Supporting Information for

Supramolecular Cage Encapsulation as Versatile Tool for the Experimental Quantification of Aromatic Interactions

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Contents

1 General Methods

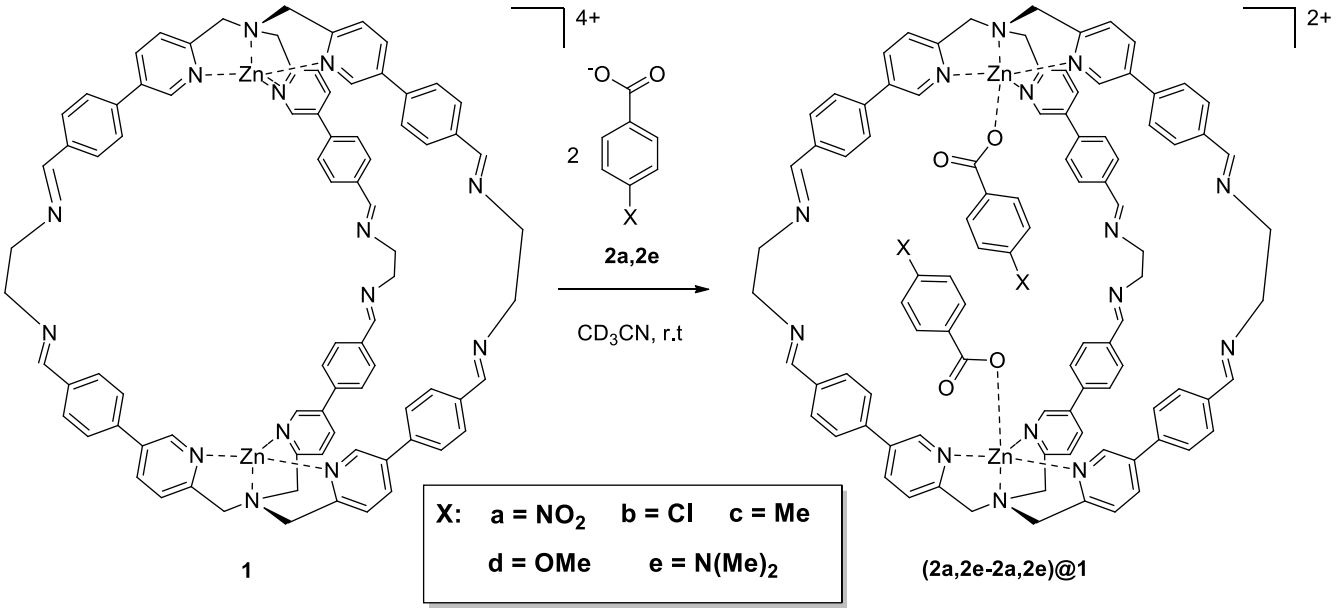
NMR spectra were recorded at 301 K on a Bruker 500 MHz Avance TCI Cryoprobe spectrometer and on a Bruker 400 Avance III BBi-z grad 5 mm. All the ^{1}H NMR spectra were referenced to residual isotopic impurity of CD_3CN (1.98 ppm). The following abbreviations are used in reporting the multiplicity for NMR resonances: s=single, d=doublet, t= triplet, and m=multiplet. The NMR data were processed using Bruker Topspin 3.5 pl2 and MestReNova 10.0.2.

Low resolution electrospray ionization mass spectrometry LRMS (ESI-MS) experiments were carried out in positive mode with Agilent Technologies LC/MSD Trap SL AGILENT instrument (mobile phase Acetonitrile). MS peak intensity for each analysis is reported as monoisotopic mass and the data were processed with Data Explorer 4.2. Chemicals were purchased from Aldrich, TCI, or Apollo Scientific and used without further purification.

2 Synthesis and Characterization

Compounds **1** has been synthesized and fully characterized (^{1}H NMR, 2D NMR, MS analysis) accordingly to: C. Bravin, E. Badetti, F.A. Scaramuzzo, G. Licini, C. Zonta. *J. Am. Chem. Soc.* **2017**; *139*, 6456-6460.

2.1 General procedure for homo species



To 500 µl (0.5 µmol) of a solution 0.001 M in CD_3CN of cage **1** were added 60 µl (1.2 µmol) of a solution 0.02 M in CD_3CN of a substituted *p*-benzoate triethylammonium salt **2a,2e** in a NMR tube. The mixture was checked *via* ^{1}H NMR (^{1}H NMR yield >95% based on internal standard *p*-xilene).

(2a-2a)@1 ^{1}H NMR (500 MHz, CD_3CN) δ (ppm): 9.37 (d, 6H, *J*=2.0 Hz PyrH), 8.45 (s, 6H, NH_{imm}), 8.43 (dd, 6H, *J*=8.0 Hz, *J*=2.0 Hz, PyrH), 8.14 (d, 4H, *J*=8.0 Hz, ArH-NO_2), 7.91 (d, 12H, *J*=8.5 Hz, ArH), 7.80 (m, 12H, ArH+4H ArH-NO_2), 7.73 (dd, 6H, *J*=8.0 Hz, *J*=2.0 Hz, PyrH), 4.40 (s, 12H, CH_2), 3.93 (s, 12H, CH_{2eda}).
ESI-MS *(m/z)*: $[M]^{2+}$ calcd. for $[C_{98}H_{80}N_{16}O_8Zn_2]^{2+}$, 869.7 found; 869.9.

(2b-2b)@1 ^{1}H NMR (500 MHz, CD_3CN) δ (ppm): 9.33 (d, 6H, *J*=2.0 Hz PyrH), 8.44 (s, 6H, NH_{imm}), 8.38 (dd, 6H, *J*=8.0 Hz, *J*=2.0 Hz, PyrH), 8.06 (m, 4H, *J*=8.0 Hz, ArH-Cl) 7.90 (d, 12H, *J*=8.5 Hz, ArH), 7.73 (m, 12H+4H+6H, ArH; ArH-Cl, PyrH), 4.37 (s, 12H, CH_2), 3.94 (s, 12H, CH_{2eda}).
ESI-MS *(m/z)*: $[M]^{2+}$ calcd. for $[C_{98}H_{80}Cl_2N_{14}O_4Zn_2]^{2+}$, 857.2 found; 857.3.

(2c-2c)@1 ^{1}H NMR (500 MHz, CD_3CN) δ (ppm): 9.33 (d, 6H, *J*=2.0 Hz PyrH), 8.44 (s, 6H, NH_{imm}), 8.39 (dd, 6H, *J*=8.0 Hz, *J*=2.0 Hz, PyrH), 7.99 (m, 4H, *J*=8.0 Hz, ArH-Me), 7.88 (d, 12H, *J*=8.5 Hz, ArH), 7.68 (m, 12H+6H, ArH, PyrH), 6.97 (m, 4H, *J*=8.0 Hz, ArH-Me), 4.37 (s, 12H, CH_2), 3.94 (s, 12H, CH_{2eda}). *p*-Me proton of **2c** are hidden by water peak.

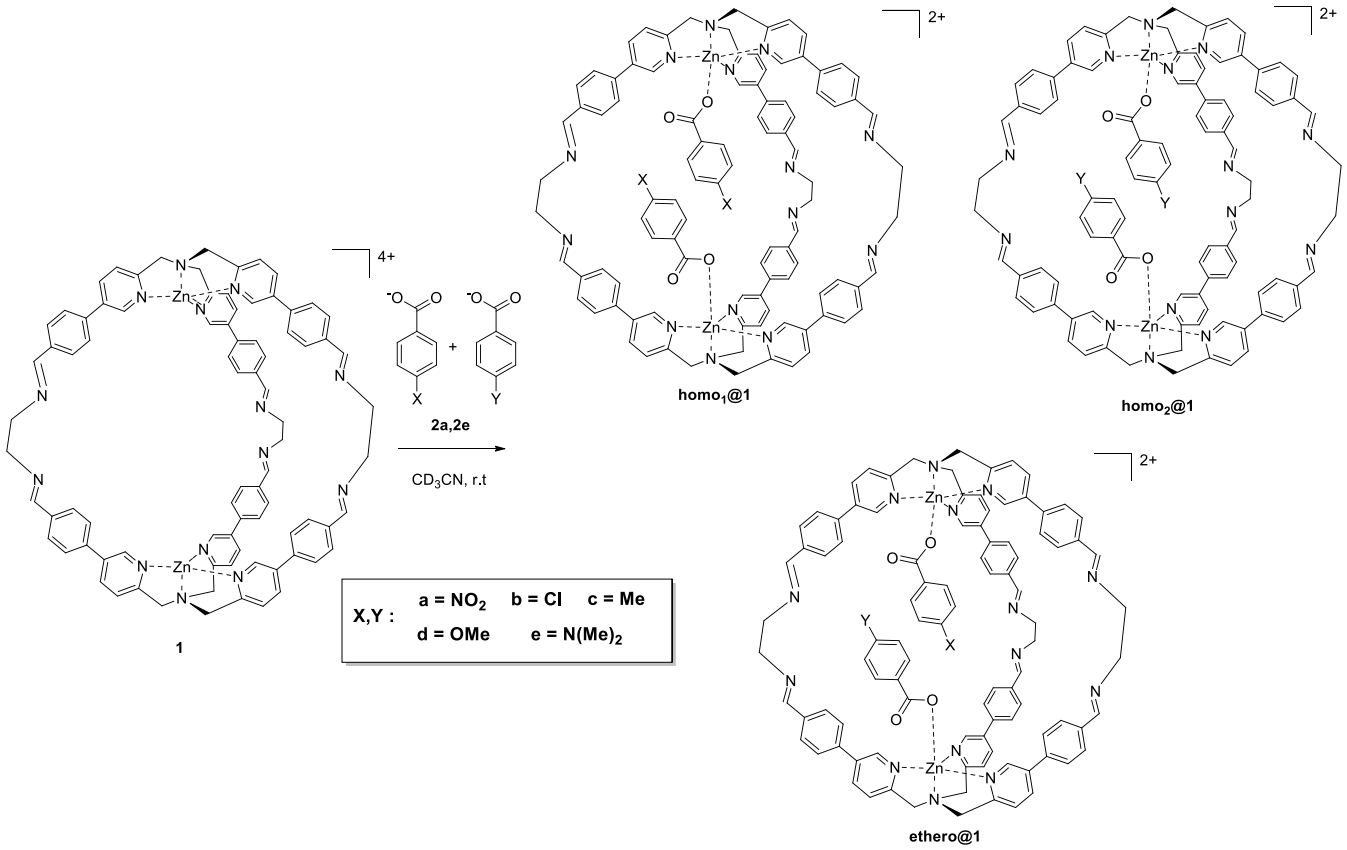
ESI-MS *(m/z)*: $[M]^{2+}$ calcd. for $[C_{100}H_{86}N_{14}O_4Zn_2]^{2+}$, 839.3 found; 839.5.

(2d-2d)@1 ^{1}H NMR (500 MHz, CD_3CN) δ (ppm): 9.33 (d, 6H, *J*=2.0 Hz PyrH), 8.44 (s, 6H, NH_{imm}), 8.39 (dd, 6H, *J*=8.0 Hz, *J*=2.0 Hz, PyrH), 7.99 (m, 4H, ArH-OMe) 7.89 (d, 12H, *J*=8.5 Hz, ArH), 7.68 (m, 12H, ArH+6H PyrH), 6.97 (m, 4H, ArH-OMe), 4.37 (s, 12H, CH_2), 3.94 (s, 12H, CH_{2eda}). *p*-OMe proton of **2d** are hidden by water peak.
ESI-MS *(m/z)*: $[M]^{2+}$ calcd. for $[C_{100}H_{86}N_{14}O_6Zn_2]^{2+}$, 853.3 found; 853.2

(2e-2e)@1 ^{1}H NMR (500 MHz, CD_3CN) δ (ppm): 9.40 (d, 6H, *J*=2.0 Hz PyrH), 8.45 (s, 6H, NH_{imm}), 8.38 (dd, 6H, *J*=8.0 Hz, *J*=2.0 Hz, PyrH), 7.97 (m, 4H, ArH-$N(Me)_2$) 7.90 (d, 12H, *J*=8.5 Hz, ArH), 7.71 (m, 12H, ArH+6H PyrH), 6.50 (m, 4H, ArH-$N(Me)_2$), 4.39 (s, 12H, CH_2), 3.93 (s, 12H, CH_{2eda}). *p*-NMe_2 proton of **2e** are hidden by water peak.
ESI-MS *(m/z)*: $[M]^{2+}$ calcd. for $[C_{102}H_{92}N_{16}O_4Zn_2]^{2+}$, 866.3 found; 866.1

(HexA-HexA)@1 ^{1}H NMR (500 MHz, CD_3CN) δ (ppm): 9.21 (d, 6H, *J*=2.0 Hz PyrH), 8.45 (s, 6H, NH_{imm}), 8.35 (dd, 6H, *J*=8.0 Hz, *J*=2.0 Hz, PyrH), 7.94 (d, 12H, *J*=8.5 Hz, ArH), 7.76 (d, 12H, *J*=8.5 Hz, ArH), 7.76 (d, 6H, *J*=8.0 Hz, PyrH), 4.33 (s, 12H, CH_2), 3.96 (s, 12H, CH_{2eda}), 1.39 (m, 4H, $CH_{2\beta}$, HexA), 0.74 (m, 8H, $CH_{2\gamma}$, $CH_{2\delta}$, HexA). $CH_{2\alpha}$ of **HexA** are hidden by solvent peak.
ESI-MS *(m/z)*: $[M]^{2+}$ calcd. for $[C_{96}H_{94}N_{14}O_4Zn_2]^{2+}$, 819.3 found; 819.4

2.2 General Procedure for Competition Experiment



To 500 µl (0.5 µmol) of a solution 0.001 M of cage **1** (based on *p*-xylene standard) in CD_3CN, 20 µl (0.24 µmol) of a solution 0.012 M in CD_3CN of *p*-xylene were added. Then 10 µl (0.1 µmol) of a 0.01 M mixed solution of two guests of the series **2a,2e** were introduced. The mixture was monitored with ^1H NMR.

3 Results and Discussion

3.1 ^{1}H NMR determination of Binding Stoichiometry and Binding constant along the titration points for (2a-2a)@1

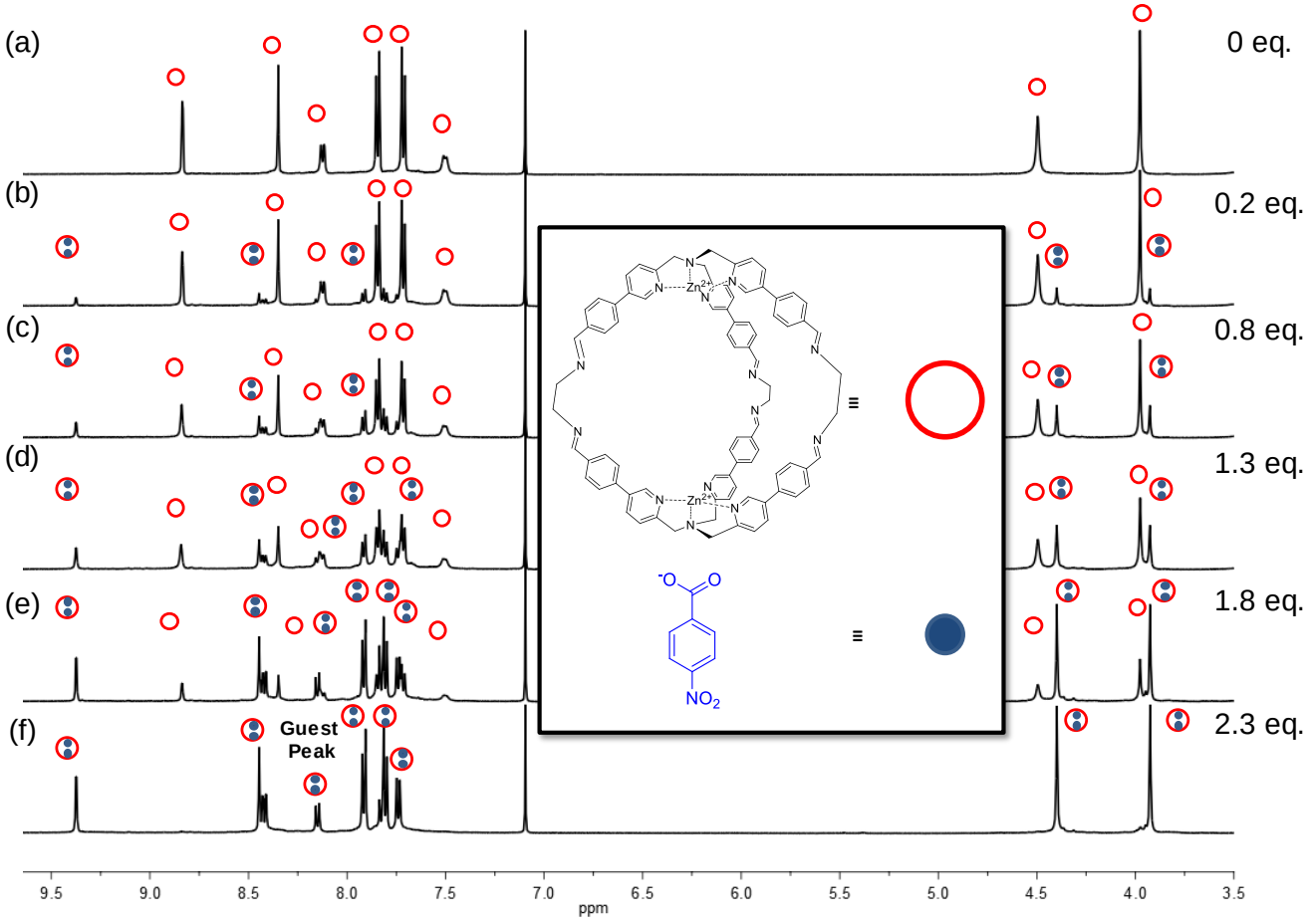


Figure S1 ^{1}H NMR inclusion experiments. Addition of *p*-Nitrobenzoate **2a** to cage **1** in CD_3CN. (a) Preformed cage **1** (0.001 M cage).(b)-(f) Addition of sub-stoichiometric amounts (0.2-1.8 equiv) of **2a** results in the formation of a new species which could be attributed to 1:2 H:G complex. (f) Addition of 2.3 equiv of **2a** totally shift the system to the new species **(2a-2a)@1** Counter anions are perchlorates.

The determination of binding stoichiometry was possible thanks to the integration of the signals of the pyridine ring α proton of the filled cage **(2a-2a)@1** and a guest signal. It results a 1:2 ratio H:G binding. The overall equilibrium constant for formation of the 1:2 complex (K1•K2) was determined (42 ± 4) x 10^6 M^{-2}

3.2 Identification of 1:1 and 1:2 binding species for HexA

The evidence for a 1:1 adduct were recorded in the case of mono carboxylate guest with lower binding constant in as example for triethylammonium hexanoate **HexA**. In this case are reported the ^{1}H NMR titration in which is highlighted the formation of the 1:1 and 1:2 Host:Guest (H:G) species in the region between 8.0 and 9.5 ppm corresponding to the α-proton pyridine ring of the cage for **HexA** (Figure S2 and Figure S3).

