The Supporting Information has been revised and is available with the second correction to this paper
(*Org. Lett.* **2014**, *16*, 4692. DOI: 10.1021/ol502316x).

Supporting Information

Experimental Procedure and Characterization Data

Total Synthesis of Lysergic Acid

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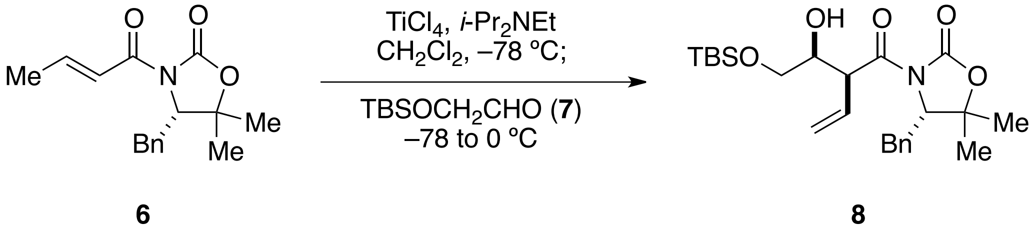
Technical notes: Nuclear magnetic resonance (^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)) spectra were determined on a JEOL-ECX400 instrument. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm) downfields from tetramethylsilane (δ) in deuteriochloroform as the internal standard or the centerline of a quintet at 2.49 ppm for dimethylsulfoxide in deuteriodimethylsulfoxide, and coupling constants are in hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Chemical shifts for ^{13}C NMR were reported in ppm relative to the centerline of a triplet at 77.0 ppm for deuteriochloroform, the centerline at 49.0 ppm for deuteriomethanol, or the centerline at 39.7 ppm for deuteriodimethylsulfoxide. Infrared spectra (IR) were recorded on a JASCO FT/IR-4100 Fourier Transform Infrared Spectrophotometer, and are reported in wavenumbers (cm^{-1}). High resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100LP AccuTOF LC-plus either in positive electrospray ionization (ESI) method, using PEG as the internal standard. Optical rotations were measured on a JASCO P-2200 Digital Polarimeter at room temperature, using the sodium D line. Melting points, determined on a Yanaco Micro Melting Point Apparatus, are uncorected.

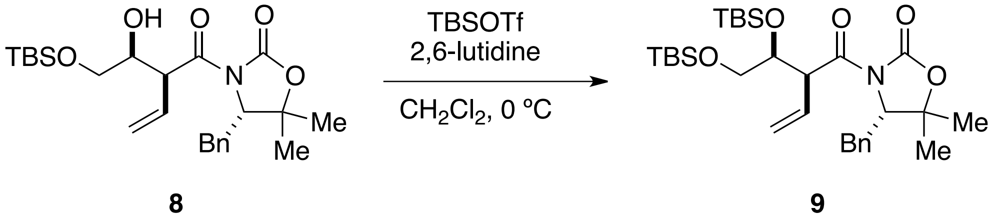
All non-aqueous reactions were carried out under an inert atmosphere of argon in oven-dried glassware unless otherwise noted. Dehydrated diethyl ether, tetrahydrofuran, methylene chloride and toluene were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Dehydrated *N*,*N*-dimethylformamide was purchased from Kanto Chemicals Co., Inc. and stored over activated MS4A. Dehydrated methanol, ethanol and acetonitrile were also purchased from Kanto Chemicals Co., Inc. and stored over activated MS3A. All other reagents were commercially available and used without further purification. Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60F$_{254}$. Preparative flash chromatography was performed using Silica Gel 60 (spherical, 40-100 μm) purchased from Kanto Chemical Co., Inc.

(*S*)-4-benzyl-3-((*S*)-2-((*S*)-2-((*tert*-butyldimethylsilyl)oxy)-1-hydroxyethyl)but-3-enoyl)-5,5-dimethyloxazolidin-2-one (8)



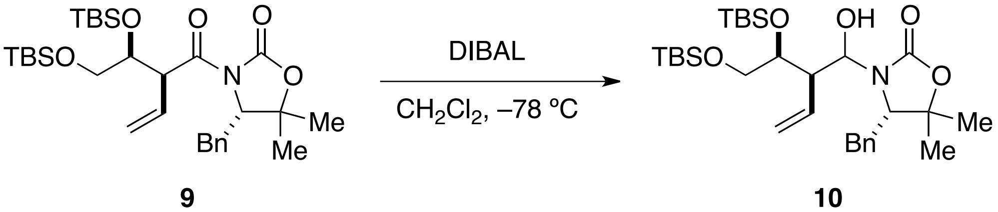
To a solution of **6** (10.20 g, 37.31 mmol) in CH_2Cl_2 (350 ml) was added $TiCl_4$ (4.30 ml, 39.2 mmol) dropwise at –78 °C. After stirring for 5 minutes, *N*,*N*-diisopropylethylamine (16.2 mL, 93.3 mmol) was added to the resultant yellow solution at –78 °C. The dark purple solution of a titanium enolate was stirred for 1 hours at –78 °C. To this solution was added **7** (7.16 g, 41.0 mmol) dropwise at –78 °C. The resulting mixture was stirred for 1 hour at –78 °C and warmed to 0 ºC. After stirred for 1 hour at same temperature, the reaction mixture was poured into saturated aq. NH_4Cl, and the resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, and filtrated. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (10 % AcOEt in hexane) to afford **8** (13.10 g, 78.42%) as colorless oil. $[\alpha]_D^{24}$ –62.5° (*c* 1.00, $CHCl_3$); IR (film) 2953, 2929, 2857, 1780, 1686, 1359 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18 (m, 5 H), 5.86-5.98 (m, 1H), 5.37 (d, *J* = 17.4 Hz, 1H), 5.31 (dd, *J* = 1.4 Hz, 11.2 Hz, 1 H), 4.76 (dd, *J* = 5.3 Hz, 8.9 Hz, 1 H), 4.53 (dd, *J* = 3.9 Hz, 9.4 Hz, 1 H), 4.04 (d, *J* = 5.0 Hz, 1 H), 3.56-3.69 (m, 2 H), 3.19 (dd, *J* = 3.9 Hz, 14.4 Hz, 1 H), 2.86 (dd, *J* = 9.4 Hz, 14.4 Hz, 1 H), 2.85 (br s, 1 H), 1.37 (s, 6 H), 0.89 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 151.9, 136.7, 131.7, 129.0, 128.6, 126.7, 120.6, 81.9, 71.9, 49.3, 35.0, 28.3, 25.7, 22.1, 18.1, -5.5; HRMS (ESI) calcd for $C_{24}H_{37}NO_5SiNa$ $(M+Na)^+$: 470.2339, found 470.2322.

(*S*)-4-benzyl-5,5-dimethyl-3-((*S*)-2-((*S*)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)but-3-enoyl)oxazolidin-2-one (9)



To a stirred solution of **8** (5.82 g 13.0 mmol) and 2,6-lutidine (2.27 ml, 19.5 mmol) in CH_2Cl_2 (150 ml) was added TMSOTf (3.59 ml, 15.6 mmol) at 0 ºC. After stirring for 1 hour, the reaction mixture was quenched with saturated aq. $NaHCO_3$. The resulting solution was extracted with CH_2Cl_2 three times, and the combined organic layer was washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (5 % AcOEt in hexane) to afford **9** (5.85 g, 80.0%) as colorless oil. $[\alpha]_D^{25}$ –30.0° (*c* 1.11, $CHCl_3$); IR (film) 2953, 2929, 2857, 1780, 1698, 1472, 1354, 1253 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18-7.32 (m, 5 H), 5.85-5.98 (m, 1H), 5.25 (d, *J* = 17.4 Hz, 1H), 5.22 (dd, *J* = 1.4 Hz, 10.3 Hz, 1 H), 4.73 (dd, *J* = 6.4 Hz, 9.2 Hz, 1 H), 4.47 (dd, *J* = 3.2 Hz, 10.0 Hz, 1 H), 4.08 (td, *J* = 5.3 Hz, 6.0 Hz, 1 H), 3.56-3.69 (m, 2 H), 3.14 (dd, *J* = 3.2 Hz, 14.5 Hz, 1 H), 2.84 (dd, *J* = 10.0 Hz, 14.5 Hz, 1 H), 1.35 (s, 3 H), 1.34 (s, 3 H), 0.89 (s, 9 H), 0.87 (s, 9 H), 0.06 (s, 6 H), 0.05 (s, 3 H), 0.04 (3 H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 151.9, 137.0, 138.8, 129.0, 128.6, 126.6, 119.3, 81.5, 74.2, 66.3, 63.7, 51.4, 34.8, 28.5, 25.9, 25.8, 22.3, 18.4, 18.1, -4.1, -4.7, -5.3, -5.4; HRMS (ESI) calcd for $C_{30}H_{51}NO_5Si_2Na$ $(M+Na)^+$: 584.3203, found 584.3199.

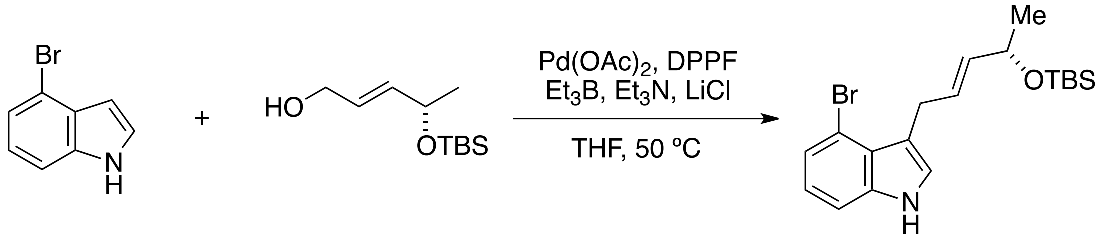
(4*S*)-4-benzyl-3-((2*S*)-1-hydroxy-2-((*S*)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)but-3-en-1-yl)-5,5-dimethyloxazolidin-2-one (10)



9 **10**

To a stirred solution of **9** (8.17 g, 14.5 mmol) in CH_2Cl_2 (150 ml) was added DIBAL (1.02 mol/l hexane solution, 35.5 ml, 36.3 mmol) at –78 °C. After stirring for 20 minutes, sat. NH_4Cl (15 ml) and water (15 ml) were added to the reaction mixture dropwise at –78 °C and the resulting mixture was allowed to warm to 0 °C and the reaction mixture was stirred for 20 minutes. After filtration, the residue was extracted with CH_2Cl_2 three times. The combined organic extracts were dried over Na_2SO_4, and filtrated. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (5 % AcOEt in hexane) to afford **10** (6.51 g, 79.4%) as colorless oil. $[\alpha]_D^{24}$ +7.0° (*c* 1.22, $CHCl_3$); IR (film) 3425, 2978, 2933, 1730, 1693, 1441, 1391, 1361, 1160, 1116 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15-7.34 (m, 5 H), 5.72 (ddd, *J* = 8.7 Hz, 8.7 Hz, 17.0 Hz, 1 H), 5.23-5.40 (m, 3 H), 4.02-4.15 (m, 2 H), 3.32-3.57 (m, 3 H), 3.06 (dd, *J* = 1.8 Hz, 10.7 Hz, 1 H), 2.76 (dd, *J* =, 10.7 Hz, 14.9 Hz, 1 H), 1.27 (s, 3H), 1.50 (s, 3 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.12 (s, 3 H), 0.08 (s, 3 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 137.2, 133.7, 128.7, 128.7, 126.6, 119.5, 81.6, 77.9, 72.2, 64.4, 63.7, 49.9, 35.6, 27.9, 25.9, 25.8, 22.4, 18.2, 18.0, –4.3, –5.0, –5.4, –5.4; HRMS (ESI) calcd for $C_{30}H_{53}NO_5Si_2Na$ $(M+Na)^+$: 586.3360, found 586.3350.

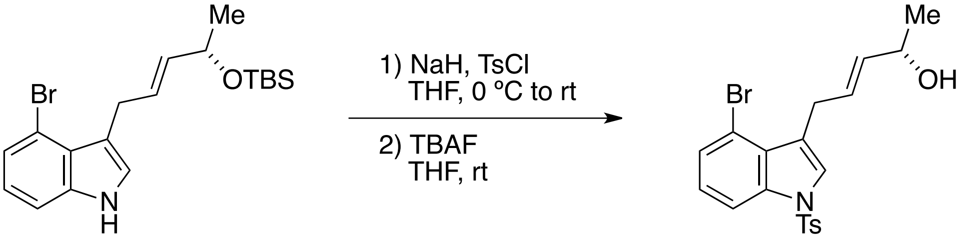
(*S*,*E*)-4-bromo-3-(4-((*tert*-butyldimethylsilyl)oxy)pent-2-en-1-yl)-1*H*-indole (13)



11 **12** **13**

To a stirred solution of 4-bromoindole (**11**, 8.56 g, 43.7 mmol), allylic alcohol **12** (11.34 g, 52.40 mmol), triethylamine (7.30 ml, 52.4 mmol), LiCl (2.22 g, 52.4 mmol), palladium acetate (490.6 mg, 2.185 mmol), and DPPF (2.42 g, 4.37 mmol), in THF (500 ml) was added triehylborane (1.0 mol/l hexane solution, 52.4 ml, 52.4 mmol) at room temperature. After stirring at 50 ºC for 8 hours, the reaction mixture was quenched with saturated aq. $NaHCO_3$. The resulting mixture was extracted with AcOEt three times, and the combined organic extracts were dried over Na_2SO_4, and filtrated. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (50% CH_2Cl_2 in hexane) to afford **13** (15.51 g, 90.03%) as dark red oil. $[\alpha]_D^{25}$ −3.5° (*c* 1.07, $CHCl_3$); IR (film) 3423, 3287, 2954, 2927, 2885, 2856, 1472, 1335, 1254 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1 H), 7.20-7.31 (m, 2 H), 6.93-7.03 (m, 2 H), 5.87 (td, *J* = 6.4 Hz, 15.6 Hz, 1 H), 5.53 (dd, *J* = 5.5 Hz, 15.6 Hz, 1 H), 4.32 (qd, *J* =, 6.4 Hz, 6.4 Hz, 1 H), 3.72 (d, *J* = 6.4 Hz, 2 H), 1.21 (d, *J* = 6.4 Hz, 3 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 135.5, 128.2, 125.3, 123.6, 123.4, 122.6, 115.9, 114.3, 110.4, 69.4, 29.0, 25.9, 24.6, 18.3, −4.5, −4.7; HRMS (ESI) calcd for $C_{19}H_{28}BrNOSiNa$ $(M+Na)^+$: 416.1021, found 416.1014.

(*S*,*E*)-5-(4-bromo-1-tosyl-1*H*-indol-3-yl)pent-3-en-2-ol (S1)

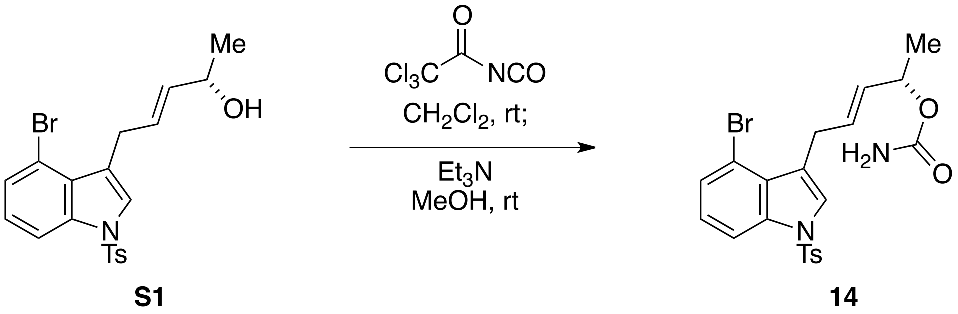


13 **S1**

To a stirred solution of **13** (6.57 g, 16.7 mmol) in THF (200 ml) was added sodium hydride (60% dispersion in mineral oil, 1.60 g, 19.8 mmol) at 0 ºC. After stirring at same temperature for 5 min, to the reaction mixture was added tosyl chloride (7.62 g, 19.8 mmol). After the reaction mixture was warm up to room temperature, the resulting mixture was stirred for 1 hour. Then the reaction mixture was quenched with sat. aq. NH_4Cl. The resulting mixture was extracted with AcOEt three times and the combined organic extracts were dried over Na_2SO_4, and filtrated. Concentration of the residue afforded crude products, which was used for the next step without further purification.

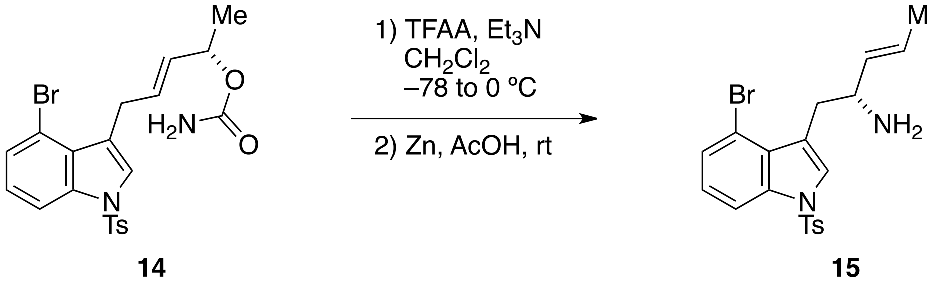
To a stirred solution of the crude products in THF (200 ml) was added TBAF (1.0 mol/l THF solution, 19.8 ml, 19.8 mmol) at room temperature. After stirring 1 hour, the reaction mixture was quenched with saturated aq. NH_4Cl and the resulting mixture was extracted with AcOEt three times. The combined organic layer was washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (30% AcOEt in hexane) to afford **S1** (6.53 g, 90.3%) as brown foam. $[\alpha]_D^{24}$ −1.10° (*c* 1.03, $CHCl_3$); IR (film) 3362, 2970, 1596, 1556, 1411, 1372 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.9 Hz, 1 H), 7.73 (d, *J* = 8.2 Hz, 2 H), 7.37 (d, *J* = 7.9 Hz, 1 H), 7.36 (s, 1 H), 7.23 (d, *J* = 8.2 Hz, 2 H), 7.11 (dd, *J* = 7.9 Hz, 7.9 Hz, 1 H), 5.90 (td, *J* = 6.4 Hz, 15.2 Hz, 1 H), 5.54 (dd, *J* = 6.6 Hz, 15.2 Hz, 1 H), 4.34 (qd, *J* =6.1 Hz, 6.2 Hz, 1 H), 3.69 (d, *J* = 6.4 Hz, 2 H), 2.35 (s, 3 H), 1.27 (d, *J* = 6.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 136.3, 136.3, 134.5, 129.7, 128.5, 127.6, 127.3, 126.6, 125.2, 124.7, 121.9, 114.3, 112.7, 68.3, 29.0, 23.2, 21.3; HRMS (ESI) calcd for $C_{20}H_{20}BrNO_3SNa$ $(M+Na)^+$: 456.0245, found 456.0228.

(*S*,*E*)-5-(4-bromo-1-tosyl-1*H*-indol-3-yl)pent-3-en-2-yl carbamate (14)



To a solution of **S1** (6.53 g, 15.0 mmol) in CH_2Cl_2 (150 ml) was added trichloroacetyl isocyanate (1.96 ml, 16.5 mmol) at room temperature. After stirring 1 hour at same temperature, methanol (150 ml) and triethylamine (0.15 ml) was added. After stirring for additional 4 hours, the reaction mixture concentrated *in vacuo*. Trituration of crude product and wash of the resulting solid with Et_2O and hexane afforded **14** (7.16 g, quant.) as a off white solid. $[\alpha]_D^{21}$ +22.6° (*c* 1.00, $CHCl_3$); mp: 166-167 °C; IR (film) 3649, 3489, 2978, 1716, 1596, 1373, 1189 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.7 Hz, 1 H), 7.74 (d, *J* = 8.2 Hz, 2 H), 7.36 (s, 1 H), 7.36 (d, *J* = 8.7 Hz, 1 H), 7.23 (d, *J* = 8.2 Hz, 2 H), 7.11 (dd, *J* = 8.7 Hz, 8.7 Hz, 1 H), 5.97 (td, *J* = 6.4 Hz, 15.6 Hz, 1 H), 5.51 (dd, *J* = 6.6 Hz, 15.6 Hz, 1 H), 5.28 (qd, *J* =6.4 Hz, 6.4 Hz, 1 H), 4.62 (s, 2 H), 3.69 (d, *J* = 6.2 Hz, 2 H), 2.35 (s, 3 H), 1.33 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 145.3, 136.7, 135.0, 132.2, 130.1, 130.0, 128.9, 127.9, 127.0, 125.5, 125.2, 121.9, 114.7, 113.0, 71.7, 29.5, 21.7, 20.6; HRMS (ESI) calcd for $C_{21}H_{21}BrN_2O_4SNa$ $(M+Na)^+$: 499.0303, found 499.0307.

(***R*,*E***)-1-(4-bromo-1-tosyl-1*H*-indol-3-yl)pent-3-en-2-amine (15)

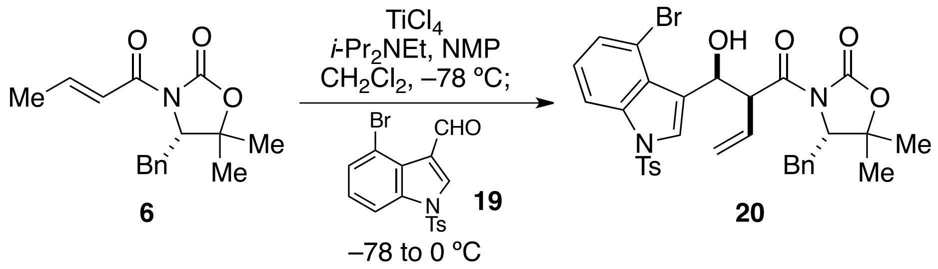


To a stirred suspension of **14** (7.16 g, 15.0 mmol) and triethylamine (8.36 ml, 60.0 mmol) in CH_2Cl_2 (150 ml) was added trifluoroacetic anhydride (3.15 ml, 22.5 mmol) at –78 °C. After stirring at –78 °C for 10 minutes, the reaction mixture was warm up to 0 °C and stirred for additional 1 hour. To the reaction mixture was added 2,2,2-trichloroethanol (2.15 ml, 22.5 mmol), and the reaction mixture was stirred at room temperature for additional 2 hours. Then the reaction mixture was quenched with saturated aq. $NaHCO_3$, and the resulting mixture was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and filtered. Concentration of the filtrate afforded crude products, which was used for next step without further purification.

To a stirred solution of the crude products in acetic acid (150 ml) was added zinc powder (1.90 g, 75.0 mmol) portionwise at 0 °C. After stirring for 5 minutes, the reaction mixture was warm up to room temperature, and stirred for additional 2 hours. Then the resulting mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was partitioned between AcOEt and water, and the aqueous layer was extracted twice with AcOEt. The combined organic layer was washed with water, saturated aq. $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4 and filtrated. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (AcOEt) to afford **15** (6.35 g, 97.7%) as brown oil. $[\alpha]_D^{24}$ +18.1° (*c* 1.00, $CHCl_3$); IR (film) 2919, 1595, 1555, 1411, 1372 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.0 Hz, 1 H), 7.73 (d, J = 8.0 Hz, 2 H), 7.55 (s, 1 H), 7.36 (d, J = 8.0 Hz, 1 H), 7.21 (d, J = 8.0 Hz, 2 H), 7.10 (dd, J = 8.0 Hz, 8.0 Hz, 1 H), 5.50-5.71 (m, 2 H) 3.24 (br s, 2 H), 2.33 (s, 3 H), 1.67 (br s, 2 H), 1.65 (d, J = 5.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 136.2, 134.7, 132.8, 129.8, 128.2, 127.6, 127.4, 126.9, 126.0, 125.4, 116.7, 114.3, 112.7, 54.6, 30.3, 21.5, 17.8; HRMS (ESI) calcd for $C_{20}H_{22}BrN_2O_2S$ $(M+H)^+$: 433.0585, found 433.0576.

(*S*)-4-benzyl-3-((*S*)-2-((*S*)-hydroxy(1-tosyl-1*H*-indol-3-yl)methyl)but-3-enoyl)-5,5-dimethyloxa-

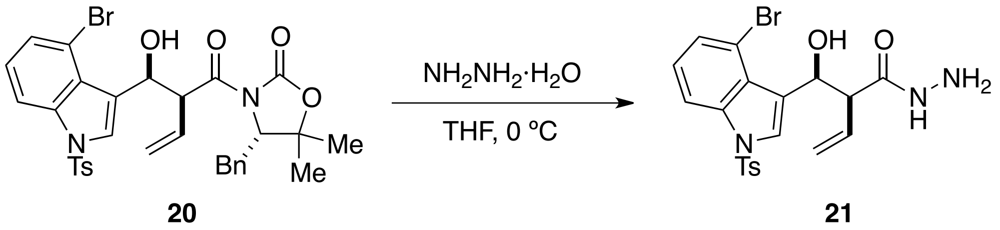
zolidin-2-one (20)



To a solution of **6** (10.43 g, 38.16 mmol) in CH_2Cl_2 (400 ml) was added $TiCl_4$ (4.39 ml, 40.1 mmol) dropwise at –78 °C. After stirring for 5 minutes, *N,N*-diisopropylethylamine (16.5 mL, 95.5 mmol) was added to the resultant yellow solution at –78 °C. The dark purple solution of a titanium enolate was stirred for 1 hours at –78 °C. To a solution of the titanium enolate was added *N*-methlpyrrolidone (3.66 ml, 38.2 mmol). After stirred for 15 minutes, to this solution was added **19** (14.43 g, 38.16 mmol) portionwise at –78 °C. The resulting mixture was stirred for 1 hour at –78 °C and warmed to 0 °C. After stirred for 1 hour at same temperature, the reaction mixture was poured into sat. NH_4Cl, and the resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtrated, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (20% AcOEt in hexane) to afford **20** (20.26 g, 81.50%) as a yellow solid. $[\alpha]_D^{22}$ +111° (*c* 1.00, $CHCl_3$);

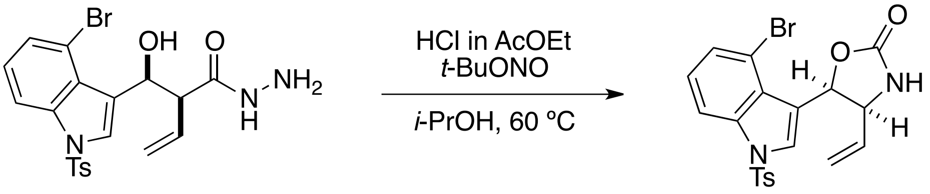
mp: 71-74 °C; IR (film) 3525, 3028, 2981, 1779, 1682, 1411, 1373, 1173, 1098 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.1 Hz, 1 H), 7.73 (d, *J* = 8.0 Hz, 2 H), 7.69 (d, *J* = 0.9 Hz, 1 H), 7.24-7.39 (m, 6 H), 7.22 (d, *J* = 8.0 Hz, 2 H) 7.12 (dd, *J* = 8.1 Hz, 8.1 Hz, 1 H), 6.05 (br s, 1 H), 5.66-5.82 (m, 1 H), 5.25 (d, *J* = 10.6 Hz, 1 H), 5.02 (d, *J* = 17.4 Hz, 1 H), 4.92 (dd, *J* = 2.3 Hz, 8.2 Hz, 1 H), 4.58 (dd, *J* = 4.4 Hz, 9.4 Hz, 1 H), 3.77 (d, *J* = 2.3 Hz, 1H), 3.09 (dd, *J* = 4.4 Hz, 14.4 Hz, 1 H), 2.90 (dd, *J* =9.4 Hz, 14.4 Hz, 1 H), 2.35 (s, 3 H), 1.37 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 151.6, 145.3, 136.5, 136.5, 134.7, 129.9, 129.5, 129.1, 128.7, 128.0, 127.0, 126.9, 126.9, 126.1, 125.4, 122.3, 121.9, 113.5, 113.0, 82.4, 63.4, 52.1, 35.2, 28.4, 22.1, 21.6, 18.1; HRMS (ESI) calcd for $C_{32}H_{31}BrN_2O_6SNa$ $(M+NA)^+$: 673.0984, found 673.0997.

(*S*)-2-((*S*)-(4-bromo-1-tosyl-1*H*-indol-3-yl)(hydroxy)methyl)but-3-enehydrazide (21)



To a stirred solution of **20** (18.85 g, 28.93 mmol) in THF (300 ml) was added hydrazine monohydrate (4.21 ml, 57.9 mmol). After stirring at 0 ºC for 1 h, silica gel (100 g) was added to the solution. The suspension was concentrated *in vacuo*, and the residue was purified with flash column chromatography (ethyl acetate) to afford **21** (12.99 g, 93.86%) as a white foam. $[\alpha]_D^{22}$ −40.6° (*c* 1.03, MeOH); IR (film) 3320, 1653, 1556, 1411, 1370, 1173 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.1 Hz, 1 H), 7.74 (d, *J* = 8.2 Hz, 2 H), 7.71(s, 1 H), 7.38 (d, *J* = 8.1 Hz, 1 H), 7.22 (d, *J* = 8.2 Hz, 2 H), 7.13 (dd, *J* = 8.1 Hz, 8.1 Hz, 1 H), 7.05 (br s, 1 H), 6.11 (s, 1 H), 5.86-5.99 (m, 1 H), 5.11 (d, *J* = 10.6 Hz, 1 H), 4.76 (d, *J* = 17.0 Hz, 1 H), 4.07 (br s, 2 H), 3.40 (d, *J* = 9.2 Hz, 1 H), 2.35 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 145.3, 136.5, 134.8, 130.4, 129.9, 127.8, 127.0, 126.9, 126.4, 125.3, 122.6, 121.2, 113.3, 113.1, 67.0, 54.3, 21.6; HRMS (ESI) calcd for $C_{20}H_{20}BrN_3O_4SNa$ $(M+NA)^+$: 500.0256, found 500.0277.

