

# Supplementary Information

## Exploiting the Hydrophobicity of Calixarene Macrocycles for Catalysis Under "On-Water" Conditions

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**General Methods.** Flash chromatography was performed on Merck silica gel (60, 40-63  $\mu\text{m}$ ). All chemicals were reagent grade and were used without further purification. Anhydrous solvents were purchased from Aldrich. Reaction temperatures were measured externally; reactions were monitored by TLC on Merck silica gel plates (0.25 mm) and visualized by UV light and spraying with  $\text{H}_2\text{SO}_4$ - $\text{Ce}(\text{SO}_4)_2$  or phosphomolybdic acid. NMR spectra were recorded on Bruker Avance-600 spectrometer [600.13 MHz ( $^1\text{H}$ ) and 150.03 MHz ( $^{13}\text{C}$ )], Bruker Avance-400 spectrometer [400 ( $^1\text{H}$ ) and 100.57 MHz ( $^{13}\text{C}$ )], Bruker Avance-300 spectrometer [300 ( $^1\text{H}$ ) and 75.48 MHz ( $^{13}\text{C}$ )], or Bruker Avance-250 spectrometer [250 ( $^1\text{H}$ ) and 62.80 MHz ( $^{13}\text{C}$ )]; chemical shifts are reported relative to the residual solvent peak ( $\text{CHCl}_3$ :  $\delta$  7.26,  $\text{CDCl}_3$ :  $\delta$  77.23). Derivatives: **10**<sup>1</sup>, **12**<sup>2</sup>, **11**<sup>3</sup>, **7a**<sup>4</sup>, **7d**<sup>5</sup>, and **7c**<sup>6</sup> were synthesized according to literature procedures. Melting points were measured with a Stuart melting point apparatus (SMP3).

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<sup>1</sup> A. M. A. Wageningen, E. Snip, W. Verboom, D. N. Reinhoudt, H. Boerrigter, *Liebigs Ann./Recueil*, 1997, 2235.

<sup>2</sup> M. De Rosa, A. Soriente, G. Concilio, C. Talotta, C. Gaeta, P. Neri, *J. Org. Chem*, 2015, **80**, 7295.

<sup>3</sup> I-T. Ho, J. H. Chu, W. S. Chung, *Eur. J. Org. Chem.*, 2011, **8**, 1472.

<sup>4</sup> A. Sagar, S. Vidyacharan, D. S. Sharada, *RSC. Adv.*, 2014, **4**, 37047.

<sup>5</sup> W. J. Quan, D. Q. Man, W. Liang, X. Kai, W. Hao, L. Ren-Rong, G. Jian-Rong, J. Yi-Xia, *Org. Lett.*, 2014, **16**, 776.

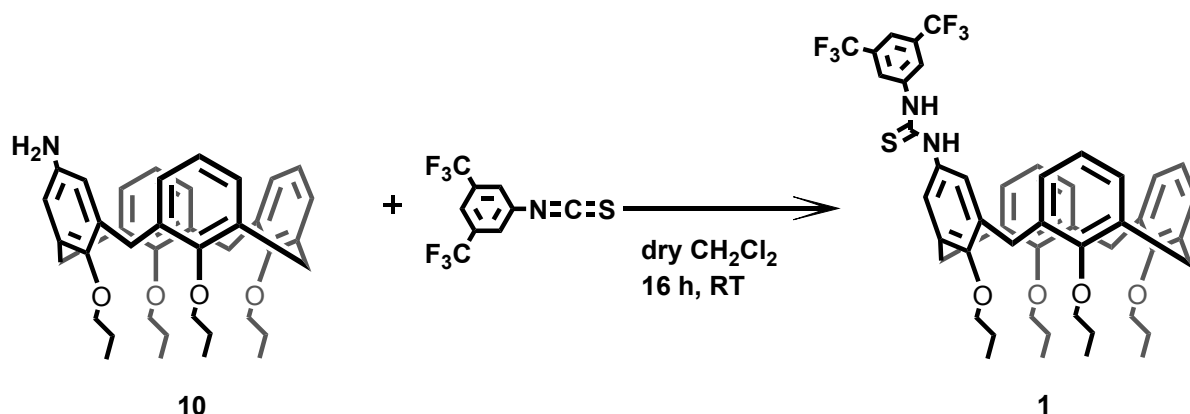
<sup>6</sup> N. J. A. Martin, X. Cheng, B. List, *J. Am. Chem. Soc.*, 2008, **130**, 13862.

**General procedure for on water catalysis of VMAR in the presence of calixarene catalyst.** A mixture of the appropriate  $\alpha$ -ketoester **7a-d** (0.22 mmol) and catalyst (0.011 mmol) was stirred in the presence of 2-(trimethylsilyloxy)furan (TMSOF) **6** (0.33 mmol) in deionized water (1 mL) as medium. The reaction mixture was kept under magnetic stirring (1400 rpm) at 30 °C for the appropriate time (see Table 3), then it was extracted with ethyl acetate (3 x 5 mL). Organic layers were collected and dried over Na<sub>2</sub>SO<sub>4</sub>, then filtered and evaporated under reduced pressure. Diastereoisomeric ratios and percentage of conversion to  $\gamma$ -adducts **8a**, **8b**, and **8d** were determined by integration of the <sup>1</sup>H NMR signals of the crude reaction mixtures in comparison with the literature values.<sup>4-7</sup> In the case of **8c**, the crude reaction mixture was purified by flash chromatography on silica gel using a gradient from *n*-hexane to a mixture of *n*-hexane/ethyl acetate (90/10) to give *syn* and *anti* diastereomers of **8c**. The relative configuration of **8c** was assigned in analogy to other derivatives **8a**, **8b**, and **8d**<sup>20a</sup> by comparison <sup>1</sup>H-NMR chemical shifts of the characteristic -CH and =CH signals of the  $\gamma$ -hydroxybutenolide ring (see page S37).

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<sup>7</sup> M. Frings, I. Atodiresei, J. Runsink, G. Raabe, C. Bolm, *Chem. Eur. J.* 2009, **15**, 1566.

## Synthesis of catalyst 1

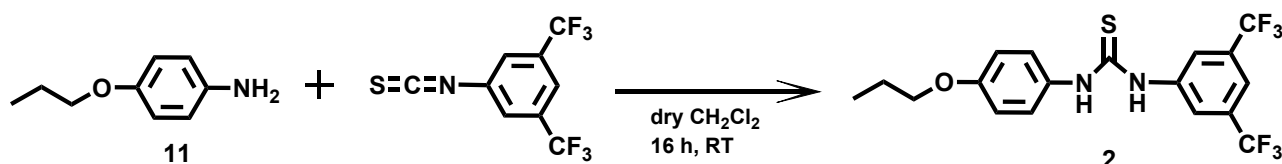


**Scheme S1.** Synthesis of **1**.

To a solution of **10** (0.14 g, 0.23 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (7 mL) 3,5-bis(trifluoromethyl)phenylisothiocyanate (0.07 g, 0.26 mmol) was added. The reaction mixture was stirred under a nitrogen atmosphere for 16 h at rt. The solvent was removed under reduced pressure and the crude mixture was purified by flash chromatography on silica gel (hexanes/ $\text{CHCl}_3$ , 80/20) to give derivative **1** as a light yellow solid (0.16 g, 0.18 mmol, 78.3 %).  $^1\text{H NMR}$  (250 MHz,  $\text{CDCl}_3$ , 298 K):  $\delta$  0.88-1.14 (overlapped,  $-\text{OCH}_2\text{CH}_2\text{CH}_3$ , 12H), 1.86-2.03 (overlapped,  $-\text{OCH}_2\text{CH}_2\text{CH}_3$ , 8H), 3.14 (d,  $J = 13.2$  Hz, 2H,  $\text{ArCH}_2\text{Ar}$ ), 3.17 (d,  $J = 13.2$  Hz, 2H,  $\text{ArCH}_2\text{Ar}$ ), 3.63-3.75 (overlapped,  $-\text{OCH}_2\text{CH}_2\text{CH}_3$ , 4H), 3.98-4.08 (m,  $-\text{OCH}_2\text{CH}_2\text{CH}_3$ , 4H), 4.43 (d,  $J = 13.2$  Hz, 2H,  $\text{ArCH}_2\text{Ar}$ ), 4.49 (d,  $J = 13.2$  Hz, 2H,  $\text{ArCH}_2\text{Ar}$ ), 5.94 (br t, ArH, 1H), 6.06 (d, ArH,  $J = 7.3$  Hz, 2H), 6.18 (s, ArH, 2H), 6.90-7.10 (overlapped, ArH + NH, 7H), 7.61 (s, NH,

1H), 7.71 (s, CF<sub>3</sub>ArH, 1H), 7.78 (s, CF<sub>3</sub>ArH, 2H). <sup>13</sup>C NMR (63 MHz, CDCl<sub>3</sub>, 298 K): δ 9.7, 10.56, 10.61, 22.8, 23.3, 30.8, 30.9, 76.5, 77.1, 77.3, 119.6, 120.9, 122.4, 124.0, 125.1, 126.2, 127.1, 128.5, 128.9, 129.3, 131.4, 133.6, 135.8, 136.3, 136.9, 139.6, 155.1, 155.5, 157.3, 179.1. HRMS (MALDI-FTICR), calcd for C<sub>49</sub>H<sub>52</sub>N<sub>2</sub>O<sub>4</sub>S [M + H<sup>+</sup>]: 879.36205, found: 879.36198. M.p: 117-118 °C.

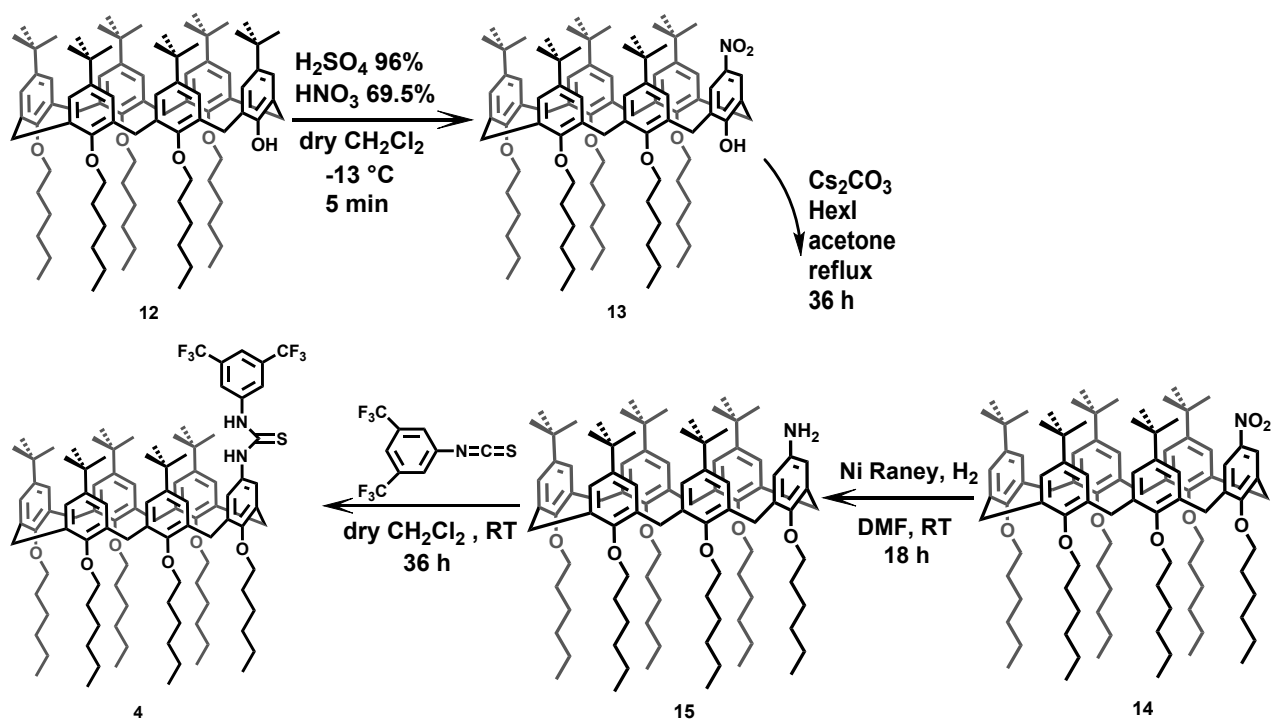
### Synthesis of catalyst 2



Scheme S2. Synthesis of 2.

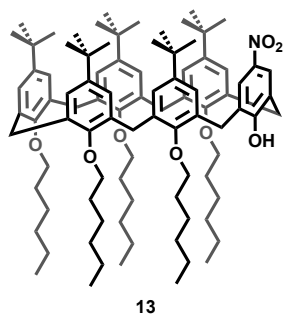
To a solution of **11** (0.10 g, 0.66 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL) 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.21 g, 0.79 mmol) was added under N<sub>2</sub>. The solution was stirred under nitrogen atmosphere for 16 h at rt. Then, the solvent was removed under reduced pressure and the crude mixture was purified by flash chromatography on silica gel (hexanes/CHCl<sub>3</sub>, 65/35) to give **2** as an ocher solid (0.22 g, 0.52 mmol, 79.0 %). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>, 298 K): δ 1.05 (t, *J* = 7.4 Hz, 3H, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.84 (m, 2H, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.95 (t, *J* = 6.5 Hz, 2H, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 7.00 (d, *J* = 8.9 Hz, 2H, ArH), 7.25 (d, *J* = 8.9 Hz, 2H, ArH), 7.57 (s, 1H, NH), 7.66 (s, 1H, CF<sub>3</sub>ArH), 7.99 (s, 2H, CF<sub>3</sub>ArH), 8.16 (s, 1H, NH). <sup>13</sup>C NMR (63, CDCl<sub>3</sub>, 298 K): δ 10.4, 22.3, 69.8, 116.1, 119.2, 120.7, 124.4, 127.2, 127.8, 131.0, 131.8, 139.6, 159.2, 180.1. HRMS (MALDI-FTICR), calcd for C<sub>18</sub>H<sub>17</sub>F<sub>6</sub>N<sub>2</sub>OS [M + H<sup>+</sup>]: 423.09603, found: 423.09608. M.p: 121-122 °C.

## Synthesis of catalyst 4



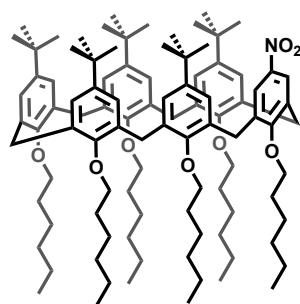
Scheme S3. Synthesis of 4.

## Derivative 13



To a solution of **12** (0.43 g, 0.31 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (7 mL), at -13 °C, HNO<sub>3</sub> (69.5%, 0.035 mL) and H<sub>2</sub>SO<sub>4</sub> (96%, 0.035 mL) were added under N<sub>2</sub>. After 5 minutes the reaction mixture was quenched with H<sub>2</sub>O (20 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 10 mL). The organic layers were collected and dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated under reduced pressure to give a yellow crude solid, which was purified by flash chromatography on silica gel (hexanes/CHCl<sub>3</sub>, 70/30) to give derivative **13** as a yellow solid (0.32 g, 0.23 mmol, 74.2%). <sup>1</sup>H NMR (300 MHz, TCDE, 363 K): δ 0.69-1.65 (overlapped, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> + -C(CH<sub>3</sub>), 100H), 3.07-3.76 (overlapped, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> + ArCH<sub>2</sub>Ar, 22H), 6.64-6.69 (overlapped, ArH, 4H), 6.78 (s, ArH, 2H), 6.91 (s, ArH, 2H), 7.02 (s, ArH, 2H), 7.84 (s, NO<sub>2</sub>-ArH, 2H), 8.62 (bs, OH, 1H). <sup>13</sup>C NMR (75 MHz, TCDE, 363 K): δ 13.7, 22.2, 22.3, 22.5, 25.5, 25.6, 29.6, 30.3, 30.5, 31.2, 31.3, 31.4, 31.6, 31.9, 33.8, 72.9, 73.5, 73.8, 124.6, 124.9, 125.8, 126.8, 127.0, 128.1, 129.9, 131.5, 132.8, 133.3, 133.4, 140.3, 144.5, 144.9, 146.4, 151.5, 153.3, 159.4. HRMS (MALDI-FTICR), calcd for C<sub>92</sub>H<sub>135</sub>NO<sub>8</sub>K [M + K<sup>+</sup>]: 1421.98531, found: 1421.98945. M.p: 181-182°C.

