

Supporting information

Near-Infrared Molecular photosensitizer Decorated with Quaternary Ammonium for high-efficiency photothermal treatment of bacterial infections

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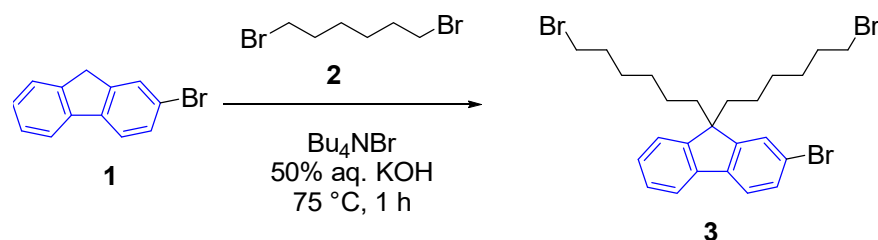
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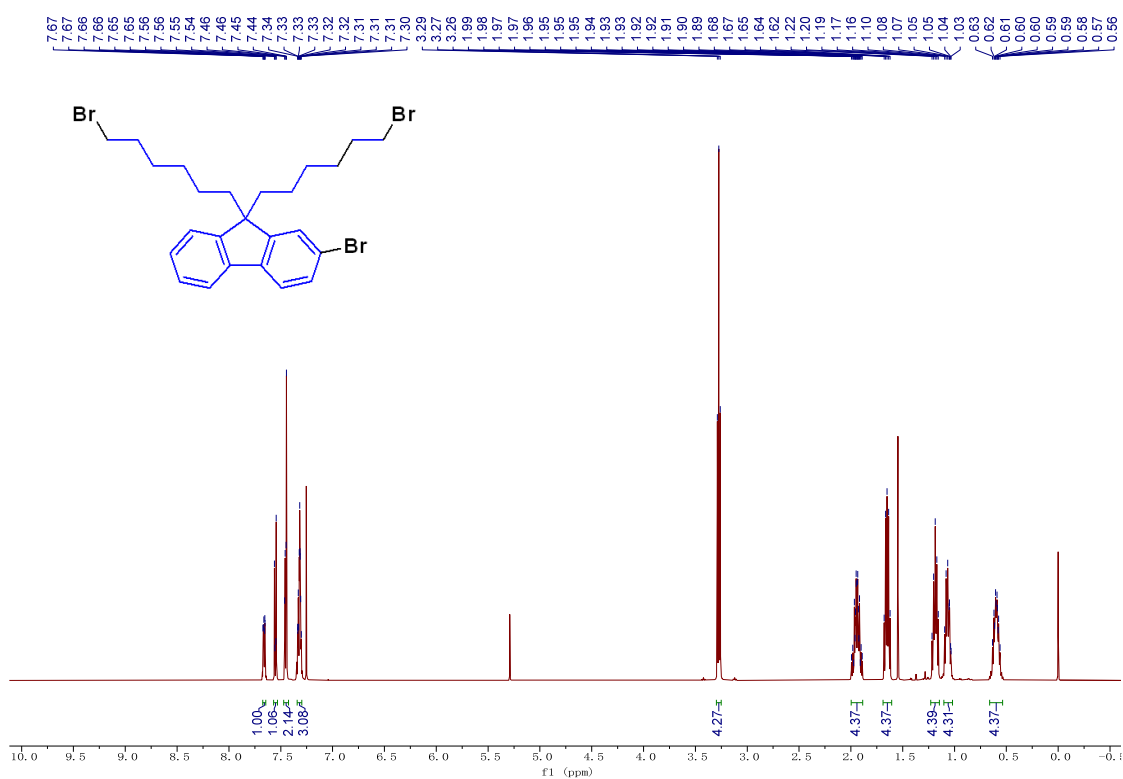
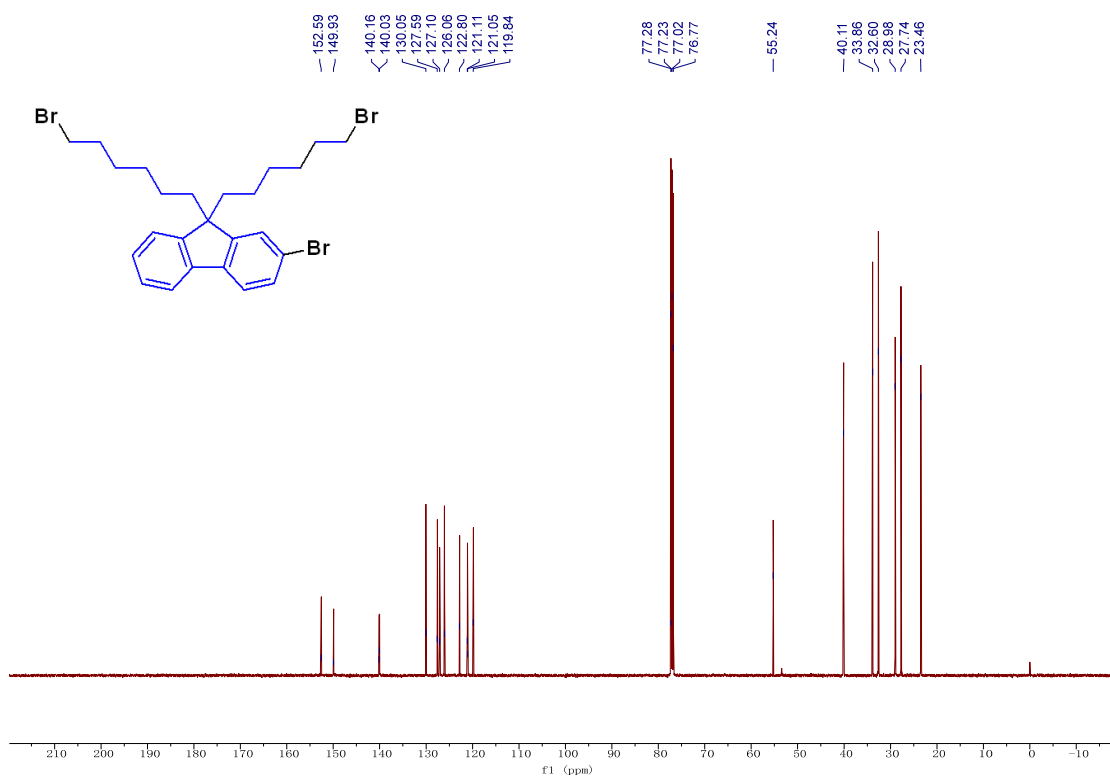
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Experimental Section

