# Supporting Information

**Water-Soluble Aryl-Extended Calix[4]pyrroles with Unperturbed Aromatic Cavities: Synthesis and Binding Studies**

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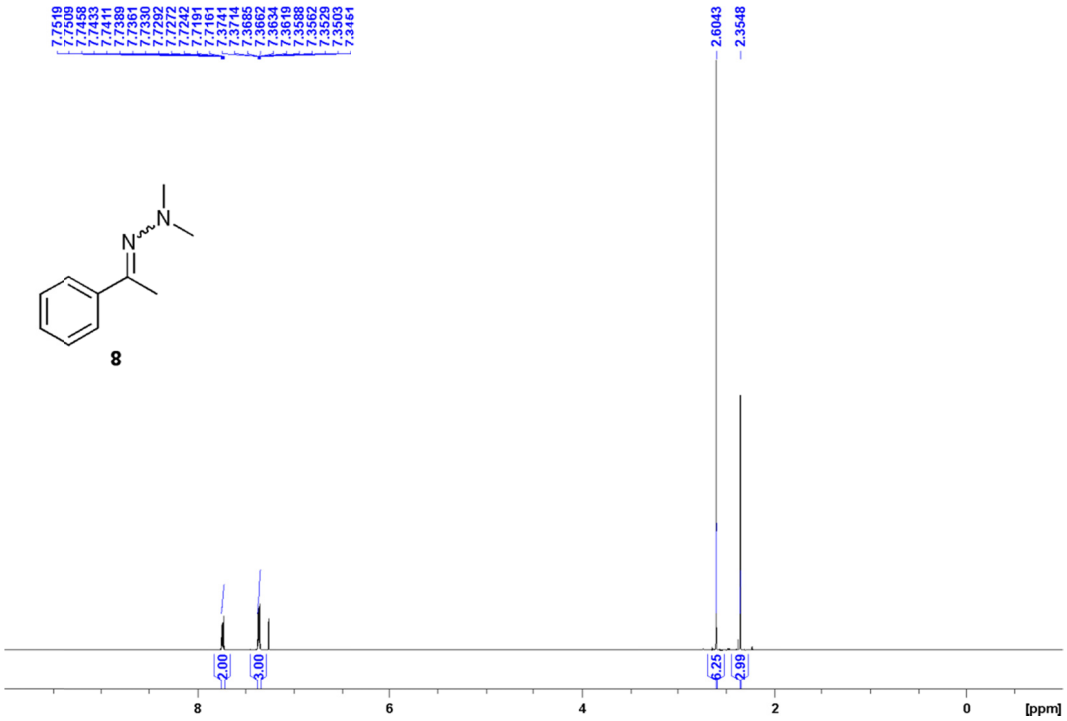
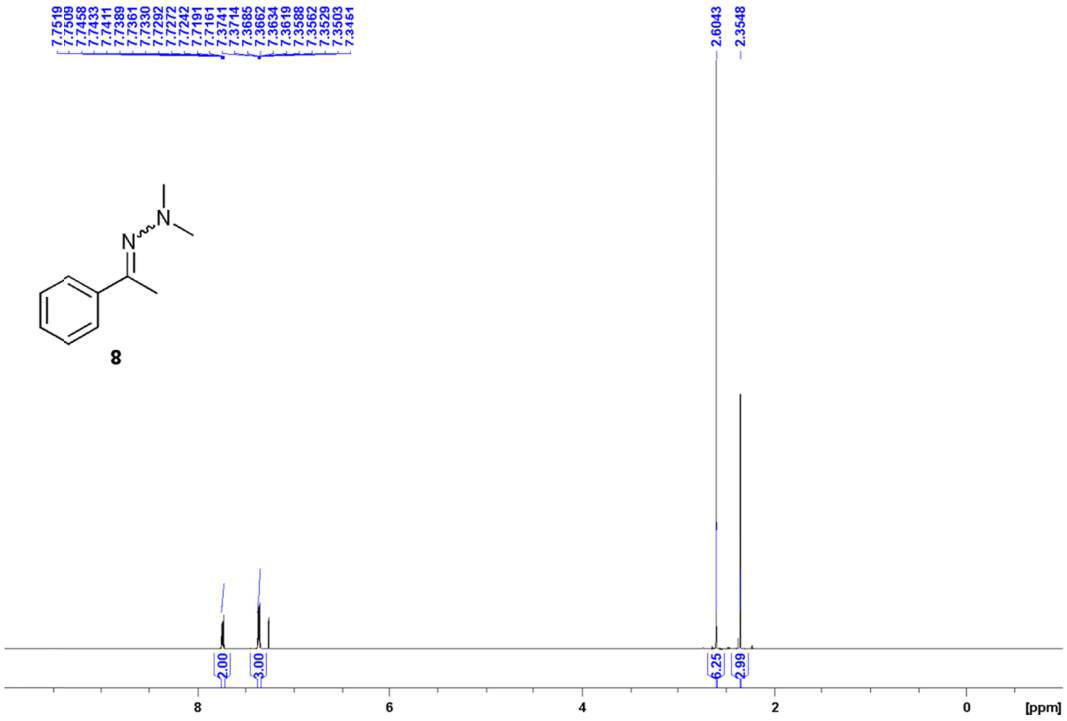
**$^{1}$H and $^{13}$C{$^{1}$H}-NMR spectra of compounds.** All the NMR spectra were measured at 25ºC

