Supporting Information for

Confined Pool-Buried Water-Soluble Nanoparticles from Reverse Micelles

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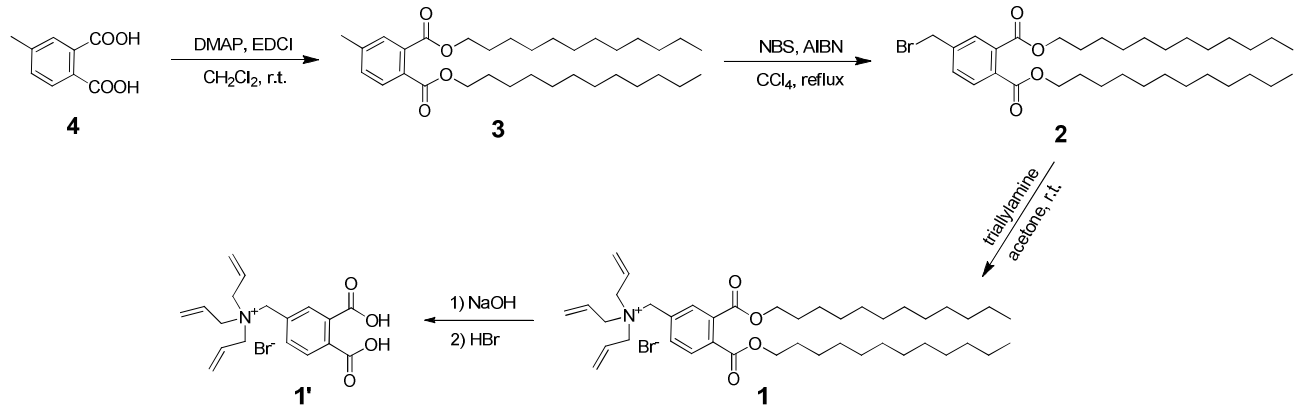
Synthesis

Scheme 1. Synthesis of compound **1** and **1′**



Compound 3.[1] To a stirred solution of 1-Ethyl-3-(3-dimethyllaminopropyl) carbodiimide hydrochloride (EDCI) (11.70 g, 61.05 mmol) and 4-dimethylaminopyridine (DMAP) (678 mg, 5.55 mmol) in anhydrous dichloroethane (60 mL) at 0 ºC, was syringed a solution of 4-methylphthalic acid **4** (5.0 g, 27.75 mmol) and 1-dodecanol (15.6 mL, 69.38 mmol) in anhydrous tetrahydrofuran (THF) (20 mL). The reaction was allowed to warm to room temperature and proceed until completion as monitored by TLC (10 h). After stirring, the reaction was acidified with 0.1 M HCl and extracted with dichloroethane (3 × 100 mL). The combined organic layer was further washed with brine (80 mL), dried over Na_2SO_4 and concentrated by under vacuum and the residue was purified by column chromatography (Petroleum ether : ethyl acetate = 50:1) to give **3** as a white solid (7.17 g, 50%). ^{1}HNMR ($CDCl_3$, 400 MHz): δ (ppm) 7.67-7.65 (m, 1H), 7.46-7.45 (m, 1H), 7.32-7.30 (m, 1H), 4.27 (q, *J* = 6.8 Hz, 4H), 2.41 (s, 3H), 1.75-1.67 (m, 4H), 1.40-1.25 (m, 36H), 0.88 (t, *J* = 6.7 Hz, 6H).

Compound 2.[2] A mixture of compound **3** (3.0 g, 5.80 mmol), *N*-bromosuccinimide (NBS) (1.14 g, 6.39 mmol) and azodiisobutyronitrile (AIBN) (95.0 mg, 0.58 mmol) in carbon tetrachloride (CCl_4) (50

mL) was refluxed for 12 h. Then the mixture was filtered and concentrated to afford the crude product of **2** (4.2 g), which was used in the next step without further purification.

