Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Alkaloids from the Traditional Chinese Medicine ChanSu: Synthesis-enabled structural reassignment of bufopyramide to bufoserotonin C†

Emma K. Davison and Jonathan Sperry*

School of Chemical Sciences, University of Auckland, 23 Symonds St., Auckland, New Zealand

SUPPORTING INFORMATION

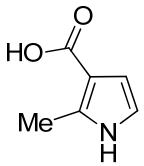
Contents

Page

General

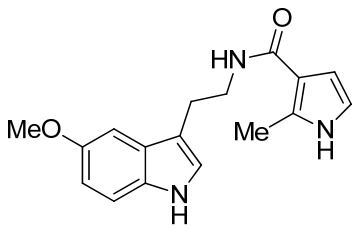
Commercially available reagents were used throughout without purification unless otherwise stated. Anhydrous solvents were used as supplied. Tetrahydrofuran was distilled from sodium benzophenone ketyl under nitrogen atmosphere. Dichloromethane was distilled from calcium hydride under a nitrogen atmosphere. Ether refers to diethyl ether. All reactions were routinely carried out in oven-dried glassware under a nitrogen or argon atmosphere unless otherwise stated. Analytical thin layer chromatography was performed using silica plates and compounds were visualized at 254 and/or 360 nm ultraviolet irradiation followed by staining with either alkaline permanganate or ethanolic vanillin solution. Infrared spectra were obtained using a Perkin Elmer spectrum One Fourier Transform Infrared spectrometer as thin films between sodium chloride plates. Absorption maxima are expressed in wavenumbers (cm^{-1}). Melting points were recorded on an Electrothermal melting point apparatus and are uncorrected. NMR spectra were recorded as indicated on either a spectrometer operating at 400 MHz for ^{1}H nuclei and 100 MHz for ^{13}C nuclei or on a spectrometer operating at 500 MHz and 125 MHz for ^{1}H and ^{13}C nuclei, respectively. Chemical shifts are reported in parts per million (ppm) relative to the tetramethylsilane peak recorded as δ 0.00 ppm in $CDCl_3$/ TMS solvent, or the residual chloroform (δ 7.26 ppm), DMSO (δ 2.50 ppm) or methanol (δ 3.31 ppm) peaks. The ^{13}C NMR values were referenced to the residual chloroform (δ 77.1 ppm), DMSO (δ 39.5 ppm) or methanol (δ 49.0 ppm) peaks. ^{13}C NMR values are reported as chemical shift δ, multiplicity and assignment. ^{1}H NMR shift values are reported as chemical shift δ, relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant (*J* in Hz) and assignment. Assignments are made with the aid of DEPT 135, COSY, NOESY, HMBC and HSQC experiments. High resolution mass spectra were obtained by electrospray ionization in positive ion mode at a nominal accelerating voltage of 70 eV on a microTOF mass spectrometer.

2-Methylpyrrole-3-carboxylic acid (**3**)



To a stirred solution of ethyl 2-methyl-pyrrole-3-carboxylate (0.494 g, 3.23 mmol) in methanol (24 mL) and water (5 mL), was added a solution of potassium hydroxide (7.96 g, 0.142 mol) in methanol (25 mL) slowly. The resulting solution was heated to reflux for 16 h, before removal of the methanol *in vacuo*. The resulting aqueous solution was neutralised with 10% aq. HCl, then acidified to ~pH 4 with acetic acid. The acidic solution was then extracted exhaustively with dichloromethane and the combined organic extracts were dried using Na_2SO_4, filtered, then concentrated *in vacuo* to afford the *title compound* (308 mg, 2.46 mmol, 76%) as an orange/brown solid without further purification. **Mp**: 185 – 190 °C; **HRMS** Found: $[M + Na]^+$, 148.0373, $[C_6H_7NO_2 + Na^+]$ requires 148.0369; **IR** (neat): 3295, 2921, 2852, 1635, 1479, 1336, 1279, 1193, 1144, 897 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6): δ_H = 11.45 (1 H, br s, COOH), 11.07 (1 H, br s, NH), 6.56 (1 H, t, *J* = 2.8, ArH), 6.28 (1 H, t, *J* = 2.8, ArH), 2.38 (3 H, s, Me); **^{13}C NMR** (100 MHz, DMSO-d_6): δ_C = 166.4, 134.4, 115.9 (CH), 110.5 (CH), 109.7, 12.7 (Me).

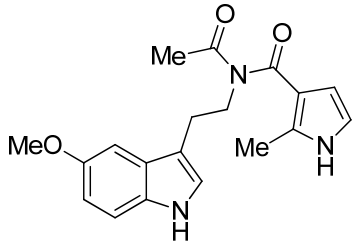
***N*-3-[2-(5-Methoxy-3-indolyl)ethyl]-2-methyl-3-pyrrolecarboxamide** (**4**)



To a stirred solution of 5-MT hydrochloride (100 mg, 0.442 mmol) in dichloromethane (8 mL), was added pyrrole **3** (50 mg, 0.400 mmol), 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-

triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU) (160 mg, 0.421 mmol), and *N*,*N*-diisopropylethylamine (0.175 mL, 1.00 mmol). The resulting solution was stirred at room temperature for 20 h, before diluting with dichloromethane (20 mL) and 10% aq. HCl (30 mL). The organic layer was separated and washed with sat. sodium bicarbonate solution (4 x 20 mL). The combined aqueous layers were then extracted with dichloromethane (3 x 10 mL) and the combined organic extracts were dried using Na_2SO_4, filtered, then concentrated *in vacuo.* The crude product was purified by flash chromatography eluting with ethyl acetate – hexanes (4:1) to afford the *title compound* (76 mg, 0.256 mmol, 64%) as a cream coloured solid. **Mp**: 184 – 189 °C; **HRMS** Found: $[M + Na]^+$, 320.1367, $[C_{17}H_{19}N_3O_2 + Na^+]$ requires 320.1369; **IR** (neat): 3377, 1602, 1572, 1530, 1483, 1440, 1215, 830 cm^{-1}; **^{1}H NMR** (400 MHz, acetone-d_6): δ_H = 10.07 (1 H, br s, NH), 9.83 (1 H, br s, NH), 7.26 (1 H, d, *J* = 8.8, ArH), 7.16 (1 H, d, *J* = 2.4, ArH), 7.15 – 7.14 (1 H, m, ArH), 6.95 (1 H, br s, NH), 6.74 (1 H, dd, *J* = 8.8, 2.4, ArH), 6.56 (1 H, t, *J* = 2.7, ArH), 6.36 (1 H, t, *J* = 2.7, ArH), 3.77 (3 H, s, OMe), 3.62 – 3.57 (2 H, m, CH_2), 2.97 (2 H, t, *J* = 7.2, CH_2), 2.50 (3 H, s, Me); **^{13}C NMR** (100 MHz, DMSO-d_6): δ_C = 152.9, 139.6, 131.6, 131.4, 127.7, 123.1 (CH), 115.4, 115.1 (CH), 112.1, 111.9 (CH), 111.0 (CH), 107.0 (CH), 100.3 (CH), 55.3 (OMe), 39.3 (CH_2), 25.7 (CH_2), 12.6 (Me).

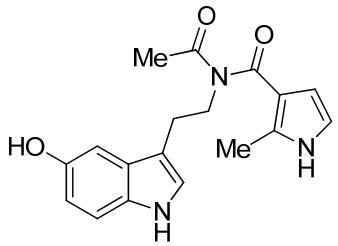
_N_-3-Acetyl-_N_-3-[2-(5-methoxy-3-indolyl)ethyl]-2-methyl-3-pyrrolecarboxamide (**5**)



To a stirred solution of **4** (48 mg, 0.162 mmol) in dichloromethane (5 mL), was added triethylamine (0.025 mL, 0.179 mmol) and acetyl chloride (0.013 mL, 0.183 mmol). The

resulting solution was then heated to 30 °C and stirred for 2.5 h. The solution was then cooled to room temperature, diluted with dichloromethane (10 mL) and washed with sat. sodium bicarbonate solution (10 mL) and water (3 x 10 mL). The combined aqueous layers were then extracted with dichloromethane (3 x 10 mL). The combined organic extracts were dried using Na_2SO_4, filtered, then concentrated *in vacuo*. The crude product was purified by flash chromatography eluting with ethyl acetate – hexanes (3:2) to afford the *title compound* (21 mg, 0.0619 mmol, 38% (44%brsm)) as a yellow oil. **HRMS** Found: $[M + H]^+$, 340.1668, $[C_{19}H_{21}N_3O_3 + H^+]$ requires 340.1656; **IR** (neat): 3309, 2926, 1635, 1438, 1367, 1348, 1265, 1212, 1171, 1136, 989, 727 cm^{-1}; **^{1}H NMR** (400 MHz, acetone-d_6): δ_H = 10.48 (1 H, br s, NH), 9.80 (1 H, br s, NH), 7.23 (1 H, d, *J* = 8.8, ArH), 7.06 – 7.03 (2 H, m, 2 x ArH), 6.73 – 6.69 (2 H, m, 2 x ArH), 6.29 – 6.28 (1 H, m, ArH), 4.06 – 4.02 (2 H, m, CH_2), 3.76 (3 H, s, OMe), 2.98 – 2.94 (2 H, m, CH_2), 2.36 (3 H, s, Me), 2.12 (3 H, s, Me); **^{13}C NMR** (100 MHz, acetone-d_6): δ_C = 172.6, 171.6, 154.7, 137.2, 132.8, 128.8, 124.2 (CH), 117.5 (CH), 116.6, 112.7 (CH), 112.6, 112.5 (CH), 110.5 (CH), 101.0 (CH), 55.8 (OMe), 47.3 (CH_2), 25.9 (CH_2), 25.1 (Me), 12.6 (Me).

Putative Bufopyramide (**1**)

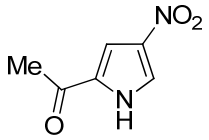


A stirred solution of **5** (21 mg, 0.0619 mmol) in dichloromethane (6 mL) was cooled to -78 °C prior to the dropwise addition of boron tribromide (0.025 mL, 0.264 mmol). The solution was allowed to warm to room temperature with stirring over 15.5 h. The reaction mixture was then quenched with ice and water (10 mL) and neutralised with aq. sodium hydrogen

carbonate solution (10 mL). The aqueous layer was extracted with dichloromethane (3 x 20 mL) and the combined organic extracts were dried using Na_2SO_4, filtered, then concentrated *in vacuo*. The crude product was purified by flash chromatography eluting with dichloromethane - methanol (19:1) to afford the *title compound* (2 mg, 0.00615 mmol, 10%) as an orange oil. **HRMS** Found: $[M + Na]^+$, 348.1309, $[C_{18}H_{19}N_3O_3 + Na^+]$ requires 348.1319; **IR** (neat): 3288, 2925, 1629, 1437, 1366, 1257, 1175, 989, 796, 727 cm^{-1}

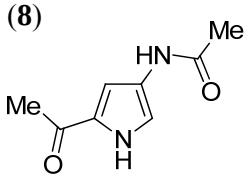
For NMR data, see **Table 1** in the manuscript

5-Acetyl-3-nitropyrrole (**7**)



A stirred solution of 2-acetylpyrrole (1.00 g, 9.17 mmol) in acetic anhydride (12.5 mL) was cooled to -40 °C prior to the dropwise addition of 69% nitric acid (0.82 mL) over 40 min. The reaction mixture was warmed to room temperature and stirred for 1.5 h. The solution was then poured onto ice water, and neutralised with sat. sodium bicarbonate solution. The aqueous layer was then separated, and extracted with ethyl acetate (4 x 50 mL). The combined organic extracts were then dried using $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by flash column chromatography on silica gel eluting with dichloromethane – ethyl acetate (9:1) afforded the *title compound* (503 mg, 3.27 mmol, 36%) as a yellow powder. **Mp**: 194.8 – 198.2 °C; **HRMS** Found: $[M + Na]^+$, 177.0275. $[C_6H_6N_2O_3 + Na]^+$ requires 177.0271; **IR** (neat): 3231, 3136, 1652, 1555, 1480, 1392, 1358, 1317, 1258, 1172, 1147, 984, 938, 854, 792, 748 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H = 9.83 (1 H, br s, NH), 7.82 (1 H, dd, J = 3.5, 1.5, ArH), 7.39 (1 H, dd, J = 2.5, 1.5, ArH), 2.50 (3 H, s, COMe); **^{13}C NMR** (100 MHz, DMSO-d_6): δ_C = 188.3, 136.6, 131.4, 125.1 (CH), 111.1 (CH), 25.7 (CO<u>Me</u>). ^{1}H-NMR data consistent with the literature. [1]

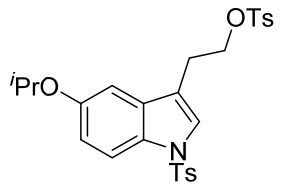
***N*-(5-Acetylpyrrol-3-yl)-acetamide (8)**



To a stirred solution of **7** (485 mg, 3.15 mmol) in ethanol (8 mL) was added iron (913 mg, 16.3 mmol) and aq. ammonium chloride (24%, 2.54 mL). The mixture was then heated to 70 °C for 1.5 h, before being cooled to room temperature and filtered through celite. The filtrate was then concentrated *in vacuo*, and the residue redissolved in ethyl acetate (20 mL). The resulting solution was then washed with aq. sodium hydroxide (1 M, 10 mL) and brine (10 mL) and the organic layer was then dried using $MgSO_4$, filtered, then concentrated *in vacuo*. The crude amine intermediate was then dissolved in THF (14 mL) at -5 °C, before adding triethylamine (0.55 mL, 3.94 mmol), acetic anhydride (0.37 mL, 3.92 mmol) and dimethylaminopyridine (19 mg, 0.156 mmol, 5 mol%). The resulting solution was then stirred at room temperature for 2.5 h, before being diluted with ethyl acetate (20 mL) and water (20 mL). The aqueous layer was separated and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were washed with brine (20 mL) and sat. sodium bicarbonate solution (20 mL), then were dried using $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel eluting with dichloromethane – methanol (19:1) afforded the *title compound* (185 mg, 1.11 mmol, 35%) as a brown powder. **Mp**: Degraded at 182.4 – 185.8 °C; **HRMS** Found: $[M + Na]^+$, 189.0638. $[C_8H_{10}N_2O_2 + Na]^+$ requires 189.0634; **IR** (neat): 3306, 3148, 2922, 2853, 1629, 1581, 1452, 1386, 1211, 1124, 1025, 919, 808, 729 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6): δ_H = 11.50 (1 H, br s, NH), 9.85 (1 H, br s, NH), 7.22 (1 H, dd, *J* = 2.9, 1.5, ArH), 6.78 (1 H, dd, *J* = 2.7, 1.5, ArH), 2.30 (3 H, s, COMe), 1.96 (3 H, s, NHCOMe); **^{13}C NMR** (100 MHz, DMSO-d_6): δ_C = 186.7, 166.7, 128.9, 124.9, 115.2 (CH), 106.9 (CH), 25.5 (Me), 23.0 (Me).

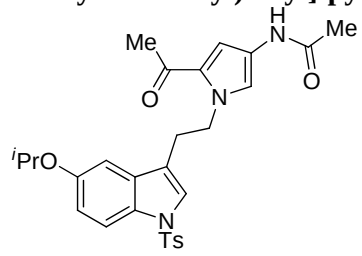
Spectroscopic data consistent with the literature. [2]

2-(5-Isopropoxy-1-tosyl-indol-3-yl)ethyl-4-methylbenzenesulfonate (**9**)



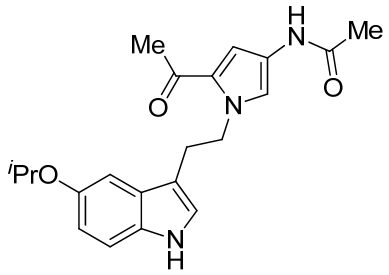
To a stirred solution of 5-isopropoxytryptophol [3] (69 mg, 0.315 mmol) in THF (10 mL) at 0 °C was added sodium hydride (60% in mineral oil, 274 mg, 6.85 mmol). The reaction mixture was stirred for 1 h at 0 °C before the careful addition of p-toluenesulfonyl chloride (375 mg, 1.97 mmol). The reaction mixture was then warmed to room temperature and was stirred vigorously for 25 h, before carefully quenching with water (20 mL) and ethyl acetate (10 mL). The aqueous layer was then separated, and extracted with ethyl acetate (4 x 20 mL). The combined organic extracts were then dried using Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel eluting with ethyl acetate – hexanes (1:4) afforded the *title compound* (102 mg, 0.193 mmol, 61%) as a yellow oil. **HRMS** Found: $[M + Na]^+$, 550.1333. $[C_{27}H_{29}NO_6S_2 + Na]^+$ requires 550.1329; **IR** (neat): 2977, 1597, 1463, 1360, 1188, 1170, 1114, 1095, 965, 81, 811, 664 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H = 7.80 (1 H, d, *J* = 9.0, ArH), 7.71 (2 H, d, *J* = 8.4, 2 x ArH), 7.56 (2 H, d, *J* = 8.3, 2 x ArH), 7.25 (1 H, s, ArH), 7.21 (2 H, d, *J* = 8.2, 2 x ArH), 7.16 (2 H, d, *J* = 8.2, 2 x ArH), 6.88 (1 H, dd, *J* = 9.0, 2.4, ArH), 6.73 (1 H, d, *J* = 2.4, ArH), 4.47 (1 H, sept, *J* = 6.1, CH), 4.22 (2 H, t, *J* = 6.6, CH_2), 2.95 (2 H, td, *J* = 6.6, 0.7, CH_2), 2.39 (3 H, s, Me), 2.33 (3 H, s, Me), 1.31 (6 H, d, *J* = 6.1, CH$\underline{Me_2}$); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C = 154.7, 144.98, 144.94, 135.4, 132.7, 131.4, 130.0 (2 x CH), 129.8 (2 x CH), 127.8 (2 x CH), 126.9 (2 x CH), 124.9 (CH), 117.3, 115.5 (CH), 114.7 (CH), 104.6 (CH), 70.8 (O$\underline{CH}Me_2$), 68.8 (CH_2), 25.1 (CH_2), 22.2 (OCH$\underline{Me_2}$), 21.8 (Me), 21.7 (Me), 1 x C not observed.

***N*-{5-Acetyl-1-[2-(5-isopropoxy-1-tosyl-indol-3-yl)ethyl]-pyrrol-3-yl}acetamide** (**10**)



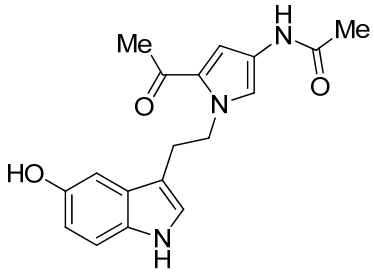
To a stirred solution of pyrrole **8** (130 mg, 0.783 mmol) in DMF (12 mL) at 0 °C was added sodium hydride (60% in mineral oil, 36 mg, 0.900 mmol). The reaction mixture was allowed to warm to room temperature, and was stirred for 40 min. The solution was then cooled to 0 °C before the dropwise addition of a solution of tosylate **9** (454 mg, 0.861 mmol) in DMF (12 mL). The reaction mixture was again warmed to room temperature and stirring continued for 24 h, before being carefully quenched by the cautious addition of water (10 mL). The aqueous layer was then separated, and extracted with ether (4 x 20 mL). The combined organic extracts were then dried using $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel eluting with ethyl acetate – hexanes (4:1) afforded the *title compound* (235 mg, 0.451 mmol, 58%) as a brown solid. **Mp**: 57.3 – 63.1 °C; **HRMS** Found: $[M + Na]^+$, 544.1881. $[C_{28}H_{31}N_3O_5S + Na]^+$ requires 544.1877; **IR** (neat): 2928, 1647, 1594, 1462, 1401, 1368, 1169, 1114, 1094, 960, 810, 667 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H = 7.81 (1 H, d, *J* = 9.0, ArH), 7.70 (2 H, d, *J* = 8.4, 2 x ArH), 7.47 (1 H, br s, NH), 7.22 (1 H, s, ArH), 7.19 (2 H, d, *J* = 8.2, 2 x ArH), 7.16 (1 H, d, *J* = 1.6, 2 x ArH), 7.14 (1 H, d, *J* = 2.4, ArH), 6.88 (1 H, dd, *J* = 9.0, 2.4, ArH), 6.83 (1 H, d, *J* = 1.9, ArH), 4.59 (1 H, sept, *J* = 6.0, CH), 4.44 (2 H, t, *J* = 7.6, CH_2), 3.00 (2 H, t, *J* = 7.5, CH_2), 2.37 (3 H, s, Me), 2.32 (3 H, s, Me), 2.10 (3 H, s, Me), 1.33 (6 H, d, *J* = 6.0, $CH\underline{Me_2}$); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C = 188.2, 167.8, 154.8, 144.8, 135.3, 131.9, 129.94 (2 x CH), 129.87, 127.4, 126.9 (2 x CH), 124.4 (CH), 122.2, 121.6 (CH), 119.4 , 115.6 (CH), 114.6 (CH), 111.0 (CH), 104.9 (CH), 70.8 ($\underline{CH}Me_2$), 49.5 (CH_2), 27.5 (CH_2), 27.4 (Me), 23.7 (Me), 22.2 ($CH\underline{Me_2}$), 21.7 (Me).

