3CN, 300 K) of [Zn(**6**)(CD_3CN)]$(OTf)_2$.

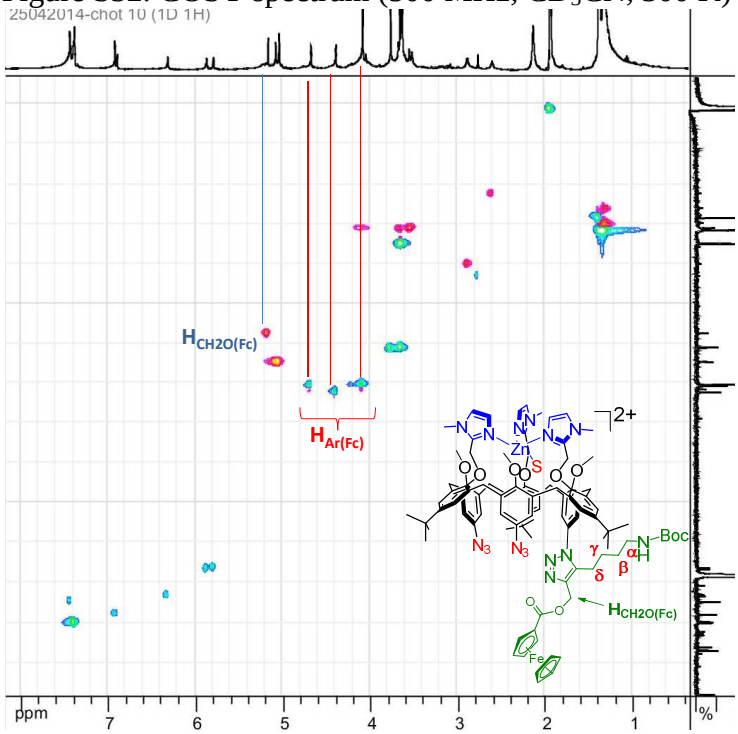


Figure S33. HSQC spectrum (500 MHz, CD_3CN, 300 K) of [Zn(**6**)(CD_3CN)]$(OTf)_2$.

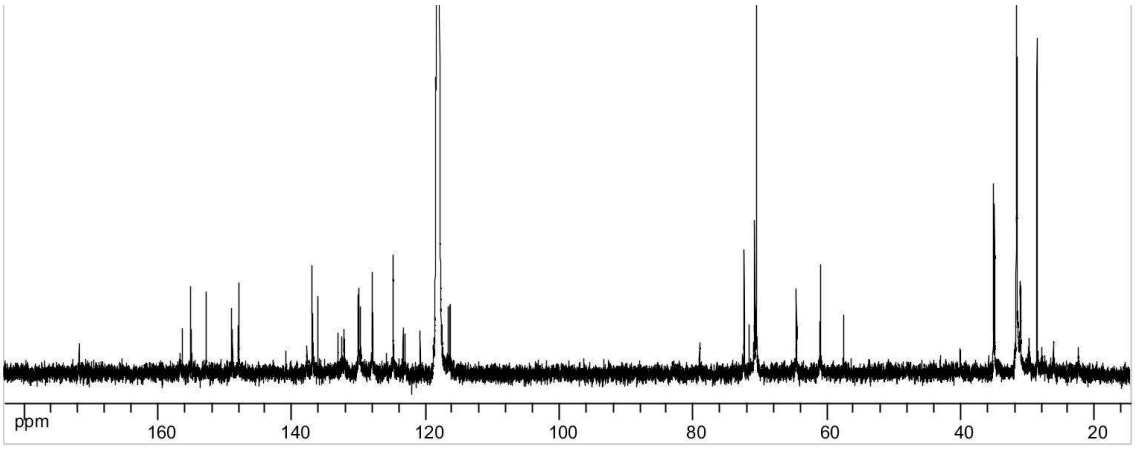


Figure S34. ^{13}C NMR spectrum (500 MHz, CD_3CN, 300 K) of [Zn(**6**)(CD_3CN)](OTf)$_2$.

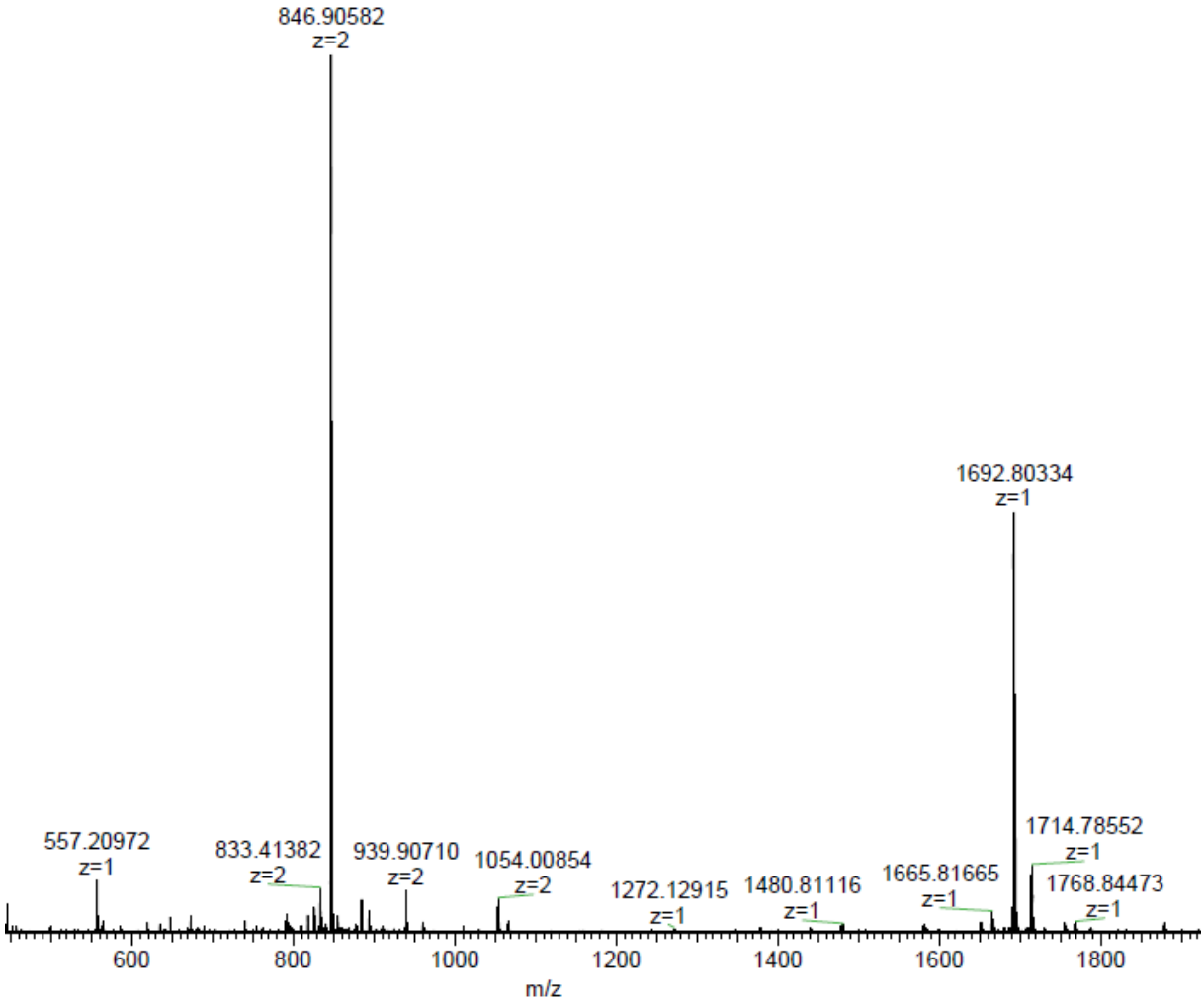
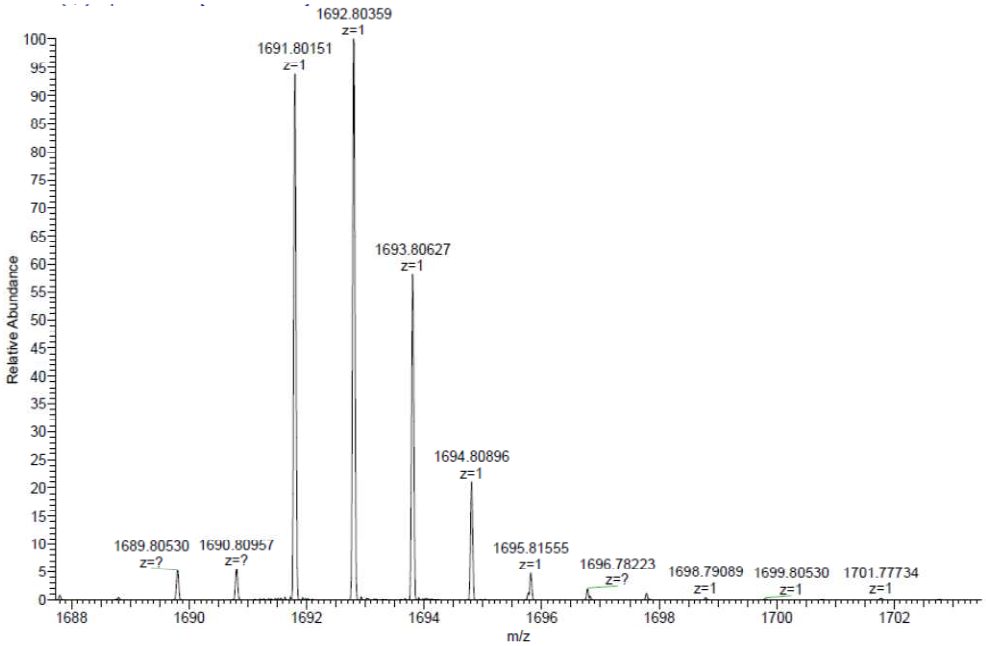


