Total Synthesis of (+)-Nakadomarin A

Supporting Information

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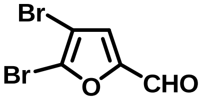
Experimental

General

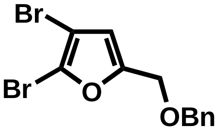
Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were obtained as thin films on NaCl plates using a Bruker Vector 33 FT-IR instrument. NMR experiments were performed on Varian Mercury 400, Varian Inova 600 and Inova 400 instruments and samples were obtained in $CDCl_3$ (referenced to 7.26 ppm for ^1H and 77.0 for ^{13}C) or Methanol-d_4 (referenced to 3.30 for ^1H). Coupling constants (J) are in Hz. The multiplicities of the signals are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad. High resolution mass spectra (HRMS) were obtained on a Finnigan MAT 8200 spectrometer at 70 eV. Optical rotations of the intermediates were recorded in cells of 10 cm path length using an Atago Polax-2L polarimeter. The optical rotation of Nakadomarin A was measured on a Perkin-Elmer 241 digital polarimeter.

All reactions were performed under an atmosphere of argon unless otherwise indicated. Toluene, tetrahydrofuran (THF), ether, N,N-dimethylformamide (DMF), and methylene chloride were dried and deoxygenated by passing the nitrogen purged solvents through activated alumina columns. All other reagents and solvents were used as purchased from Aldrich, Strem, Caledon or VWR. Reaction progress was followed by thin layer chromatography (TLC) (EM Science, silica gel 60 F_{254}) visualizing with UV light, and the plates developed using acidic anisaldehyde, phosphomolybdic acid or basic potassium permanganate. Flash chromatography was performed using silica gel purchased from Silicycle Chemical Division Inc. (230-400 mesh). Preparative TLC was performed on glass backed 0.25 mm silica plates (Rose Scientific, silica gel 60 F_{254}).



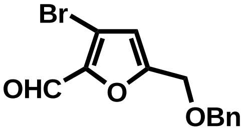
Compound 24a

Compound 24a was prepared using the procedure of Chiarello, J.; Joullie, M. M. *Tetrahedron* **1988**, *44*, 41-8, with changes made to the purification procedure. Freshly distilled furfural (20.00 g, 208.13 mmol) was added dropwise at 0 °C to aluminum chloride (61.06 g, 457.90 mmol) over a two hour period with mechanical stirring. Bromine (73.17 g, 457.90 mmol) was then added dropwise at 0 °C over a two hour period, after which stirring was discontinued and the reaction allowed to stand overnight. The reaction was quenched by carefully pouring the mixture into ice (800 mL) and then extracting the aqueous layer three times with ether. The combined organics were washed twice with saturated sodium bicarbonate, once with brine, and dried with $MgSO_4$. The solvent was removed under reduced pressure to yield a red oil. In the above reference the product was purified by distillation, but heating led to a black tar and no product being recovered. Purification using column chromatography on silica (hexanes / ethyl acetate as eluent) yielded **24a** (24.85 g, 97.81 mmol, 47%, R_f = 0.48, 20% ethyl acetate in hexanes) as an orange oil. Less than 5% of what might be another bromination isomer is present.



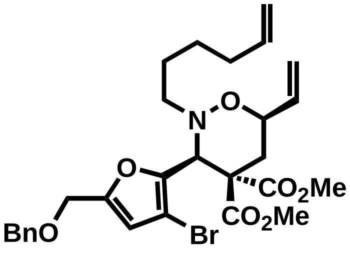
Compound 24b

Dibromoaldehyde **24a** (14.50 g, 57.07 mmol) was dissolved in methanol (175 mL) and cooled to 0 °C. $NaBH_4$ (2.16 g, 57.07 mmol) was added in four portions over 15 minutes. After 1 hour, water (5 mL) was added and the methanol removed under reduced pressure. The residual material was added to water (200 mL) and 5% HCl (20 mL) and the aqueous layer extracted 3 times with ethyl acetate. The combined organics were washed with water and dried with $MgSO_4$, and the solvent removed under reduced pressure. The resulting crude dibromoalcohol (13.61 g, 53.14 mmol, 94%) was recovered as a red oil, and was of sufficient purity to be directly benzylated. THF (200 mL) was added to sodium hydride (2.70 g, 3.38 g of 80%, 112.50 mmol) that was washed with hexanes, and the resulting slurry cooled to 0 ^oC. The crude dibromoalcohol from above (13.61 g, 53.14 mmol) was added as a solution in THF (100 mL) via a dropping funnel, and once the addition was complete, the mixture was stirred for 30 minutes. Benzyl bromide (8.18 g, 51.51 mmol) dissolved in THF (100 mL) was added via cannula, and the mixture warmed to room temperature and stirred for 13 hours. Water (50 mL) was added and the THF removed under reduced pressure. Water (200 mL) was added and the aqueous phase extracted 3 times with ethyl acetate. The combined organics were washed with water, brine and then dried with $MgSO_4$. Removal of the solvent under reduced pressure produced benzylated product **24b** (15.53 g, 44.87 mmol, 84%) as an orange oil which was not purified.



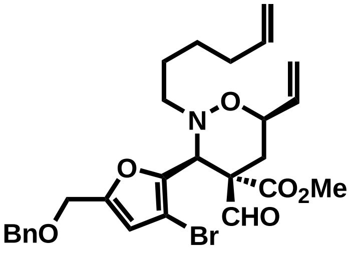
Compound 24

The procedure used is an adaptation from Zaluski, M-C., Robba, M., Bonhomme, M. *Bull. Soc. Chim. Fr.* **1970**, 1838 for the preparation of a similar compound. n-BuLi (21.70 mL of 1.6 M in hexanes, 34.72 mmol) was added to anhydrous ether (150 mL) and the solution was cooled to -78 ^oC. A solution of **24b** (7.77 g, 22.45 mmol) in ether (100 mL) was added dropwise to the n-BuLi, and after addition was complete the mixture was stirred for 30 minutes at -78 ^oC. DMF (1.98 g, 31.43 mmol) in ether (100 mL) was then added dropwise, and after addition was complete the reaction was warmed to room temperature over two hours, and then refluxed for 30 minutes. The reaction was quenched by the addition of water (5 mL), and then 5% HCl (300 mL) was added. The layers were separated and the aqueous extracted 3 times with ether. The combined organics were washed with water, dried with $MgSO_4$ and the solvent removed under reduced pressure. Flash column chromatography on silica gel (hexanes / ethyl acetate as eluent) afforded **24** (3.41 g, 11.55 mmol, 51%) as a pale yellow oil. R_f = 0.42, 20% ethyl acetate in hexanes; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.69 (s, 1H), 7.39-7.30 (m, 5H), 6.62 (s, 1H), 4.60 (s, 2H), 4.55 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =176.0, 158.4, 147.6, 136.9, 128.5, 128.0, 127.8, 114.7, 113.3, 73.0, 63.9; IR (thin film): 3119, 3032, 2856, 1679, 1575, 1520, 1454, 1352, 1274, 1209, 1094, 1033, 973, 794, 739, 699 cm^{-1}; HRMS calc'd for $C_{13}H_{11}BrO_3$ = 293.9892, found = 293.9887.



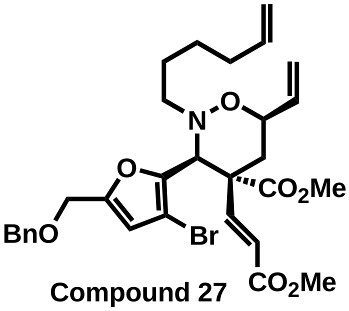
Compound 25

Aldehyde **24** (1.13 g, 3.81 mmol) and hydroxylamine **22** (0.44 g, 3.81 mmol) were added to toluene (30 mL) containing 4A molecular sieves. $Yb(OTf)_3$•xH_2O (0.197 g, 0.318 mmol) was added and the mixture stirred for three hours, after which cyclopropane **23** (0.585 g, 3.17 mmol) was added. The reaction was stirred at room temperature, and after 24 hours a small amount of cyclopropane remained, so additional hydroxylamine **22** (35 mg, 0.304 mmol) was added and the reaction stirred for 24 more hours. The reaction was then filtered through celite, and the filter cake washed with ether. The excess aldehyde **24** had a R_f similar to the product, so the solvent was removed under reduced pressure and the residual material dissolved in methanol (30mL). $NaBH_4$ (100 mg, 2.65 mmol) was added and after 30 minutes water (25 mL) was added and the methanol removed under reduced pressure. Ethyl acetate (25 mL) was added and the layers separated. The aqueous layer was extracted once with ethyl acetate and then twice with ether. The combine organics were washed with water, brine, dried with $MgSO_4$ and the solvent removed under reduced pressure. The resulting crude material was purified by flash column chromatography on silica (hexanes / ethyl acetate as eluent) to yield cycloadduct **25** (1.52 g, 2.63 mmol, 82%) as a colorless oil. Proton NMR indicates that there was approximately 8 % of what might be the other diastereomer. This impurity is removed upon formation of **27**. R_f = 0.48, 25% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.36-7.33 (m, 4H), 7.31-7.28 (m, 1H), 6.38 (s, 1H), 5.88 (ddd, J = 16.8, 10.8, 6.0 Hz, 1H), 5.83-5.76 (m, 1H), 5.35 (ddd, J = 18.0, 1.8, 1.2 Hz, 1H), 5.20 (ddd, J = 10.8, 2.4, 1.8 Hz, 1H), 5.01 (s, 1H), 5.01-4.97 (m, 1H), 4.93 (ddd, J = 10.8, 1.8, 0.6 Hz, 1H), 4.52-4.38 (m, 5H), 3.84 (s, 3H), 3.54 (s, 3H), 2.60-2.50 (m, 4H), 2.06-2.02 (m, 2H), 1.63-1.55 (m, 2H), 1.54-1.48 (m, 1H), 1.43-1.37 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.2, 168.1, 153.2, 147.0, 138.8, 137.7, 136.5, 128.3, 127.8, 127.7, 117.1, 114.3, 112.3, 103.1, 76.6, 71.7, 63.7, 58.0, 57.7, 54.8, 53.2, 52.7, 33.4, 31.4, 26.4, 26.1; IR (thin film): 2951, 2927, 2856, 1743, 1641, 1436, 1358, 1257, 1208, 1173, 1114, 1074, 1032, 990, 912, 828, 816, 739, 698 cm^{-1}; HRMS calc'd for $C_{28}H_{34}BrNO_7$ = 575.1519, found = 575.1511.



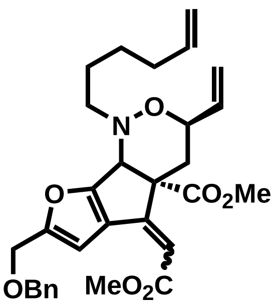
Compound 26

Cycloadduct **25** (300 mg, 0.521 mmol) was dissolved in methylene chloride (60 mL) and then cooled to –78 °C. DIBAL (2.1 mL of 1.5M solution in toluene, 3.15 mmol) was added dropwise and the reaction stirred for 15 minutes, after which multiply eluted TLC showed complete consumption of the starting material. Methanol (5 mL) was then added slowly to quench the excess DIBAL, and the mixture stirred at –78 °C for 20 minutes, after which it was removed from the dry ice bath and allowed to warm to room temperature. The reaction was then poured into 5% HCl (20 mL) and the layers separated. The aqueous layer was extracted 3 times with methylene chloride, and the combined organics washed with 5% HCl. The organic layer was dried with $MgSO_4$, and the solvent removed under reduced pressure. The residual material was purified by flash column chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield aldehyde **26** (276 mg, 0.505 mmol, 97%) as a yellow oil. R_f = 0.50, 25% ethyl acetate in hexanes; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.26 (s, 1H), 7.35-7.31 (m, 5H), 6.38 (s, 1H), 5.93-5.84 (m, 1H), 5.82-5.74 (m, 1H), 5.36 (d, J = 17.6 Hz, 1H), 5.21 (d, J = 10.8 Hz, 1H), 5.08 (s, 1H), 4.98 (dd, J = 17.2, 1.2 Hz, 1H), 4.93 (d, J = 10.4 Hz, 1H), 4.53-4.43 (m, 5H), 3.87 (s, 3H), 2.60-2.48 (m, 2H), 2.38-2.33 (m, 2H), 2.06-2.01 (m, 2H), 1.62-1.48 (m, 3H), 1.43-1.36 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 195.0, 168.8, 154.1, 146.0, 138.8, 137.5, 136.5, 128.4, 127.9, 127.8, 117.2, 114.4, 112.3, 103.9, 76.6, 71.9, 63.7, 63.1, 57.3, 54.7, 53.3, 33.4, 28.4, 26.3, 26.0; IR (thin film): 3076, 3032, 2947, 2935, 2857, 1752, 1722, 1641, 1452, 1438, 1358, 1239, 1220, 1114, 1073, 1031, 996, 909, 809, 743, 698 cm^{-1}; HRMS calc'd for $C_{27}H_{32}BrNO_6$ = 545.1413, found = 545.1403.

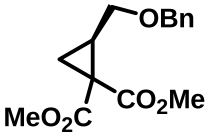


Compound 27

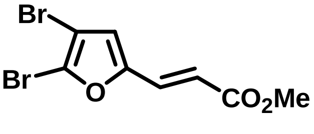
Trimethyl phosphonoacetate (1.04 g, 5.69 mmol) was dissolved in THF (75 mL) and cooled in an ice bath. t-BuOK (0.638 g, 5.69 mmol) was added and the slurry was stirred for 10 minutes. Aldehyde **26** (2.07 g, 3.79 mmol) in THF (75 mL) was then added slowly via cannula, and TLC indicated complete consumption of the starting material after 13 hours. Water (20 mL) was added, and the THF removed under reduced pressure. To the resulting residue was added water (50 mL), 5% HCl (10 mL) and ethyl acetate (50mL). The layers were separated, and the aqueous washed 3 times with ethyl acetate. The combined organics were washed with water, brine and dried with $MgSO_4$. The solvent was removed under reduced pressure and the residual material purified by column chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield enoate **27** (1.82 g, 3.02 mmol, 80%) as a pale yellow oil. R_f = 0.33, 25% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.35-7.28 (m, 5H), 6.63 (d, J = 16.2 Hz, 1H), 6.36 (s, 1H), 5.91-5.85 (m, 1H), 5.83 (d, J = 16.2 Hz, 1H), 5.82-5.76 (m, 1H), 5.35 (dt, J = 16.2, 1.8 Hz, 1H), 5.20 (dt, J = 10.2, 1.8 Hz, 1H), 4.99 (ddd, J = 16.8, 3.6, 1.8 Hz, 1H), 4.94-4.92 (m, 1H), 4.86 (s, 1H), 4.53-4.47 (m, 3H), 4.42 (d, J = 4.2 Hz, 1H), 4.40 (d, J = 6.0 Hz, 1H), 3.81 (s, 3H), 3.61 (s, 3H), 2.57-2.48 (m, 2H), 2.38 (dd, J = 13.2, 2.1 Hz, 1H), 2.24 (dd, J = 13.2, 11.4 Hz, 1H), 2.05-2.01 (m, 2H), 1.61-1.54 (m, 1H), 1.52-1.46 (m, 1H), 1.45-1.35 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 171.9, 166.0, 153.2, 146.9, 145.7, 138.9, 137.6, 136.7, 128.4, 127.8 (2 signals), 122.4, 117.1, 114.3, 112.4, 103.9, 71.7, 63.8, 60.0, 54.9, 53.0, 52.9, 51.7, 33.4, 32.9, 26.4, 26.1 (1 sp^3 signal missing); IR (thin film): 2950, 2854, 1733, 1648, 1436, 1318, 1280, 1213, 1173, 1070, 1032, 985, 915, 828, 741, 687 cm^{-1}; HRMS calc'd for $C_{30}H_{36}BrNO_7$ = 601.1675, found = 601.1681.


Compound 28

Enoate **27** (150 mg, 0.248 mmol) was dissolved in DMF (10 mL) and Ag_2SO_4 (154 mg, 0.496 mmol), NEt_3 (125 mg, 1.24 mmol), and $Pd(PPh_3)_4$ (86 mg, 0.075 mmol) added. The mixture was refluxed for 6.5 hour, after which TLC indicated complete consumption of the starting material. The reaction mixture was poured into water (50 mL) and 5% HCl (10 mL) and extracted 4 times with ether. The combined organics were washed with water, and dried with $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica (hexanes / ethyl acetate as eluent) to produce **28** (110 mg, 0.211 mmol, 85%) as a yellow oil. Only one double bond isomer was produced but the configuration was not determined since the double bond would be reduced at a later stage. R_f = 0.32, 25% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.37-7.36 (m, 4H), 7.32-7.31 (m, 1H), 6.40 (s, 1H), 5.98-5.92 (m, 1H), 5.84-5.77 (m, 2H), 5.20 (d, J = 17.4 Hz, 1H), 5.09 (d, J = 10.2 Hz, 1H), 5.01 (d, J = 17.4 Hz, 1H), 4.94 (d, J = 10.2 Hz, 1H), 4.86-4.82 (m, 1H), 4.59 (s, 2H), 4.49 (d, J = 13.2 Hz, 1H), 4.45 (d, J = 13.2 Hz, 1H), 4.11 (s, 1H), 3.73 (s, 3H), 3.70 (s, 3H), 3.19-3.14 (m, 1H), 2.90 (dd, J = 7.8, 6.0 Hz, 1H), 2.73-2.69 (m, 1H), 2.09-2.05 (m, 2H), 1.69-1.58 (m, 3H), 1.51-1.42 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 172.8, 166.5, 164.0, 159.7, 154.0, 139.0, 138.8, 137.4, 131.5, 128.5, 127.9 (2 signals), 116.0, 114.4, 107.2, 104.5, 76.0, 72.3, 68.7, 64.2, 61.1, 56.2, 52.3, 51.2, 33.5, 32.1, 26.6, 26.3; IR (thin film): 3075, 2950, 2855, 1750, 1713, 1638, 1497, 1435, 1344, 1266, 1230, 1195, 1156, 1072, 994, 921, 855, 806, 771, 740, 699 cm^{-1}; HRMS calc'd for $C_{30}H_{35}NO_7$ = 521.2414, found = 521.2427.

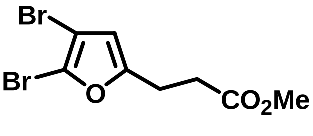

Compound 30

Cyclopropane **30** was prepared using the literature procedure Burgess, K., and Ke, C-Y. *Synthesis* **1996**, *12*, 1463, except that dimethyl malonate (15.47 g, 117.09 mmol) was used instead of diethyl malonate to yield cyclopropane **11** (25.10 g, 90.23 mmol, 77%) as a colorless oil. Also, the compound was purified by chromatography on silica gel (hexanes / ethyl acetate as eluent) instead of distillation. R_f = 0.46, 30% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.35-7.26 (m, 5H), 4.51 (d, J = 12.0 Hz, 1H), 4.43 (d, J = 12.0 Hz, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 3.59 (dd, J = 10.5, 5.4 Hz, 1H), 3.46 (dd, J = 10.5, 7.2 Hz, 1H), 2.29-2.25 (m, 1H), 1.59 (dd, J = 7.8, 4.8 Hz, 1H), 1.46 (dd, J = 9.6, 4.8 Hz, 1H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ = 170.2, 168.0, 137.8, 128.2, 127.5 (two signals), 72.7, 67.6, 52.5, 52.4, 32.6, 27.2, 18.7; IR (thin film): 3032, 2954, 2923, 2855, 1734, 1456, 1437, 1334, 1291, 1213, 1130, 927, 740 cm^{-1}; HRMS [M+H] calc'd for $C_{15}H_{19}O_5$ = 279.1232, found = 279.1236; $[\alpha]_D$ = -30 (*c* = 3.9, $CHCl_3$)



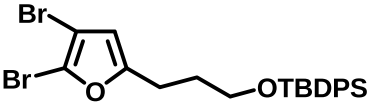
Compound 31b

The procedure is taken from Rathke, M.W.; Nowak, M. *J. Org. Chem.* **1985**, *50*, 2624. Lithium bromide (14.50 g, 167.55 mmol) was added to THF (350 mL) and cooled to 0 °C. Trimethylphosphonoacetate (27.84 g, 152.87 mmol) was added and the mixture stirred for 5 minutes. Triethylamine (15.47 g, 152.88 mmol) was added and the mixtures stirred for 10 minutes. **24a** (35.28 g, 138.85 mmol) was added as a solution in THF (50 mL) via cannula, and the reaction stirred for 2 hours at 0 °C, after which TLC indicated complete consumption of the starting material. Water (100 mL) was added, and the THF removed under reduced pressure. To the remaining aqueous layer was added water (300 mL) and ethyl acetate (300 mL) and the layers separated. The aqueous layer was washed three times with ethyl acetate and the combined organic layers were washed twice with 1 M sodium hydroxide, twice with water and once with brine. The organic layer was dried with $MgSO_4$, and concentrated under reduce pressure to yield **31b** (41.21 g, 132.88 mmol, 96%) as a brown solid which was of sufficient purity to be used directly in the next step Approximately 5-10% of an unidentifiable and inseparable isomer was present. If KOtBu was used as the base in this reaction a larger proportion (10-30%) of this byproduct resulted. R_f = 0.52 (20% ethyl acetate in hexanes) ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, J = 15.6 Hz, 1H), 6.63 (s, 1H), 6.34 (d, J = 15.6 Hz, 1H), 3.80 (s, 3H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ = 166.6, 152.5, 129.1, 126.0, 118.3, 117.4, 104.1, 51.8; IR (thin film): 1718, 1645, 1559, 1431, 1305, 1249, 1188, 1167, 1156, 981, 963, 817 cm^{-1}; HRMS calc'd for $C_8H_6Br_2O_3$ = 307.8684, found = 307.8690.



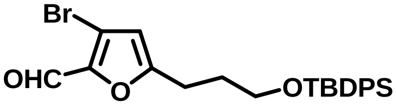
Compound 31c

Sodium acetate (39.68 g, 483.73 mmol), p-toluenesulfonhydrazide (63.04 g, 338.51 mmol) and **31b** (30.00 g, 97.64 mmol) were added to water (500 mL) and THF (500 mL) and the mixture was refluxed for 14 hrs, after which TLC indicated a small amount of starting material remained. Sodium acetate (6.00 g, 73.14 mmol) and p-toluenesulfonhydrazide (9.00 g, 48.33 mmol) were added and after refluxing for 4 more hours, TLC indicated complete consumption of the starting material. The reaction was cooled to room temperature and the THF was removed under reduced pressure. The resulting slurry was extracted three times with ether, and the combined organics washed with water then brine and dried with $MgSO_4$. The solvent was removed under reduced pressure and the resulting material was purified by flash column chromatography on silica gel (ethyl acetate / hexanes as eluent) to yield **31c** (28.92 g, 92.65 mmol, 96%) as a yellow oil. R_f = 0.49, 15% ethyl acetate in hexanes; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 6.13 (s, 1H), 3.70 (s, 3H), 2.94 (t, J = 8.0 Hz, 2H), 2.63 (t, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1, 156.4, 120.6, 111.2, 101.7, 51.7, 31.7, 23.5; IR (thin film): 3121, 2998, 2953, 2847, 1741, 1597, 1524, 1438, 1371, 1336, 1294, 1260, 1200, 1175, 1155, 975, 802 cm^{-1}; HRMS calc'd for $C_8H_8Br_2O_3$ = 309.8840, found = 309.8845.



Compound 31d

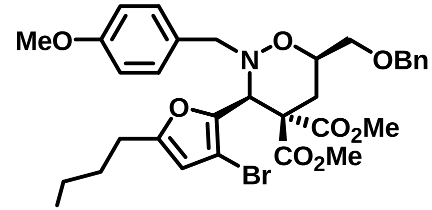
Dibromoester **31c** (27.65 g, 88.55 mmol) was dissolved in CH_2Cl_2 (800 mL) and cooled to 0 ^oC. DIBAL (135 mL of 1.5 M solution in toluene, 202.50 mmol) was added dropwise over 30 minutes, and after the addition was complete the reaction was stirred for 30 minutes at 0 ^oC. Water (20 mL) was added to quench the excess DIBAL (cautiously at first) and the mixture was stirred at 0 ^oC for 20 minutes, and then at room temperature for 40 minutes. The reaction was then filtered through celite to remove the gelatinous aluminum precipitate and the filter cake washed with CH_2Cl_2. The filtrate was dried with $MgSO_4$, and the solvent removed under reduced pressure to yield the crude alcohol as a yellow oil. Selected data for alcohol : R_f = 0.10, 20% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 6.12 (s, 1H), 3.69 (t, J = 6.3 Hz, 2H), 2.72 (t, J = 7.5 Hz, 2H), 1.90-1.85 (m, 2H); IR (thin film): ν_{max} = 3346 (broad), 3123, 2944, 2879, 1595, 1523, 1446, 1433, 1298, 1215, 1154, 1058, 995, 977, 949, 933, 795; HRMS calc'd for $C_7H_8Br_2O_2$ = 281.8891, found = 281.8884. The alcohol would decompose over a few days at room temperature, and was immediately dissolved in DMF (200 mL). Imidazole (6.32 g, 92.95 mmol) and N,N-dimethylaminopyridine (a few crystals) were added and the mixture cooled to 0 ^oC and stirred for 15 minutes. TBDPSCl (24.32 g, 88.55 mmol) was added and the reaction allowed to warm to room temperature and stirred for 14 hours. The reaction was poured into water (1 L) and extracted 3 times with ether (250 mL). The combined organics were washed with water, dried with $MgSO_4$ and the solvent removed under reduced pressure. The resulting crude oil was purified by flash column chromatography on silica gel (ethyl acetate / hexanes as eluent) to yield **31d** (41.76 g, 80.54 mmol, 91% for two steps) as a pale yellow oil. R_f = 0.71, 10% ethyl acetate in hexanes; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.71-7.68 (m, 4H), 7.49-7.40 (m, 6H), 6.04 (t, J = 0.8 Hz, 1H), 3.72 (t, J = 6.2 Hz, 2H), 2.77 (dt, J = 7.2, 0.8 Hz, 2H), 1.89 (app p, J = 7.0 Hz, 2H), 1.10 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.3, 135.5, 133.6, 129.7, 127.7, 120.0, 110.8, 101.6, 62.3, 30.2, 26.8, 24.7, 19.2; ; IR (thin film): 3071, 3049, 2931, 2894, 2857, 1591, 1472, 1428, 1390, 1361, 1154, 1112, 979, 823, 794, 738 cm^{-1}; HRMS calc'd for [M+H] $C_{23}H_{27}Br_2O_2Si$ = 521.0147, found = 521.0152.



Compound 31

The procedure used is an adaptation from Zaluski, M-C., Robba, M., and Bonhomme, M. *Bull. Soc. Chim. Fr.* **1970**, 1838 for the preparation of a similar compound. n-BuLi (13.3 mL of 1.6 M in hexanes, 21.28 mmol) was added to anhydrous ether (150 mL) and the solution was cooled to -78 ^oC. A solution of the dibromofuran **31d** (10.00 g, 19.28 mmol) in ether (75 mL) was added dropwise to the n-BuLi, and after addition was complete the mixture was stirred for 30 minutes at -78 ^oC. DMF (1.70 g, 26.98 mmol) in ether (75 mL) was then added dropwise, and after addition was complete the reaction was warmed to room temperature over two hours, and then refluxed for 30 minutes. Water (5 ml) was added to quench the reaction, followed by 5% HCl (300 mL). The layers were separated and the aqueous extracted 3 times with ether. The combined organics were washed with water and dried with $MgSO_4$ and the solvent removed under reduced pressure. Flash column chromatography on silica gel (hexanes / ethyl acetate as eluent) afforded **31** (5.82 g, 12.45 mmol, 65%) as a pale yellow oil. R_f = 0.45, 10% ethyl acetate in hexanes; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.60 (s, 1H), 7.66-7.63 (m, 4H), 7.46-7.36 (m, 6H), 6.22 (s, 1H), 3.69 (t, J = 5.8 Hz, 2H), 2.85 (t, J = 7.6 Hz, 2H), 1.96-1.89 (m, 2H), 1.05 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 175.2, 163.2, 146.9, 135.4, 133.4, 129.6, 127.6, 112.5, 62.2, 29.8, 26.7, 24.9, 19.1;

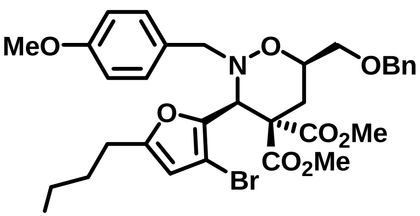
IR (thin film): 3071, 3049, 2931, 2857, 1677, 1571, 1519, 1472, 1463, 1428, 1384, 1361, 1279, 1112, 1020, 974, 823, 787, 741 cm^{-1}; HRMS - calc'd for [M+H] $C_{24}H_{28Br}O_3Si$ = 471.0991, found = 471.0998.



Compound 32

p-Methoxybenzylhydroxylamine **29** (1.73 g, 11.32 mmol), aldehyde **31** (5.29 g, 11.32 mmol), Yb(OTf)$_3$•xH$_2$O (0.88 g, 1.41 mmol) and molecular sieves were added to toluene (100 mL) and the reaction stirred at room temperature for 3 hours. Cyclopropane **30** (2.62 g, 9.43 mmol) was then added and the reaction heated to 100 °C for 20 hrs, after which NMR analysis of the crude reaction mixture indicated that the cyclopropane had been consumed. The reaction mixture was then cooled to room temperature and filtered through celite. The filter cake was washed with ethyl acetate and the solvent was removed under reduced pressure. The resulting crude residue was purified by flash column chromatography on silca gel (ethyl acetate/hexanes as eluent) to yield cycloadduct **32** (7.22 g, 8.20 mmol, 87%) as a viscous orange oil. R_f = 0.50, 40% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, CDCl$_3$): δ = 7.66-7.65 (m, 4H), 7.43-7.36 (m, 6H), 7.26-7.24 (m, 2H), 7.21-7.17 (m, 5H), 6.79 (d, J = 8.4 Hz, 2H), 6.01 (s, 1H), 4.98 (s, 1H), 4.38 (s, 2H), 4.21-4.19 (m, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 3.71 (d, J = 13.8 Hz, 1H), 3.66-3.60 (m, 3H), 3.53 (d, J = 5.4 Hz, 2H), 3.46 (s, 3H), 2.72 (t, J = 7.8 Hz, 2H), 2.47 (dd, J = 13.8, 12.0 Hz, 1H), 2.35 (dd, J = 13.8, 2.4 Hz, 1H), 1.90-1.79 (m, 2H), 1.06 (s, 9H); ^{13}C-NMR (150 MHz, CDCl$_3$): δ = 169.2, 168.1, 158.6, 157.0, 144.8, 138.2, 135.4, 133.6, 129.8, 129.5, 128.9, 128.0, 127.6, 127.4, 127.2, 113.2, 108.8, 103.0, 76.1, 72.9, 71.8, 62.4, 58.4, 57.7, 57.5, 55.0, 53.0, 52.5, 30.1, 28.1, 26.8, 24.5, 19.1; IR (thin film): 3000, 2953, 2858, 1743, 1613, 1589, 1514, 1430, 1362, 1303, 1250, 1179, 1112, 1038, 1008, 965, 824, 739, 703 cm^{-1}; HRMS calc'd for $C_{47}H_{54}BrNO_9Si$ = 883.2751, found = 883.2730; $[\alpha]_D$ = +35.9 (*c* = 11.52, CHCl$_3$)

The enantiomeric excess of **32** could not be determined due to the –TBDPS making it difficult to separate the enantiomers of a racemic sample of **32** using chiral HPLC. As a result, **HPLC Compound 1** was prepared from **32.**

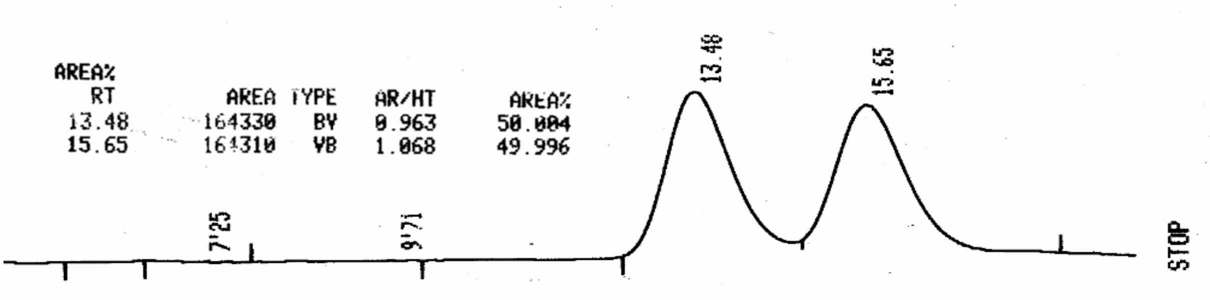


HPLC Compound 1

Compound **32** (160 mg, 0.181 mmol) was dissolved in THF (10 mL). TBAF (0.36 mL of a 1M solution in THF, 0.36 mmol) was added, and after 1 hour TLC indicated complete consumption of the starting material. Saturated ammonium chloride (1 mL) was added and the THF removed under reduced pressure. Water (15 mL) and EtOAc (15 mL) were added to the residue and the layers separated. The aqueous layer was washed 3 times with ethyl acetate, and the combined organics dried with MgSO$_4$. Removal of the solvent under reduced pressure produced an oil that was purified by column chromatography on silica gel (ethyl acetate / hexanes as eluent) to yield **HPLC Compound 1** (108 mg, 0.167 mmol, 92 %) as a pale yellow oil. R_f = 0.30, 60% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, CDCl$_3$): δ = 7.31 (t, 7.5 Hz, 2H), 7.27-7.21 (m, 5H), 6.81 (d, J = 6.6 Hz, 2H), 6.08 (s, 1H), 4.99 (s, 1H), 4.48-4.42 (m, 2H), 4.19-4.17 (m, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 3.73 (d, J = 13.8 Hz, 1H), 3.64 (d, J = 13.8 Hz, 1H), 3.60-3.55 (m, 4 H), 3.53 (s, 3H), 2.73-2.65 (m, 2H), 2.56 (dd, J = 13.8, 12.0 Hz, 1H), 2.35 (dd, J

= 13.8, 1.8 Hz, 1H), 1.88-1.79 (m, 2 H), 1.63 (br s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 169.3, 168.4, 158.6, 157.1, 144.8, 138.2, 130.0, 128.8, 128.2, 127.6, 127.4, 113.3, 108.9, 103.3, 76.1, 73.1, 71.6, 61.4, 58.5, 57.8, 57.4, 55.1, 53.2, 52.7, 30.6, 28.0, 24.6; IR (thin film): 3448, 3032, 3002, 2953, 1741, 1616, 1514, 1465, 1457, 1437, 1302, 1250, 1176, 1102, 1036, 1006, 969, 918, 825, 739, cm^{-1}; HRMS calc'd for $C_{31}H_{36}BrNO_9$ = 645.1574, found = 645.1578; $[\alpha]_D$ = +46.5 (*c* = 1.80, $CHCl_3$).

The enantiomeric excess was determined to be >95% by chiral HPLC (Chiralcel OD-H, 250 x 4.6 mm^2, Diacel Chemical Industries; 93:7 Hexanes / *i*-PrOH at 1.5 mL/min; 220 nm; The retention time for the enantiomers of the racemic sample were r_t(+) = 13.5 min, r_t (-) = 15.7 min.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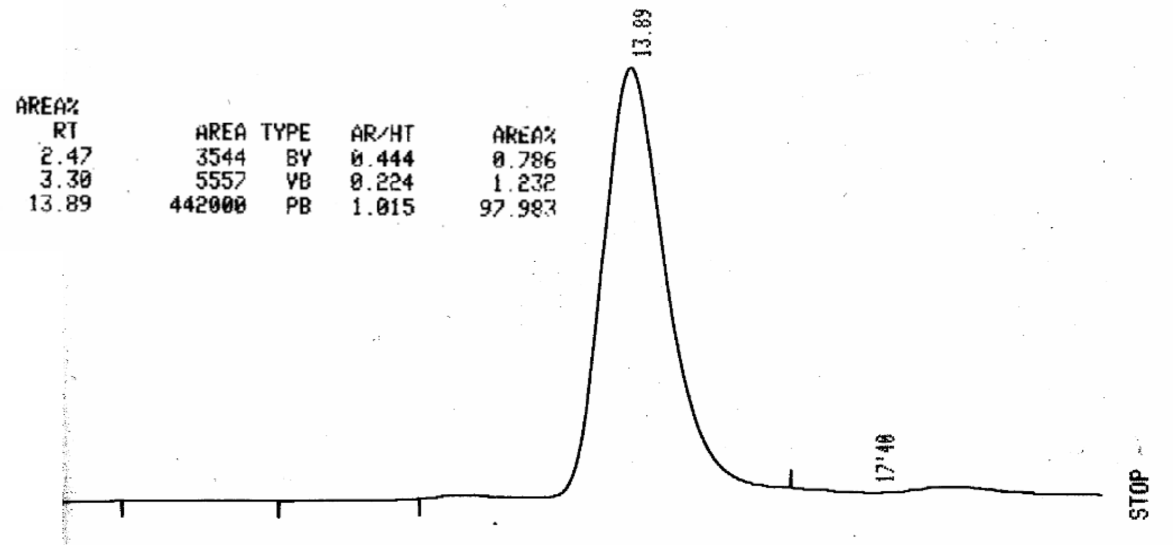
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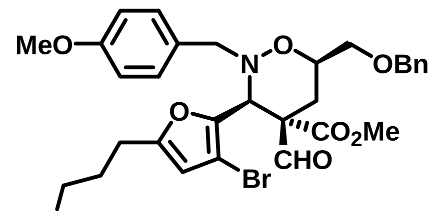
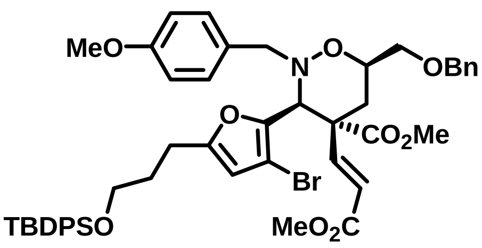


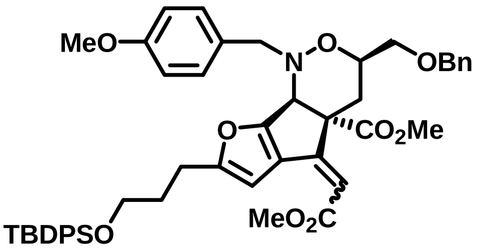
Compound 33

Cycloadduct **32** (7.20 g, 8.17 mmol) was dissolved in methylene chloride (300 mL) and then cooled to –78 °C. DIBAL (28.8 mL of 1.5M solution in toluene, 43.20 mmol) was added dropwise and the reaction stirred for 15 minutes, after which multiply eluted TLC showed complete consumption of the starting material. Methanol (20 mL) was then added slowly to quench the excess DIBAL, and the mixture stirred at –78 °C for 20 minutes, after which it was removed from the dry ice bath and allowed to warm to room temperature. The reaction was then poured into 5% HCl (300 mL) and the layers separated. The aqueous layer was extracted 3 times with methylene chloride, and the combined organics washed with 5% HCl. The organic layer was dried with $MgSO_4$, and the solvent removed under reduced pressure. The residual material was purified by flash column chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield aldehyde **33** (6.08 g, 7.15 mmol, 87%) as viscous yellow oil. R_f = 0.50, 40% ethyl acetate in hexanes; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.17 (s, 1H), 7.66-7.64 (m, 4H), 7.44-7.36 (m, 6H), 7.28-7.24 (m, 2H), 7.22-7.17 (m, 5H), 6.88 (d, J = 8.4 Hz, 2H), 6.01 (s, 1H), 5.05 (s, 1H), 4.40 (s, 2H), 4.40-4.34 (m, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 3.75 (d, J = 13.6 Hz, 1H), 3.65-3.60 (m 3H), 3.55-3.54 (m, 2H), 2.70 (t, J = 7.4 Hz, 2H), 2.26 (dd, J = 13.8, 11.4 Hz, 1H), 2.18 (dd, J = 13.8, 2.8 Hz, 1H), 1.86-1.78 (m, 2H), 1.06 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 194.8, 168.7, 158.6, 158.0, 143.7, 138.1, 135.4, 133.5, 129.8, 129.5, 128.5, 128.1, 127.6, 127.4, 127.3, 113.2, 108.8, 103.8, 75.9, 72.9, 71.7, 62.8, 62.4, 58.1, 56.7, 55.0, 53.1, 30.1, 26.7, 24.9, 24.5, 19.1; IR (thin film): 3071, 3048, 3032, 3012, 3000, 2954, 2932, 2906, 2897, 2858, 1751, 1722, 1613, 1514, 1429, 1389, 1362, 1303, 1248, 1174, 1111, 1107, 1035, 1009, 999, 970, 823, 806, 740, 701 cm^{-1}; HRMS calc'd for $C_{46}H_{52}BrNO_8Si$ = 853.2646, found = 853.2619; $[\alpha]_D$ = +34.4 (*c* = 1.67 $CHCl_3$)



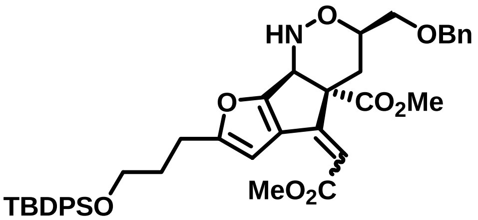
Compound 34

Trimethyl phosphonoacetate (2.96 g, 16.28 mmol) was dissolved in THF (400 mL) and cooled in an ice bath. KO*t*Bu (1.83 g, 16.28 mmol) was added in small portions and after addition was complete, the slurry was stirred for 10 minutes. Aldehyde **33** (11.54 g, 13.57 mmol) in THF (100 mL) was then added slowly via cannula, and TLC indicated complete consumption of the starting material after 11 hours. Water (50 mL) was added, and the THF removed under reduced pressure. To the resulting residue was added water (500 mL), 5% HCl (20 mL) and ethyl acetate (200 mL). The layers were separated, and the aqueous washed 3 times with ethyl acetate. The combined organics were washed once with 1M NaOH and twice with water, followed by brine. The combined organics were dried with $MgSO_4$, the solvent removed under reduced pressure, and the residual material purified by column chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield enoate **34** (11.40 g, 12.54 mmol, 93%) as a viscous yellow oil. In most cases this compound was of high purity and did not need to be purified by column. R_f = 0.50, 40% ethyl acetate in hexanes; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.66-7.64 (m, 4H), 7.45-7.36 (m, 6H), 7.28-7.24 (m, 2H), 7.22-7.15 (m, 5H), 6.79 (d, J = 8.8 Hz, 2H), 6.58 (d, J = 16.0 Hz, 1H), 5.99 (s, 1H), 5.75 (d, J = 16.0 Hz, 1H), 4.81 (s, 1H), 4.40 (s, 2H), 4.40-4.32 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.71 (d, J = 13.6 Hz, 1H), 3.64-3.60 (m, 3H), 3.58 (s, 3H), 3.53 (d, J = 4.8 Hz, 2H), 2.69 (t, J = 7.4 Hz, 2H), 2.23 (dd, J = 13.8, 2.4 Hz, 1H), 2.14 (dd, J = 13.8, 13.4 Hz, 1H), 1.89-1.84 (m, 2H), 1.05 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 171.7, 165.7, 158.5, 157.1, 145.8, 144.6, 138.1, 135.3, 133.5, 129.7, 129.5, 128.8, 128.0, 127.5, 127.4, 127.3, 121.9, 113.1, 108.7, 103.7, 76.1, 72.8, 71.6, 62.2, 59.2, 58.3, 54.9, 52.7 (2 signals), 51.4, 30.2, 29.1, 26.7, 24.4, 19.0; IR (thin film): 3071, 3047, 3030, 3011, 2999, 2952, 2933, 2898, 2858, 1734, 1653, 1613, 1589, 1514, 1429, 1317, 1247, 1173, 1111, 1106, 1037, 976, 912, 824, 739, 702 cm^{-1}; HRMS calc'd for $C_{49}H_{56}BrNO_9Si$ = 909.2908, found = 909.2873; $[\alpha]_D$ = +45.2 (*c* = 3.07, $CHCl_3$)



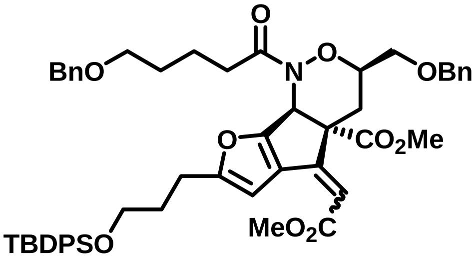
Compound 35

Enoate **34** (11.44 g, 12.62 mmol) was dissolved in DMF (300 mL) and Ag_2SO_4 (3.92 g, 12.62 mmol), NEt_3 (5.10 g, 50.46 mmol), and $Pd(PPh_3)_4$ (1.46 g, 1.26 mmol) added. The mixture was refluxed for 1 hour, after which TLC indicated complete consumption of the starting material. The reaction mixture was poured into water (1200 mL) and 5% HCl (200 mL) and extracted 4 times with ether. The combined organics were washed with water, and dried with $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica (hexanes/ethyl acetate as eluent) to produce **35** (8.56 g, 10.37 mmol, 82%) as an orange foam. Only one double bond isomer was produced but the configuration was not determined since the double bond would be reduced at a later stage. R_f = 0.39, 40% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.67-7.66 (m, 4H), 7.44-7.42 (m, 2H), 7.40-7.37 (m, 4H), 7.30-7.27 (m, 4H), 7.23-7.21 (m, 1H), 7.16-7.14 (m, 2H), 6.80-6.78 (m, 2H), 6.02 (s, 1H), 5.78 (s, 1H), 4.64-4.59 (m, 1H), 4.26 (d, J = 12.6 Hz, 1H), 4.20 (s, 1H), 4.13 (d, J = 12.6 Hz, 1H), 3.91 (d, J = 12.0 Hz, 1H), 3.76-3.74 (m, 6H), 3.70 (s, 3H), 3.68 (s, 3H), 3.18-3.11 (m, 2H), 2.82-2.77 (m, 3H), 1.92 (p, J = 7.2 Hz, 2H), 1.44 (dd, J = 13.2, 10.2 Hz, 1H), 1.06 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ = 172.5, 166.2, 164.4, 162.1, 158.6, 154.3, 138.4, 135.2, 133.4, 130.7, 129.4, 128.9, 127.8, 127.5, 127.1, 126.9, 113.1, 106.3, 100.3, 74.3, 72.5, 71.9, 68.2, 62.3, 60.7, 59.5, 54.7, 51.8, 50.8, 30.1, 28.7, 26.6, 24.9, 18.9; IR (thin film): 3070, 3031, 299, 2951, 2857, 1751, 1717, 1635, 1513, 1457, 1430, 1341, 1250, 1195, 1155, 1107, 1030, 982, 925, 855, 822, 804, 738, 702 cm^{-1}; HRMS calc'd for $C_{49}H_{55}NO_9Si$ = 829.3646, found = 829.3662; $[\alpha]_D$ = -65.5 (*c* = 2.50, $CHCl_3$).



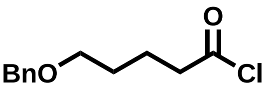
Compound 36

Heck product **35** **(**25.20 g, 30.51 mmol) was dissolved in CH_2Cl_2 (450 mL) and water (45 mL) was added. The reaction was stirred vigorously and cooled to 0 °C, and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (7.43 g, 32.73 mmol) was added. The reaction was kept at 0 °C for 20 minutes, and then allowed to stir at room temperature for 5 hours. TLC analysis of the reaction mixture showed that starting material still remained, but the reaction was stopped due to the formation of imine by-product. Ethyl acetate was added (1.2 litres) and the reaction mixture poured into 500 mL of saturated $NaHCO_3$ solution. The layers were separated, and the aqueous layer was extracted 3 times with ethyl acetate, and the combined organic layers were washed with saturated $NaHCO_3$ and brine and dried with $MgSO_4$. The solvent was removed under reduced pressure to yield a residue that was purified by column chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield the product **36** (9.66 g, 13.71 mmol, 45 %) as an off white foam. 8.32 g of a 3:1 mix of starting material to imine by-product was also recovered and was resubjected to the reaction above using 4.01 g (17.68 mmol) of DDQ, 135 mL of CH_2Cl_2 and 15 mL of water. After 2 hours the reaction was worked up and purified as above to yield an additional 2.88 g (4.09 mmol) of product, bringing the overall yield after one recycle to 12.54 g, 17.79 mmol, 58 %. R_f = 0.30, 40% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.66-7.65 (m, 4H), 7.44-7.41 (m, 2H), 7.39-7.37 (m, 4H), 7.33-7.24 (m, 5H), 5.99 (s, 1H), 5.79 (s, 1H), 5.40 (d, J = 4.5 Hz, 1H), 4.56 (d, J = 12.3 Hz, 1H), 4.50 (d, J = 12.3 Hz, 1H), 4.47 (d, J = 4.5 Hz, 1H), 4.34-4.31 (m, 1H), 3.72-3.70 (m, 5H), 3.69 (s, 3H), 3.48 (dd, J = 11.1, 3.0 Hz, 1H), 3.41 (dd, J = 11.1, 6.0 Hz, 1H), 2.84 (dd, J = 14.4, 3.0 Hz, 1H), 2.79 (t, J = 7.5 Hz, 2H), 1.91 (p, J = 7.5 Hz, 2H), 1.63 (dd, J = 14.4, 11.4 Hz, 1H), 1.06 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 172.7, 166.8, 164.8, 161.8, 154.5, 137.9, 135.5, 133.7, 130.2, 129.6, 128.3 127.7, 127.6 (2 signals), 106.5, 100.5, 76.0, 73.4, 72.1, 62.6, 61.1, 55.9, 52.3, 51.2, 30.3, 30.0, 26.8, 25.2, 19.2; IR (thin film): 3256, 3089, 3071, 3051, 3030, 2999, 2951, 2931, 2896, 2858, 1737, 1710, 1638, 1429, 1343, 1231, 1197, 1168, 1155, 1111, 1029, 824, 738, 702 cm^{-1}; HRMS calc'd for $C_{41}H_{47}NO_8Si$ = 709.3071, found = 709.3076; $[\alpha]_D$ = -38.6 (*c* = 2.33, $CHCl_3$).



Compound 37

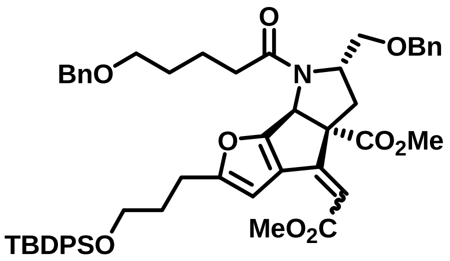
Oxazine **36** (12.54 g, 17.79 mmol) and triethylamine (5.40 g, 53.36 mmol) were dissolved in CH_2Cl_2 (160 mL) and cooled to 0 ^{o}C. A solution of acid chloride (5.70 g, 24.92 mmol, see preparation below) in CH_2Cl_2 (80 mL) was added dropwise and the reaction stirred at room temperature for 18 hours. The reaction was poured into water (200 mL) and the layers separated. The aqueous layer was extracted three times with CH_2Cl_2 and the combined organics were washed with 5% HCl, 1M NaOH, and brine, and then dried with $MgSO_4$. The solvent was removed under reduced pressure to yield a residue that was purified by column chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield the product **37** (14.27 g, 15.91 mmol, 89 %) as a viscous yellow oil. A small amount of starting material **36** (0.43 g, 0.61 mmol) was also recovered. R_f = 0.40, 40% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.66-7.65 (m, 4H), 7.44-7.41 (m, 2H), 7.38 (t, J = 7.4 Hz, 4H), 7.33-7.25 (m, 10H), 6.08 (s, 1H), 5.98 (s, 1H), 5.79 (s, 1H), 4.52 (s, 2H), 4.48 (s, 2H), 4.44-4.40 (m, 1H), 3.71-3.69 (m, 8H), 3.51 (dd, J = 11.4, 2.4 Hz, 2H), 3.48 (t, J = 6.3 Hz, 2H), 3.41 (dd, J = 11.4, 7.2 Hz, 1H), 2.83 (dd, J = 13.8, 2.4 Hz, 1H), 2.77 (t, J = 7.8 Hz, 2H), 2.73-2.67 (m, 1H), 2.61-2.56 (m, 1H), 1.91-1.86 (m, 2H), 1.80-1.75 (m, 2H), 1.67 (p, J = 7.8 Hz, 2H), 1.61 (dd, J = 13.8, 11.7 Hz, 1H), 1.06 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 173.7, 171.3, 166.5, 164.7, 160.3, 153.1, 138.4, 137.5, 135.3, 133.3 (2 signals), 129.9, 129.4, 128.1, 128.0, 127.4, 127.3, 127.1, 109.4, 106.6, 100.4, 79.1, 73.0, 72.5, 70.8, 69.7, 62.3, 55.8, 53.0, 52.2, 51.0, 31.6, 31.0, 30.0, 29.0, 26.6, 24.9, 20.9, 18.9; IR (thin film): 3069, 3031, 2931, 2857, 1741, 1707, 1676, 1636, 1560, 1473, 1457, 1430, 1395, 1344, 1201, 1152, 1106, 1017, 965, 923, 852, 823, 739, 702 cm^{-1}; HRMS calc'd for $C_{53}H_{61}NO_{10}Si$ = 899.4065, found = 899.4045; $[\alpha]_D$ = -77.7 (*c* = 3.24, $CHCl_3$).



5-benzyloxy-n-pentanoic acid was prepared by modifying the procedure of Borjesson, L.; Corsegh, I.; and Welch, C.A. *J. Org. Chem.* **1995**, *60*, 2989. For a reference that contains full data for the acid, as well as scans of the proton and carbon spectra, see Jacobi, P.A.; Li, Y.; *Org. Lett.* **2003**, *5*, 701. A solution of 1,5-pentanediol (98.91 g, 949.68 mmol) in THF (200 mL) was added via an addition funnel over 30 minutes to a slurry of NaH (3.91 g, 6.51 g of 60% suspension in mineral oil, 162.84 mmol) in THF (400 mL) at 0 ^{o}C. After stirring for 30 minutes at this temperature, a solution of benzyl bromide (23.20 g, 135.64 mmol) in THF (200 mL) was added over 30 minutes via an addition funnel. The reaction was warmed to room temperature, and stirred for 20 hours. Water (20 mL) was then added, and the THF removed under reduced pressure to yield an oil that was partitioned between water (1 L) and ethyl acetate (250 mL). The layers were separated, and the aqueous layer washed 3 times with EtOAc. The combined organic layers were washed 6 times with water (150 mL each wash), and then dried with $MgSO_4$. Removal of the solvent under reduced pressure produced a colorless oil (24.60 g, 126.62 mmol, 98%)

that was of high purity and could be used without further purification. 5-benzyloxy-1-pentanol (14.32 g, 73.71 mmol) was dissolved in acetone (400 mL) and the solution cooled to 0 ^{o}C. Jones Reagent (184.25 mmol, 275 mL of an ~0.67 M solution) was added dropwise over 20 minutes, and the reaction was kept at 0 ^{o}C for one hour. Isopropanol (20 mL) was then added, and stirring at 0 ^{o}C continued for 30 minutes. Solid sodium bicarbonate was added cautiously until the solution was neutral, and the chromium precipitate was removed by filtration through celite with the filter cake being washed with acetone and ether. The acetone and ether were removed under reduced pressure, and the solution was made basic (pH > 12) with solid NaOH. The aqueous layer was extracted 3 times with ether, and then made acidic (pH < 1) with concentrated HCl. The aqueous layer was extracted 3 times with ether, and the combined organics dried with $MgSO_4$ and the solvent removed under reduced pressure to produce the acid as a dark green oil, which was of high purity by NMR. Purification by a small silica column (hexanes / ethyl acetate as eluent, $R_f = 0.50$, 50% ethyl acetate/hexanes) yielded the desired acid (8.81 g, 41.90 mmol, 57%) as a white, low melting solid. Spectroscopic data was consistent with the literature references The desired acid chloride was prepared according to the following procedure; 5-benzyloxy-n-pentanoic acid (5.52 g, 26.22 mmol) was dissolved in 80 mL of toluene, and 8 drops of DMF was added. Oxalyl chloride (4.66 g, 36.74 mmol) was then added dropwise, and the reaction stirred at room temperature for 30 minutes. The reaction was then heated to 60 ^{o}C for 1.5 hours. After cooling to room temperature, the toluene was removed under reduced pressure to produce the acid chloride as an orange oil. This acid chloride was dissolved in CH_2Cl_2 (80 mL) and used directly in the reaction above.

Compounds 39 were prepared in three steps from **37** without full characterization of the intermediates. The aminoalcohols resulting from N-O bond cleavage were susceptible to lactonization, and as a result were immediately mesylated after rapid column chromatography. The mesylates were also unstable, with decomposition products visible 30 minutes after rapid chromatography. As a result **37** was quickly converted into the appropriate pyrrolidines **39** over three successive steps.