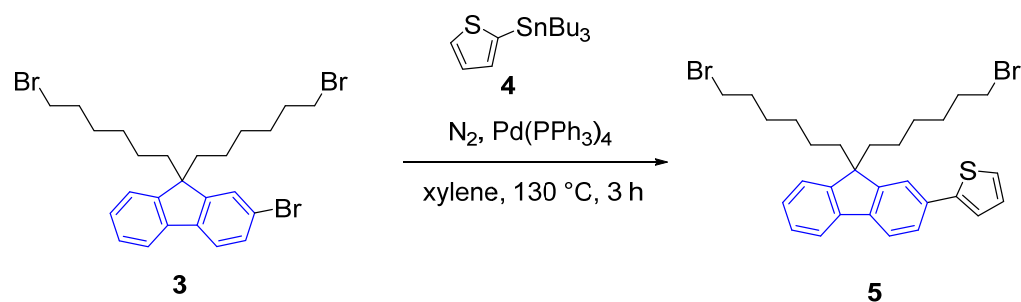
Synthesis of Product 3



2-bromo-9,9-bis(6-bromohexyl)-9H-fluorene(3): To a 150 ml of 45% aqueous potassium hydroxide was added 6.0 g (24.4 mmol) 2-bromofluorene **1**, 59.3 g (0.244 mol) 1,6-dibromohexane **2** and 0.78 g (2.4 mmol) tetrabutylammonium bromide at 75°C . The mixture was stirring for one hour, and then cooled down to room temperature. The aqueous layer was extracted with dichloromethane. The organic layer was washed with 1.0 M aqueous HCl, then brine and water, and dried over anhydrous magnesium sulfate. After removal of the solvent and the excess 1,6-dibromohexane under reduced pressure, the residue was purified by column chromatography on silica gel (eluent petroleum ether) to afford yellow, which was further purified by recrystallization by petroleum ether under -20°C to give white solid product 8.79 g (63%). ^1H NMR (500 MHz, CDCl_3). δ (ppm): δ 7.67 – 7.64 (m, 1H), 7.57 – 7.53 (m, 1H), 7.47 – 7.42 (m, 2H), 7.34 – 7.30 (m, 3H), 3.27 (t, J = 6.8 Hz, 4H), 2.00 – 1.89 (m, 4H), 1.69 – 1.61 (m, 4H), 1.23 – 1.15 (m, 4H), 1.10 – 1.02 (m, 4H), 0.66 – 0.54 (m, 4H). ^{13}C NMR (125 MHz, CDCl_3). δ (ppm): 152.59, 149.93, 140.16, 140.03, 130.05, 127.59, 127.10, 126.06, 122.80, 121.11, 121.05, 119.84, 55.24, 40.11, 33.86, 32.60, 28.98, 27.74, 23.46.

Figure S1. ¹H NMR of compound 3.Figure S2. ¹³C NMR of compound 3.

Synthesis of Product 5



2-(9,9-bis(6-bromohexyl)-9H-fluoren-2-yl)thiophene (5): To a solution of compound **3** (5.71 g, 10.00 mmol) and the compound **4** (5.60 g, 15.00 mmol) in xylene (100 mL) under nitrogen, Pd(PPh₃)₄ (1.16 g) was added. The mixture was stirred at 130 °C for 5 h. After cooling to room temperature, the mixture was poured into water and extracted twice with ethyl acetate, dried with MgSO₄ and evaporated in vacuo. The crude product was subjected to column chromatography on silica gel to afford compound **5** as pale yellow oil (3.36 g, 58.5%). ¹H NMR (500 MHz, CDCl₃) δ (ppm): δ 7.69 (dd, *J* = 7.6, 3.2 Hz, 2H), 7.60 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.55 (d, *J* = 1.6 Hz, 1H), 7.38 (d, *J* = 3.6 Hz, 1H), 7.36–7.27 (m, 4H), 7.11 (dd, *J* = 5.1, 3.6 Hz, 1H), 3.26 (t, *J* = 6.8 Hz, 4H), 2.07–1.93 (m, 4H), 1.70–1.59 (m, 4H), 1.23–1.12 (m, 4H), 1.12–1.02 (m, 4H), 0.73–0.59 (m, 4H). ¹³C NMR (125 MHz, CDCl₃) δ 151.15, 150.50, 145.11, 140.72, 140.67, 133.32, 128.08, 127.23, 127.00, 125.02, 124.55, 122.93, 122.80, 120.14, 120.08, 119.79, 77.27, 77.02, 76.77, 55.05, 40.24, 33.90, 32.62, 29.03, 27.74, 23.52.

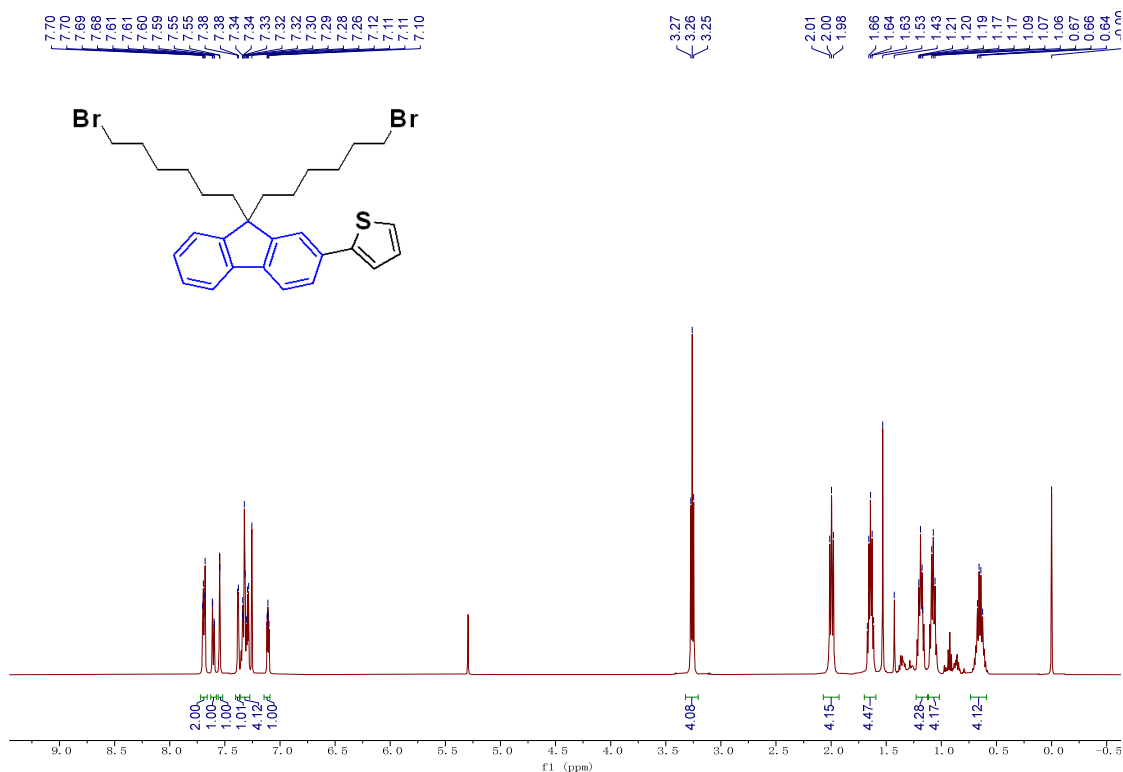


Figure S3. ¹H NMR of compound **5**.