Compound 1.[3] Triallylamine (1.51 mL, 8.70 mmol) in acetone (3 mL) was slowly added to a solution of compound **2** (3.46 g, 5.80 mmol) in acetone (12 mL). After 3 days at room temperature, acetone was removed by rotary evaporation and the residue purified by column chromatography over silica gel with CH_2Cl_2 /MeOH from 60/1 to 20/1 as the eluents to give **1** as a white powder (1.3 g, 47%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.24-8.21 (m, 1H), 7.87 (d, *J* = 1.5 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 6.13-6.03 (m, 3H), 5.79-5.69 (m, 6H), 5.20 (s, 2H), 4.32-4.21 (m, 10H), 1.80-1.68 (m, 6H), 1.39-1.24 (m, 34H), 0.86 (t, *J* = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.8, 166.4, 136.6, 134.7, 132.9, 132.6, 130.5, 129.8, 129.1, 124.8, 66.4, 66.3, 62.7, 62.3, 31.9, 29.6, 29.6, 29.5, 29.3, 29.2, 28.5, 28.4, 25.9, 22.7, 14.1. HRMS calcd for $C_{42}H_{70}NO_4^+$ $[M]^+$ 652.5299, found: 652.5288.

Synthesis of Compound 1′. The suspension of sodium hydroxide (240 mg, 6 mmol) in water (0.6 mL) was added to compound **1** (220 mg, 0.3 mmol) in methanol (5 mL) mixture. The reaction was allowed to stir at room temperature for about 12 h. Then the reaction mixture was adjusted to pH 5 with hydrobromic acid solution, and the mixture was evaporated the solvents. The residue was purified by column chromatography over silica gel with DCM /MeOH 20/1 to 10/1 to give **1′** (74.0 mg) as white solid with 62% yield. ^{1}H NMR (CD_3OD, 400 MHz): δ (ppm) 8.0 (s, 1H), 7.95-7.93 (m, 1H), 7.74-7.72 (m, 1H), 6.02-5.92 (m, 2H), 5.58-5.45 (m, 5H), 5.12-5.01 (m, 2H), 4.60-5.57 (m, 1H), 3.89-3.84 (m, 2H), 3.71-3.66 (m, 2H), 3.07-2.96 (m, 2H). ^{13}C NMR (100 MHz, CDCl3): δ (ppm) 169.3, 135.3, 133.9, 132.0, 131.2, 130.8, 130.1, 126.7, 125.0, 119.1, 65.4, 33.7, 52.9. HRMS calcd for $C_{18}H_{20}NO_4^-$ $[M]^-$ 314.1398, found: 314.1394.

Reference

(1) Juwarker, H.; Lenhardt, J. M.; Pham, D. M.; Craig, S. L. 1,2,3-Triazole CH···Cl Contacts Guide Anion Binding and Concomitant Folding in 1,4-Diaryl Triazole Oligomers. *Angew. Chem. Int. Ed*. **2008**, *47*, 3740-3743.

(2) Harvey, J. H.; Long, D. H.; England, P. M.; Whistler, J. L. Tuned-Affinity Bivalent Ligands for the Characterization of Opioid Receptor Heteromers. *ACS Med. Chem. Lett.* **2012**, *3*, 640-644.

(3) Zhang, S.; Zhao, Y. Facile Synthesis of Multivalent Water-Soluble Organic Nanoparticles via "Surface Clicking" of Alkynylated Surfactant Micelles. *Macromolecules* **2010**, *43*, 4020-4022.

