Supporting Information

Recognition and Catalysis by a Cavitand Receptor Bearing a Zinc(II)-Salen Wall

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I. Synthesis of new cavitands

I-1. General Experimental

All reagents were obtained from commercial suppliers and were used without further purification unless otherwise noted. Dichloromethane and THF used for synthesis were dried using columns of activated alumina. All other solvents were purchased as such and used directly. All reactions were carried under a dry nitrogen atmosphere. The progression of reactions were monitored with thin layer chromatography on Merck 60 F_{254} 0.25 μm silica plates. Flash chromatography was carried out using Silicycle R10030B 60 Å 230-400 mesh silica gel. ^{1}H NMR spectra were obtained using a Brucker DRX-600 MHz spectrometer at 300 K. High accurancy mass spectra were obtained with an ESI-TOF mass spectrometer.

I-2. Synthesis of Cavitands 1 and Zn-1

Salen Cavitand 1

Hexa-amide cavitand (660 mg, 0.52 mmol) and 1,2 difluoro-4,5-dinitrobenzene (120 mg, 0.58 mmol) were dissolved in dry DMF (120 ml) under nitrogen. Triethylamine (240 μL, 0.86 mmol) was added dropwise and the reaction mixture was stirred at 70°C overnight. The solvent was removed by rotary evaporation and the residue was purified by column chromatography on

silicagel (eluant : EtOAc/CH_2Cl_2 1/1). The hexa-amide-di-nitro cavitand was precipitated with diethyl ether and dried under vacuo (356 mg, 48 % yield). This compound (350 mg, 0.25 mmol) was dissolved in THF, Raney nickel was added and the mixture was stirred at 40°C under hydrogen overnight. The mixture was filtered through celite, washed with THF and evaporated to give the crude diamino cavitand as a clear oil, which was dried *under vacuo* in the dark. The oil was then dissolved in toluene (120 mL) with an excess of 2-hydroxy-3,5-di-*t*-butylbenzaldehyde (3.9 g, ~100 eq). The mixture was stirred at reflux under nitrogen for 48 hours. After evaporation of the solvent, the residue was chromatographied on silicagel (CH_2Cl_2 to 15% EtOAc). The salen cavitand **1** was precipitated in a mix diethyl ether / hexanes and obtained as a yellow solid (275 mg, 62 % yield).

^{1}H NMR 600MHz CD_2Cl_2 25°C :13.43 (s, 2H, OH), 9.51 (br s, 2H, NH), 9.30 (br s, 2H, NH), 8.78 (s, 2H, H imine), 8.57 (br s, 2H, NH), 7.57 (s, 2H, Ar H), 7.50 (s, 2H, Ar H), 7.49 (s, 2H Ar H), 7.48 (s, 2H, Ar H), 7.37 (s, 2H, Ar H), 7.35 (s, 2H, Ar H), 7.30 (s, 4H, Ar H), 7.25 (s, 2H, Ar H), 7.16 (s, 2H, Ar H), 5.74 (t, 2H, *J* = 8.3 Hz, H benz.), 5.59 (t, 2H, *J* = 8.3 Hz, H benz.), 2.54-2.20 (m, 20H, CH_2), 1.45 (s, 18H, *t*-Bu), 1.34 (s, 18H, *t*-Bu), 1.27 (t, 6H, *J* = 7.7 Hz, CH_3), 1.15 (t, 12H, *J* = 7.5 Hz, CH_3), 0.97 (t, 6H, *J* = 7.3 Hz, CH_3), 0.75 (t, 6H, *J* = 7.5 Hz, CH_3)

ESI-TOF high-acc : calculated for $C_{108}H_{120}N_8O_{16}$: 1785.8895 ; found 1785.8866

UV-Visible : λ_{nm} (ε) : 283 (30100), 347 (19000)

