

## Supporting Information

### Selective Hetero-Trisfunctionalization of the Large Rim of a Biomimetic Calix[6]arene Using Host-Guest Chemistry as a Synthetic Tool.

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#### Table of Contents

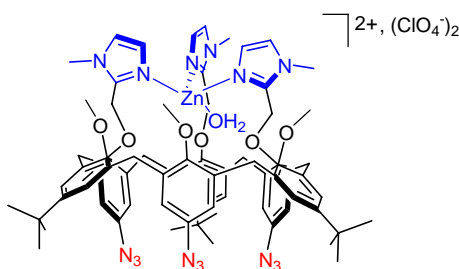
<b>Experimental Section</b>	S2
[Zn(1)](ClO <sub>4</sub> ) <sub>2</sub>	S2
[Zn(2)](ClO <sub>4</sub> ) <sub>2</sub>	S4
Calixarene <b>2</b>	S6
Calixarene <b>3</b>	S7
[Zn(3)](ClO <sub>4</sub> ) <sub>2</sub>	S8
[Zn(4)](ClO <sub>4</sub> ) <sub>2</sub>	S10
<b><sup>1</sup>H NMR of [Zn(1)(CD<sub>3</sub>CN)](ClO<sub>4</sub>)<sub>2</sub>, [Zn(1)(NH<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>C≡CH)](ClO<sub>4</sub>)<sub>2</sub> and [Zn(2)](ClO<sub>4</sub>)<sub>2</sub></b>	S13
<b>Schematic representation of the enantiomerization process of the helical binding at the metal core</b>	S14
<b>Variable temperature <sup>1</sup>H NMR experiments (500MHz, CD<sub>3</sub>CN) with [Zn(4)](ClO<sub>4</sub>)<sub>2</sub></b>	S14
<b>NMR COSY experiment of [Zn(4)](ClO<sub>4</sub>)<sub>2</sub> (500 MHz, CD<sub>3</sub>CN, 300K)</b>	S17
<b>Question/answer relative to the regioselectivity of the cycloaddition</b>	S19
<b>References</b>	S19

## Experimental Section.

**Safety Note.** Caution ! Although we have not encountered any problems, it is noted that perchlorate salts of metal complexes with organic ligands are potentially explosive and should be handled only in small quantities with appropriate precautions. Identically, organic azides are potentially explosive and should be manipulated carefully.

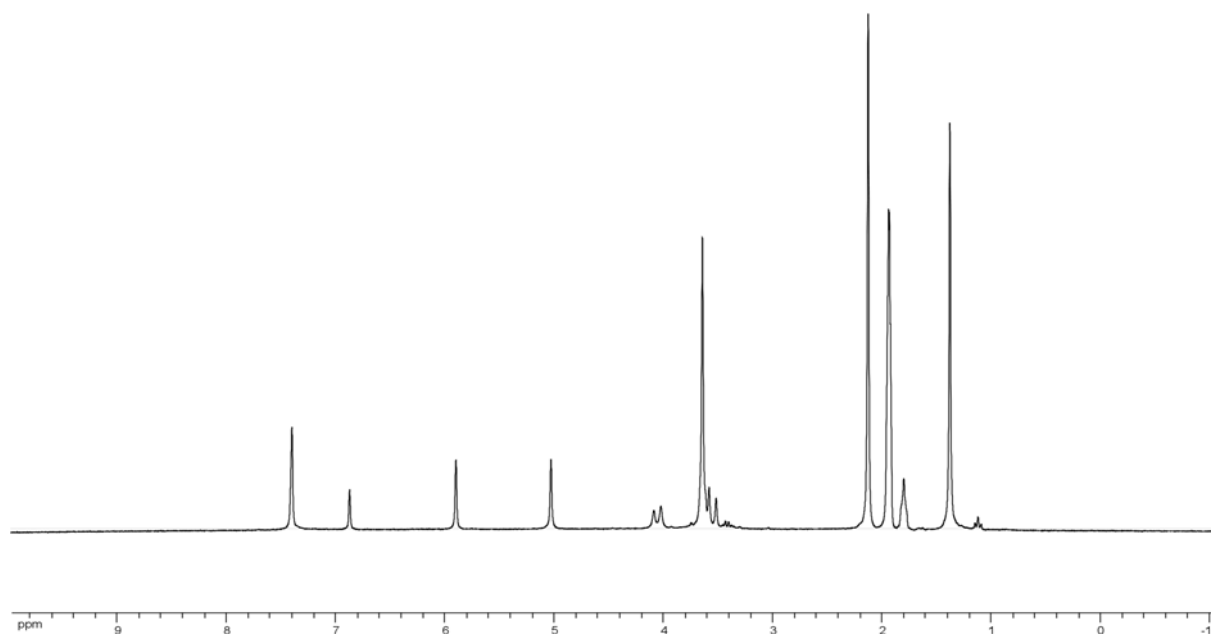
**General experimental methods.** Solvents and chemicals were of reagent grade and were used without purification. THF was dried over Na/benzophenone and distilled. All the reactions were performed under an Ar atmosphere. 5-aminopentyne was prepared following a procedure described elsewhere.<sup>1</sup> Tris(azido)calix[6]arene **1** was described in a previous publication.<sup>2</sup> Elemental analyses were performed at the Institut de Chimie des Substances Naturelles, France. <sup>1</sup>H, <sup>13</sup>C NMR spectra and COSY experiments were recorded on a Bruker ARX250 MHz spectrometer or an Advance 500 spectrometer. MS (ESI) analyses were obtained with a ThermoFinnigan LCQ Advantage spectrometer using methanol or dichloromethane as solvents. IR spectra were obtained with a Perkin-Elmer Spectrum on FTIR spectrometer equipped with a MIRacle™ single reflection horizontal ATR unit (germanium crystal).

[Zn(**1**)](ClO<sub>4</sub>)<sub>2</sub>:

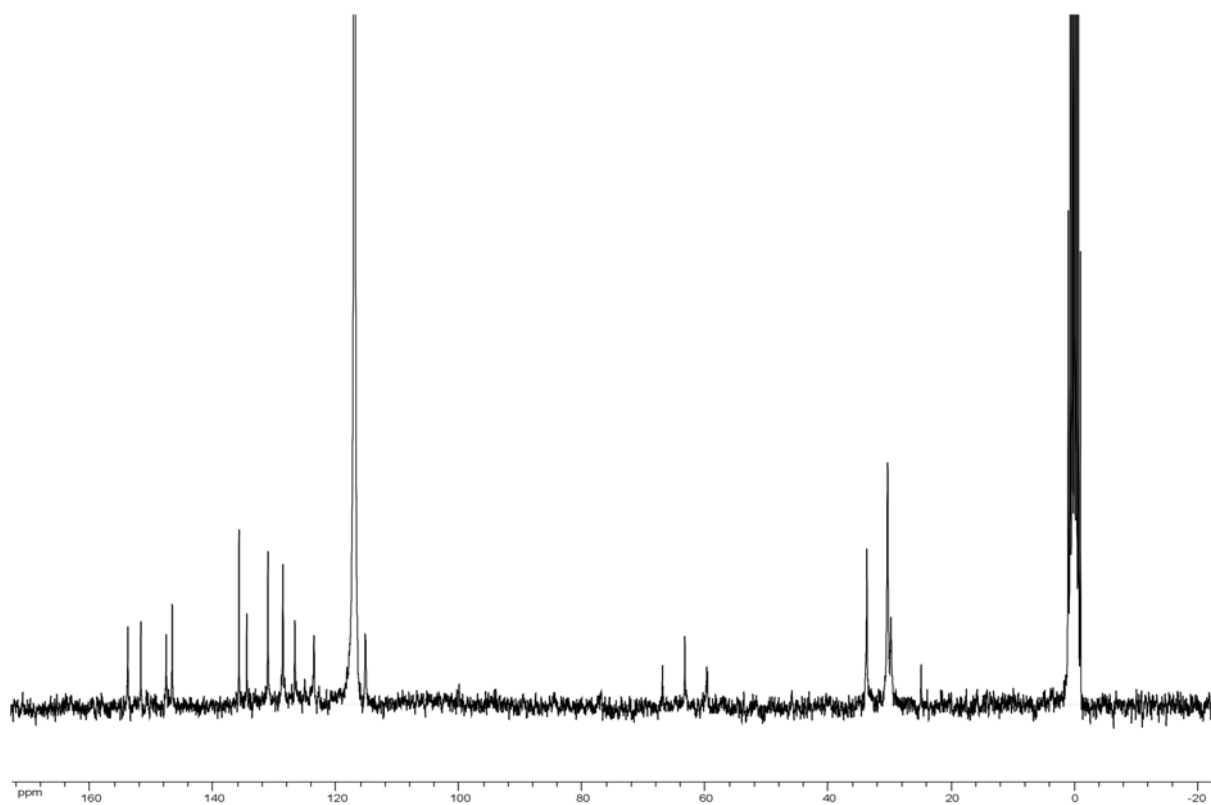


Zn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O (44.1 mg, 118 μmol) was poured into a flask containing calixN3 **1** (148.4 mg, 118 μmol) in THF (3 mL). The solution was stirred for 2h at room temperature. 10mL of Et<sub>2</sub>O were added which resulted in the precipitation of a white solid. The mixture was centrifugated and the solid was washed with 5mL of Et<sub>2</sub>O. The solid was dried under vacuum and [Zn(**1**)](ClO<sub>4</sub>)<sub>2</sub> (180 mg, 99% yield) was obtained as a white powder.

**<sup>1</sup>H NMR (250 MHz, CD<sub>3</sub>CN, 300 K)** δ (ppm): 1.40 (*t*-Bu, s, 27H), 3.47 (ArCH<sub>2</sub>, d, J= 16.2 Hz, 6H), 3.67 (OCH<sub>3</sub> and NCH<sub>3</sub>, s, 18H), 4.07 (ArCH<sub>2</sub>, d, J= 16.2 Hz, 6H), 5.06 (CH<sub>2</sub>Im, s, 6H), 5.93 (H<sub>ArN3</sub>, s, 6H), 6.90 (H<sub>Im</sub>, s, 3H), 7.43 (H<sub>Ar*t*-Bu</sub> and H<sub>Im</sub>, s, 9H); **<sup>13</sup>C NMR (62 MHz, CD<sub>3</sub>CN, 300 K)** δ (ppm): 31.07, 31.63, 34.97, 61.00, 64.58, 116.54, 124.85, 127.96, 129.90, 132.34, 135.79, 137.04, 147.90, 148.89, 153.00, 155.12. **ES-MS** (CH<sub>2</sub>Cl<sub>2</sub>) *m/z*: 666.1 (calcd for [M+H<sub>2</sub>O-2ClO<sub>4</sub>]<sup>2+</sup> 666.8). **Elemental Analysis:** C<sub>72</sub>H<sub>81</sub>Cl<sub>2</sub>N<sub>15</sub>O<sub>14</sub>Zn-H<sub>2</sub>O-CH<sub>2</sub>Cl<sub>2</sub> Found: C 54.11 H 5.33 N 12.16 Calculated: C 54.13 H 5.29 N 12.97. **IR** (ATR, cm<sup>-1</sup>): 2111 (s), 1597 (w), 1505 (w), 1475 (m), 1434 (w), 1363 (w), 1299 (w), 1243 (w), 1188 (w), 1165 (w), 1103 (s), 1001 (m), 976 (w), 866 (w), 760 (w).

