Supporting Information

Cell-penetrating poly(disulfide)s-based nanoquenchers (*q*CPDs) for self-monitoring of intracellular gene delivery

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General Information

Chemicals

Oligonucleotides (shown in Table S1) were synthesized and HPLC purified by Qingke Biotechnology Co., Ltd (Beijing, China). Hoechst 33342 were purchased from Thermo Fisher Scientific Inc (USA). Anti-Survivin monoclonal antibody (EP2880Y) was purchased from Abcam (USA) and the secondary antibody (Anti-Rabbit, P0488) was obtained from Cell Signaling Technology (USA). 1,1'-Carbonyldiimidazole (CDI), 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC), *N*-Hydroxysuccinimide (NHS), 2-(7-Azabenzotriazol-1-yl)-*N, N, N′, N′*-tetramethyluronium hexafluorophosphate (HATU), Trifluoroacetic acid (TFA) and Ethyldiisopropylamine (DIEA) were purchased from Adamas. Dichloromethane (DCM), and tetrahydrofuran (THF) were purchased from HUSHI. Ultrapure water was obtained from a Milli-Q® water purification system (resistivity 18.2 MΩ cm^{-1}, Millipore). All reagents were received and used without further purification.

Table S1. The detailed information of ONs

Name	Detailed sequence information
Survivin-FAM	5’- CC AGC CTT CCA GCT CCT T (FAM) -3’
Survivin-TMR	5’- CC AGC CTT CCA GCT CCT T (TMR) -3’
Survivin	5’- CC AGC CTT CCA GCT CCT -3’
Pink 1(siRNA)	Sense: 5’- GACGCUGUUCCUCGUUAUGAA -3’ Antisense: 5’- UUCAUAACGAGGAACAGCGUC -3’
NC-siRNA	Sense: 5’-UUCUCCGAACGUGUCACGUTT-3’ Anti-sense: 5’-ACGUGACACGUUCGGAGAATT-3’

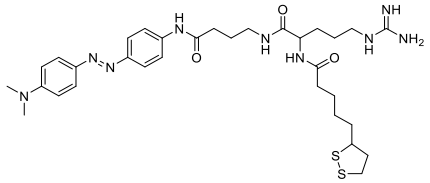
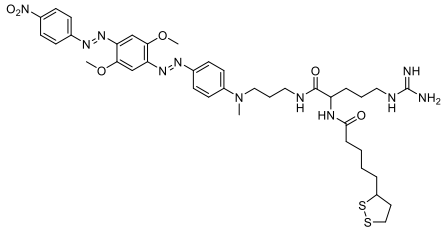
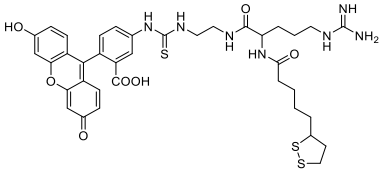
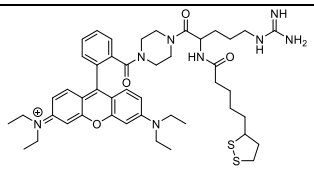
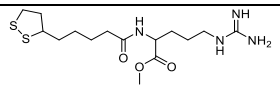
Apparatus

^{1}H NMR spectra were recorded on a Bruker AvanceIII 500 MHz spectrometer (Germany). The UV-vis absorption spectra and fluorescence spectra were recorded using a SYNERGY H1 microplate reader (BioTek). The confocal laser scanning microscopy (CLSM) images of cells were taken on Leica. Western blot and fluorescent image were recorded using Invitrogen iBright 1500. Transmission electron microscopy (TEM) images were obtained by HT7700 (HITACHI, Japan) operated at an accelerating voltage of 200 kV. Zeta potential were measured using

dynamic light scattering (DLS) on a Zetasizer Nano particle analyser Nano-ZS90 (Malvern Instruments Ltd., England).

Experimental Details and Procedures

Table S2. Summary of all the monomers used in this project

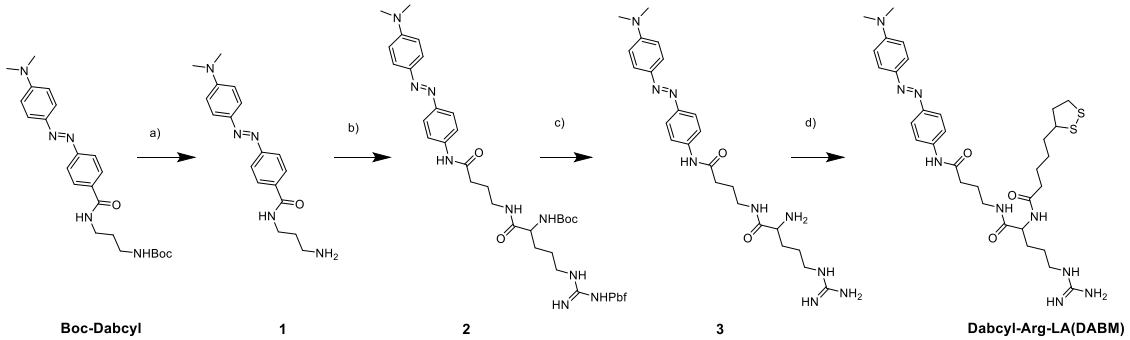
Name	Structure
DABM (Quencher: Dabcyl)	
BHQM (Quencher: BHQ-2)	
FITM (Fluorophore: FITC)	
TERM (Fluorophore: Rhodamine B)	
NORM	

Synthesis and characterization of disulfide monomers:

LA-NHS

Scheme S1. Synthesis of LA-NHS

Lipoic Acid (500 mg, 2.42 mmol) was dissolved in DCM (15 mL) at 0°C. EDC (465 mg, 2.42 mmol) and NHS (280 mg, 2.42 mmol) were added. The mixture was warmed to room temperature (r. t.). After 1 h, the reaction was washed with ether/DCM (5/1) for 3 times to yield as a yellow solid (440 mg, 60% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.56 (dq, *J* = 12.9, 6.4 Hz, 1H), 3.13 - 3.21 (m, 1H), 3.06 - 3.31 (m, 1H), 2.82 (d, *J* = 1.9 Hz, 4H), 2.61 (t, *J* = 7.4 Hz, 2H), 2.45 (td, *J* = 12.5, 6.3 Hz, 1H), 1.91 (dq, *J* = 13.5, 6.9 Hz, 1H), 1.78 (dd, *J* = 15.1, 7.5 Hz, 2H), 1.69 (dd, *J* = 14.5, 8.8 Hz, 2H), 1.61 - 1.47 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 168.4, 56.1, 40.2, 38.5, 34.4, 30.8, 28.3, 25.6, 24.4.

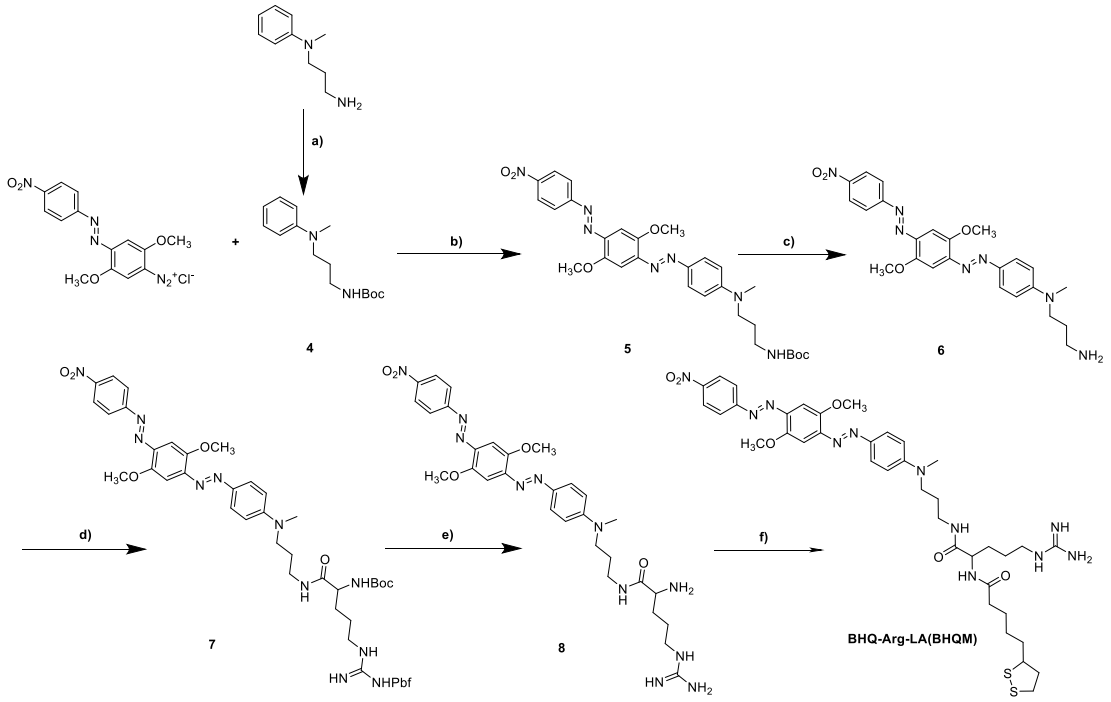


Scheme S2 Synthesis of quench-monomer DABM a) TFA, DCM, 2 h, r. t., 78%; b) HATU, DIEA, DMF, 3 h, 0 °C to r. t., 42%; c) TFA, DCM, 2 h, r. t., 89%; d) DIEA, DMF, 3 h, 0 °C to r. t., 68.3%.

Compound 1: Boc-Dabcyl (498 mg, 1.172 mmol) was dissolved into the mixture of DCM (20 mL) and TFA (6 mL) at r. t. for 3 h. Volatiles were removed and the crude material was purified by column chromatography to get as an orange solid (350 mg, 92% yield).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (dt, *J* = 16.5, 7.0 Hz, 6H), 7.80 (s, 1H), 6.76 (d, *J* = 9.0 Hz, 2H), 3.61 (dd, *J* = 11.9, 5.8 Hz, 2H), 3.10 (s, 6H), 2.91 - 2.97 (m, 2H), 1.76 (m, 2H).

Compound 3: Boc-Arg(Pbf)-OH (526 mg, 1 mmol) was dissolved in dry DMF (15 mL) at 0℃. HATU (380 mg, 1 mmol) and DIEA (181 μL, 1.32 mmol) were added followed by **1** (325 mg, 1 mmol). The solution was allowed to warm up from 0 ℃ to room temperature and stirred for 4 h under N_2 atmosphere. EtOAc (40 mL) was then added and organic layer was washed with H_2O and brine (2*40 mL each). Then the organic layer was then dried with Na_2SO_4 and evaporated under reduced pressure. Volatiles were removed and the crude material was purified by column chromatography to get as an orange solid **2** (350 mg, 42% yield). Then, **2** (250 mg, 0.3 mmol) was dissolved into the mixture of DCM (4 mL) and TFA (6 mL) was stirred at r. t. for 2 h. The resulting solution was concentrated under reduced pressure and purified by semi-preparative HPLC. Then the product was freeze-dried to yield as a dark yellow solid **3** (180 mg, 89% yield). ^{1}H NMR (400 MHz, MeOD) δ 7.95 (d, *J* = 8.7 Hz, 2H), 7.89 – 7.82 (m, 4H), 6.92 (d, *J* = 9.4 Hz, 2H), 3.90 (t, *J* = 6.5 Hz, 1H), 3.47 (dd, *J* = 10.2, 6.9 Hz, 2H), 3.44 - 3.32 (m, 2H), 3.26 (t, *J* = 6.9 Hz, 2H), 3.17 (s, 6H), 1.93 (dd, *J* = 14.6, 7.7 Hz, 2H), 1.86 (dd, *J* = 13.6, 6.9 Hz, 2H), 1.78 - 1.65 (m, 2H). ^{13}C NMR (126 MHz, MeOD) δ 168.6, 168.3, 157.4, 153.9, 153.4, 142.8, 134.1, 128.0, 126.2, 121.0, 112.4, 52.8, 40.4, 39.5, 39.0, 36.9, 36.6, 28.7, 28.3, 24.1.

DABM: 3 (20 mg, 0.0416 mmol) was dissolved in DMF (5 mL). Then LA-NHS (13 mg, 0.043 mmol) and DIEA (60 μL, 0.336 mmol) was added to this reaction for overnight. The crude reaction production was purified by semi-preparative HPLC. The product was freeze-dried to yield as an orange solid (19 mg, 68% yield). ^{1}H NMR (500 MHz, MeOD) δ 7.98 (d, *J* = 8.5 Hz, 2H), 7.88 (dd, *J* = 14.2, 8.8 Hz, 4H), 6.92 (d, *J* = 9.2 Hz, 2H), 4.35 (dd, *J* = 7.5, 6.2 Hz, 1H), 3.56 (dd, *J* = 8.3, 6.2 Hz, 1H), 3.47 (dd, *J* = 6.2, 4.5 Hz, 2H), 3.24 (t, *J* = 6.7 Hz, 2H), 3.17 (s, 6H), 3.14 (s, 1H), 3.11 - 3.05 (m, 1H), 2.43 (dt, *J* = 12.3, 6.2 Hz, 1H), 2.33 (dd, *J* = 13.1, 5.9 Hz, 2H), 1.91 - 1.80 (m, 4H), 1.78 - 1.59 (m, 8H), 1.48 (dd, *J* = 15.6, 6.4 Hz, 2H). ESI-MS calcd. For $C_{32}H_{48}N_9O_3S_2^+$ [m/z]$^+$: 670.32, found: 670.35.



Scheme S3. a) Boc_2O, TEA, DCM, 2 h, r. t., 68%; b) THF, MeOH, 2 h, r. t., 24%; c) TFA, DCM, 2 h, r. t., 84%; d) HATU, DIEA, DCM, 2 h,0 °C to r. t., 58%; e) TFA, DCM, 2 h, r. t.,89%; f) LA-NHS, DIEA, DMF, 0°C to r. t., 50%.

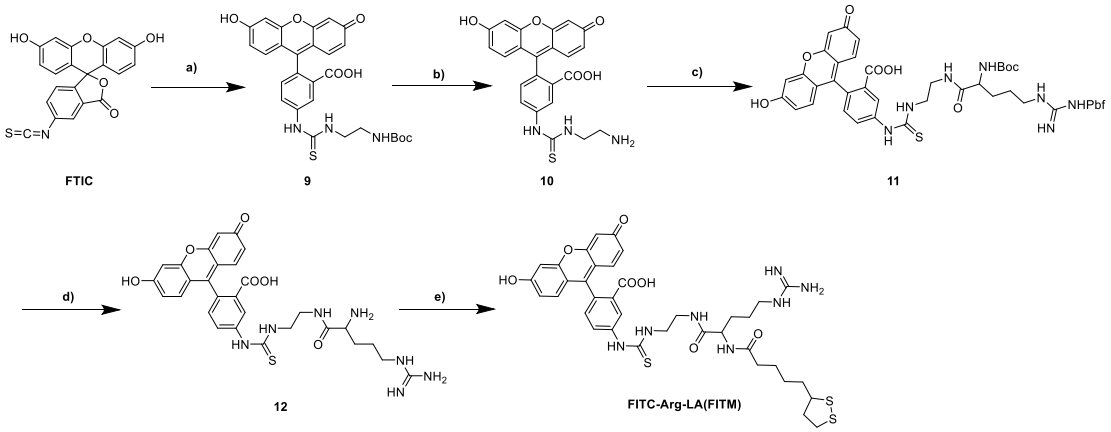
Compound 4: N-(3-Aminopropyl)-N-methylaniline (200 mg, 1.22 mmol) and TEA (225 μL, 1.83 mmol) were dissolved in DCM (10 mL) at r. t. Boc_2O (319 mg,1.46 mmol) was dissolved in DCM (3 mL), and then the mixture was dropped into the previous bottle slowly. Volatiles were removed and the crude material was purified by column chromatography to yield as a transparent oily liquid (220 mg, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 8.7, 7.1 Hz, 2H), 6.70 (dd, *J* = 8.2, 7.4 Hz, 3H), 3.38 - 3.33 (m, 2H), 3.17 (d, *J* = 6.2 Hz, 2H), 2.92 (s, 3H), 1.81 - 1.74 (m, 2H), 1.61 (s, 1H), 1.45 (s, 9H).

Compound 6: 4 (164 mg, 1 mmol) and Fast Black K salt (1.25 g, 3.6 mmol) were dissolved into the mixture of THF (15 mL) and MeOH (3 mL). The red-brown suspension was stirred at room temperature for 2 h and the color of the solution became dark purple slowly. Volatiles were removed and the crude material was purified by column chromatography to yield as a black purple solid **5** (135 mg, 23% yield). **Compound 6:** The solution of **5** (110 mg, 0.19 mmol) which was dissolved in 6 mL DCM and 4 mL TFA and stirred at r. t. for 2 h, Volatiles were removed and the crude material was purified by column chromatography to yield as a dark purple solid (77 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, *J* = 9.0 Hz, 2H), 8.02 (d, *J* = 8.9 Hz, 2H), 7.88 (d, *J* = 9.0 Hz, 2H), 7.44 (d, *J* = 17.7 Hz, 2H), 6.73 (d, *J* = 9.1 Hz, 2H), 4.02 (s, 3H), 4.04 (s, 3H), 3.50 (t, *J* = 7.1 Hz, 2H), 3.01 (s, 3H), 2.97 (s, 2H), 2.07 - 2.01 (m, 2H).

Compound 7: Boc-Arg(Pbf)-OH (53 mg, 0.10 mmol), HATU (38 mg, 0.10 mmol) and DIEA (22 μL, 0.158 mmol) was dissolved in dry DMF (15 mL) at 0 ℃. Then **6** (40 mg, 0.084 mmol) was added followed. The solution was allowed to warm up from 0 ℃ to rt and stirred for 4 h under N_2 atmosphere. EtOAc (40 mL) was then added, organic layer was washed with H_2O and brine (2*40 mL each). Then the organic layer was then dried with Na_2SO_4 and evaporated under reduced pressure, then using 2 mL of DMSO to dissolve the crude solid and purified by semi-preparative HPLC to get as a dark purple solid (48mg,58%yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 - 8.32 (m, 2H), 8.03 - 7.99 (m, 2H), 7.87 (d, *J* = 9.0 Hz, 2H), 7.47 (s, 1H), 7.44 (s, 1H), 7.23 - 7.13 (m, 2H), 6.70 (d, *J* = 9.2 Hz, 2H), 4.22 (s, 1H), 4.06 (s, 3H), 4.00 (s, 3H), 3.46 (d, *J* = 6.9 Hz, 2H), 3.31 - 3.27 (m, 2H), 3.25 - 3.21 (m, 2H), 3.03 (s, 3H), 2.92 (s, 3H), 2.85 (s, 2H), 2.49 (d, *J* = 2.3 Hz, 6H), 2.00 (s, 1H), 1.86 - 1.82 (m, 2H), 1.78 - 1.72 (m, 2H), 1.59 - 1.56 (m, 2H), 1.40 (s, 9H), 1.38 (s, 6H), 1.24 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 157.0, 156.5, 156.4, 153.7, 152.1, 150.8, 148.3, 146.7, 144.3, 142.0, 138.3, 132.6, 132.2, 129.2, 126.2, 124.7, 123.5, 117.6, 112.5, 111.5, 101.0, 100.0, 86.5, 56.7, 56.7, 50.6, 50.3, 50.1, 43.2, 38.6, 38.4, 37.6, 37.1, 28.6, 28.4, 27.0, 26.6, 19.4, 18.0, 12.5.