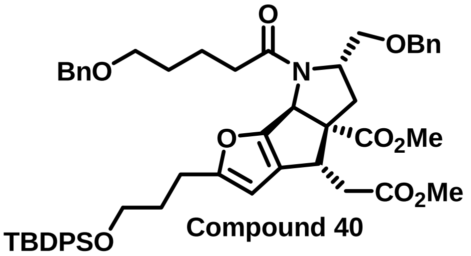


Compound 39

Compound 37 (1.97 g, 2.20 mmol) was dissolved in THF (30 mL) and cooled to 0 ^{o}C. A 0.1M solution of SmI_2 (prepared by refluxing 3.43g (13.50 mmol) of iodine and 2.23 g (14.81 mmol) of Sm metal (~40 mesh) in THF (135 mL) for three hours (the deep blue color should be present after ~20 min)) cooled to 0 ^{o}C was added rapidly via cannula, and after 30 minutes the deep blue color had faded. Saturated $NaHCO_3$ (30 mL) was added, and the mixture stirred for 5 minutes. The resulting precipitate was removed by filtration through celite, the filter cake was washed with EtOAc, and the THF and EtOAc was removed under reduce pressure, with a rotory evaporator bath at less than 30 ^{o}C. Water was added (100 mL) and the aqueous layer extracted 3 times with EtOAc. The combined organics were dried with $MgSO_4$, and concentrated under reduced pressure with a bath temp of less than 30 ^{o}C. TLC analysis of the worked up reaction mixture indicated that lactonization was starting to occur, so the resulting orange oil was subjected to rapid flash column chromatography on silica (ethyl acetate / hexanes as eluent) to yield the non-isomerized amidoalcohol (1.36 g, 1.51 mmol, $R_f = 0.18$, 50% ethyl acetate in hexanes) and an amidoalcohol in which the double bond had isomerised (0.273 g, 0.306 mmol, $R_f = 0.36$, 50% ethyl acetate in hexanes) as yellow oils. Each amidoalcohol was independently subjected to the following procedure. The amidoalcohol (non-isomerized, 1.36 g, 1.51 mmol; isomerized, 0.273 g, 0.306 mmol) was dissolved in CH_2Cl_2 (non-isomerized 50 mL; isomerized 20 mL). Triethylamine (non-isomerized, 0.460 g, 4.55 mmol; isomerized, 0.092 g, 0.909 mmol) and a few crystals of DMAP were added. The reaction was cooled to 0 ^oC, and methanesulfonyl chloride (non-isomerized, 0.347 g, 3.03 mmol; isomerized, 0.069 g, 0.606 mmol) was added dropwise. TLC indicated the reaction was complete within 20 minutes, and the reaction mixture was directly absorbed onto silica gel in preparation for column chromatography. Rapid column chromatography on silica gel (hexanes / ethyl acetate as eluent) yielded the amidomesylate (non-isomerized, 1.34 g, 1.37 mmol, R_f = 0.42, 50% ethyl acetate in hexanes; isomerized, 0.230 g, 0.235 mmol, Rf = 0.55, 50% ethyl acetate in hexanes) as yellow oils. Each amidomesylate was independently subjected to the following procedure to form the stable pyrrolidine. The amidomesylate (non-isomerized, 1.34 g, 1.37 mmol; isomerized, 0.230 g, 0.235 mmol) was dissolved in THF (non-isomerized, 50 mL; isomerized, 20 mL) and the solution cooled to -20 to -30 ^oC. This temperature is crucial because lower temperatures lead to slower reaction and decomposition, while higher temperatures lead to rapid formation of side products in some instances. KOtBu was added (non-isomerized, 0.269 g, 2.40 mmol; isomerized, 0.053 g, 0.47 mmol) and after 20 minutes TLC indicated that a small quantity of starting material remained, so 20 mg of KOtBu was added to each reaction, and the reactions were complete by TLC after 15 additional minutes. Saturated ammonium chloride solution was added, and the reaction was warmed to room temperature. The THF was removed under reduced pressure, and the resulting residue was partitioned between water and ethyl acetate, and the layers were separated. The aqueous layer was washed 3 times with ethyl acetate, and the combined organics dried with $MgSO_4$. The solvent was removed under reduced pressure, and the resulting residue purified by column chromatography on silica gel (ethyl acetate / hexanes as eluent to yield **39 (non-isomerized)** (1.10 g, 1.24 mmol, 56% overall for 3 steps) and **39 (isomerized)** (0.180 g, 0.204 mmol, 9% overall for 3 steps) for an overall yield of 65%. The non-isomerized pyrrolidine was always the major product, but more of the isomerized product could be obtained if a larger excess of SmI_2 was used.

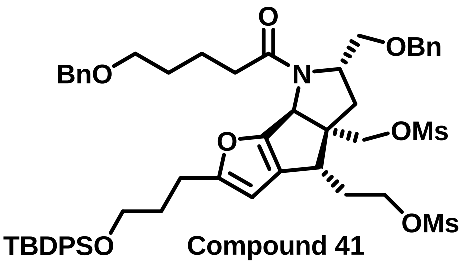
39 (non-isomerized) was formed in a 50:43 mixture of rotamers. A single proton of the major rotamer was set to one for proton integration. R_f = 0.70, 50% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.66-7.65 (m, 7.9H), 7.44-7.41 (m, 4.1H), 7.39-7.24 (m, 25.9H), 5.95 (s, 0.9H), 5.91 (s,1.0H), 5.80 (s, 0.9H), 5.76 (s, 1.0H), 5.32 (s, 1.0H), 5.17 (s, 0.9H), 4.64 (d, J = 12.0 Hz, 1.1H), 4.56 (m, 1.9H), 4.50 (d, J = 12.0 Hz, 1.2H), 4.47 (s, 1.9H), 4.43 (s, 2.2H), 4.30-4.23 (m, 2.0H), 4.10 (dd, J = 8.4, 3.0 Hz, 0.9H), 3.86 (m, 1.2H), 3.76 (t, J = 9.0 Hz, 1.0H), 3.71-3.65 (m, 16.9H), 3.49 (t, J = 6.3 Hz, 2.0H), 3.39 (t, J = 6.3 Hz, 2.0H), 3.36- 3.29 (m, 2.1H), 2.80- 2.68 (m, 5.0H), 2.51-2.46 (m, 0.9H), 2.44-2.39 (m, 1.1H), 2.35-2.30 (m, 1.1H), 2.22-2.17 (m, 2.0H), 1.91-1.83 (4.1H), 1.80-1.52 (10.2H), 1.06 (s, 8.0H), 1.05 (s, 9.0H) ; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 172.8, 172.4, 172.3, 171.9, 166.5, 166.2, 164.7, 163.8, 161.6, 153.4, 152.3, 138.4, 138.3, 135.3, 133.4, 133.3, 130.2, 129.4, 130.2, 129.4 (2 signals), 128.1, 128.0 (2signals), 127.6, 127.4, 127.3, 127.2, 127.1, 106.9, 105.9, 100.1, 99.4, 73.2, 73.0, 69.8, 69.5, 68.5, 66.5, 65.1, 62.4, 62.2, 60.0, 59.0, 52.4, 52.3, 51.0, 50.9, 35.8, 34.6, 33.6, 30.0, 29.1, 28.9, 26.6, 25.0, 24.9, 21.9, 21.7, 18.9; IR (thin film): 3069, 3055, 3049, 2950, 2932, 2857, 1745, 1708, 1654, 1641, 1473, 1454, 1429, 1400, 1362, 1344, 1231, 1195, 1167, 1154, 1111, 1028, 823, 812, 738, 702 cm^{-1}; HRMS calc'd for $C_{53}H_{61}NO_9Si$ = 883.4116, found = 883.4125; $[\alpha]_D$ = -96.2 (*c* = 2.35, $CHCl_3$).

39 (isomerized) was formed in a 100:37 mixture of rotamers. A single proton of the major rotamer was set to one for proton integration. R_f = 0.56, 40% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.66-7.64 (m, 6.0H), 7.43-7.36 (m, 9.2H), 7.37-7.24 (m, 12.3H), 6.70 (s, 1.0H), 6.67 (s, 0.4H), 5.74 (s, 1.0H), 5.74 (s, 0.3H), 5.66 (s, 1.0H), 5.62 (s, 0.3H), 4.49 (s, 2.1H), 4.43-4.42 (m, 1.6H), 4.40-4.38 (m, 3.2H), 4.12-4.09 (m, 0.4H), 3.82 (dd, J = 8.7, 3.9 Hz, 1.1H), 3.73 (s, 4.3H), 3.70 (app. t, J = 6.0 Hz, 3.0H), 3.52 (t, J = 6.6 Hz, 2.2H), 3.46 (s, 4.2H), 3.43-3.73 (m, 2.4H), 3.33 (dd, J = 9.3, 3.3 Hz, 0.4 Hz,), 3.04 (d, J = 13.8 Hz, 0.4H), 2.97 (dd, J = 14.4 Hz, 1.1H), 2.84-2.79 (m, 1.9H), 2.76 (t, J = 8.1 Hz, 2.2H), 2.61-2.56 (m, 1.1H), 2.31-2.28 (m, 0.8H), 2.20-2.12 (m, 1.5H), 1.95-1.87 (m, 3.2H), 1.84-1.68 (m, 5.2H), 1.05-1.04 (m, 13.2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 172.2, 172.1, 171.4, 170.6, 166.7, 166.6, 165.8, 163.9, 163.1, 162.9, 152.3, 151.3, 138.3, 137.7, 137.1, 135.3, 133.5, 133.4, 129.4, 129.3, 128.3, 128.1 (2 signals), 127.6 (2 signals), 127.4, 127.3, 127.2, 126.2, 126.1, 106.9, 106.0, 105.6, 104.7, 73.1, 72.7, 72.6, 71.8, 70.6, 69.9, 69.7, 67.5, 65.6, 62.7, 62.5, 61.8, 61.4, 59.1, 58.9, 57.8, 52.5, 50.9 (2 signals), 38.1, 37.4, 34.3, 33.4, 30.3, 30.2, 29.2, 28.9, 26.6, 25.1, 25.0, 22.0, 21.8, 18.9; IR (thin film): 3070, 3031, 2951, 2932, 2858, 1738, 1723, 1638, 1460, 1454, 1429, 1407, 1384, 1361, 1289, 1241, 1221, 1196, 1111, 1061, 1028, 1010, 857, 824, 739, 702 cm^{-1}; HRMS calc'd for $C_{53}H_{61}NO_9Si$ = 883.4116, found = 883.4125; $[\alpha]_D$ = -108.8 (*c* = 1.47, $CHCl_3$).



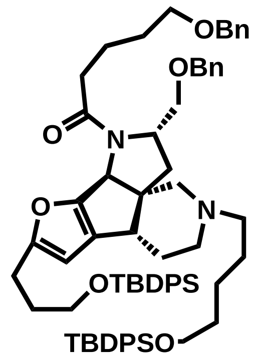
Compound 40

Both **39 (non-isomerized) and 39 (isomerized)** yielded **20** in approximately the same yield, so a representative experimental procedure will be given using **39 (non-isomerized)**. Compound **39** (0.970 g, 1.10 mmol) and $NiCl_2{\bullet}6H_2O$ (0.104 g, 0.439 mmol) were dissolved in a mixture of methanol (100 mL) and THF (15 mL). Na_2CO_3 (0.600 g) was added, and the reaction mixture cooled to -50 °C. $NaBH_4$ (0.414 g, 10.97 mmol, 10eq) was added, and after 20 minutes another 10 eq of $NaBH_4$ was added. The reaction was stirred for another 30 minutes after which it turned black and hydrogen evolution started to occur. In some instances, it took more than an hour to initiate so it was warmed to -40 °C. Once the reaction initiated, the reaction was kept between -50 and -55 °C and 40 more equivalents of $NaBH_4$ (10 eq every 20 minutes) was added (the isomerized sample needed 100 more equivalents). Stirring occurred for an additional two hours at -50 °C, after which the cold solution was rapidly filtered through a pad of celite to remove the black precipitate. The filter cake was washed with EtOAc, and 20 mL of water was added to the filtrate. The organic solvent was removed under reduced pressure, and to the resulting aqueous phase was added 30 mL of water and 50 mL of ethyl acetate. 20 mL of 5% HCl was also added to destroy the emulsion. The layers were separated, and the aqueous layer extracted three times with EtOAc. The combined organics were washed with water then brine, and dried with $MgSO_4$ The solvent was removed under reduced pressure to yield a crude oil that was purified by column chromatography on silica gel (ethyl acetate / hexanes as eluent) to yield **40** (0.642 g, 0.722 mmol, 67 %) as a yellow oil. The NMR shows that there may be ~7% of what might be the diastereomer resulting from hydrogen delivery from the opposite face. The isomerized compound produces a slightly higher percentage (13%) of the undesired diastereomer. Product formed as a 9:1 mixture of rotamers. A single proton of the major rotamer was set to one for proton integration. R_f = 0.70, 50% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.65-7.63 (m, 5.1H), 7.43-7.40 (m, 2.4H), 7.33-7.22 (m, 13.2H), 5.84 (s, 0.1H), 5.75 (s, 1.0H), 5.71 (s, 0.1H), 5.67 (s, 1.0H), 4.49-4.48 (m, 2.4H), 4.47-4.43 (m, 1.6H), 4.40-4.38 (m, 1.4H), 4.27-4.24 (m, 1.1H), 3.69-3.65 (m, 6.3H), 3.56 (d, J = 6.0Hz, 0.9H), 3.54-3.51 (m, 6.8H), 3.46-3.42 (m, 1.7H), 3.31-3.28 (m, 1.3H), 3.02 (d, J = 13.2 Hz, 0.1H), 2.96 (d, J = 13.8 Hz, 1.0H), 2.84 (dd, J = 15.9, 2.9 Hz, 0.2H), 2.79-2.74 (m, 1.3H), 2.70-2.65 (m, 2.4H), 2.59-2.54 (m, 1.4H), 2.46-2.41 (m, 1.3H), 2.20-2.15 (m, 2.4H), 1.85-1.78 (m, 5.0H), 1.75-1.70 (m, 2.9H), 1.04-1.03 (m, 12.0H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 172.5, 172.2, 171.6, 161.5, 153.3, 138.4, 137.9, 135.3, 133.6, 129.4, 128.2, 128.1, 127.6, 127.5, 127.4 (2 signals), 127.2 (2 signals), 103.7, 73.1, 72.7, 70.1, 69.0, 68.3, 62.7, 61.5, 57.0, 52.0, 51.5, 42.4, 38.7, 37.0, 34.3, 30.4, 29.6, 26.7, 25.1, 21.6, 19.0; IR (thin film): 3068, 3029, 2951, 2930, 2857, 1737, 1655, 1471, 1461, 1454, 1446, 1439, 1360, 1291, 1214, 1111, 1095, 1074, 883, 740, 701 cm^{-1}; HRMS calc'd for $C_{53}H_{63}NO_9Si$ = 885.4272, found = 885.4286; $[\alpha]_D$ = -87.1 (*c* = 2.34, $CHCl_3$).



Compound 41

The preparation of bis-mesylate **41** was accomplished in two steps from **40** without purification of the intermediate diol. Compound **40** (1.31 g, 1.48 mmol) was dissolved in THF (100 mL) and cooled to 0 ^{o}C. Lithium aluminum hydride (4.44 mmol, 4.44 mL of a 1M solution in ether) was added dropwise and after 15 minutes TLC indicated complete consumption of the starting material (R_f of diol = 0.15, 70% ethyl acetate in hexanes). Water (2 mL) was cautiously added dropwise, and the reaction was stirred at 0 ^{o}C for 30 minutes, and then room temperature for 30 minutes. After this time a gelatinous precipitate formed, and this was removed by filtration through celite. The filter cake was washed with ethyl acetate, and the filtrate was dried with $MgSO_4$. Removal of the solvent under reduced pressure yielded diol of sufficient purity (1.19 g) to be used in the next step. The crude diol from above was dissolved in 50 mL of CH_2Cl_2 and triethylamine (599 mg, 5.92 mmol) and DMAP (a few crystals) were added and the solution cooled to 0 ^{o}C. Methanesulfonyl chloride (508 mg, 4.44 mmol) was added dropwise and after 1 hour TLC indicated complete conversion to the product with no evidence of the intermediate mono-mesylate. The reaction mixture was directly absorbed onto silica gel, and purified by column chromatography on silica (hexanes / ethyl acetate as eluent) to yield the bis-mesylate **41** (1.232 g, 1.35 mmol, 85% for two steps) as a thick, yellow foam. There are some minor impurities present, one of which might be the other rotamer. A single proton of the major rotamer was set to one for proton integration. The impurities are removed in the next step. R_f = 0.67, 70% ethyl acetate in hexanes;. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.66-7.65 (m, 4H), 7.44-7.37 (m, 6H), 7.35-7.24 (m, 10H), 5.92 (s, 1H), 4.94 (s, 1H), 4.57 (d, J = 11.4 Hz, 1H), 4.53-4.47 (m, 5H), 4.32-4.23 (m, 2H), 4.19-4.17 (m, 1H), 4.05 (dd, J = 10.2, 4.8 Hz, 1H), 3.70-3.66 (m, 2H), 3.61 (dd, J = 9.6, 2.4 Hz, 1H), 3.53 (t, J = 6.3 Hz, 2H), 3.03 (s, 3H), 2.85 (dd, J = 12.0, 3.0 Hz, 1H), 2.69 (m, 6H), 2.58-2.53 (m, 1H), 2.41-2.31 (m, 2H), 2.06 (dd, J = 11.1, 5.7 Hz, 1H), 1.88-1.80 (m, 4H), 1.74-1.70 (m, 2H), 1.58-1.52 (m, 1H), 1.05 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ =173.1, 161.6, 152.7, 138.3, 137.7, 135.1, 133.4, 129.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.3, 127.2, 127.1, 103.9, 73.1, 72.5, 69.9, 69.6, 68.8, 67.6, 62.6, 61.5, 60.4, 56.8, 41.4, 37.2, 36.2, 34.3, 31.1, 30.3, 28.9, 26.5, 25.0, 21.6, 18.8; IR (thin film): 3029, 2932, 2857, 1653, 1428, 1409, 1357, 1176, 1111, 959, 917, 824, 740, 702 cm^{-1}; HRMS calc'd for $C_{53}H_{67}NO_{11}S_2Si$ = 985.3925, found = 985.3898; $[\alpha]_D$ = -55.5 (*c* = 3.04, $CHCl_3$).

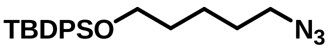


Compound 42

Bis-mesylate **41** (0.644 g, 0.662 mmol) was dissolved in THF (5 mL) and then absolute ethanol (60 mL) was added. 5-tert-butyldiphenylsiloxy-n-pentylamine (2.02 g, 5.98 mmol, see preparation below) was added, and the solution was refluxed for 32 hours, after which TLC indicated that some starting material remained. Additional amine (0.250 g, 0.736 mmol) was added and the solution was refluxed an additional 22 hours, after which TLC indicated complete consumption of the starting mesylate. The solution was cooled to room temperature, and the solvent removed under reduced pressure. The residue was dissolved in EtOAc (50 mL), and 1M NaOH (50 mL) was added. The layers were separated, and the aqueous layer was washed two times with EtOAc, and the combined organics washed with brine and dried with $MgSO_4$. Removal of the solvent under reduced pressure produced an oil that was purified by flash column chromatography on silica (ethyl acetate / hexanes as eluent) to yield **42** (0.600 g, 0.530 mmol, 80%) as a colorless oil. R_f = 0.50, 40% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.67-7.64 (m, 8H), 7.42-7.35 (m, 12H), 7.32-7.28 (m, 8H), 7.25-7.22 (m, 2H), 5.76 (s, 1H), 4.89 (s, 1H), 4.58 (d, J = 11.7 Hz, 1H), 4.47 (s, 2H), 4.40 (d, J = 11.7 Hz, 1H), 4.20-4.17 (m, 1H), 3.91 (dd, J = 9.0, 3.6 Hz, 1H), 3.67 (t, J = 6.6 Hz, 2H), 3.64 (t, J = 6.6 Hz, 2H), 3.49 (ddd, J = 7.6, 7.6, 1.8 Hz, 2H), 3.44 (t, J = 8.7 Hz, 1H), 3.00 (d, J = 12.0 Hz, 1H), 2.74-2.63 (m, 4H), 2.53-2.48 (m, 1H), 2.43 (dd, J = 9.6, 6.6 Hz, 1H), 2.27-2.16 (m, 2H), 2.11 (dd, J = 13.2, 9.6 Hz, 1H), 2.03-2.01 (m, 2H), 1.94-1.90 (m, 2H), 1.83 (p, J = 7.6 Hz, 2H), 1.78 (p, J = 7.6 Hz, 2H), 1.69 (p, J = 7.6 Hz, 2H), 1.54 (p, J = 7.6 Hz, 2H), 1.37-1.27 (m, 6H), 1.05 (s, 9H), 1.04 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 173.8, 160.6, 153.9, 138.6, 138.4, 135.5, 134.0, 133.8, 132.0, 129.5 (2 signals), 128.2, 127.8, 127.6, 127.5, 127.3, 102.9, 73.0, 72.8, 70.6, 70.3, 63.9, 63.4, 62.8, 61.8, 58.7, 58.6, 56.9, 51.8, 39.6, 39.0, 34.6, 32.6, 32.4, 30.7, 29.4, 26.8, 26.7, 25.3, 23.8, 21.7, 19.2 (2 signals) (one sp^3 and four sp^2 carbons are missing, presumably due to overlap); IR (thin film): 2930, 2901, 2896, 2857, 1651, 1472, 1462, 1454, 1428, 1408, 1112, 824, 738, 701 cm^{-1}; HRMS calc'd for $C_{72}H_{90}N_2O_6Si_2$ = 1134.6347, found = 1134.6337

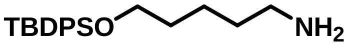
Amine Precursor 1

Mono-TBDPS protected 1,5-pentanediol (16.50 g, 48.17 mmol) and triethylamine (6.33 g, 62.62 mmol) were added to CH_2Cl_2 and cooled to 0 ^{o}C. Methanesulfonyl chloride (6.62 g, 57.80 mmol) was added dropwise, and the reaction stirred for 1 hour at 0 ^{o}C. The reaction was warmed to room temperature and washed with 5% HCl (100 mL), water and then brine. The organic layer was dried with $MgSO_4$ and the solvent removed under reduced pressure. The resulting oil was purified by flash column chromatography on silica gel (ethyl acetate / hexanes as eluent) to yield **Amine Precursor 1** (17.10 g, 40.65 mmol, 84%) as a colorless oil. R_f = 0.66, 40% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.76-7.65 (m, 4H), 7.43 (tt, J = 7.2, 1.8 Hz, 2H), 7.40-7.37 (m, 4H), 4.21 (t, J = 7.6 Hz, 2H), 3.67 (t, J = 7.6 Hz, 2 H), 2.98 (s, 3H), 1.76-1.72 (m, 2H), 1.61-1.56 (m, 2H), 1.52-1.47 (m, 2H), 1.05 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 135.5, 133.8, 129.5, 127.6, 69.9, 63.3, 37.2, 31.7, 28.7, 26.8, 21.7, 19.1; IR (thin film): 3072, 2932, 2858, 1473, 1428, 1390, 1357, 1112, 952, 823, 742, 703 cm^{-1}; HRMS [M+H] calc'd for $C_{22}H_{23}O_4SSi$ = 421.1869, found = 421.1873.



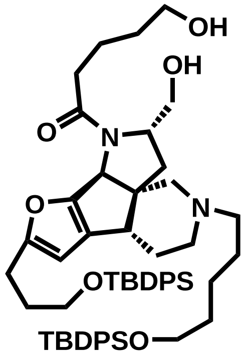
Amine Precursor 2

Mesylate **Amine Precursor 1** (17.10 g, 40.65 mmol) and sodium azide (6.61 g, 101.62 mmol) were added to DMF (171 mL) and water (22 mL) and the resulting mixture heated to 50 ^{o}C for 15 hours. After cooling to room temperature, the reaction mixture was poured into water (500 mL) and the aqueous layer extracted 3 times with ether. The combined organic layers were washed with water and brine and then dried with MgSO$_4$. Removal of the solvent under reduced pressure yielded pure **Amine Precursor 2** (13.99 g, 38.05 mmol, 94%) as a colorless oil. R$_f$ = 0.86, 30% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, CDCl$_3$): δ = 7.67-7.66 (m, 4H), 7.44-7.41 (m, 2H), 7.40-7.37 (m, 4H), 3.67 (t, 7.6 Hz, 2H), 3.24 (t, J = 7.6 Hz, 2H), 1.61-1.55 (m, 4H), 1.48-1.43 (m, 2H), 1.05 (s, 9H); ^{13}C-NMR (150 MHz, CDCl$_3$): δ = 135.5, 133.9, 129.5, 127.6, 63.5, 51.3, 31.9, 28.5, 26.8, 23.0, 19.2; IR (thin film): 3072, 2933, 2859, 2096, 1472, 1428, 1390, 1362, 1265, 1112, 998, 824, 741, 701 cm^{-1}; HRMS [M+H] calc'd for C$_{21}$H$_{30}$N$_3$OSi = 368.2158, found = 368.2162.



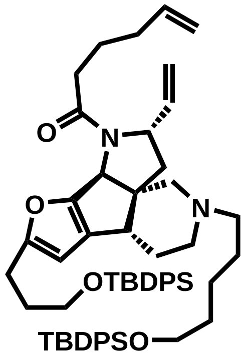
5-tert-butyldiphenylsiloxy-n-pentylamine

Azide **Amine Precursor 2** (13.80 g, 37.54 mmol) was dissolved in ether (450 mL) and placed in a water bath. Lithium aluminum hydride powder (1.43 g, 37.54 mmol) was added in three portions over 15 minutes, and the reaction was stirred at room temperature for 1.5 hours. The reaction was cooled in an ice bath and quenched with water (20 mL, cautiously at first) and stirred at room temperature for 20 minutes. 1M sodium hydroxide solution (300 mL) was added and the layers separated. The aqueous layer was washed 2 more times with ether, and the organic washes combined. The organic washes had a significant amount of gelatinous precipitate/water present, so it was filtered through celite, and then the layers were separated. The organic layer was dried with MgSO$_4$ and concentrated under reduced pressure to yield the desired amine (12.35 g, 36.4 mmol, 97%) as a colorless oil. R$_f$ = baseline, 30% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, CDCl$_3$): δ = 7.68-7.66 (m, 4H), 7.43-7.41 (m, 2H), 7.39-7.36 (m, 4H), 3.66 (t, J = 6.6 Hz, 2H), 2.66 (t, J = 6.6 Hz, 2H), 1.57 (p, J = 6.6 Hz, 2H), 1.43-1.36 (m, 4H), 1.05 (s, 9H); ^{13}C-NMR (150 MHz, CDCl$_3$): δ = 135.4, 134.0, 129.4, 127.5, 63.7, 42.1, 33.4, 32.3, 26.8, 22.9, 19.1; IR (thin film): 3071, 2931, 2858, 1589, 1473, 1428, 1389, 1307, 1112, 823, 739, 701 cm^{-1}; HRMS - calc'd for C$_{21}$H$_{31}$NOSi = 341.2175, found = 341.2179



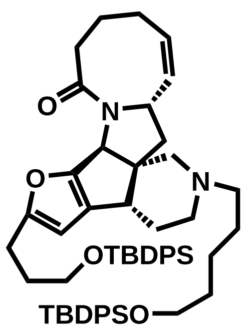
Compound 43

Compound **42** (885 mg, 0.781 mmol) was dissolved in methylene chloride (90 mL) and the solution cooled to -78 ^{o}C. Boron trichloride (6.0 mL of a 1M solution in methylene chloride, 6.0 mmol) was added dropwise and the reaction stirred for 3.5 hours at -78 ^{o}C. Saturated aqueous NaHCO$_3$ (10 mL) was added (slowly at first) and the reaction stirred at -78 ^{o}C for 20 minutes, then removed from the cold bath and allowed to warm to room temperature. The reaction mixture was added to 1M NaOH (30 mL) and the layers separated. The aqueous layer was washed 3 times with methylene chloride and the combined organics washed with brine and dried with MgSO$_4$. The solvent was removed under reduced pressure and the resulting residue purified by flash column chromatography on silica gel (hexanes /ethyl acetate to methanol / ethyl acetate) to yield diol **43** (343 mg, 0.360 mmol, 45%) as a yellow oil along with a mixture of products (302 mg) that was mostly the mono-debenzylated compound. This mixture was resubjected to the above condition using 30 mL of methylene chloride and 2.0 mL of BCl_3 solution to yield an additional 102 mg of **43** to bring the total yield after 1 recycle to 445 mg, 0.467 mmol, 60%. R_f = 0.47, 8% methanol in ethyl acetate; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.66-7.65 (m, 8H), 7.42-7.36 (m, 12H), 5.80 (s, 1H), 5.57 (d, J = 9.0 Hz, 1H), 4.91 (s, 1H), 4.18-4.12 (m, 1H), 3.72-3.59 (m, 8H), 2.82 (d, J = 12.0 Hz, 1H), 2.80-2.75 (m, 1H), 2.70 (dd, J = 7.8, 7.2 Hz, 2H), 2.60-2.50 (m, 3H), 2.32-2.29 (m, 3H), 2.04-2.00 (m, 3H), 1.88-1.76 (m, 5H), 1.67-1.51 (m, 6H), 1.47-1.42 (m, 2H), 1.40-1.34 (m, 3H), 1.06 (s, 9H), 1.04 (s, 9H); IR (thin film): 3500-3100 broad, 3075, 2937, 2859, 1646, 1624, 1420, 1105, 823 cm^{-1}; HRMS - calc'd for $C_{58}H_{78}N_2O_6Si_2$ = 954.5398, found = 954.5351.



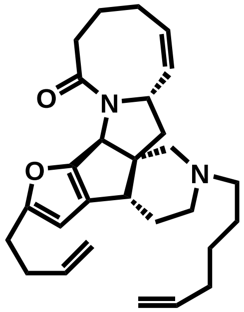
Compound 45

Bis-alkene **45** was prepared in two steps from diol **43** without purification of the intermediate bis-aldehyde. Diol **43** (210 mg, 0.22 mmol) was dissolved in DMSO (25 mL) and IBX (566 mg, 1.98 mmol) was added. The reaction was stirred under argon for 2.5 hours after which TLC indicated complete consumption of the starting material and no mono-alcohol. The reaction mixture was poured into 200 mL of saturated $NaHCO_3$, and the aqueous layer was extracted four times with ether. The combined organics were washed once with water and dried with $MgSO_4$. The solvent was removed under reduced pressure to yield a yellow oil (215 mg) that was used directly in the next step. $MePPh_3I$ (1.07 g, 2.64 mmol) was added to THF (40 mL) and the slurry cooled to 0 ^{o}C. KOtBu (0.247 g, 2.20 mmol) was added and the mixture stirred at 0 ^{o}C for 15 minutes. A THF solution of the bis-aldehyde generated above (10 mL) was added rapidly via cannula and the mixture stirred for 15 minutes, after which TLC indicated complete consumption of the starting material. Water (5 mL) was then added and the THF was removed under reduced pressure. To the resulting residue was added water (30 mL), 1M NaOH (5 mL), and EtOAc (20 mL). The layers were separated, and the aqueous layer was extracted 3 times with EtOAc. The combined organics were dried with $MgSO_4$, and the solvent was removed under reduced pressure to yield a crude residue that was purified by column chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield bis-alkene **45** (110 mg, 0.116 mmol, 52 % for two steps) as a pale yellow oil. R_f = 0.61, 50% ethyl acetate in hexanes; Proton NMR showed that the product was a 10:3 mixture of rotational isomers. A single proton of the major rotamer was set to one for proton integration. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.67-7.66 (m, 12.0H), 7-44-7.36 (m, 18.6H), 5.89-5.75 (m, 4.3H), 5.25 (s, 0.3H), 5.14-5.02 (m, 5.3H), 4.98-4.89 (m, 2.0H), 4.59-4.56 (m, 1.0H), 4.37-4.34 (m, 0.3H), 3.70-3.65 (m, 6.5H), 3.11 (d, J = 12.6 Hz, 1H), 2.95 (d, J = 12.0 Hz, 0.3H), 2.79-2.67 (m, 5.7H), 2.59-2.52 (m, 1.7H), 2.44-2.27 (m, 6.8H), 2.18-2.11 (m, 2.6H), 2.09-2.03 (m, 3.0H), 1.98-1.92 (m, 3.2H), 1.89-1.82 (m, 6.3H), 1.78-1.74 (m, 1.9H), 1.60-1.55 (m, 4.1H), 1.46-1.21 (m, 17.3H, includes grease), 1.06-1.05 (m, 28.7H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 173.1 (2 signals), 160.5, 154.0, 140.0, 138.4, 135.5, 134.0, 133.8, 131.7, 129.5 (2 signals), 127.5 (2 signals), 114.8, 113.7, 102.9, 102.2, 63.8, 63.0, 62.9, 59.4, 59.0, 58.5, 54.0, 42.3, 38.4, 33.9, 33.7, 33.3, 33.1, 32.4, 30.7, 29.6, 26.8, 25.4, 24.3, 24.2, 23.7, 19.2 (2 signals); IR (thin film): 3069, 3048, 2933, 2857, 2804, 2769, 1652, 1464, 1430, 1406, 1110, 910, 823, 740 cm^{-1}; HRMS calc'd for $C_{68}H_{78}N_2O_4Si_2$ = 946.5500, found = 946.5462.



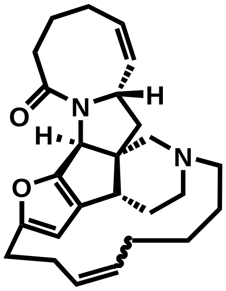
Compound 46

Compound **45** (61 mg, 0.064 mmol) was dissolved in CH_2Cl_2 and Grubbs1st generation catalyst (6 mg, 0.00707 mmol, 11 mol%) was added. The reaction was evacuated and backfilled with argon five times, and then refluxed for 2 hours, after which TLC indicated complete consumption of the starting material. The reaction mixture was directly absorbed onto silica, and purified by column chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield **46** (44 mg, 0.048 mmol, 75%) as an orange film. R_f = 0.26, 40% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.67-766 (m, 8H), 7.43-7.36 (m, 12H), 5.76 (s, 1H), 5.62-5.58 (m, 1H), 5.41 (d, J = 12.6 Hz, 1H), 5.18 (s, 1H), 4.50 (d, J = 9.6 Hz, 1H), 3.69 (t, J = 6.6 Hz, 2H), 3.65 (t, J = 6.6 Hz, 2H), 3.02 (d, J = 12.0 Hz, 1H), 2.75 (t, J = 7.8 Hz, 2H), 2.66-2.59 (m, 2H), 2.43-2.40 (m, 2H), 2.37-2.28 (m, 3H), 2.19-2.16 (m, 1H), 2.05-1.87 (m, 8H), 1.78 (d, J = 12.7 Hz, 1H), 1.71-1.66 (m, 1H), 1.58 (p, J = 6.6 Hz, 2H), 1.40-1.32 (m, 6H), 1.049 (s, 9H), 1.046 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ = 173.1, 160.5, 155.1, 135.4, 134.7, 134.0, 133.8, 131.2, 129.4 (2 signals), 127.5 (2 signals), 125.8, 102.4, 63.7, 63.2, 63.0, 59.8, 58.2, 56.2, 52.1, 43.9, 38.2, 32.4, 32.3, 30.6, 29.5, 26.8, 26.7, 26.1, 25.3, 23.4, 22.6, 19.1, 19.09 (one sp^2 and two sp^3 signals missing, presumably due to overlap); IR (thin film): 3071, 2931, 2902, 2857, 1653, 1647, 1472, 1462, 1458, 1427, 1406, 1399, 1110, 823, 740; HRMS calc'd for $C_{58}H_{74}N_2O_4Si_2$ = 918.5187, found = 918.5154.



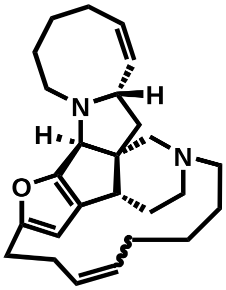
Compound 49

Since the Nakadomarin A produced by this route could not be separated from the E-isomer, the following procedure was not optimized. Diene **49** was prepared in 3 steps from **46**. Data is not given for the intermediate diol or dial because the TBAF used for silyl removal co-elutes with the product and a pure sample could not be obtained. The low yield for this sequence may be attributed to the residual TBAF contamination. For the bis-amide **57** it was found that acidic methanol deprotection lead to a higher overall yield for the desilylation, oxidation, Wittig sequence. Compound **46** (147 mg, 0.160 mmol) was dissolved in THF (25 mL) and TBAF (0.64 mL of a 1M solution in THF, 0.64 mmol) added. After 7 hours the starting material was consumed and there was no indication of the mono-TBDPS compound remaining by TLC, so the THF was removed under reduced pressure and the residue dissolved in methylene chloride. The material was pre-absorbed on silica and subjected to chromatography on silica gel (methanol / ethyl acetate as eluent) to yield the TBAF contaminated diol (71 mg for mixture, ~20-25% by weight TBAF), R_f = 0.15 (25% methanol in ethyl acetate). Half of this mixture (35 mg) was dissolved in methylene chloride (10 mL) and cooled to 0 ^{o}C. Dess-Martin periodinane (168 mg, 0.395 mmol) was added and the reaction stirred at 0 ^{o}C for 1 hour and then room temperature for 2 hours (R_f of dial = 0.42 (25% methanol in ethyl acetate)). Saturated aqueous $NaHCO_3$ (3 mL) and $Na_2S_2O_3$ (3 mL) were added and the mixture stirred vigorously for 30 minutes. The layers were separated, and the aqueous layer extracted 2 times with methylene chloride. The combined organics were dried and the solvent removed under reduced pressure to yield 35 mg of crude product. Crude NMR analysis indicated that the correct product was formed, but the ratio of TBAF to product has increased slightly. A solution of the crude oxidation product in THF (3 mL) was added to a slurry of Wittig ylide (prepared by stirring t-BuOK (89 mg, 0.793 mmol) and $MePPh_3I$ (383 mg, 0.948 mmol) in THF (8 mL) for 30 minutes) via cannula at 0 ^{o}C. After 10 minutes TLC indicated complete consumption of the starting material, and water (2 mL) was added. The THF was removed under reduced pressure, and water (3 mL) and ethyl acetate (5 mL) were added. The layers were separated and the aqueous layer was extracted 3 times with ethyl acetate and the combined organics washed with water and then dried with $MgSO_4$. Removal of the solvent under reduced pressure and purification of the residue by flash column chromatography on silica gel (hexanes / ethyl acetate as eluent) yielded diene **49** (8 mg, 0.0184 mmol, 23% for 3 steps) as a yellow oil. The yields for this sequence were variable and range from 20-30%. R_f = 0.33, 100% ethyl acetate; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 5.87-5.74 (m, 3H), 5.66-5.62 (m, 1H), 5.42 (d, J = 12.0 Hz, 1H), 5.20 (s, 1H), 5.03 (dd, J = 17.1, 1.5 Hz, 1H), 4.99-4.96 (m, 2H), 4.92 (d, J = 10.2 Hz, 1H), 4.51 (d, J = 10.2 Hz, 1H), 3.05 (d, J = 12.6 Hz, 1H), 2.74-2.60 (m, 4H), 2.44-2.32 (m, 7H), 2.20-2.18 (m, 1H), 2.06-1.95 (m, 6H), 1.89 (d, J = 12.0 Hz, 1H), 1.79 (d, J = 12.0 Hz, 1H), 1.74-1.69 (m, 2H), 1.39-1.35 (m, 5H).



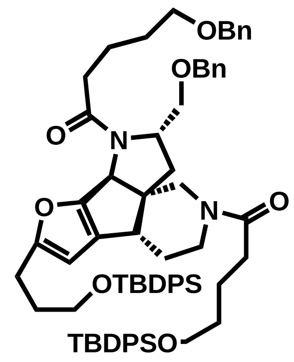
Mixture 50

Diene **49** (18 mg, 0.0414 mmol) was dissolved in CH_2Cl_2 (200 mL) and to this solution was added Grubbs First Generation Catalyst (13 mg, 0.0164 mmol, ~40 mol%). The reaction flask was evacuated and back filled with argon five times, and then refluxed for 20 hours. The solvent was removed under reduced pressure, and a crude NMR indicated that the reaction had gone to completion and that the ratio of *E*:*Z* isomers was approximately 5:3. The reaction mixture was then subjected to column chromatography on silica gel, (hexanes / ethyl acetate to methanol / ethyl acetate as eluent) to yield a mixture of the *E*-and Z-isomers (12 mg, 0.0295 mmol, 71% combined) as a brown film in a ratio that was similar to the crude. Attempted separation of the isomers by chromatography on silica, silver impregnated preparative TLC, and HPLC on both standard and reversed phase columns failed in our hands, so the mixture would be subjected to Red-Al reduction in hopes that the final product could be separated. R_f of **mixture 50** = 0.20 (20% methanol in ethyl acetate).



(+)-Nakadomarin A and *E*-isomer

Mixture 50 was subjected to the procedure of Nishida (*Angew. Chem. Int. Ed.* **2004**, *43*, 2020). A solution of **Mixture 50** (8.0 mg, 0.0197 mmol) in toluene (5 mL) was cooled to 0 ^{o}C. Red-Al (80 μL of a 65% solution in toluene) was added and stirring continued for 10 minutes at this temperature. The reaction was then heated to reflux for 3 hours, then quenched at -30 ^{o}C with saturated aqueous Rochelle’s salt (3 mL). After warming to room temperature, the mixture was stirred vigorously for 1 hour, then ethyl acetate (5 mL) was added, and vigorous stirring continued for an additional hour. The layers were separated, and the aqueous layer extracted 4 times with ethyl acetate. The combined organics were washed with saturated aqueous Rochelle’s salt, twice with brine and the solvent removed under reduced pressure. The residue was subjected to column chromatography on silica gel (methanol / ethyl acetate as eluent) to produce a mixture of **nakadomarin A** and the ***E*-isomer** (6.0 mg, 0.0153 mmol, 75% combined) as a pale brown film. The ratio of the compounds was 5:4 *E*-isomer:Nakadomarin A after the reduction. As with **mixture 50**, we were unable to successfully separate the two compounds. R_f of mixture = 0.16 (80 % methanol in ethyl acetate). A ^{1}H-NMR of the mixture is included in the spectral section.

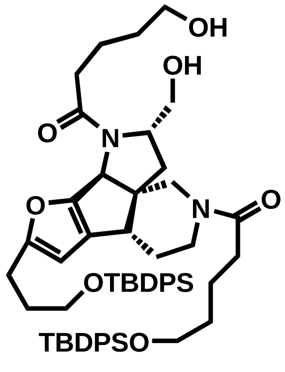


Compound 53

Compound **53** was prepared in two steps from bis-mesylate **41**, without purification of the intermediate secondary amine. Bis-mesylate **41** (0.950 g, 0.992 mmol) was dissolved in a minimum volume of tetrahydrofuran (~ 3 mL) and transferred to a pressure tube. A solution of ammonia in absolute ethanol (20 mL of an approximately 2.8 M solution) was then added, the head space purged with argon, and the tube heated to 85 ^{o}C for 13 hours. The solution was then cooled to room temperature, and the solvent removed under reduced pressure to yield a crude yellow residue. To this residue was added water (50 mL), 1 molar NaOH (50 mL) and ethyl acetate (100 mL) and the layers separated. The aqueous layer was washed twice with ethyl acetate and the combined organics washed with water and brine and dried with $MgSO_4$. Removal of the solvent under reduce pressure produced a yellow oil that was of high enough purity to be used directly in the next step. NMR showed approximately 8% of the other diastereomer still present from the double bond reduction. R_f of intermediate secondary amine = 0.51, 50% methanol in ethyl acetate. The crude amine (750 mg of mixture) was dissolved in methylene chloride (30 mL) and triethylamine (388 mg, 3.83 mmol) was added. The solution was cooled to 0 ^{o}C, and 5-tert-butyldiphenylsiloxy-n-pentanoyl chloride (953 mg, 2.39 mmol, see preparation below) was added dropwise as a solution in methylene chloride (15 mL), and the reaction kept at 0 ^{o}C for 2 hours before being stirred at room temperature for 16 hours. The solvent was then removed under reduced pressure, and the residue dissolved in ether (100 mL). Water (100 mL) was added and the layers separated. The aqueous layer was washed 2 times with ether and the combined organics washed once with 5% HCl, 1 M NaOH, water and then brine and dried with $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue purified by column chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield bis-amide **53** (847 mg, 0.739 mmol, 77% over two steps) as a yellow viscous oil. Compound was formed in what appears to be a 5:3:1 mixture of rotamers. A single proton of the major rotamer was set to one for proton integration R_f = 0.54, 50% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.66-7.64 (m, 14.5H), 7.43-7.28 (m, 34.5H), 7.26-7.22 (m, 6.0H), 5.75 (s, 1.4H), 5.72 (s, 0.2H), 4.71 (s, 1H), 4.70 (s, 0.5H), 4.58 (d, J = 11.4 Hz, 0.2H), 4.54 (s, 1.4H), 4.50-4.44 (m, 6.0H), 4.34-4.26 (m, 2.3H), 3.99-3.95 (m, 1.8H), 3.85 (d, J = 13.8Hz, 1H), 3.68-3.66 (m, 5.9H), 3.61 (dd, J = 6.0, 6.6 Hz, 2H), 3.54-3.40 (m, 7.9H), 3.35-3.27 (m, 1.6H), 3.18-3.10 (m, 1.9H), 2.83 (d, J = 10.8 Hz, 0.2H), 2.80-2.67 (m, 7.4H), 2.51-2.44 (m, 1.8H), 2.31-2.00 (m, 10.2H), 1.86-1.57 (m, 24.2H), 1.47 (p, J = 7.2 Hz, 2.4H), 1.05-1.03 (m, 32.7H), 0.89-0.84 (m, 1.8H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 172.9, 172.8, 172.7, 172.5, 161.8, 161.7, 153.8, 153.3, 138.4, 138.3, 138.1, 137.6, 135.2, 133.6, 133.5, 133.4, 129.3 (2 signals), 128.1, 128.0, 127.5 (2 signals), 127.3 (2 signals), 127.2 (2 signals), 127.1, 127.0, 102.6, 102.5, 73.1, 72.9, 72.5 (2 signals), 69.9 (2 signals), 69.6, 63.4. 63.3 (3 signals), 62.5 (2 signals), 60.5, 59.9, 57.5, 57.2, 47.2, 44.7, 41.7, 40.8, 40.7, 39.3, 39.1, 38.9, 36.8, 35.0, 34.3, 34.2, 33.4, 32.7, 32.0, 31.9, 31.8, 31.7, 30.4 (2 signals), 29.1, 26.6, 25.9, 25.0 (2 signals), 21.7, 21.5, 21.2, 21.1, 21.0, 18.9; IR (thin film): 3070, 3048, 3030, 2931, 2893, 2857, 1647, 1472, 1462, 1454, 1428, 1414, 1392, 1111, 823, 740, 702 cm^{-1}; HRMS calc'd for $C_{72}H_{88}N_2O_7Si_2$ = 1148.6130, found = 1148.6178. Attempts to determine the optical rotation of **22** were unsuccessful, as solutions with concentrations as high as 1.70 in $CHCl_3$, did not produce appreciable readings.

5-tert-butyldiphenylsiloxy-n-pentanoic acid was prepared in three steps according to the following procedure: 1,5-pentanediol (18.94 g, 180.55 mmol) was dissolved in N,N-dimethylformamide (100 mL) and imidazole (0.248 g, 3.64 mmol) and DMAP (a few crystals) were added. Tert-butyldiphenylsilylchloride (4.97 g, 18.10 mmol) was added via syringe and the reaction stirred at room temperature for 18 hours. The reaction was poured into water (500 mL) and extracted 5 times with ether. The combined organics were washed 5 times with water (50 mL portions), then once with brine and dried with $MgSO_4$. Removal of the solvent under reduced pressure produced the mono-silylated alcohol (5.26 g, 15.36 mmol, 84% crude yield) as a yellow oil. This material was of sufficient purity to be used without directly in the next step. The TBDPS-protected monoalcohol (5.00 g, 14.60 mmol) from above was dissolved in DMSO (50 mL) under argon, and to this was added IBX (6.10 g, 21.35 mmol). After 2 hours the reaction was complete by TLC, and the reaction was added to water (500 mL) and extracted 5 times with ether. The combined organics were washed 3 times with water, once with brine, and dried with $MgSO_4$. Removal of the solvent under reduced pressure produced the aldehyde (4.84 g, 14.21 mmol, 97% crude yield) as a yellow oil. The material was of sufficient purity to be used in the next step without further purification. The crude aldehyde (4.84 g, 14.21 mmol) was dissolved in tert-butanol (90 mL) and water (30 mL), cooled to 0 ^{o}C and 2-methyl-2-butene (5.98 g, 85.26 mmol) added. A solution of sodium chlorite (2.57 g, 3.21 g of 80% reagent, 28.42 mmol) and sodium dihydrogen phosphate (7.84 g, 56.82 mmol) in water (60 mL) was then added dropwise. After 1 hour the reaction was complete by TLC, and water (150 mL) was added. Acetic acid was added to adjust the pH to 5. The reaction mixture was then washed 3 times with ether and dried with $MgSO_4$. The solvent was removed under reduced pressure to produce an oil that was purified by flash column chromatography (hexanes / ethyl acetate as eluent) to yield the acid (4.28 g, 12.02 mmol, 84% over 2 steps) as a yellow solid. This material was identical spectroscopically with that reported by Jacobi, P.A.; Li, Y.; *Org. Lett.* **2003**, *5*, 701.

5-tert-butyldiphenylsiloxy-n-pentanoyl chloride – 5-tert-butyldiphenylsiloxy-n-pentanoic acid (0.909 g, 2.39 mmol) was dissolved in 20 mL of toluene, and 3 drops of DMF was added. Oxalyl chloride (0.425 g, 3.35 mmol) was then added dropwise, and the reaction stirred at room temperature for 30 minutes. The reaction was then heated to 50 ^{o}C for 1 hour. After cooling to room temperature, the toluene was removed under reduced pressure to produce the acid chloride as an orange oil. This acid chloride was dissolved in CH_2Cl_2 (15 mL) and used directly in the reaction above.

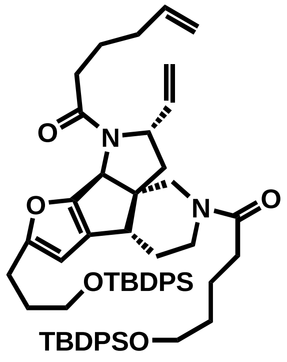


Compound 54

Bis-amide **53** (700 mg, 0.610 mmol) was dissolved in methylene chloride (70 mL) and the solution cooled to -78 ^{o}C. Boron trichloride (3.66 mmol, 3.66 mL of a 1M solution in methylene chloride) was added dropwise, and the reaction was allowed to warm slowly to -50 ^{o}C (about 1.5 hours). The reaction was maintained at -50 ^{o}C for two hours, and then cooled to -78 ^{o}C. A saturated solution of sodium bicarbonate (4 mL) was then cautiously added, and the reaction stirred at -78 ^{o}C for 20 minutes, after which it was removed from the cooling bath, and allowed to warm to room temperature. The reaction mixture was added to water (20 mL) and 1 M NaOH (20 mL) and layers were separated. The aqueous layer was extracted twice with methylene chloride, and the combined organics washed twice with brine and dried with $MgSO_4$. The solvent was removed under reduced pressure to yield a crude residue that was purified by column chromatography on silica gel (hexane / ethyl acetate to methanol / ethyl aceate as eluent) to yield diol **54** (420 mg, 0.434 mmol, 71%) as a yellow oil/foam. Diol **54** was formed as a 5:2 ratio of rotamers. A single proton of the major rotamer was set to one for proton integration. R_f = 0.17, 100% ethyl acetate; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.67-7.64 (m, 12H). 7.44-7.35 (m, 18H), 5.78 (s, 1.4 H), 5.46 (br. s, 1H), 4.84 (s, 1H), 4.75 (s, 0.4H), 4.19 (d, J =

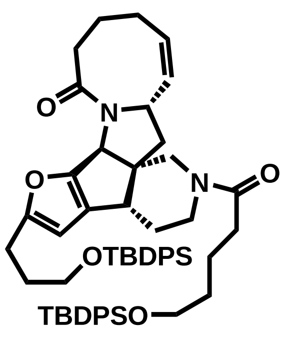
13.2 Hz, 1H), 4.06-4.04 (m, 0.4H), 3.83 (d, J = 11.4 Hz, 0.4H), 3.72-3.59 (m, 13.2H), 3.53 (dd, J = 10.2, 10.2 Hz, 0.4Hz), 3.49-3.42 (m, 1.4H), 3.33-3.29 (m, 2.1H), 3.26-3.19 (m, 1.4H), 2.88-2.84 (m, 1.4H), 2.80-2.61 (m, 6.6H), 2.57-2.52 (m, 0.7H), 2.42-2.29 (m, 1.6H), 2.24-2.08 (m, 4.6H), 1.99 (dd, J = 7.2, 13.2 Hz, 1H), 1.87-1.55 (m, 19.2H), 1.41-1.35 (m, 0.5H), 1.06-1.04 (m, 26.3H), 0.98-0.86 (m, 1.8H)**;** ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 174.7, 173.3, 162.4, 153.0, 135.0, 133.7, 133.6, 129.8, 129.5 (2 signals), 127.5 (2 signals), 102.5, 65.1, 64.8, 63.4, 62.7, 62.2, 61.8, 58.4, 48.5, 44.7, 41.2, 40.7, 40.1, 34.3, 33.4, 32.9, 32.1, 32.0, 31.9, 31.8, 30.5, 26.8, 25.8, 25.3, 21.5, 21.2, 20.8, 19.11, 19.07; IR (thin film): 3415 (broad), 3071, 2953, 2950, 2932, 2895, 2859, 1635, 1628, 1473, 1428, 1112, 1070, 823, 741, 703, 688 cm^{-1}; HRMS [M+H] calc'd for $C_{58}H_{77}N_2O_7Si_2$ = 969.5260, found = 969.5238. Attempts to determine the optical rotation of **23** were unsuccessful, as solutions with concentrations as high as 2.1 in $CHCl_3$, did not produce appreciable readings.

Compound **56** was prepared in two steps from the diol without purification of the intermediate bis-aldehyde, as the crude aldehyde was of high purity. Subsequent purification of the aldehyde did not lead to increased yields over the two step sequence.



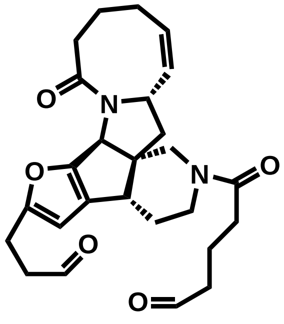
Compound 56

Diol **54** (378 mg, 0.391 mmol) was dissolved in dimethyl sulfoxide (20 mL) and *o*-Iodoxybenzoic Acid (IBX) (1.33 g, 4.69 mmol) was added and the reaction stirred for 13 hours. TLC indicated the presence of the intermediate mono-aldehyde, so more IBX was added (200 mg, 0.701 mmol) and the reaction stirred for an additional 4 hours. TLC indicated complete conversion to the bis-aldehyde (R_f = 0.61, 100% ethyl acetate), and the reaction mixture was poured into saturated sodium bicarbonate (120 mL) and extracted 5 times with ether. The combined organics were washed twice with water and once with brine, dried with $MgSO_4$ and the solvent removed under reduced pressure to produce crude aldehyde (347 mg) as a yellow oil. The resulting crude product was divided into three equivalent portions (~115 mg each) for the Wittig, because on rare occasions the reaction can lead to decomposition. In this instance all three reactions were successful, so they were combined afterwards for work up and column. The procedure will be given for one of the three portions. The crude bis-aldehyde from above was dissolved in THF (4 mL). The ylide solution in toluene (4 mL) (prepared by stirring $MePPh_3Br$ (488 mg, 1.38 mmol) and KOtBu (127 mg, 1.14 mmol) in toluene (4 mL) for 1.5 hours) was added quickly via a large bore cannula, and after 10 minutes TLC indicated consumption of the starting material. Water (2 mL) was added, and at this point all three reactions were combined. The THF/toluene was removed under reduced pressure, and water (10 mL) and ethyl acetate (10 mL) were added to the residue. The layers were separated, and the aqueous layer was washed 3 times with ethyl acetate. The combined organics were washed once with water, then with brine, and dried with $MgSO_4$. The solvent was then removed under reduced pressure, yielding a residue that was purified by chromatography on silica gel (hexanes / ethyl acetate as eluent) to yield diene **56** (124 mg, 0.129 mmol, 36%) as a yellow oil. Diene **56** was formed as a 5:4:3 mixture of identifiable rotamers. A single proton of the major rotamer was set to one for proton integration. R_f = 0.68, 60% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.67-7.65 (m, 24.4H), 7.43-7.36 (m, 36.7H), 5.98-5.72 (m, 9.4H), 5.28 (d, J = 10.2 Hz, 1H), 5.20-4.90 (m, 13.3H), 4.81 (s, 0.8H), 4.80-4.78 (m, 1.4H), 4.68-4.64 (m, 0.8H), 4.52-4.48 (m, 0.6H), 4.47-4.45 (m, 1H), 4.23 (d, J = 13.2 Hz, 0.8H), 4.00 (d, J = 13.8 Hz, 1H), 3.74-3.67 (m, 13.4H), 3.58-3.50 (m, 3.6H), 3.43 (d, J = 13.8 Hz, 1H), 3.37-3.31 (m, 2.6H), 3.24-3.12 (m, 3.1H), 2.87-2.68 (m, 10.6H), 2.64-2.62 (m, 0.7H), 2.55-2.48 (m, 1.7H), 2.31-2.04 (m, 23.9H), 1.97-1.57 (m, 33.8H), 1.06-1.04 (m, 54.0H); Due to the number or rotamers present, the carbon spectrum was not resolved well. Only the peaks that were clearly identifiable will be reported. ^{13}C-NMR (100 MHz, CDCl$_3$): δ = 172.9, 172.8, 172.7, 172.6, 172.5, 172.4, 172.3, 172.1, 162.1, 162.0, 161.8, 155.2, 154.4, 153.9, 153.3, 138.2, 138.1, 138.0, 135.7, 135.4, 135.4, 135.0, 129.6, 129.4, 129.3, 127.7, 127.4, 127.2, 114.9, 114.7 (2 signals), 102.8, 102.7, 102.6, 102.5, 102.0, 101.8, 63.6, 63.4, 63.1, 62.8, 62.7, 62.6, 61.3, 60.7, 60.1, 59.9, 59.3, 58.3, 57.9, 33.4, 33.2, 33.1, 33.0, 32.9, 32.8, 32.2, 32.0, 31.9, 30.5 (2 signals), 29.5, 26.7, 24.1, 23.9, 19.1; IR (thin film): 3072, 2953, 2931, 2898, 2858, 1653, 1648, 1473, 1462, 1443, 1427, 1419, 1274, 1185, 1112, 998, 913, 823, 741, 702, 688 cm^{-1}; HRMS [M+H] calc'd for $C_{60}H_{77}N_2O_5Si_2$ = 961.5371, found = 961.5388.