Figure S35. ESI-MS spectrum of **6** (MeOH). m/z = 1692.80 (calcd for [**6**+H]$^+$: 1692.80); 846.90 (calcd for [**6**+2H]$^{2+}$: 846.89).



Elemental composition search on mass 1691.80

m/z= 1686.80-1696.80

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
1691.80176	1691.80130	0.27	48.5	$C_{95}H_{111}O_{10}N_{16}Fe$
	1691.81254	-6.37	43.0	$C_{95}H_{117}O_{14}N_{11}Fe$
	1691.78873	7.70	43.5	$C_{95}H_{115}O_{15}N_{10}Fe$
	1691.83635	-20.45	42.5	$C_{95}H_{119}O_{13}N_{12}Fe$
	1691.86609	-38.02	45.5	$C_{95}H_{115}O_{15}N_{14}$
	1691.88989	-52.10	45.0	$C_{95}H_{117}O_{14}N_{15}$
	1691.91370	-66.17	44.5	$C_{95}H_{119}O_{13}N_{16}$

Figure S36. HR-MS spectrum of **6** (MeOH). peak at mass 1691.8017 corresponds to the formula $C_{95}H_{111}N_{16}O_{10}Fe$ in agreement with $[\mathbf{6}+H]^+$ (mass error: 0.3 ppm).

b) Synthesis of **7**

5 ($L_{CHO}^{C4\,NHBoc}$) (21 mg, 14.2 µmol) and 1-aminomethylanthracene (2.9 mg, 14.2 µmol) were mixed in EtOH (2 mL) and refluxed overnight. The mixture was evaporated to dryness and dried under vacuum to yield a light solid (23.5mg, quantitative).
For ^{1}H NMR, the system was characterized as its mononuclear Zn^{II} complex in CD_3CN.

^{1}H (500 MHz, CD_3CN, 300 K) δ (ppm): 1.03 (m, 2H, γ); 1.12 (m, 2H, β);1.29 (s, 18H, *t*Bu); 1.38 (s, 9H, *t*Bu); 1.39 (s, 9H, *t*Bu Boc); 2.57 (m, 4H, α+δ); 3.53 (d, 4H, J = 16 Hz, CH_2Ar); 3.61 (s, 6H, NCH_3); 3.63 (s, 6H, OCH_3); 3.62 (d, 2H, J = 16 Hz, CH_2Ar); 3.65 (s, 3H, NCH_3); 3.73 (s, 3H, OCH_3); 3.94 - 4.15 (m, 6H, CH_2Ar); 4.85 (s, 1H, NHBoc); 5.02 (s, 4H, CH_2Im); 5.06 (s, 2H, CH_2Im); 5.75 (s, 4H, H_{CH2Ant} + H_{ArN3}); 5.84 (s, 2H, H_{ArN3}); 6.25 (s 2H, H_{ArTria}); 6.87(d, 1H, J = 1.6 Hz, H_{Im}); 6.90 (d, 2H, J = 1.6 Hz, H_{Im}); 7.34 (s, 4H, H_{ArtBu}); 7.37 (s, 2H, H_{ArtBu}); 7.41 (m, 3H, H_{Im}); 7.52 (m, 4H, H_2 + H_3); 8.07 (d, 2H, J = 9.8 Hz, H_4); 8.41 (d, 2H, J = 9.8 Hz, H_1); 8.52 (s, 1H, H_5); 8.53 (s, 1H, H_{imine})

^{13}C (500 MHz, CD_3CN, 300 K) δ (ppm): 23.28; 25.95; 28.81; 30.97; 31.21; 31.25; 31.79; 35.10; 35.13; 35.28; 37.99; 40.42; 55.40; 57.05; 61.11; 61.20; 64.70; 64.74; 79.24; 116.55; 116.79; 121.01; 123.55; 123.58; 124.56; 125.02; 125.55; 126.27; 127.30; 127.89; 128.09; 128.16; 128.34; 128.50; 129.89; 130.10; 130.13; 130.23; 131.32; 131.37; 132.28; 132.39; 132.66; 132.69; 136.21; 136.97; 137.03; 137.10; 142.80; 145.76; 148.11; 148.16; 152.99; 155.30; 155.40; 156.71

ESI-MS (CH_3OH): m/z = 1667.1 (calcd for [**7**+H]$^+$: 1666.8); 834.6 (calcd for [**7**+2H]$^{2+}$: 833.9)

HRMS: peak at mass 1666.8918 corresponds to the formula $C_{99}H_{112}N_{17}O_8$ in agreement with [**7**+H]$^+$ (mass error: 4.05 mmu; 2.43 ppm).