Compound 8: Compound 7 (70 mg, 0.071 mmol) was stirred into the mixture of DCM (4 mL) and TFA (6 mL) at r. t. for 2 h. Volatiles were removed and the crude material was purified by semi-preparative HPLC to yield as a dark purple solid (40 mg, 89% yield).^{1}H NMR (500 MHz, MeOD) δ 8.28 (d, *J* = 9.0 Hz, 2H), 7.96 (d, *J* = 9.0 Hz, 2H), 7.77 (d, *J* = 9.2 Hz, 2H), 7.37 (d, *J* = 22.1 Hz, 2H), 6.80 (d, *J* = 9.3 Hz, 2H), 4.04 (s, 3H), 4.00 (s, 3H), 3.93 (t, *J* = 6.6 Hz, 1H), 3.57 (t, *J* = 7.4 Hz, 2H), 3.38 (t, *J* = 7.1 Hz, 2H), 3.27 (t, *J* = 7.0 Hz, 2H), 3.12 (s, 3H), 2.68 (s, 6H), 1.95 (dd, *J* = 15.0, 7.2 Hz, 4H), 1.72 (dd, *J* = 10.2, 3.0 Hz, 2H).^{13}C NMR (126 MHz, MeOD) δ 168.5, 157.3, 156.0, 153.4, 152.2, 150.7, 148.3, 146.1, 144.0, 141.8, 125.8, 124.3, 123.3, 111.2, 100.5, 99.7, 55.7, 52.8, 49.6, 40.4, 39.0, 37.6, 37.1, 28.4, 26.5, 24.1.

BHQM: 8 (20 mg, 0.0316 mmol) was pre-dissolved in DMF. LA-NHS (10 mg, 0.0316 mmol) and DIEA (33 μL, 0.19 mmol) was added followed. The reaction was stirred at r.t. for overnight, and the crude material was purified by semi-preparative HPLC and freeze-dried to yield as a dark purple solid (13mg, 50.3% yield). ^{1}H NMR (500 MHz, Acetone-D_6) δ 8.47 (d, *J* = 9.0 Hz, 2H), 8.14 (d, *J* = 9.1 Hz, 2H), 7.98 (s, 2H), 7.90 (d, *J* = 9.0 Hz, 2H), 7.56 (s, 1H), 7.50 (s, 1H), 6.91 (d, *J* = 9.1 Hz, 2H), 4.45 (d, *J* = 10.6 Hz, 1H), 4.08 (s, 3H), 4.02 (s, 3H), 3.61 - 3.56 (m, 3H), 3.35 - 3.31 (m, 3H), 3.15 (s, 3H), 2.96 (s, 6H), 2.80 (s, 6H), 2.57 (s, 46H), 2.47 - 2.43 (m, 1H), 2.33 (t, *J* = 7.3 Hz, 2H), 1.95 - 1.84 (m, 4H), 1.80 - 1.61 (m, 8H), 1.56 - 1.43 (m, 4H). ESI-MS calcd. For $C_{38}H_{52}N_{11}O_6S_2^+$ [m/z]$^+$: 822.35, found: 822.35.



Scheme S4. a) DMF,1.5 h, r. t.,78%; b) TFA, DCM,2 h, r. t., 86%; c) HATU, DIEA, DMF, 2h, r. t.,3 9%; d) TFA, DCM, 2 h, r. t., 89%; e) LA-NHS, DIEA, Overnight, r. t., 60%.

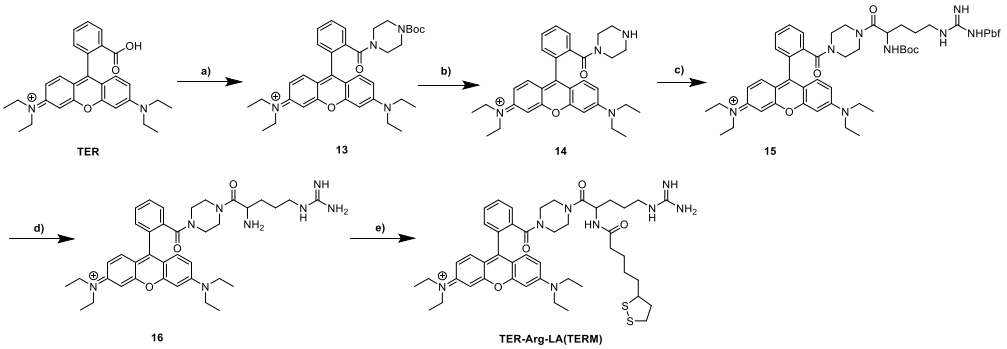
Compound 9: FITC (200 mg, 0.514 mmol) was dissolved in DMF (6 mL). The resulting yellow solution was dropped slowly to Boc protected ethylenediamine (165 mg, 1.028 mmol) under vigorous stirring. After the reaction mixture was stirred at r.t. for 2 h. Most volatiles were removed and the oily residue was drop into Et_2O. The crude material was purified by column chromatography to yield as an orange solid (220 mg, 78% yield).^{1}H NMR (500 MHz, MeOD) δ 8.15 (s, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 6.70 (d, *J* = 1.7 Hz, 3H), 6.68 (s, 1H), 6.55 (dd, *J* = 8.7, 2.3 Hz, 2H), 3.73 (s, 2H), 3.33 (t, *J* = 5.9 Hz, 2H), 1.43 (s, 11H). ^{13}C NMR (126 MHz, MeOD) δ 181.8, 169.8, 160.1, 157.5, 152.8, 129.0, 127.7, 124.4, 112.4, 110.1, 102.2, 79.0, 48.6, 44.4, 39.3, 27.5.

Compound 10: 9 (100 mg, 0.182 mmol) was dissolved into the mixture of DCM (6 mL) and TFA (4 mL) at r. t. for 2 h. Volatiles were removed and the crude material was purified by semi-prep HPLC and freeze-dried to yield as an orange solid (70 mg, 86% yield).^{1}H NMR (400 MHz, MeOD) δ 8.44 (d, *J* = 2.0 Hz, 1H), 7.95 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.28 (d, *J* = 8.3 Hz, 1H), 7.12 (d, *J* = 9.0 Hz, 2H), 6.99 (d, *J* = 2.3 Hz, 2H), 6.86 (dd, *J* = 9.0, 2.3 Hz, 2H), 4.00 (t, *J* = 6.0 Hz, 2H), 3.30 (t, *J* = 6.0 Hz, 2H). ^{13}C NMR (101 MHz, MeOD) δ 182.8, 168.1, 165.3, 160.9, 160.5, 155.9, 141.5, 130.8, 129.3, 128.9, 127.1, 122.2, 120.5, 117.6, 115.8, 114.8, 113.3, 102.1, 42.8, 41.2, 39.0.

Compound 12: Boc-Arg (Pbf)-OH (70 mg, 0.134 mmol) was dissolved in 10mL dry DMF (15 mL) at 0°C. HATU (51 mg, 0.134 mmol), DIEA (70 μL, 0.402 mmol) and **10** (60 mg, 0.134 mmol) were added followed. The solution was allowed to warm up from 0°C to r. t. and stirred for 4 h under N_2 atmosphere. EtOAc (40 mL) was then added. The organic layer was washed with H_2O and brine (2*40 mL each). Then the organic layer was then dried with Na_2SO_4 and evaporated under reduced pressure, then using 2 mL of DMSO to dissolve the crude solid and purified by prep-HPLC and freeze-dried to get as an orange solid **11** (50 mg, 39%yield). Then, **11** (50 mg, 0.0522 mmol) was stirred at the mixture of DCM (4 mL) and TFA(6 mL) at r.t. for 2 h. Volatiles were removed and the crude material was purified by semi-prep HPLC to yield as an orange solid (28 mg, 89% yield).^{1}H NMR (500 MHz, MeOD) δ 8.35

(s, 2H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 4H), 6.90 (d, *J* = 2.1 Hz, 4H), 6.76 (dd, *J* = 8.9, 2.1 Hz, 5H), 3.95 (t, *J* = 6.2 Hz, 2H), 3.83 (d, *J* = 17.1 Hz, 4H), 3.60 - 3.50 (m, 4H), 3.35 (s, 2H), 3.24 (t, *J* = 6.8 Hz, 4H), 2.04 - 1.89 (m, 5H), 1.72 (dt, *J* = 15.1, 7.5 Hz, 5H). ^{13}C NMR (101 MHz, MeOD) δ 181.8, 169.0, 168.8, 163.5, 163.4, 161.3, 161.0, 157.3, 154.8, 141.4, 130.1, 129.3, 128.6, 126.0, 120.8, 117.9, 114.6, 112.1, 102.3, 102.1, 53.4, 52.82, 43.30, 40.37, 39.1, 38.7, 28.2, 24.0.

FITM: Compound 12 (28 mg, 0.0463 mmol) was dissolved in DMF (6 mL). LA-NHS (14 mg, 0.0463 mmol) and DIEA (33 μL, 0.185 mmol) was add followed. After overnight, the crude material was purified by semi-prep HPLC and freeze-dried to yield as an orange yellow solid (22 mg, 60% yield). ^{1}H NMR (500 MHz, MeOD) δ 8.20 (d, *J* = 1.1 Hz, 3H), 7.79 (d, *J* = 7.7 Hz, 3H), 7.22 (d, *J* = 8.2 Hz, 3H), 6.83 (dd, *J* = 8.3, 6.1 Hz, 6H), 6.77 (dd, *J* = 18.2, 1.9 Hz, 6H), 6.65 (d, *J* = 8.7 Hz, 6H), 4.32 (dd, *J* = 8.3, 5.5 Hz, 3H), 3.80 (s, 6H), 3.50 (dt, *J* = 11.1, 3.7 Hz, 9H), 3.23 - 3.17 (m, 6H), 3.12 (dd, *J* = 11.6, 4.8 Hz, 3H), 3.08 - 3.02 (m, 3H), 2.66 (s, 1H), 2.40 (td, *J* = 13.0, 6.7 Hz, 3H), 2.28 (t, *J* = 7.2 Hz, 6H), 2.03 (s, 1H), 1.92 - 1.79 (m, 6H), 1.74 - 1.51 (m, 24H), 1.49 - 1.35 (m, 7H). ESI-MS calcd. For $C_{37}H_{44}N_7O_7S_3^+$ [m/z]$^+$: 794.24, found: 794.15.



Scheme S5. a) HATU, DIEA, DMF, 5 h, r. t.,76%; b) TFA, DCM, 2h, r. t., 84%; c) HATU, DIEA, DMF, 2h, r. t.,71%; d) TFA, DCM, 2h, r. t., 98%; e) LA-NHS, DIEA, Overnight, r. t., 76%.

Compound 14: TER (222 mg, 0.5 mmol), DIEA (261 μL, 1.5 mmol) and HATU (286 mg, 0.75 mmol) was dissolved in DMF (6 mL), and then tert-butyl piperazine-1-carboxylate (140 mg, 0.752 mmol) was dropped to the mixture at rt for 5h. The reaction solution was drop into ice H_2O and centrifuge at 4000 rpm for 5 minutes to yield as a red solid **13** (240 mg, 76% yield). Then, **13** (120 mg, 0.196 mmol) was dissolved into the mixture of DCM (6 mL) and TFA(4 mL) at r. t. for 2 h. Volatiles were removed and the crude material was purified by semi-prep HPLC to yield as a red sticky solid **14** (84 mg, 84% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 - 7.63 (m, 2H), 7.58 - 7.51 (m, 1H), 7.36 - 7.29 (m, 1H), 7.13 (d, *J* = 9.5 Hz, 2H), 6.88 (dd, *J* = 9.5, 1.8 Hz, 2H), 6.72 (d, *J* = 2.1 Hz, 2H), 3.70 (s, 4H), 3.62 (dd, *J* = 14.5, 7.2 Hz, 4H), 3.52 (dd, *J* = 14.7, 7.3 Hz, 4H), 3.07 (d, *J* = 21.1 Hz, 4H), 1.28 (t, *J* = 6.9 Hz, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 161.3, 160.9, 157.7, 155.7, 155.6, 134.3, 131.5, 131.0, 130.4, 130.3, 130.2, 128.8, 127.6, 125.8, 114.2, 113.6, 96.3, 46.0, 44.2, 43.1, 42.8, 40.8, 38.4, 12.4.

Compound 15: Boc-Arg(Pbf)-OH (46 mg, 0.088 mmol), HATU (34 mg, 0.088 mmol) and DIEA (46 μL, 0.264 mmol) were dissolved in 10 mL dry DMF (15 mL) at 0℃, and then **14** (45 mg, 0.088 mmol) was added followed. The solution was allowed to warm up from 0℃ to r. t. and stirred for 4 h under N_2 atmosphere. EtOAc (40 mL) was then added. Organic layer was washed with H_2O and brine (2*40 mL each), and evaporated under reduced pressure. The crude solid and purified by semi-prep HPLC and freeze-dried with lyophilizer to get as a dark red solid (64 mg, 71% yield).

Compound 16: 15 (64 mg, 0.063 mmol) was dissolved into the mixture of DCM (6 mL) and TFA (4 mL) at r.t. for 2 h. Volatiles were removed and the crude material was purified by semi-prep HPLC to yield as an orange solid (41 mg, 97% yield). ^{1}H NMR (400 MHz, MeOD) δ 7.83 – 7.77 (m, 2H), 7.73 (dd, *J* = 5.8, 3.1 Hz, 1H), 7.53 (dd, *J* = 5.8, 3.1 Hz, 1H), 7.30 (d, *J* = 9.4 Hz, 2H), 7.10 (d, *J* = 9.1 Hz, 2H), 6.98 (d, *J* = 2.4 Hz, 2H), 4.47 (s, 1H), 3.71 (q, *J* = 7.0 Hz, 8H), 3.66 – 3.36 (m, 6H), 3.23 (s, 2H), 2.68 (s, 2H), 1.84 (s, 2H), 1.70 (s, 2H), 1.33 (t, *J* = 7.1 Hz, 12H). ^{13}C NMR (101 MHz, MeOD) δ 168.27, 167.30, 157.90, 157.40, 155.85, 134.89, 131.91, 131.74, 130.42, 130.00, 127.51, 114.05, 114.00, 113.52, 113.44, 95.98, 50.00, 45.50, 44.42, 42.10, 41.45, 40.33, 39.07, 27.54, 23.52, 11.44.
TERM: Compound 16 (40 mg, 0.06 mmol) was dissolved in DMF (10 mL). LA-NHS (18 mg, 0.06 mmol) and DIEA (42 μL, 0.24 mmol) was added followed and stirred at r. t. for overnight. The crude material was purified by semi-prep HPLC and freeze-dried to yield as a red solid (38 mg, 76% yield). ^{1}H NMR (500 MHz, MeOD) δ 7.84 - 7.74 (m, 4H), 7.72 (dd, *J* = 9.9, 4.9 Hz, 2H), 7.53 (s, 2H), 7.29 (t, *J* = 11.4 Hz, 4H), 7.09 (d, *J* = 9.5 Hz, 4H), 7.01 -

6.91 (m, 4H), 4.81 - 4.73 (m, 2H), 3.76 - 3.65 (m, 16H), 3.64 - 3.40 (m, 12H), 3.28 - 3.07 (m, 8H), 2.84 (d, J = 13.8 Hz, 4H), 2.68 (d, J = 17.8 Hz, 2H), 2.47 (dt, J = 12.2, 6.1 Hz, 1H), 2.25 (t, J = 6.6 Hz, 4H), 2.04 - 1.85 (m, 4H), 1.79 - 1.70 (m, 4H), 1.68 - 1.58 (m, 12H), 1.46 - 1.38 (m, 4H), 1.33 (t, J = 7.1 Hz, 24H). ^{13}C NMR (75 MHz, MeOD) δ 174.1, 170.8, 170.3, 168.2, 157.9, 157.4, 156.0, 155.6, 135.0, 131.7, 130.7, 130.3, 129.9, 129.8, 127.4, 114.0, 113.5, 96.0, 56.2, 56.2, 45.4, 40.7, 39.8, 39.7, 37.8, 35.0, 34.1, 28.6, 28.2, 25.0, 24.9, 24.9, 24.6, 24.0, 11.5, 11.3. ESI-MS calcd. For $C_{46}H_{63}N_8O_4S_2^+$ [m/z]$^+$: 855.44, found: 855.40.

Procedure for the synthesis of self-quenched CPD-gene polymers

1) Quenched CPD with dye-modified oligonucleotide:

The mixture of quencher-based monomer **BHQM or DABM** (1 mM) with monomer **NORM** (500 μM) in Tris-HCl buffer (20 mM, pH = 7.5) were shaken in a 37 °C shaker for 5 min. Then 1 μM of TMR or FITC labeled oligonucleotide was added as the reaction template for another 2 h, respectively. Subsequently, the crude complex was dialyzed against purified water with dialysis bag (MWCO ~ 3.5KDa, Thermo Scientific) to remove salts and unreacted monomers. Further purification was performed with NAP-5 purchased from GE.

2) Self-quenched CPD with oligonucleotide (without dye modification):

The mixture of fluorophore-based monomer **TERM or FITM** (1 μM), and 1 μM of oligonucleotide in Tris-HCl buffer (20 mM, pH = 7.5) were shaken in a 37 °C shaker for 5 min. Then quencher-based monomer **BHQM or DABM** (1 mM) and monomer **NORM** (500 μM) were added as the reaction template for another 2 h. Subsequently, the crude complex was dialyzed against purified water with dialysis bag (MWCO ~ 3.5KDa, Thermo Scientific) to remove salts and unreacted monomers. Further purification was performed with NAP-5 purchased from GE.

The nanoparticles were dried in the freeze dryer and then characterized using DLS, zeta potential and TEM.

Agarose gel electrophoresis analysis (electrophoretic mobility shift assay, EMSA)

Agarose gel was performed to evaluate assembly and disassembly of qCPD-gene nanoquenchers. 8 μL samples were loaded onto 4% Agarose gel (pre-stained by GelRed) with 2 μL 5 × loading buffer. After electrophoresis at 80 V for 30 min, gels were then analyzed with iBright System.

Fluorescence measurement

The fluorescence spectra were analyzed to monitor the quenching and turn-on efficiency of qCPD-gene assemble and disassemble. Different concentrations of quench monomers were added to a buffer containing 1 μM oligonucleotide. The mixture was reacted at 37 °C for 2 h, and then analyzed the fluorescent intensity on Cytation (Biotek). In contrast, 1 μM of nanocarriers was added with 10 mM DTT and then measured the fluorescence intensity at different time points.

Cell uptake

HeLa cells were cultured in DMEM medium (HyClone) supplemented with 10% fetal bovine serum (FBS, Gibco) and 100 IU/mL penicillin-streptomycin at 37°C in 5% CO_2 atmosphere. HeLa cells were seeded in a 4-well glass-bottom dish and grown for 24 h until 60% ~ 80% confluency. Upon medium removal, cells were treated with 200 nM different nanocarriers for different time points (1 h, 3 h and 6 h). Oligonucleotides (200 nM) only were done concurrently as negative controls. Where applicable, HeLa cells were further co-stained with Hoechst (1:30000 dilution). After washing, cells were imaged in Olympus FV3000 inverted microscope with filter sets specific for DAPI, GFP and Cy3 (Figure 3) or a Leica DMi8 confocal microscopy system at different detection channels (FTIC channel: λ_{ex} = 488 nm, λ_{em} = 500-560 nm TER (TAMRA) channel: λ_{ex} = 552 nm, λ_{em} = 570-620 nm, Hoechst channel: λ_{ex} = 405 nm, λ_{em} = 420-460 nm) (other confocal images).