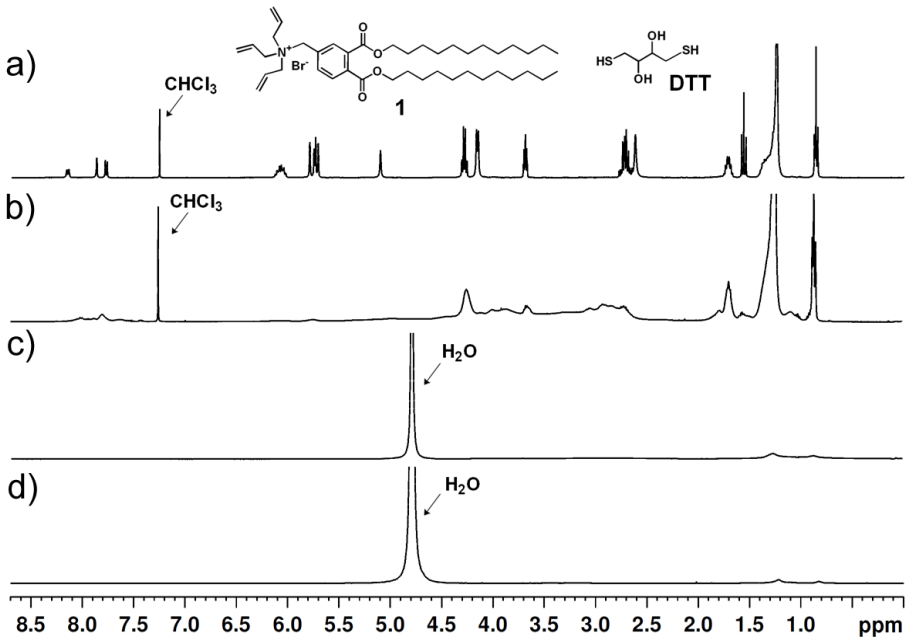


Figure S1. ^{1}H NMR spectra of a 2:3 mixture of **1** and DTT (a) before cross-linking (in $CDCl_3$), (b) after cross-linking (in $CDCl_3$), (c) after hydrolysis (in D_2O), and (d) after amidation (in D_2O). $W_0 = 5$.

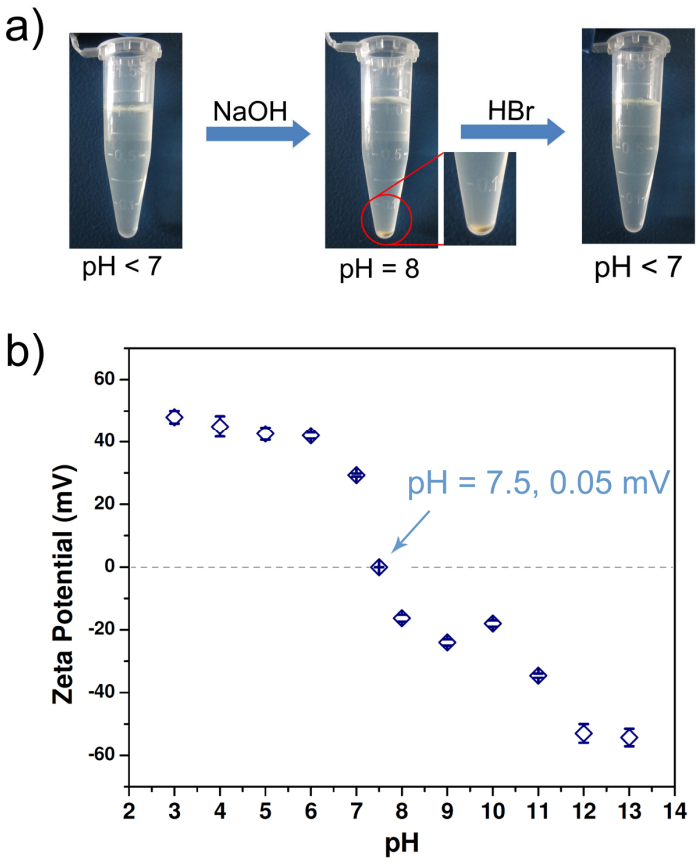


Figure S2. Solubility (a) and zeta potential (b) of PWNP_NH_2 in water at different pH values.

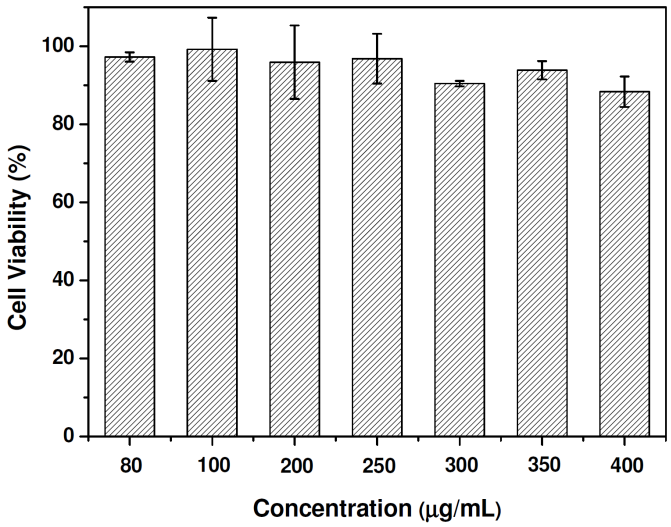


Figure S3. Cytotoxicity of ThT@PWNP_COOH against HepG2 cells for 24 h incubation. $W_0 = 5$.