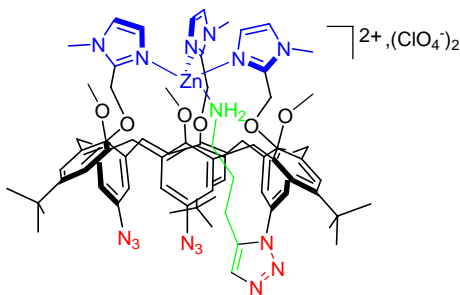


<sup>1</sup>H NMR spectrum of [Zn(**1**)](ClO<sub>4</sub>)<sub>2</sub> (250 MHz, CD<sub>3</sub>CN, 300 K).



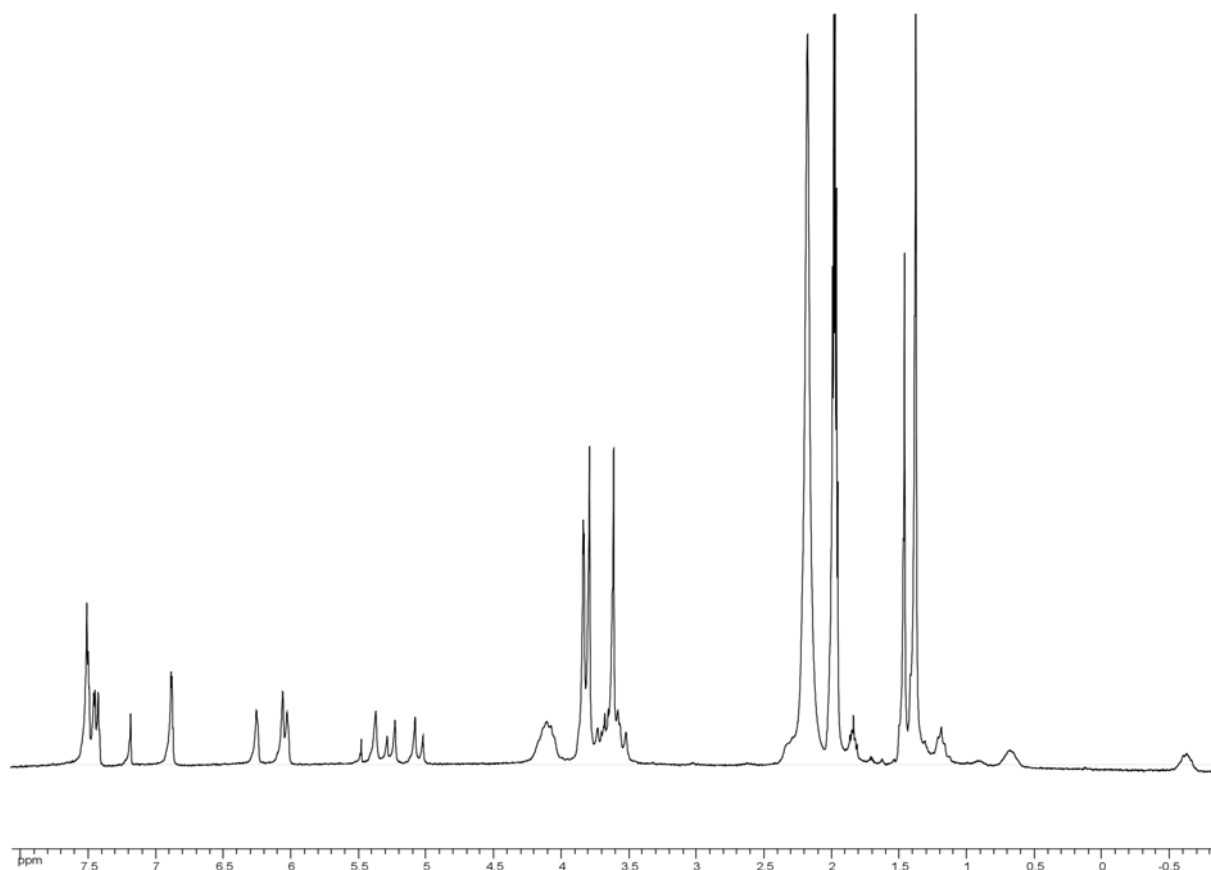
$^{13}\text{C}$  NMR spectrum of  $[\text{Zn}(\mathbf{1})](\text{ClO}_4)_2$  (62 MHz,  $\text{CD}_3\text{CN}$ , 300 K).

$[\text{Zn}(\mathbf{2})](\text{ClO}_4)_2$ :

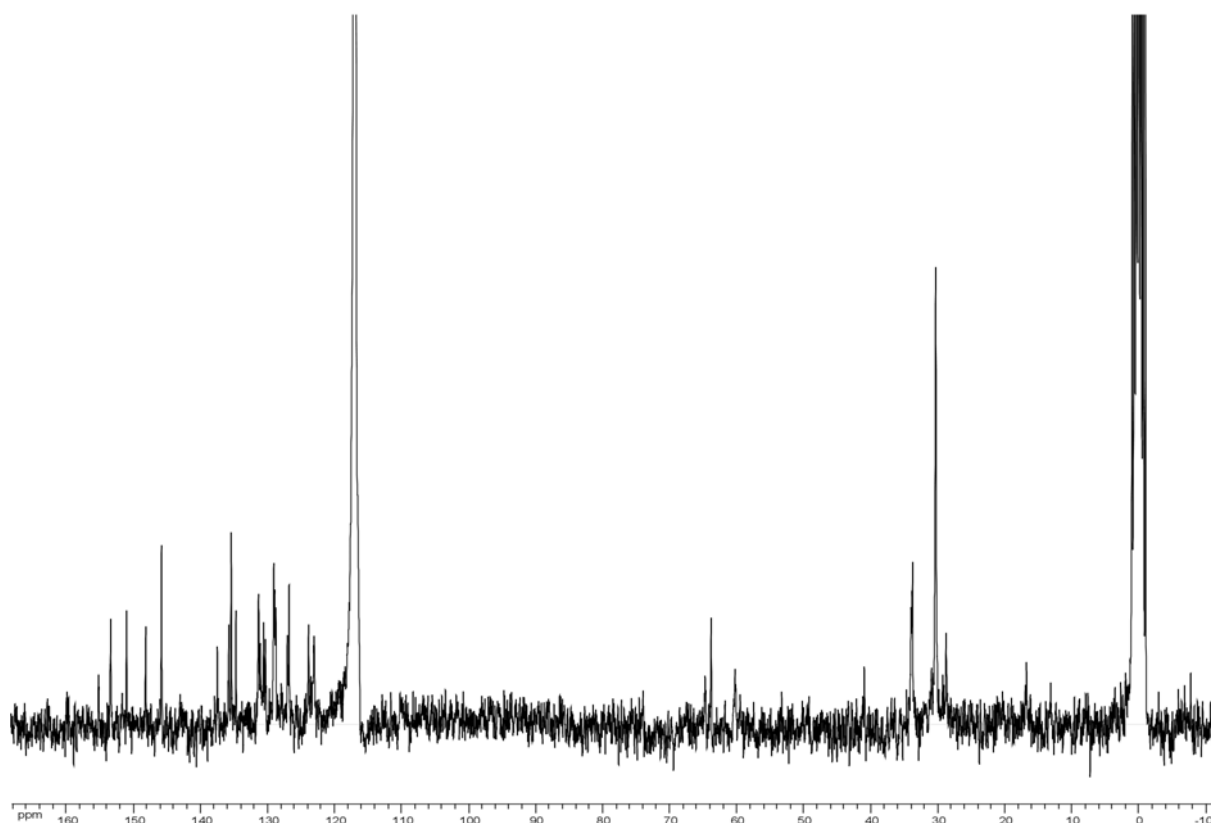


$[\text{Zn}(\mathbf{1})](\text{ClO}_4)_2$  (252 mg, 164  $\mu\text{mol}$ ) was dissolved in freshly distilled THF (15 mL). 1.2 mL of a  $\text{CH}_2\text{Cl}_2$  solution of 5-aminopentyne (27 mg, 328  $\mu\text{mol}$ ) was added and the solution was stirred for 17h at  $65^\circ\text{C}$ . Then, 0.6mL of the same 5-aminopentyne solution (13 mg, 164  $\mu\text{mol}$ ) was added and the solution was stirred at  $65^\circ\text{C}$  for 24h. The solution was cooled down to room temperature then 20mL of  $\text{Et}_2\text{O}$  were added. The mixture was centrifugated and the solid was washed twice with 5mL of  $\text{Et}_2\text{O}$ . The solid was dried under vacuum and  $[\text{Zn}(\mathbf{2})](\text{ClO}_4)_2$  (237 mg, 91% yield) was obtained as a white powder.

**$^1\text{H}$  NMR (500 MHz,  $\text{CD}_3\text{CN}$ , 300 K)**  $\delta$  (ppm): -0.67 ( $\text{H}_2$ , m, 2H), 0.65 ( $\text{H}_1$ , m, 2H), 1.15 ( $\text{H}_3$ , m, 2H), 1.33 ( $t\text{-Bu}$ , s, 18H), 1.42 ( $t\text{-Bu}$ , s, 9H), 3.54 ( $\text{ArCH}_2$ , m, 6H), 3.57 ( $\text{OCH}_3$ , s, 6H), 3.75 ( $\text{NCH}_3$ , s, 6H), 3.79 ( $\text{OCH}_3$ , s, 3H), 3.81 ( $\text{NCH}_3$ , s, 3H), 4.05 ( $\text{ArCH}_2$ , m, 6H), 5.02 ( $\text{CH}_2\text{Im}$ , d,  $J = 14.4$  Hz, 2H), 5.21 ( $\text{CH}_2\text{Im}$ , d,  $J = 14.4$  Hz, 2H), 5.33 ( $\text{CH}_2\text{Im}$ , s, 2H), 5.98 ( $\text{H}_{\text{ArN}3}$ , d,  $J = 2.3$  Hz, 2H), 6.02 ( $\text{H}_{\text{Artria}}$ , s, 2H), 6.21 ( $\text{H}_{\text{ArN}3}$ , d,  $J = 2.3$  Hz, 2H), 6.84 ( $\text{H}_{\text{Im}}$ , d,  $J = 1.6$  Hz, 1H), 6.85 ( $\text{H}_{\text{Im}}$ , d,  $J = 1.6$  Hz, 2H), 7.14 ( $\text{H}_{\text{tria}}$ , s, 1H), 7.38 ( $\text{H}_{\text{Arr-Bu}}$ , d,  $J = 2.5$  Hz, 2H), 7.41 ( $\text{H}_{\text{Arr-Bu}}$ , d,  $J = 2.5$  Hz, 2H), 7.46 ( $\text{H}_{\text{Arr-Bu}}$  and  $\text{H}_{\text{Im}}$ , m, 5H);  **$^{13}\text{C}$  NMR (62 MHz,  $\text{CD}_3\text{CN}$ , 300 K)**  $\delta$  (ppm): 28.77, 30.32, 33.76, 40.98, 60.27, 63.83, 64.75, 123.08, 123.92, 126.82, 127.07, 128.97, 129.11, 130.36, 130.62, 131.13, 131.38, 134.75, 135.46, 135.81, 137.53, 145.86, 148.31, 151.08, 153.44, 155.25. **ES-MS** ( $\text{CH}_2\text{Cl}_2$ )  $m/z$ : 699.2 (calcd for  $[\text{M}-2\text{ClO}_4]^{2+}$  699.2). **Elemental Analysis:**  $\text{C}_{77}\text{H}_{90}\text{Cl}_2\text{N}_{16}\text{O}_{14}\text{Zn}-\text{CH}_2\text{Cl}_2$  Found: C 55.54 H 5.67 N 12.61 Calculated: C 55.60 H 5.50 N 13.30. **IR** (ATR,  $\text{cm}^{-1}$ ): 2956 (w), 2109 (m), 1587 (w), 1503 (w), 1480 (m), 1460 (m), 1364 (w), 1291 (w), 1235 (w), 1201 (w), 1160 (w), 1100 (s), 998 (m), 975 (w), 871 (w), 763 (w).

