Supporting materials

Design and Synthesis of a Novel Rhodamine B [2]Rotaxane

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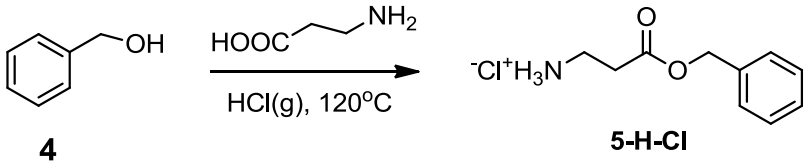
EXPERIMENTAL SECTION

MATERIALS AND GENERAL METHODS.

All reagents and organic solvents were ACS grade or higher and used without further purification. Unless otherwise noted, all chemicals were purchased from J&K Scientific (Shanghai, China). Reactions were performed under argon atmosphere with standard Schlenk techniques. Thin-layer chromatography was performed on a HAIYANG silica gel F254 plate, and the compounds were visualized under UV light (λ = 254 nm). Column chromatography was carried out using HAIYANG silica gel (type: 200–300 mesh ZCX-2). ^{1}H (500 MHz) and ^{13}C NMR (126 MHz) spectra were recorded on an Avance 500 spectrometer (Bruker; Billerica, MA, USA). Chemical shifts are reported in δ units (ppm) downfield relative to the chemical shift for tetramethylsilane.

SYNTHESIS.

Scheme **1**. Synthesis of the ether **5-H-Cl**.



4 **5-H-Cl**

3-(benzyloxy)-3-oxopropan-1-aminium chloride (5-H-Cl**).** β-Alanine **4** (2.3 g, 25.8 mmol) was suspended in 20 mL of phenylmethanol. Hydrogen chloride was passed through the solution for 15 min at room temperature. The reaction mixture was stirred at 120 °C for 4 h., cooled to room temperature, and then dried under vacuum. Flash chromatography (silica gel; MeOH/DCM, 5:95,v/v; R_f=0.3) of the residue gave **5-H-Cl** as a white solid (4.3 g, 78%). ^{1}H NMR ($CDCl_3$): δ = 7.72 (s, 1H), 7.29-7.25 (m, 5H), 5.09 (s, 2H), 3.35(t, J=5.5 Hz, 2H), 2.92(t, J=6.5 Hz, 2H).

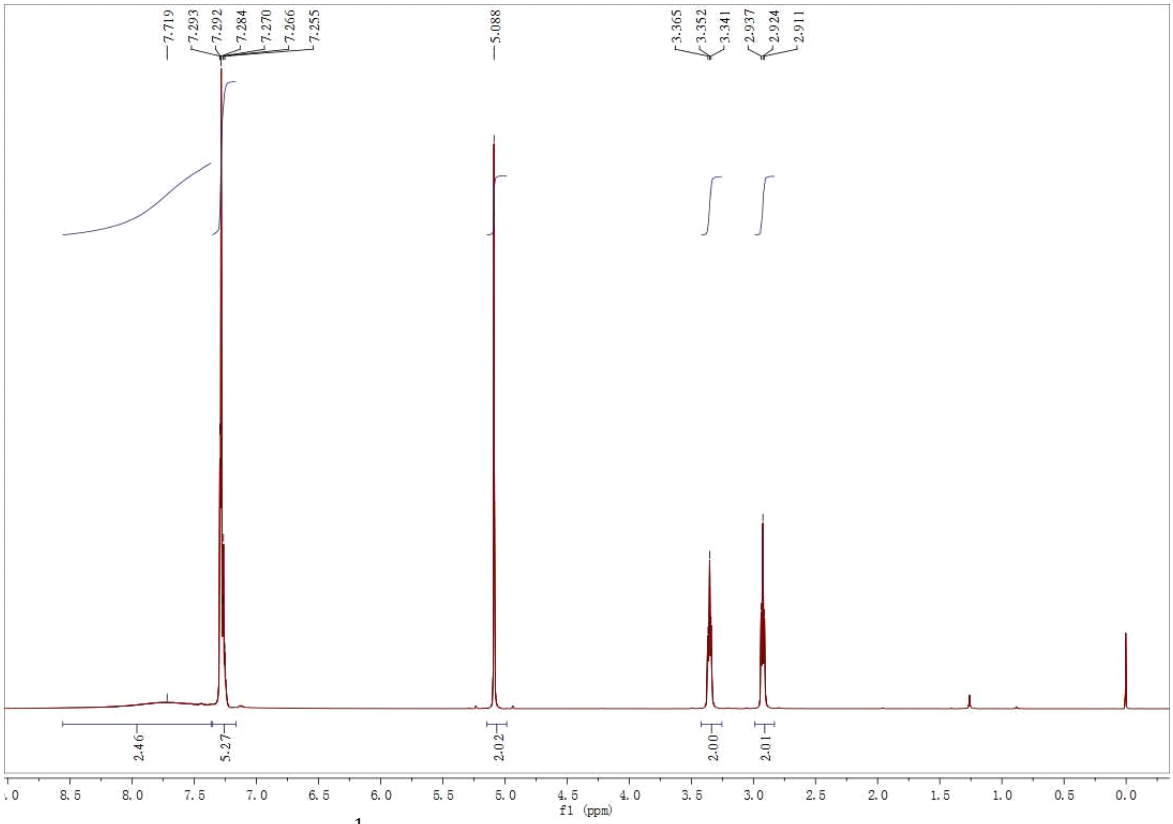
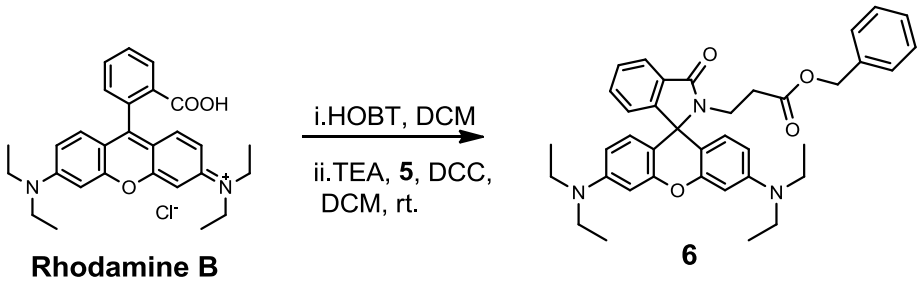


Figure 1. ^{1}H NMR spectrum ($CDCl_3$) of compound **5**-H-Cl

Scheme **2**. Synthesis of compound **6**.



Rhodamine B **6**

Benzyl 3-(3', 6'-bis(diethylamino)-3-oxospiro[isoindoline-1,9'-xanthen]-2-yl)-propanoate (6). A solution of **5**-H-Cl (1.07 g, 5 mmol) and triethylamine (405 µL, 5 mmol) in 15 mL CH_2Cl_2 was added to a solution of **Rhodamine B** (2 g, 4.2 mmol) and HOBt (0.567 g, 4.2 mmol) in 15 mL CH_2Cl_2. The reaction mixture was stirred at room temperature for 6 h., filtered through a pad of Celite and then dried under vacuum. Flash chromatography (silica gel; MeOH/DCM, 2/98, v/v; R_f= 0.3) of the residue gave **6** as a bright-red solid (2.1 g, 81%). ^{1}H NMR ($CDCl_3$): δ =7.90-7.91(m, 1H), 7.41-7.43(m, 2H), 7.26-7.30(m, 5H), 7.05-7.07(m, 1H), 4.99(s, 2H), 3.49(t, J=8.5 Hz, 2H), 3.31-3.36(m, 8H), 2.35(t, J=8.0 Hz, 2H), 1.16(t, J=7.0 Hz, 12H); ^{13}C NMR (126 MHz, $CDCl_3$, 298 K): δ =171.6, 168.2, 153.9, 153.4, 148.9, 136.0, 132.5, 130.9, 128.9, 128.5, 128.2, 128.05, 123.8, 122.9, 108.3, 105.4, 98.2, 66.2, 65.0, 44.5, 35.9, 32.9, 29.8, 12.7. ESI-MS (m/s): calcd. for $[M+H]^+$ $C_{38}H_{42}N_3O_4^+$, 604.3170; MS found, 604.15;HRMS found, 604.3180.