***N*-{5-Acetyl-1-[2-(5-isopropoxyindol-3-yl)ethyl]-pyrrol-3-yl}acetamide** (**S1**)



To a stirred solution of **10** (235 mg, 0.451 mmol) in methanol (5 mL) was added a freshly prepared solution of sodium methoxide (24% in methanol, 3 mL). The resulting solution was heated to reflux for 20 h. The reaction mixture was then cooled to 0 °C and acidified to ~ pH 2 with 10% aq. sulfuric acid. The mixture was then partitioned between dichloromethane (20 mL) and water (20 mL). The aqueous layer was separated then further extracted with dichloromethane (20 mL) and ethyl acetate (2 x 20 mL). The combined organic extracts were washed with sat. sodium bicarbonate solution (2 x 30 mL), dried using Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel eluting with ethyl acetate – hexanes (9:1) afforded the *title compound* (121 mg, 0.330 mmol, 73%) as a yellow solid. **Mp**: 68.1 – 64.4 °C; **HRMS** Found: $[M + Na]^+$, 390.1780. [$C_{21}H_{25}N_3O_3$ + $Na]^+$ requires 390.1788; **IR** (neat): 3290, 2974, 1634, 1580, 1457, 1401, 1352, 1192, 1112, 1031, 958, 910, 796, 728 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ_H = 7.86 (1 H, br s, NH), 7.22 (1 H, d, *J* = 8.7, ArH), 7.20 (1 H, d, *J* = 2.2, ArH), 7.11 (1 H, d, *J* = 1.8, ArH), 6.98 (1 H, br s, NH), 6.92 (1 H, d, *J* = 2.4, ArH), 6.86 – 6.83 (2 H, m, 2 x ArH), 4.58 (1 H, sept, *J* = 6.1, CH), 4.51 (2 H, t, *J* = 7.5, CH_2), 3.11 (2 H, t, *J* = 7.5, CH_2), 2.42 (3 H, s, Me), 2.11 (3 H, s, Me), 1.37 (6 H, d, *J* = 6.0, CH$\underline{Me_2}$); **^{13}C NMR** (100 MHz, $CDCl_3$): δ_C = 188.2, 167.8, 152.0, 131.8, 128.1, 127.4, 123.3 (CH), 121.8 (CH + C), 114.4 (CH), 112.3, 111.8 (CH), 111.0 (CH), 104.8 (CH), 71.5 ($\underline{CH}Me_2$), 50.6 (CH_2), 27.7 (CH_2), 27.4 (Me), 23.7 (Me), 22.4 ($CH\underline{Me_2}$).

Bufoserotonin C (**6**)

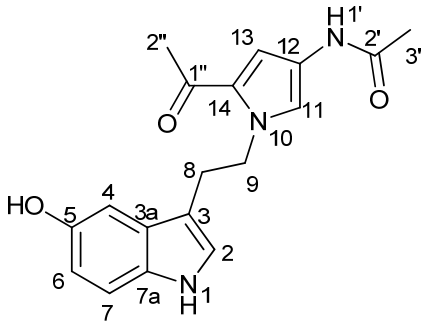


To a stirred solution of **S1** (58 mg, 0.158 mmol) in dichloromethane (12 mL) at 0 °C was added aluminium chloride (128.5 mg, 0.964 mmol). The reaction mixture was stirred at 0 °C for 3 h, then was warmed to room temperature and stirring continued for 2 h. A solution of aq. ammonium chloride (10 mL) was then added and the mixture was stirred vigorously for 40 min. The organic layer was then separated, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried using Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel eluting with dichloromethane – methanol (19:1) afforded the *title compound* (13 mg, 0.0400 mmol, 25%) as a dark brown solid. **Mp**: degraded at 159.1 – 163.2 °C; **HRMS** Found: $[M + Na]^+$, 348.1321. $[C_{18}H_{19}N_3O_3 + Na]^+$ requires 348.1319; **IR** (neat): 3282, 1628, 1582, 1455, 1402, 1134, 1031, 950, 796, 732 cm^{-1}.

For a comparison of the NMR data for synthetic bufoserotonin C to natural bufopyramide, see Table 2 in the manuscript.

For a comparison of the NMR data for synthetic bufoserotonin C to natural bufoserotonin C, see **Table S1**

Table S1 – NMR data for synthetic bufoserotonin C (**6**) and authentic bufoserotonin C[4]



Position	Literature[4] (500 MHz, DMSO-d_6)	Found (400 MHz, DMSO-d_6)	Literature[4] (125 MHz, DMSO-d_6)	Found (100 MHz, DMSO-d_6)
NH (1)	10.51 (s)	10.49 (br s)	-	-
CH (2)	6.97 (d, *J* 2.3)	6.99 – 6.98 (m)	123.5	123.5
C (3)	-	-	109.8	109.8
C (3a)	-	-	127.8	127.8
CH (4)	6.98 (d, *J* 2.2)	6.99 – 6.98 (m)	102.4	102.4
C(5)-OH	-	8.57 (br s)	150.2	150.2
CH (6)	6.59 (dd, *J* 8.6, 2.2)	6.61 (dd, *J* 8.6, 2.3)	111.3	111.3
CH (7)	7.10 (d, *J* 8.6)	7.11 (d, *J* 8.6)	111.6	111.5
C (7a)	-	-	130.7	130.7
CH_2 (8)	2.90 (t, *J* 7.6)	2.91 (t, *J* 7.8)	27.5	27.5
CH_2 (9)	4.41 (t, *J* 7.6)	4.42 (t, *J* 7.8)	49.4	49.4
CH (11)	7.29 (d, *J* 1.7)	7.30 (d, *J* 1.8)	120.8	120.8
C (12)	-	-	122.9	122.8
CH (13)	6.89 (d, *J* 1.7)	6.89 (d, *J* 1.8)	110.2	110.2
C (14)	-		126.4	126.4
NH (1')	9.93 (s)	9.86 (br s)	-	-
CO (2')	-	-	166.7	166.6
Me (3')	1.95 (s)	1.96 (s)	23.0	23.0
CO (1")	-	-	187.3	187.3
Me (2")	2.38 (s)	2.38 (s)	27.1	27.1

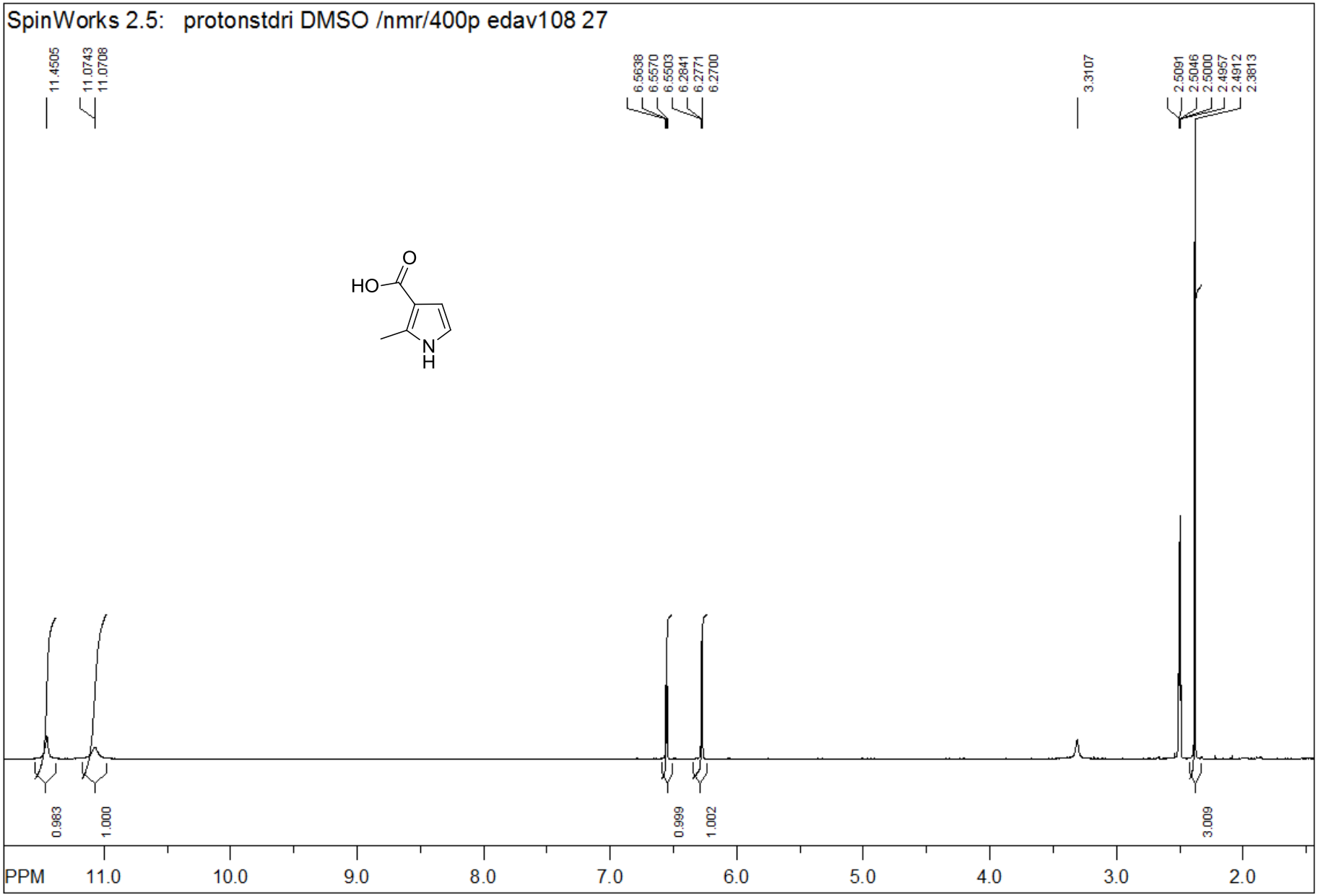
References

1. H. Oda, T. Hanami, T. Iwashita, M. Kojima, M. Itoh and Y. Hayashizaki, Y. *Tetrahedron*, 2007, **63**, 12747–12753

2. R.-H. Liu, H. Luo, Y. L. Li, M. Yang, X.K. Xu, H. L. Li, Y. H. Shen, C. Zhang, J. Su, and W. D. Zhang, *Chem. Nat. Compd.,* 2009*,* **45,** 599–600.

3. L. M. Blair and J. Sperry, *Tetrahedron Lett.,* **2013***, 54*, 1980-1982.

4. R.-H. Liu, H. Luo, Y.-L. Li, M. Yang, H.-L Li, Y.-H. Shen, C. Zhang, J. Su and W.-D. Zhang, *Helv. Chim. Acta.,* 2007, **90**, 2427–2431



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time domain size: 32768 points
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number of scans: 60

freq. of 0 ppm: 399.870007 MHz
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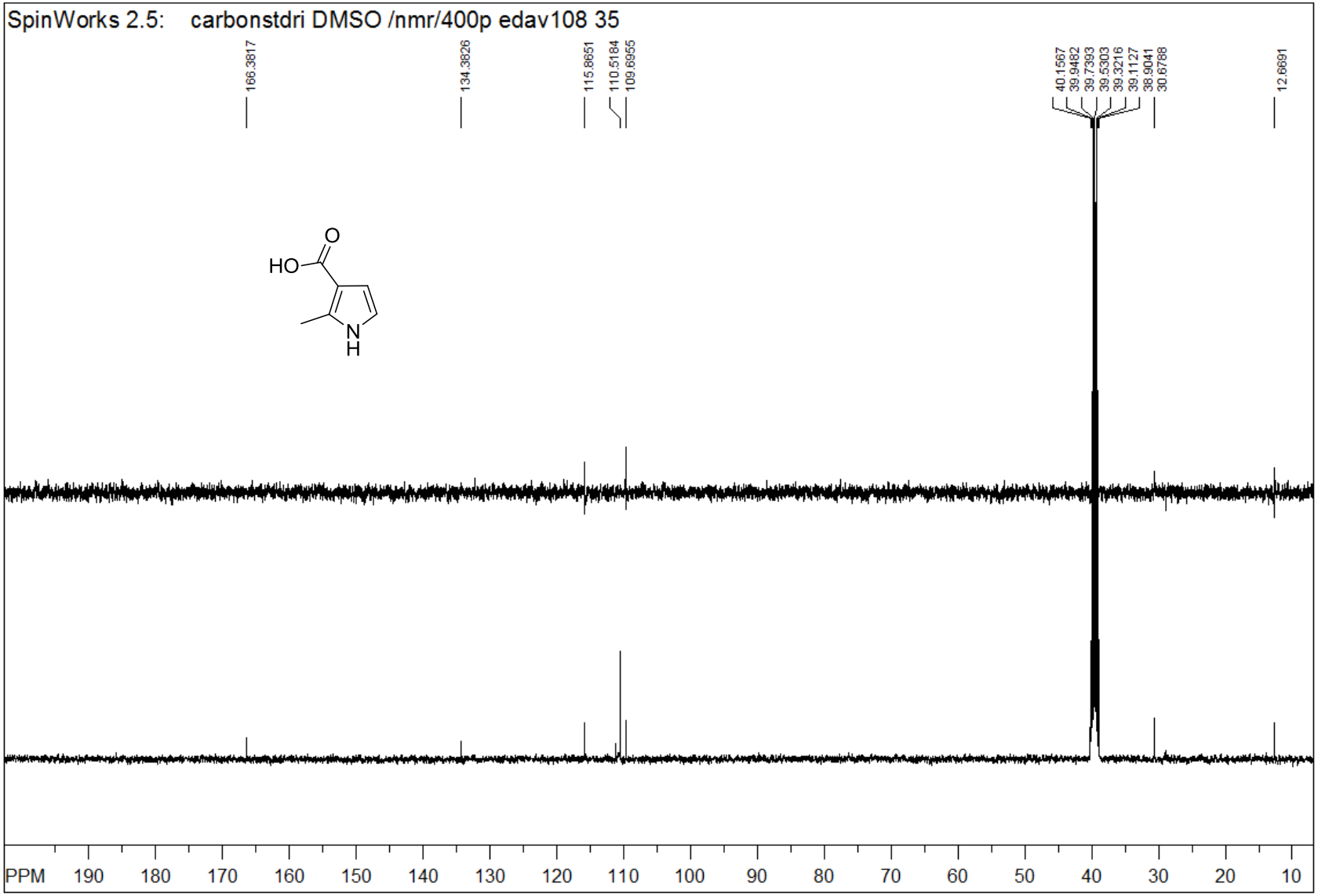
Hz/cm: 165.532 ppm/cm: 0.41396



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time domain size: 65536 points
width: 24038.46 Hz = 239.049398 ppm = 0.366798 Hz/pt
number of scans: 400

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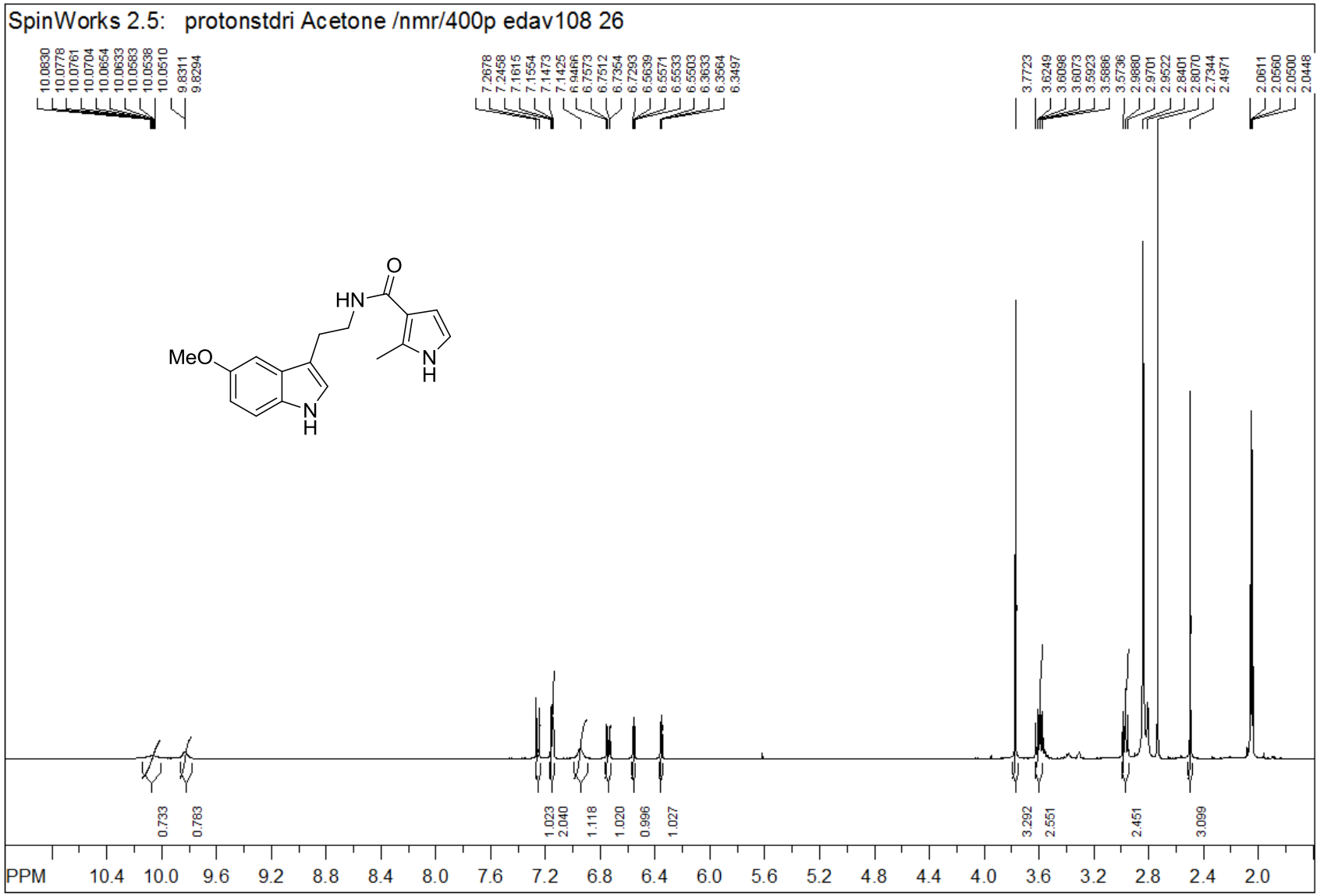

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time domain size: 32768 points
width: 8169.93 Hz = 20.431370 ppm = 0.249327 Hz/pt
number of scans: 40