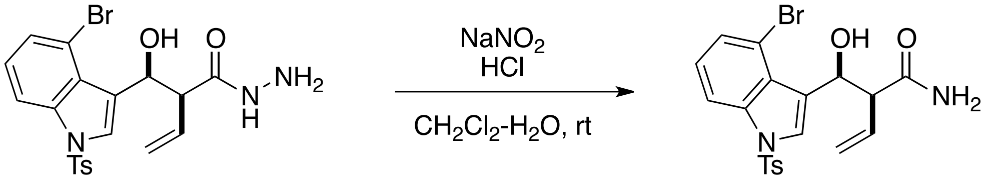
(4*S*,5*R*)-5-(4-bromo-1-tosyl-1*H*-indol-3-yl)-4-vinyloxazolidin-2-one (22)



21 **22**

To a stirred solution of **21** (12.99 g, 27.16 mmol) and hydrogen chloride (4 M ethyl acetate solution, 13.6 ml, 54.4 mmol) in *iso*-propyl alcohol (300 ml) was added *tert*-butyl nitrite (6.44 ml, 54.4 mmol). After stirring at 60 ºC for 1 hour, the solution was concentrated *in vacuo*, and the residue was purified with flash column chromatography (50% ethyl acetate in *n*-hexane) to afford **22** (12.12 g, 96.54%) as a yellow foam. $[\alpha]_D^{23}$ −244.3° (*c* 1.25, $CHCl_3$); IR (film) 3272, 3157, 3016, 1759, 1596, 1556, 1414, 137, 1174 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 1 H), 7.73-7.77 (m, 3 H), 7.38 (d, *J* = 8.2 Hz, 1 H), 7.23-7.30 (m, 2 H), 7.17 (dd, *J* = 8.2 Hz, 8.2 Hz, 1 H), 6.55 (d, *J* = 8.5 Hz, 1 H), 5.24-5.40 (m, 2 H), 5.19 (d, *J* = 17.0 Hz, 1 H), 4.90 (d, *J* = 10.1 Hz, 1 H), 4.87 (dd, *J* = 8.5 Hz, 16.9 Hz, 1 H), 2.36 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 145.6, 136.4, 134.5, 133.4, 130.0, 127.6, 127.3, 126.9, 125.8, 125.5, 118.7, 117.5, 113.2, 113.1, 75.6, 58.8, 21.6; HRMS (ESI) calcd for $C_{20}H_{17}BrN_2O_4SNa$ $(M+NA)^+$: 483.0000, found 482.9993.

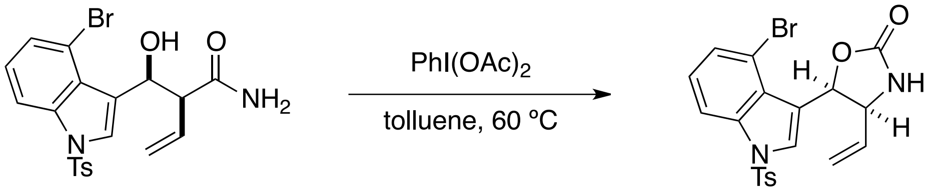
(*S*)-2-((*S*)-(4-bromo-1-tosyl-1*H*-indol-3-yl)(hydroxy)methyl)but-3-enamide (29)



21 **29**

To a stirred solution of **21** (17.3 mg, 0.0361 mmol) and hydrogen chloride (1 M aqueous solution, 0.1 ml, 0.1 mmol) in *iso*-propyl alcohol (0.5 ml) was added sodium nitrite (1 M aqueous solution, 0.1 ml, 0.1 mmol). After stirring at room temperature for 1 hour, the resulting mixture was extracted with CH_2Cl_2 three times. The combined organic layer was dried over sodium sulfate, and filtered. The filtrate was concentrated *in vacuo* and the residue was subjected to preparative thin layer chromatography (50% AcOEt in hexane) to afford **29** (12.3 mg, 73.4%) as yellow solid. $[\alpha]_D^{23}$ –244.3° (*c* 1.25, $CHCl_3$); mp: 84-85 °C; IR (film) 3272, 3157, 3016, 1759, 1596, 1556, 1414, 137, 1174 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 1 H), 7.73-7.77 (m, 3 H), 7.38 (d, *J* = 8.2 Hz, 1 H), 7.23-7.30 (m, 2 H), 7.17 (dd, *J* = 8.2 Hz, 8.2 Hz, 1 H), 6.55 (d, *J* = 8.5 Hz, 1 H), 5.24-5.40 (m, 2 H), 5.19 (d, *J* = 17.0 Hz, 1 H), 4.90 (d, *J* = 10.1 Hz, 1 H), 4.87 (dd, *J* = 8.5 Hz, 16.9 Hz, 1 H), 2.36 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 145.6, 136.4, 134.5, 133.4, 130.0, 127.6, 127.3, 126.9, 125.8, 125.5, 118.7, 117.5, 113.2, 113.1, 75.6, 58.8, 21.6; HRMS (ESI) calcd for $C_{20}H_{19}BrN_2O_4SNa$ $(M+Na)^+$: 485.0147, found 485.0151.

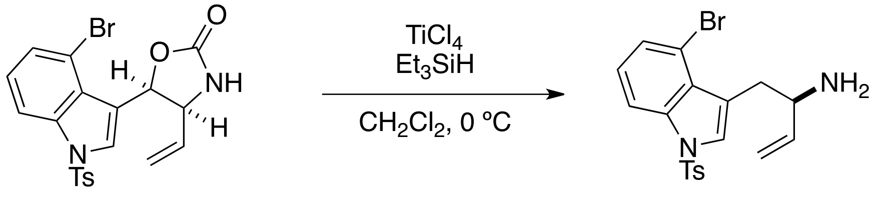
(4*S*,5*R*)-5-(4-bromo-1-tosyl-1*H*-indol-3-yl)-4-vinyloxazolidin-2-one (22)



29 **22**

To a stirred solution of **29** (3.0 mg, 6.5 μmol) in toluene (0.3 ml) was added $PhI(OAc)_2$ (3.1 mg, 9.6 μmol). After stirring at 60 °C for 1 hour, the solution was concentrated *in vacuo*, and the residue was subjected to preparative thin layer chromatography (50% ethyl acetate in *n*-hexane) to afford **22** (3.0 mg, quant.) as a yellow foam. All spectral data were in agreement with those shown in above.

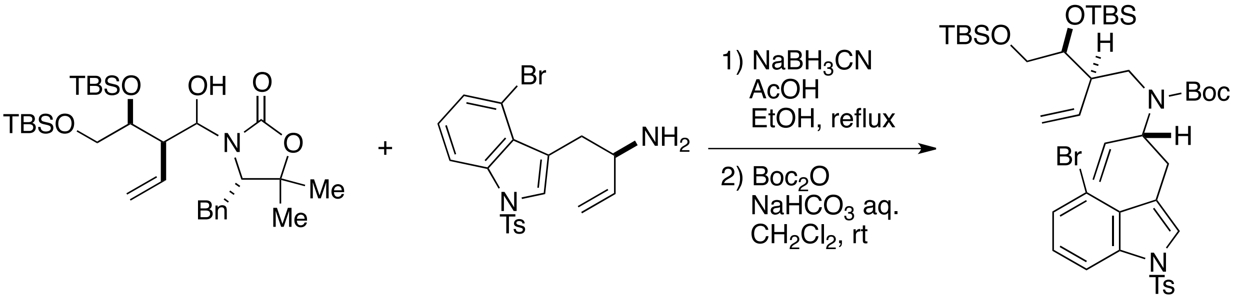
(*R*)-1-(4-bromo-1-tosyl-1*H*-indol-3-yl)but-3-en-2-amine (23)



22 **23**

To a solution of **22** (12.12 g, 26.27 mmol) and triethylsilane (8.40 ml, 52.6 mmol) in CH_2Cl_2 (300 ml) was added titanium tetrachloride (5.76 ml, 52.6 mmol) at 0 ºC, and the solution was stirred for 1 hour. After dilution with CH_2Cl_2, the reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate, and the resulting mixture was stirred for additional 15 minutes. The resulting suspension was filtered through pad of Celite, and the filter cake was washed with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (5% methanol in CH_2Cl_2) to afford **23** (10.24 g, 92.95%) as a brown oil. $[\alpha]_D^{21}$ +14.8° (*c* 1.03, $CHCl_3$); IR (film) 3102, 2919, 1595, 1554, 1411, 1371, 1173 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.0 Hz, 1 H), 7.72 (d, *J* = 8.2 Hz, 2 H), 7.45 (s, 1 H), 7.38 (d, *J* = 8.0 Hz, 1 H), 7.22 (d, *J* =, 8.2 Hz, 2 H), 7.12 (dd, *J* = 8.0 Hz, 8.0 Hz, 1 H), 5.88 (ddd, *J* = 6.4 Hz, 10.5 Hz, 17.4 Hz, 1 H), 5.10 (d, *J* = 17.4 Hz, 1 H), 5.05 (d, *J* = 10.5 Hz, 1 H), 3.74 (ddd, *J* = 6.4 Hz, 6.4 Hz, 6.4 Hz, 1 H), 3.16 (dd, *J* = 6.0 Hz, 14.2 Hz, 1 H), 2.87 (dd, *J* = 7.3 Hz, 14.2 Hz, 1 H), 2.35 (s, 3 H), 1.56 (br s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 141.6, 136.5, 134.7, 129.8, 128.6, 127.9, 126.7, 126.1, 125.3, 119.8, 114.3, 114.3, 112.9, 54.1, 34.3, 21.5; HRMS (ESI) calcd for $C_{19}H_{19}BrN_2O_2SNa$ $(M+Na)^+$: 441.0248, found 441. 0235.

tert-butyl ((*R*)-1-(4-bromo-1-tosyl-1*H*-indol-3-yl)but-3-en-2-yl)((*R*)-2-((*S*)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)but-3-en-1-yl)carbamate (24)

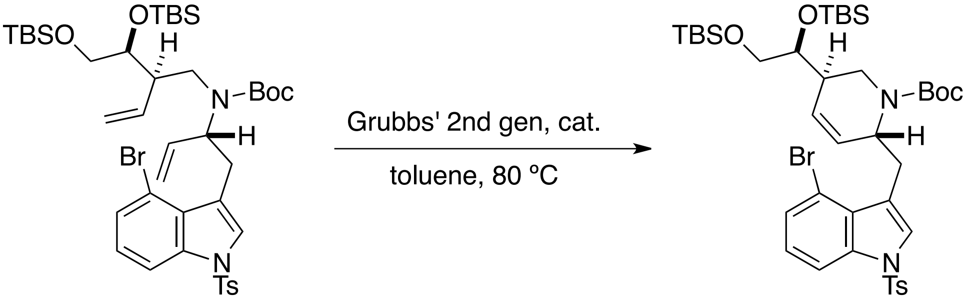


10 **23** **24**

To a solution of hemiaminal **10** (1.89 g, 3.55 mmol) and allylamine **23** (1.24 g, 2.96 mmol) in ethanol (50 ml) were added sodium cyanoborohydride (372.0 mg, 5.92 mmol) and acetic acid (0.169 ml, 2.96 mmol) at room temperature. The reaction mixture was stirred at 80 ºC for 4 hours. Then the reaction mixture was concentrated *in vacuo*. The residue was diluted with AcOEt, and the resulting solution was filtered through a pad of Celite. Concentration of the filtrate afforded crude products, which was used for next step without further purification.

To a solution of the crude products in CH_2Cl_2 (50 ml) and saturated aq. $NaHCO_3$ (50 ml) was added Boc_2O (1.29 g, 5.92 mmol) at room temperature. After stirring for 8 hours, the resulting mixture was partitioned. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was washed with brine, dried over MgSO4, filtered. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (5 % AcOEt in hexane) to afford **24** (1.53 g, 60.0%) as colorless oil. $[\alpha]_D^{20}$ +49.2° (*c* 1.00, $CHCl_3$); IR (film) 2954, 2929, 2857, 1688, 1469, 1412, 1250, 1174 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1 H), 7.75 (d, *J* = 8.3 Hz, 2 H), 7.42 (s, 1 H), 7.35 (d, *J* = 8.0 Hz, 1 H), 7.24 (br s, 2 H), 7.09 (dd, *J* = 8.0 Hz, 8.0 Hz, 1 H), 6.09 (br s, 1 H), 5.60 (br s, 1 H), 5.11 (d, *J* = 5.0 Hz, 1 H), 5.08 (br s, 1 H), 4.89 (br s, 1 H), 4.76 (d, *J* = 16.5 Hz, 1 H), 4.46 (br s, 0.4 H), 4.36 (br s, 0.6 H), 3.24-3.45 (m, 5 H), 2.92 (dd, *J* = 3.7 Hz, 13.7 Hz, 1 H), 2.79 (br s, 1 H), 2.58 (br s, 1 H), 2.35 (s, 3 H), 11.52 (s, 6 H), 1.40 (s, 3 H), 0.90 (s, 9 H), 0.76 (s, 9 H), 0.00 (s, 6 H), –0.10 (s, 3 H), –0.42 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 145.0, 139.0, 138.3, 136.3, 135.6, 135.0, 129.9, 128.9, 127.7, 127.0, 126.4, 125.1, 119.6, 118.7, 115.1, 115.1, 114.2, 112.8, 79.6, 74.1, 74.1, 65.8, 64.9, 62.4, 61.2, 52.5, 51.3, 46.9, 46.6, 28.5, 27.8, 26.0, 25.8, 21.5, 18.3, 17.9, –4.3, –5.4, –5.4; HRMS (ESI) calcd for $C_{42}H_{65}BrN_2O_6SSi_2Na$ $(M+Na)^+$: 883.3183, found 883.3205.

(2*R*,5*R*)-*tert*-butyl 2-((4-bromo-1-tosyl-1*H*-indol-3-yl)methyl)-5-((*S*)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)-5,6-dihydropyridine-1(2*H*)-carboxylate (17)

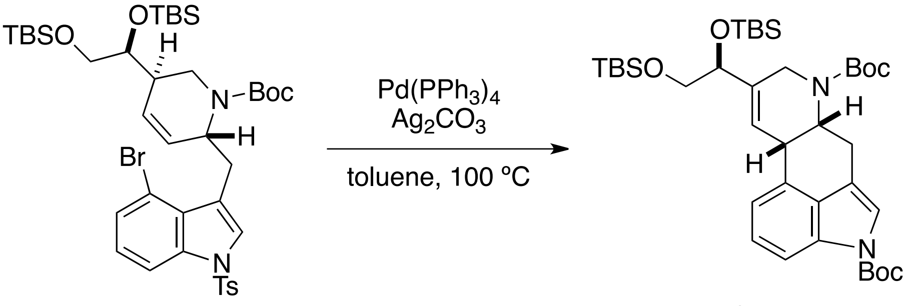


24 **17**

To a solution of **24** (3.25 g, 3.77 mmol) in toluene (50 ml) was added Grubbs' 2nd generation catalyst (96.0 mg, 0.11 mmol, 3 mol%) at room temperature and the reaction mixture was stirred at 80 ºC for 1 hour. Then the reaction mixture was concentrated *in vacuo* and the residue was purified with flash column chromatography (5 % AcOEt in hexane) to afford **17** (3.10 g, 98.6%) as off white foam. $[\alpha]_D^{21}$ –59.8° (*c* 1.06, $CHCl_3$); IR (film) 2954, 2928, 1690, 1415, 1252, 1174 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 1 H), 7.73 (d, *J* = 8.0 Hz, 2 H), 7.37

(d, *J* = 8.0 Hz, 1 H), 7.36 (s, 1 H), 7.24 (d, *J* = 8.0 Hz, 1 H), 7.10 (dd, *J* = 8.0 Hz, 8.0 Hz, 1 H), 5.89 (br s, 1 H), 5.74 (br s, 1 H), 4.82 (t, *J* = 4.1 Hz, 1 H), 4.24 (br s, 1 H), 3.52-3.88 (m, 3 H), 3.38 (d, *J* =11.4 Hz, 1 H), 2.97 (dd, *J* = 4.6 Hz, 13.8 Hz, 1 H), 2.72 (br s, 0.5 H), 2.43 (br s, 0.5 H), 2.34 (s, 3 H), 1.41 (s, 3 H), 0.89 (s, 9 H), 0.89 (s, 9 H), 0.84 (s, 6 H), 0.03 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 145.3, 136.5, 135.1, 130.2, 129.2, 128.7, 127.9, 127.1, 126.3, 125.4, 119.7, 114.9, 113.0, 78.9, 45.5, 75.5, 65.7, 53.0, 38.7, 36.7, 29.5, 28.6, 27.8, 26.3, 26.2, 21.7, 21.7, 18.6, 18.4, –3.9, –4.6, –5.0; HRMS (ESI) calcd for $C_{40}H_{61}BrN_2O_6SSi_2Na$ $(M+Na)^+$: 855.2870, found 855.2844.

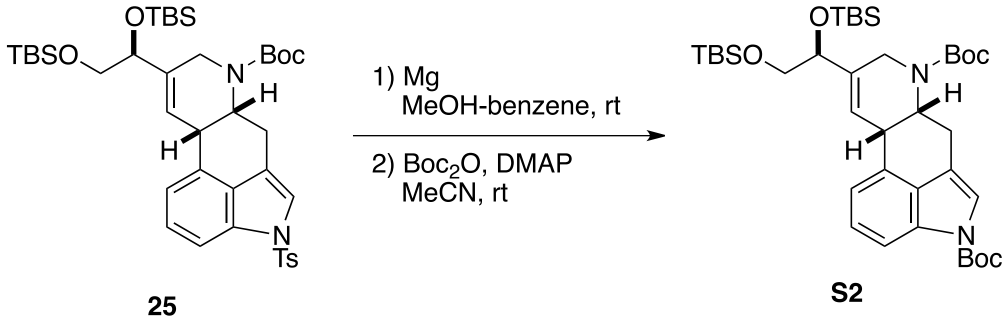
(6a*R*,10a*S*)-di-*tert*-butyl 9-((*S*)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)-6,6a-dihydroindolo[4,3-*fg*]quinoline-4,7(8*H*,10a*H*)-dicarboxylate (25)



17 **25**

To a solution of **17** (3.10 g, 3.72 mmol) in toluene (50 ml) was added catalytic amount of $Pd(PPh_3)_4$ (429.9 mg, 0.3720 mmol, 10 mol%) and Ag_2CO_3 (2.05 g, 7.44 mmol) at room temperature and the reaction mixture was stirred at 100 ºC for 4 hours. Then the reaction mixture was concentrated *in vacuo* and the residue was purified with flash column chromatography (10% AcOEt in hexane) to afford **25** (2.50 g, 89.3%) as white foam. $[\alpha]_D^{23}$ –73.0º (*c* 1.00, $CHCl_3$); IR (film) 2954, 2929, 1695, 1362, 1252, 1175 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 6.4 Hz, 2 H), 7.70 (d, *J* = 7.3 Hz, 1 H), 7.10-7.36 (m, 4 H), 6.99-7.08 (m, 1 H), 5.57 (d, *J* = 14.7 Hz, 1 H), 4.72 (br s, 0.6 H), 4.60 (br s, 0.4 H), 4.24 (d, *J* = 18.4 Hz, 0.4 H), 4.12 (d, *J* = 16.8 Hz, 0.65 H), 4.02 (t, *J* = 6.0 Hz, 1 H), 3.53-3.56 (m, 2 H), 3.49-3.51 (m, 2 H), 2.64-2.88 (m, 2 H), 2.34 (s, 3 H), 1.50 (s, 5 H), 1.45 (s, 4 H), 0.83 (s, 9 H), 0.82 (s, 9 H), 0.00 (s, 3 H), –0.02 (s, 6 H), –0.07 (s, 1.5 H), –0.11 (s, 1.5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 144.6, 134.3, 133.8, 129.8, 129.7, 126.8, 126.6, 125.8, 124.8, 124.1, 120.4, 120.3, 119.6, 118.3, 117.8, 111.8, 111.8, 111.7, 80.0, 75.7, 75.2, 49.4, 48.3, 40.6, 37.4, 28.4, 25.8, 25.7, 21.5, 21.2, 18.2, 18.1, –4.9, –5.4, –5.5; HRMS (ESI) calcd for $C_{40}H_{60}N_2O_6SSi_2Na$ $(M+Na)^+$: 775.3608, found 775.3585.

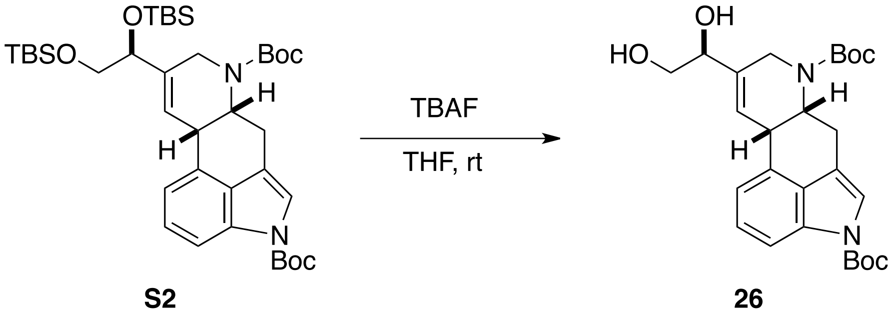
(6a*R*,10a*S*)-di-*tert*-butyl 9-((*S*)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)-6,6a-dihydroindolo[4,3-*fg*]quinoline-4,7(8*H*,10a*H*)-dicarboxylate (S2)



To a solution of **25** (2.45 g, 3.25 mmol) in methanol (50 ml) and benzene (50 ml) was added magnesium turning (0.79 g, 32.5 mmol) at room temperature. After stirring at the same temperature for 1 hour, the reaction mixture was quenched with 1 M aq. HCl, and the resulting mixture was extracted with AcOEt three times. The combined organic layer was washed with brine, dried over sodium sulfate, and filtered. Concentration of the filtrate gave the crude products, which was used for next step without further purification.

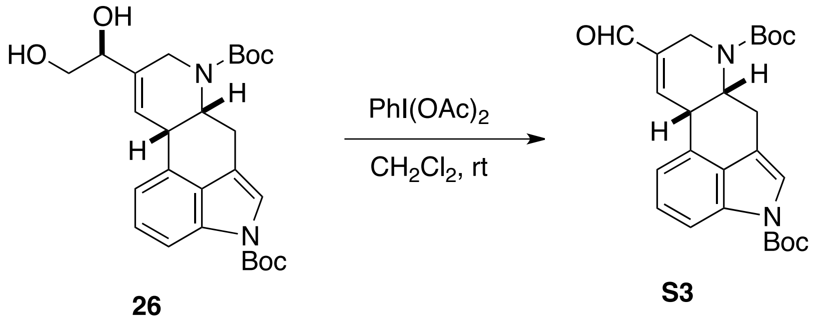
To a solution of crude mixture in MeCN (50 ml) was added Boc_2O (0.92 g, 4.2 mmol) and DMAP (34.5 mg, 0.28 mmol) at room temperature. After stirring at the same temperature for 1 hour, the solution was concentrated *in vacuo* and the residue was purified with flash column chromatography (10% AcOEt in hexane) to afford **S2** (1.91 g, 84.0%) as colorless oil. $[\alpha]_D^{25}$ –45.2° (*c* 1.00, $CHCl_3$); IR (film) 2955, 2930, 2857, 1732, 1698, 1441, 1390, 1360, 1254 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (br s, 1 H), 7.17-7.35 (m, 2 H), 7.06 (d, *J* = 7.4 Hz, 0.6 H), 7.03 (d, *J* = 7.4 Hz, 0.4 H), 5.63 (s, 1 H), 4.82 (br s, 0.4 H), 4.65 (dd, *J* = 6.0 Hz, 6.0 Hz, 0.6 H), 4.27 (d, *J* = 18.4 Hz, , 0.6 H), 4.17 (d, *J* = 17.9 Hz, 0.4 H), 4.07 (br s, 1 H), 3.70-3.83 (m, 2 H), 3.47-3.58 (m, 2 H), 2.67-2.93 (m, 2 H), 1.67 (s, 9 H), 1.51 (s, 4 H), 1.46 (s, 5 H), 0.88 (s, 9 H), 0.84 (s, 9 H), 0.03 (s, 6 H), 0.00 (s, 3 H), –0.03 (s, 1.5 H), –0.06 (s, 1.5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 154.7, 150.1, 131.3, 133.9, 133.3, 128.4, 125.4, 125.2, 124.5, 119.7, 119.4, 115.9, 113.3, 113.3, 84.7, 83.3, 79.9, 76.0, 75.4, 67.0, 66.8, 49.9, 48.6, 40.3, 39.6, 37.8, 37.6, 31.6, 28.5, 28.2, 25.9, 25.7, 22.6, 21.8, 21.2, 18.3, 18.1, 14.1, –4.9, –5.0, –5.4, –5.4; HRMS (ESI) calcd for $C_{38}H_{62}N_2O_6Si_2Na$ $(M+Na)^+$: 721.4044, found 721.4052.

(6a*R*,10a*S*)-di-*tert*-butyl 9-((*S*)-1,2-dihydroxyethyl)-6,6a-dihydroindolo[4,3-*fg*]quinoline-4,7(8*H*, 10a*H*)-dicarboxylate (26)



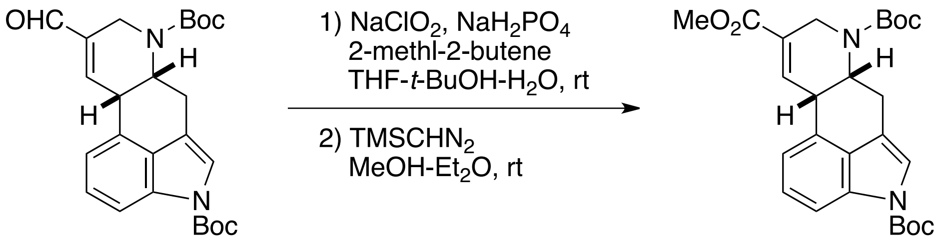
To a solution of **S2** (1.91 g, 2.73 mmol) in THF (50 ml) was added TBAF (1.0 mol/l THF solution, 6.83 ml, 6.83mmol) at room temperature. After stirring at same temperature for 2 hour, the solution was quenched with saturated aq. NH_4Cl, and the resulting mixture was extracted with AcOEt three times. The combined organic layer was washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (AcOEt) to afford **26** (1.21 g, 94.1%) as pale yellow foam. $[\alpha]_D^{23}$ −103° (*c* 1.00, $CHCl_3$); IR (film) 3378, 2954, 2929, 2857, 1733, 1254, 1106, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (br s, 1 H), 7.20-7.34 (m, 2 H), 7.08 (br s, 1 H), 5.75 (s, 1 H), 4.83 (br s, 0.4 H), 4.67 (br s, 0.6 H), 4.16-4.38 (m, 2 H), 3.85 (d, *J* = 1.4 Hz, 1 H), 3.66-3.77 (m, 2 H), 3.58 (dd, *J* = 7.8 Hz, 11.0 Hz, 1 H), 2.61-2.98 (m, 2H), 1.66 (s, 9 H), 1.51 (s, 3 H), 1.45 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 154.7, 149.7, 133.0, 132.6, 128.0, 125.3, 124.6, 124.1, 119.7, 119.2, 115.5, 113.2, 83.1, 80.2, 80.0, 73.4, 65.3, 49.5, 48.1, 40.6, 39.8, 37.4, 37.2, 28.2, 27.9, 21.8, 21.4; HRMS (ESI) calcd for $C_{26}H_{34}N_2O_6Na$ $(M+Na)^+$: 493.2315, found 493.2307.

(6a*R*,10a*S*)-di-*tert*-butyl
9-formyl-6,6a-dihydroindolo[4,3-*fg*]quinoline-4,7(8*H*,10a*H*)-dicarboxylate (S3)



To a solution of **26** (1.21 g, 2.57 mmol) in CH_2Cl_2 (50 ml) was added $PhI(OAc)_2$ (0.99 g, 3.08 mmol) at room temperature. After stirring at same temperature for 1 hour, the solution was quenched with saturated aq. $NaHCO_3$, and the resulting mixture was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (10 % AcOEt in hexane) to afford **S3** (0.91 g, 81%) as off-white foam. $[\alpha]_D^{24}$ −140° (*c* 0.31, $CHCl_3$); IR (film) 2976, 1731, 1696, 1441, 1390, 1345, 1161, 1115 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.41 (s, 1 H), 7.87 (br s, 1 H), 7.24-7.38 (m, 2 H), 7.16 (br s, 1 H), 6.80 (br s, 0.6 H), 6.76 (br s, 0.4 H), 5.00 (br s, 0.6 H), 4.81 (br s, 0.4 H), 4.68 (d, *J* = 19.0 Hz, 0.4 H), 4.53 (d, *J* = 18.1 Hz, 0.6 H), 4.10 (br s, 1 H), 3.88 (d, *J* = 18.1, 0.6 H), 3.84 (d, *J* = 19.0 Hz, 0.4 H), 2.62-2.94 (m, 2 H), 1.66 (s, 9 H), 1.51 (s, 5.4 H), 1.47 (s, 3.6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 191.2, 154.5, 154.3, 150.6, 149.8, 149.3, 136.5, 136.1, 133.4, 130.3, 130.1, 128.4, 125.6, 119.9, 119.7, 114.8, 114.0, 83.5, 80.5, 49.5, 48.1, 39.0, 39.0, 38.2, 37.5, 28.3, 28.1, 21.9, 21.3; HRMS (ESI) calcd for $C_{25}H_{30}N_2O_5Na$ $(M+Na)^+$: 461.2052, found 461.2062.