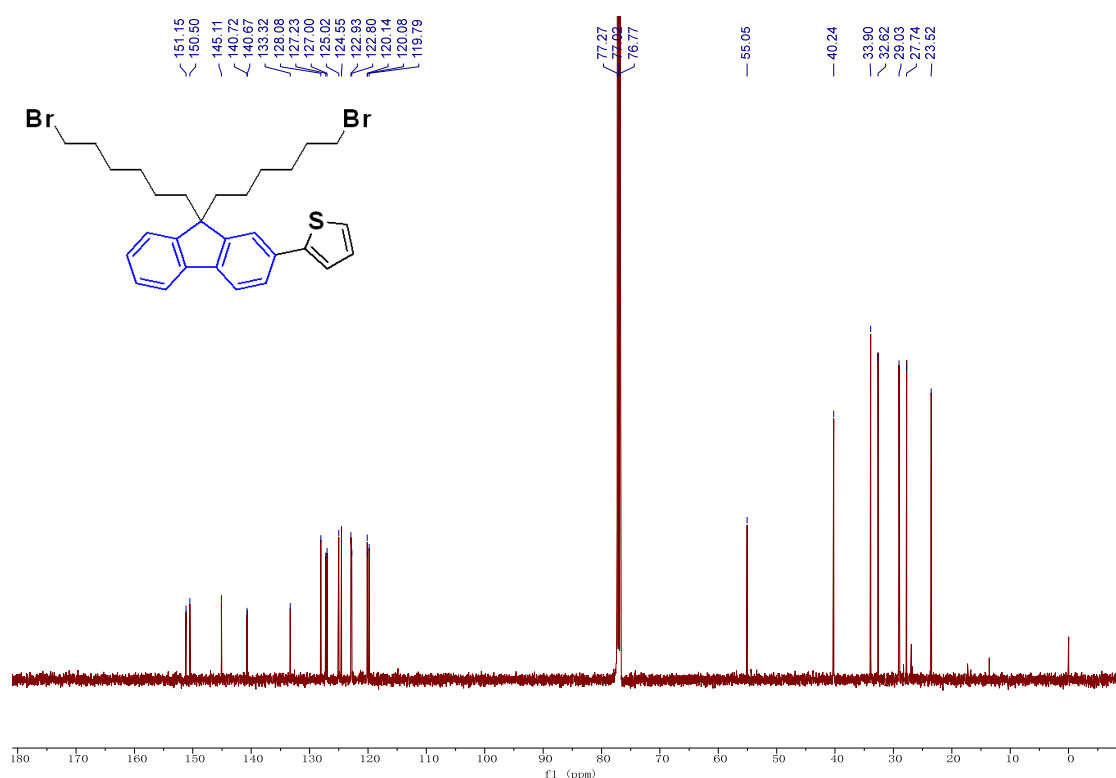
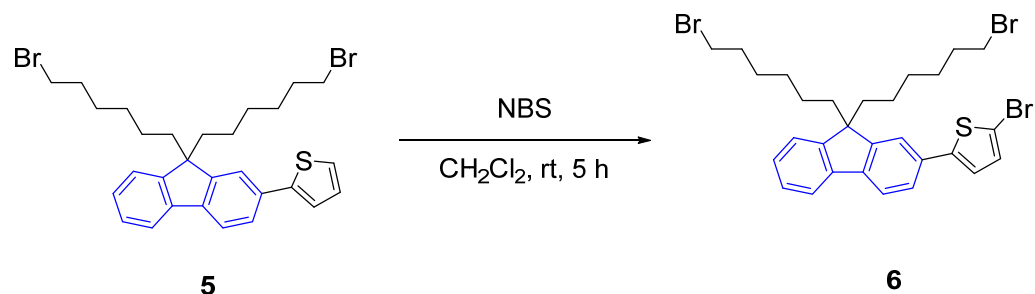
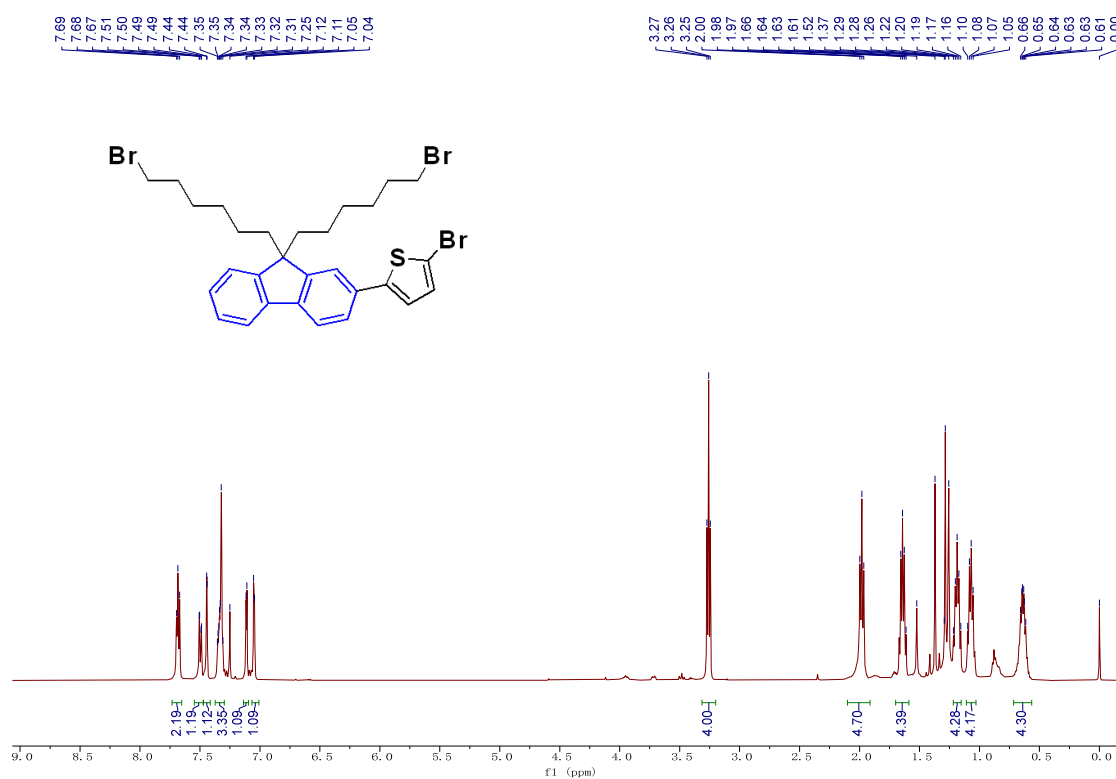
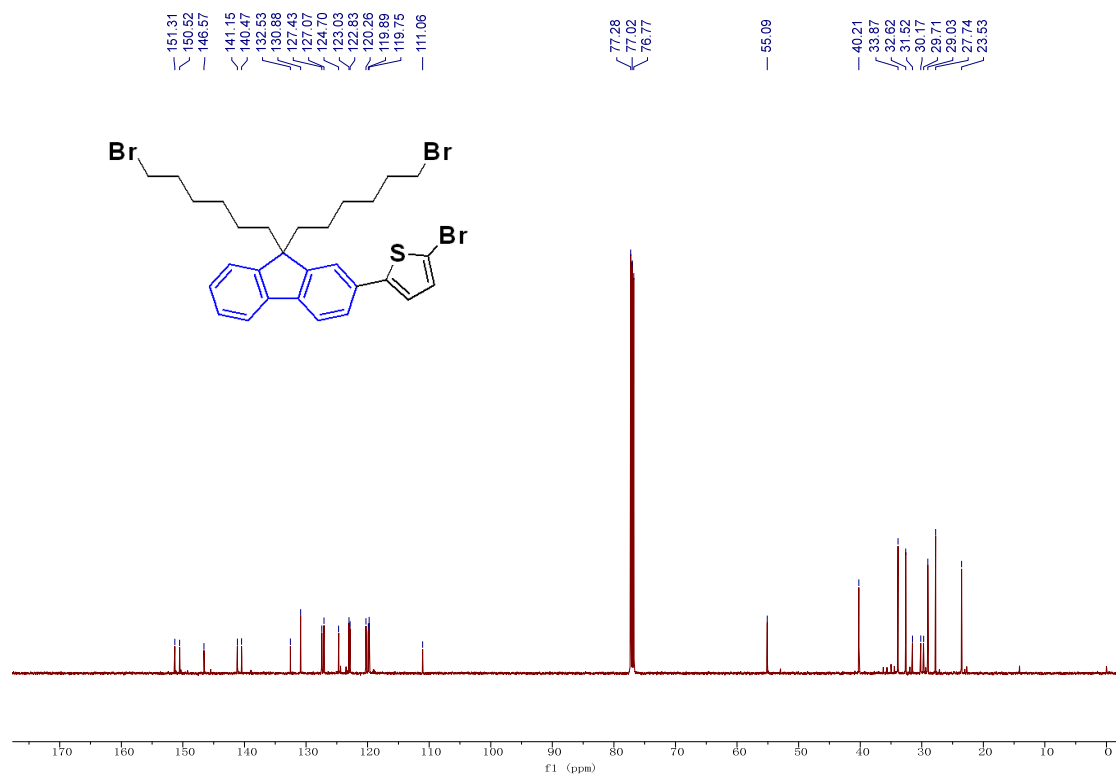


