A supramolecular hyperbranched polymer based on molecular recognition between benzo-21-crown-7 and secondary ammonium salt

Hui Li, Xiaodong Fan*, Wei Tian*, Haitao Zhang, Wanbin Zhang, and Zhen Yang

The Key Laboratory of Space Applied Physics and Chemistry, Ministry of Education and Shaanxi Key Laboratory of Macromolecular Science and Technology, School of Science, Northwestern Polytechnical University, Xi'an 710072, P. R. China

E-mail: xfand@126.com, happytw_3000@nwpu.edu.cn

Supporting information

1. Materials and Methods

Compound **3**[S1], **6**[S2], **7**[S3], were synthesized according to the literature procedure. The other reagents and solvents were either employed as purchased or dried prior to use by usual laboratory methods. Column chromatography was performed on silica gel (200-300 mesh). All reactions were carried out in atmosphere unless noted.

NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer with TMS as the internal standard. NOESY experiments were performed on a Bruker AVANCE III 400 MHz spectrometer. High-resolution electrospray ionization mass spectra (HR-ESI-MS) were obtained on a Bruker Esquire 3000 plus mass spectrometer equipped with an ESI interface and ion trap analyzer. MALDI-TOF-MASS spectrometry was performed on a AXIMA-CFR plus mass spectrometer . Viscosity measurements were carried out with Ubbelohde micro viscometers (Shanghai Liangjing Glass Instrument Factory, 0.40 mm and 0.71 mm inner diameter) at 298 K in chloroform/acetonitrile (1/1, v/v). Transmission electron microscope (TEM) experiments were carried out on a JEM-2100 instrument. Dynamic light scattering (DLS) measurements were carried out on a Brookhaven BI-9000AT system (Brookhaven Instruments Corporation, USA), using a 200-mW polarized laser source (λ = 630 nm).

2. Concentration-dependent ^{1}H NMR spectrum

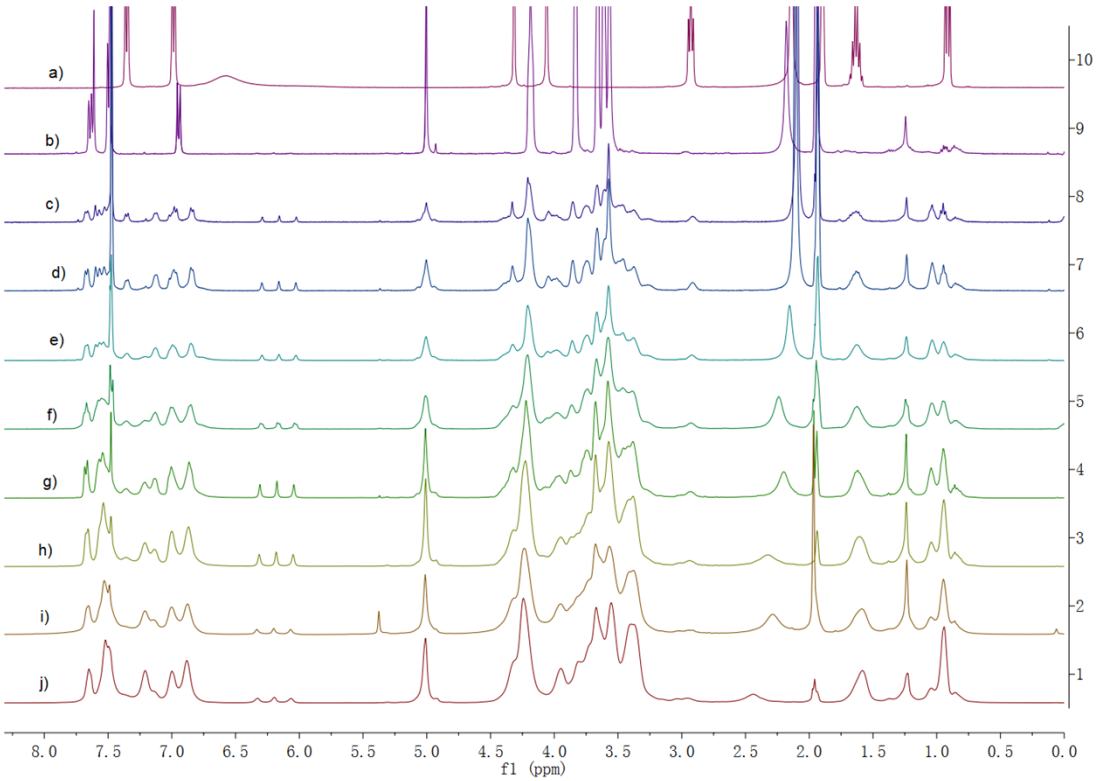
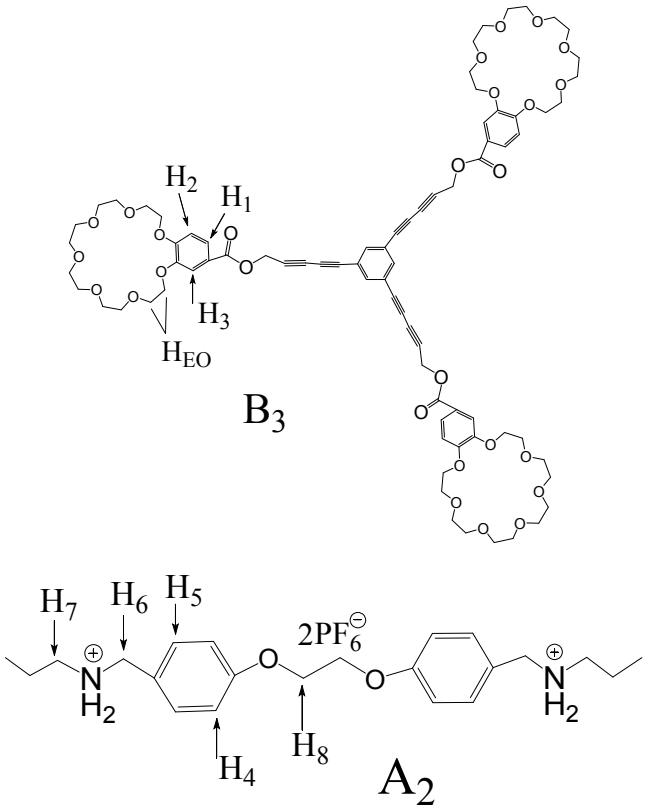


Figure S1. ^{1}H NMR spectra (400 MHz, $CDCl_3$–CD_3CN = 1/1, v/v, 298 K) of (a) individual A_2 (b)

individual B_3; mixtures of B_3 and 1.50 equiv. A_2 at different B_3 concentrations (c) 1mM, (d)2mM, (e)4mM, (f) 8mM, (g) 12mM, (h)24mM, (i)35mmol, (j)70mM.

3. ^{1}H-^{1}H COSY NMR spectrum

The ^{1}H-^{1}H COSY NMR experiment was carried out at a concentration of 10.0 mM(B_3) to identify the signals of protons of A_2 and B_3. The signal peaks including uncomplexed and complexed (branched and cyclic species) molecules all appeared at the concentration region. As shown in Figure S2, strong correlations were observed between the aromatic protons H_4 and H_5 on A_2, such as H_4uc and H_5uc, H_4cyc and H_5cyc, H_4br and H_5br. The correlation (hyperbranched peaks) between H_1br and H_3br on B_3 were also observed at the same time. The signals of complicated concentration-dependent ^{1}H NMR spectra (Fig. 1) were accurately identified with the assistance of ^{1}H–^{1}H COSY experiment.