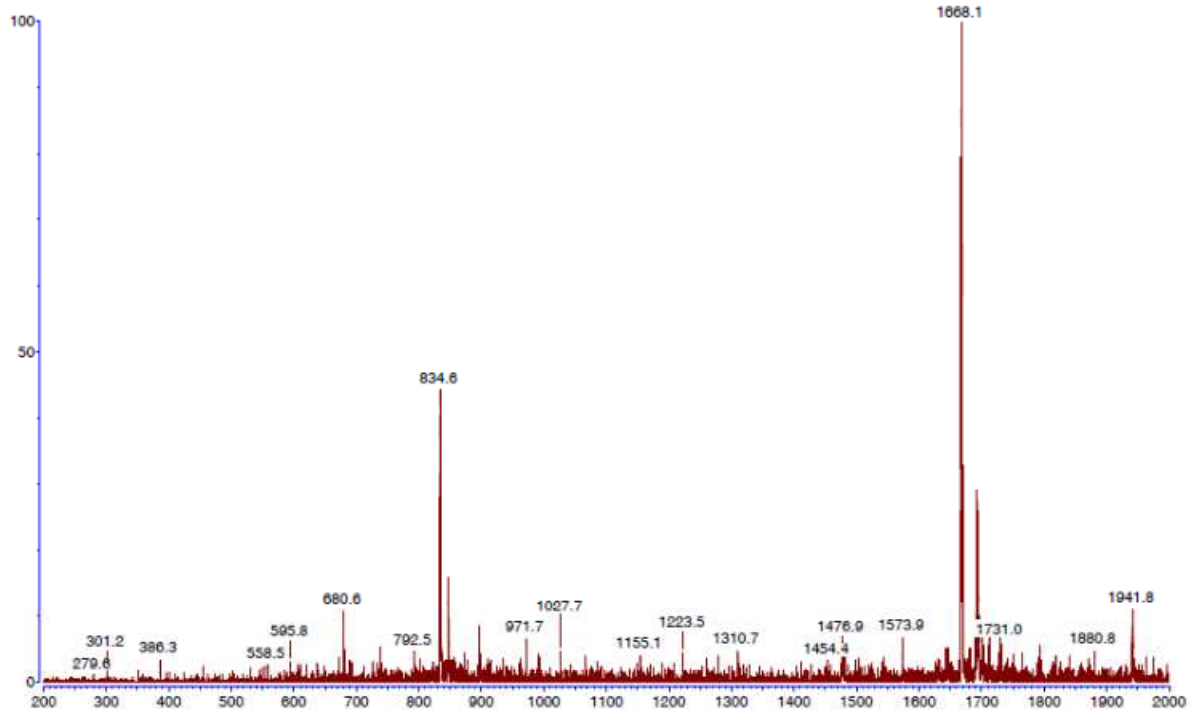
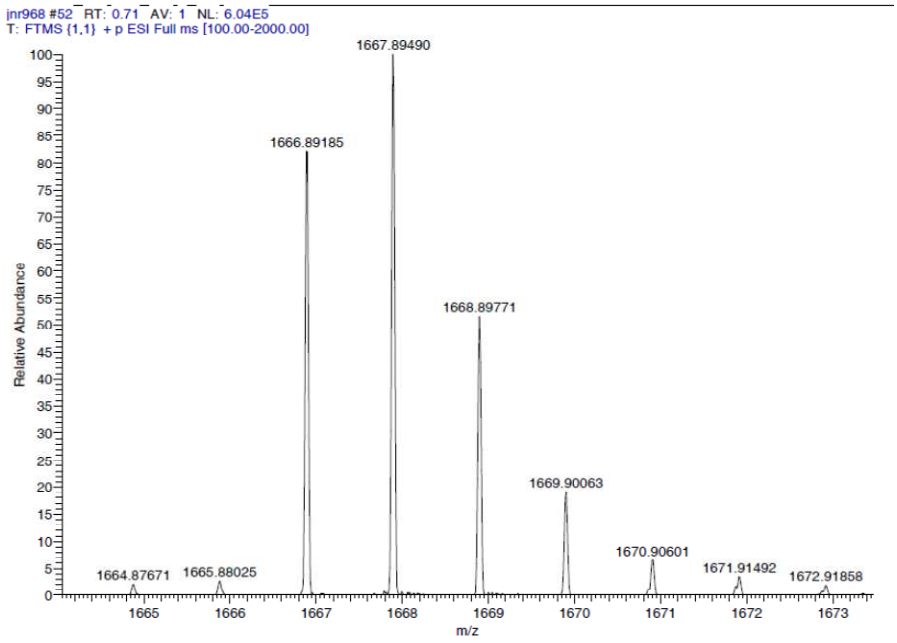


Figure S37. ESI-MS spectrum of **7** (MeOH). m/z = 1667.4 (calcd for [**7**+H]$^+$: 1667.89); 1689.5 (calcd for [**7**+Na]$^+$ 1689.87); 834.3 (calcd for [**7**+2H]$^{2+}$: 834.45).



Elemental composition search on mass 1666.89

m/z= 1661.89-1671.89

m/z	Theo. Mass	Delta (mmu)	RDB equiv.	Composition
1666.89	1666.89	4.05	52.5	$C_{99}H_{112}O_8N_{17}$
	1666.90	-8.53	52.0	$C_{100}H_{114}O_8N_{16}$
	1666.87	16.62	47.5	$C_{99}H_{116}O_{13}N_{11}$
	1666.86	27.85	47.5	$C_{100}H_{116}O_{14}N_9$
	1666.86	27.86	53.0	$C_{99}H_{110}O_9N_{16}$

Figure S38. HRMS spectrum of **7.** the peak associated to mass 1666.8918 corresponds to the formula $C_{99}H_{112}N_{17}O_8$ in agreement with $[\mathbf{7}+H]^+$ (mass error: 4.05 mmu; 2.43 ppm).