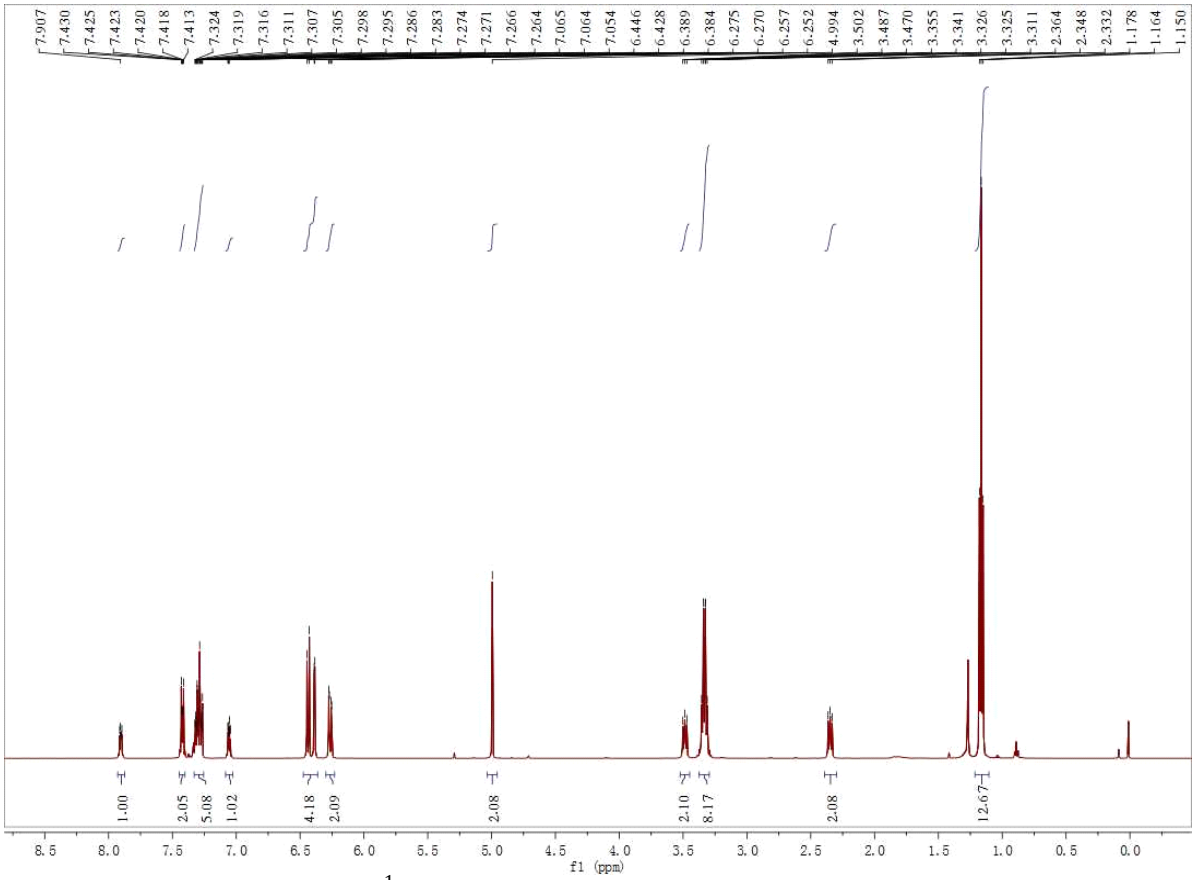


Figure 2. ^{1}H NMR spectrum (CDCl3) of compound **6**.

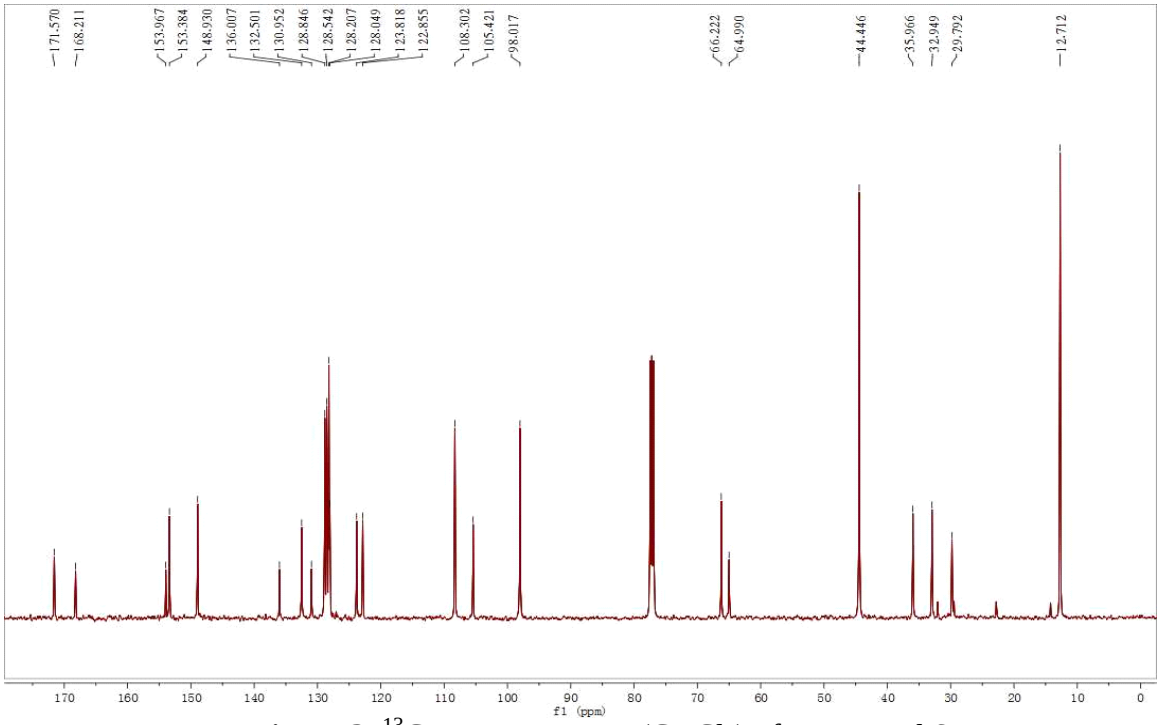
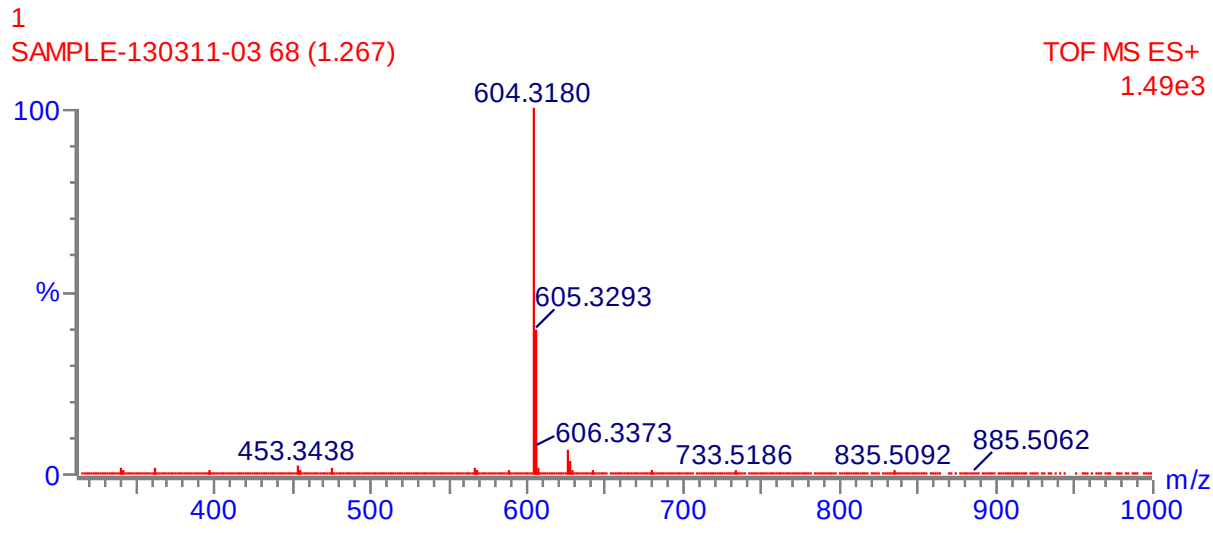


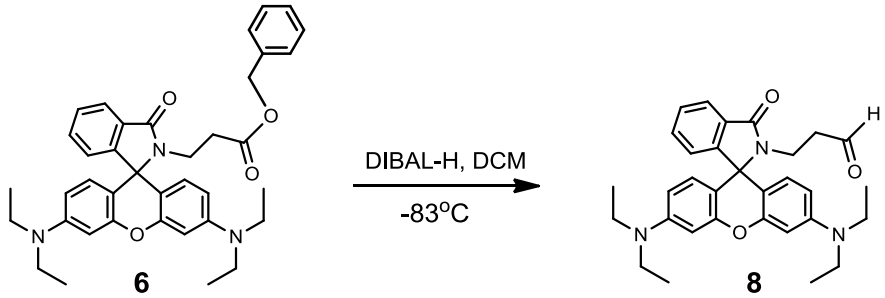
Figure 3. ^{13}C NMR spectrum ($CDCl_3$).of compound **6**.



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
604.3180	604.3175	0.5	0.8	19.5	15.0	C38 H42 N3 O4

Figure 4. HRMS of compound **6**.

Scheme **3.** Synthesis of compound **8**.



