

# Electronic Supplementary Information

## Nano onions based on an amphiphilic $\text{Au}_3(\text{pyrazolate})_3$ complex

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## 1 General

All chemicals were obtained from commercial sources and used without further purification unless stated otherwise.

NMR spectra were measured on a Bruker Avance III HD spectrometer ( $^1\text{H}$ : 400 MHz) equipped with a BBFO-Plus<sub>z</sub> 5 mm probe or on a Bruker Avance III HD spectrometer ( $^1\text{H}$ : 600 MHz) equipped with a CPPBBO<sub>z</sub> 5 mm probe.

High-resolution mass spectrometry was carried out using a hybrid ion trap-Orbitrap Fourier transform mass spectrometer, Orbitrap Elite (Thermo Scientific) equipped with a TriVersa Nanomate (Advion) nano-electrospray ionization source. MALDI spectra were recorded on a MALDI-TOF/TOF AutoFlex Speed spectrometer from Bruker, using graphite as a matrix.

Dynamic light scattering (DLS) and zeta potential measurements were performed on a Nano ZS from Malvern.

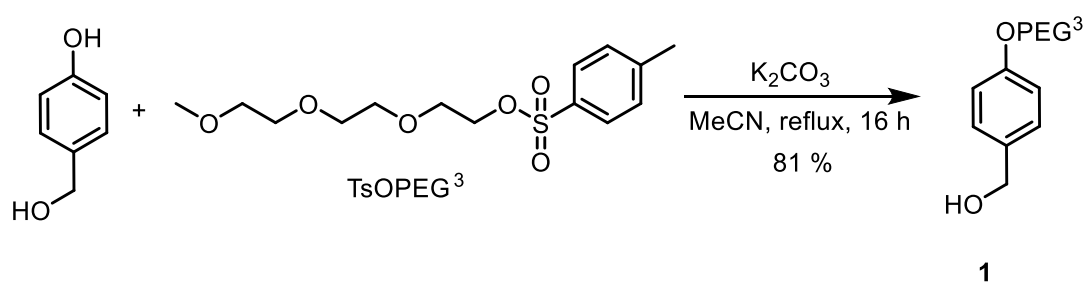
The emission spectra were measured on a Cary Eclipse fluorimeter.

The PEGylated precursor **1** was synthesized following a modified reported procedure.<sup>1</sup> Precursor **2** was synthesized following a reported procedure.<sup>2</sup>

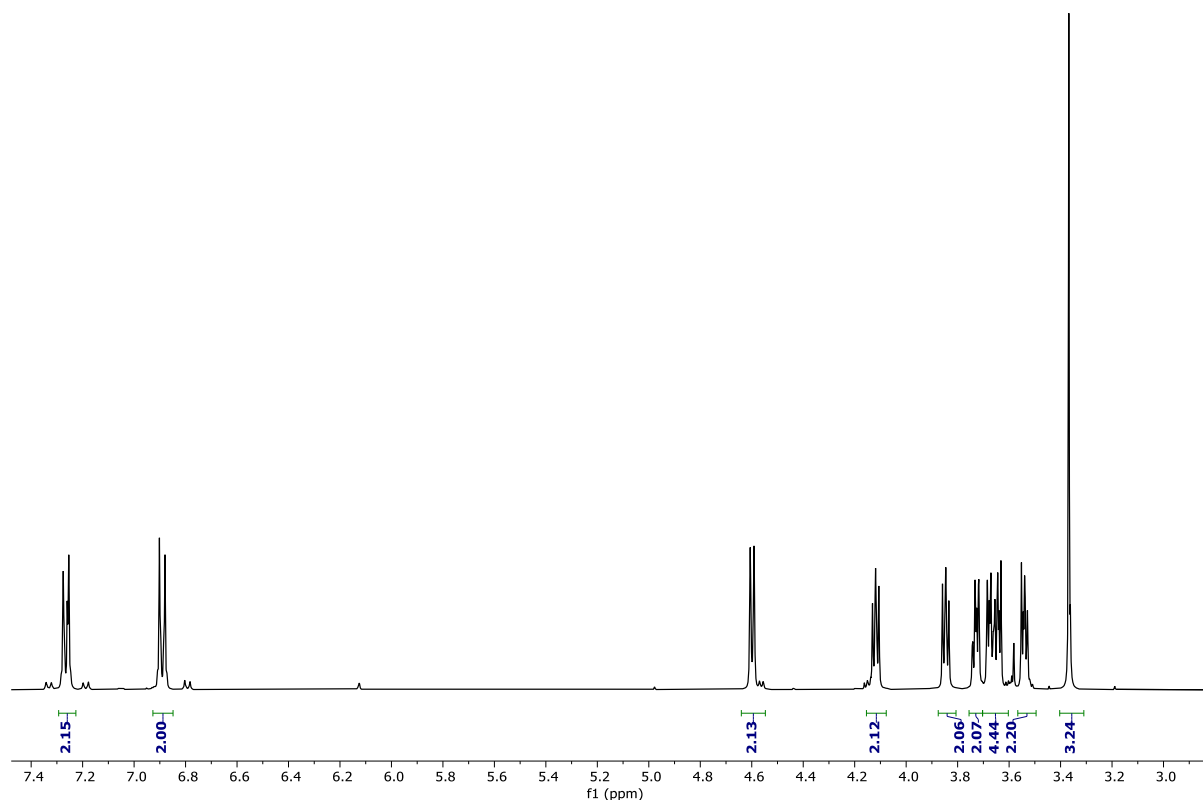
The gold complex  $\text{Au}_3(\text{L}3)$  was prepared in analogy to a known procedure.<sup>3</sup> The NMR data of the complex were in accordance to what was reported.

## 2 Synthesis of the precursors

### 2.1 Synthesis of compound **1**

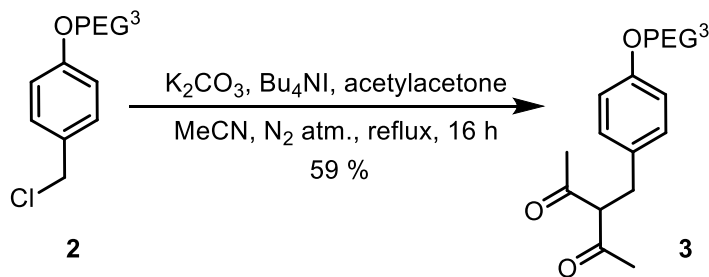


A mixture of 4-hydroxy benzyl alcohol (500 mg, 4.03 mmol, 1 eq.), TsOPEG<sup>3</sup> (1.28 g, 4.03 mmol, 1 eq.) and  $\text{K}_2\text{CO}_3$  (1.34 g, 9.67 mmol, 2.4 eq.) was placed in a round bottom flask equipped with a condenser. MeCN (40 mL) was added and the mixture was heated under reflux for 16 h. After allowing the mixture to reach room temperature, the white precipitate was filtered over silica, and the filtrate was concentrated under reduced pressure to give the product in the form of a light-yellow oil. Yield: 882 mg, 81%. The NMR data of **1** are in line with what was reported in the literature.<sup>1</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 – 7.22 (m, 2H), 6.93 – 6.85 (m, 2H), 4.60 (d,  $J = 5.8$  Hz, 2H), 4.12 (dd,  $J = 5.7, 4.1$  Hz, 2H), 3.85 (dd,  $J = 5.7, 4.1$  Hz, 2H), 3.77 – 3.70 (m, 2H), 3.70 – 3.62 (m, 4H), 3.57 – 3.50 (m, 2H), 3.37 (s, 3H).



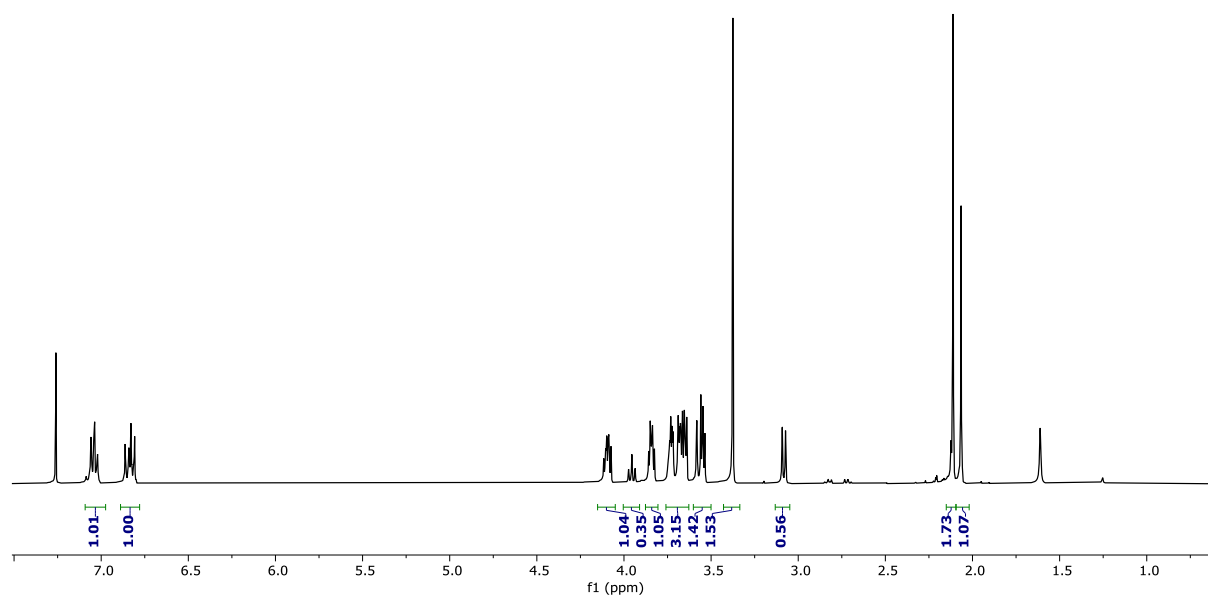
**Figure S1.**  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ , 400 MHz) of compound **1**.

## 2.2 Synthesis of compound **3**

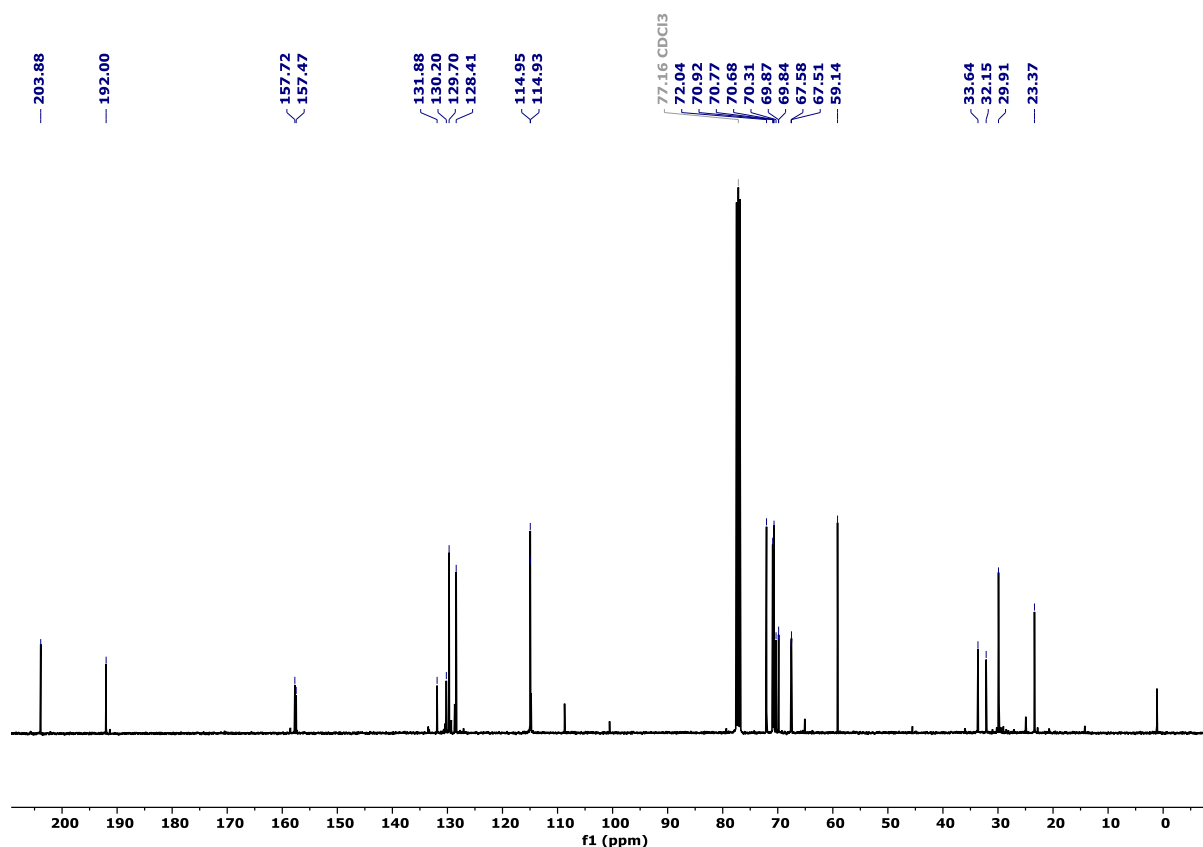


A mixture of **2** (400 mg, 1.38 mmol, 1 eq.), tetrabutylammonium iodide (52 mg, 0.14 mmol, 0.1 eq.),  $\text{K}_2\text{CO}_3$  (1.15 g, 8.31 mmol, 6 eq.) and acetylacetone (143  $\mu\text{L}$ , 1.38 mmol, 1 eq.) in anhydrous acetonitrile (15 mL) was placed in a two-neck flask equipped with a condenser. The mixture was heated under reflux under  $\text{N}_2$  overnight. The solvent was removed under reduced pressure and  $\text{CHCl}_3$  (100 mL) was added. The precipitate was filtered off and the crude product was purified by column chromatography on silica gel, using hexane/EtOAc as eluent, with a gradient from 90/10 to 50/50 to give the product in the form of a light-yellow oil.  $R_f$  0.25. Yield: 290 mg, 59%.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.11 – 6.99 (m, 2H, overlapped,  $\text{H}_{\text{arom}}$ ), 6.89 – 6.78 (m, 2H, overlapped,  $\text{H}_{\text{arom}}$ ), 4.14 – 4.05 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.99 – 3.92 (m, 1H,  $\text{H}_{\text{acac}}$ , *keto-form*), 3.88 – 3.80 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.77 – 3.62 (m, 6H,  $\text{H}_{\text{peg}}$ ), 3.60 – 3.51 (m, 3H,

overlapped, H<sub>peg</sub>, H<sub>benzyl</sub>, *enol-form*), 3.38 (s, 3H, H<sub>peg</sub>), 3.08 (d, *J* = 7.5 Hz, 1H, H<sub>benzyl</sub>, *keto-form*) 2.11 (s, 3H, H<sub>Me</sub>, *keto-form*), 2.07 (s, 3H, H<sub>Me</sub>, *enol-form*). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 203.88, 192.00, 157.72, 157.47, 131.88, 130.20, 129.70, 128.41, 114.95, 114.93, 72.04, 70.92, 70.77, 70.68, 70.31, 69.87, 69.84, 67.58, 67.51, 59.14, 33.64, 32.15, 29.91, 23.37. HRMS (ESI/Ion Trap) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>29</sub>O<sub>6</sub><sup>+</sup> 353.1959; Found 353.0761.

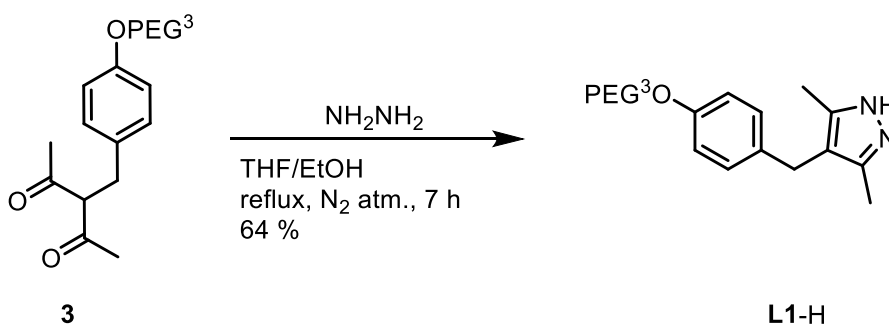


**Figure S2.** <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>, 400 MHz) of compound **3**.



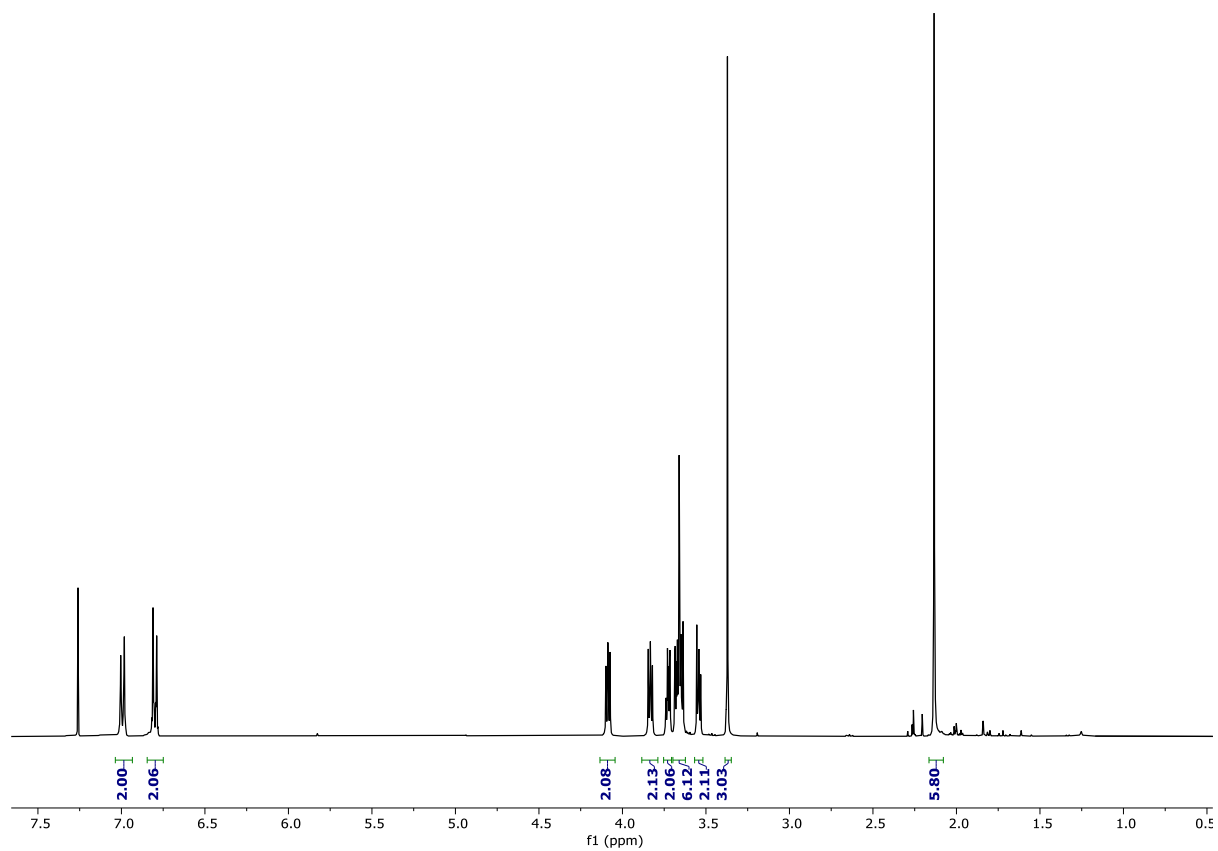
**Figure S3.**  $^{13}\text{C}$  NMR spectrum ( $\text{CDCl}_3$ , 101 MHz) of compound **3**.