(6a*R*,10a*S*)-4,7-di-*tert*-butyl 9-methyl 6,6a-dihydroindolo[4,3-*fg*]quinoline-4,7,9(8*H*,10a*H*)-tricarboxylate (27)

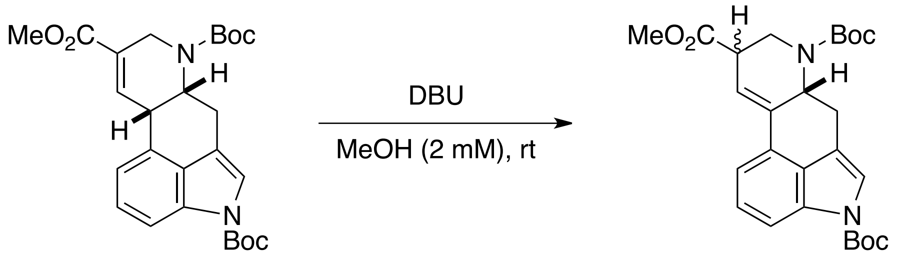


S3 **27**

To a stirred solution of **S3** (0.91 g, 2.1 mmol), $NaH_2PO_4{\cdot}2H_2O$ (0.65 g, 4.1 mmol), and 2-methyl-2-butene (2.2 ml, 21.0 mmol) in THF (15 ml), *tert*-butanol (15 ml) and H_2O (5 ml) was added $NaClO_2$ (0.95 g, 10 mmol) at room temperature. After stirring at same temperature for 4 hour, the solution was quenched with saturated aq. $NaHSO_3$, and the resulting mixture was extracted with AcOEt three times. The combined organic layer was washed with brine, dried over sodium sulfate, and filtered. Concentration of the filtrate gave the crude products, which was used for next step without further purification.

To a solution of the crude carboxylic acid in methanol (20 ml) and Et_2O (20 ml) was added TMS diazomethane (1.0 M Et_2O solution, 4.16 ml, 4.16 mmol) at room temperature. After stirring at same temperature for 15 minutes, the solution was quenched with 1 M aq. HCl, and the resulting mixture was extracted with AcOEt three times. The combined organic layer was washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (10 % AcOEt in hexane) to afford **27** (0.85 g, 87%) as off-white foam. $[\alpha]_D^{23}$ −112° (*c* 1.05, $CHCl_3$); IR (film) 2977, 1721, 1697, 1440, 1391, 1361, 1251, 1165, 1114 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (br s, 1 H), 7.22-7.36 (m, 2 H), 7.13 (br s, 1 H), 6.96 (br s, 1 H), 4.92 (br s, 0.5 H), 4.66-4.80 (m, 1.5 H), 3.96 (s, 1 H), 3.88 (d, *J* = 17.4 Hz, 17.4 Hz, 1 H), 3.54 (s, 3 H), 2.70-2.88 (m, 2 H), 1.66 (s, 9 H), 1.52 (s, 5 H), 1.46 (s, 4 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.3, 165.2, 154.3, 149.7, 140.6, 139.8, 133.2, 130.9, 128.3, 125.8, 125.4, 119.7, 119.6, 115.0, 113.7, 83.2, 80.2, 51.6, 48.9, 47.3, 39.7, 38.4, 38.2, 28.3, 28.0, 21.5, 21.3; HRMS (ESI) calcd for $C_{26}H_{32}N_2O_6Na$ (M+Na)$^+$: 491.2158, found 491.2170.

(6a*R*)-4,7-di-*tert*-butyl 9-methyl 6,6a,8,9-tetrahydroindolo[4,3-*fg*]quinoline-4,7,9-tricarboxylate (S4)

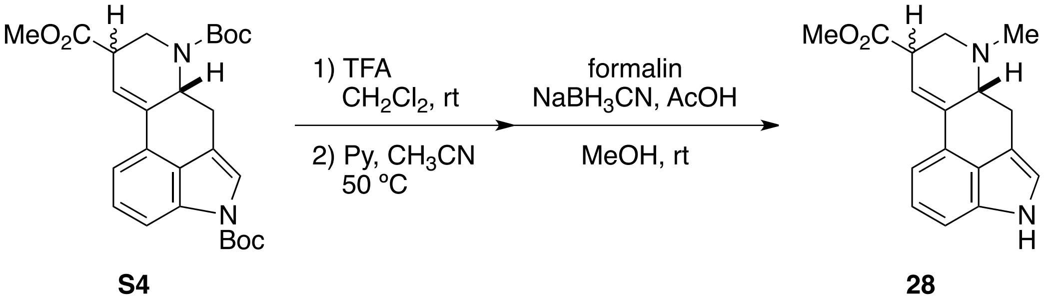


27

S4

To a stirred solution of **27** (370.0 mg, 0.790 mmol) in methanol (400 ml) added 1,8-diazabicyclo[5.4.0]undec-7-ene (0.12 ml, 0.79 mmol) at room temperature. After stirred at same temperature for 8 hours, 1 M aq. HCl (5ml) was added to the reaction mixture, which was then evaporated *in vacuo*. The residue was partitioned between AcOEt and water, and the organic extracts were washed with brine, dried over Na_2SO_4, and filtered. Concentration of the filtrate gave the crude products, which was used for the next step without further purification. Two diastereomers could be separated with flash column chromatography (10 to 20% AcOEt in hexane) to afford **S4a** and **S4b** for spectral analysis. Less polar isomer: $[\alpha]_D^{23}$ –206° (*c* 1.21, CHCl$_3$); IR (film) 2976, 1731, 1696, 1441, 1389, 1164, 1122 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.83 (s, 1 H), 7.25-7.31 (m, 3 H), 6.57 (br s, 1H), 4.37-4.85 (m, 2 H,), 3.76 (s, 3 H), 3.48 (br s, 1 H), 3.21 (br s, 1 H), 2.96 (br s, 1H), 2.83 (br s, 1 H), 1.67 (s, 9 H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 172.0, 154.2, 150.0, 135.0, 133.5, 129.4, 128.2, 125.3, 120.4, 120.1, 119.8, 115.6, 115.3, 114.4, 83.5, 80.4, 52.6, 52.2, 51.8, 41.9, 38.8, 29.7, 28.4, 28.2; HRMS (ESI) calcd for $C_{26}H_{32}N_2O_6Na$ (M+Na)$^+$: 491.2158, found 491.2144. More polar isomer: $[\alpha]_D^{23}$ –81.7° (*c* 1.10, CHCl$_3$); IR (film) 2977, 2930, 1733, 1696, 1389, 1354, 1296, 1164 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.83 (s, 1 H), 7.26-7.33 (m, 3 H), 6.47 (d, *J* = 6.0 Hz, 1H), 4.83 (br s, 1 H), 4.68 (d, *J* = 12.4 Hz, 1 H), 3.73 (s, 3 H), 3.35 (br s, 1 H), 3.22 (d, *J* = 11.0 Hz, 1 H), 3.08 (d, *J* = 11.9 Hz, 1 H), 2.78 (dd, *J* = 13.3 Hz, 13.3 Hz, 1 H), 1.67 (s, 9 H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 171.9, 154.2, 150.0, 136.1, 133.5, 129.3, 128.2, 125.3, 120.1, 118.3, 115.7, 115.4, 114.4, 83.5, 80.0, 52.2, 52.2, 41.5, 39.5, 28.4, 28.2, 26.8; HRMS (ESI) calcd for $C_{26}H_{32}N_2O_6Na$ (M+Na)$^+$: 491.2158, found 491.2154.

Lysergic acid methyl ester (60a) and *iso*-lysergic acid methyl ester (28)

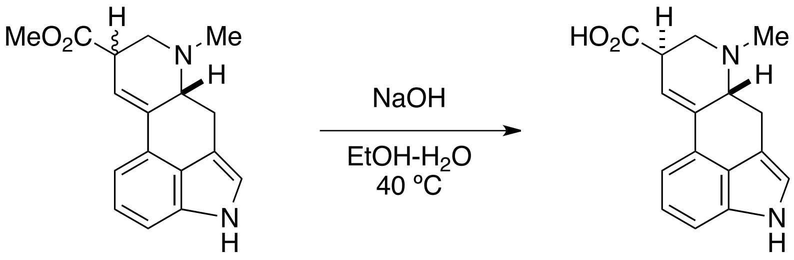


To a stirred solution of the diastereomixture of **S4** in CH_2Cl_2 (8 ml) and dimethyl sulfide (1 ml) was added trifluoroacetic acid (2 ml) at room temperature. After stirring at same temperature for 1 hour, the reaction mixture was diluted with toluene (10 ml). Concentration of the reaction mixture gave the crude product, which was used for next step without further purification.

To a stirred solution of the crude product in CH_3CN (10 ml) was added pyridine (0.2 ml) at room temperature. After stirred at 50 °C for 30 minutes, the reaction mixture was concentrated *in vacuo*. The crude product was used for next step without further purification.

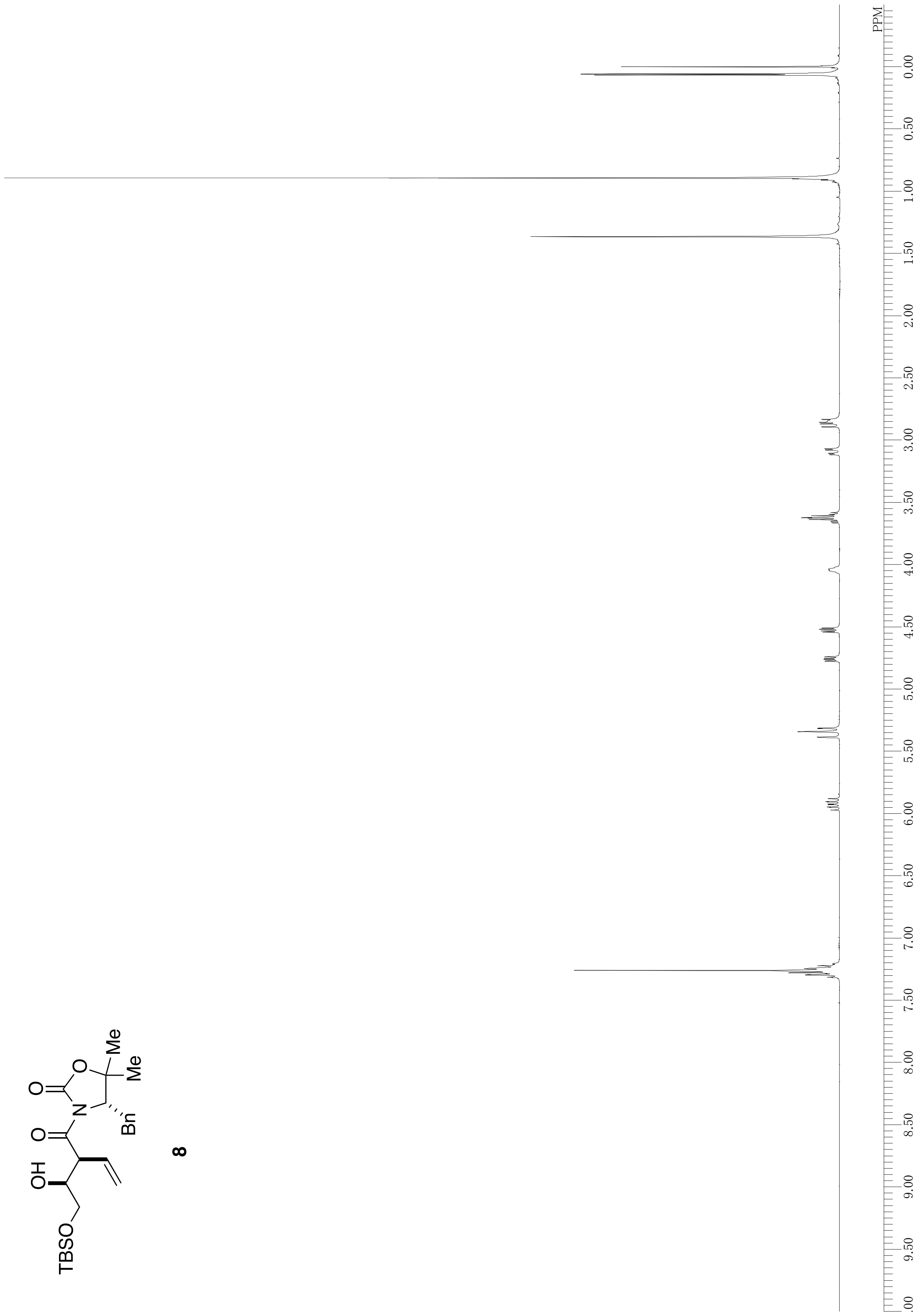
To a stirred solution of this crude product, formalin (0.2 ml), $NaBH_3CN$ (148.9 mg, 2.37 mmol) in methanol (10 ml) added AcOH (1 ml) at room temperature. After stirring for 1 hour at this temperature, the mixture was quenched with saturated aq. $NaHCO_3$. The resulting mixture was extracted with AcOEt, three times. The combined organic layer was washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified with flash column chromatography (AcOEt) to afford a diastereomixture of **28a** and **28b** (168.3 mg, 75.5%, **28a**:**28b** = 2:1) as brown solid. IR (film) 2977, 2930, 1733, 1696, 1389, 1354, 1296, 1164 cm^{-1}; ^1H NMR spectra of **28a** and **28b** were in agreement with those reported by Ohno [Inuki, S.; Oishi, S.; Fujii, N.; Ohno, H. *Org. Lett.* **2008**, *10*, 5239.] ^1H NMR (400 MHz, $CDCl_3$) of methyl lysergate : δ 7.92 (br s, 1H), 7.14-7.35 (m, 3H), 6.90 (br s, 1H), 6.60 (br s, 1H), 3.78 (s, 3H), 3.68-3.80 (m, 1H), 3.52 (dd, *J* = 14.2, 5.2 Hz, 1H), 3.17-3.33 (m, 2H), 2.64-2.83 (m, 2H), 2.61 (s, 3H). ^1H NMR (400 MHz, $CDCl_3$) of methyl isolysergate : δ 7.92 (br s, 1H), 7.14-7.35 (m, 3H), 6.91 (br s, 1H), 6.55 (d, *J* = 5.4 Hz, 1H), 3.73 (s, 3H), 3.68-3.80 (m, 1H), 3.43 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.35 (dd, *J* = 11.2, 2.8 Hz, 1H), 3.17-3.33 (m, 1H), 2.64-2.83 (m, 2H), 2.58 (s, 3H). HRMS (ESI) calcd for $C_{17}H_{19}N_2O_2$ $(M+H)^+$: 283.1447, found 283.1441.

Lysergic acid (1)



28 lysergic acid (**1**)

To solution of diastereomixture of methyl lysergate and isolysergate (141.8 mg, 0.502 mmol, **28a**:**28b** = 2:1) in EtOH (5.0 ml) was added 1 *N* NaOH (5.0 ml). The reaction mixture was stirred at 40 °C for 2 h. 1 *N* aqueous HCl solution was used to carefully adjust the pH to 6. The resulting mixture was concentrated *in vacuo*. The residue was washed with ice cold water (1 ml) three times, and acetone (1 ml). The resulting solid was dried *in vacuo* to afford **1** (105.6 mg, 78.4%) as brown solid. $[\alpha]_D^{23}$ 40.3° (*c* 0.42, pyridine); mp: 220-230 °C (decomp.); IR (film) 3396, 1599, 1449, 1380 cm^{-1}; ^{1}H NMR (400 MHz, C_5D_5N) δ 11.69 (s, 1 H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.30 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.16-7.26 (m, 2H), 4.05 (br s, 1H), 3.63 (dd, *J* = 14.4 Hz, 4.8 Hz, 1H), 3.53 (br s, 1H), 3.29 (br s, 1H), 2.84-2.97 (m, 2H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, C_5D_5N) δ 175.0, 136.8, 135.8, 128.8, 127.3, 120.1, 119.8, 112.2, 110.5, 110.4, 63.7, 56.1, 43.9 (2C), 27.8 (one of the sp$_2$ carbons was overlapped with C_5D_5N solvent peaks)



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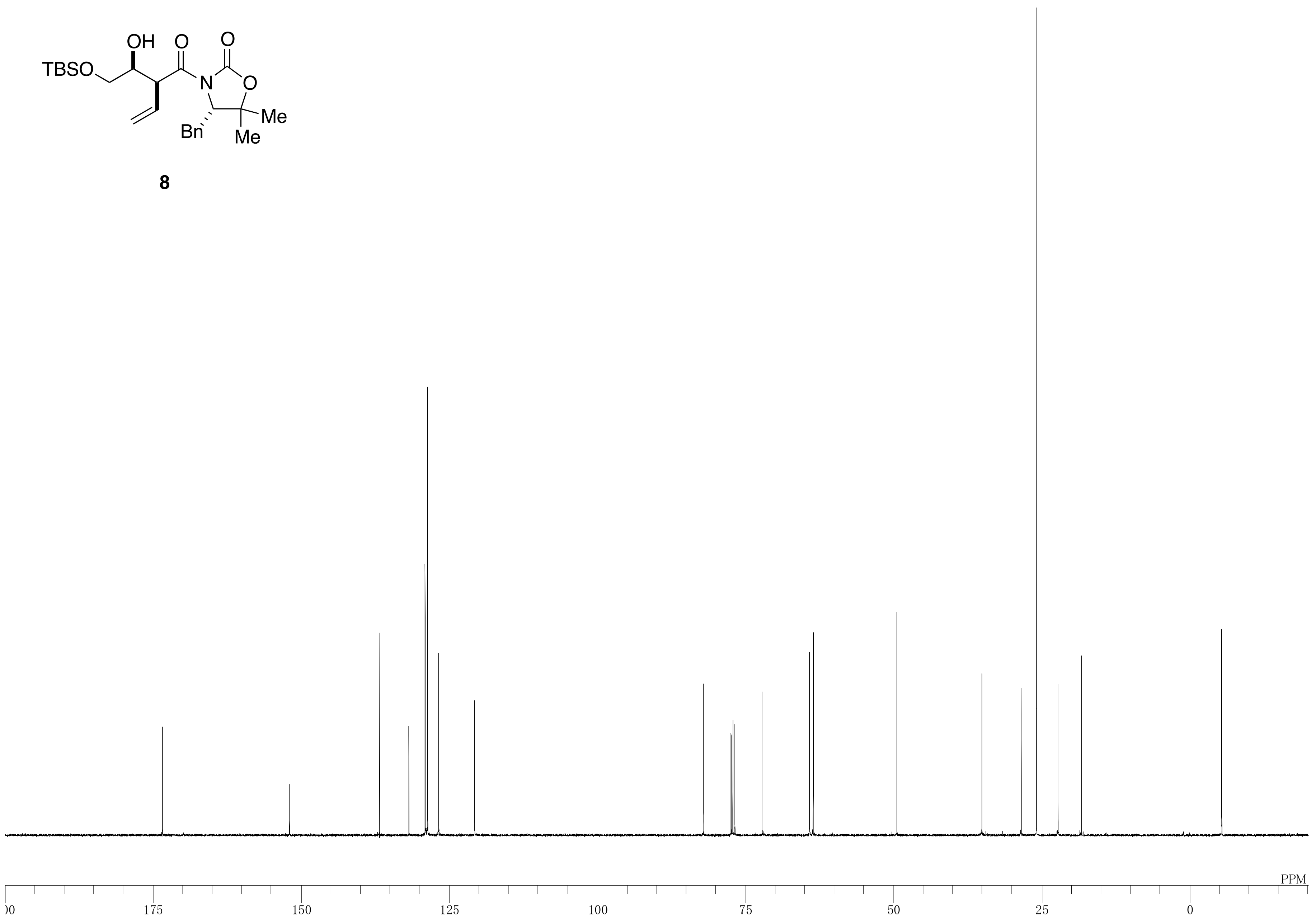
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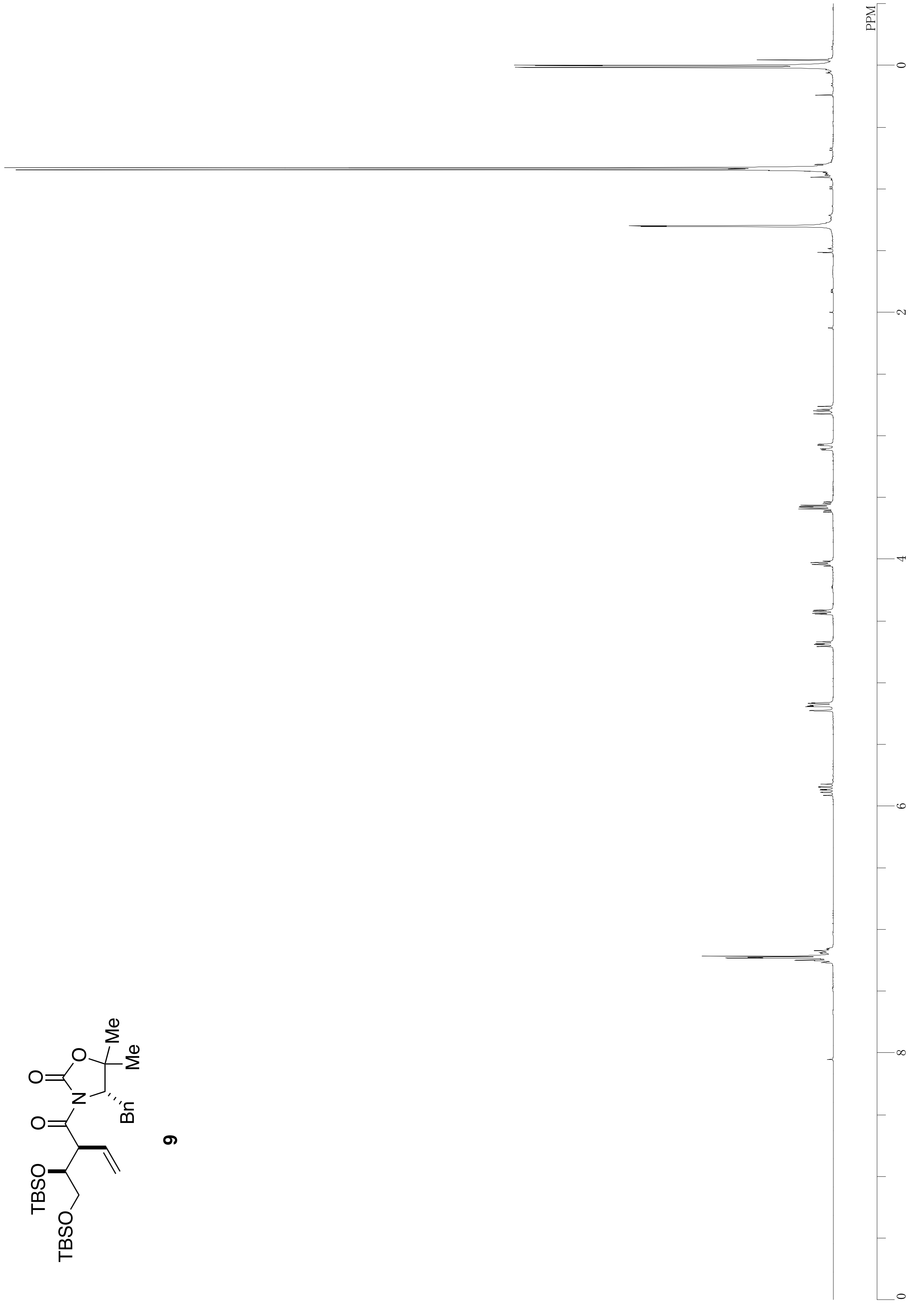

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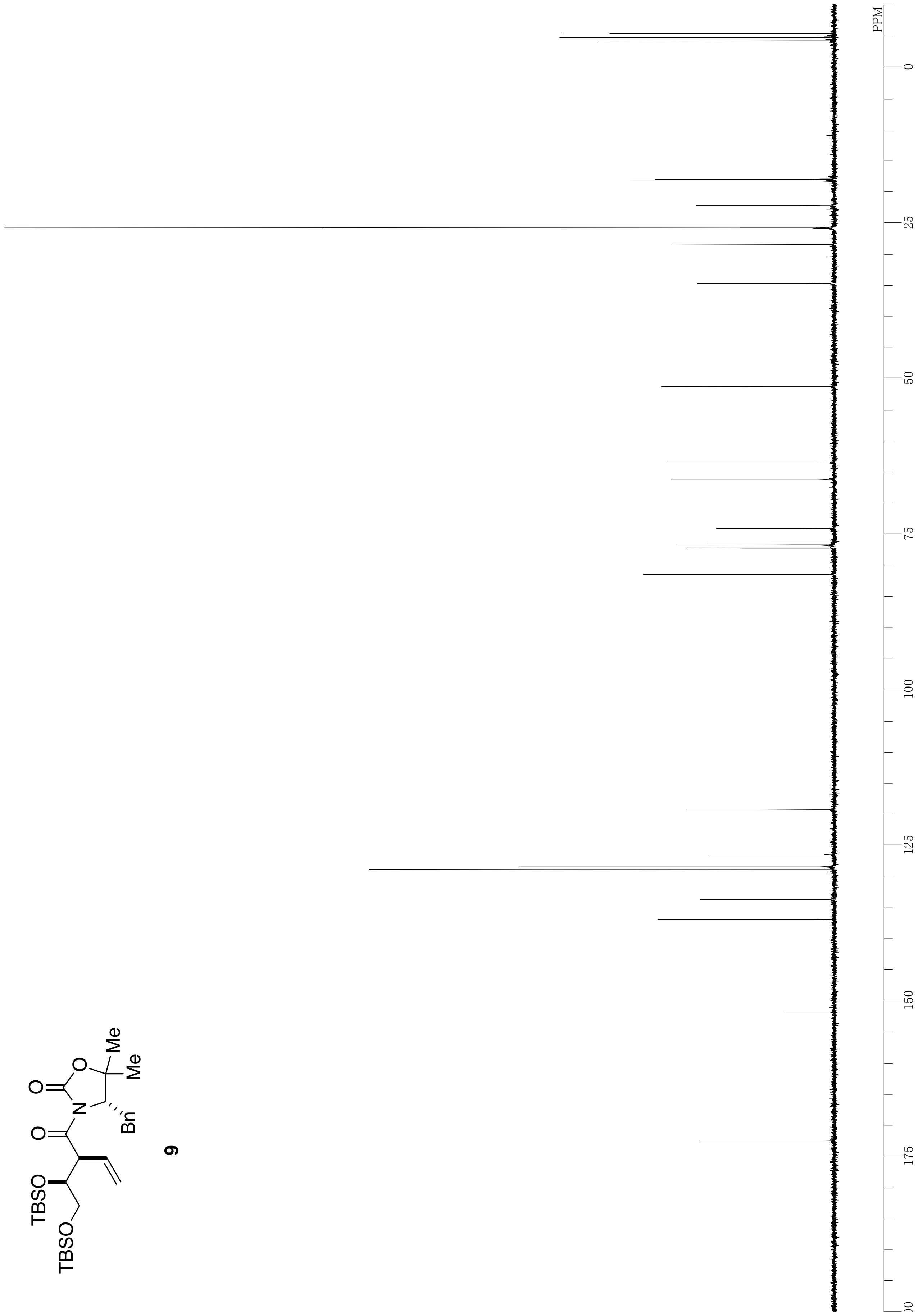

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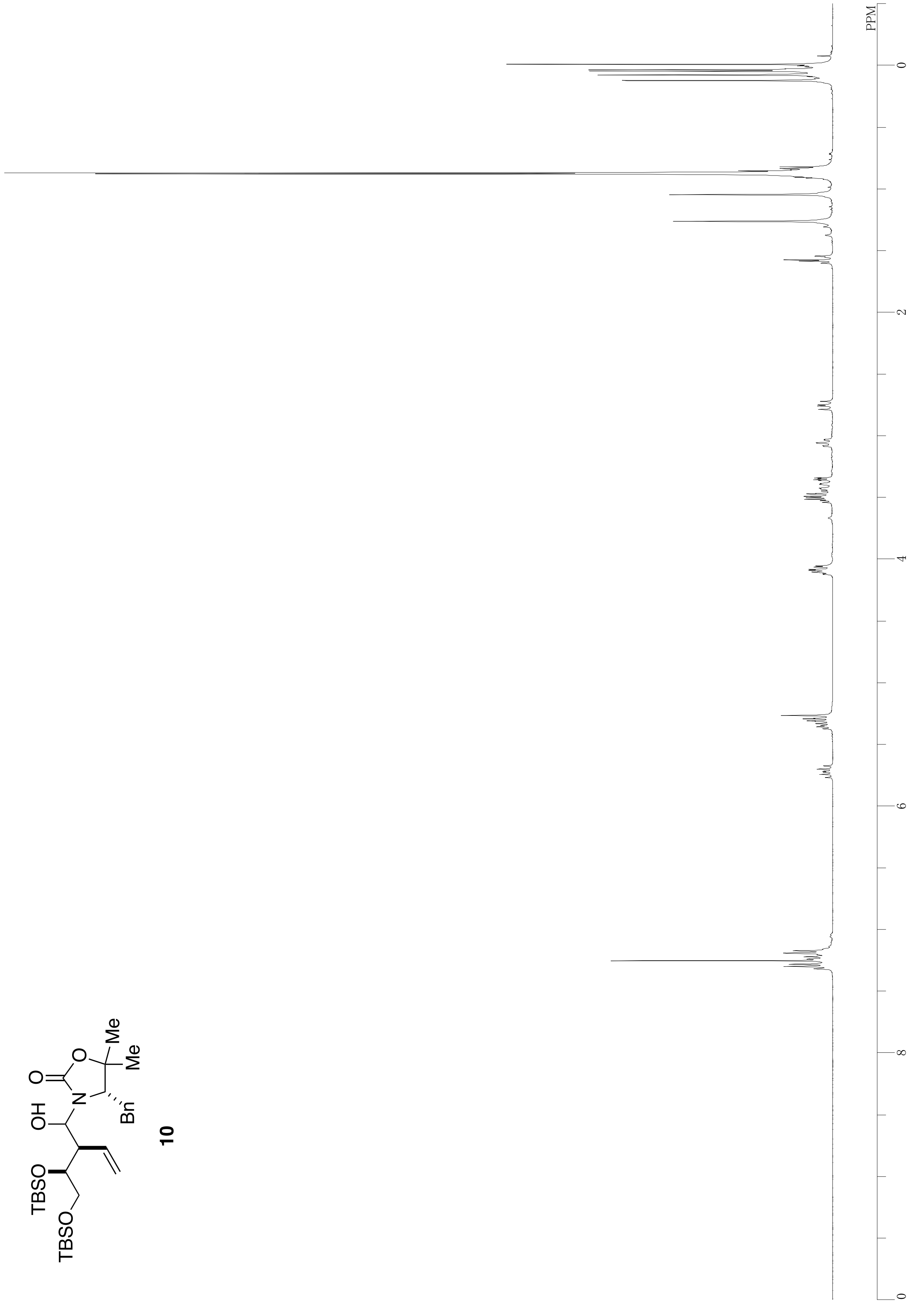