3-(3',6'-bis(diethylamino)-3-oxospiro[isoindoline-1,9'-xanthen] -2-yl)propanal (8). In a 100 mL dried round bottom flask, **6** (2 g, 3.32 mmol) in 50 mL CH_2Cl_2 was purged with nitrogen for 10 to 20 min., cooled to -83°C, treated with a solution of 1.2 M diisobutylaluminum hydride (DIBAL) in toluene (4.2 mL, 5.0 mmol), and stirred at -83°C for 2 h under nitrogen. 15 mL methanol was slowly added into the reaction mixture, and then stirred at rt. for 30 min. The crude mixture was then taken to dryness under vacuum, extracted with DCM (3 x 40 mL), and dried with $MgSO_4$. Flash chromatography (silica gel; Hexane/EtOAc, 7:3 v/v; R_f= 0.3) of the residue yielded **8** as a white solid (926 mg, 56%). ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ =9.54(s, 1H), 7.88-7.90(m, 1H), 7.42-7.44(m, 2H), 7.06-7.08(m, 1H), 6.38-6.44(m, 4H), 6.27-6.29(m, 2H), 3.47(t, J=14.5 Hz, 2H), 3.32-3.36(m, 8H), 2.35-2.38(m, 2H), 1.17(t, J=14.0 Hz, 12H); ^{13}C NMR (500 MHz, $CDCl_3$, 298 K): δ=201.2, 168.2, 153.7, 153.4, 148.9, 132.6, 131.0, 128.8, 128.1, 123.9, 122.8, 108.3, 105.2, 97.9, 65.0, 44.5, 42.65, 34.0, 12.7. ESI-MS (m/s): calcd. for $[M+H]^+$ $C_{31}H_{36}N_3O_3^+$, 498.2751; MS found, 498.14. HRMS found, 498.2761.

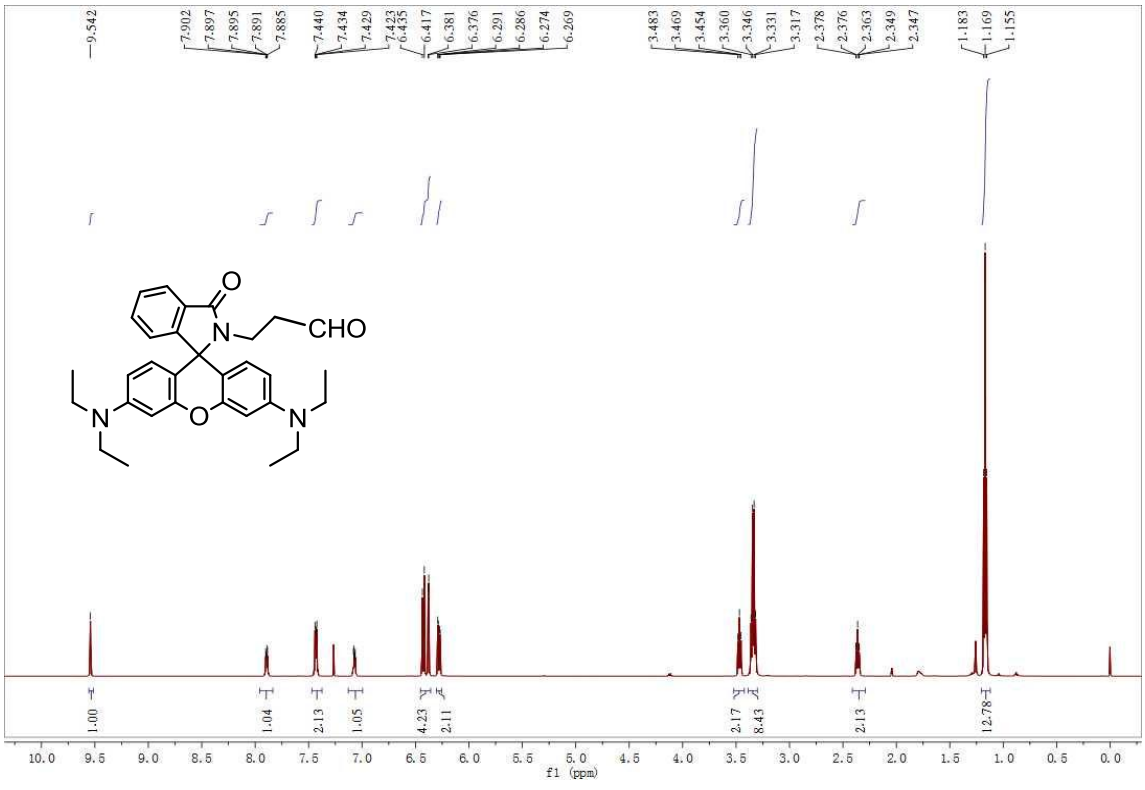


Figure 5. ^{1}H NMR spectrum ($CDCl_3$) of compound **8**.