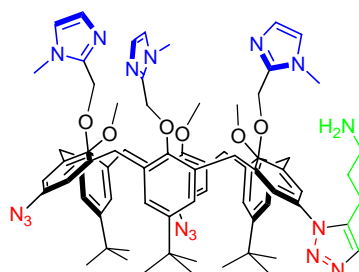


$^1\text{H}$  NMR spectrum of  $[\text{Zn}(\mathbf{2})](\text{ClO}_4)_2$  (250 MHz,  $\text{CD}_3\text{CN}$ , 300 K).



$^{13}\text{C}$  NMR spectrum of  $[\text{Zn}(\mathbf{2})](\text{ClO}_4)_2$  (62 MHz,  $\text{CD}_3\text{CN}$ , 300 K).

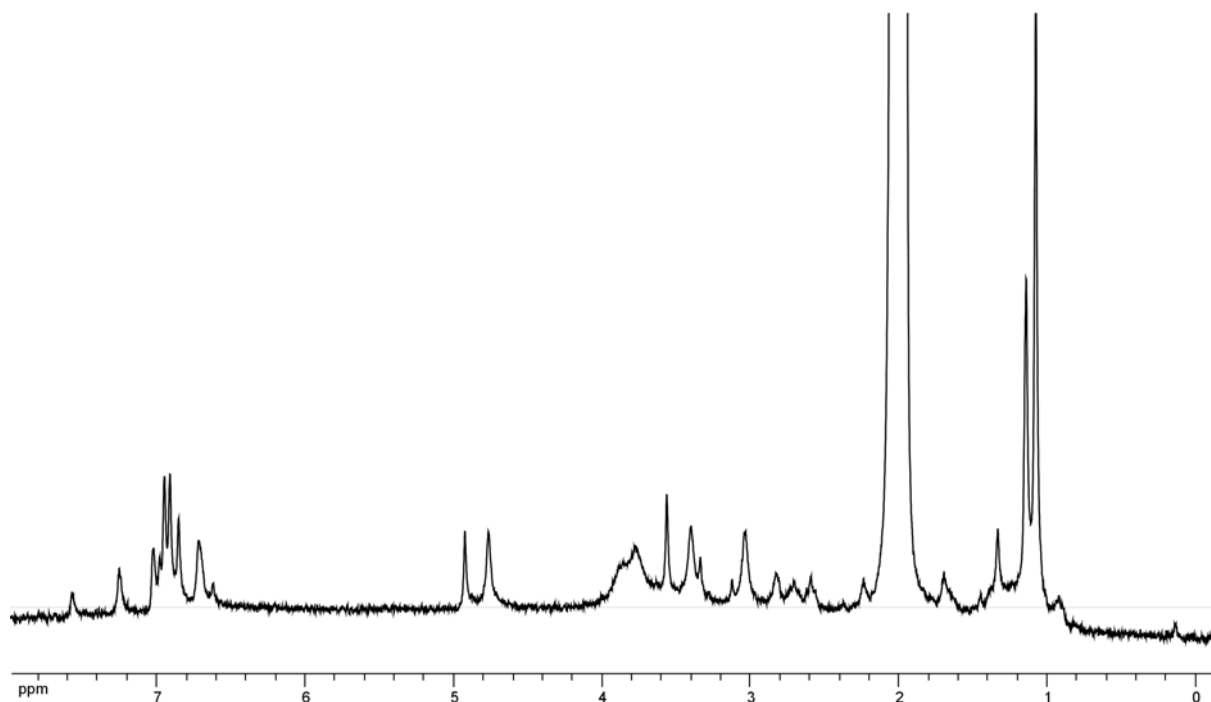
Calixarene **2**:



$[\text{Zn}(\mathbf{2})](\text{ClO}_4)_2$  (205 mg, 128  $\mu\text{mol}$ ) was dissolved in 4 mL of  $\text{CH}_2\text{Cl}_2$ . 3 mL of aqueous NaOH (1M) was added and the biphasic solution was stirred overnight at room temperature. The organic layer was separated. The aqueous layer was extracted twice with 5 mL of  $\text{CH}_2\text{Cl}_2$ . The organic phases were combined, washed with 10 mL of  $\text{H}_2\text{O}$  and dried over  $\text{Na}_2\text{SO}_4$ . After filtration, **2** was obtained as a green solid (166 mg, 97% yield).

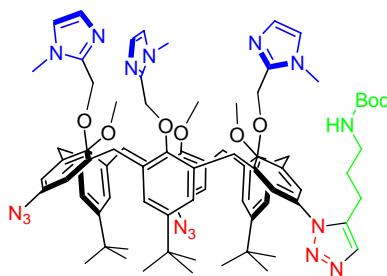
$^1\text{H}$  NMR (300 MHz,  $\text{CD}_3\text{CN}$ , 300 K)  $\delta$  (ppm): the peaks are large at room temperature. No attribution was made;  $^{13}\text{C}$  NMR (62 MHz,  $\text{CD}_3\text{CN}$ , 300 K)  $\delta$  (ppm): the peaks are large at room temperature. No spectrum was recorded. ES-MS (MeOH)  $m/z$ : 1335.7 (calcd for  $[\text{M}+\text{H}]^+$  1335.7); 668.3 (calcd for  $[\text{M}+2\text{H}]^{2+}$  668.3). **Elemental Analysis:**  $\text{C}_{77}\text{H}_{90}\text{N}_{16}\text{O}_6$ -

0.5H<sub>2</sub>O-0.5CH<sub>2</sub>Cl<sub>2</sub> Found: C 66.76 H 6.78 N 15.71 Calculated: C 67.11 H 6.69 N 16.16. **IR** (ATR, cm<sup>-1</sup>): 2957 (m), 2109 (s), 1596 (w), 1477 (s), 1362 (w), 1284 (w), 1241 (s), 1205 (w), 1183 (w), 1111 (w), 1080 (w), 1005 (m), 979 (m), 876 (w), 743 (w).



<sup>1</sup>H NMR spectrum of calix **2** (250 MHz, CD<sub>3</sub>CN, 340 K).

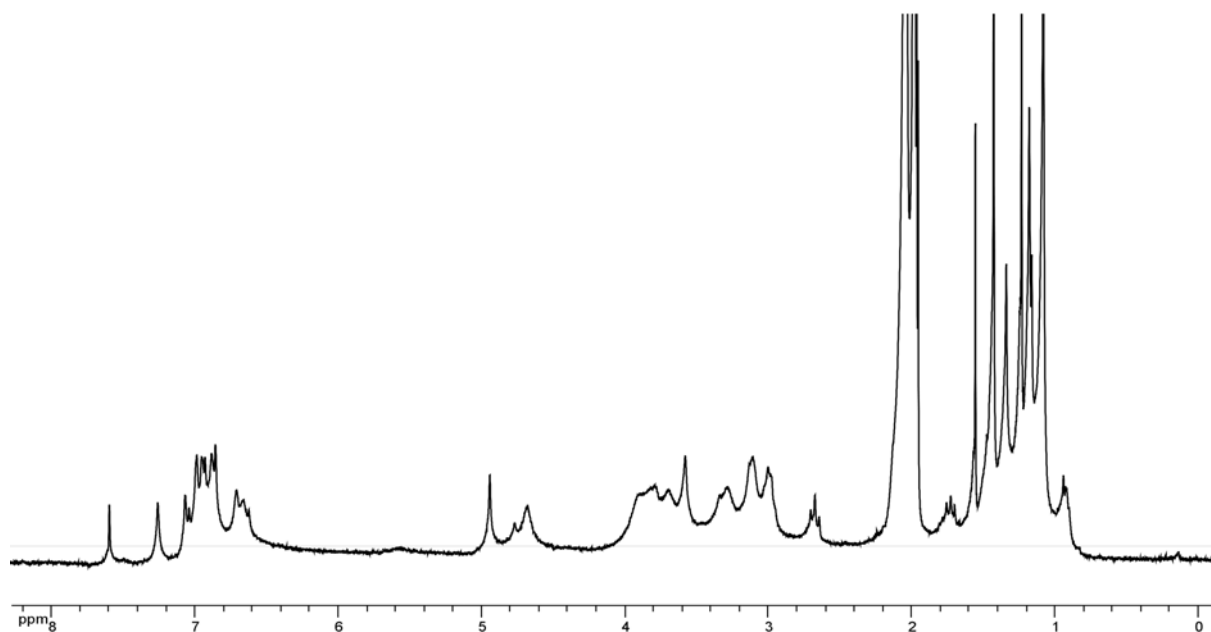
Calixarene **3**:



Calixarene **2** (151mg, 113  $\mu$ mol) was dissolved in dry THF. The solution was cooled to 0°C. Et<sub>3</sub>N (23  $\mu$ L, 168  $\mu$ mol) and Boc<sub>2</sub>O (37mg, 168  $\mu$ mol) were added into the solution after which it was stirred at room temperature for 4h. The solvent was then removed under vacuum, and the residue was taken in CH<sub>2</sub>Cl<sub>2</sub> (15mL) and a saturated NH<sub>4</sub>Cl aqueous solution (15mL). The organic layer was then washed three times with 10mL of H<sub>2</sub>O and dried with Na<sub>2</sub>SO<sub>4</sub>. After filtration, **3** was obtained in 92% yield as beige solid.