Compound 57

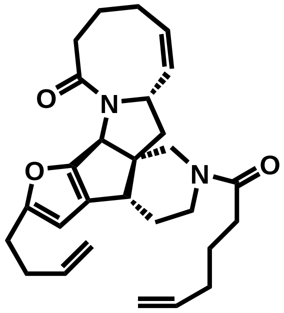
Alkene **56** (80 mg, 0.0834 mmol) was dissolved in methylene chloride (120 mL) and to this solution was added Grubbs 2nd generation catalyst (14 mg, 0.0167 mmol, 20 mol%). The reaction flask was evacuated and backfilled with argon four times and then refluxed for 2.5 hours, after which TLC indicated complete consumption of the starting material. The solvent was removed under reduced pressure, and the residue purified by flash column chromatography (hexanes / ethyl acetate as eluent) to yield azocine **57** (65 mg, 0.0696 mmol, 84%) as a beige foam. The compound was produced as a 5:3 mixture of rotamers. A single proton of the major rotamer was set to one for proton integration. R_f = 0.26, 50% ethyl acetate in hexanes; ^{1}H-NMR (600 MHz, CDCl$_3$): δ = 7.66-7.65 (m, 13.4H), 7.43-7.35 (m, 20.1H), 5.82-5.76 (m, 2.6H), 5.70-5.65 (m, 0.6H), 5.49-5.44 (m, 1.6H), 4.96 (s, 0.6H), 4.89 (s, 1H), 4.61-4.57 (m, 1.6H), 4.13 (d, J = 14.4 Hz, 1H), 3.73-3.64 (m, 8.1H), 3.51-3.48 (m, 1H), 3.43 (d, J = 14.4 Hz, 0.6H), 3.37 (d, J = 13.8 Hz, 1H), 3.32-3.25 (m, 1.6H), 3.21-3.17 (m, 1H), 2.78-2.59 (m, 7.3H), 2.40-1.87 (m, 21.5H), 1.74-1.60 (m, 11.8H), 1.05-1.04 (m, 30.0H); ^{13}C-NMR (150 MHz, CDCl$_3$): δ = 173.4, 173.1, 172.6, 171.8, 162.0, 161.9, 155.0, 154.3, 135.3, 134.1, 133.7, 133.6, 133.3, 129.3 (2 signals), 128.3, 127.8, 127.6, 127.4, 127.2, 102.2, 102.1, 63.4, 63.3, 62.8, 62.7, 59.5, 57.3, 57.1, 47.7, 43.6, 43.2, 42.7, 40.8, 40.1, 39.7, 39.4, 33.2, 32.9, 32.5, 32.2, 32.0, 30.4, 29.4, 27.1 26.6, 26.5, 26.4, 25.3, 22.8, 22.6, 21.3, 21.0, 18.98, 18.96; IR (thin film): 3071, 3049, 3014, 2999, 2953, 2931, 2895, 2858, 1656, 1650, 1645, 1471, 1461, 1428, 1409, 1270, 1112, 823, 741, 703 cm^{-1}; HRMS [M+H] calc'd for $C_{58}H_{73}N_2O_5Si_2$ = 933.5058, found = 933.5393.



Compound 59

Compound **57** (40 mg, 0.0428 mmol) was divided into four approximately equal portions (10 mg) for the next two reactions, due to the Dess-Martin producing an unidentifiable and inseparable by-product on rare occasions. The procedure will be given for one of these four equivalent reactions, and all operations were performed independently. To **57** was added methanol (3 mL). Acidic methanol (10 drops, prepared by adding 20 drops of acetyl chloride to 5 mL of methanol) was added, and the reaction monitored by TLC (R_f = 0.25, 20% methanol in ethyl acetate for desired diol). More HCl solution was added as follows, after 45 minutes 5 drops, after 2 hours 5 drops, after 3 hours 7 drops. After 4.5 hours TLC indicated complete consumption of the starting material and no evidence of the mono-silylated compound. Solid sodium bicarbonate was added to neutralize the acid, and the solution was filtered through a plug of cotton wool. The salt remaining in the flask was washed with methanol and methylene chloride. Removal of the solvent under reduced pressure yielded a solid film that was the result of a minor amount of salt being soluble in the methanol, so to this was added methylene chloride and then it was filtered again through a plug of cotton. Removal of the solvent under reduced pressure yielded a yellow oil, (approximately 10 mg), that was of very high purity by NMR, except for the presence of the cleaved silyl groups.

Again, the oxidation with Dess-Martin periodinane was performed in four separate batches, and the procedure for one will be given. To the crude diol (10 mg, (5 mg, 0.0107 mmol of which is diol)) was added methylene chloride (4 mL). The solution was cooled to 0 ^{o}C, and to this was added Dess-Martin periodinane (23 mg, 0.0535 mmol) and the reaction maintained at this temperature for 30 minutes. The reaction was then stirred at room temperature for 2.5 hours, after which TLC indicated complete consumption of the starting material and no evidence of the unknown by-product (R_f = 0.43, 35% methanol in ethyl acetate). Saturated sodium bicarbonate (1 mL) and saturated sodium thiosulfate (1 mL) was then added and the reaction stirred for one hour. At this point, since there was no evidence of by-product formation in any of the four reactions, they were combined for work up and purification. The layers were separated, and the aqueous layer washed 3 times with methylene chloride. The combined organics were washed with saturated sodium thiosulfate and brine, dried with $MgSO_4$ and concentrated under reduced pressure. The compound was then purified by column chromatography (ethyl acetate / hexanes to methanol / ethyl acetate as eluent) to yield bis-aldehyde **59** (14 mg, 0.0316 mmol, 70% for 2 steps) as a yellow oil. Bis-aldehyde **59** was formed as a 5:3 mixture of rotamers. A single proton of the major rotamer was set to one for proton integration. R_f = 0.43, 35% methanol in ethyl acetate; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.78 (s, 1.4H), 9.75 (s, 1.4H), 5.84-5.83 (m, 1.4H), 5.80-5.75 (m, 1.7H), 5.51-5.46 (m, 1.6H), 4.95 (s, 0.6H), 4.86 (s, 1.0H), 4.65-4.58 (m, 1.6H), 4.19 (d, J = 13.2 Hz, 1H), 3.66 (d, J = 13.2 Hz, 0.6H), 3.50-3.46 (m, 0.6H), 3.42 (d, J = 13.8 Hz, 1H), 3.35-3.26 (m, 2.2H), 3.23-3.17 (m, 1.6H), 2.97-2.95 (m, 3.3H), 2.82-2.70 (m, 5.0H), 2.66-2.48 (m, 5.7H), 2.39-1.89 (m, 21.0H), 1.80-1.60 (m, 5.5H), 0.88-0.83 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 202.3, 202.1, 201.1, 201.0, 173.7, 173.5, 172.0, 171.1, 159.9, 159.8, 155.7, 155.0, 134.1, 133.3, 128.6, 128.1, 127.9, 127.6, 103.3, 63.4, 59.7, 59.6, 57.5, 57.3, 47.7, 43.8, 43.4, 43.2, 43.0, 41.8 (2 signals), 40.9, 40.4, 39.9, 39.5, 32.6, 32.4, 32.2, 32.1, 29.6, 27.0, 26.6, 26.5, 23.0, 22.8, 21.5, 17.3, 17.2; IR (thin film): 2928, 2893, 2872, 2728, 1718, 1646, 1642, 1457, 1437, 1420, 1277, 1270, 1158, 1075, 1054, 1031, 936, 933, 798, 732 cm^{-1}; HRMS calc'd for $C_{26}H_{32}N_2O_5$ = 452.2311, found = 452.2303.

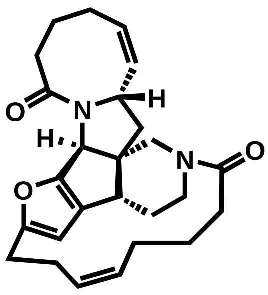


Compound 51

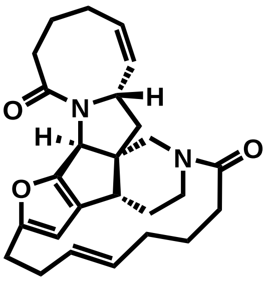
Compound **59** was divided into three equivalent portions (~4 mg each) for the Wittig, and they were combined for work up and column after each reaction was determined to be successful. The procedure for one of these 4 mg samples will be given. Compound **59** was dissolved in THF (0.5 mL). A solution of the Wittig ylide (prepared by stirring $MePPh_3Br$ (330 mg, 0.923 mmol) and KOtBu (80 mg, 0.713 mmol) for 1.5 hours in toluene (3 mL)) was added via cannula until the reaction was yellow/brown (~2 mL). Upon initial addition of the ylide solution, the reaction turns bright red/purple, and if addition is stopped at this stage, little to no product can be isolated. After 10 minutes, water (2 mL) was added to the reaction. At this stage all three reactions were combined, and the organic solvent removed under reduced pressure. Ethyl acetate (10 mL) and water (5 mL) was added to the residue and the layers were separated. The aqueous layer was extracted three times with ethyl acetate, and the combined organics were washed with water, brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate as eluent) to yield the desired bis-alkene **51** which was contaminated with triphenylphosphine oxide (23 mg total mass of mixture). The triphenylphosphine oxide did not affect the following metathesis step, but a small portion (~ 1 mg) of **51** was purified by preparative TLC (4% methanol in CH_2Cl_2, eluted 4 times) for characterization by ^{1}H-NMR, IR and HRMS. A ^{13}C-NMR was run with the triphenylphosphine oxide present. Due to the limited material, not all peaks were observed. A comparison of the peaks observed for ^{13}C-NMR with those reported by Nishida is presented in the following table. A visual comparison of the ^{1}H- and ^{13}C-spectra is in the spectral section of the supporting information. Bis-alkene **51** was formed as a 5:3 mixture of rotamers. A single proton of the major rotamer was set to one for proton integration. R_f = 0.38, 100% ethyl acetate; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 5.86-5.74 (m, 5.9H, contains furan singlets at 5.83 (0.6H) and 5.82 (1H)), 5.50 (dd, J = 12.0, 9.6 Hz, 1.6H), 5.07-4.95 (m, 6.7H), 4.90 (s, 1H), 4.64 (d, J = 9.6 Hz, 0.6H), 4.59 (d, J = 9.0 Hz, 1H), 4.17 (d, J = 14.4 Hz, 1H), 3.68 (d, J = 13.8 Hz, 0.6H), 3.52-3.46 (m, 0.6H), 3.46 (d, J = 13.8 Hz, 0.6H), 3.37-3.34 (m, 2H), 3.29-3.21 (m, 1.6H), 2.74-2.62 (m, 6.5H), 2.40-1.99 (m, 24.5H), 1.80-1.56 (m, 8.6H), 0.89-0.81 (m, 4.1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 173.6, 172.8, 161.9, 155.4, 154.6, 138.2, 137.54, 137.49, 134.4, 133.5, 128.0, 127.9, 127.5, 115.16, 115.1, 102.5, 102.4, 63.57, 59.7, 57.6, 57.4, 43.9, 43.5, 43.1, 41.1, 40.1, 33.4, 33.3, 32.9, 32.7, 32.6, 32.5, 31.9, 28.4, 27.3, 26.6, 24.1, 23.9, 23.1, 22.9 (see following table for not observed signals); IR (thin film): 3005, 2953, 2924, 2851, 2242, 1651, 1646, 1637, 1464, 1419, 1269, 1157, 993, 912 cm^{-1}; HRMS calc'd for $C_{28}H_{36}N_2O_3$ = 448.2726, found = 448.2728. Compound **51** is spectroscopically identical to that reported by Nishida (*J. Am. Chem. Soc*. **2003**, *125*, 7484 and *Angew. Chem. Int. Ed*. **2004**, *43*, 2020).

Comparison of observed ^{13}C-NMR signals with those reported by Nishida (*Angew. Chem. Int. Ed*. **2004**, *43*, 2020)

Nishida	**Kerr (Observed)**
173.7	173.6
173.4	
172.9	172.8
172.1	
161.9	161.9
161.8	
155.3	155.4
154.6	154.6
138.2	138.2
138.1	
137.54	137.54
137.49	137.49
134.4	134.4
133.5	133.5
128.6	
128.0	128.0
127.9	127.9
127.6	127.5
115.20	
115.19	
115.17	115.16
115.1	115.1
102.5	102.5
102.4	102.4
63.61	
63.57	63.57
59.7 (2C)	59.7
57.6	57.6
57.4	57.4
48.0	
43.9	43.9
43.5	43.5
43.1	43.1
41.1	41.1
40.6	
40.1	40.1
39.8	
33.4	33.4
33.3	33.3
32.9	32.9
32.7	32.7
32.6	32.6
32.5	32.5
31.9 (2C)	31.9
28.4 (2C)	28.4
27.3	27.3
26.9	
26.7	
26.6	26.6
24.1	24.1
23.9	23.9
23.1	23.1
22.9	22.9



Compound 52-*Z*

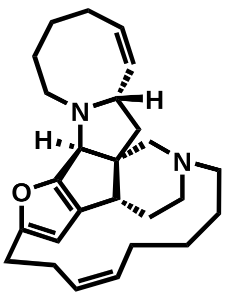


Compound 52-*E*

The mixture of **51** and triphenylphosphine oxide (23 mg) was dissolved in CH_2Cl_2 (70 mL) and to this solution was added Grubbs First Generation Catalyst (3.6 mg, 0.0044 mmol, ~30 mol%). The reaction flask was evacuated and back filled with argon five times, and then refluxed for 23 hours. The solvent was removed under reduced pressure, and a crude NMR indicated that the reaction had gone to completion and that the ratio of *E*:*Z* isomers was approximately 6:5. The reaction mixture was then purified by column chromatography on silica gel, (hexanes / ethyl acetate as eluent) to yield the undesired **52-*E*** (6.2 mg) and **52-*Z*** (4.0 mg). Due to the small scale and similarity in R_f, a large volume of chromatography solvents was required for complete separation. **52-*E*** contained substantial solvent derived impurities so it was resubjected to chromatography to yield **52-*E*** (3.2 mg, 0.0077 mmol, 28% over 2 steps). Compound **52-*Z*** had a lesser degree of chromatography solvent derived impurities, so it was used directly in the next step, and the yield will be given over a three step sequence. A visual comparison of the proton spectra to Nishida's is included for **52-*E*** and crude **52-*Z*** in the spectral section.

Compound 52-*E* (undesired isomer) - R_f = 0.28, 100% ethyl acetate; ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 5.81 (s, 1H), 5.60 (dd, J = 2.7, 12.3 Hz, 1H), 5.56-5.51 (m, 1H), 5.30-5.19 (m, 2H), 4.99 (s, 1H), 4.60 (d, J = 13.8 Hz, 1H), 4.48-4.45 (m, 1H), 3.36-3.30 (m, 1H), 3.23 (dd, J = 11.4, 6.6 Hz, 1H), 3.04 (s, 1H), 2.88-2.84 (m, 2H), 2.65-2.57 (m, 3H), 2.42-2.36 (m, 1H), 2.24-2.17 (m, 5H), 2.07-2.01 (m, 3H), 1.97-1.80 (m, 5H), 1.74-1.60 (m, 4H), 1.52-1.41 (m, 3H), 0.96-0.80 (m, 4H). Accurate integration of the protons from 1.7-0.8 ppm was difficult due to grease contamination; HRMS calc'd for $C_{26}H_{32}N_2O_3$ = 420.2413, found = 420.2422

Compound 52-*Z* –R_f = 0.13, 100% ethyl acetate; **52-*Z*** contained chromatography solvent impurities and was used directly in the next step.



(+)-ent-Nakadomarin A

(+)-Nakadomarin A is prepared from **52-*Z*** using the procedure of Nishida (*Angew. Chem. Int. Ed.* **2004**, *43*, 2020). A solution of the bis-amide **52-*Z*** (4.0 mg with impurities) in toluene (4 mL) was cooled to 0 °C. Red-Al (80 μL of a 65% solution in toluene) was added and stirring continued for 10 minutes at this temperature. The reaction was then heated to reflux for 3 hours, then quenched at -30 °C with saturated aqueous Rochelle's salt (3 mL). After warming to room temperature, the mixture was stirred vigorously for 1 hour, then ethyl acetate (3 mL) was added, and vigorous stirring continued for an additional hour. The layers were separated, and the aqueous layer extracted 4 times with ethyl acetate. The combined organics were washed with saturated aqueous Rochelle's salt, twice with brine and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica (methanol / ethyl acetate as eluent) to yield **(+)-ent-Nakadomarin A** (2.1 mg, 0.00535 mmol, 20% over 3 steps) as pale yellow film. The chemical shifts of the protons next to the amines showed some variance with respect to those reported by Nishida, and Nishida attributed this to trace acid in his initial publication, *J. Am.*

Chem. Soc. **2003**, *125*, 7484. MeOH-d_4 (1 mL) filtered through basic alumina was added to the sample and then removed under reduced pressure (running this sample directly led to a large water peak). Fresh MeOH-d_4 was added to yield a spectrum that was identical to that published by Nishida. A comparison of the proton spectra (both the initial and neutralized) to Nishida's is included in the spectral section.

(+)-Nakadomarin A - R_f = 0.18, 75% methanol in ethyl acetate; ^{1}H-NMR (600 MHz, MeOH-d_4): δ = 5.87 (s, 1H), 5.83-5.79 (m, 1H), 5.50 (dd, J = 9.0, 8.7 Hz, 1H), 5.46-5.42 (m, 1H), 5.28-5.24 (m, 1H), 3.94 (s, 1H), 3.75-3.71 (m, 1H), 3.04 (d, J = 12.6 Hz, 1H),. 3.04-3.00 (m, 1H), 2.84 (br. s, 1H), 2.82-2.75 (m, 1H), 2.71 (dd, J = 6.0, 12.0 Hz, 1H), 2.64-2.59 (m, 2H), 2.51-2.46 (m, 1H), 2.40 (ddd, J = 3.6, 3.0, 11.4 Hz, 1H), 2.36-2.29 (m, 2H), 2.30 (d, J = 12.6 Hz, 1H), 2.19-1.97 (m, 5H), 1.94-1.89 (m, 2H), 1.82 (ddd, J = 3.0, 7.2, 14.0 Hz, 1H), 1.74-1.59 (m, 4H), 1.49 (dd, J = 9.9, 12.3 Hz, 1H), 1.42-1.23 (m, 2H), 1.09-1.04 (m, 1H), 0.91-0.84 (m, 2H). Accurate integration of the protons from 1.7-0.8 ppm was difficult due to grease contamination; IR (thin film): 3006, 2926, 2857, 2793, 1457, 1132, 1081, 954 cm^{-1}; HRMS calc'd for $C_{26}H_{36}N_2O$= 392.2828, found = 392.2815; $[\alpha]_D$ = +60.7 (*c* = 0.27, MeOH), literature $[\alpha]_D$ = -73.0 (*c* = 0.08, MeOH) (*Angew. Chem. Int. Ed*. **2004**, *43*, 2020).

```
IY-7-9 Inova 400

exp1  s2pul

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solvent      CDCl3  gain        not used
file           exp  spin              20
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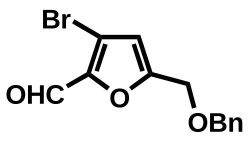
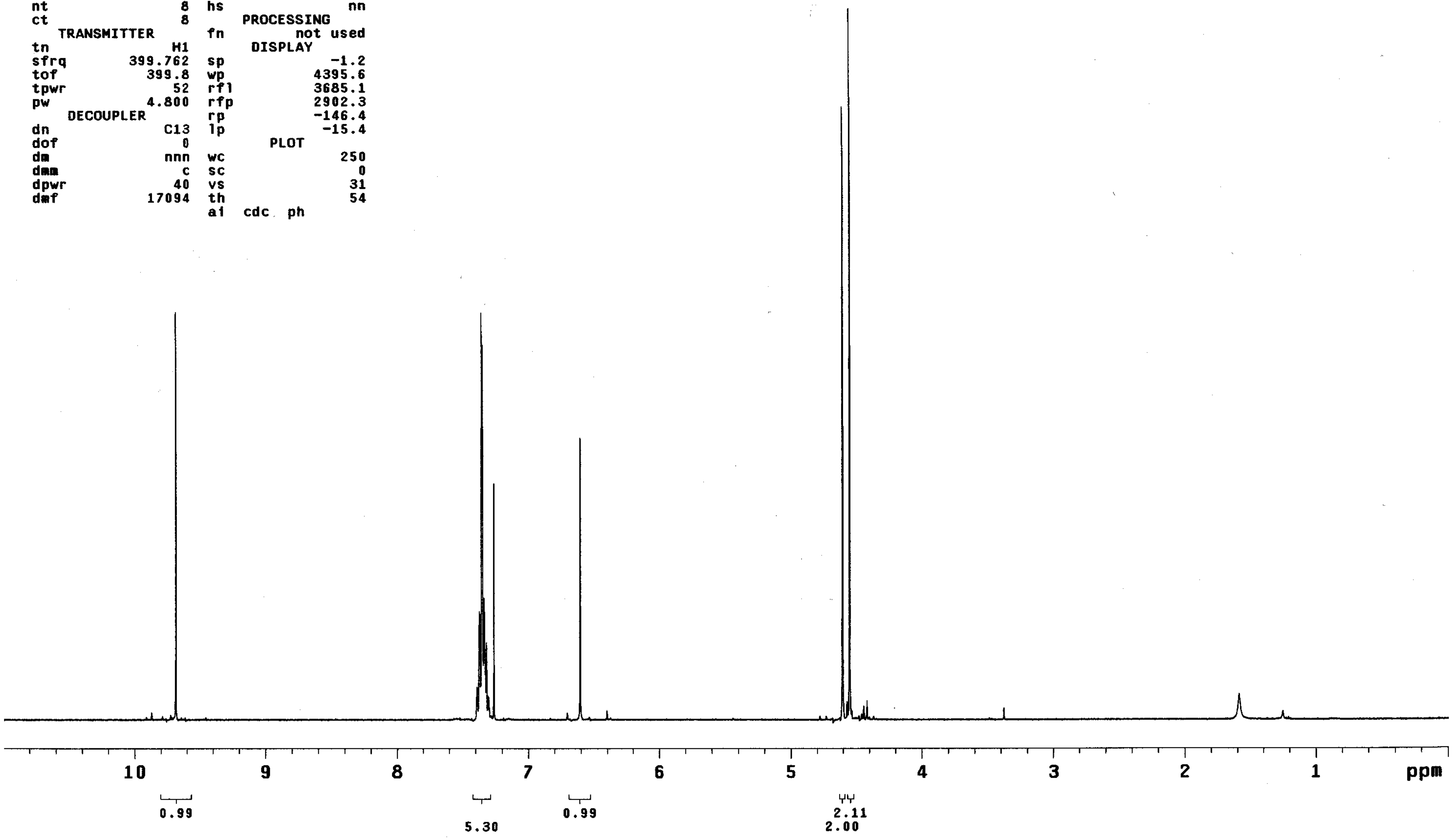
sw          6395.9  pw90           9.600
at           3.744  alfa           6.600
np           47892          FLAGS
fb            4000  il                 n
bs              16  in                 n
d1           1.000  dp                 y
nt               8  hs                nn
ct               8        PROCESSING
   TRANSMITTER      fn          not used
tn              H1         DISPLAY
sfrq       399.762  sp              -1.2
tof          399.8  wp            4395.6
tpwr            52  rfl           3685.1
pw           4.800  rfp           2902.3
    DECOUPLER       rp            -146.4
dn             C13  lp             -15.4
dof              0           PLOT
dm             nnn  wc               250
dmm              c  sc                 0
dpwr            40  vs                31
dmf          17094  th                54
                    ai  cdc  ph
```



Compound 24



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IY-7-9ccc
STANDARD 1H OBSERVE

exp12  s2pul

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date   Mar 18 2004  temp      not used
solvent      cdcl3  gain      not used
file /export/home/~ spin      not used
vnmr1/vnmrsys/data~ hst          0.008
/iyoung/IY-7-9ccc/~ pw90        11.600
        CARBON.fid  alfa        20.000
   ACQUISITION            FLAGS
sw         25125.6  il               n
at           1.199  in               n
np           60270  dp               y
fb           13800  hs              nn
bs              64       PROCESSING
d1           1.000  lb            1.00
nt            1000  fn        not used
ct             128        DISPLAY
   TRANSMITTER      sp           -14.4
tn             C13  wp         20140.7
sfrq       100.613  rfl         9275.9
tof         1550.8  rfp         7746.3
tpwr            57  rp          -121.7
pw           5.800  lp          -397.6
    DECOUPLER             PLOT
dn              H1  wc             250
dof              0  sc               0
dm             yyy  vs              73
dmm              w  th               9
dpwr            40  ai   no   ph
dmf           9300
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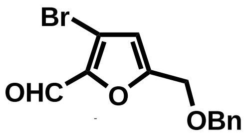
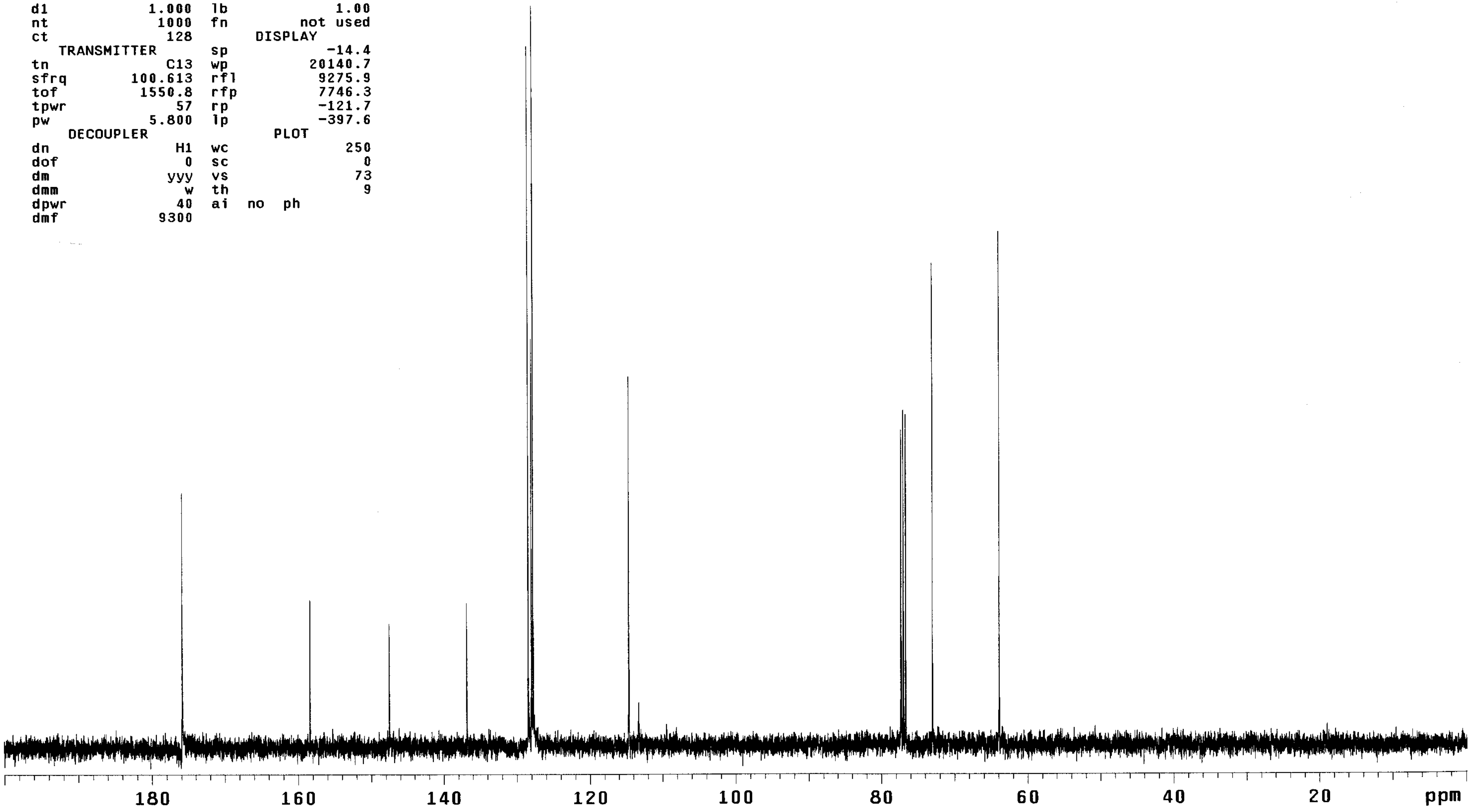
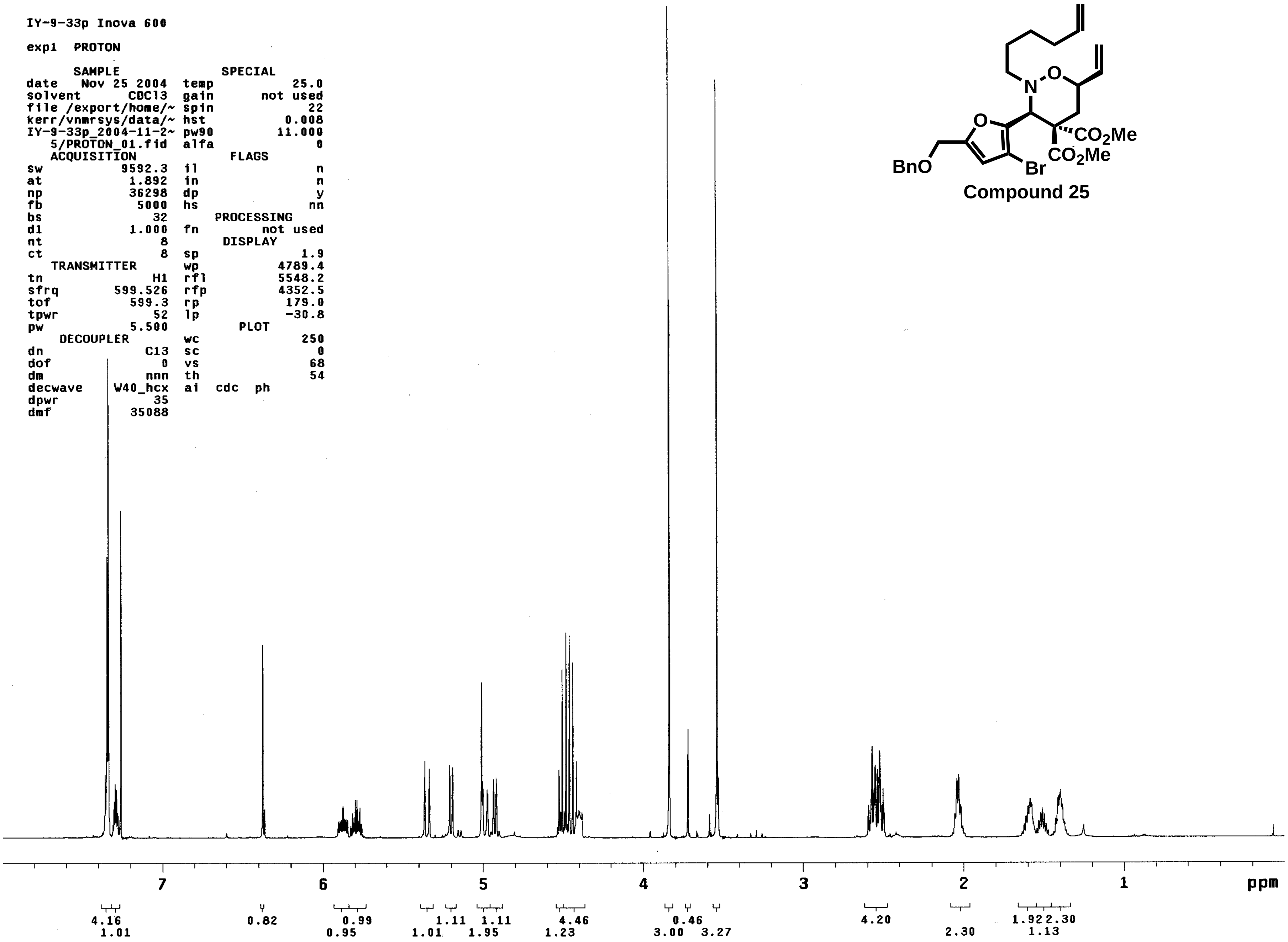


Compound 24





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IY-9-33p Inova 600

exp1  PROTON

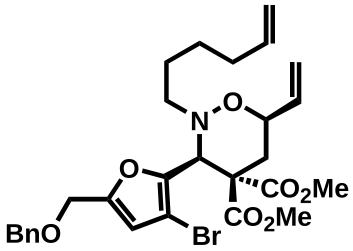
     SAMPLE                SPECIAL
date   Nov 25 2004  temp             25.0
solvent      CDCl3  gain         not used
file /export/home/~ spin               22
kerr/vnmrsys/data/~ hst             0.008
IY-9-33p_2004-11-2~ pw90           11.000
   5/PROTON_01.fid  alfa                0
   ACQUISITION              FLAGS
sw          9592.3  il                  n
at           1.892  in                  n
np           36298  dp                  y
fb            5000  hs                 nn
bs              32        PROCESSING
d1           1.000  fn           not used
nt               8         DISPLAY
ct               8  sp                1.9
   TRANSMITTER      wp             4789.4
tn              H1  rfl            5548.2
sfrq       599.526  rfp            4352.5
tof          599.3  rp              179.0
tpwr            52  lp              -30.8
pw           5.500           PLOT
    DECOUPLER       wc                250
dn             C13  sc                  0
dof              0  vs                 68
dm             nnn  th                 54
decwave    W40_hcx  ai   cdc  ph
dpwr            35
dmf          35088
```

Compound 25

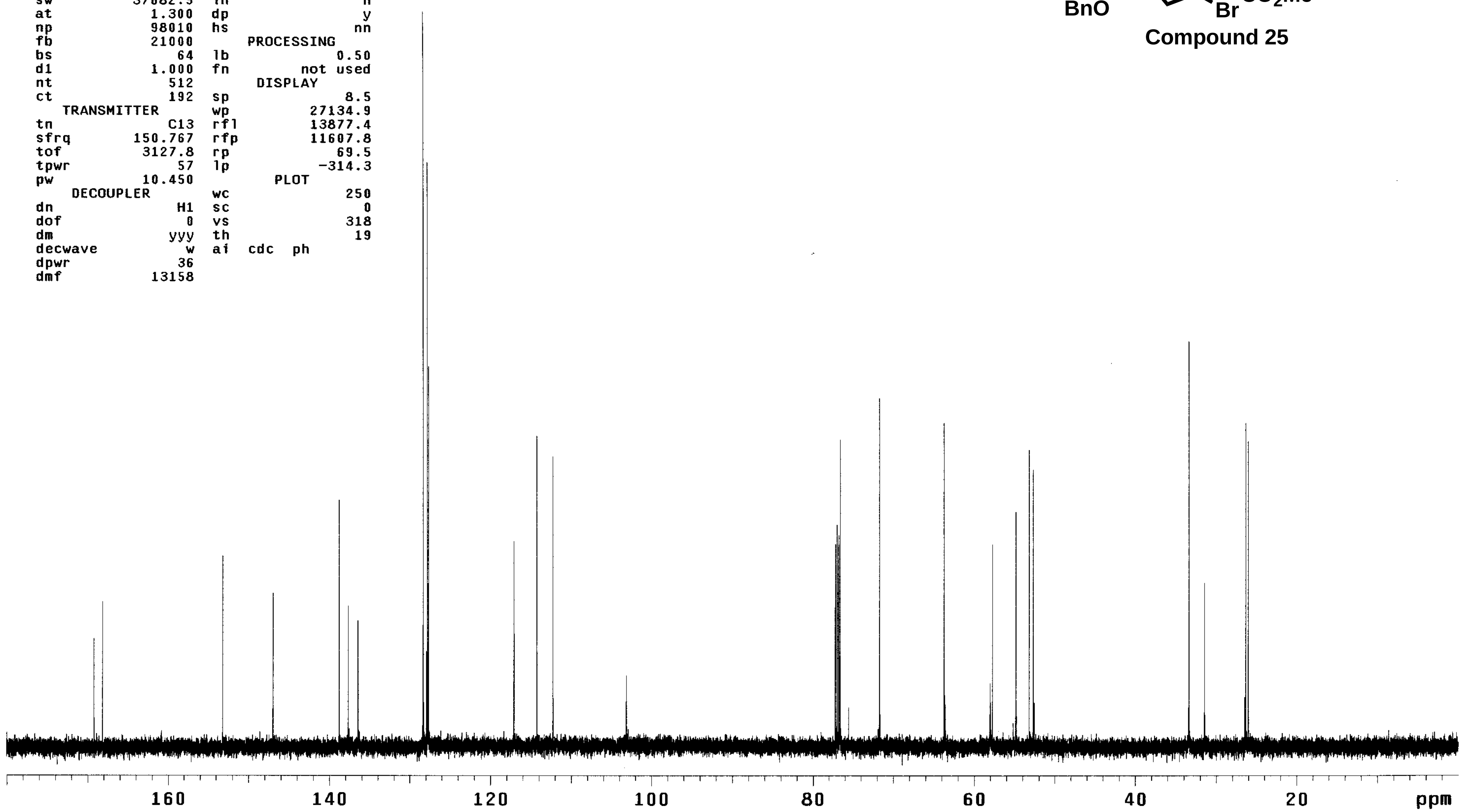
```
IY-9-33carbon Inova 600

exp1  CARBON

      SAMPLE                SPECIAL
date   Nov 25 2004  temp            25.0
solvent      CDCl3  gain        not used
file /export/home/~ spin              16
kerr/vnmrsys/data/~ hst            0.008
IY-9-33carbon_2004~ pw90          20.900
-11-25/CARBON_01.f~ alfa          10.000
                id           FLAGS
   ACQUISITION      il                 n
sw         37682.5  in                 n
at           1.300  dp                 y
np           98010  hs                nn
fb           21000        PROCESSING
bs              64  lb              0.50
d1           1.000  fn          not used
nt             512           DISPLAY
ct             192  sp               8.5
   TRANSMITTER      wp           27134.9
tn             C13  rfl          13877.4
sfrq       150.767  rfp          11607.8
tof         3127.8  rp              69.5
tpwr            57  lp            -314.3
pw          10.450             PLOT
    DECOUPLER       wc               250
dn              H1  sc                 0
dof              0  vs               318
dm             yyy  th                19
decwave          w  ai    cdc  ph
dpwr            36
dmf          13158
```



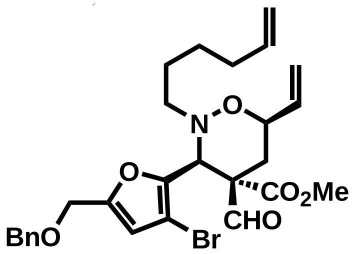
Compound 25



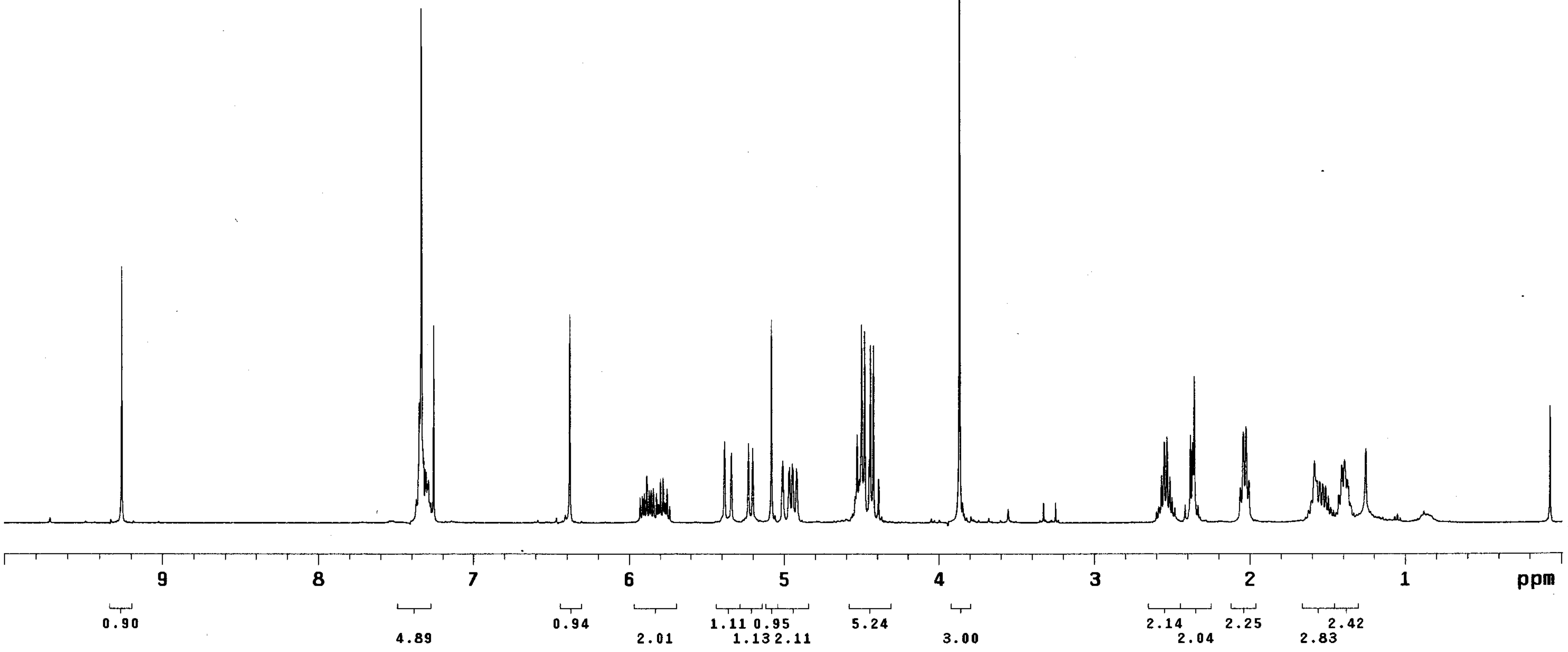
```
IY-7-93spt2 Inova 400

exp1  s2pul

      SAMPLE               SPECIAL
date   Apr 29 2004   temp        not used
solvent      CDCl3   gain        not used
file           exp   spin              20
    ACQUISITION      hst            0.008
sw          6395.9   pw90           9.600
at           3.744   alfa           6.600
np           47892          FLAGS
fb            4000   il                 n
bs              16   in                 n
d1           1.000   dp                 y
nt               8   hs                nn
ct               8        PROCESSING
    TRANSMITTER      fn          not used
tn              H1         DISPLAY
sfrq       399.762   sp              -2.4
tof          399.8   wp            4000.5
tpwr            52   rfl           3686.2
pw           4.800   rfp           2902.3
     DECOUPLER       rp             -75.4
dn             C13   lp             -23.0
dof              0           PLOT
dm             nnn   wc               250
dmm              c   sc                 0
dpwr            40   vs                85
dmf          17094   th                 2
                     ai   cdc   ph
```



Compound 26



```
IY-8-77c
STANDARD 1H OBSERVE

exp3  s2pul

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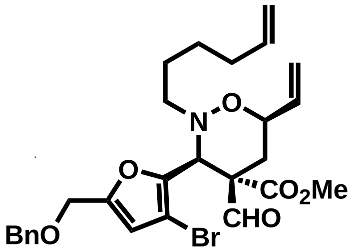
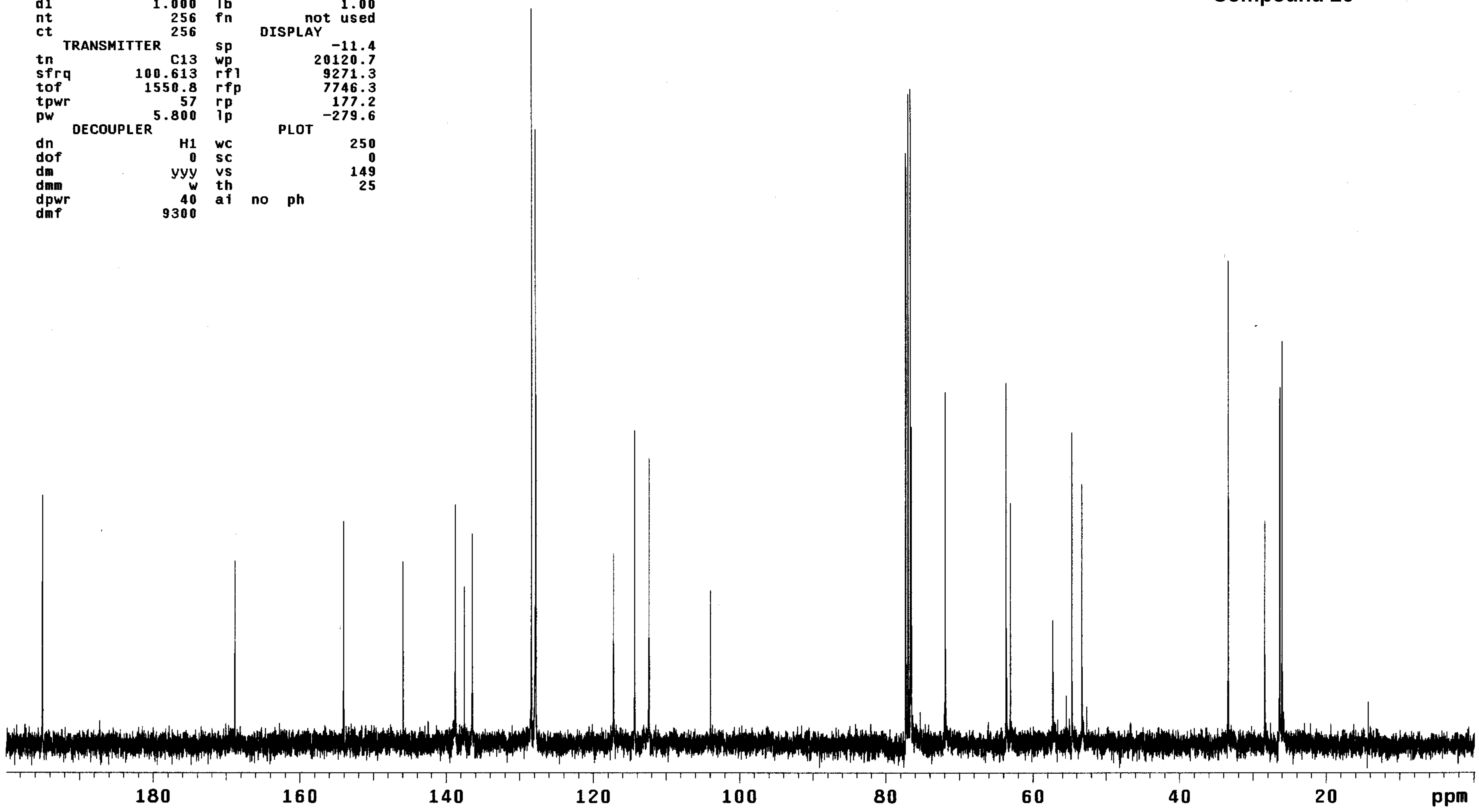
date   Jul 15 2004  temp       not used
solvent      cdcl3  gain       not used
file /export/home/~ spin       not used
vnmr1/vnmrsys/data~ hst           0.008
/iyoung/IY-8-77c/C~ pw90         11.600
         ARBON.fid  alfa         20.000
   ACQUISITION              FLAGS
sw         25125.6  il                n
at           1.199  in                n
np           60270  dp                y
fb           13800  hs               nn
bs              64        PROCESSING
d1           1.000  lb             1.00
nt             256  fn         not used
ct             256         DISPLAY
   TRANSMITTER      sp            -11.4
tn             C13  wp          20120.7
sfrq       100.613  rfl          9271.3
tof         1550.8  rfp          7746.3
tpwr            57  rp            177.2
pw           5.800  lp           -279.6
    DECOUPLER               PLOT
dn              H1  wc              250
dof              0  sc                0
dm             yyy  vs              149
dmm              w  th               25
dpwr            40  ai  no  ph
dmf           9300
```



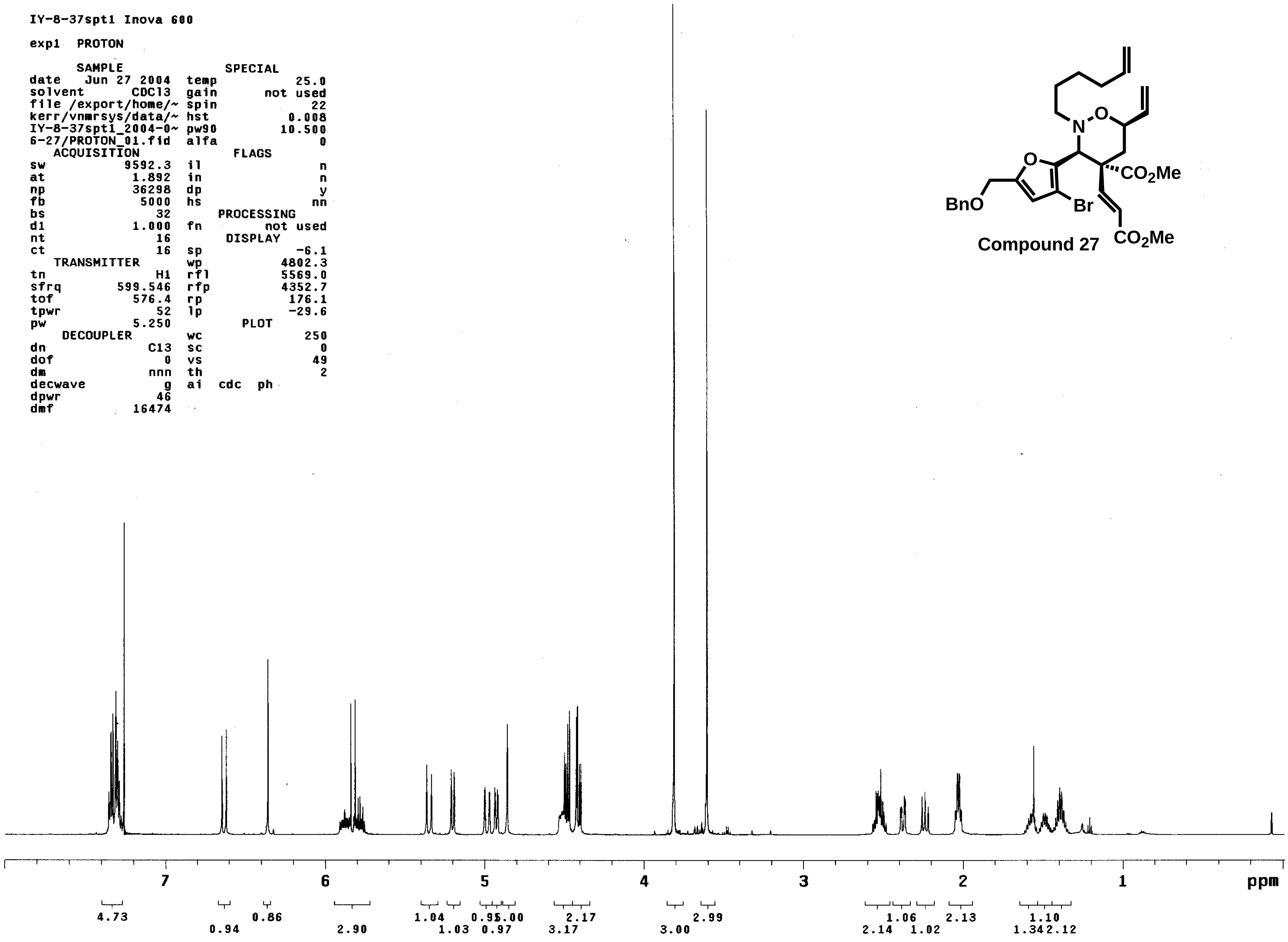
Compound 26



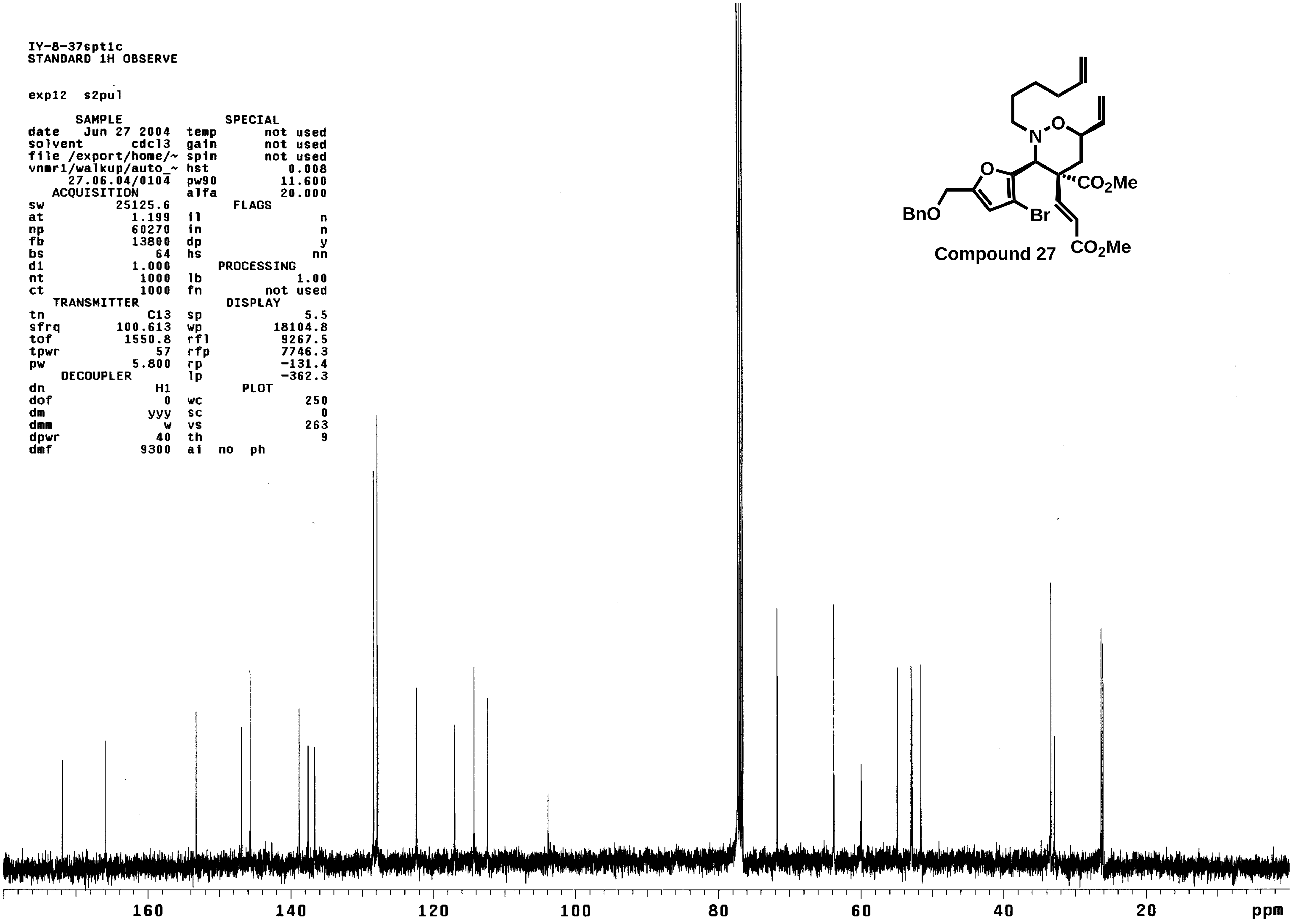
```
IY-8-37spt1 Inova 600

exp1  PROTON

      SAMPLE              SPECIAL
date   Jun 27 2004  temp          25.0
solvent      CDCl3  gain      not used
file /export/home/~ spin            22
kerr/vnmrsys/data/~ hst          0.008
IY-8-37spt1_2004-0~ pw90        10.500
6-27/PROTON_01.fid  alfa             0
   ACQUISITION            FLAGS
sw          9592.3  il               n
at           1.892  in               n
np           36298  dp               y
fb            5000  hs              nn
bs              32       PROCESSING
d1           1.000  fn        not used
nt              16         DISPLAY
ct              16  sp            -6.1
   TRANSMITTER      wp          4802.3
tn              H1  rfl         5569.0
sfrq       599.546  rfp         4352.7
tof          576.4  rp           176.1
tpwr            52  lp           -29.6
pw           5.250            PLOT
    DECOUPLER       wc             250
dn             C13  sc               0
dof              0  vs              49
dm             nnn  th               2
decwave          g  ai   cdc  ph
dpwr            46
dmf          16474
```



Compound 27