Zn(II)-Salen-Cavitand Zn-1

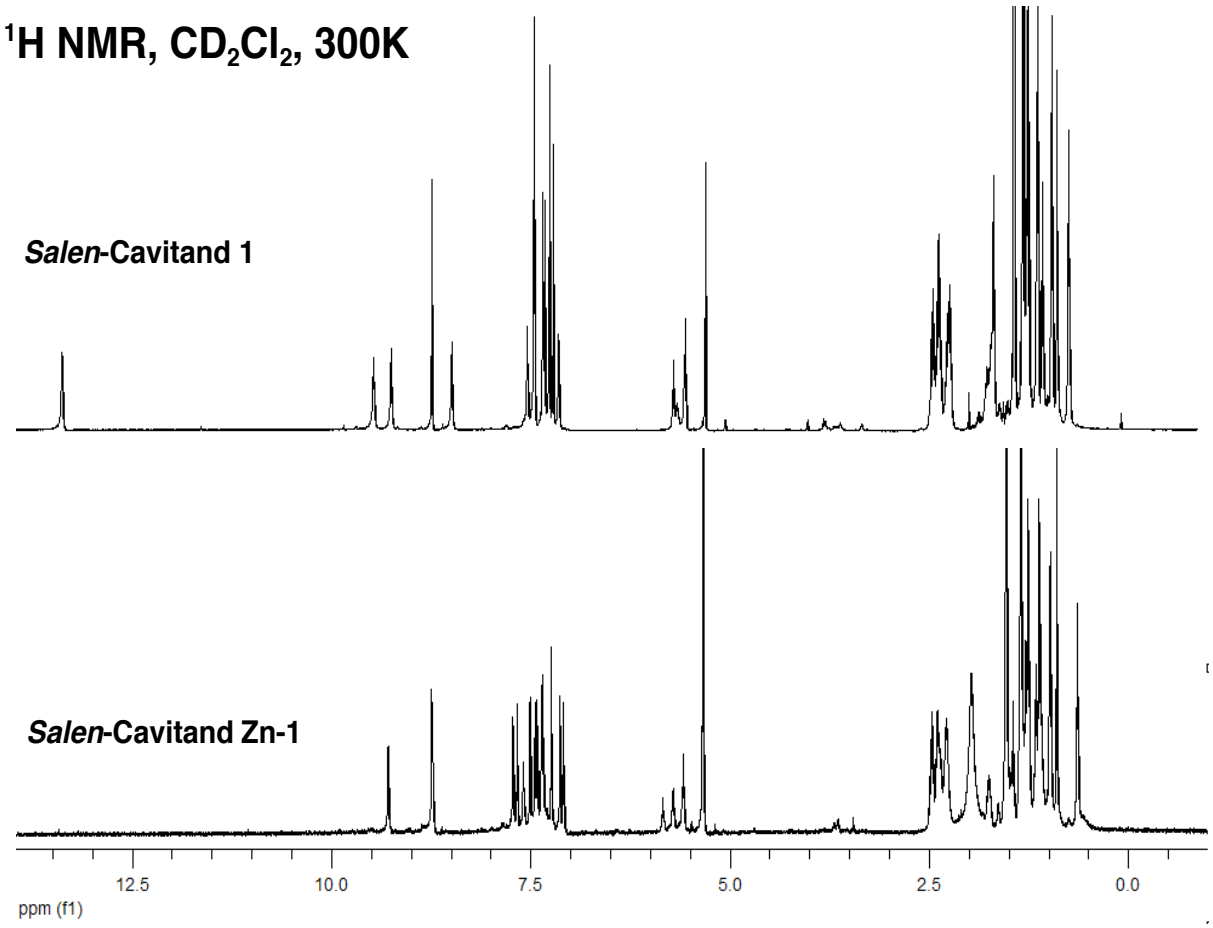
$ZnEt_2$ (110 µL) was added to a solution of salen-cavitand **1** (125 mg, 7.10^{-5} mol) in THF (10 mL) at room temperature under nitrogen. The mixture was stirred for 12 hours. The color of the solution changed from yellow to orange. After rotary evaporation of the solvent, the Zn(II)-cavitand **Zn-1** was precipitated in a mix diethyl ether / hexanes and obtained as an orange powder (94 mg, 73 % yield).

