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SUPPORTING INFORMATION

Molecular Engineering of Organic Small Molecular Photothermal agents by Changing donor group for Photothermal Therapy and Photoacoustic Imaging of tumor

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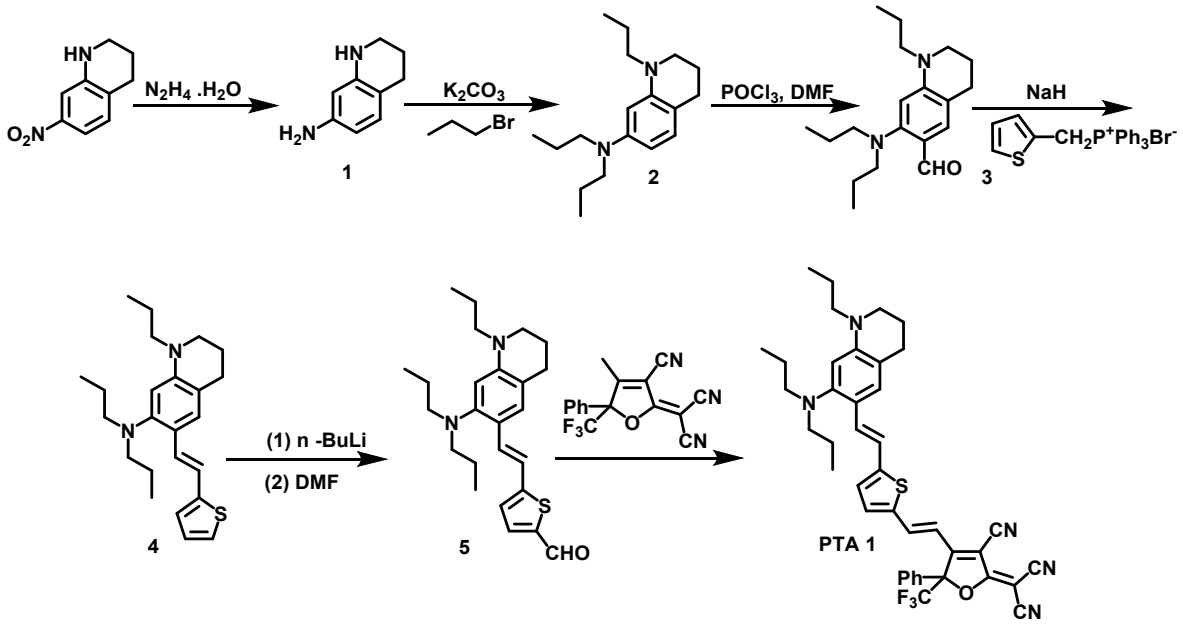
Experimental Procedures

General Information

All chemical reagents were purchased from Beijing InnoChem Science & Technology Co (Beijing, China) and used without further purification. Electron acceptor Ph-CF_3-TCF was prepare according to the reported literature [1]. Absorption spectra were recorded on a Hitachi UV-3010 (Hitachi, Tokyo, Japan). ^{1}H NMR spectra were obtained on BrukerAvance III 400 H (400 MHz) spectrometers (Bruker, Karlsruhe, Germany). The HRMS spectra were analyzed on the Q-Exactive instrument. Zetasizer 90 (Malvern, U.K.) was selected to measure the size of the nanoparticles. We used the optical power density meter (LP-3C50, CHINA) to calibrate the output power density to 0.6 W cm^{-2}). A thermal imaging camera (226s, FOTRIC, CHINA) were used to record the temperature rise process. Photoacoustic imaging was performed on multimode photoacoustic imaging system for small animals (Vevo LAZR-X, Fujifilm viualsonic, Canada).

Synthetic details of PTA 1



Scheme S1. The synthetic route to compound PTA 1.

Synthesis of Compound 2

To a solution of 7-nitro-1,2,3,4-tetrahydroquinoline(5g, 28mmol) in 20 mL EtOH, $FeCl_3$ (100mg) and activated carbon (1g) were added. The mixture was heated to reflux, and 5mL of hydrazine hydrate was added dropwise. The reaction mixture was stirred under reflux for another 3h. After cooled to the room temperature, the activated carbon was filtrated, and the filtrate was dried over Na_2SO_4. After removal of the solvent, the crude product **1** was obtained as colorless oil. Without further purification, the crude product 1, 1-bromopropane (17.8g, 100mmol) and K_2CO_3(13.8g, 100mmol) were dissolved in 30 mL acetonitrile. The obtained mixture was stirred under reflux overnight. The inorganic salt was removed through filtration, and the filtrate was concentrated. Finally, the concentrated crude product was purified through column chromatography using hexane as the eluent. Compound **2** was obtained as colorless oil (5.38g, total yield: 70%). HRMS: m/z calcd for $[M+H]^+$ $C_{18}H_{31}N_2$: 275.2482; found: 275.2482. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.72 (d, *J* = 8.2 Hz, 1H), 5.92 (dd, *J* = 8.2, 2.4 Hz, 1H), 5.86 (d, *J* = 2.4 Hz, 1H), 3.27 (t, *J* = 5.6 Hz, 2H), 3.23 – 3.17 (m, 6H), 2.64 (t, *J* = 6.3 Hz, 2H), 1.97 – 1.85 (m, 2H), 1.62 (m, 7.4 Hz, 6H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 147.79, 145.89, 129.30, 110.19, 100.25, 95.16, 53.51, 49.81, 27.20, 22.99, 20.67, 19.52, 11.37, 11.26.

Synthesis of Compound 3

Compound 2 (3g, 11mmol) was dissolved in 10 mL DMF. After cooled to 0 ℃, 1.2 mL $POCl_3$ was added to the solution dropwise. The reaction mixture was stirred at 0 ℃ for another 3h, and then poured into 100 mL 1M K_2CO_3 aqueous solution, extracted by ethyl acetate. The organic layer was dried over Na_2SO_4. After removal of the solvent, the crude product was purified by column chromatography (hexane: ethyl acetate =10:1), and compound 3 was obtained as yellow oil (2.5g, yield: 75.5%). HRMS: m/z calcd for $[M+H]^+$ $C_{19}H_{31}N_2O$: 303.2431; found: 303.2431. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 10.08 (s, 1H), 7.40 (s, 1H), 6.21 (s, 1H), 3.38(t, *J* = 4.4 Hz, 2H), 3.29 (t, *J* = 7.6 Hz, 2H), 3.06 (t, *J* = 7.2 Hz, 4H), 2.72 (t, *J* = 6.2 Hz, 1H), 1.99 – 1.87 (m, 2H), 1.71-1.64 (m, 2H), 1.58 – 1.46 (m, 4H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 188.85, 156.08, 150.38, 128.87, 119.27, 117.06, 101.77, 57.09, 53.05, 49.79, 27.37, 21.89, 20.37, 19.67, 11.46, 11.29.

Synthesis of Compound 4

To a solution of compound 3 (1g, 3.3mmol) and triphenyl(2-thienylmethyl)phosphonium bromide (1.7 g, 3.87 mmol) in dry THF, and NaH (100mg, 4.16mmol) was added slowly. The reaction mixture was stirred at room temperature overnight. And then, the reaction mixture was poured into 100 mL H_2O, extracted by ethyl acetate, and the organic layer was dried over Na_2SO_4. After removal of solvent, the crude product was purified by column chromatography using hexane as eluent, and compound 4 was obtained as oil(0.88g, yield: 70%). HRMS: m/z calcd for $[M+H]^+$ $C_{24}H_{35}N_2S$: 383.2515; found: 383.2513. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.42 (d, *J* = 16.4 Hz, 1H), 7.22 (s, 1H), 7.13 (d, *J* = 5.0 Hz, 1H), 7.04 – 6.96 (m, 3H), 6.34 (s, 1H), 3.33 (t, *J* = 5.6 Hz, 2H), 3.25 (t, *J* = 7.2 Hz, 2H), 2.92 (t, *J* = 4.8 Hz, 4H), 2.77 (t, *J* = 6.3 Hz, 2H), 2.02 – 1.91 (m, 2H), 1.68-1.60 (m, 2H), 1.58 – 1.44 (m, 4H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 149.48, 145.42, 145.34, 127.40, 126.40, 125.93, 123.66, 122.26, 120.53, 117.93, 115.75, 104.01, 56.47, 53.11, 49.53, 27.75, 22.47, 20.56, 19.52, 11.64, 11.41.