For Flow cytometry analysis, HeLa cells (3×10^5 cells/well) grown for 24 h in 12-well plates were pretreated with 200 nM BN^{SurTMR} or FDN^{Sur} for different time points (1 h, 3 h, 6 h). Then cell was detached from the plate by treatment with 500 μL of trypsin at 37°C for 5 min. The detached cells were collected by centrifugation, further cells were washed 3 times and suspended with PBS (500 μL). Cells were analyzed on a BD FACS Canto^{TM} III Flow Cytometer (10,000 cells were counted for each event).

Mechanistic studies of nanoquencher uptakes

HeLa cells were seeded in a 4-well confocal dish for 24 h before experiments. The cells were pretreated with different inhibitors (4.8 mM 5, 5'-dithioobis-2-nitrobenzoic acid, 10 μg/mL chlorpromazine, 50 nM wortmannin or 50 μM methyl-β-cyclodextrin) in DMEM for 30 min at 37°C. Then, 200 nM nanoquencher was added into cells for another 4 h incubation, during which period the inhibitor concentrations were kept constant. After that, cells were washed with cell medium and co-stained with Hoechst (1:30000 dilution) according to the manufacture's protocol. After washing with PBS three times, cells were then imaged by CLSM.

Cytotoxicity Assay

The XTT Colorimetric Cell Proliferation Kit is used to determine cell viability in accordance with the manufacturer's guidelines and the protocol we previously reported. Briefly the cells were seeded in 96-well plates and grown overnight before treatment with different concentrations of monomer (100 μM, 300 μM, 500 μM in DMEM medium) for 24 h. At the same time, cells without monomer treatment were run as a negative control. After that, add 50 μL of XTT reagent solution to each well, incubate at 37°C for 2 h, and then measure the proliferation absorbance at λ_{abs} = 450 nm and λ_{abs} = 650 nm on microplate reader. All experiments were performed in triplicate, and the cell viability of each sample was calculated accordingly.

Western Blot (WB) Assay

HeLa cells (3×10^5 cells/well) grown for 24 h in 12-well plates were treated with 200 nM nanocarriers for different time points (1 h, 3 h, 6 h), After washing off, cells were continued with 24 h incubation. Then, the cells were washed with cold PBS twice and lysed in 80 μL PBS lysis buffer containing 0.2% Triton-X and 100 μM PMSF. Then 20 μL 5×SDS loading buffer was added into cell lysates and heated for 10 min at 95 ℃. the samples were separated by 15% SDS-polyacrylamide gels and transferred to PVDF membranes, and then the membranes were blocked with 5% milk/TBST for 1 h. The primary antibody (survivin, 1:5000 dilutions; PINK1 1:1000) and HRP-conjugated mouse anti-actin (1:7500 dilutions) were incubated overnight at 4°C. After several washes, then HRP-conjugated goat anti-rabbit IgG (1:7500 dilutions) was added with further incubation for 1 h at room temperature. The blot was recorded by Invitrogen iBright 1500.

Table S3 Summary of all the complexes prepared in this work.

Name	Material Composition	Gene type (single or double strand)	Oligo used
DN^{SurFAM}	DN (DABM/NORM)		Survivin-FAM (Sur^{FAM})
BN^{SurTMR}	BN (BHQM/NORM)		Survivin-TMR (Sur^{TMR})
FDN^{Sur}	FDN (FITM/DABM/NORM)		Survivin (Sur)
TBN^{Sur}	TBN (FITM/DABM/NORM)		Survivin (Sur)
TN^{SurFAM}	TN (TERM/NORM)		Survivin-FAM (Sur^{FAM})
TBN^{PINK}	TBN (TERM/BHQM/NORM)		PINK1
$TBN^{NCsiRNA}$	TBN (TERM/BHQM/NORM)		NC-siRNA

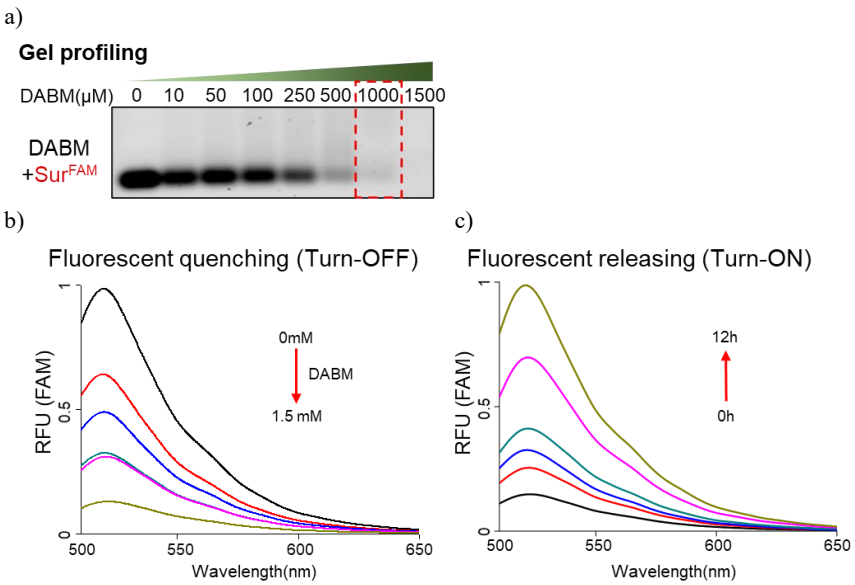


Figure S1 Agarose gel electrophoresis assay of A) different concentrations of DABM with Sur^{FAM} (1 μM) in 37 ºC at Tris-HCl buffer for 2 h. Concentration-dependent emission spectra (λ_{ex} = 488 nm) of B) Quenching Reaction with DABM (0, 0.1 mM, 0.25 mM, 0.5 mM, 1 mM, 1.5 mM). C) Time dependent emission spectra of fluorescent releasing of nanocarriers (Red Box) in A) in the present of DTT (10 mM).

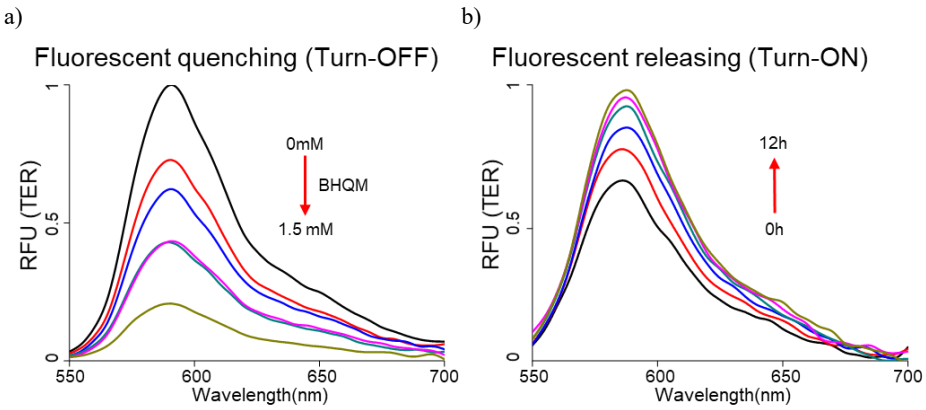


Figure S2 a). Different concentrations (0 mM, 0.2 mM, 0.4 mM, 0.8 mM, 1 mM, 1.5 mM) of BHQM add to the mixture of 1 μM Survivin and 1 μM TERM in Tris-HCl buffer at 37℃ for 2 h. b). Nanoquencher (TBN^{Sur}) was release by 10 mM DTT, and fluorescence was detected on the microplate reader at different time points (0 h, 1 h, 2 h, 4 h, 8 h, 12 h).

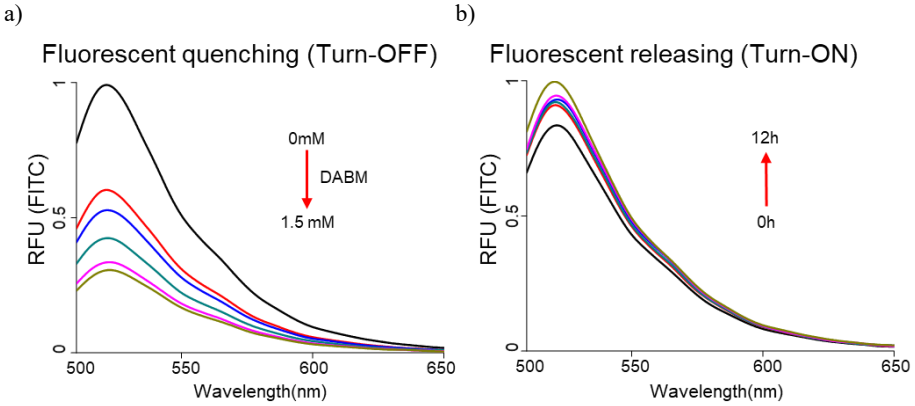
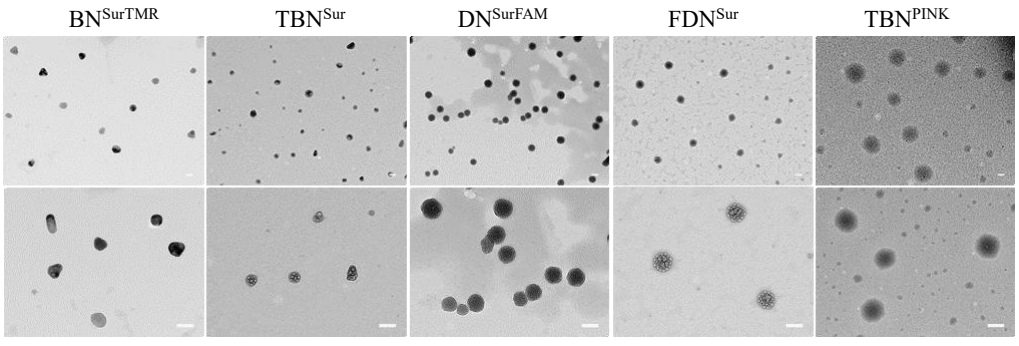


Figure S3 a). Different concentration (0 mM, 0.2 mM, 0.4 mM, 0.8 mM, 1 mM, 1.5 mM) of DABM add to the mixture of 1 μM survivin and 1 μM FITM in Tris-HCl buffer at 37℃ for 2 h. b). Nanoquencher (FDN^{Sur}) was release by 10 mM DTT, and fluorescence was detected on the microplate reader at different time points (0 h, 1 h, 2 h, 4 h, 8 h, 12 h).

a)



b)

Nanoparticle	BN^{SurTMR}	TBN^{Sur}	DN^{SurFAM}	FDN^{Sur}	TBN^{PINK}
Size (nm)	83 ± 9	61 ± 17	97 ± 5	46 ± 12	177 ± 21

Figure S4 a) TEM image of CPD related nanoparticles. Scale bar = 200 nm. b) Table of DLS data.

Table S4 Zeta potential value of nanoparticles.

Nanoparticle	Zeta potential (mV)
BN^{SurTMR}	-2.7 ± 1
TBN^{Sur}	6.1 ± 2.1
DN^{SurFAM}	-8 ± 1.1
FDN^{Sur}	3.3 ± 0.3
TBN^{PINK}	1.6 ± 0.8

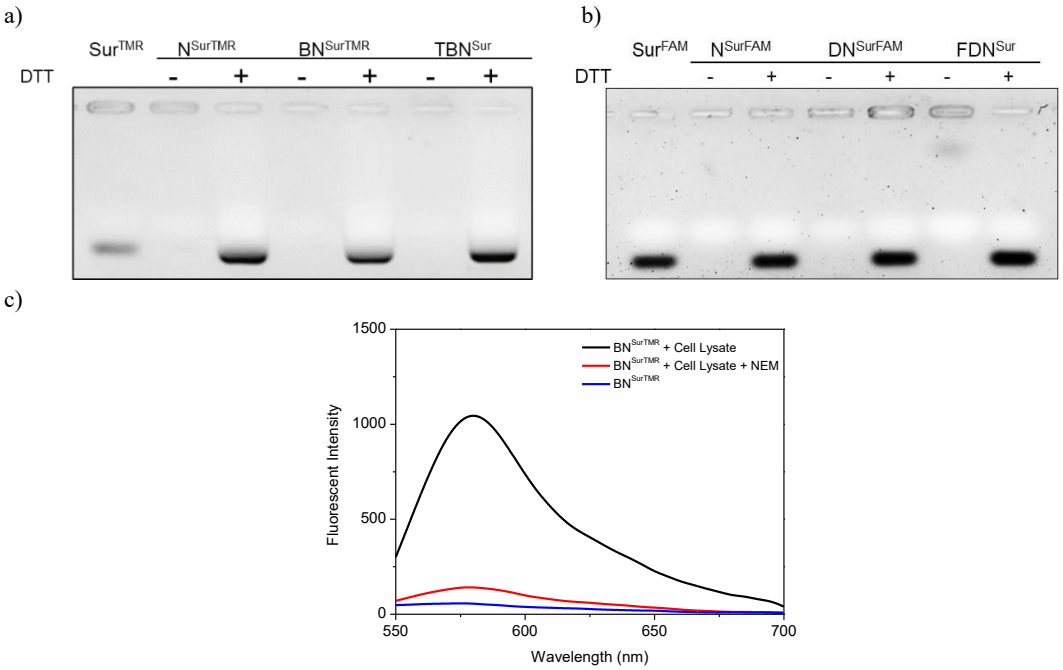


Figure S5 Using agarose gel (with gel red) to monitor gene release of different nanoquenchers by 10 mM DTT treatment. a) and b) was acquired using iBright at Cy3 channel. c) Fluorescent spectra of 200 nM $BNSur^{TMR}$ in present of 1 mg/mL cell lysate in PBS buffer (w/w or w/o 5 mM *N*-Ethylmaleimide (NEM)) after 24 h gentle mix. Fluorescent spectra were acquired using Biotek with 520 nm excitation.

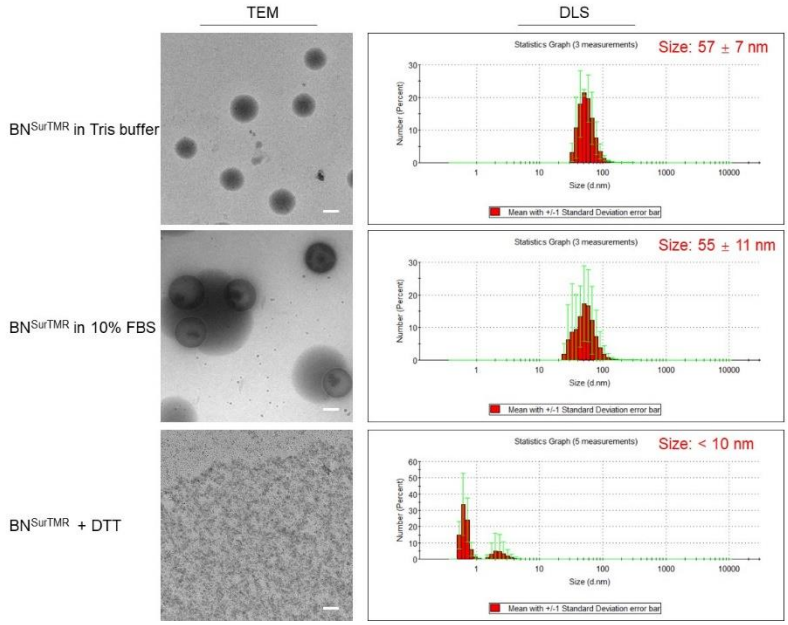
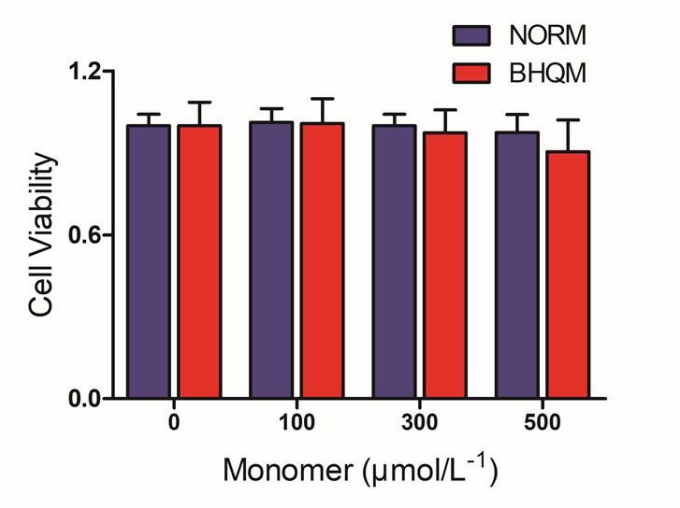


Figure S6 TEM image and DLS measurement of BN^{SurTMR} after incubation with Tris buffer (control), 10% FBS and DTT (10 mM) for 48 h, respectively. Scale bar = 250 nm.

a)



b)

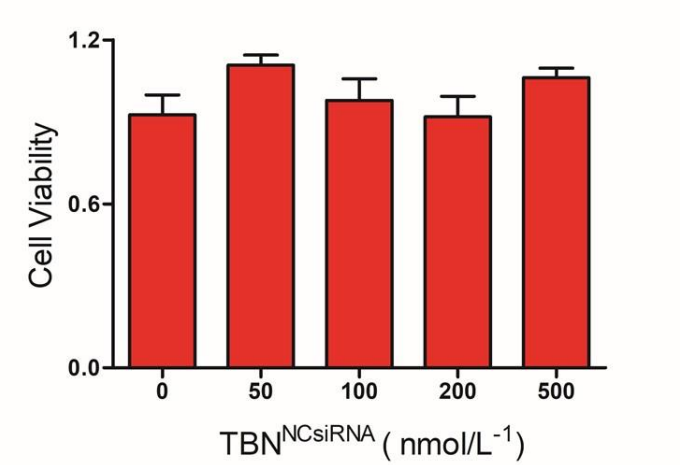


Figure S7 Cell viability of HeLa cells treated with a) different concentrations of Monomers (NORM and BHQM) and b) $TBN^{NCsiRNA}$ (the concentration was dependent on the gene amount) for 24 h.

a) b)

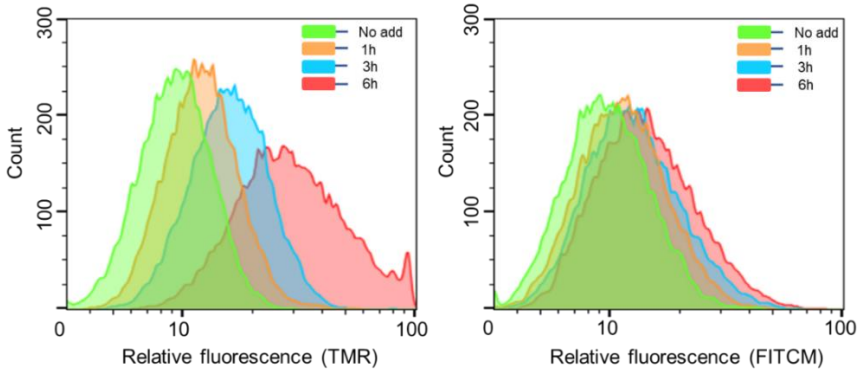


Figure S8 Flow cytometry analysis of time-dependent uptake of Nanoquencher a) BN^{SurTMR} and b) FDN^{Sur} against HeLa cells.