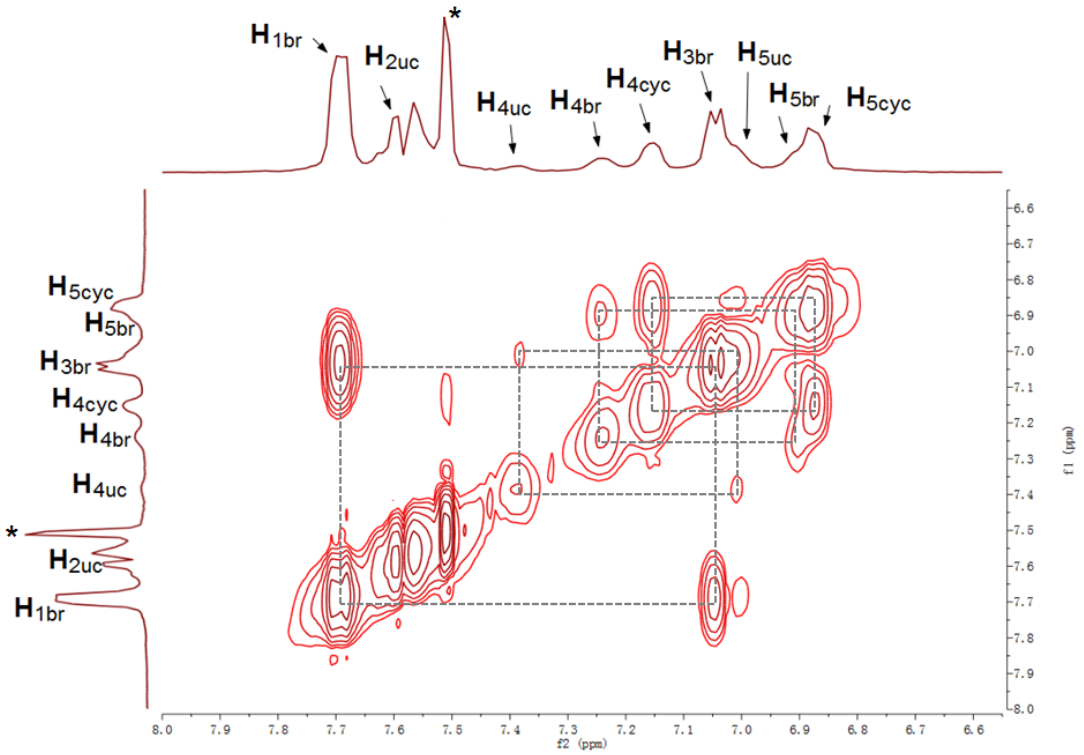
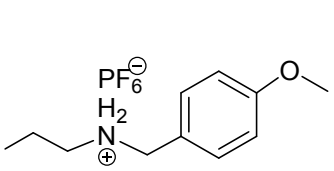
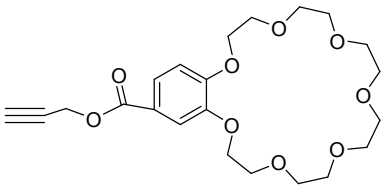


Figure S2. Partial COSY NMR (400 MHz, $CDCl_3/CD_3CN$ = 1/1, v/v, 298 K) spectrum of a solution of B_3(10mM) and 1.50 equiv A_2(15mM).Peaks of linear polymers, cyclic oligomers, and uncomplexed monomer are designated by lin, cyc, and uc, respectively. Peaks of uncomplexed monomer, cyclic oligomers, and the hyperbranched polymers, are designated as uc, cyc, and br, respectively. Signals affiliated with solvents are denoted by star symbols.

4. The discussion of the K_a values of Benzo-21-crown-7/secondary ammonium salt recognition motif



A_1



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To estimate the *K*a value for interaction of A_2 with B_3 **,** we use compound 4 and the model compound A_1 to determine the association constant K_a of the B21C7/Dialkylammonium system according to the reference method[S1]. The K_a value of B21C7-Dialkylammonium complexes, slow-exchange systems, could be calculated from integrations of complexed and uncomplexed peaks in ^{1}H NMR spectrum. The *K*a value was determined at 10.00 mM host and guest in $CDCl_3/CD_3CN$(1/1,v/v)solution. Using the reference method[S1], *K*a {[4**.** $\mathbf{A_1}$]/[4][$\mathbf{A_1}$] }

is equal to 710 ± 72 M^{-1} in chloroform/acetonitrile solution(1/1, v/v), which is close to the literature value.

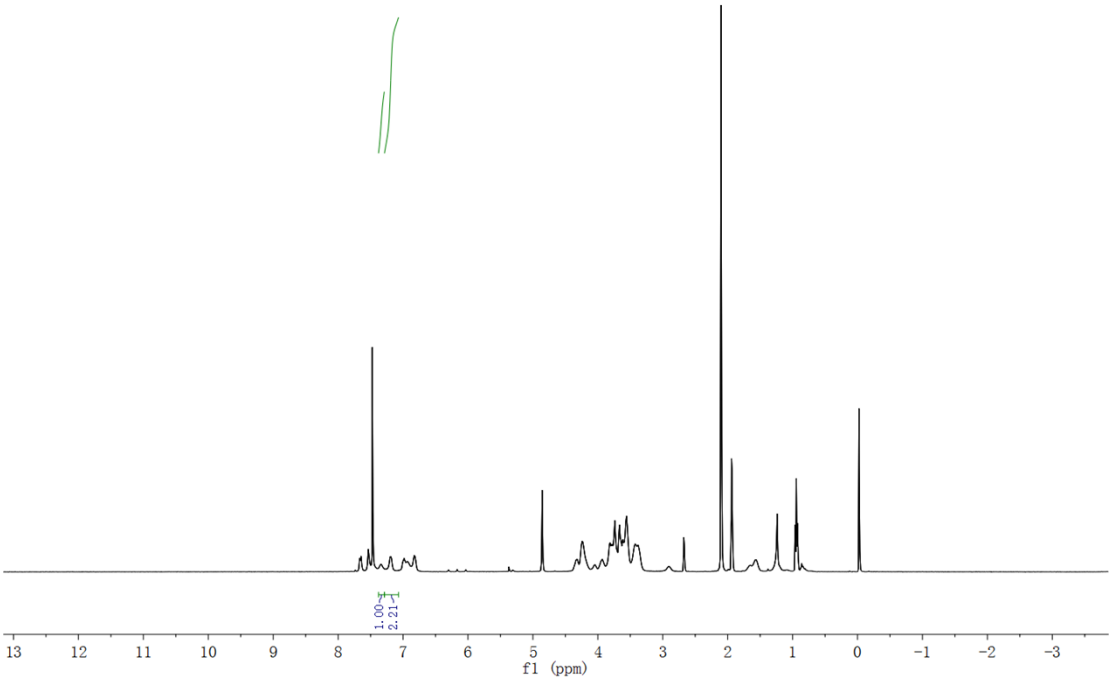


Figure S3. ^{1}HNMR spectra (400 MHz, $CDCl_3/CD_3CN$ = 1/1, v/v, 298 K) of 10.00 mM **4** and $\mathbf{A_1}$.

5. XRD study of supramolecular hyperbranched polymer

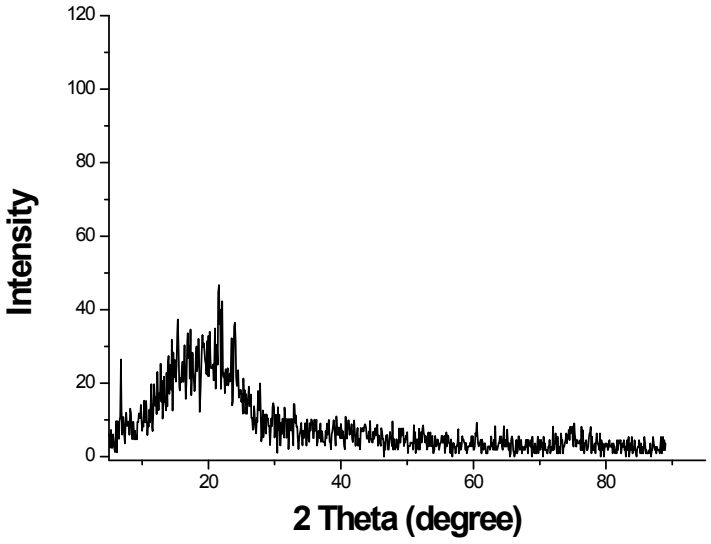


Figure S4. XRD analysis of sample obtained from concentrated mixed solution of B_3 and A_2.

XRD analysis of sample obtained from concentrated mixed solution of B_3 and A_2 indicating that it is amorphous.

6. Stimuli-Responsiveness of the supramolecular hyperbranched polymer investigated by NOESY and DLS experiments

The reversible disassembly–assembly process was also investigated by NOESY NMR experiments (B_3= 45 mM). As shown in Figure S5, the signal peak of H_{4br} and H_{5br} from A_2 disappeared after the addition of K^+, the broad peaks of the ^1H NMR became sharp and simple, suggesting that the polyether ring of the B21C7 group of B_3 was occupied by K^+ and the large aggregates were disassembled into low-molecular-weight species. Upon subsequent addition of B18C6, the correlation between H_{4br} from A_2 and H_{EO} from B_3 was recovered and the peaks became broad again, indicating the hyperbranched polymer was reformed.