Synthesis of Compound 5

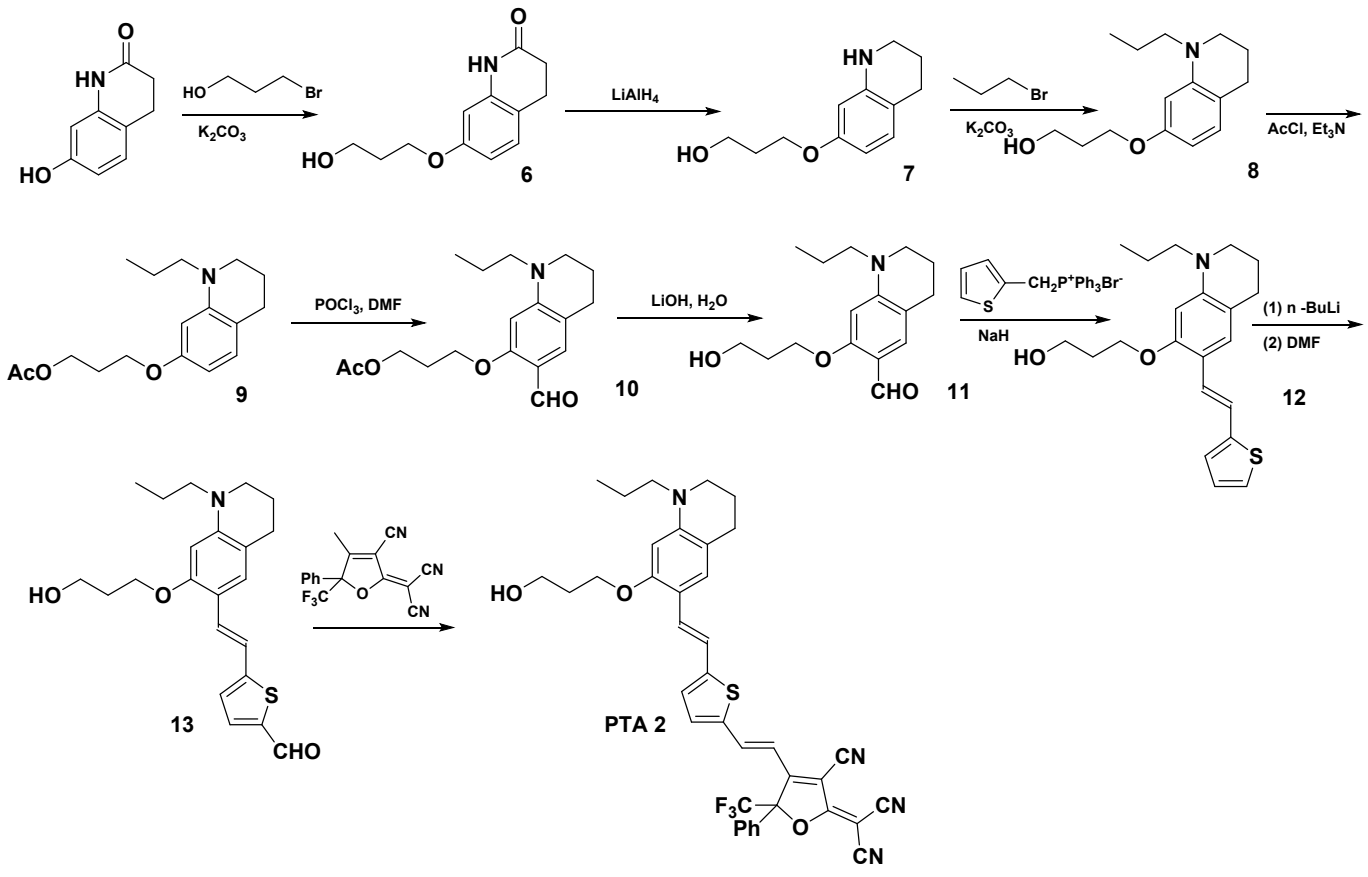
Compound 5 (0.8g, 2.09mmol) was dissolved in 10 mL dry THF, and cooled down to -78℃. n-BuLi (3 mmol) was added dropwise under the protection of N_2. Keep the temperature and stirred for 2h, DMF (0.5g, 6.85mmol) was added, and the mixture was reacted for another 2h. Next, the reaction was quenched by H_2O and extracted by ethyl acetate, and the organic phase was dried over Na_2SO_4. Finally, the solvent was removed, and compound 5 was obtained as a Z/E mixture (1:1) through column chromatography (hexane: ethyl acetate =10:1). (0.63g, yield: 73%). HRMS: m/z calcd for $[M+H]^+$ $C_{25}H_{35}N_2OS$:411.2465; found: 411.2464. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 9.80 (s, 0.5H), 9.79 (s, 0.5H), 7.71 (d, *J* = 16.2 Hz, 0.5H), 7.67 (d, *J* = 3.9 Hz, 0.5H), 7.67 (d, *J* = 3.9 Hz, 0.5H), 7.60 (d, *J* = 4.0 Hz, 0.5H), 7.59 (t, *J* = 4.2 Hz, 0.5H), 7.03 (d, *J* = 16 Hz, 0.5H), 7.25 (s, 1H), 6.79 (d, *J* = 11.5 Hz, 0.5H), 6.50 (d, *J* = 11.8 Hz, 0.5H), 6.32 (s, 0.5H), 6.25 (s, 0.5H), 4.35 – 4.23 (m, 2H), 3.39 – 3.21 (m, 4H), 3.02 – 2.89 (m, 4H), 2.02 – 1.88 (m, 2H), 1.71 – 1.62 (m, 2H), 1.56 – 1.42 (m, 4H), 1.04 – 0.77 (m, 9H).

Synthesis of PTA 1

Compound 5(100mg, 0.244mmol) and CF_3-Ph-TCF (100mg, 0.318mmol) was dissolved in 5 mL ethanol, and the reaction mixture was stirred under refluxing. Finally, the solvent was removed, and the

crude product was purified through column chromatography (hexane: ethyl acetate =5:1). The target compound PTA 1 was obtained as dark green powder (69mg, yield: 40%). HRMS: m/z calcd for $[M+H]^+$ $C_{41}H_{41}F_3N_5OS$: 708.2978; found: 708.2980. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.79 (d, *J* = 11.5 Hz, 1H), 7.75 (d, *J* = 15.0 Hz, 1H), 7.63 – 7.55 (m, 5H), 7.37 (d, *J* = 4.3 Hz, 1H), 7.27 (s, 1H), 7.06 (s, 1H), 7.03 (d, *J* = 11.5 Hz, 1H), 6.60 (d, *J* = 15.0 Hz, 1H), 6.30 (s, 1H), 3.44 – 3.35 (m, 2H), 3.34 – 3.27 (m, 2H), 3.02 – 2.93 (m, 4H), 2.75 (t, *J* = 6.1 Hz, 2H), 2.03 – 1.91 (m, 2H), 1.67 (td, *J* = 14.9, 7.4 Hz, 2H), 1.52 (dt, *J* = 14.7, 7.3 Hz, 4H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 175.70, 161.15, 160.62, 152.70, 148.04, 141.32, 140.60, 137.65, 135.15, 131.37, 130.04, 129.66, 127.37, 127.32, 126.86, 126.85, 119.32, 118.74, 114.24, 111.60, 111.45, 111.30, 110.80, 103.76, 56.76, 49.81, 29.68, 27.64, 22.05, 20.51, 19.80, 11.55, 11.29.

Synthetic details of PTA 2



Scheme S2. The synthetic route to compound PTA 2.

Synthesis of Compound 6

7-hydroxy-3,4-dihydroquinolin-2(1H)-one (3.26g, 20mmol), 3-bromo-1-propanol (4.17g, 30mmol) and K_2CO_3(4.14g, 30mmol) were added into 20mL DMF. The reaction mixture was stirred at 90 ℃ overnight. Next, the reaction mixture was poured into 200 mL H_2O, and the precipitate was filtered. The filter cake was dried, and used directly for the next step without further purification. HRMS: m/z calcd for $[M+H]^+$ $C_{12}H_{16}NO_3$: 222.1125; found: 222.1123. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.10 (d, *J* = 8.3 Hz, 1H), 6.56 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.34 (d, *J* = 2.4 Hz, 1H), 4.10 (t, *J* = 6.1 Hz, 2H), 3.83 (t, *J* = 5.9 Hz, 2H), 2.92 (t, *J* = 6.8 Hz, 2H), 2.60 (t, *J* = 7.2Hz, 2H), 2.06 – 1.99 (m, 2H).

Synthesis of Compound 7

Compound 6 (2.21g, 10mmol) was dissolved in 10 mL dry THF, and then $LiAlH_4$(0.4g, 10.5mmol) was added slowly. The reaction mixture was stirred at room temperature for another 3h. And then, the reaction mixture was poured into H_2O slowly, extracted by ethyl acetate, dried over Na_2SO_4. After removal of the solvent, the crude product was purified by column chromatography (hexane: ethyl acetate =2:1), and compound 7 was obtained as colorless oil(1.8g, yield: 87%). HRMS: m/z calcd for $[M+H]^+$ $C_{12}H_{18}NO_2$: 208.1332; found: 208.1333. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.83 (d, *J* = 8.2 Hz, 1H), 6.18 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.05 (d, *J* = 2.5 Hz, 1H), 4.04 (t, *J* = 6.0 Hz, 2H), 3.81 (t, *J* = 6.0 Hz, 2H), 3.30 – 3.27 (m, 2H), 2.70 (t, *J* = 6.4 Hz, 2H), 2.03 – 1.95 (m, 2H), 1.95 – 1.86 (m, 2H), 1.30 (s, 1H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 157.98, 145.71, 129.89, 114.16, 103.14, 99.75, 65.66, 60.38, 41.83, 32.16, 26.24, 22.43.