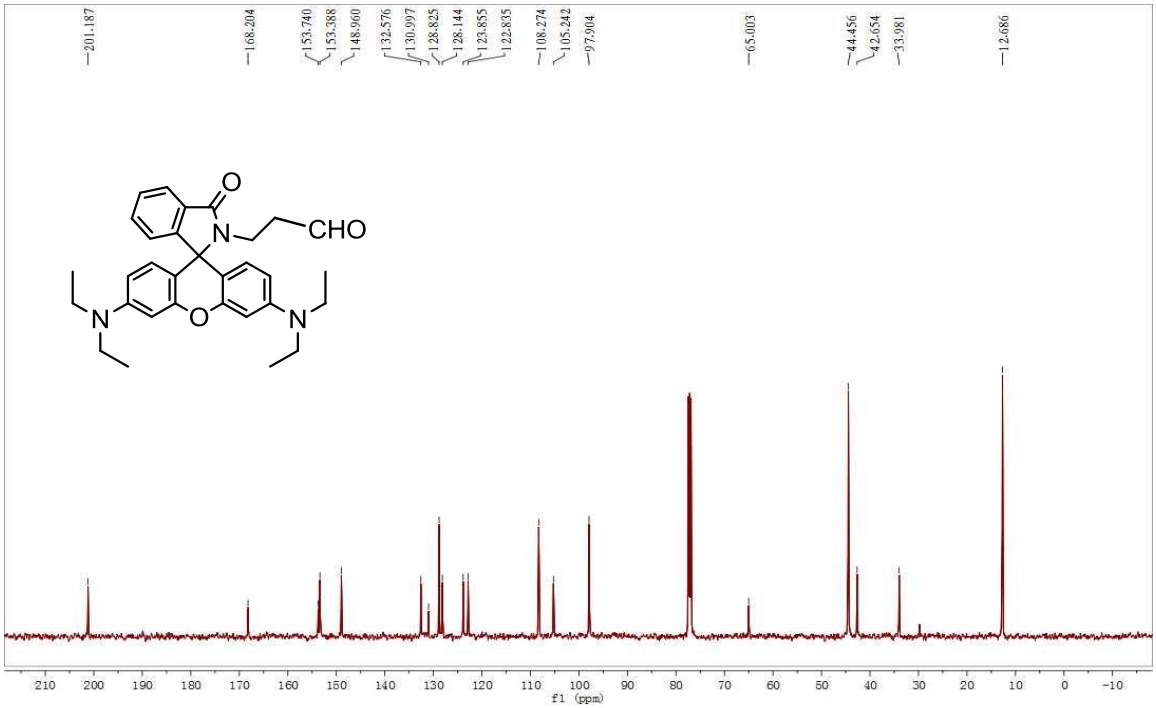


Figure 6. ^{13}C NMR spectrum ($CDCl_3$) of compound **8**

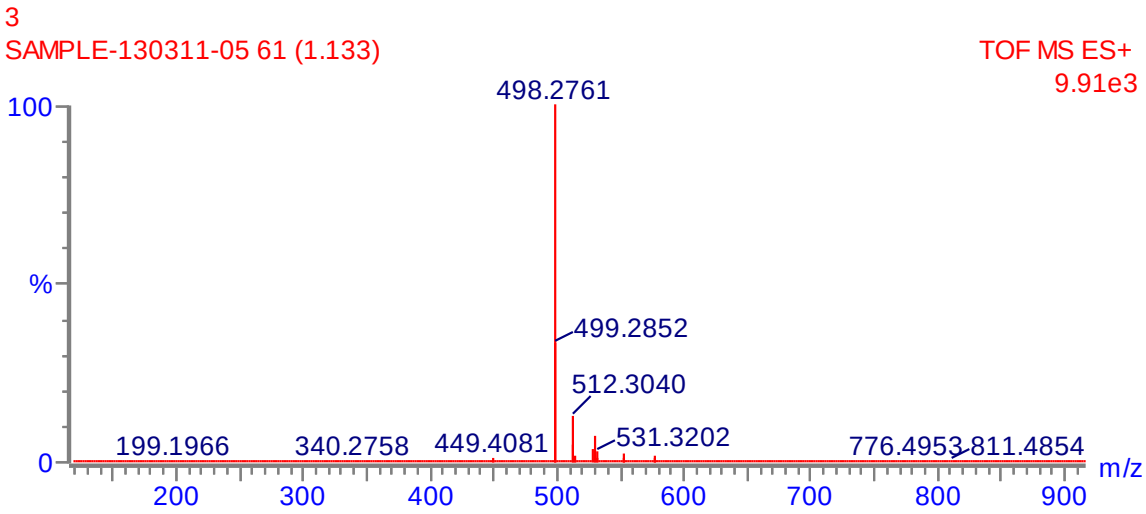
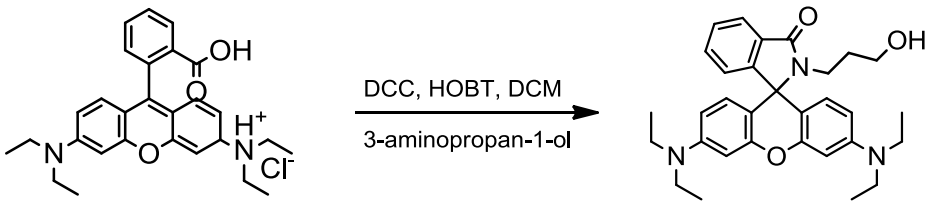


Figure 7. HRMS of compound **8**

Scheme **4**. Synthesis of compound **7**.



Rhodamine B **7**

3',6'-bis(diethylamino)-2-(3-hydroxypropyl)spiro[isoindoline-1,9'-xanthen]-3-one (7) To a solution of rhodamine B (500 mg, 1.044 mmol), DCC (215 mg, 1.566 mmol) and triethylamine (145 μL, 1.044 mmol) in 15 mL of anhydrous DCM was added HOBt (141 mg, 1.044 mmol), and the resulting mixture was stirred at room temperature for 30 min. 3-Aminopropan-1-ol (115 μL, 1.044 mmol) was added, and the mixture was stirred for an additional 5 h. The precipitated DCU was filtered; the residue was extracted with DCM/H2O, dried with $MgSO_4$, and concentrated under vacuum. Chromatography (silica gel; EtOAc/hexane 1:1 v/v; R_f=0.4) to afford **7** (250 mg, 48%) as a white solid. ^{1}H NMR($CDCl_3$): 7.92-7.90(m, 1H), 7.48-7.46(m, 2H), 7.13-7.11(m, 1H), 6.40-6.48(t, 4H), 6,27-6.25(dd, 2H), 4.42(s, 1H), 3.40-3.30(m, 12H), 1.17-1.15(t, J=7.0 Hz, 12H), 1.11-1.07(m, 2H); ^{13}C NMR ($CDCl_3$): δ 169.3, 153.5, 148.9, 132.7, 131.1, 128.7, 128.3, 123.9, 122.9, 108.2, 105.3, 97.8, 65.5, 58.4, 44.5, 35.6, 30.9, 12.7. ESI-MS (m/s): calcd. for $[M+H]^+$ $C_{31}H_{38}N_3O_3^+$, 500.2908; MS found, 500.11; HRMS found, 500.2917.