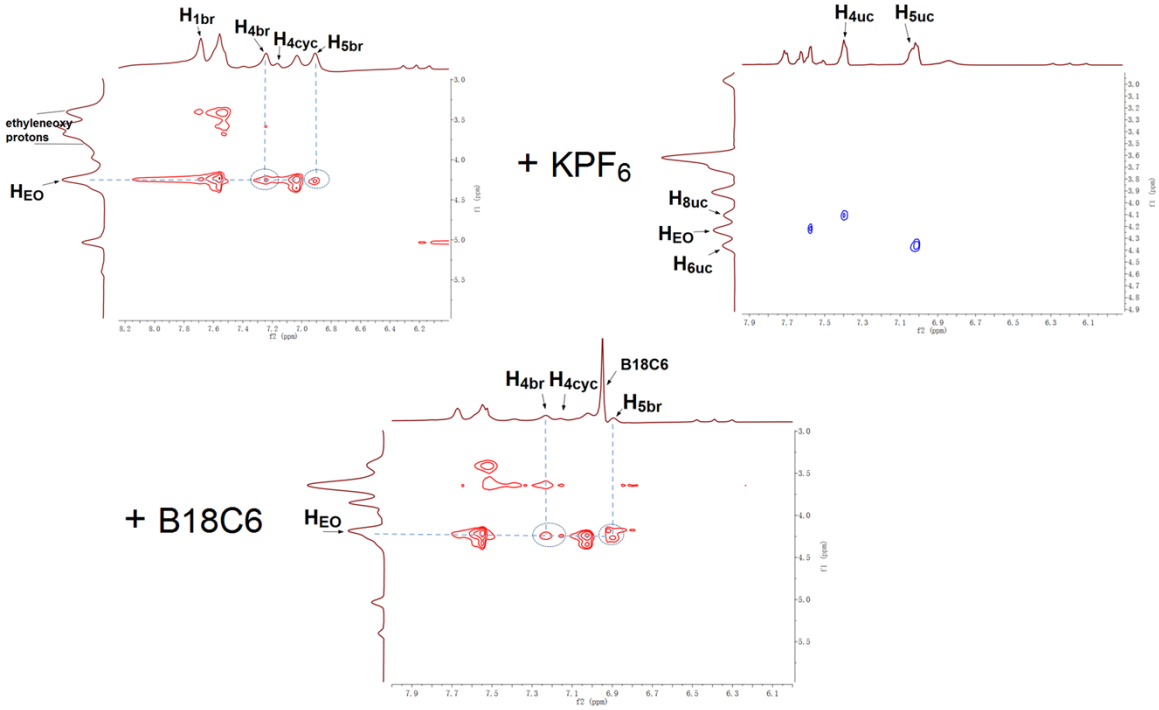


Figure S5. Partial NOESY NMR spectra (400 MHz, $CDCl_3$–CD_3CN = 1/1, v/v, 298 K) of (a) B_3 (45 mM) with 1.5 equiv. A_2, (b) after addition of 3 equiv. KPF_6, and (c) after addition of 3 equiv. B18C6.

DLS was conducted to verify the concentration-dependent formation of SHP. As shown in Figure S6 (a), almost no aggregation was observed in 10 mM B_3 and 1.5 equiv. A_2 in chloroform/acetonitrile solution. When the concentration of B_3 was increased to 65 mM, the solution of B_3 and 1.5 equiv. A_2 has an average hydrodynamic diameter (D_H) value of 531 nm (Figure S6 (b)), manifesting the concentration-dependent formation of SHP. This result also indicated that the as-prepared hyperbranched polymers without aggregation could be obtained by controlling the concentration.

DLS was also used to confirm the disassembly–assembly process of SHP. As shown in Figure S6 (b), an evident decrease of the average D_H from 531 nm to 2.32

nm was found after adding KPF_6 to the solution of B_3 (65mM) and 1.5 equiv. A_2, indicating that the complexation between B21C7 and Dialkylammonium salt was destroyed and the disassembly occurred. The average D_H value was then recovered after the addition of B18C6, implying that the formation of SHP again.

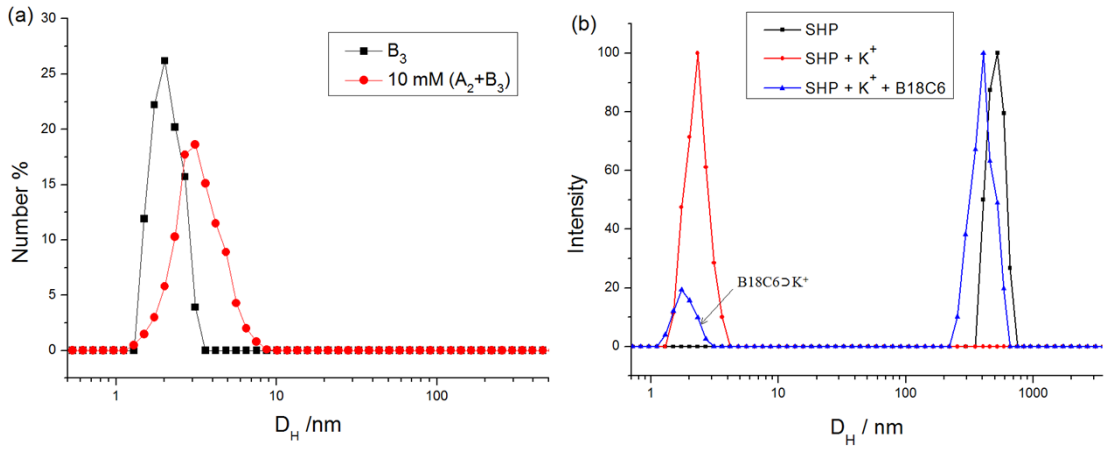


Figure S6. **(a)** Distributions of the hydrodynamic diameter of B_3 and a mixture of 10 mM B_3 and 1.5 equiv. A_2 in chloroform/ acetonitrile (1 : 1, v/v) at 298 K. **(b)** Size distributions of SHP (B_3=65mM) in chloroform/ acetonitrile (1 : 1, v/v) at 298 K before and after addition of KPF_6, and removal of K^+.

7. The discussion of molar ratio between A_2 and B_3 for the formation of supramolecular hyperbranched polymer.

It is well known that the crown ether recognition system assembles usually in $CHCl_3/CH_3CN$ (1 : 1, v/v) mixture and one B21C7 unit bind one secondary ammonium salt unit.[S1] Different molar ratios between A_2 and B_3 may affect the formation of SHP. Thus, we checked the effect of different ratios between A_2 and B_3 for the formation of SHP by NMR analysis - equivalent between B_3 and A_2, and 1 : 1.5 molar ratio of B_3 and A_2. No precipitation (fixed B_3 concentration 15 mM) was observed when B_3 and A_2 were mixed for 1:1 or 1:1.5 molar ratio in $CHCl_3/CH_3CN$ solution. Their ^1H NMR spectra were listed in Figure S7. H_4 from A_2 were all split into two sets of peaks in Figure S7 (a) and (b), corresponding to complexed cyclic oligomers (H_{4cyc}) and hyperbranched assembly (H_{4br}). As shown in Figure S7 (b), the relative intensity of peak (7.21 ppm) corresponding to hyperbranched assembly slightly increased compared with that of Figure S7 (a). Considering the fixed B_3 concentration, the increasing hyperbranched assembly (comparated with 1:1 ratio) is similar to the effect of increasing concentration. Thus, we found the ratio between A_2 and B_3 (1 : 1 or 1 : 1.5) do not markedly affect the formation of SHP in this system. In previous work, we found the precipitation appeared for the ratio range from 0.3-1.8 between A_2 and B_3 (PEG-NP_2 and β-CD_3) if guest adopt long flexible chain.[S5] Therefore, the structure of precursors may play important role in the formation of SHP instead of changing the molar ratio between host and guest molecules in this system.