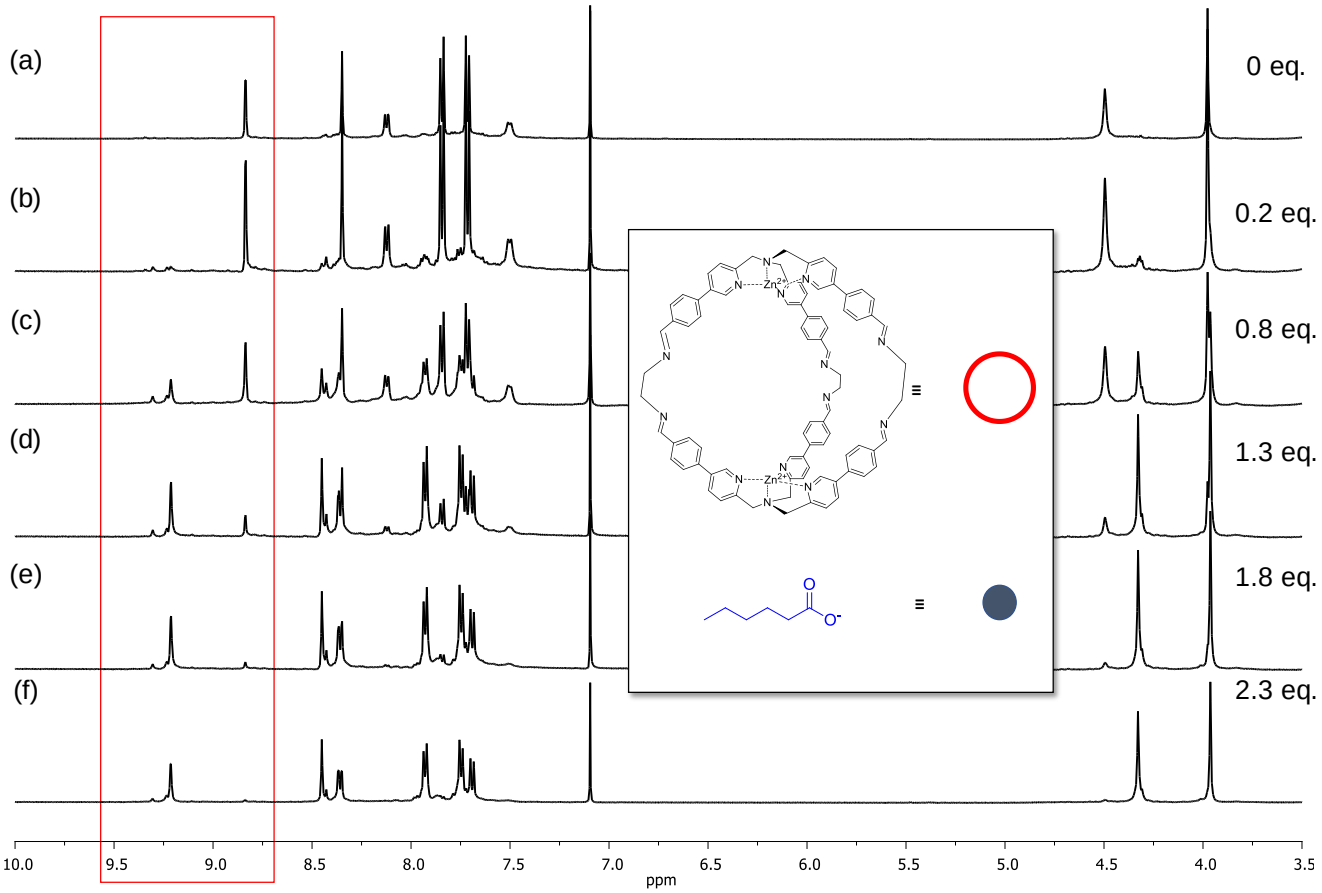


Figure S2 ^{1}H NMR inclusion experiments with Hexanoate **HexA**. Counter anions are perchlorates

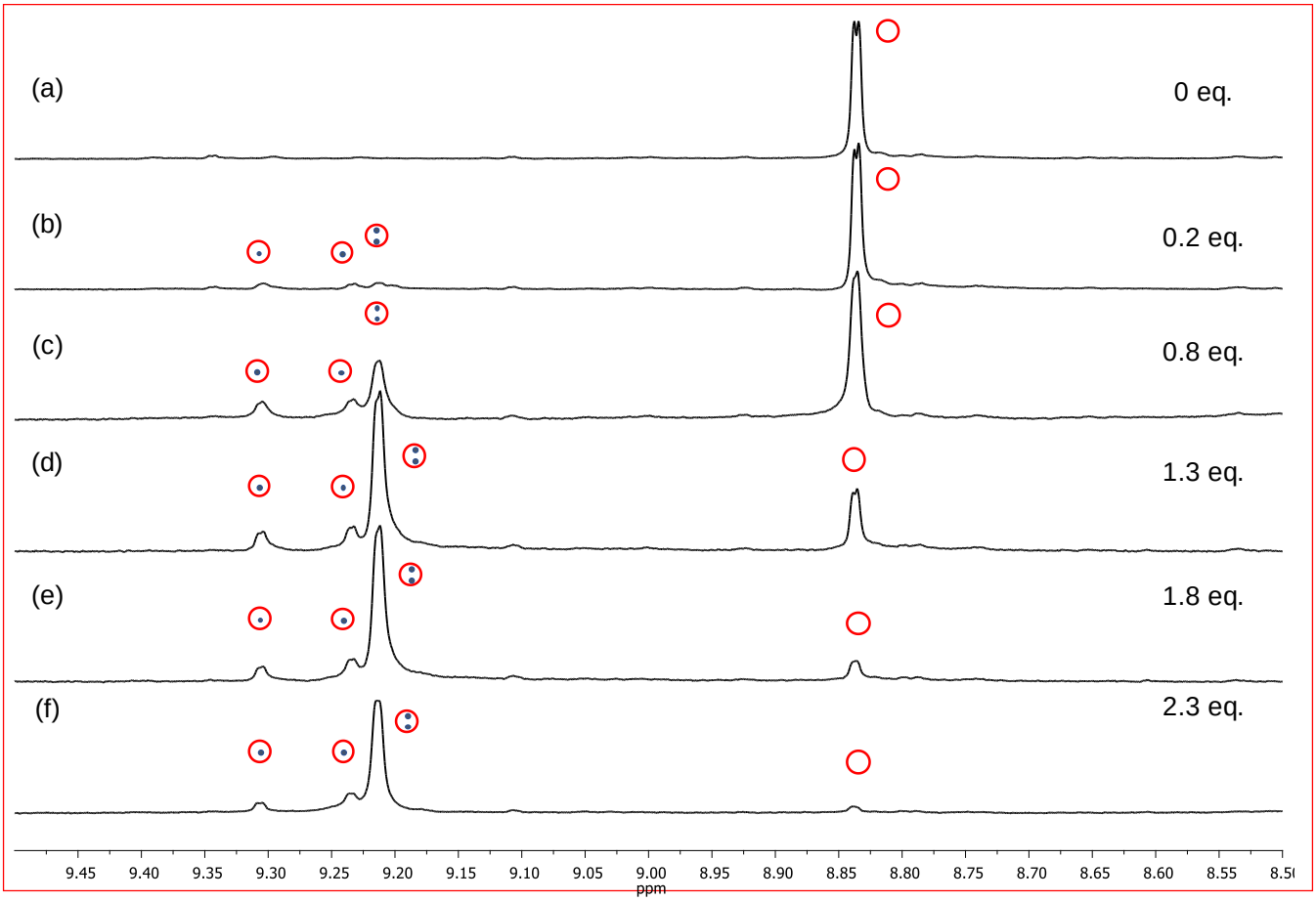


Figure S3 ^{1}H NMR inclusion experiments with hexanoate **HexA**. The characteristic region of the α-proton pyridine ring of cage **1** and **HexA@1** or **(HexA-HexA)@1**

The binding constant values for **HexA** in 1:1 (K_1) and 1:2 (K_2) are respectively 1093±203 $M^{-1}$and 8513±1055 M^{-1}. The resulting product of the two binding event (K_b=K_1 * K_2) corresponds to (11.75±0.76) * 10^6 M^{-2}.

3.3 ^{1}H NMR of α-pyridin proton ring of filled cages in competition experiments

The ^{1}H ROESY spectrum for the competition between guests **2a** and **2e** with the magnified range of interest is displayed in Figure S4. It is possible to notice the cross peak correlation between the hetero filled species **(2a-2e)@1** and the homo species **(2a-2a)@1** and **(2e-2e)@1** allowing the full assignment of each species in solution.

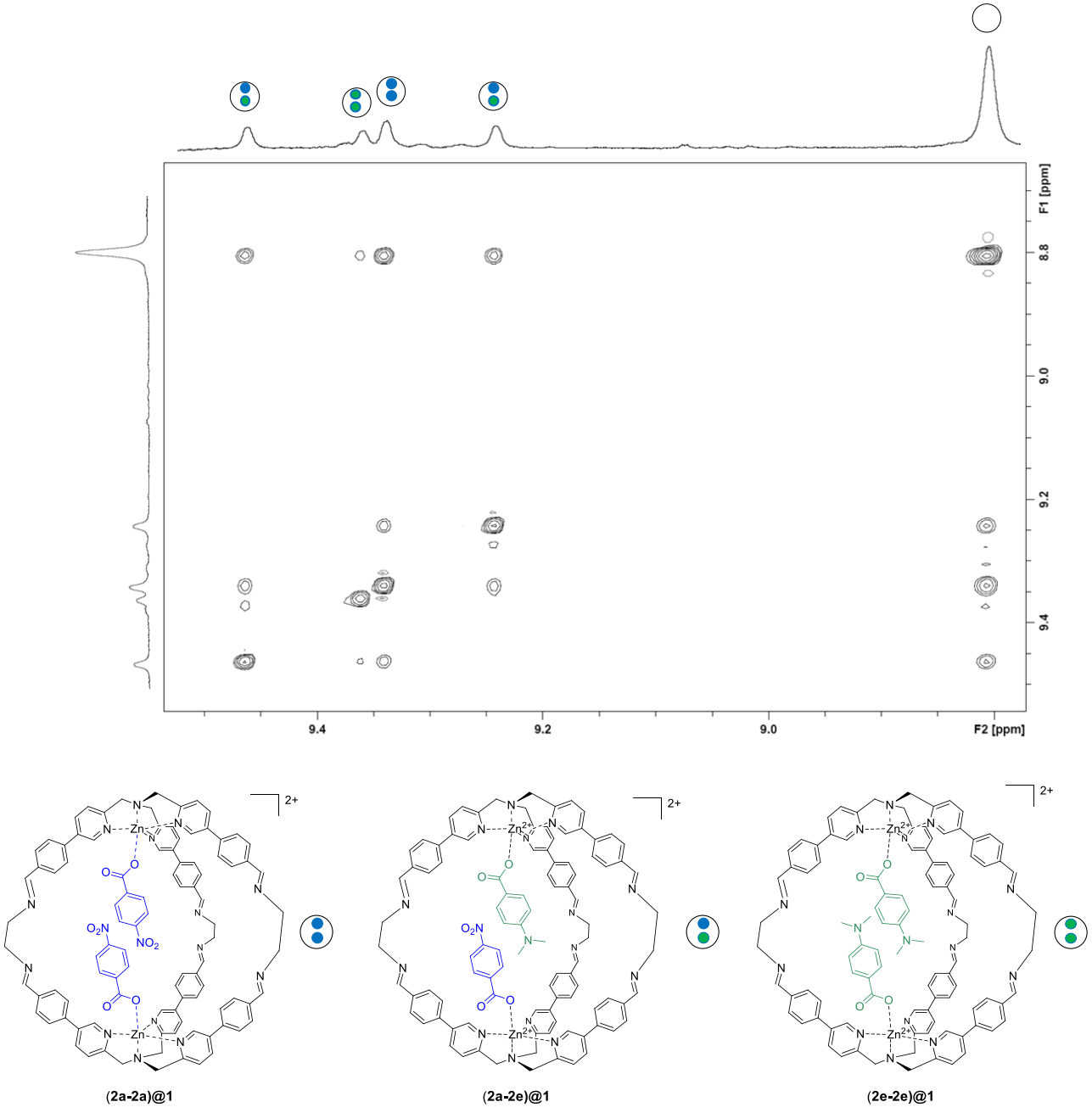
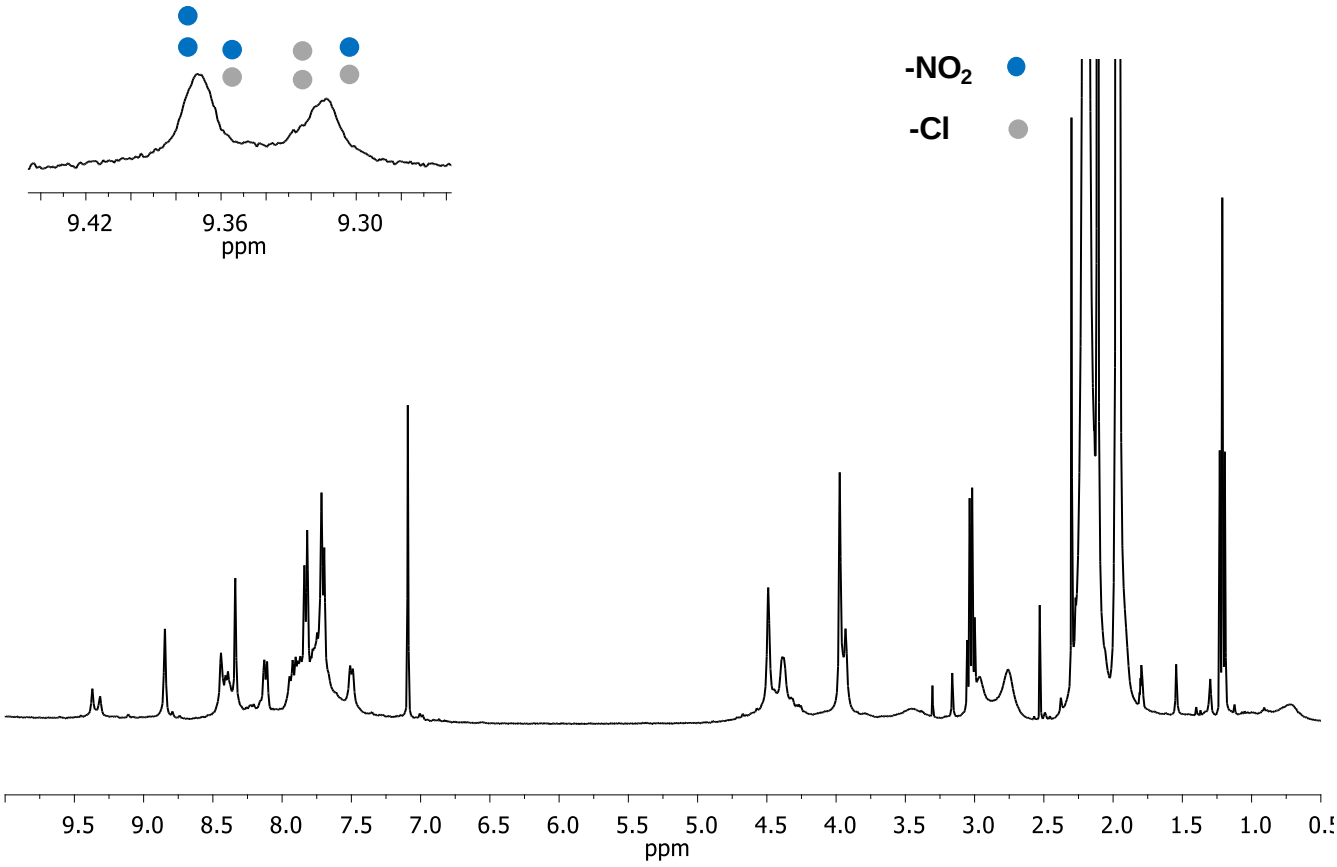


Figure S4 ^{1}H ROESY for the competition experiment between guests **2a** and **2e**.

