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# Cooperative Complexation of Amino Acid Derivatives to Platinum Acetylide-Based Bolaamphiphile

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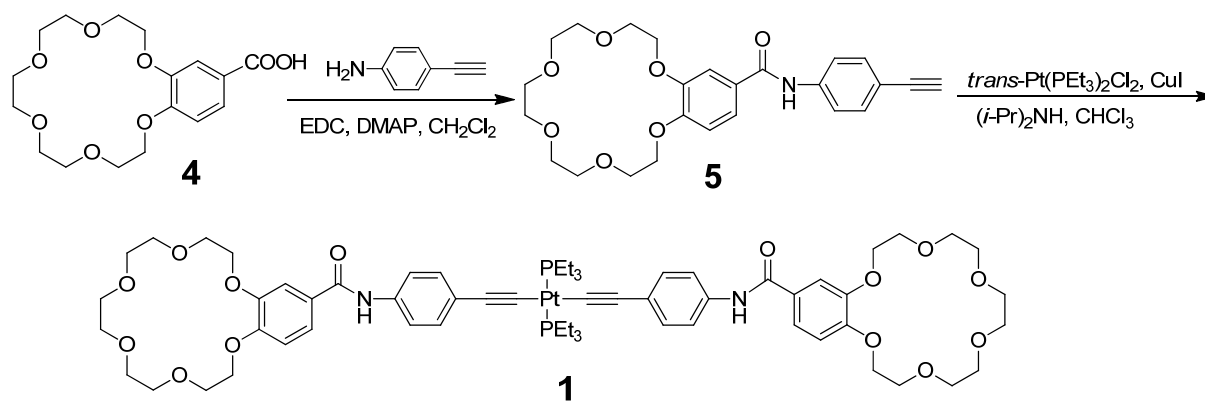
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## 1. Materials and methods

L-alanine methyl ester salt **2**, pentaethylene glycol, *p*-toluenesulfonyl chloride, 3,4-dihydroxybenzaldehyde, *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC•HCl) and 4-dimethylamino pyridine (DMAP) were reagent grade and used as received. 4-Ethynylaniline and B18C6 acid **4** were synthesized according to the previously reported procedure.<sup>[S1–2]</sup> Other reagents and solvents were employed as purchased.

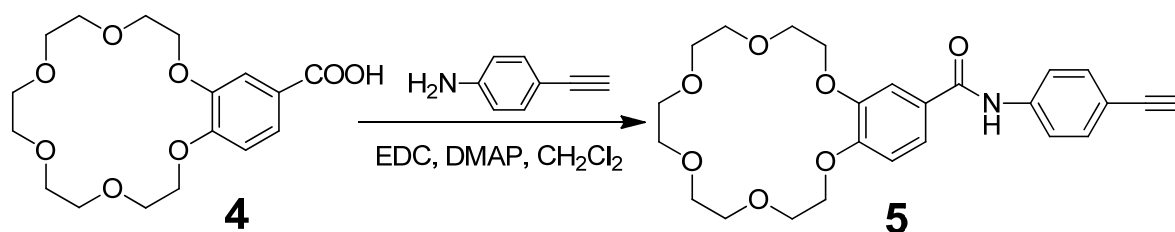
NMR spectra were collected on a Varian Unity INOVA-300 spectrometer, for which the <sup>1</sup>H NMR were performed with TMS as the internal standard and the <sup>13</sup>C NMR were reported relative to the resonance of CDCl<sub>3</sub> as internal standard. Electrospray ionization mass spectra (ESI-MS) were obtained on a Bruker Esquire 3000 plus mass spectrometer (Bruker-Franzen Analytik GmbH Bremen, Germany) equipped with an ESI interface and ion trap analyzer. UV/Vis spectra were recorded on a Beijing Persee TU-1901 UV-Vis spectrometer. The FETEM spectra were observed on a JEM-2100F (Japan). AFM spectra were obtained on a DI MultiMode V (Veeco).