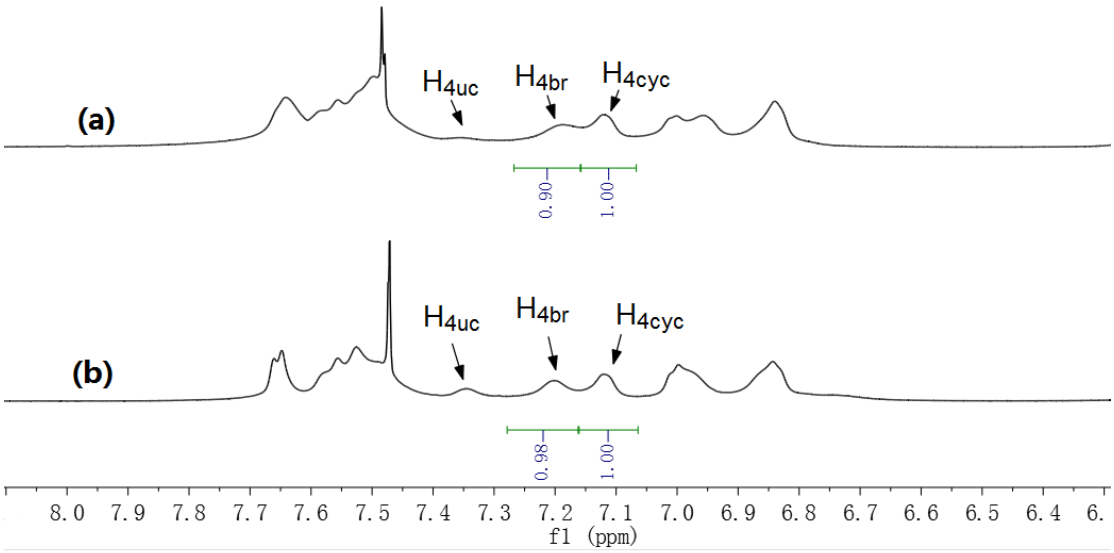
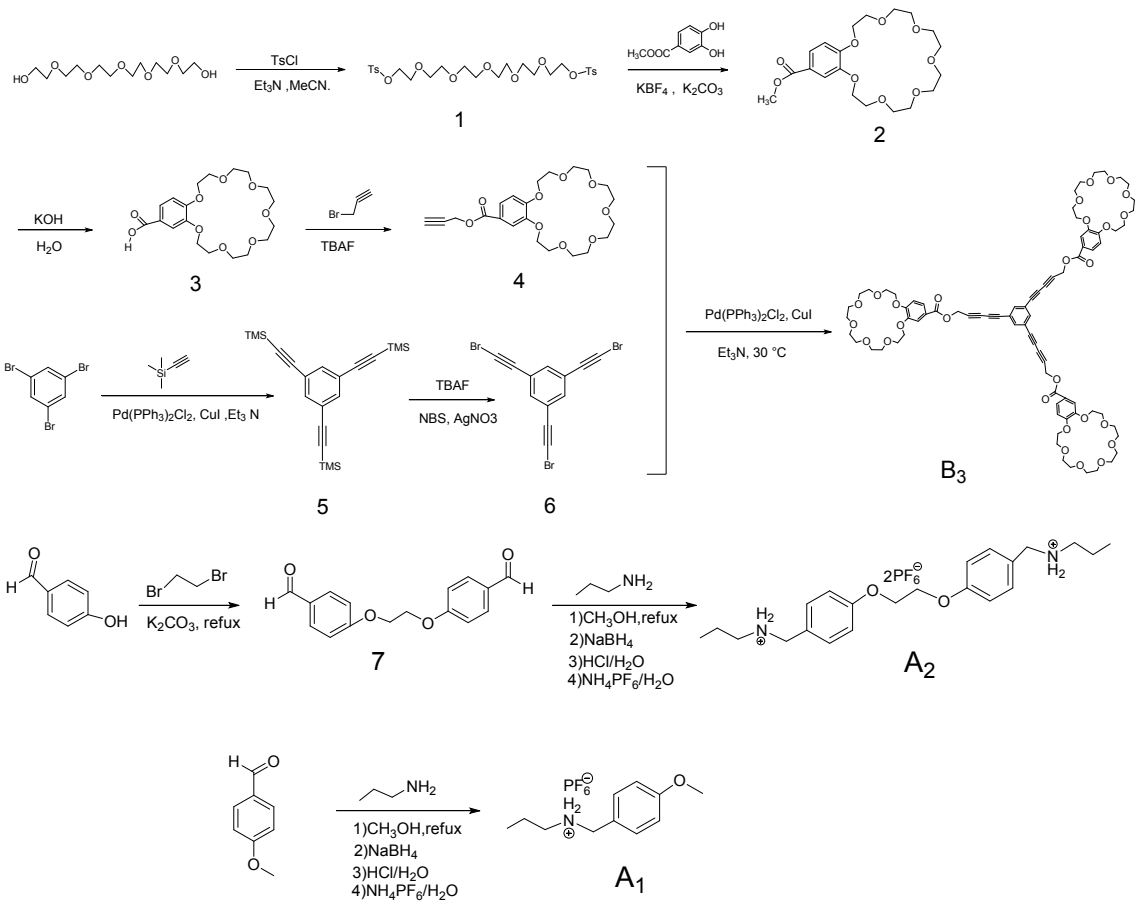


Figure S7. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$–CD_3CN = 1/1, v/v, 298 K, fixed B_3 concentration 15mM) of (a) equimolar mixture of B_3 and A_2 (b) 1 : 1.5 molar ratio of B_3 and A_2. Peaks of uncomplexed monomers, cyclic oligomers, and the hyperbranched assembly, are designated as uc, cyc, and br, respectively.

8. Synthesis of the monomers B_3, A_2, and A_1.

Design and Synthesis of Monomers. The synthetic routes of the desired compounds A_2, B_3, and A_1 are showed in Scheme S1. TBAF-mediated alkylation is an efficient, mild, and reliable approach for the rapid synthesis of esters[S4], compound 4 was prepared by the reaction of 3 and Propargyl bromide in the presence of TBAF. Monomer B_3 was obtained by coupling between core1,3,5-tris(bromoethynyl)benzene (6) and compound 4, in which the core 6 serves as the backbone to ensure the rigidity of the monomer B_3 and increases the solubility of B_3 in organic solvents. The analysis of proton NMR can also be simplified because of the lack of proton on rigid alkynyl chain. Monomer A_2 was synthesized starting with the Knoevenagel condensation reaction between 7 and propylamine followed by acidification and anion exchange. Model compound A_1 was obtained under similar synthetic method as A_2. These monomers were fully characterized.



Scheme S1 Synthetic routes of the homotritopic B21C7 host B_3 , the homoditopic dialkylammonium salt guest A_2, and the monotopic dialkylammonium salt guest A_1

Synthesis of Compound 4

A solution of compound 3(2.00g, 5mmol), 3-Bromo-1-propyne（0.72g，6mmol）, and Tetrabutylammonium fluoride (1mol/L in THF, 6ml) in tetrahydrofuran (25 mL) was stirred for 12 h at room temperature, The solvent was evaporated under reduced pressure and the residue was partitioned between dichloromethane (50 mL) and water (50 mL). The aqueous layer was further washed with dichloromethane (3 × 100 mL). The organic phases were combined and dried over anhydrous Na_2SO_4. After the solvent was removed, the resulting residue was subjected to column chromatography (CH_2Cl_2/CH_3OH= 60:1), to give 4 (1.68g, 96 %) as a white solid. ^{1}HNMR (400 MHz, CDCl3): δ (ppm) = 2.50(t, *J* = 2.4 Hz ,1H), 3.63–3.69 (m, 8H),3.70–3.75 (m, 4H), 3.77–3.82 (m, 4H), 3.91–3.97 (m, 4H),4.18–4.24 (m, 4H), 6.87 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 2.0 Hz,1H), 7.68 (dd, *J1* = 2.0 Hz, *J2* = 2.0 Hz, 1H). ^{13}C NMR (75MHz, CDCl3): δ (ppm) =165.22, 153.11, 148.13, 124.09, 121.85, 114.49, 112.10, 77.81, 77.48, 76.84, 74.94, 71.11, 71.00, 70.89, 70.86, 70.80, 70.78, 70.37, 69.42, 69.27, 69.12, 68.91, 52.08. HR-ESI-MS ($C_{78}H_{90}O_{27}$): *m/z* calcd for $[M + Na]^+$ = 461.1782, found =461.1799.