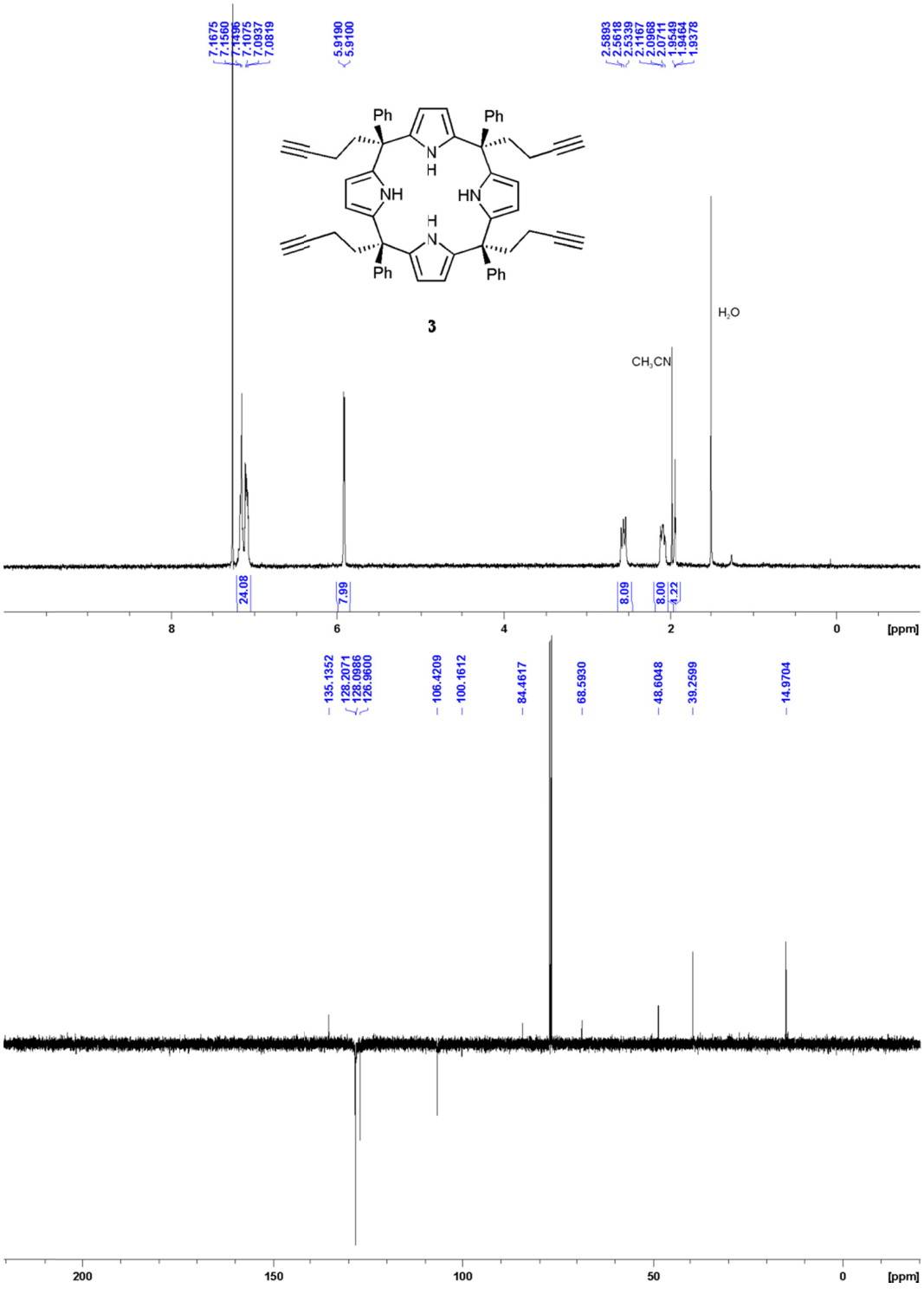
$^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **8**