The ^{1}H NMR spectra for each competition with the magnified range of interest for the binding constant determination are displayed in Figure S5. The magnified region between 9.5 and 9.0 ppm is related to the α proton of the pyridine ring of the filled cage at guests ratio 1:1. The coloured dots represent the guests contained within the cage in each competition experiment.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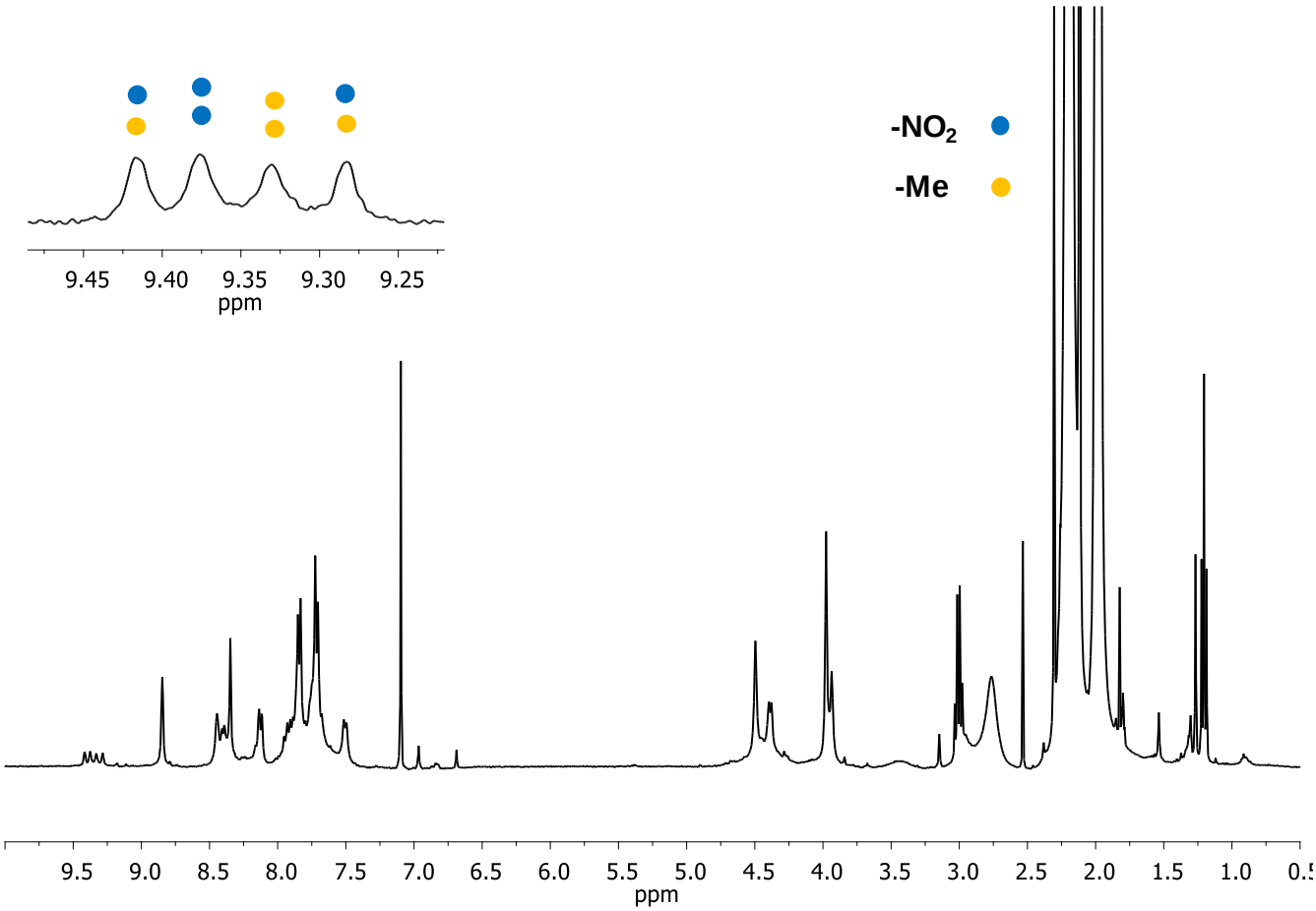
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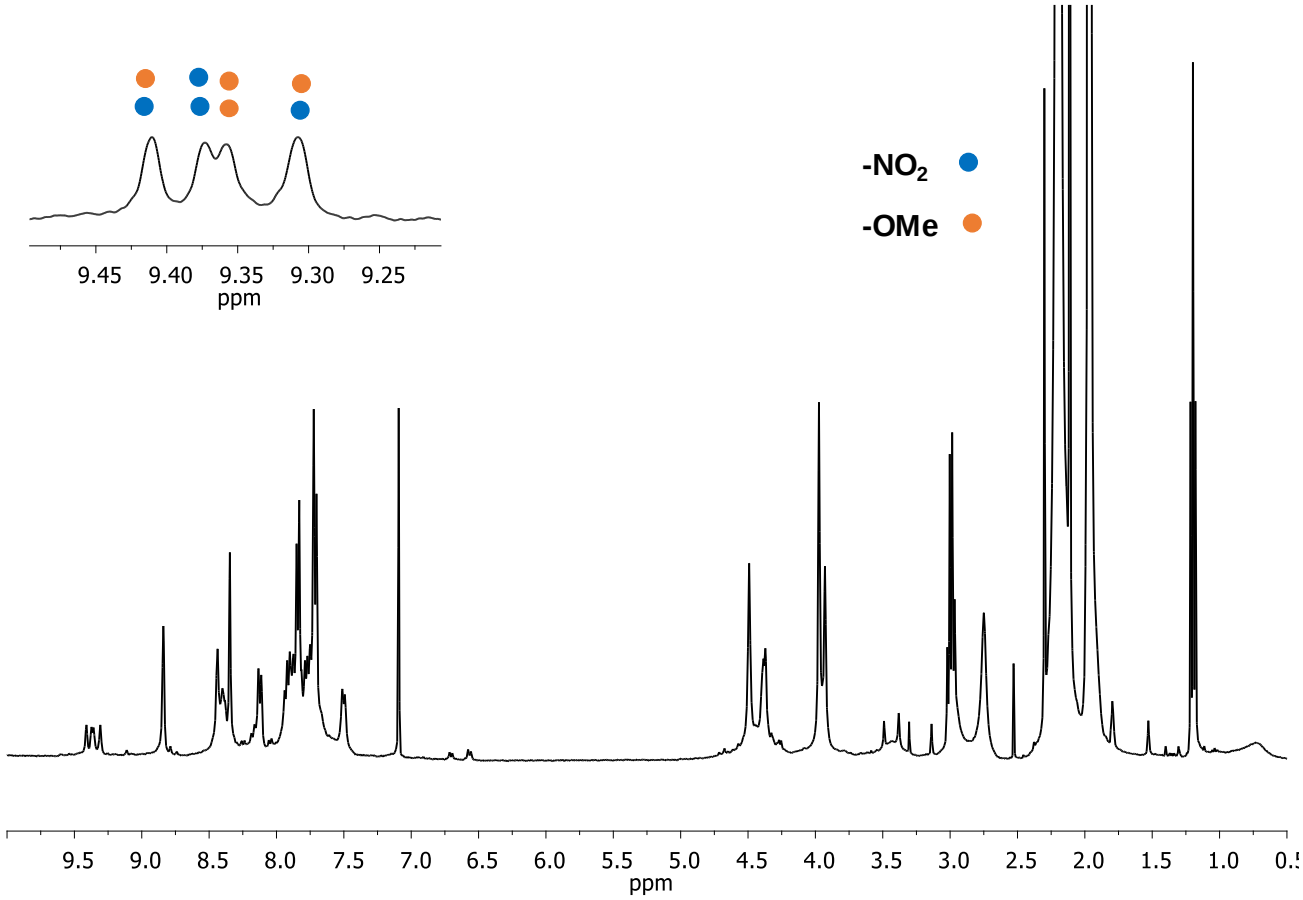
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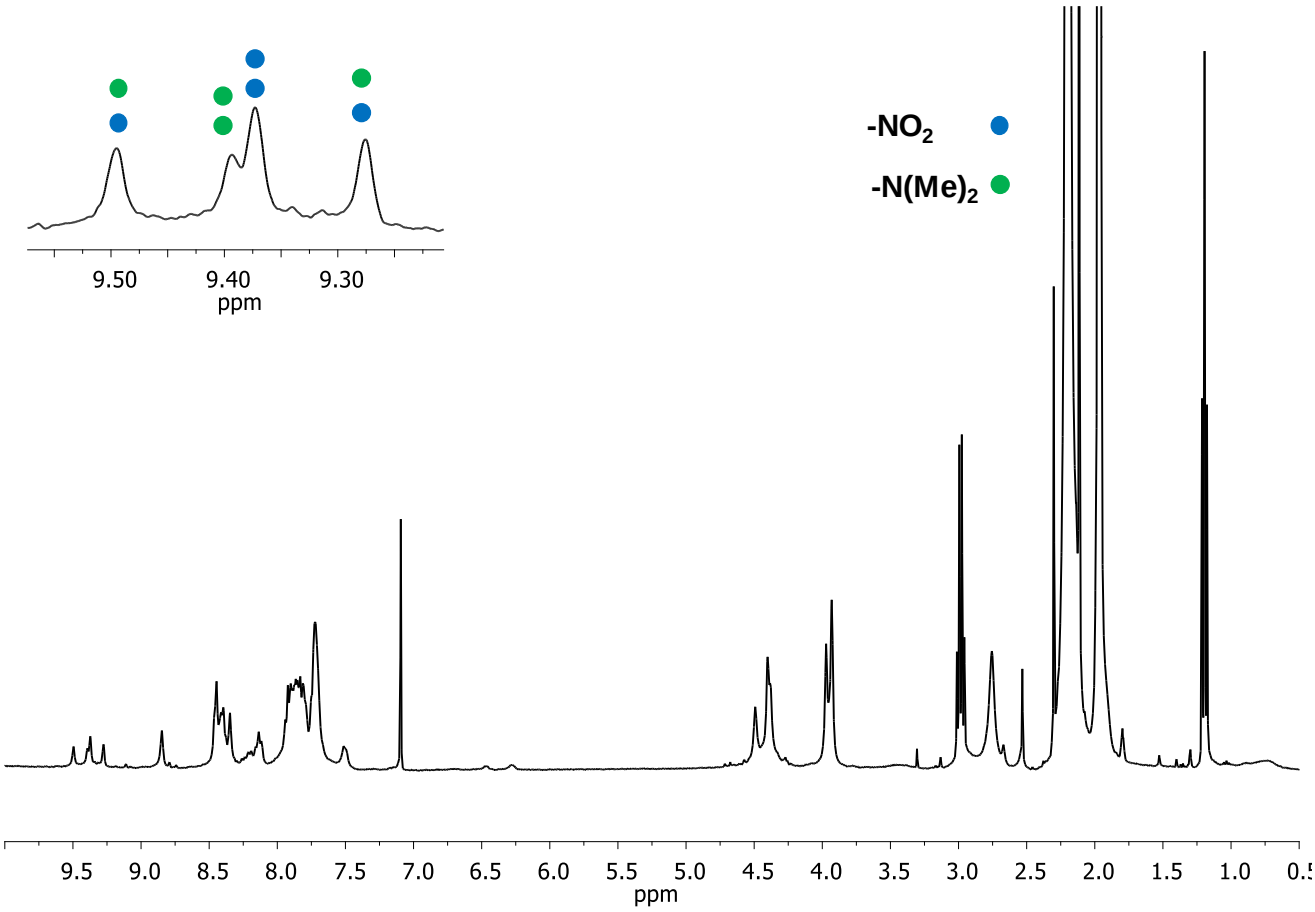
ppm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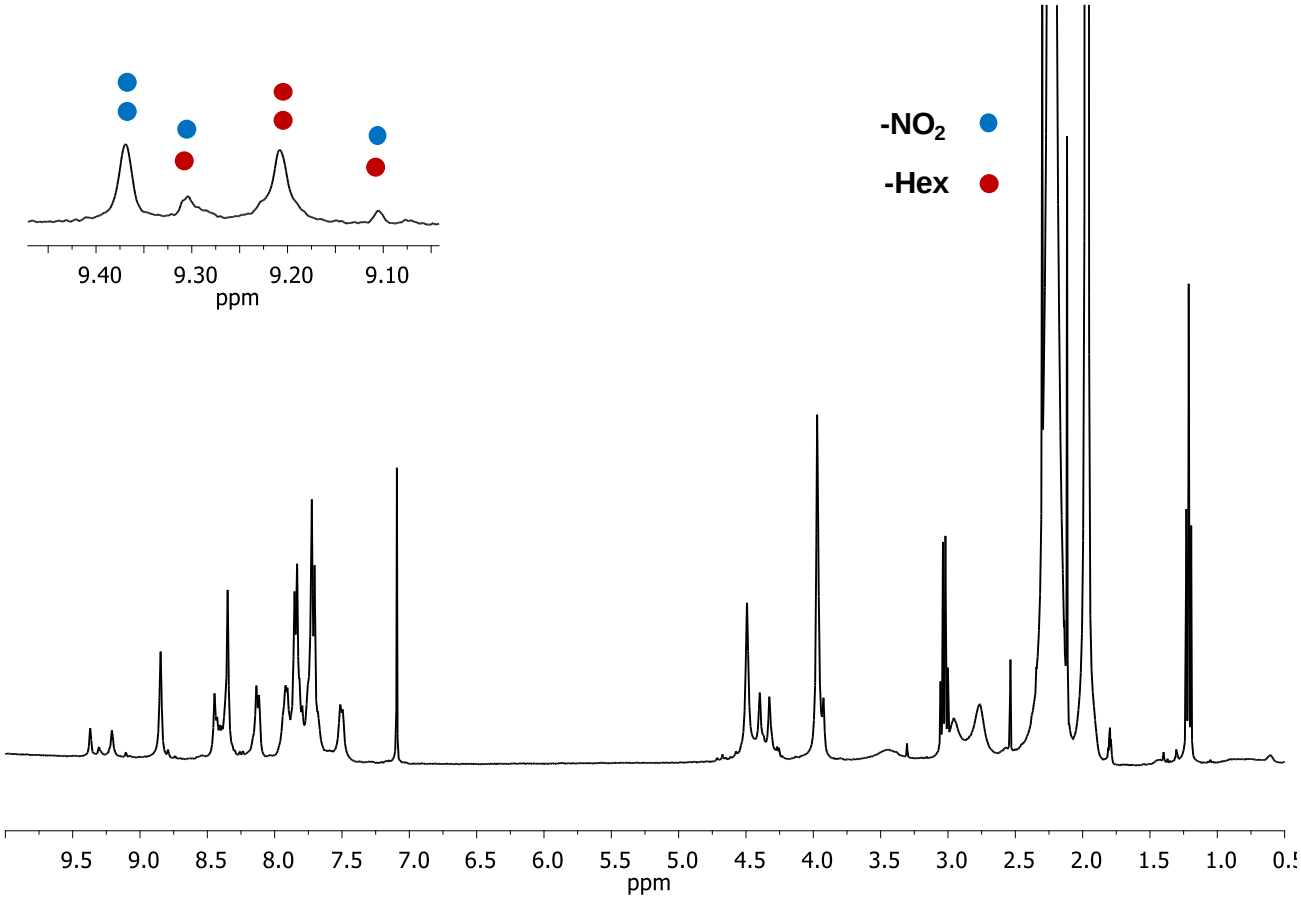
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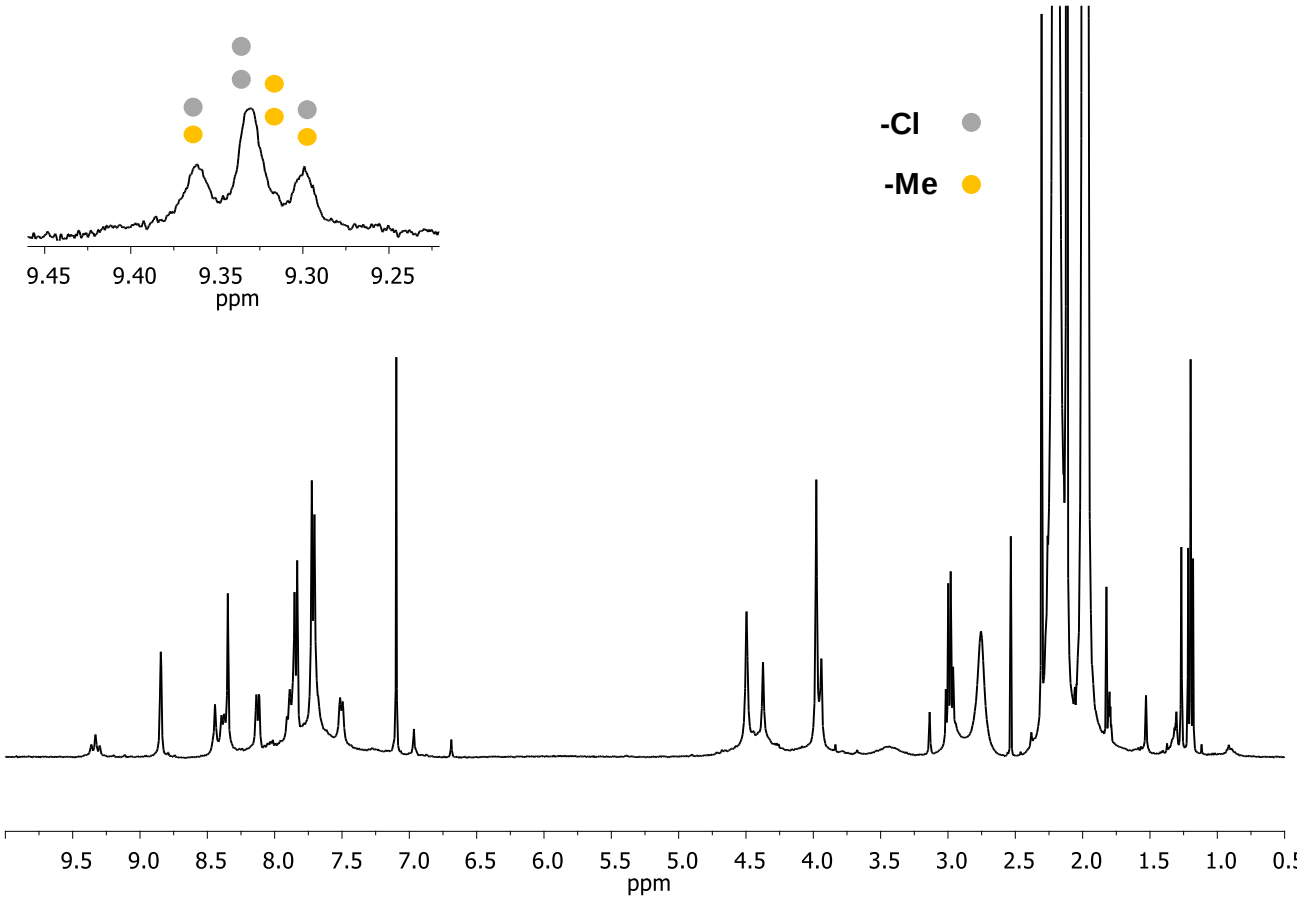