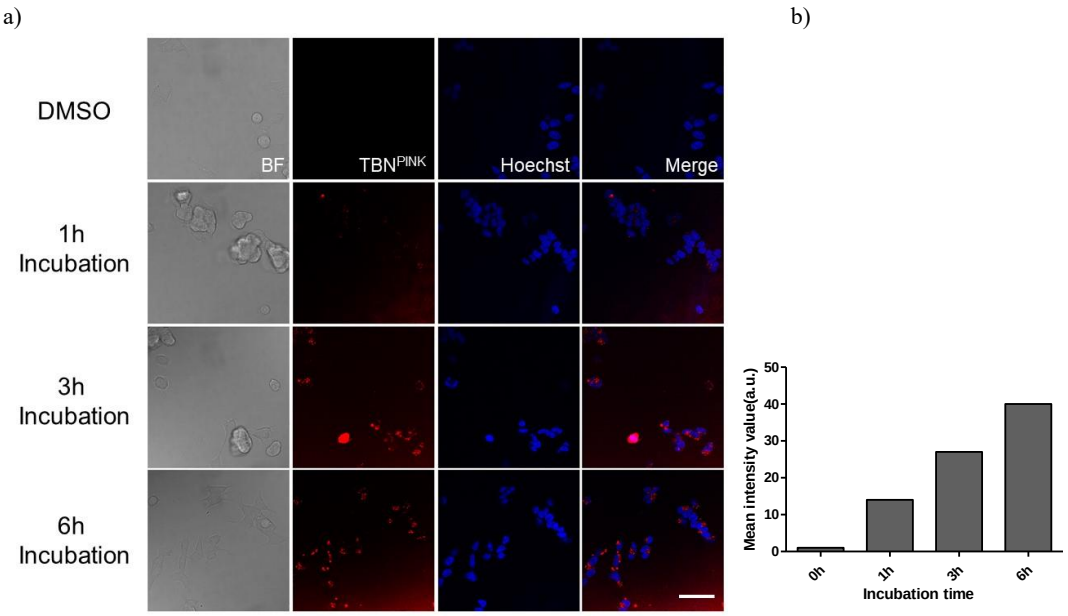


Figure S9 Confocal images of SHSY-5Y cells treated with Nanoquencher (TBN^{PINK}) at different time points (1 h, 3 h, 6 h). Red channel: fluorescence from TBN material; Blue channel: Hoechst nucleus stain. Scale bars: 25 μm. b) Quantification of the average fluorescence intensity (Red channel) after treatment with Nanoquencher (TBN^{PINK}).

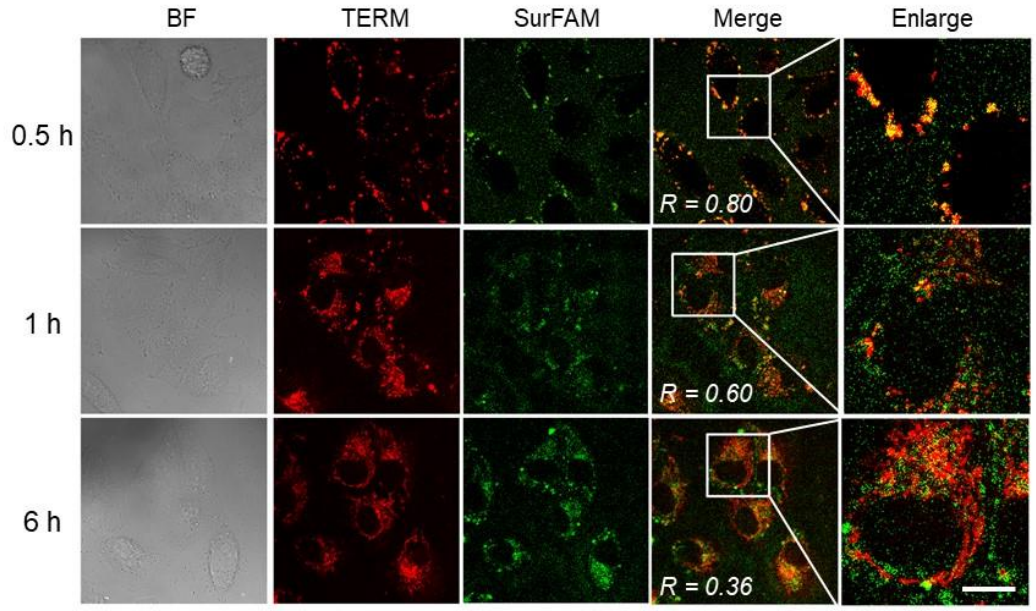


Figure S10 Confocal images of HeLa cells treated with 200 nM TN^{SurFAM} (composed of TERM and NORM monomers together with Sur^{FAM} gene) at different time points (0.5 h, 1 h, 6 h). Red channel: fluorescence from Rhodamine dye in TERM monomer (TN material); Green channel: fluorescence from FAM in Sur^{FAM} gene. Merge is the overlapped image of red and green channel. Scale bars: 10 μm. Pearson's correlation coefficient (*R*) was calculated by ImageJ.

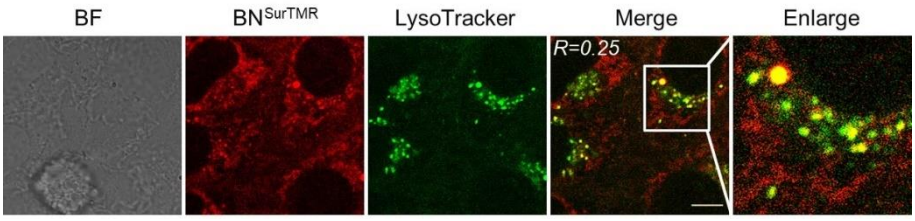


Figure S11 Confocal images of HeLa cells treated with 200 nM BN^{SurTMR} for 6 h and then co-stained with LysoTracker Green (Invitrogen) for 30 min. Merge is the overlapped image of TMR channel (gene) and lysosome green channel. Scale bar = 5 μm. Pearson's correlation coefficient (*R*) was calculated by ImageJ.

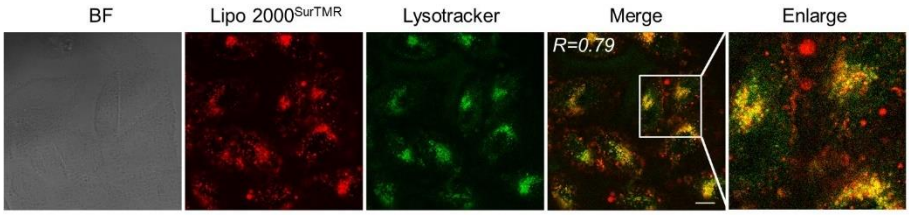


Figure S12 Confocal images of HeLa cells treated with 200 nM Sur^{TMR} with Lipofectamine 2000 (Lipo2000) transfection reagent for 6 h and then co-stained with LysoTracker Green (Invitrogen) for 30 min. Merge is the overlapped image of TMR channel (gene) and lysosome green channel. Scale bar = 10 μm. Pearson's correlation coefficient (*R*) was calculated by ImageJ.

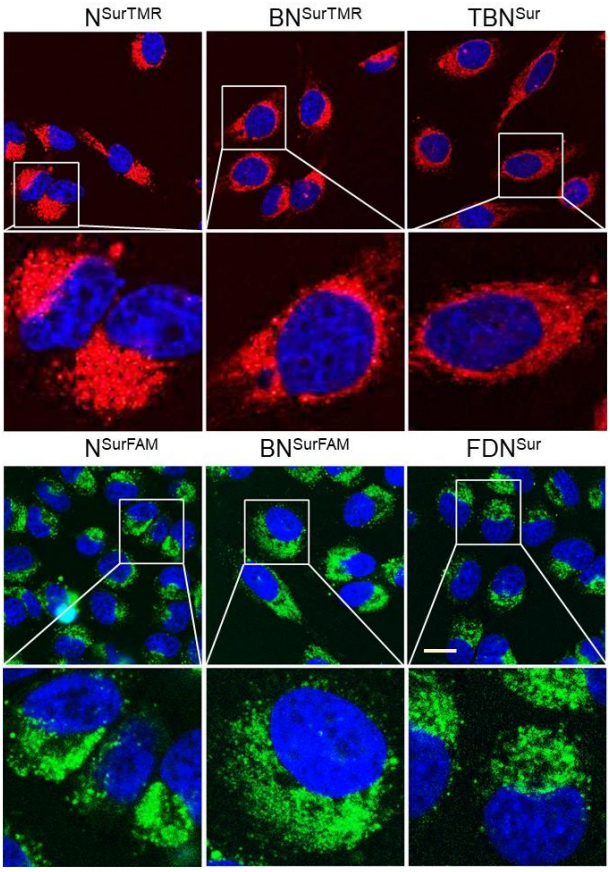


Figure S13 Enlarged images of merge images in Figure 3. Scale bars: 10 μm.

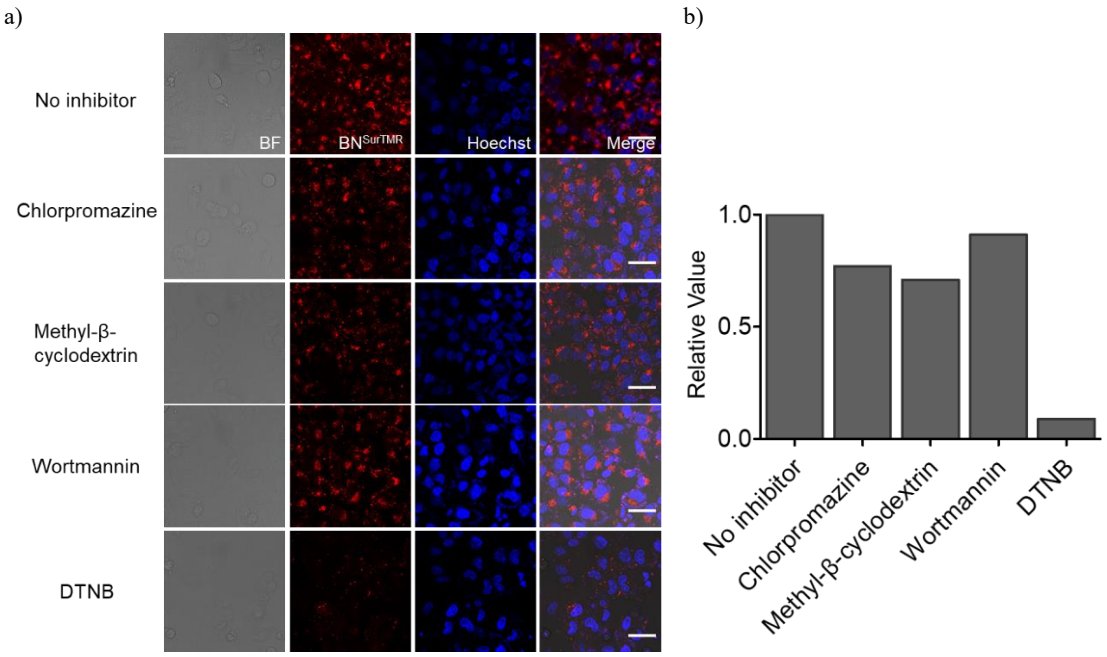


Figure S14 a) CLSM images of Nanoquencher (BN^{SurTMR}) treated HeLa cells with pre-treatment of different inhibitors, including DTNB (4.8 mM), chlorpromazine (10 μg/mL), wortmannin (50 nM) or methyl-β-cyclodextrin (50 μM). Red channel: fluorescence from delivered gene SurTMR; Blue channel: Hoechst nucleus stain. Scale bar: 50 μm. b) Quantification of the average fluorescence intensity (Red Channel) after treatment with different inhibitors.

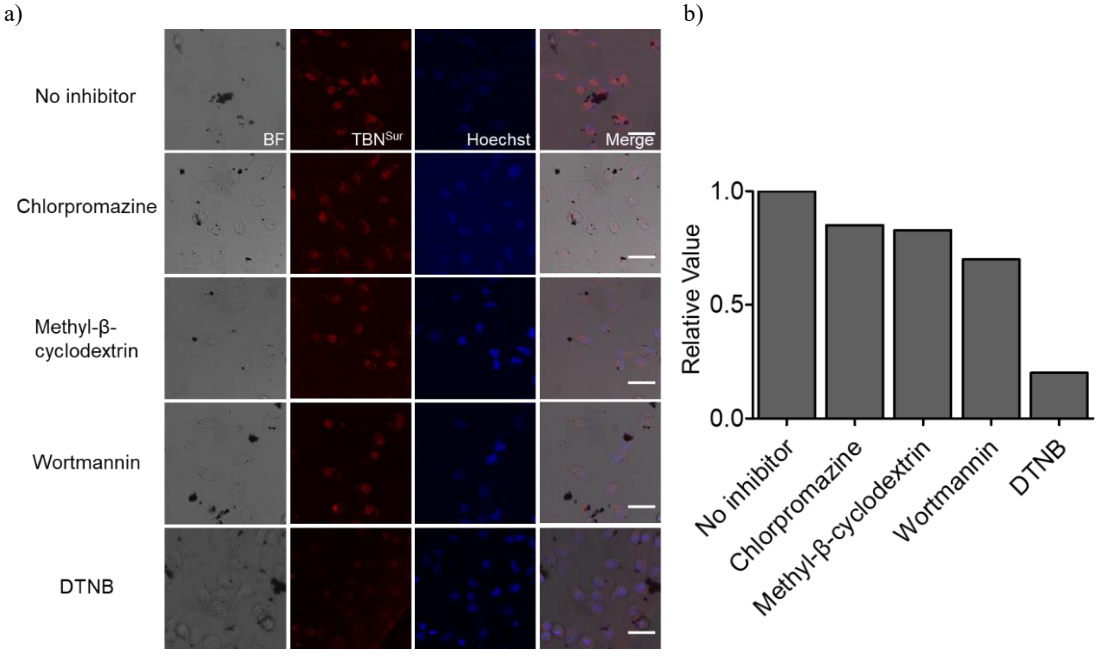


Figure S15 a) CLSM images of nanoquencher (TBN^{Sur}) treated HeLa cells with pre-treatment of different inhibitors, including DTNB (4.8 mM), chlorpromazine (10 μg/mL), wortmannin (50 nM) or methyl-β-cyclodextrin (50 μM). Scale bar: 50 μm. Red channel: fluorescence from material TBN; Blue channel: Hoechst nucleus stain. b) Quantification of the average fluorescence intensity (Red channel) after inhibitor treatment.

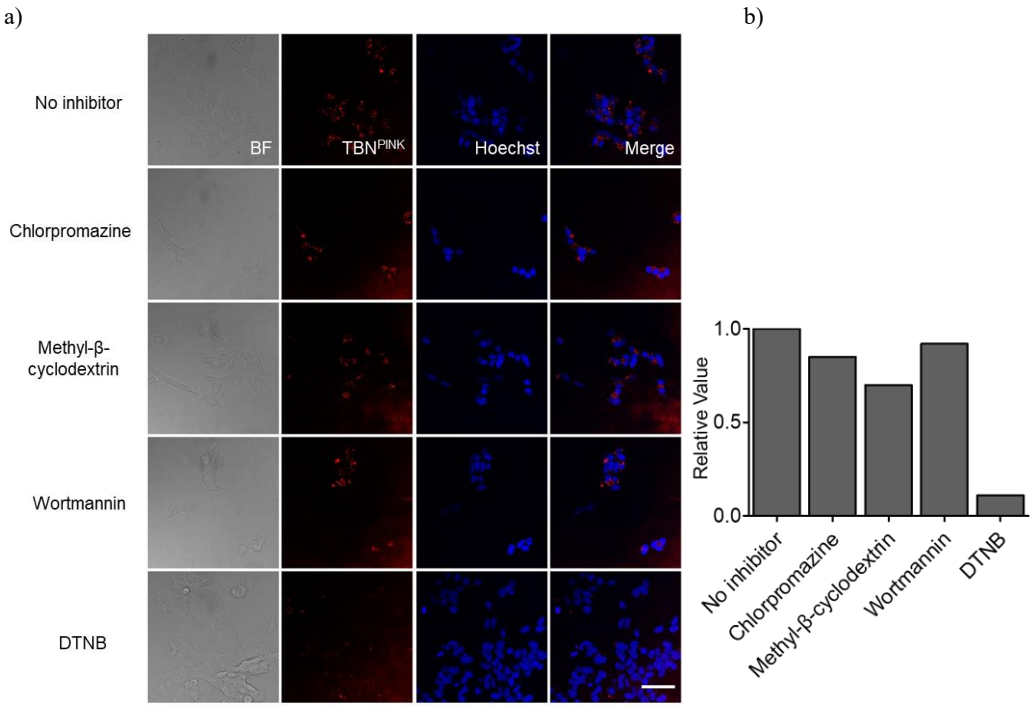


Figure S16 a) CLSM images of nanoquencher (TBN^{PINK}) treated SH-SY5Y cells with pre-treatment of different inhibitors, including DTNB (4.8 mM), chlorpromazine (10 μg/mL), wortmannin (50 nM) or methyl-β-cyclodextrin (50 μM). Scale bar: 25 μm. Red channel: fluorescence from material TBN; Blue channel: Hoechst nucleus stain. b) Quantification of the average fluorescence intensity (Red Channel) after inhibitor treatment.

