

Supplementary Information for:

## Dynamic Combinatorial Libraries for the Recognition of Heavy Metal Ions

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### General remarks

Solvents were purchased from Romil (LC-MS grade CHCl<sub>3</sub>), Fisher (HPLC grade MeOH) and Aldrich (TFA). Metal salts were purchased from Sigma-Aldrich (RbCl), Lancaster (LiCl), Breckland (NaCl, KCl), Alpha Aesar (CsCl). 4-Methoxypyridine-2,6-dicarbaldehyde<sup>1</sup> **1** and 2,6-bis(2-carboxyphenoxy)methylpyridine<sup>2</sup> **2a** were synthesized according to literature procedures.

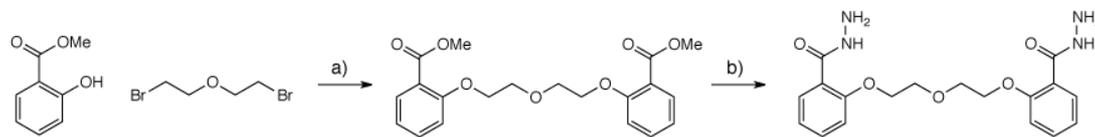
<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Bruker DPX-400, DRX 500 or AV 600 or Advance 500 TCI Cryo Spectrometers. All signals were internally referenced to the solvent residue (3.31 ppm for MeOD). All high-resolution (HR) electrospray ionisation (ESI) mass spectra were recorded on a Waters LCT Premier XE instrument.

<sup>1</sup>U. Lüning, R. Baumstark, K. Peters and H. G. von Schnering, *Liebigs Ann. Chem.*, 1990, 129.

<sup>2</sup>J. M. Klein, V. Saggiomo, L. Reck, G. D. Pantos, U. Lüning and J. K. M. Sanders, *Chem. Commun.*, 2011, **47**, 3371-3373.

UV-Vis spectra were recorded in a 1 cm quartz cuvette using a Lambda 14 spectrometer from Perkin Elmer at 22 °C, unless otherwise stated. The DCLs were analysed by LCMS using an Agilent 1100 series HPLC coupled to an Agilent XCT Ion-Trap.

## Synthesis



**Fig. 1** Synthesis of **2b**. a)  $K_2CO_3$ , acetone, reflux, 7 d, 55%; b)  $N_2H_4$ , reflux, 12 h, 99%.

1,7-Bis[2-(methoxycarbonyl)phenyl]-1,4,7-trioxaheptane was prepared as described in the literature.<sup>3</sup>

### 1,7-Bis[2-(hydrazinocarbonyl)phenyl]-1,4,7-trioxaheptane.

1,7-Bis[2-(methoxycarbonyl)phenyl]-1,4,7-trioxaheptane (374 mg, 1.00 mmol) was suspended in a solution composed of 5.00 mL of EtOH and 254  $\mu$ L (4.00 mmol) of hydrazine monohydrate. The reaction was refluxed for 12 h. The final product was obtained by recrystallization from EtOH in quantitative yield.

$^1H$ -NMR (600 MHz,  $CDCl_3$ ):  $\delta$  = 9.22 (s, 2H, NH), 8.15 (dd,  $^3J$  = 7.8 Hz,  $^4J$  = 1.8 Hz, 2H, 6- $C_{Ar}$ -H), 7.42 (ddd,  $^3J$  = 8.2 Hz,  $^3J$  = 7.3 Hz,  $^4J$  = 1.8 Hz, 2H, 4- $C_{Ar}$ -H), 7.09 (m, 2H, 5- $C_{Ar}$ -H), 6.98 (dd,  $^3J$  = 8.3 Hz,  $^4J$  = 0.8 Hz, 2H, 3- $C_{Ar}$ -H), 4.40 (m, 4H, Ar-O- $CH_2$ ), 4.02 (s, 4H,  $NH_2$ ), 3.98 (m, 4H,  $CH_2$ -O- $CH_2$ ) ppm.

$^{13}C$ -NMR (150 MHz,  $CDCl_3$ ):  $\delta$  = 166.3 (COON $_2$ H $_3$ ), 156.5 (2- $C_{Ar}$ ), 132.7 (4- $C_{Ar}$ ), 132.0 (6- $C_{Ar}$ ), 121.9 (5- $C_{Ar}$ ), 120.9 (1- $C_{Ar}$ ), 113.3 (3- $C_{Ar}$ ), 69.3 68.3 (2  $CH_2$ ) ppm.

ESI-MS (pos. mode):  $C_{18}H_{22}N_4O_5Na^+$  calcd. 397.1482, found 397.1416.

$C_{18}H_{22}N_4O_5$ : calcd. C 57.75, H 5.92, N 14.96; found. C 57.15, H 6.04, N 14.02

## Library Preparation

Templated DCLs were prepared by mixing stock solutions of building blocks (20 mM in  $CHCl_3$ ) and metal salts (50 mM in MeOH) and adding the appropriate amount of  $CHCl_3$  and MeOH. Exchange was initiated by addition of 5% TFA to the DCLs. DCLs were typically prepared on a 1 mL scale (1 mM, analytical for metal screening) or on a 10 mL scale (10 mM, preparative to isolate the 2+2 macrocycles).

<sup>3</sup> H. Sharghi and H. Eshghi, *Tetrahedron*, **1995**, *51*, 913-922

## **LC-MS Analysis**

The DCLs were analysed by LCMS using an Agilent 1100 series HPLC coupled to an Agilent XCT Ion-Trap. Water was obtained from a MilliQ purification system. MeOH (Fisher Scientific, LC-MS grade) and formic acid (Fluka, p.a. puriss. for mass spectrometry) were purchased. Samples were analysed using either method A or B:

### Method A:

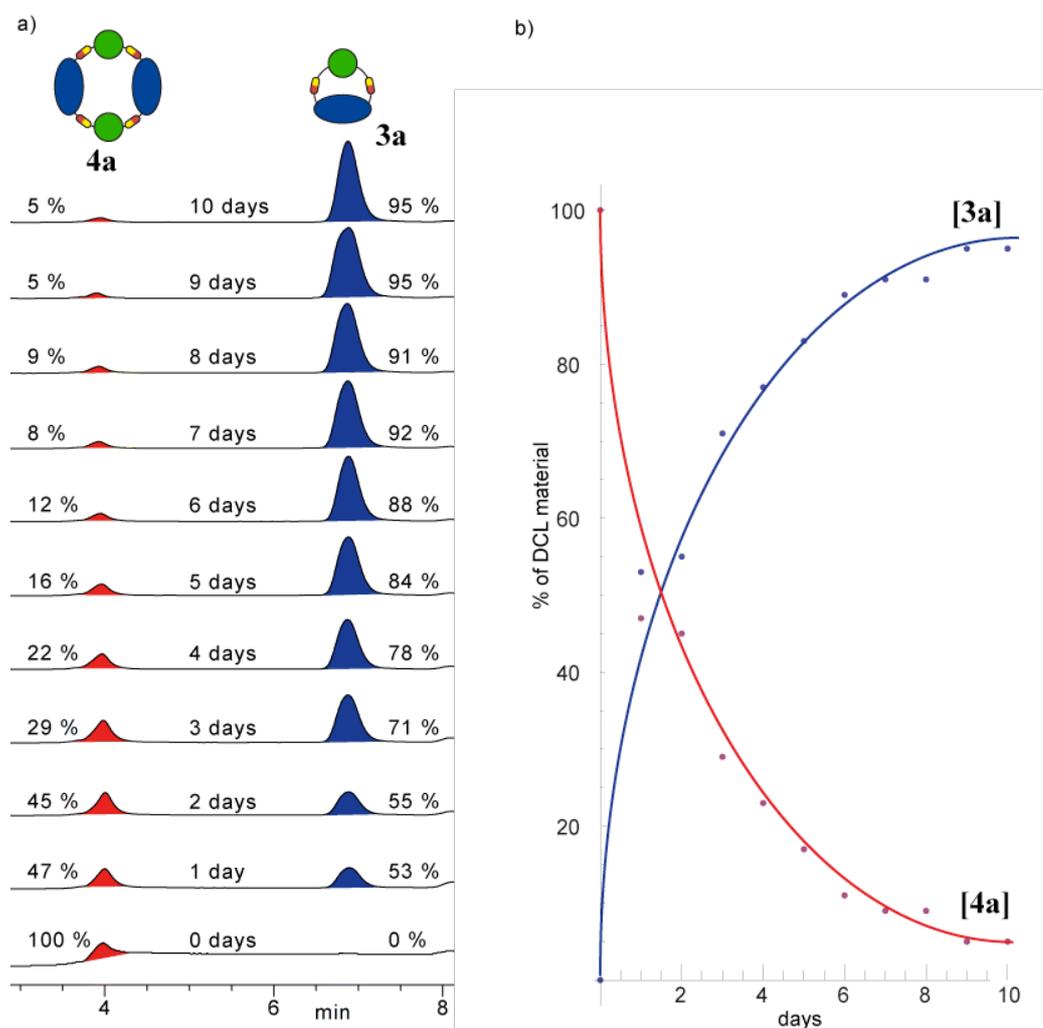
Column: Phenomenex Prodigy 5 ODS-2 column (150 x 4.60 mm, particle size: 5 µm)  
Injection volume: 5 µl  
Flow rate: 1.0 ml/min  
Gradient: MeOH in water (60% to 70% in 10 min, then to 100% in 1 min, both containing 0.1% formic acid) at 323 K. UV absorption was detected at 290 nm and referenced against 550 nm.

### Method B:

Column: Water Symmetry C<sub>8</sub> (150 x 3.90 mm, particle size: 5 µm)  
Injection volume: 1 µl  
Flow rate: 1.0 ml/min  
Gradient: MeCN in water (35% 0-15 min, then to 100% in 5 min, both containing 0.1% formic acid) at 323 K. UV absorption was detected at 290 nm and referenced against 550 nm.

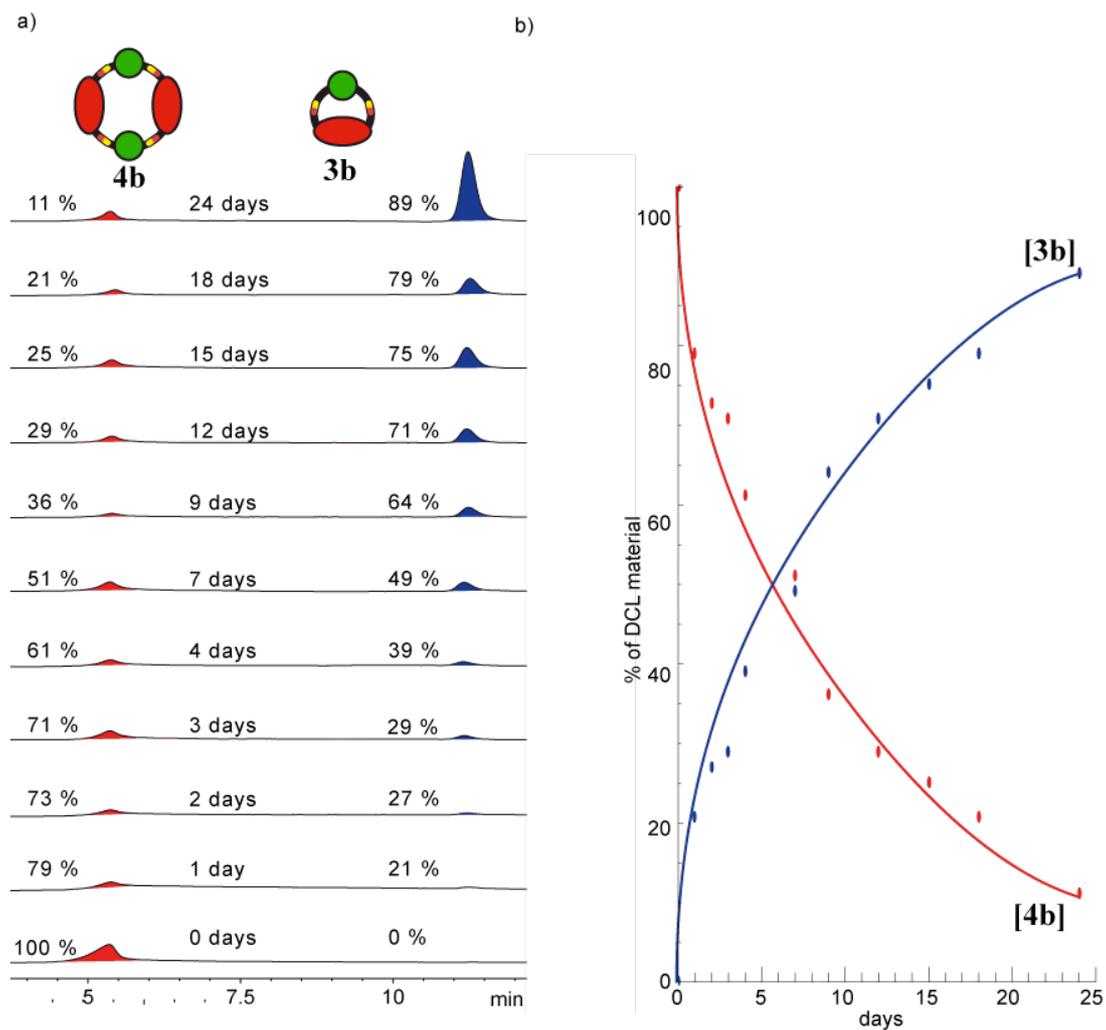
Positive ion mass spectra were acquired in standard enhanced mode using electrospray ionisation (drying temperature: 350 °C; nebuliser pressure: 18 psi; drying gas flow: 8 l/min; ICC target: 200 000; range: 400-1700 m/z)

## Reversibility



**Fig. 2** Conversion of **4a** into **3a** over time.

The isolated sample of **4a** was dissolved in  $\text{CHCl}_3/\text{MeOH}/\text{TFA}$  (50/50/5, 1 mM) and stirred. A sample of the mixture was taken daily, basified (to halt the exchange) and stored at  $-20\text{ }^\circ\text{C}$ . After 19 days, the samples were analysed by LCMS and the relative peak of the two products (**3a** and **4a**) were plotted over time. Original DCL distribution was reached after approx. 10 days.