```
IY-8-37spt1c
STANDARD 1H OBSERVE

exp12  s2pul

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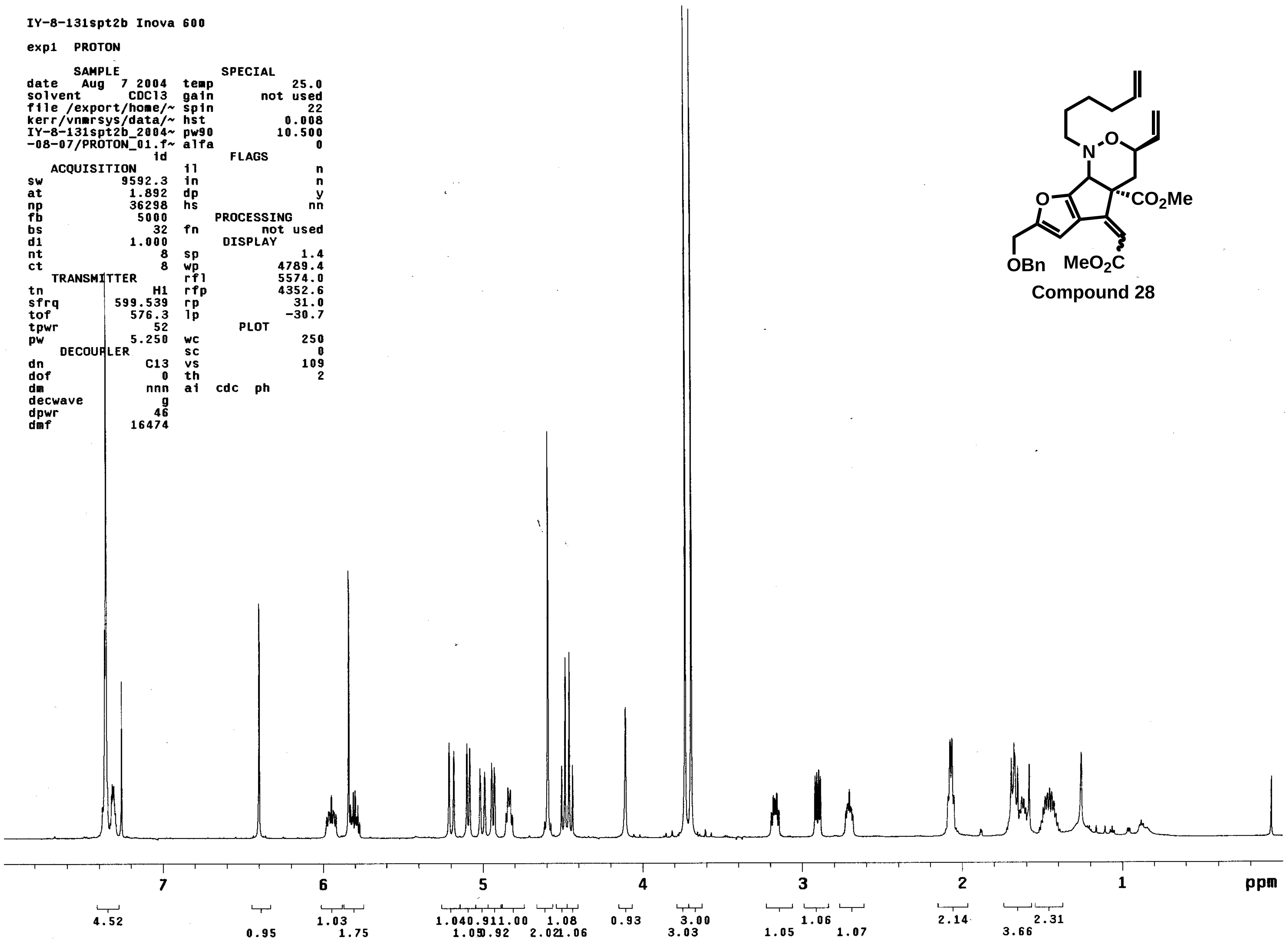
solvent      cdcl3  gain       not used
file /export/home/~ spin       not used
vnmr1/walkup/auto_~ hst           0.008
     27.06.04/0104  pw90         11.600
   ACQUISITION      alfa         20.000
sw         25125.6          FLAGS
at           1.199  il                n
np           60270  in                n
fb           13800  dp                y
bs              64  hs               nn
d1           1.000        PROCESSING
nt            1000  lb             1.00
ct            1000  fn         not used
   TRANSMITTER             DISPLAY
tn             C13  sp              5.5
sfrq       100.613  wp          18104.8
tof         1550.8  rfl          9267.5
tpwr            57  rfp          7746.3
pw           5.800  rp           -131.4
    DECOUPLER       lp           -362.3
dn              H1          PLOT
dof              0  wc              250
dm             yyy  sc                0
dmm              w  vs              263
dpwr            40  th                9
dmf           9300  ai   no  ph
```

Compound 27



Compound 28

```
IY-8-131spt2b Inova 600

exp1  PROTON

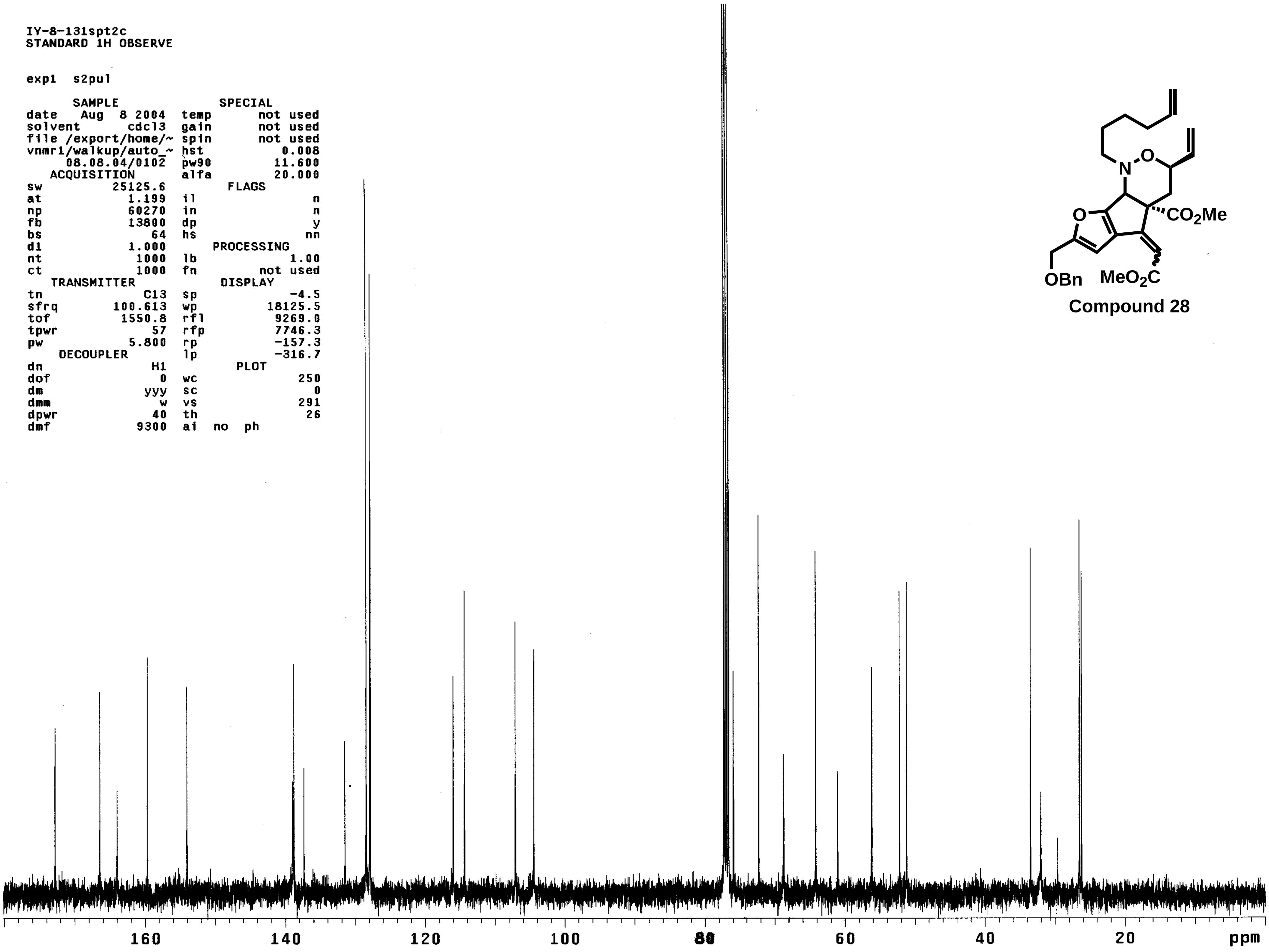
      SAMPLE              SPECIAL
date   Aug  7 2004  temp           25.0
solvent      CDCl3  gain       not used
file /export/home/~ spin             22
kerr/vnmrsys/data/~ hst           0.008
IY-8-131spt2b_2004~ pw90         10.500
-08-07/PROTON_01.f~ alfa              0
                 id         FLAGS
   ACQUISITION      il                n
sw           9592.3 in                n
at            1.892 dp                y
np            36298 hs               nn
fb             5000      PROCESSING
bs               32 fn         not used
d1            1.000        DISPLAY
nt                8 sp              1.4
ct                8 wp           4789.4
   TRANSMITTER      rfl          5574.0
tn               H1 rfp          4352.6
sfrq        599.539 rp             31.0
tof           576.3 lp            -30.7
tpwr             52          PLOT
pw            5.250 wc              250
    DECOUPLER       sc                0
dn              C13 vs              109
dof               0 th                2
dm              nnn ai   cdc   ph
decwave           g
dpwr             46
dmf           16474
```

```
IY-8-131spt2c
STANDARD 1H OBSERVE

exp1  s2pul

      SAMPLE              SPECIAL
date   Aug  8 2004  temp      not used
solvent      cdcl3  gain      not used
file /export/home/~ spin      not used
vnmr1/walkup/auto_~ hst          0.008
     08.08.04/0102  pw90        11.600
   ACQUISITION      alfa        20.000
sw         25125.6          FLAGS
at           1.199  il               n
np           60270  in               n
fb           13800  dp               y
bs              64  hs              nn
d1           1.000         PROCESSING
nt            1000  lb            1.00
ct            1000  fn        not used
   TRANSMITTER              DISPLAY
tn             C13  sp            -4.5
sfrq       100.613  wp         18125.5
tof         1550.8  rfl         9269.0
tpwr            57  rfp         7746.3
pw           5.800  rp          -157.3
    DECOUPLER       lp          -316.7
dn              H1           PLOT
dof              0  wc             250
dm             yyy  sc               0
dmm              w  vs             291
dpwr            40  th              26
dmf           9300  ai  no  ph
```

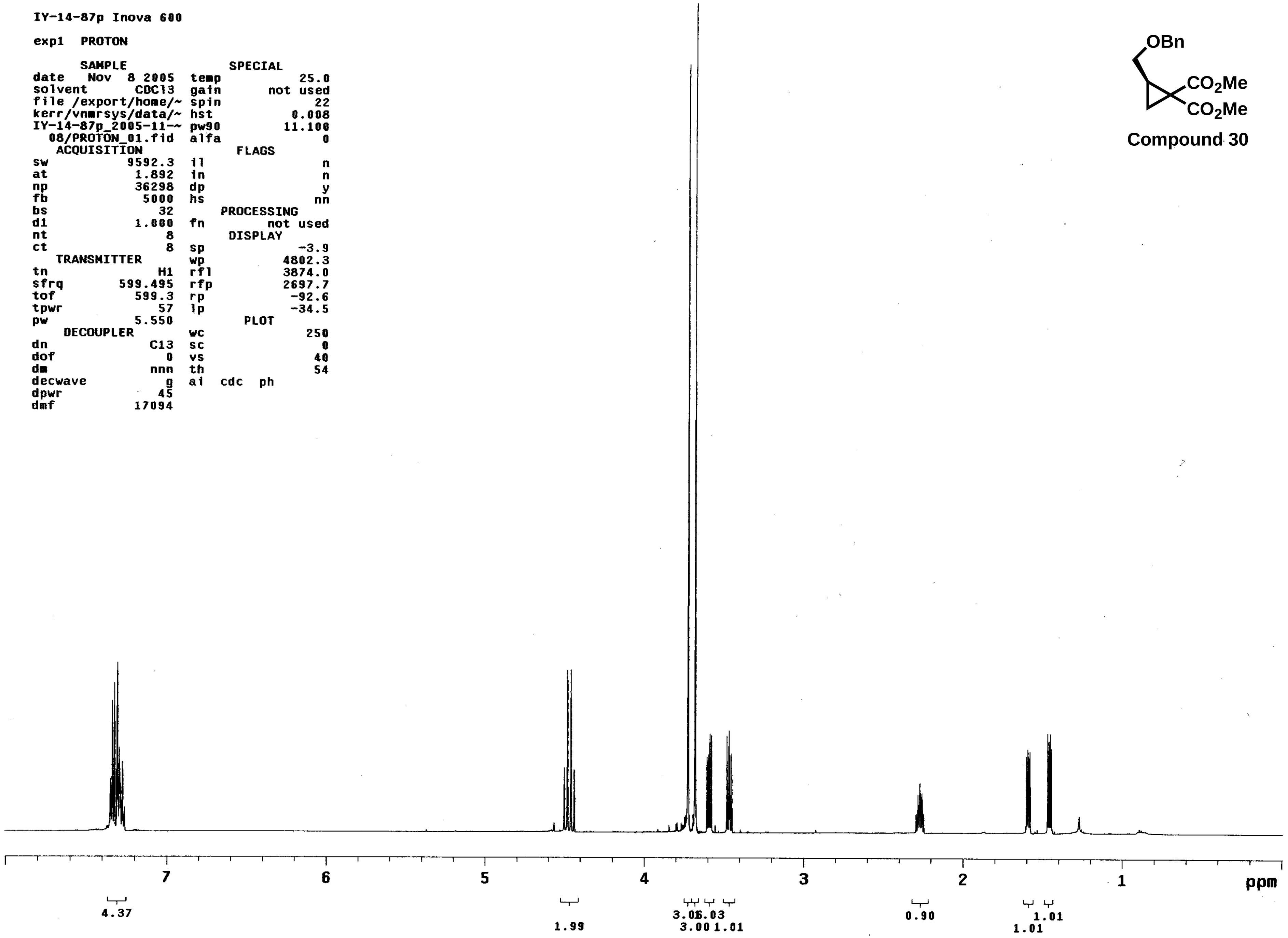
Compound 28



```
IY-14-87p Inova 600

exp1  PROTON

    SAMPLE              SPECIAL
date   Nov  8 2005  temp          25.0
solvent      CDCl3  gain      not used
file /export/home/~ spin            22
kerr/vnmrsys/data/~ hst          0.008
IY-14-87p_2005-11-~ pw90        11.100
  08/PROTON_01.fid  alfa             0
   ACQUISITION           FLAGS
sw          9592.3  il               n
at           1.892  in               n
np           36298  dp               y
fb            5000  hs              nn
bs              32      PROCESSING
d1           1.000  fn        not used
nt               8       DISPLAY
ct               8  sp            -3.9
   TRANSMITTER      wp          4802.3
tn              H1  rfl         3874.0
sfrq       599.495  rfp         2697.7
tof          599.3  rp           -92.6
tpwr            57  lp           -34.5
pw           5.550         PLOT
    DECOUPLER       wc             250
dn             C13  sc               0
dof              0  vs              40
dm             nnn  th              54
decwave          g  ai  cdc  ph
dpwr            45
dmf          17094
```

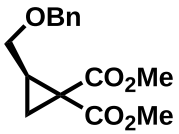


Compound 30

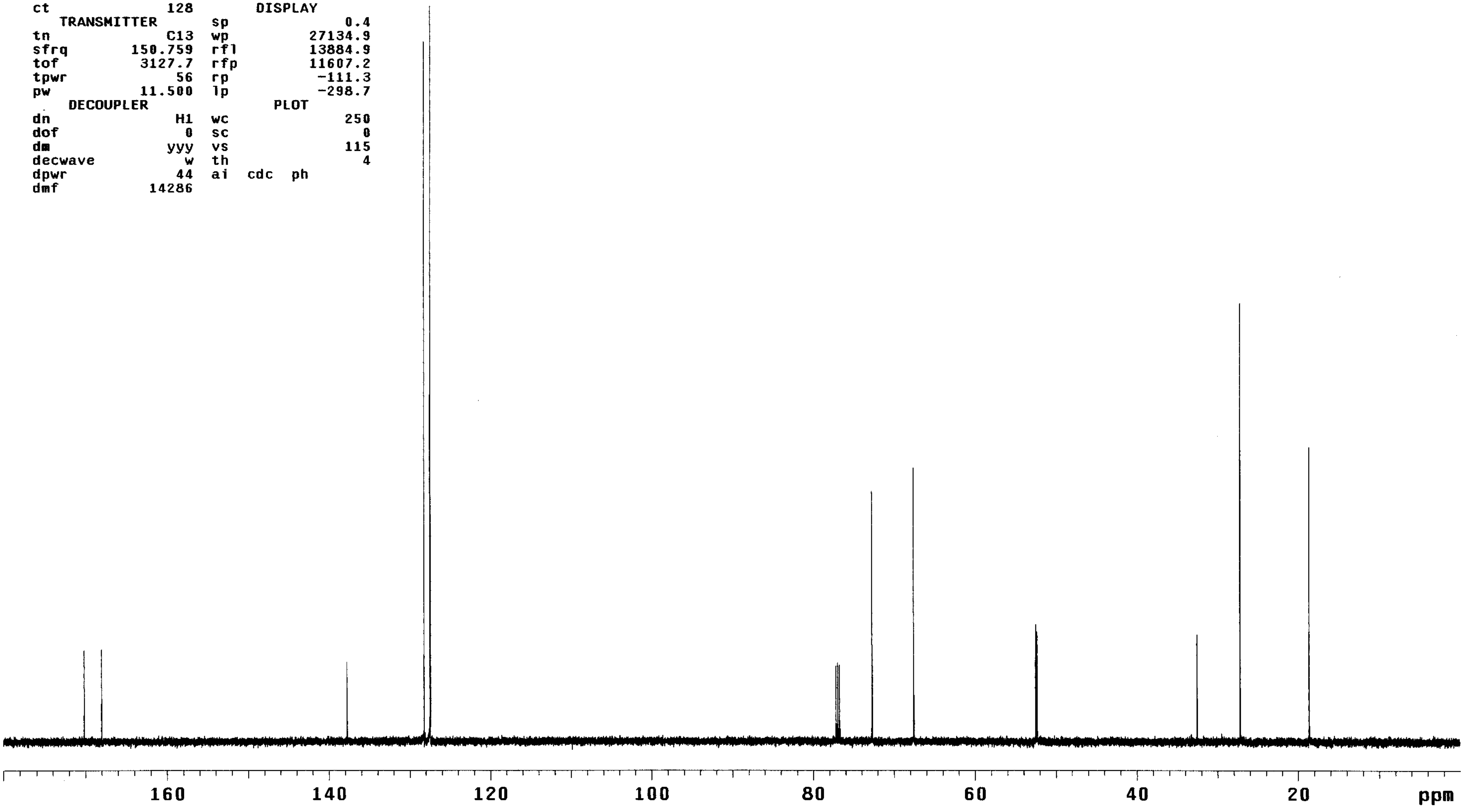
```
IY-14-87c Inova 600

exp1  CARBON

      SAMPLE              SPECIAL
date   Nov  8 2005  temp          25.0
solvent      CDCl3  gain      not used
file /export/home/~ spin            16
kerr/vnmrsys/data/~ hst          0.008
IY-14-87c_2005-11-~ pw90        23.000
  08/CARBON_01.fid  alfa        10.000
   ACQUISITION             FLAGS
sw         37682.5  il               n
at           1.300  in               n
np           98010  dp               y
fb           21000  hs              nn
bs              64       PROCESSING
d1           1.000  lb            0.50
nt             512  fn        not used
ct             128        DISPLAY
   TRANSMITTER      sp             0.4
tn             C13  wp         27134.9
sfrq       150.759  rfl        13884.9
tof         3127.7  rfp        11607.2
tpwr            56  rp          -111.3
pw          11.500  lp          -298.7
    DECOUPLER              PLOT
dn              H1  wc             250
dof              0  sc               0
dm             yyy  vs             115
decwave          w  th               4
dpwr            44  ai  cdc  ph
dmf          14286
```



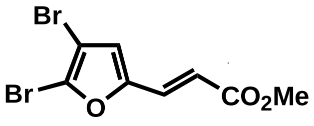
Compound 30



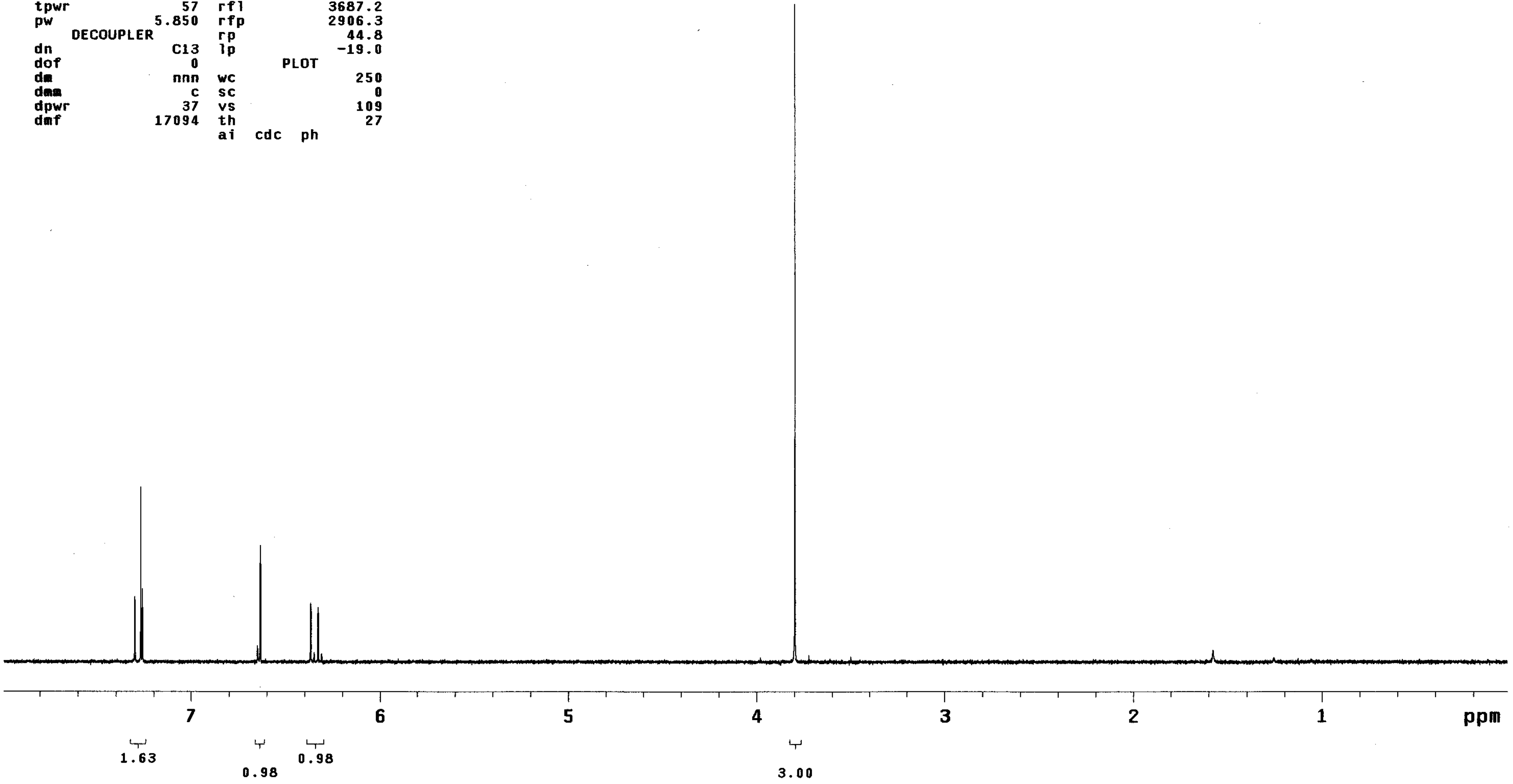
```
IY-furanenoate Inova 400

exp1  s2pul

      SAMPLE               SPECIAL
date   Aug  6 2005   temp       not used
solvent      CDCl3   gain       not used
file           exp   spin             20
   ACQUISITION       hst           0.008
sw          6395.9   pw90         11.700
at           3.744   alfa          6.600
np           47892           FLAGS
fb            4000   il                n
bs              16   in                n
d1           1.000   dp                y
nt               8   hs               nn
ct               8         PROCESSING
   TRANSMITTER       fn         not used
tn              H1          DISPLAY
sfrq       399.762   sp              9.0
tof          399.8   wp           3185.2
tpwr            57   rfl          3687.2
pw           5.850   rfp          2906.3
    DECOUPLER        rp             44.8
dn             C13   lp            -19.0
dof              0            PLOT
dm             nnn   wc              250
dmm              c   sc                0
dpwr            37   vs              109
dmf          17094   th               27
                     ai   cdc   ph
```



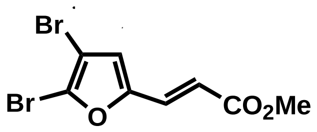
Compound 31b



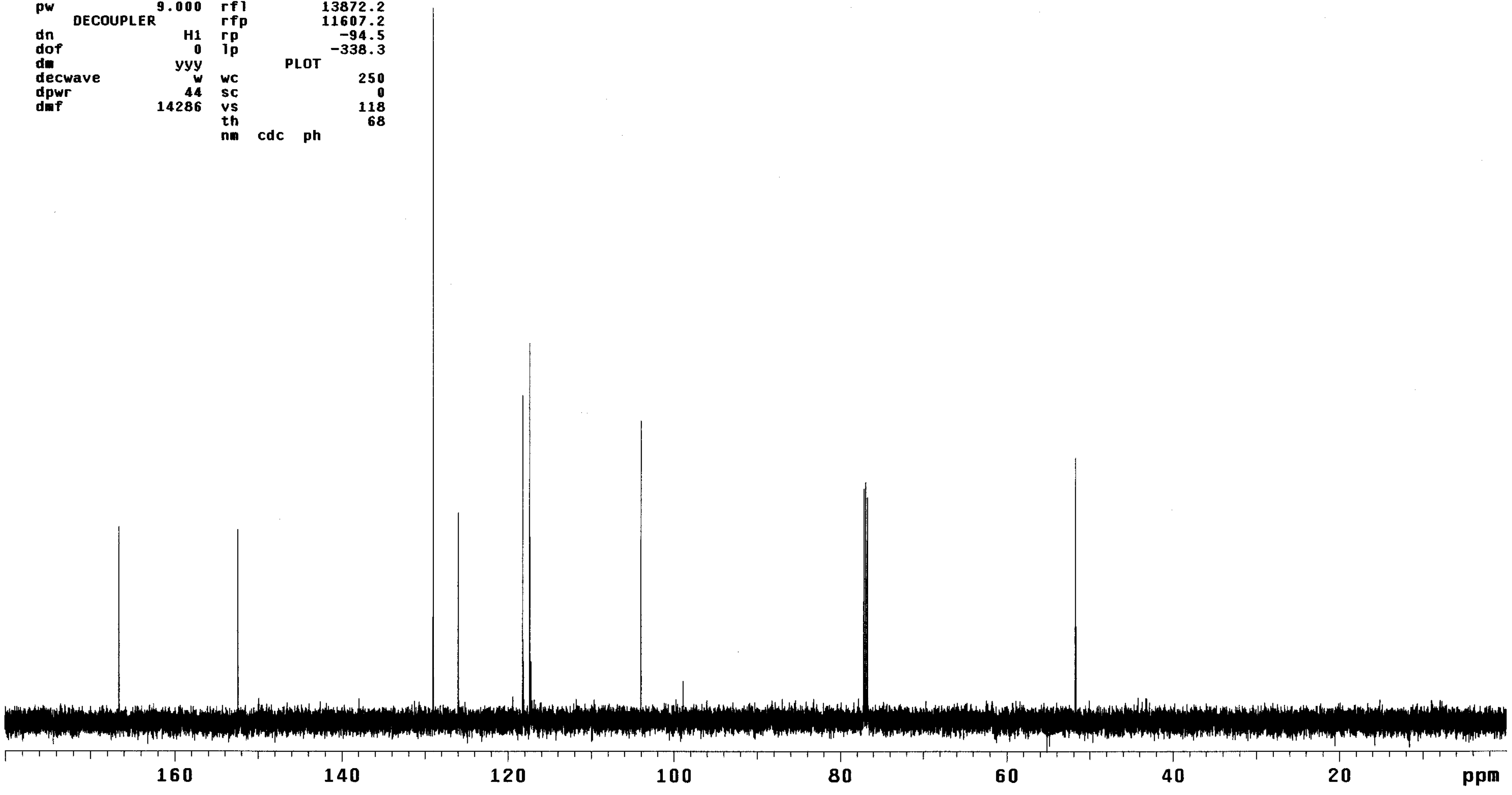
```
IY-15-61c Inova 600

exp1  CARBON

      SAMPLE             SPECIAL
date   Nov 29 2005  temp          25.0
solvent      CDCl3  gain      not used
file           exp  spin            16
   ACQUISITION      hst          0.008
sw         37682.5  pw90        18.000
at           1.300  alfa        10.000
np           98010          FLAGS
fb           21000  il               n
bs              64  in               n
d1           1.000  dp               y
nt             256  hs              nn
ct              64        PROCESSING
   TRANSMITTER      lb            0.50
tn             C13  fn        not used
sfrq       150.759          DISPLAY
tof         3127.7  sp            13.1
tpwr            56  wp         27134.9
pw           9.000  rfl        13872.2
    DECOUPLER       rfp        11607.2
dn              H1  rp           -94.5
dof              0  lp          -338.3
dm             yyy           PLOT
decwave          w  wc             250
dpwr            44  sc               0
dmf          14286  vs             118
                    th              68
                    nm  cdc  ph
```



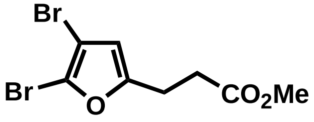
Compound 31b



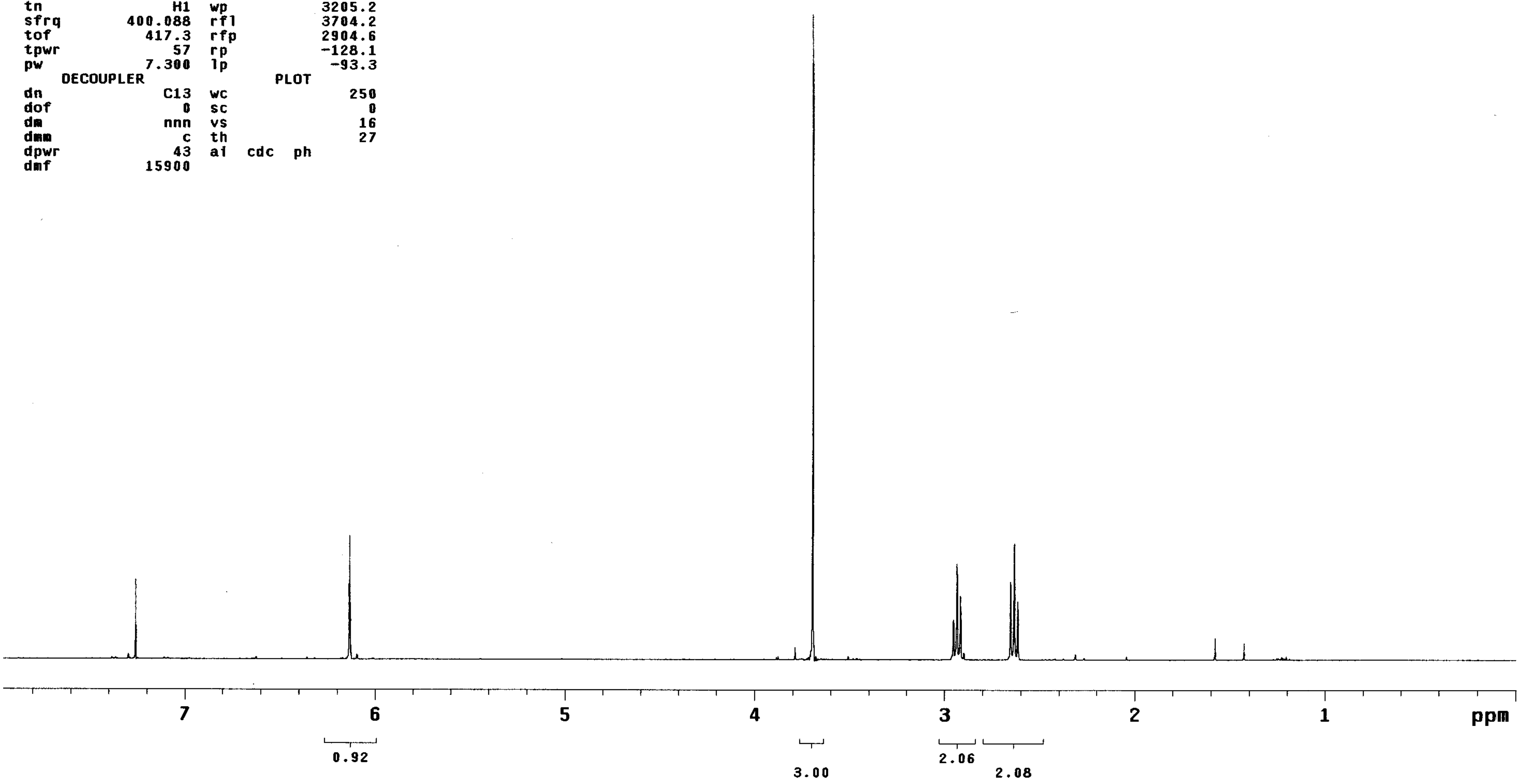
```
IY-13-199mercury
STANDARD 1H OBSERVE

exp1  s2pul

      SAMPLE                SPECIAL
date   Aug  7 2005  temp      not used
solvent      cdcl3  gain      not used
file /export/home/~ spin            20
vnmr1/walkup/auto_~ hst          0.008
     07.08.05/0203  pw90        14.600
   ACQUISITION      alfa        20.000
sw          6402.0          FLAGS
at           4.000  il               n
np           51216  in               n
fb        not used  dp               y
bs              16  hs              nn
d1           1.000        PROCESSING
nt               8  fn        not used
ct               8          DISPLAY
   TRANSMITTER      sp            -0.5
tn              H1  wp          3205.2
sfrq       400.088  rfl         3704.2
tof          417.3  rfp         2904.6
tpwr            57  rp          -128.1
pw           7.300  lp           -93.3
    DECOUPLER                PLOT
dn             C13  wc             250
dof              0  sc               0
dm             nnn  vs              16
dmm              c  th              27
dpwr            43  ai  cdc  ph
dmf          15900
```



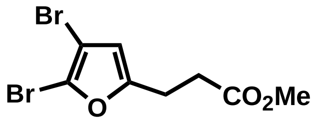
Compound 31c



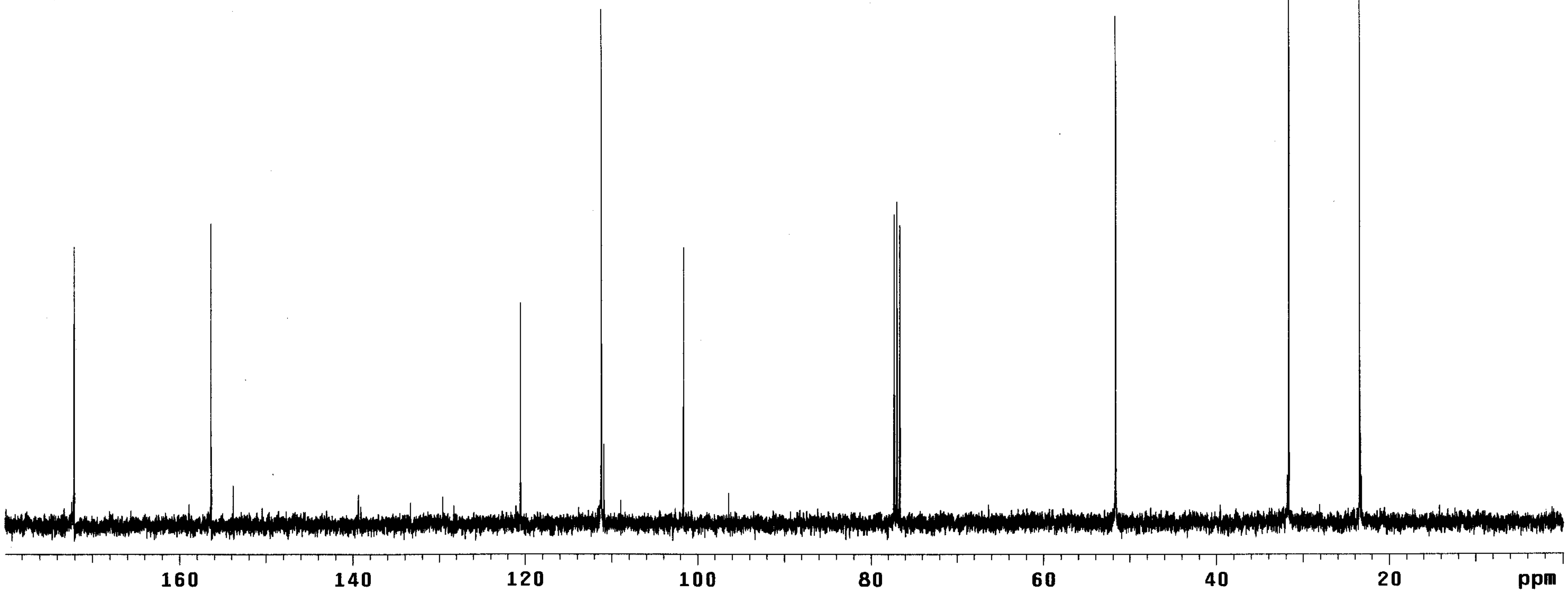
```
IY-13-199c Mercury
STANDARD 1H OBSERVE

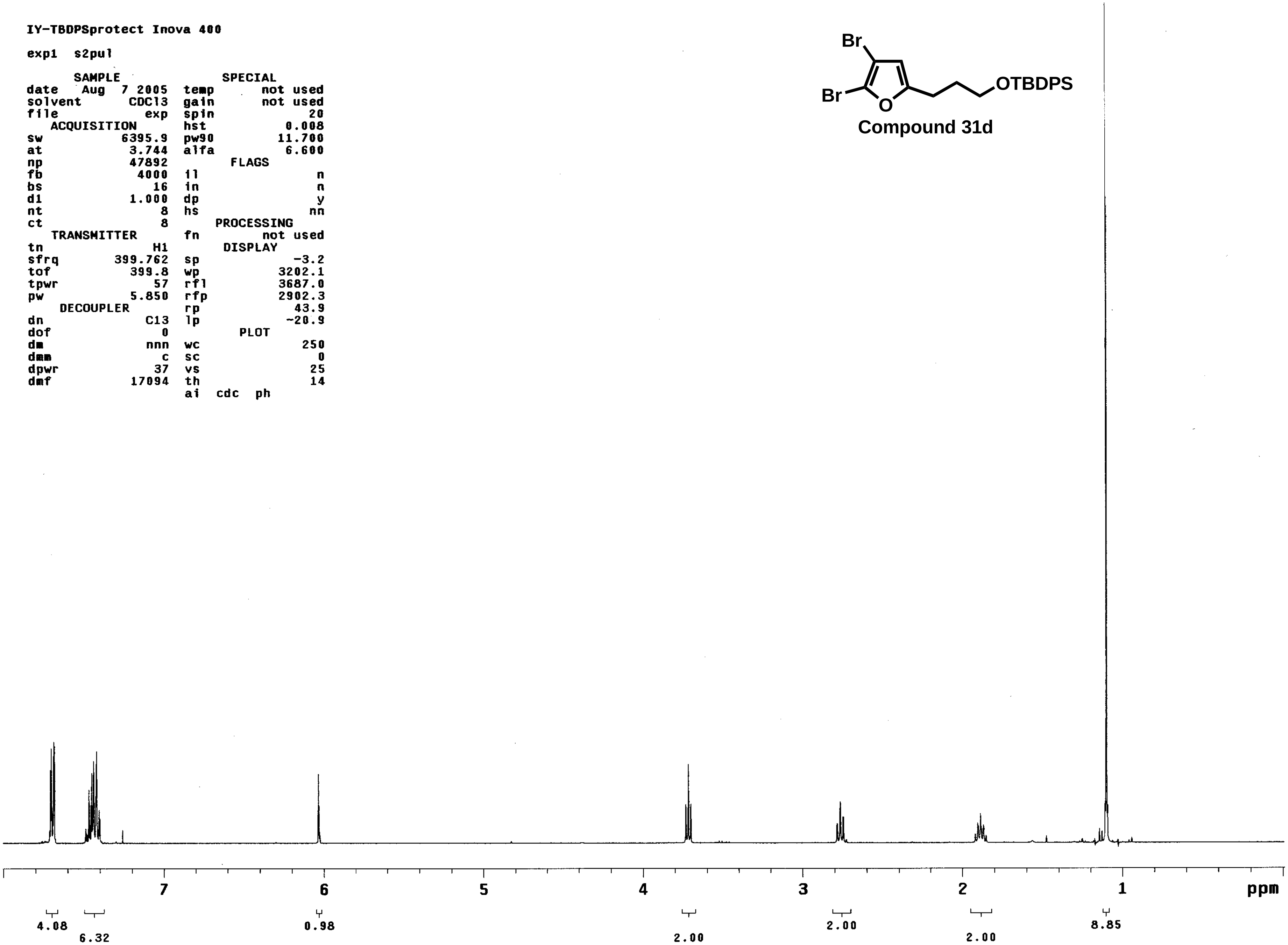
exp1  s2pul

      SAMPLE                 SPECIAL
date   Aug  7 2005  temp       not used
solvent      cdcl3  gain       not used
file /export/home/~ spin       not used
vnmr1/walkup/auto_~ hst           0.008
     07.08.05/0205  pw90         11.600
   ACQUISITION      alfa         20.000
sw         25125.6          FLAGS
at           1.199  il                n
np           60270  in                n
fb           13800  dp                y
bs              64  hs               nn
d1           1.000         PROCESSING
nt             256  lb             1.00
ct              64  fn         not used
   TRANSMITTER              DISPLAY
tn             C13  sp             -6.8
sfrq       100.613  wp          18107.9
tof         1550.8  rfl          9280.5
tpwr            57  rfp          7746.3
pw           5.800  rp           -131.5
    DECOUPLER       lp           -294.6
dn              H1          PLOT
dof              0  wc              250
dm             yyy  sc                0
dmm              w  vs               49
dpwr            40  th                8
dmf           9300  ai  no  ph
```



Compound 31c





Compound 31d

```
IY-TBDPSprotect Inova 400

exp1  s2pul

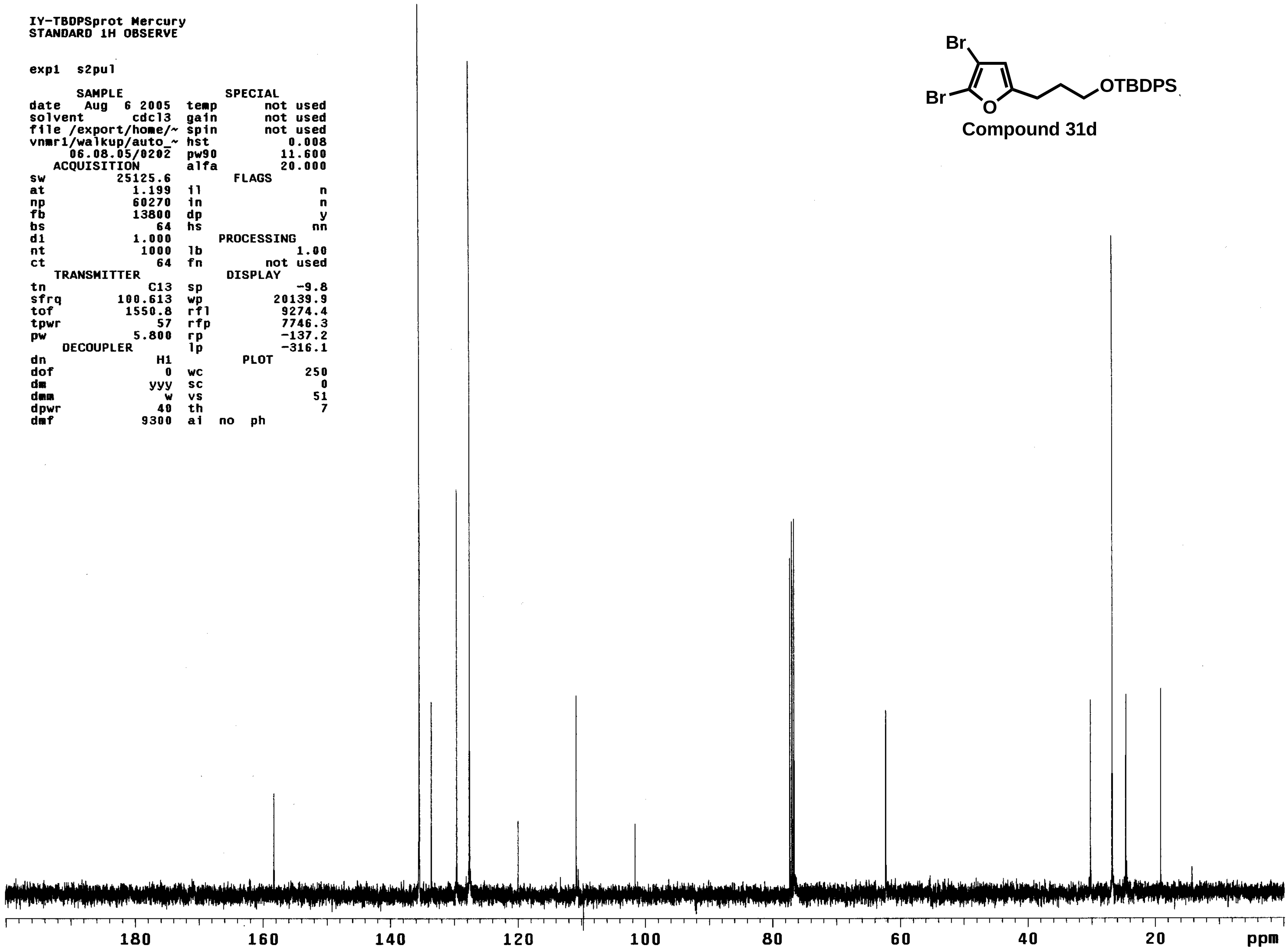
      SAMPLE                SPECIAL
date   Aug  7 2005  temp       not used
solvent      CDCl3  gain       not used
file           exp  spin             20
   ACQUISITION      hst           0.008
sw          6395.9  pw90         11.700
at           3.744  alfa          6.600
np           47892         FLAGS
fb            4000  il                n
bs              16  in                n
d1           1.000  dp                y
nt               8  hs               nn
ct               8       PROCESSING
   TRANSMITTER      fn         not used
tn              H1         DISPLAY
sfrq       399.762  sp             -3.2
tof          399.8  wp           3202.1
tpwr            57  rfl          3687.0
pw           5.850  rfp          2902.3
     DECOUPLER      rp             43.9
dn             C13  lp            -20.9
dof              0          PLOT
dm             nnn  wc              250
dmm              c  sc                0
dpwr            37  vs               25
dmf          17094  th               14
                    ai  cdc  ph
```

```
IY-TBDPSprot Mercury
STANDARD 1H OBSERVE

exp1  s2pul

      SAMPLE              SPECIAL
date   Aug  6 2005  temp      not used
solvent      cdcl3  gain      not used
file /export/home/~ spin      not used
vnmr1/walkup/auto_~ hst          0.008
     06.08.05/0202  pw90        11.600
   ACQUISITION      alfa        20.000
sw         25125.6         FLAGS
at           1.199  il               n
np           60270  in               n
fb           13800  dp               y
bs              64  hs              nn
d1           1.000       PROCESSING
nt            1000  lb            1.00
ct              64  fn        not used
   TRANSMITTER            DISPLAY
tn             C13  sp            -9.8
sfrq       100.613  wp         20139.9
tof         1550.8  rfl         9274.4
tpwr            57  rfp         7746.3
pw           5.800  rp          -137.2
    DECOUPLER       lp          -316.1
dn              H1          PLOT
dof              0  wc             250
dm             yyy  sc               0
dmm              w  vs              51
dpwr            40  th               7
dmf           9300  ai   no  ph
```

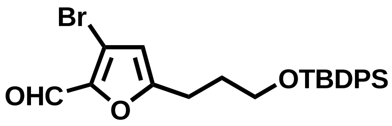
Compound 31d



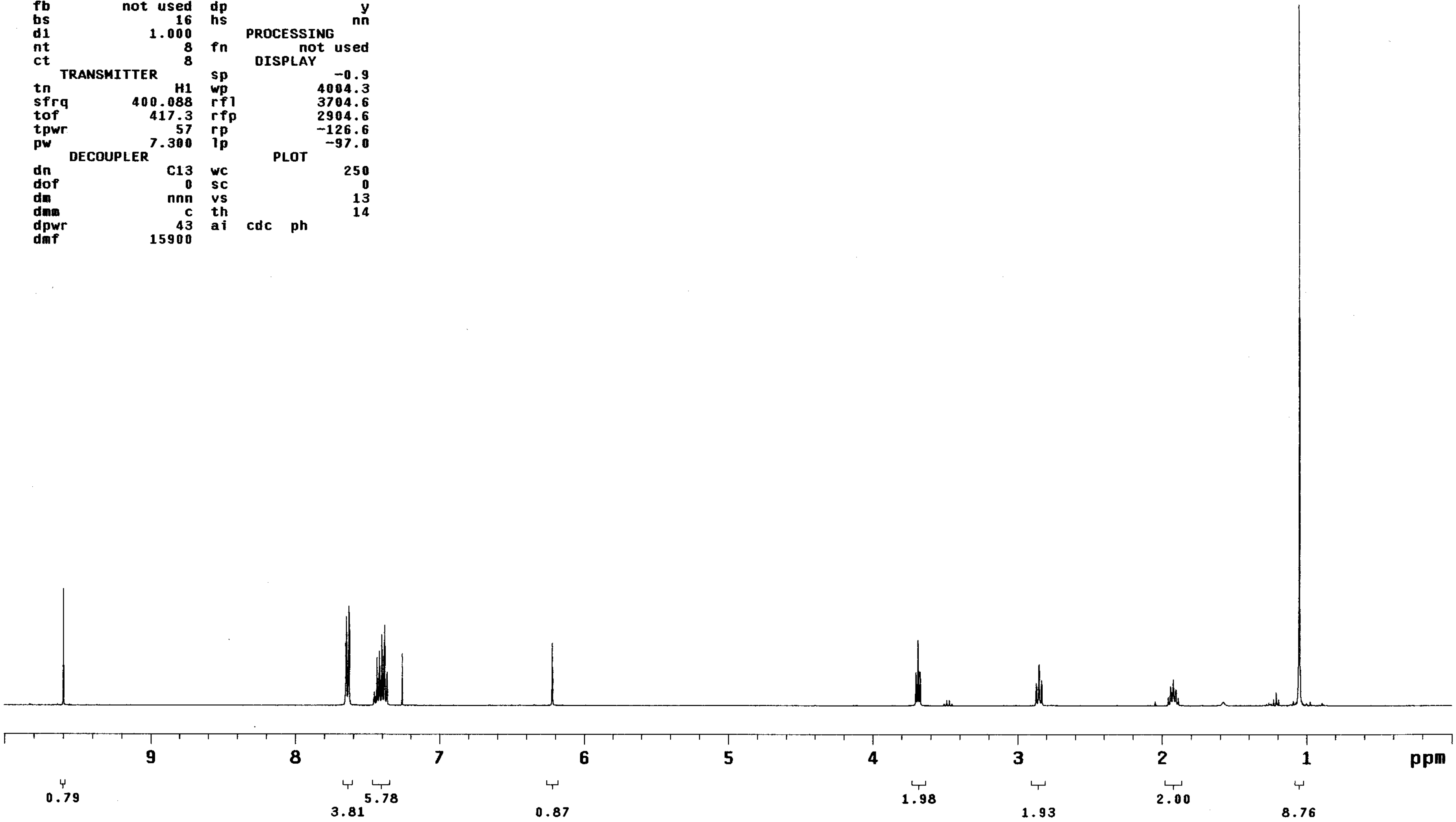
```
IY-15-83p mercury
STANDARD 1H OBSERVE

exp12  s2pul

      SAMPLE               SPECIAL
date   Nov 23 2005  temp       not used
solvent       cdcl3  gain       not used
file /export/home/~ spin             20
vnmr1/walkup/auto_~ hst           0.008
     23.11.05/0201  pw90         14.600
   ACQUISITION      alfa         20.000
sw           6402.0           FLAGS
at            4.000  il               n
np            51216  in               n
fb         not used  dp               y
bs               16  hs              nn
d1            1.000         PROCESSING
nt                8  fn        not used
ct                8          DISPLAY
   TRANSMITTER       sp            -0.9
tn               H1  wp          4004.3
sfrq        400.088  rfl         3704.6
tof           417.3  rfp         2904.6
tpwr             57  rp          -126.6
pw            7.300  lp           -97.0
    DECOUPLER                PLOT
dn              C13  wc             250
dof               0  sc               0
dm              nnn  vs              13
dmm               c  th              14
dpwr             43  ai  cdc  ph
dmf           15900
```



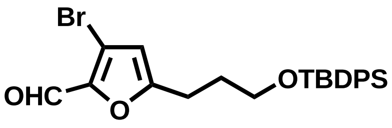
Compound 31



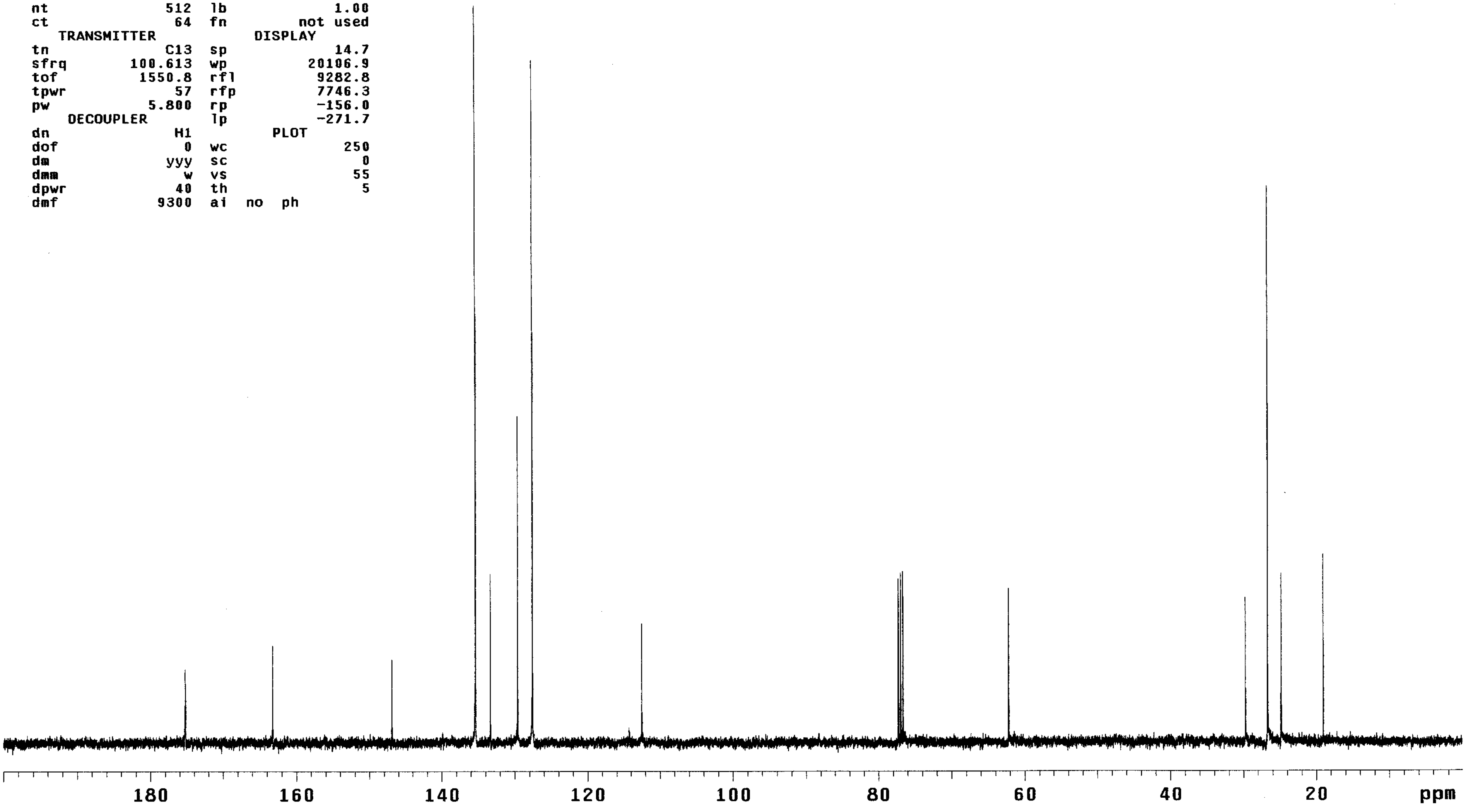
```
IY-15-83c mercury
STANDARD 1H OBSERVE

exp12  s2pul

      SAMPLE                SPECIAL
date   Nov 23 2005  temp       not used
solvent      cdcl3  gain       not used
file /export/home/~ spin       not used
vnmr1/walkup/auto_~ hst           0.008
     23.11.05/0103  pw90         11.600
   ACQUISITION      alfa         20.000
sw         25125.6           FLAGS
at           1.199  il                n
np           60270  in                n
fb           13800  dp                y
bs              64  hs               nn
d1           1.000         PROCESSING
nt             512  lb             1.00
ct              64  fn         not used
   TRANSMITTER              DISPLAY
tn             C13  sp             14.7
sfrq       100.613  wp          20106.9
tof         1550.8  rfl          9282.8
tpwr            57  rfp          7746.3
pw           5.800  rp           -156.0
    DECOUPLER       lp           -271.7
dn              H1            PLOT
dof              0  wc              250
dm             yyy  sc                0
dmm              w  vs               55
dpwr            40  th                5
dmf           9300  ai   no  ph
```



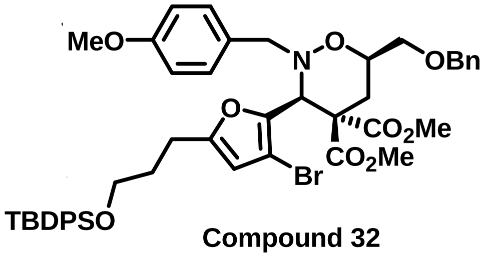
Compound 31



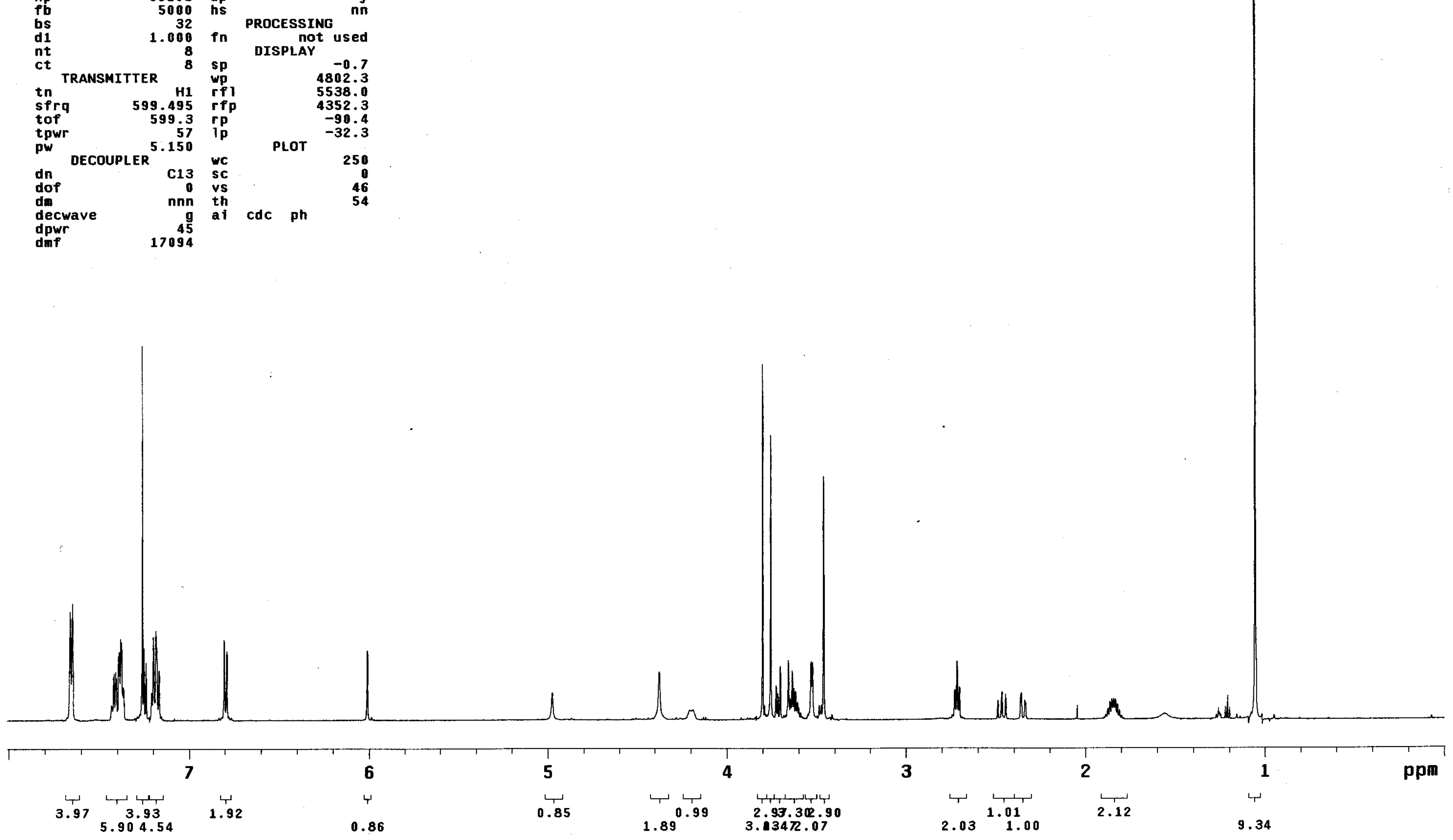
```
I-15-93p Inova 600

