– Electronic Supplementary Information –

Photocontrol of Ion Permeation in Lipid Vesicles with (Bola)amphiphilic Spirooxazines

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Procedures for the synthesis of 2 and 3

15-(4-Bromophenyl)pentadec-14-yn-1-ol (4)

The preparation of **4** has been adapted from a previously published procedure.[1] Starting material, pentadec-14-yn-1-ol, was synthesized following a reported procedure.[2] Pentadec-14-yn-1-ol (6.65 g, 29.6 mmol) was added to a solution of 1-bromo-4-iodobenzene (8.80 g, 31.1 mmol) in triethylamine (210 mL) followed by the addition of $Pd(Ph_3P)_2Cl_2$ (193 mg, 0.275 mmol) and copper (I) iodide (116 mg, 0.609 mmol) under an atmosphere of argon at 0 °C. After stirring for 10 min, the ice bath was removed and the reaction mixture continued to stir for another 2 h while it warmed to room temperature. The reaction mixture was diluted with diethyl ether (60 mL) and poured into water (100 mL) to give a biphasic mixture. This mixture was extracted with diethyl ether (3 × 100 mL). The combined organic extracts were washed with aqueous hydrochloric acid (2 × 70 mL, 1M), washed with a saturated aqueous solution of sodium chloride (2 × 100 mL), dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (silica gel; 1:1 petroleum ether/diethyl ether) gave pure **4** as an off-white solid (6.98 g, 62%). ^{1}H NMR ($CDCl_3$, δ): 1.27 (m, 16H, CH_2), 1.43 (t, J = 7.6 Hz, 2H, CH_2), 1.56 (m, 4H, CH_2), 2.37 (t, J = 7.2 Hz, 2H, CH_2), 3.63 (t, J = 7.4 Hz, 2H, CH_2), 7.19–7.29 (m, 2H, Ar H), 7.35–7.45 (m, 2H, Ar H). ^{13}C NMR ($CDCl_3$, δ): 19.6, 25.9, 28.8, 29.1, 29.3, 29.6, 29.7, 29.8, 33.0, 63.2, 79.7, 92.0, 121.6, 123.2, 131.5, 133.2. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{21}H_{31}O^{79}Br$, 378.1558; found 378.1545.

15-(4-Bromophenyl)pentadecan-1-ol (5)

The preparation of **5** has been adapted from a previously published procedure.[3] Platinum (IV) oxide (100 mg, 0.440 mmol) was added to a solution of **4** (6.90 g, 18.2 mmol) in dry methanol. This reaction mixture was shaken in a hydrogenation apparatus under an atmosphere of hydrogen (1.7 atm) at room temperature. After 2 h, the reaction mixture was concentrated under reduced pressure. Purification of the crude product by flash column chromatography (silica gel; 1:1 petroleum ether/diethyl ether) gave pure **5** as an off-white solid (6.80 g, 98%). ^{1}H NMR ($CDCl_3$, δ): 1.25 (m, 22H, CH_2), 1.56 (m, 4H, CH_2), 2.55 (t, J = 7.6 Hz, 2H, CH_2), 3.64 (t, J = 6.6 Hz, 2H, CH_2), 7.00–7.10 (m, 2H, Ar H), 7.34–7.42 (m, 2H, Ar H). ^{13}C NMR ($CDCl_3$, δ): 25.9, 29.3, 29.6, 29.7, 29.8, 31.5, 33.0, 35.5, 63.3, 119.4, 130.3, 131.4, 142.0. HRMS-EI (m/z): $[M]^+$ calcd for $C_{21}H_{35}O^{79}Br$, 382.1871; found 382.1865.

(15-(4-Bromophenyl)pentadecyloxy)(*tert*-butyl)dimethylsilane (6)

The preparation of **6** has been adapted from a previously published procedure.[4] Imidazole (3.01 g, 44.2 mmol) was added to a solution of **5** (6.80 g, 17.7 mmol) in dimethylformamide (40 mL) followed by the addition of *tert*-butyldimethylsilyl chloride (3.20 g, 21.2 mmol) at room temperature. After stirring at 40 °C for 2 h, ice water (50 mL) was added to the reaction mixture. The mixture was extracted with diethyl ether (3 × 50 mL), washed with a saturated aqueous solution of sodium chloride (80 mL), dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (silica gel; 1:5 diethyl ether/ petroleum ether) gave pure **6** as a colorless oil (7.54 g, 85%). ^{1}H NMR ($CDCl_3$, δ): 0.05 (s, 6H, CH_3), 0.90 (s, 9H, CH_3), 1.26 (m, 22H, CH_2), 1.40–1.70 (m, 4H, CH_2), 2.55 (t, J = 7.8 Hz, 2H, CH_2), 3.60 (t, J = 6.6 Hz, 2H, CH_2), 6.95–7.09

(m, 2H, Ar H), 7.34–7.43 (m, 2H, Ar H). ^{13}C NMR ($CDCl_3$, δ): –5.1, 18.5, 26.0, 26.2, 29.3, 29.6, 29.7, 29.8, 31.5, 33.1, 35.5, 63.5, 119.4, 130.3, 131.4, 142.0. HRMS-CI (*m*/*z*): $[M+H]^+$ calcd for $C_{27}H_{50}OSi^{79}Br$, 497.2814; found 497.2803.

***tert*-Butyldimethyl(15-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pentadecyloxy)silane (7)**

The precursor boronic acid was initially prepared by adding *n*-BuLi (6.96 mL of a 2.5 M solution in hexanes, 17.4 mmol) dropwise to a solution of **6** (7.20 g, 14.5 mmol) in tetrahydrofuran (80 mL) at –78 °C under an atmosphere of argon. After stirring for 30 min, trimethoxyborane (1.95 g, 18.7 mmol) was added dropwise to the reaction mixture at –78 °C and then the mixture was allowed to warm to room temperature. After stirring for 12 h, deionized water (60 mL) was added followed by the addition of aqueous ammonium chloride (15 mL, 1.0 M). The mixture was extracted with ethyl acetate (3 × 70 mL). The combined organic extracts were washed with a saturated aqueous solution of sodium chloride (70 mL), dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The boronic acid was obtained as a colorless oil (6.69 g, 100%) and was used to prepare **7** without further purification. Pinacol (1.89 g, 16.0 mmol) was added to a solution of the boronic acid (6.69 g, 14.5 mmol) in toluene (100 mL) as one portion at room temperature. After refluxing the reaction mixture for 1 h, water produced during the reaction was removed using a Dean-Stark trap. The remaining mixture was concentrated under reduced pressure. Purification of the crude product by flash column chromatography (silica gel; 1:20 diethyl ether/petroleum ether) gave pure **7** as a colorless oil (4.70 g, 54%). ^{1}H NMR ($CDCl_3$, δ): 0.05 (s, 6H, CH_3), 0.91 (s, 9H, CH_3), 1.26 (m, 22H, CH_2), 1.34 (s, 12H, CH_3), 1.40–1.70 (m, 4H, CH_2), 2.62 (t, J = 7.8 Hz, 2H, CH_2), 3.60 (t, J = 6.6 Hz, 2H, CH_2), 7.13–7.23 (m, 2H, Ar H), 7.65–7.75 (m, 2H, Ar H). ^{13}C NMR ($CDCl_3$, δ): –5.1, 18.5, 25.0, 26.0, 26.2, 29.5, 29.6, 29.7, 29.8, 31.5, 33.1, 36.4, 63.5, 83.7, 128.0, 135.0, 146.6. HRMS-EI (*m*/*z*): $[M+Na]^+$ calcd for $C_{33}H_{61}{}^{11}BO_3NaSi$, 567.4375; found 567.4394.

15-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pentadecan-1-ol (8)

Hydrochloric acid (75 mL, 1 M) in methanol was added to a solution of **7** (4.65 g, 10.8 mmol) in dichloromethane (26 mL) at 0 °C. After stirring for 30 min, the reaction mixture was diluted with deionized water (80 mL) and was extracted with dichloromethane (3 × 70 mL). The combined organic extracts were washed with a saturated aqueous solution of sodium chloride (80 mL), dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (silica gel; 1:1 diethyl ether/petroleum ether) gave pure **8** as a colorless solid (3.36 g, 92%). ^1H NMR ($CDCl_3$, δ): 1.25 (m, 22H, CH_2), 1.34 (s, 12H, CH_3), 1.47–1.70 (m, 4H, CH_2), 2.61 (t, J = 7.8 Hz, 2H, CH_2), 3.64 (t, J = 6.6 Hz, 2H, CH_2), 7.13–7.23 (m, 2H, Ar H), 7.65–7.75 (m, 2H, Ar H). ^{13}C NMR ($CDCl_3$, δ): 25.0, 25.9, 29.4, 29.6, 29.7, 29.8, 31.5, 32.9, 36.3, 63.2, 83.7, 128.0, 134.9, 146.6. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{27}H_{47}{}^{11}BO_3$, 430.3618; found 430.3622.

2-(4-(15-Bromopentadecyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**9**)

The preparation of **9** has been adapted from a previously published procedure.[5] *N*-Bromosuccinamide (1.64 g, 9.20 mmol) was added to a stirred solution of triphenylphosphine (2.41 g, 9.20 mmol) and **8** (3.30 g, 7.67 mmol) in dry dichloromethane (40 mL) at 0 °C. After stirring for 1 h, the reaction mixture was diluted with deionized water (40 mL) and was extracted with dichloromethane (3 × 40 mL). The combined organic extracts were washed with a saturated aqueous solution of sodium chloride (70 mL), dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (silica gel; 1:40 diethyl ether/petroleum ether) gave pure **9** as a colorless solid (2.26 g, 60%). ^{1}H NMR (CDCl$_3$, δ): 1.26 (m, 20H, CH$_2$), 1.34 (s, 12H, CH$_3$), 1.41 (m, 2H, CH$_2$), 1.59 (m, 2H, CH$_2$), 1.86 (m, 2H, CH$_2$), 2.62 (t, *J* = 7.5 Hz, 2H, CH$_2$), 3.41 (t, *J* = 6.6 Hz, 2H, CH$_2$), 7.15–7.24 (m, 2H, Ar H), 7.68–7.79 (m, 2H, Ar H). ^{13}C NMR (CDCl$_3$, δ): 25.0, 28.3, 28.9, 29.5, 29.6, 29.7, 29.8, 31.5, 33.0, 34.2, 36.3, 83.7, 128.0, 134.9, 146.5. HRMS-EI (*m*/*z*): [M]$^+$ calcd for $C_{27}H_{46}{}^{11}BO_2{}^{79}Br$, 492.2774; found 492.2770.

N,N,N-Triethyl-15-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pentadecan-1-aminium bromide (10)

A solution of **9** (895 mg, 1.8 mmol) in triethylamine (2.2 mL, 15.8 mmol) and ethanol (9 mL) was refluxed for 24 h. After allowing the reaction mixture to cool to room temperature, it was concentrated under reduced pressure. The residual solid was then washed with diethyl ether (2 × 10 mL) to give pure **10** as a colorless solid (0.984 g, 92 %). ^{1}H NMR (CDCl$_3$, δ): 1.10–1.45 (m, 43H, CH$_2$ and CH$_3$), 1.50–1.75 (m, 4H, CH$_2$), 2.58 (t, *J* = 7.5 Hz, 2H, CH$_2$), 3.25 (t, *J* = 7.5 Hz, 2H, CH$_2$), 3.47 (q, *J* = 7.5 Hz, 6H, CH$_2$), 7.13–7.20 (m, 2H, Ar H), 7.65–7.80 (m, 2H, Ar H). ^{13}C NMR (CDCl$_3$, δ): 8.2, 22.2, 24.9, 26.6, 29.2, 29.4, 29.5, 29.6, 29.7, 31.4, 31.6, 36.0, 36.2, 53.7, 83.7, 127.9, 134.8, 146.5. HRMS-ESI (*m*/*z*): [M]$^+$ calcd for $C_{33}H_{61}{}^{11}BNO_2$ 514.4790; found 514.4779.

Potassium 4-(15-(*N*,*N*,*N*-triethylpentadecan)aminium bromide)phenyltrifluoroborate (11)

The preparation of **11** has been adapted from a previously published procedure.[6] Aqueous potassium hydrogen fluoride (0.520 mL, 2.34 mmol, 4.5 M) was added dropwise to the solution of **10** (240 mg, 0.404 mmol) in methanol (6 mL) at room temperature. After stirring for 15 min, the resulting white slurry was concentrated under reduced pressure. The residual solid was then washed with 1:1 water/methanol (2 × 5 mL) followed by dichloromethane (2 × 5 mL) to give **11** as an off-white solid (195 mg, 84%). ^{1}H NMR ($CDCl_3$, δ): 0.90–1.35 (m, 31H, CH_2 and CH_3), 1.38–1.65 (m, 4H, CH_2), 2.46 (t, J = 7.5 Hz, 2H, CH_2), 3.08 (t, J = 7.5 Hz, 2H, CH_2), 3.19 (q, J = 7.5 Hz, 6H, CH_2), 6.82–6.92 (m, 2H, Ar H), 7.16–7.26 (m, 2H, Ar H). ^{13}C NMR (DMSO-d_6, δ): 7.1, 20.7, 20.8, 25.3, 28.1, 28.5, 28.6, 28.7, 28.8, 29.0, 31.2, 31.3, 35.1, 35.2, 51.7, 63.8, 126.2, 131.3, 138.2, 170.4. HRMS-ESI (*m*/*z*): $[M]^+$ calcd for $C_{27}H_{49}{}^{11}BNF_3K$, 494.3542; found 494.3534.

10-(Hydroxyimino)-2-iodophenanthren-9-one (12)

The preparation of **12** has been adapted from a previously published procedure.[7] Initially, the precursor 2-iodo-9,10-phenanthrenedione was prepared with minor modification of a published procedure.[8] Phenanthrenequinone (6.08 g, 29.3 mmol) was dissolved in acetic acid (100 mL) and sulfuric acid (7.5 mL). Iodine (15.3 g, 60.1 mmol) was slowly added to this solution over 30 min. The mixture was heated to 100 °C and nitric acid (3 mL) was added. The reaction mixture was refluxed for 6 h and then cooled to room temperature. The mixture was poured into water (300 mL) and the resulting precipitate was collected by vacuum filtration, washed with water (3 × 30 mL), a 10% aqueous solution of sodium carbonate (3 × 30 mL) and a 1 N aqueous solution of sodium thiosulfate (3 × 30 mL). The crude product was filtered with a short silica gel column (chloroform), recrystallized thrice from ethyl acetate to remove starting material, and purified by gravity column chromatography (silica gel; dichloromethane) to give pure 2-iodo-9,10-phenanthrenedione as orange crystals (1.18 g, 12%), mp 224–225 °C (lit. 225 °C[9]). ^{1}H NMR ($CDCl_3$, δ): 7.47 (ddd, *J* = 0.9, 7.5, 7.5 Hz, 1H, Ar H-7), 7.67–7.74 (m, 2H, Ar H-4,5) 7.95–8.04 (m, 2H, Ar H-6,8), 8.18 (dd, *J* = 1.2, 6.3 Hz, 1H, Ar H-3), 8.47 (d, *J* = 1.2 Hz, 1H, Ar H-1). ^{13}C NMR ($CDCl_3$, δ): 96.3, 125.1, 127.2, 129.9, 130.4, 132.1, 133.4, 135.3, 135.3, 136.1, 137.7, 144.0, 178.4, 178.8. HRMS-EI (*m/z*): $[M]^+$ calcd for $C_{14}H_7O_2I$, 333.9485; found 333.9488. Subsequently, a mixture of 2-iodo-9,10-phenanthrenedione (715 mg, 2.14 mmol), ethanol (40 mL), pyridine (1.4 mL) and hydroxylamine hydrochloride (205 mg, 2.95 mmol) was refluxed for 3 h. The reaction mixture was cooled to room temperature and then concentrated under reduced pressure. Purification of the crude product by flash column chromatography (silica gel; 1:1 petroleum ether/dichloromethane) gave pure **12** as a yellow solid (682 mg, 91%), mp 153–155 °C. ^{1}H NMR ($CDCl_3$, δ): 7.40–7.57 (m, 1H, Ar H), 7.69–7.88 (m, 3H, Ar H), 7.95–8.12(m, 1H, Ar H), 8.23–8.39 (m, 1H, Ar H), 8.57–8.67 (m, 1H, Ar H). ^{13}C NMR ($CDCl_3$, δ): 95.7, 123.5, 124.2, 124.9, 127.7, 128.9, 129.5, 130.1, 130.4, 132.9, 136.5, 138.9, 144.8, 181.7. HRMS-EI (*m/z*): $[M]^+$ calcd for $C_{14}H_8NO_2I$, 348.9600; found 348.9601.

1,4-Bis(6'-iodo-3,3-dimethylspiro[indoline-2,2'-[2H]phenanthro[9,10-b][1,4]oxazine]-1-yl)butane (13)

Initially, the precursor bisindoline was prepared in two steps with minor modification of a published procedure.[10] Briefly, 2,3,3-trimethylindolenine (6.67 g, 41.9 mmol) and 1,4-dibromobutane (2.57 g, 11.9 mmol) were stirred at 140 °C. After stirring for 22 h, the resulting precipitate was collected by vacuum filtration, washed with diethyl ether (3 × 30 mL) and acetone (3 × 30 mL). Recrystallization from water gave 1-(4-(3,3-dimethyl-2-methyleneindolin-1-yl)butyl)-2,3,3-trimethyl-3H-indolium bromide as purple crystals (3.24 g, 60%) Subsequently, the indoleninium salt (1.26 g, 2.77 mmol) was added to a 1 N aqueous solution of potassium hydroxide (11 mL, 11mmol) and was stirred vigorously at room temperature. After stirring for 2 h, the reaction mixture was extracted with diethyl ether (3 × 8 mL). The combined organic extracts were washed with a saturated aqueous solution of sodium chloride (2 × 8 mL), dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (basic aluminum oxide; 10:1 petroleum ether/diethyl ether) gave pure 1,4-bis(3,3-dimethyl-2-methyleneindolin-1-yl)butane as pink crystals (605 mg, 59%), mp 103–105 °C. ^{1}H NMR ($CDCl_3$, δ): 1.34 (s, 12H, CH_3), 1.74 (m, 4H, CH_2), 3.55 (t, *J* = 6 Hz, 4H, CH_2), 3.87 (m, 4H, CH_2), 6.51 (d, *J* = 7.5 Hz, 2H, Ar H-7), 6.77 (dt, *J* =1.0, 7.5 Hz, 2H, Ar H-5), 7.09 –7.15 (m, 4 H, Ar H-4,6). ^{13}C NMR ($CDCl_3$, δ): 24.3, 30.3, 42.4, 44.4, 73.4, 105.3, 118.5, 122.1, 127.7, 137.8, 146.1, 161.8. A solution of **12** (393 mg, 1.06 mmol) in ethanol (100 mL) was added dropwise over 3 h to a refluxing solution of the bisindoline (740 mg, 2.12 mmol) in ethanol (25 mL). After refluxing for an additional 18 h, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. Purification of the crude product twice by flash column chromatography (neutral aluminum oxide; 3:1 petroleum ether/dichloromethane) and recrystallization from diethyl ether gave **13** as a blue solid (285 mg, 26%), mp 207–208 °C. ^{1}H NMR ($CDCl_3$, δ): 1.15–1.35 (m, 12H, CH_3), 1.45–1.60 (m, 4H, CH_2), 2.95–3.20 (m, 4H, CH_2), 6.30–6.45 (m, 2H, Ar H-7), 6.77–6.92 (m, 2H, Ar H-5), 6.97–7.19 (m, 4H, Ar H-4,6), 7.38–7.52 (m, 2H, Ar H-11’), 7.53–7.69 (m, 4H, Ar H-10’,3’), 7.73–7.89 (m, 2H, Ar H-12’), 7.93–8.06 (m, 2H, Ar H-8’), 8.17–8.31 (m, 2H, Ar H-7’), 8.42–8.56 (m, 2H, Ar H-5’), 8.93–9.05 (m, 2H, Ar H-9’). ^{13}C NMR ($CDCl_3$, δ): 14.3, 22.8, 25.4, 31.7, 44.2, 51.9, 94.0, 99.6, 106.9, 118.6, 119.7, 121.9, 122.6, 122.8, 124.3, 124.5, 125.5, 127.3, 128.1, 128.2, 131.0, 131.3, 131.6, 133.6, 135.6, 146.7, 151.2. HRMS-FD (*m/z*): $[M]^+$ calcd for $C_{54}H_{44}N_4O_2I_2$, 1034.1554; found 1034.1529.

1,4-Bis(6'-(4-(15-(triethylammonio)pentadecyl)phenyl)-3,3-dimethylspiro[indoline-2,2'-[2H]phenanthro[9,10-b][1,4]oxazine]-1-yl)butane dibromide (2)

Initially, the precursor 15-(4-boronophenyl)-*N,N,N*-triethylpentadecan-1-aminium bromide was prepared with minor modification of a published procedure.[6] Briefly, trimethylsilyl chloride (106 µL, 0.836 mmol) was added dropwise to a stirred suspension of **11** (160 mg, 0.279 mmol) in acetonitrile (5 mL) and water (15 µL, 0.836 mmol) at room temperature. After stirring for 1 h, the reaction mixture was quenched with a saturated aqueous solution of sodium bicarbonate (0.5 mL) and concentrated under reduced pressure. The residual white solid was used to prepare **2** without further purification. The boronic acid (90 mg, 0.18 mmol), **13** (60 mg, 0.058 mmol), $Pd(Ph_3P)_4$ (15 mg, 0.013 mmol) and 1,4-dioxane (5 mL) were refluxed under an atmosphere of argon. This was followed by the dropwise addition of aqueous sodium carbonate (0.2 mL, 2.0 M). After stirring for 15 h, the reaction mixture was cooled to room temperature, filtered with a short basic aluminum oxide column (methanol) and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (basic aluminum oxide; 20:1 acetonitrile/methanol) gave pure **2** as a blue solid (22 mg, 22%). ^{1}H NMR ($CDCl_3$, δ): 1.00–1.49 (m, 74H, CH_2 and CH_3), 1.50–1.80 (m, 12H, CH_2), 2.53–2.75 (m, 4H, CH_2), 3.15–3.33 (m, 4H, CH_2), 3.38–3.57 (m, 16H, CH_2), 6.25–6.40 (m, 2H, Ar H), 6.75–6.90 (m, 2H, Ar H), 6.95–7.15 (m, 4H, Ar H), 7.20–8.25 (m, 17H, Ar H), 8.49–8.70 (m, 4H, Ar H), 8.73–8.81 (m, 1H, Ar H), 8.83–8.92 (m, 1H, Ar H), 9.00–9.20 (m, 1H, Ar H). We were unable to obtain a ^{13}C NMR spectrum for **2** due to its low solubility. HRMS-ESI (*m/z*): $[M + 2H]^{2+}$ calcd for $C_{108}H_{142}N_6O_2$, 777.5591; found 777.5582.

