Supporting Information

for

Binding selectivity and separation for *p*-functionalized toluene with metallo cavitand in water

Faiz-Ur Rahman,[a] Ji-min Yang,[c] Yunhui Wan,[a] Hui-bin Zhang,[a] Ioannis D. Petsalakis,[b] Giannoula Theodorakopoulos,[b] Julius Rebek Jr.,*[a,c] Yang Yu*[a]

Author Affiliations:

[a]Center for Supramolecular Chemistry & Catalysis and Department of Chemistry, College of Science, Shanghai University, 99 Shang-Da Road, Shanghai 200444, China

[b]Theoretical and Physical Chemistry Institute, The National Hellenic Research Foundation, 48 Vassileos Constantinou Ave. Athens 116 35, Greece

[c]Skaggs Institute for Chemical Biology and Department of Chemistry, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA

***Corresponding authors:**

Julius Rebek Jr.: jrebek@scripps.edu

Yang Yu: yangyu2017@shu.edu.cn

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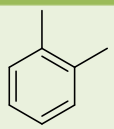
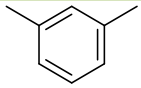
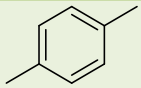
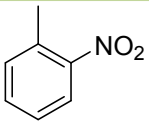
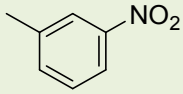
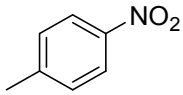
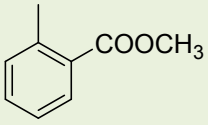
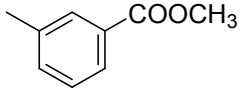
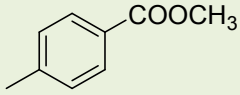
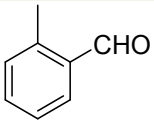
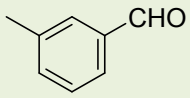
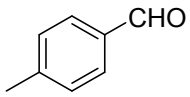
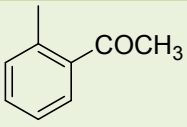
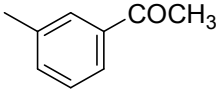
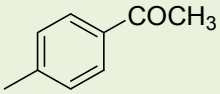
General experimental

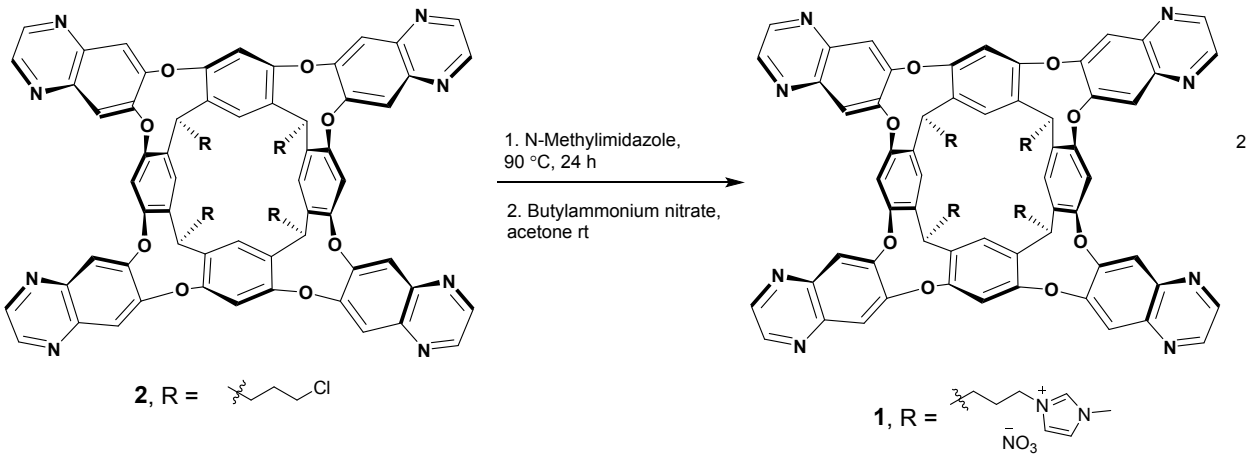
All analytical grade solvents and reagents purchased from commercial sources were used without further purification. Functionalized toluene isomers were purchased from commercial sources and used without further purification. Commercially available Pd(ethylene diamine).2NO_3 was used. D_2O, DMSO-d_6, $CDCl_3$ and CD_3OD were used as NMR analysis solvents. ^{1}H COSY, ^{1}H and ^{13}C NMR analyses were performed using Bruker AVANCE III HD 600 MHz spectrophotometer.

Table S1, Melting points and boiling points of different functionalized toluene isomers acquired from online sources.

No	Compound	Melting point (°C)	Boiling point (°C)
1		-25	144
2		-47	139
3		13	136
4		-9	225
5		15	230
6		53	238
7		-50	207
8		-	113
9		33	103
10		-35	200
11		25	199
12		-6	204
13		107	214

14		-9	218
15		45	226

Synthesis of water soluble cavitand 1 with nitrate anions



A similar procedure as we previously reported was used[1], 200 mg of **2** was taken in 20 mL 1-methylimidazole in a 50 mL round bottom flask, the mixture in the flask was stirred magnetically and heated in an oil bath at 90 °C under nitrogen for 24 h. After cooling the mixture to rt excess of n-butyl ammonium nitrate dissolved in 50 mL of acetone was added with vigorous stirring that resulted in a white solid precipitation. The solid was filtered and washed thoroughly with acetone. The recovered solid was suspended in 50 mL of acetone, vigorously stirred and heated at reflux for 2 h. It was cooled to rt, filtered, washed with excess acetone and dried under high vacuum. **1** was obtained in not less than 90% yield each time. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9·29 (s, 4H), 8.71 (s, 8H), 8.59 (s, 8H), 8.16 (s, 4H), 7.96 (s, 4H), 7.90 (s, 4H), 7.77 (s, 4H), 5.56 (s, br, 4H), 4.40 – 4.30 (m, 8H), 2.67 – 2.57 (m, 8H), 1.83 (s, br, 8H) ppm. ^{13}C NMR (150 MHz, DMSO-d_6) δ 154.9, 154.1, 145.7, 141.2, 137.1, 135.6, 125.6, 124.1, 123.5, 122.9, 117.0, 49.6, 40.5, 36.3, 34.0, 28.5 ppm. HR-MS (ESI): Calcd. for chemical formula $C_{88}H_{76}N_{16}O_8 \cdot 4NO_3$: 1732.5545, found: 1670.5679 $[M\text{-}NO_3]^+$, 804.2905 $[M\text{-}2NO_3]^{2+}$.

Computational details

The M062X functional[2, 3] was employed along with the and Lanl2dz basis set[4, 5], provided in the gaussian 16 suit of programs[6]. The optimized structures for **1-2Pd** and with *p*-xylene in the cavity

are displayed in Figure 3. NMR spectra were obtained using the Gauge-Independent Atomic Orbital (GIAO) method[7].

Optimized (computational) figures

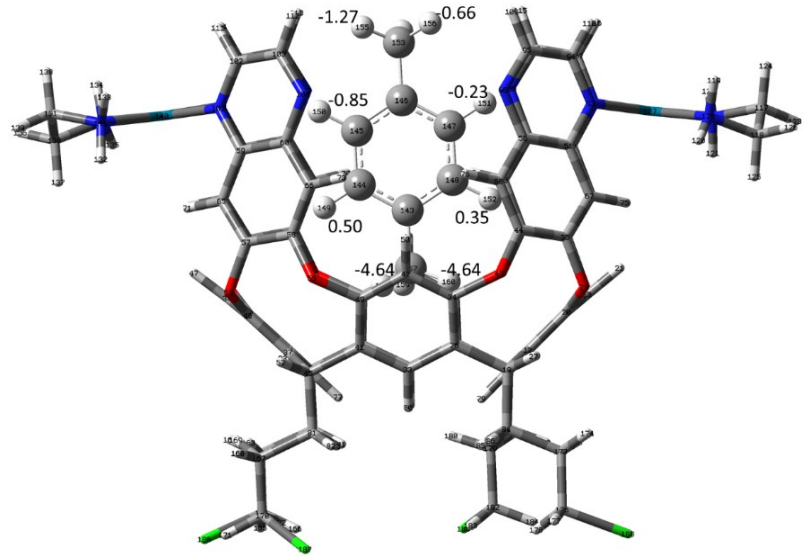


Figure S1 Calculated [1]H NMR chemical shifts of *p*-xylene in optimized **1-2Pd** with one methyl up and other at the bottom of the cavity

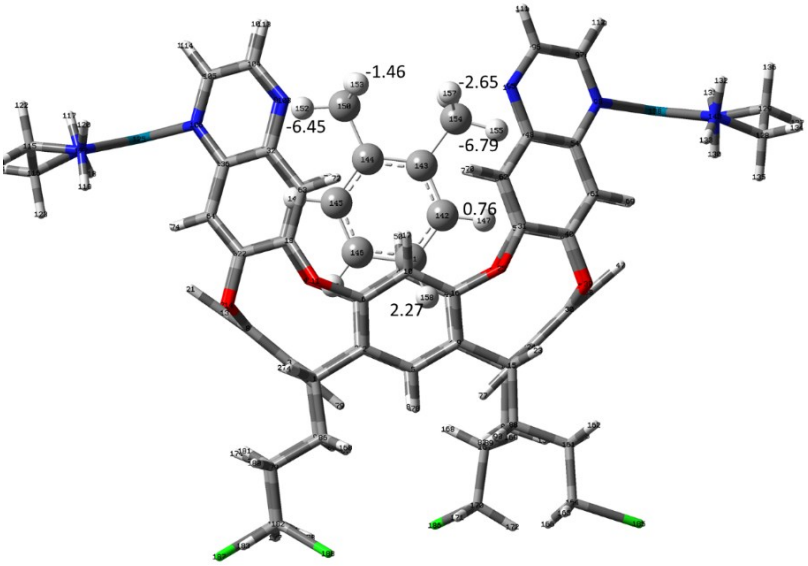


Figure S2 Calculated [1]H NMR chemical shifts of *o*-xylene in optimized **1-2Pd** with methyls up in the cavity

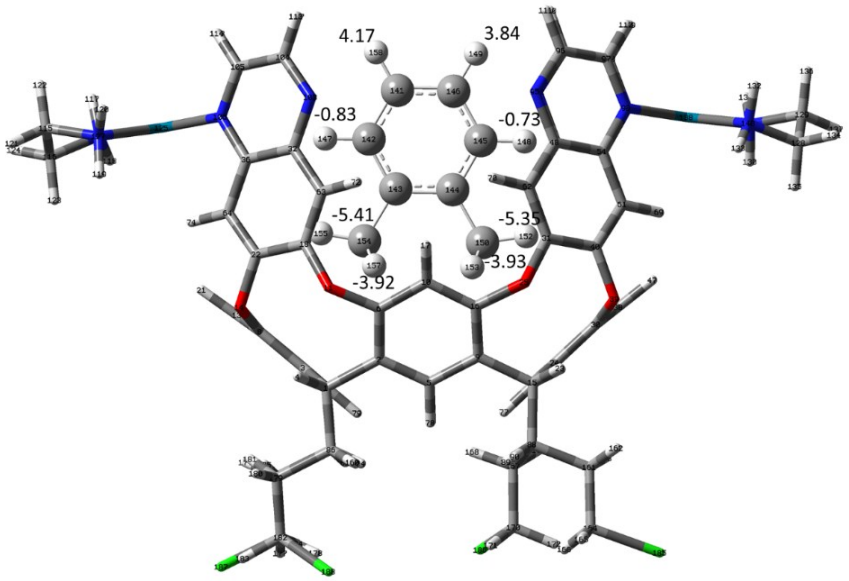


Figure S3 Calculated ^{1}H NMR chemical shifts of *o*-xylene in optimized **1-2Pd** with methyls down in the cavity

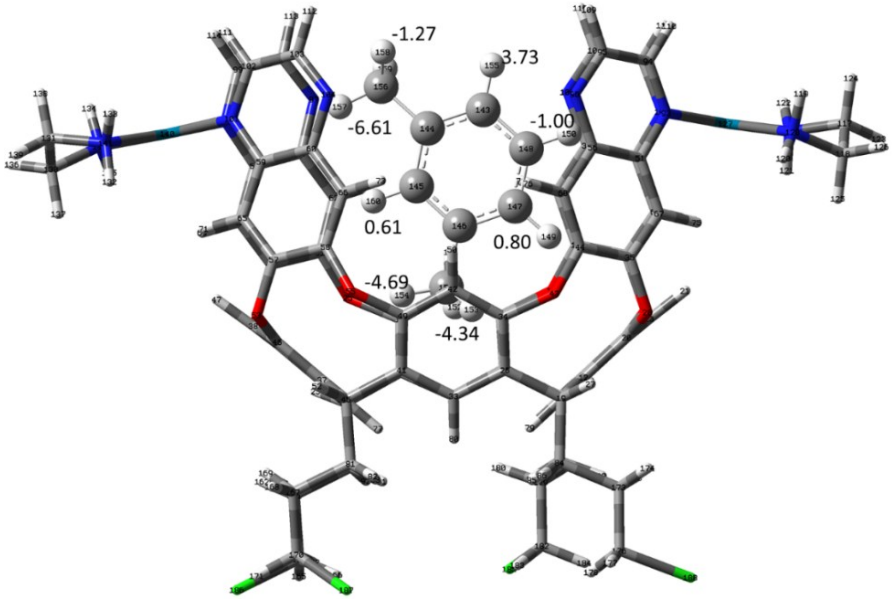


Figure S4 Calculated ^{1}H NMR chemical shifts of *m*-xylene in optimized **1-2Pd** with methyl tumbling in the cavity

^{1}H COSY NMR spectra and protons chemical shifts of the free and bound guests

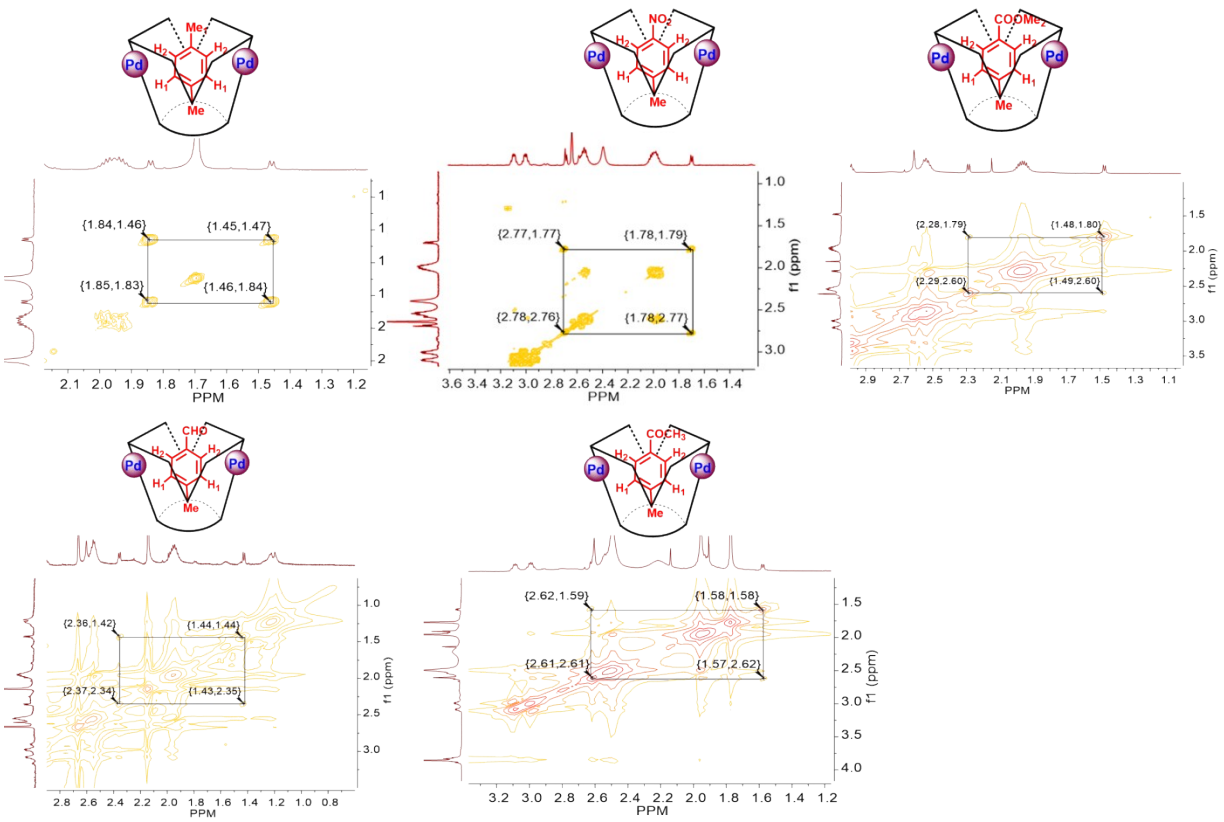
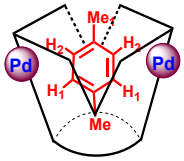
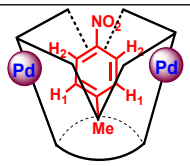
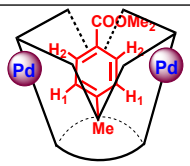
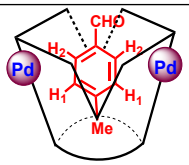
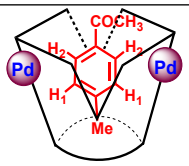


Figure S5 ^{1}H COSY NMR spectra of the complexes formed between **1-2Pd**, 1 mM + excess *p*-functionalized toluene in D_2O, analyzed at rt

Table S2 Chemical shifts (ppm) for free and bound protons of the guests and respective Δδ (ppm) value

S/No	Guest/host	Protons	Free (ppm)	Bound (ppm)	-Δδ (ppm)
1		Me	2.20	-3.31	5.51
		H^1	7.07	1.86	5.21
		H^2	7.07	1.47	5.6
		Me_1	2.20	0.90	3.1
2		Me	2.40	-3.05	5.45
		H^1	7.37	1.7	5.67
		H^2	8.1	2.7	5.4
3		Me	2.40	-3.05	5.45
		H^1	7.37	1.57	5.8
		H^2	7.92	2.37	5.55

		COOMe	3.92	-	-
4		Me	2.35	-3.19	5.54
		H^1	7.36	1.43	5.93
		H^2	7.76	2.36	5.4
5		Me	2.33	-3.14	5.47
		H^1	7.3	1.61	5.69
		H^2	7.83	2.62	5.21
		CH_3	2.61	-	-

^{1}H NMR spectra of 1-2Pd in water in the presence of xylenes as binding guests

General procedure for the binding analyses

1 mM, 0.5 mL solution of **1-2Pd** in D_2O was taken in NMR tube and excess pure xylene isomer or their mixture (~0.25 µL) was added to the tube, it was shaken well to mix the guest in water. The sample was sonicated for 1 h and analyzed by ^{1}H NMR spectroscopy.

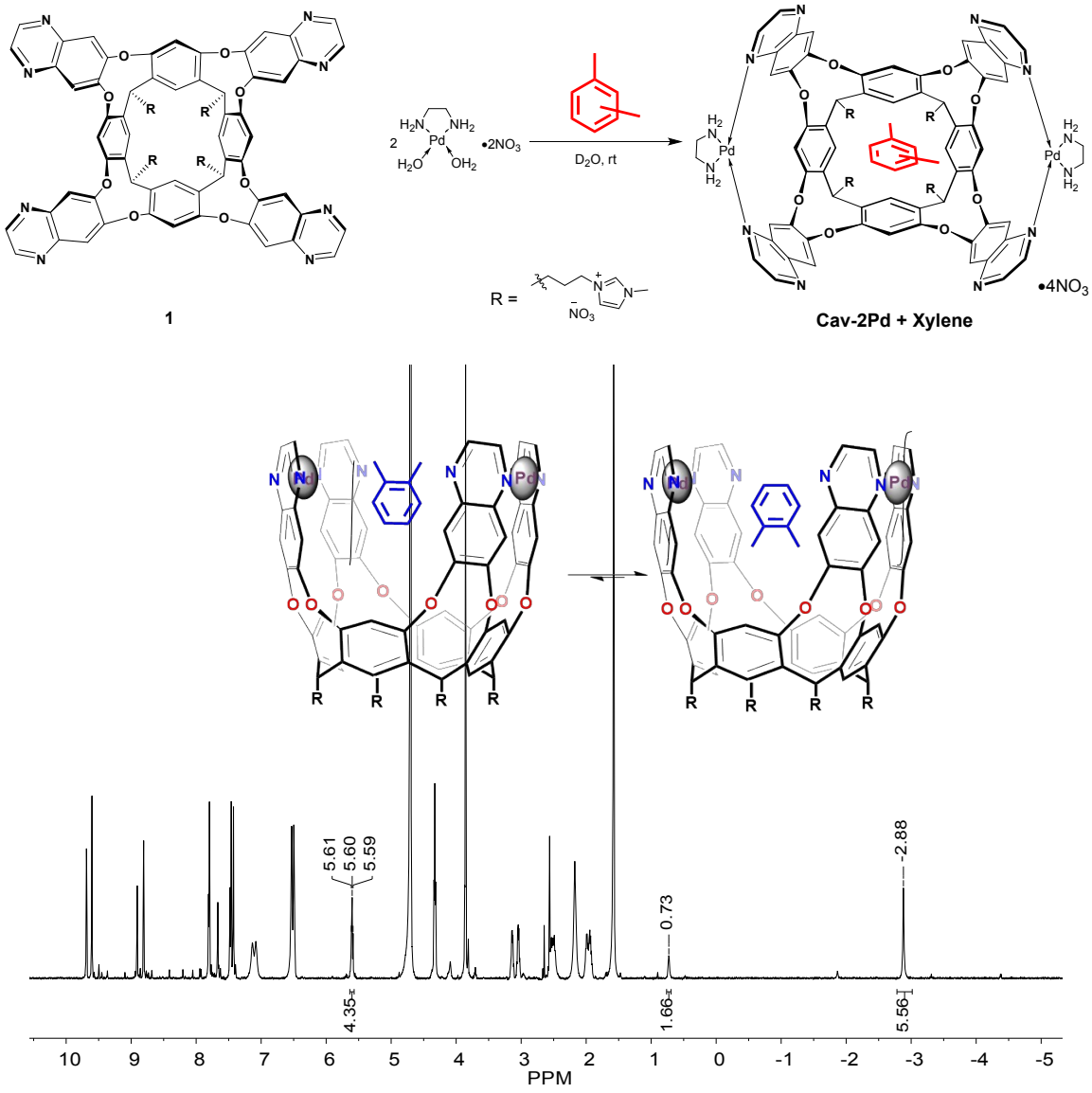


Figure S6 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*-xylene in D_2O, analyzed at rt

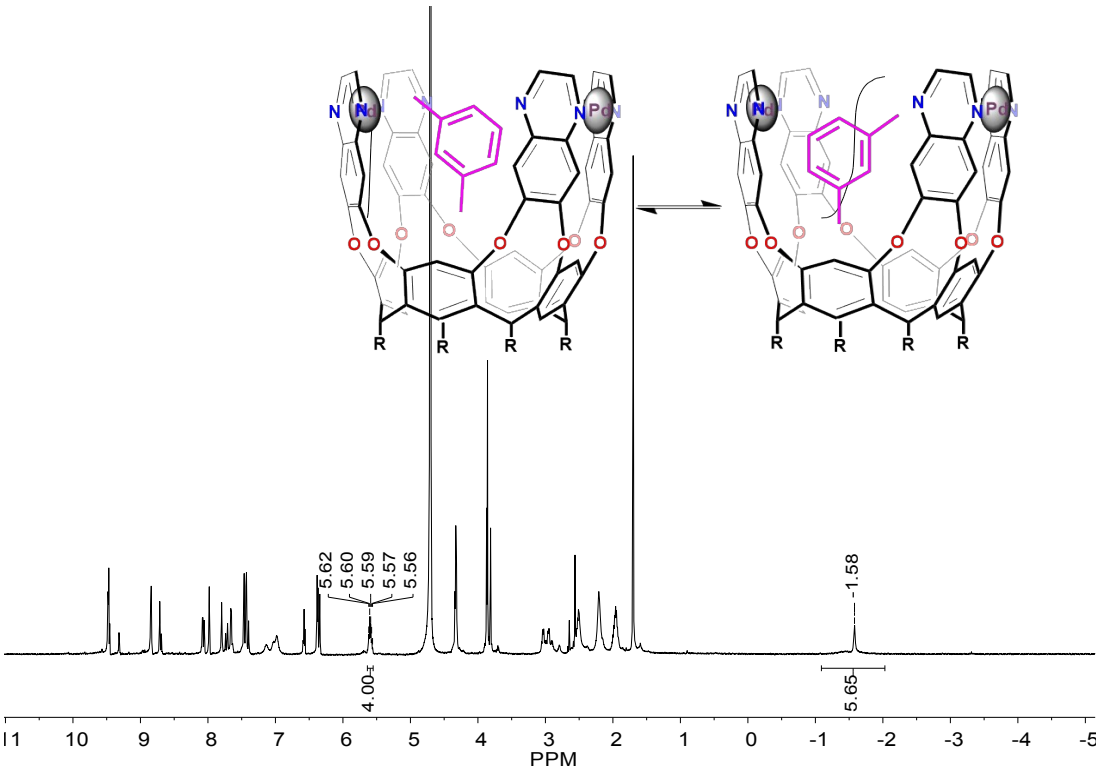


Figure S7 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *m*-xylene in D_2O, analyzed at rt

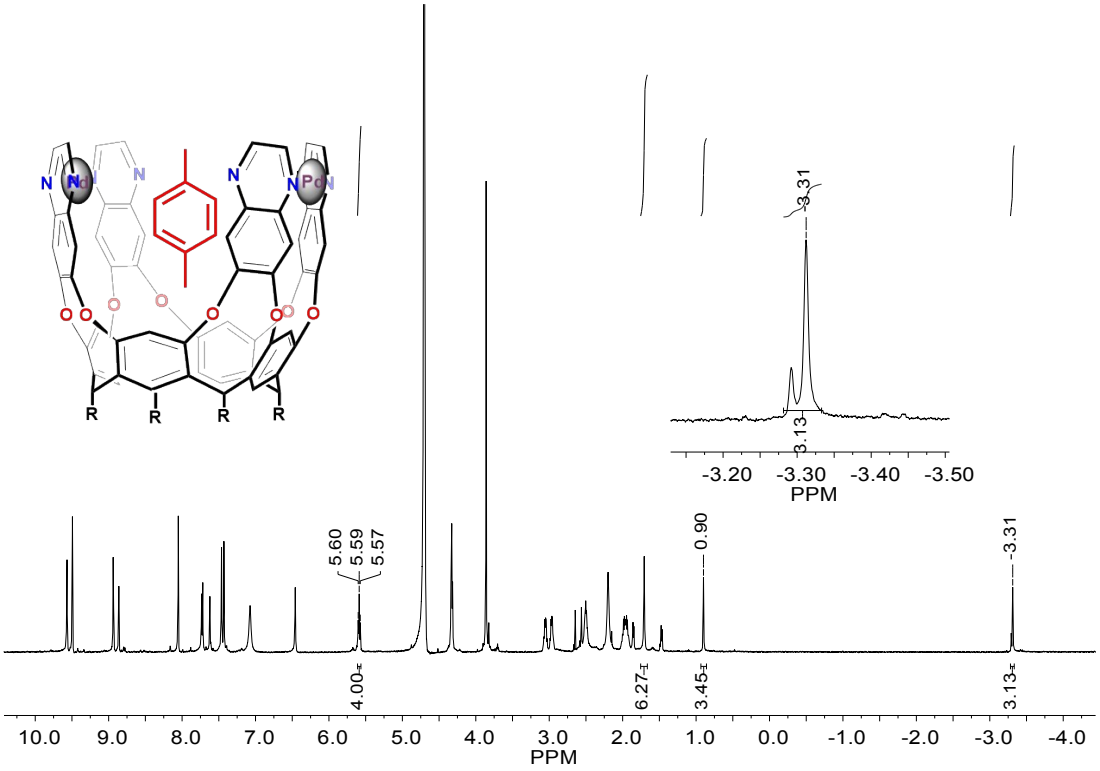
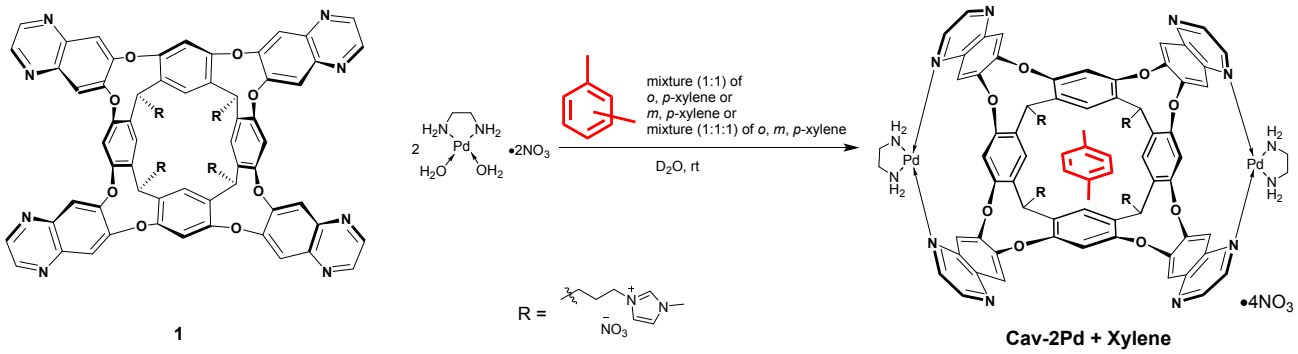


Figure S8 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *p*-xylene in D_2O, analyzed at rt

^{1}H NMR spectra of 1-2Pd in water in the presence of xylenes (mixture of xylene isomers) as binding guests

General procedure for the binding analyses

1 mM, 0.5 mL solution of **1-2Pd** in D_2O was taken in NMR tube and excess of *o*- + *p*-xylene (1:1) mixture or *m*- + *p*-xylene (1:1) mixture or *o*- + *m*- + *p*-xylene (1:1:1) mixture (~0.25 µL) was added to the tube respectively, it was shaken well to mix the guest in water. The sample was sonicated for 1 h and analyzed by ^{1}H NMR spectroscopy.