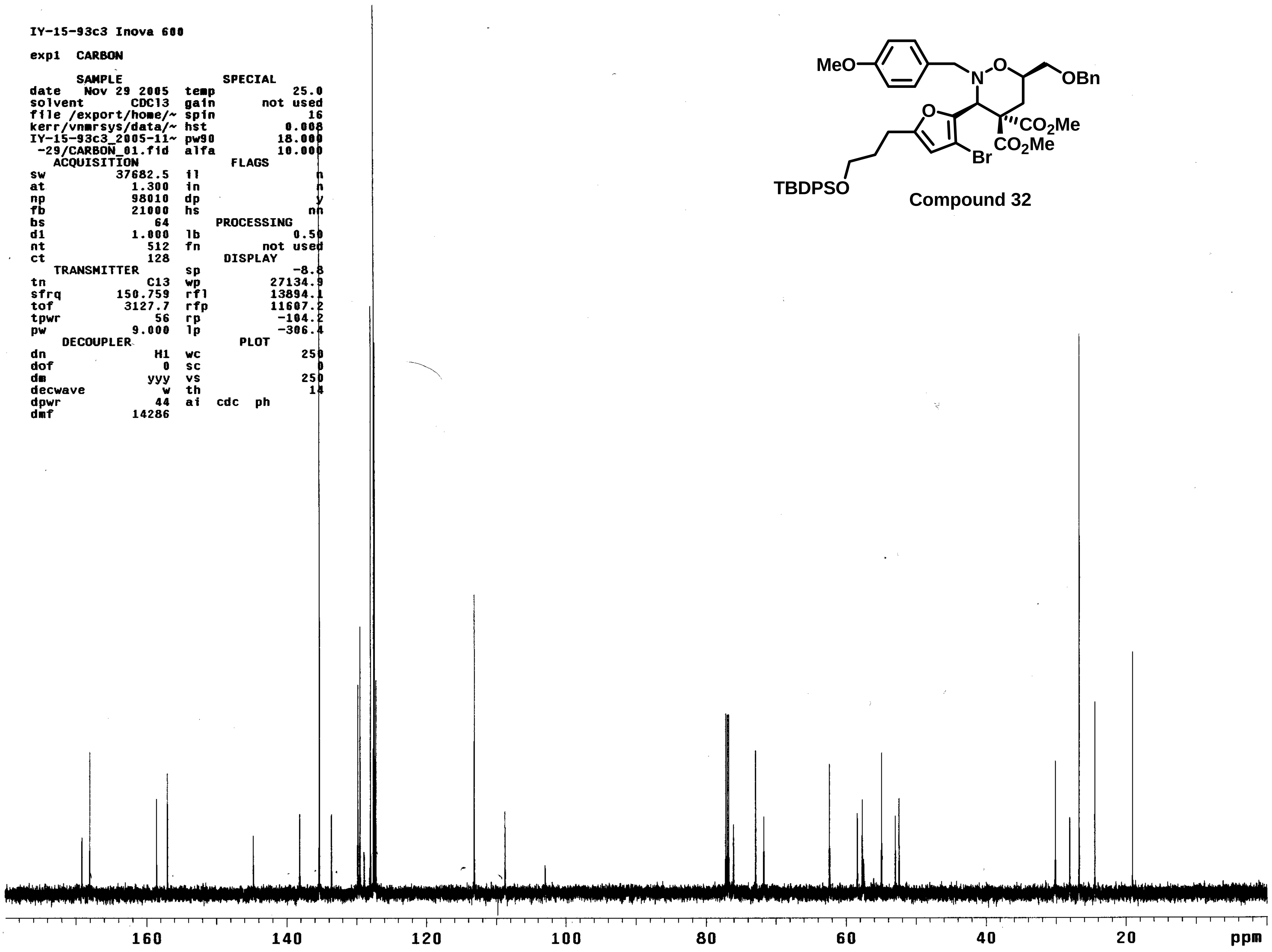
exp1  PROTON

      SAMPLE              SPECIAL
date   Nov 29 2005  temp            25.0
solvent      CDCl3  gain        not used
file /export/home/~ spin              22
kerr/vnmrsys/data/~ hst            0.008
IY-15-93p_2005-11-~ pw90          10.300
  29/PROTON_01.fid  alfa               0
    ACQUISITION            FLAGS
sw          9592.3  il                 n
at           1.892  in                 n
np           36298  dp                 y
fb            5000  hs                nn
bs              32       PROCESSING
d1           1.000  fn          not used
nt               8         DISPLAY
ct               8  sp              -0.7
   TRANSMITTER      wp            4802.3
tn              H1  rfl           5538.0
sfrq       599.495  rfp           4352.3
tof          599.3  rp             -90.4
tpwr            57  lp             -32.3
pw           5.150          PLOT
     DECOUPLER      wc               250
dn             C13  sc                 0
dof              0  vs                46
dm             nnn  th                54
decwave          g  ai  cdc  ph
dpwr            45
dmf          17094
```



Compound 32



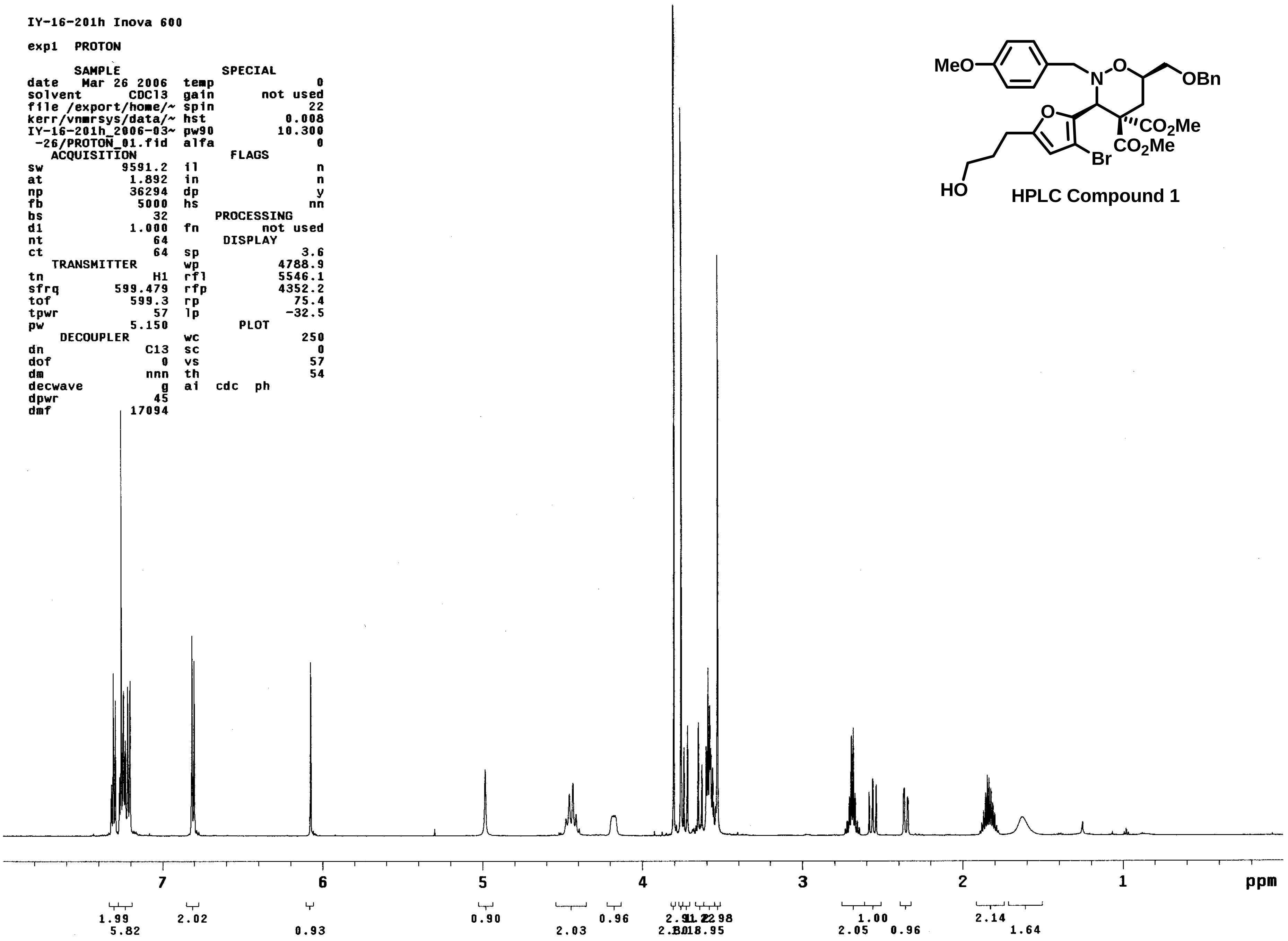


Compound 32

```
IY-15-93c3 Inova 600

exp1  CARBON

      SAMPLE              SPECIAL
date   Nov 29 2005  temp           25.0
solvent       CDCl3  gain       not used
file /export/home/~  spin             16
kerr/vnmrsys/data/~  hst           0.008
IY-15-93c3_2005-11~  pw90         18.000
 -29/CARBON_01.fid   alfa         10.000
   ACQUISITION            FLAGS
sw          37682.5  il                n
at            1.300  in                n
np            98010  dp                y
fb            21000  hs               nn
bs               64      PROCESSING
d1            1.000  lb             0.50
nt              512  fn         not used
ct              128       DISPLAY
   TRANSMITTER       sp             -8.8
tn              C13  wp          27134.9
sfrq        150.759  rfl         13894.1
tof          3127.7  rfp         11607.2
tpwr             56  rp           -104.2
pw            9.000  lp           -306.4
    DECOUPLER              PLOT
dn               H1  wc              250
dof               0  sc                0
dm              yyy  vs              250
decwave           w  th               14
dpwr             44  ai   cdc   ph
dmf           14286
```



HPLC Compound 1

```
IY-16-201h Inova 600

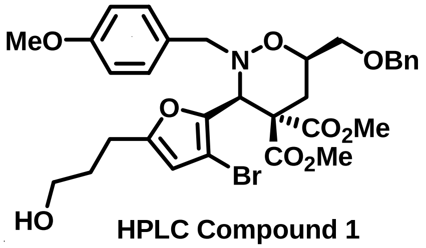
exp1  PROTON

      SAMPLE                SPECIAL
date   Mar 26 2006  temp            0
solvent      CDCl3  gain     not used
file /export/home/~ spin           22
kerr/vnmrsys/data/~ hst         0.008
IY-16-201h_2006-03~ pw90       10.300
 -26/PROTON_01.fid  alfa            0
   ACQUISITION             FLAGS
sw          9591.2  il              n
at           1.892  in              n
np           36294  dp              y
fb            5000  hs             nn
bs              32        PROCESSING
d1           1.000  fn       not used
nt              64         DISPLAY
ct              64  sp            3.6
   TRANSMITTER      wp         4788.9
tn              H1  rfl        5546.1
sfrq       599.479  rfp        4352.2
tof          599.3  rp           75.4
tpwr            57  lp          -32.5
pw           5.150           PLOT
    DECOUPLER       wc            250
dn             C13  sc              0
dof              0  vs             57
dm             nnn  th             54
decwave          g  ai   cdc   ph
dpwr            45
dmf          17094
```

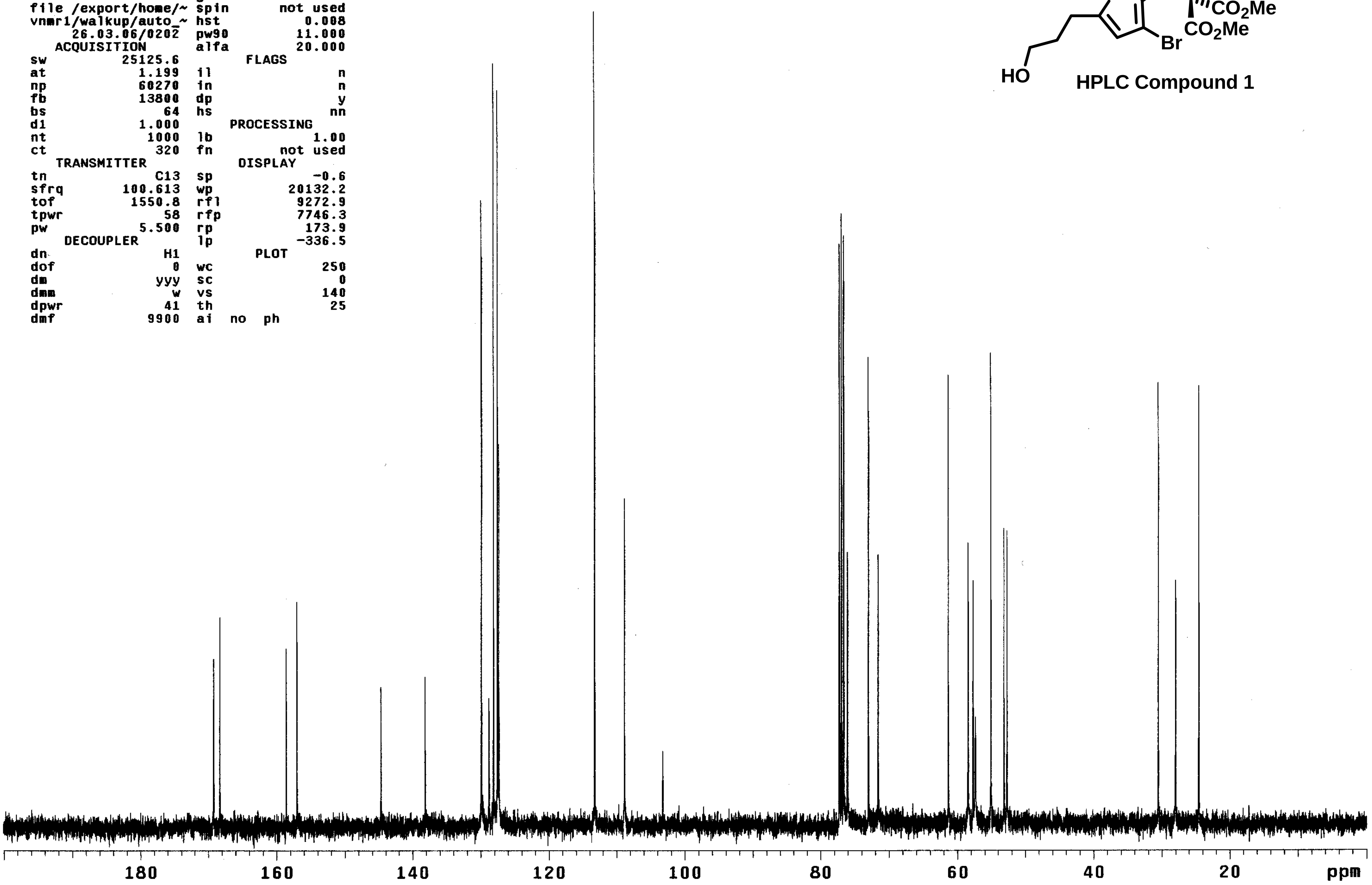
```
IY-16-201c
STANDARD 1H OBSERVE

exp1  s2pul

      SAMPLE              SPECIAL
date   Mar 26 2006  temp       not used
solvent      cdcl3  gain       not used
file /export/home/~ spin       not used
vnmr1/walkup/auto_~ hst           0.008
    26.03.06/0202   pw90         11.000
   ACQUISITION      alfa         20.000
sw         25125.6          FLAGS
at           1.199  il                n
np           60270  in                n
fb           13800  dp                y
bs              64  hs               nn
d1           1.000       PROCESSING
nt            1000  lb             1.00
ct             320  fn         not used
   TRANSMITTER            DISPLAY
tn             C13  sp             -0.6
sfrq       100.613  wp          20132.2
tof         1550.8  rfl          9272.9
tpwr            58  rfp          7746.3
pw           5.500  rp            173.9
    DECOUPLER       lp           -336.5
dn              H1          PLOT
dof              0  wc              250
dm             yyy  sc                0
dmm              w  vs              140
dpwr            41  th               25
dmf           9900  ai   no   ph
```



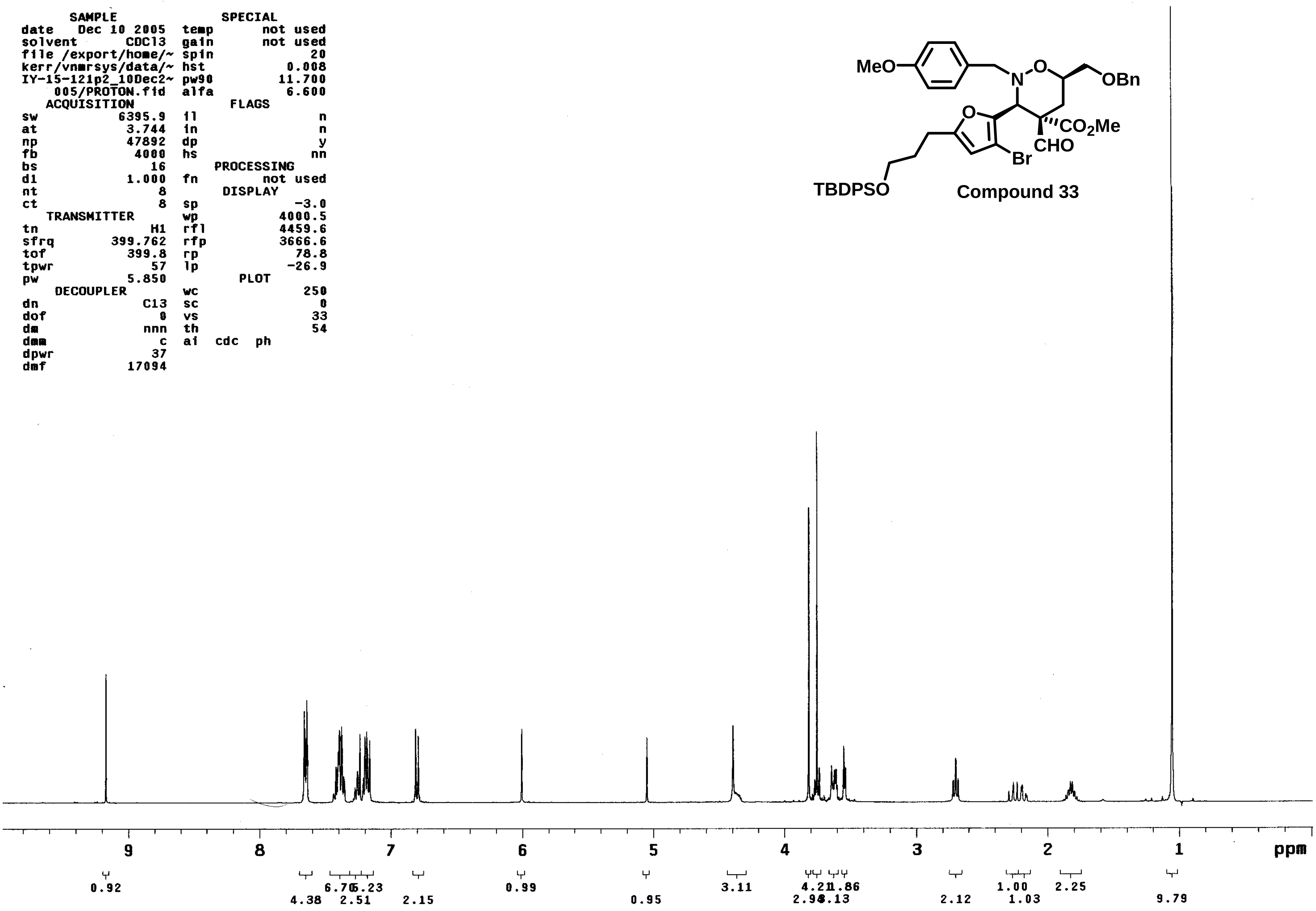
HPLC Compound 1



```
IY-15-121p2 Inova 400

exp1  s2pul

      SAMPLE                 SPECIAL
date   Dec 10 2005  temp       not used
solvent      CDCl3  gain       not used
file /export/home/~ spin             20
kerr/vnmrsys/data/~ hst           0.008
IY-15-121p2_10Dec2~ pw90         11.700
    005/PROTON.fid  alfa          6.600
   ACQUISITION             FLAGS
sw          6395.9  il                n
at           3.744  in                n
np           47892  dp                y
fb            4000  hs               nn
bs              16        PROCESSING
d1           1.000  fn         not used
nt               8          DISPLAY
ct               8  sp             -3.0
   TRANSMITTER      wp           4000.5
tn              H1  rfl          4459.6
sfrq       399.762  rfp          3666.6
tof          399.8  rp             78.8
tpwr            57  lp            -26.9
pw           5.850            PLOT
    DECOUPLER       wc              250
dn             C13  sc                0
dof              0  vs               33
dm             nnn  th               54
dmm              c  ai  cdc  ph
dpwr            37
dmf          17094
```

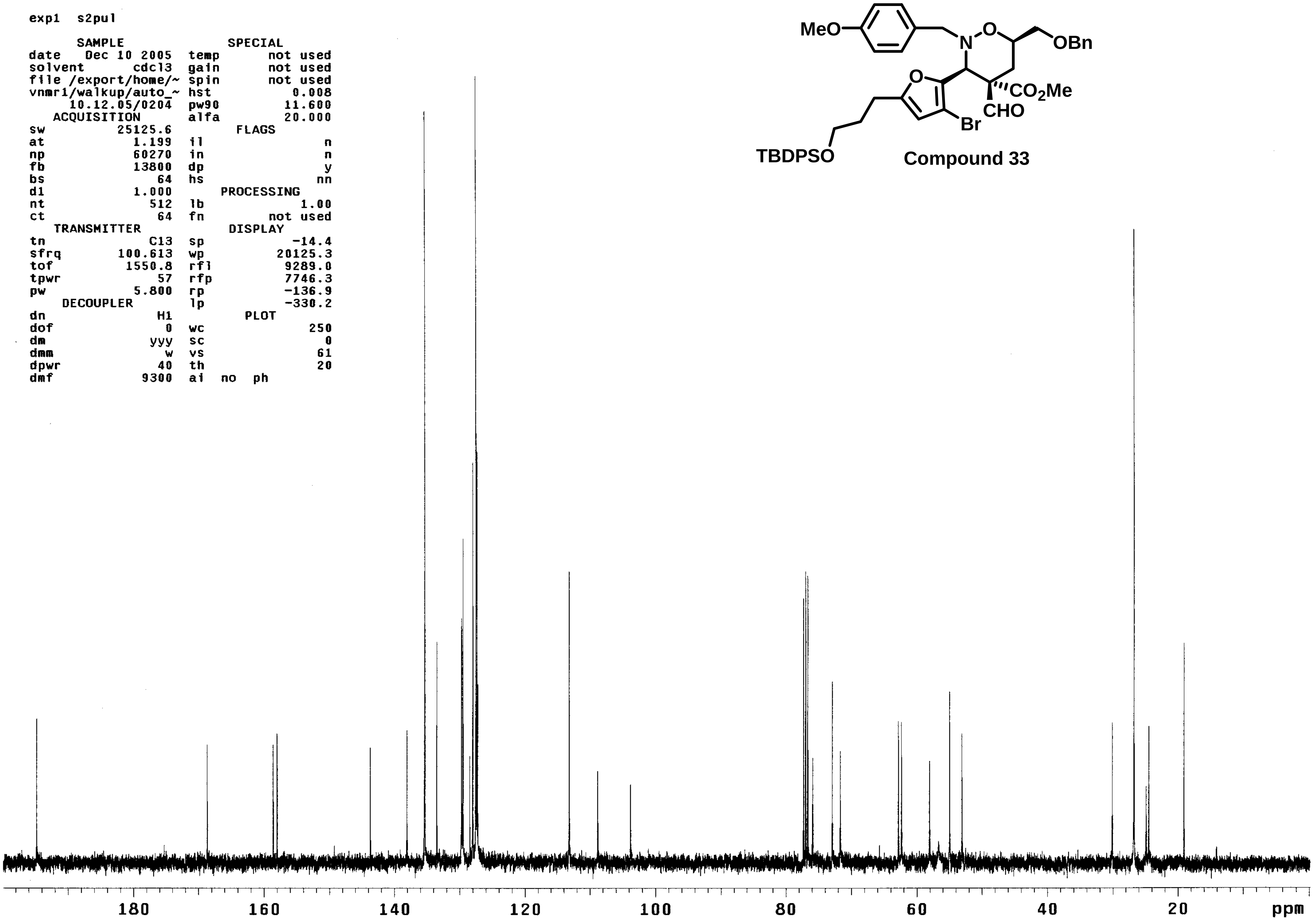


Compound 33

```
IY-15-121c2 Mercury
STANDARD 1H OBSERVE

exp1  s2pul

      SAMPLE             SPECIAL
date   Dec 10 2005  temp      not used
solvent      cdcl3  gain      not used
file /export/home/~ spin      not used
vnmr1/walkup/auto_~ hst          0.008
    10.12.05/0204   pw90        11.600
   ACQUISITION      alfa        20.000
sw         25125.6          FLAGS
at           1.199  il               n
np           60270  in               n
fb           13800  dp               y
bs              64  hs              nn
d1           1.000        PROCESSING
nt             512  lb            1.00
ct              64  fn        not used
   TRANSMITTER             DISPLAY
tn             C13  sp           -14.4
sfrq       100.613  wp         20125.3
tof         1550.8  rfl         9289.0
tpwr            57  rfp         7746.3
pw           5.800  rp          -136.9
    DECOUPLER       lp          -330.2
dn              H1          PLOT
dof              0  wc             250
dm             yyy  sc               0
dmm              w  vs              61
dpwr            40  th              20
dmf           9300  ai  no  ph
```

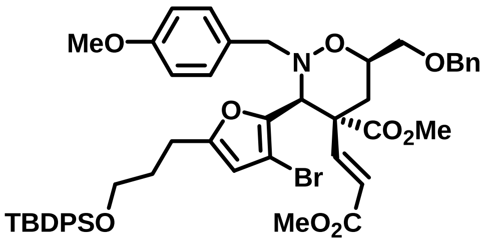


Compound 33

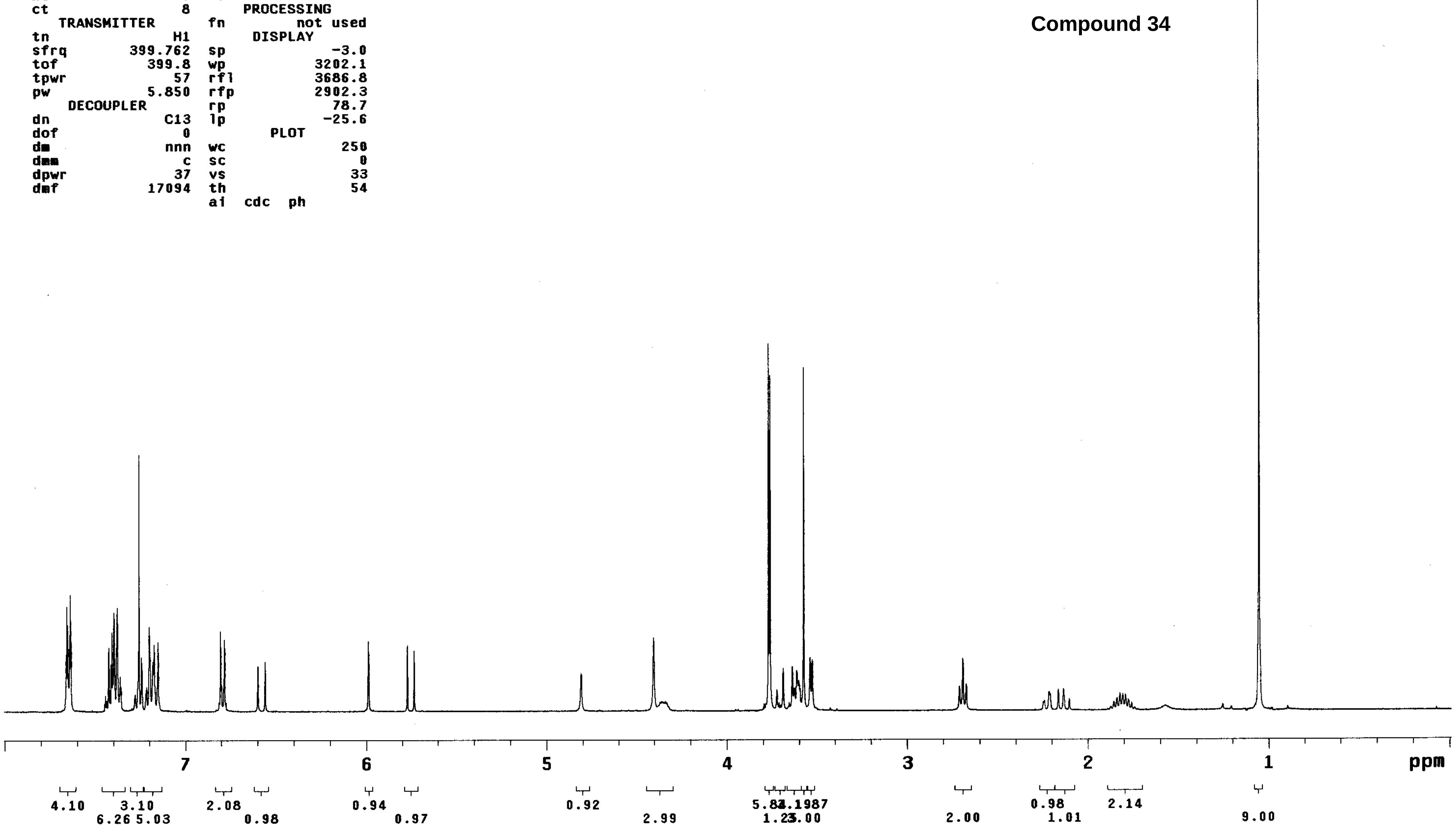
```
IY-15-115P3 Inova 400

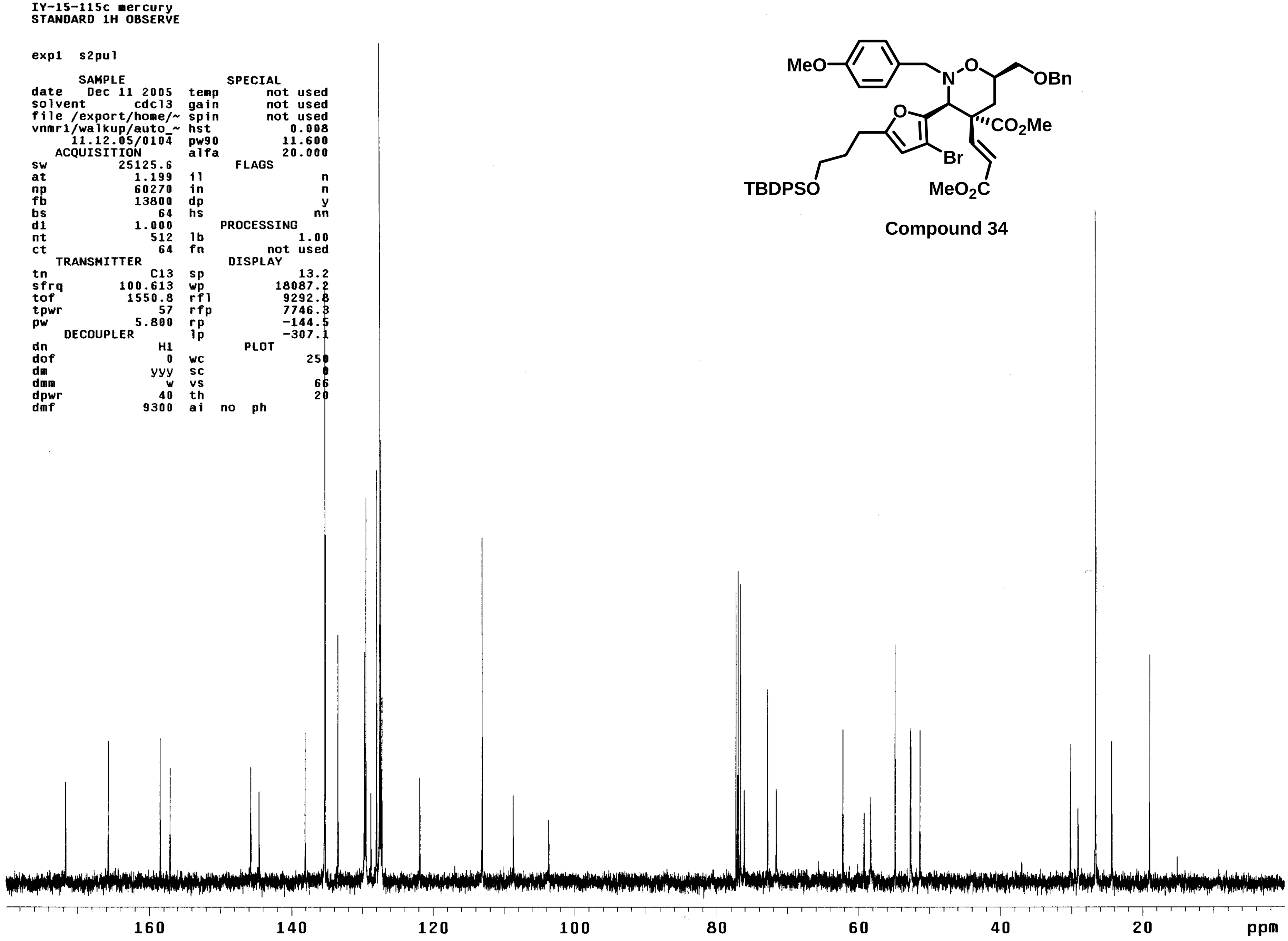
exp1  s2pul

      SAMPLE                  SPECIAL
date   Dec 11 2005   temp        not used
solvent      CDCl3   gain        not used
file           exp   spin              20
   ACQUISITION       hst            0.008
sw          6395.9   pw90          11.700
at           3.744   alfa           6.600
np           47892          FLAGS
fb            4000   il                 n
bs              16   in                 n
d1           1.000   dp                 y
nt               8   hs                nn
ct               8       PROCESSING
   TRANSMITTER       fn          not used
tn              H1          DISPLAY
sfrq       399.762   sp              -3.0
tof          399.8   wp            3202.1
tpwr            57   rfl           3686.8
pw           5.850   rfp           2902.3
    DECOUPLER        rp              78.7
dn             C13   lp             -25.6
dof              0            PLOT
dm             nnn   wc               250
dmm              c   sc                 0
dpwr            37   vs                33
dmf          17094   th                54
                     ai   cdc   ph
```



Compound 34



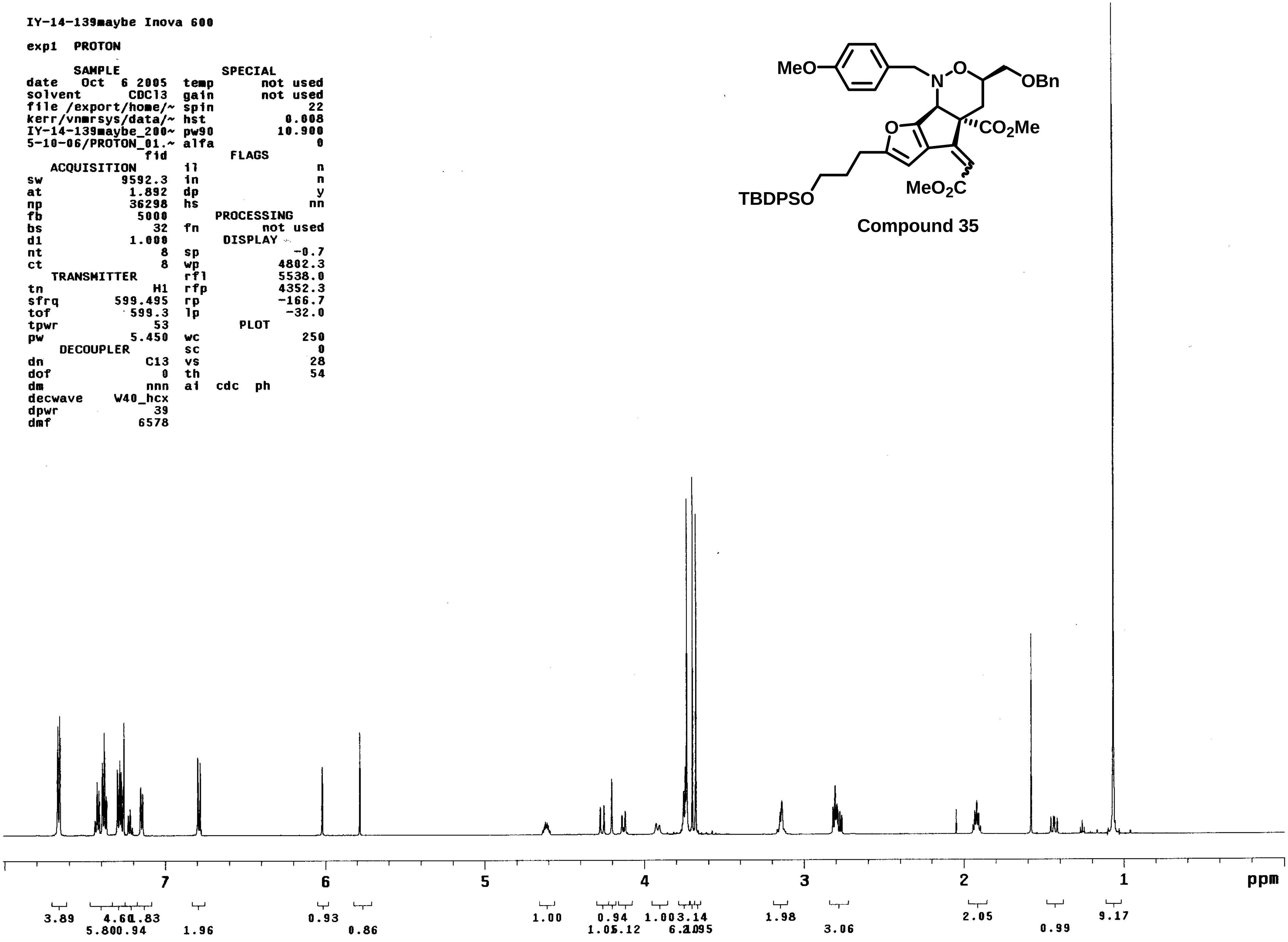


```
IY-15-115c mercury
STANDARD 1H OBSERVE

exp1  s2pul

      SAMPLE               SPECIAL
date   Dec 11 2005  temp       not used
solvent       cdcl3  gain       not used
file /export/home/~  spin       not used
vnmr1/walkup/auto_~  hst           0.008
     11.12.05/0104  pw90         11.600
   ACQUISITION       alfa         20.000
sw          25125.6           FLAGS
at            1.199  il                n
np            60270  in                n
fb            13800  dp                y
bs               64  hs               nn
d1            1.000         PROCESSING
nt              512  lb             1.00
ct               64  fn         not used
   TRANSMITTER               DISPLAY
tn              C13  sp             13.2
sfrq        100.613  wp          18087.2
tof          1550.8  rfl          9292.8
tpwr             57  rfp          7746.3
pw            5.800  rp           -144.5
    DECOUPLER        lp           -307.1
dn               H1           PLOT
dof               0  wc              250
dm              yyy  sc                0
dmm               w  vs               66
dpwr             40  th               20
dmf            9300  ai   no  ph
```

Compound 34



```
IY-14-139maybe Inova 600

exp1  PROTON

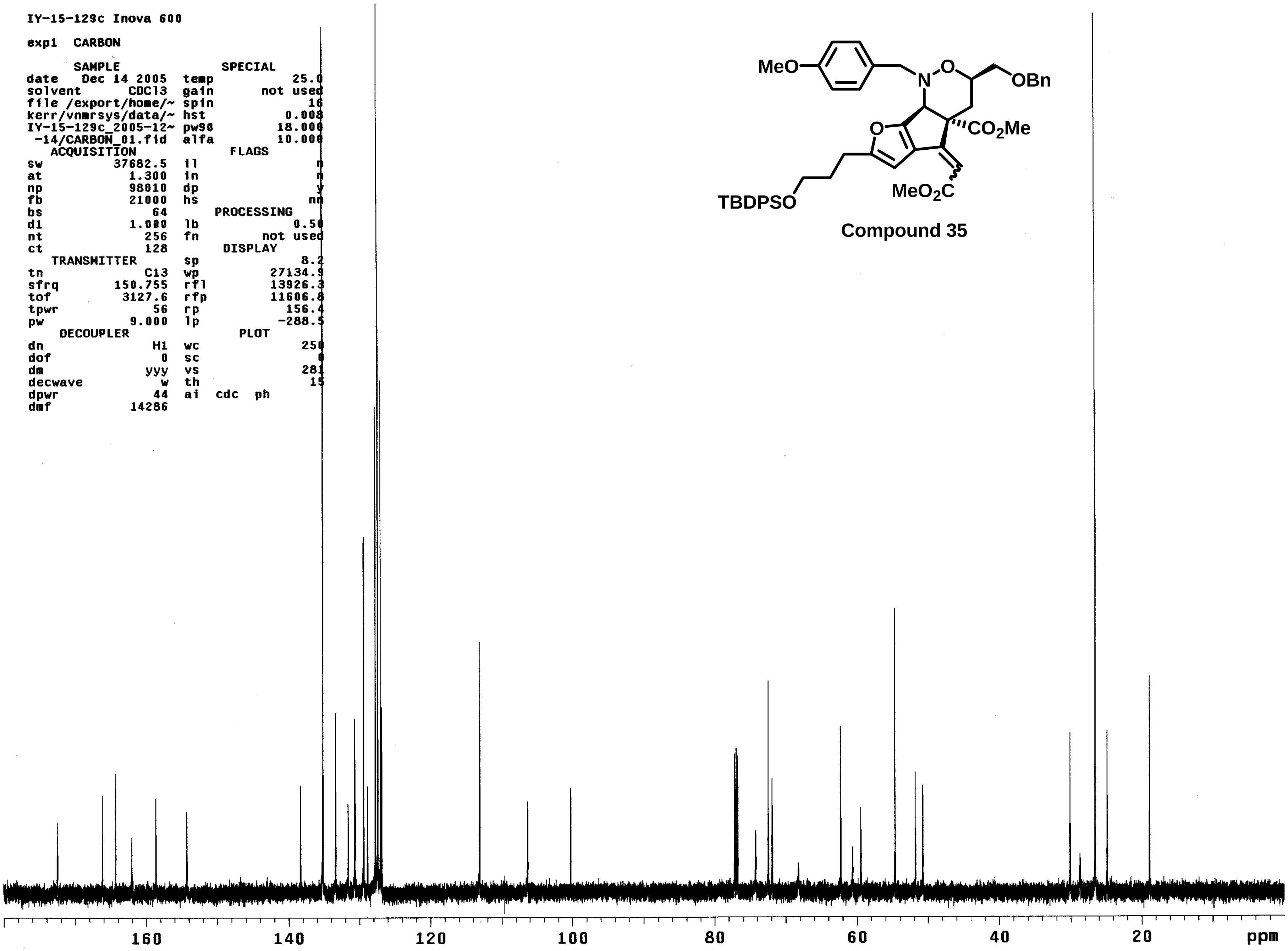
    SAMPLE              SPECIAL
date   Oct  6 2005  temp       not used
solvent      CDCl3  gain       not used
file /export/home/~ spin             22
kerr/vnmrsys/data/~ hst           0.008
IY-14-139maybe_200~ pw90         10.900
5-10-06/PROTON_01.~ alfa              0
               fid          FLAGS
   ACQUISITION      il                n
sw          9592.3  in                n
at           1.892  dp                y
np           36298  hs               nn
fb            5000       PROCESSING
bs              32  fn         not used
d1           1.000        DISPLAY
nt               8  sp             -0.7
ct               8  wp           4802.3
   TRANSMITTER      rfl          5538.0
tn              H1  rfp          4352.3
sfrq       599.495  rp           -166.7
tof          599.3  lp            -32.0
tpwr            53          PLOT
pw           5.450  wc              250
   DECOUPLER        sc                0
dn             C13  vs               28
dof              0  th               54
dm             nnn  ai  cdc  ph
decwave    W40_hcx
dpwr            39
dmf           6578
```

Compound 35

```
IY-15-129c Inova 600

exp1  CARBON

      SAMPLE                SPECIAL
date   Dec 14 2005  temp          25.0
solvent      CDCl3  gain      not used
file /export/home/~ spin            16
kerr/vnmrsys/data/~ hst          0.008
IY-15-129c_2005-12~ pw90        18.000
 -14/CARBON_01.fid  alfa        10.000
   ACQUISITION              FLAGS
sw         37682.5  il               n
at           1.300  in               n
np           98010  dp               y
fb           21000  hs              nn
bs              64        PROCESSING
d1           1.000  lb            0.50
nt             256  fn        not used
ct             128         DISPLAY
   TRANSMITTER      sp             8.2
tn             C13  wp         27134.9
sfrq       150.755  rfl        13926.3
tof         3127.6  rfp        11606.8
tpwr            56  rp           156.4
pw           9.000  lp          -288.5
    DECOUPLER                PLOT
dn              H1  wc             250
dof              0  sc               0
dm             yyy  vs             281
decwave          w  th              15
dpwr            44  ai   cdc   ph
dmf          14286
```

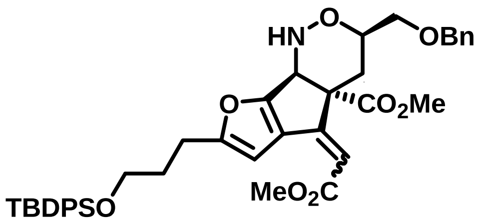


Compound 35

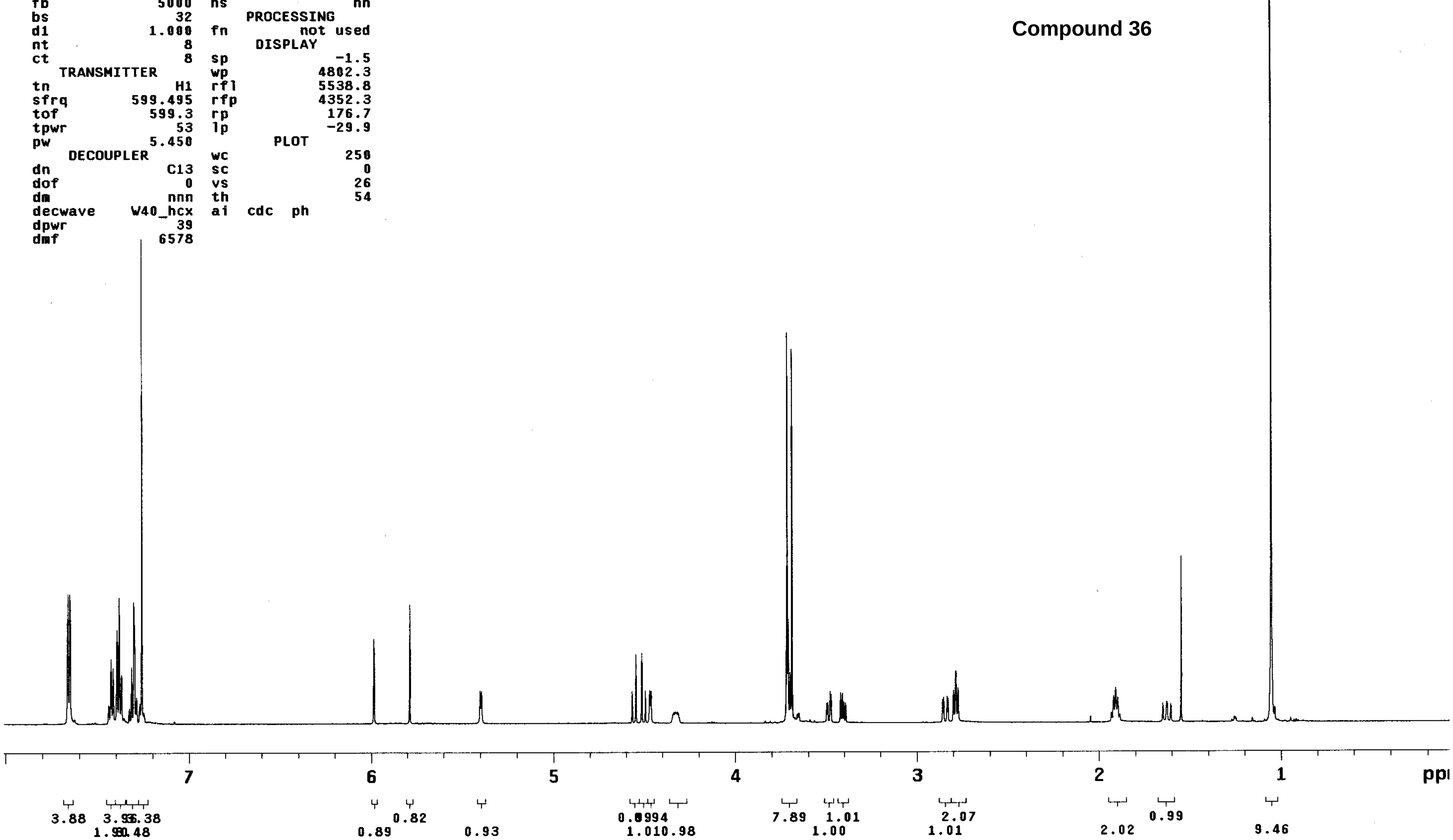
```
IY-13-85p Inova 600