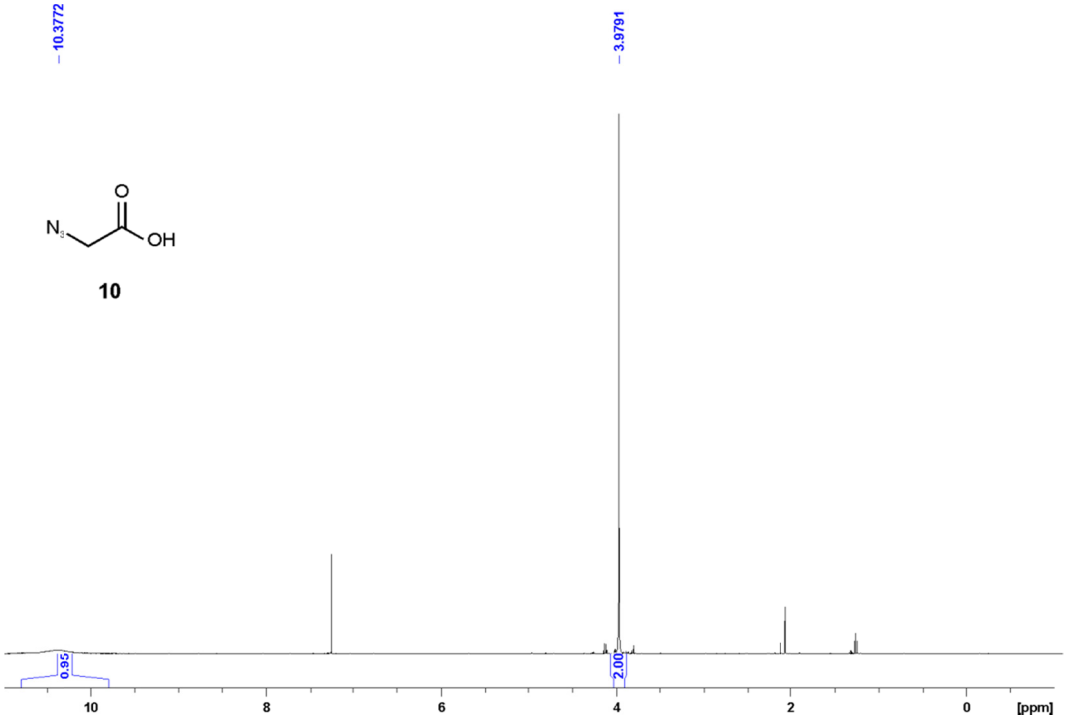

$^{1}$H NMR (300 MHz, $CDCl_3$) spectrum of compound **4**



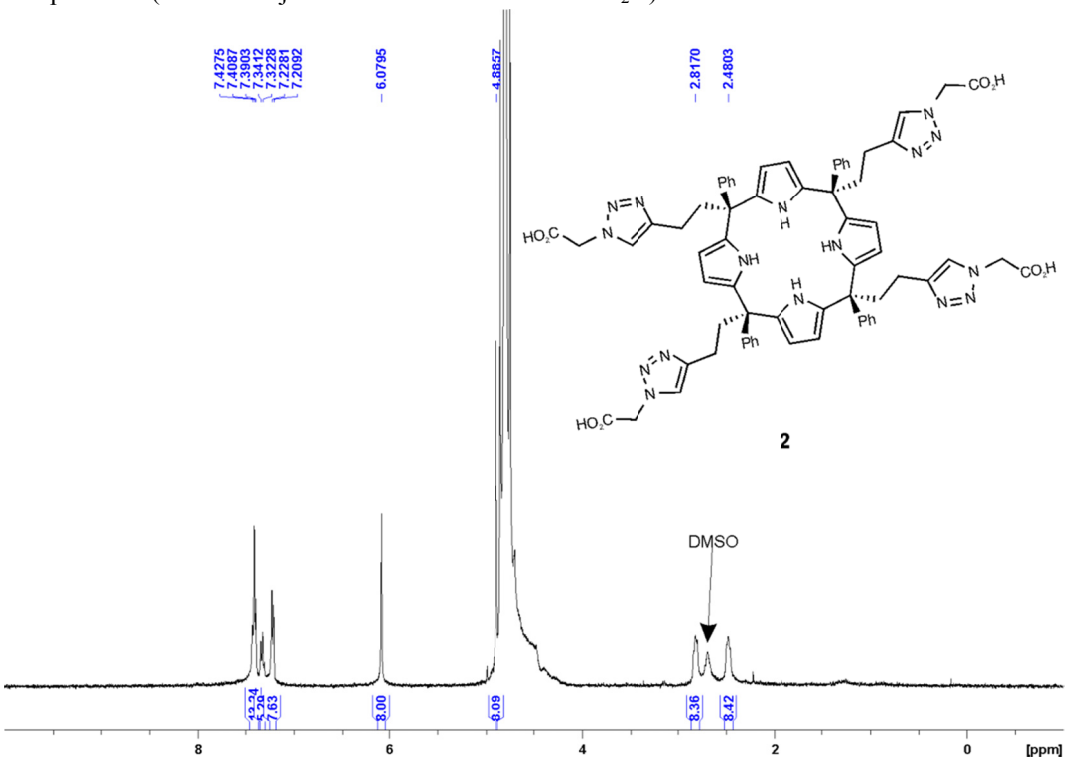
$^{1}$H NMR (300 MHz, $CDCl_3$) and $^{13}$C NMR {$^{1}$H} DEPTQ 135 (125 MHz, $CDCl_3$) spectra of compound **3**

