Supplementary information

Spectacular Induced-Fit Process for Guest Binding by a Calix[6]arene Zn(II) *Funnel Complex*

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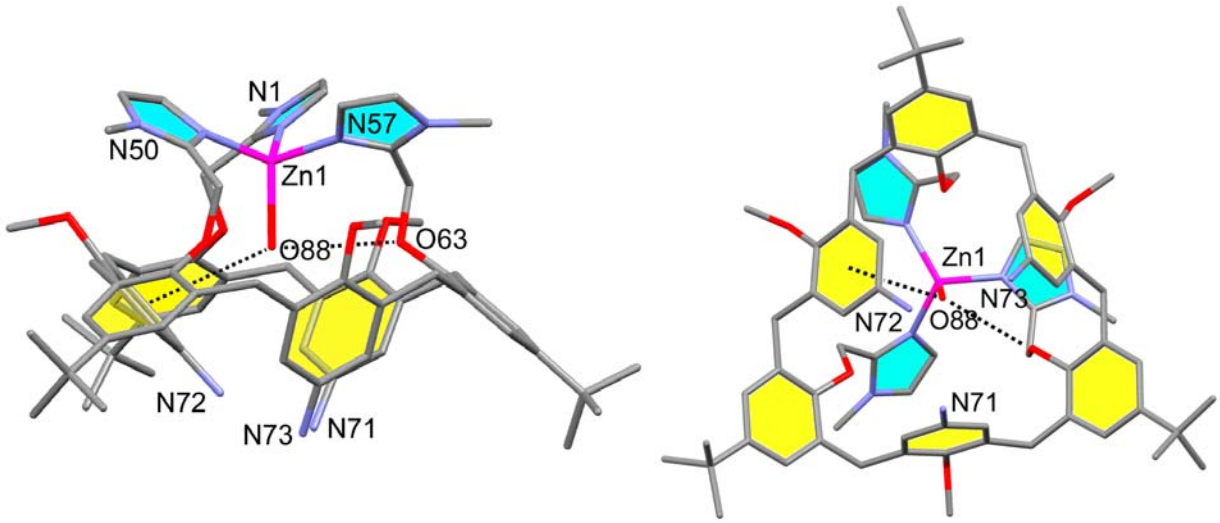
XRD of the aqua complex 3

Slow diethyl ether diffusion into a CH_2Cl_2 solution (0.5 mL) of complex **3** (≈ 3 mg) resulted in the formation of colourless crystals suitable for X-Ray analysis.