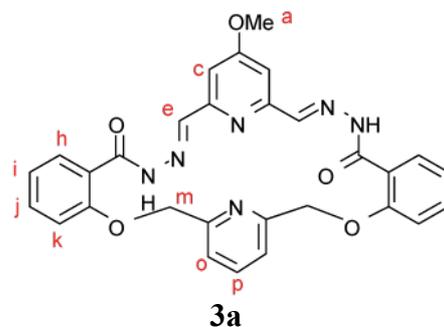


**Fig. 3** Conversion of **4b** into **3b** over time.

The isolated sample of **4b** was dissolved in  $\text{CHCl}_3/\text{MeOH}/\text{TFA}$  (70/30/5, 1 mM) and stirred. A sample of the mixture was taken daily, basified (to halt the exchange) and stored at  $-20\text{ }^\circ\text{C}$ . After 19 days, the samples were analysed by LCMS and the relative peak of the two products (**3b** and **4b**) were plotted over time. Original DCL distribution was reached after approx. 24 days.

## Isolation of Macrocycle and Characterisation

The free macrocycles were isolated as described below. Metal complexes were synthesised by adding 1.0 eq. of a metal chloride (as a 50 mM solution in MeOD) to a 1.0 mM solution of the free macrocycle.

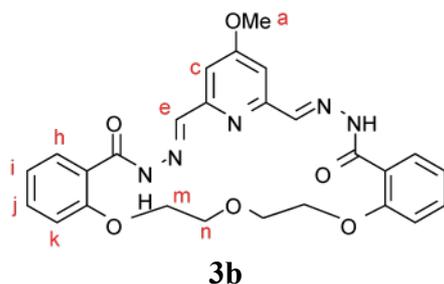


Dialdehyde **1** (33.0 mg, 200  $\mu$ mol) and dihydrazone **2a** (81.4 mg, 200  $\mu$ mol) were dissolved in 200 ml of  $\text{CHCl}_3/\text{MeOH}/\text{TFA}$  (90:10:5). After 17 days, exchange was stopped by adding  $\text{NEt}_3$  (11 ml, 1.1 eq. with respect to TFA). The solution was concentrated in vacuo to ca. 10 ml and the product was precipitated by addition of  $\text{Na}_2\text{CO}_3$  (aq., sat., 50 ml) and  $\text{H}_2\text{O}$  (150 ml). The precipitate was collected by filtration and washed with  $\text{H}_2\text{O}$  (100 ml) to give a beige powder (97.0 mg, 90%).

$^1\text{H-NMR}$  (500 MHz, 300 K,  $\text{CDCl}_3/\text{MeOD}$ , 1:3, v/v).  $\delta$  = 8.99 (s, 1H, *e*), 8.24 (dd, 1H,  $^3J = 7.8$  Hz,  $^4J = 1.7$  Hz, *h*), 8.19 (dd, 1H,  $^3J = 7.2$  Hz,  $^4J = 2.3$  Hz, *h*), 8.14 (d, 1H,  $^3J = 2.3$  Hz, *c*), 7.74 (t, 1H,  $^3J = 7.7$  Hz, *j*), 7.67 (dt, 1H,  $^3J = 7.8$  Hz,  $^4J = 1.8$  Hz, *p*), 7.59 (s, 1H, *e*), 7.46 (d, 1H,  $^3J = 7.8$  Hz, *o*), 7.41 (d, 1H,  $^3J = 8.2$  Hz, *k*), 7.20 - 7.28 (m, 4H, 2*i*, *j*, *c*), 7.05 (d, 1H,  $^3J = 7.6$  Hz, *o*), 6.61 (dd, 1H,  $^3J = 7.7$  Hz,  $^4J = 1.5$  Hz, *k*), 5.39 (s, 2H, *m*), 5.25 (s, 2H, *m*), 4.01 (s, 3H, *a*), ppm.

$^{13}\text{C-NMR}$  (125 MHz, 300 K,  $\text{CDCl}_3/\text{MeOD}$ , 1:3, v/v).  $\delta$  = 169.0, 165.1, 165.1, 158.6, 158.3, 157.5, 157.1, 156.7, 153.7, 149.2, 141.3, 139.1, 135.8, 134.6, 133.9, 133.7, 126.5, 125.0, 125.0, 123.4, 123.3, 116.2, 114.6, 107.3, 78.1, 72.5, 57.0 ppm.

HRMS (ESI+) calcd. for  $\text{C}_{29}\text{H}_{24}\text{N}_6\text{O}_5$ :  $[\text{MH}]^+$  ( $m/z$ ) = 537.1881, found: 537.1913.



Dialdehyde **1** (8.30 mg, 50.0  $\mu$ mol) and dihydrazone **2b** (18.7 mg, 50.0  $\mu$ mol) were dissolved in 50 ml of  $\text{CHCl}_3/\text{MeOH}/\text{TFA}$  (90:10:5). After three days the solution was washed with  $\text{Na}_2\text{CO}_3$  (aq., sat., 3  $\times$  50.0 ml) and the combined organic layers were evaporated to dryness. After recrystallization from  $\text{Et}_2\text{O}/\text{hexanes}$ , a beige powder was obtained (12.0 mg, 48%).

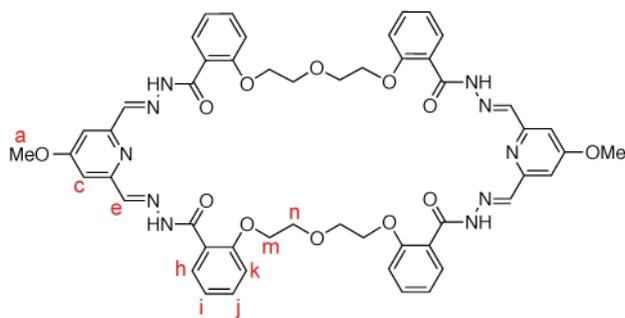
$^1\text{H-NMR}$  (400 MHz, 298 K,  $\text{CDCl}_3/\text{MeOD}$ , 3:1, v/v).  $\delta$  = 8.51 (s, 1H, *e*), 8.16 (dd, 1H,  $^3J = 7.8$  Hz,  $^4J = 1.7$  Hz, *h*), 8.02 (m, 2H, *h*, *c*), 7.56 (dt, 1H,  $^3J = 7.8$  Hz,  $^4J = 1.8$  Hz, *j*), 7.51 (dt, 1H,  $^3J = 7.8$  Hz,  $^4J = 1.8$  Hz, *j*), 7.49 (s, 1H, *e*), 7.28 (d, 1H,  $^3J = 8.2$  Hz, *k*), 7.24 (t, 1H,  $^3J = 7.6$  Hz, *i*), 7.18 (t, 1H,  $^3J = 7.6$  Hz, *i*), 7.14 (d, 1H,  $^3J = 8.3$

Hz, *k*), 7.05 (d, 1H,  $^3J = 2.3$  Hz, *c*), 4.42 (m, 2H, *m*), 4.28 (m, 2H, *m*), 4.02 (m, 2H, *n*), 3.98 (s, 3H, *a*), 3.82 (m, 2H, *n*), ppm.

$^{13}\text{C}$ -NMR (100 MHz, 300 K,  $\text{CDCl}_3/\text{MeOD}$ , 3:1, v/v).  $\delta = 167.9, 164.6, 163.8, 157.4, 157.2, 155.2, 152.7, 148.6, 148.5, 140.1, 134.7, 134.1, 132.7, 125.7, 125.0, 123.1, 122.9, 121.2, 115.0, 114.8, 106.2, 77.7$  (under solvent peak, located by HMQC), 74.5, 69.7, 69.5, 56.3 ppm.

HRMS (ESI+) calcd. for  $\text{C}_{26}\text{H}_{25}\text{N}_5\text{O}_6$ :  $[\text{MH}]^+$  ( $m/z$ ) = 504.1878, found: 504.2041.

**4a** and its complex with  $\text{Ba}^{2+}$  were described earlier.<sup>4</sup>



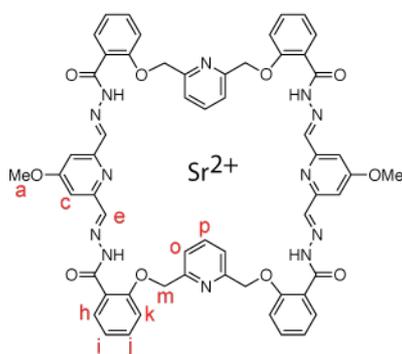
**4b**

Dialdehyde **1** (33.0 mg, 200  $\mu\text{mol}$ ) and dihydrazide **2b** (75.0 mg, 200  $\mu\text{mol}$ ) were dissolved in 10 ml of  $\text{CHCl}_3/\text{MeOH}/\text{TFA}$  (90:10:5). After 14 days, a white precipitate was collected by filtration, suspended in  $\text{Na}_2\text{CO}_3$  (sat. aq., 10 ml) and sonicated (5 min). The white solid was collected by filtration, washed with water (5 ml) and dried in vacuo (95.0 mg, 95%).

$^1\text{H}$ -NMR (400 MHz, 298 K,  $\text{CDCl}_3/\text{MeOD}$ , 7:3, v/v).  $\delta = 8.05$  (dd, 4H,  $^3J = 8.0$  Hz,  $^4J = 1.7$  Hz, *h*), 8.02 (s, 4H, *e*), 7.53 (s, 4H, *c*), 7.37 (t, 4H,  $^3J = 7.8$  Hz, *j*), 7.08 (m, 8H, *k, i*), 4.43 (t, 8H,  $^3J = 4.2$  Hz, *m*), 4.13 (t, 8H,  $^3J = 4.2$  Hz, *n*), 3.92 (s, 6H, *a*) ppm.

$^{13}\text{C}$ -NMR (100 MHz, 300 K,  $\text{CDCl}_3/\text{MeOD}$ , 7:3, v/v).  $\delta = 167.5, 163.0, 157.2, 154.3, 147.5, 134.3, 132.5, 122.6, 120.4, 114.1, 108.6, 70.0, 69.4, 56.1$  ppm.

HRMS (ESI+) calcd. for  $\text{C}_{52}\text{H}_{50}\text{N}_{10}\text{O}_{12}$ :  $[\text{MH}]^+$  ( $m/z$ ) = 1007.3682, found: 1007.3770;  $[\text{MH}_2]^{2+}$  ( $m/z$ ): 504.1884. found: 504.1920.

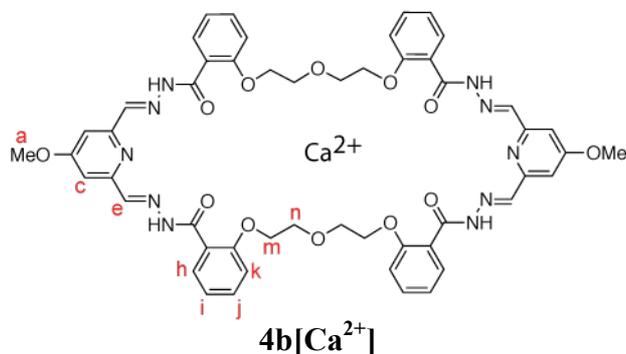


**4a[Sr<sup>2+</sup>]**

$^1\text{H}$ -NMR (500 MHz, 300 K,  $\text{CDCl}_3/\text{MeOD}$ , 1:1, v/v),  $\delta = 8.33$  (s, 4H, *e*), 7.93 (t, 2H,  $^3J = 7.8$  Hz, *p*), 7.55 (d, 4H,  $^3J = 7.8$  Hz, *o*), 7.48 (dt, 4H,  $^3J = 7.8$  Hz,  $^4J = 1.7$  Hz, *j*), 7.41 (dd, 4H,  $^3J = 7.8$  Hz,  $^4J = 1.7$  Hz, *h*), 7.26 (s, 4H, *c*), 7.18 (d, 4H,  $^3J = 8.4$  Hz, *k*), 6.94 (dt, 4H,  $^3J = 7.5$  Hz,  $^4J = 0.6$  Hz, *i*), 5.44 (s, 8H, *m*), 4.04 (s, 6H, *a*) ppm.

<sup>4</sup> J. M. Klein, V. S. Saggiomo, L. Reck, G. D. Pantos, U. Lüning and J. K. M. Sanders, *Chem. Commun.*, 2011, **47**, 3371-3373.