### Derivative 14

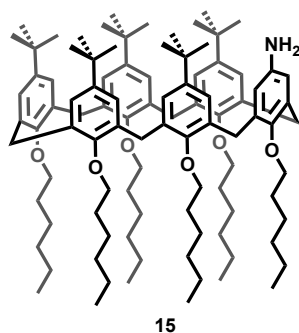


14



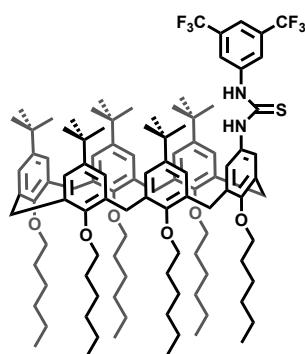
$\text{Cs}_2\text{CO}_3$  (0.75 g, 2.31 mmol) was added to a suspension of derivative **13** (0.32 g, 0.23 mmol) in acetone (20 mL). The reaction mixture was refluxed for 2 hours, then was allowed to cool slowly to room temperature. 1-Iodohexane (0.98 g, 4.62 mmol) was added and the reaction mixture was refluxed for 36 hours, then it was cooled to rt and concentrated under vacuum. The crude product was dissolved in  $\text{CH}_2\text{Cl}_2$  (50 mL), washed with aqueous 1N HCl (20 mL) and the organic layer was dried over  $\text{Na}_2\text{SO}_4$ , filtered and the crude product was evaporated to dryness and then purified by flash chromatography on silica gel using a gradient of *n*-Hexane/ $\text{CHCl}_3$  (from 90/10 to 75/25) to give derivative **14** (0.29 g, 0.20 mmol, 87.0 %).  $^1\text{H NMR}$  (300 MHz, TCDE, 363 K):  $\delta$  0.71-1.80 (overlapped,  $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 + -\text{C}(\text{CH}_3)$ , 111H), 3.18-3.80 (overlapped,  $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 + \text{ArCH}_2\text{Ar}$ , 24H), 6.58 (bs, ArH, 2H), 6.73 (bs, ArH, 2H), 6.86-7.04 (overlapped, ArH, 6H), 7.56 (s,  $\text{NO}_2\text{-ArH}$ , 2H).  $^{13}\text{C NMR}$  (75 MHz, TCDE, 363 K):  $\delta$  13.8, 22.4, 22.5, 25.9, 29.6, 30.1, 30.2, 30.5, 31.2, 31.4, 31.6, 31.7, 31.8, 33.7, 33.8, 33.9, 73.0, 73.3, 73.5, 73.7, 123.2, 124.9, 125.3, 126.2, 126.5, 127.7, 131.2, 132.5, 132.8, 132.9, 133.5, 135.8, 143.6, 145.0, 145.6, 152.8, 153.7, 160.3. **HRMS (MALDI-FTICR)**, calcd for  $\text{C}_{98}\text{H}_{147}\text{NO}_8\text{Na}$  [ $M + \text{Na}^+$ ]: 1490.10527, found: 1490.10384. M.p: 243-244 °C.

### Derivative 15



Raney nickel (cat. amounts) was added to a solution of derivative **14** (0.42 g, 0.29 mmol) in hot DMF (230 mL). The resulting black suspension was stirred under H<sub>2</sub> (1 atm) at rt for 18 hours, then was filtered through a celite pad. Concentration of the filtrate to dryness give a crude product, which was purified by flash chromatography on silica gel (hexanes/CH<sub>2</sub>Cl<sub>2</sub>, 80/20) to give derivative **15** (0.36 g, 0.25 mmol, 86.2 %). <sup>1</sup>H NMR (300 MHz, TCDE, 363 K): δ 0.39-1.78 (overlapped, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> + -C(CH<sub>3</sub>), 111H), 3.63-3.77 (overlapped, ArCH<sub>2</sub>Ar + OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, 24 H), 6.73-7.07 (overlapped, ArH, 12H). <sup>13</sup>C NMR (75 MHz, TCDE, 363 K): δ 13.3, 13.4, 25.2, 25.3, 25.4, 29.9, 30.6, 30.9, 31.0, 31.2, 31.4, 33.4, 73.6, 113.5 (*broad*), 125.5 (*broad*), 132.4 (*broad*), 145.0, 145.2, 154.0 (*broad*). HRMS (ESI-FTICR), calcd for C<sub>98</sub>H<sub>150</sub>NO<sub>6</sub> [*M* + H<sup>+</sup>]: 1438.14915, found: 1438.12274. Decomposes to light red oil at 151.5 °C.

### Catalyst 4



4

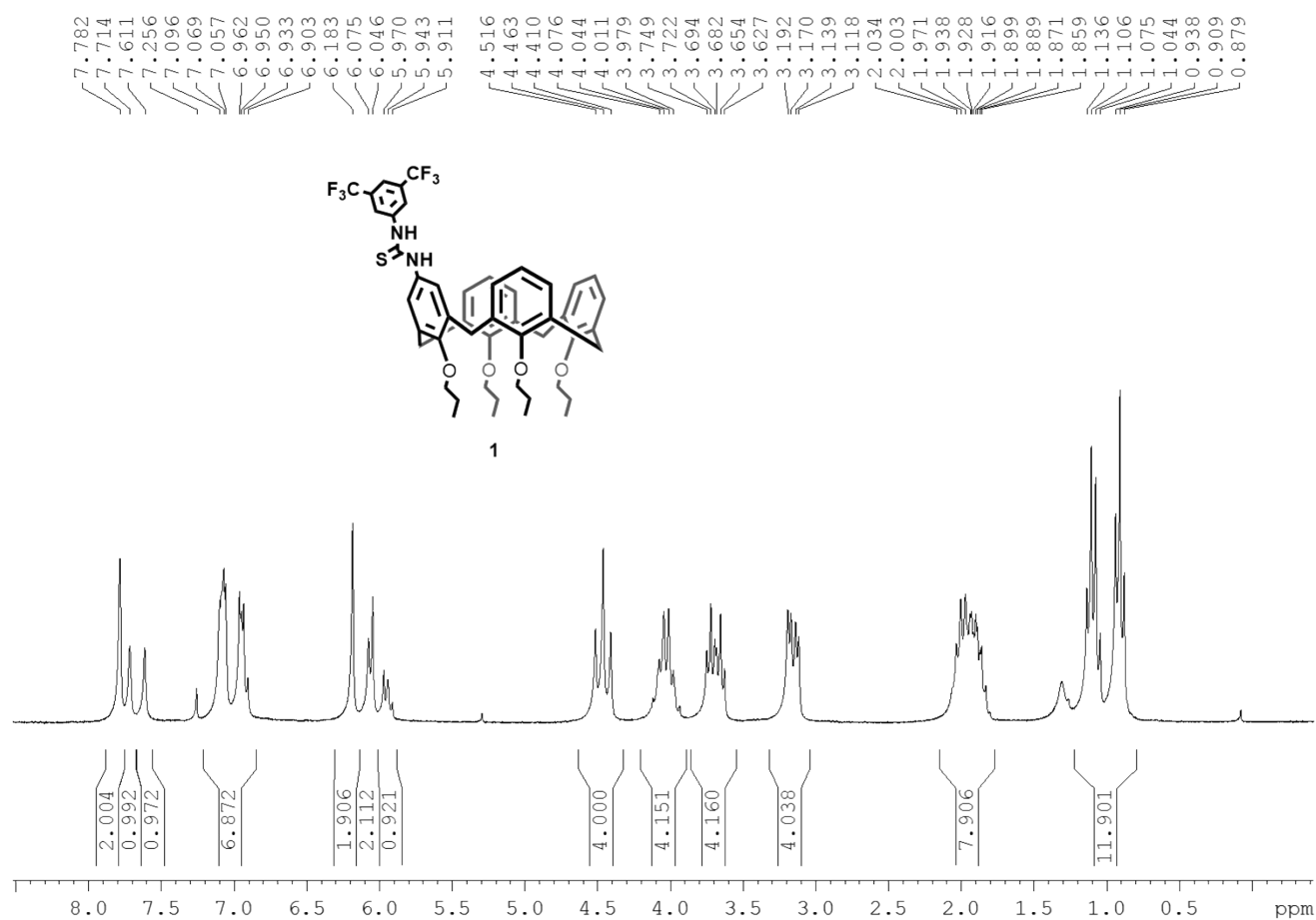
3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.08 g, 0.30 mmol) was added to a solution of derivative **15** (0.32 g, 0.22 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL). The reaction mixture was stirred for 24 hours at rt under N<sub>2</sub> atmosphere, then other isothiocyanate (0.03 g, 0.11 mmol) was added. After other 12 hours, solvent was evaporated to give a brown oil, which was purified by flash column chromatography on silica gel (hexanes) to obtain catalyst **4** as a white solid (0.32 g, 0.19 mmol, 86.4 %). <sup>1</sup>H NMR (300 MHz, TCDE, 363 K): δ 0.31-1.82 (overlapped, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> + -C(CH<sub>3</sub>), 111H), 3.48-3.75 (overlapped, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> + ArCH<sub>2</sub>Ar, 24H), 6.80-7.42 (overlapped, ArH + CF<sub>3</sub>ArH, 13H), 8.10 (s, CF<sub>3</sub>ArH, 2H). <sup>13</sup>C NMR (75 MHz, TCDE, 363 K): δ 13.7, 22.4, 25.6, 30.0, 31.0, 31.4, 33.8, 126.2 (*broad*), 133.1 (*broad*), 145.6 (*broad*), 154.0 (*broad*). HRMS (ESI-FTICR), calcd for C<sub>107</sub>H<sub>153</sub>F<sub>6</sub>N<sub>2</sub>O<sub>6</sub>S : 1709.13814 [*M* + H<sup>+</sup>], found : 1709.13571. M.p.: 214-215 °C.

### Derivative **8c**

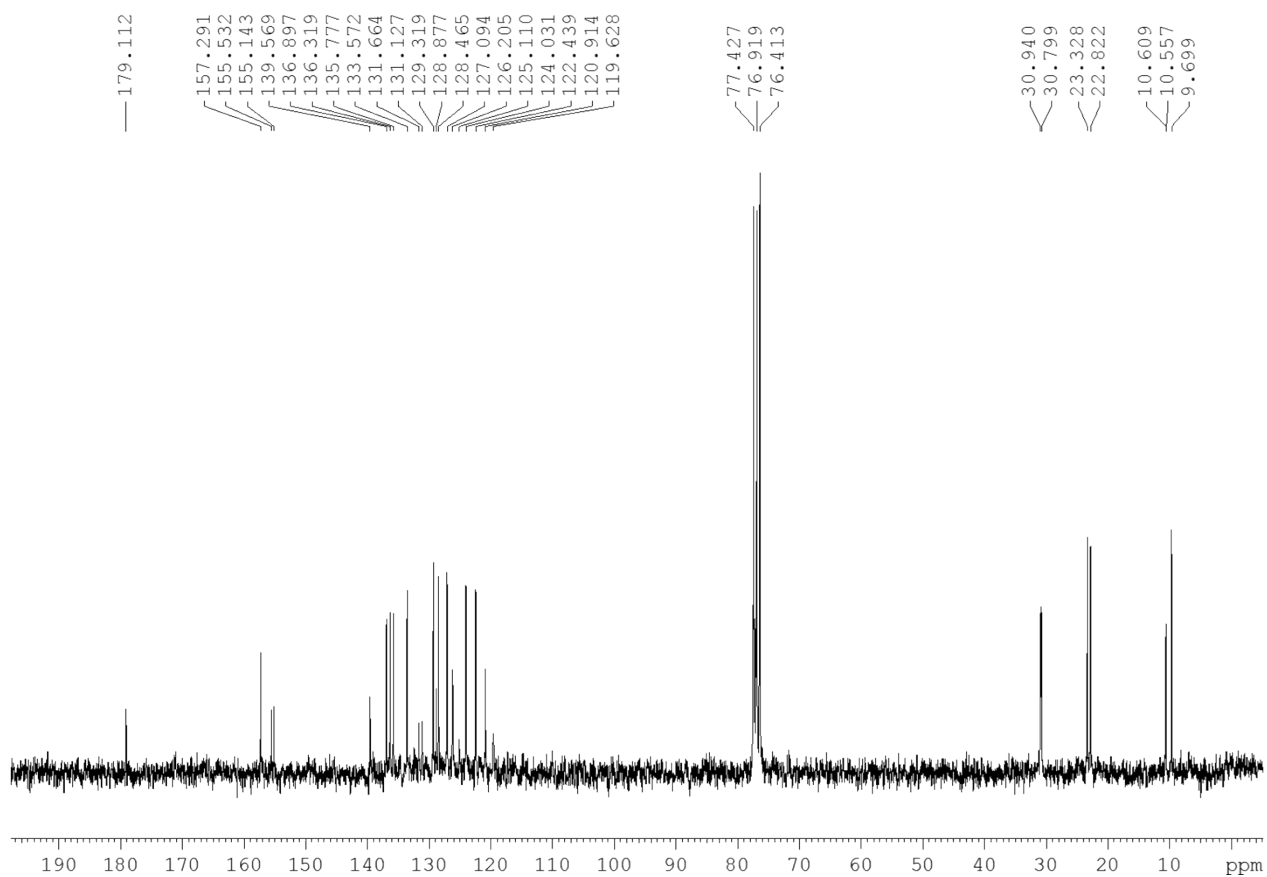
Prepared according to the general procedure from **7c**, 2-(trimethylsilyloxy)furan **6** and catalyst **1**. The residue was purified by flash column chromatography on silica gel using a gradient from *n*-hexane to a mixture of *n*-hexane/ethyl acetate (90/10) to give *anti* and *syn* diastereomers. **Anti isomer** (isolated as a colorless oil) (0.012 g, 0.037 mmol, 16.7%): <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>, 298 K): δ 3.60 (broad, 1H, OH), 5.25

(d, 1H,  $J = 12.1$  Hz, CH<sub>2 benz</sub>), 5.32 (d,  $J = 12.1$  Hz, 1H, CH<sub>2 benz</sub>), 5.55 (s, 1H, -CH), 6.10 (dd,  $J_2 = 1.8$  Hz,  $J_1 = 5.4$  Hz, 1H, =CH), 7.18 (dd,  $J_2 = 1.2$  Hz,  $J_1 = 5.4$  Hz, 1H, =CH), 7.32-7.37 (overlapped, ArH, 8H), 7.57-7.59 (overlapped, ArH, 2H). **<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>, 298 K):  $\delta$  69.0, 78.4, 85.8, 124.1, 126.0, 128.75, 128.76, 129.0, 129.1, 129.2, 134.4, 136.8, 152.1, 171.4, 172.4. **Syn isomer** (isolated as a colorless oil) (0.010 g, 0.031 mmol, 14.2%): **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>, 298 K):  $\delta$  3.88 (s, 1H, OH), 5.28 (d, 1H,  $J = 12.1$  Hz, CH<sub>2 benz</sub>), 5.34 (d, 1H,  $J = 12.1$  Hz, CH<sub>2 benz</sub>), 5.78-5.79 (m, 1H, -CH), 6.16 (dd,  $J_2 = 2.0$  Hz,  $J_1 = 6.0$  Hz, 1H, =CH), 6.95 (dd,  $J_2 = 1.6$  Hz,  $J_1 = 5.6$  Hz, 1H, =CH), 7.31-7.42 (overlapped, ArH, 8H), 7.66-7.69 (overlapped, ArH, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>, 298 K):  $\delta$  69.4, 77.6, 86.3, 124.1, 125.7, 128.5, 128.9, 129.0, 129.1, 129.3, 134.5, 136.3, 151.5, 171.7, 172.7. **HRMS (ESI-FTICR)**, calcd for C<sub>19</sub>H<sub>16</sub>O<sub>5</sub>Na : 347.08899 [ $M + Na^+$ ], found : 347.08931.