### 2.3 Synthesis of L1-H

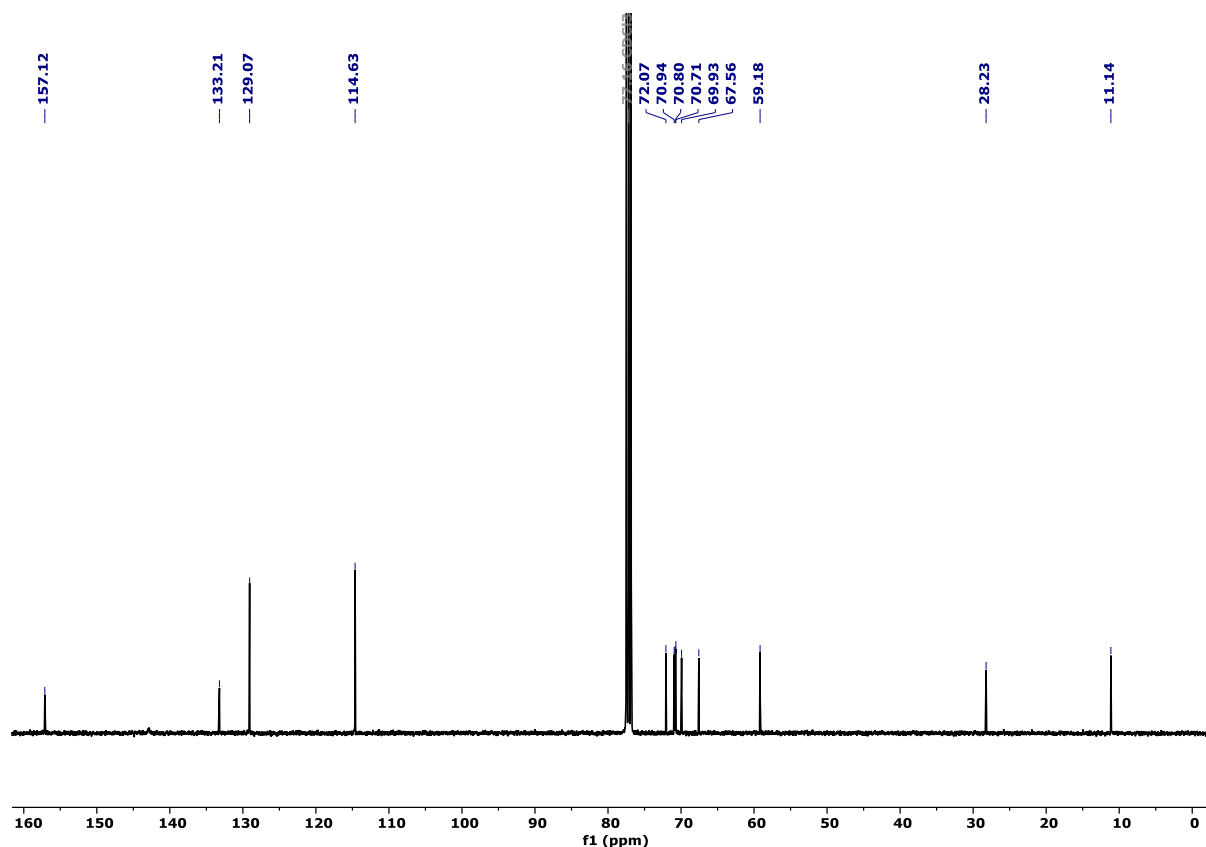


A mixture of **3** (150 mg, 0.42 mmol, 1 eq.) and hydrazine hydrate ( $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$ ) (0.15 mL, 2.30 mmol, 8.4 eq.), absolute EtOH (5 mL) and THF (5 mL) were added into a two-neck flask equipped with a condenser. The mixture was stirred at 70 °C overnight under an inert atmosphere. The volatiles were removed under reduced pressure and the product was further dried under high vacuum. The crude was purified by column chromatography on  $\text{SiO}_2$  with EtOAc as eluent to give the product in the form of a light-yellow oil.  $R_f = 0.17$ . Yield: 94 mg, 64%.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.03 – 6.95 (m, 2H,  $\text{H}_{\text{arom}}$ ), 6.80 (d,  $J = 8.6$  Hz, 2H,  $\text{H}_{\text{arom}}$ ), 4.09 (dd,  $J = 5.7, 4.2$  Hz, 2H,  $\text{H}_{\text{peg}}$ ), 3.87 – 3.80 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.76 – 3.70 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.70 – 3.62 (m, 6H,  $\text{H}_{\text{peg}}$ ,  $\text{H}_{\text{benzyl}}$ ), 3.59 – 3.51 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.37 (s, 3H,  $\text{H}_{\text{peg}}$ ), 2.13

(s, 6H, H<sub>Me-Pz</sub>). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 157.12, 133.21, 129.07, 114.63, 72.07, 70.94, 70.80, 70.71, 69.93, 67.56, 59.18, 28.23, 11.14. HRMS (ESI/QTOF) *m/z*: [M + Na]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>28</sub>NaO<sub>6</sub><sup>+</sup> 375.1778; Found 375.1779.

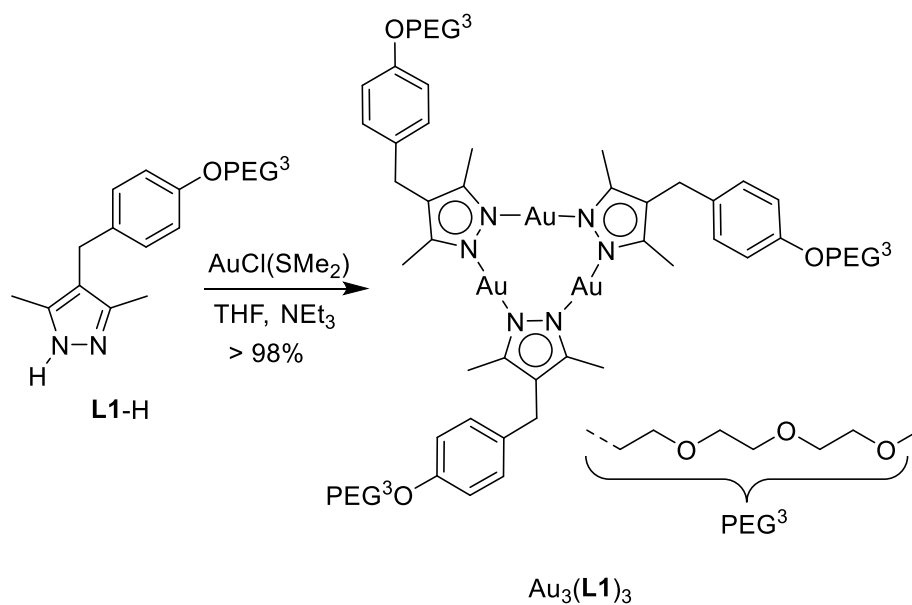


**Figure S4.** <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>, 400 MHz) of compound **L1-H**.



**Figure S5.**  $^{13}\text{C}$  NMR spectrum ( $\text{CDCl}_3$ , 101 MHz) of compound **L1-H**.

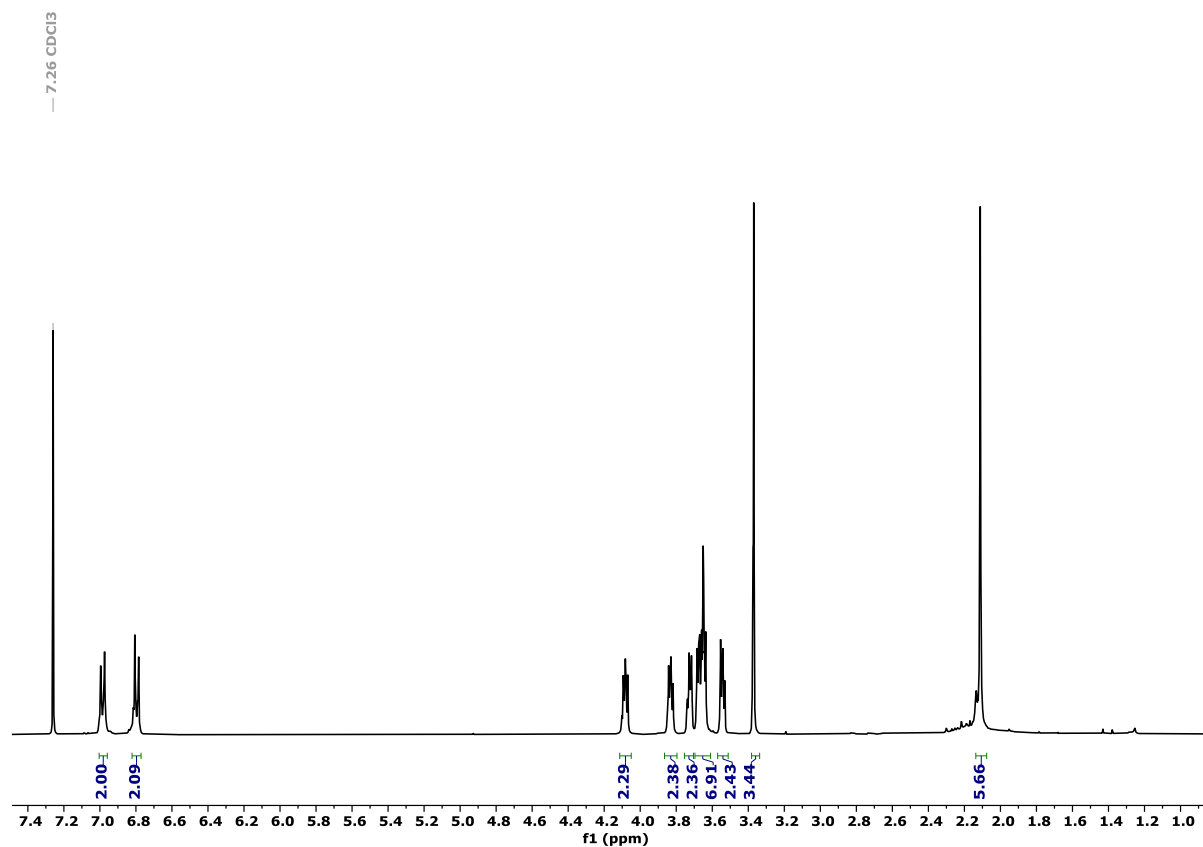
#### 2.4 Synthesis of $\text{Au}_3(\text{L1})_3$



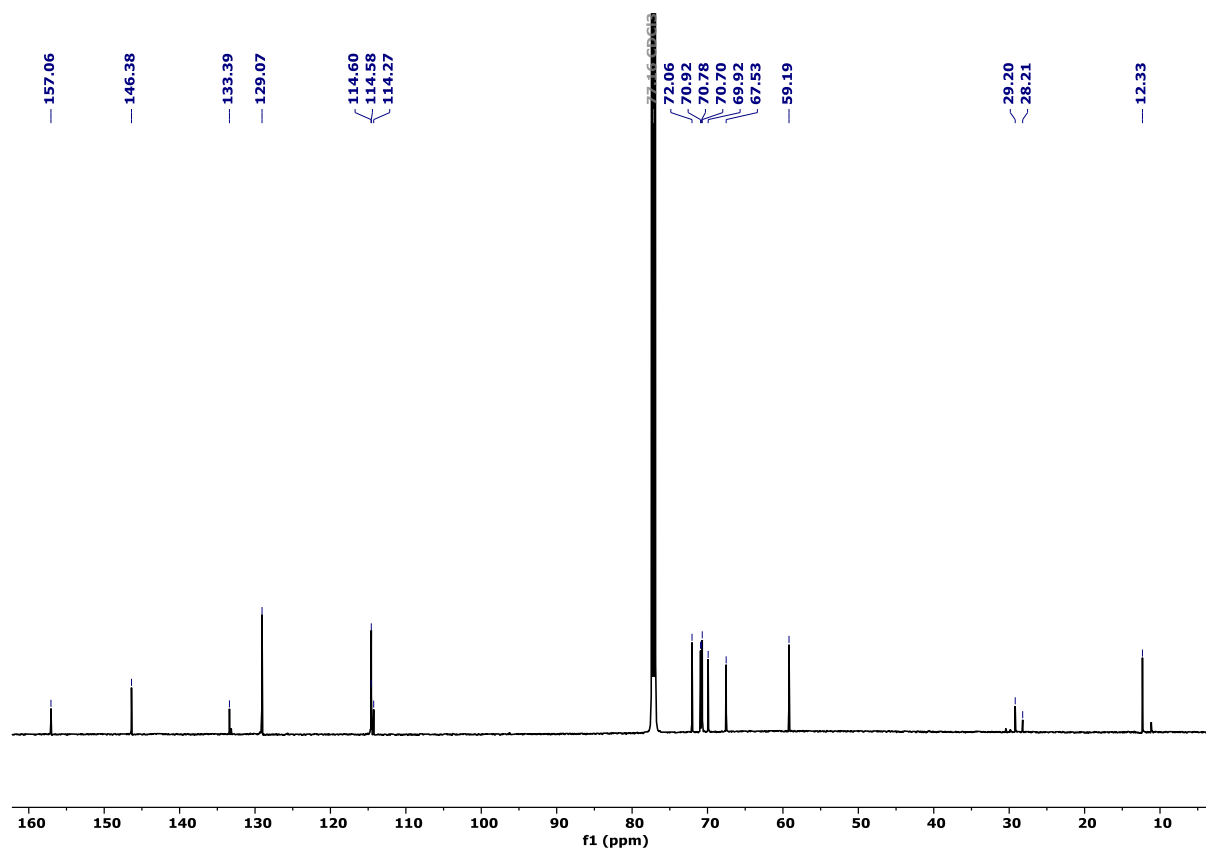
A solution of **L1-H** (348 mg, 0.44 mmol, 1 eq.) was prepared in THF (15 mL) in a round bottom flask.  $\text{NEt}_3$  (0.2 mL, excess) was added and the mixture was stirred at room temperature for 10 min.  $\text{Au}(\text{SMe}_2)\text{Cl}$  (128 mg, 0.44 mmol, 1 eq.) was added and the mixture was stirred for 16 h at room temperature. All solids were removed by filtration. The filtrate was dried under reduced pressure and redissolved in  $\text{CH}_2\text{Cl}_2$  and filtered over celite. The solvent was removed under reduced pressure and



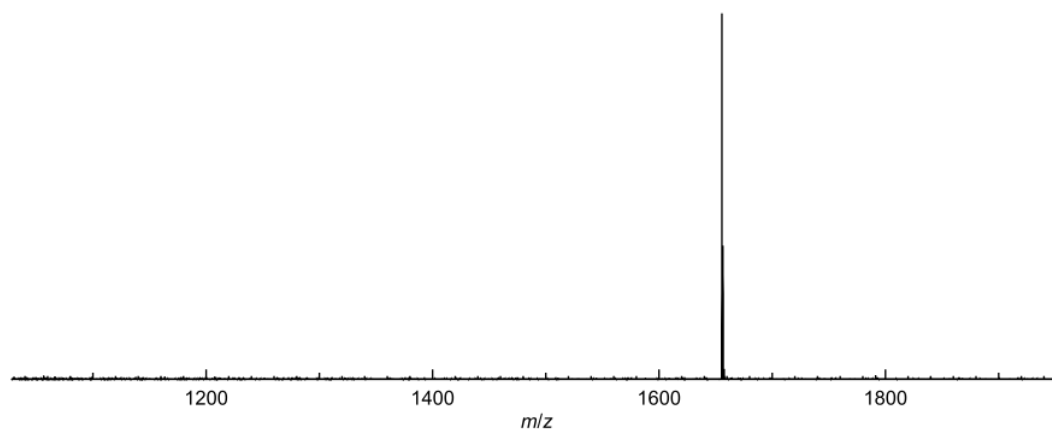
the product was further dried under high vacuum to give the product in the form of a white solid. Yield: 202 mg, 85%.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.00 – 6.96 (m, 2H,  $\text{H}_{\text{arom}}$ ), 6.81 – 6.77 (m, 2H,  $\text{H}_{\text{arom}}$ ), 4.11 – 4.05 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.86 – 3.80 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.73 (ddd,  $J = 5.1, 3.2, 1.1$  Hz, 2H,  $\text{H}_{\text{peg}}$ ), 3.69 – 3.62 (m, 6H,  $\text{H}_{\text{benzyl}}$ ,  $\text{H}_{\text{peg}}$ ), 3.57 – 3.52 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.37 (s, 3H,  $\text{H}_{\text{peg}}$ ), 2.11 (s, 6H,  $\text{H}_{\text{Me-Pz}}$ ).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  157.06, 146.38, 133.39, 129.07, 114.60, 114.58, 114.27, 72.06, 70.92, 70.78, 70.70, 69.92, 67.53, 59.19, 29.20, 28.21, 12.33. MALDI/TOF  $m/z$ :  $[\text{M} + \text{Na}]^+$  Calcd for  $\text{C}_{57}\text{H}_{81}\text{Au}_3\text{N}_6\text{NaO}_{12}^+$  1655.5; Found 1655.6. HRMS (ESI/QTOF)  $m/z$ :  $[\text{M} + \text{Na}]^+$  Calcd for  $\text{C}_{57}\text{H}_{81}\text{Au}_3\text{N}_6\text{NaO}_{12}^+$  1655.4802; Found 1655.4839.



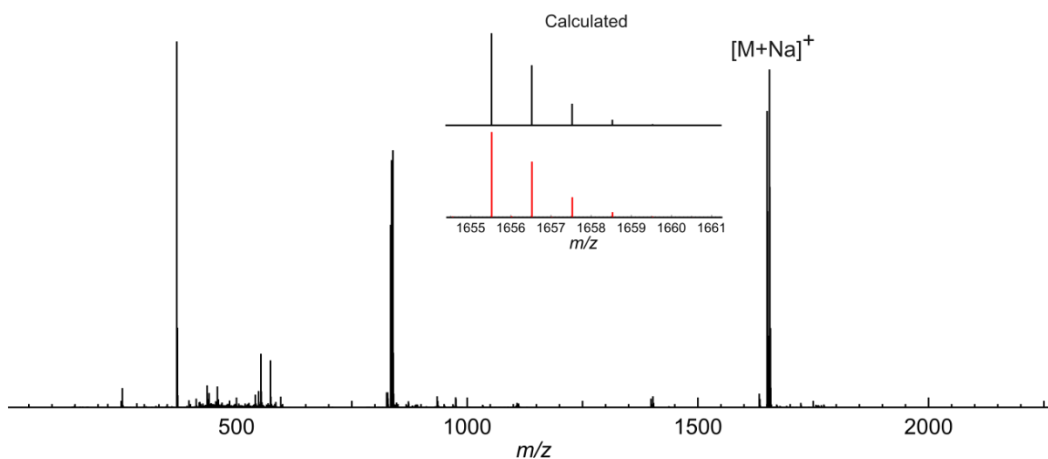
**Figure S6.**  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ , 400 MHz) of complex  $\text{Au}_3(\text{L}1)_3$ .