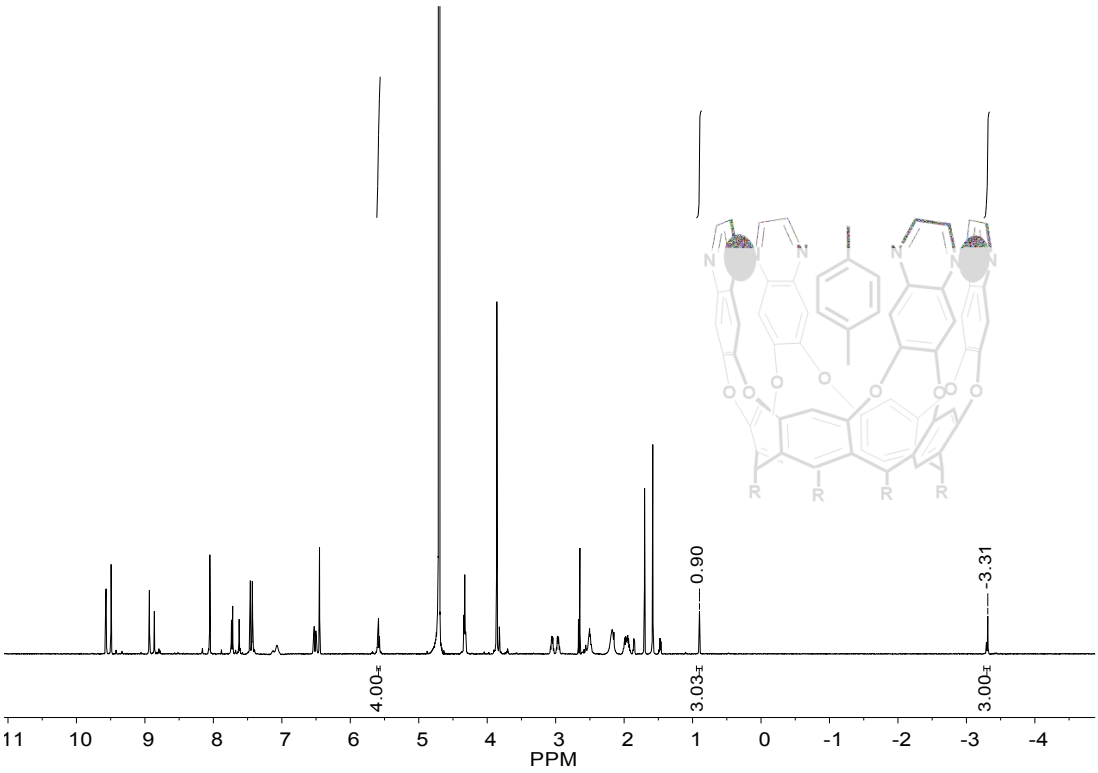


Figure S9 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*- + *p*-xylene (1:1) mixture in D_2O, analyzed at rt; only *p*-xylene was captured by the **1-2Pd**

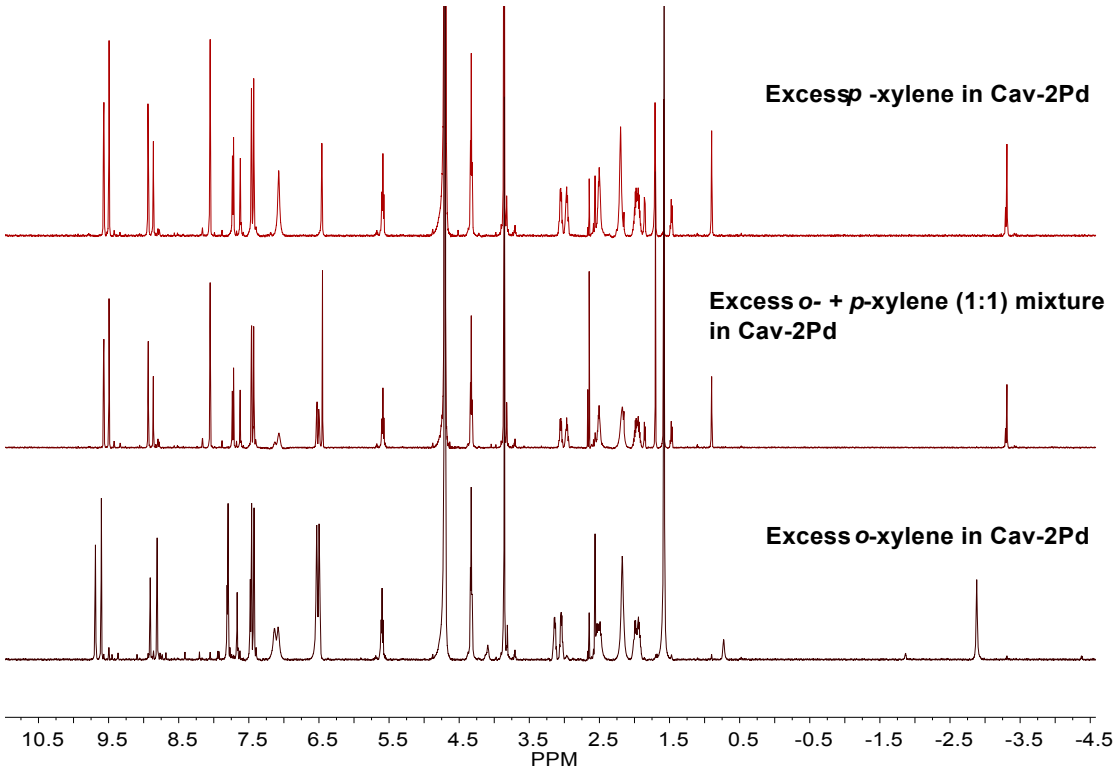


Figure S10 Comparative ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + from bottom to top, excess of *o*-xylene *o*- + *p*-xylene (1:1) mixture and *p*-xylene in D_2O, analyzed at rt; In the middle spectrum only *p*-xylene was captured by the **1-2Pd**

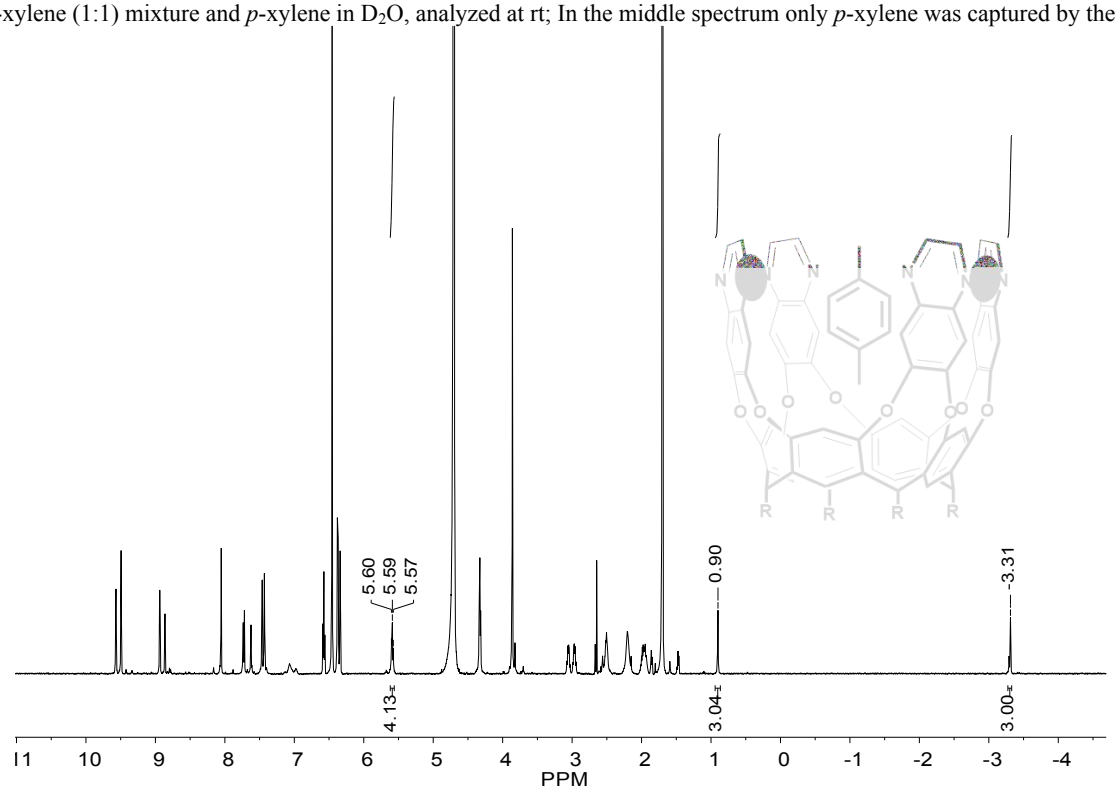


Figure S11 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *m*- + *p*-xylene (1:1) mixture in D_2O, analyzed at rt; only *p*-xylene was captured by the **1-2Pd**

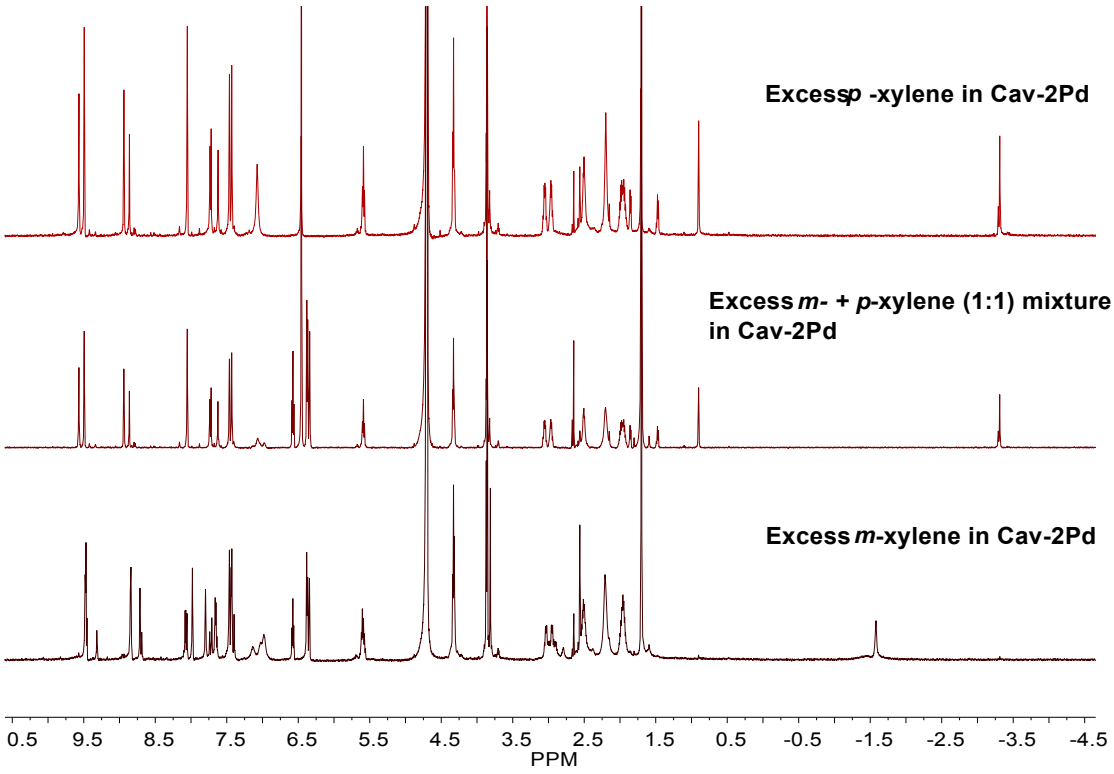


Figure S12 Comparative ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + from bottom to top, excess of *m*-xylene *m*- + *p*-xylene (1:1) mixture and *p*-xylene in D_2O, analyzed at rt; In the middle spectrum only *p*-xylene was captured by the **1-2Pd**

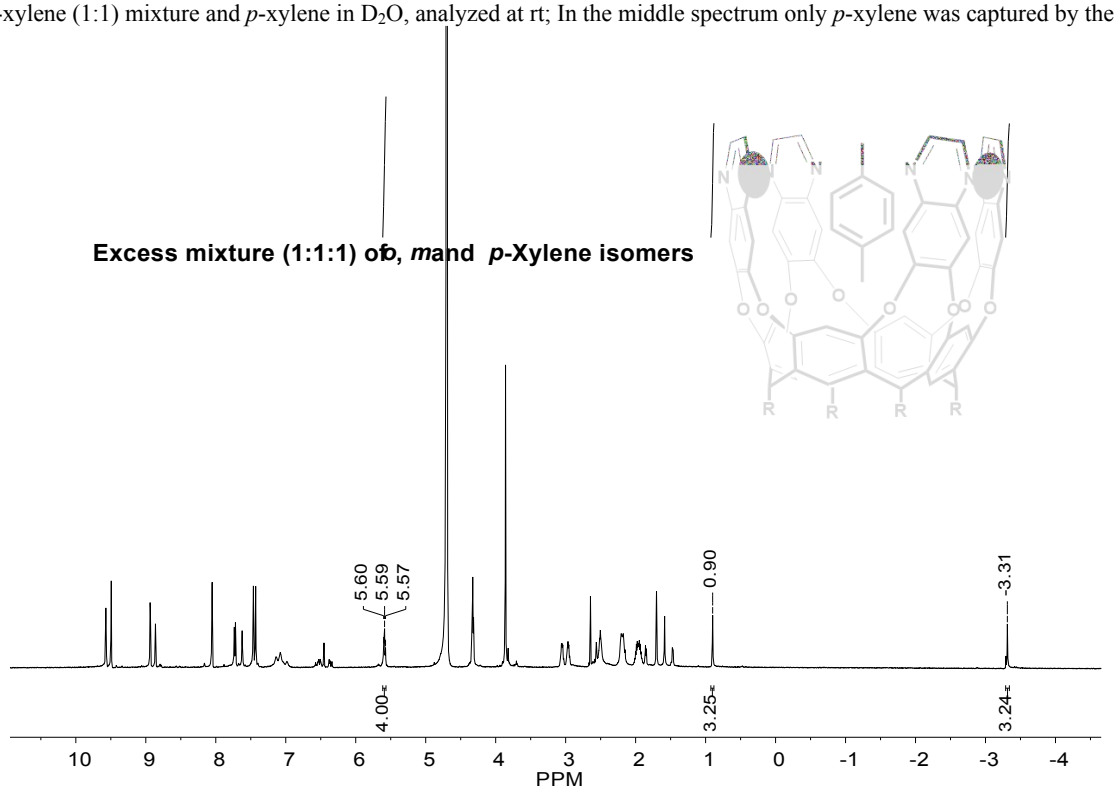


Figure S13 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*- + *m*- + *p*-xylene (1:1:1) mixture in D_2O, analyzed at rt; only *p*-xylene was captured by the **1-2Pd**

^{1}H NMR spectra of 1-2Pd in water in the presence of xylenes (mixture of xylene isomers) as binding guests while keeping host : guest 1:1

General procedure for the binding analyses

1 mM, 0.5 mL solution of **1-2Pd** in D_2O was taken in NMR tube and 1 equivalent of xylene mixture of single isomers (stock solution in methanol-d_4) was added to the tube, it was shaken well to mix the guest in water. The sample was sonicated for 1 h and analyzed by ^{1}H NMR spectroscopy.

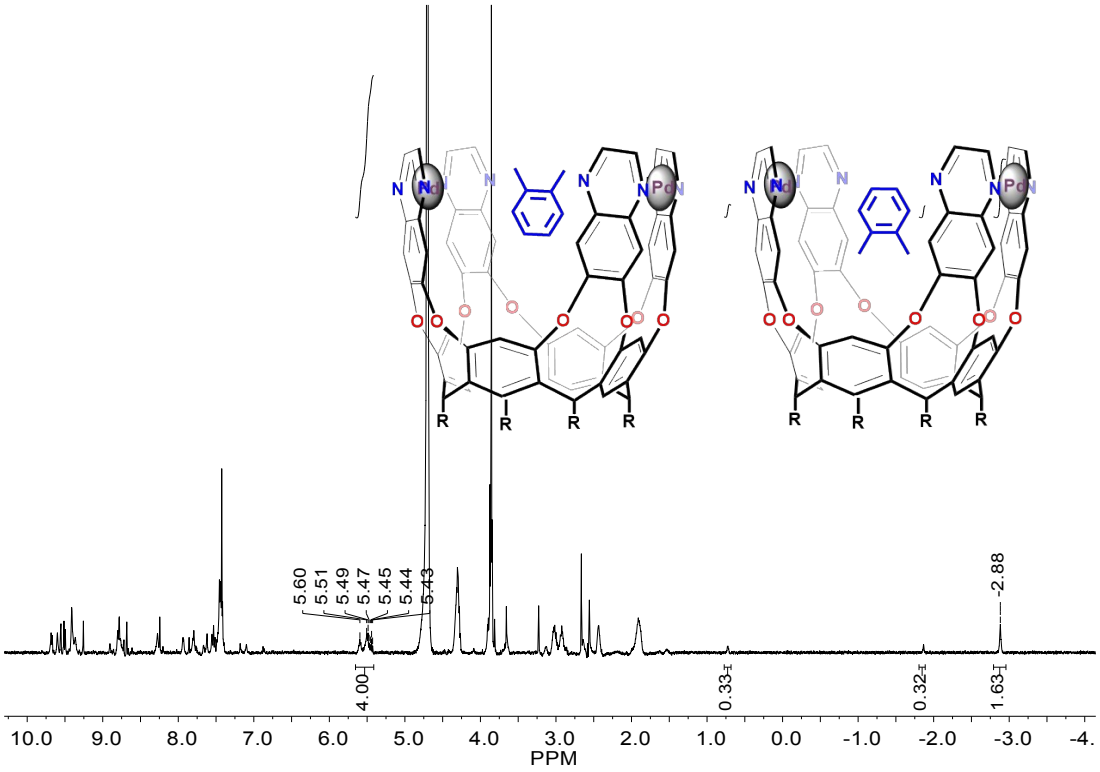


Figure S14 ^{1}H NMR spectra of the complex formed between 1 mM of **1-2Pd** in D_2O + 1 equivalent of *o*-xylene (added 5 µL 100 mM stock solution in methanol-d_4), analyzed at rt

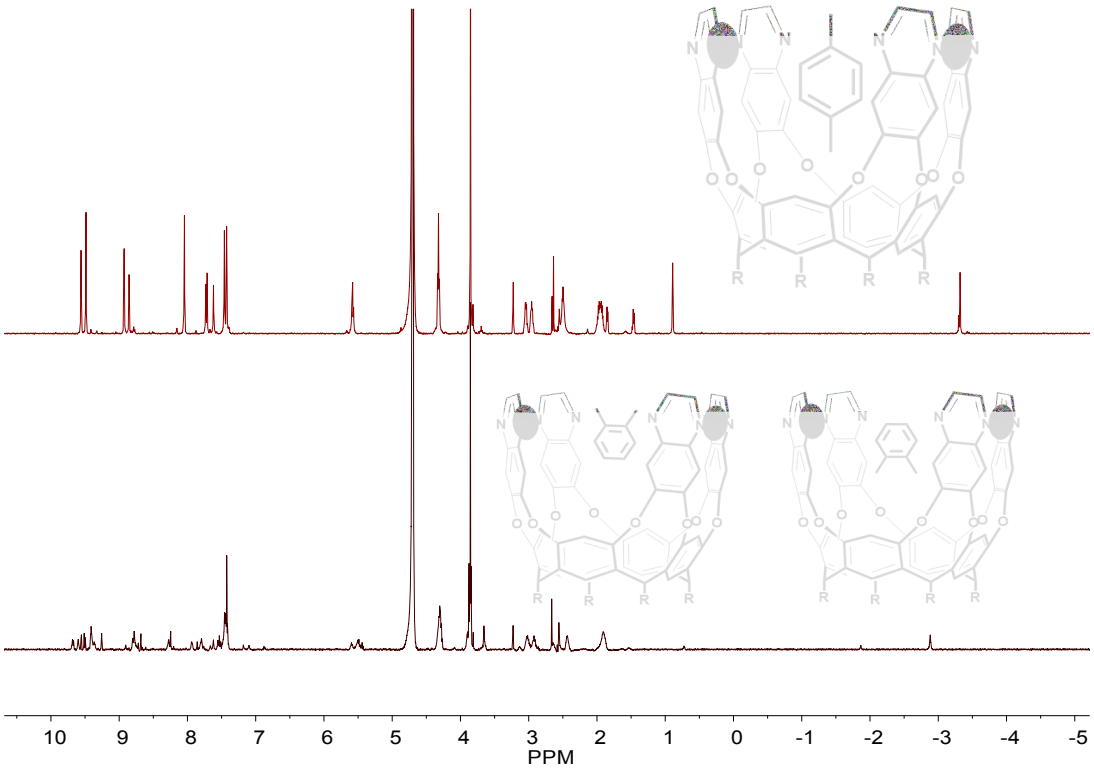


Figure S15 ^{1}H NMR spectra of the complex formed between 1 mM of **1-2Pd** in D_2O + 1 equivalent of *o*-xylene (added 5 µL 100 mM stock solution in methanol-d_4) (bottom) and then added with 1 equivalent of *p*-xylene (added 5 µL 100 mM stock solution in methanol-d_4) (top), analyzed at rt

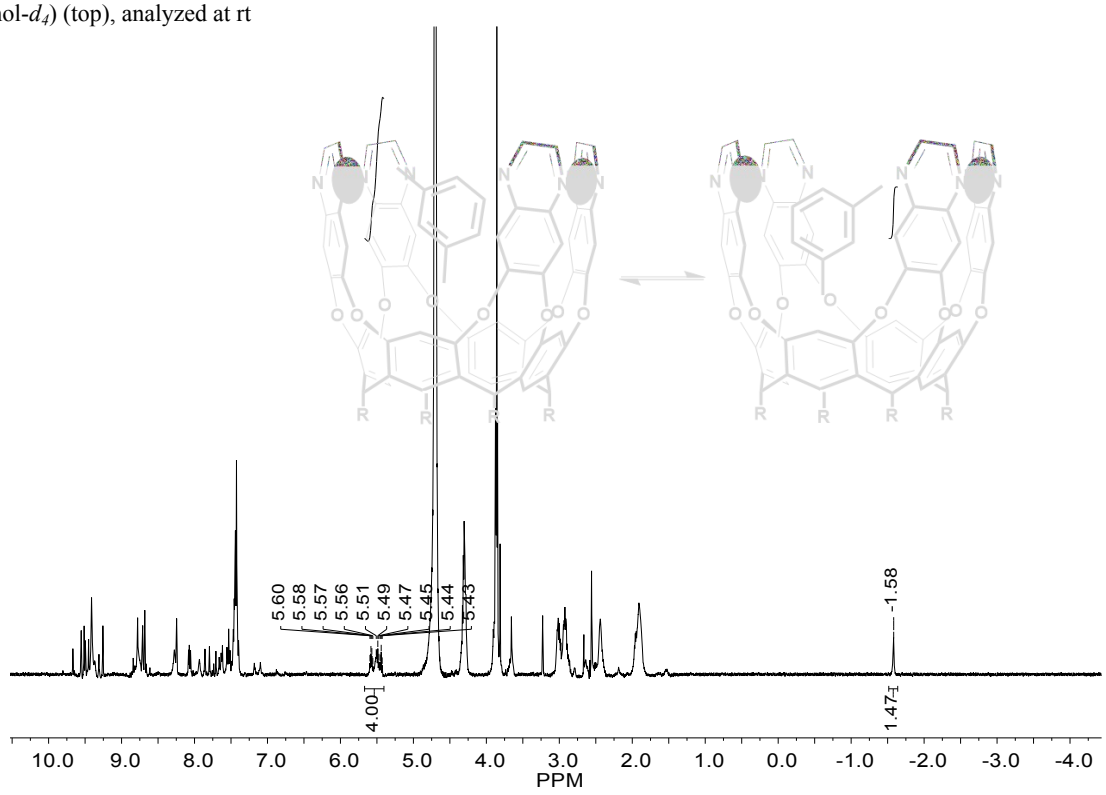


Figure S16 ^{1}H NMR spectra of the complex formed between 1 mM of **1-2Pd** in D_2O + 1 equivalent of *m*-xylene (added 5 µL 100 mM stock solution in methanol-d_4), analyzed at rt

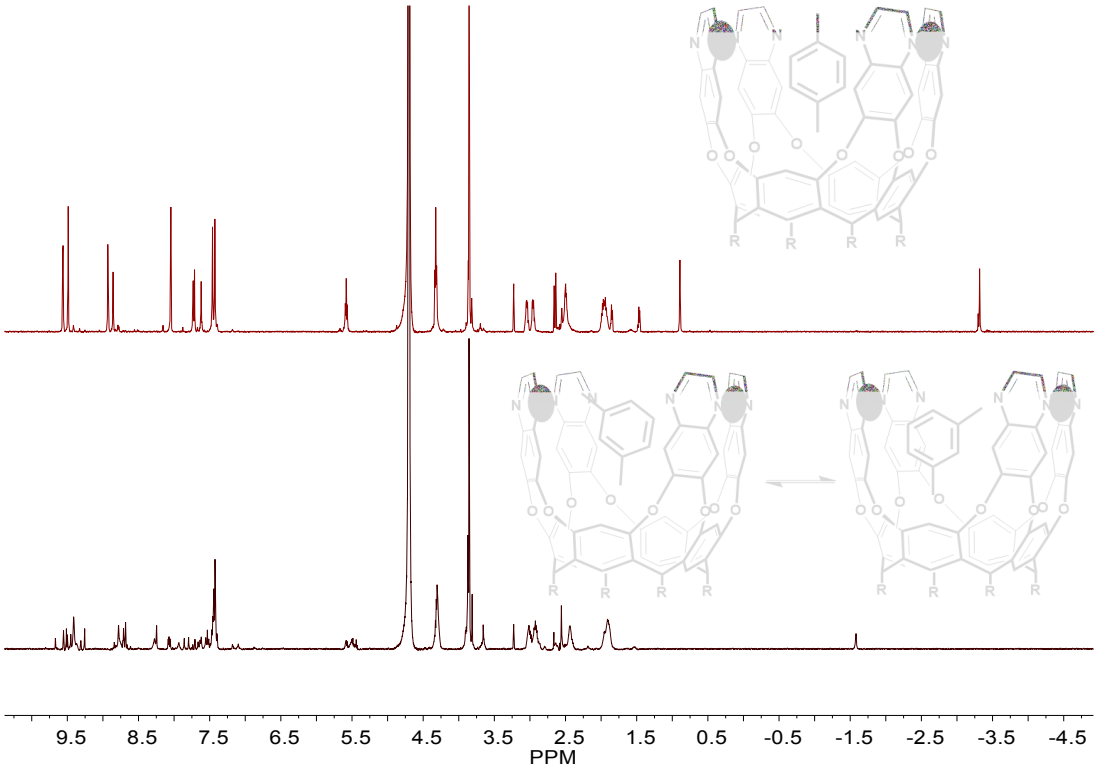


Figure S17 ^{1}H NMR spectra of the complex formed between 1 mM of **1-2Pd** in D_2O + 1 equivalent of *m*-xylene (added 5 µL 100 mM stock solution in methanol-d_4) (bottom) and then added with 1 equivalent of *p*-xylene (added 5 µL 100 mM stock solution in methanol-d_4) (top), analyzed at rt

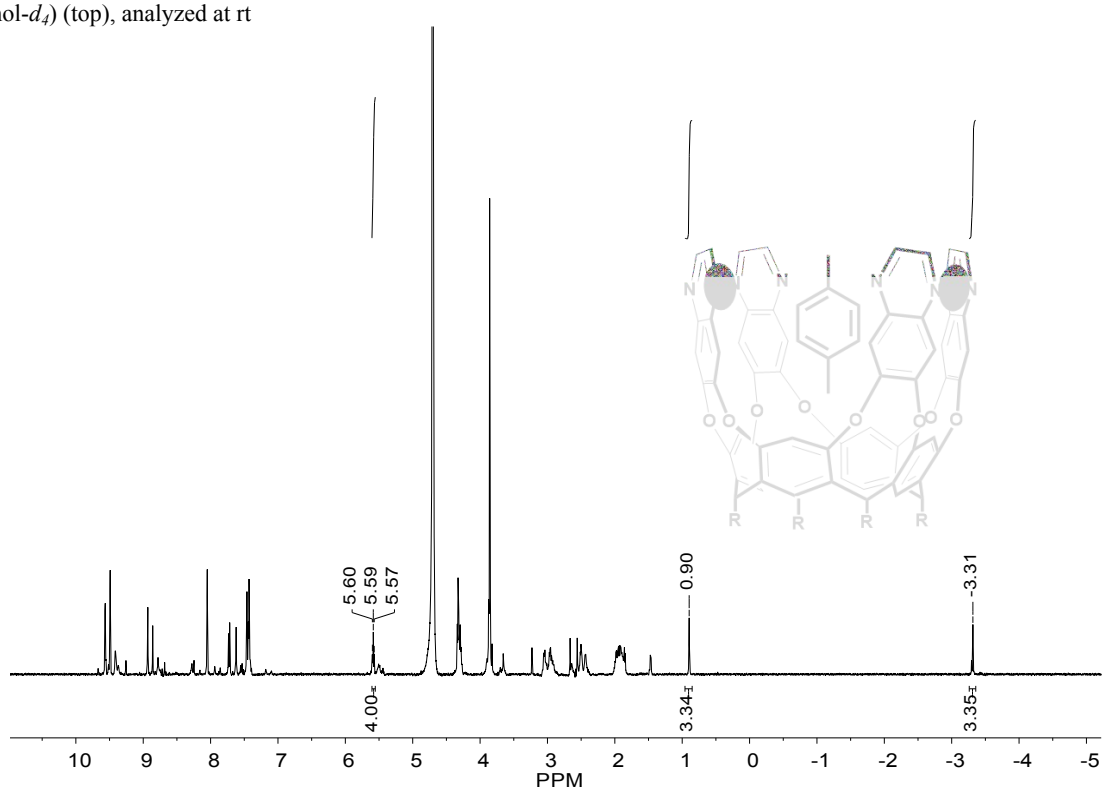


Figure S18 ^{1}H NMR spectra of the complex formed between 1 mM of **1-2Pd** in D_2O + 1 equivalent of *p*-xylene (added 5 µL 100 mM stock solution in methanol-d_4), analyzed at rt

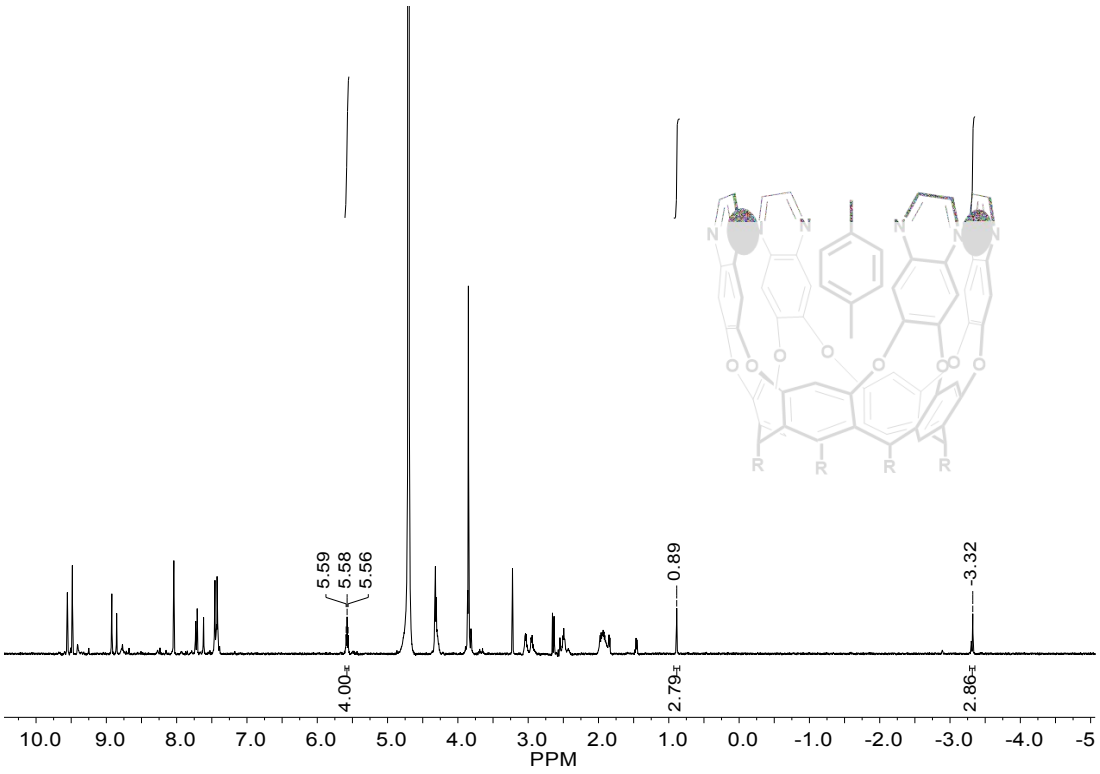


Figure S19 ^{1}H NMR spectra of the complex formed between 1 mM of **1-2Pd** in D_2O + 1 equivalent of *o*-, *m*- and *p*-xylene (added each isomer in 5 μL 100 mM stock solution in methanol-d_4), analyzed at rt

Selective capture of *p*-xylene in real time mixture studied by ^{1}H NMR spectroscopy

Fossil fuel xylenes distillate contains *o*-:*m*-:*p*-xylene 1:3:1, so this ideal mixture was prepared by mixing of these isomers in the mentioned ratio.