^{1}H NMR 600MHz CD_2Cl_2 25°C : 9.29 (br s, 2H, NH), 8.75 (s, 2H, H imine), 8.74 (br s, 2H, NH), 7.72 (s, 2H, Ar H) 7.67 (s, 2H, Ar H), 7.59 (br s, 2H, NH), 7.51 (s, 2H, Ar H), 7. 45 (s, 2H, Ar H), 7.42 (s, 2H, Ar H), 7.37 (s, 2H, Ar-H), 7.35 (s, 2H, Ar H), 7.24 (s, 2H, Ar H), 7.13 (s, 2H, Ar H), 7.09 (s, 2H, Ar H), 5.84 (t, 1H, *J* = 8.3 Hz, H benz.), 5.72 (t, 1H, *J* = 8.3 Hz, H benz.),

5.59 (t, 2H, *J* = 8.3 Hz, H benz.), 2.60-2.20 (m, 20H, CH_2), 1.54 (s, 18H, *t*-Bu), 1.36 (s, 18H, *t*-Bu), 1.30-0.94 (m, 18H, CH_3), 0.90 (t, 6H, *J* = 7.2 Hz, CH_3), 0.65 (t, 6H, *J* = 7.5 Hz, CH_3)

ESI-TOF high-acc : calculated for $C_{108}H_{118}N_8O_{16}Zn$: 1847.803 ; found 1847.7998

UV-Visible : λ_{nm} (ε) : 288 (19000), 426 (15000)



II. Kinetic tudy of the PNPCC hydrolysis

II-1. General Experimental

All reagents were obtained from commercial suppliers and used without further purification. The PNPCC was synthesized as previously described.[1] The salen ligand **2** and its zinc(II) complex **Zn-2** have been synthetized according to the procedure described by G.A.

Morris *et al.*[2] Dichloromethane used for the kinetic study was obtained from Fisher Scientific's (CH_2Cl_2 UN1593 HPLC-GC/MS grade containing 0.01 % of water). Kinetic experiments were performed in 1 mL quartz cells (10 mm) in a UV-visible Varian Cary 50 Bio Spectrometer (software : Varian Cary Win-UV Kinetic Application).

II-2. Kinetic experiments

Typical conditions used for the experiments were 40 μM of PNPCC, 20 mM of Hünig's base and 0.5 mM of TFA in CH_2Cl_2 at room temperature. A stock solution of buffered dichloromethane was prepared : 8.75 mL of Hünig's base and 0.1 mL of TFA in dichloromethane (final volume : 250 mL). Stock solutions of 80 μM of cavitand **1**, **Zn-1** and **Zn-2** were also prepared. For each experiment, a fresh solution 0.4 mM of PNPCC was prepared in dichloromethane (4 mg in 25 mL, sonication for 10 minutes).

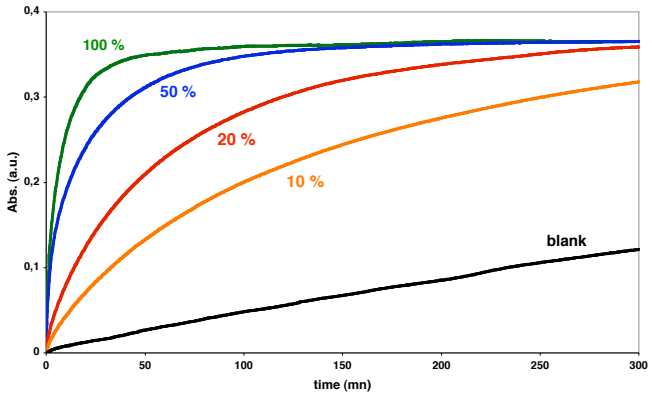
In a typical experiment, the different components are :

0.1 mL of stock buffered dichloromethane,
0.1 mL of stock PNPCC,
V mL of stock catalyst
0.8-V mL of dichloromethane.

