Enantioselective Total Synthesis of (+)-galbulin via organocatalytic domino Michael–Michael–aldol condensation.

Bor-Cherng Hong,*[,†] Che-Sheng Hsu,[†] and Gene-Hsiang Lee[‡]

[†]*Department of Chemistry and Biochemistry, National Chung Cheng University, Chia-Yi, 621, Taiwan, R.O.C., and* [‡]*Instrumentation Center, National Taiwan University, Taipei, 106, Taiwan, R.O.C.*

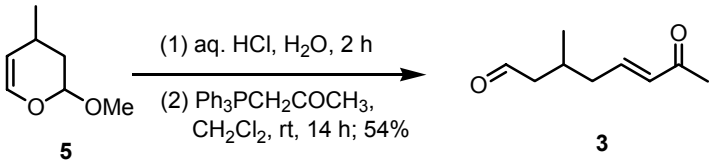
chebch@ccu.edu.tw

SUPPORTING INFORMATION:

Contents: (1) Experimental procedures and characterization data for compounds **1-10**.
(2) Spectra data for compounds **1-10**.

General Procedure. All solvents were reagent grade. L-proline (99+%) was purchased from Bachem. Other chemicals were purchased from Aldrich or Acros Chemical Co. Reactions were normally carried out under argon atmosphere in glassware. Merck silica gel 60 (particle size 0.04-0.063 mm) was employed for flash chromatography. Melting points are uncorrected. ^{1}H NMR spectra were obtained in $CDCl_3$ unless otherwise noted at 400 MHz (Bruker DPX-400) or 500 MHz (Varian-Unity INOVA-500). ^{13}C NMR spectra were obtained at 100 MHz or 125 MHz. *E.e.* values were measured by HPLC on a chiral column (chiralpak IA, chiralpak IB, chiralpak IC or chiralcel OD-H, 0.46 cm ID x 25 cm, particle size 5 μ) by elution with IPA-hexane. The flow rate of the indicated elution solvent is maintained at 1 mL/min, and the retention time of a compound is recorded accordingly. HPLC was equipped with the ultraviolet and refractive index detectors. The melting point was recorded on a melting point apparatus (MPA100 – Automated melting point system, Stanford Research Systems, Inc.) and is uncorrected. The optical rotation values were recorded with a Jasco-P-2000 digital polarimeter.

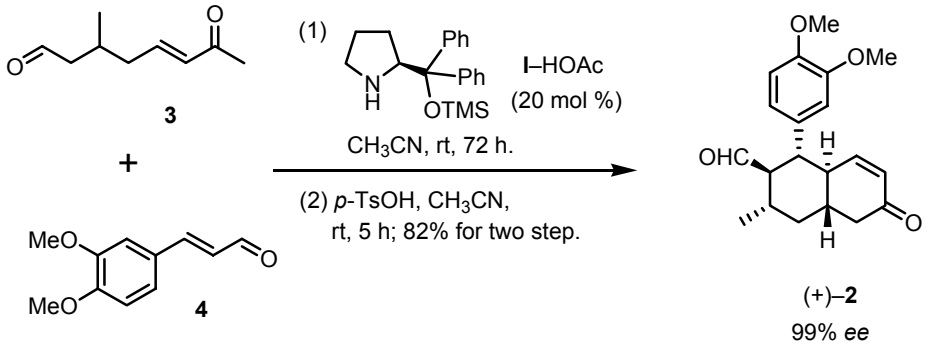
Preparation of ketoaldehyde 3.



5 **3**

To a solution of 3,4-dihydro-2-methoxy-4-methyl-2*H*-pyran **5** (300 mg, 2.34 mmol) in H_2O (5.0 mL) was added a concentrate aqueous HCl solution (0.5 mL). The resulting mixture was stirred at 25 °C for 2 h until the solution turned to clear. The solution was neutralized to pH 7 by slow addition of $NaHCO_3$, monitored by pH indictor paper. To this mixture was slowly added a solution of 1-(triphenylphosphoranylidene)acetone (460.0 mg, 1.445 mmol) in CH_2Cl_2 (2 mL) over 1.5 h. After the addition, the resulting mixture was stirred at ambient temperature for 14 h until the completion of reaction, as monitored by TLC. The reaction mixture was extracted with EtOAc (25 mL x 2), and the organic solution was washed with brine (10 mL x 2), dried over Na_2SO_4, concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 25% EtOAc-hexane (R_f = 0.56 for **3** in 50 % EtOAc-hexane) to give **3** as a colorless oil (120 mg, 54% yield). Selected spectroscopic data: IR (neat): 3428, 2960, 2727, 1722, 1671, 1626, 1363, 1255, 1175, 984 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.74 (t, J = 1.5 Hz, 1 H), 6.75-6.67 (m, 1 H), 6.06 (d, J = 15.5 Hz, 1 H), 2.50 – 2.10 (m, 5 H), 2.22 (s, 3 H), 0.99 (d, J = 6.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.6 (CH), 198.2 (C), 145.3 (CH), 133.0 (CH), 50.3 (CH_2), 39.4 (CH_2), 27.5 (CH), 27.1 (CH_3), 19.9 (CH_3); MS (*m/z*, relative intensity): 55 (M^+ +1, 32.57), 154 (M^+, 2.), 129 (58), 111 (63), 99 (64), 95 (47), 85 (49), 71 (67), 69 (100), 58 (62), 55 (70); exact mass calculate for $C_9H_{14}O_2$ (M^+): 154.0994; found (M^+): 154.0984.

Preparation of (+)-2.



To a solution of (*E*)-3-(3,4-dimethoxyphenyl)acrylaldehyde **4** (290 mg, 1.51 mmol) and (*E*)-3-methyl-7-oxooct-5-enal **3** (565 mg, 3.66 mmol) in CH_3CN (5.0 mL) was added dropwise a solution of catalyst **I** (98 mg, 0.30 mmol) and acetic acid (18 mg, 0.30 mmol) in CH_3CN (1 mL). The resulting solution was stirred at ambient temperature for 72 h until the completion of reaction, as monitored by TLC, and followed by the addition of *p*-TsOH (430 mg, 2.50 mmol), and stirring for an additional 5 h. The solution was extracted with EtOAc (10 mL x 3), washed with brine (5 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 25% EtOAc–hexane (R_f = 0.43 for **2** in 20% EtOAc–hexane) to give **2** as a white solid (407 mg, 82% yield); mp. 109-111 °C. Selected spectroscopic data for (+)-**2**: $[\alpha]_D^{26}$ +58.9 (*c* 6.3, $CHCl_3$); IR (neat): 2957, 1723, 1678, 1516, 1463, 1262, 1226, 1142, 1026, 759, 668 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.37 (d, J = 4.5 Hz, 1 H), 6.82 – 6.78 (m, 1 H), 6.74 – 6.65 (m, 1 H), 6.62 – 6.60 (m, 1 H), 6.48 (d, J = 10.0 Hz, 1 H), 5.88 (dd, J = 10.0, 2.5 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 2.64 (t, J = 11.5 Hz, 1 H), 2.50 (dd, J = 16.5, 3.0, 1 H), 2.44 – 2.38 (m, 1 H), 2.35 – 2.25 (m, 1 H), 2.23 – 2.15 (m, 1 H), 2.05 – 1.80 (m, 3 H), 1.30 –1.08 (m, 1 H), 0.96 (d, J = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 203.7 (CH), 199.2 (C), 150.6 (CH), 148.3 (C), 131.8 (C), 130.0 (CH), 111.5 (CH), 63.7 (CH), 55.9 (CH_3), 55.8 (CH_3), 47.8 (CH), 46.2 (CH), 44.8 (CH_2), 40.6 (CH), 40.3 (CH_2), 32.1 (CH), 19.9 (CH_3), some aryl carbons are broadened and disappeared due to the slow rotation and coalescence phenomenon; MS (*m*/*z*, relative intensity): 328 (M^+, 66), 243 (5), 221(5), 194 (11), 151 (100), 138 (30), 128 (6), 115 (11), 91 (9), 77 (11), 73 (7), 66 (6); exact mass calculated for $C_{20}H_{24}O_4$ (M^+): 328.1675; found 328.1673.

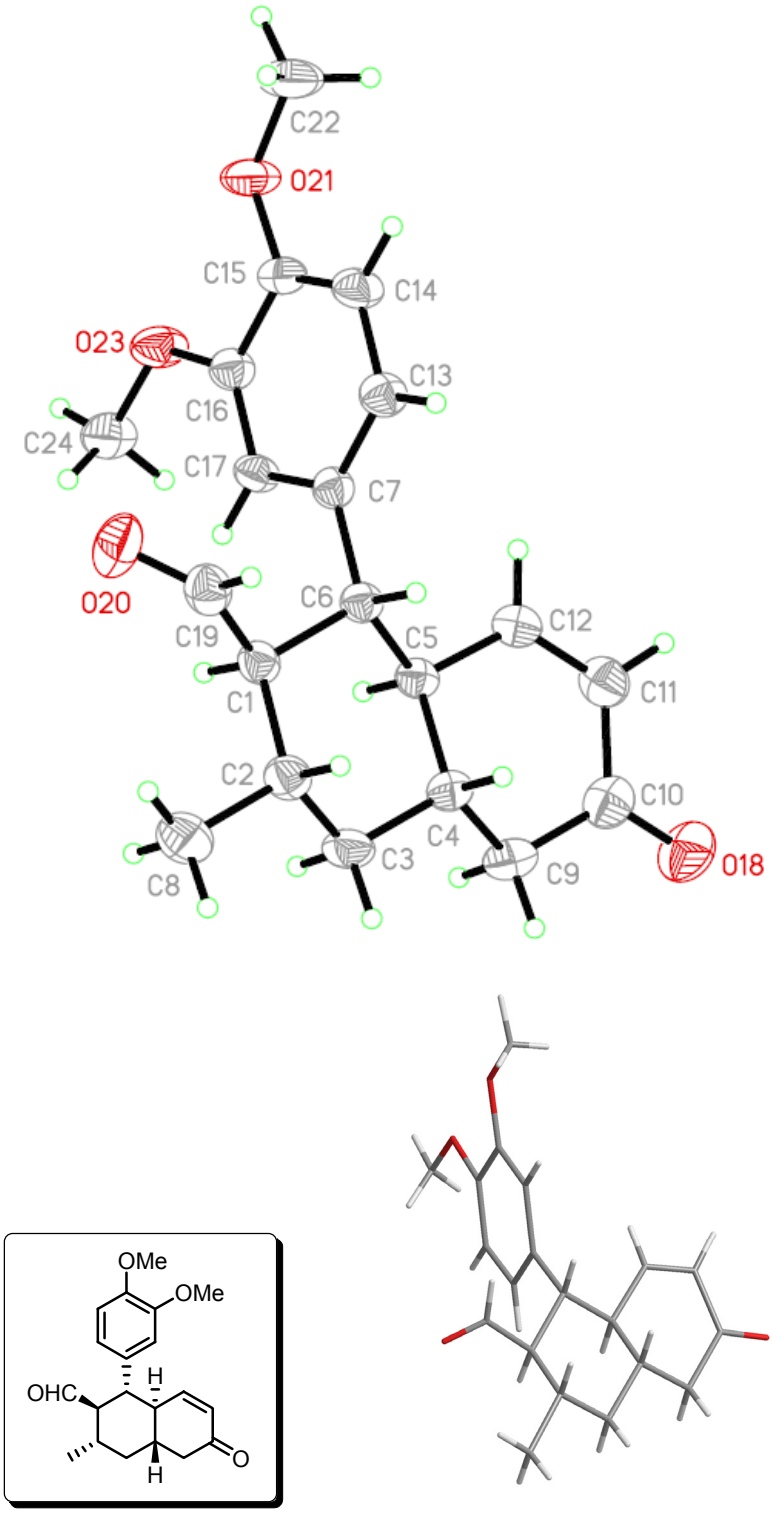
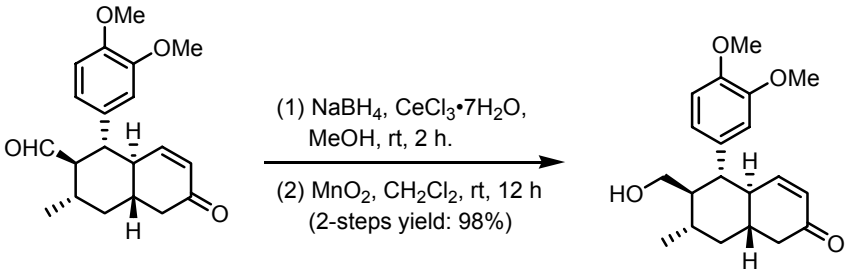


Figure S1 Stereo plots of the X-ray crystal structures of (+)-**2**: C, gray; O, red, and the ORTEP diagram.

CCDC 844400 contains the supplementary crystallographic data for (+)-**2**. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Preparation of alcohol 6.

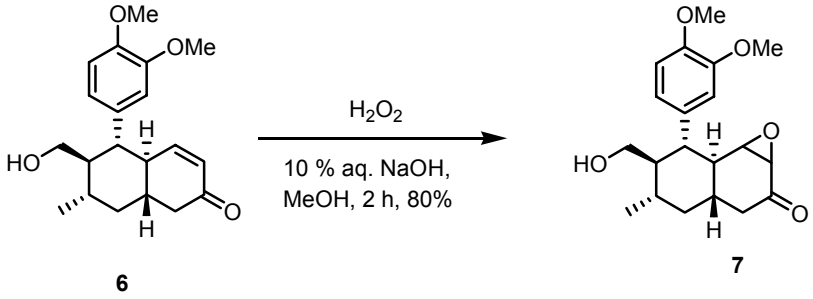


(+)–**2**
99% *ee*

6

To a solution of **2** (20.0 mg, 0.06 mmol) and $CeCl_3$•$7H_2O$ (34.0 mg, 0.09 mmol) in MeOH (3 mL) was added $NaBH_4$ (3.0 mg, 0.08 mmol) at 0 °C. The resulting solution was stirred at ambient temperature for 2 h until the completion of reaction, monitored by TLC, followed by addition of a 1N aqueous NaOH solution (1.0 mL). The resulting mixture was filtered through Celite and extracted with EtOAc (15 mL x 2). The organic solution was washed with brine (5 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. To a solution of this residue in CH_2Cl_2 (3.0 mL) was added MnO_2 (80.0 mg, 0.92 mmol) and the resulting mixture was stirred at room temperature for 12 h until the completion of reaction, monitored by TLC. The resulting mixture was filtered through Celite and extracted with EtOAc (10 mL x 2). The organic solution was washed with brine (5 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 40% EtOAc–hexane (R_f = 0.33 for **6** in 60% EtOAc–hexane) to give **6** as a colorless oil (19.7 mg, 98% yield). Selected spectroscopic data: $[\alpha]_D^{26}$ +30.2 (*c* 2.4, $CHCl_3$); IR (neat): 3478, 3006, 2903, 2839, 1668, 1516, 1464, 1261, 1225, 1153, 1027, 806, 755, 665 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 6.90 – 6.61 (m, 3 H), 6.45 (dd, J = 10.2, 1.3 Hz, 1 H), 5.83 (dd, J = 10.2, 2.6 Hz, 1 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.64 (dd, J = 11.2, 2.6 Hz, 1 H), 3.21 (dd, J = 11.2, 1.7 Hz, 1 H), 2.65 – 2.42 (m, 2 H), 2.32 – 2.18 (m, 2 H), 2.02 – 1.85 (m, 1 H), 1.80 – 1.70 (m, 1 H), 1.40 – 1.00 (m, 4 H), 1.04 (d, J = 6.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.9 (C), 152.9 (CH), 129.4 (CH), 60.5 (CH_2), 55.9 (CH_3), 55.8 (CH_3), 48.3 (CH), 45.1 (CH_2), 41.6 (CH_2), 40.9 (CH), 31.5 (CH), 19.9 (CH_3); Some aryl carbons are broadened and disappeared due to the slow rotation and coalescence phenomenon; MS (*m*/*z*, relative intensity): 330 (M^+, 47), 316 (1), 314 (0.86), 284 (0.86), 267 (0.61), 256 (0.66), 243 (1), 239 (1), 205 (5), 191 (3), 177 (5), 153 (6), 151 (100), 138 (7), 115 (5), 107 (5), 91 (6), 77 (5), 57 (4), 55 (4); exact mass calculated for $C_{20}H_{26}O_4$ (M^+): 330.1831; found 330.1832.

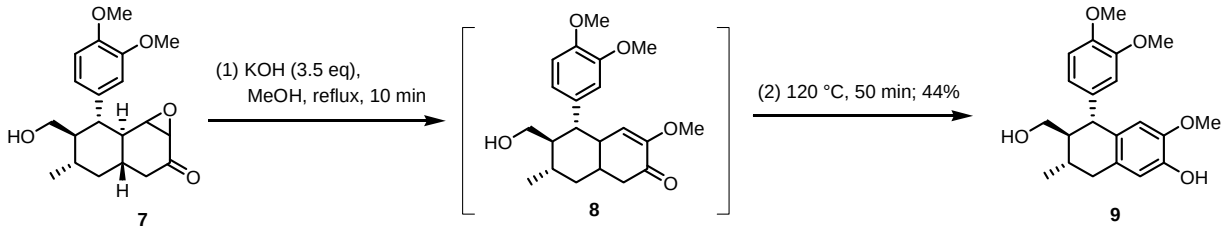
Preparation of epoxide7.



6 **7**

To a solution of **6** (20.0 mg, 0.06 mmol) in MeOH (1 mL) was added a 10% aqueous solution of NaOH (0.005 mL) and H_2O_2 (30%, 0.016 mL) at 0 °C. After the addition, the resulting solution was stirred at ambient temperature for 2 h until the completion of reaction, monitored by TLC. In order to remove methanol, the solution was concentrated *in vacuo* to *ca.* 3/4 of the original volume. To the resulting mixture was added ice water (2.0 mL), and the solution was extracted with EtOAc (5.0 mL x 2), washed with brine (5.0 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 40% EtOAc–hexane (R_f = 0.42 for **7** in 60% EtOAc–hexane) to give **7** as a colorless oil (17 mg, 80% yield). Selected spectroscopic data: $[\alpha]_D^{26}$ +65 (*c* 2.45, $CHCl_3$); IR (neat): 3515, 3009, 2960, 2913, 2839, 1706, 1516, 1261, 1027, 808, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.93 – 6.63 (m, 3 H), 3.87 (s, 3 H), 3.86 (s, 3 H), 3.66 (d, J = 12.0 Hz, 1 H), 3.25 (d, J = 12.0 Hz, 1 H), 3.09 (d, J = 3.5 Hz, 1 H), 2.97 (brs, 1 H), 2.85 – 2.70 (m, 1 H), 2.48 (dd, J = 19.0, 4.5 Hz, 1 H), 2.10 – 1.95 (m, 1 H), 1.88 – 1.70 (m, 4 H), 1.31 (t, J = 11.0 Hz, 1 H), 1.03 (d, J = 6.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 205.0 (C), 60.6 (CH_2), 56.3 (CH), 56.0 (2 CH_3), 55.7 (2 CH), 47.6 (CH), 43.6 (CH_2), 41.7 (CH_2), 31.5 (CH), 30.0 (CH), 19.9 (CH_3); Some aryl protons and carbons are broadened and disappeared due to the slow rotation and coalescence phenomenon; MS (*m*/*z*, relative intensity): 346 (M^+, 72), 330 (2), 310 (2), 295 (3), 284 (6), 267 (3), 256 (19), 239 (5), 213 (14), 211 (5), 185 (10), 169 (9), 151 (53), 149 (26), 129 (25), 111 (28), 97 (41), 85 (70), 71 (90), 57 (100); exact mass calculated for $C_{20}H_{26}O_5$ (M^+): 346.1780; found 346.1779.

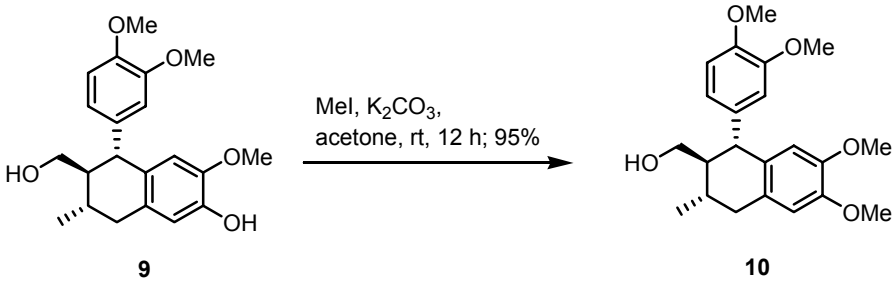
Preparation of alcohol 9.



A solution of **7** (10.0 mg, 0.03 mmol) and NaOH (5.7 mg, 0.14 mmol) in MeOH (0.11 mL) was heated to reflux for 10 min. The solution was concentrated *in vacuo* to remove most methanol but not dried and gave a sticky reside. The residue **8** was heated to 120 °C under N_2, with a reflux condenser, for 50 min until the completion of reaction, as monitored by TLC. The solution was washed with aqueous saturated $NaHCO_3$ solution, extracted with CH_2Cl_2 (5 mL x 2). The combined organic solution was washed with brine (5 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 40% EtOAc–hexane (R_f = 0.33 for **9** in 50% EtOAc–hexane) to give **9 as** a yellow oil (4.4 mg, 44% yield). Selected spectroscopic data: $[\alpha]_D^{26}$ +8.4 (*c* 2.15, $CHCl_3$); IR (neat): 3401, 3003, 2959, 2926, 1726, 1666, 1593, 1513, 1464, 1260, 1026, 759 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.78 (d, J = 8.0 Hz, 1 H), 6.74 (d, J = 8.0 Hz, 1 H), 6.61 (d, J = 12.0 Hz, 2 H), 6.17 (s, 1 H), 5.40 (s, 1 H), 3.97 (d, J = 11.0 Hz, 1 H), 3.87 (s, 3 H), 3.80 – 3.75 (m, 1 H), 3.79 (s, 3 H), 3.58 (s, 3 H), 3.43 (d, J = 11.0 Hz, 1 H), 2.75 (dd, J = 16.0, 4.5 Hz, 1 H), 2.62 – 2.56 (m, 1 H), 2.07 – 1.98 (m, 1 H), 1.59 – 1.52 (m, 2 H), 1.12 (d, J = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 149.0 (C), 147.5 (C), 144.8 (C), 143.6 (C), 138.5 (C), 131.8 (C), 129.6 (C), 121.7 (CH), 113.4 (CH), 112.1 (CH), 111.9 (CH), 110.9 (CH), 61.1 (CH_2), 55.9 (2 CH_3), 55.8 (CH_3), 50.7 (CH), 47.4 (CH), 38.6 (CH_2), 30.1 (CH), 19.7 (CH_3); MS (*m*/*z*, relative intensity): 358 (M^+, 11), 339 (15), 323 (12), 309 (7), 299 (5), 285 (6), 269 (24), 255 (10), 254 (7), 211 (4), 203 (16), 189 (7), 178 (8), 167 (7), 151 (15), 149 (14), 111 (14), 97 (20), 85 (20), 71 (28), 58 (100), 57 (35); exact mass calculated for $C_{21}H_{26}O_5$ (M^+): 358.1780; found: 358.1777.

R_f = 0.12 for **8** in 50% EtOAc–hexane. Selected spectroscopic data for **8**: $[\alpha]_D^{26}$ +31.6 (*c* 2.26, $CHCl_3$); IR (neat): 3515, 3010, 2925, 2839, 1687, 1619, 1515, 1464, 1261, 1155, 1027, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.82 – 6.69 (m, 3 H), 5.28 (s, 1 H), 3.87 (s, 6 H), 3.64 (d, J = 11.0 Hz, 1 H), 3.32 (s, 3 H), 3.20 (d, J = 11.0 Hz, 1 H), 2.58–2.47 (m, 2 H), 2.37 (t, J = 10.5 Hz, 1 H), 2.24 (dd, J = 16.5, 14 Hz, 1 H), 1.92–1.89 (m, 1 H), 1.79 – 1.75 (m, 2 H), 1.31 (t, J = 10.5 Hz, 1 H), 1.20 (brs, 1 H), 1.03 (d, J = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 194.0 (C), 151.4 (C), 147.8 (C), 134.4 (C), 122.9 (CH), 118.6 (CH), 117.6 (CH), 114.5 (C), 112.2 (C), 110.8 (CH), 108.1 (CH), 60.6 (CH_2), 55.9 (CH_3), 55.8 (CH_3), 54.7 (CH_3), 49.4 (CH), 41.0 (CH), 40.9 (CH_2), 31.5 (CH), 47.4 (CH), 19.9 (CH_3); MS (*m*/*z*, relative intensity): 360 (M^+, 15), 347 (2), 333 (2), 320 (2), 305 (3), 285 (5), 277 (3), 263 (3), 249 (4), 239 (7), 221 (15), 205 (20), 193 (12), 191 (11), 165 (15), 151 (43), 137 (24), 125 (36), 97 (81), 83 (73), 71 (84), 57 (100); exact mass calculated for $C_{22}H_{28}O_4$ (M^+): 360.1937; found: 360.1937.

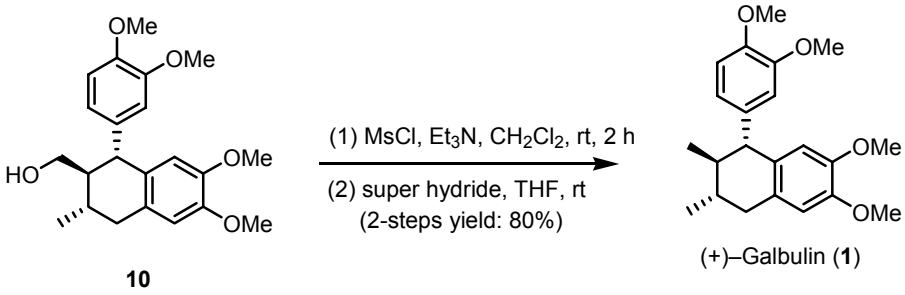
Preparation of 10.



9 **10**

To a solution of **9** (10.0 mg, 0.03 mmol) and K_2CO_3 (8.0 mg, 0.06 mmol) in acetone (1 mL) was added MeI (6.0 mg, 0.04 mmol). The solution was stirred at room temperature for 12 h until the completion of reaction, as monitored by TLC, followed by addition of H_2O (4 mL). The solution was extracted with EtOAc (15 mL x 2), washed with brine (10 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 30% EtOAc–hexane (R_f = 0.38 for **10** in 50% EtOAc–hexane) to give **10** as a yellow oil (9.9 mg, 95% yield). Selected spectroscopic data: $[\alpha]_D^{26}$ -4.5 (*c* 2.2, $CHCl_3$); IR (neat): 3469, 2926, 2850, 2834, 1738, 1607, 1514, 1464, 1256, 1028, 808, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.79 (d, J = 8.0 Hz, 1 H), 6.74 (dd, J = 8.0, 2.0 Hz, 1 H), 6.59 (d, J = 2.0 Hz, 1 H), 6.56 (s, 1 H), 6.20 (s, 1 H), 3.99 (dd, J = 10.0, 1.0 Hz, 1 H), 3.86 (s, 3 H), 3.83 (s, 3 H), 3.80 – 3.76 (m, 1 H), 3.78 (s, 3 H), 3.56 (s, 3 H), 3.47 – 3.42 (m, 1 H), 2.79 (dd, J = 16.0, 4.5 Hz, 1 H), 2.67 – 2.59 (m, 1 H), 2.06 – 1.97 (m, 1 H), 1.54 – 1.50 (m, 2 H), 1.14 (d, J = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 149.0 (C), 147.5 (C), 147.1 (C), 147.0 (C), 138.4 (C), 132.2 (C), 128.8 (C), 121.8 (CH), 112.9 (CH), 112.0 (CH), 110.9 (CH), 110.6 (CH), 61.1 (CH_2), 55.9 (CH_3), 55.83 (2 CH_3), 55.78 (CH_3), 50.7 (CH), 47.3 (CH), 38.9 (CH_2), 30.2 (CH), 19.7 (CH_3); MS (*m*/*z*, relative intensity): 372 (M^+, 100), 356 (9), 339 (16), 323 (18), 313 (7), 299 (9), 284 (16), 269 (65), 256 (10), 239 (21), 238 (10), 203 (22), 189 (6), 178 (10), 165 (8), 151 (22), 133 (7), 118 (7), 98 (9), 91 (43), 71 (14), 58 (61), 57 (19); exact mass calculated for $C_{22}H_{28}O_5$ (M^+): 372.1937; found: 372.1936.

Synthesis of (+)-Galbulin.



10 (+)–Galbulin (**1**)

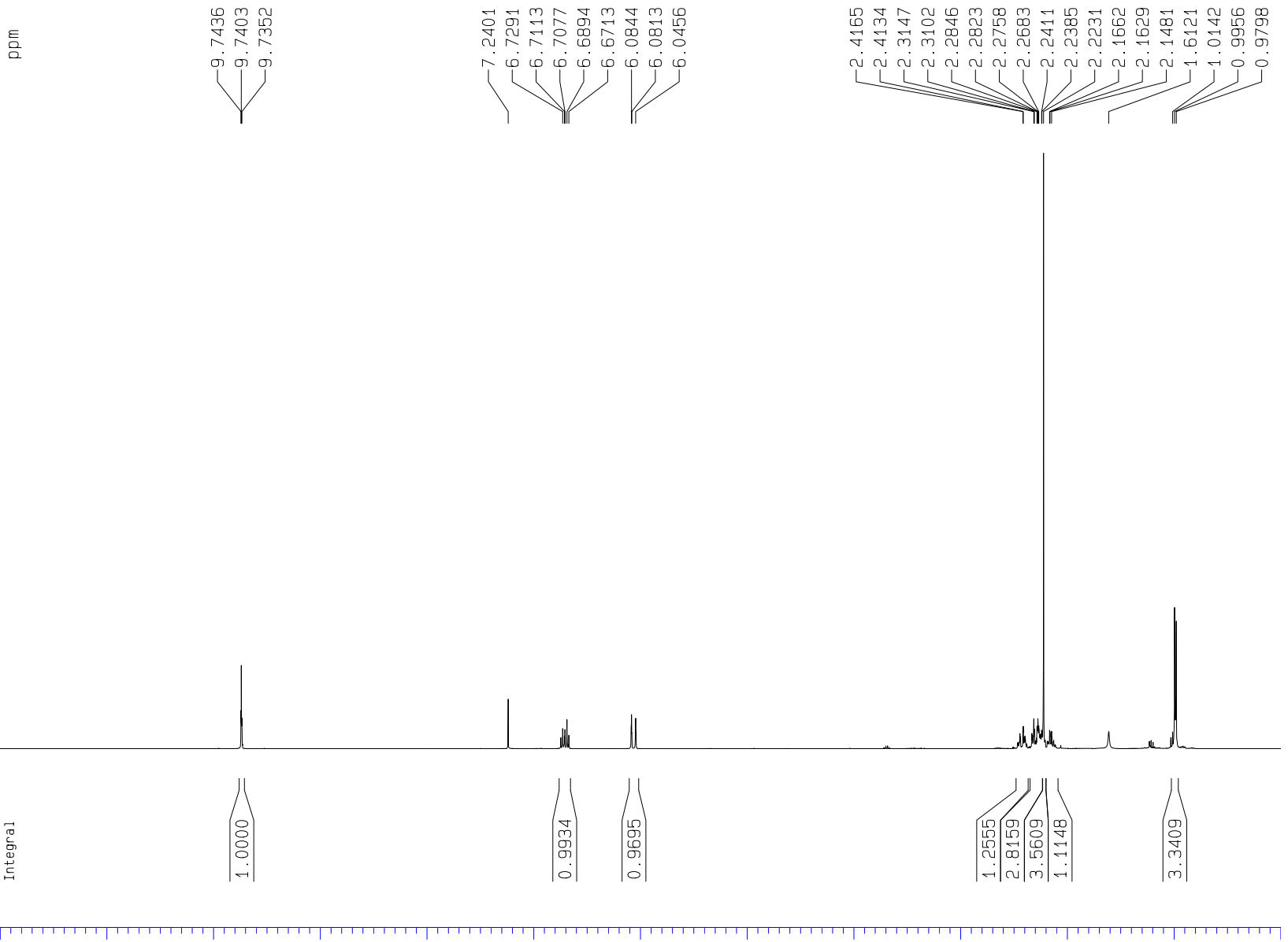
To a solution of **10** (12.0 mg, 0.03 mmol) and Et_3N (6.5 mg, 0.06 mmol) in CH_2Cl_2 (2 mL) was added methanesulfonyl chloride (7.4 mg, 0.06 mmol). The resulting solution was stirred at ambient temperature for 2 h until the completion of reaction, as monitored by TLC, and followed by addition of H_2O (3 mL). The solution was extracted with CH_2Cl_2 (10 mL x 2), washed with brine (10 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. To a solution of the residue in THF (2.0 mL) was added a Super-Hydride® solution (lithium triethylborohydride, 1M in THF, 0.071 mL, 0.07 mmol), and the resulting solution was stirred at ambient temperature for 2 h until the completion of reaction, as monitored by TLC. To the reaction mixture was added H_2O (3 mL). The solution was extracted with EtOAc (15 mL x 2), washed with brine (10 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give the crude product. The residue was purified by flash column chromatography with 10% EtOAc–hexane (R_f = 0.71 for **1** in 50% EtOAc–hexane) to give **1** as a white solid (9.1 mg, 80% yield); mp. 130-131 °C. Selected spectroscopic data: $[\alpha]_D^{30}$ +8.0 (*c* 0.3, $CHCl_3$); IR (neat): 2960, 2872, 2833, 1607, 1516, 1464, 1417, 1249, 1217, 1029, 801, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.78 (d, J = 8.5 Hz, 1 H), 6.69 (dd, J = 8.0, 1.5 Hz, 1 H), 6.56 – 6.54 (m, 2 H), 6.14 (s, 1 H), 3.86 (s, 3 H), 3.82 (s, 3 H), 3.79 (s, 3 H), 3.54 (s, 3 H), 3.41 (d, J = 10.5 Hz, 1 H), 2.74 (dd, J = 16.0, 4.5 Hz, 1 H), 2.63 – 2.56 (m, 1 H), 1.68 – 1.58 (m, 1 H), 1.56 – 1.45 (m, 1 H), 1.06 (d, J = 6.5 Hz, 3 H), 0.85 (d, J = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 148.8 (C), 147.3 (C), 147.0 (C), 146.9 (C), 139.0 (C), 132.4 (C), 129.1 (C), 121.9 (CH), 112.8 (CH), 112.0 (CH), 110.7 (CH), 110.6 (CH), 55.9 (2 CH_3), 55.8 (2 CH_3), 54.3 (CH), 43.8 (CH), 39.0 (CH_2), 35.5 (CH), 20.0 (CH_3), 17.2 (CH_3); MS (*m*/*z*, relative intensity): 356 (M^+, 4), 355 (M^+-1, 11), 341 (4), 339 (2), 316 (4), 295 (21), 281 (13), 269 (4), 256 (5), 239 (6), 221 (38), 207 (10), 185 (4), 167 (4), 147 (20), 141 (5), 129 (11), 111 (11), 97 (17), 85 (24), 71 (35), 58 (100), 57 (44); exact mass calculated for $C_{22}H_{28}O_4$ (M^+): 356.1988; found: 356.1988.