The binding in **1-2Pd** was measured in D_2O using;

1. Excess of *o*-:*m*-:*p*-xylene 1:3:1 mixture in **1-2Pd**
2. 1-6 equivalents of the mixture was added as 100 mM stock solution in CD_3OD to **1-2Pd** solution in D_2O and analysed at rt over 2 and 24 h.

General procedure for the binding analyses

1 mM, 0.5 mL solution of **1-2Pd** in D_2O was taken in NMR tube and excess of the xylene mixture or 1-6 equivalents of xylene mixture stock solution in methanol-d_4 (15 µL) was added to the tube, it was shaken well to mix the guest in water. The sample was sonicated for 2 h and analyzed by ^{1}H NMR spectroscopy, the analyses of the same samples were repeated after 24 h.

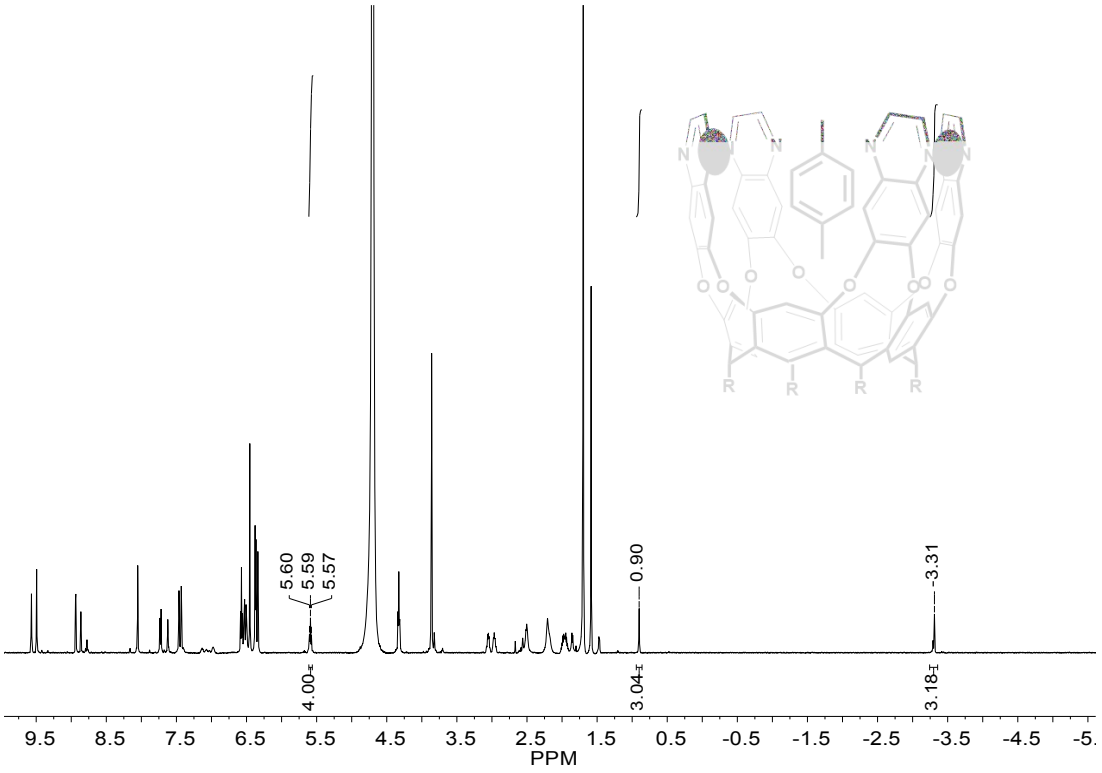


Figure S20 ^{1}H NMR spectra of the complex formed between 1 mM of **1-2Pd** in D_2O + Excess of *o-, m-* and *p*-xylene (1:3:1) mixture sonicated for 2 h, analyzed at rt

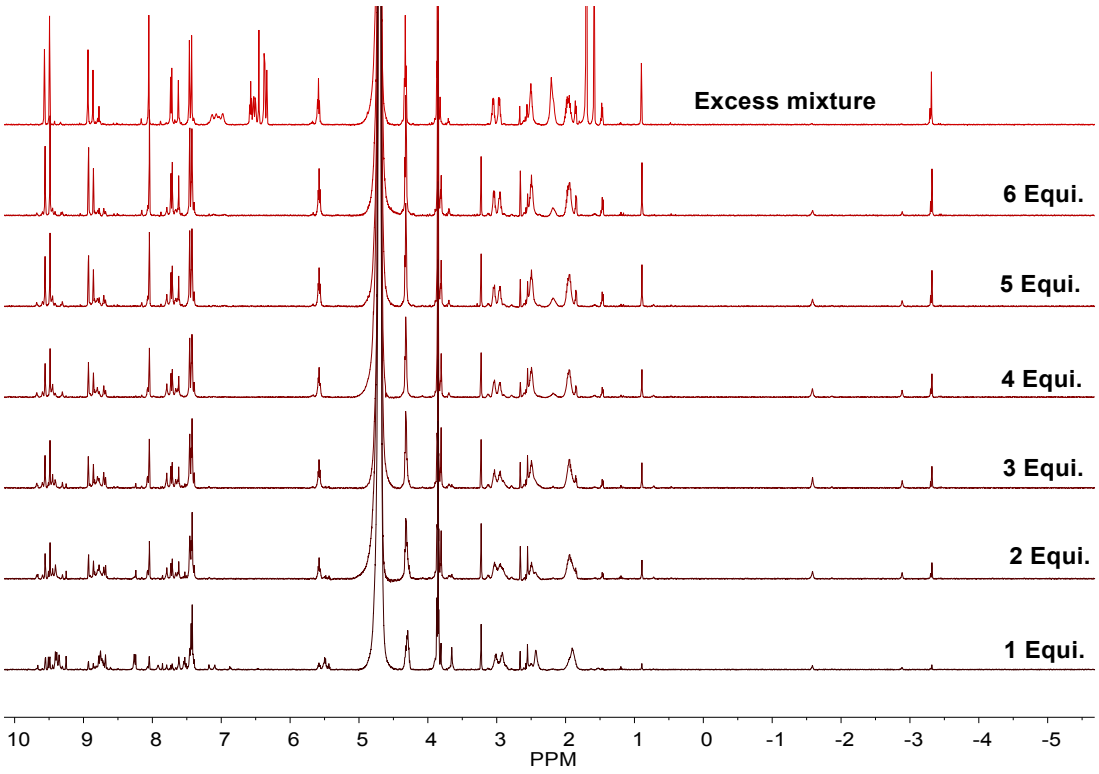


Figure S21 ^{1}H NMR spectra of the complex formed between 1 mM of **1-2Pd** in D_2O + 1-6 equivalents of *o-, m-* and *p*-xylene (1:3:1) mixture; 15 µL stock solution of the mixture in CD_3OD was added and the mixture sonicated for 2 h, analyzed at rt

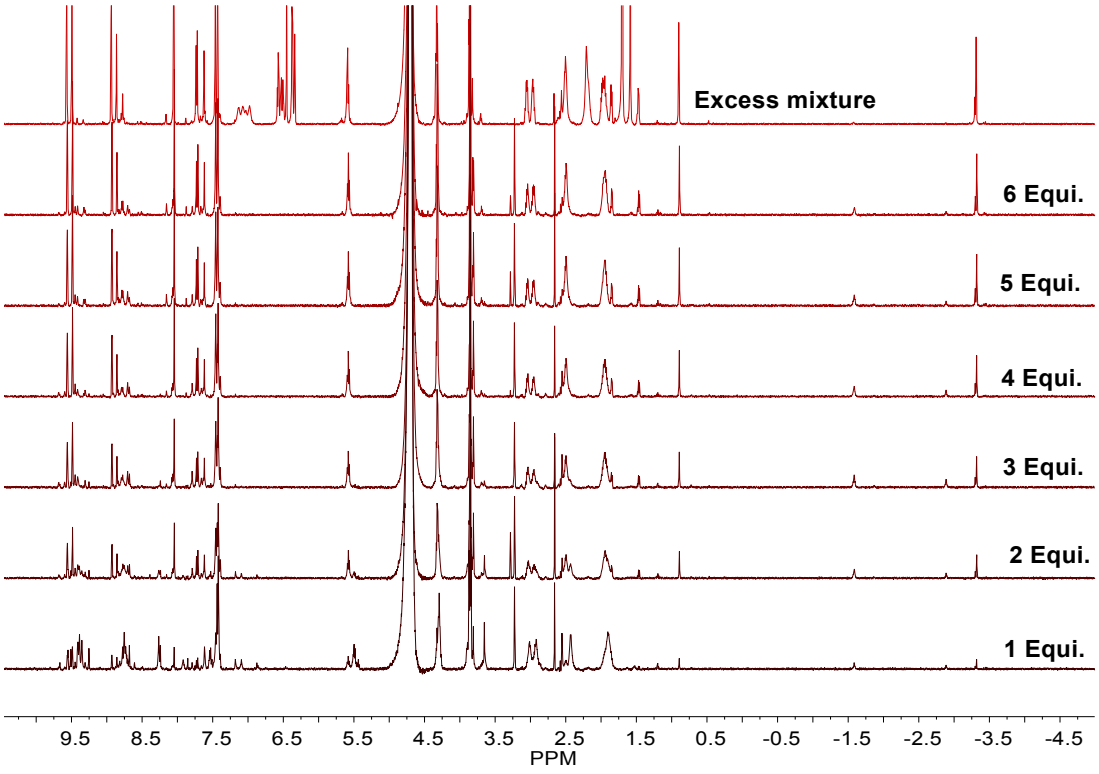
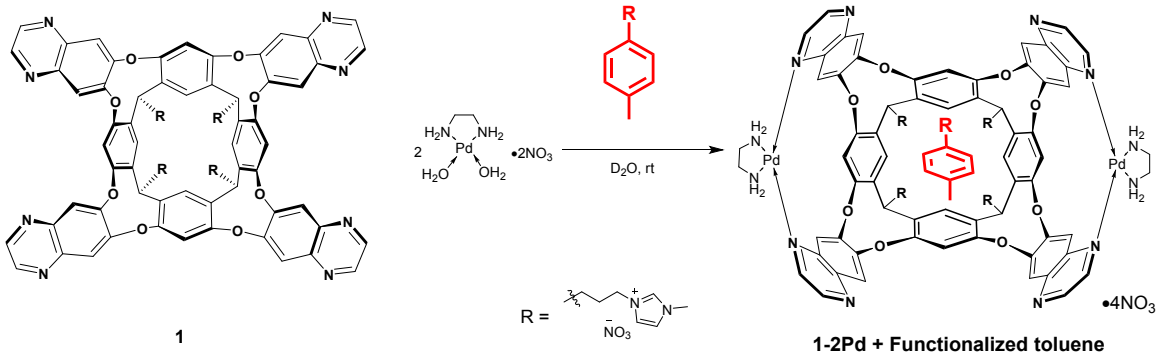


Figure S22 ^{1}H NMR spectra of the complex formed between 1 mM of **1-2Pd** in D_2O + 1-6 equivalents of *o-, m-* and *p*-xylene (1:3:1), 15 µL stock solution (in CD_3OD) was added and mixture sonicated for 2 h, analyzed after 24 h at rt

Binding and competition study of functionalized toluene isomers in 1-2Pd

General procedure for the binding analyses

1 mM, 0.5 mL solution of **1-2Pd** in D_2O was taken in NMR tube and excess pure particular isomer or mixture (~0.25 µL) or equivalent quantity as CD_3OD stock solution was added to the tube, it was shaken well to mix the guest in water. The sample was sonicated for 1 h and analyzed by ^1H NMR spectroscopy.



Nitrotoluene isomers binding in 1-2Pd

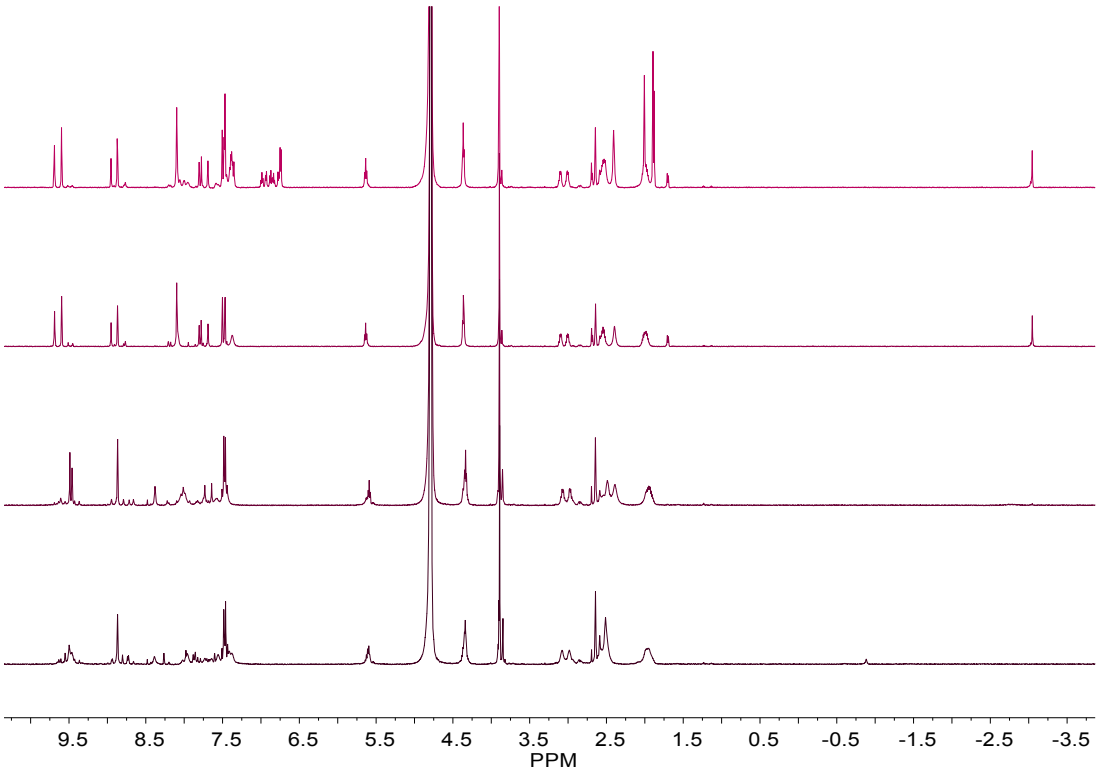


Figure S23 Comparative ^1H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*- (bottom) or *m*- (second from bottom), or *p*- isomer (third from bottom) and excess 1:1:1 mixture of these isomers (top), in D_2O, analyzed at rt

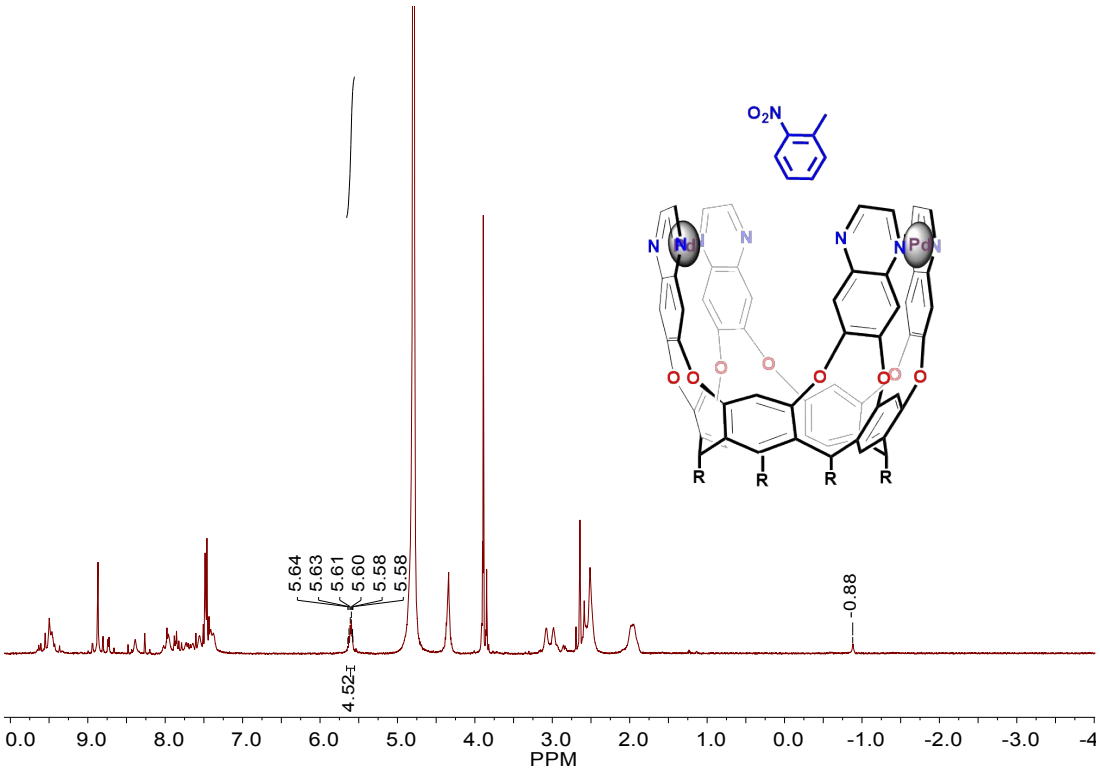


Figure S24 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*-nitrotoluene in D_2O, analyzed at rt

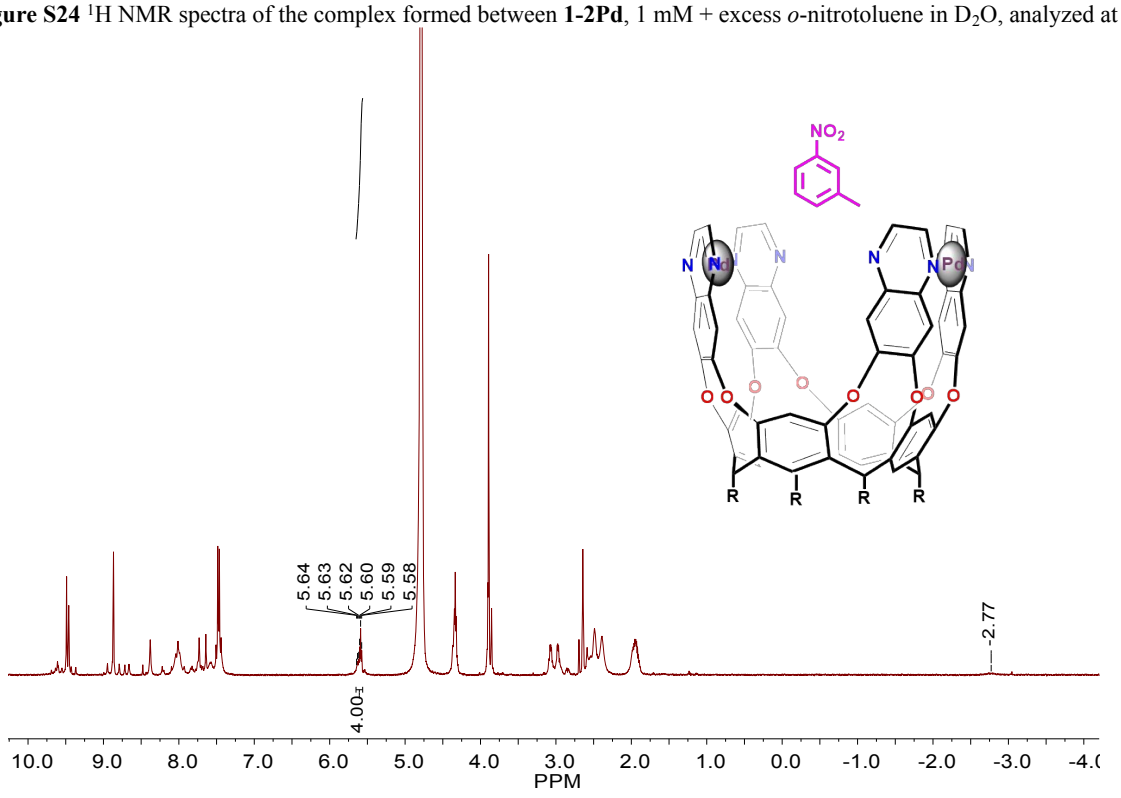


Figure S25 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *m*-nitrotoluene in D_2O, analyzed at rt

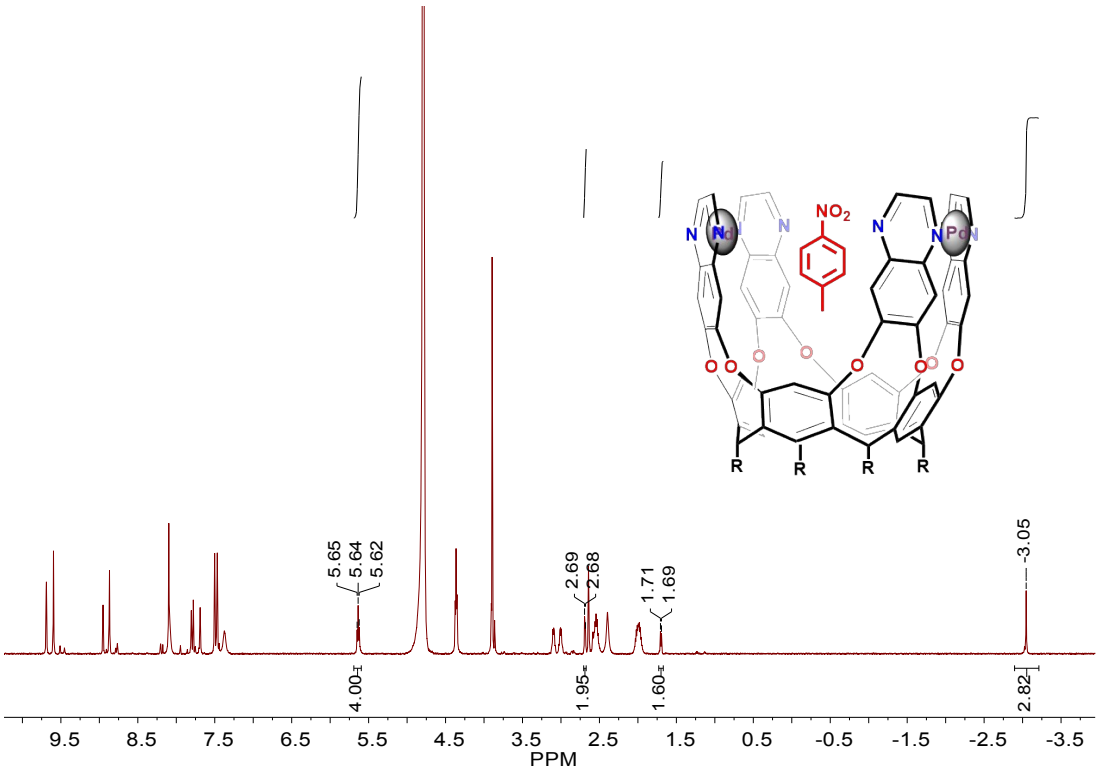


Figure S26 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *p*-nitrotoluene in D_2O, analyzed at rt

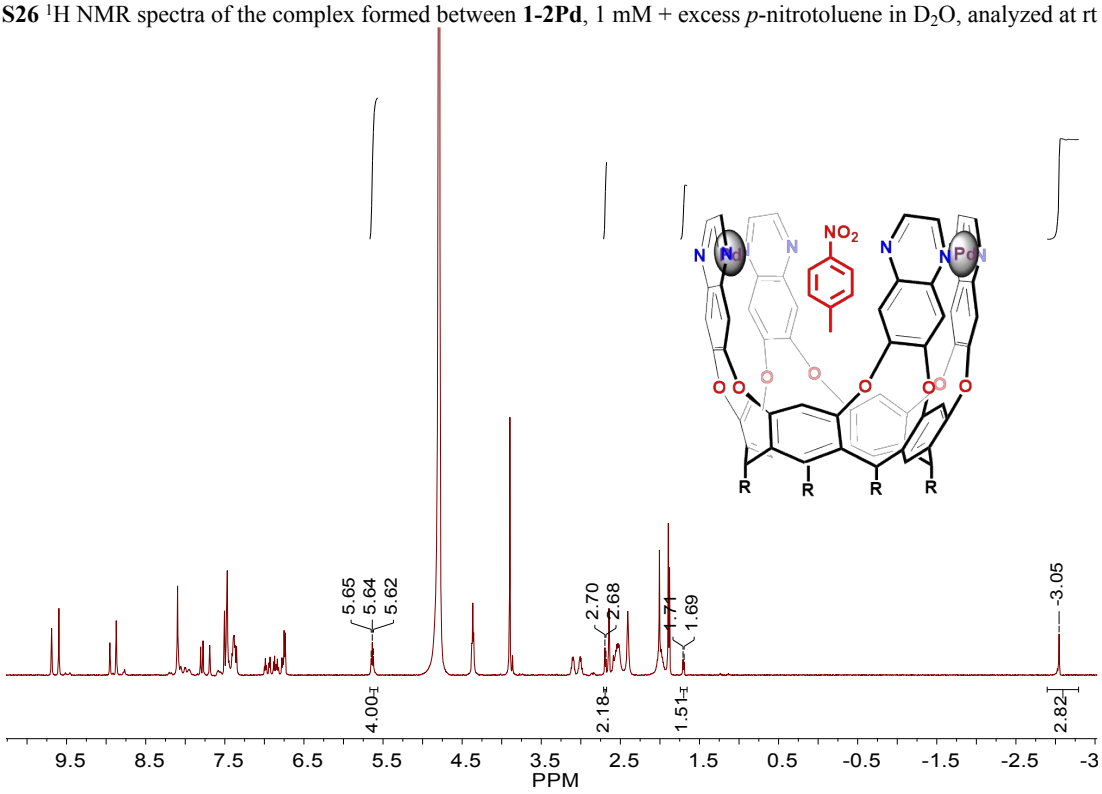


Figure S27 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*-, *m*-, *p*-nitrotoluene (1:1:1) mixture in D_2O, analyzed at rt

Methyltoluate isomers binding in 1-2Pd

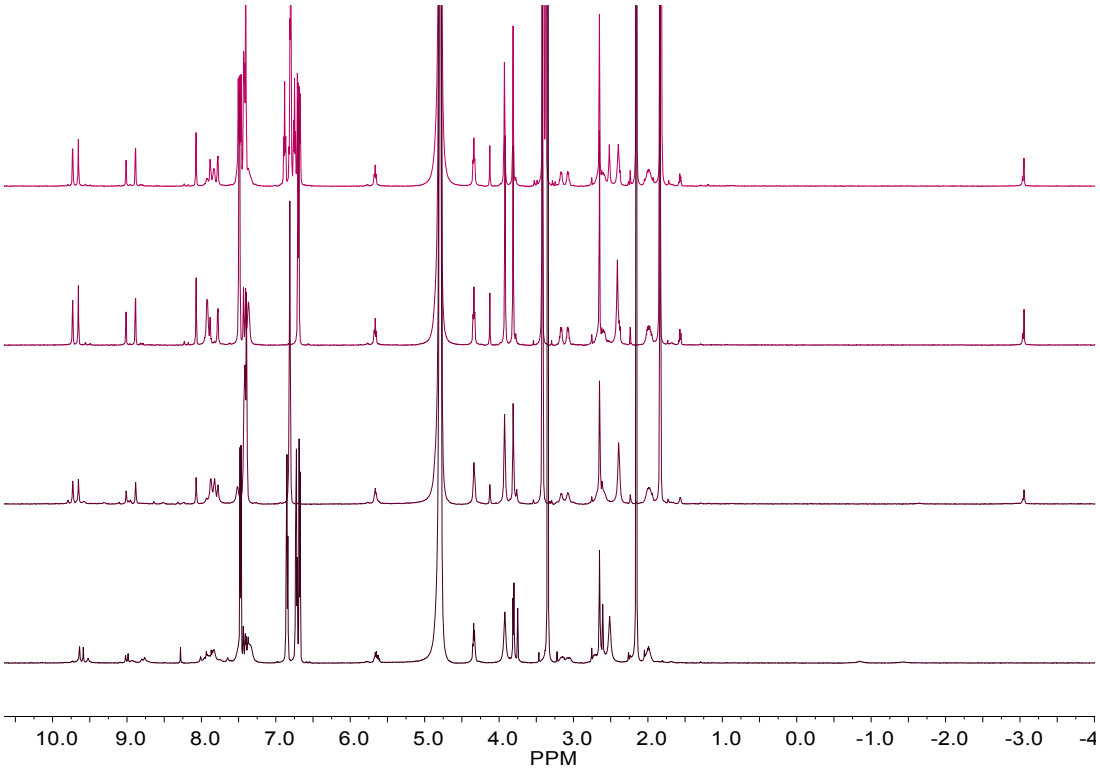


Figure S28 Comparative ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*- (bottom) or *m*- (second from bottom), or *p*- isomer (third from bottom) and excess 1:1:1 mixture of these isomers (top), in D_2O, analyzed at rt