## 2. Synthetic route to the bolaamphiphile **1**

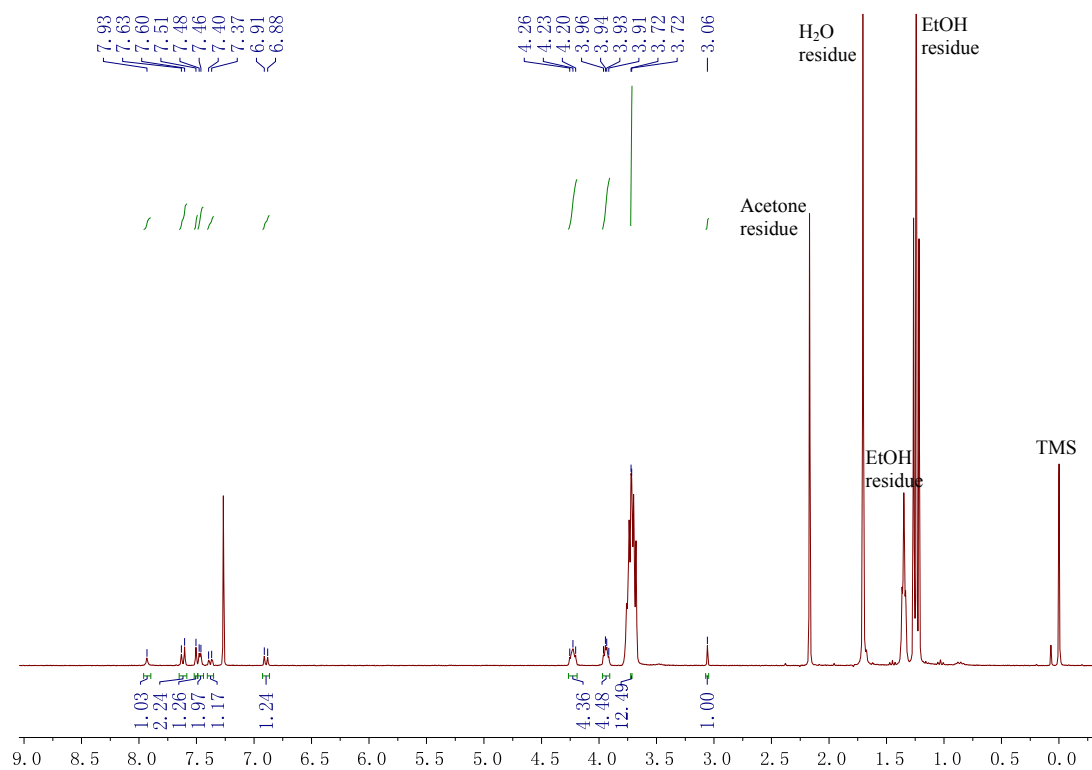


**Scheme S1.** Synthetic route to the bolaamphiphile **1**.

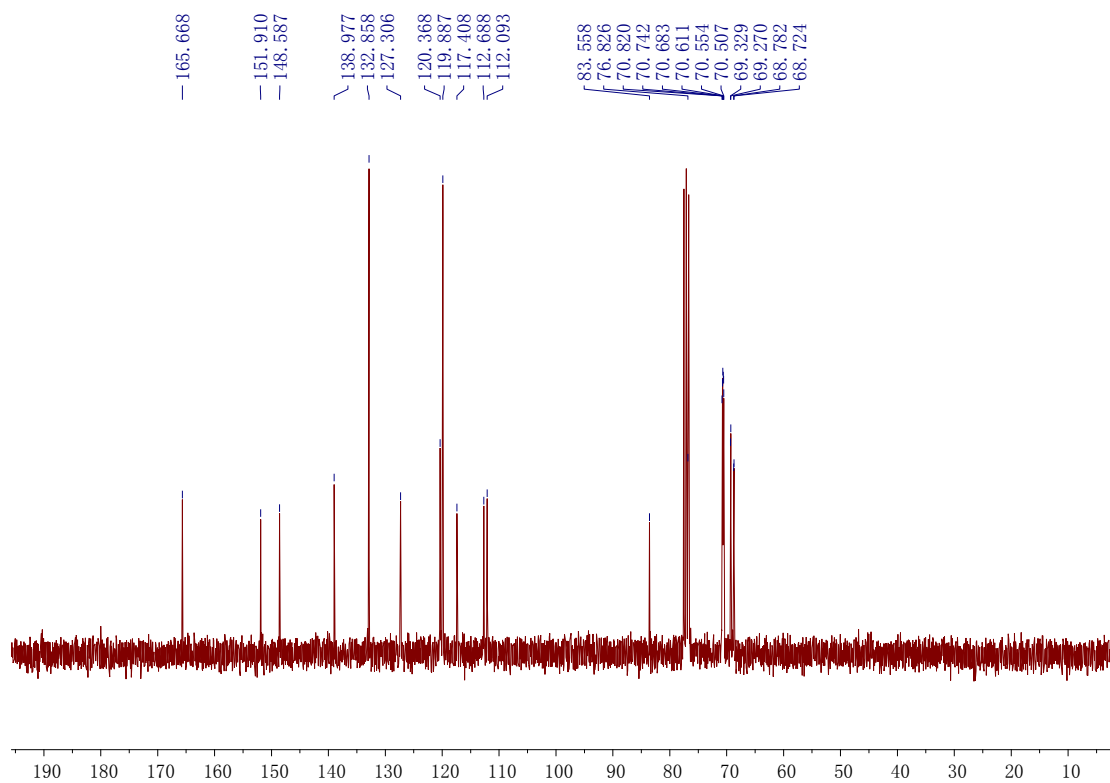
### 2.1 Synthesis of compound **5**



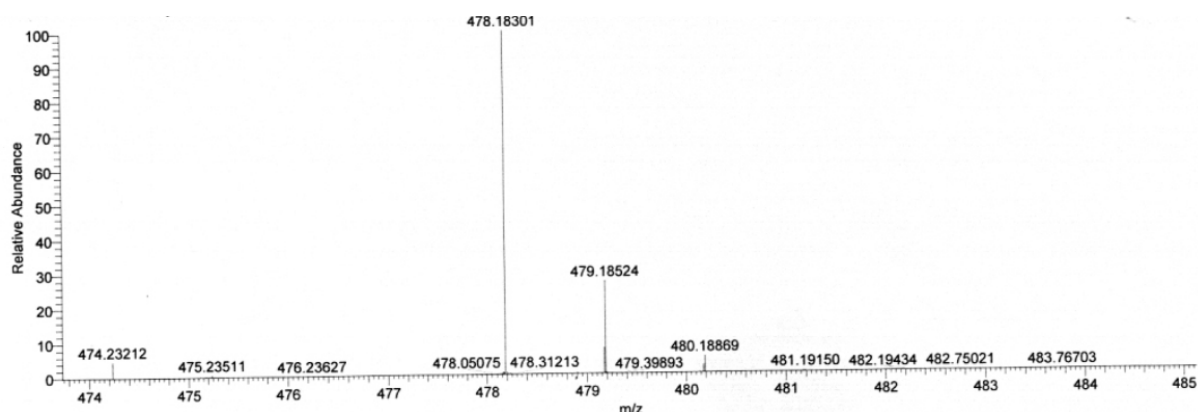
Compound **4** (671 mg, 1.67 mmol), 4-ethynylaniline (215 mg, 1.84 mmol), EDC•HCl (449 mg, 2.34 mmol) and DMAP (204 mg, 1.67 mmol) were dissolved in  $\text{CH}_2\text{Cl}_2$  and stirred for 2 days under nitrogen. The resulting mixture was subsequently extracted with  $\text{CH}_2\text{Cl}_2$  (3×) and washed with water. The organic layer was evaporated to dryness and the residue was purified by flash column chromatograph ( $\text{CH}_2\text{Cl}_2/\text{MeOH}$ , 40 : 1, v/v as the eluent) to afford **5** as a white solid (599 mg, 79%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , room temperature)  $\delta$ (ppm): 7.93 (s, 1H), 7.62 (d, 2H), 7.51 (s, 1H), 7.47 (d, 2H), 7.38 (d, 1H), 6.90 (d, 1H), 4.23 (m, 4H), 3.94 (m, 4H), 3.72 (m, 12H), 3.06 (s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ , room temperature)  $\delta$ (ppm): 165.67, 151.91, 148.59, 138.98, 132.86, 127.31, 120.37, 119.89, 117.41, 112.69, 112.09, 83.56, 76.83, 70.82, 70.74, 70.68, 70.61, 70.55, 70.51, 69.33, 69.27, 68.78, 68.72; ESI-MS  $m/z$ :  $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{25}\text{H}_{29}\text{NNaO}_7$ , 478.1842; found, 478.1830; error, 2.5 ppm.