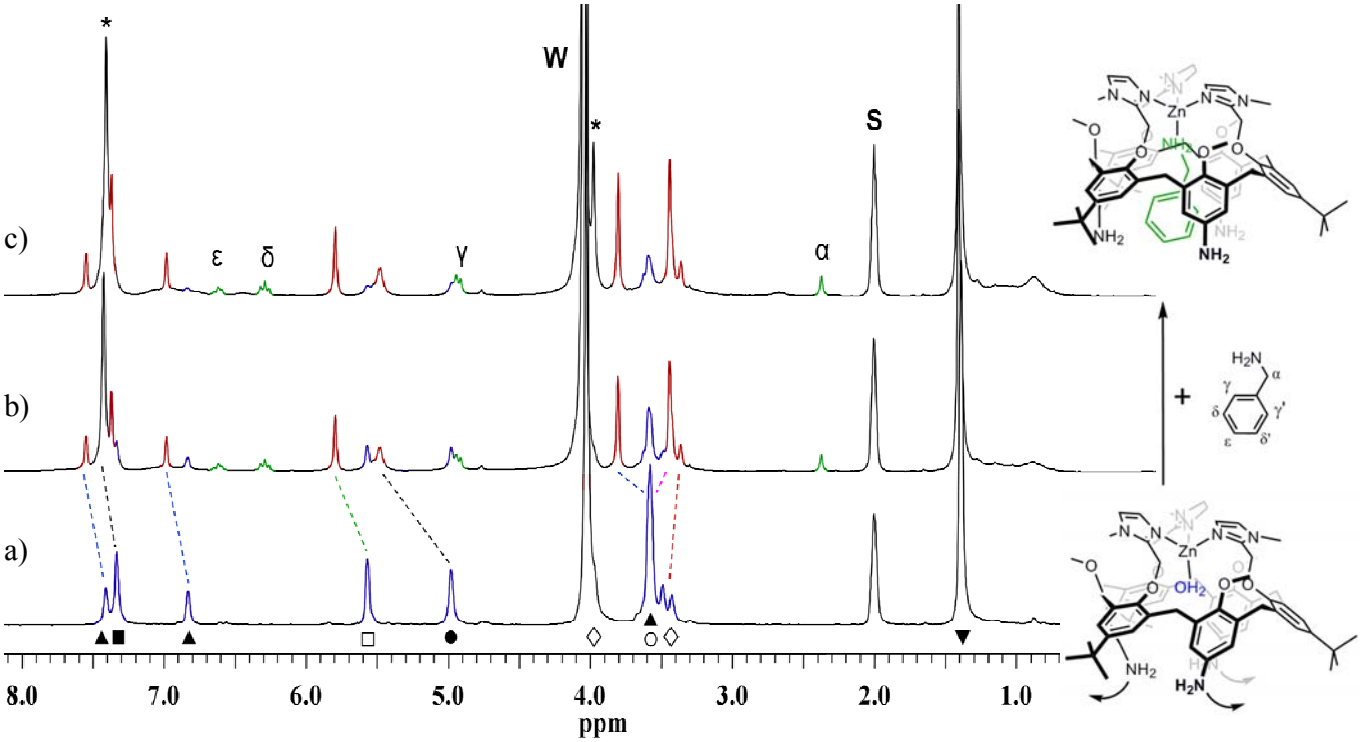
Crystal data: $C_{88}\ H_{129}\ Cl_2\ N_9\ O_{19}\ Zn$, M_w = 1753.27, monoclinic, space group $P2_1/c$; dimensions: a = 16.4885(3) Å, b = 26.3581(6) Å, c = 23.3178(5) Å, β = 109.279(1)°, V = 9565.7(3) $Å^3$; Z = 4; μ = 0.381 mm^{-1}; 117512 reflections measured at 100 K; independent reflections: 28046 [19361 Fo > 4σ (Fo)]; data were collected up to a 2Θmax value of 60.16° (99.8 % coverage). Number of variables: 995; R_1 = 0.0608, wR_2 = 0.1782, S = 1.109; highest residual electron density 1.285 e.$Å^{-3}$ (all data R_1 = 0.0874, wR_2 = 0.1922). CCDC 690395.



XRD structures of the aqua-complex **3**. Left: side view; right: bottom view. Hydrogen atoms, counter anions and solvent molecules (four molecules of diethylether) have been omitted for clarity. Dotted lines: hydrogen bonds (OH···O) and CH-π interactions.

Distances (Å):	d(Zn(1)-N(50)) =	1,9766(17)
	d(Zn(1)-N(1)) =	1,9980(17)
	d(Zn(1)-N(57)) =	1,9972(18)
	d(Zn(1)-O(88)) =	2,041(2)
	d(N(71)···N(72)) =	3,14
	d(N(71)···N(73)) =	4,37
	d(N(72)···N(73)) =	3,24.
Angles (degree):	N(50)-Zn(1)-N(1) =	112,50(7)
	N(50)-Zn(1)-N(57) =	109,74(7)
	N(1)-Zn(1)-N(57) =	104,05(7)
	N(50)-Zn(1)-O(88) =	112,09(8)
	N(1)-Zn(1)-O(88) =	110,25(8)
	N(57)-Zn(1)-O(88) =	107,81(8)
Hydrogen bond (Å):	d(O(88)···O(63)) =	3,10
CH-π interaction (Å):	d(O(88)···centroïd) =	3,48

Evolution of ^{1}H NMR spectrum (250 MHz, 300 K) of complex 3 upon addition of benzylamine



Bottom to top: ^{1}H NMR spectra (250 MHz, CD_3CN/D_2O 1:1, 300 K) of complex **3** (6 mM) a) before and after the addition of b) 2 equiv. and c) 5 equiv. of benzylamine. ▼ $(CH_3)_3C$, o OCH_3, ▲ NCH_3 and H_{Im}, ◊ CH_2Ar, • CH_{2Im}, □ H_{ArNH2} and ■ H_{ArtBu}; * uncoordinated benzylamine; α, γ, δ and ε guest benzylamine; S: solvent; W: water.