Synthesis of Compound 8

To a solution of compound 7(2g, 9.66mmol), 1-bromopropane (2.36g, 19.3mmol) and K_2CO_3(6g, 43.5mmol) in 10 mL acetonitrile, and the reaction mixture was stirred under reflux for 6h. The inorganic salt was removed through filtration, and the filtrate was concentrated. Finally, the concentrated crude product was purified through column chromatography (hexane: ethyl acetate =4:1). Compound 8 was obtained as oil (1.7g, yield: 70.5%). HRMS: m/z calcd for $[M+H]^+$ $C_{15}H_{24}NO_2$: 250.1802; found: 250.1791. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.81 (d, *J* = 7.9 Hz, 1H), 6.12 (dd, *J* = 4.8, 2.3 Hz, 1H), 6.09 (d, *J* = 2.4 Hz, 1H), 4.07 (t, *J* = 6.0 Hz, 2H), 3.83 (t, *J* = 6.0 Hz, 2H), 3.30 – 3.26 (m, 2H), 3.22 – 3.17 (m, 2H), 2.68 (t, *J* = 6.3

Hz, 2H), 2.00 (p, *J* = 6.0 Hz, 2H), 1.91 (tt, *J* = 14.1, 5.7 Hz, 2H), 1.69 – 1.57 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 158.42, 146.27, 129.23, 115.27, 100.14, 97.57, 65.70, 60.48, 49.31, 32.23, 27.43, 22.49, 19.35, 11.28.

Synthesis of Compound 9

To a solution of compound 8 (2g, 8mmol), acetyl chloride (0.7g, 8.9mmol) and 2mL Et_3N in 10 mL dry CH_2Cl_2, and the solution was stirred at room temperature for 5h. Then, the reaction solution was poured into H_2O, extracted with CH_2Cl_2, and dried over Na_2SO_4. After removal of the solvent, the crude product was purified by column chromatography (hexane: ethyl acetate =5:1), and compound 9 was obtained as oil (2g, yield: 85.8%). HRMS: m/z calcd for $[M+H]^+$ $C_{17}H_{26}NO_3$: 292.1907; found: 292.1900. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.82 (d, *J* = 8.0 Hz, 1H), 6.13 (d, *J* = 2.3 Hz, 1H), 6.10 (dd, *J* = 8.0, 2.4 Hz, 1H), 4.26 (t, *J* = 6.4 Hz, 2H), 4.02 (t, *J* = 6.2 Hz, 2H), 3.31 – 3.27 (m, 2H), 3.23 – 3.18 (m, 2H), 2.69 (t, *J* = 6.3 Hz, 2H), 2.11 (dd, *J* = 12.6, 6.3 Hz, 2H), 2.07 (s, 3H), 1.97 – 1.88 (m, 2H), 1.69 – 1.59 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 170.80, 158.45, 146.29, 129.23, 115.26, 100.10, 97.69, 64.22, 61.35, 49.33, 28.77, 27.44, 22.52, 20.69, 19.36, 11.29.

Synthesis of Compound 10

Compound 9 (2g, 6.86mmol) was dissolved in 10 mL dry DMF. After cool down to 0 ℃, $POCl_3$ (1.2g, 7.8 mmol) was added to the solution slowly. The reaction was stirred at room temperature for 2h, and room temperature for another 12h. The reaction mixture was poured into 50 mL 100 mL 1M K_2CO_3 aqueous solution, extracted by ethyl acetate. The organic layer was dried over Na_2SO_4. After removal of the solvent, the crude product was purified by column chromatography (hexane: ethyl acetate =2:1), and compound 10 was obtained as yellow oil (1.5g, yield: 75%). HRMS: m/z calcd for $[M+H]^+$ $C_{18}H_{26}NO_4$: 320.1856; found: 292.1852. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 10.11 (s, 1H), 7.38 (s, 1H), 6.01 (s, 1H), 4.29 (t, *J* = 6.3 Hz, 2H), 4.13 (t, *J* = 6.1 Hz, 2H), 3.41 – 3.37 (m, 2H), 3.35 – 3.30 (m, 2H), 2.73 – 2.67 (m, 2H), 2.18 (p, *J* = 6.2 Hz, 2H), 2.07 (s, 3H), 1.93 (dt, *J* = 11.5, 6.0 Hz, 2H), 1.78 – 1.65 (m, 2H), 1.01 (t, *J* = 8.4 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 186.05, 170.77, 162.27, 151.66, 128.04, 115.12, 113.65, 92.49, 64.83, 61.16, 49.84, 28.61, 27.13, 21.82, 20.68, 19.67, 11.28.

Synthesis of Compound11

Compound 10 (1.5g, 4.7mmol) was dissolved in a mixture of THF/H_2O(v/v=1:1), and NaOH(0.25g, 6.25mmol) was added. The reaction mixture was stirred at 40 ℃ for 6h. The reaction mixture was extracted by ethyl acetate, dried over Na_2SO_4. After removal of the solvent, the crude product was purified by column chromatography (hexane: ethyl acetate =3:1), and compound 11 was obtained as yellow powder (0.95 g, yield: 73%). HRMS: m/z calcd for $[M+H]^+$ $C_{16}H_{24}NO_3$: 278.1751; found: 278.1743. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 9.88 (s, 1H), 7.29 (s, 1H), 6.03 (s, 1H), 4.18 (t, *J* = 4.7 Hz, 2H), 3.84 (s, 2H), 3.39 (s, 2H), 3.32 (t, *J* = 6.7 Hz, 2H), 2.70 (s, 2H), 2.16 – 2.00 (m, 2H), 1.93 (s, 2H), 1.70 (dd, *J* = 13.8, 6.8 Hz, 2H), 1.00 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 186.83, 161.70, 151.69, 130.87, 114.76, 113.43, 92.58, 66.37, 60.05, 49.83, 32.12, 27.08, 21.78, 19.68, 11.26.

Synthesis of Compound 12

To a solution of compound 11 (0.8g, 2.9mmol) and triphenyl(2-thienylmethyl)phosphonium bromide (1.6 g, 3.6 mmol) in dry THF, and NaH (200mg, 8.32mmol) was added slowly. The reaction mixture was stirred at room temperature overnight. And then, the reaction mixture was poured into 100 mL H_2O, extracted by ethyl acetate, and the organic layer was dried over Na_2SO_4. After removal of solvent, the crude product was purified by column chromatography (hexane: ethyl acetate =3:1),, and compound 12 was obtained as oil (0.6g, yield: 57.8%). HRMS: m/z calcd for $[M+H]^+$ $C_{21}H_{28}NO_2S$: 358.1835; found: 358.1830. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.15 (d, *J* = 16.2 Hz, 1H), 7.12 (d, *J* = 7.1 Hz, 1H), 7.11 (s, 1H), 7.07 (d, *J* = 16.2 Hz, 1H), 7.00 (d, *J* = 3.5 Hz, 1H), 6.98 (dd, *J* = 2.8, 1.9 Hz, 1H), 6.15 (s, 1H), 4.15 (t, *J* = 6.0 Hz, 2H), 3.91 (t, *J* = 6.0 Hz, 2H), 3.35 – 3.31 (m, 2H), 3.29 – 3.24 (m, 2H), 2.73 (t, *J* = 6.3 Hz, 2H), 2.11 (p, *J* = 6.0 Hz, 2H), 2.01 – 1.90 (m, 4H), 1.68 (dq, *J* = 14.8, 7.4 Hz, 2H), 1.00 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 156.15, 146.13, 144.96, 127.42, 126.78, 123.82, 123.76, 122.39, 116.73, 115.17, 112.93, 95.28, 66.23, 60.11, 49.49, 32.38, 27.44, 22.40, 19.66, 11.36.

Synthesis of Compound 13

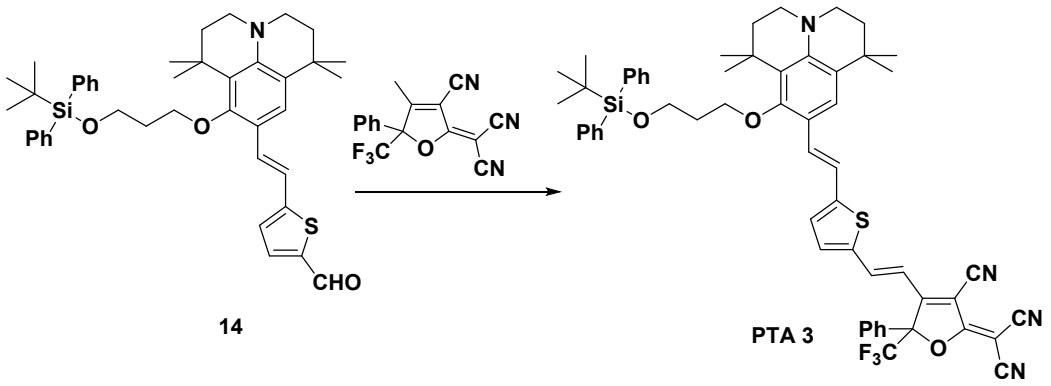
Compound 12 (0.5g, 1.4mmol) was dissolved in 10 mL dry THF, and cooled down to -78℃. n-BuLi (3 mmol) was added dropwise under the protection of N_2. Keep the temperature and stirred for 2h, DMF (0.3g, 4.11mmol) was added, and the mixture was reacted for another 2h. Next, the reaction was quenched by H_2O and extracted by ethyl acetate, and the organic phase was dried over Na_2SO_4. Finally, the solvent