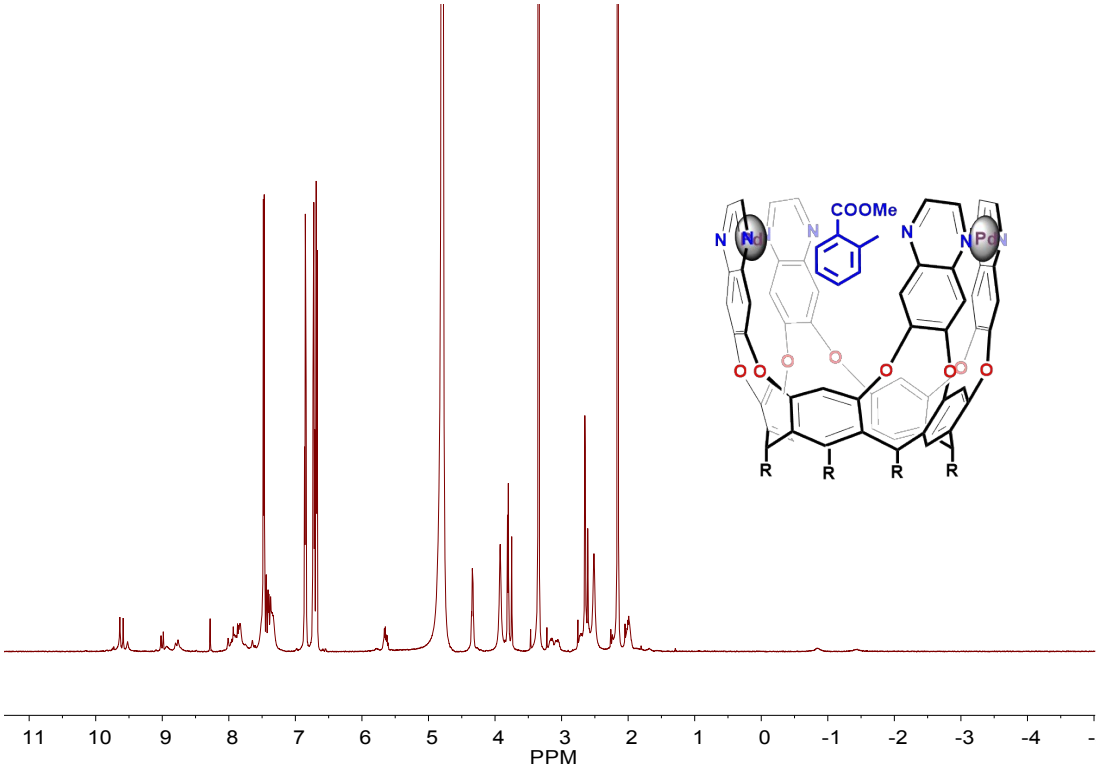


Figure S29 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess methyl-*o*-toluate in D_2O, analyzed at rt

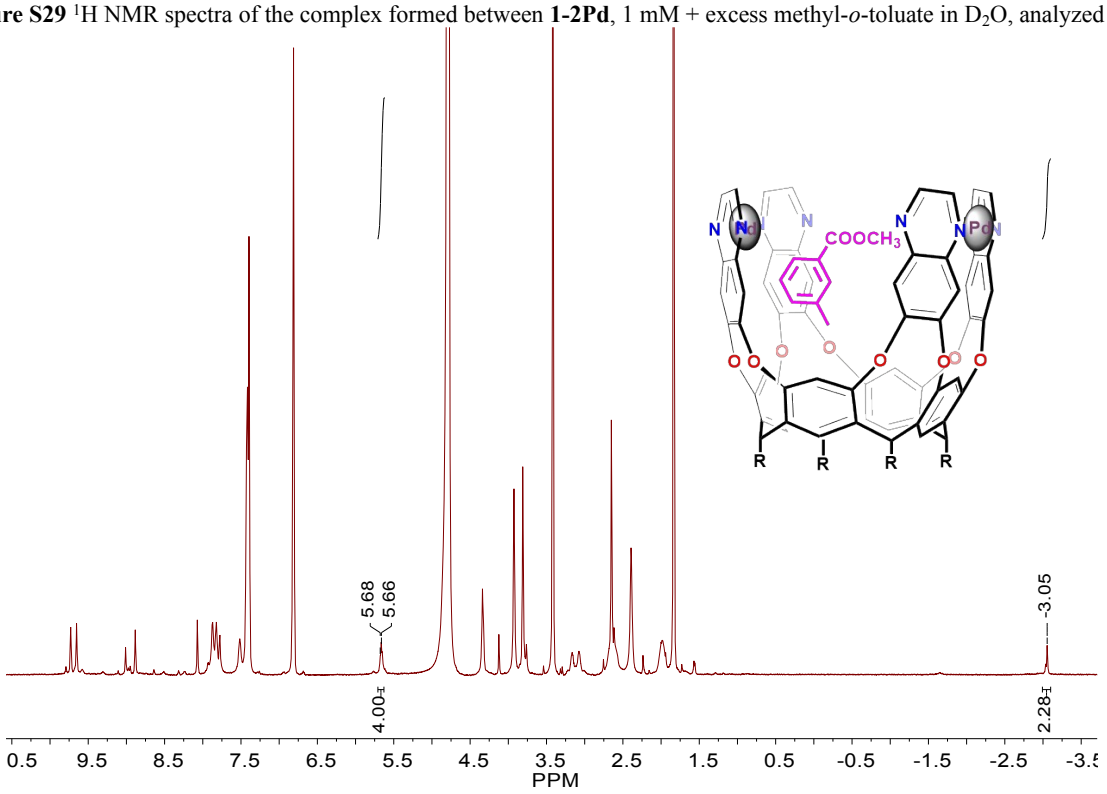


Figure S30 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess methyl-*m*-toluate in D_2O, analyzed at rt

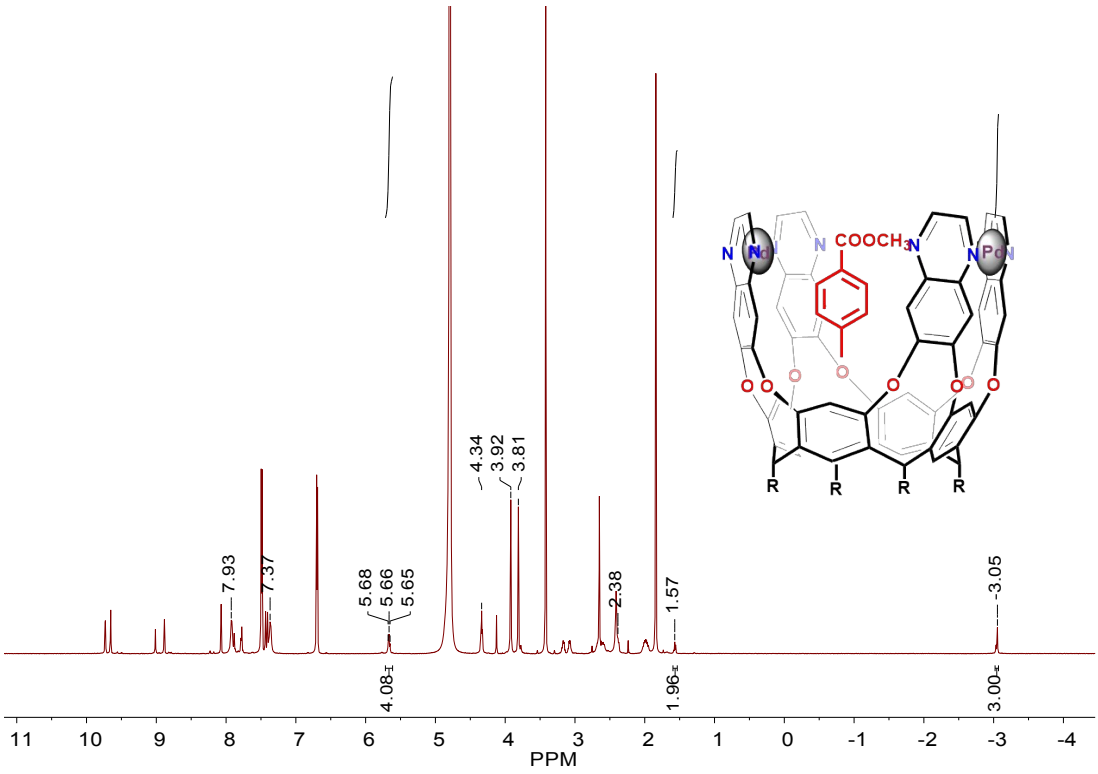


Figure S31 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess methyl-*p*-toluate in D_2O, analyzed at rt

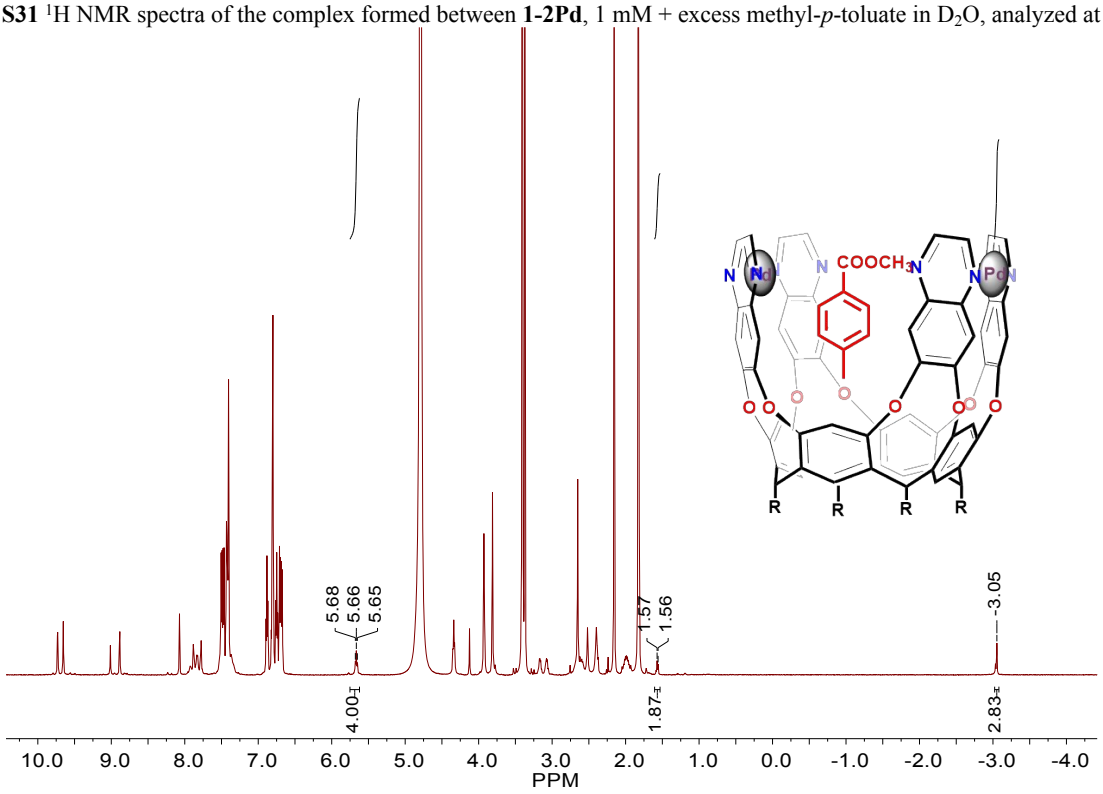


Figure S32 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess methyl-*o*-toluate, methyl-*m*-toluate, methyl-*p*-toluate (1:1:1) mixture in D_2O, analyzed at rt, only *p*-tolualdehyde was captured by the **1-2Pd**

Tolualdehyde isomers binding in 1-2Pd

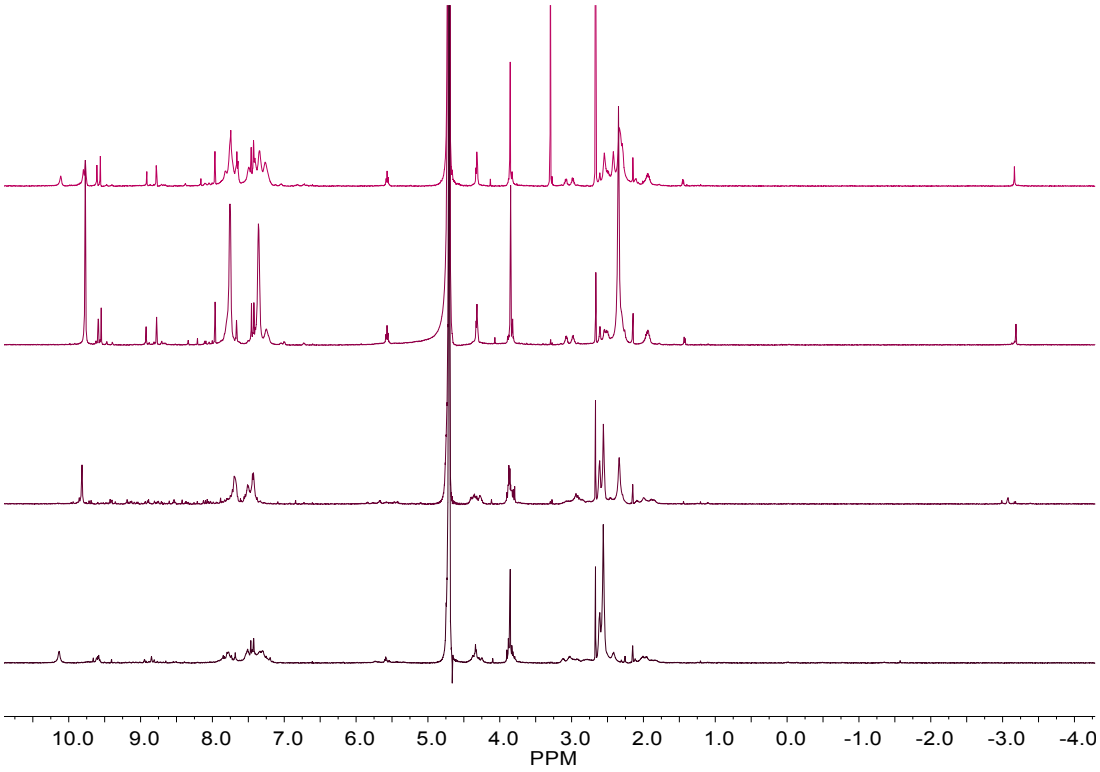


Figure S33 Comparative ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*- (bottom) or *m*- (second from bottom), or *p*-tolualdehyde (third from bottom) and excess 1:1:1 mixture of these isomers (top), in D_2O, analyzed at rt

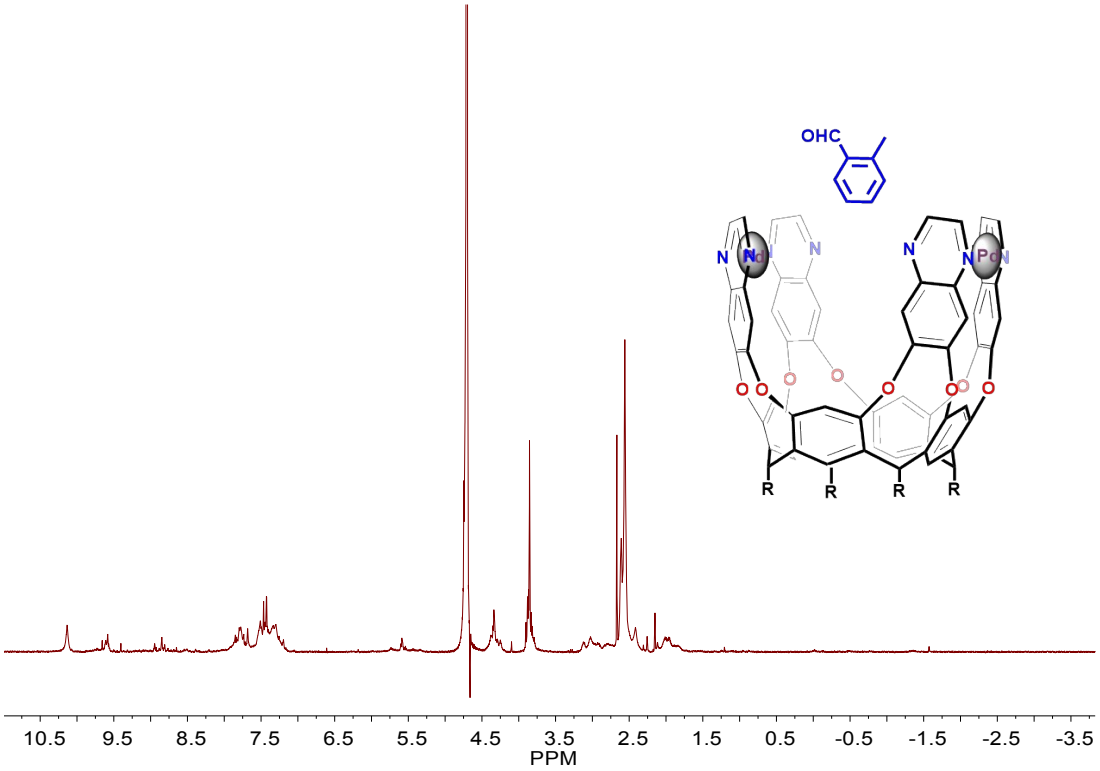


Figure S34 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*- tolualdehyde in D_2O, analyzed at rt

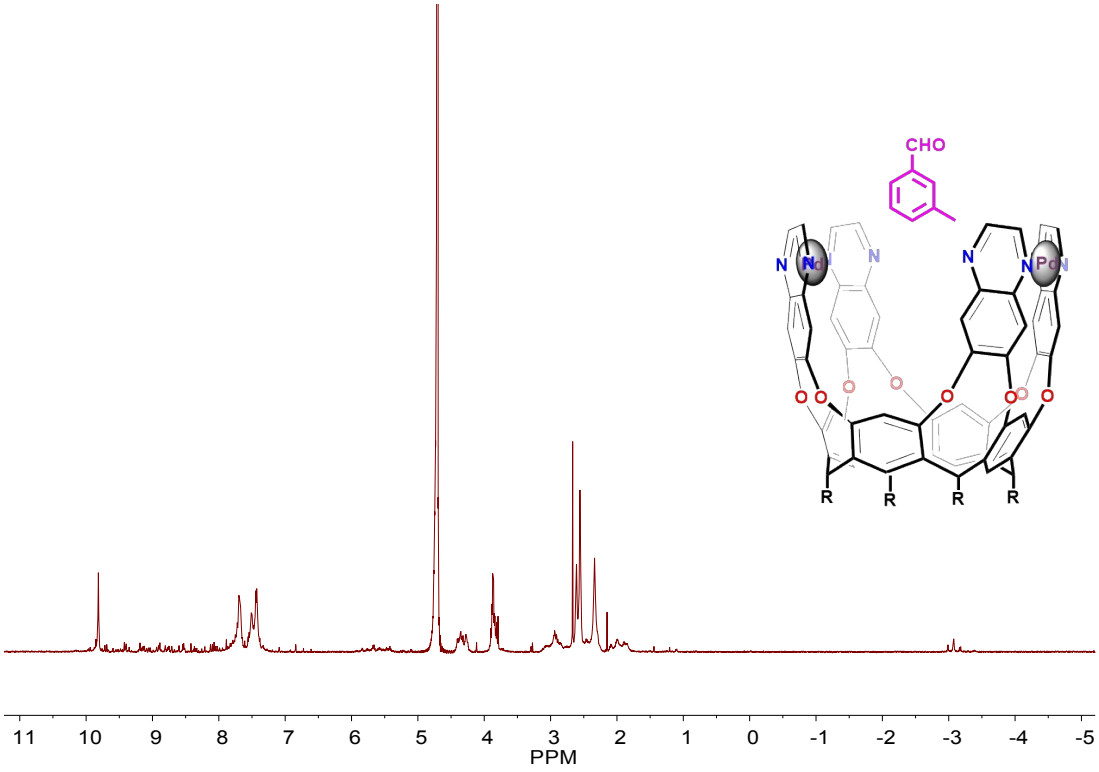


Figure S35 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *m*-tolualdehyde in D_2O, analyzed at rt

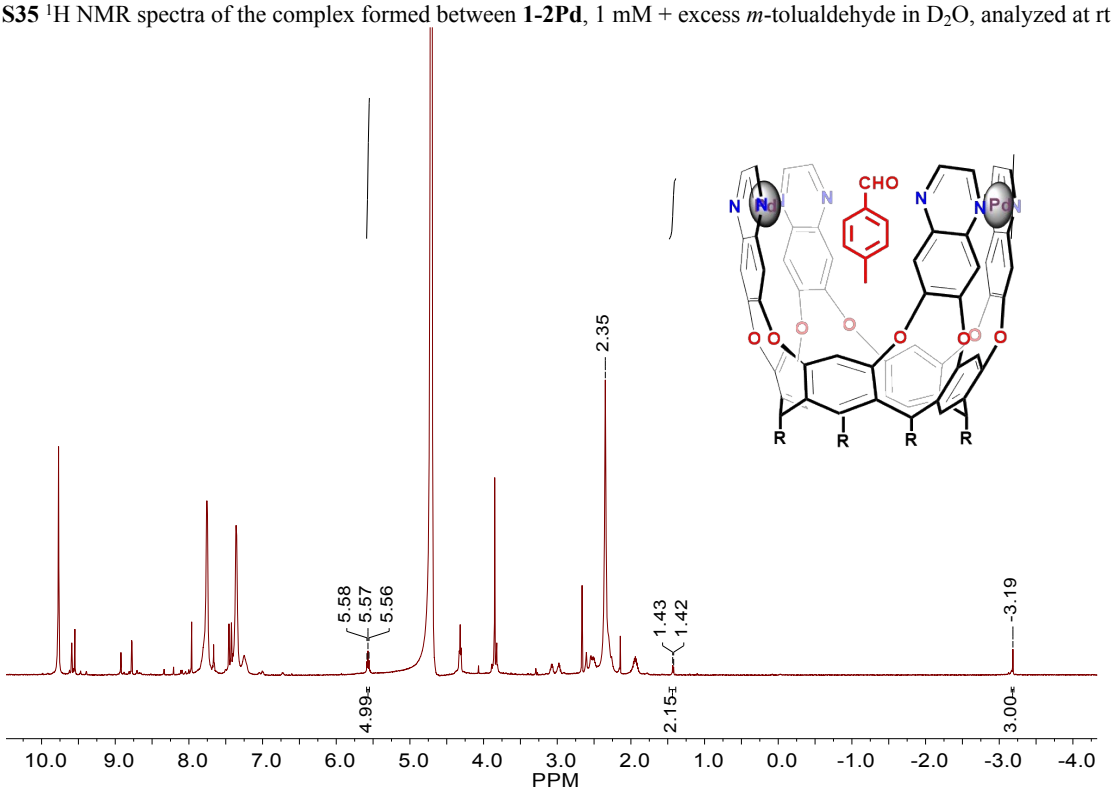


Figure S36 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *p*-tolualdehyde in D_2O, analyzed at rt

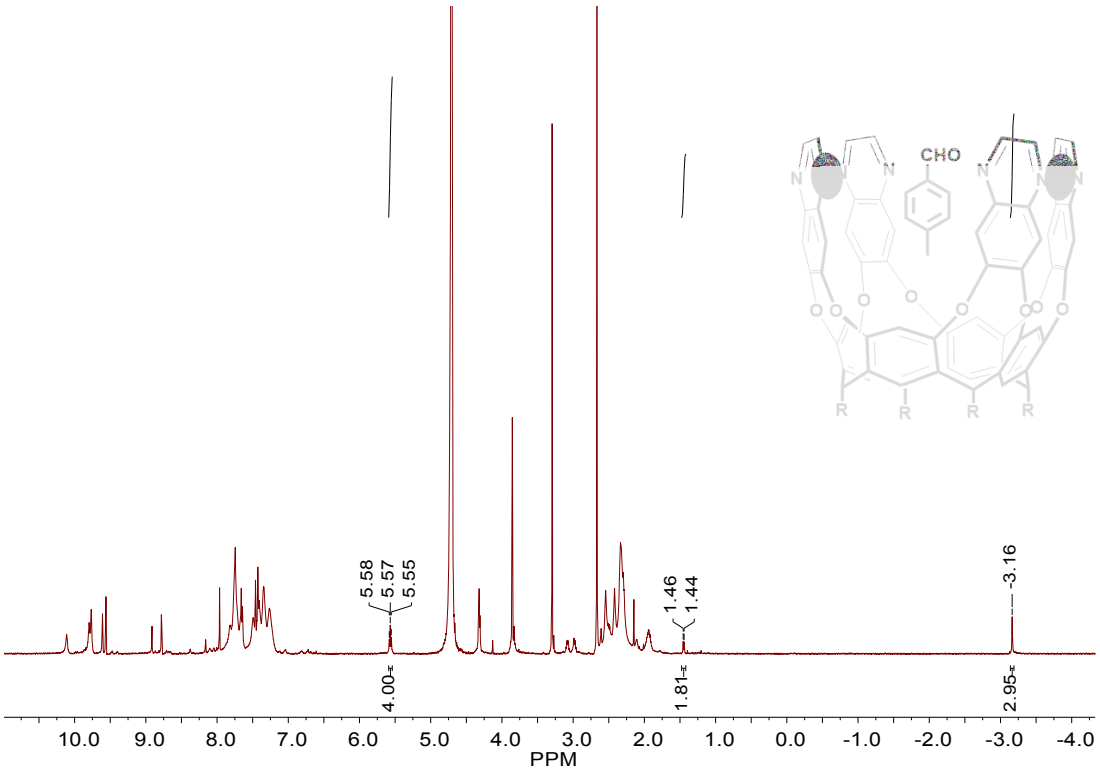


Figure S37 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*- + *m*- + *p*-tolualdehyde (1:1:1) mixture in D_2O, analyzed at rt only *p*-tolualdehyde was captured by the **1-2Pd**

Acetyl toluene isomers binding in 1-2Pd

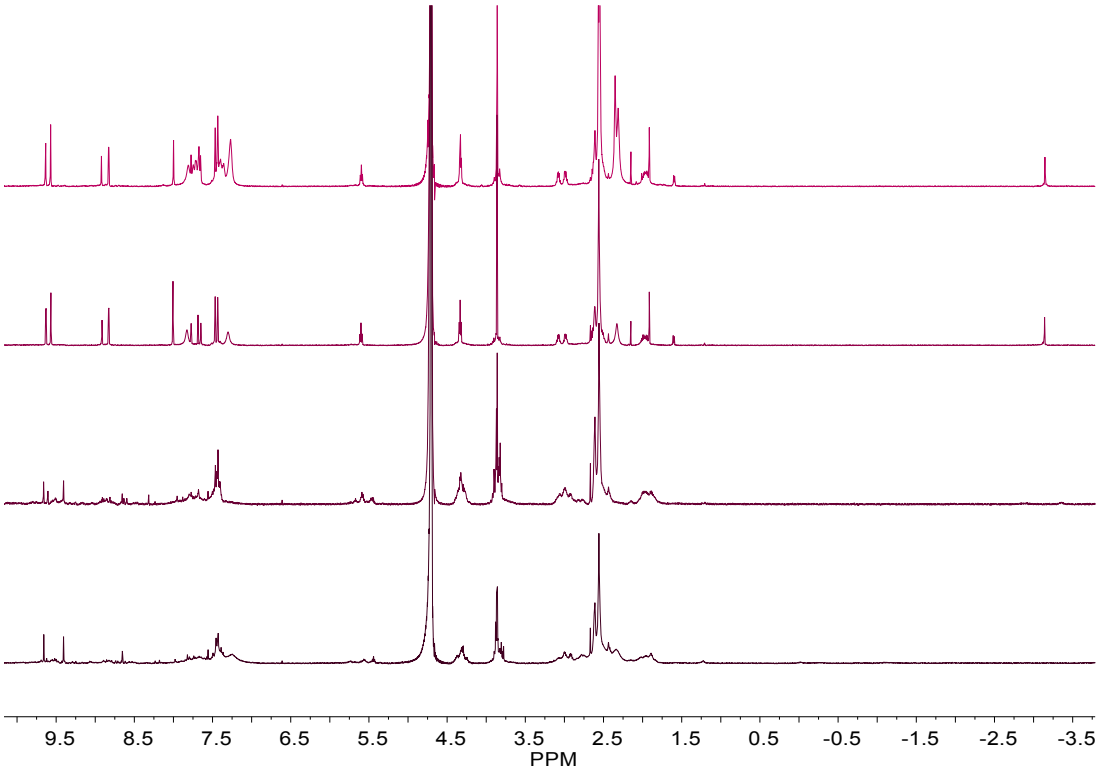


Figure S38 Comparative ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*- (bottom) or *m*- (second from bottom), or *p*-acetyltoluene (third from bottom) and excess 1:1:1 mixture of these isomers (top), in D_2O, analyzed at rt