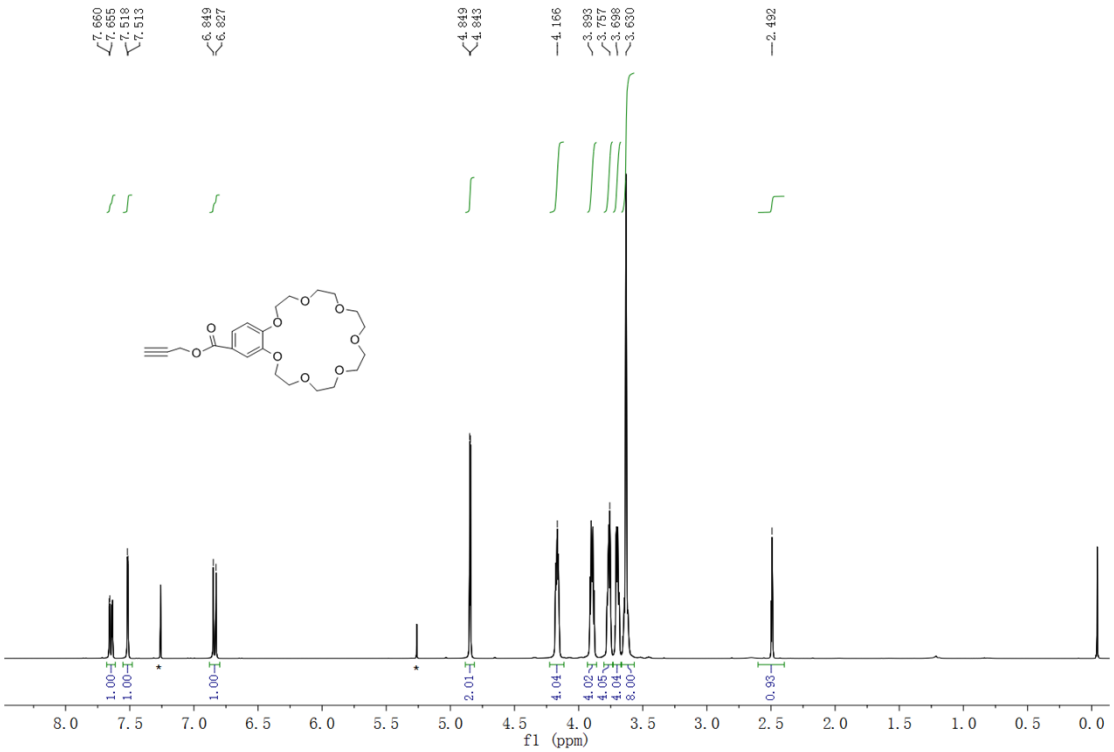


Figure S8. [1]H NMR spectrum (400 MHz, CDCl3) of compound **4**

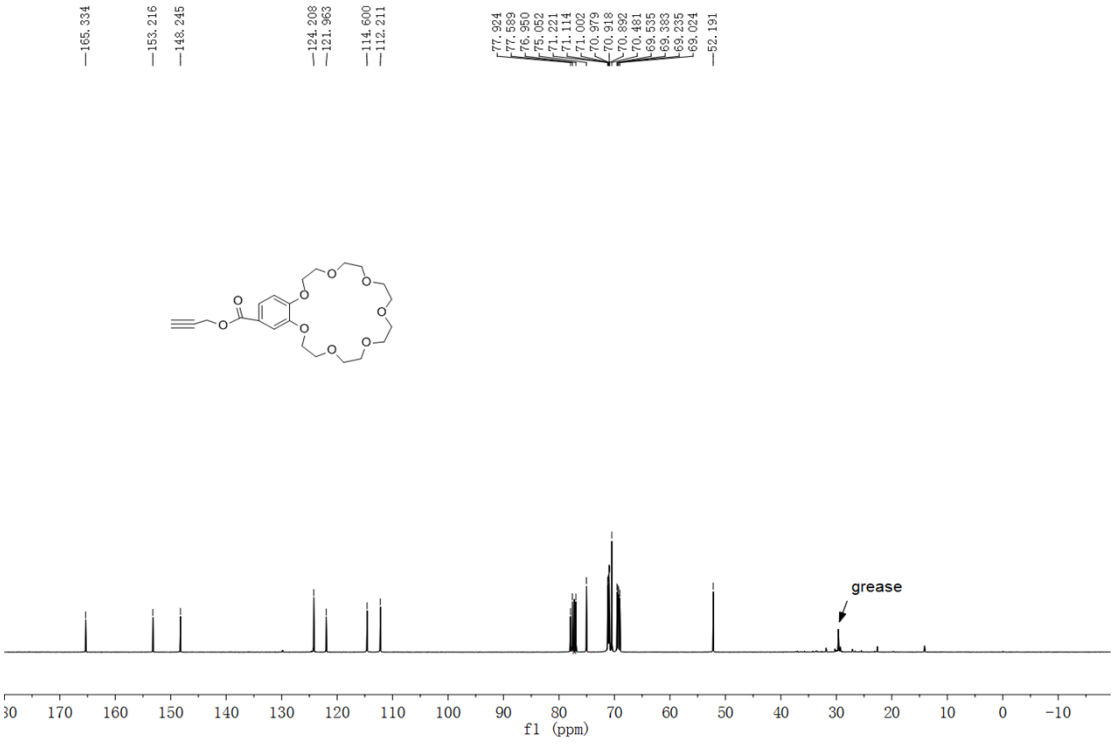


Figure S9.[13]C NMR spectrum (75 MHz, CDCl3, room temperature) of compound **4**.

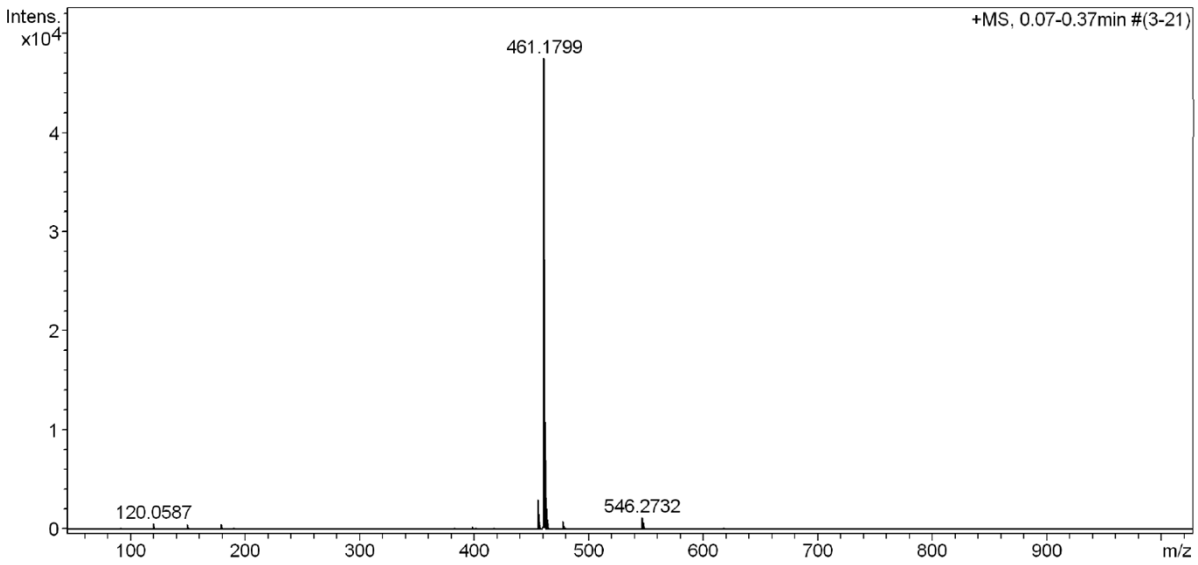


Figure S10. Electrospray ionization mass spectrum of compound **4**

Synthesis of Compound B_3

In a sealed tube, 30 mL of 20% Et_3N in tetrahydrofuran was degassed vigorously for 30 minutes. The following compounds were then added in order: compound 4 (2.22g, 5.04mmol), compound 6（0.5g，1.29mmol）, dichlorobis(triphenylphosphine) palladium(II) (0.027g, 0.038mmol) and Cu(I)I (0.007g, 0.038mmol). The dark mixture was stirred at 35 ℃ for 12 h. The organic solvent was evaporated under reduced pressure and the residue was partitioned between dichloromethane (50 mL) and water (50 mL). The aqueous layer was further washed with dichloromethane (3 × 100 mL). The organic phases were combined and dried over anhydrous Na_2SO_4. After the solvent was removed, The brown residue was purified by column chromatography (CH_2Cl_2/CH_3OH= 15:1), to afford B_3 (1.68g, 30 %) as a white solid. ^{1}HNMR (400 MHz, CDCl3): δ (ppm) = 3.63–3.69 (m, 24H),3.75–3.76 (m, 12H), 3.82–3.83 (m, 12H), 3.95–3.96 (m, 12H), 4.21–4.24 (m, 12H), 6.89 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 2.0 Hz,1H), 7.70 (d, *J*=2.0 Hz, 1H). ^{13}C NMR (75MHz, CDCl3): δ (ppm) = 165.4, 153.4, 148.4, 136.8, 124.4, 122.7,121.8, 114.6, 112.2, 77.8, 77.3, 75.9, 75.1, 71.48, 71.36, 71,24, 71.21, 71.12, 71.11, 70.7,70.6, 69.7, 69.5, 69.3, 69.2, 52.8ppm. MALDI-TOF-MS: *m/z* calcd for $[M + Na]^+$ = 1481.5419, found =1481.5421.