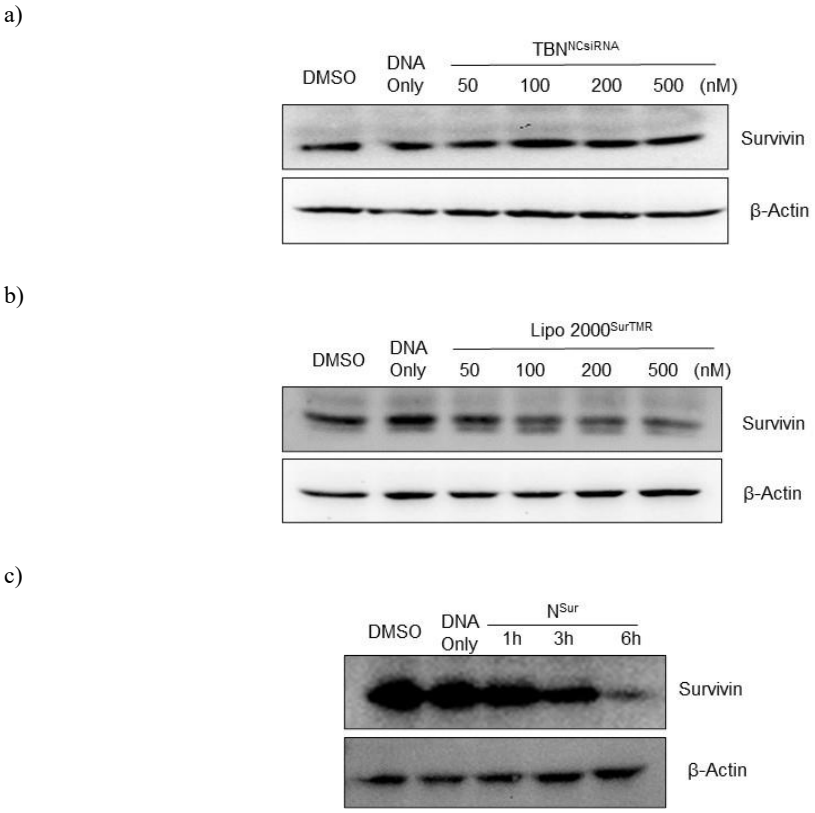
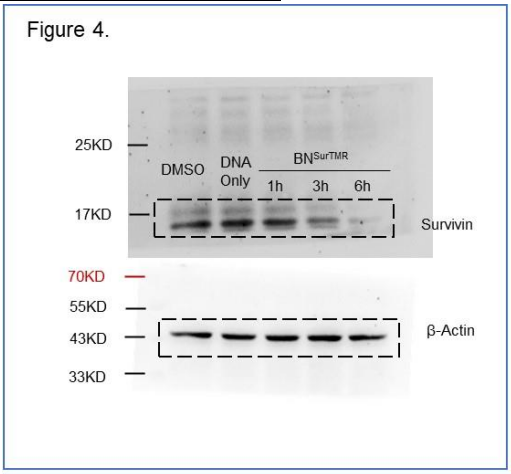
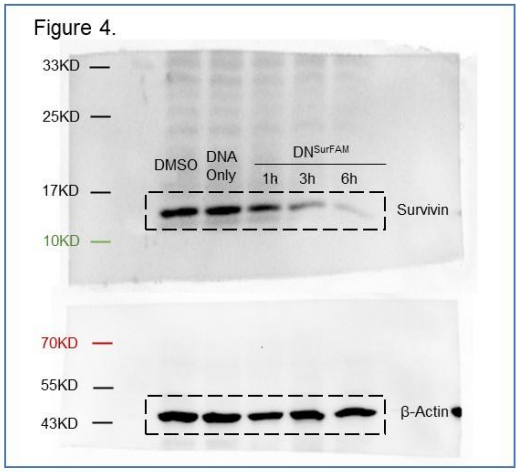
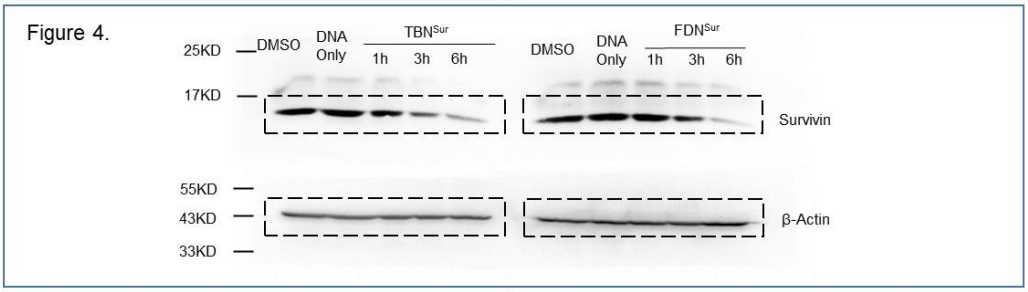


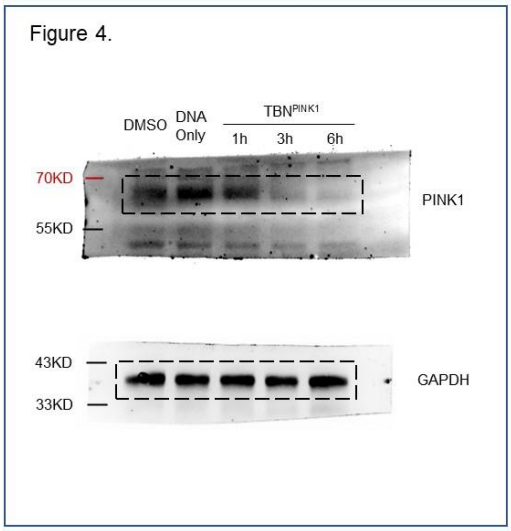
Figure S17 Western blot analysis of survivin protein expression in HeLa cells for 48 h after pre-treated with different concentrations of a) $TBN^{NCsiRNA}$ for 6 h and b) Survivin using lipofectamine 2000 for 6 h and c) 200 nM nanocarrier (N^{Sur}) for different time points.

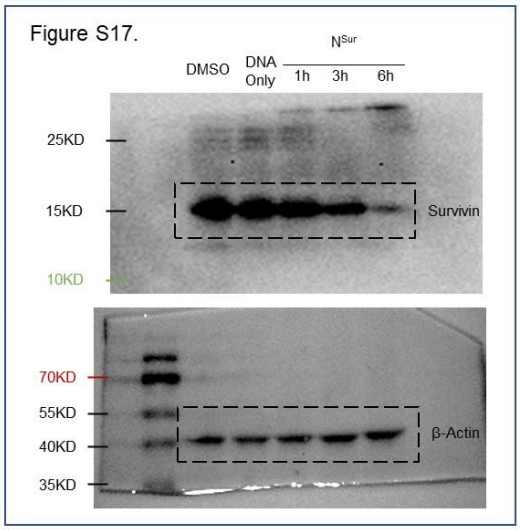
Uncropped western blot image

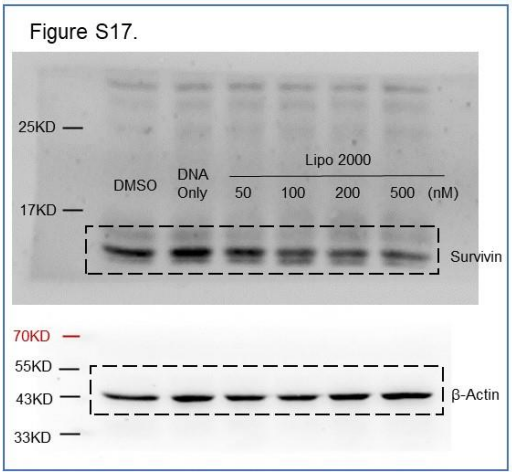


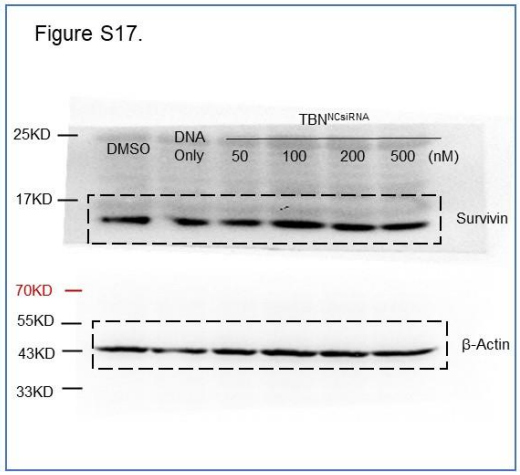




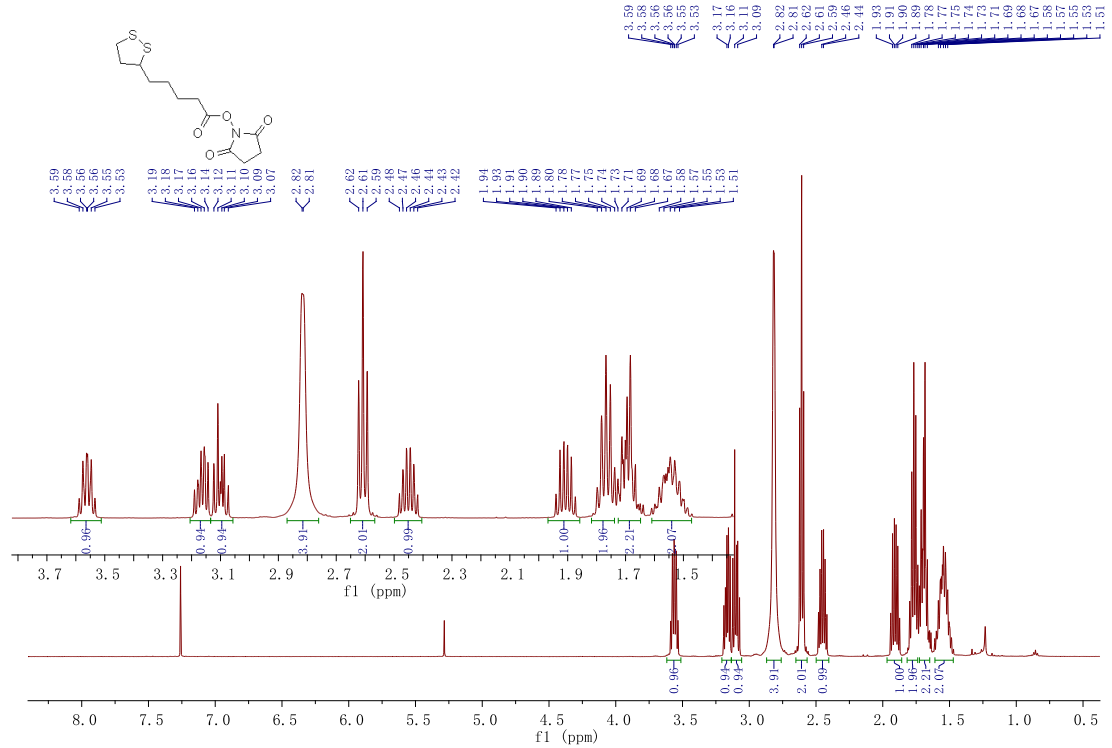


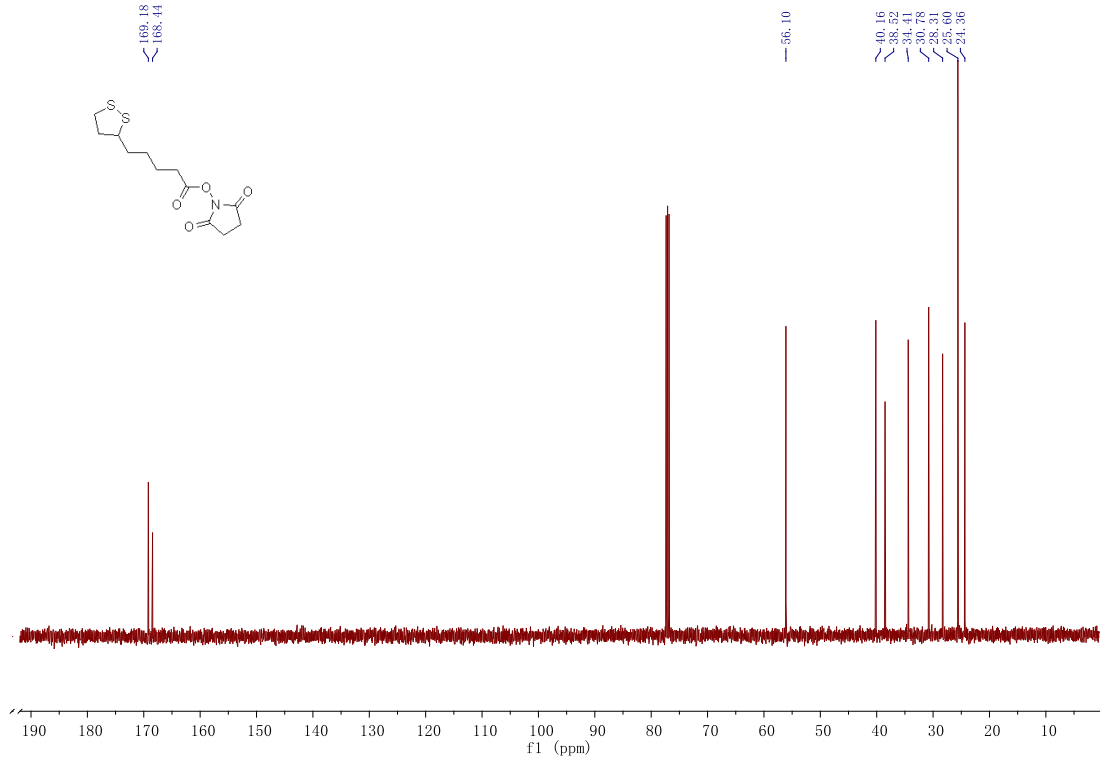


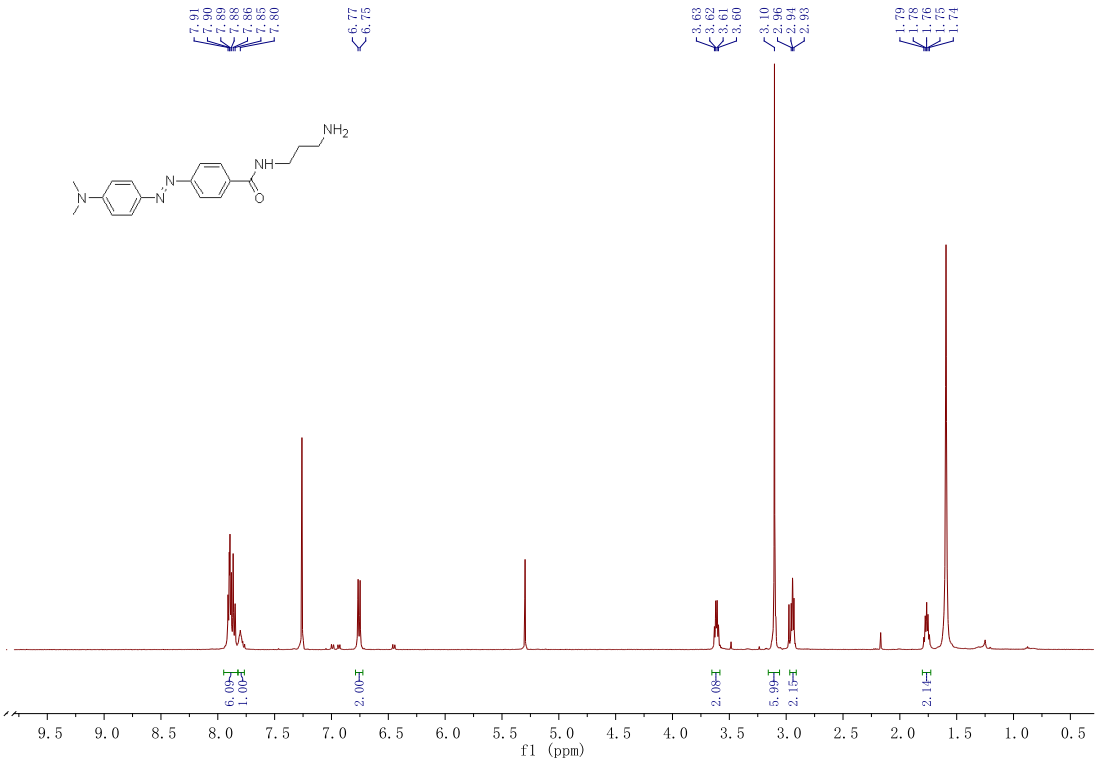




NMR Spectra



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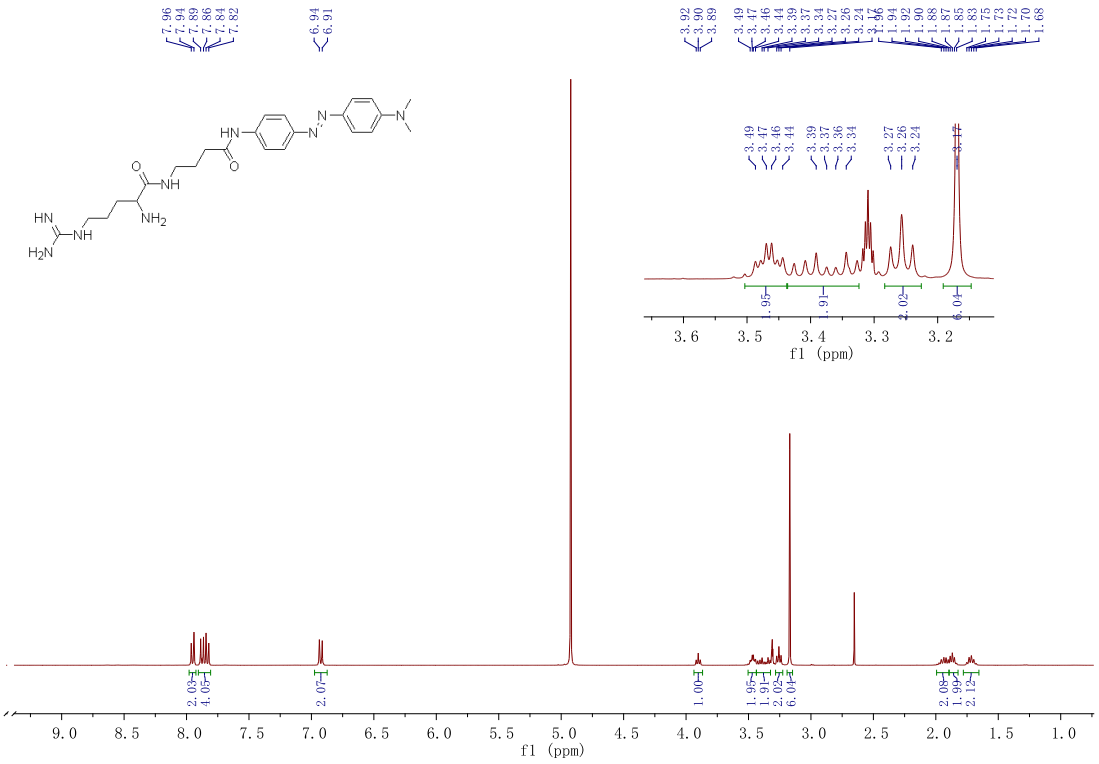
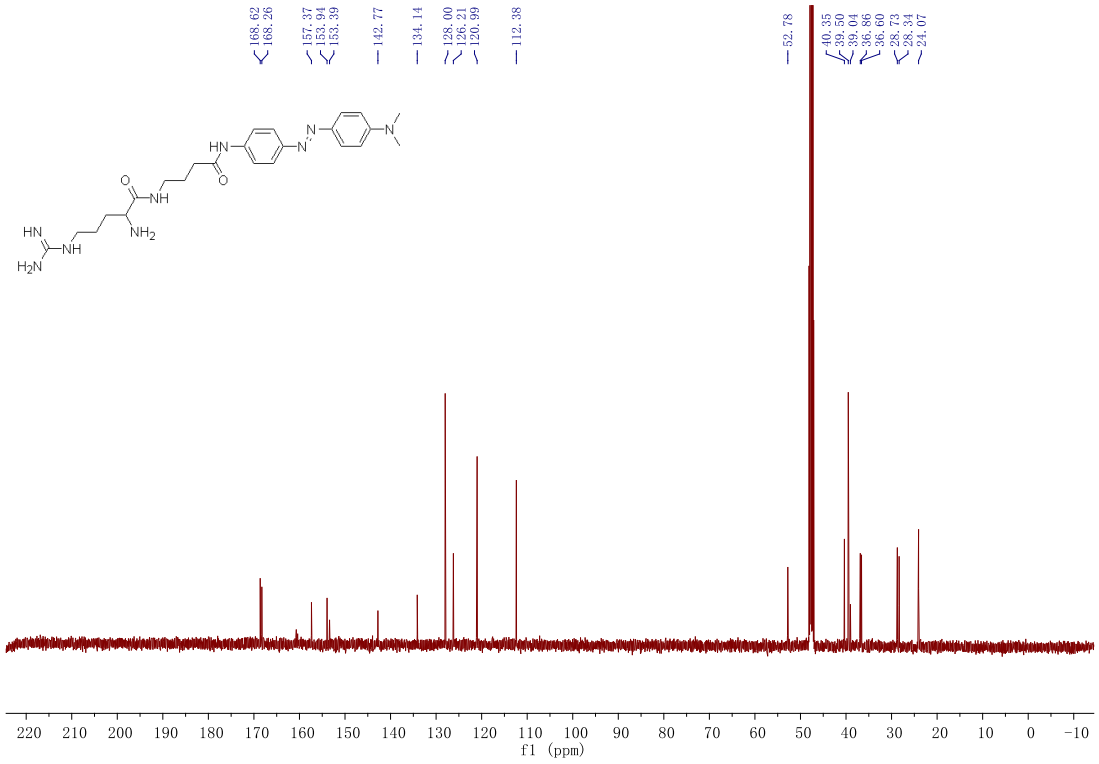
7.90
7.89
7.88
7.86
7.85
7.80
6.77
6.75
3.63
3.62
3.61
3.60
3.10
2.96
2.94
2.93
1.79
1.78
1.76
1.75
1.74
NH2
NH
N
N
O
6.09
1.00
2.00
2.08
5.99
2.15
2.14
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