**Figure S1.** <sup>1</sup>H NMR spectrum (300 MHz, CDCl<sub>3</sub>, room temperature) of compound **5**.

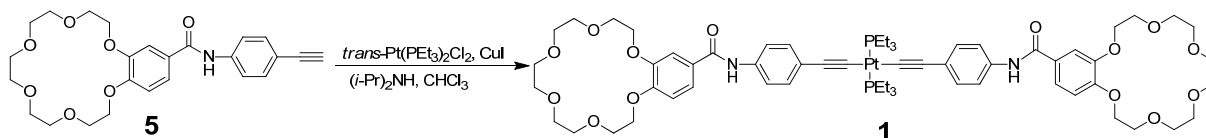


**Figure S2.** <sup>13</sup>C NMR spectrum (75 MHz, CDCl<sub>3</sub>, room temperature) of compound **5**.

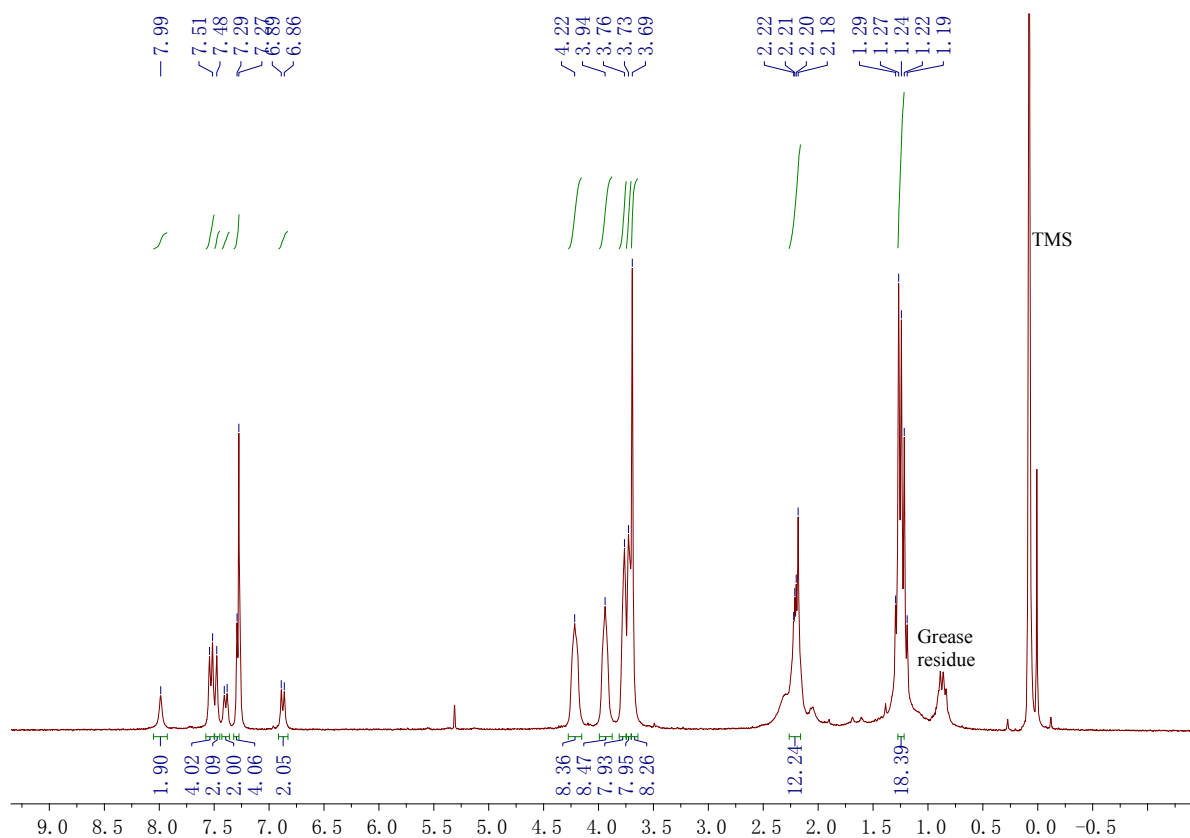


**Figure S3.** Electrospray ionization mass spectrum of compound **5**.

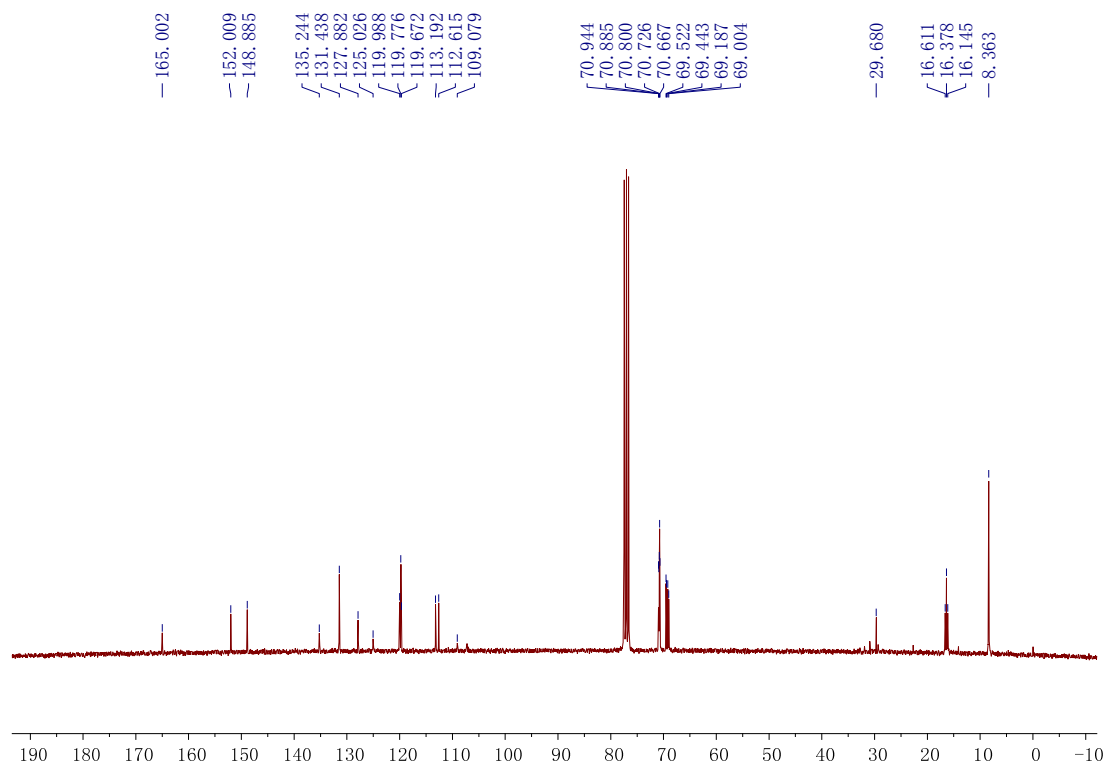
## 2.2 Synthesis of compound **1**



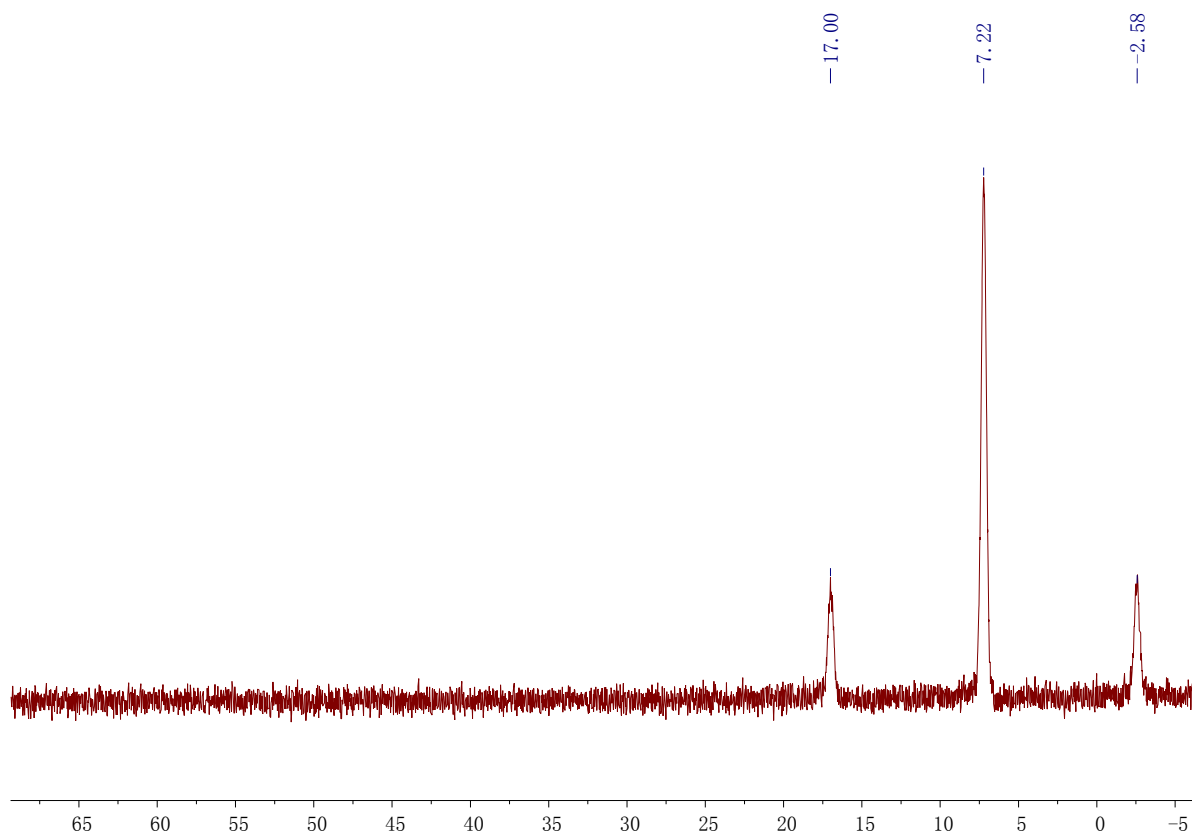
Compound **5** (100 mg, 0.22 mmol), *trans*-Pt(PEt<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (55 mg, 0.11 mmol), CuI (2 mg, 0.01 mmol) was dissolved in a mixture of CHCl<sub>3</sub>/(*i*-Pr)<sub>2</sub>NH (20 mL, 1 : 1, v/v). The solution was stirred for 3 days at 45 °C, after which all solvents were removed under reduced pressure. The residue was extracted with H<sub>2</sub>O/CH<sub>2</sub>Cl<sub>2</sub>. The combined organic extracts were then removed with a rotary evaporator. It