For each ^{1}H NMR spectrum, the number and relative intensities of proton signals are in agreement with C_{3v} symmetrical compounds. The chemical shifts of the tertiobutyl (1.41 ppm) and methoxy protons (3.53 ppm) show that these groups are projected away from the calixarene cavity, in agreement with the flattened cone conformation above schematized.[1] In spectrum b, the resonances of both complexes (with and without benzylamine endo-coordinate) are observable. This shows that the guest exchange was slow vs. the time scale of the NMR analysis.

Integration of the resonances that are characteristic of both complexes (with and without benzylamine in the cavity) indicated that *ca.* 73% of benzylamine encapsulation is obtained after addition of 2 equivalents of benzylamine to the solution of the complex (spectrum b). The corresponding tertiobutyle resonance, did not shift significantly as it remains in position *out* whatever this guest is. However, important shifts are observed for

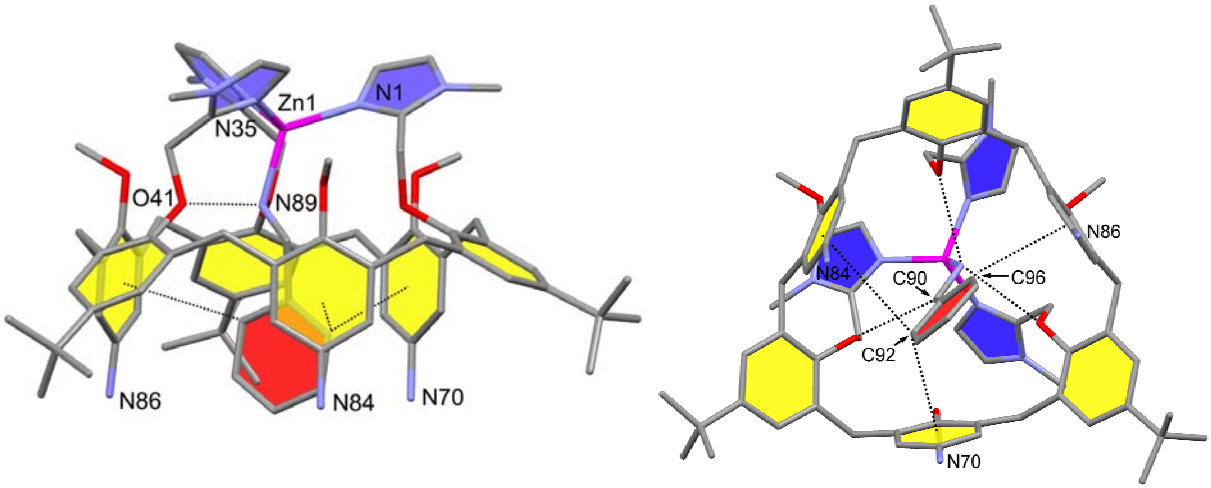
[1] Coquiere, D.; Marrot, J.; Reinaud, O. *Chem. Commun.* **2006**, 3924-3926.

H_{ArNH2} (in position *in*) and CH_{2Im} signals with $\Delta\delta$ = + 0.25 ppm and + 0.48 ppm, respectively. These low-field shifts are rationalized by the endo-coordination of the large benzylamine guest (green NMR signature), which pushes away these groups from the center of the cone (red NMR signature), in full agreement with the solid state structure. Such a geometrical change allows the cavity size to increase and the calixarene to accommodate benzylamine thanks to a more straight conformation. Consequently, the rest of the host signals (o OCH_3, ▲ NCH_3 and H_{Im}, ◊ CH_2Ar, and ■ H_{ArtBu}) are also slightly shifted. The signals of protons α, γ, δ and ε of the coordinated guest gradually appeared during the titration at 2.38 ppm (s), 4.93 ppm (d), 6.28 ppm (t) and 6.59 ppm (t), respectively (for $\Delta\delta$ see Figure 3 of the manuscript).