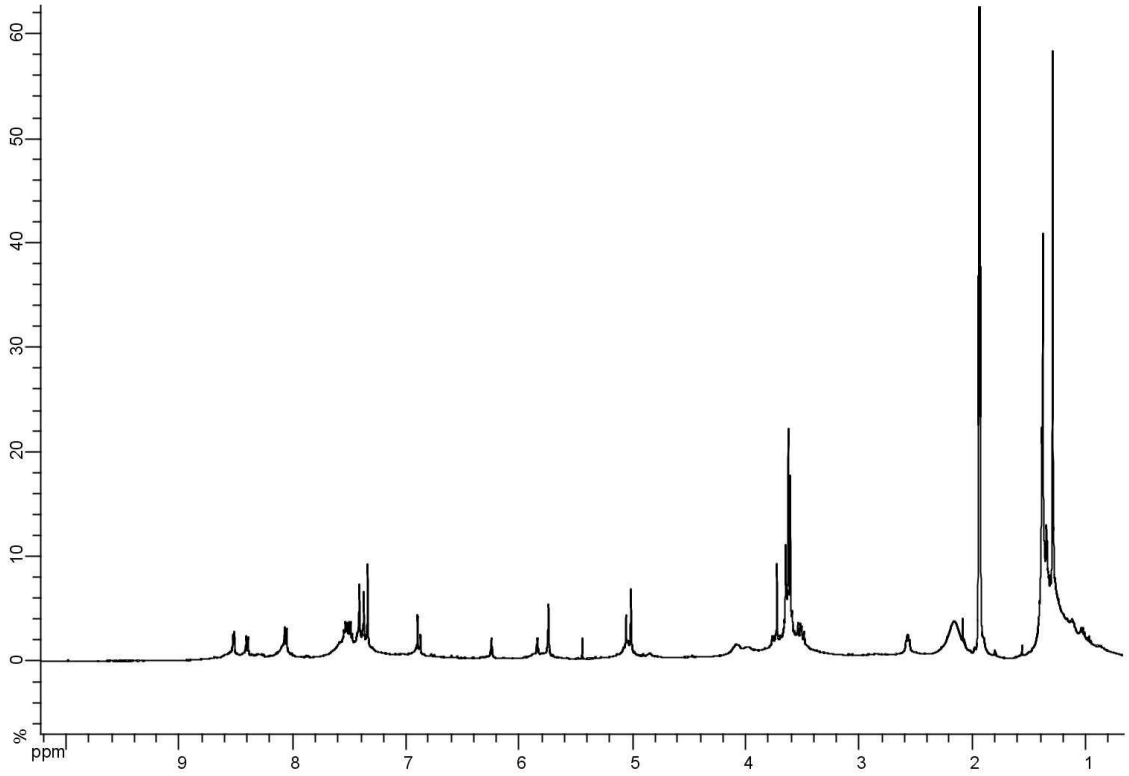


Figure S39. ^{1}H spectrum of [Zn(**7**)(CD_3CN)($OTf)_2$] (500 MHz, CD_3CN, 300 K)

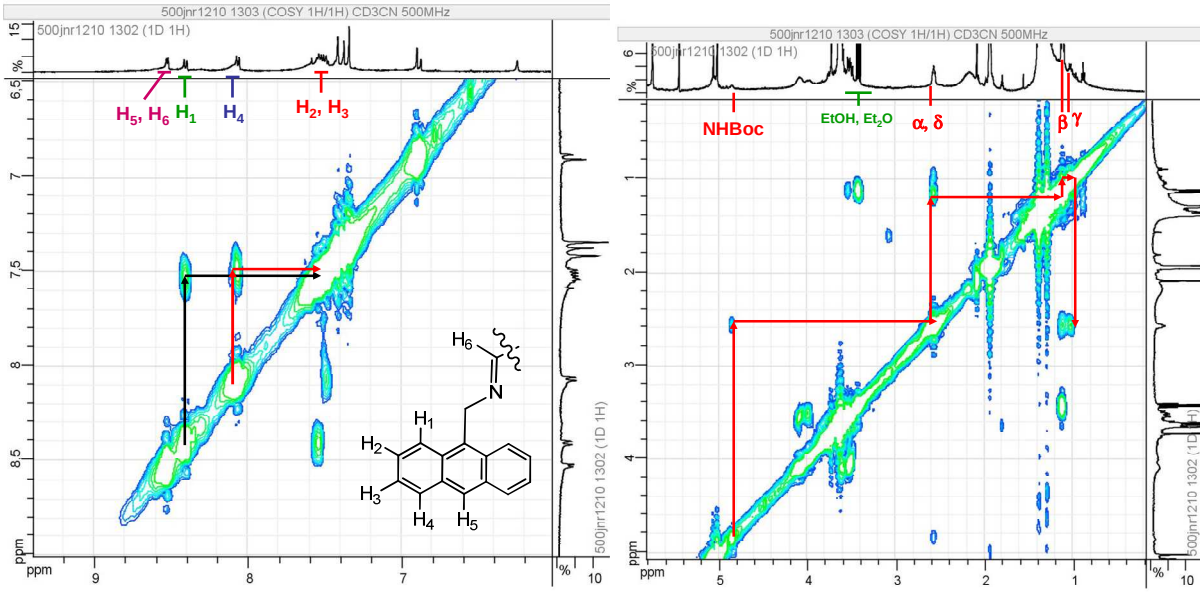


Figure S40. COSY spectrum of [Zn(**7**)(CD_3CN)($OTf)_2$] (500 MHz, CD_3CN, 300 K)

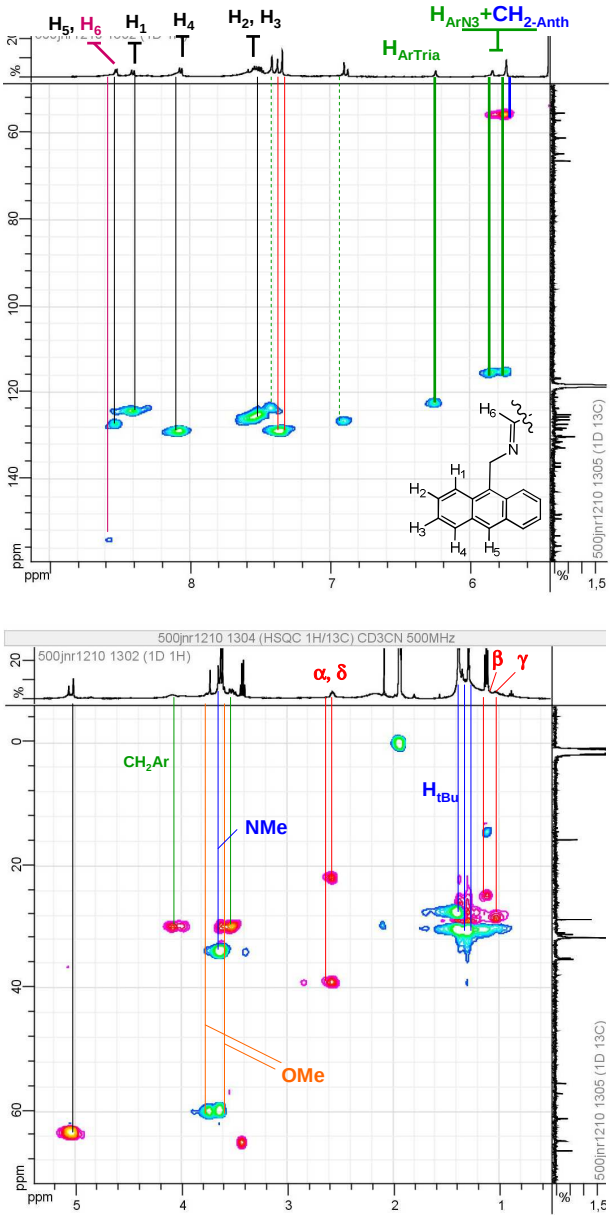


Figure S41. HSQC spectrum of [Zn(**7**)(CD_3CN)($OTf)_2$] (500 MHz, CD_3CN, 300 K)

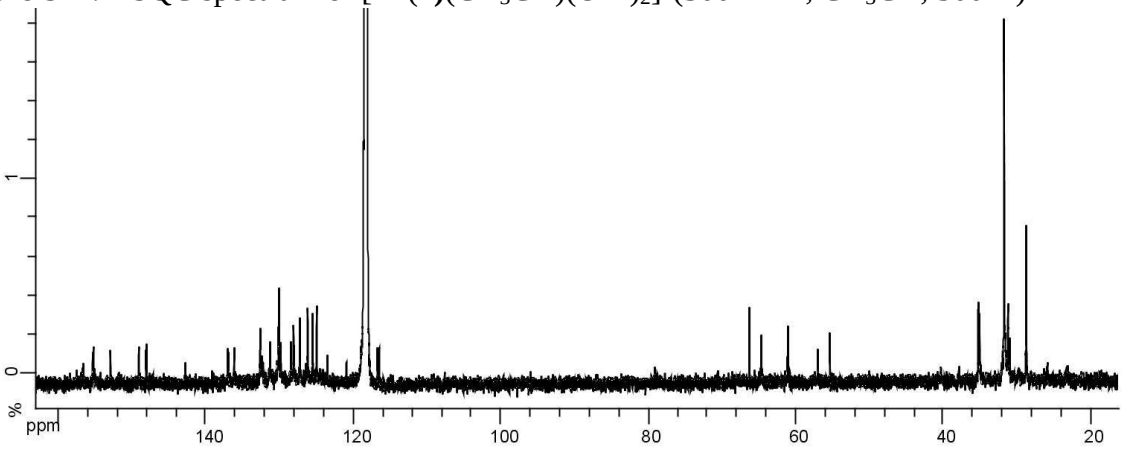


Figure S42. ^{13}C spectrum of (**7**)Zn(CD_3CN)($OTf)_2$ (125 MHz, CD_3CN, 300 K)

