Supporting Information

Metal-Free Stereoselective C(sp^3)-H Indolation of N-heterocycles to Potent Antimicrobial Non-Canonical Tryp-Pro Hybrids

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Experimental Section:

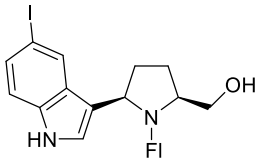
General: All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in oven-dried glassware under an argon atmosphere. Dichloromethane (CH_2Cl_2) was freshly distilled from phosphorus(V)oxide (P_2O_5). Triethylamine (Et_3N) was distilled from CaH_2 and stored under argon. Commercial grade xylene, benzene and toluene were distilled before use. All other solvents and reagents were purified according to standard procedures or were used as received from Aldrich, Acros, Merck and Spectrochem. ^1H, ^{13}C NMR spectroscopy: Bruker 400, 500 and 600 MHz (at 298 K). Chemical shifts, δ (in ppm), are reported relative to TMS (1H) 0.0 ppm, δ (^{13}C) 0.0 ppm) which was used as the inner reference. Otherwise, the solvents residual proton resonance and carbon resonance ($CHCl_3$, δ (1H) 7.26 ppm, δ (^{13}C) 77.26 ppm) were used for calibration. Column chromatography: Merck or Spectrochem silica gel 60-120, 100-200 under gravity or 230-400 silica in Flash Chromatography. IR: spectra were recorded on Perkin Elmer Instrument at normal temperature in neat. MS (ESI-HRMS): Mass spectra were recorded on an Agilent 6546 LC/Q-TOF, and peaks are given in m/z (% of basis peak). HPLC: 1260, Infinity II Prime LC, make: Agilent;

and Dionex Ultimate 3000, make: Thermo Scientific. Polarimetry: MCP5100, make: Anton Paar. Single crystal X-ray data was collected on a Bruker SMART APEX equipped with a CCD area detector using Mo/Kα radiation and the structure was solved by direct method using SHELXT- 2018/2 (Göttingen, Germany)

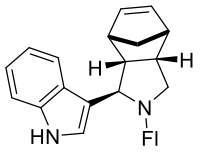
Table s1: Additional conditions for the reaction optimization

entry	conditions	Yield %
1	Neat, MW, 90 ºC, 60 min	26
2	Neat, MW, 100 ºC, 60 min	30
3	Neat, MW, 120 ºC, 60 min	32
4	Neat, MW, 75 ºC- 120 ºC, 40 min	43
5	Anisole (0.1 mL), MW, 120 ºC, 40 min	30
6	Toluene (0.1 mL), MW, 120 ºC, 40 min	52
7	Toluene (0.2 mL), MW, 120 ºC, 40 min	63
8	Sulfolane (0.1 mL), MW, 120 ºC, 40 min	Trace
9	EtOH (0.1 mL), MW, 120 ºC, 40 min	35
10	Toluene, 110 ºC, 2 days	50
11	^{i}PrOH (0.1 mL), MW, 120 ºC, 40 min	50
12	^{n}BuOH (0.1 mL), MW, 120 ºC, 60 min	52
13	**^{n}BuOH (0.1 mL), MW, 120 ºC, 100 min**	**60**
14	2-MeTHF (0.2 mL), 120 ºC, 40 min	19

Additional Substrates:



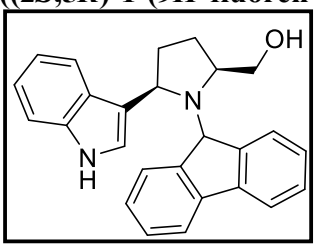
12k', 60%



16d, 70%

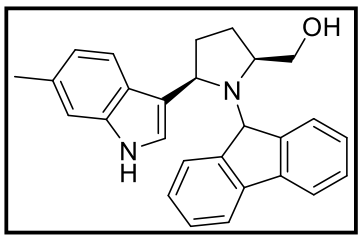
General procedure I: Indole (0.2 mmol, 1 equiv.), 9*H*-fluoren-9-one (0.24 mmol, 1.2 euiv.), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv.) were dissolved in 1 mL of toluene in a microwave tube. Then acetic acid (0.2 mmol, 1 equiv.) was added to the mixture and the tube was sealed. The reaction mixture was then heated for 60 min under microwave irradiation at 145 ºC. After completion of the reaction the solvent was evaporated under reduced pressure and the residue was purified by column chromatography to obtain the desired *cis*-α-indolyl (*S*)-prolinol.

((2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(1*H*-indol-3-yl)pyrrolidin-2-yl)methanol (12a):



According to general procedure **I:** 1*H*-Indole (0.20 mmol, 1equiv., 23.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43.2 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:4 ethyl acetate:hexane) to afford **12a** as white-yellow foam (47.5 mg, 63% yield). **FTIR** (neat): ŭ = 3417, 3294, 3066, 2928, 288, 1449, 1210, 1095, 102, 739 cm^{-1}. $[\alpha]_D^{25}$ = +221.678 (c = 0.30 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-d) δ = 8.14 (s, 1H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.33 – 7.26 (m, 3H), 7.24 – 7.16 (m, 5H), 5.08 (s, 1H), 4.93 – 4.90 (m, 1H), 3.04 – 3.01 (m, 1H), 2.96 – 2.92 (m, 1H), 2.73 – 2.70 (m, 1H), 2.44 – 2.30 (m, 1H), 2.27 – 2.20 (m, 1H), 2.18 – 2.12 (m, 1H), 2.00 – 1.90 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 146.2, 144.1, 141.3, 139.8, 137.2, 128.1, 127.9, 127.5, 126.7, 126.4, 125.9, 124.7, 122.9, 122.2, 120.09, 120.06, 119.8, 119.5, 117.7, 111.6, 63.9, 63.2, 62.9, 59.6, 32.3, 28.3 ppm. **HRMS** (**ESI):** exact mass calculated for $C_{26}H_{25}N_2O^+$ ($[M+H]^+$): 381.1961, found: 381.1963. **HPLC analysis:** ee = 99.24%; Chiralpak IA column; hexane: *i*PrOH = 85:15; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 12.65 min, t_{minor} = 13.81 min).

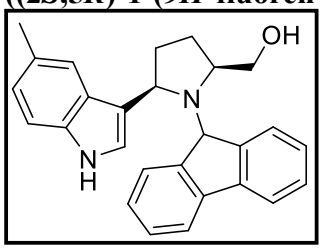
((2*S*,5*R*)-1-(9H-fluoren-9-yl)-5-(6-methyl-1*H*-indol-3-yl)pyrrolidin-2-yl)methanol (12b):



According to general procedure **I:** 6-Methylindole (0.2 mmol, 1 equiv., 26.2 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43.2 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:5 ethyl acetate:hexane) to give **12b** as maroon gum (45.5 mg, 58% yield). **FTIR** (neat): ŭ = 3401, 3299, 3063, 2924, 2872, 1712, 1611, 1449, 1195, 1088, 1027, 800, 735 cm^{-1}. $[\alpha]_D^{25}$ = +204.101 (c = 0.22 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.97 (s, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.18 (m, 3H), 7.14 (s, 1H), 7.03 – 7.00 (m, 1H), 5.09 (s, 1H), 4.92 – 4.89 (m, 1H), 3.01 – 2.98 (m, 1H), 2.93 – 2.88 (m, 1H), 2.68 – 2.65 (m, 1H), 2.47 (s, 3H), 2.26 – 2.18 (m, 1H), 2.17 – 2.11 (m, 1H), 2.01 – 1.92 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 146.3,

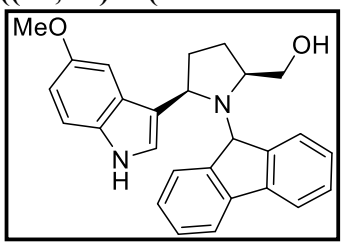
144.1, 141.4, 139.7, 137.6, 132.0, 128.0, 127.9, 127.5, 126.7, 125.9, 124.7, 124.2, 122.2, 121.3, 120.1, 119.73, 119.70, 117.5, 111.5, 63.8, 63.13, 63.10, 59.4, 32.27, 28.4, 21.8 ppm. **HRMS (ESI):** exact mass calculated for $C_{27}H_{26}N_2O^+$ ($[M+H]^+$): 395.2118, found: 395.2113. **HPLC analysis:** ee = 99.04%; Chiralpak IB column; hexane: *i*PrOH = 90:10; flow rate 1 mL/min; λ = 254 nm; (t_{major} = 20.26 min, t_{minor} = 13.43 min).

((2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(5-methyl-1*H*-indol-3-yl)pyrrolidin-2-yl)methanol (12c):



According to general procedure **I:** 5-Methylindole (0.2 mmol, 1 equiv., 26.2 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:5 ethyl acetate:hexane) to give **12c** as a maroon gum (47 mg, 60% yield). **FTIR** (neat): ῡ = 3406, 3295, 3046, 2927, 2872, 1712, 1611, 1447, 1264, 1090, 1024, 794, 733. $[\alpha]_D^{25}$ = +183.759 (c = 0.24 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-d) δ = 8.01 (s, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.66 – 7.64 (m, 2H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 7.0 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.27 – 7.21 (m, 4H), 7.05 – 7.03 (m, 1H), 5.11 (s, 1H), 4.94 – 4.91 (m, 1H), 3.04 – 3.01 (m, 1H), 2.95 – 2.93 (m, 1H), 2.73 – 2.70 (m, 1H), 2.50 (s, 3H), 2.21 – 2.16 (m, 2H), 2.03 – 1.90 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 146.2, 144.2, 141.3, 139.8, 135.4, 128.7, 128.0, 127.9, 127.5, 126.73, 126.70, 125.9, 124.7, 123.8, 122.7, 120.0, 119.7, 119.5, 117.3, 111.1, 63.9, 63.3, 62.7, 59.5, 32.6, 28.4, 21.7 ppm. **HRMS (ESI):** exact mass calculated for $C_{27}H_{26}N_2O^+$ ($[M+H]^+$): 395.2118, found: 395.2110. **HPLC analysis:** ee = 99.06%; Chiralpak IB column; hexane: *i*PrOH = 90:10; flow rate 1 mL/min; λ = 254 nm; (t_{major} = 16.31 min, t_{minor} = 13.40 min).

((2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(5-methoxy-1*H*-indol-3-yl)pyrrolidin-2-yl)methanol

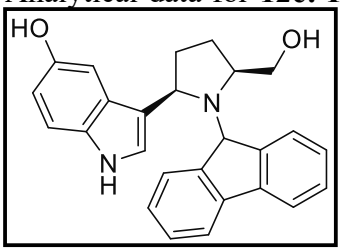


(12d): According to general procedure **I:** 5-methoxyindole (0.2 mmol, 1 equiv., 29.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:5 ethyl acetate:hexane) to afford **12d** as greenish-blue gum (49 mg, 60% yield). **FTIR** (neat): ῡ = 3544, 3414, 3326 3067, 2926, 2872, 2832, 1710, 1624, 1583, 1483, 1449, 1210, 1028, 797, 735 cm-

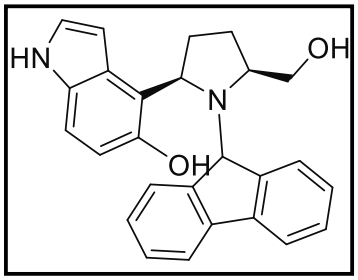
[1]. $[\alpha]_D^{25}$ = +204.455 (c = 0.09 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-d) δ = 8.00 (s, 1H), 7.59 (d, *J* = 7.2 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.24 – 7.19 (m, 2H), 7.14 – 7.09 (m, 4H), 6.79 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.00 (s, 1H), 4.81 – 4.77 (m, 1H), 3.81 (s, 3H), 2.98 – 2.95 (m, 1H), 2.90 – 2.85 (m, 1H), 2.70 – 2.66 (m, 1H), 2.19 – 2.02 (m, 2H), 1.96 – 1.81 (m, 2H) ppm. **^{13}C NMR** (101 MHz, Chloroform-d) δ = 153.8, 146.2, 144.1, 141.3, 139.8, 132.3, 128.1, 127.9, 127.4, 126.74, 126.68, 125.8, 124.8, 123.7, 120.1, 119.8, 117.3, 112.5, 112.2, 101.9, 64.1, 63.3, 62.8, 59.7, 56.0, 32.1, 28.4 ppm. **HRMS (ESI):** exact mass calculated for $C_{27}H_{27}N_2O_2^+$ ($[M+H]^+$): 411.2067, found: 411.2064. **HPLC analysis:** ee = 99.66%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 90:10; flow rate 1.0 mL/min; λ = 254 nm, (t_{major} = 52.34 min, t_{minor} = 33.84 min).

4-((2*R*,5*S*)-1-(9*H*-fluoren-9-yl)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indol-5-ol (12e) and **4-((2*R*,5*S*)-1-(9*H*-fluoren-9-yl)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indol-5-ol (12e$^/$):**According to general procedure **I:** 5-hydroxyindole (0.2 mmol, 1 equiv., 26.6 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:2 ethyl acetate:hexane) to afford both **12e** as pale white gummy (36 mg, 46% yield) and **12e$^/$** as pale white solid crystal (36 mg, 46% yield, mp: 213-215 ºC). The regioisomeric ratio of **12e** and **12e$^/$** is 1:1.

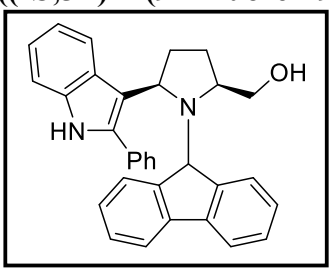
Analytical data for **12e: FTIR** (neat): ῡ = 3407, 3329, 2925, 2854, 1712, 1611, 1450, 1262, 1195, 1097, 797, 736 cm^{-1}. $[\alpha]_D^{25}$ = +202.01 (c = 0.05 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-d) δ = 7.89 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 2H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.32 – 7.28 (m, 2H), 7.26 – 7.17 (m, 4H), 6.84 – 6.82 (m, 1H), 5.09 (s, 1H), 4.84 – 4.81 (m, 1H), 3.10 – 3.08 (m, 1H), 2.99 – 2.87 (m, 1H), 2.78 – 2.76 (m, 1H), 2.31 – 2.23 (m, 1H), 2.15 – 2.09 (m, 1H), 2.05 – 1.99 (m, 1H), 1.97 – 1.90 (m, 1H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 149.7, 146.0, 144.0, 141.2, 139.8, 132.3, 128.1, 127.9, 127.5, 126.7, 126.6, 125.8, 124.8, 124.0, 120.0, 119.7, 116.9, 112.1, 112.1, 104.5, 63.8, 63.2, 63.0, 59.5, 31.7, 28.4 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{24}N_2O_2^+$ ($[M+H]^+$): 397.1911, found 397.1915. **HPLC analysis:** ee = 99.24%; phenomenex lux 5u cellulose-2 column; hexane: *i*PrOH = 85:15; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 17.72 min, t_{minor} = 15.29 min).



Analytical data for **12e′: FTIR** (neat): ῡ = 3402, 3320, 3060, 2926, 2871, 1449, 1265, 1191, 732, 703 cm^{-1}. $[\alpha]_D^{25}$ = +124.292 (c = 0.28 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-d) δ = 11.16 (brs, 1H), 8.12 (s, 1H), 7.90 – 7.85 (m, 2H), 7.70 – 7.68 (m, 1H), 7.66 – 7.61 (m, 1H), 7.42 – 7.29 (m, 4H), 7.26 – 7.24 (m, 1H), 7.23 – 7.21 (m, 1H), 6.92 (d, *J* = 8.6 Hz, 1H), 6.59 – 6.58 (m, 1H), 5.40 – 5.35 m, 1H), 5.09 (s, 1H), 3.09 – 3.05 (m, 1H), 2.96 – 2.92 (m, 1H), 2.74 – 2.69 m, 1H), 2.30 – 2.14 (m, 2H), 1.94 – 1.89 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 151.0, 144.8, 142.5, 142.0, 140.0, 130.3, 128.6, 128.5, 128.1, 127.9, 127.1, 126.1, 125.9, 124.7, 120.2, 119.8, 113.6, 113.1, 111.0, 99.4, 67.1, 65.1, 63.6, 59.6, 30.3, 28.0 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{24}N_2O_2^+$ ($[M+H]^+$): 397.1911, found 397.1915. **HPLC analysis:** ee = 92.5%; Chiralpak IA column; hexane: *i*PrOH = 90:10; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 48.18 min, t_{minor} = 37.70 min).

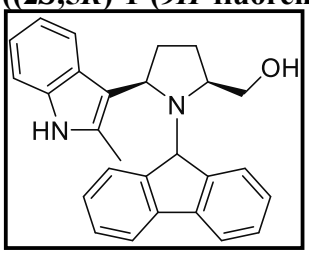


((2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(2-phenyl-1H-indol-3-yl)pyrrolidin-2-yl)methanol (**12f**):



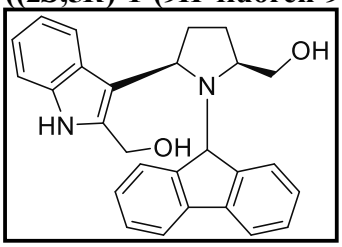
According to general procedure **I:** 2-Phenylindole (0.25 mmol, 1 equiv., 48.3 mg), 9*H*-fluoren-9-one (0.3 mmol, 1.2 equiv., 54 mg), (*S*)-pyrrolidin-2-ylmethanol (0.625 mmol, 2.5 equiv., 63.1 mg) were reacted in presence of acetic acid (0.25 mmol, 1 equiv., 15 mg). The reaction mixture was purified in silica column chromatography (1:8 ethyl acetate:hexane) to afford **12f** as maroon gummy (51.3 mg, 45% yield). FTIR: ῡ = 3410, 3283, 3061, 2923, 2853, 1706, 1604, 1449, 1378, 1298, 1188, 1073, 1028, 740, 700 $cm^{-1.}$ $[\alpha]_D^{25}$ = +167.49 (c = 0.163 g/100 mL, DCM). **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 11.25 (s, 1H), 8.23 – 8.21 (m, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.50 (m, 4H), 7.47 – 7.43 (m, 1H), 7.41 – 7.38 (m, 1H), 7.31 – 7.23 (m, 2H), 7.19 – 7.12 (m, 4H), 7.08 – 7.02 (d, 2H), 5.04 – 5.00 (m, 1H), 4.70 (s, 1H), 4.17 – 4.14 (m, 1H), 3.59 – 3.54 (m, 1H), 2.96 – 2.90 (m, 1H), 2.67 – 2.62 (m, 1H), 2.40 – 2.29 (m, 1H), 2.08 – 2.04 (m, 1H), 1.87 – 1.81 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 146.8, 144.2, 140.8, 138.9, 137.6, 136.7, 132.7, 129.0, 128.6, 127.8, 127.73, 127.67, 126.9, 126.7, 126.6, 125.6, 125.2, 121.5, 121.2, 120.1, 119.7, 118.4, 111.5, 111.5, 65.2, 62.8, 61.4, 59.6, 29.9, 28.0 ppm. **HRMS (ESI):** exact mass calculated for $C_{28}H_{27}N_2O_2^+$ ($[M+H]^+$): 457.2274, found: 457.2269. **HPLC analysis:** ee = 99.05%; Chiralpak IA column; hexane: *i*PrOH = 93:7; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 64.4 min, t_{minor} = 26.97 min).

((2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(2-methyl-1*H*-indol-3-yl)pyrrolidin-2-yl)methanol (12g):



According to general procedure **I:** 2-Methylindole (0.2 mmol, 1 equiv., 26.2 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43.2 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:5 ethyl acetate:hexane) to give **12g** as maroon yellow solid (36 mg, 46% yield, mp.: 209 – 212 ºC). **FTIR** (neat): ῡ = 3405, 3279, 3060, 2925, 2873, 1741, 1620, 1459, 144, 1299, 1027, 739 cm^{-1}. $[\alpha]_D^{25}$ = +275.014 (c = 0.108 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ = 7.97 – 7.96 (m, 1H), 7.84 – 7.74 (m, 1H), 7.65 – 7.61 (m, 2H), 7.36 – 7.11 (m, 8H), 4.99 (s, 1H)), 4.92 – 4.74 (m, 1H), 3.09 (bs, 2H), 2.80 (bs, 1H), 2.57 – 2.25 (m, 4H), 2.07 – 1.98 (m, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 146.3, 144.1, 141.1, 139.9, 135.9, 133.3, 128.0, 127.8, 127.6, 127.4, 126.6, 125.6, 125.1, 121.2, 120.14, 120.03, 119.8, 119.4, 111.4, 110.6, 63.5, 63.0, 62.0, 60.1, 30.2, 27.7, 12.1 ppm. **HRMS** (**ESI):** exact mass calculated for $C_{27}H_{26}N_2O^+$ ($[M+H]^+$): 395.2118, found: 395.2125. **HPLC analysis:** ee = 98.7%; phenomenex lux 5u cellulose-2 column; n-hexane: *i*PrOH = 95:5; flow rate 0.5 mL/min; λ = 254 nm; (t_{major} = 64.83 min, t_{minor} = 60.53 min).

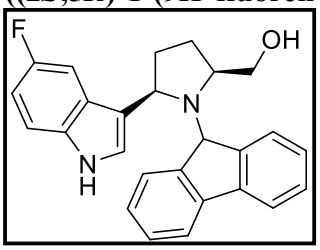
((2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(2-(hydroxymethyl)-1*H*-indol-3-yl)pyrrolidin-2-yl)methanol (12h):



According to general procedure **I:** 1H-Indole-2-methanol (0.2 mmol, 1 equiv., 29.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43.2 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:1 ethyl acetate:hexane) to afford **12h** as yellow-maroon gum (46.5 mg, 57% yield). **FTIR** (neat): ῡ = 3384, 3272, 3066, 2925, 2852, 1662, 1449, 1037, 739 cm^{-1}. $[\alpha]_D^{25}$ = +183.539 (c = 0.085 g/100 mL, DCM). **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 10.89 (s, 1H), 8.04 – 8.01 (m, 1H), 7.87 (s, 1H), 7.80 (d, *J* = 7.2 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.39 – 7.26 (m, 4H), 7.22 – 7.14 (m, 2H), 7.09 – 7.03 (m, 2H), 5.19 – 5.17 (m, 1H), 5.04 – 5.02 (m, 1H), 4.86 (s, 1H), 4.71 (bs, 2H), 4.15 – 4.12 (m, 1H), 2.93 (s, 1H), 2.69 – 2.61 (m, 2H), 2.26 – 2.16 (m, 1H), 1.95 – 1.83 (m, 3H) ppm. **^{13}C NMR** (126 MHz, DMSO-d_6) δ = 147.1, 144.8, 140.7, 139.1, 137.8, 136.0, 127.7, 127.6, 126.9, 126.7, 125.8, 125.7, 120.7, 120.4, 120.1, 119.7, 118.0, 111.3, 110.7, 65.3, 63.0, 61.1, 59.7, 55.0, 30.1, 28.0 ppm. (overlap of signals at aromatic region leading to 1

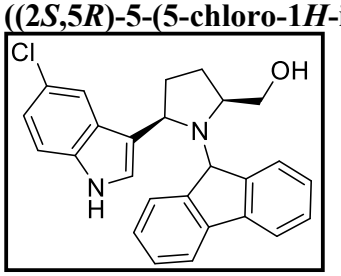
carbon less in count) **HRMS (ESI):** exact mass calculated for $C_{27}H_{27}N_2O_2^+$ ($[M+H]^+$) 411.2067, found: 411.2072. **HPLC analysis:** ee = 99.76%; Chiralpak IA column; hexane: *i*PrOH = 90:10; flow rate 1.0 mL/ min; λ = 254 nm; (t_{major} = 36.45 min, t_{minor} = 29.80 min).

((2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(5-fluoro-1*H*-indol-3-yl)pyrrolidin-2-yl)methanol (12i):



According to general procedure **I:** 5-fluoroindole (0.2 mmol, 1 equiv., 27 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:3 ethyl acetate:hexane) to give **12i** as maroon gum (51.5 mg, 65% yield). **FTIR** (neat): ʊ = 3432, 3288, 3062, 2942, 2874, 1711, 1581, 1482, 1264, 1174, 1026, 933, 796, 732 cm^{-1}. $[\alpha]_D^{25}$ = +198.939 (c = 0.28 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-d) δ = 8.15 (s, 1H), 7.64 – 7.60 (m, 3H), 7.51 – 7.48 (m, 1H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.25 – 7.17 (m, 4H), 6.94 (td, *J* = 9.0, 2.5 Hz, 1H), 5.05 (s, 1H), 4.84 – 4.81 (m, 1H), 3.08 – 3.06 (m, 1H), 3.01 – 2.97 (m, 1H), 2.84 – 2.81 (m, 1H), 2.18 – 2.12 (m, 2H), 2.04 – 1.90 (m, 2H) ppm. **13C NMR** (126 MHz, Chloroform-d) δ = 157.55 (158.49, 156.62, d, *J* = 234.9 Hz), 145.9, 144.1, 141.1, 139.9, 133.5, 128.1, 127.9, 127.5, 126.7, 126.66 (126.70, 126.63, d, *J* = 9.3 Hz), 125.8, 124.7, 124.5, 120.0, 119.8, 117.88 (117.90, 117.87, d, *J* = 4.8 Hz), 112.02 (112.06, 111.99, d, J = 9.5 Hz), 110.54 (110.64, 110.43, d, J = 26.6 Hz), 104.86 (104.96, 104.77, d, J = 23.18 Hz), 63.9, 63.3, 62.3, 59.9, 32.2, 28.2 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{24}FN_2O^+$ ($[M+H]^+$): 399.1867, found 399.1868. **HPLC analysis:** ee = 99.8%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 92:8; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 53.50 min, t_{minor} = 37.97 min).

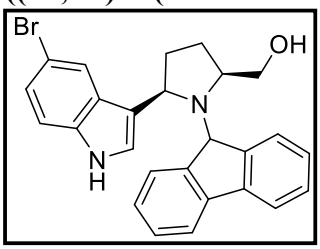
((2*S*,5*R*)-5-(5-chloro-1*H*-indol-3-yl)-1-(9*H*-fluoren-9-yl)pyrrolidin-2-yl)methanol (12j):



According to general procedure **I:** 5-chloro-1*H*-indole (0.2 mmol, 1equiv., 30.2 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) and acetic acid (0.2 mmol, 1 equiv., 12 mg) were reacted. The reaction mixture is purified in silica column chromatography (1:3 ethyl acetate:hexane) to afford **12j** as light-yellow foam (50.5 mg, 61% yield). **FTIR** (neat): ʊ = 3667, 3423, 3277, 3066, 2940, 2877, 1718, 1611, 1449, 1100, 1026, 892, 796, 742, 675, 421 cm^{-1}. $[\alpha]_D^{25}$ =

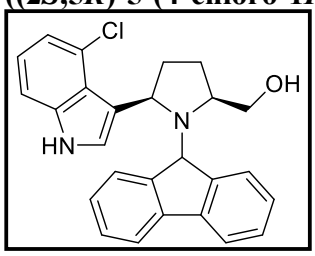
+144.007 (c = 0.10 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-d) δ = 8.07 (s, 1H), 7.67 (s, 1H), 7.55 - 7.52 (m, 3H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.22 – 7.14 (m, 4H), 7.11 – 7.05 (m, 2H), 4.99 (s, 1H), 4.75 – 4.71 (m, 1H), 3.06 – 2.98 (m, 2H), 2.87 – 2.80 (m, 1H), 2.10 – 2.02 (m, 2H), 1.98 – 1.85 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 145.7, 144.1, 141.0, 140.0, 135.2, 128.2, 127.8, 127.48, 127.45, 126.7, 125.7, 125.1, 124.7, 123.8, 122.5, 119.92, 119.85, 119.38, 117.9, 112.3, 63.9, 63.5, 61.8, 60.2, 32.6, 28.1 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{24}ClN_2O^+$ ($[M+H]^+$): 415.1572, found: 415.1583. **HPLC analysis:** ee = 99.28%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 90:10; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 44.37 min, t_{minor} = 32.91 min).

((2*S*,5*R*)-5-(5-bromo-1*H*-indol-3-yl)-1-(9*H*-fluoren-9-yl)pyrrolidin-2-yl)methanol (12k):



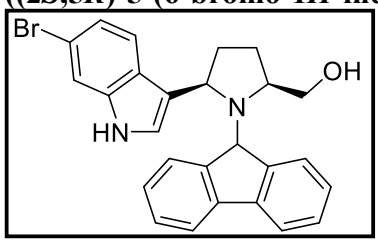
According to general procedure **I:** 5-bromoindole (0.2 mmol, 1 equiv., 38.8 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:3 ethyl acetate:hexane) to afford **12k** as maroon-brown gum (49 mg, 54% yield). **FTIR** (neat): ῡ = 3423, 3276, 3063, 2942, 2875, 1607, 1566, 1448, 1295, 1204, 1092, 883, 737 cm^{-1}. $[\alpha]_D^{25}$ = +201.314 (c = 0.23 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-d) = δ 8.16 (s, 1H), 7.91 (s, 1H), 7.62 - 7.59 (m, 3H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 7.35 Hz, 1H), 7.29 - 7.24 (m, 3H), 7.21 - 7.16 (m, 3H), 5.04 (s, 1H), 4.82 - 4.78 (m, 1H), 3.12 – 3.10 (m, 1H), 3.05 - 3.01 (m, 1H), 2.91 – 2.88 (m, 1H), 2.19 – 2.08 (m, 2H), 2.03 – 1.90 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 145.7, 144.1, 141.0, 140.1, 135.5, 128.18, 128.16, 127.9, 127.5, 126.7, 125.7, 124.9, 124.7, 123.7, 122.5, 119.93, 119.87, 117.8, 112.8, 112.6, 64.0, 63.5, 61.8, 60.2, 32.7, 28.2 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{24}BrN_2O^+$ ($[M+H]^+$): 459.1067, found: 459.1076. **HPLC analysis:** ee = 99.28%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 90:10; flow rate 1.0 mL/ min; λ = 254 nm; (t_{major} = 45.23 min, t_{minor} = 35.09 min).

((2*S*,5*R*)-5-(4-chloro-1*H*-indol-3-yl)-1-(9*H*-fluoren-9-yl)pyrrolidin-2-yl)methanol (12l):



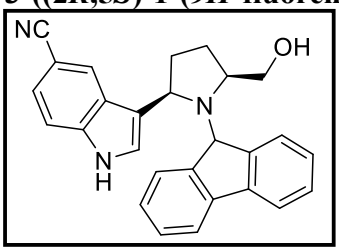
According to general procedure **I:** 4-chloroindole (0.2 mmol, 1equiv., 30.2 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) and acetic acid (0.2 mmol, 1 equiv., 12 mg) were reacted. The reaction mixture is purified in silica column chromatography (1:3 ethyl acetate:hexane) to afford **12l** as maroon gum (35 mg, 42% yield). **FTIR** (neat): ŭ = 3422, 3301, 3059, 2924, 2854, 1699, 1449, 1263, 1023, 737 cm^{-1}. $[\alpha]_D^{25}$ = +80.913 (c = 0.11 g/100 ml, DCM). **^{1}H NMR** (500 MHz, Chloroform-d) δ = 8.41 (s, 1H), 7.83 – 7.63 (m, 5H), 7.37 – 7.25 (m, 5H), 7.12 – 7.06 (m, 2H), 5.76 (s, 1H), 5.20 (s, 1H), 3.01 – 2.99 (m, 1H), 2.82 – 2.68 (m, 2H), 2.50 – 2.46 (m, 1H), 1.99 – 1.90 (m, 1H), 1.82 – 1.65 (m, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 146.23, 144.4, 141.58, 140.0, 138.2, 128.4, 128.2, 127.5, 127.2, 126.2, 126.1, 124.43, 124.38, 122.6, 121.0, 120.1, 120.0, 110.3, 64.7, 64.2, 62.2, 59.5, 36.1, 28.9 ppm. (overlap of signals at aromatic region leading to 2 carbons less in count). **HRMS (ESI):** exact mass calculated for $C_{26}H_{24}ClN_2O^+$ ($[M+H]^+$): 415.1572, found 415.1570. **HPLC analysis:** ee = 99.75%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 94:6; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 49.39 min, t_{minor} = 34.00 min).

((2*S*,5*R*)-5-(6-bromo-1*H*-indol-3-yl)-1-(9*H*-fluoren-9-yl)pyrrolidin-2-yl)methanol (12m):

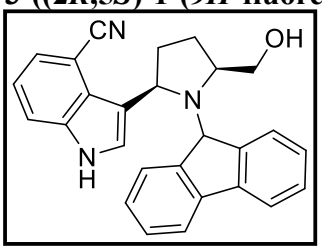


According to general procedure **I:** 6-bromoindole (0.2 mmol, 1equiv., 38.8 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:5 ethyl acetate:hexane) to afford **12m** as maroon-red gum (50.5 mg, 55% yield). **FTIR** (neat): ŭ = 3422, 3284, 3064, 2924, 2853, 1711, 1611, 1449, 1088, 1026, 801, 737 cm^{-1}. $[\alpha]_D^{25}$ = +177.009 (c = 0.10 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ = 8.09 (s, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.65 – 7.62 (m, 3H), 7.51 (d, *J* = 1.8 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.29 – 7.24 (m, 2H), 7.22 – 7.18 (m, 2H), 5.06 (s, 1H), 4.87 – 4.83 (m, 1H), 3.10 – 3.02 (m, 2H), 2.83 – 2.79 (m, 1H), 2.23 – 2.13 (m, 2H), 2.03 – 1.95 (m, 2H) ppm. ^{13}C NMR (126 MHz, Chloroform-d) δ = 145.8, 143.9, 141.1, 139.9, 137.9, 128.2, 127.9, 127.5, 126.7, 125.7, 125.2, 124.7, 123.4, 122.8, 121.3, 120.0, 119.8, 118.0, 115.7, 114.4, 63.7, 63.3, 62.4, 60.0, 32.2, 28.1 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{24}BrN_2O^+$ ($[M+H]^+$):

459.1067, found: 459.1066. **HPLC analysis:** ee = 99.58%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 90:10; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 40.18 min, t_{minor} = 30.96 min).

3-((2*R*,5*S*)-1-(9*H*-fluoren-9-yl)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indole-5-carbonitrile (12n): 

According to general procedure **I:** 5-cyanoindole (0.2 mmol, 1equiv., 28.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:4 ethyl acetate:hexane) to afford **12n** as maroon-pink gum (46.3 mg, 57% yield). **FTIR** (neat): ῡ = 3419, 3314, 3062, 2926, 2877, 2218, 1712, 1616, 1448, 1264, 1024, 805, 733 cm^{-1}. $[\alpha]_D^{25}$ = +184.384 (c = 0.16 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ = 8.59 – 8.51 (m, 1H), 8.00 – 7.99 (m, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.40 – 7.38 (m, 1H), 7.36 – 7.32 (m, 2H), 7.30 – 7.26 (m, 2H), 7.25 – 7.21 (m, 1H), 7.13 – 7.09 (m, 1H), 5.03 (s, 1H), 4.78 – 4.74 (m, 1H), 3.24 – 3.17 (m, 2H), 3.10 – 3.06 (m, 1H), 2.22 – 2.14 (m, 1H), 2.12 – 2.05 (m, 2H), 2.01 – 1.98 (m, 1H), 1.92 – 1.89 (m, 1H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 145.2, 144.2, 140.9, 140.4, 138.5, 128.4, 127.9, 127.5, 126.8, 126.3, 125.6, 125.5, 125.0, 124.9, 124.7, 121.0, 120.1, 119.9, 119.3, 112.2, 102.4, 64.1, 63.8, 61.0, 60.8, 33.1, 28.2 ppm. **HRMS (ESI):** exact mass calculated for $C_{27}H_{24}N_3O^+$ ($[M+H]^+$): 406.1914, found: 406.1919. **HPLC analysis:** ee = 99.73%; Chiralpak IA column; hexane: *i*PrOH = 88:12; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 19.14 min, t_{minor} = 27.01 min).

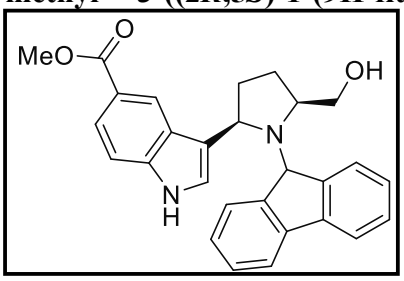
3-((2*R*,5*S*)-1-(9*H*-fluoren-9-yl)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indole-4-carbonitrile (12o): 

According to general procedure **I:** 4-cyanoindole (0.2 mmol, 1 equiv., 28.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:4 ethyl acetate:hexane) to afford **12o** as maroon-pink gum (35 mg, 43% yield). **FTIR** (neat): ῡ = 3332, 3059, 2926, 2860, 2215, 1720, 1447, 1346, 1108, 1028, 742 cm^{-1}. $[\alpha]_D^{25}$ = +80.004 (c = 0.15 g/100 mL, DCM).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ = 8.76 (s, 1H), 7.87 (d, *J* = 7.5

Hz, 1H), 7.80 – 7.68 (m, 1H), 7.66 – 7.61 (m, 3H), 7.58 – 7.56 (m, 1H), 7.52 – 7.49 (m, 1H), 7.37 – 7.34 (m, 1H), 7.30 – 7.25 (m, 3H), 7.22 – 7.19 (m, 1H), 5.55 (s, 1H), 5.11 (s, 1H), 3.10 – 3.07 (m, 1H), 2.99 – 2.78 (m, 2H), 2.50 – 2.48 (m, 1H), 2.05 – 1.97 (m, 2H), 1.91 – 1.85 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 145.7, 144.0, 141.20, 140.2, 137.0, 128.4, 128.1, 127.41, 127.38, 126.8, 126.6, 126.2, 124.9, 124.5, 121.6, 120.03, 119.97, 116.5, 102.0, 64.2, 61.2, 60.1, 35.1, 28.3 ppm. (overlap of signals at aromatic and aliphatic region leading to 2 carbon less in count). **HRMS (ESI):** exact mass calculated for $C_{27}H_{24}N_3O^+$ ($[M+H]^+$): 406.1914, found: 406.1922. **HPLC analysis:** ee = 99.82%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 92:8; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 50.37 min, t_{minor} = 33.81 min).

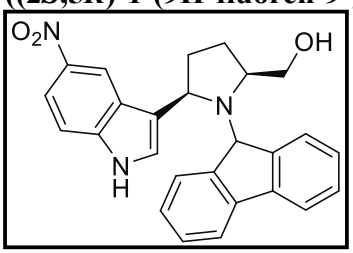
methyl 3-((2*R*,5*S*)-1-(9*H*-fluoren-9-yl)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indole-6-carboxylate (12p): According to general procedure **I:** Methyl indole-6-carboxylate (0.2 mmol, 1 equiv., 35 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:5 ethyl acetate:hexane) to afford **12p** as maroon gum (55 mg, 63% yield). **FTIR** (neat): ῡ = 3422, 3326, 3060, 2950, 1875, 1698, 1622, 1449, 1315, 1250, 1294, 1264, 1087, 1025, 732 cm^{-1}. $[\alpha]_D^{25}$ = +175.179 (c = 0.294 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-d) δ = 8.62 (s, 1H), 8.12 (s, 1H), 7.90 – 7.84 (m, 2H), 7.64 - 7.60 (m, 3H), 7.40 – 7.38 (m, 2H), 7.33 – 7.27 (m, 2H), 7.23 – 7.20 (m, 1H), 7.19 – 7.15 (m, 1H), 5.05 (s, 1H), 4.89 – 4.85 (m, 1H), 3.95 (s, 3H), 3.13 – 3.10 (m, 1H), 3.06 (bs, 1H), 2.88 – 2.85 (m, 1H), 2.24 – 2.16 (m, 2H), 2.07 – 1.95 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 168.3, 145.7, 144.0, 141.1, 140.0, 136.4, 130.0, 128.2, 127.9, 127.4, 126.7, 126.3, 125.7, 124.7, 123.7, 120.4, 120.0, 119.8, 119.5, 118.2, 113.9, 63.8, 63.4, 62.1, 60.1, 52.0, 32.4, 28.2 ppm. **HRMS (ESI):** exact mass calculated for $C_{28}H_{27}N_2O_3^+$ ($[M+H]^+$): 439.2016, found: 439.2019. **HPLC analysis:** ee = 99.92%; phenomenex lux 5u cellulose-2 column; hexane: *i*PrOH = 85:15; flow rate 1.0 mL/min; λ = 254 nm, (t_{major} = 27.19 min, t_{minor} = 16.72 min)

methyl 3-((2*R*,5*S*)-1-(9H-fluoren-9-yl)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indole-5-carboxylate (12q):



According to general procedure **I:** Methyl indole-5-carboxylate (0.2 mmol, 1 equiv., 35 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:5 ethyl acetate:hexane) to afford **12q** as maroon gum (56 mg, 64% yield). **FTIR** (neat): ŭ = 3539, 3417, 3331,3048, 2950, 1694, 1694, 1618, 1447, 1265, 1112, 1029, 742 cm^{-1}. $[\alpha]_D^{25}$ = +211.677 (c = 0.18 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-d) δ = 8.62 (s, 1H), 8.43 (s, 1H), 7.92 – 7.90 (m, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.62 – 7.60 (m, 2H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.34 – 7.30 (m, 3H), 7.28 – 7.22 (m, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 5.07 (s, 1H), 4.95 – 4.92 (m, 1H), 3.97 (s, 3H), 3.13 - 310 (m, 1H), 3.05 – 3.01 (m, 1H), 2.90 – 2.87 (m, 1H), 2.25 – 2.19 (m, 1H), 2.15 – 2.11 (m, 1H), 2.04 – 1.99 (m, 1H), 1.97 – 1.93 (m, 1H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 168.3, 145.7, 144.1, 141.1, 140.0, 139.5, 128.2, 127.9, 127.4, 126.7, 126.1, 125.8, 124.7, 123.6, 123.5, 122.8, 121.4, 119.9, 119.8, 119.7, 111.1, 64.1, 63.6, 61.9, 60.1, 52.0, 33.1, 28.3 ppm. **HRMS (ESI):** exact mass calculated for $C_{28}H_{27}N_2O_3^+$ ($[M+H]^+$): 439.2016, found: 439.2024. **HPLC analysis:** ee = 99.70%; Chiralpak IA column; hexane: *i*PrOH = 90:10; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 22.36 min, t_{minor} = 32.20 min).

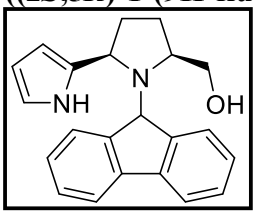
((2*S*,5*R*)-1-(9H-fluoren-9-yl)-5-(5-nitro-1*H*-indol-3-yl)pyrrolidin-2-yl)methanol (12r):



According to general procedure **I:** 5-nitroindole (0.2 mmol, 1equiv., 32.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (S)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:2 ethyl acetate:hexane) to afford **12r** as maroon-brown gum (35 mg, 41% yield). **FTIR** (neat): ŭ = 3559, 3402, 3237, 3069, 2925, 2855, 1717, 1518, 1469, 1331, 1028, 813, 739 cm^{-1}. $[\alpha]_D^{25}$ = +187.656 (c = 0.17 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-d) δ = 8.69 – 8.65 (m, 2H), 8.08 – 8.05 (m, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.55 – 7.49 (m, 3H), 7.37 – 7.19 (m, 5H), 7.11 – 7.07 (m, 1H), 5.05 (s, 1H), 4.82 – 4.78 (m, 1H), 3.28 – 3.24 (m, 1H), 3.22 – 3.11 (m, 2H), 2.24 – 2.16 (m, 1H), 2.13 – 1.99 (m, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 145.1, 144.1, 141.3, 140.8, 140.3, 139.7, 128.3, 127.8, 127.4, 126.7, 125.8, 125.6, 125.4, 124.8,

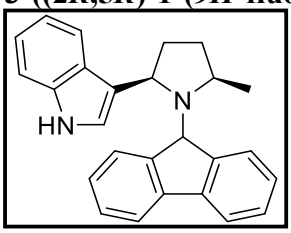
121.0, 120.0, 119.8, 117.7, 117.1, 111.2, 64.2, 63.9, 60.9, 60.7, 33.3, 28.2 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{24}N_3O_3^+$ ($[M+H]^+$): 426.1812, found 426.1820. **HPLC analysis:** ee = 99.50%; phenomenex lux 5u cellulose-2 column; hexane: *i*PrOH = 96:4; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 161.45 min, t_{minor} = 176.04 min).

((2*S*,5*R*)-1-(9H-fluoren-9-yl)-5-(1*H*-pyrrol-2-yl)pyrrolidin-2-yl)methanol (12s):



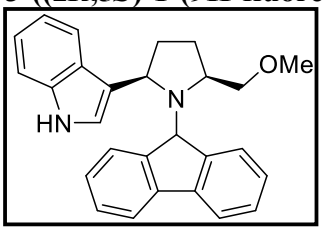
According to general procedure **I:** pyrrole (0.2 mmol, 1 equiv., 13.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:5 ethyl acetate:hexane) to afford **12s** as maroon gum (41.5 mg, 63% yield). **FTIR** (neat): ῡ = 3434, 3311, 3068, 2924, 2854, 1698, 1449, 1265, 1025, 795, 740 cm^{-1}. $[\alpha]_D^{25}$ = +76.927 (c = 0.052 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-d) δ = 8.70 (s, 1H), 7.70 – 7.66 (m, 2H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.31 – 7.25 (m, 3H), 6.74 – 6.72 (m, 1H), 6.11 – 6.10 (m, 2H), 5.04 (s, 1H), 4.61 – 4.57 (m, 1H), 3.11 – 3.08 (m, 1H), 3.03 – 3.00 (m, 1H), 2.91 – 2.87 (m, 1H), 2.17 – 2.10 (m, 1H), 1.96 – 1.86 (m, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 145.6, 144.1, 141.1, 140.1, 133.7, 128.3, 128.1, 127.4, 127.0, 125.6, 124.6, 120.1, 119.9, 117.3, 108.1, 106.4, 64.1, 64.0, 62.2, 60.3, 33.1, 28.3 ppm. **HRMS (ESI):** exact mass calculated for $C_{22}H_{23}N_2O^+$ ($[M+H]^+$): 331.1805, found: 331.1821. **HPLC analysis:** ee = 99.72%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 94:6; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 28.64 min, t_{minor} = 21.96 min).

3-((2*R*,5*R*)-1-(9*H*-fluoren-9-yl)-5-methylpyrrolidin-2-yl)-1*H*-indole (12t): According to general procedure **I:** Indole (0.2 mmol, 1 equiv., 23.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*R*)-2-methylpyrrolidine (0.5 mmol, 2.5 equiv., 42.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:9 ethyl acetate:hexane) to afford **12t** as maroon gum (37 mg, 51% yield). **FTIR** (neat): ῡ = 3427, 3060, 2924, 2854, 1714, 1450, 1264, 736, 703 cm^{-1}. $[\alpha]_D^{25}$ = +147.007 (c = 0.10 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ = 8.05 (d, *J* = 7.2 Hz, 1H), 7.94 (s, 1H), 7.69 – 7.64 (m, 2H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.35 – 7.25 (m, 4H), 7.22 – 7.15 (m, 4H), 5.04 (s, 1H), 4.85 – 4.10 (m, 1H), 2.98 – 2.93 (m,



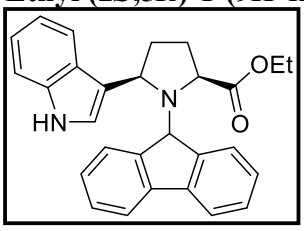
1H), 2.21 – 2.09 (m, 2H), 2.00 – 1.91 (m, 1H), 1.60 – 1.52 (m, 1H), 0.61 (d, *J* = 6.0 Hz, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 147.7, 145.0, 141.3, 139.8, 137.3, 134.9, 127.5, 127.4, 126.9, 126.5, 126.3, 126.1, 122.9, 122.1, 120.8, 119.9, 119.3, 119.2, 119.1, 111.3, 63.4, 62.2, 55.2, 33.0, 31.6, 22.7 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{25}N_2^+$ ([M+H]$^+$): 365.2012, found: 365.2019. **HPLC analysis:** ee = 99.56%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 95:5; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 23.2 min, t_{minor} = 14.3 min).

3-((2*R*,5*S*)-1-(9H-fluoren-9-yl)-5-(methoxymethyl)pyrrolidin-2-yl)-1*H*-indole (12u):



According to general procedure **I:** Indole (0.2 mmol, 1 equiv., 23.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-2-(methoxymethyl)pyrrolidine (0.5 mmol, 2.5 equiv., 57.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:7 ethyl acetate:hexane) to afford **12u** as maroon gum (40 mg, 51% yield). **FTIR** (neat): ῡ = 3416, 3297, 3059, 2926, 1618, 1554, 1449, 1335 1264, 1202, 1093, 1010, 939, 737 cm^{-1}. $[\alpha]_D^{25}$ = +163.510 (c = 0.337 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ = 7.99 (d, *J* = 7.5 Hz, 1H), 7.93 (s, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.63 – 7.59 (m, 2H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.32 – 7.26 (m, 3H), 7.22 – 7.15 (m, 5H), 5.06 (s, 1H), 4.90 – 4.87 (m, 1H), 3.04 – 3.02 (m, 4H), 2.98 – 2.94 (m, 1H), 2.84 – 2.82 (m, 1H), 2.23 – 2.17 (m, 1H), 2.15 – 2.09 (m, 1H), 1.99 – 1.91 (m, 1H), 1.87 – 1.82 (m, 1H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 146.8, 145.3, 141.4, 140.0, 137.3, 127.7, 127.7, 126.9, 126.6, 126.5, 126.2, 125.8, 122.9, 122.1, 120.7, 119.9, 119.5, 119.2, 118.5, 111.4, 77.3, 64.2, 62.4, 58.7, 58.1, 32.2, 28.8 ppm. **HRMS (ESI):** exact mass calculated for $C_{27}H_{26}N_2O^+$ ([M+H]$^+$): 395.2118, found: 395.2110.