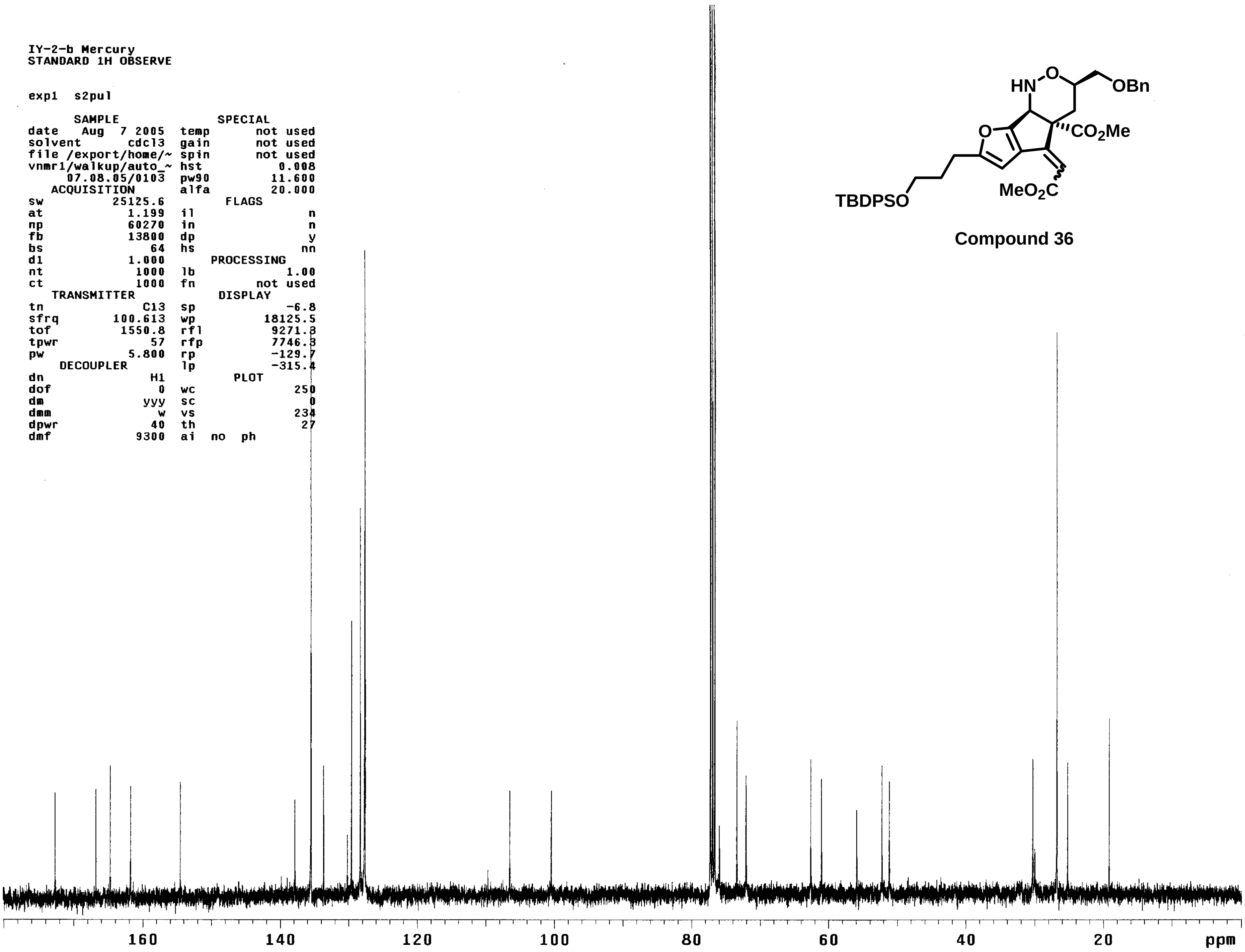
exp1  PROTON

      SAMPLE              SPECIAL
date   Jul  9 2005  temp           25.0
solvent       CDCl3  gain       not used
file /export/home/~ spin             22
kerr/vnmrsys/data/~ hst           0.008
IY-13-85p_2005-07-~ pw90         10.900
  09/PROTON_01.fid  alfa              0
    ACQUISITION           FLAGS
sw           9592.3  il                n
at            1.892  in                n
np            36298  dp                y
fb             5000  hs               nn
bs               32      PROCESSING
d1            1.000  fn       not used
nt                8       DISPLAY
ct                8  sp            -1.5
   TRANSMITTER       wp          4802.3
tn               H1  rfl         5538.8
sfrq        599.495  rfp         4352.3
tof           599.3  rp           176.7
tpwr             53  lp           -29.9
pw            5.450        PLOT
    DECOUPLER        wc             250
dn              C13  sc               0
dof               0  vs              26
dm              nnn  th              54
decwave     W40_hcx  ai   cdc  ph
dpwr             39
dmf            6578
```



Compound 36





```
IY-2-b Mercury
STANDARD 1H OBSERVE

exp1  s2pul

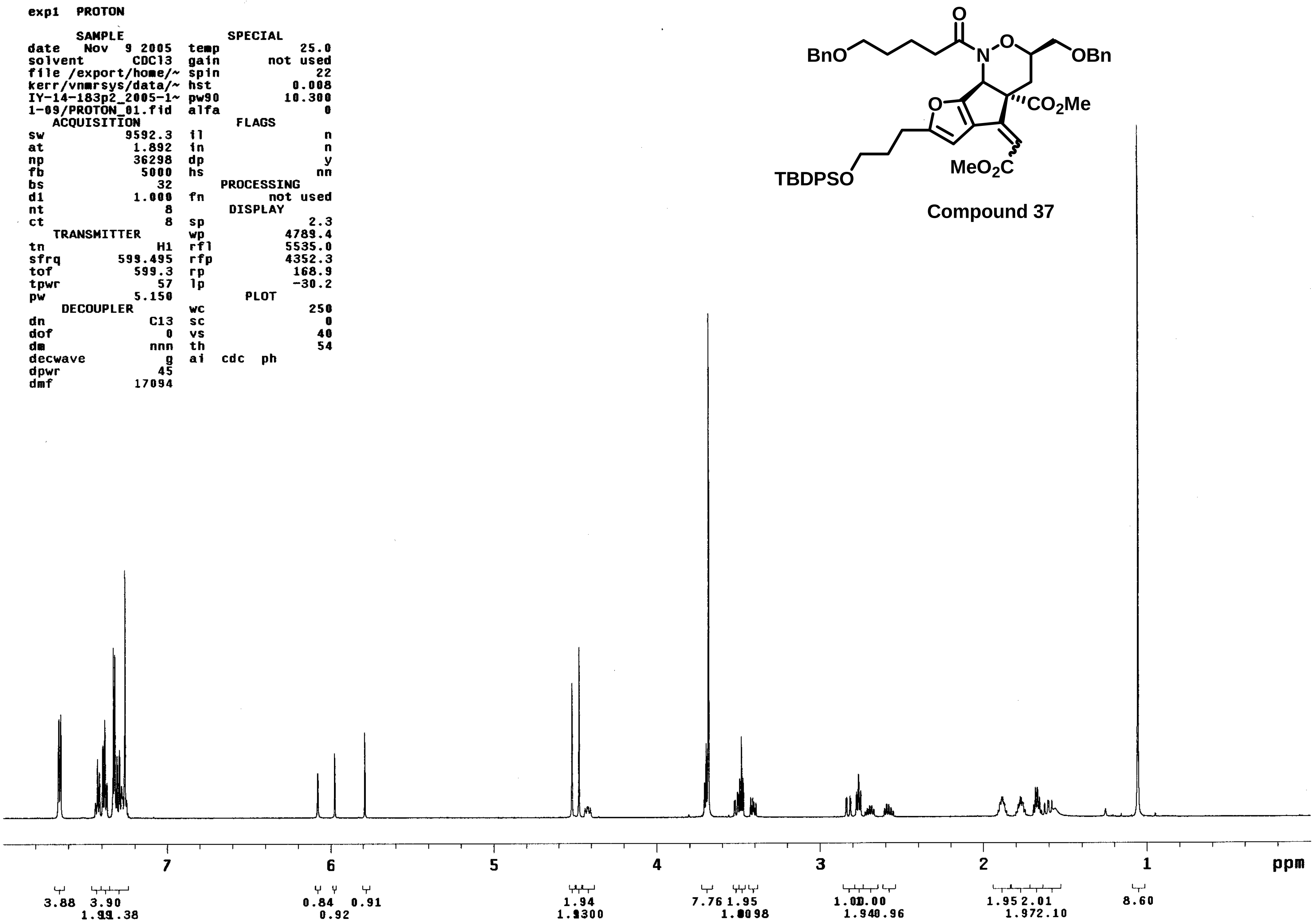
      SAMPLE                SPECIAL
date   Aug  7 2005  temp       not used
solvent       cdcl3  gain       not used
file /export/home/~ spin       not used
vnmr1/walkup/auto_~ hst           0.008
    07.08.05/0103   pw90         11.600
   ACQUISITION      alfa         20.000
sw          25125.6          FLAGS
at            1.199  il                n
np            60270  in                n
fb            13800  dp                y
bs               64  hs               nn
d1            1.000       PROCESSING
nt             1000  lb             1.00
ct             1000  fn         not used
   TRANSMITTER             DISPLAY
tn              C13  sp             -6.8
sfrq        100.613  wp          18125.5
tof          1550.8  rfl          9271.8
tpwr             57  rfp          7746.8
pw            5.800  rp           -129.7
    DECOUPLER        lp           -315.4
dn               H1            PLOT
dof               0  wc              250
dm              yyy  sc                0
dmm               w  vs              234
dpwr             40  th               27
dmf            9300  ai   no   ph
```

Compound 36

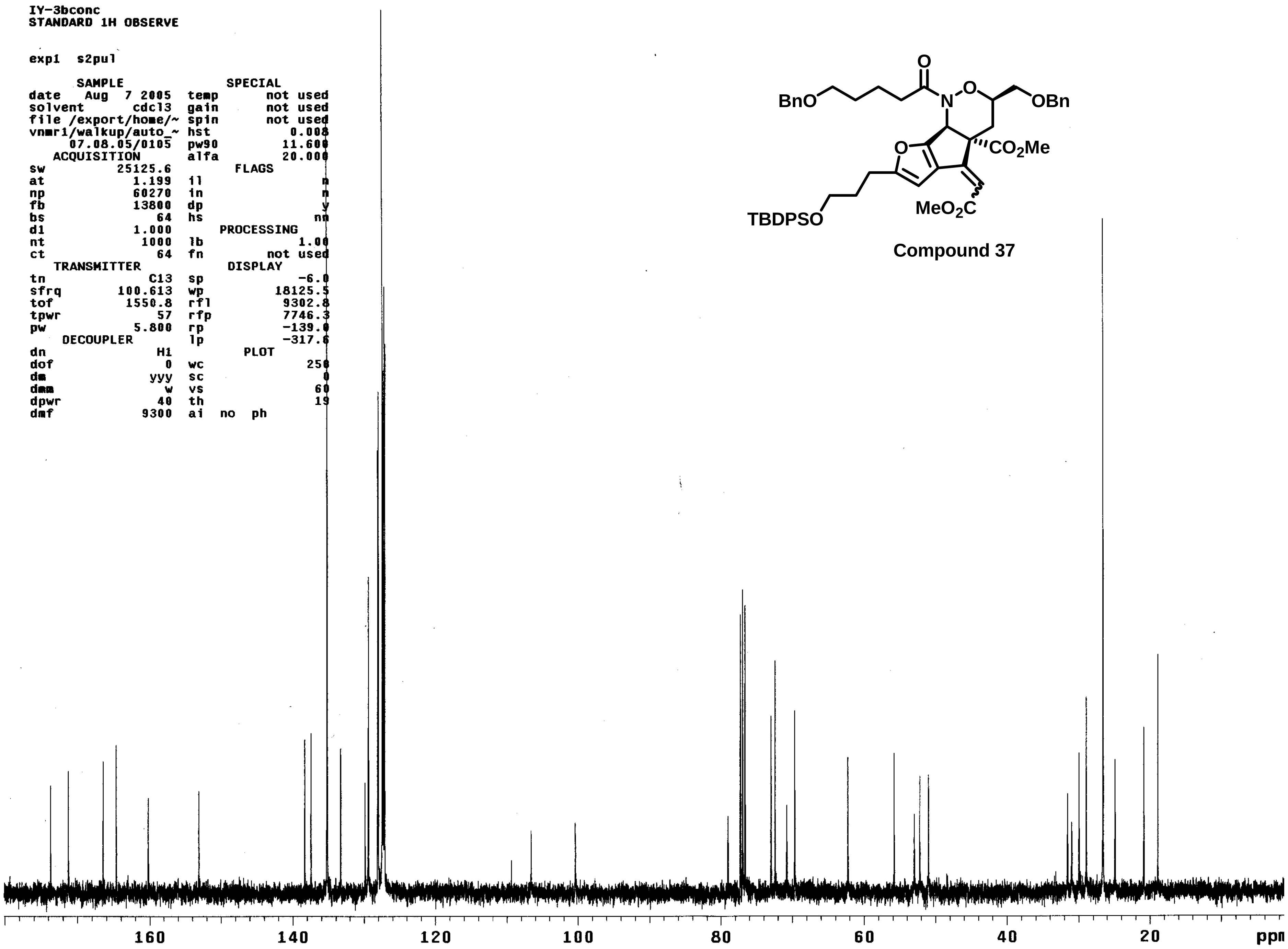
```
IY-14-183p2 Inova 600

exp1  PROTON

      SAMPLE                SPECIAL
date   Nov  9 2005  temp           25.0
solvent       CDCl3  gain       not used
file /export/home/~  spin             22
kerr/vnmrsys/data/~  hst           0.008
IY-14-183p2_2005-1~  pw90         10.300
1-09/PROTON_01.fid   alfa              0
    ACQUISITION              FLAGS
sw             9592.3  il                n
at              1.892  in                n
np              36298  dp                y
fb               5000  hs               nn
bs                 32       PROCESSING
d1              1.000  fn        not used
nt                  8        DISPLAY
ct                  8  sp              2.3
    TRANSMITTER        wp           4789.4
tn                 H1  rfl          5535.0
sfrq          599.495  rfp          4352.3
tof             599.3  rp            168.9
tpwr               57  lp            -30.2
pw              5.150          PLOT
     DECOUPLER         wc              250
dn                C13  sc                0
dof                 0  vs               40
dm                nnn  th               54
decwave             g  ai   cdc   ph
dpwr               45
dmf             17094
```



Compound 37



Compound 37

```
IY-3bconc
STANDARD 1H OBSERVE

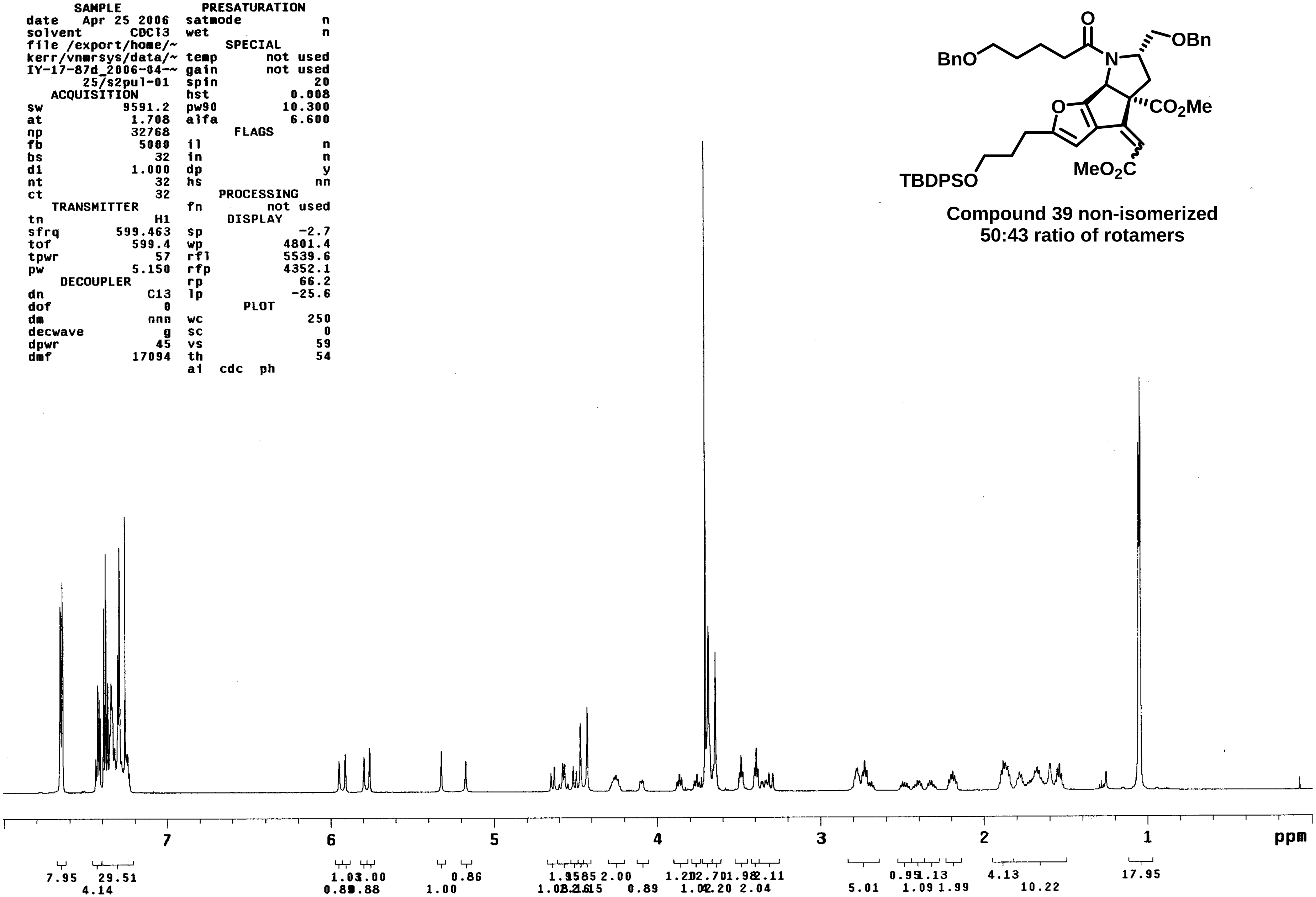
exp1  s2pul

      SAMPLE              SPECIAL
date   Aug  7 2005  temp       not used
solvent       cdcl3  gain       not used
file /export/home/~ spin       not used
vnmr1/walkup/auto_~ hst           0.008
    07.08.05/0105   pw90         11.600
   ACQUISITION      alfa         20.000
sw           25125.6          FLAGS
at             1.199  il                 n
np             60270  in                 n
fb             13800  dp                 y
bs                64  hs                nn
d1             1.000         PROCESSING
nt              1000  lb              1.00
ct                64  fn          not used
   TRANSMITTER               DISPLAY
tn               C13  sp              -6.0
sfrq         100.613  wp           18125.5
tof           1550.8  rfl           9302.8
tpwr              57  rfp           7746.3
pw             5.800  rp            -139.0
    DECOUPLER         lp            -317.6
dn                H1           PLOT
dof                0  wc               250
dm               yyy  sc                 0
dmm                w  vs                60
dpwr              40  th                19
dmf             9300  ai   no   ph
```

```
IY-17-87d Inova 600

exp1  PROTON

      SAMPLE              PRESATURATION
date   Apr 25 2006   satmode              n
solvent      CDCl3   wet                  n
file /export/home/~        SPECIAL
kerr/vnmrsys/data/~  temp          not used
IY-17-87d_2006-04-~  gain          not used
     25/s2pul-01     spin                20
   ACQUISITION       hst              0.008
sw          9591.2   pw90            10.300
at           1.708   alfa             6.600
np           32768          FLAGS
fb            5000   il                   n
bs              32   in                   n
d1           1.000   dp                   y
nt              32   hs                  nn
ct              32         PROCESSING
   TRANSMITTER       fn            not used
tn              H1          DISPLAY
sfrq       599.463   sp                -2.7
tof          599.4   wp              4801.4
tpwr            57   rfl             5539.6
pw           5.150   rfp             4352.1
    DECOUPLER        rp                66.2
dn             C13   lp               -25.6
dof              0            PLOT
dm             nnn   wc                 250
decwave          g   sc                   0
dpwr            45   vs                  59
dmf          17094   th                  54
                     ai   cdc   ph
```

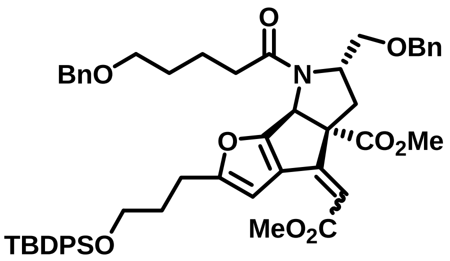


Compound 39 non-isomerized
50:43 ratio of rotamers

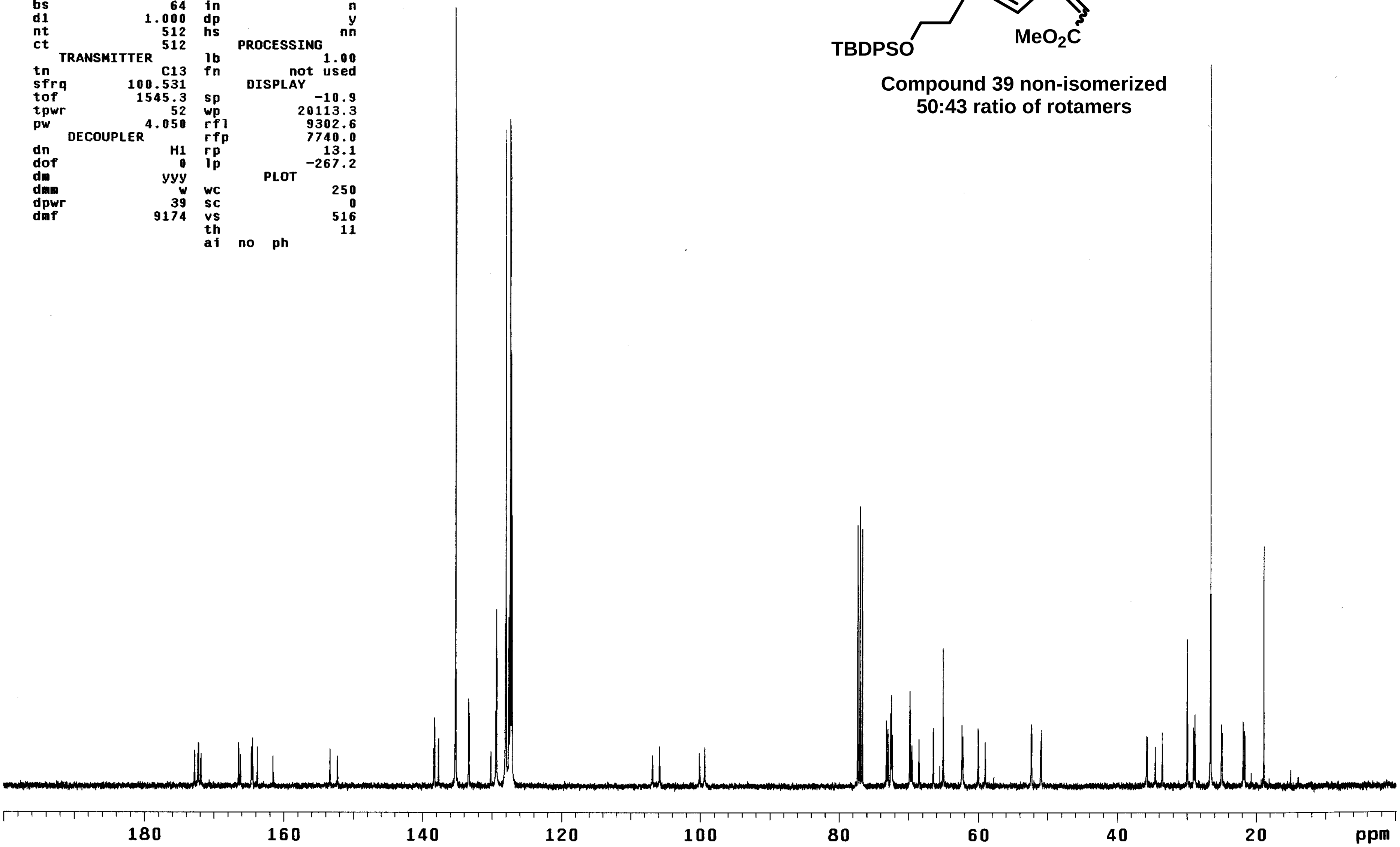
```
IY-17-97c Inova 400

exp1  s2pul

     SAMPLE              SPECIAL
date   Apr 25 2006  temp       not used
solvent      CDCl3  gain       not used
file           exp  spin             20
   ACQUISITION      hst           0.008
sw         25133.5  pw90          8.100
at           1.199  alfa         20.000
np           60288          FLAGS
fb           14000  il                n
bs              64  in                n
d1           1.000  dp                y
nt             512  hs               nn
ct             512        PROCESSING
   TRANSMITTER      lb             1.00
tn             C13  fn         not used
sfrq       100.531        DISPLAY
tof         1545.3  sp            -10.9
tpwr            52  wp          20113.3
pw           4.050  rfl          9302.6
    DECOUPLER       rfp          7740.0
dn              H1  rp             13.1
dof              0  lp           -267.2
dm             yyy          PLOT
dmm              w  wc              250
dpwr            39  sc                0
dmf           9174  vs              516
                    th               11
                    ai   no   ph
```



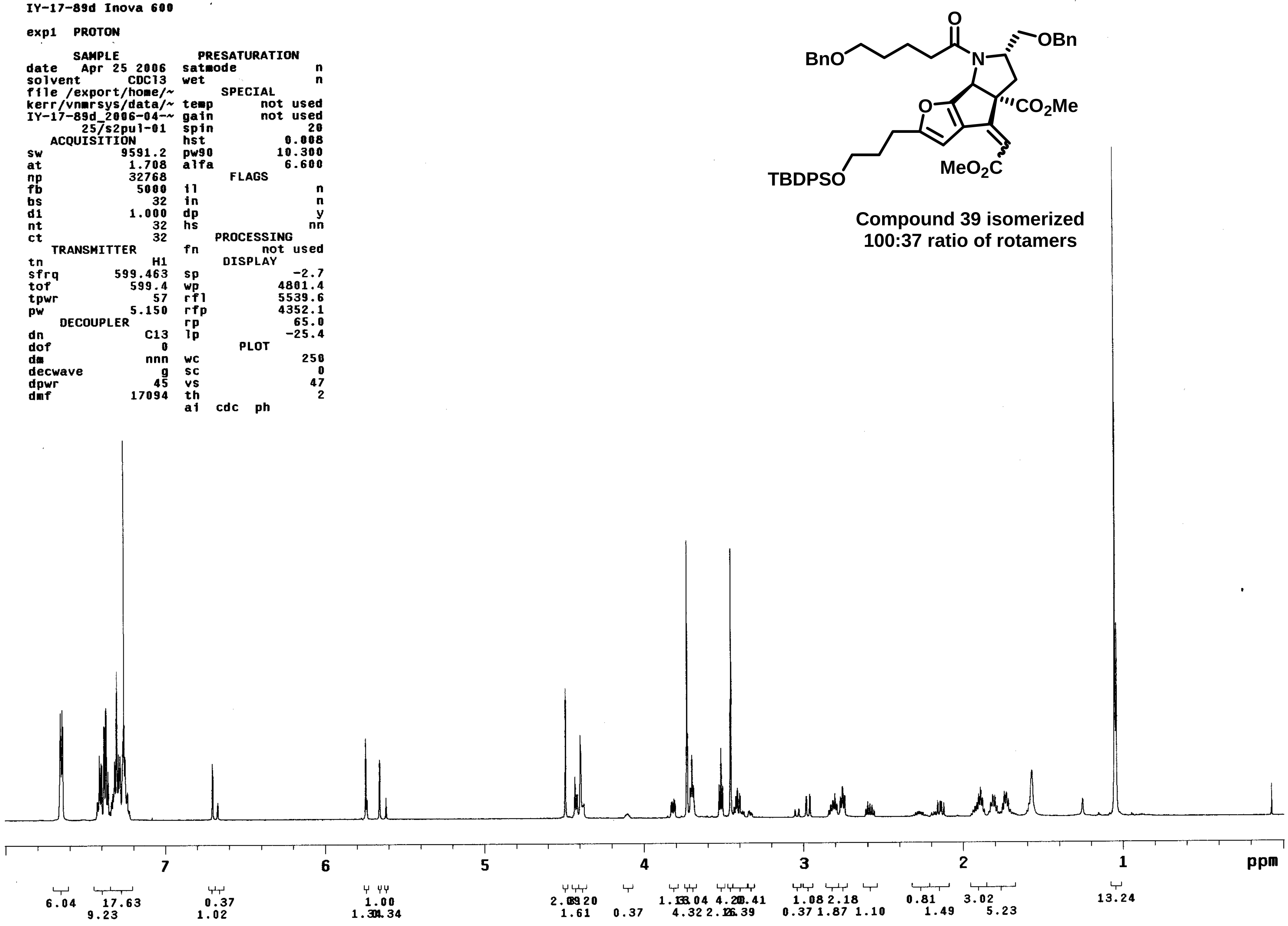
Compound 39 non-isomerized
50:43 ratio of rotamers



```
IY-17-89d Inova 600

exp1  PROTON

      SAMPLE             PRESATURATION
date   Apr 25 2006     satmode            n
solvent       CDCl3    wet                n
file /export/home/~           SPECIAL
kerr/vnmrsys/data/~    temp        not used
IY-17-89d_2006-04-~    gain        not used
      25/s2pul-01      spin              20
   ACQUISITION         hst            0.008
sw            9591.2   pw90          10.300
at             1.708   alfa           6.600
np             32768            FLAGS
fb              5000   il                 n
bs                32   in                 n
d1             1.000   dp                 y
nt                32   hs                nn
ct                32          PROCESSING
   TRANSMITTER         fn          not used
tn                H1            DISPLAY
sfrq         599.463   sp              -2.7
tof            599.4   wp            4801.4
tpwr              57   rfl           5539.6
pw             5.150   rfp           4352.1
    DECOUPLER          rp              65.0
dn               C13   lp             -25.4
dof                0             PLOT
dm               nnn   wc               250
decwave            g   sc                 0
dpwr              45   vs                47
dmf            17094   th                 2
                       ai   cdc   ph
```

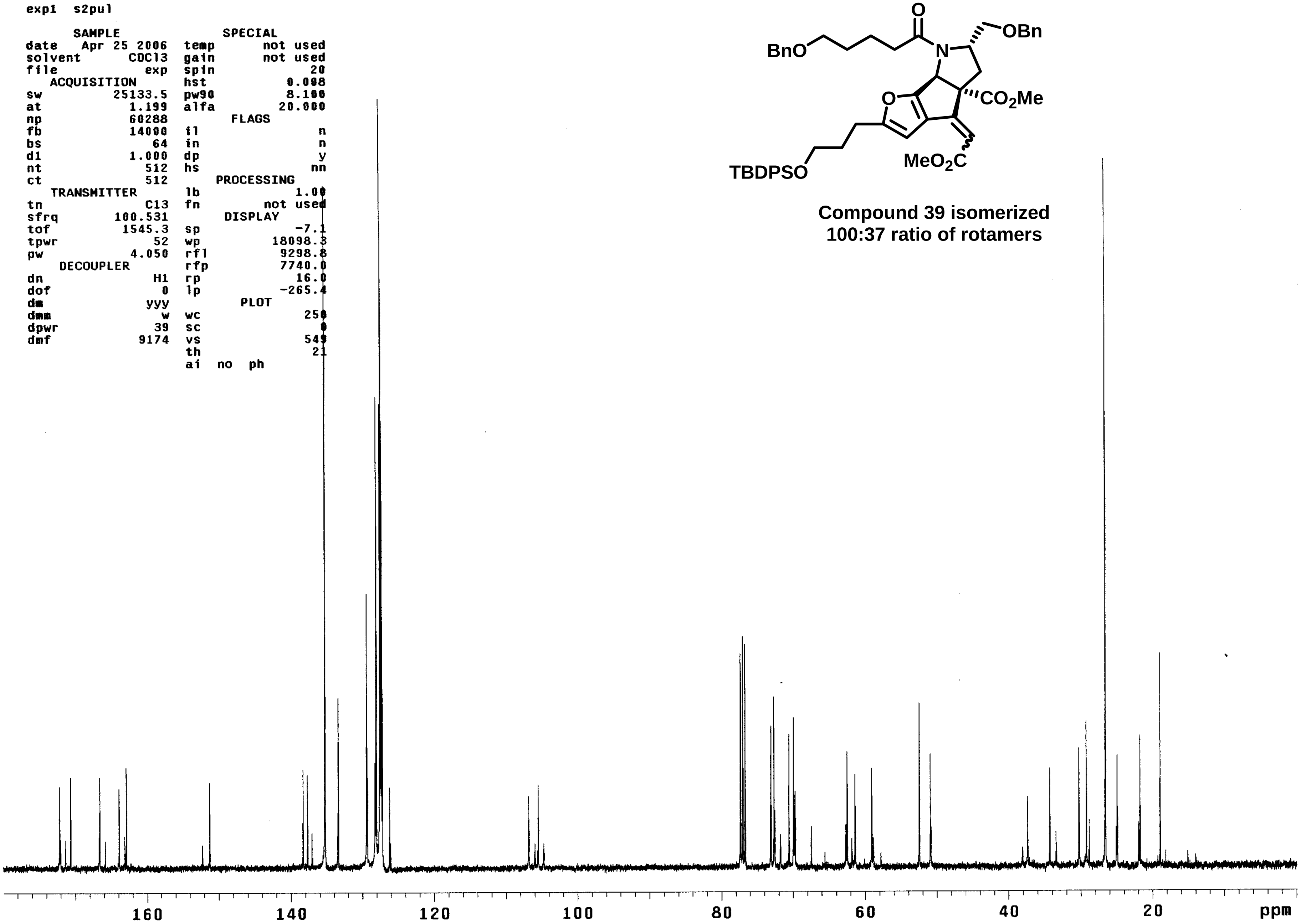


Compound 39 isomerized
100:37 ratio of rotamers

```
IY-17-89c Inova 400

exp1  s2pul

      SAMPLE                 SPECIAL
date   Apr 25 2006   temp       not used
solvent       CDCl3  gain       not used
file            exp  spin             20
    ACQUISITION      hst           0.008
sw          25133.5  pw90          8.100
at            1.199  alfa         20.000
np            60288          FLAGS
fb            14000  il                n
bs               64  in                n
d1            1.000  dp                y
nt              512  hs               nn
ct              512        PROCESSING
    TRANSMITTER      lb             1.00
tn              C13  fn         not used
sfrq        100.531         DISPLAY
tof          1545.3  sp             -7.1
tpwr             52  wp          18098.3
pw            4.050  rfl          9298.8
     DECOUPLER       rfp          7740.0
dn               H1  rp             16.0
dof               0  lp           -265.4
dm              yyy          PLOT
dmm               w  wc              250
dpwr             39  sc                0
dmf            9174  vs              549
                     th               21
                     ai  no  ph
```

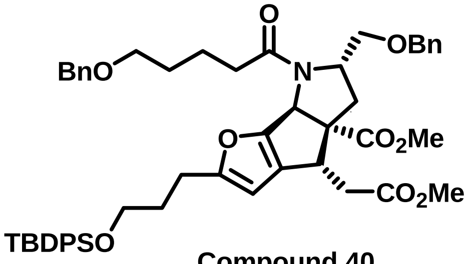


Compound 39 isomerized
100:37 ratio of rotamers

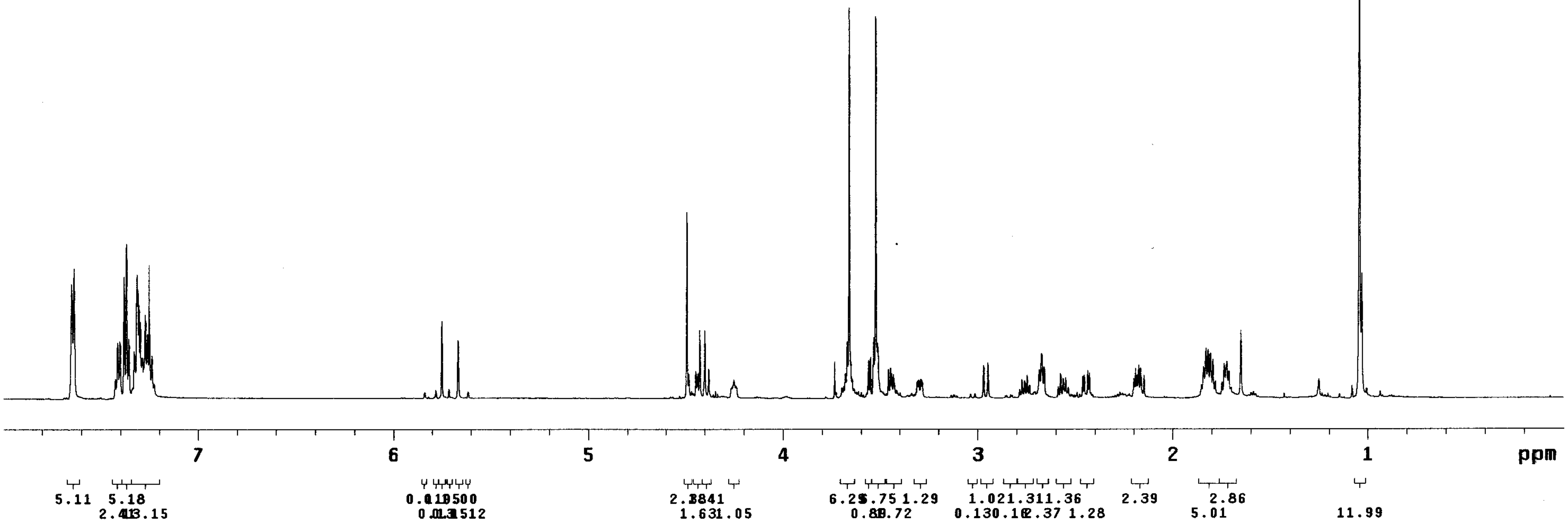
```
IY-14-131spt1 Inova 600

exp1  PROTON

      SAMPLE                SPECIAL
date   Sep 27 2005  temp       not used
solvent      CDCl3  gain       not used
file /export/home/~ spin             22
kerr/vnmrsys/data/~ hst           0.008
IY-14-131spt1_2005~ pw90         10.900
-09-27/PROTON_01.f~ alfa              0
                id          FLAGS
   ACQUISITION      il                n
sw          9592.3  in                n
at           1.892  dp                y
np           36298  hs               nn
fb            5000       PROCESSING
bs              32  fn         not used
d1           1.000        DISPLAY
nt               8  sp              0.7
ct               8  wp           4791.8
   TRANSMITTER      rfl          4636.6
tn              H1  rfp          3447.1
sfrq       599.495  rp           -177.7
tof          599.3  lp            -34.5
tpwr            53           PLOT
pw           5.450  wc              250
    DECOUPLER       sc                0
dn             C13  vs               47
dof              0  th               54
dm             nnn  ai   cdc   ph
decwave    W40_hcx
dpwr            39
dmf           6578
```



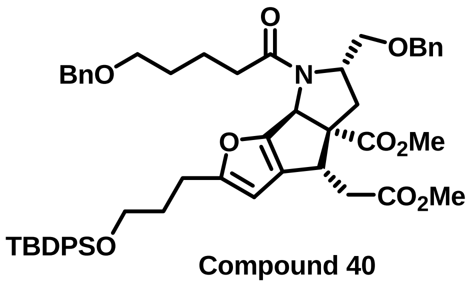
Compound 40
9:1 ratio of rotamers



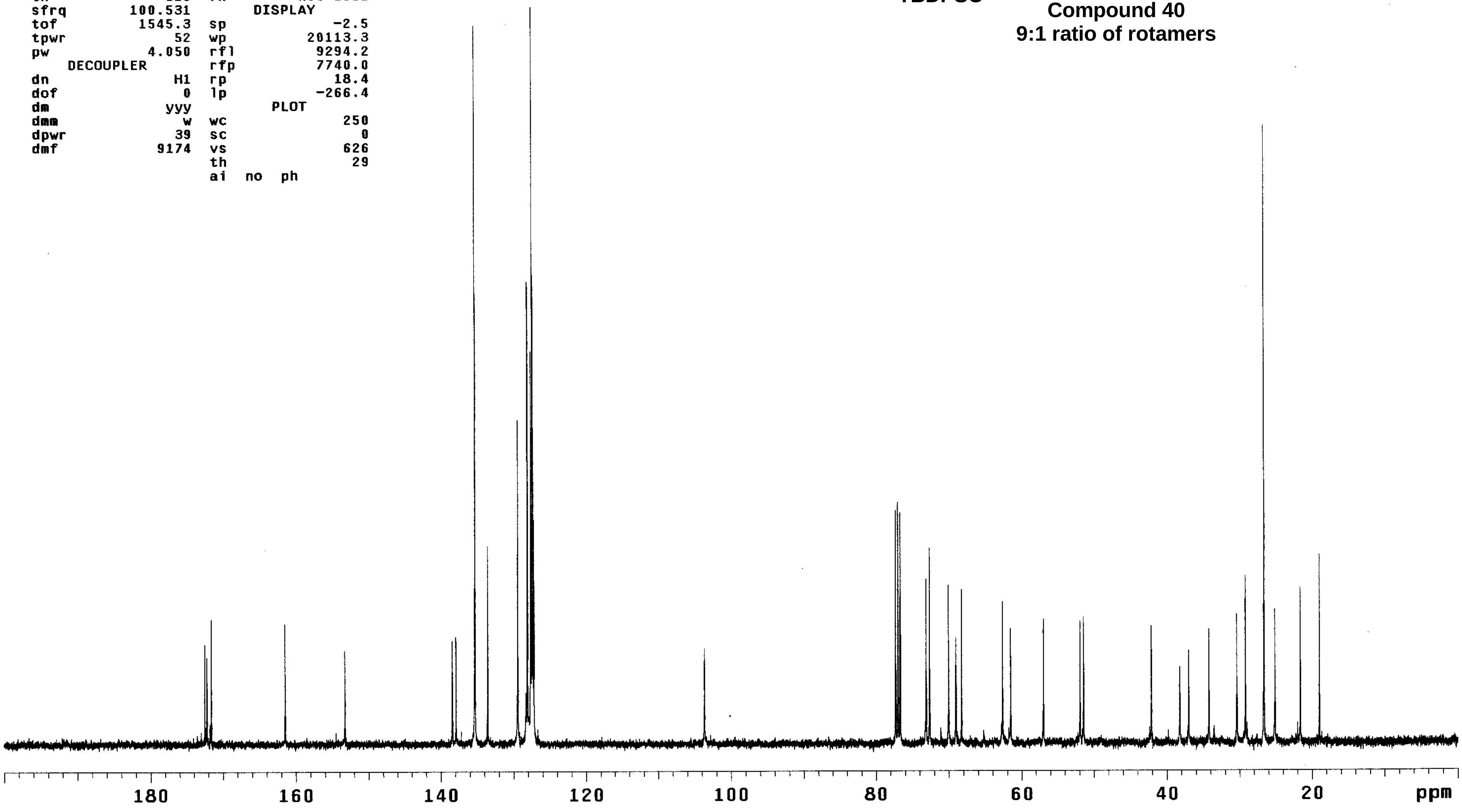
```
IY-17-101C Inova 400

exp1  s2pul

    SAMPLE                  SPECIAL
date   Apr 27 2006  temp       not used
solvent      CDCl3  gain       not used
file           exp  spin             20
   ACQUISITION      hst           0.008
sw         25133.5  pw90          8.100
at           1.199  alfa         20.000
np           60288         FLAGS
fb           14000  il                n
bs              64  in                n
d1           1.000  dp                y
nt             512  hs               nn
ct             512       PROCESSING
   TRANSMITTER      lb             1.00
tn             C13  fn         not used
sfrq       100.531        DISPLAY
tof         1545.3  sp             -2.5
tpwr            52  wp          20113.3
pw           4.050  rfl          9294.2
    DECOUPLER       rfp          7740.0
dn              H1  rp             18.4
dof              0  lp           -266.4
dm             yyy          PLOT
dmm              w  wc              250
dpwr            39  sc                0
dmf           9174  vs              626
                    th               29
                    ai   no   ph
```



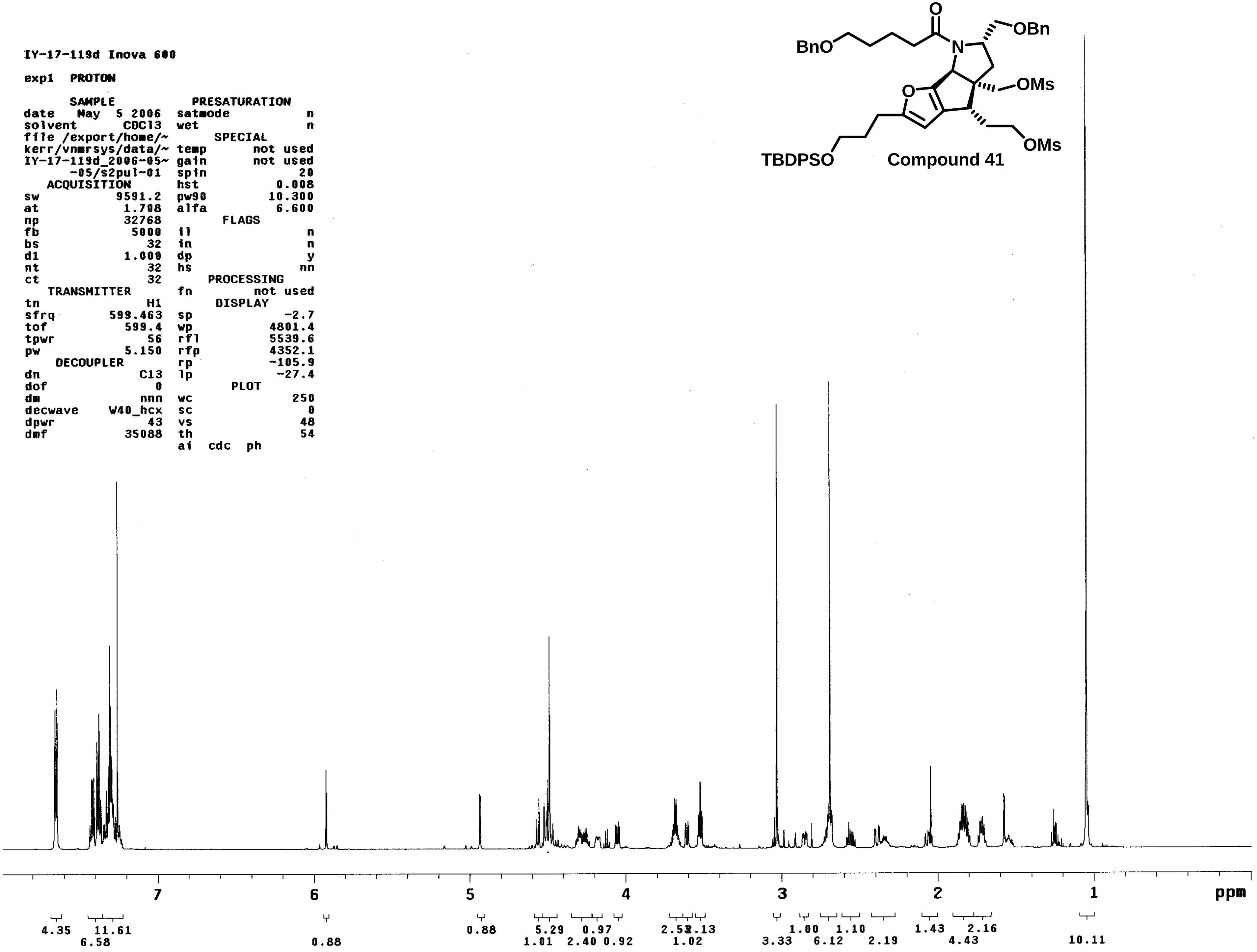
Compound 40
9:1 ratio of rotamers



```
IY-17-119d Inova 600

exp1  PROTON

      SAMPLE              PRESATURATION
date   May  5 2006   satmode            n
solvent      CDCl3   wet                n
file /export/home/~       SPECIAL
kerr/vnmrsys/data/~  temp        not used
IY-17-119d_2006-05~  gain        not used
      -05/s2pul-01   spin              20
   ACQUISITION       hst            0.008
sw          9591.2   pw90          10.300
at           1.708   alfa           6.600
np           32768         FLAGS
fb            5000   il                 n
bs              32   in                 n
d1           1.000   dp                 y
nt              32   hs                nn
ct              32       PROCESSING
   TRANSMITTER       fn          not used
tn              H1        DISPLAY
sfrq       599.463   sp              -2.7
tof          599.4   wp            4801.4
tpwr            56   rfl           5539.6
pw           5.150   rfp           4352.1
   DECOUPLER         rp            -105.9
dn             C13   lp             -27.4
dof              0          PLOT
dm             nnn   wc               250
decwave    W40_hcx   sc                 0
dpwr            43   vs                48
dmf          35088   th                54
                     ai   cdc   ph
```

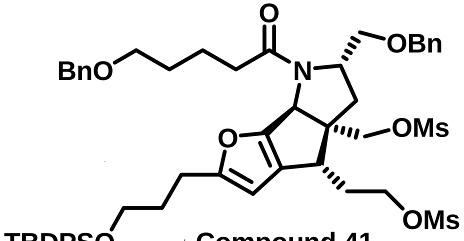


Compound 41

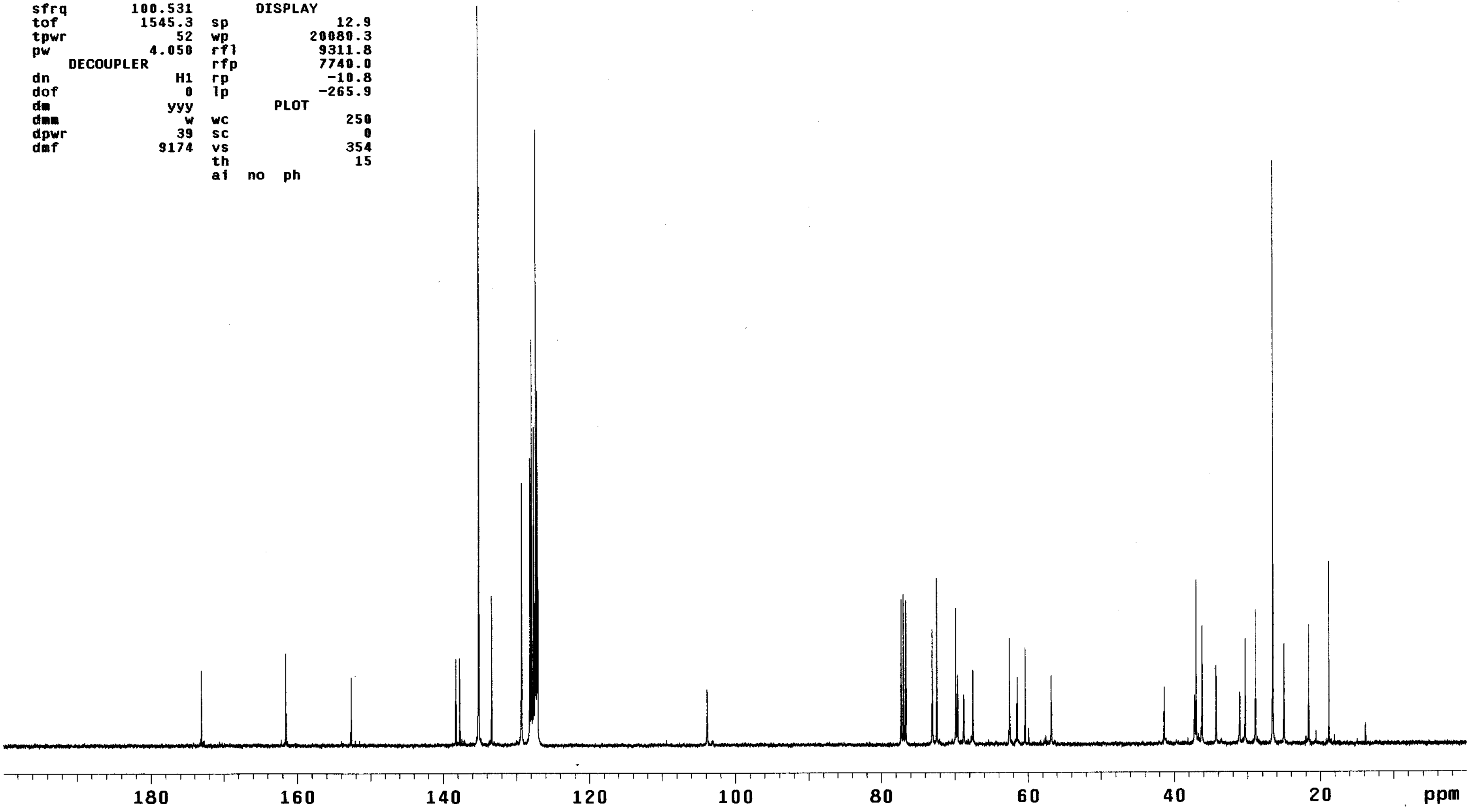
```
IY-17-119carbon Inova 400

exp1  s2pul

      SAMPLE                 SPECIAL
date   May  5 2006   temp        not used
solvent       CDCl3  gain        not used
file            exp  spin              20
   ACQUISITION       hst            0.008
sw          25133.5  pw90           8.100
at            1.199  alfa          20.000
np            60288          FLAGS
fb            14000  il                 n
bs               64  in                 n
d1            1.000  dp                 y
nt             1000  hs                nn
ct             1000        PROCESSING
   TRANSMITTER       lb              1.00
tn              C13  fn          not used
sfrq        100.531          DISPLAY
tof          1545.3  sp              12.9
tpwr             52  wp           20080.3
pw            4.050  rfl           9311.8
    DECOUPLER        rfp           7740.0
dn               H1  rp             -10.8
dof               0  lp            -265.9
dm              yyy           PLOT
dmm               w  wc               250
dpwr             39  sc                 0
dmf            9174  vs               354
                     th                15
                     ai  no  ph
```



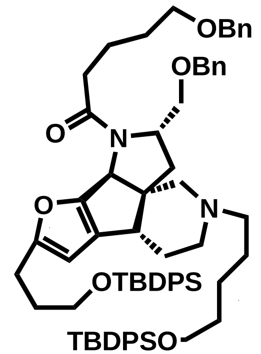
Compound 41



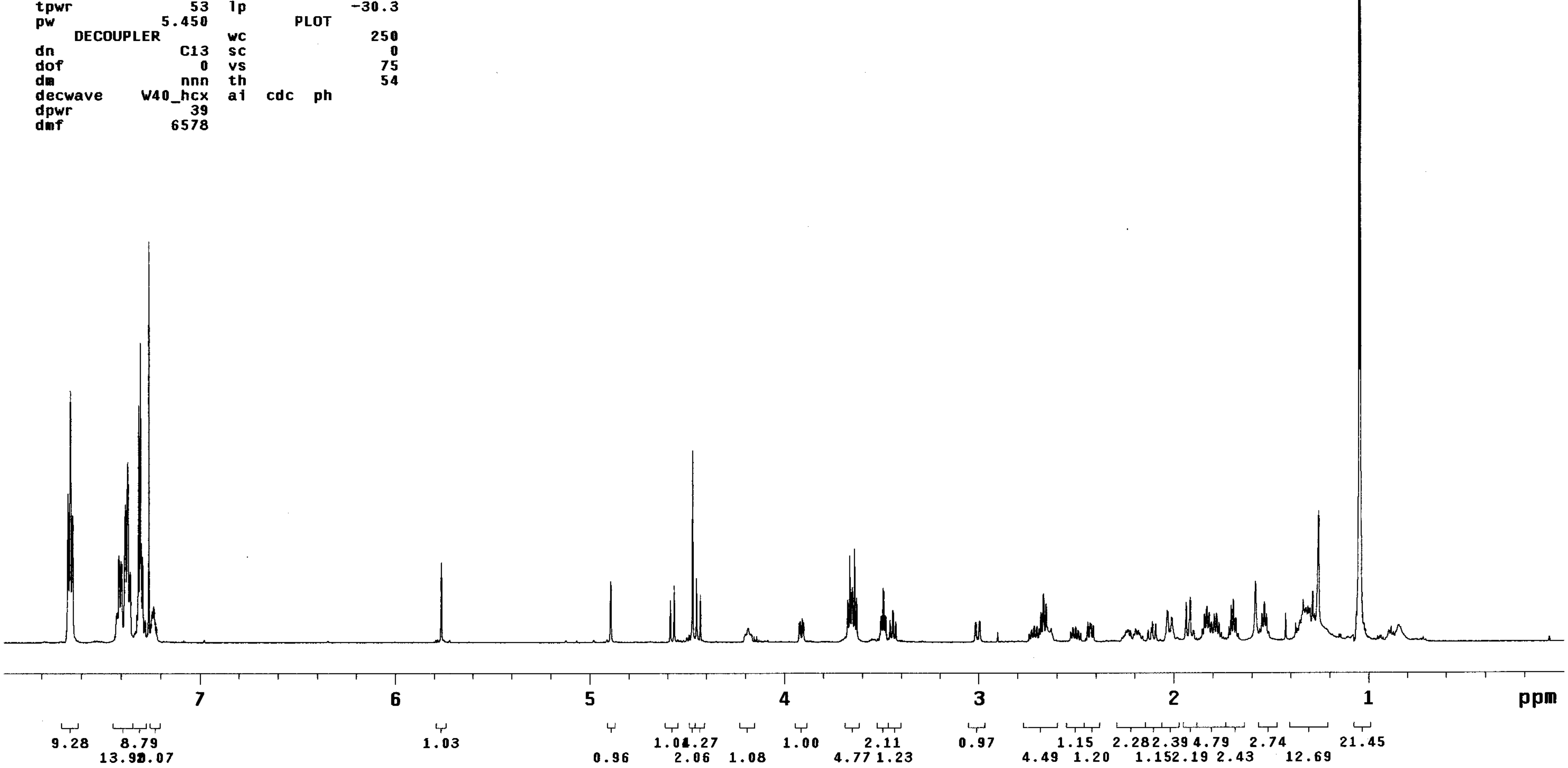
```
IY-14-173g Inova 600