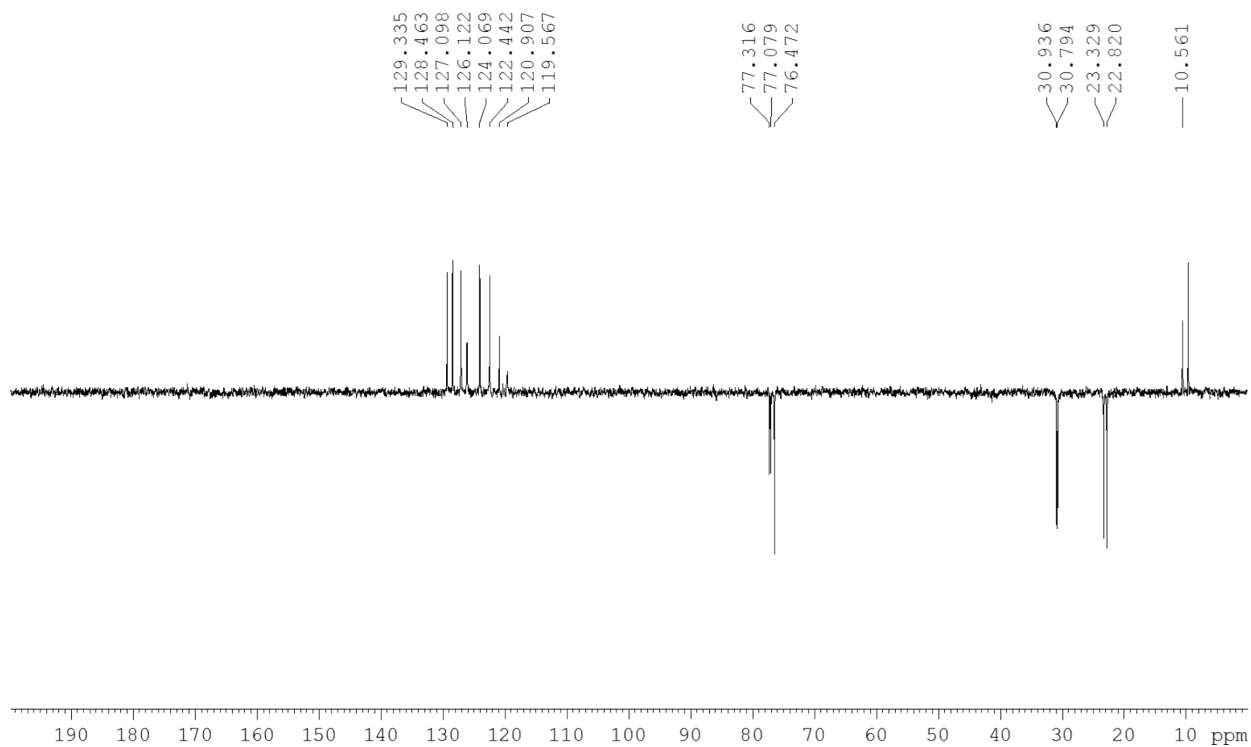
# Copies of $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and MS spectra of synthesized derivatives



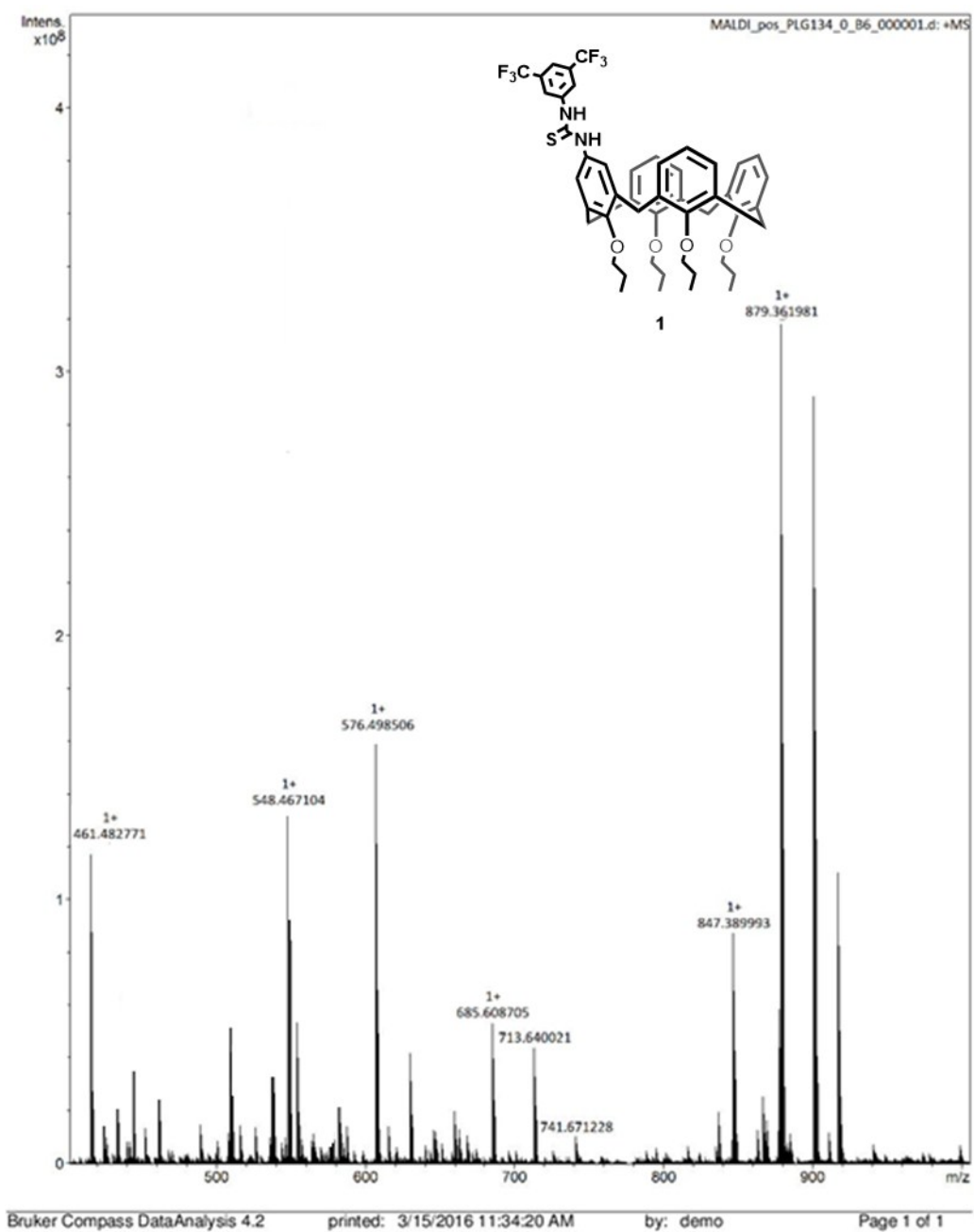
**Figure S1.**  $^1\text{H}$  NMR spectrum of catalyst **1** (250 MHz,  $\text{CDCl}_3$ , 298 K).



**Figure S2.**  $^{13}\text{C}$  NMR spectrum of catalyst **1** (63 MHz,  $\text{CDCl}_3$ , 298 K).



**Figure S3.** DEPT 135 spectrum of catalyst **1** (63 MHz,  $\text{CDCl}_3$ , 298 K).



**Figure S4.** MALDI MS spectrum of catalyst **1**.

## Catalyst 2

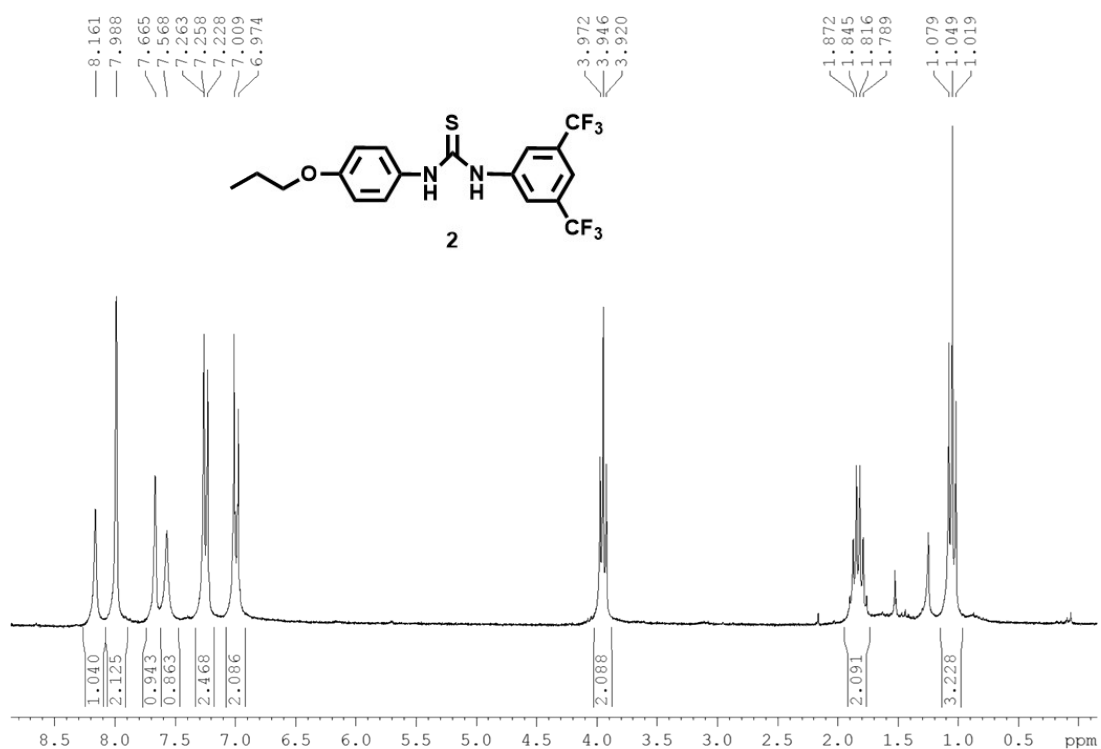


Figure S5. <sup>1</sup>H NMR spectrum of catalyst 2 (250 MHz, CDCl<sub>3</sub>, 298 K).

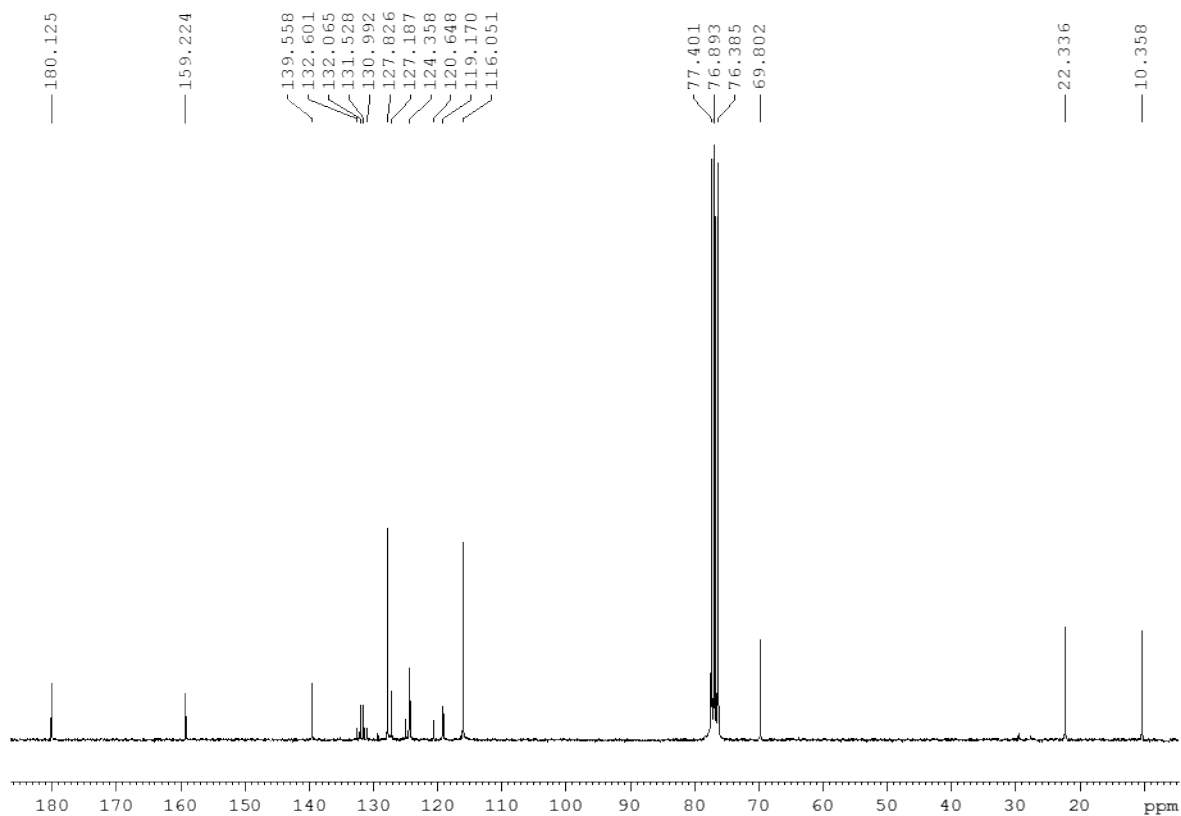
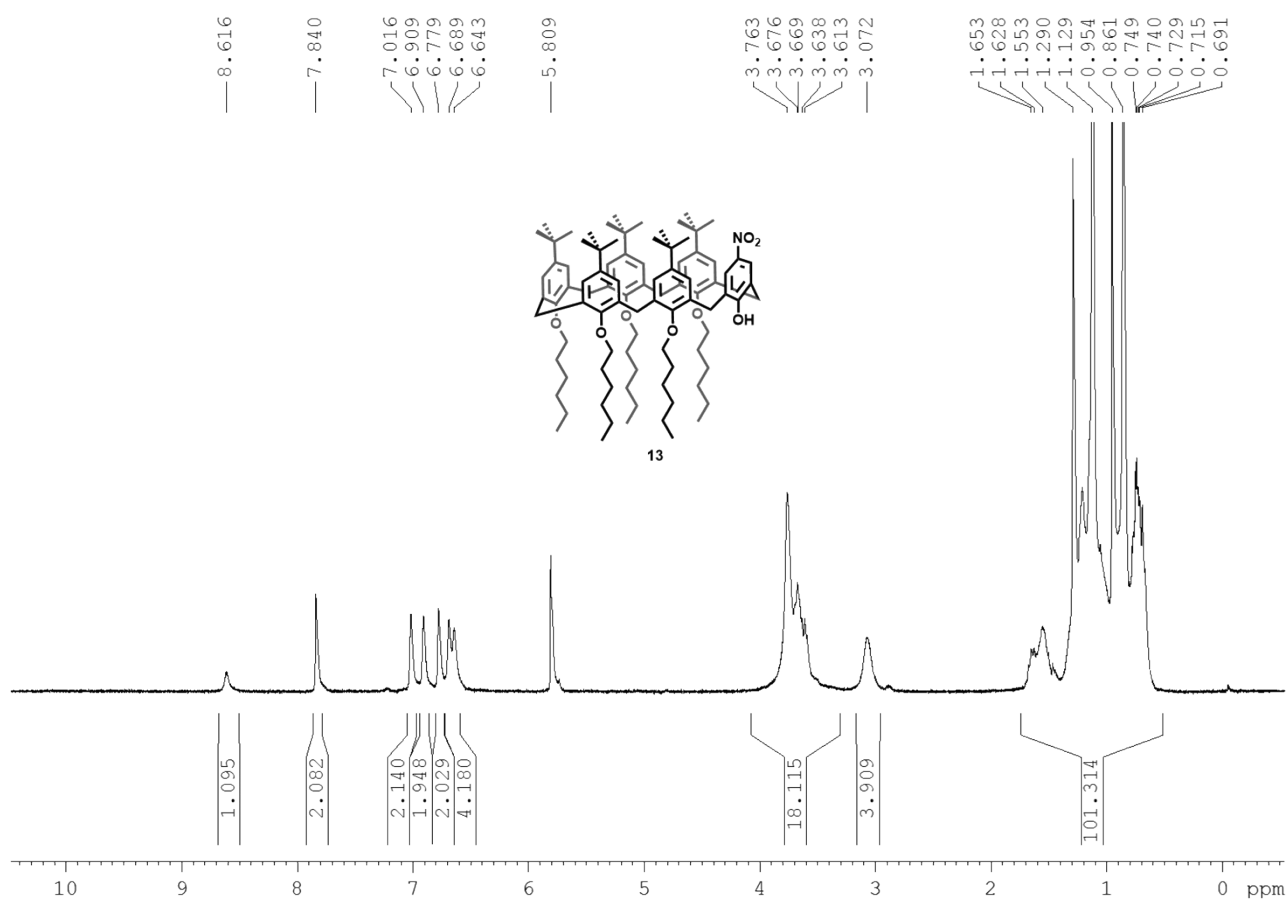