7.96
7.94
7.89
7.86
7.84
7.82
6.94
6.91
3.92
3.90
3.89
3.49
3.47
3.46
3.44
3.39
3.37
3.34
3.27
3.26
3.24
3.17
1.94
1.92
1.90
1.88
1.87
1.85
1.83
1.75
1.73
1.72
1.70
1.68
HN
N
N
NH
O
O
NH
NH2
HN
NH
H2N
1.95
1.91
2.02
6.04
3.6 3.5 3.4 3.3 3.2
f1 (ppm)
2.03
4.05
2.07
1.00
1.95
1.91
2.02
6.04
2.08
1.99
2.12
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)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168.26
157.37
153.94
153.39
142.77
134.14
128.00
126.21
120.99
112.38
52.78
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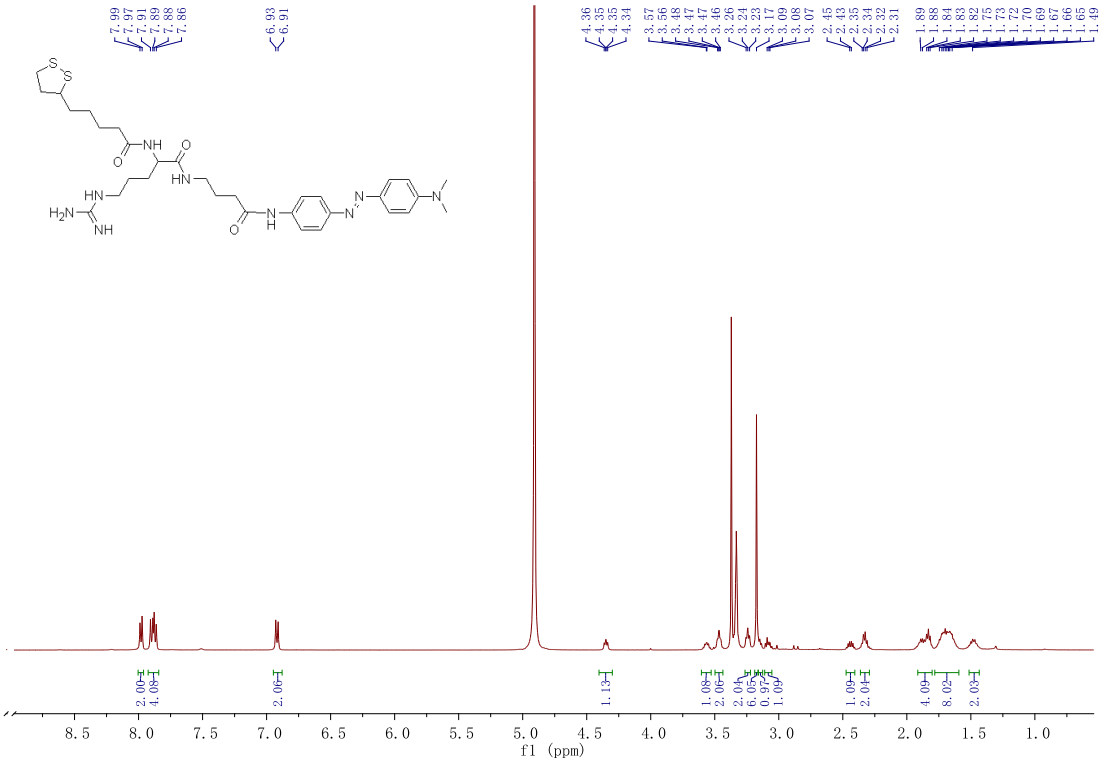
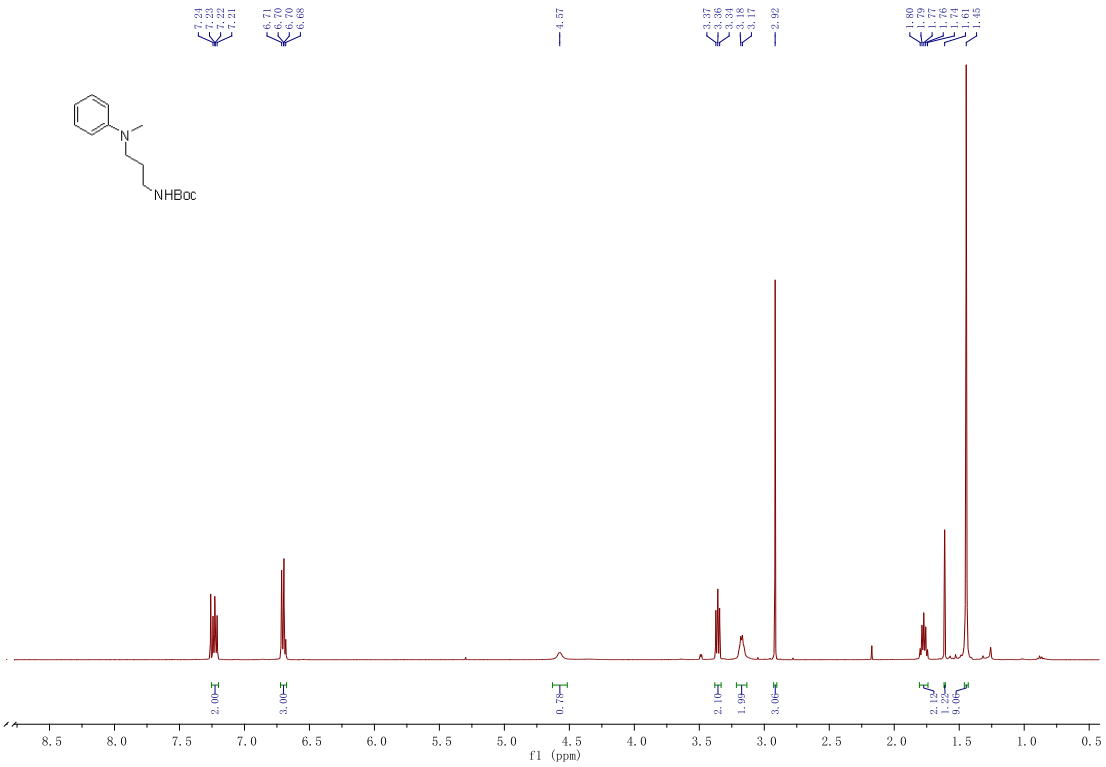
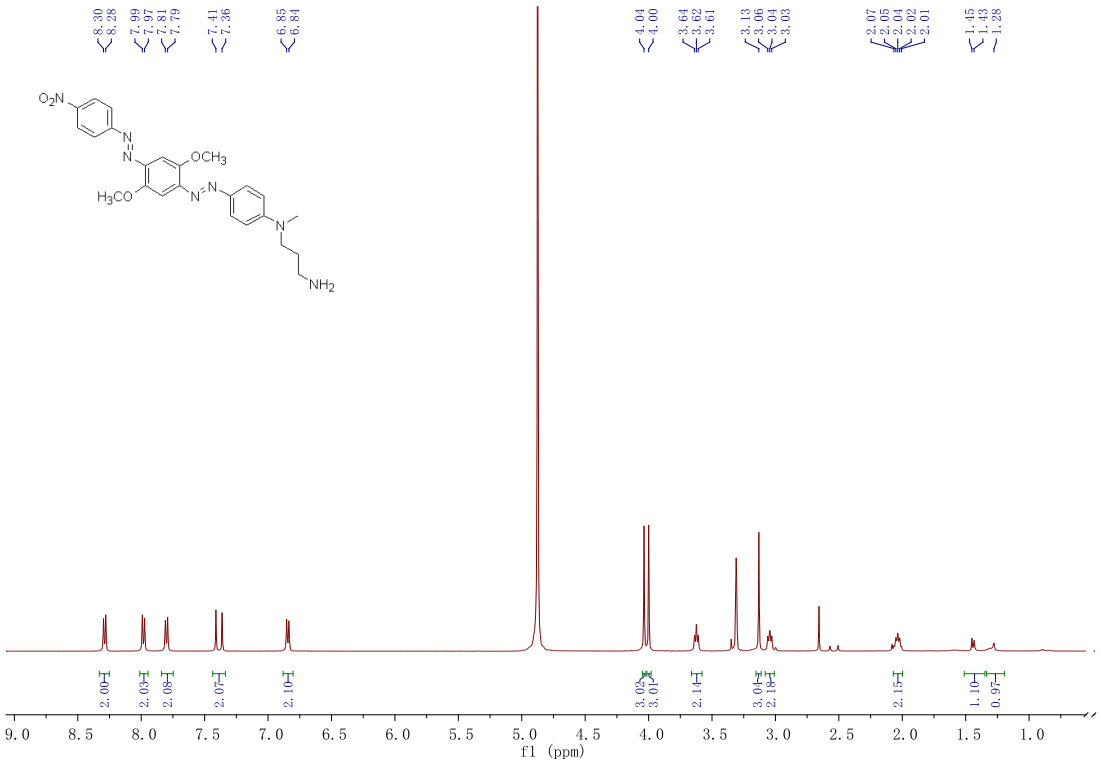
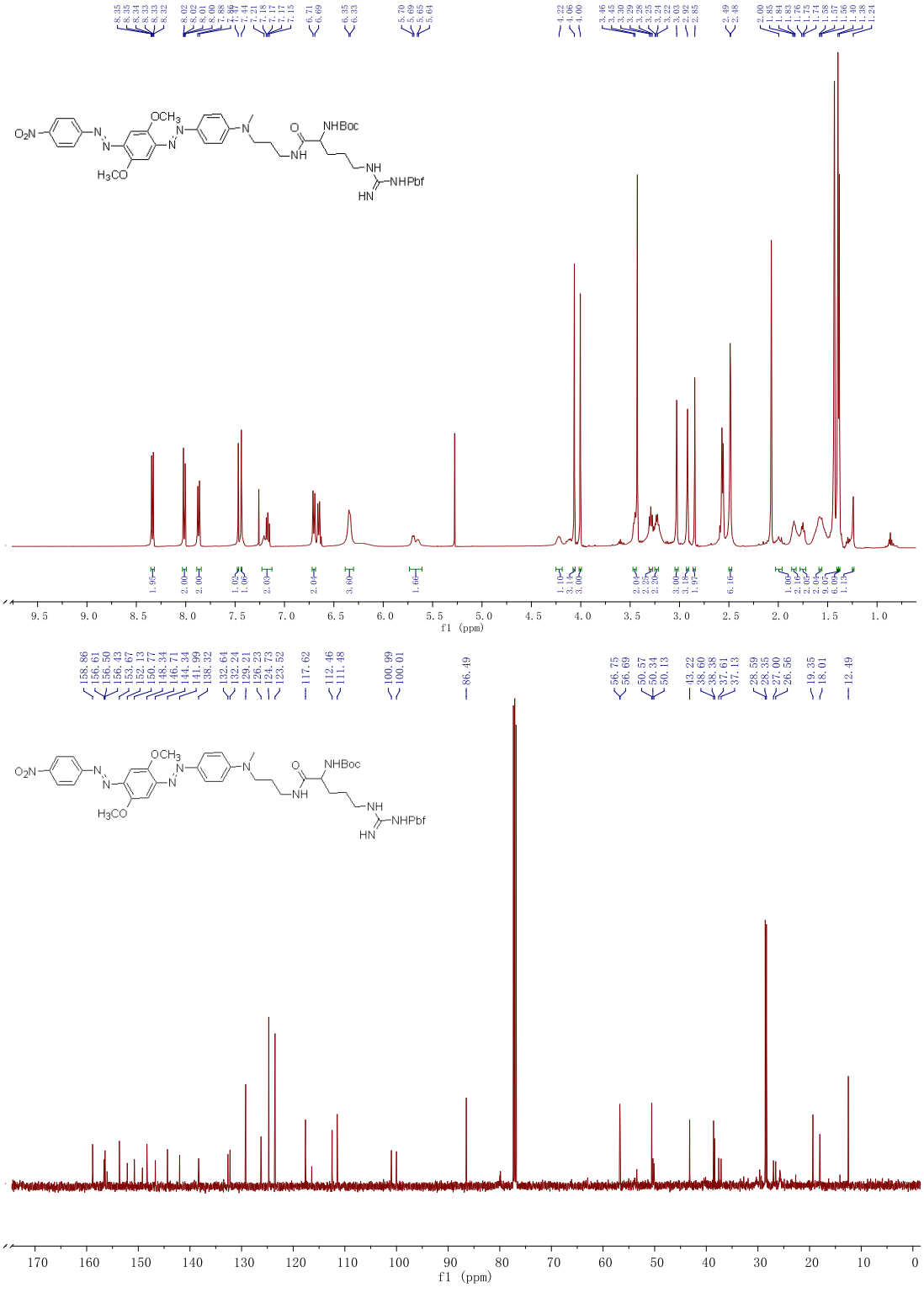
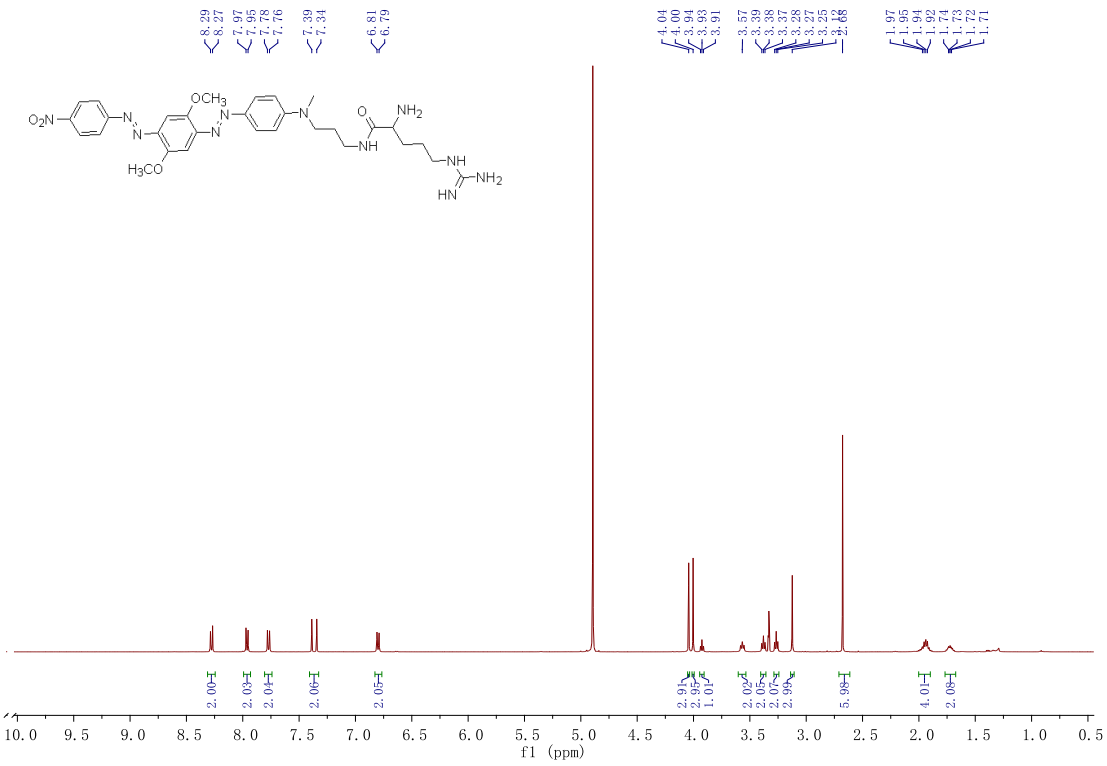
36.60
28.73
28.34
24.07
f1 (ppm)


7.99
7.97
7.91
7.89
7.88
7.86
6.93
6.91
4.36
4.35
4.35
4.34
3.57
3.56
3.48
3.47
3.47
3.46
3.26
3.24
3.23
3.17
3.09
3.08
3.07
2.45
2.43
2.35
2.34
2.32
2.31
1.89
1.88
1.84
1.83
1.82
1.75
1.73
1.72
1.70
1.69
1.67
1.66
1.65
1.49
2.00
4.08
2.06
1.13
1.08
2.06
2.04
6.05
0.97
1.09
1.09
2.04
4.09
8.02
2.03
f1 (ppm)


NHBoc
f1 (ppm)


f1 (ppm)