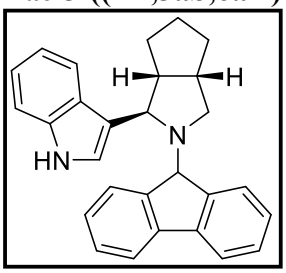
Ethyl (2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(1*H*-indol-3-yl)pyrrolidine-2-carboxylate (12v):



According to general procedure **I:** Indole (0.2 mmol, 1 equiv., 23.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), ethyl L-prolinate (0.5 mmol, 2.5 equiv., 71.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:9 ethyl acetate:hexane) to afford **12v** as pale white solid (50.5 mg, 60% yield, mp:142 – 145 ºC). **FTIR** (neat): ῡ = 3410, 3368, 3061, 2926, 1726, 1450, 13788, 1186, 1119, 1023, 741 cm^{-1}. $[\alpha]_D^{25}$ = -44.778 (c = 0.067 g/100 mL, DCM). **^{1}H**

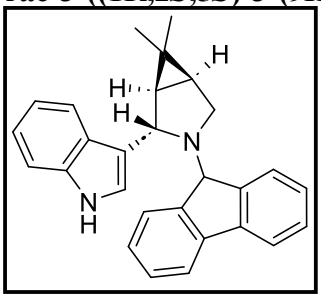
NMR (400 MHz, Chloroform-*d*) δ = 8.43 – 8.41 (m, 1H), 8.05 (s, 1H), 7.73 – 7.71 (m, 1H), 7.68 – 7.66 (m, 1H), 7.60 – 7.58 (m, 1H), 7.45 – 7.43 (m, 2H), 7.39 – 7.36 (m, 1H), 7.36 – 7.33 (m, 1H), 7.28 – 7.21 (m, 4H), 7.17 – 7.13 (m, 1H), 5.06 (s, 1H), 5.00 (dd, *J* = 9.6, 5.2 Hz, 1H), 3.83 – 3.75 (m, 1H), 3.73 – 3.65 (m, 1H), 3.14 (dd, *J* = 9.6, 3.2 Hz, 1H), 2.54 – 2.44 (m, 1H), 2.16 – 2.09 (m, 1H), 2.07 – 1.99 (m, 1H), 1.97 – 1.89 (m, 1H), 1.04 (t, *J* = 7.2 Hz, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 176.3, 145.0, 144.6, 142.1, 140.2, 137.3, 128.1, 127.9, 127.1, 126.9, 126.8, 126.5, 126.0, 123.4, 122.3, 121.3, 120.0, 119.5, 119.4, 117.5, 111.3, 63.5, 62.1, 60.2, 59.3, 33.1, 30.3, 14.1 ppm. **HRMS (ESI):** exact mass calculated for $C_{28}H_{27}N_2O_2^+$ ([M+H]$^+$): 423.2067, found: 423.2061. **HPLC analysis:** ee = 11.7%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 95:5; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 57.72 min, t_{minor} = 52.83 min).

rac-3-((1R,3aS,6aR)-2-(9H-fluoren-9-yl)octahydrocyclopenta[c]pyrrol-1-yl)-1H-indole



(16a): According to general procedure **I:** Indole (0.2 mmol, 1 equiv., 23.4 mg), 9H-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), octahydrocyclopenta[c]pyrrole (0.5 mmol, 2.5 equiv., 55.6 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:10 ethyl acetate:hexane) to afford **16a** as white-pink solid (43 mg, 55% yield, mp 181-184 ºC). **FTIR** (neat): ῡ = 3417, 3057, 2934, 2860, 2802, 1715, 1556, 1449, 1264, 1089, 1009, 801, 735 cm^{-1}. **^{1}H NMR** (500 MHz, Chloroform-d) δ = 8.24 – 8.22 (m, 1H), 7.87 (s, 1H), 7.63 – 7.60 (m, 1H), 7.56 – 7.54 (m, 3H), 7.30 – 7.17 (m, 8H), 4.80 (s, 1H), 3.99 – 3.96 (m, 1H), 2.87 – 2.82 (m, 1H), 2.65 – 2.57 (m, 2H), 1.65 – 1.60 (m, 1H), 1.59 – 1.55 (m, 1H), 1.52 - 146 (m, 2H), 1.40 – 1.34 (m, 2H), 1.23 – 1.19 (m, 1H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 146.6, 144.0, 141.7, 140.1, 137.4, 127.7, 127.6, 127.3, 126.7, 126.5, 126.3, 125.6, 123.1, 122.3, 121.2, 120.0, 119.4, 119.3, 117.1, 111.5, 67.1, 62.5, 52.5, 50.9, 40.5, 31.6, 30.8, 24.8 ppm. **HRMS (ESI):** exact mass calculated for $C_{28}H_{27}N_2^+$ ([M+H]$^+$): 391.2169, found: 391.2172.

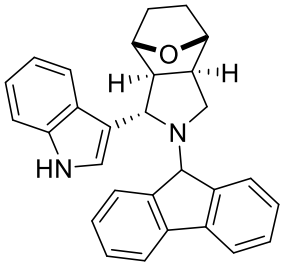
rac-3-((1R,2*S*,5*S*)-3-(9*H*-fluoren-9-yl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexan-2-yl)-1*H*-



indole (16b): According to general procedure **I:** Indole (0.2 mmol, 1 equiv., 23.4 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), 6,6-dimethyl-3-azabicyclo[3.1.0]hexane (0.5 mmol, 2.5 equiv., 55.6 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture is purified in silica column chromatography (1:10 ethyl acetate:hexane) to afford **16b** as maroon gum (31.5 mg, 40%

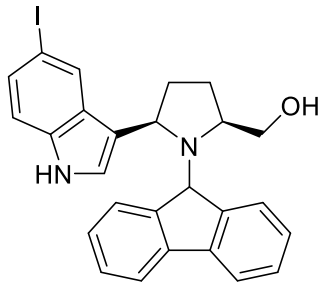
yield). **FTIR** (neat): ῡ = 3418, 3304, 3059, 2952, 2867, 1713, 6151, 1611, 1450, 1364, 1264, 1149, 1121, 1009, 882, 736, 670, 621 cm^{-1}. **^{1}H NMR** (500 MHz, Chloroform-d) δ = 8.01 (d, *J* = 8.0 Hz, 1H), 7.94 (s, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.37 – 3.35 (m, 1H), 7.28 – 7.15 (m, 6H), 7.12 – 7.09 (m, 1H), 7.06 – 7.04 (m, 1H), 4.95 (s, 1H), 4.74 (s, 1H), 2.98 – 2.95 (m, 1H), 2.24 – 2.22 (m, 1H), 1.61 – 1.59 (m, 1H), 1.51 – 1.48 (m, 1H), 1.17 (s, 3H), 0.99 (s, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 146.3, 145.4, 140.9, 139.9, 137.3, 127.5, 127.4, 127.2, 126.9, 126.8, 126.51, 126.48, 125.9, 122.5, 122.1, 120.9, 119.6, 119.4, 119.3, 111.2, 62.3, 57.8, 45.0, 37.1, 29.9, 27.2, 23.0, 14.6 ppm. **HRMS (ESI):** exact mass calculated for $C_{28}H_{27}N_2^+$ ($[M+H]^+$): 391.2169, found 391.2168.

***rac*-(1R,3aR,7aS)-2-(9H-fluoren-9-yl)-1-(1H-indol-3-yl)octahydro-1H-4,7-epoxyisoindole**



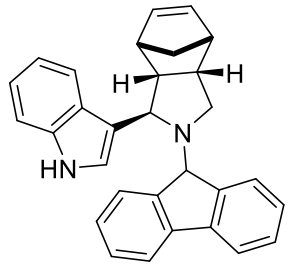
16c: Indole (0.23 mmol, 1 equiv., 27 mg), 9H-fluoren-9-one (0.276 mmol, 1.2 equiv., 50 mg), (3aR,7aS)-octahydro-1H-4,7-epoxyisoindole (0.58 mmol, 2.5 equiv., 80 mg) were dissolved in 0.2 mL of toluene in a microwave tube. Then acetic acid (0.23 mmol, 1 equiv., 14 mg) was added to the mixture, and the tube was sealed. The reaction mixture was then heated for 60 min under microwave irradiation at 120 °C. After completion of the reaction, the solvent was evaporated under reduced pressure. The reaction mixture is purified in silica column chromatography (1:7 ethyl acetate:hexane) to afford **16c** as a pale white solid (82 mg, 85% yield, mp 225.5 – 226.5 °C). **FTIR** (neat): ῡ = 3415, 3306, 3060, 2956, 2817, 1733, 1619, 1556, 1449, 1373, 1240, 1141, 1111, 1044, 988, 807, 737, 674, 621, 606, 587 cm^{-1}. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ = 8.22 - 819 (m, 2H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.52 (d, *J* = 7.2 Hz, 1H), 7.35 – 7.31 (m, 2H), 7.29 – 7.18 (m, 6H), 4.80 (s, 1H), 4.40 (d, *J* = 4.4 Hz, 1H), 4.29 (d, *J* = 7.6 Hz, 1H), 4.07 (d, *J* = 4.4 Hz, 1H), 2.62 – 2.57 (m, 2H), 2.36 – 2.30 (m, 1H), 1.94 – 1.90 (m, 1H), 1.63 – 1.53 (m, 2H), 1.31 – 1.22 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 146.4, 143.7, 141.4, 140.1, 137.4, 127.7, 127.6, 127.2, 126.7, 126.6, 126.5, 125.4, 123.5, 122.4, 121.0, 119.9, 119.4, 119.3, 116.26, 111.6, 79.3, 78.6, 64.2, 62.1, 56.6, 49.7, 46.9, 28.8, 28.4 ppm. **HRMS (ESI):** exact mass calculated for $C_{29}H_{27}N_2O^+$ ($[M+H]^+$): 419.2118, found: 419.2115.

((2S,5R)-1-(9H-fluoren-9-yl)-5-(5-iodo-1H-indol-3-yl)pyrrolidin-2-yl)methanol (12k/):



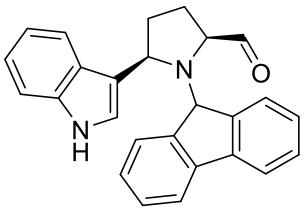
According to general procedure **I:** 5-iodo-1*H*-indole (0.2 mmol, 1 equiv., 49 mg), 9*H*-fluoren-9-one (0.24 mmol, 1.2 equiv., 43 mg), (*S*)-pyrrolidin-2-ylmethanol (0.5 mmol, 2.5 equiv., 50.5 mg) were reacted in presence of acetic acid (0.2 mmol, 1 equiv., 12 mg). The reaction mixture was purified in silica column chromatography (1:3 ethyl acetate:hexane) to afford **12@** as maroon gummy (60.5 mg, 60% yield). **FTIR:** ʊ̃ = 3414, 3287, 3069, 2934, 2882, 1718, 1615, 1449, 1301, 1208, 1096, 1023, 881, 796, 742 cm^{-1}. $[\alpha]_D^{25}$ = +162.97 (c = 0.27 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ = 8.13 – 8.12 (m, 2H), 7.63 – 7.59 (m, 3H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 8.6 Hz, 1H), 7.35 – 7.32 (m, 1H), 7.28 – 7.24 (m, 2H), 7.18 – 7.15 (m, 2H), 7.08 (d, *J* = 8.5 Hz, 1H), 5.03 (s, 1H), 4.81 – 4.78 (m, 1H), 3.12 (m, 1H), 3.05 – 3.03 (m, 1H), 2.92 – 2.89 (m, 1H), 2.16 – 2.13 (m, 1H), 2.10 – 2.06 (m, 1H), 2.01 – 1.94 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 145.7, 144.1, 141.0, 140.1, 135.9, 130.4, 129.0, 128.8, 128.2, 127.8, 127.5, 126.7, 125.7, 124.7, 123.2, 119.9, 119.9, 117.6, 113.3, 82.9, 64.0, 63.5, 61.7, 60.2, 32.8, 28.2 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{24}IN_2O^+$ ($[M+H]^+$): 507.0928, found: 507.0917. **HPLC analysis:** ee = 99.5%; phenomenex lux 5u cellulose-1 column; hexane: *i*PrOH = 90:10; flow rate 1.0 mL/min; λ = 254 nm; (t_{major} = 46.13 min, t_{minor} = 35.3 min).

***rac*-(1R,3aS,4R,7S,7aR)-2-(9H-fluoren-9-yl)-1-(1H-indol-3-yl)-2,3,3a,4,7,7a-hexahydro-1H-4,7-methanoisoindole (16d):** Indole (0.18 mmol, 1 equiv., 21 mg), 9H-fluoren-9-one (0.22 mmol, 1.2 equiv., 40 mg), *rac*-(3aR,4S,7R,7aS)-2,3,3a,4,7,7a-hexahydro-1H-4,7-methanoisoindole (0.45 mmol, 2.5 equiv., 61 mg) were dissolved in 0.2 mL of n-butyl alcohol in a microwave tube. Then acetic acid (0.22 mmol, 1 equiv., 11 mg) was added to the mixture, and the tube was sealed. The reaction mixture was then heated for 60 min under microwave irradiation at 120 ºC. After the reaction was completed, the solvent was evaporated under reduced pressure. The reaction mixture is purified in silica column chromatography (1:12 ethyl acetate:hexane) to afford **16d** as a colourless gummy compound (52 mg, 70% yield). **FTIR** (neat): ʊ̃ = 3421, 3285, 3061, 2961, 2929, 2848, 1626, 1451, 1341, 1090, 908, 799, 738 cm^{-1}. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ = 8.11 – 8.08 (m, 1H), 8.01 (s, 1H), 7.65 – 7.63 (m, 2H), 7.59 – 7.57 (m, 1H), 7.49 – 7.47 (m, 1H), 7.37 – 7.35 (m, 1H), 7.33 – 7.28 (m, 2H), 7.26 – 7.19 (m, 5H), 6.41 – 6.39 (m, 1H), 5.98 – 5.96 (m, 1H), 4.83 (s,



1H), 4.50 (d, *J* = 7.2 Hz, 1H), 3.20 – 3.15 (m, 1H), 3.02 – 2.94 (m, 1H), 2.85 – 2.83 (m, 1H), 2.66 – 2.64 (m, 1H), 2.47 – 2.43 (m, 1H), 1.95 – 1.90 (m, 1H), 1.66 – 1.63 (m, 1H), 1.52 – 1.49 (m, 1H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 146.5, 145.0, 141.6, 140.0, 138.6, 137.8, 137.3, 127.6, 127.6, 127.2, 126.8, 126.7, 126.3, 125.5, 122.6, 122.2, 120.8, 119.9, 119.4, 119.2, 118.1, 111.5, 63.1, 62.0, 55.7, 53.6, 48.4, 45.3, 45.0, 44.3 ppm. **HRMS (ESI):** exact mass calculated for $C_{30}H_{27}N_2^+$ ([M+H]$^+$): 415.2169, found: 415.2168.

(2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(1*H*-indol-3-yl)pyrrolidine-2-carbaldehyde (**19**): To an



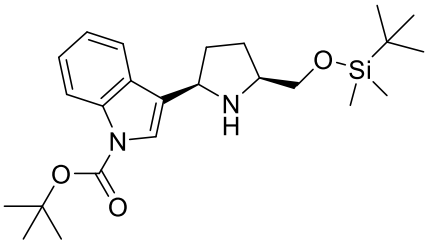
oven-dried round-bottom flask under an argon atmosphere, 2 mL of dry DCM was added and cooled to -78 °C. Next, 0.77 mmol (2.8 equivalents, 66 µL) of oxalyl chloride was introduced, followed by the addition of 1.33 mmol (4.8 equivalents, 94 µL) of dry DMSO. After 15 minutes, a solution of (2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(1*H*-indol-3-yl)pyrrolidin-2-yl (**12a**) (0.276 mmol, 1 equiv., 105 mg) in 1 mL of dry DCM was carefully added using a syringe. After 60 minutes, 1.33 mmol (4.5 equivalents, 184 µL) of dry triethylamine was introduced, and the mixture was stirred at -78 °C for an additional 60 minutes. The reaction mixture was then gradually brought to room temperature and quenched by adding 1 mL of water. Subsequently, the mixture was extracted with DCM, dried over sodium sulfate (Na_2SO_4), and purified through column chromatography using a hexane:ethyl acetate mixture (7:1) on neutral alumina gave the product **19** as a maroon gummy (73 mg, 70%). **FTIR** (neat): ῡ = 3062, 2930, 2830, 2710, 1730, 1454, 1327, 1218, 1045, 800, 735, 638 cm^{-1} $[\alpha]_D^{25}$ = +158.01 (c = 0.20 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ = 9.17 (d, *J* = 3.5 Hz, 1H), 8.09 (s, 1H), 7.99 (d, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.38 (s, 1H), 7.35 (d, *J* = 8 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.23 (m, 1H), 7.22 – 7.20 (m, 1H), 7.20 – 7.18 (m, 1H), 7.17 – 7.16 (m, 1H), 7.14 – 7.13 (m, 1H), 5.01 (s, 1H), 4.99 – 4.96 (m, 1H), 2.83 – 2.79 (m, 1H), 2.16 – 2.10 (m, 2H), 1.92 – 1.87 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 202.9, 145.3, 143.5, 142.0, 140.4, 137.4, 128.67, 128.46, 127.34, 127.08, 126.37, 126.31, 126.04, 123.1, 122.5, 120.4, 120.32, 119.79, 119.65, 117.00, 111.7, 65.4, 63.1, 62.3, 33.00, 26.6 ppm. **HRMS (ESI):** exact mass calculated for $C_{26}H_{23}N_2O^+$ ([M + H]$^+$): 379.1805, found: 379.1807.

***tert*-butyl 3-((2*R*,5*S*)-1-(9*H*-fluoren-9-yl)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indole-1-carboxylate (S1)**: ((2*S*,5*R*)-1-(9*H*-fluoren-9-yl)-5-(1*H*-indol-3-yl)pyrrolidin-2-yl) (**12a**, 0.389 mmol, 1 equiv., 148 mg) dissolved in acetonitrile (1.5 mL, HPLC grade) then Di-*tert*-butyl dicarbonate (0.43 mmol, 1.1 equiv., 94 mg) and 4-(dimethylamino)pyridine (0.05 mmol, 0.13 equiv., 6 mg) were added to the solution. The reaction mixture was heated to 50 °C for 1 hour. After removing the solvent the crude was purified in flash chromatography (hexane:ethyl acetate, 10:1) to give **S1** as yellow-brown gummy (150 mg, 80%). **FTIR** (neat): ῡ = 3381, 3064, 2928, 2872, 1731, 1475, 1450, 1369, 1308, 1254, 1089, 1029, 855, 742 cm^{-1}. $[\alpha]_D^{25}$ = +165.34 (c = 0.075 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ = 8.15 – 8.13 (m, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.64 – 7.60 (m, 4H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.35 – 7.27 (m, 4H), 7.25 – 7.23 (m, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 5.10 (s, 1H), 4.84 – 4.80 (m, 1H), 3.11 – 3.04 (m, 2H), 2.89 – 8.87 (m, 1H), 2.22 – 2.15 (m, 2H), 2.13 – 2.11 (m, 1H), 2.04 – 1.97 (m, 2H), 1.68 (s, 9H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 149.7, 145.8, 144.0, 141.2, 140.2, 136.5, 129.2, 128.3, 128.1, 127.6, 126.8, 125.8, 124.9, 124.6, 124.08, 122.52, 122.42, 120.37, 120.09, 119.98, 115.65, 83.69, 64.01, 63.71, 62.19, 60.4, 31.7, 28.4, 28.2 ppm. **HRMS (ESI):** exact mass calculated for $C_{31}H_{33}N_2O_3^+$ ($[M+H]^+$): 481.2486, found: 481.2486.

***tert*-butyl 3-((2*R*,5*S*)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indole-1-carboxylate (20)**: In a 25 mL round-bottom flask, *tert*-butyl 3-((2*R*,5*S*)-1-(9*H*-fluoren-9-yl)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indole-1-carboxylate (**S1**, 0.27 mmol, 130 mg, 1 equiv.) was dissolved in a mixture of methanol and ethyl acetate (HPLC grade, 4 mL, 3:1 v/v). Palladium on charcoal (10%, 0.054 mmol, 57 mg, 0.2 equiv.) was then added to the solution. The round-bottom flask was connected to a hydrogen balloon, and the air was purged out, followed by refilling it with hydrogen. This purging and refilling process was repeated three times. The reaction mixture was stirred at room temperature, and after 24 hours, the crude product was filtered through Celite and concentrated under vacuum. The product was then purified using preparative thin layer chromatography (TLC) with 100% ethyl acetate solvent system to afford the product (**20)** as a colourless gummy substance (54 mg, 63%). **FTIR** (neat): ῡ = 3334, 2925, 2854, 1731, 1699, 1601, 1485, 1453, 1390, 1367, 1253, 1143, 1088, 1042, 1016, 855, 747 cm^{-1}. $[\alpha]_D^{25}$ = +30.00 (c = 0.10 g/100 mL, DCM). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ = 8.12 – 8.10 (m, 1H), 7.92 (s, 1H), 7.83 (d, *J* =

7.8 Hz, 1H), 7.31 – 7.29 (m, 1H), 7.24 – 7.22 (m, 1H), 4.82 – 4.79 (m, 1H), 3.78 (s, 1H), 3.58 – 3.50 (m, 2H), 2.38 – 2.35 (m, 2H), 2.09 – 2.06 (m, 2H), 1.65 (s, 9H) ppm. **^{13}C NMR** (151 MHz, Chloroform-*d*) δ = 149.4, 135.6, 128.5, 125.3, 125.2, 123.2, 119.5, 115.6, 114.5, 84.7, 61.9, 60.4, 56.0, 30.7, 28.3, 26.1 ppm. **HRMS** (**ESI):** exact mass calculated for $C_{18}H_{25}N_2O_3^+$ ($[M+H]^+$): 317.1860, found: 317.1856.

***tert*-butyl 3-((2*R*,5*S*)-5-(((tert-butyldimethylsilyl)oxy)methyl)pyrrolidin-2-yl)-1*H*-indole-1-carboxylate** (**21**): In an inert atmosphere, a mixture of *tert*-butyl 3-((2*R*,5*S*)-5-(hydroxymethyl)pyrrolidin-2-yl)-1*H*-indole-1-carboxylate **20** (0.079 mmol, 25 mg), imidazole (0.316 mmol, 21.49 mg, 4 equiv.) and 4-(dimethylamino)pyridine (DMAP, 1 mg, 0.008 mmol 0.1 equiv.) was prepared in dry dichloromethane (DCM, 0.5 mL). The mixture was then cooled to 0 °C. Next, a solution of *tert*-butyldimethylsilyl chloride (0.17 mmol, 2.1 equiv., 25 mg) in dry DCM (0.5 mL) was prepared in a round-bottom flask in inert atmosphere and this solution was then added slowly to the above reaction mixture through syringe. The mixture was allowed to return to room temperature and stirred for several hours, monitored by thin-layer chromatography (TLC). After completion of the reaction (4 h) the DCM was removed. The crude product was purified using silica column chromatography (hexane:ethyl acetate, 7:1) to afford **21** as colourless gummy (27.5 mg, 81%). **FTIR** (neat): ῡ = 2955, 2924, 2855, 1736, 1455, 1375, 1254, 1158, 1083, 838, 768,747 cm^{-1}. $[\alpha]_D^{25}$ = -18.00 (c = 0.16 g/100 mL, DCM). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ = 8.15 – 8.13 (m, 1H), 7.67 – 7.64 (m, 1H), 7.5 (s, 1H), 7.32 – 7.28 (m, 1H), 7.24 – 7.19 (m, 1H), 4.40 – 4.36 (m, 1H), 3.76 – 3.64 (m, 2H), 3.40 – 3.34 (m, 1H), 2.27 – 2.19 (m, 1H), 2.00 – 1.98 (m, 1H), 1.94 – 1.89 (m, 1H), 1.86 – 1.79 (m, 1H), 1.77 – 1.71 (m, 1H), 1.66 (s, 9H), 0.90 (s, 9H), 0.09 – 0.07 (m, 6H) ppm. **^{13}C NMR** (126 MHz, Chloroform-*d*) δ = 150.0, 136.2, 129.6, 124.4, 124.1, 122.4, 122.0, 119.9, 115.5, 83.5, 66.5, 60.4, 55.6, 32.4, 28.4, 27.9, 26.1, 18.5, -5.1 ppm. (overlap at -5.1 ppm leading to 1 carbon less in count). **HRMS** (**ESI):** exact mass calculated for $C_{24}H_{39}N_2O_3Si^+$ ($[M+H]^+$): 431.2724, found: 431.2734.

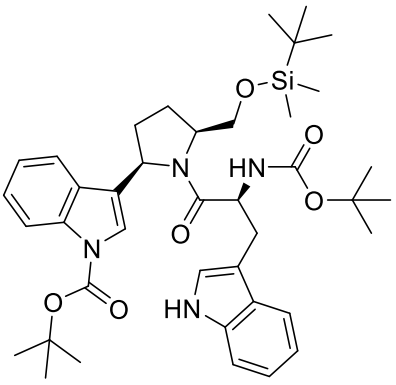


***tert*-butyl 3-((2*R*,5*S*)-1-((3,5-bis(trifluoromethyl)phenyl)carbamothioyl)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)pyrrolidin-2-yl)-1*H*-indole-1-carboxylate** (**22**): In a round-bottom flask *tert*-butyl 3-((2*R*,5*S*)-5-(((tert-butyldimethylsilyl)oxy)methyl)pyrrolidin-2-yl)-1*H*-indole-1-carboxylate (**21**, 0.023 mmol, 1 equiv., 10 mg) was dissolved in dry THF (2 mL) and 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.025 mmol, 1.1 equiv., 6.92 mg) added. The reaction mixture was then stirred overnight. After removing the solvent, the crude was purified in silica column chromatography (hexane:ethyl acetate, 25:1) to get **22** as colourless gummy (14.5 mg, 90%). **FTIR** (neat): ῡ = 3248, 3113, 2932, 2860, 1732, 1587, 1472, 1452, 1360, 1275, 1169, 1130, 1071, 1022, 1001, 882, 831, 784, 741, 681 cm^{-1}. $[\alpha]_D^{25}$ = -27.00 (c = 0.10 g/100 mL, DCM). **^{1}H NMR** (500 MHz, Chloroform-d) δ = 9.78 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.01 (s, 2H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.61 (s, 1H), 7.44 (s, 1H), 7.34 – 7.31 (m, 1H), 7.24 – 7.22 (m, 1H), 6.36 (s, 1H), 4.52 (s, 1H), 3.88 – 3.85 (m, 1H), 3.80 – 3.76 (m, 1H), 2.50 – 2.43 (m, 1H), 2.34 – 2.20 (m, 2H), 1.90 – 1.85 (m, 1H), 1.67 (s, 9H), 0.87 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ = 182.71, 149.83, 141.58, 136.04, 131.72 (132.12, 131.85, 131.59, 131.32, q, *J* = 33.4 Hz), 128.86, 124.88, 124.70, 124.67, 124.45, 122.28, 122.90, 122.02, 121.95, 120.01, 118.30, 118.27, 118.23, 118.20, 115.61, 84.10, 68.50, 64.83, 60.07, 30.68, 28.38, 28.32, 25.98, 18.70, -5.03, -5.45. (Other coupling F-C patterns could not be determined unambiguously due to overlapping signals) **HRMS (ESI):** exact mass calculated for $C_{33}H_{42}F_6N_3O_3SSi^+$ ($[M+H]^+$): 702.2615, found: 702.2599.

***tert*-butyl 3-((2*R*,5*S*)-1-((*tert*-butoxycarbonyl)-L-prolyl)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)pyrrolidin-2-yl)-1*H*-indole-1-carboxylate** (**23**): In a round-bottom flask, N-(tert-butoxycarbonyl)-L-proline (0.031 mmol, 1.2 equiv., 6.7 mg) was dissolved in dry DCM (0.5 mL) and cooled to 0 °C. In another round-bottom flask, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl, 0.0286 mmol, 1.1 equiv., 5.5 mg) and 1-Hydroxybenzotriazole ($HOBt.H_2O$, 0.026 mmol, 1 equiv., 3.5 mg) were dissolved in dry DCM (0.5 mL) and also cooled to 0 °C. This mixture was then added to the first round-bottom flask using a syringe and stirred for 15 minutes at 0 °C. In a

third round-bottom flask, dry DCM (0.5 mL) was added along with *tert*-butyl 3-((2R,5S)-5-(((tert-butyldimethylsilyl)oxy)methyl)pyrrolidin-2-yl)-1H-indole-1-carboxylate (**21**, 0.026 mmol, 1 equiv., 11 mg) and N,N-diisopropyl ethylamine (0.069 mmol, 2.8 equiv., 12.1 µL), which were cooled to 0 °C. This mixture was then added to the first round-bottom flask using a syringe. The resulting mixture was gradually warmed back to 30 °C and stirred for an additional 15 hours. After this period, the mixture was concentrated under vacuum, and the product, **23** (colourless gummy substance, 13 mg, 80.3% yield) was purified by flash chromatography (silica, hexane:ethyl acetate, 6:1). The final product, **23**, was obtained as 1:1 inseparable rotational isomers. **FTIR** (neat): ŭ = 2955, 2930, 2857, 1733, 1689, 1657, 1452, 1392, 1368, 1308, 1249, 1153, 1115, 1076, 1020, 1005, 836, 767, 745 cm^{-1}. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ = 8.14 – 8.11 (m, 1H), 7.63 – 7.52 (m, 1H), 7.44 – 7.23 (m, 3H), 5.72 – 5.38 (m, 1H), 4.33 – 4.28 (m, 1H), 4.25 – 4.17 (m, 1H), 4.11 – 4.05 (m, 1H), 3.86 – 3.76 (m, 1H), 3.56 – 3.29 (m, 2H), 2.49 – 2.29 (m, 1H), 2.17 – 1.92 (m, 4H), 1.81 – 1.73 (m, 1H), 1.67 – 1.63 (m, 9H), 1.59 – 1.56 (m, 1H), 1.49 1.42 (m, 9H), 1.27 – 1.25 (m, 1H), 0.90 – 0.87 (m, 9H), 0.10 – 0.04 (m, 6H) ppm. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ = 175.0, 174.7, 155.0, 153.7, 149.74, 149.65, 136.0, 128.38, 128.19, 125.0, 124.8, 124.2, 123.4, 123.3, 122.9, 122.7, 119.6, 118.9, 115.8, 115.5, 84.23, 83.95, 79.4, 64.05, 63.98, 60.4, 60.1, 57.4, 57.3, 56.2, 56.0, 47.47, 47.37, 33.1, 32.8, 32.3, 31.1, 28.87, 28.66, 28.45, 28.35, 26.71, 26.67, 26.10, 26.09, 24.7, 23.7, 18.51, 18.47, -5.1, -5.2 ppm. **HRMS** (**ESI):** exact mass calculated for $C_{34}H_{54}N_3O_6Si^+$ ([M+H]$^+$): 628.3776, found: 628.3748.

***tert*-butyl 3-((2R,5S)-1-((tert-butoxycarbonyl)-L-prolyl)-5-(((tert-butyldimethylsilyl)oxy)methyl)pyrrolidin-2-yl)-1H-indole-1-carboxylate(24):**



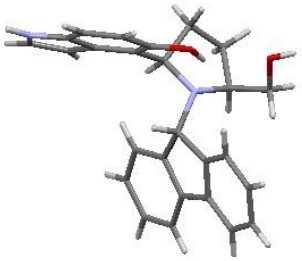
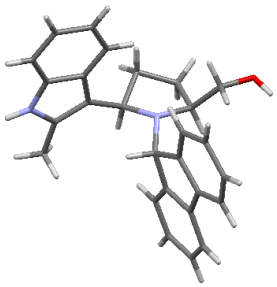
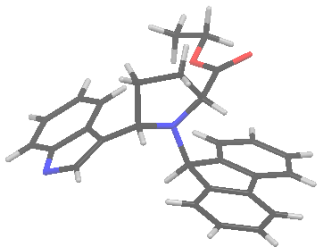
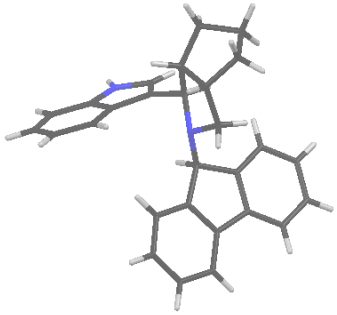
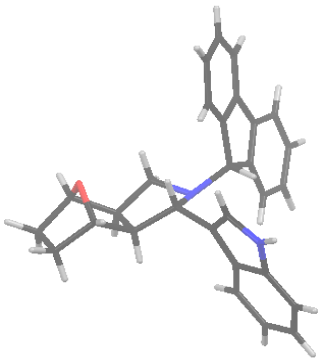
In a round-bottom flask, N- (tert-Butoxycarbonyl)-L-tryptophan (0.049 mmol, 1.2 equiv., 15 mg) was dissolved in dry DCM (0.5 mL) and cooled to 0 °C. In another round-bottom flask, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl, 0.045 mmol, 1.1 equiv., 8.6 mg) and 1-hydroxybenzotriazole (HOBt. H_2O, 0.041 mmol, 1.1 equiv., 6.2 mg) were dissolved in dry DCM (0.5 mL) and also cooled to 0 °C. This mixture was then added to the first round-bottom flask using a syringe and stirred for 15 minutes at 0 °C. In a third round-bottom flask, dry DCM (0.5 mL) was added along with *tert*-butyl 3-((2R,5S)-5-

(((tert-butyldimethylsilyl)oxy)methyl)pyrrolidin-2-yl)-1H-indole-1-carboxylate **21** (0.041 mmol, 1 equiv., 18 mg) and N,N-diisopropyl ethylamine (0.135 mmol, 3.3 equiv., 23.5 µL), which were cooled to 0 °C. This mixture was then added to the first round-bottom flask using a syringe. The resulting mixture was gradually warmed back to 30 °C and stirred for an additional 15 hours. After this period, the mixture was concentrated under vacuum, and the product, **24** (colourless gummy substance, 17 mg, 58% yield) was purified by flash chromatography (silica, hexane:ethyl acetate, 6:1). The final product, **24**, was obtained as 4.2:4.2:1.6 inseparable rotational isomers. **FTIR: ŭ** = 3312, 2928, 2856, 1733, 1709, 1634, 1451, 1368, 1308, 1250, 1224, 1155, 1077, 1018, 908, 836, 766, 737, 669 cm^{-1}. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ = 8.22 – 7.90 (m, 2H), 7.74 – 7.62 (m, 1H), 7.51 – 7.27 (m, 3H), 7.25 – 7.12 (m, 3H), 7.02 – 6.77 (m, 1H), 6.67 – 6.33 (m, 1H), 5.76 – 5.36 (m, 1H), 5.07 – 4.98 (m, 1H), 4.88 – 4.53 (m, 1H), 4.26 – 4.16 (m, 1H), 3.84 – 3.64 (m, 1H), 3.35 – 3.13 (m, 2H), 2.98 – 2.85 (m, 1H), 2.32 – 2.08 (m, 2H), 1.99 – 1.79 (m, 1H), 1.63 – 1.58 (m, 9H), 1.46 – 1.32 m, 9H), 0.91 (s, 5H), 0.81 – 0.77 (m, 4H), 0.12 – 0.11 (m, 3H), 0.01 – -0.03 (m, 3H). **^{13}C NMR** (126 MHz, Chloroform-*d*) δ 174.4, 172.2, 155.5, 155.2, 149.9, 149.8, 136.4, 136.1, 136.0, 129.1, 128.5, 127.8, 127.5, 125.0, 124.4, 123.6, 123.2, 123.1, 123.0, 122.7, 122.6, 122.5, 122.0, 121.3, 120.0, 119.7, 119.6, 119.4, 118.6, 115.7, 115.5, 111.5, 111.2, 111.1, 111.0, 84.1, 83.6, 79.6, 79.6, 64.8, 64.5, 60.5, 59.4, 56.3, 54.6, 53.7, 52.5, 32.8, 30.8, 30.5, 29.9, 29.3, 28.6, 28.5, 28.41, 28.38, 27.7, 27.2, 26.7, 26.21, 26.17, 18.6, 18.5, 14.43, 14.37, 1.3, 0.2, -4.96, -5.04, -5.11, -5.4. **HRMS (ESI):** exact mass calculated for $C_{34}H_{54}N_3O_6Si^+$ ($[M+H]^+$): 717.4042, found: 717.4008.

Gram Scale Reaction:

In a 125 mL pressure tube indole (17.09 mmol, 1 equiv., 2.0 G), 40 mL toluene, (S)-prolinol (42.73 mmol, 2.5 equiv., 4.315 G), 9H-fluoren-9-one (20.5 mmol,1.2 equiv., 3.690 G) and acetic acid (17.09 mmol,1 equiv., 1.025 G) were taken in the sequence. Then the mixture was heated to 150 ºC for 40 h. Toluene was then evaporated in rotary evaporator and the crude was then directly injected in silica column for purification to afford **12a** as white-yellow foam (3.27 G, 50.4% yield).

Crystallographic data

12e'	
12g	
12v	
16a	
16c	

Crystallographic data and refinement parameters.

Entry	**12e'**	**12g**	**12v**	**16a**	**16c**
Formula	$C_{26}H_{24}N_2O_2$	$C_{27}H_{26}N_2O$	$C_{28}H_{26}N_2O_2$	$C_{28}H_{26}N_2$	$C_{58}H_{52}N_4O_2$
CCDC No.	2420329	2420321	2420325	2420327	2503126
Mol. wt.	396.47	394.5	422.51	390.51	837.03
Cryst.color, habit	colourless	yellow	colourless	colourless	Pale yellow
T, K	298	295	299	295	297
Cryst. syst.	monoclinic	Tetragonal	monoclinic	monoclinic	triclinic
Space group	$P2_1$	$P4_3$	$P2_1/c$	$P2_1/n$	*P-1*
a, Å	12.203(3)	13.5803(14)	9.1088(3)	10.2031(11)	11.2946(13)
b, Å	7.0304(14)	13.5803(14)	10.6818(4)	18.048(2)	13.8524(16)
c, Å	12.614(3)	11.6172(17)	23.1277(9)	12.5014(14)	15.5340(18)
α ,deg	90	90	90	90	71.090(3)
β, deg	103.755(7)	90	95.5270(10)	109.100(3)	78.320(4)
γ ,deg	90	90	90	90	79.922(4)
V, Å^3	1051.1(4)	2142.5(5)	2239.83(14)	2175.3(4)	2235.9(5)
Z	2	4	4	4	2
*D*calcd, g cm^{-3}	1.253	1.223	1.253	1.192	1.243
μ, mm^{-1}	0.080	0.074	0.079	0.069	0.075
GOF[a] on F^2	1.141	1.093	1.095	1.096	1.260
F(000)	420.0	840.0	896.0	832.0	888.0
Reflection collected	27945	50204	49815	49012	52455
Unique reflections	4616	3730	3919	3846	7778
R_1[b], wR_2[c] ($I \geq 2\sigma(I)$)	0.0508, 0.1203	0.0498, 0.1358	0.0395, 0.0918	0.0634, 0.1543	0.0664, 0.0647
R_1[b], wR_2[c] (all data)	0.0547, 0.1227	0.0574, 0.1467	0.0489, 0.1016	0.0834,0.1709	0.1706, 0.1993

[a]GOF (Goodness-of-fit) = $[\sum[w(F_0^2 - F_c^2)^2] / M - N]^{1/2}$ (M =number of reflections, N = number of parameters refined). [b] $R_1 = \sum \| F_0| - |Fc \| / \sum |F_0|$. [c]$wR_2 = [\sum[w(F_0^2 - F_c^2)^2] / \sum[w(F_0^2)^2]]$.

Materials and Methods for biological studies:

Bacterial Strains

All the molecules synthesized were primarily screened by following Clinical and Laboratory Standard Institute (CLSI) guidelines against *E. coli* ATCC 25922, *S. aureus* ATCC 29213, *K. pneumoniae* BAA 1705, *A. baumannii* BAA 1605, *P. aeruginosa* ATCC 27853 and *Enterococcus* spp., collectively known as ESKAPE pathogens. The panel includes the type strains as well the drug-resistant clinical strains of *S. aureus* and *Enterococcus* spp. including methicillin-resistant *S. aureus* (MRSA) and vancomycin resistant *S. aureus* (VRSA) and other MDR bacterial isolates. These strains were procured from the Biodefense and Emerging Infections Research Resources Repository/Network on Antimicrobial Resistance in *Staphylococcus aureus*/American Type Culture Collection (BEI/NARSA/ATCC, U.S.A.) and routinely cultivated on MHA and MHBII. To obtain the starter culture, a single colony was picked from the culture-streaked MHA plate, inoculated in MHBII, and incubated overnight at 37°C with shaking at 180 rpm for 18–24 h.

Growth Media and Reagents

All bacterial media and supplements, including cation-supplemented Mueller–Hinton broth II (MHBII), Mueller–Hinton agar (MHA), and tryptic soy broth (TSB) were purchased from Becton-Dickinson (Franklin Lakes, NJ, U.S.A.). All other chemicals and antibiotics were procured from Sigma-Aldrich (St. Louis, MO, U.S.A.). While performing the experiments, all the relevant guidelines and regulations were followed.

Antibiotic Susceptibility Testing

CLSI guidelines for microdilution assay were followed to conduct the preliminary antibiotic susceptibility testing (4). 10 mg/mL stock solutions of tested compounds were prepared in dimethyl sulfoxide (DMSO)/water as per their solubility. MHBII was used growth medium to inoculate the bacterial culture and optical density (O.D.) was measured at 600 nm. This was followed by diluting the culture to obtain the culture with $\sim 10^5$ colony-forming units (CFU)/mL. The compounds were screened for their antibacterial activity with concentrations ranging from 64 to 0.5 µg/mL, in a 2-fold serial dilution manner. To achieve this concentration, 2.5 µL of compound of desired concentration was added to the wells of 96-well round-bottomed microtiter plate. Later, 97.5 µL of bacterial suspension was added to each well containing either the test compound or appropriate control. The plates were incubated at 37 °C for 18–24 h, and minimum inhibitory concentration (MIC) was determined as the lowest concentration of the test compounds at which no visible bacterial growth was observed. MIC determination for each test compound was carried out independently three times using duplicate samples.

Cytotoxicity against Vero Cells (ATCC CCL-81)

The cytotoxicity of all compounds was assessed against eukaryotic Vero cells via MTT assay (5). Here, 10^4 cells in RPMI, supplemented with 10% FBS, were seeded in each well of 96 flat bottom plate. The plates were incubated at 37^0C and 5% CO_2. After 24 h incubation, the test compounds, or the control drug, prepared in RPMI+10 FBS, were added to the wells at desired concentrations, in triplicates. Plates were then incubated at 37^0C CO_2 for 72hr.

After incubation, 20µL of MTT at 5mg/mL concentration was added to each well of 96 well flat bottom plate. Plates were further incubated for 4h at 37^0C. Purple coloured formazan crystals are formed on reduction of MTT by live cells. The well components were then discarded and formed formazon crystals were dissolved in 100µLDMSO. Absorbance was recorded at 575nm using a plate reader. CC_{50} was determined as the concentration of compound at which 50% of the cell proliferation is inhibited. Selectivity index was calculated by the formula: CC_{50}/MIC. Doxorubicin was used as a positive control, and each experiment was repeated in triplicate.

12j Drug interaction study

Drug interaction study was conducted to analyse the interaction of 12j with standard approved drugs (6). The analysis was carried out chequerboard method where one the test compound was added along the abscissa whereas the antibiotic of the combination was added along the ordinate of the 96-well microtiter plate, in a serially diluted manner. Bacterial culture of ~10^5 CFU/mL were then added to the plates. These microtiter plates were then incubated at 37°C for 18-24hr. FICI (Fractional Inhibitory Concentration Index) was calculated as: FICI=FICA+FICB where, FICA= MIC of drug A in combination/MIC of drug A alone, FICB= MIC of drug B in combination/MIC of drug B alone. The combination is considered synergistic when ∑FICI is ≤0.5, indifferent when ∑FICI is >0.5 to 4, and antagonistic when ∑FICI is >4.

Time-kill kinetics assay

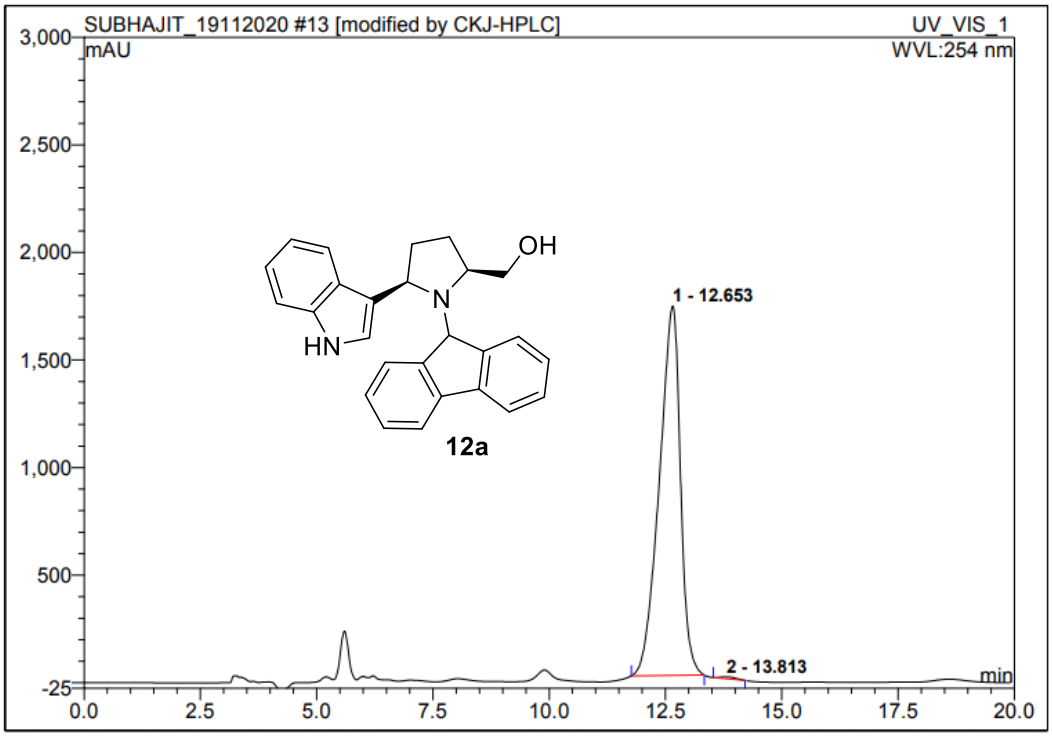
The experiment was conducted to evaluate the concentration and time dependent anti-bacterial activity of the compound (7). For the same, antibacterial effect of 1x and 10x MIC concentration of 12jwas studied at 0, 1, 6 and 24^{th} hr. Vancomycin at same concentrations was taken as the control drug. The compound treated tubes were inoculated with the bacterial load of ~5.9 Log_{10} CFU/ml and bacterial CFU/mL was plated at each time points. This experiment was repeated thrice in duplicate and the mean values were plotted on graph.

Induction of resistance in *S. aureus* ATCC 29213 against 12j

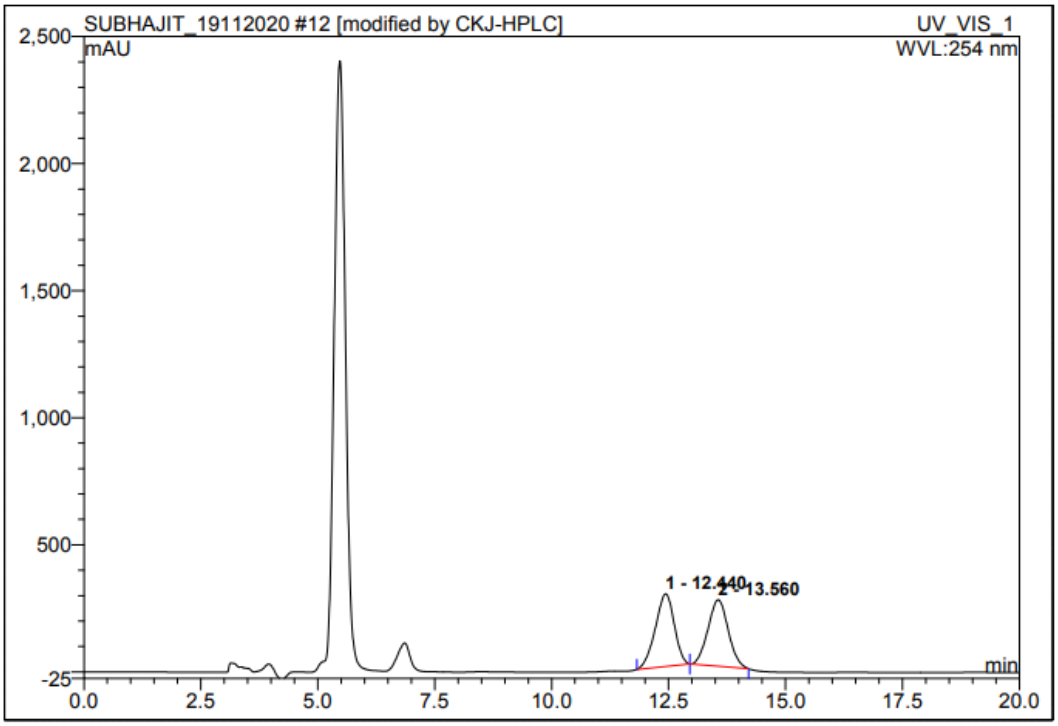
S. aureus ATCC 2913 culture of ~10^5 CFU/mL was treated with either **12j** or the control drug levofloxacin at sub-inhibitory concentrations (i.e. 1/2x MIC) (8). The culture was then allowed to grow in 37°C shaking incubator at 180 rpm for 24hr. After incubation, the culture is further passaged in fresh tubes containing the compound/control at sub-inhibitory concentrations. MIC of the compound/drug is monitored regularly and concentration to be added is changed accordingly. The change in MIC of compound/control against the passaged culture was monitored for 36 days to check for the induction of mutation, if possible, in the bacteria, grown continuously in the presence of antibacterial agents.