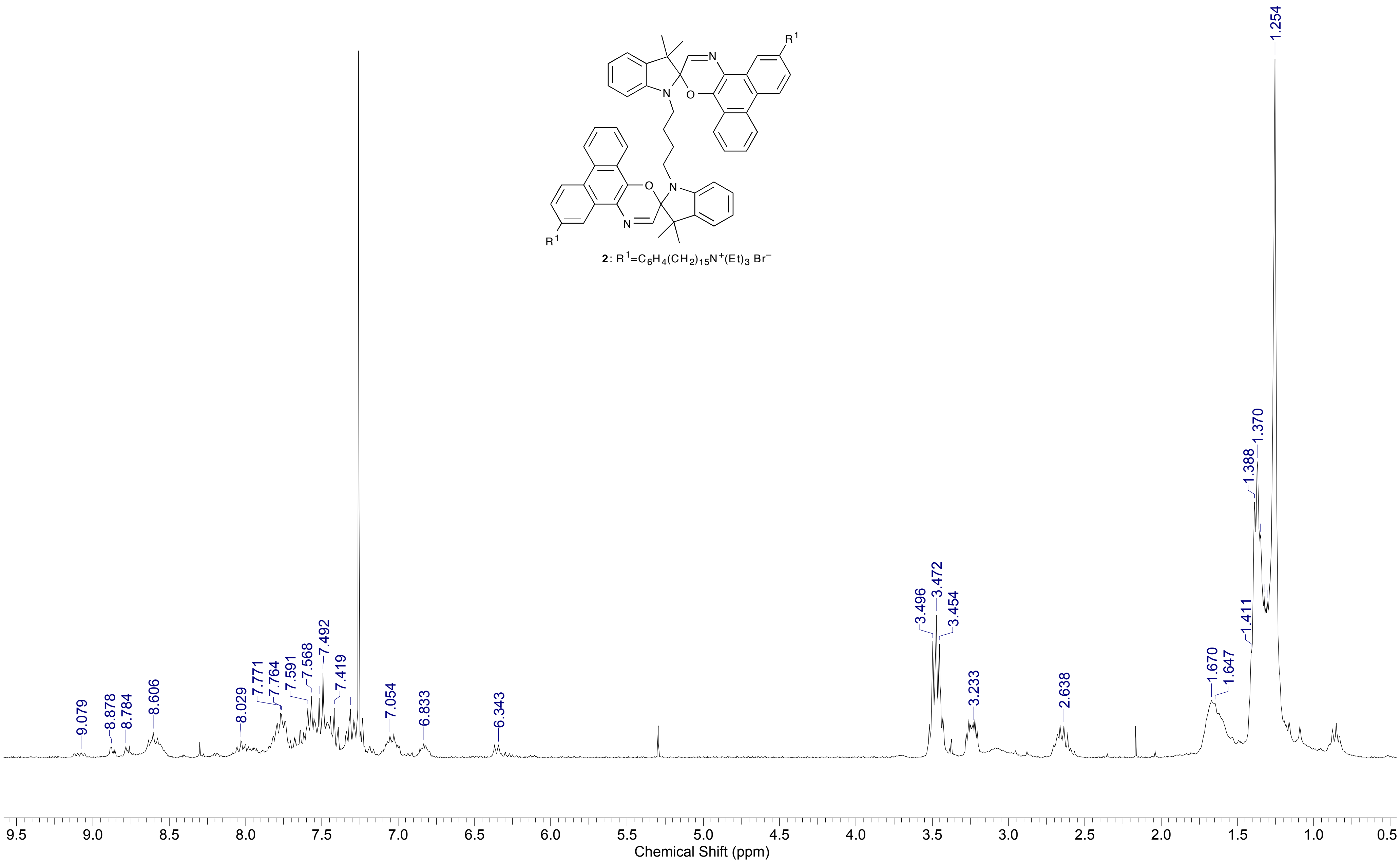
N-(6-Bromohexyl)-3,3-dimethylspiro[indoline-2,2'-[2H]phenanthro[9,10-b][1,4]oxazine] (14)

The preparation of **14** has been adapted from a previously published procedure.[11] A solution of 10-(hydroxyimino)phenanthren-9-one (1.91 g, 8.56 mmol) in ethanol (150 mL) was added dropwise over 3 h to a refluxing solution of *N*-(12-bromohexyl)-3,3dimethyl-2-methyleneindoline (2.75 g, 8.56 mmol) in ethanol (120 mL). After refluxing for an additional 7 h, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. Purification of the crude product twice by flash column chromatography (silica gel; 1:40 ethyl acetate/petroleum ether w/ 0.5% ammonium hydroxide) gave **14** as a blue oil (1.13 g, 15%). ^{1}H NMR ($CDCl_3$, δ): 1.25–1.34 (m, 4H, CH_2), 1.39 (s, 6H, CH_3), 1.57 (m, 2H, CH_2), 1.68 (m, 2H, CH_2), 3.24 (m, 4H, CH_2), 6.60 (d, *J* = 7.6 Hz, 1H, H-7), 6.89 (dt, *J* = 0.9, 7.1 Hz, 1H, H-5), 7.08 (dd, *J* = 0.9, 6.5 Hz, 1H, H-4), 7.22 (dt, *J* = 1.2, 7.6 Hz, 1H, H-6), 7.61 (m, 4H, H-6’7’10’11’), 7.81 (s, 1H, H-3’), 8.12 (dd, *J* = 1.2, 8.2 Hz, 1H, H-12’), 8.62 (m, 3H, H-5’8’9’). ^{13}C NMR ($CDCl_3$, δ): 21.3, 25.8, 26.7, 28.0, 28.8, 32.8, 33.8, 44.5, 52.0, 99.6, 107.0, 119.6, 119.9, 122.0, 122.4, 122.7, 122.9, 124.7, 125.1, 126.6, 126.9, 127.6, 127.9, 128.1, 129.1, 130.2, 131.1, 131.6, 136.0, 139.5, 147.1, 151.0. HRMS-EI (*m/z*): $[M]^+$ calcd for $C_{31}H_{31}N_2O^{81}Br$, 526.1599; found 528.1620.

N-(6-(Triethylammonio)hexyl)-3,3-dimethylspiro[indoline-2,2'-[2H]phenanthro[9,10-b][1,4]oxazine] bromide (3)

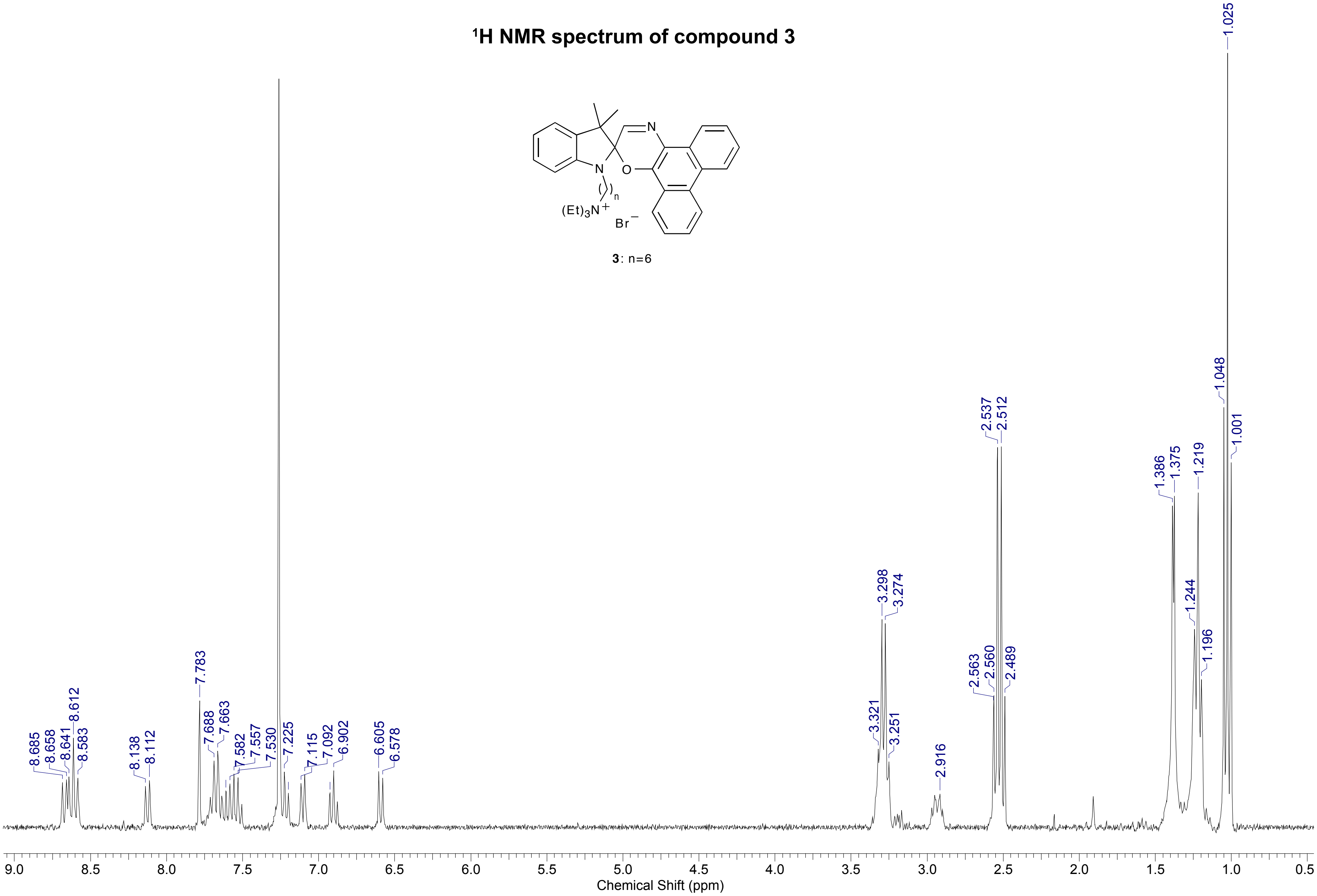
The preparation of **3** has been adapted from a previously published procedure.[11] A solution of **14** (1.13 g, 2.14 mmol) in triethylamine (3.00 mL, 40.8 mmol) and benzene (4.35 mL) was refluxed for 6 h. After allowing the reaction mixture to cool to room temperature, it was concentrated under reduced pressure. Purification of the crude product three times by flash column chromatography (silica gel; 1:8 ethyl acetate/petroleum ether once and 50:10:1 chloroform/methanol/water twice) gave **3** as a blue solid (300 mg, 22%). ^{1}H NMR ($CDCl_3$, δ): 1.02 (t, *J* = 7.4 Hz, 9H, CH_3), 1.22 (m, 8H, CH_2), 1.38 (m, 6H, CH_3), 2.53 (q, *J* = 7.0 Hz, 6H, CH_3), 3.25–3.40 (m, 4H, CH_2), 6.60 (d, *J* = 7.9 Hz, 1H, H-7), 6.89 (d, *J* = 7.4 Hz, 1H, H-5), 7.08 (d, *J* = 7.1, 1H, H-4), 7.22 (t, *J* = 7.6, 1H, H-6), 7.63 (m, 4H, H-6’7’10’11’), 7.78 (s, 1H, H-3’), 8.12 (d, *J* = 8.2 Hz, 1H, H-12’), 8.61 (m, 3H, H-5’8’9’). ^{13}C NMR ($CDCl_3$, δ): 8.2, 9.0, 9.2, 21.2, 21.9, 25.6, 26.1, 26.9, 28.4, 44.1, 46.4, 46.7, 52.0, 53.7, 99.4, 107.0, 119.7, 122.0, 122.4, 122.7, 122.8, 122.9, 124.6, 125.2, 126.4, 127.1, 127.6, 128.1, 128.1, 130.1, 131.4, 135.6, 146.8, 151.1. HRMS-ESI (*m*/*z*): $[M]^+$ calcd for $C_{37}H_{46}N_3O$, 548.3635; found 548.3639.