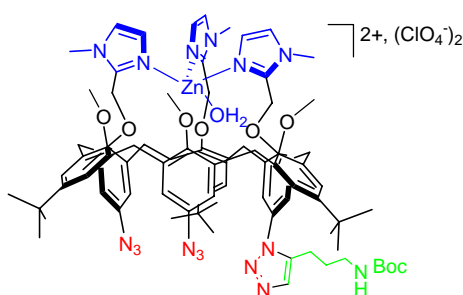
**<sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>CN, 300 K)**  $\delta$  (ppm): the peaks are large at room temperature. No attribution was made; **<sup>13</sup>C NMR (62 MHz, CD<sub>3</sub>CN, 300 K)**  $\delta$  (ppm): the peaks are large a

room temperature. No spectrum was recorded. **ES-MS** (MeOH)  $m/z$ : 1435.6 (calcd for  $[M+H]^+$  1435.7); 718.4 (calcd for  $[M+2H]^{2+}$  718.3). **Elemental Analysis**:  $C_{82}H_{98}N_{16}O_8 \cdot 0.5CH_2Cl_2$  Found: C 67.12 H 7.04 N 14.72 Calculated: C 67.03 H 6.75 N 15.16. **IR** (ATR,  $cm^{-1}$ ): 2957 (m), 2109 (s), 1707 (m), 1596 (w), 1477 (s), 1364 (w), 1284 (w), 1242 (s), 1205 (w), 1181 (m), 1112 (w), 1078 (w), 1007 (m), 979 (m), 875 (w), 746 (w).



$^1H$  NMR spectrum of calix **3** (250 MHz,  $CD_3CN$ , 340 K).

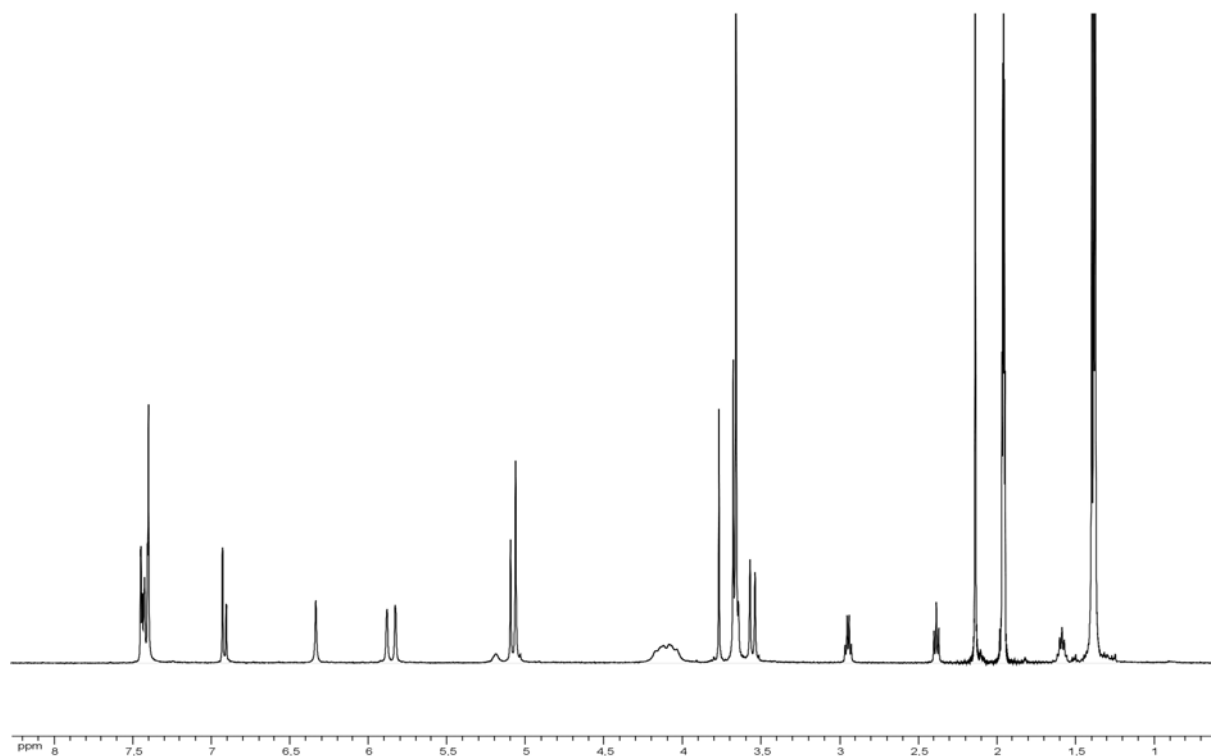
$[Zn(\mathbf{3})](ClO_4)_2$ :



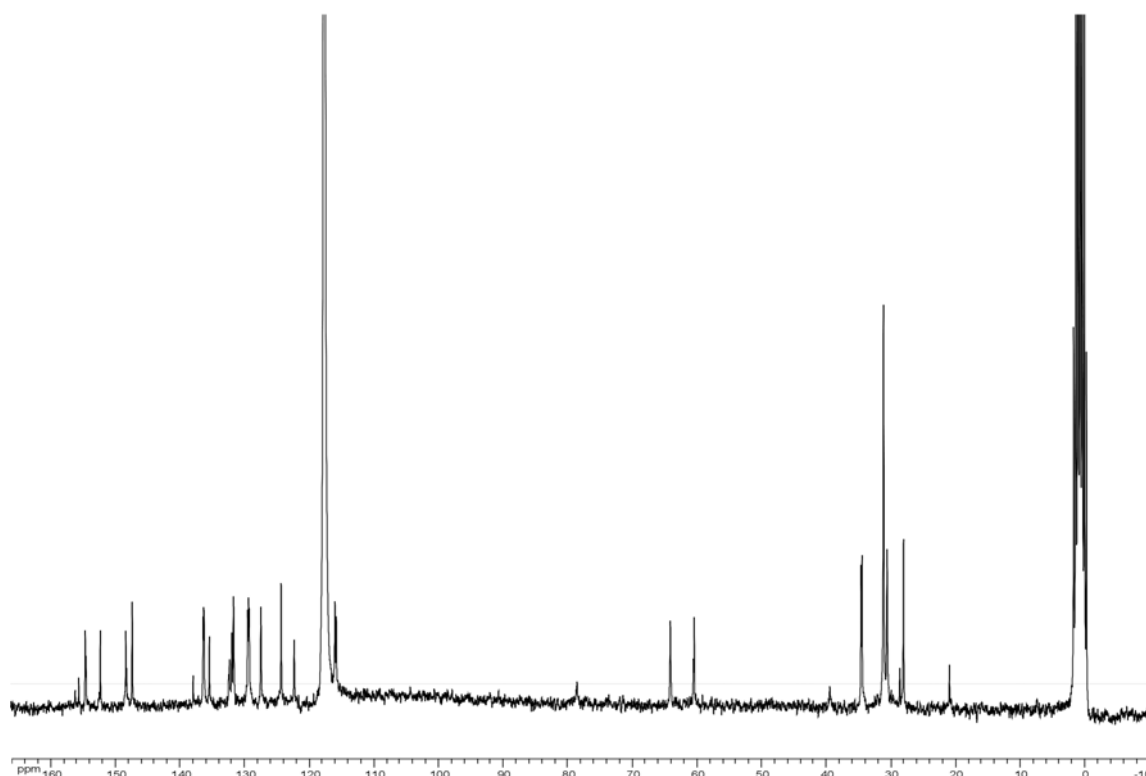
$Zn(ClO_4)_2 \cdot 6H_2O$  (34.5 mg, 92  $\mu$ mol) was poured into a flask containing calixarene **3** (130 mg, 91  $\mu$ mol) in dry THF (2 mL). The solution was stirred for 2h at room temperature. 5mL of  $Et_2O$  were added which resulted in the precipitation of a white solid. The mixture was centrifuged and the solid was washed with 5mL of  $Et_2O$ . The solid was dried under vacuum and  $[Zn(\mathbf{3})](ClO_4)_2$  (160 mg, 97% yield) was obtained as a white powder.



**<sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>CN, 300 K)** δ (ppm): 1.37 (*t*-Bu, s, 18H), 1.38 (*t*-Bu, s, 9H), 1.40 (*t*-Bu, s, 9H), 1.59 (H<sub>2</sub>, q, 2H), 2.39 (H<sub>3</sub>, t, J = 7.2 Hz, 2H), 2.95 (H<sub>1</sub>, m, 2H), 3.56 (ArCH<sub>2</sub>, m, 4H), 3.65 (ArCH<sub>2</sub> and NCH<sub>3</sub>, m, 11H), 3.68 (OCH<sub>3</sub>, s, 6H), 3.77 (OCH<sub>3</sub>, s, 3H), 4.09 (ArCH<sub>2</sub>, m, 6H), 5.06 (CH<sub>2</sub>Im, s, 4H), 5.10 (CH<sub>2</sub>Im, s, 2H), 5.19 (NHBoc, bs, 1H), 5.83 (H<sub>ArN3</sub>, s, 2H), 5.88 (H<sub>ArN3</sub>, s, 2H), 6.34 (H<sub>Artria</sub>, s, 2H), 6.91 (H<sub>Im</sub>, d, J = 1.6 Hz, 1H), 6.93 (H<sub>Im</sub>, d, J = 1.2 Hz, 2H), 7.41 (H<sub>Ar*t*-Bu</sub>, m, 1H), 7.43 (H<sub>tria</sub>, s, 1H), 7.44 (H<sub>Im</sub>, d, J = 1.6 Hz, 1H), 7.45 (H<sub>Im</sub>, d, J = 1.2 Hz, 2H); **<sup>13</sup>C NMR (62 MHz, CD<sub>3</sub>CN, 300 K)** δ (ppm): 19.64, 26.76, 27.32, 29.30, 29.53, 29.87, 33.18, 33.33, 59.16, 62.87, 77.29, 114.55, 114.76, 121.07, 123.09, 126.25, 128.02, 128.14, 128.26, 130.47, 130.74, 131.09, 131.20, 134.19, 135.02, 135.08, 135.17, 136.71, 146.14, 147.01, 147.14, 151.08, 153.30, 153.42, 154.42. **ES-MS** (CH<sub>2</sub>Cl<sub>2</sub>) *m/z*: 758.2 (calcd for [M+H<sub>2</sub>O-2ClO<sub>4</sub>]<sup>2+</sup> 758.3). **Elemental Analysis:** C<sub>82</sub>H<sub>98</sub>Cl<sub>2</sub>N<sub>16</sub>O<sub>16</sub>Zn-H<sub>2</sub>O-CH<sub>2</sub>Cl<sub>2</sub> Found: C 55.47 H 5.75 N 12.37 Calculated: C 55.29 H 5.70 N 12.43. **IR** (ATR, cm<sup>-1</sup>): 2957 (w), 2110 (m), 1707 (w), 1594 (w), 1504 (w), 1480 (m), 1364 (w), 1292 (w), 1244 (w), 1188 (w), 1164 (w), 1098 (s), 1001 (m), 974 (w), 875 (w), 763 (w).