exp1  PROTON

      SAMPLE              SPECIAL
date   Oct 16 2005  temp            25.0
solvent       CDCl3  gain       not used
file /export/home/~ spin              22
kerr/vnmrsys/data/~ hst            0.008
IY-14-173g_2005-10~ pw90          10.900
 -16/PROTON_01.fid  alfa               0
   ACQUISITION            FLAGS
sw           9592.3  il                n
at            1.892  in                n
np            36298  dp                y
fb             5000  hs               nn
bs               32      PROCESSING
d1            1.000  fn         not used
nt                8       DISPLAY
ct                8  sp              0.5
   TRANSMITTER       wp           4789.4
tn               H1  rfl          5536.8
sfrq        599.495  rfp          4352.3
tof           599.3  rp             51.6
tpwr             53  lp            -30.3
pw            5.450          PLOT
    DECOUPLER        wc              250
dn              C13  sc                0
dof               0  vs               75
dm              nnn  th               54
decwave     W40_hcx  ai   cdc  ph
dpwr             39
dmf            6578
```



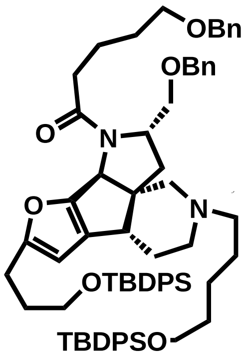
Compound 42



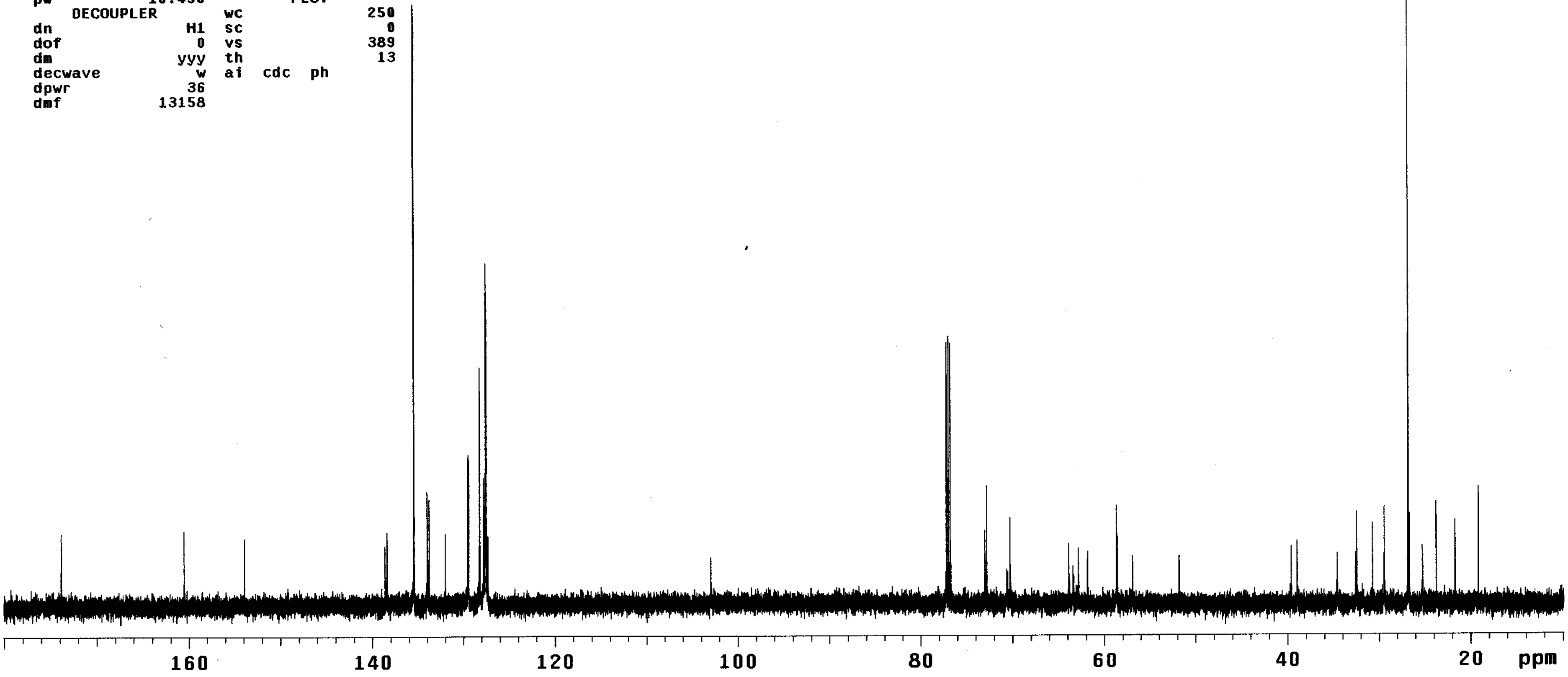
```
IY-15-3carbon Inova 600

exp1  CARBON

      SAMPLE               SPECIAL
date   Oct 23 2005  temp            25.0
solvent       CDCl3  gain       not used
file /export/home/~ spin              16
kerr/vnmrsys/data/~ hst            0.008
IY-15-3carbon_2005~ pw90          20.900
-10-23/CARBON_01.f~ alfa          10.000
                 id           FLAGS
   ACQUISITION      il                 n
sw          37682.5 in                 n
at            1.300 dp                 y
np            98010 hs                nn
fb            21000        PROCESSING
bs               64 lb              0.50
d1            1.000 fn          not used
nt              512         DISPLAY
ct              256 sp            1496.0
   TRANSMITTER      wp           25649.1
tn              C13 rfl          13874.5
sfrq        150.759 rfp          11607.2
tof          3127.7 rp            -135.0
tpwr             57 lp            -297.1
pw           10.450           PLOT
    DECOUPLER       wc               250
dn               H1 sc                 0
dof               0 vs               389
dm              yyy th                13
decwave           w ai   cdc  ph
dpwr             36
dmf           13158
```



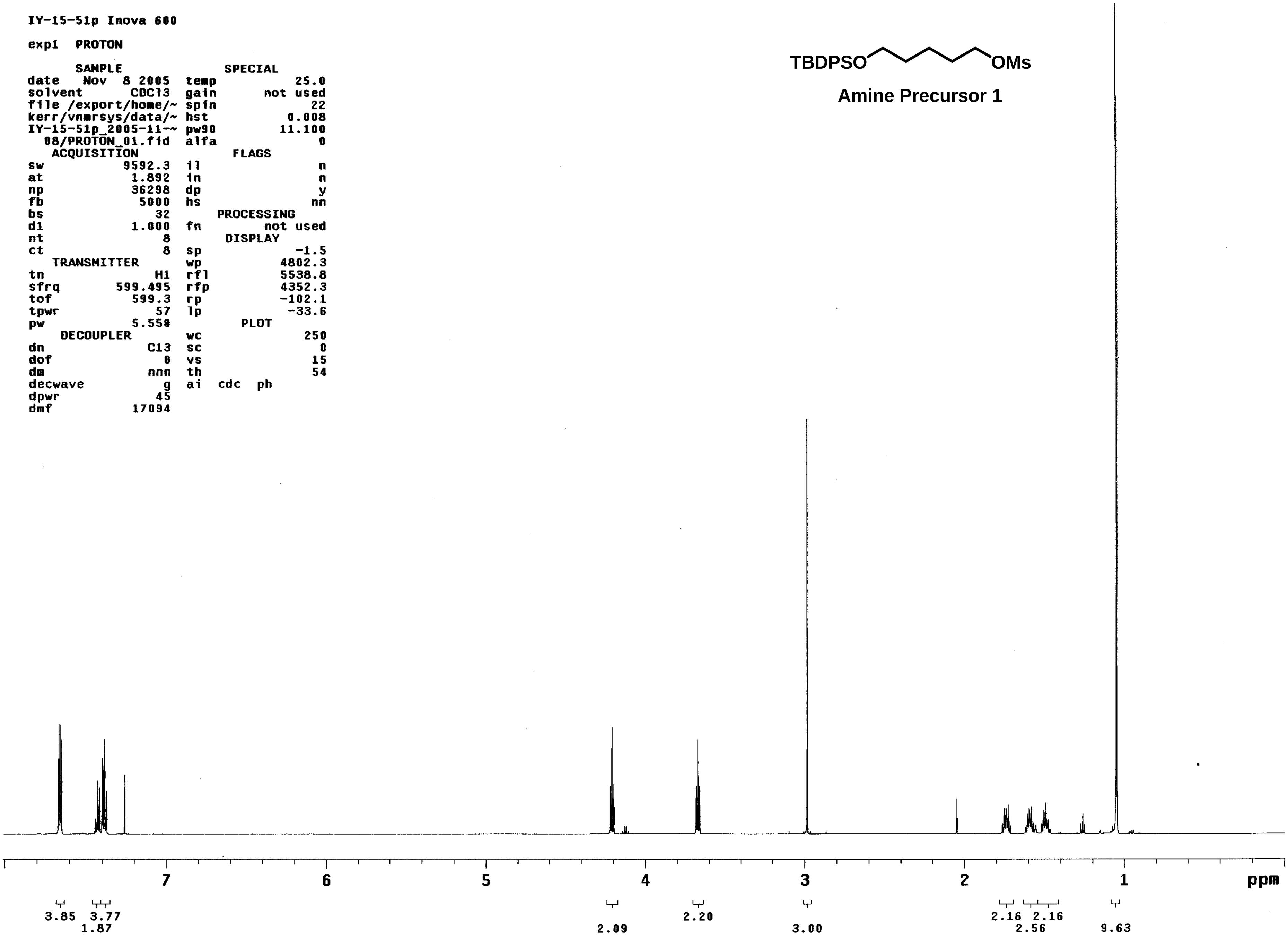
Compound 42



```
IY-15-51p Inova 600

exp1  PROTON

      SAMPLE                SPECIAL
date    Nov  8 2005  temp             25.0
solvent       CDCl3  gain         not used
file /export/home/~  spin               22
kerr/vnmrsys/data/~  hst             0.008
IY-15-51p_2005-11-~  pw90           11.100
  08/PROTON_01.fid   alfa                0
   ACQUISITION              FLAGS
sw           9592.3  il                  n
at            1.892  in                  n
np            36298  dp                  y
fb             5000  hs                 nn
bs               32        PROCESSING
d1            1.000  fn           not used
nt                8          DISPLAY
ct                8  sp               -1.5
   TRANSMITTER       wp             4802.3
tn               H1  rfl            5538.8
sfrq        599.495  rfp            4352.3
tof           599.3  rp             -102.1
tpwr             57  lp              -33.6
pw            5.550          PLOT
    DECOUPLER        wc                250
dn              C13  sc                  0
dof               0  vs                 15
dm              nnn  th                 54
decwave           g  ai   cdc   ph
dpwr             45
dmf           17094
```



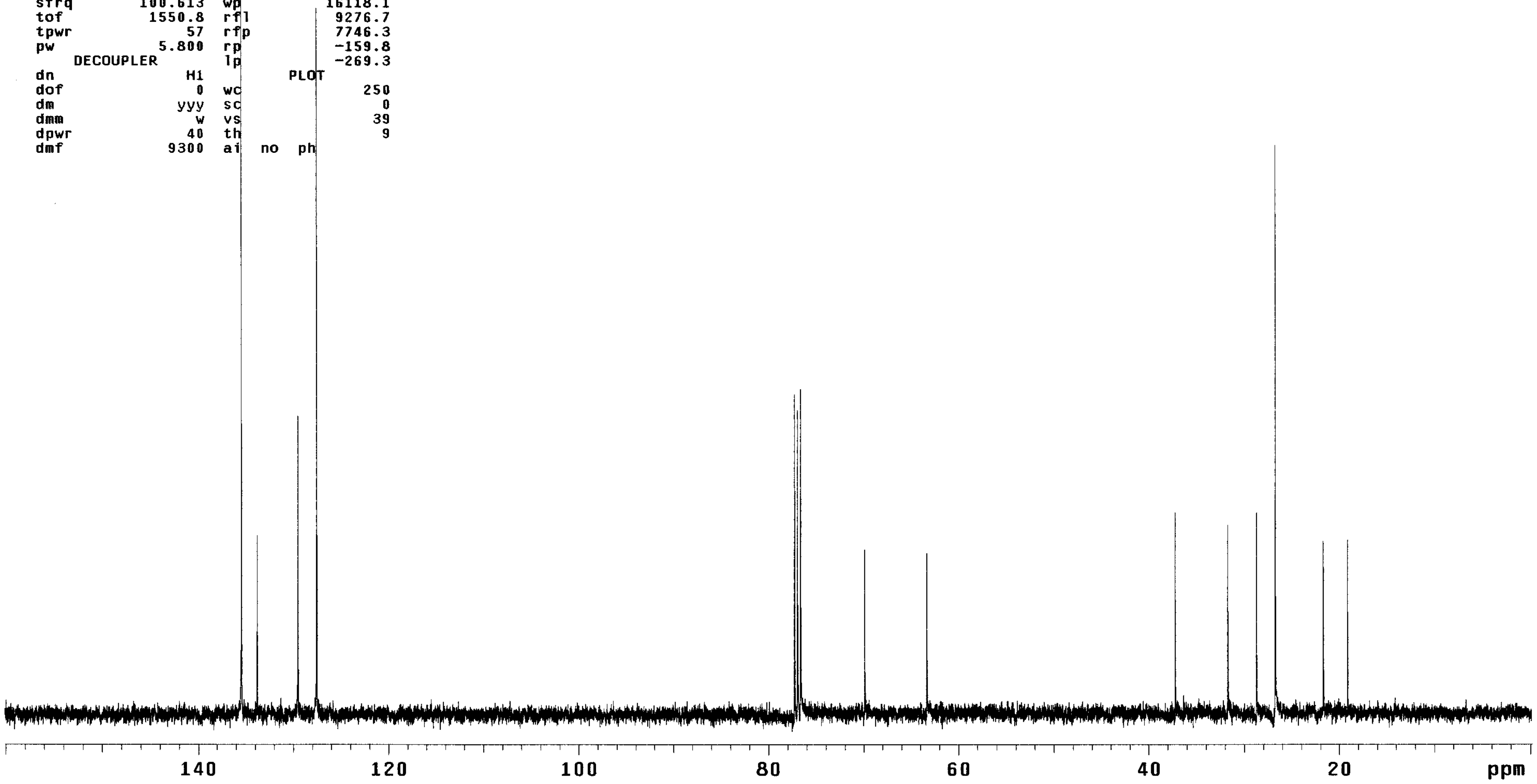
Amine Precursor 1

```
IY-15-51c mercury
STANDARD 1H OBSERVE

exp1  s2pul

      SAMPLE              SPECIAL
date   Nov 10 2005  temp      not used
solvent      cdcl3  gain      not used
file /export/home/~ spin      not used
vnmr1/walkup/auto_~ hst          0.008
     10.11.05/0102  pw90        11.600
   ACQUISITION      alfa        20.000
sw         25125.6          FLAGS
at           1.199  il               n
np           60270  in               n
fb           13800  dp               y
bs              64  hs              nn
d1           1.000        PROCESSING
nt             512  lb            1.00
ct              64  fn        not used
   TRANSMITTER             DISPLAY
tn             C13  sp           -13.7
sfrq       100.613  wp         16118.1
tof         1550.8  rfl         9276.7
tpwr            57  rfp         7746.3
pw           5.800  rp          -159.8
    DECOUPLER       lp          -269.3
dn              H1           PLOT
dof              0  wc             250
dm             yyy  sc               0
dmm              w  vs              39
dpwr            40  th               9
dmf           9300  ai   no  ph
```

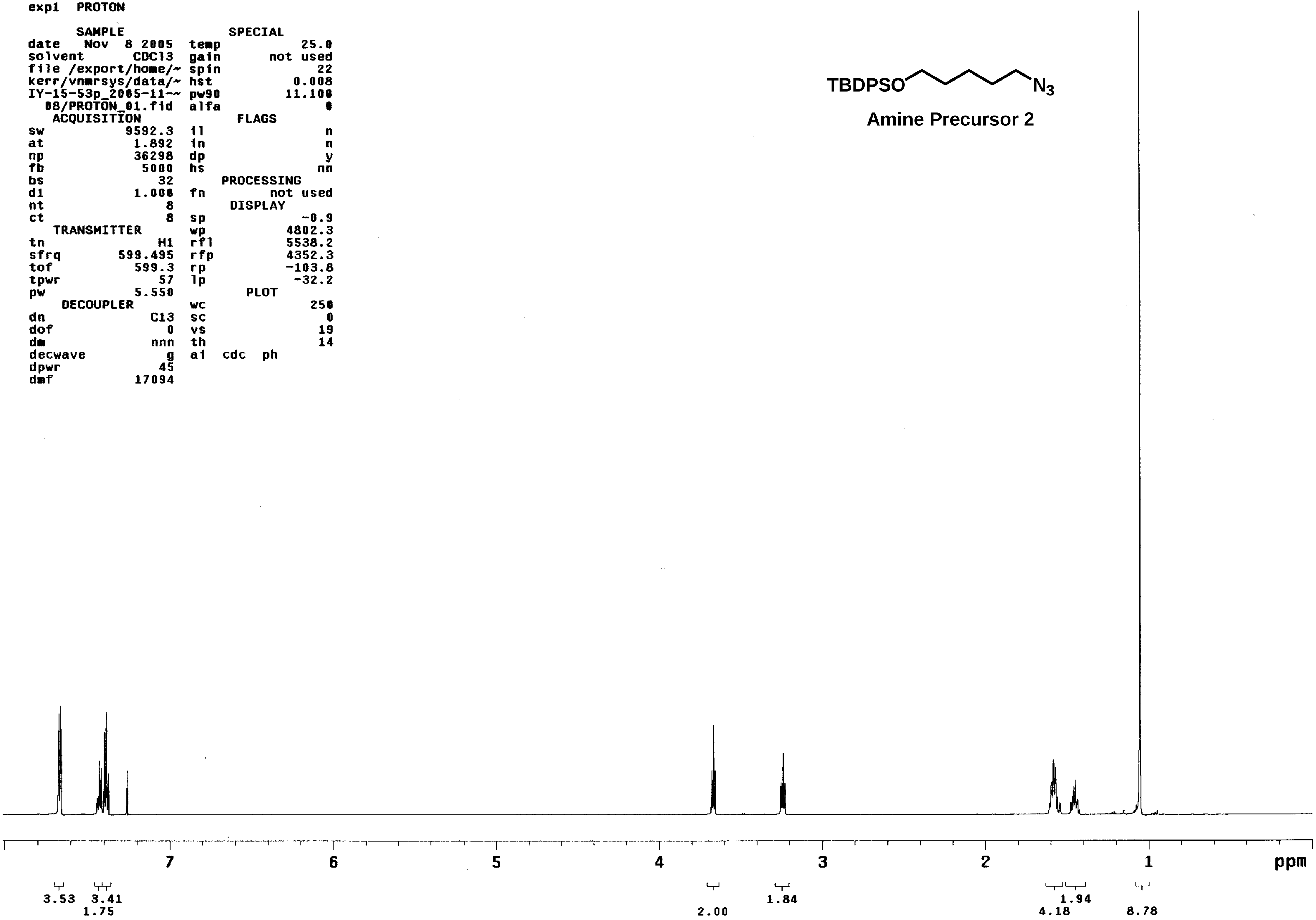
Amine Precursor 1



```
IY-15-53p Inova 600

exp1  PROTON

     SAMPLE                SPECIAL
date   Nov  8 2005  temp             25.0
solvent      CDCl3  gain         not used
file /export/home/~ spin               22
kerr/vnmrsys/data/~ hst             0.008
IY-15-53p_2005-11-~ pw90           11.100
  08/PROTON_01.fid  alfa                0
   ACQUISITION              FLAGS
sw          9592.3  il                  n
at           1.892  in                  n
np           36298  dp                  y
fb            5000  hs                 nn
bs              32        PROCESSING
d1           1.000  fn           not used
nt               8          DISPLAY
ct               8  sp               -0.9
   TRANSMITTER      wp             4802.3
tn              H1  rfl            5538.2
sfrq       599.495  rfp            4352.3
tof          599.3  rp             -103.8
tpwr            57  lp              -32.2
pw           5.550           PLOT
    DECOUPLER       wc                250
dn             C13  sc                  0
dof              0  vs                 19
dm             nnn  th                 14
decwave          g  ai   cdc   ph
dpwr            45
dmf          17094
```

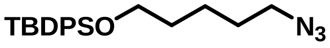


Amine Precursor 2

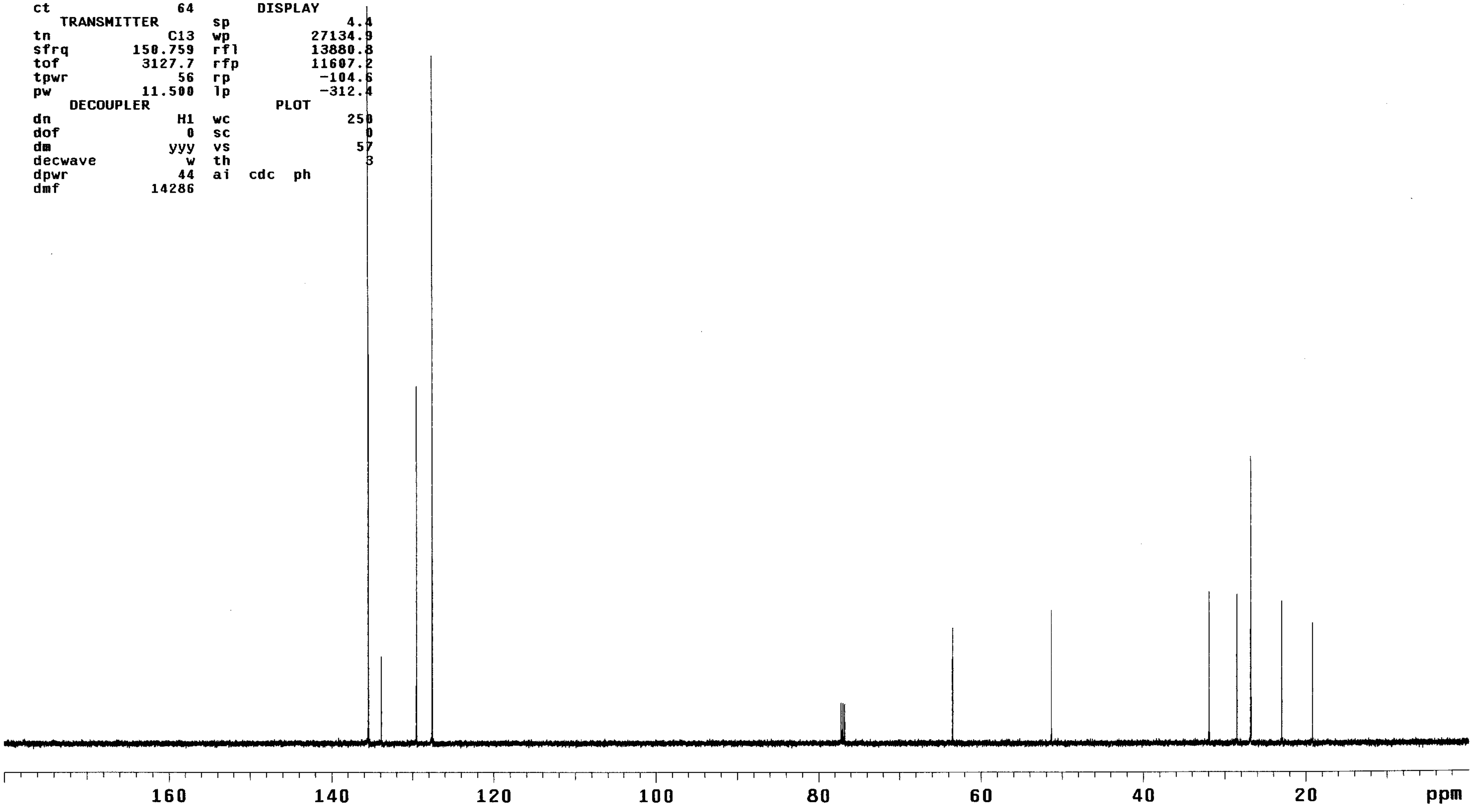
```
IY-15-53c Inova 600

exp1  CARBON

     SAMPLE               SPECIAL
date   Nov  8 2005  temp          25.0
solvent       CDCl3  gain      not used
file /export/home/~ spin            16
kerr/vnmrsys/data/~ hst          0.008
IY-15-53c_2005-11-~ pw90        23.000
  08/CARBON_01.fid  alfa        10.000
   ACQUISITION              FLAGS
sw          37682.5  il              n
at            1.300  in              n
np            98010  dp              y
fb            21000  hs             nn
bs               64       PROCESSING
d1            1.000  lb           0.50
nt              256  fn       not used
ct               64        DISPLAY
   TRANSMITTER       sp            4.4
tn              C13  wp        27134.9
sfrq        150.759  rfl       13880.8
tof          3127.7  rfp       11607.2
tpwr             56  rp         -104.6
pw           11.500  lp         -312.4
    DECOUPLER                PLOT
dn               H1  wc            250
dof               0  sc              0
dm              yyy  vs             57
decwave           w  th              3
dpwr             44  ai   cdc  ph
dmf           14286
```



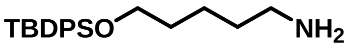
Amine Precursor 2



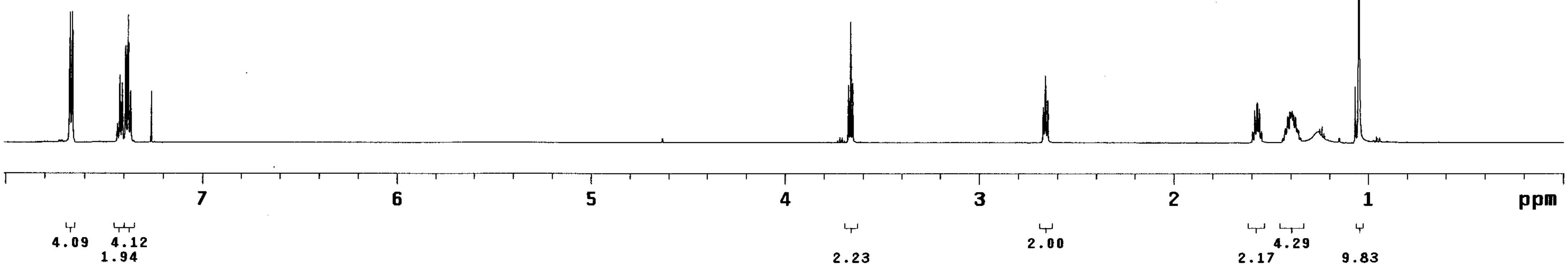
```
IY-14-167p Inova 600

exp1  PROTON

      SAMPLE                SPECIAL
date   Nov  8 2005  temp            25.0
solvent      CDCl3  gain        not used
file /export/home/~ spin              22
kerr/vnmrsys/data/~ hst            0.008
IY-14-167p_2005-11~ pw90          11.100
 -08/PROTON_01.fid  alfa               0
   ACQUISITION             FLAGS
sw          9592.3  il                 n
at           1.892  in                 n
np           36298  dp                 y
fb            5000  hs                nn
bs              32        PROCESSING
d1           1.000  fn          not used
nt               8         DISPLAY
ct               8  sp              -1.5
   TRANSMITTER      wp            4802.3
tn              H1  rfl           5538.8
sfrq       599.495  rfp           4352.3
tof          599.3  rp            -112.5
tpwr            57  lp             -22.5
pw           5.550           PLOT
    DECOUPLER       wc               250
dn             C13  sc                 0
dof              0  vs                23
dm             nnn  th                14
decwave          g  ai   cdc  ph
dpwr            45
dmf          17094
```



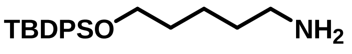
5-tert-butyldiphenylsiloxy-n-pentylamine



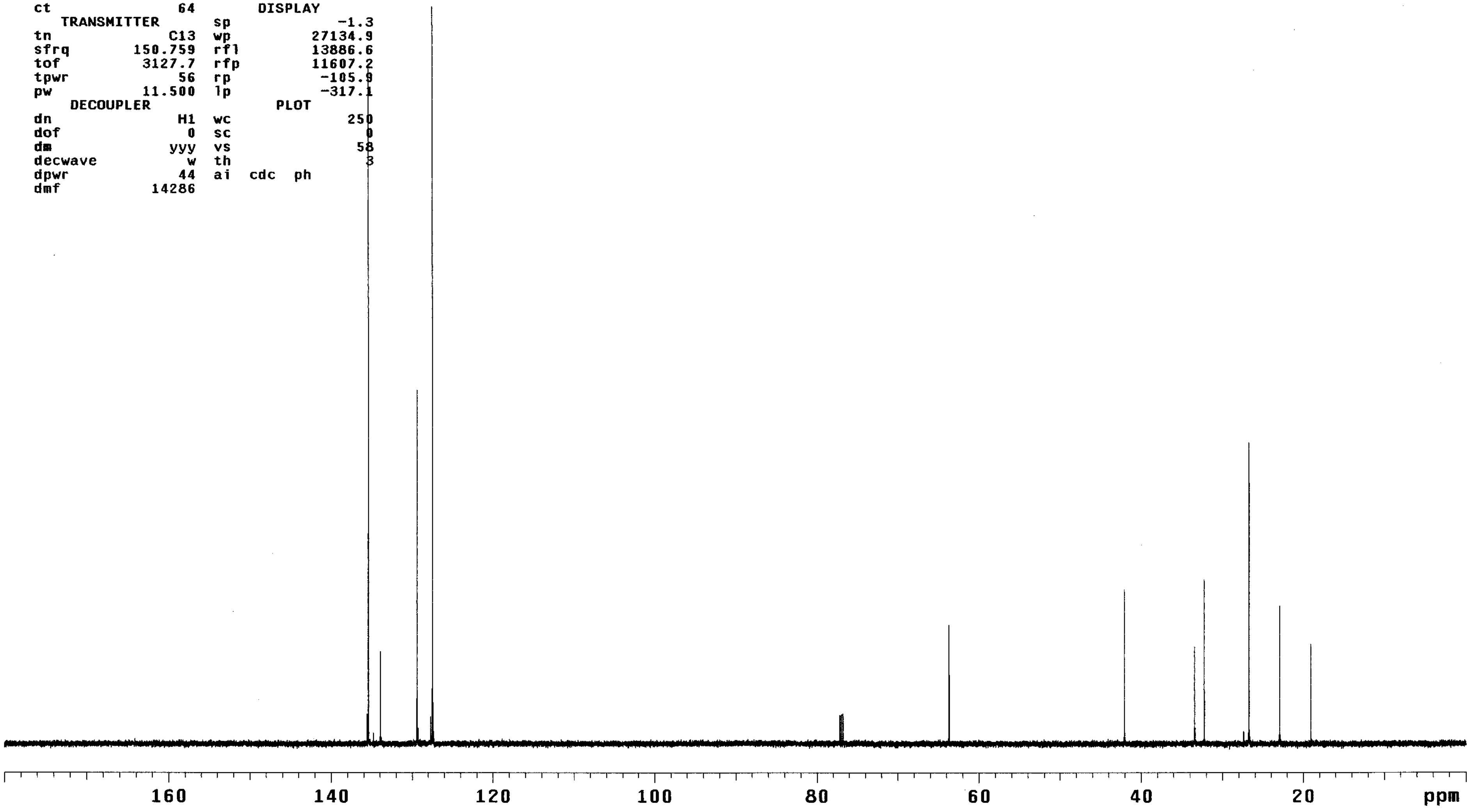
```
IY-14-167c Inova 600

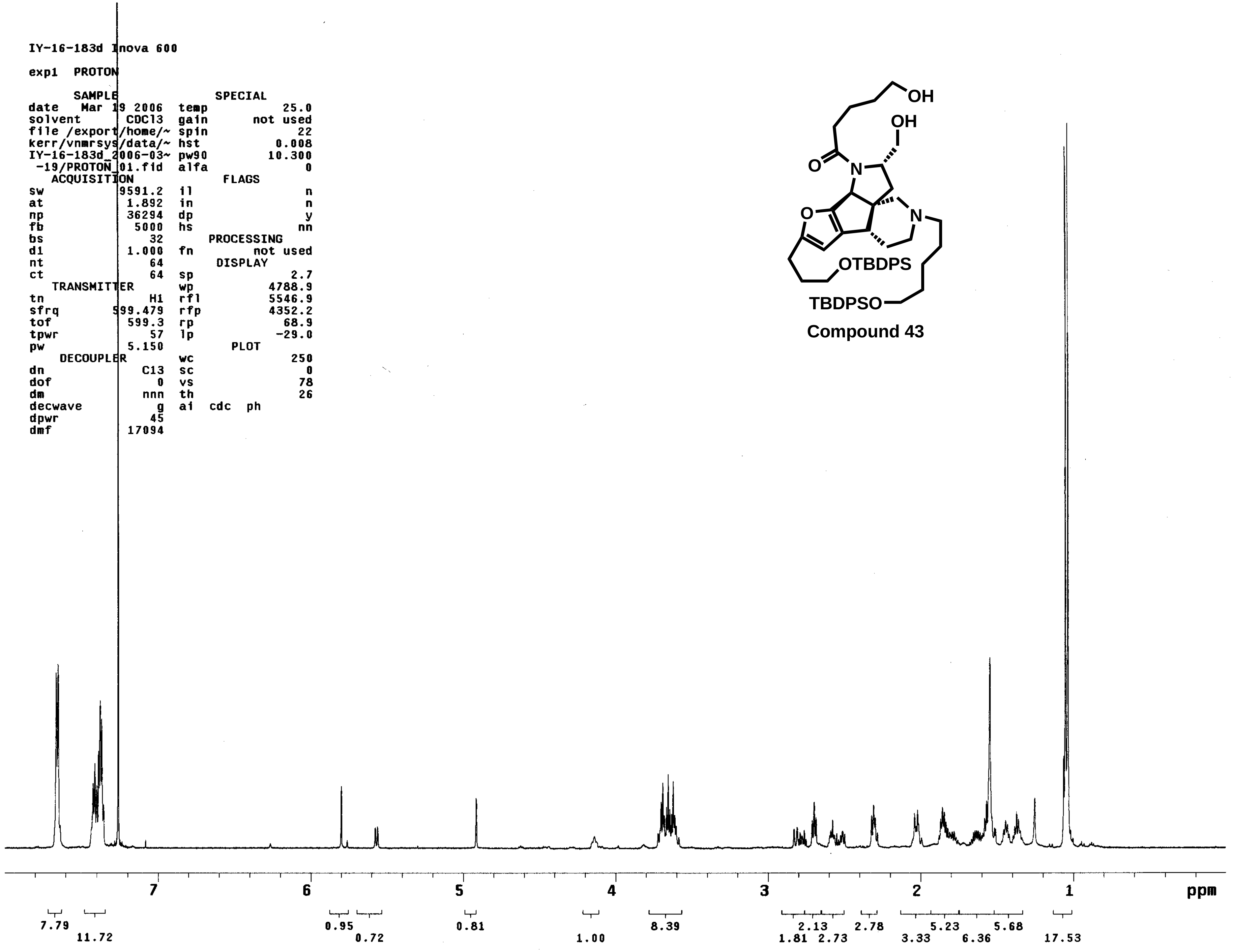
exp1  CARBON

     SAMPLE              SPECIAL
date   Nov  8 2005  temp          25.0
solvent      CDCl3  gain      not used
file /export/home/~ spin            16
kerr/vnmrsys/data/~ hst          0.008
IY-14-167c_2005-11~ pw90        23.000
 -08/CARBON_01.fid  alfa        10.000
   ACQUISITION            FLAGS
sw         37682.5  il               n
at           1.300  in               n
np           98010  dp               y
fb           21000  hs              nn
bs              64       PROCESSING
d1           1.000  lb            0.50
nt             512  fn        not used
ct              64        DISPLAY
   TRANSMITTER      sp            -1.3
tn             C13  wp         27134.9
sfrq       150.759  rfl        13886.6
tof         3127.7  rfp        11607.2
tpwr            56  rp          -105.9
pw          11.500  lp          -317.1
    DECOUPLER               PLOT
dn              H1  wc             250
dof              0  sc               0
dm             yyy  vs              58
decwave          w  th               3
dpwr            44  ai  cdc  ph
dmf          14286
```



5-tert-butyldiphenylsiloxy-n-pentylamine



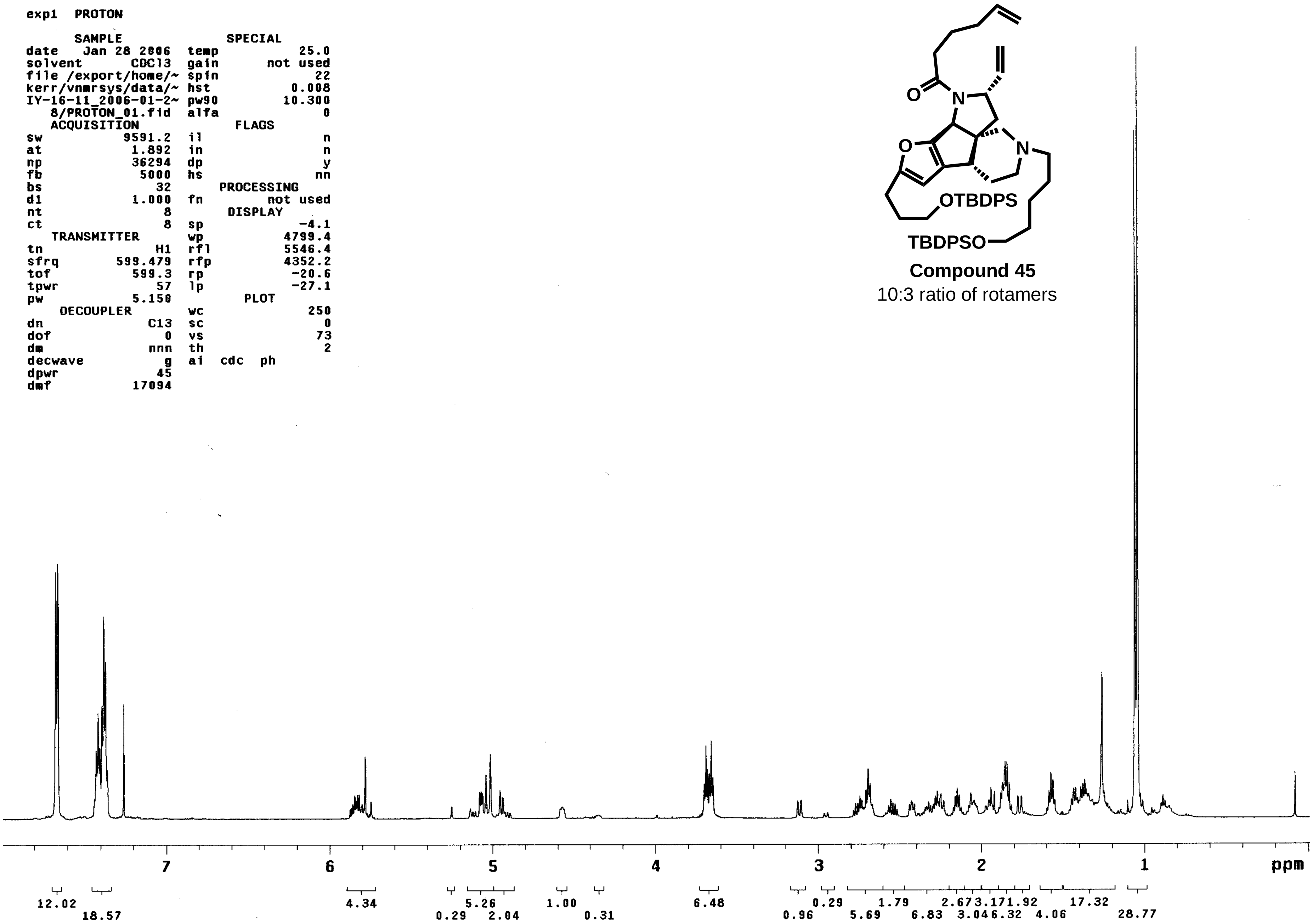


```
IY-16-183d Inova 600

exp1  PROTON

      SAMPLE                SPECIAL
date   Mar 19 2006  temp             25.0
solvent      CDCl3  gain         not used
file /export/home/~ spin               22
kerr/vnmrsys/data/~ hst             0.008
IY-16-183d_2006-03~ pw90           10.300
 -19/PROTON_01.fid  alfa                0
   ACQUISITION               FLAGS
sw          9591.2  il                  n
at           1.892  in                  n
np           36294  dp                  y
fb            5000  hs                 nn
bs              32        PROCESSING
d1           1.000  fn           not used
nt              64          DISPLAY
ct              64  sp                2.7
   TRANSMITTER      wp             4788.9
tn              H1  rfl            5546.9
sfrq       599.479  rfp            4352.2
tof          599.3  rp               68.9
tpwr            57  lp              -29.0
pw           5.150           PLOT
    DECOUPLER       wc                250
dn             C13  sc                  0
dof              0  vs                 78
dm             nnn  th                 26
decwave          g  ai   cdc  ph
dpwr            45
dmf          17094
```

Compound 43



```
IY-16-11 Inova 600

exp1  PROTON

      SAMPLE                SPECIAL
date   Jan 28 2006  temp             25.0
solvent      CDCl3  gain         not used
file /export/home/~ spin               22
kerr/vnmrsys/data/~ hst             0.008
IY-16-11_2006-01-2~ pw90           10.300
   8/PROTON_01.fid  alfa                0
   ACQUISITION              FLAGS
sw          9591.2  il                  n
at           1.892  in                  n
np           36294  dp                  y
fb            5000  hs                 nn
bs              32        PROCESSING
d1           1.000  fn           not used
nt               8          DISPLAY
ct               8  sp               -4.1
   TRANSMITTER      wp             4799.4
tn              H1  rfl            5546.4
sfrq       599.479  rfp            4352.2
tof          599.3  rp              -20.6
tpwr            57  lp              -27.1
pw           5.150           PLOT
    DECOUPLER       wc                250
dn             C13  sc                  0
dof              0  vs                 73
dm             nnn  th                  2
decwave          g  ai   cdc   ph
dpwr            45
dmf          17094
```

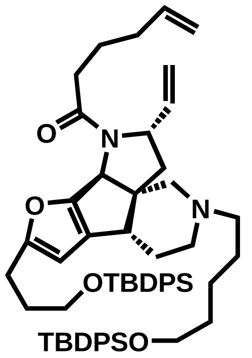
Compound 45

10:3 ratio of rotamers

```
IY-17-137c Inova 400

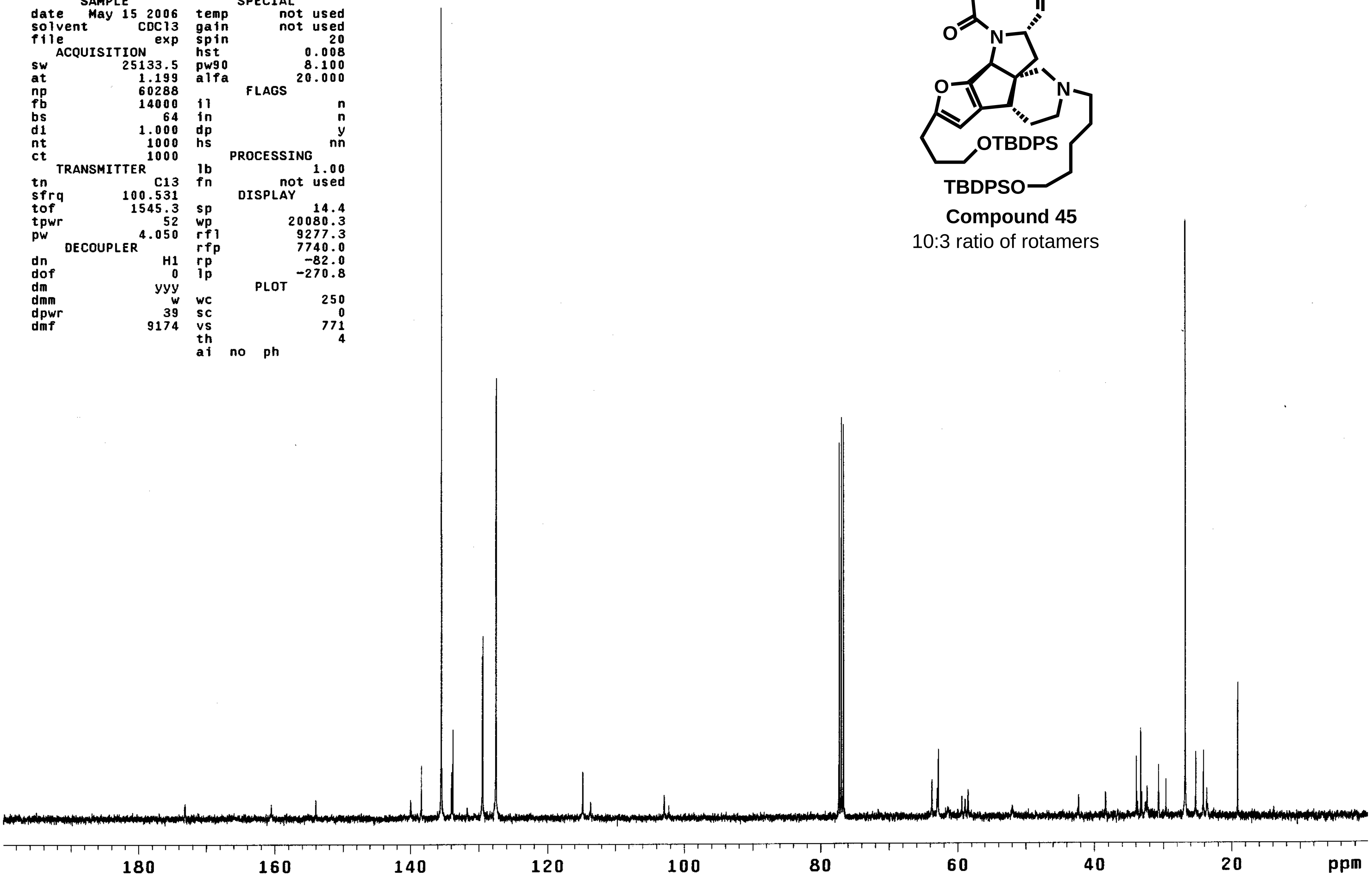
exp1  s2pul

      SAMPLE               SPECIAL
date   May 15 2006   temp       not used
solvent      CDCl3   gain       not used
file           exp   spin             20
   ACQUISITION       hst           0.008
sw         25133.5   pw90          8.100
at           1.199   alfa         20.000
np           60288            FLAGS
fb           14000   il                n
bs              64   in                n
d1           1.000   dp                y
nt            1000   hs               nn
ct            1000          PROCESSING
   TRANSMITTER       lb             1.00
tn             C13   fn         not used
sfrq       100.531           DISPLAY
tof         1545.3   sp             14.4
tpwr            52   wp          20080.3
pw           4.050   rfl          9277.3
    DECOUPLER        rfp          7740.0
dn              H1   rp            -82.0
dof              0   lp           -270.8
dm             yyy             PLOT
dmm              w   wc              250
dpwr            39   sc                0
dmf           9174   vs              771
                     th                4
                     ai  no  ph
```



Compound 45

10:3 ratio of rotamers

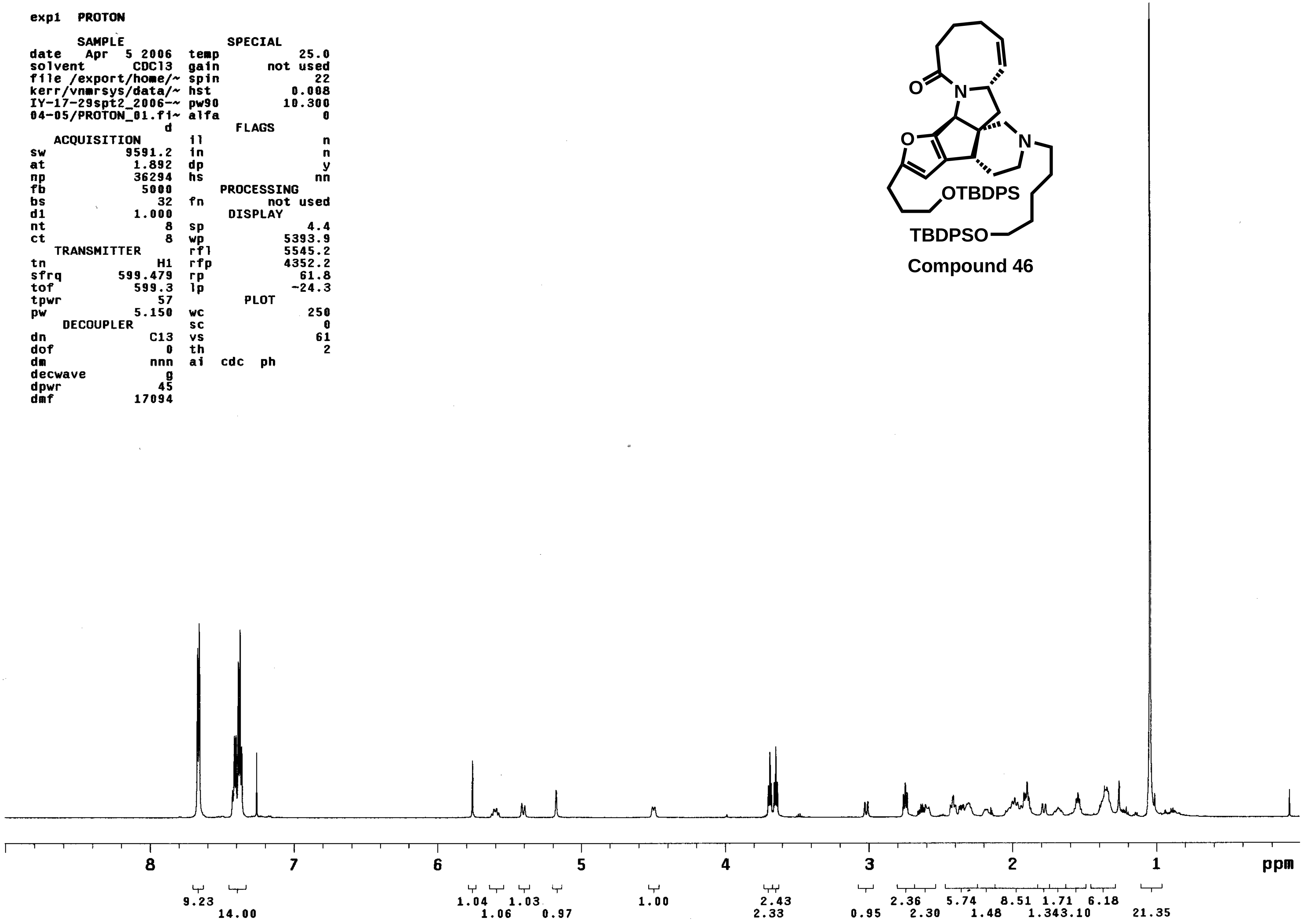