^{1}H NMR spectrum of compound 2

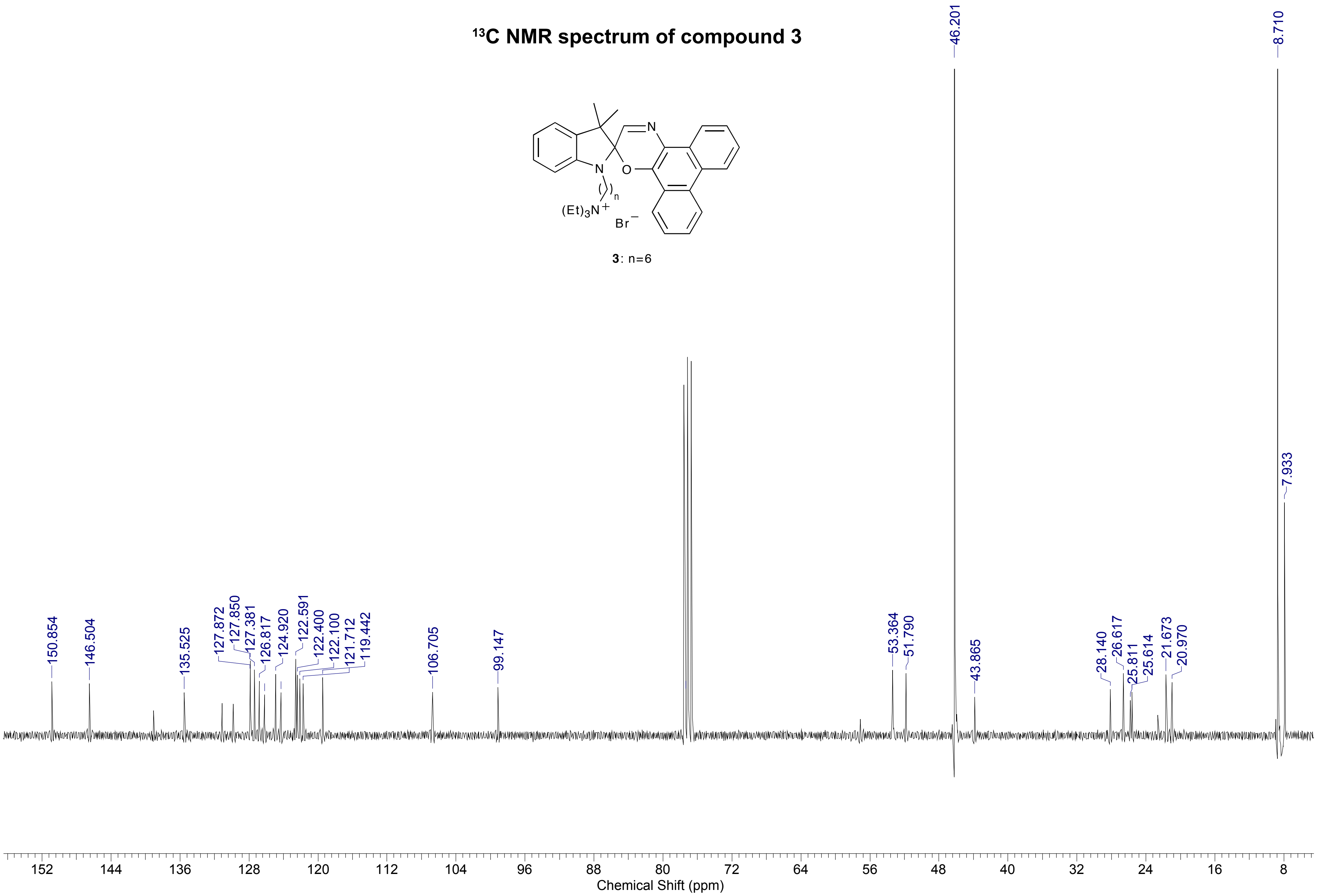


2: R^1=$C_6H_4(CH_2)_{15}N^+(Et)_3$ Br^-

^{1}H NMR spectrum of compound 3

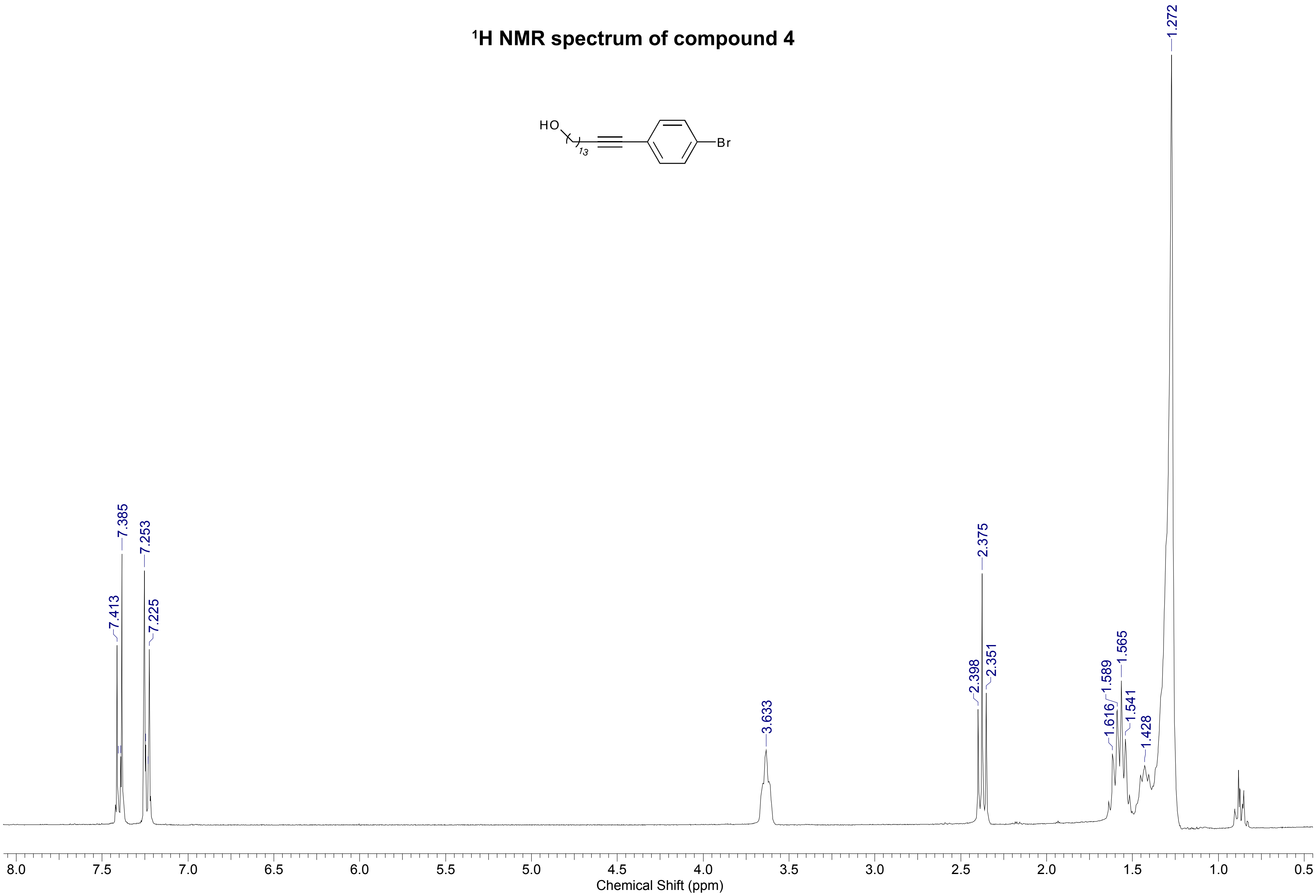


¹³C NMR spectrum of compound 3

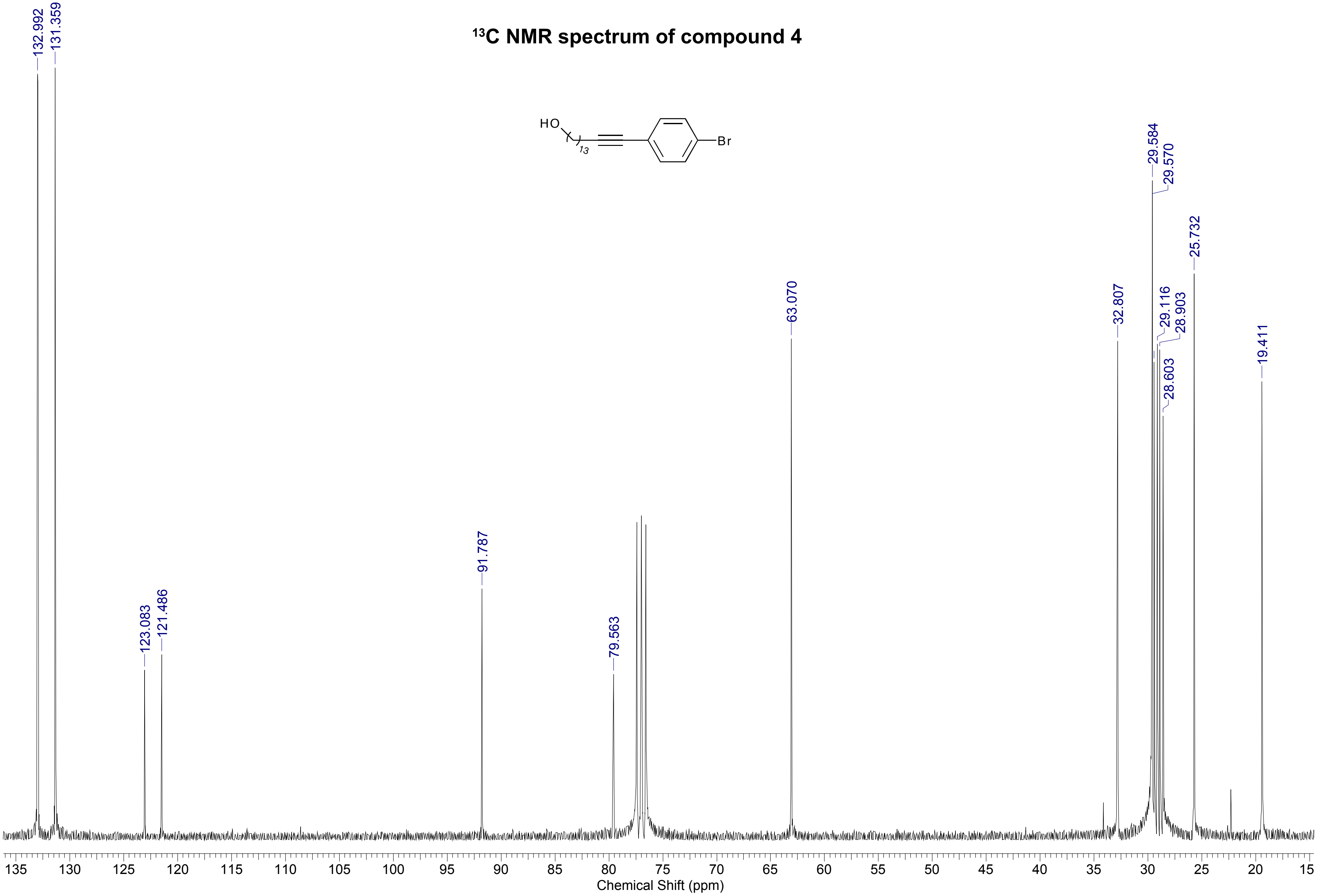


3: n=6

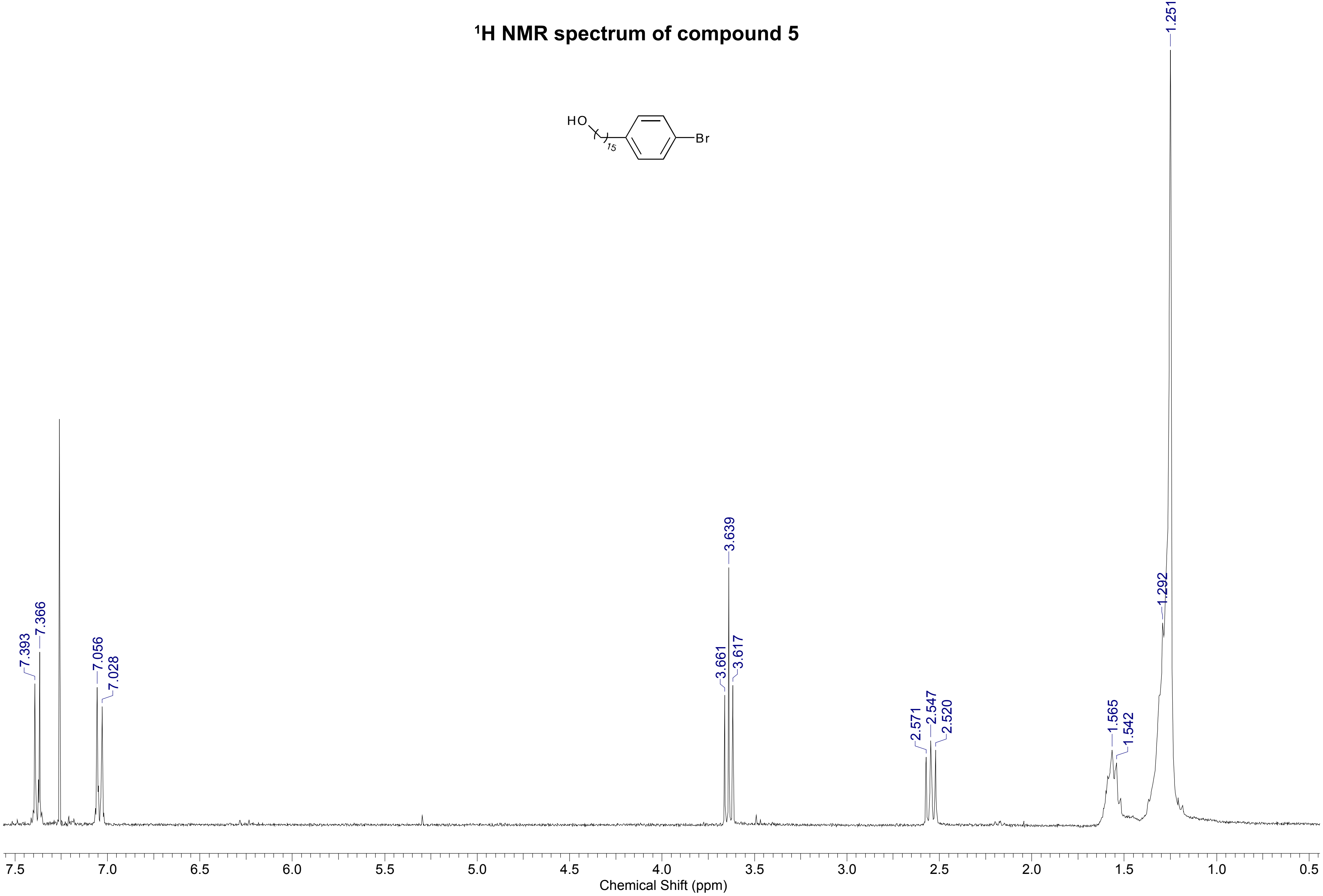
¹H NMR spectrum of compound 4



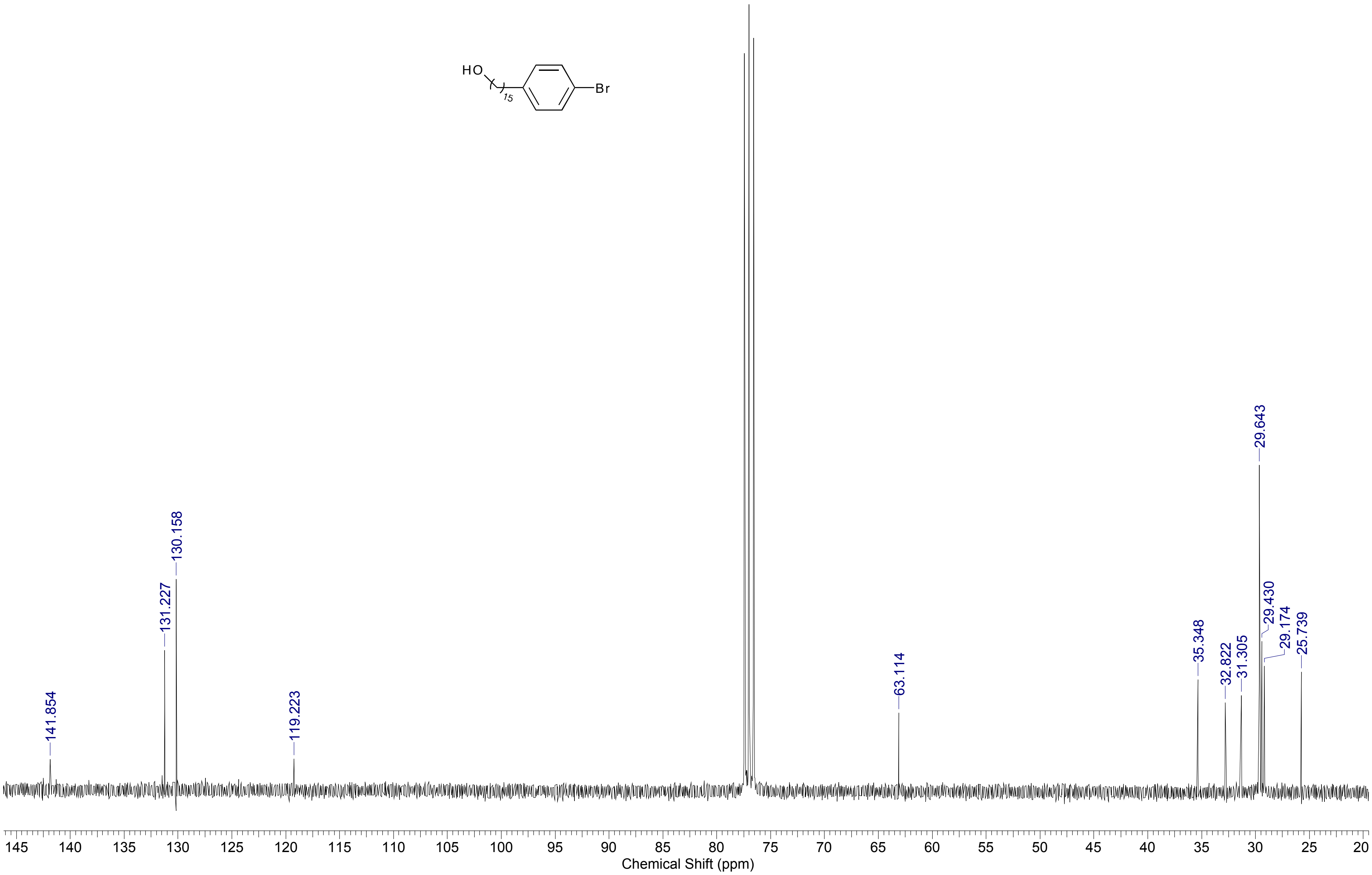
^{13}C NMR spectrum of compound 4



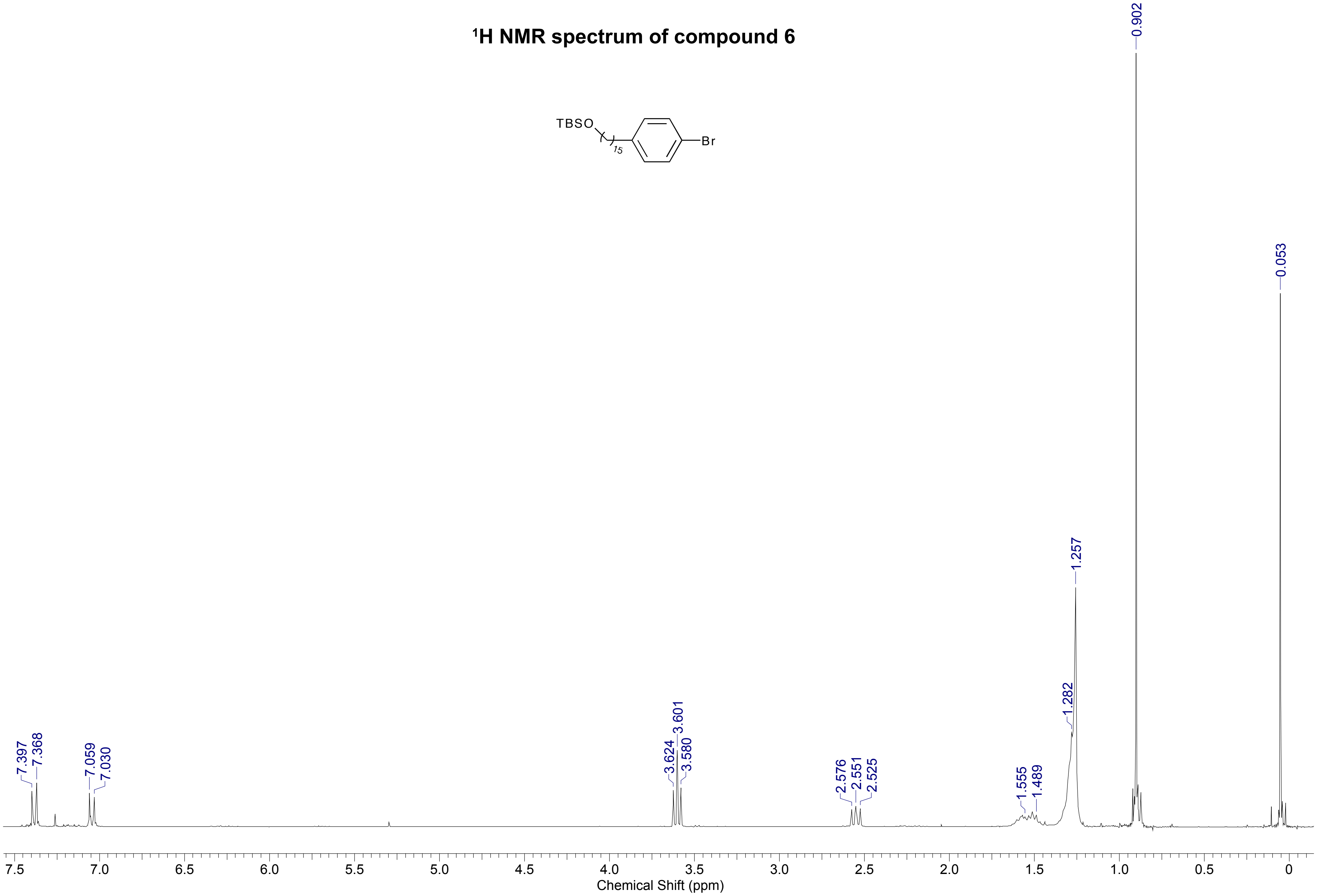
^{1}H NMR spectrum of compound 5



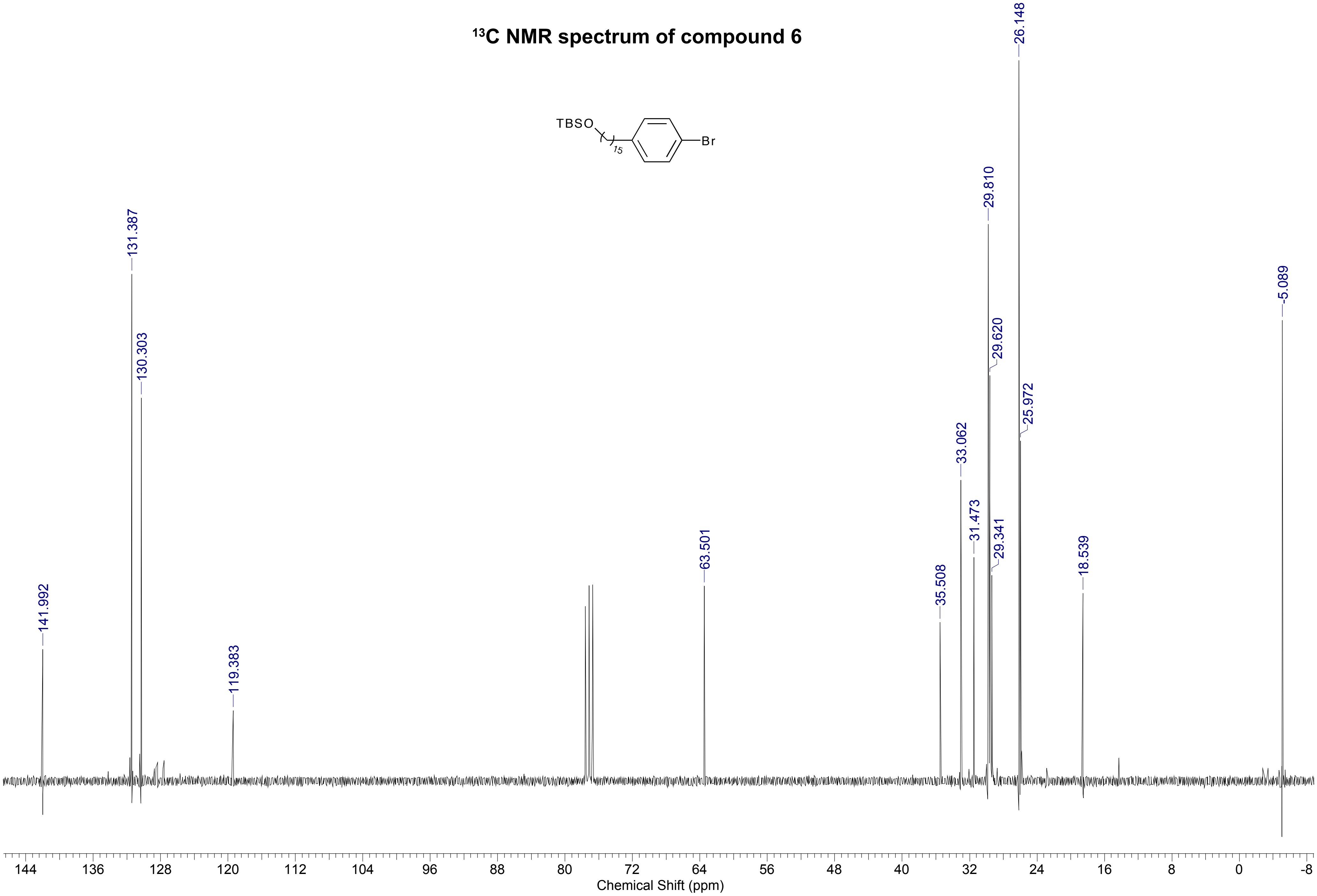
^{13}C NMR spectrum of compound 5



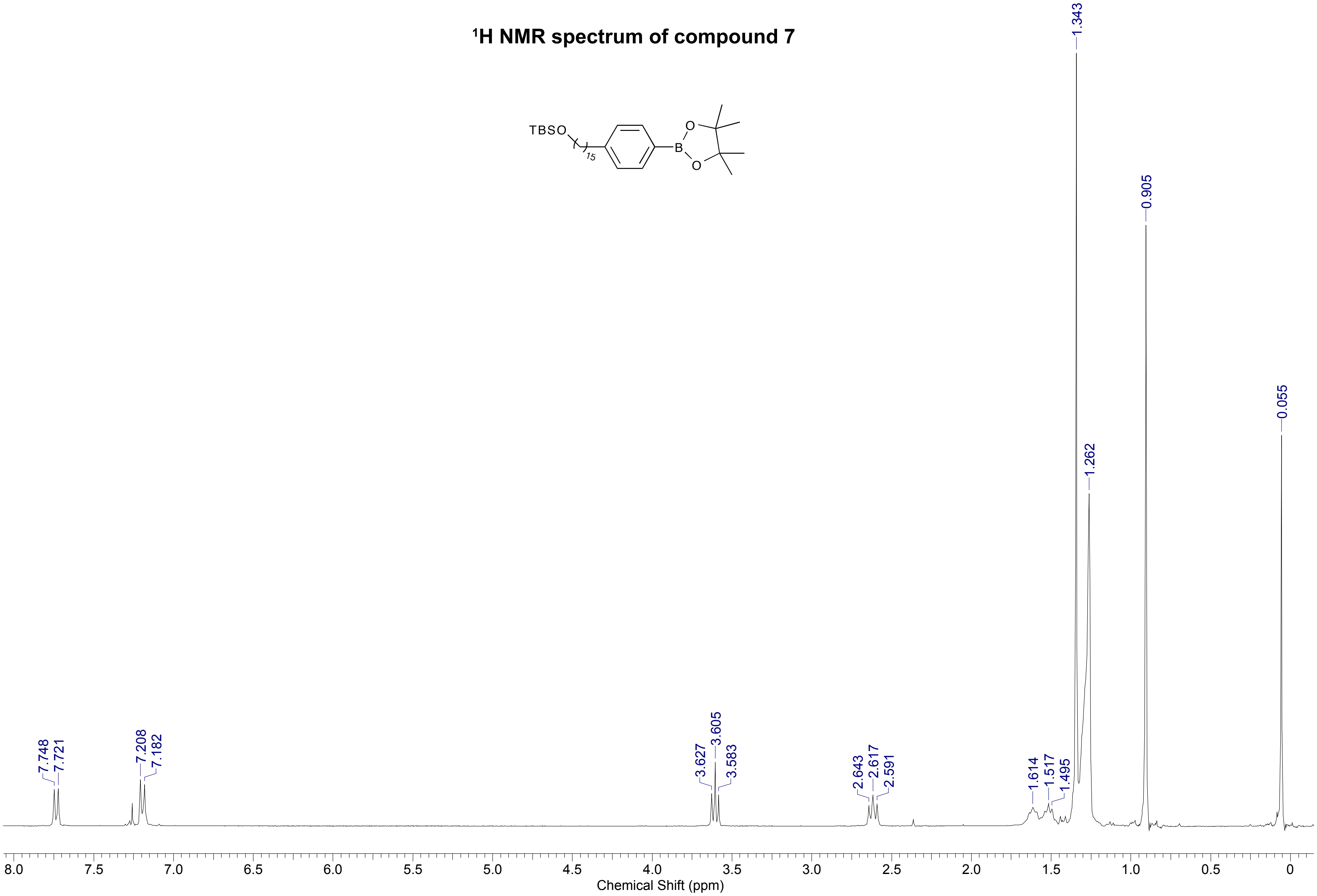
^{1}H NMR spectrum of compound 6



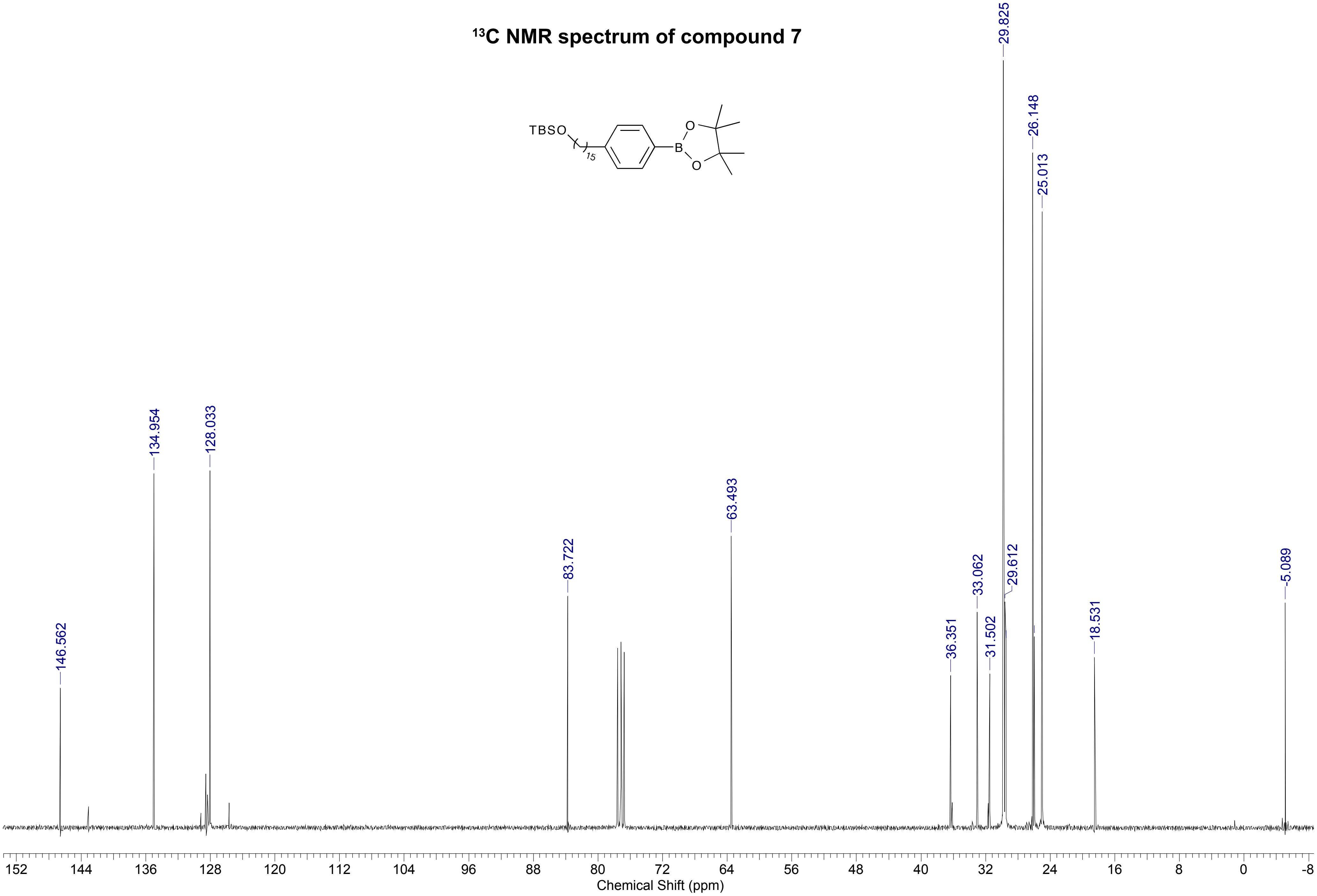