Statistical Analysis

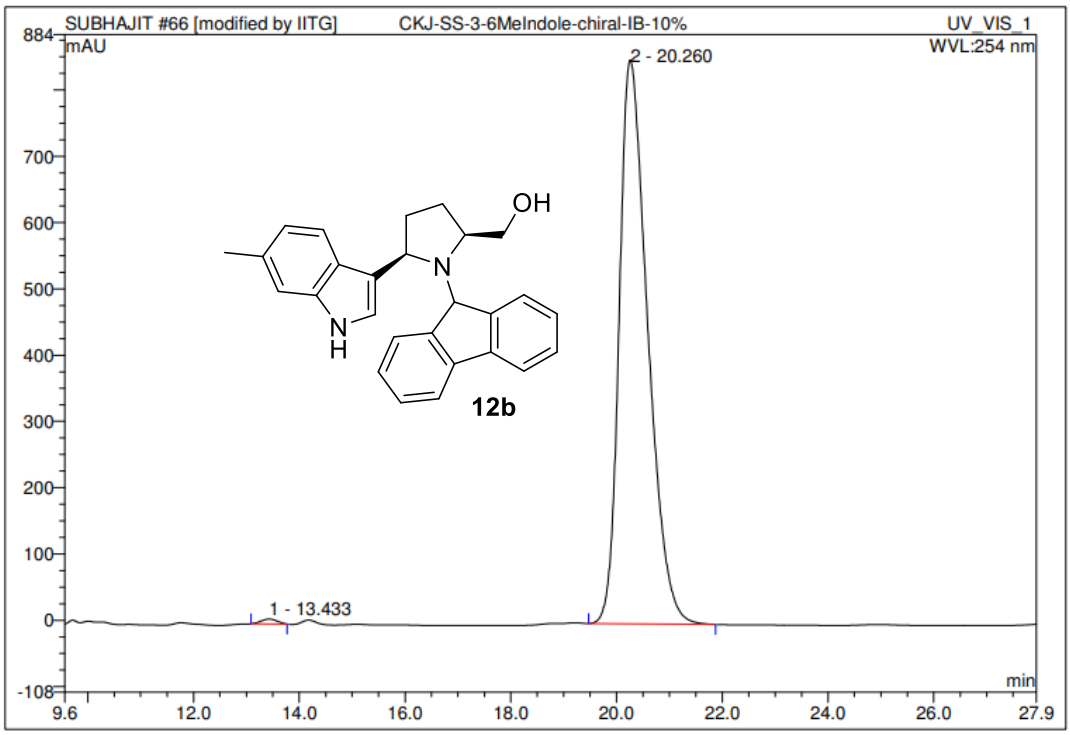
Statistical analysis was performed using GraphPad Prism 8.0.2 software (GraphPad Software, La Jolla, CA, U.S.A.). Comparison between three or more groups was analysed using a one-way analysis of variance with Dunnett's multiple comparison test. *P*-values < 0.0001 were considered to indicate significance.



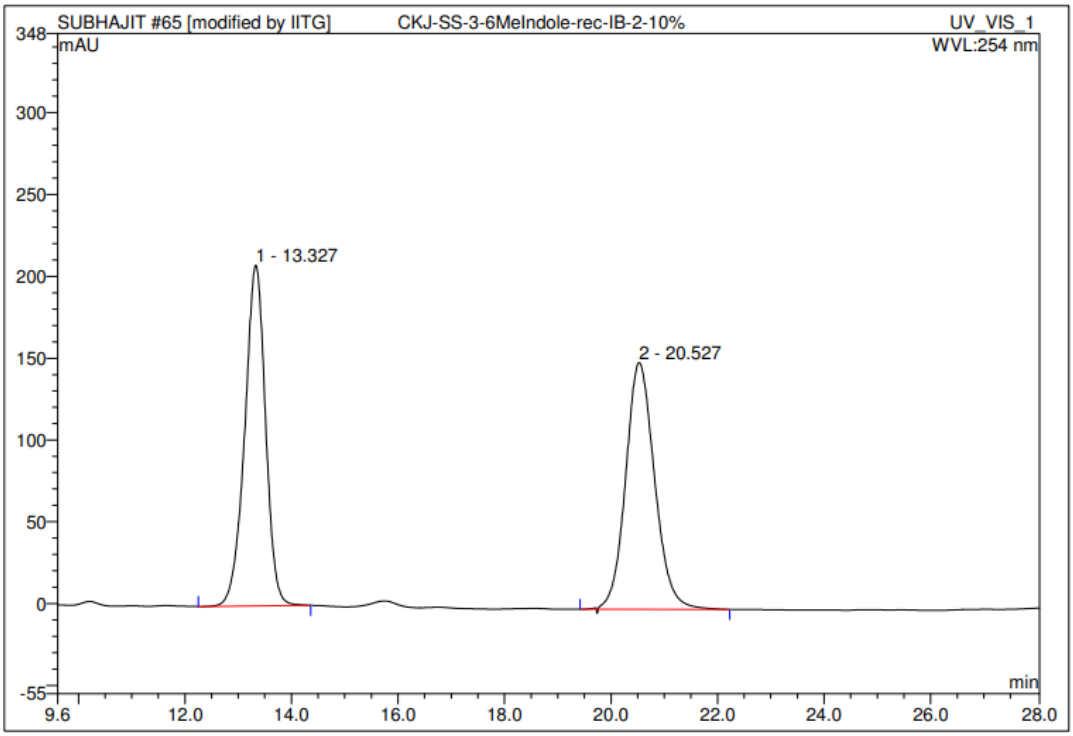
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	12.65	n.a.	1716.177	901.303	99.62	n.a.	BMB*
2	13.81	n.a.	8.524	3.420	0.38	n.a.	BMB*
Total:			1724.701	904.723	100.00	0.000	



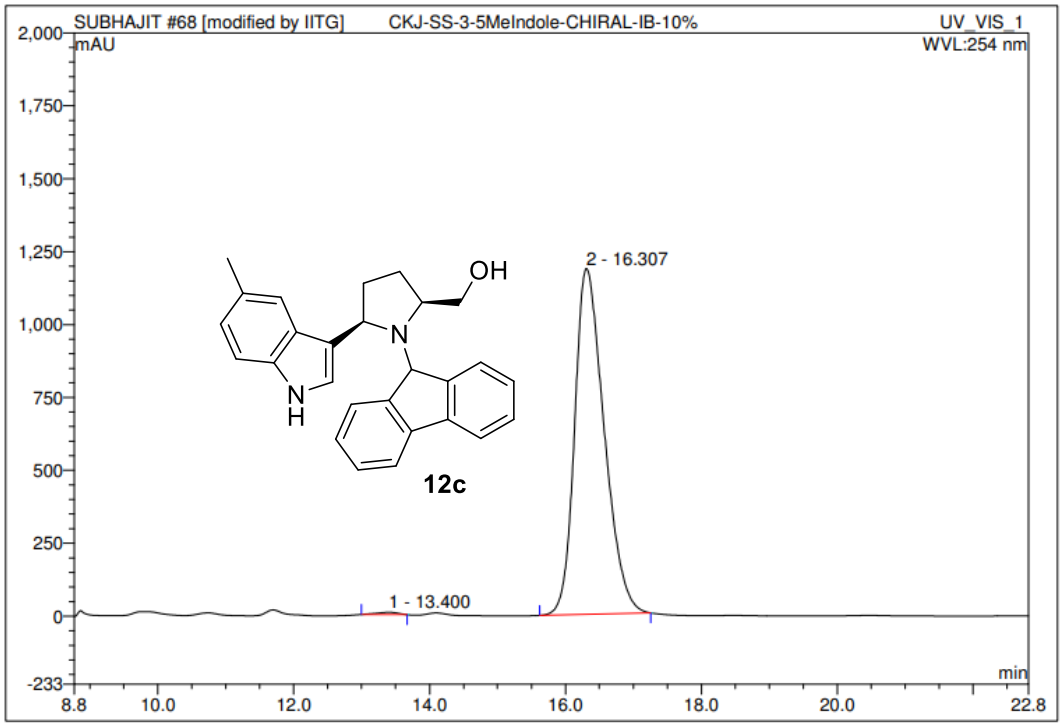
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	12.44	n.a.	285.682	134.358	50.55	n.a.	BMb*
2	13.56	n.a.	261.626	131.458	49.45	n.a.	bMB*
Total:			547.307	265.816	100.00	0.000	



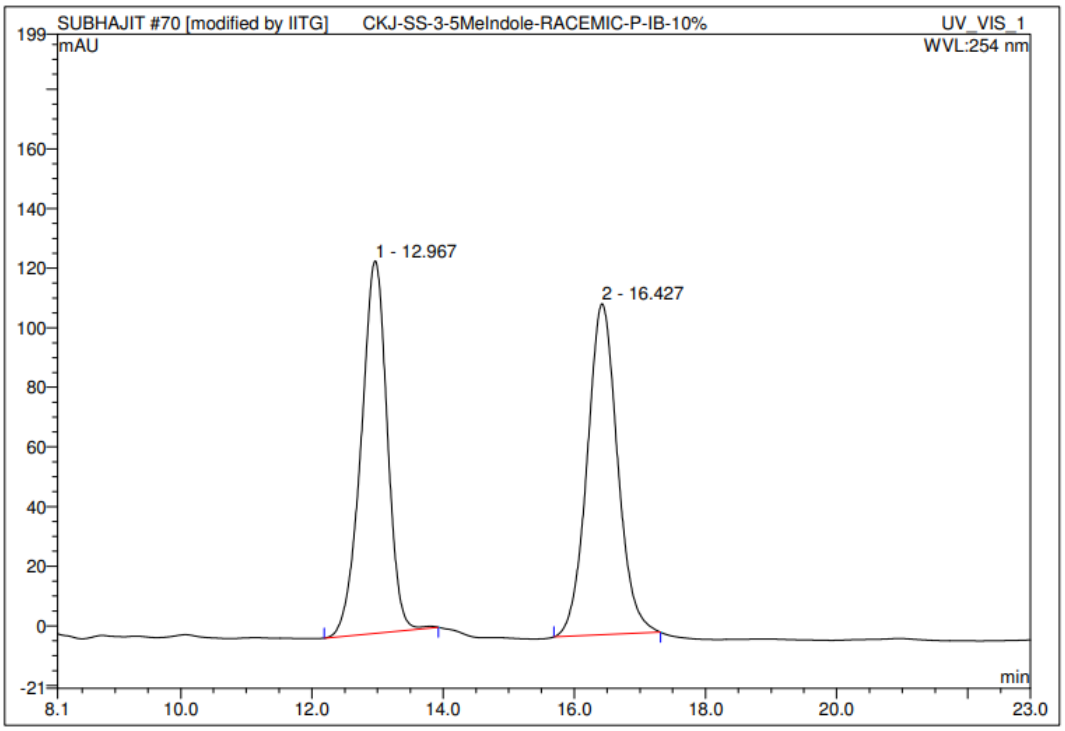
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	13.43	n.a.	7.289	2.573	0.48	n.a.	BMB*
2	20.26	n.a.	850.434	529.055	99.52	n.a.	BMB*
Total:			857.722	531.627	100.00	0.000	



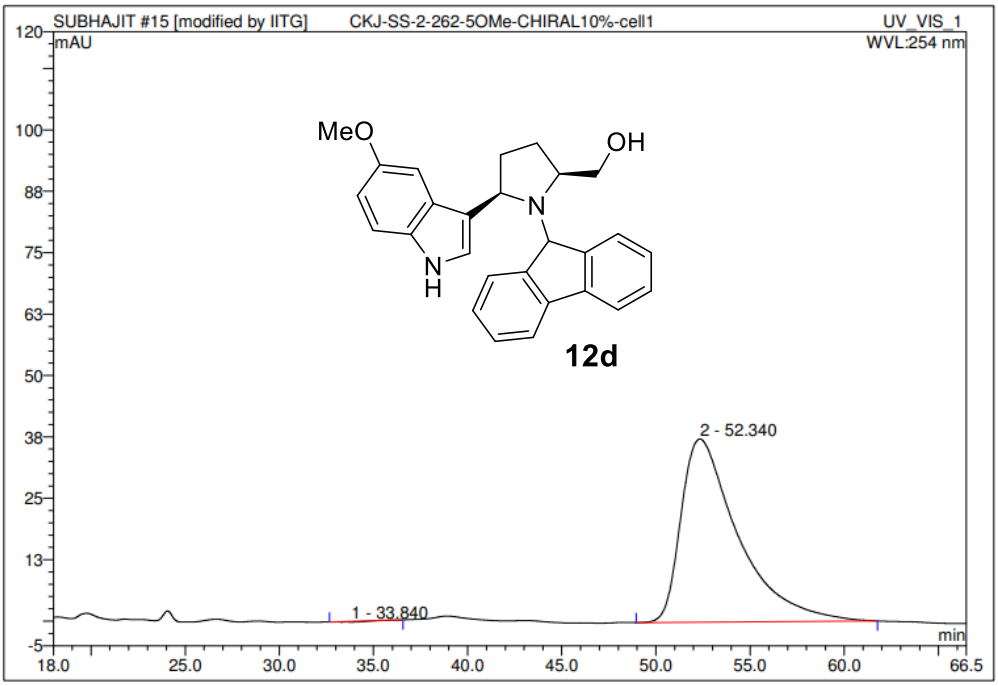
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	13.33	n.a.	208.018	94.239	49.77	n.a.	BMB*
2	20.53	n.a.	150.754	95.125	50.23	n.a.	BMB*
Total:			358.772	189.364	100.00	0.000	



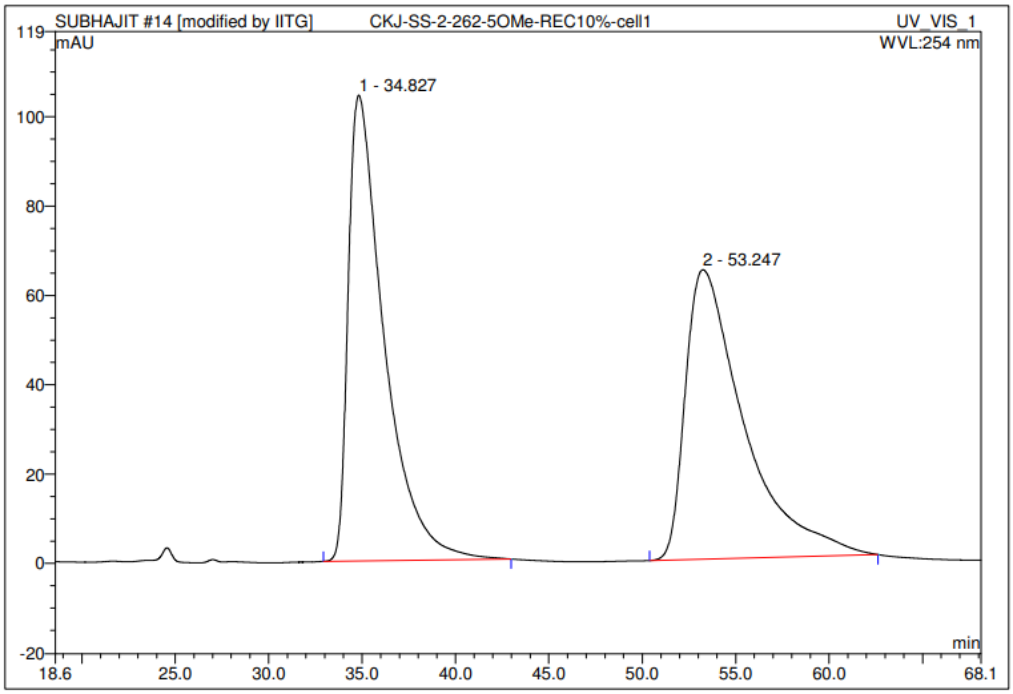
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	13.40	n.a.	7.777	2.816	0.47	n.a.	BMB*
2	16.31	n.a.	1185.919	596.185	99.53	n.a.	BMB*
Total:			1193.696	599.000	100.00	0.000	



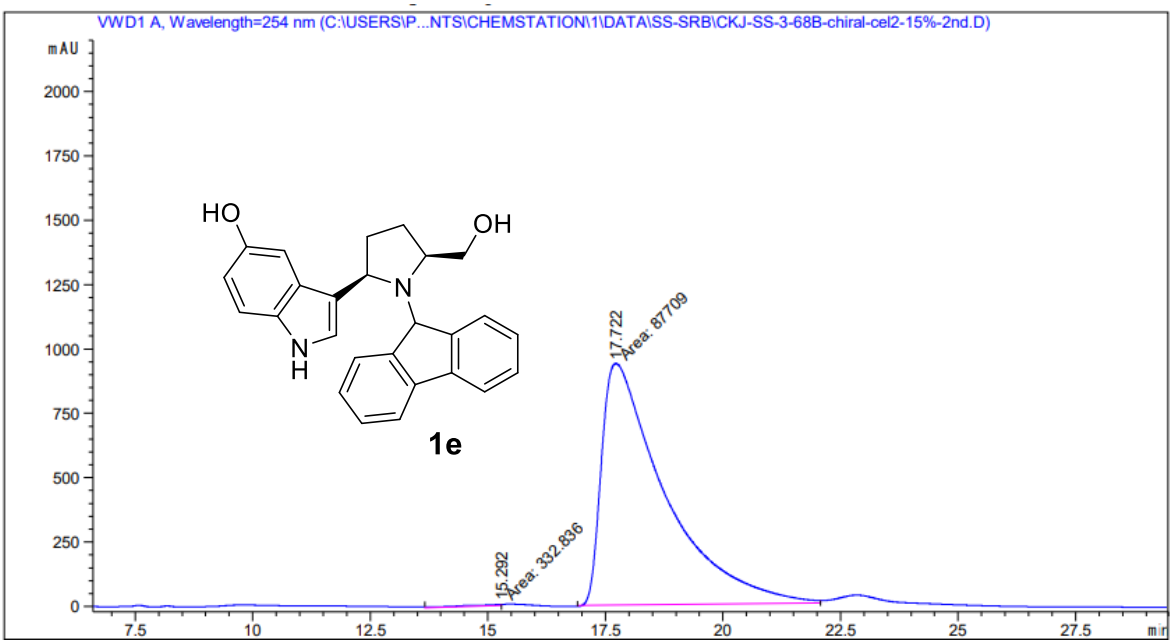
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	12.97	n.a.	124.949	57.565	49.19	n.a.	BMB*
2	16.43	n.a.	111.027	59.452	50.81	n.a.	BMB*
Total:			235.975	117.016	100.00	0.000	



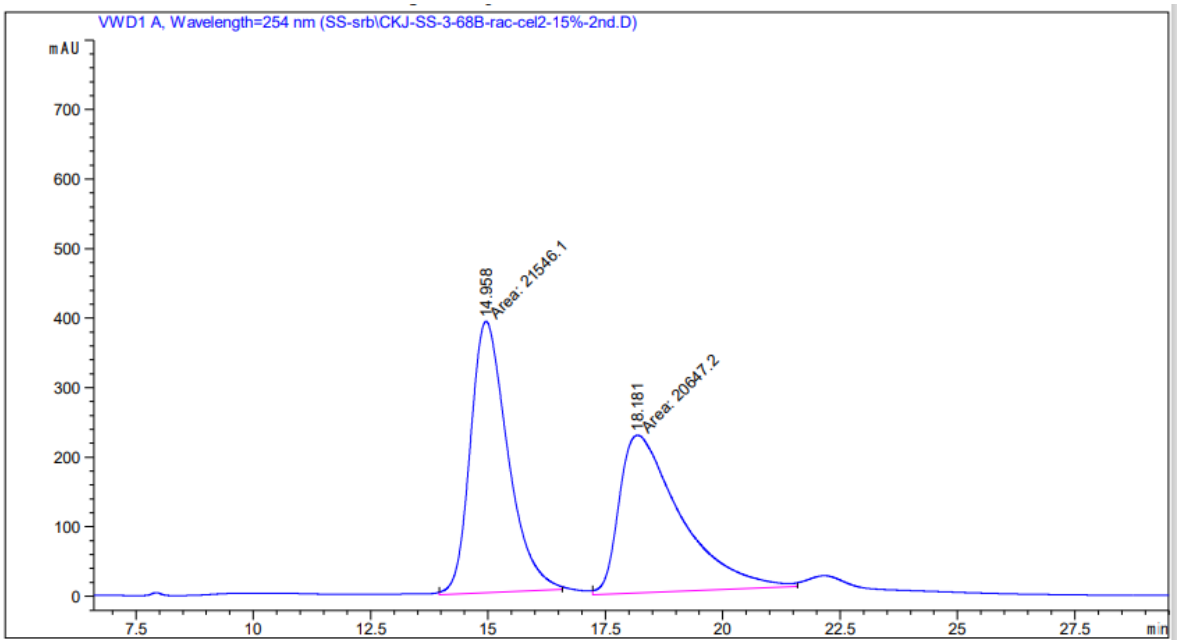
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	33.84	n.a.	0.157	0.222	0.17	n.a.	BMB*
2	52.34	n.a.	37.274	131.001	99.83	n.a.	BMB*
Total:			37.431	131.223	100.00	0.000	



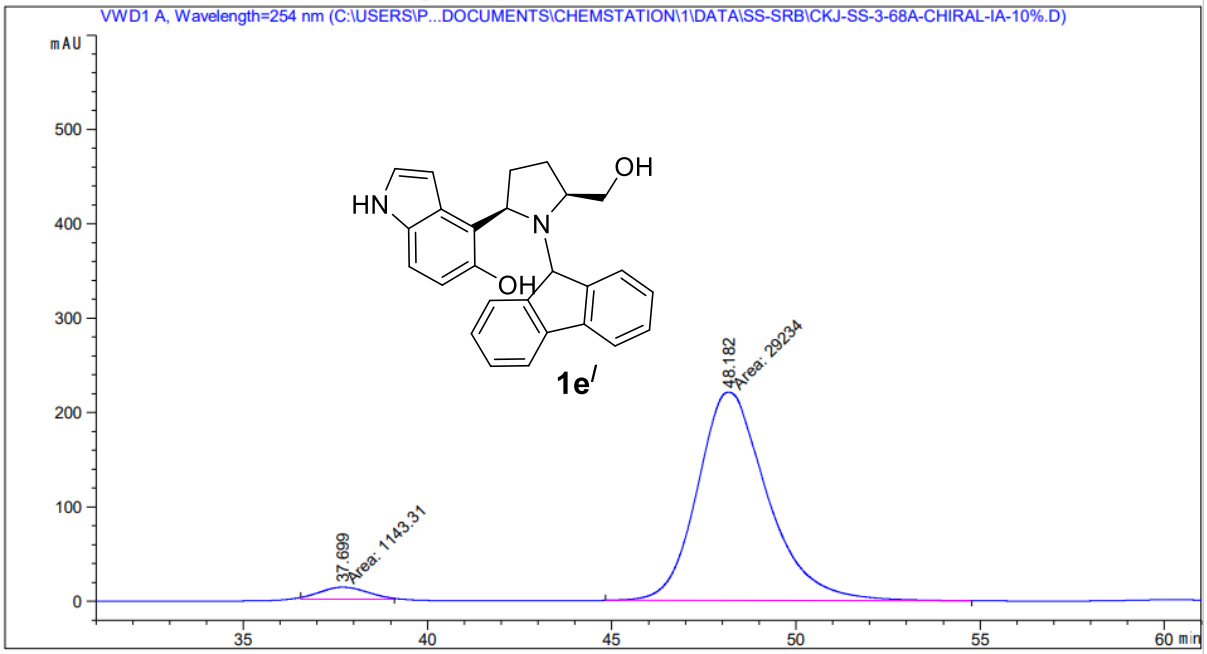
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	34.83	n.a.	104.290	232.472	49.65	n.a.	BMB*
2	53.25	n.a.	64.825	235.748	50.35	n.a.	BMB*
Total:			169.115	468.220	100.00	0.000	



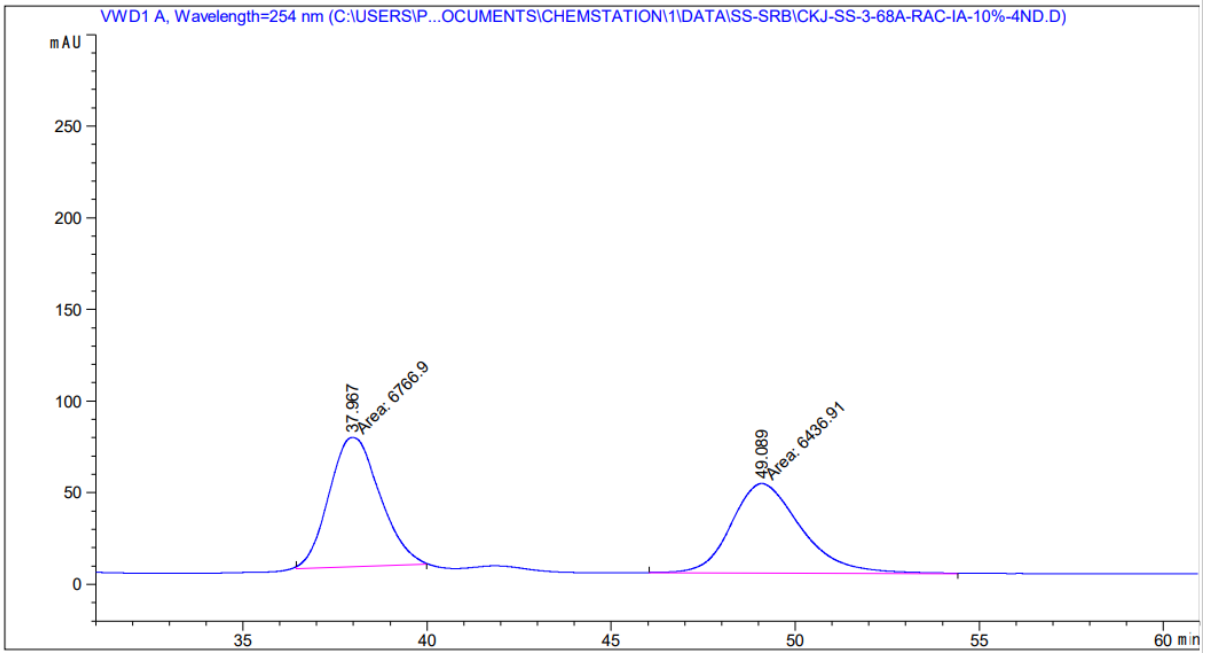
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.292	MM T	1.0954	332.83627	5.06395	0.3780
2	17.722	MM T	1.5584	8.77090e4	938.05060	99.6220



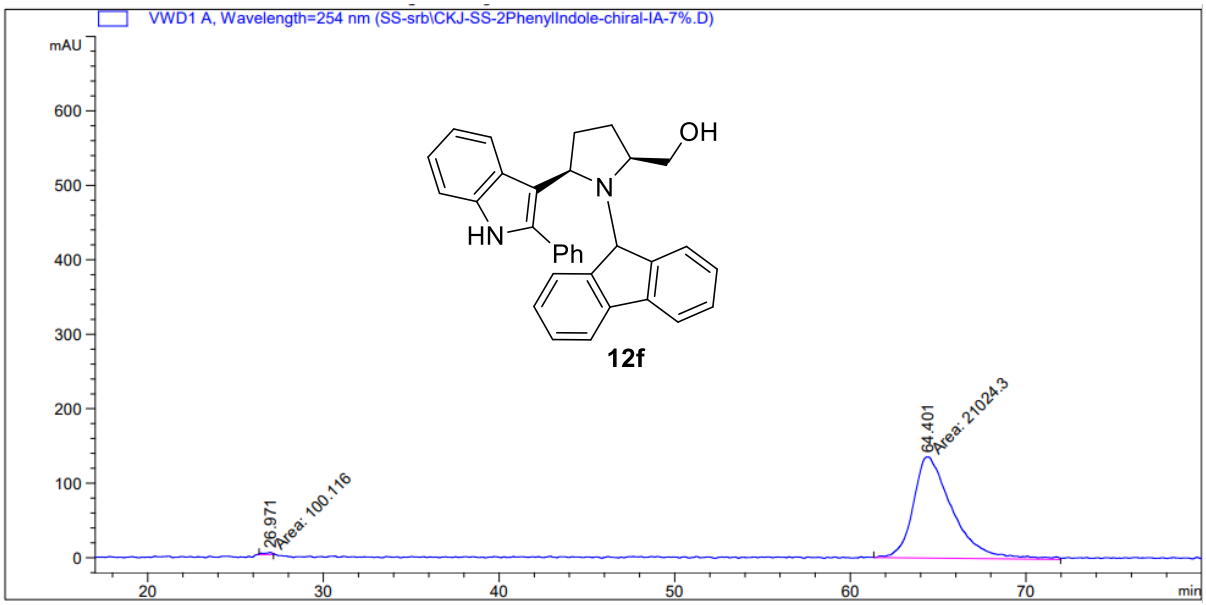
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.958	MM T	0.9210	2.15461e4	389.90381	51.0652
2	18.181	MM T	1.5202	2.06472e4	226.37149	48.9348



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.699	MM T	1.4971	1143.31409	12.72826	3.7637
2	48.182	MM T	2.2060	2.92340e4	220.86681	96.2363



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.967	MM T	1.5982	6766.89795	70.56595	51.2496
2	49.089	MM T	2.1953	6436.91455	48.86962	48.7504



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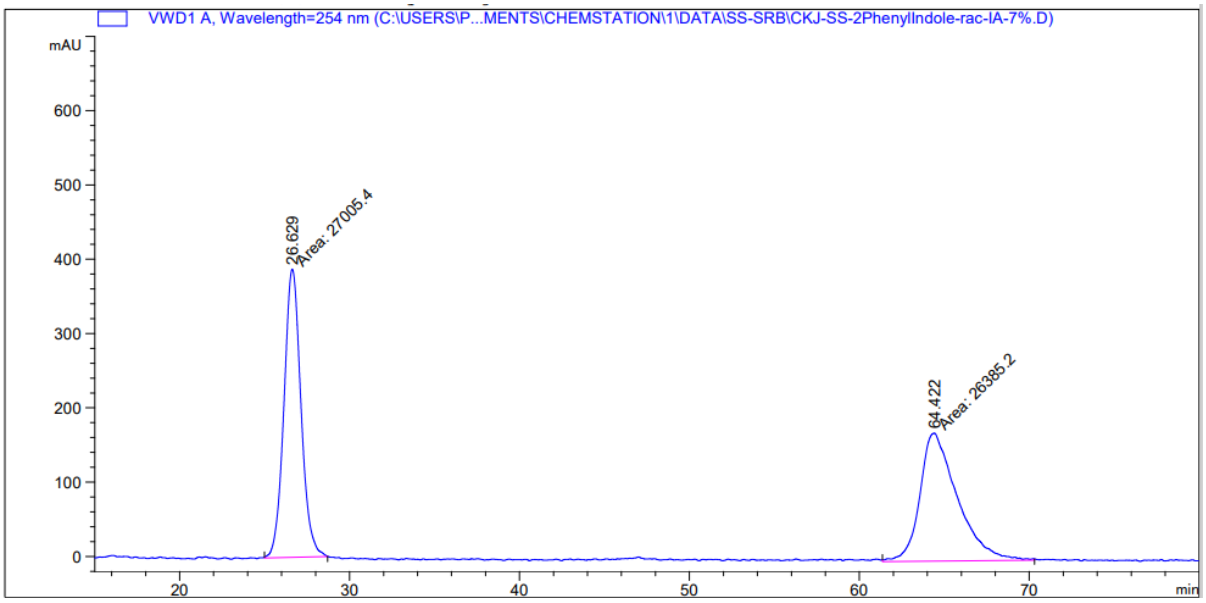
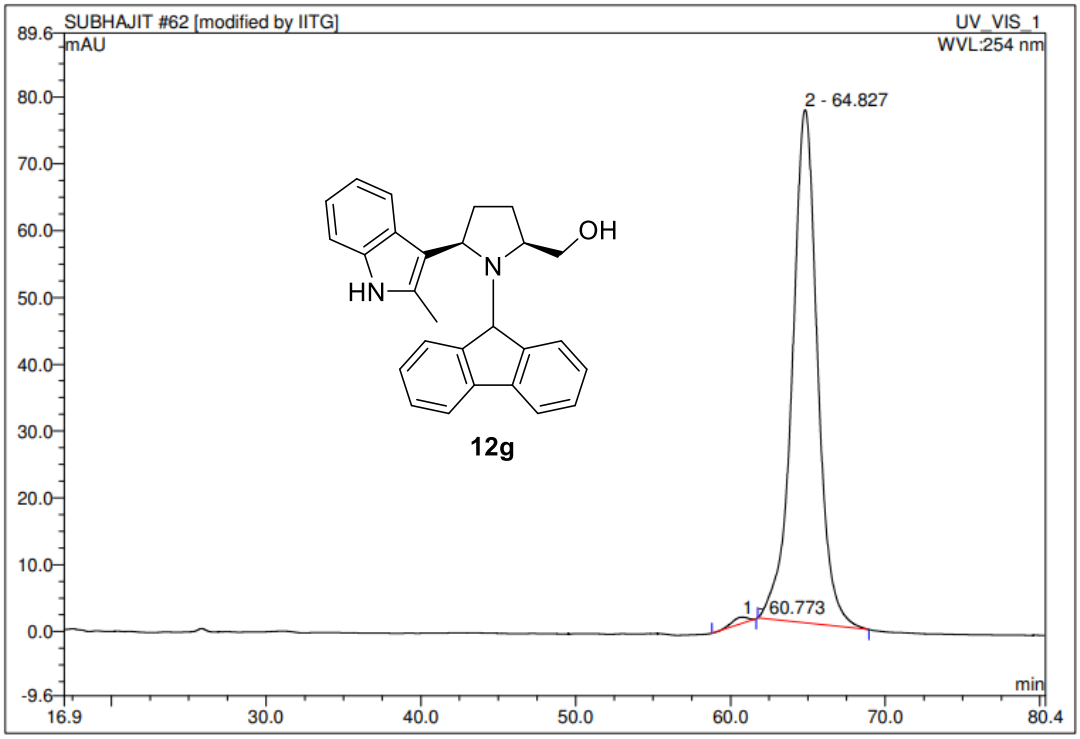
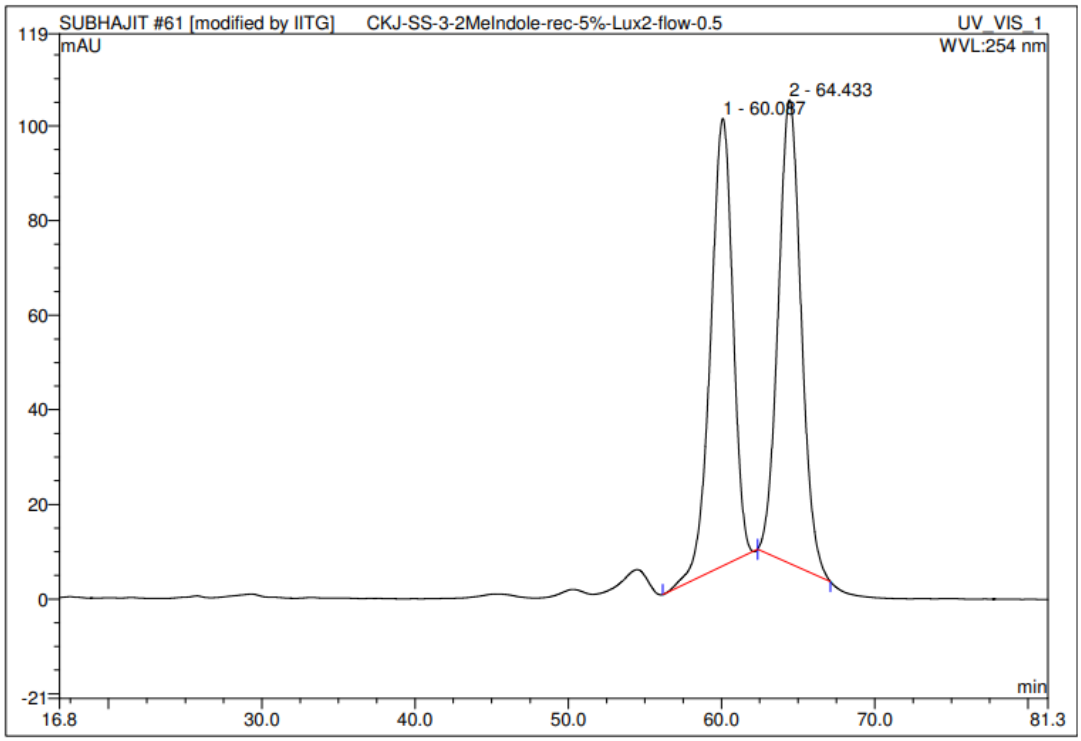
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.971	MM T	0.5665	100.11552	2.94533	0.4739
2	64.401	MM T	2.5826	2.10243e4	135.68031	99.5261



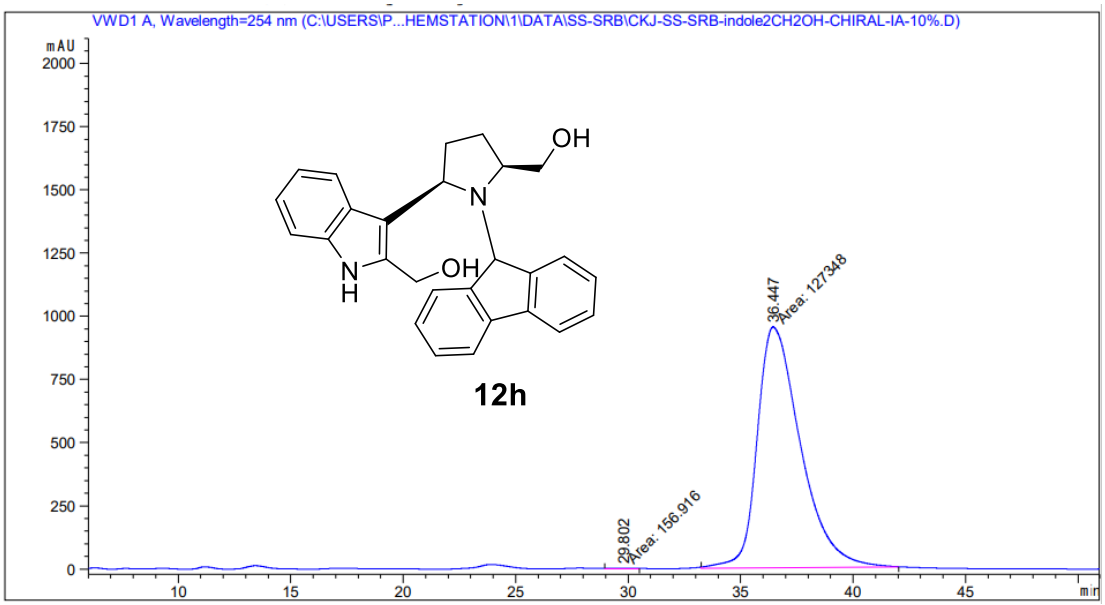
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.629	MM T	1.1603	2.70054e4	387.89258	50.5808
2	64.422	MM T	2.5538	2.63852e4	172.19530	49.4192



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	60.77	n.a.	0.921	1.166	0.80	n.a.	BMB*
2	64.83	n.a.	76.767	145.111	99.20	n.a.	BMB*
Total:			77.687	146.277	100.00	0.000	

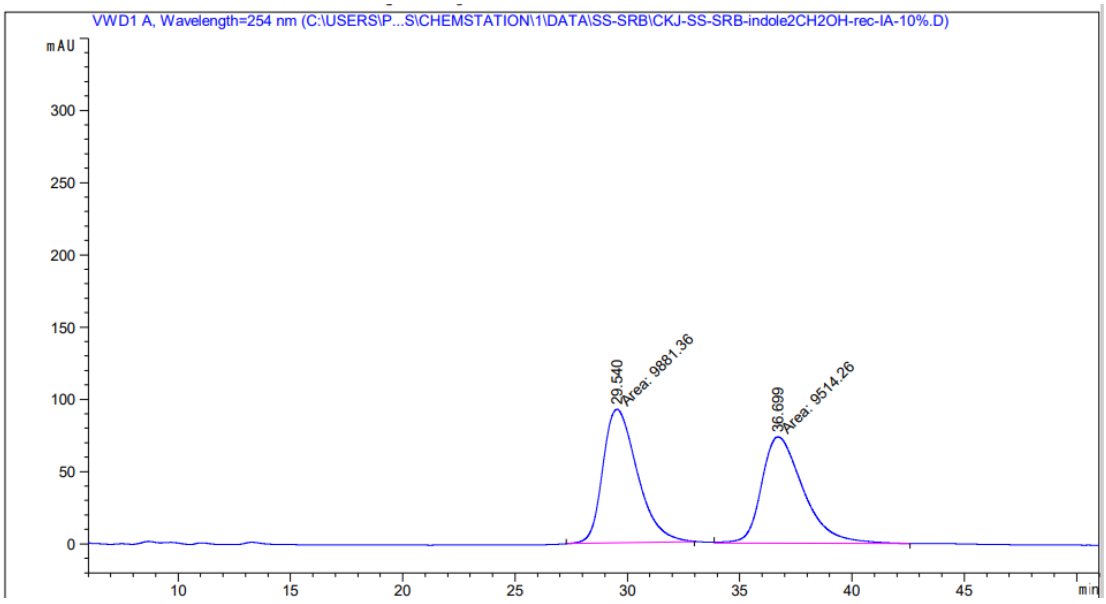


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	60.09	n.a.	94.567	159.690	48.41	n.a.	BMb*
2	64.43	n.a.	97.957	170.182	51.59	n.a.	bMB*
Total:			192.524	329.872	100.00	0.000	



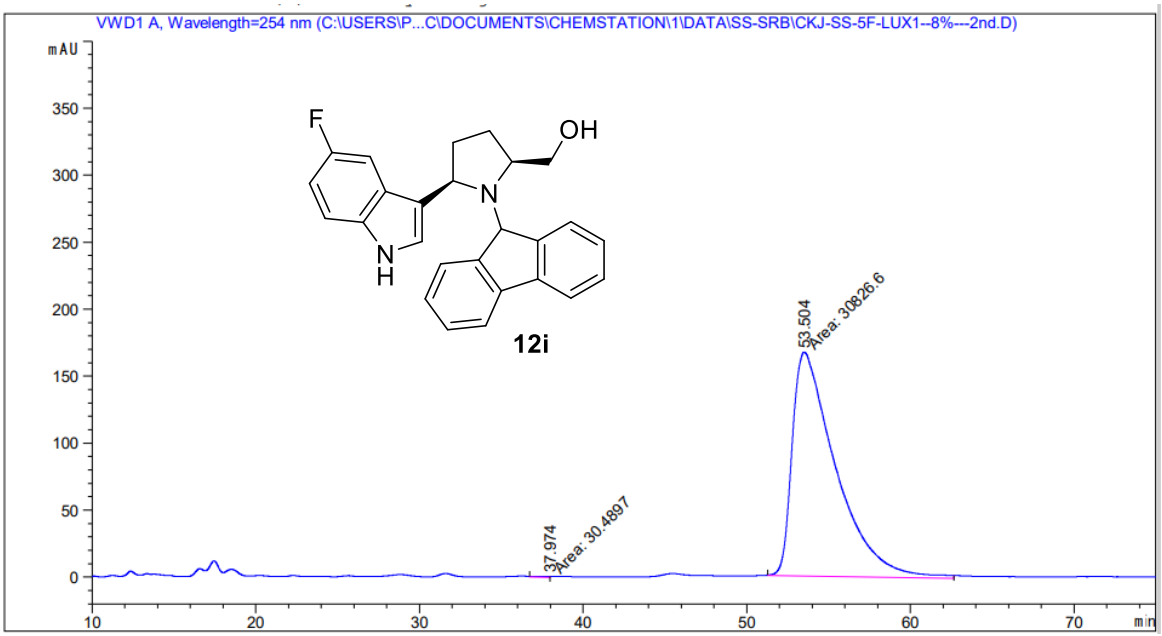
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.802	MM T	1.2301	156.91586	2.12599	0.1231
2	36.447	MM T	2.2278	1.27348e5	952.72479	99.8769



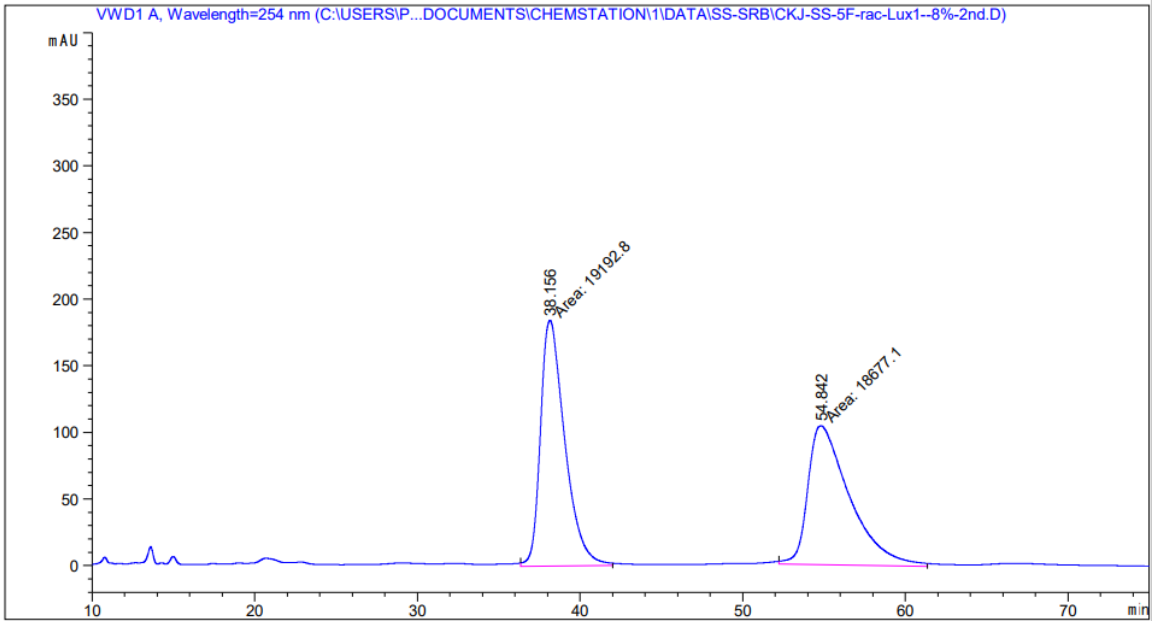
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.540	MM T	1.7799	9881.36035	92.52948	50.9463
2	36.699	MM T	2.1568	9514.26270	73.52216	49.0537



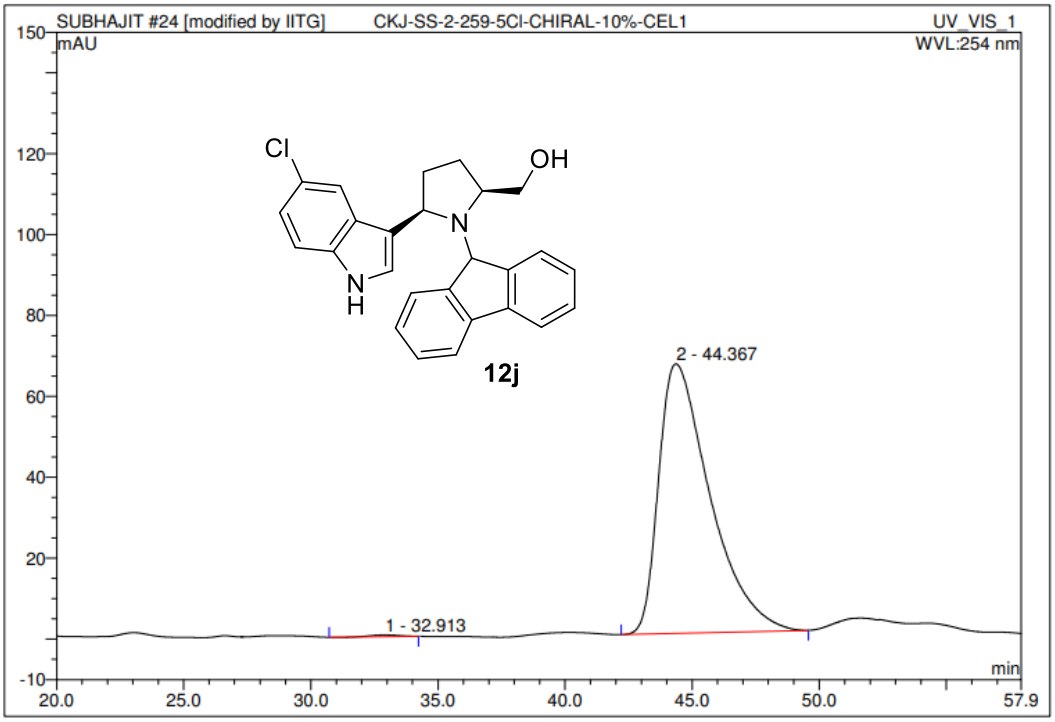
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.974	MM T	0.7632	30.48970	6.65814e-1	0.0988
2	53.504	MM T	3.0749	3.08266e4	167.08862	99.9012