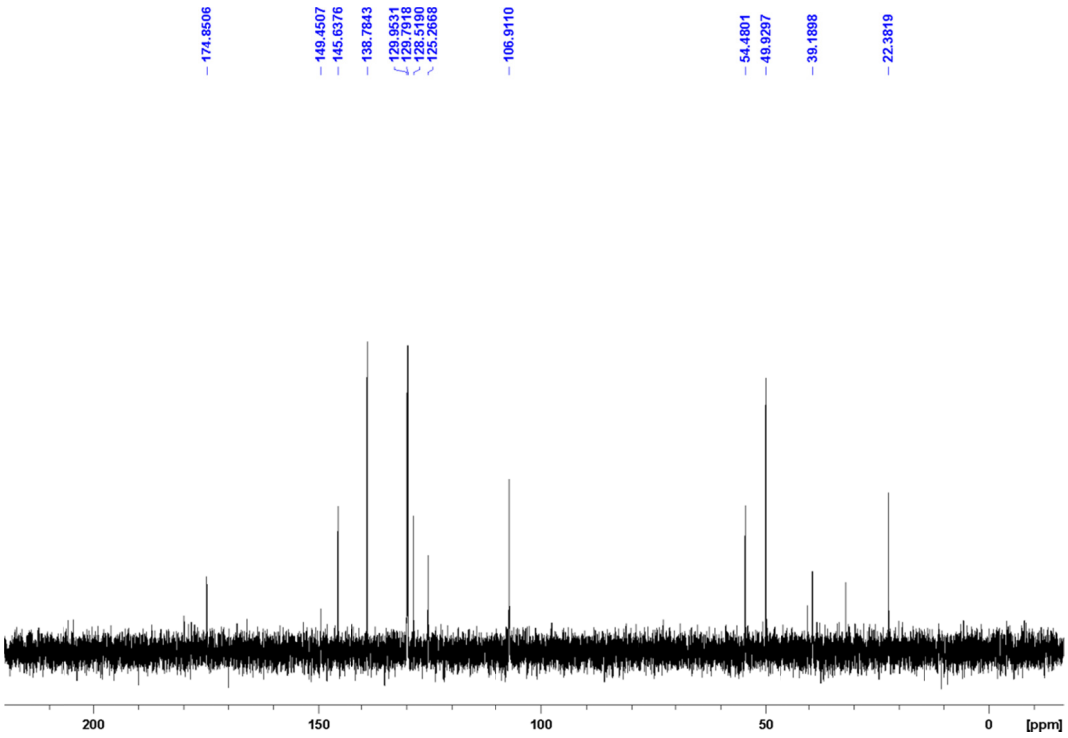


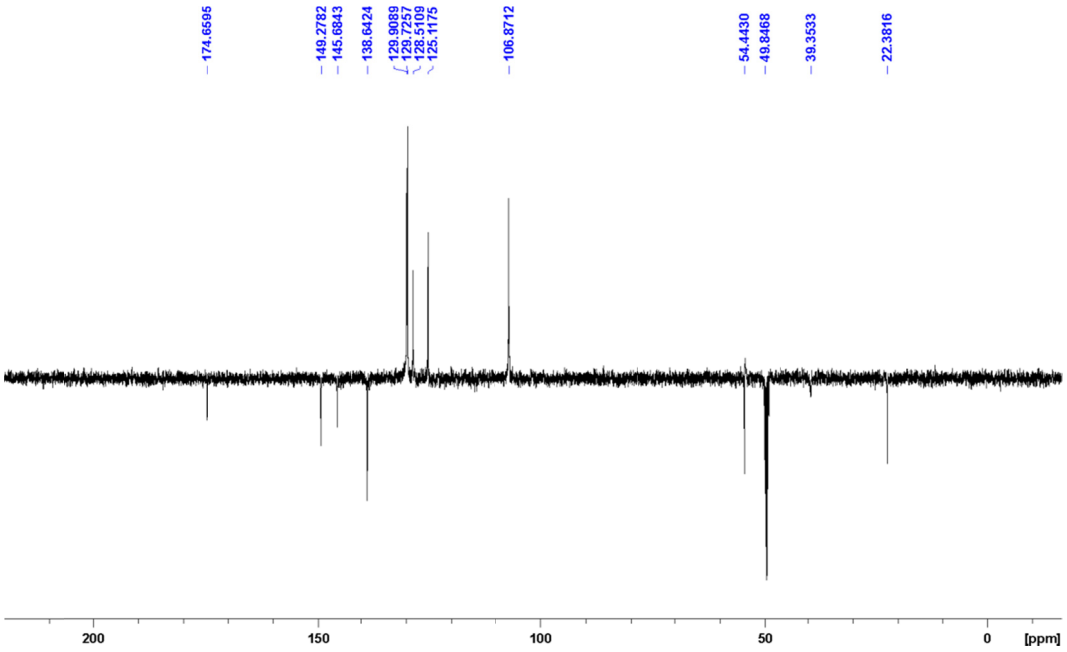
$^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **10**

