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


# Supporting Information

## First Water-Soluble *Bowl* Complex: Molecular Recognition of Acetate by the Biomimetic Tris(imidazole) Zn(II) System at pH 7.4

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**General experimental methods.** All solvents and reagents were obtained commercially. THF and $CH_2Cl_2$ were freshly distilled under Argon over sodium/benzophenone and $CaH_2$, respectively. Anhydrous "extra-dry" DMF and DMA ($H_2O$ < 30 ppm, Acros) were used as received and kept over molecular sieves under Argon. The one- and two-dimensional $^1H$ and $^{13}C$ NMR spectra were recorded with a Bruker ARX250 MHz spectrometer and Advance 500 spectrometer (500 MHz). The $^1H$ and $^{13}C$ chemical shifts (δ) were referred to $SiMe_4$. Standard HSQC and HMBC experiments were used for peak assignments. MS (ESI) analyses were obtained with a ThermoFinnigen LCQ Advantage spectrometer using methanol, dichloromethane or acetonitrile as solvents. HRMS (ESI) analyses were obtained with a Spectrometer (LC) ESI/TOF (LCT, Waters) and with a Spectrometer ES/Orbitrap (Exactive, ThermoScientific). IR spectra were obtained with a Perkin-Elmer Spectrum on FTIR spectrometer equipped with a MIRacleTM single reflection horizontal ATR unit (germanium crystal). Elemental analyses were performed at the Institut de Chimie des Substances Naturelles (France). For this purpose, the products were dried for at least one night under vacuum at 60-70°C. The pD values of the solutions were corrected considering $pD = pH_{read} + 0.4$ at 25°C.

**Experimental procedures**

Methylene bridged cavitand **1** was obtained by following ref: Gibb, B. C.; Chapman, R. G.; Sherman, J. C. *J. Org. Chem.* **1996**, *61*, 1505-1509.

**Tetrabromocavitand (R= $(CH_2)_3$OTIPS) (2)**

Tetrabromocavitand **1** (1.0 g, 0.923 mmol) was dissolved in anhydrous DMF (10 ml) under argon. Imidazole (0.954 g, 14.0 mmol) was added to the solution. After 10 min, triisopropylsilyl chloride (2.69 mL, 12.6 mmol) was added and the solution was stirred at room temperature for 24 h. DMF was removed under reduced pressure. The residue was dissolved in $CH_2Cl_2$ (20 ml) and washed with water (3x5 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated. The crude was purified by flash column chromatography ($SiO_2$, $CH_2Cl_2$/cyclohexane 1:3 then 2:3) to yield silylated product **2** as a white foam (1.30 g, 82%). $^1$H NMR (500 MHz, $CDCl_3$, 300 K) δ (ppm): 7.06 (m, 4H, Ar-H down), 5.96 (d, *J* = 7.4 Hz, 4H, -O-$CH_{2out}$-O-), 4.89 (t, *J* = 8.0 Hz, 4H, $CH_2$-CH), 4.40 (d, *J* = 7.4 Hz, 2H, -O-$CH_{2in}$-O-), 3.77 (t, *J* = 6.0 Hz, 8H, $CH_2$-OTIPS), 2.36-2.21 (m, 8H, $CH_2$-$CH_2$-CH), 1.67-1.55 ($CH_2$, m, 8H), 1.09 (s, 72H, $Si(CH_3)_2$); 1.08 (s, 12H, SiCH); $^{13}$C NMR (125 MHz, $CDCl_3$, 300 K) δ (ppm): 152.3, 139.3, 119.2, 113.7, 98.6, 62.8, 37.3, 30.9, 27.1, 26.2, 18.2, 12.2; IR (ATR): ν = 2942, 2854, 1464, 1449, 1417, 1382, 1312, 1261, 1231, 1177, 1105, 1086, 1021, 1011, 964, 888, 789, 727 cm$^{-1}$; Anal. Calcd for $C_{80}H_{124}Br_4O_{12}Si_4 \cdot H_2O$ : C, 55.61; H, 7.35; found: C, 55.63; H, 7.32.

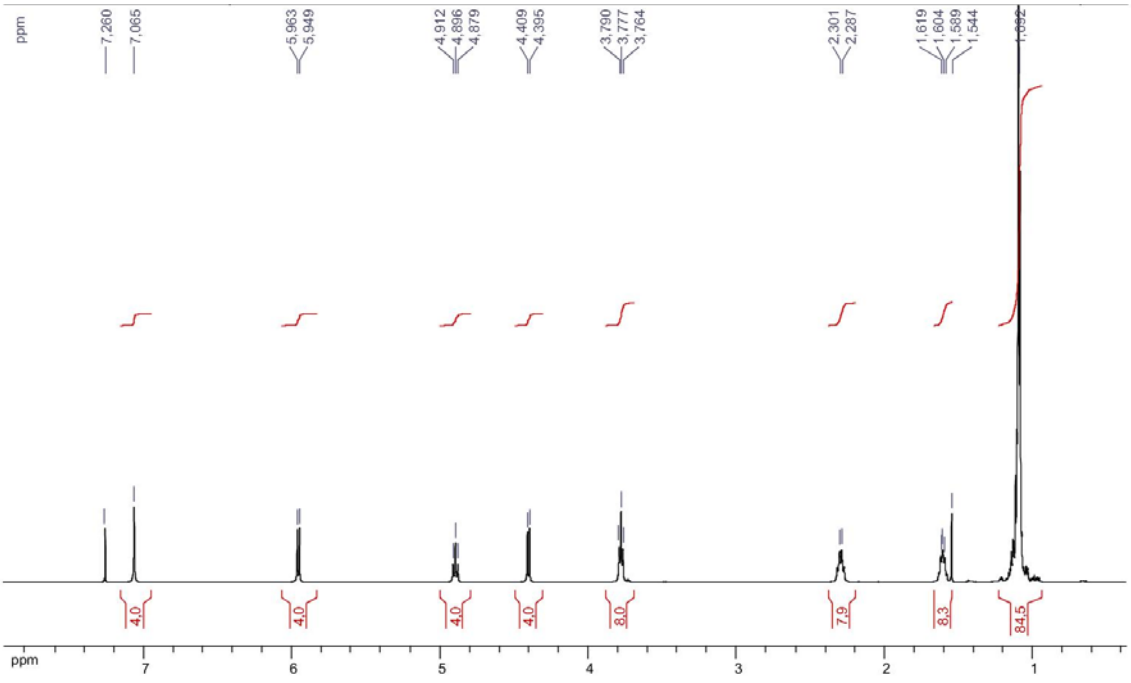



**Figure S1.** $^{1}$H NMR (500 MHz) spectrum of **2** recorded at 300 K in $CDCl_3$.

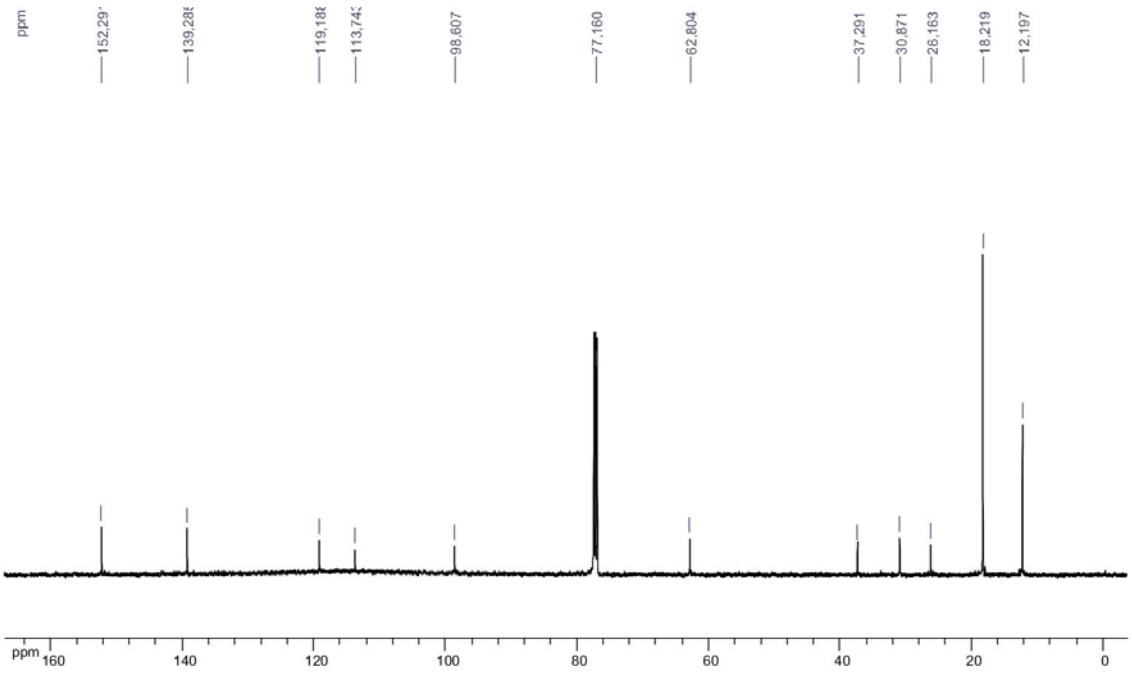



**Figure S2.** $^{13}$C NMR (125 MHz) spectrum of **2** recorded at 300 K in $CDCl_3$.

**Tribromocavitand (3)**

To the tetrabromocavitand **2** (3.2 g, 1.9 mmol) was added freshly distilled dry THF (10 mL) under argon and the solution was evaporated to dryness and then heated to 80°C at 0.1 mmHg over 1h. Repeating this process twice gave a material sufficiently dried for the selective