Table S1. Comparison of compound **1** and Galbulin (^{13}C NMR spectra with literature data).

Lit.[1]	Lit.[2]	Compound 1
148.9	148.9	148.8
147.4	147.3	147.3
147.0	147.0	147.0
146.9	146.9	146.9
139.1	139.0	139.0
132.5	132.5	132.4
129.1	129.1	129.1
121.9	121.9	121.9
112.9	112.9	112.8
112.2	112.1	112.0
110.8	110.7	110.7
110.7	110.6	110.6
55.9 (2C)	55.9 (2C)	55.9 (2C)
55.8 (2C)	55.8, 55.7	55.8 (2C)
54.3	54.3	54.3
43.8	43.8	43.8
39.1	39.0	39.0
35.6	35.6	35.5
20.0	20.0	20.0
17.2	17.2	17.2

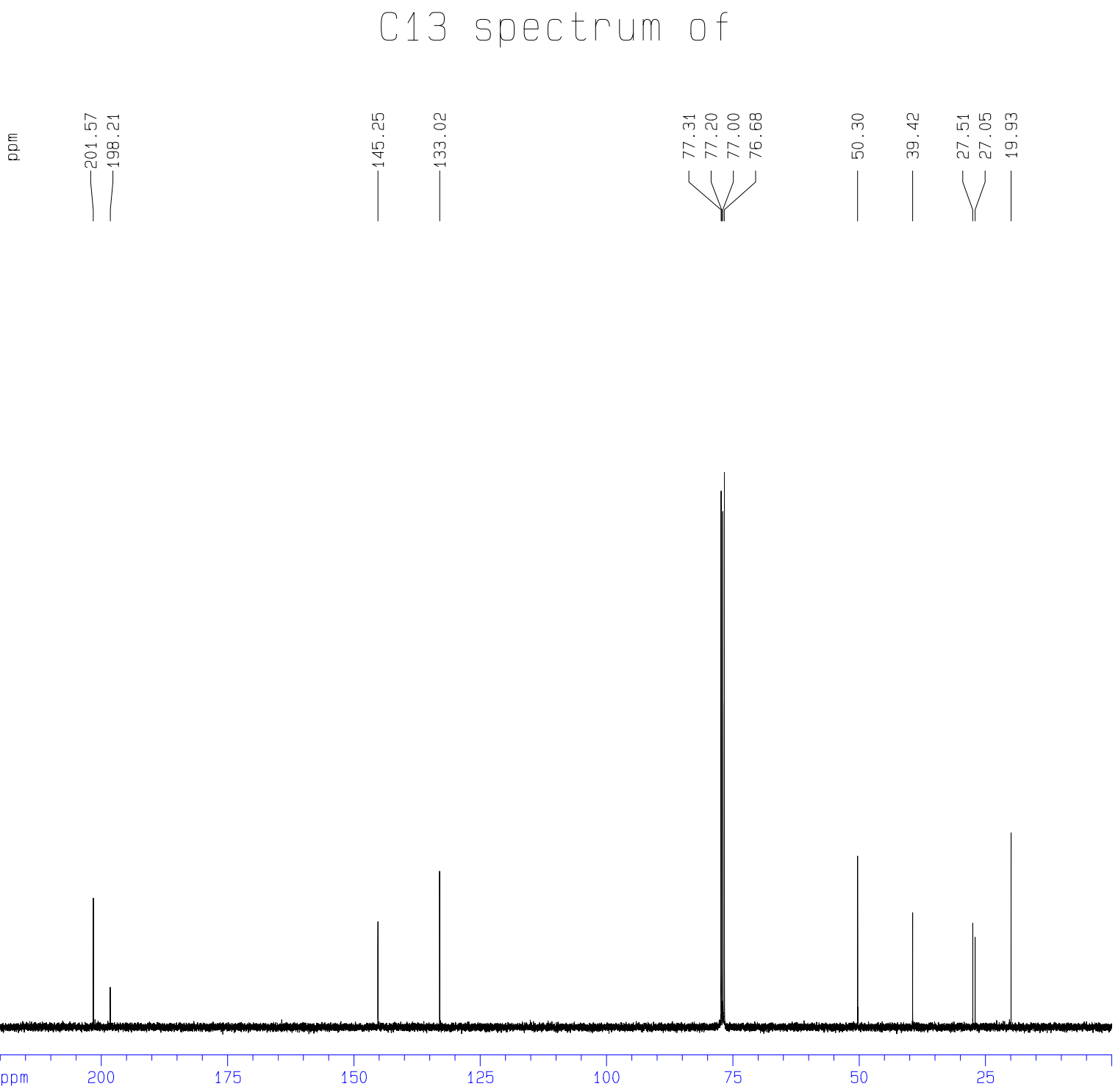
[1] Buckleton, J. S.; Cambie, R. C.; Clark, G. R.; Craw, P. A.; Rickard, C. E. F.; Rutledge, P. S.; Woodgate, P. D. *Aust. J. Chem*. **1988**, *41*, 305-324.
[2] Datta, P. K.; Yau, C.; Hooper, T. S.; Yvon, B. L.; Charlton, J. L. *J. Org. Chem.* **2001,** *66,* 8606-8611.

Fig S11. 1H NMR (CDCl3, 400 MHz) of compound 3.



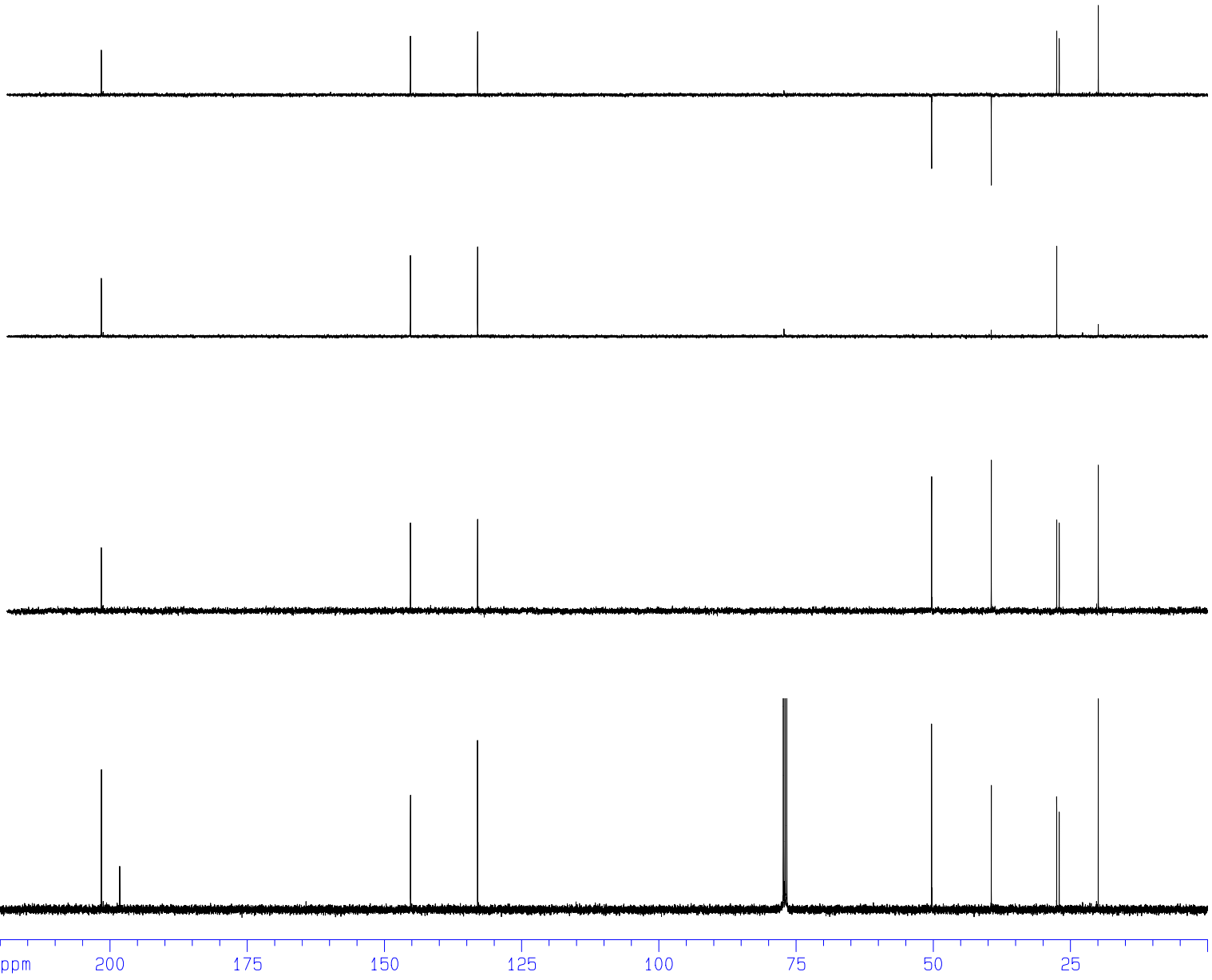

```
Current Data Parameters
NAME                  HCS-005
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20110106
Time                  21.06
INSTRUM               spect
PROBHD      5 mm QNP  1H
PULPROG                zg30
TD                    16384
SOLVENT               CDCl3
NS                       16
DS                        0
SWH                5995.204 Hz
FIDRES             0.365918 Hz
AQ                 1.3664756 sec
RG                    1290.2
DW                    83.400 usec
DE                     6.50 usec
TE                    300.0 K
D1                 1.50000000 sec

============ CHANNEL f1 =============
NUC1                      1H
P1                    10.90 usec
PL1                   -3.00 dB
SFO1            400.1326008 MHz

F2 - Processing parameters
SI                        8192
SF              400.1300171 MHz
WDW                       EM
SSB                       0
LB                     0.10 Hz
GB                        0
PC                     1.00

1D NMR plot parameters
CX                    21.50 cm
CY                    10.00 cm
F1P                  12.000 ppm
F1                  4801.56 Hz
F2P                  -0.000 ppm
F2                   -0.00 Hz
PPMCM              0.55814 ppm/cm
HZCM             223.32838 Hz/cm
```

Fig S12. 13C NMR (CDCl3, 100 MHz) of compound 3.




```
Current Data Parameters
NAME                  HCS-005
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_              20110106
Time                  22.06
INSTRUM               spect
PROBHD     5 mm QNP  1H
PULPROG               zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     1024
DS                        4
SWH              25125.629 Hz
FIDRES            0.383387 Hz
AQ                1.3042164 sec
RG                      256
DW                   19.900 usec
DE                    6.50 usec
TE                   300.0 K
D1               2.00000000 sec
d11              0.03000000 sec
d12              0.00002000 sec

============ CHANNEL f1 =============
NUC1                    13C
P1                   10.00 usec
PL1                   0.00 dB
SFO1            100.6237959 MHz

============ CHANNEL f2 =============
CPDPRG2             waltz16
NUC2                    1H
PCPD2                90.00 usec
PL2                  -3.00 dB
PL12                 15.70 dB
PL13                 18.70 dB
SFO2            400.1326008 MHz

F2 - Processing parameters
SI                    32768
SF              100.6127715 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
CY                   10.00 cm
F1P                 220.000 ppm
F1                22134.81 Hz
F2P                   0.000 ppm
F2                    0.00 Hz
PPMCM             11.00000 ppm/cm
HZCM            1106.74048 Hz/cm
```

Fig S13. DEPTof compound 3.




```
Current Data Parameters
NAME            HCS-005
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20110106
Time              22.06
INSTRUM           spect
PROBHD     5 mm QNP  1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           25125.629 Hz
FIDRES         0.383387 Hz
AQ             1.3042164 sec
RG                  256
DW               19.900 usec
DE                6.50 usec
TE               300.0 K
D1            2.00000000 sec
d11           0.03000000 sec
d12           0.00002000 sec

============ CHANNEL f1 =============
NUC1                13C
P1                10.00 usec
PL1                0.00 dB
SFO1         100.6237959 MHz

============ CHANNEL f2 =============
CPDPRG2         waltz16
NUC2                1H
PCPD2             90.00 usec
PL2               -3.00 dB
PL12              15.70 dB
PL13              18.70 dB
SFO2         400.1326008 MHz

F2 - Processing parameters
SI                32768
SF           100.6127715 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.40

1D NMR plot parameters
CX                20.00 cm
CY                10.00 cm
F1P              220.000 ppm
F1             22134.81 Hz
F2P               0.000 ppm
F2                 0.00 Hz
PPMCM          11.00000 ppm/cm
HZCM         1106.74048 Hz/cm
```

Fig S14. 1H NMR (CDCl3, 500 MHz) of compound 2.

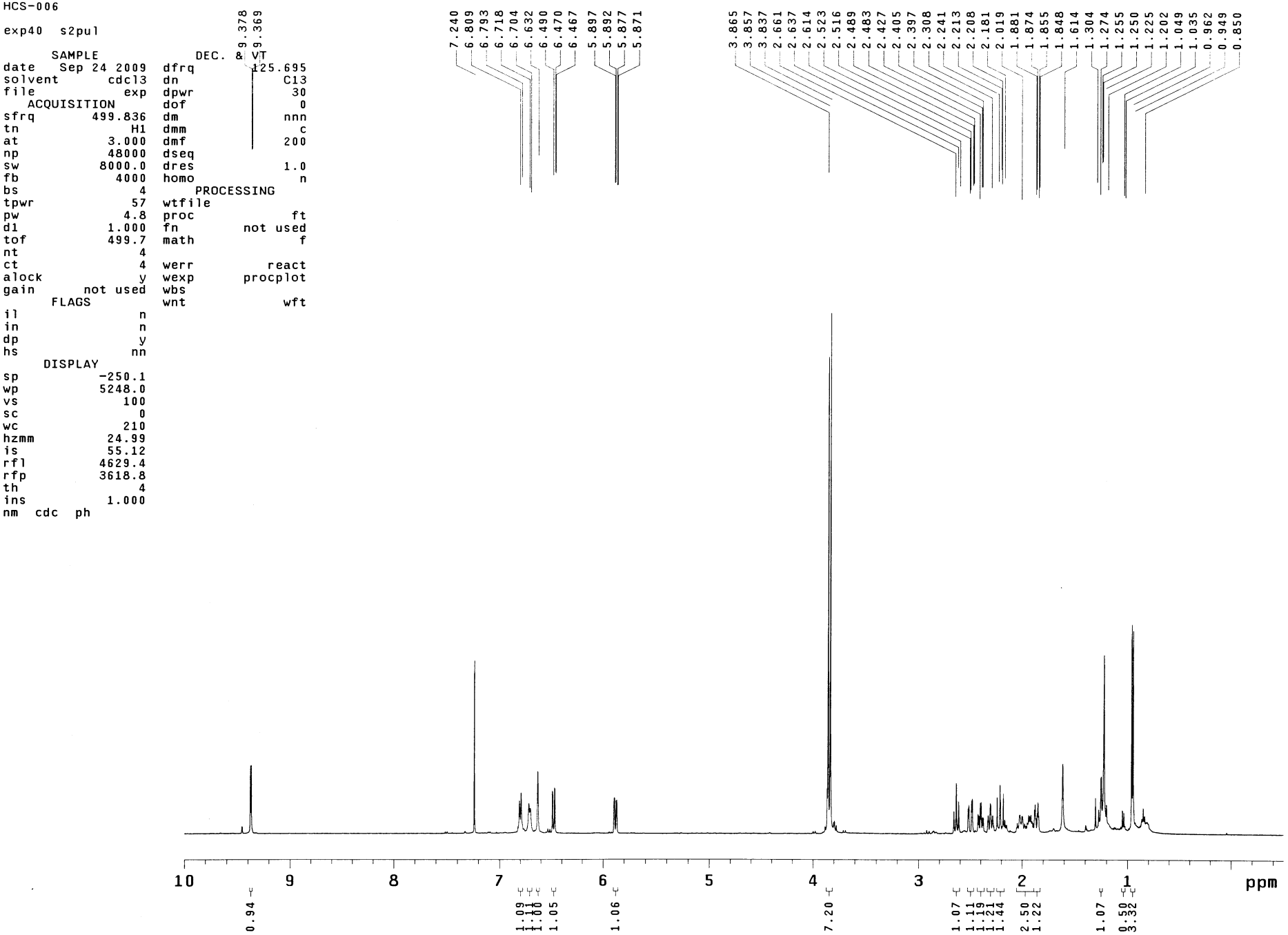


Fig S15. 13C NMR (CDCl3, 126 MHz) of compound 2.

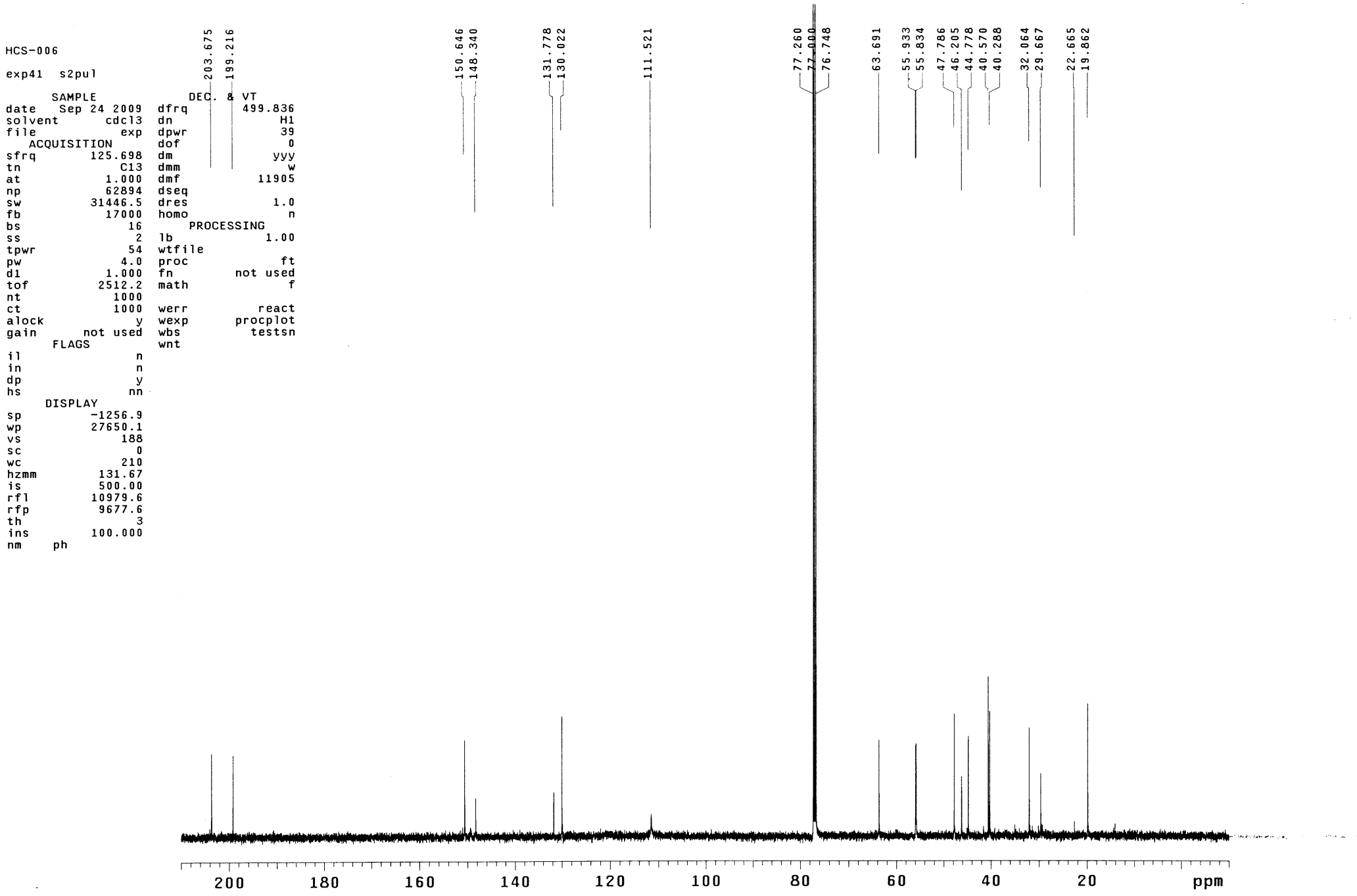


Fig S16. DEPT of compound 2.

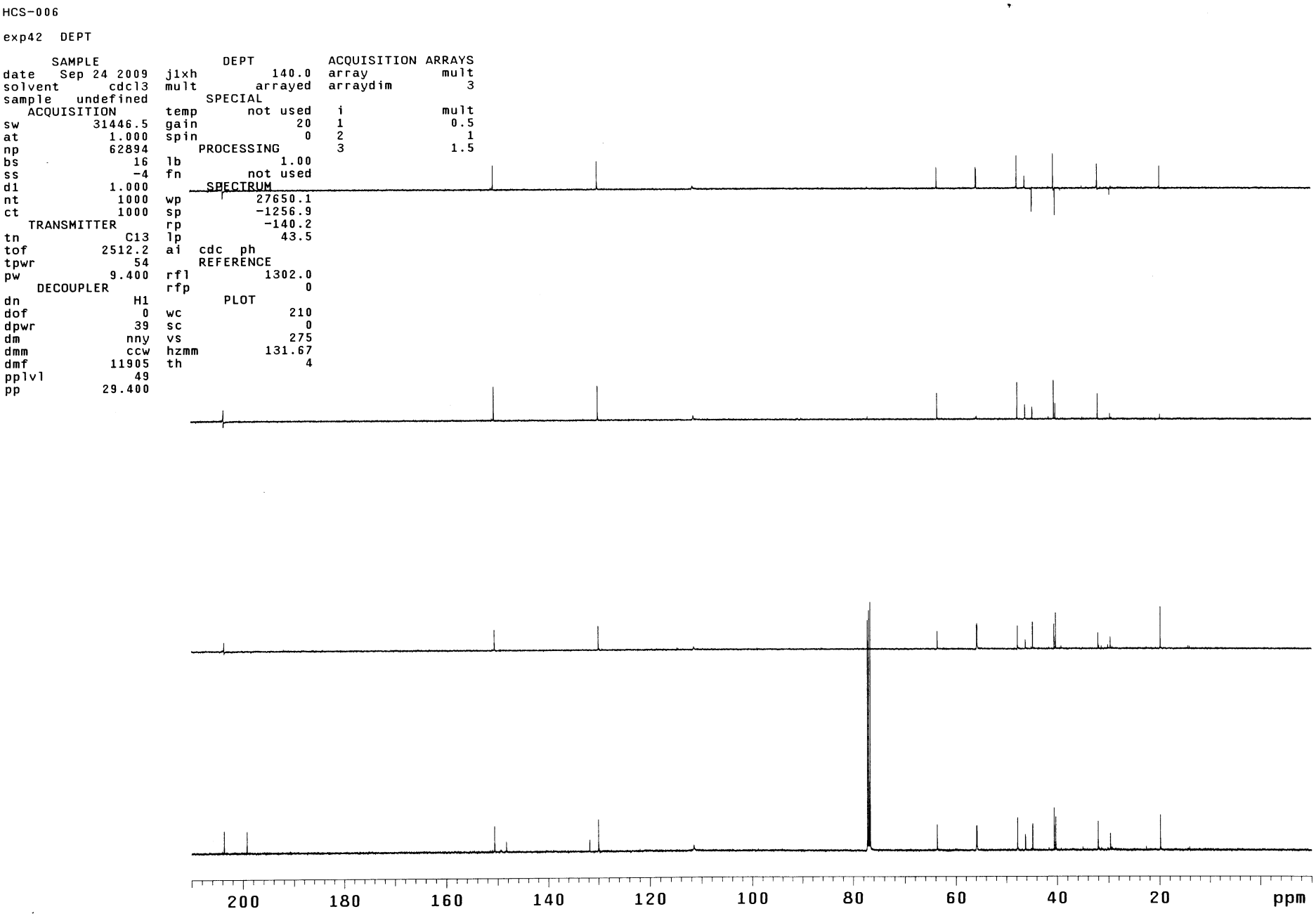


Fig S17. COSY of compound 2.

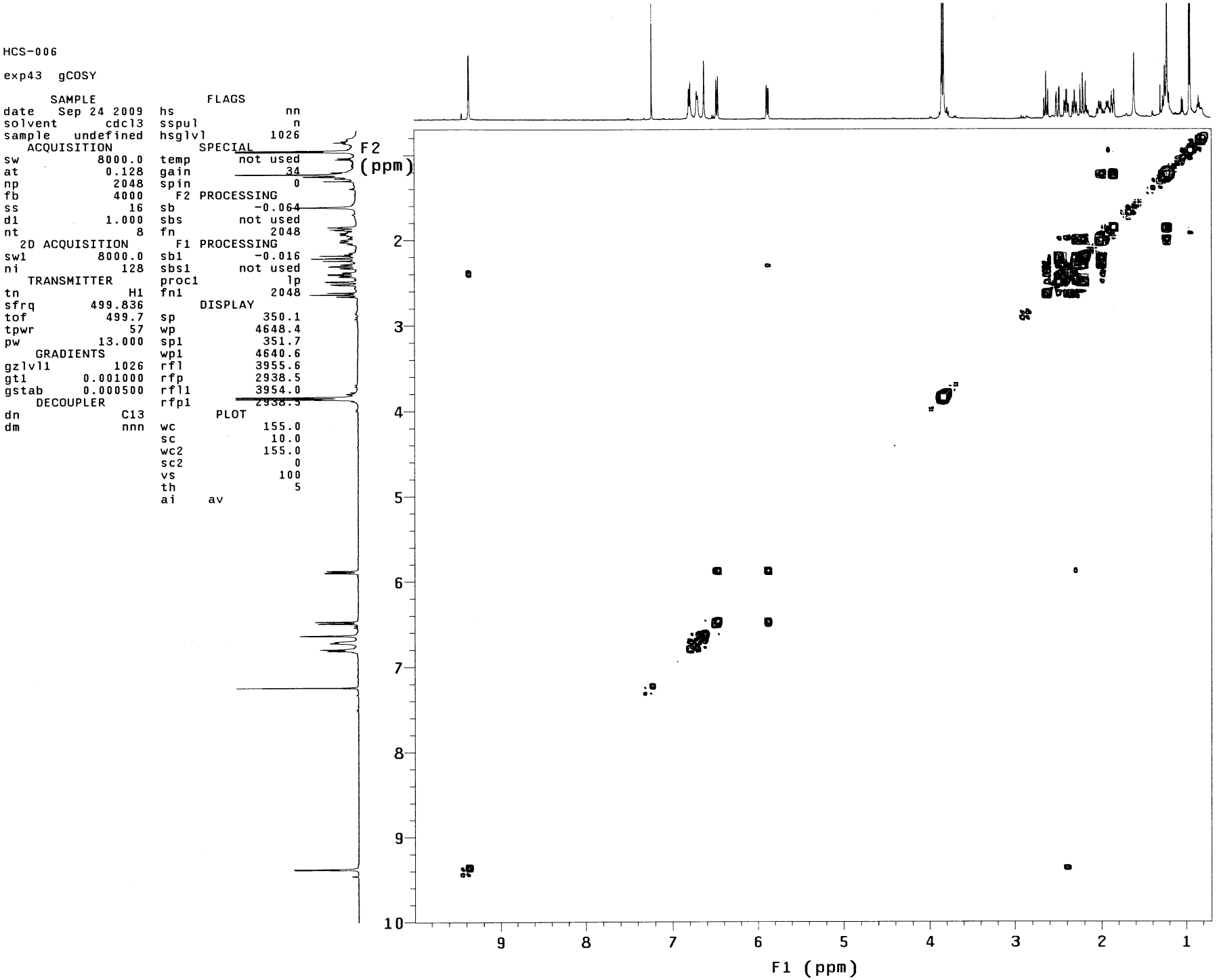


Fig S18. COSY of compound 2, expanded.