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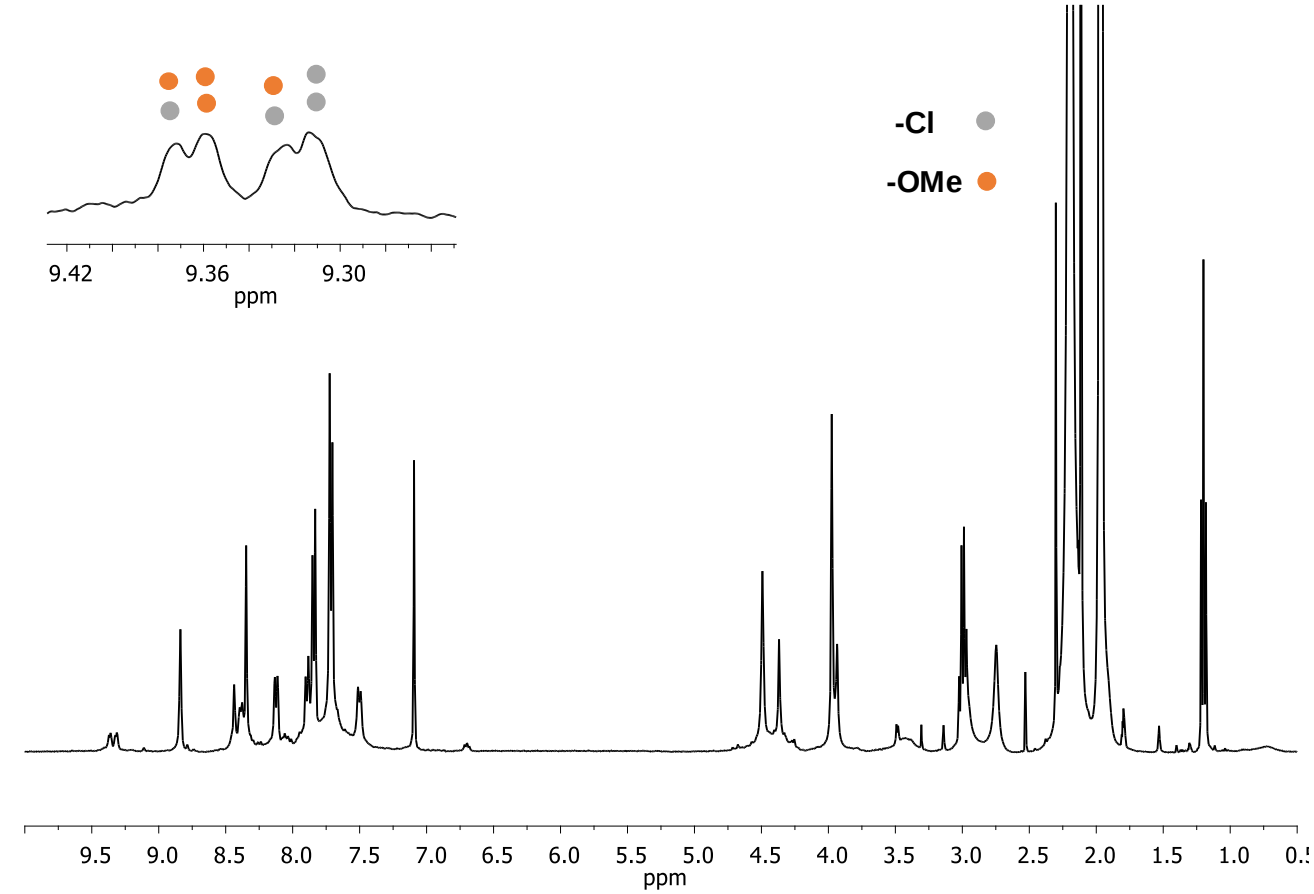
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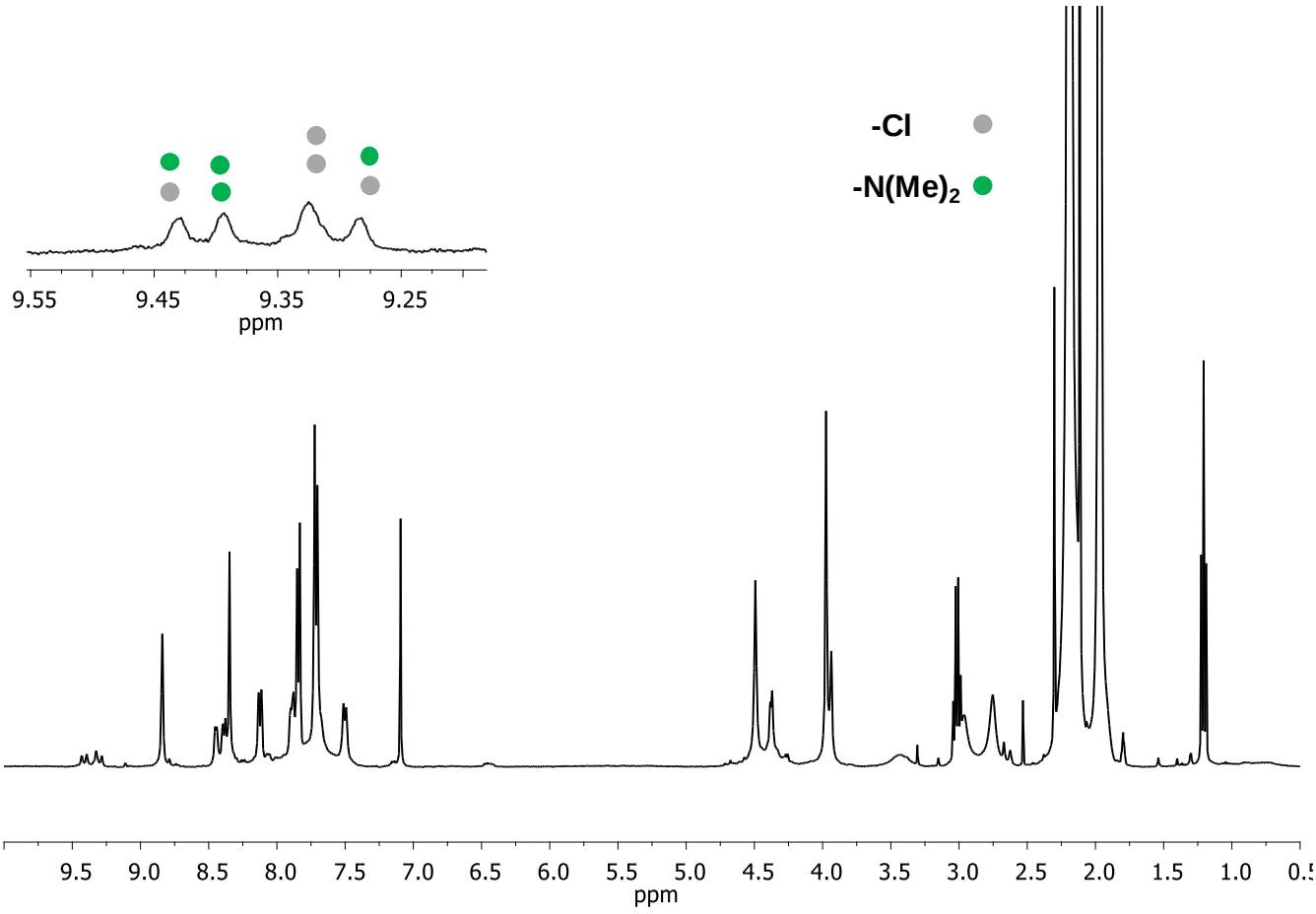
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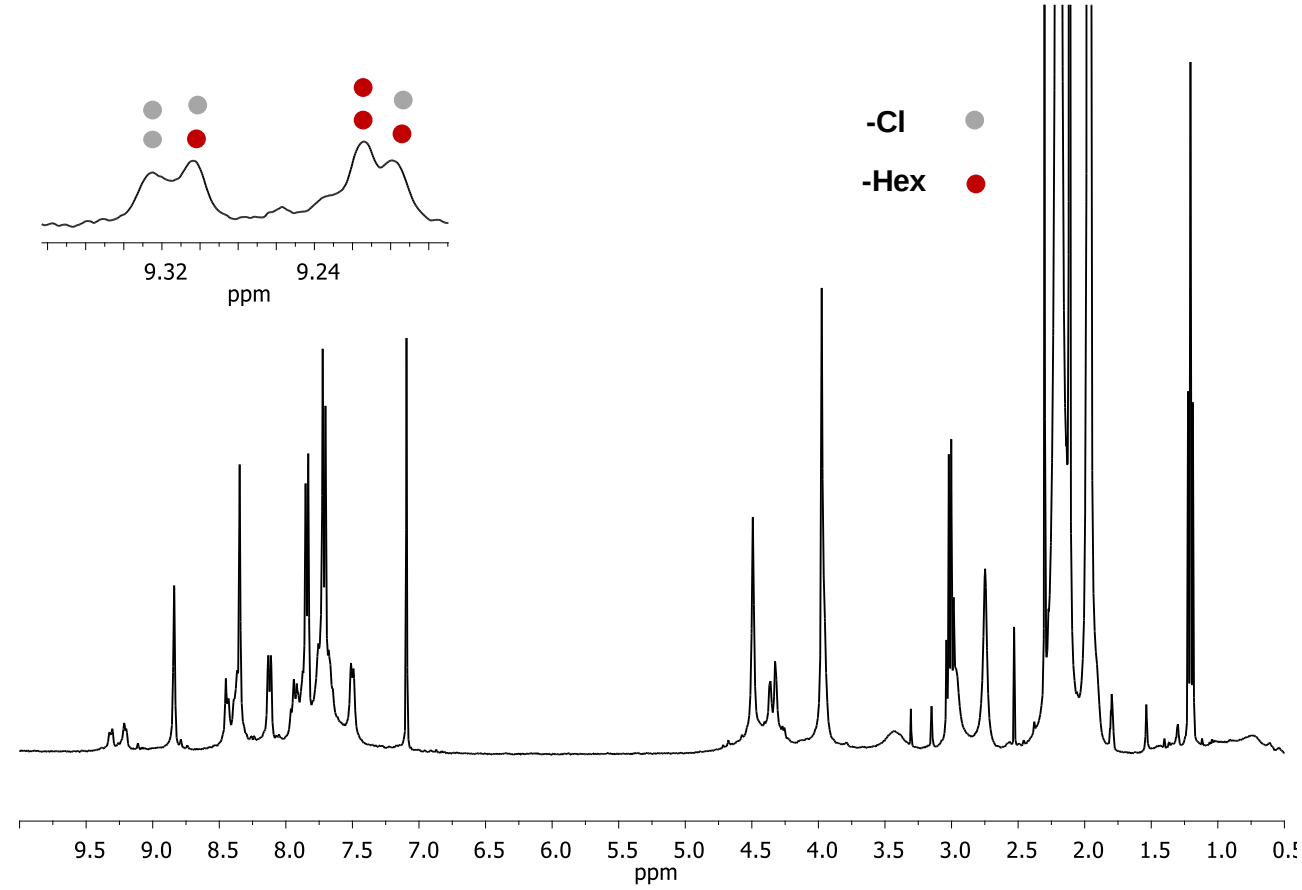
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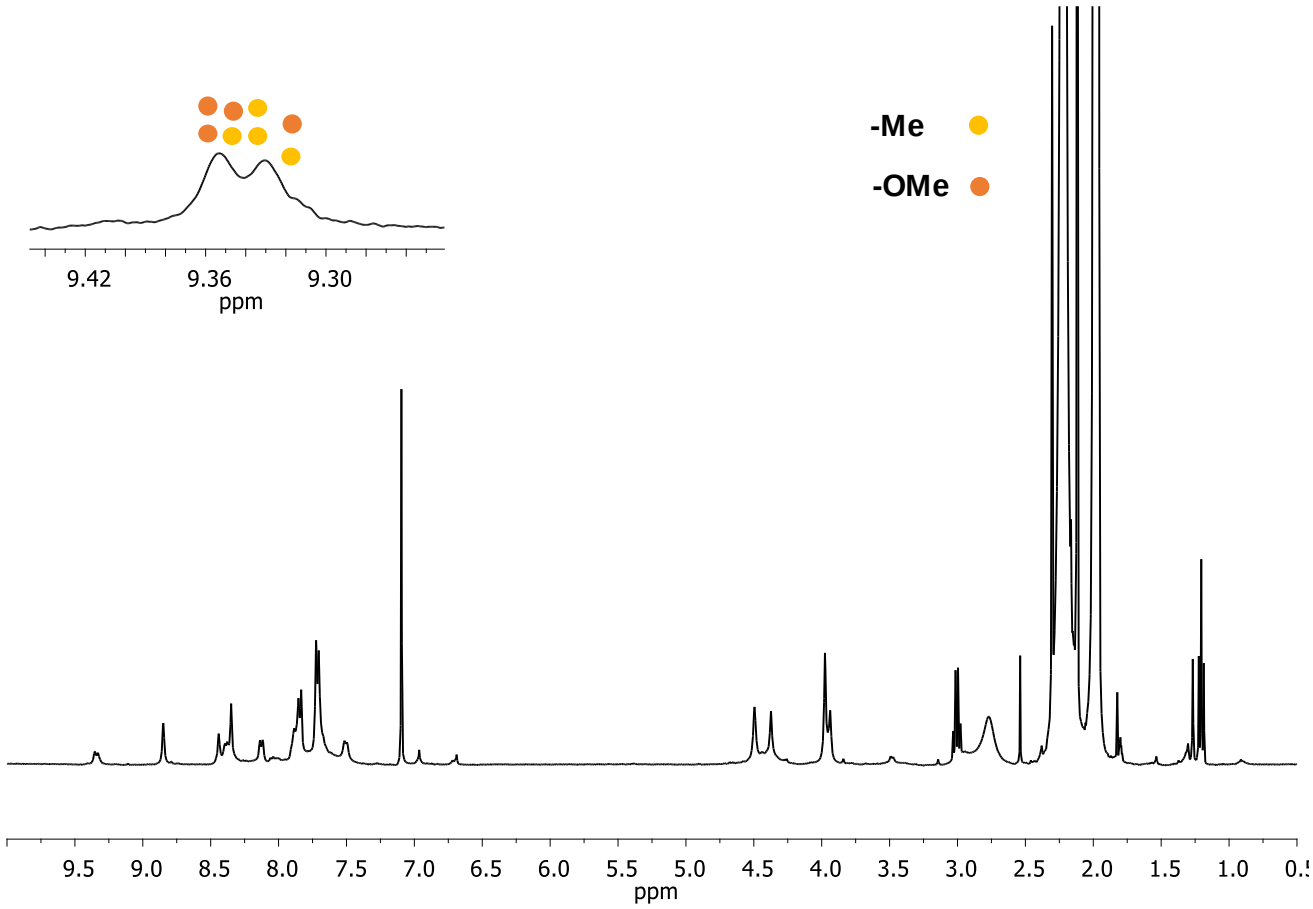
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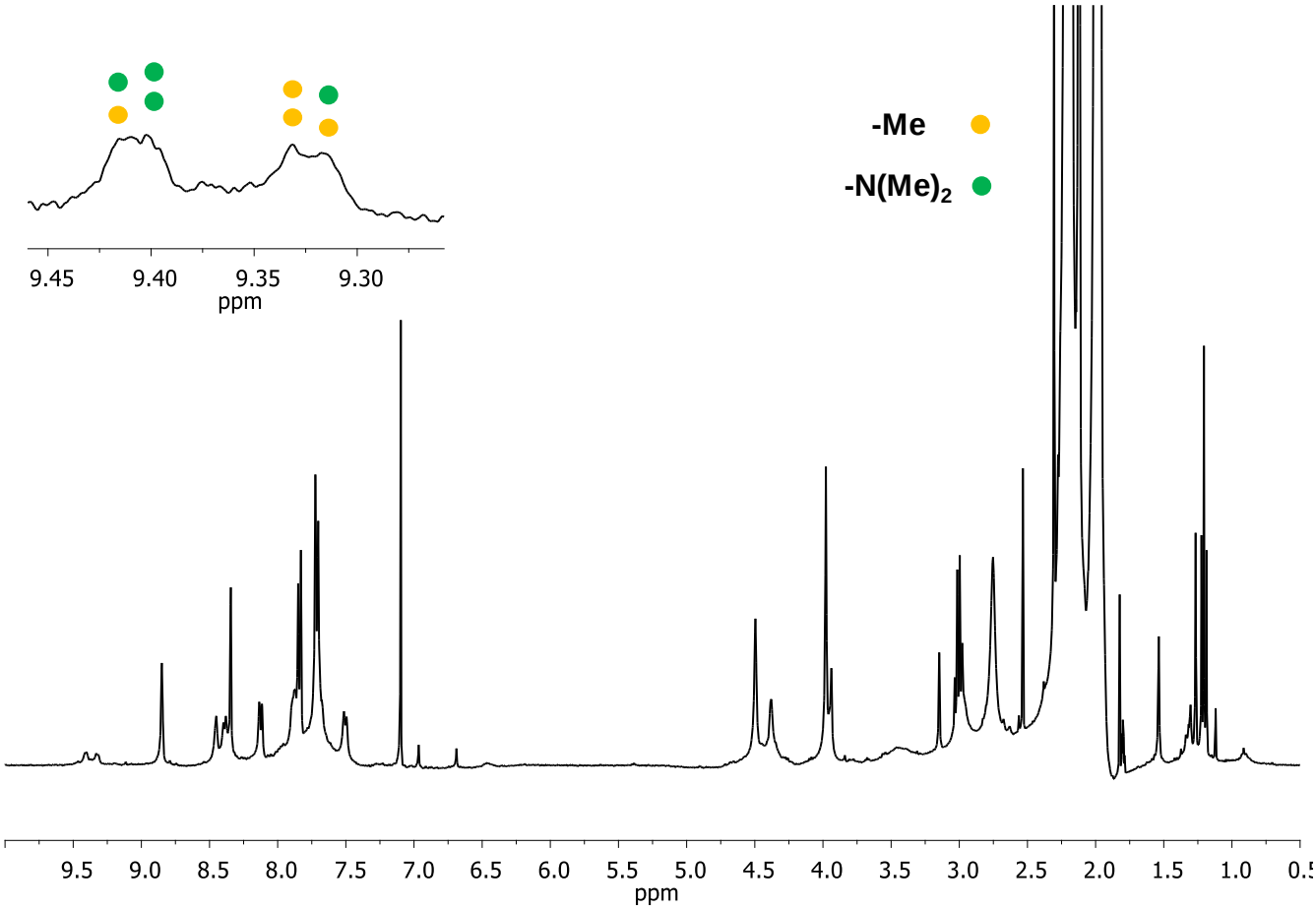
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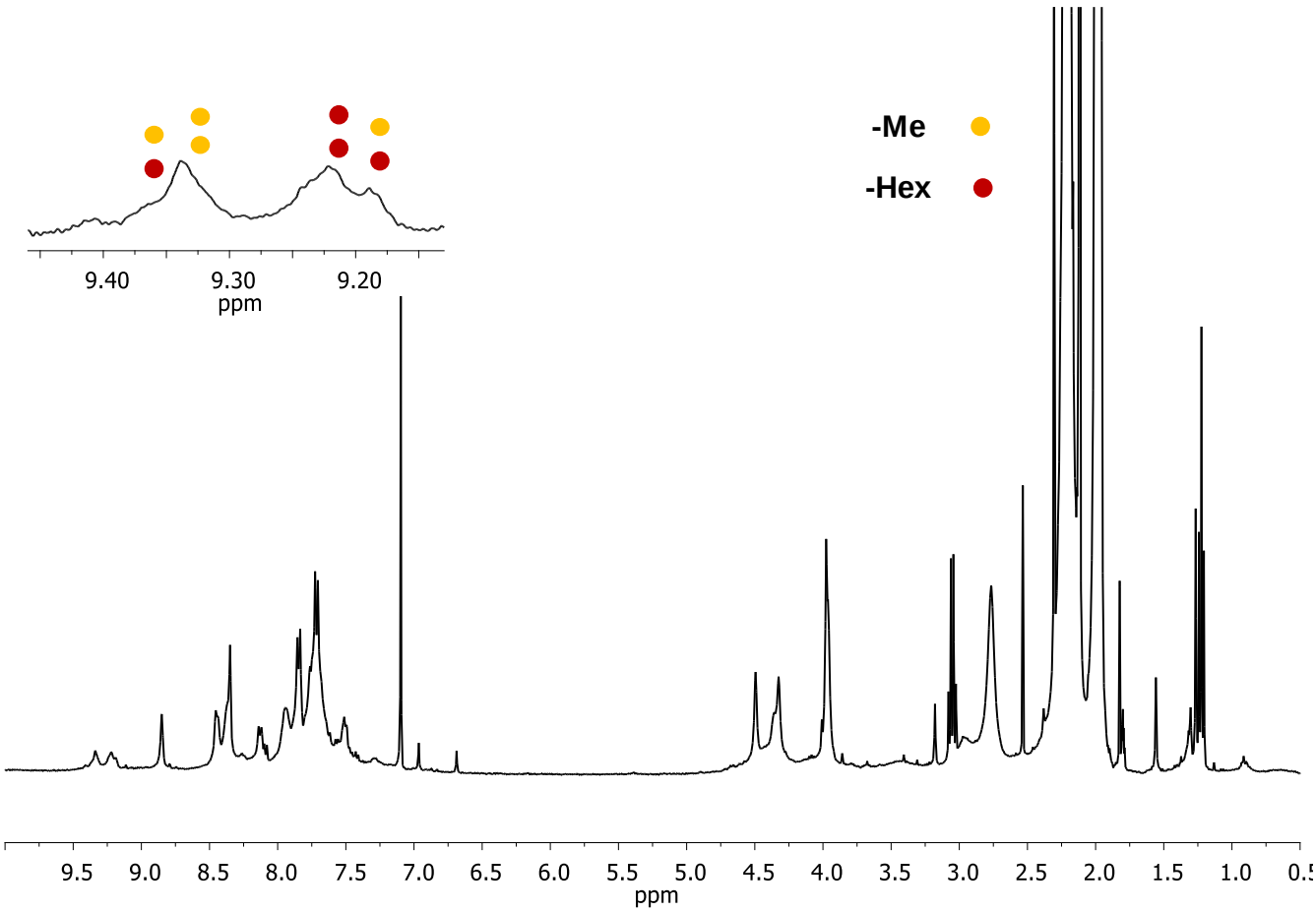
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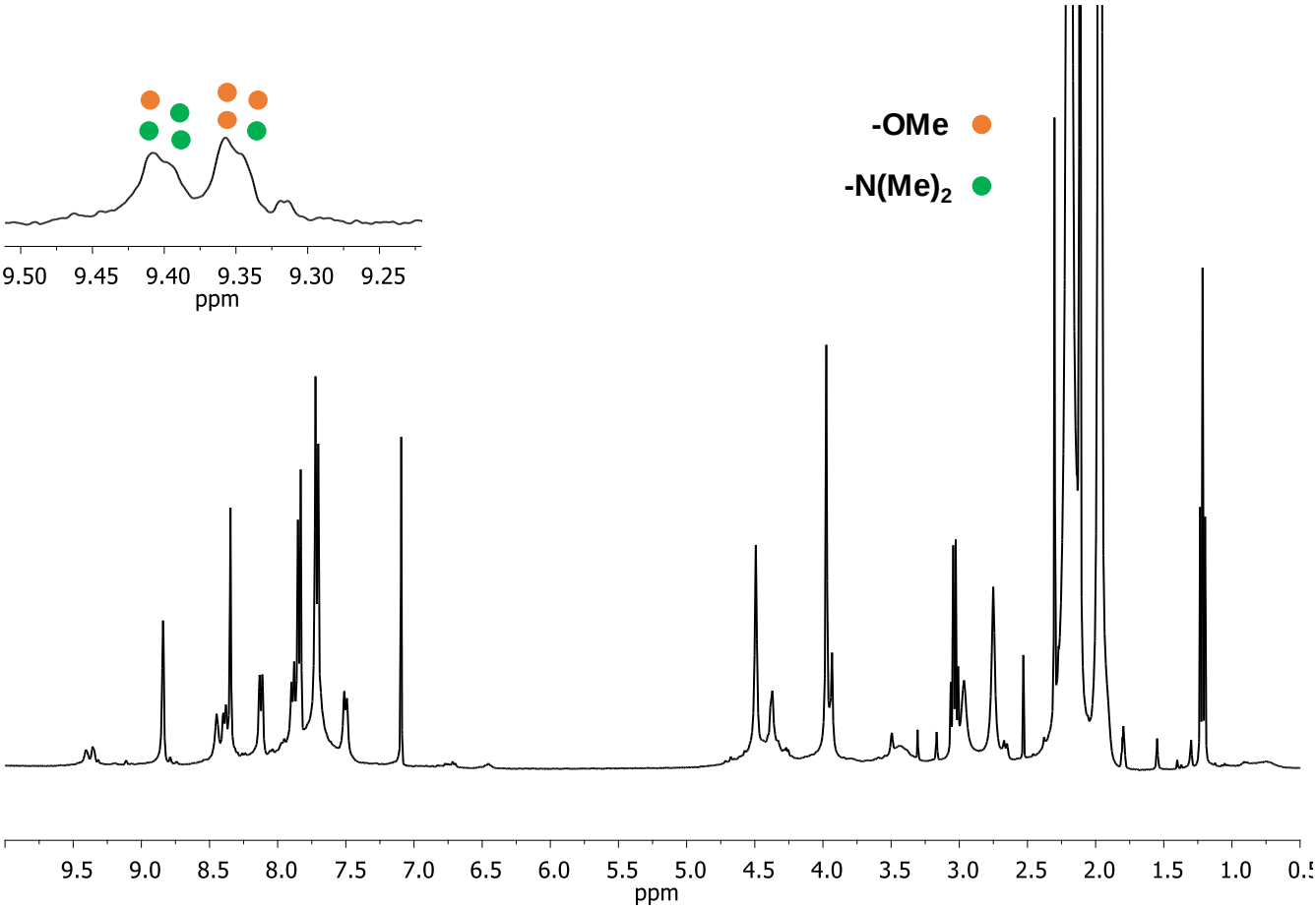
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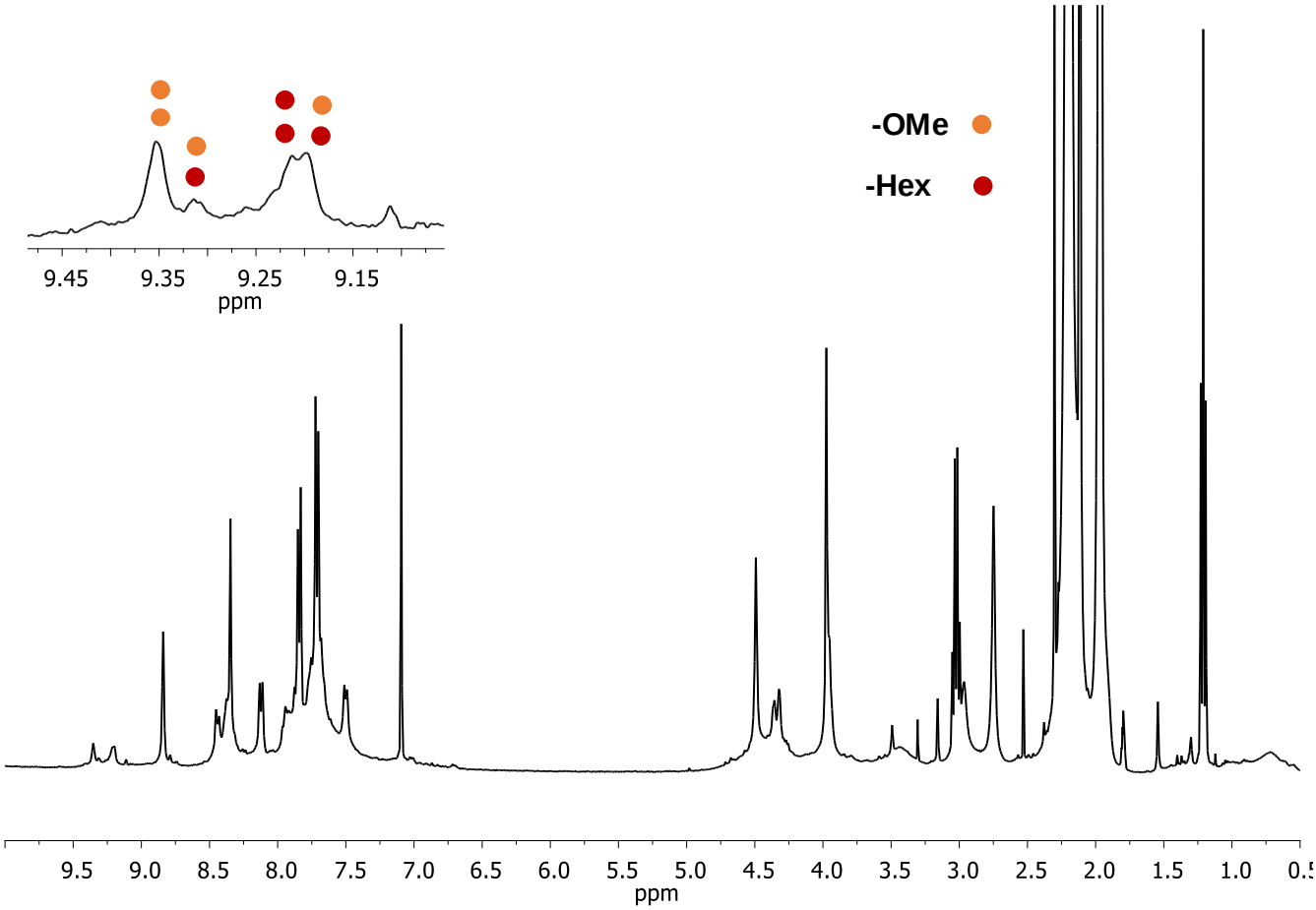
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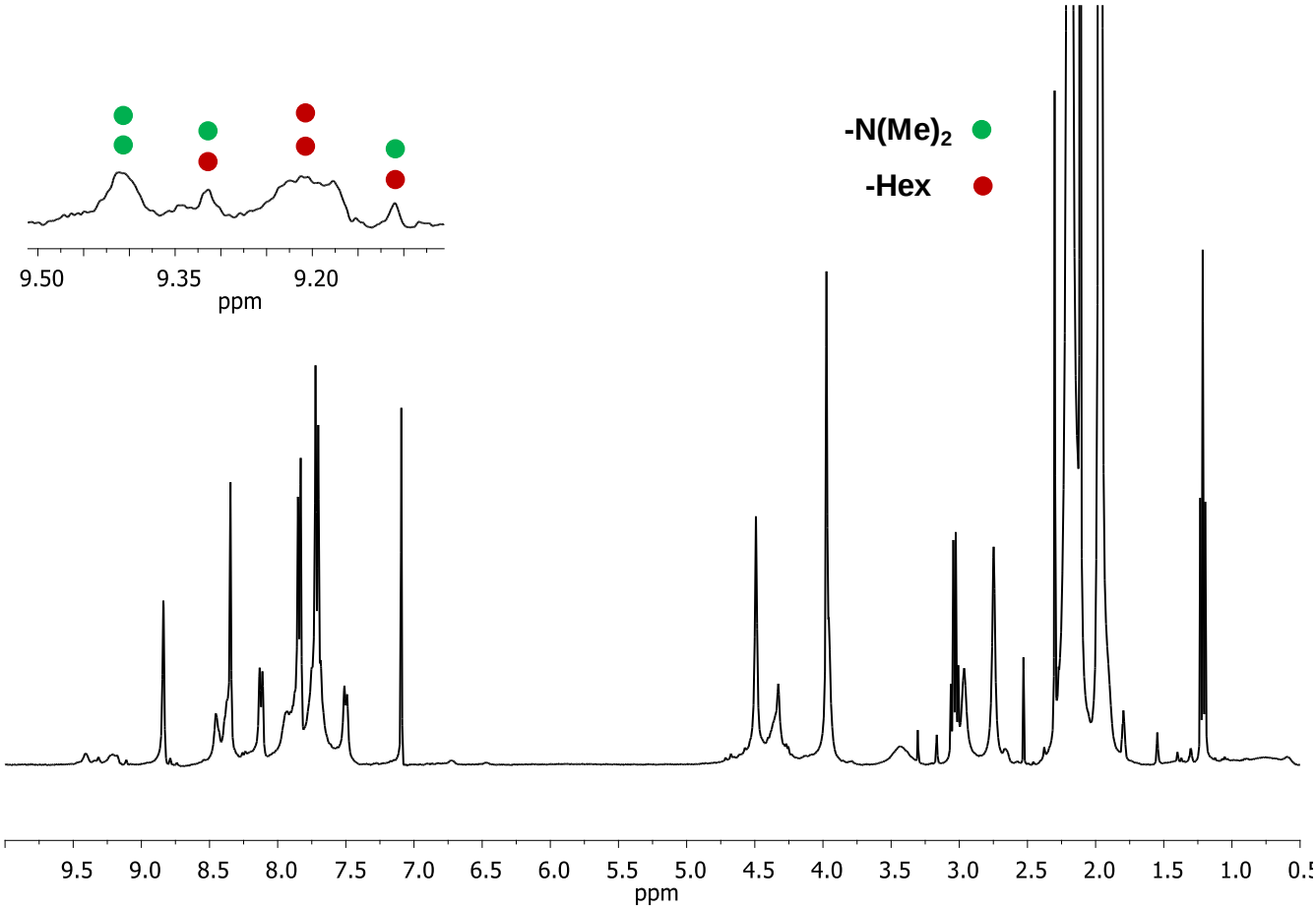
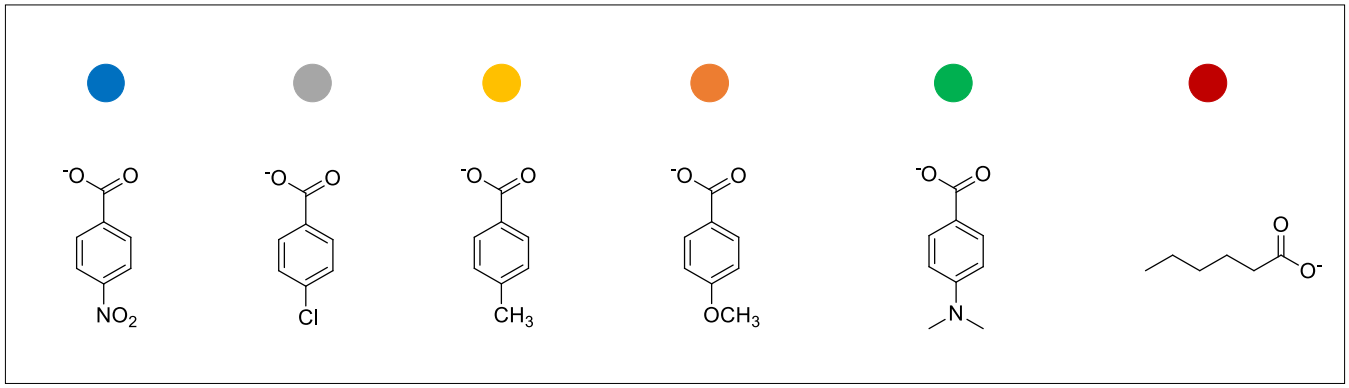