f1 (ppm)
f1 (ppm)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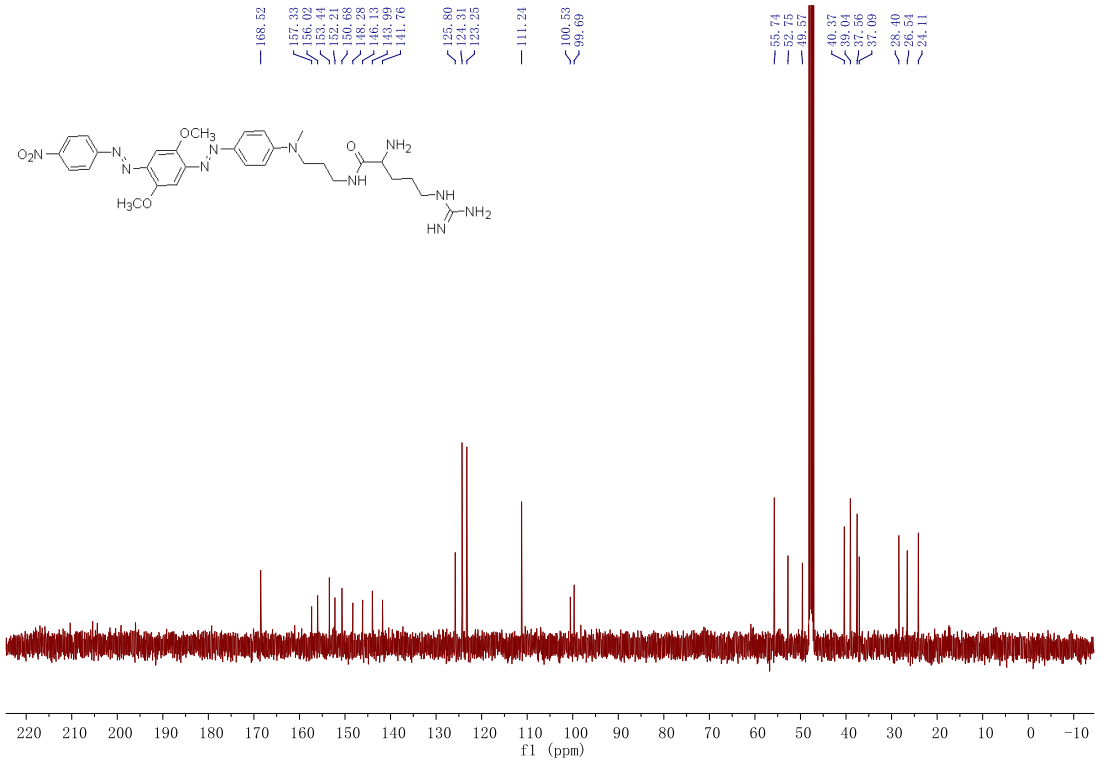
7.97
7.95
7.78
7.76
7.39
7.34
6.81
6.79
4.04
4.00
3.94
3.93
3.91
3.57
3.39
3.38
3.37
3.28
3.27
3.25
1.97
1.95
1.94
1.92
1.74
1.73
1.72
1.71
2.00
2.03
2.04
2.06
2.05
2.91
2.99
1.01
2.02
2.05
2.07
2.99
5.98
4.01
2.08
f1 (ppm)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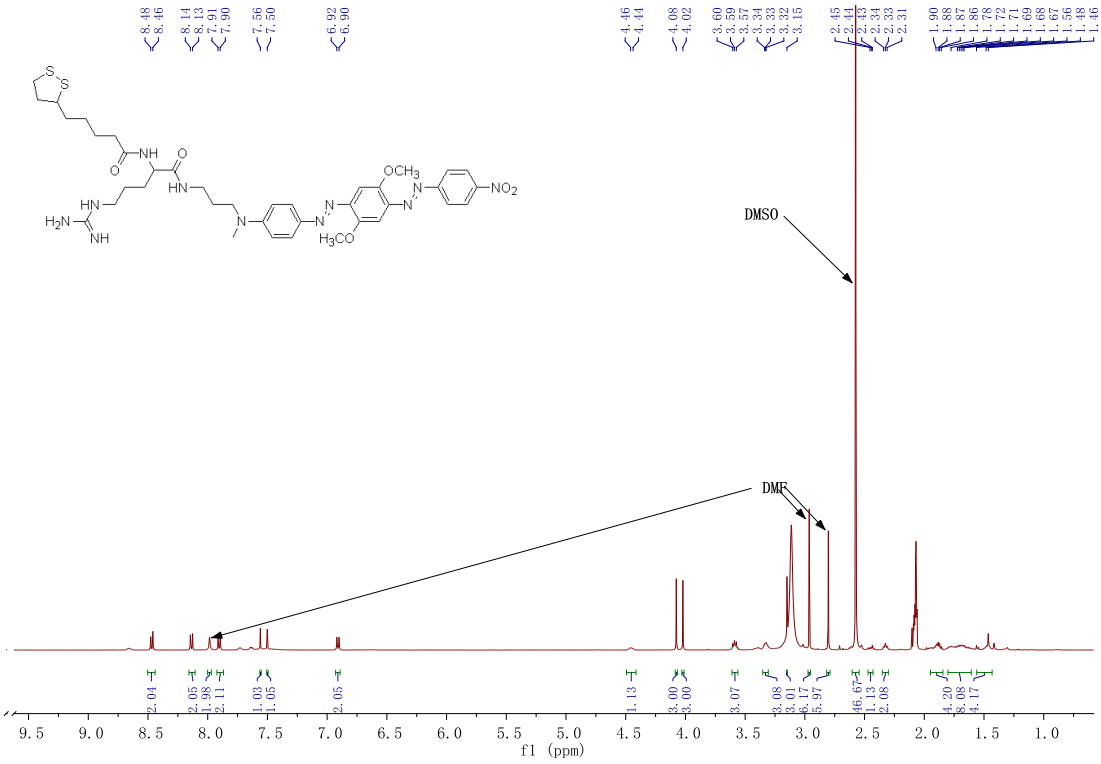
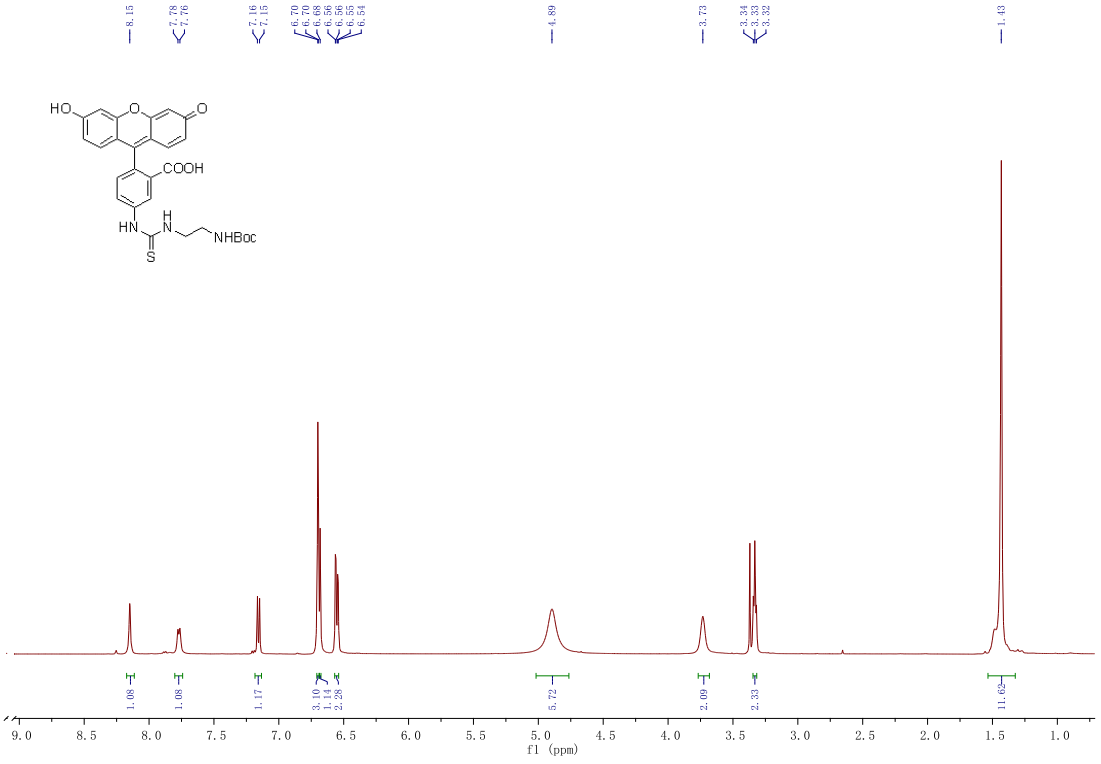
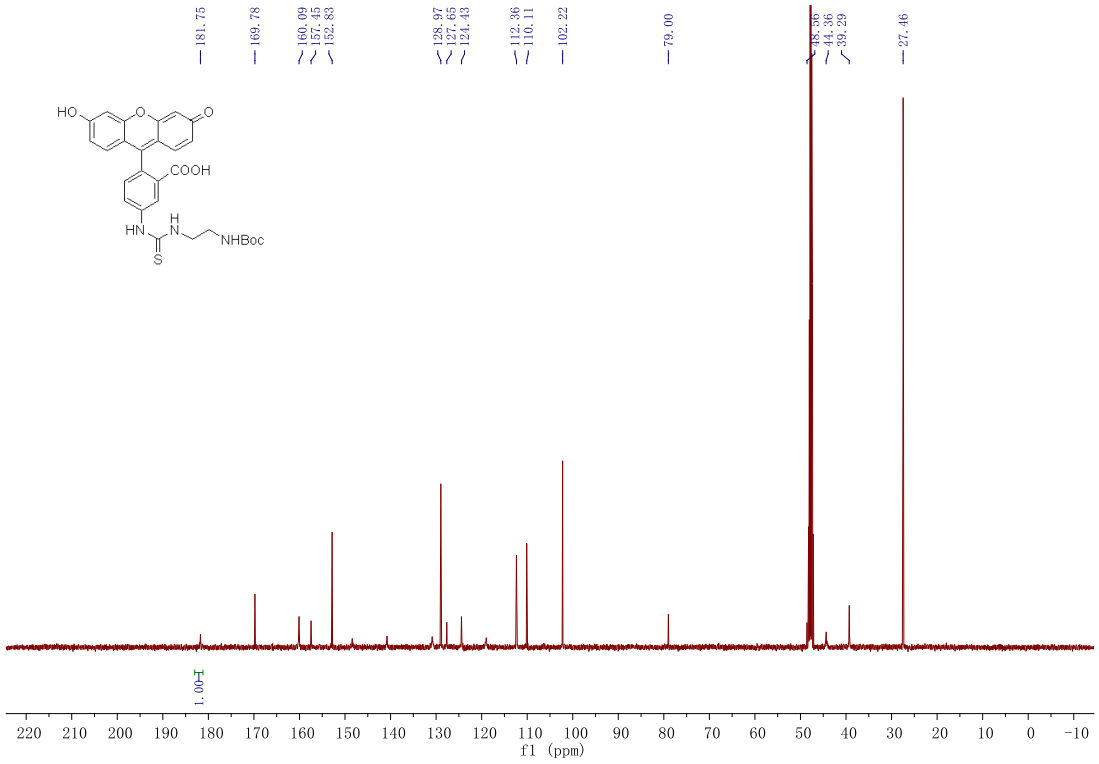
157.33
156.02
153.44
152.21
150.68
148.28
146.13
143.99
141.76
125.80
124.31
123.25
111.24
100.53
99.69
55.74
52.75
49.57
40.37
39.04
37.56
37.09
28.40
26.54
24.11
f1 (ppm)


DMSO
DMF
f1 (ppm)