was then purified by flash column chromatography (CHCl<sub>3</sub>/THF/CH<sub>3</sub>OH, 40 : 1 : 1, v/v/v as the eluent) to afford compound **1** as a pale yellow solid (122 mg, 83%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, room temperature) δ (ppm): 7.99 (s, 2H), 7.53 (d, 4H), 7.48 (s, 2H), 7.39 (d, 2H), 7.28 (d, 4H), 6.87 (d, 2H), 4.22 (m, 8H), 3.94 (m, 8H), 3.76 (m, 8H), 3.73 (m, 8H), 3.69 (m, 8H), 2.20 (m, 12H), 1.25 (m, 18H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, room temperature) δ (ppm): 165.00, 152.01, 148.89, 135.24, 131.44, 127.88, 125.03, 119.99, 119.78, 119.67, 113.19, 112.61, 109.08, 70.94, 70.88, 70.80, 70.73, 70.67, 69.52, 69.44, 69.19, 69.00, 29.68, 16.61, 16.38, 16.15, 8.36; <sup>31</sup>P NMR (121 MHz, CDCl<sub>3</sub>, room temperature) δ (ppm): 7.22 (triplet peak); ESI-MS m/z: [M + H]<sup>+</sup> calcd for C<sub>62</sub>H<sub>87</sub>N<sub>2</sub>O<sub>14</sub>P<sub>2</sub>Pt, 1340.5280; found, 1340.5255; error, 1.9 ppm.