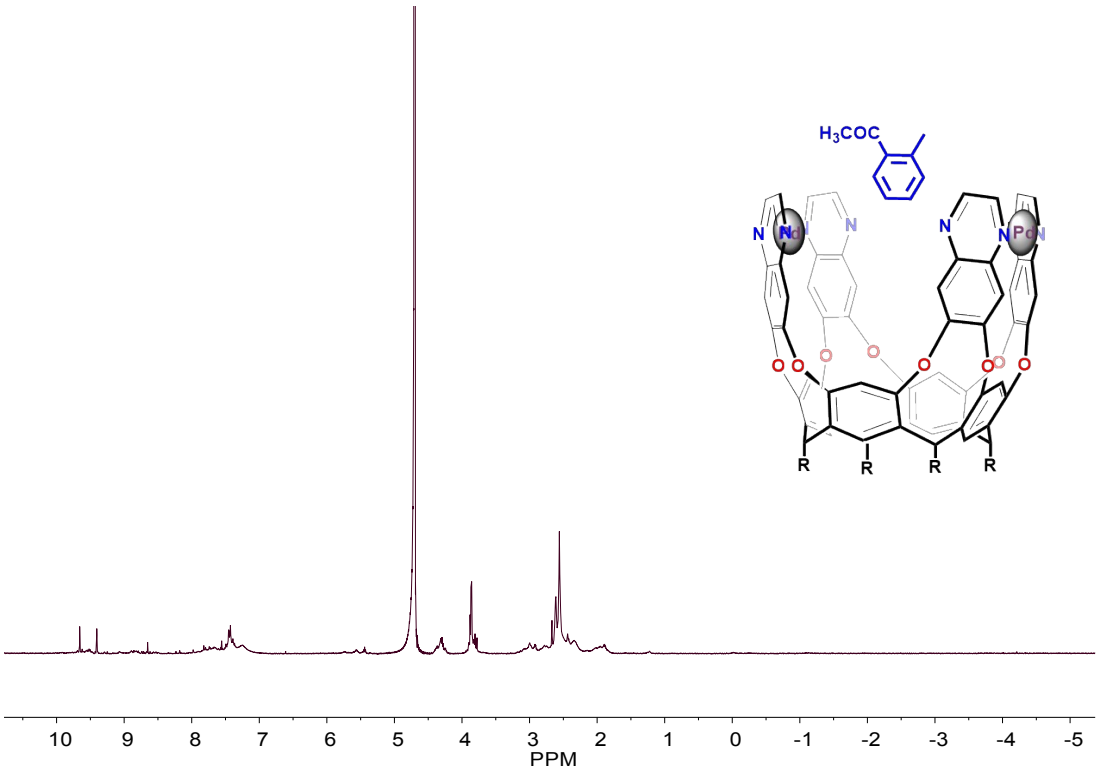


Figure S39 ^{1}H NMR spectrum of the complex formed between **1-2Pd**, 1 mM + excess *o*-acetyltoluene in D_2O, analyzed at rt

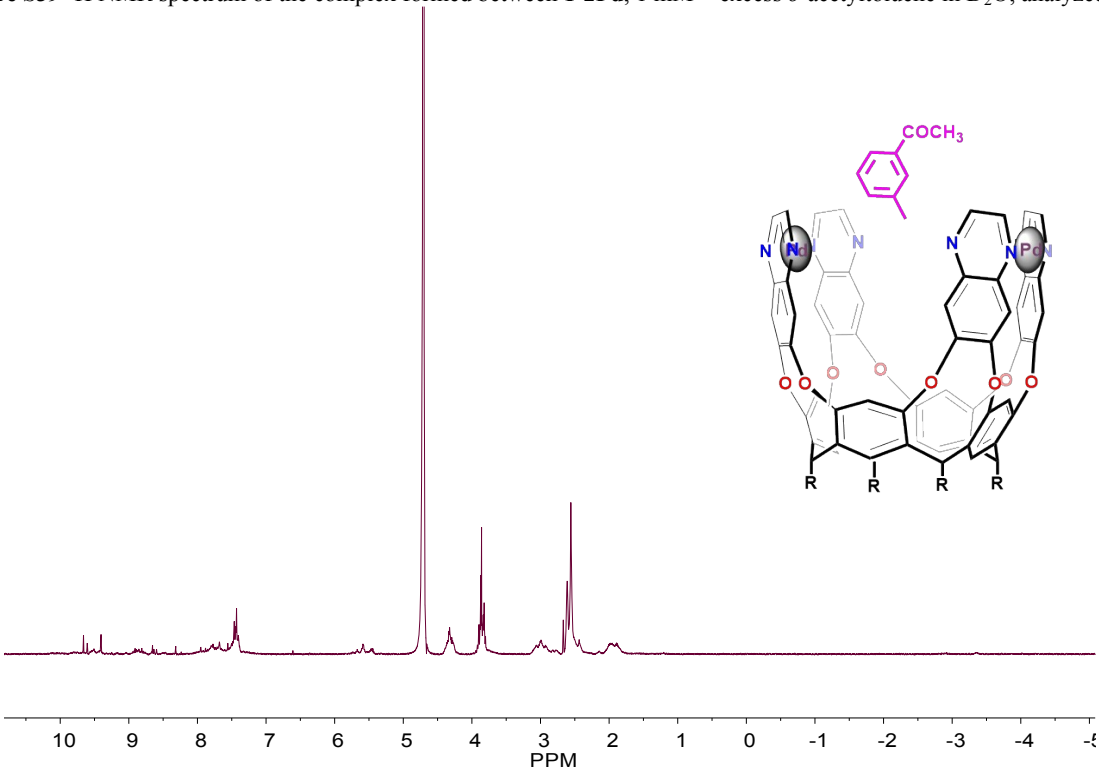


Figure S40 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *m*-acetyltoluene in D_2O, analyzed at rt

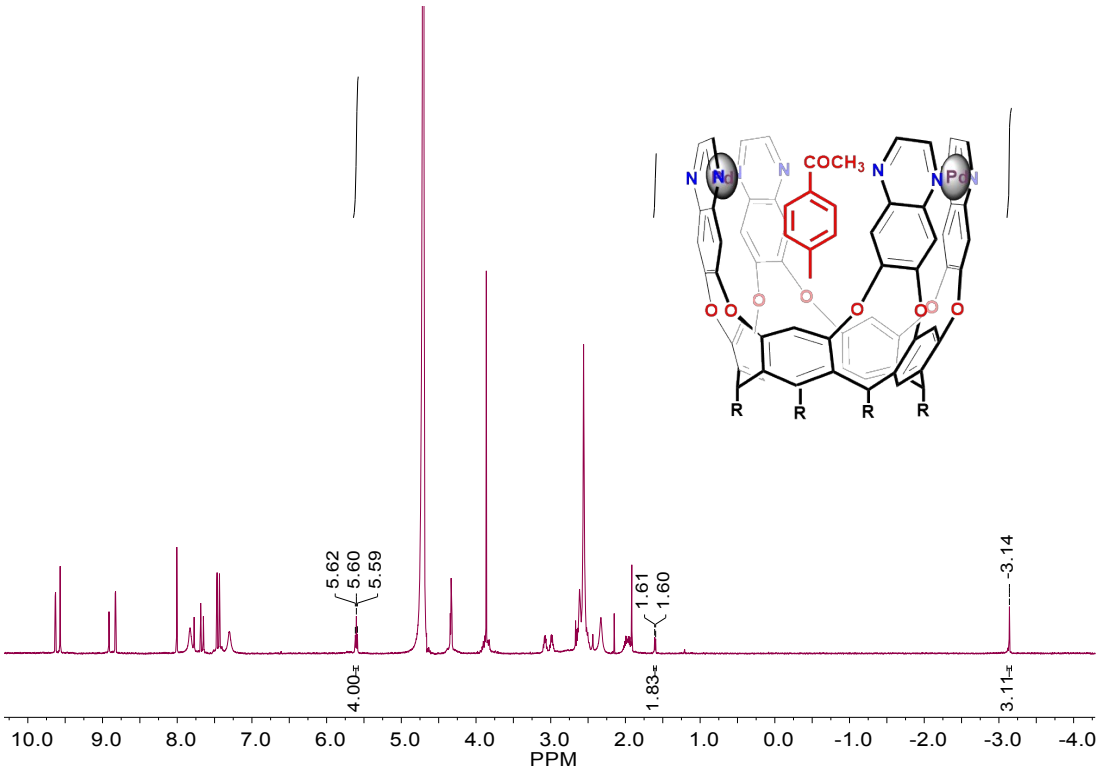


Figure S41 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *p*-acetyltoluene in D_2O, analyzed at rt

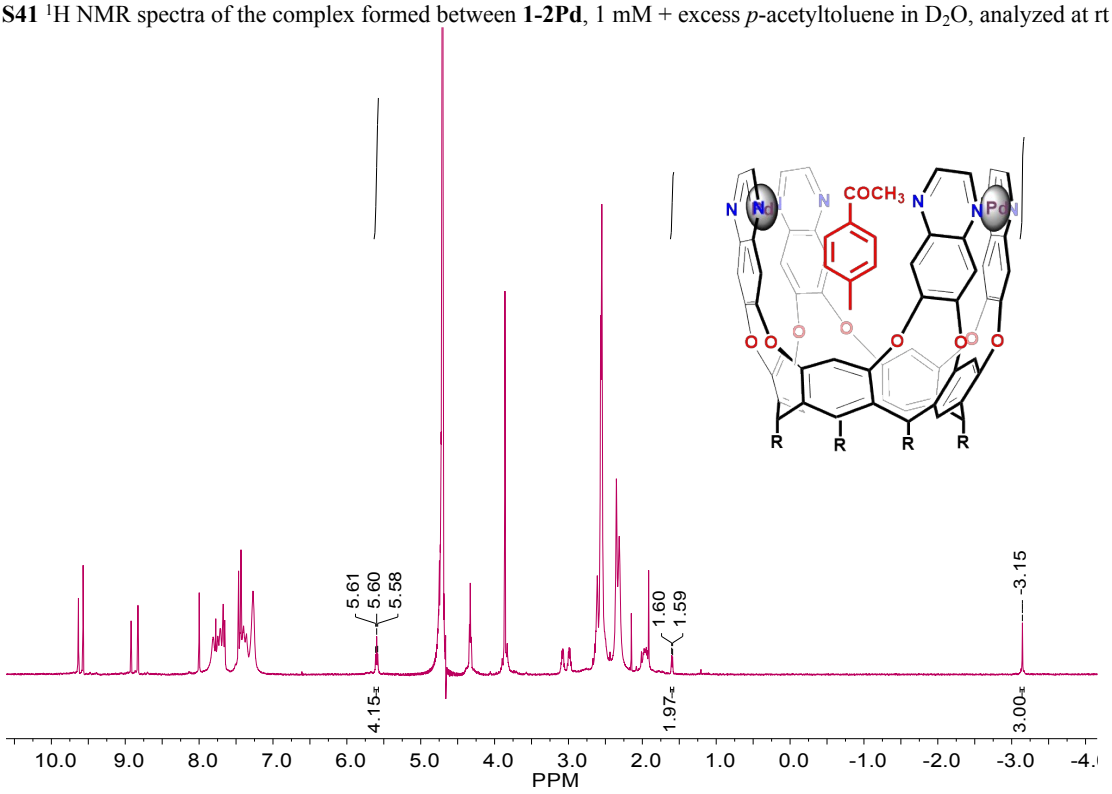


Figure S42 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess *o*- + *m*- + *p*-acetyltoluene (1:1:1) mixture in D_2O, analyzed at rt, only p-tolualdehyde was captured by the **1-2Pd**

Binding constant for xylene isomers

As xylenes are not soluble in water so it is difficult to perform binding constant experiments in pure water using isothermal titration calorimetry (ITC), but we used a comparative method to deduce binding constant for xylene isomers. The binding constant was calculated for n-butanol (a water-soluble guest) using ITC.

The binding constant and thermodynamic parameters for **1-2Pd** complexation with *n*-butanol as a reference water-soluble guest were obtained through isothermal titration calorimetry (ITC). Increasing amounts of 5 mM aqueous *n*-butanol solution was added to 0.5 mM solution of **1** + 2.2 equivalents of $Pd(EDA)\cdot 2NO_3$ (**1-2Pd)** in water. The trace showed 1:1 complex formation with a binding constant $K = 1.54 \times 10^5$ M^{-1} (Figure 8). The complex formation was exothermic (ΔH = - 5942 cal mol^{-1}) showing favorable binding of the guest in **1-2Pd**. A positive change in entropy (ΔS = 3.81 cal mol^{-1} deg^{-1}) was observed that may be due to liberation of water from the host.

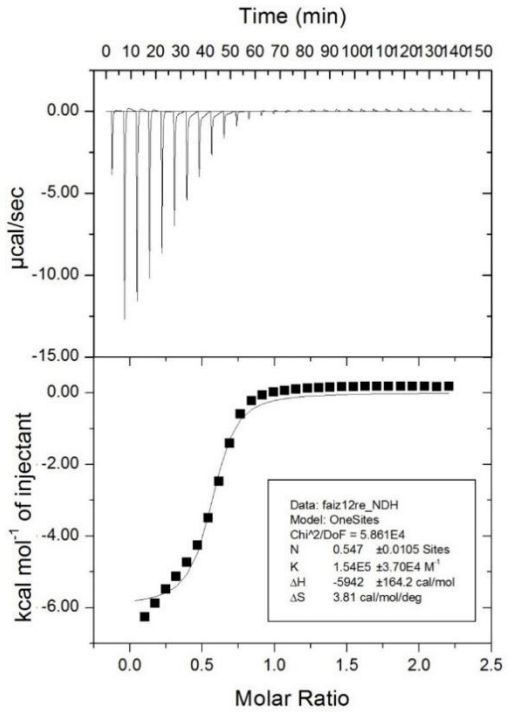


Figure S43 ITC titration curve of **1-2Pd** vs. n-butanol.

We compared *o*-, *m*- and *p*-xylene binding with **1-2Pd** in the presence of 1 equivalent of n-butanol by using ^{1}H NMR spectroscopy. 1 equivalent of **1-2Pd** 1 mM water solution was added with 2 equivalents of each n-butanol and 2 equivalents of *o*- or *m*- or *p*-xylene as CD_3OD stock solution (10 µL) and analysed by ^{1}H NMR spectroscopy at 2 h sonication or 24 h at rt time points.

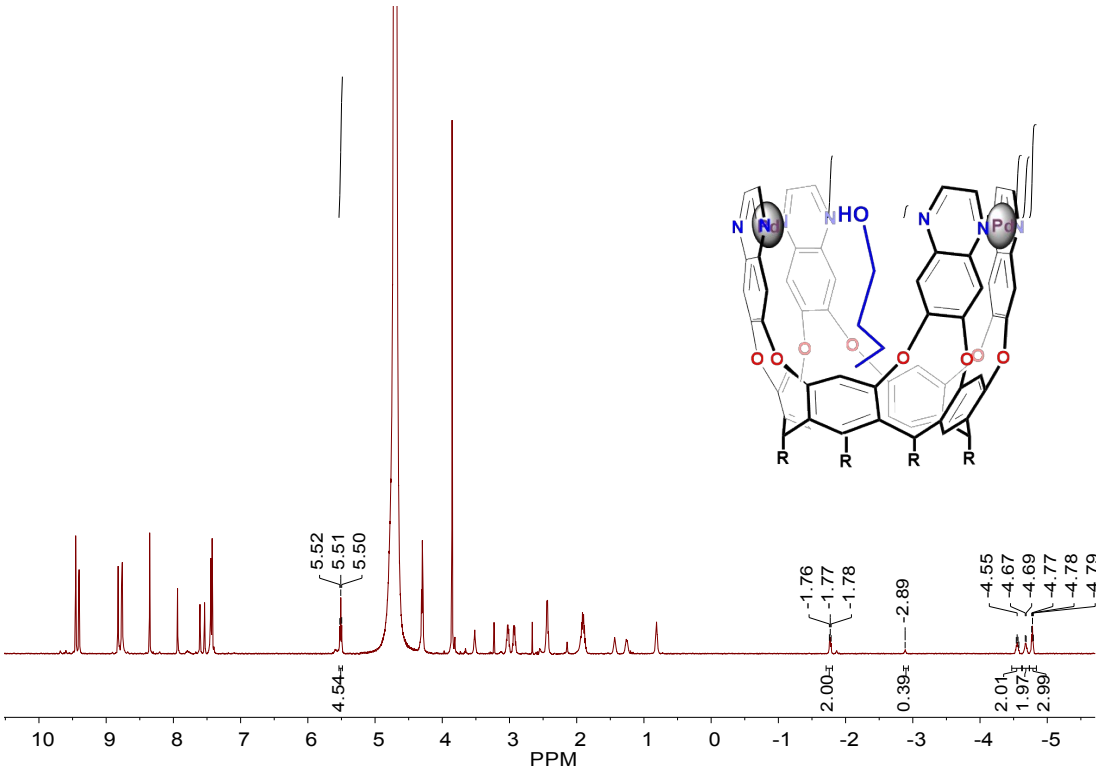


Figure S44 ^{1}H NMR spectrum of the complex formed between 1 mM of **1-2Pd** in D_2O + 2 equivalents *o*-xylene and 2 equivalents of n-butanol, analyzed at rt

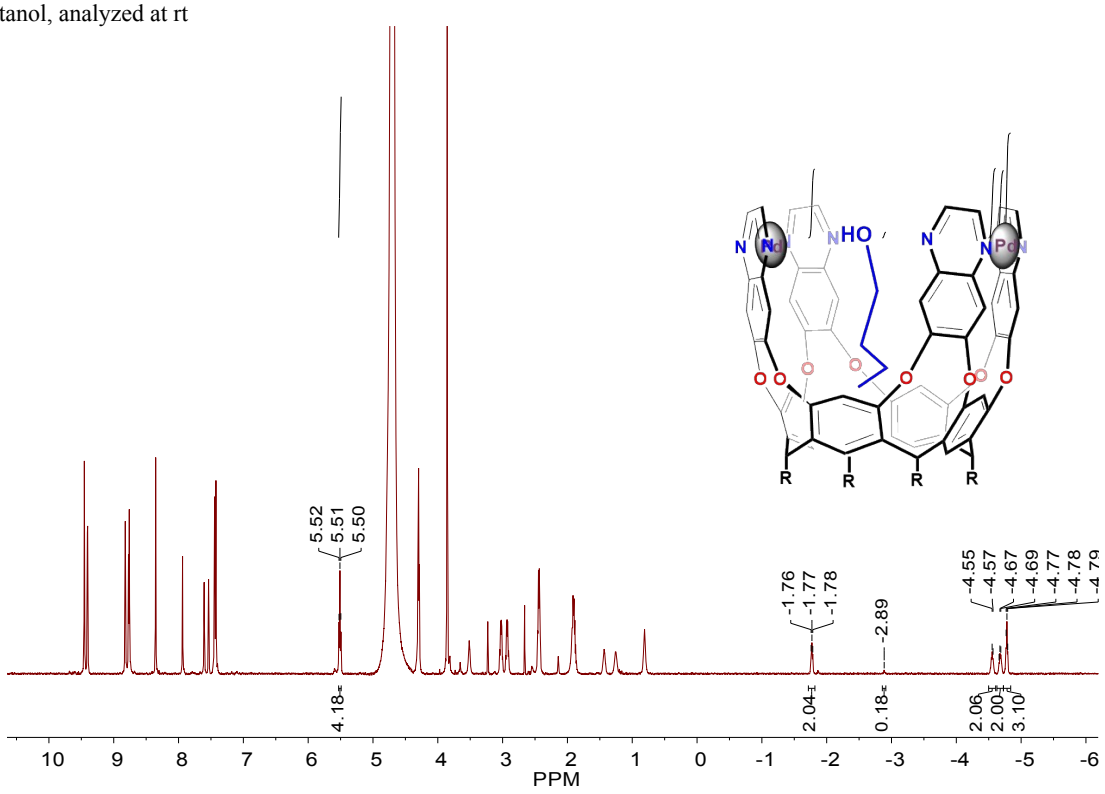


Figure S45 ^{1}H NMR spectrum of the complex formed between 1 mM of **1-2Pd** in D_2O + 2 equivalents *o*-xylene and 2 equivalents of n-butanol, analyzed at rt after 24 h

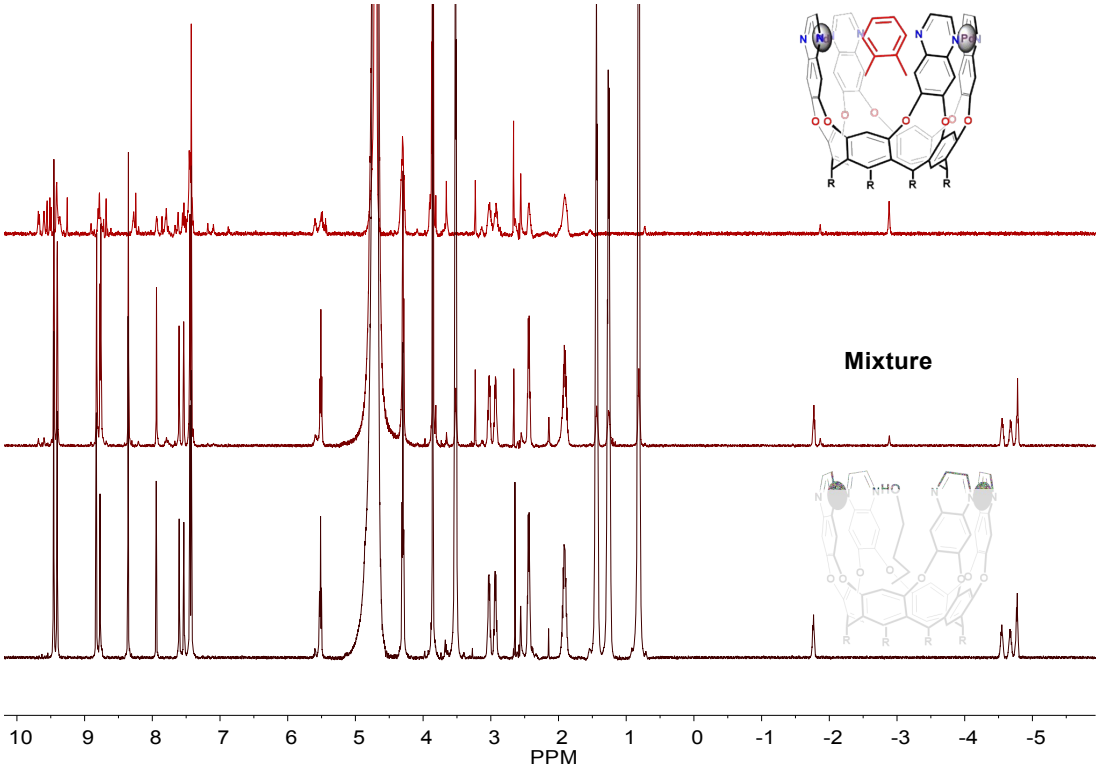


Figure S46 Comparative ^{1}H NMR spectra plot of the complex formed between 1 mM of **1-2Pd** and excess n-butanol (bottom), 1 mM of **1-2Pd** in D_2O + 2 equivalents *o*-xylene and 2 equivalents of n-butanol (middle) and 1 mM of **1-2Pd** in D_2O + 1 equivalent *o*-xylene (top) in D_2O, analyzed at rt

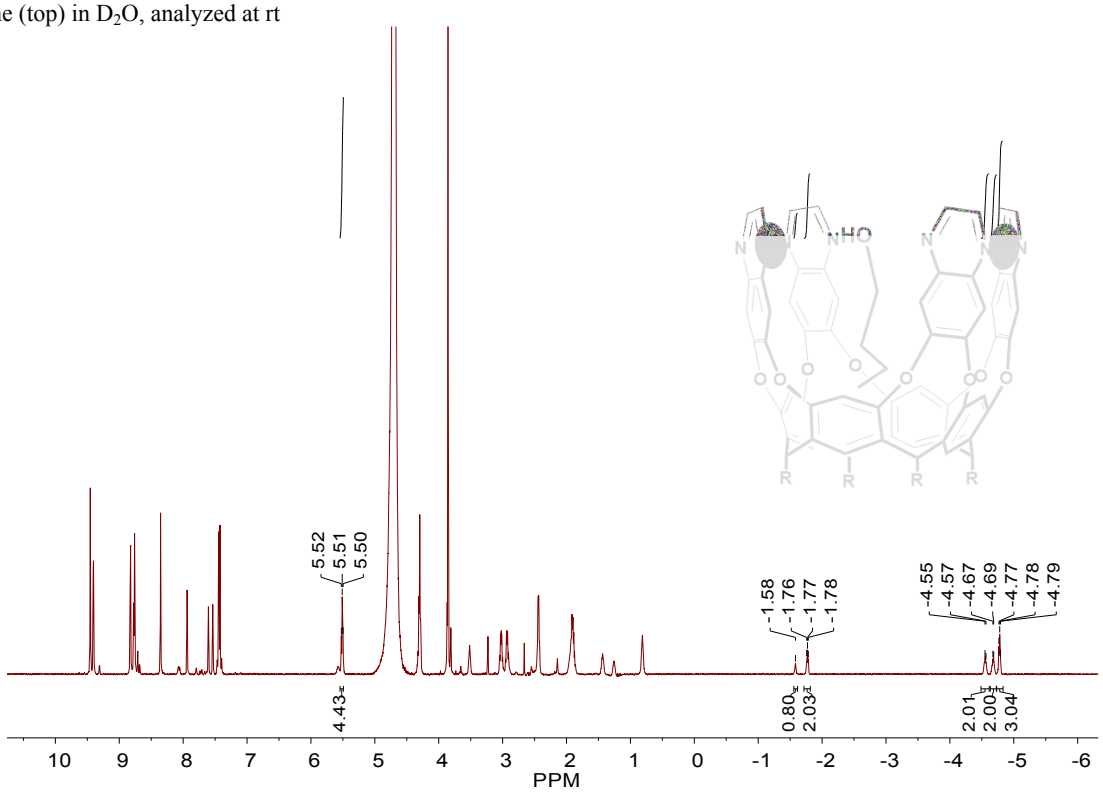


Figure S47 ^{1}H NMR spectrum of the complex formed between 1 mM of **1-2Pd** in D_2O + 2 equivalents *m*-xylene and 2 equivalents of n-butanol, analyzed at rt

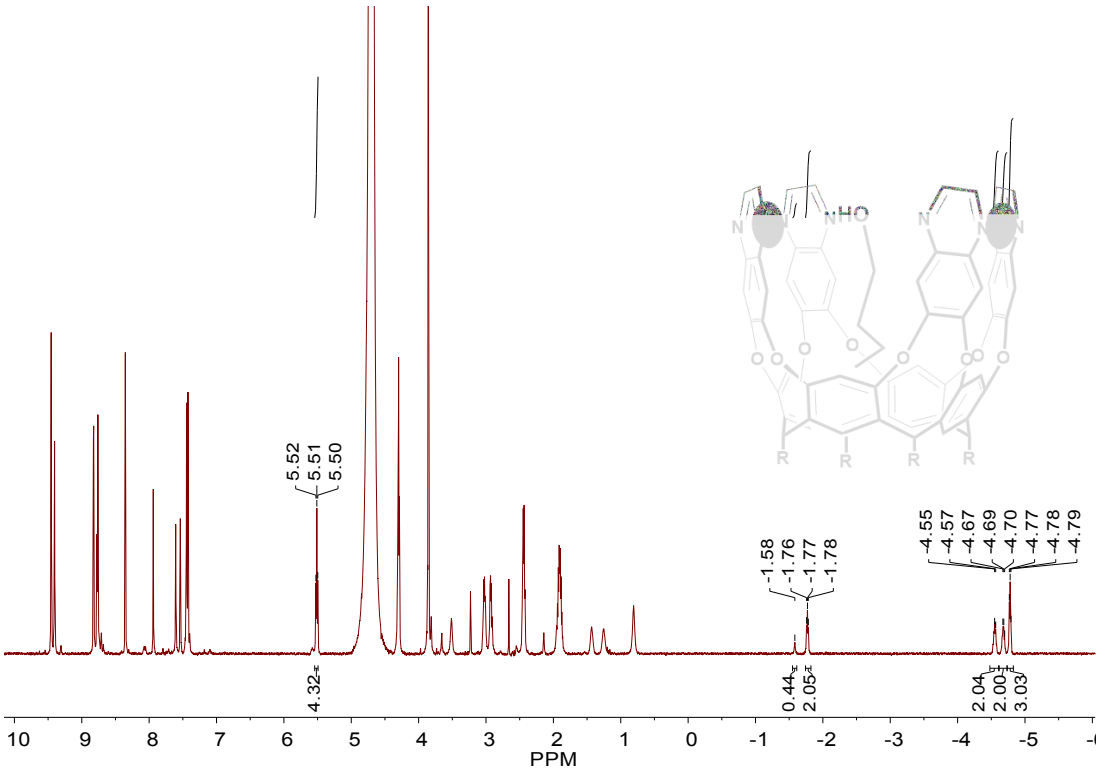


Figure S48 [1]H NMR spectrum of the complex formed between 1 mM of **1-2Pd** in D_2O + 2 equivalents *m*-xylene and 2 equivalents of n-butanol, analyzed at rt after 24 h