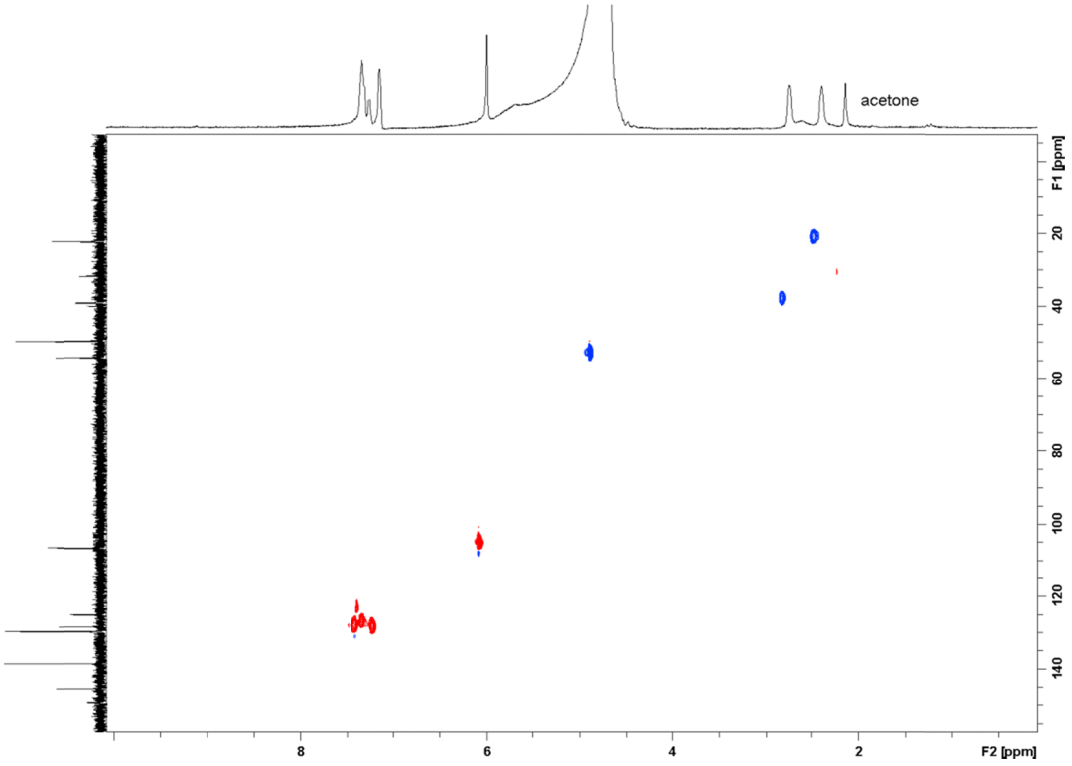



$^{1}$H NMR (400 MHz, $D_2O$), $^{13}$C NMR {$^{1}$H} (125 MHz with cryoprobe, $D_2O$), $^{13}$C NMR {$^{1}$H} DEPTQ 135 (125 MHz with cryoprobe, $D_2O$) and $^{13}$C NMR {$^{1}$H} HSQC (125 MHz with cryoprobe, $D_2O$) spectra of compound **2**. (PD≈ 7.2 adjusted with NaOD solution in $D_2O$)



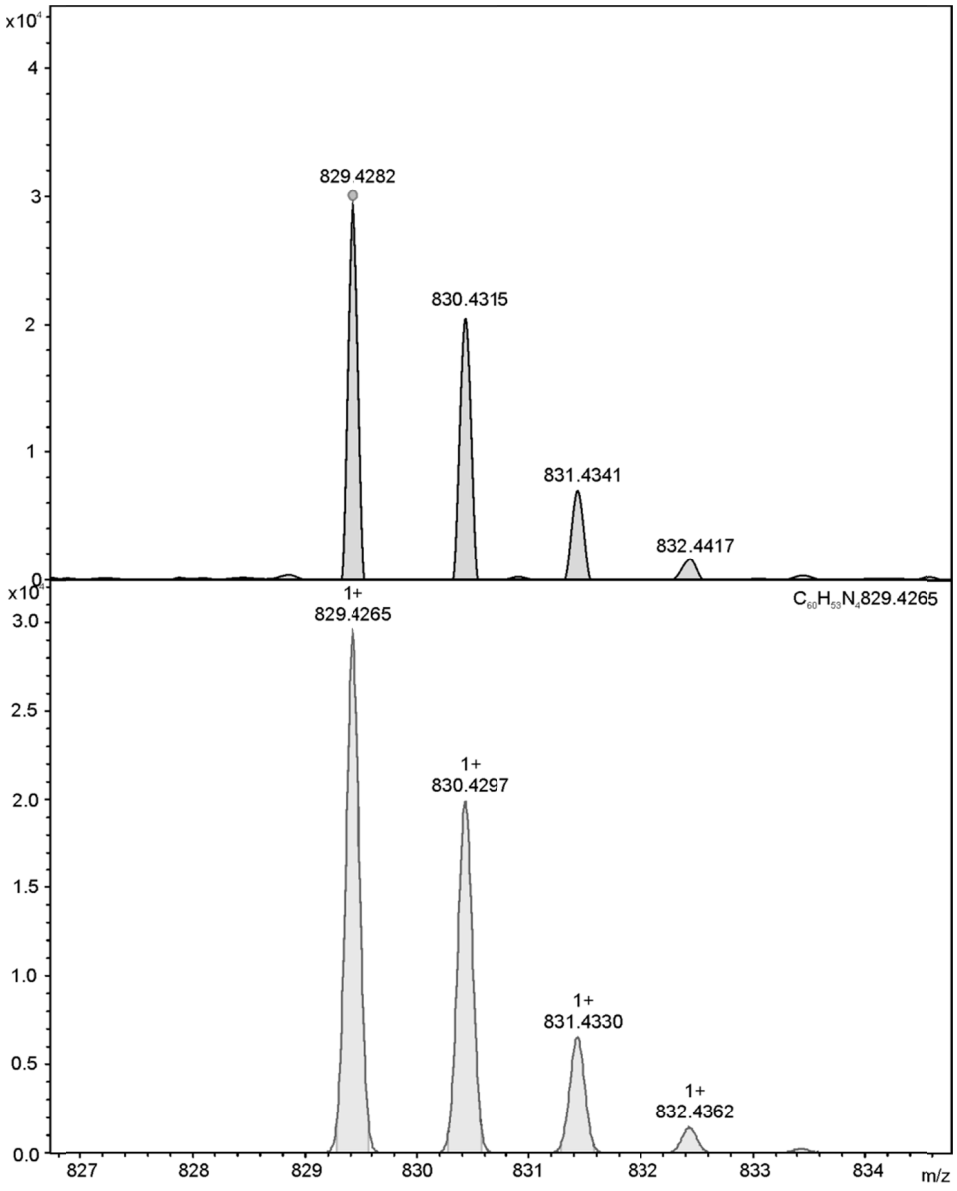

174.8506
149.4507
145.6376
138.7843
129.9531
129.7918
128.5190
125.2668
106.9110
54.4801
49.9297
39.1898
22.3819
200
150
100
50
0
[ppm]


174.6595
149.2782
145.6843
138.6424
129.9089
129.7257
128.5109
125.1175
106.8712
54.4430
49.8468
39.3533
22.3816
200
150
100
50
0
[ppm]