HCS-006

exp43 gCOSY

SAMPLE		FLAGS	
date	Sep 24 2009	hs	nn
solvent	cdcl3	sspul	n
sample	undefined	hsglvl	1026
ACQUISITION		SPECIAL	
sw	8000.0	temp	not used
at	0.128	gain	34
np	2048	spin	0
fb	4000	F2 PROCESSING	
ss	16	sb	-0.064
d1	1.000	sbs	not used
nt	8	fn	2048
2D ACQUISITION		F1 PROCESSING	
sw1	8000.0	sb1	-0.016
ni	128	sbs1	not used
TRANSMITTER		proc1	lp
tn	H1	fn1	2048
sfrq	499.836	DISPLAY	
tof	499.7	sp	365.7
tpwr	57	wp	1218.8
pw	13.000	sp1	359.5
GRADIENTS		wp1	1226.6
gzlvl1	1026	rfl	3955.6
gt1	0.001000	rfp	2938.5
gstab	0.000500	rfl1	3954.0
DECOUPLER		rfp1	2938.5
dn	C13	PLOT	
dm	nnn	wc	155.0
		sc	10.0
		wc2	155.0
		sc2	0
		vs	100
		th	5
		ai av	

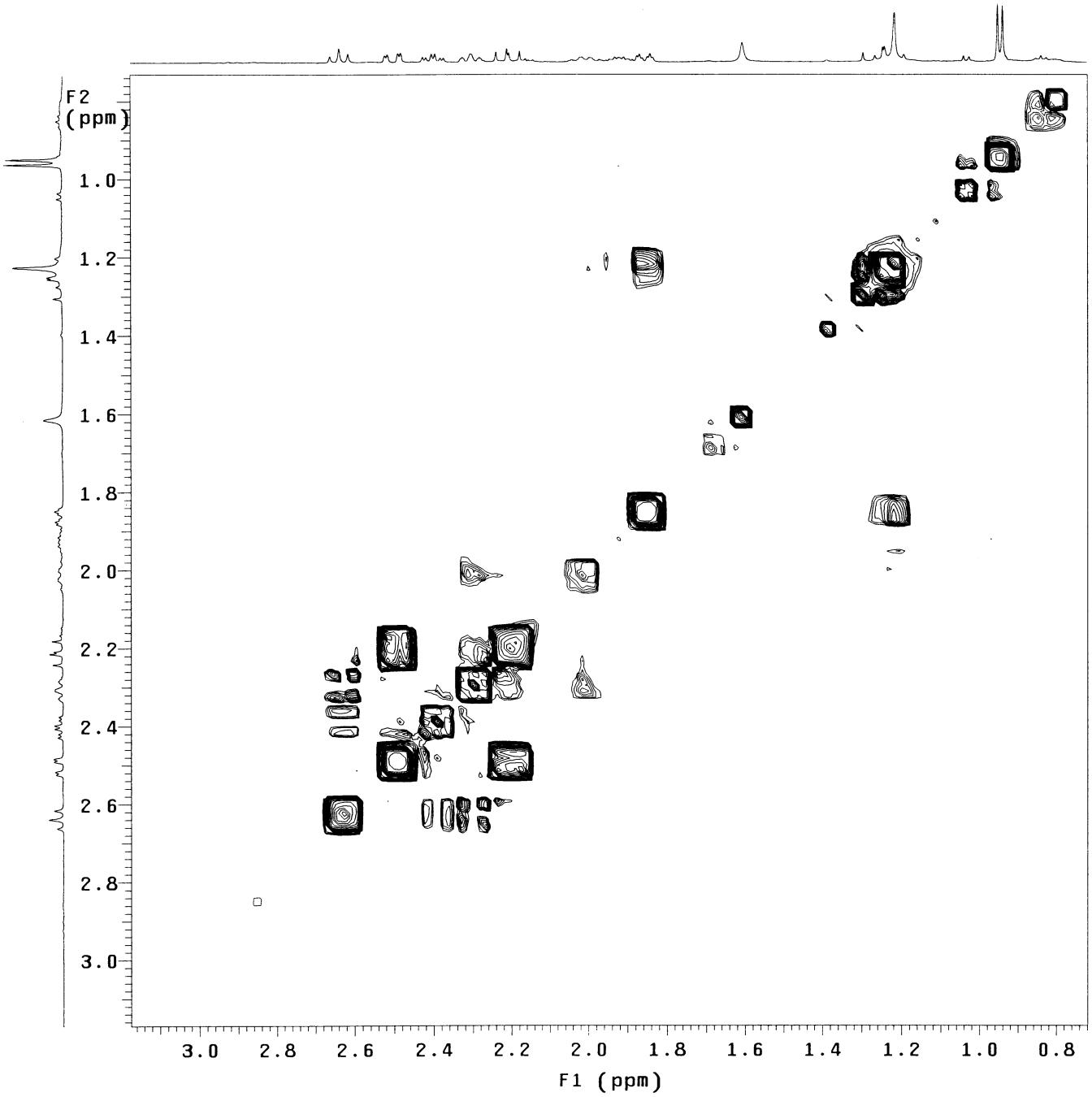


Fig S19. HMQC of compound 2.

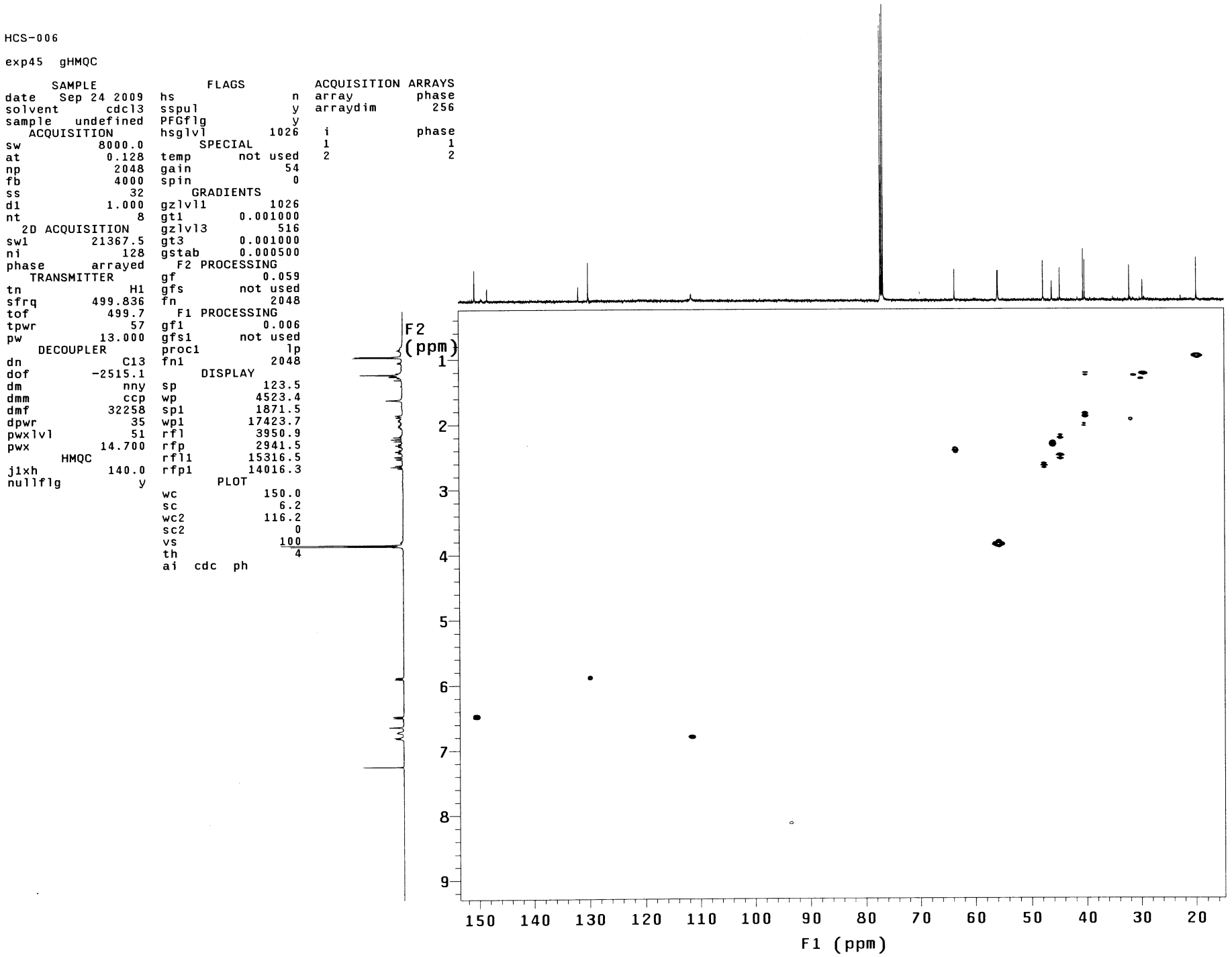


Fig S20. NOESY of compound 2.

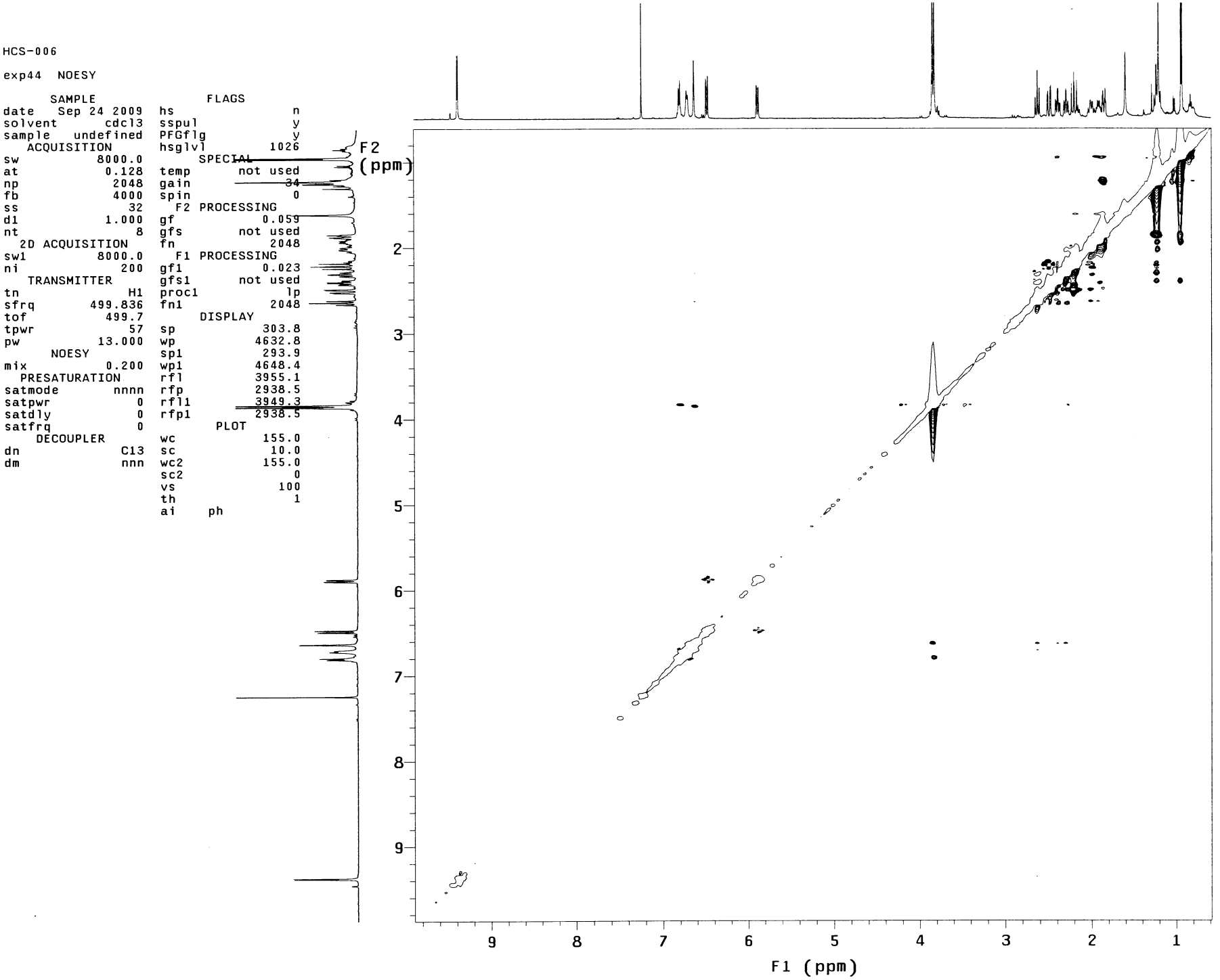
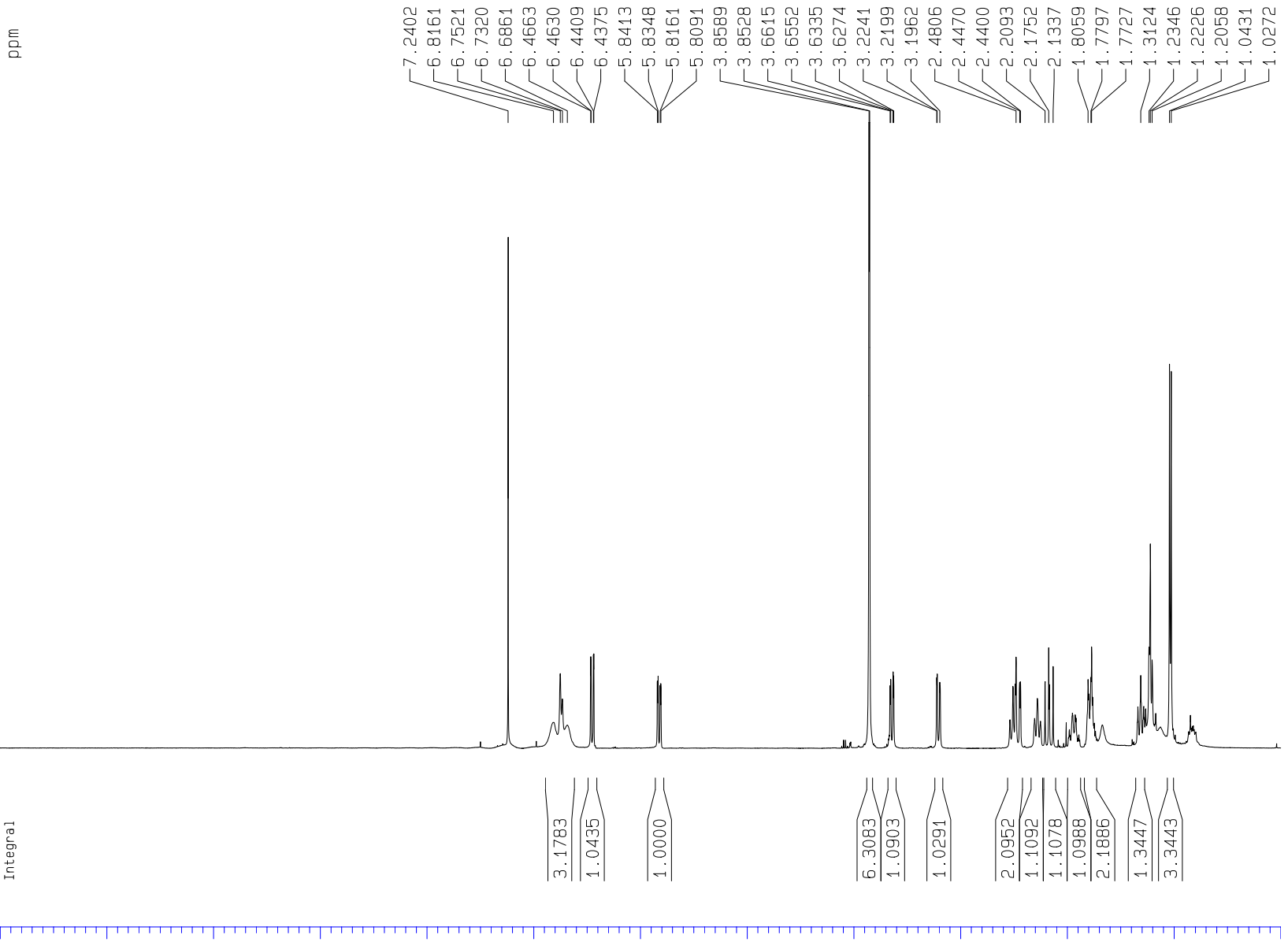
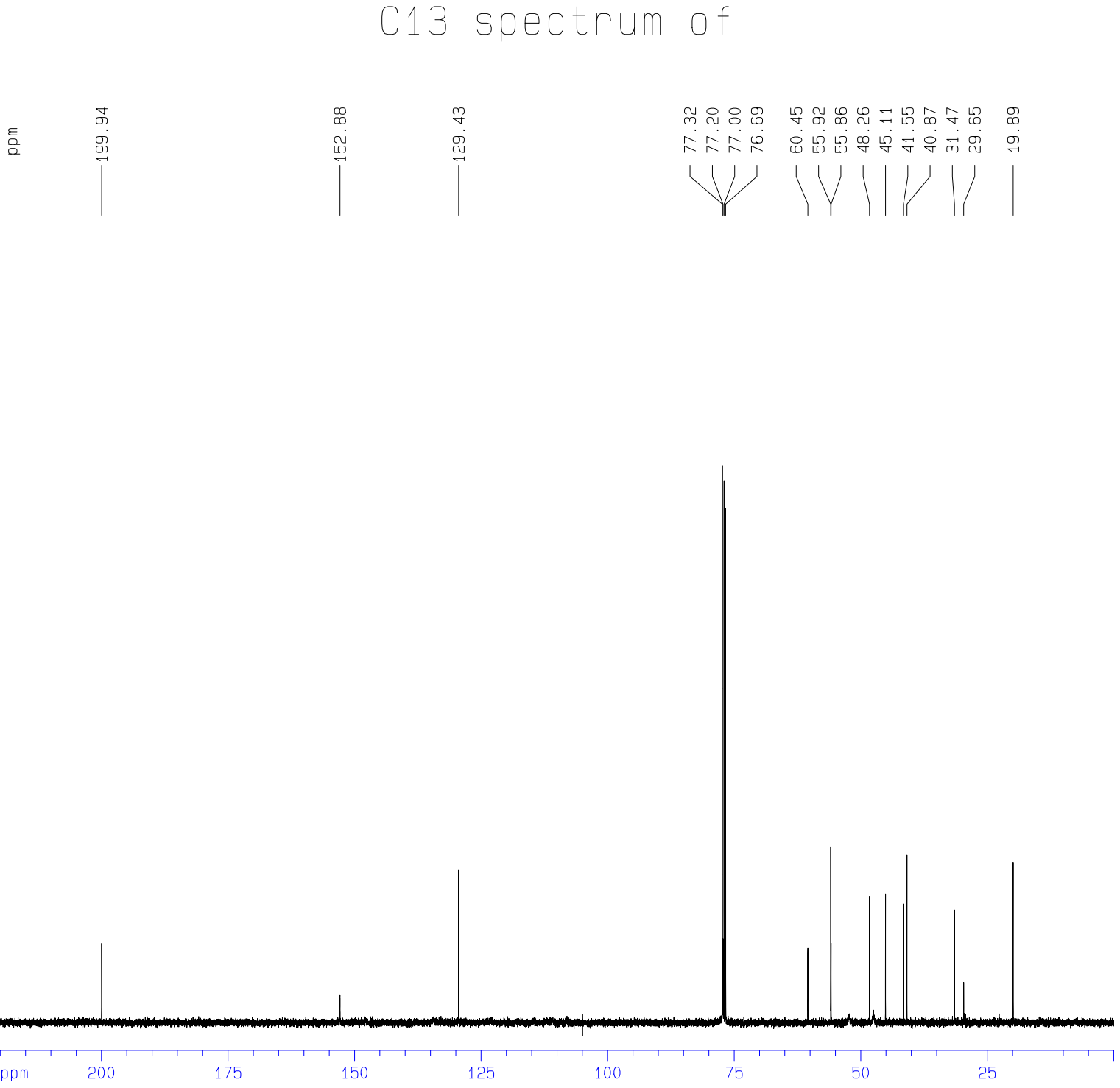


Fig S21. 1H NMR (CDCl3, 400 MHz) of compound 6.



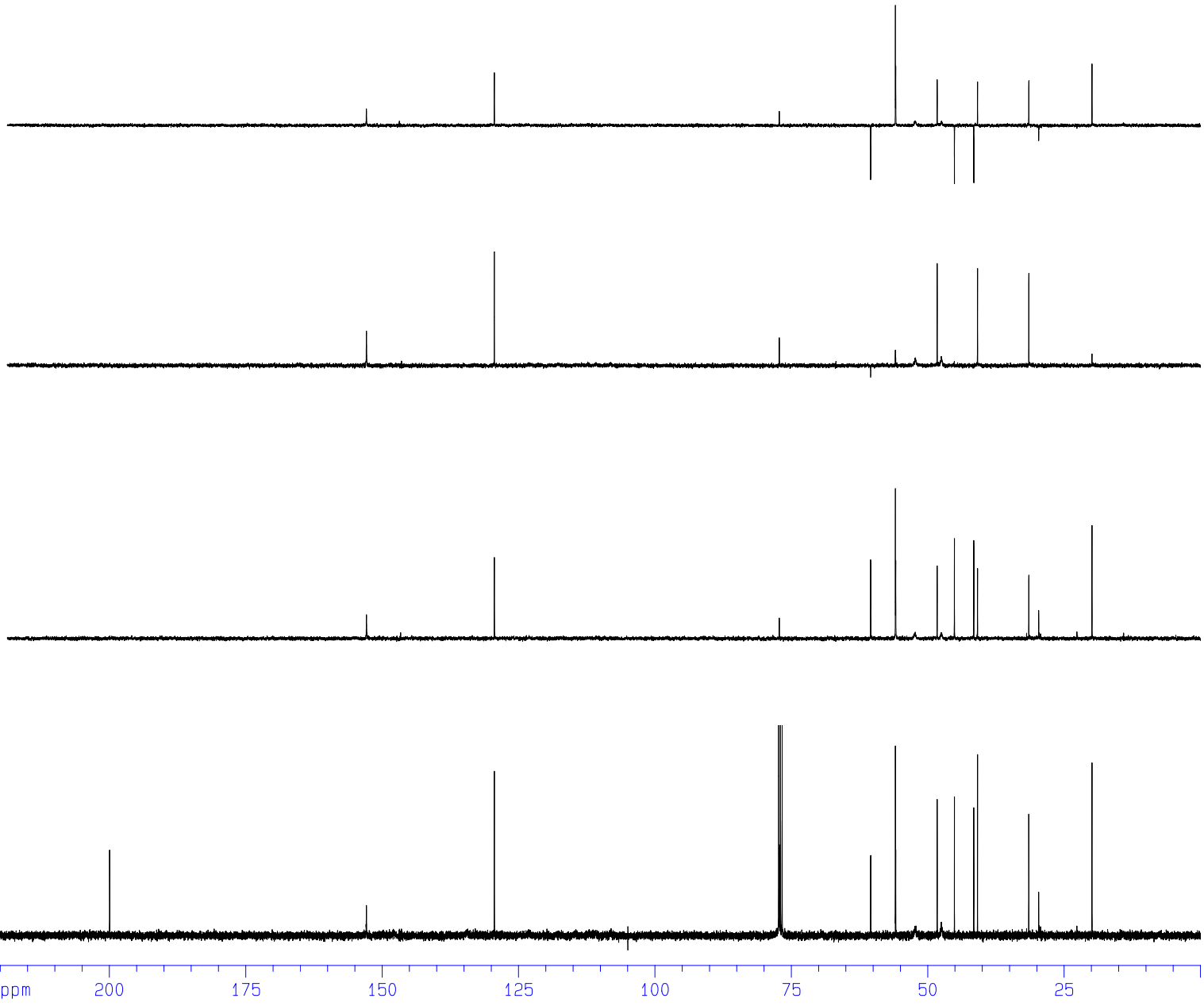

```
Current Data Parameters
NAME          HCS-3-80-P
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20110405
Time               15.44
INSTRUM            spect
PROBHD     5 mm QNP  1H
PULPROG             zg30
TD                 16384
SOLVENT            CDCl3
NS                    16
DS                     0
SWH             5995.204 Hz
FIDRES          0.365918 Hz
AQ             1.3664756 sec
RG                 645.1
DW                83.400 usec
DE                 6.50 usec
TE                300.0 K
D1             1.50000000 sec

============ CHANNEL f1 =============
NUC1                   1H
P1                 10.90 usec
PL1                -3.00 dB
SFO1         400.1326008 MHz

F2 - Processing parameters
SI                  8192
SF          400.1300171 MHz
WDW                   EM
SSB                    0
LB                  0.10 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 21.50 cm
CY                 25.00 cm
F1P               12.000 ppm
F1                4801.56 Hz
F2P               -0.000 ppm
F2                 -0.00 Hz
PPMCM           0.55814 ppm/cm
HZCM          223.32838 Hz/cm
```

Fig. S22. 13C NMR (CDCl3, 100 MHz) of compound 6.




```
Current Data Parameters
NAME          HCS-3-80-P
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20110405
Time               16.24
INSTRUM            spect
PROBHD     5 mm QNP  1H
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           25125.629 Hz
FIDRES         0.383387 Hz
AQ             1.3042164 sec
RG                   256
DW                19.900 usec
DE                 6.50 usec
TE                300.0 K
D1             2.00000000 sec
d11            0.03000000 sec
d12            0.00002000 sec

============ CHANNEL f1 =============
NUC1                 13C
P1                 10.00 usec
PL1                 0.00 dB
SFO1         100.6237959 MHz

============ CHANNEL f2 =============
CPDPRG2          waltz16
NUC2                 1H
PCPD2              90.00 usec
PL2                -3.00 dB
PL12               15.70 dB
PL13               18.70 dB
SFO2         400.1326008 MHz

F2 - Processing parameters
SI                 32768
SF           100.6127738 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.40

1D NMR plot parameters
CX                 20.00 cm
CY                 10.00 cm
F1P              220.000 ppm
F1             22134.81 Hz
F2P                0.000 ppm
F2                 0.00 Hz
PPMCM          11.00000 ppm/cm
HZCM         1106.74048 Hz/cm
```

Fig S23. DEPT of compound 6.




```
Current Data Parameters
NAME          HCS-3-80-P
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20110405
Time               16.24
INSTRUM            spect
PROBHD     5 mm QNP  1H
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           25125.629 Hz
FIDRES         0.383387 Hz
AQ             1.3042164 sec
RG                   256
DW                19.900 usec
DE                 6.50 usec
TE                300.0 K
D1            2.00000000 sec
d11           0.03000000 sec
d12           0.00002000 sec

============ CHANNEL f1 =============
NUC1                13C
P1                10.00 usec
PL1                0.00 dB
SFO1         100.6237959 MHz

============ CHANNEL f2 =============
CPDPRG2          waltz16
NUC2                1H
PCPD2             90.00 usec
PL2               -3.00 dB
PL12              15.70 dB
PL13              18.70 dB
SFO2         400.1326008 MHz

F2 - Processing parameters
SI                 32768
SF           100.6127738 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.40

1D NMR plot parameters
CX                 20.00 cm
CY                 10.00 cm
F1P              220.000 ppm
F1             22134.81 Hz
F2P                0.000 ppm
F2                 0.00 Hz
PPMCM          11.00000 ppm/cm
HZCM         1106.74048 Hz/cm
```

Fig S24. 1H NMR (CDCl3, 500 MHz) of compound 7.

HCS-3-82-c

exp51 s2pul

SAMPLE		DEC. & VT	
date	Jul 17 2011	dfrq	125.693
solvent	cdcl3	dn	C13
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.830	dm	nnn
tn	H1	dmm	c
at	3.000	dmf	200
np	48000	dseq	
sw	8000.0	dres	1.0
fb	not used	homo	n
bs	4	PROCESSING	
tpwr	58	wtfile	
pw	4.8	proc	ft
d1	1.000	fn	not used
tof	499.7	math	f
nt	4		
ct	4	werr	react
alock	y	wexp	procplot
gain	not used	wbs	
FLAGS		wnt	wft
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.1		
wp	5747.8		
vs	85		
sc	0		
wc	210		
hzmm	27.37		
is	284.06		
rfl	4637.9		
rfp	3618.7		
th	2		
ins	100.000		
nm cdc ph			

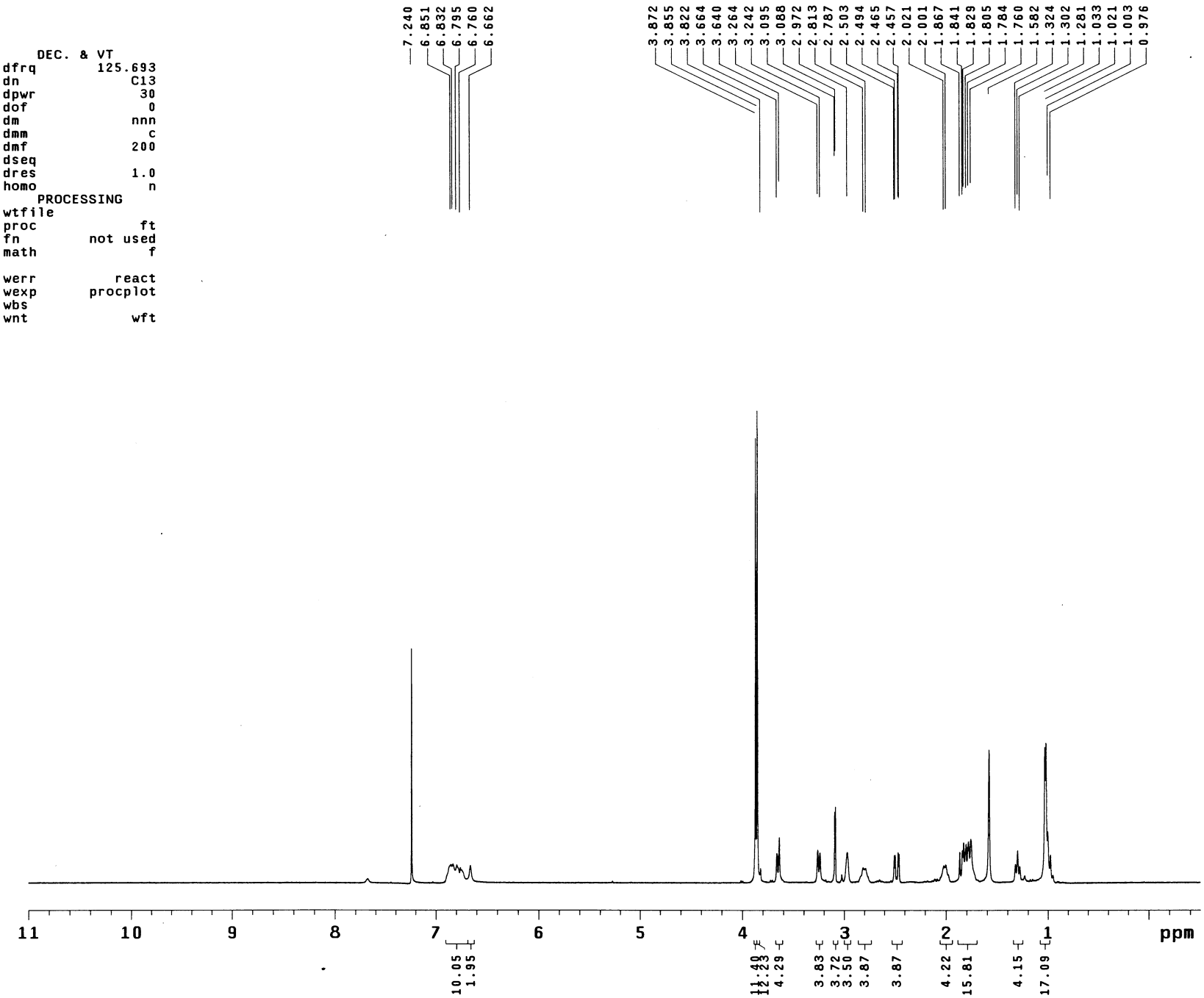


Fig S25. 13C NMR (CDCl3, 126 MHz) of compound 7.