Figure S4. ¹³CNMR of compound 5.

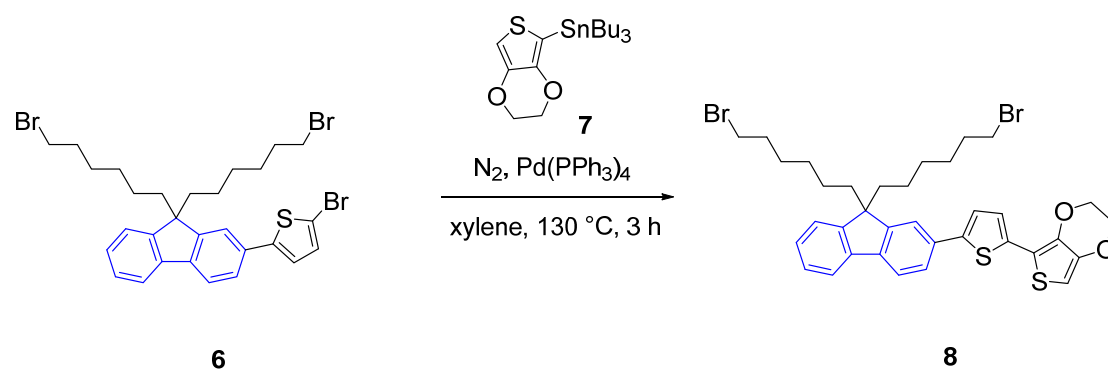
Synthesis of Product 6



2-(9,9-bis(6-bromohexyl)-9H-fluoren-2-yl)-5-bromothiophene (6): 2-(9,9-bis(6-bromohexyl)-9H-fluoren-2-yl)thiophene **5** (1.18 g, 2.05 mmol) was dissolved in CH₂Cl₂ (30 mL). NBS (402 mg, 2.26 mmol) was dissolved in CH₂Cl₂ then dropwise added to the solution and the mixture was stirred overnight at room temperature in the dark. Until the reaction completion as shown by TLC analyses, the solvent was removed. The residue was purified by silica gel column chromatography eluting with PE/CH₂Cl₂ (1:1) to give compound **6** (1.23 g, 92%) as a yellow solid. ¹H NMR (500 MHz, CDCl₃) δ 7.73 – 7.65 (m, 2H), 7.50 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.44 (d, *J* = 1.6 Hz, 1H), 7.37 – 7.29 (m, 3H), 7.11 (d, *J* = 3.8 Hz, 1H), 7.05 (d, *J* = 3.9 Hz, 1H), 3.26 (t, *J* = 6.8 Hz, 4H), 1.98 (t, *J* = 8.1 Hz, 5H), 1.70 – 1.59 (m, 4H), 1.23 – 1.14 (m, 5H), 1.08 (q, *J* = 7.5 Hz, 4H), 0.72 – 0.56 (m, 4H). ¹³C NMR (125 MHz, CDCl₃) δ 151.31, 150.52, 146.57, 141.15, 140.47, 132.53, 130.88, 127.43, 127.07, 124.70, 123.03, 122.83, 120.26, 119.89, 119.75, 111.06, 55.09, 40.21, 33.87, 32.62, 31.52, 30.17, 29.71, 29.03, 27.74, 23.53.

Figure S5. ¹H NMR of compound 6.Figure S6. ¹³C NMR of compound 6.