Figure S6. <sup>13</sup>C NMR spectrum of catalyst 2 (63 MHz, CDCl<sub>3</sub>, 298 K).

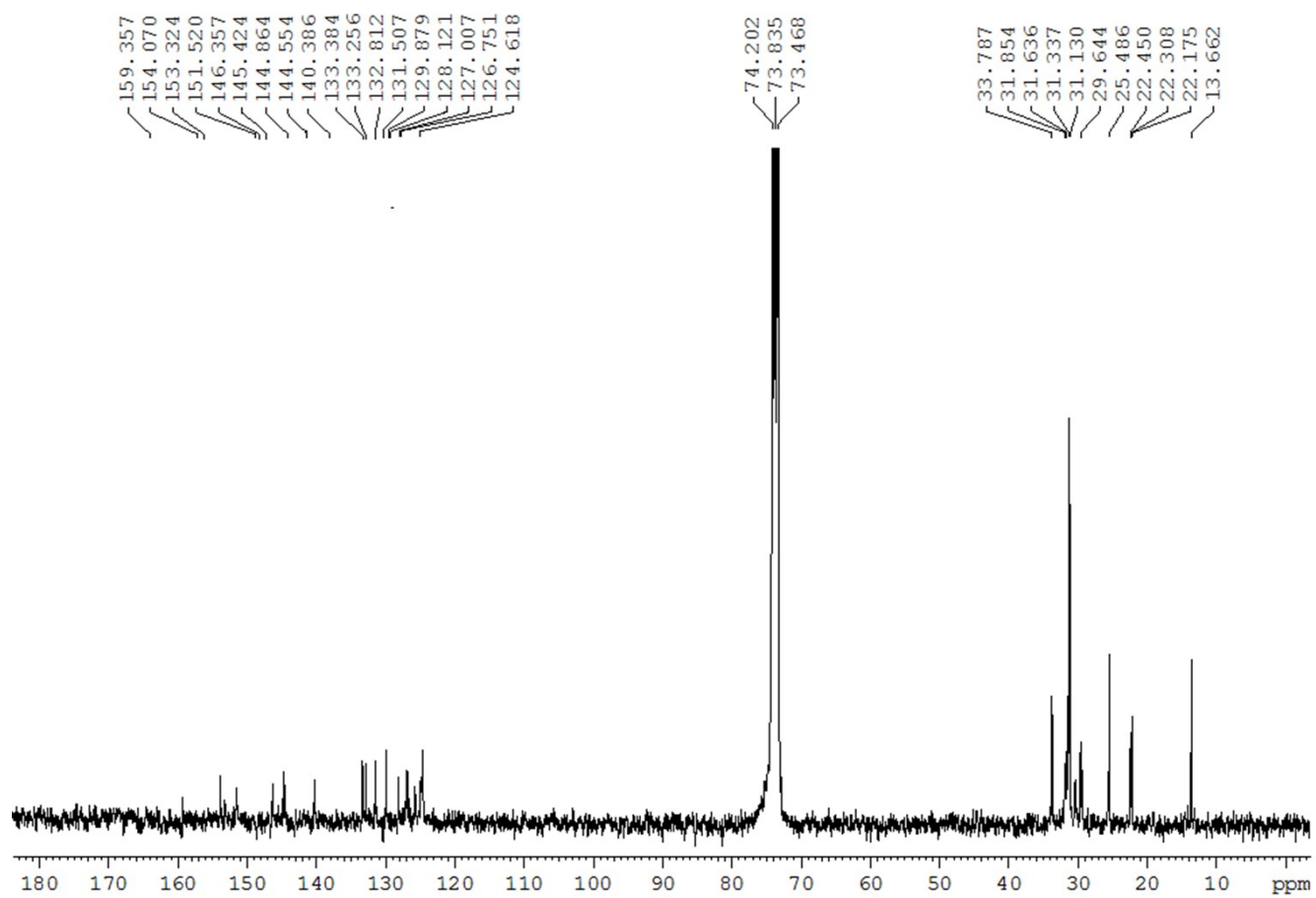




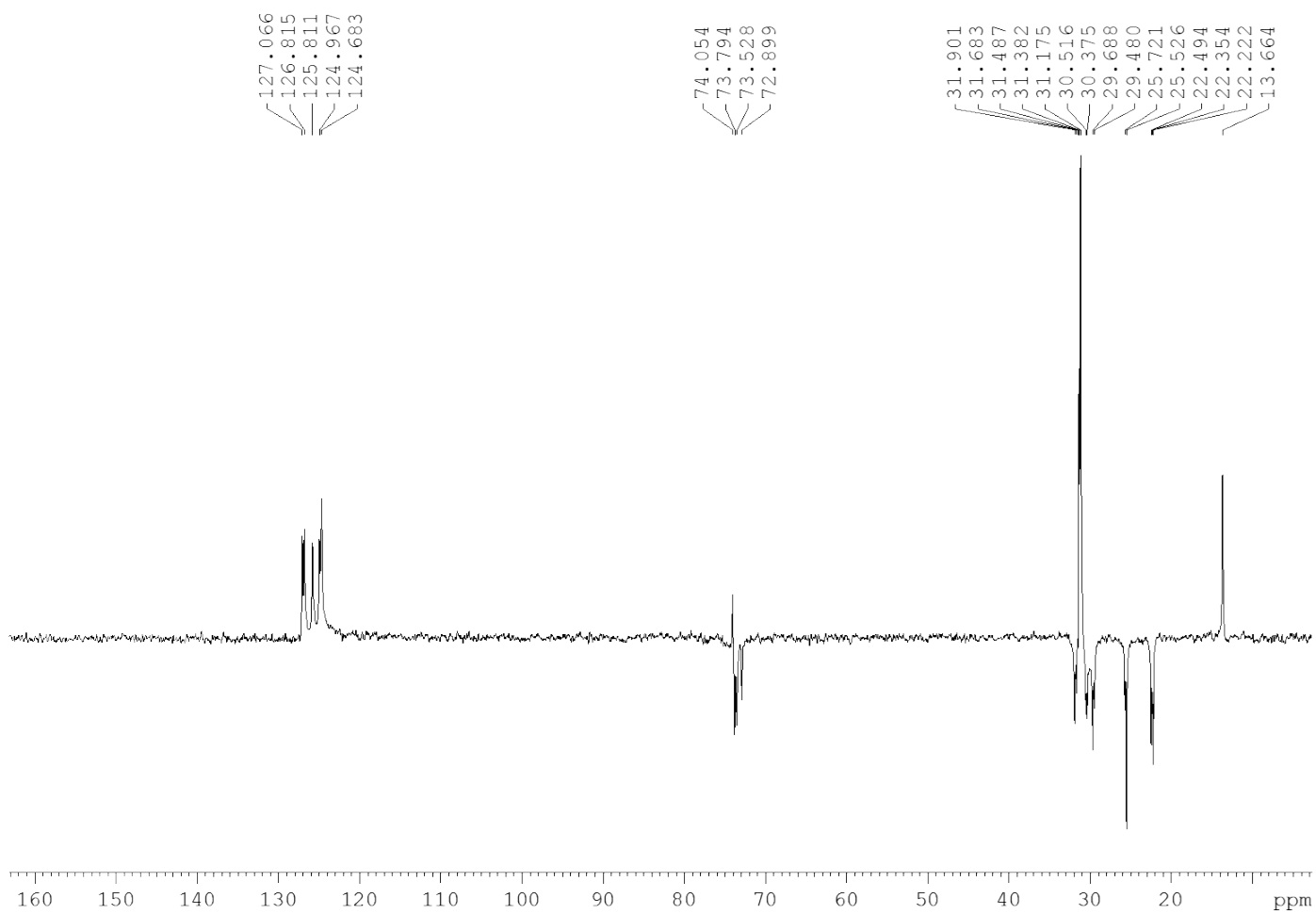
## Derivative 13



**Figure S8.** <sup>1</sup>H NMR spectrum of derivative **13** (300 MHz, TCDE, 363 K).



**Figure S9.**  $^{13}\text{C}$  NMR spectrum of derivative **13** (75 MHz, TCDE, 363 K).



**Figure S10.** DEPT 135 spectrum of derivative **13** (75 MHz, TCDE, 363 K).

Generic Display Report (all)