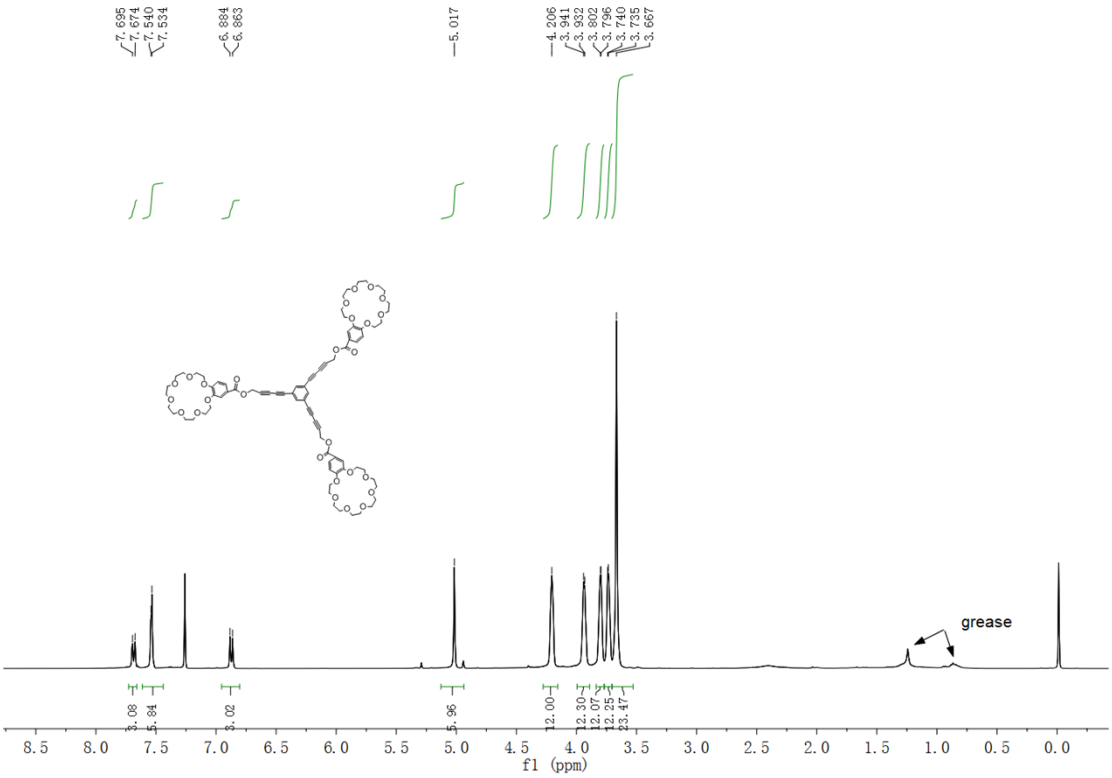


Figure S11. [1]H NMR spectrum (400 MHz, CDCl3) of compound **B_3**

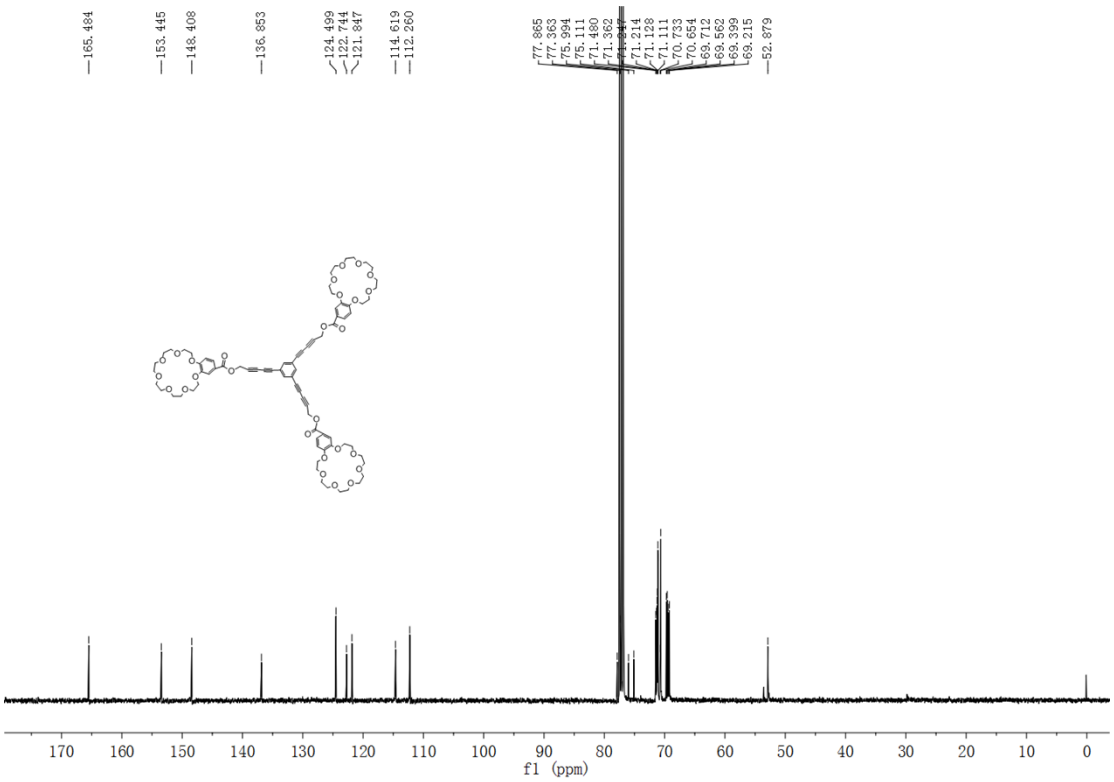


Figure S12.[13]C NMR spectrum (75 MHz, CDCl3, room temperature) of compound **B_3**.

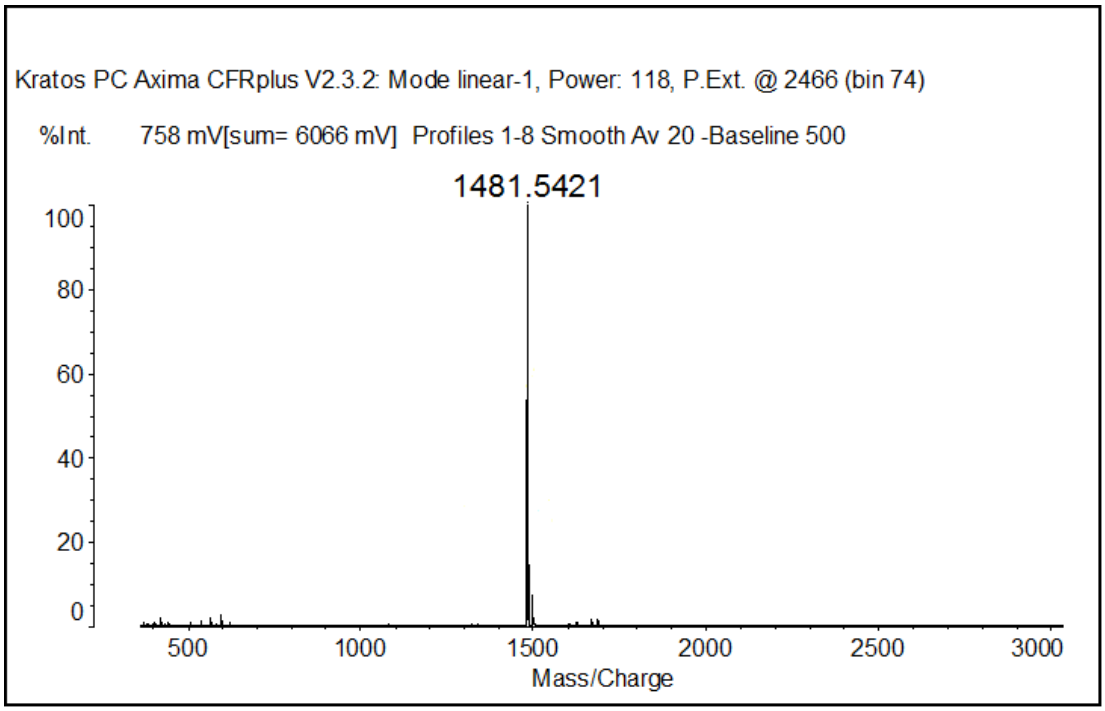


Figure S13. MALDI-TOF-MASS spectrum of compound $\mathbf{B_3}$.

Synthesis of Compound A_2

Bisaldehyde 7 (1.00g, 3.7mmol) and propylamine (0.44g, 7.4mmol) were dissolved in methanol (60 mL) and heated at 65 ℃ under N_2 atmosphere overnight. After the reaction mixture was cooled to ambient temperature, $NaBH_4$(0.56 g, 15.0 mmol) was added to the solution in small portion and the mixture was stirred at room temperature for another 12 h. Water (30 mL) was added to quench the remaining $NaBH_4$, and 2 M HCl was added to acidify the amine. The solvent was removed under reduced pressure to give a white solid which was dissolved in deionized water/methanol (150 mL, 5:1, v/v). A saturated aqueous solution of NH_4PF_6 was added to afford a white precipitate which was filtered off and washed with deionized water to afford A_2 as a white solid (1.07 g, 45%).^{1}H NMR (400 MHz, CD_3CN, 298 K): ppm = 0.95(t, J = 7.2 Hz,6H), 1.65(m, 4H), 2.95(t, J = 7.2 Hz, 4H), 4.07 (s, 4H), 4.35 (s, 4H), 6.62(br, 2H), 7.01(d, J = 8.4 Hz, 4H), 7.39 (d, J = 8.8 Hz, 4H), ^{13}C NMR (75MHz, CDCl3): δ (ppm) = 160.53, 132.70, 123.75, 115.75, 67.52, 51.83, 50.03, 20.01, 11.01ppm. HR-ESI-MS ($C_{22}H_{34}F_{12}N_2O_2P_2$): *m/z* calcd for $[M\text{-}PF_6^-]^+$ = 503.2251, found =503.2252.