c) Synthesis of **8**

4 ($L_{Cl}^{C4NHBoc}$) (31 mg, 20.7 µmol), di-(2-picolyl)amine (11 mg, 55.3 µmol) and K_2CO_3 (15 mg, 108.7 µmol) were mixed in dry THF (5mL) and refluxed overnight under Ar. The solvent was evaporated and the residue taken up in CH_2Cl_2 (20 mL) and water (10mL). The aqueous phase was extracted with CH_2Cl_2 (20 mL) and the organic phases were gathered, washed with water (3 x 5 mL), dried over Na_2SO_4 and evaporated. The solid was washed with 2 x 4 mL of diethyl ether and dried under vacuum (27 mg, 80 %).
NMR Characterization was attempted in DMSO, giving rise to broad resonances (^{1}H, COSY and HSQC spectra are given as an example). For full characterization, the system was studied as a Zn^{II} complex.
From the NMR spectra in the presence of Zn^{II}, an impurity can be detected (9%) identified as **3** ($L_{OH}^{C4NHBoc}$), product of the competitive hydrolysis of **4** ($L_{Cl}^{C4NHBoc}$).

^{1}H NMR characterization (500 MHz, CD_3CN, 300 K): As the scaffold displays multiple coordination sites, several species are to be expected. Zn^{II} addition was thus carried out stepwise (NMR titration, Fig. S48). The ligand itself displays broad resonances, due to the calixarene conformational motion, but sharp resonances for the pyridyl ones, indicating faster motion of the large rim group. A first coordination event happens around 0.5 equiv. of Zn^{II}, with a complete downfield shift of the pyridyl peaks, indicative of their coordination to Zn^{II}. The calixarene resonances remain broad, as no Zn is bound at the imidazole site. A **8**:Zn 2:1 complex can be proposed. Between 0.5 and 1.5 equivalents, the pyridines remain bound, as their resonances are poorly affected, but the calixarene peaks shapen significantly, which is the signature of Zn coordination at the small rim. Indeed, the macrocycle is frozen in a cone conformation, as attested by the *Cs* symmetry of the species. A **8**:Zn 2:3 complex can thus be proposed (Fig. S48).
Characterization of the ligand was thus carried out for the **8**:Zn 2:3 stoichiometry, where a single species with sharp signals is obtained (^{1}H, COSY, HSQC, ^{13}C).
^{1}H (500 MHz, CD_3CN, 300 K) δ (ppm): 1.25 (m, 2H, γ); 1.23 (m, 2H, β); 1.28 (s, 18H, *t*Bu); 1.38 (s, 9H, *t*Bu); 1.43 (s, 9H, *t*Bu Boc); 2.43 (t, J = 7.2 Hz, 2H, δ); 2.87 (m, 2H, α); 3.51 (d, 2H, J = 16 Hz, CH_2Ar); 3.56 (d, 2H, J = 16 Hz, CH_2Ar); 3.63 (s, 12H, NCH_3+ OMe); 3.66 (m, 2H, J = 16 Hz, CH_2Ar); 3.70 (s, 3H, NCH_3); 3.74 (s, 3H, OCH_3); 3.94 (s, 2H, CH_{2Tria}); 4.06-4.14 (dd, 4H, AB system, J = 15 Hz, CH_{2py}) 4.06 - 4.20 (m, 6H, CH_2Ar); 5.05-5.13 (m, 6H, CH_2Im); 5.18 (s, 1H, NHBoc); 5.71 (s, 2H, H_{ArN3}); 6.04 (s, 2H, H_{ArN3}); 6.39 (s 2H, H_{ArTria}); 6.88 (d, 1H, J = 1.6 Hz, H_{Im}); 6.94 (d, 2H, J = 1.6 Hz, H_{Im}); 7.34 (d, 2H, J = 2.7 Hz, H_{ArtBu}); 7.38 (d, 2H, , J = 2.7 Hz, H_{ArtBu}); 7.44 (d, 1H, J = 1.6 Hz, H_{Im}); 7.45 (s, 2H, H_{ArtBu}); 7.46 (d, 1H, J = 1.6 Hz, H_{Im}), 7.51 (d, 2H, J = 7.6 Hz, py), 7.57 (t, 2H, J = 7.6 Hz, py), 8.04 (dt, 2H, J_1 = 7.6 Hz, J_2 = 1.8 Hz, py), 8.04 (d, 2H, J = 5.0 Hz, py).
^{13}C (500 MHz, CD_3CN, 300 K) δ (ppm): 22.37; 25.69; 28.80; 28.81; 30.99; 31.11; 31.27; 31.76; 31.81; 31.87; 35.12; 35.19; 35.28; 40.21; 40.36; 40.52; 40.68; 49.26; 57.70; 61.31; 64.84; 65.04; 79.32; 116.59; 117.10; 120.91; 123.48; 124.24; 125.06; 125.84; 126.02; 126.11; 128.07; 128.29; 129.97; 130.12; 130.34; 131.72; 132.29; 132.44; 132.89; 136.09; 136.29; 136.78; 136.94; 137.17; 137.28; 137.68; 138.58; 142.40; 142.58; 148.09; 148.22; 149.0; 149.26; 150.05; 153.08; 155.55; 156.41; 157.09; 157.85**.**
ESI-MS (CH_3OH): m/z = 1660.1 (calcd for [**8**+H]$^+$: 1660.91); 830.9 (calcd for [**8**+2H]$^{2+}$: 830.96), 554.7 (calcd for [**8**+3H]$^{3+}$: 554.31).
HRMS: peak at mass 1479.9116 corresponds to the formula $C_{96}H_{114}N_{19}O_8$ in agreement with [**8**+H]$^+$ (mass error: 2.27 mmu; 1.4 ppm).