^{13}C NMR spectrum of compound 6



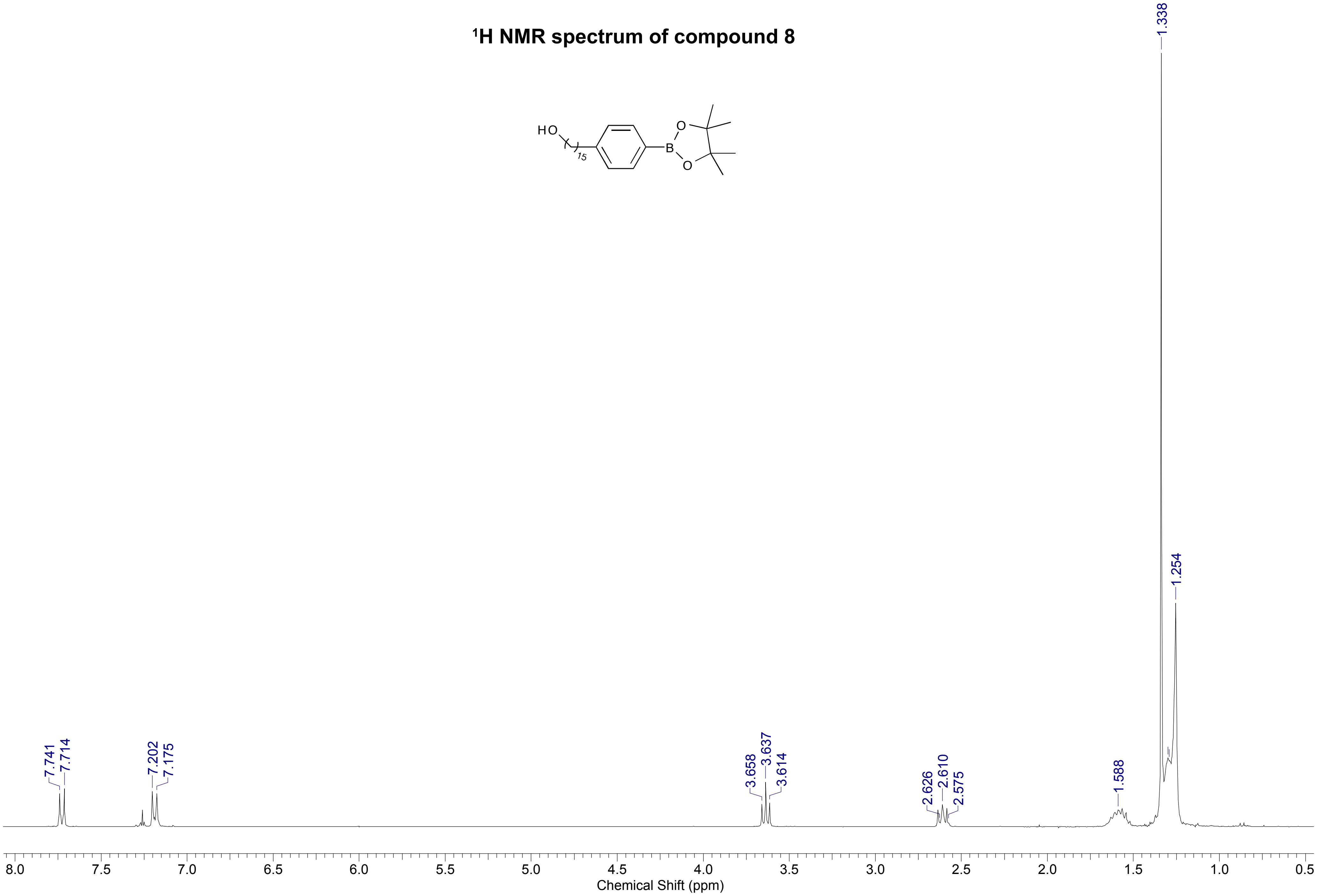
^{1}H NMR spectrum of compound 7



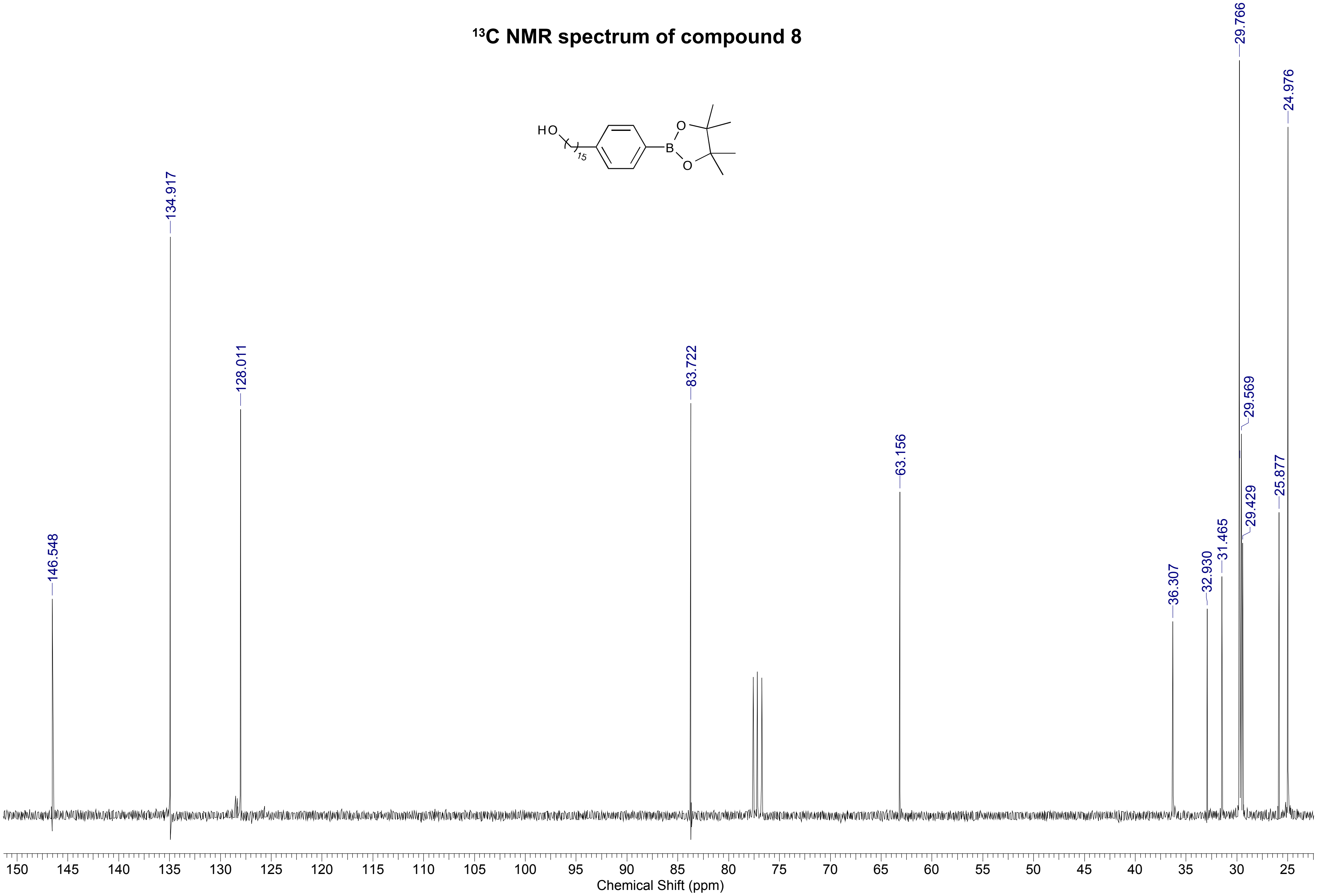
^{13}C NMR spectrum of compound 7



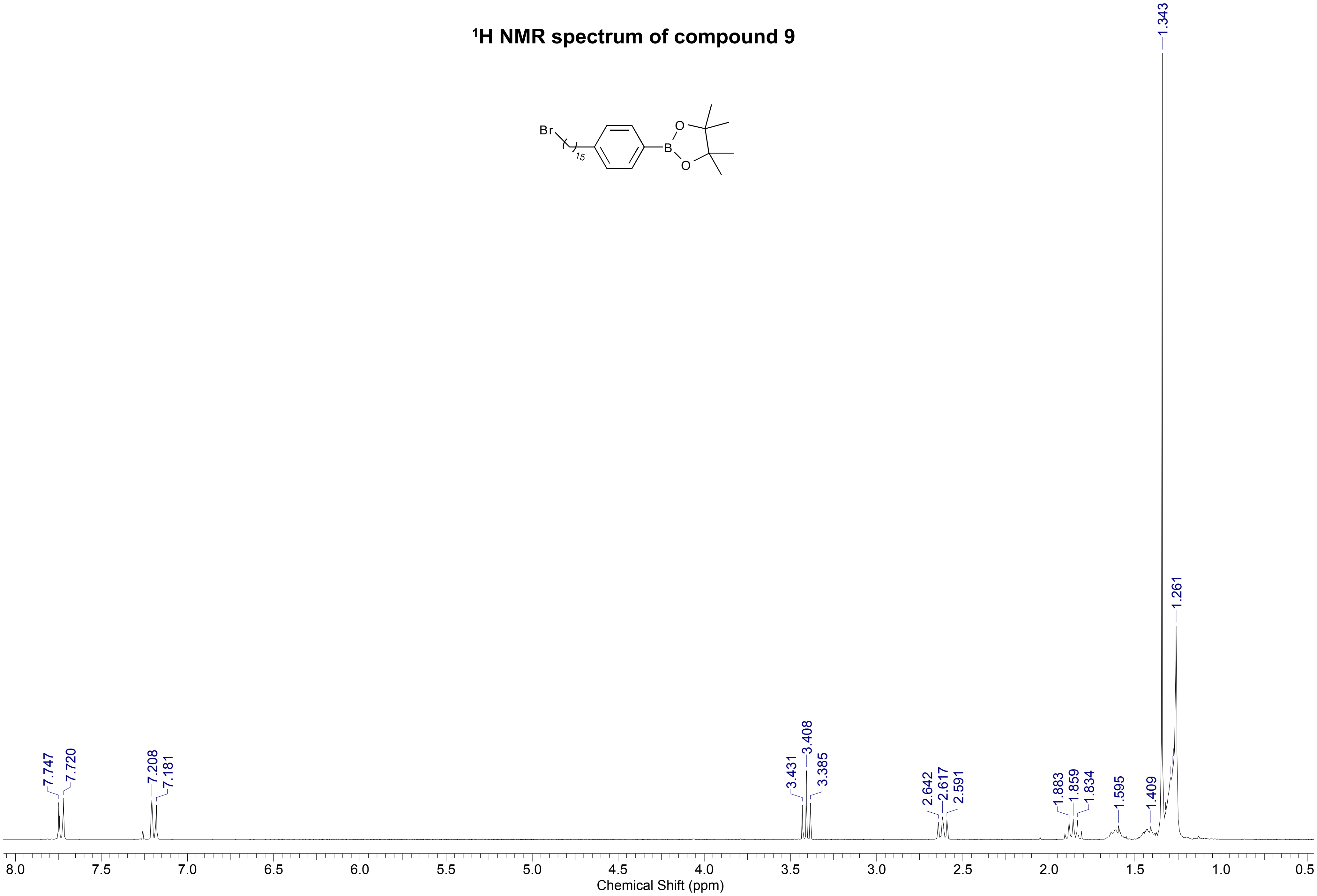
^{1}H NMR spectrum of compound 8



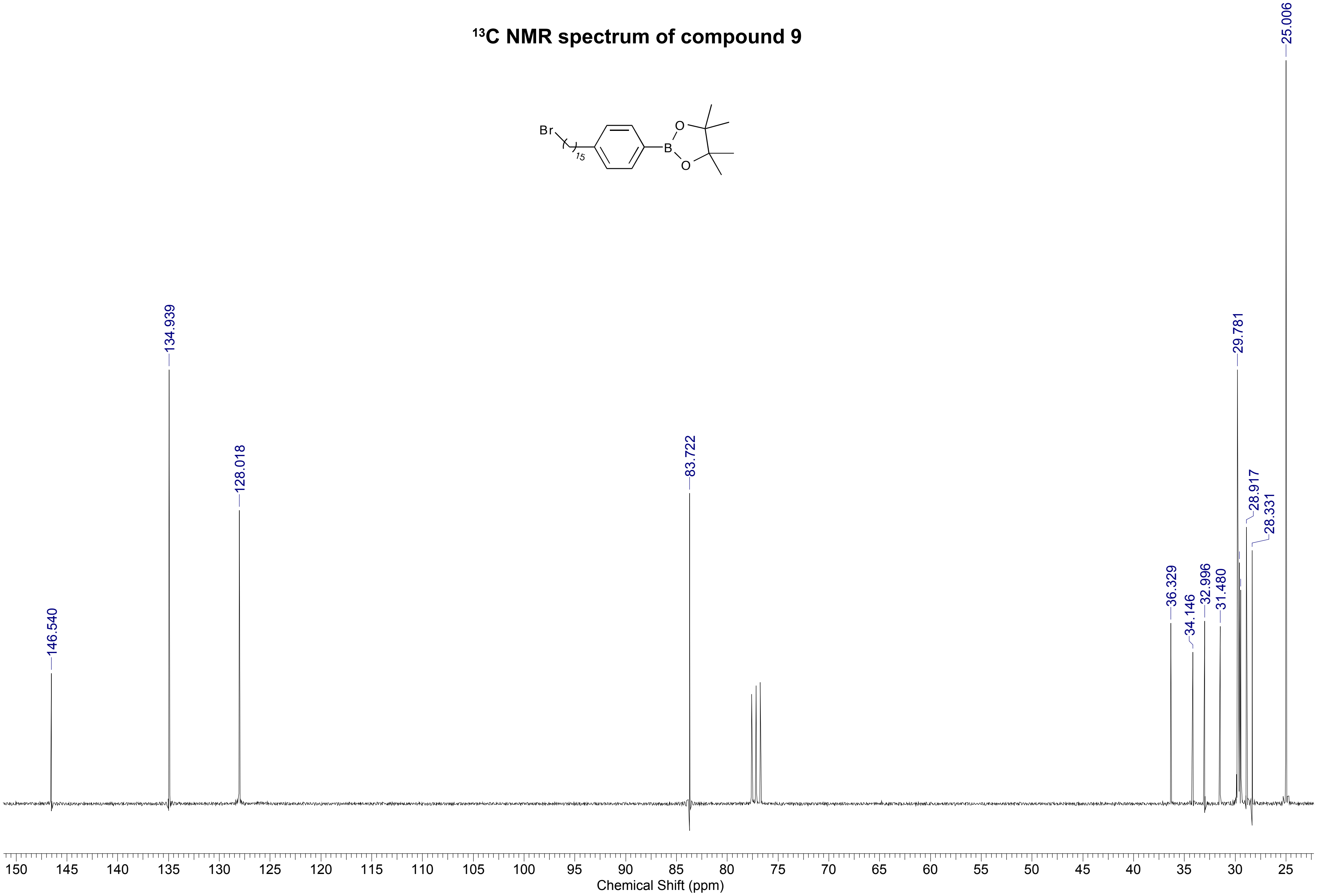
^{13}C NMR spectrum of compound 8



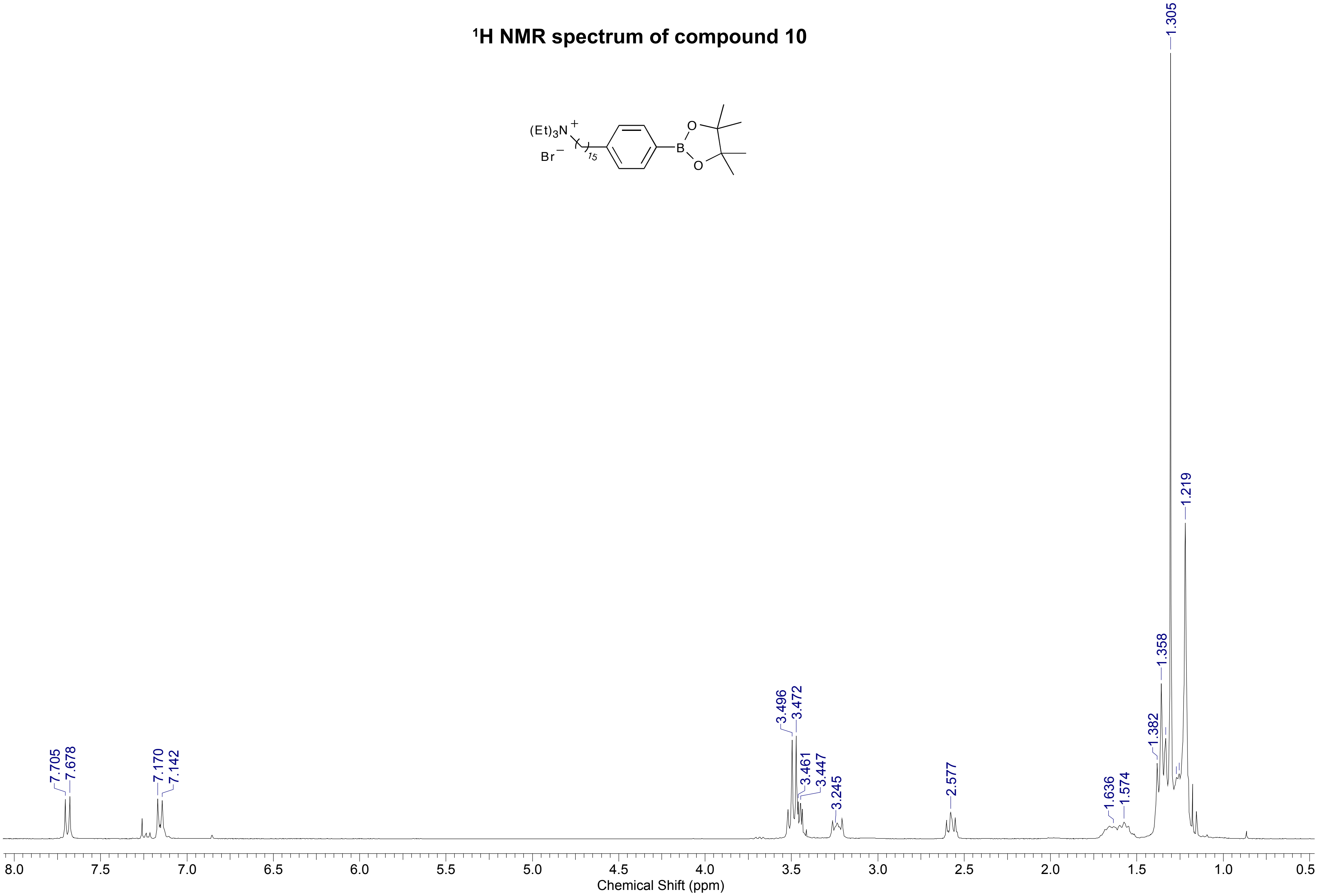
^{1}H NMR spectrum of compound 9



^{13}C NMR spectrum of compound 9



^{1}H NMR spectrum of compound 10



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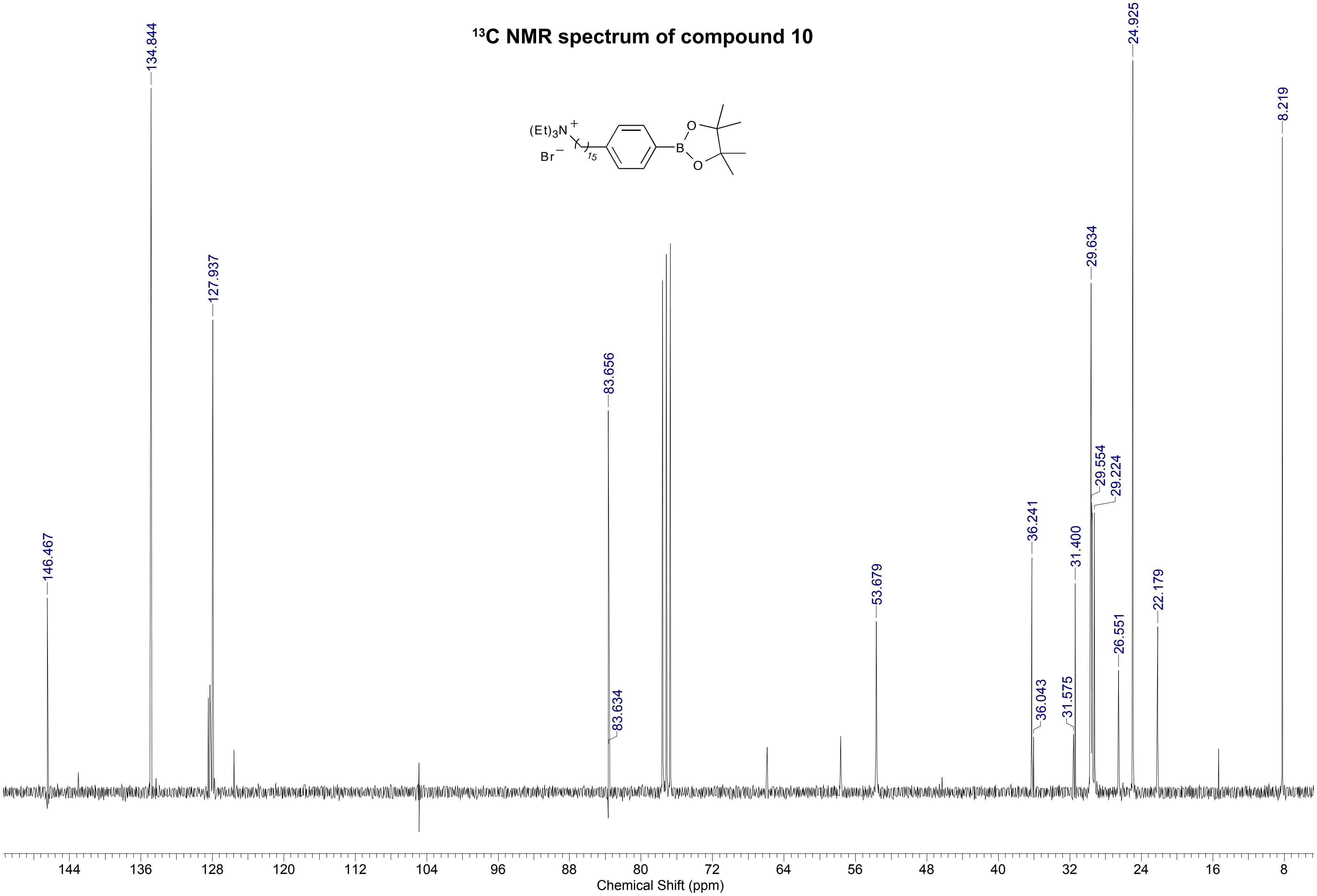
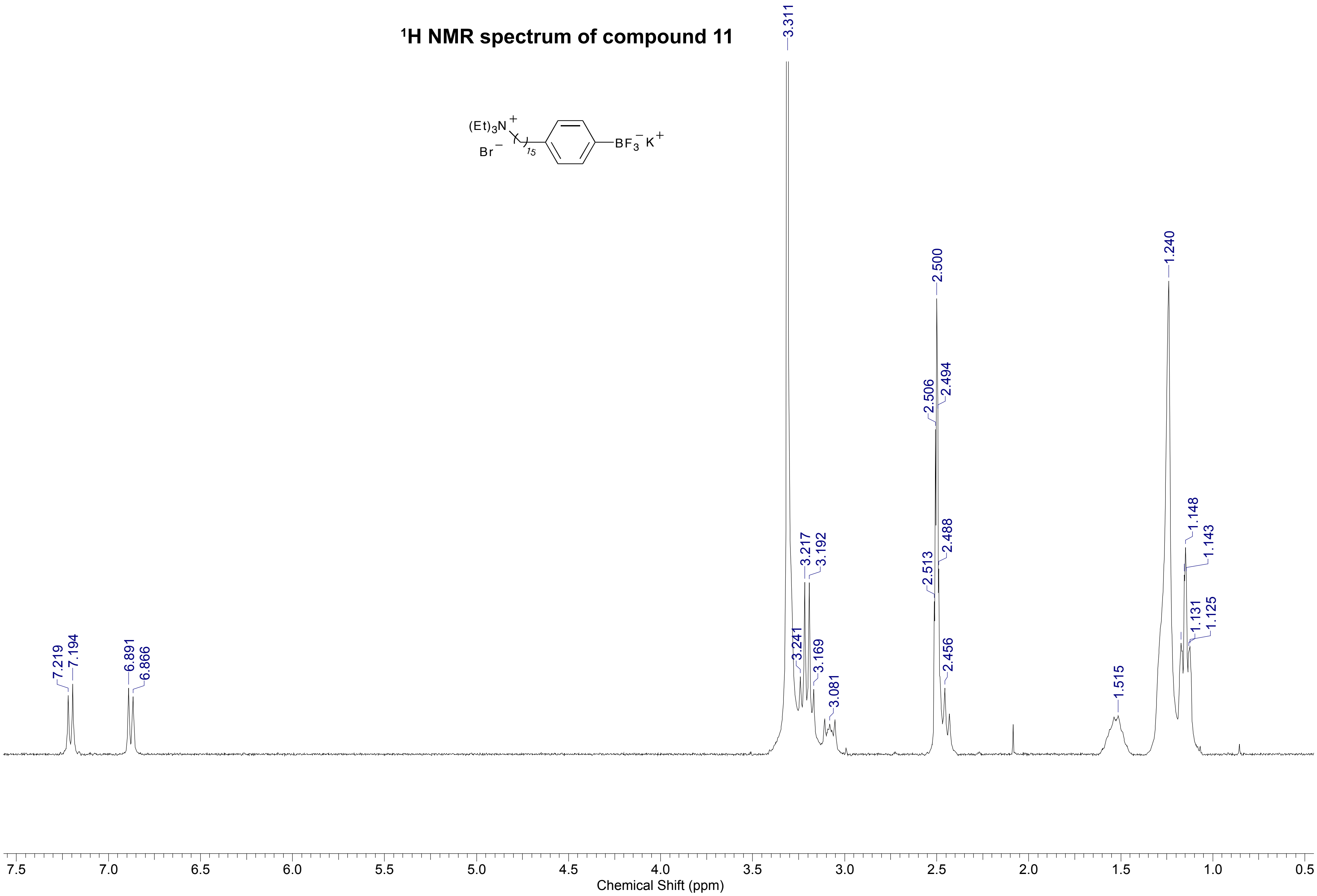
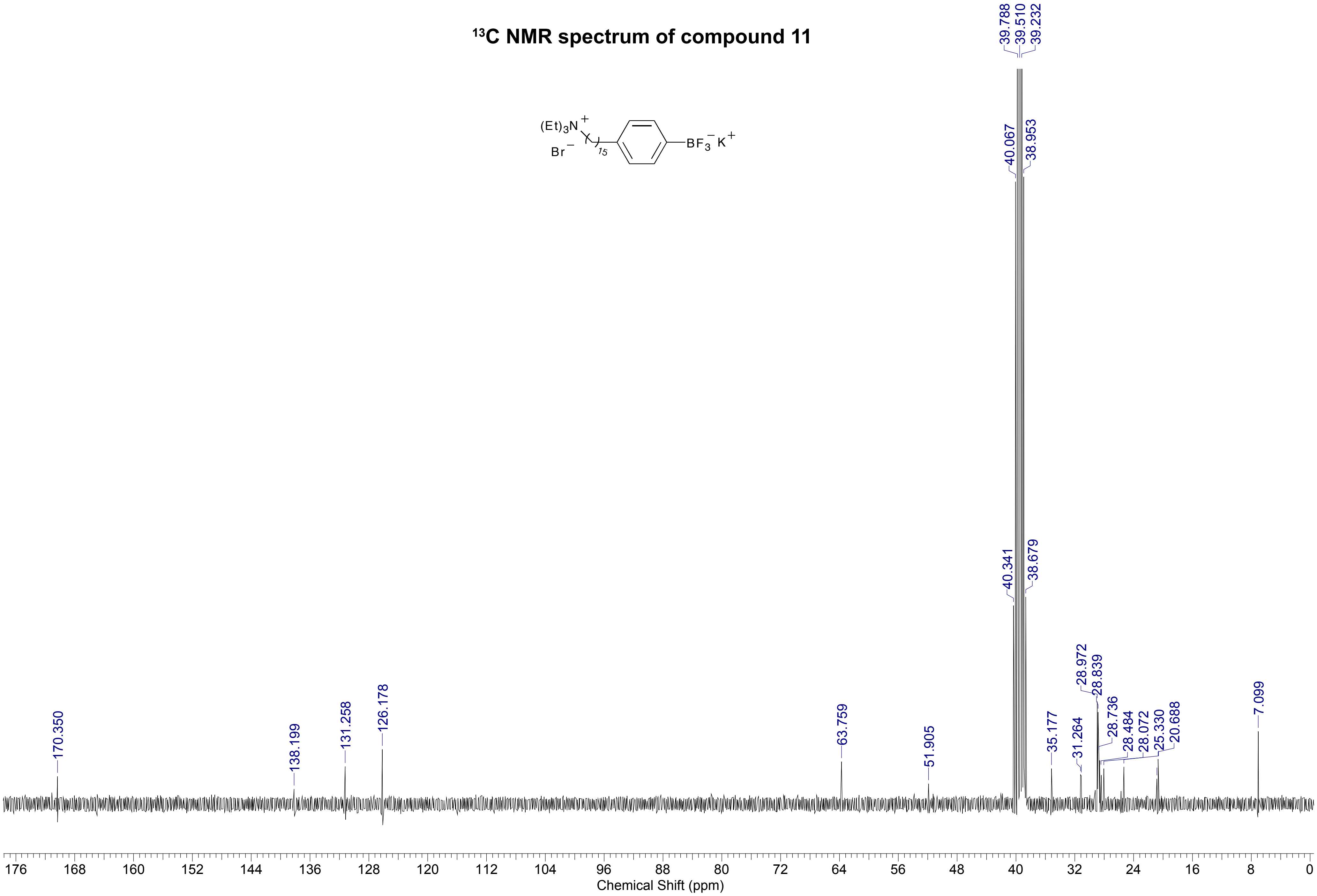