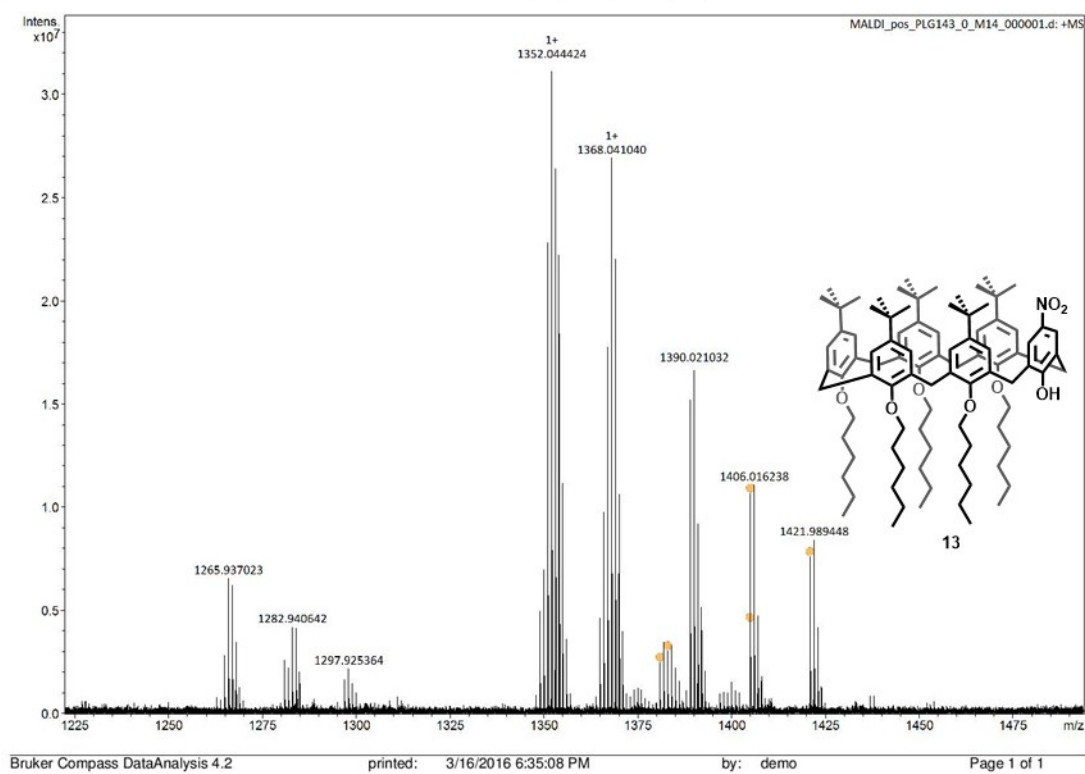
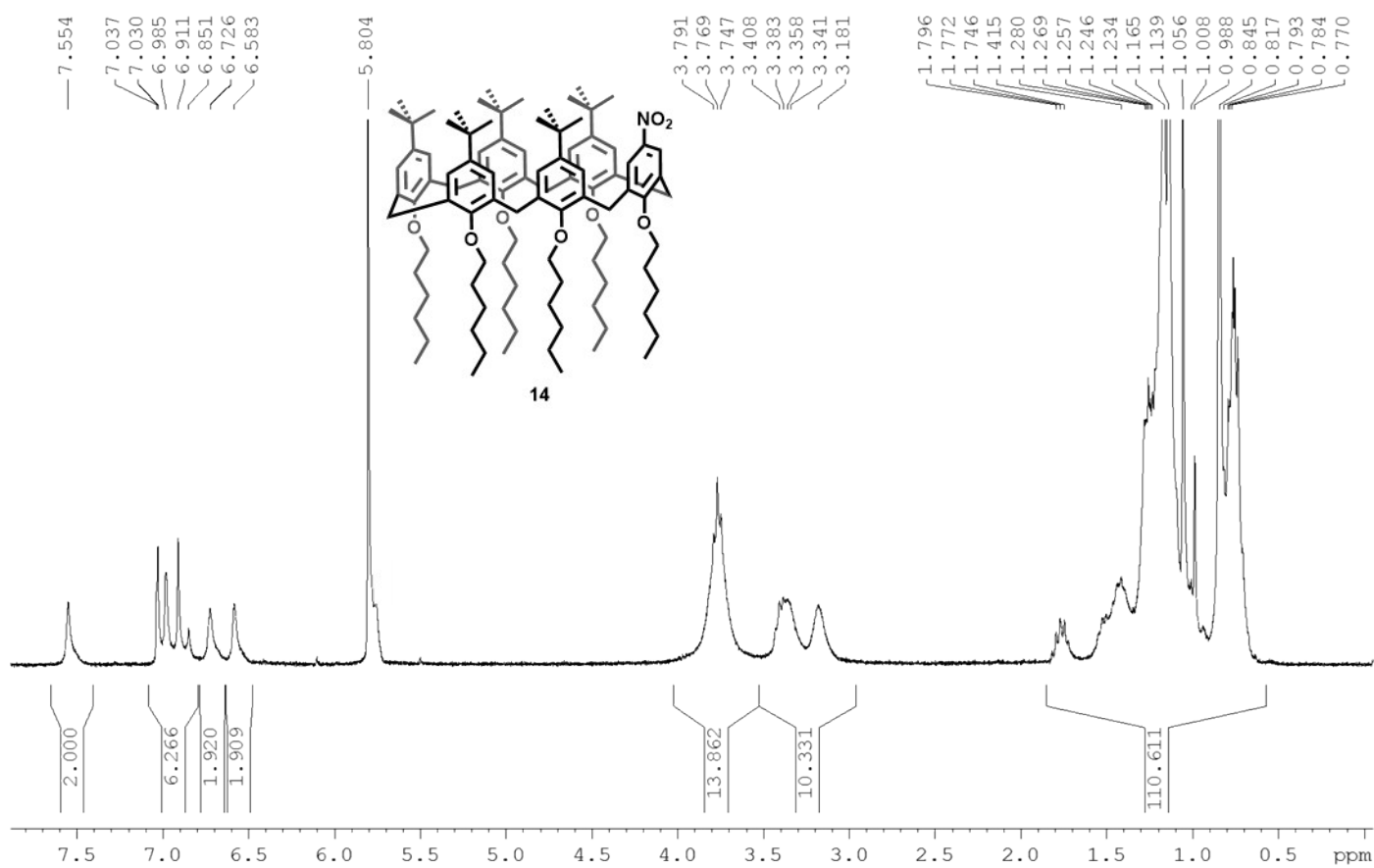
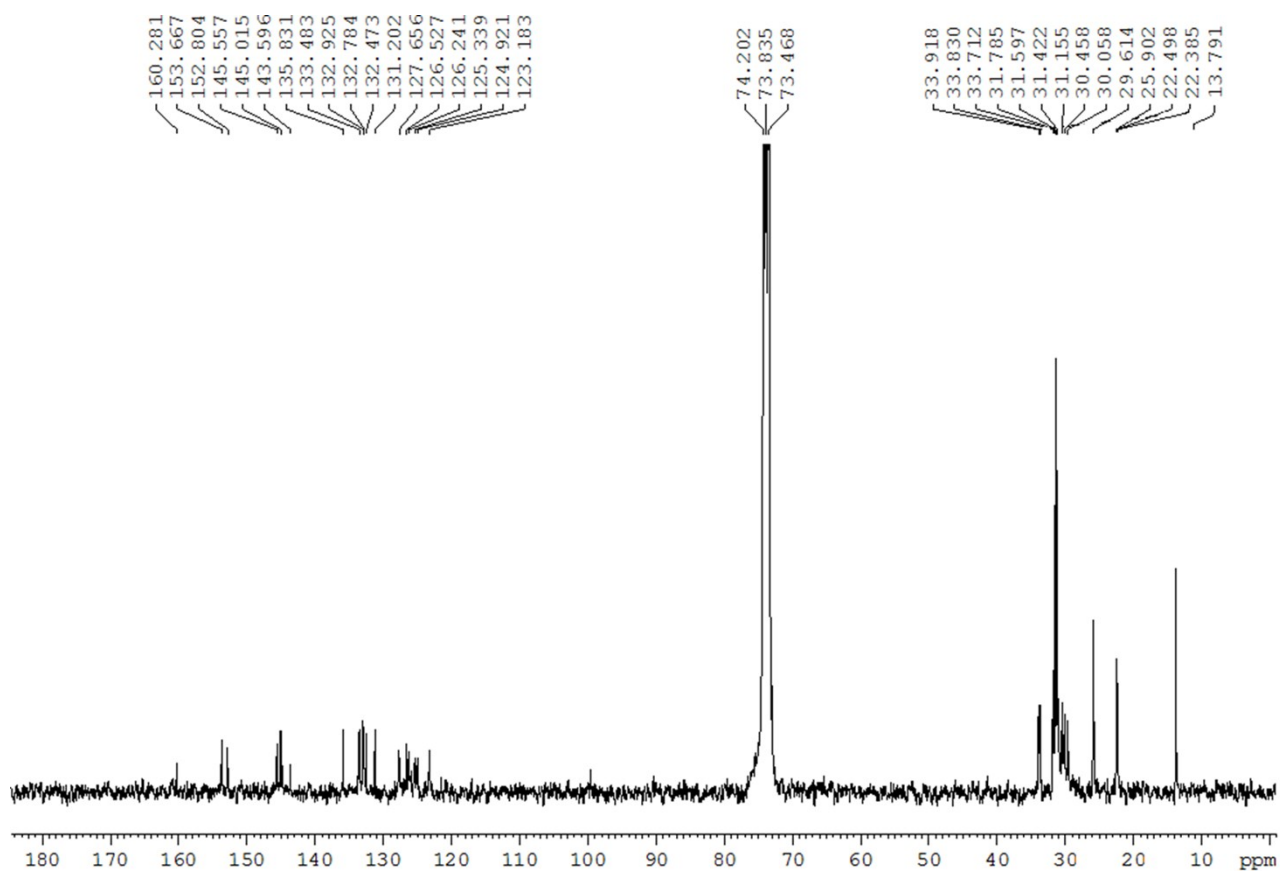


Figure S11. MALDI MS spectrum of derivative 13.