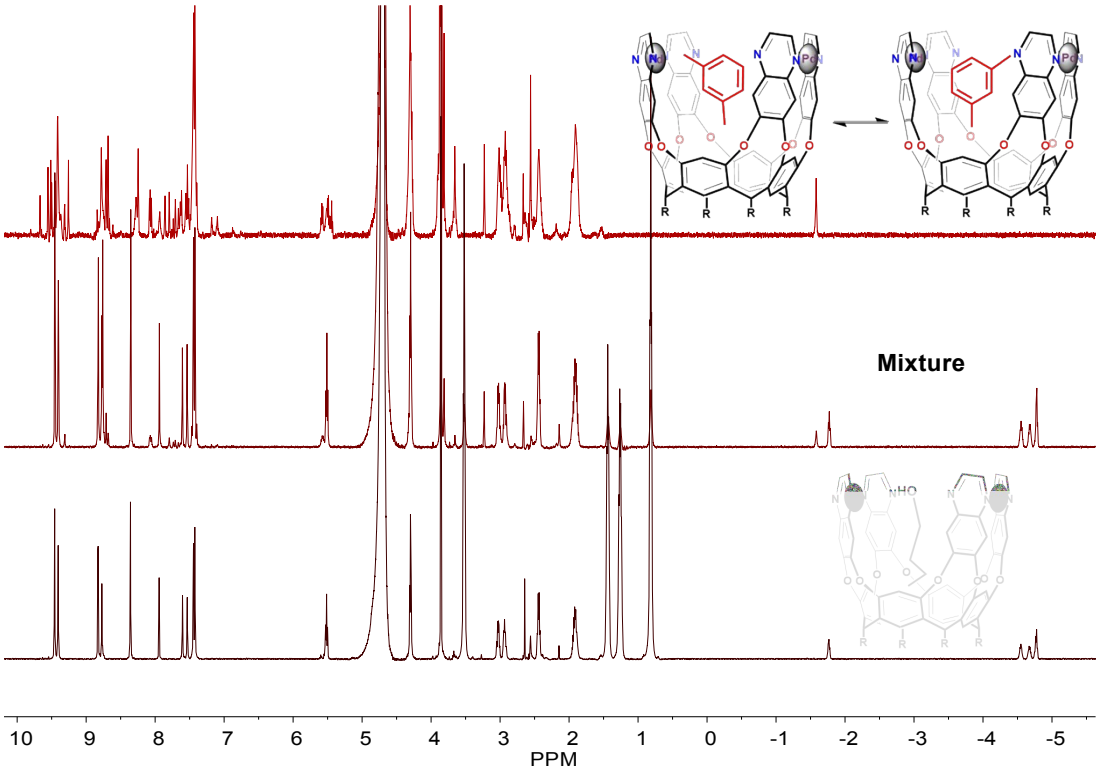


Figure S49 Comparative [1]H NMR spectra plot of the complex formed between 1 mM of **1-2Pd** and excess n-butanol (bottom), 1 mM of **1-2Pd** in D_2O + 2 equivalents *m*-xylene and 2 equivalents of n-butanol (middle) and 1 mM of **1-2Pd** in D_2O + 1 equivalents *m*-xylene (top) in D_2O, analyzed at rt

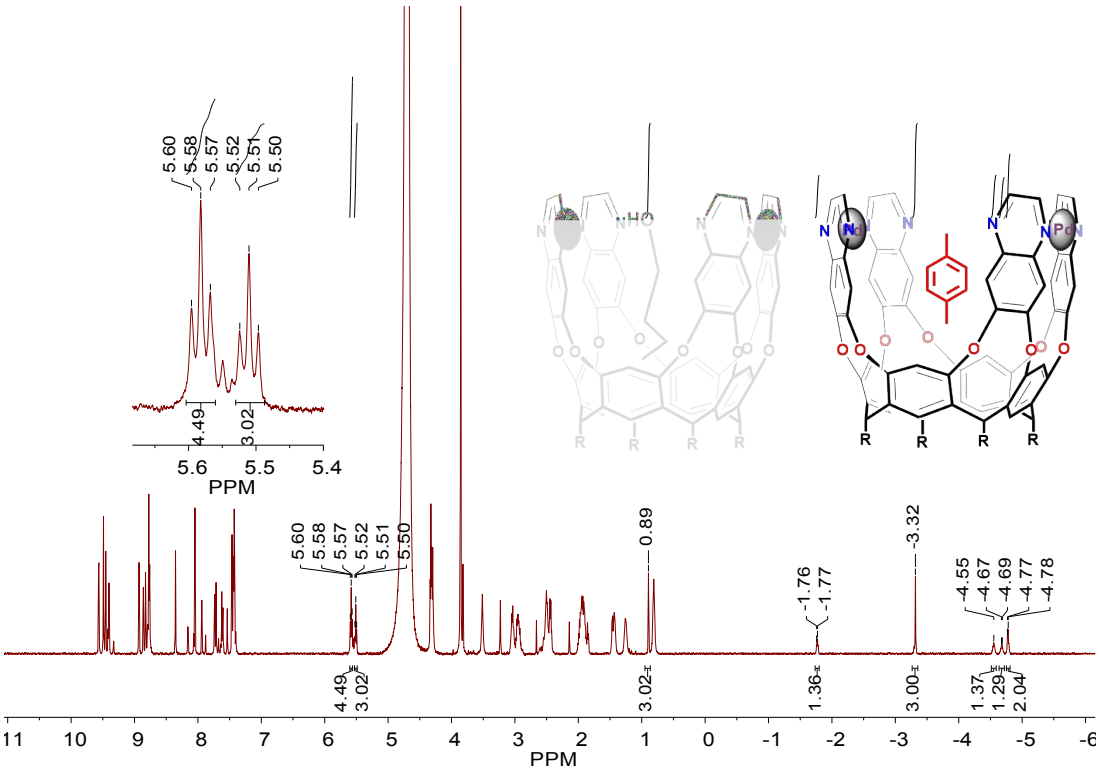


Figure S50 ^{1}H NMR spectrum of the complex formed between 1 mM of **1-2Pd** in D_2O + 2 equivalents *p*-xylene and 2 equivalents of n-butanol, analyzed at rt

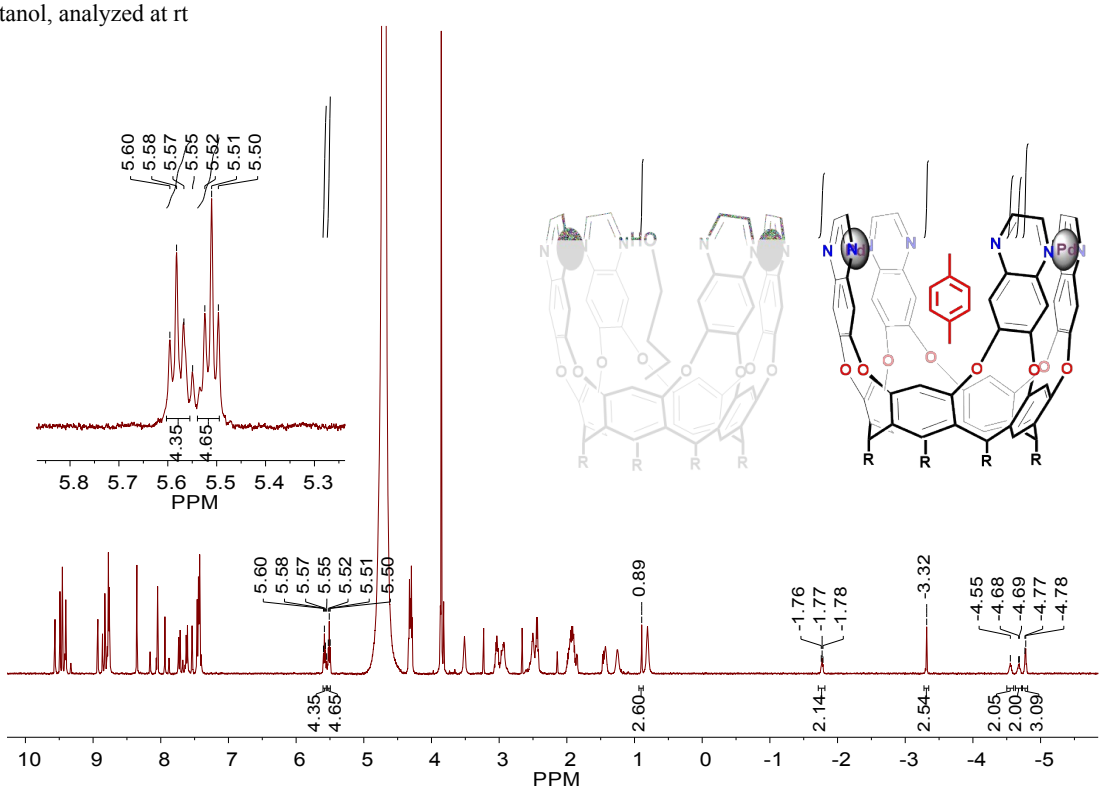


Figure S51 ^{1}H NMR spectrum of the complex formed between 1 mM of **1-2Pd** in D_2O + 2 equivalents *p*-xylene and 2 equivalents of n-butanol, analyzed at rt after 24 h

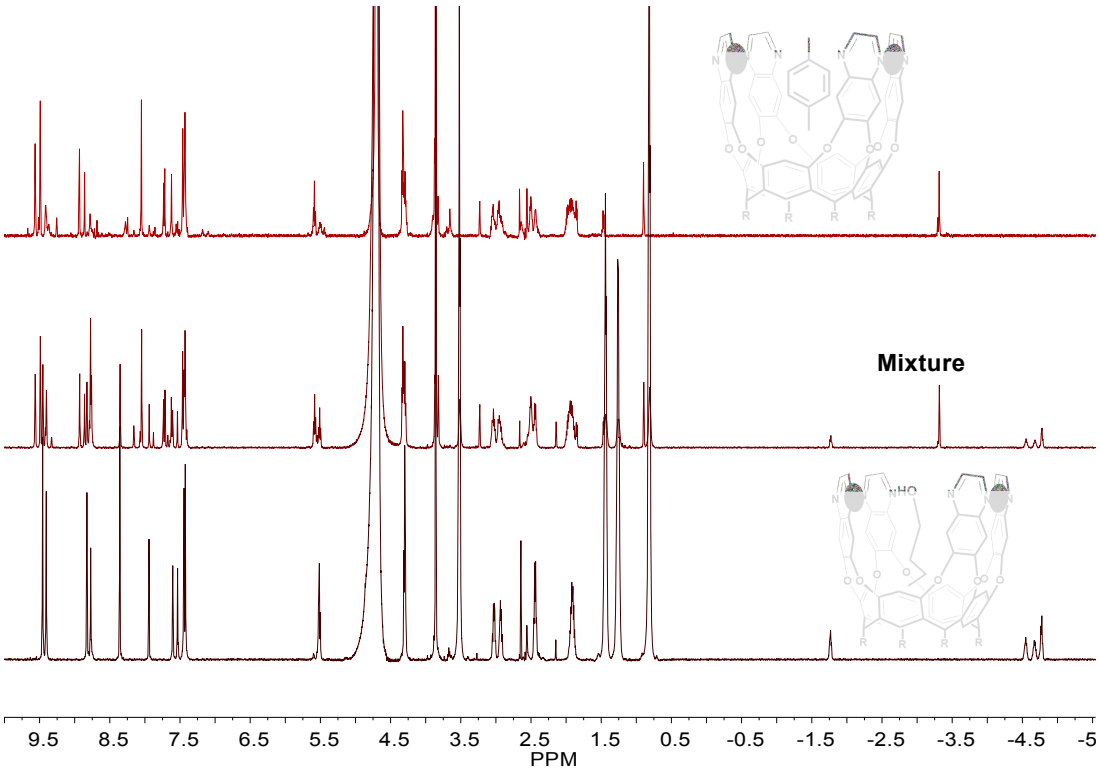


Figure S52 Comparative ^{1}H NMR spectra plot of the complex formed between 1 mM of **1-2Pd** and excess n-butanol (bottom), 1 mM of **1-2Pd** in D_2O + 2 equivalents *p*-xylene and 2 equivalents of n-butanol (middle) and 1 mM of **1-2Pd** in D_2O + 1 equivalents *p*-xylene (top) in D_2O, analyzed at rt

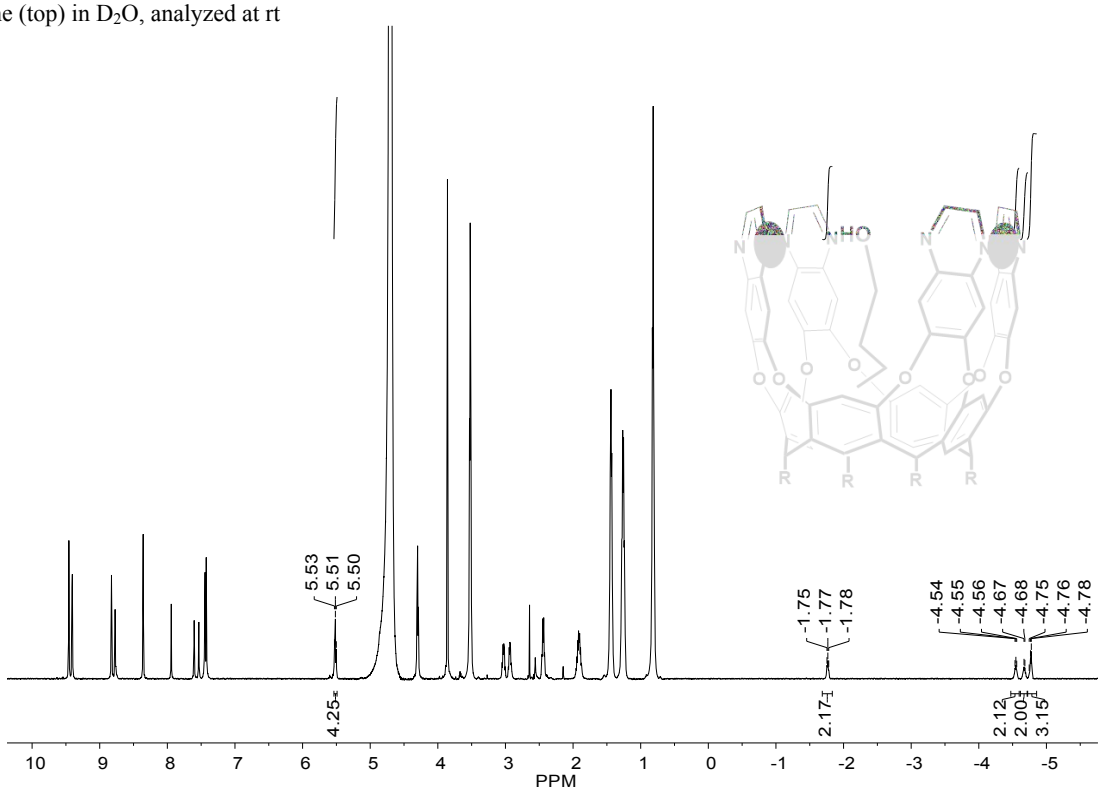


Figure S53 ^{1}H NMR spectra of the complex formed between **1-2Pd**, 1 mM + excess n-butanol in D_2O, analyzed at rt

Separation of *p*-xylene form xylene mixture and recycling of the host

A scheme was devised for the selective separation of *p*-xylene from *o*- or *m*-isomers (Figure S54) An aqueous solution of **1-2Pd** was added with a mixture of xylenes and stirred at rt for 2 h. The mixture was allowed to settle down and the layers formed were separated. The water layer was extracted with organic solvent to separate bound *p*-xylene from **1-2Pd**. The recovered, water portion containing **1-2Pd** was recycled for the next separating cycle.

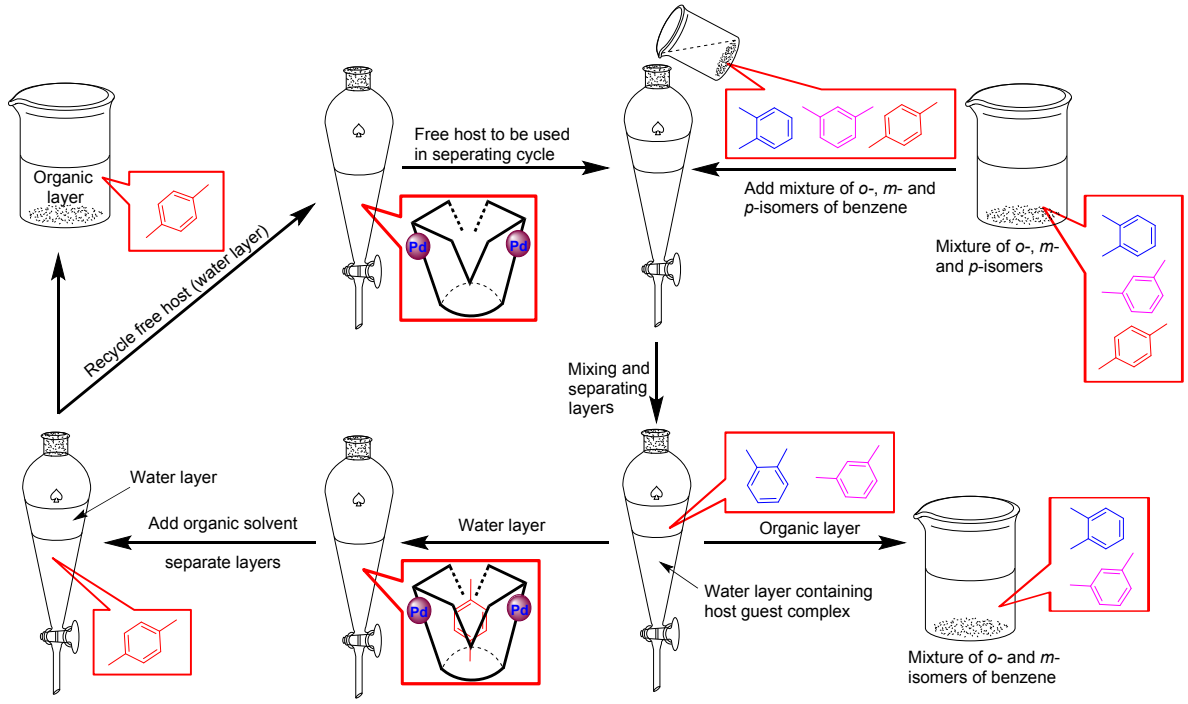


Figure S54 Liquid-liquid separation chart for *p*-xylene using **1-2Pd**

The binding and extraction of *p*-xylene using **1-2Pd** was quantified and the recyclability of this supramolecular host system was confirmed using liquid-liquid extraction method (Figure S36). 25 µL of *p*-xylene in 0.5 mL of mesitylene (mesitylene is a bad guest (Figure S56) and could not bind in **1-2Pd** in the presence of any xylene) was vigorously stirred with 5 mL, 2 mM solution of **1-2Pd** in D_2O in a 10 mL glass vial. After 2 h of stirring the mixture was allowed to stand for 4 h to separate layers. The organic layer was separated and the water layer was analyzed by ^{1}H NMR spectroscopy (ESI Figure S57). 500 uL of water portion was extracted with 1 mL of $CDCl_3$ and both aqueous and organic portions were analyzed by ^{1}H NMR spectroscopy (ESI Figure S58-S59). The $CDCl_3$ layer was added with 1 mM DMSO as internal standard to quantify the amount of *p*-xylene in the mixture and we found a quantitative amount of *p*-xylene product extracted to $CDCl_3$ (ESI Figure S59). The recovered solution of **1-2Pd** in water was used in the second cycle (ESI Figure S60-S62) and the same results were obtained.

Procedure of Cycle 1

5 mL, 2 mM **1-2Pd** solution was prepared in D_2O, 0.5 mL *p*-xylene in mesitylene (50 µL/mL) was added to water solution and vigorously stirred over 2 h. the mixture was allowed to stand for 4 h to separate layers. The water layer was separated and the mesitylene layer was kept to be used in the 2nd cycle.

1. 250 µL of water portion was diluted to 0.5 mL with D_2O to make 1 mM solution and analyzed by ^1H NMR spectroscopy (Figure S57)

2. 0.5 mL of the water portion was added with 1 mL $CDCl_3$ and shaken well with hands, the layers were settled down for 2 h. 250 µL of water portion was taken from it and diluted to 0.5 mL with D_2O to make 1 mM solution and analyzed by ^1H NMR spectroscopy (Figure S58)

3. 0.5 mL of $CDCl_3$ portion (theoretically contained 1 mM *p*-xylene) was added with 1 mM DMSO standard (5 µL, 100 mM DMSO solution in $CDCl_3$) and analyzed by ^1H NMR spectroscopy (Figure S59)

The remaining water portion (4.25 mL) was washed 5x 0.5 mL $CDCl_3$ and used in cycle 2.

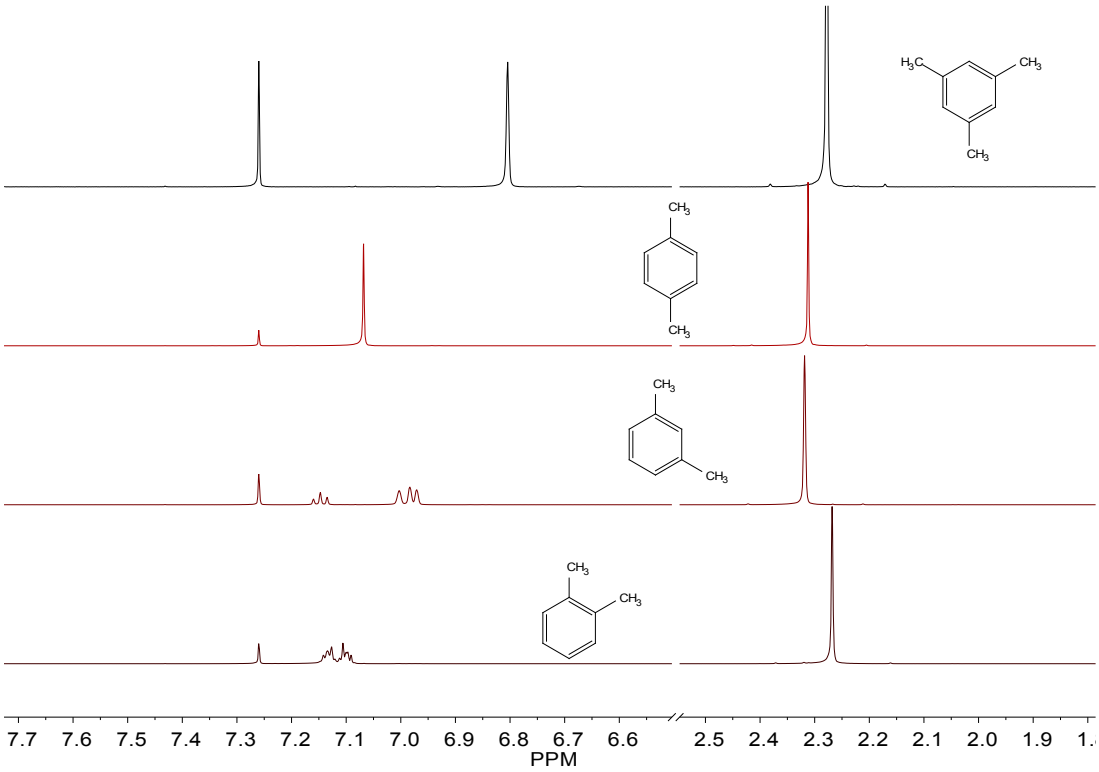


Figure S55 ^1H NMR spectra (selected part) of xylene isomers and mesitylene in $CDCl_3$, analyzed at rt

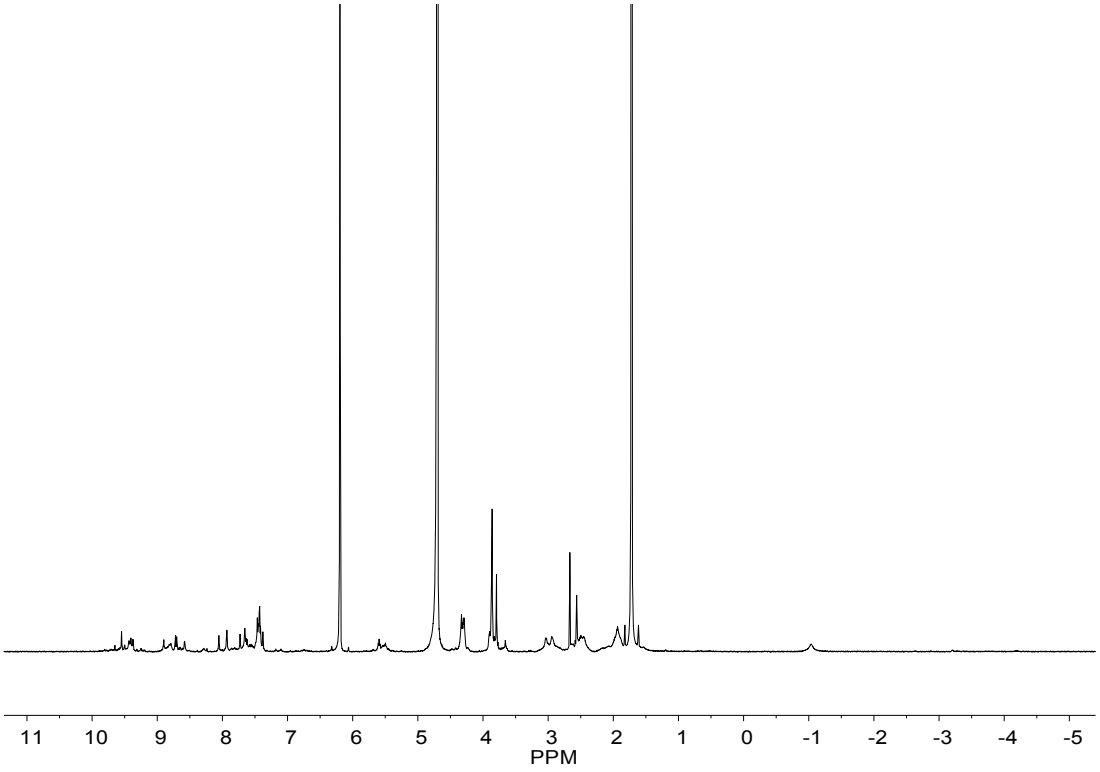


Figure S56 ^{1}H NMR spectrum of 1 mM **1-2Pd** solution in D_2O + excess of pure mesitylene, analyzed at rt

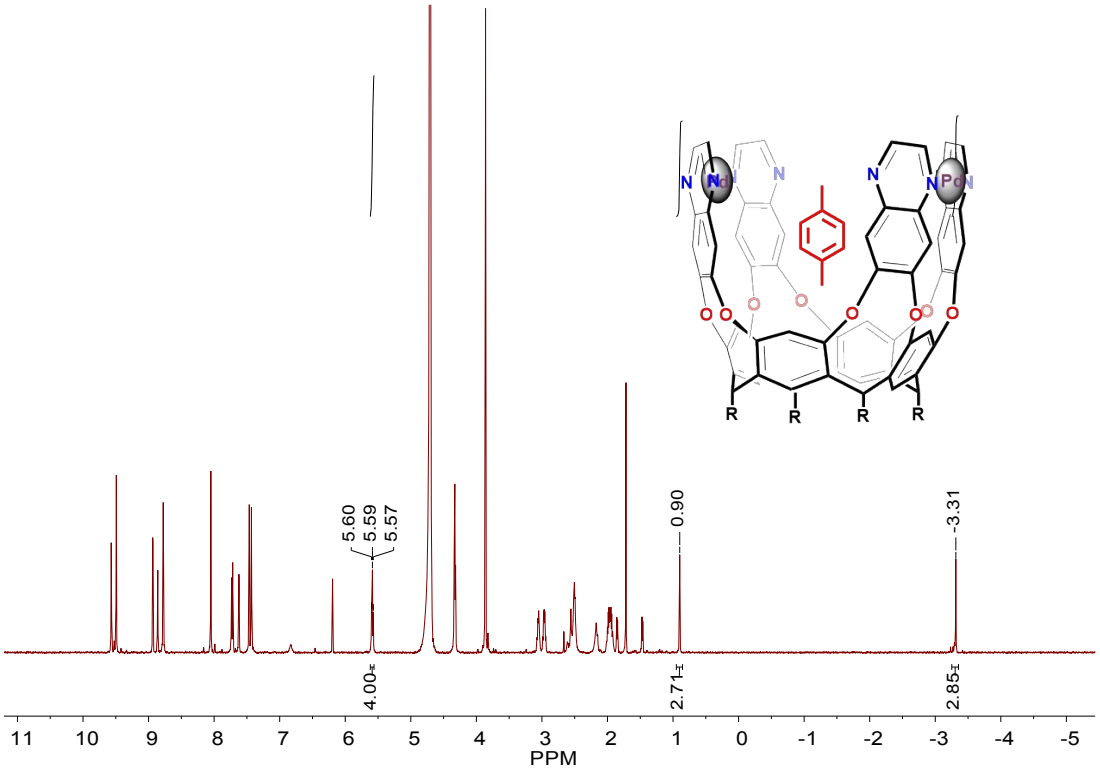


Figure S57 ^{1}H NMR spectrum of the aqueous layer (1 mM **1-2Pd** solution in D_2O containing bound *p*-xylene), analyzed at rt

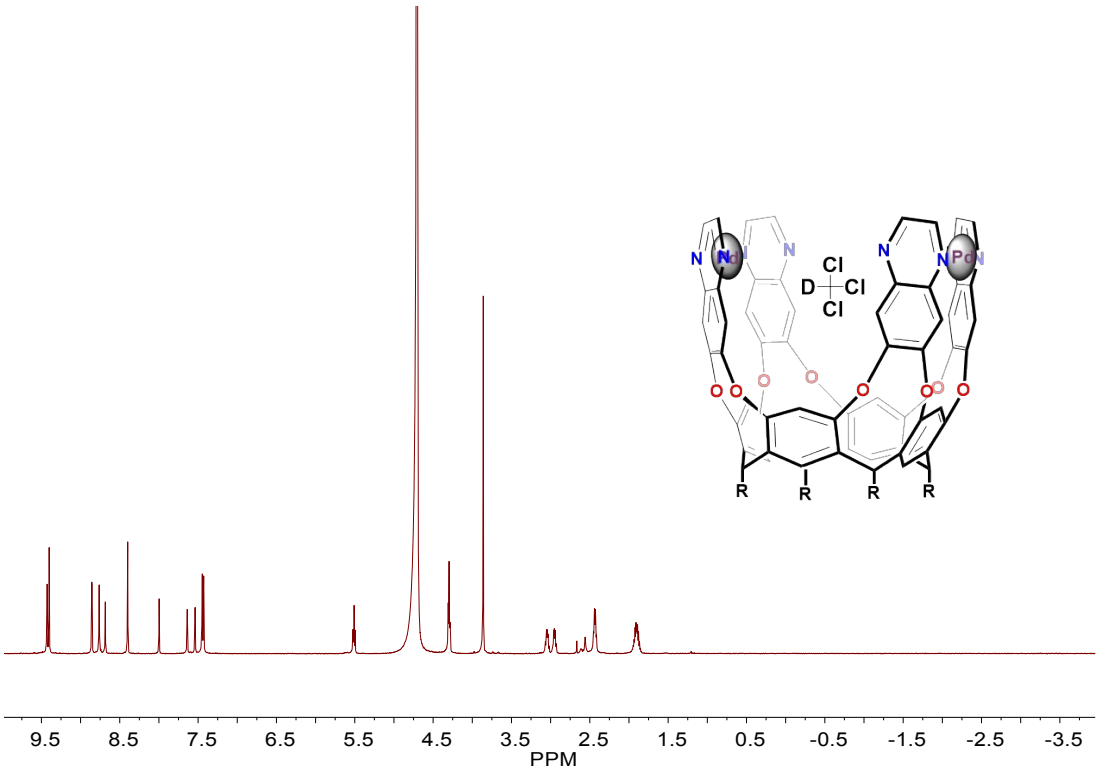


Figure S58 ^{1}H NMR spectrum of the aqueous layer extracted with $CDCl_3$ to remove the bound *p*-xylene, analyzed at rt

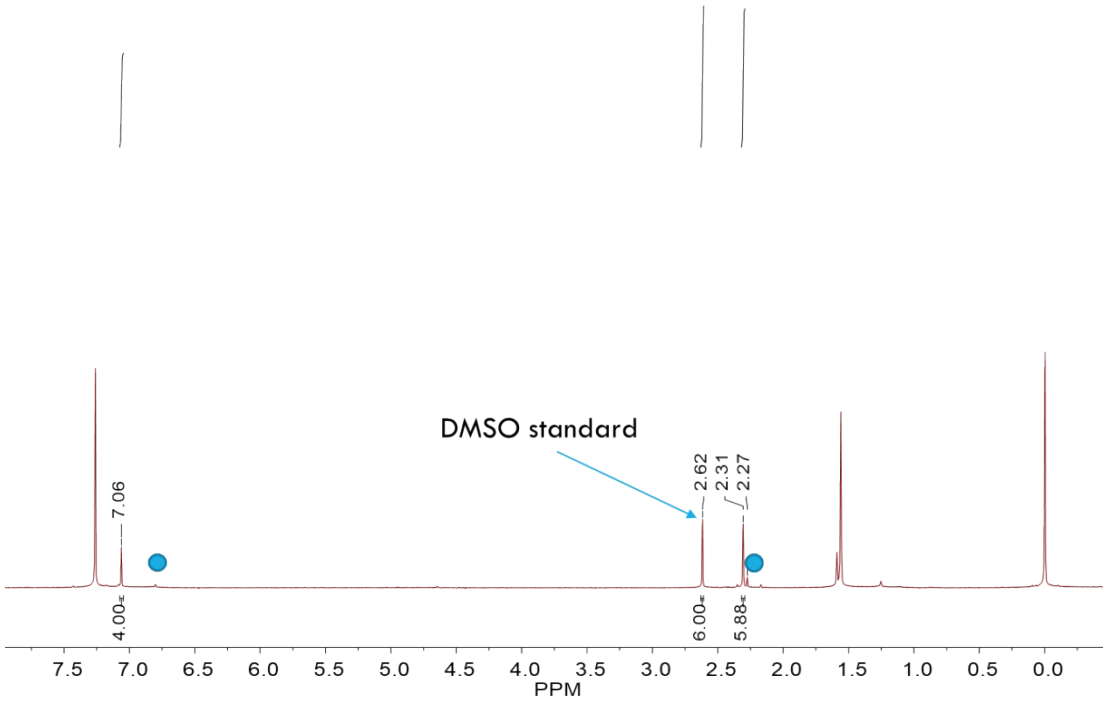


Figure S59 ^{1}H NMR spectrum *p*-xylene extracted to $CDCl_3$, 1 mM of DMSO was added as internal standard and we see the ratio of DMSO and *p*-xylene methyl protons is almost 1:1 showing 1 mM of *p*-xylene is present in the mixture, blue circles showed small amount of mesitylene (solvent) suspended in water portion extracted to $CDCl_3$

Procedure of Cycle 2

1-2Pd solution (2 mM) 4.25 mL recovered from cycle 1 was added with the mesitylene layer separated in cycle 1 and vigorously stirred for 12 h at rt. The mixture was allowed to stand for 4 h to separate layers. The water layer was separated.