Figure S5 ^{1}H NMR experiment for the competition experiment of all possible combination of guests **2a,2e**. The guest are described as in the legend below



3.4 Binding constant determination of the homo and hetero co-encapsulated species and ^{1}H NMR of α-pyridin proton ring of filled cages in competition experiments

By the integration of each peak related to the filled species and the cage **1** (Table S1) is possible to determine the binding constant for each homo by each competition experiment species (Table S2). The integrals are defined *via* fitting of the characteristic peaks when partial overlap is present. Then is possible to obtain the binding constant for the hetero species which are reported in Table S3. The integral peaks are referred to internal standard *p*-xylene and their values are reported with the error calculated repeating the experiments three times. The binding constants obtained for the homo species for each competition experiment agree with the values reported by the titration experiments.

The method adopted for binding constant determination is based on the following procedure.

Total cage concentration in solution [H_0] is known and verified with the internal standard (*p*-xylene). Due to slow exchange is possible to integrate the distinct signals related to: free host (I_H), homo encapsulated cages ($I_{AA@H}$ and $I_{BB@H}$) and hetero encapsulated cage ($I_{AB@H}$) as shown in Figure S6 for the case of guest A= 4-nitrobenzoate **2a** and B= 4-dimethylaminobenzoate **2e**. No signals of the 1:1 inclusion species were detected, therefore they were not taken into account in the model.

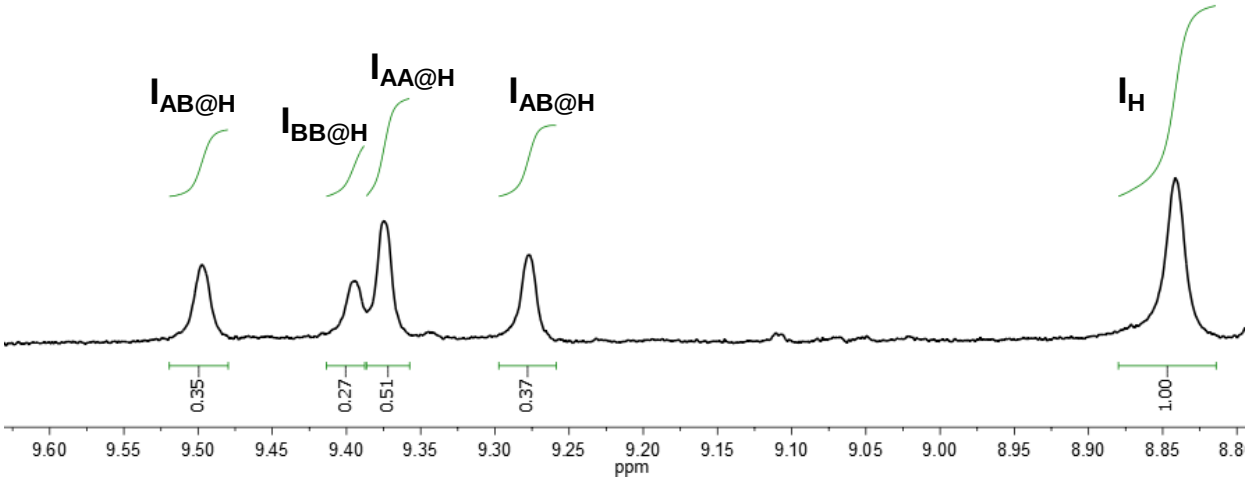


Figure S6. Integration of the signals related to homo and hetero cages formed during the competition experiment between guests **2a** and **2e**.