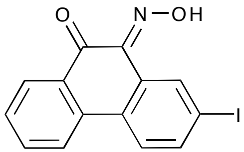


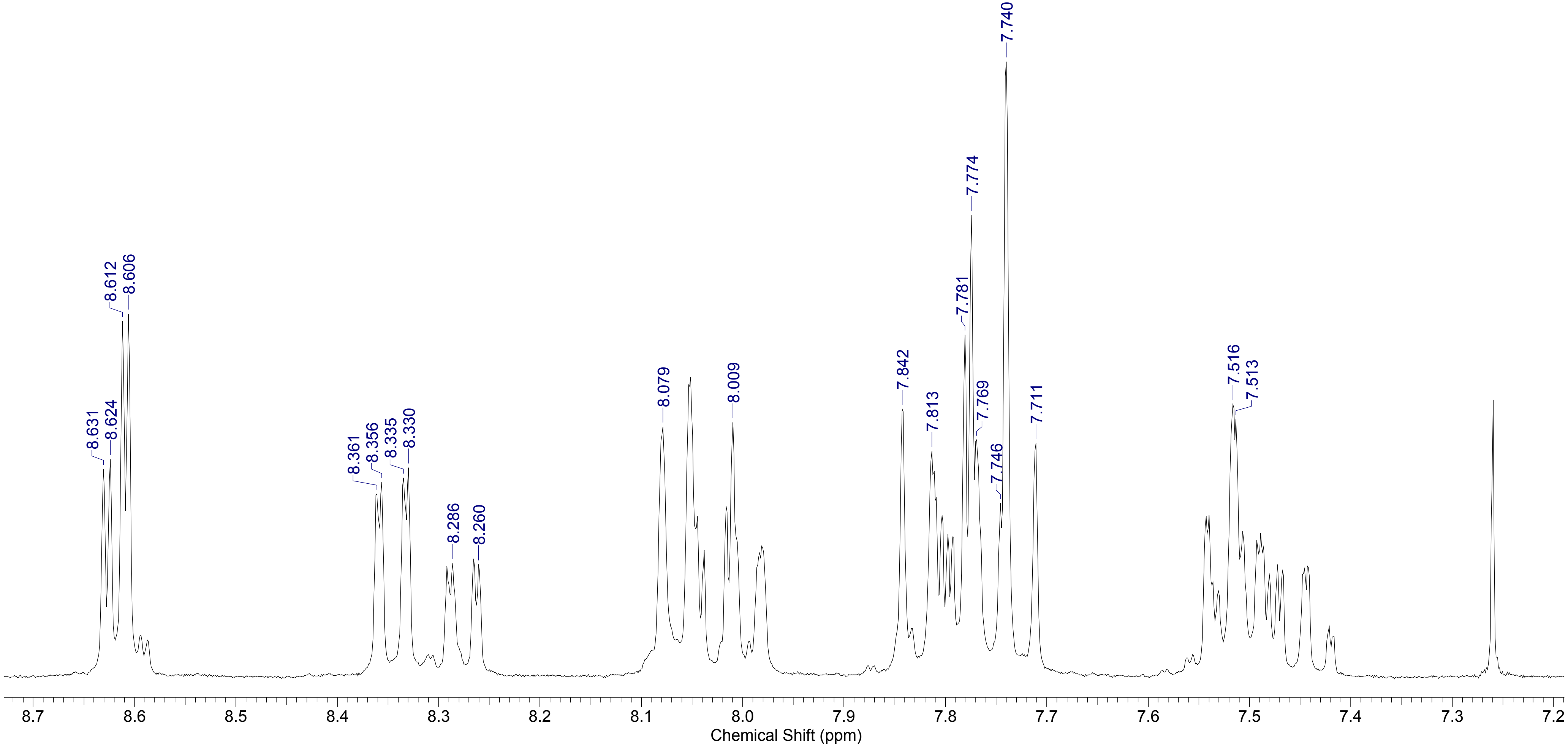
^{1}H NMR spectrum of compound 11

^{13}C NMR spectrum of compound 11

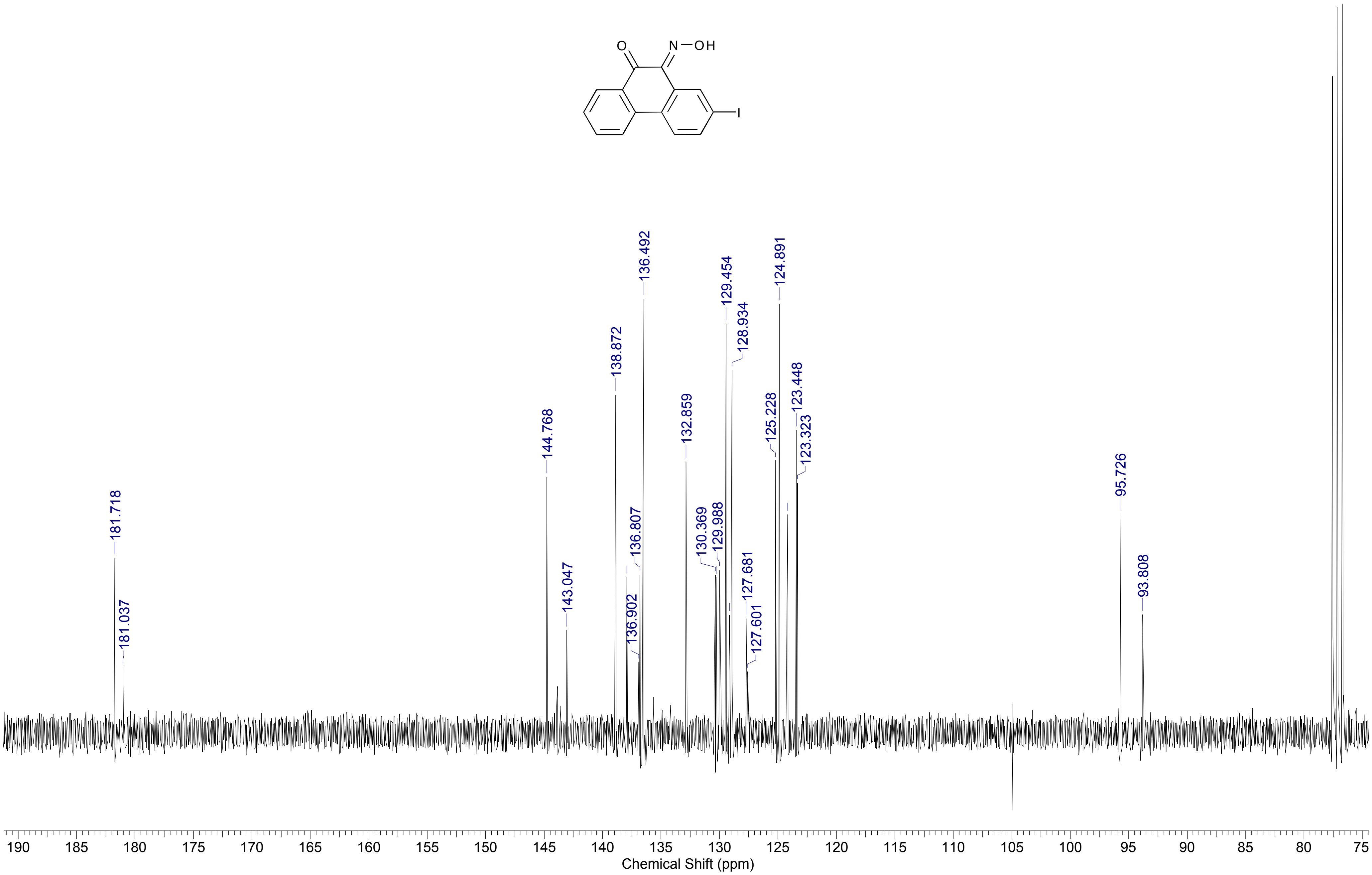


^{1}H NMR spectrum of compound 12

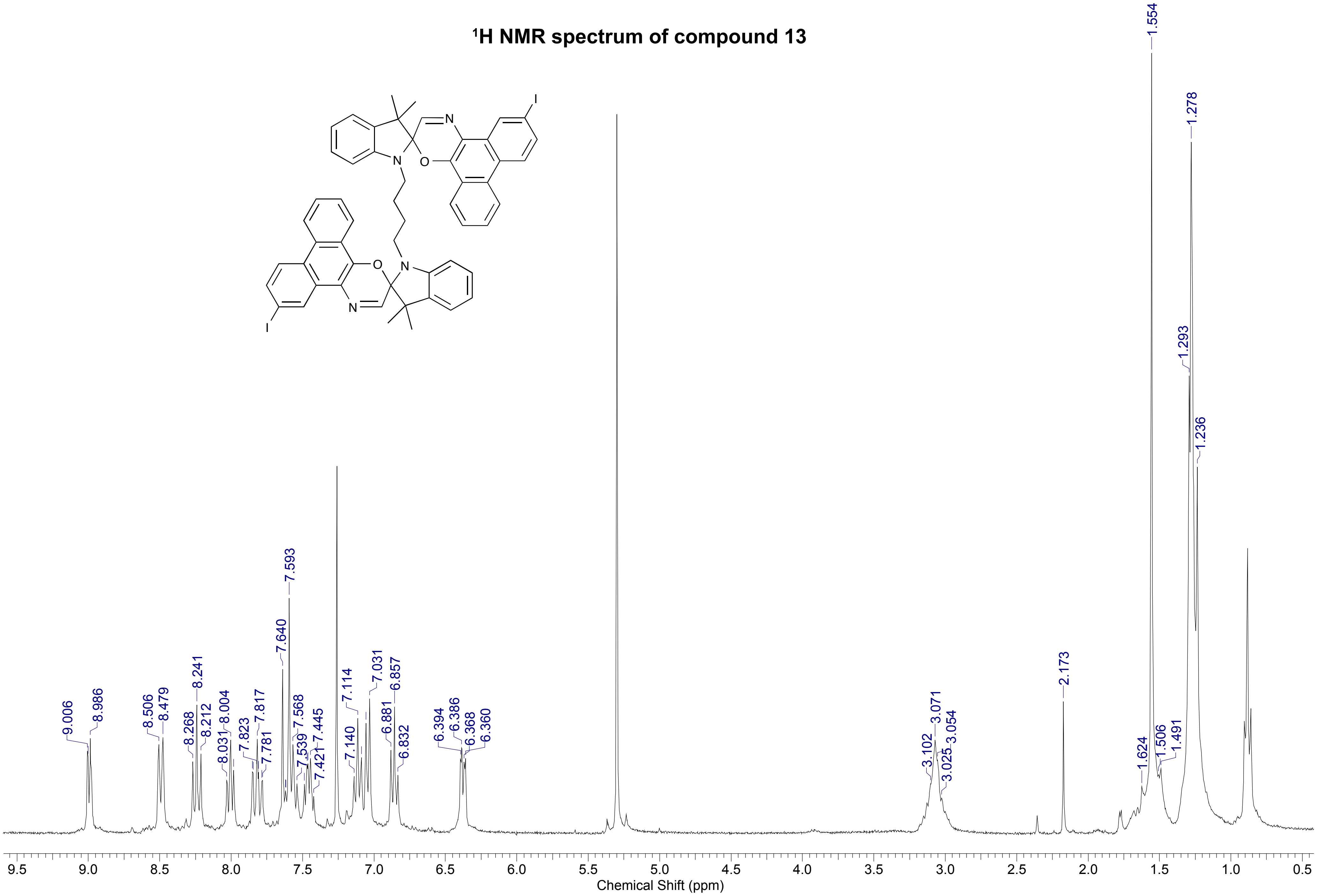




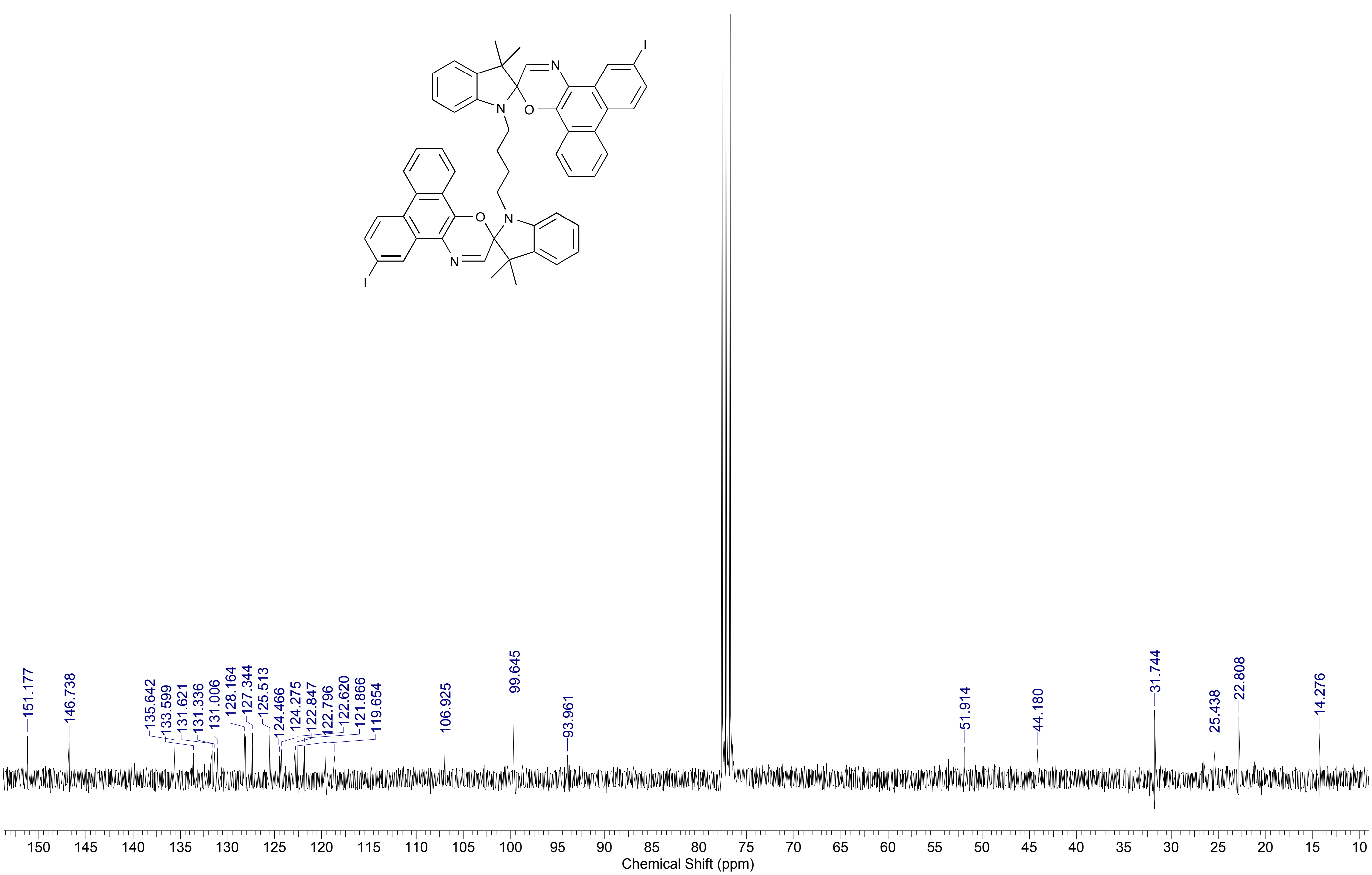
^{13}C NMR spectrum of compound 12



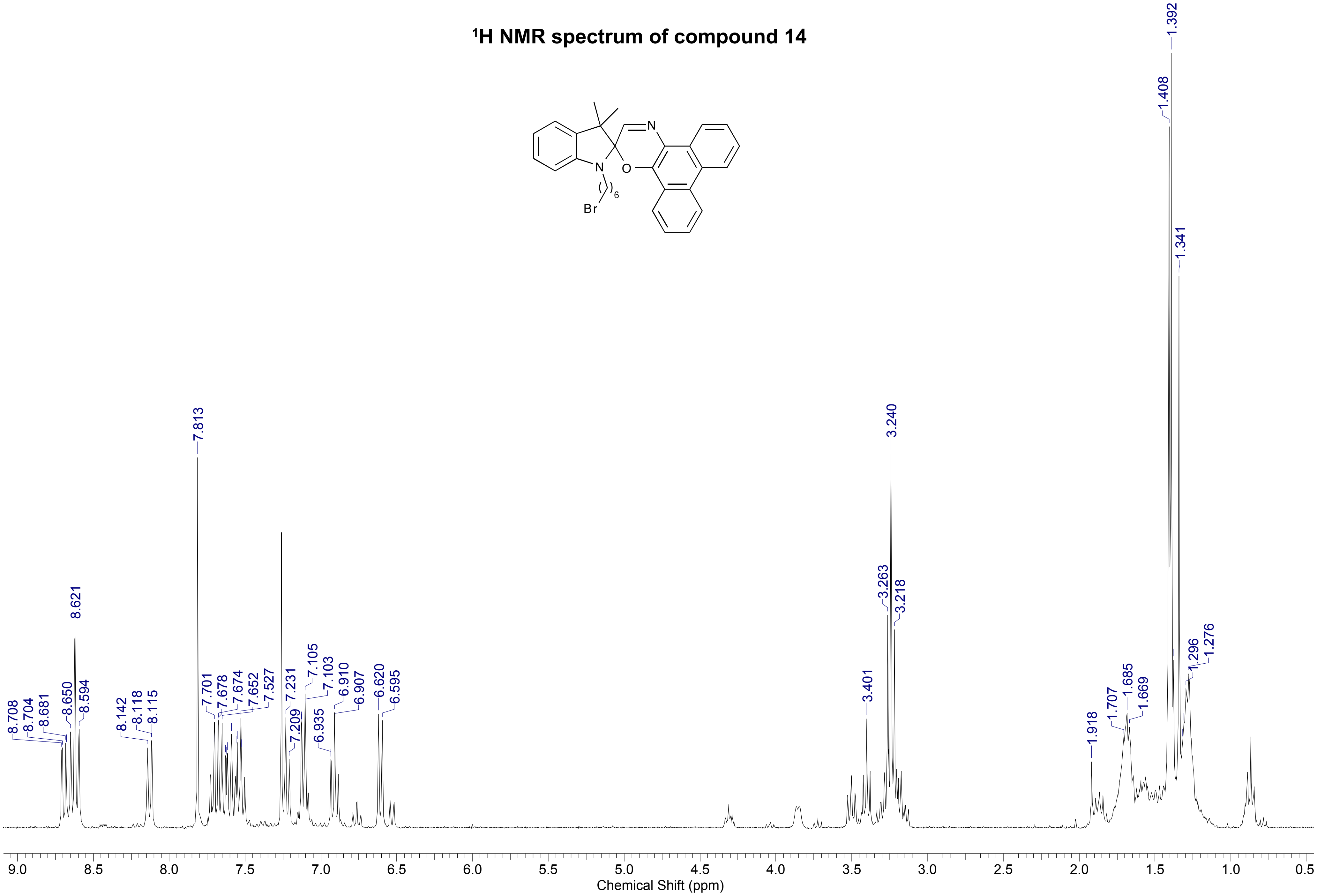
^{1}H NMR spectrum of compound 13



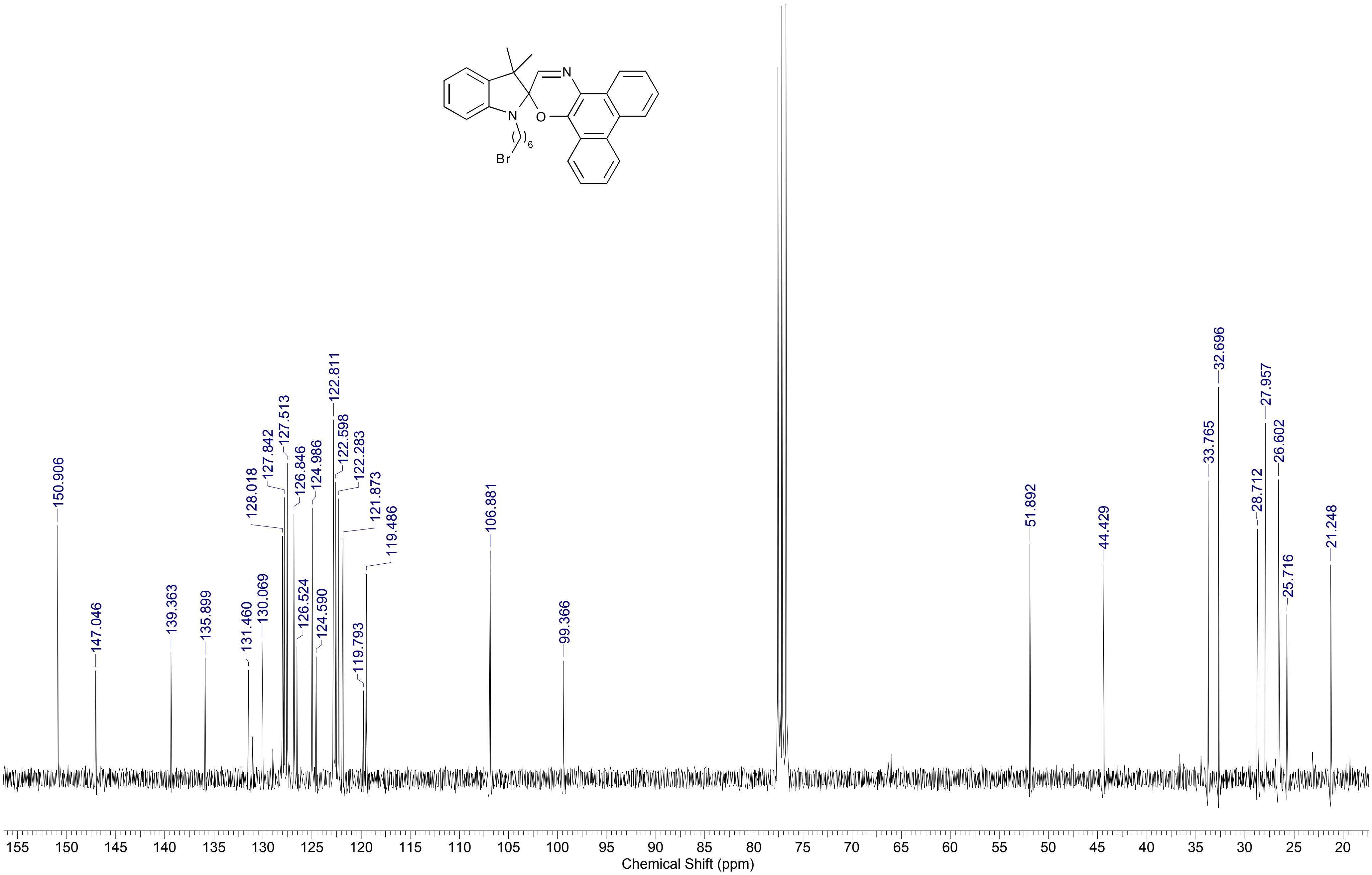
^{13}C NMR spectrum of compound 13

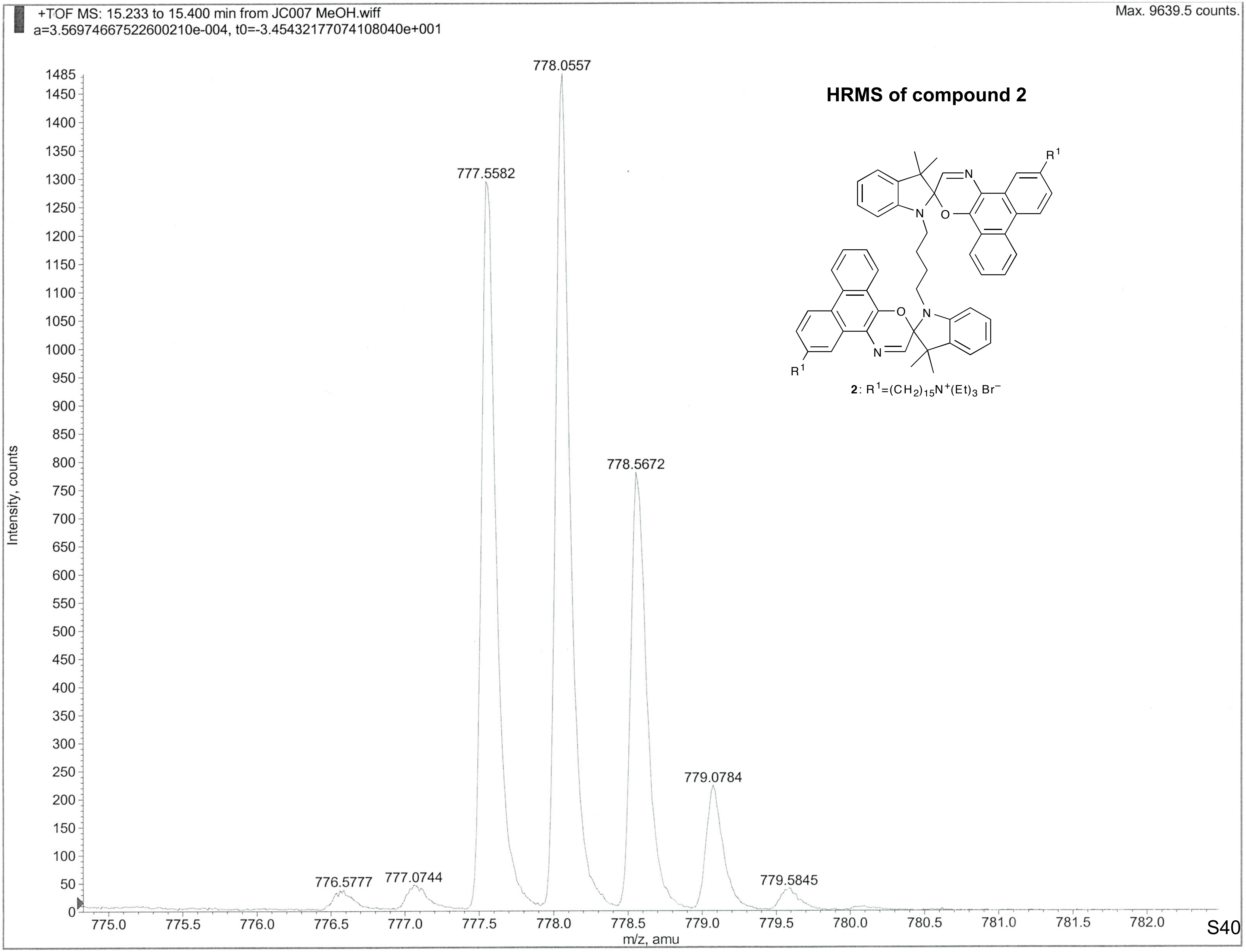


^{1}H NMR spectrum of compound 14



^{1}H NMR spectrum of compound 14



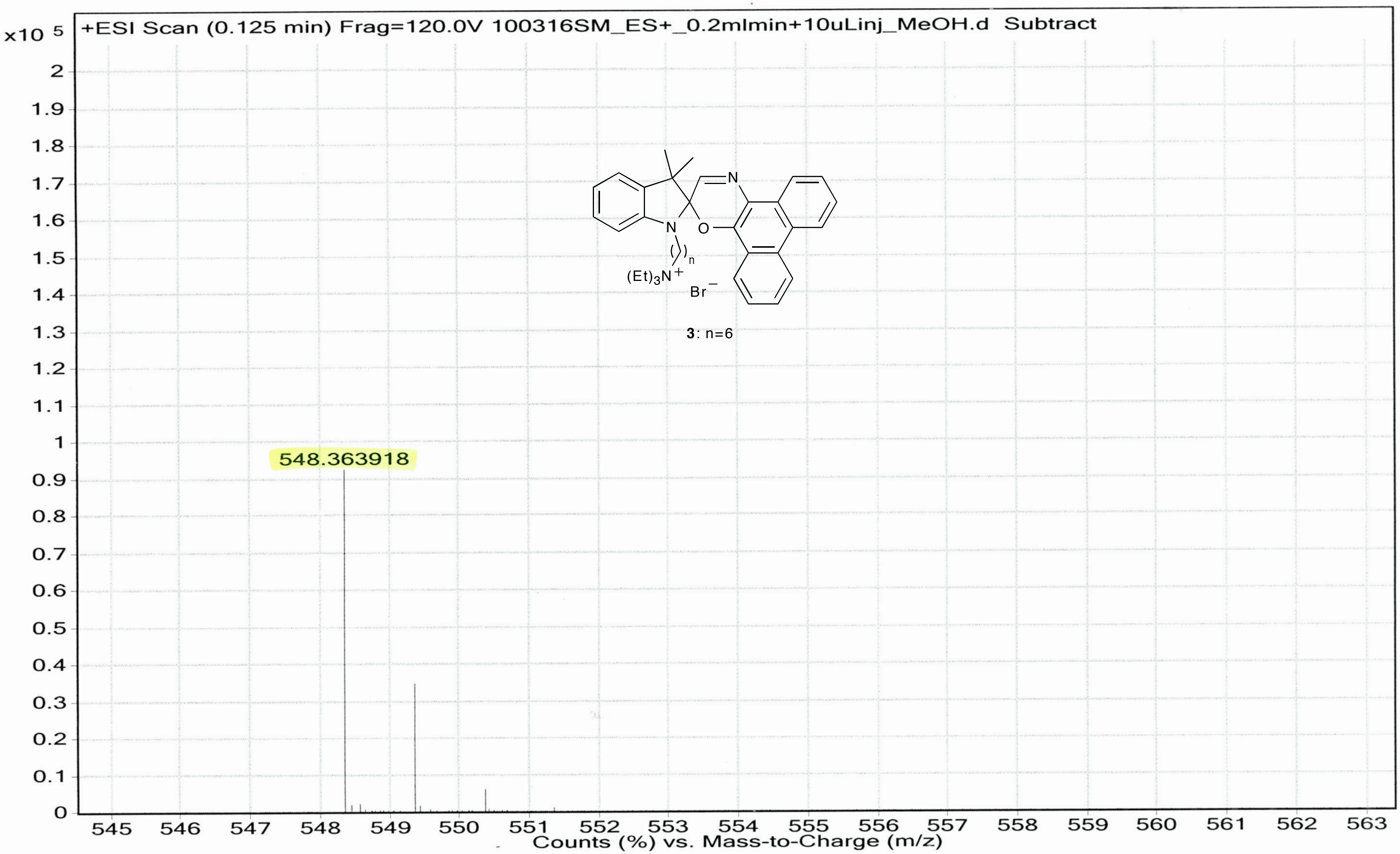


HRMS of compound 2

2: $R^1=(CH_2)_{15}N^+(Et)_3\ Br^-$

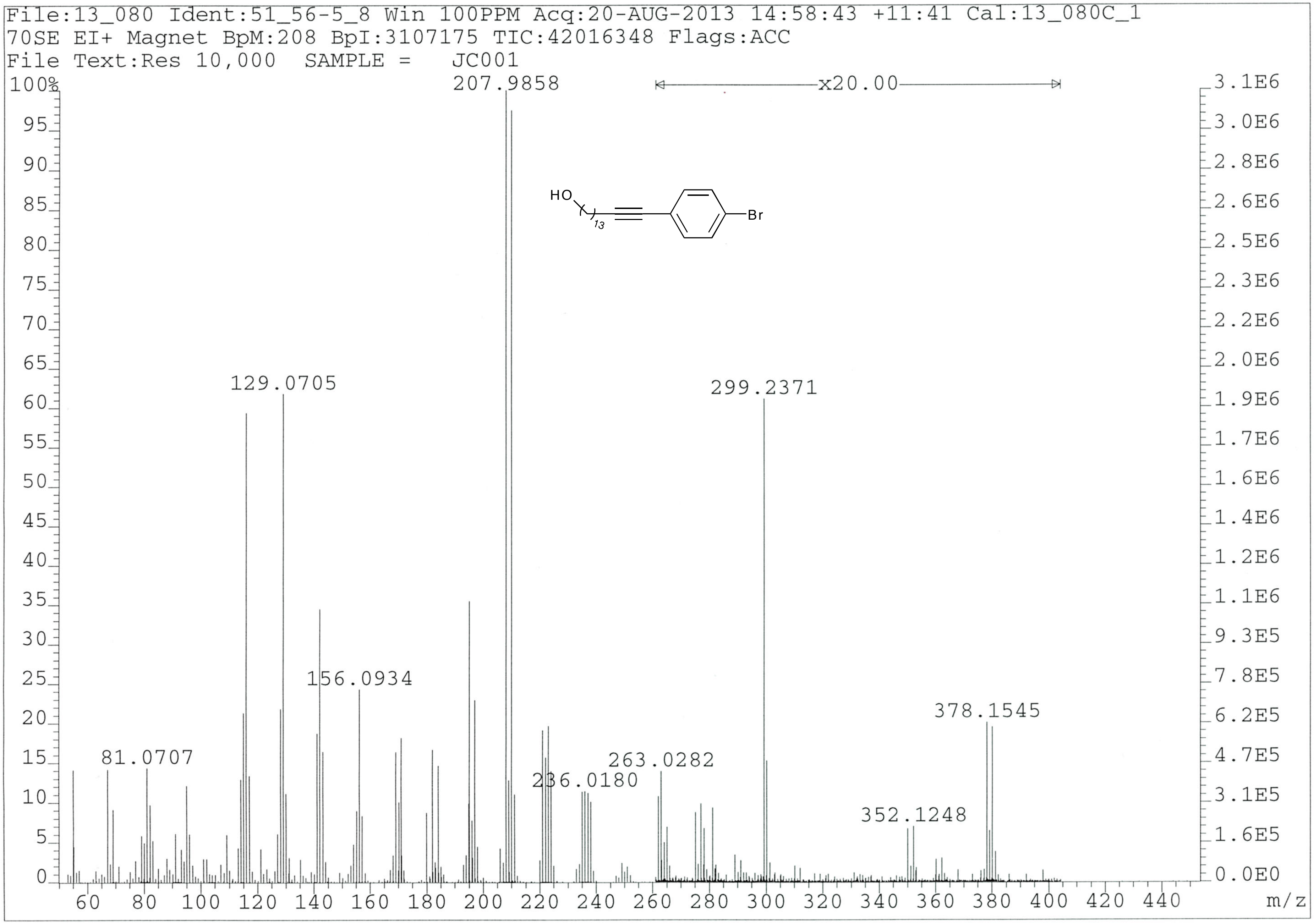
HRMS of compound 3

Sample Name	RSM005_6c_NEt3	**Position**	Vial 19	**Instrument Name**	QTOF_01	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	100316SM_ES+_0.2mlmi	**ACQ Method**	ES+_FIA_100MeOH_0.2m	**Comment**		**Acquired Time**	3/16/2010 12:29:49 PM