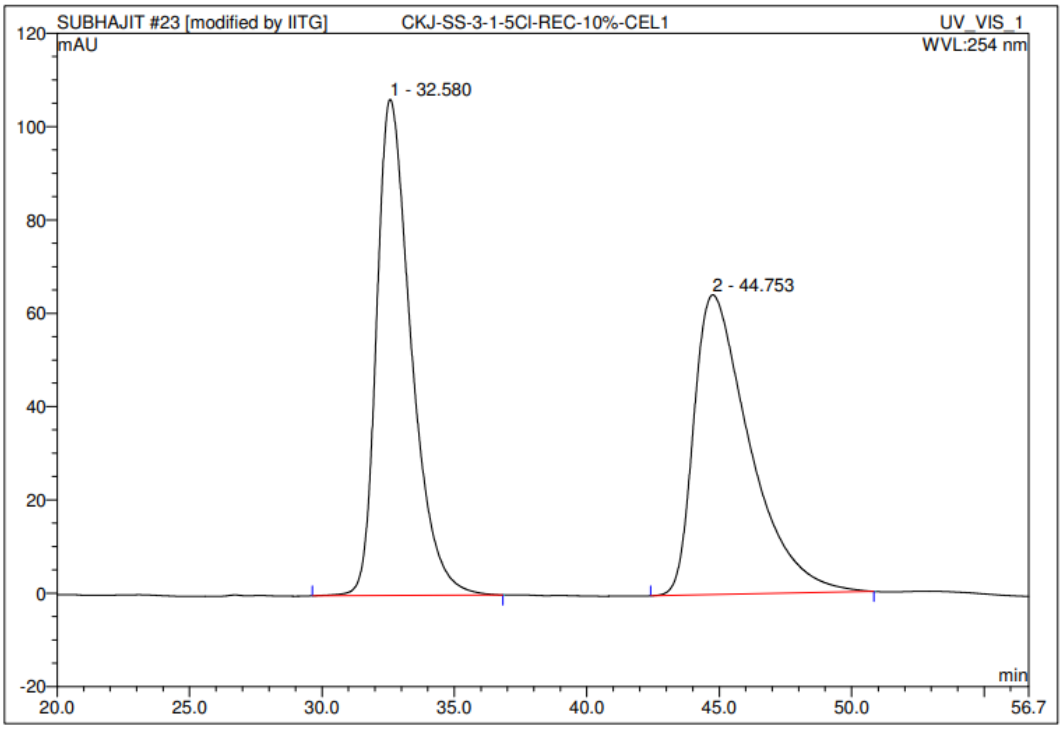


Signal 1: VWD1 A, Wavelength=254 nm

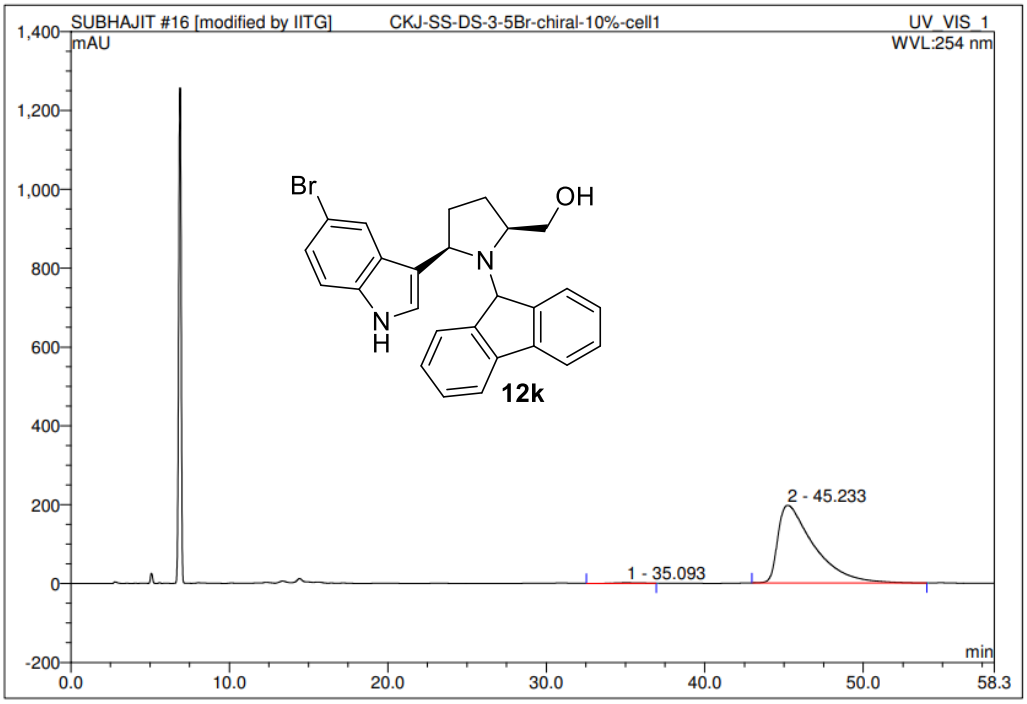
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	38.156	MM T	1.7321	1.91928e4	184.67920	50.6809
2	54.842	MM T	2.9866	1.86771e4	104.22842	49.3191



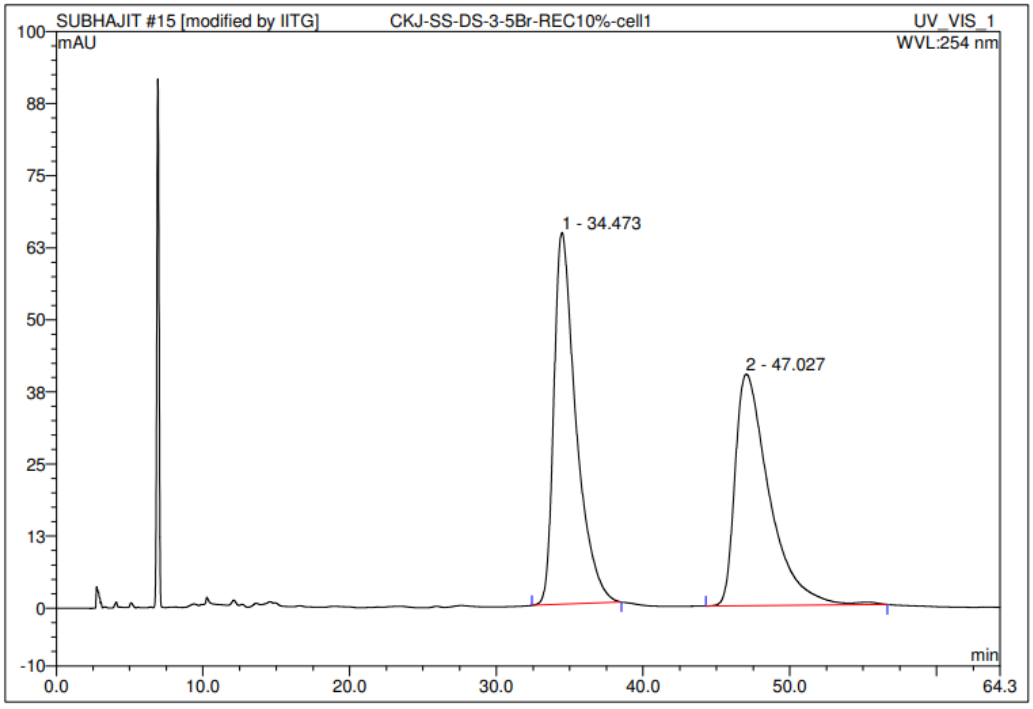
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	32.91	n.a.	0.444	0.566	0.36	n.a.	BMB*
2	44.37	n.a.	66.645	155.742	99.64	n.a.	BMB*
Total:			67.089	156.308	100.00	0.000	



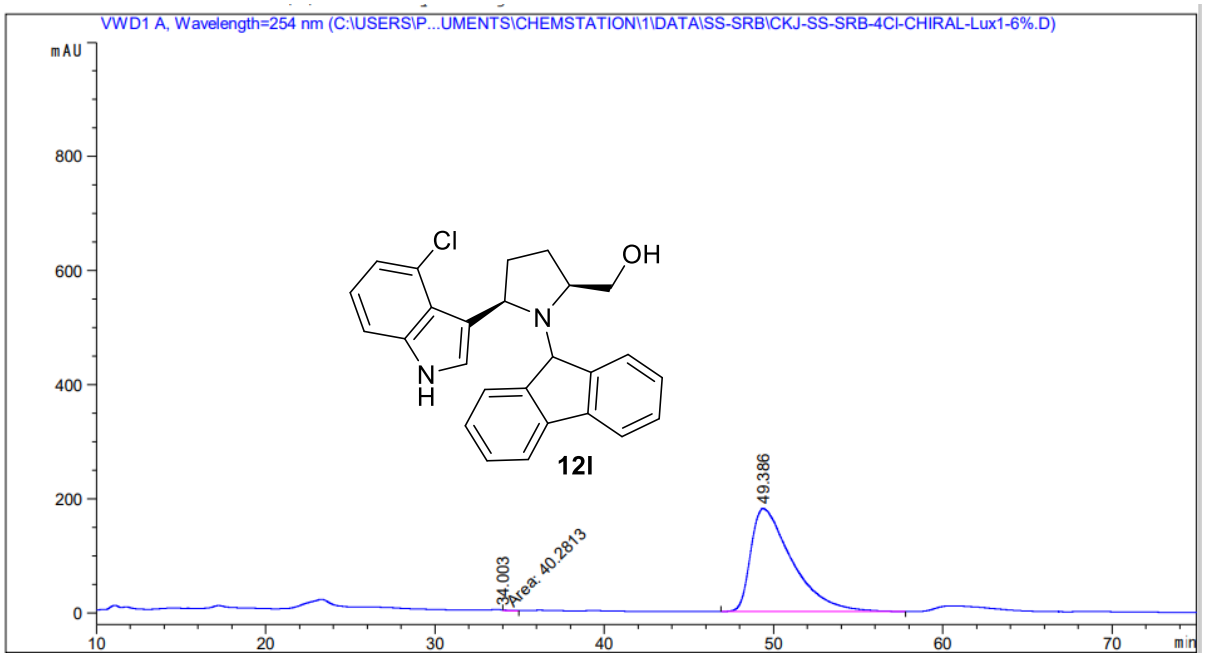
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	32.58	n.a.	106.302	160.827	50.60	n.a.	BMB*
2	44.75	n.a.	64.256	157.022	49.40	n.a.	BMB*
Total:			170.558	317.849	100.00	0.000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	35.09	n.a.	1.233	1.888	0.36	n.a.	BMB*
2	45.23	n.a.	196.526	516.427	99.64	n.a.	BMB*
Total:			197.759	518.315	100.00	0.000	

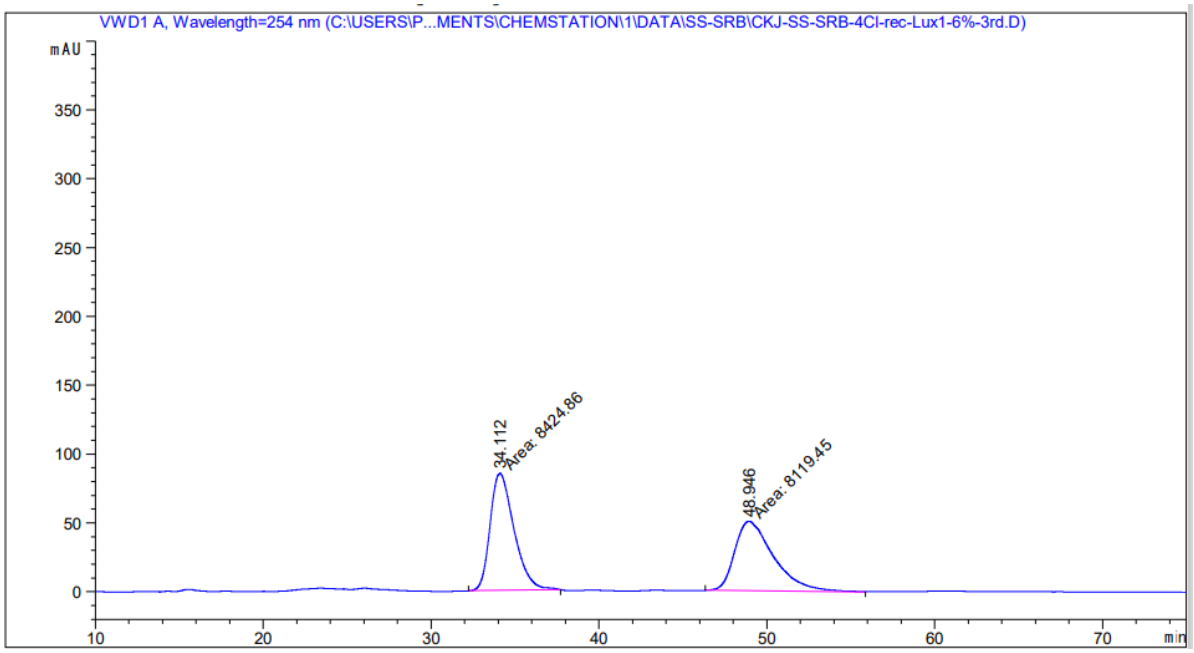


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	34.47	n.a.	64.434	112.719	50.98	n.a.	BMB*
2	47.03	n.a.	40.139	108.401	49.02	n.a.	BMB*
Total:			104.573	221.120	100.00	0.000	



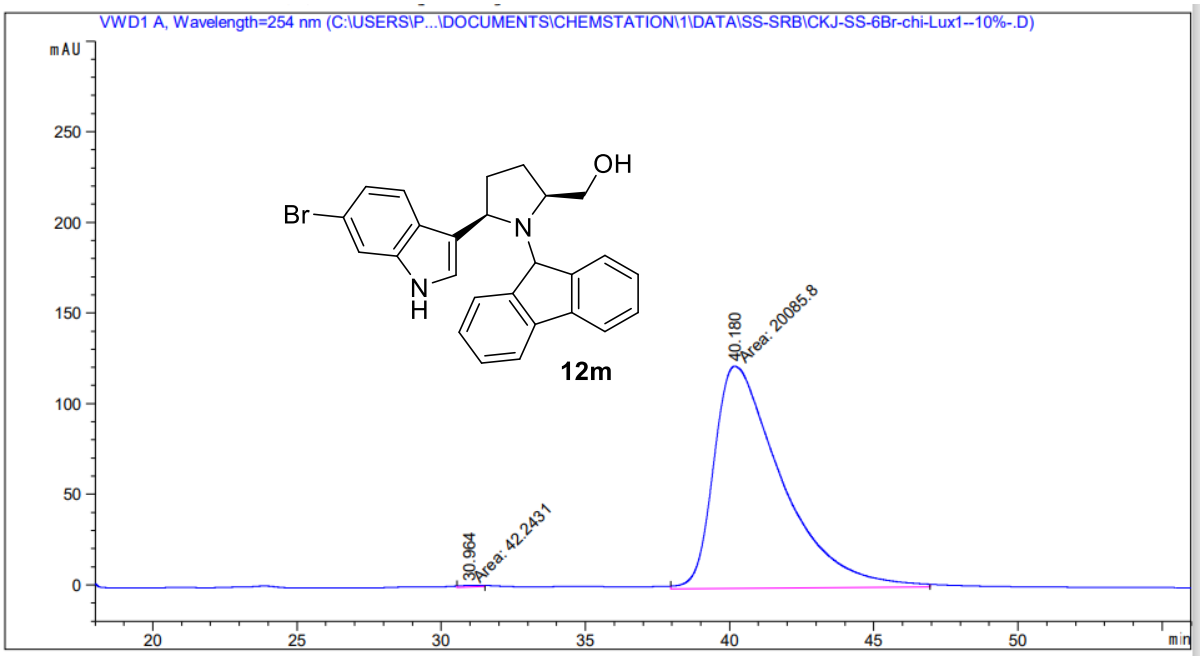
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.003	MM T	0.4704	40.28127	1.02066	0.1315
2	49.386	BB	2.1466	3.05819e4	181.24040	99.8685



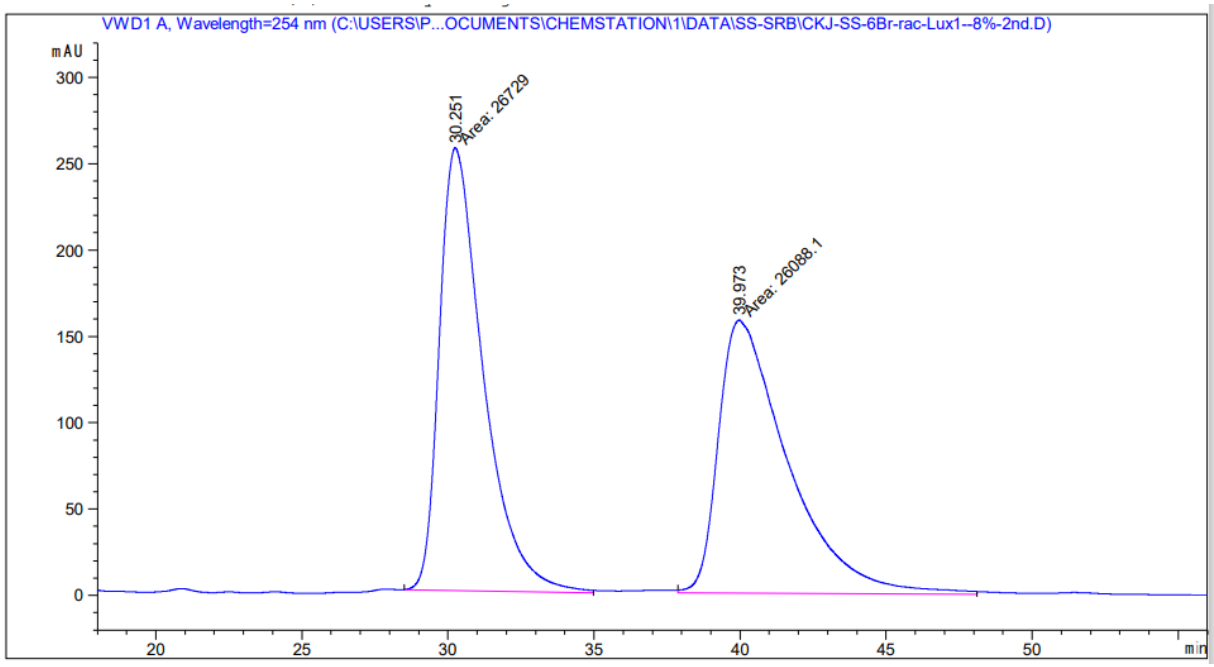
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.112	MM T	1.6513	8424.85645	85.03491	50.9230
2	48.946	MM T	2.6836	8119.44629	50.42616	49.0770

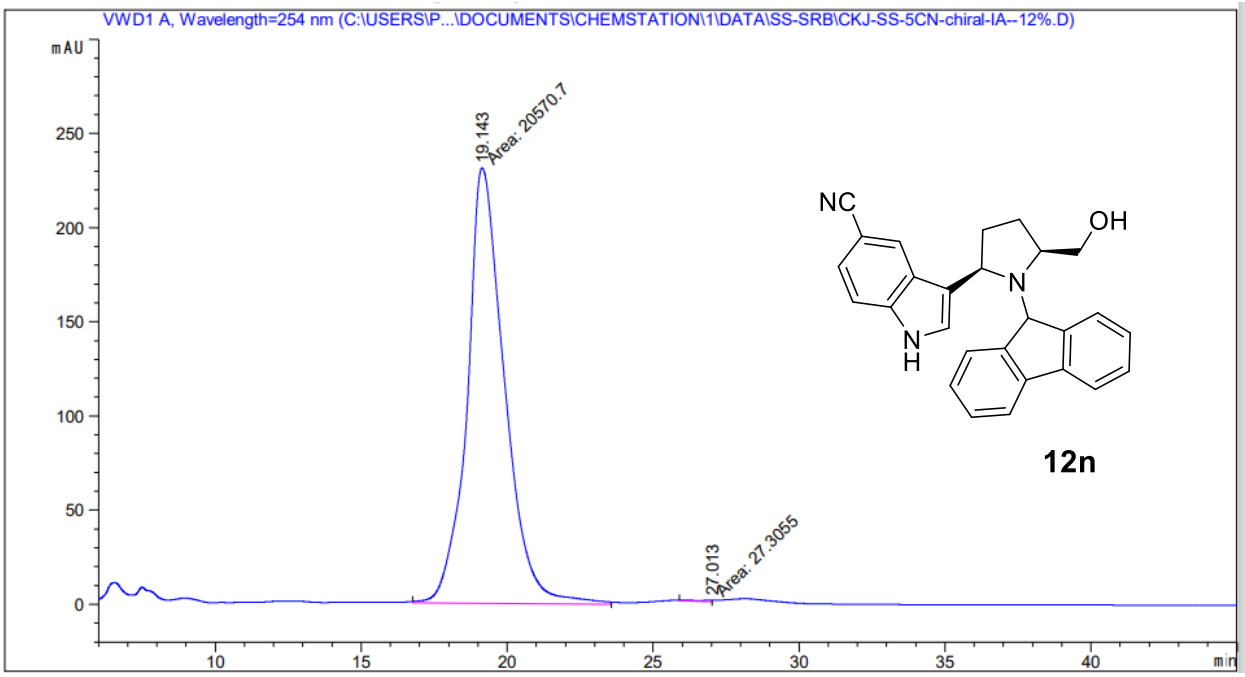


Signal 1: VWD1 A, Wavelength=254 nm

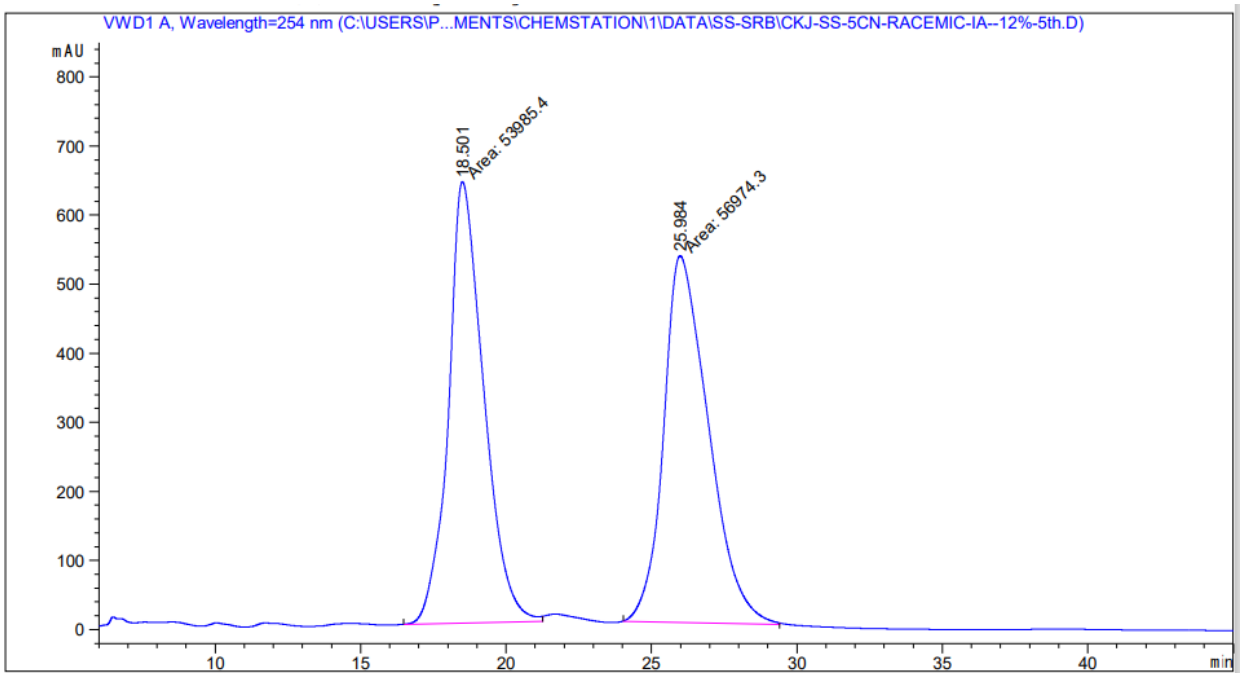
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.964	MM T	0.8889	42.24310	7.92073e-1	0.2099
2	40.180	MM T	2.7304	2.00858e4	122.60794	99.7901



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.251	MM T	1.7380	2.67290e4	256.32043	50.6067
2	39.973	MM T	2.7516	2.60881e4	158.01570	49.3933

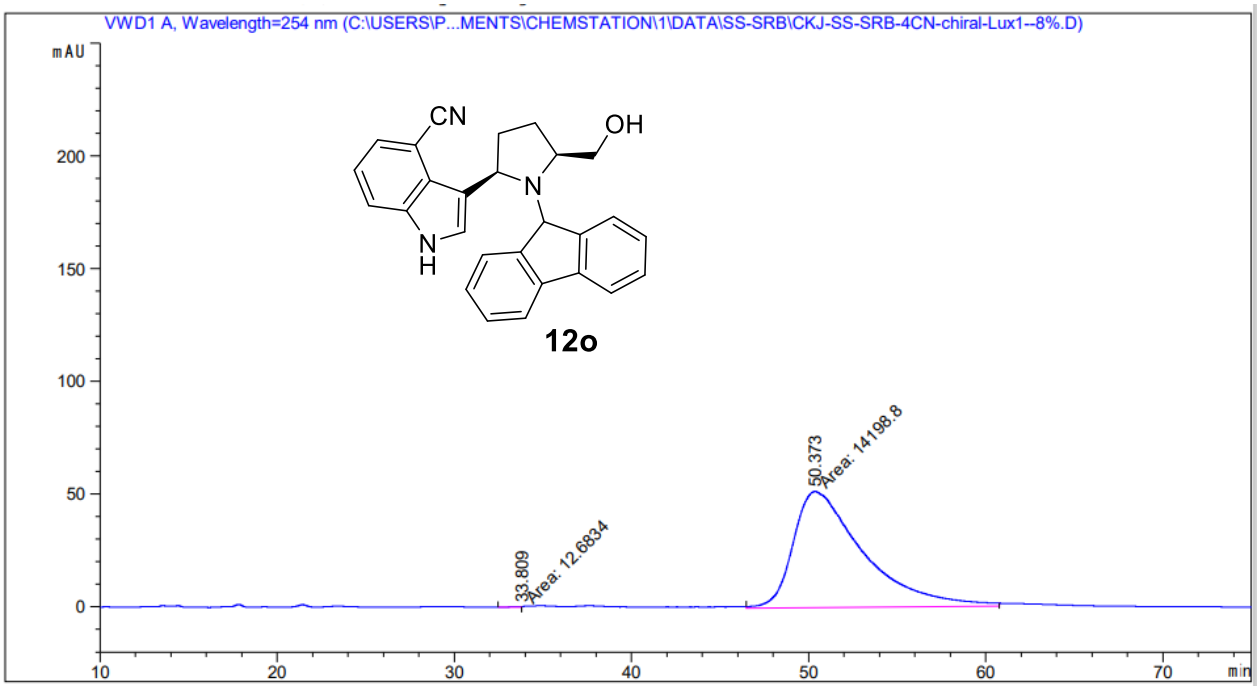


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.143	MM T	1.4830	2.05707e4	231.18570	99.8674
2	27.013	MM T	0.7117	27.30551	6.39461e-1	0.1326

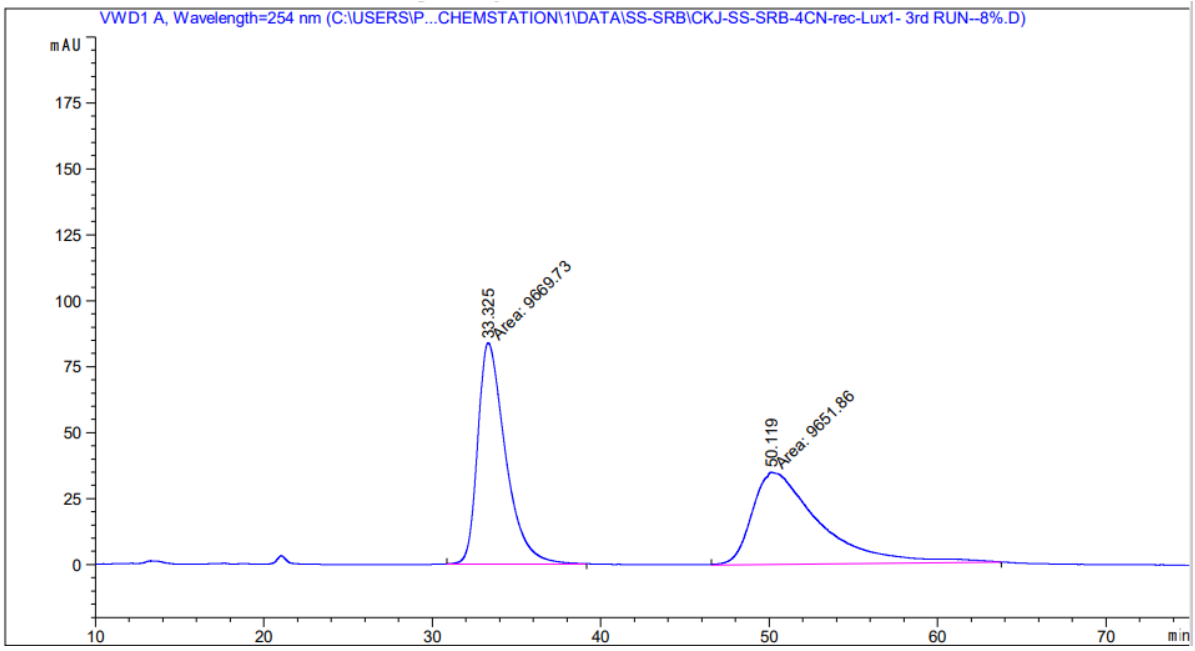


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.501	MM T	1.4076	5.39854e4	639.21326	48.6531
2	25.984	MM T	1.7882	5.69743e4	531.02997	51.3469

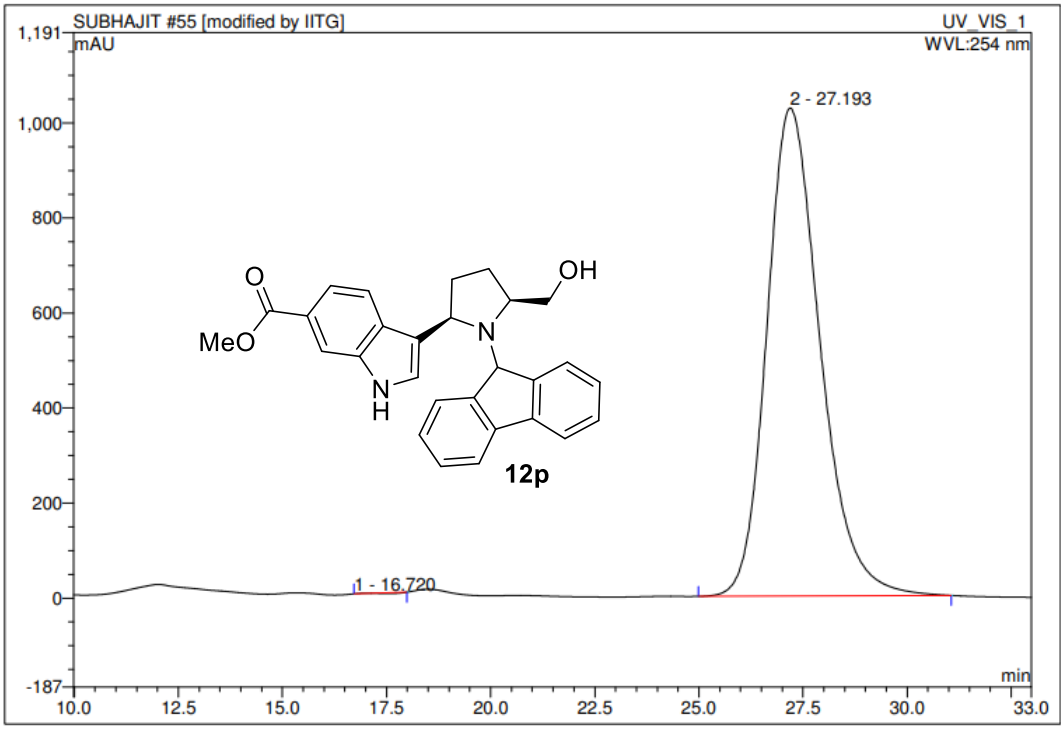


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.809	MM T	0.9107	12.68340	2.32120e-1	0.0892
2	50.373	MM T	4.5876	1.41988e4	51.58429	99.9108

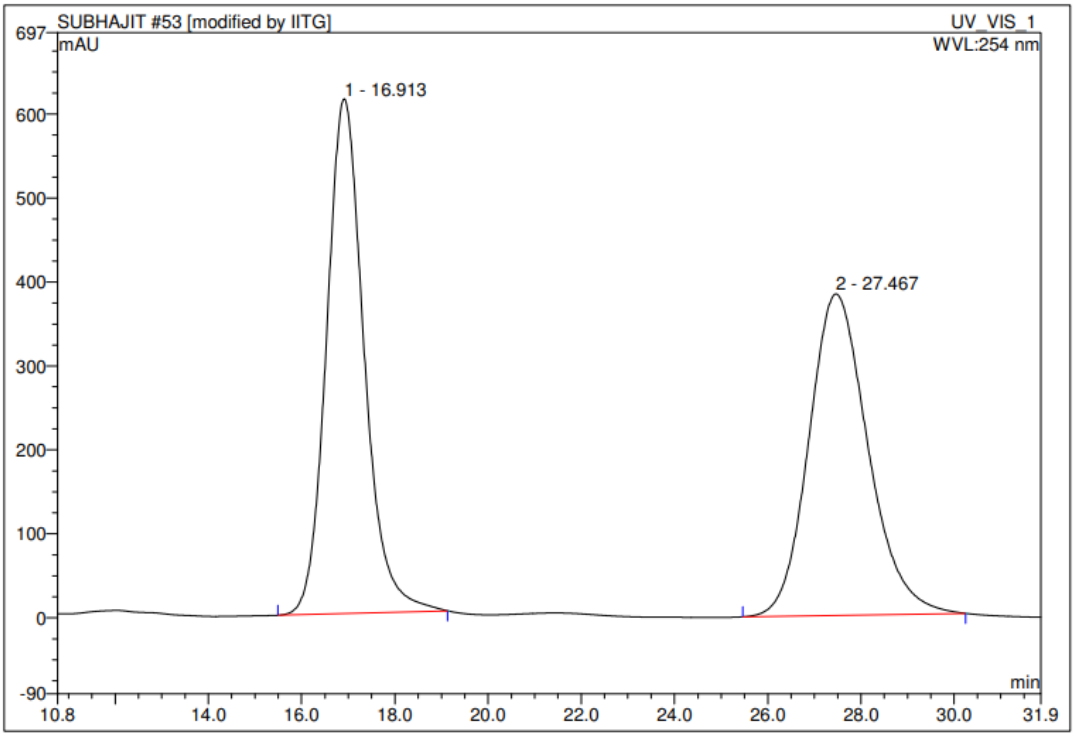


Signal 1: VWD1 A, Wavelength=254 nm

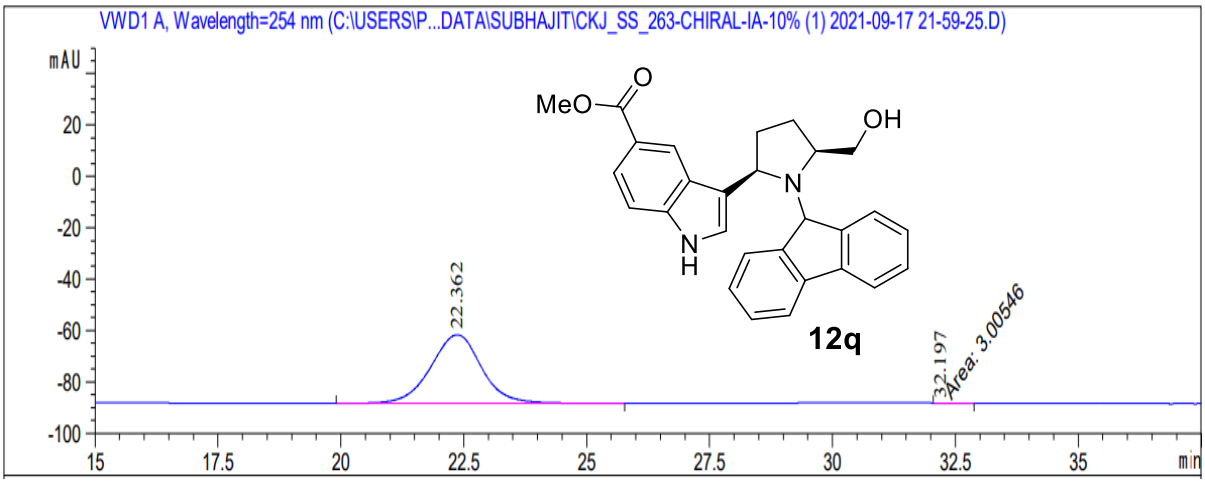
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.325	MM T	1.9195	9669.72949	83.95963	50.0462
2	50.119	MM T	4.6087	9651.86426	34.90455	49.9538



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	16.72	n.a.	0.035	0.638	0.04	n.a.	BMB*
2	27.19	n.a.	1027.101	1524.408	99.96	n.a.	BMB*
Total:			1027.136	1525.046	100.00	0.000	

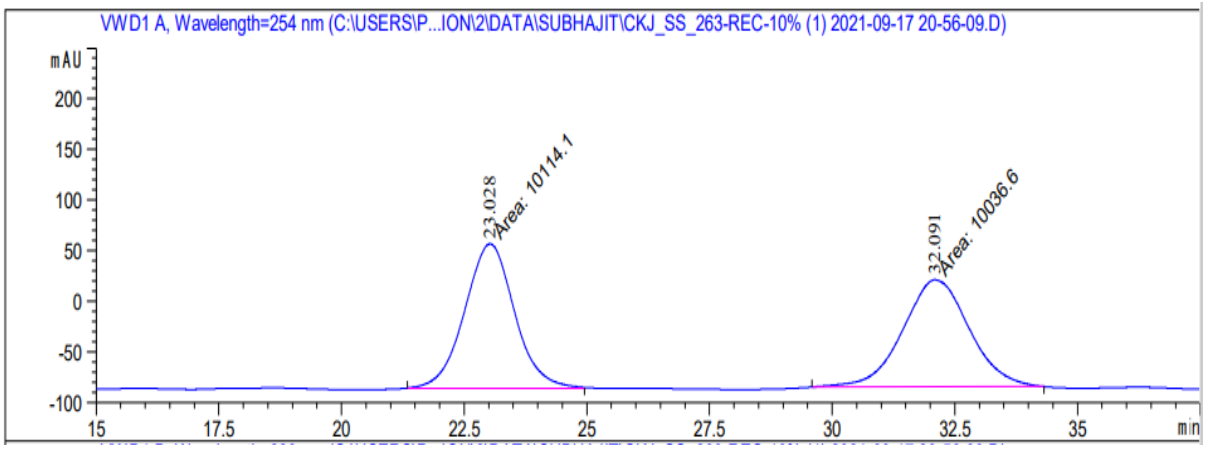


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	16.91	n.a.	612.933	572.390	50.43	n.a.	BMB*
2	27.47	n.a.	382.840	562.536	49.57	n.a.	BMB*
Total:			995.773	1134.926	100.00	0.000	



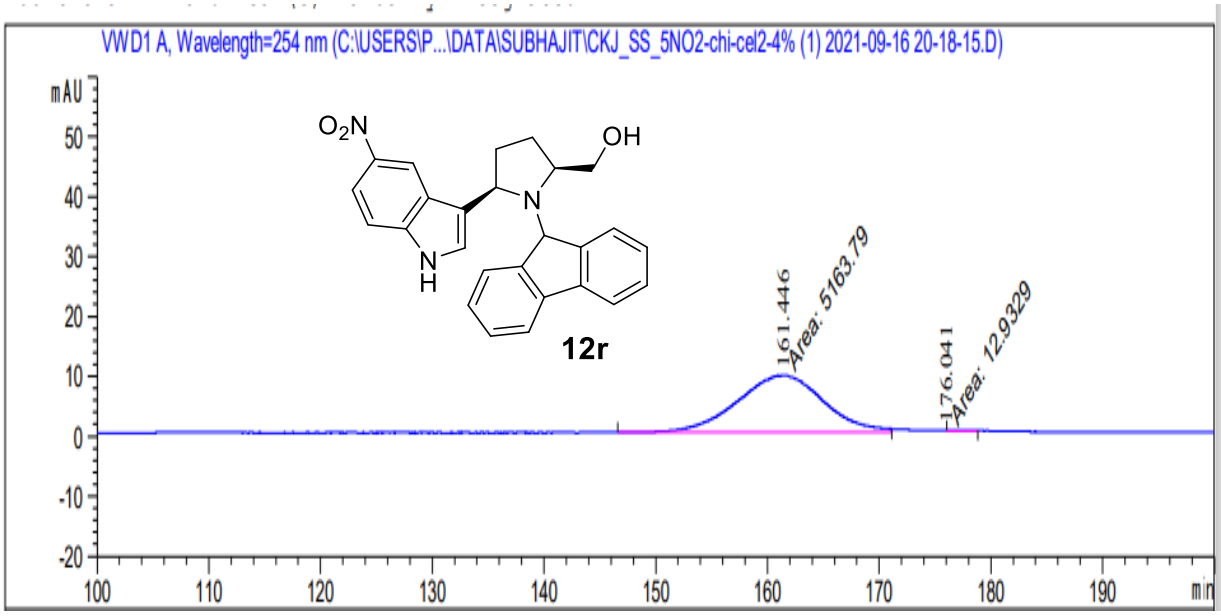
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.362	BB	1.1014	1934.25977	26.69254	99.8449
2	32.197	MM T	0.5799	3.00546	6.85413e-2	0.1551

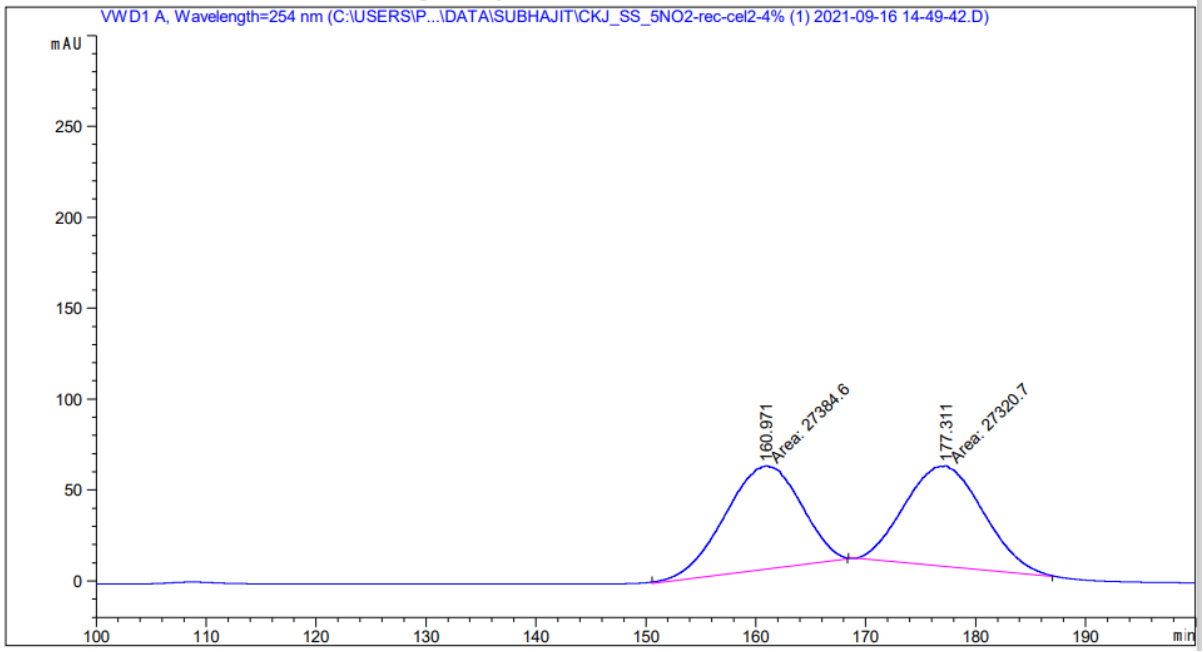


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.028	MM T	1.1807	1.01141e4	142.77248	50.1924
2	32.091	MM T	1.5790	1.00366e4	105.94098	49.8076

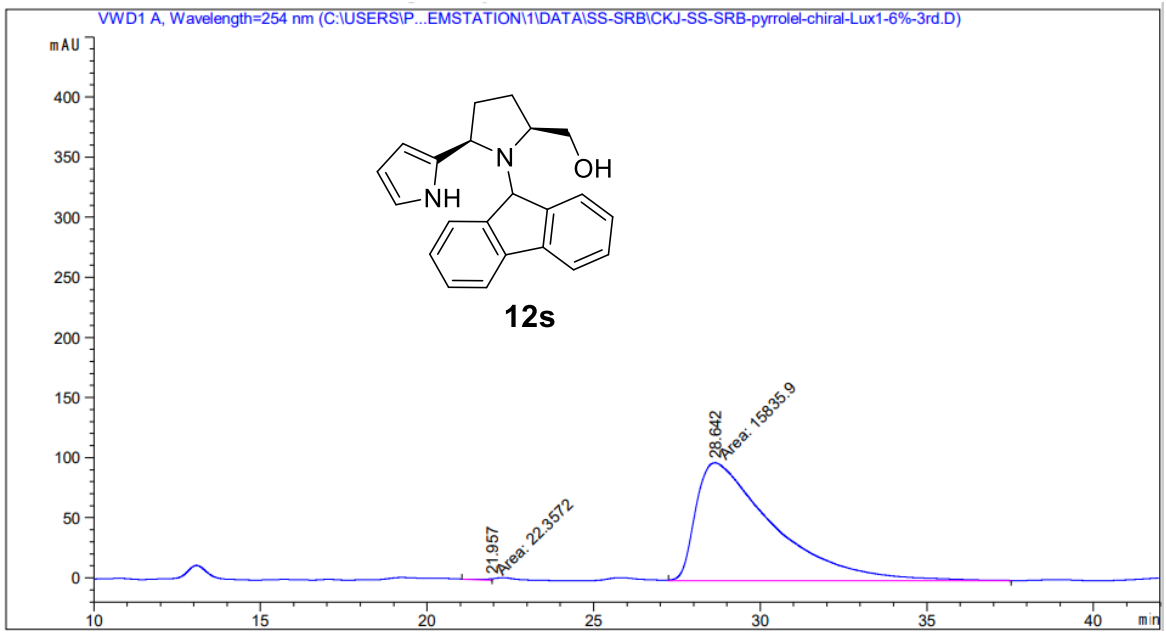


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	161.446	MM T	8.9929	5163.79346	9.57013	99.7502
2	176.041	MM T	2.0742	12.93292	1.03917e-1	0.2498



Signal 1: VWD1 A, Wavelength=254 nm

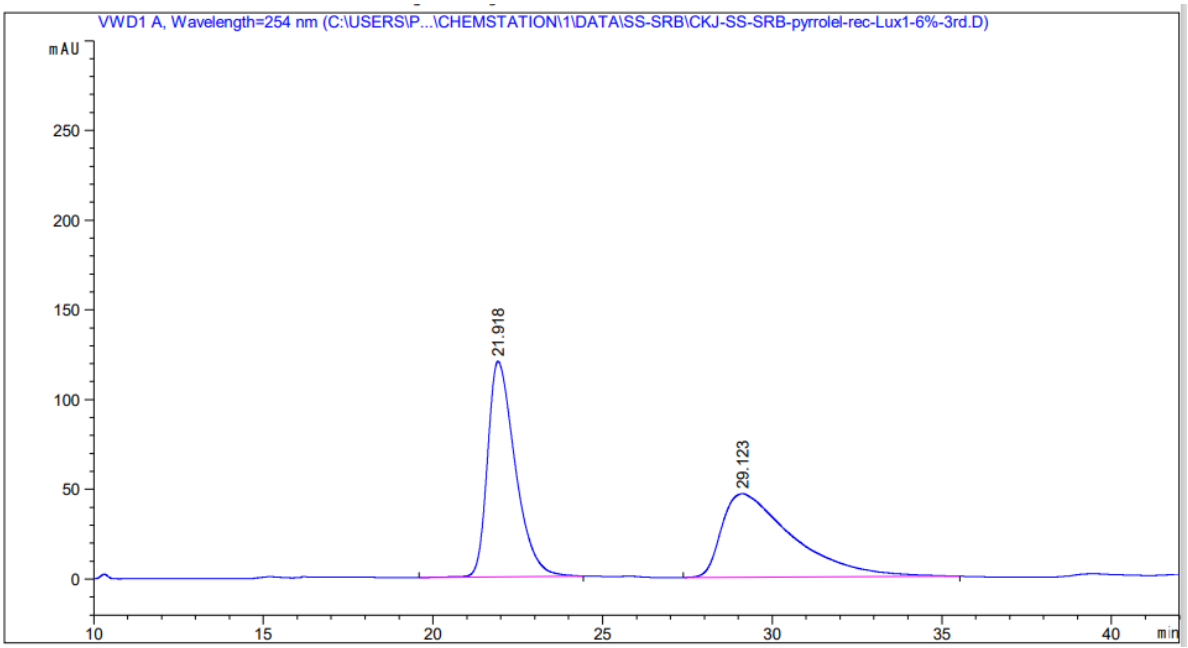
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	160.971	MM T	8.7676	2.73846e4	56.77050	50.0584
2	177.311	MM T	8.4897	2.73207e4	55.34008	49.9416



12s

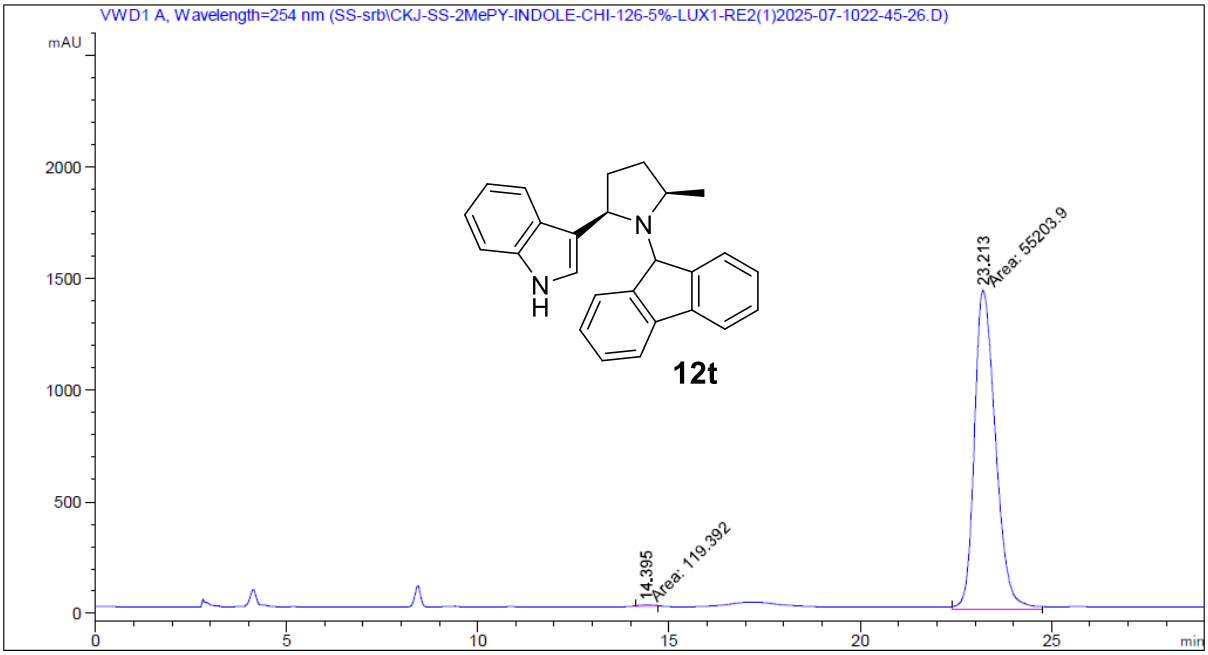
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.957	MM T	0.3016	22.35720	1.23567	0.1410
2	28.642	MM T	2.6880	1.58359e4	98.18993	99.8590