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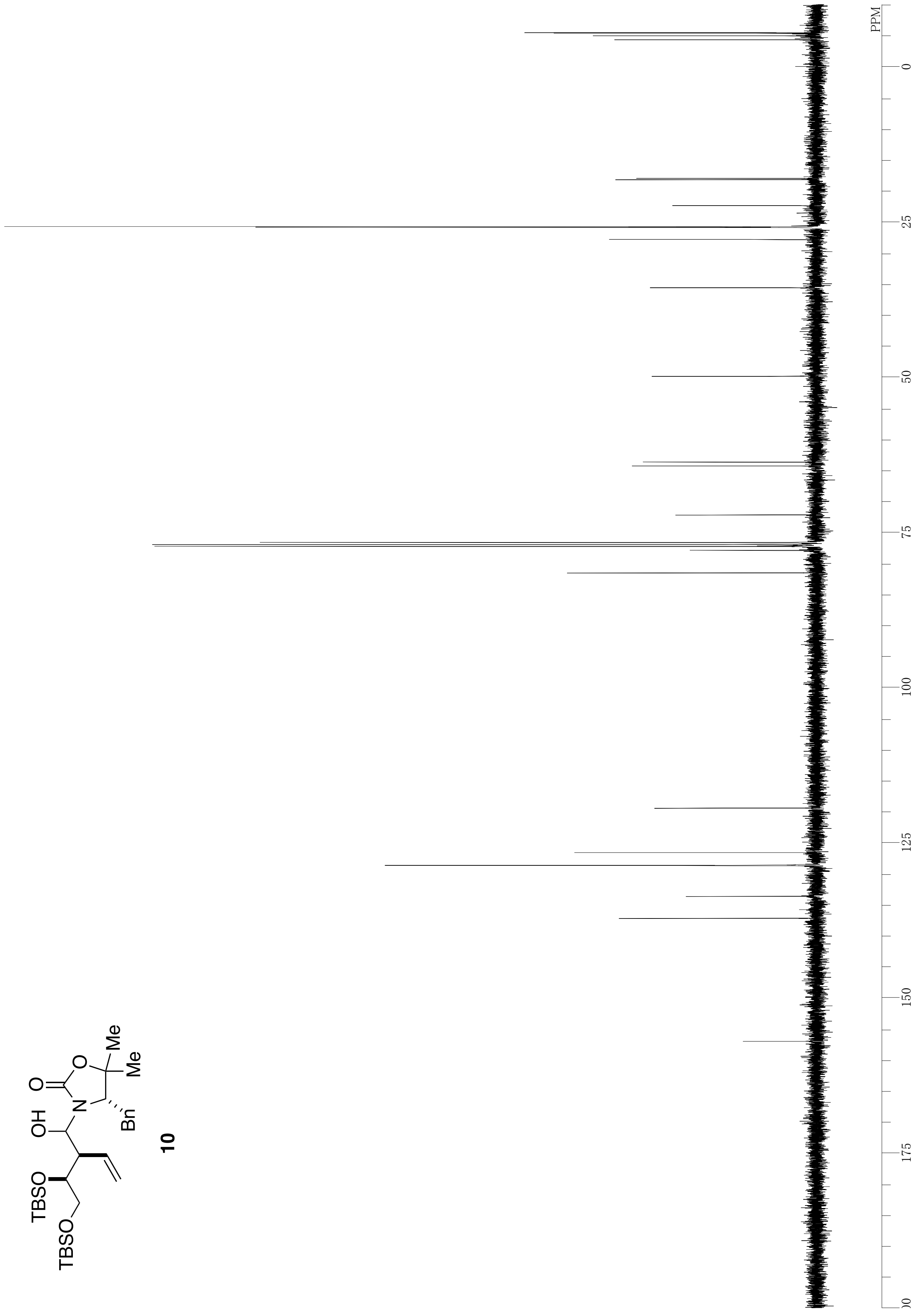

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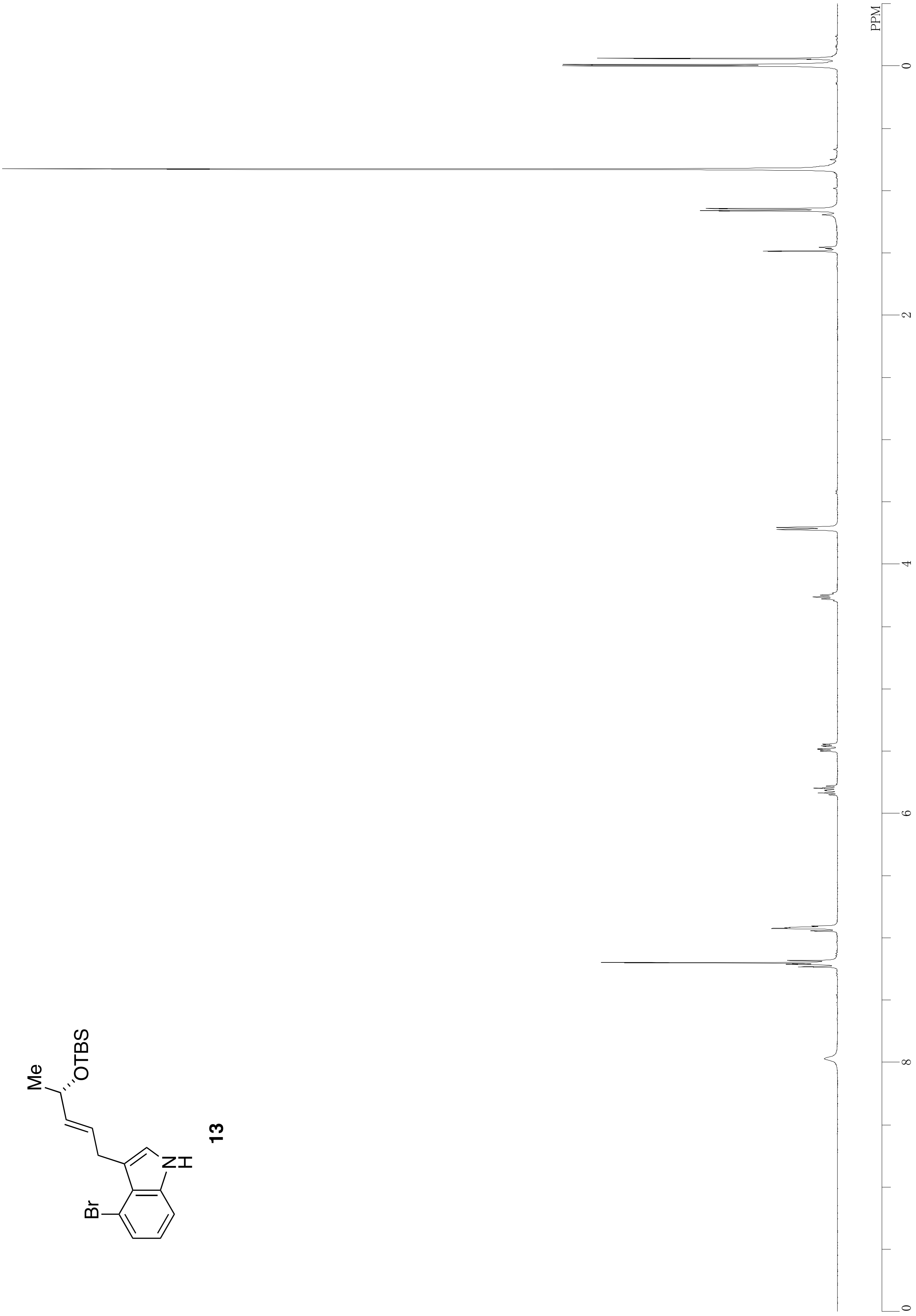

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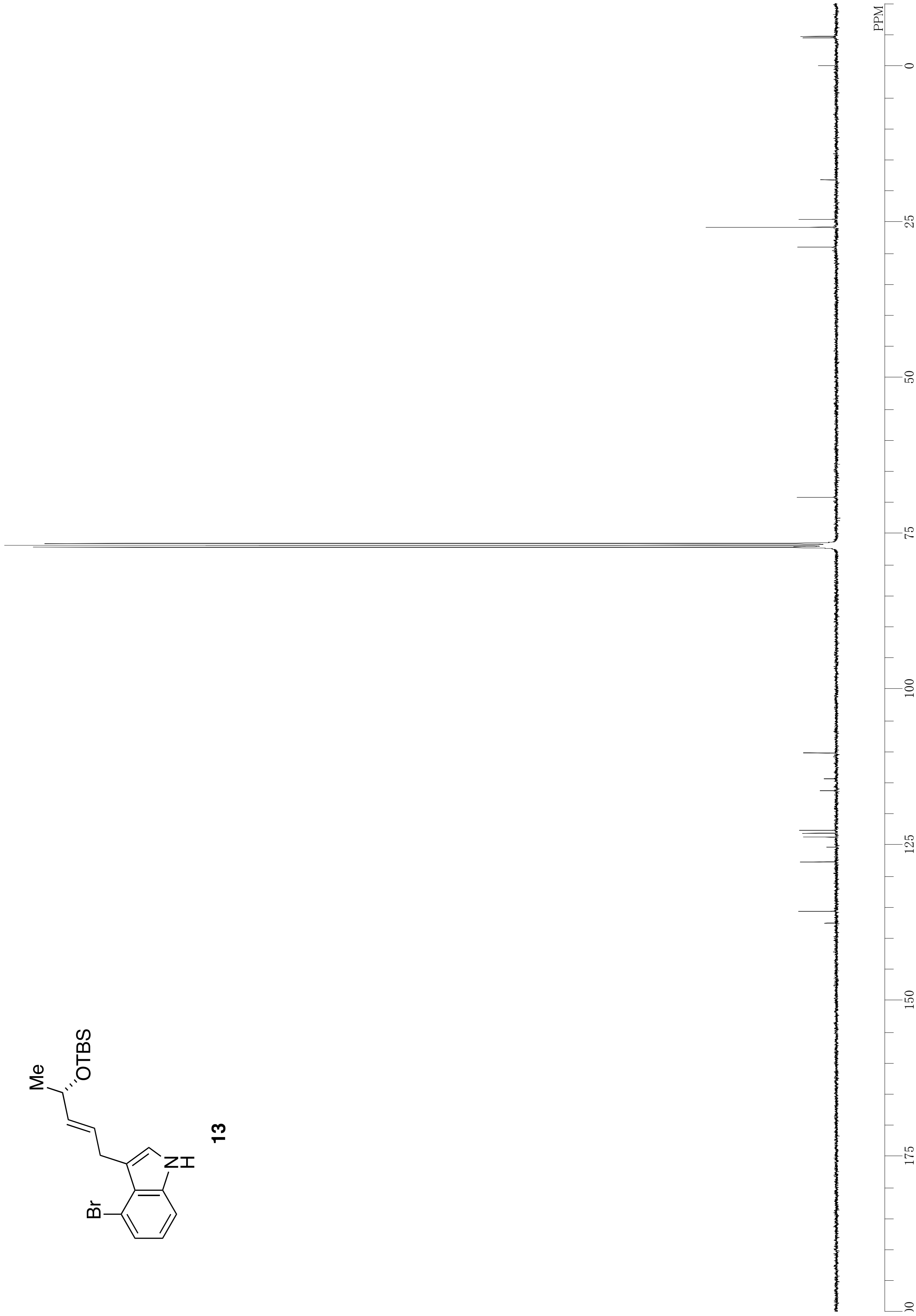

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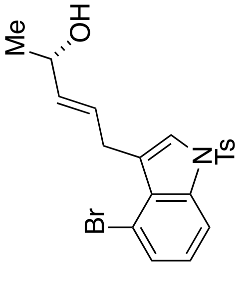
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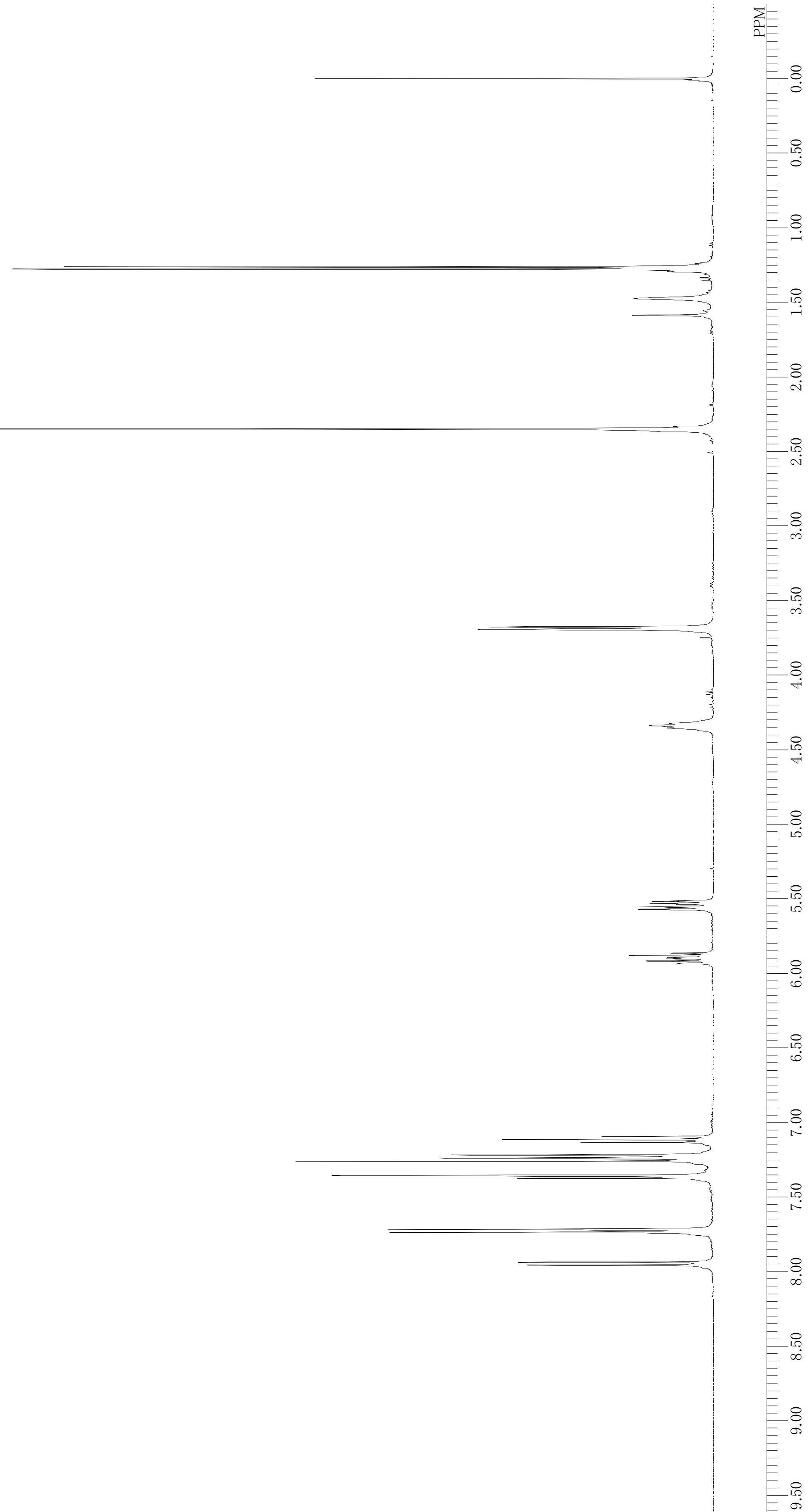
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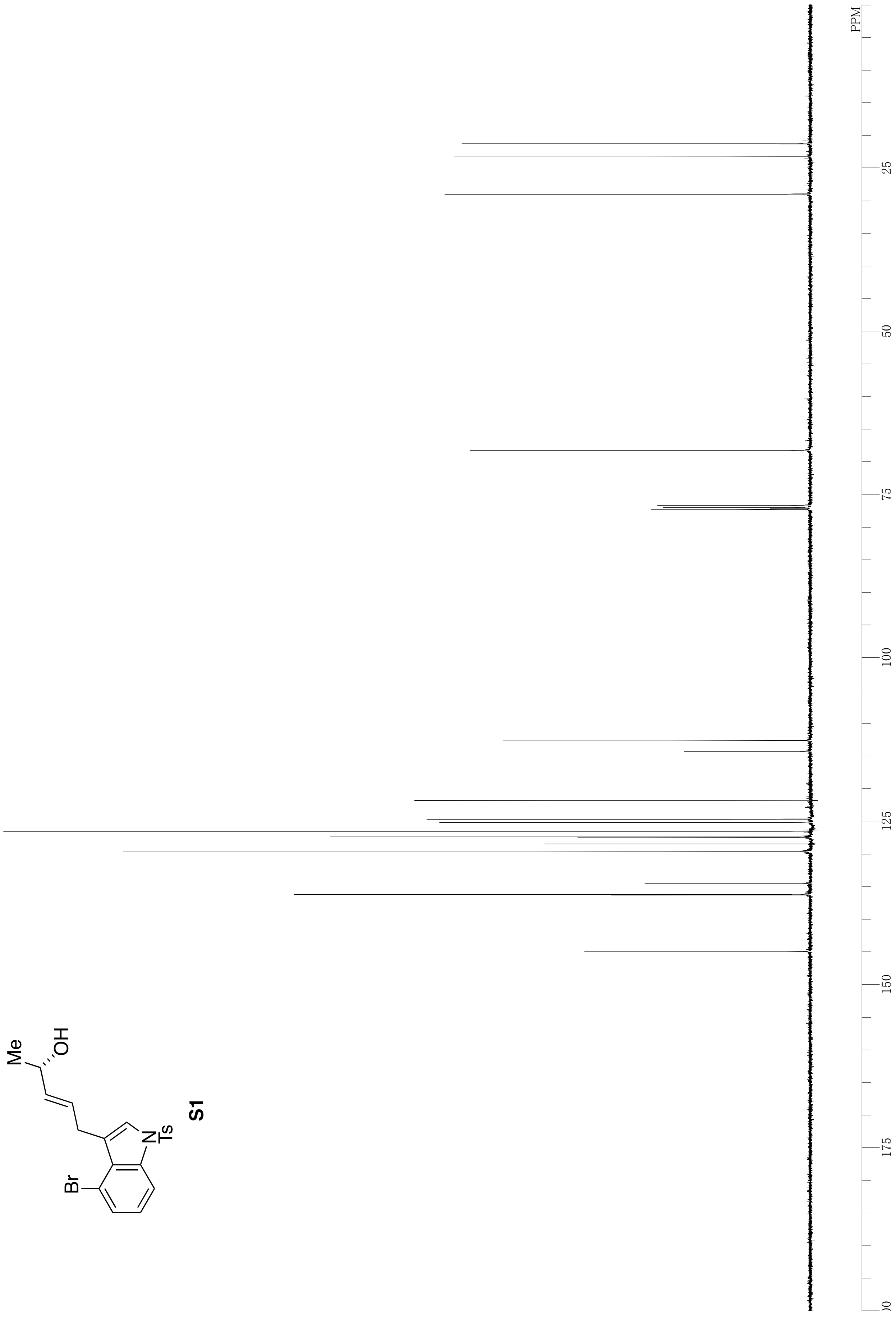

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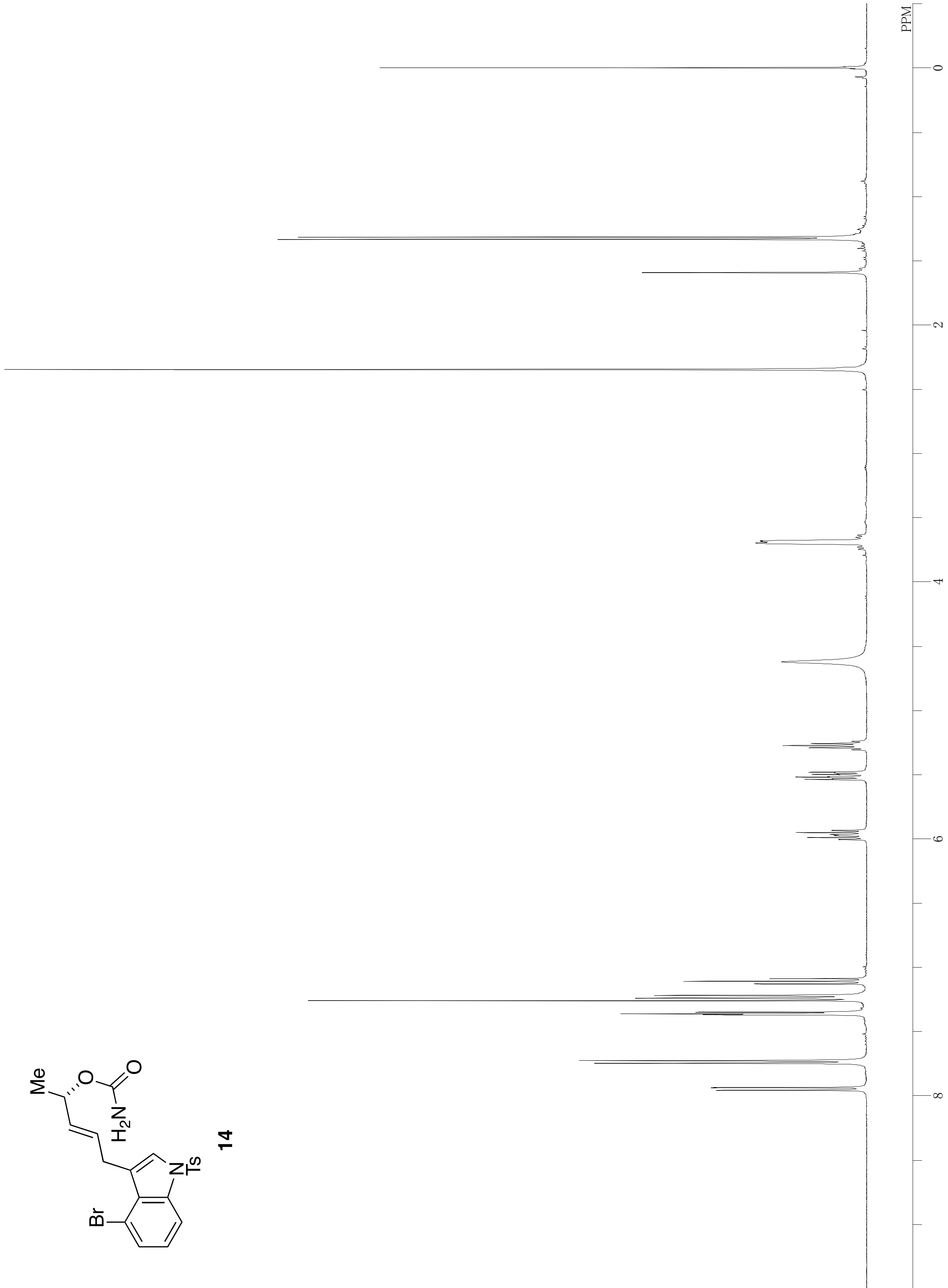

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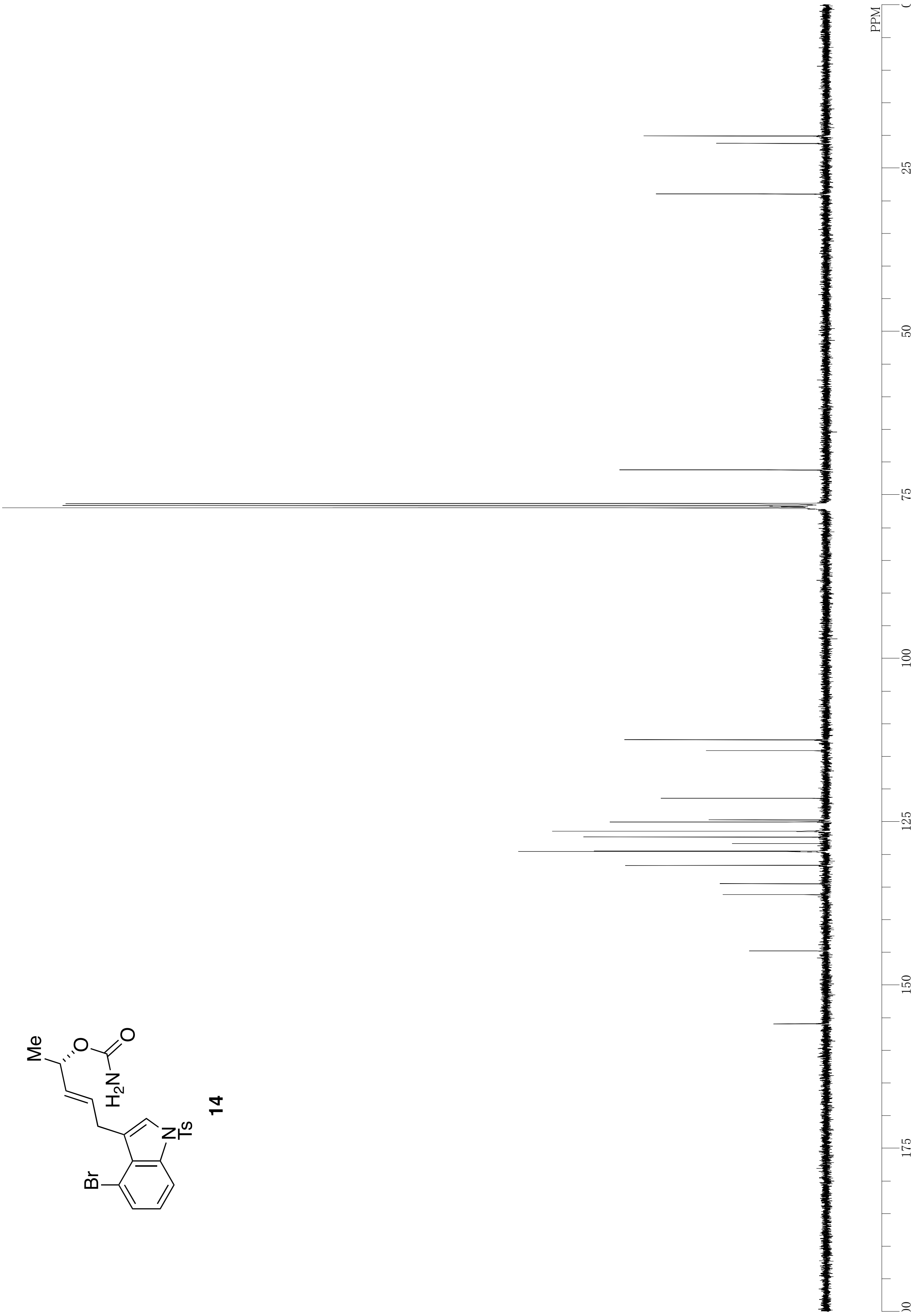

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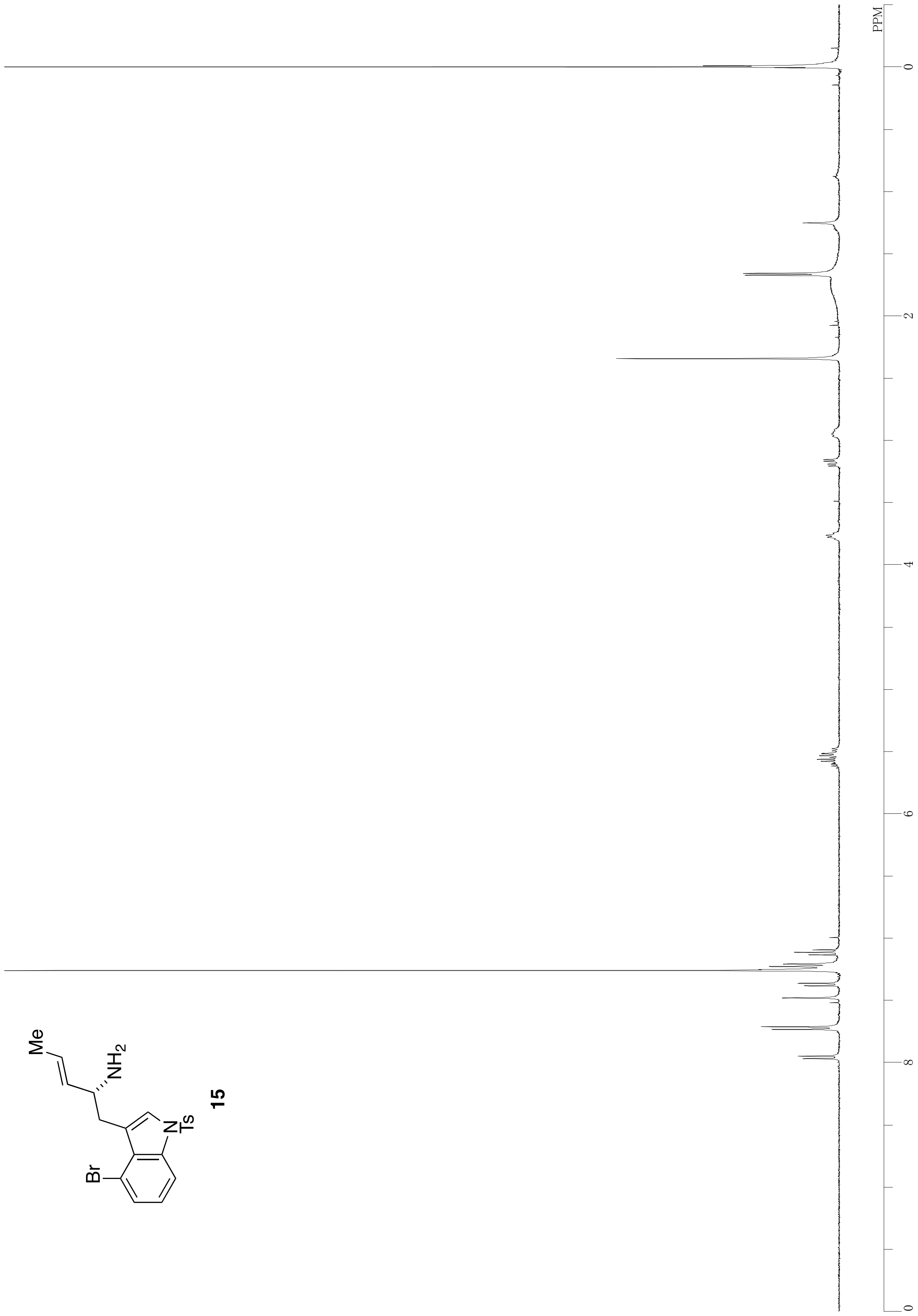