Knowing that:

$[H_0] = [H] + [AA@H] + [BB@H] + [AB@H]$

concentrations are calculated using equations (1-4):

$$[H] = \frac{I_H}{(I_{AA@H} + I_{BB@H} + I_{AB@H} + I_H)} \cdot [H_0] \qquad (1)$$

$$[AA@H] = \frac{I_{AA@H}}{(I_{AA@H} + I_{BB@H} + I_{AB@H} + I_H)} \cdot [H_0] \qquad (2)$$

$$[BB@H] = \frac{I_{BB@H}}{(I_{AA@H} + I_{BB@H} + I_{AB@H} + I_H)} \cdot [H_0] \qquad (3)$$

$$[AB@H] = \frac{I_{AB@H}}{(I_{AA@H} + I_{BB@H} + I_{AB@H} + I_H)} \cdot [H_0] \qquad (4)$$

Free carboxylates concentrations [A] and [B] are obtained by difference from the known $[A_0]$ and $[B_0]$ taking into account the stoichiometry of the included complexes with equations (5) and (6):

$$[A] = [A_0] - \{2 \cdot [AA@H] + [AB@H]\} \qquad (5)$$

$$[B] = [B_0] - \{2 \cdot [BB@H] + [AB@H]\} \qquad (6)$$

Binding constant for the Host-Guest 1:2 species formed are obtained with equations (7-9) for homo (K_{AA} and K_{BB}) and hetero (K_{AB}), taking into account of a statistical factor 2 for the formation of the hetero species.

$$K_{AA} = \frac{[AA@H]}{[A]^2 \cdot [H]} \qquad (7)$$

$$K_{BB} = \frac{[BB@H]}{[B]^2 \cdot [H]} \qquad (8)$$

$$K_{AB} = \frac{[AB@H]}{[A] \cdot [B] \cdot [H]} \cdot \frac{1}{2} \qquad (9)$$

Integral Values

Competition Experiment	Guest X	Guest Y	Integral value of Homo species (X-X)	Integral value of Homo species (Y-Y)	Integral value of Hetero species (X-Y)	Integral value of Cage 1
1	NO_2	Cl	0.172±0.011	0.161±0.021	0.166±0.025	0.904±0.042
2	NO_2	Me	0.145±0.013	0.124±0.016	0.221±0.021	0.773±0.032
3	NO_2	OMe	0.174±0.012	0.137±0.011	0.316±0.024	0.988±0.041
4	NO_2	$N(Me)_2$	0.152±0.020	0.077±0.013	0.304±0.024	0.911±0.024
5	NO_2	HexA	0.211±0.018	0.152±0.020	0.227±0.020	1.052±0.032
6	Cl	Me	0.111±0.015	0.105±0.022	0.158±0.016	0.637±0.024
7	Cl	OMe	0.157±0.026	0.123±0.012	0.204±0.017	0.847±0.033
8	Cl	$N(Me)_2$	0.128±0.015	0.082±0.022	0.228±0.022	0.852±0.026
9	Cl	HexA	0.142±0.012	0.118±0.008	0.181±0.018	0.809±0.025
10	Me	OMe	0.118±0.024	0.144±0.026	0.218±0.018	0.913±0.028
11	Me	$N(Me)_2$	0.112±0.018	0.068±0.011	0.163±0.012	0.778±0.024
12	Me	HexA	0.115±0.017	0.102±0.015	0.159±0.012	0.824±0.027
13	OMe	$N(Me)_2$	0.132±0.012	0.093±0.017	0.187±0.013	0.847±0.029
14	OMe	HexA	0.137±0.016	0.124±0.011	0.228±0.013	0.933±0.026
15	$N(Me)_2$	HexA	0.126±0.017	0.118±0.016	0.243±0.011	0.938±0.030

Table S1 Integral values obtained for each competition experiment related to the filled cage specie

Binding constant for homo species obtained by competition experiment

Competition Experiment	Guest X	Guest Y	Binding constant for the Homo species (X-X) ($1*10^6$ M^{-2})	Binding constant for the Homo species (Y-Y) ($1*10^6$ M^{-2})	Binding constant for the Hetero species (X-Y) ($1*10^6$ M^{-2})
1	NO_2	Cl	43.76±4.63	24.52±2.44	27.63±2.42
2	NO_2	Me	42.94±4.31	18.78±2.33	26.27±2.13
3	NO_2	OMe	47.29±4.01	12.99±1.25	25.00±1.09
4	NO_2	$N(Me)_2$	43.00±4.24	4.96±1.2	20.34±0.20
5	NO_2	HexA	40.23±4.42	8.53±1.98	11.48±2.86
6	Cl	Me	26.87±2.58	17.00±1.33	16.30±3.63
7	Cl	OMe	23.60±2.44	9.81±1.01	13.65±0.24
8	Cl	$N(Me)_2$	23.46±2.11	4.62±0.87	11.74±2.79
9	Cl	HexA	21.27±2.19	11.04±1.08	10.63±3.23
10	Me	OMe	17.83±2.13	10.95±1.00	13.82±0.82
11	Me	$N(Me)_2$	18.44±2.01	4.23±0.67	8.05±0.22
12	Me	HexA	19.56±1.66	11.88±1.11	10.60±1.58
13	OMe	$N(Me)_2$	15.64±1.78	4.73±1.02	7.55±0.99
14	OMe	HexA	15.90±1.33	8.99±0.77	10.61±2.58
15	$N(Me)_2$	HexA	5.89±1.11	9.90±0.86	10.98±0.44

Table S2 Binding constant values obtained in each competition experiment for the homo species and hetero species considering the integral valued reported in Table S1

Binding constant values from all the experiments for Homo and Hetero species

Guest X / Guest Y	NO_2	Cl	Me	OMe	$N(Me)_2$	HexA
NO_2	40.96±2.49					
Cl	27.63±2.42	22.09±2.30				
Me	26.27±2.13	16.30±3.63	16.00±2.25			
OMe	25.00±1.09	13.65±0.24	13.82±0.82	10.89±2.24		
$N(Me)_2$	20.34±0.20	11.74±2.79	8.05±0.22	7.55±0.99	5.28±1.30	
HexA	11.48±2.86	10.63±3.23	10.60±1.58	10.61±2.58	10.98±0.44	10.17±0.76

Table S3 Binding constant values obtained by competition and titration experiment. The values are expressed as ($1*10^6$ M^{-2})

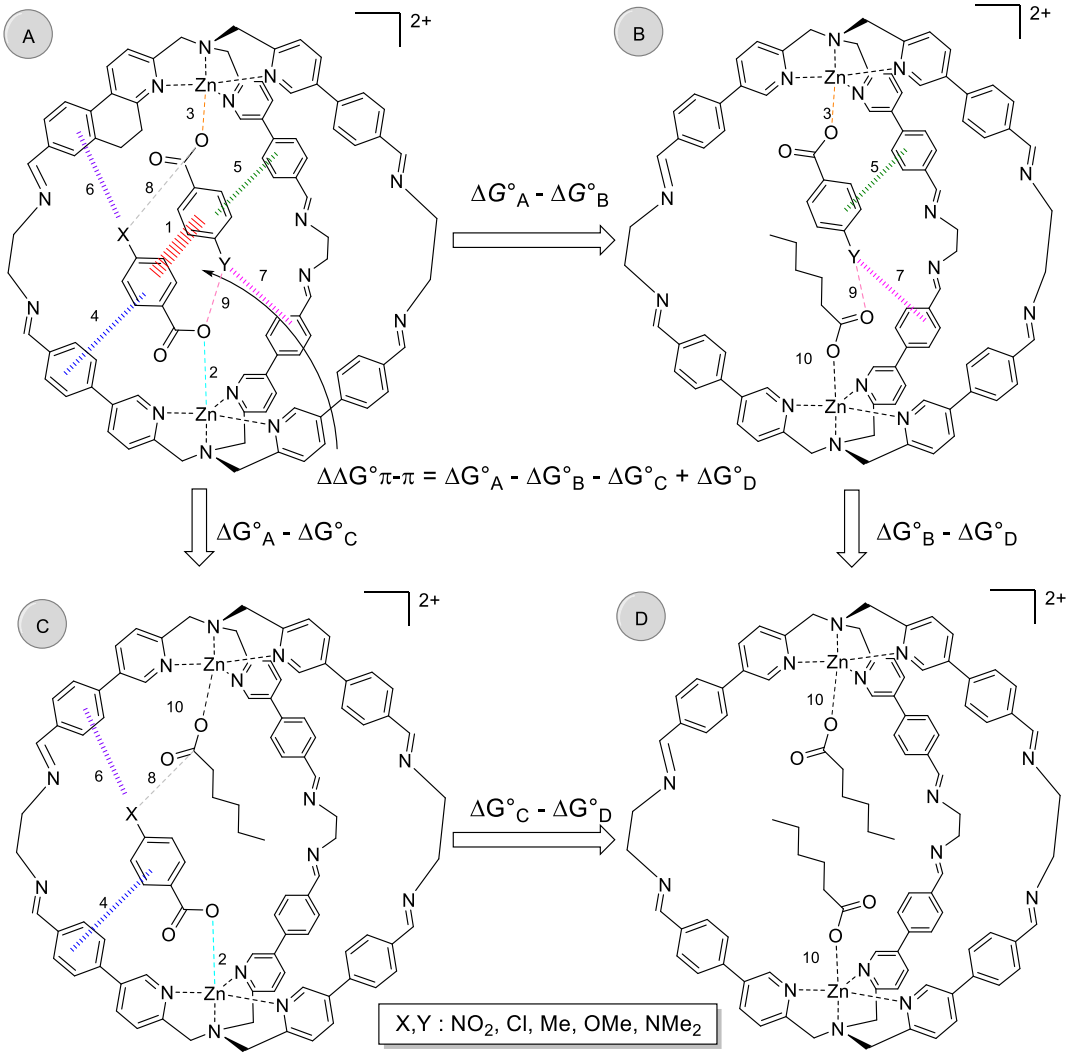
After the binding constant determination for each cage filled species, it was possible to obtain the corresponding $\Delta G°$ using the Gibbs equation and consequently these values were used for $\Delta\Delta G°$ calculation in the DMC (Table S4).

ΔG° values

Guest X / Guest Y	NO_2	Cl	Me	OMe	$N(Me)_2$	HexA
NO_2	-43.41±1.15					
Cl	-42.43±1.24	-41.88±1.26				
Me	-42.31±1.39	-41.12±1.32	-41.08±1.16			
OMe	-42.18±1.21	-40.69±1.56	-40.71±1.16	-40.13±1.51		
$N(Me)_2$	-41.67±1.11	-40.31±1.08	-39.38±1.26	-39.22±1.08	-38.34±1.72	
HexA	-40.26±1.08	-40.07±1.48	-40.06±1.04	-40.06±1.02	-40.15±1.10	-39.96±1.32

Table S4 $\Delta G°$ values obtained using the Gibbs equation from binding constant displayed in Table S3. The values are expressed in (kJ/mol)

3.5 Double Mutant Cycle-Description of the Interactions



1. Aromatic stacking interaction between the two guests
2. Coordination interaction between the carboxylate group of the guest with substituent X and the zinc ion
3. Coordination interaction between the carboxylate group of the guest with substituent Y and the zinc ion
4. Interactions of the edges of the aromatic ring with substituent X with the internal walls of the cage
5. Interactions of the edges of the aromatic ring with substituent Y with the internal walls of the cage
6. Interactions of substituent X with the walls of the cage
7. Interactions of substituent Y with the walls of the cage
8. Interactions between the carboxylate group of one guest and substituent X on the other guest.
9. Interactions between the carboxylate group of one guest and substituent Y on the other guest.
10. Interaction between aliphatic guest with the other guest and the cage

Figure S7 Chemical DMC for measuring the aromatic stacking interaction between two guests. All the interactions present are explained.

3.6 Correlation of the experimental aromatic stacking interactions with the electrostatic potential (ESP) of the aromatic rings

The correlation plot between the electrostatic potential of the aromatic ring (ESP) obtained using Spartan02 which are listed in the table above, and the aromatic interaction energies is displayed in Figure S8.

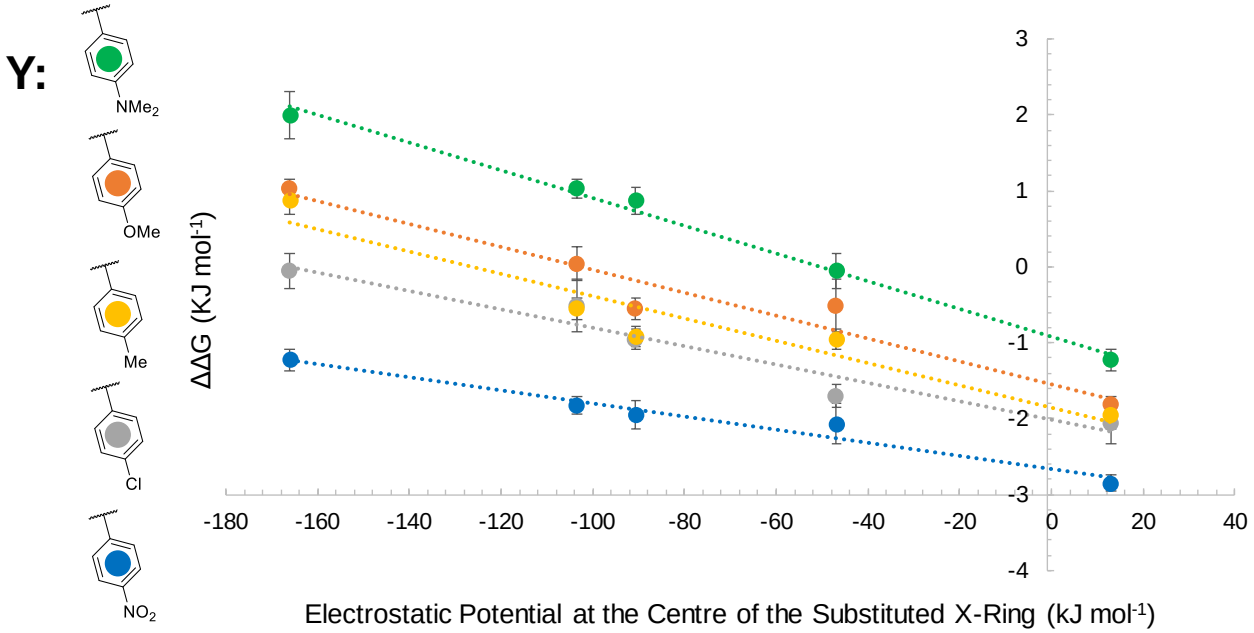


Figure S8 Plot of experimental aromatic stacking interaction energies measured with the cage system (y-axis) against the B3LYP/6-31G calculated electrostatic surface potential at the ring centre of substituted benzoate (X = NMe_2 to X = NO_2) (x-axis).

Substituent	Electrostatic potential (ESP) (kJ mol^{-1})
NMe_2	-166.1
OMe	-103.5
Me	-90.6
Cl	-46.9
NO_2	12.9

3.7 Hammet plot of slopes and intercept values of ΔΔ*G*° correlation

After the correlation of the ΔΔ*G*° values with of Hammet constant for each substituent it was possible to determine a correlation between the slope (Figure S6) and intercept (Figure S7) values for each substituent. The fitting values define the coefficient for equation (1).

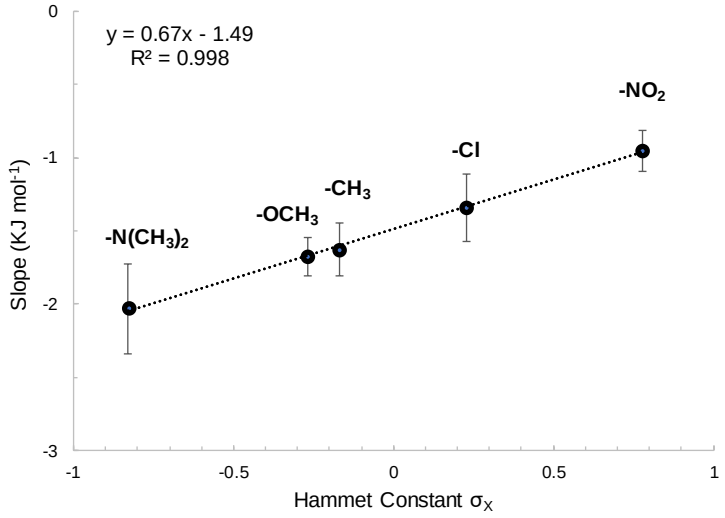


Figure S9 Correlation plot between the slopes of each correlation represented in Figure 1 (ΔΔ*G*° for each substituent against Hammet constant)

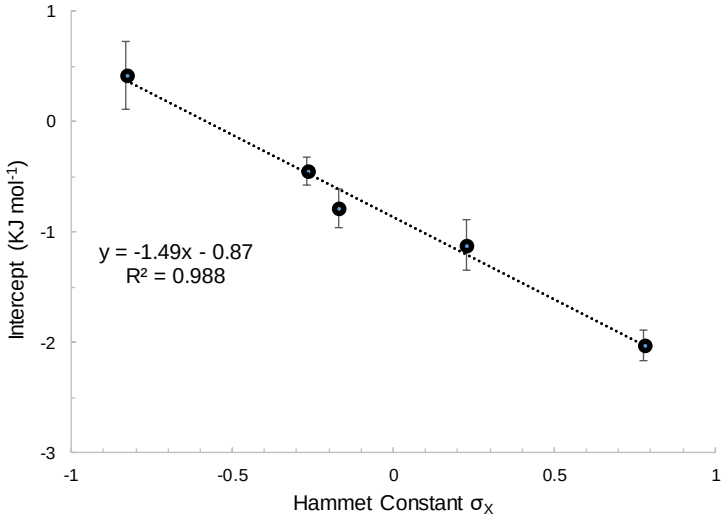


Figure S10 Correlation plot between the intercepts of each correlation represented in Figure 1 (ΔΔ*G*° for each substituent against Hammet constant)

4 ^{1}H NMR and MS characterization

4.1 (2a-2a)@1

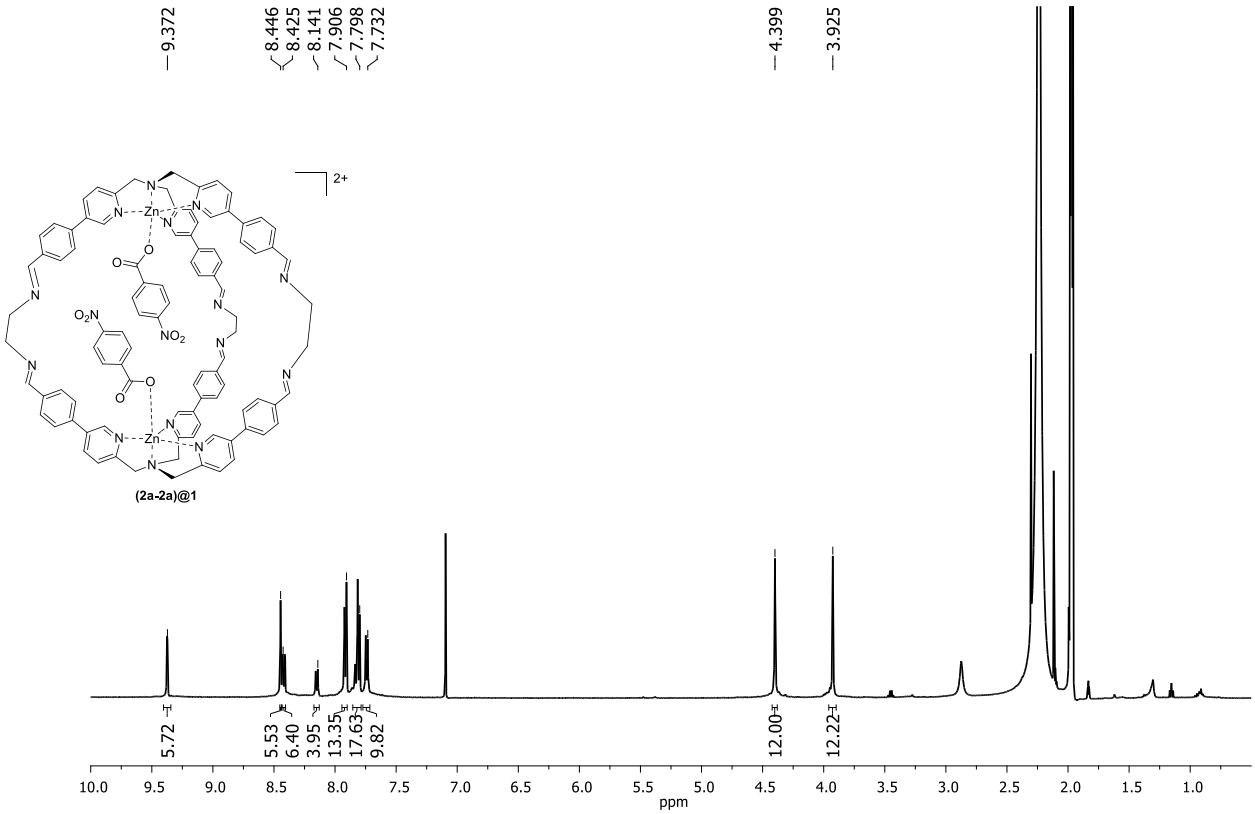


Figure S11 ^{1}H NMR spectrum (500 MHz, 301 K, CD_3CN) of cage **(2a-2a)@1.** (*p*-xylene is used as internal standard 7.095 ppm)