1. 250 µL of water portion was diluted to 0.5 mL with D_2O to make 1 mM solution and analyzed by ^{1}H NMR spectroscopy (Figure S60)

2. 0.5 mL of the water portion was added with 1 mL $CDCl_3$ and shaken well with hands, the layers were settled down for 2 h. 250 µL of water portion was taken from it and diluted to 0.5 mL with D_2O to make 1 mM solution and analyzed by ^{1}H NMR spectroscopy (Figure S61)

3. 0.5 mL of $CDCl_3$ portion (theoretically contained 1 mM *p*-xylene) was added with 1 mM DMSO standard (5 µL, 100 mM DMSO solution in $CDCl_3$) and analyzed by ^{1}H NMR spectroscopy (Figure S62)

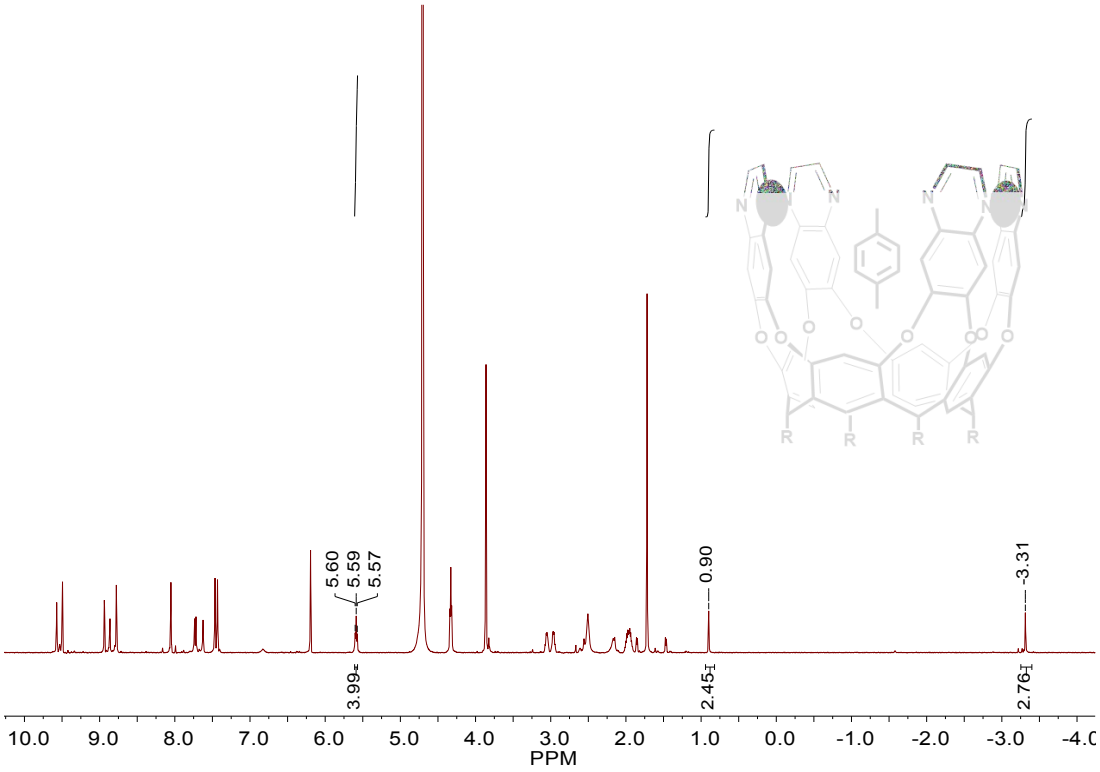


Figure S60 ^{1}H NMR spectrum of **1-2Pd** D2O solution recovered from first cycle and stirred with solution of *p*-xylene 25 µL in 0.5 mL of mesitylene for 12 h, analyzed at rt

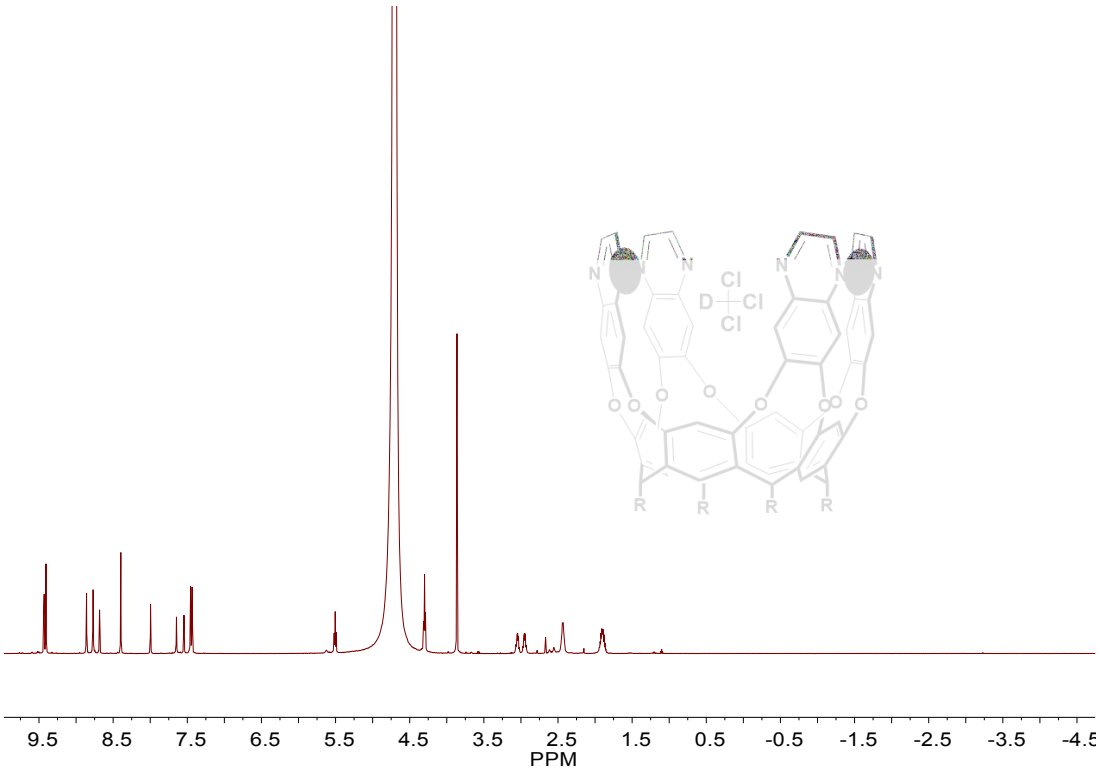


Figure S61 ^{1}H NMR spectrum of the aqueous layer of cycle 2 extracted with $CDCl_3$ to remove the bound *p*-xylene, analyzed at rt

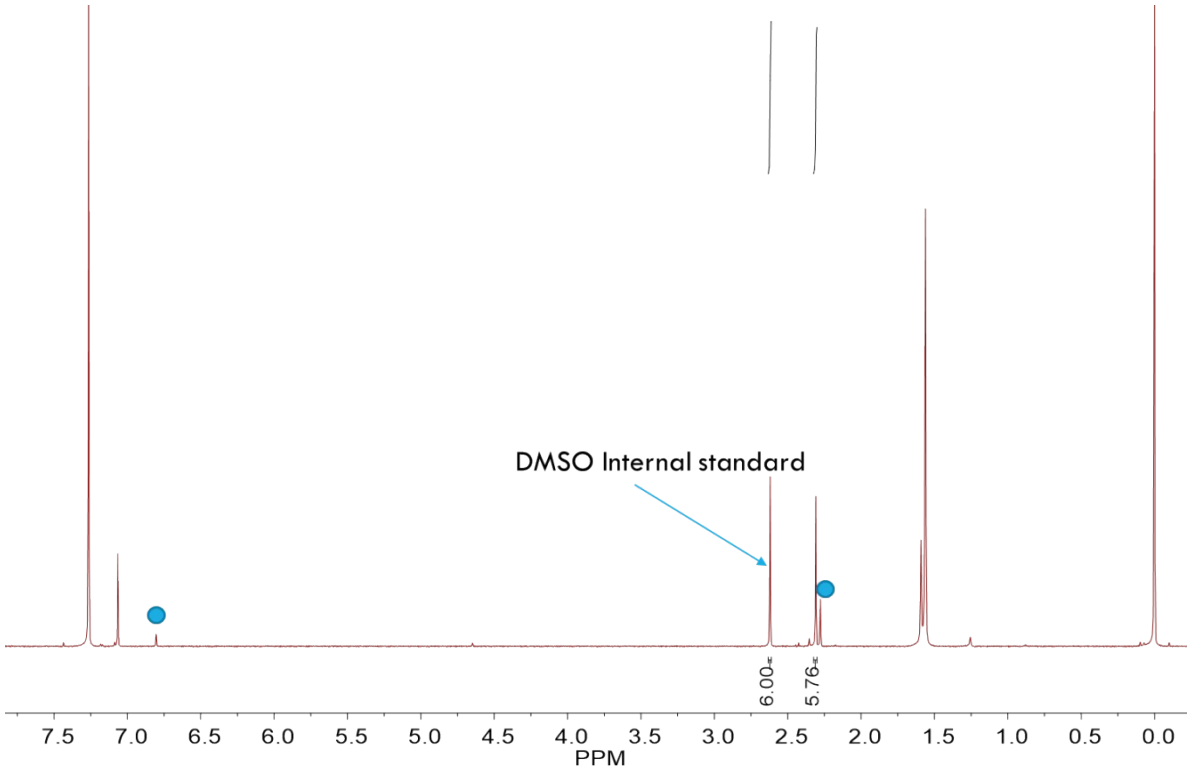


Figure S62 ^{1}H NMR spectrum of *p*-xylene extracted to $CDCl_3$, 1 mM of DMSO was added as internal standard and we see the ratio of DMSO and *p*-xylene methyl protons is almost 1:1 showing 1 mM of *p*-xylene is present in the mixture, blue circle showed small amount of mesitylene (solvent) suspended in water portion extracted to $CDCl_3$

Procedure for separation of *p*-xylene from ideal xylene mixture (mixture obtained from crude oil distillation plant) and recycling of the host

5 mL, 2 mM **1-2Pd** solution was prepared in D_2O, 0.5 mL *p*-xylene ideal mixture was added to water solution and vigorously stirred over 2 h. the mixture was allowed to stand for 12 h to separate layers. The water layer was separated and analyzed for the constituent.

1. 250 µL of water portion was diluted to 0.5 mL with D_2O to make 1 mM solution and analyzed by ^{1}H NMR spectroscopy (Figure S63)

2. 0.5 mL of the water portion was added with 1 mL $CDCl_3$ and shaken well with hands, the layers were settled down for 4 h. 250 µL of water portion was taken from it and diluted to 0.5 mL with D_2O to make 1 mM solution and analyzed by ^{1}H NMR spectroscopy (Figure S64)

3. 0.5 mL of $CDCl_3$ portion (theoretically contained 1 mM *p*-xylene) was added with 1 mM DMSO standard (5 µL, 100 mM DMSO solution in $CDCl_3$) and analyzed by ^{1}H NMR spectroscopy (Figure S65)

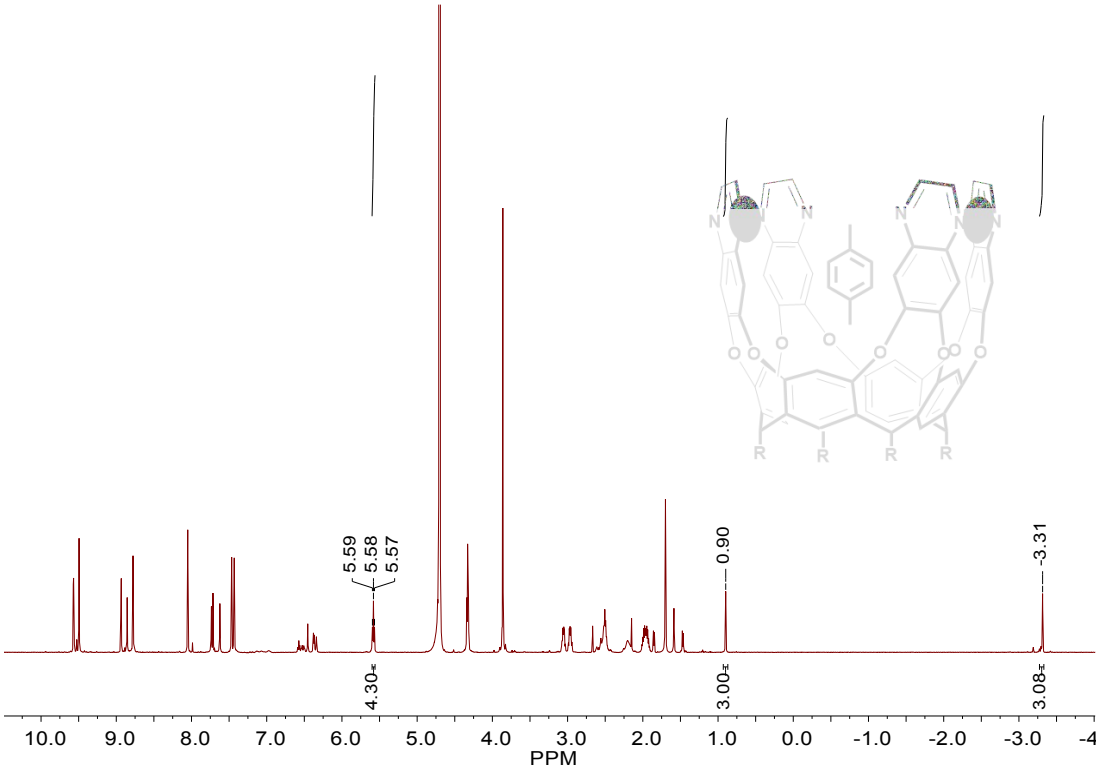


Figure S63 ^{1}H NMR spectrum of the aqueous layer (1 mM **1-2Pd** solution in D_2O containing bound *p*-xylene), analyzed at rt

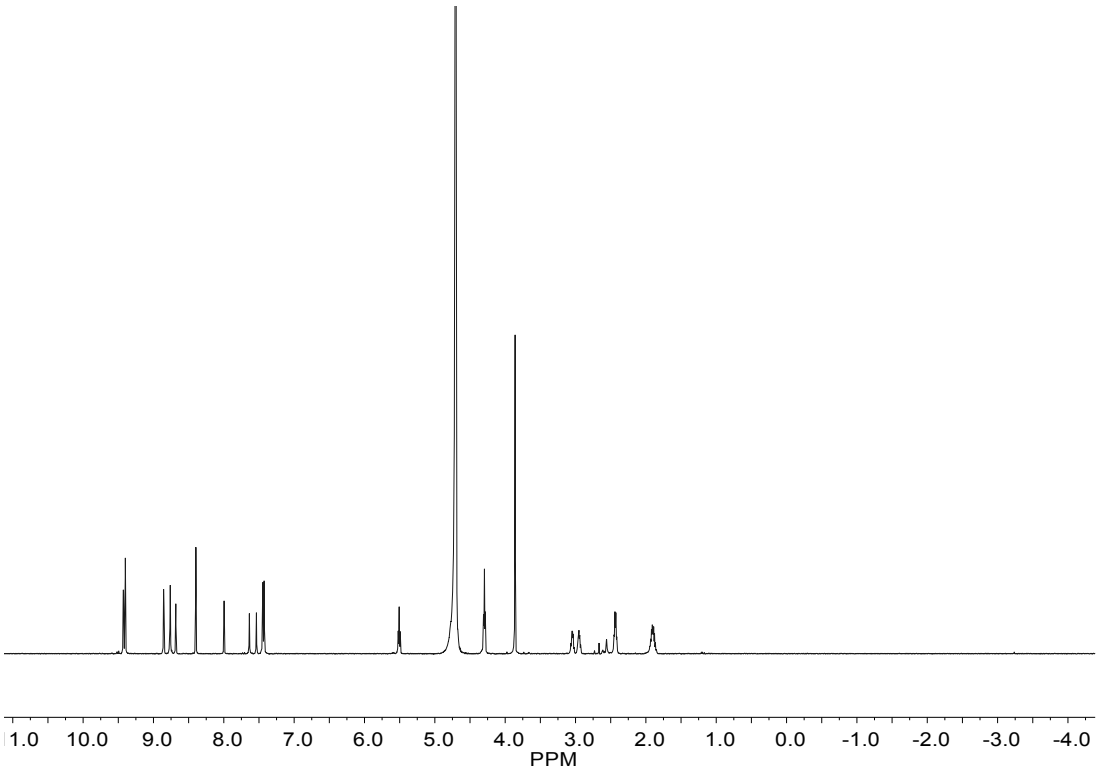


Figure S64 ^{1}H NMR spectrum of the aqueous layer of extracted with $CDCl_3$ to remove the bound *p*-xylene, analyzed at rt

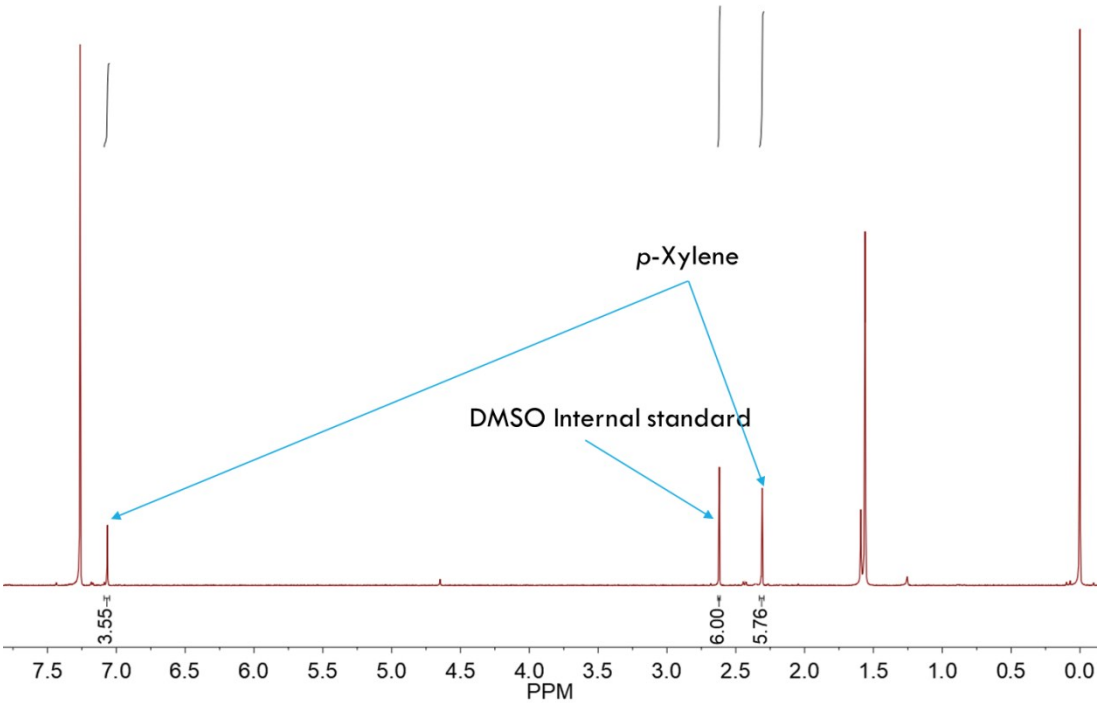


Figure S65 ^{1}H NMR spectrum of *p*-xylene extracted to $CDCl_3$, 1 mM of DMSO was added as internal standard and we see the ratio of DMSO and *p*-xylene methyl protons is almost 1:1 showing 1 mM of *p*-xylene is present in the mixture

Separation cycle using ethyl acetate as extracting organic solvent

5 mL, 2 mM **1-2Pd** solution was prepared in D_2O, 0.5 mL *p*-xylene ideal mixture was added to water solution and vigorously stirred over 2 h. the mixture was allowed to stand for 12 h to separate layers. The water layer was separated and analyzed for the constituent.

1. 250 µL of water portion was diluted to 0.5 mL with D_2O to make 1 mM solution and analyzed by ^{1}H NMR spectroscopy (Figure S66)

2. 0.5 mL of the water portion was added with 1 mL ethyl acetate and shaken well with hands, the layers were settled down for 4 h. 250 µL of water portion was taken from it and diluted to 0.5 mL with D_2O to make 1 mM solution and analyzed by ^{1}H NMR spectroscopy (Figure S67)

The recovered **1-2Pd** solution from cycle 1 was added with 0.5 mL xylene ideal mixture and vigorously stirred for 12 h at rt. The mixture was allowed to stand for 4 h to separate layers. The water layer was separated and analyzed by ^{1}H NMR spectroscopy (Figure S68).

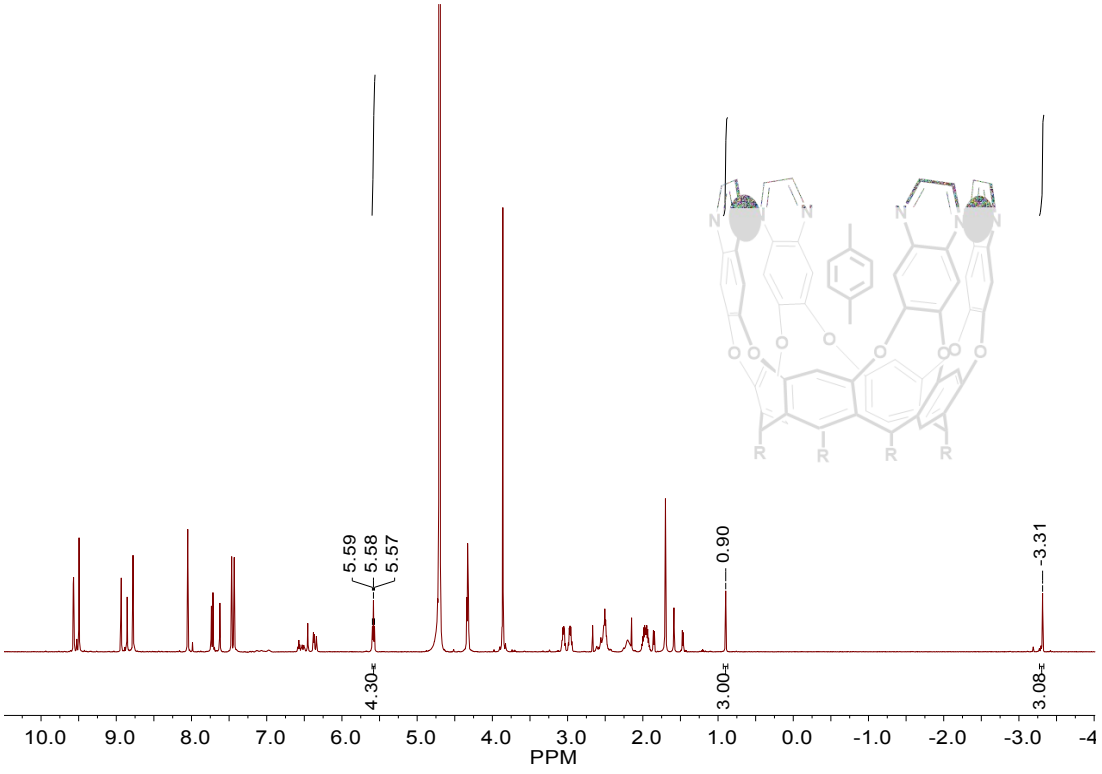


Figure S66 ^{1}H NMR spectrum of the aqueous layer (1 mM **1-2Pd** solution in D_2O containing bound *p*-xylene), analyzed at rt

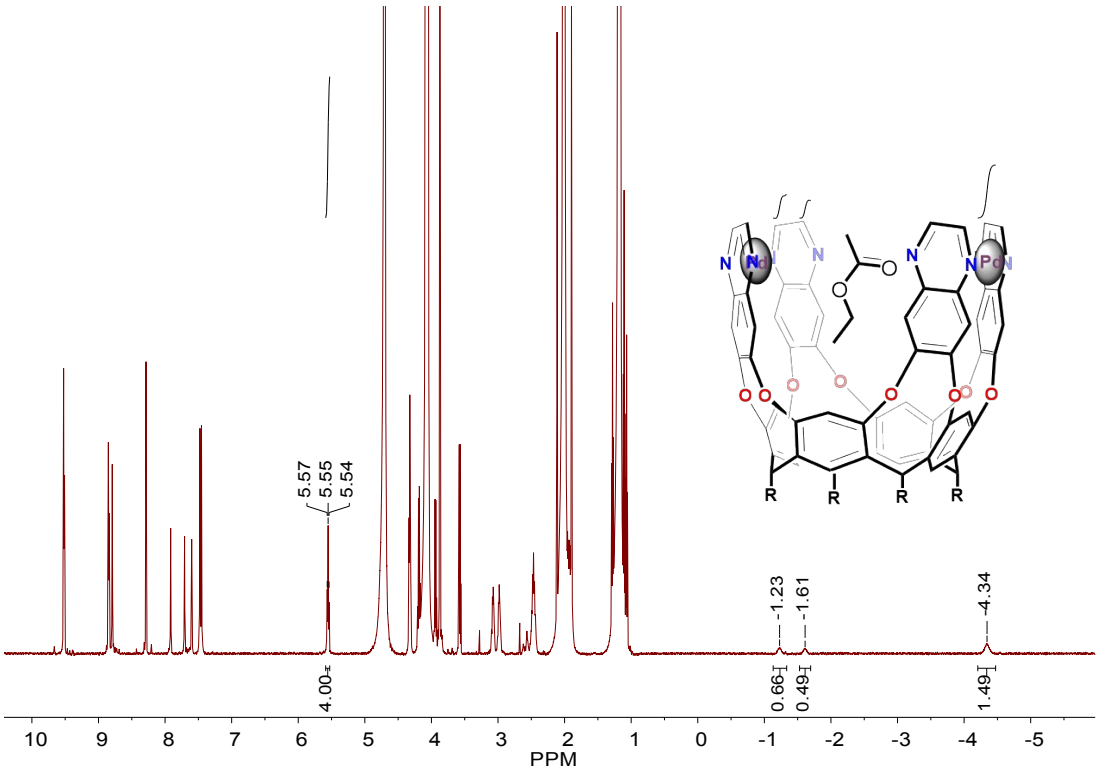


Figure S67 [1]H NMR spectrum of the aqueous layer extracted with ethyl acetate (mixture 3 extracted with ethyl acetate instead chloroform) to remove the bound *p*-xylene, analyzed at rt

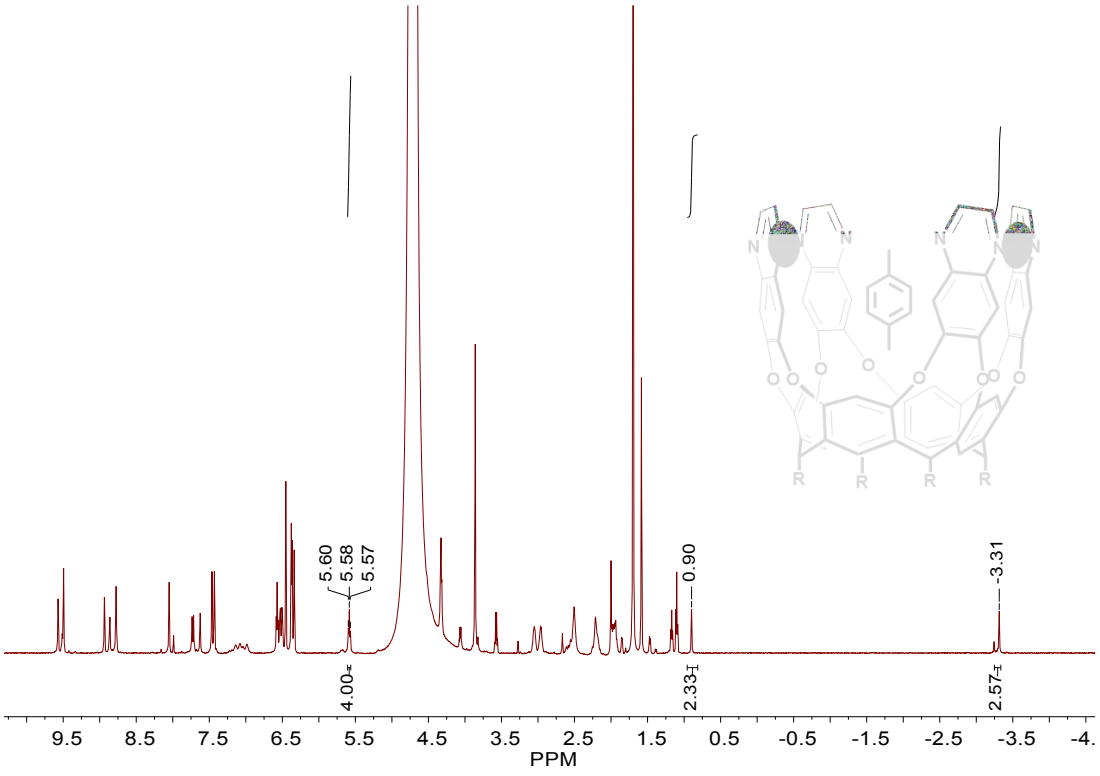


Figure S68 [1]H NMR spectrum of the aqueous layer extracted with ethyl acetate and added with xylene ideal mixture and stirred vigorously for 6 h, analyzed at rt

Separation cycle using dichloromethane as extracting organic solvent

5 mL, 2 mM **1-2Pd** solution was prepared in D_2O, 0.5 mL *p*-xylene ideal mixture was added to water solution and vigorously stirred over 2 h. the mixture was allowed to stand for 12 h to separate layers. The water layer was separated and analyzed for the constituent.