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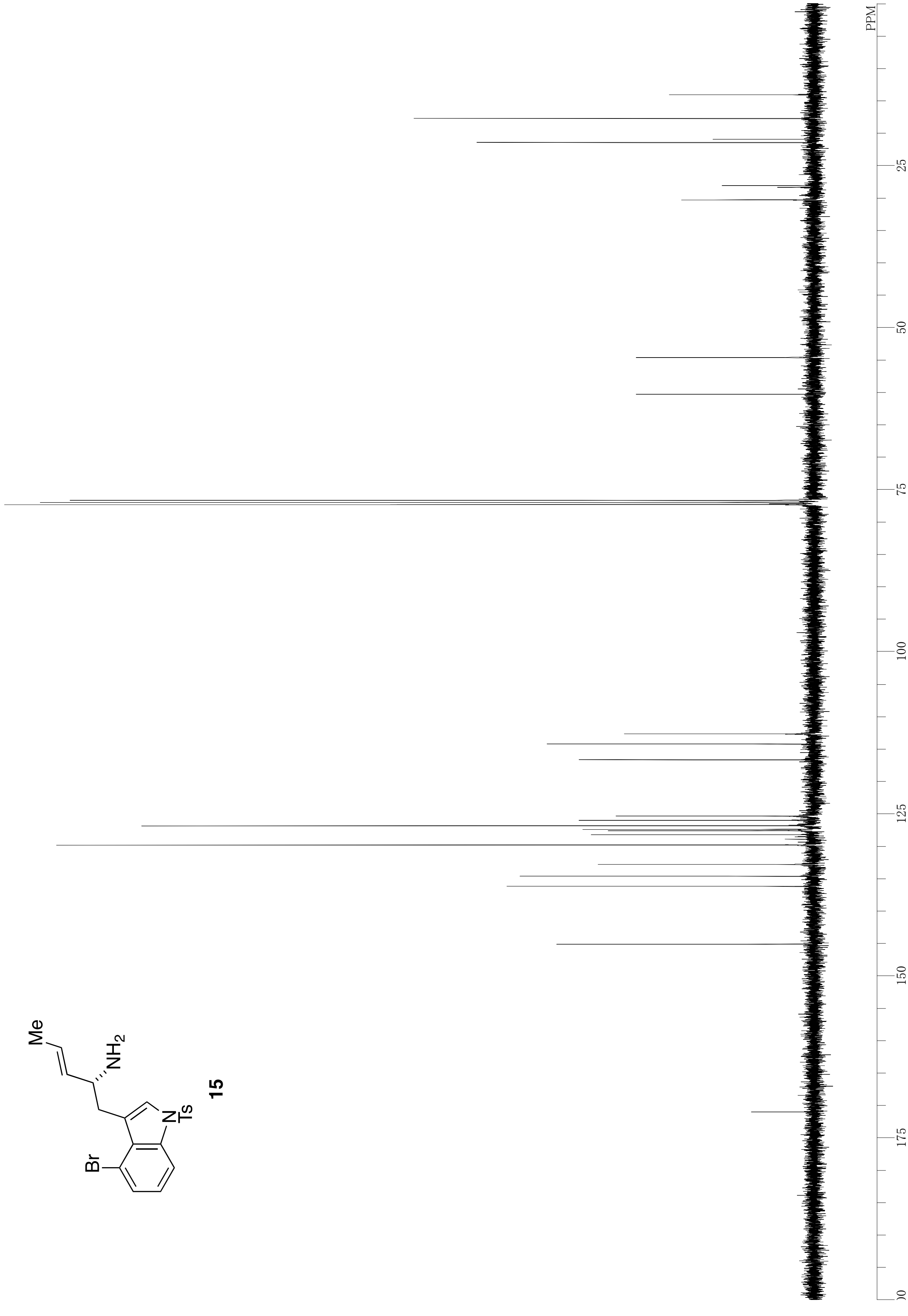

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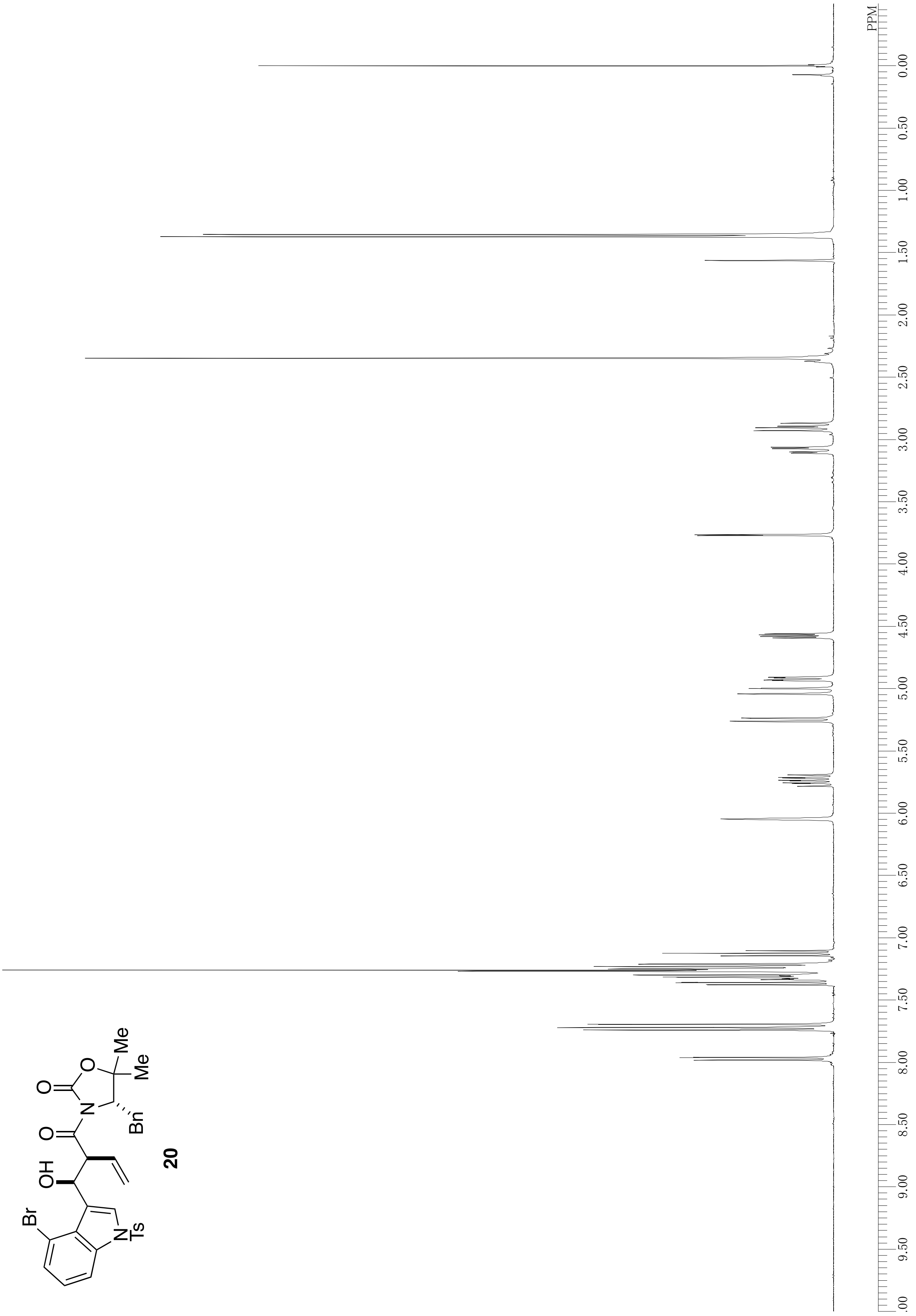
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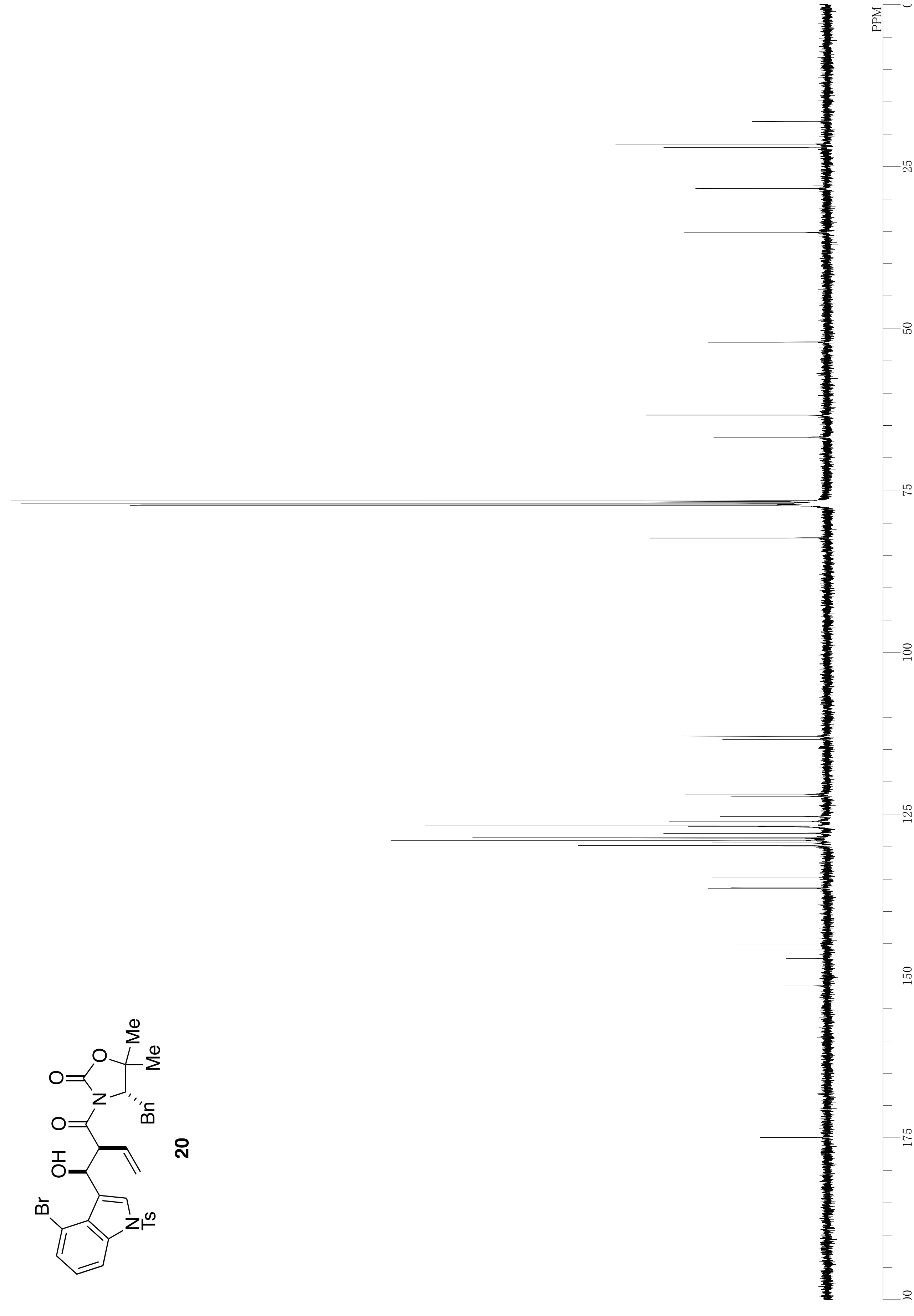

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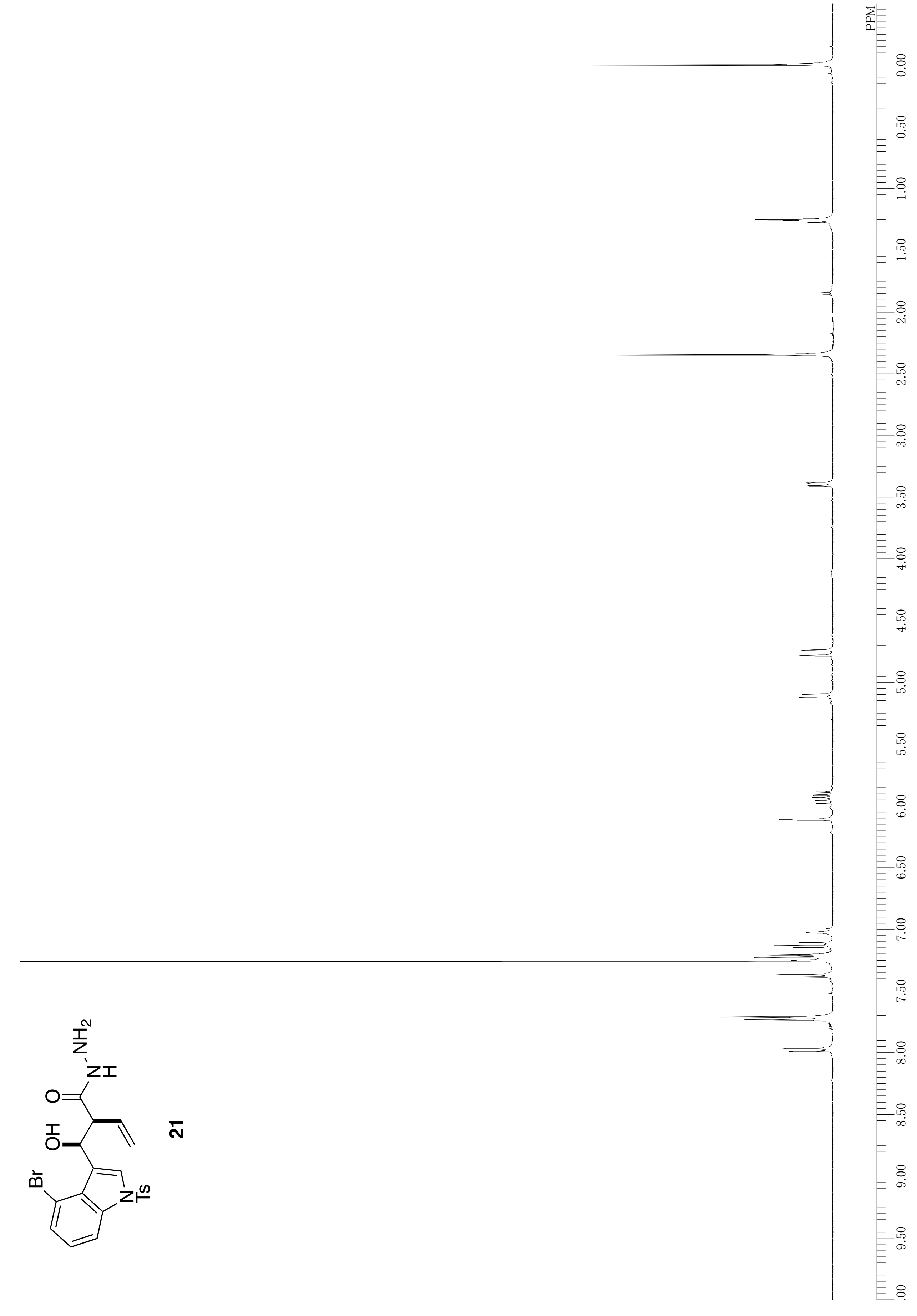
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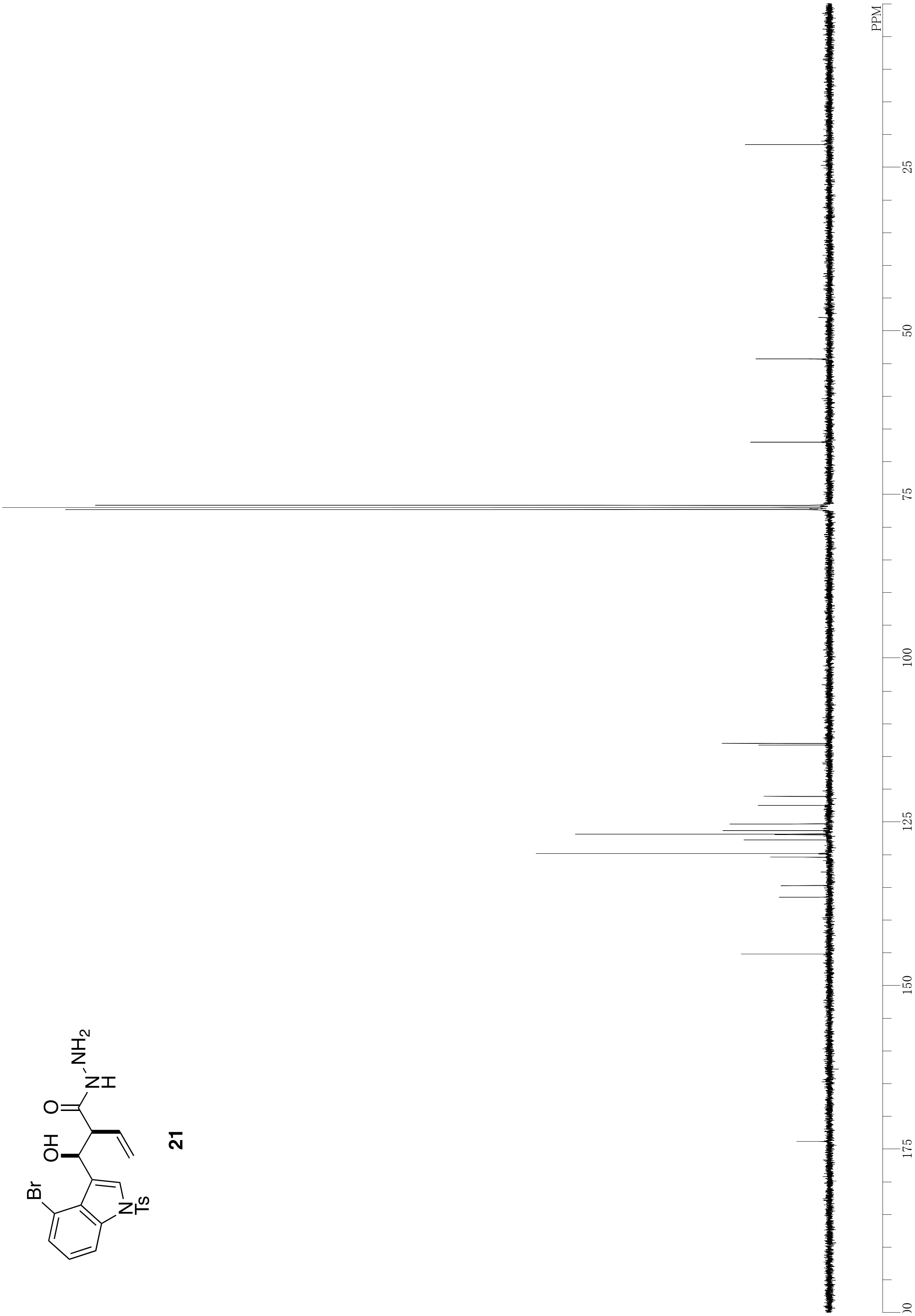

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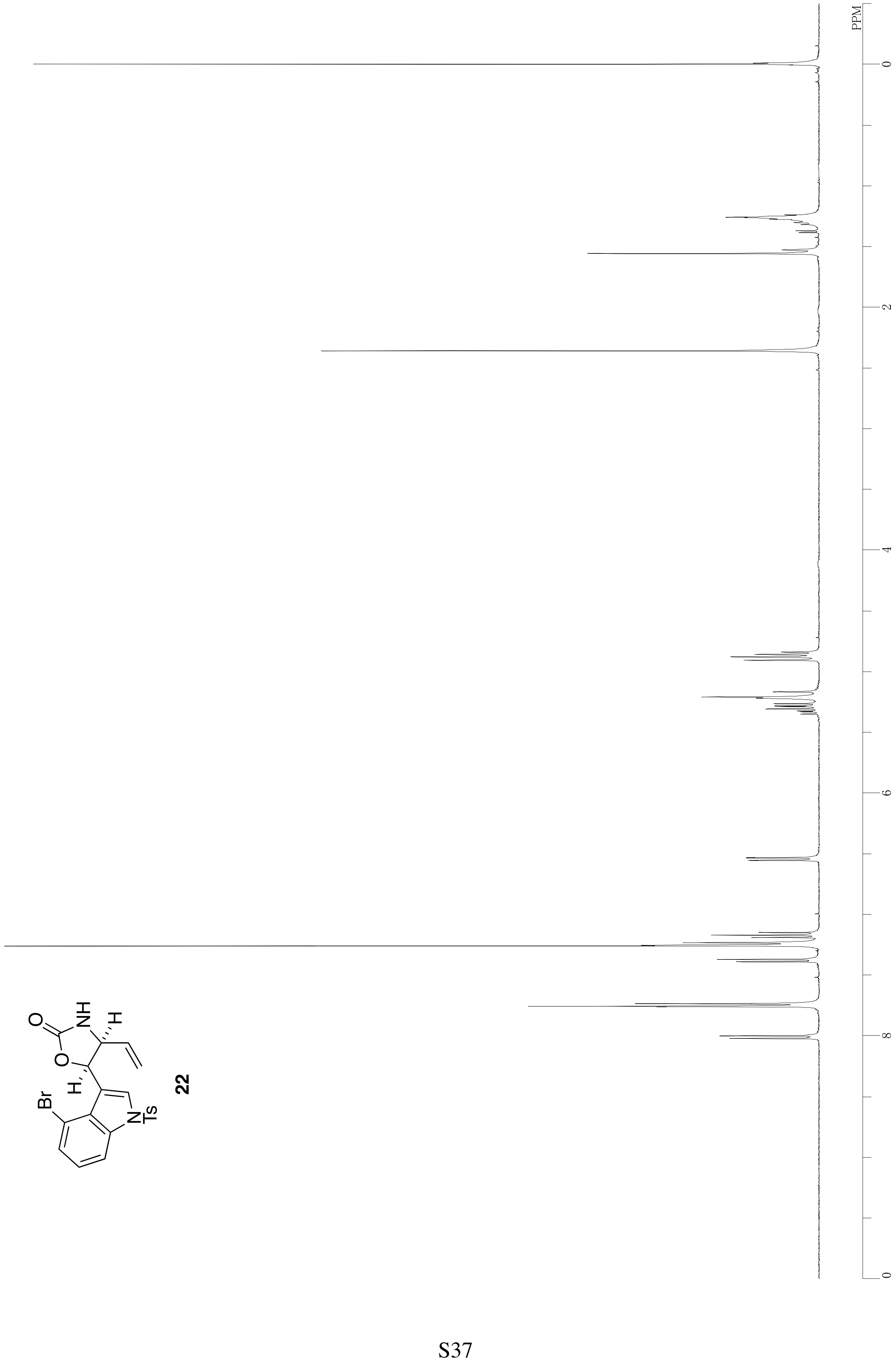

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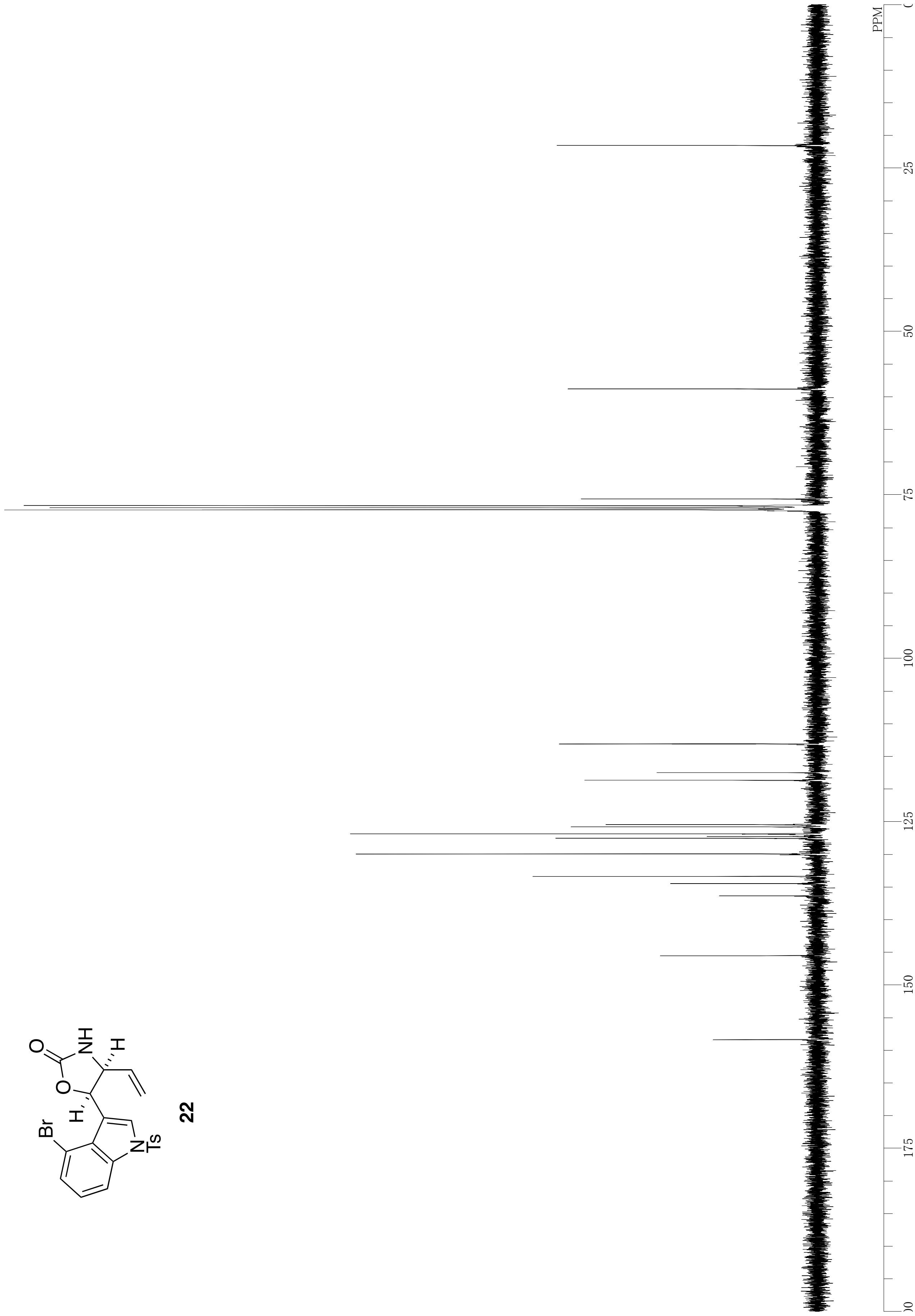

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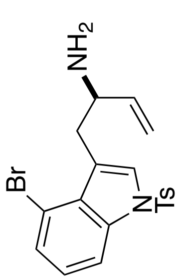

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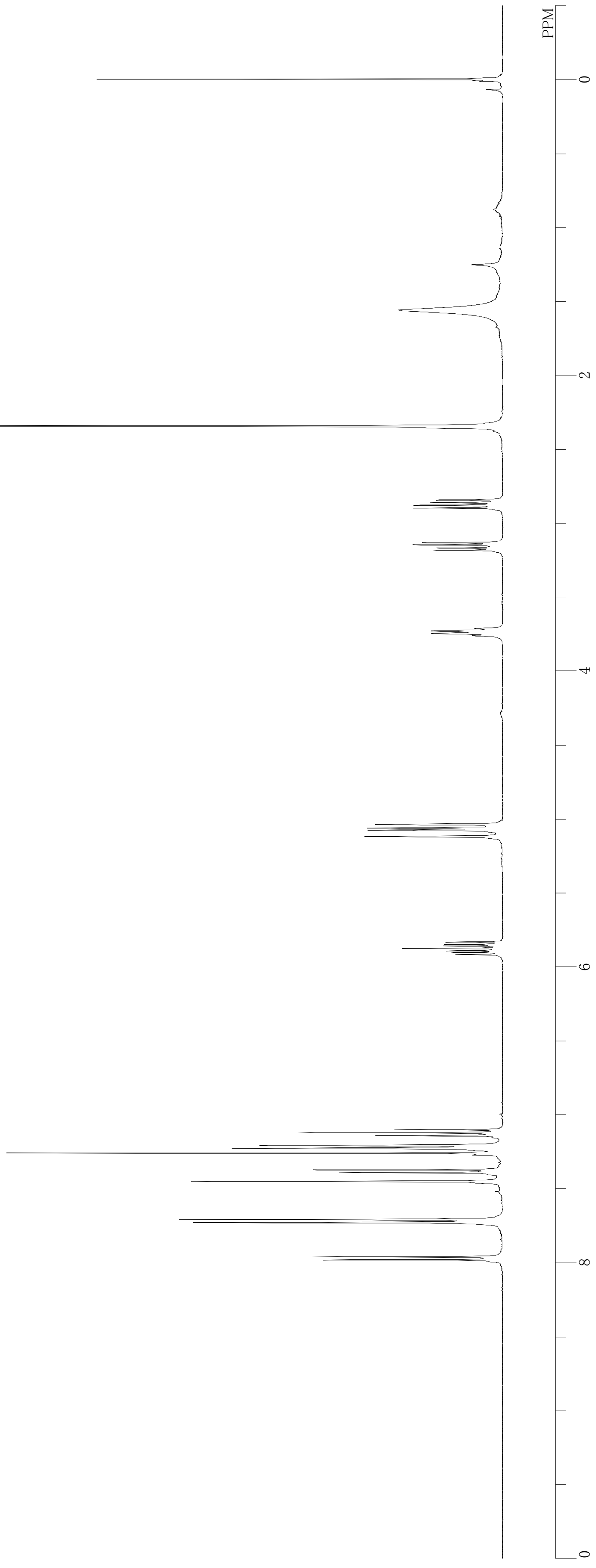