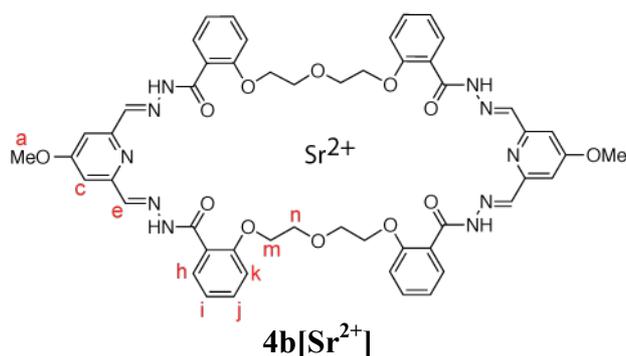
$^{13}\text{C}$ -NMR (125 MHz, 300 K,  $\text{CDCl}_3/\text{MeOD}$ , 1:1, v/v).  $\delta = 169.1, 167.0, 157.4, 156.2, 153.7, 147.8, 139.1, 134.9, 131.7, 123.4, 122.2, 120.4, 114.2, 113.3, 70.7, 56.7$  ppm.  
HRMS (ESI+) calcd. for  $\text{C}_{58}\text{H}_{46}\text{N}_{12}\text{O}_{10}\text{Sr}$ :  $[\text{MH}]^+$  (m/z) = 1159.2589, found: 1159.2614;  $[\text{MH}_2]^{2+}$  (m/z): 580.1331. found: 580.1315.



$^1\text{H}$ -NMR (400 MHz, 298 K,  $\text{CDCl}_3/\text{MeOD}$ , 7:3, v/v).  $\delta = 8.30$  (s, 4H, *e*), 7.46 (m, *j* overlaps with residual solvent peak for  $\text{CDCl}_3$ ), 7.30 (d, 4H,  $^3J = 7.8$  Hz, *h*), 7.07 (s, 4H, *c*), 7.02 (d, 4H,  $^3J = 8.4$  Hz, *k*), 6.90 (t, 4H,  $^3J = 7.5$  Hz, *i*), 4.40 (t, 8H,  $^3J = 4.2$  Hz, *m*), 4.04 (br s, 8H, *n*), 3.91 (s, 6H, *a*), ppm.

$^{13}\text{C}$ -NMR (100 MHz, 298 K,  $\text{CDCl}_3/\text{MeOD}$ , 7:3, v/v).  $\delta = 168.6, 166.6, 157.3, 152.4, 146.6, 134.9, 131.7, 121.9, 119.6, 113.3, 112.4, 69.4, 68.0, 56.5$  ppm.

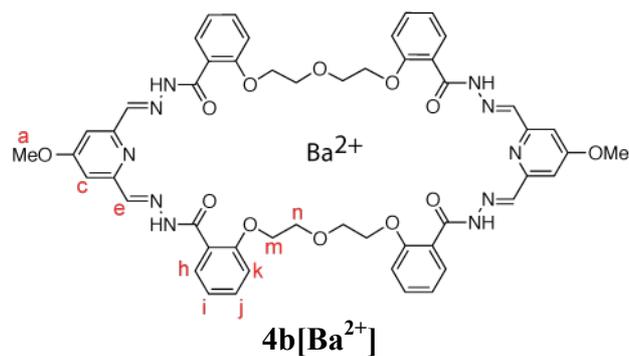
In HRMS only the free macrocycle is observed.



$^1\text{H}$ -NMR (500 MHz, 300 K,  $\text{CDCl}_3/\text{MeOD}$ , 7:3, v/v).  $\delta = 8.38$  (s, 4H, *e*), 7.48 (dt, 4H,  $^3J = 7.8$  Hz,  $^4J = 1.7$  Hz, *j*), 7.38 (dd, 4H,  $^3J = 7.8$  Hz,  $^4J = 1.7$  Hz, *h*), 7.14 (s, 4H, *c*), 7.02 (t, 4H,  $^3J = 8.4$  Hz, *k*), 6.94 (t, 4H,  $^3J = 7.5$  Hz, *i*), 4.40 (br s, 8H, *m*), 3.96-4.20 (br s, 8H, *n*), 3.96 (s, 6H, *a*) ppm.

$^{13}\text{C}$ -NMR (125 MHz, 300 K,  $\text{CDCl}_3/\text{MeOD}$ , 7:3, v/v).  $\delta = 168.7, 166.6, 157.4, 153.4, 147.0, 134.8, 131.6, 121.9, 119.9, 113.6, 113.0, 69.4, 68.3, 56.5$  ppm.

HRMS (ESI+) calcd. for  $\text{C}_{58}\text{H}_{48}\text{N}_{10}\text{O}_{12}\text{Sr}$ :  $[\text{MH}]^+$  (m/z) = 1093.2582, found: 1093.2706;  $[\text{MH}_2]^{2+}$  (m/z): 547.1327. found: 547.1381.

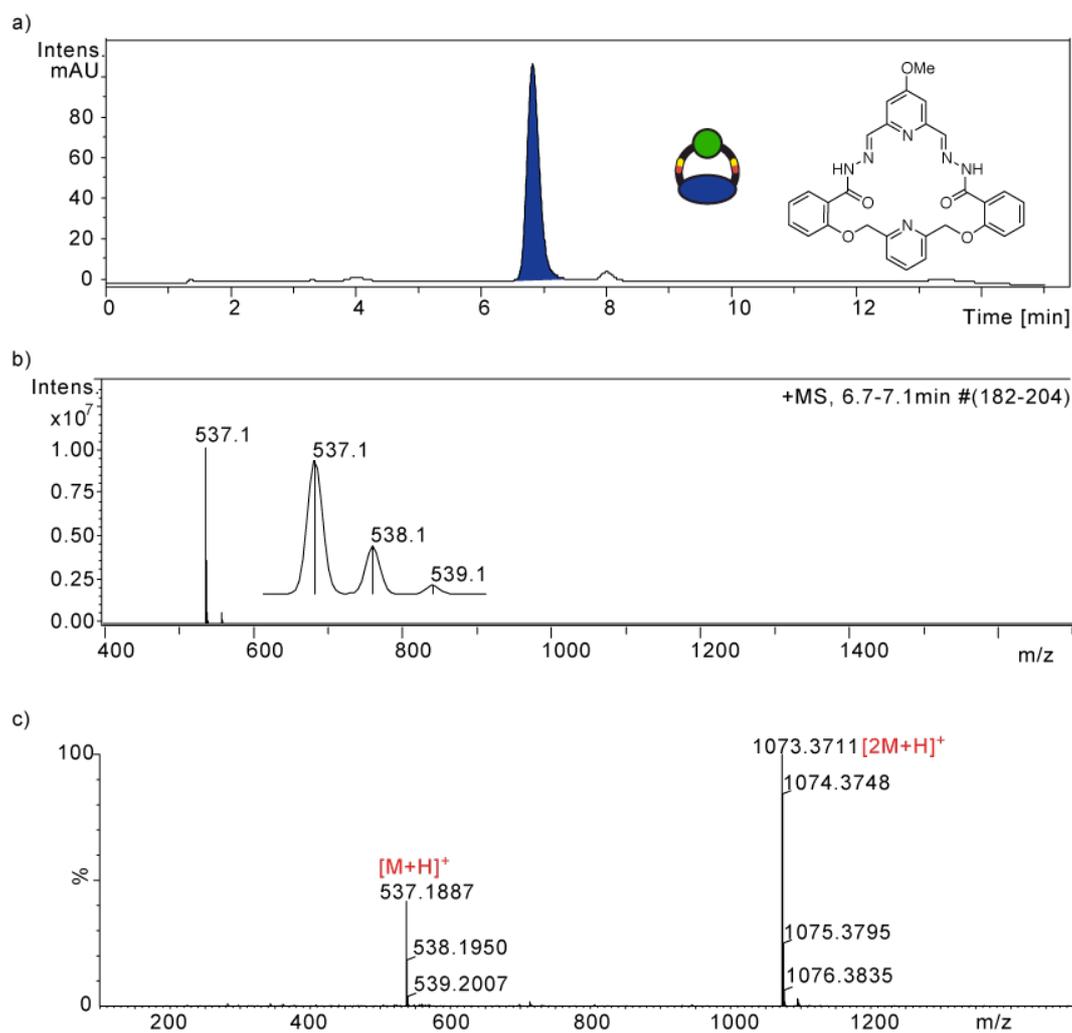


<sup>1</sup>H-NMR (400 MHz, 298 K, CDCl<sub>3</sub>/MeOD, 7:3, v/v).  $\delta$  = 8.35 (s, 4H, *e*), 7.42-7.46 (m, 8H, *h, j*), 7.19 (s, 4H, *c*), 6.98 (d, 4H, <sup>3</sup>*J* = 8.3 Hz, *k*), 6.94 (t, 4H, <sup>3</sup>*J* = 7.6 Hz, *i*), 4.34 (s, 8H, *m*), 4.00 (broad s, 8H, *n*), 3.98 (s, 6H, *a*) ppm.

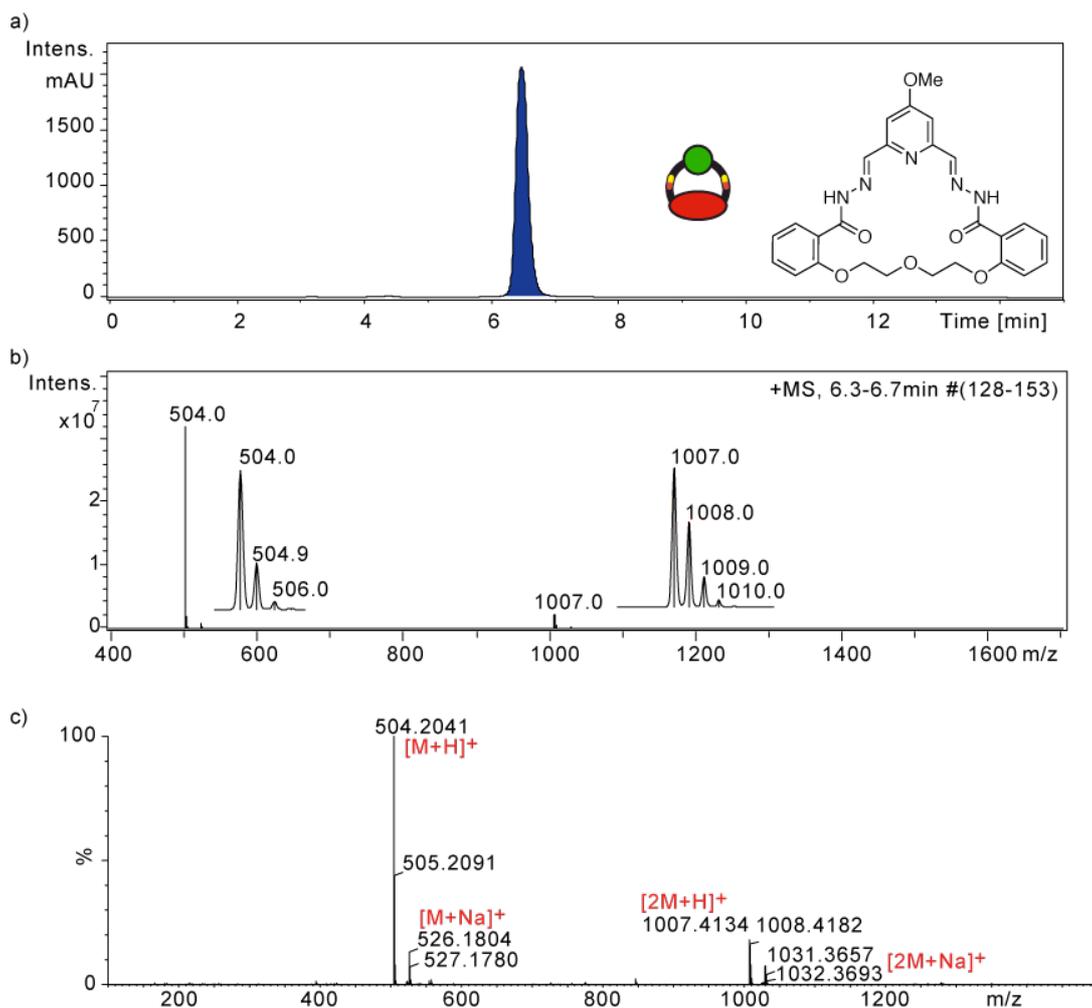
<sup>13</sup>C-NMR (100 MHz, 300 K, CDCl<sub>3</sub>/MeOD, 1:1, v/v).  $\delta$  = 168.0, 165.4, 162.3, 156.6, 153.6, 146.7, 133.7, 130.7, 121.1, 119.7, 113.1, 112.7, 68.5, 67.6, 55.7 ppm.

HRMS (ESI+) calcd. for C<sub>52</sub>H<sub>48</sub>N<sub>10</sub>O<sub>12</sub>Ba: [MH]<sup>+</sup> (m/z) = 1143.2578, found: 1143.2592; [MH<sub>2</sub>]<sup>2+</sup> (m/z): 572.1325. found: 572.1287.