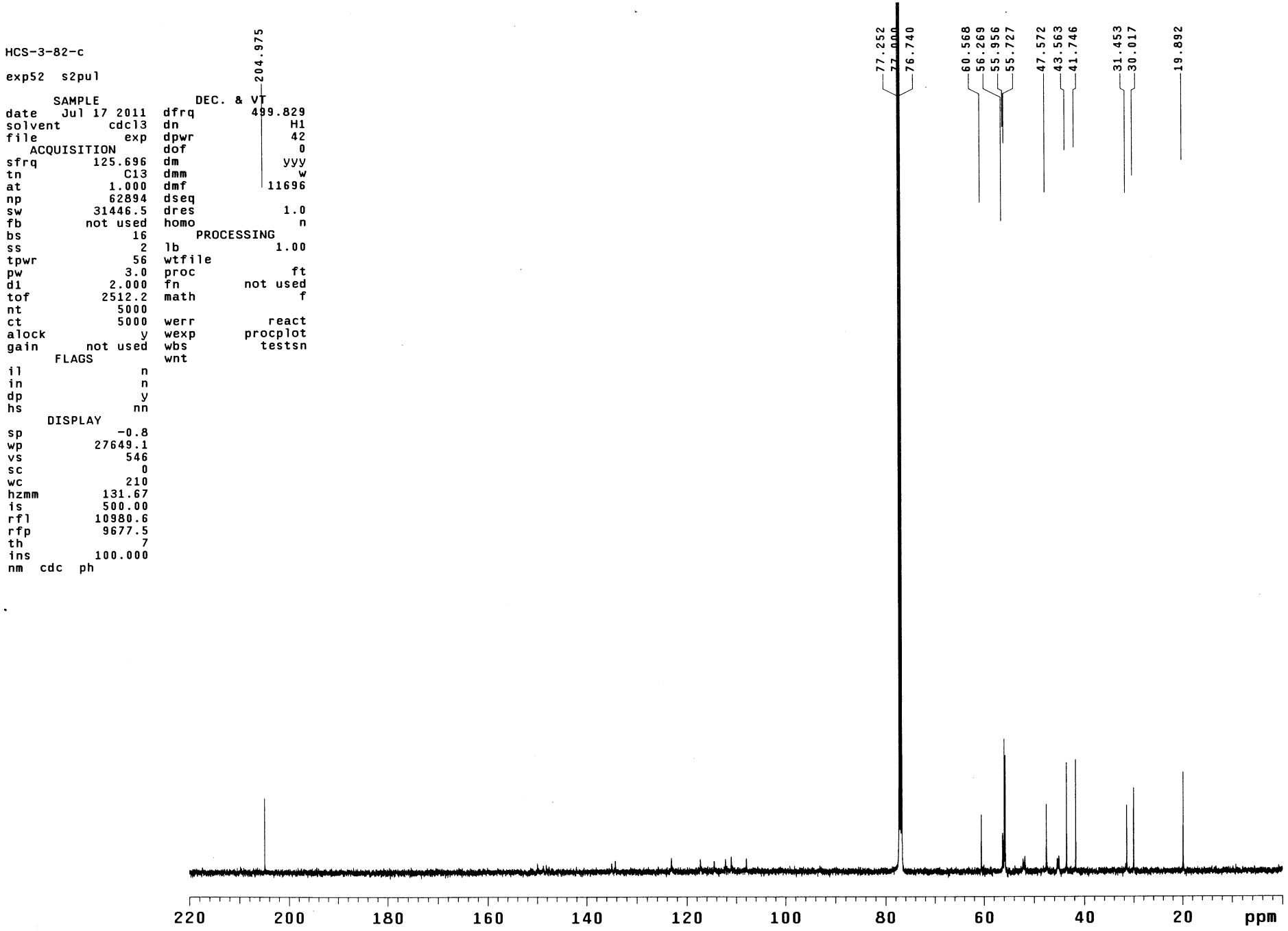


Fig S26. 13C NMR (CDCl3, 126 MHz) of compound 7.

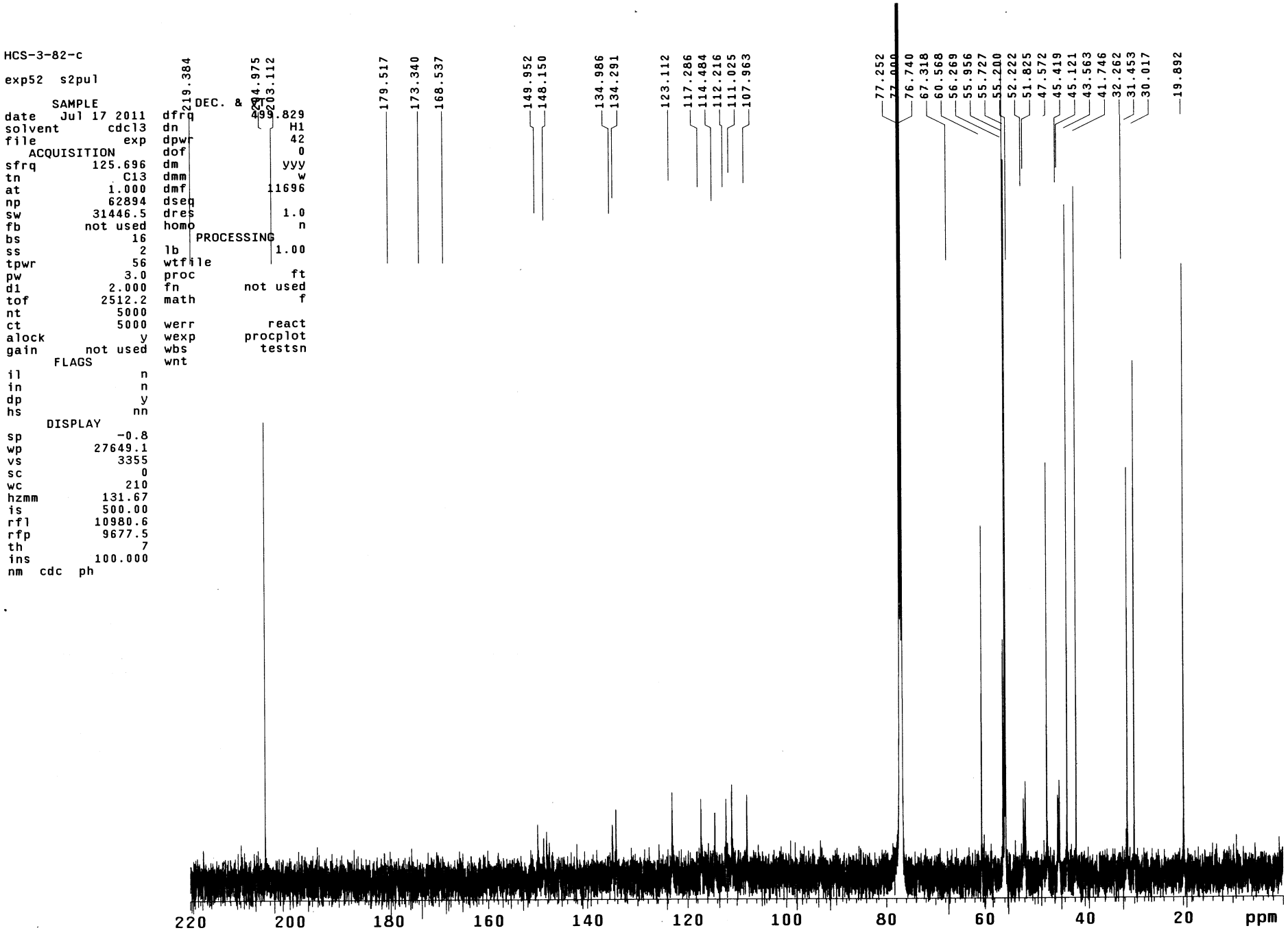


Fig S27. 13C NMR (CDCl3, 126 MHz) of compound 7, expanded.


```
HCS-3-82-c

exp52  s2pul

      SAMPLE
date   Jul 17 2011
solvent      cdcl3
file           exp
   ACQUISITION
sfrq        125.696
tn              C13
at             1.000
np             62894
sw          31446.5
fb         not used
bs               16
ss                2
tpwr             56
pw              3.0
d1            2.000
tof          2512.2
nt             5000
ct             5000
alock             y
gain       not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp          12568.0
wp           7540.1
vs             3466
sc                0
wc              210
hzmm          35.91
is           500.00
rfl         10980.6
rfp          9677.5
th                8
ins         100.000
nm  cdc  ph

      DEC. & VT
dfrq         499.829
dn                H1
dpwr              42
dof                0
dm               yyy
dmm                w
dmf            11696
dseq
dres             1.0
homo               n
     PROCESSING
lb              1.00
wtfile
proc              ft
fn         not used
math               f

werr           react
wexp       procplot
wbs          testsn
wnt
```

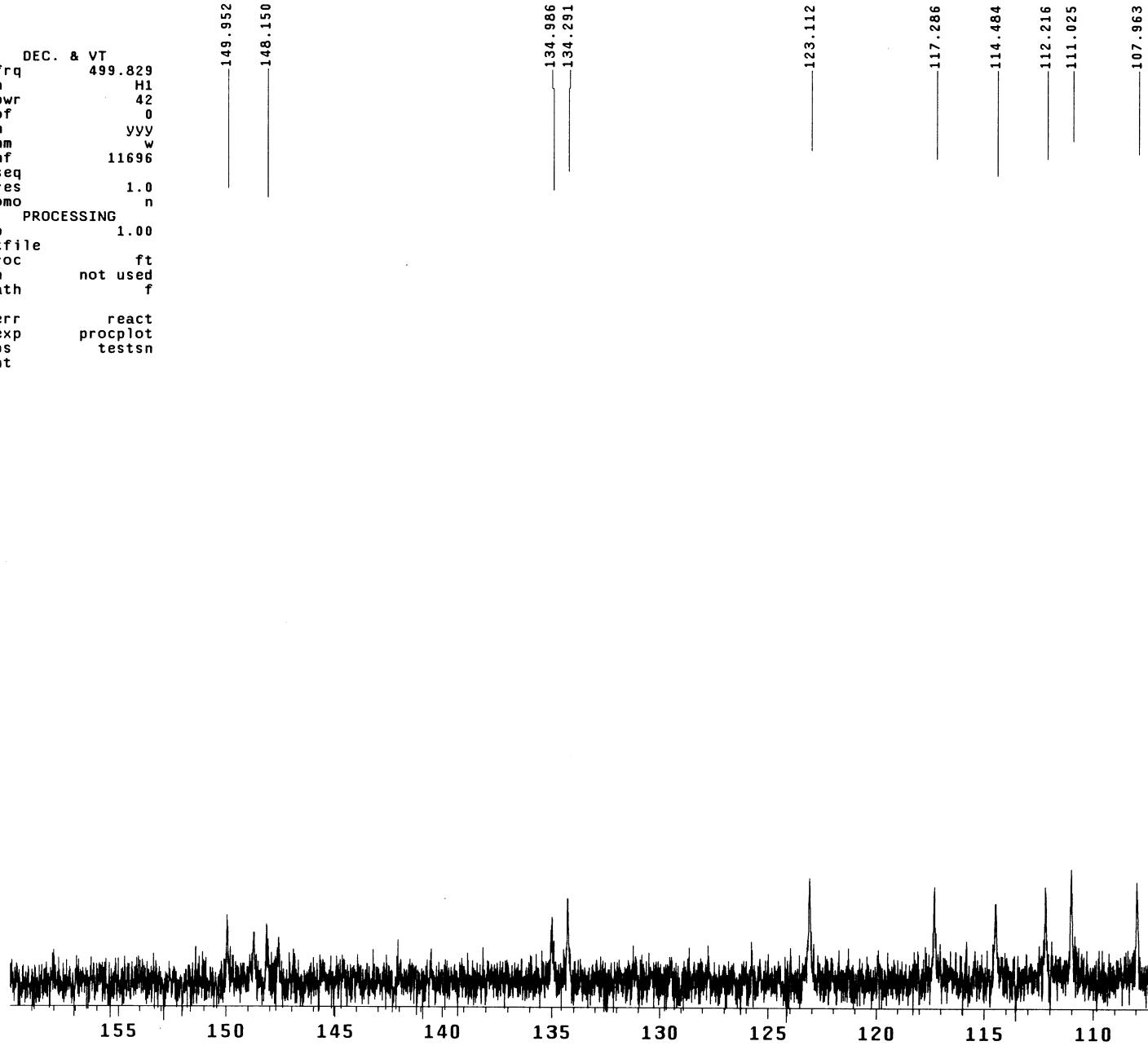


Fig S28. DEPT of compound 7.

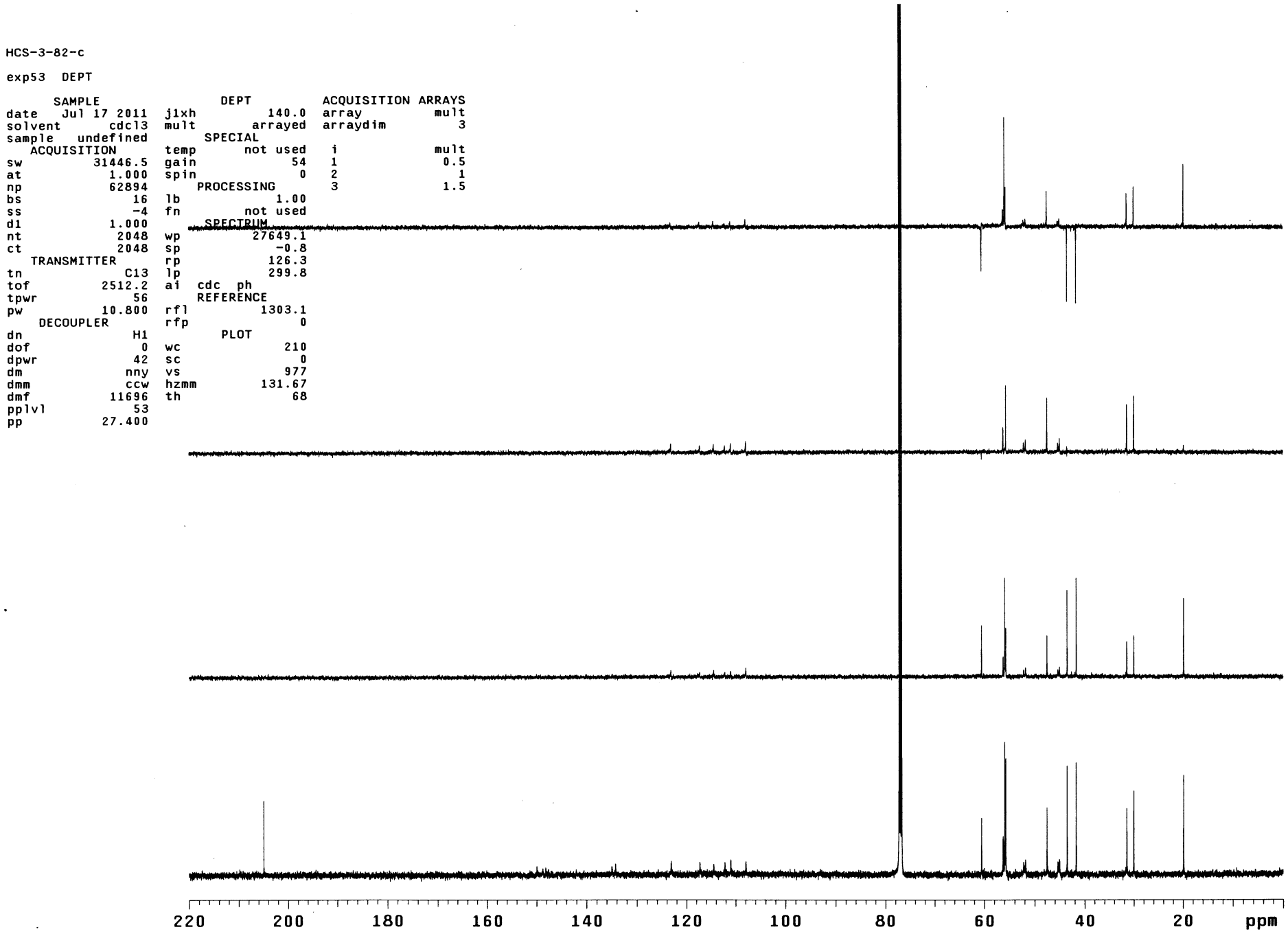


Fig S29. DEPT of compound 7, expanded.

HCS-3-82-c

exp53 DEPT

SAMPLE		DEPT		ACQUISITION ARRAYS	
date	Jul 17 2011	j1xh	140.0	array	mult
solvent	cdcl3	mult	arrayed	arraydim	3
sample	undefined	SPECIAL			
ACQUISITION		temp	not used	i	mult
sw	31446.5	gain	54	1	0.5
at	1.000	spin	0	2	1
np	62894	PROCESSING		3	1.5
bs	16	lb	1.00		
ss	-4	fn	not used		
d1	1.000				
nt	2048	wp	15041.1		
ct	2048	sp	12568.0		
TRANSMITTER		rp	126.3		
tn	C13	lp	299.8		
tof	2512.2	ai	cdc ph		
tpwr	56	REFERENCE			
pw	10.800	rfl	1303.1		
DECOUPLER		rfp	0		
dn	H1	PLOT			
dof	0	wc	210		
dpwr	42	sc	0		
dm	nny	vs	7192		
dmm	ccw	hzmm	35.91		
dmf	11696	th	68		
pplvl	53				
pp	27.400				

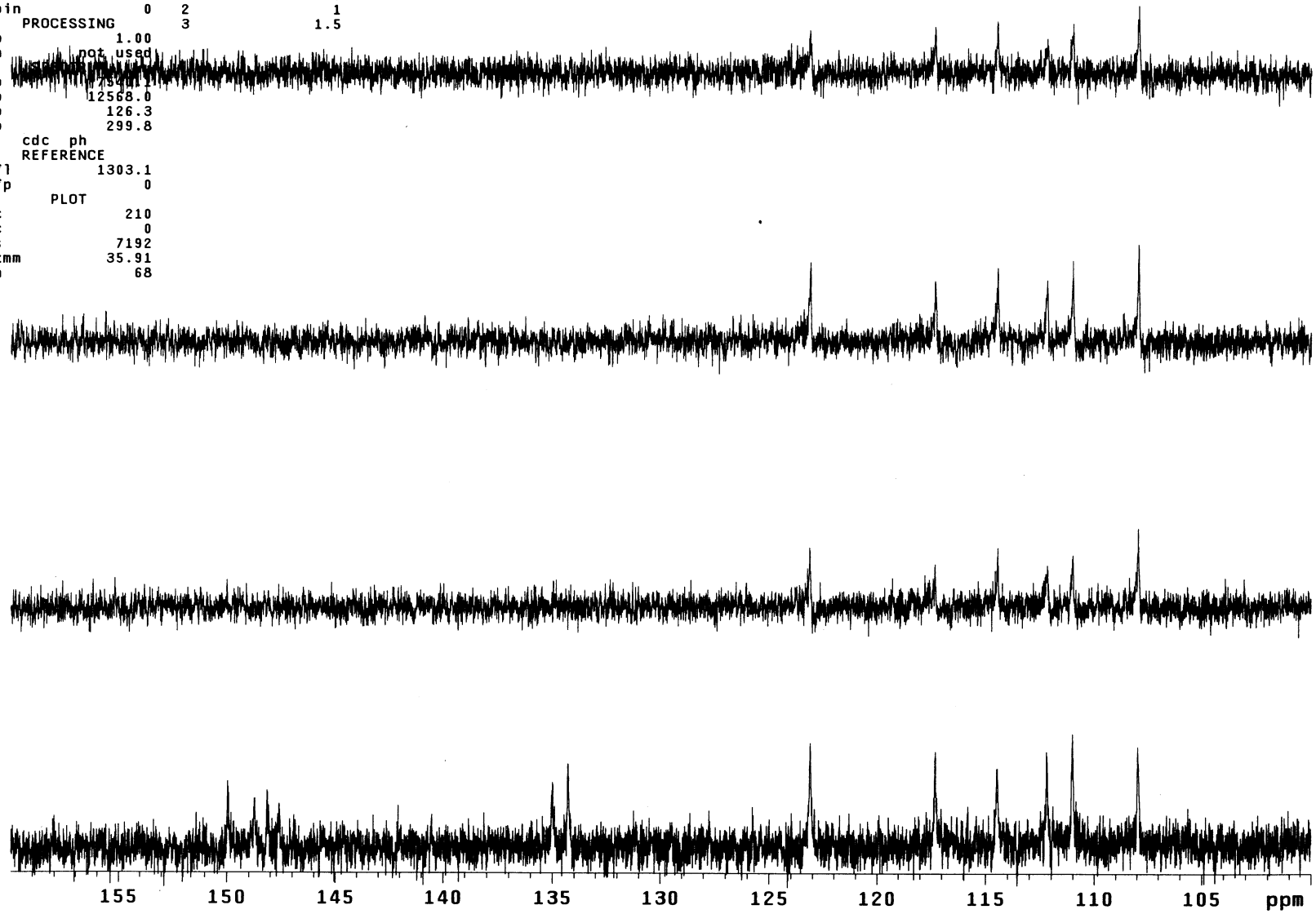


Fig S30. HSQC of compound 7.

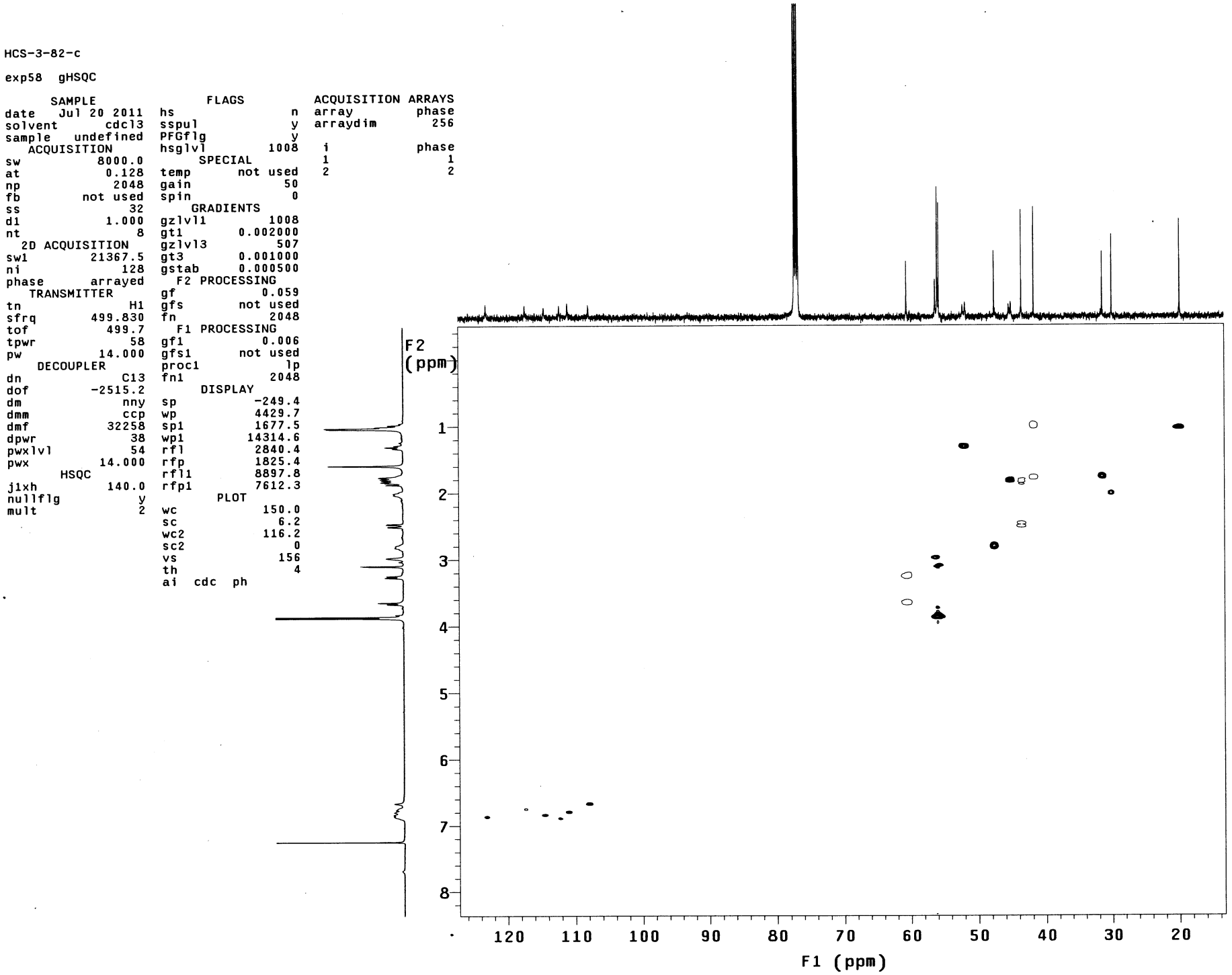


Fig S31. HSQC of compound 7, expanded.

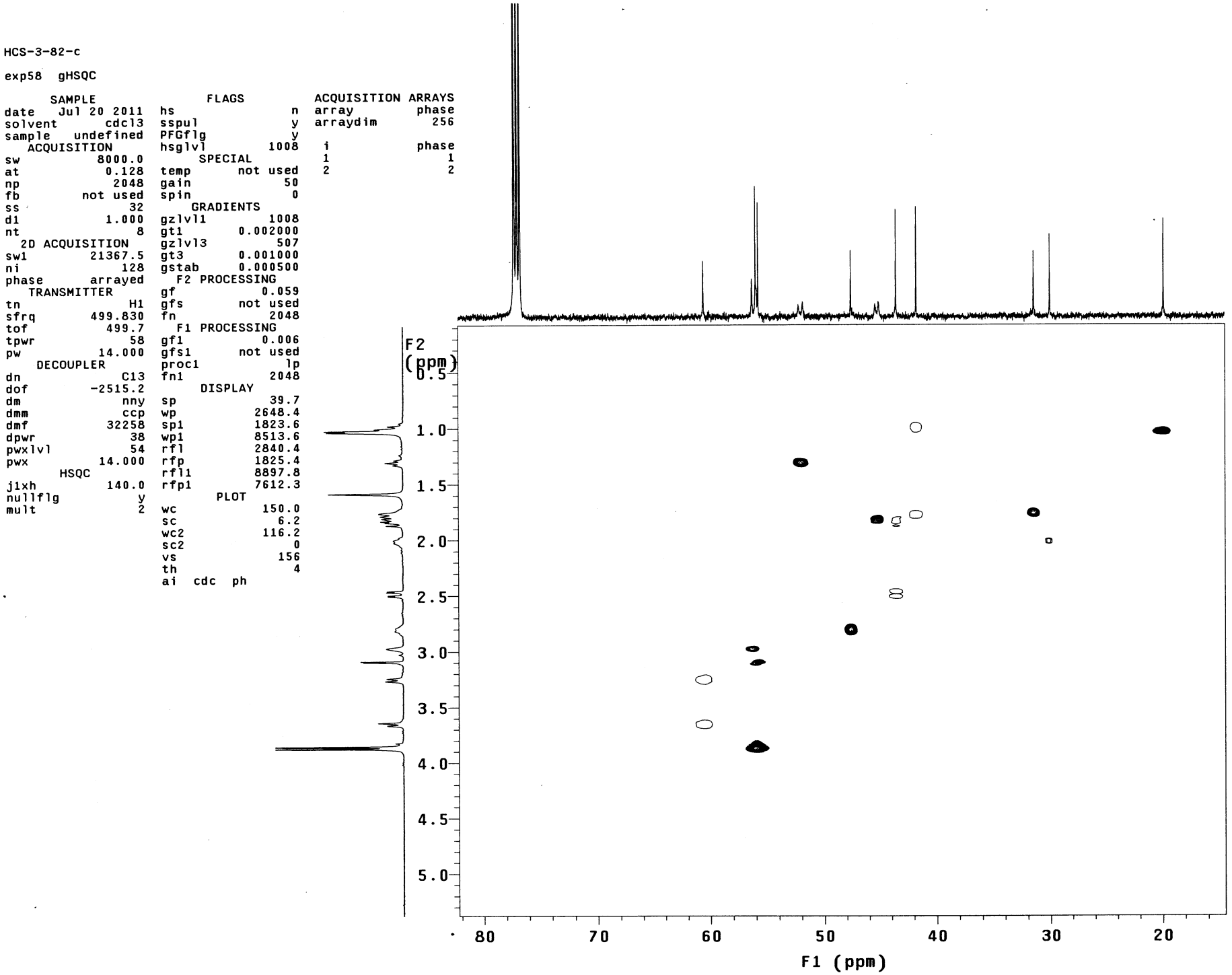


Fig S32. COSY of compound 7.

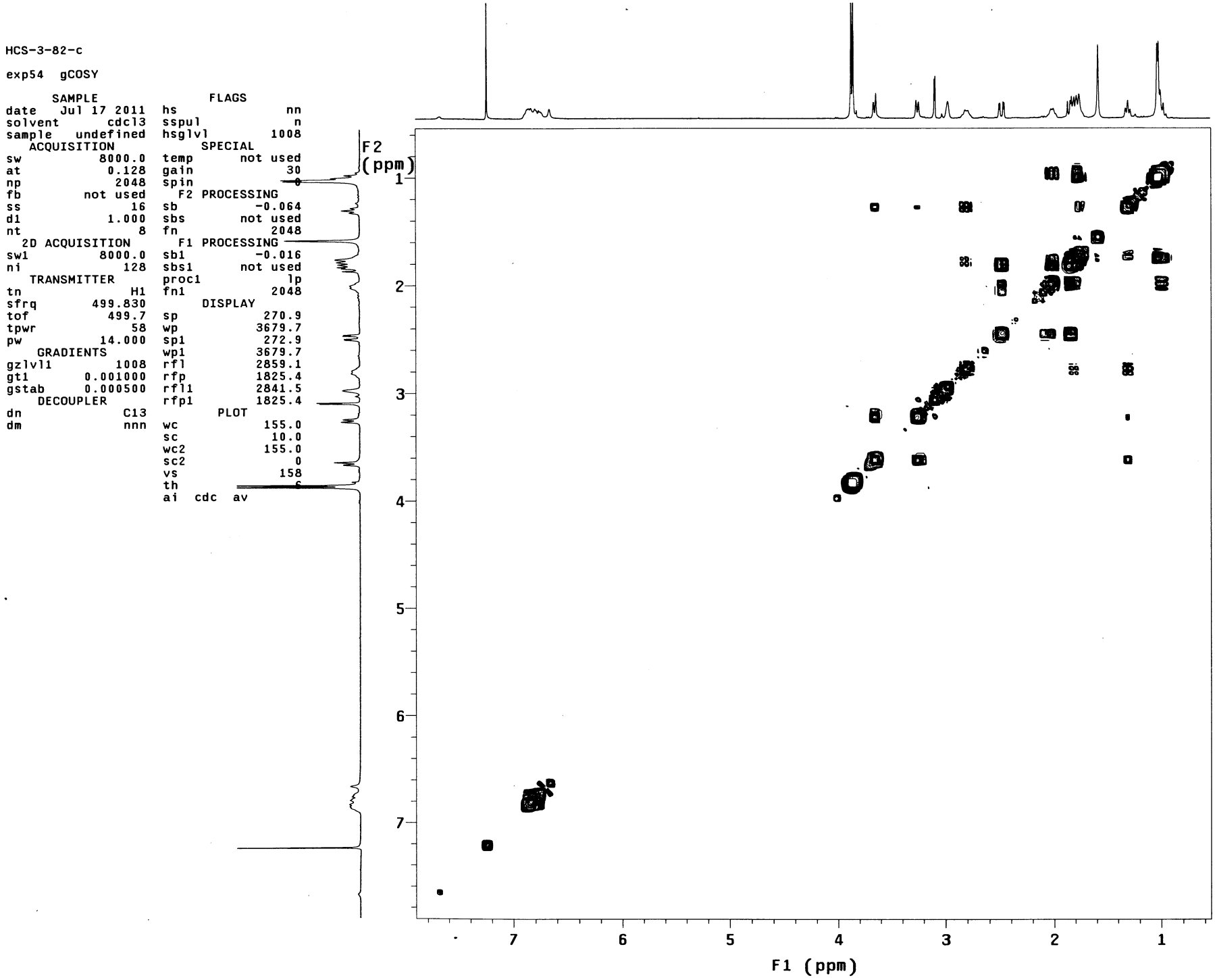


Fig S33. NOESY of compound 7.