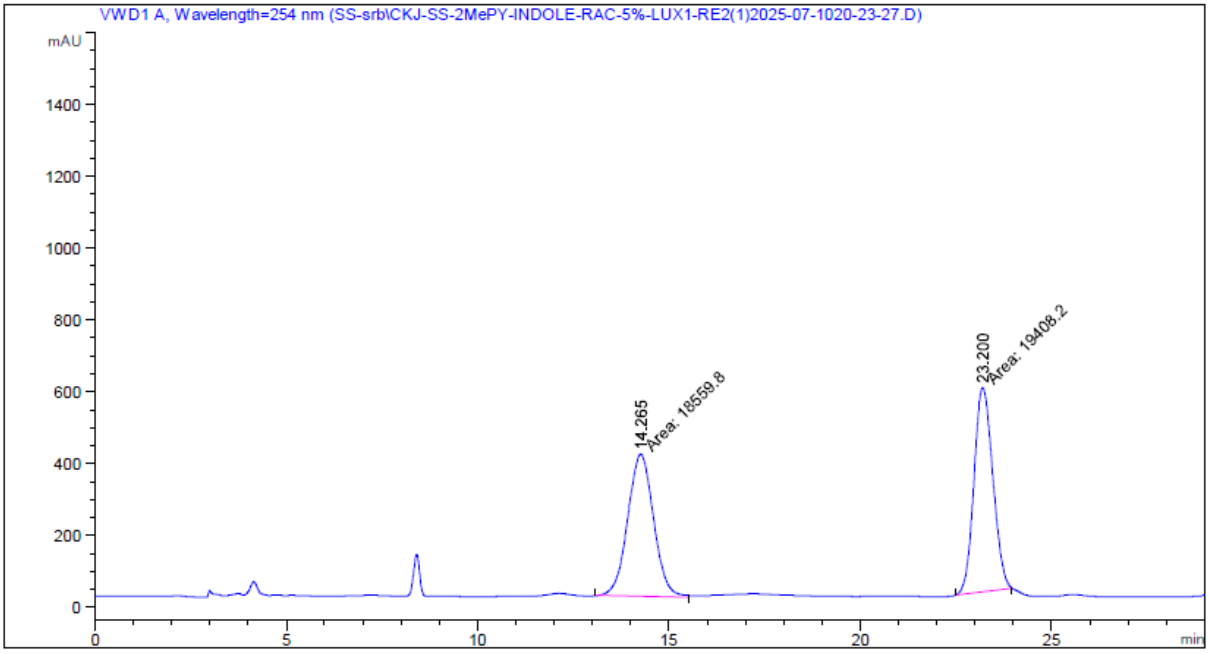
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.918	BB	0.8526	6800.90771	120.11452	50.2005
2	29.123	BB	1.9528	6746.58301	46.52406	49.7995



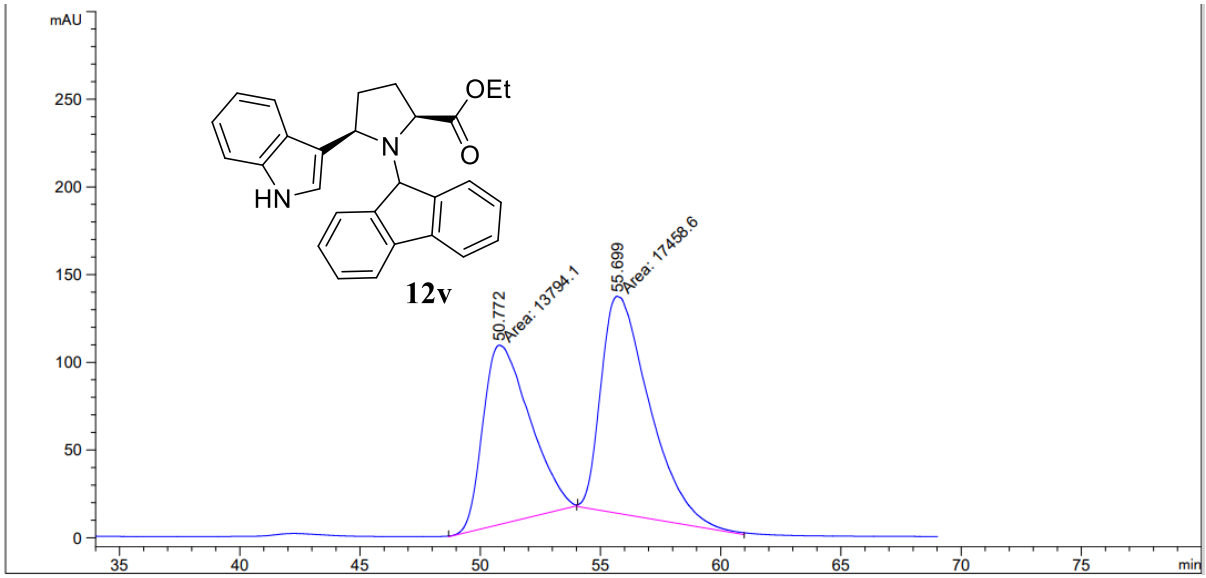
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.395	MM T	0.4224	119.39164	4.71080	0.2158
2	23.213	MM T	0.6423	5.52039e4	1432.46912	99.7842

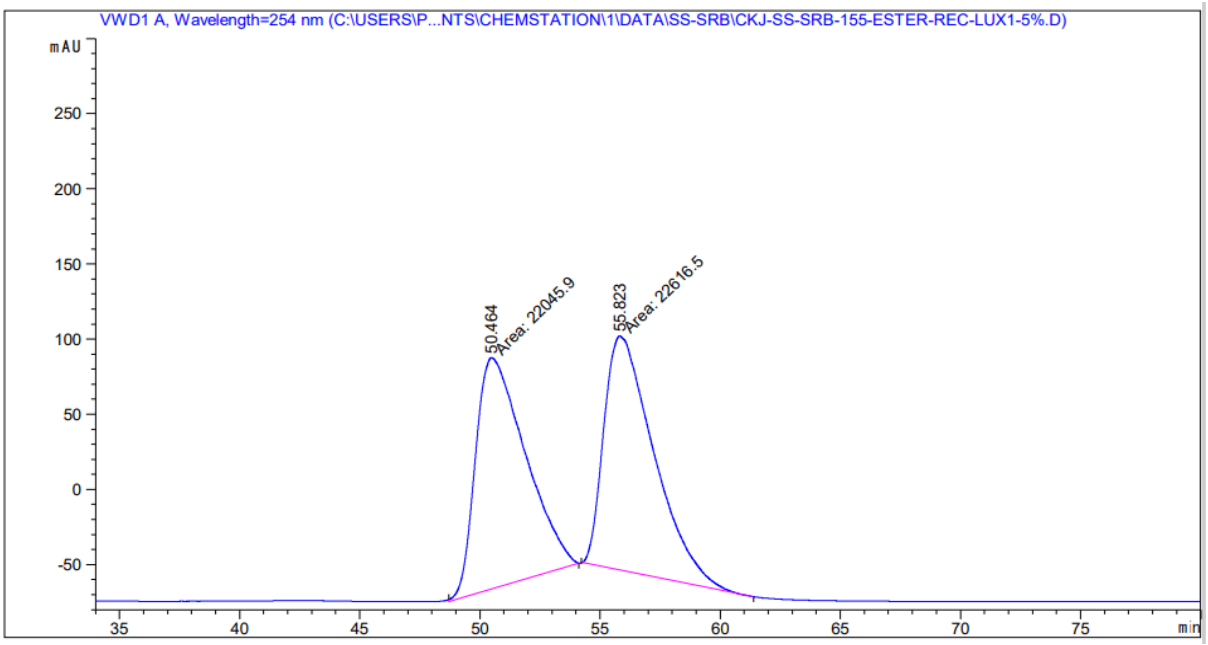


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.265	MM T	0.7829	1.85598e4	395.10114	48.8827
2	23.200	MM T	0.5687	1.94082e4	568.83203	51.1173

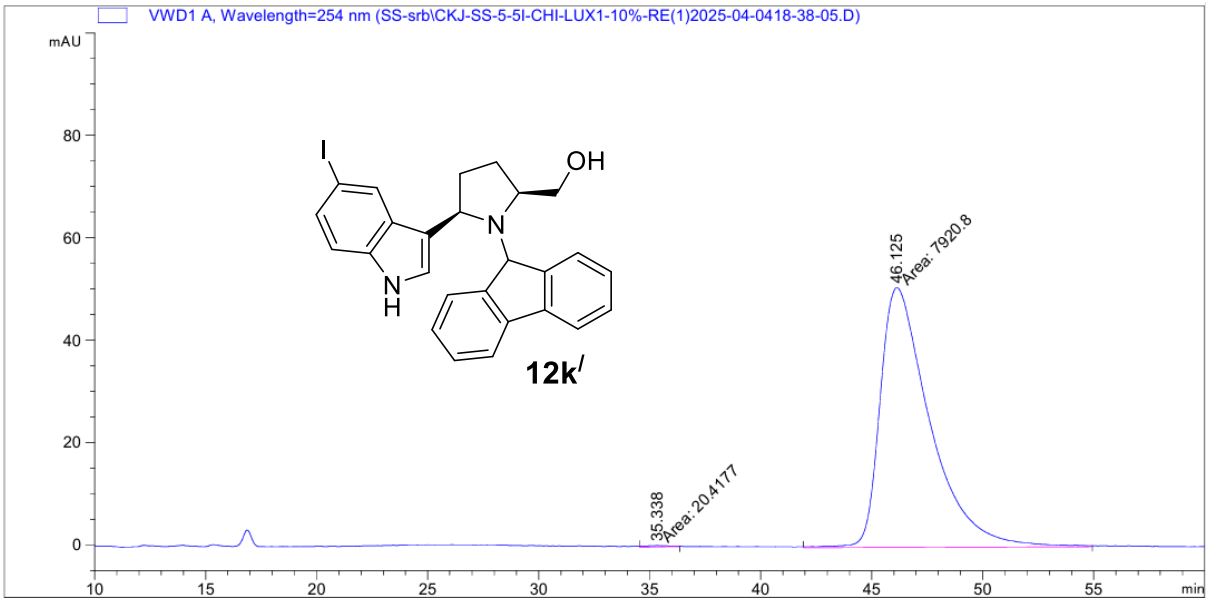


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	50.772	MM T	2.3790	1.37941e4	102.34458	44.1374
2	55.699	MM T	2.3527	1.74586e4	123.67685	55.8626



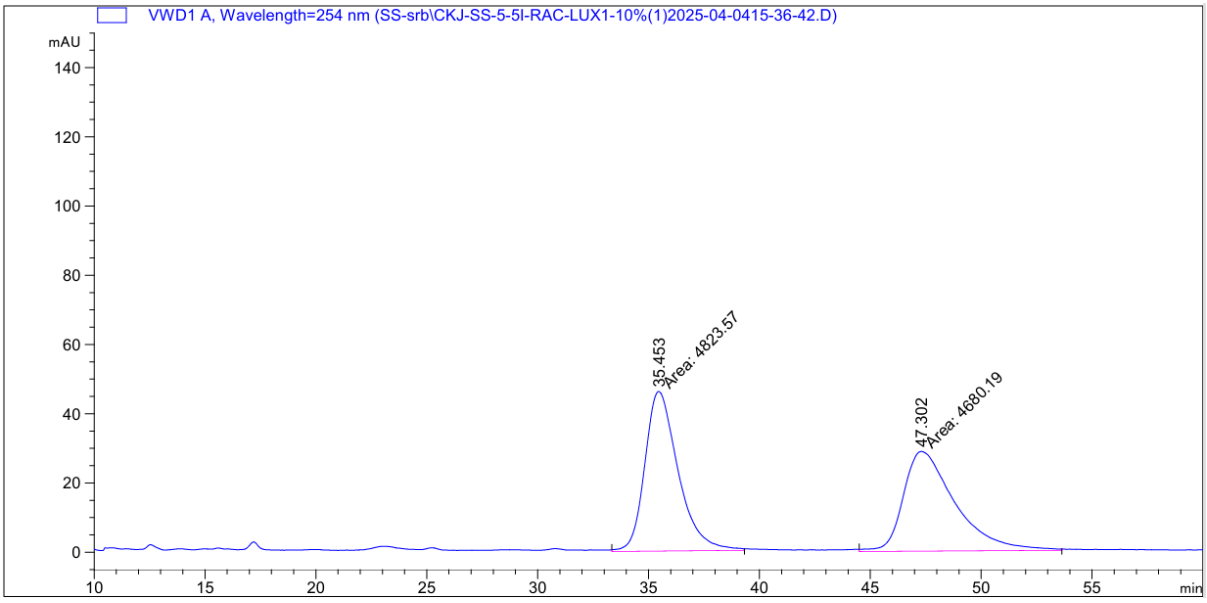
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	50.464	MM T	2.3856	2.20459e4	154.02017	49.3612
2	55.823	MM T	2.4207	2.26165e4	155.71281	50.6388



Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.338	MM T	1.3196	20.41767	2.57870e-1	0.2571
2	46.125	MM T	3.2226	7920.79541	50.73524	99.7429

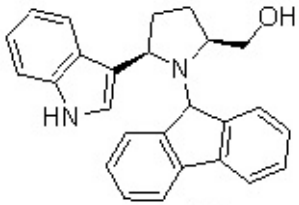


Signal 1: VWD1 A, Wavelength=254 nm

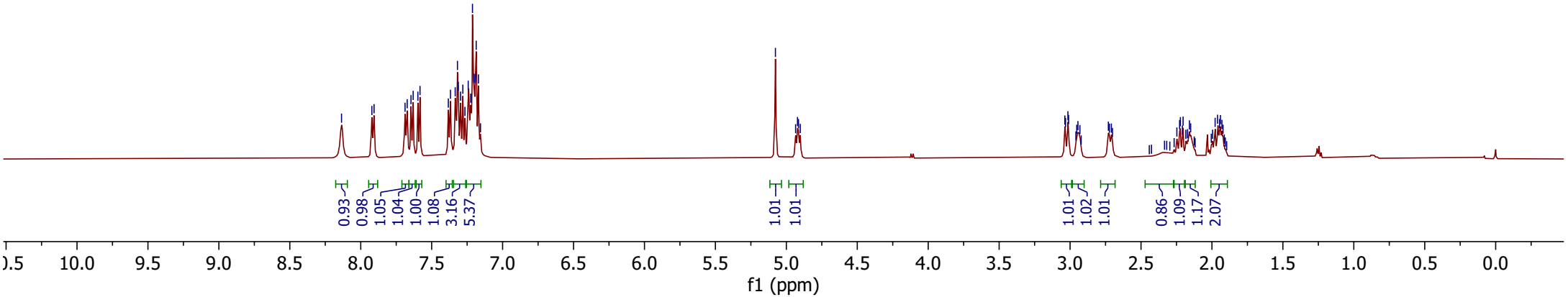
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.453	MM T	1.7437	4823.56689	46.10353	50.7543
2	47.302	MM T	2.8783	4680.19092	28.79363	49.2457

^{1}H NMR


8.1355
7.9215
7.9061
7.6875
7.6726
7.6457
7.6307
7.5972
7.5822
7.3825
7.3675
7.3342
7.3183
7.3124
7.2966
7.2804
7.2655
7.2424
7.2248
7.2124
7.2014
7.1933
7.1862
7.1705
7.1559
5.0770
4.9346
4.9214
4.9143
4.9019
3.0367
3.0320
3.0152
3.0103
2.9590
2.9530
2.9445
2.9307
2.9218
2.7301
2.7227
2.7089
2.7013
2.3342
2.3187
2.2665
2.2472
2.2279
2.2225
2.2083
2.2034
2.1840
2.1720
2.1589
2.1499
2.1250
2.1188
2.0046
1.9952
1.9776
1.9605
1.9462
1.9402
1.9297
1.9218
1.9131


OH
N
HN

12a

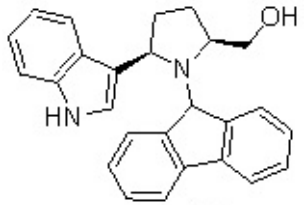

0.93
0.98
1.05
1.04
1.00
1.08
3.16
5.37
1.01
1.01
1.01
1.02
1.01
0.86
1.09
1.17
2.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

^{13}C NMR

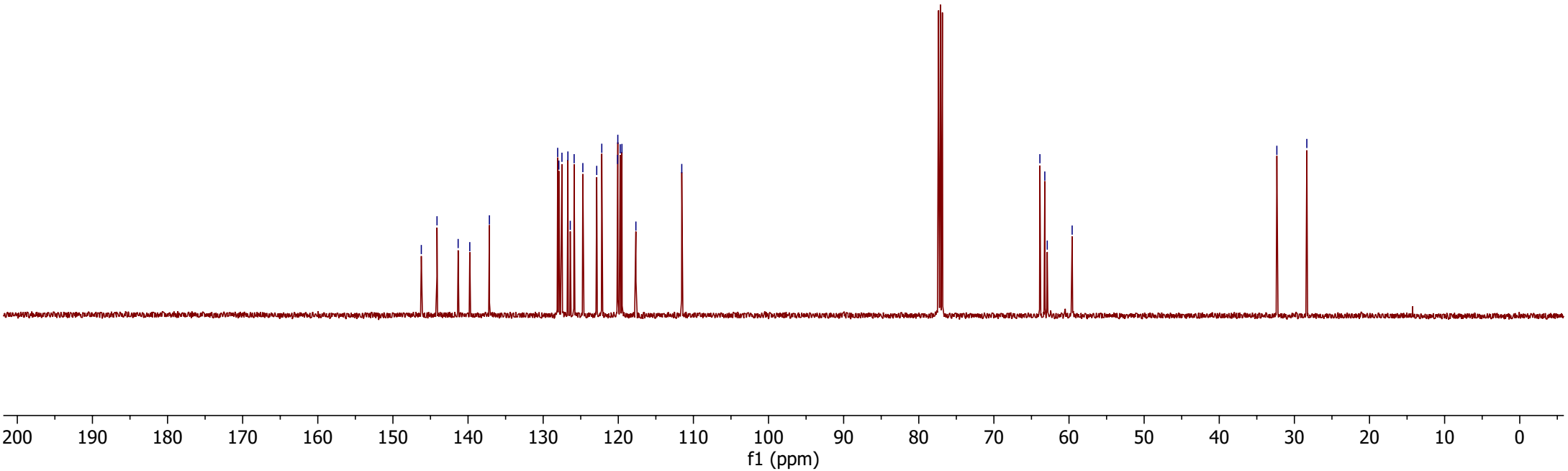
146.22
144.13
141.32
139.77
137.16
128.07
127.91
127.50
126.71
126.39
125.88
124.72
122.87
122.20
120.09
120.06
119.75
119.51
117.66
111.55

63.88
63.22
62.90
59.58

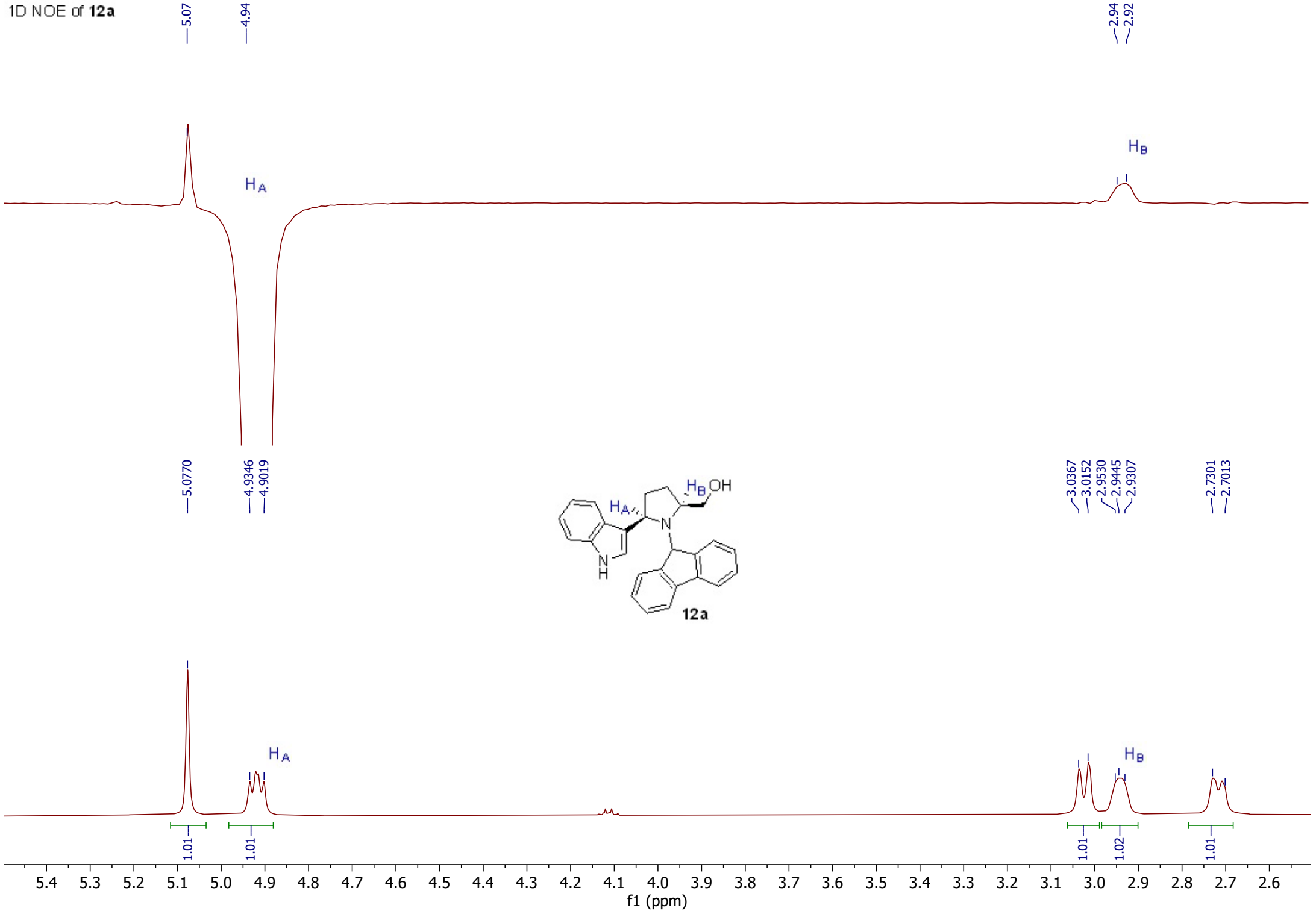
32.33
28.34



12a



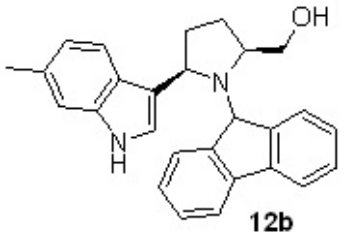
1D NOE of **12a**


5.07
4.94
2.94
2.92
H_A
H_B
5.0770
4.9346
4.9019
3.0367
3.0152
2.9530
2.9445
2.9307
2.7301
2.7013
H_BOH
H_A
N
H
12a
H_A
H_B
1.01
1.01
1.01
1.02
1.01
5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6
f1 (ppm)

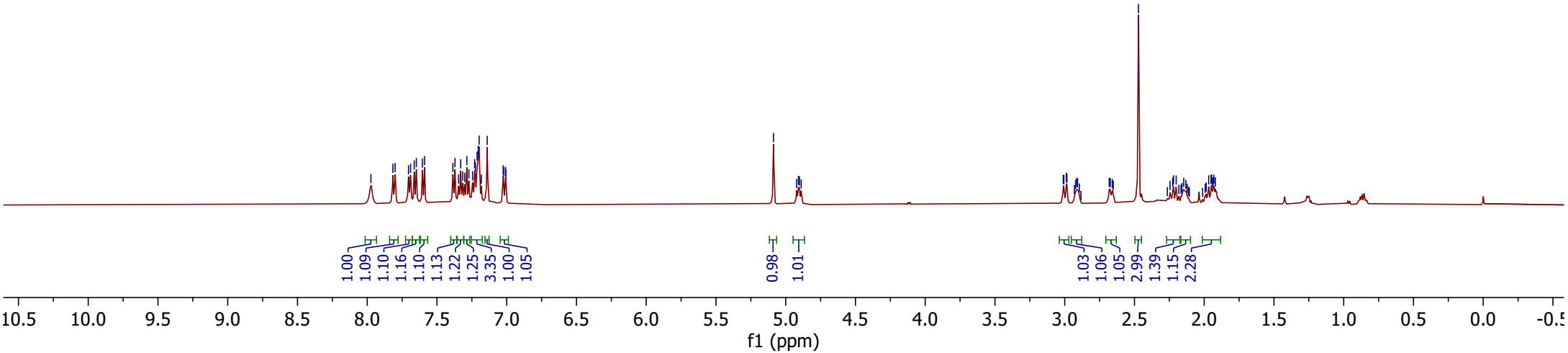
^{1}H NMR

7.973 7.816 7.800 7.704 7.689 7.663 7.648 7.604 7.589 7.386 7.371 7.345 7.330 7.315 7.301 7.286 7.271 7.245 7.230 7.224 7.212 7.204 7.198 7.182 7.140 7.026 7.023 7.009 7.006

5.088 4.921 4.909 4.901 4.889 3.011 3.006 2.989 2.984 2.931 2.922 2.914 2.908 2.895 2.884 2.681 2.673 2.659 2.652 2.471 2.264 2.245 2.226 2.220 2.201 2.182 2.166 2.160 2.147 2.131 2.123 2.113 2.107 2.011 1.993 1.986 1.968 1.951 1.947 1.940 1.937 1.931 1.920



12b

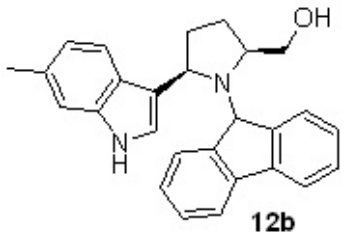


^{13}C NMR

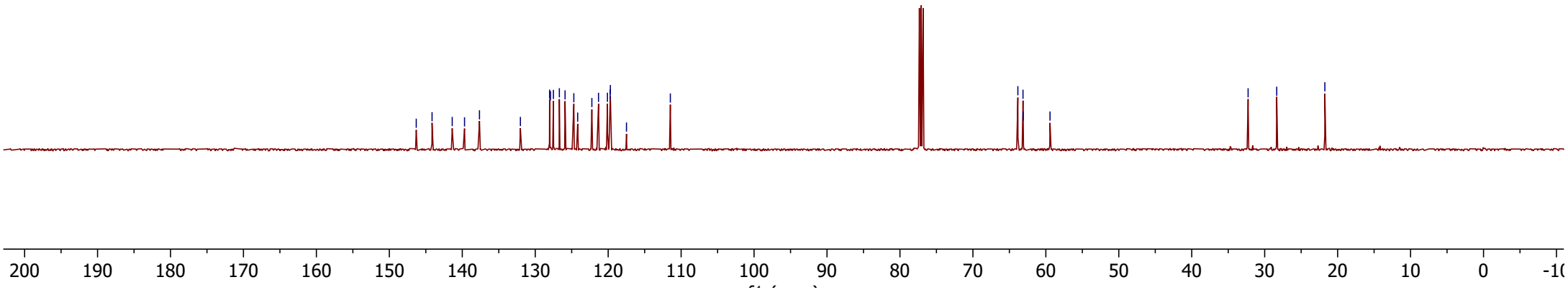
146.31
144.14
141.38
139.69
137.64
132.03
128.03
127.91
127.51
126.69
125.91
124.71
124.18
122.24
121.32
120.10
119.73
119.70
117.49
111.48

63.84
63.13
63.10
59.43

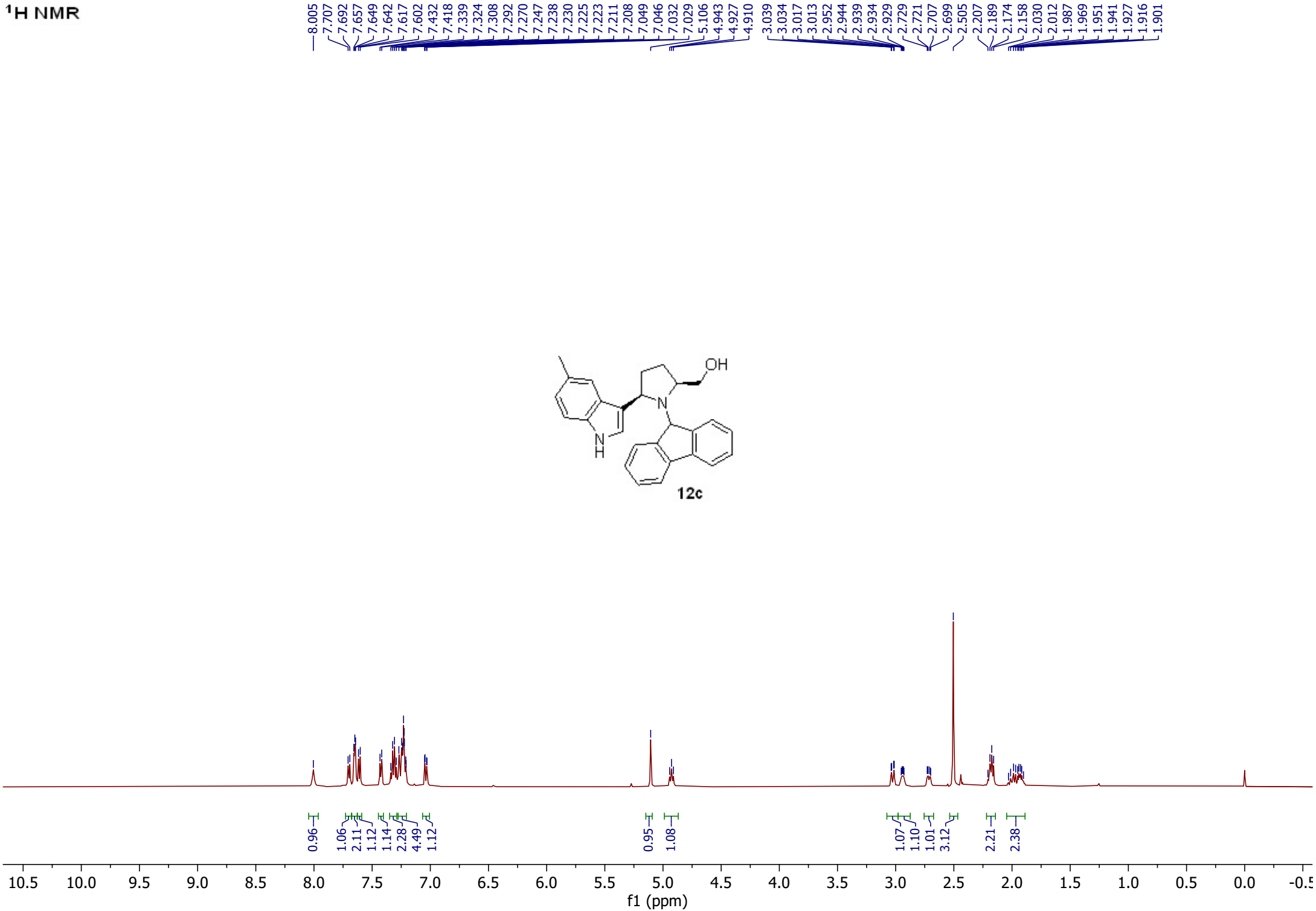
32.27
28.35
21.75



12b



^{1}H NMR

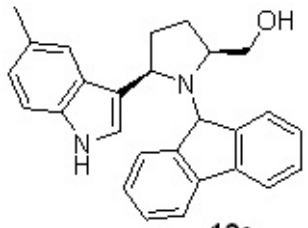

8.005
7.707
7.692
7.657
7.649
7.642
7.617
7.602
7.432
7.418
7.339
7.324
7.308
7.292
7.270
7.247
7.238
7.230
7.225
7.223
7.211
7.208
7.049
7.046
7.032
7.029
5.106
4.943
4.927
4.910
3.039
3.034
3.017
3.013
2.952
2.944
2.939
2.934
2.929
2.729
2.721
2.707
2.699
2.505
2.207
2.189
2.174
2.158
2.030
2.012
1.987
1.969
1.951
1.941
1.927
1.916
1.901
OH
N
H
12c
0.96
1.06
2.11
1.12
1.14
2.28
4.49
1.12
0.95
1.08
1.07
1.10
1.01
3.12
2.21
2.38
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

^{13}C NMR

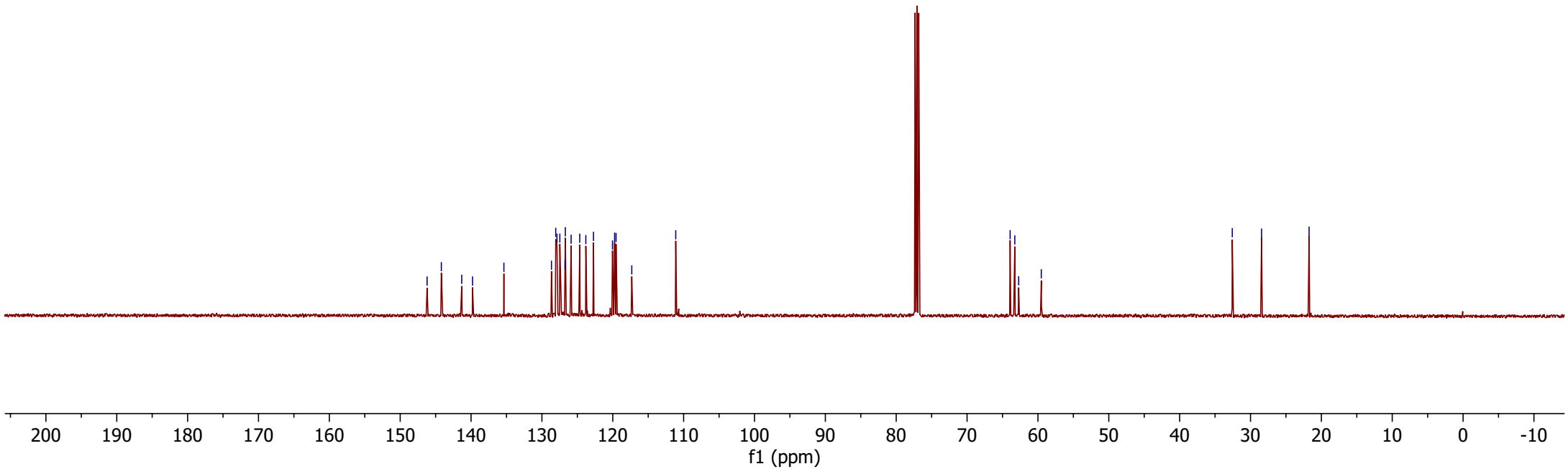
146.20
144.19
141.31
139.79
135.36
128.65
128.05
127.88
127.47
126.73
126.70
125.88
124.66
123.80
122.72
120.04
119.74
119.54
117.32
111.11

63.92
63.27
62.72
59.53

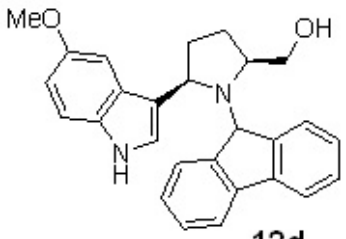
32.57
28.44
21.73



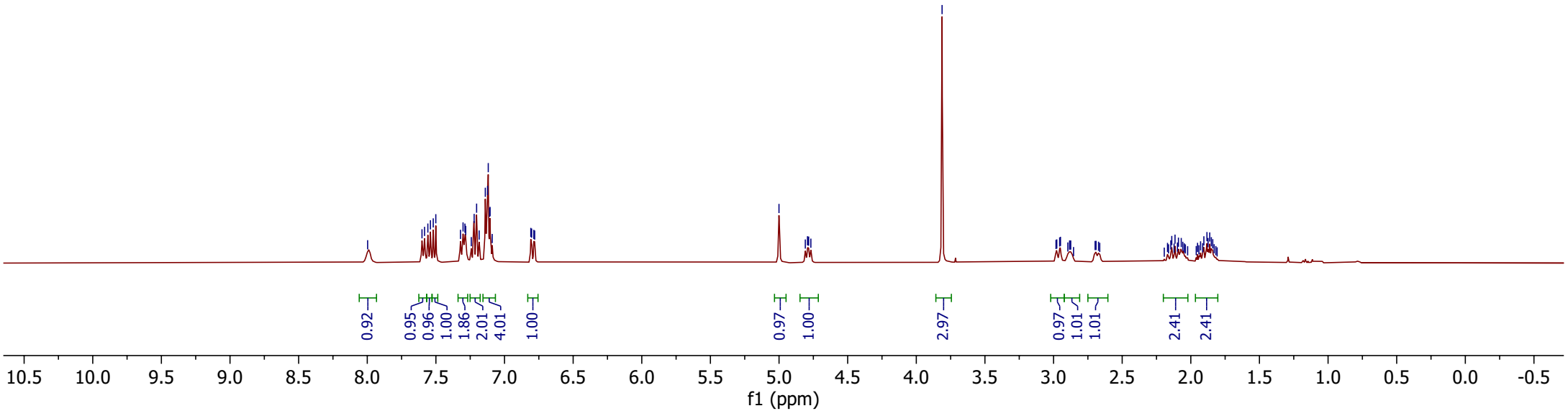
12c



^{1}H NMR

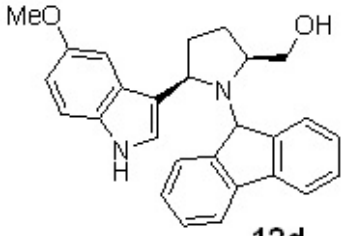

MeO
OH
N
N
H

12d

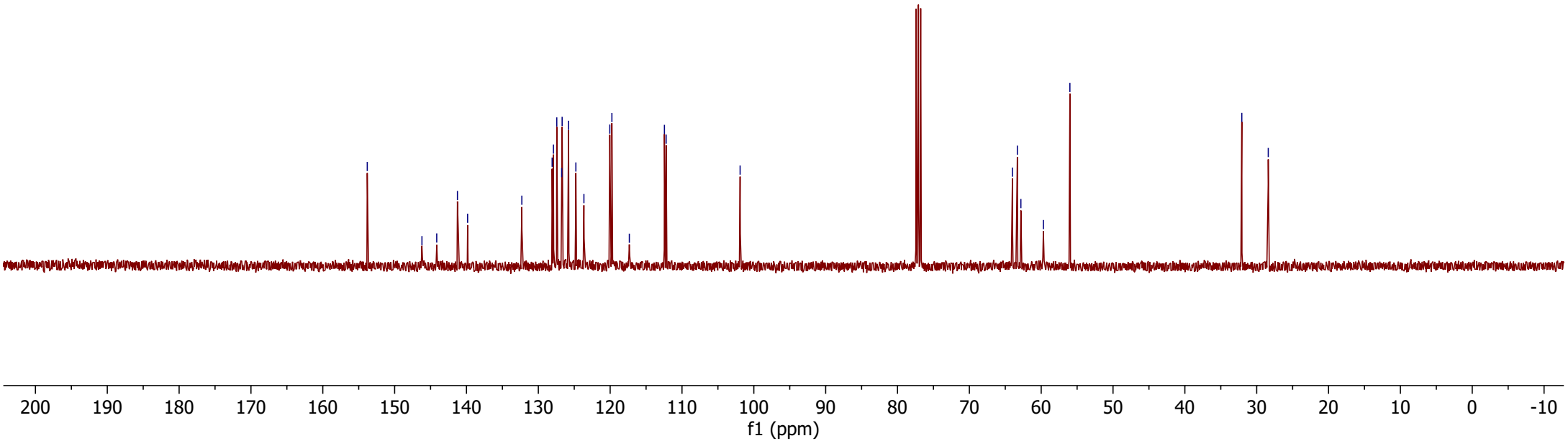

0.92
0.95
0.96
1.00
1.86
2.01
4.01
1.00
0.97
1.00
2.97
0.97
1.01
1.01
2.41
2.41
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

^{13}C NMR

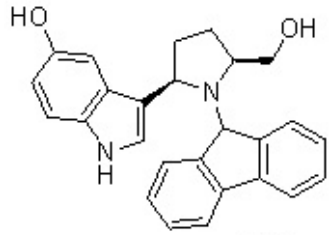
153.81
146.20
144.14
141.26
139.84
132.29
128.08
127.90
127.43
126.74
126.68
125.79
124.77
123.65
120.05
119.76
117.33
112.45
112.21
101.91
64.01
63.32
62.83
59.69
56.00
32.07
28.39



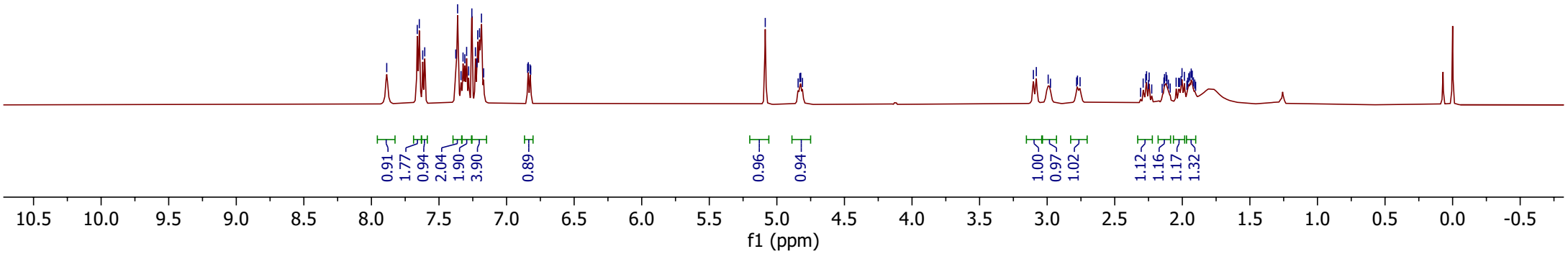
12d



^{1}H NMR

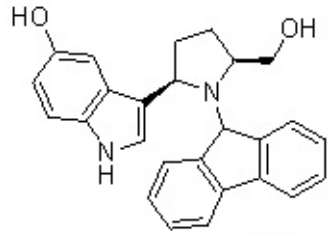

HO
OH
N
N
H

12e


0.91
1.77
0.94
2.04
1.90
3.90
0.89
0.96
0.94
1.00
0.97
1.02
1.12
1.16
1.17
1.32
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

^{13}C NMR

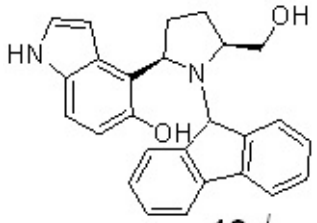
149.73
146.00
144.02
141.22
139.80
132.28
128.05
127.86
127.54
126.72
126.64
125.75
124.84
123.99
119.99
119.69
116.86
112.13
112.11
104.53
63.77
63.21
63.01
59.46
31.71
28.42



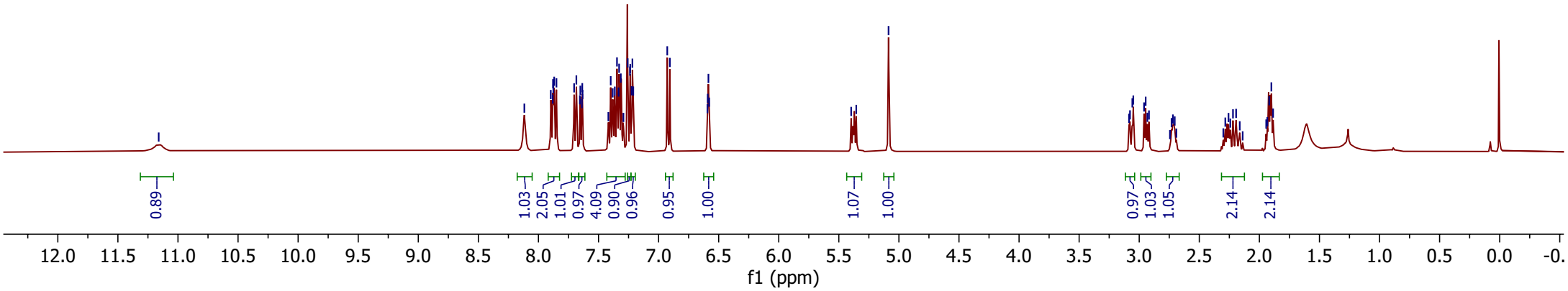
12e

^{1}H NMR

11.160 8.117 7.897 7.881 7.879 7.876 7.869 7.850 7.703 7.684 7.655 7.651 7.638 7.635 7.633 7.418 7.398 7.382 7.364 7.346 7.333 7.329 7.314 7.293 7.257 7.238 7.236 7.225 7.218 7.211 6.928 6.906 6.594 6.591 6.585 6.579 5.397 5.355 5.086 3.085 3.077 3.057 3.049 2.960 2.946 2.932 2.919 2.744 2.731 2.720 2.704 2.691 2.300 2.284 2.257 2.242 2.220 2.194 2.163 2.139 1.943 1.934 1.918 1.900 1.886

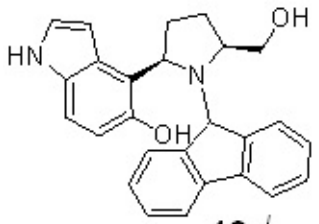


12e'

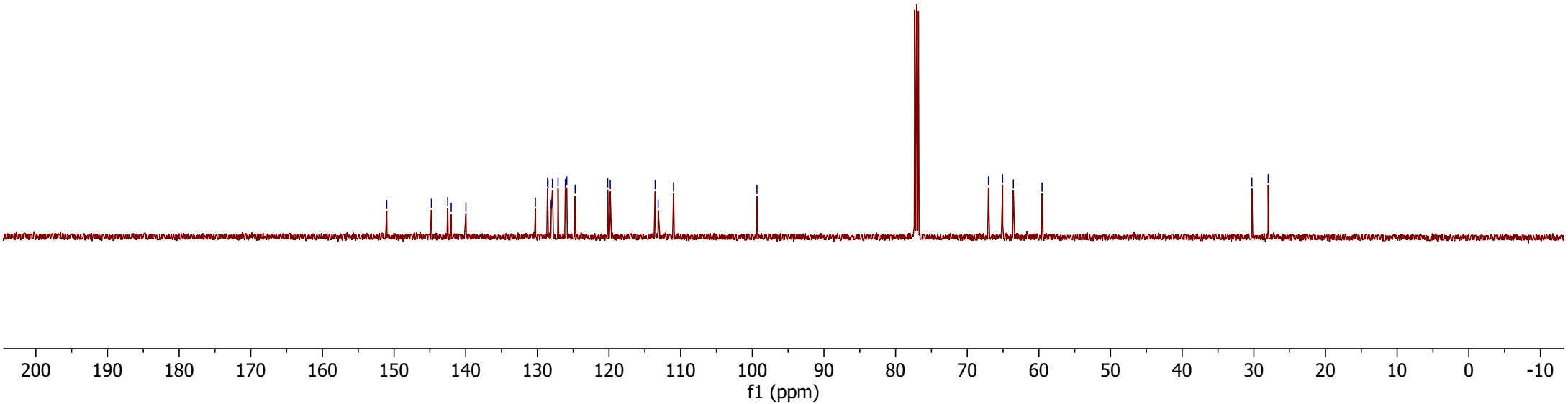


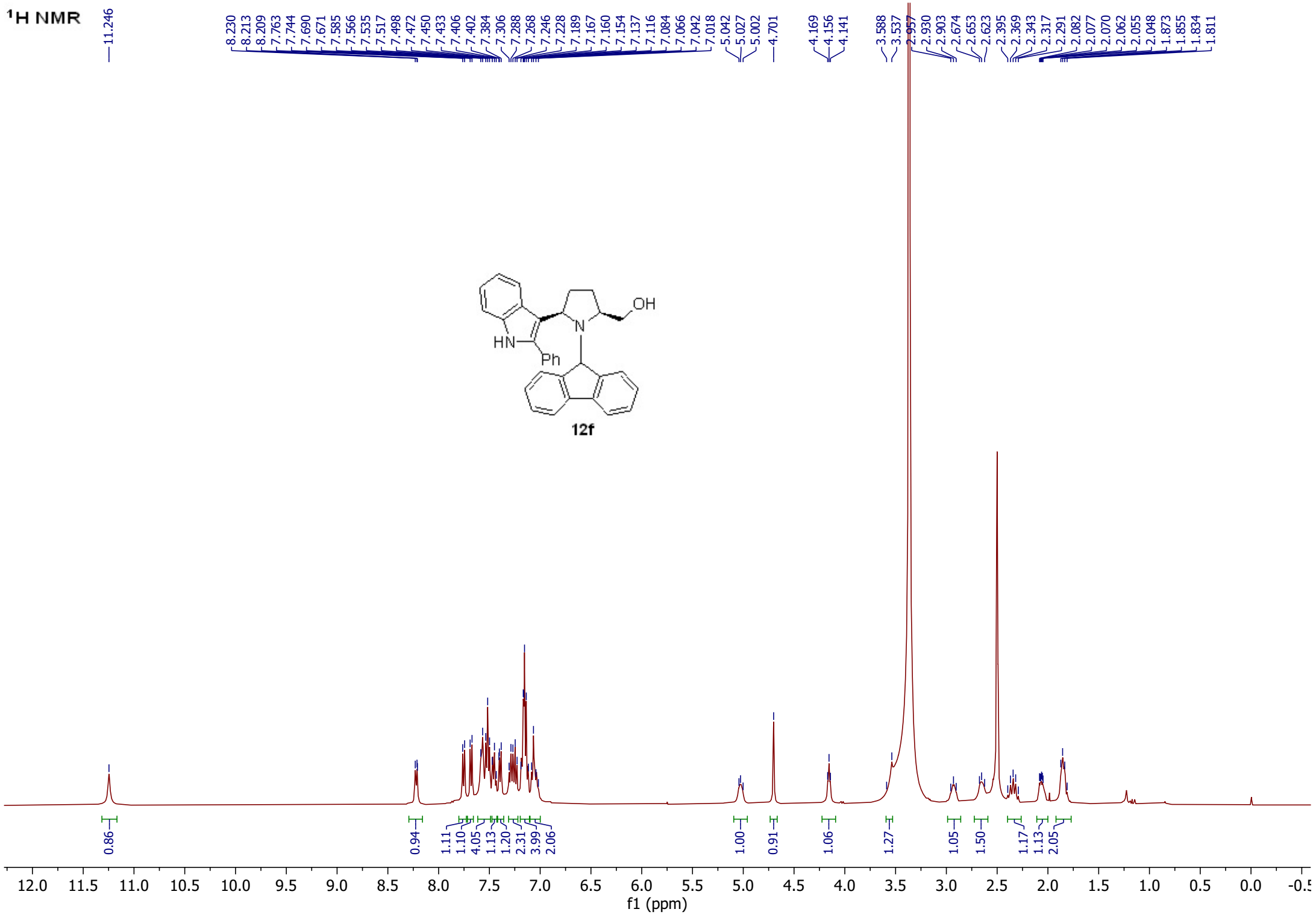
^{13}C NMR

151.03
144.79
142.51
142.03
139.97
130.28
128.58
128.52
128.06
127.90
127.12
126.10
125.90
124.73
120.19
119.83
113.55
113.14
111.00
99.35
67.04
65.06
63.56
59.56
30.27
27.99