was removed, and compound 13 was obtained through column chromatography (hexane: ethyl acetate =2:1) as yellow oil (0.35g, yield: 64.8%). HRMS: m/z calcd for $[M+H]^+$ $C_{22}H_{28}NO_3S$: 386.1784; found: 386.1780. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 9.79 (s, 1H), 7.66 (d, *J* = 4.0 Hz, 1H), 7.43 (d, *J* = 16.1 Hz, 1H), 7.14 (s, 1H), 7.07 (d, *J* = 14.8 Hz, 1H), 7.05 (d, *J* = 2.7 Hz, 1H), 6.13 (s, 1H), 4.16 (t, *J* = 6.0 Hz, 2H), 3.92 (t, *J* = 6.0 Hz, 2H), 3.38 – 3.32 (m, 2H), 3.30 – 3.26 (m, 2H), 2.72 (t, *J* = 6.2 Hz, 2H), 2.10 (m, 2H), 1.95 (dd, *J* = 15.1, 8.8 Hz, 2H), 1.67 (dt, *J* = 14.7, 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 182.11, 157.10, 155.47, 147.28, 139.46, 137.94, 128.83, 127.44, 124.38, 115.22, 115.06, 111.75, 94.51, 65.78, 59.86, 49.57, 32.29, 27.39, 22.22, 19.69, 11.35.

Synthesis of PTA 2

Compound 13 (100mg, 0.259mmol) and CF_3-Ph-TCF (100mg, 0.318mmol) was dissolved in 5 mL ethanol, and the reaction mixture was stirred under refluxing. Finally, the solvent was removed, and the crude product was purified through column chromatography (hexane: ethyl acetate =1:1). The target compound PTA 2 was obtained as dark green powder (50mg, yield: 28%). HRMS: m/z calcd for $[M]^+$ $C_{38}H_{33}F_3N_4O_3S$: 682.2225; found: 682.2203. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.75 (d, *J* = 14.9 Hz, 1H), 7.64 – 7.56 (m, 5H), 7.53 (d, *J* = 15.7 Hz, 1H), 7.35 (d, *J* = 4.3 Hz, 1H), 7.13 (d, *J* = 15.5 Hz, 1H), 7.11(s, 1H), 7.05 (d, *J* = 4.3 Hz, 1H), 6.59 (d, *J* = 15.0 Hz, 1H), 6.12 (s, 1H), 4.20 (t, *J* = 6.1 Hz, 2H), 3.92 (t, *J* = 6.0 Hz, 2H), 3.44 – 3.37 (m, 2H), 3.36 – 3.28 (m, 2H), 2.71 (t, *J* = 6.2 Hz, 2H), 2.18 – 2.08 (m, 2H), 2.01 – 1.88 (m, 2H), 1.71 (dt, *J* = 21.2, 6.9 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 175.66, 161.08, 160.37, 158.59, 148.96, 141.25, 140.59, 137.73, 132.96, 131.39, 130.02, 129.67, 128.56, 127.29, 126.87, 116.04, 115.06, 112.32, 111.59, 111.48, 111.30, 110.84, 94.04, 65.68, 59.68, 49.85, 32.20, 29.68, 27.31, 22.01, 19.85, 11.30.

Synthetic details of PTA 3



Scheme S3. The synthetic route to compound PTA 3.

The synthesis of PTA 3 is similar to the previously reported literature [2, 3]. Phenyl-vinylene-thiophene aldehyde 14 and CF_3-Ph-TCF were reacted in ethanol and purified through column chromatography (hexane: ethyl acetate =3:1). HRMS: m/z calcd for $[M+Na]^+$ $C_{58}H_{57}F_3N_4NaO_3SSi$: 997.3765; found: 997.3776. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.76 (d, *J* = 15.1 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 4H), 7.54 (s, 5H), 7.48 – 7.32 (m, 8H), 7.30 (d, *J* = 3.7 Hz, 1H), 7.06 (d, *J* = 16.5 Hz, 1H), 7.04 (s, 1H), 6.57 (d, *J* = 14.9 Hz, 1H), 4.02 (t, *J* = 6.8 Hz, 2H), 3.91 (t, *J* = 5.6 Hz, 2H), 3.32 (s, 2H), 3.25 (s, 2H), 2.27 – 2.14 (m, 2H), 1.77-1.74 (m, 4H), 1.45 (s, 6H), 1.32 (s, 6H), 1.00 (s, 9H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 175.63, 161.45, 159.11, 157.90, 145.33, 141.48, 140.20, 137.82, 135.46, 133.67, 133.18, 131.35, 129.77, 129.68, 129.61, 127.62, 127.26, 127.16, 126.77, 123.50, 122.41, 116.27, 115.19, 111.43, 111.25, 111.15, 111.11, 73.51, 60.78, 57.08, 47.39, 46.82, 39.58, 35.94, 33.08, 32.56, 32.10, 30.31, 29.76, 26.49, 18.94.

Fabrication of PTA-1-cRGD, PTA-2-cRGD and PTA-3-cRGD

First, a solution of 0.5umol PTA 1 (PTA 2 or PTA 3), DSPE-PEG2000 (0.5 mg), and DSPE-PEG2000 maleimide (0.5 mg) in acetone (1 mL) was injected into 10 mL of water. A microtip probe sonicator (12 W) was subsequently applied for 2 minutes to vigorously disperse the organic phase in water. The mixture was stirred in fume hood for two days and was further filtered through a membrane filter (diameter = 200 nm). Subsequently, a solution of c-RGD (0.5 mg) in water (about 1 mL) was added into the dot suspension to further react for 12 h. After the dot suspension was dialyzed against water for two days

The calculation of PTCE, *η*

The photothermal conversion efficiency, *η*, temperature changes during a cycle of laser-caused heating and cooling of the PTA—1-cRGD, PTA-2-cRGD and PTA-3-cRGD water solution were measured. η was calculated following the eq 1:

$$\eta = \frac{hS(T_{max} - T_{amb}) - Q_0}{I(1 - 10^{-A})} \quad (1)$$

where h corresponds to the heat transfer coefficient and S is the lateral surface area of the PTA-cRGD-1, PTA-cRGD-2 and PTA-cRGD-3 solution in the quartz cuvette. T_{max} is the maximum temperature of their solution during the lasercaused heating and T_{amb} is the ambient temperature. A is optical density of these solution at a wavelength of 808 nm. Q_0 is the loss of heat from the light absorbed by the solvent and quartz cuvette and I is the laser power density (0.6W/cm^2). The value of hS is obtained according to eq 2

$$\tau_s = \frac{m_D c_D}{hS} \quad (2)$$

where m_D is the mass (1.0 g) and c_D is the heat capacity (4.2 J g^{-1}) of the deionized water. τ_s means the sample system time constant.

Tumor Model

Nude mice 6−7 weeks old were provided by the Laboratory Animal Center of North Sichuan Medical College, Nanchong, China. All procedures involving animals were performed according to a protocol approved by the Institutional Animal Care and Treatment Committee of North Sichuan Medical College. These nude mice were subcutaneously injected with 1 × 10^6 SKOV-3 cells in the right axillary under aseptic conditions. Then, they were individually housed under specific pathogenfree conditions with free access to food and water until the formed tumor grew to approximately 1 cm in diameter by measuring with a caliper; tumor growth to this size took about a month. These tumor-bearing mice were further used to conduct photothermal experiments.

Results and Discussion

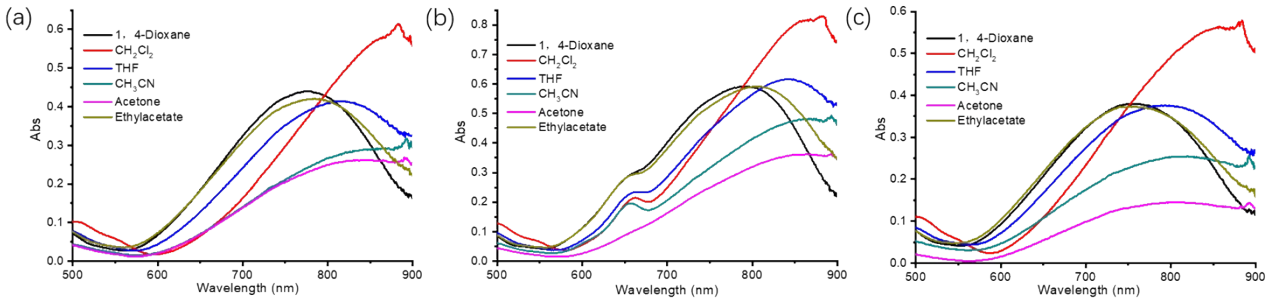


Figure S1. UV absorption spectra of 5uM (a)PTA 1, (b) PTA 2 and (c) PTA 3 in various solvents.