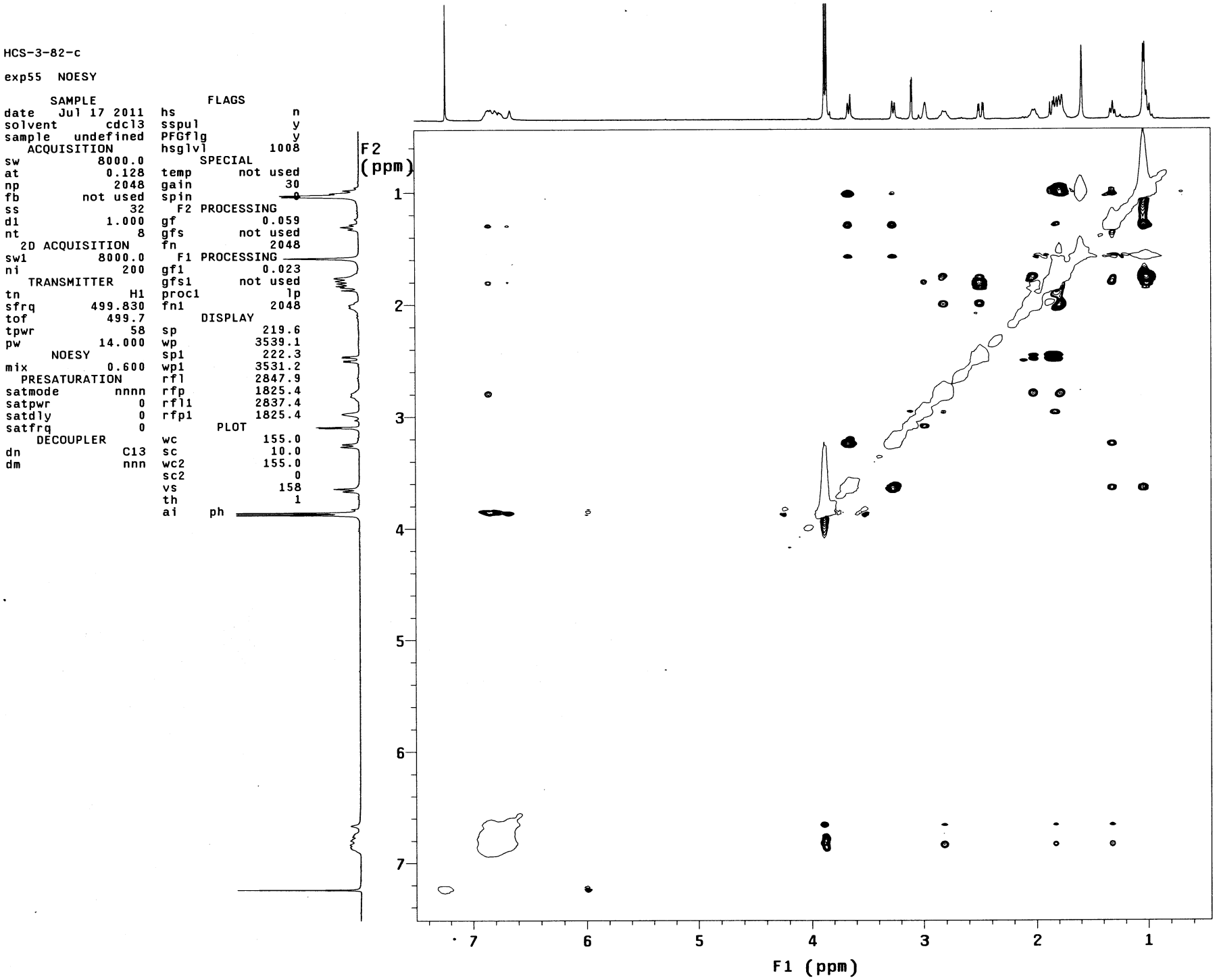


Fig S34. 1H NMR (CDCl3, 500 MHz) of compound 8.

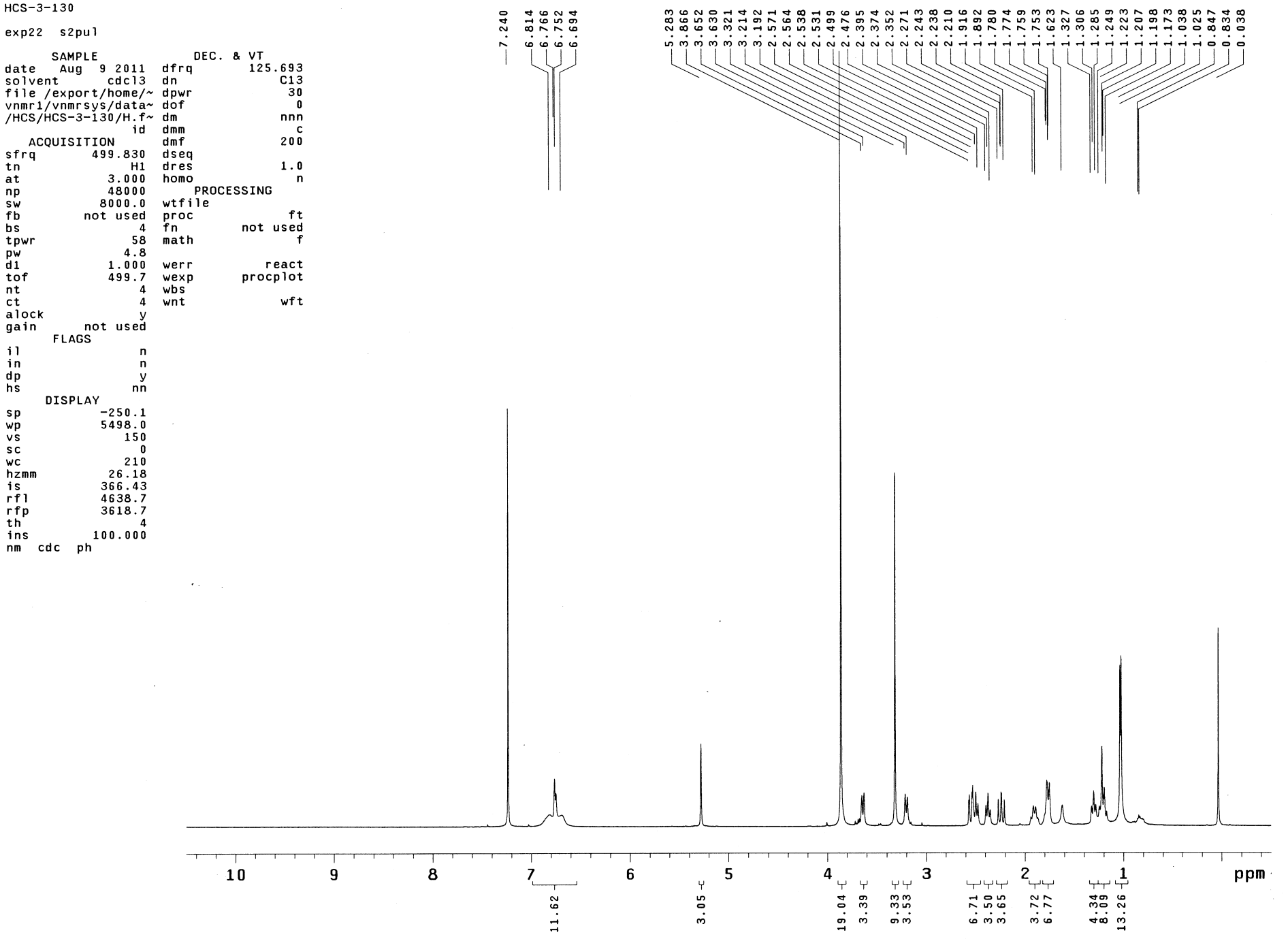


Fig. S35. 13C NMR (CDCl3, 126 MHz) of compound 8.

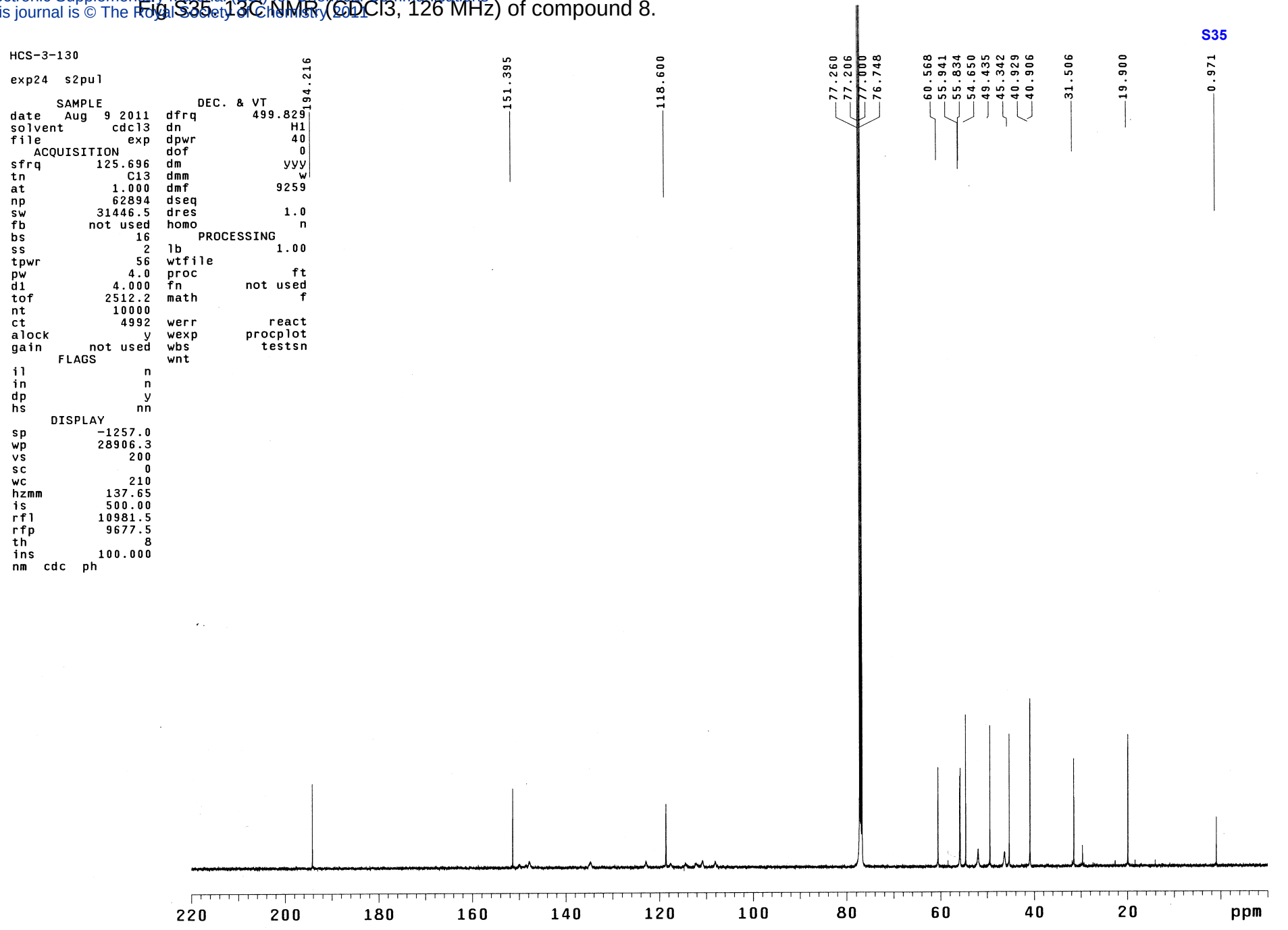


Fig S36. ^{13}C NMR (CDCl3, 126 MHz) of compound 8, expanded.

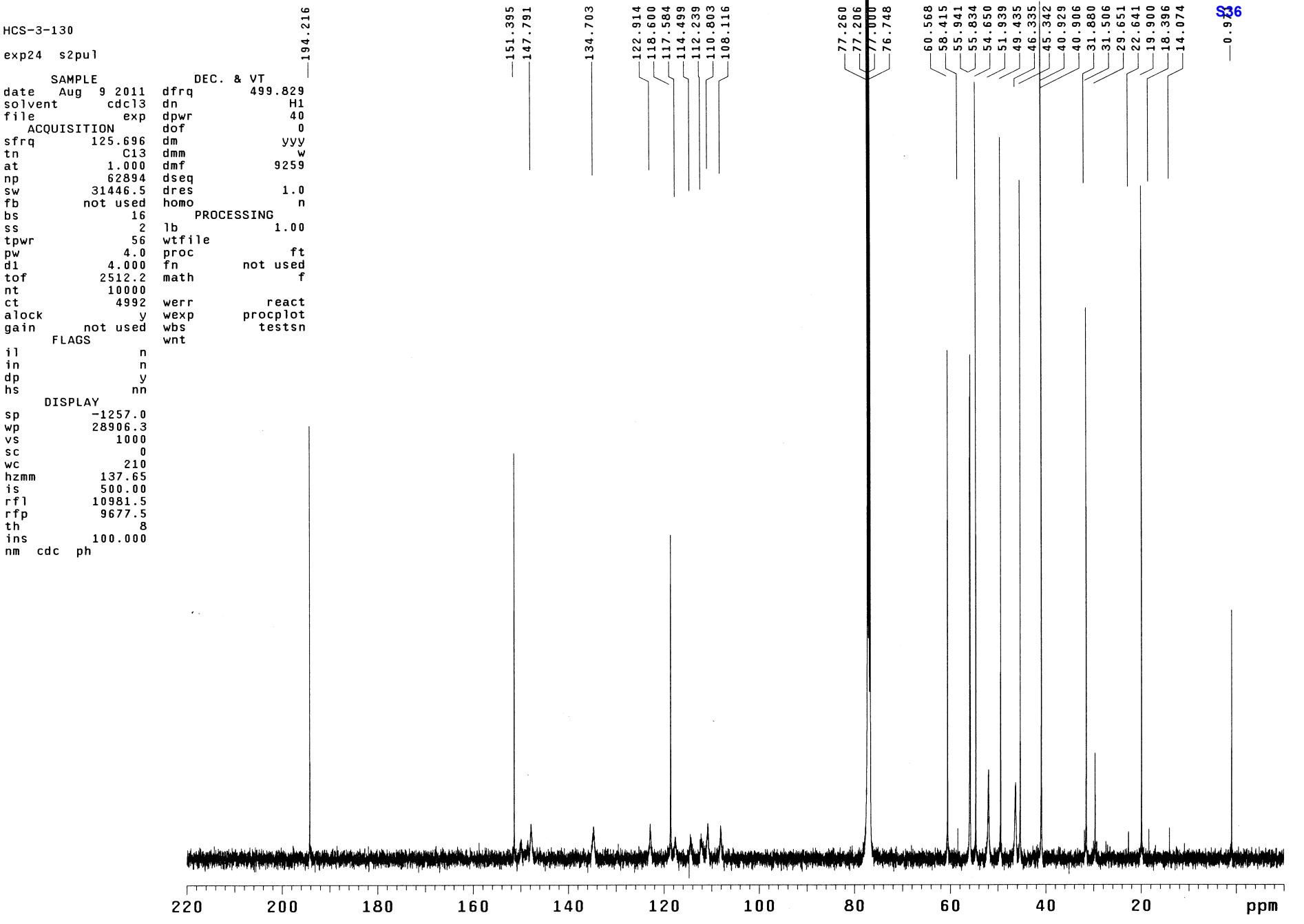


Fig S37. HSQC of compound 8.

HCS-3-130

exp26 gHSQC

SAMPLE		FLAGS		ACQUISITION ARRAYS	
date	Aug 9 2011	hs	n	array	phase
solvent	cdcl3	sspul	y	arraydim	256
sample	undefined	PFGflg	y		
ACQUISITION		hsglvl	1008	i	phase
sw	5006.3	SPECIAL		1	1
at	0.205	temp	not used	2	2
np	2048	gain	48		
fb	not used	spin	0		
ss	32	GRADIENTS			
d1	1.000	gzlvl1	1008		
nt	16	gt1	0.002000		
2D ACQUISITION		gzlvl3	507		
sw1	21367.5	gt3	0.001000		
ni	128	gstab	0.000500		
phase	arrayed	F2 PROCESSING			
TRANSMITTER		gf	0.094		
tn	H1	gfs	not used		
sfrq	499.829	fn	2048		
tof	-499.9	F1 PROCESSING			
tpwr	58	gf1	0.006		
pw	14.000	gfs1	not used		
DECOUPLER		proc1	lp		
dn	C13	fn1	2048		
dof	-2515.2	DISPLAY			
dm	nny	sp	195.6		
dmm	ccp	wp	3608.0		
dmf	32258	sp1	1550.4		
dpwr	38	wp1	17945.4		
pwxlvl	54	rf1	3163.7		
pwx	14.000	rfp	2640.6		
HSQC		rfl1	16193.4		
j1xh	140.0	rfp1	14905.8		
nullflg	y	PLOT			
mult	2	wc	150.0		
		sc	6.2		
		wc2	116.2		
		sc2	0		
		vs	100		
		th	2		
		ai cdc ph			

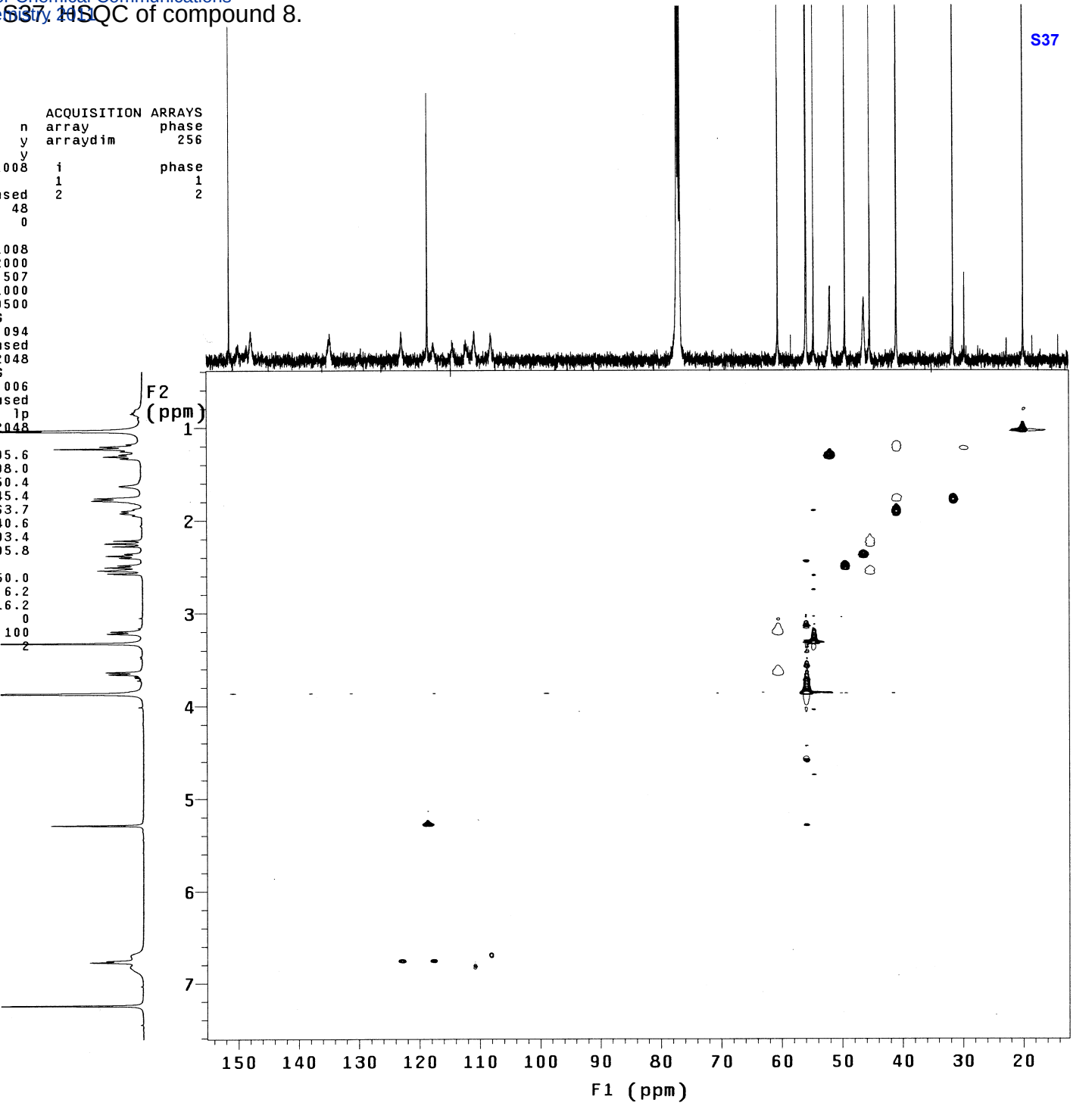


Fig S38. COSY of compound 8.

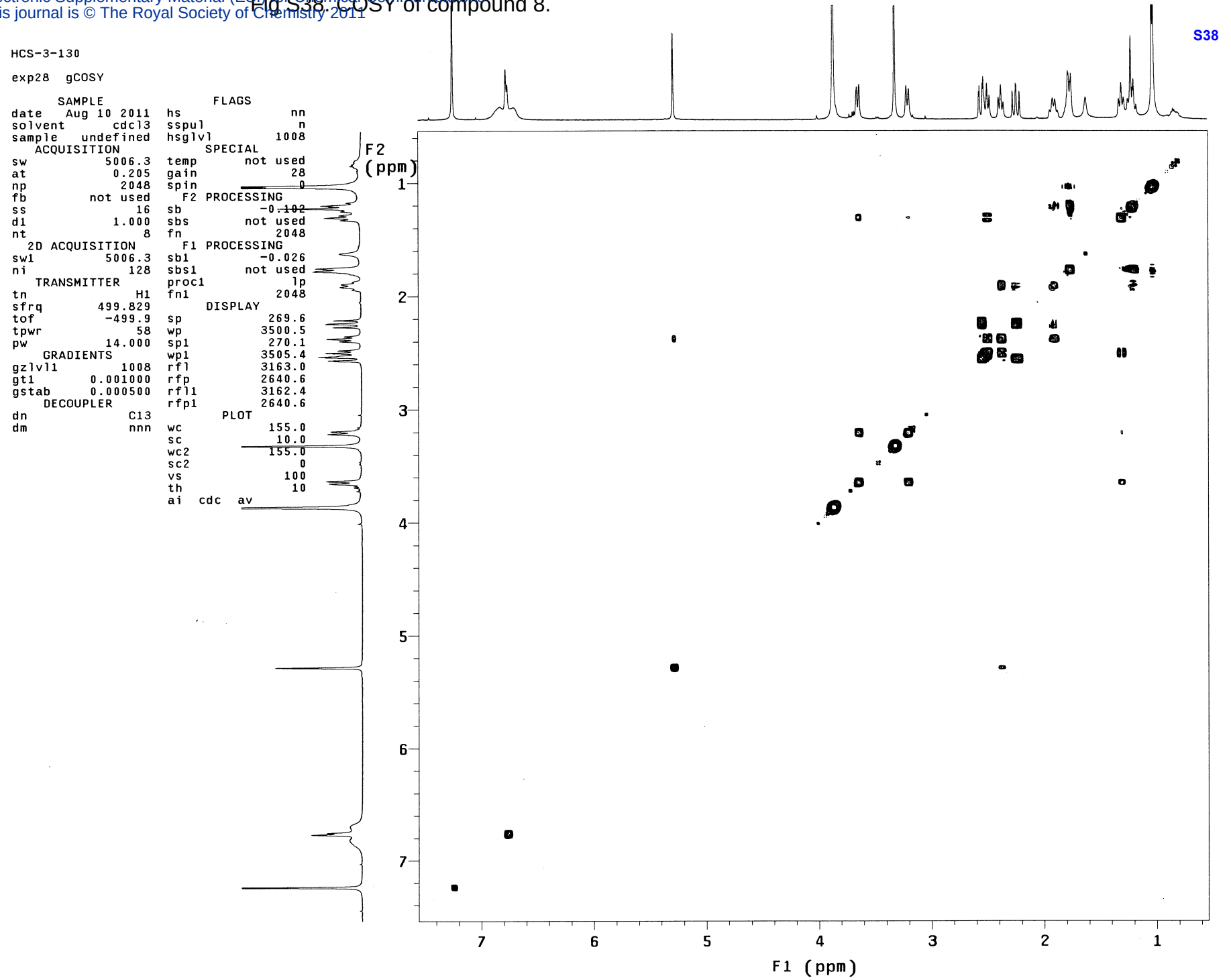


Fig. S39. NOESY of compound 8.

HCS-3-130

exp29 NOESY

SAMPLE		FLAGS	
date	Aug 10 2011	hs	n
solvent	cdcl3	sspul	y
sample	undefined	PFGflg	y
ACQUISITION		hsglvl	1008
sw	5006.3	SPECIAL	
at	0.205	temp	not used
np	2048	gain	28
fb	not used	spin	0
ss	32	F2 PROCESSING	
d1	1.000	gf	0.094
nt	16	gfs	not used
2D ACQUISITION		fn	2048
sw1	5006.3	F1 PROCESSING	
ni	200	gf1	0.037
TRANSMITTER		gfs1	not used
tn	H1	proc1	lp
sfrq	499.829	fn1	2048
tof	-499.9	DISPLAY	
tpwr	58	sp	286.0
pw	14.000	wp	3500.5
NOESY		sp1	287.3
mix	0.600	wp1	3495.6
PRESATURATION		rfl	3166.1
satmode	nnnn	rfp	2640.6
satpwr	0	rfl1	3164.8
satdly	0	rfp1	2640.6
satfrq	0	PLOT	
DECOUPLER		wc	155.0
dn	C13	sc	10.0
dm	nnn	wc2	155.0
		sc2	0
		vs	100
		th	1
		ai ph	

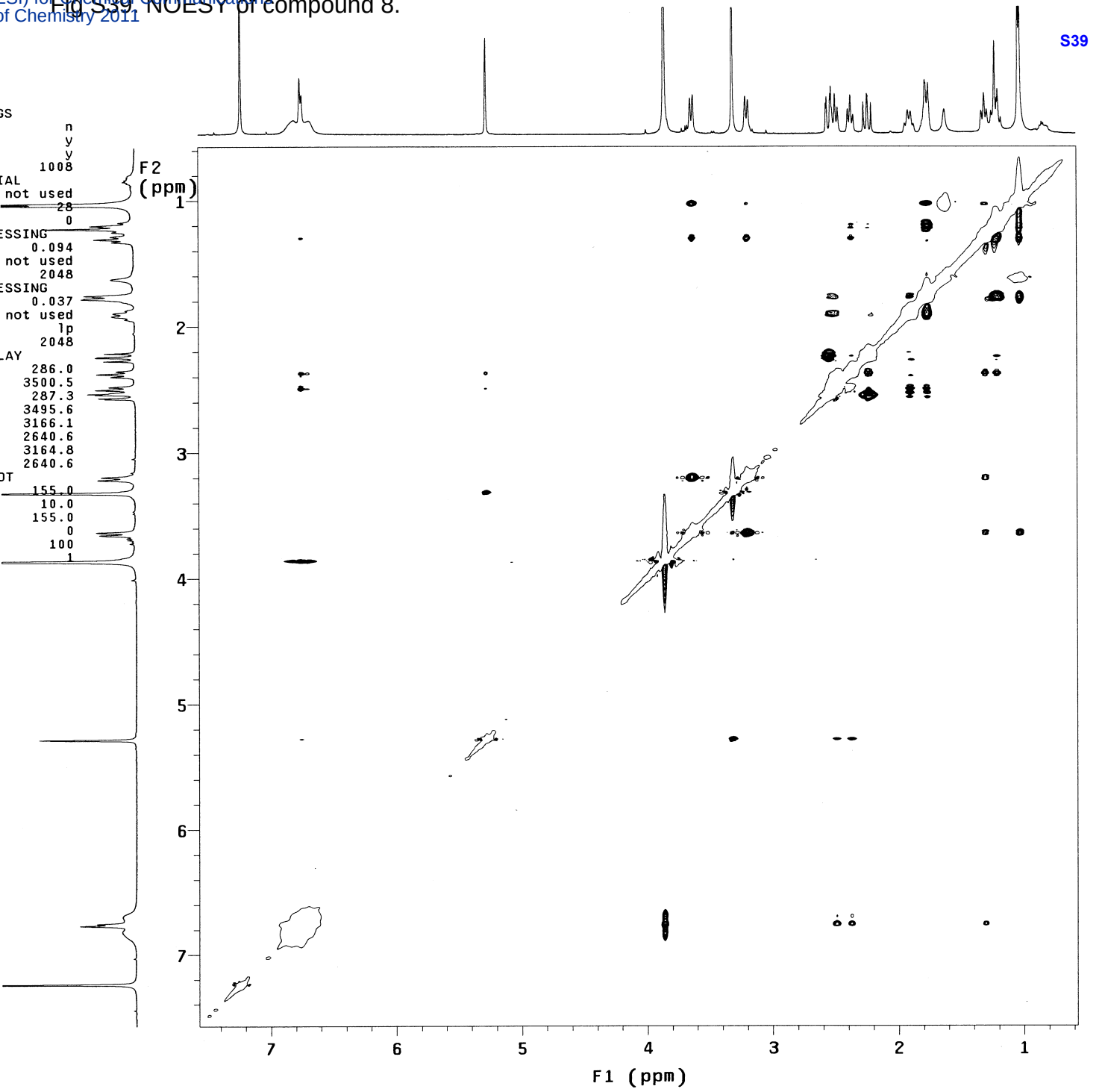


Fig. S40. HMBC of compound 8.

HCS-3-130

exp27 gHMBC

SAMPLE		FLAGS	
date	Aug 9 2011	hs	n
solvent	cdcl3	sspul	n
sample	undefined	PFGflg	y
ACQUISITION		hsglvl	1008
sw	5006.3	SPECIAL	
at	0.205	temp	not used
np	2048	gain	20
fb	not used	spin	0
ss	32	GRADIENTS	
d1	1.000	gzlvl1	1008
nt	16	gt1	0.001000
2D ACQUISITION		gzlvl3	507
sw1	30165.9	gt3	0.001000
ni	400	gstab	0.000500
phase	0	F2 PROCESSING	
TRANSMITTER		sb	0.102
tn	H1	sbs	not used
sfrq	499.829	fn	2048
tof	-499.9	F1 PROCESSING	
tpwr	58	sb1	0.007
pw	14.000	sbs1	not used
DECOUPLER		fn1	2048
dn	C13	DISPLAY	
dof	1255.3	sp	262.0
dm	nnn	wp	3788.9
dmm	ccc	sp1	1083.6
dmf	32258	wp1	25275.7
dpwr	38	rf1	3165.7
pwxlvl	54	rfp	2640.6
pwx	14.000	rf1	26330.5
HMBC		rfp1	24409.4
j1xh	140.0	PLOT	
jnxh	8.0	wc	150.0
		sc	6.2
		wc2	116.2
		sc2	0
		vs	100
		th	13
		ai cdc av	

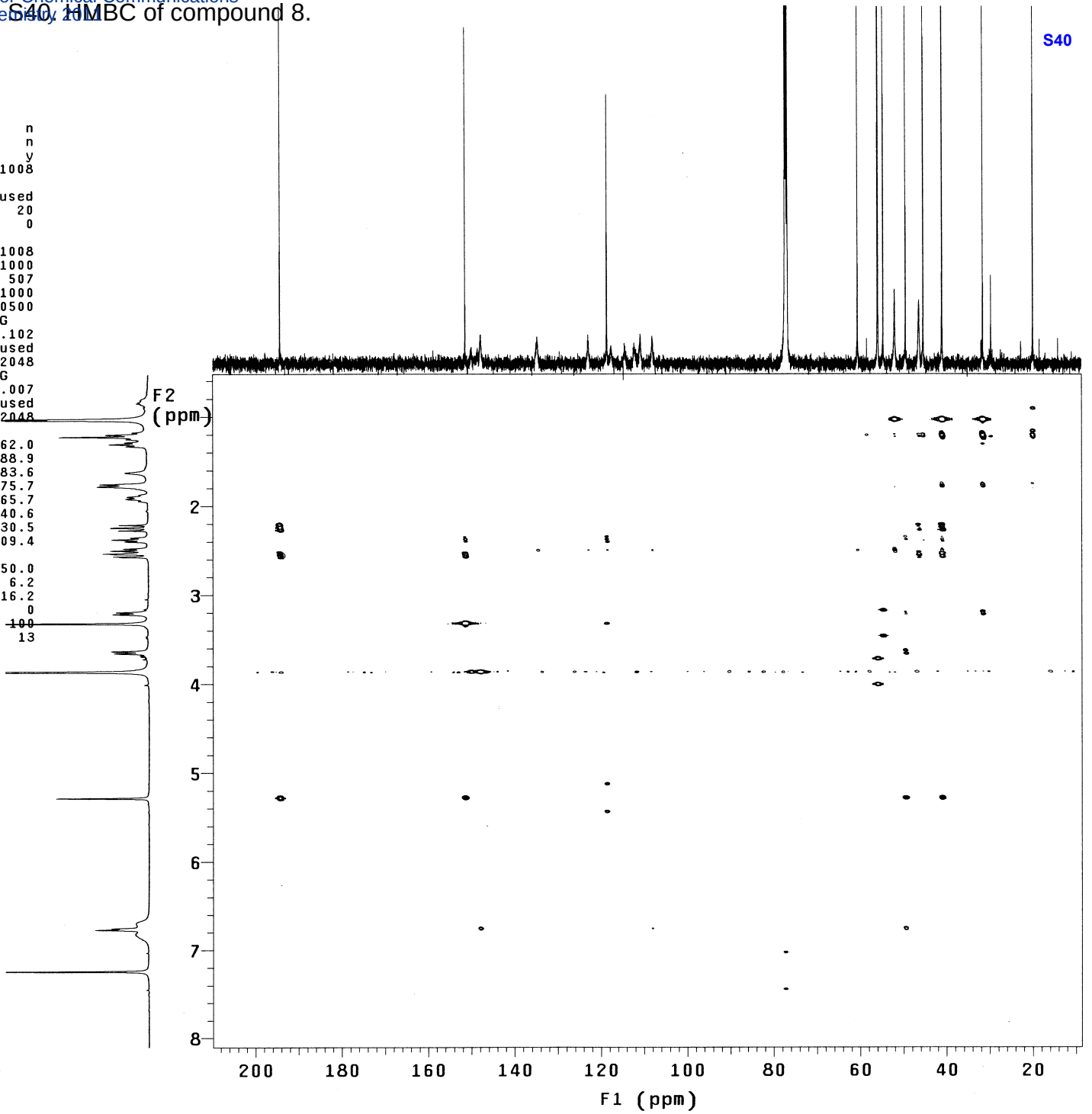


Fig S41. 1H NMR (CDCl3, 500 MHz) of compound 9.