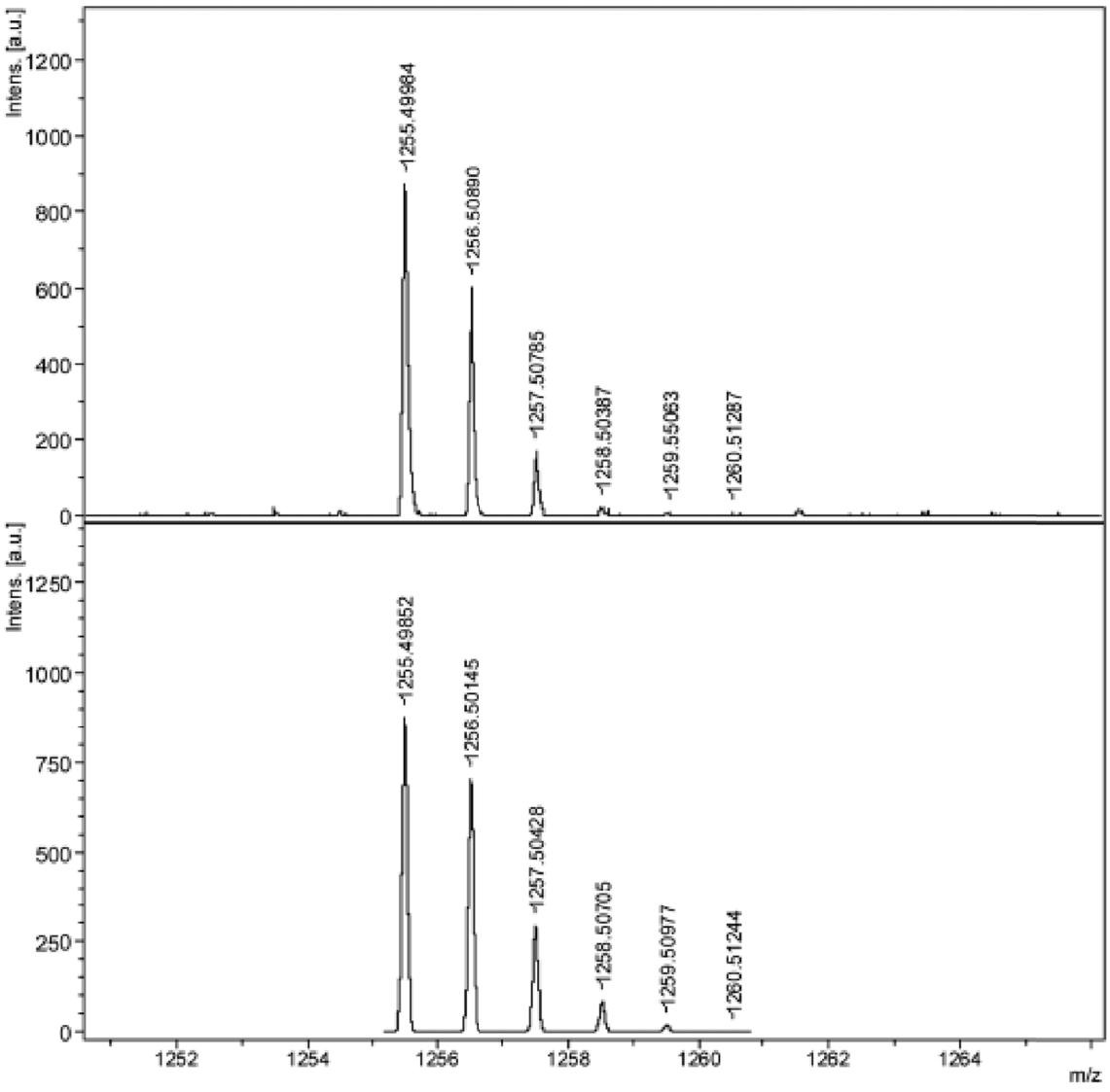

acetone
F1 [ppm]
20
40
60
80
100
120
140
8
6
4
2
F2 [ppm]

**HRMS spectra**

HRMS (ESI-TOF) m/z: $[M + Na]^+$spectrum of compound **3.** Top measured, bottom calculated)



HRMS (MALDI-TOF) spectrum of compound **2** $[M + Na]^+$ (top measured, bottom calculated)