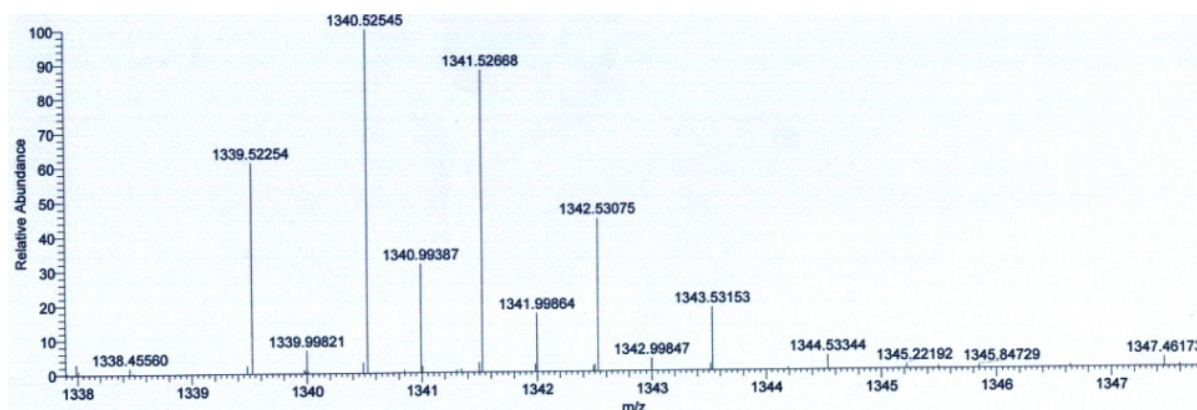
**Figure S4.**  $^1\text{H}$  NMR spectrum (300 MHz,  $\text{CDCl}_3$ , room temperature) of compound **1**.