HCS-3-137-F3

exp51 s2pul

SAMPLE		DEC. & VT	
date	Jul 6 2011	dfrq	125.693
solvent	cdcl3	dn	C13
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.830	dm	nnn
tn	H1	dmm	c
at	3.000	dmf	200
np	48000	dseq	
sw	8000.0	dres	1.0
fb	not used	homo	n
bs	4	PROCESSING	
tpwr	58	wtfile	
pw	4.8	proc	ft
d1	1.000	fn	not used
tof	499.7	math	f
nt	4		
ct	4	werr	react
alock	y	wexp	procplot
gain	not used	wbs	
FLAGS		wnt	wft
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.1		
wp	5747.8		
vs	80		
sc	0		
wc	210		
hzmm	27.37		
is	610.94		
rfl	4638.4		
rfp	3618.7		
th	3		
ins	100.000		
nm cdc ph			

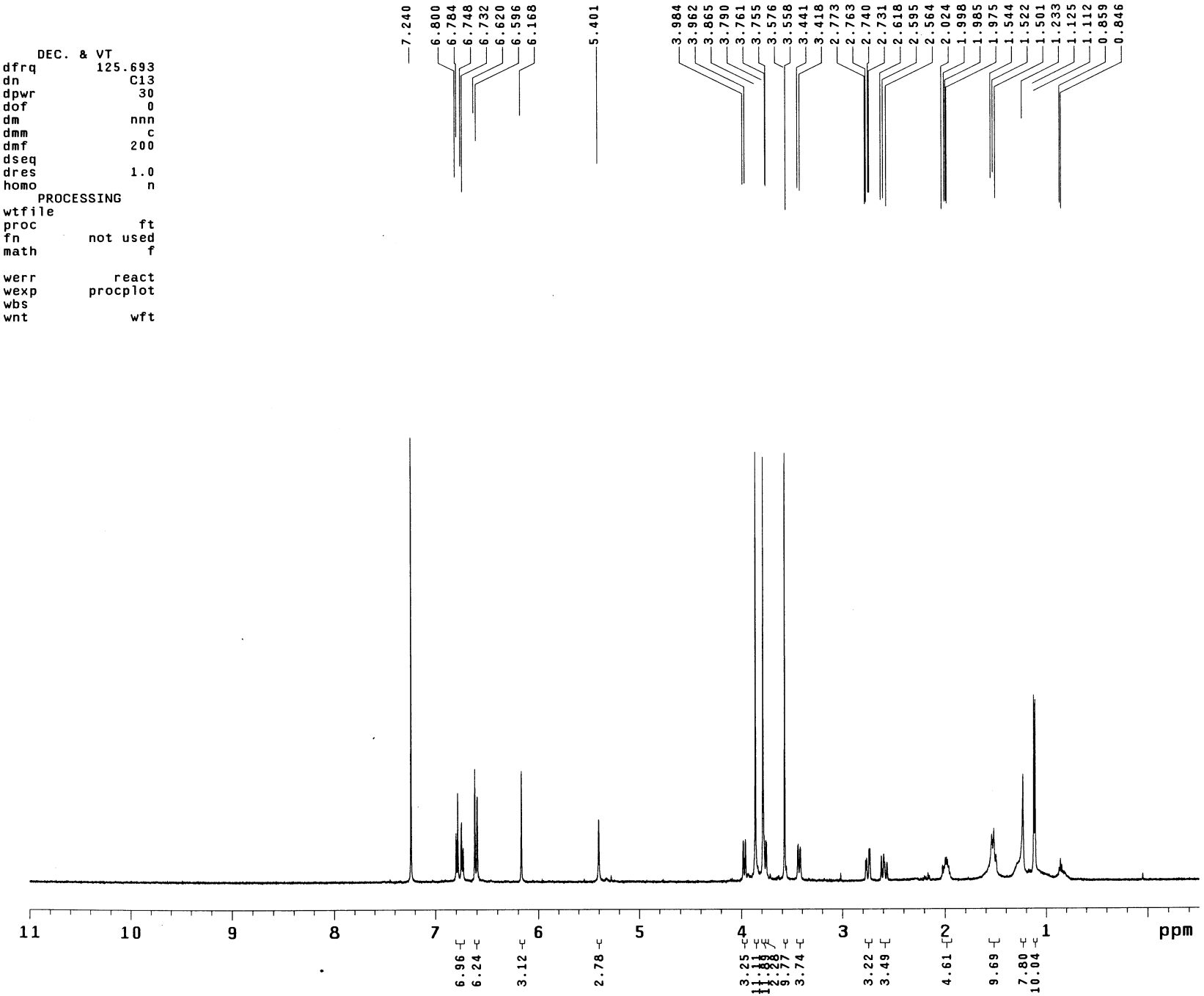


Fig S42. 13C NMR (CDCl3, 126 MHz) of compound 9.

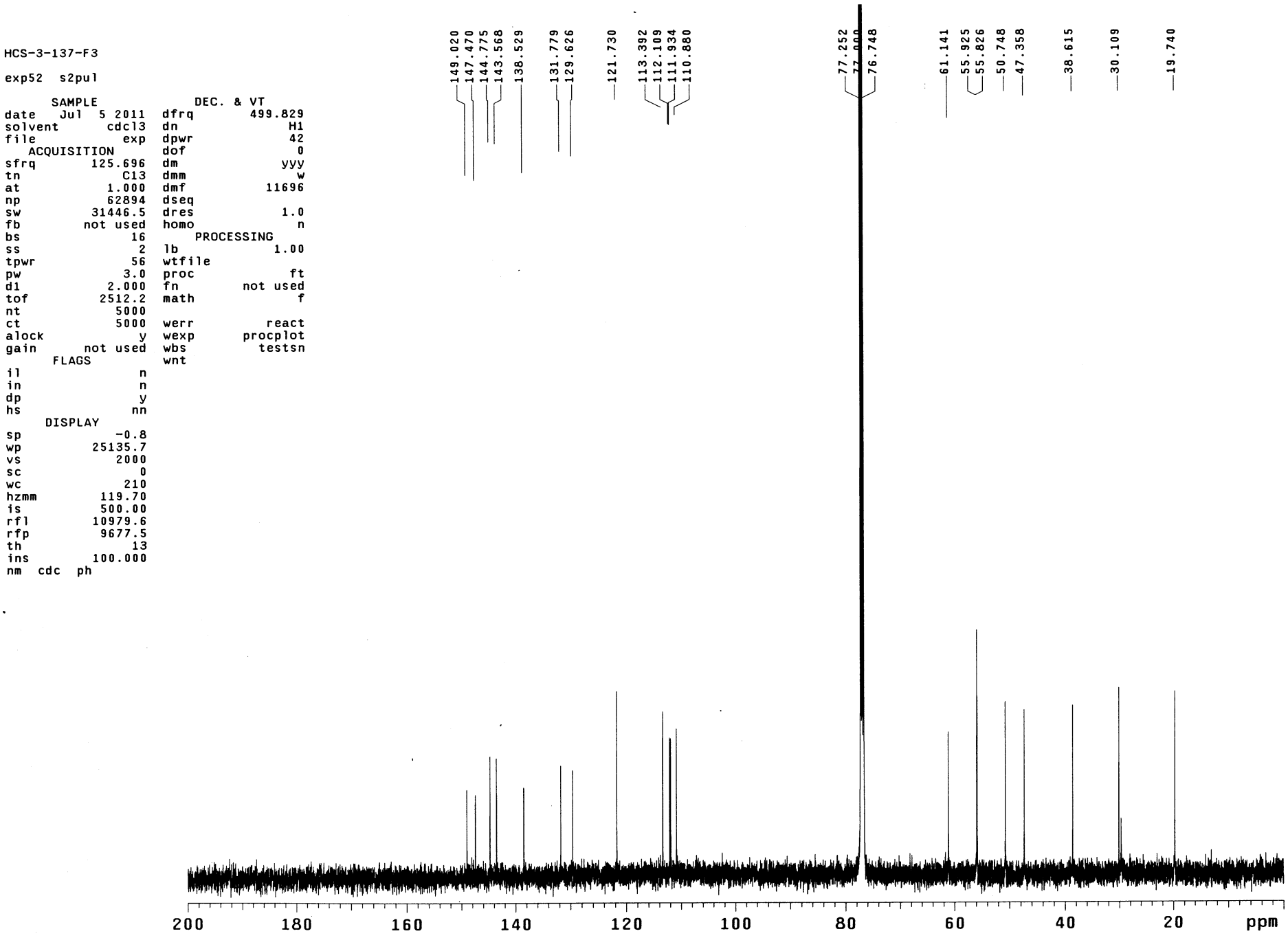


Fig S43. DEPT of compound 9.

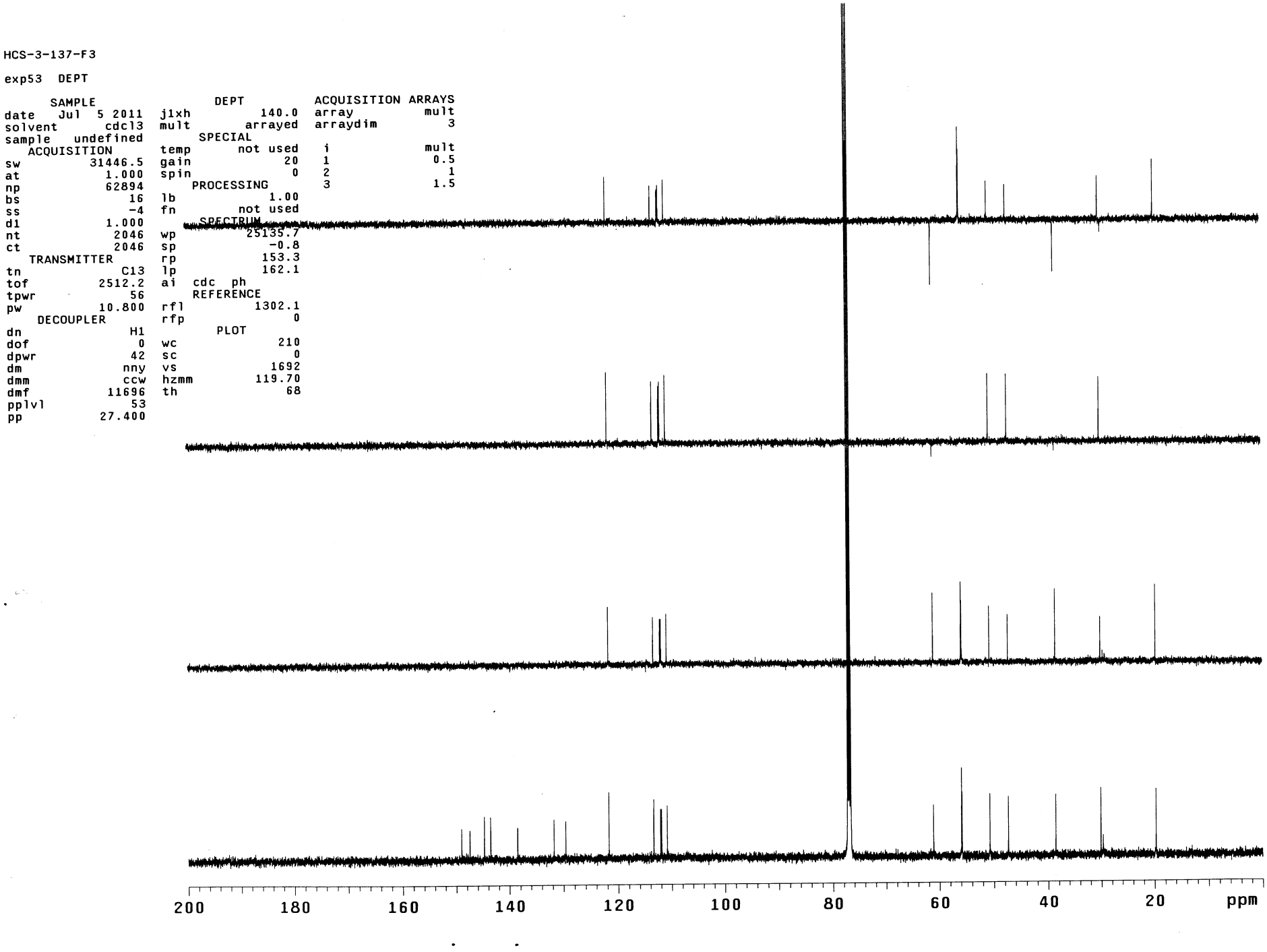


Fig S44. COSY of compound 9.

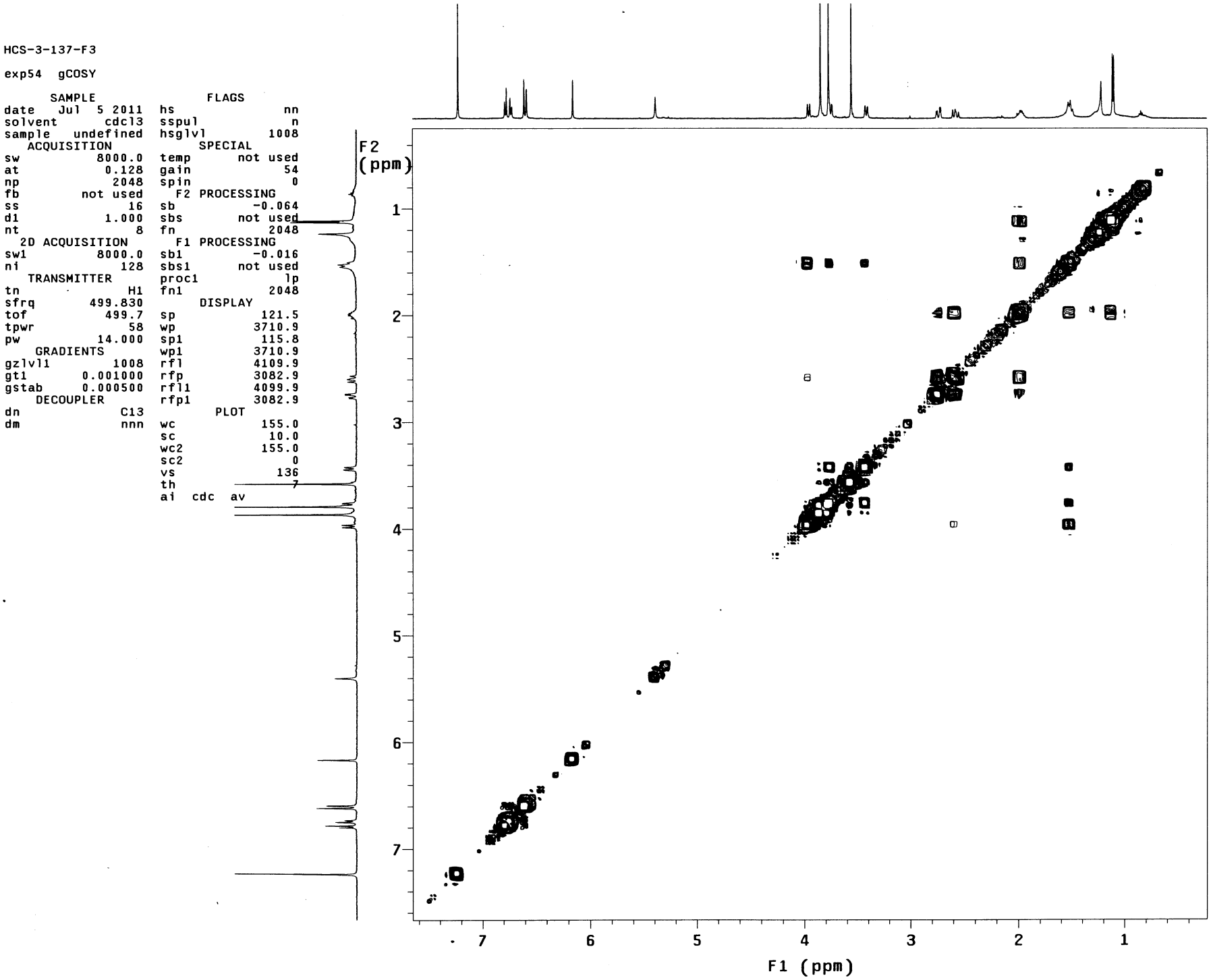


Fig S45. HSQC of compound 9.

HCS-3-137-F3

exp56 gHSQC

SAMPLE		FLAGS		ACQUISITION ARRAYS	
date	Jul 5 2011	hs	n	array	phase
solvent	cdcl3	sspul	y	arraydim	256
sample	undefined	PFGflg	y		
ACQUISITION		hsglvl	1008	i	phase
sw	8000.0	SPECIAL		1	1
at	0.128	temp	not used	2	2
np	2048	gain	34		
fb	not used	spin	0		
ss	32	GRADIENTS			
d1	1.000	gzlvl1	1008		
nt	8	gt1	0.002000		
2D ACQUISITION		gzlvl3	507		
sw1	21367.5	gt3	0.001000		
ni	128	gstab	0.000500		
phase	arrayed	F2 PROCESSING			
TRANSMITTER		gf	0.059		
tn	H1	gfs	not used		
sfrq	499.830	fn	2048		
tof	499.7	F1 PROCESSING			
tpwr	58	gf1	0.006		
pw	14.000	gfs1	not used		
DECOUPLER		proc1	lp		
dn	C13	fn1	2048		
dof	-2515.2	DISPLAY			
dm	nny	sp	285.0		
dmm	ccp	wp	3656.2		
dmf	32258	sp1	1581.7		
dpwr	38	wp1	14502.4		
pwxlvl	54	rfl	4102.7		
pwx	14.000	rfp	3082.9		
HSQC		rfl1	15387.9		
j1xh	140.0	rfp1	14090.0		
nullflg	y	PLOT			
mult	2	wc	150.0		
		sc	6.2		
		wc2	116.2		
		sc2	0		
		vs	136		
		th	6		
		ai cdc ph			

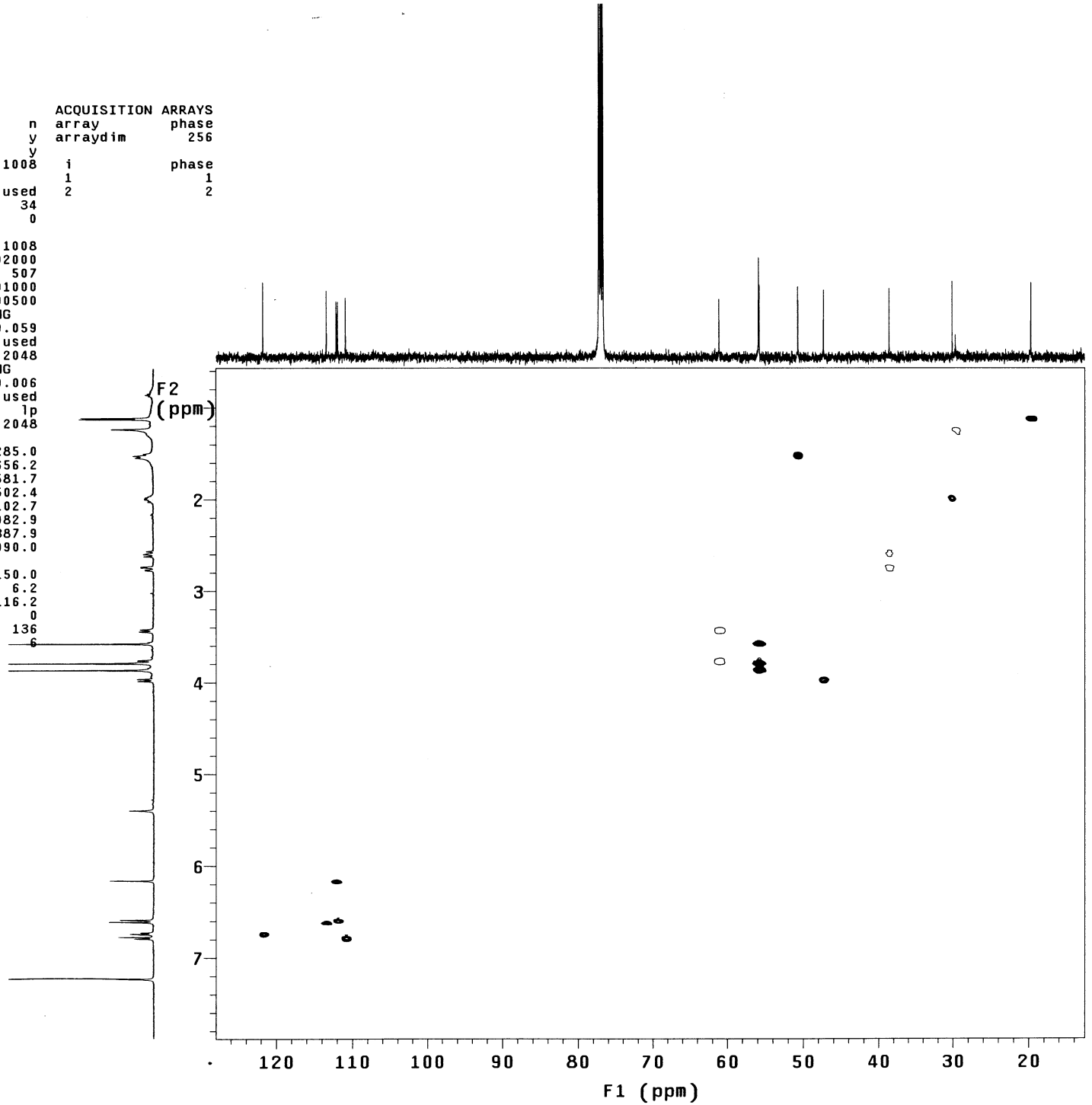


Fig S46. COSY of compound 9.

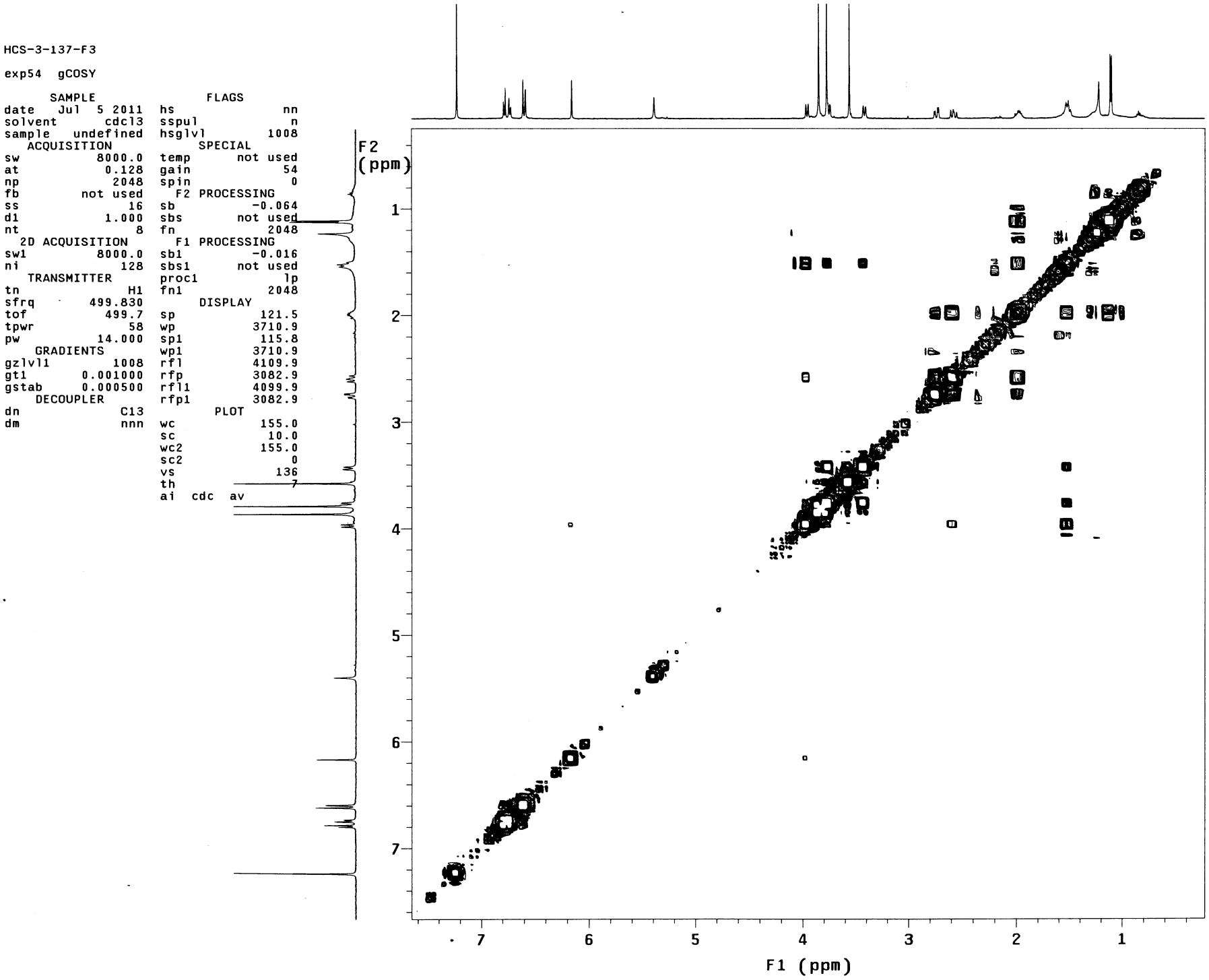


Fig S47. NOESY of compound 9.

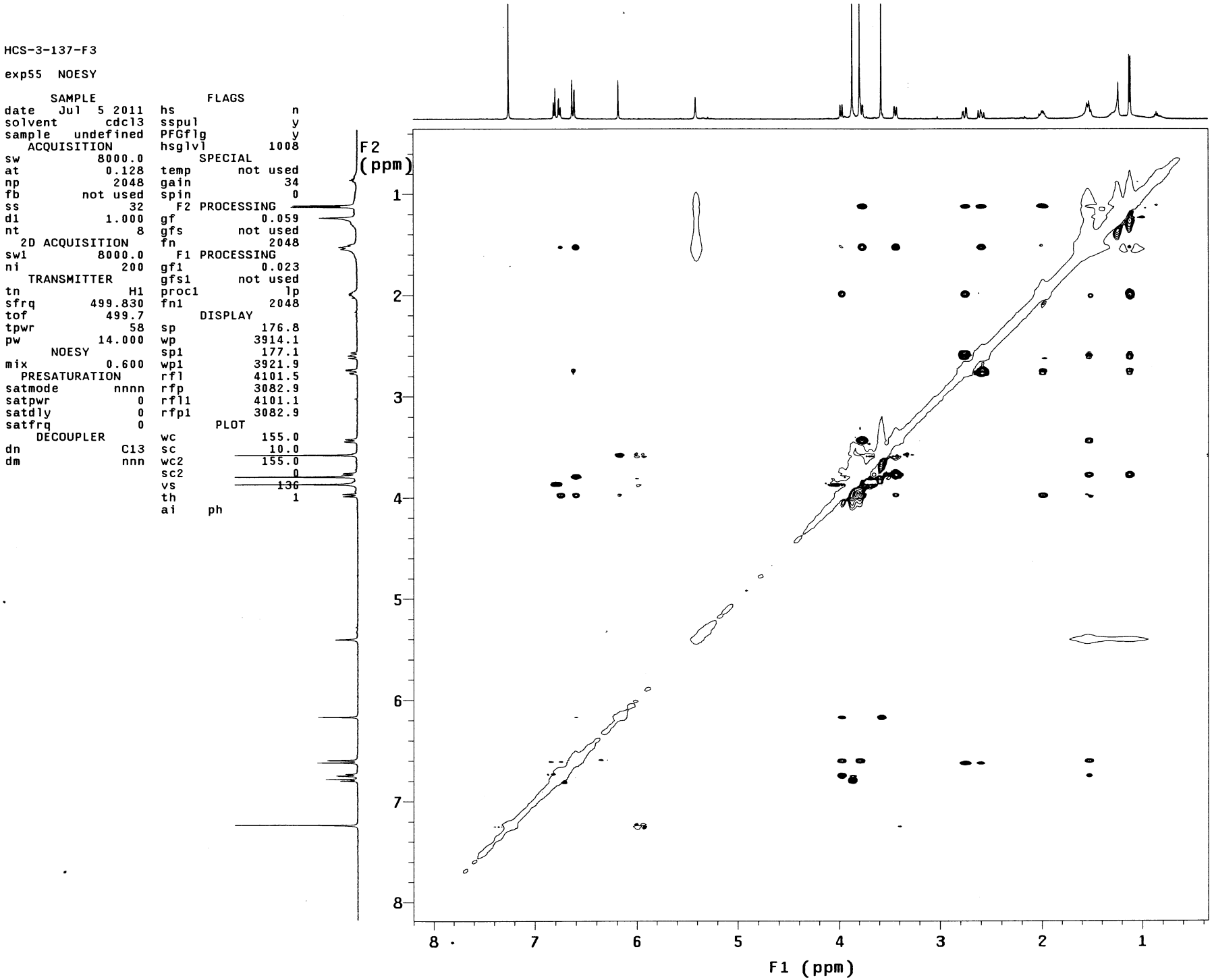


Fig S48. 1H NMR (CDCl3, 500 MHz) of compound 10.

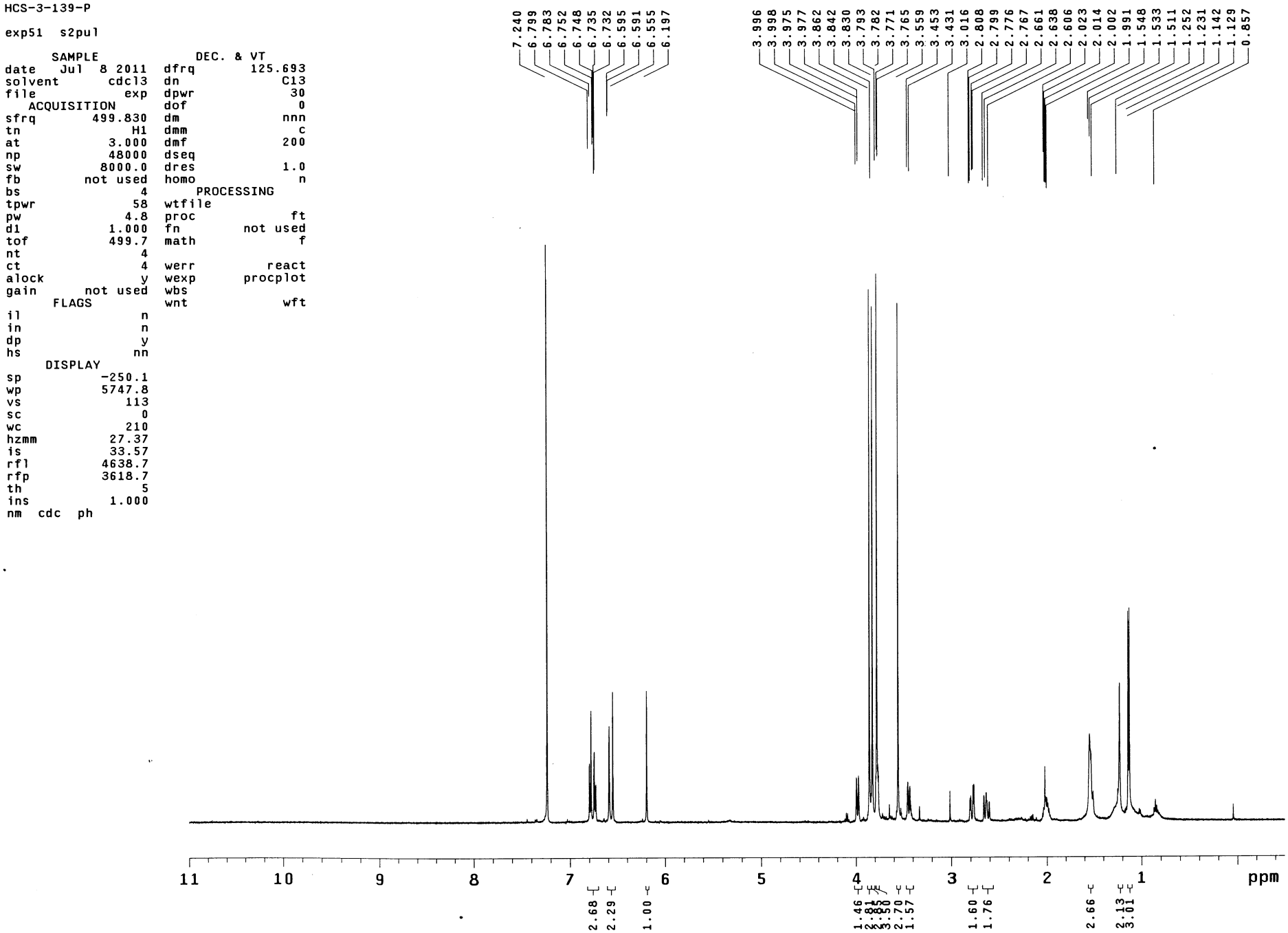


Fig S49. 13C NMR (CDCl3, 126 MHz) of compound 10.