**[1]HNMR titration of receptor 2 with PNO13 and ROESY [1]HNMR of the complex in presence of an excess of PNO13.**

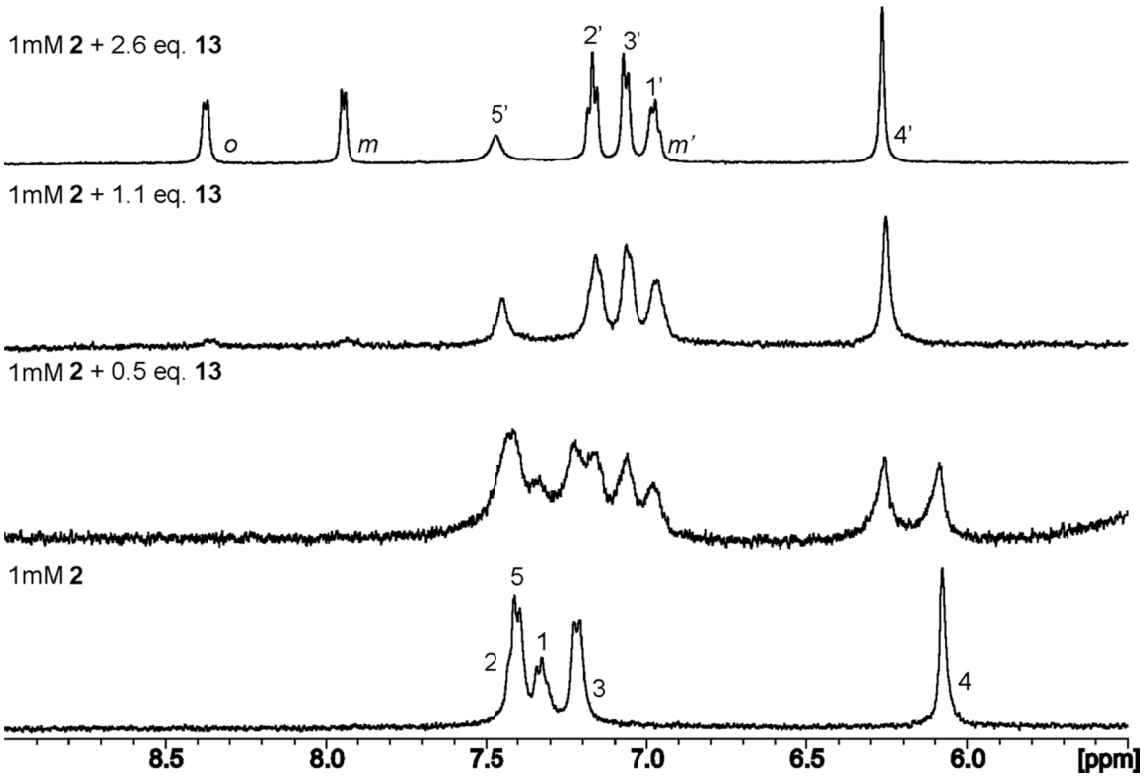



**Figure S1:** Selected downfield regions of the [1]H-NMR spectra (400 MHz, $D_2O$ adjusted to pD≈7.2 with NaOD, 273 K) obtained during the titration of calix[4]pyrrole **2** (1 mM) with incremental amounts of PNO **13**. See figure 3 in the manuscript for proton numbering. Prime letters and numbers represent proton signals corresponding to encapsulation complex PNO**13**⊂**2**.

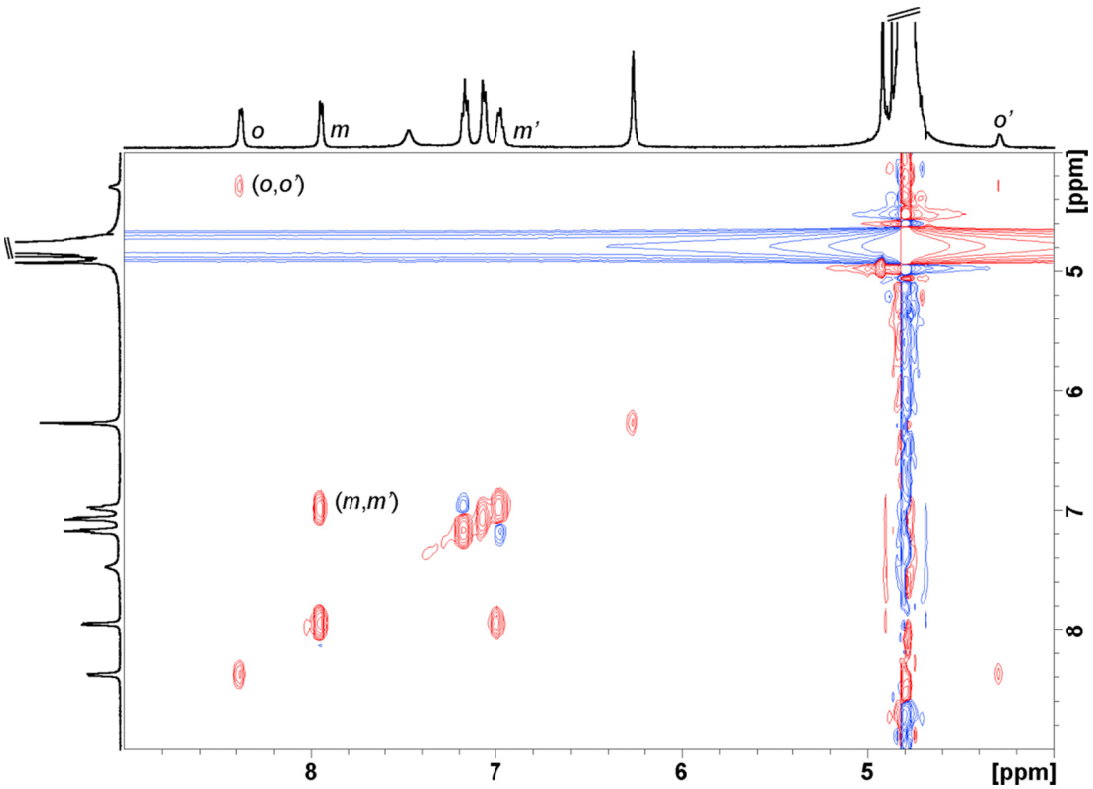



**Figure S2:** Selected region of ROESY $^{1}$H NMR experiment of complex **13**⊂**2** in presence of 2.6 eq of PNO **13**. Prime letters represent proton signals corresponding to PNO **13** in complex **13**⊂**2**. See figure 3 in the manuscript for proton lettering.