**Figure S7.**  $^{13}\text{C}$  NMR spectrum ( $\text{CDCl}_3$ , 151 MHz) of complex  $\text{Au}_3(\text{L1})_3$ .

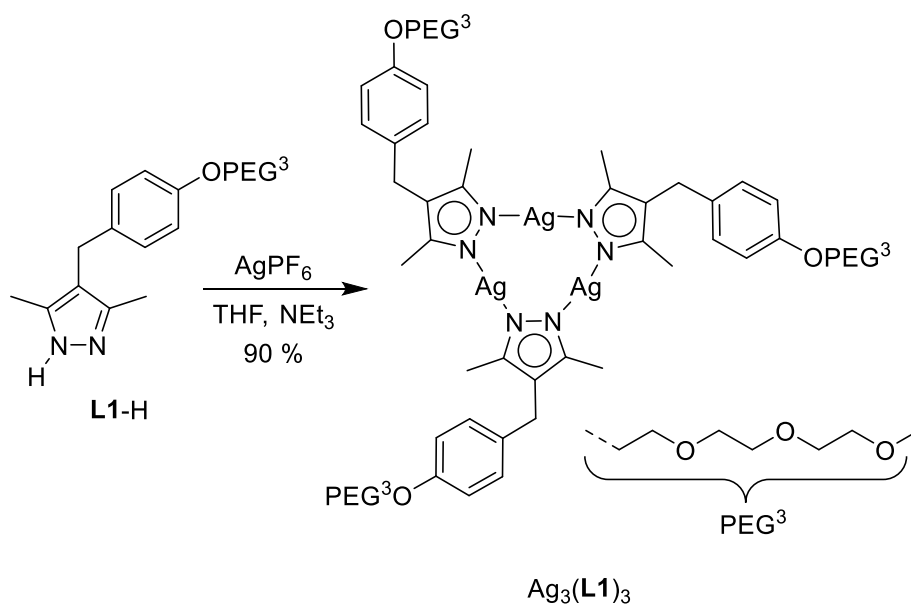


**Figure S8.** MALDI spectrum of  $\text{Au}_3(\text{L1})_3$ .



**Figure S9.** HRMS spectrum of  $\text{Au}_3(\text{L1})_3$ .

### 2.5 Synthesis of $\text{Ag}_3(\text{L1})_3$



A solution of **L1-H** (10.0 mg, 0.05 mmol, 1 eq.) was prepared in anhydrous THF (3 mL) under inert atmosphere.  $\text{NEt}_3$  (7.5  $\mu\text{L}$ , 1 eq.) was added and the mixture was stirred at room temperature for 10 min.  $\text{AgPF}_6$  (14 mg, 0.05 mmol, 1 eq.) was added and the mixture was stirred at room temperature for 16 h, shielded from light. The precipitate was filtered off and the filtrate was dried under reduced pressure to give the product in the form of a light-yellow oil. Yield: 246 mg, 90%.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.00 (d,  $J = 8.5$  Hz, 2H,  $\text{H}_{\text{arom}}$ ), 6.83 – 6.75 (m, 2H,  $\text{H}_{\text{arom}}$ ), 4.08 (dd,  $J = 5.8, 4.2$  Hz, 2H,  $\text{H}_{\text{peg}}$ ), 3.83 (dd,  $J = 5.7, 4.2$  Hz, 2H,  $\text{H}_{\text{peg}}$ ), 3.76 – 3.69 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.68 (m, 6H,  $\text{H}_{\text{benzyl}}$ ,  $\text{H}_{\text{peg}}$ ), 3.59 – 3.51 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.37 (s, 3H,  $\text{H}_{\text{peg}}$ ), 2.07 (s, 6H,  $\text{H}_{\text{Me-Pz}}$ ).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  156.92, 147.64, 134.05, 129.07, 114.52, 112.49, 72.03, 70.90, 70.74, 70.66, 69.91, 67.53, 59.14, 29.04, 12.85. MALDI/TOF  $m/z$ :  $[\text{M} + \text{Na}]^+$  Calcd for  $\text{C}_{57}\text{H}_{81}\text{Ag}_3\text{N}_6\text{NaO}_{12}^+$  1385.3; Found 1385.6.

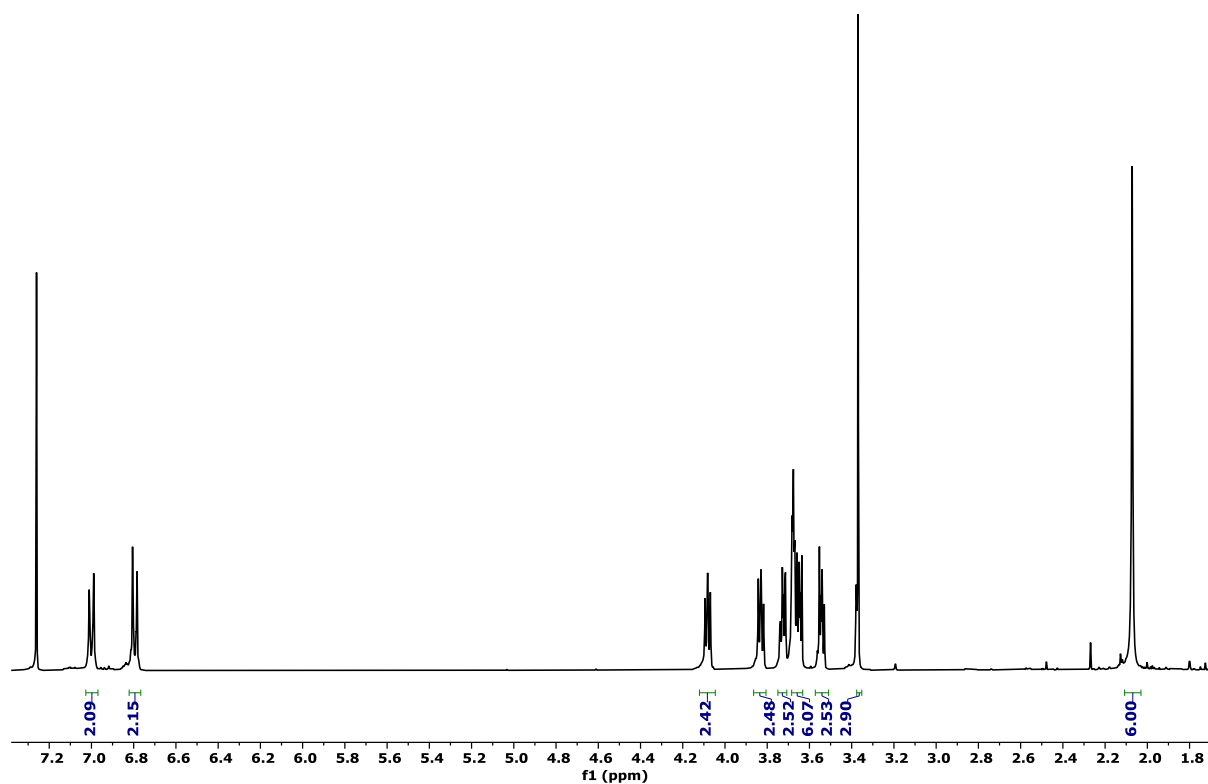


Figure S10.  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ , 400 MHz) of complex  $\text{Ag}_3(\text{L1})_3$ .

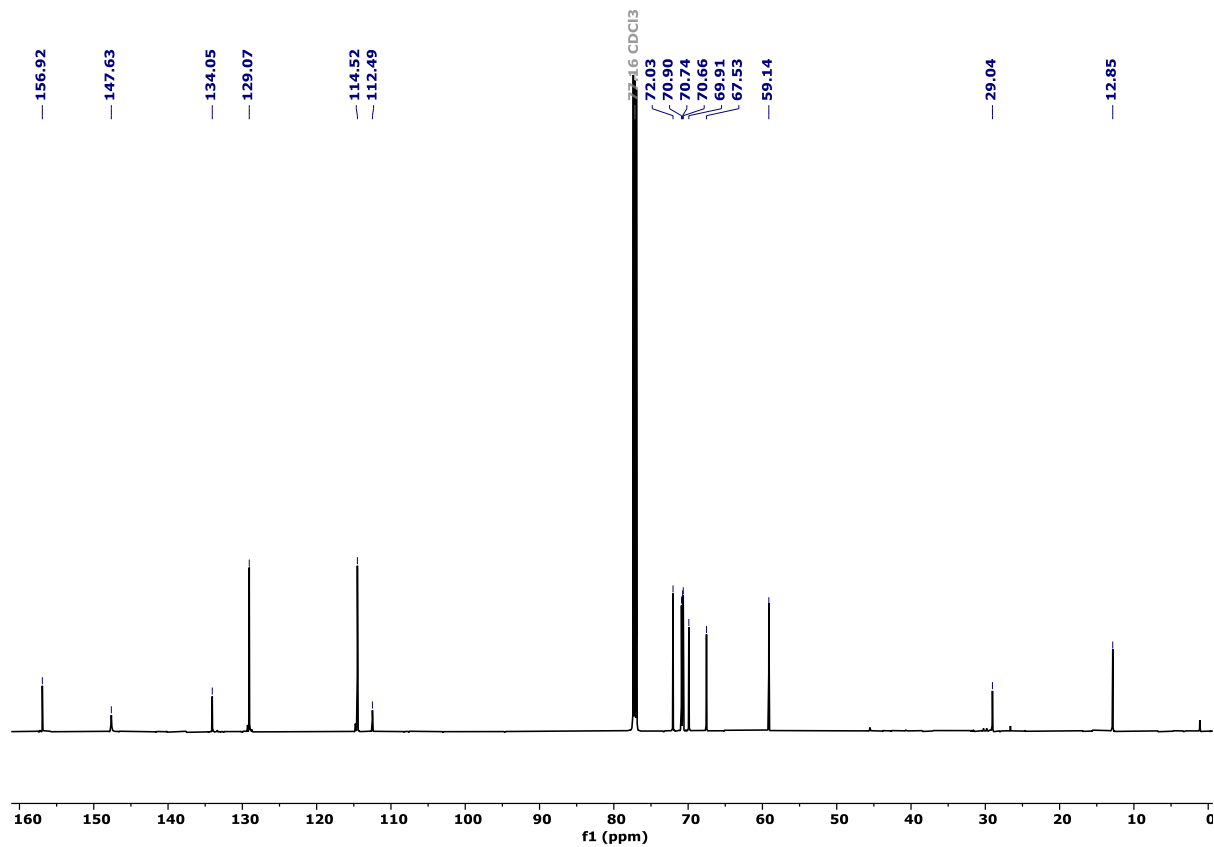
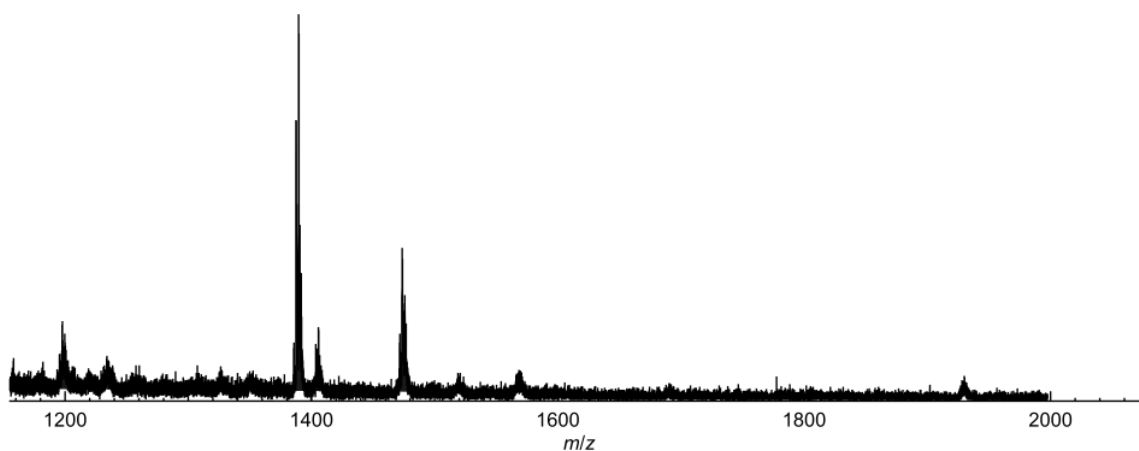
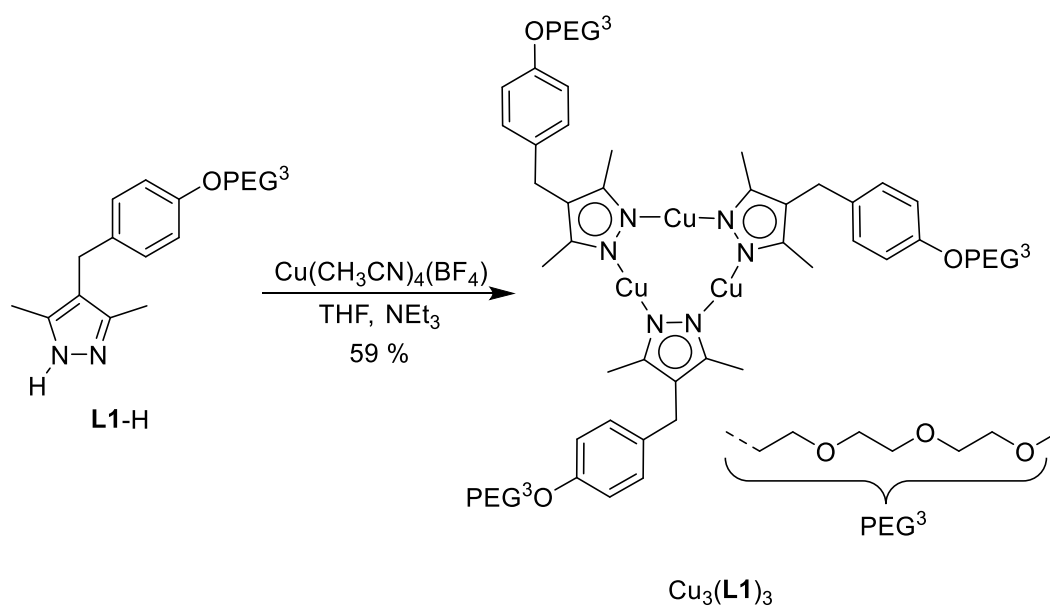


Figure S11.  $^{13}\text{C}$  NMR spectrum ( $\text{CDCl}_3$ , 151 MHz) of complex  $\text{Ag}_3(\text{L1})_3$ .

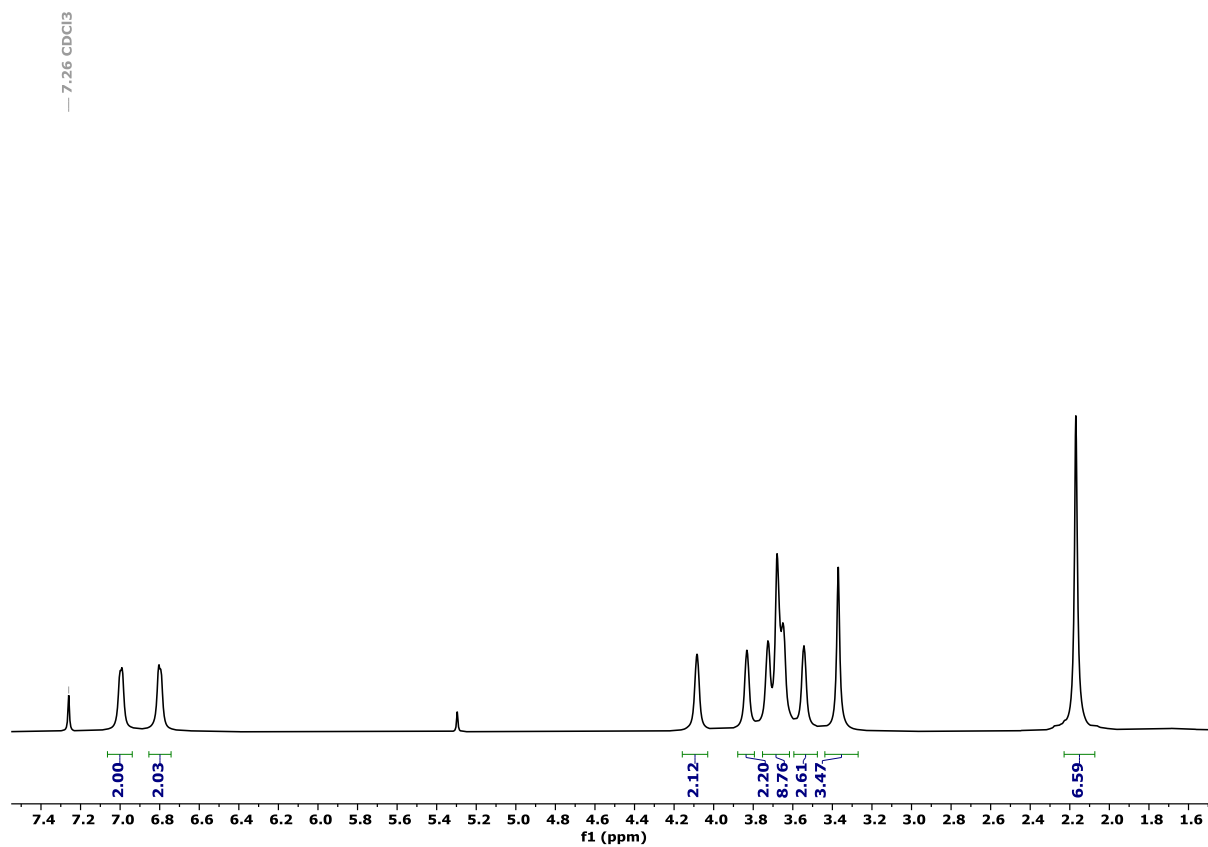


**Figure S12.** MALDI spectrum of  $\text{Ag}_3(\text{L1})_3$ .

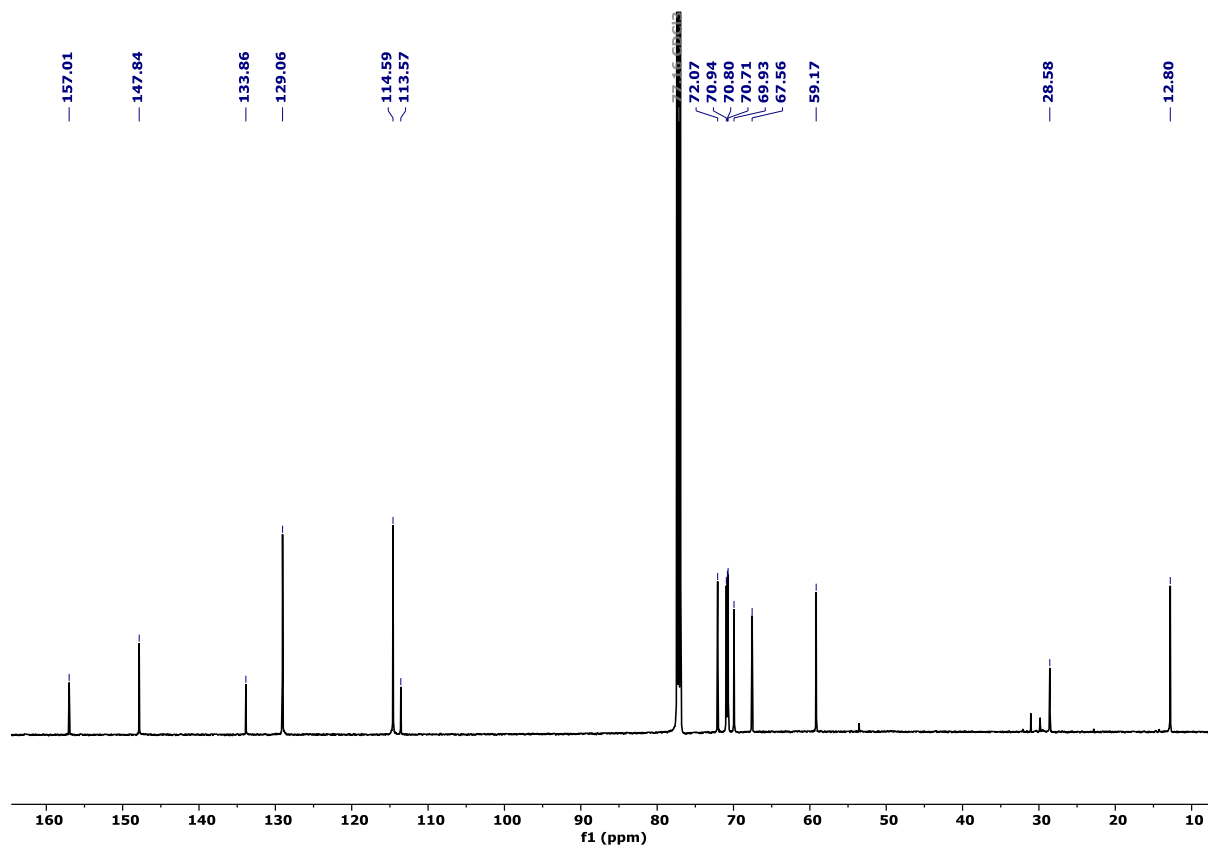
## 2.6 Synthesis of $\text{Cu}_3(\text{L1})_3$