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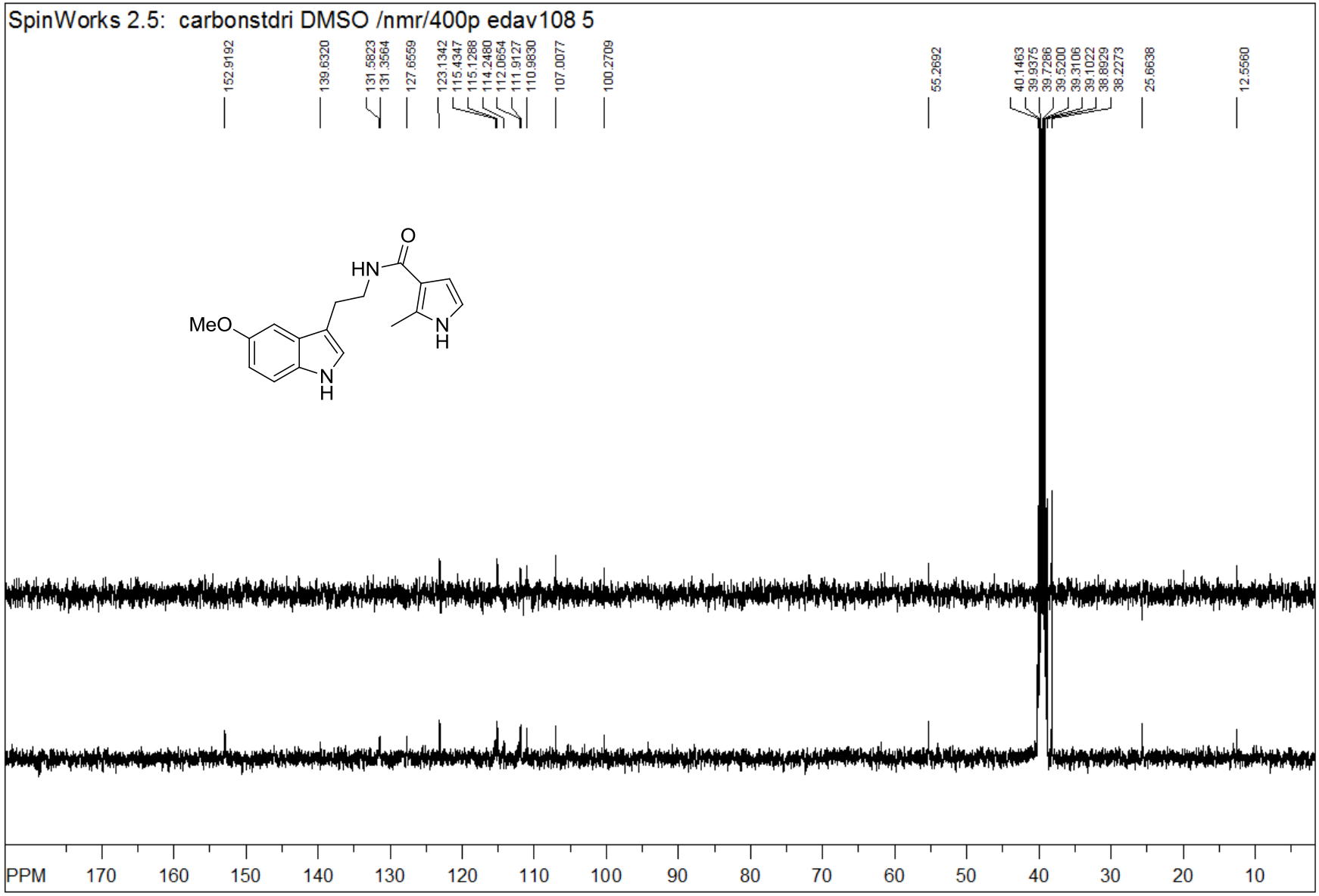

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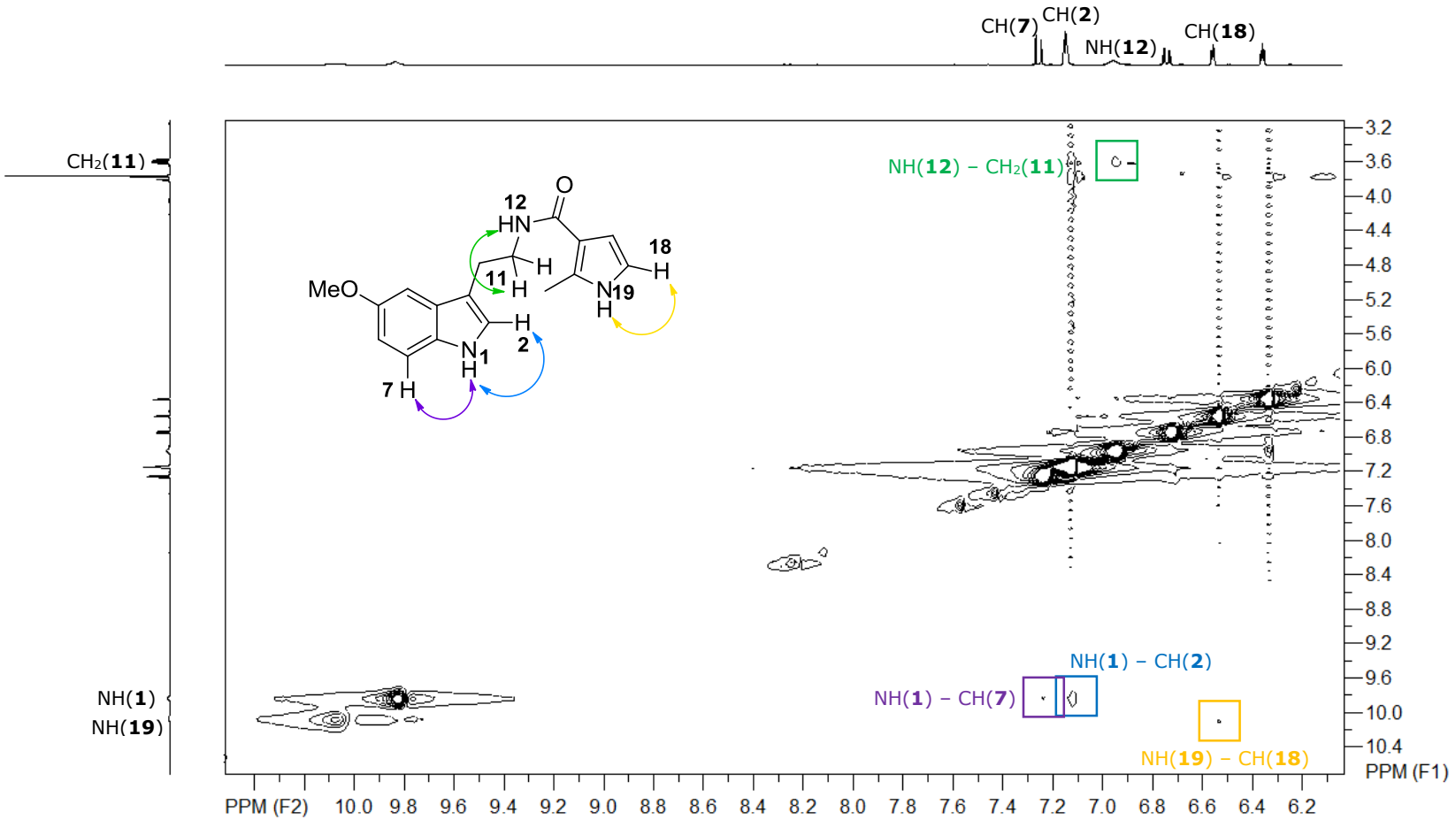
time domain size: 65536 points
width: 24038.46 Hz = 239.049398 ppm = 0.366798 Hz/pt
number of scans: 400

freq. of 0 ppm: 100.547441 MHz
processed size: 32768 complex points
LB: 2.000 GB: 0.0000
Hz/cm: 730.568 ppm/cm: 7.26510

SpinWorks 2.5 2D: noesystdi Acetone /nmr/400p edav108 29



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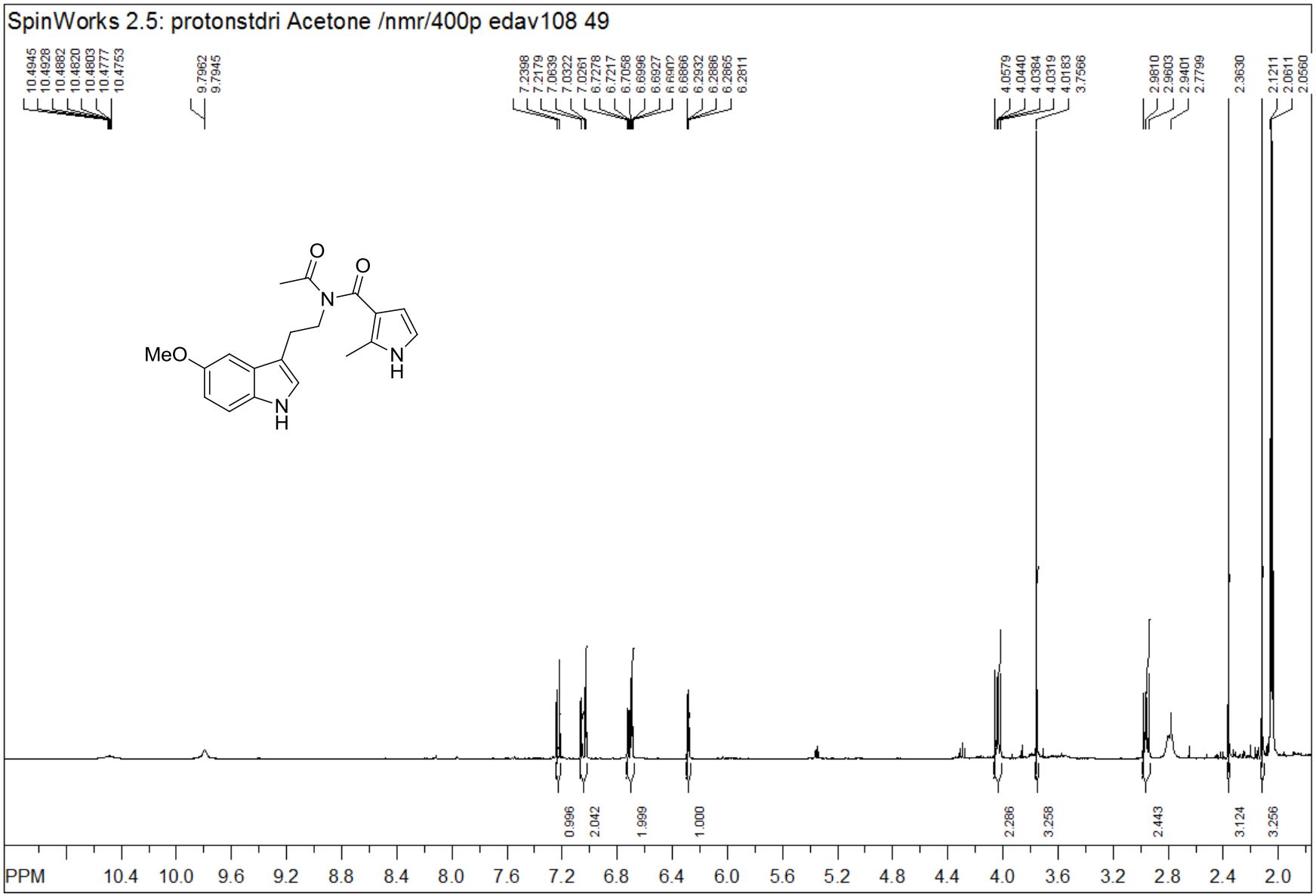
time domain size: 2048 by 256 points
width (F2): 5580.33 Hz = 13.955368 ppm = 2.724772 Hz/pt
number of scans: 10

F2: freq. of 0 ppm: 399.870024 MHz
processed size: 1024 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 87.479 ppm/cm: 0.21877

F1: freq. of 0 ppm: 399.870010 MHz
processed size: 256 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 253.548 ppm/cm: 0.63407



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time domain size: 32768 points
width: 8169.93 Hz = 20.431370 ppm = 0.249327 Hz/pt
number of scans: 50

freq. of 0 ppm: 399.870011 MHz
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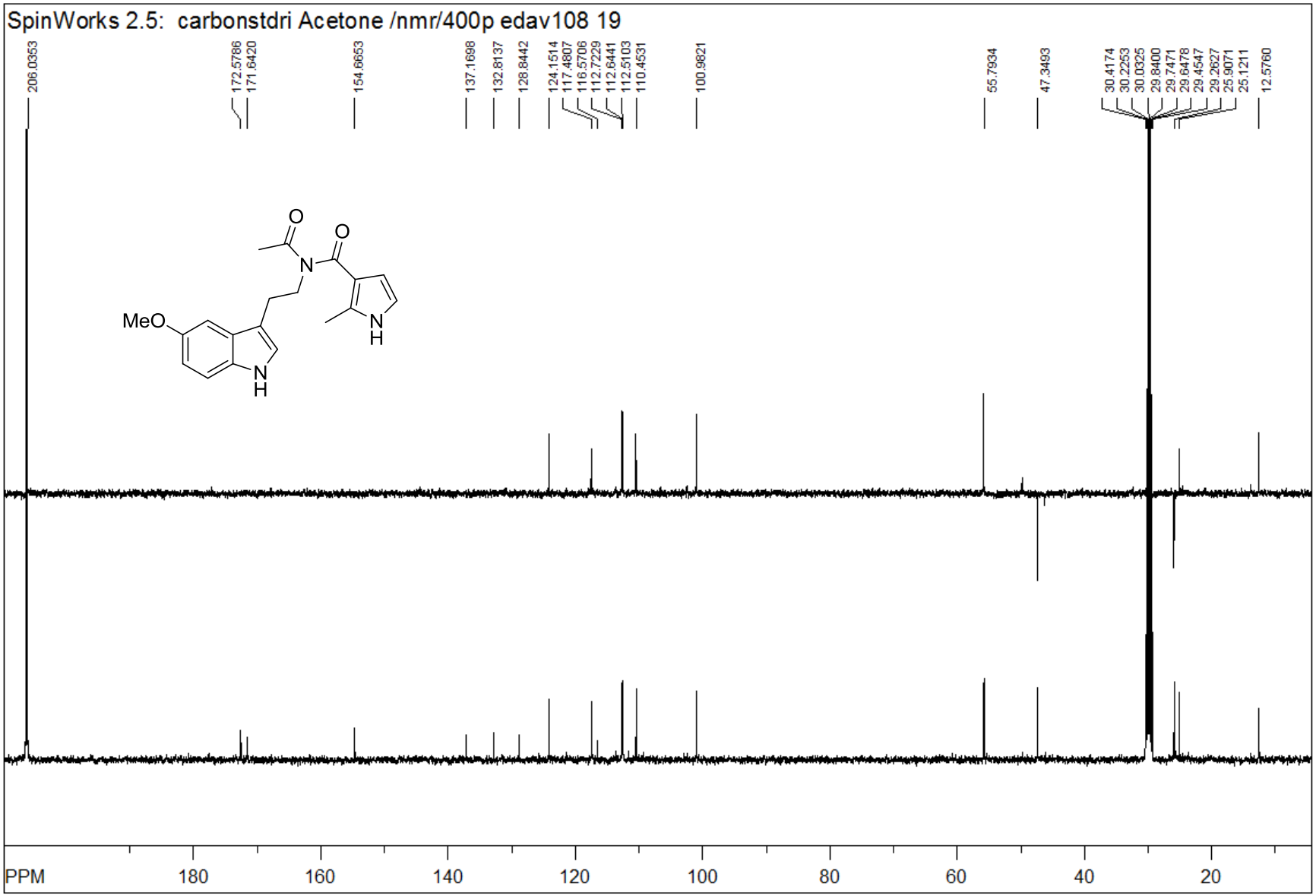
Hz/cm: 151.709 ppm/cm: 0.37939



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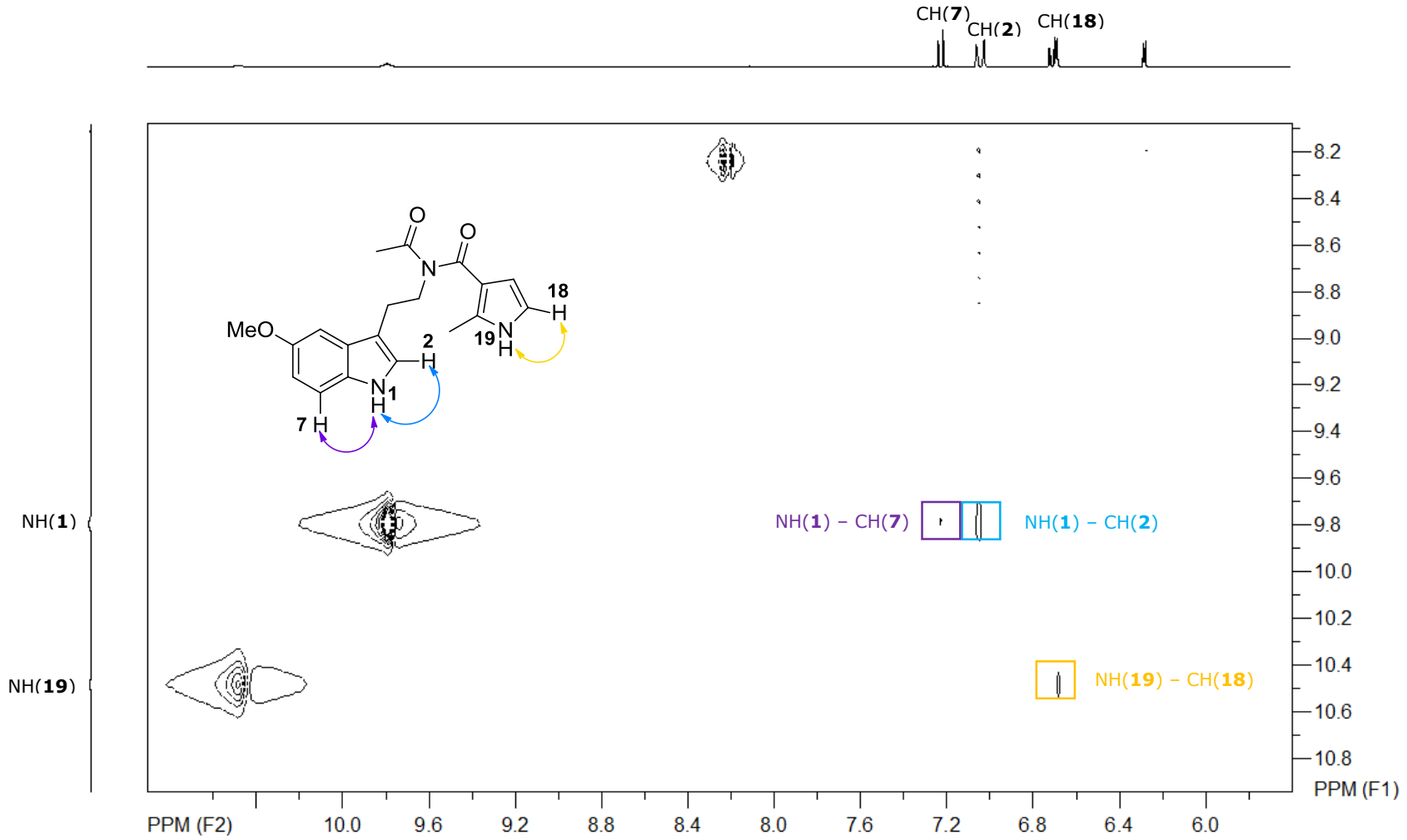
width: 24038.46 Hz = 239.049398 ppm = 0.366798 Hz/pt
number of scans: 200

freq. of 0 ppm: 100.547302 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000
Hz/cm: 825.969 ppm/cm: 8.21381