reductive debromination reaction. After dissolution in freshly distilled anhydrous THF (90 mL), the reaction mixture was cooled to -78°C, and freshly titrated *n*-butyllithium (1.28 ml of a 1.6 M solution in hexanes, 2.0 mmol) was added. After 15 min, methanol (2.0 mL) was added, and the mixture was allowed to warm to room temperature. Solvent evaporation gave a residue which was dissolved in $CH_2Cl_2$, washed with water, then saturated brine and dried over anhydrous $MgSO_4$. The organic layer was filtered and the solvent was evaporated under vacuum. Purification by flash column chromatography on silica gel (60 g of $SiO_2$, cyclohexane/$CH_2Cl_2$ from 3:2 to 2:3) gave compound **3** as white foam (2.5 g, 81 %). $^1$H NMR (500 MHz, $CDCl_3$, 300 K) δ (ppm): 7.11 (s, 1H, Ar-H down), 7.08 (s, 3H, Ar-H down), 6.55 (s, 1H, Ar-H up), 5.96 (d, *J* = 7.3 Hz, 2H, -O-$CH_{2,out}$-O-), 5.86 (d, *J* = 7.3 Hz, 2H, -O-$CH_{2,out}$-O-), 4.90 (t, *J* = 8.25 Hz, $CH_2$-CH , 2H), 4.84 (t, *J* = 8.25 Hz, $CH_2$-CH , 2H), 4.43 (d, *J* = 7.3 Hz, 2H, -O-$CH_{2,in}$-O-), 4.40 (d, *J* = 7.3 Hz, 2H, -O-$CH_{2,in}$-O), 3.79 (t, *J* = 6.3 Hz, 8H, $CH_2$-OTIPS), 2.40-2.20 (m, 8H, $CH_2$-$CH_2$ -CH), 1.72-1.52 (m, 8H, $CH_2$), 1.09 (m, 72H, $Si(CH_3)_2$), 1.08 (m, 12H, SiCH); $^{13}$C NMR (125 MHz, $CDCl_3$, 300 K) δ (ppm): 155.1, 152.4, 152.2, 152.1, 139.6, 139.3, 139.1, 138.3, 120.9, 119.3, 119.06, 117.1, 113.6, 99.1, 98.6, 76.9, 62.9, 62.8, 37.3, 36.6, 30.9, 30.9, 27.1, 26.1, 18.2, 12.2; IR (ATR): ν = 2942, 2854, 1464, 1449, 1417, 1382, 1312, 1261, 1231, 1177, 1105, 1086, 1021, 1011, 964, 888, 789, 727 cm$^{-1}$; Anal. Calcd for $C_{80}H_{125}Br_3O_{12}Si_4 \cdot H_2O$ : C,58.27; H,7.76; found: C,58.56 ; H,7.77 .

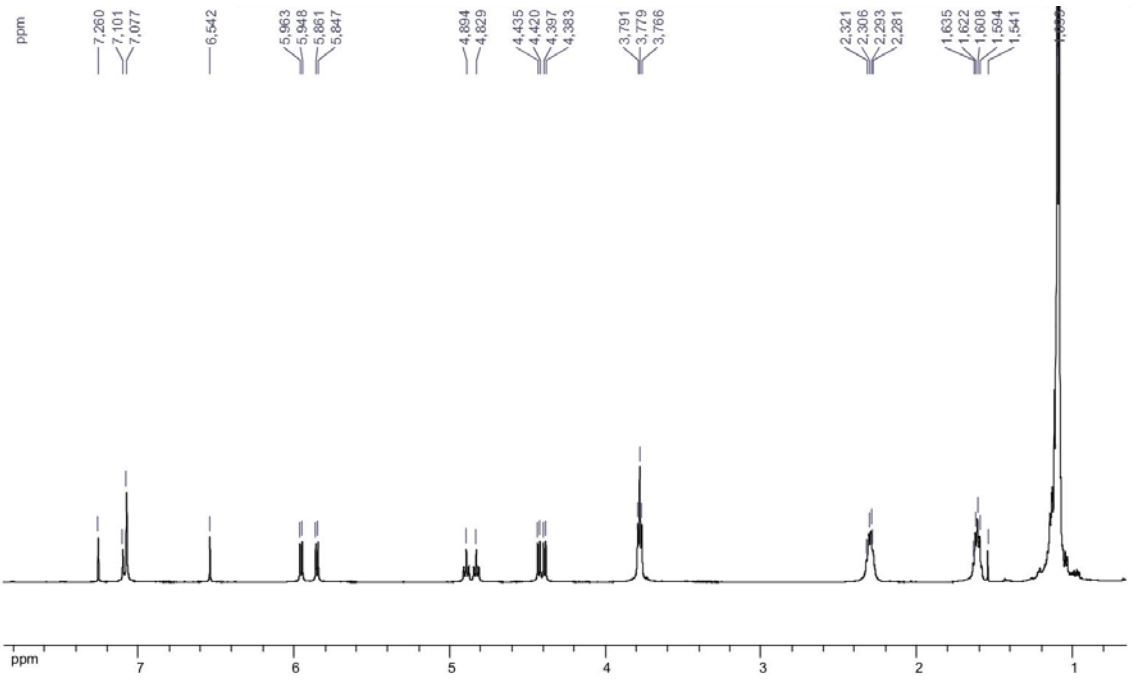



**Figure S3.** $^1$H NMR (500 MHz) spectrum of **3** recorded at 300 K in $CDCl_3$.

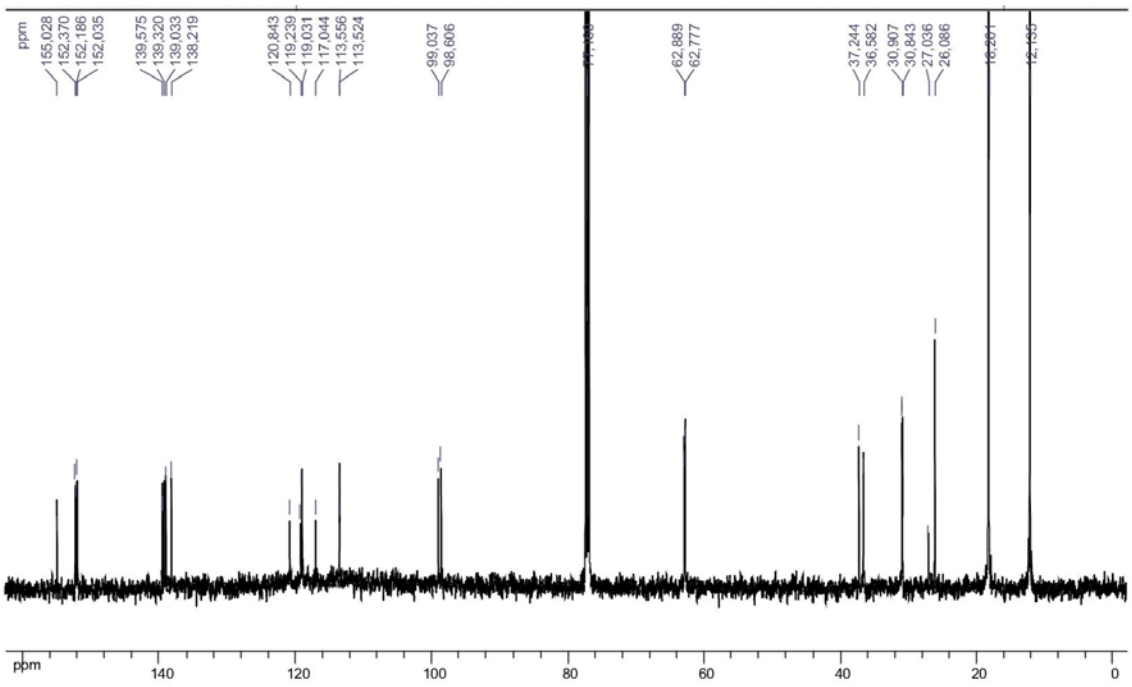



**Figure S4.** $^{13}C$ NMR (125 MHz) spectrum of **3** recorded at 300 K in $CDCl_3$.

**Triestercavitand**

Tribromocavitand **3** (1.17 g, 0.72 mmol) was dissolved in freshly distilled THF (2 mL) under argon and the solution was evaporated to dryness and then heated to 80°C at 0.1 mmHg over 1 h. The procedure was repeated twice. To a solution of the dried tribromocavitand in THF (26 mL) at -78 ˚C, was slowly added freshly titrated *n*-butyllithium (1.56 mL, 1.52 M solution, 2.37 mmol). After two hours, methyl chloroformate (554 µL, 7.17 mmol) was rapidly added and the reaction mixture was stirred for 12 hours at room temperature. Water (2 mL) was added at 0°C and the solvents were evaporated under vacuum. The residue was taken up in $CH_2Cl_2$ (50 mL), washed with water (2 x 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated to give 1.20 g of white foam. The product was used in the next step without further purification.

**Triolcavitand (4)**

The crude triestercavitand (0.72 mmol) was dissolved in freshly distilled THF (2 mL) under argon and the solution was evaporated to dryness and then heated to 80°C at 0.1 mmHg over 1 h. The procedure was repeated twice. Under an inert atmosphere, the solution of this dried triestercavitand in dry THF (27 mL) was introduced into a flask containing $LiAlH_4$ (273 mg, 7.2 mmol) and dry THF (27 mL) at 0°C. The mixture was stirred at 0°C for 10 min then at room

temperature for 3 h. To this mixture was added dropwise at 0°C ethyl acetate (30 mL) , MeOH (2 mL) and finally water (2 mL). The mixture was stirred at room temperature for 1h. $Na_2SO_4$ was added and stirring was followed for 30 min. The reaction mixture was filtered over Büchner. The filtrate was concentrated to yield the crude product, which was then purified by flash column chromatography on silica gel (DCM/MeOH, 94:6) to give triol **4** (784 mg) in 74 % yield over 2 steps.

$^1$H NMR (500 MHz, $CDCl_3$, 300 K) δ (ppm): 7.14 (s, 3H, Ar-H down), 7.13 (s, 1H, Ar-H down), 6.50 (Ar-H up, s, 1H), 5.90 (d, *J* = 7.3 Hz, 2H, -O-$CH_{2out}$-O-), 5.81 (d, *J* = 7.3 Hz, 2H, -O-$CH_{2out}$-O-), 4.82 (t, *J* = 7.8 Hz, $CH_2$-CH, 2H), 4.79 (t, *J* = 7.8 Hz, $CH_2$-CH, 2H), 4.58 (br s, 4H $CH_2OH$), 4.52 (br s, $CH_2OH$), 4.49 (d, *J* = 7.4 Hz, 2H, -O-$CH_{2in}$-O-), 4.40 (d, *J* = 7.3 Hz, 2H -O-$CH_{2in}$-O-), 3.78 (t, *J* = 6.5 Hz, 8H, $CH_2$-OTIPS), 2.36-2.22 (m, 8H, $CH_2$-$CH_2$-CH), 1.70-1.52 (m, 8H, $CH_2$), 1.09 (s, 72H, $Si(CH_3)_2$); 1.08 (s, 12H, SiCH); $^{13}$C NMR (125 MHz, $CDCl_3$, 300 K) δ (ppm): 155.0, 153.9, 153.7, 138.3, 138.2, 138.1, 126.5, 126.3, 120.6, 120.4, 120.3, 117.0, 99.9, 99.7, 63.1, 55.7, 55.5, 36.5, 36.2, 31.1, 26.3, 26.3, 18.2, 12.2. – IR (ATR): ν = 2948, 2858, 2119, 1597, 1483, 1461 1387, 1300, 1241, 1100, 1086, 1016, 1001, 964, 882 cm$^{-1}$. Anal. Calcd for $C_{83}H_{134}O_{15}Si_4 \cdot 3H_2O$ : C, 64.80; H, 9.17; found : C, 64.80; H, 8.82.