The volume V depends of the desired catalyst concentration (for example, 0.1 mL of catalyst solution used for 20 % of catalyst / PNPCC). For the blank experiment the catalyst solution was replaced by dichloromethane.

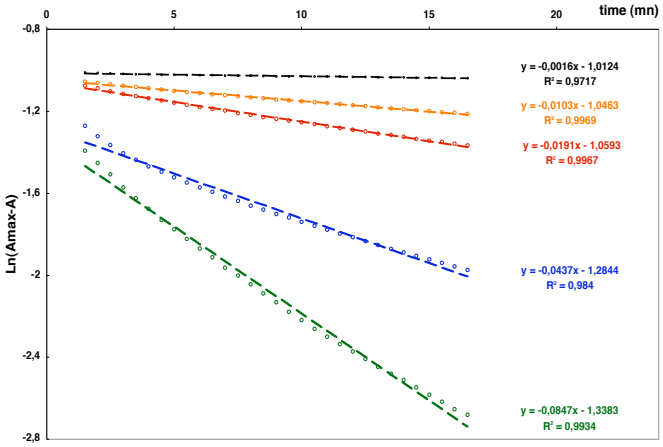
The catalyst was added at the last moment and immediately upon mixing, the sample was placed in the UV-visible spectrometer at the desired wavelenght (λ = 405 nm) and the reaction monitored by periodic absorbance acquisition (every 30 seconds during 5 hours). Each experiment was at least repetead two times.

II-2. Experimental kinetic curves obtained



The quantity of **Zn-1** used for each experiment is indicated with the corresponding kinetic curve. These experimental curves correspond to the entries 1 to 5 of the Table 1.

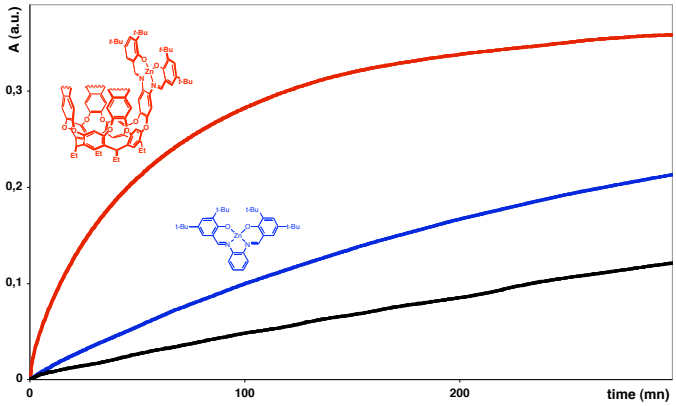
II-2. First order in PNPCC : $Ln(A_{max}-A) = - k_{obsvd}\, t + Ln(A_{max})$



The first order rate in PNPCC was determined by $Ln(A_{max}-A)$ *vs.* time plots. The rates were estimated by the slopes of the straight lines obtained by linear correlation on a common time window (black, blank reaction; orange, 10% of **Zn-1**; red, 20% of **Zn-1**; blue 50% of **Zn-1**; green 100 % of **Zn-1**).

II-3. Control experiments

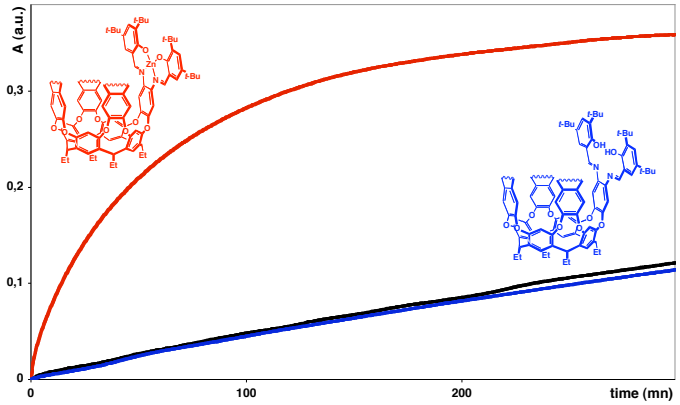
II-3-a. *Role of the cavity : kinetic experiment with the zinc(II) salen wall* ***Zn-2***