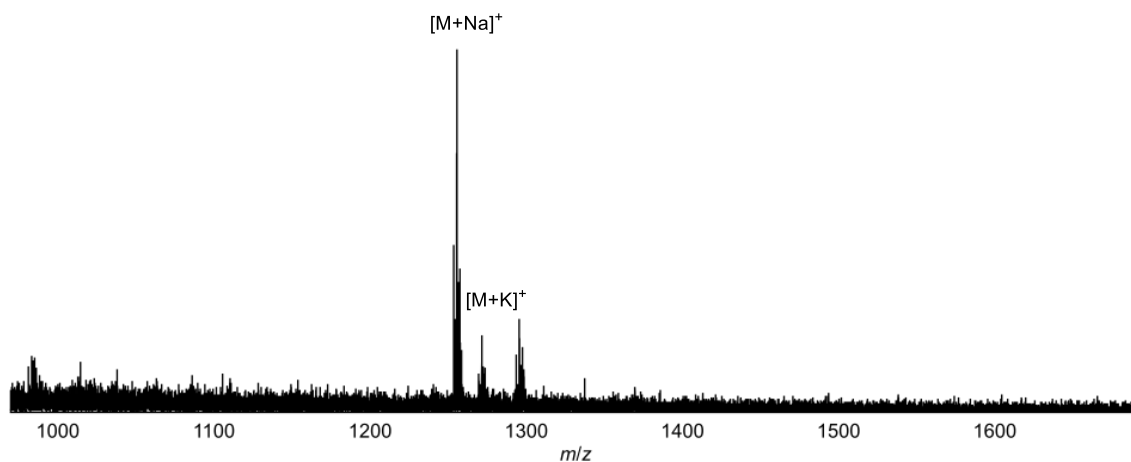
Under inert atmosphere, a solution of  $\text{NEt}_3$  (92  $\mu\text{L}$ , 0.7 mmol, 3.3 eq.) and **L1-H** (70 mg, 0.2 mmol, 1 eq.) was prepared in anhydrous THF (5 mL).  $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{BF}_4)$  (63 mg, 0.2 mmol, 1 eq.) was added and the mixture was stirred at room temperature for 16 h. The precipitate was filtered off and the filtrate was dried under reduced pressure to give the product in the form of a light-yellow oil. Yield: 48 mg, 59%.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.00 (d,  $J = 8.1$  Hz, 2H,  $\text{H}_{\text{arom}}$ ), 6.80 (d,  $J = 8.1$  Hz, 2H,  $\text{H}_{\text{arom}}$ ), 4.08 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.88 – 3.73 (m, 2H,  $\text{H}_{\text{peg}}$ ), 3.73 – 3.53 (m, 6H,  $\text{H}_{\text{benzyl}}$ ,  $\text{H}_{\text{peg}}$ ), 3.37 (s, 3H,  $\text{H}_{\text{peg}}$ ), 2.17 (s, 6H,  $\text{H}_{\text{Me-Pz}}$ ).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  157.01, 147.84, 133.86, 129.06, 114.59, 113.57, 72.07, 70.94, 70.80, 70.71, 69.93, 67.56, 59.17, 28.58, 12.80. MALDI/TOF  $m/z$ :  $[\text{M} + \text{Na}]^+$  Calcd for  $\text{C}_{57}\text{H}_{81}\text{Cu}_3\text{N}_6\text{NaO}_{12}^+$  1253.4; Found 1253.7.



**Figure S13.** <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>, 600 MHz) of complex Cu<sub>3</sub>(L1)<sub>3</sub>.

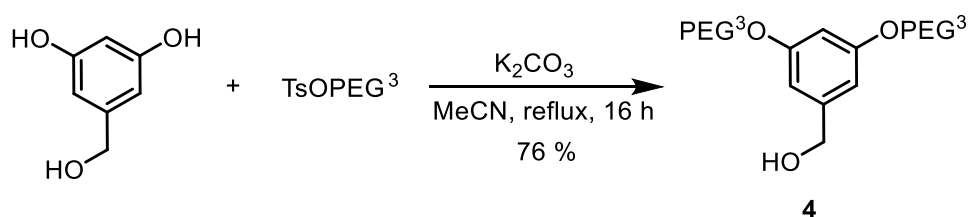


**Figure S14.** <sup>13</sup>C NMR spectrum CDCl<sub>3</sub>, 151 MHz) of complex Cu<sub>3</sub>(L1)<sub>3</sub>.



**Figure S15.** MALDI spectrum of  $\text{Cu}_3(\text{L1})_3$ .

## 2.7 Synthesis of compound **4**



A mixture of 3,5-dihydroxybenzyl alcohol (500 mg, 3.57 mmol, 1 eq.), TsOPEG<sup>3</sup> (2.272 g, 7.136 mmol, 2 eq.) and K<sub>2</sub>CO<sub>3</sub> (2.367 g, 17.13 mmol, 4.8 eq.) was placed in a round bottom flask equipped with a condenser. MeCN (40 mL) was added and the mixture was heated under reflux for 16 h. After allowing the mixture to reach room temperature, the white precipitate was filtered over silica and the filtrate was concentrated under reduced pressure to give the product in the form of a light-yellow oil. Yield: 1.175 g, 76%. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 6.49 (d, *J* = 2.3 Hz, 2H, H<sub>arom</sub>), 6.36 (t, *J* = 2.3 Hz, 1H, H<sub>arom</sub>), 4.55 (s, 2H, H<sub>benzyl</sub>), 4.06 (dd, *J* = 5.6, 3.9 Hz, 4H, H<sub>peg</sub>), 3.82 – 3.77 (m, 4H, H<sub>peg</sub>), 3.72 – 3.66 (m, 4H, H<sub>peg</sub>), 3.66 – 3.58 (m, 8H, H<sub>peg</sub>), 3.54 – 3.49 (m, 4H, H<sub>peg</sub>), 3.34 (s, 6H, H<sub>peg</sub>). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 159.97, 143.66, 105.39, 100.71, 71.89, 70.77, 70.62, 70.51, 69.71, 67.41, 65.01, 59.06. HRMS (ESI/QTOF) *m/z*: [M + Na]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>36</sub>NaO<sub>9</sub><sup>+</sup> 455.2252; Found 455.2244.

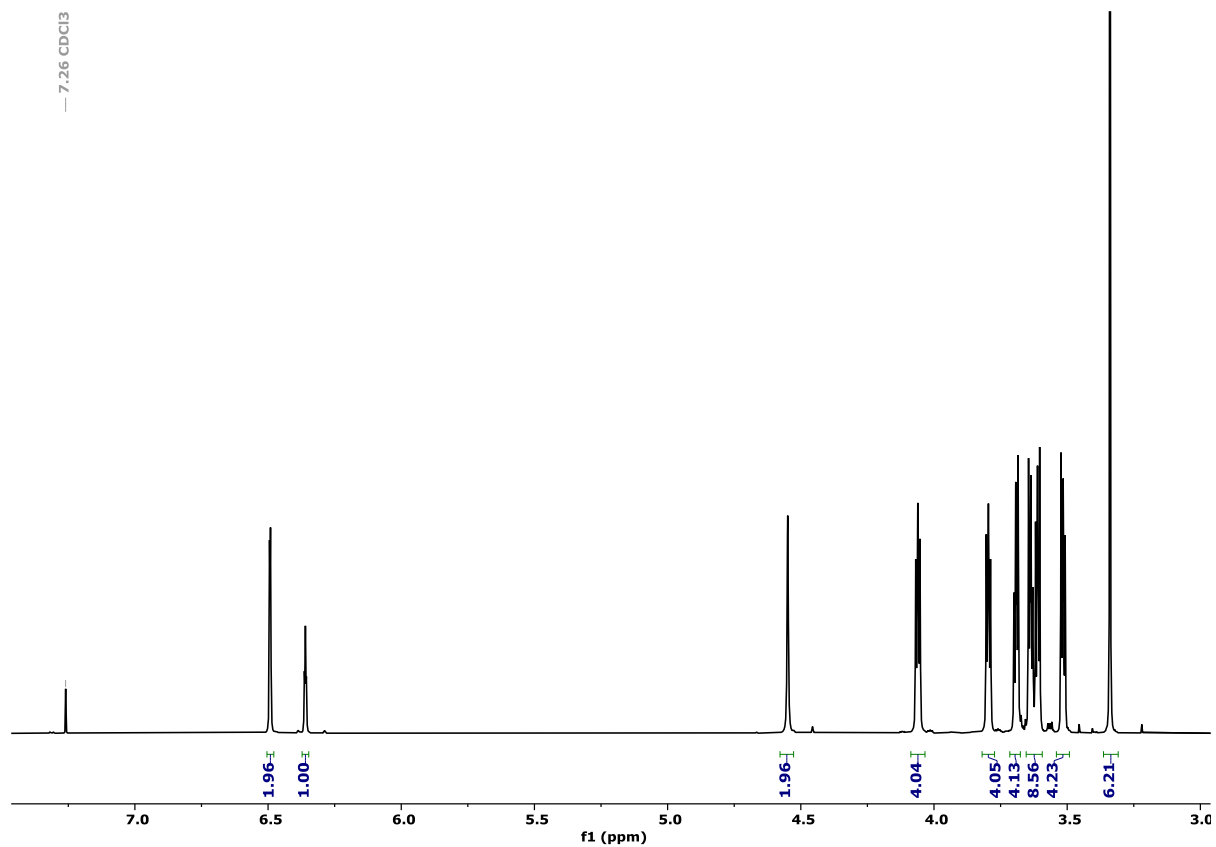


Figure S16. <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>, 600 MHz) of compound 4.

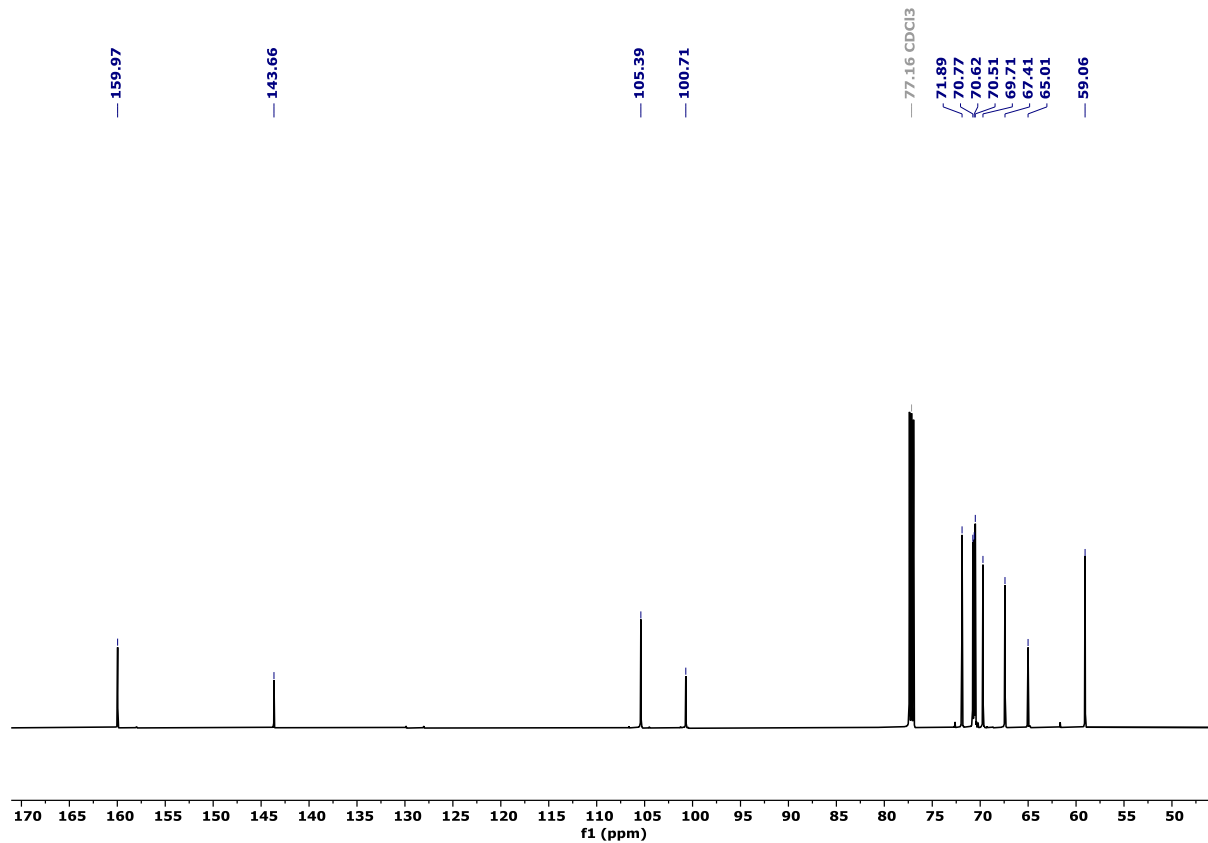
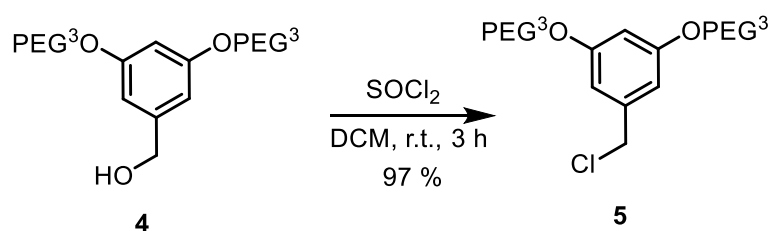


Figure S17. <sup>13</sup>C NMR spectrum (CDCl<sub>3</sub>, 151 MHz) of compound 4.



## 2.8 Synthesis of compound 5



The substrate **4** (500 mg, 1.85 mmol, 1 eq.) was placed in a round bottom flask. CH<sub>2</sub>Cl<sub>2</sub> (60 mL) was added, followed by the dropwise addition of SOCl<sub>2</sub> (600 μL, 963 mg, 8.09 mmol, 7 eq.) under stirring. The mixture was stirred at room temperature for 2.5 h. The volatiles were removed under reduced pressure and the product was dried under high vacuum to give the product in the form of a light-yellow oil. Yield: 506 mg, 97%. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.54 (d, *J* = 2.2 Hz, 2H, H<sub>arom</sub>), 6.44 (t, *J* = 2.3 Hz, 1H, H<sub>arom</sub>), 4.48 (s, 2H, H<sub>benzyl</sub>), 4.13 – 4.07 (m, 4H, H<sub>peg</sub>), 3.87 – 3.81 (m, 4H, H<sub>peg</sub>), 3.75 – 3.71 (m, 4H, H<sub>peg</sub>), 3.69 – 3.64 (m, 8H, H<sub>peg</sub>), 3.57 – 3.52 (m, 4H, H<sub>peg</sub>), 3.37 (s, 6H, H<sub>peg</sub>). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 160.18, 139.53, 107.51, 101.75, 72.07, 70.97, 70.80, 70.72, 69.78, 67.69, 59.18, 46.43. HRMS (ESI/QTOF) *m/z*: [M + Na]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>35</sub>ClNaO<sub>8</sub><sup>+</sup> 473.1913; Found 473.1921.