3: n=6

HRMS of compound 4



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File Text:Res 10,000  SAMPLE =   JC001
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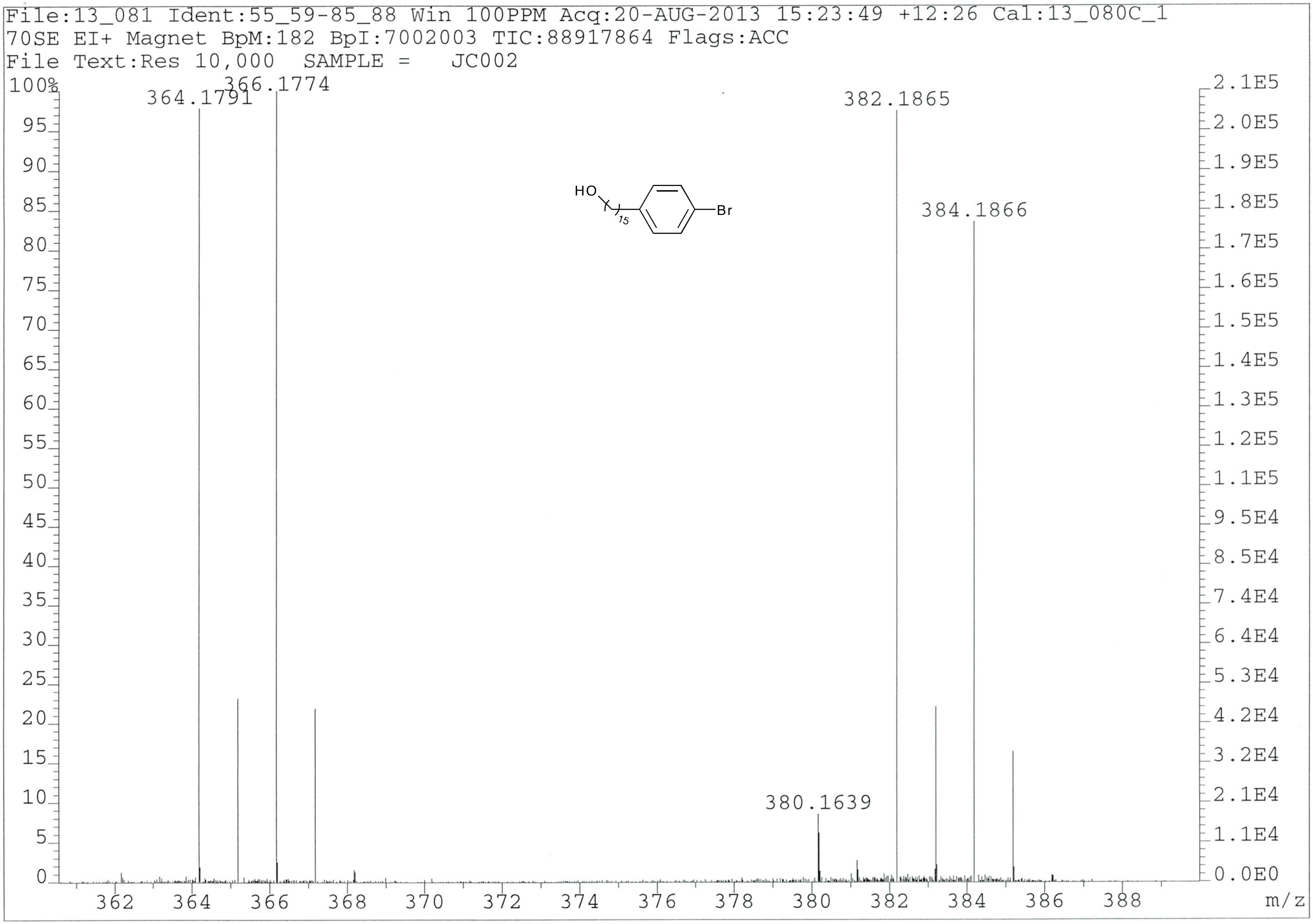
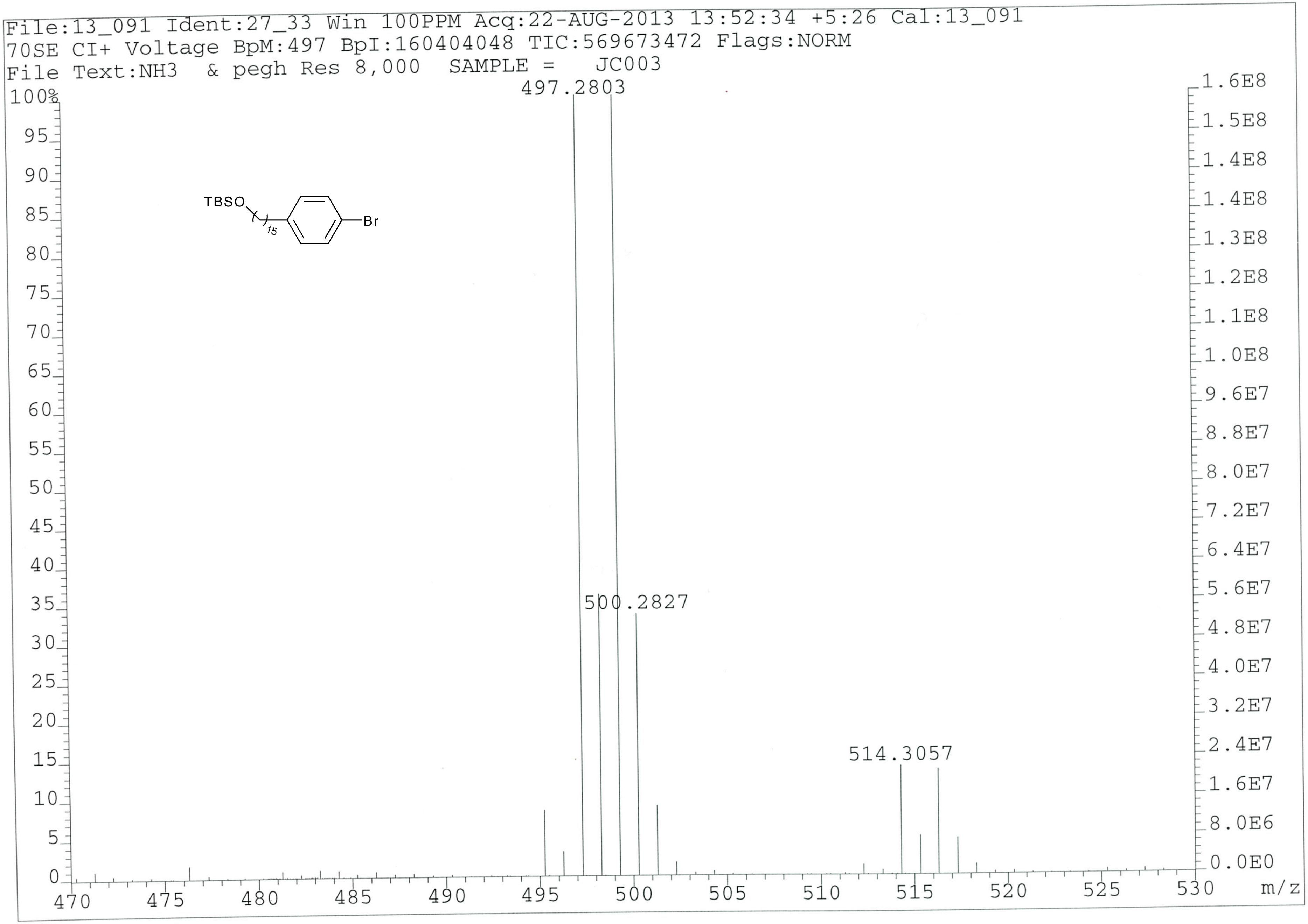
HRMS of compound 5



HRMS of compound 6



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70SE CI+ Voltage BpM:497 BpI:160404048 TIC:569673472 Flags:NORM
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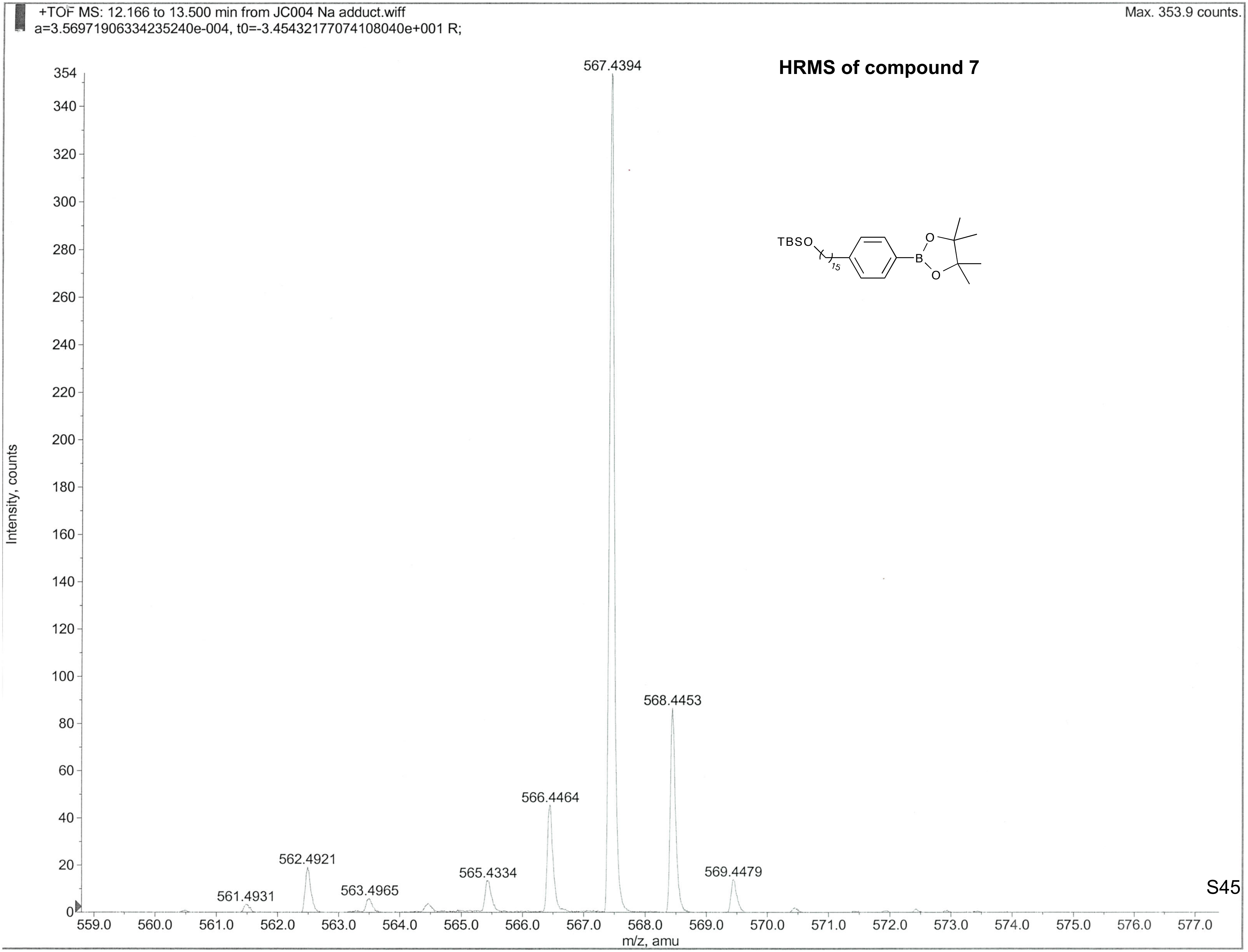
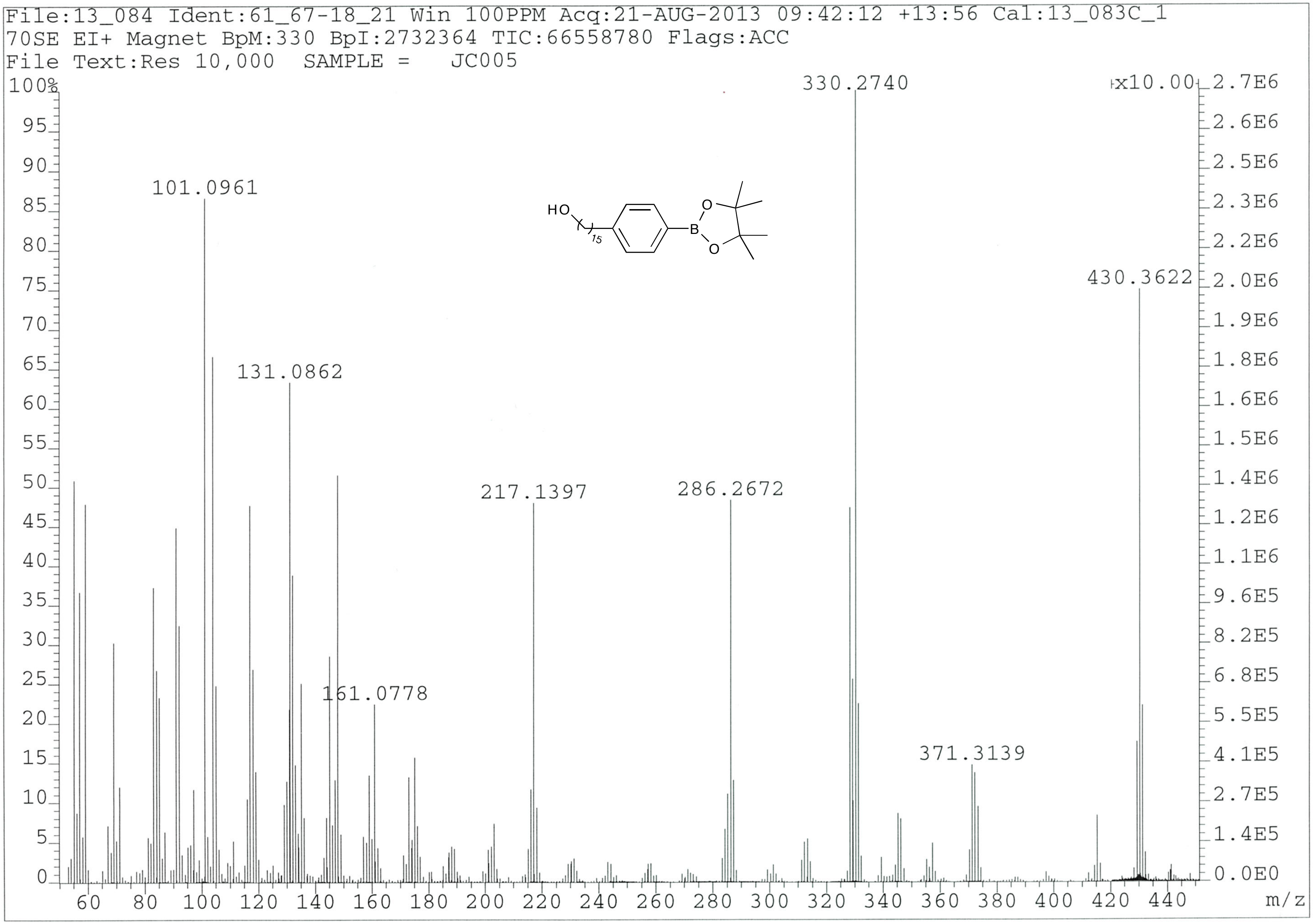
HRMS of compound 7



HRMS of compound 8



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File Text:Res 10,000  SAMPLE =   JC005
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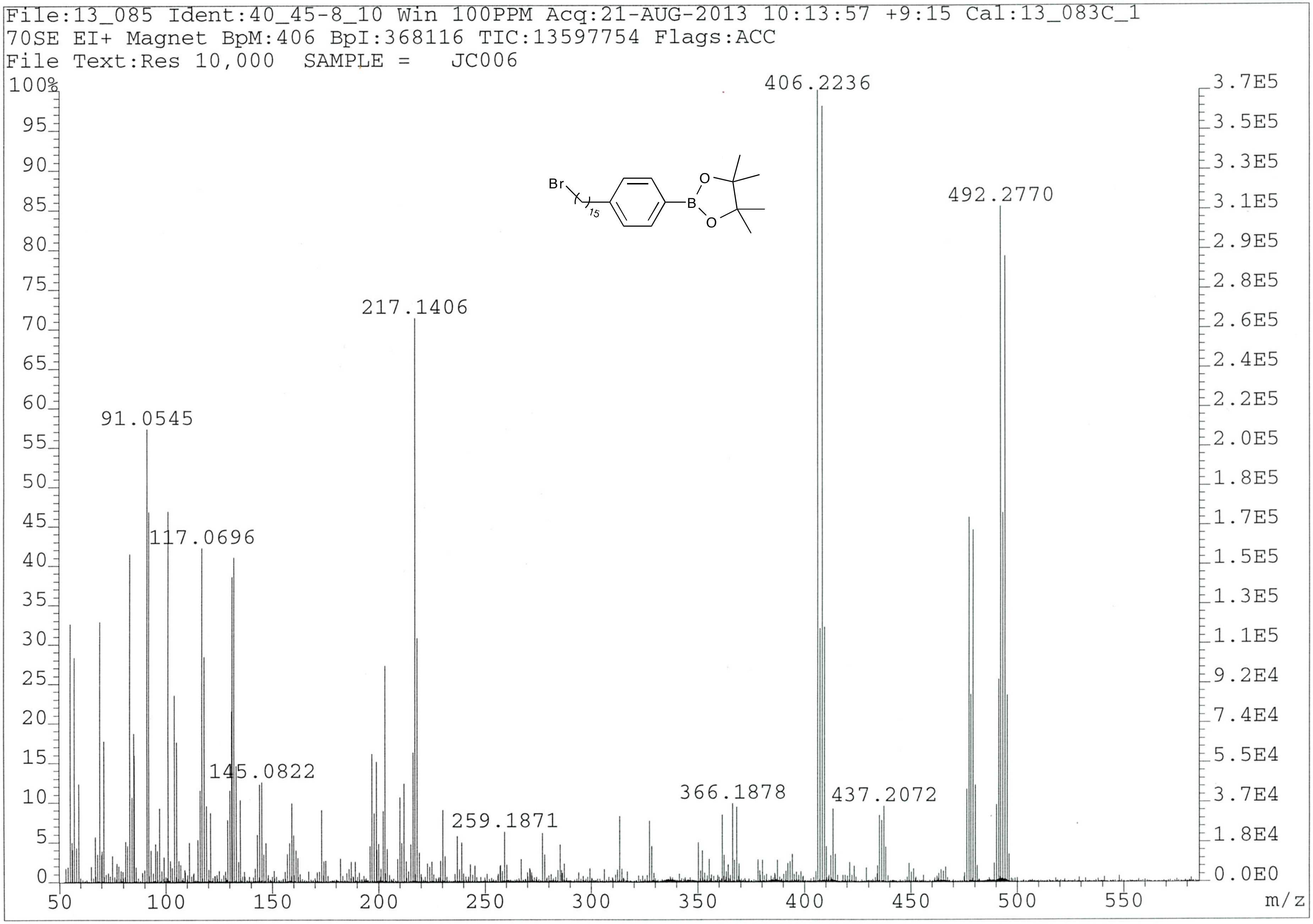
HRMS of compound 9



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File Text:Res 10,000  SAMPLE =   JC006
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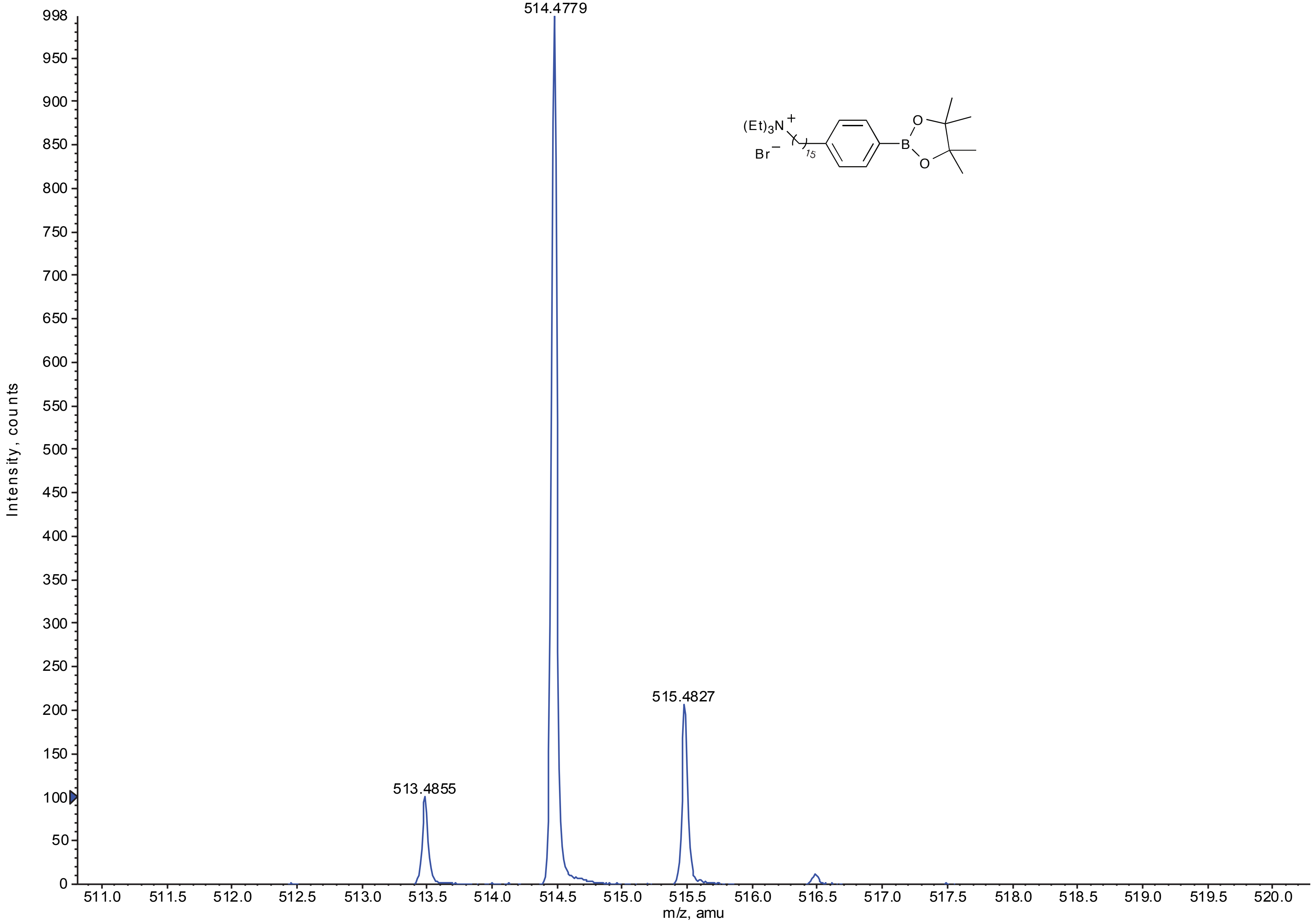
HRMS of compound 10

Max. 998.1 counts.