**ITC Experiments**

Titrations were carried out on a Microcal VP-ITC microcalorimeter, at 298 K, in water adjusting the pH by addition of $NaOH_{(aq.)}$ solution until pH≈ 11 and then adjusting with $HCl_{(aq.)}$ solution until pH≈7.2. The association constants between receptor **2** and pyridine *N*-oxide **11**, **12** and **13** were determined by monitoring the heat released by the system as incremental amounts of the *N*-oxide **11**, **12** or **13** were added. The values of the association constant $K_a$ and the enthalpy of binding $\Delta H$ were calculated using the Origin 7 software package which uses least-squares minimization to obtain globally optimized parameters as described in Wiseman *et al*.[1] In all cases the data fit well to a simple 1:1 binding model.

Specifically, the association constants were determined using solution of **2** in water at 296 K, and adding aliquots of a solution of pyridine *N*-oxide derivatives, approximately 10 times more concentrated, also in the same media. The association constant ($K_a$), $T\Delta S$ and $\Delta H$ values for the binding process were determined by averaging the values from the titrations.

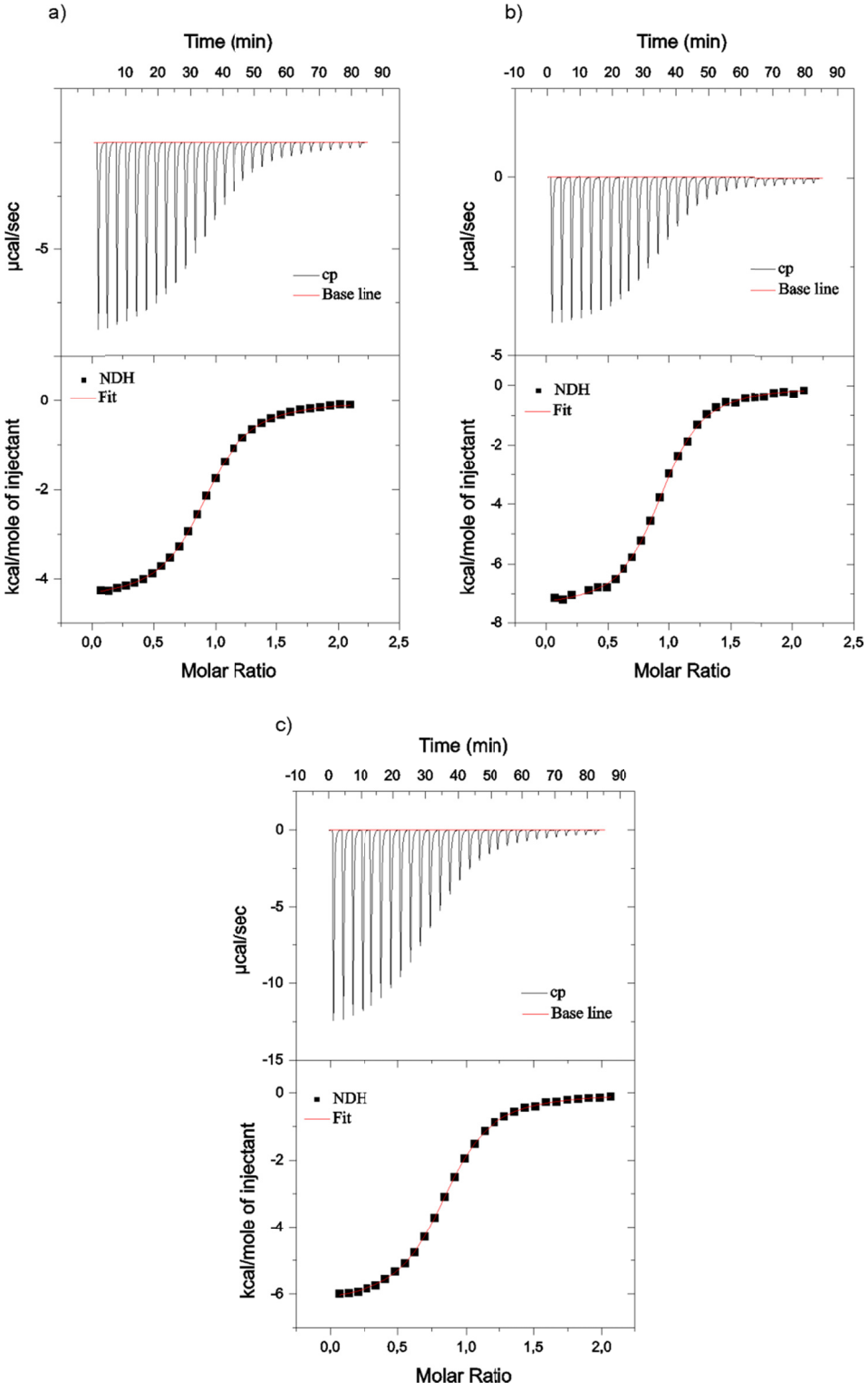



**Figure S3**: Top: Raw data for the ITC titration in water of PNO derivatives into **r**eceptor **2**. Bottom: Binding isotherm of calorimetric titration data shown on top. a) PNO**11** over [**2**] = 0.62mM in $H_2O$; pH= 7.22. b) PNO **12** over [**2**] = 0.17mM in $H_2O$; pH = 7.21. c) PNO **13** over [**2**] = 0.63mM in $H_2O$; pH = 7.23. c) = 7.43.

(1) Wiseman, T.; Williston, S.; Brandts, J. F.; Lin, L. N. *Anal. Biochem.* **1989**, *179*, 131.