Synthesis of Product 8



5-(5-(9,9-bis(6-bromohexyl)-9H-fluoren-2-yl)thiophen-2-yl)-2,3-dihydrothieno[3,4-b][1,4]dioxine (8): To a solution of compound **6** (1.31 g, 2.00 mmol) and the compound **7** (3.00 mmol) in xylene (30 mL) under nitrogen, Pd(PPh₃)₄ (231 mg, 0.20 mmol) was added. The mixture was stirred at 130 °C for 5 h. After cooling to room temperature, the mixture was poured into water and extracted twice with ethyl acetate, dried with MgSO₄ and evaporated in vacuo. The crude product was subjected to column chromatography on silica gel to afford compound **8** as yellow oil (673 mg, 47.1%). ¹H NMR (500 MHz, CDCl₃) δ 7.72–7.65 (m, 2H), 7.63–7.58 (m, 1H), 7.53 (d, *J* = 1.6 Hz, 1H), 7.36–7.27 (m, 4H), 7.21 (d, *J* = 3.7 Hz, 1H), 6.25 (s, 1H), 4.44–4.35 (m, 2H), 4.31–4.22 (m, 2H), 3.27 (t, *J* = 6.8 Hz, 4H), 2.00 (t, *J* = 8.3 Hz, 4H), 1.70–1.60 (m, 4H), 1.23–1.14 (m, 4H), 1.11–1.03 (m, 4H), 0.70–0.55 (m, 4H). ¹³C NMR (125 MHz, CDCl₃) δ 151.12, 150.43, 142.97, 141.89, 140.65, 140.54, 137.53, 133.96, 133.13, 127.17, 126.96, 124.48, 123.78, 123.02, 122.74, 120.12, 119.73, 119.60, 112.38, 96.97, 65.10, 64.59, 55.02, 40.23, 34.04, 32.59, 29.00, 27.72, 26.89, 23.47.

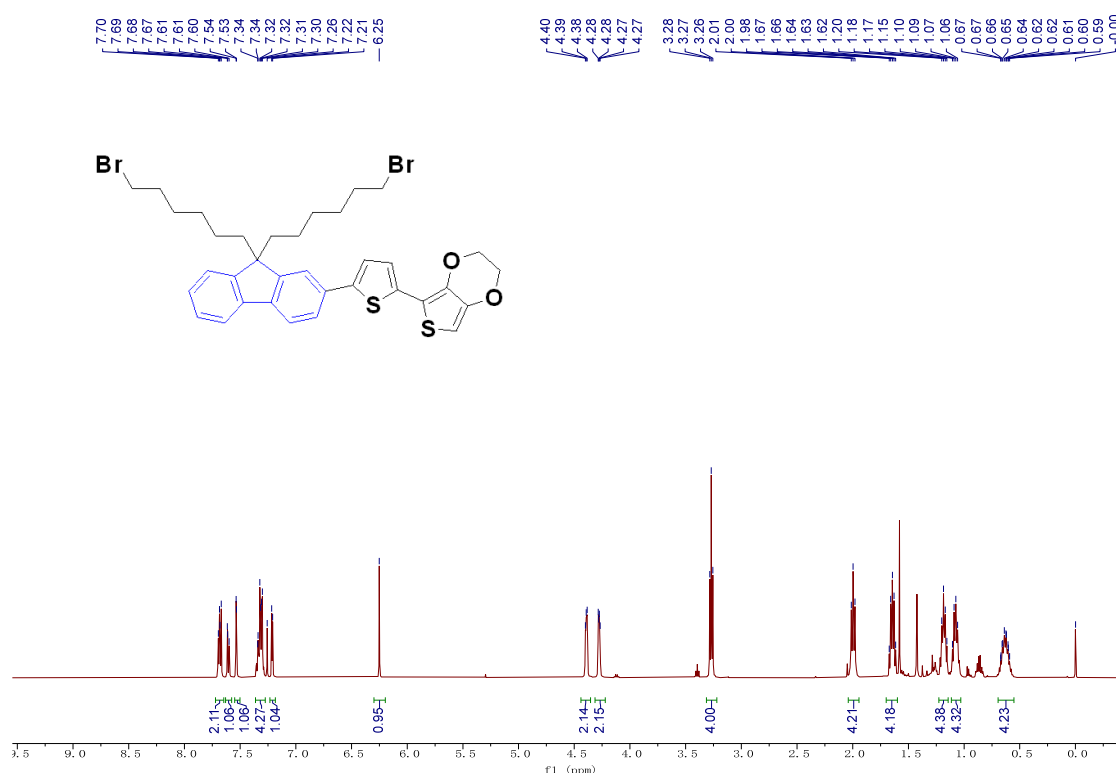


Figure S7. ¹H NMR of compound **8**.

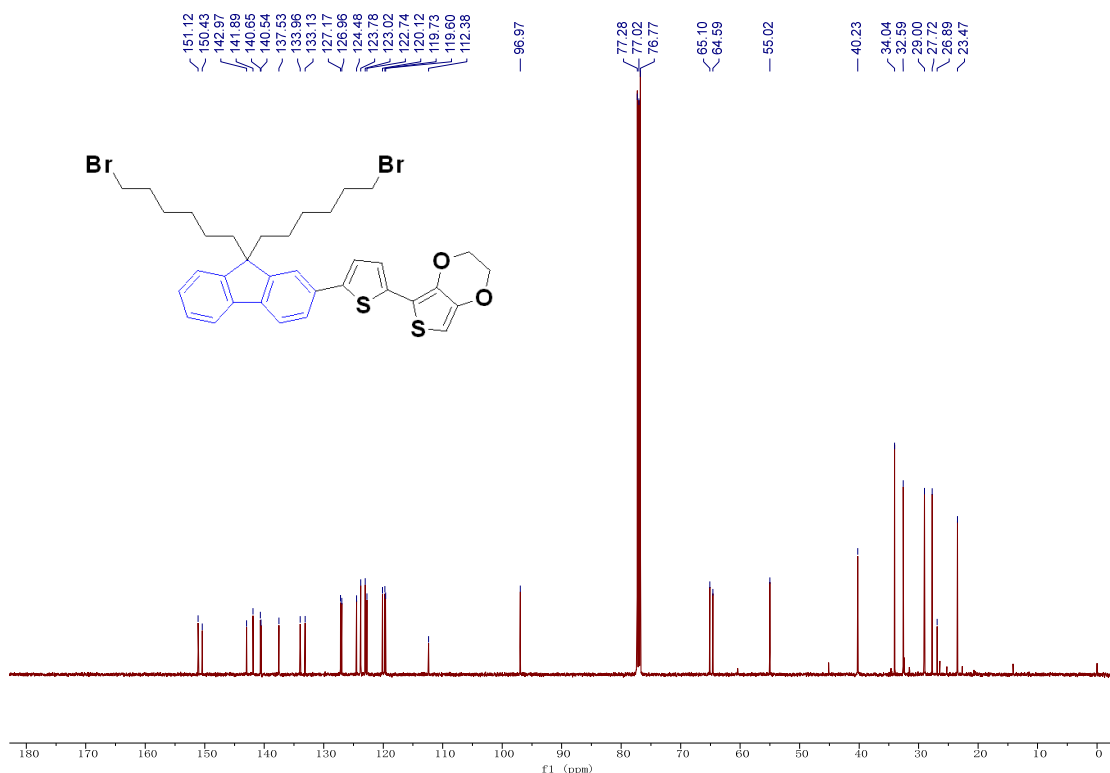
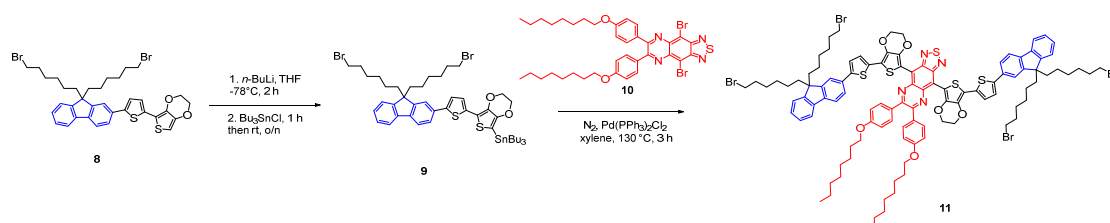


Figure S8. ^{13}C NMR of compound 8.