XRD of complex 3 with benzylamine as a guest

Slow diethyl ether diffusion into a methanol solution (0.5 mL) of complex **3** (≈ 3 mg) and 5 equiv. of benzylamine resulted in the formation of colourless crystals suitable for X-Ray analysis.

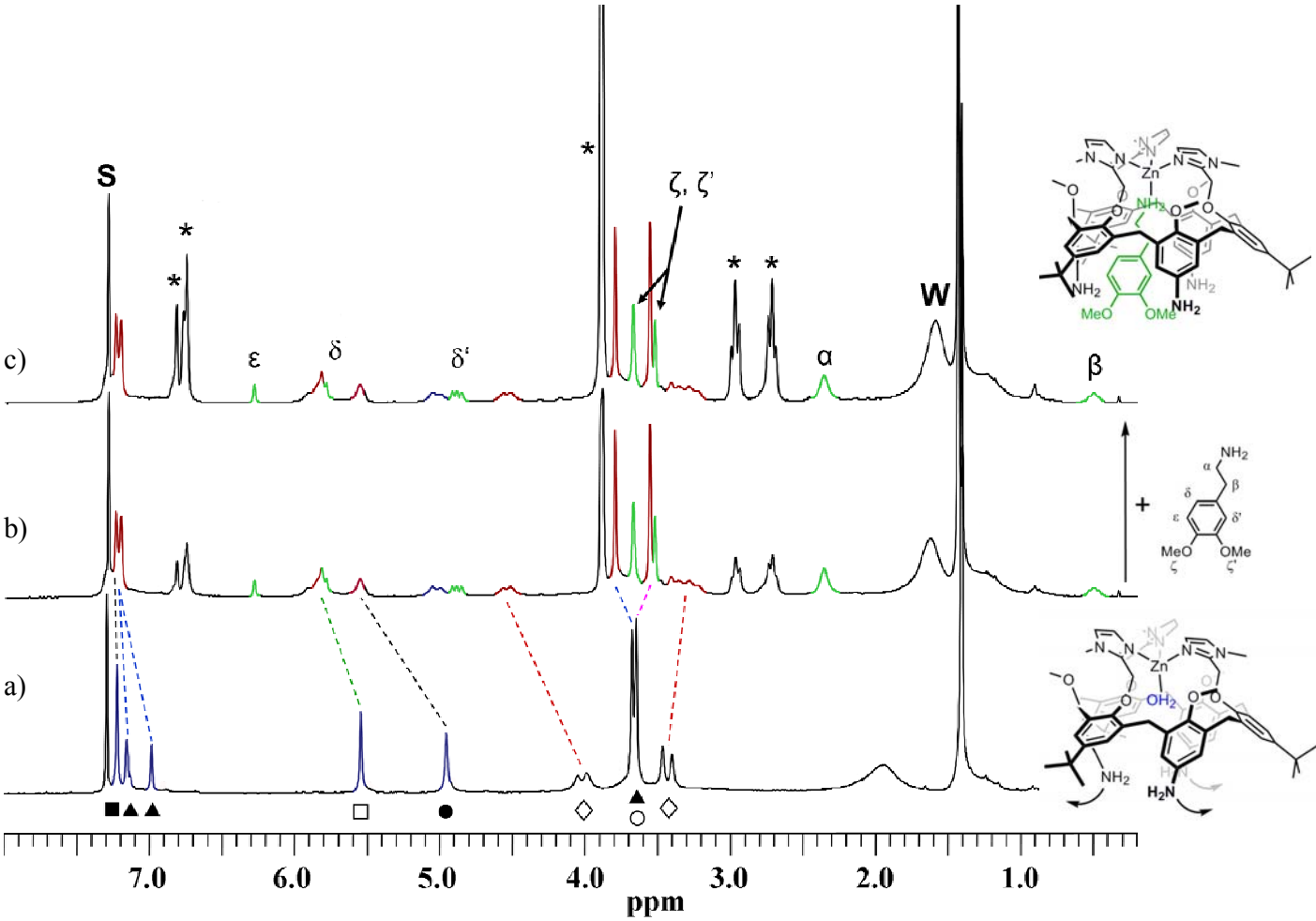
Crystal data: C_{79} H_{96} Cl_2 N_{10} O_{14} Zn, M_w = 1545.93, monoclinic, space group $P2_1/n$; dimensions: a = 19.874(3) Å, b = 25.382(4) Å, c = 23.188(3) Å, β = 114.988(6)°, V = 10602(3)Å^3; Z = 4; μ = 0.333 mm^{-1}; 284267 reflections measured at 100 K; independent reflections: 18776 [9992 Fo > 4σ (Fo)]; data were collected up to a 2Θmax value of 50.40° (98.3 % coverage). Number of variables: 915; R_1 = 0.1406, wR_2 = 0.3437, S = 1.040; highest residual electron density 1.701 e.Å^{-3} (all data R_1 = 0.1910, wR_2 = 0.3715). CCDC 690397.