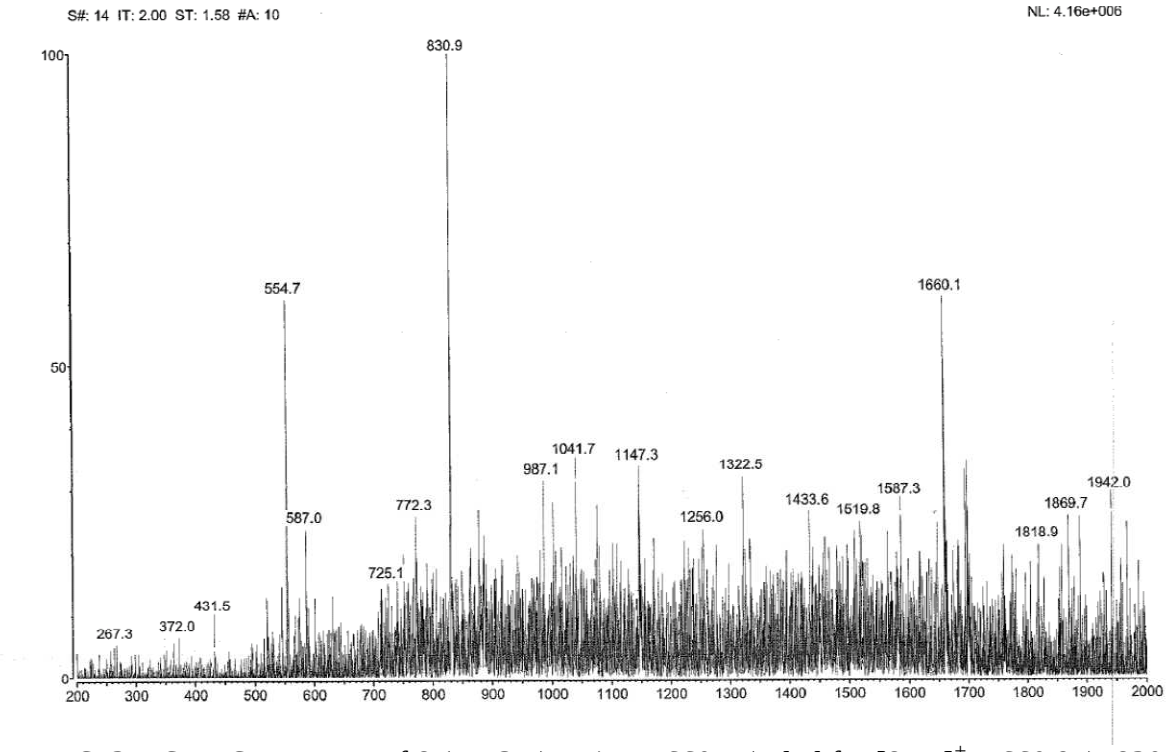
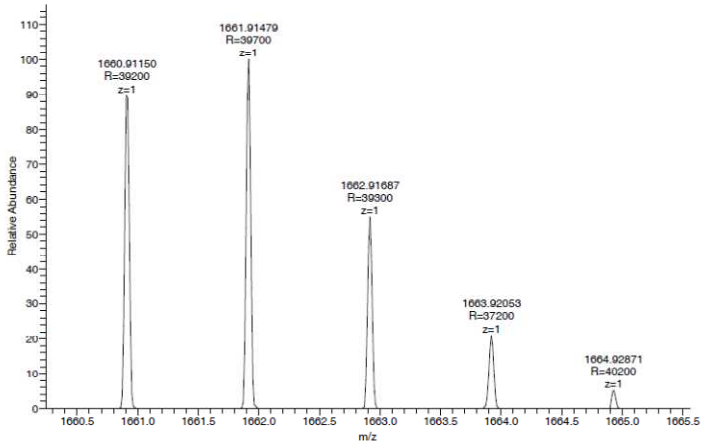


Figure S43. ESI-MS spectrum of **8** (MeOH). m/z = 1660.1 (calcd for [**8**+H]$^{+}$: 1660.91); 830.9 (calcd for [**8**+2H]$^{2+}$: 830.96), 554.7 (calcd for [**8**+3H]$^{3+}$: 554.31).



Elemental composition search on mass 1660.91

m/z= 1655.91-1665.91

m/z	Theo. Mass	Delta (mmu)	RDB equiv.	Composition
1660.91	1660.91	2.27	49.5	$C_{96}H_{114}O_8N_{19}$
	1660.89	26.08	50.0	$C_{96}H_{112}O_9N_{18}$
	1660.86	49.89	50.5	$C_{96}H_{110}O_{10}N_{17}$
	1660.78	132.56	57.5	$C_{96}H_{98}O_9N_{19}$
	1660.76	156.37	58.0	$C_{96}H_{96}O_{10}N_{18}$

Figure S44. HRMS spectrum of **8** (MeOH).the peak associated to mass 1479.9116 corresponds to the formula $C_{96}H_{114}N_{19}O_8$ in agreement with [**8**+H]$^{+}$ (mass error: 2.27 mmu; 1.4 ppm).

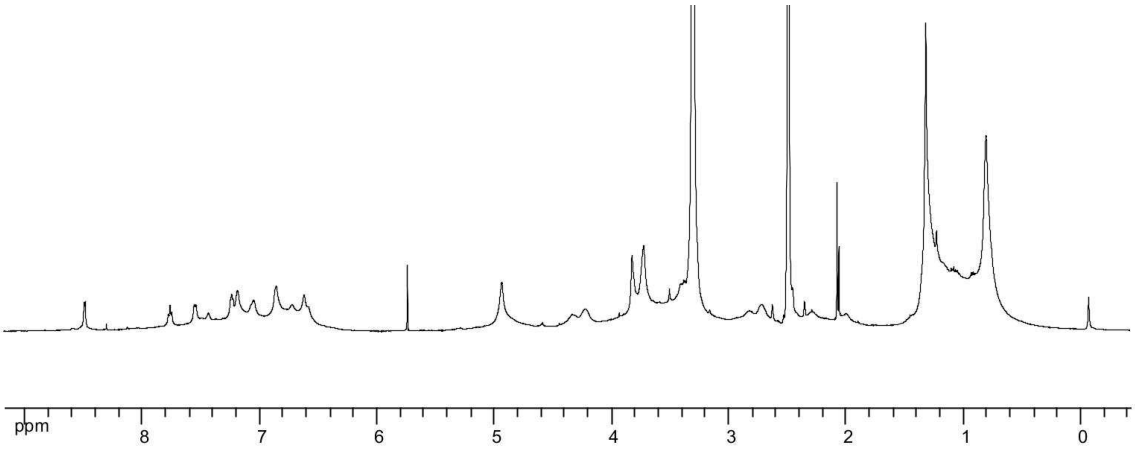


Figure S45. ^{1}H spectrum of ligand **8** (500 MHz, DMSO d^{6}, 300 K)

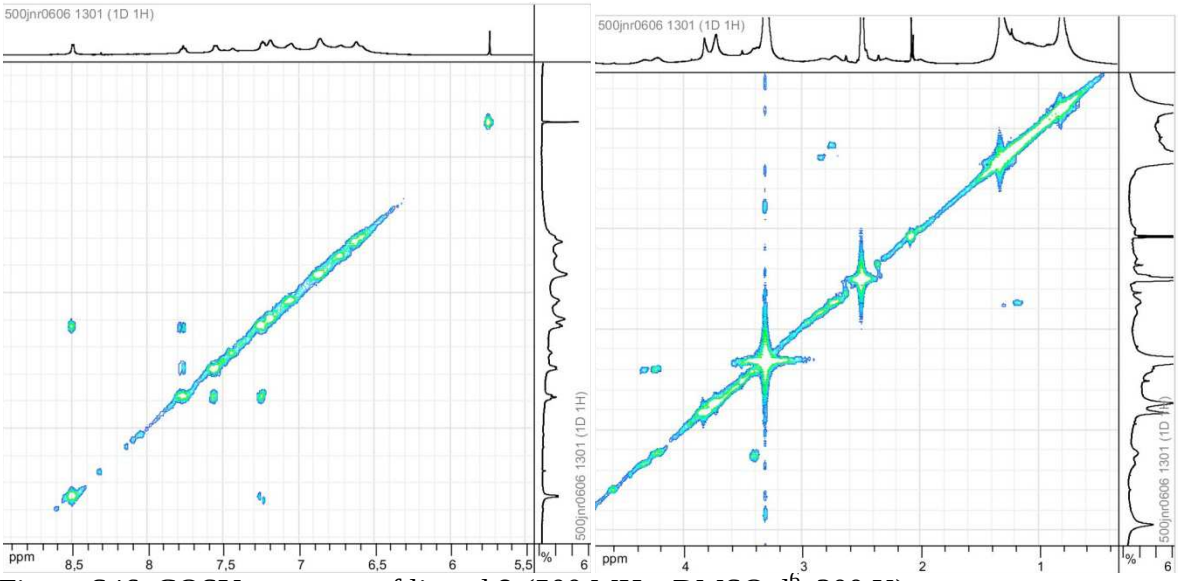


Figure S46. COSY spectrum of ligand **8** (500 MHz, DMSO d^{6}, 300 K)