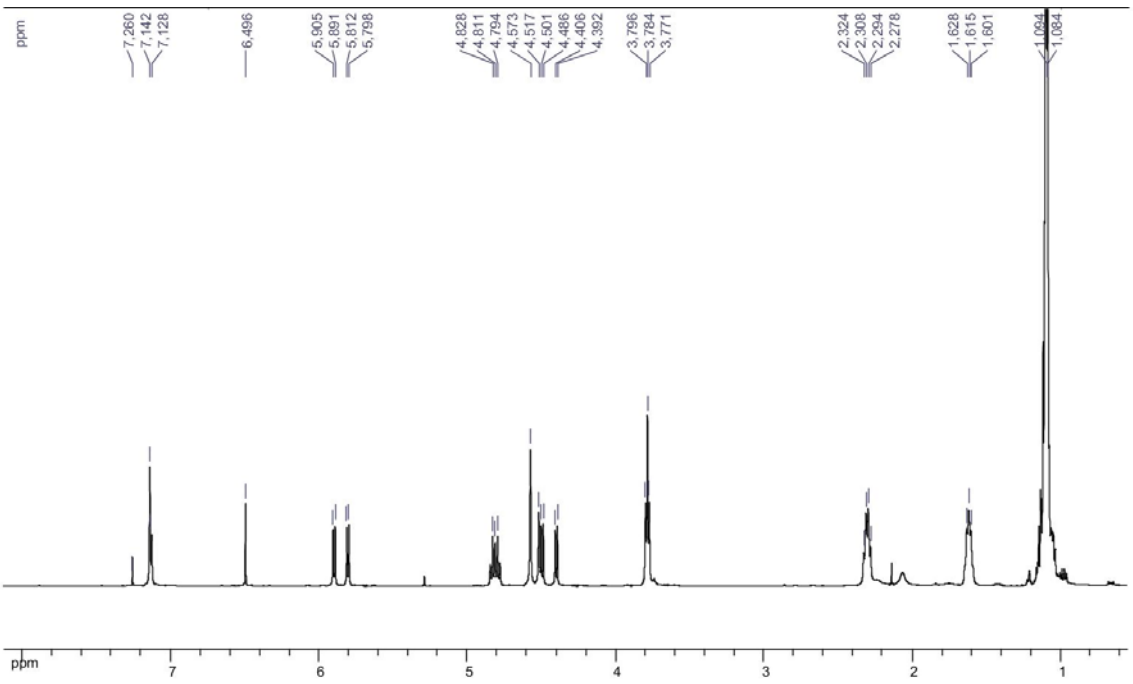



**Figure S5.** $^1$H NMR (500 MHz) spectrum of **4** recorded at 300 K in $CDCl_3$.

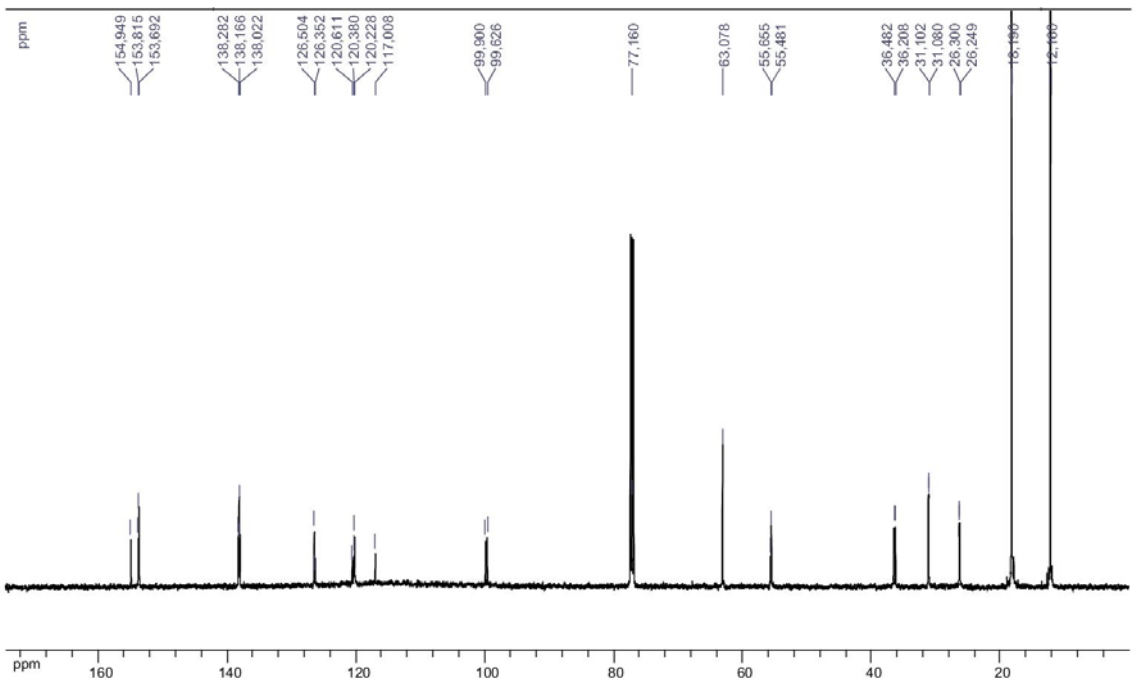



**Figure S6.** $^{13}$C NMR (125 MHz) spectrum of **4** recorded at 300 K in $CDCl_3$.

**Bowl-ligand (5)**

Triol **4** (383 mg, 0.26 mmol) was dissolved in freshly distilled THF (2 mL) under argon and the solution was evaporated to dryness and then heated to 80°C at 0.1 mmHg over 1 h. The procedure was repeated twice. Under an inert atmosphere, a solution of this dried triol in dry DMF (9 mL) was introduced into a flask containing sodium hydride (60% in oil, washed with pentane, 310 mg, 7.74 mmol) in dry DMF (9 mL) at 0°C. The reaction mixture was stirred at 0°C for 30 minutes then 1h at r.t. At 0°C, 2-chloromethyl-1-methyl-1H-imidazole hydrochloride (180 mg, 1.08 mmol) was added to the reaction mixture, which was then stirred at 0°C for 30 minutes. Further addition of 2-chloromethyl-1-methyl-1H-imidazole hydrochloride (180 mg, 1.08 mmol) was realized at 0°C and the mixture stirred at 0°C for additional 30 minutes. This procedure was repeated once again. The reaction mixture was subsequently stirred overnight at r.t. and then poured dropwise at 0°C into water (100 mL) to precipitate the product. The solid was filtered over Büchner, and washed with water. It was subsequently dissolved in dichloromethane (50 mL), washed with water twice (2*30 mL), dried over $Na_2SO_4$, filtered and concentrated. The crude product was triturated with pentane (2*5 mL) to give ligand **5** (337 mg, 74%) as a white powder. $^1$H NMR (500 MHz, $CDCl_3$, 300 K) δ (ppm) : 7.09 (s, 3H, Ar-H down), 7.05 (s, 1H, Ar-H down), 6.95 (br s, 1H, Im-H), 6.94 (br s, 2H, Im-H), 6.92 (br s, 1H, Im-H), 6.86 (br s, 2H, Im-H), 6.40 (s, 1H, Ar-H up), 5.65 (d, *J* = 7.0

Hz, 2H, -O-$CH_{2out}$-O-), 5.60 (d, *J* = 7.0 Hz, 2H, -O-$CH_{2out}$-O-), 4.76 (t, *J* = 8.0 Hz, $CH_2$-CH, m, 2H), 4.73 (t, *J* = 8.0 Hz, $CH_2$-CH, m, 2H), 4.60 (s, 2H, Im-$CH_2$-O-), 4.58 (s, 4H, Im-$CH_2$-O-), 4.35 (d, *J* = 7.0 Hz, 2H, -O-$CH_{2in}$-O-), 4.32 (s, 4H, Ar-$CH_2$-O-), 4.19 (d, *J* = 7.0 Hz, 2H, -O-$CH_{2in}$-O-), 4.17 (s, 2H, Ar-$CH_2$-O-), 3.75 (t, *J* = 6.7 Hz, 8H, $CH_2$-OH), 3.66 (s, 3H, $NCH_3$), 3.62 (s, 6H, $NCH_3$), 2.25 (m, 8H, $CH_2$-$CH_2$-CH), 1.57 (m, 8H, OH-$CH_2$-$CH_2$), 1.09-1.06 (m, 84H, Si-CH-$(CH_3)_2$); $^{13}$C NMR (125 MHz, $CDCl_3$, 300 K) δ (ppm) : 154.9, 154.3, 154.1, 144.6, 144.4, 138.1, 138.0, 137.8, 127.8, 127.5, 123.9, 123.5, 122.3, 122.1, 120.9, 120.7, 120.5, 117.1, 99.6, 99.5, 64.8, 63.1, 62.3, 61.9, 36.5, 36.2, 33.0, 32.9, 31.2, 31.1, 26.3, 26.2, 18.2, 12.2; ESI-MS (MeOH) m/z: 1766.5 $[Rim_{(OTIPS)4}H]^+$. ESI-MS (MeOH) m/z: 1766.05 $[Rim(OTIPS)_4 + H]^+$; HRMS (ESI+, Orbitrap) m/z: 1767.05078 (calcd for $[M+H]^+$ 1767.05045 (0.2 ppm)); Anal. Calcd for $C_{98}H_{152}N_6O_{15}Si_4.H_2O$ : C, 65.95 ; H, 8.70 ; found : C, 65.71 ; H, 8.70.