Synthesis of Product 11

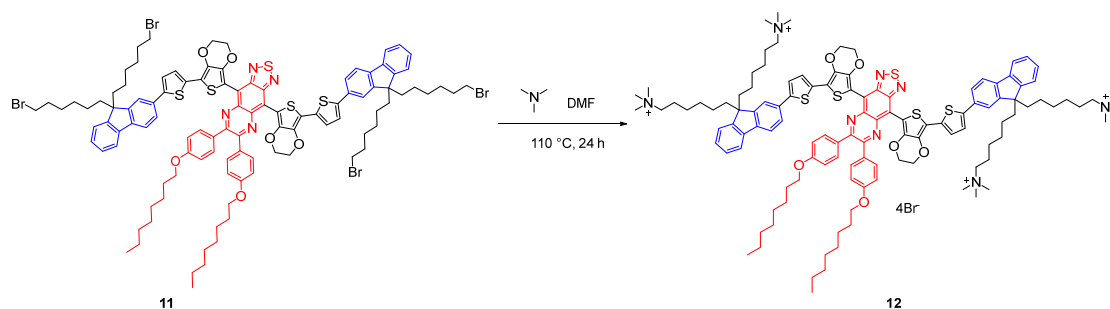


(7-(5-(9,9-bis(6-bromohexyl)-9H-fluoren-2-yl)thiophen-2-yl)-2,3-dihydrothieno[3,4-b][1,4]dioxin-5-yl)tributylstannane (9): To a solution of compound 8 (0.69 g, 1.50 mmol) in THF (15.00 mL) at $-78\text{ }^{\circ}\text{C}$ under nitrogen, *n*-BuLi solution (2.50 M in hexane, 0.90 mL, 2.25 mmol) was added dropwise. After the mixture was stirred at this temperature for another 2.0 h, tributyltin chloride (0.73 g, 2.25 mmol) was added to the solution. The reaction mixture was then slowly warmed to room temperature and stirred for overnight. After that the mixture was poured into water and extracted twice with ethyl acetate, the combined organic phase was dried with MgSO_4 and evaporated in vacuo without further purification.

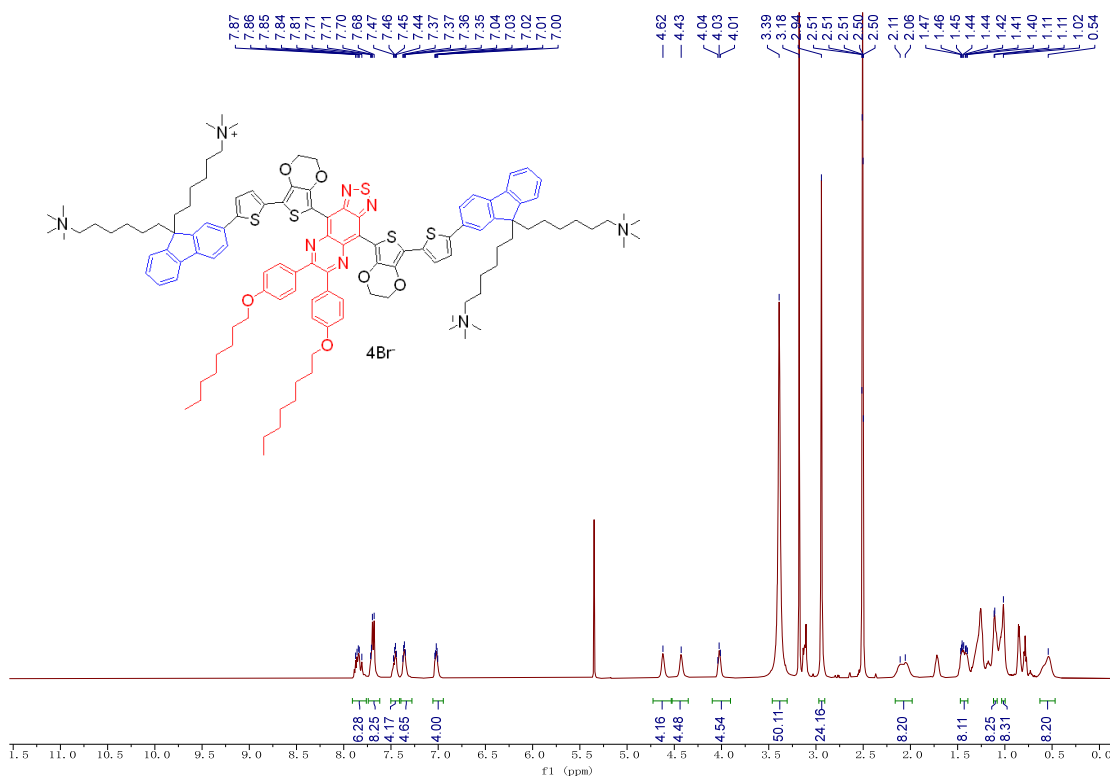
IRFT (11): To a solution of compound 10 (377 mg, 0.5 mmol) and the crude product 9 from previous step in xylene (20 mL) under nitrogen, $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (70 mg, 0.1 mmol) was added. The mixture was stirred at $130\text{ }^{\circ}\text{C}$ for 10 h. After cooling to room temperature, the mixture was poured into water and extracted twice with ethyl acetate, dried with MgSO_4 and evaporated in vacuo. The crude product was subjected to column chromatography on silica gel to afford 11 as a dark green solid (405 mg, 40.1%). ^1H NMR (500 MHz, CDCl_3) δ 7.77 (d, $J = 8.5\text{ Hz}$, 4H), 7.71 (d, $J = 7.5\text{ Hz}$, 4H), 7.69–7.65 (m, 2H), 7.60 (s, 2H), 7.39 (s, 4H), 7.37–7.29 (m, 6H), 6.88 (d, $J = 8.6\text{ Hz}$, 4H), 4.66–4.55 (m, 4H), 4.43–4.34 (m, 4H), 3.99 (t, $J = 6.6\text{ Hz}$, 4H), 3.29 (t, $J = 6.8\text{ Hz}$, 7H), 2.07–2.00 (m, 8H), 1.67 (p, $J = 7.0\text{ Hz}$, 8H), 1.23–1.17 (m, 8H), 1.14–1.07 (m, 8H), 0.73–0.57 (m, 8H). ^{13}C NMR (125 MHz, CDCl_3)