12e



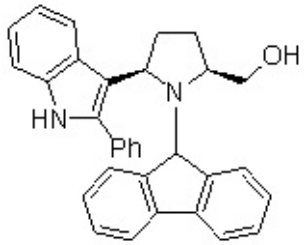

^{1}H NMR
11.246
8.230
8.213
8.209
7.763
7.744
7.690
7.671
7.585
7.566
7.535
7.517
7.498
7.472
7.450
7.433
7.406
7.402
7.384
7.306
7.288
7.268
7.246
7.228
7.189
7.167
7.160
7.154
7.137
7.116
7.084
7.066
7.042
7.018
5.042
5.027
5.002
4.701
4.169
4.156
4.141
3.588
3.537
2.957
2.930
2.903
2.674
2.653
2.623
2.395
2.369
2.343
2.317
2.291
2.082
2.077
2.070
2.062
2.055
2.048
1.873
1.855
1.834
1.811
OH
N
HN
Ph
12f
0.86
0.94
1.11
1.10
4.05
1.13
1.20
2.31
3.99
2.06
1.00
0.91
1.06
1.27
1.05
1.50
1.17
1.13
2.05
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

^{13}C NMR

146.776
144.186
140.835
138.912
137.569
136.683
132.733
129.019
128.554
127.808
127.730
127.665
126.849
126.739
126.578
125.643
125.168
121.484
121.232
120.143
119.664
118.418
111.531
111.472

65.172
62.747
61.433
59.548

29.935
27.995



12f

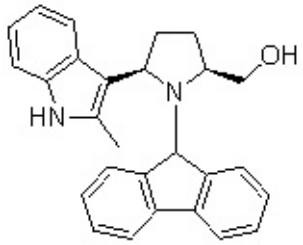
f1 (ppm)

^{1}H NMR

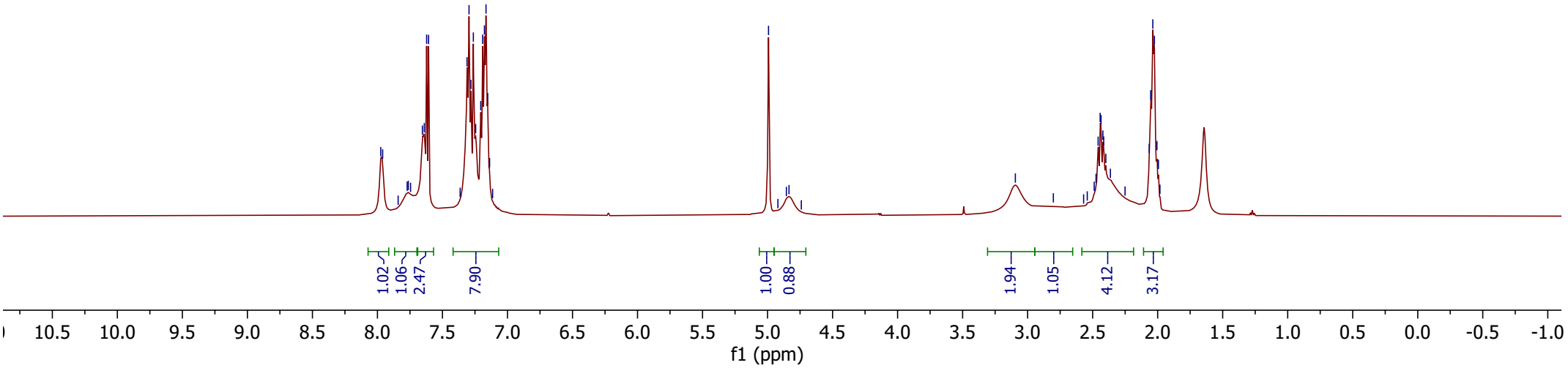
7.974 7.960 7.841 7.771 7.763 7.745 7.654 7.640 7.622 7.607 7.364 7.311 7.296 7.281 7.262 7.245 7.206 7.191 7.177 7.165 7.152 7.138 7.114

4.993 4.920 4.855 4.835 4.740

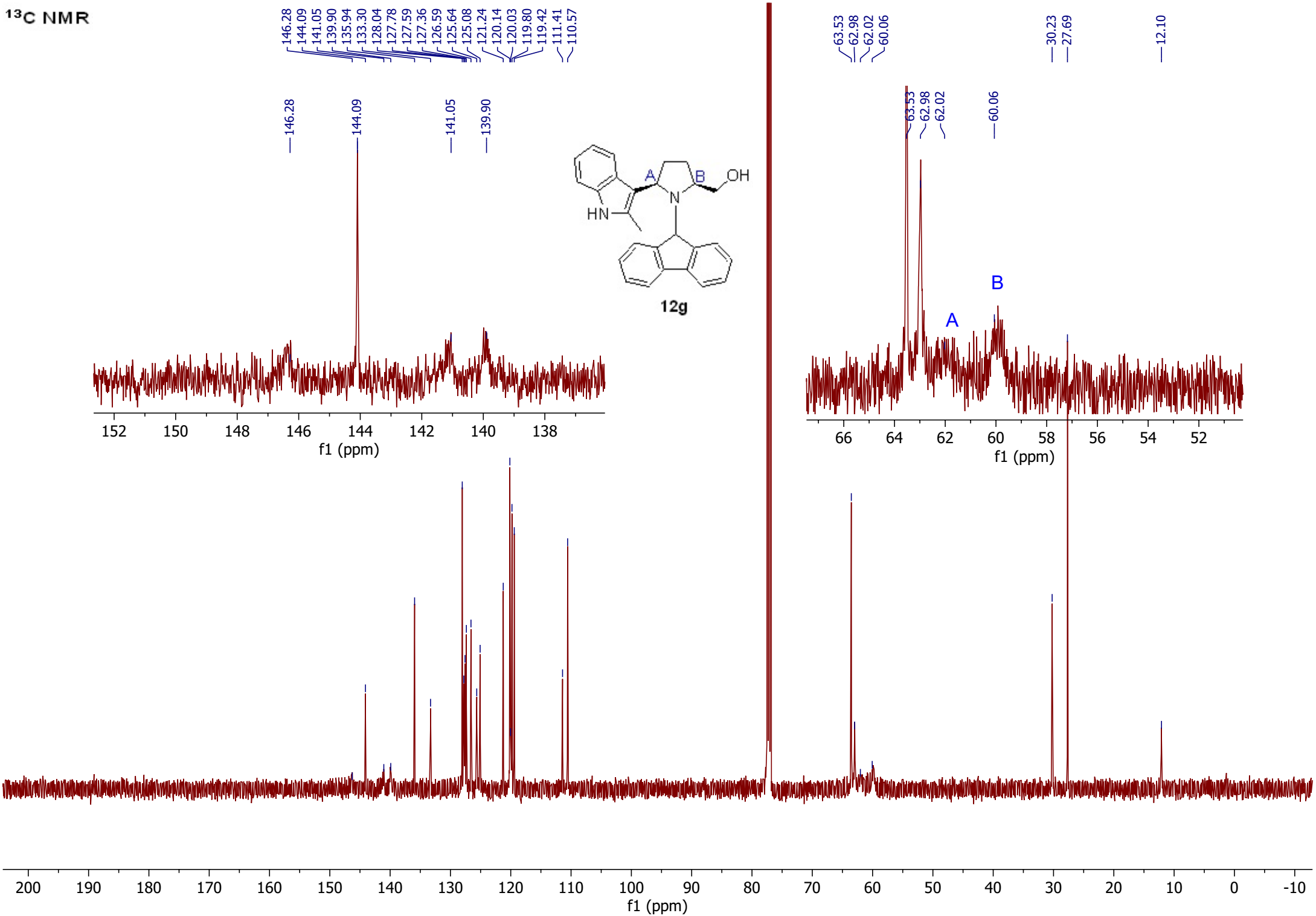
3.094 2.802 2.570 2.541 2.488 2.474 2.458 2.442 2.436 2.421 2.415 2.399 2.363 2.251 2.065 2.053 2.037 2.025 2.006 1.994 1.983

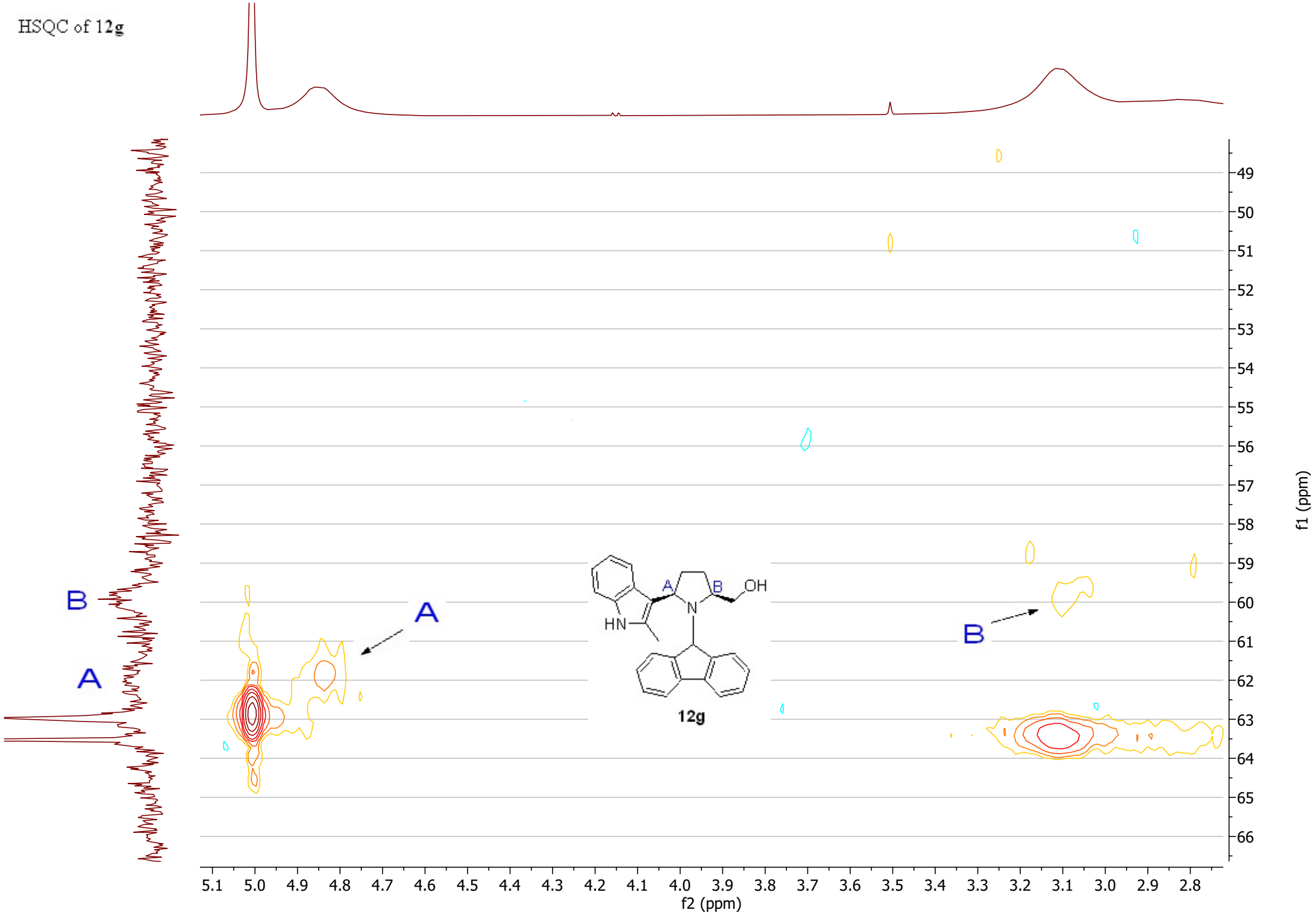


12g

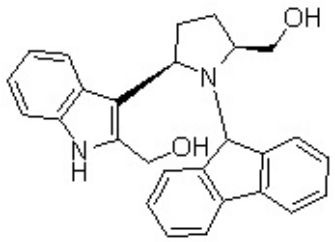


^{13}C NMR


146.28
144.09
141.05
139.90
135.94
133.30
128.04
127.78
127.59
127.36
126.59
125.64
125.08
121.24
120.14
120.03
119.80
119.42
111.41
110.57
63.53
62.98
62.02
60.06
30.23
27.69
12.10
A
B
OH
N
HN
12g
f1 (ppm)
f1 (ppm)
f1 (ppm)


HSQC of 12g
B
A
A
B
A
B
OH
HN
N
12g
5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8
f2 (ppm)
49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66
f1 (ppm)

^{1}H NMR



12h

f1 (ppm)

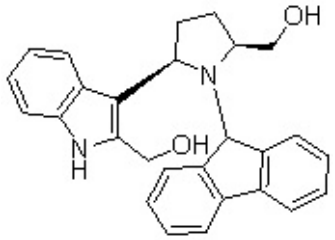
^{13}C NMR

147.06
144.79
140.74
139.04
137.84
135.98
127.70
127.60
126.85
126.71
125.80
125.66
120.70
120.37
120.07
119.65
118.03
111.31
110.69

65.25
62.95
61.09
59.65
54.96

39.53

30.11
28.01



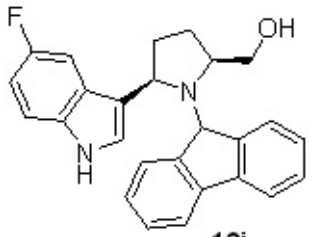
12h

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

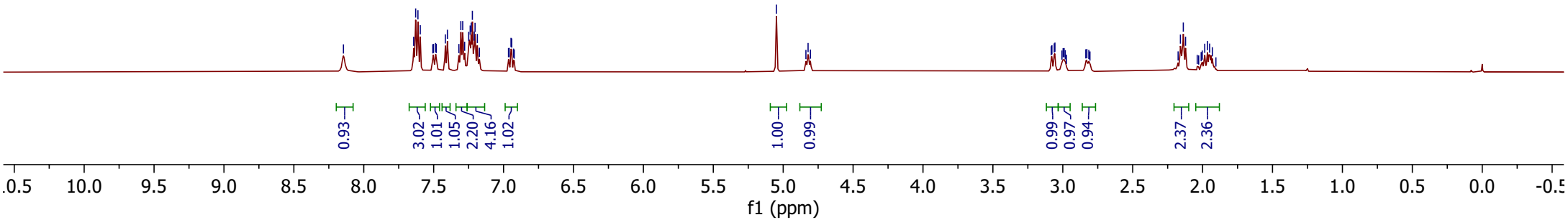
f1 (ppm)

^{1}H NMR

8.145 7.643 7.629 7.612 7.596 7.506 7.501 7.486 7.481 7.417 7.402 7.320 7.306 7.292 7.279 7.249 7.239 7.231 7.223 7.210 7.204 7.188 7.173 6.965 6.960 6.947 6.942 6.929 6.924 5.049 4.837 4.822 4.805 3.083 3.078 3.061 3.056 3.006 2.998 2.991 2.983 2.974 2.835 2.828 2.814 2.806 2.175 2.159 2.138 2.122 2.039 2.028 2.010 2.003 1.985 1.965 1.950 1.930 1.905

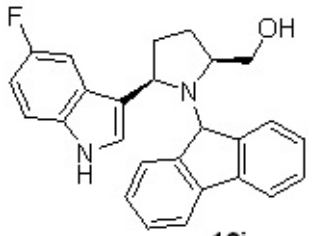


12i

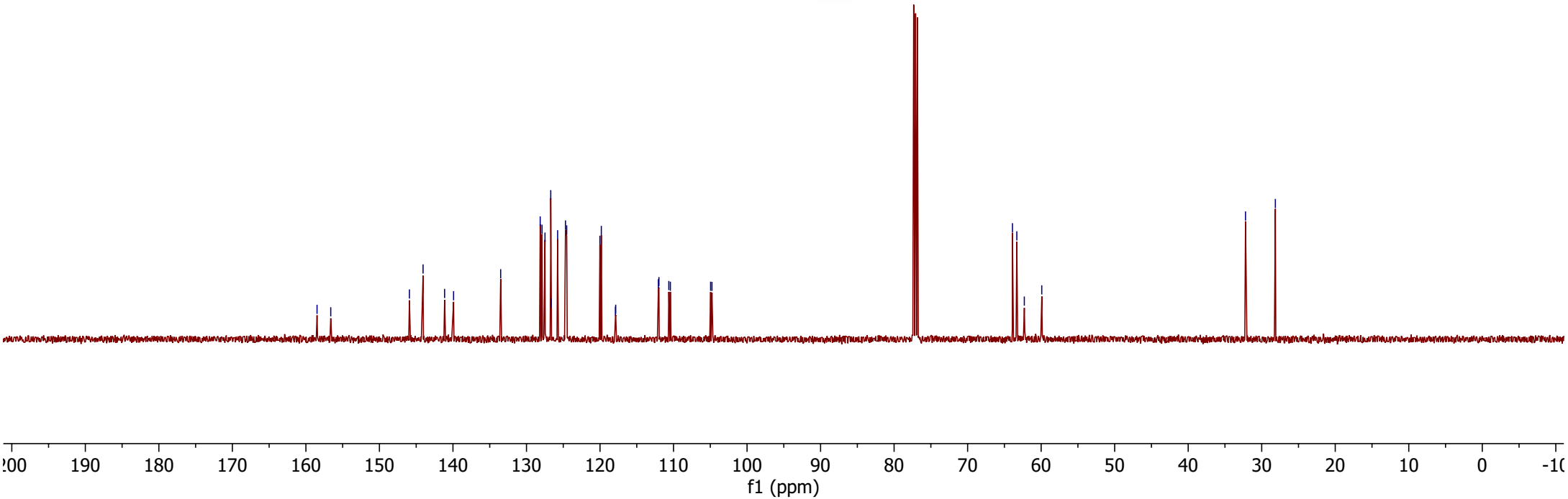


^{13}C NMR

158.485
156.621
145.921
144.065
141.135
139.916
133.510
128.132
127.884
127.483
126.700
126.626
125.763
124.696
124.529
120.012
119.821
117.903
117.865
112.061
111.986
110.641
110.430
104.956
104.772
63.900
63.309
62.289
59.915
32.203
28.147



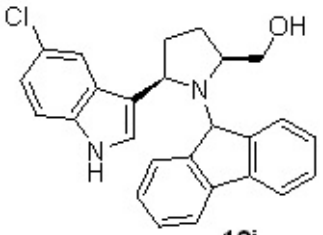
12i



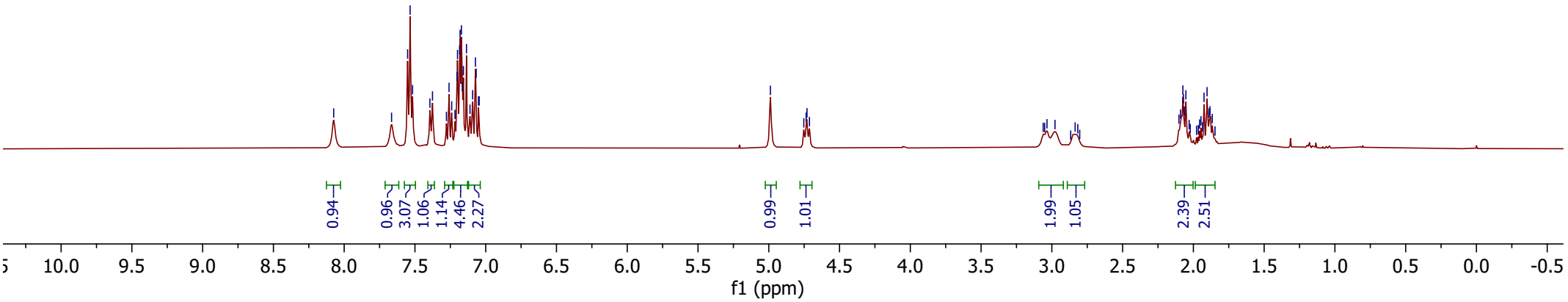
^{1}H NMR

8.074 7.665 7.552 7.534 7.517 7.394 7.376 7.278 7.259 7.240 7.217 7.203 7.199 7.184 7.181 7.172 7.165 7.157 7.136 7.111 7.092 7.073 7.067 7.051 7.046 4.988 4.752 4.736 4.730 4.713

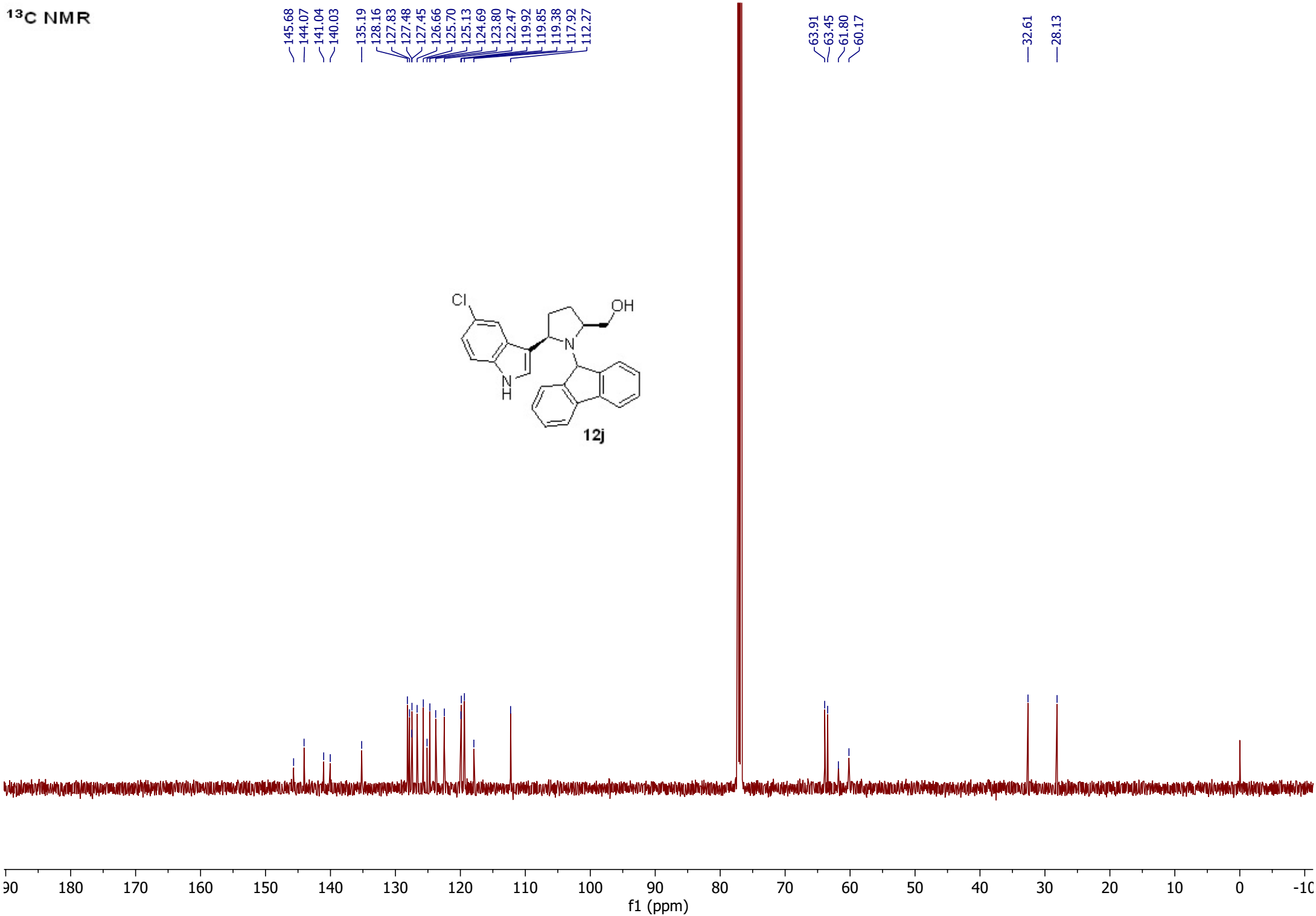
3.061 3.051 3.034 2.978 2.867 2.835 2.816 2.803 2.102 2.091 2.074 2.070 2.064 2.053 2.030 2.022 1.978 1.965 1.956 1.946 1.935 1.925 1.903 1.888 1.882 1.866 1.847



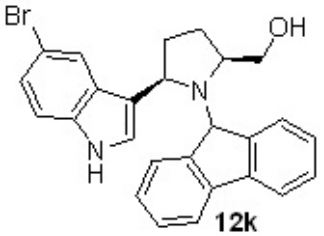
12j



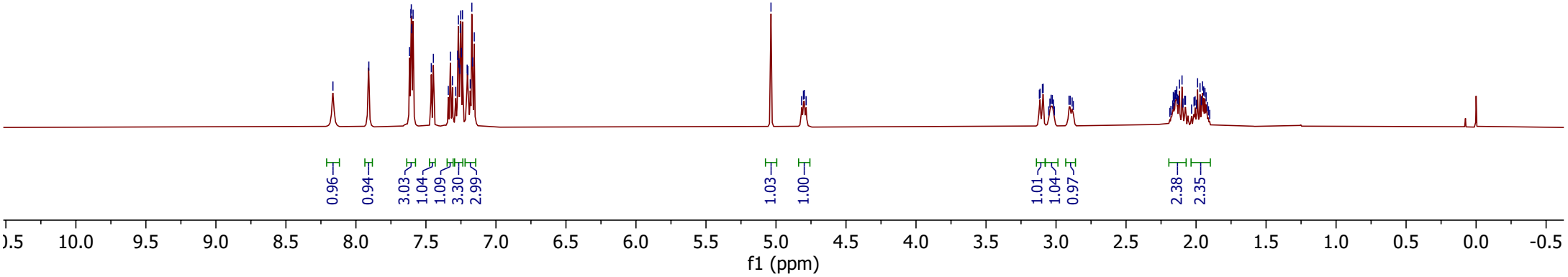
^{13}C NMR


145.68
144.07
141.04
140.03
135.19
128.16
127.83
127.48
127.45
126.66
125.70
125.13
124.69
123.80
122.47
119.92
119.85
119.38
117.92
112.27
63.91
63.45
61.80
60.17
32.61
28.13
Cl
OH
N
N
H
12j
f1 (ppm)

^{1}H NMR


Br
OH
N
H
N

12k

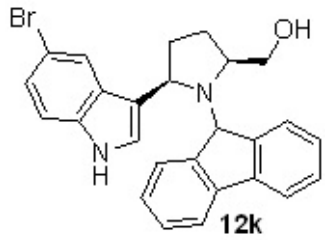

0.96
0.94
3.03
1.04
1.09
3.30
2.99
1.03
1.00
1.01
1.04
0.97
2.38
2.35
f1 (ppm)

^{13}C NMR

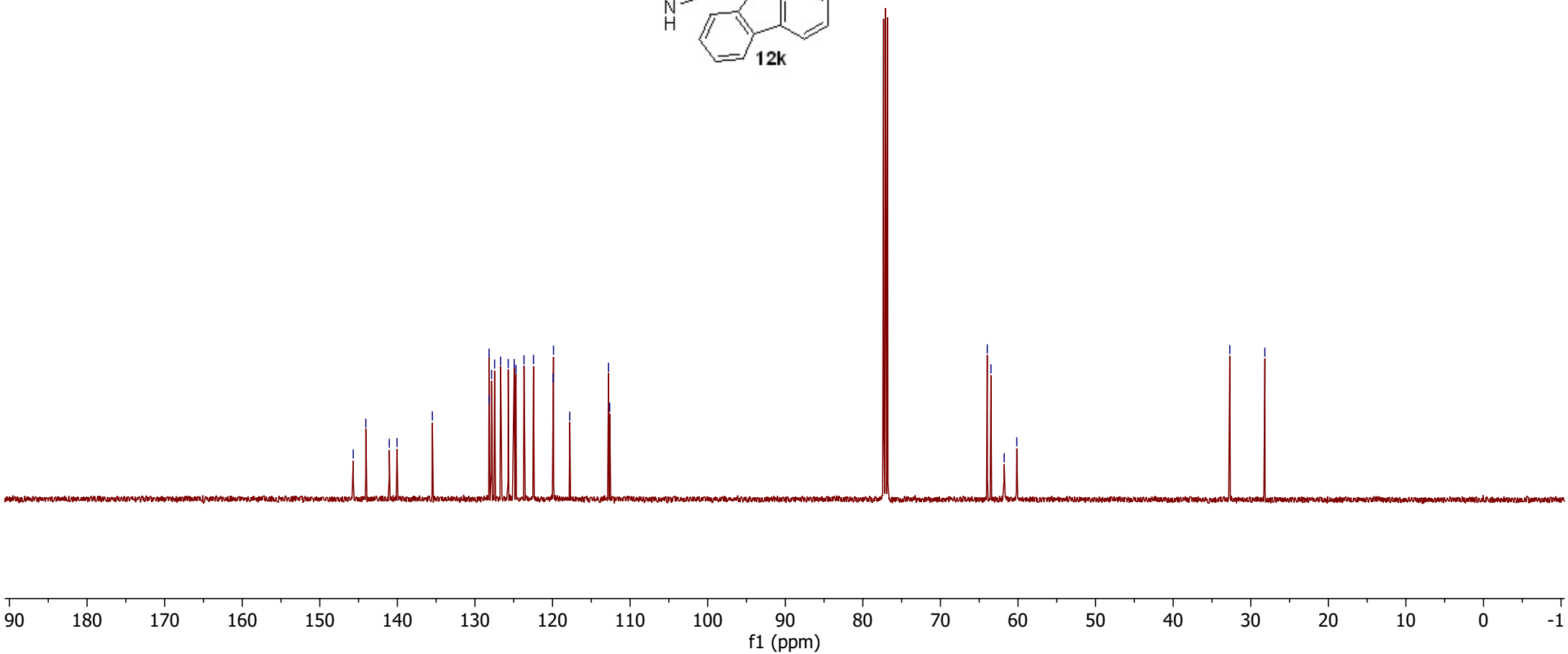
145.69
144.06
141.04
140.05
135.49
128.18
128.16
127.86
127.47
126.69
125.71
124.94
124.71
123.68
122.45
119.93
119.87
117.77
112.78
112.63

63.96
63.49
61.78
60.16

32.70
28.18



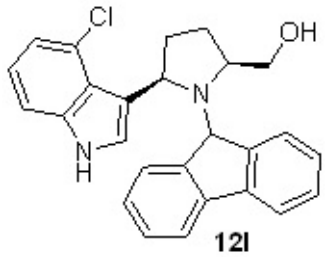
12k



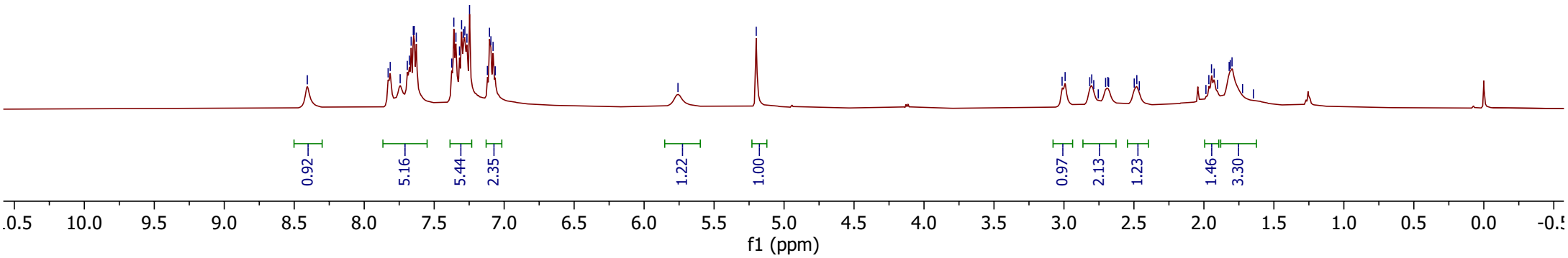
^{1}H NMR

8.407 7.829 7.814 7.743 7.692 7.678 7.664 7.649 7.642 7.628 7.375 7.360 7.345 7.319 7.304 7.290 7.281 7.266 7.247 7.120 7.105 7.095 7.079 7.064 5.758 5.199

3.013 2.992 2.816 2.802 2.787 2.755 2.702 2.686 2.681 2.498 2.479 2.461 1.986 1.965 1.946 1.927 1.902 1.820 1.812 1.799 1.724 1.646

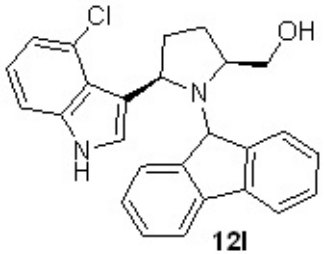


12l



^{13}C NMR

146.23
144.37
141.58
140.03
138.18
128.37
128.15
127.50
127.18
126.20
126.06
124.43
124.38
122.62
120.95
120.13
120.02
110.27
64.68
64.17
62.19
59.53
36.09
28.91

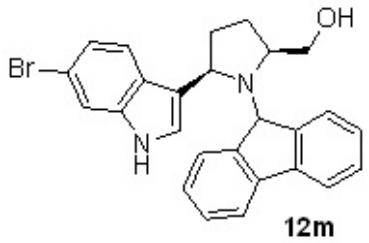


12l

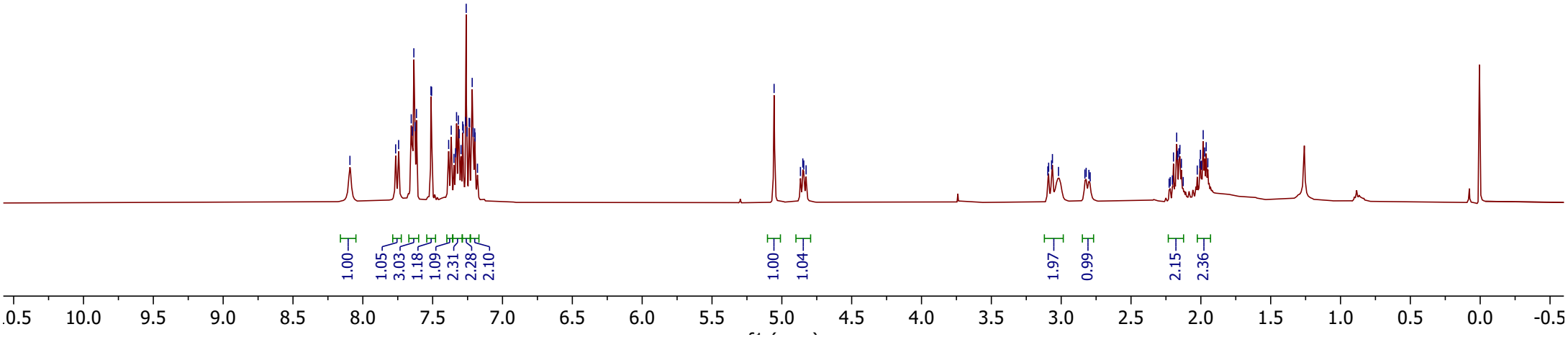
f1 (ppm)

^{1}H NMR


8.092
7.765
7.744
7.653
7.646
7.635
7.627
7.616
7.512
7.508
7.386
7.367
7.347
7.336
7.329
7.316
7.311
7.297
7.285
7.281
7.264
7.260
7.254
7.239
7.236
7.217
7.210
7.199
7.196
7.179
5.056
4.867
4.850
4.843
4.826
3.096
3.090
3.069
3.063
3.019
2.830
2.821
2.802
2.792
2.227
2.219
2.204
2.196
2.173
2.167
2.157
2.150
2.139
2.126
2.026
2.007
2.003
1.995
1.983
1.973
1.962
1.950

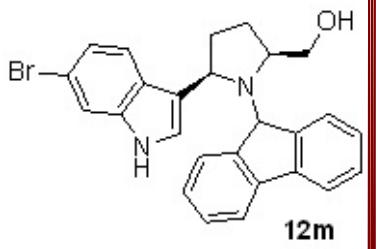

Br
OH
N
H

12m


1.00
1.05
3.03
1.18
1.09
2.31
2.28
2.10
1.00
1.04
1.97
0.99
2.15
2.36
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

^{13}C NMR

145.80
143.92
141.14
139.89
137.85
128.16
127.91
127.48
126.68
125.72
125.16
124.66
123.41
122.78
121.29
120.03
119.82
118.02
115.73
114.36
63.73
63.28
62.37
59.94
32.21
28.12

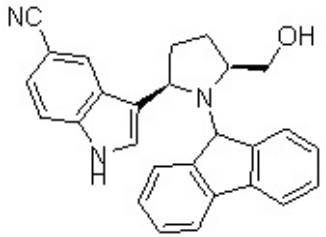


12m

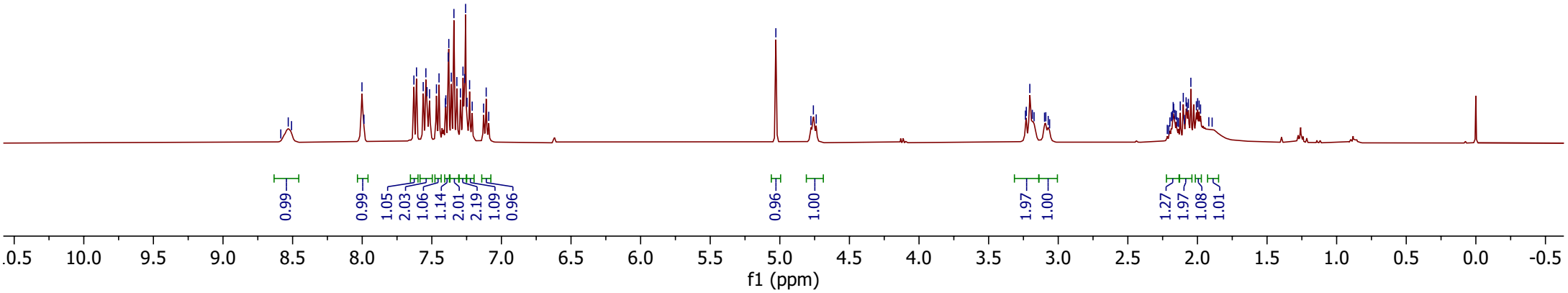
f1 (ppm)

^{1}H NMR

8.585 8.531 8.508 8.002 7.988 7.629 7.610 7.562 7.543 7.535 7.516 7.467 7.448 7.403 7.399 7.382 7.378 7.360 7.341 7.320 7.295 7.276 7.264 7.257 7.247 7.229 7.210 7.128 7.109 7.091 5.028 4.777 4.759 4.739 3.236 3.229 3.204 3.186 3.174 3.098 3.089 3.072 3.062 2.217 2.206 2.198 2.187 2.179 2.174 2.171 2.161 2.152 2.145 2.136 2.123 2.102 2.094 2.081 2.074 2.065 2.047 2.008 1.998 1.988 1.978 1.918 1.894

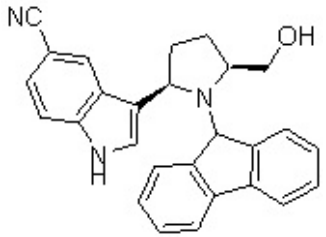


12n



^{13}C NMR

145.19
144.19
140.85
140.42
138.48
128.43
127.92
127.47
126.78
126.34
125.64
125.51
125.03
124.89
124.67
120.99
120.10
119.90
119.33
112.24
102.42
64.11
63.84
61.01
60.75
33.07
28.21



12n

f1 (ppm)

^{1}H NMR

8.759
7.882
7.867
7.797
7.781
7.752
7.738
7.710
7.705
7.693
7.676
7.659
7.641
7.626
7.614
7.605
7.578
7.562
7.518
7.506
7.492
7.365
7.350
7.335
7.304
7.290
7.274
7.253
7.220
7.205
7.189
5.550
5.107
3.095
3.091
3.073
2.988
2.953
2.933
2.897
2.851
2.845
2.784
2.501
2.478
2.052
2.045
2.033
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2.015
2.009
1.998
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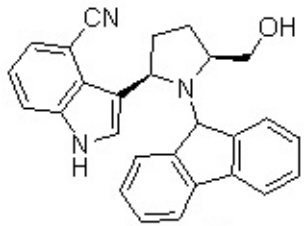
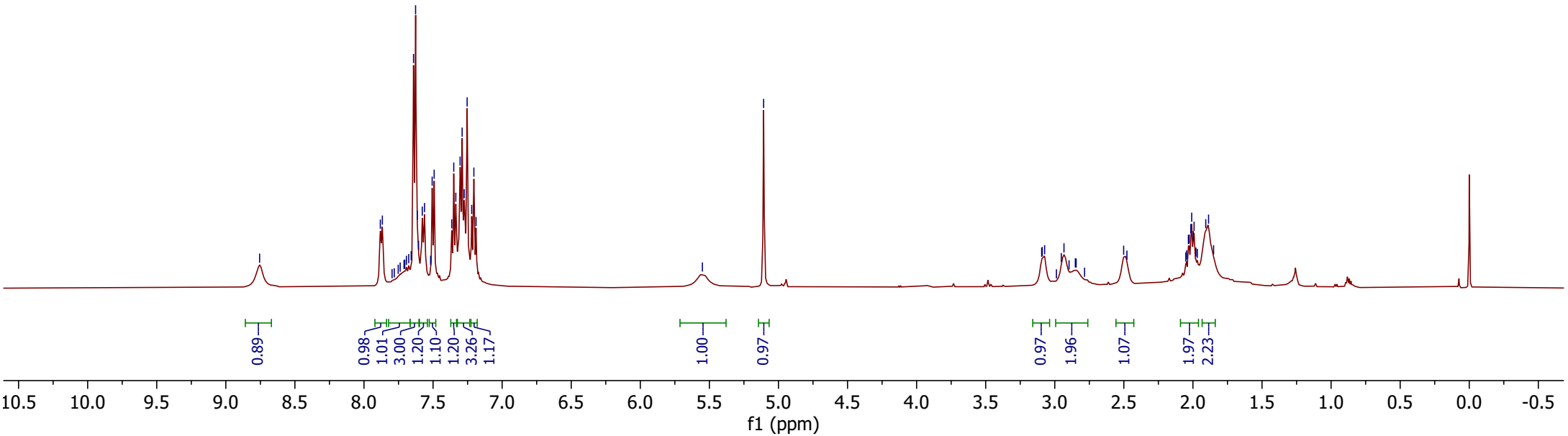
1.979
1.968
1.907
1.887
1.850

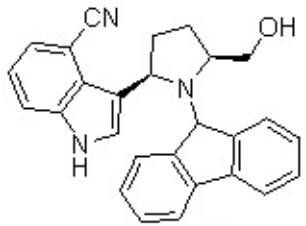


12o



^{13}C NMR

145.71
144.03
141.20
140.19
136.95
128.41
128.10
127.41
127.38
126.79
126.59
126.23
124.91
124.54
121.64
120.03
119.97
116.46
102.02
64.21
61.19
60.07
35.11
28.30

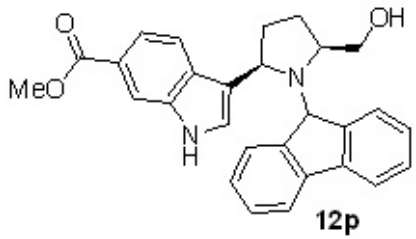


12o

f1 (ppm)

^{1}H NMR

8.620 8.122 7.895 7.873 7.860 7.839 7.638 7.619 7.600 7.401 7.382 7.331 7.313 7.305 7.294 7.286 7.268 7.260 7.233 7.215 7.196 7.187 7.169 7.150 5.054 4.892 4.875 4.869 4.853 3.953 3.131 3.104 3.057 2.882 2.855 2.236 2.213 2.190 2.179 2.161 2.077 2.054 2.022 2.002 1.981 1.949



12p

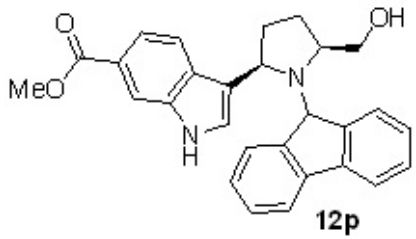
0.94 0.97 1.93 3.16 1.96 2.23 1.26 1.11 1.01 1.10 3.07 1.00 1.00 1.05 2.20 3.01

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.

f1 (ppm)

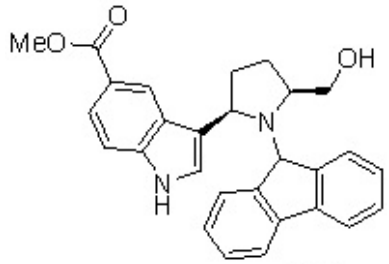
^{13}C NMR

168.30
145.73
143.97
141.06
139.97
136.37
129.94
128.17
127.89
127.44
126.69
126.29
125.69
124.72
123.72
120.44
119.98
119.83
119.53
118.24
113.87
63.82
63.41
62.12
60.10
52.02
32.39
28.16

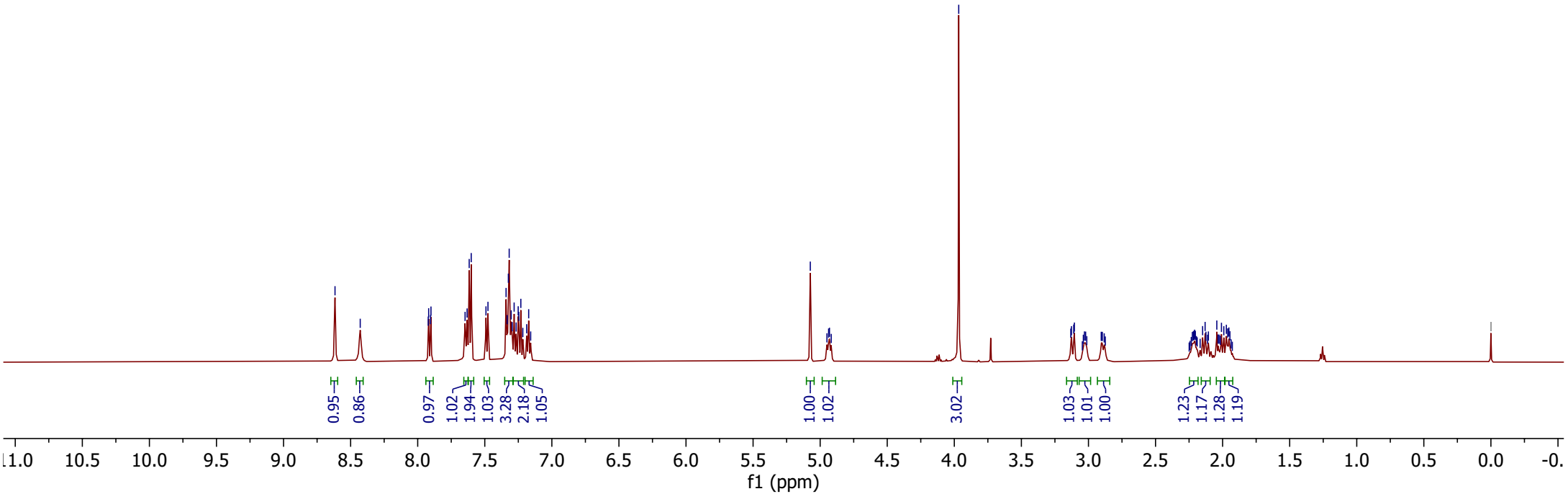


12p

^{1}H NMR

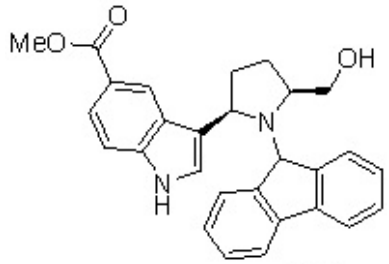

MeO
O
OH
N
H
N

12q

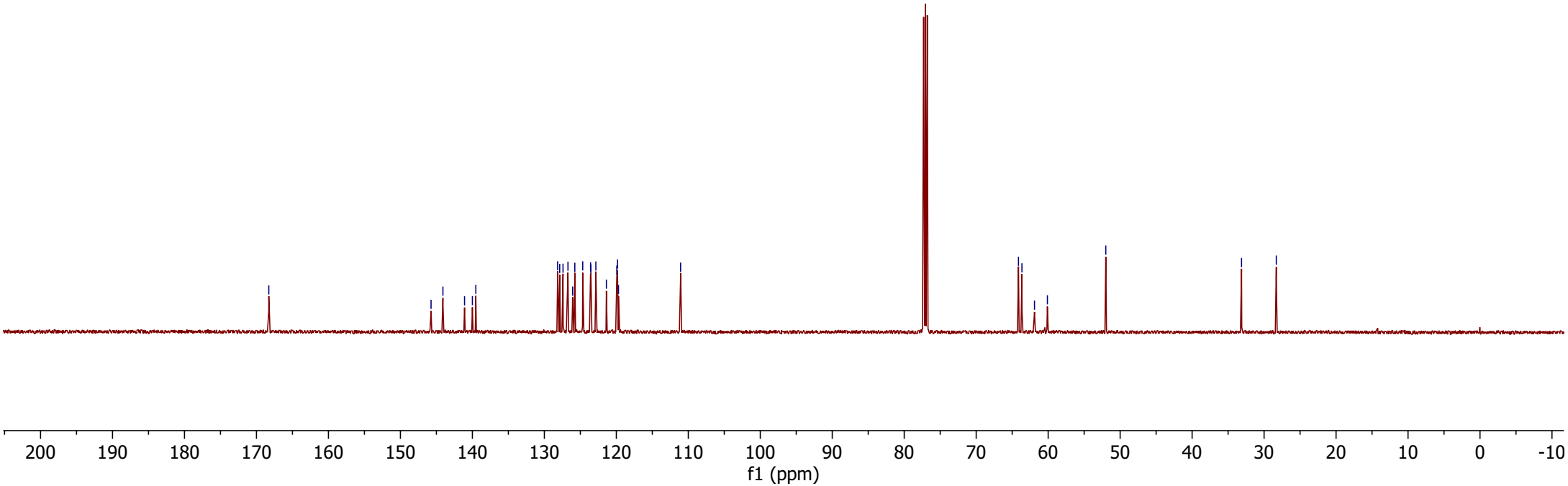

0.95
0.86
0.97
1.02
1.94
1.03
3.28
2.18
1.05
1.00
1.02
3.02
1.03
1.01
1.00
1.23
1.17
1.28
1.19
f1 (ppm)