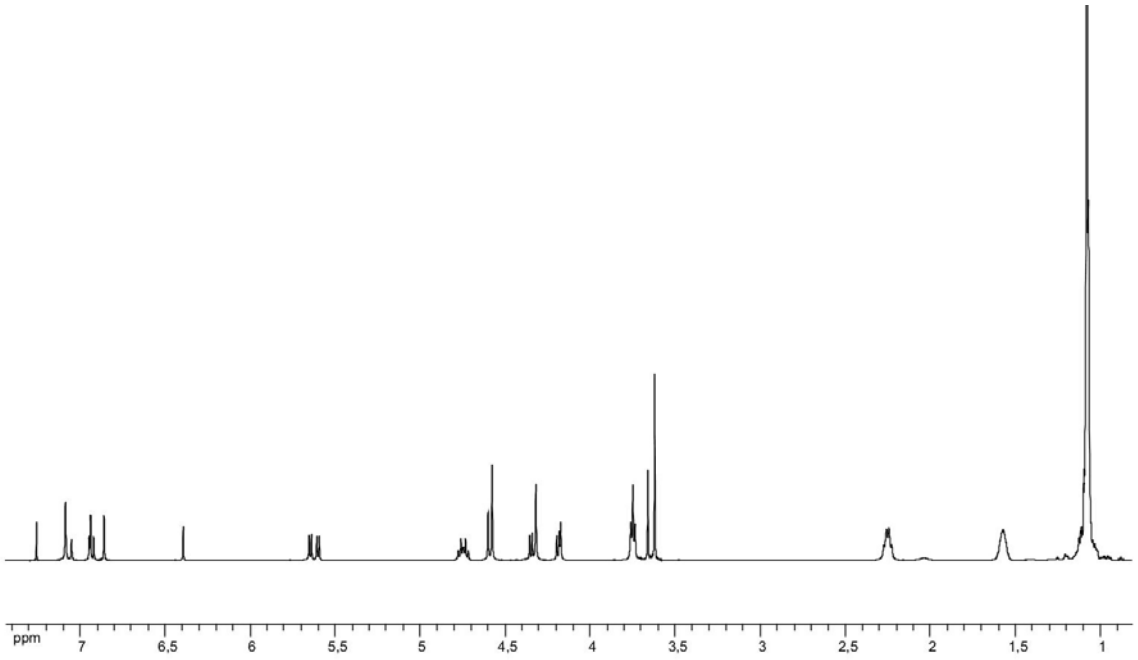



**Figure S7.** $^1$H NMR (500 MHz) spectrum of **5** recorded at 300 K in $CDCl_3$.

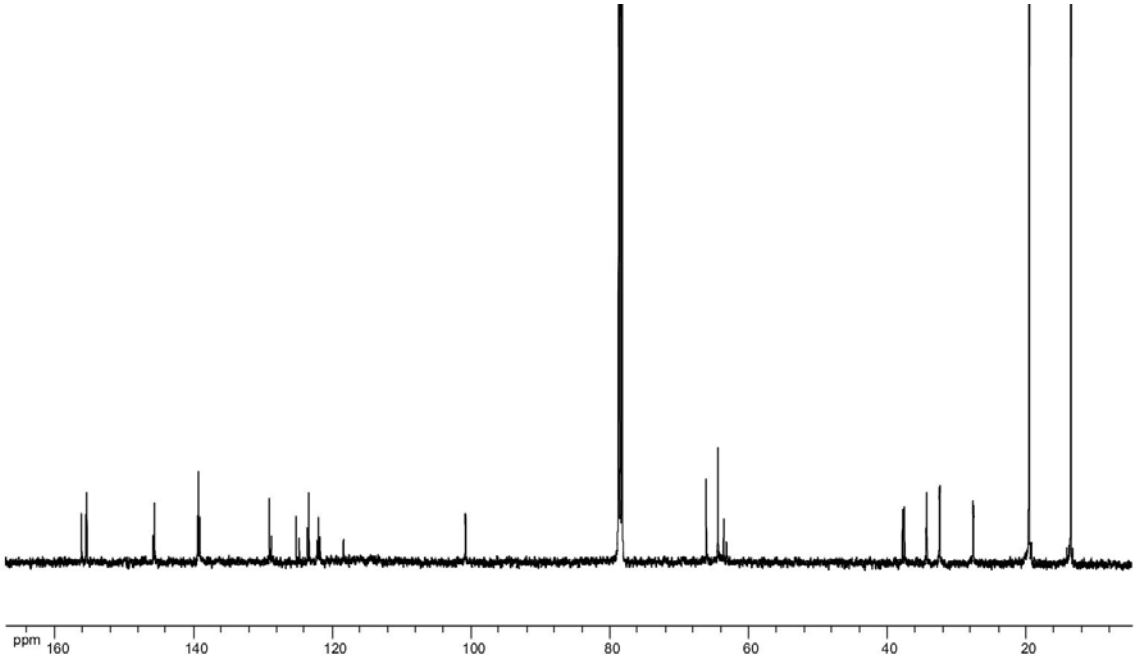



**Figure S8.** $^{13}C$ NMR (125 MHz) spectrum of **5** recorded at 300 K in $CDCl_3$.

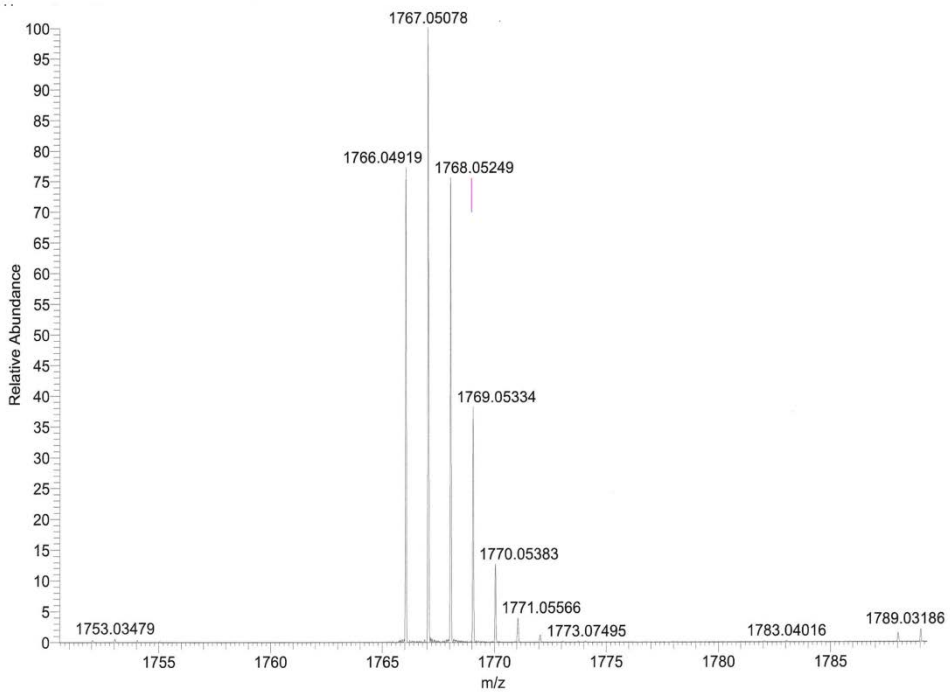



**Figure S9.** HRMS (ES, Orbitrap) of bowl-ligand **5**

**Bowl-ligand deprotected (6)**

Ligand **5** (0.050 g, 0.028 mmol) was dissolved in a THF/$H_2O$ (1:1) mixture (3 mL). TFA (0.3 mL, 4.040 mmol) was added dropwise and the mixture was stirred overnight at r.t. TFA was evaporated, after which the resulting solid was suspended in toluene (2 mL). Solvents were

evaporated. Toluene was again and solvents were evaporated. The resulting solid was dried at the vacuum ramp. It was then dissolved in MeOH (4 mL) and stirred with DOWEX $OH^-$ resin (BioRad, AG-1*4 resin, 200-400 mesh, chloride form transformed to hydroxide form by treating the commercial resin with 2M NaOH solution and rinsing it with water until neutral pH). The resin was filtered off over a frit filter (pore size nº 3) and washed with MeOH. The filtrate was concentrated, suspended in a (1:1) mixture of toluene/MeOH, solvents were evaporated and the resulting solid was dried under vacuum, than triturated with pentane (3*3 mL), centrifugated and dried over vacuum ramp, yielding product **6** as a white powder (0.041 g, 91%).

$^1$H NMR (500 MHz, $CDCl_3$/MeOD, 300K) δ (ppm): δ (ppm) : 7.07 (s, 3H, Ar-H down), 7.03 (s, 1H, Ar-H down), 6.79 (s, 1H, Im-H), 6.75 (s, 1H, Im-H), 6.73 (s, 2H, Im-H), 6.26 (s, 1H, Ar-H up), 5.49 (d, *J* = 2.4 Hz, 2H, -O-$CH_{2,out}$-O-), 5.48 (d, *J* = 2.2 Hz, 2H, -O-$CH_{2,out}$-O-), 4.58 (t, *J* = 8.1 Hz, 2H, $CH_2$-CH), 4.53 (t, *J* = 8.1 Hz, 2H, $CH_2$-CH), 4.60 (s, 2H, Im-$CH_2$-O-), 4.58 (s, 4H, Im-$CH_2$-O-), 4.37 (s, 4H, Ar-$CH_2$-O-), 4.36 (s, 2H, Ar-$CH_2$-O-), 4.17-4.14 (m, 6H, Ar-$CH_2$-O, -O-$CH_{2in}$-O-), 4.12-4.00 (m, 8H, Ar-$CH_2$-O, OH, -O-$CH_{2in}$-O-), 3.51 (t, *J* = 5.9 Hz, 8H, $CH_2$OH), 3.47 (s, 3H, $NCH_3$), 3.46 (s, 6H, $NCH_3$), 2.21-2.10 (m, 8H, $CH_2$-$CH_2$-CH), 1.44-.1.32 (m, 8H, $CH_2$); $^{13}$C NMR (125 MHz, $CDCl_3$/MeOD, 300 K) δ (ppm): 154.6, 154.0, 153.9, 153.8, 144.2, 144.0, 137.9, 137.8, 137.6, 126.7, 126.5, 123.4, 123.0, 122.3, 122.1, 121.2, 121.0, 120.7, 116.6, 99.3, 63.8, 63.7, 62.0, 61.8, 36.7, 36.5, 32.6, 30.8, 26.15, 26.1; IR (ATR): ν = 3290, 2937, 2883, 1590, 1495, 1471, 1461, 1421, 1401, 1288, 1239, 1150, 1060, 1019, 1001, 744 $cm^{-1}$; ESI-MS (MeOH) m/z: 1141.5 $[Rim(OH)_4 + H]^+$ 1163.5; HRMS (TOF ES+) m/z: 1141.5150 (calcd for $[M+H]^+$ 1141.5134 (1.4 ppm))