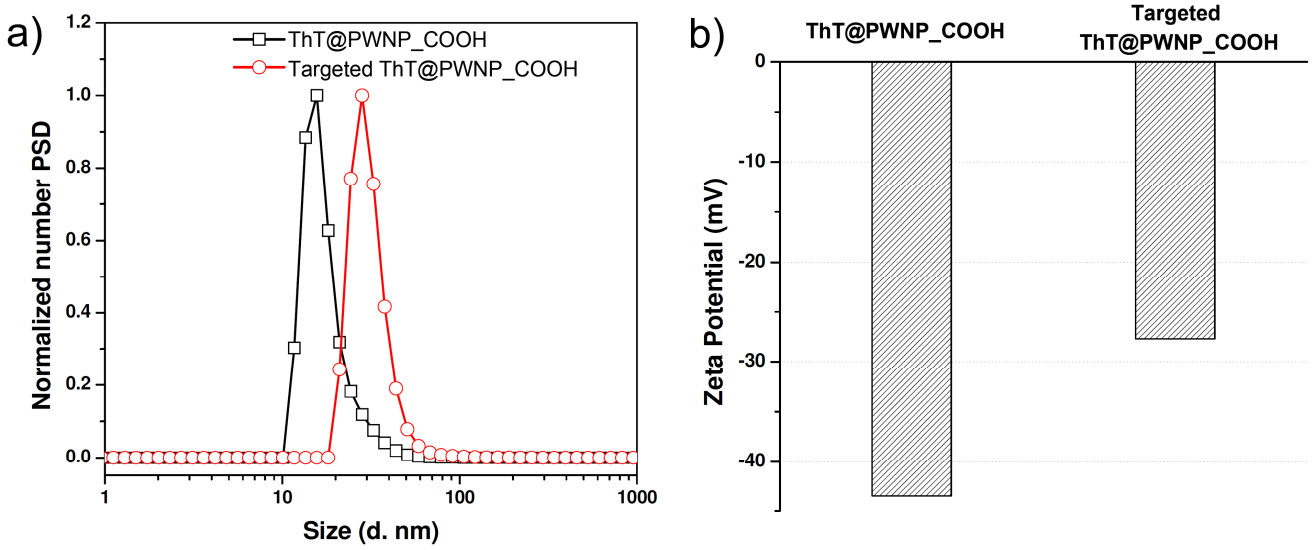


Figure S4. Comparison of DLS and zeta potentials of ThT@PWNP_COOH and targeted ThT@PWNP_COOH with a glucose unit (D-glucosamine), respectively. [**1**] = 0.02 M, [ThT] = 4.5×10^{-5} M, $W_0 = 5$.