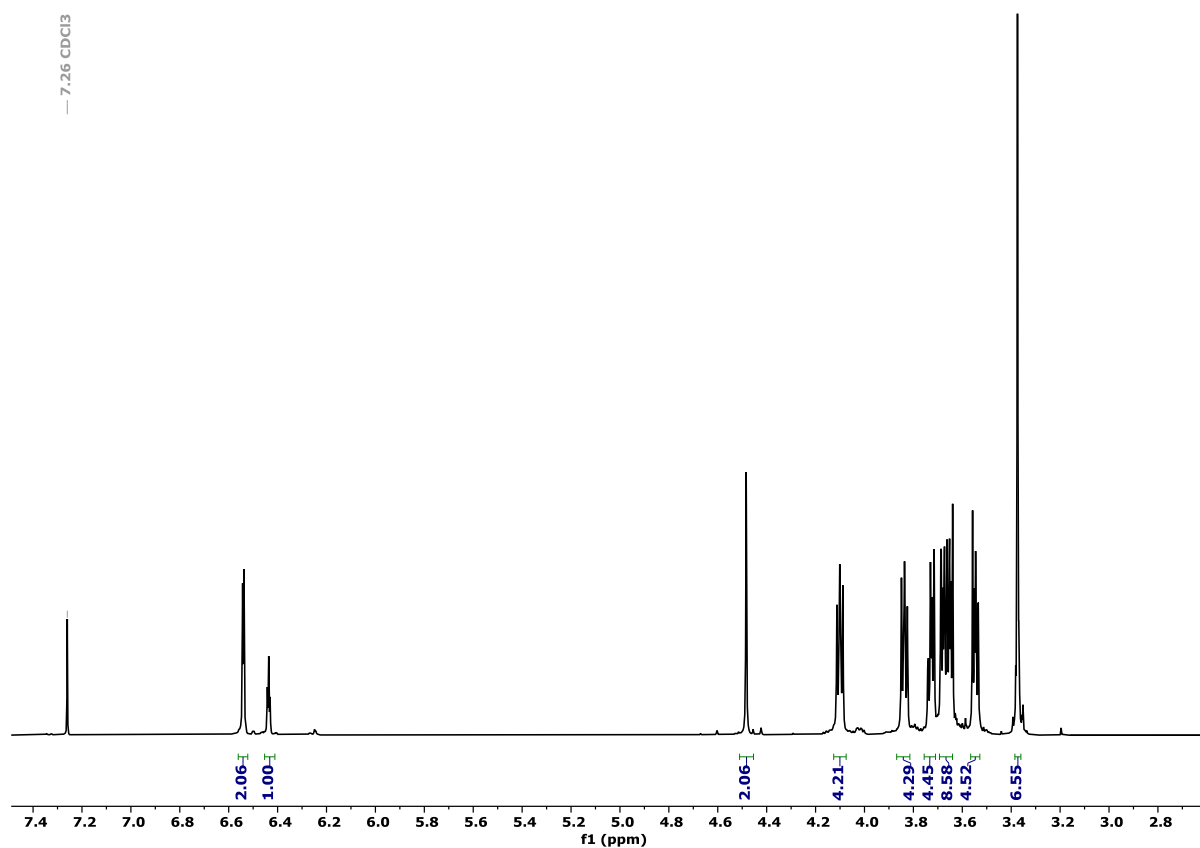
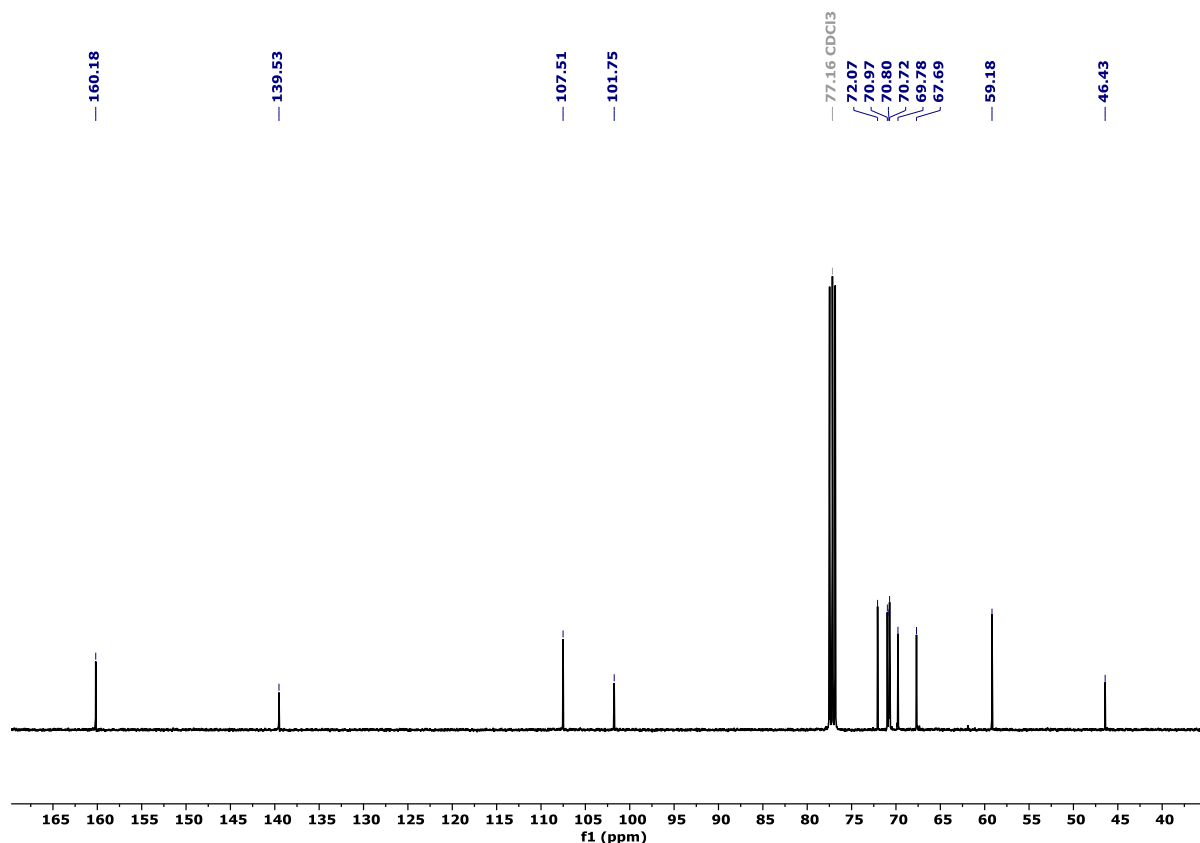
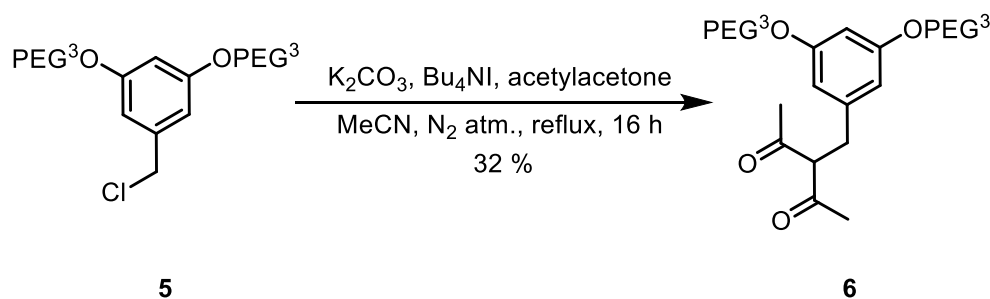


Figure S18. <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>, 400 MHz) of compound **5**.



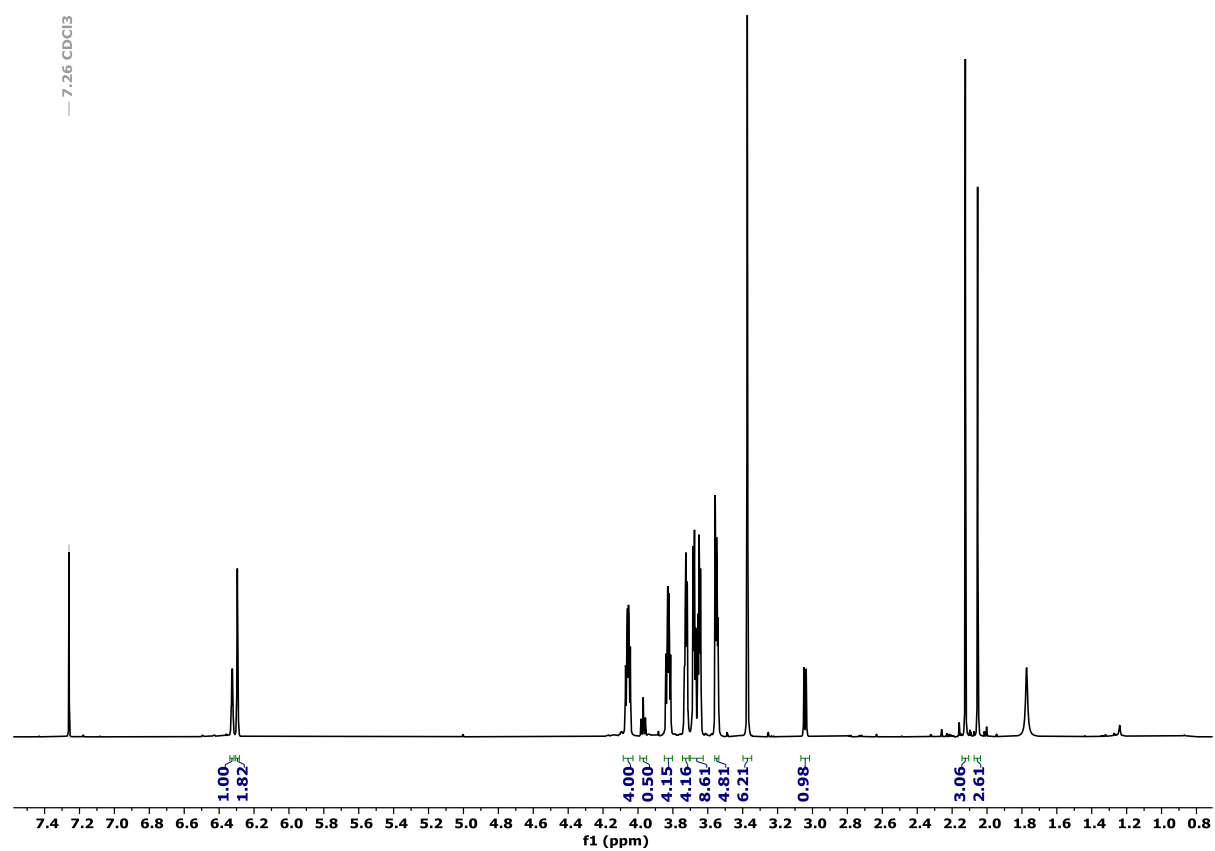
**Figure S19.**  $^{13}\text{C}$  NMR spectrum ( $\text{CDCl}_3$ , 101 MHz) of compound **5**.

## 2.9 Synthesis of compound **6**

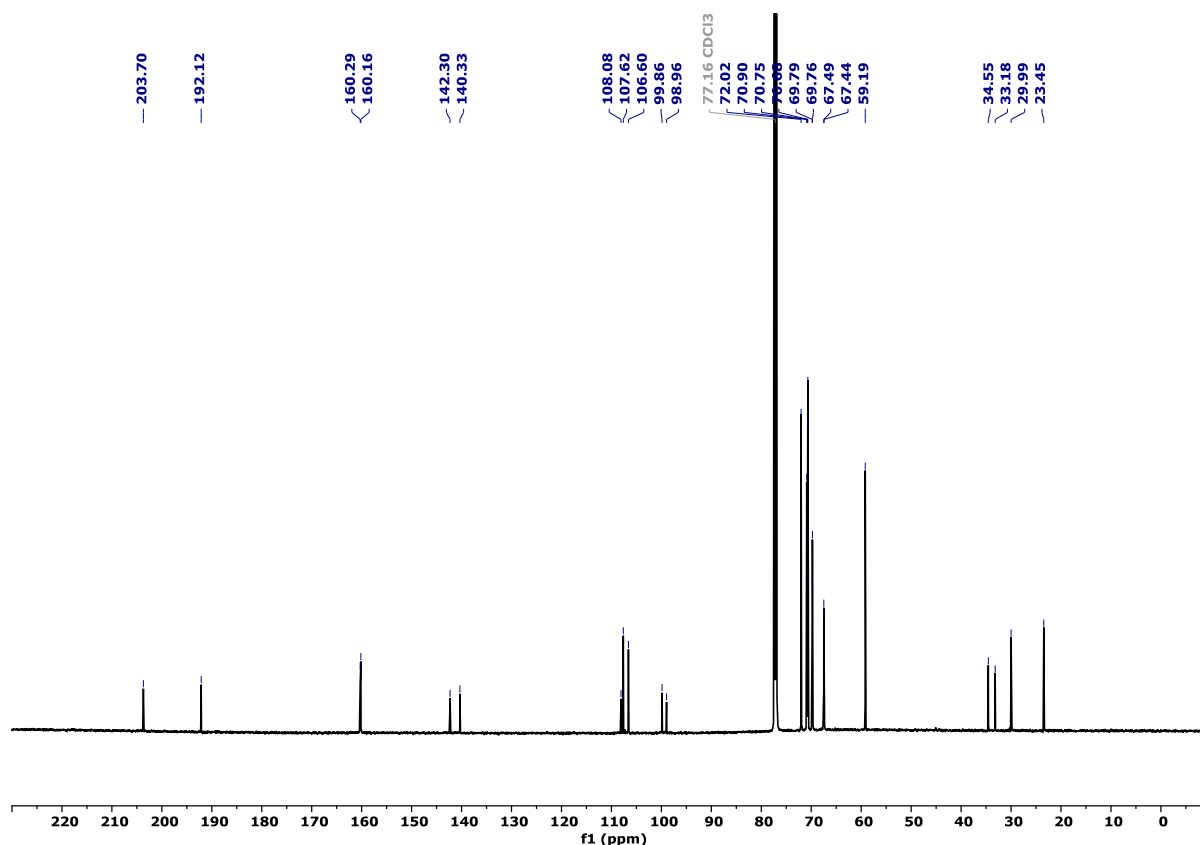


A solution of **5** (3.398 g, 7.535 mmol, 1 eq.) was prepared in MeCN (90 mL) under inert atmosphere in a two-neck flask equipped with a condenser.  $\text{Bu}_4\text{NI}$  (279 mg, 0.75 mmol, 0.1 eq.),  $\text{K}_2\text{CO}_3$  (6.248 g, 45.21 mmol, 6 eq.) and acetylacetone (774  $\mu\text{L}$ , 7.54 mmol, 1 eq.) were successively added. The mixture was heated under reflux under inert atmosphere for 16 h, then the volatiles were removed under reduced pressure.  $\text{CHCl}_3$  (100 mL) was added and the insoluble residue was filtered off. The filtrate was evaporated to dryness and subjected to column chromatography purification on  $\text{SiO}_2$ , using EtOAc as eluent to give **6** in the form of a light-yellow oil.  $R_f = 0.2$  (drags). Yield: 1.254 g, 32%.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  6.33 (overlapped, 1H,  $\text{H}_{\text{arom}}$ ), 6.30 – 6.29 (overlapped, m, 2H,  $\text{H}_{\text{arom}}$ ), 4.09 – 4.03 (m, 4H,  $\text{H}_{\text{peg}}$ ), 3.97 (t,  $J = 7.5$  Hz, 0.5H,  $\text{H}_{\text{acac keto-form}}$ ), 3.85 – 3.80 (m, 4H,  $\text{H}_{\text{peg}}$ ), 3.75 – 3.71 (m, 4H,  $\text{H}_{\text{peg}}$ ), 3.70 – 3.63 (m, 8H,  $\text{H}_{\text{peg}}$ ), 3.58 – 3.52 (overlapped, m, 5H,  $\text{H}_{\text{peg}}$ ,  $\text{H}_{\text{benzyl}}$ , *enol-form*), 3.37 (d,  $J = 1.4$  Hz, 6H,  $\text{H}_{\text{peg}}$ ), 3.04 (d,  $J = 7.5$  Hz, 1H,  $\text{H}_{\text{benzyl keto-form}}$ ), 2.12 (s, 3H, Me, *keto-form*), 2.05 (s, 3H,

H<sub>Me</sub>, *enol-form*). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 203.70, 192.12, 160.29, 160.16, 142.30, 140.33, 108.08, 107.62, 106.60, 99.86, 98.96, 72.02, 70.90, 70.75, 70.68, 69.79, 69.76, 67.49, 67.44, 59.19, 34.55, 33.18, 29.99, 23.45. HRMS (ESI/QTOF) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>26</sub>H<sub>43</sub>O<sub>10</sub><sup>+</sup> 515.2851; Found 515.2853.



**Figure S20.** <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>, 600 MHz) of compound **6**.



**Figure S21.**  $^{13}\text{C}$  NMR spectrum ( $\text{CDCl}_3$ , 151 MHz) of compound **6**.

### 2.10 Synthesis of **L2-H**

Under inert atmosphere, **6** (700 mg, 1.36 mmol, 1 eq.) THF (12 mL), absolute EtOH (12 mL) and hydrazine hydrate ( $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$ ) (0.36 mL, 7.36 mmol, 5.4 eq.) were placed in a two-neck flask equipped with a condenser. THF (12 mL) and absolute EtOH (12 mL) were added and the mixture was stirred at 70 °C overnight. The volatiles were removed under reduced pressure and the product was further dried under high vacuum to give **L2-H** in the form of a light-yellow oil. Yield: 692 mg, quantitative.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  6.29 (t,  $J = 2.3$  Hz, 1H,  $\text{H}_{\text{arom}}$ ), 6.26 (d,  $J = 2.2$  Hz, 2H,  $\text{H}_{\text{arom}}$ ), 4.04 (dd,  $J = 5.7, 4.0$  Hz, 4H,  $\text{H}_{\text{peg}}$ ), 3.84 – 3.77 (m, 4H,  $\text{H}_{\text{peg}}$ ), 3.74 – 3.69 (m, 4H,  $\text{H}_{\text{peg}}$ ), 3.69 – 3.61 (m, 10H,  $\text{H}_{\text{peg}}$ ,  $\text{H}_{\text{benzyl}}$ ), 3.58 – 3.52 (m, 4H,  $\text{H}_{\text{peg}}$ ), 3.37 (s, 6H,  $\text{H}_{\text{peg}}$ ), 2.14 (s, 6H,  $\text{H}_{\text{Me-Pz}}$ ).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  159.87, 143.16, 142.78, 113.80, 107.14, 98.85, 71.92, 70.77, 70.63, 70.56, 69.68, 67.28, 59.06, 29.09, 11.01. HRMS (ESI/QTOF)  $m/z$ :  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{26}\text{H}_{43}\text{N}_2\text{O}_8^+$  511.3014; Found 511.3019.

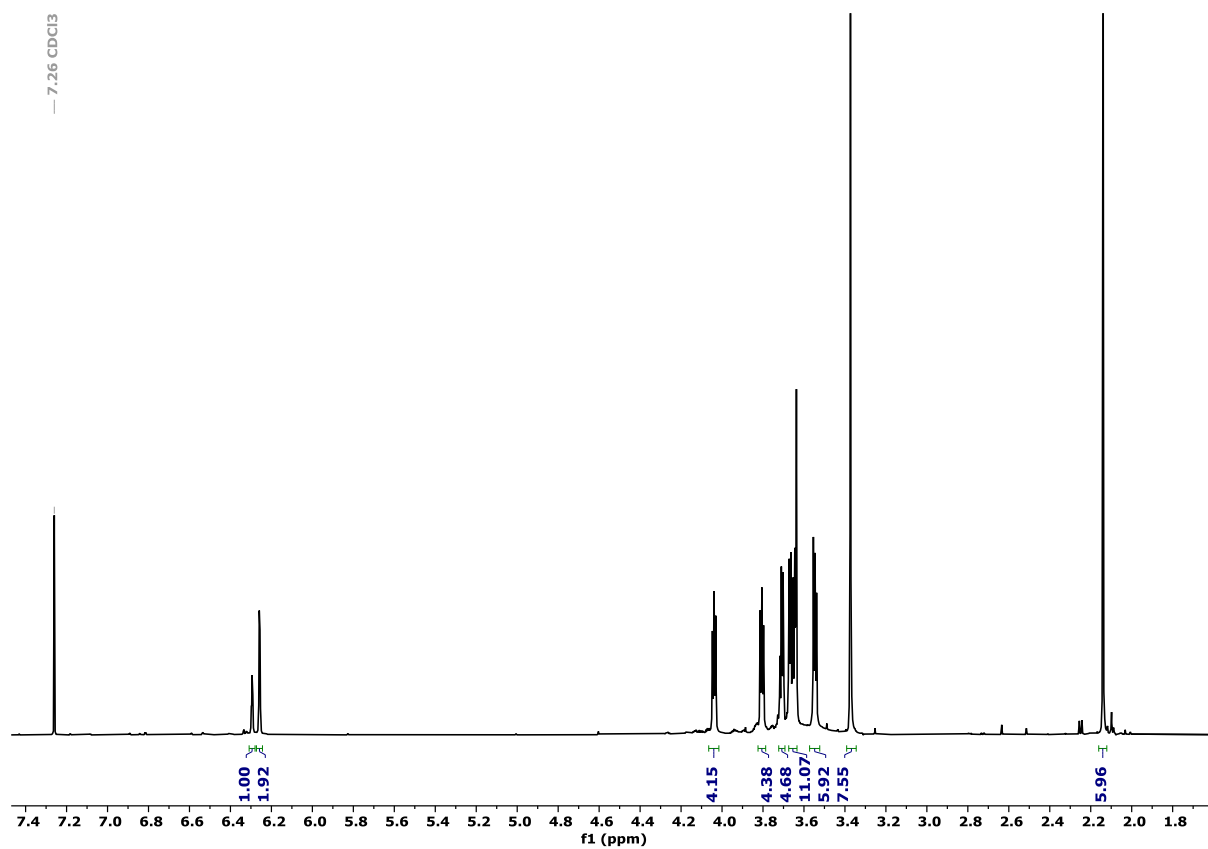


Figure S22. <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>, 600 MHz) of compound L2-H.