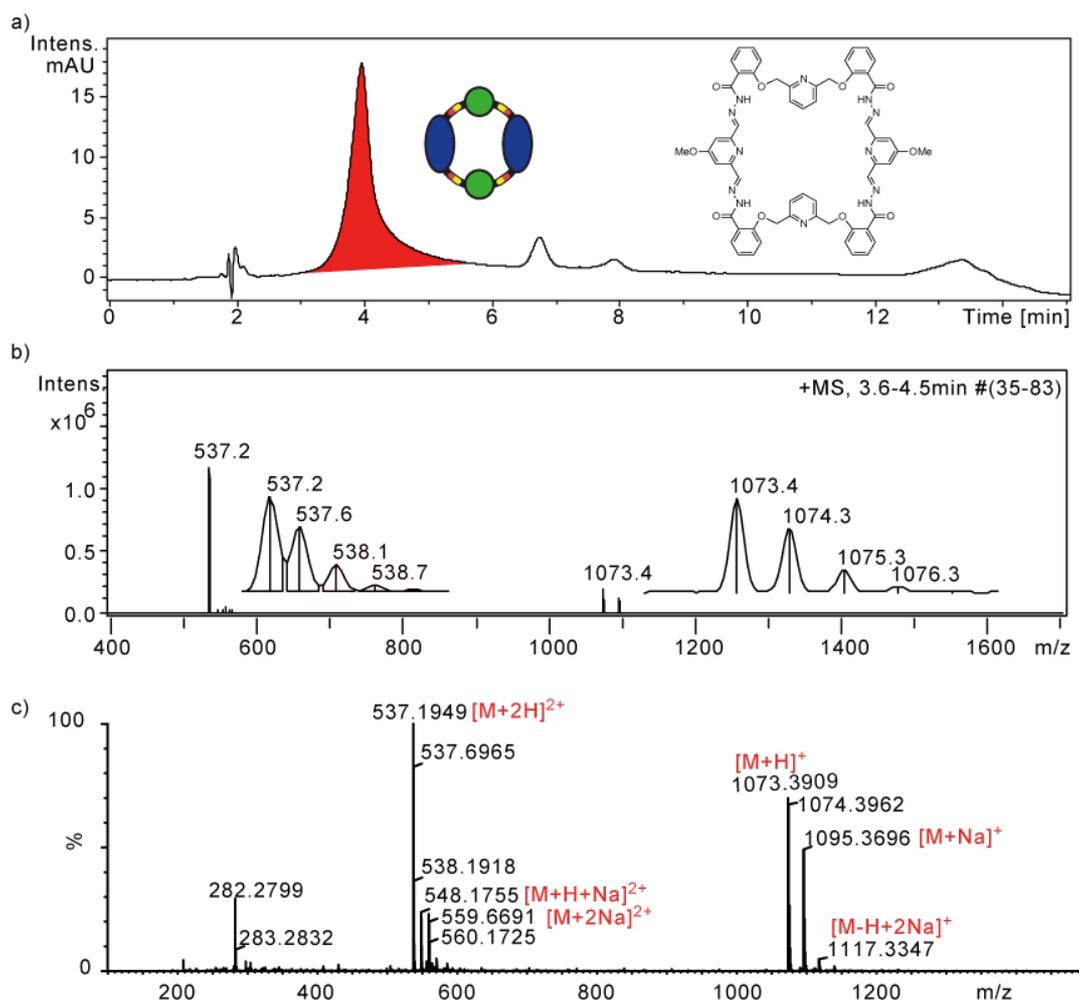
## LC-MS and HRMS



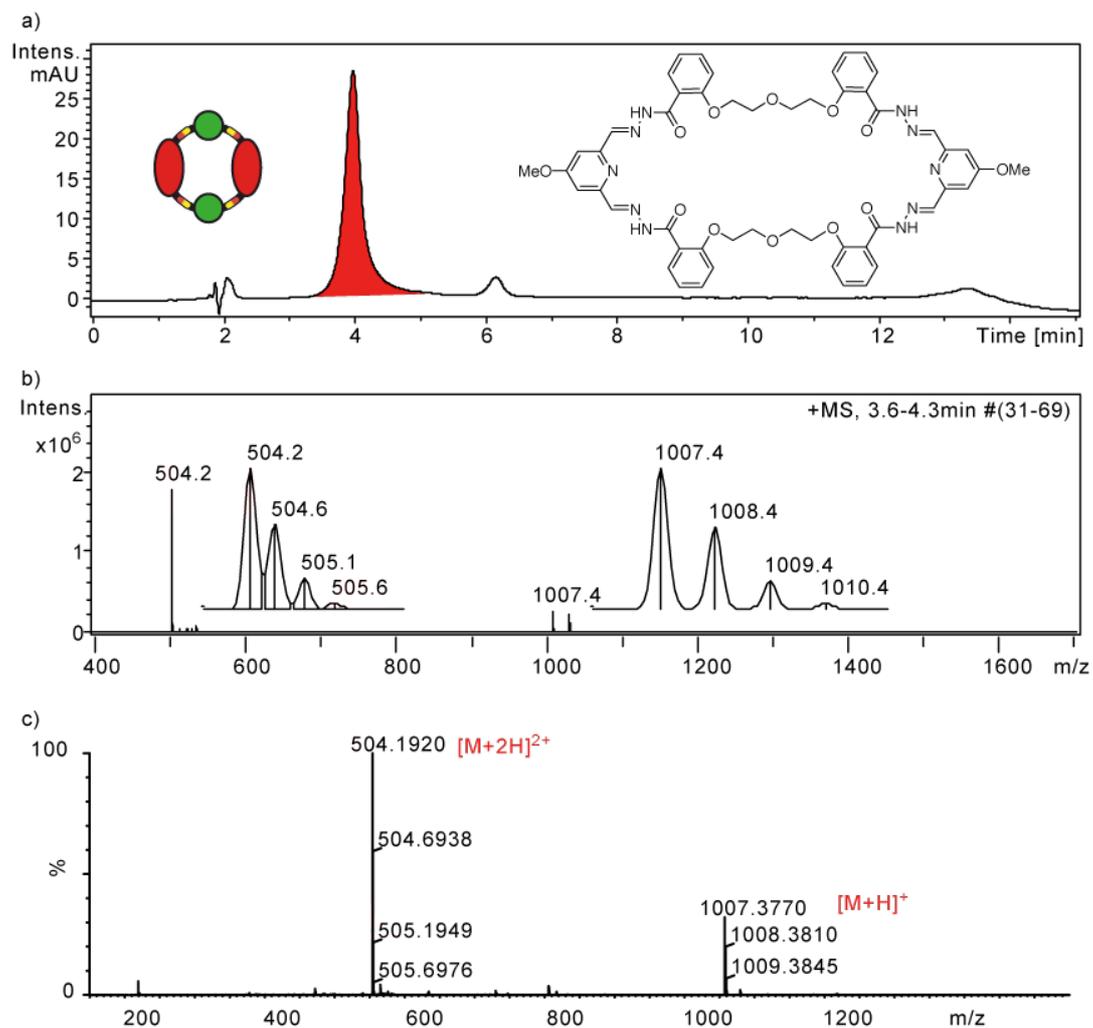
**Fig. 4:** LCMS and HRMS analysis of the 1+1 macrocycle with pyridyl linker **3a** (Method A). a) HPLC trace recorded at 290 nm showing the isolated material to consist of 1+1 macrocycle (**3a**, 97%, blue peak) and the 2+2 macrocycle (**4a**, 3%, peak at 8 mins); b) low resolution mass spectrum of the blue peak in a); c) ESI(+)-HRMS spectrum of the isolated material. The isotope pattern in b) and c) show that the isolated material is the 1+1 and not the 2+2 macrocycle.



**Fig. 5:** LCMS and HRMS analysis of the 1+1 macrocycle with ethyleneglycol linker **3b** (Method A). a) HPLC trace recorded at 290 nm showing the isolated material to consist of 1+1 macrocycle (**3b**, >99%, blue peak); b) low resolution mass spectrum of the blue peak in a); c) ESI(+)-HRMS spectrum of the isolated material. The isotope pattern in b) and c) show that the isolated material is the 1+1 and not the 2+2 macrocycle.

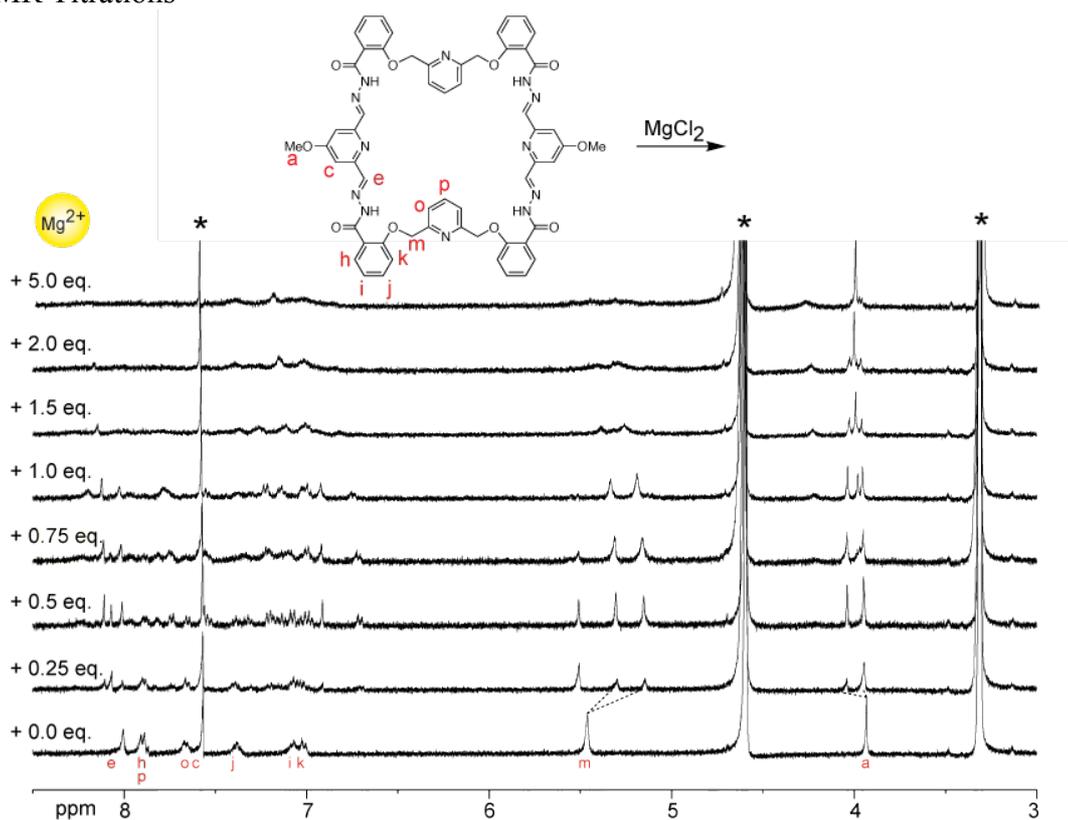


**Fig. 6:** LCMS and HRMS analysis of the 2+2 macrocycle with pyridyl linker **4a** (Method A). a) HPLC trace recorded at 290 nm showing the isolated material to consist of 1+1 macrocycle (**3a**, 6%, 6.8 mins) and the 2+2 macrocycle (**4a**, 91%, red peak, the MS of the peak at 8 mins is identical to that of the red peak, it is possibly a conformational isomer of **4b**, 3%); b) mass spectrum of the red peak in a); c) ESI(+)-HRMS spectrum of the isolated material. The isotope pattern in b) and c) show that the isolated material is the 2+2 and not the 1+1 macrocycle.

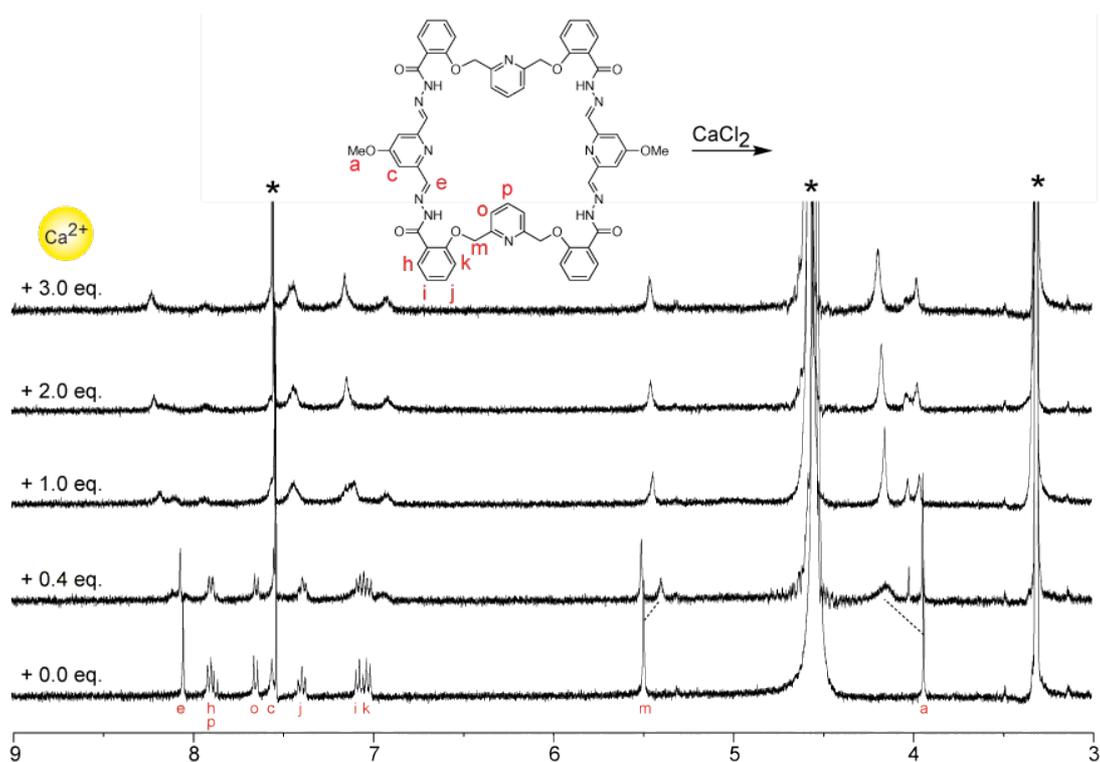


**Fig. 7:** LCMS and HRMS analysis of the 2+2 macrocycle with ethyleneglycol linker **4b** (Method A). a) HPLC trace recorded at 290 nm showing the isolated material to consist of two isomers of the 2+2 macrocycle (**4b**, 95%, red peak and peak at 6.1 mins, 5%); b) mass spectrum of the red peak in a); c) ESI(+)-HRMS spectrum of the isolated material. The isotope pattern in b) and c) show that the isolated material is the 2+2 (**4b**) and not the 1+1 macrocycle (**3b**).