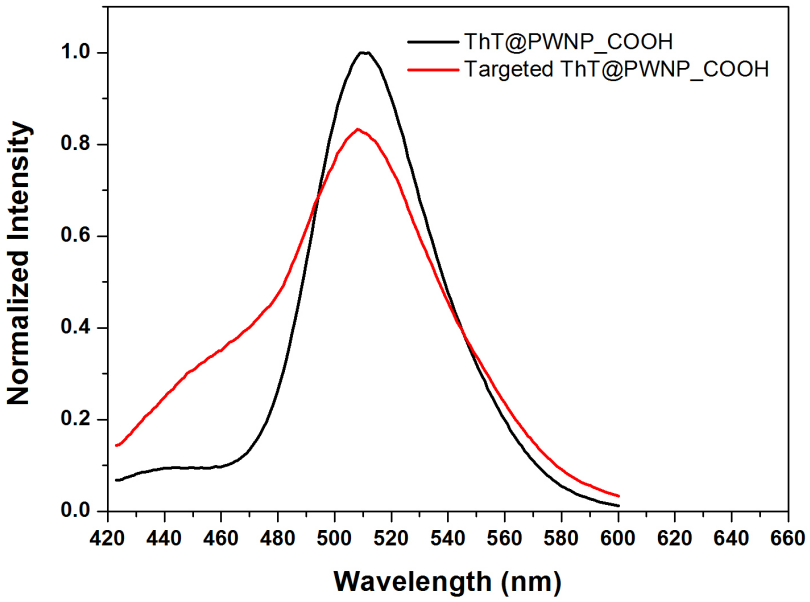


Figure S5. Comparison of fluorescence spectra of ThT@PWNP_COOH (λ_{ex} = 403 nm) and targeted ThT@PWNP_COOH (λ_{ex} = 403 nm), respectively. [**1**] = 0.02 M, [ThT] = 4.5×10^{-5} M, W_0 = 5.

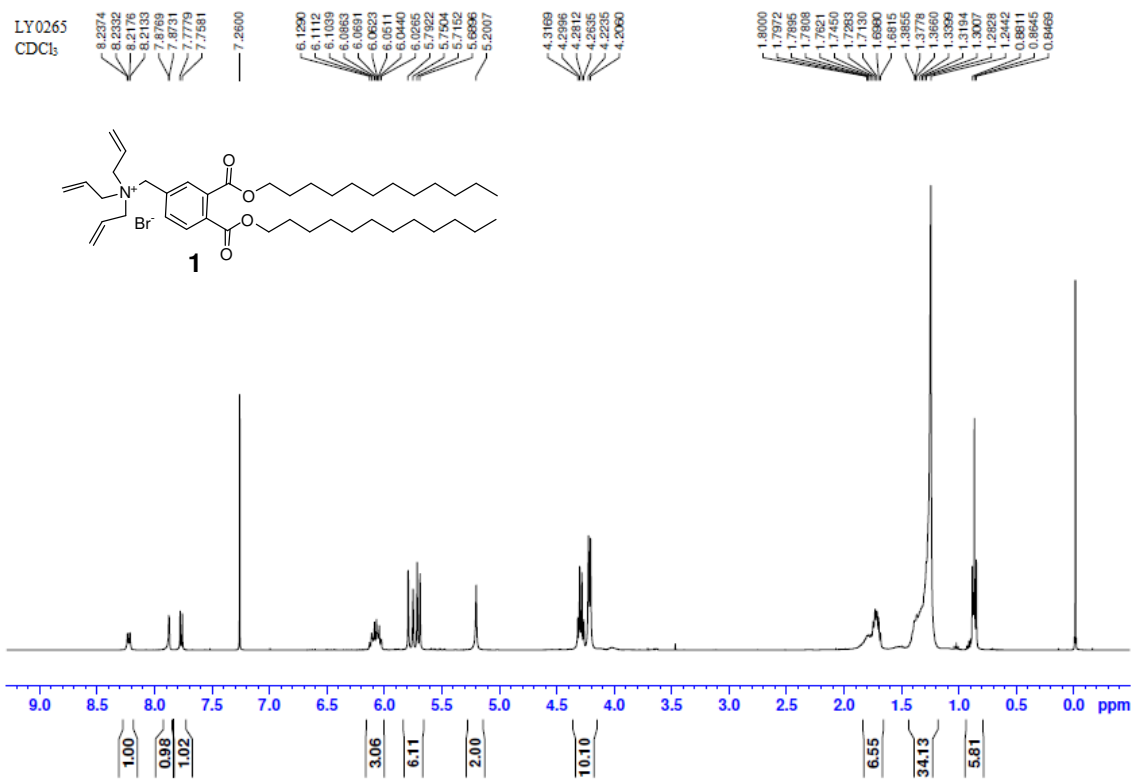


Figure S6. ^{1}H NMR spectrum of compound **1** in $CDCl_3$.