**Figure S5.**  $^{13}\text{C}$  NMR spectrum (75 MHz,  $\text{CDCl}_3$ , room temperature) of compound **1**.

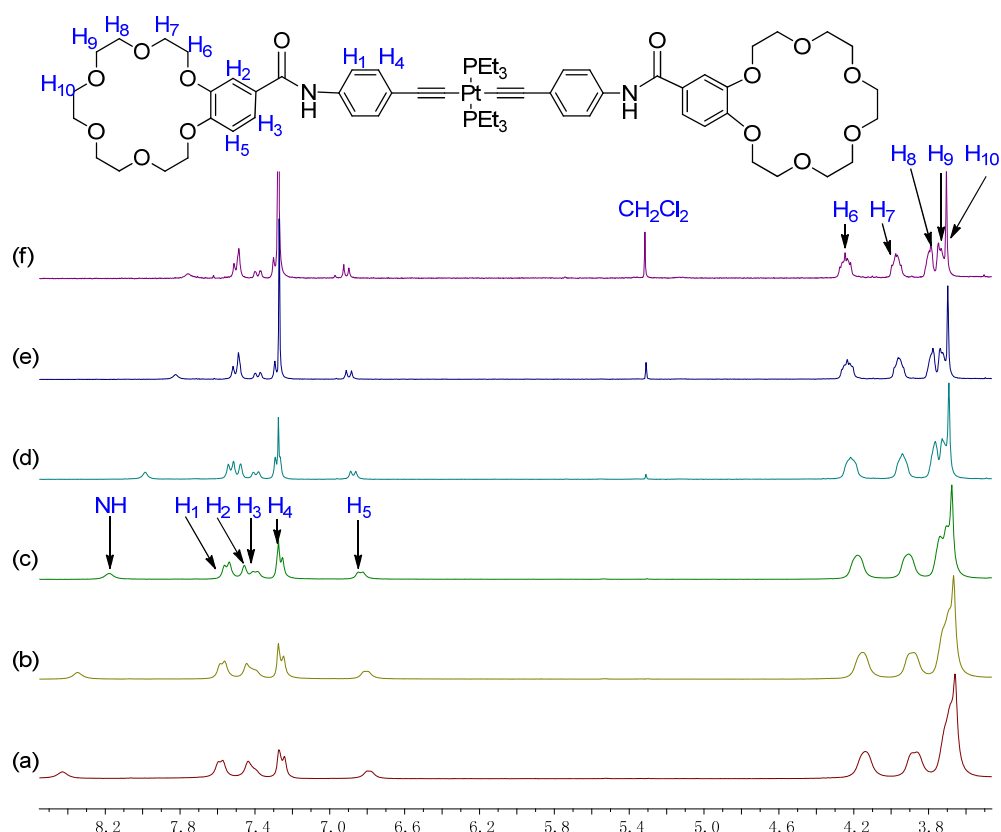


**Figure S6.**  $^{31}\text{P}$  NMR spectrum (121 MHz,  $\text{CDCl}_3$ , room temperature) of compound **1**.

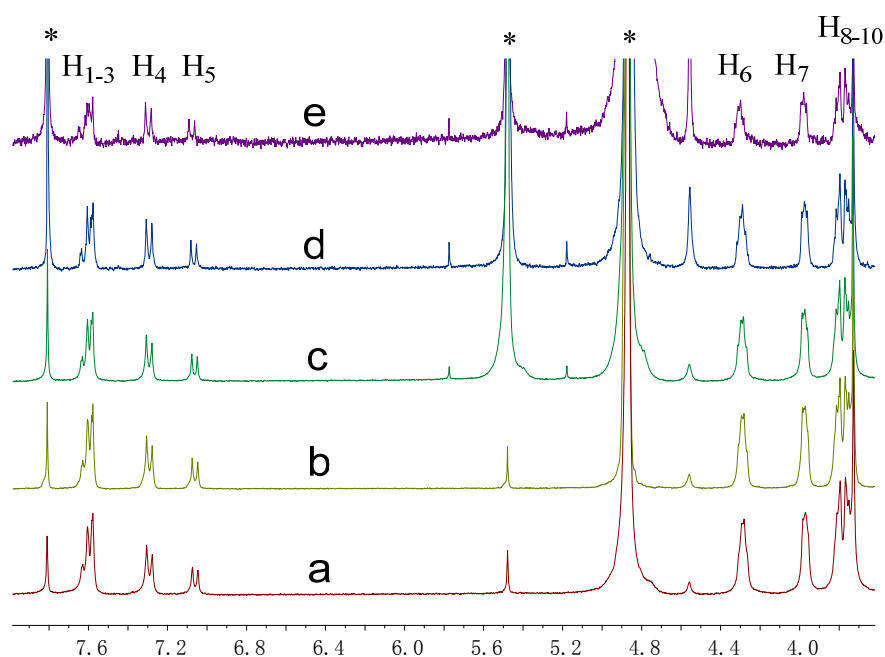


**Figure S7.** Electrospray ionization mass spectrum of compound **1**.

### 3. Concentration-dependent $^1\text{H}$ NMR spectra of **1**



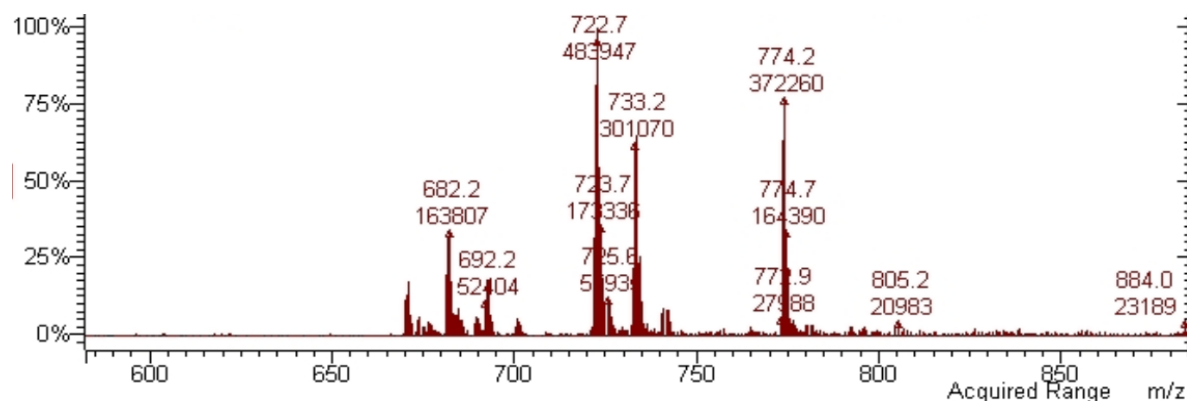
**Figure S8.** Partial concentration-dependent  $^1\text{H}$  NMR spectra of **1** in  $d$ -chloroform at different monomer concentrations: (a) 45.8; (b) 38.1; (c) 24.5; (d) 11.1; (e) 3.34; (f) 1.11 mM. (all measurements:  $T = 25\text{ }^\circ\text{C}$ ).



**Figure S9.** Partial concentration-dependent  $^1\text{H}$  NMR spectra of **1** in  $d_4$ -methanol/ $d$ -chloroform (3/1,  $v/v$ ) at different monomer concentrations: (a) 6.12; (b) 3.06; (c) 1.53; (d) 0.51; (e) 0.15 mM. (all measurements:  $T = 25\text{ }^\circ\text{C}$ ).