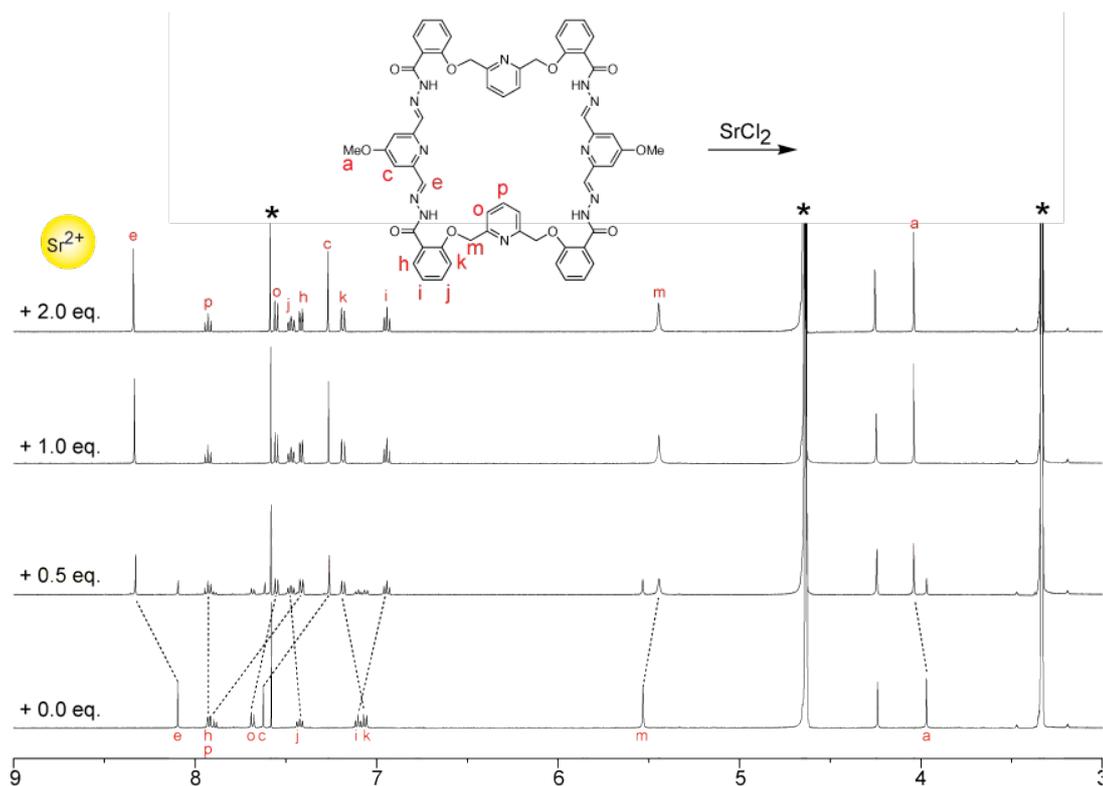
### NMR Titrations



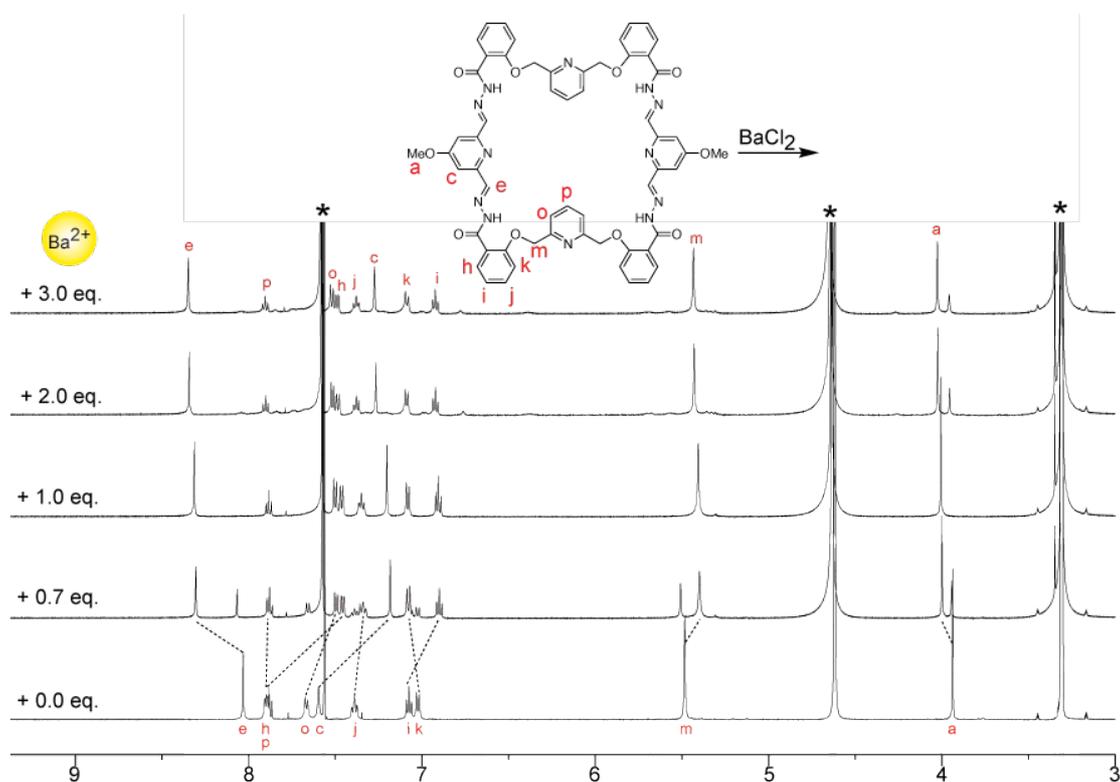
**Fig. 8:** NMR spectra of **4a** in CDCl<sub>3</sub>/MeOD (1:1) after addition of different amounts of MgCl<sub>2</sub>. Residual solvent signals are marked with asterisk.



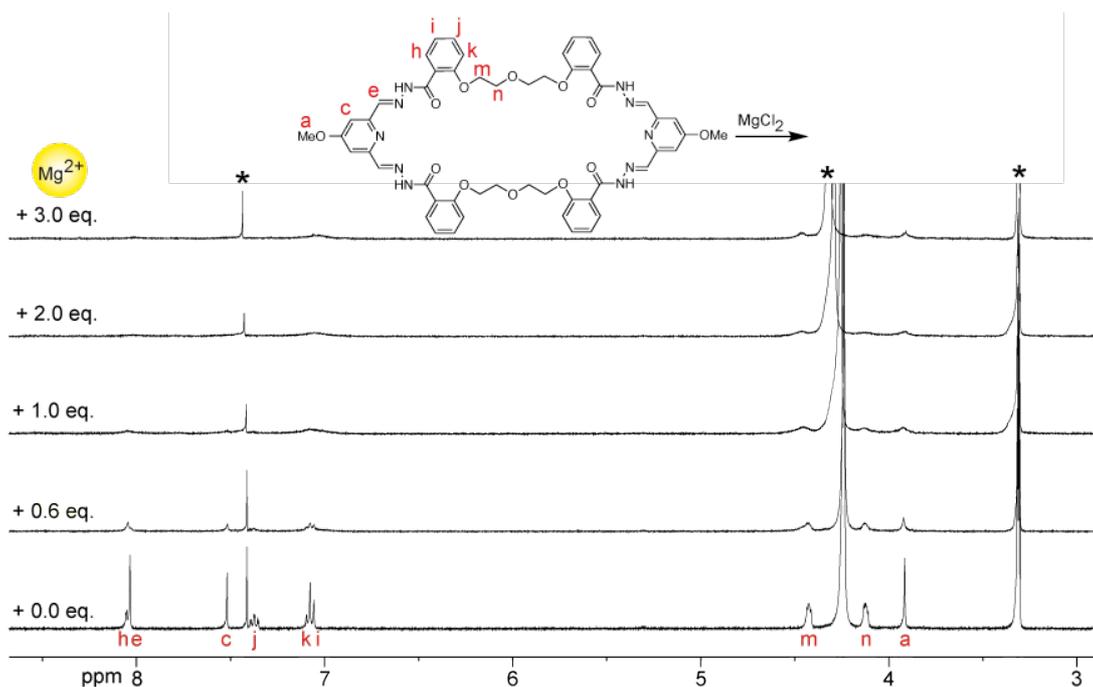
**Fig. 9:** NMR spectra of **4a** in CDCl<sub>3</sub>/MeOD (1:1) after addition of different amounts of CaCl<sub>2</sub>. Residual solvent signals are marked with asterisk.



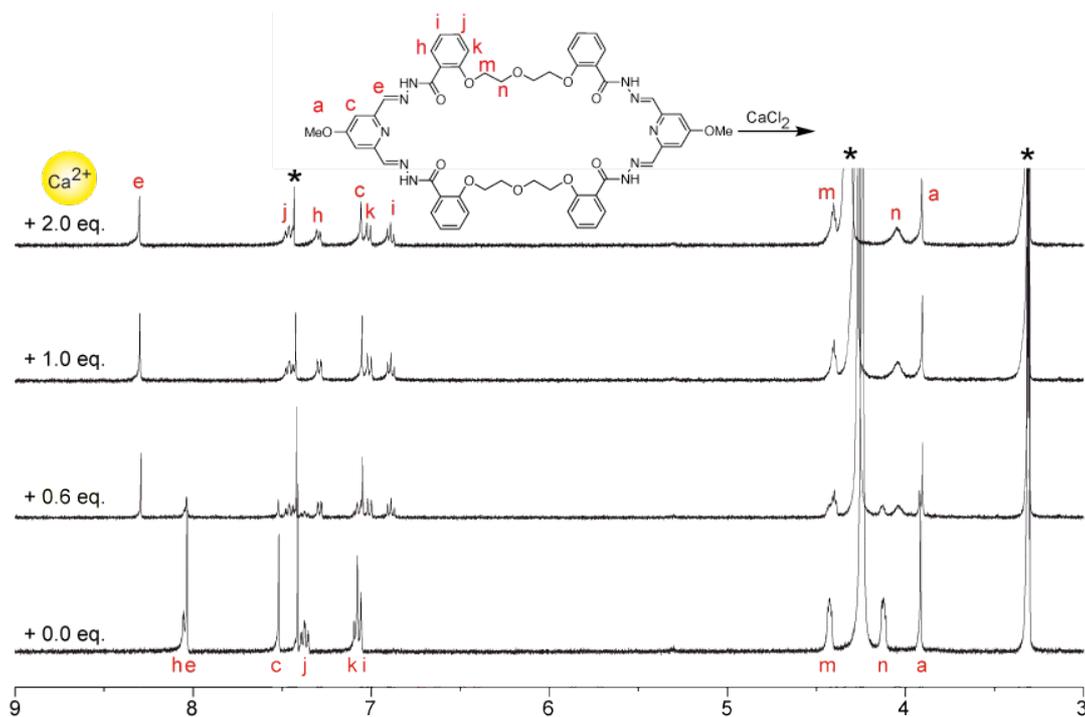
**Fig. 10:** NMR spectra of **4a** in CDCl<sub>3</sub>/MeOD (1:1) after addition of different amounts of SrCl<sub>2</sub>. Residual solvent signals are marked with asterisk.