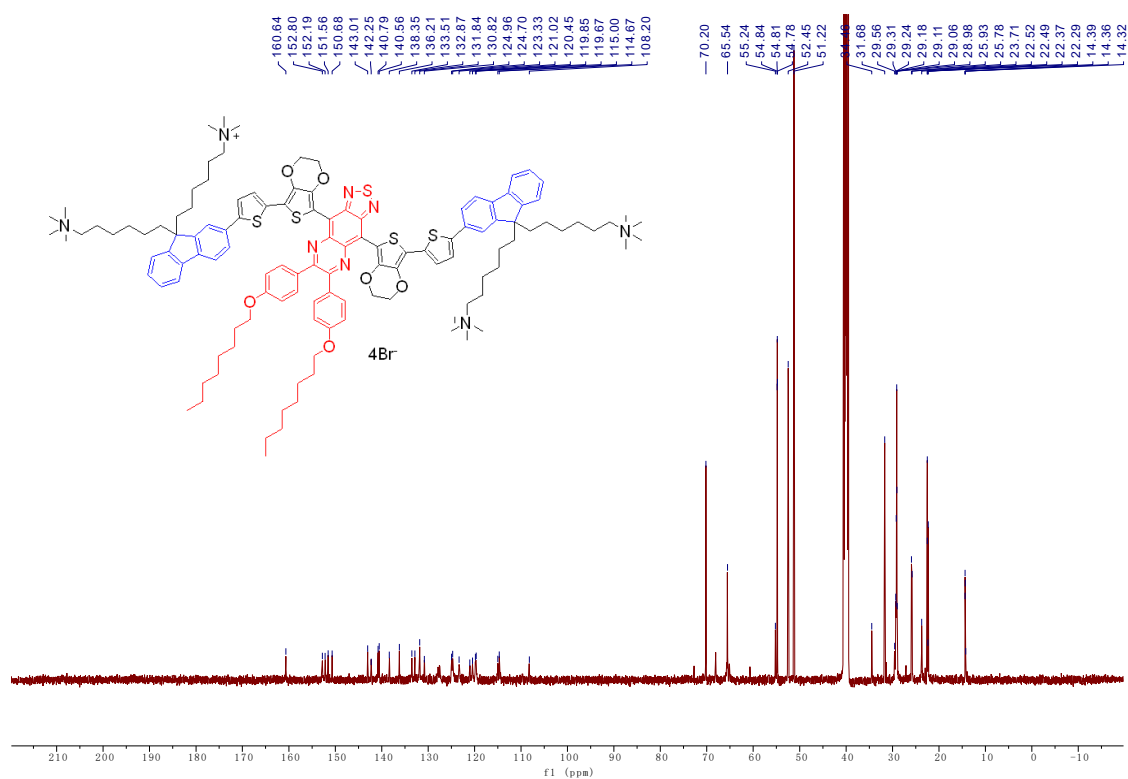
Chemical Structure of Compound 10:

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)S(=O)(=O)c289ccc(Br)cc289)nc290c288c(nc291c290sc(cc291)S(=O)(=O)c292ccc(Br)cc292)nc293c291c(nc294c293sc(cc294)S(=O)(=O

Figure S10. ^{13}C NMR of compound 11.*Synthesis of RT-MN*

RT-MN (12): A pressure bottle equipped with stir bar, DMF (5 mL), compound 11 (101 mg, 0.50 mmol), and trimethylamine in THF solution (118 mg, 2.00 mmol, 1.0 M, 2.0 mL). After the bottle was sealed, the solution was stirred at 110 °C for 24 h. After cool to room temperature, the solution was added to 40 mL of methyl tert-butyl ether (MTBE), then the heterogeneous mixture was separated by high-speed centrifugation. The dark green solid (97 mg) was obtained by 5 times of washed by MTBE. ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 7.91 – 7.76 (m, 6H), 7.74 – 7.62 (m, 8H), 7.50 – 7.41 (m, 4H), 7.40 – 7.28 (m, 5H), 7.06 – 6.95 (m, 4H), 4.73 – 4.53 (m, 4H), 4.52 – 4.35 (m, 4H), 4.10 – 3.91 (m, 5H), 3.39 (s, 50H), 2.94 (s, 24H), 2.16 – 1.98 (m, 8H), 1.49 – 1.38 (m, 10H), 1.13 – 1.08 (m, 10H), 1.03 – 1.00 (m, 8H), 0.63 – 0.47 (m, 8H). ^{13}C NMR (126 MHz, DMSO) δ 160.64, 152.80, 152.19, 151.56, 150.68, 143.01, 142.25, 140.79, 140.56, 138.35, 136.21, 133.51, 132.87, 131.84, 130.82, 124.96, 124.70, 123.33, 121.02, 120.45, 119.85, 119.67, 115.00, 114.67, 108.20, 70.20, 65.54, 55.24, 54.84, 54.81, 54.78, 52.45, 51.22, 34.46, 31.68, 29.56, 29.31, 29.24, 29.18, 29.11, 29.06, 28.98, 25.93, 25.78, 23.71, 22.52, 22.49, 22.37, 22.29, 14.39, 14.36, 14.32, 14.22. HRMS (ESI) m/z 484.5098 $[(\text{M}-4\text{Br})^+]$, Cal. $\text{C}_{118}\text{H}_{152}\text{N}_8\text{O}_6\text{S}_5^{4+}$, 484.5112.

**Figure S11.** ^1H NMR of compound 12.

Figure S12. ^{13}C NMR of compound 12.