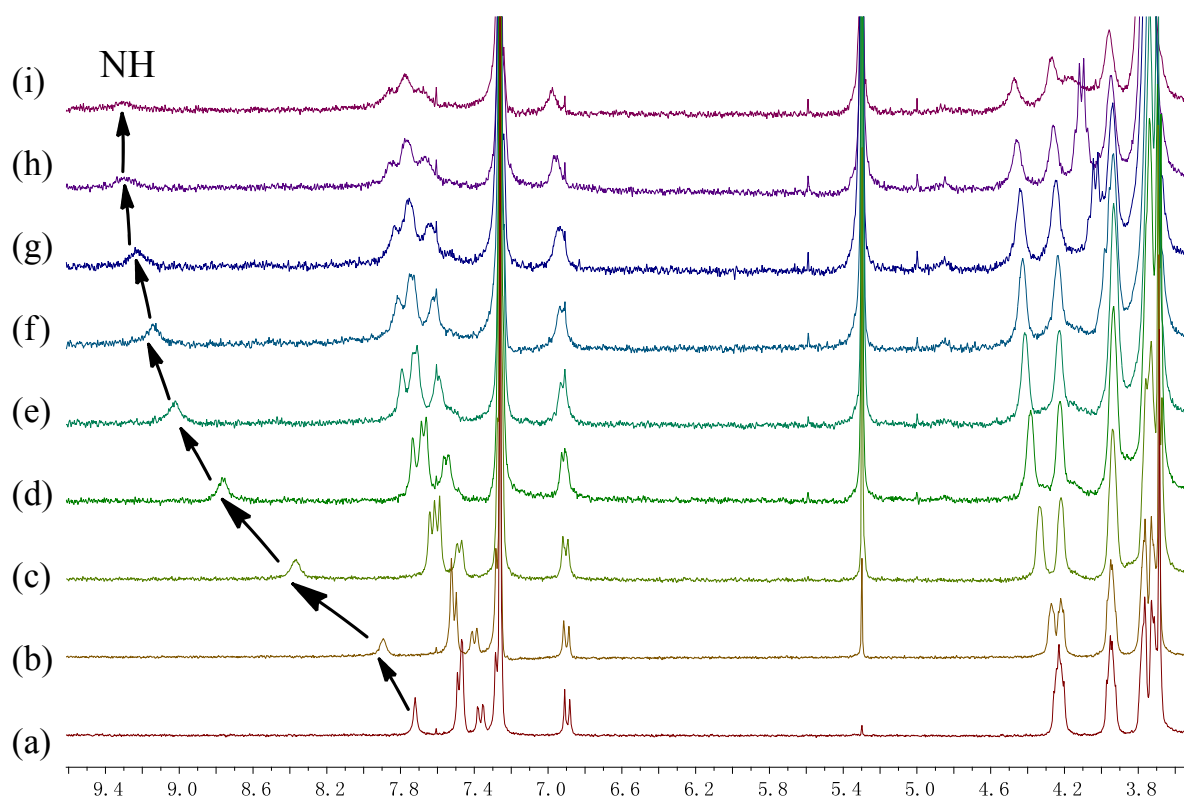


#### 4. Electrospray ionization mass spectrometry for the mixture of **1** and **2**



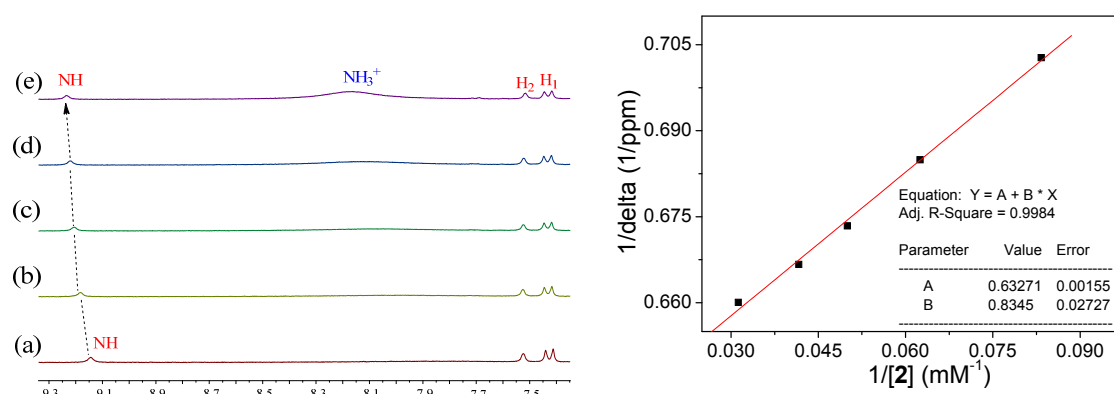
**Figure S10.** Electrospray ionization mass spectrum for the mixture of **1** and **2**. The spectrum displays two intense peaks locating at  $m/z$  722.7 (100%) and 774.2 (76%), corresponding to  $[\mathbf{1} \cdot \mathbf{2} - \text{Cl} - \text{H}]^{2+}$  and  $[\mathbf{1} \cdot \mathbf{2}_2 - 2\text{Cl}]^{2+}$ , respectively.

#### 5. $^1\text{H}$ NMR titration between **1** and **2** in $\text{CDCl}_3$



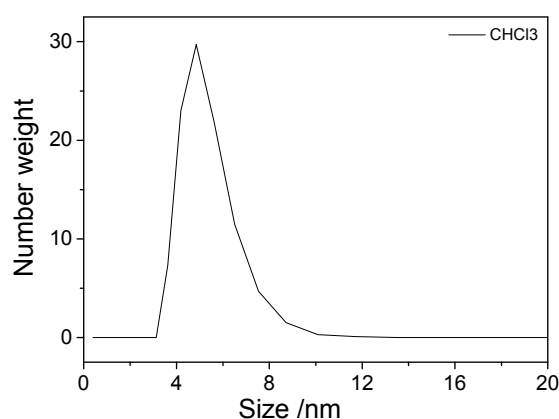
**Figure S11.**  $^1\text{H}$  NMR titration spectra (300 MHz, chloroform- $d$ , room temperature) of **1** at the concentration of 2 mM upon stepwise addition of **2**: (a) 0 mM, (b) 0.2 mM, (c) 0.6 mM, (d) 1.0 mM, (e) 1.5 mM, (f) 2.0 mM, (g) 3.0 mM, (h) 6.0 mM, (i) 10 mM.