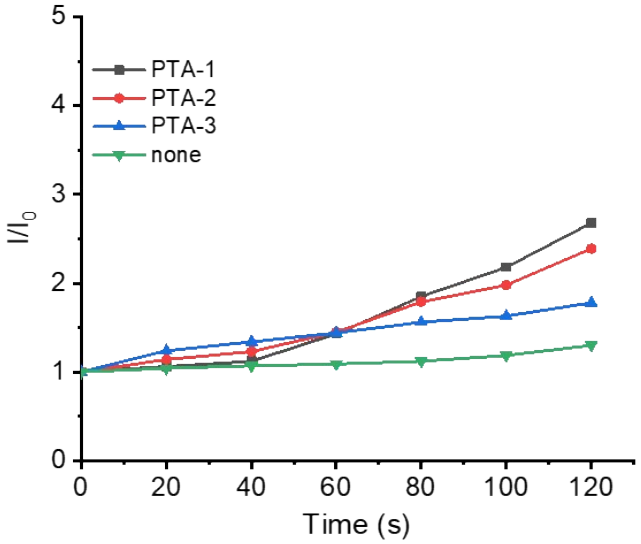


Figure S2. The ROS ability in the presence or absence of each probe via fluorescence enhancement at 525 nm referred to H_2DCF-DA under 808nm laser (0.6 W/cm^2). Test according to the method reported in the literature. [16]

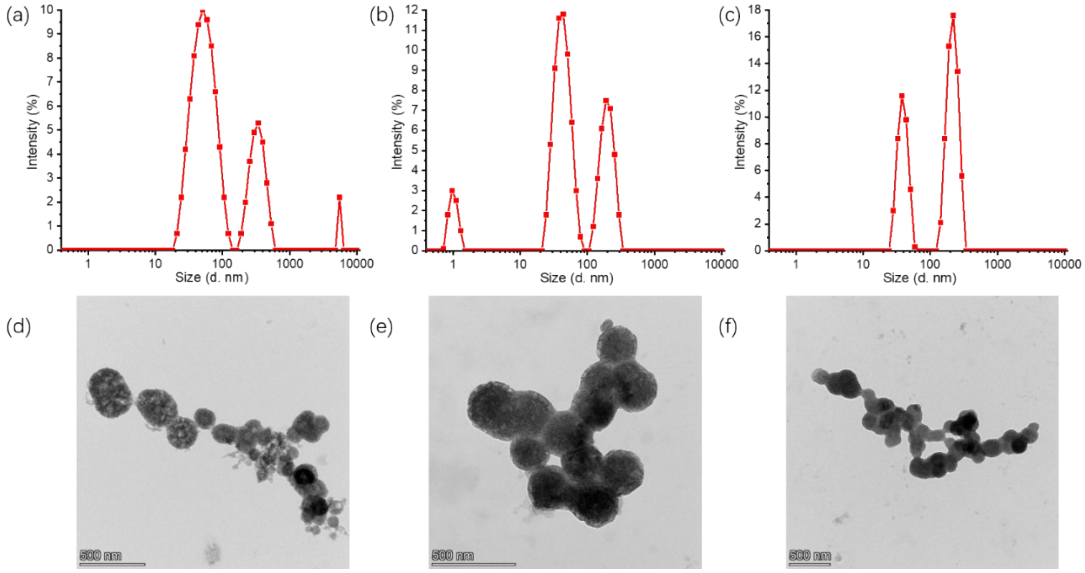
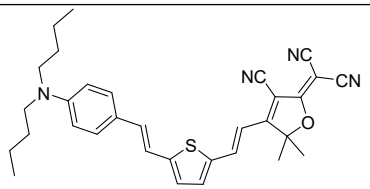
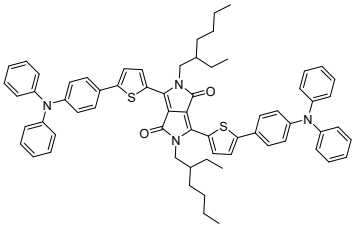
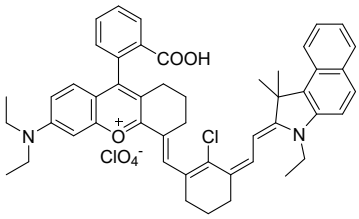
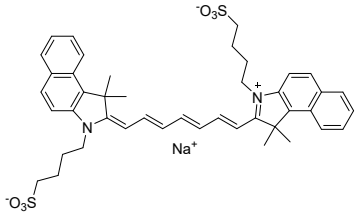
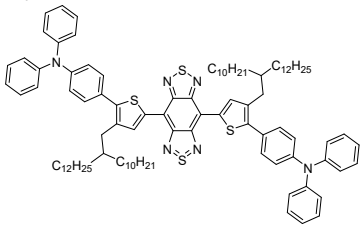
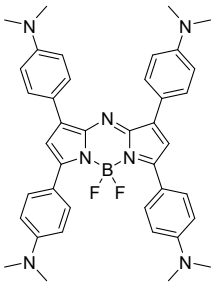
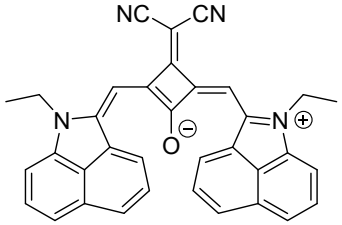
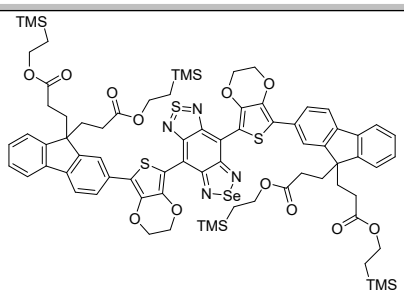
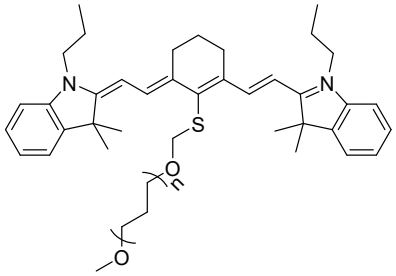
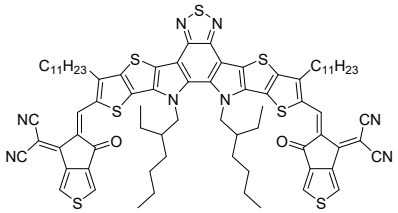
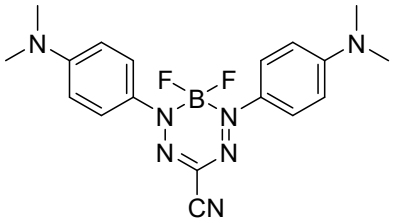
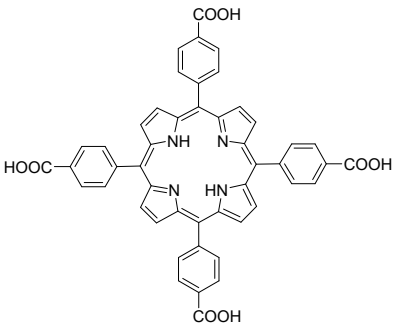
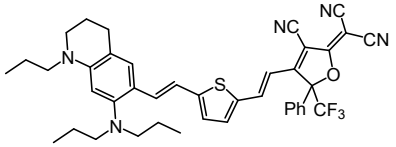
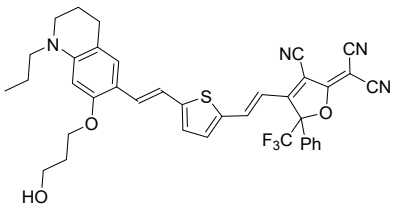
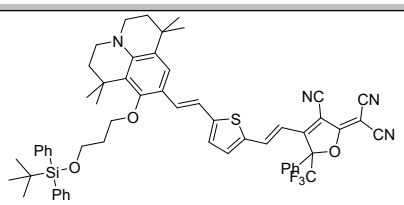


Figure S3. Size distribution of (a)PTA-1-cRGD, (b) PTA-2-cRGD and (c) PTA-3-cRGD measured by DLS in water . TEM image of (c)PTA-1-cRGD, (d) PTA-2-cRGD and (f) PTA-3-cRGD.