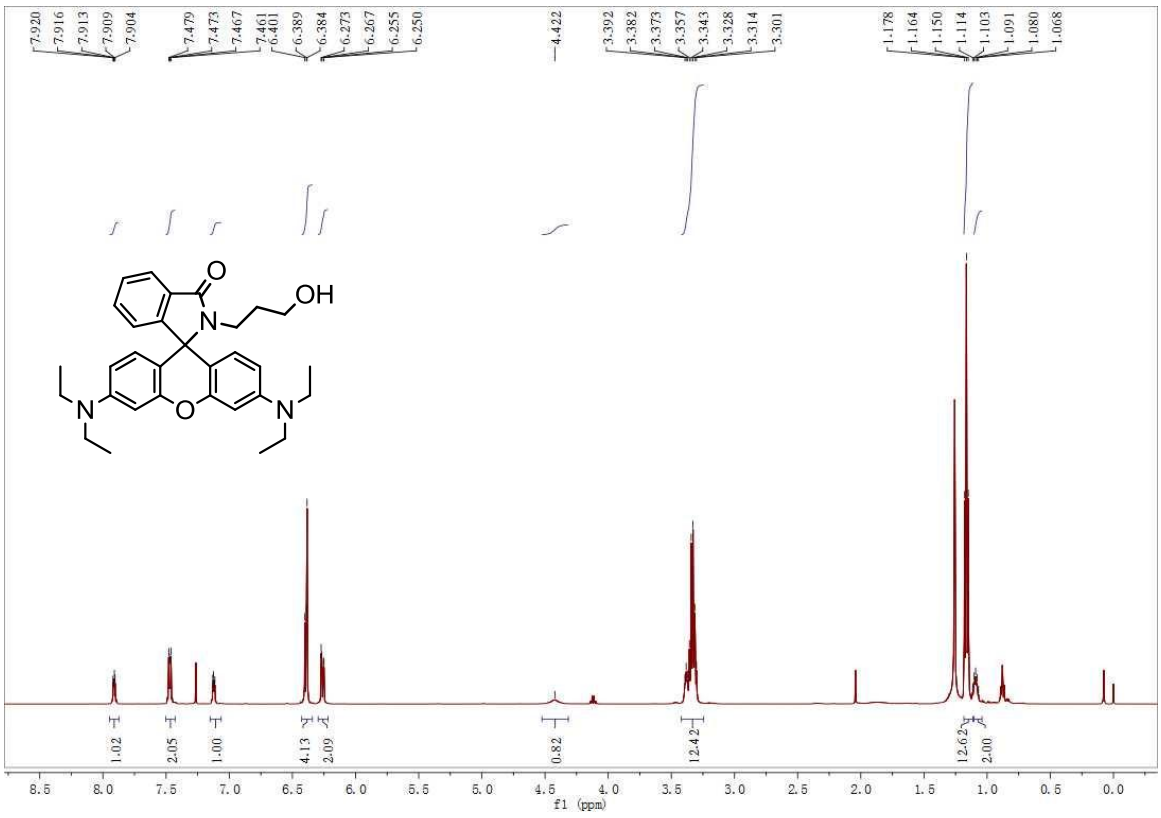


Figure 8. ^{1}H NMR spectrum ($CDCl_3$) of compound **7**

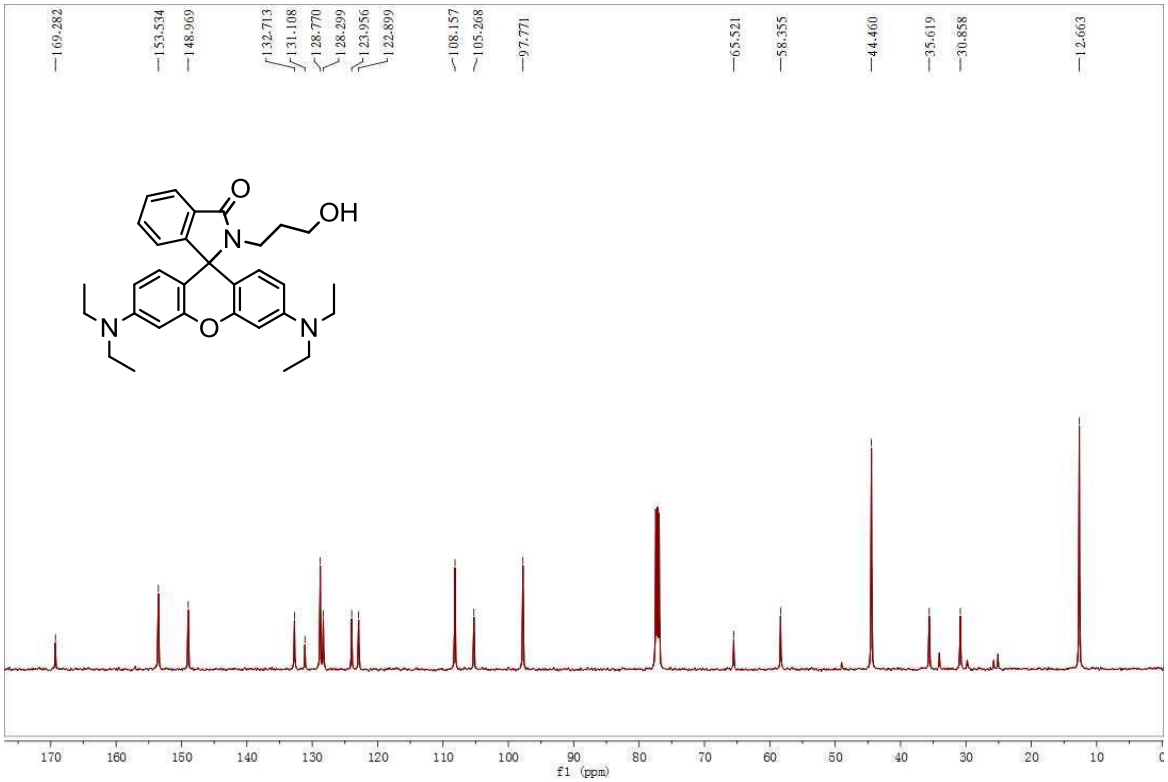


Figure 9. ^{13}C NMR spectrum ($CDCl_3$) of compound **7**

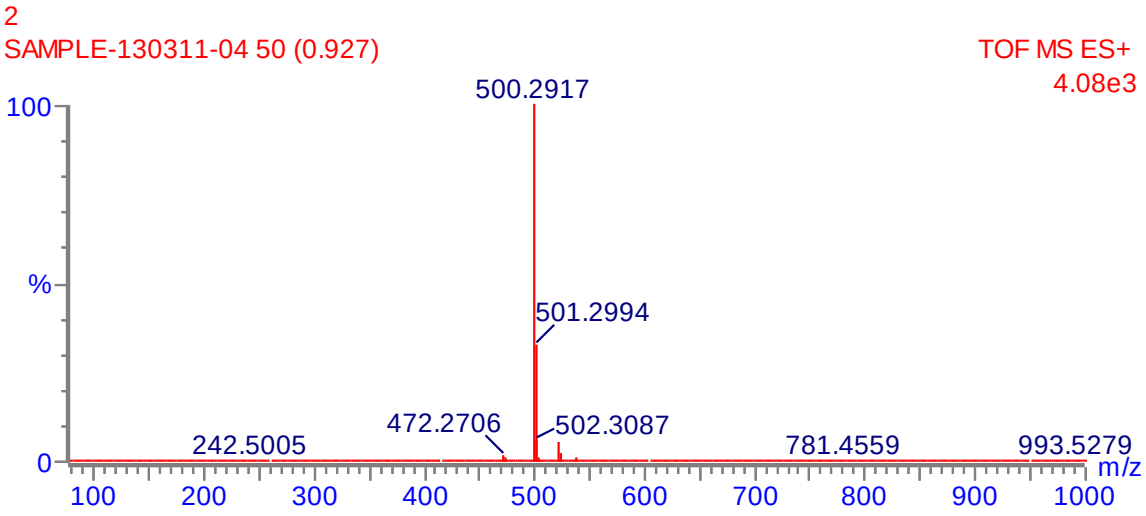
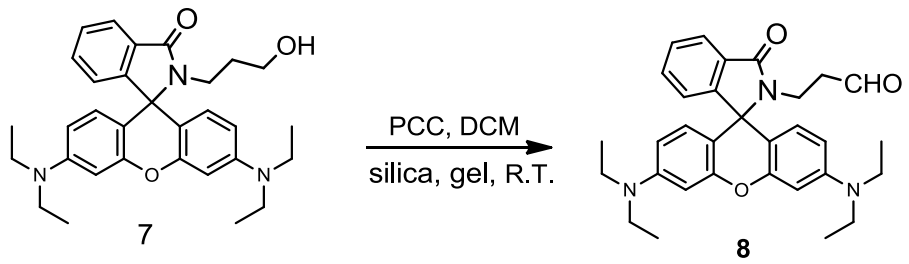


Figure 10. HRMS of compound **7**

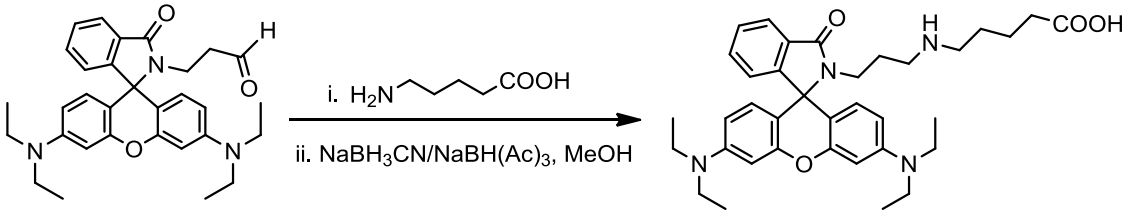
Scheme **5**. Synthesis of compound **8**.



7 **8**

3-(3',6'-bis(diethylamino)-3-oxospiro[isoindoline-1,9'-xanthen]-2-yl)propanal. (8) Pyridinium chlorochromate (144 mg, 0.6692 mmol) was added to a solution of **7** (180 mg, 0.36 mmol) and silica gel (200 mg, 300 mesh) in 15 mL DCM. The reaction mixture was stirred at room temperature overnight, and then introduced onto a short silica column (3.5x8 cm) which was eluted with EtOAc. The organic layer was collected and concentrated under vacuum. Chromatography (silica gel; EtOAc/hexane,2:3 v/v; R_f=0.5) of the residue gave **8** (35 mg, 20%) as a pale-red solid. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ =9.54(s, 1H), 7.88-7.90(m, 1H), 7.42-7.44(m, 2H), 7.06-7.08(m, 1H), 6.38-6.44(m, 4H), 6.27-6.29(m, 2H), 3.47(t, J=14.5 Hz, 2H), 3.32-3.36(m, 8H), 2.35-2.38(m, 2H), 1.17(t, J=14.0 Hz, 12H); ^{13}C NMR (500 MHz, $CDCl_3$, 298 K): δ=201.2, 168.2, 153.7, 153.4, 148.9, 132.6, 131.0, 128.8, 128.1, 123.9, 122.8, 108.3, 105.2, 97.9, 65.0, 44.5, 42.65, 34.0, 12.7. ESI-MS (m/s): calcd. for $[M+H]^+$ $C_{31}H_{36}N_3O_3^+$, 498.2751; MS found, 498.14. HRMS found, 498.2761.

Scheme **6**. Synthesis of compound **9**.



8 **9**

5-((3-(3',6'-bis(diethylamino)-3-oxospiro[isoindoline-1,9'-xanthen]-2-yl)propyl) amino)pentanoic acid (9) To a solution of **8** (1 g, 2.012 mmol) in 15 mL of anhydrous methanol was added 5-aminopentanoic acid (705 mg, 6.02 mmol) in 5 mL anhydrous methanol and the reaction was stirred at room temperature for 1 h. Sodium triacetoborohydride (852 mg, 4.02 mmol) in 5 mL of anhydrous methanol was then added, and the resulting mixture was stirred at room temperature overnight while monitoring by TLC. After the reaction was complete, 5 mL of saturated aqueous $NaHCO_3$ was added to and the solution was stirred for an additional 30 min. The reaction mixture was then dried under vacuum and washed with DCM three times. The combined organic layers were dried over $MgSO_4$, concentrated and purified on a silica column with MeOH/ DCM (3:17 v/v; R_f= 0.3) to afford **9** (434 mg, 36%) as a pale-red solid. ^{1}H NMR ($CDCl_3$): δ 8.20(s, 1H), 7.89-7.84(m, 2H), 7.48-7.46(t, J=7.5 Hz, 1H), 6.37-6.34(m, 4H), 6.25-6.23(dd, 2H), 3.34-3.30(m, 8H), 3.26-3.24(t, J=5.5 Hz, 2H), 2.79-2.77(t, J=7.5 Hz, 2H), 2.66-2.63(t, J=6 Hz, 2H), 2.20-2.18(t, J=5.5 Hz, 2H), 1.75-1.72(t, J =8 Hz, 2H), 1.38(m, 2H), 1.17-1.14(t, J =7 Hz, 12H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.5, 169.2, 153.5, 153.3, 149.0, 132.9, 130.9, 128.5, 128.4, 124.1, 123.0, 108.2, 105.0, 97.8, 65.6, 47.6, 44.50, 36.7, 36.2, 26.5, 25.2, 23.3, 12.7. ESI-MS: calcd. for $[M+H]^+$ $C_{36}H_{47}N_4O_4^+$, 599.3592; MS found 599.18. HRMS found, 599.3603.