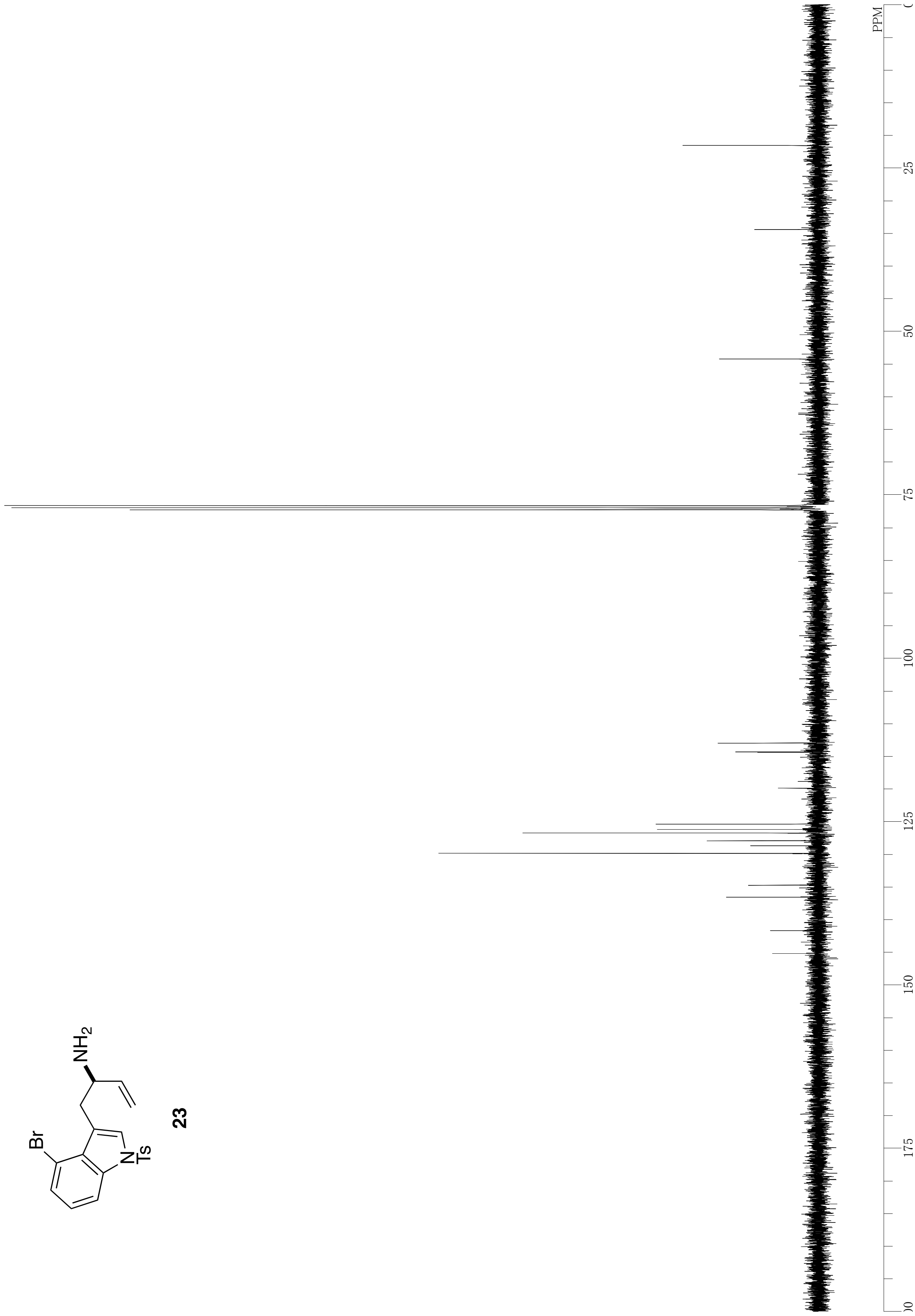

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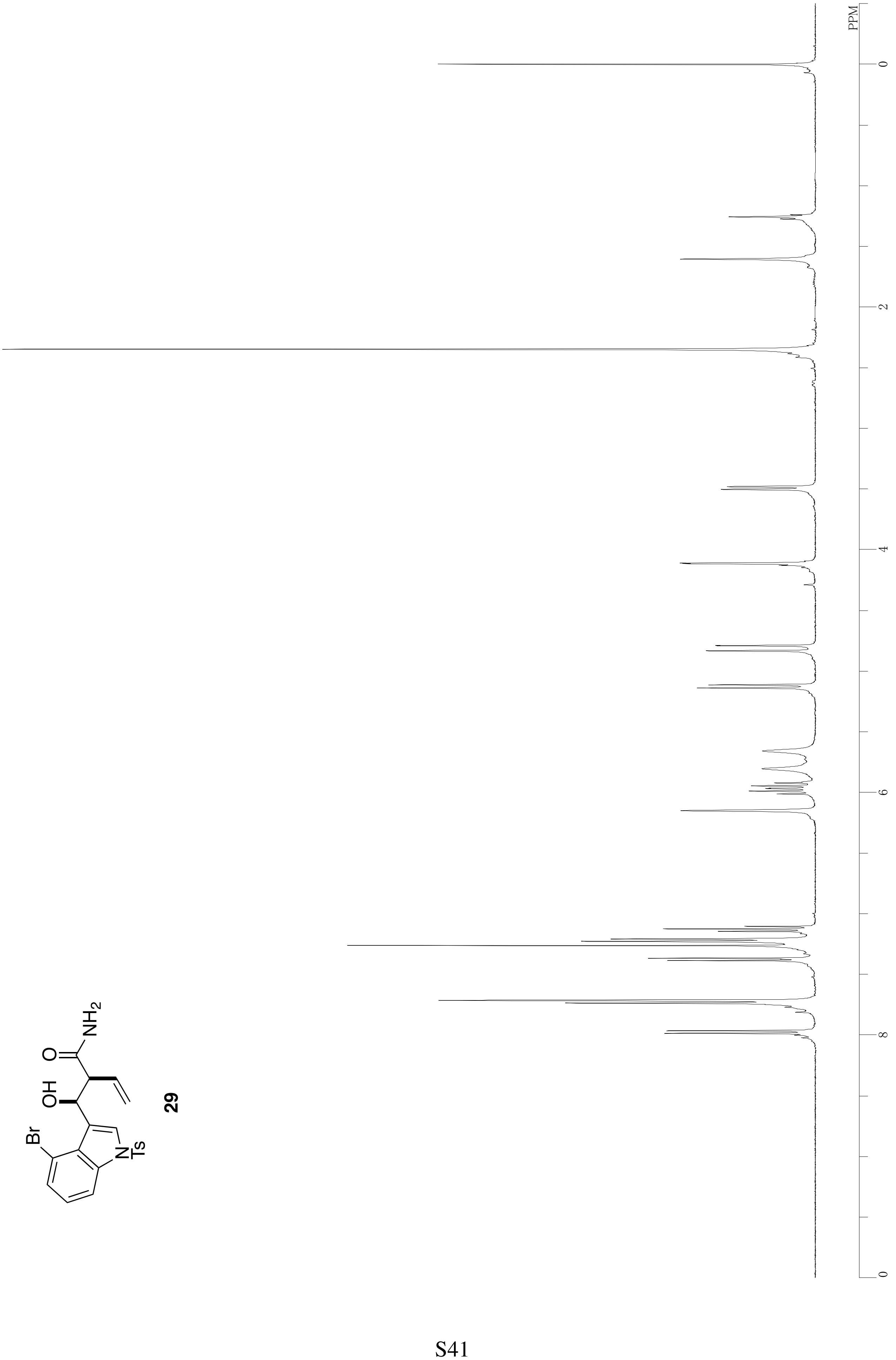

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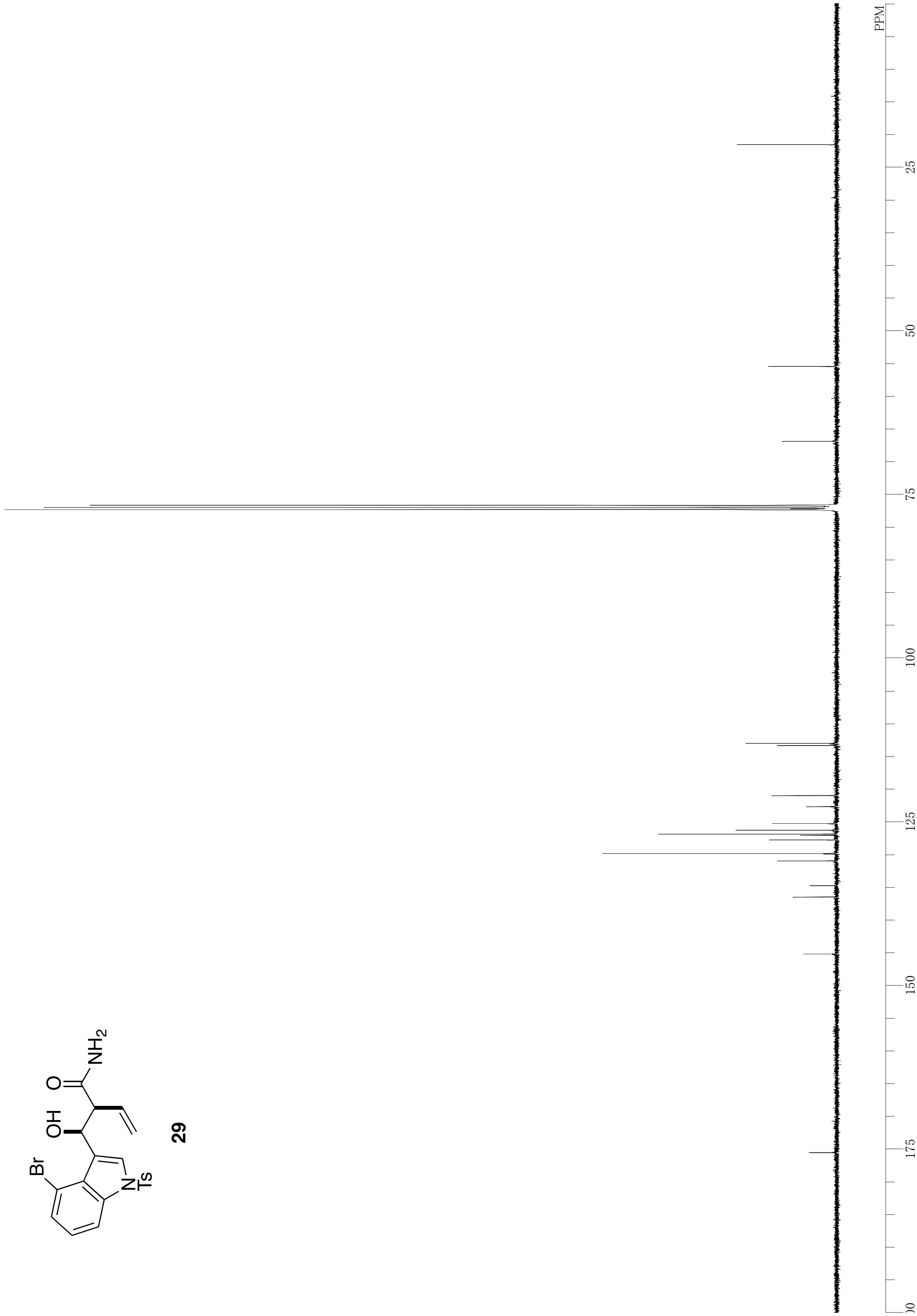

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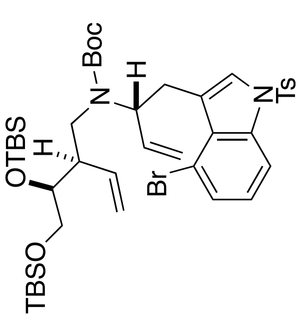

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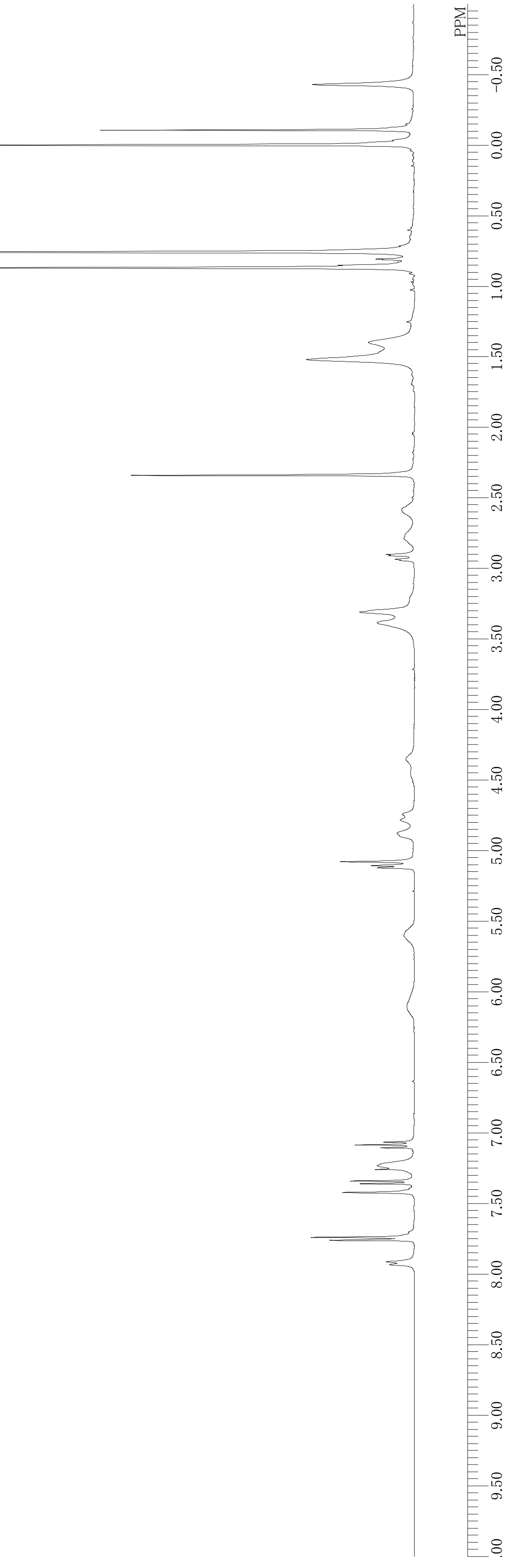

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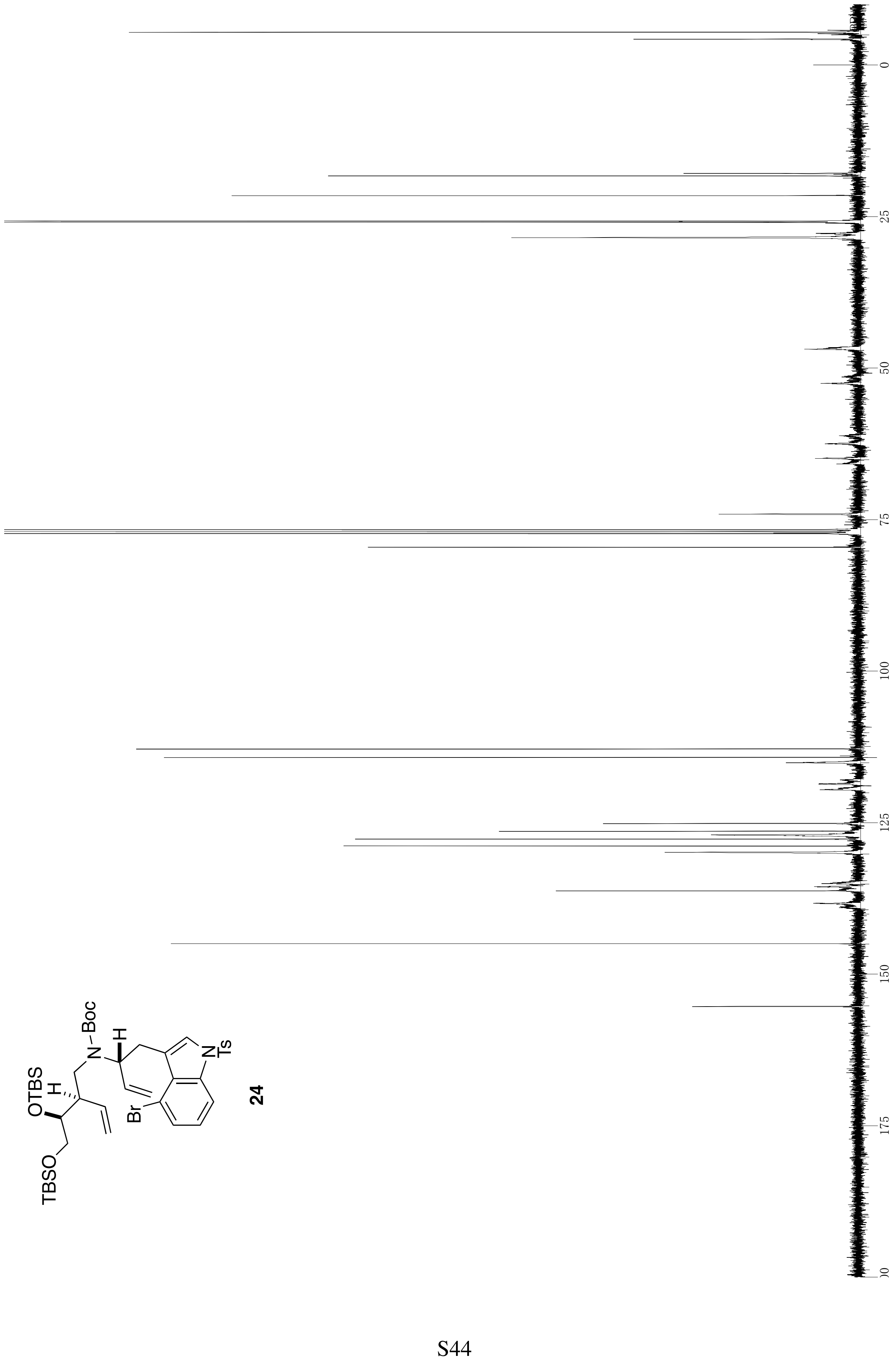
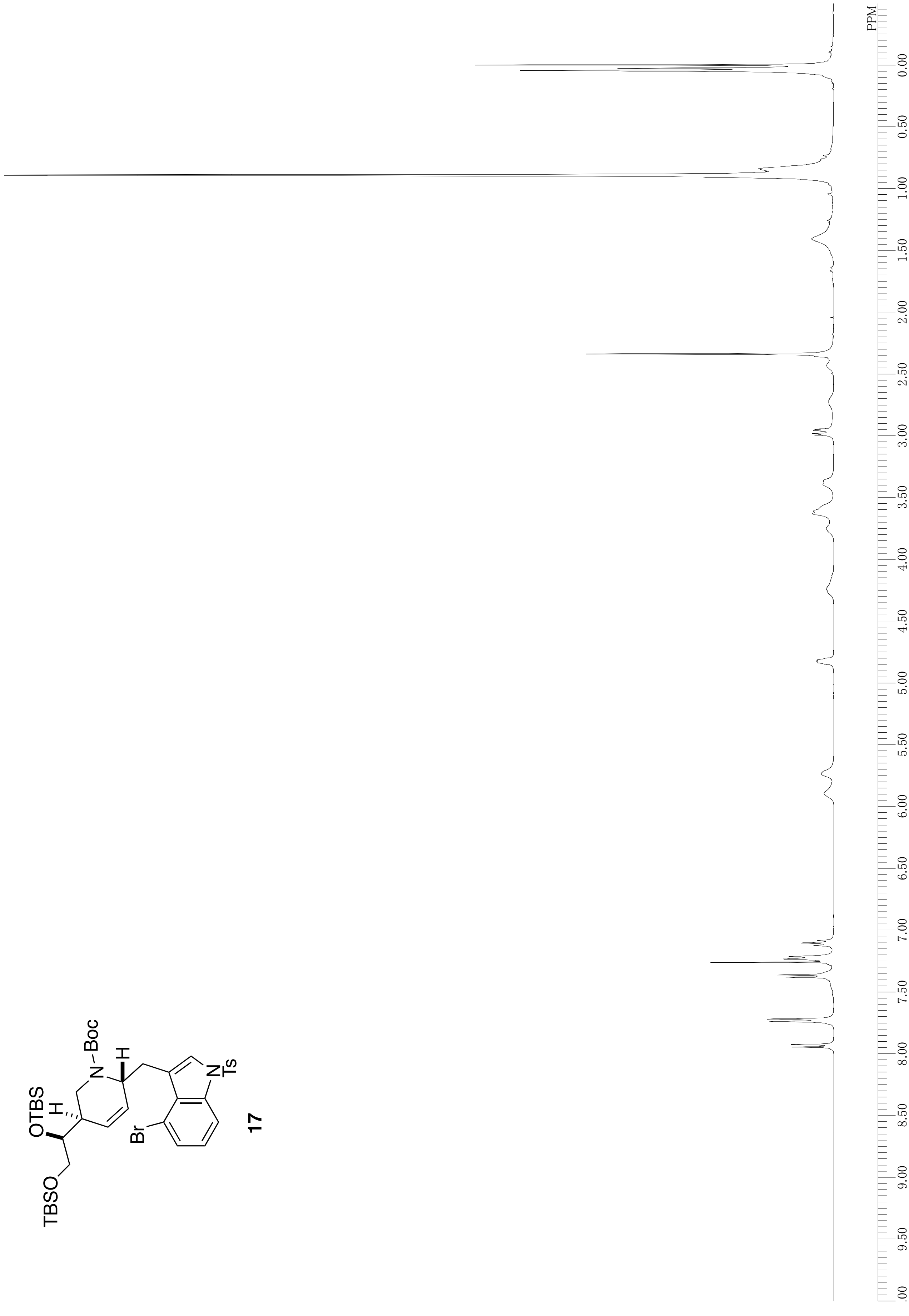
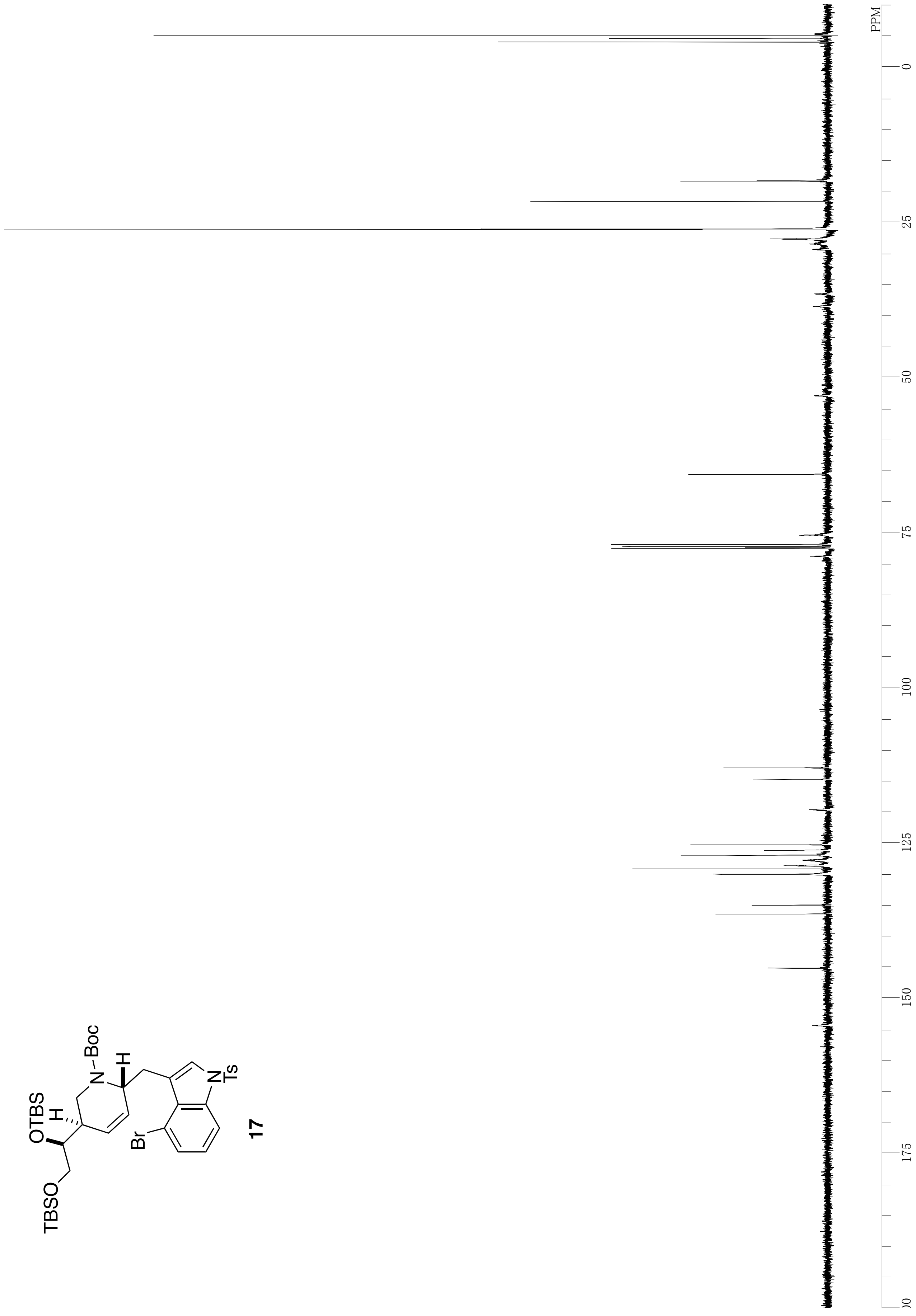
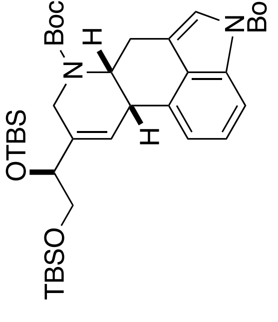

TBSO
OTBS
H
N–Boc
H
N
Ts
Br
24
0
25
50
75
100
125
150
175
ppm


TBSO
OTBS
H
N–Boc
H
N
Ts
Br
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50
.00