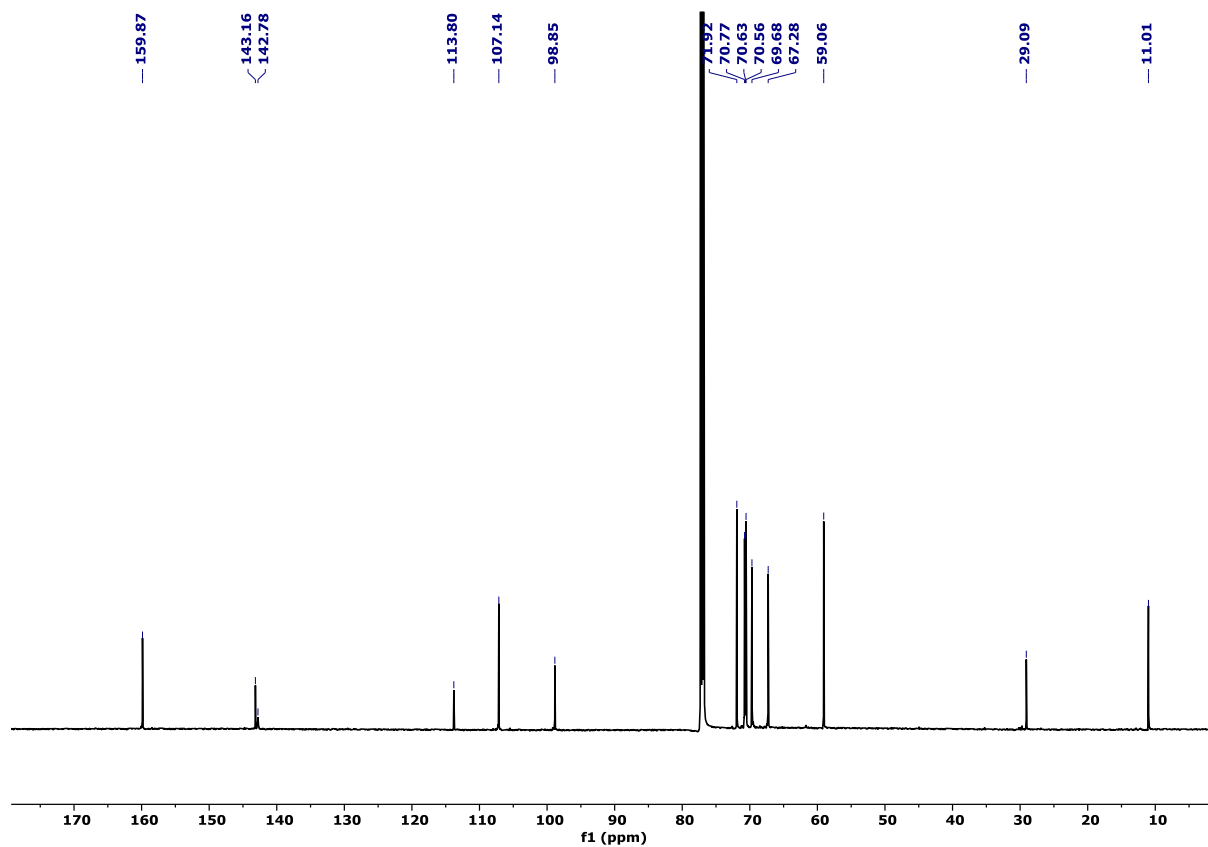
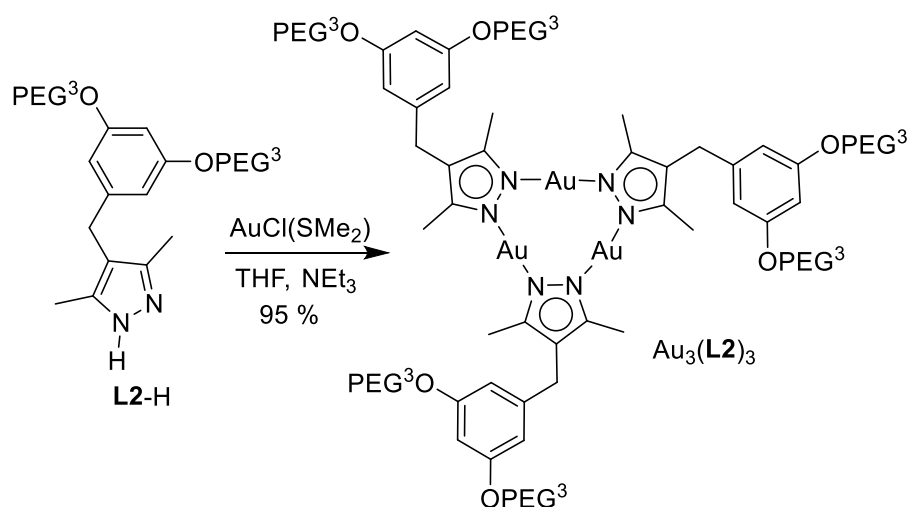


Figure S23. <sup>13</sup>C NMR spectrum (CDCl<sub>3</sub>, 151 MHz) of compound L2-H.

## 2.11 Synthesis of Au<sub>3</sub>(L2)<sub>3</sub>



**L2-H** (50 mg, 0.1 mmol, 1 eq.) was placed in a round bottom flask. THF (3 mL) was added, followed by NEt<sub>3</sub> (0.1 mL, excess) and the mixture was stirred at room temperature for 10 min. Au(SMe<sub>2</sub>)Cl (29 mg, 0.1 mmol, 1 eq.) was added and the mixture was stirred for 16 h at room temperature. Solids were removed by filtration. The filtrate was dried under reduced pressure and redissolved in CH<sub>2</sub>Cl<sub>2</sub> and filtered over celite. The solvent was removed under reduced pressure and the product was further dried under high vacuum to give Au<sub>3</sub>(L2)<sub>3</sub> in the form of a light-yellow oil. Yield: 66 mg, 95%. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 6.30 (t, *J* = 2.3 Hz, 1H, H<sub>arom</sub>), 6.27 (d, *J* = 2.2 Hz, 2H, H<sub>arom</sub>), 4.05 (dd, *J* = 5.8, 4.1 Hz, 4H, H<sub>peg</sub>), 3.83 – 3.79 (m, 4H, H<sub>peg</sub>), 3.75 – 3.69 (m, 4H, H<sub>peg</sub>), 3.69 – 3.62 (m, 10H, H<sub>benzyl</sub>, H<sub>peg</sub>), 3.58 – 3.52 (m, 4H, H<sub>peg</sub>), 3.36 (s, 6H, H<sub>peg</sub>), 2.17 (s, 6H, H<sub>Me-Pz</sub>). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 160.04, 146.76, 143.51, 113.76, 107.29, 99.00, 72.07, 70.93, 70.79, 70.70, 69.84, 67.47, 59.18, 30.28, 12.44. MALDI/TOF *m/z*: [M + Na]<sup>+</sup> Calcd for C<sub>78</sub>H<sub>123</sub>Au<sub>3</sub>NaN<sub>6</sub>O<sub>24</sub><sup>+</sup> 2141.8; Found 2141.7. HRMS (Nanochip-based ESI/LTQ-Orbitrap) *m/z*: [M + Na]<sup>+</sup> Calcd for C<sub>78</sub>H<sub>123</sub>Au<sub>3</sub>N<sub>6</sub>NaO<sub>24</sub><sup>+</sup> 2141.7478; Found 2141.7456, [M + K]<sup>+</sup> Calcd for C<sub>78</sub>H<sub>123</sub>Au<sub>3</sub>KN<sub>6</sub>O<sub>24</sub><sup>+</sup> 2157.7217; Found 2157.7219

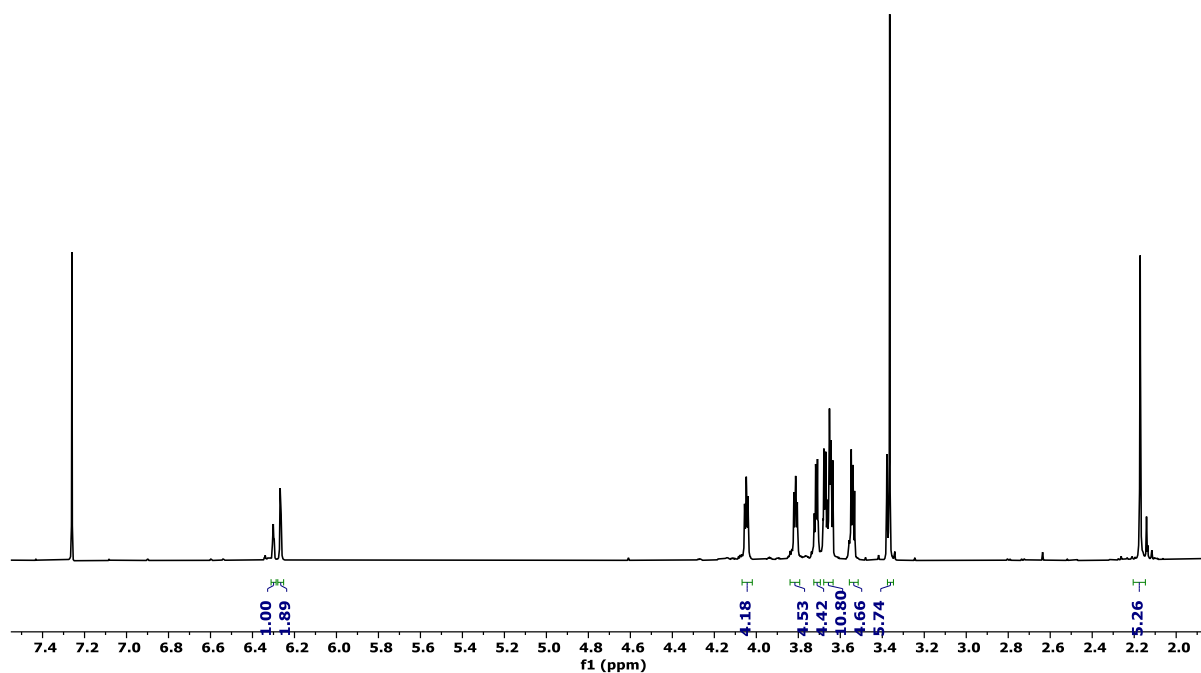


Figure S24.  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ , 600 MHz) of  $\text{Au}_3(\text{L}2)_3$ .

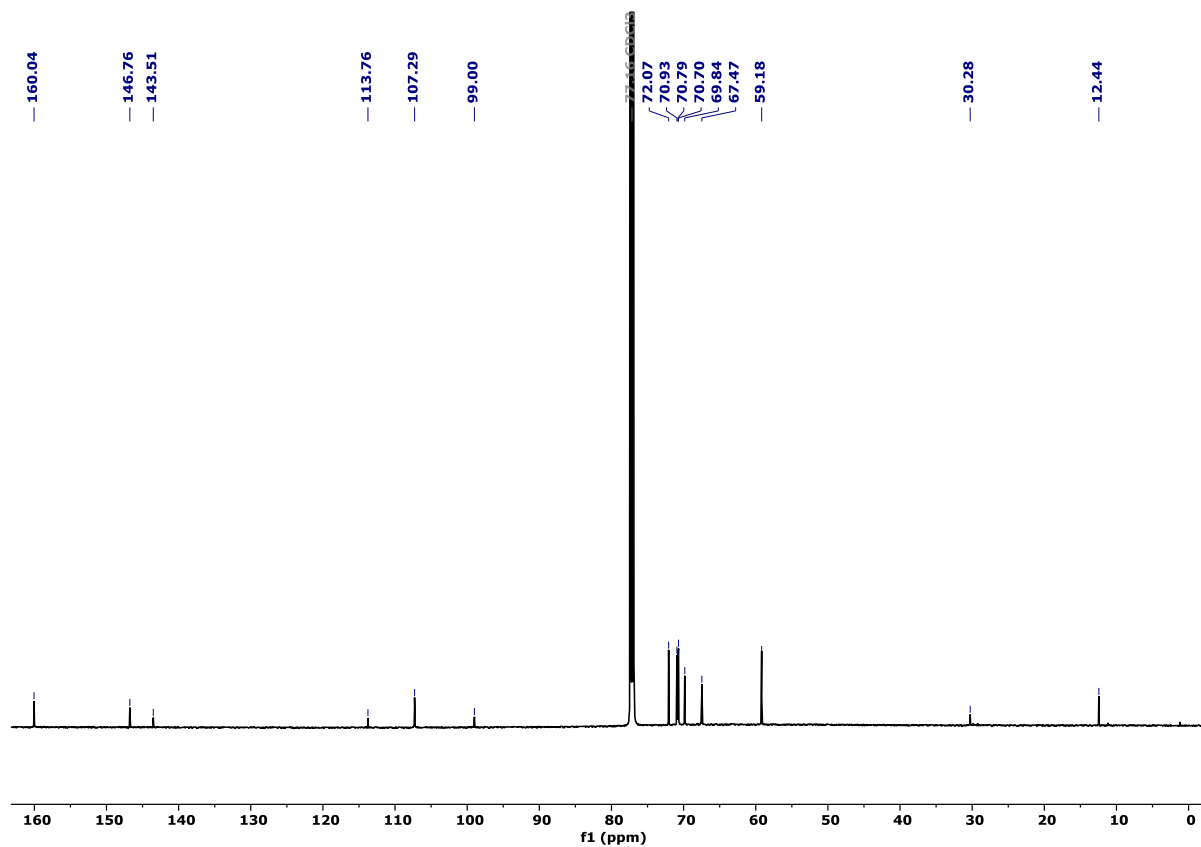
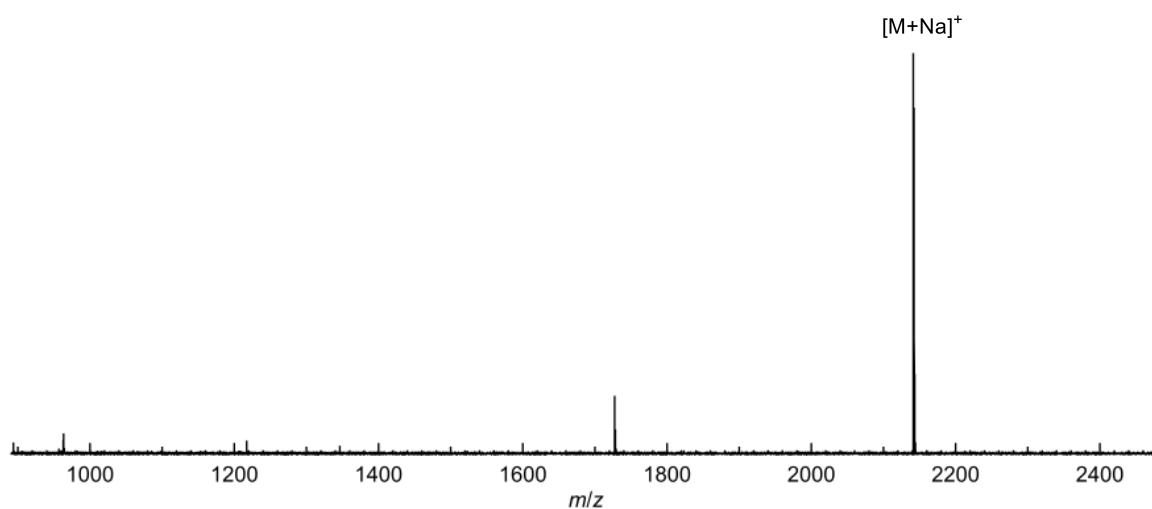
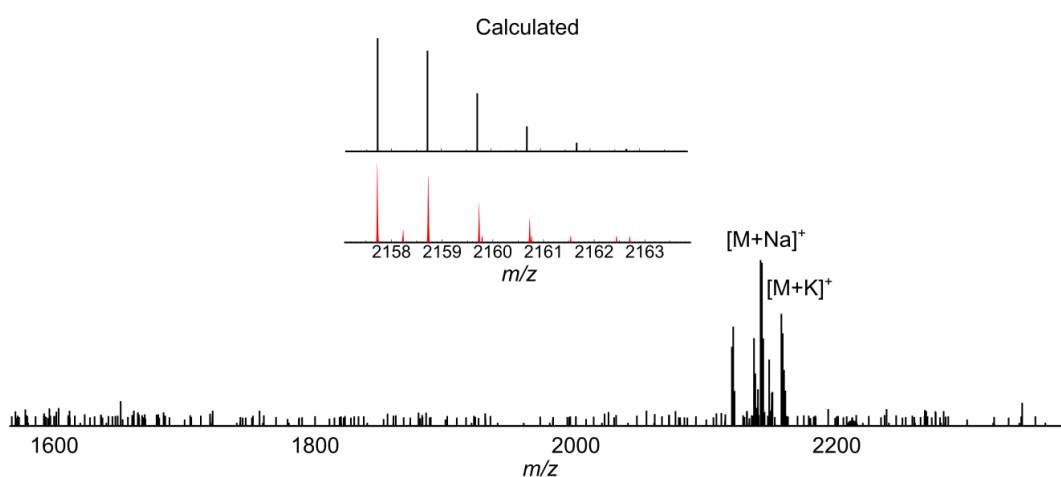


Figure S25.  $^{13}\text{C}$  NMR spectrum ( $\text{CDCl}_3$ , 151 MHz) of  $\text{Au}_3(\text{L}2)_3$ .