## 6. Benesi-Hildebrand plot for the complexation between **1** and **2**



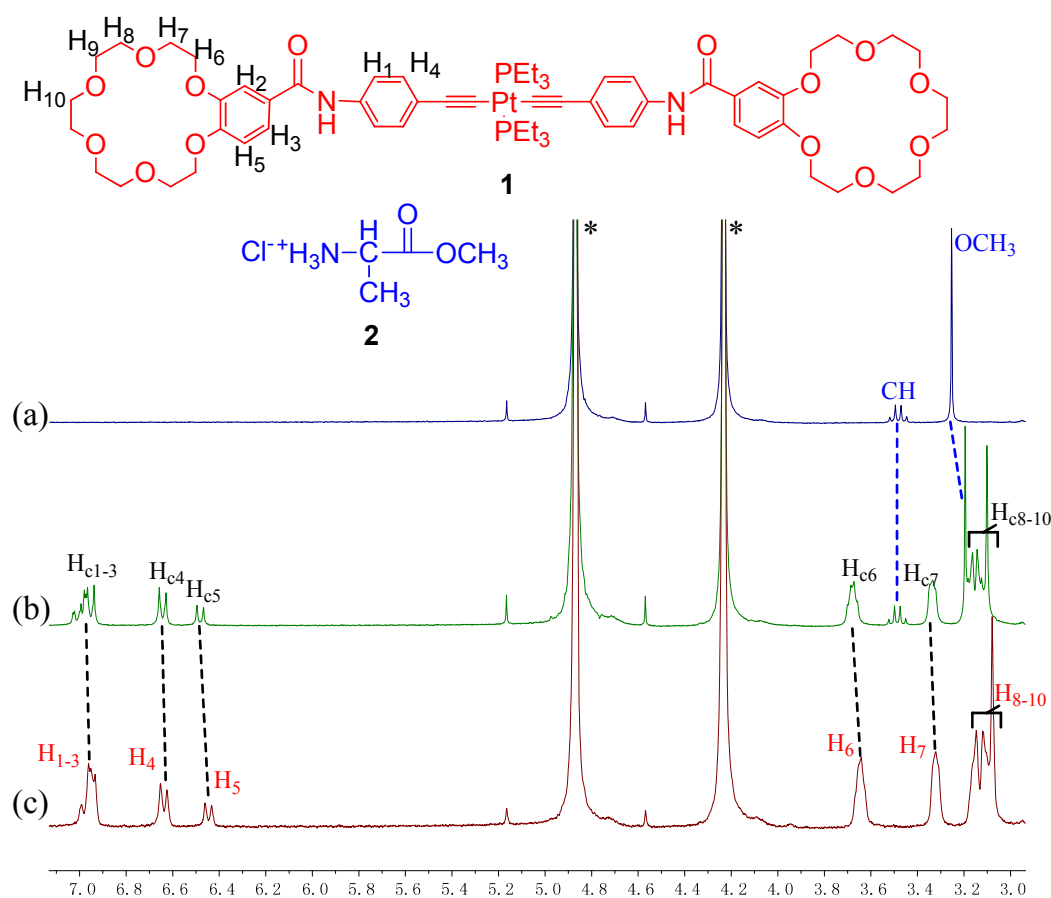
**Figure S12.** *left*, <sup>1</sup>H NMR titration spectra (300 MHz, chloroform-*d*, room temperature) of **1** at the concentration of 2.00 mM upon stepwise addition of **2**: (a) 12.0 mM, (b) 16.0 mM, (c) 20.0 mM, (d) 24.0 mM, (e) 32.0 mM; *right*, Benesi-Hildebrand plot for the complexation between **1** and **2**. Δ<sub>0</sub>, representing the chemical shift difference between the uncomplexed and fully complexed species, is the reciprocal value of the plot intercept. Hence, Δ<sub>0</sub> value is determined to be 1.581 ppm.

## 7. DLS measurement of **1** in chloroform



**Figure S13.** Hydrodynamic size distributions of a 10<sup>-4</sup> M solution of **1** measured by DLS at 25 °C in CHCl<sub>3</sub>. Very small aggregates (average hydrodynamic diameter ≈ 5 nm) are detected for a 10<sup>-4</sup> M solution of **1** in chloroform, proving that monomer **1** maintains monomer state in CHCl<sub>3</sub>.

8.  $^1\text{H}$  NMR spectra for the complexation between **1** and **2** in  $\text{CD}_3\text{OD}/\text{CDCl}_3$



**Figure S14.** Partial  $^1\text{H}$  NMR spectra (300 MHz,  $d_4$ -methanol/ $d$ -chloroform (3/1, v/v), 25 °C): (a) 4.00 mM **2**; (b) a 1 : 2 mixture of **1** and **2** ( $[\mathbf{1}] = 2\text{ mM}$ ,  $[\mathbf{2}] = 4\text{ mM}$ ); (c) 2.00 mM **1**. Signals affiliated with solvents are denoted by star symbols. Herein “c” denotes complexed species.

*References:*

- S1. Pagliai, F.; Pirali, T.; Del Grosso, E.; Di Brisco, R.; Tron, G. C.; Sorba, G.; Genazzani, A. *A. J. Med. Chem.* **2006**, *49*, 467–470.
- S2. Calderon, V.; Schwarz, G.; Garcia, F.; Tapia, M. J.; Valente, A. J. M.; Burrows, H. D.; Garcia, J. M. *J. Polym. Sci. Part A: Polym. Chem.*, **2006**, *44*, 6252–6269.