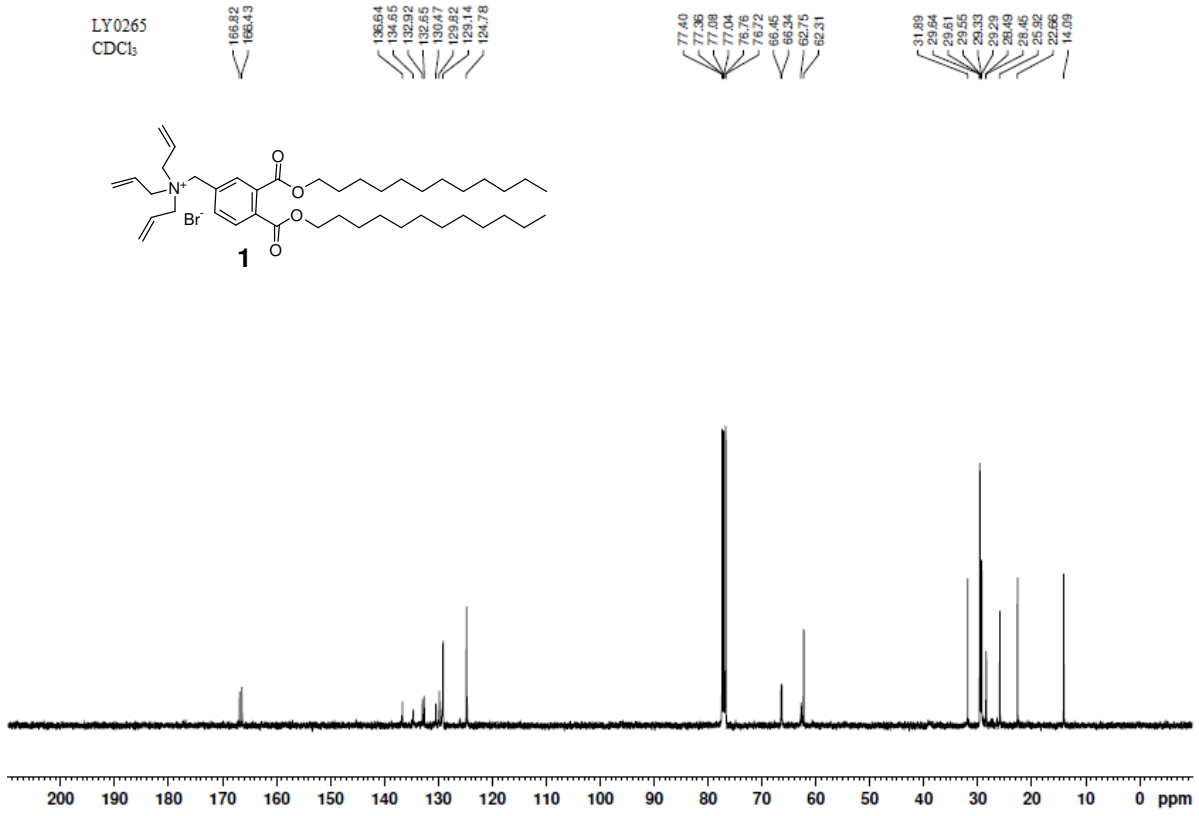


Figure S7. ^{13}C NMR spectrum of compound **1** in $CDCl_3$.