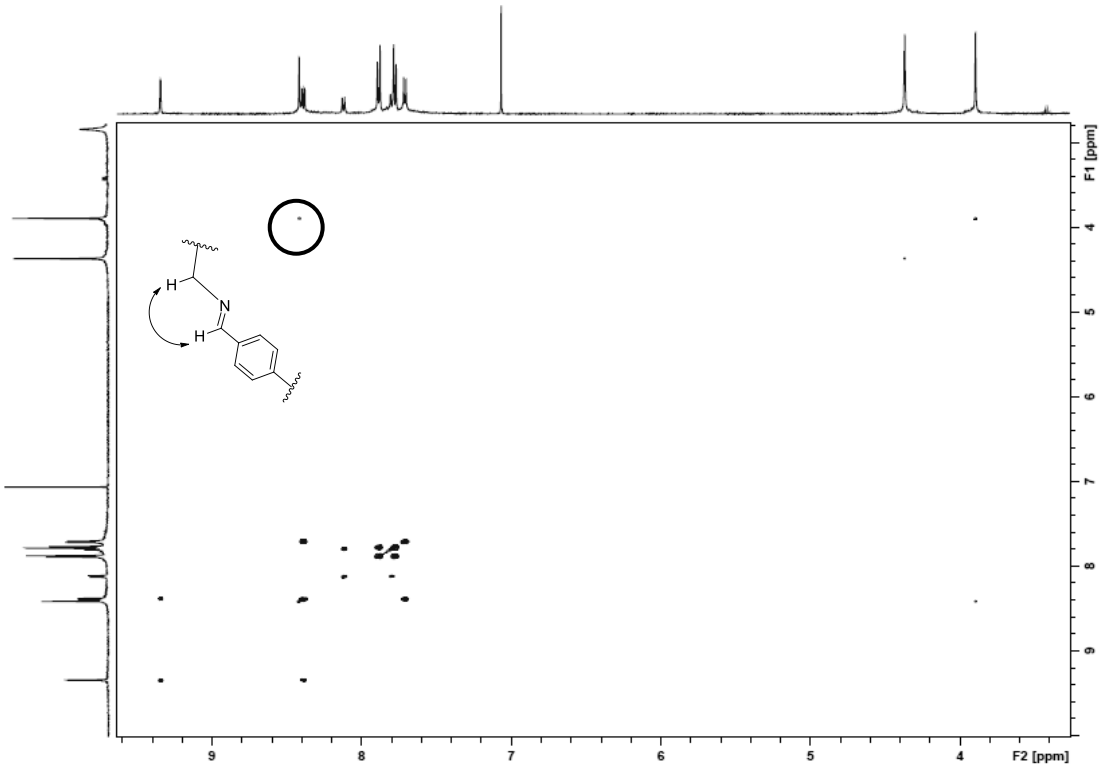


Figure S12 ^{1}H-^{1}H COSY spectrum (500 MHz, 301 K, CD_3CN) of cage **(2a-2a)@1**

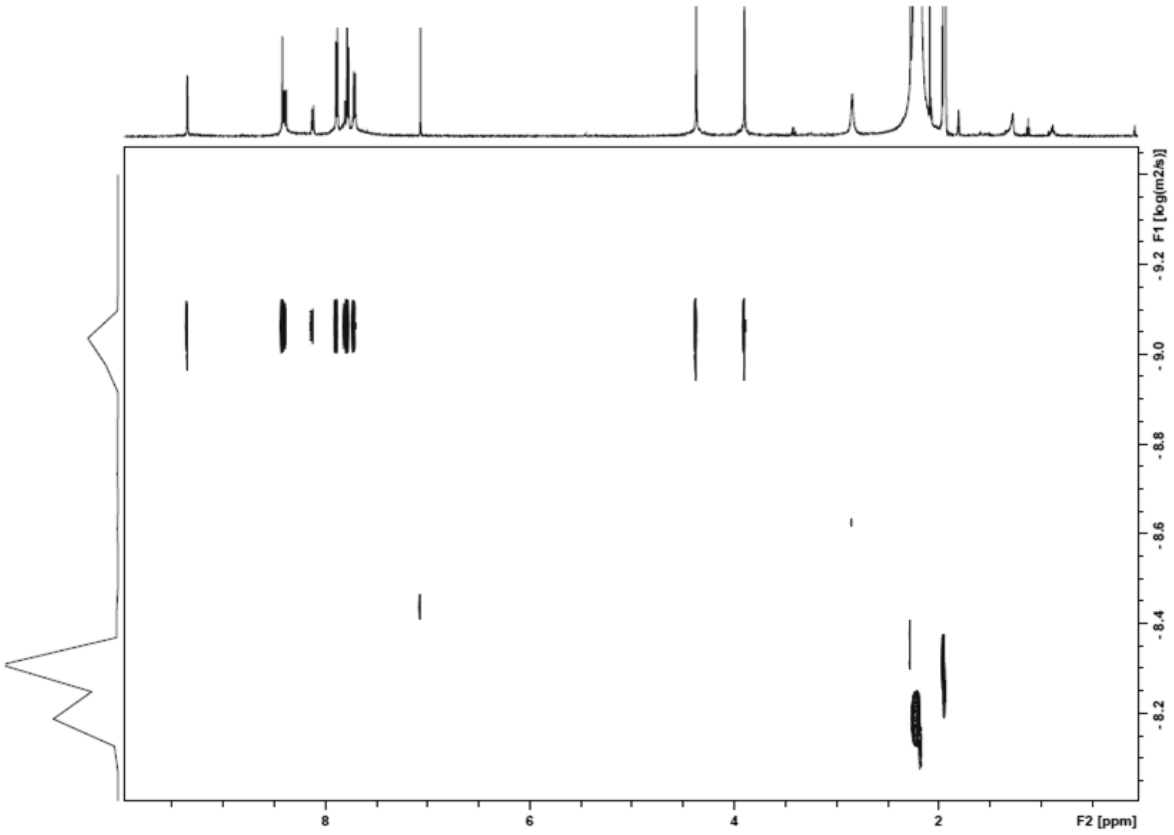


Figure S13 DOSY spectrum (500 MHz, 301 K, CD_3CN) of **(2a-2a)@1**. The diffusion coefficient corresponding hydrodynamic radius (r_H) was calculated to be 12±0.3 Å by using the Stokes-Einstein equation.[1]

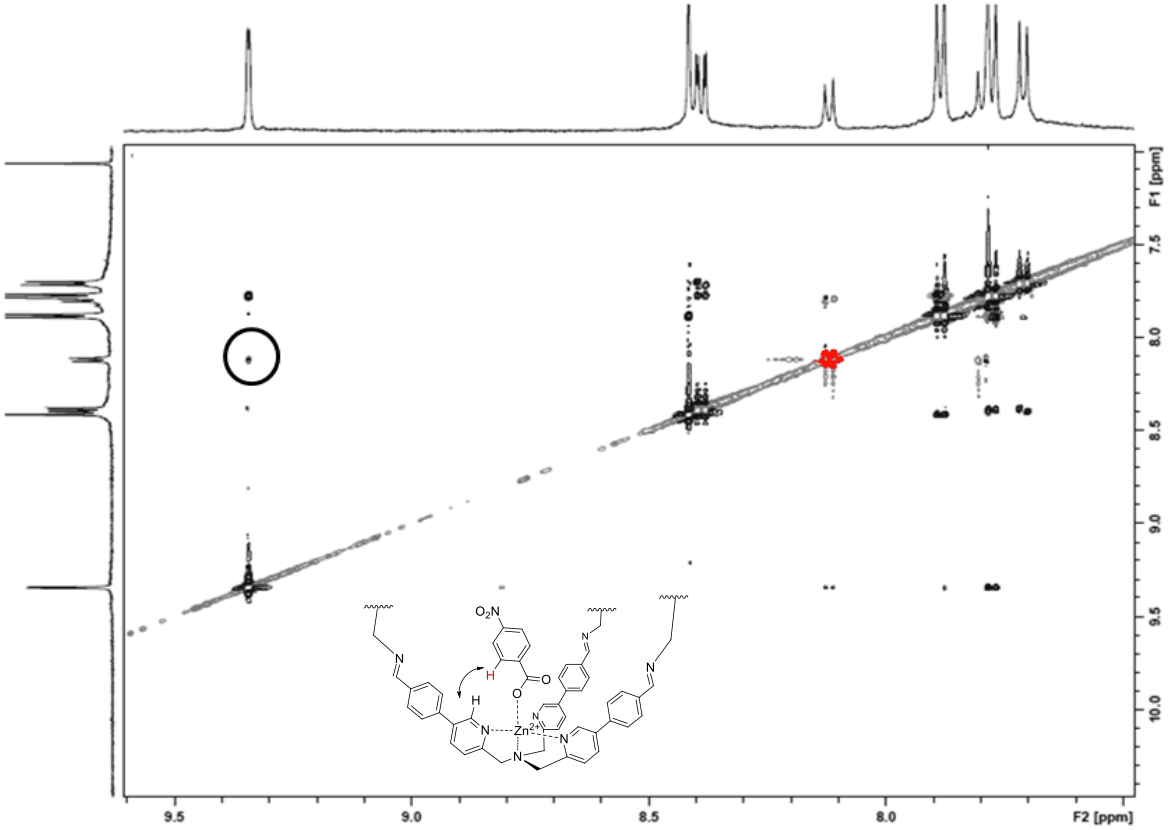


Figure S14 Particular of ^{1}H-^{1}H ROESY spectrum (500 MHz, 301 K, CD_3CN)of cage **(2a-2a)@1**

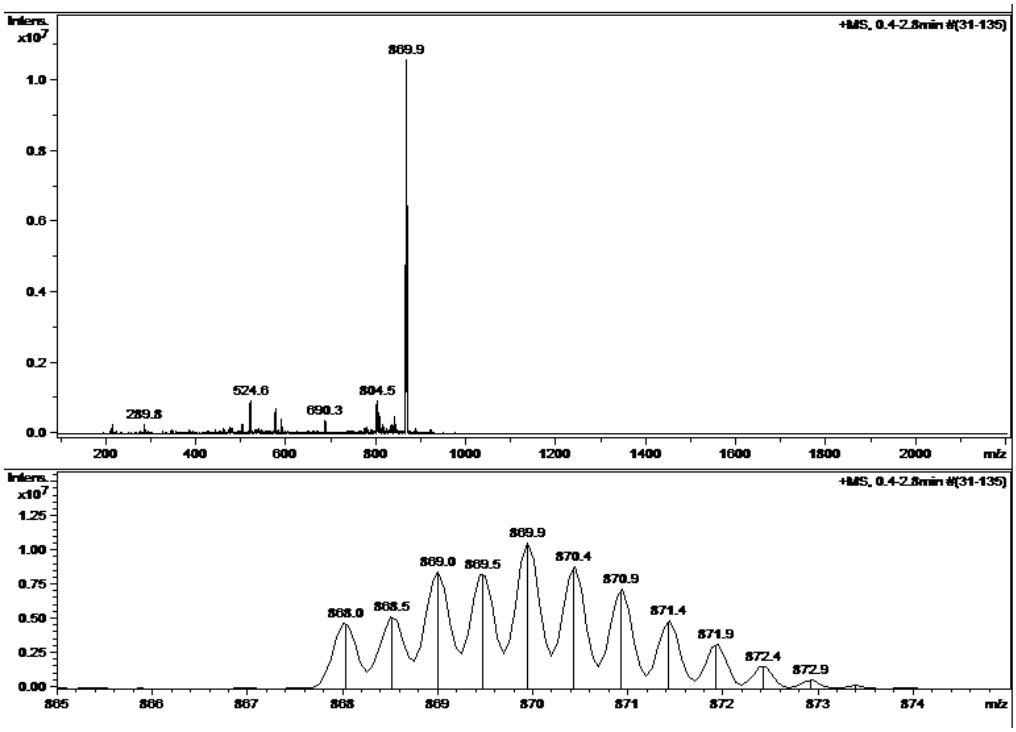


Figure S15 Experimental ESI-MS of **(2a-2a)@1** corresponding to $[C_{98}H_{80}N_{16}O_8Zn_2]^{2+}$.

4.2 (2b-2b)@1

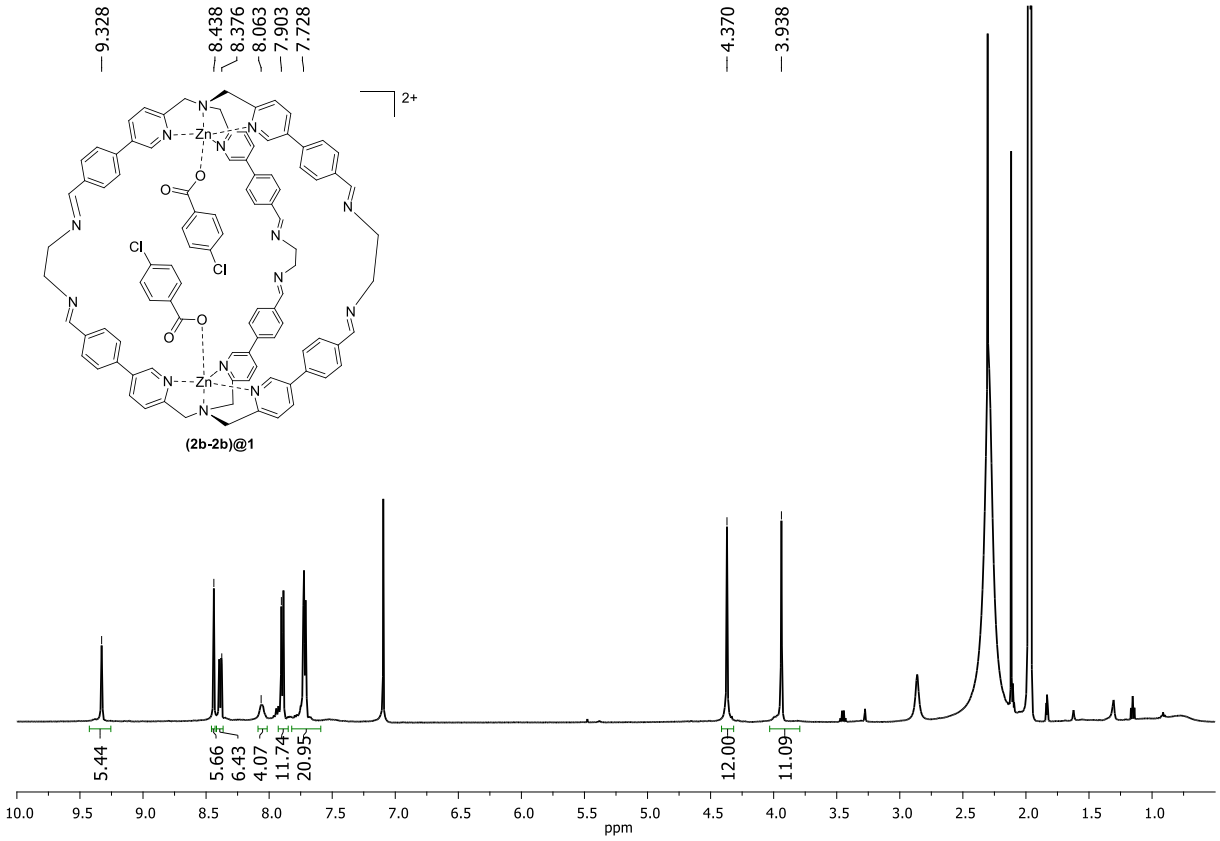


Figure S16 ^{1}H NMR spectrum (500 MHz, 301 K, CD_3CN)of cage **(2b-2b)@1.** (*p*-xylene is used as internal standard 7.095 ppm)

4.3 (2c-2c)@1

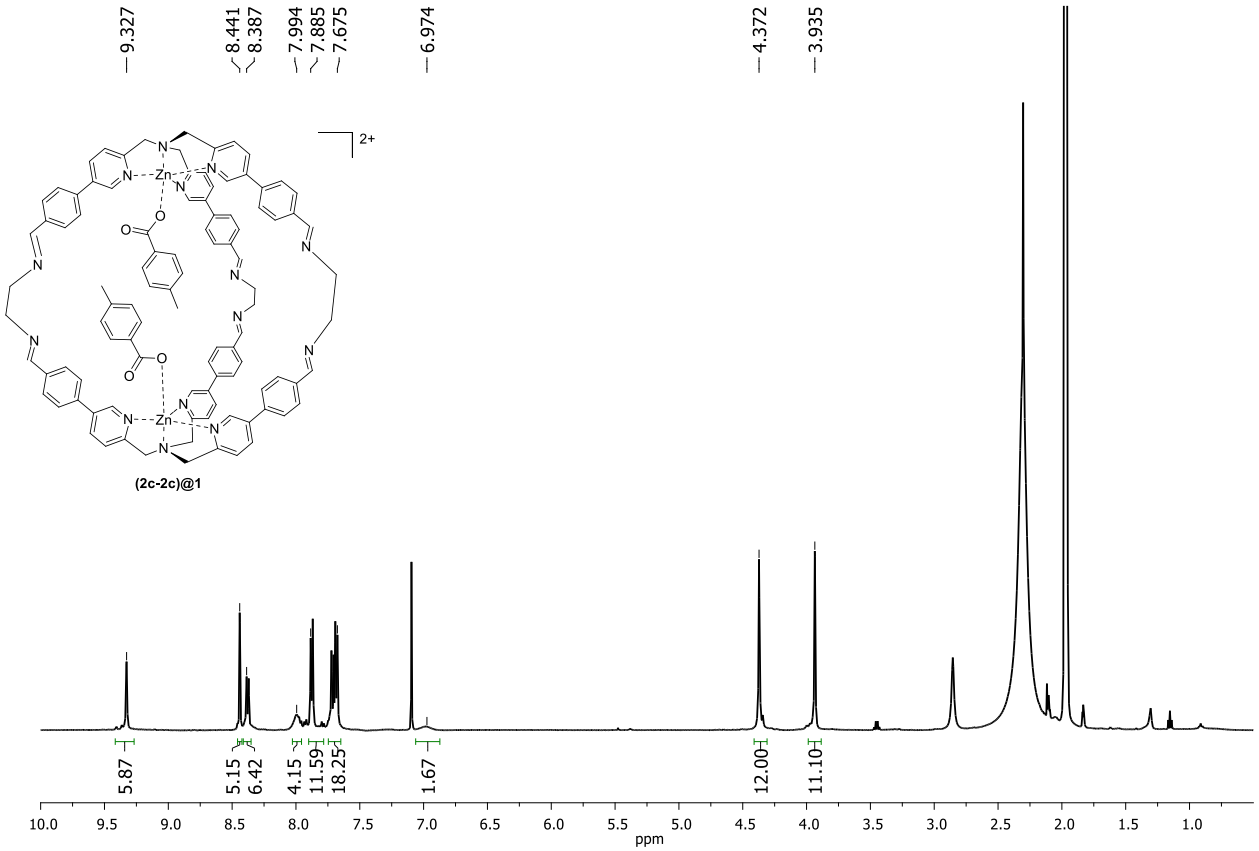


Figure S17 ^{1}H NMR spectrum (500 MHz, 301 K, CD_3CN)of cage **(2c-2c)@1.** (*p*-xylene is used as internal standard 7.095 ppm)