Table S1 Summary of the organic photothermal small molecule dyes

PTT agents	Organic dyes	λ_{max}（nm）after being loaded	PTCE	Reference
FTC NPs		635	52.71%（635nm）	4
DPP-TPA NPs		660	34.5%（660nm）	5
RC-BSA NPs		868	28.7%（915nm）	6
FA-INPs		787	17.3%（808nm）	7
NIRb14 NPs		822	31.2%（808nm）	8
A1-NPs		---	35.0%（808nm）	9
SQ1 Nanoprobe		940	25.6%（915nm）	10

SY1080 NPs		820	22.3%（808nm）	11
PEG-IR780-BIIB021		785nm	29.23%（808nm）	12
Y8 NPs		793nm	228.04（808nm）	13
Nano-BFF		broad absorption ranging from 900nm to 1200nm	28.6%（808nm） 34.3%（1064nm）	14
TCPP nanoparticles		—	31%（650nm）	15
PTA-1-cRGD		888	32.8%（808nm）	In this work
PTA-2-cRGD		758	57.0%（808nm）	In this work

PTA-3-cRGD		840	67.9%（808nm）	In this work

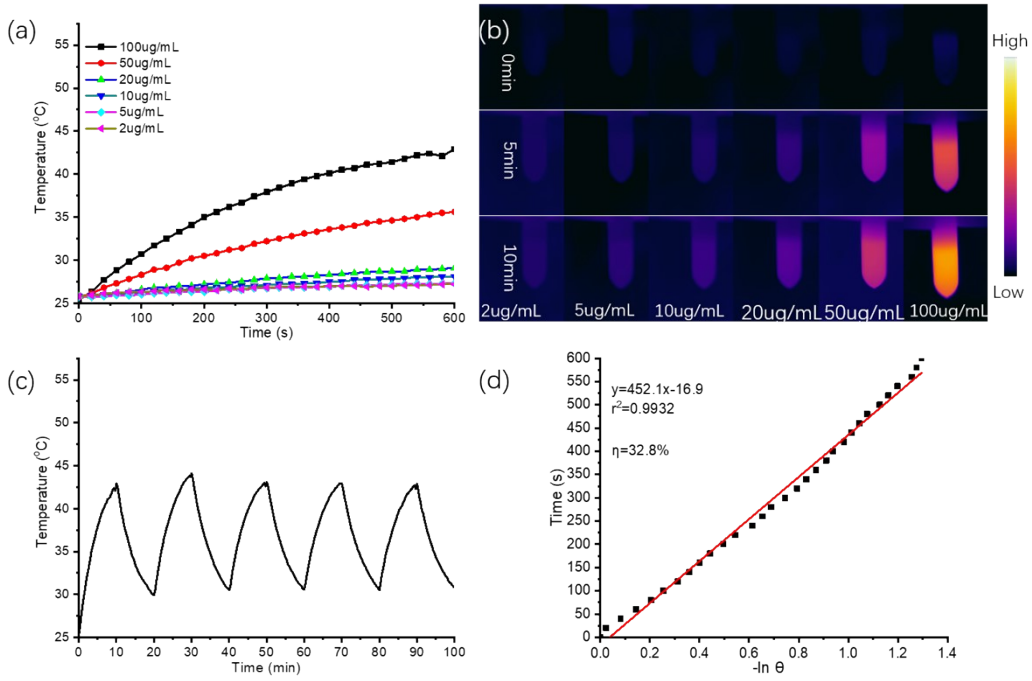


Figure S4. (a) Concentration-dependent temperature variation of PTA-1-cRGD with 808 nm (0.6 W cm^{-2}) laser irradiation; (b) IR image of PTA-1-cRGD solution with different concentration under laser irradiation; (c) Temperature variations of PTA-1-cRGD water solution (100 μg /mL) using laser irradiation for five cycles.; (d) Plot of cooling time (10 min) and the negative natural logarithm of the temperature driving force.

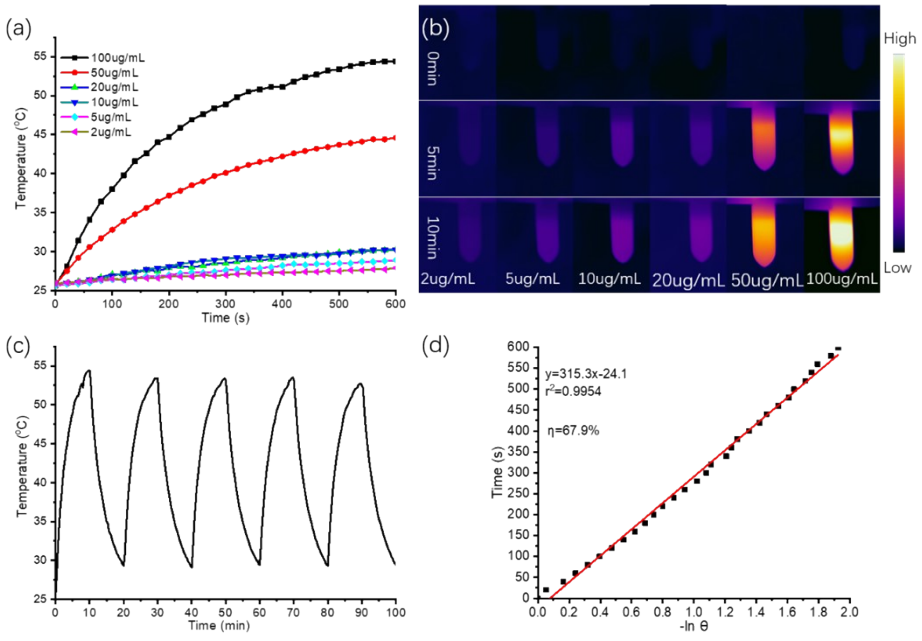


Figure S5. (a) Concentration-dependent temperature variation of PTA-3-cRGD with 808 nm (0.6 W cm^{-2}) laser irradiation; (b) IR image of PTA-3-cRGD solution with different concentration under laser irradiation; (c) Temperature variations of PTA-3-cRGD water solution (100 μg /mL) using laser irradiation for five cycles.; (d) Plot of cooling time (10 min) and the negative natural logarithm of the temperature driving force.

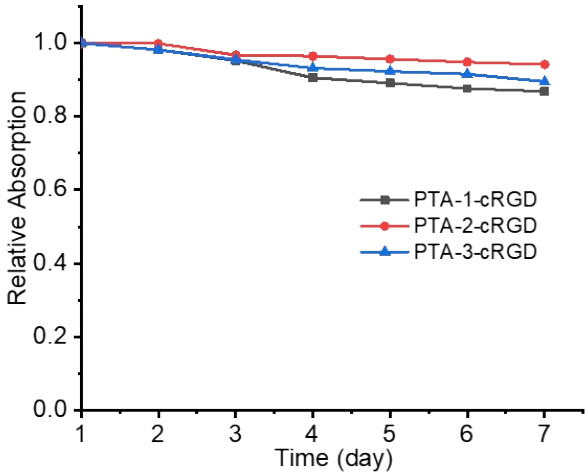


Figure S6. The change of relative absorption value at their maximum absorption wavelength.

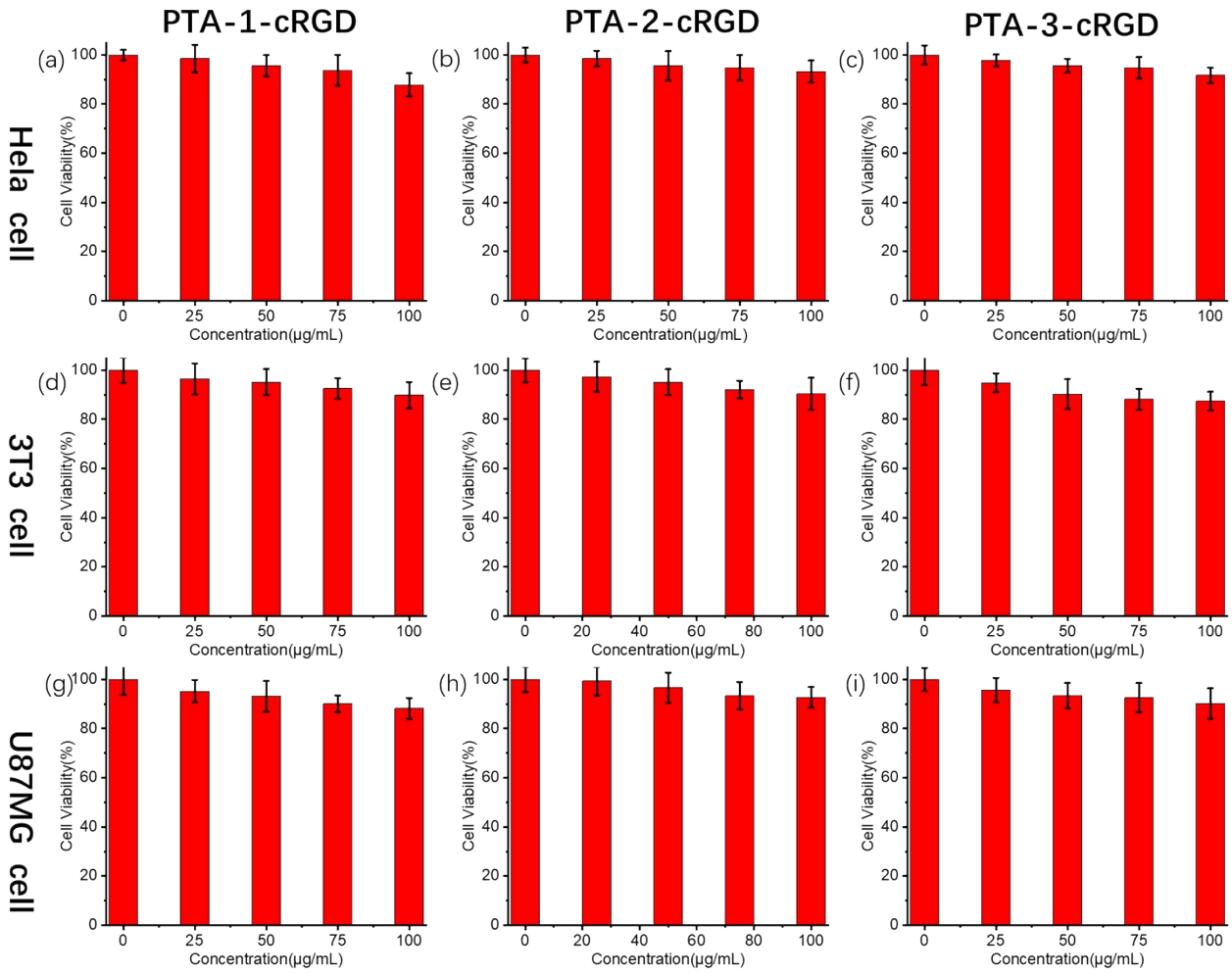


Figure S7. Cytotoxicity of PTA-1-cRGD, PTA-2-cRGD and PTA-3-cRGD on various cells determined by MTT assay.