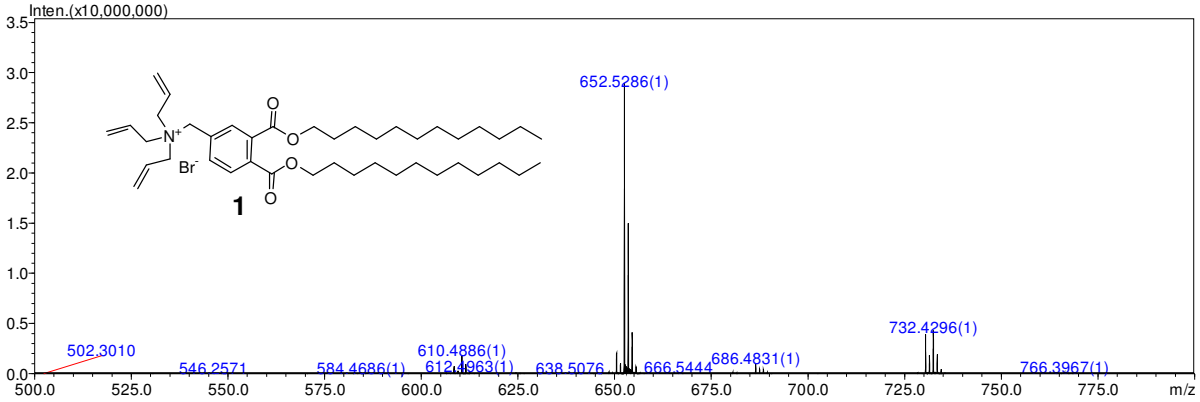


Figure S8. Mass spectrum of compound **1**. HRMS: calcd. for $C_{42}H_{70}NO_4^+$ $[M]^+$: 652.5299, found: 652.5288.

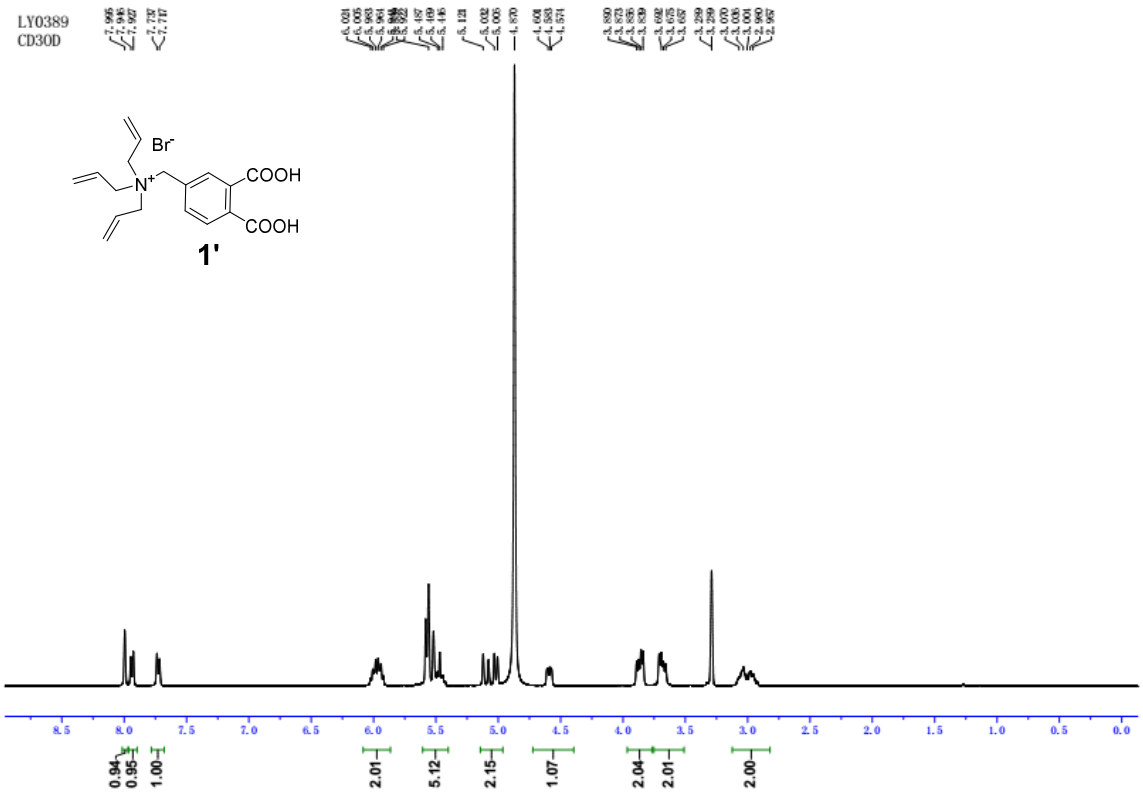


Figure S9. ^{1}H NMR spectrum of compound **1′** in CD_3OD.