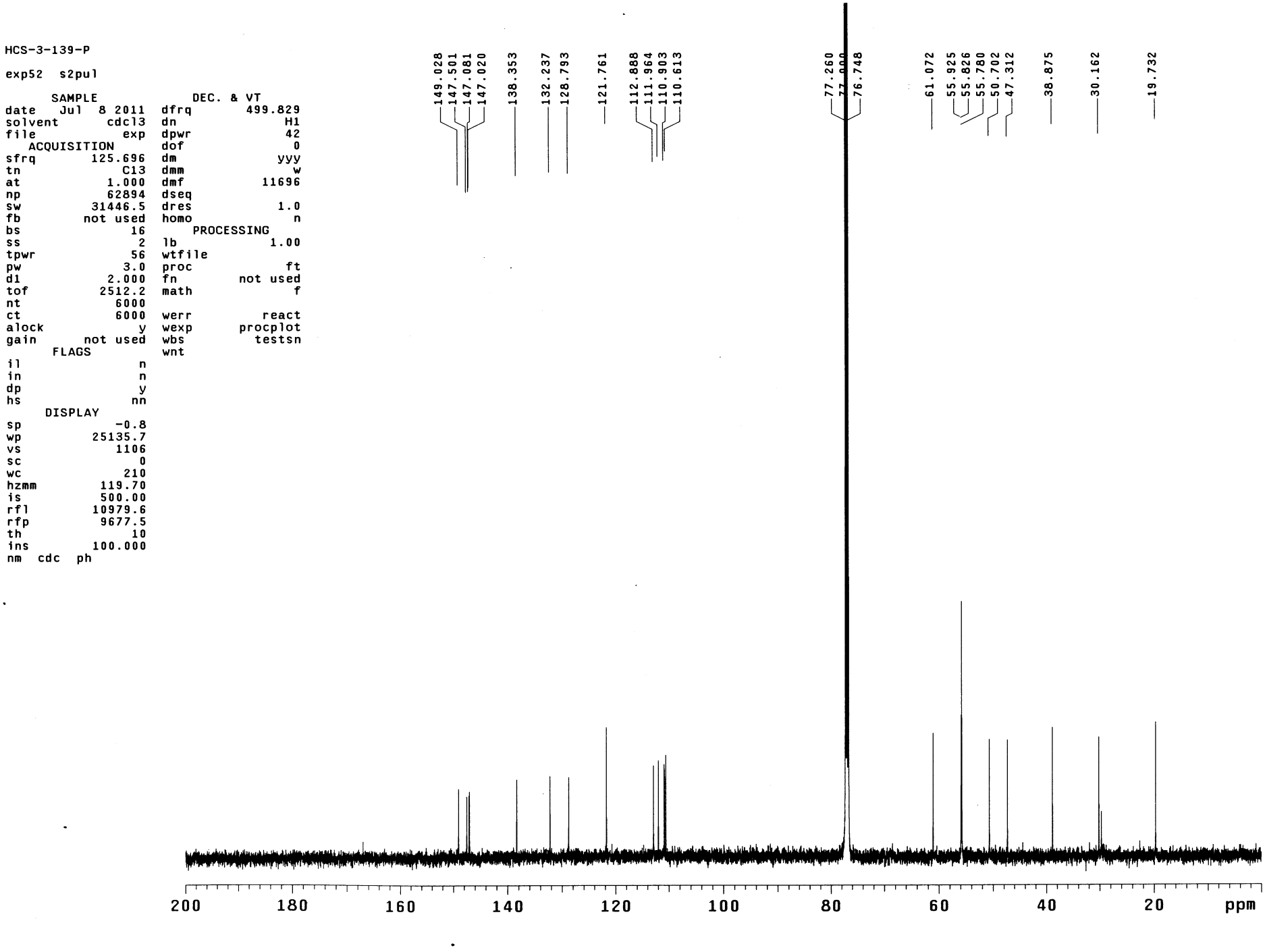


Fig S50. DEPT of compound 10.

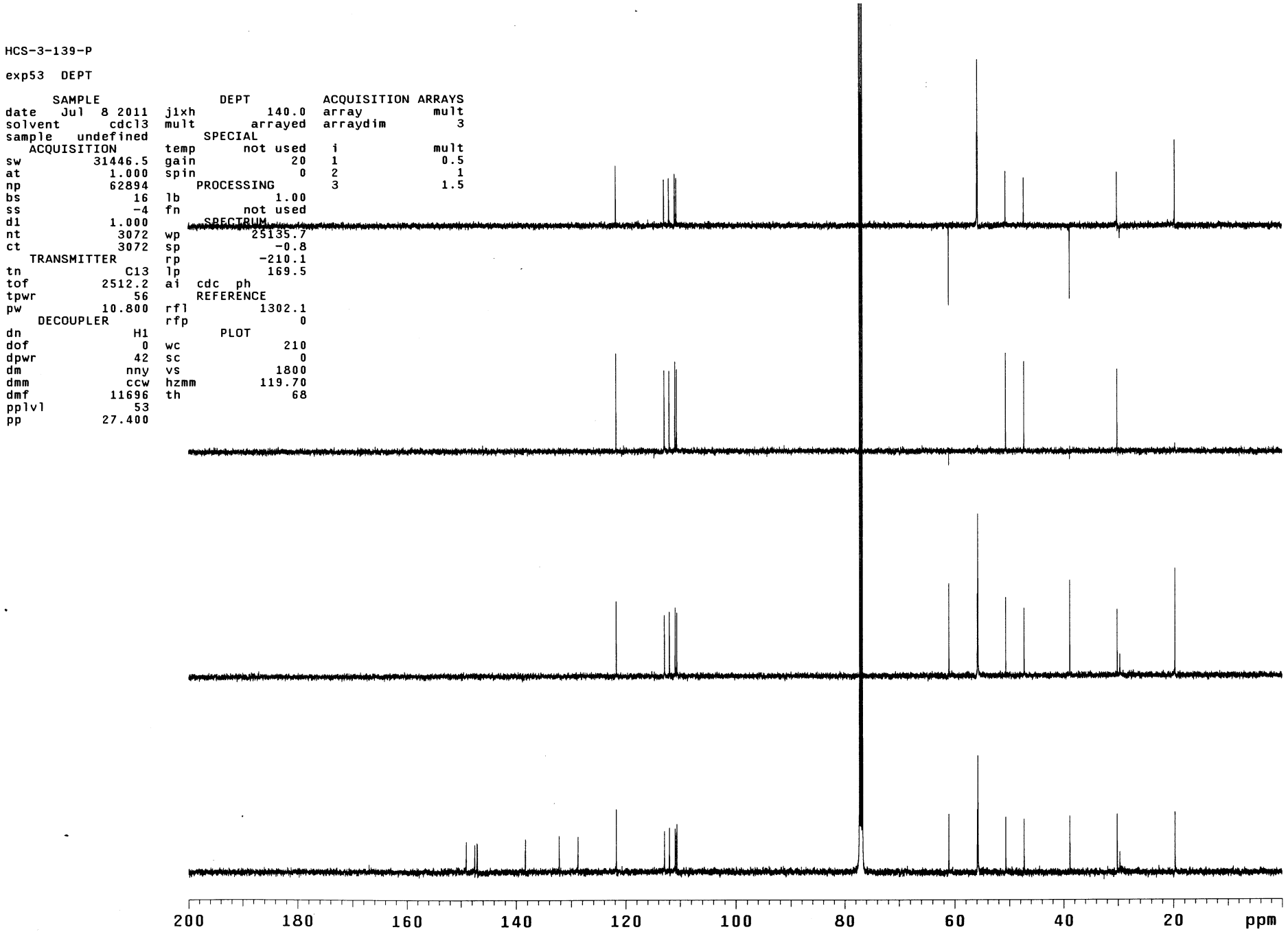


Fig S51. HSQC of compound 10.

HCS-3-139-P

exp56 gHSQC

SAMPLE		FLAGS		ACQUISITION ARRAYS	
date	Jul 8 2011	hs	n	array	phase
solvent	cdcl3	sspul	y	arraydim	256
sample	undefined	PFGflg	y		
ACQUISITION		hsglvl	1008	i	phase
sw	8000.0	SPECIAL		1	1
at	0.128	temp	not used	2	2
np	2048	gain	50		
fb	not used	spin	0		
ss	32	GRADIENTS			
d1	1.000	gzlvl1	1008		
nt	12	gt1	0.002000		
2D ACQUISITION		gzlvl3	507		
sw1	21367.5	gt3	0.001000		
ni	128	gstab	0.000500		
phase	arrayed	F2 PROCESSING			
TRANSMITTER		gf	0.059		
tn	H1	gfs	not used		
sfrq	499.830	fn	2048		
tof	499.7	F1 PROCESSING			
tpwr	58	gf1	0.006		
pw	14.000	gfs1	not used		
DECOUPLER		proc1	lp		
dn	C13	fn1	2048		
dof	-2515.2	DISPLAY			
dm	nny	sp	173.3		
dmm	ccp	wp	3640.6		
dmf	32258	sp1	1909.4		
dpwr	38	wp1	13897.2		
pwxlvl	54	rfl	4119.5		
pwx	14.000	rfp	3097.4		
HSQC		rfl1	15472.1		
j1xh	140.0	rfp1	14188.9		
nullflg	y	PLOT			
mult	2	wc	150.0		
		sc	6.2		
		wc2	116.2		
		sc2	0		
		vs	113		
		th	5		
		ai cdc ph			

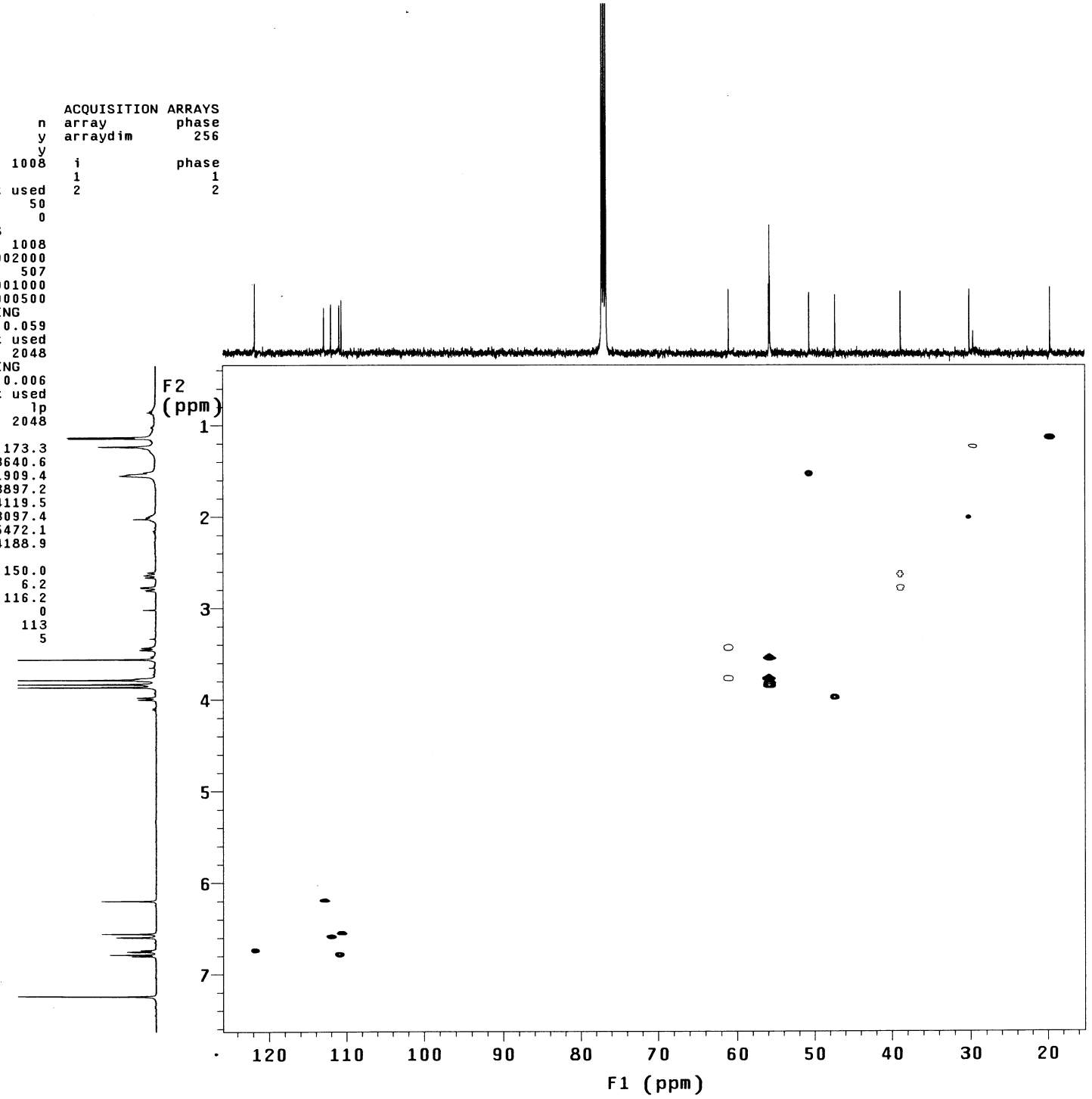


Fig S52. COSY of compound 10.

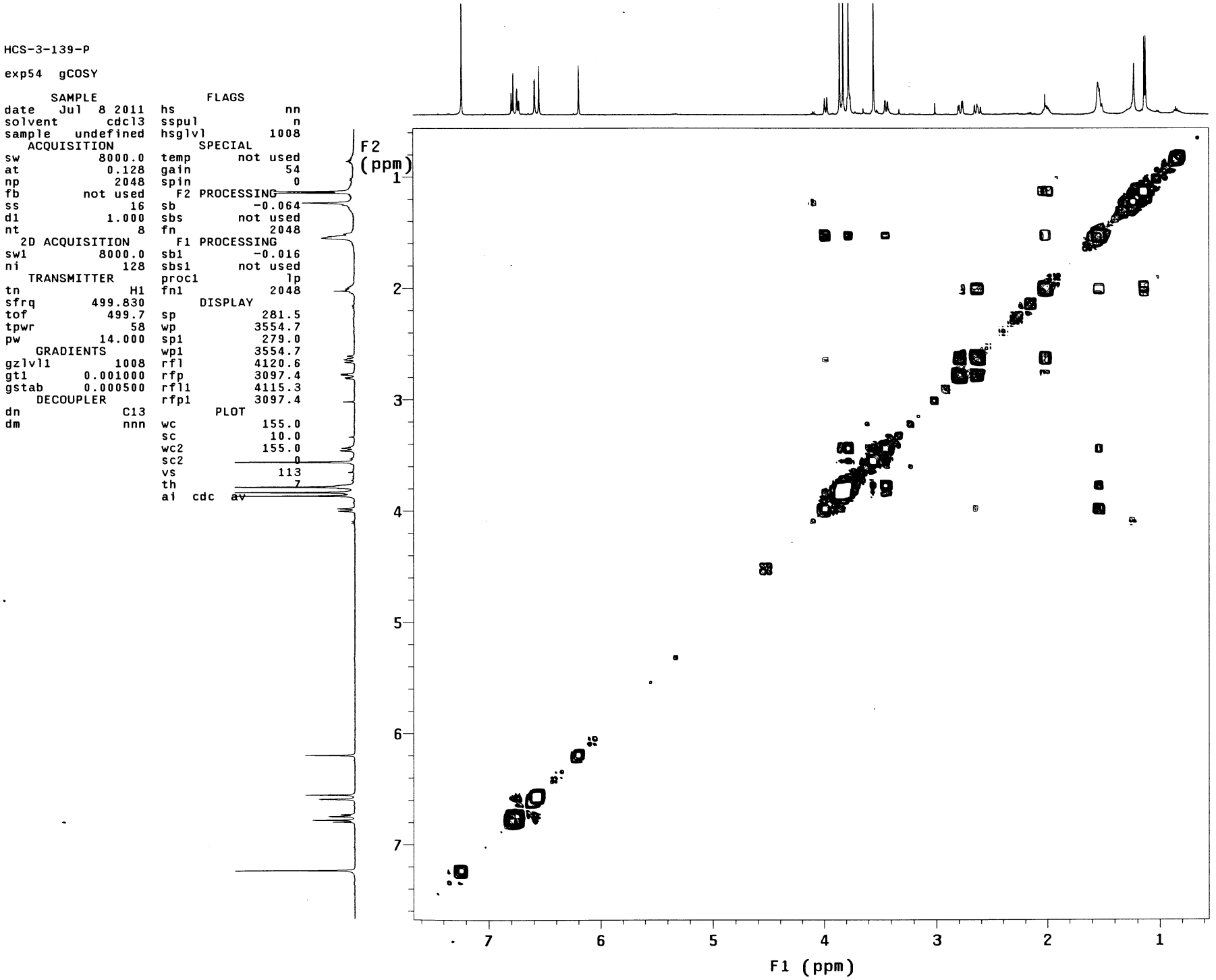


Fig S53. NOESY of compound 10.

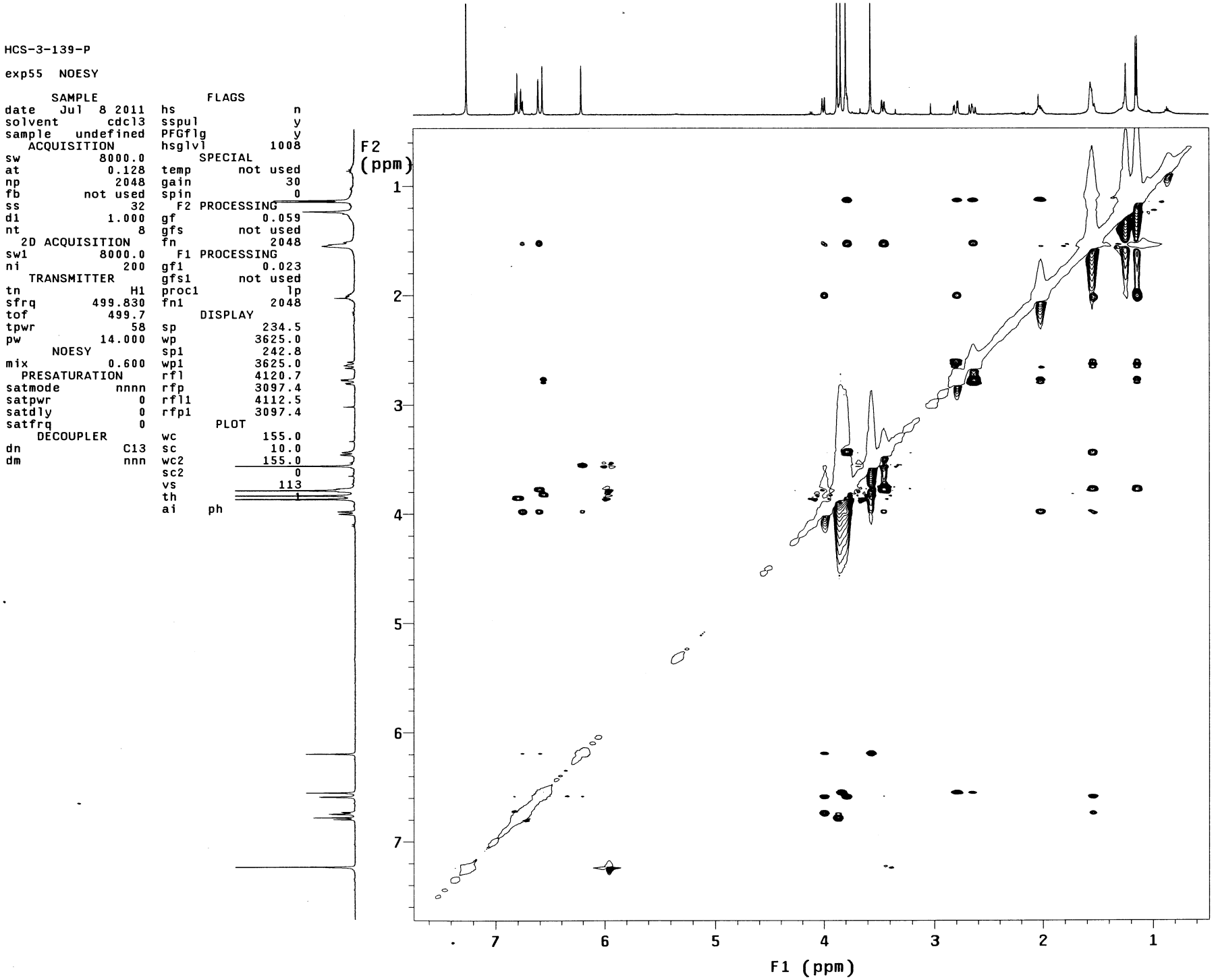


Fig S54. 1H NMR (CDCl3, 500 MHz) of compound 1.

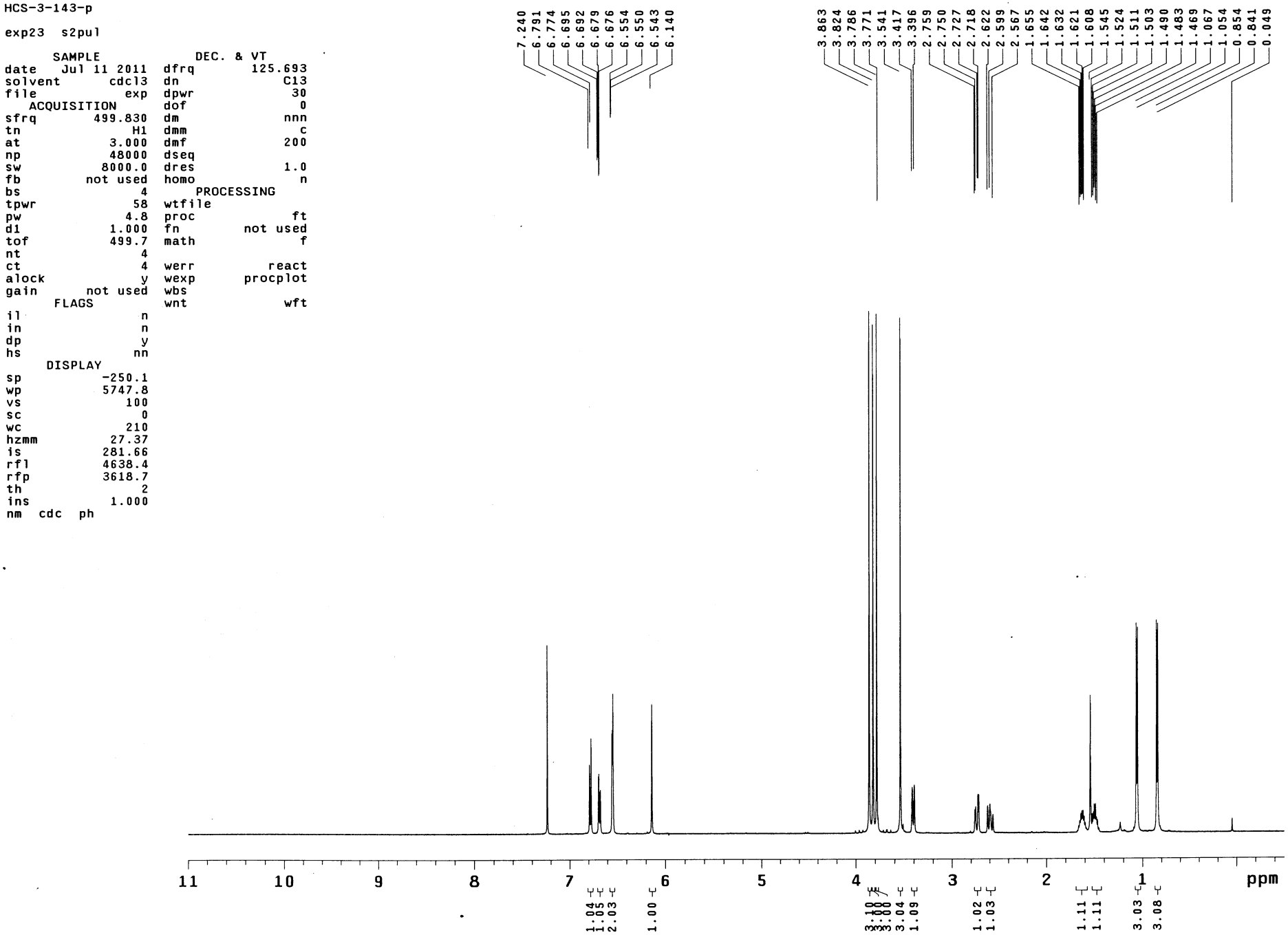


Fig. S52 ^{1}H NMR of galbulin (1), reprinted (adapted) with permission from (J. Org. Chem., 2001, 66 (25), pp 8606–8611, Supporting information). Copyright (2001) American Chemical Society. (For comparison)

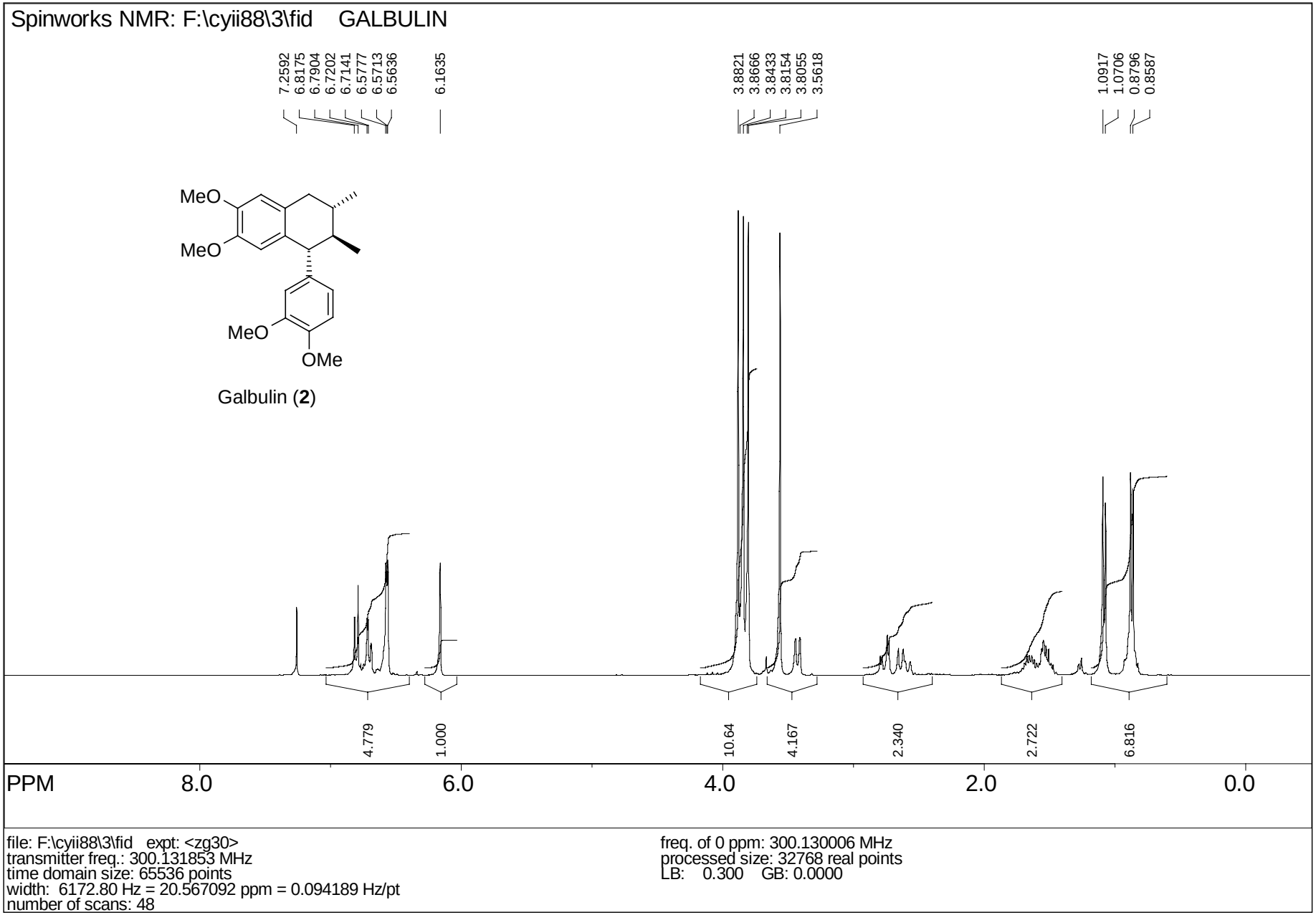


Fig S56. 13C NMR (CDCl3, 126 MHz) of compound 1.