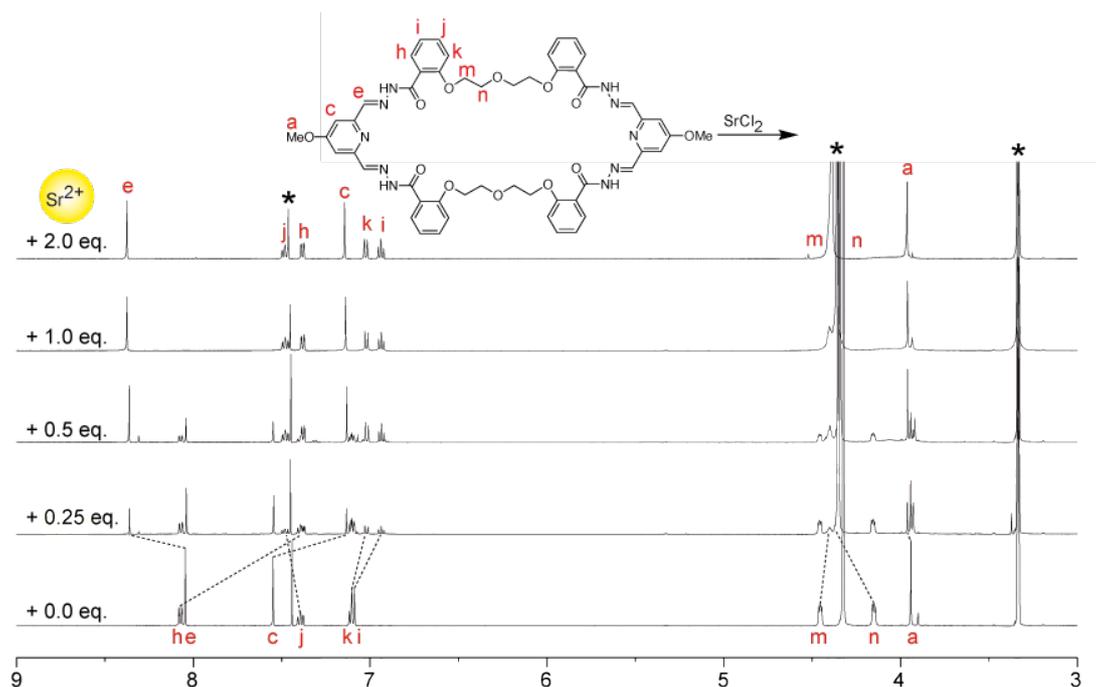
**Fig. 11:** NMR spectra of **4a** in CDCl<sub>3</sub>/MeOD (1:1) after addition of different amounts of BaCl<sub>2</sub>. Residual solvent signals are marked with asterisk.



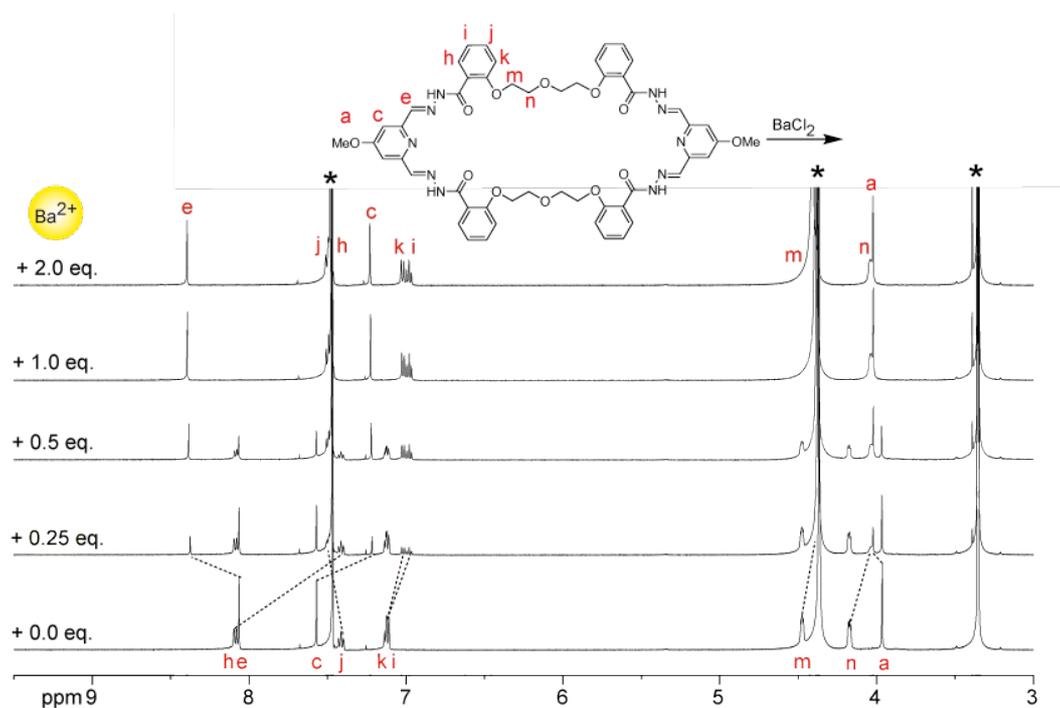
**Fig. 12:** NMR spectra of **4b** in CDCl<sub>3</sub>/MeOD (7:3) after addition of different amounts of MgCl<sub>2</sub>. Residual solvent signals are marked with asterisk.



**Fig. 13:** NMR spectra of **4b** in CDCl<sub>3</sub>/MeOD (7:3) after addition of different amounts of CaCl<sub>2</sub>. Residual solvent signals are marked with asterisk.

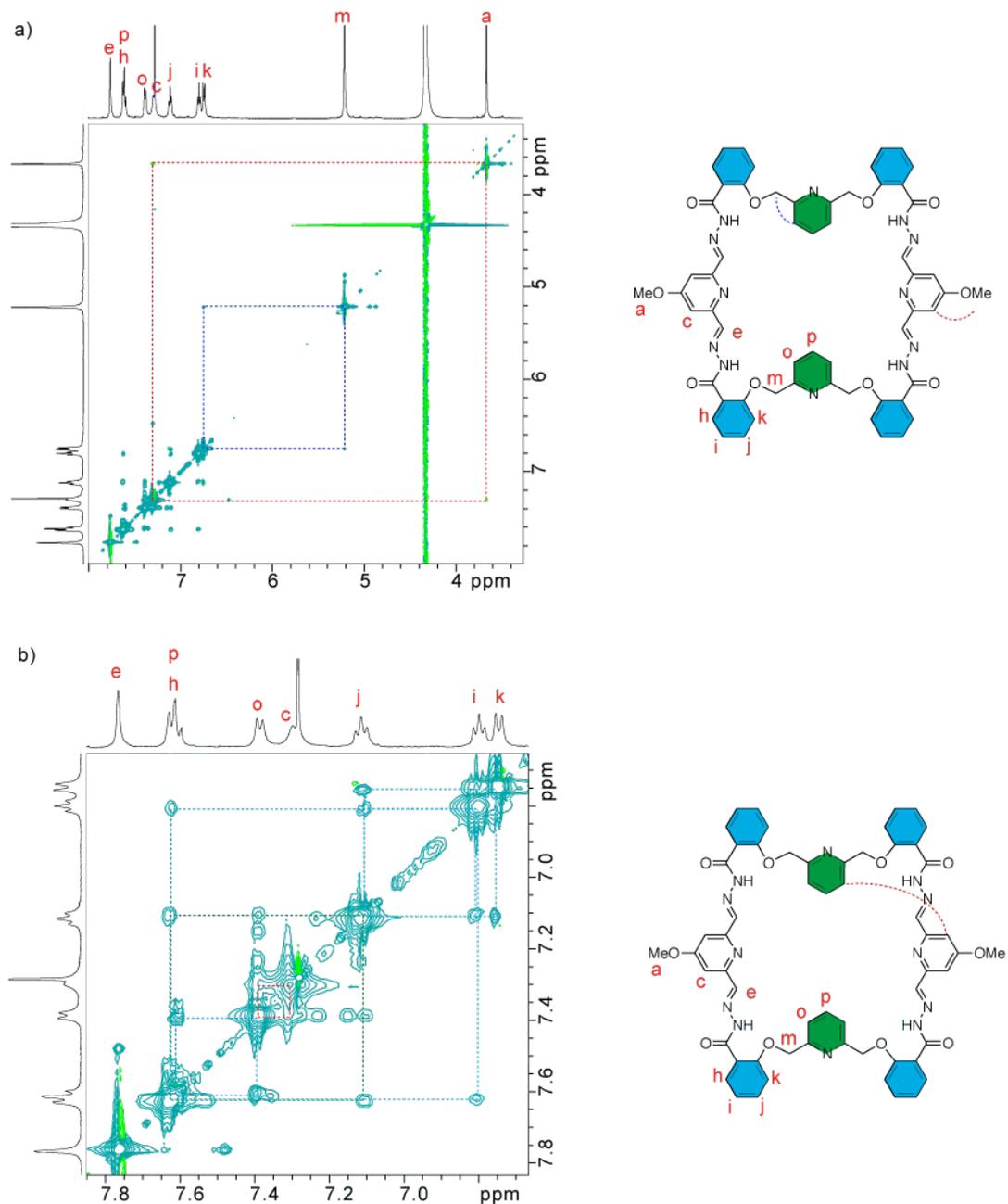


**Fig. 14:** NMR spectra of **4b** in CDCl<sub>3</sub>/MeOD (7:3) after addition of different amounts of SrCl<sub>2</sub>. Residual solvent signals are marked with asterisk.

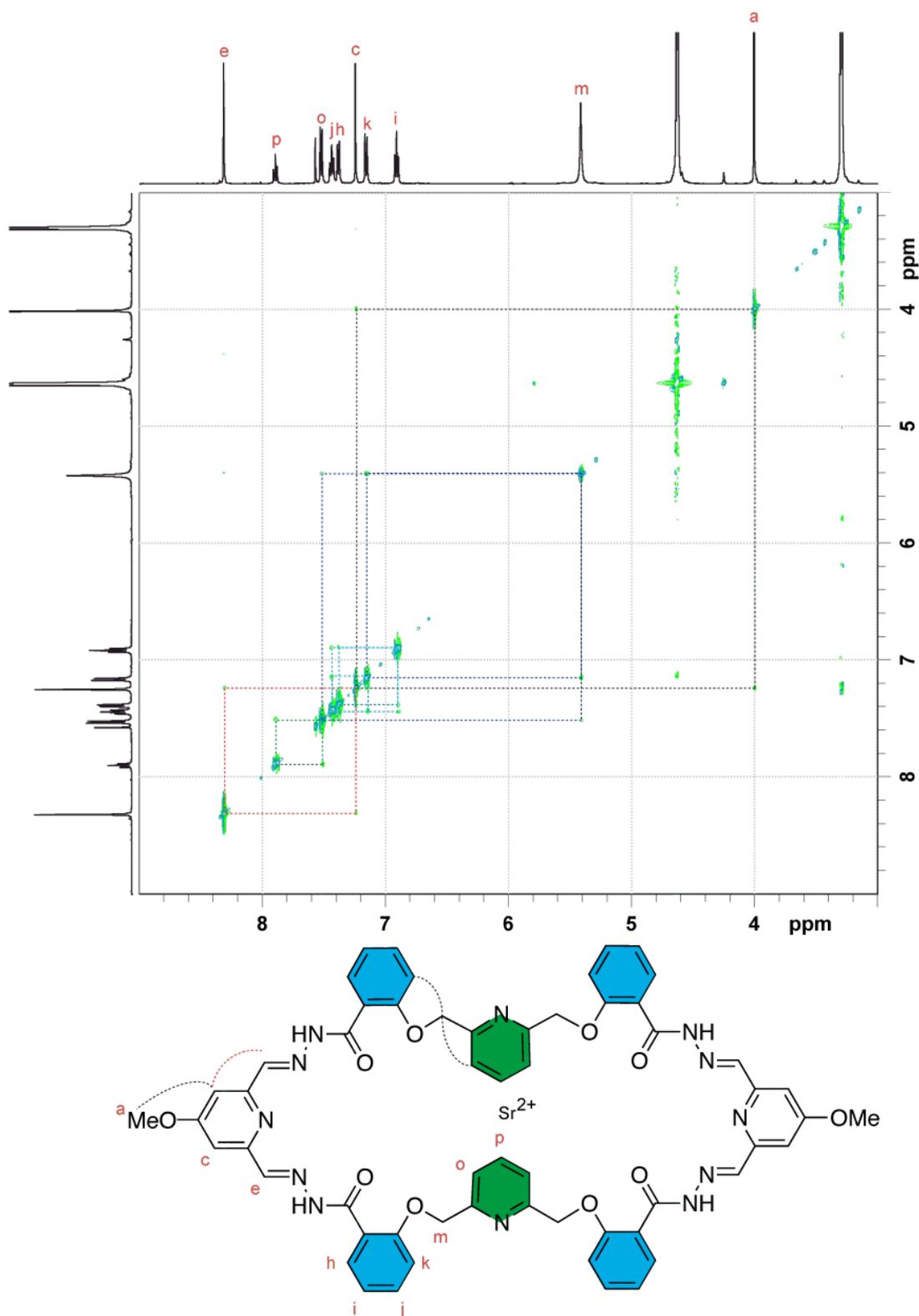


**Fig. 15:** NMR spectra of **4b** in CDCl<sub>3</sub>/MeOD (7:3) after addition of different amounts of BaCl<sub>2</sub>. Residual solvent signals are marked with asterisk.