SpinWorks 2.5 2D: noesystdi Acetone /nmr/400p edav108 28



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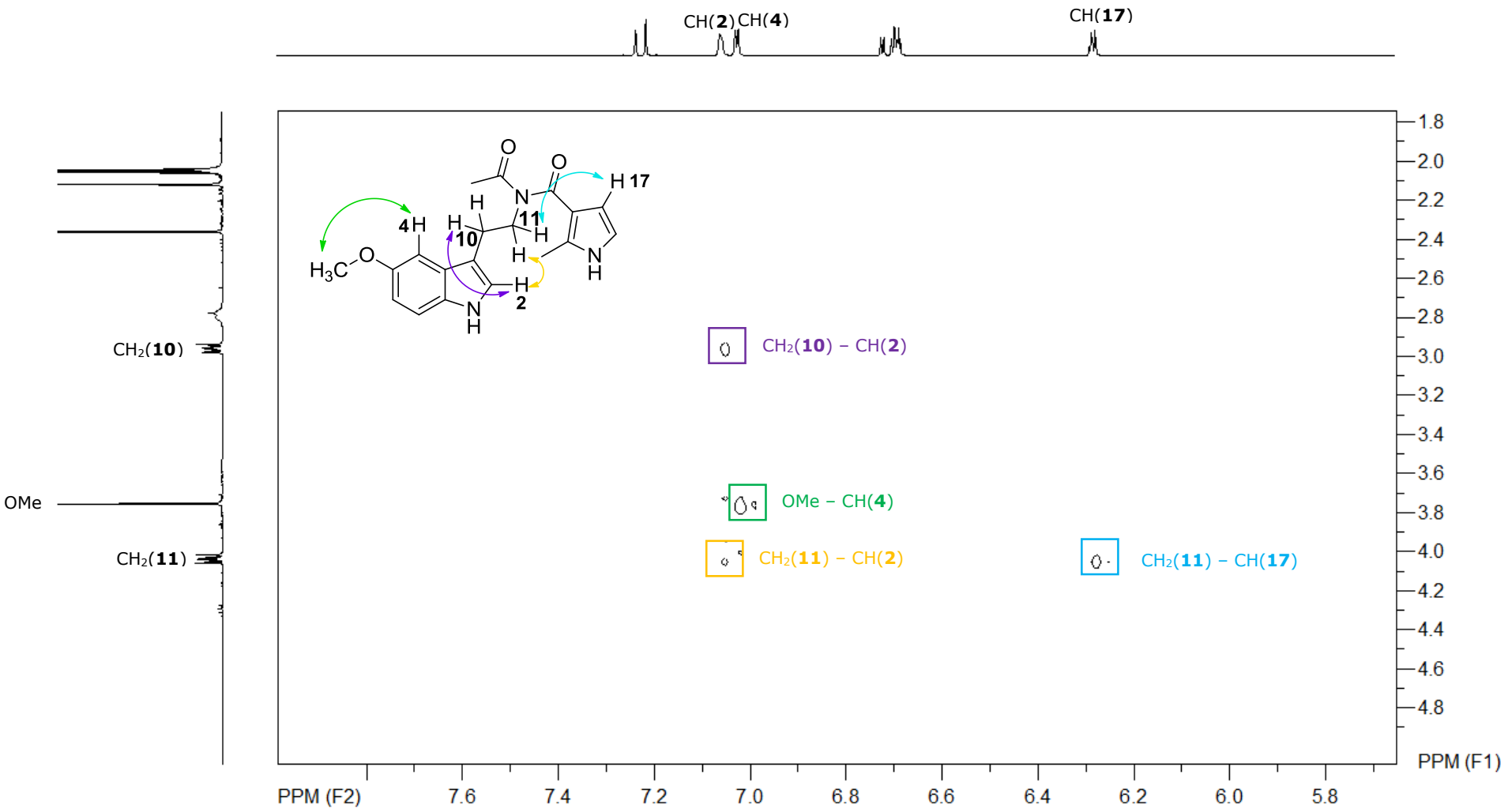
time domain size: 2048 by 256 points
width (F2): 5580.33 Hz = 13.955368 ppm = 2.724772 Hz/pt
number of scans: 8

F2: freq. of 0 ppm: 399.870017 MHz
processed size: 1024 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 103.491 ppm/cm: 0.25881

F1: freq. of 0 ppm: 399.870011 MHz
processed size: 256 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 95.501 ppm/cm: 0.23883

SpinWorks 2.5 2D: noesystdi Acetone /nmr/400p edav108 28



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time domain size: 2048 by 256 points
width (F2): 5580.33 Hz = 13.955368 ppm = 2.724772 Hz/pt
number of scans: 8

F2: freq. of 0 ppm: 399.870017 MHz
processed size: 1024 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 45.509 ppm/cm: 0.11381

F1: freq. of 0 ppm: 399.870011 MHz
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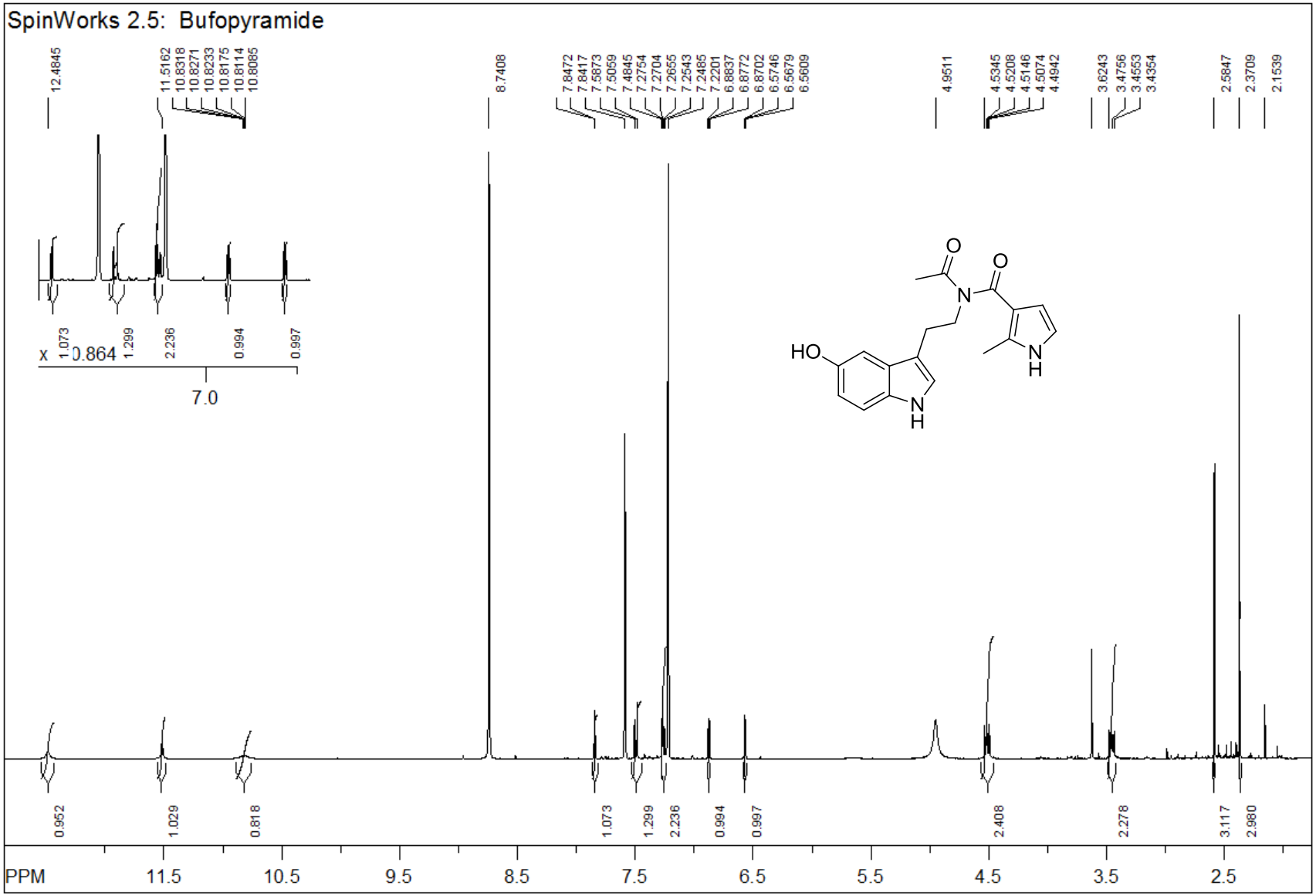
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 111.642 ppm/cm: 0.27919



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time domain size: 32768 points
width: 8169.93 Hz = 20.431370 ppm = 0.249327 Hz/pt
number of scans: 64

freq. of 0 ppm: 399.869989 MHz
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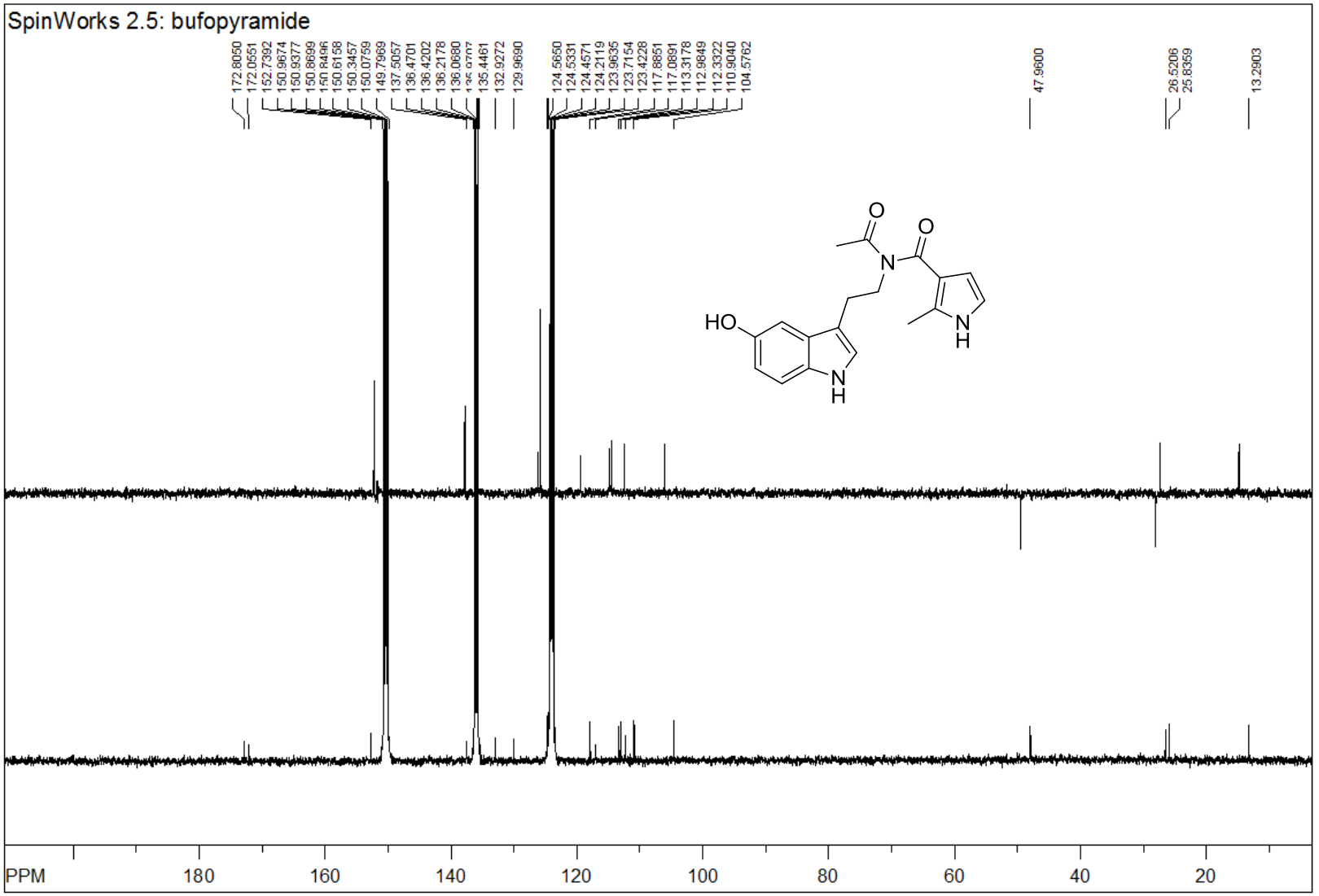
Hz/cm: 177.477 ppm/cm: 0.44384



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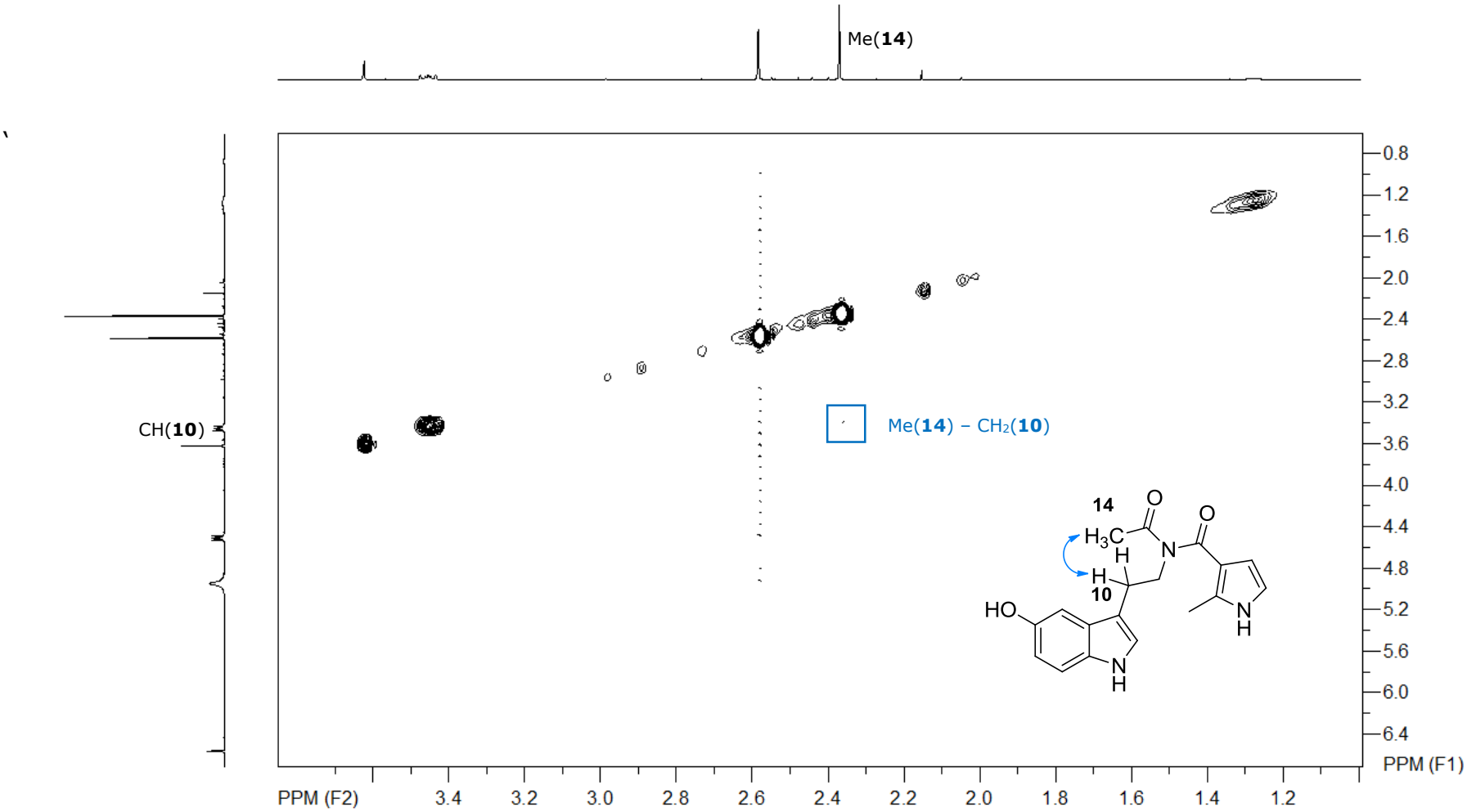
time domain size: 65536 points
width: 24038.46 Hz = 239.049640 ppm = 0.366798 Hz/pt
number of scans: 2500

freq. of 0 ppm: 100.547473 MHz
processed size: 32768 complex points
LB: 2.000 GB: 0.0000
Hz/cm: 835.007 ppm/cm: 8.30370

SpinWorks 2.5 2D: noesystdi Pyr /nmr/400p edav108 28



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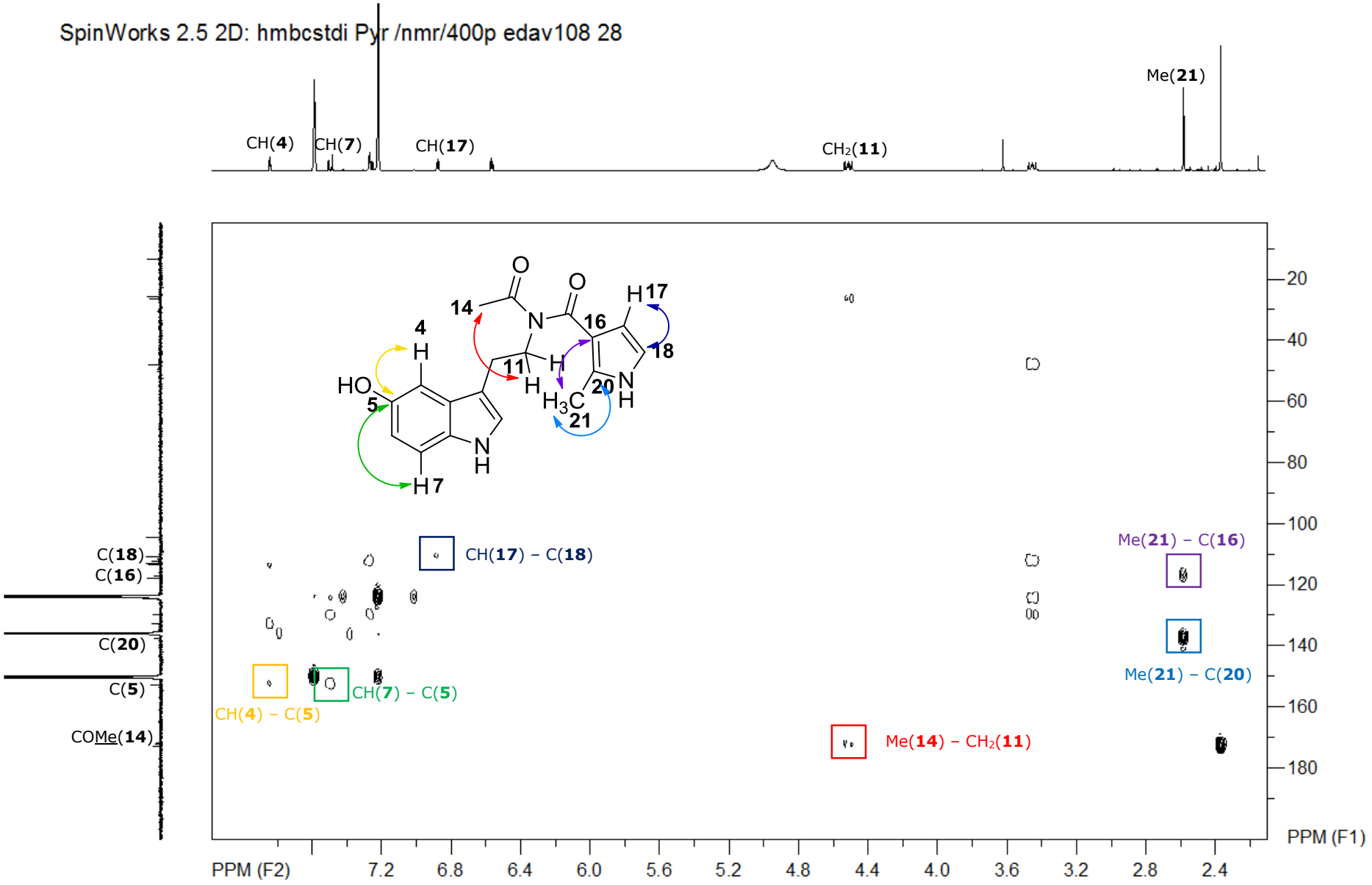
transmitter freq.: 399.871719 MHz
time domain size: 2048 by 256 points
width (F2): 5580.34 Hz = 13.955368 ppm = 2.724776 Hz/pt
number of scans: 12