XRD structures of complex **3** with benzylamine as a guest. Left: side view; right: bottom view. Hydrogen atoms and counter anions have been omitted for clarity. Dotted lines: hydrogen bonds (NH···O) and CH-π interactions.

Distances (Å):	d(Zn(1)-N(1)) =	1.995(3)
	d(Zn(1)-N(34)) =	1.991(2)
	d(Zn(1)-N(35)) =	2.000(2)
	d(Zn(1)-N(89)) =	2.020(4)
Angles (degree):	N(1)-Zn(1)-N(34) =	107.40(10)
	N(1)-Zn(1)-N(35) =	106.38(10)
	N(34)-Zn(1)-N(35) =	108.95(9)
	N(1)-Zn(1)-N(89) =	122.00(12)
	N(34)-Zn(1)-N(89) =	101.36(12)
	N(35)-Zn(1)-N(89) =	110.17(12)
Hydrogen bonds (Å):	d(N(89)···O(28)) =	2,92
	d(N(89)···O(41)) =	2,94
CH-π interactions (Å):	d(C(92)···centroïd) =	3,64 and 4,14
	d(C(96)···centroïd) =	3,45

Evolution of ^{1}H NMR spectrum (250 MHz, 300 K) of complex 3 upon addition of dimethyldopamine