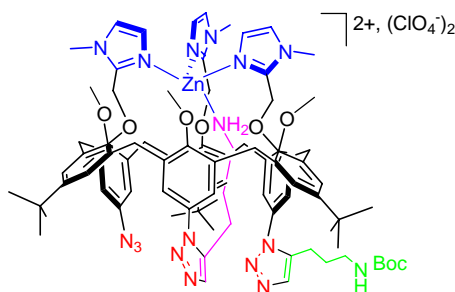


<sup>1</sup>H NMR spectrum of [Zn(**3**)](ClO<sub>4</sub>)<sub>2</sub> (500 MHz, CD<sub>3</sub>CN, 300 K).



$^{13}\text{C}$  NMR spectrum of  $[\text{Zn}(\mathbf{3})](\text{ClO}_4)_2$  (62 MHz,  $\text{CD}_3\text{CN}$ , 300 K).

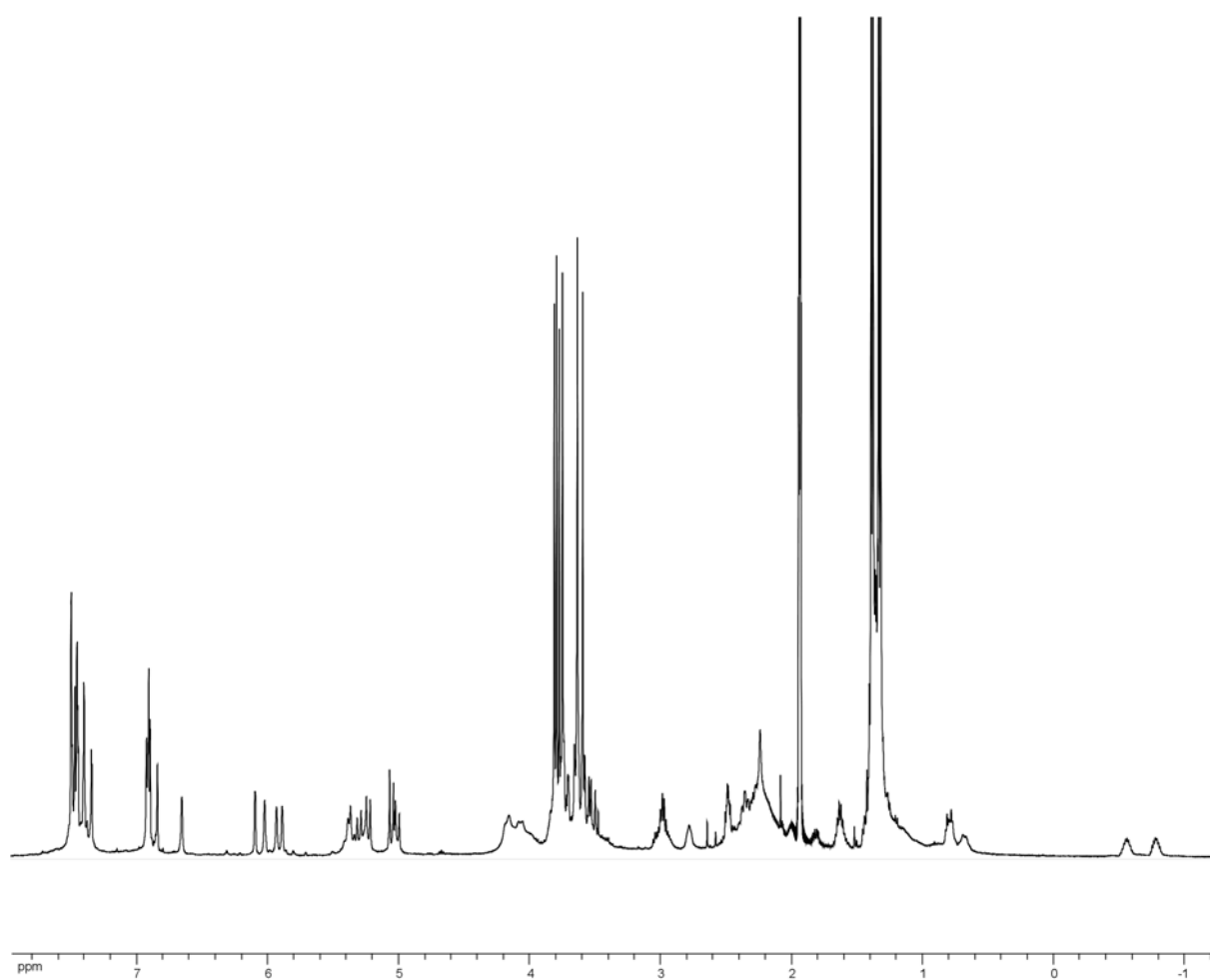
$[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$ :



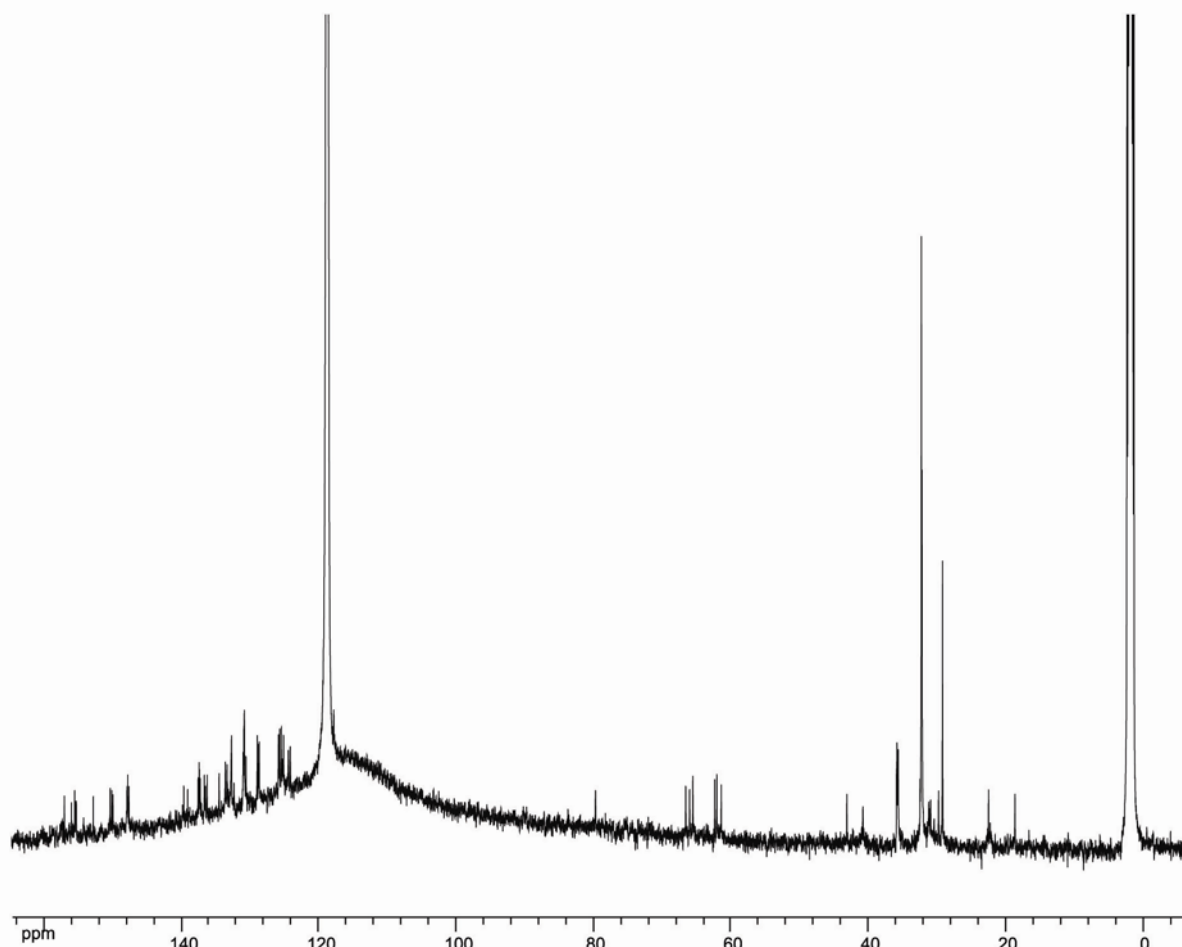
$[\text{Zn}(\mathbf{3})](\text{ClO}_4)_2$  (40.7 mg, 22  $\mu\text{mol}$ ) was dissolved in freshly distilled THF (2 mL). 320  $\mu\text{L}$  of a  $\text{CH}_2\text{Cl}_2$  solution of 5-aminopentyne (3.9 mg, 46  $\mu\text{mol}$ ) was added and the solution was stirred for 24h at 65°C. Then, 300  $\mu\text{L}$  of the same 5-aminopentyne solution (43  $\mu\text{mol}$ ) was added every 24h during 4 days. The solution was cooled down to room temperature then 8mL of  $\text{Et}_2\text{O}$  were added. The mixture was centrifugated and the solid was washed twice with 5mL of  $\text{Et}_2\text{O}$ . The solid was dried under vacuum and  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  (40 mg, 95% yield) was obtained as a white powder.

$^1\text{H}$  NMR (500 MHz,  $\text{CD}_3\text{CN}$ , 300 K)  $\delta$  (ppm): -0.76 ( $\text{H}_2$ , m, 1H), -0.54 ( $\text{H}_2$ , m, 1H), 0.71 ( $\text{H}_1$ , m, 1H), 0.83 ( $\text{H}_1$ , m, 1H), 1.34 (*t*-Bu, s, 9H), 1.36 (*t*-Bu, s, 9H), 1.38 ( $\text{H}_3$ , m, 2H), 1.40 (*t*-