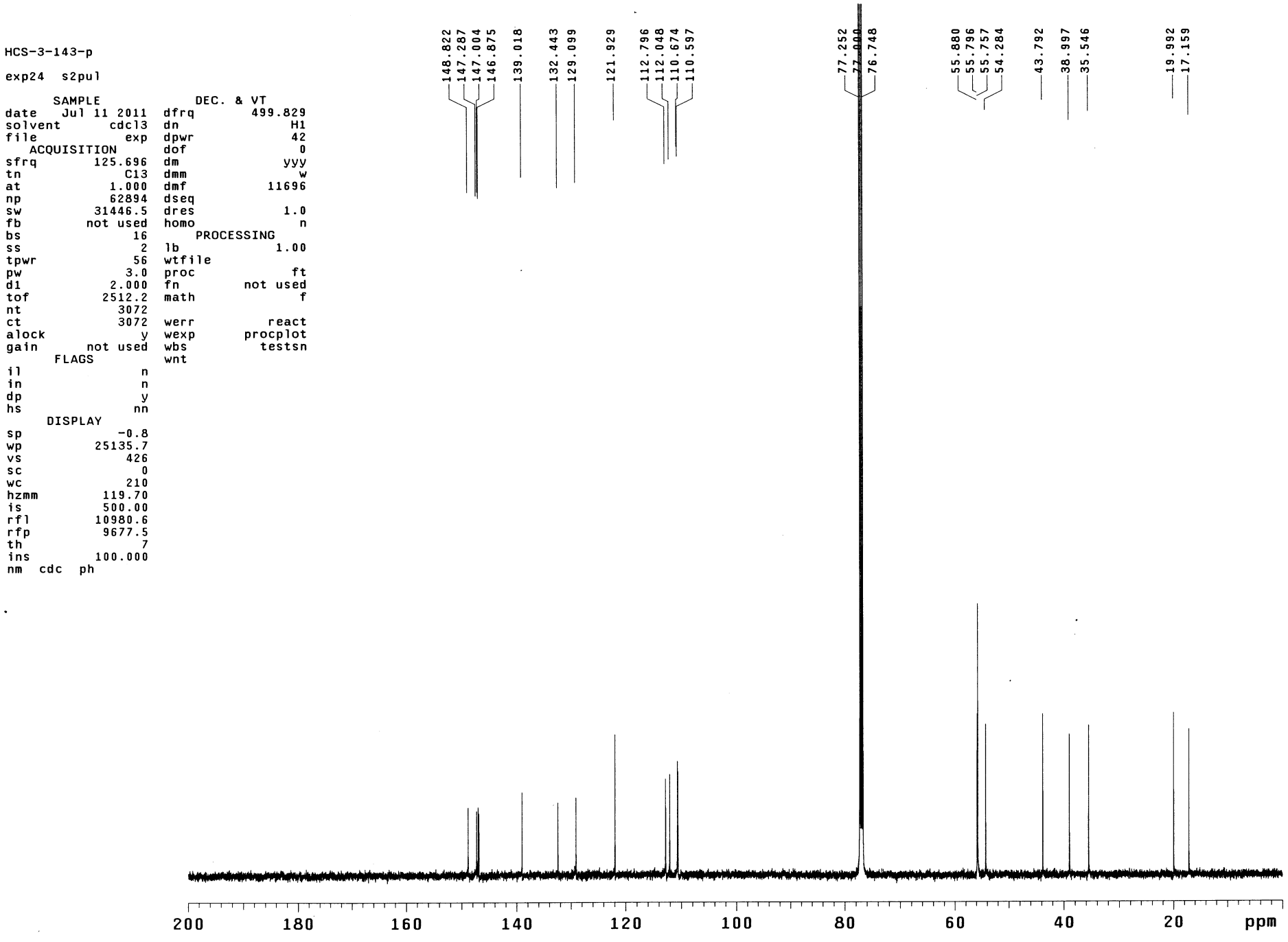


Fig. S57 ^{13}C NMR of galbulin (1).

 (For comparison)

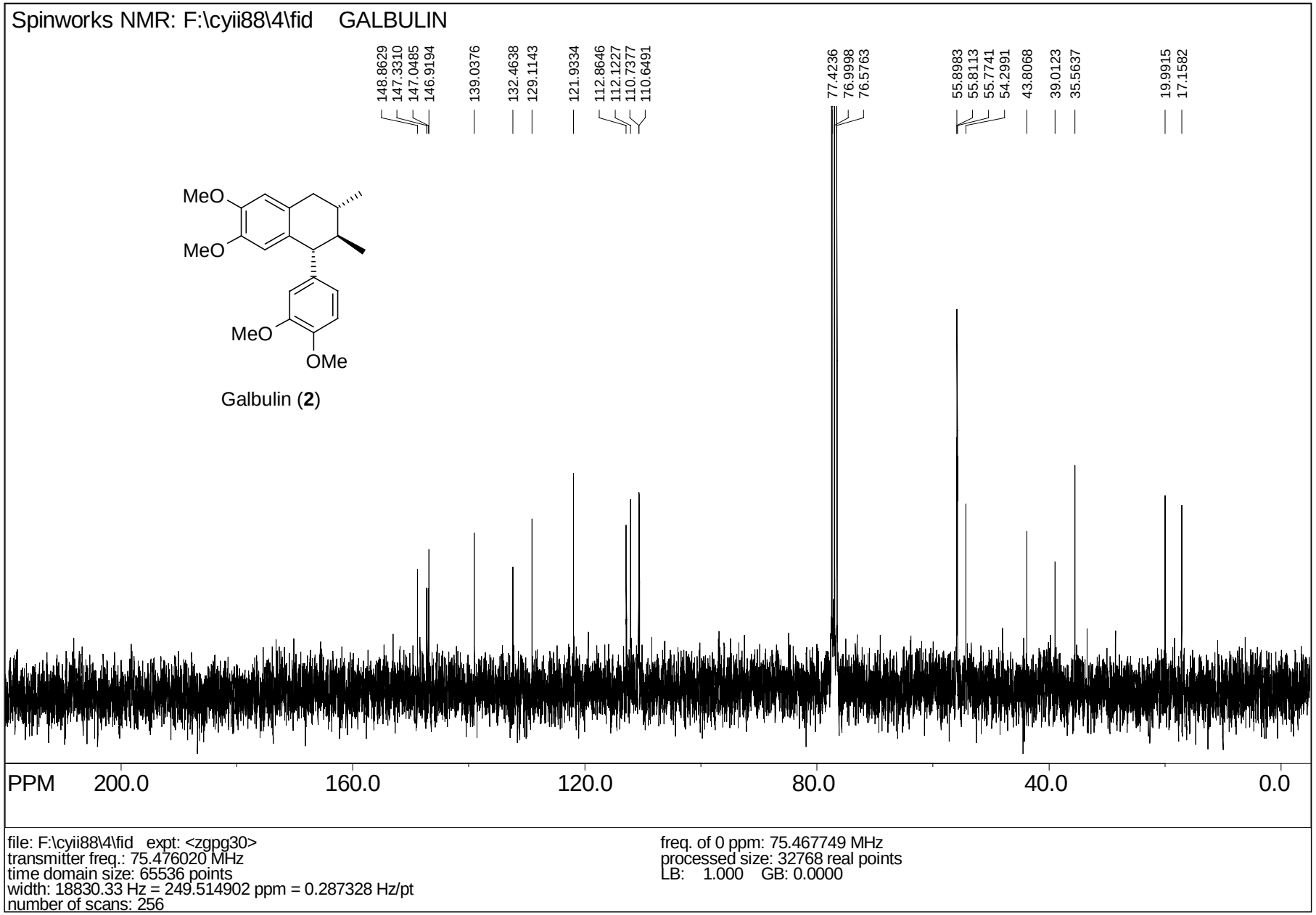


Fig S58. DEPT of compound 1.

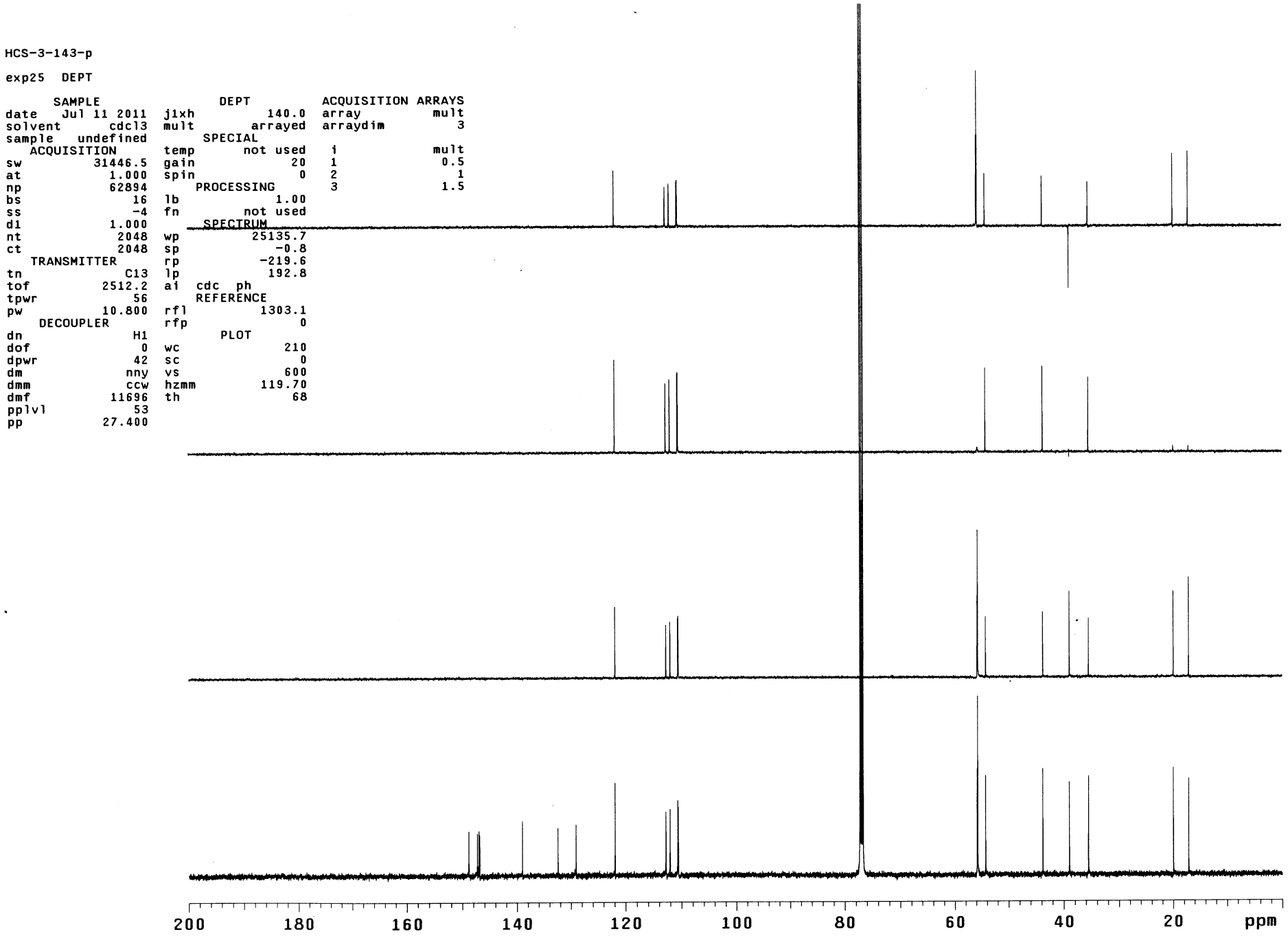


Fig S59. HSQC of compound 1.

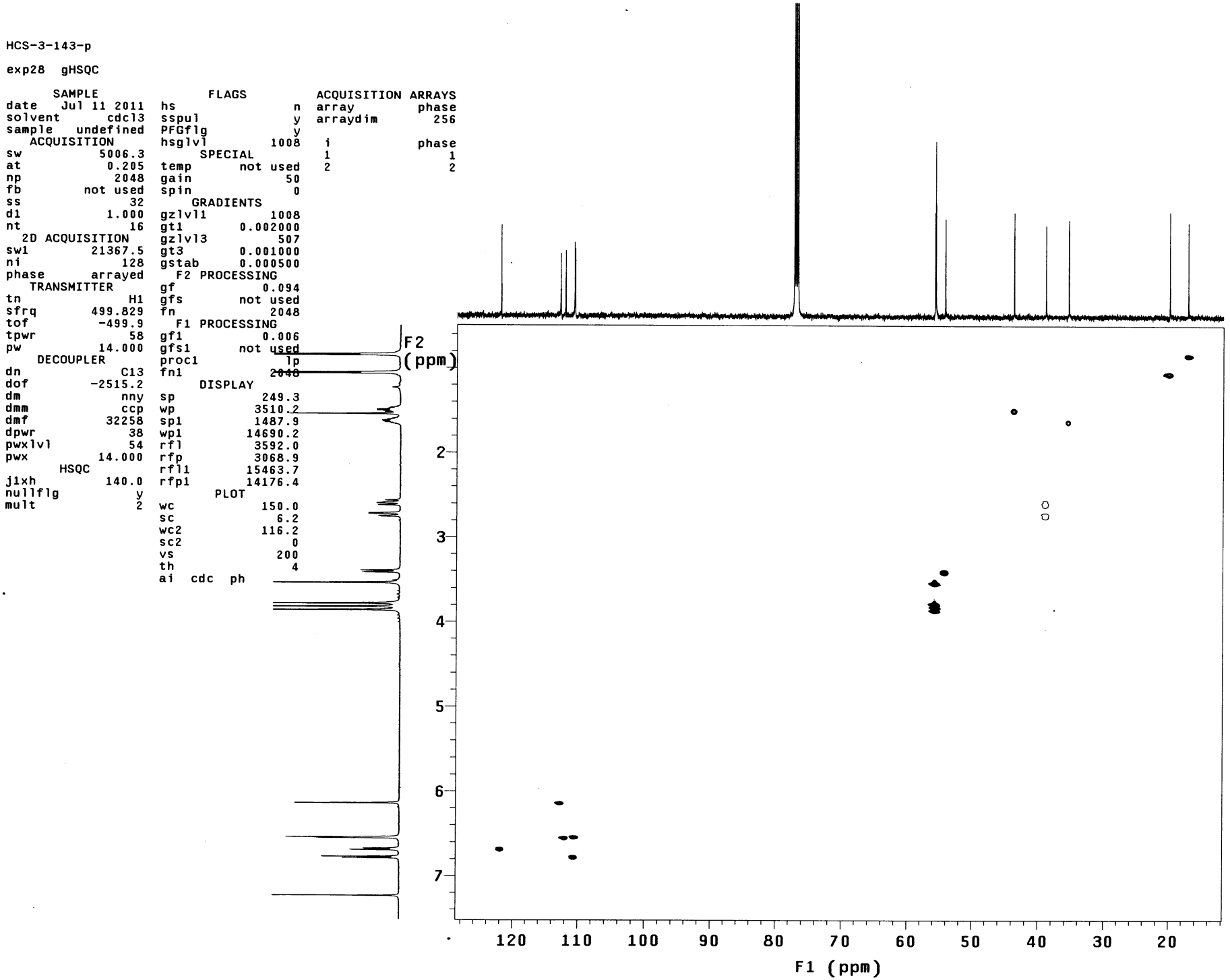


Fig. S60. COSY of compound 1.

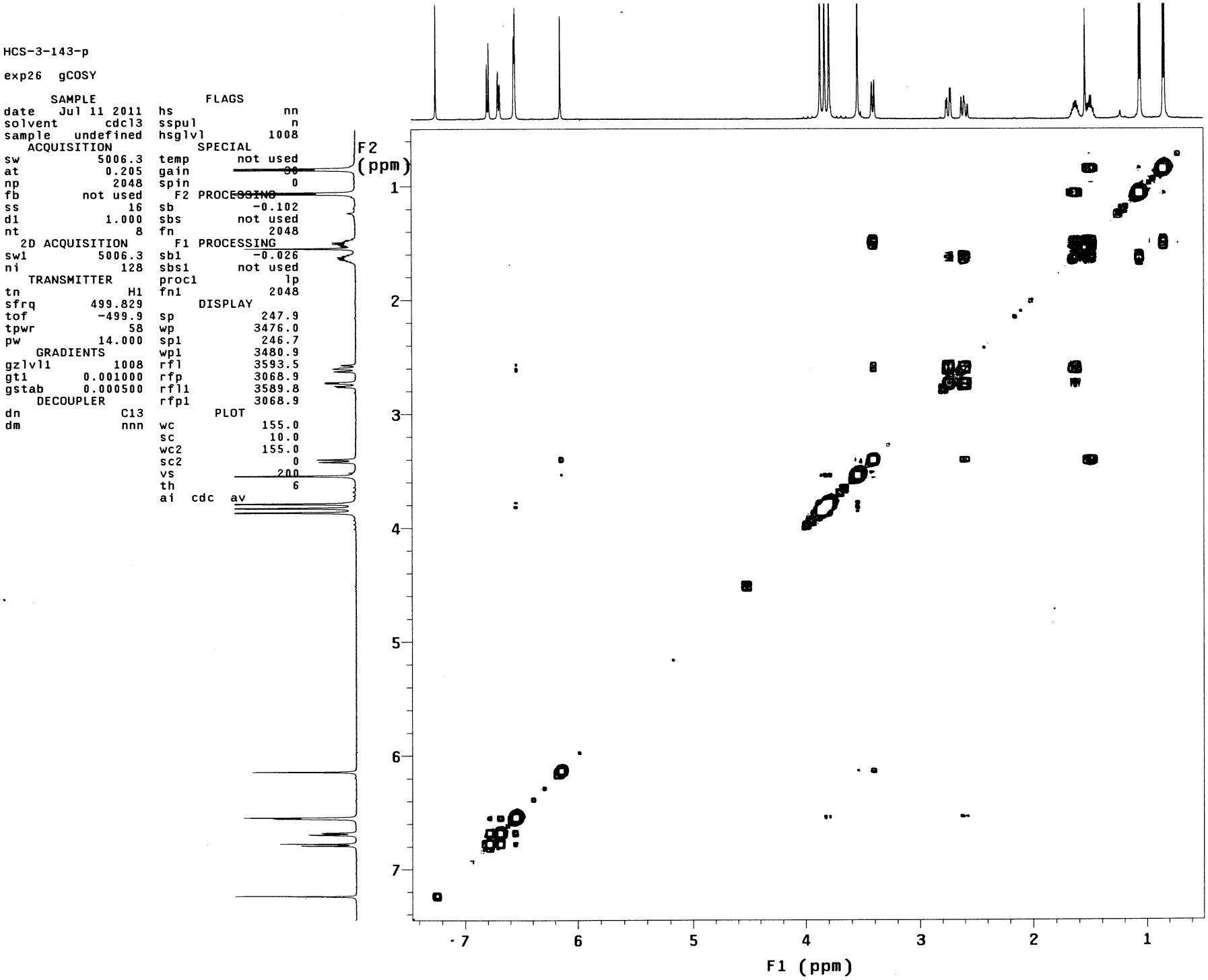


Fig S61. NOESY of compound 1.

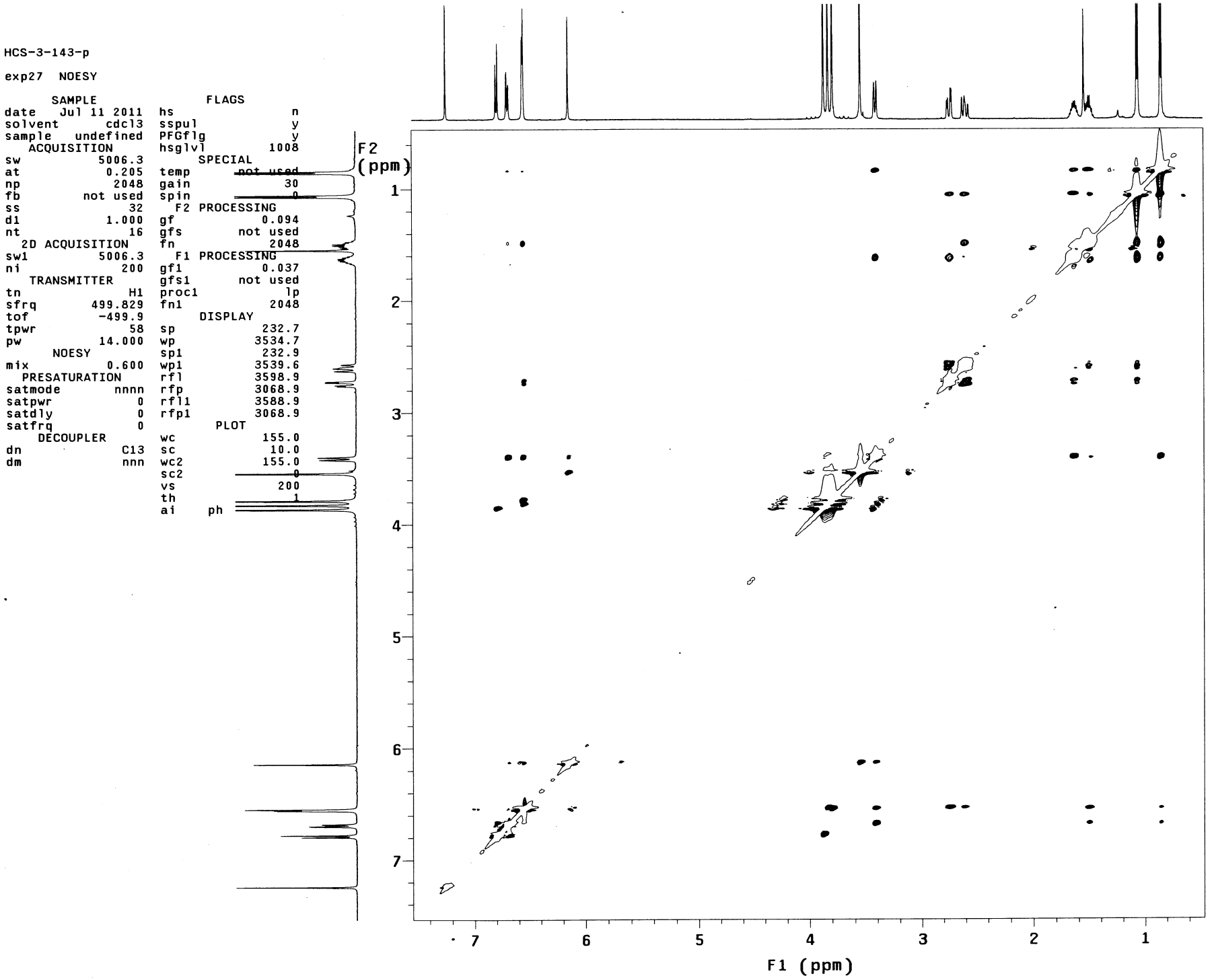


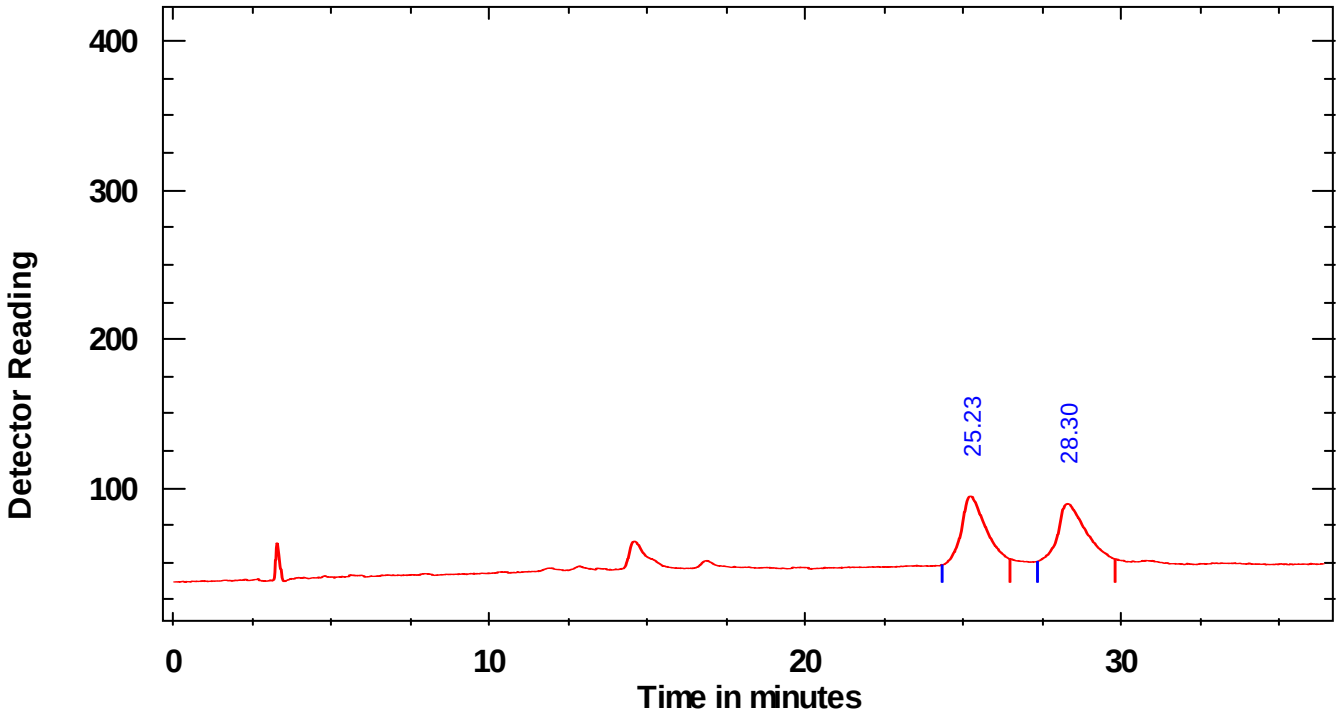
Fig S62. HPLC analysis of the racemic 3. (For comparison)

Chromatogram Report

First line of organization's address
Second line of organization's address

HCS-3-81-RACEMATE-COL-IA-20%-EA/HEX

Report produced on 2011/7/26 at 下午 01:31:04 by Put your name here



2011/7/26 ¤W¤È 11:52:04 Flow set to 1.00 at 0.00 minutes

2011/7/26 ¤U¤È 12:28:32 Run stopped by operator

PEAK REPORT

#	begin	end	area	percent	maximum	time	begins as	name
1	24.33	26.48	2292	50.4	94.39	25.23	Baseline	
2	27.35	29.81	2257	49.6	89.36	28.30	Baseline	

Data taken from file [A00861 HCS-3-81-RACEMATE-COL-IA-20%-EA_HEX on 七月 26 2011 12 28 下午 12_28 .chr]
D-Star Instruments - 8424 Quarry Rd., Manassas VA 20110 - 800-DSTAR12

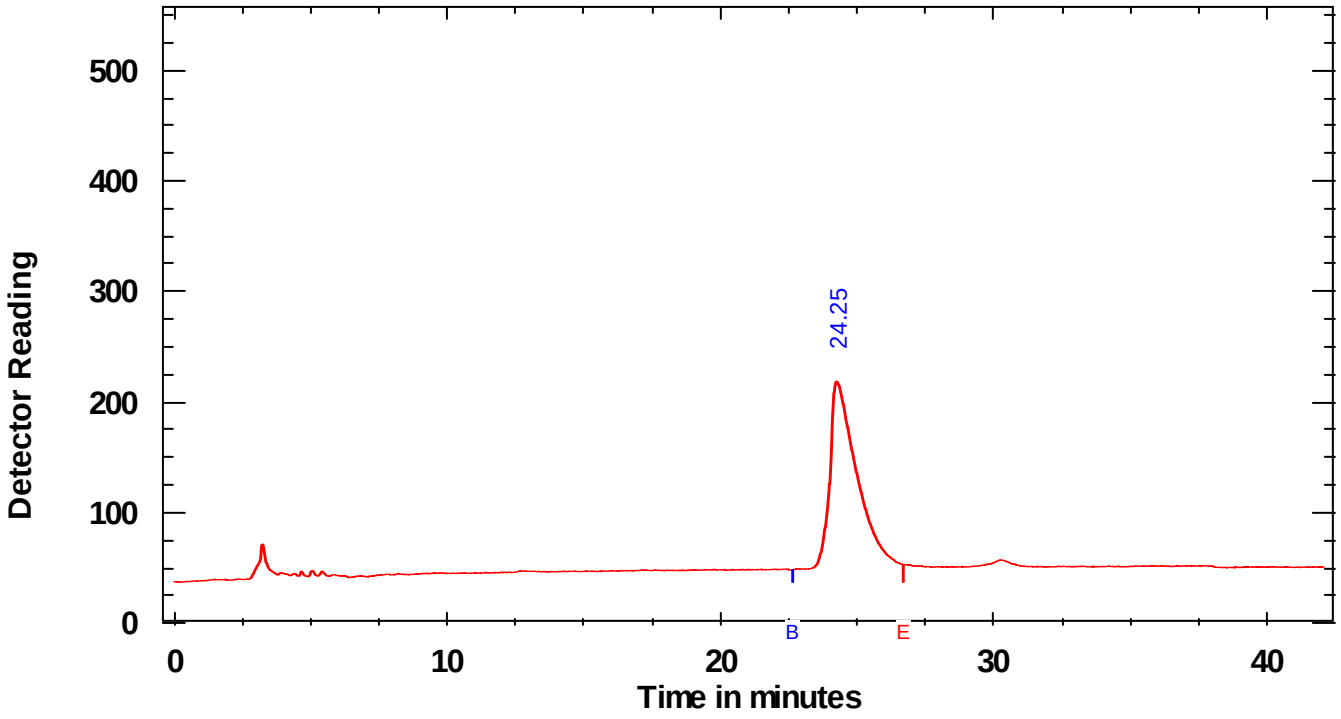
Fig S63. HPLC analysis of the chiral compound (+)-3 obtained.

Chromatogram Report

First line of organization's address
Second line of organization's address

HCS-006(CHIRAL)COL-IA 20% EA+HX

Report produced on 2011/7/26 at 下午 02:33:10 by Put your name here



2011/7/26 ¤U¤È 01:49:21 Flow set to 1.00 at 0.00 minutes
2011/7/26 ¤U¤È 02:31:29 Run stopped by operator

PEAK REPORT

#	begin	end	area	percent	maximum	time	begins as	name
1	22.64	26.69	11390	100.0	218.31	24.25	Baseline	

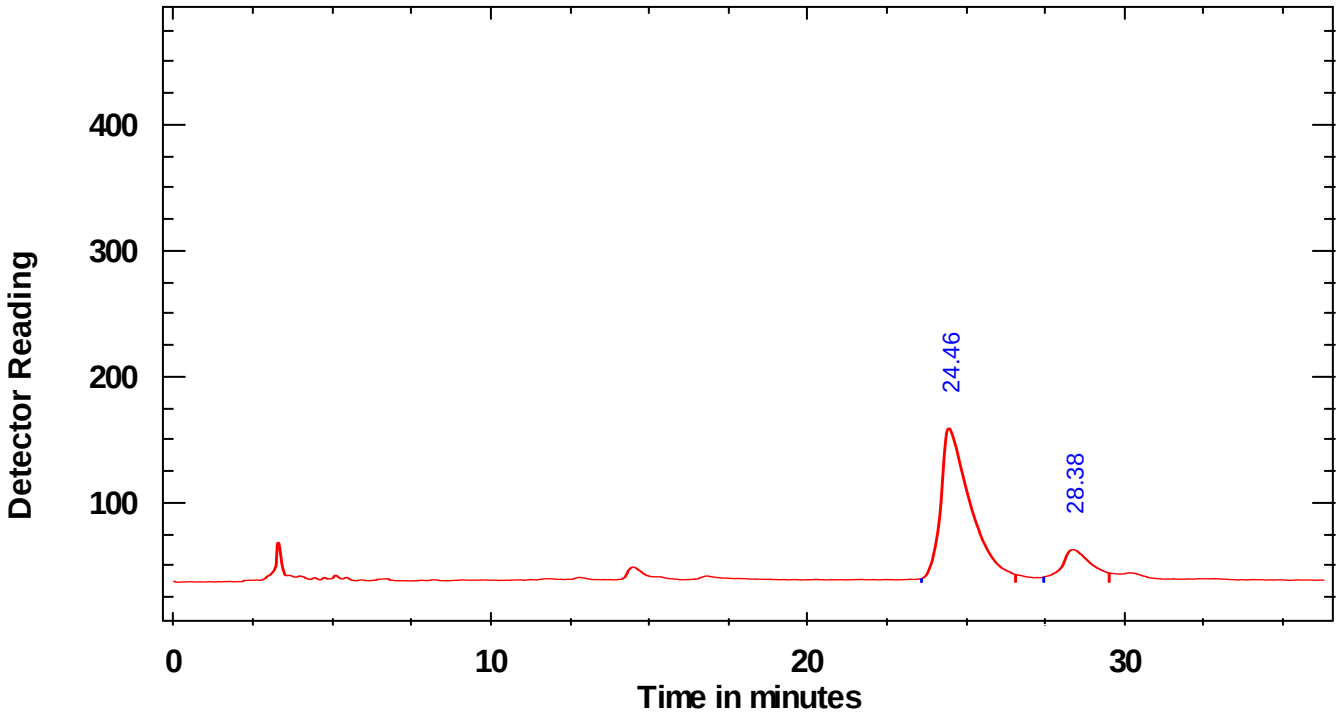
Fig. S64 HPLC analysis of the mixture of racemic and chiral compound (+)-3 obtained.
(For comparison)

Chromatogram Report

First line of organization's address
Second line of organization's address

HCS-006(CO)COL-IA 20% EA+HX

Report produced on 2011/7/26 at 下午 03:13:54 by Put your name here



2011/7/26 ¤U¤È 02:34:54 Flow set to 1.00 at 0.00 minutes
2011/7/26 ¤U¤È 03:11:15 Run stopped by operator

PEAK REPORT

#	begin	end	area	percent	maximum	time	begins as	name
1	23.59	26.56	7389	87.5	159.20	24.46	Baseline	
2	27.45	29.51	1052	12.5	62.81	28.38	Baseline	