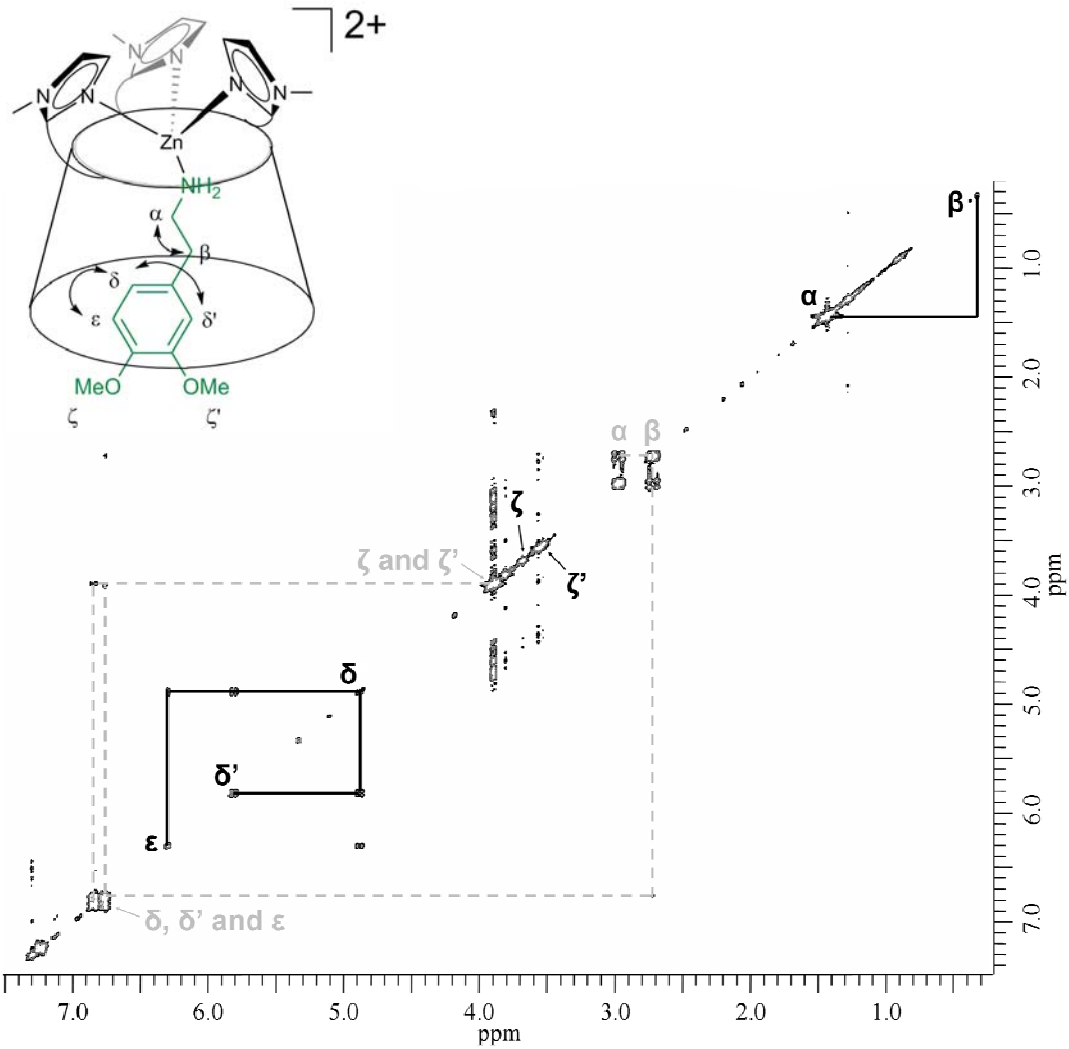


Bottom to top: ^{1}H NMR spectra (250 MHz, $CDCl_3$, 300 K) of complex **3** (5 mM) a) before and after the addition of b) 3 equiv. and c) 6 equiv. of dimethyldopamine in total. ▼ $(CH_3)_3C$, o OCH_3, ▲ NCH_3 and H_{Im}, ◊ CH_2Ar, • CH_{2Im}, □ H_{ArNH2} and ■ H_{ArtBu}; α, β, δ, δ', ε, ζ and ζ': guest dimethyldopamine; *: free dimethyldopamine; S: solvents; W: water.

The addition of 3 equivalents of dimethyldopamine led to a growing new ^{1}H NMR signature that is characteristic of calixarene **3** (red resonances) hosting one equivalent of dimethyldopamine (green resonances) (spectra b and c). The most significant resonance shifts were observed for the CH_{2Im}, H_{ArNH2} and CH_{2Ar} groups with $\Delta\delta$ = + 0.63 ppm, + 0.35 ppm and 0.47 ppm, respectively. Dimethyldopamine endo-coordination was characterized by 2D ^{1}H NMR analysis (see below). α, β and methoxy proton signals were observed at δ = 1.38 ppm, 0.50 ppm and 3.40 ppm and 3.60 ppm ($\Delta\delta$ of 1.58 ppm, 2.28 ppm, 0.55 ppm and 0.35 ppm), respectively. Aromatic proton δ, δ' and ε appeared at 4.92 ppm ($\Delta\delta$ = 1.90 ppm), 5.83 ppm ($\Delta\delta$ = 0.93 ppm) and 6.28 ppm ($\Delta\delta$ = 0.42 ppm), respectively.

The chemical shifts of the complexes in $CDCl_3$ and CD_3CN/D_2O (see page S-3) are slightly different. However, the most significant changes observed during the titration are similar in both solvents, which indicates similar host structural modifications upon inclusion of a voluminous guest. Again, for each ^1H NMR spectrum, the number and relative intensities of proton signals are in agreement with C_{3v} symmetrical compounds. The chemical shifts of the tertiobutyl (1.34 ppm) and methoxy protons (3.42 ppm) show that these groups are projected away from the calixarene cavity, in agreement with a flattened cone conformation **Erreur ! Signet non défini.**

COSY ^{1}H NMR spectrum (250 MHz, $CDCl_3$, 300 K) of complex 3 with dimethyldopamine as a guest