^{13}C NMR

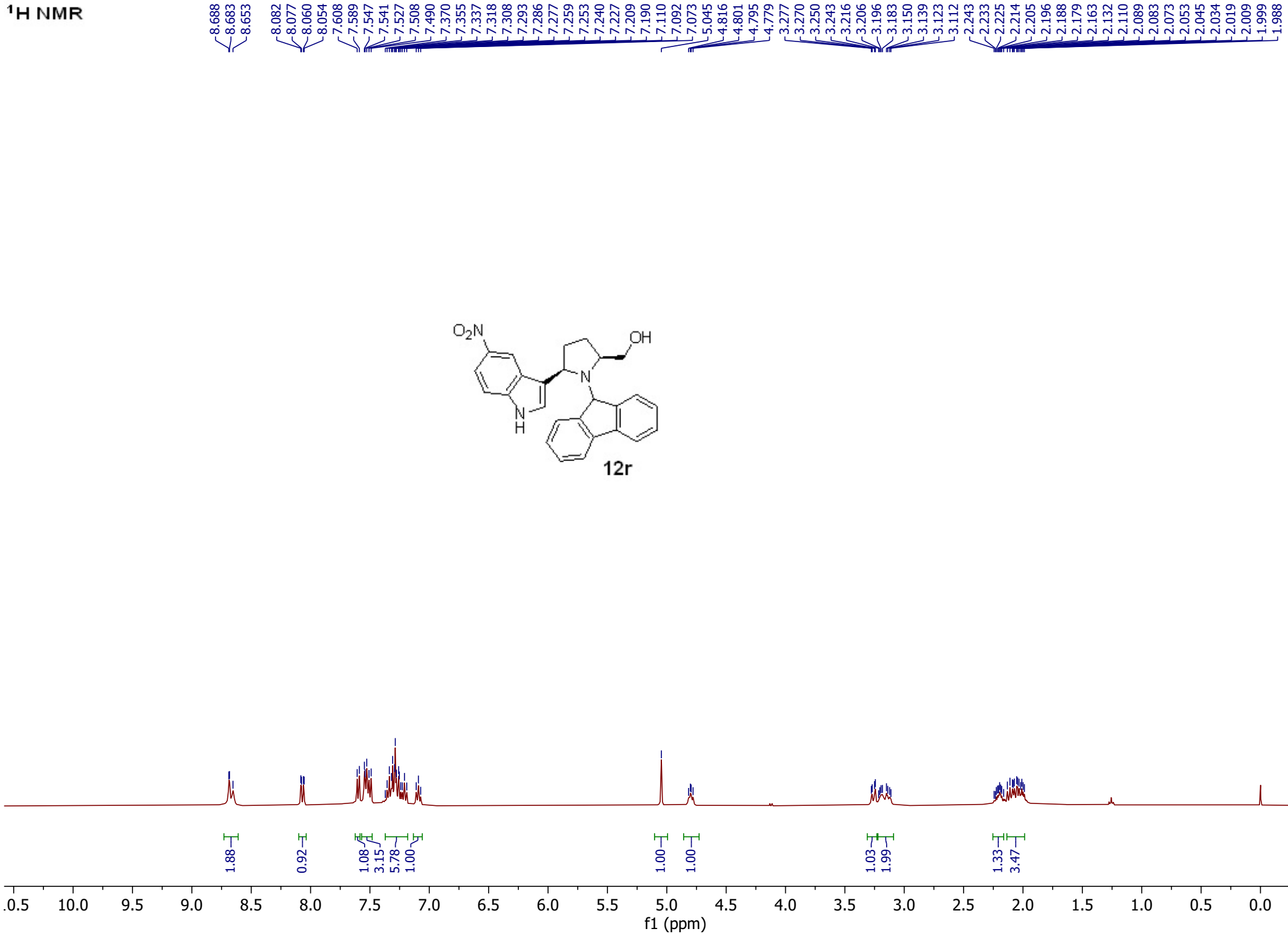
168.29
145.74
144.09
141.09
140.00
139.52
128.15
127.87
127.41
126.72
126.07
125.77
124.67
123.58
123.53
122.84
121.38
119.93
119.83
119.70
111.06
64.13
63.64
61.90
60.11
51.99
33.13
28.30



12q



^{1}H NMR


8.688
8.683
8.653
8.082
8.077
8.060
8.054
7.608
7.589
7.547
7.541
7.527
7.508
7.490
7.370
7.355
7.337
7.318
7.308
7.293
7.286
7.277
7.259
7.253
7.240
7.227
7.209
7.190
7.110
7.092
7.073
5.045
4.816
4.801
4.795
4.779
3.277
3.270
3.250
3.243
3.216
3.206
3.196
3.183
3.150
3.139
3.123
3.112
2.243
2.233
2.225
2.214
2.205
2.196
2.188
2.179
2.163
2.132
2.110
2.089
2.083
2.073
2.053
2.045
2.034
2.019
2.009
1.999
1.988
O2N
OH
N
N
H
12r
1.88
0.92
1.08
3.15
5.78
1.00
1.00
1.00
1.03
1.99
1.33
3.47
f1 (ppm)

^{13}C NMR

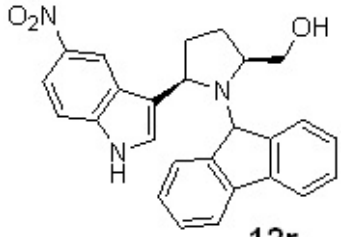
145.07
144.10
141.30
140.79
140.29
139.70
128.34
127.82
127.41
126.69
125.77
125.59
125.38
124.78
120.97
119.96
119.80
117.66
117.14
111.21

64.15
63.86
60.89
60.72

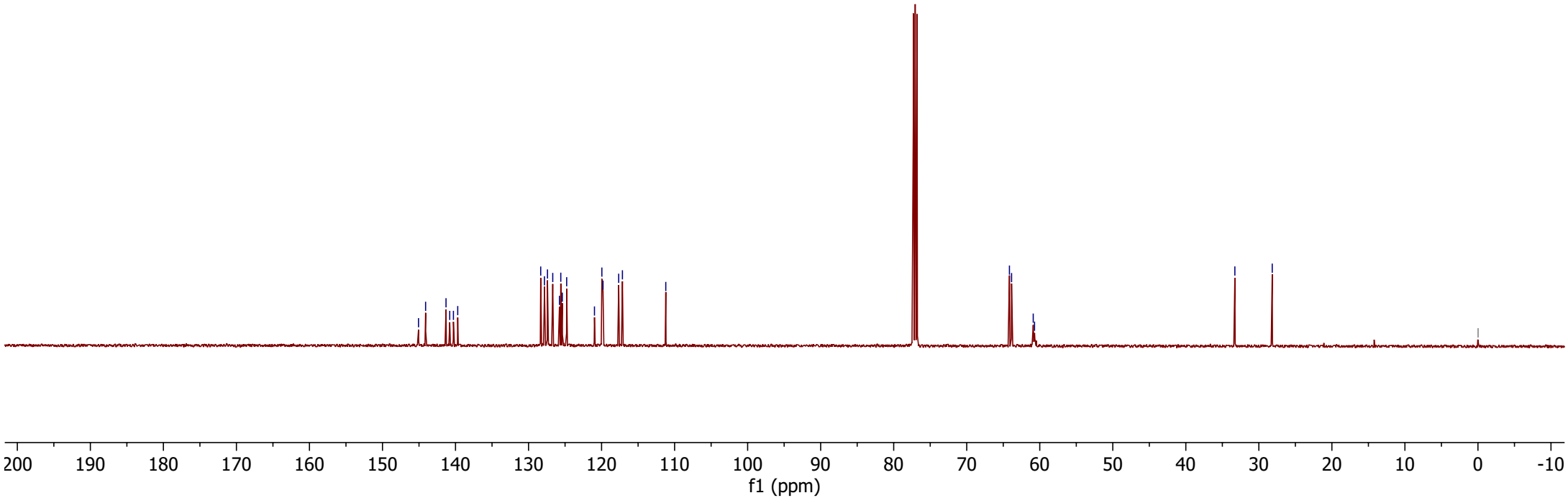
33.29

28.17

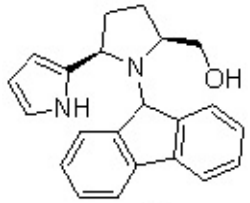
0.02



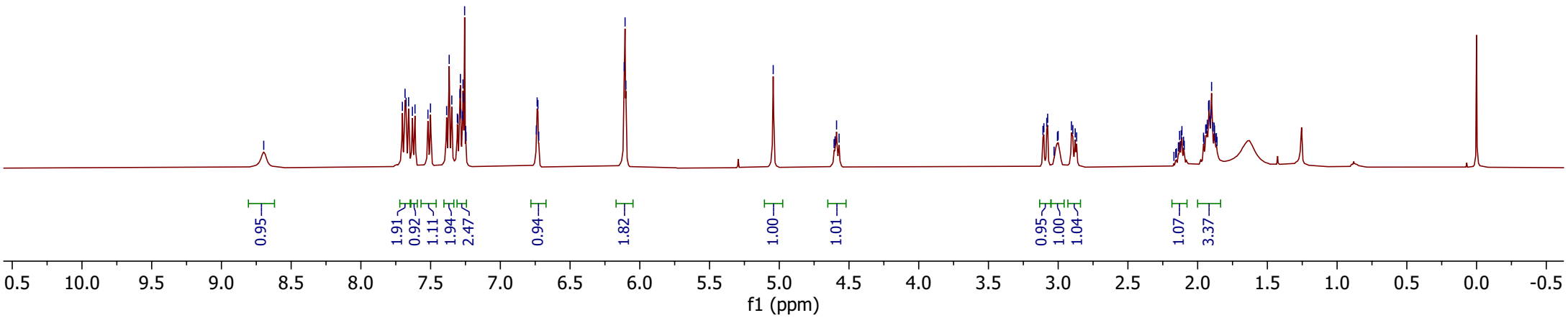
12r



^{1}H NMR

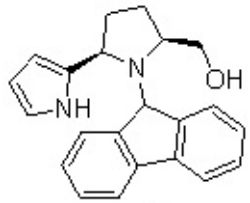

N
OH
NH

12s


0.95
1.91
0.92
1.11
1.94
2.47
0.94
1.82
1.00
1.01
0.95
1.00
1.04
1.07
3.37
f1 (ppm)

^{13}C NMR

145.59
144.12
141.10
140.09
133.72
128.31
128.12
127.41
127.00
125.61
124.55
120.12
119.93
117.31
108.07
106.38
64.10
63.95
62.24
60.33
33.11
28.33

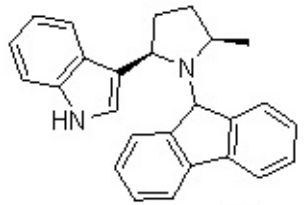


12s

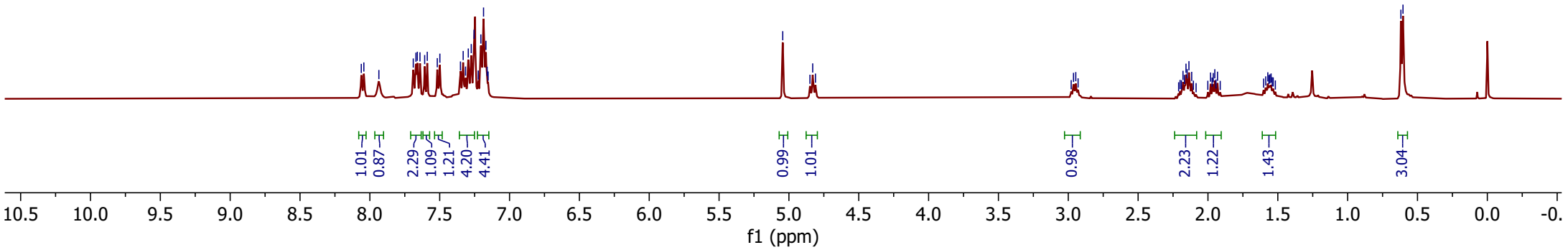
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)

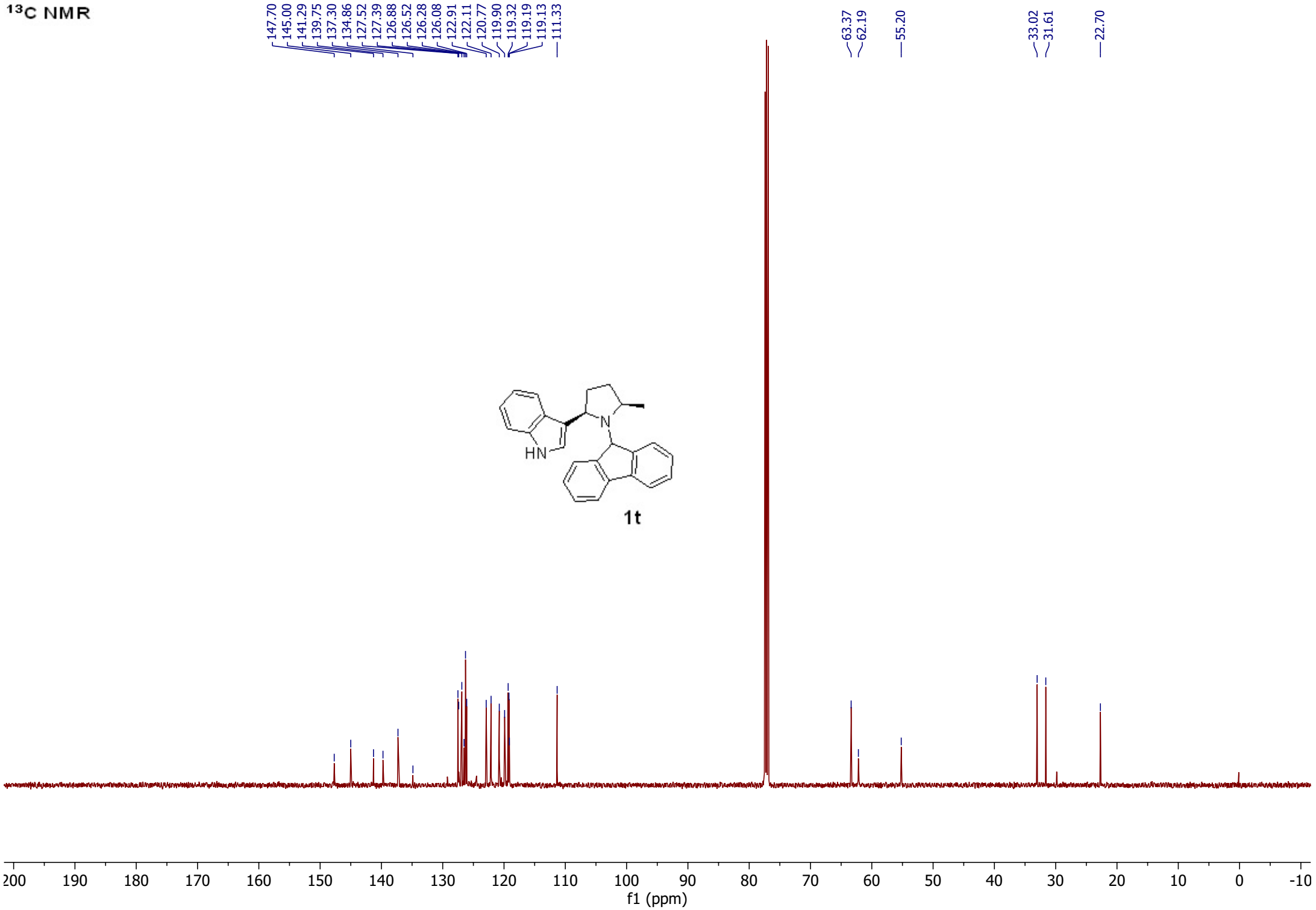
^{1}H NMR

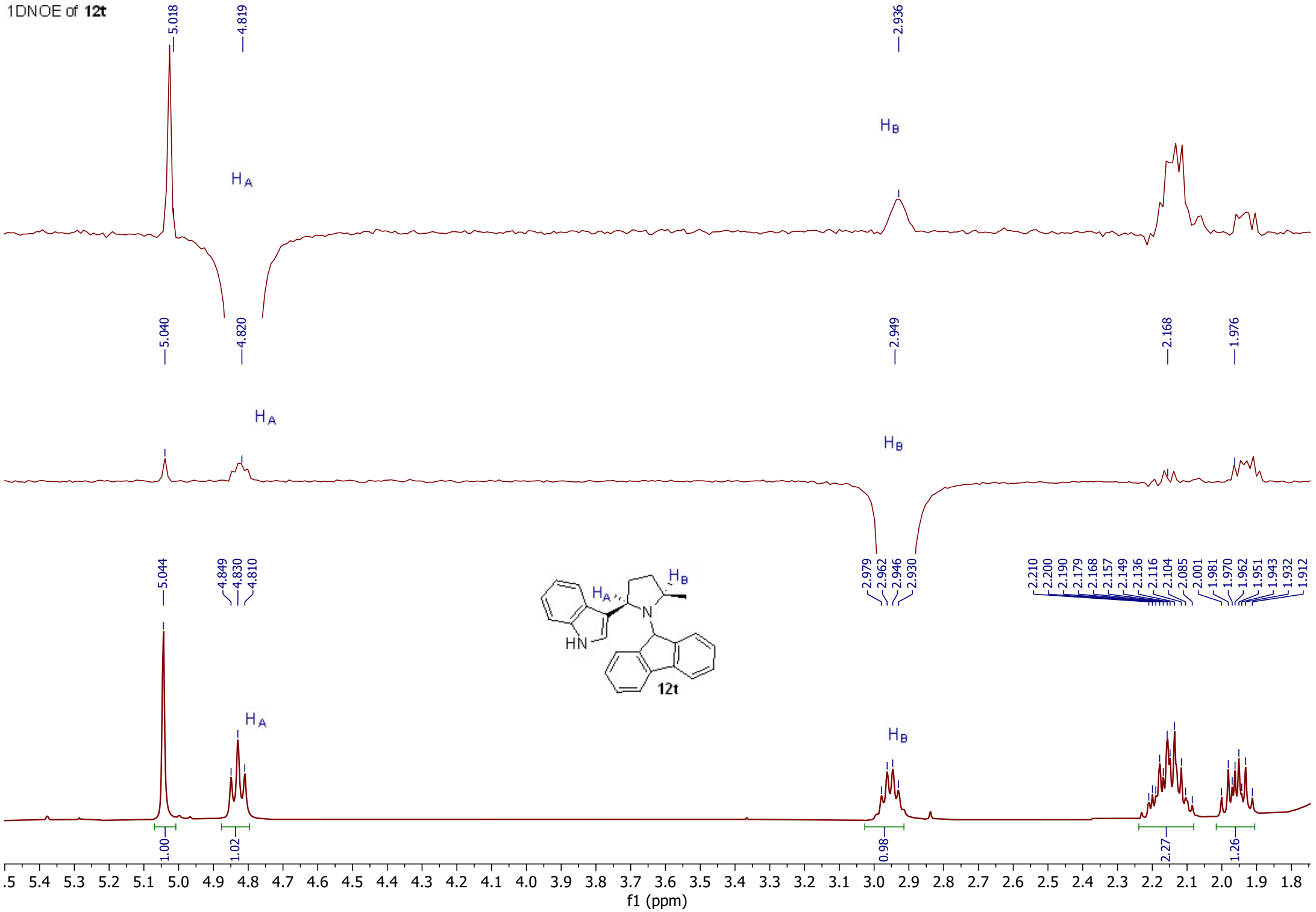


12t

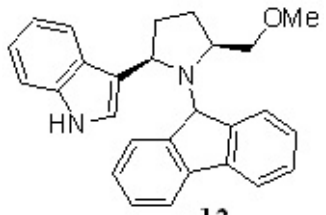


^{13}C NMR


147.70
145.00
141.29
139.75
137.30
134.86
127.52
127.39
126.88
126.52
126.28
126.08
122.91
122.11
120.77
119.90
119.32
119.19
119.13
111.33
63.37
62.19
55.20
33.02
31.61
22.70
HN
N
1t
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


1DNOE of 12t
5.018
4.819
2.936
HB
HA
5.040
4.820
2.949
2.168
1.976
HA
HB
5.044
4.849
4.830
4.810
2.979
2.962
2.946
2.930
2.210
2.200
2.190
2.179
2.168
2.157
2.149
2.136
2.116
2.104
2.085
2.001
1.981
1.970
1.962
1.951
1.943
1.932
1.912
HA
HB
HN
N
12t
HA
HB
1.00
1.02
0.98
2.27
1.26
f1 (ppm)

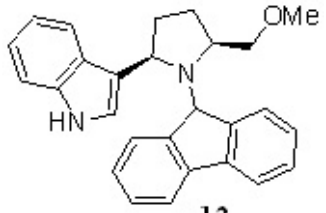
^{1}H NMR



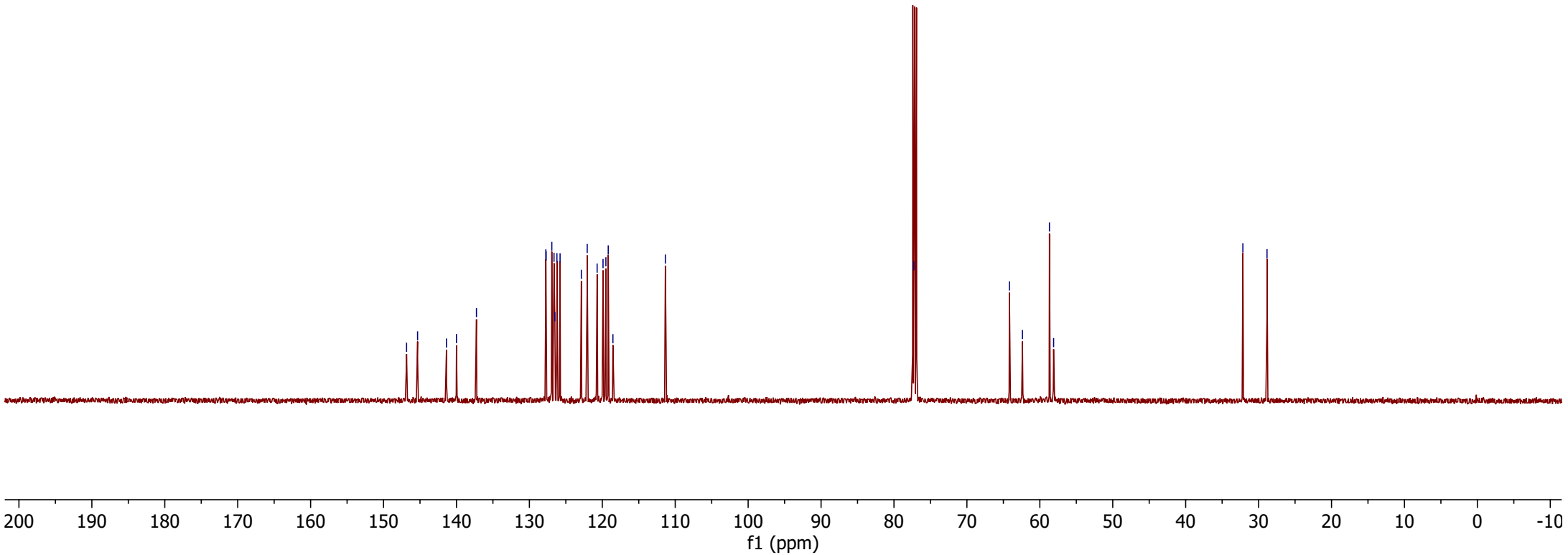
12u

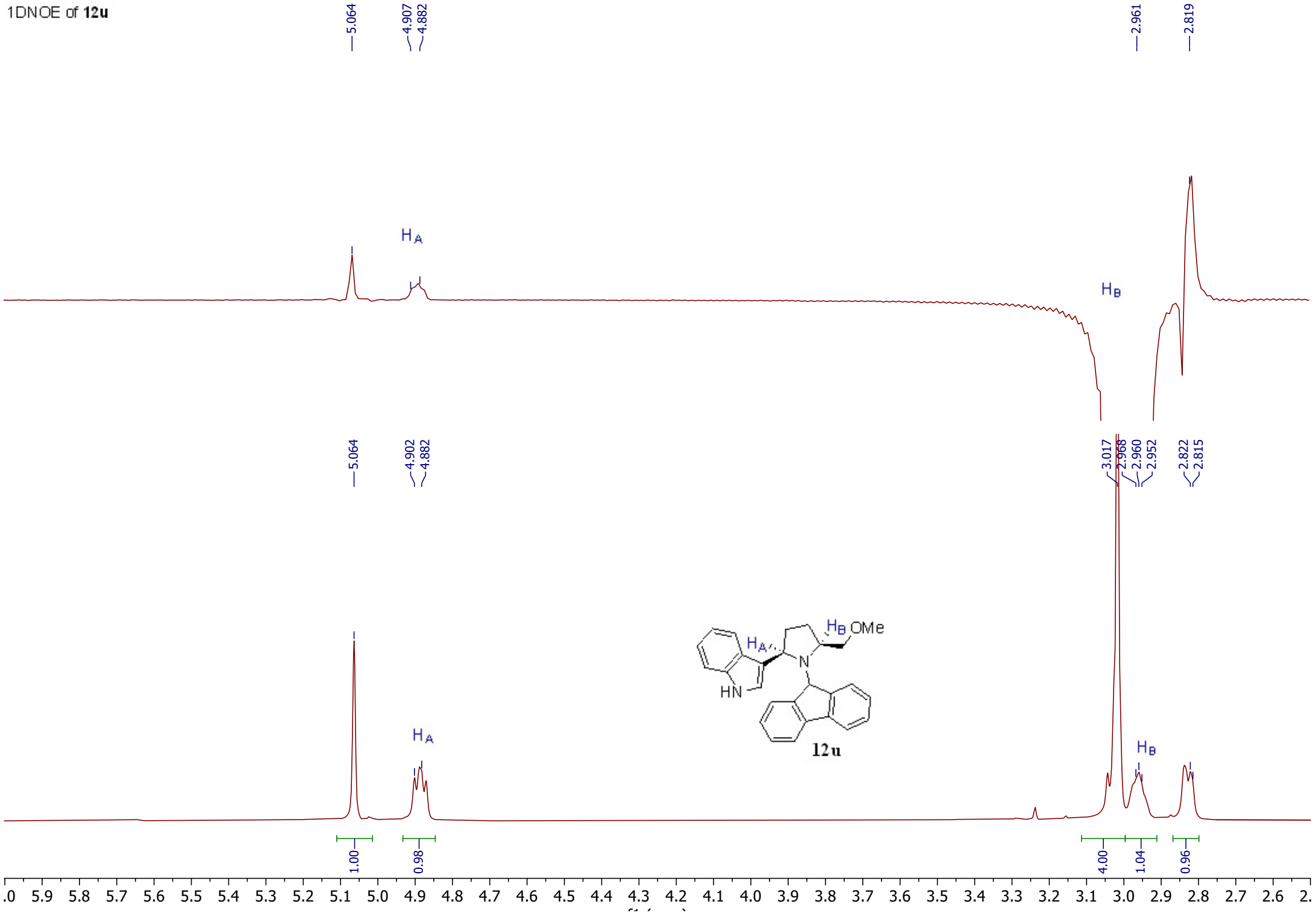
^{13}C NMR

146.84
145.33
141.37
140.00
137.26
127.74
127.70
126.92
126.62
126.50
126.22
125.79
122.87
122.07
120.71
119.90
119.51
119.19
118.54
111.35
77.28
64.17
62.38
58.68
58.11
32.16
28.84



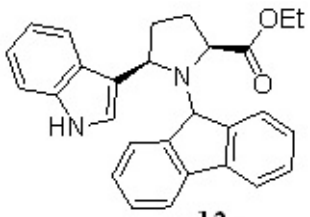
12u



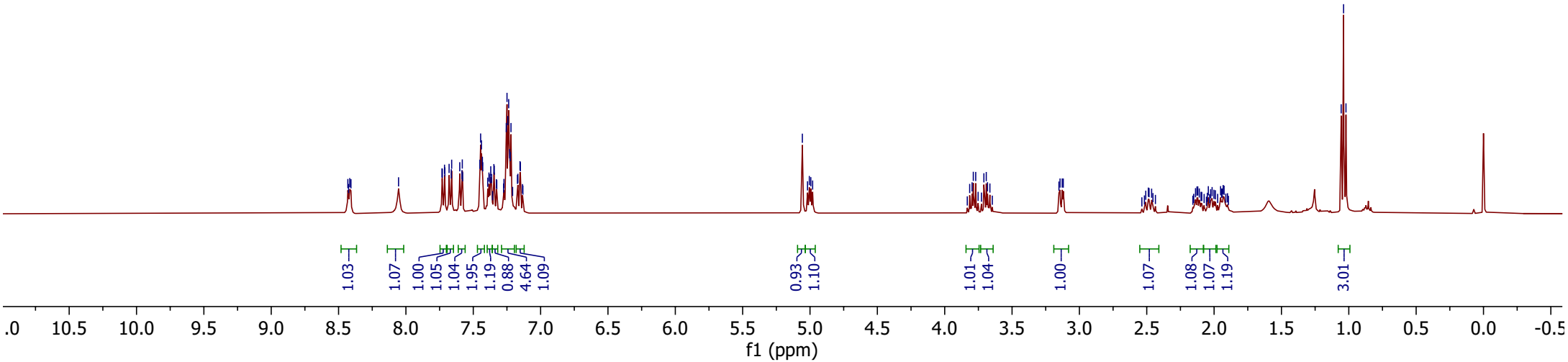

1DNOE of 12u
5.064
4.907
4.882
2.961
2.819
HA
HB
5.064
4.902
4.882
3.017
2.968
2.960
2.952
2.822
2.815
HB OMe
HA
HN
N
12u
HA
HB
1.00
0.98
4.00
1.04
0.96
.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.

8.431 8.426 8.417 8.408 8.055 7.732 7.730 7.713 7.711 7.679 7.663 7.660 7.600 7.584 7.581 7.579 7.451 7.445 7.439 7.432 7.430 7.393 7.384 7.375 7.370 7.364 7.357 7.347 7.344 7.328 7.325 7.275 7.272 7.255 7.250 7.243 7.237 7.230 7.226 7.220 7.208 7.172 7.169 7.153 7.150 7.135 7.132 5.057 5.018 5.005 4.994 4.981 3.814 3.797 3.788 3.770 3.752 3.709 3.691 3.682 3.664 3.152 3.144 3.128 3.120 2.507 2.488 2.483 2.464 2.138 2.127 2.121 2.110 2.097 2.043 2.025 2.015 2.001 1.991 1.952 1.945 1.940 1.933 1.926 1.057 1.039 1.021

^{1}H NMR

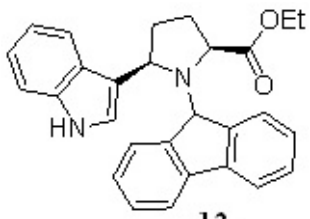


12v



^{13}C NMR

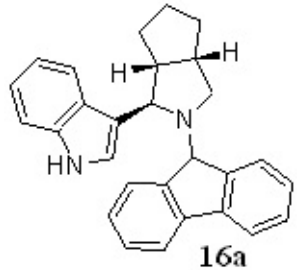
176.303
144.981
144.643
142.076
140.207
137.289
128.091
127.928
127.047
126.861
126.822
126.507
125.962
123.434
122.251
121.251
120.029
119.471
119.398
117.495
111.288
63.491
62.119
60.202
59.287
33.083
30.252
14.099



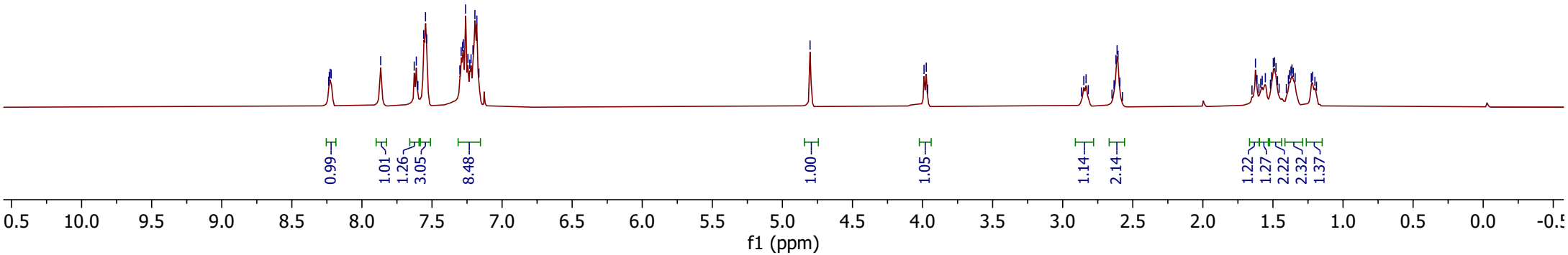
12v

f1 (ppm)

^{1}H NMR


H
H
N
HN

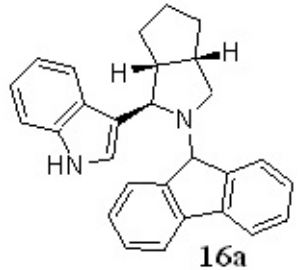
16a


0.99
1.01
1.26
3.05
8.48
1.00
1.05
1.14
2.14
1.22
1.27
2.22
2.32
1.37
f1 (ppm)

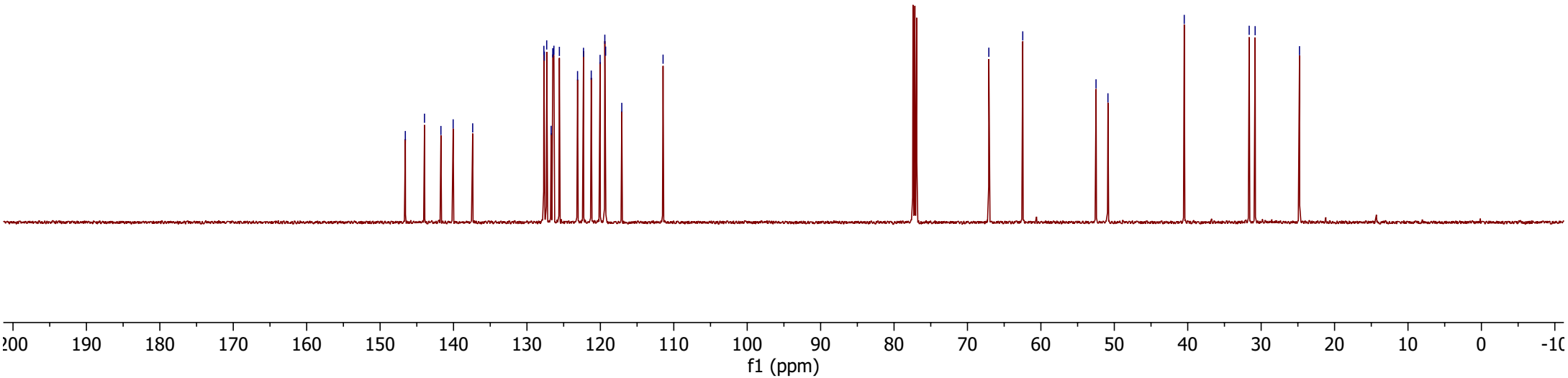
^{13}C NMR

146.57
143.95
141.72
140.05
137.39
127.70
127.63
127.31
126.70
126.48
126.33
125.58
123.11
122.30
121.24
120.04
119.39
119.28
117.08
111.46

67.09
62.47
52.49
50.87
40.47
31.63
30.82
24.78



16a

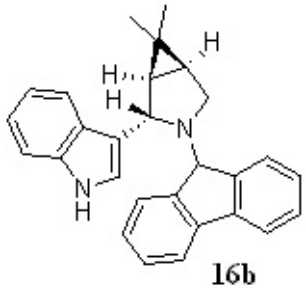


^{1}H NMR

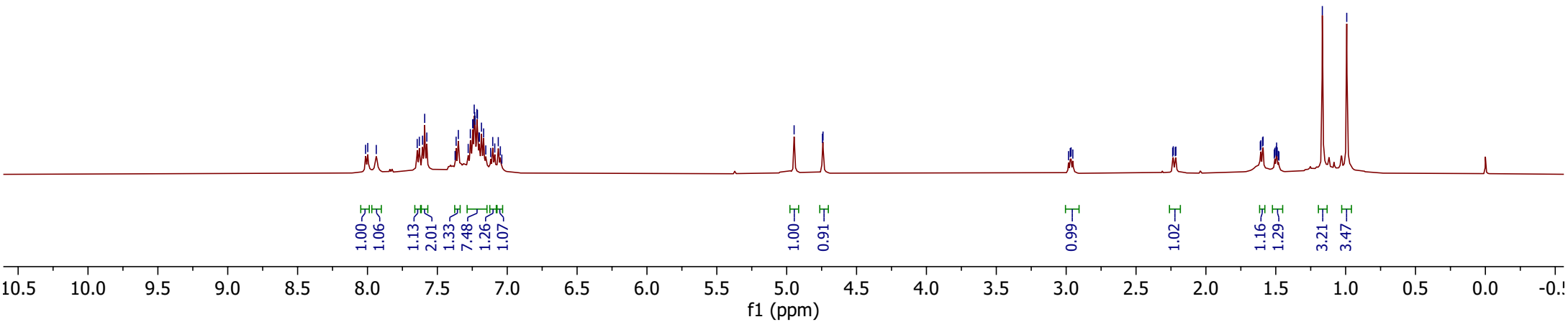
8.014 7.998 7.937 7.644 7.629 7.606 7.591 7.575 7.373 7.366 7.350 7.279 7.264 7.247 7.244 7.236 7.232 7.229 7.217 7.213 7.202 7.199 7.184 7.169 7.153 7.118 7.104 7.089 7.064 7.049 7.039 4.947 4.744 4.740

2.983 2.971 2.965 2.952

2.238 2.233 2.219 2.215 1.611 1.607 1.594 1.591 1.511 1.506 1.498 1.494 1.490 1.482 1.477 1.167 0.992



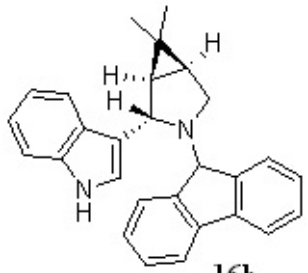
16b



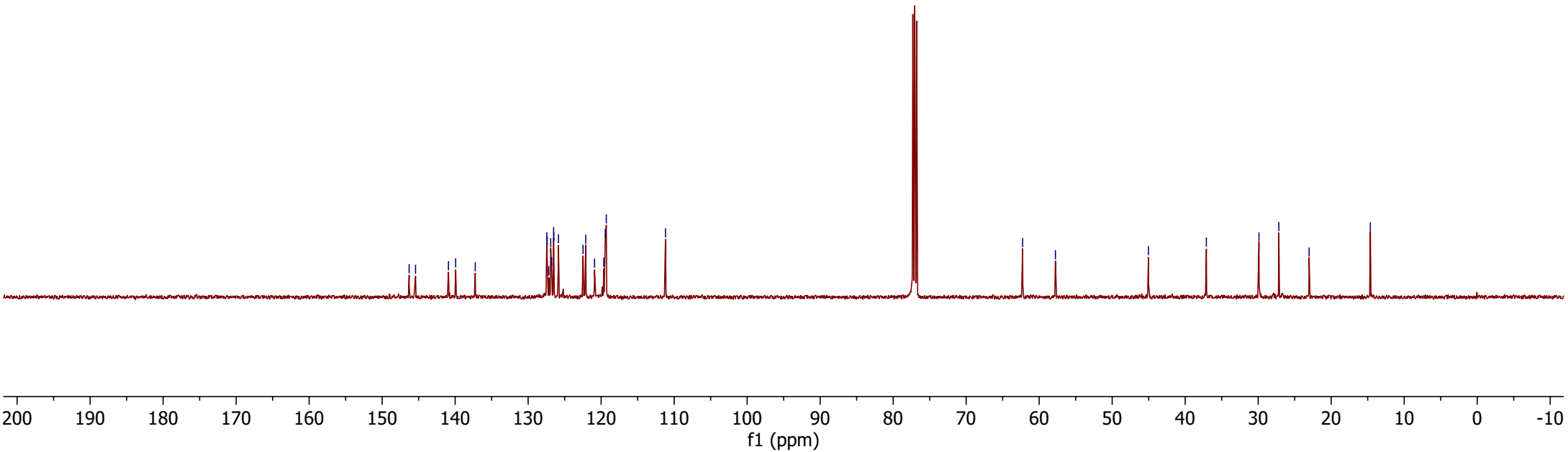
^{13}C NMR

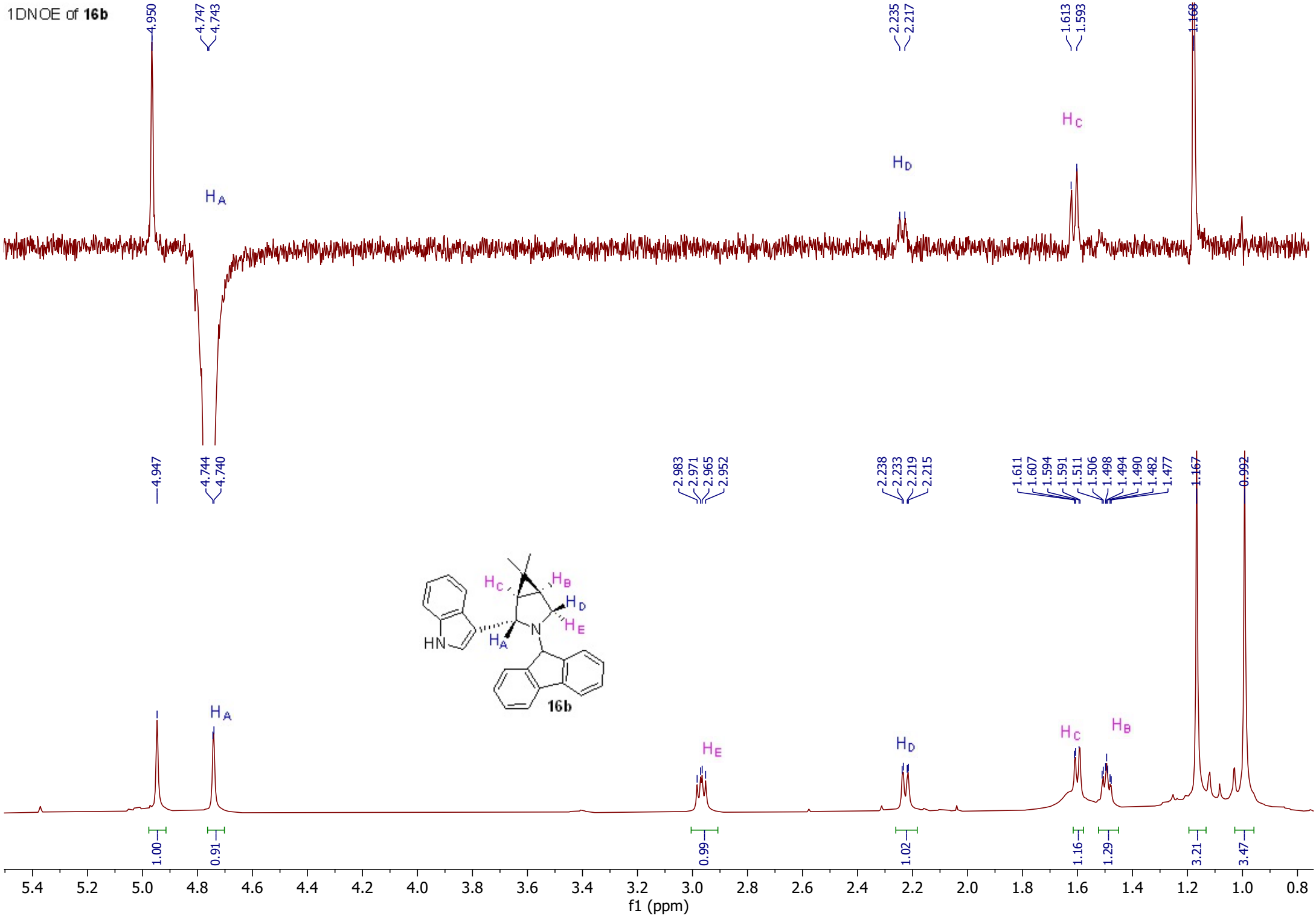
146.30
145.42
140.92
139.93
137.25
127.45
127.39
127.17
126.91
126.79
126.51
126.48
125.85
122.48
122.12
120.90
119.64
119.43
119.29
111.19

62.26
57.78
45.03
37.10
29.89
27.17
23.02
14.64



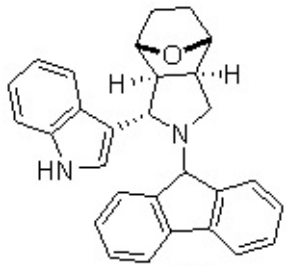
16b



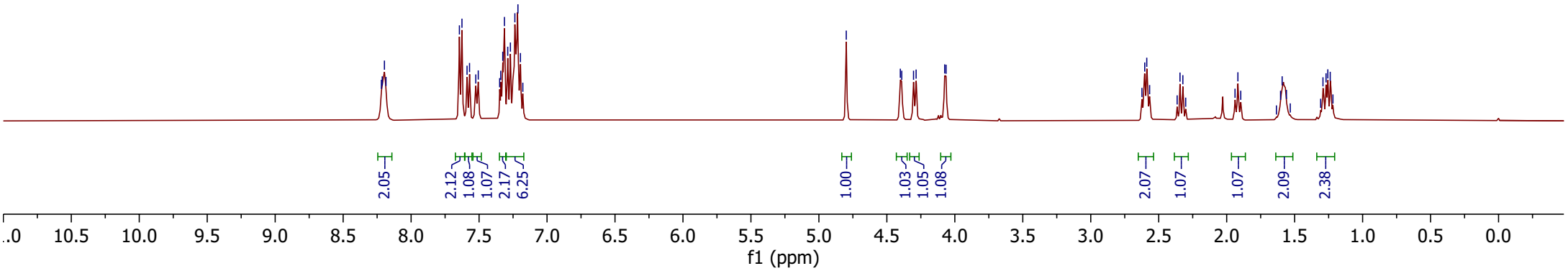

1DNOE of 16b
4.950
4.747
4.743
2.235
2.217
1.613
1.593
1.168
HA
HD
HC
4.947
4.744
4.740
2.983
2.971
2.965
2.952
2.238
2.233
2.219
2.215
1.611
1.607
1.594
1.591
1.511
1.506
1.498
1.494
1.490
1.482
1.477
1.167
0.992
HC
HB
HD
HE
HA
HN
N
16b
HA
HE
HD
HC
HB
1.00
0.91
0.99
1.02
1.16
1.29
3.21
3.47
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
f1 (ppm)

^{1}H NMR

8.219 8.212 8.196 8.185 7.645 7.626 7.588 7.570 7.524 7.506 7.349 7.341 7.326 7.313 7.289 7.270 7.237 7.214 7.196 7.178 4.799 4.401 4.390 4.304 4.285 4.075 4.064 2.623 2.603 2.588 2.567 2.364 2.343 2.322 2.302 1.939 1.918 1.896 1.634 1.604 1.592 1.560 1.532 1.309 1.292 1.269 1.256 1.238 1.218

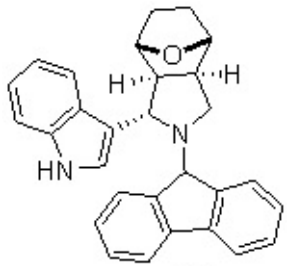


16c

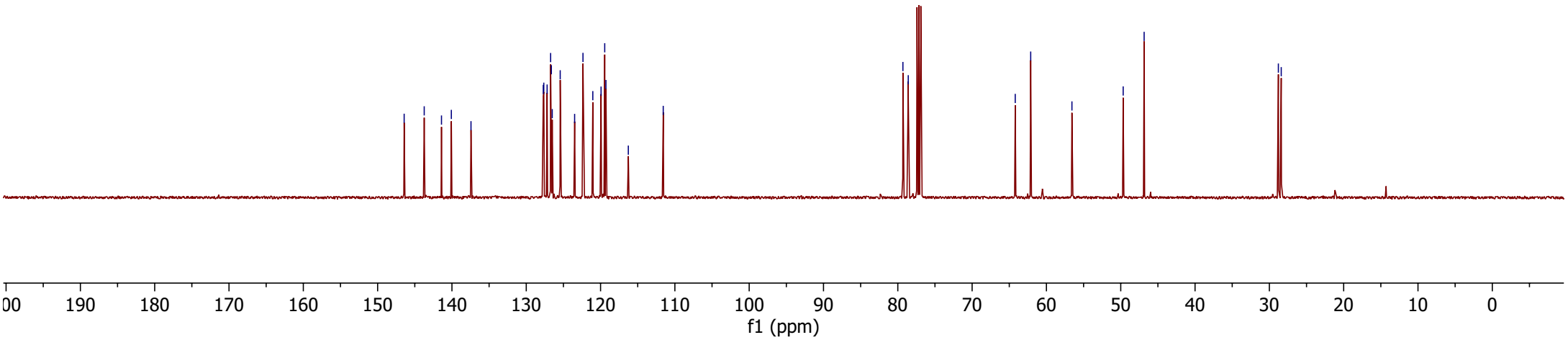


^{13}C NMR

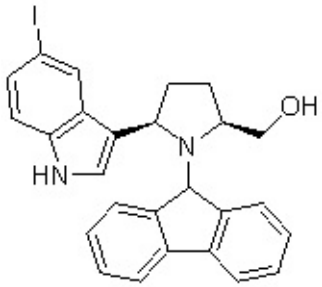
146.430
143.732
141.407
140.080
137.436
127.710
127.640
127.193
126.720
126.621
126.504
125.430
123.491
122.367
121.044
119.932
119.440
119.277
116.265
111.567
79.314
78.594
64.198
62.117
56.568
49.672
46.852
28.788
28.403