Red : 20% of the cavitand **Zn-1**
Blue : 20% of the zinc(II) salen wall **Zn-2**
Black : no catalyst (blank reaction)

The reaction is five times faster with the cavitand (Table 1, entry 6).

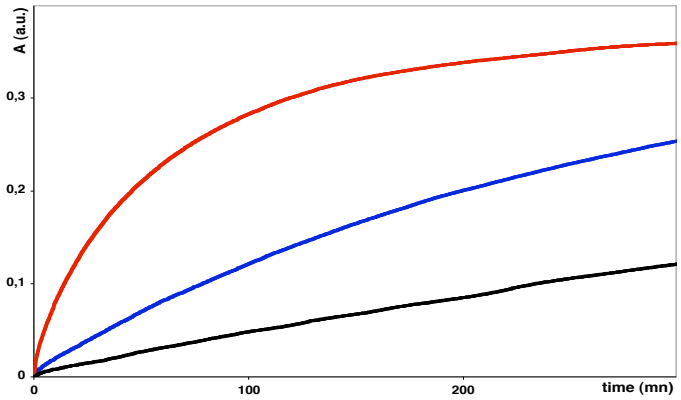
II-3-b. *Role of the zinc(II) : kinetic experiment with the metal free cavitand* ***1***



Red : 20% of the cavitand **Zn-1**
Blue : 20% of the cavitand **1**
Black : no-catalyst (blank reaction)

Without the zinc(II), **no catalysis** is observed (Table 1, entry 7).

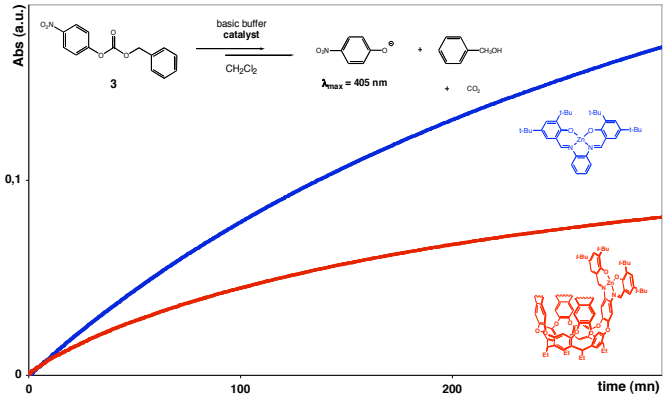
II-3-c. *Inhibition of the **Zn-1** catalyst by acetylcholine chloride*



Red : 20% of the cavitand **Zn-1**
Blue : 20% of the cavitand **Zn-1 + 65 µM acetylcholine chloride**
Black : no catalyst (blank reaction)