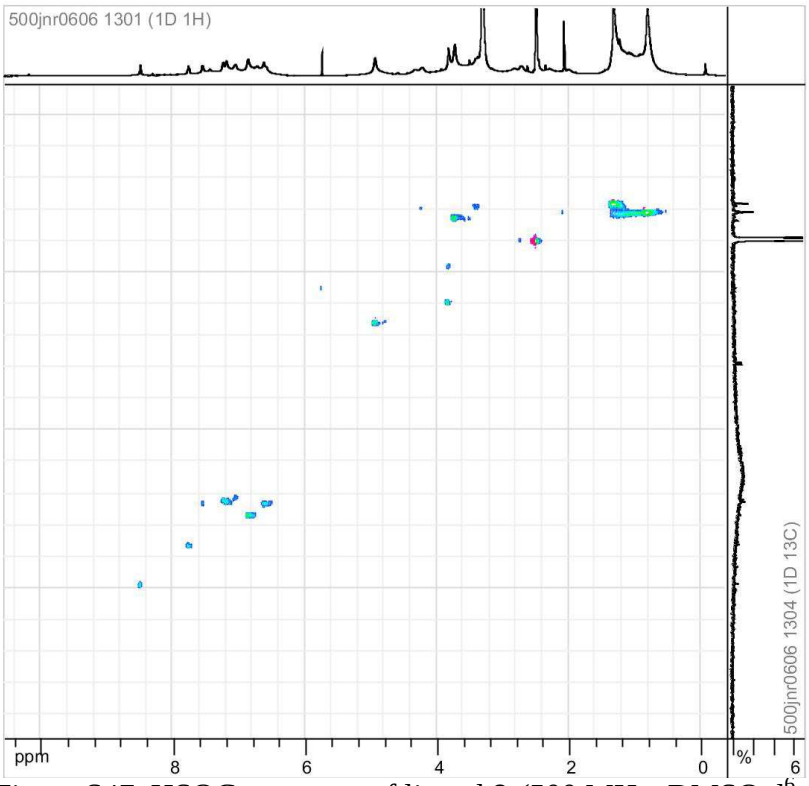


Figure S47. HSQC spectrum of ligand **8** (500 MHz, DMSO d^6, 300 K)

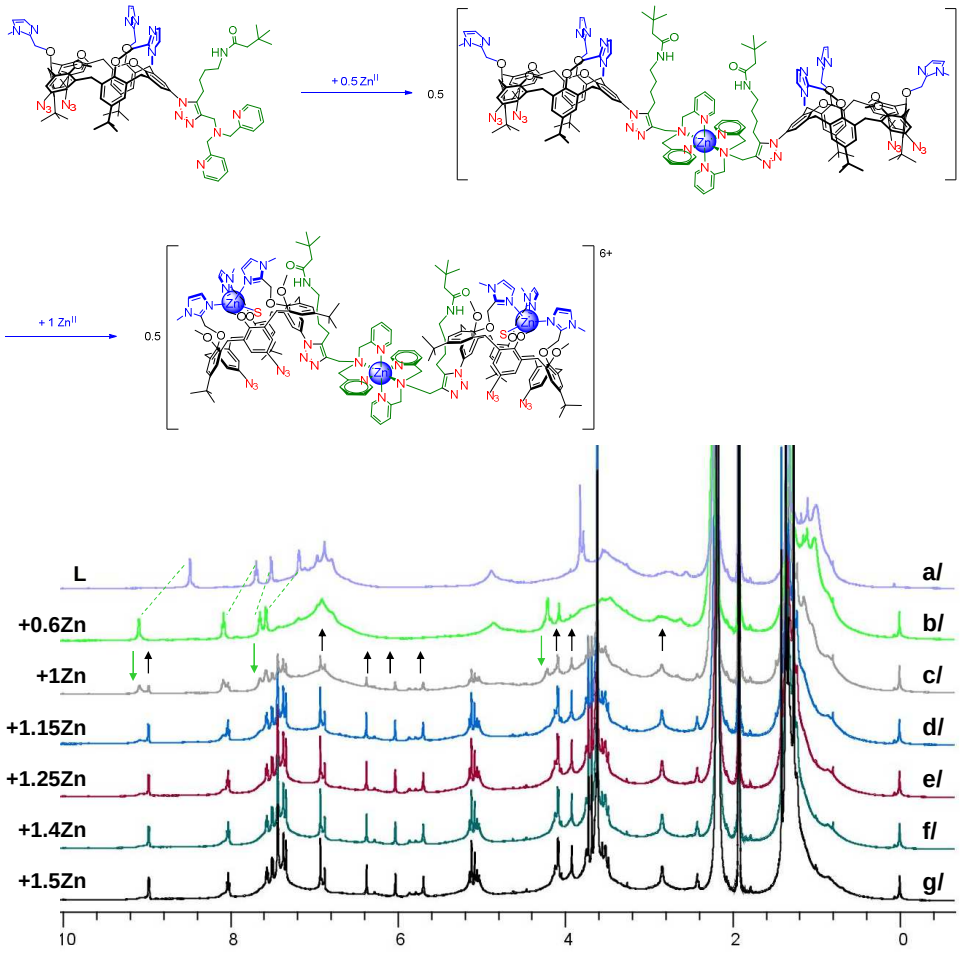


Figure S48. ^{1}H NMR Titration of **8** by $Zn(OTf)_2$ in CD3CN (500 MHz, 300 K). The trace peaks observed at 6.29, 5.87, 579 ppm correspond to an impurity (9%) identified as the Zn^{II} complex of **3**($L_{OH}^{C4NHBoc}$). The presence of **3**($L_{OH}^{C4NHBoc}$) is very likely resulting from the competitive hydrolysis of **4** ($L_{Cl}^{C4NHBoc}$) in the basic reaction conditions.