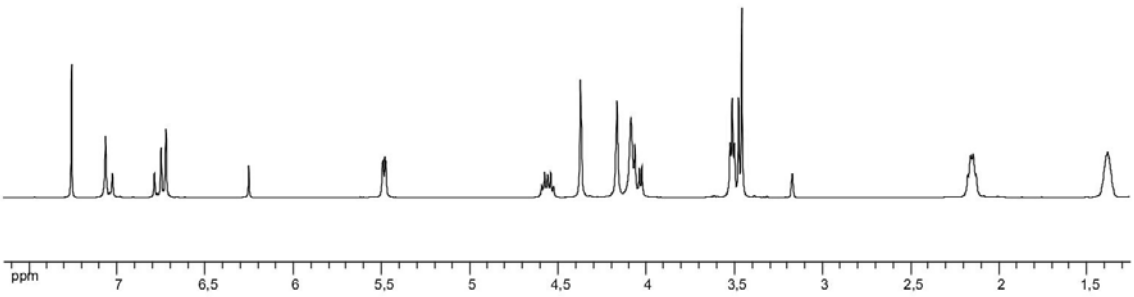



**Figure S10.** $^{1}$H NMR (500 MHz) spectrum of **6** recorded at 300 K in $CDCl_3$/MeOD.

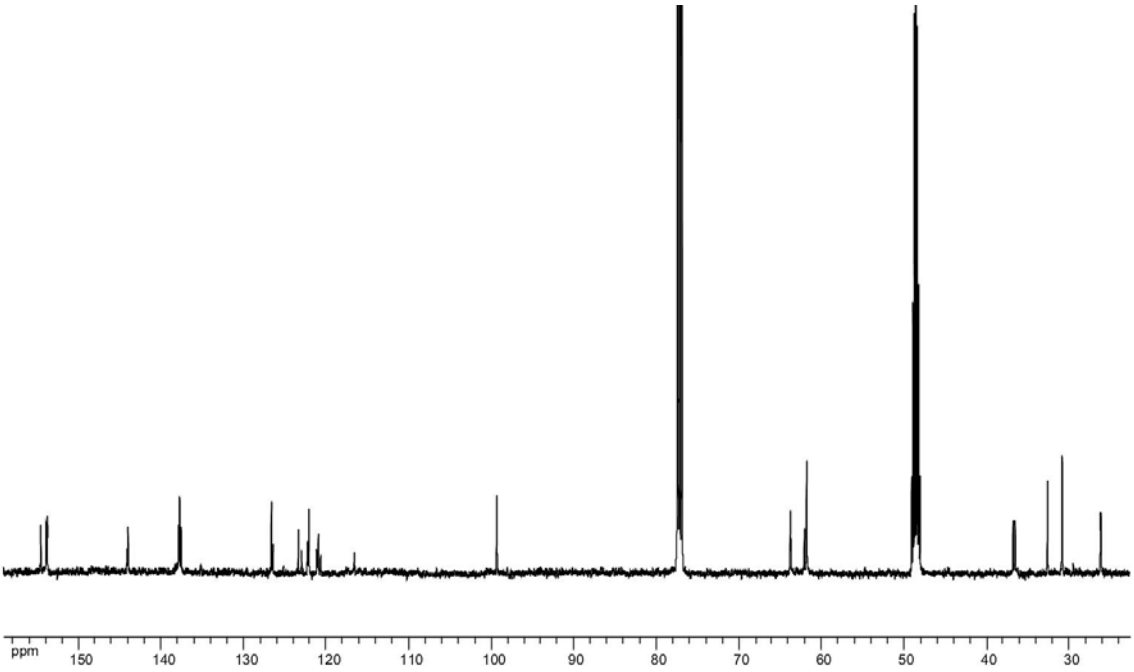



**Figure S11.** $^{13}$C NMR (125 MHz) spectrum of **6** recorded at 300 K in $CDCl_3$/MeOD.

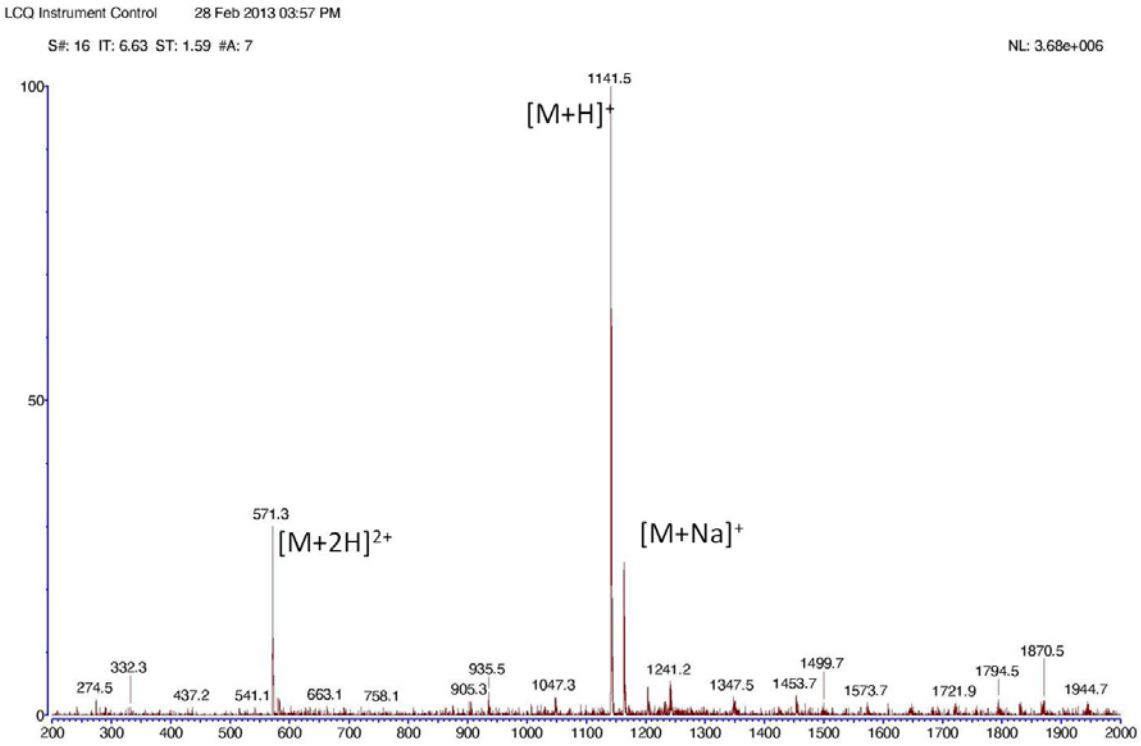



**Figure S12.** MS (ESI) of bowl-ligand **6**

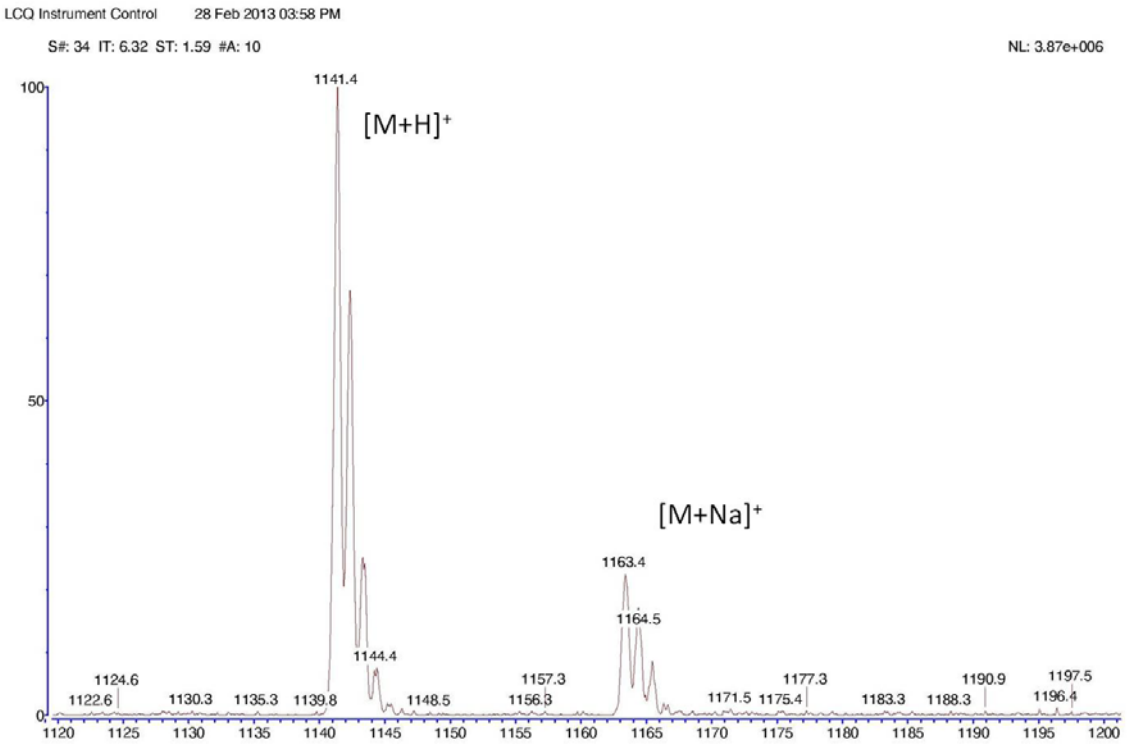



**Figure S13.** MS (ESI) of bowl-ligand **6** - Zoom

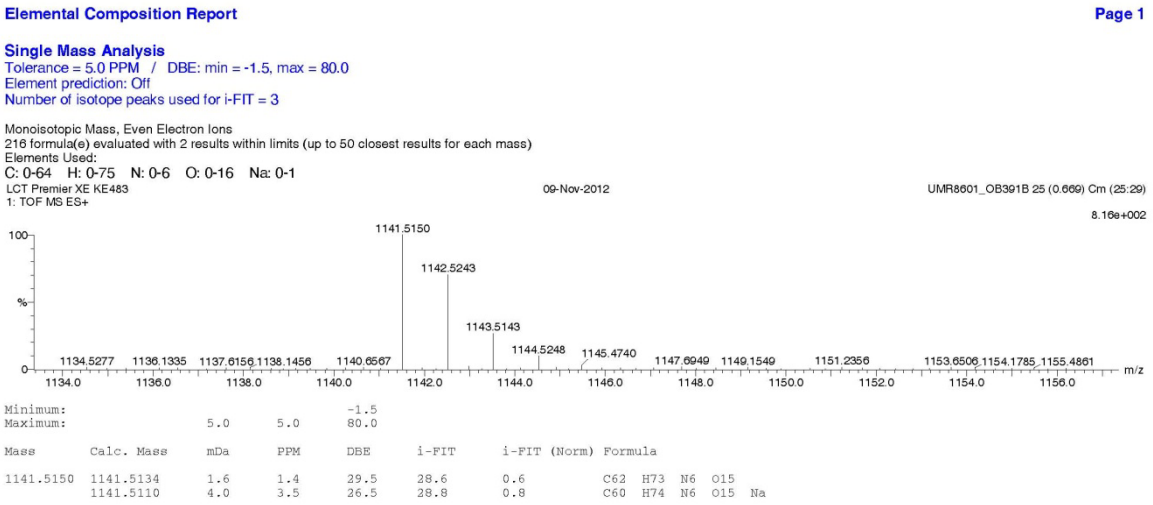



**Figure S14.** HRMS (TOF ES+) of bowl-ligand **6**

### Water-soluble bowl-ligand WRim$_3$ (7)

Bowl ligand **6** (200 mg, 0.175 mmol) was dissolved in DMF (10 mL). To this solution was added at 0°C N,N-diisopropylethylamine (360 µL, 2.18 mmol) followed by mesyl chloride (160 µL, 2.06 mmol). The reaction mixture was stirred at r.t. overnight. Dichloromethane (10 mL) was added and the organic layer was washed twice with a saturated solution of $NaHCO_3$ followed by brine. Organic layer was dried over $Na_2SO_4$, filtered and concentrated.