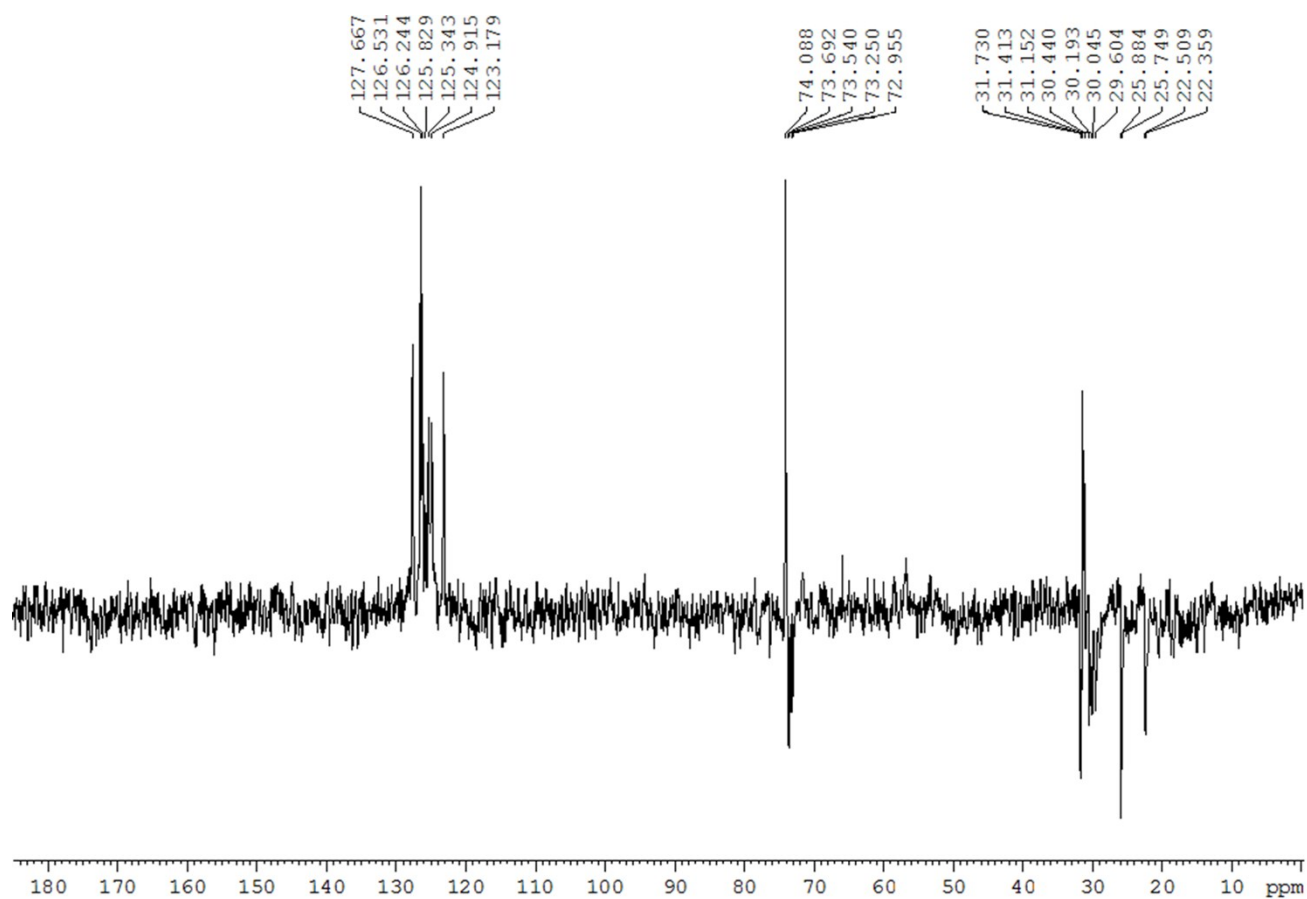
## Derivative 14



**Figure S12.**  $^1\text{H}$  NMR spectrum of derivative **14** (300 MHz, TCDE, 363 K).



**Figure S13.**  $^{13}\text{C}$  NMR of derivative **14** (75 MHz, TCDE, 363 K).

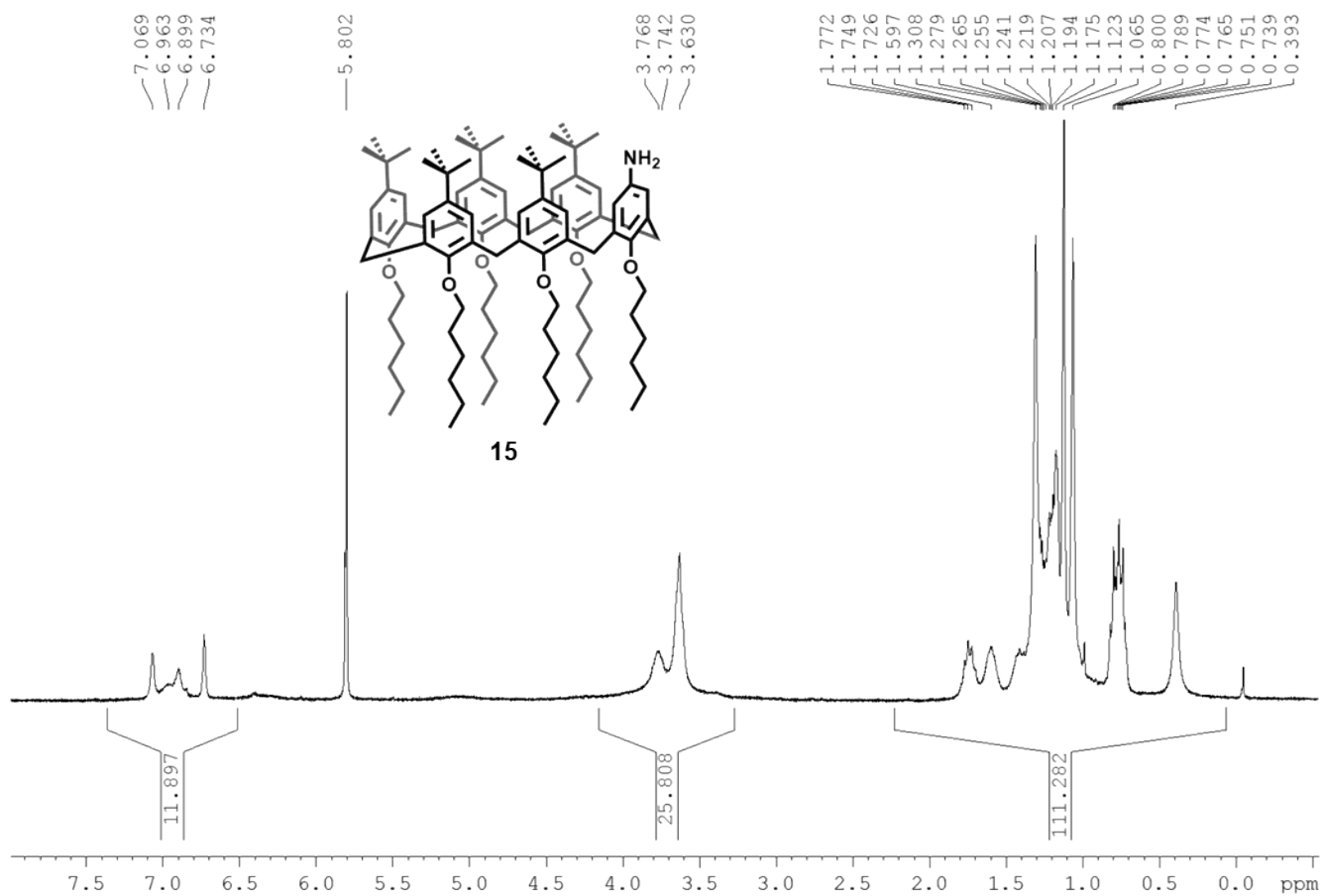


**Figure S14.** DEPT 135 spectrum of derivative **14** (300 MHz, TCDE, 363 K).

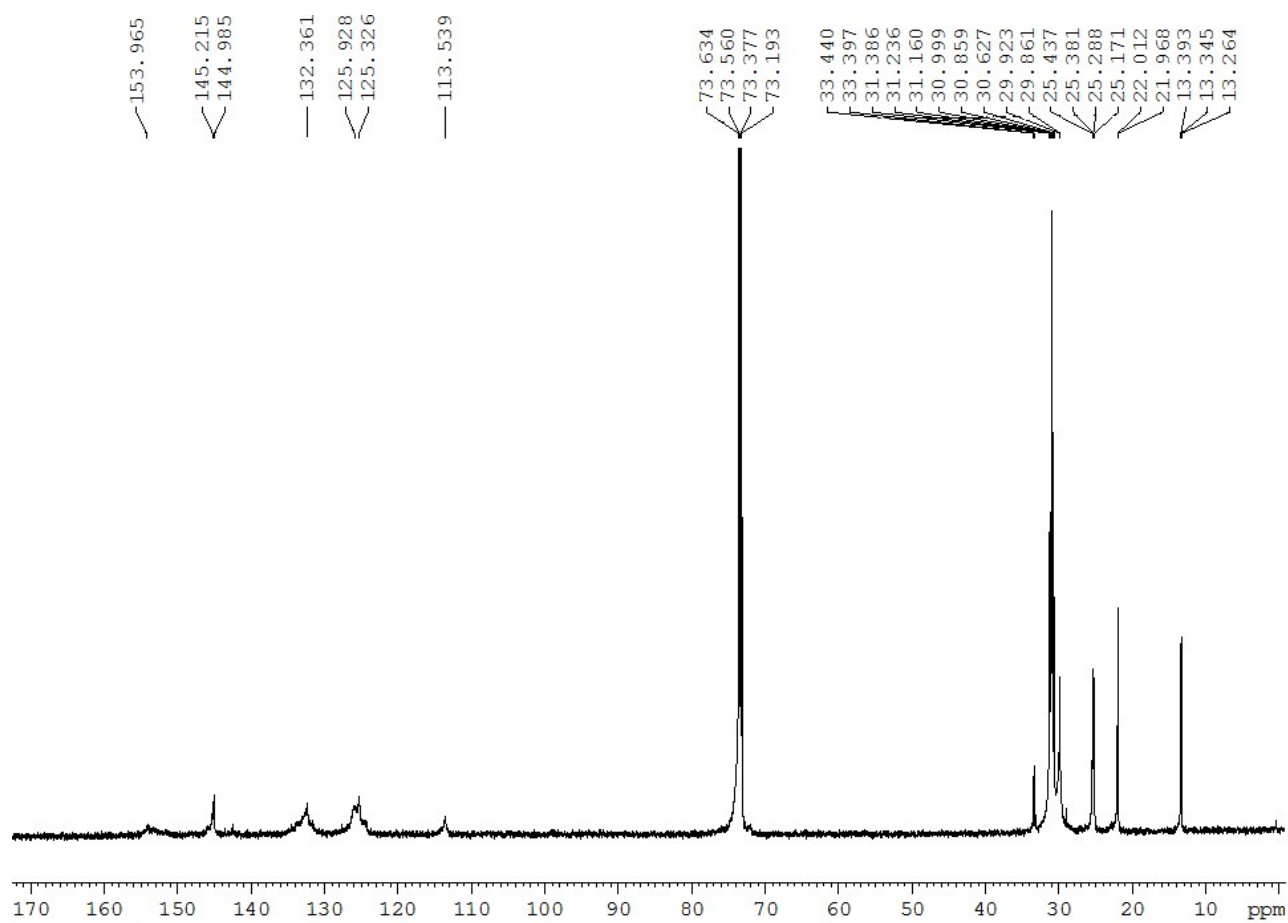




## Derivative 15



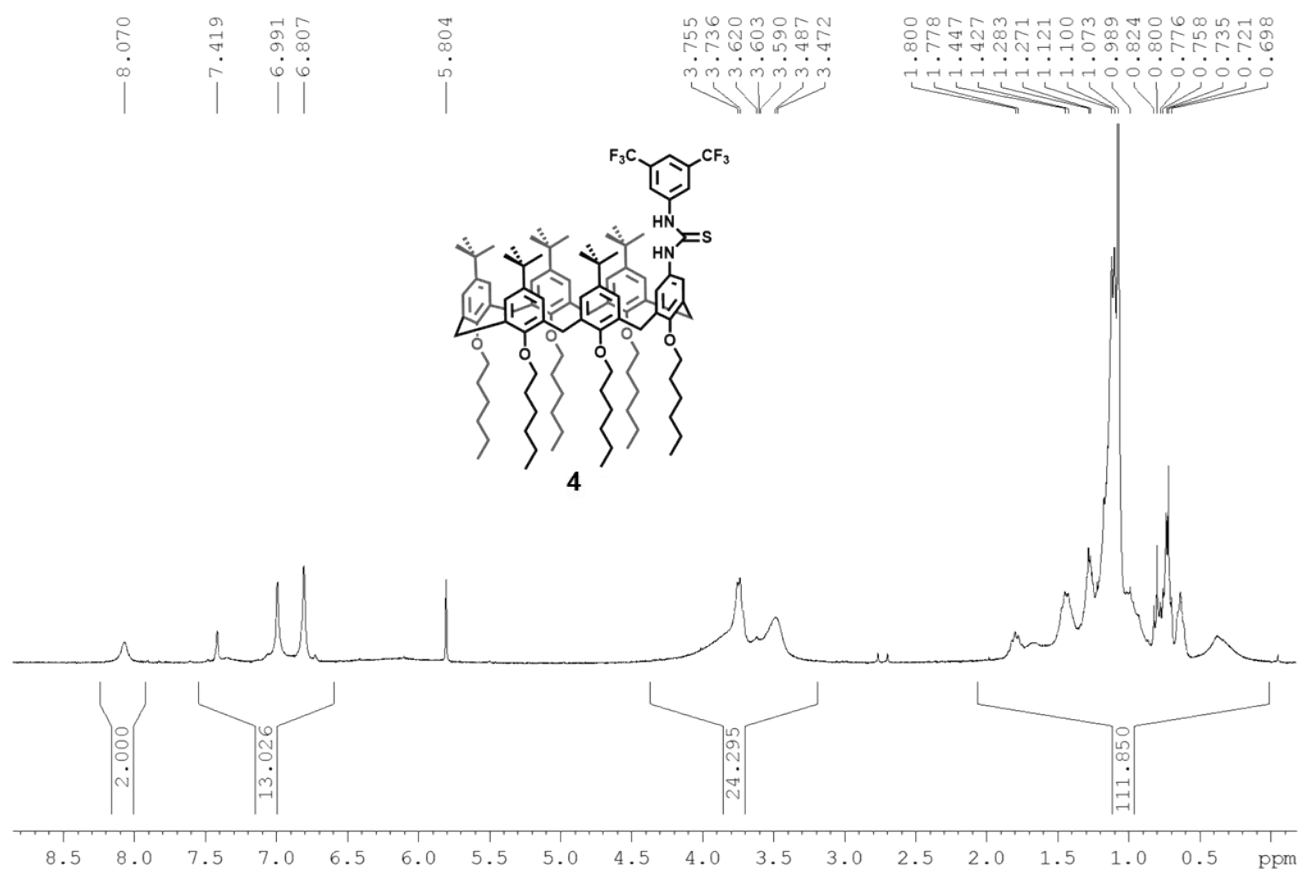
**Figure S16.** <sup>1</sup>H NMR spectrum (300 MHz, TCDE, 363 K) of derivative 15.



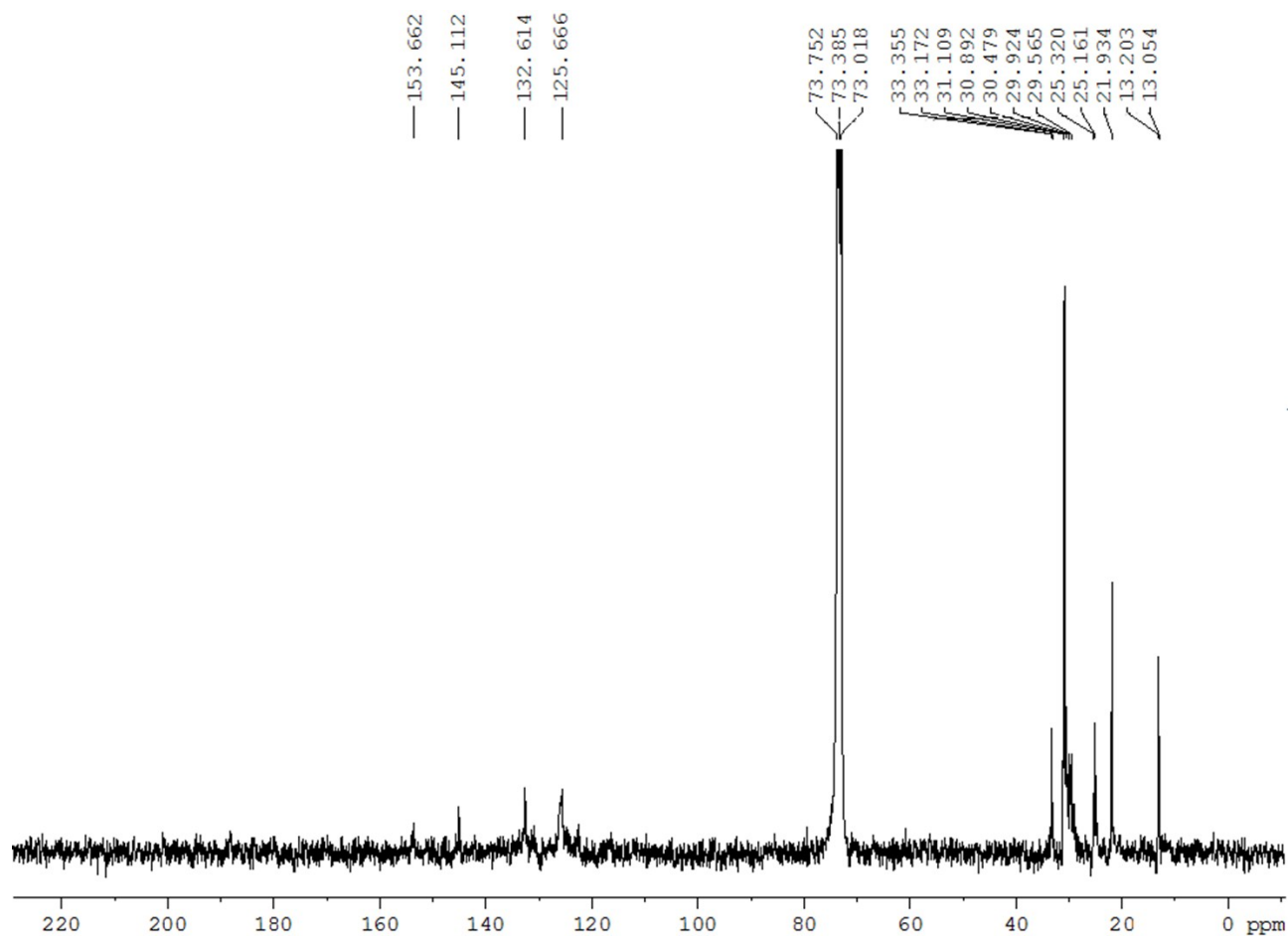
**Figure S17.**  $^{13}\text{C}$  NMR of derivative **15** (75 MHz, TCDE, 363 K).



### Catalyst 4



**Figure S19.** <sup>1</sup>H NMR spectrum of catalyst 4 (300 MHz, TCDE, 363 K).



**Figure S20.**  $^{13}\text{C}$  NMR spectrum of catalyst 4 (75 MHz, TCDE, 363 K).

Generic Display Report (all)

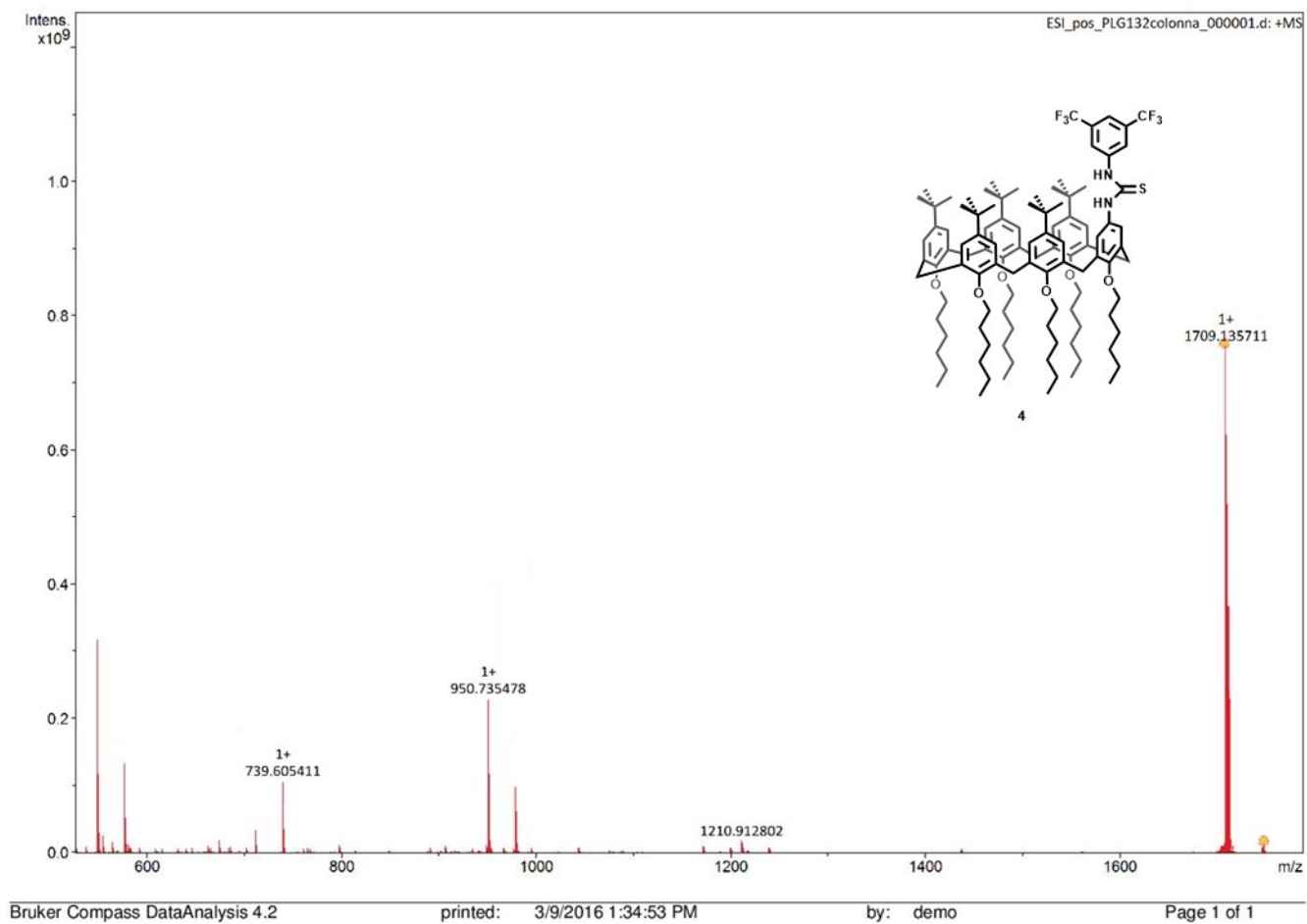
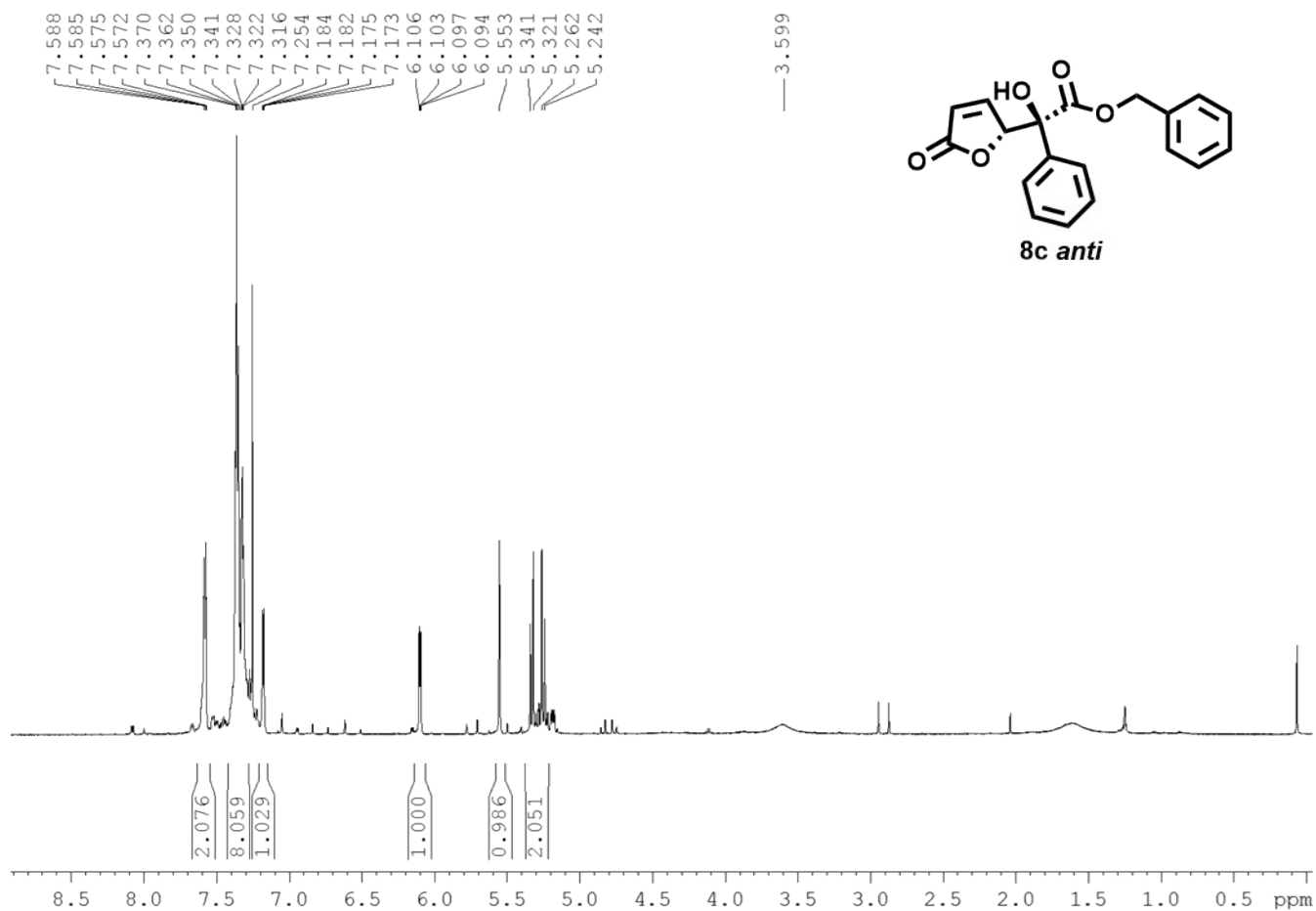


Figure S21. ESI MS spectrum of catalyst 4.