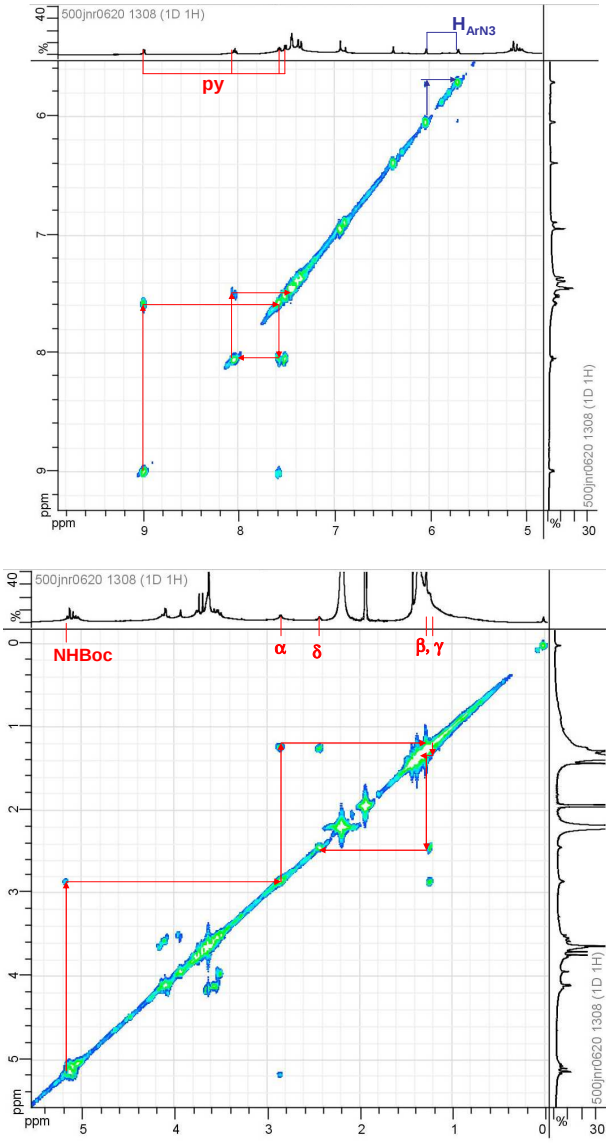


Figure S49. COSY spectrum of a mixture of **8** and $Zn(OTf)_2$ 2:3(500 MHz, CD_3CN, 300 K)

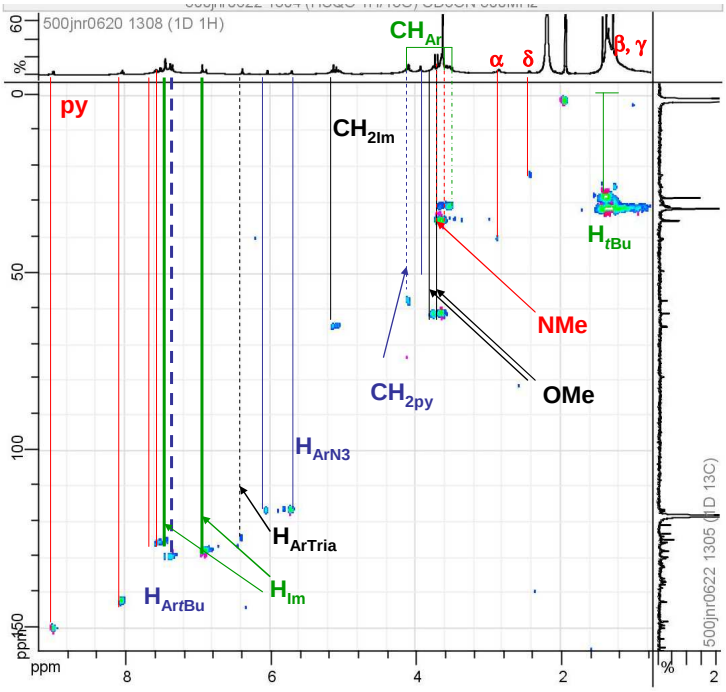


Figure S50. HSQC spectrum of a mixture of **8** and $Zn(OTf)_2$ 2:3 (500 MHz, CD_3CN, 300 K)

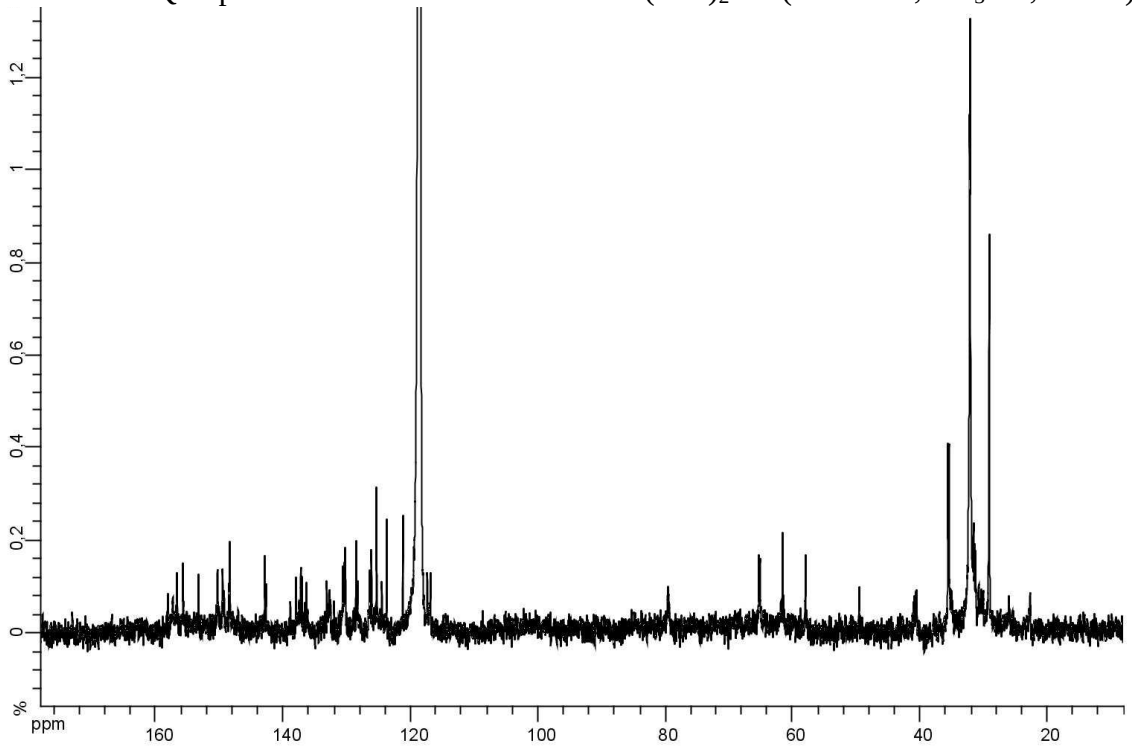


Figure S51. ^{13}C spectrum of a mixture of **8** and $Zn(OTf)_2$ 2:3 (125 MHz, CD_3CN, 300 K)

(1) Larrosa, I.; Da Silva, M. I.; Gómez , P. M.; Hannen, P.; Ko, E.; Lenger, S. R.; Linke, S. R.; White, A. J. P.; Wilton, D.; Barrett, A. G. M. *J. Am. Chem. Soc.* **2006**, *128*, 14042-14043.

(2) Coquière, D.; Marrot, J.; Reinaud, O. *Chem. Commun.* **2006**, 3924-3926.
(3) Sénèque, O.; Rager, M. N.; Giorgi, M.; Reinaud, O. *J. Am. Chem. Soc.* **2000**, *122*, 6183-6189.
(4) Colasson, B.; Save, M.; Milko, P.; Roithova, J.; Schroder, D.; Reinaud, O. *Org. Lett.* **2007**, *9*, 4987-4990.
(5) Redon, S.; Li, Y.; Reinaud, O. *J. Org. Chem.* **2003**, *68*, 7004-7008.
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(7) Colasson, B.; Reinaud, O. *J. Am. Chem. Soc.* **2008**, *130*, 15226-15227.