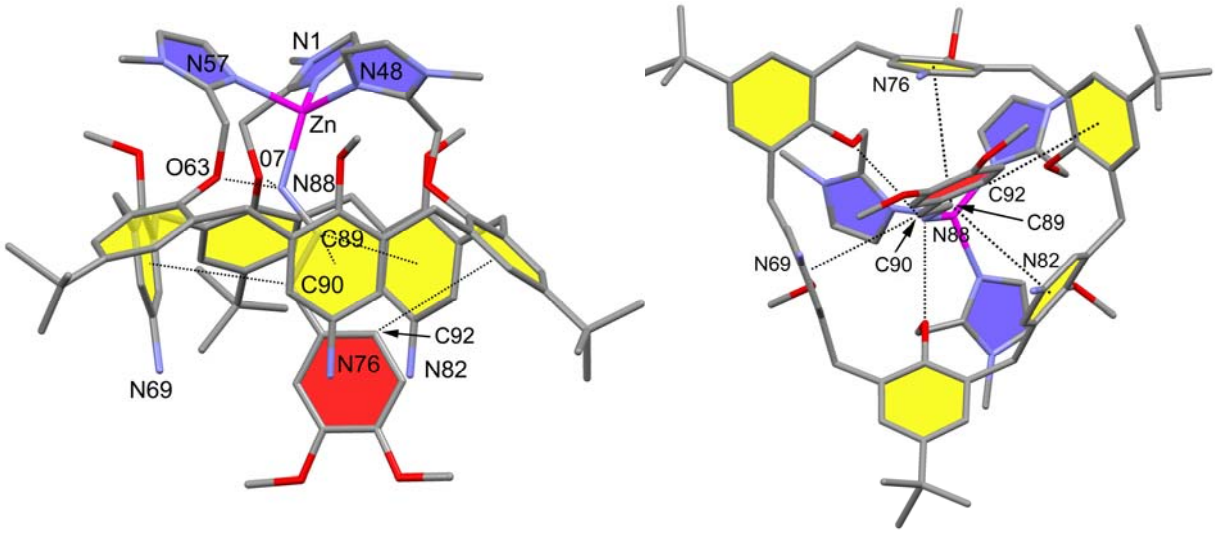
COSY ^{1}H NMR spectrum (250 MHz, $CDCl_3$, 300 K) of complex **3** (5 mM) with 6 equiv. of dimethyldopamine (it corresponds to the ^{1}H NMR spectrum c) above reported). α, β, δ, δ', ε, ζ and ζ': guest dimethyldopamine; α, β, δ, δ', ε, ζ and ζ' (in grey): free dimethyldopamine; dotted lines: correlations.

The determination of the endo-coordinated dimethyldopamine proton signals required a COSY ^{1}H NMR analysis. It was performed with the sample corresponding to spectrum c (page S-6) and showed $^3J_{HH}$ correlations for the α (1.38 ppm) and β (0.50 ppm) protons as well as for aromatic protons δ (4.92 ppm) and ε (6.28 ppm). Surprisingly, the resonance of the δ' proton (5.83 ppm) have been identified through a $^4J_{HH}$ correlation with the δ proton (4.92 ppm).

XRD of complex 3 with dimethyldopamine as a guest

Slow diethyl ether diffusion onto a solution of complex **3** (≈ 3 mg) and 6 equiv. of dimethyldopamine in CH_2Cl_2/CH_3CN (1:1; 0.5 mL) resulted in the formation of colourless crystals suitable for X-Ray analysis.