F2: freq. of 0 ppm: 399.870596 MHz
processed size: 1024 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 55.791 ppm/cm: 0.13952

F1: freq. of 0 ppm: 399.870602 MHz
processed size: 256 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 203.780 ppm/cm: 0.50961



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time domain size: 2048 by 128 points
width (F2): 5580.34 Hz = 13.955368 ppm = 2.724776 Hz/pt
number of scans: 12

F2: freq. of 0 ppm: 399.870593 MHz
processed size: 1024 complex points
window function: Sine
shift: 90.0 degrees
Hz/cm: 118.493 ppm/cm: 0.29633

F1: freq. of 0 ppm: 100.547499 MHz
processed size: 256 complex points
window function: Sine
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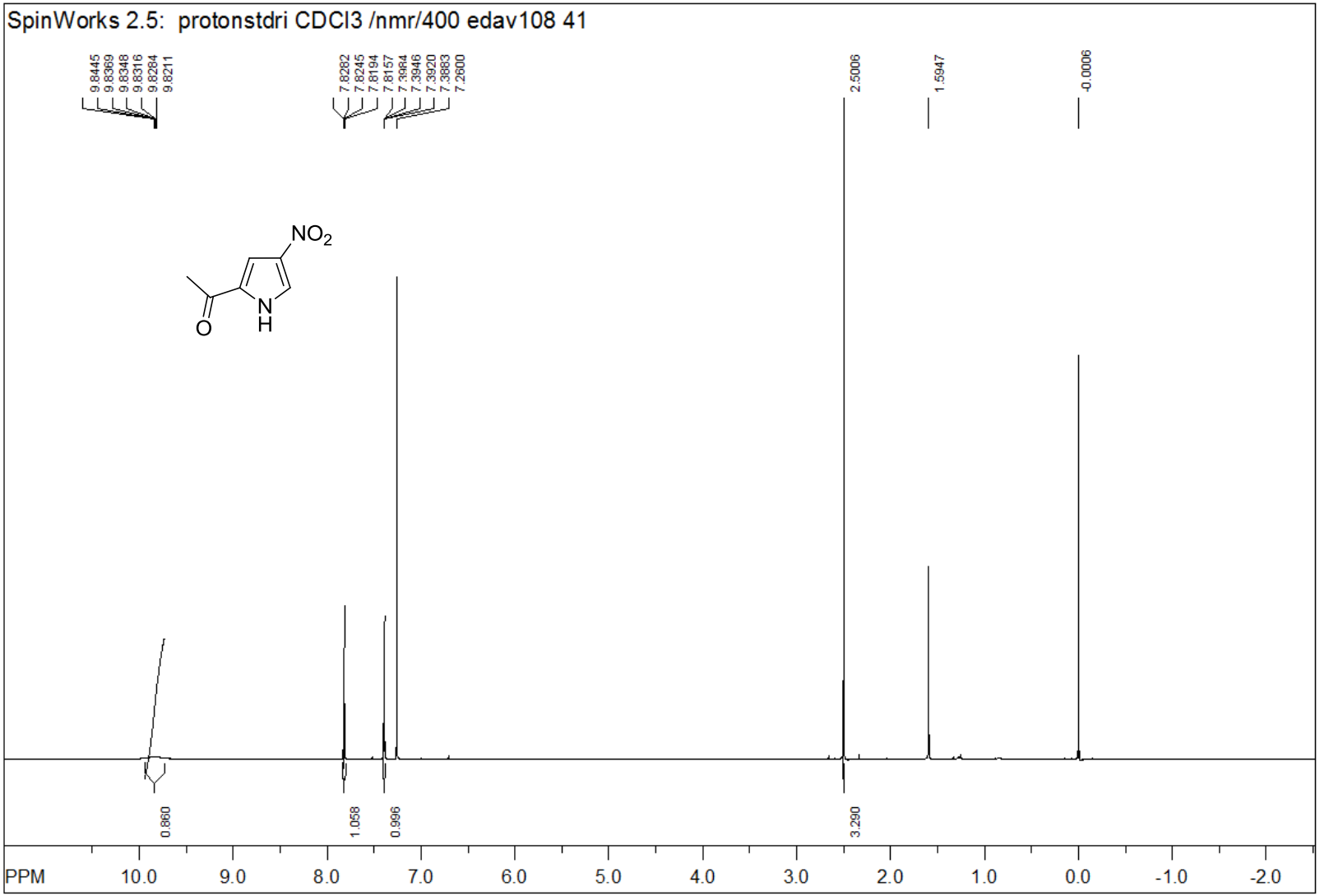
Hz/cm: 1693.922 ppm/cm: 16.84515



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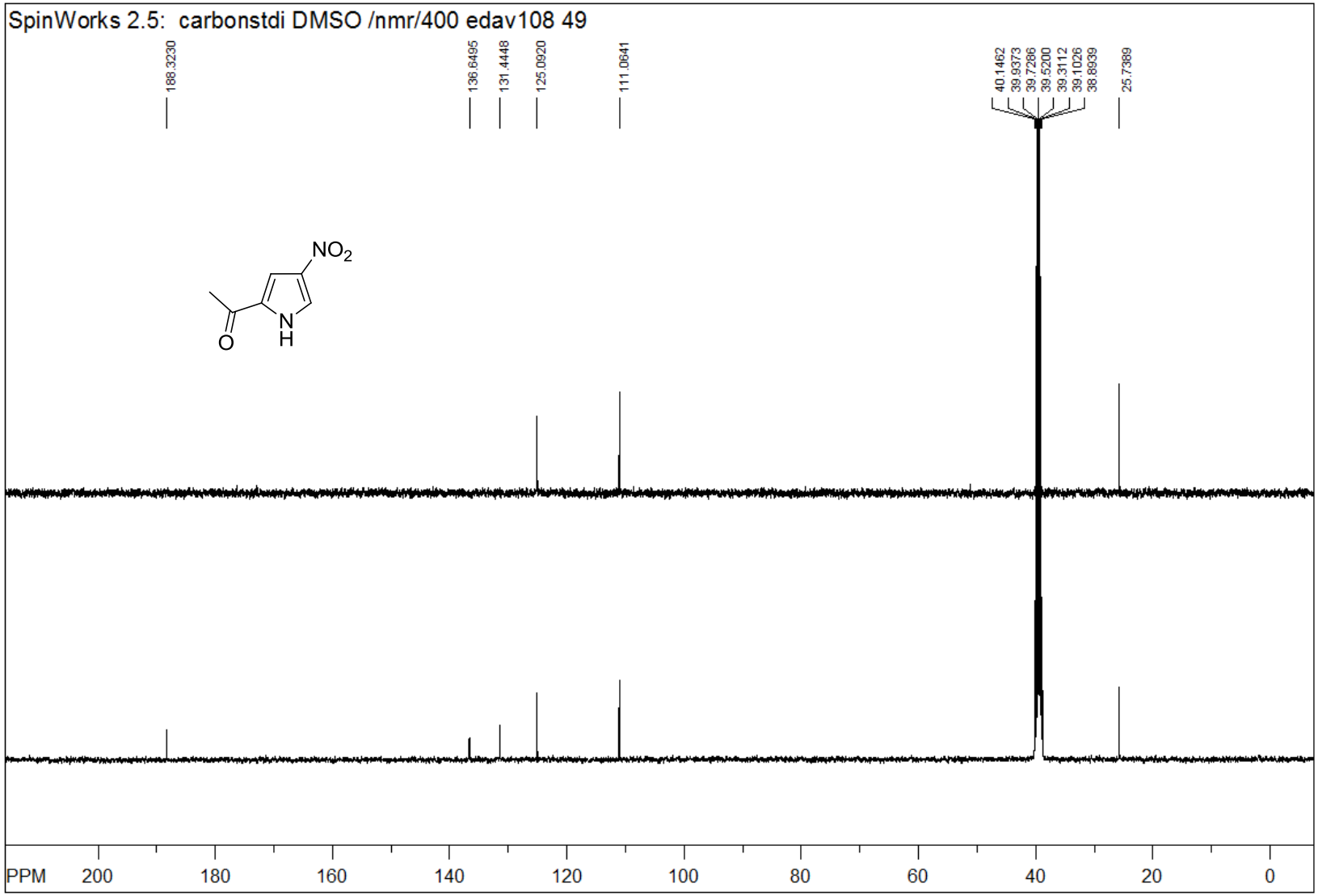
transmitter freq.: 400.132101 MHz
time domain size: 32768 points
width: 8169.93 Hz = 20.418093 ppm = 0.249327 Hz/pt
number of scans: 50

freq. of 0 ppm: 400.130010 MHz
processed size: 16384 complex points
LB: 0.000 GB: 0.0000
Hz/cm: 223.383 ppm/cm: 0.55827



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time domain size: 65536 points
width: 24038.46 Hz = 238.894065 ppm = 0.366798 Hz/pt
number of scans: 2000

freq. of 0 ppm: 100.612817 MHz
processed size: 32768 complex points
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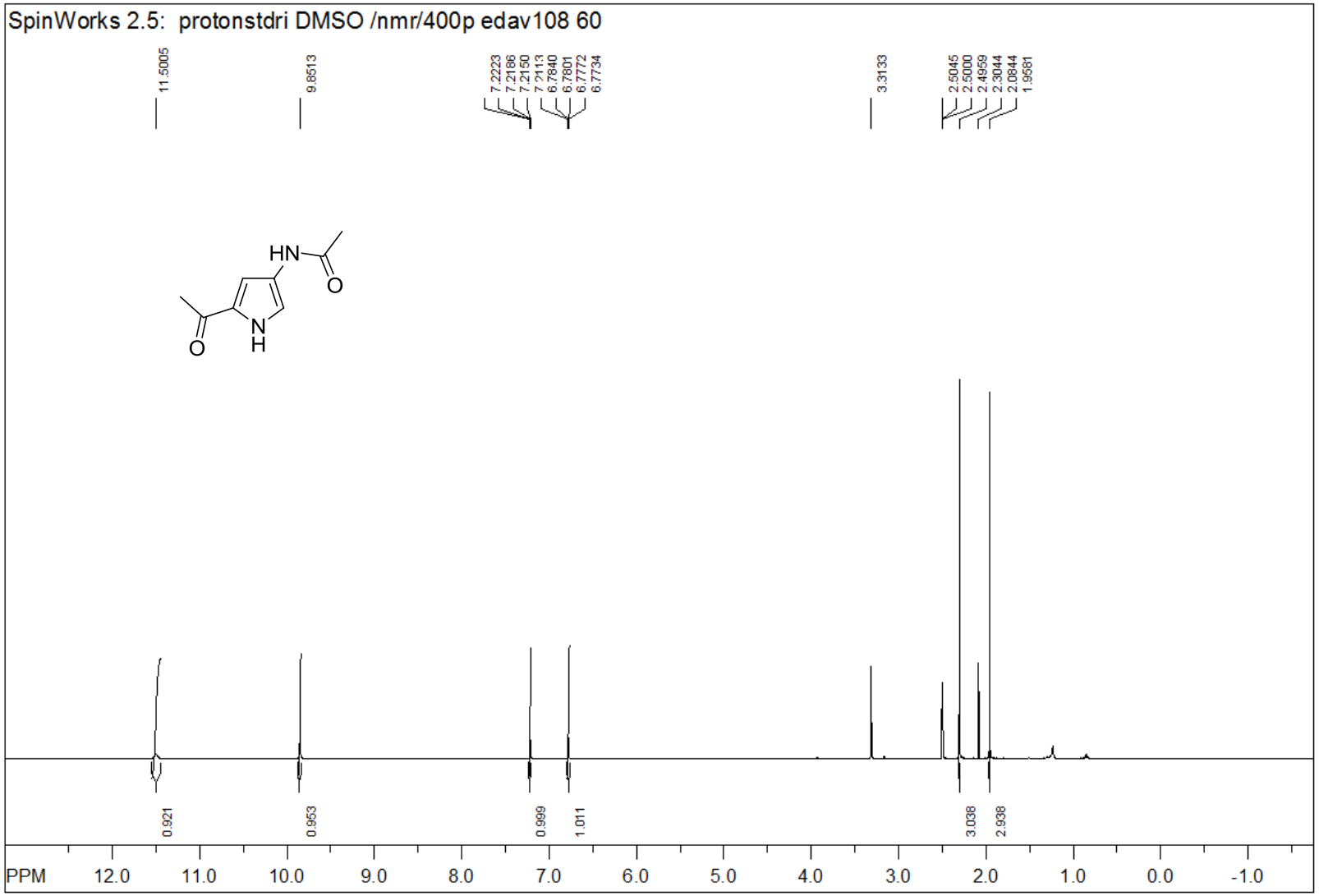

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time domain size: 32768 points
width: 8169.93 Hz = 20.431370 ppm = 0.249327 Hz/pt
number of scans: 50

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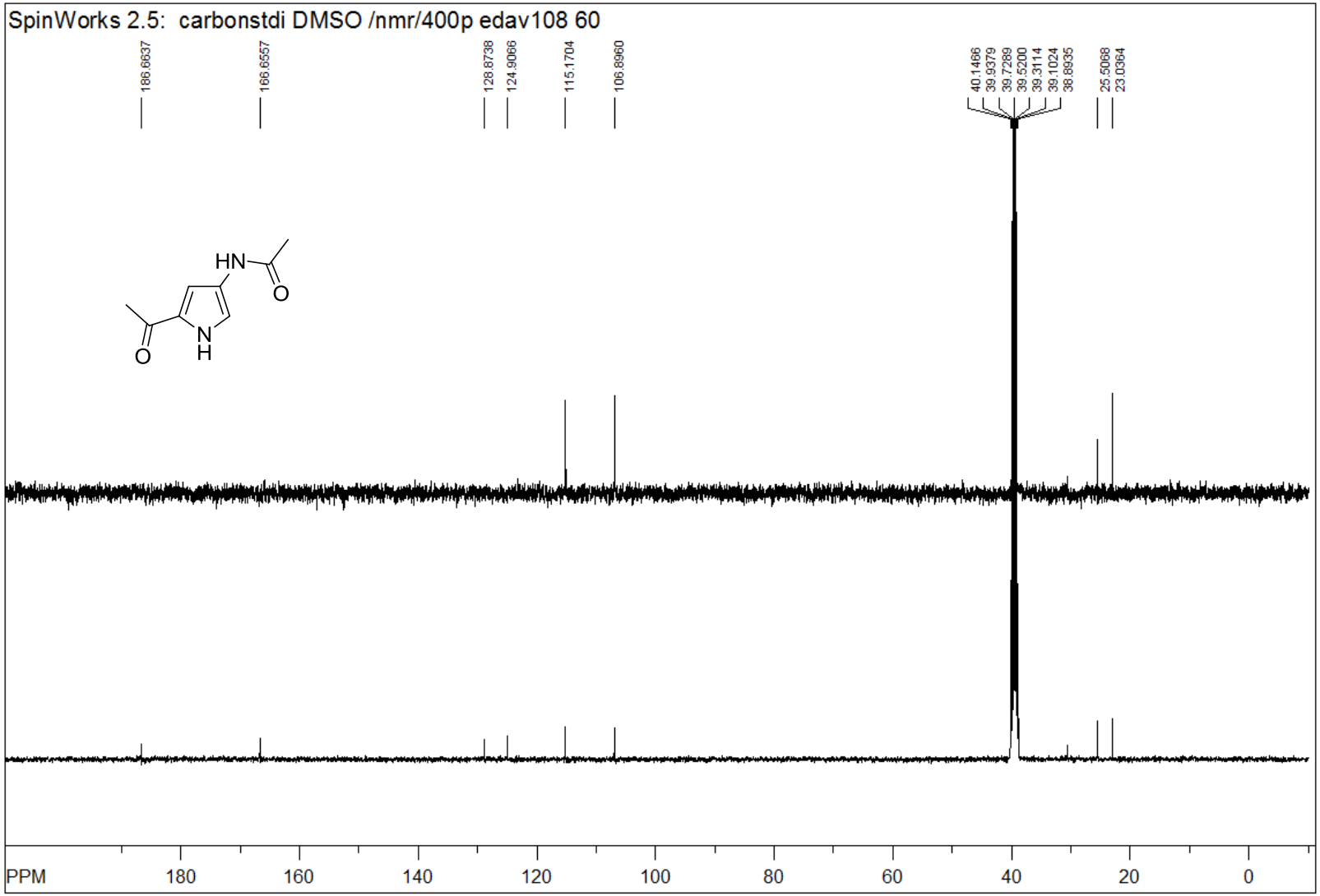
Hz/cm: 239.424 ppm/cm: 0.59875



file: Z:\data\edav108\nmr\ED63.1_spot2\22\fid expt: <zgpg30>
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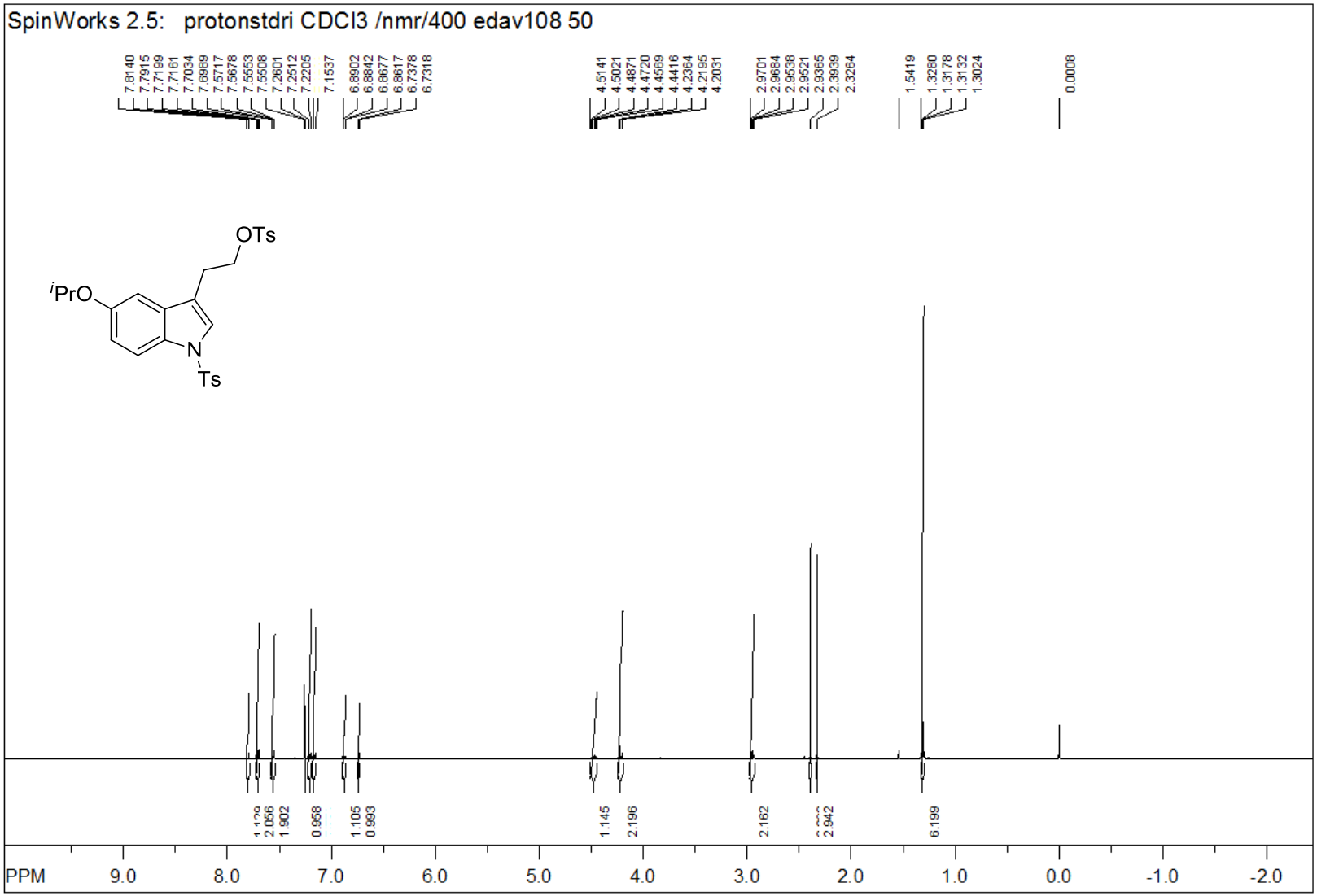
time domain size: 65536 points
width: 24038.46 Hz = 239.049640 ppm = 0.366798 Hz/pt
number of scans: 1500

freq. of 0 ppm: 100.547440 MHz
processed size: 32768 complex points
LB: 0.100 GB: 0.0000
Hz/cm: 887.728 ppm/cm: 8.82798