f1 (ppm)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169.78
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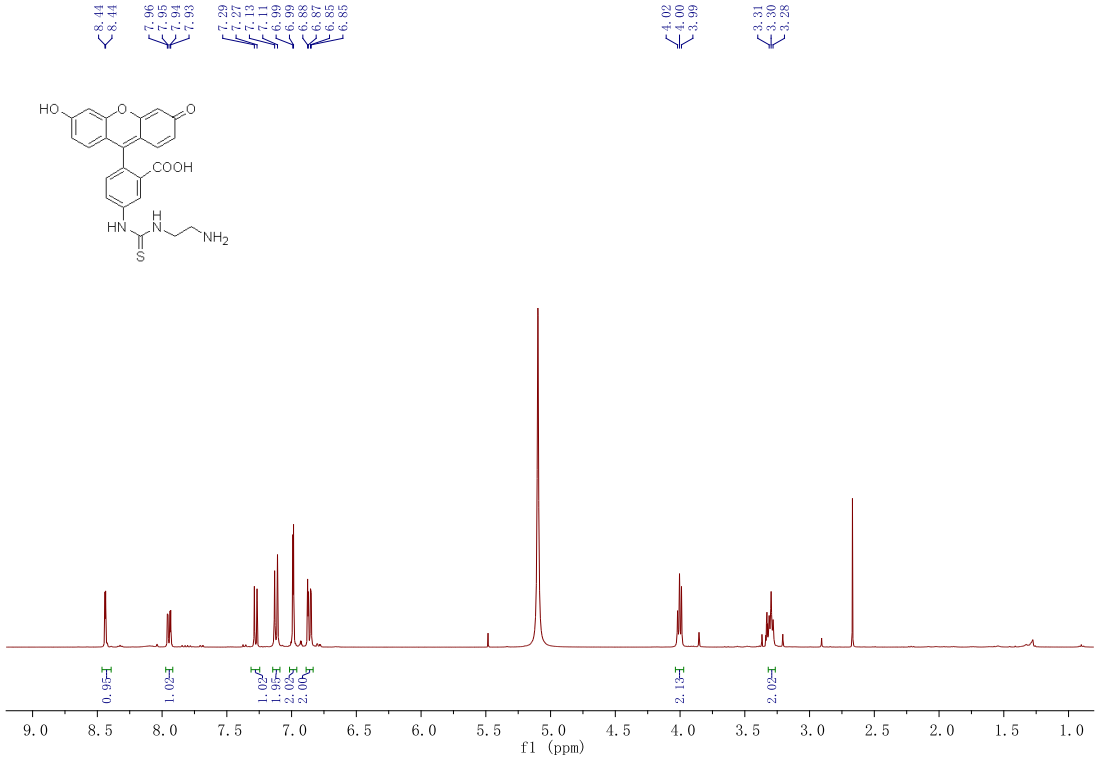
157.45
152.83
128.97
127.65
124.43
112.36
110.11
102.22
79.00
48.36
44.36
39.29
27.46
HO
O
O
COOH
HN
H
N
NHBoc
S
1.00
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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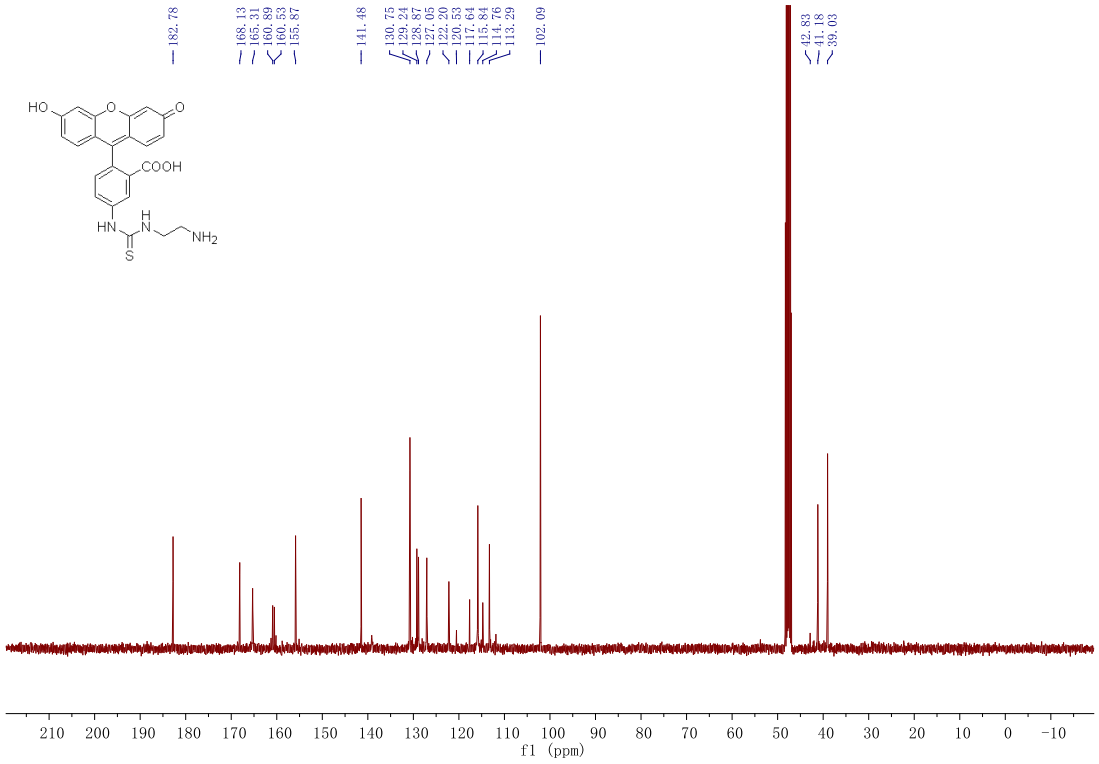
7.94
7.93
7.29
7.27
7.13
7.11
6.99
6.99
6.88
6.87
6.85
6.85
4.02
4.00
3.99
3.31
3.30
3.28
HO
O
O
COOH
HN
H
N
NH2
S
0.95
1.02
1.02
1.95
2.02
2.00
2.13
2.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)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160.53
155.87
141.48
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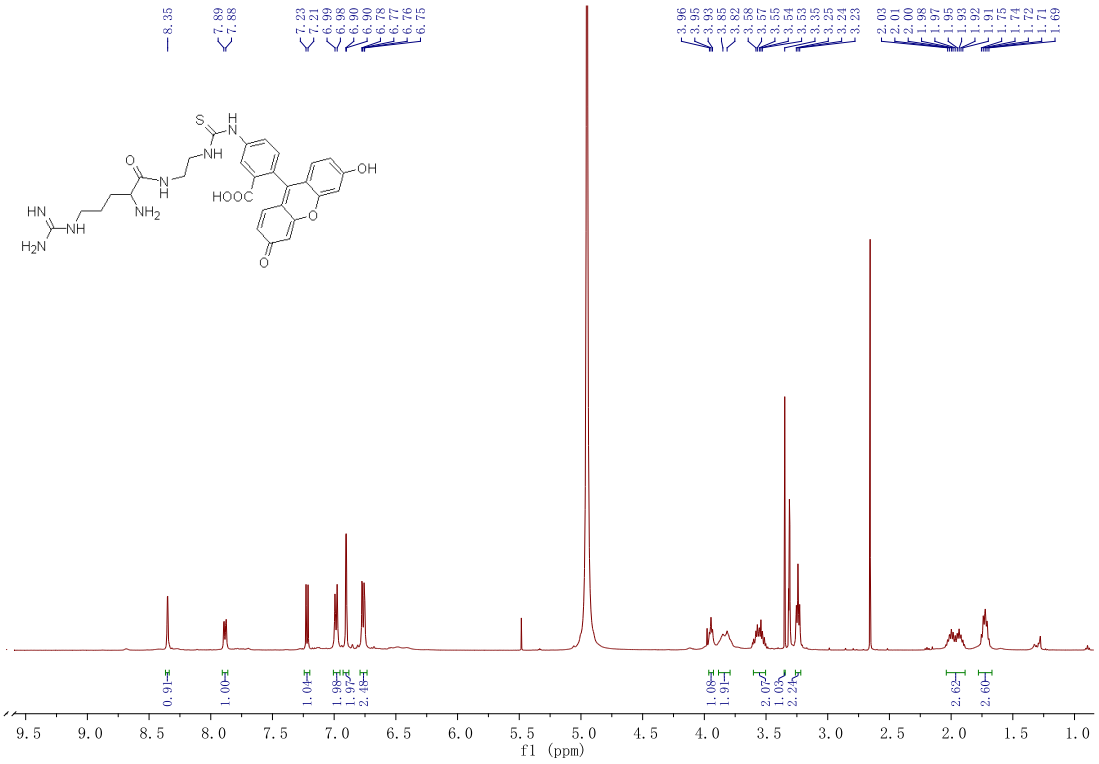
129.24
128.87
127.05
122.20
120.53
117.64
115.84
114.76
113.29
102.09
42.83
41.18
39.03
HO
O
O
COOH
HN
H
N
NH2
S
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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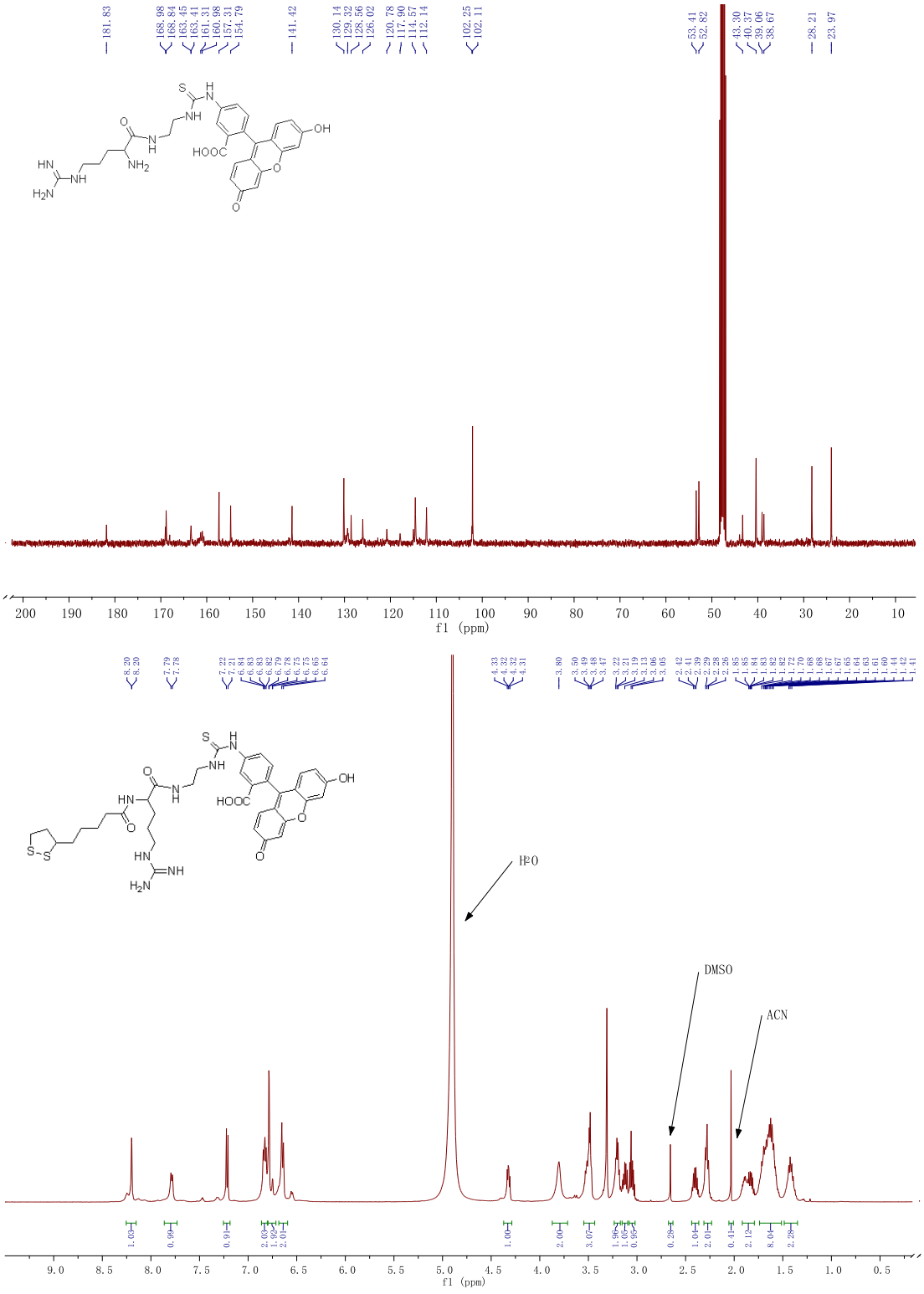
7.88
7.23
7.21
6.99
6.98
6.90
6.90
6.78
6.77
6.76
6.75
3.96
3.95
3.93
3.85
3.82
3.58
3.57
3.55
3.54
3.53
3.35
3.25
3.24
3.23
2.03
2.01
2.00
1.98
1.97
1.95
1.93
1.92
1.91
1.75
1.74
1.72
1.71
1.69
S
NH
N
H
O
NH
NH2
HN
NH
H2N
HOOC
OH
O
O
0.91
1.00
1.04
1.98
1.97
2.48
1.08
1.91
2.07
1.05
2.24
2.62
2.60
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)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160.98
157.31
154.79
141.42
130.14
129.32
128.56
126.02
120.78
117.90
114.57
112.14
102.25
102.11
53.41
52.82
43.30
40.37
39.06
38.67
28.21
23.97
f1 (ppm)
8.20
8.20
7.79
7.78
7.22
7.21
6.84
6.83
6.83
6.82
6.79
6.78
6.75
6.65
6.64
4.33
4.32
4.32
4.31
3.80
3.50
3.49
3.48
3.47
3.22
3.21
3.19
3.13
3.06
3.05
2.42
2.41
2.39
2.29
2.28
2.26
1.85
1.84
1.83
1.82
1.82
1.72
1.70
1.68
1.68
1.67
1.67
1.65
1.64
1.63
1.61
1.60
1.44
1.42
1.41
H2O
DMSO
ACN
1.03
0.99
0.91
2.03
1.92
2.01
1.00
2.00
3.07
1.99
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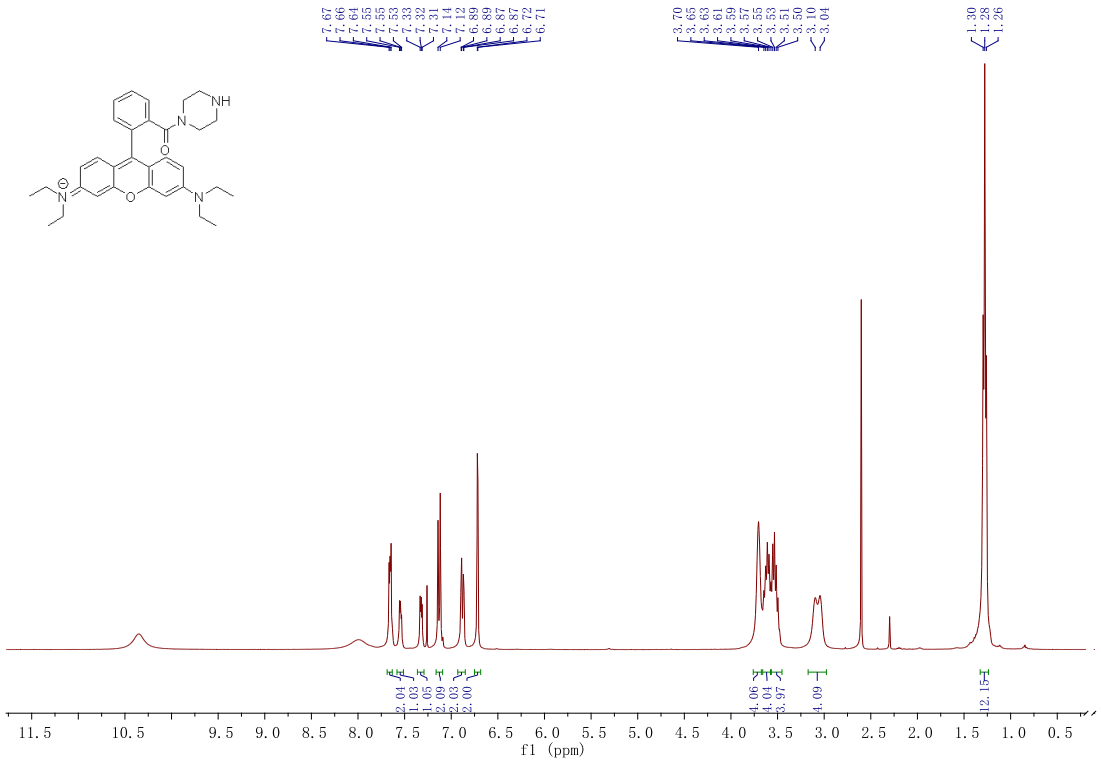
0.95
0.28
1.04
2.01
0.41
2.12
8.04
2.28
f1 (ppm)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7.33
7.32
7.31
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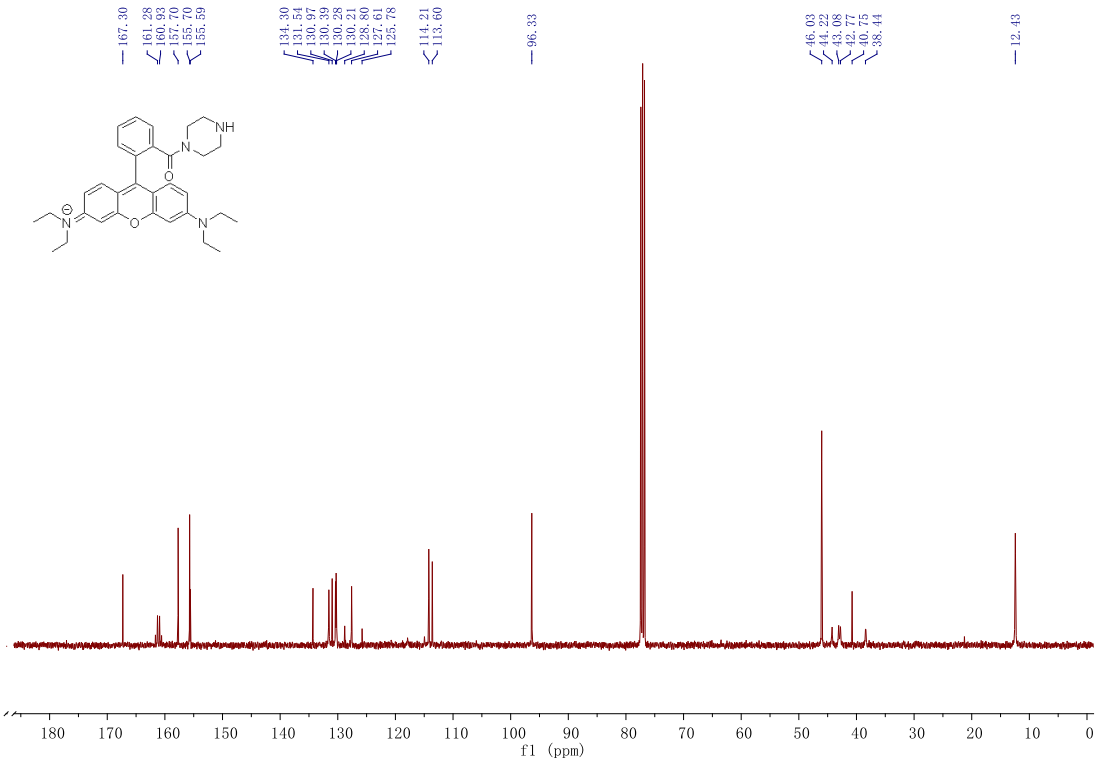
7.12
6.89
6.87
6.72
6.71
3.70
3.65
3.63
3.61
3.59
3.57
3.55
3.53
3.51
3.50
3.10
3.04
1.30
1.28
1.26
2.04
2.03
1.05
1.09
2.03
2.00
4.06
4.04
3.97
4.09
12.15
NH
O
O
N
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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155.70
155.59
134.30
131.54
130.97
130.39
130.28
130.21
128.80
127.61
125.78
114.21
113.60
96.33
46.03
44.22
43.08
42.77
40.75
38.44
12.43
NH
O
O
N
180
170
160
150
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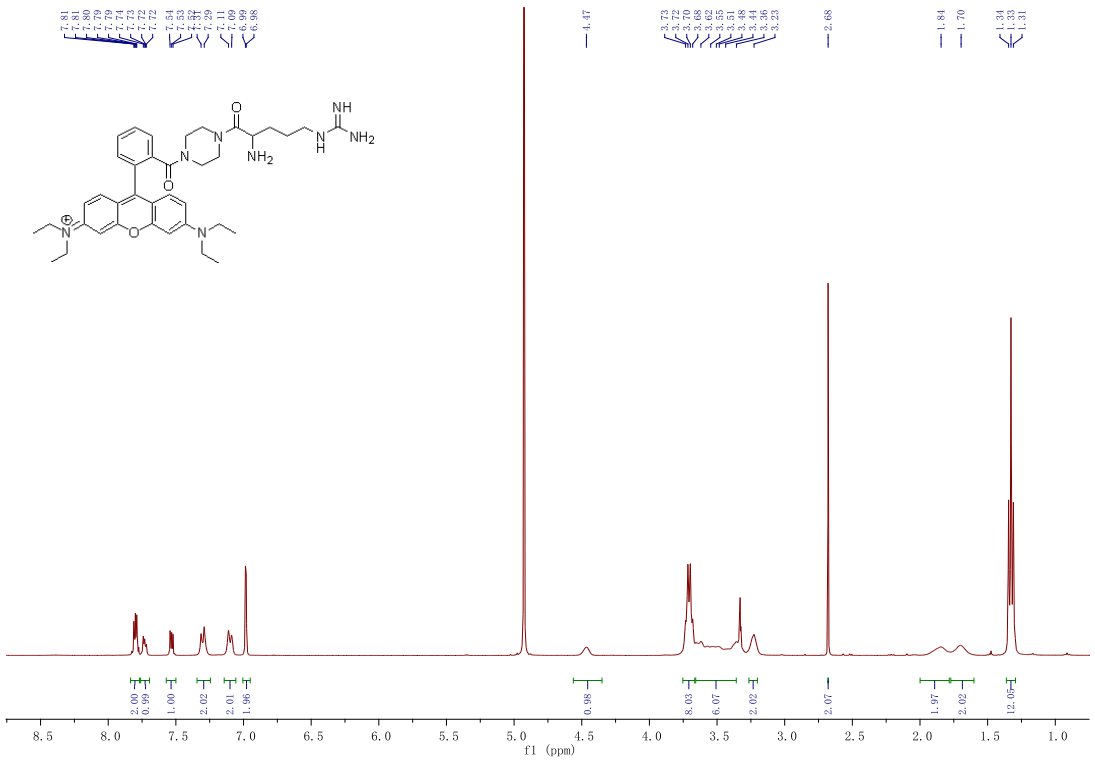
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.79
7.74
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7.72
7.54
7.53
7.37
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3.73
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3.70
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3.44
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2.68
1.84
1.70
1.34
1.33
1.31
2.00
6.99
1.00
2.02
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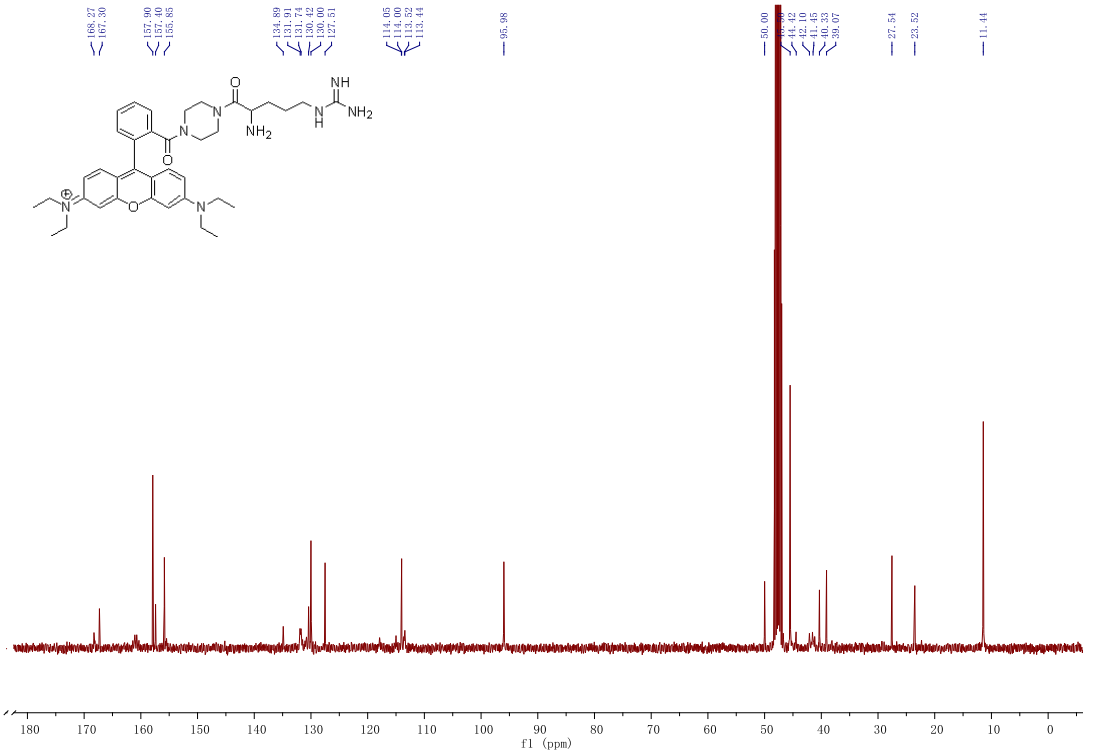
0.98
8.03
6.07
2.02
2.07
1.97
2.02
12.05
f1 (ppm)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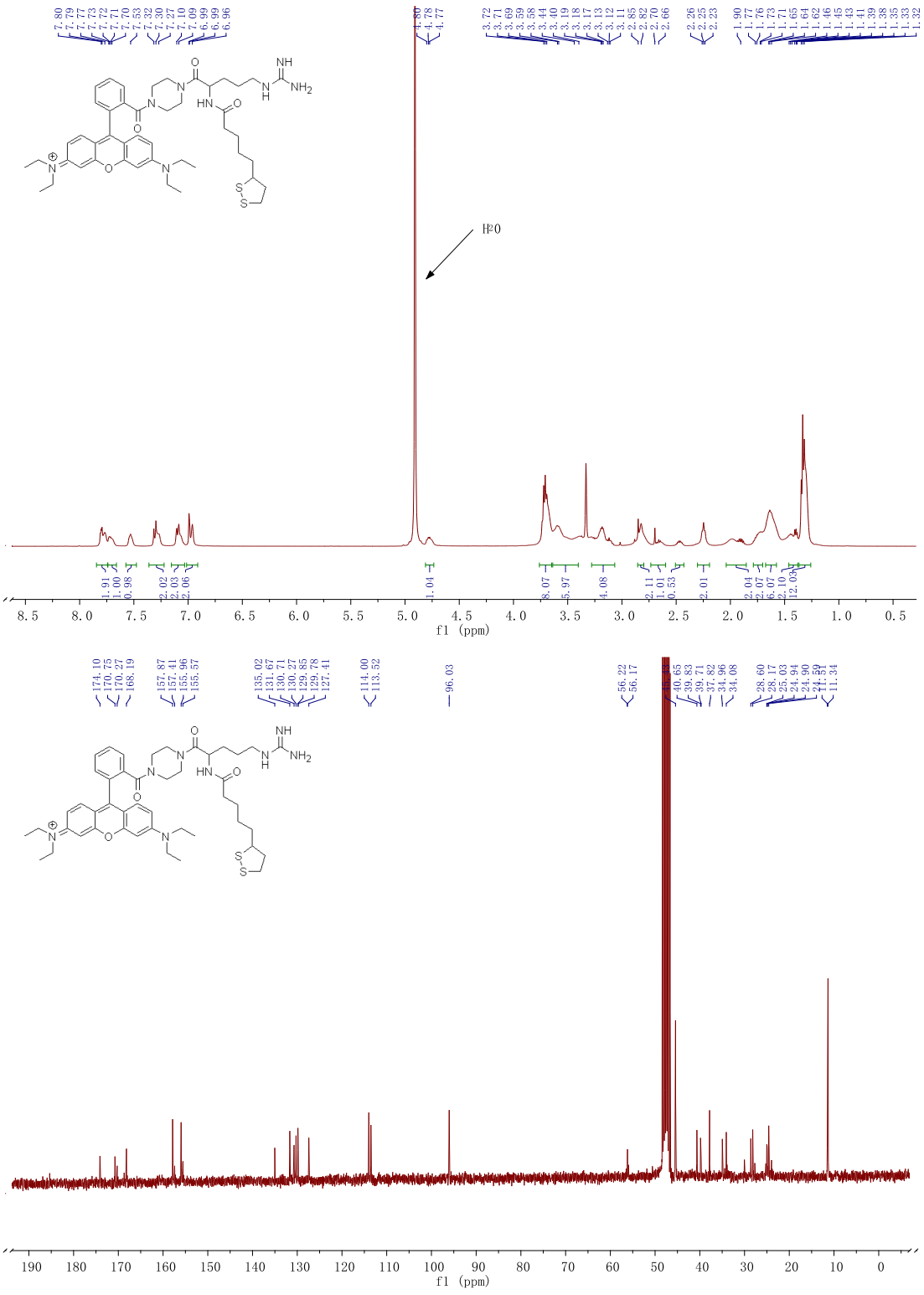
133.91
131.74
130.42
130.00
127.51
114.05
114.00
113.52
113.44
95.98
50.00
44.22
42.10
41.45
40.33
39.07
27.54
23.52
11.44
f1 (ppm)


H2O
f1 (ppm)
f1 (ppm)