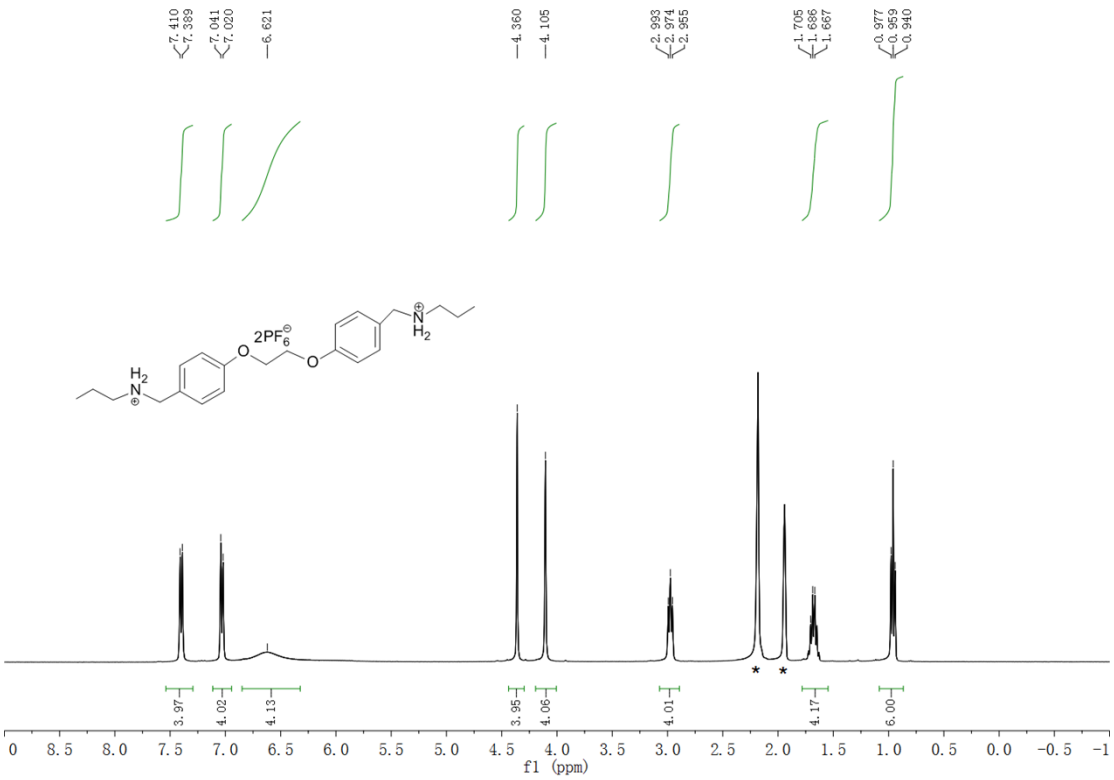


Figure S14. [1]H NMR spectrum (400 MHz, CDCl3) of compound $\mathbf{A_2}$

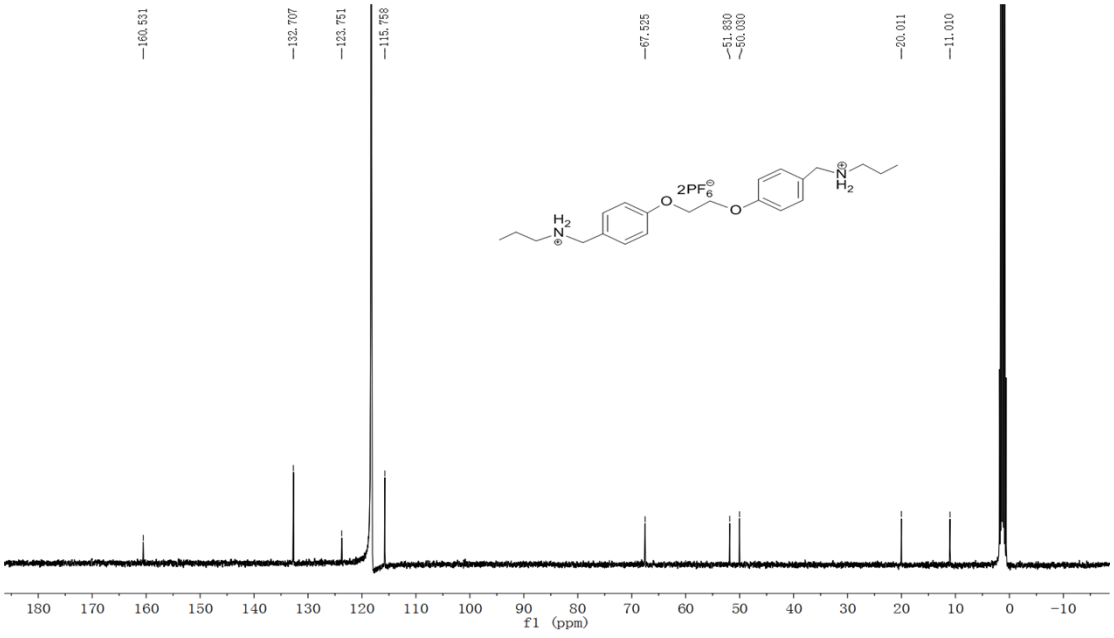


Figure S15.[13]C NMR spectrum (75 MHz, CDCl3, room temperature) of compound $\mathbf{A_2}$.

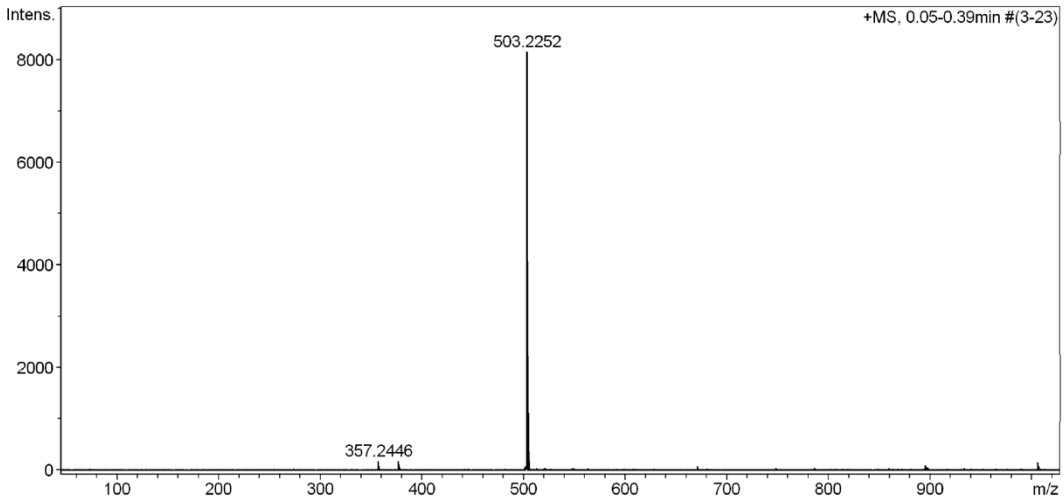


Figure S16. Electrospray ionization mass spectrum of compound $\mathbf{A_2}$

Synthesis of Compound A_1

p-anisaldehyde (1.00g, 7.3mmol) and propylamine (0.43g, 7.3mmol) were dissolved in methanol (60 mL) and heated at 65 ℃ under N_2 atmosphere overnight. After the reaction mixture was cooled to ambient temperature, $NaBH_4$(0.28 g, 7.5 mmol) was added to the solution in small portion and the mixture was stirred at room temperature for another 12 h. Water (30mL) was added to quench the remaining $NaBH_4$, and 2 M HCl was added to acidify the amine. The solvent was removed under reduced pressure to give a white solid which was dissolved in deionized water/methanol (100 mL, 5:1, v/v). A saturated aqueous solution of NH_4PF_6 was added to afford a white precipitate which was filtered off and washed with deionized water to afford A_1 as a white solid (1.18 g, 50%).^{1}H NMR (400 MHz, CD_3CN, 298 K): ppm = 0.95(t, J = 7.2 Hz,3H), 1.66(m, 2H), 2.97(t, J = 7.2 Hz, 2H), 3.81 (s, 3H), 4.09(s, 2H), 6.69(br, 2H), 6.99(d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.8 Hz, 2H), ^{13}C NMR (75MHz, CDCl3): δ (ppm) = 161.60, 132.60, 123.29, 115.24, 55.98, 51.96, 50.09, 20.00, 10.99ppm. HR-ESI-MS ($C_{11}H_{18}F_6NOP$): m/z calcd for $[M\text{-}PF_6^-]^+$ = 180.1388, found =180.1388.