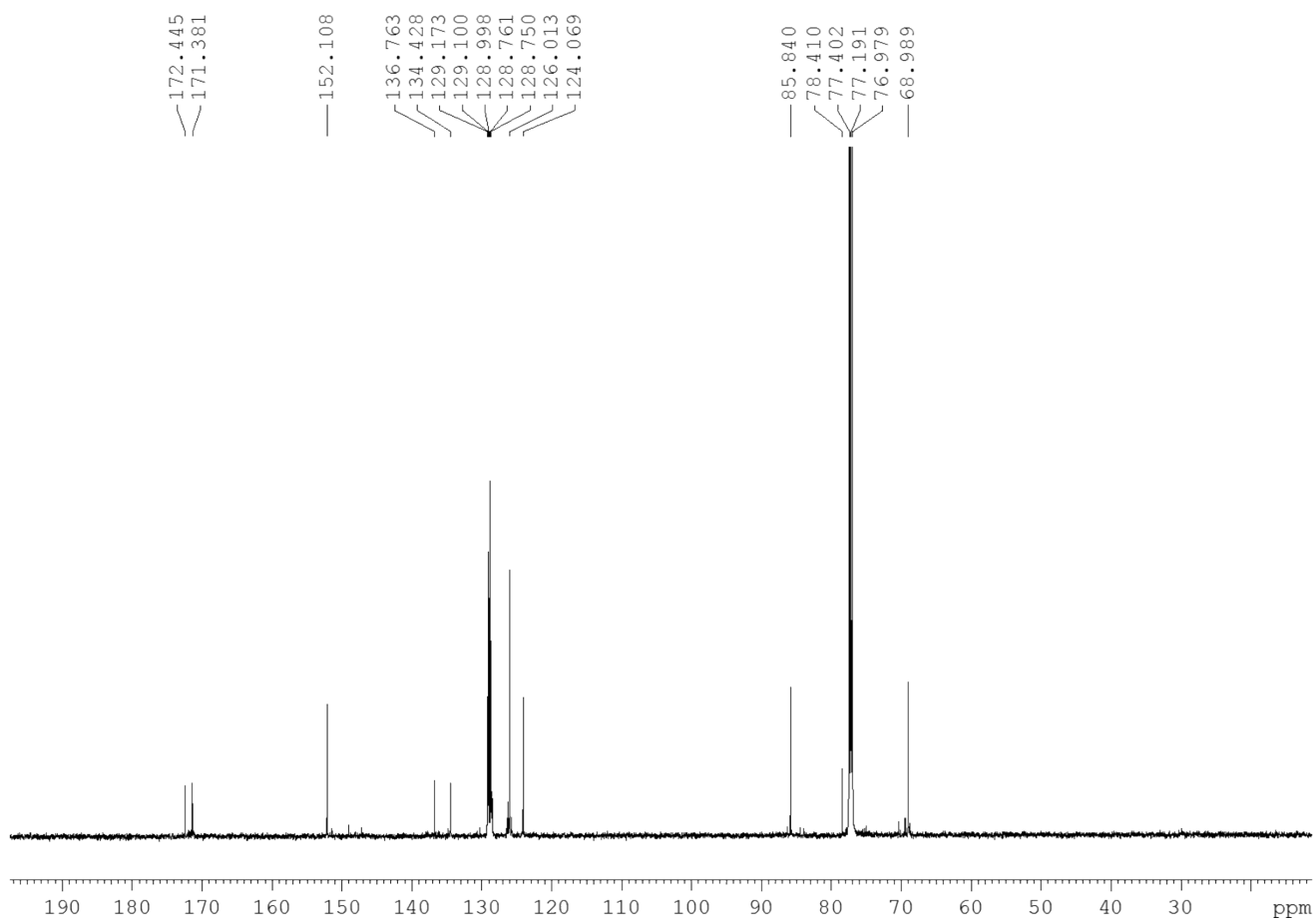
## Derivative 8c

### *Anti* Isomer



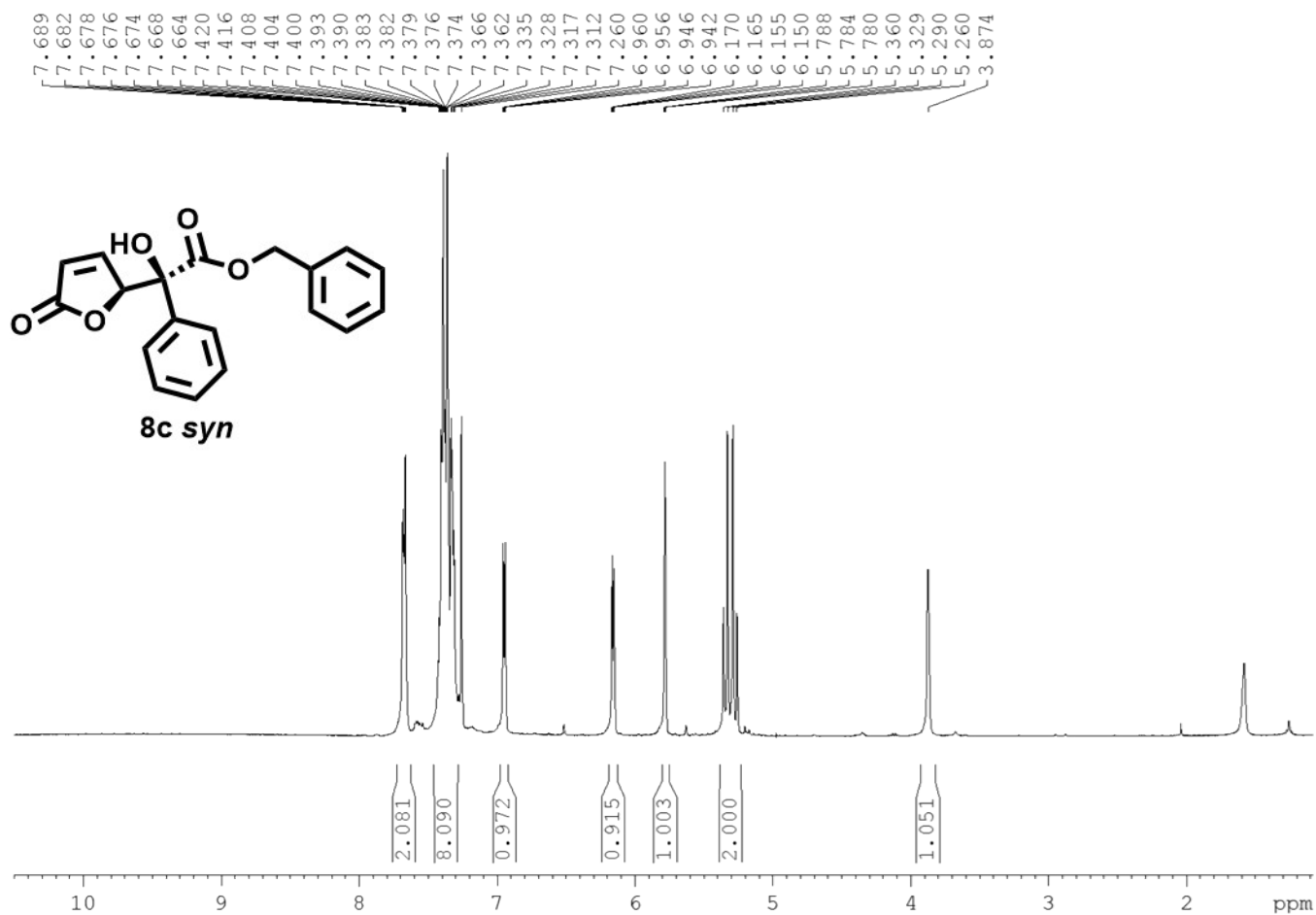
**Figure S22.** <sup>1</sup>H NMR spectrum of *anti* isomer of derivative **8c** (600 MHz, CDCl<sub>3</sub>, 298 K).



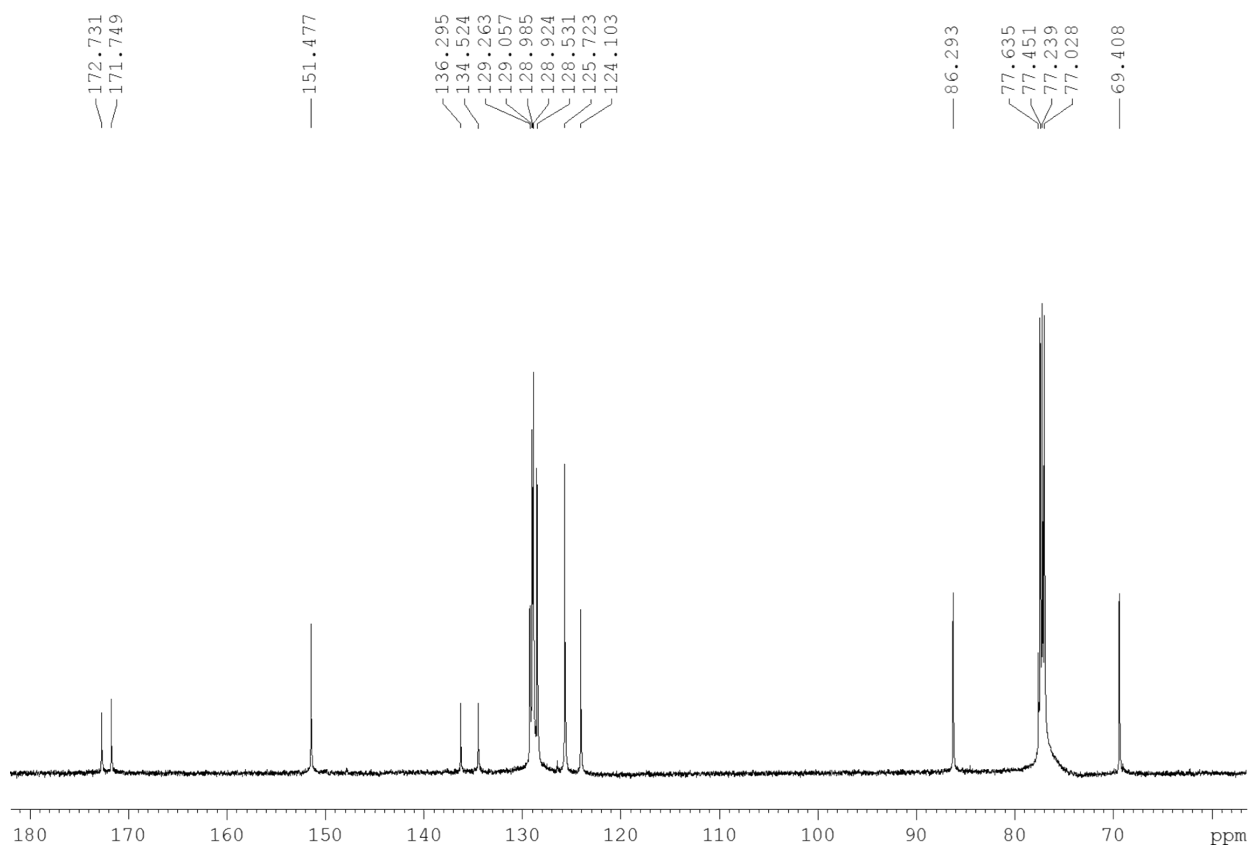


**Figure S23.**  $^{13}\text{C}$  NMR spectrum of *anti* isomer of derivative **8c** (150 MHz,  $\text{CDCl}_3$ , 298 K).

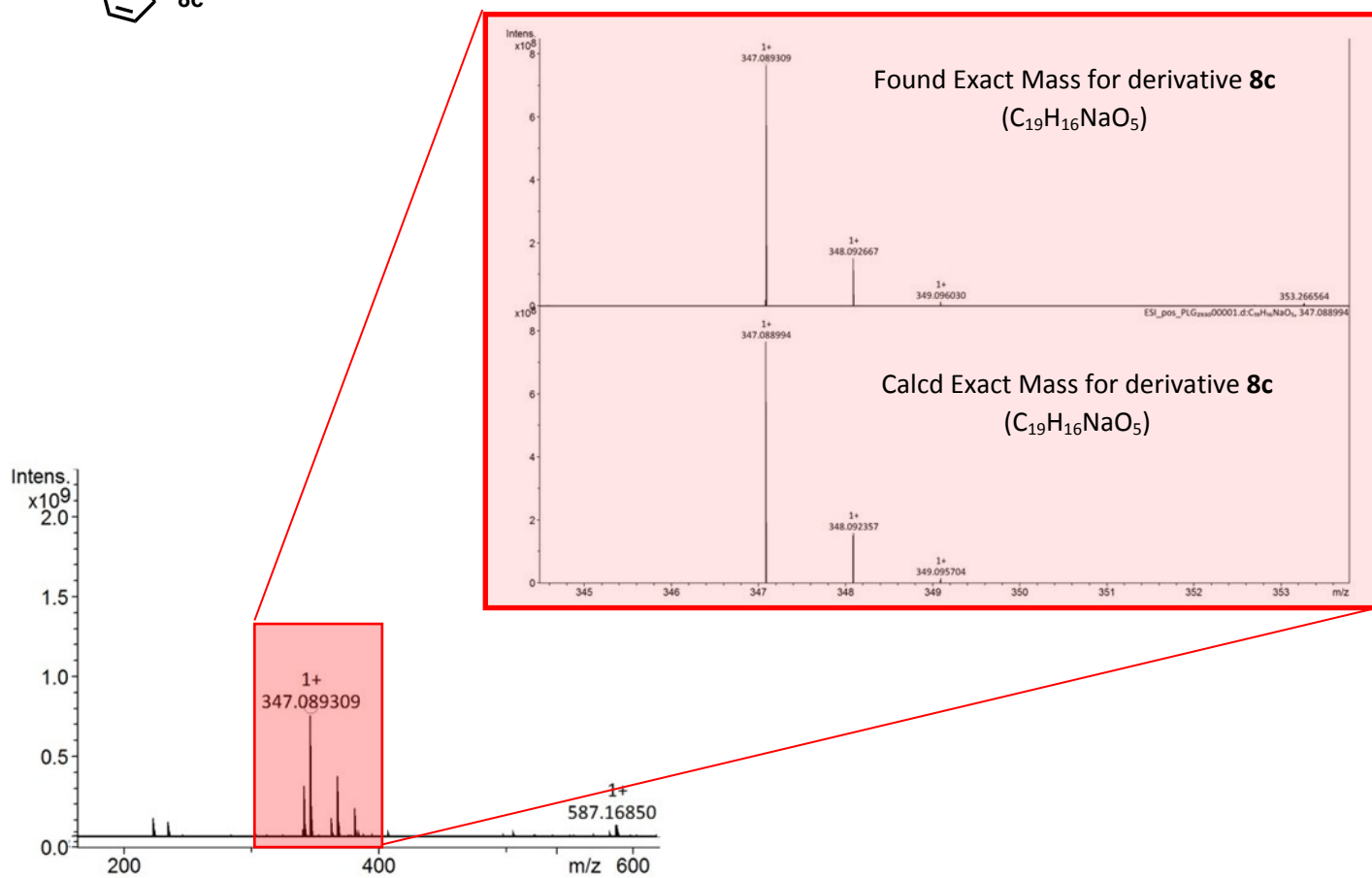
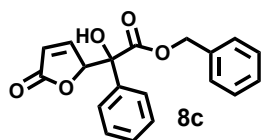
## Syn Isomer