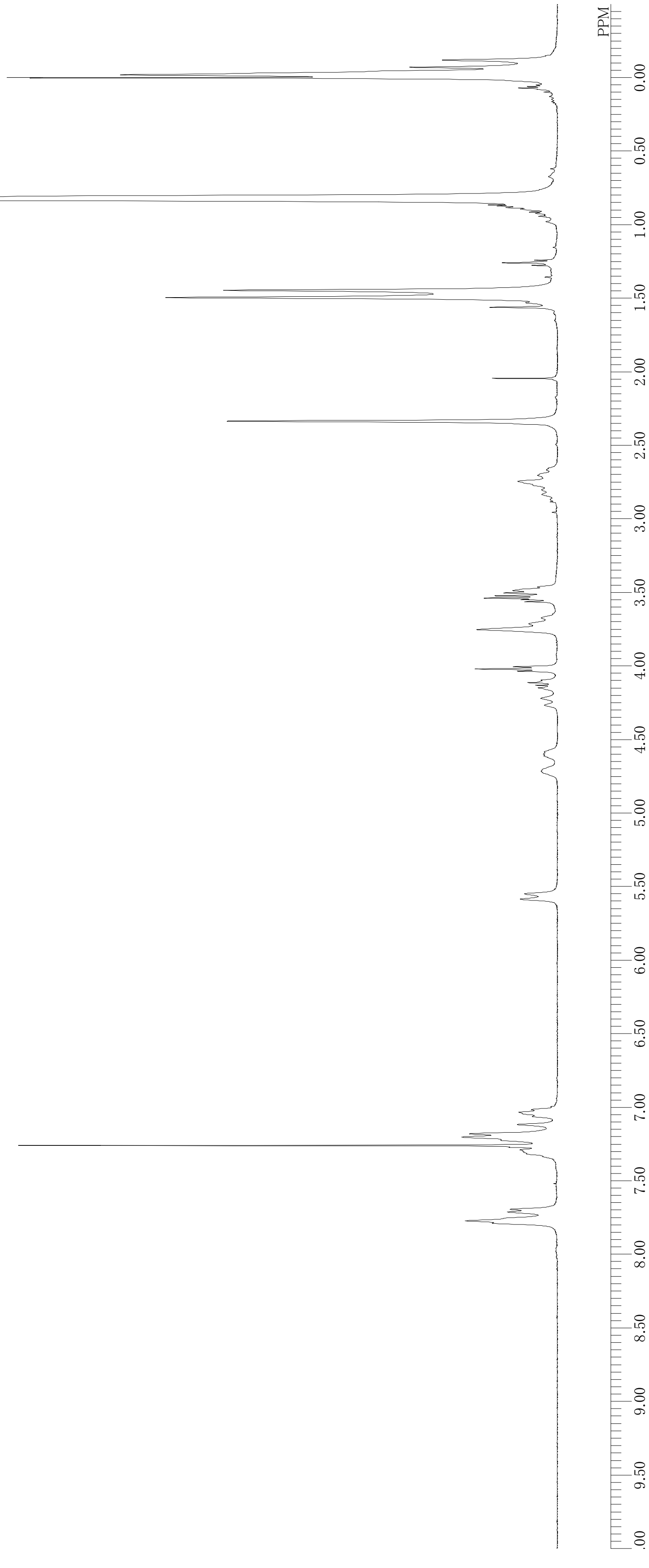
17

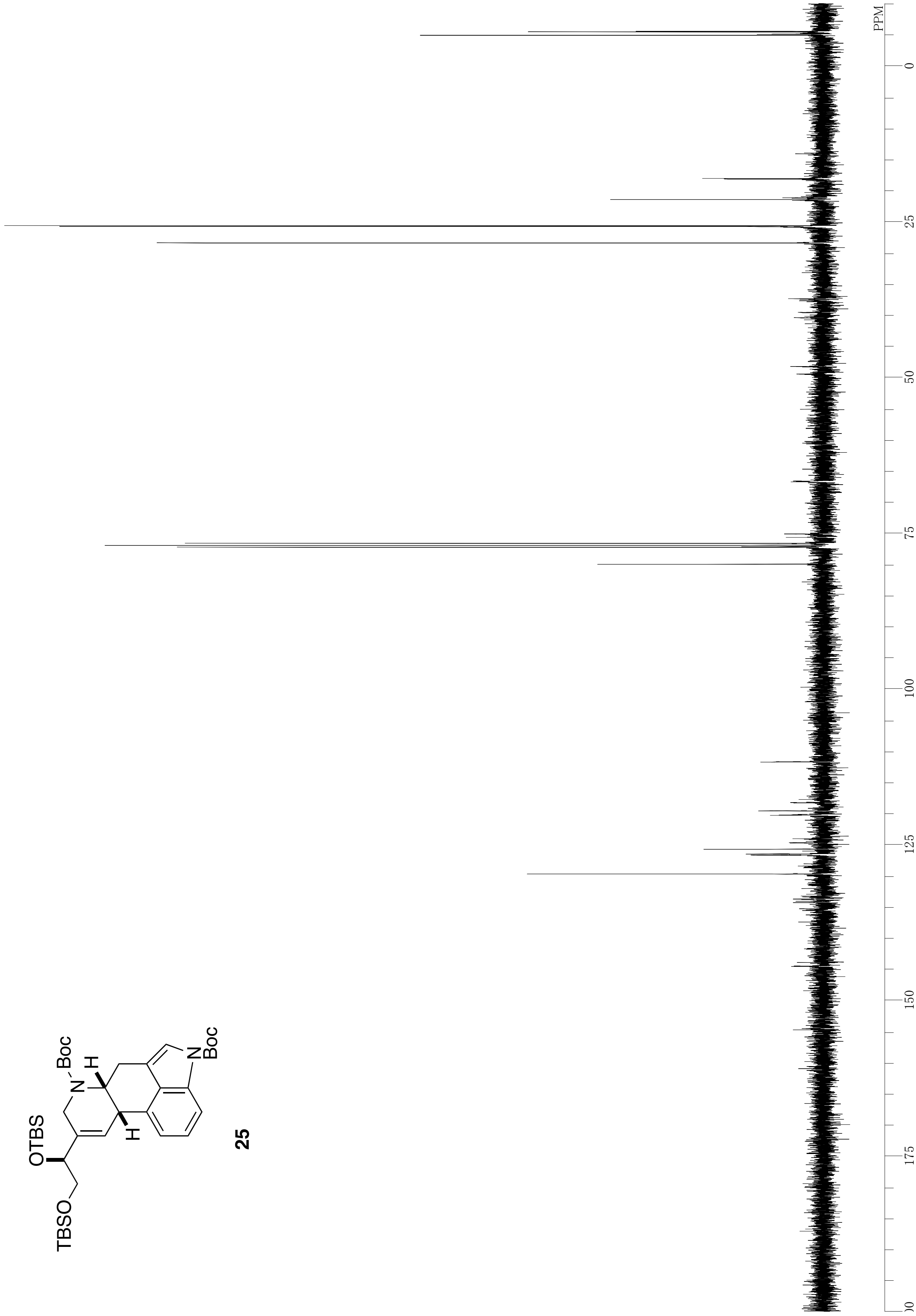


17

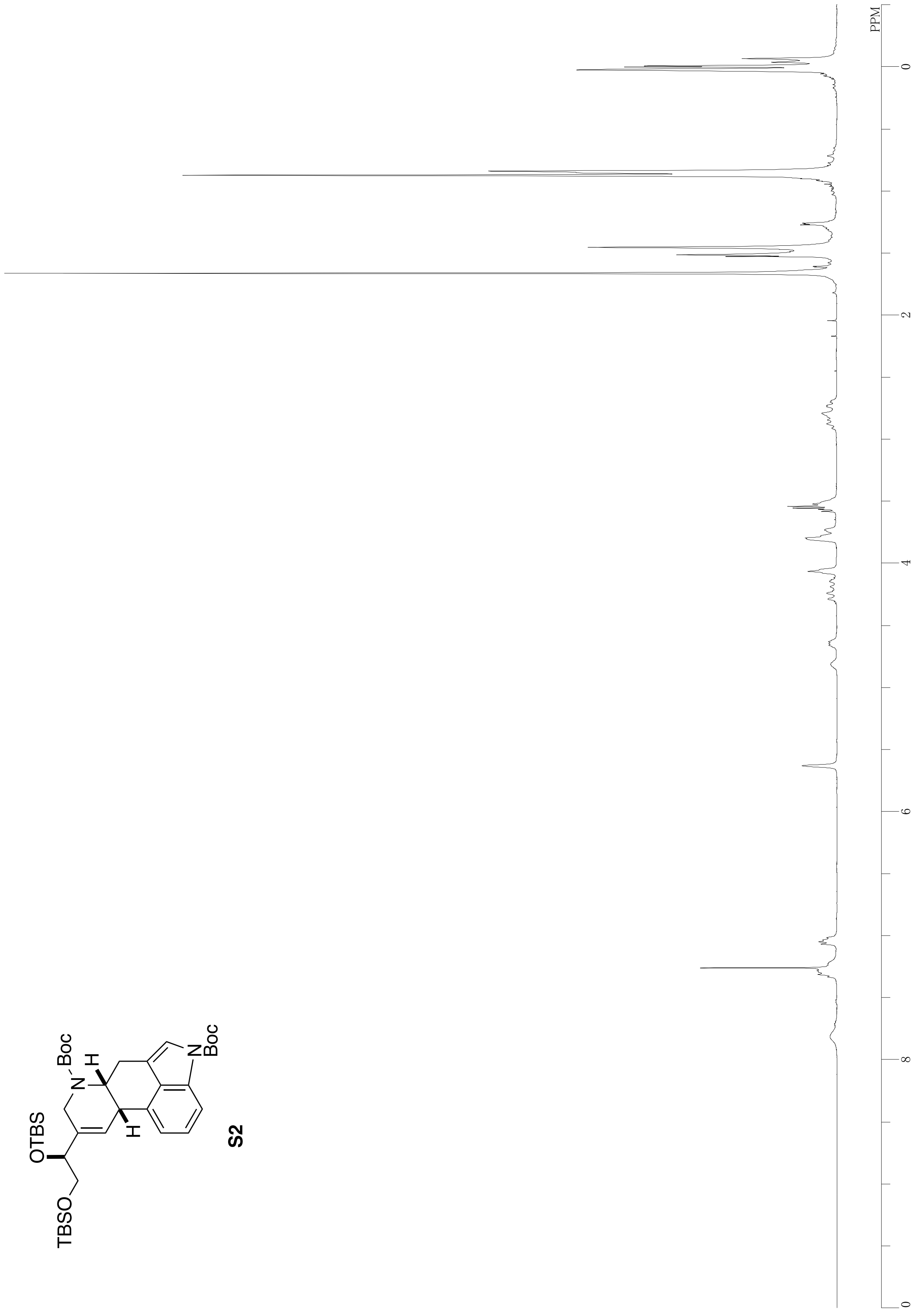

OTBS
TBSO
N
Boc
H
H
N
Boc

25

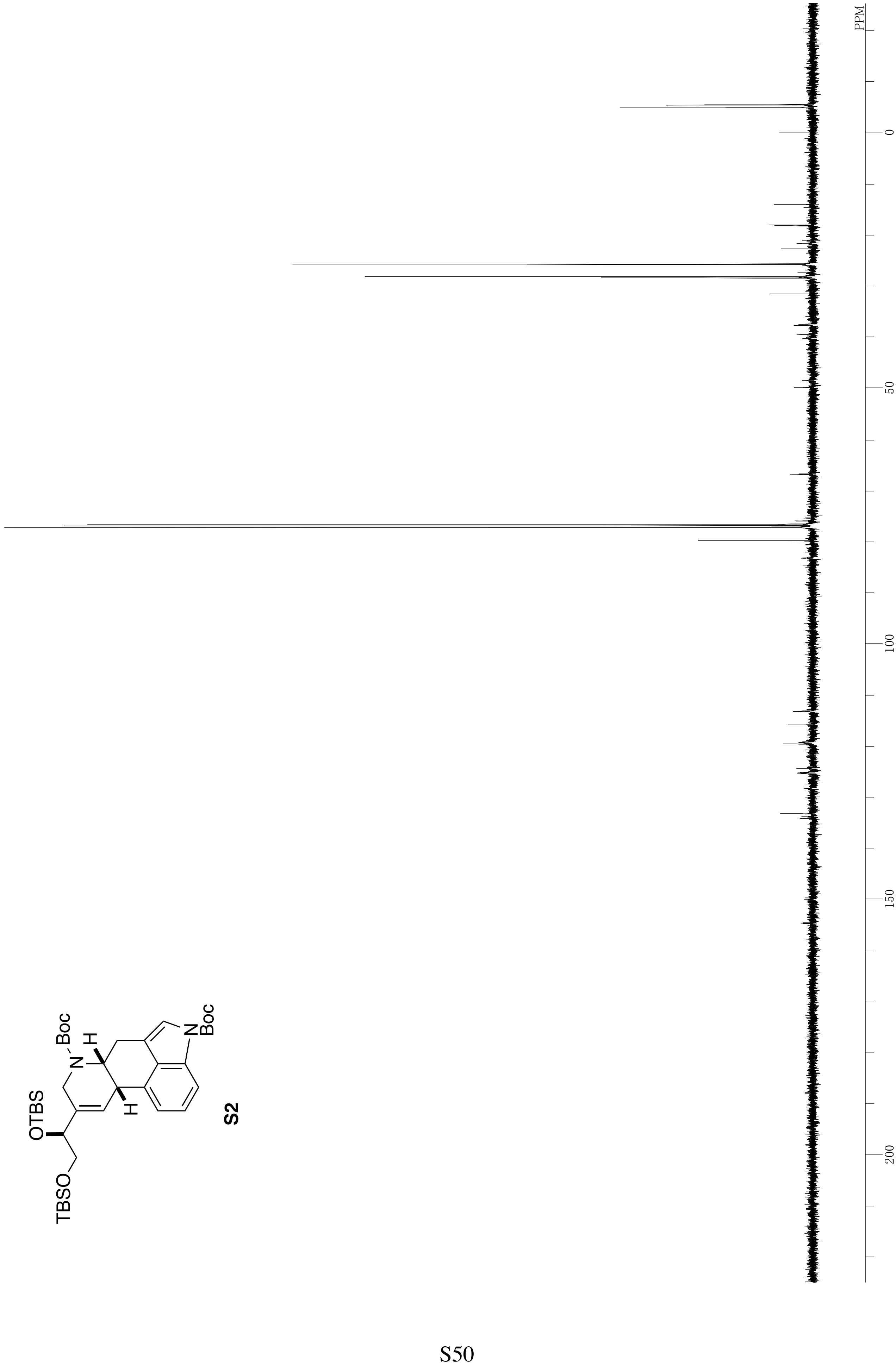

PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50
.00



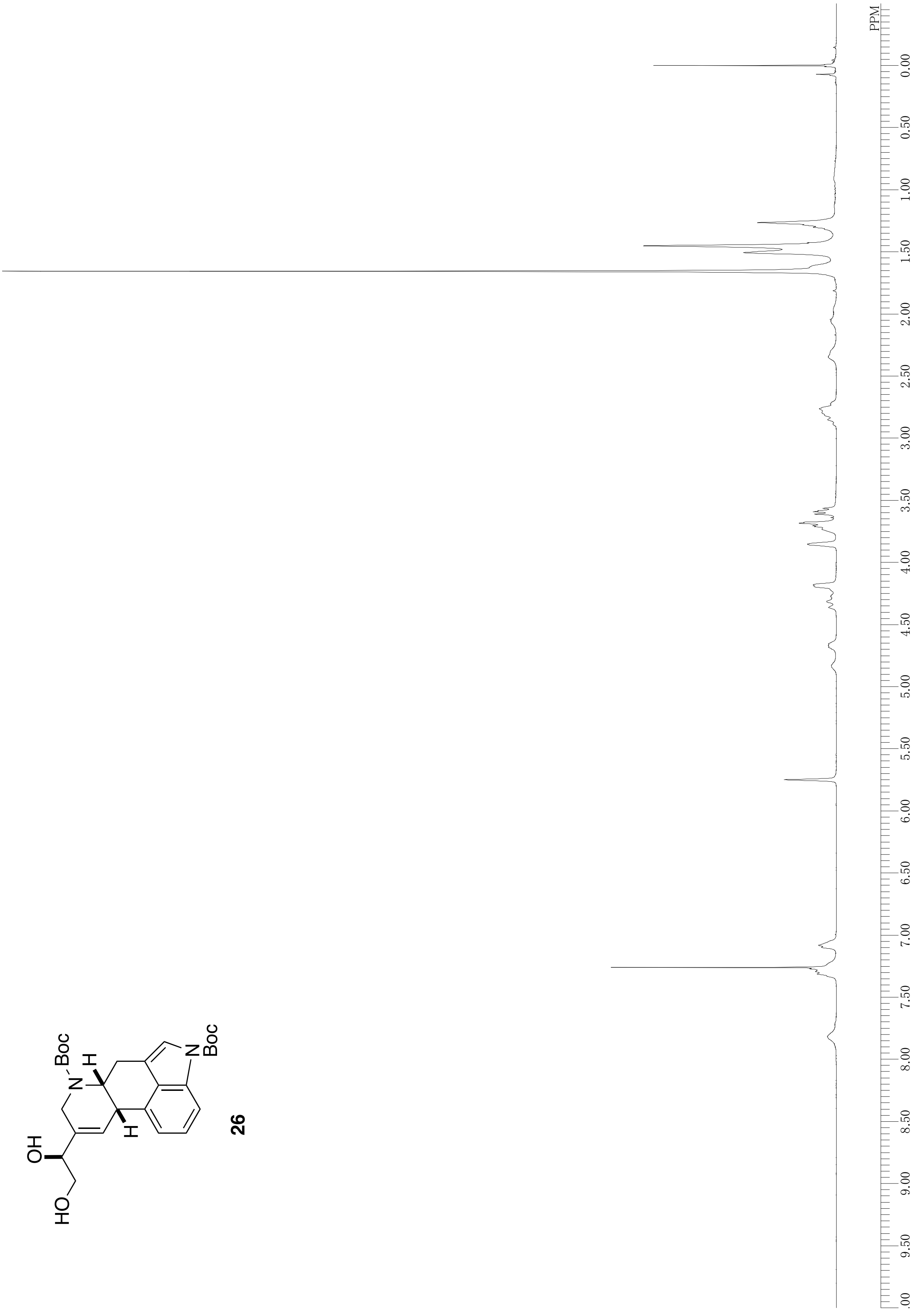
25



S2



S2



PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
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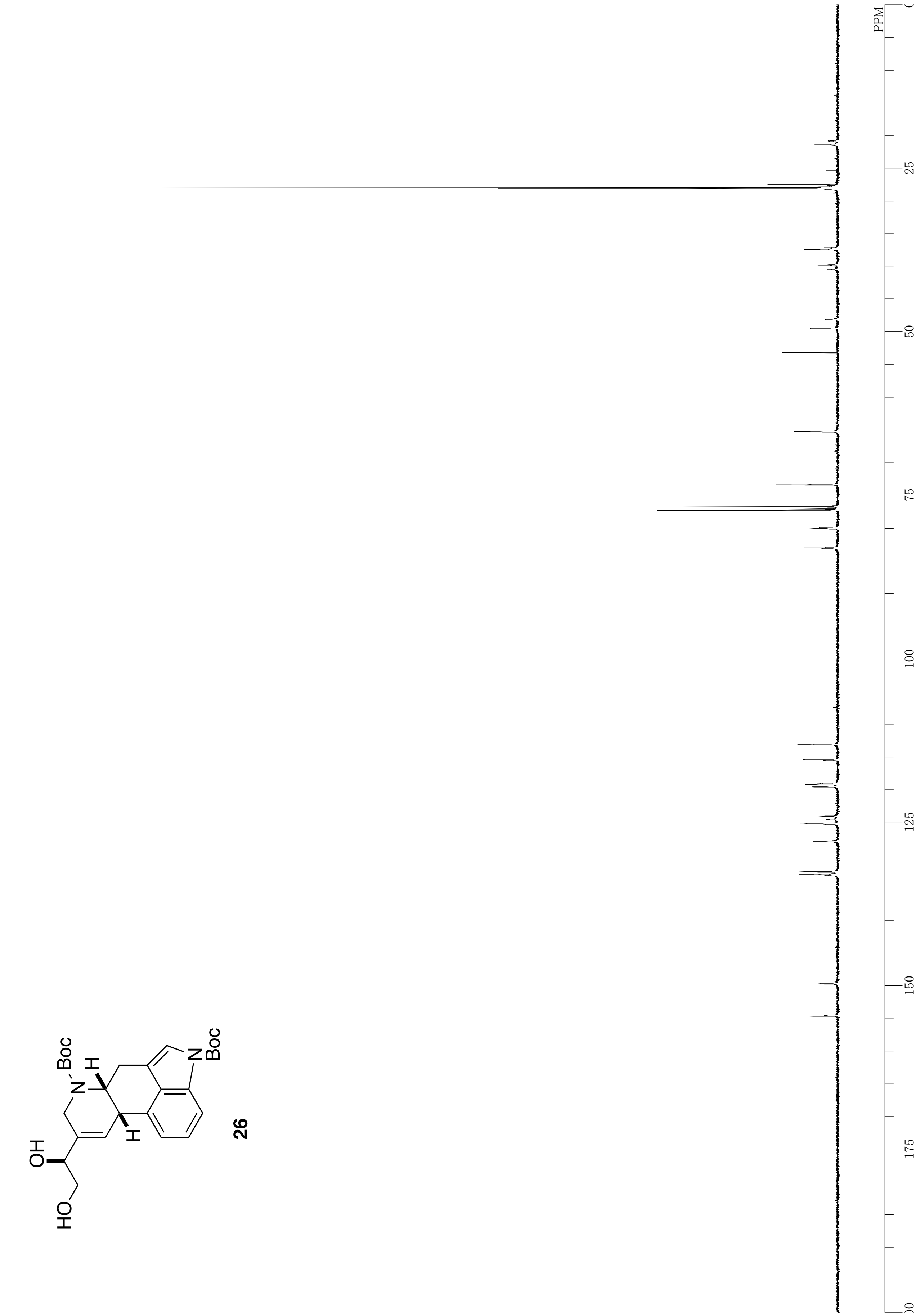
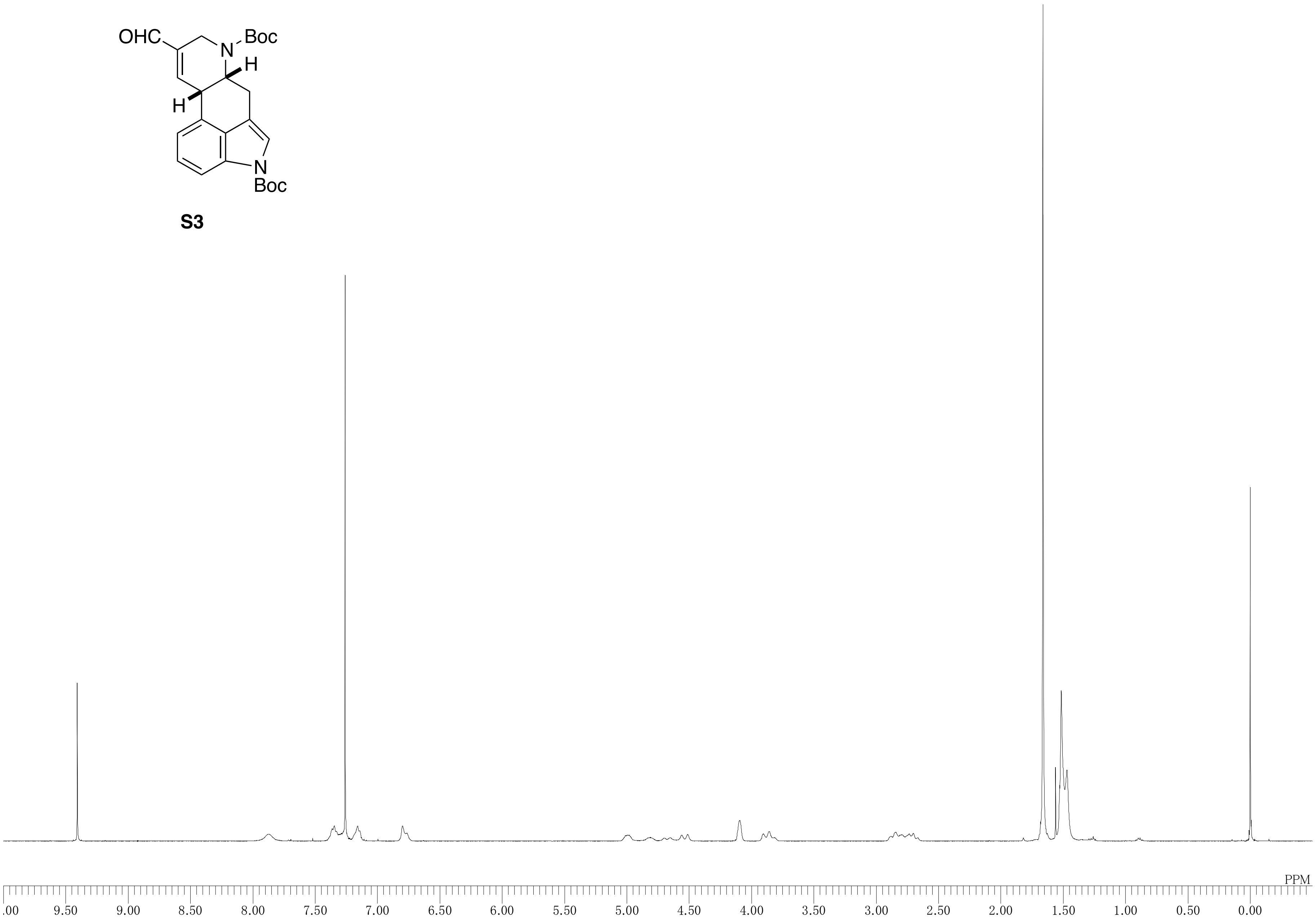
9.50
.00
HO
OH
N
Boc
H
H
N
Boc

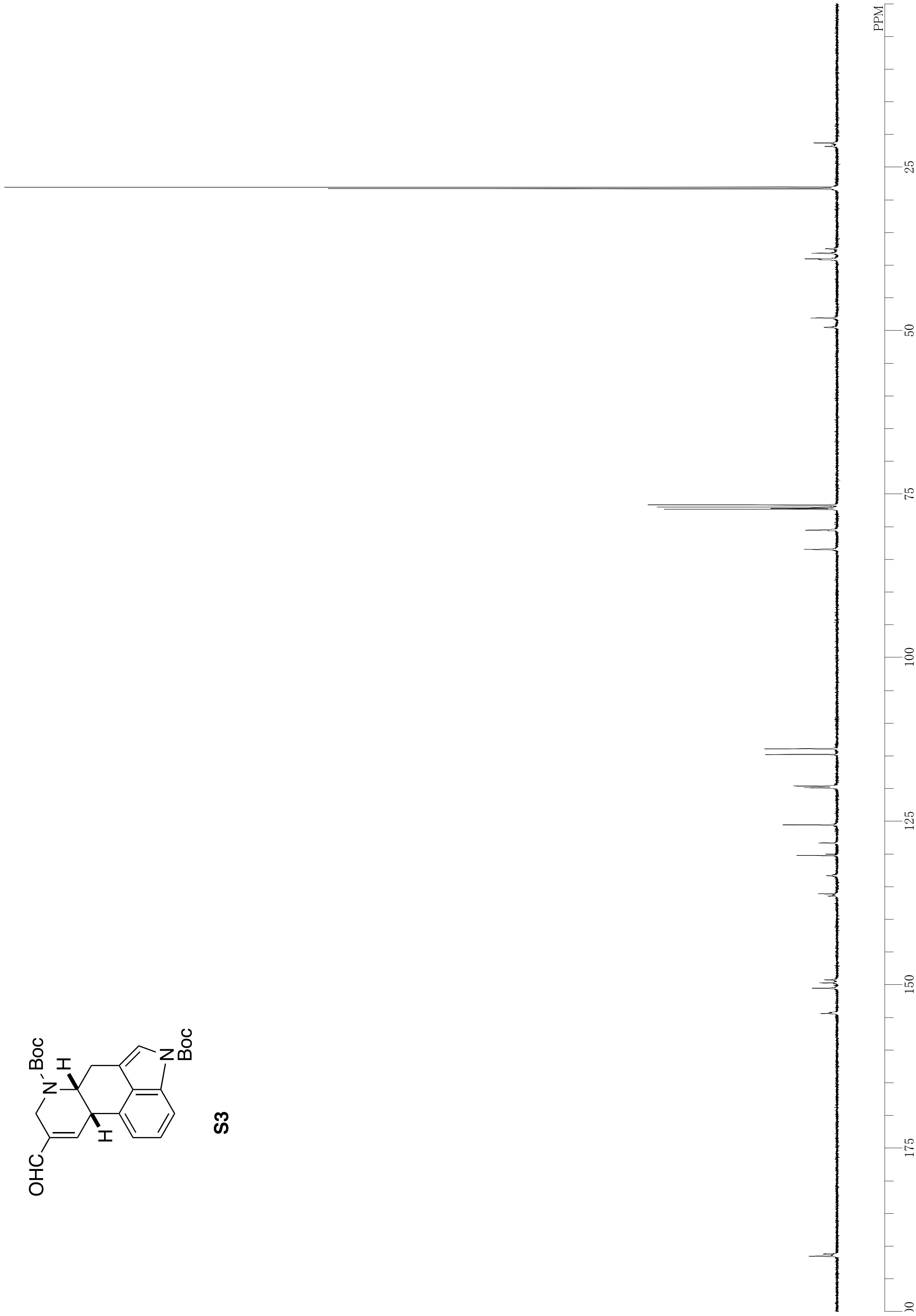
26



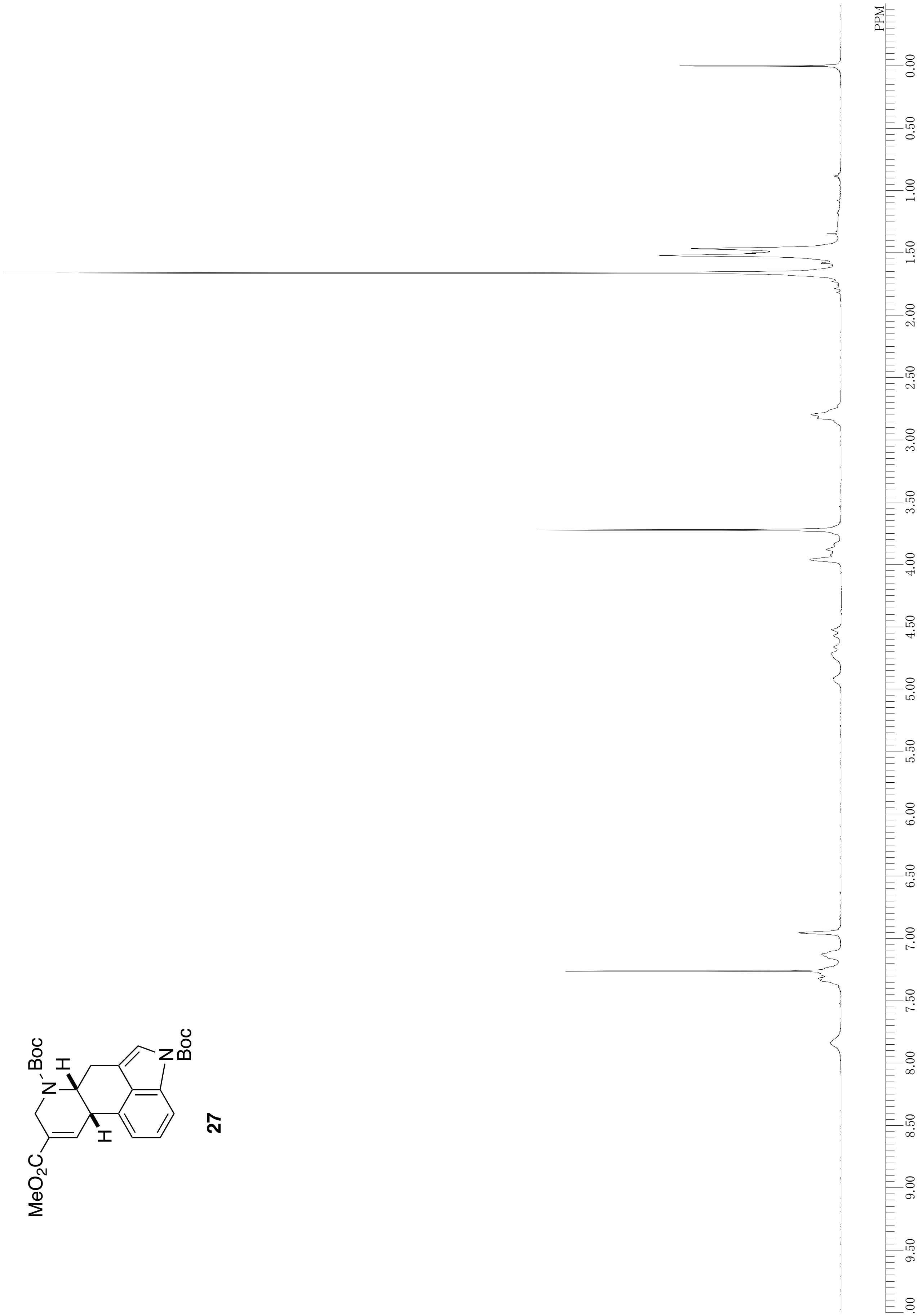
26


OHC
N
Boc
H
H
N
Boc
PPM
.00
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00