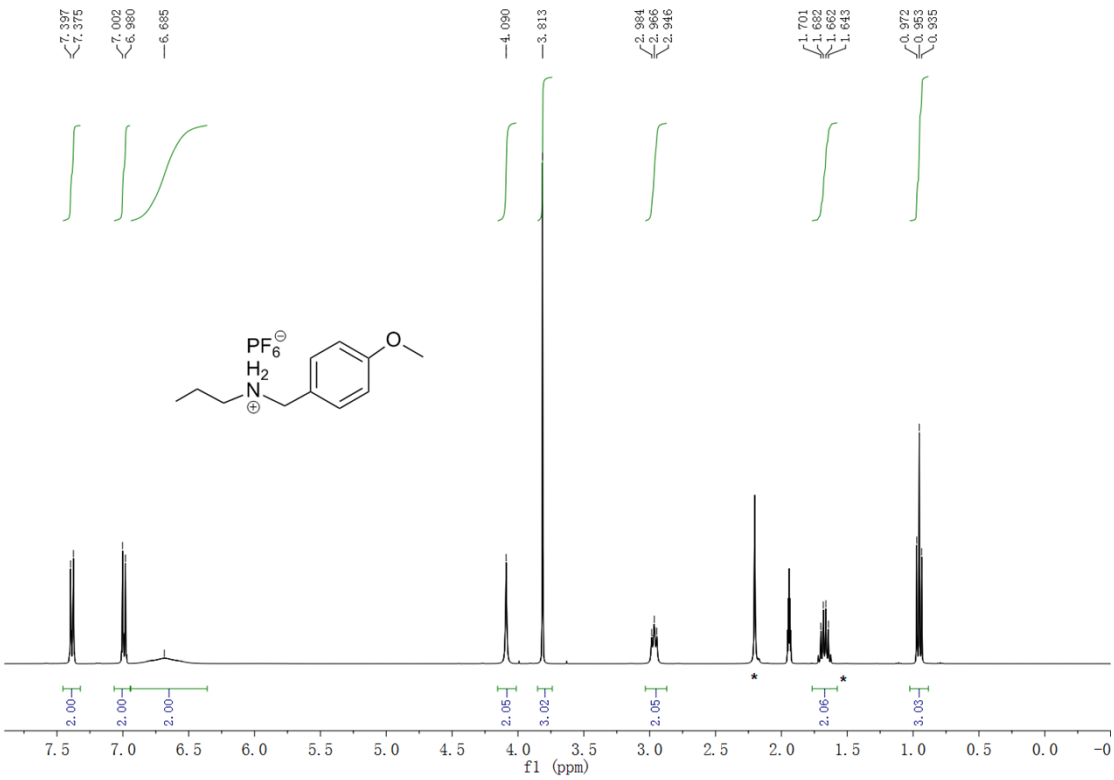


Figure S17. ^{1}H NMR spectrum (400 MHz, CDCl3) of compound $\mathbf{A_1}$

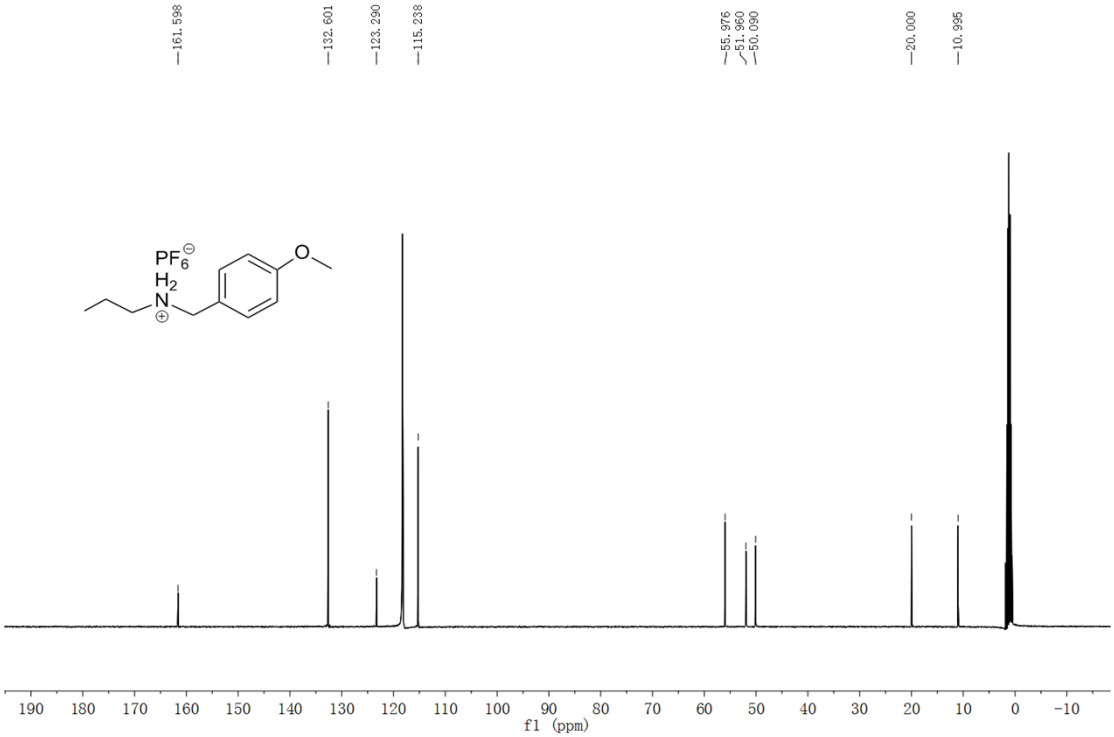


Figure S18. ^{13}C NMR spectrum (75 MHz, CDCl3, room temperature) of compound $\mathbf{A_1}$

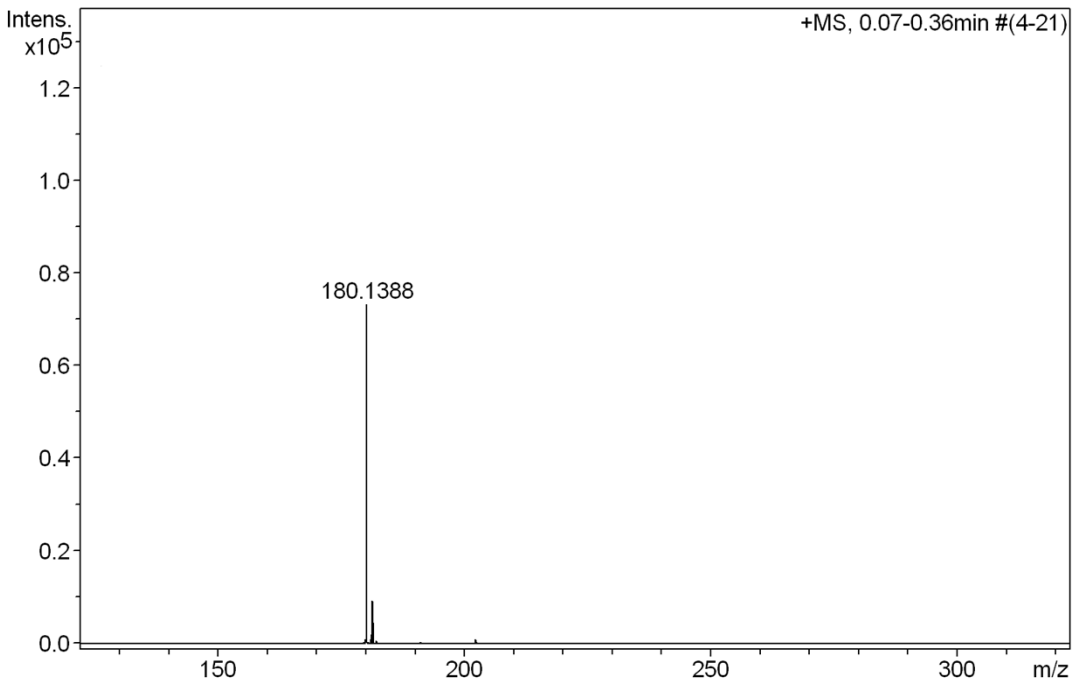


Figure S19. Electrospray ionization mass spectrum of compound $\mathbf{A_1}$

References:

S1. (a) C. J. Zhang, S. J. Li, J. Q. Zhang, K. L. Zhu, N. Li and F. H. Huang, *Org. Lett*., 2007, **9**, 5553-5556; (b) T. X. Xiao, X. Q. Feng, Q. Wang, C. Lin, L. Y. Wang and Y. Pan, *Chem. Commun*., 2013, **49**, 8329-8331.

S2. M. I .Mangione, R .A. Spanevello, *Macromolecules.,* 2013, **46**, 4754−4763.

S3. W. Jiang, K. Nowosinski, N. L. Löw, E. V. Dzyuba, F. Klautzsch, A. Schafer, J. Huuskonen, K. Rissanen and C. A. Schalley, *J. Am. Chem. Soc*., 2012, **134**, 1860−1868.

S4. C. Y. Wu, A. Brik, S. K. Wang, Y. H. Chen, C. H. Wong, *ChemBioChem*., 2005, **6**, 2176 – 2180.

S5. Z. Yang, X. D. Fan, W. Tian, D. Wang, H. T. Zhang and Y. Bai, *Langmuir*., 2014, **30**, 7319−7326.