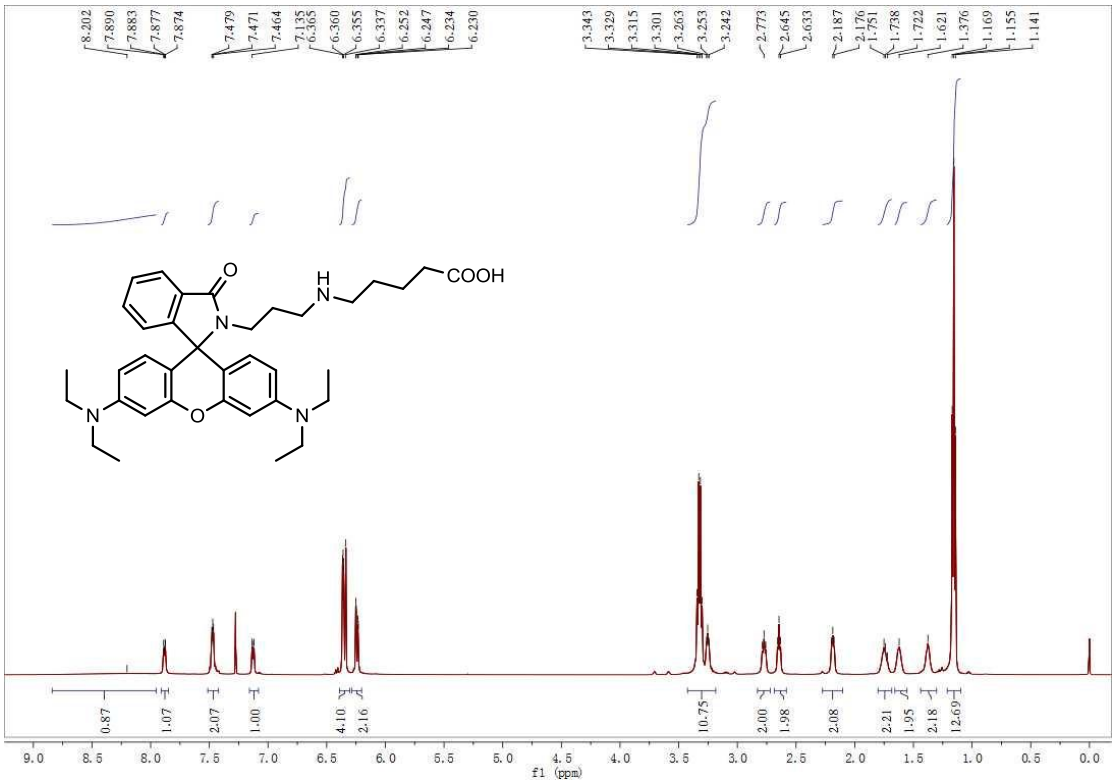


Figure 11. ^{1}H NMR spectrum ($CDCl_3$) of compound **9**

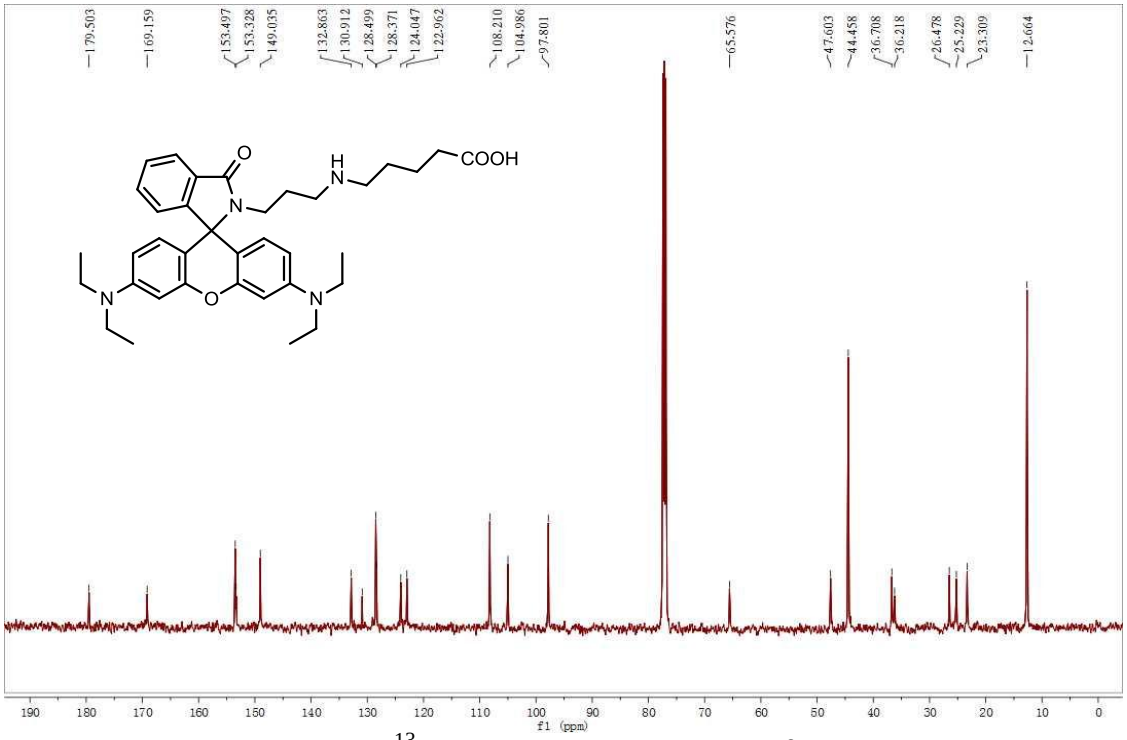


Figure 12. ^{13}C NMR spectrum ($CDCl_3$) of compound **9**

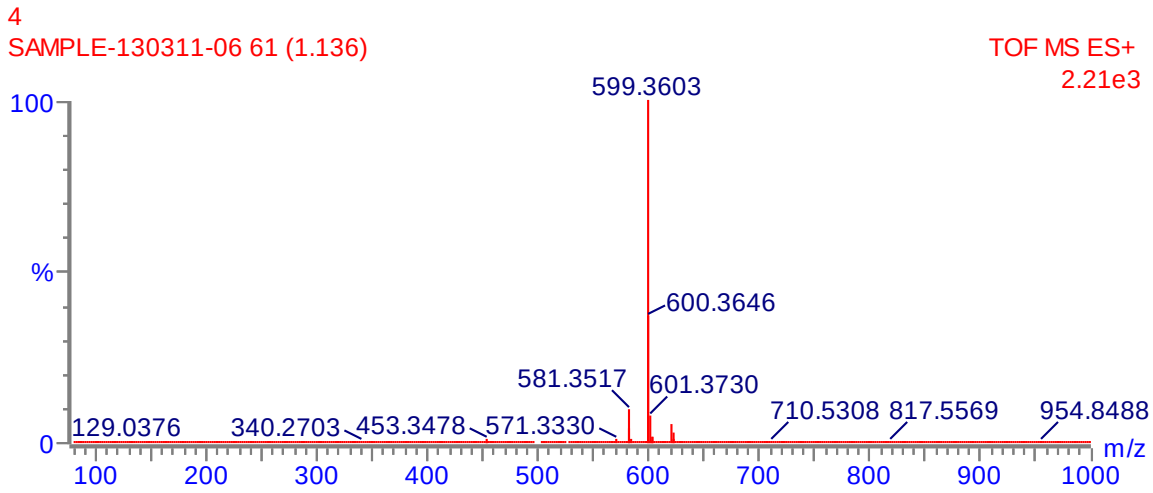
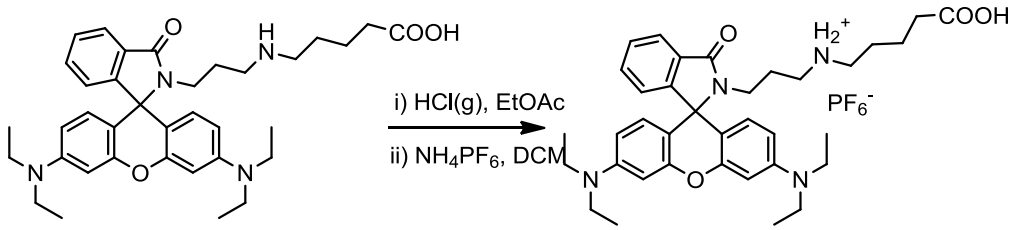


Figure 13. HRMS of compound **9**.

Scheme **7.** Synthesis of **8-H-PF$_6$.**



9 **10-H-PF$_6$**

N-(3-(3',6'-bis(diethylamino)-3-oxospiro[isoindoline-1,9'--anthen]-2-yl)propyl)-4-carboxybutan-1-aminium hexafluorophosphate(V). (10-H-PF$_6$) Hydrogen chloride gas was passed through a solution of **9** (100 mg, 0.167 mmol) in 10 mL of EtOAc for 15 min until a red precipitates was observed. The mixture was then stirred for another 30 min. and concentrated under vacuum to provide a red solid. A 2 mL solution of NH_4PF_6 (200 mg, 1.22 mmol) in water (2 mL) was added into a suspension of this solid in 10 mL of DCM. The biphasic solution was stirred vigorously for 3 h until the solid had dissolved in the organic layer. The organic layer was concentrated under vacuum to afford **10-H-PF$_6$** as a pale-red solid (120 mg, 97%). ^{1}H NMR(500 MHz, $CDCl_3$, 298 K): δ 7.88-7.87(m, 1H), 7.47-7.45(m, 2H), 7.12-7.11(dd, 1H), 6.36-6.33(m, 4H), 6.25-6.23(m, 2H), 3.34-3.30(m, 8H), 3.25-3.23(t, J=6.0 Hz, 2H), 2.80-2.77(t, J=7.5 Hz, 2H), 2.66-2.64(t, J=6.0 Hz, 2H), 2.21-2.19(t, J= 5.5 Hz, 2H), 1.75-1.72(t, J=7.0 Hz, 2H), 1.62(m, 2H), 1.41-1.40(m, 2H), 1.16-1.13(t, J=7.0 Hz, 12H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.2, 169.7, 153.5, 153.4, 149.2, 133.2, 130.4, 128.6, 128.4, 124.1, 123.1, 108.4, 108.2, 104.5, 97.8, 66.0, 47.7, 44.7, 44.5, 35.9, 35.8, 32.0, 29.8, 29.4, 26.1, 25.1, 22.8, 22.6, 14.2, 12.7. TOF-ESI-MS: calcd. for $[M-PF_6]^+$ $C_{36}H_{47}N_4O_4^+$, 599.3592; HRMS found 599.3602.