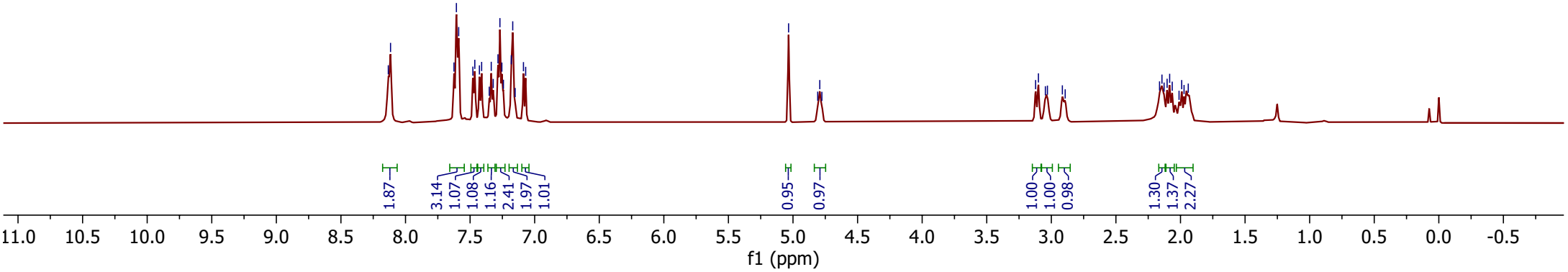
16c

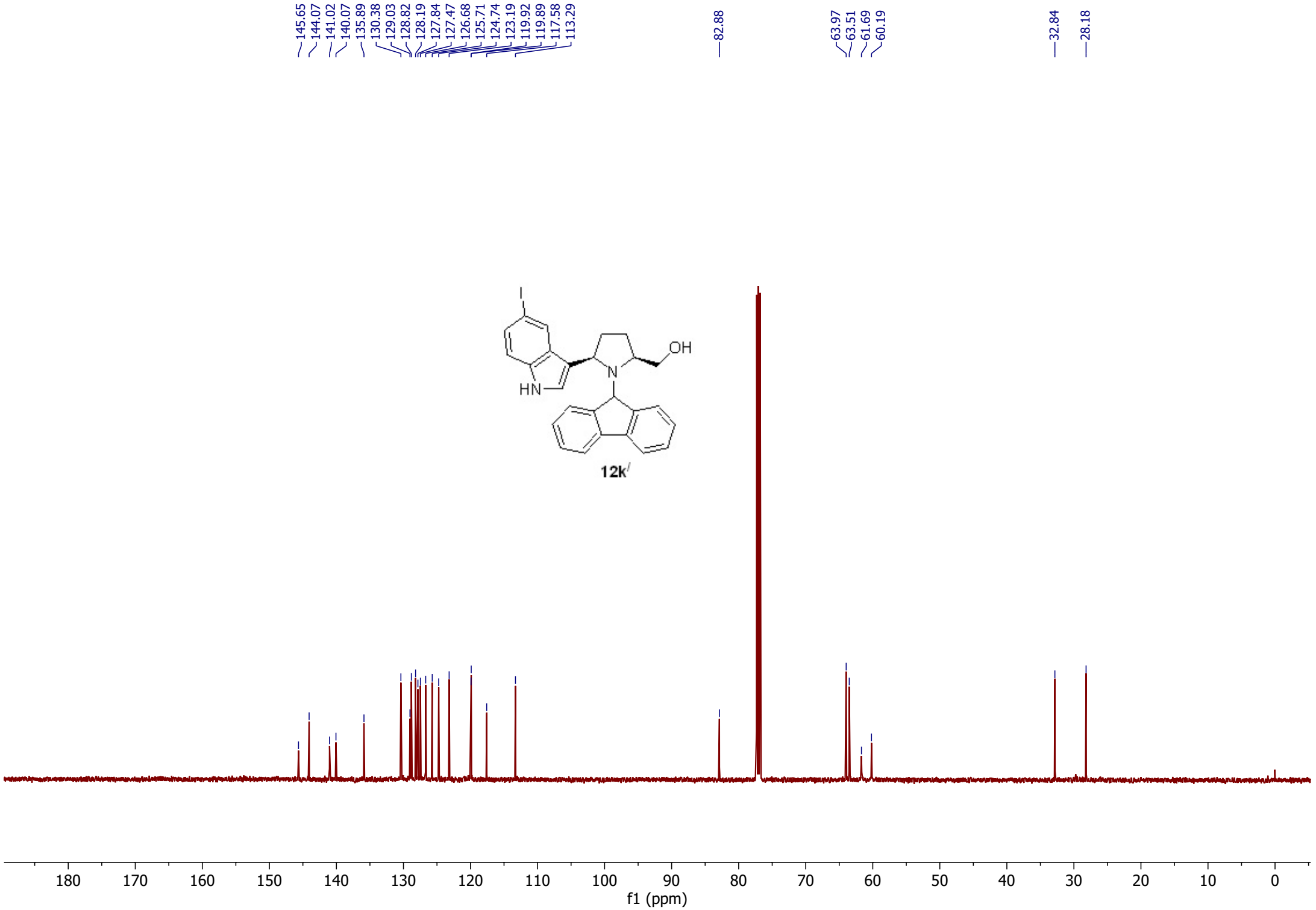


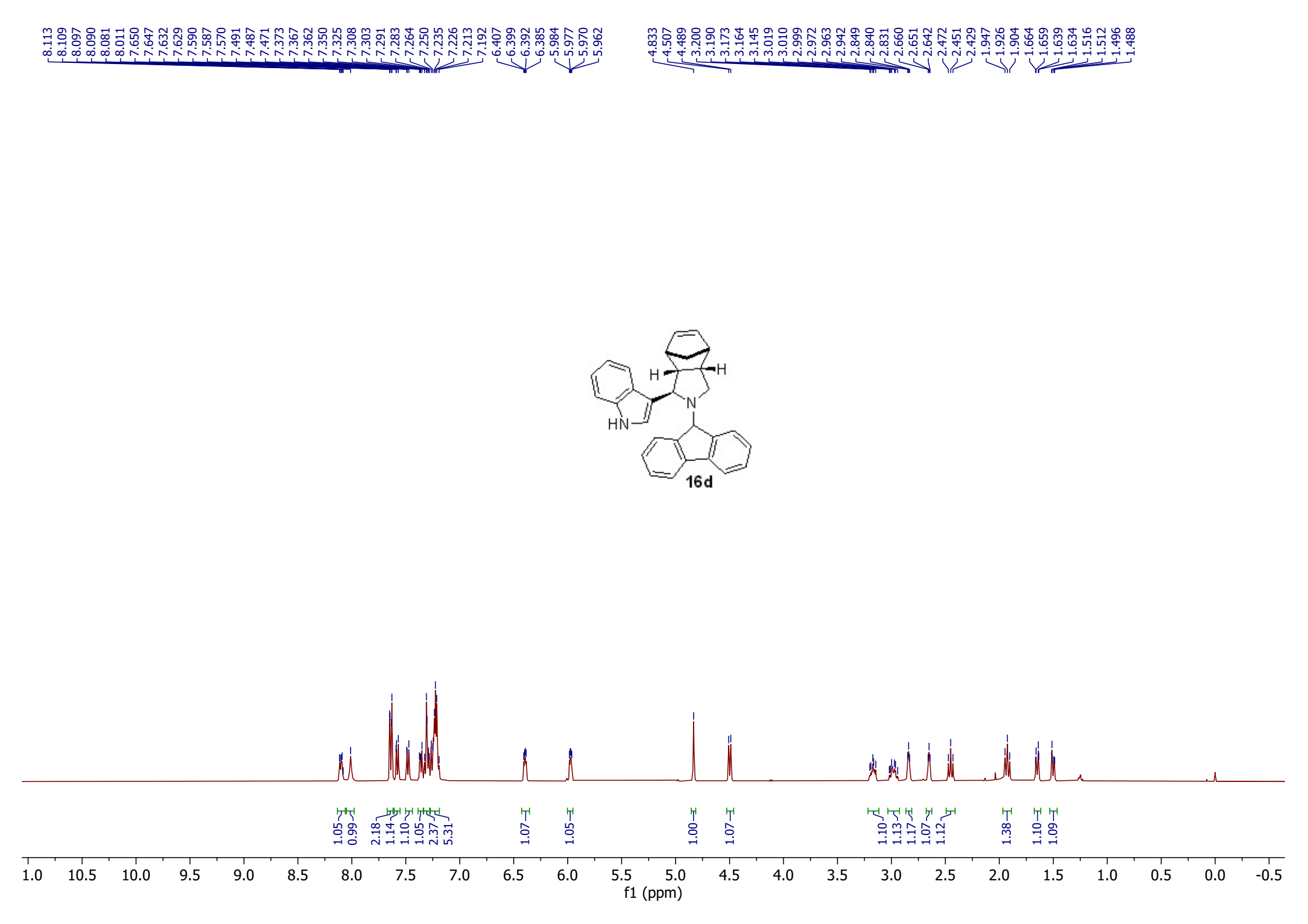
8.133 8.116 7.625 7.606 7.588 7.479 7.463 7.428 7.411 7.352 7.336 7.321 7.284 7.269 7.254 7.242 7.181 7.170 7.151 7.087 7.070 5.034 4.809 4.793 4.776 3.122 3.100 3.046 3.030 2.915 2.893 2.162 2.144 2.127 2.104 2.084 2.064 2.011 1.991 1.972 1.940

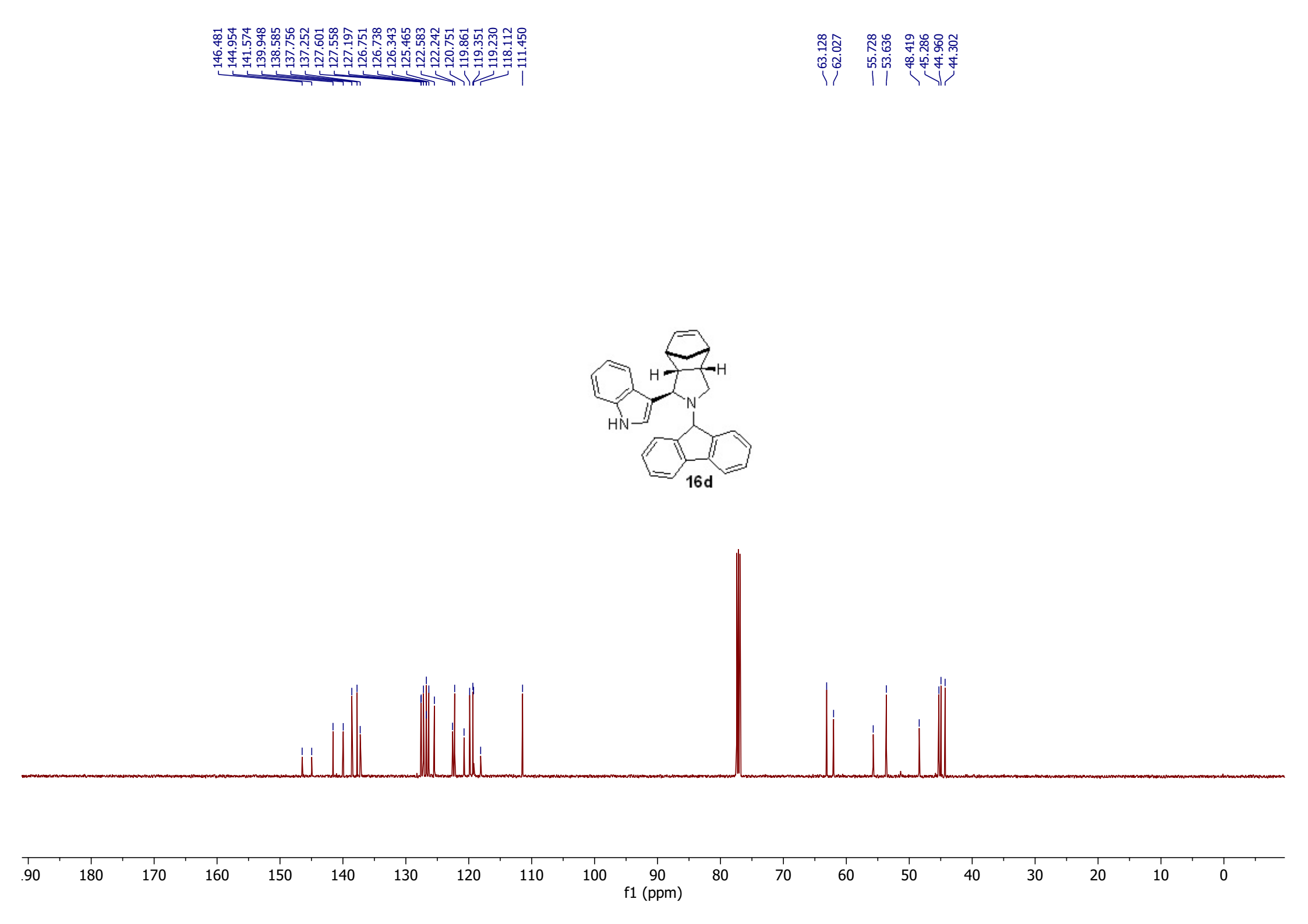


12k'



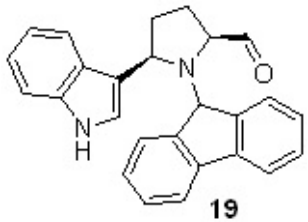

145.65
144.07
141.02
140.07
135.89
130.38
129.03
128.82
128.19
127.84
127.47
126.68
125.71
124.74
123.19
119.92
119.89
117.58
113.29
82.88
63.97
63.51
61.69
60.19
32.84
28.18
I
OH
N
HN
12k'
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.113
8.109
8.097
8.090
8.081
8.011
7.650
7.647
7.632
7.629
7.590
7.587
7.570
7.491
7.487
7.471
7.373
7.367
7.362
7.350
7.325
7.308
7.303
7.291
7.283
7.264
7.250
7.235
7.226
7.213
7.192
6.407
6.399
6.392
6.385
5.984
5.977
5.970
5.962
4.833
4.507
4.489
3.200
3.190
3.173
3.164
3.145
3.019
3.010
2.999
2.972
2.963
2.942
2.849
2.840
2.831
2.660
2.651
2.642
2.472
2.451
2.429
1.947
1.926
1.904
1.664
1.659
1.639
1.634
1.516
1.512
1.496
1.488
H
H
N
HN
16d
1.05
0.99
2.18
1.14
1.10
1.05
2.37
5.31
1.07
1.05
1.00
1.07
1.10
1.13
1.17
1.07
1.12
1.38
1.10
1.09
1.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

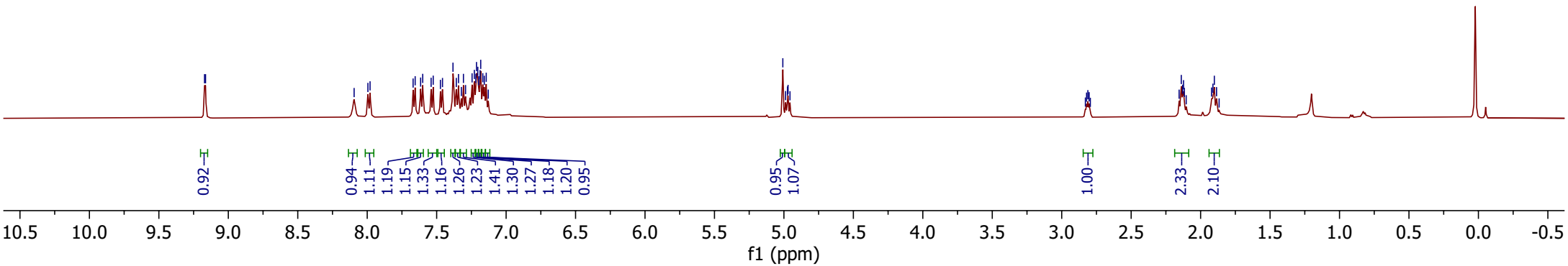

146.481
144.954
141.574
139.948
138.585
137.756
137.252
127.601
127.558
127.197
126.751
126.738
126.343
125.465
122.583
122.242
120.751
119.861
119.351
119.230
118.112
111.450
63.128
62.027
55.728
53.636
48.419
45.286
44.960
44.302
H
H
N
HN
16d
f1 (ppm)

^{1}H NMR

9.171
9.164
8.094
7.995
7.980
7.670
7.655
7.615
7.600
7.540
7.525
7.473
7.458
7.382
7.359
7.343
7.322
7.307
7.292
7.245
7.229
7.217
7.213
7.204
7.198
7.188
7.183
7.168
7.157
7.143
7.128
5.008
4.988
4.974
4.970
4.956
2.830
2.821
2.812
2.803
2.794
2.155
2.139
2.130
2.123
2.117
2.104
1.921
1.911
1.901
1.885
1.867

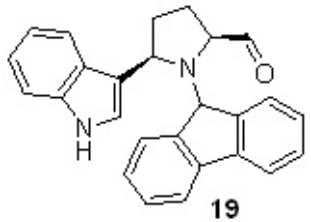


19

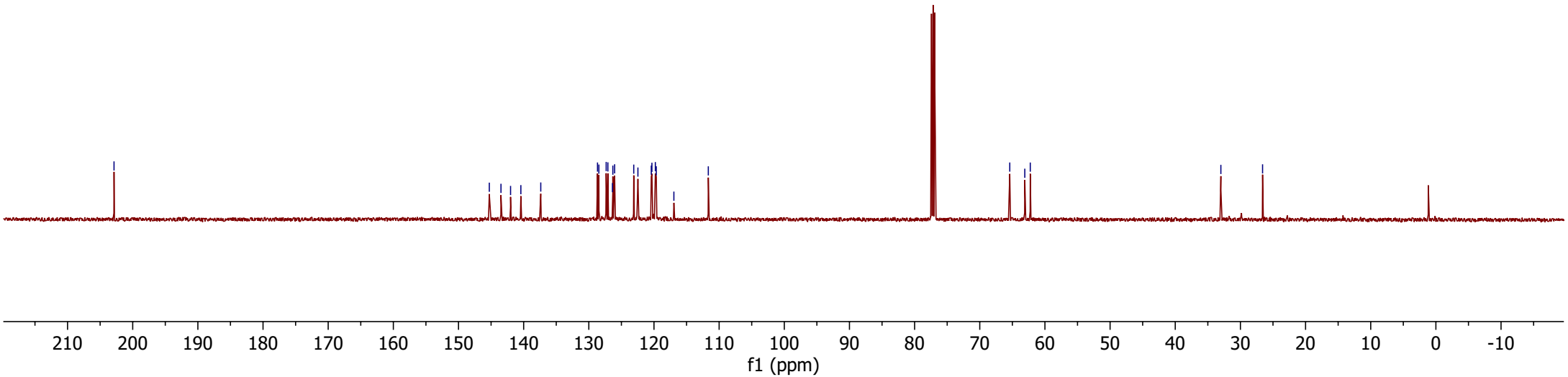


^{13}C NMR

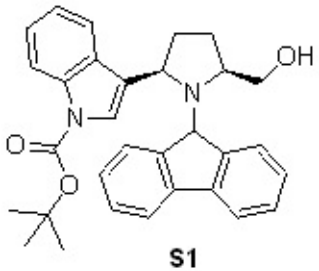
202.87
145.27
143.48
142.01
140.43
137.37
128.67
128.46
127.34
127.08
126.37
126.31
126.04
123.11
122.47
120.41
120.32
119.79
119.65
116.95
111.66
65.40
63.09
62.25
33.00
26.60



19



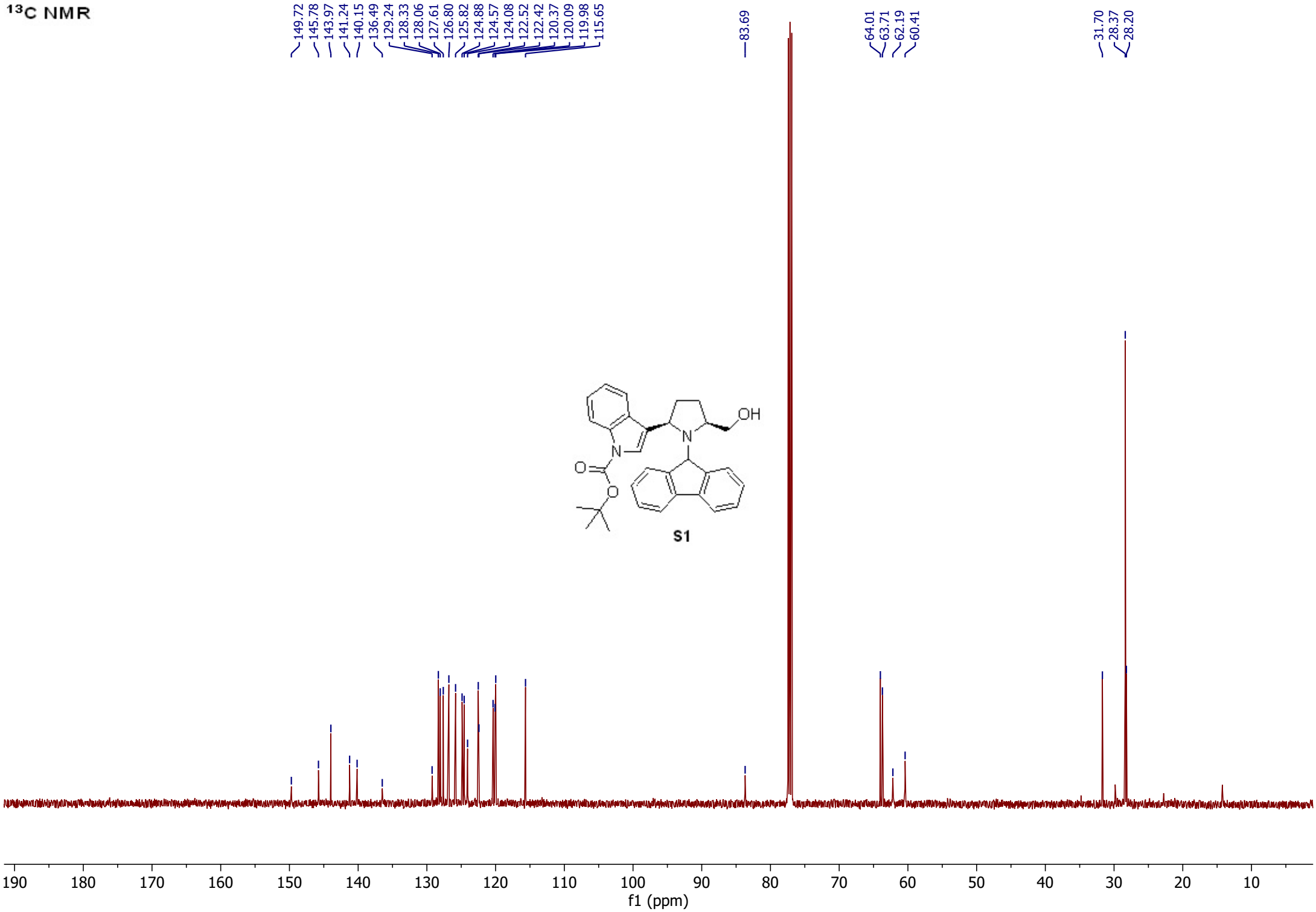
^{1}H NMR



S1

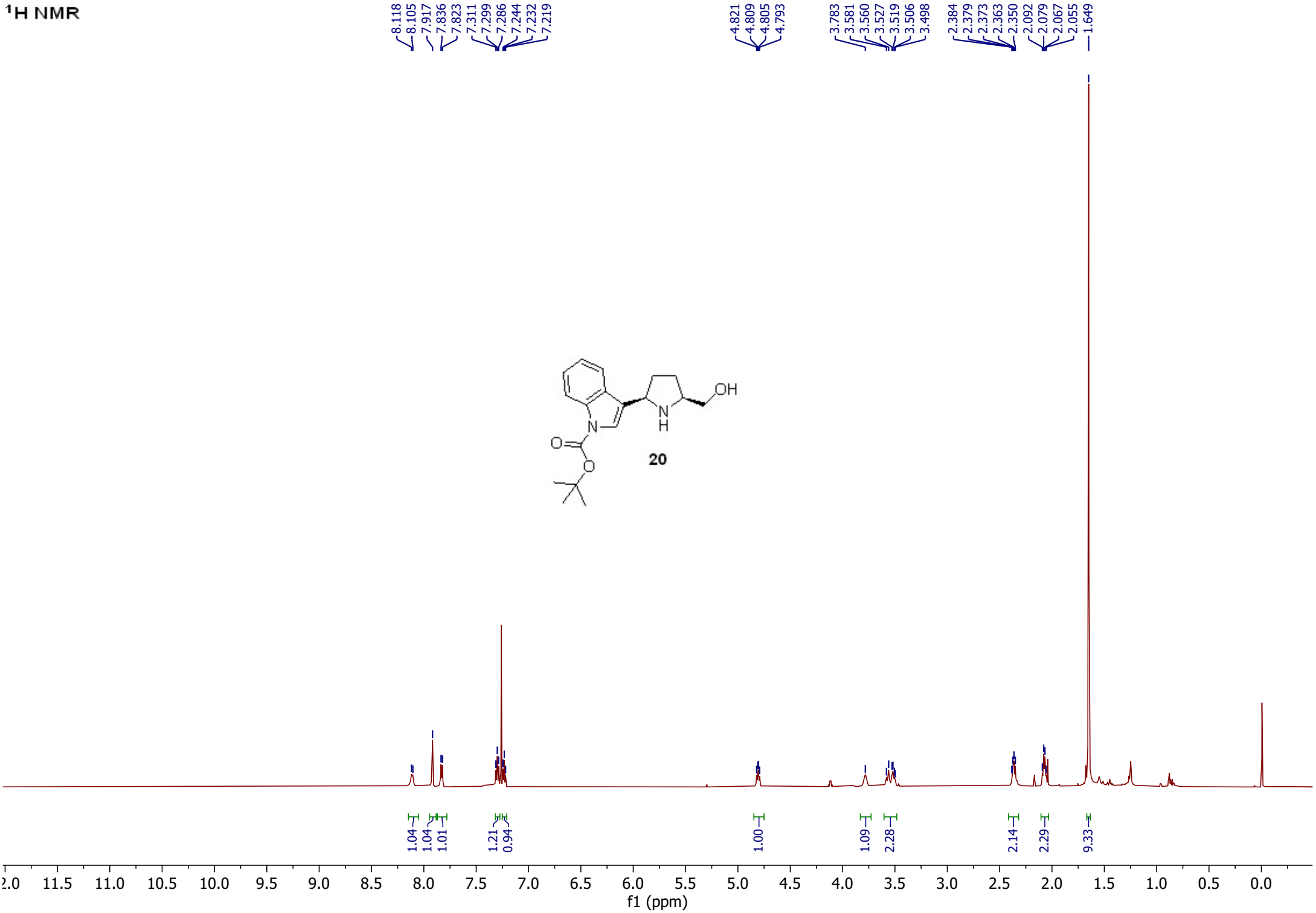
f1 (ppm)

^{13}C NMR


149.72
145.78
143.97
141.24
140.15
136.49
129.24
128.33
128.06
127.61
126.80
125.82
124.88
124.57
124.08
122.52
122.42
120.37
120.09
119.98
115.65
83.69
64.01
63.71
62.19
60.41
31.70
28.37
28.20
OH
N
N
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

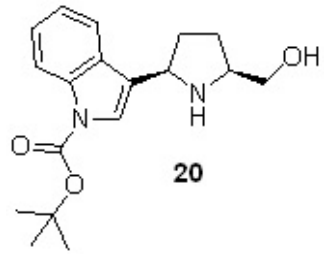
S1

^{1}H NMR


8.118
8.105
7.917
7.836
7.823
7.311
7.299
7.286
7.244
7.232
7.219
4.821
4.809
4.805
4.793
3.783
3.581
3.560
3.527
3.519
3.506
3.498
2.384
2.379
2.373
2.363
2.350
2.092
2.079
2.067
2.055
1.649
OH
N
H
N
O
O
20
1.04
1.04
1.01
1.21
0.94
1.00
1.09
2.28
2.14
2.29
9.33
f1 (ppm)

^{13}C NMR

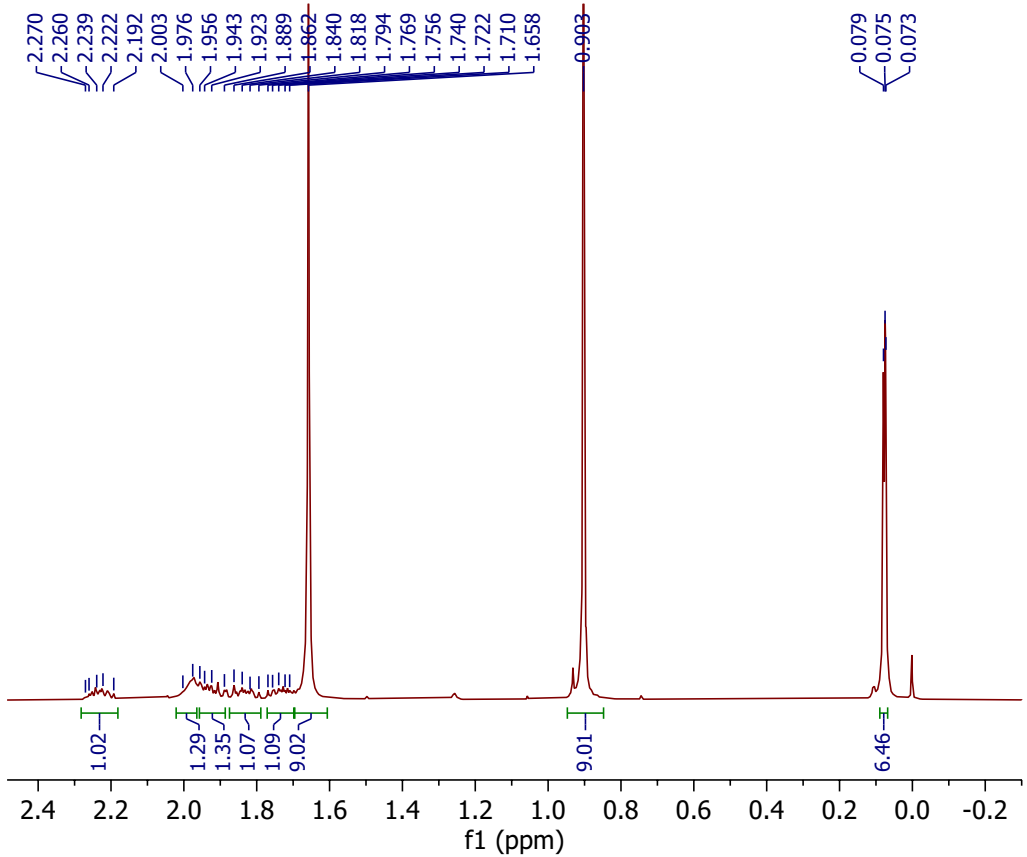
149.44
135.64
128.46
125.30
125.17
123.16
119.49
115.56
114.49
84.70
61.92
60.38
55.99
30.66
28.28
26.05

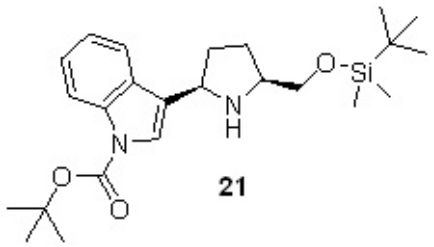


20

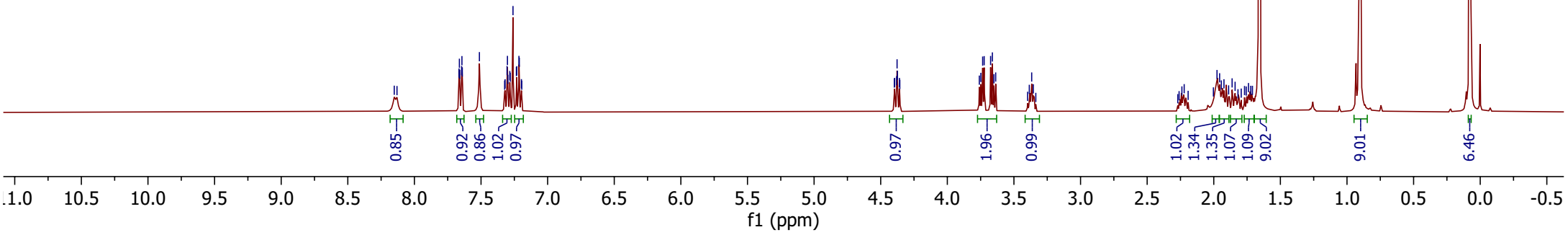
f1 (ppm)

^{1}H NMR



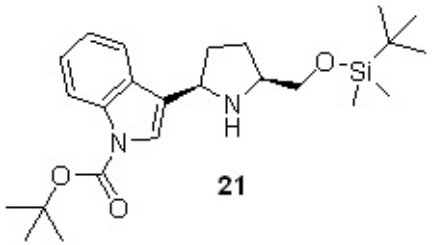


21



^{13}C NMR

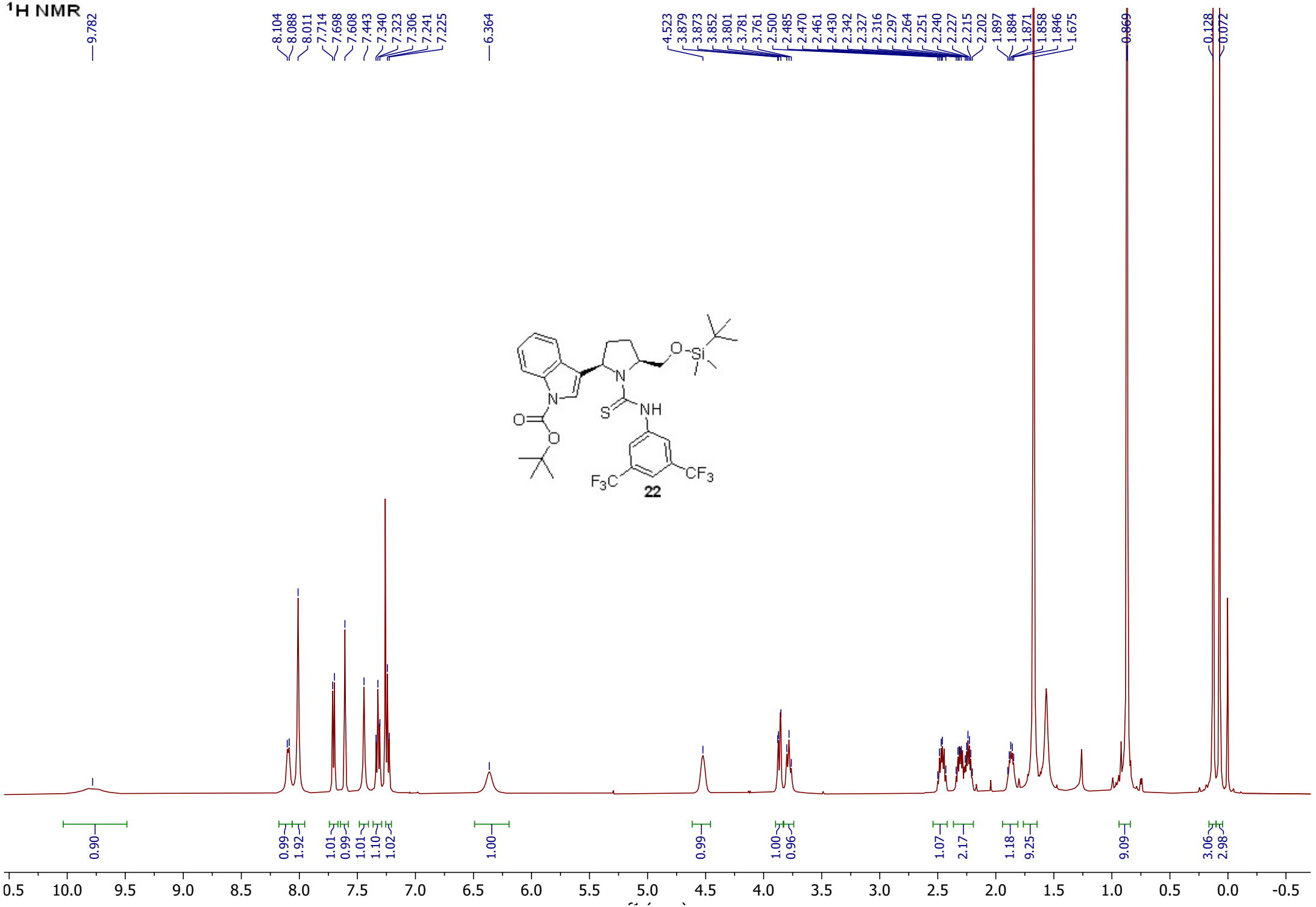
149.961
136.164
129.612
124.422
124.127
122.443
121.977
119.936
115.462
83.479
66.517
60.422
55.602
32.357
28.372
27.871
26.110
18.524
-5.143



21

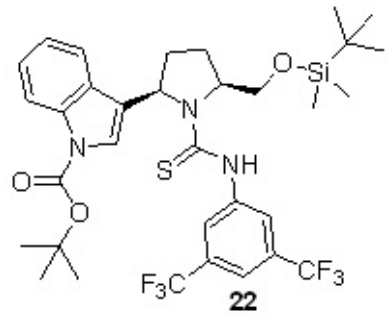
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)


1H NMR
9.782
8.104
8.088
8.011
7.714
7.698
7.608
7.443
7.340
7.323
7.306
7.241
7.225
6.364
4.523
3.879
3.873
3.852
3.801
3.781
3.761
2.500
2.485
2.470
2.461
2.430
2.342
2.327
2.316
2.297
2.264
2.251
2.240
2.227
2.215
2.202
1.897
1.884
1.871
1.858
1.846
1.675
0.869
0.128
0.072
O
Si
N
S
NH
O
O
N
F3C
CF3
22
0.90
0.99
1.92
1.01
0.99
1.01
1.10
1.02
1.00
0.99
1.00
0.96
1.07
2.17
1.18
9.25
9.09
3.06
2.98
0.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

^{13}C NMR

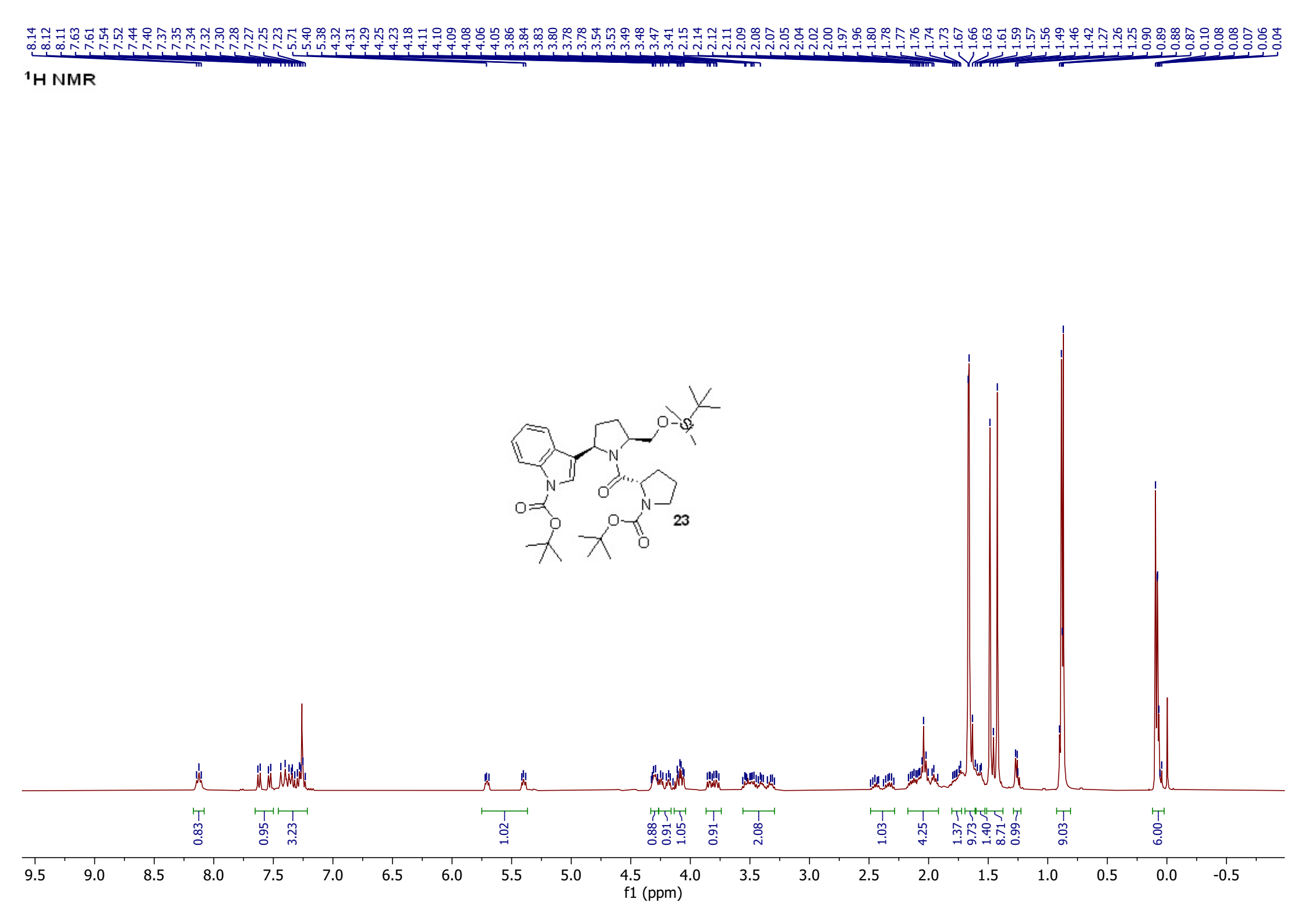
182.712
149.826
141.585
136.045
132.117
131.853
131.586
131.319
128.863
124.879
124.703
124.672
124.449
122.904
122.282
122.019
121.950
120.009
118.297
118.265
118.233
118.201
115.610
84.096
68.499
64.833
60.066
30.682
28.380
28.315
25.982
18.702
-5.026
-5.446



22

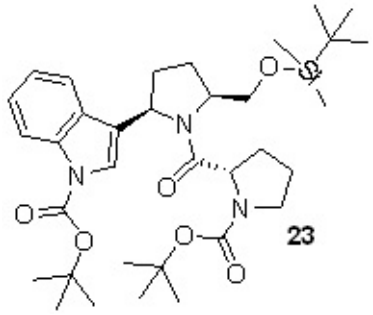
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)


8.14 8.12 8.11 7.63 7.61 7.54 7.52 7.44 7.40 7.37 7.35 7.34 7.32 7.30 7.28 7.27 7.25 7.23 5.71 5.40 5.38 4.32 4.31 4.29 4.25 4.23 4.18 4.11 4.10 4.09 4.08 4.06 4.05 3.86 3.84 3.83 3.80 3.78 3.78 3.54 3.53 3.49 3.48 3.47 3.41 2.15 2.14 2.12 2.11 2.09 2.08 2.07 2.05 2.04 2.02 2.00 1.97 1.96 1.80 1.78 1.77 1.76 1.74 1.73 1.67 1.66 1.63 1.61 1.59 1.57 1.56 1.49 1.46 1.42 1.27 1.26 1.25 0.90 0.89 0.88 0.87 0.10 0.08 0.08 0.07 0.06 0.04
1H NMR
23
0.83 0.95 3.23 1.02 0.88 0.91 1.05 0.91 2.08 1.03 4.25 1.37 9.73 1.40 8.71 0.99 9.03 6.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

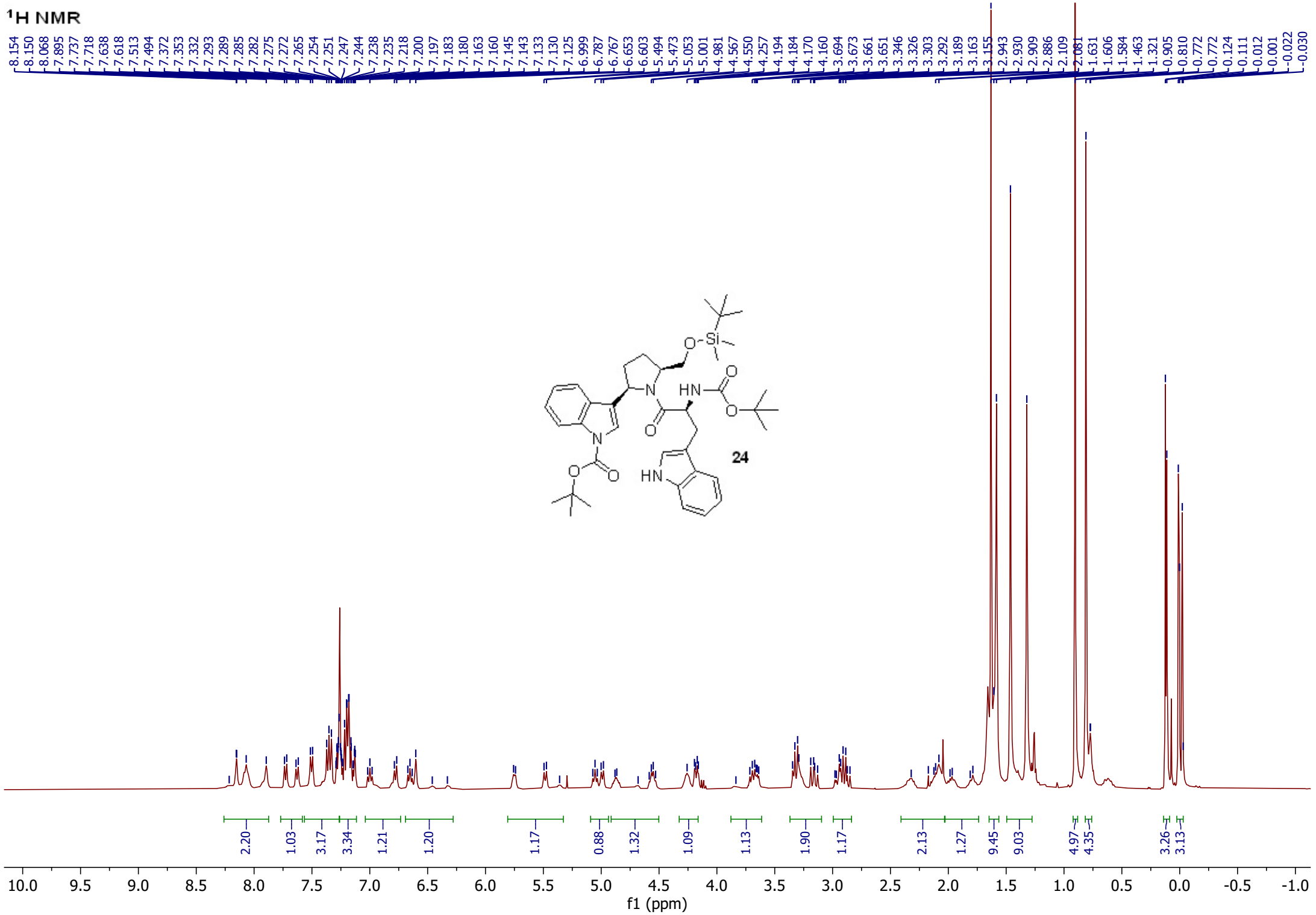
^{13}C NMR

174.995
174.682
154.486
153.665
149.744
149.653
136.036
128.383
128.191
125.038
124.833
124.209
123.355
123.276
122.911
122.732
119.637
118.875
115.771
115.528
84.225
83.954
79.813
79.357
64.048
63.984
60.352
60.113
57.429
57.329
56.182
55.979
47.471
47.365
33.079
32.820
32.265
31.055
28.872
28.664
28.597
28.453
28.349
26.707
26.673
26.103
26.086
24.668
23.722
18.508
18.467
-5.104
-5.188



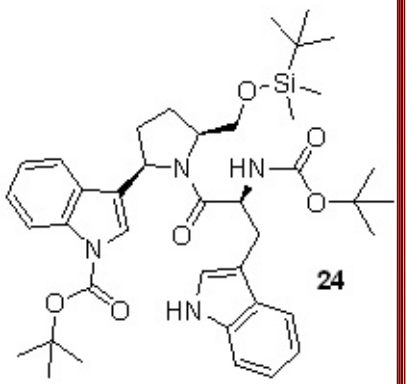
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)


1H NMR
8.154 8.150 8.068 7.895 7.737 7.718 7.638 7.618 7.513 7.494 7.372 7.353 7.332 7.293 7.289 7.285 7.282 7.275 7.272 7.265 7.254 7.251 7.247 7.244 7.238 7.235 7.218 7.200 7.197 7.183 7.180 7.163 7.160 7.145 7.143 7.133 7.130 7.125 6.999 6.787 6.767 6.653 6.603 5.494 5.473 5.053 5.001 4.981 4.567 4.550 4.257 4.194 4.184 4.170 4.160 3.694 3.673 3.661 3.651 3.346 3.326 3.303 3.292 3.189 3.163 3.155 2.943 2.930 2.909 2.886 2.109 2.081 1.631 1.606 1.584 1.463 1.321 0.905 0.810 0.772 0.772 0.124 0.111 0.012 0.001 -0.022 -0.030
O
Si
N
HN
O
O
N
O
O
HN
24
2.20 1.03 3.17 3.34 1.21 1.20 1.17 0.88 1.32 1.09 1.13 1.90 1.17 2.13 1.27 9.45 9.03 4.97 4.35 3.26 3.13
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

^{13}C NMR

174.37
172.15
155.54
155.19
149.92
149.76
136.37
136.13
135.96
129.14
128.49
127.75
127.48
125.02
124.44
123.58
123.22
123.10
123.02
122.71
122.61
122.51
121.96
121.28
119.98
119.67
119.57
119.40
118.59
115.67
115.50
111.48
111.24
111.10
111.04
84.07
83.56
79.61
79.55
64.78
64.51
60.53
59.35
56.27
54.63
53.65
52.53
32.79
30.82
30.46
29.94
29.32
28.64
28.50
28.41
28.38
27.70
27.18
26.73
26.21
26.17
18.60
18.50
14.43
14.37
1.26
0.23
-4.96
-5.04
-5.11
-5.37



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