Bu, s, 9H), 1.42 (*t*-Bu, s, 9H), 1.66 (H<sub>2</sub>, q, 2H), 2.33 (NH<sub>2</sub>, m, 2H), 2.44 (H<sub>3</sub>, t, J = 7.2 Hz, 2H), 3.01 (H<sub>1</sub>, m, 2H), 3.52 to 3.62 (ArCH<sub>2</sub>, m, 6H), 3.60 (OCH<sub>3</sub>, s, 3H), 3.62 (OCH<sub>3</sub>, s, 3H), 3.77 (OCH<sub>3</sub>, s, 3H), 3.79 (NCH<sub>3</sub>, s, 3H), 3.81 (NCH<sub>3</sub>, s, 3H), 3.82 (NCH<sub>3</sub>, s, 3H), 4.10 to 4.18 (ArCH<sub>2</sub>, m, 6H), 5.03 (CH<sub>2</sub>Im, d, J = 14.5 Hz, 1H), 5.07 (CH<sub>2</sub>Im, d, J = 14.5 Hz, 1H), 5.25 (CH<sub>2</sub>Im, d, J = 14.5 Hz, 1H), 5.27 (NHBoc, bs, 1H), 5.32 (CH<sub>2</sub>Im, d, J = 14.5 Hz, 1H), 5.40 (CH<sub>2</sub>Im, m, 2H), 5.91 (s, 1H), 5.96 (s, 1H), 6.05 (s, 1H), 6.12 (s, 1H), 6.68 (s, 1H), 6.92 (H<sub>Im</sub>, d, J = 1.6 Hz, 1H), 6.93 (H<sub>Im</sub>, d, J = 1.2 Hz, 2H), 6.94 (s, 1H), 7.36 (d, J = 5.3 Hz, 1H), 7.42 (H<sub>Arr-Bu</sub>, d, J = 5.3 Hz, 1H), 7.46 to 7.52 (H<sub>tria</sub>, H<sub>Im</sub>, H<sub>Arr-Bu</sub>, m, 8H); **<sup>13</sup>C NMR (125 MHz, CD<sub>3</sub>CN, 300 K)** δ (ppm): 18.54, 22.40, 29.10, 29.70, 30.83, 32.08, 32.17, 35.53, 35.57, 35.63, 35.68, 35.73, 35.75, 35.80, 40.70, 43.03, 61.32, 61.96, 62.27, 65.46, 65.93, 66.49, 124.08, 124.36, 125.06, 125.20, 125.38, 125.64, 125.80, 128.60, 128.68, 128.89, 130.52, 130.77, 130.81, 130.85, 130.94, 132.28, 132.64, 132.75, 133.24, 133.30, 133.54, 134.44, 136.18, 136.43, 136.59, 137.19, 137.30, 137.35, 137.49, 139.02, 139.58, 147.57, 147.76, 147.85, 150.06, 150.31, 152.76, 155.24, 155.33, 155.46, 155.93, 156.98. **ES-MS** (CH<sub>2</sub>Cl<sub>2</sub>) *m/z*: 1680.7 (calcd for [M-ClO<sub>4</sub>]<sup>+</sup> 1680.7), 790.8 (calcd for [M-2ClO<sub>4</sub>]<sup>2+</sup> 790.9). **Elemental Analysis:** C<sub>87</sub>H<sub>107</sub>Cl<sub>2</sub>N<sub>17</sub>O<sub>16</sub>Zn·1.5CH<sub>2</sub>Cl<sub>2</sub> Found: C 55.66 H 6.32 N 12.11 Calculated: C 55.63 H 5.80 N 12.46. **IR** (ATR, cm<sup>-1</sup>): 2959 (w), 2109 (w), 1707 (w), 1594 (w), 1504 (w), 1481 (m), 1365 (w), 1291 (w), 1238 (w), 1185 (w), 1162 (w), 1100 (s), 998 (w), 980 (w), 872 (w), 761 (w).



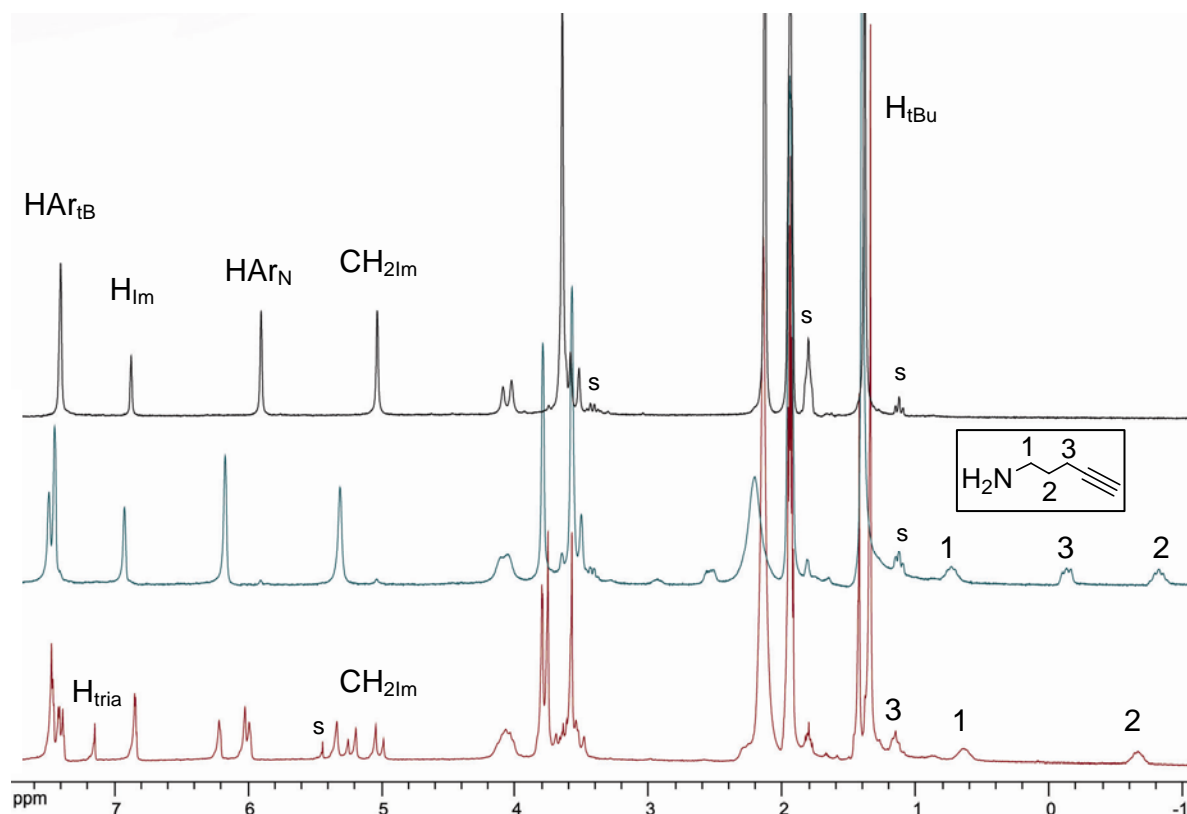
$^1\text{H}$  NMR spectrum of  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  (500 MHz,  $\text{CD}_3\text{CN}$ , 300 K).



$^{13}\text{C}$  NMR spectrum of  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  (125 MHz,  $\text{CD}_3\text{CN}$ , 300 K).

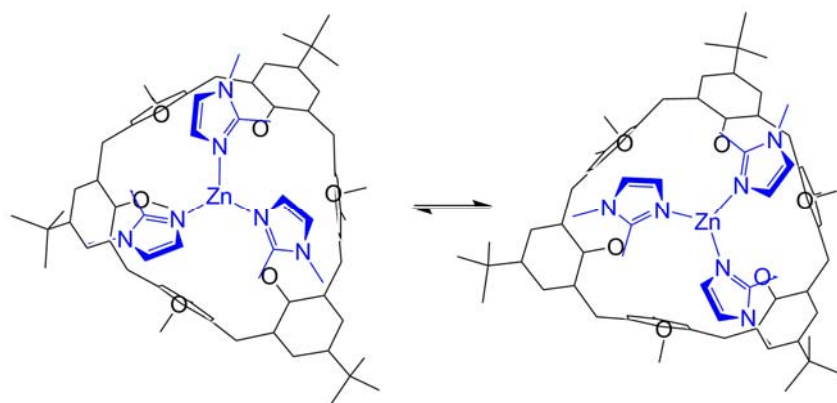
**$^1\text{H}$  NMR of  $[\text{Zn}(\mathbf{1})(\text{CD}_3\text{CN})](\text{ClO}_4)_2$ ,  $[\text{Zn}(\mathbf{1})(\text{NH}_2(\text{CH}_2)_3\text{C}\equiv\text{CH})](\text{ClO}_4)_2$  and  $[\text{Zn}(\mathbf{2})](\text{ClO}_4)_2$ :**

The overall profile also indicates that the symmetry of the complex has switched from pseudo  $C_{3v}$  to  $C_s$ . Indeed, the resonance of the *t*Bu groups has changed from one singlet (integrating for 27H) in  $[\text{Zn}(\mathbf{1})(\text{CD}_3\text{CN})](\text{ClO}_4)_2$  to two singlets (18H and 9H) for  $[\text{Zn}(\mathbf{2})](\text{ClO}_4)_2$ . The singlet accounting for the  $\text{CH}_{2\text{lm}}$  in  $[\text{Zn}(\mathbf{1})(\text{CD}_3\text{CN})](\text{ClO}_4)_2$  (6H) has been replaced by one singlet (2H) and an AB system for the diastereotopic methylene protons (2x2H). In the aromatic region, a single new resonance for the proton located on the triazole ring ( $\text{H}_{\text{tria}}$ ) can be seen at 7.15 ppm.



$^1\text{H}$  NMR spectra ( $\text{CD}_3\text{CN}$ , 250MHz, 300K). From top to bottom,  $[\text{Zn}(\mathbf{1})(\text{CD}_3\text{CN})](\text{ClO}_4)_2$ ,  $[\text{Zn}(\mathbf{1})(\text{NH}_2(\text{CH}_2)_3\text{C}\equiv\text{CH})](\text{ClO}_4)_2$  and  $[\text{Zn}(\mathbf{2})](\text{ClO}_4)_2$  (s = residual solvents, Im and tria stand for imidazole and triazole, respectively).