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time domain size: 32768 points
width: 8169.93 Hz = 20.418093 ppm = 0.249327 Hz/pt
number of scans: 50

freq. of 0 ppm: 400.130010 MHz
processed size: 16384 complex points
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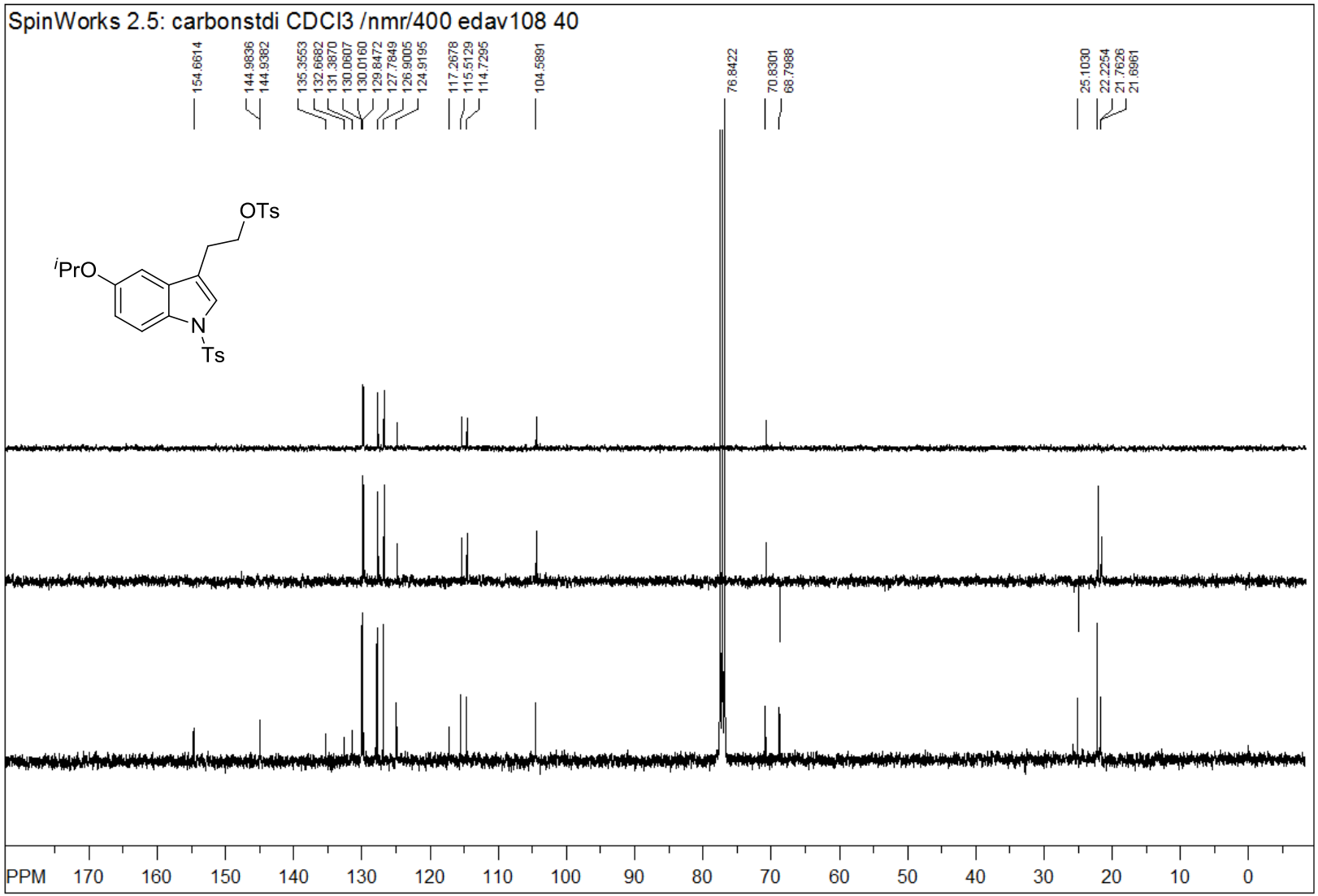
Hz/cm: 201.369 ppm/cm: 0.50326



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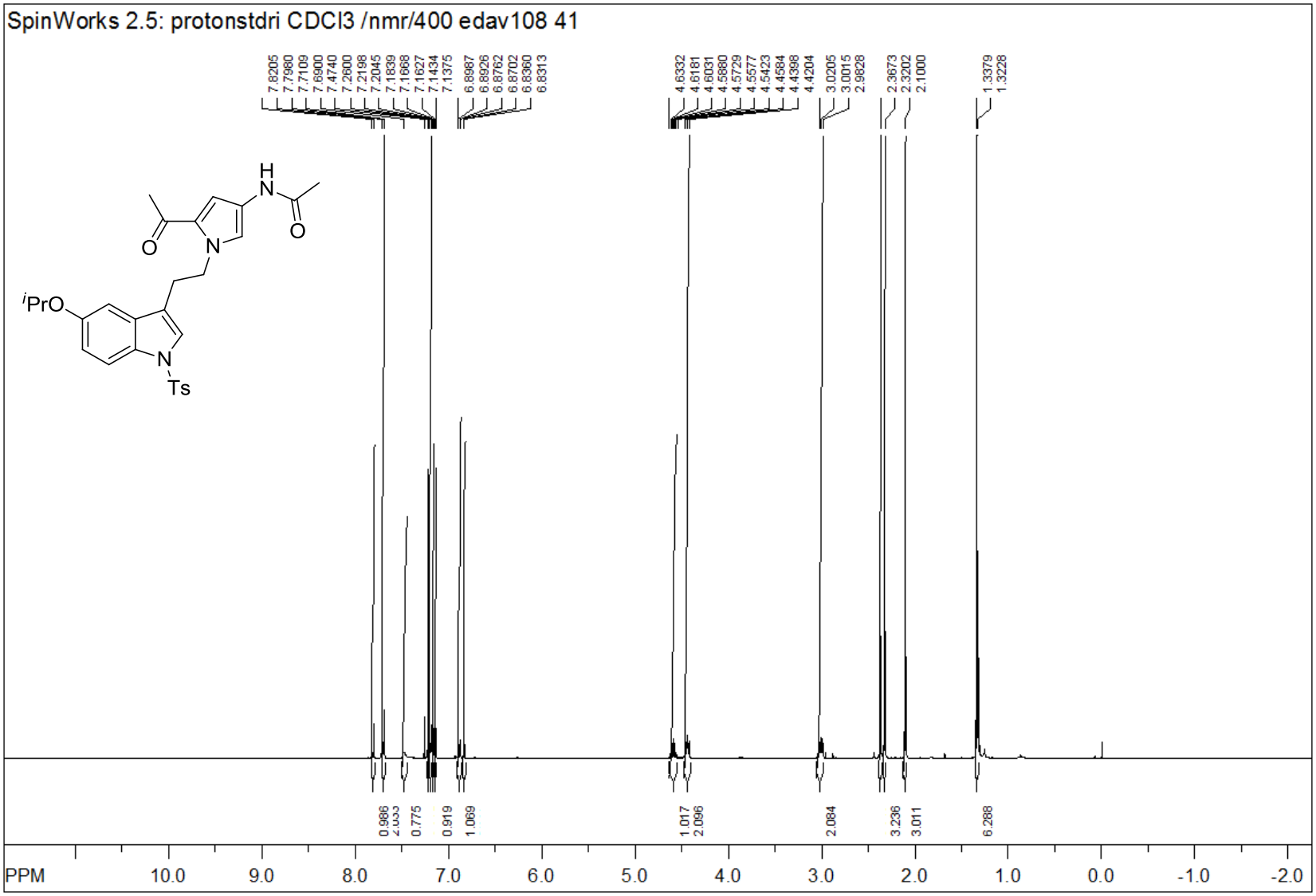
time domain size: 65536 points
width: 24038.46 Hz = 238.894065 ppm = 0.366798 Hz/pt
number of scans: 2000

freq. of 0 ppm: 100.612753 MHz
processed size: 32768 complex points
LB: 2.000 GB: 0.0000
Hz/cm: 771.741 ppm/cm: 7.66956



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time domain size: 32768 points
width: 8169.93 Hz = 20.418093 ppm = 0.249327 Hz/pt
number of scans: 30

freq. of 0 ppm: 400.130010 MHz
processed size: 16384 complex points
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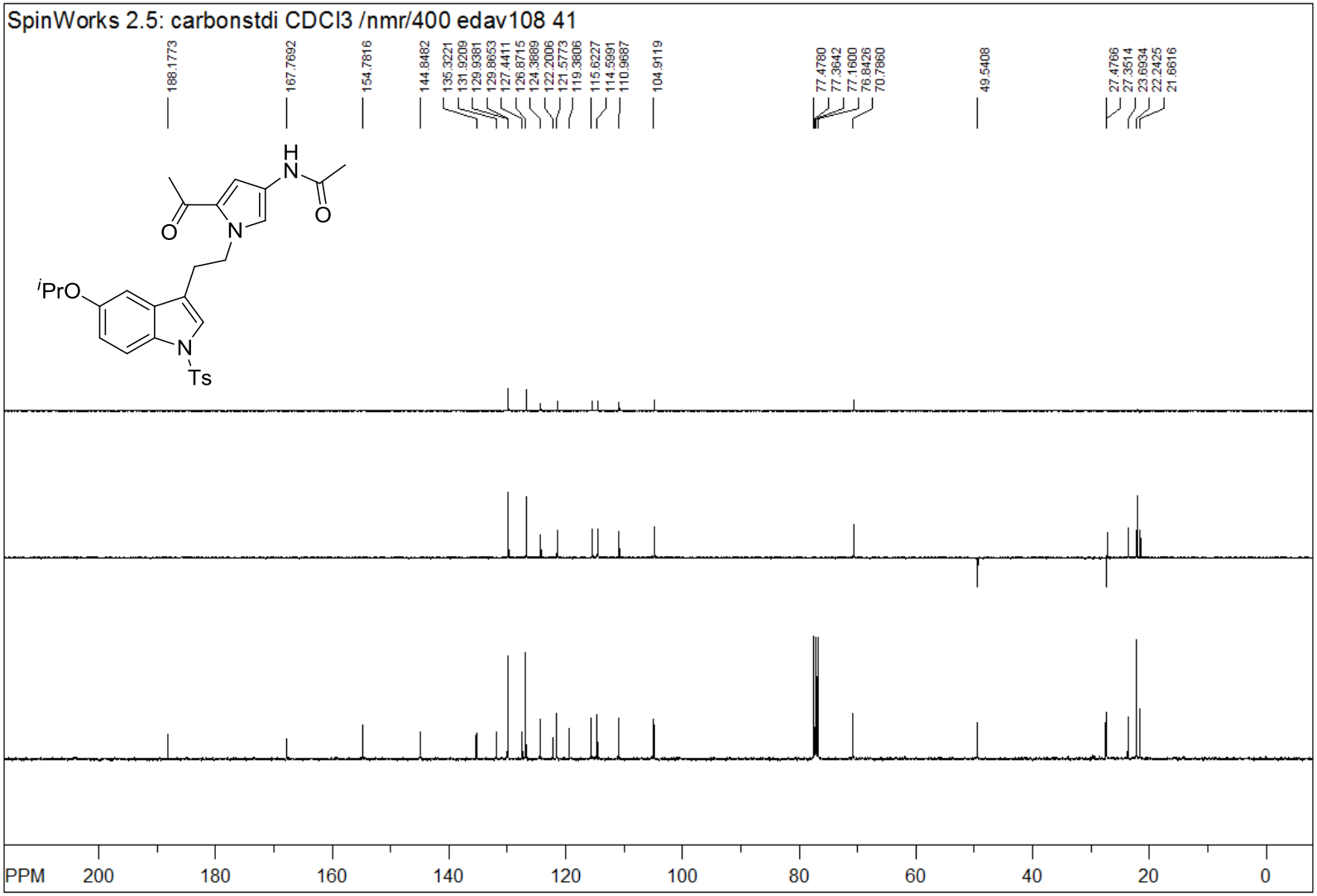
Hz/cm: 224.265 ppm/cm: 0.56048



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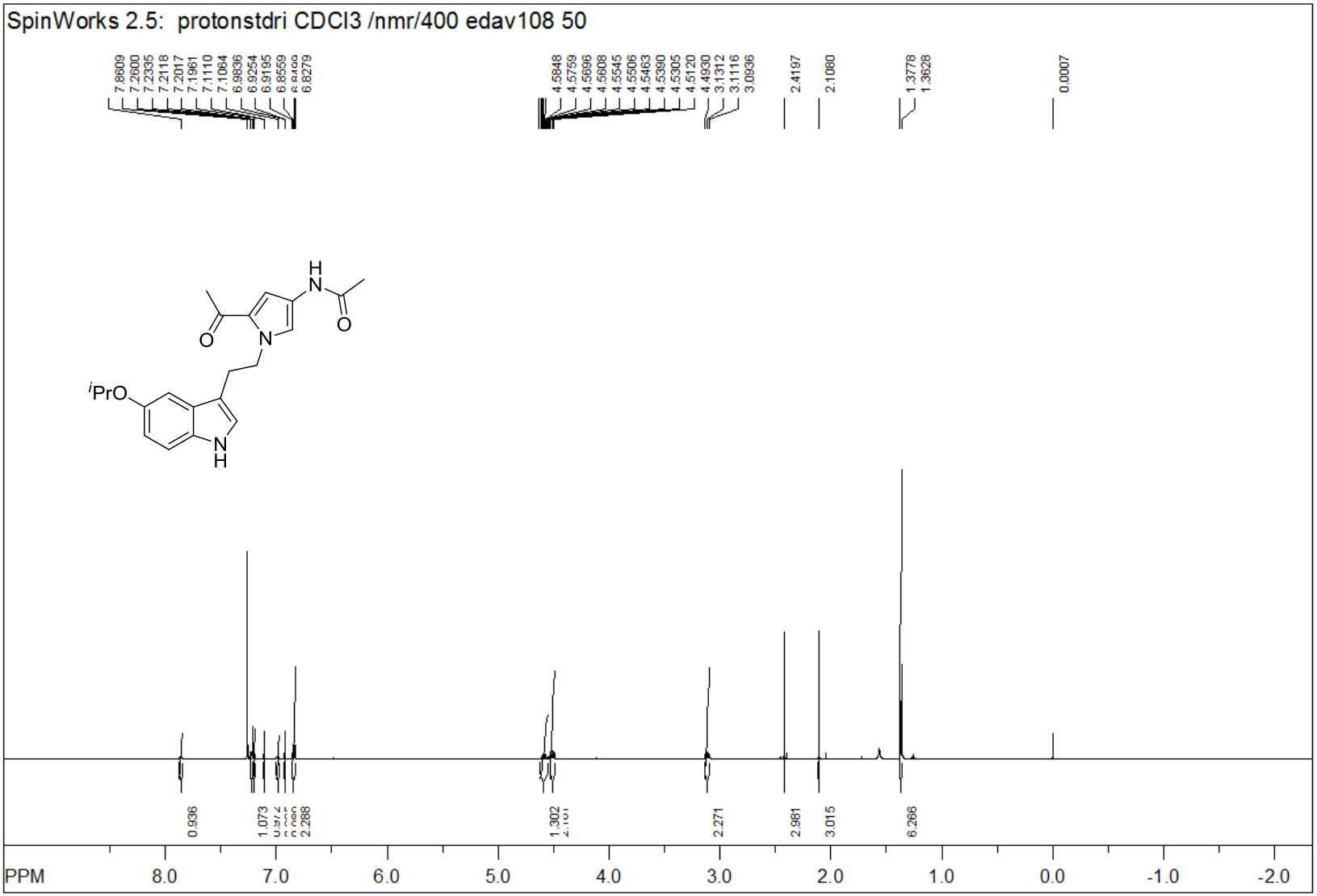
time domain size: 65536 points
width: 24038.46 Hz = 238.894065 ppm = 0.366798 Hz/pt
number of scans: 1000

freq. of 0 ppm: 100.612756 MHz
processed size: 32768 complex points
LB: 2.000 GB: 0.0000
Hz/cm: 901.788 ppm/cm: 8.96196



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time domain size: 32768 points
width: 8169.93 Hz = 20.418093 ppm = 0.249327 Hz/pt
number of scans: 40

freq. of 0 ppm: 400.130010 MHz
processed size: 16384 complex points
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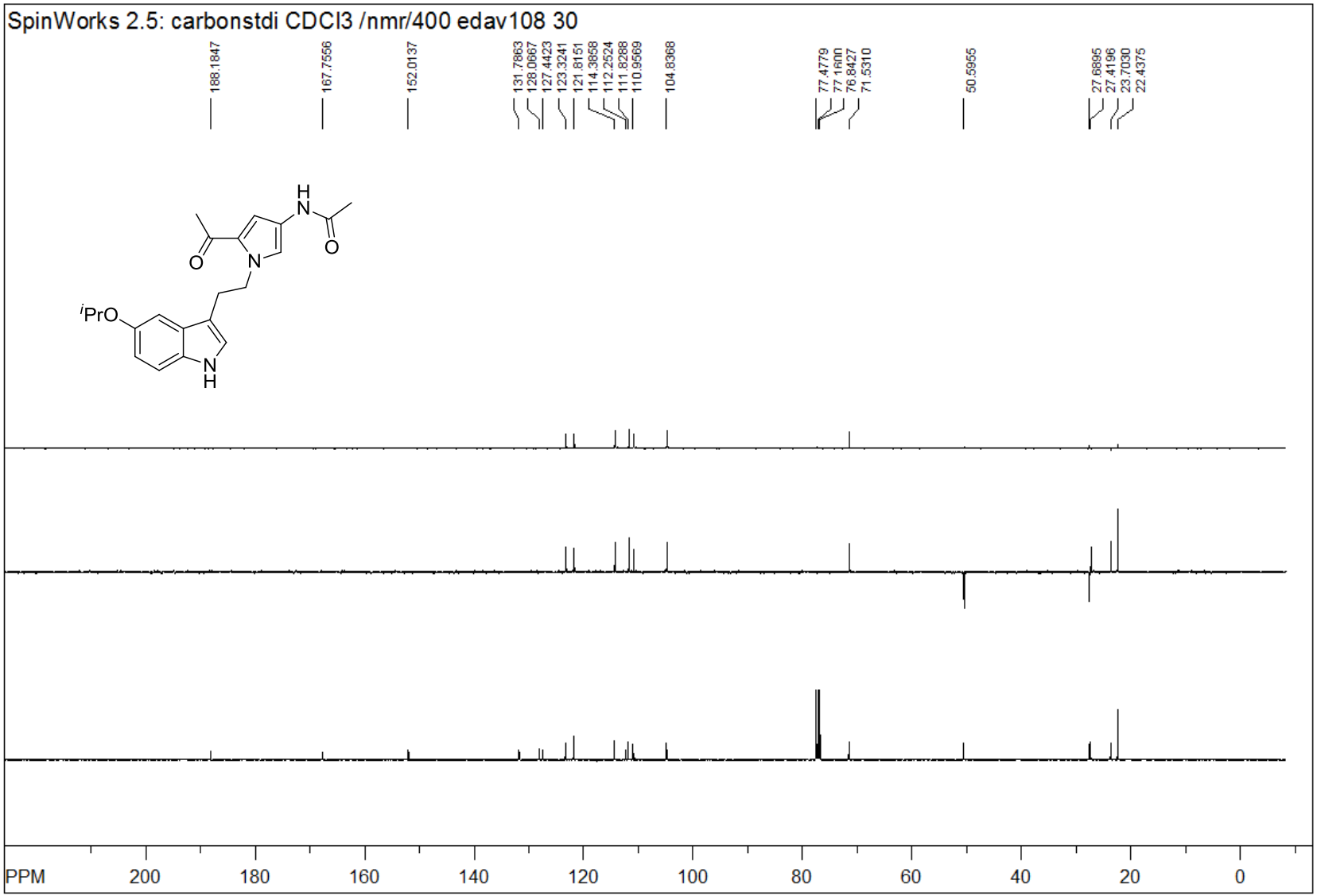
Hz/cm: 188.740 ppm/cm: 0.47170