+TOF MS: 1.183 to 1.300 min from JC-003 POS MeCl2 and Methanol mix.wiff
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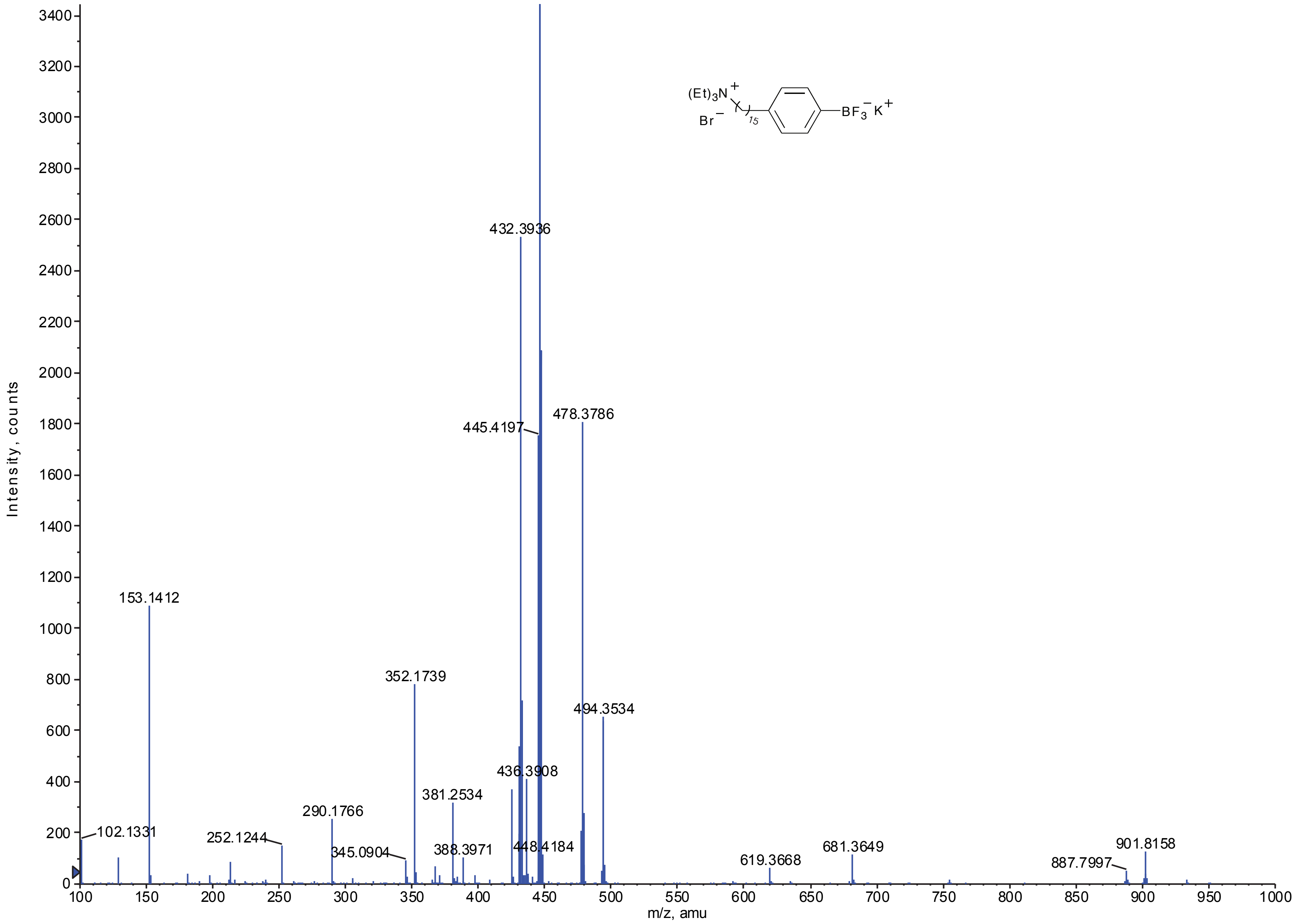
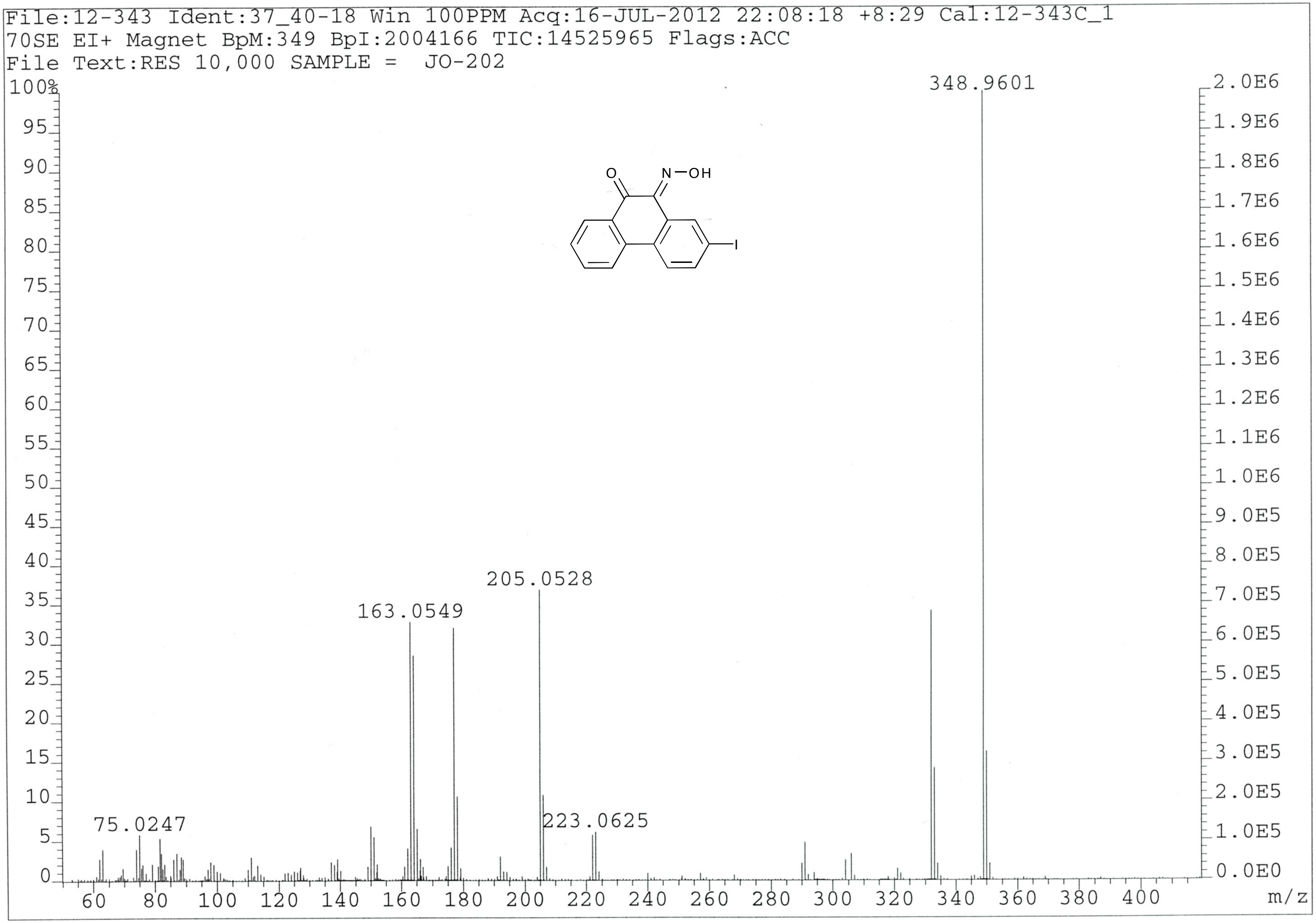
HRMS of compound 11

Max. 3443.9 counts.



HRMS of compound 12



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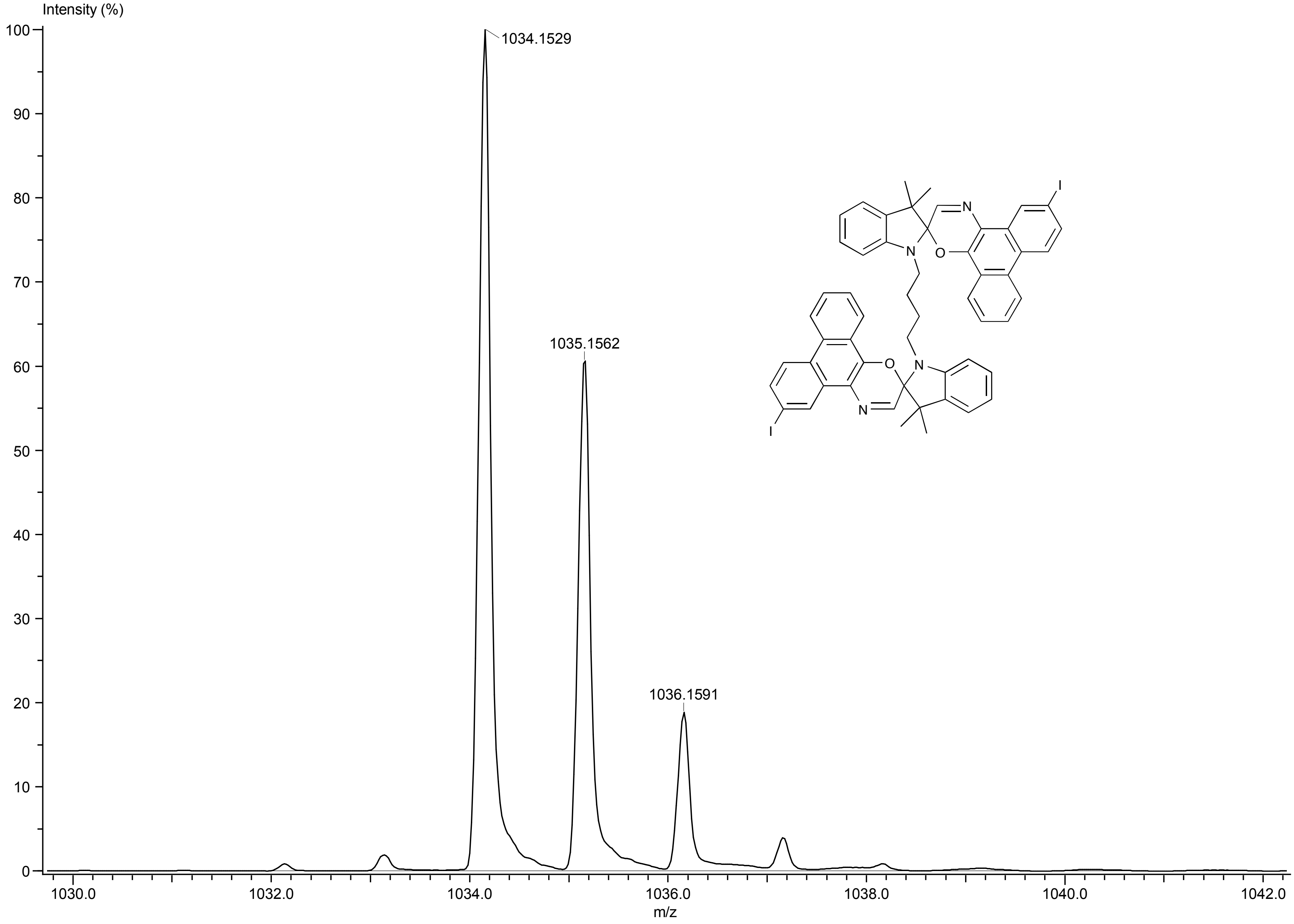
Acq. Data Name: JO-204 Spiro
Creation Parameters: Average(MS Time:0.44..0.45)

HRMS of compound 13

Experiment Date/Time: 28/04/2015 9:44:31 AM
Ionization Mode: FD+(eiFi)



HRMS of compound 14

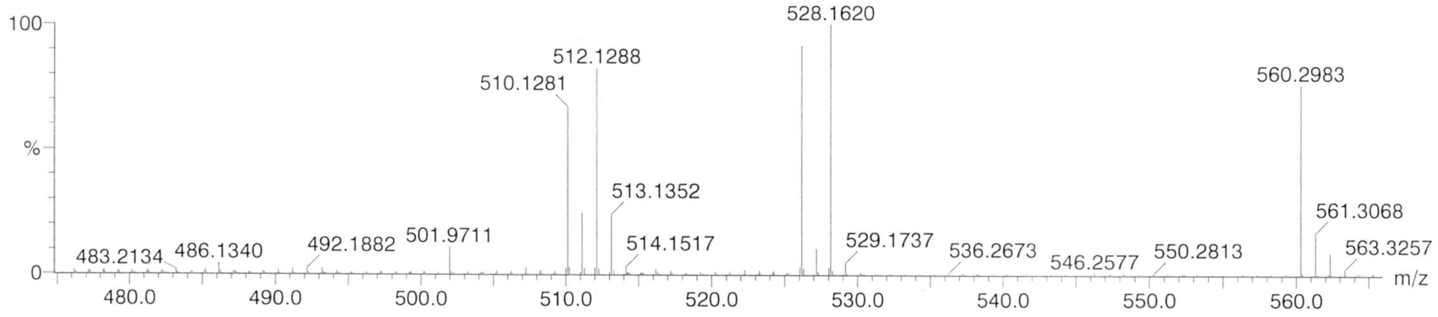
Elemental Composition Report **Page 1**

Single Mass Analysis (displaying only valid results)

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
109 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-31 H: 0-31 N: 0-2 O: 0-1 79Br: 0-2 81Br: 0-2

S MURPHY RSM004-6C-Br CAB072 19-Mar-2010 11:49:19
100319SM2 841 (15.419) Cm (841:879) TOF MS EI+
2.22e+003



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Minimum:                                   -1.5
Maximum:                  5.0      20.0    50.0

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✓m/z

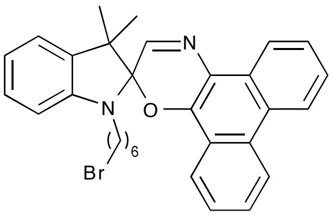

Table S1 Proton permeation rate constants and normalized extent of proton permeation determined for **3** in DOPC and DPPC vesicles at various mole ratios (i.e., **3**/lipid)[a]

DOPC	k_{H+} (10^{-4} s^{-1})		N	
UV	No	Yes	No	Yes
Control	1.8 ± 0.5 (57)	1.4 ± 0.6 (52)	0.31 ± 0.07 (47)	0.37 ± 0.06 (45)
1:10	0.89 ± 0.10 (4)	1.3 ± 0.1 (4)	0.96 ± 0.01 (4)	0.96 ± 0.03 (4)
1:20	2.2 ± 0.2 (6)	2.2 ± 0.4 (6)	0.65 ± 0.02 (6)	0.70 ± 0.02 (6)
1:30	1.8 ± 0.1 (6)	1.7 ± 0.4 (6)	0.57 ± 0.03 (6)	0.61 ± 0.03 (6)
1:40	1.6 ± 0.2 (6)	1.1 ± 0.1 (6)	0.56 ± 0.02 (6)	0.59 ± 0.01 (6)
DPPC	k_{H+} (10^{-4} s^{-1})		N	
UV	No	Yes	No	Yes
Control	0.42 ± 0.24 (61)	0.31 ± 0.27 (52)	0.07 ± 0.05 (54)	0.20 ± 0.07 (49)
1:10	0.77 ± 0.07 (3)	0.36 ± 0.05 (3)	0.98 ± 0.01 (3)	0.99 ± 0.01 (3)
1:20	1.6 ± 0.2 (6)	1.2 ± 0.3 (6)	0.78 ± 0.03 (6)	0.75 ± 0.05 (6)
1:30	1.7 ± 0.6 (6)	1.4 ± 0.6 (6)	0.22 ± 0.06 (6)	0.40 ± 0.09 (6)
1:40	1.1 ± 0.3 (6)	0.84 ± 0.28 (6)	0.08 ± 0.09 (6)	0.30 ± 0.04 (6)

[a] The error is the standard deviation of the mean taken from *n* independent measurements. The value of *n* is shown in parentheses.

Table S2 Proton permeation rate constants and normalized extent of proton permeation determined for **1** in DOPC and DPPC vesicles at various mole ratios (i.e., **1**/lipid)[a]

DOPC	k_{H+} (10^{-4} s^{-1})		N	
UV	No	Yes	No	Yes
Control	1.8 ± 0.5 (57)	1.4 ± 0.6 (52)	0.31 ± 0.07 (47)	0.37 ± 0.06 (45)
1:10	2.8 ± 0.4 (6)	2.4 ± 0.1 (6)	0.88 ± 0.02 (6)	0.88 ± 0.02 (6)
1:20	4.3 ± 0.1 (6)	3.8 ± 0.3 (6)	0.73 ± 0.01 (6)	0.78 ± 0.01 (6)
1:30	4.3 ± 0.4 (6)	4.1± 0.2 (6)	0.57 ± 0.02 (6)	0.62 ± 0.05 (6)
1:40	3.1 ± 0.2 (6)	2.5 ± 0.1 (6)	0.45 ± 0.02 (6)	0.48 ± 0.02 (6)
DPPC	k_{H+} (10^{-4} s^{-1})		N	
UV	No	Yes	No	Yes
Control	0.42 ± 0.24 (61)	0.31 ± 0.27 (52)	0.07 ± 0.05 (54)	0.20 ± 0.07 (49)
1:20	0.25 ± 0.10 (6)	0.22 ± 0.15 (6)	0.96 ± 0.01 (6)	0.96 ± 0.01 (6)
1:30	1.1 ± 0.3 (6)	0.99 ± 0.50 (6)	0.65 ± 0.05 (6)	0.71 ± 0.07 (6)
1:40	1.0 ± 0.4 (6)	0.57 ± 0.16 (6)	0.28 ± 0.02 (6)	0.55 ± 0.01 (6)
1:50	0.67 ± 0.20 (6)	0.45 ± 0.16 (6)	0.12 ± 0.04 (6)	0.22 ± 0.04 (6)

[a] The error is the standard deviation of the mean taken from *n* independent measurements. The value of *n* is shown in parentheses.

Table S3 Proton permeation rate constants and normalized extent of proton permeation determined for **2** in DOPC and DPPC vesicles at various mole ratios (i.e., **2**/lipid)[a]

DOPC	$k_{\mathrm{H+}}$ (10^{-4} s^{-1})		N	
UV	No	Yes	No	Yes
Control	1.8 ± 0.5 (57)	1.4 ± 0.6 (52)	0.31 ± 0.07 (47)	0.37 ± 0.06 (45)
1:20	0.83 ± 0.11 (4)	0.71 ± 0.37 (4)	0.97 ± 0.01 (4)	0.98 ± 0.01 (4)
1:30	8.9 ± 0.6 (6)	8.7 ± 0.2 (6)	0.89 ± 0.01 (7)	0.90 ± 0.01 (6)
1:40	7.3 ± 0.5 (8)	6.9 ± 1.1 (6)	0.87 ± 0.01 (7)	0.88 ± 0.03 (6)
1:50	5.9 ± 0.2 (7)	5.5 ± 0.2 (7)	0.73 ± 0.02 (7)	0.74 ± 0.06 (7)
1:60	5.7 ± 0.2 (6)	5.2 ± 0.4 (6)	0.64 ± 0.05 (6)	0.66 ± 0.04 (6)

DPPC	$k_{\mathrm{H+}}$ (10^{-4} s^{-1})		N	
UV	No	Yes	No	Yes
Control	0.42 ± 0.24 (61)	0.31 ± 0.27 (52)	0.07 ± 0.05 (54)	0.20 ± 0.07 (49)
1:20	0.15 ± 0.06 (6)	0.38 ± 0.12 (4)	0.98 ± 0.01 (6)	0.97 ± 0.01 (4)
1:30	1.0 ± 0.3 (6)	0.83 ± 0.35 (6)	0.53 ± 0.11 (6)	0.62 ± 0.10 (6)
1:40	0.95 ± 0.57 (6)	0.75 ± 0.40 (6)	0.25 ± 0.05 (6)	0.34 ± 0.08 (6)
1:50	0.94 ± 0.45 (6)	0.64 ± 0.37 (6)	0.17 ± 0.04 (6)	0.30 ± 0.09 (6)

[a] The error is the standard deviation of the mean taken from *n* independent measurements. The value of *n* is shown in parentheses.

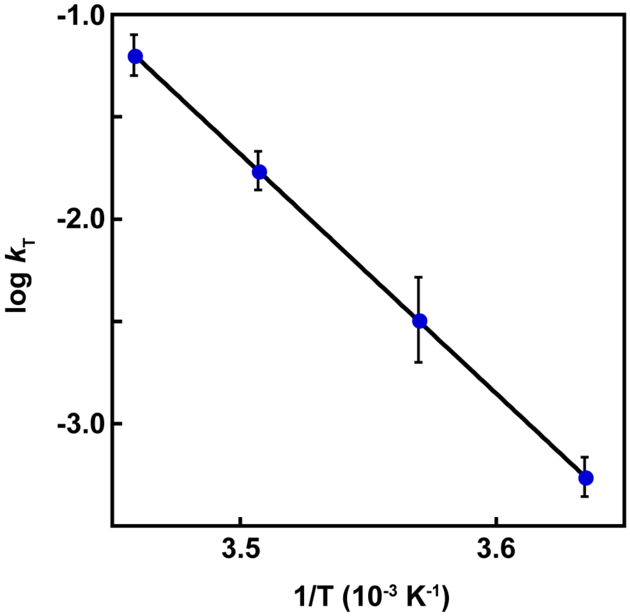

Figure S1. Arrhenius plot of the thermal ring closure rate constants (k_T) for **1** in DPPC vesicles at a mole ratio of 1:20 (i.e., **1**/DPPC). The error bars represent the standard deviation for the mean taken from a minimum of four independent measurements.