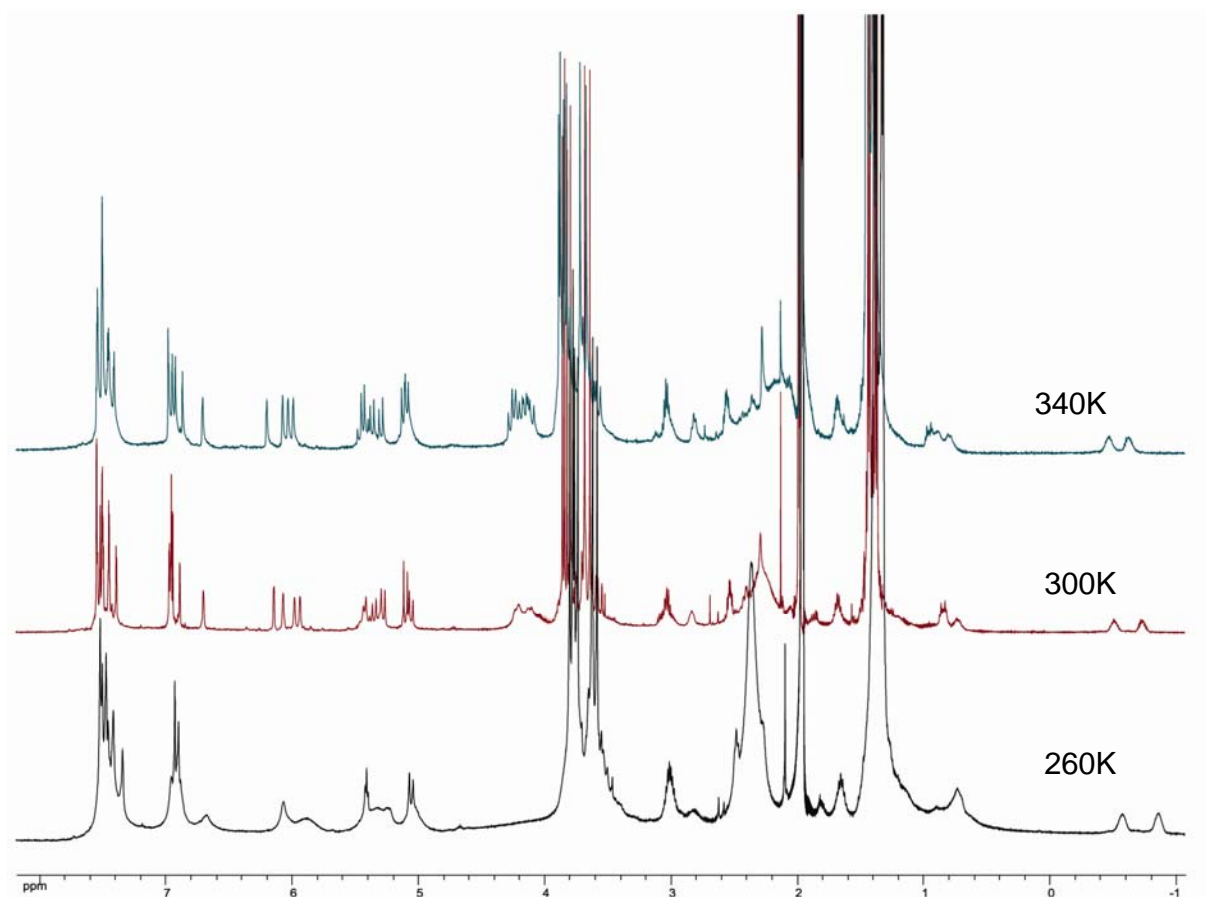
**Schematic representation of the enantiomerization process of the helical binding at the metal core:**



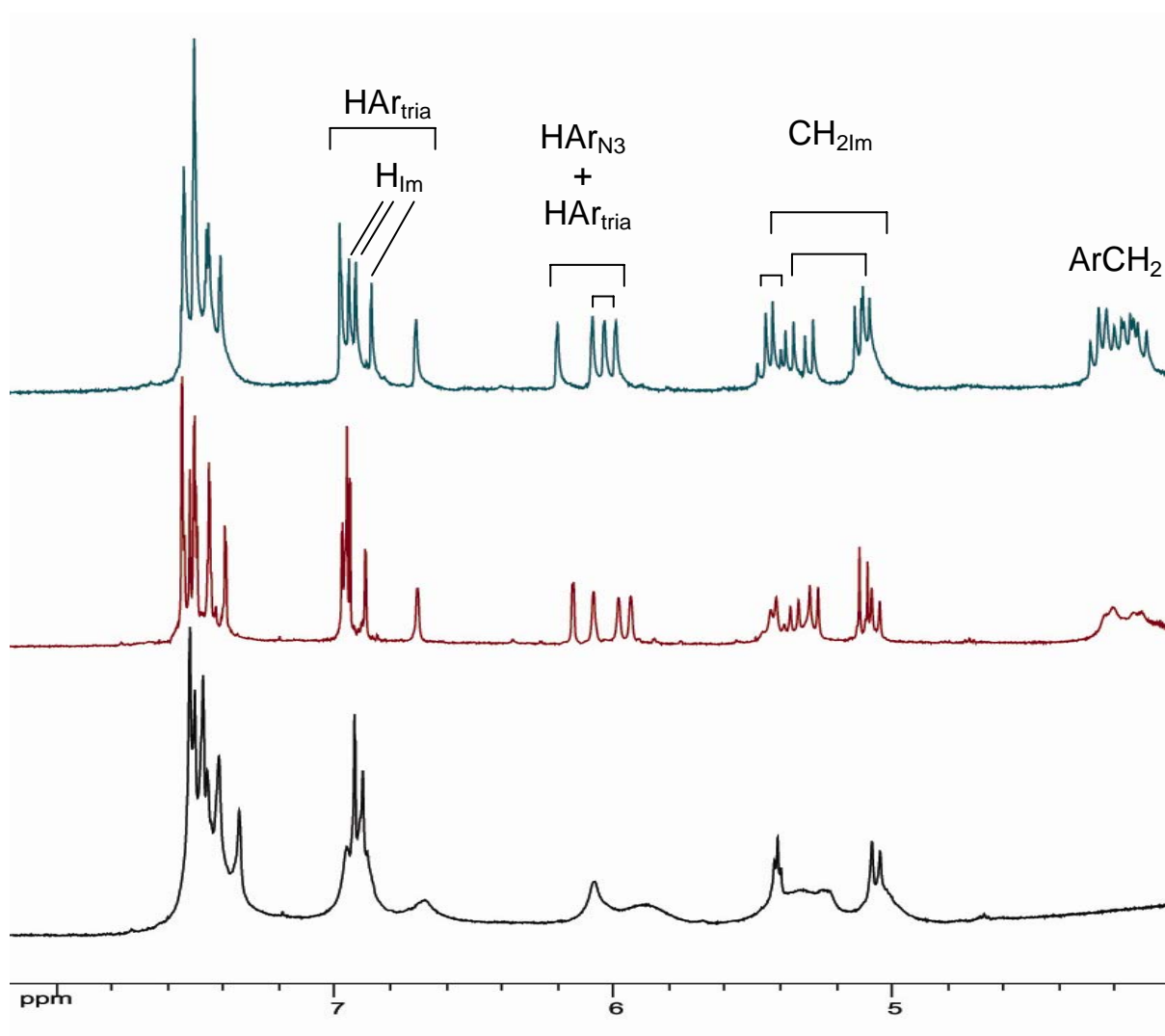
**Variable temperature  $^1\text{H}$  NMR experiments (500MHz,  $\text{CD}_3\text{CN}$ ) on  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$ :**

The  $^1\text{H}$  NMR spectrum of complex  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  attested to the complete loss of symmetry as awaited for a hetero tris-functionalized calix[6]arene. It displayed particularly sharp and well defined resonances at high T. At low T, specific resonances became very broad, whereas others remained almost unchanged. This is indicative of the left/right

inversion of the helix at the level of the tris-imidazole zinc core that was slowed down: the aromatic protons of the anisole units ( $\text{HAr}_{\text{N3}}$ ,  $\text{HAr}_{\text{tria}}$ ) that are in *in* position relative to the calixarene core are the most affected together with the methylenic H, whereas the imidazole ( $\text{H}_{\text{Im}}$ ), methoxy and *t*Bu protons are barely changed, as previously described for the  $\text{C}_3$  parent complexes.<sup>3</sup> Most interestingly, the methylene groups of the encapsulated amine appeared diastereotope whatever the temperature

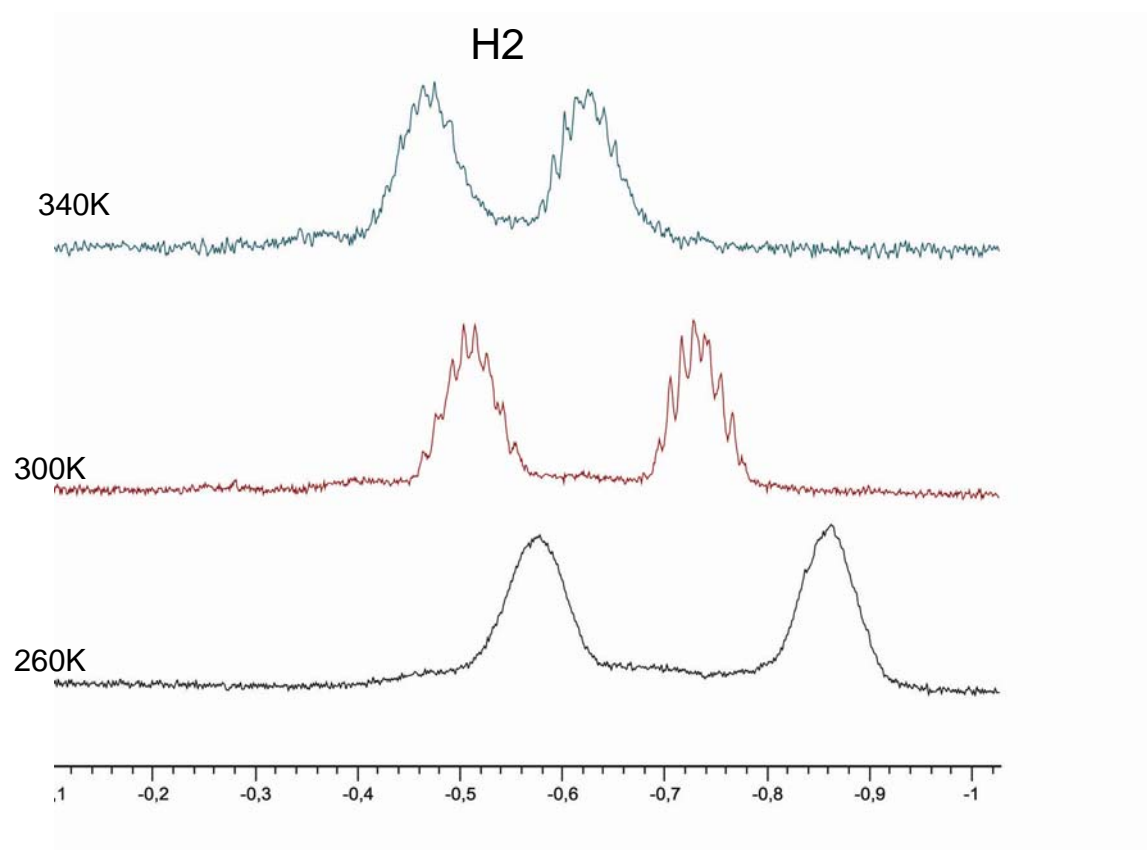


$^1\text{H}$  NMR spectrum of  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  (500 MHz,  $\text{CD}_3\text{CN}$ , 340 K, 300K and 260K).