4.4 (2d-2d)@1

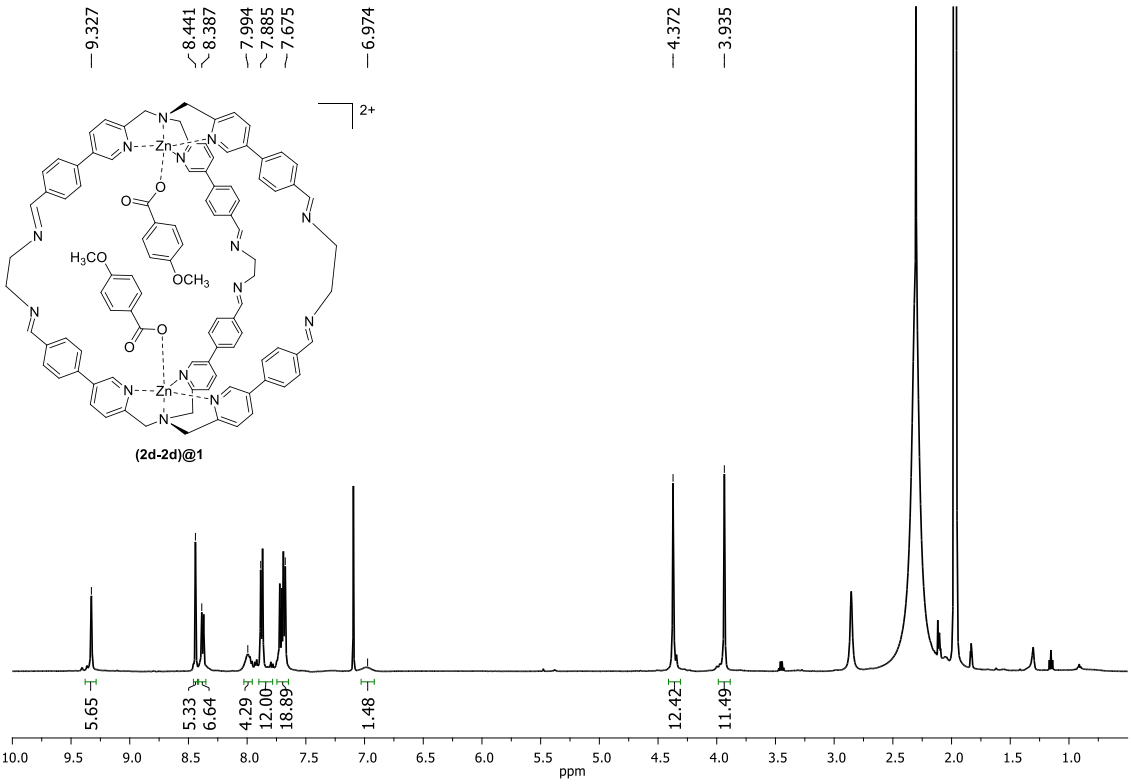


Figure S18 ^{1}H NMR spectrum (500 MHz, 301 K, CD_3CN)of cage **(2d-2d)@1.** (*p*-xylene is used as internal standard 7.095 ppm)

4.5 (2e-2e)@1

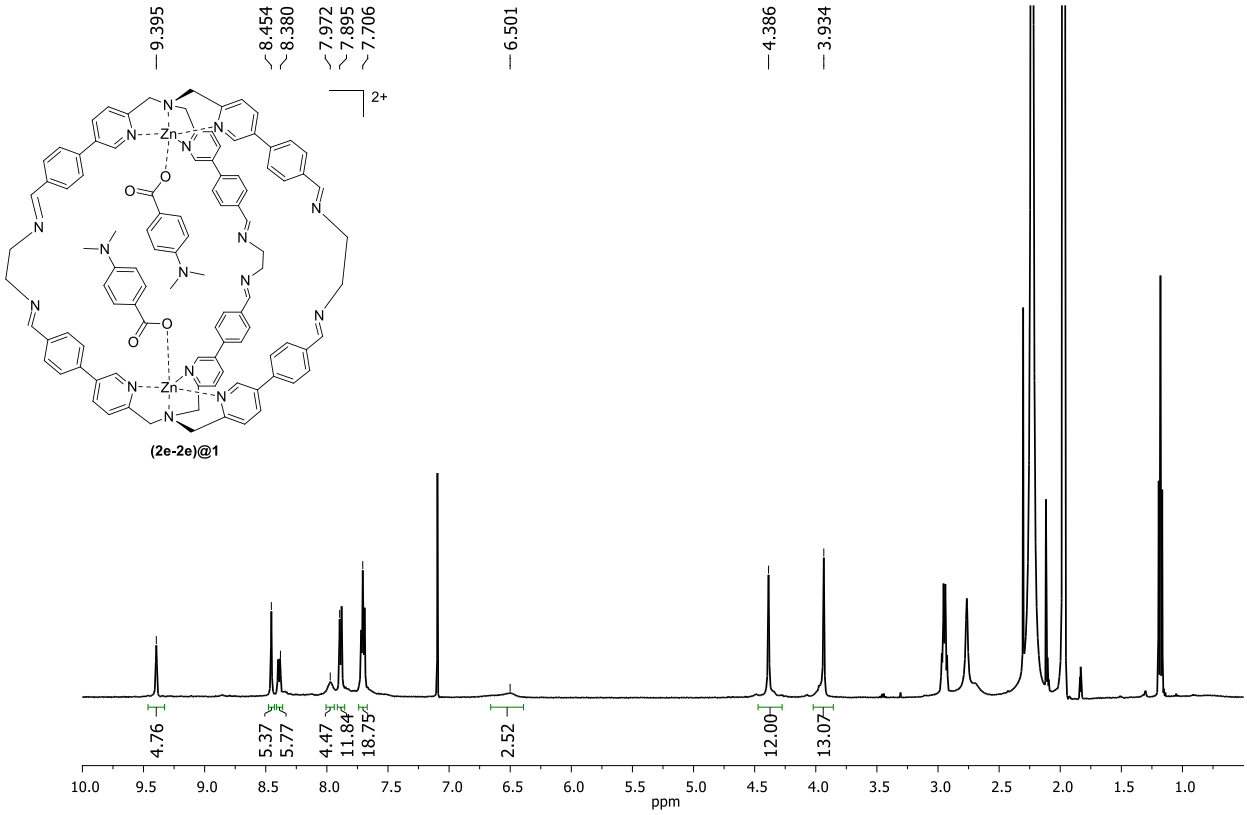


Figure S19 ^{1}H NMR spectrum (500 MHz, 301 K, CD_3CN) of cage **(2e-2e)@1.** (*p*-xylene is used as internal standard 7.095 ppm)

4.6 (HexA-HexA)@1

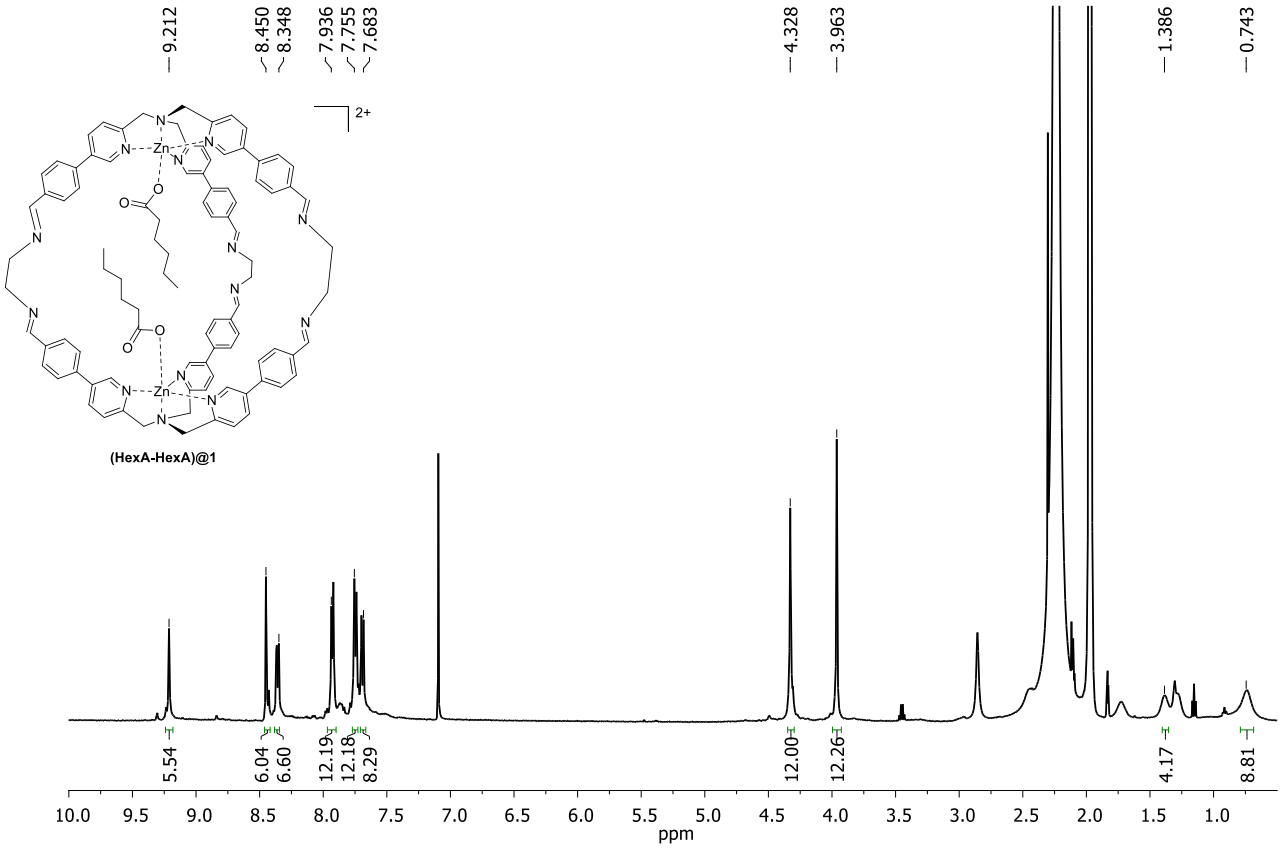


Figure S20 ^{1}H NMR spectrum (500 MHz, 301 K, CD_3CN) of cage **(HexA-HexA)@1.** (*p*-xylene is used as internal standard 7.095 ppm)

5. Computational Section

DFT and TDDFT calculations were run with Gaussian 09 package, with default grids and convergence criteria.[1] Cage **(2a-2a)@1** has been optimized employing the functional DFT (WB97XD/6-31G(d)) basis set using including the solvent effects for acetonitrile by the polarizable continuum model.

Coordinates for **(2a-2a)@1**

C	0.57997	10.17963	-3.23070
C	0.28180	-2.30328	10.43832
C	1.00511	-8.35414	-6.88398
N	1.47218	9.27947	-2.52867
N	1.16503	-2.45147	9.29951
N	1.93572	-7.33700	-6.43986
C	1.53317	8.07132	-2.92013
C	1.97747	-7.06614	-5.19848
C	1.17475	-1.53182	8.42150
C	2.42050	7.08682	-2.27051
C	2.46956	5.77467	-2.74524
C	3.25618	7.45718	-1.21040
C	3.35787	4.85744	-2.19509
H	1.82677	5.47284	-3.56809
C	4.14094	6.54392	-0.66103
H	3.20800	8.47381	-0.83479
C	4.21505	5.23514	-1.15649
H	3.41342	3.85441	-2.60843
H	4.77960	6.84574	0.16405
C	2.06829	-1.58914	7.24693
C	2.09399	-0.53033	6.33690
C	2.94404	-2.66530	7.06100
C	3.00650	-0.52079	5.28648
H	1.41794	0.31070	6.46705
C	3.85125	-2.65935	6.01490
H	2.91367	-3.49429	7.76005
C	3.90931	-1.57674	5.12651
H	3.04847	0.33544	4.61865
H	4.52635	-3.50049	5.88598
C	2.87333	-6.02427	-4.66015

C	3.75769	-5.33084	-5.49419
C	2.85627	-5.72969	-3.29557
C	4.61241	-4.37475	-4.97086
H	3.76312	-5.55425	-6.55568
C	3.71147	-4.76857	-2.76914
H	2.17679	-6.26334	-2.63629
C	4.60464	-4.08430	-3.59979
H	5.28208	-3.83488	-5.63405
H	3.70052	-4.57128	-1.70126
C	4.96245	-1.52028	4.08643
C	6.27771	-1.90320	4.36489
C	4.70380	-1.03648	2.80727
C	7.25839	-1.77475	3.39321
H	6.53980	-2.27215	5.35143
H	3.70648	-0.74740	2.50219
C	6.91713	-1.25470	2.15327
H	8.28566	-2.05381	3.59909
C	5.53252	-3.07430	-3.04144
C	5.11508	-2.21440	-2.02885
C	6.85274	-2.94576	-3.48100
H	4.10489	-2.25760	-1.63647
C	7.68714	-2.00335	-2.89655
H	7.23814	-3.60264	-4.25444
C	7.18824	-1.19372	-1.88583
H	8.72141	-1.90737	-3.20741
C	5.21288	4.28181	-0.62089
C	4.89555	2.93713	-0.45283
C	6.51576	4.67134	-0.29937
H	3.90371	2.55437	-0.65871
C	7.43044	3.72760	0.14706
H	6.82452	5.70412	-0.42741
C	7.02937	2.40451	0.26641
H	8.45100	4.00927	0.38148
H	1.35957	-7.59907	-4.46101
H	0.55124	-0.63004	8.50946
N	5.91678	-1.30181	-1.46993
N	5.65348	-0.89296	1.87597

N	5.77705	2.02737	-0.02751
C	7.95654	1.31829	0.76014
C	7.93416	-1.10193	1.04567
C	8.03329	-0.14467	-1.19835
H	9.09728	-0.40591	-1.26435
H	7.90099	0.81129	-1.71810
H	7.92029	-2.01537	0.44122
H	8.94441	-1.01060	1.46345
H	9.00242	1.58019	0.55662
H	7.84947	1.24592	1.84850
N	7.58934	0.02657	0.18367
Zn	5.30676	-0.00905	0.05732
H	0.95307	7.70360	-3.77920
C	-0.70304	10.39483	-2.41381
C	-0.22864	-7.69047	-7.51373
C	-0.94885	-3.20898	10.27941
N	-1.58075	9.25156	-2.55950
N	-1.11445	-7.19379	-6.48033
N	-1.88704	-2.60710	9.35424
C	-1.64040	8.41595	-1.60318
C	-1.91926	-3.05164	8.16356
C	-1.13076	-5.94315	-6.25146
C	-2.51102	7.22543	-1.66410
C	-3.32009	6.97889	-2.77939
C	-2.56935	6.34981	-0.57804
C	-4.18695	5.89864	-2.79324
H	-3.26535	7.65318	-3.62744
C	-3.44071	5.26631	-0.58994
H	-1.94772	6.52965	0.29521
C	-4.27004	5.03564	-1.69210
H	-4.80398	5.71762	-3.66859
H	-3.50548	4.62379	0.28345
C	-2.02955	-5.35076	-5.24015
C	-2.90853	-6.15252	-4.50254
C	-2.05754	-3.96717	-5.05384
C	-3.82106	-5.57850	-3.63341
H	-2.87669	-7.22837	-4.63786

C	-2.97501	-3.38776	-4.18289
H	-1.37887	-3.33225	-5.61734
C	-3.88126	-4.18662	-3.47850
H	-4.49854	-6.21444	-3.07086
H	-3.01839	-2.30605	-4.08949
C	-2.82366	-2.48354	7.14532
C	-3.73458	-1.47203	7.47050
C	-2.78900	-2.96972	5.83699
C	-4.59816	-0.96997	6.51093
H	-3.75498	-1.08888	8.48519
C	-3.65268	-2.46476	4.87202
H	-2.08898	-3.75762	5.57177
C	-4.57275	-1.46343	5.19949
H	-5.28977	-0.17575	6.77672
H	-3.62598	-2.87268	3.86584
C	-4.94052	-3.57284	-2.64439
C	-6.25437	-4.04959	-2.67636
C	-4.69117	-2.46651	-1.83749
C	-7.24219	-3.41464	-1.93912
H	-6.50980	-4.89832	-3.30275
H	-3.69732	-2.04980	-1.73731
C	-6.90892	-2.30112	-1.18186
H	-8.26811	-3.76409	-1.96625
C	-5.51149	-0.93991	4.18093
C	-5.09618	-0.76440	2.86370
C	-6.83921	-0.62029	4.47700
H	-4.07951	-0.99364	2.56445
C	-7.68185	-0.17031	3.47033
H	-7.22338	-0.75388	5.48337
C	-7.18547	-0.03716	2.18106
H	-8.72132	0.05892	3.67683
C	-5.24851	3.92488	-1.68047
C	-4.91968	2.68888	-1.13084
C	-6.54336	4.07079	-2.18446
H	-3.92914	2.48082	-0.74574
C	-7.44048	3.01435	-2.10650
H	-6.86033	5.01789	-2.60970

C	-7.03080	1.82448	-1.52267
H	-8.45451	3.11738	-2.47620
H	-1.28645	-3.88820	7.83273
H	-0.50942	-5.23495	-6.81902
N	-5.90661	-0.32627	1.89395
N	-5.64754	-1.84214	-1.14108
N	-5.78546	1.67459	-1.04842
C	-7.93852	0.62245	-1.40294
C	-7.93141	-1.57335	-0.33918
C	-8.04112	0.44465	1.03152
H	-9.10113	0.24216	1.23135
H	-7.93158	1.53161	0.94357
H	-7.92210	-2.01551	0.66324
H	-8.93965	-1.72291	-0.74529
H	-8.99182	0.93087	-1.40067
H	-7.79011	-0.01189	-2.28431
N	-7.58777	-0.15910	-0.21958
Zn	-5.29818	-0.11345	-0.09104
H	-1.07167	8.54987	-0.67132
H	0.10589	-6.90255	-8.20523
H	-0.77219	-8.44645	-8.08977
H	1.50052	-8.96069	-7.64888
H	0.67698	-9.01971	-6.07146
H	-0.61662	-4.20900	9.96269
H	-1.43977	-3.30056	11.25352
H	0.82876	-2.61742	11.33319
H	-0.05620	-1.26643	10.58532
H	-1.22143	11.27433	-2.80898
H	-0.43009	10.59461	-1.36670
H	1.08691	11.14365	-3.34075
H	0.30614	9.81583	-4.23242
C	-2.53974	-0.27514	0.68337
C	2.57299	-0.54306	-0.54461
O	3.47478	0.36894	-0.55981
O	2.68396	-1.64764	-0.00090
O	-3.42110	0.45248	0.09857
O	-2.65011	-1.48276	0.91816

C	1.29619	-0.19372	-1.27459
C	1.06842	1.09904	-1.74607
C	0.31928	-1.17545	-1.44953
C	-0.14747	1.43502	-2.32524
H	1.83072	1.85831	-1.62291
C	-0.89162	-0.86497	-2.04815
H	0.50968	-2.17898	-1.08760
C	-1.11725	0.44874	-2.44547
H	-0.35425	2.44722	-2.64860
H	-1.65106	-1.62282	-2.18186
C	-1.28382	0.45453	1.10576
C	-1.08719	1.79674	0.78116
C	-0.29530	-0.23930	1.80552
C	0.10709	2.43129	1.09180
H	-1.85762	2.33695	0.24575
C	0.89891	0.38097	2.13711
H	-0.46345	-1.27833	2.06336
C	1.09110	1.70192	1.74632
H	0.28829	3.45919	0.80474
H	1.66826	-0.15460	2.67535
N	2.38543	2.33680	1.98629
O	3.25671	1.68449	2.55060
O	2.54722	3.48430	1.60043
N	-2.43206	0.82367	-2.96121
O	-3.26746	-0.05896	-3.11954
O	-2.64501	2.00292	-3.19734

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