1. The water portion was analyzed by ^{1}H NMR spectroscopy (Figure S69)
2. The water portion was extracted with CH_2Cl_2, and analyzed by ^{1}H NMR spectroscopy (Figure S70).
3. The water portion was heated at 50 °C for 4 h and analyzed by ^{1}H NMR spectroscopy (Figure S71).

The recovered **1-2Pd** solution from cycle step 3 was added with 0.5 mL xylene ideal mixture and vigorously stirred for 2 h at rt. The mixture was allowed to stand for 4 h to separate layers. The water layer was separated and analyzed by ^{1}H NMR spectroscopy (Figure S72).

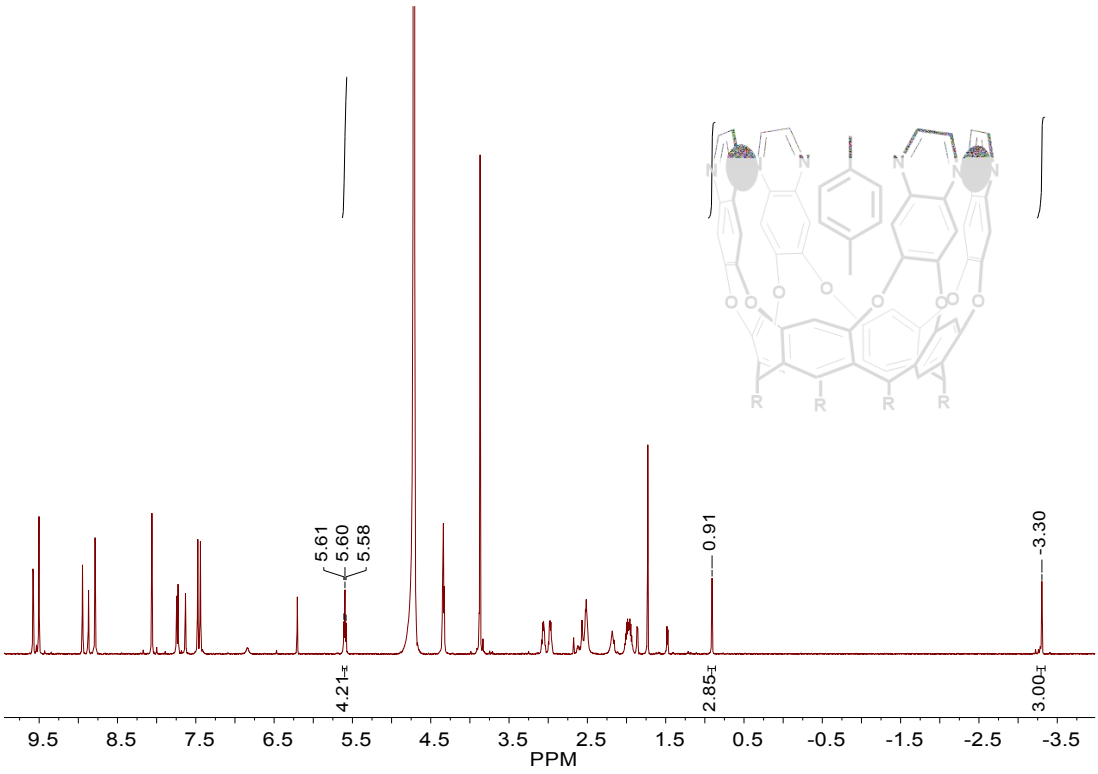


Figure S69 ^{1}H NMR spectrum of the aqueous layer (1 mM **1-2Pd** solution in D_2O containing bound *p*-xylene), analyzed at rt

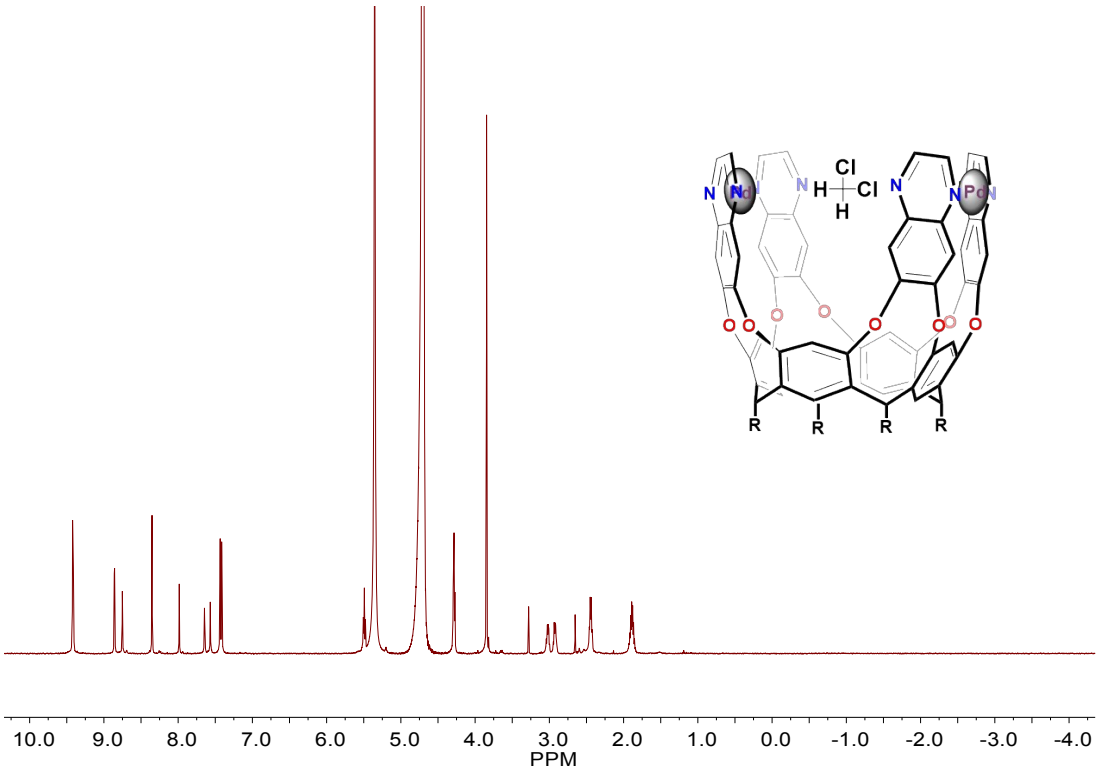


Figure S70 ^{1}H NMR spectrum of the aqueous layer extracted with dichloromethane (mixture extracted with dichloromethane instead chloroform) to remove the bound *p*-xylene, analyzed at rt

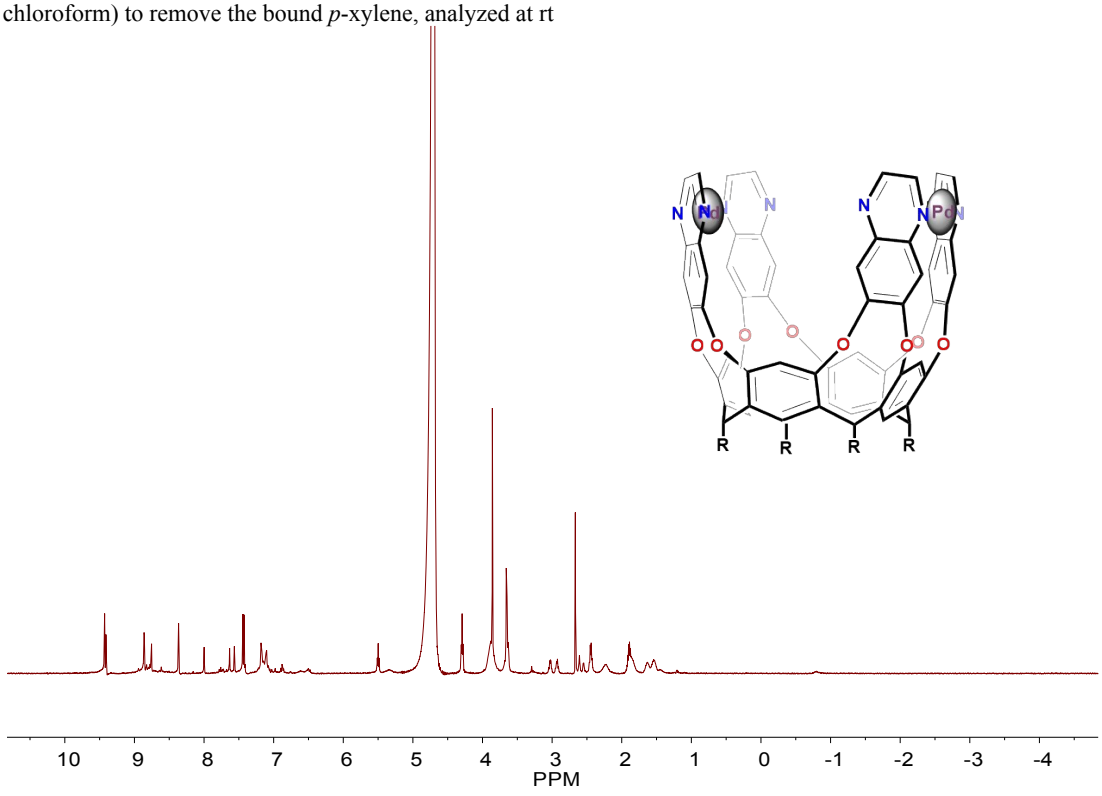


Figure S71 ^{1}H NMR spectrum of the aqueous layer extracted with dichloromethane and heated at 50 °C for 4 h to evaporate dichloromethane from the cavity and get free host, analyzed at rt

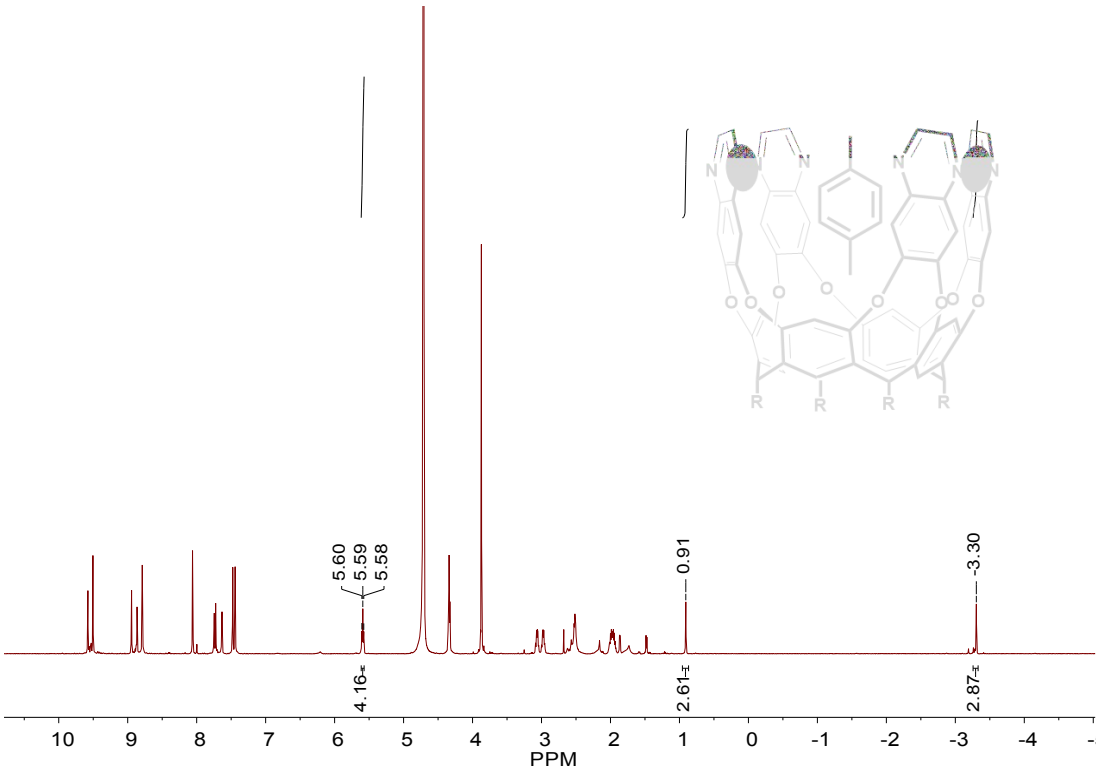


Figure S72 ^{1}H NMR spectrum of the aqueous layer extracted with dichloromethane and added with xylene ideal mixture and stirred vigorously for 2 h, analyzed at rt

Separation of *p*-nitro toluene from 1:1:1 mixture of *o*-, *m*- and *p*-nitro toluene isomers and recycling of the host

5 mL, 1 mM **1-2Pd** solution was prepared in D_2O, 0.5 g 1:1:1 mixture of *o*-, *m*- and *p*-nitro toluene was added to water solution and vigorously stirred over 2 h. the mixture was filtered to remove the solid isomers mixture

1. 0.5 mL water portion was taken in NMR tube and analyzed by ^{1}H NMR spectroscopy (Figure S75)
2. 1 mL of the water portion was added with 1 mL $CDCl_3$ and shaken well with hands, the layers were settled down. Both water and organic layers were analyzed by ^{1}H NMR spectroscopy (Figure S76-S77)
3. The $CDCl_3$ portion 0.5 mL was added with DMSO (1 mM) as internal standard to quantify the amount of *p*-nitro toluene extracted(Figure S77).

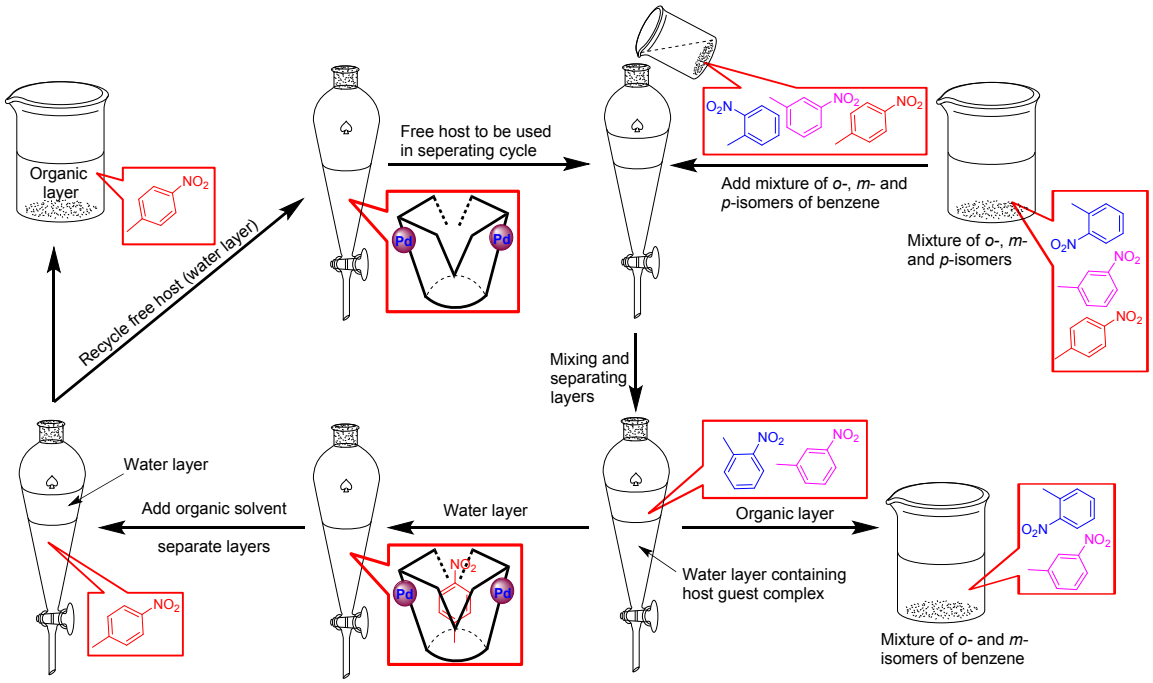


Figure S73 Liquid-liquid separation chart for *p*-nitro toluene of toluene using **1-2Pd**

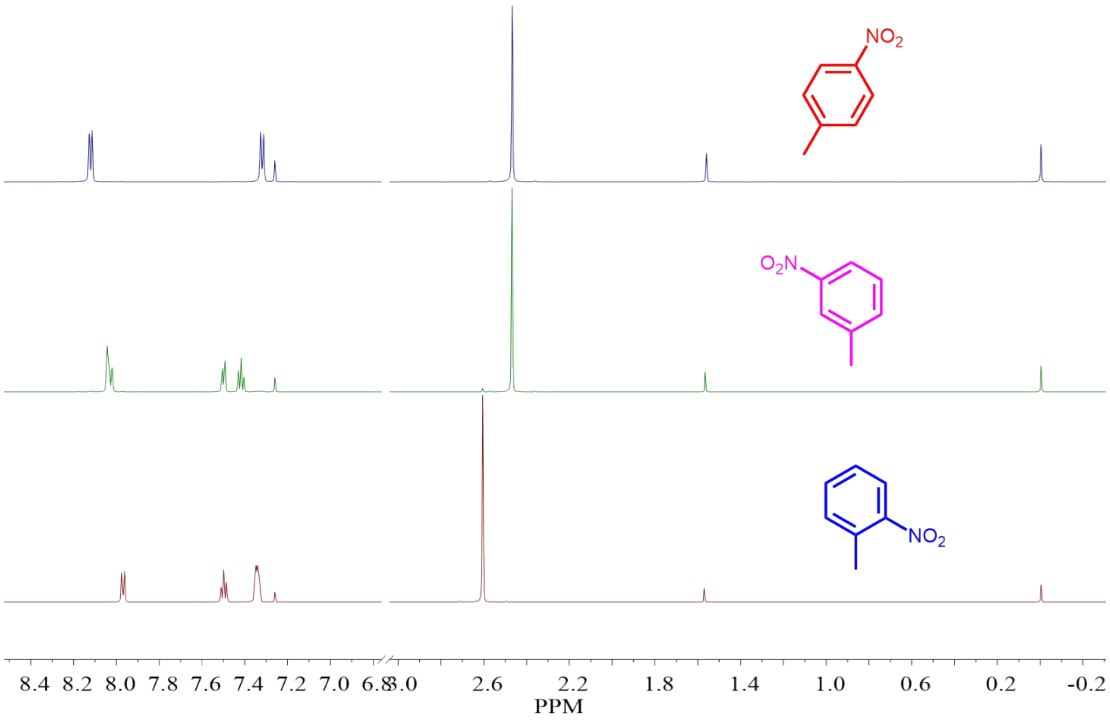


Figure S74 ^{1}H NMR spectra (selected part) of nitrotoluene isomers in $CDCl_3$, analyzed at rt

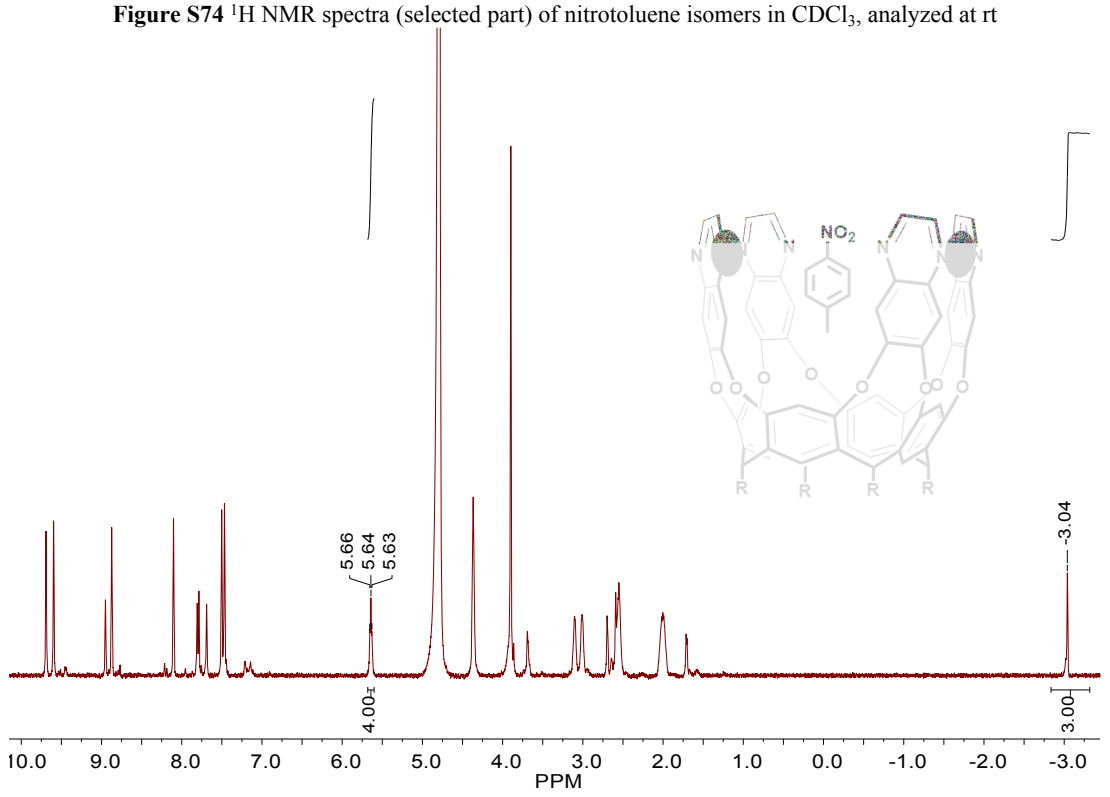


Figure S75 ^{1}H NMR spectrum of the aqueous layer (1 mM **1-2Pd** solution in D_2O containing *p*-nitro toluene), analyzed at rt

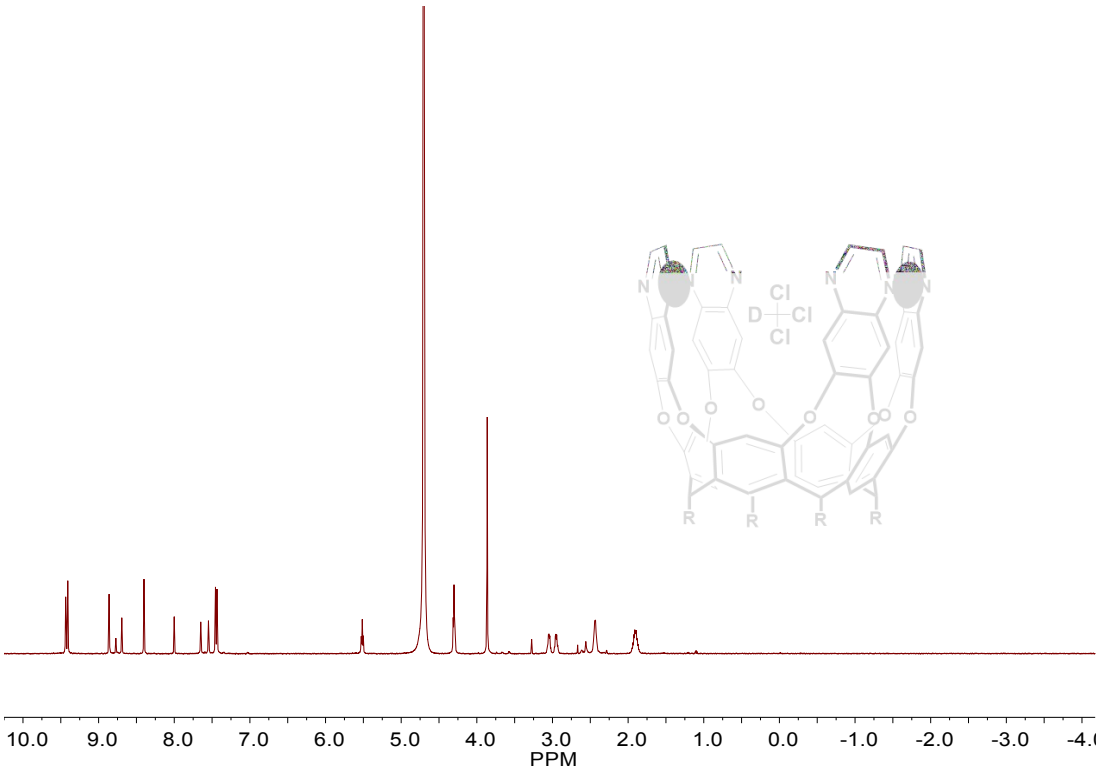


Figure S76 ^{1}H NMR spectrum of the aqueous layer extracted with $CDCl_3$ to remove the bound *p*-substituted toluene, analyzed at rt

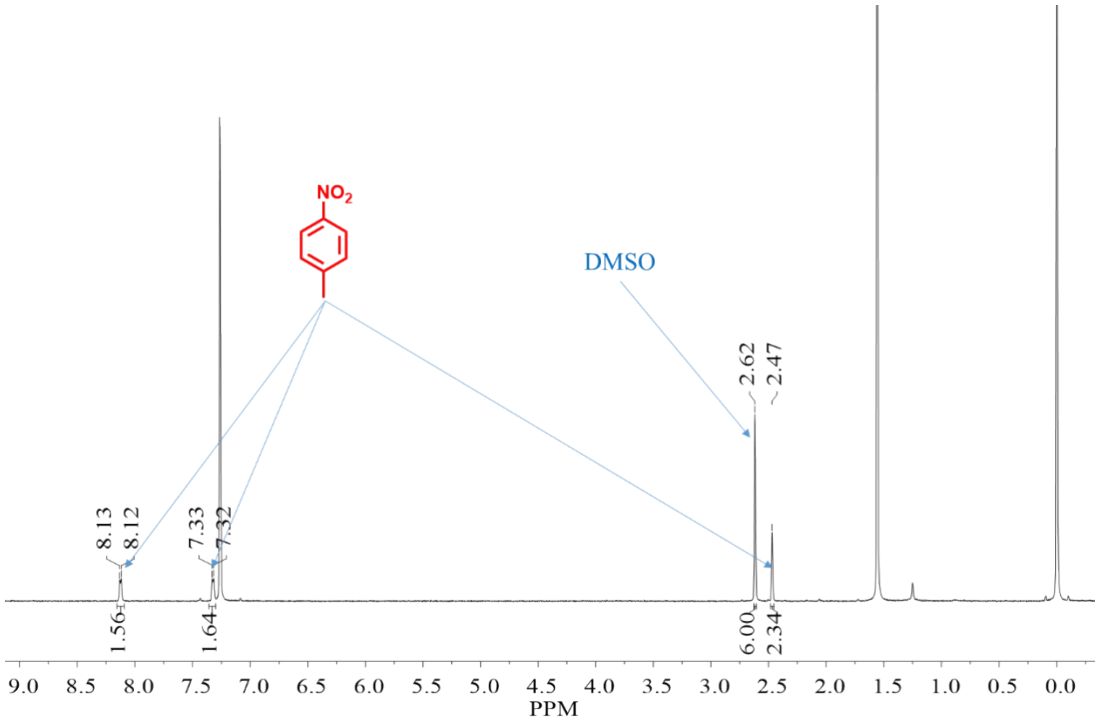


Figure S77 ^{1}H NMR spectrum of *p*-nitro toluene extracted to $CDCl_3$, 1 mM of DMSO was added as internal standard and we see the ratio of DMSO and *p*-nitro toluene methyl protons is almost 1:1 showing 1 mM of *p*-nitro toluene is present in the mixture

References

1. Faiz-Ur Rahman; Yong-sheng Li; Ioannis D. Petsalakis; Giannoula Theodorakopoulos; Jr., J. R.; Yu, Y., *Proc Natl Acad Sci USA* **2019**.
2. Zhao, Y.; Truhlar, D. G., *Theor. Chem. Acc.* **2007,** *120* (1-3), 215-241.
3. Zhao, Y.; Truhlar, D. G., *Acc. Chem. Res.* **2008,** *41* (2), 157-67.
4. T. H. Dunning Jr. and P. J. Hay, in Modern Theoretical Chemistry, Ed. H. F. Schaefer III, Vol. 3 (Plenum, New York, 1977) 1-28. .
5. Wadt, W. R.; Hay, P. J., *J. Chem. Phys.* **1985,** *82* (1), 284-298.
6. Gaussian 16, Revision B.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.4. .
7. Wolinski, K.; Hinton, J. F.; Pulay, P., *J. Am. Chem. Soc.* **1990,** *112* (23), 8251-8260.