The acetylcholine chloride slows down the reaction rate

II-3-d. *Hydrolysis of the carbonate **3***



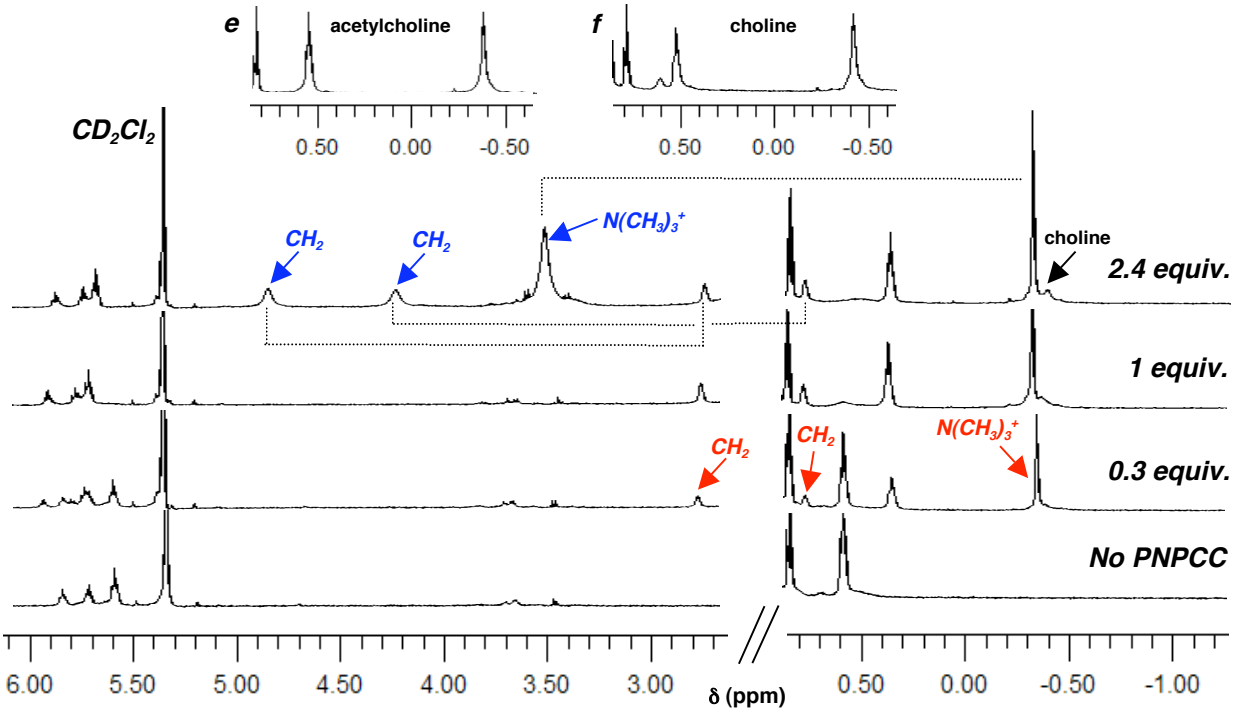
Red : 20% of the cavitand **Zn-1**
Blue : 20% of the cavitand **Zn-2**

Conditions : 40 µM of **3**, 160 mM Hünig's base, 4 mM TFA in CH_2Cl_2, room temperature

The hydrolysis is approximately two times faster with **Zn-2** than **Zn-1**
$k_{obsd\ Zn\text{-}2} / k_{obsd\ Zn\text{-}1} = 0.0025 / 0.0014 \sim 1.8$

III. ^{1}H NMR study of the PNPCC@Zn-1 complex

In the absence of buffer, the hydrolysis of the PNPCC is slow at millimolar concentrations even in the presence of **Zn-1**, making it was possible to observe the PNPCC@**Zn-**1 complex by ^{1}H NMR. A solution of **Zn-1** was prepared in dichloromethane-d_2 (3.6 mg in 0.5 mL). The PNPCC was added and immediately upon mixing, the sample was placed in the NMR for spectral acquisition. The quantity of PNPCC present in the solution was estimated by integration. The same type of experiment was performed using acetylcholine chloride and choline chloride as guests. High affinities for these guests was observed as more than one equivalent of guest was necessary to observe the free guest in solution.



Blue, free PNPCC signals. Red, encapsulated PNPCC signals

References

(1) Cuevas, F.; Di Stefano, S.; Magrans, J. O.; Prados, P.; Mandolini, L.; de Mendoza, J. *Chemistry* **2000**, *6*, 3228-3234.

(2) Morris, G. A.; Zhou, H.; Stern, C. L.; Nguyen, S. T. *Inorg. Chem.* **2001**, *40*, 3222-3227.