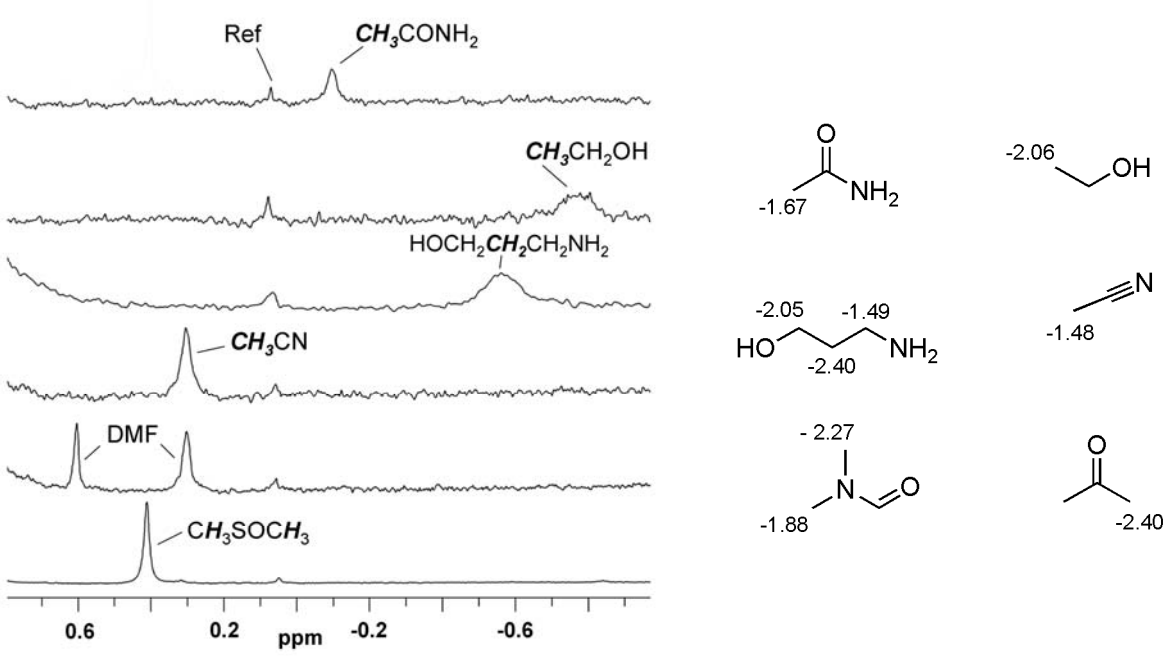
Crystal data: C_{82} H_{102} Cl_2 N_{10} O_{16} Zn, M_w = 1620.01, triclinic, space group P-1; dimensions: a = 16.0388(6) Å, b = 16.3548(7) Å, c = 20.0055(9) Å, α = 75.968(2)°, β = 78.527(2)°, γ = 88.231(2)°, V = 4988.5(4) $Å^3$; Z = 2; μ = 0.358 mm^{-1}; 76509 reflections measured at 100 K; independent reflections: 29217 [12362 Fo > 4σ (Fo)]; data were collected up to a 2Θmax value of 60.32° (99.0 % coverage). Number of variables: 1017; R_1 = 0.0741, wR_2 = 0.1927, S = 0.869; highest residual electron density 1.474 e.$Å^{-3}$ (all data R_1 = 0.1435, wR_2 = 0.2158). CCDC 690396.



XRD structures of complex **3** with dimethydopamine as a guest. Left: side view; right: bottom view. Hydrogen atoms and counter anions have been omitted for clarity. Dotted lines: hydrogen bonds (NH···O) and CH-π interactions.

Distances (Å):	d(Zn-N(1)) =	2,003(3)
	d(Zn-N(57)) =	2,027(3)
	d(Zn-N(88)) =	2,038(2)
	d(Zn-N(48)) =	1,991(2)
Angles (degree):	N(48)-Zn-N(1) =	108,71(10)
	N(48)-Zn-N(57) =	104,87(10)
	N(1)-Zn-N(57) =	104,40(11)
	N(48)-Zn-N(88) =	122,38 (10)
	N(1)-Zn-N(88) =	113,83(10)
	N(57)-Zn-N(88) =	100,28(10)
Hydrogen bonds (Å):	d(N(88)···O(7)) =	2,94
	d(N(88)···O(63)) =	3,01
CH-π interactions (Å):	d(C(89)···centroïd) =	4,02 each
	d(C(90)···centroïd) =	3,77
	d(C(92)···centroïd) =	4,10

High-field ^{1}H NMR spectrum area of complex 3 with inclusion of various organic guests and measured Δδ



Left: ^{1}H High-field NMR spectra (250 MHz, $CDCl_3$, 300 K) of complex **3** after the addition of a) $AcNH_2$, b) EtOH, c) 3-aminopropanol, d) MeCN, e) DMF, and f) DMSO. The H atoms displayed in italics correspond to the ^{1}H NMR signal. Right: measured Δδ ($\Delta\delta = \delta_{L\ endo\text{-}bound} - \delta_{L\ free}$.