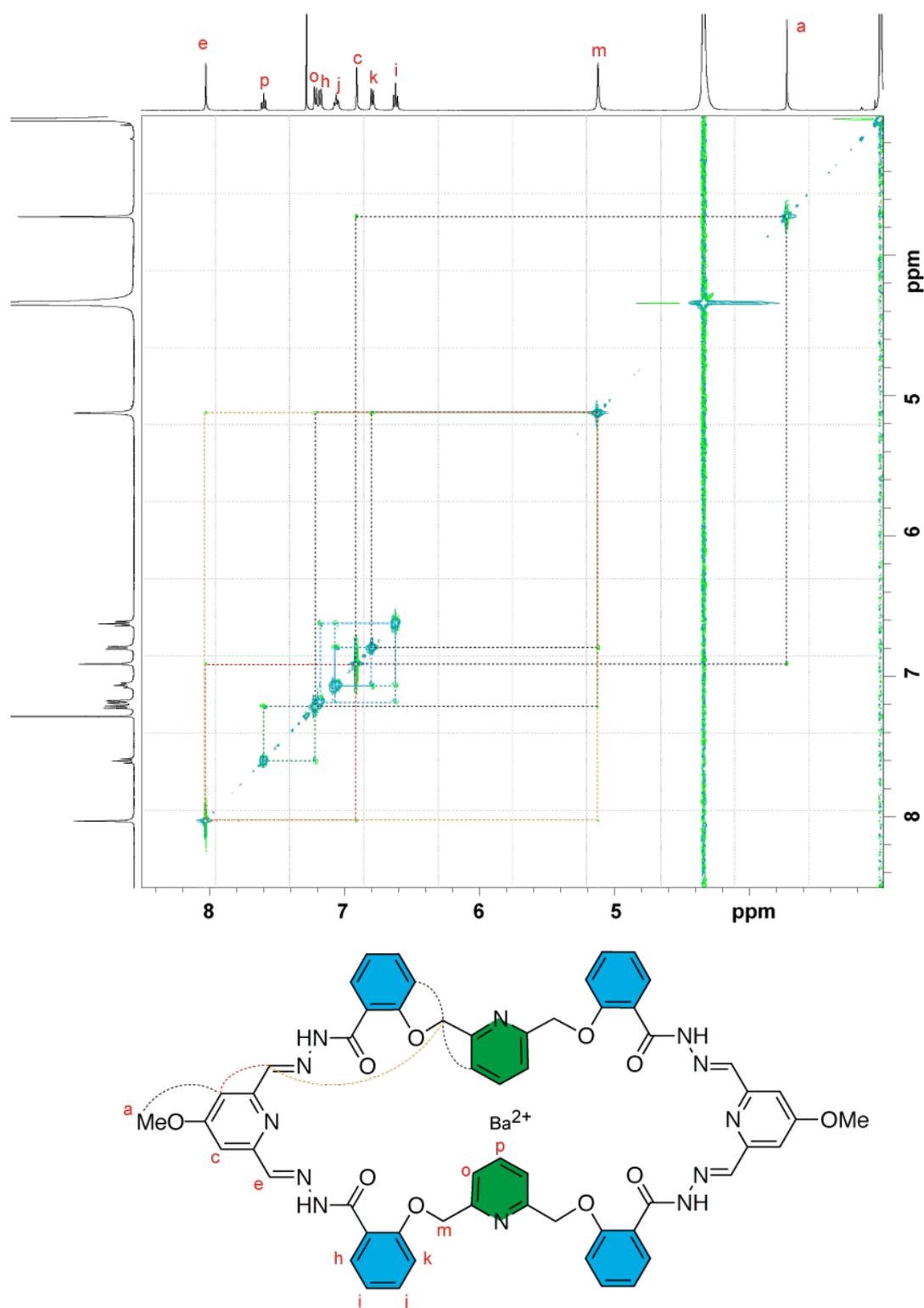
## NOESY Spectra



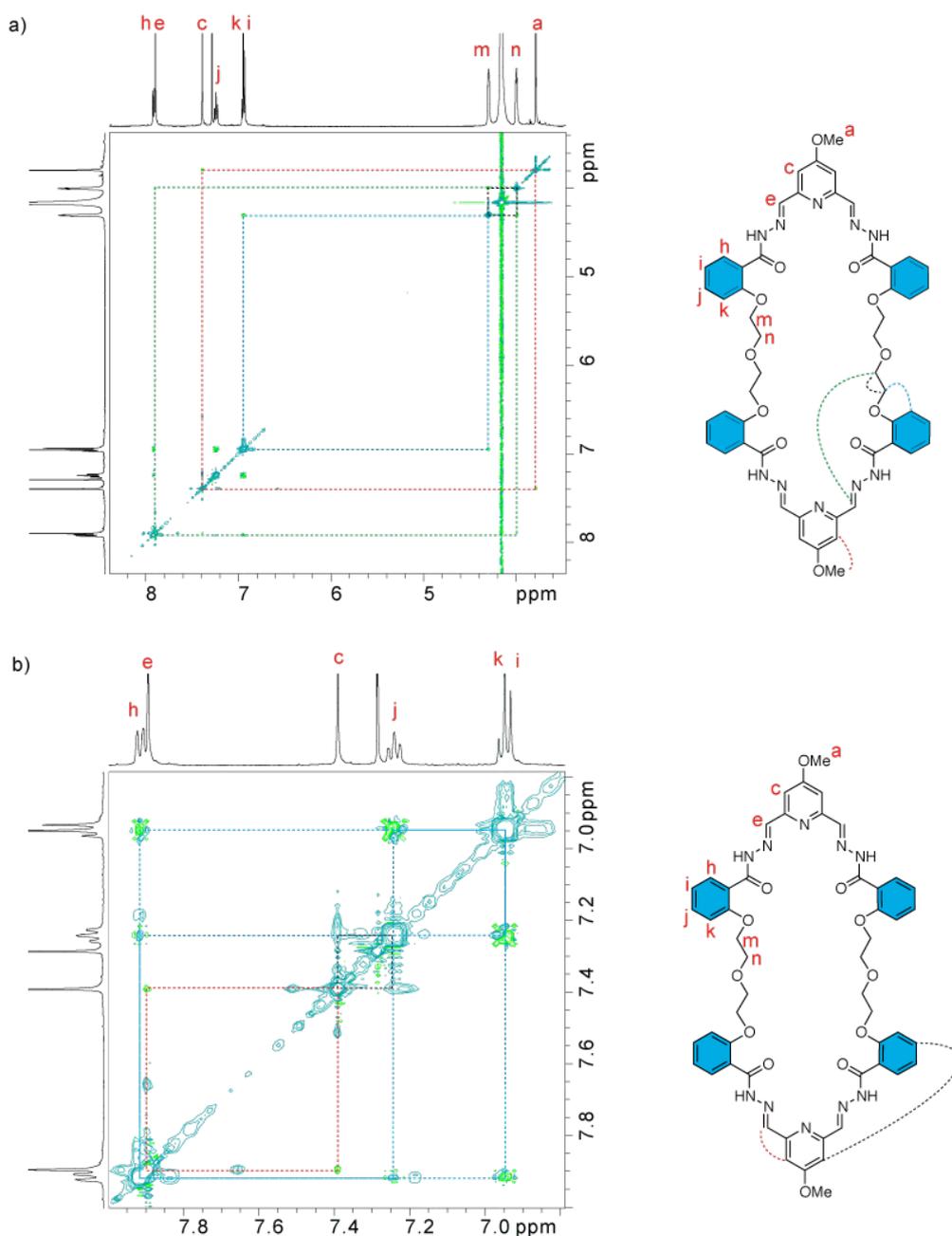
**Fig. 16:** : NOESY spectrum of **4a** (1 mM in CDCl<sub>3</sub>/MeOD, 1:1, 298 K, 500 MHz, mixing time = 800 ms). a) whole spectrum; b) aromatic region. Cross-peaks are indicated with corresponding colours in the spectrum and the structures next to the spectra. Light blue cross-peaks were assigned to the protons on the light blue ring (h, i, j, k) and green cross-peaks were assigned to the protons of green pyridine ring (o, p).



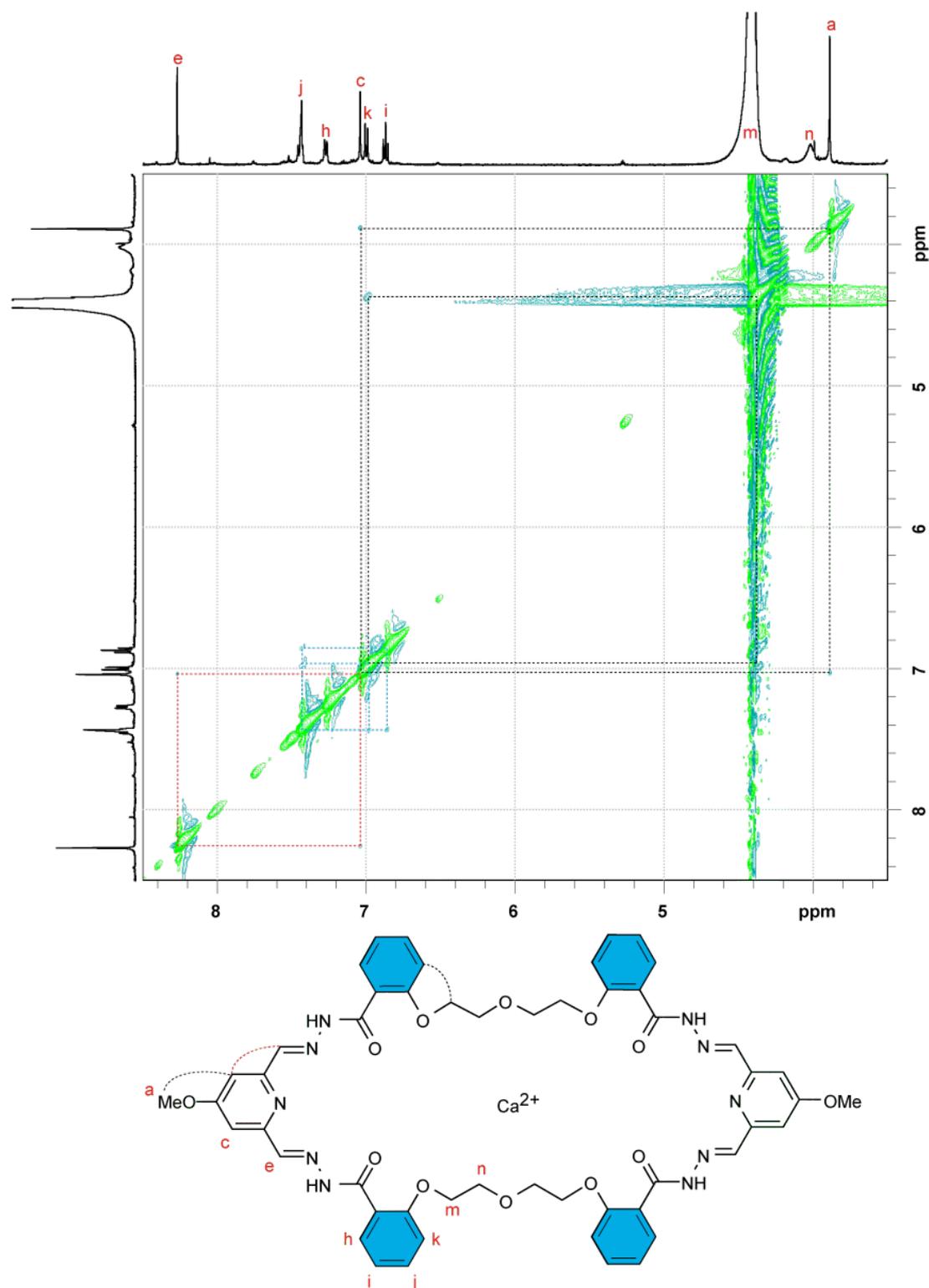
**Fig. 17:** NOESY spectrum of **4a**[Sr<sup>2+</sup>] (1 mM in CDCl<sub>3</sub>/MeOD, 1:1, 298 K, 500 MHz, mixing time = 800 ms). Cross-peaks are indicated with corresponding colours in the spectrum and the structure below the spectrum. Light blue cross-peaks were assigned to the protons on the light blue ring (h, i, j, k) and green cross-peaks were assigned to the protons of green pyridine ring (o, p).