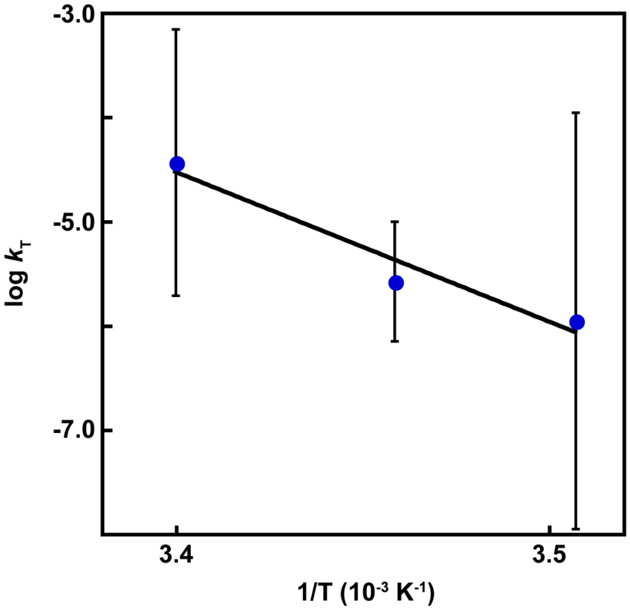

Figure S2. Arrhenius plot of the thermal ring closure rate constants (k_T) for **2** in DPPC vesicles at a mole ratio of 1:20 (i.e., **2**/DPPC). The error bars represent the standard deviation for the mean taken from a minimum of four independent measurements.

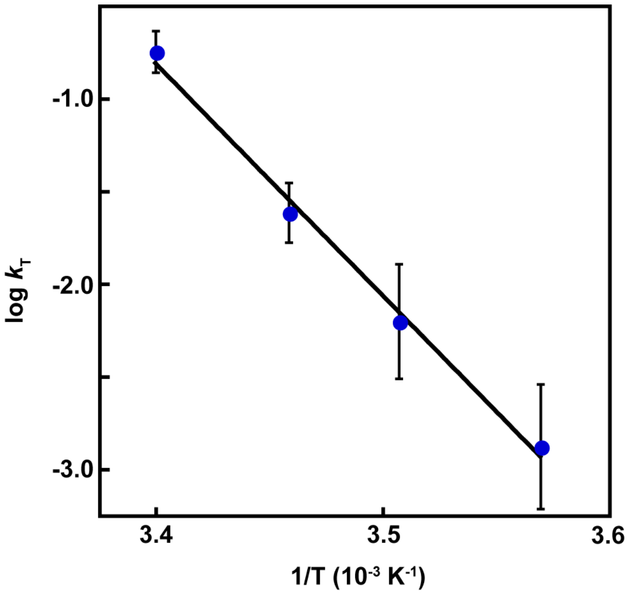

Figure S3. Arrhenius plot of the thermal ring closure rate constants (k_T) for **3** in DPPC vesicles at a mole ratio of 1:20 (i.e., **3**/DPPC). The error bars represent the standard deviation for the mean taken from a minimum of four independent measurements.

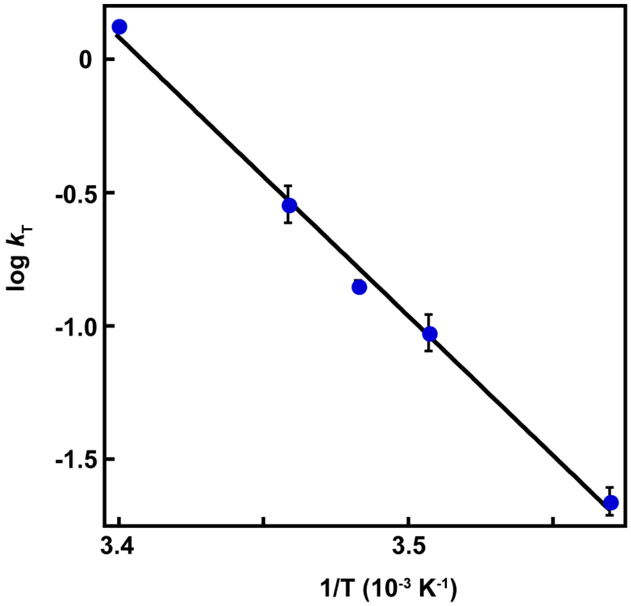

Figure S4. Arrhenius plot of the thermal ring closure rate constants (k_T) for **1** in DOPC vesicles at a mole ratio of 1:20 (i.e., **1**/DOPC). The error bars represent the standard deviation for the mean taken from a minimum of four independent measurements.

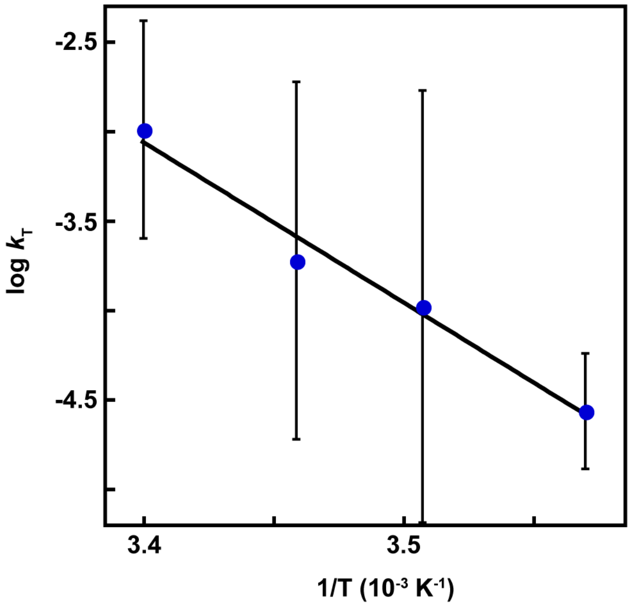

Figure S5. Arrhenius plot of the thermal ring closure rate constants (k_T) for **2** in DOPC vesicles at a mole ratio of 1:20 (i.e., **2**/DOPC). The error bars represent the standard deviation for the mean taken from a minimum of four independent measurements.

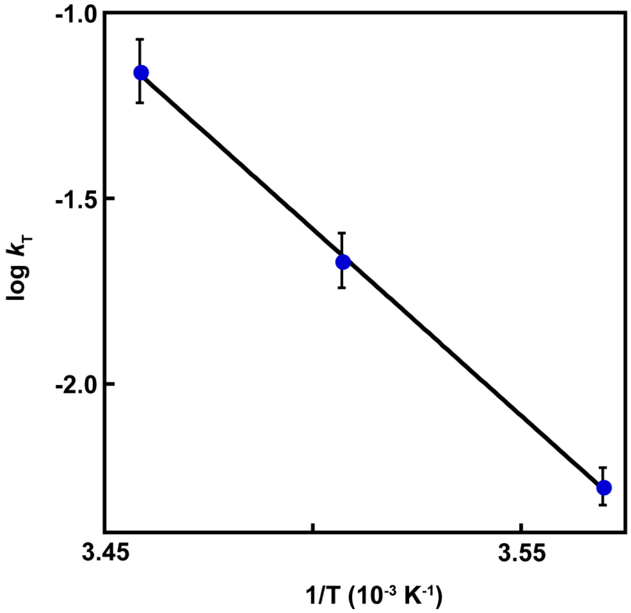

Figure S6. Arrhenius plot of the thermal ring closure rate constants (k_T) for **3** in DOPC vesicles at a mole ratio of 1:20 (i.e., **3**/DOPC). The error bars represent the standard deviation for the mean taken from a minimum of four independent measurements.

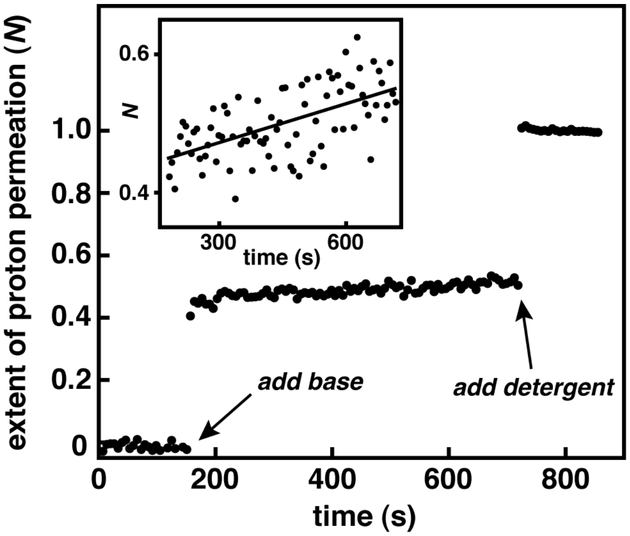

Figure S7. Normalized extent of proton permeation as a function of time for **2** in DPPC vesicles at a mole ratio of 1:30 (i.e., **2**/DPPC). The inset is a linear fit to data > 180 s.

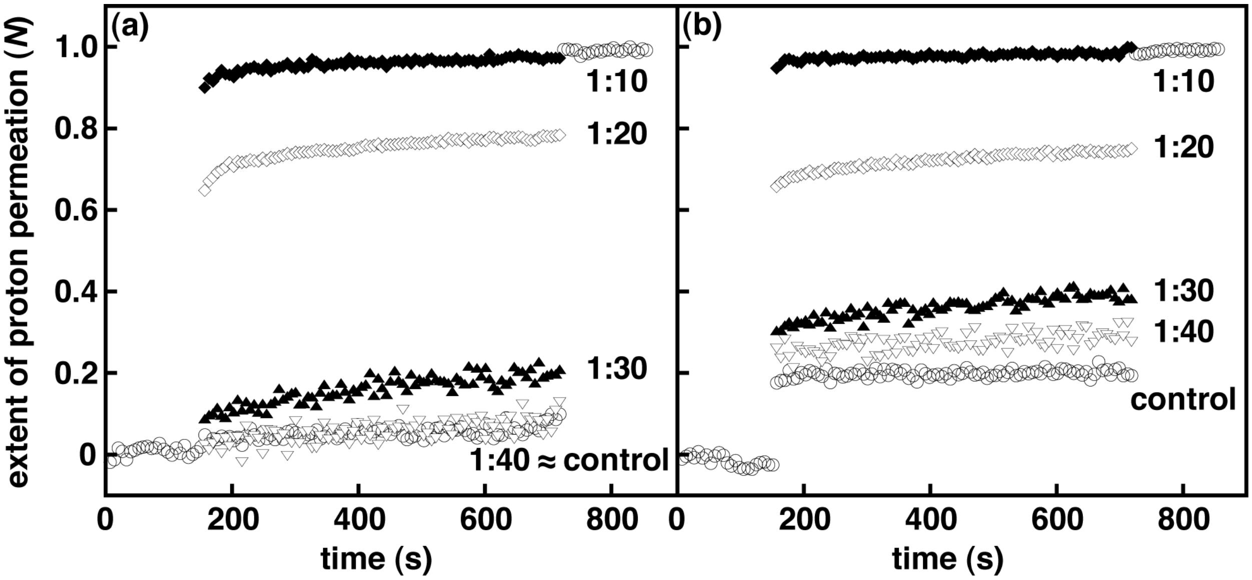

Figure S8. Normalized extent of proton permeation as a function of time for various mole ratios of **3** in DPPC vesicles (i.e., **3**/DPPC) prior to UV irradiation (a) and after 3 min of UV irradiation (b). Each plot is an average of a minimum of three independent measurements. For clarity error bars are not shown, and only the control is shown before the base pulse and after the addition of detergent.

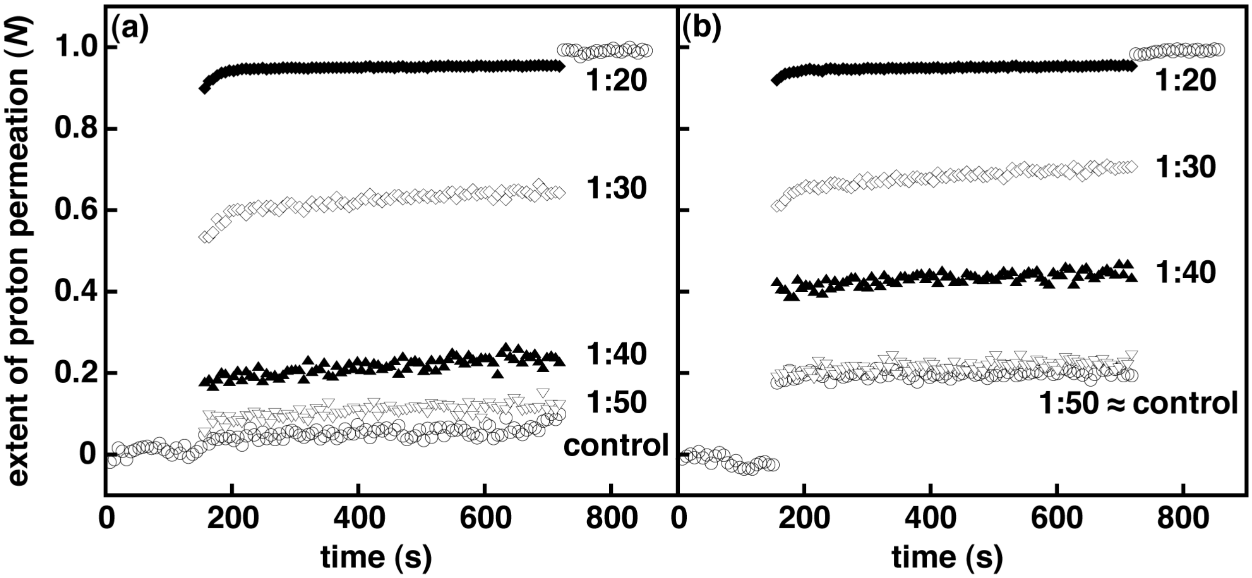

Figure S9. Normalized extent of proton permeation as a function of time for various mole ratios of **1** in DPPC vesicles (i.e., **1**/DPPC) prior to UV irradiation (a) and after 3 min of UV irradiation (b). Each plot is an average of a minimum of six independent measurements. For clarity error bars are not shown, and only the control is shown before the base pulse and after the addition of detergent.

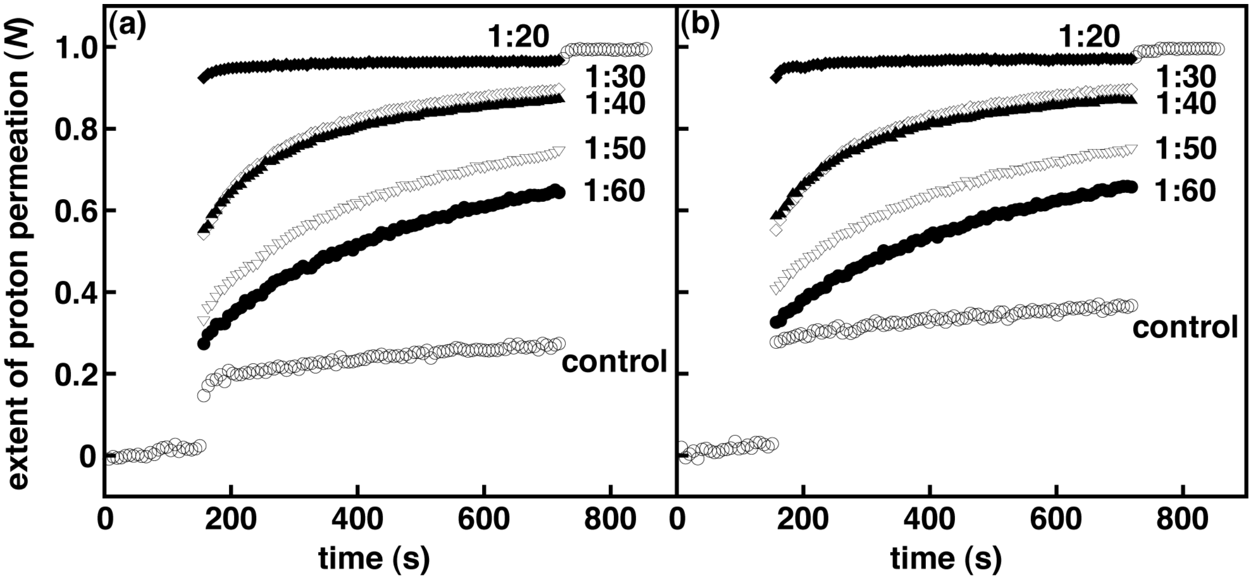

Figure S10. Normalized extent of proton permeation as a function of time for various mole ratios of **2** in DOPC vesicles (i.e., **2**/DOPC) prior to UV irradiation (a) and after 3 min of UV irradiation (b). Each plot is an average of a minimum of four independent measurements. For clarity error bars are not shown, and only the control is shown before the base pulse and after the addition of detergent.

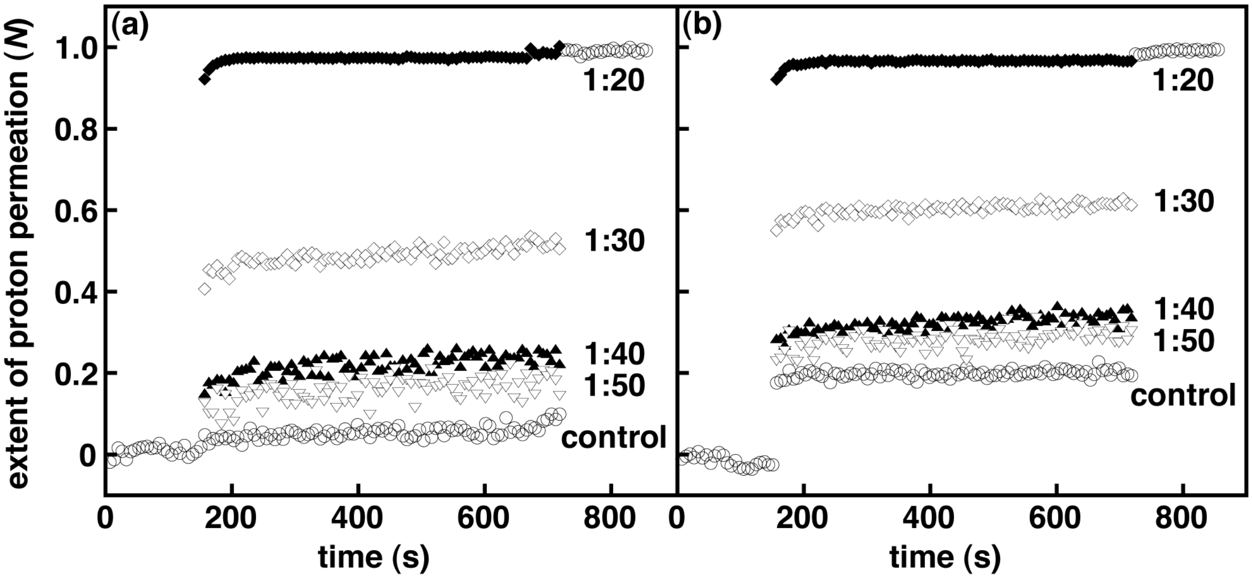

Figure S11. Normalized extent of proton permeation as a function of time for various mole ratios of **2** in DPPC vesicles (i.e., **2**/DPPC) prior to UV irradiation (a) and after 3 min of UV irradiation (b). Each plot is an average of a minimum of four independent measurements. For clarity error bars are not shown, and only the control is shown before the base pulse and after the addition of detergent.

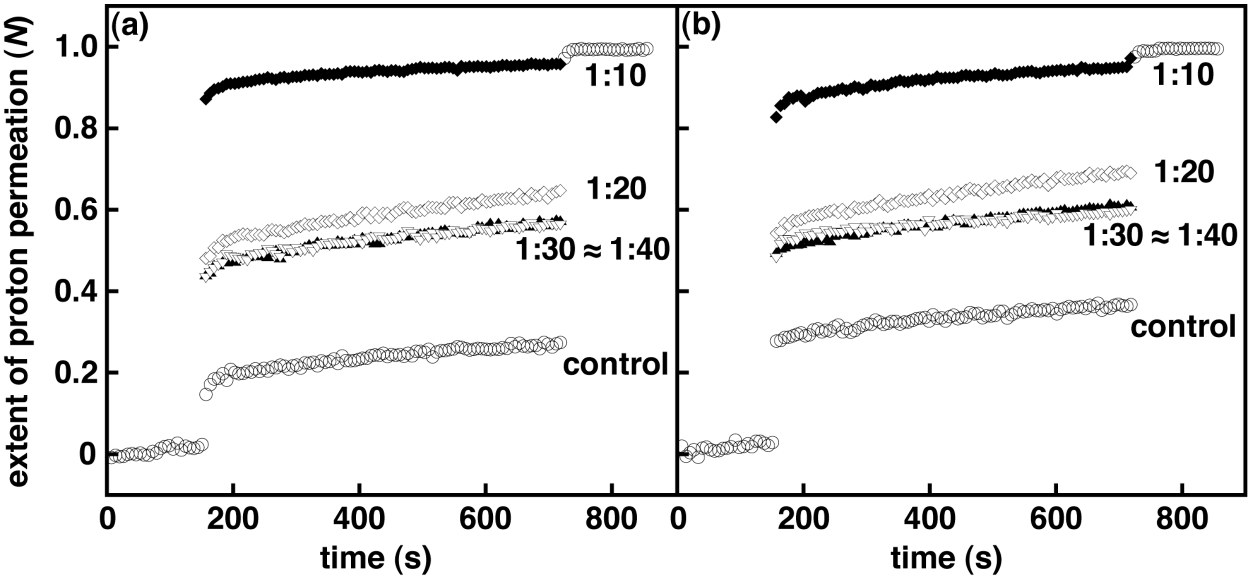

Figure S12. Normalized extent of proton permeation as a function of time for various mole ratios of **3** in DOPC vesicles (i.e., **3**/DOPC) prior to UV irradiation (a) and after 3 min of UV irradiation (b). Each plot is an average of a minimum of four independent measurements. For clarity error bars are not shown, and only the control is shown before the base pulse and after the addition of detergent.

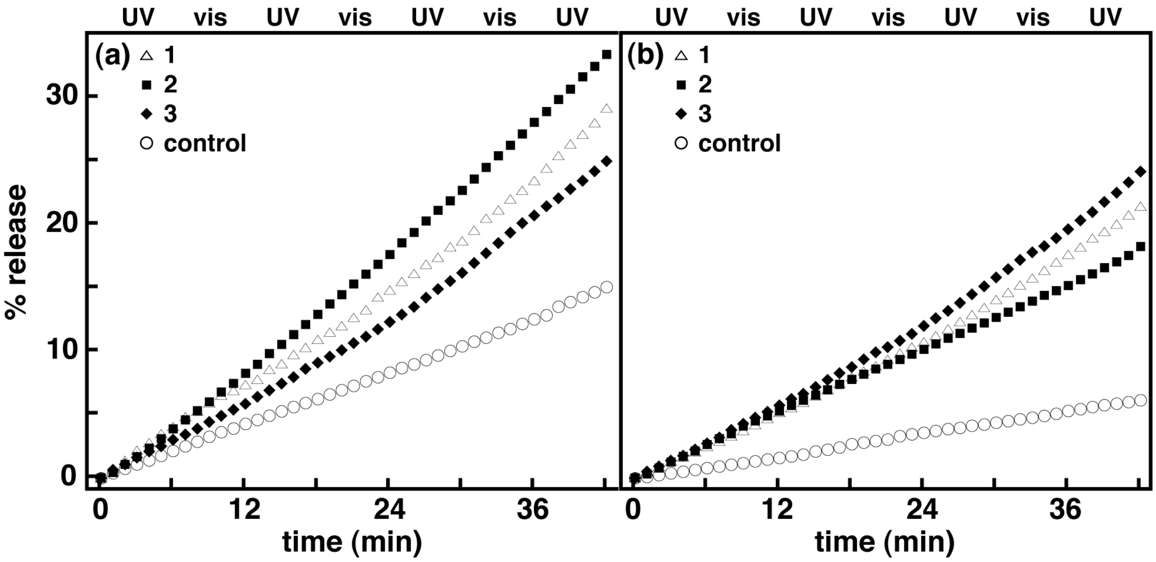

Figure S13. Normalized percentage of potassium ion release as a function of time for **1**–**3** in DOPC (a) and DPPC (b) vesicles at a mole ratio of 1:20 (i.e., spirooxazine/lipid) without irradiation. Each plot is an average of three independent measurements. For clarity error bars are not shown.

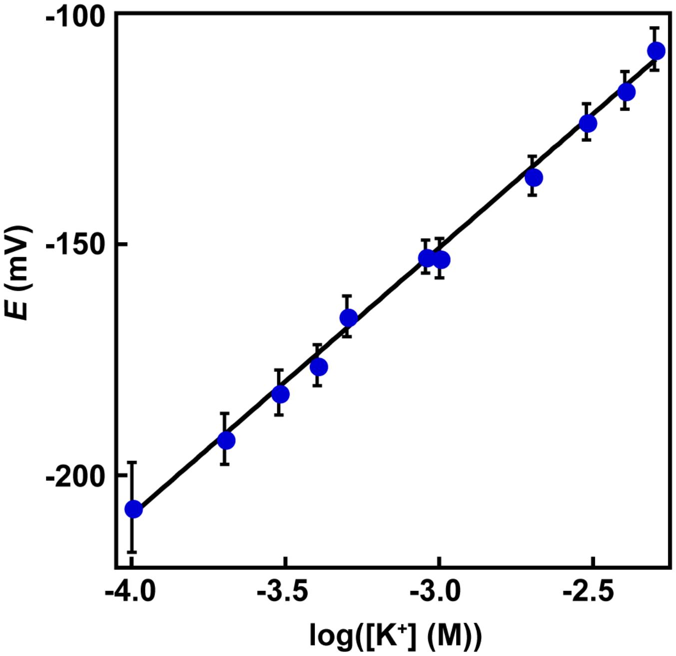

Figure S14. Calibration curve for the electrode potential of potassium ions in phosphate buffer. The error bars represent the standard deviation for the mean taken from a minimum of four independent measurements.

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