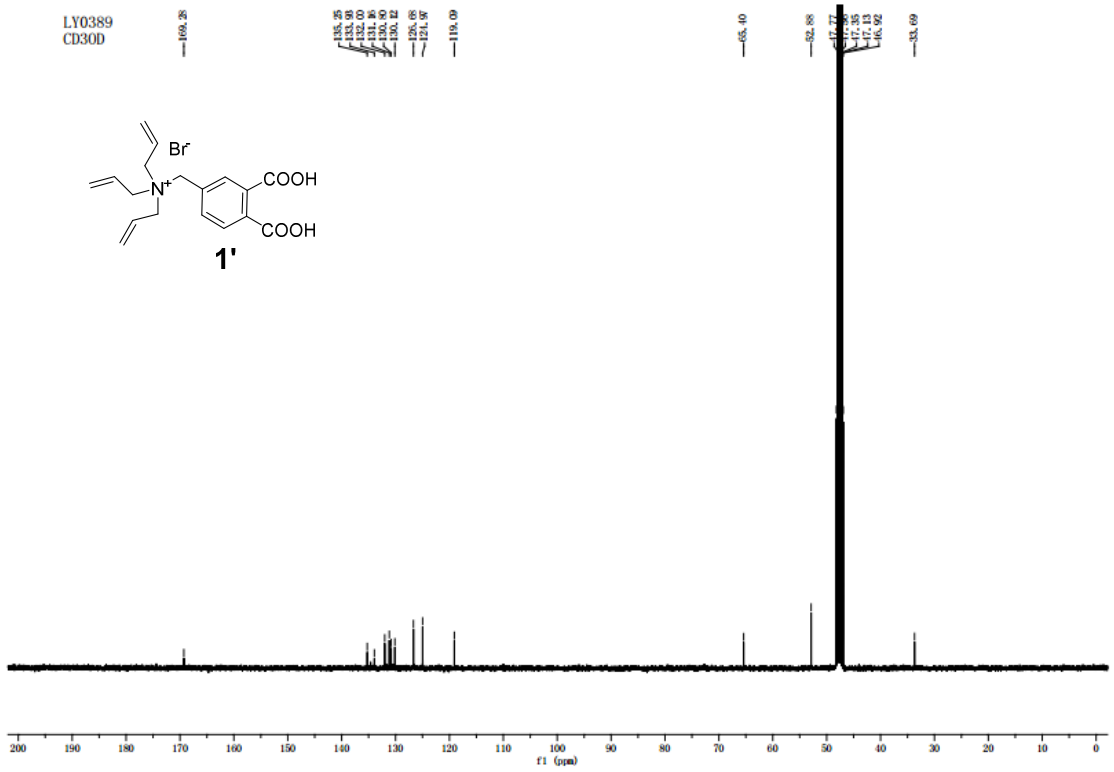


Figure S10. ^{13}C NMR spectrum of compound **1′** in CD_3OD.

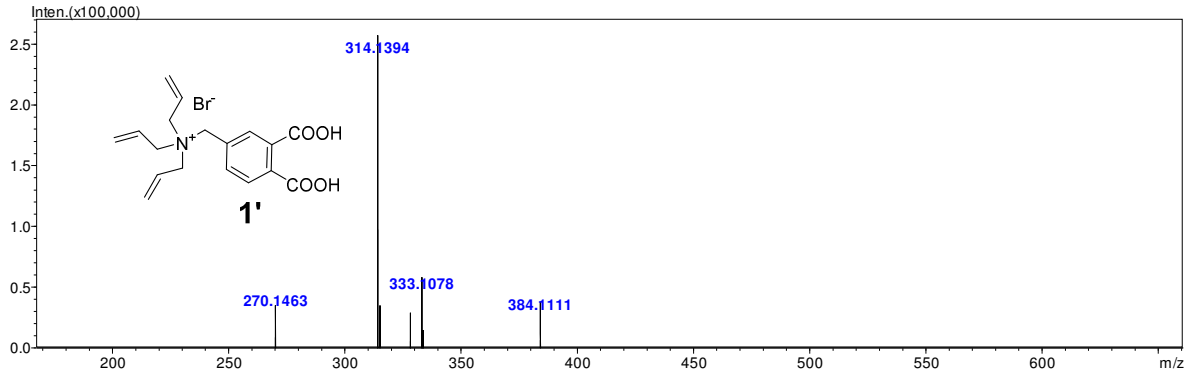


Figure S11. Mass spectrum of compound **1′**. HRMS: calcd for $C_{18}H_{20}NO_4^-$ $[M]^-$: 314.1398, found: 314.1394.