The mesylated cavitand (20 mg, 0.014 mmol) was dissolved in 500 µL of acetone in a sealed tube. Trimethylamine (500 µL of a 40% aqueous solution) was added and stirred during 12 h at 40°C. The aqueous solution was concentrated and the residue was dried under vacuum to afford 19 mg of a yellow solid (85 %). $^1$H NMR (500 MHz, $D_2O$, 300 K) δ (ppm): 7.60 (s, 3H, Ar-H down), 7.58 (s, 1H, Ar-H down), 7.18 (s, 3H, Im-H), 7.06 (s, 3H, Im-H), 6.79 (s, 1H, Ar-H up), 5.86 (d, *J* = 7.4 Hz, 2H, -O-$CH_{2,out}$-O-), 5.81 (d, *J* = 7.4 Hz, 2H, O-$CH_{2out}$-O-), 4.68 (s, 4H, Im-$CH_2$-O-), 4.62 (s, 2H, -O-$CH_2$-Im), 4.50-4.37 (m, 6H, Ar-$CH_2$-O-), 4.38 (d, *J* = 6.6 Hz, 2H, -O-$CH_{2in}$-O-), 4.27 (d, *J* = 6.6 Hz, 2H, -O-$CH_{2in}$-O-), 3.61 (s, 6H, $NCH_3$), 3.55-3.49 (m, 11H, $NCH_3$, $CH_2$-$CH_2$-$\underline{CH_2}$-$N^+Me_3$), 3.31 (s, 12H, $MsO^-$), 3.12 (s, 36 H, $N^+Me_3$), 2.43 (m, 8H, $CH_2$-$\underline{CH_2}$-CH), 1.92 (m, 8H, $N^+Me_3$-$CH_2$-$\underline{CH_2}$); $^{13}$C NMR (125 MHz, $D_2O$, 300 K) δ (ppm): 156.1, 155.4, 155.3, 155.2, 155.1, 145.6, 139.3, 139.2, 139.0, 127.1, 127.0, 126.9, 125.4, 124.8, 123.4, 118.8, 101.3, 101.2, 101.1, 101.0, 100.8, 64.6, 64.4, 64.3, 63.2, 63.1, 59.6, 54.2, 46.1, 39.0, 38.0, 37.8, 37.5, 34.0, 27.6, 27.5, 27.4, 27.2, 22.4, 22.3, 22.2, 20.6; HRMS (TOF ES+)

m/z: 467.9232 (calcd for $[WRim_3(N^+Me_3)_4(^-OMs)]^{3+}$, $C_{75}H_{107}N_{10}O_{14}S$: M = 1403.7689; m/z: 467.9229 (0.5 ppm))

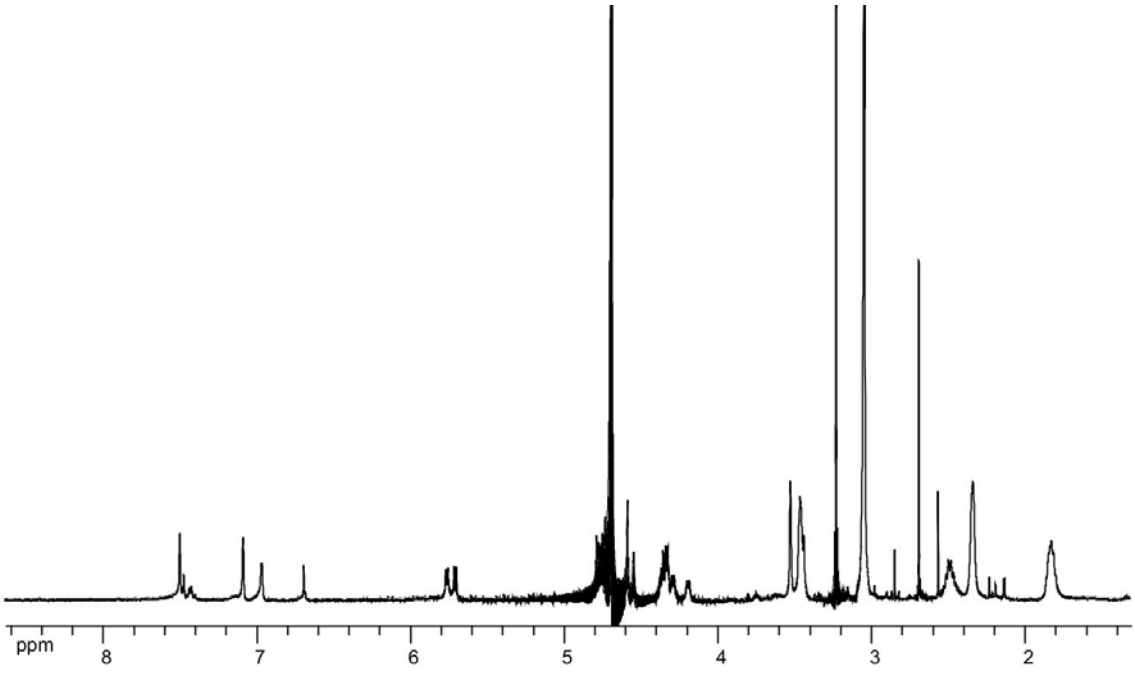



**Figure S15.** $^1$H NMR (500 MHz) spectrum of **WRim$_3$** recorded at 300 K in $D_2O$.

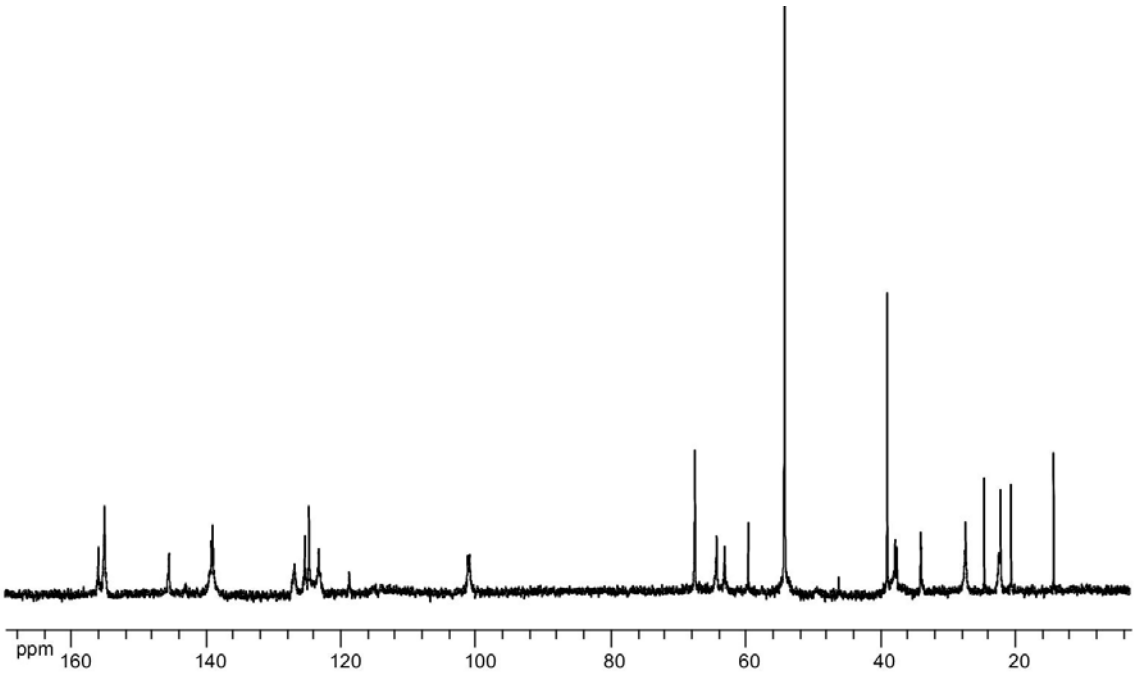


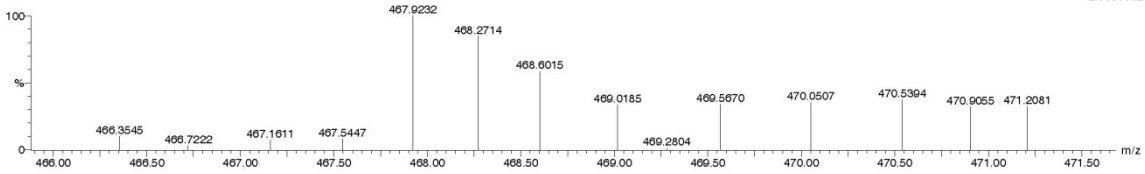

**Figure S16.** $^{13}$C NMR (125 MHz) spectrum of **WRim$_3$** recorded at 300 K in $D_2O$.

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 80.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
509 formula(e) evaluated with 5 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 70-100 H: 0-150 N: 10-10 O: 10-20 S: 0-4

LCT Premier XE KE483 01-Oct-2012 UMR8601_SR074 26 (0.680) Cm (26:28)
1: TOF MS ES+ 2.53e+002




| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | | | | | | |
| Maximum: | | 5.0 | 10.0 | 80.0 | | | | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | i-FIT (Norm) | Formula | | | | |
| 1403.7696 | 1403.7689 | 0.7 | 0.5 | 27.5 | -1.$ | n/a | C75 | H107 | N10 | O14 | S |
| | 1403.7714 | -1.8 | -1.3 | 23.5 | -1.$ | n/a | C71 | H107 | N10 | O19 | |
| | 1403.7723 | -2.7 | -1.9 | 22.5 | -1.$ | n/a | C72 | H111 | N10 | O14 | S2 |
| | 1403.7655 | 4.1 | 2.9 | 32.5 | -1.$ | n/a | C78 | H103 | N10 | O14 | |
| | 1403.7808 | -11.2 | -8.0 | 36.5 | -1.$ | n/a | C82 | H103 | N10 | O11 | |

**Figure S17.** HRMS (TOF ES+) of **WRim$_3$.**

**Estimation of the imidazole p*Ka* values**

A solution of $WRim_3$ **7** (2.0 mg, 1.2 µmol) in $D_2O$ (500 µL, [**7**] = 2.4 mM) was prepared. pD value was measured (pD = 6.42). Aliquots of a NaOD solution or a $HNO_3$ solution were gradually added to this solution and pD values and $^1H$ NMR spectra were recorded after each addition.