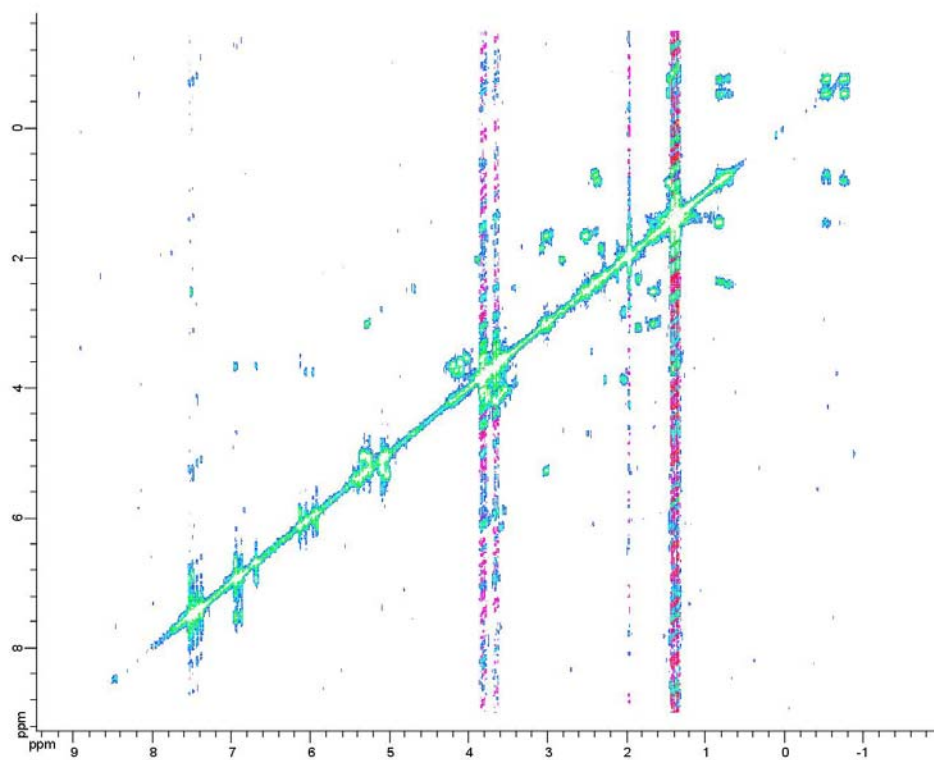


$^1\text{H}$  NMR spectrum of  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  (500 MHz,  $\text{CD}_3\text{CN}$ , 340 K, 300K and 260K).

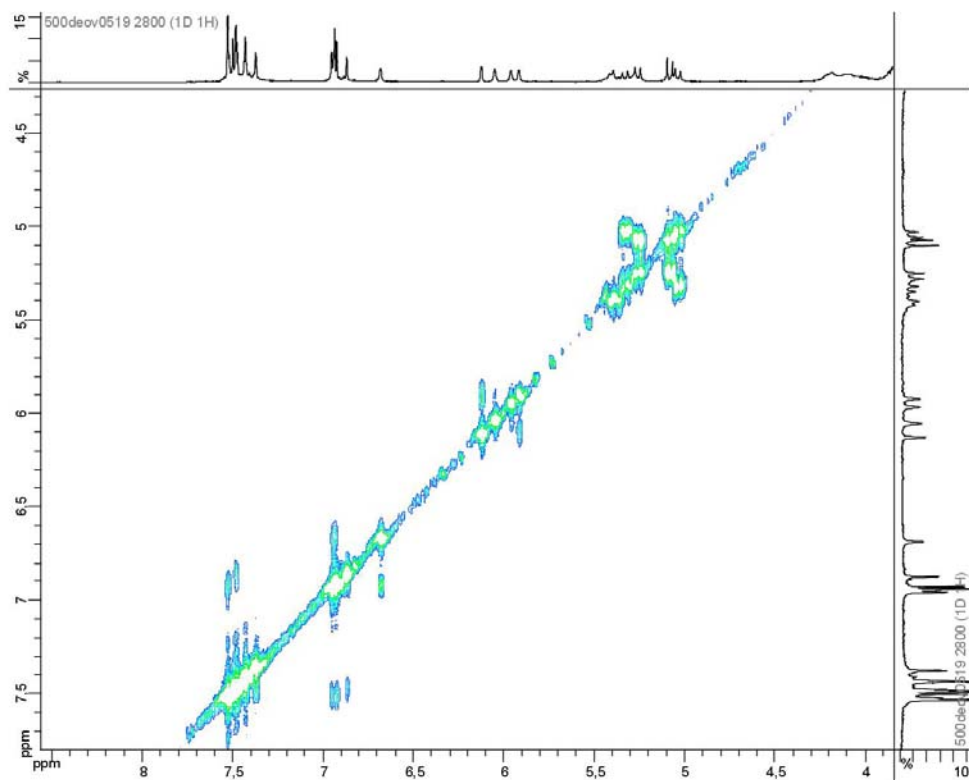




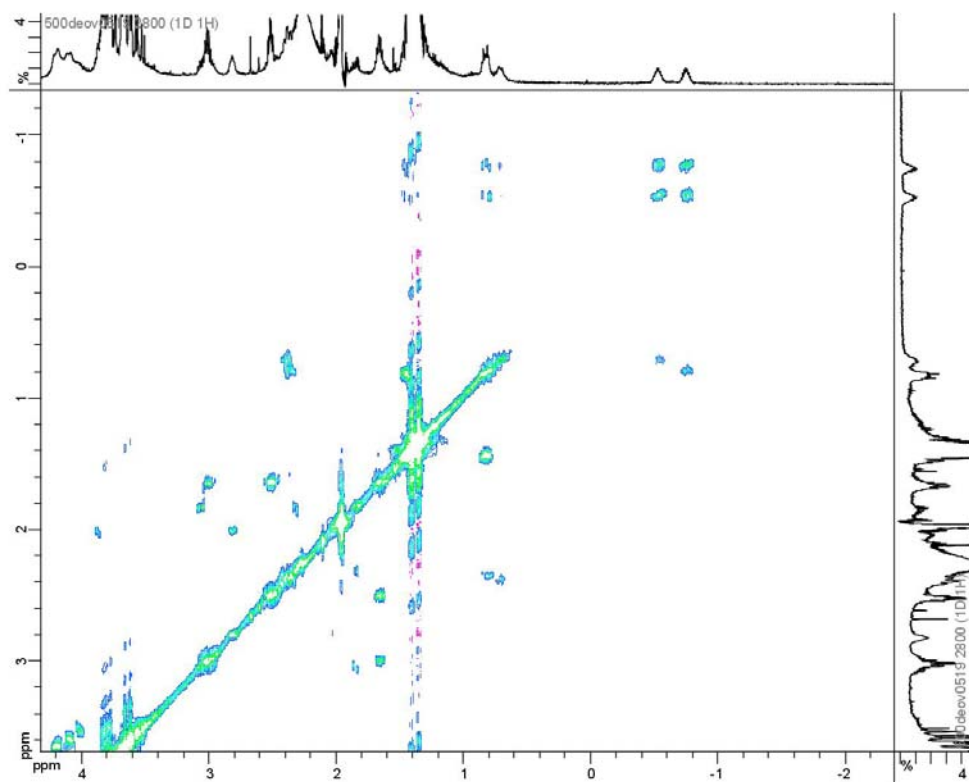
$^1\text{H}$  NMR spectrum of  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  (500 MHz,  $\text{CD}_3\text{CN}$ , 340 K, 300K and 260K).



NMR COSY experiment of  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  (500 MHz,  $\text{CD}_3\text{CN}$ , 300K).

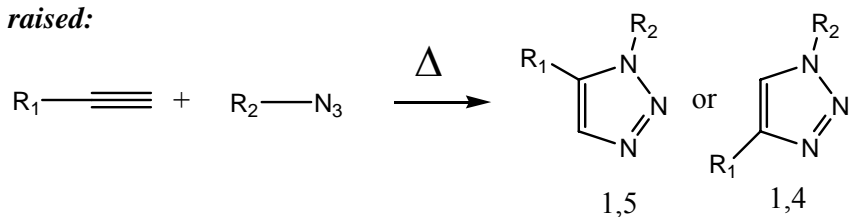


NMR COSY experiment of  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  (500 MHz,  $\text{CD}_3\text{CN}$ , 300K).

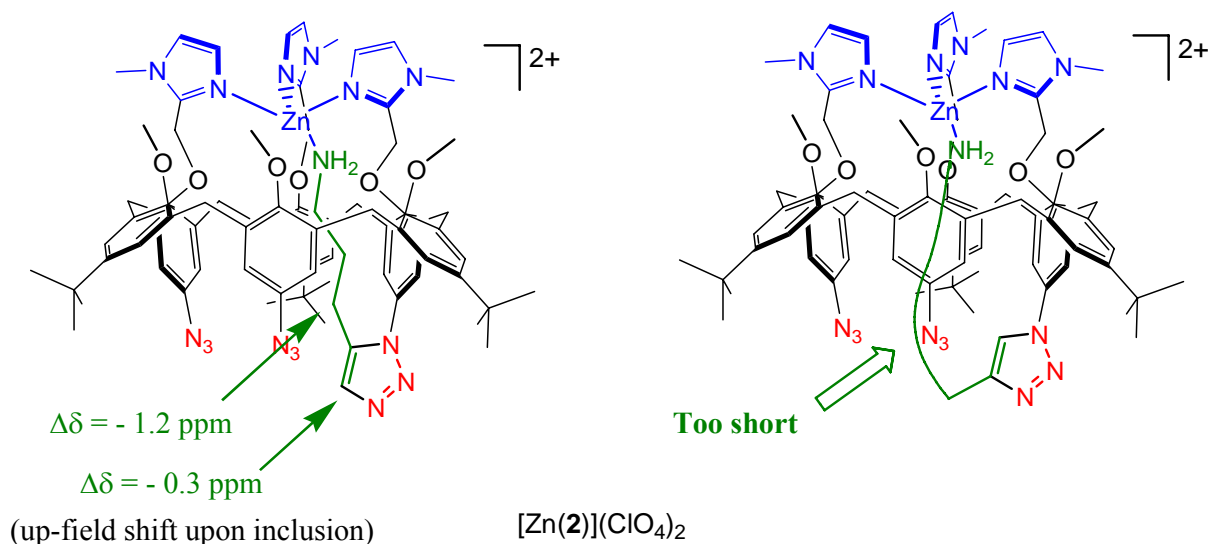


NMR COSY experiment of  $[\text{Zn}(\mathbf{4})](\text{ClO}_4)_2$  (500 MHz,  $\text{CD}_3\text{CN}$ , 300K).

**Question raised:**



**Answer:**



A comparison of the  $\delta$ -shift of the triazole proton when it is in *in* position (in complex [Zn(2)]) vs an *out* position (in complex [Zn(3)(MeCN)]) shows a  $\Delta\delta$  shift of ca. -0.3 ppm, whereas the corresponding  $\alpha$ -methylene protons undergo a  $\Delta\delta$  shift of -1.2 ppm. This shows that the latter are deeper included in the  $\pi$ -basic calixarene cavity, which is consistent with the formation of the 1,5-regioisomer, not with the 1,4-one.

Finally, when considering the 1,4-isomer, simple modeling unambiguously shows that the propylamine chain is far too short to reach the metal center at the small rim.

## References

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- (3) (a) Blanchard, S.; Rager M.-N.; Duprat A. F.; Reinaud, O. *New J. Chem.*, **1998**, 1143-1146. (b) Sènèque, O.; Rondelez, Y.; Le Clainche, L.; Inisan, C.; Rager, M.-N.; Giorgi, M.; Reinaud, O. *Eur. J. Inorg. Chem.*, **2001**, 2597-2604.