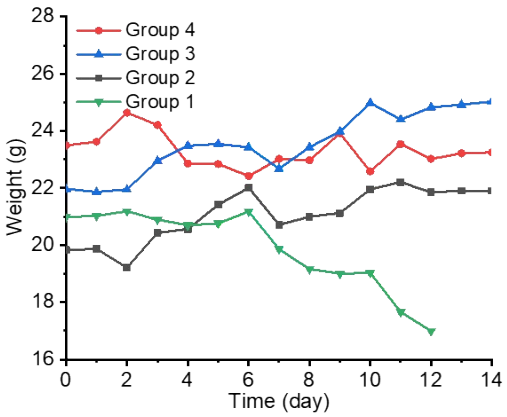


Figure S8. The changes in body weight of treated mice over time.

Table S2. the p values of (a) Group 1, (b) Group 2, (c) Group 3 and (d) Group 4.

(a)

	2	4	8
12	0.041	0.039	0.056
8	0.048	0.042	
4	0.046		

(b)

	2	4	8
12	0.038	0.049	0.065
8	0.029	0.043	
4	0.037		

(c)

	2	4	8
12	0.054	0.036	0.047
8	0.043	0.048	
4	0.043		

(d)

	0	1
2	0.041	0.039
1	0.048	

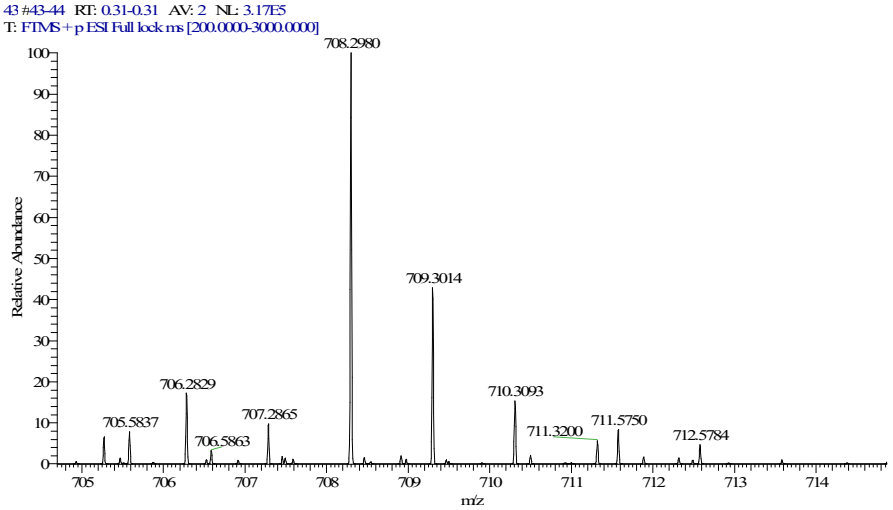


Figure S9. HRMS spectra of PTA-1.

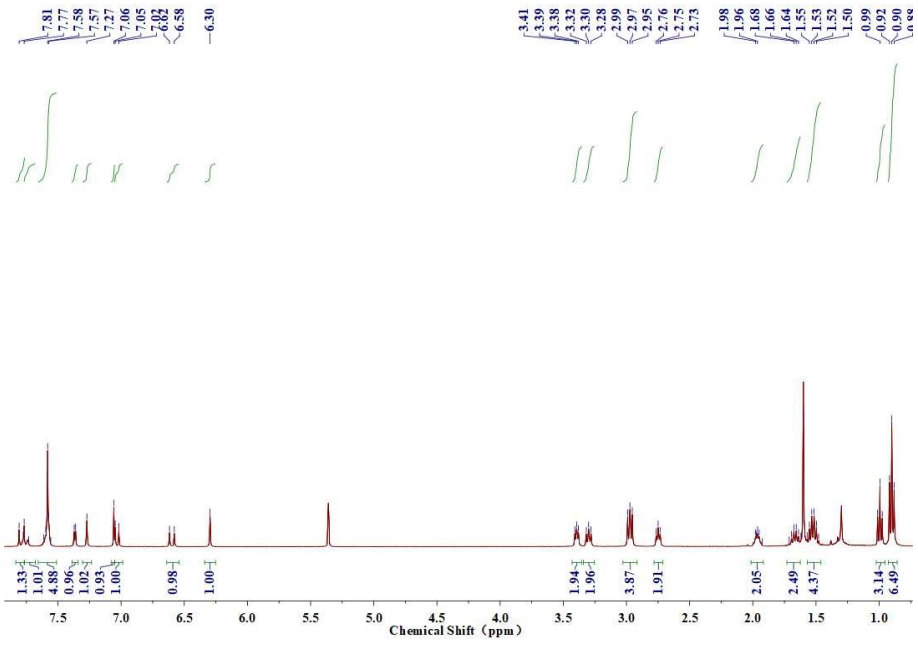


Figure S10. ^{1}H NMR spectra of PTA-1.

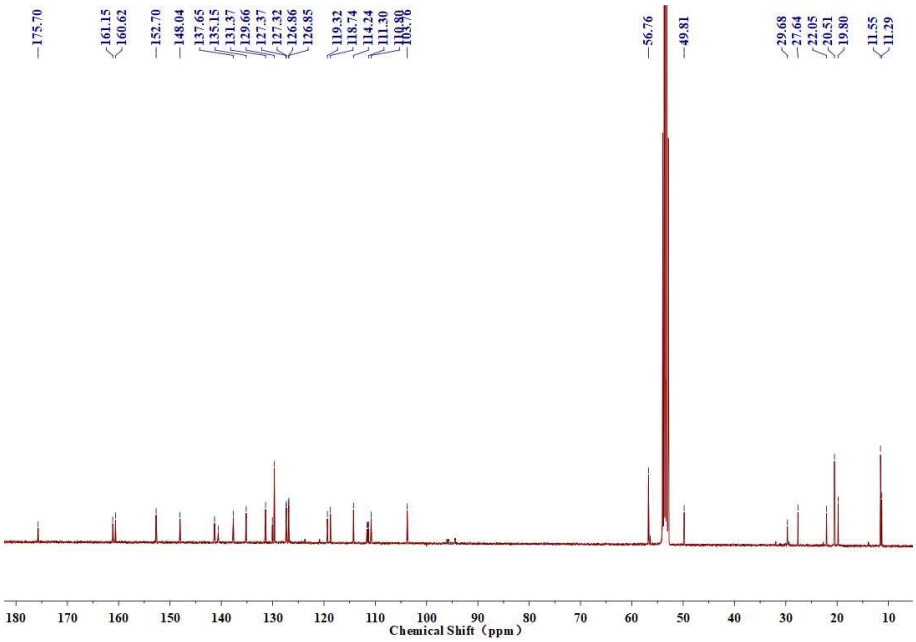


Figure S11. ^{13}C NMR spectra of PTA-1.

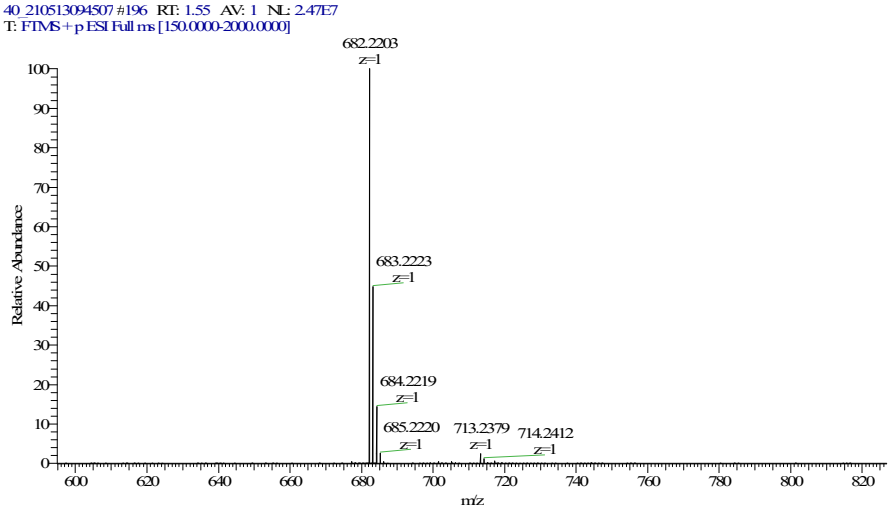


Figure S12. HRMS spectra of PTA-2.