**Figure S24.** <sup>1</sup>H NMR spectrum of *syn* isomer of derivative **8c** (400 MHz, CDCl<sub>3</sub>, 298 K).

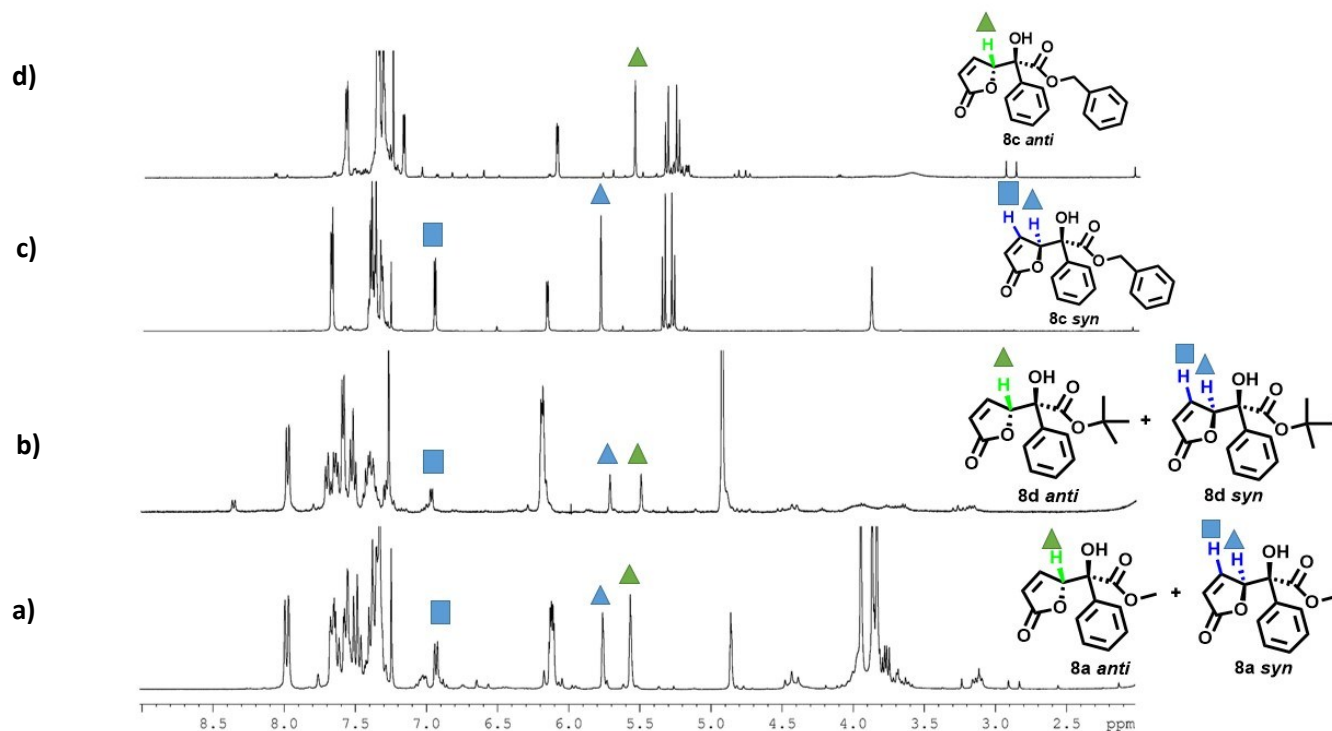


**Figure S25.**  $^{13}\text{C}$  NMR spectrum of *syn* isomer of derivative **8c** (100 MHz,  $\text{CDCl}_3$ , 298 K).



**Figure S26.** ESI Mass Spectrum of derivative **8c**.

## Determination of the relative configuration of **8c** based on the comparison $^1\text{H}$ -NMR data with known **8a** and **8d**



**Figure S27.** Representative sections of  $^1\text{H}$ -NMR spectra (400 MHz,  $\text{CDCl}_3$ , 298 K) : a) crude VMAR reaction mixture of **8a** ; b) crude VMAR reaction mixture of **8d**; c) isolated *syn*-**8c**; d) isolated *anti*-**8c**. The relative configuration of **8c** was assigned based on the comparison of  $^1\text{H}$ -NMR characteristic chemical shifts of -CH methine resonances (*anti* and *syn* diastereomers were indicated with green and blue triangles, respectively), and CH olefinic protons (*anti* and *syn* diastereomers were indicated with blue squares).

## $^1\text{H}$ NMR titrations of **7a** and **7b** with catalyst **1**

The following standard procedure was used.

**Host solution.** A 3.2 mM  $\text{CDCl}_3$  solution of catalyst **1** was prepared (2.00 mL).

In 0.5 mL of *host solution*, derivative **7a** was dissolved (*solution 7a*).

0.4 mL of host solution, in a NMR tube, was titrated with *solution 7a* in the concentration range indicated below.

[**1**] = 3.2 mM. [**7a**] concentration range during titration: 0.00-2.50 mM.

In 0.5 mL of *host solution*, derivative **7b** was dissolved (*solution 7b*).

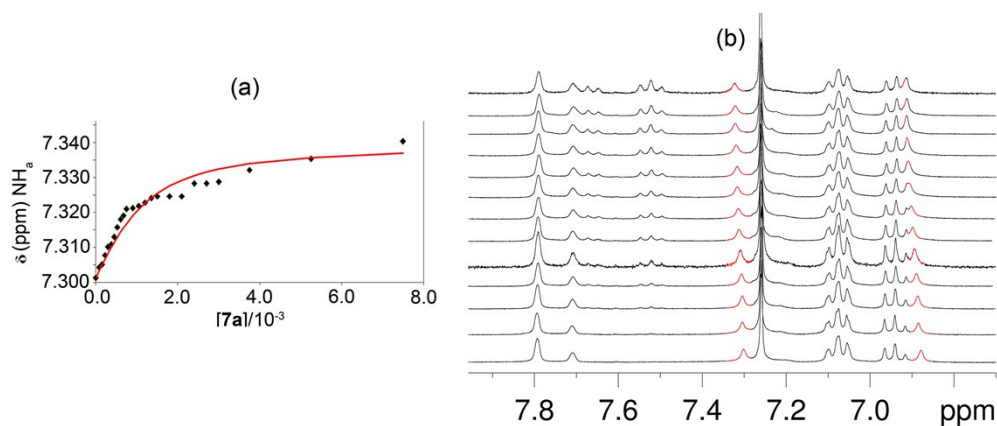
0.4 mL of host solution, in a NMR tube, was titrated with *solution 7b* in the concentration range indicated below.

[**1**] = 3.2 mM. [**7b**] concentration range during titration: 0.00-2.50 mM.

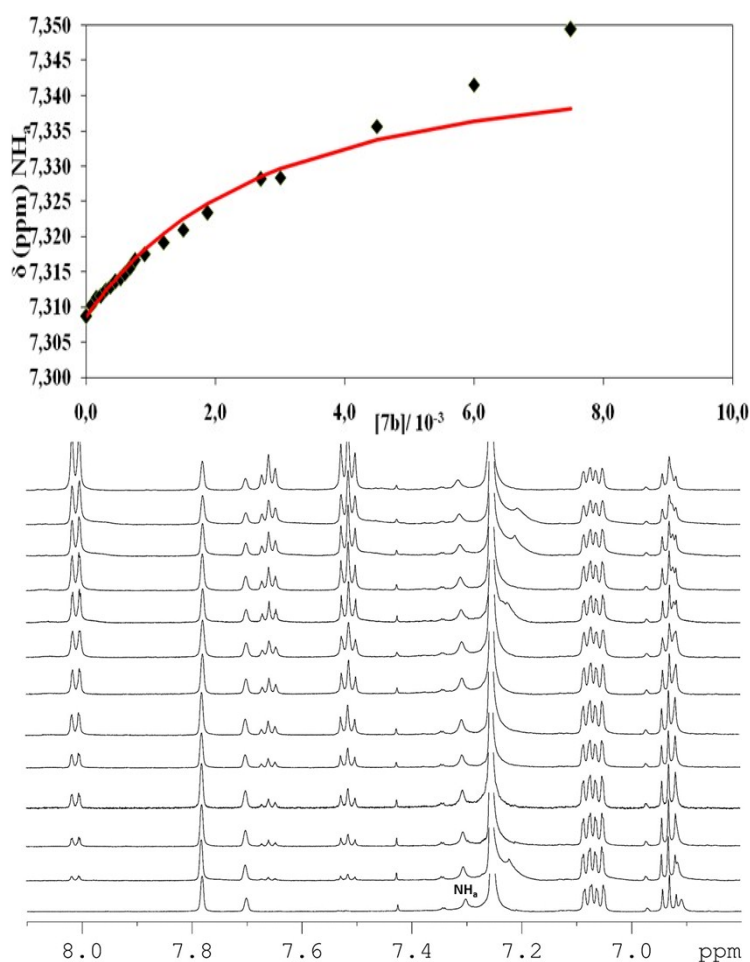
The titration data were analyzed by nonlinear least-squares fitting procedures<sup>8</sup> and in all cases a good fit of the experimental data with the theoretical model confirmed the 1:1 stoichiometry of the complexes.

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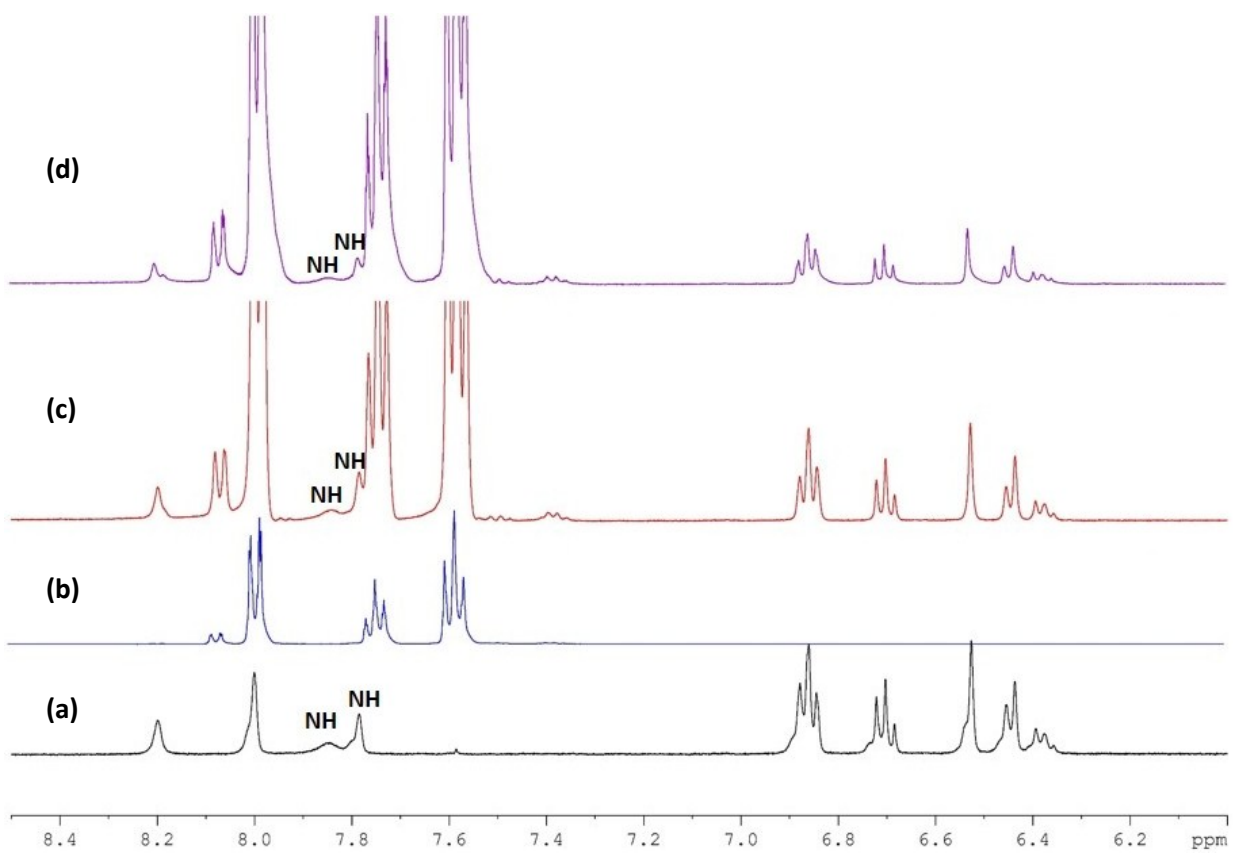
<sup>8</sup>Connors, K. A. *Binding Constants*; John Wiley & Sons: Chichester, 1987



**Figure S28.** (a) Plots of  $\delta$  for NH proton of **1** as a function of the concentration of **7a** ( $\text{CDCl}_3$ , 25 °C, 400 MHz). (b) Titration of **1** with **7a**. Aromatic region of the  $^1\text{H}$  NMR spectrum (400 MHz, 298 K) of **1** after addition of **7a** ( $[\mathbf{7a}]$  concentration range during titration: 0.00-2.50 mM, from bottom to top) (in red the NH signals of **1**).



**Figure S29. (Top)** Plot of the chemical shift of a NH proton of catalyst **1** (3.2 mM in 0.5 mL  $\text{CDCl}_3$  at 298 K) versus  $[\mathbf{7b}]/10^{-3}$  at 25 °C in  $\text{CDCl}_3$ . (Bottom) Titration of **1** with **7b**. Aromatic region of the  $^1\text{H}$  NMR spectrum (400 MHz, 298 K) of **1** after addition of **7b** ( $[\mathbf{7b}]$  concentration range during titration: 0.00-2.50 mM, from bottom to top) (in red the NH signals of **1**)



**Figure S30.** Aromatic region of the <sup>1</sup>H NMR spectrum (400 MHz, CD<sub>3</sub>CN) : (a) of **1**; (b) of **7a**; (c) of **1** after added of 4 equiv of **7a**; (d) of **1** after added of 8 equiv of **7a**.