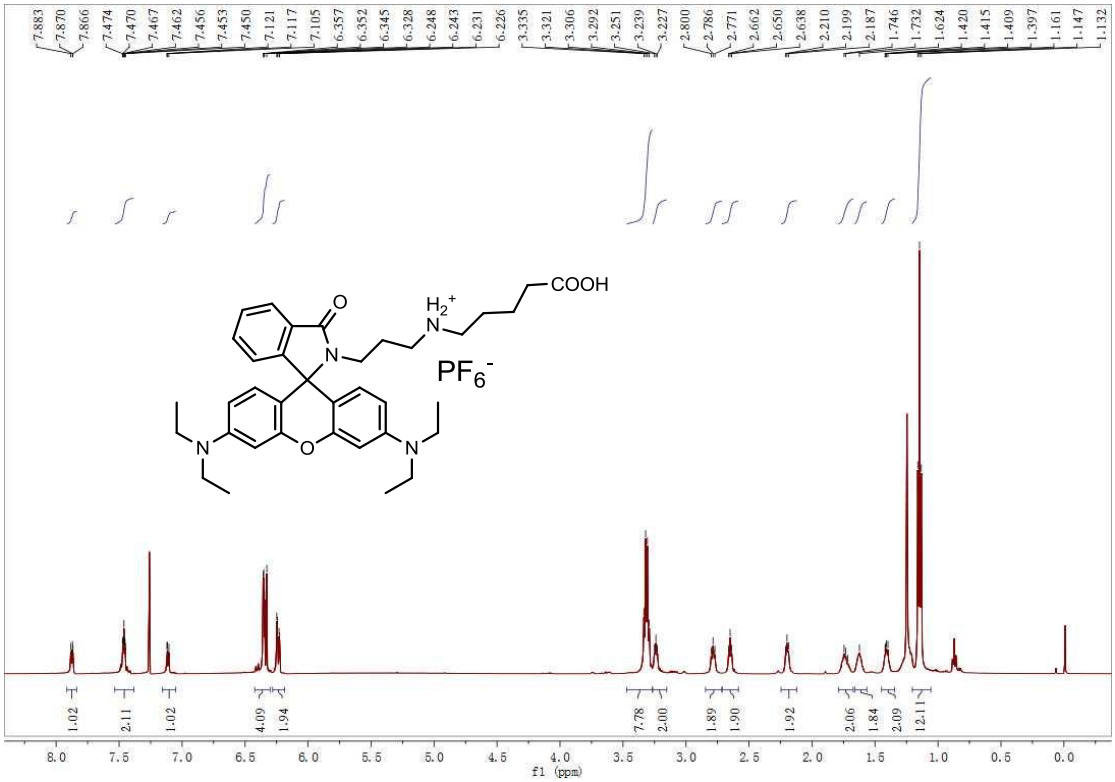


Figure 14. ^{1}H NMR spectrum ($CDCl_3$) of compound **10-H-PF$_6$**

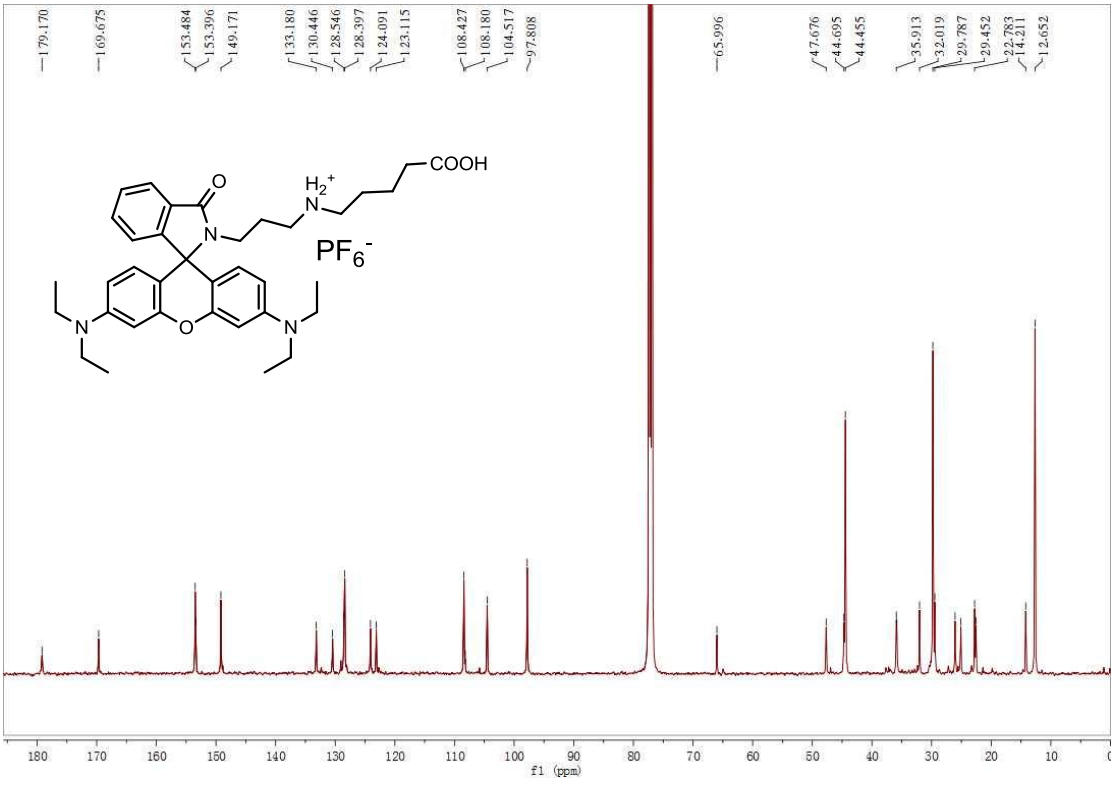


Figure 15. ^{13}C NMR spectrum ($CDCl_3$) of compound **10-H-PF$_6$**.

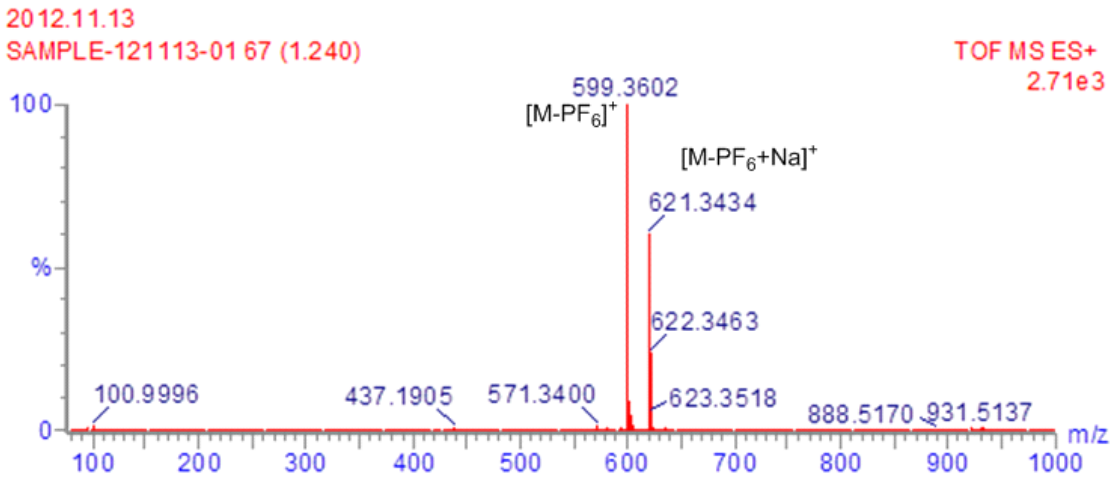
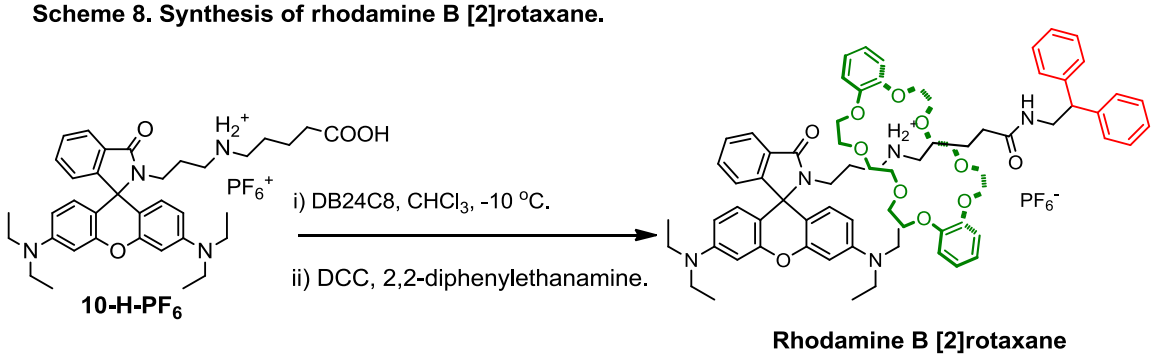


Figure 16. HRMS of compound **10-H-PF$_6$**.