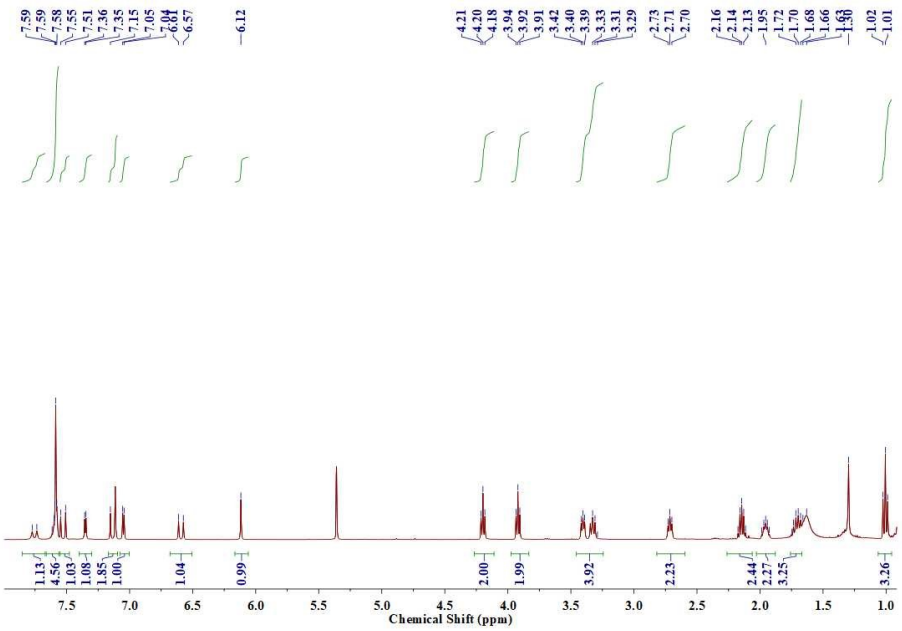


Figure S13. HRMS spectra of PTA-2.

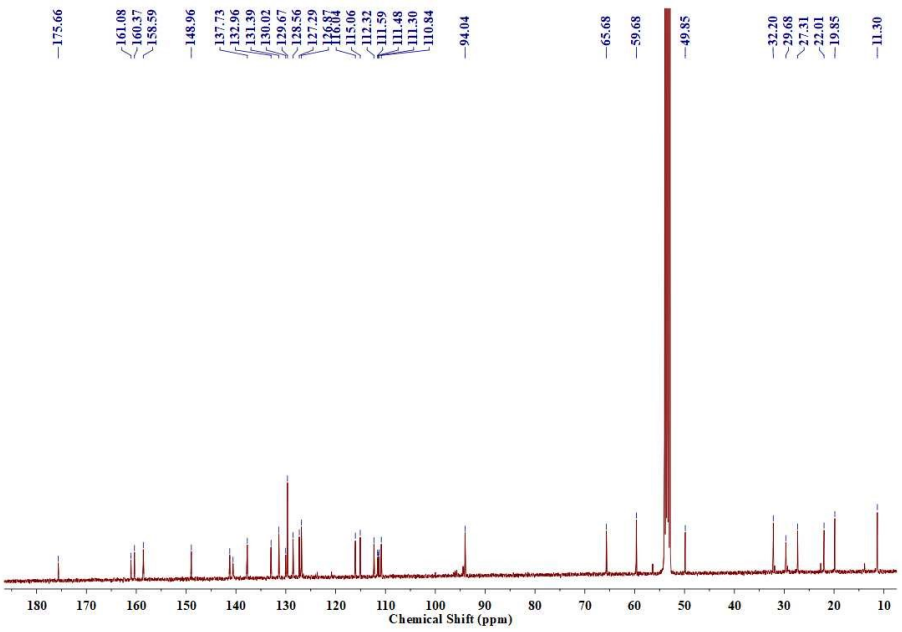


Figure S14. ^{13}C NMR spectra of PTA-2.

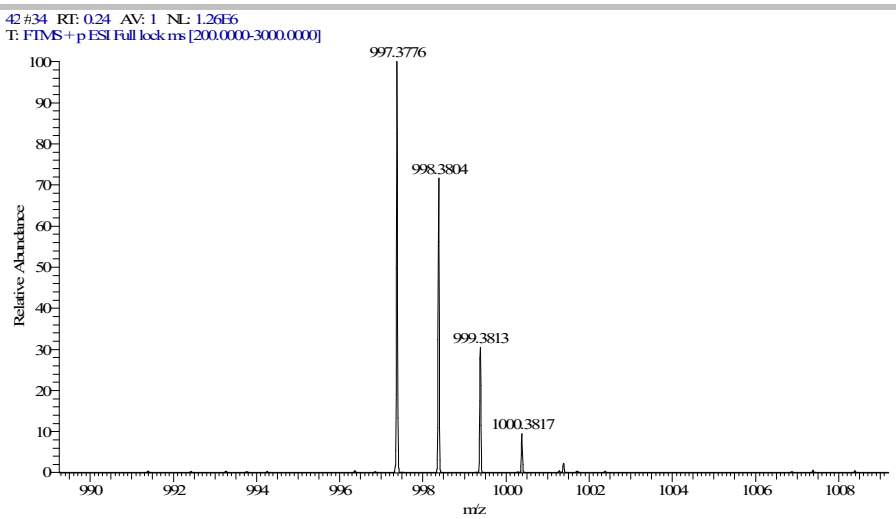


Figure S15. HRMS spectra of PTA-3.

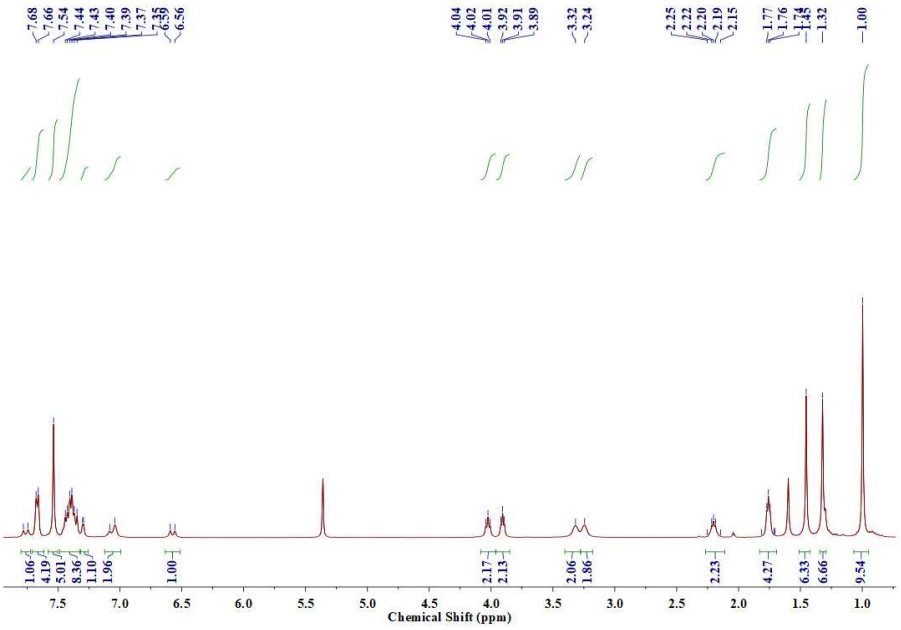


Figure S16. ^{1}H NMR spectra of PTA-3.

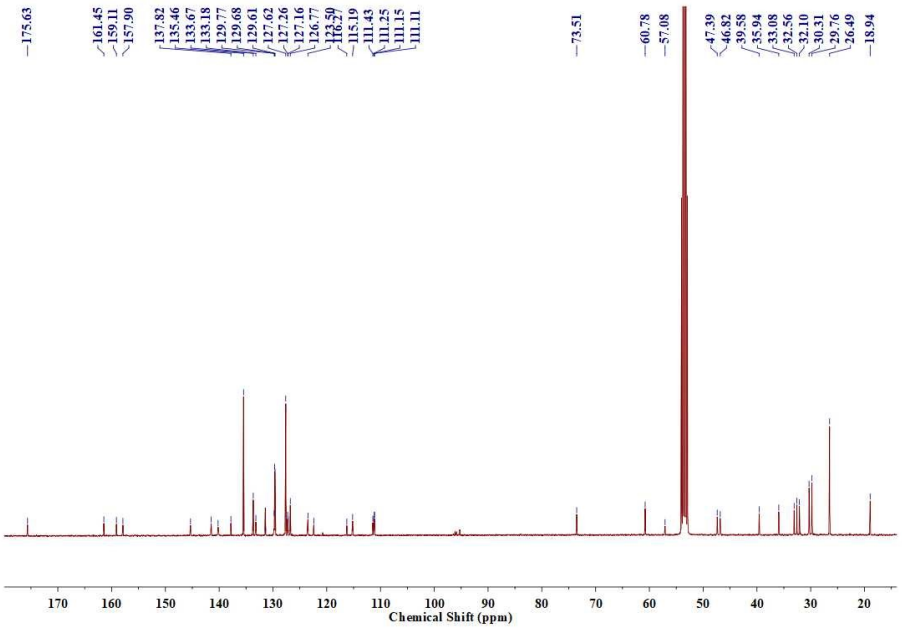


Figure S17. ^{13}C NMR spectra of PTA-3.

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