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time domain size: 65536 points
width: 24038.46 Hz = 238.894065 ppm = 0.366798 Hz/pt
number of scans: 800

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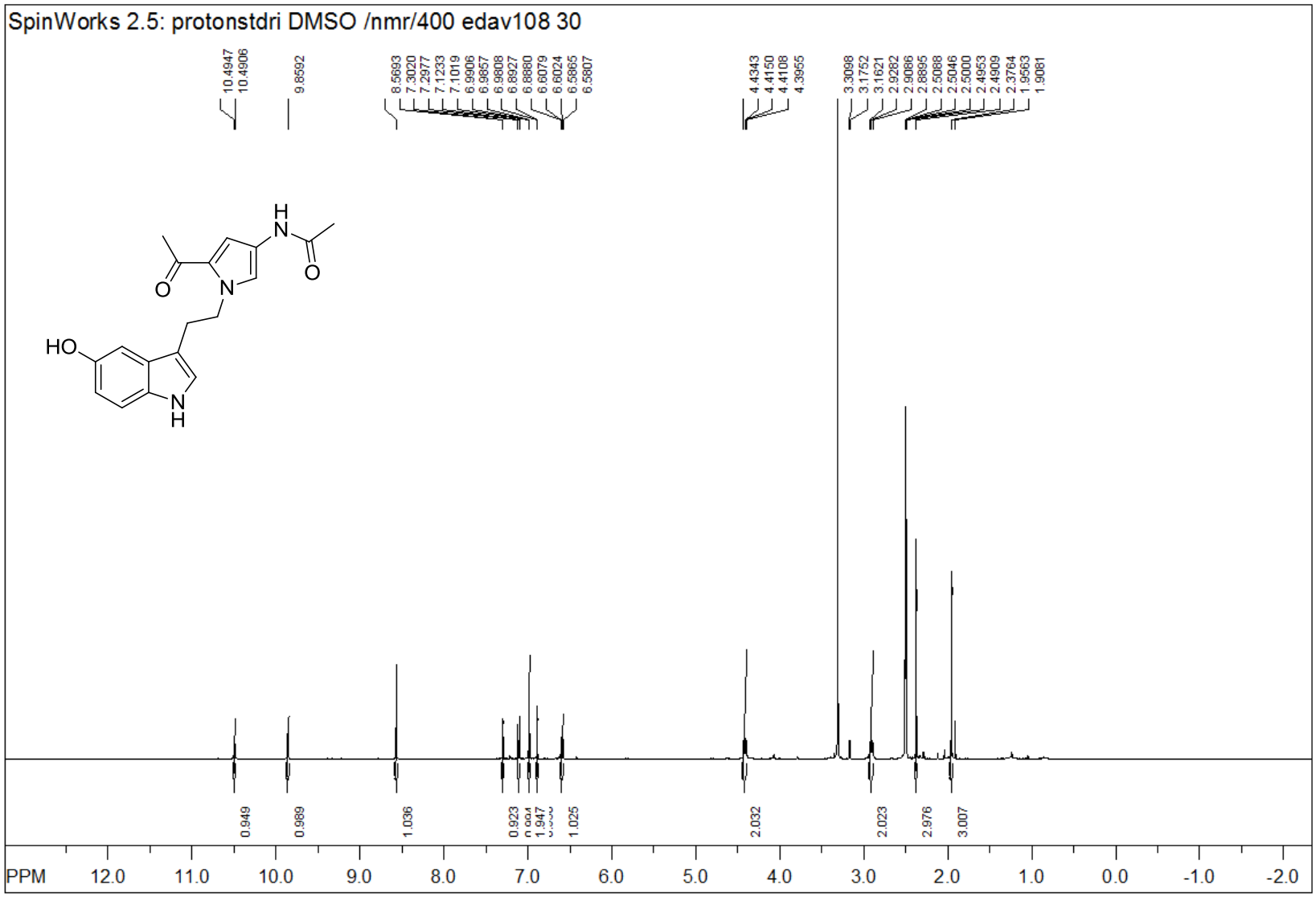
LB: 2.000 GB: 0.0000
Hz/cm: 961.538 ppm/cm: 9.55576



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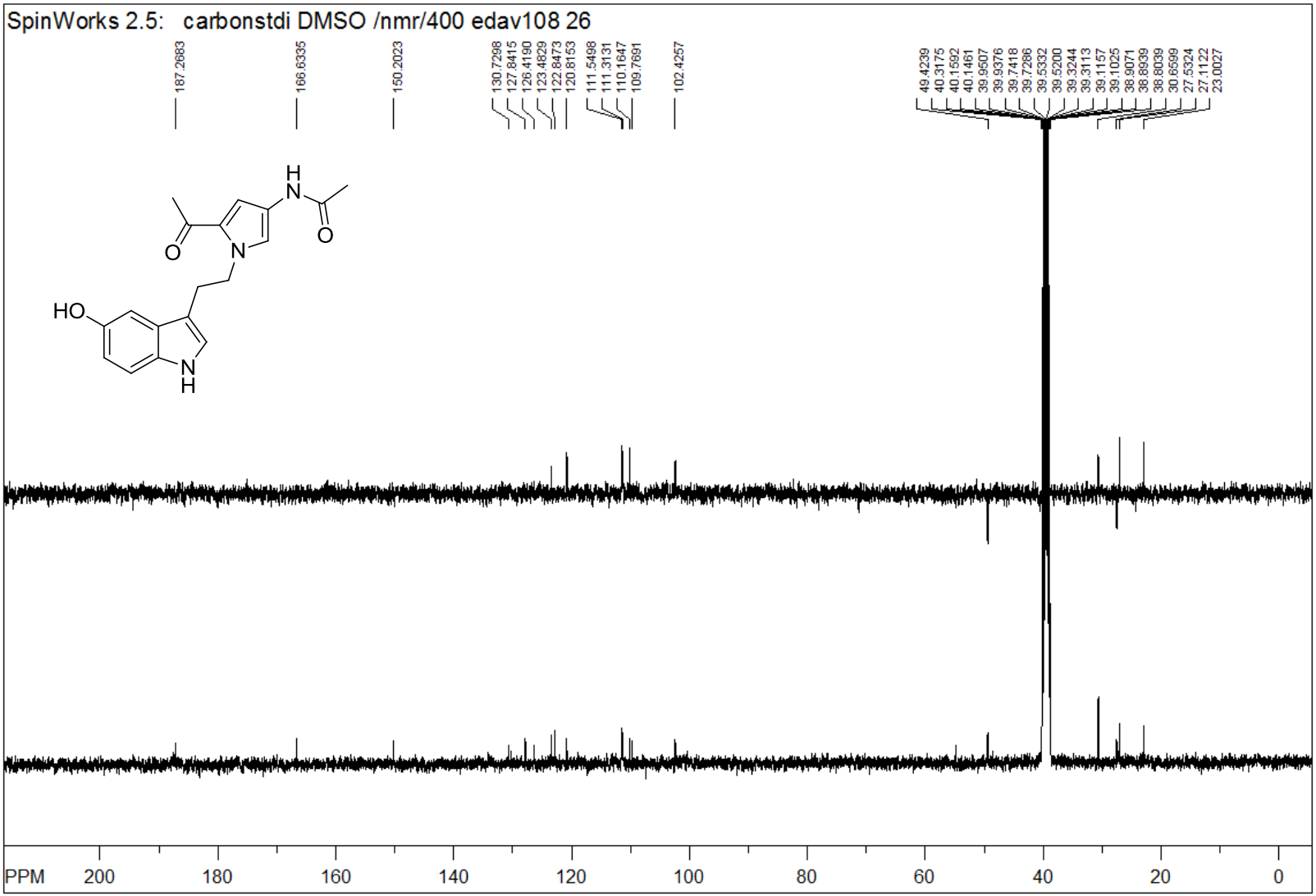
time domain size: 32768 points
width: 8169.93 Hz = 20.418093 ppm = 0.249327 Hz/pt
number of scans: 60

freq. of 0 ppm: 400.130004 MHz
processed size: 16384 complex points
LB: 0.100 GB: 0.0000
Hz/cm: 248.980 ppm/cm: 0.62225



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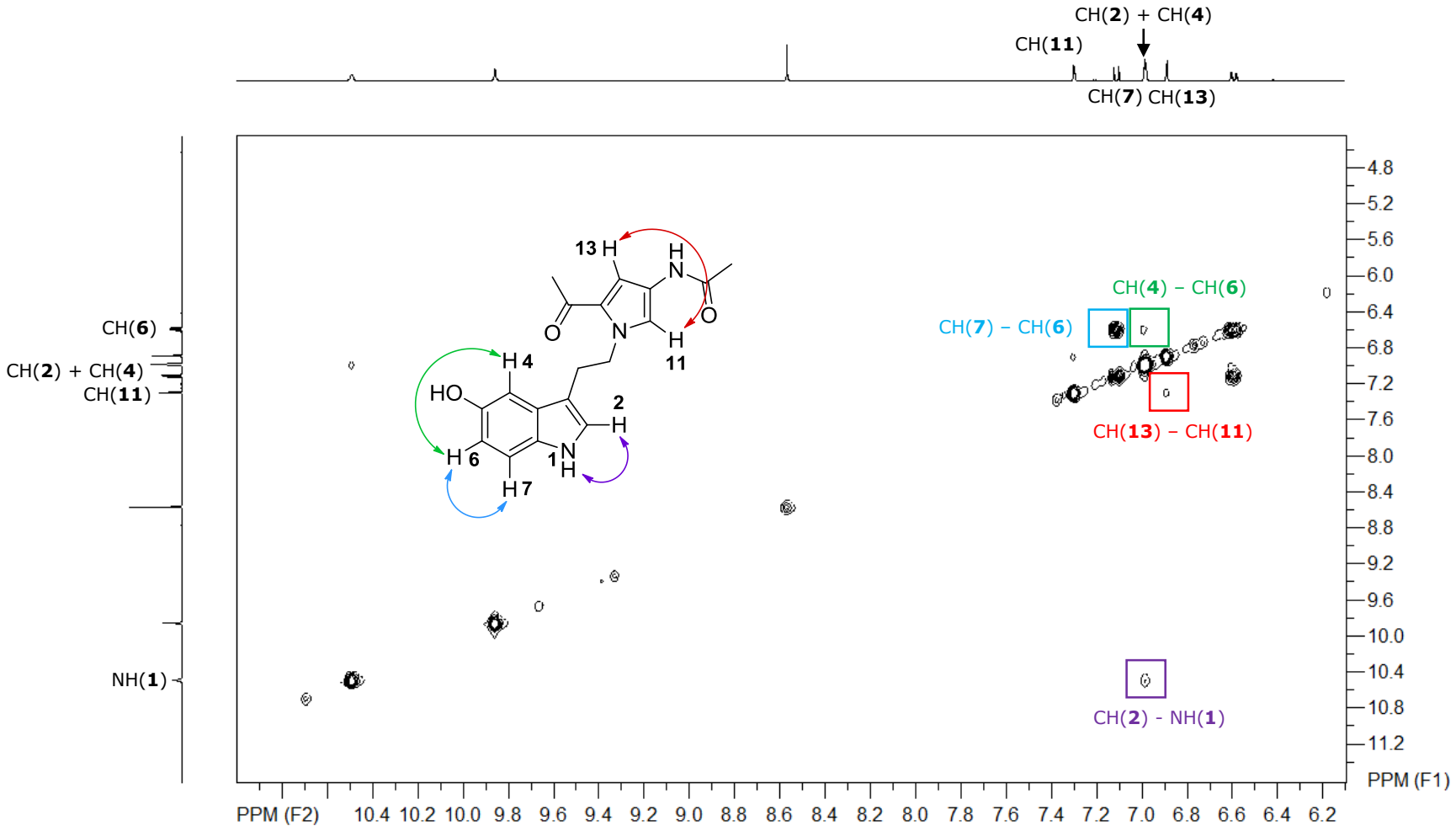
transmitter freq.: 100.623938 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.894065 ppm = 0.366798 Hz/pt
number of scans: 3000

freq. of 0 ppm: 100.612818 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000
Hz/cm: 892.750 ppm/cm: 8.87214

SpinWorks 2.5 2D: cosystdi DMSO /nmr/400 edav108 41

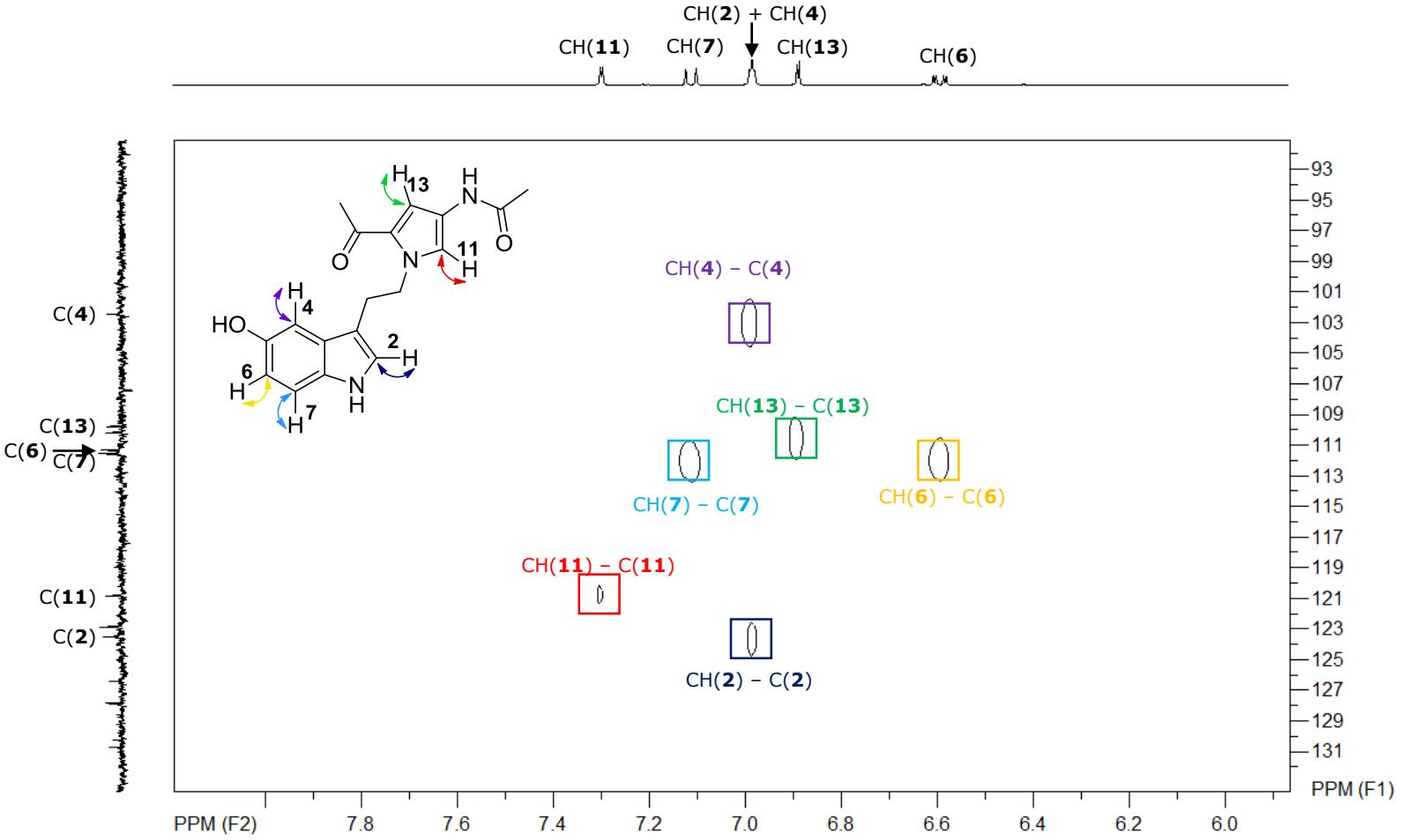


file: Y:\data\edav108\nmr\ED70.1_DMSO\20\ser expt: <cosygpppqf>
transmitter freq.: 400.132401 MHz
time domain size: 2048 by 256 points
width (F2): 6009.58 Hz = 15.019067 ppm = 2.934365 Hz/pt
number of scans: 10

F2: freq. of 0 ppm: 400.130004 MHz
processed size: 1024 complex points
window function: Sine
shift: 0.0 degrees
Hz/cm: 95.736 ppm/cm: 0.23926

F1: freq. of 0 ppm: 400.130001 MHz
processed size: 256 complex points
window function: Sine
shift: 0.0 degrees
Hz/cm: 239.888 ppm/cm: 0.59952

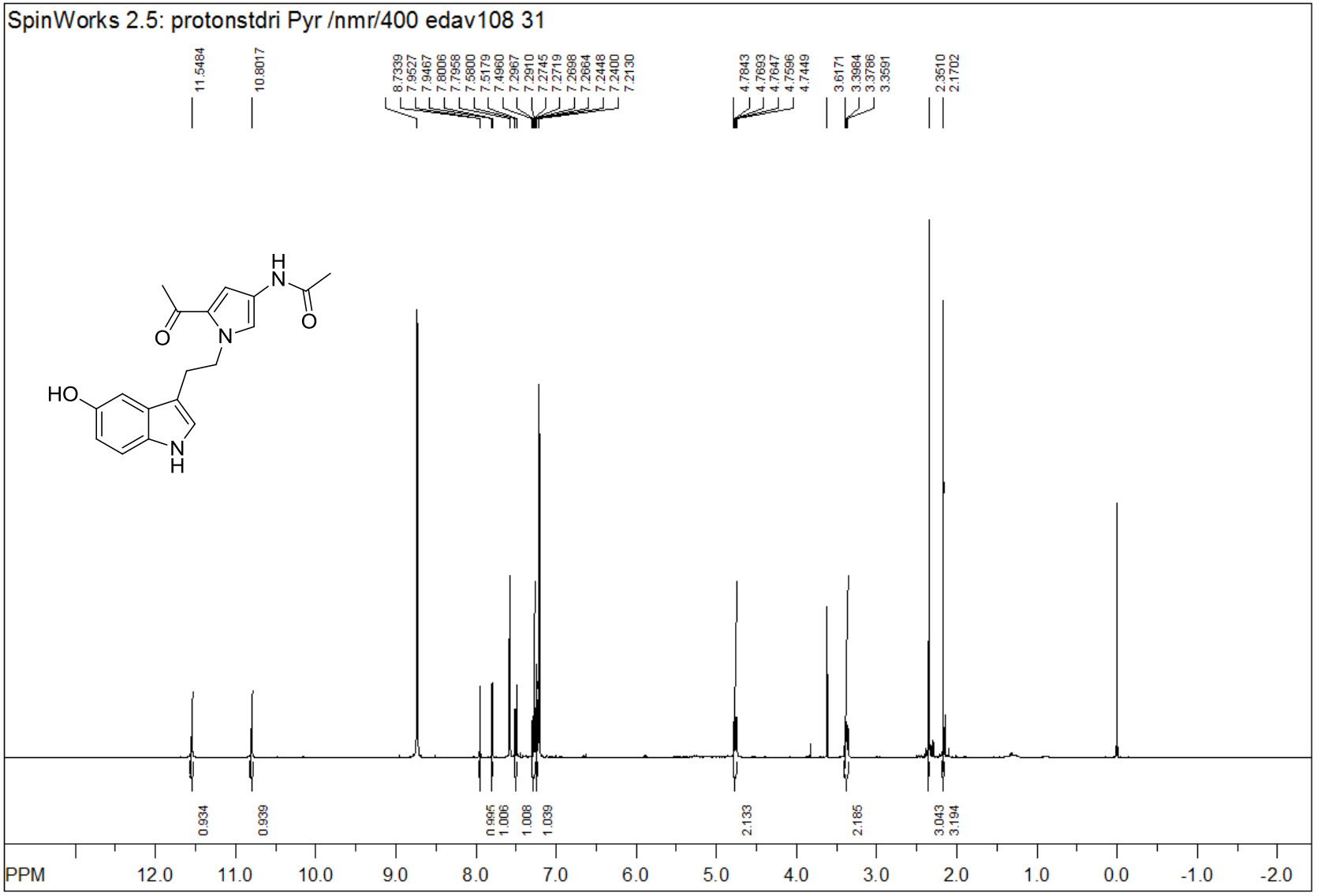
SpinWorks 2.5 2D: hsqcedstdi DMSO /nmr/400 edav108 41



file: Y:\data\edav108\nmr\ED70.1_DMSO\21\ser expt: <hsqcedetgpsisp.2>
transmitter freq.: 400.132401 MHz
time domain size: 2048 by 128 points
width (F2): 6009.58 Hz = 15.019067 ppm = 2.934365 Hz/pt
number of scans: 15