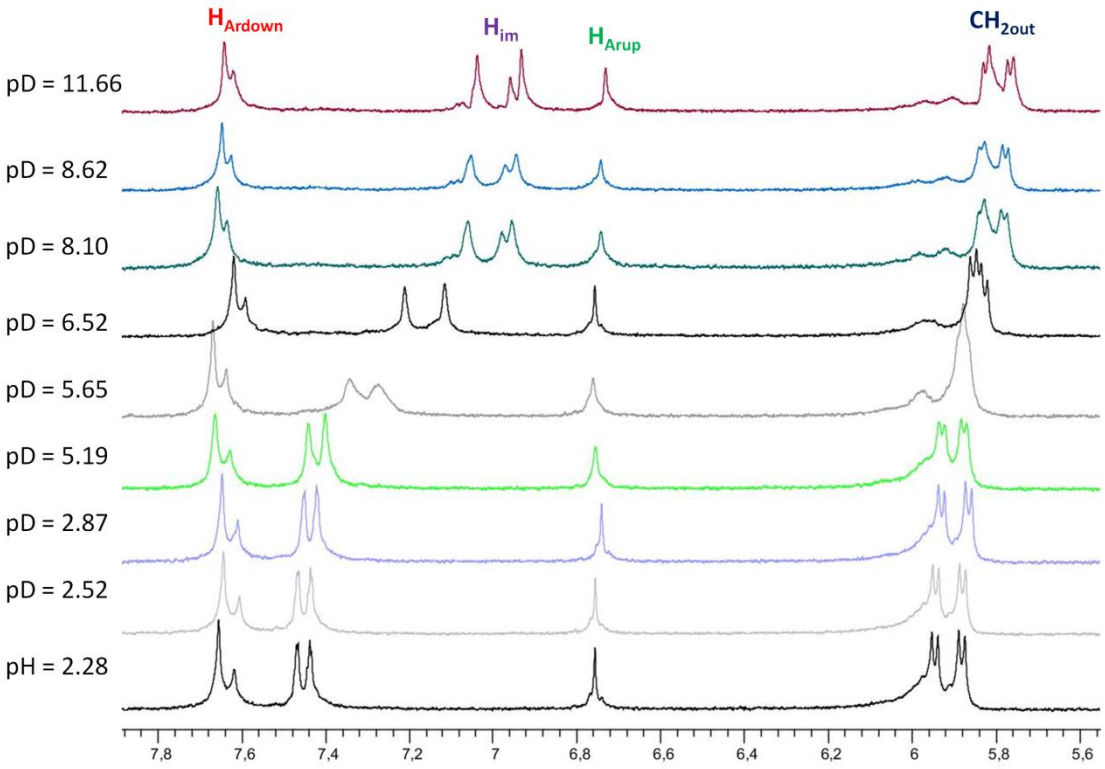



**Figure S18.** $^1H$ NMR (300K, 500 MHz) of a solution of $WRim_3$ **7** in $D_2O$ (C = 2.4 mM) at different pD values.

**pD range for $WRim_3Zn$ complex detection**

A solution of $WRim_3$ **7** (2.0 mg, 1.2 µmol) in the presence of 1 equiv. of $Zn(NO_3)_2$ in $D_2O$ (500 µL, [**7**] = 2.4 mM) was prepared. Aliquots of a NaOD solution or a $HNO_3$ solution were gradually added to this solution and pD values and $^1H$ NMR spectra were recorded after each addition.

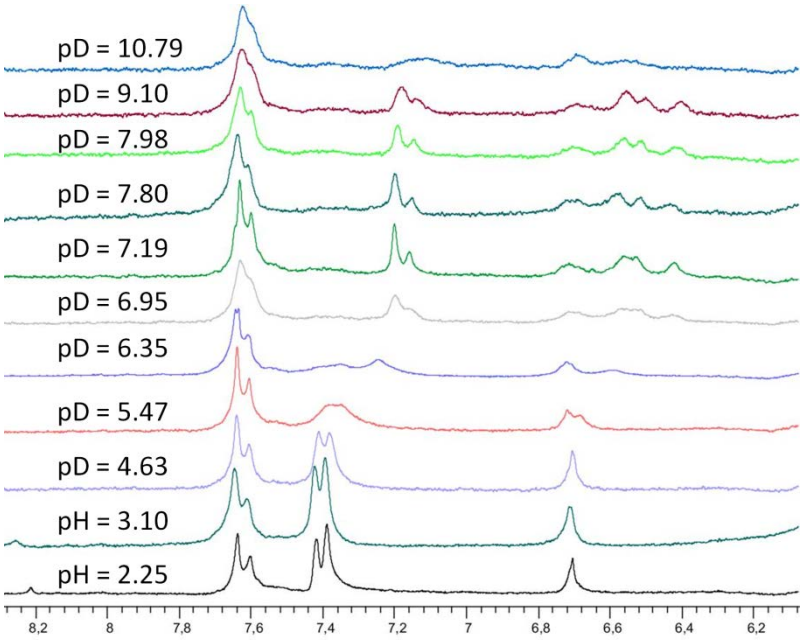



**Figure S19.** $^{1}$H NMR (300K, 500 MHz) of a solution of $WRim_3$ **7** in the presence of 1 equiv. of $Zn(NO_3)_2$ in $D_2O$ (C = 2.4 mM) at different pD values.

**Optimal pD determination**

A solution of $WRim_3$ **7** (2.4 mg, 1.5 µmol) in $D_2O$ (600 µL, [**7**] = 2.5 mM) in the presence of 1 equiv. of $Zn(OAc)_2$ and 1.1 equiv. of DMF was prepared. pD value was measured (pD = 7.15). Aliquots of a NaOD solution or a $HNO_3$ solution were gradually added to this solution and pD values and $^{1}$H NMR spectra were recorded after each addition. The integration value of the methyl of the encapsulated acetate anion signal in comparison with a reference peak (DMF) was evaluated at different pD.

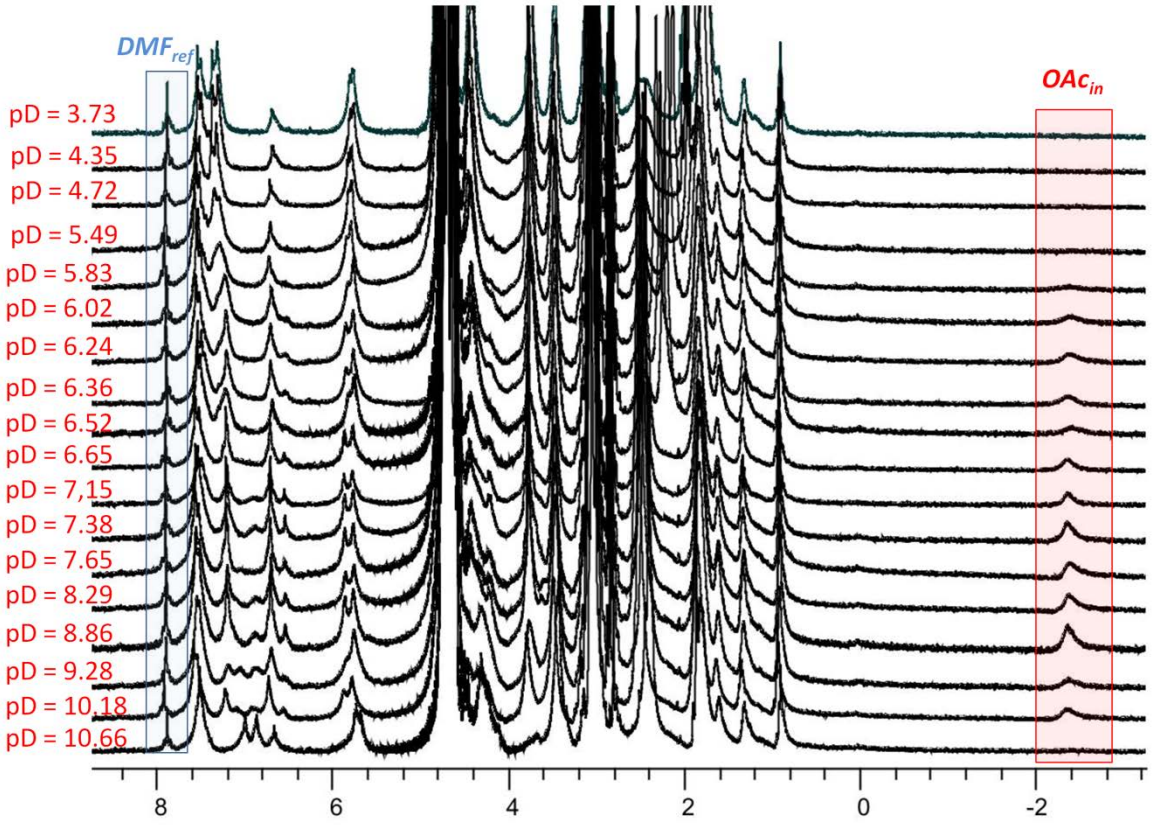



**Figure S20.** $^{1}$H NMR (300K, 500 MHz) of a solution of WRim$_3$ **7** in $D_2O$ (C = 2.5 mM) in the presence of 1 equiv. of $Zn(OAc)_2$ and 1.1 equiv. of DMF at different pD values.