**Figure S26.** MALDI spectrum of  $\text{Au}_3(\text{L2})_3$



**Figure S27.** HRMS spectrum of  $\text{Au}_3(\text{L2})_3$ .

### 3. Single-crystal X-ray diffraction

**Experimental.** Single colorless needle-shaped crystals of **AS245** were used as supplied. A suitable crystal with dimensions  $0.43 \times 0.02 \times 0.01 \text{ mm}^3$  was selected and mounted on an XtaLAB Synergy R, DW system, HyPix-Arc 150 diffractometer. The crystal was kept at a steady  $T = 139.99(10) \text{ K}$  during data collection. The structure was solved with the ShelXT 2018/2 solution program<sup>4</sup> using dual methods and by using Olex2 1.5<sup>5</sup> as the graphical interface. The model was refined with ShelXL 2019/3<sup>6</sup> using full matrix least squares minimization on  $F^2$ .

A colorless needle-shaped crystal with dimensions  $0.43 \times 0.02 \times 0.01 \text{ mm}^3$  was mounted. Data were collected using an XtaLAB Synergy R, DW system, HyPix-Arc 150 diffractometer operating at  $T =$



139.99(10) K.

Data were measured using  $w$  scans with  $\text{CuK}_\alpha$  radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program CrysAlis<sup>Pro</sup> system (CCD 43.116a 64-bit (release 22-03-2024)). The maximum resolution achieved was  $\theta = 74.630^\circ$  (0.80 Å).

The unit cell was refined using CrysAlis<sup>Pro</sup> 1.171.43.115a<sup>7</sup> on 13283 reflections, 50% of the observed reflections.

Data reduction, scaling and absorption corrections were performed using CrysAlis<sup>Pro</sup> 1.171.43.115a.<sup>7</sup> The final completeness is 99.50 % out to  $74.630^\circ$  in  $\theta$ . A Gaussian absorption correction was performed using CrysAlis<sup>Pro</sup> 1.171.43.115a.<sup>7</sup> Numerical absorption correction based on Gaussian integration over a multifaceted crystal model. Empirical absorption correction using spherical harmonics as implemented in SCALE3 ABSPACK scaling algorithm. The absorption coefficient  $\mu$  of this material is  $24.942 \text{ mm}^{-1}$  at this wavelength ( $\lambda = 1.54184 \text{ \AA}$ ) and the minimum and maximum transmissions are 0.030 and 1.000.

The structure was solved in the space group  $P\bar{1}$  (# 2) by the ShelXT 2018/2 (Sheldrick, 2015) structure solution program using dual methods and refined by full matrix least squares minimization on  $F^2$  using version 2019/3 of ShelXL 2019/3.<sup>4</sup> All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model.

There is a single formula unit in the asymmetric unit, which is represented by the reported sum formula. In other words:  $Z$  is 2 and  $Z'$  is 1. The moiety formula is  $\text{C}_{36}\text{H}_{39}\text{Au}_3\text{N}_6$ .

**Crystal Data.**  $\text{C}_{36}\text{H}_{39}\text{N}_6\text{Au}_3$ ,  $M_r = 1146.63$ , triclinic,  $P\bar{1}$  (No. 2),  $a = 5.92744(9) \text{ \AA}$ ,  $b = 13.7395(3) \text{ \AA}$ ,  $c = 20.7053(4) \text{ \AA}$ ,  $\alpha = 79.4971(16)^\circ$ ,  $\beta = 83.0769(13)^\circ$ ,  $\gamma = 85.9397(13)^\circ$ ,  $V = 1643.84(5) \text{ \AA}^3$ ,  $T = 139.99(10) \text{ K}$ ,  $Z = 2$ ,  $Z' = 1$ ,  $m(\text{Cu K}_\alpha) = 24.942$ , 26455 reflections measured, 6463 unique ( $R_{\text{int}} = 0.0424$ ) which were used in all calculations. The final  $wR_2$  was 0.0814 (all data) and  $R_1$  was 0.0306 ( $I \geq 2\sigma(I)$ ).

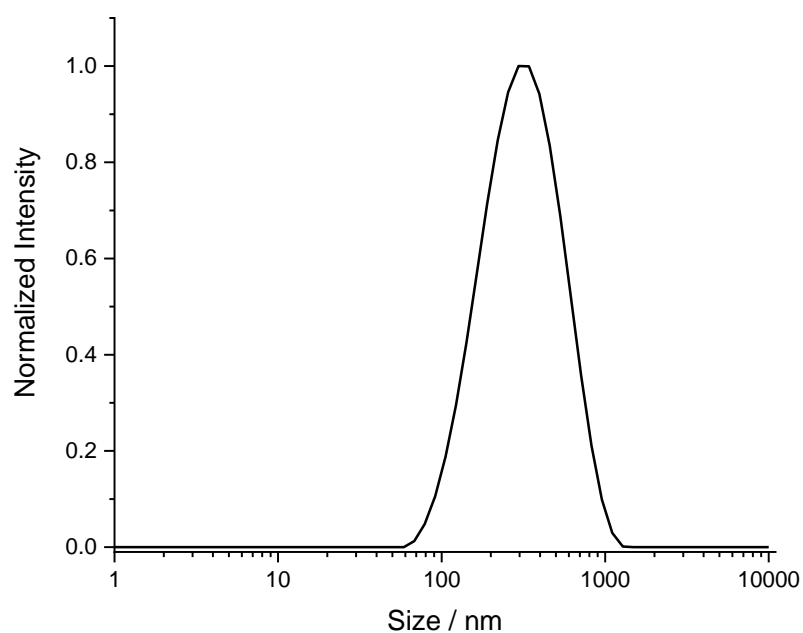
**Table S1.** Crystal data for Au<sub>3</sub>(L1)<sub>3</sub>.

<b>Compound</b>	<b>AS245</b>
Formula	C <sub>36</sub> H <sub>39</sub> N <sub>6</sub> Au <sub>3</sub>
$D_{calc.}/\text{g cm}^{-3}$	2.317
$m/\text{mm}^{-1}$	24.942
Formula Weight	1146.63
Color	colorless
Shape	needle-shaped
Size/ $\text{mm}^3$	0.43×0.02×0.01
$T/\text{K}$	139.99(10)
Crystal System	triclinic
Space Group	$P\bar{1}$
$a/\text{\AA}$	5.92744(9)
$b/\text{\AA}$	13.7395(3)
$c/\text{\AA}$	20.7053(4)
$\alpha/^\circ$	79.4971(16)
$\beta/^\circ$	83.0769(13)
$\gamma/^\circ$	85.9397(13)
$V/\text{\AA}^3$	1643.84(5)
$Z$	2
$Z'$	1
Wavelength/ $\text{\AA}$	1.54184
Radiation type	CuK $\alpha$
$\theta_{min}/^\circ$	2.183
$\theta_{max}/^\circ$	74.630
Measured Refl's.	26455
Indep't Refl's	6463
Refl's $I \geq 2\sigma(I)$	5633
$R_{int}$	0.0424
Parameters	412
Restraints	0
Largest Peak/ $e \text{\AA}^{-3}$	1.550
Deepest Hole/ $e \text{\AA}^{-3}$	-1.663
Goof	1.083
$wR_2$ (all data)	0.0814
$wR_2$	0.0789
$R_1$ (all data)	0.0372
$R_1$	0.0306
CCDC number	2357277

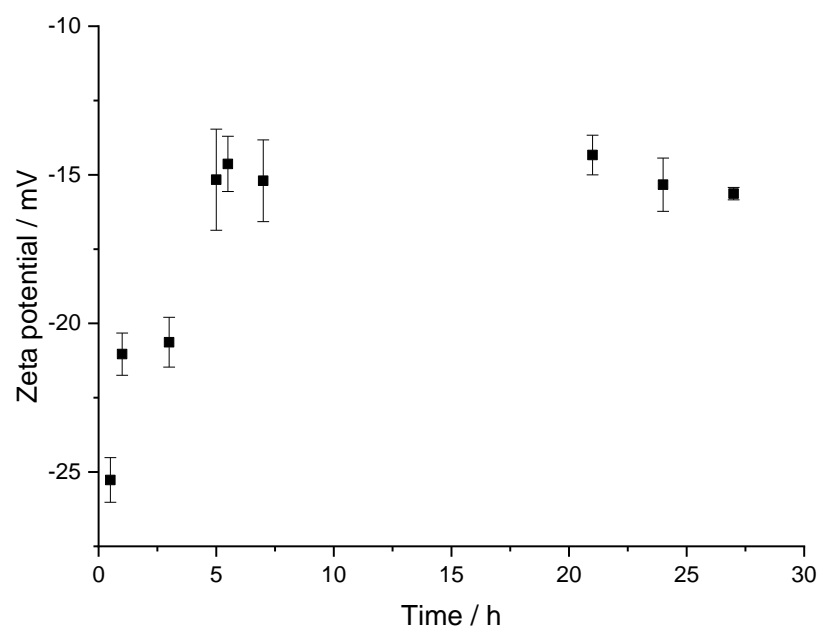
#### 4. Dynamic light scattering and zeta potential measurements

Colloidal suspensions of  $M_3(\mathbf{L1})_3$  ( $M = \text{Cu, Ag, Au}$ ) in  $\text{H}_2\text{O}$  (0.1 mM) were prepared by quick addition of an aliquot (3.3  $\mu\text{L}$ ) of an  $M_3(\mathbf{L1})_3$  stock solution in MeCN (61.22 mM) to 2000  $\mu\text{L}$   $\text{H}_2\text{O}$  under intense stirring. The resulting mixtures were stirred under high vacuum for 30 min to remove all traces of MeCN. The samples were analyzed 30 minutes after preparation following filtration (filter pore size: 1.2  $\mu\text{m}$ ).

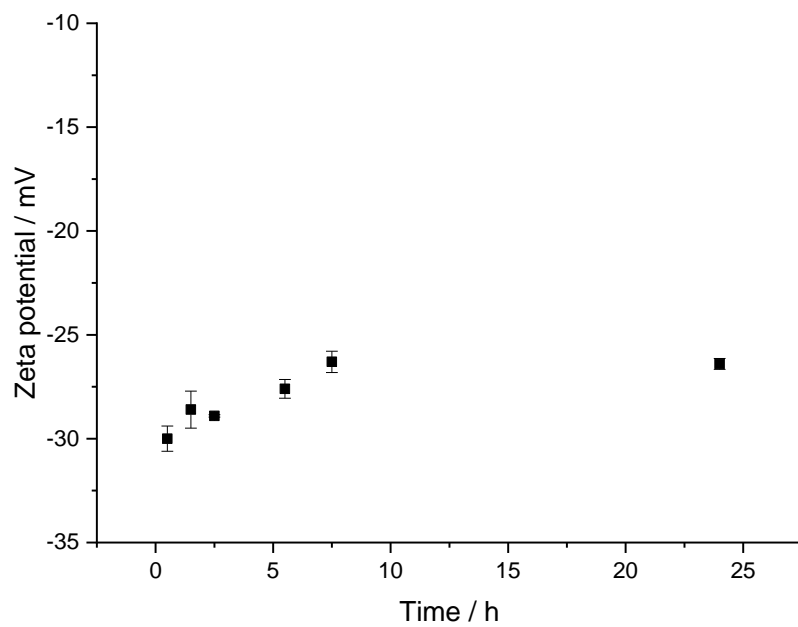
Time-dependent zeta potential measurements were performed using samples of  $\text{Au}_3(\mathbf{L1})_3$ , which were prepared as described above, with and without a filtering step (filter pore size: 1.2  $\mu\text{m}$ ).



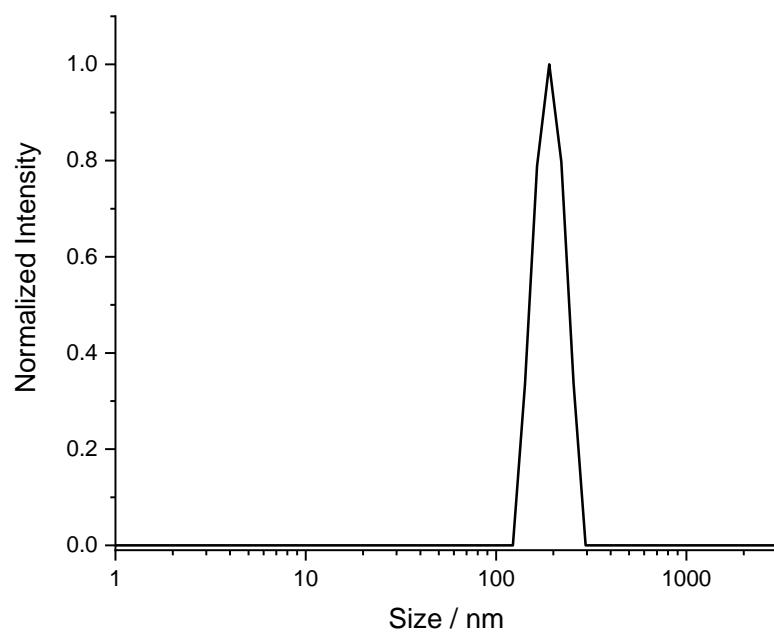
**Figure S28.** Dynamic light scattering measurement of a 0.1 mM colloidal suspension of  $\text{Au}_3(\mathbf{L1})_3$  in water.



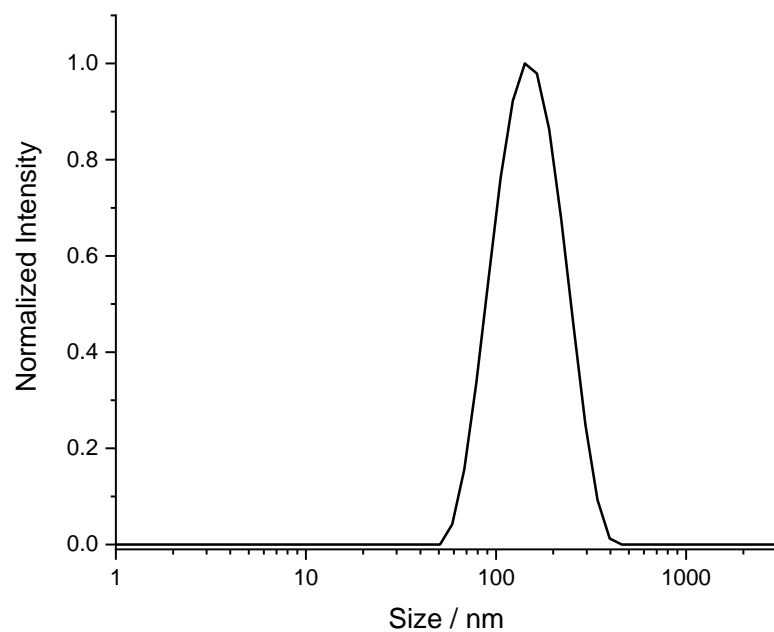
**Figure S29.** Time-dependent zeta potential measurements of a 0.1 mM colloidal suspension of  $\text{Au}_3(\text{L1})_3$ .



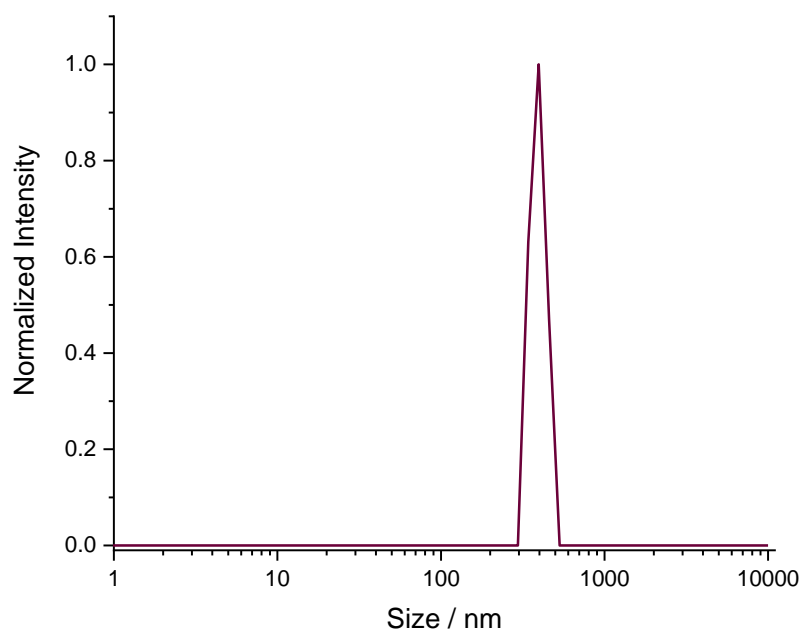
**Figure S30.** Time-dependent zeta potential measurements of a filtered (1.2  $\mu\text{m}$  pore size), 0.1 mM colloidal suspension of  $\text{Au}_3(\text{L1})_3$ .



**Figure S31.** Dynamic light scattering measurement of a 0.1 mM colloidal suspension of  $\text{Ag}_3(\text{L1})_3$  in water.



**Figure S32.** Dynamic light scattering measurement of a 0.1 mM colloidal suspension of  $\text{Cu}_3(\text{L1})_3$  in water.



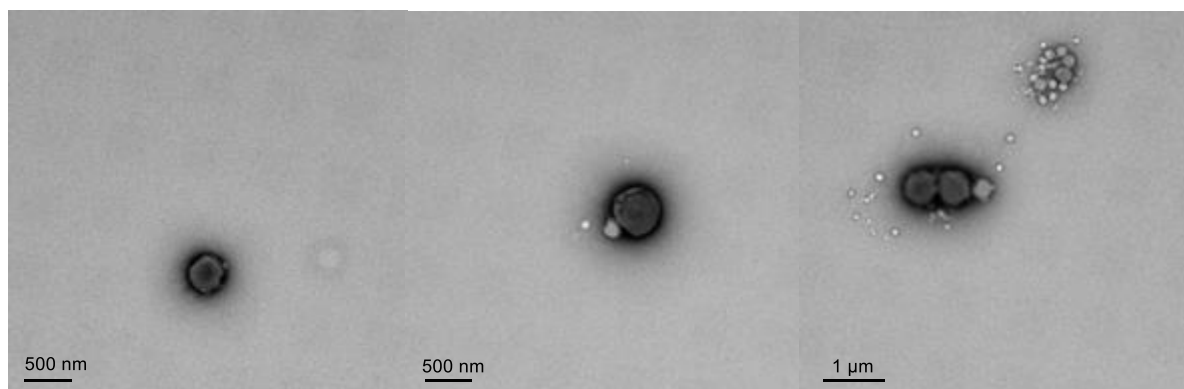
**Figure S33.** Dynamic light scattering measurement of a 0.1 mM colloidal suspension of  $\text{Au}_3(\text{L2})_3$  in water.