S3



S3


PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
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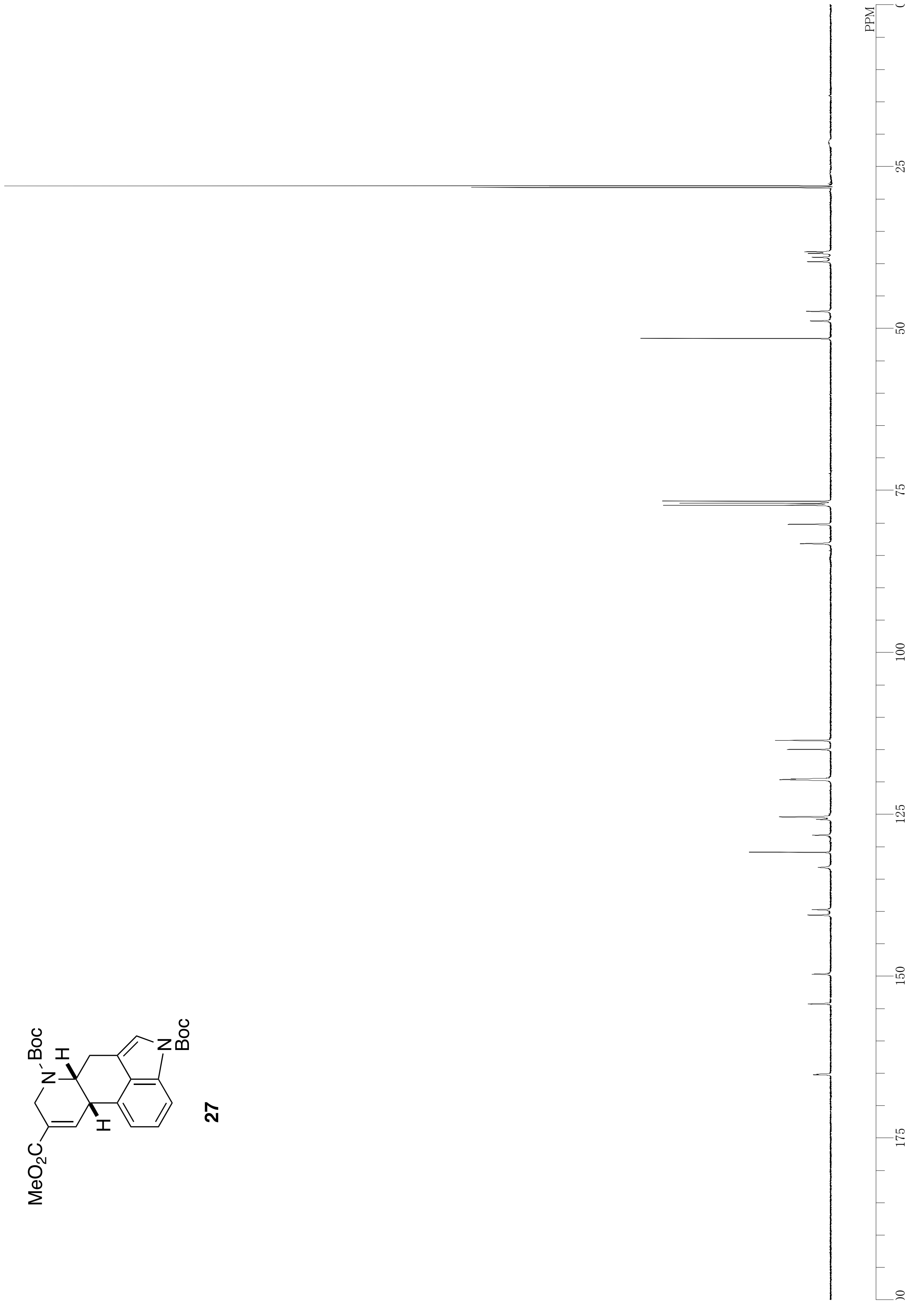
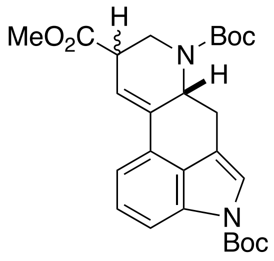
8.50
9.00
9.50
.00
MeO2C
N
Boc
H
H
N
Boc

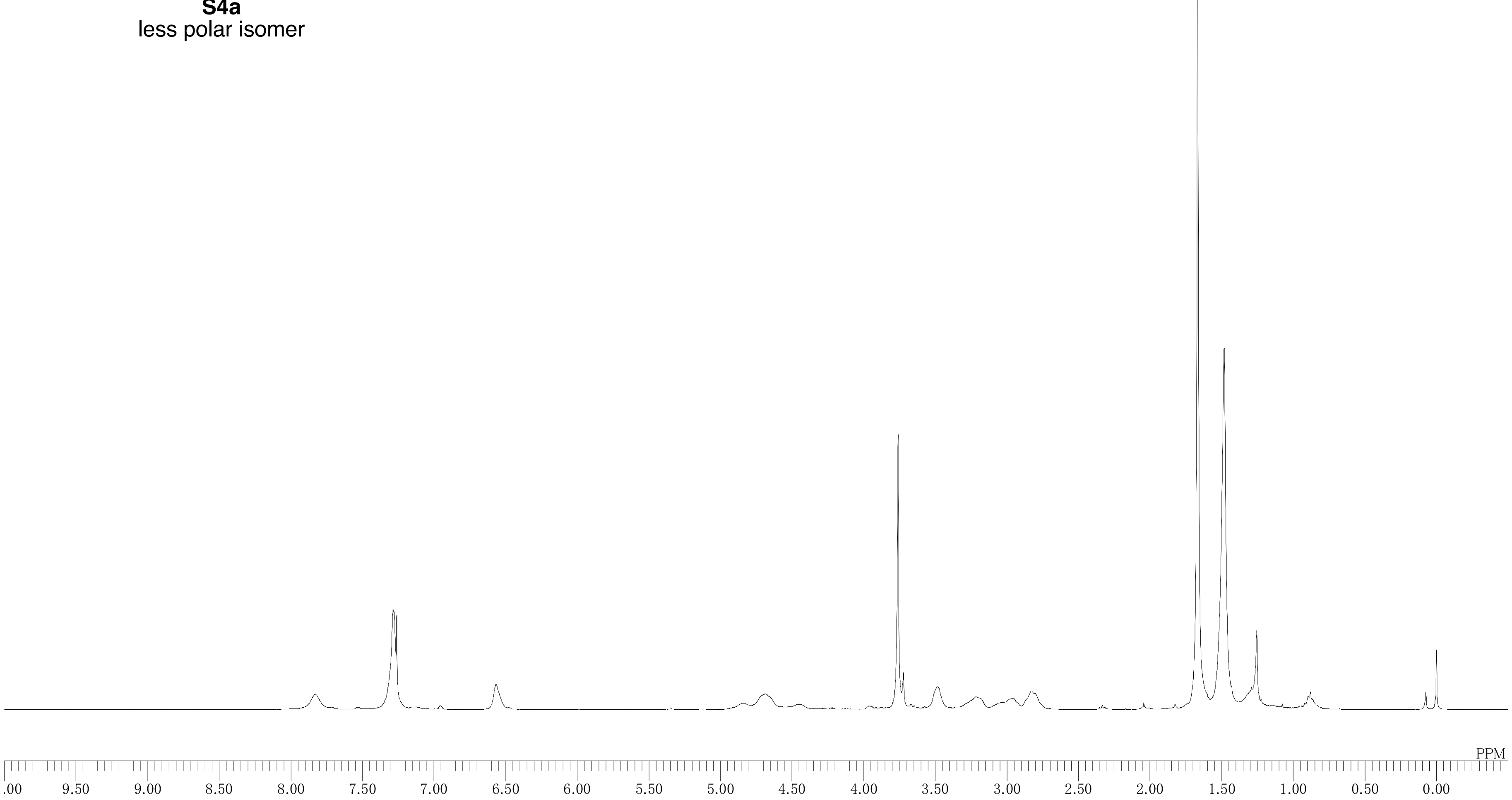
27

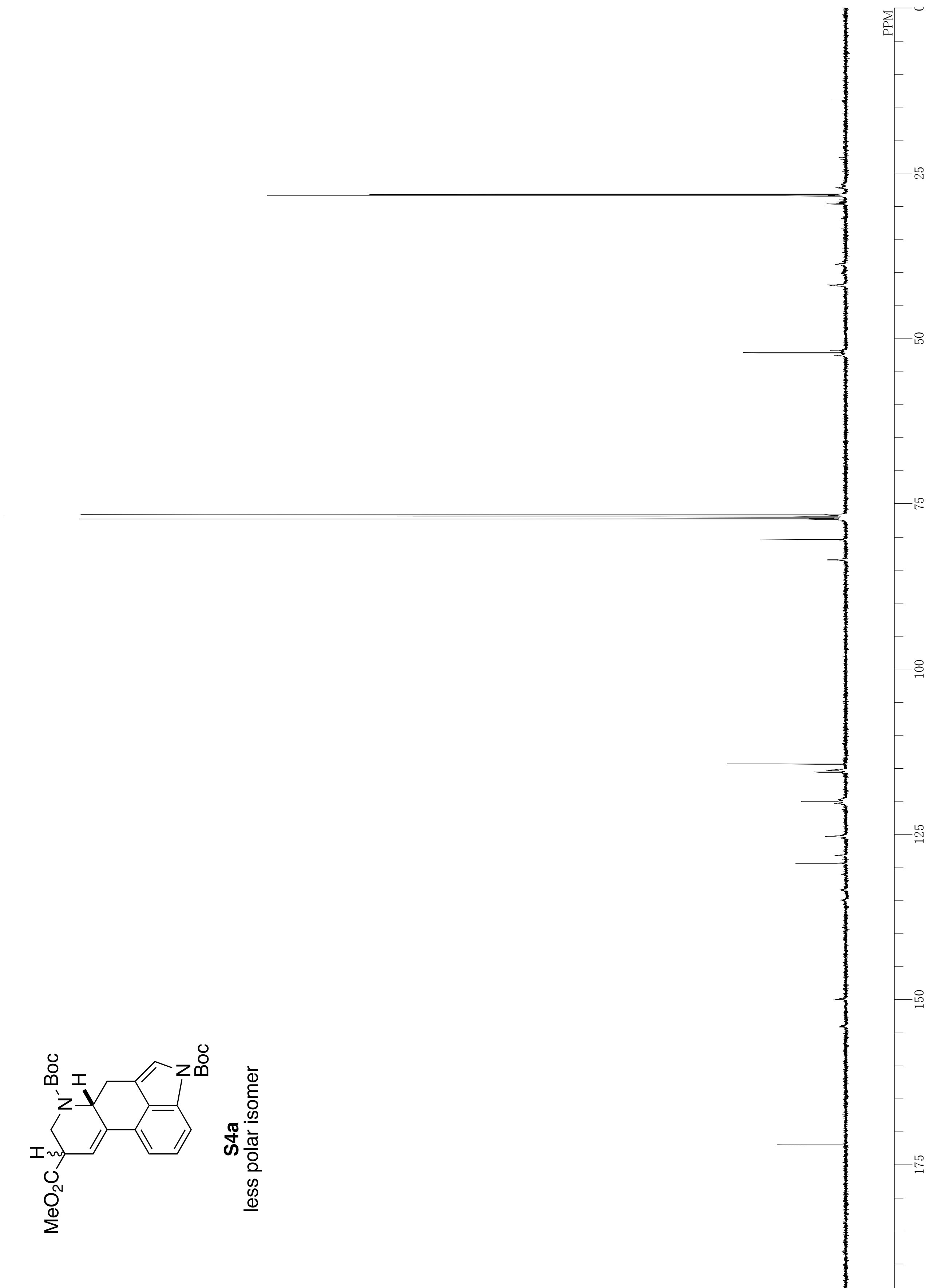


27

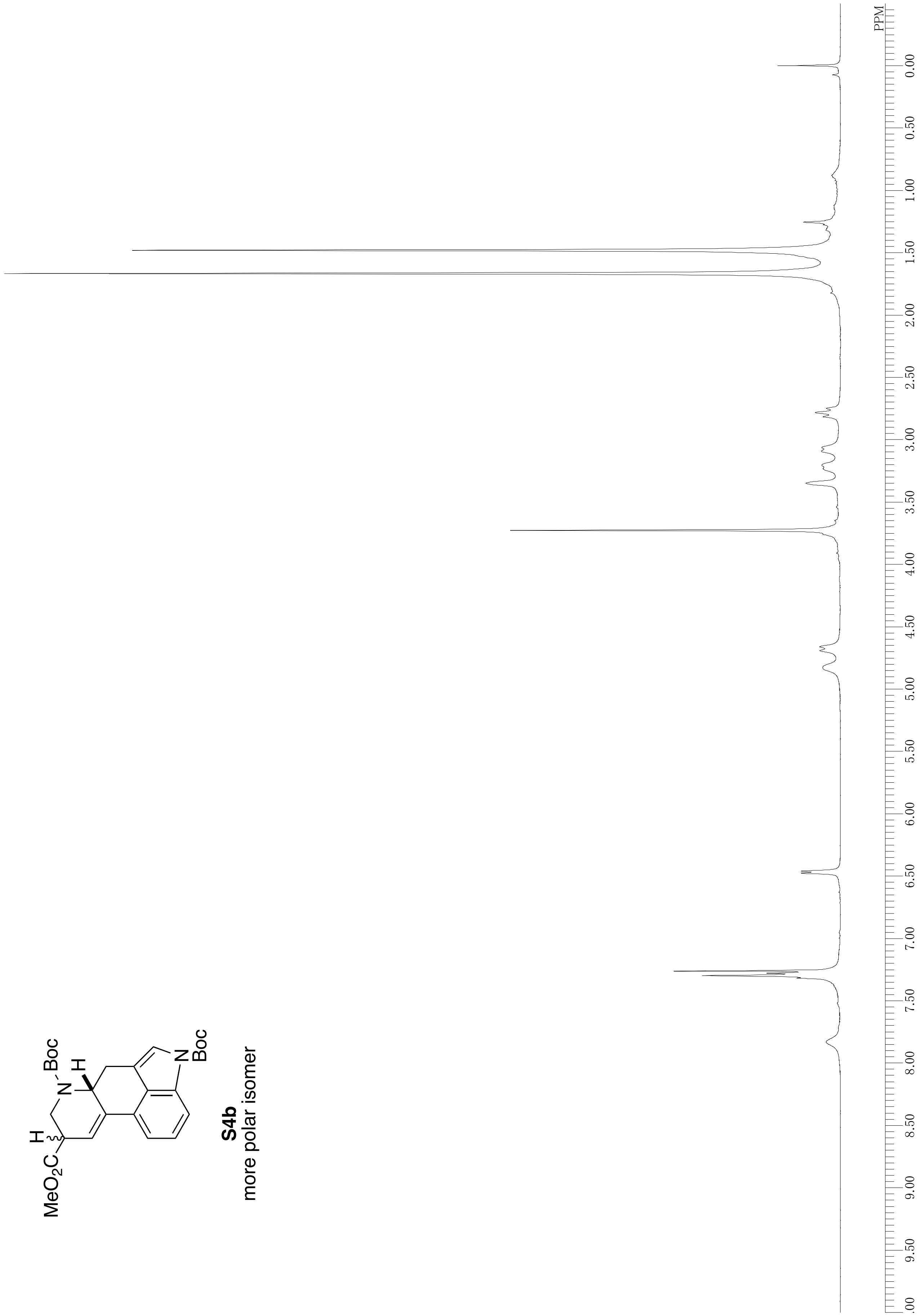


S4a
less polar isomer

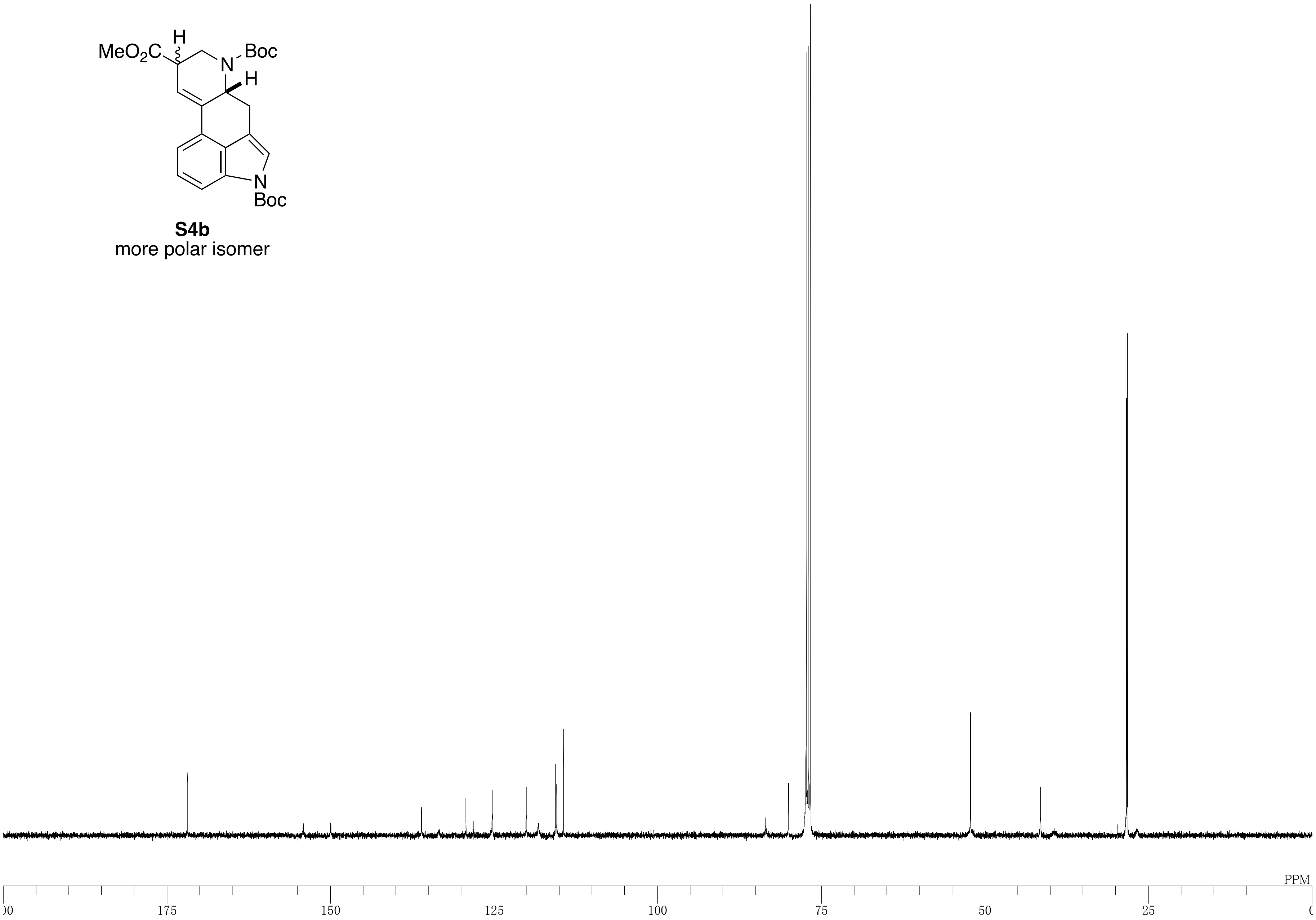




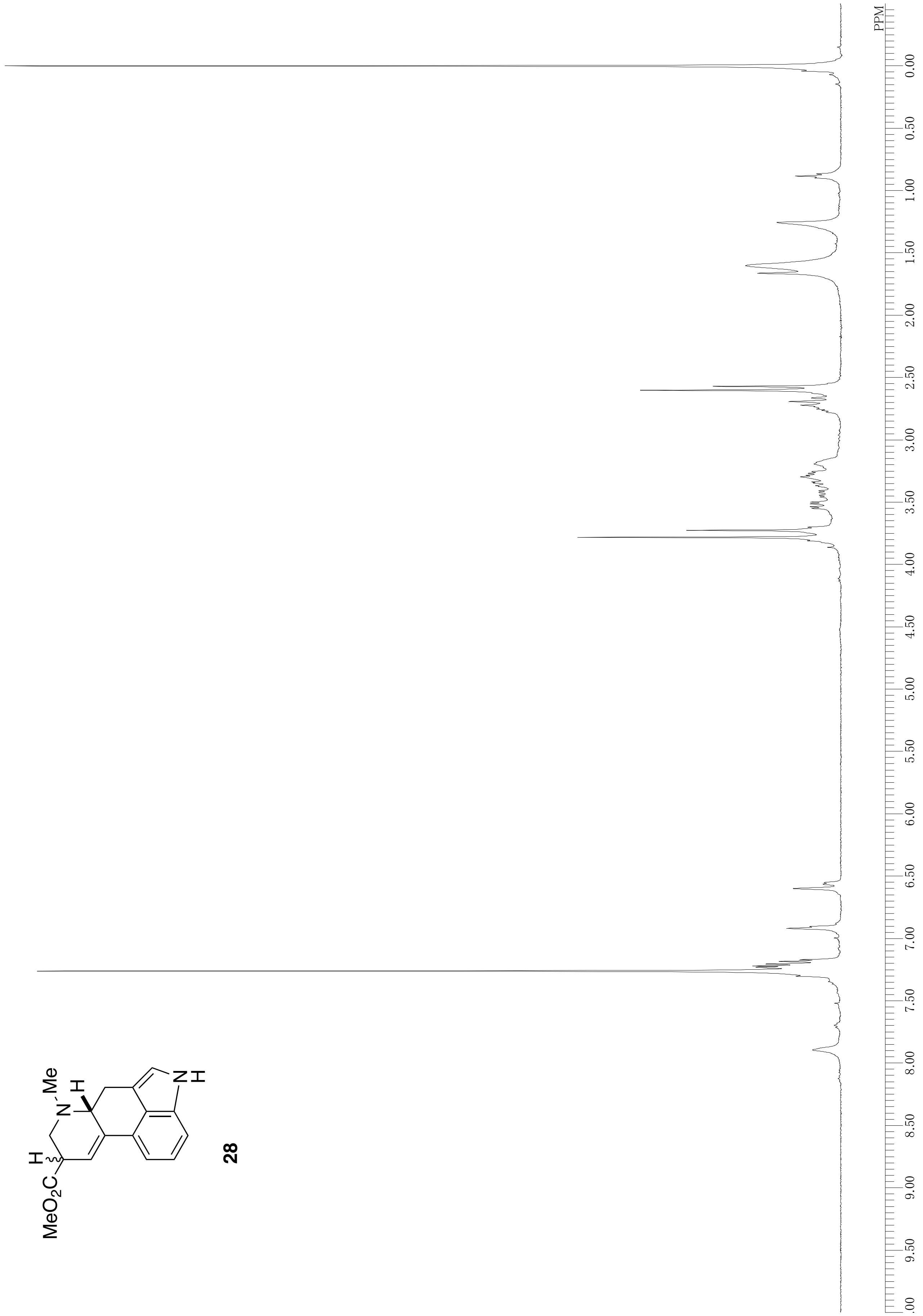
S4a
less polar isomer



S4b
more polar isomer



S4b
more polar isomer


PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
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8.50
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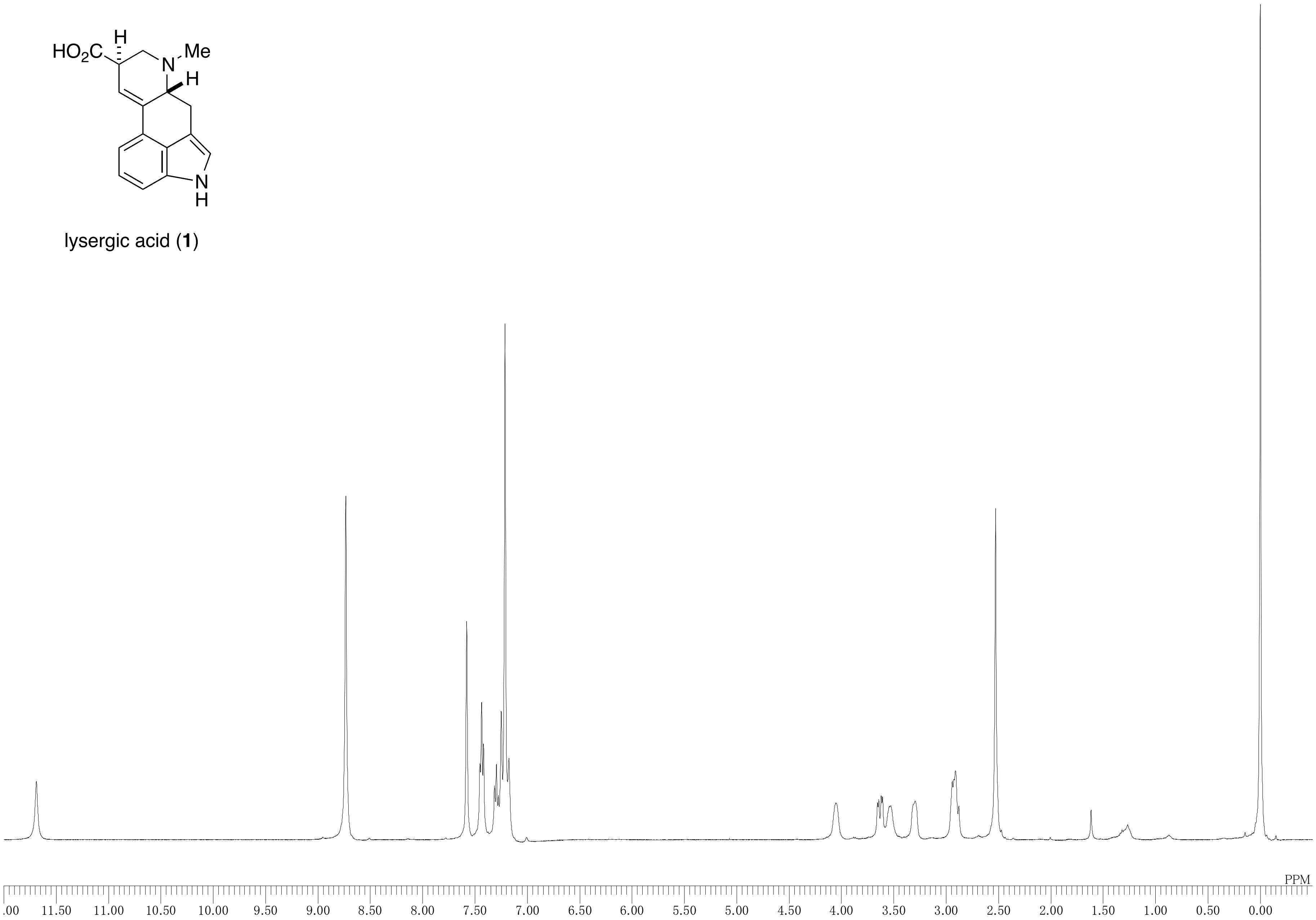
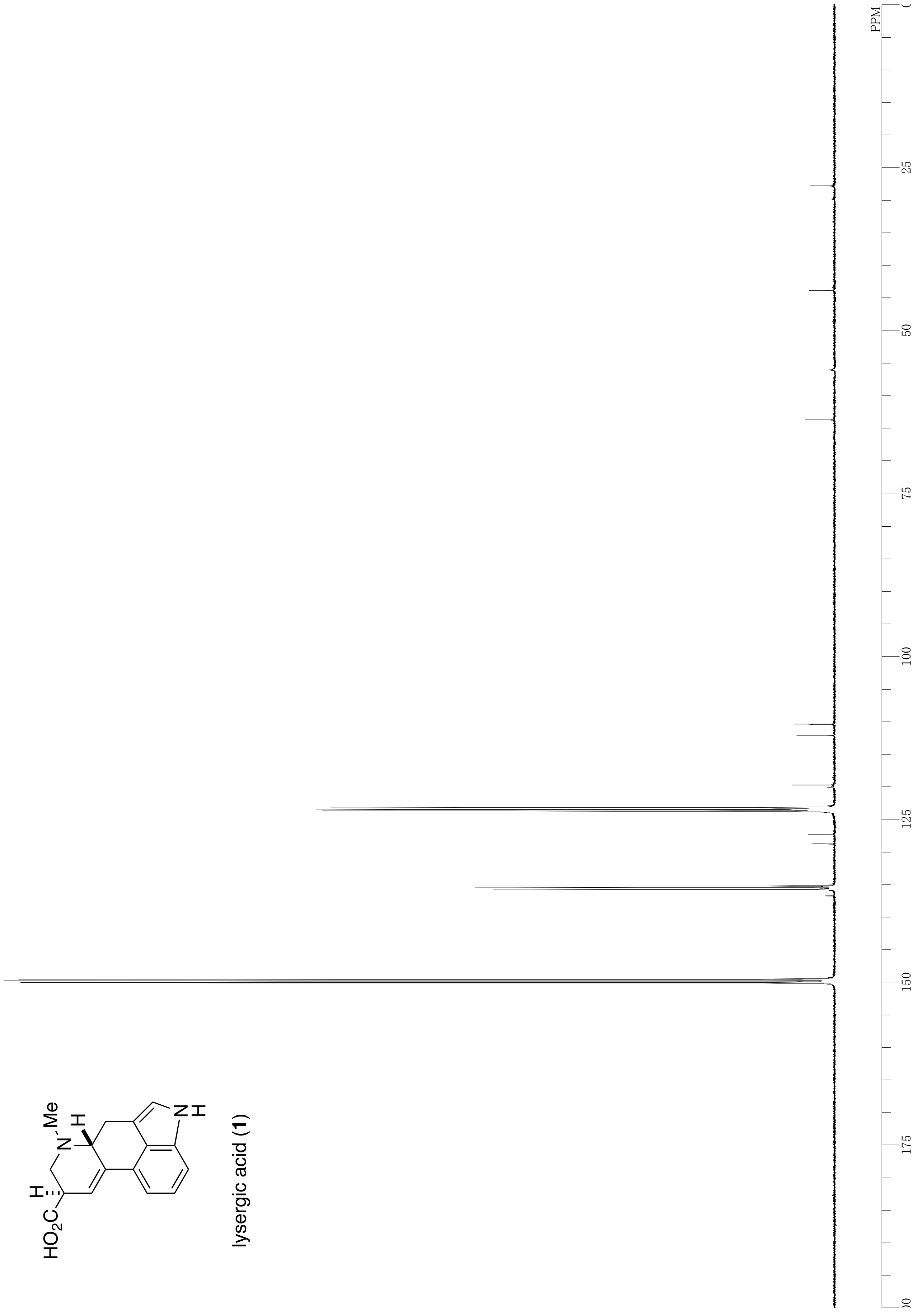
9.50
.00
MeO$_2$C
H
N
Me
H
NH

28



lysergic acid (**1**)



lysergic acid (**1**)