**K' determination at various pD**

$WRim_3Zn + AcO^- = WRim_3ZnOAc$

$$\frac{I}{Iref} = \frac{[WRim_3ZnOAc]}{[DMF]} = \frac{[WRim_3ZnOAc]}{1.1*[WRim_3Zn]_0}$$

$[WRim_3Zn]_0$ = 2.5 mM and $[OAc]_0 = 2*[WRim_3Zn]_0 = 5$ mM

$$K'_{pD} = \frac{[WRim_3ZnOAc]}{[WRim_3Zn][OAc]}$$

$$K'_{pD} = 1.1*(I/Iref)*1/([WRim_3Zn]_0*(1-1{,}1I/Iref)*(2-1{,}1*I/Iref))$$

| **pD** | **I/Iref** | ***K'*pD** |
|---|---|---|
| 5,83 | 0,2 | 63 |

| | | |
|---|---|---|
| 6,02 | 0,2467 | 86 |
| 6,24 | 0,4233 | 227 |
| 6,65 | 0,4933 | 326 |
| 7,38 | 0,6067 | 602 |
| 8,29 | 0,5167 | 368 |
| 9,28 | 0,2067 | 66 |
| 10,18 | 0,14 | 39 |
| 3,73 | 0 | 0 |
| 10,66 | 0 | 0 |

**Full pictures of $^{1}$H NMR spectra cited in the article**

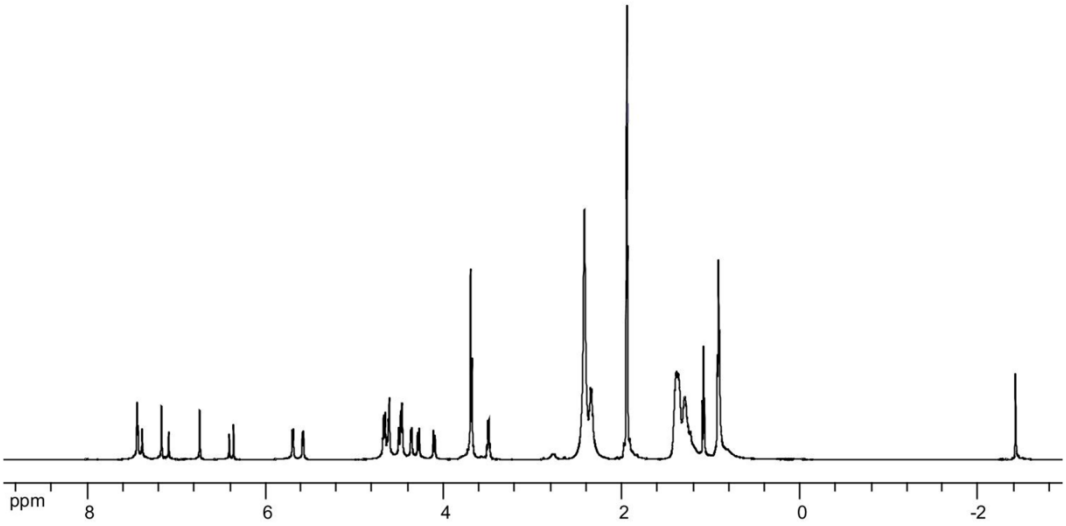



**Figure S21.** $^{1}$H NMR (253 K, 600 MHz) of organosoluble $Rim_3Zn(OAc)$ in $CD_3CN$.

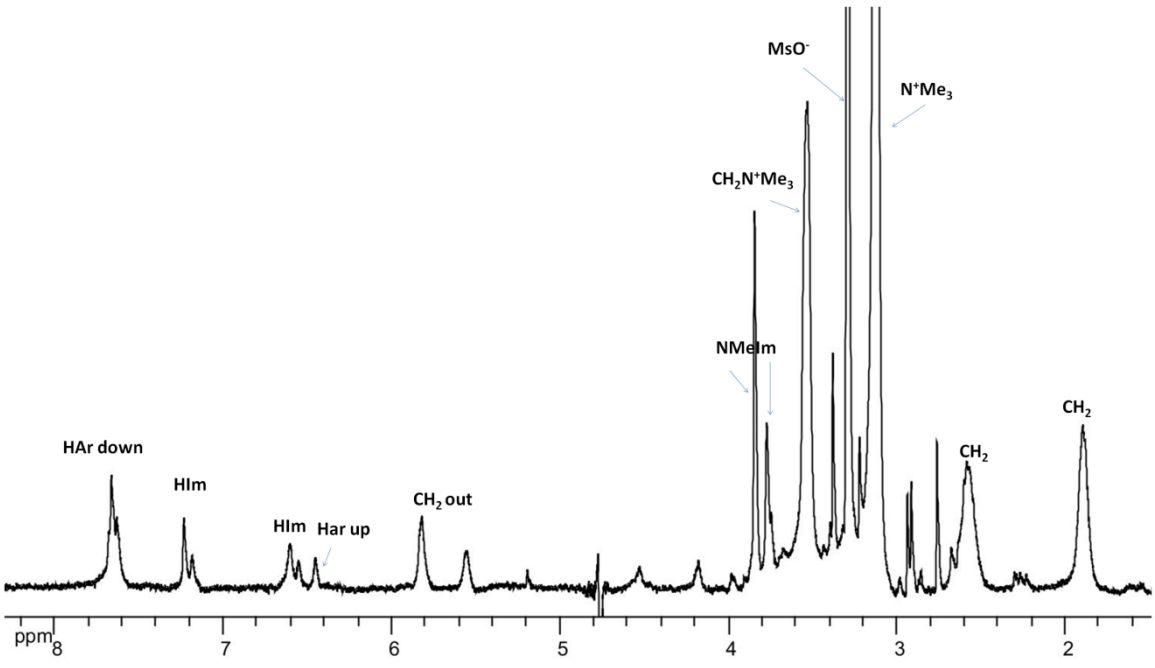



**Figure S22 (Full spectrum of Figure 2b).** $^{1}$H (WATERGATE solvent suppression) NMR spectrum (500 MHz) of free ligand **$WRim_3$** (2.4 mM) in the presence of 1 equiv. of $Zn(NO_3)_2$ in $D_2O$, pD = 7.3 at 300 K.

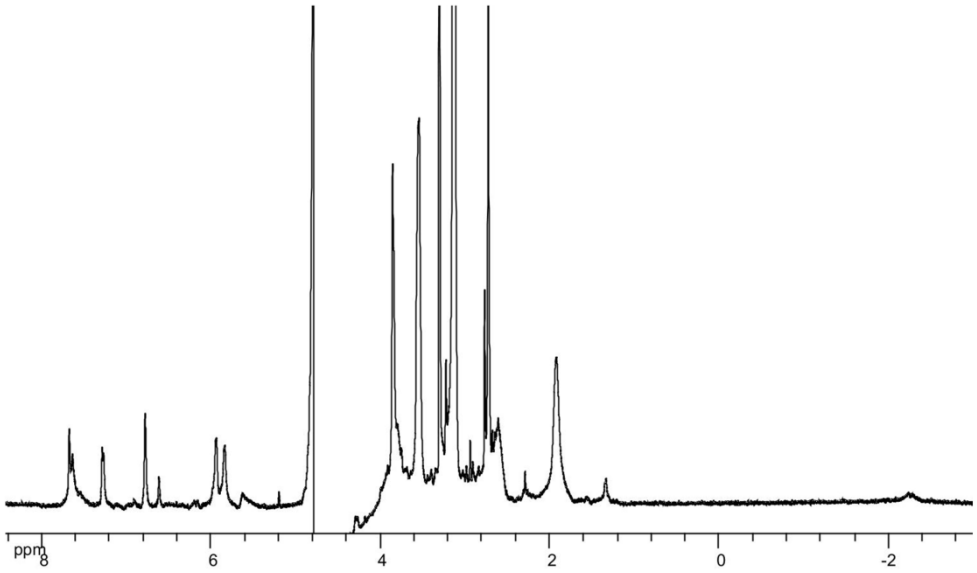



**Figure S23 (Full spectrum of Figure 2c).** $^{1}$H (WATERGATE solvent suppression) NMR spectrum (500 MHz) of free ligand **WRim$_3$** (2.9 mM) in the presence of 1 equiv. of $Zn(OAc)_2$ in $H_2O$, pH = 7.2 at 300 K.

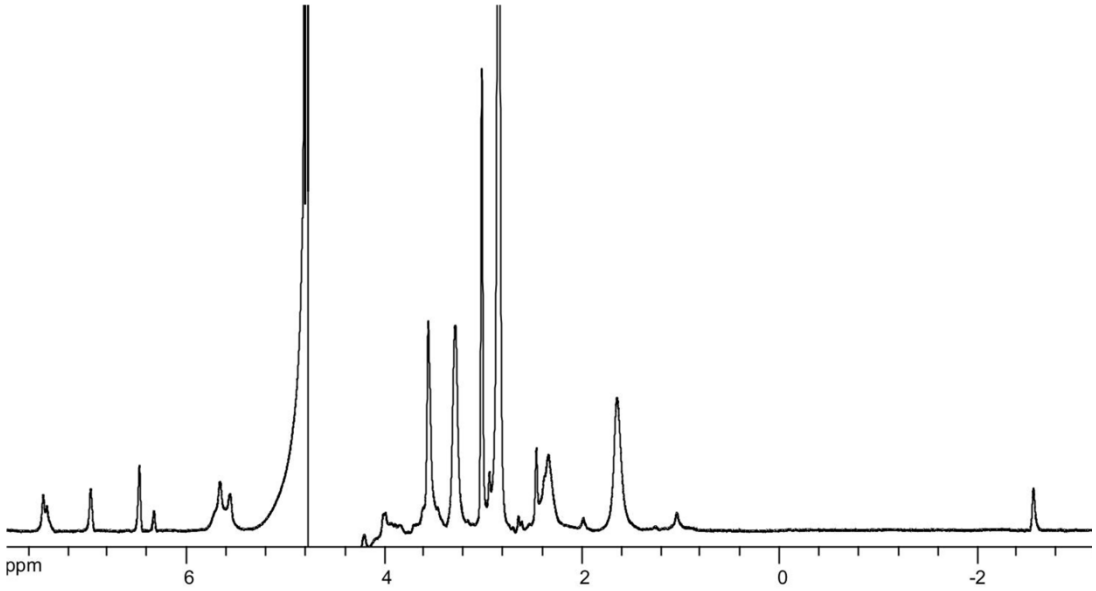



**Figure S24 (Full spectrum of Figure 2d).** $^{1}$H (WATERGATE solvent suppression) NMR spectrum (500 MHz) of free ligand **WRim$_3$** (2.9 mM) in the presence of 1 equiv. of $Zn(OAc)_2$ in $H_2O$, pH = 7.2 at 280 K.

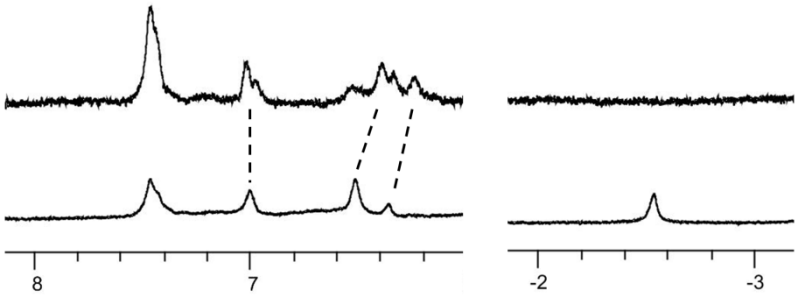



**Figure S25.** $^{1}$H (WATERGATE solvent suppression) NMR spectra (500 MHz) of free ligand **WRim$_3$** (2.4 mM) in the presence of 1 equiv. of $Zn(NO_3)_2$ in $D_2O$, pD = 7.9 at 280 K (top); and after addition of 3 equiv. of NaOAc at pD = 7.4 at 280 K (pD value of the solution was adjusted to this value by addition of aqueous $HNO_3$ solution aliquots).