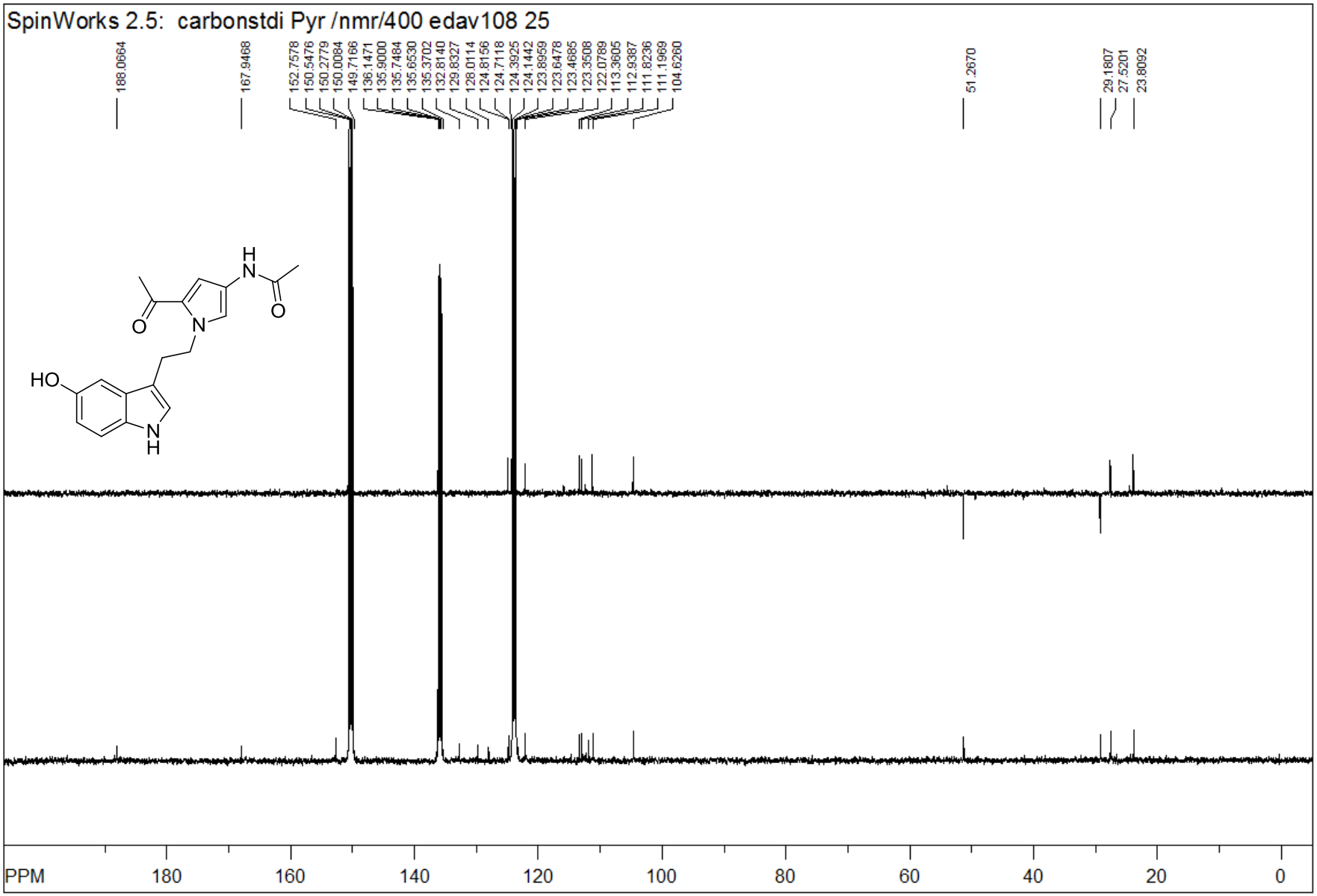
F2: freq. of 0 ppm: 400.130004 MHz
processed size: 1024 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 45.380 ppm/cm: 0.11341

F1: freq. of 0 ppm: 100.612739 MHz
processed size: 256 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 356.892 ppm/cm: 3.54688



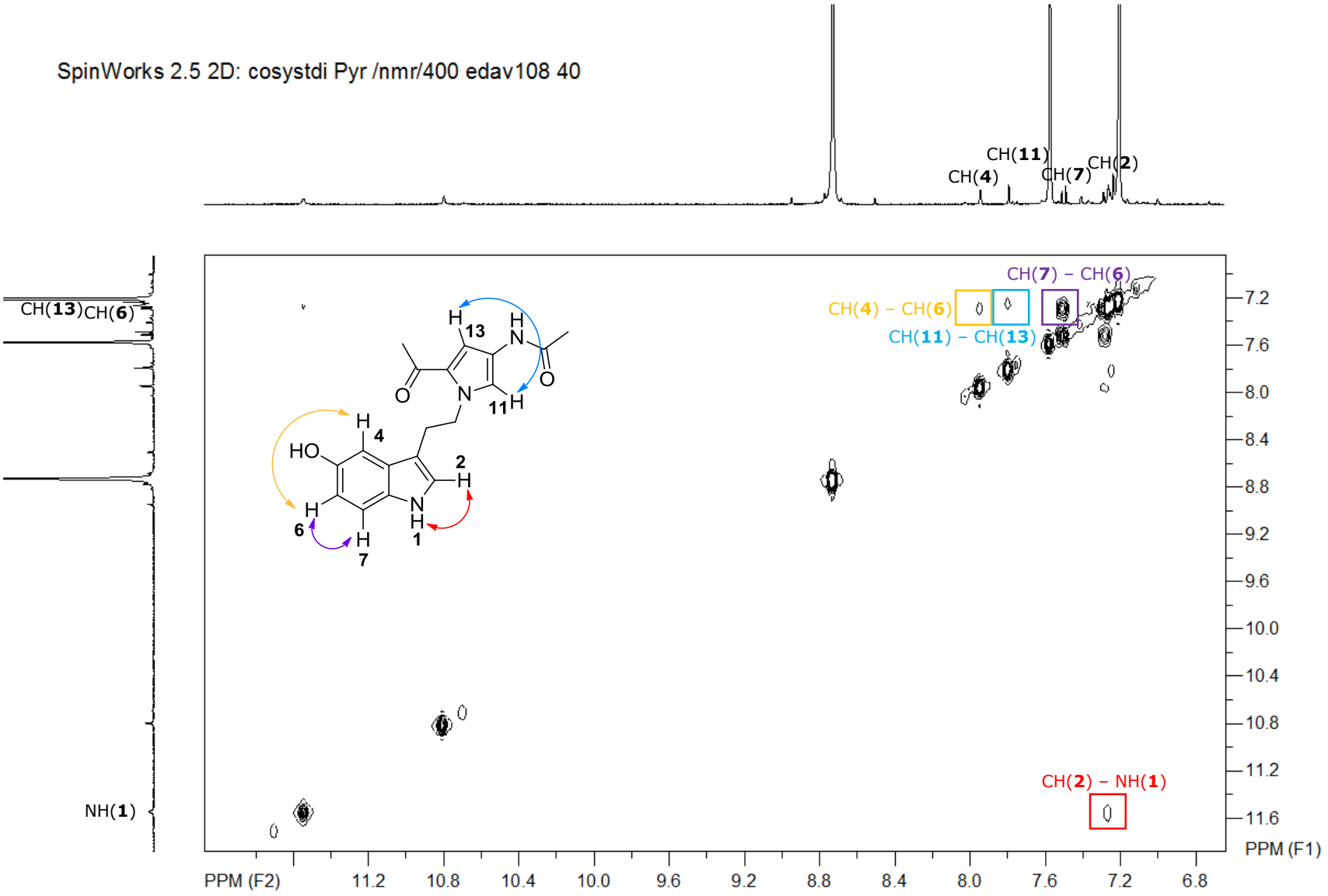
file: Y:\data\edav108\nmr\ED70.2_Pyr\1\fid expt: <zg30>
transmitter freq.: 400.132101 MHz
time domain size: 32768 points
width: 8169.93 Hz = 20.418093 ppm = 0.249327 Hz/pt
number of scans: 60

freq. of 0 ppm: 400.130594 MHz
processed size: 16384 complex points
LB: 0.100 GB: 0.0000
Hz/cm: 260.926 ppm/cm: 0.65210



file: Y:\data\edav108\nmr\ED70.1_Pyr\12\fid expt: <zgpg30>
transmitter freq.: 100.623938 MHz
time domain size: 65536 points
width: 24038.46 Hz = 238.894065 ppm = 0.366798 Hz/pt
number of scans: 1000

freq. of 0 ppm: 100.612704 MHz
processed size: 32768 complex points
LB: 0.100 GB: 0.0000
Hz/cm: 850.572 ppm/cm: 8.45298

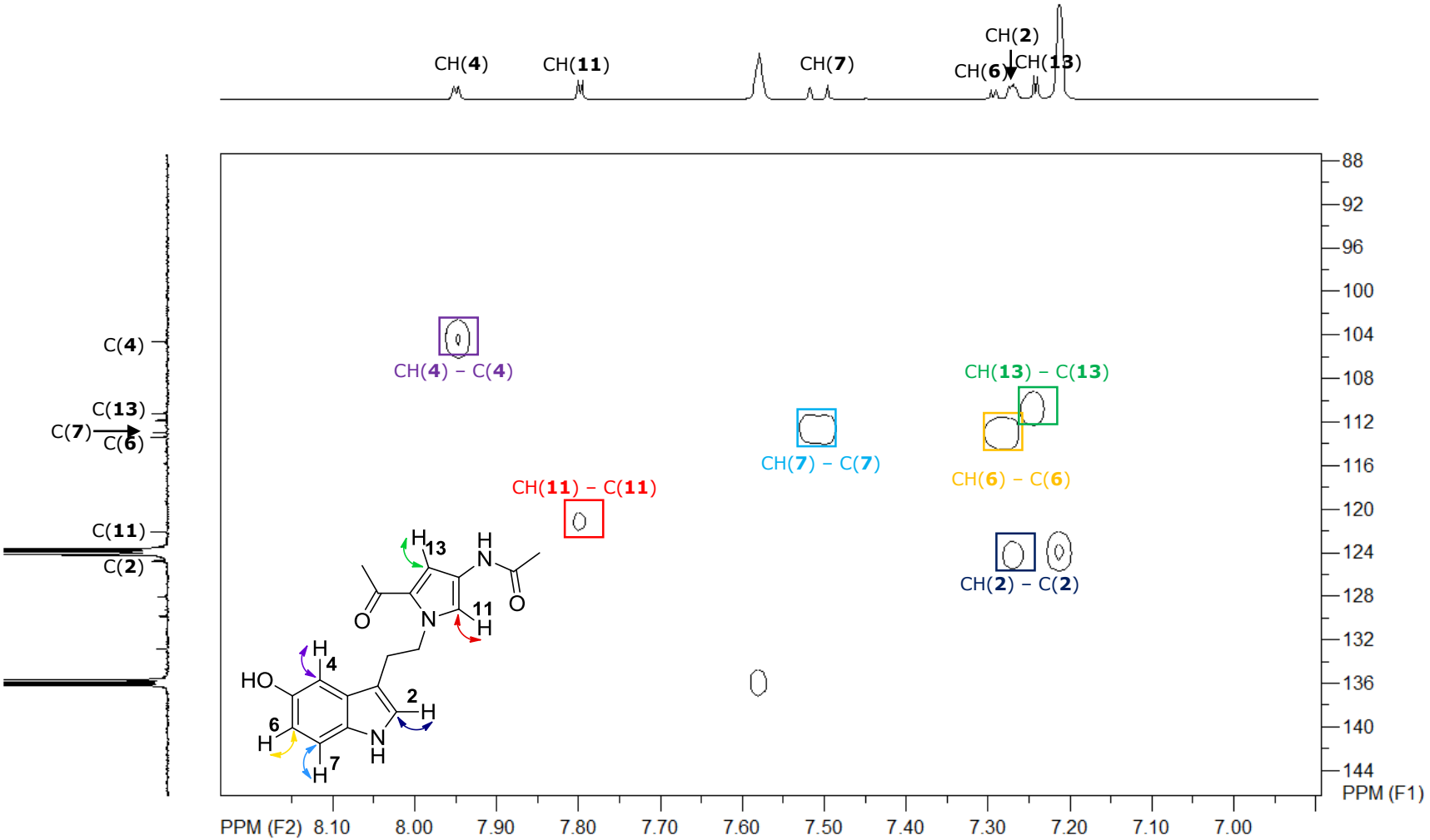


file: Y:\data\edav108\nmr\ED70.1_Pyr\21\ser expt: <cosygpppqf>
transmitter freq.: 400.132401 MHz
time domain size: 2048 by 256 points
width (F2): 6009.58 Hz = 15.019067 ppm = 2.934365 Hz/pt
number of scans: 10

F2: freq. of 0 ppm: 400.129989 MHz
processed size: 1024 complex points
window function: Sine
shift: 0.0 degrees
Hz/cm: 106.044 ppm/cm: 0.26502

F1: freq. of 0 ppm: 400.129985 MHz
processed size: 256 complex points
window function: Sine
shift: 0.0 degrees
Hz/cm: 168.402 ppm/cm: 0.42087

SpinWorks 2.5 2D: hsqcedstdi Pyr /nmr/400 edav108 40

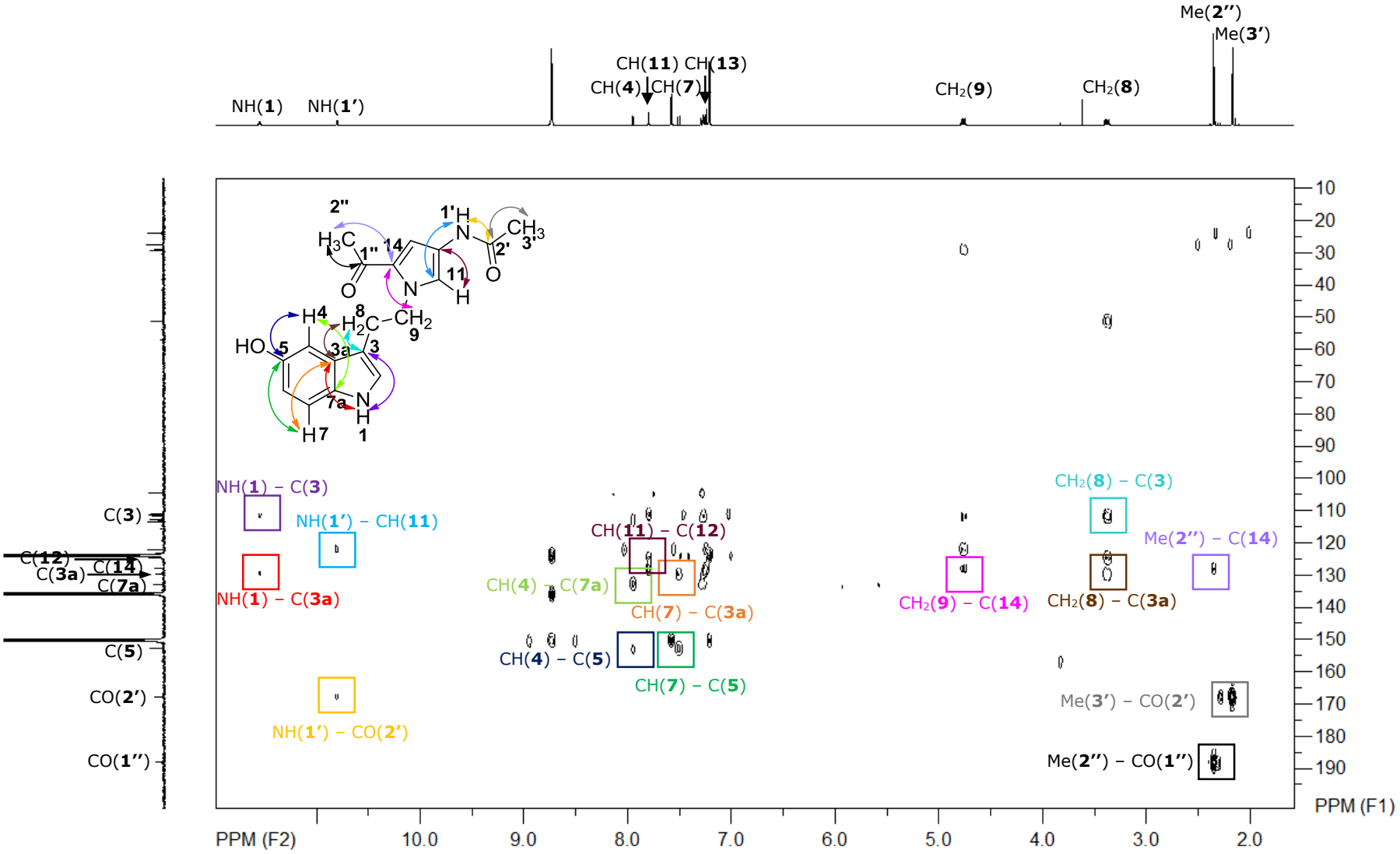


file: Y:\data\edav108\nmr\ED70.1_Pyr\22\ser expt: <hsqcedetgpsisp.2>
transmitter freq.: 400.132401 MHz
time domain size: 2048 by 128 points
width (F2): 6009.58 Hz = 15.019067 ppm = 2.934365 Hz/pt
number of scans: 12

F2: freq. of 0 ppm: 400.129990 MHz
processed size: 1024 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 26.240 ppm/cm: 0.06558

F1: freq. of 0 ppm: 100.612710 MHz
processed size: 256 complex points
window function: Sine Squared
shift: 90.0 degrees
Hz/cm: 494.840 ppm/cm: 4.91785

SpinWorks 2.5 2D: hmbcstdi Pyr /nmr/400 edav108 40



file: Y:\data\edav108\nmr\ED70.1_Pyr\23\ser expt: <hmbcgplpndqf>
transmitter freq.: 400.132401 MHz
time domain size: 2048 by 128 points
width (F2): 6009.58 Hz = 15.019067 ppm = 2.934365 Hz/pt
number of scans: 10

F2: freq. of 0 ppm: 400.129990 MHz
processed size: 1024 complex points
window function: Sine
shift: 90.0 degrees
Hz/cm: 202.937 ppm/cm: 0.50718

F1: freq. of 0 ppm: 100.612707 MHz
processed size: 256 complex points
window function: Sine
shift: 0.0 degrees
Hz/cm: 1639.688 ppm/cm: 16.29522