2_20220629171829#7 RT: 0.07 AV: 1 NL: 2.69E6 T:
FTMS + p ESI Full ms [300.0000-1000.0000]

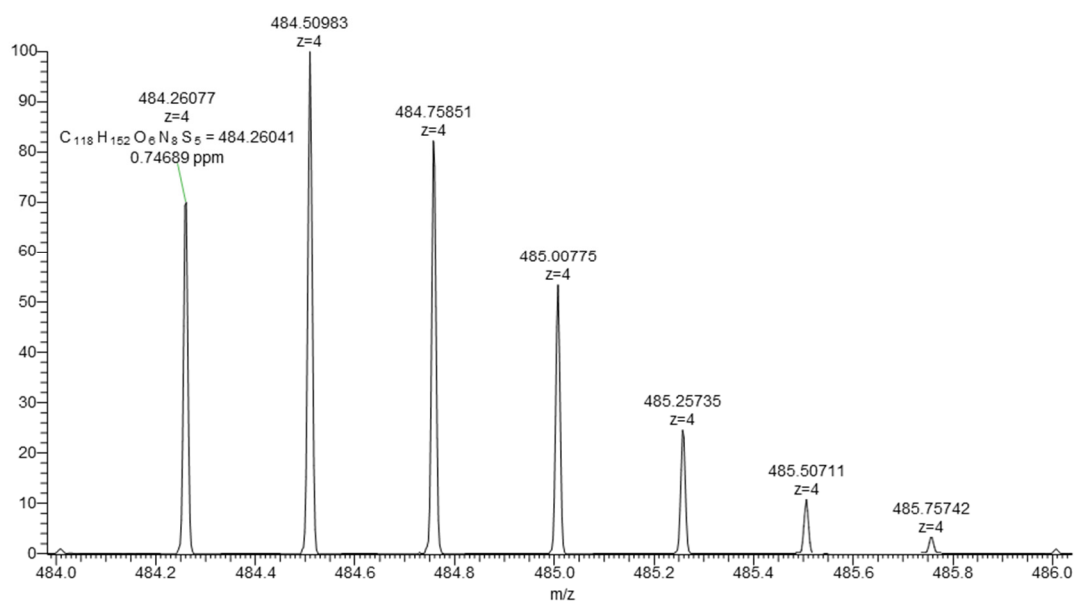


Figure S13. HRMS of compound 12.

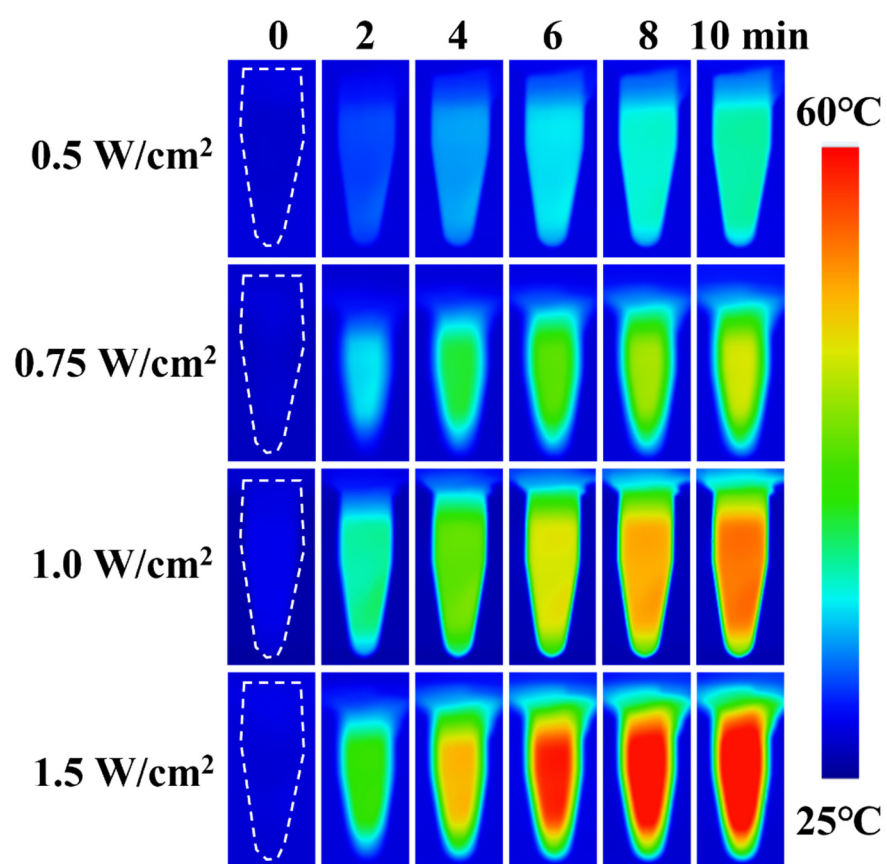


Figure S14. Infrared thermal images of RT-MN with different laser power density.

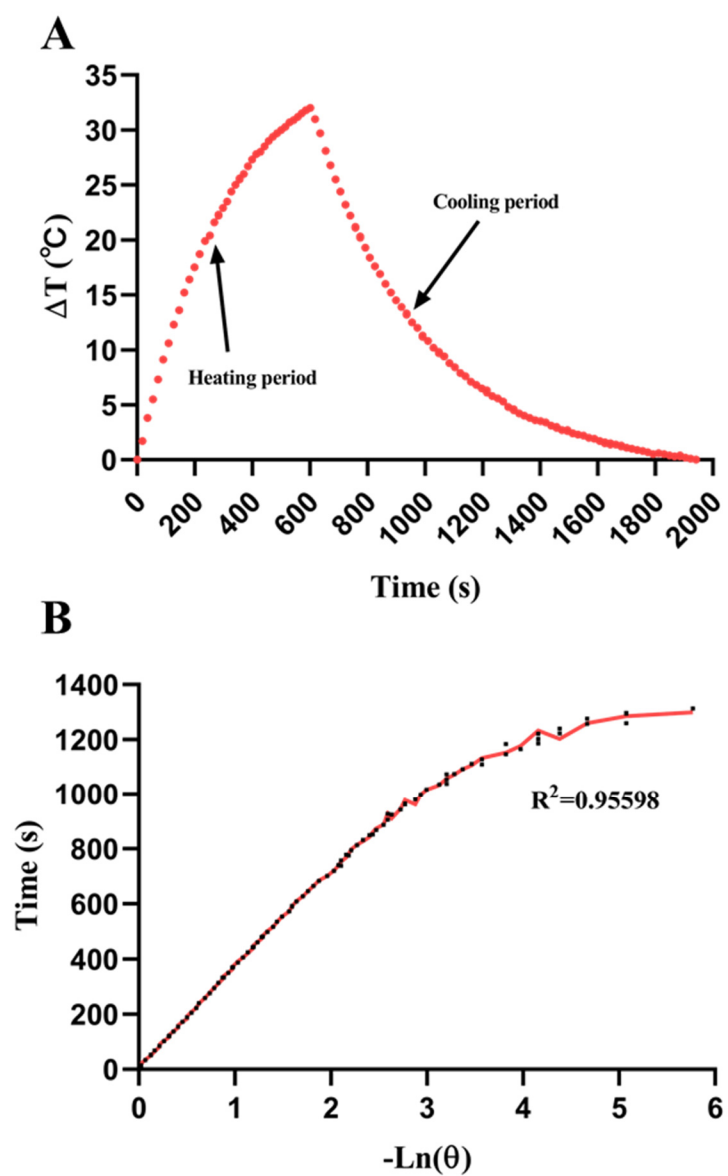


Figure S15. Photothermal effect of RT-MN in water when irradiated with an 808 nm laser ($1.0 \text{ W}\cdot\text{cm}^{-2}$). The laser was switched off after irradiation for 10 minutes.