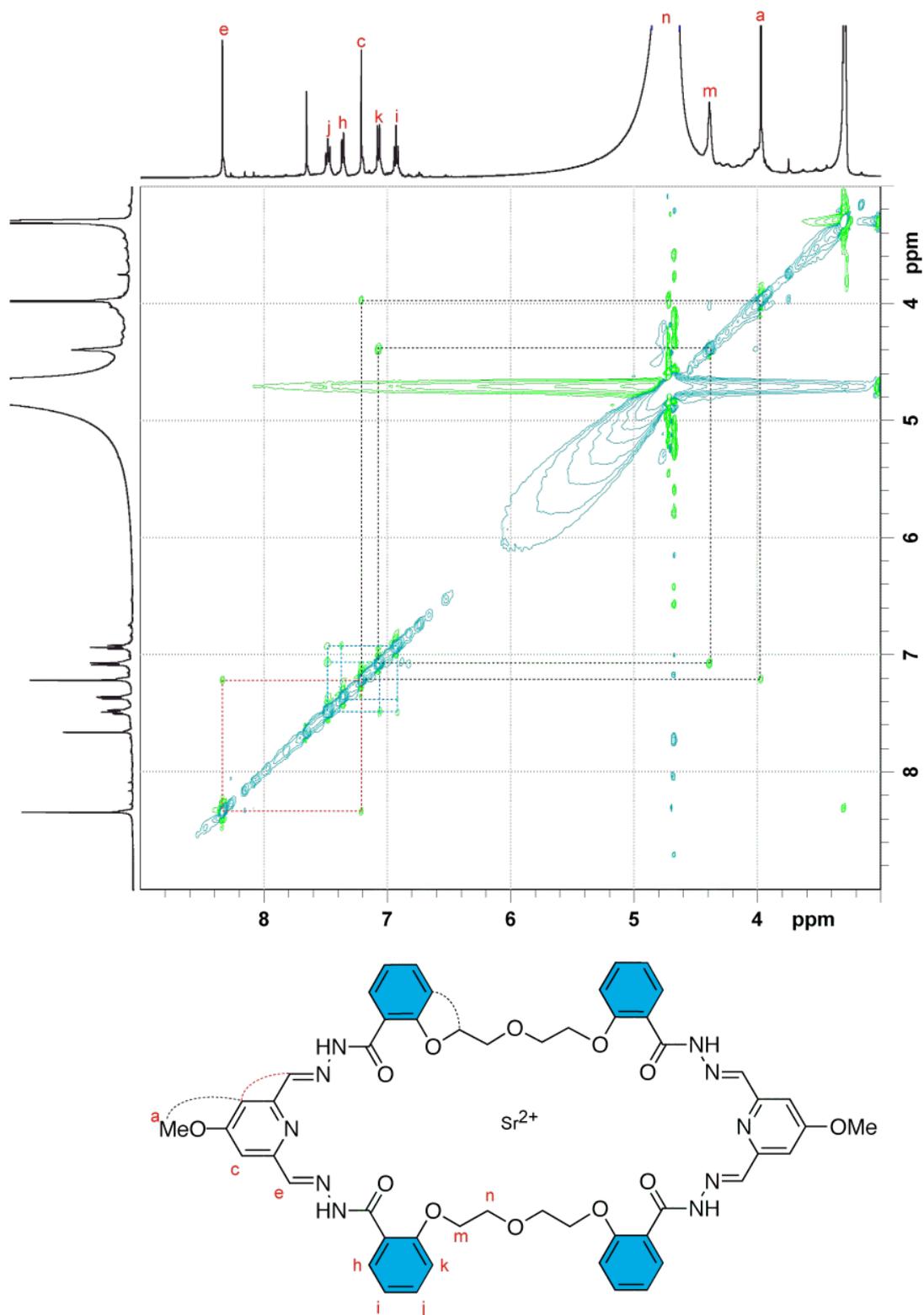
**Fig. 18:** NOESY spectrum of **4a**[Ba<sup>2+</sup>] (1 mM in CDCl<sub>3</sub>/MeOD, 1:1, 298 K, 500 MHz, mixing time = 800 ms). Cross-peaks are indicated with corresponding colours in the spectrum and the structure below the spectrum. Light blue cross-peaks were assigned to the protons on the light blue ring (h, i, j, k) and green cross-peaks were assigned to the protons of green pyridine ring (o, p).



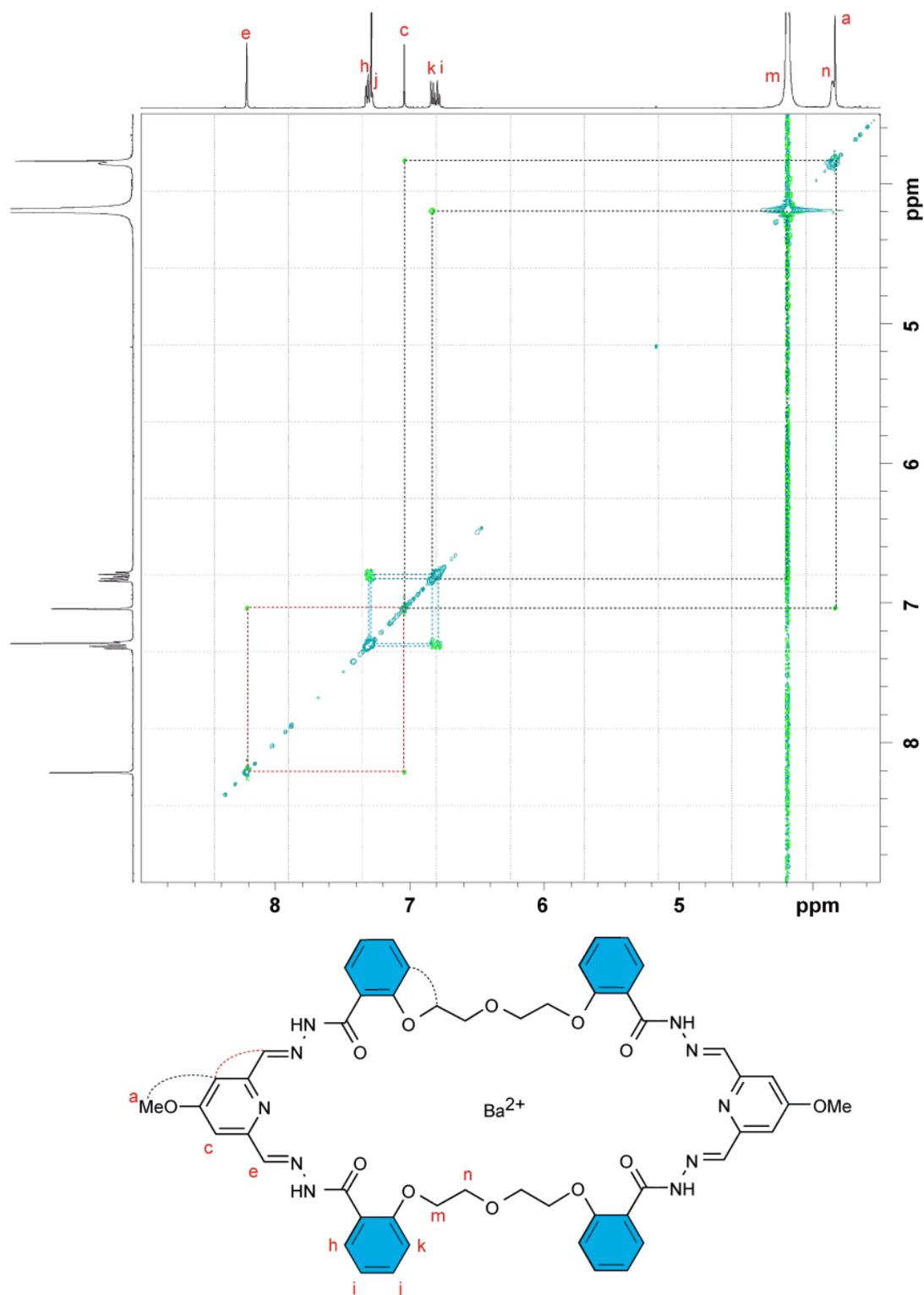
**Fig. 19:** NOESY spectrum of **4b** (1 mM in CDCl<sub>3</sub>/MeOD, 7:3, 298 K, 500 MHz, mixing time = 800 ms). a) whole spectrum; b) aromatic region. Cross-peaks are indicated with corresponding colours in the spectrum and the structures next to the spectra. Light blue cross-peaks were assigned to the protons on the light blue ring (h, i, j, k).



**Fig. 20:** NOESY spectrum of **4b**[Ca<sup>2+</sup>] (1 mM in CDCl<sub>3</sub>/MeOD, 7:3, 298 K, 500 MHz, mixing time = 800 ms). Cross-peaks are indicated with corresponding colours in the spectrum and the structure below the spectrum. Light blue cross-peaks were assigned to the protons on the light blue ring (h, i, j, k).



**Fig. 21:** NOESY spectrum of  $4b[Sr^{2+}]$  (1 mM in  $CDCl_3/MeOD$ , 7:3, 298 K, 500 MHz, mixing time = 800 ms). Cross-peaks are indicated with corresponding colours in the spectrum and the structure below the spectrum. Light blue cross-peaks were assigned to the protons on the light blue ring (h, i, j, k).



**Fig. 22:** NOESY spectrum of **4b**[Ba<sup>2+</sup>] (1 mM in CDCl<sub>3</sub>/MeOD, 7:3, 298 K, 500 MHz, mixing time = 800 ms). Cross-peaks are indicated with corresponding colours in the spectrum and the structure below the spectrum. Light blue cross-peaks were assigned to the protons on the light blue ring (h, i, j, k).

### **UV-Vis Titrations**

The results for **4a** have been reported previously<sup>5</sup> and the results for **4b** are shown in Fig. 23.

Host **4b** was dissolved in CHCl<sub>3</sub>/MeOH (7:3, v/v) to give a solution of 0.010 mM. Metal salts were dissolved in the solution of **4b** to give solutions containing 0.010 mM **4b** and 1.0 mM.

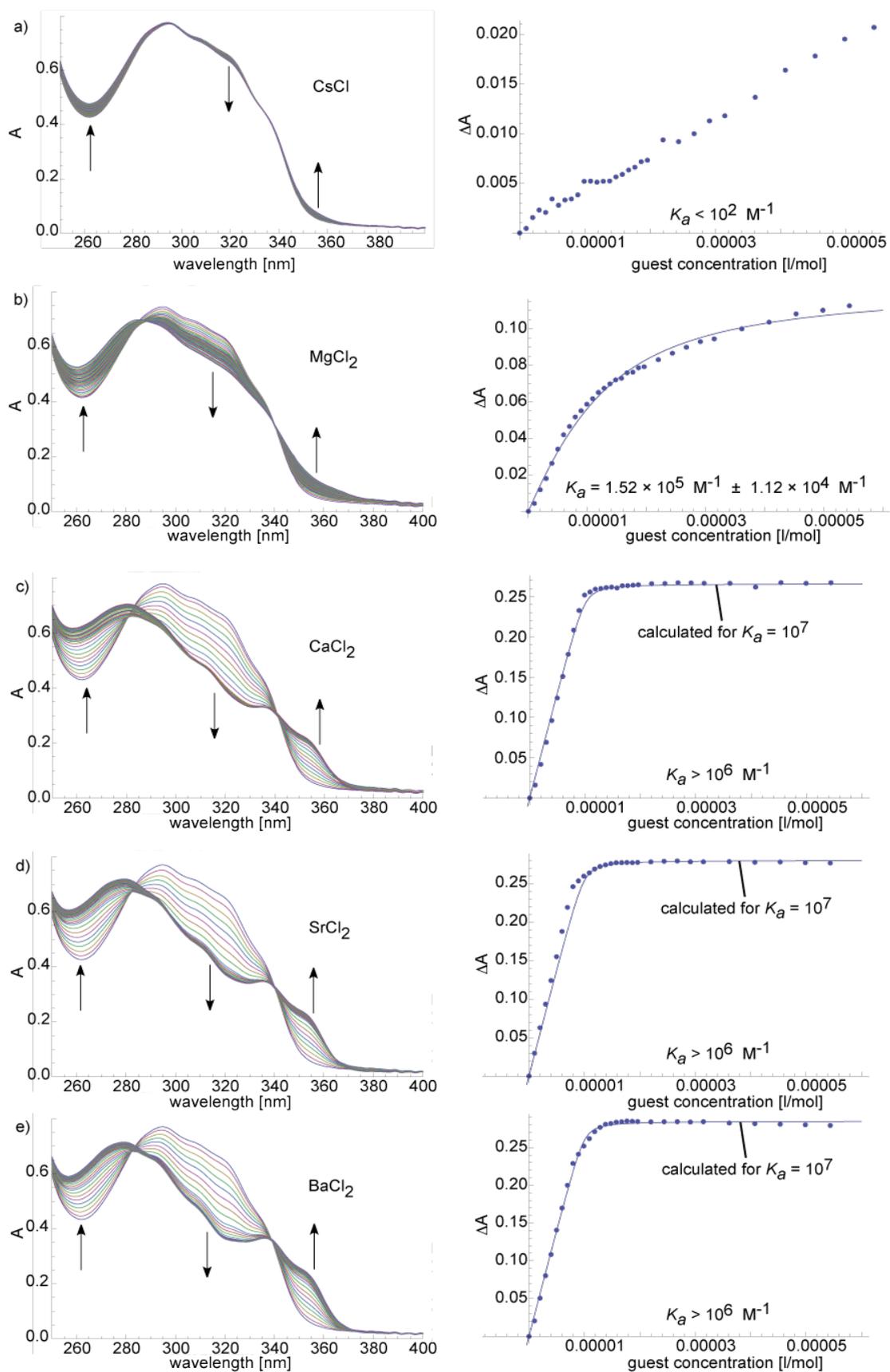
Procedure of the binding studies involved making sequential additions (20 × 2.0 μl, then 5 × 5.0 μl, then 5 × 10 μl) of metal salts using Eppendorf pipettes to a 2.0 ml solution of **4a** or **4b** in a spectrometric cell (*b* = 1.0 cm). UV–Vis spectra were then combined to produce plots that showed the changes in the spectral features as a function of changes in the concentration of metal salts.

Binding constants were calculated using a model derived by Maarten Smoulders.<sup>6</sup>

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<sup>5</sup> J. M. Klein, V. Saggiomo, L. Reck, G. D. Pantos, U. Lüning and J. K. M. Sanders, *Chem. Commun.*, 2011, **47**, 3371-3373.

<sup>6</sup> Y. R. Hristova, M. M. J. Smulders, J. K. Clegg, B. Breiner and J. R. Nitschke, *Chem. Sci.* 2011, **2**, 638-641.



**Fig. 23** UV spectra of **4b** with different amounts of metal guests (left). Binding isotherms for the binding of different guests to **4b** at 23 °C (right).

## ***Crystallographic Data***

The .cif files for **3b** and **4b** can be downloaded separately and the data for **4a** has been published.<sup>7</sup>

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<sup>7</sup> J. M. Klein, V. Saggiomo, L. Reck, G. D. Pantos, U. Lüning and J. K. M. Sanders, *Chem. Commun.* 2011, **47**, 3371-3373.