## 5. TEM observations by negative stain

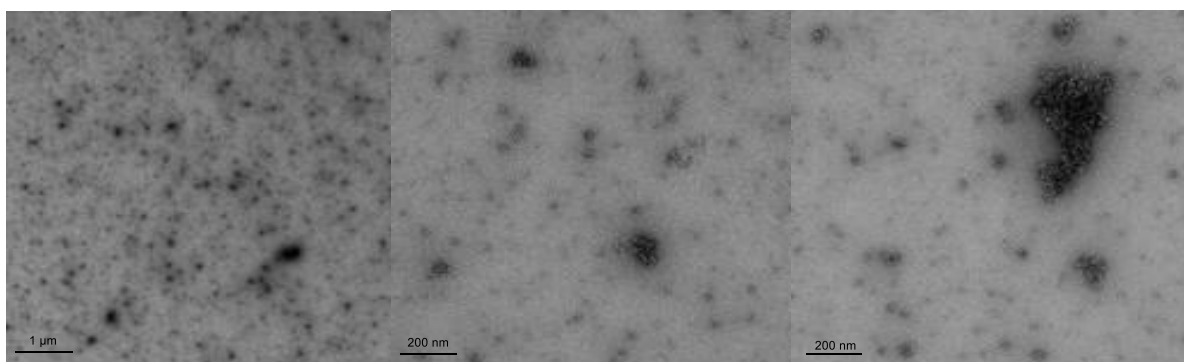
Colloidal suspensions of  $\text{Au}_3(\text{L})_3$  ( $\text{L} = \text{L1}, \text{L2}$ ) in  $\text{H}_2\text{O}$  (0.33 mM) were prepared by the quick addition of an aliquot (10  $\mu\text{L}$ ) of a  $\text{Au}_3(\text{L})_3$  stock solution in MeCN (61.22 mM) to 2000  $\mu\text{L}$   $\text{H}_2\text{O}$  under intense stirring. The resulting mixtures were stirred under high vacuum for 30 min to remove all traces of MeCN.

The samples were adsorbed on a glow-discharged carbon-coated copper grid 400mesh (EMS, Hatfield, PA, USA) washed with deionized water and stained with uranyl acetate 1% for 30 seconds.

Observations were made using a Talos L120C electron microscope (Thermo Fisher, Hillsboro, USA) operated at 120 kV. Digital images were collected using a CMOS camera Ceta-S (Thermo Fisher, Hillsboro, USA) (4098  $\times$  4098 pixels.), using a defocus range between  $-1.5 \mu\text{m}$  and  $-2.5 \mu\text{m}$ .



**Figure S34.** TEM images of Au<sub>3</sub>(L1)<sub>3</sub> in dried state.



**Figure S35.** TEM images of Au<sub>3</sub>(L2)<sub>3</sub> in dried state.

## 6. CryoEM imaging and tomography analysis

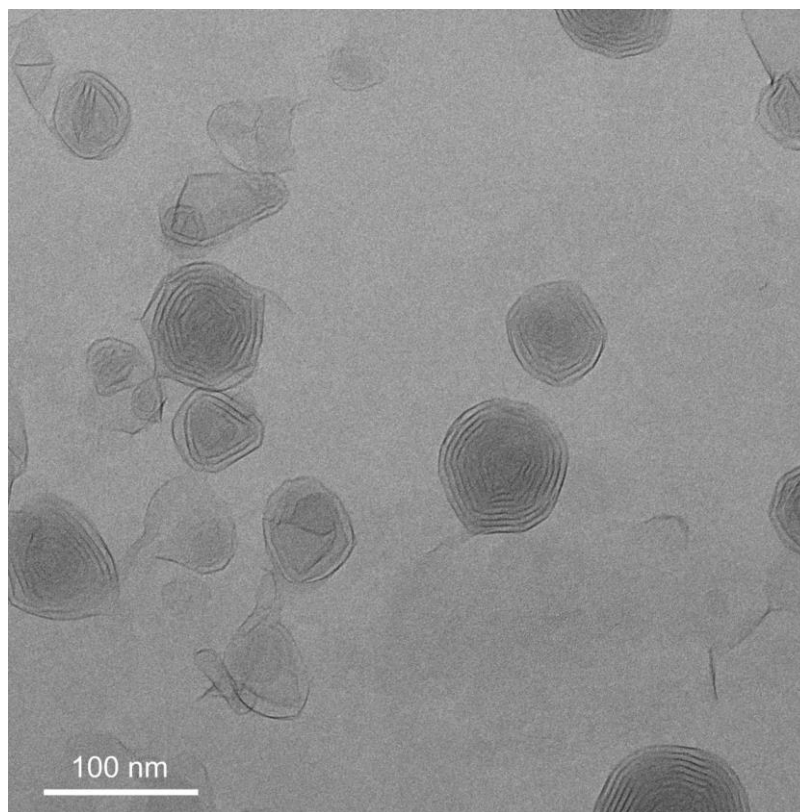
A colloidal suspension of  $M_3(\mathbf{L1})_3$  ( $M = \text{Au, Ag, Cu}$ ) in  $\text{H}_2\text{O}$  (0.33 mM) was prepared by the quick addition of an aliquot (10  $\mu\text{L}$ ) of a  $\text{Au}_3(\mathbf{L1})_3$  stock solution in MeCN (61.22 mM) to 2000  $\mu\text{L}$   $\text{H}_2\text{O}$  under intense stirring. The resulting mixture was stirred under high vacuum for 30 min to remove all traces of MeCN. The sample was stored at 4  $^\circ\text{C}$  until the images were collected. Unless otherwise mentioned, observations were made at least 24 h after the sample was prepared.

A Lacey EM grid (EMS, Hatfield, PA, USA) 300 mesh was held in a tweezer and 4–5  $\mu\text{L}$  of sample solution was applied on the grid. The tweezer has been mounted in an automatic plunge freezing apparatus Vitrobot Mark IV (Thermo Fisher, Hillsboro, USA) to control humidity and temperature. After blotting, the grid was plunged in a small metal container with liquid ethane.

Observations were made at  $-170$   $^\circ\text{C}$  in a Tecnai F 20 microscope (Thermo Fisher, Hillsboro, USA) operating at 200 kV equipped with a cryo-specimen holder Gatan 626 (Warrendale, PA).

For tomography, acquisition tilt-series were collected automatically on Tecnai F20 from  $-60^\circ$  to  $+60^\circ$  degrees with  $2^\circ$  angular increment using the tomography software Tomo 4.0 (Thermo Fisher, Hillsboro, USA)

Digital images were drift corrected with a direct detector camera FalconIII (FEI) 4098 X 4098 pixels using a defocus range from  $-3$   $\mu\text{m}$  to  $-4$   $\mu\text{m}$  for a total dose of  $40$   $\text{e}^-/\text{\AA}^2$ . Alignments of tilted stack and tomography reconstruction was made using Inspect3D software (Thermo Fisher, Hillsboro, USA).



**Figure S36.** CryoEM images of the fresh aggregates obtained from  $\text{Au}_3(\mathbf{L1})_3$ .

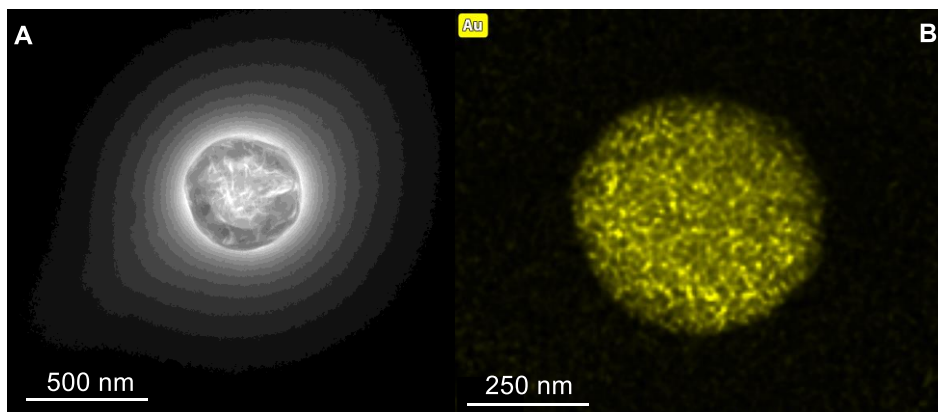


## 7. EDX mapping

A colloidal suspension of  $M_3(\mathbf{L1})_3$  ( $M = \text{Au, Ag, Cu}$ ) in  $\text{H}_2\text{O}$  (0.33 mM) was prepared by the quick addition of an aliquot (10  $\mu\text{L}$ ) of a  $\text{Au}_3(\mathbf{L1})_3$  stock solution in MeCN (61.22 mM) to 2000  $\mu\text{L}$   $\text{H}_2\text{O}$  under intense stirring. The resulting mixture was stirred under high vacuum for 30 min to remove all traces of MeCN. The sample was stored at 4  $^\circ\text{C}$  until the images were collected. Unless otherwise mentioned, observations were made at least 24 h after the sample was prepared.

Cu TEM grids with a continuous carbon film were used. First, the TEM grid was submitted to a glow discharge process in order to make its surface hydrophobic. Then a drop of the particle solution was deposited and let in on top of the grid for around 1 minute. The particles were attached electrostatically to the carbon film. Finally, the TEM grid was dried under vacuum for at least 1 night.

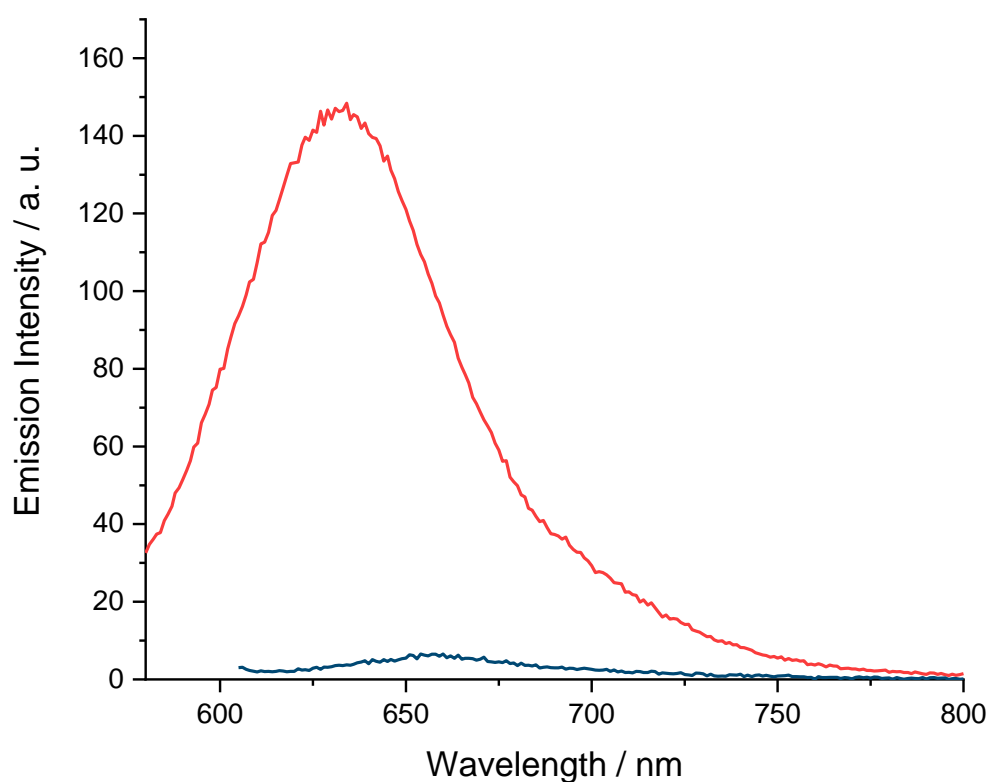
Elemental maps were obtained from EDX experiments performed on Tecnai Osiris equipped with a Super-X SDD EDX detectors integrated into the pole piece. The microscope was operated on STEM mode at 200 kV. Several scans were performed on the sample during some minutes to acquire the X-rays resulting of the excitation of the electrons with the sample. Each pixel of the image corresponds to a spectrum. In order to obtain the EDX elemental maps the peaks of the spectrum were identified and the background was removed.



**Figure S37.** SEM (A) and EDX Au mapping (B) of  $\text{Au}_3(\mathbf{L1})_3$  particles in dried state.

## 8. Uptake study

A colloidal suspension of  $\text{Au}_3(\text{L1})_3$  in  $\text{H}_2\text{O}$  (0.1 mM) was prepared by the quick addition of an aliquot (6.5  $\mu\text{L}$ ) of a  $\text{Au}_3(\text{L1})_3$  stock solution in MeCN (30.6 mM) to 2000  $\mu\text{L}$   $\text{H}_2\text{O}$  under intense stirring. The resulting mixture was stirred under high vacuum for 30 min to remove all traces of MeCN. Subsequently, an aliquot (4  $\mu\text{L}$ ) of a stock solution of the dye Nile Red in MeOH (10 mM) was added under stirring. The mixture was stirred under high vacuum for 10 minutes to remove any traces of MeOH. As a control, an aliquot (4  $\mu\text{L}$ ) of a stock solution of Nile Red in MeOH (10 mM) was added under stirring to 2000  $\mu\text{L}$   $\text{H}_2\text{O}$ . The MeOH was removed by stirring the sample under high vacuum for 10 minutes.



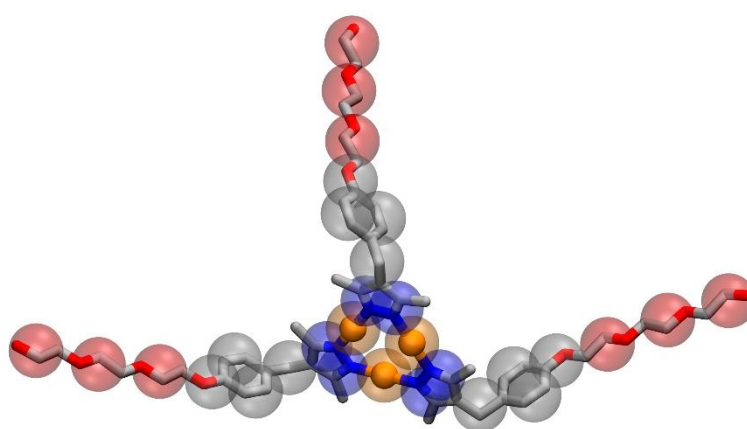
**Figure S38.** Emission of Nile Red in the nano onions (red,  $\lambda_{\text{ex}} = 566$  nm) and control (blue,  $\lambda_{\text{ex}} = 595$  nm).

## 9. Modelling summary

### All-atom and Coarse-grained modeling

The all-atom (AA) model of  $\text{Au}_3(\text{L1})_3$  was built using the Generalized Amber Force Field (GAFF)<sup>8</sup> with RESP charges,<sup>9</sup> computed with the M06 functional<sup>10</sup> and CEP-31G basis set,<sup>11</sup> as implemented in Gaussian16.<sup>12</sup> The AmberTools21 package<sup>13</sup> was employed for system parameterization, except for the bonded parameters involving the Au atoms, which were parameterized using Seminario's method.<sup>14</sup> The TIP3P water model<sup>15</sup> was used to represent the water solvent.

The AA model was subsequently used to develop a coarse-grained (CG) model of  $\text{Au}_3(\text{L1})_3$ , based on the MARTINI force field<sup>16</sup> mapping scheme, with three SQ0 beads representing the Au atoms.

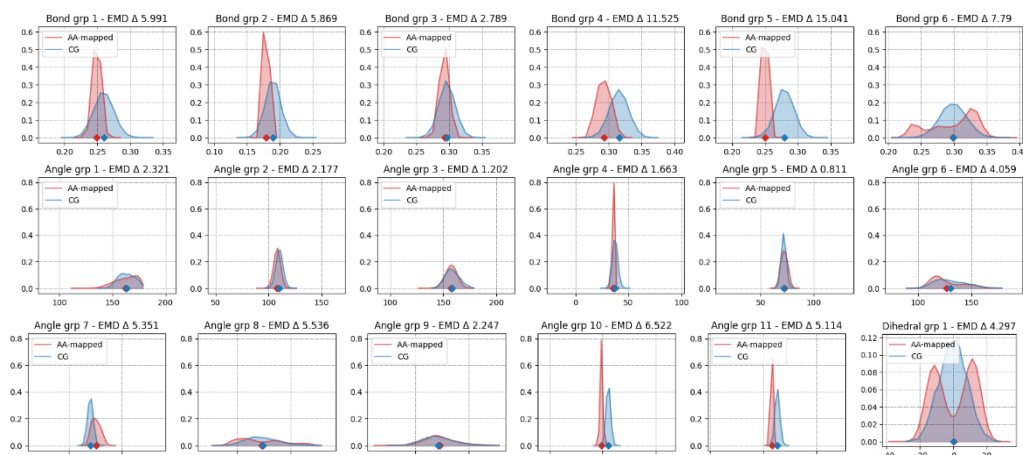


**Figure S39.** Mapping scheme of the  $\text{Au}_3(\text{L1})_3$  complex.

The solvent was represented implicitly through the noise term in Langevin dynamics and the interaction between the beads of monomers.

The bonded parameters of the CG model (bonds, angles, dihedrals) were optimized using the SWARM-CG software.<sup>17</sup>

The non-bonded parameters between bead cores (SQ0-SQ0, SQ0-TN3a, SQ0-TC4) were optimized to reproduce the dimerization free energy of two AA cores. Two AA cores were placed in a box, and their dimerization free energy was estimated via well-tempered metadynamics (WT-MetaD).<sup>18</sup> The same WT-MetaD setup was applied to two CG cores, and the non-bonded interactions between the CG beads were iteratively adjusted to match the AA dimerization free energy. This protocol has been successfully applied previously on similar supramolecular systems.<sup>19</sup>



**Figure S40.** Distribution of bonds, angles, and dihedrals.

The non-bonded parameters for the beads representing the PEG arms were obtained from the literature.<sup>20</sup>

### Molecular simulations

All simulations were performed using GROMACS version 2022.5,<sup>21</sup> patched with the PLUMED plugin version 2.7.0,<sup>22</sup> and conducted at 300 K. Each AA and CG system was minimized using the steepest descent algorithm. The AA systems were pre-equilibrated under NPT conditions, employing the Berendsen barostat<sup>23</sup> with a coupling constant of 1 ps. In the AA production runs, we used the leap-frog integrator with a time step of 2 fs, the v-rescale thermostat<sup>24</sup> with a coupling constant of 0.2 ps, and the Parrinello-Rahman barostat<sup>25</sup> with a coupling constant of 4 ps. Non-bonded interactions were treated using a cutoff distance of 0.9 nm, and long-range electrostatic interactions were evaluated using the Particle Mesh Ewald (PME) method.<sup>26</sup> The LINCS algorithm<sup>27</sup> has been used to constrain all the bonds involving hydrogens.

For the CG production runs, we applied the leapfrog stochastic dynamics integrator with a time step of 10 fs, the v-rescale thermostat with a time constant of 0.1 ps. The friction coefficient parameter  $bd\text{-}fric$  was set to 0 amu ps<sup>-1</sup>.

All the AA and CG WT-MetaD simulations for the estimation of dimerization free energies have been performed using the distance between the center of geometry between the Au atoms of the monomers (CV1), and the torsional angle between the planes formed by the Au atoms of the monomers (CV2) as collective variables. We used a bias factor of 20, a gaussian height of 0.4186 kJ/mol, a gaussian width of 0.06 nm and 0.04 rad for CV1 and CV2, respectively, and a deposition rate of one gaussian every 2000 simulations steps.

### Self-assembly simulations of CG-Au<sub>3</sub>(pyrazolate)<sub>3</sub>

To investigate the spontaneous self-assembly of Au<sub>3</sub>(L1)<sub>3</sub> monomers in solution, 1000 CG monomers were placed in a 70x70x70 nm simulation box. The system was simulated for approximately 90,000,000 CG steps.

Subsequently, 500 additional monomers were introduced to the system to explore the interactions between free monomers and pre-existing aggregates. This second system was simulated for 12,000,000 CG steps.

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