Scheme 8. Synthesis of rhodamine B [2]rotaxane.



Rhodamine B [2]Rotaxane. (12) **10-H-PF$_6$** (100 mg, 0.1344 mmol) and DB24C8 (120 mg, 0.2688 mmol) was dissolved in 15 mL $CHCl_3$ and stirred in an ice-salt bath for 30 min.; DCC (41 mg, 0.2016 mmol) was then added and the reaction was stirred for an additional 2 h, followed by the addition of 2,2-diphenylthanamine (39 mg,0.2016 mmol.). The reaction mixture was stirred overnight at room temperature, concentrated, and dissolved in CH_3CN. The precipitated DCU was removed by filtration. Chromatography (silica gel; MeOH/ DCM, 2:98, v/v (R_f= 0.1); 5: 95 v/v (R_f= 0.3)) of the residue gave **12** (24 mg, 15%) as a pale-red solid. ^{1}H NMR ($CDCl_3$): δ 7.88(m, 1H), 7.44-7.42(m, 2H), 7.12-6.89(m, 18H), 6.42-6.38(m, 4H), 6.27-6.25(dd, 2H), 4.13-4.81(m, 16H), 3.78(s, 1H), 3.70-3.79(d, 2H), 3.35-3.31(m, 8H), 3.22-3.20(t, J=6.5 Hz, 2H), 3.11-3.08(t, J=7.5 Hz, 2H), 3.02(m, 2H), 2.28(m, 2H), 1.72-1.71(m, 4H), 1.43-1.40(t, J=7.5, 2H), 1.18-1.15(m, J=7.0 Hz, 12H); ESI-MS: m/z calcd. for $[M-PF_6]^+$ $C_{74}H_{92}N_5O_{11}^+$, 1226.68; found 1226.88.

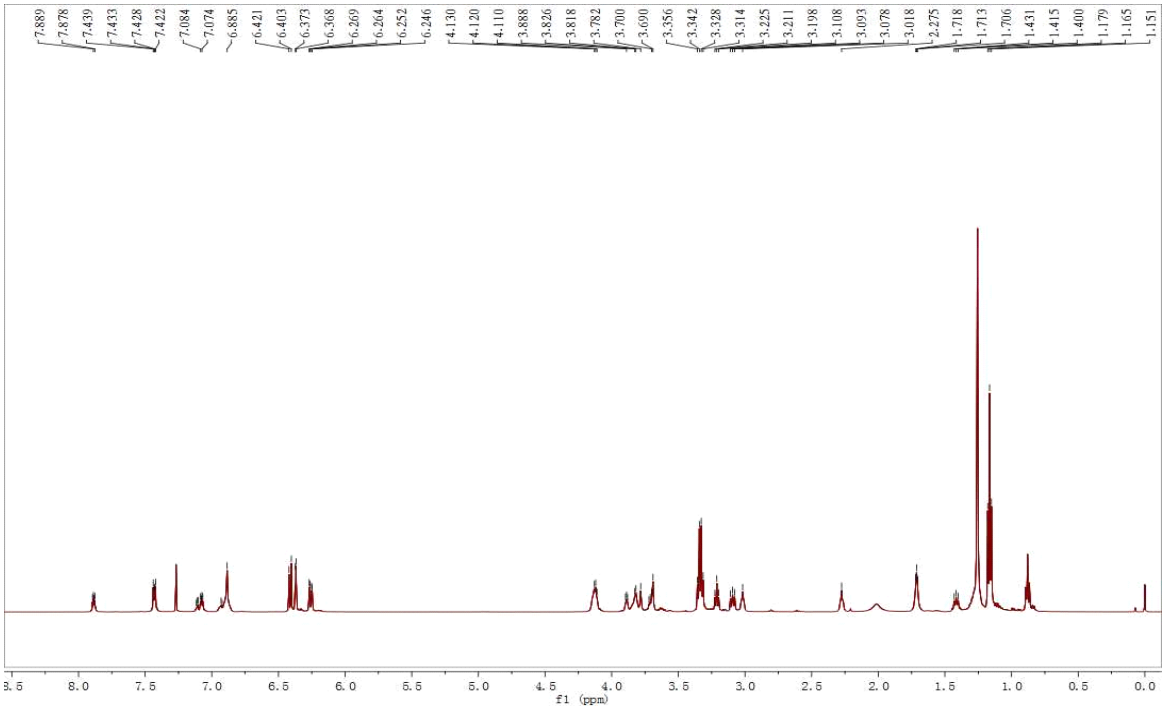


Figure 17. ^{1}H NMR spectrum (in $CDCl_3$) of compound **Rhodamine-[2]rotaxane**.

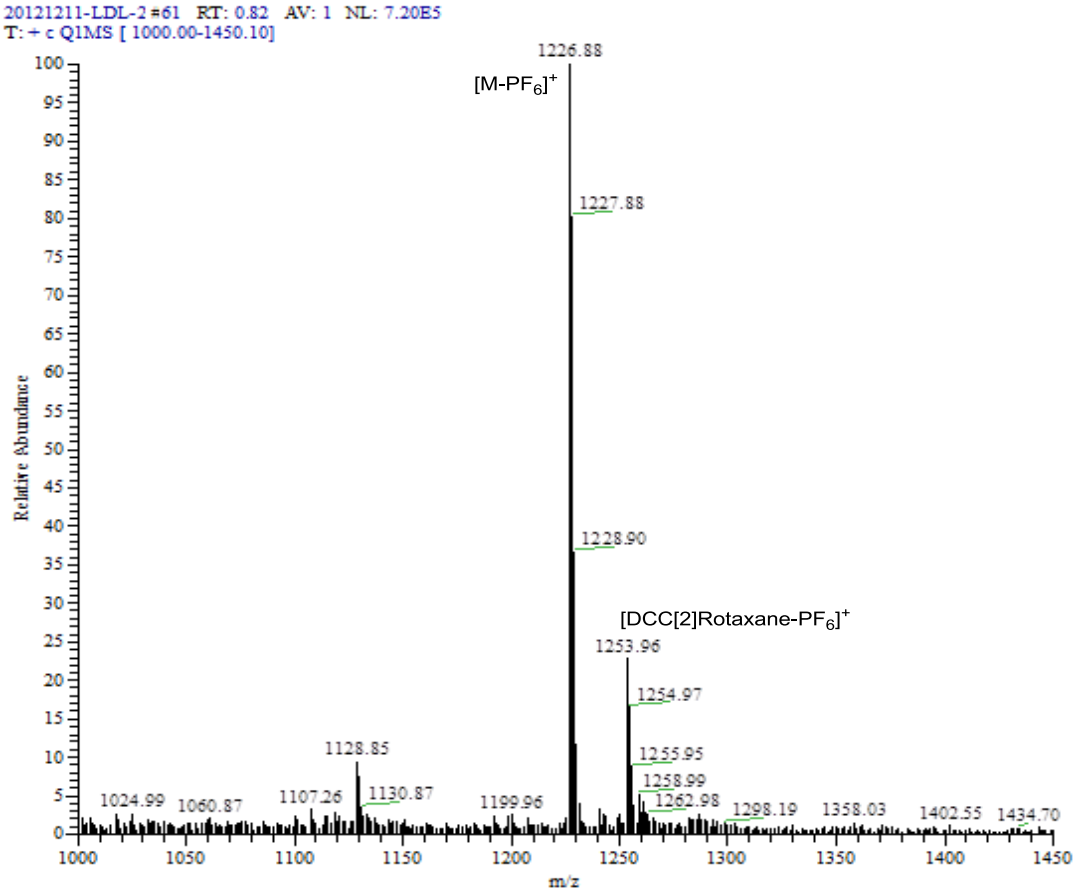


Figure 18. MS of **Rhodamine B [2]rotaxane**