```
IY-17-29spt2 Inova 600

exp1  PROTON

      SAMPLE              SPECIAL
date    Apr  5 2006  temp           25.0
solvent       CDCl3  gain       not used
file /export/home/~  spin             22
kerr/vnmrsys/data/~  hst           0.008
IY-17-29spt2_2006-~  pw90         10.300
04-05/PROTON_01.fi~  alfa              0
                  d          FLAGS
   ACQUISITION       il                n
sw           9591.2  in                n
at            1.892  dp                y
np            36294  hs               nn
fb             5000         PROCESSING
bs               32  fn         not used
d1            1.000          DISPLAY
nt                8  sp              4.4
ct                8  wp           5393.9
   TRANSMITTER       rfl          5545.2
tn               H1  rfp          4352.2
sfrq        599.479  rp             61.8
tof           599.3  lp            -24.3
tpwr             57            PLOT
pw            5.150  wc              250
     DECOUPLER       sc                0
dn              C13  vs               61
dof               0  th                2
dm              nnn  ai   cdc  ph
decwave           g
dpwr             45
dmf           17094
```

Compound 46

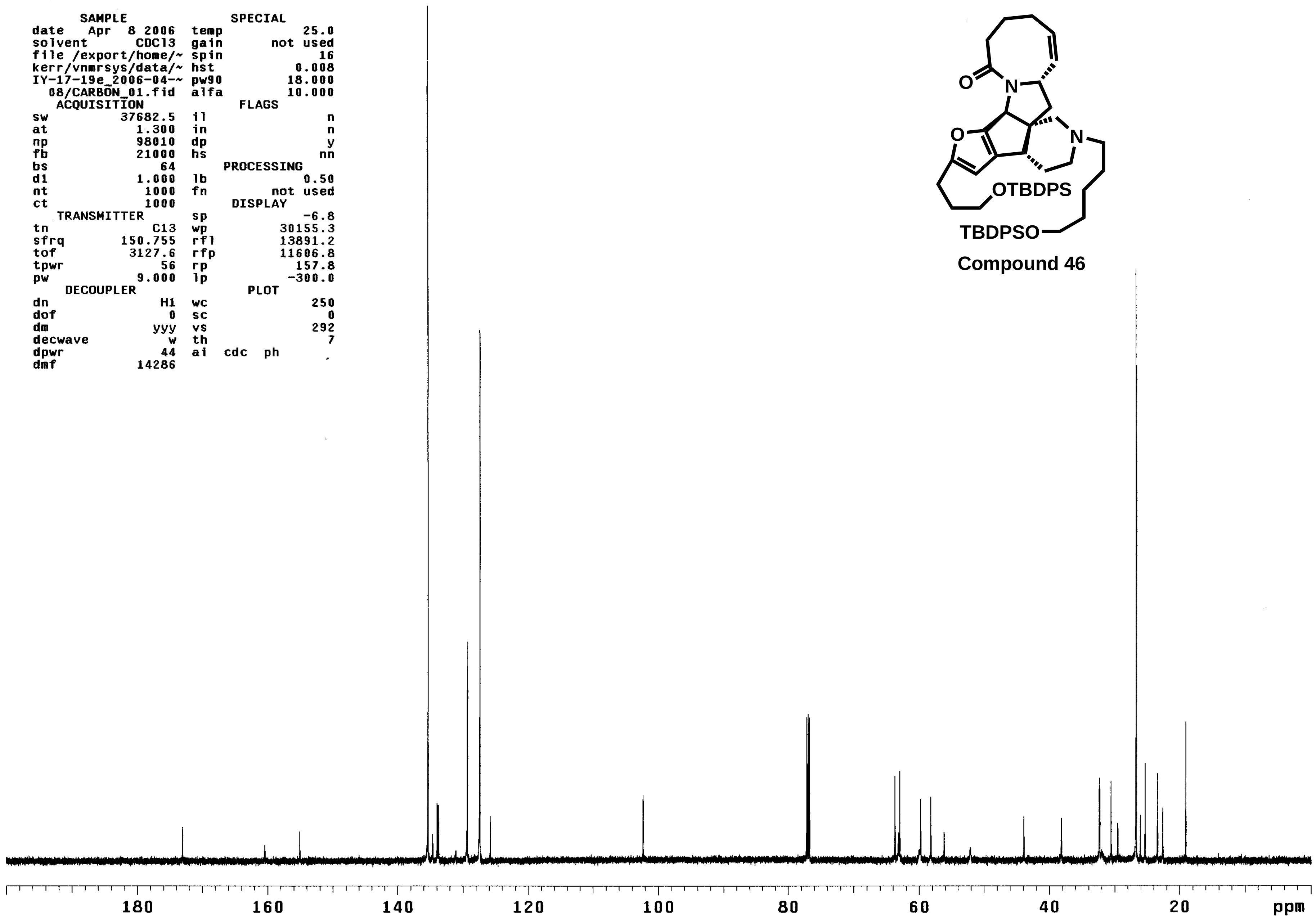


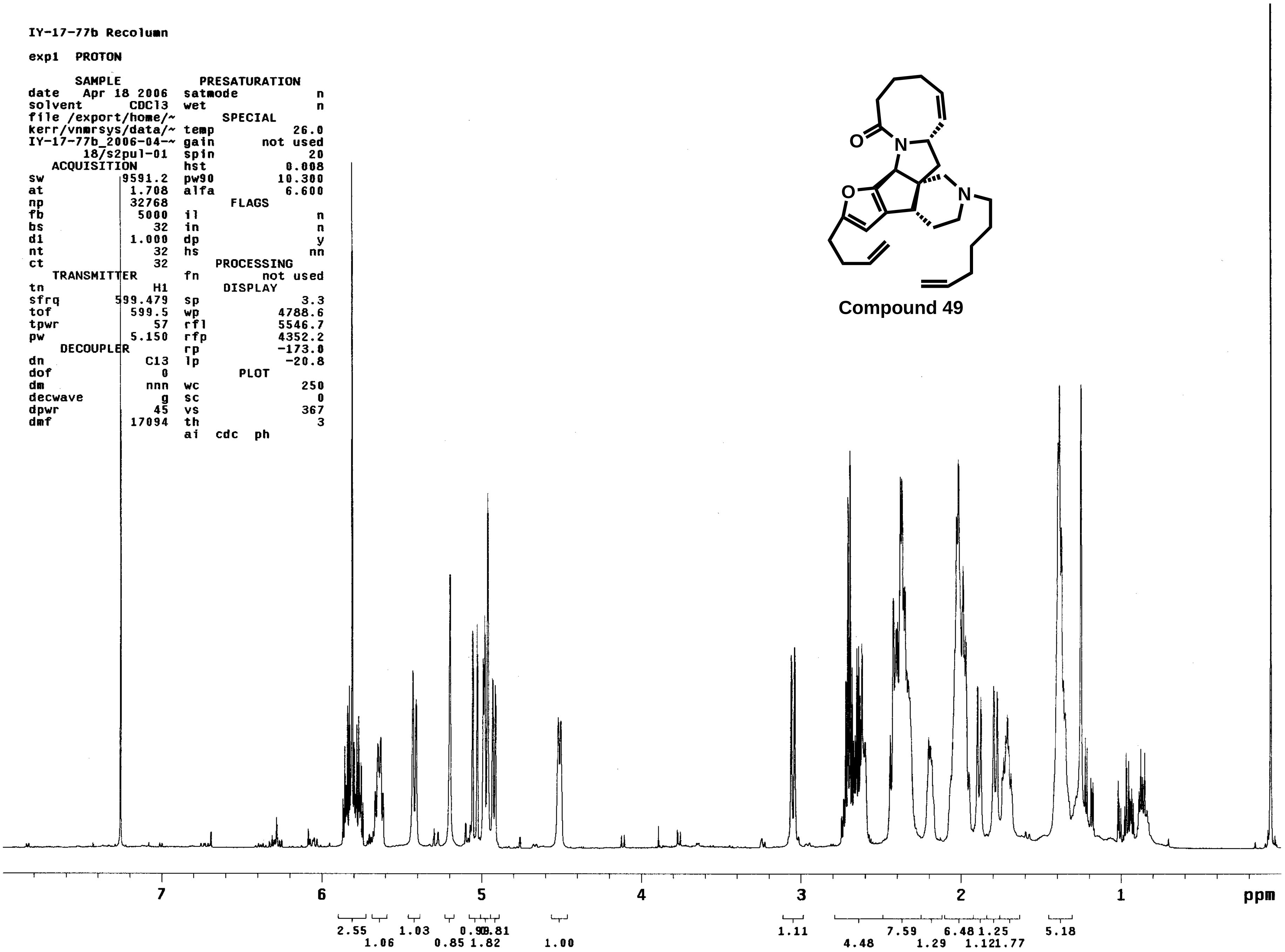
```
IY-17-19e Inova 600

exp1  CARBON

      SAMPLE              SPECIAL
date   Apr  8 2006  temp            25.0
solvent      CDCl3  gain        not used
file /export/home/~ spin              16
kerr/vnmrsys/data/~ hst            0.008
IY-17-19e_2006-04-~ pw90          18.000
  08/CARBON_01.fid  alfa          10.000
   ACQUISITION            FLAGS
sw         37682.5  il                 n
at           1.300  in                 n
np           98010  dp                 y
fb           21000  hs                nn
bs              64       PROCESSING
d1           1.000  lb              0.50
nt            1000  fn          not used
ct            1000        DISPLAY
   TRANSMITTER      sp              -6.8
tn             C13  wp           30155.3
sfrq       150.755  rfl          13891.2
tof         3127.6  rfp          11606.8
tpwr            56  rp             157.8
pw           9.000  lp            -300.0
    DECOUPLER              PLOT
dn              H1  wc               250
dof              0  sc                 0
dm             yyy  vs               292
decwave          w  th                 7
dpwr            44  ai   cdc  ph
dmf          14286
```

Compound 46



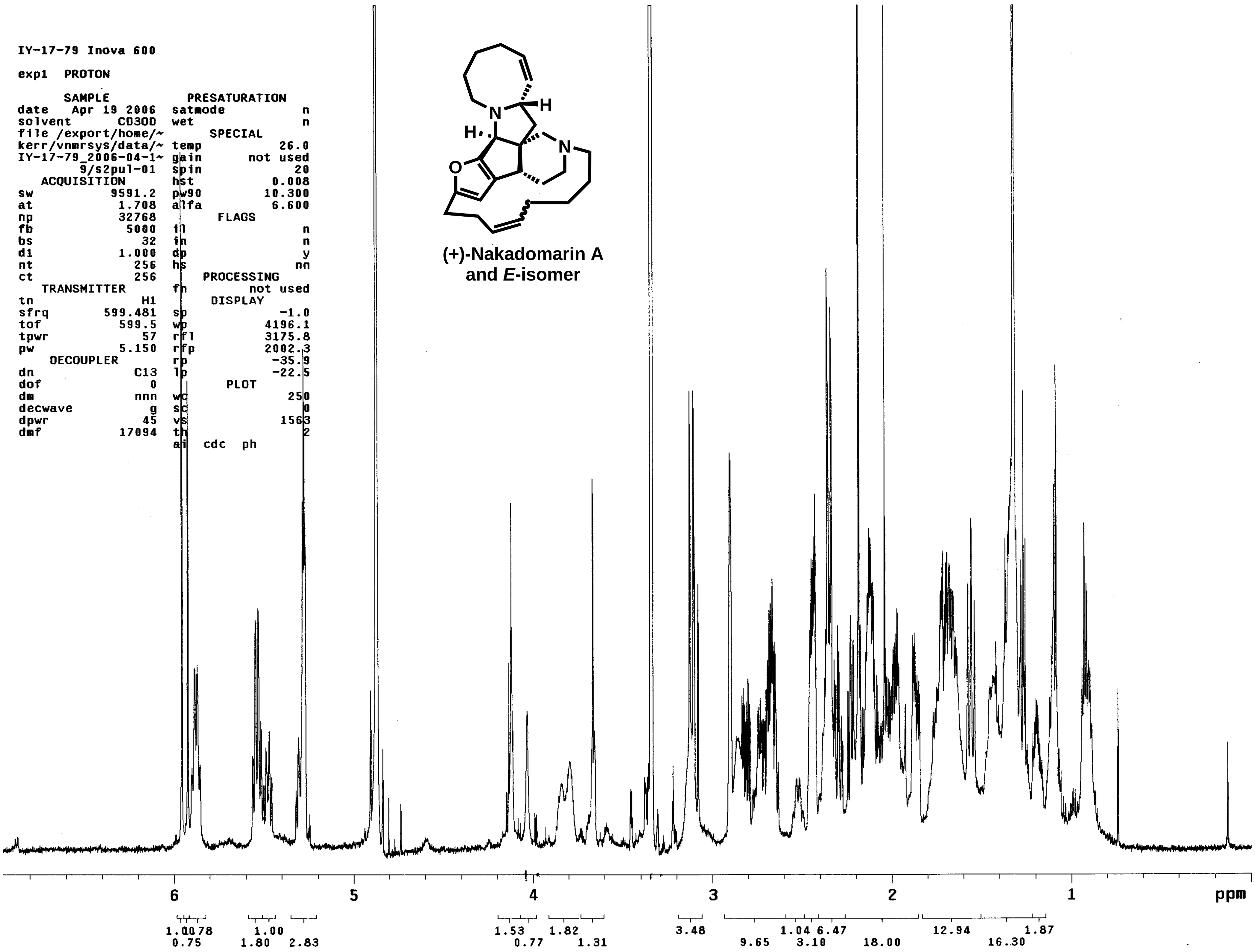


```
IY-17-77b Recolumn

exp1  PROTON

      SAMPLE               PRESATURATION
date    Apr 18 2006   satmode              n
solvent       CDCl3   wet                  n
file /export/home/~          SPECIAL
kerr/vnmrsys/data/~   temp              26.0
IY-17-77b_2006-04-~   gain          not used
     18/s2pul-01      spin                20
   ACQUISITION        hst              0.008
sw           9591.2   pw90            10.300
at            1.708   alfa             6.600
np            32768          FLAGS
fb             5000   il                   n
bs               32   in                   n
d1            1.000   dp                   y
nt               32   hs                  nn
ct               32       PROCESSING
   TRANSMITTER        fn            not used
tn               H1          DISPLAY
sfrq        599.479   sp                 3.3
tof           599.5   wp              4788.6
tpwr             57   rfl             5546.7
pw            5.150   rfp             4352.2
    DECOUPLER         rp              -173.0
dn              C13   lp               -20.8
dof               0          PLOT
dm              nnn   wc                 250
decwave           g   sc                   0
dpwr             45   vs                 367
dmf           17094   th                   3
                      ai   cdc   ph
```

Compound 49



```
IY-17-79 Inova 600

exp1  PROTON

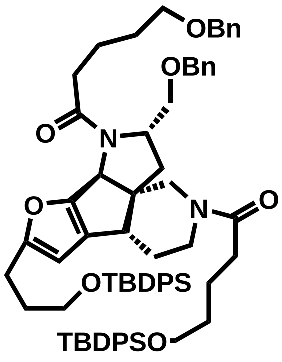
      SAMPLE                PRESATURATION
date    Apr 19 2006   satmode              n
solvent       CD3OD   wet                  n
file /export/home/~          SPECIAL
kerr/vnmrsys/data/~   temp              26.0
IY-17-79_2006-04-1~   gain          not used
         9/s2pul-01   spin                20
     ACQUISITION      hst              0.008
sw           9591.2   pw90            10.300
at            1.708   alfa             6.600
np            32768            FLAGS
fb             5000   il                   n
bs               32   in                   n
d1            1.000   dp                   y
nt              256   hs                  nn
ct              256        PROCESSING
     TRANSMITTER      fn            not used
tn               H1           DISPLAY
sfrq        599.481   sp                -1.0
tof           599.5   wp              4196.1
tpwr             57   rfl             3175.8
pw            5.150   rfp             2002.3
     DECOUPLER        rp               -35.9
dn              C13   lp               -22.5
dof               0            PLOT
dm              nnn   wc                 250
decwave           g   sc                   0
dpwr             45   vs                1563
dmf           17094   th                   2
                      ai    cdc   ph
```

(+)-Nakadomarin A and *E*-isomer

```
IY-bisamidespt2 Inova 600

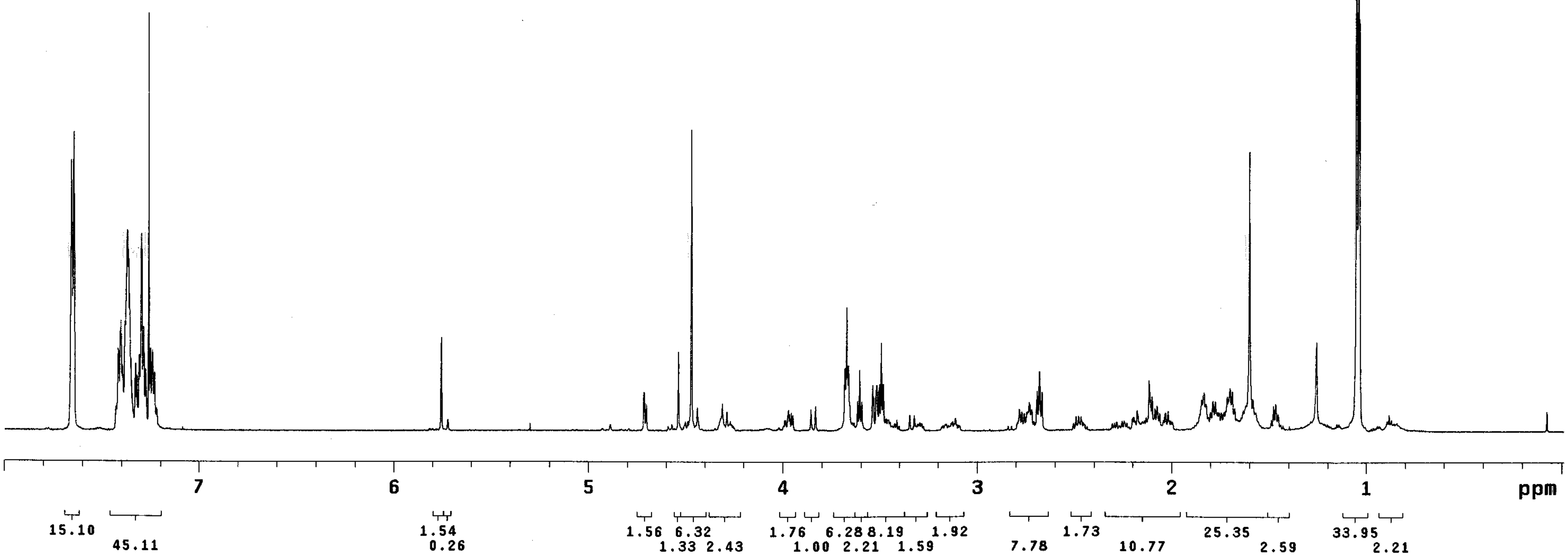
exp1  PROTON

      SAMPLE              PRESATURATION
date   Oct 24 2006   satmode            n
solvent       CDCl3   wet                n
file /export/home/~       SPECIAL
kerr/vnmrsys/data/~  temp       not used
IY-19-bisamidespt2~  gain       not used
_2006-10-24/s2pul-~  spin             20
             01.fid  hst           0.008
    ACQUISITION      pw90         10.300
sw           9591.2  alfa          6.600
at            1.708          FLAGS
np            32768  il                 n
fb             5000  in                 n
bs               32  dp                 y
d1            1.000  hs                nn
nt               32        PROCESSING
ct               32  fn         not used
    TRANSMITTER             DISPLAY
tn               H1  sp             -6.3
sfrq        599.454  wp           4801.4
tof           599.4  rfl          5543.1
tpwr             56  rfp          4352.0
pw            5.150  rp              4.4
     DECOUPLER       lp            -32.6
dn              C13          PLOT
dof               0  wc              250
dm              nnn  sc                0
decwave     W40_hcx  vs               82
dpwr             43  th                2
dmf           35088  ai   cdc   ph
```



Compound 53

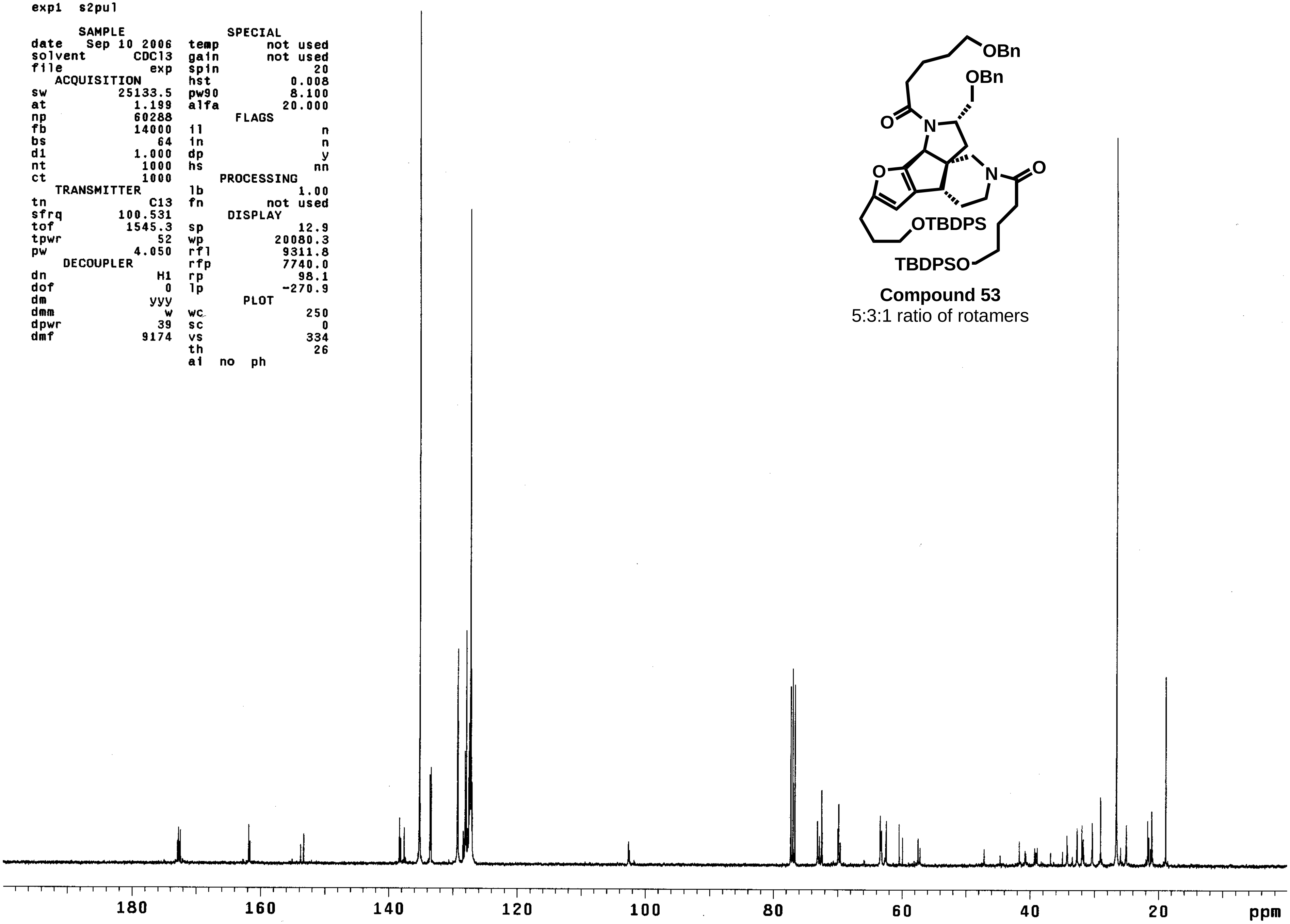
5:3:1 ratio of rotamers



```
IY-bisamidec Inova 400

exp1  s2pul

      SAMPLE                 SPECIAL
date   Sep 10 2006   temp       not used
solvent      CDCl3   gain       not used
file           exp   spin             20
   ACQUISITION       hst           0.008
sw         25133.5   pw90          8.100
at           1.199   alfa         20.000
np           60288          FLAGS
fb           14000   il                n
bs              64   in                n
d1           1.000   dp                y
nt            1000   hs               nn
ct            1000        PROCESSING
   TRANSMITTER       lb             1.00
tn             C13   fn         not used
sfrq       100.531         DISPLAY
tof         1545.3   sp             12.9
tpwr            52   wp          20080.3
pw           4.050   rfl          9311.8
   DECOUPLER         rfp          7740.0
dn              H1   rp             98.1
dof              0   lp           -270.9
dm             yyy           PLOT
dmm              w   wc              250
dpwr            39   sc                0
dmf           9174   vs              334
                     th               26
                     ai   no  ph
```



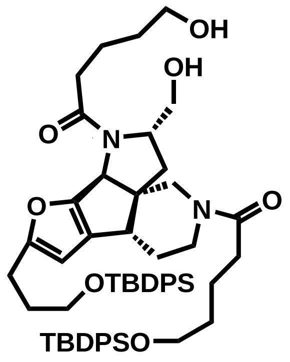
Compound 53

5:3:1 ratio of rotamers

```
IY-diolproton Inova 600

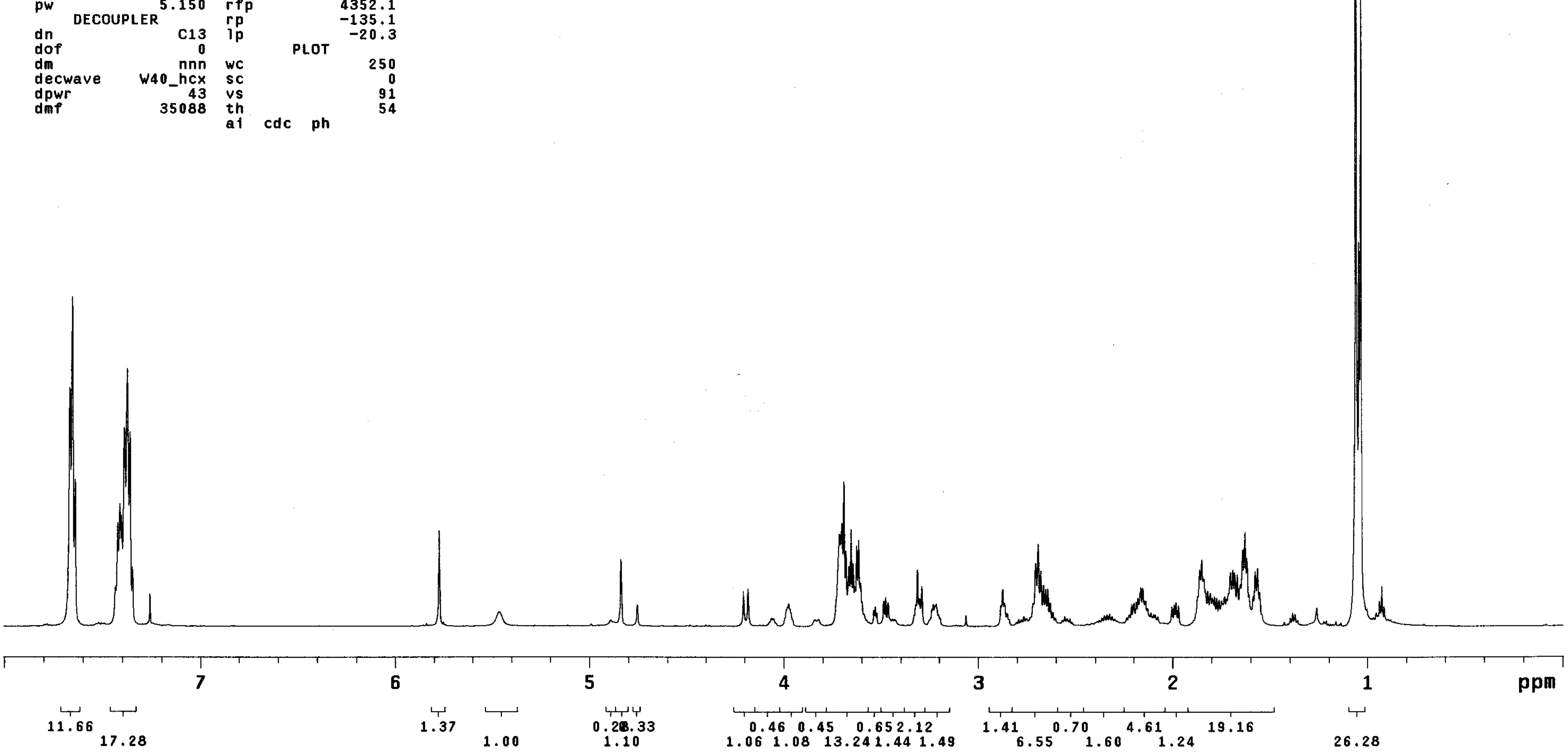
exp1  PROTON

      SAMPLE              PRESATURATION
date   Sep 10 2006   satmode           n
solvent      CDCl3   wet               n
file /export/home/~        SPECIAL
kerr/vnmrsys/data/~  temp           20.0
IY-diolproton_2006~  gain       not used
   -09-10/s2pul-01   spin             20
    ACQUISITION      hst           0.008
sw          9591.2   pw90         10.300
at           1.708   alfa          6.600
np           32768          FLAGS
fb            5000   il                n
bs              32   in                n
d1           1.000   dp                y
nt               8   hs               nn
ct               8        PROCESSING
    TRANSMITTER      fn         not used
tn              H1          DISPLAY
sfrq       599.463   sp             -1.5
tof          599.4   wp           4801.4
tpwr            56   rfl          5538.5
pw           5.150   rfp          4352.1
     DECOUPLER       rp           -135.1
dn             C13   lp            -20.3
dof              0           PLOT
dm             nnn   wc              250
decwave    W40_hcx   sc                0
dpwr            43   vs               91
dmf          35088   th               54
                     ai   cdc   ph
```



Compound 54

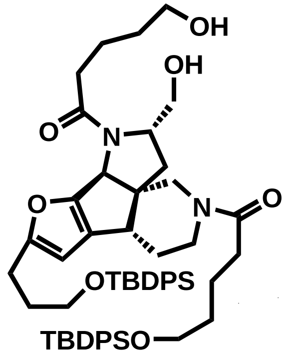
5:2 ratio of rotamers



```
IY-diol carbon Inova 600

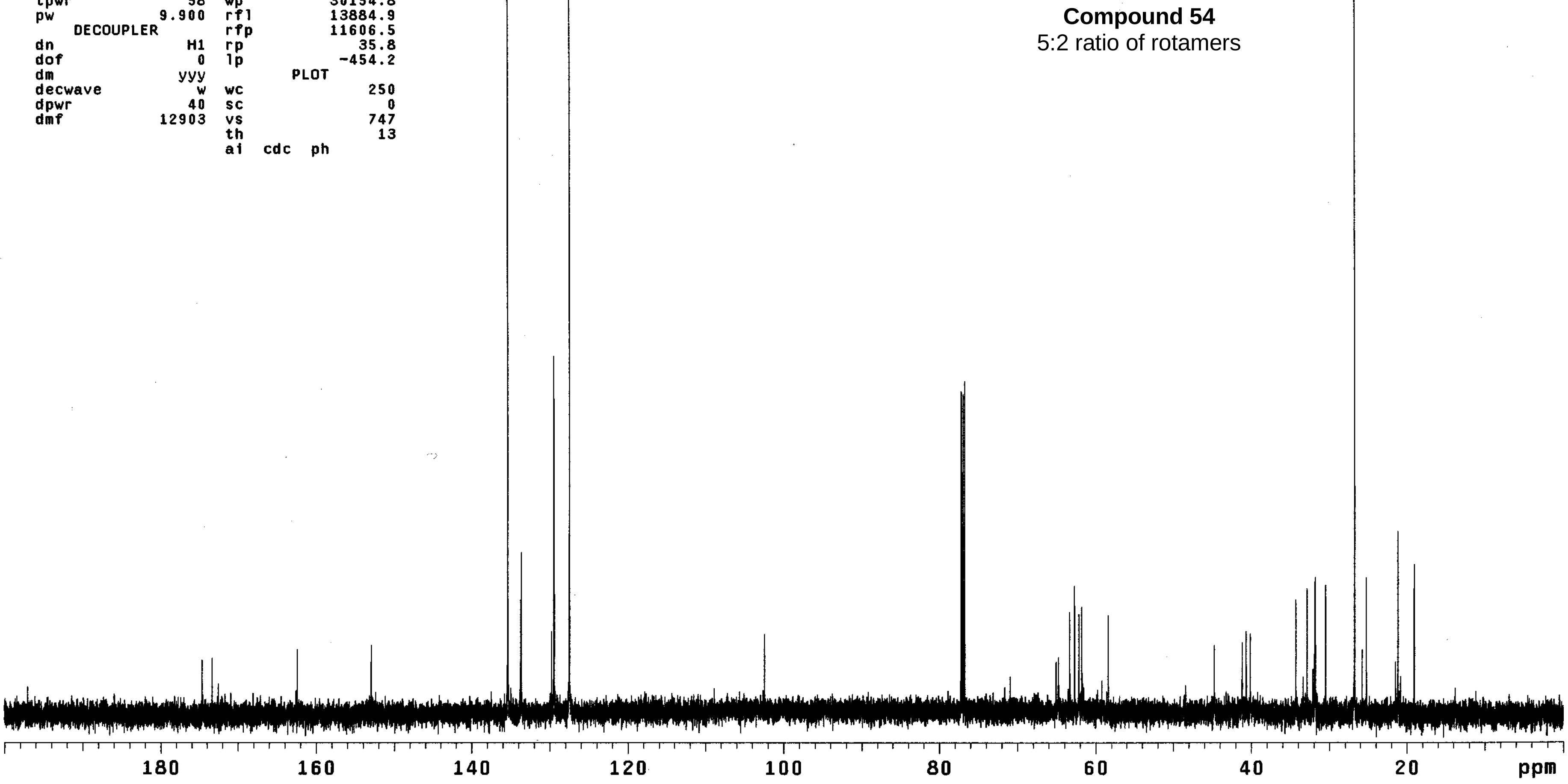
exp1  CARBON

      SAMPLE              PRESATURATION
date   Sep 10 2006   satmode           n
solvent       CDCl3  wet               n
file /export/home/~       SPECIAL
kerr/vnmrsys/data/~  temp           20.0
IY-diolcarbon_2006~  gain       not used
   -09-10/s2pul-01   spin             20
   ACQUISITION       hst           0.008
sw          37682.5  pw90         19.800
at            0.870  alfa         20.000
np            65536         FLAGS
fb            21000  il                n
bs               64  in                n
d1            1.000  dp                y
nt             1000  hs               nn
ct              384       PROCESSING
   TRANSMITTER       lb             0.50
tn              C13  fn         not used
sfrq        150.751         DISPLAY
tof          2295.2  sp             -0.2
tpwr             58  wp          30154.8
pw            9.900  rfl         13884.9
    DECOUPLER        rfp         11606.5
dn               H1  rp             35.8
dof               0  lp           -454.2
dm              yyy          PLOT
decwave           w  wc              250
dpwr             40  sc                0
dmf           12903  vs              747
                     th               13
                     ai  cdc  ph
```



Compound 54

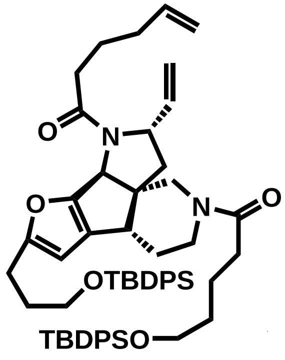
5:2 ratio of rotamers



```
IY-19-43 Inova 600

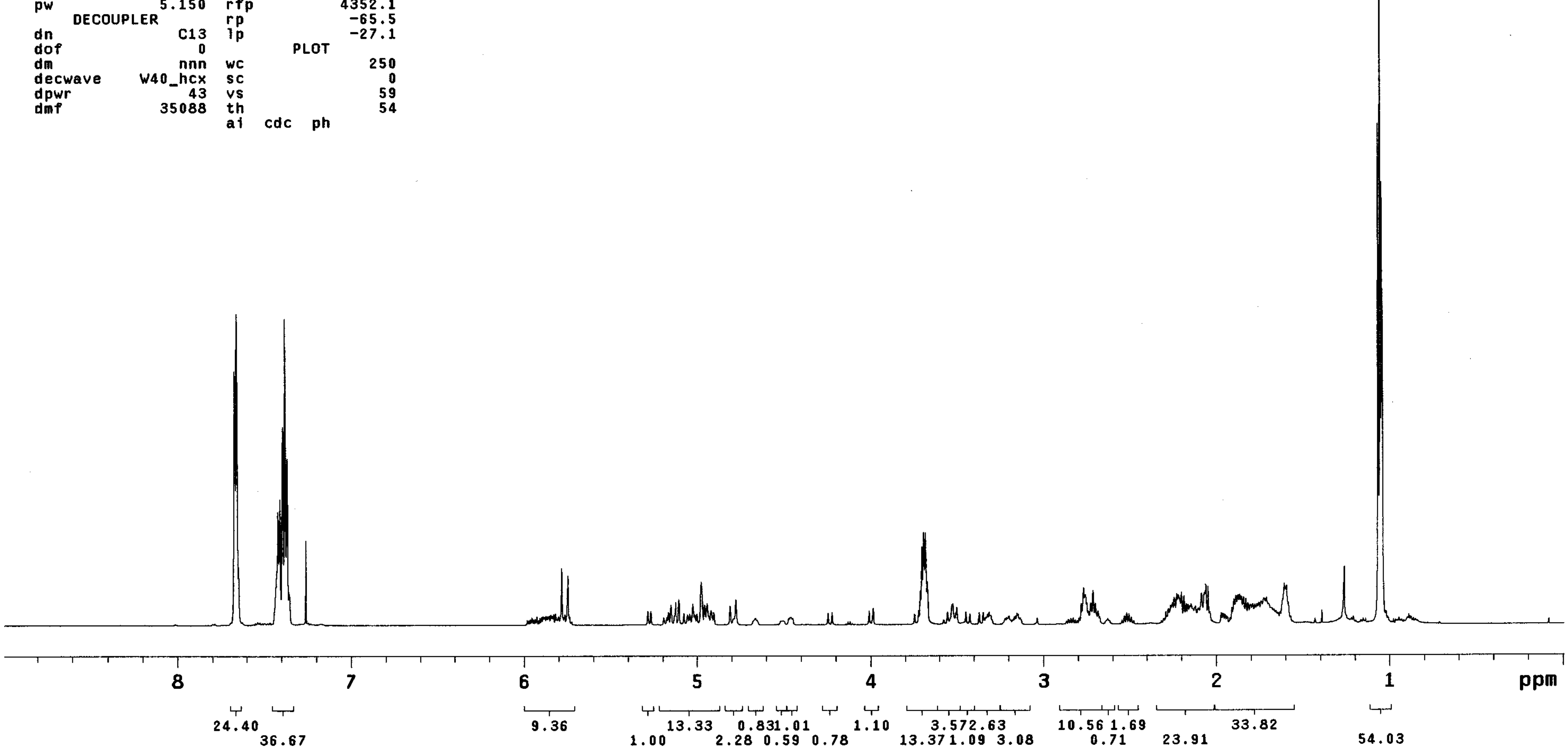
exp1  PROTON

      SAMPLE              PRESATURATION
date   Sep 28 2006   satmode              n
solvent        CDCl3   wet                  n
file /export/home/~        SPECIAL
kerr/vnmrsys/data/~   temp          not used
IY-19-43_2006-09-2~   gain          not used
   8/s2pul-01.fid     spin                20
   ACQUISITION        hst              0.008
sw            9591.2   pw90            10.300
at             1.708   alfa             6.600
np             32768           FLAGS
fb              5000   il                   n
bs                32   in                   n
d1             1.000   dp                   y
nt                16   hs                  nn
ct                16          PROCESSING
   TRANSMITTER         fn            not used
tn                H1            DISPLAY
sfrq         599.463   sp                -3.3
tof            599.4   wp              5393.9
tpwr              56   rfl             5540.2
pw             5.150   rfp             4352.1
    DECOUPLER          rp               -65.5
dn               C13   lp               -27.1
dof                0             PLOT
dm               nnn   wc                 250
decwave     W40_hcx   sc                   0
dpwr              43   vs                  59
dmf            35088   th                  54
                       ai   cdc   ph
```



Compound 56

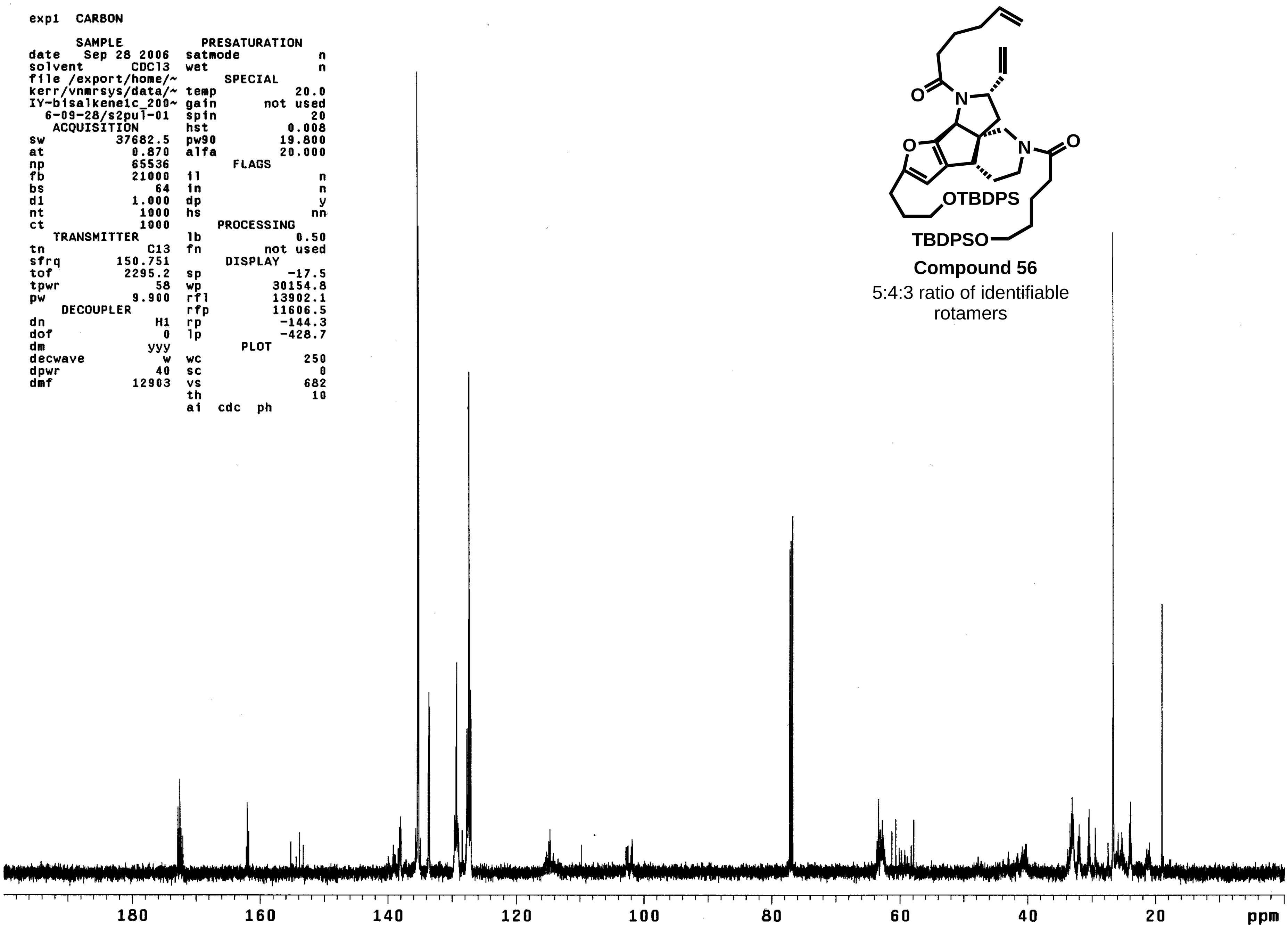
5:4:3 ratio of identifiable rotamers



```
IY-bisalkene1 Inova 600 carbon

exp1  CARBON

      SAMPLE              PRESATURATION
date   Sep 28 2006   satmode            n
solvent      CDCl3   wet                n
file /export/home/~       SPECIAL
kerr/vnmrsys/data/~  temp            20.0
IY-bisalkene1c_200~  gain        not used
  6-09-28/s2pul-01   spin              20
    ACQUISITION      hst            0.008
sw         37682.5   pw90          19.800
at           0.870   alfa          20.000
np           65536          FLAGS
fb           21000   il                 n
bs              64   in                 n
d1           1.000   dp                 y
nt            1000   hs                nn
ct            1000        PROCESSING
   TRANSMITTER       lb              0.50
tn             C13   fn          not used
sfrq       150.751         DISPLAY
tof         2295.2   sp             -17.5
tpwr            58   wp           30154.8
pw           9.900   rfl          13902.1
    DECOUPLER        rfp          11606.5
dn              H1   rp            -144.3
dof              0   lp            -428.7
dm             yyy           PLOT
decwave          w   wc               250
dpwr            40   sc                 0
dmf          12903   vs               682
                     th                10
                     ai  cdc  ph
```



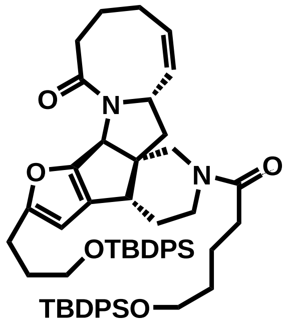
Compound 56

5:4:3 ratio of identifiable rotamers

```
IY-19-47spt2 Inova 600

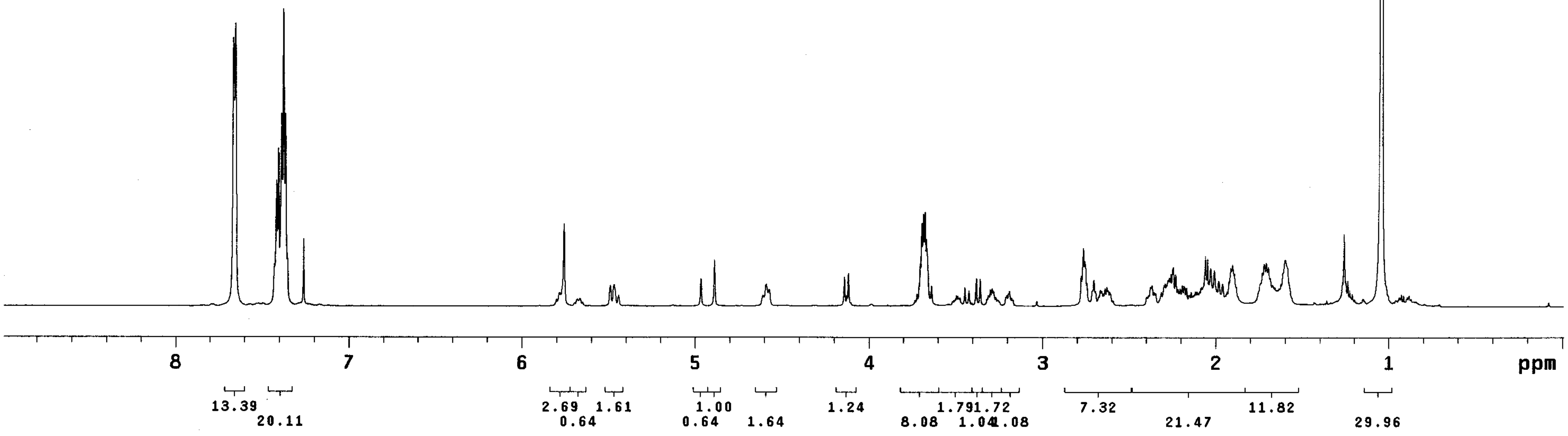
exp1  PROTON

       SAMPLE              PRESATURATION
date   Sep 29 2006   satmode              n
solvent       CDCl3  wet                  n
file /export/home/~         SPECIAL
kerr/vnmrsys/data/~  temp              20.0
IY-19-47spt2_2006-~  gain          not used
    09-29/s2pul-01   spin                20
   ACQUISITION       hst              0.008
sw           9591.2  pw90            10.300
at            1.708  alfa             6.600
np            32768          FLAGS
fb             5000  il                   n
bs               32  in                   n
d1            1.000  dp                   y
nt               32  hs                  nn
ct               32        PROCESSING
   TRANSMITTER       fn            not used
tn               H1          DISPLAY
sfrq        599.463  sp                -3.3
tof           599.4  wp              5393.9
tpwr             56  rfl             5540.2
pw            5.150  rfp             4352.1
    DECOUPLER        rp               -72.7
dn              C13  lp               -26.6
dof               0          PLOT
dm              nnn  wc                 250
decwave     W40_hcx  sc                   0
dpwr             43  vs                  93
dmf           35088  th                  54
                     ai   cdc   ph
```



Compound 57

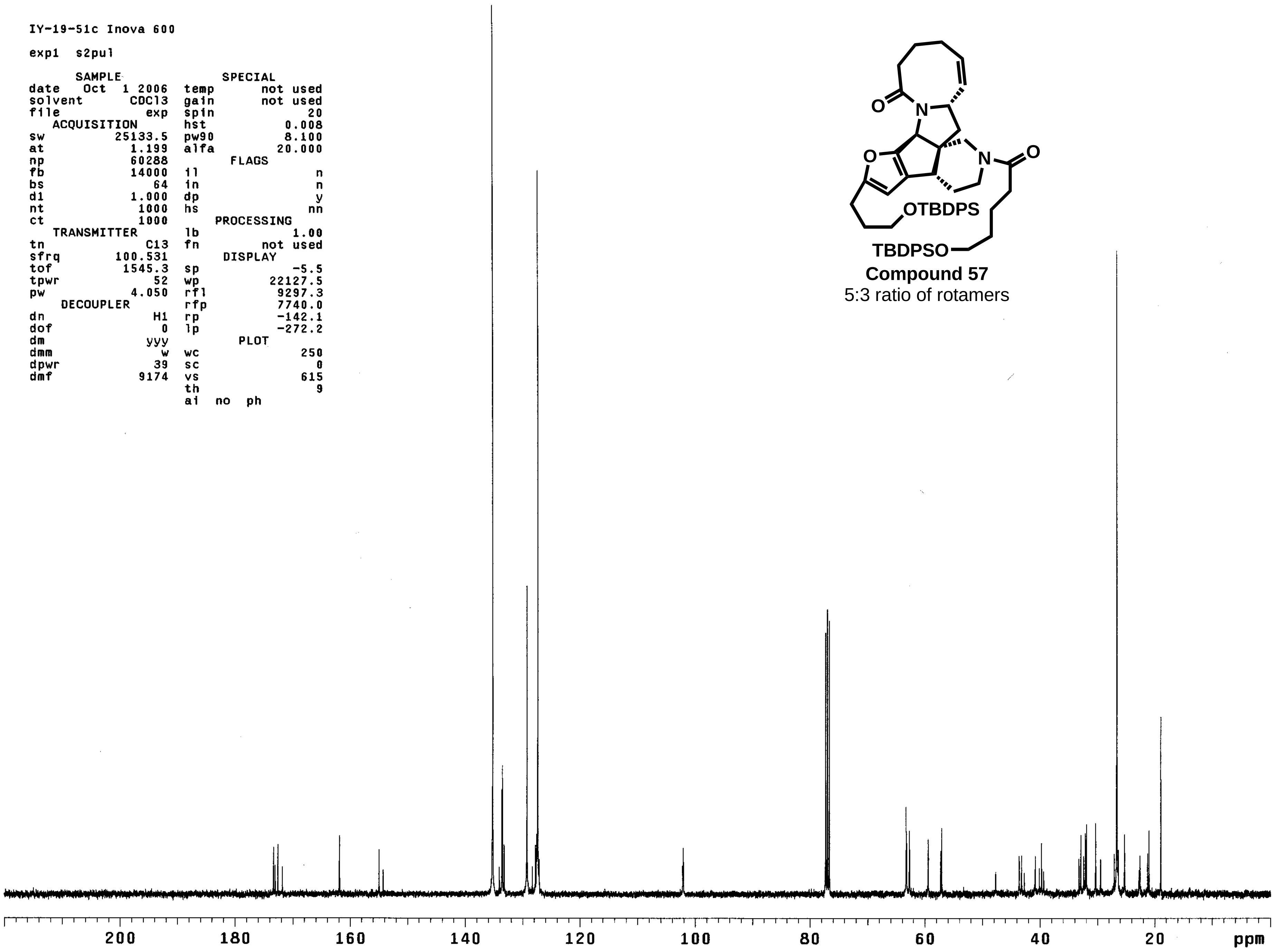
5:3 ratio of rotamers



```
IY-19-51c Inova 600

exp1  s2pul

      SAMPLE              SPECIAL
date   Oct  1 2006   temp       not used
solvent       CDCl3  gain       not used
file            exp  spin             20
   ACQUISITION       hst           0.008
sw          25133.5  pw90          8.100
at            1.199  alfa         20.000
np            60288           FLAGS
fb            14000  il                n
bs               64  in                n
d1            1.000  dp                y
nt             1000  hs               nn
ct             1000        PROCESSING
   TRANSMITTER       lb             1.00
tn              C13  fn         not used
sfrq        100.531         DISPLAY
tof          1545.3  sp             -5.5
tpwr             52  wp          22127.5
pw            4.050  rfl          9297.3
    DECOUPLER        rfp          7740.0
dn               H1  rp           -142.1
dof               0  lp           -272.2
dm              yyy           PLOT
dmm               w  wc              250
dpwr             39  sc                0
dmf            9174  vs              615
                     th                9
                     ai   no  ph
```



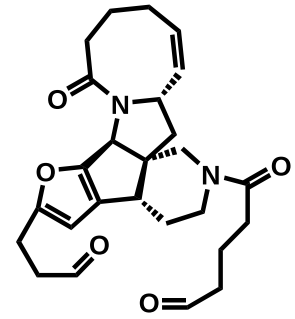
Compound 57

5:3 ratio of rotamers

```
IY-aldehyde2 proton Inova 600

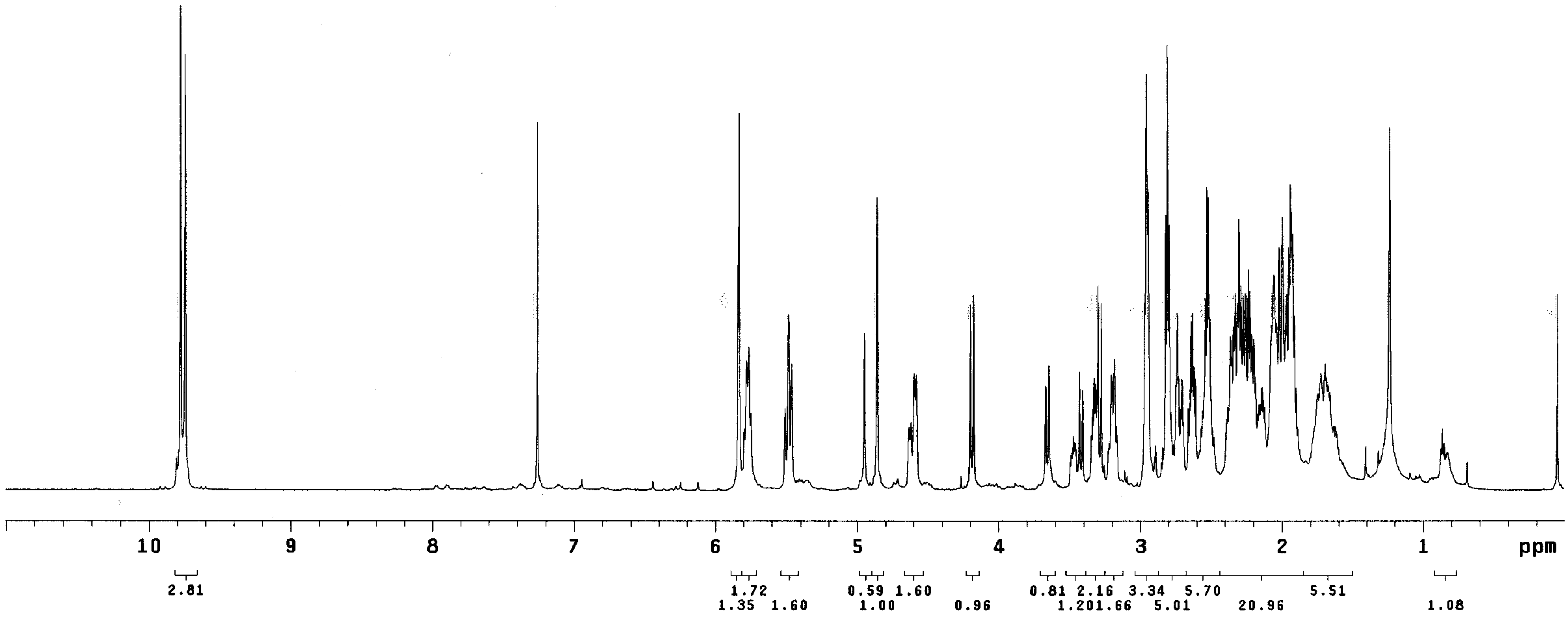
exp1  PROTON

      SAMPLE              PRESATURATION
date   Oct 23 2006  satmode             n
solvent      CDCl3  wet                 n
file /export/home/~       SPECIAL
kerr/vnmrsys/data/~ temp         not used
IY-aldp2_2006-10-2~ gain         not used
       3/s2pul-01   spin               20
   ACQUISITION      hst             0.008
sw          9591.2  pw90           10.300
at           1.708  alfa            6.600
np           32768         FLAGS
fb            5000  il                  n
bs              32  in                  n
d1           1.000  dp                  y
nt              64  hs                 nn
ct              64       PROCESSING
   TRANSMITTER      fn           not used
tn              H1         DISPLAY
sfrq       599.454  sp                6.0
tof          599.4  wp             6591.0
tpwr            56  rfl            5543.7
pw           5.150  rfp            4352.0
    DECOUPLER       rp              142.6
dn             C13  lp              -22.5
dof              0           PLOT
dm             nnn  wc                250
decwave    W40_hcx  sc                  0
dpwr            43  vs                295
dmf          35088  th                  2
                    ai  cdc  ph
```



Compound 59

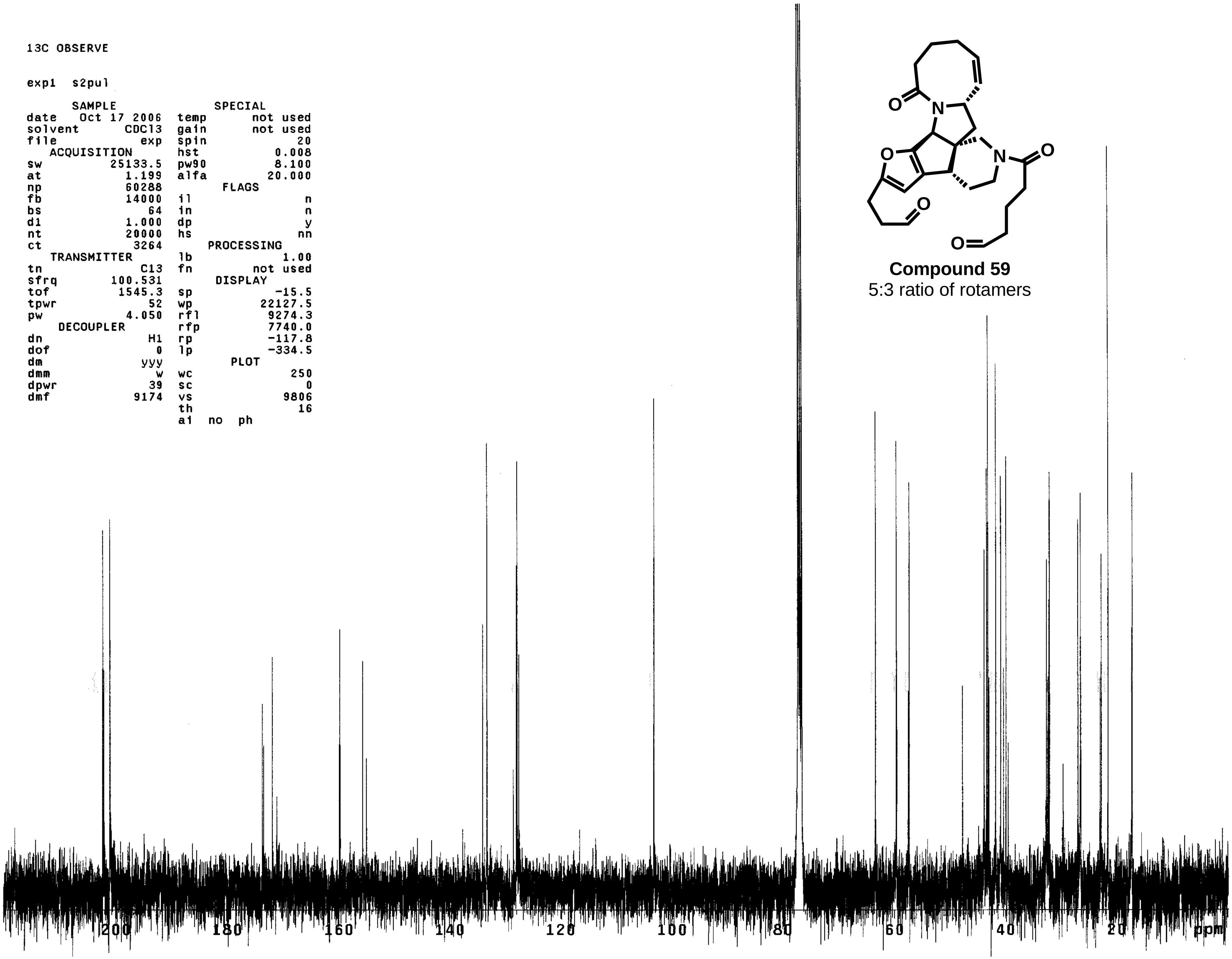
5:3 ratio of rotamers



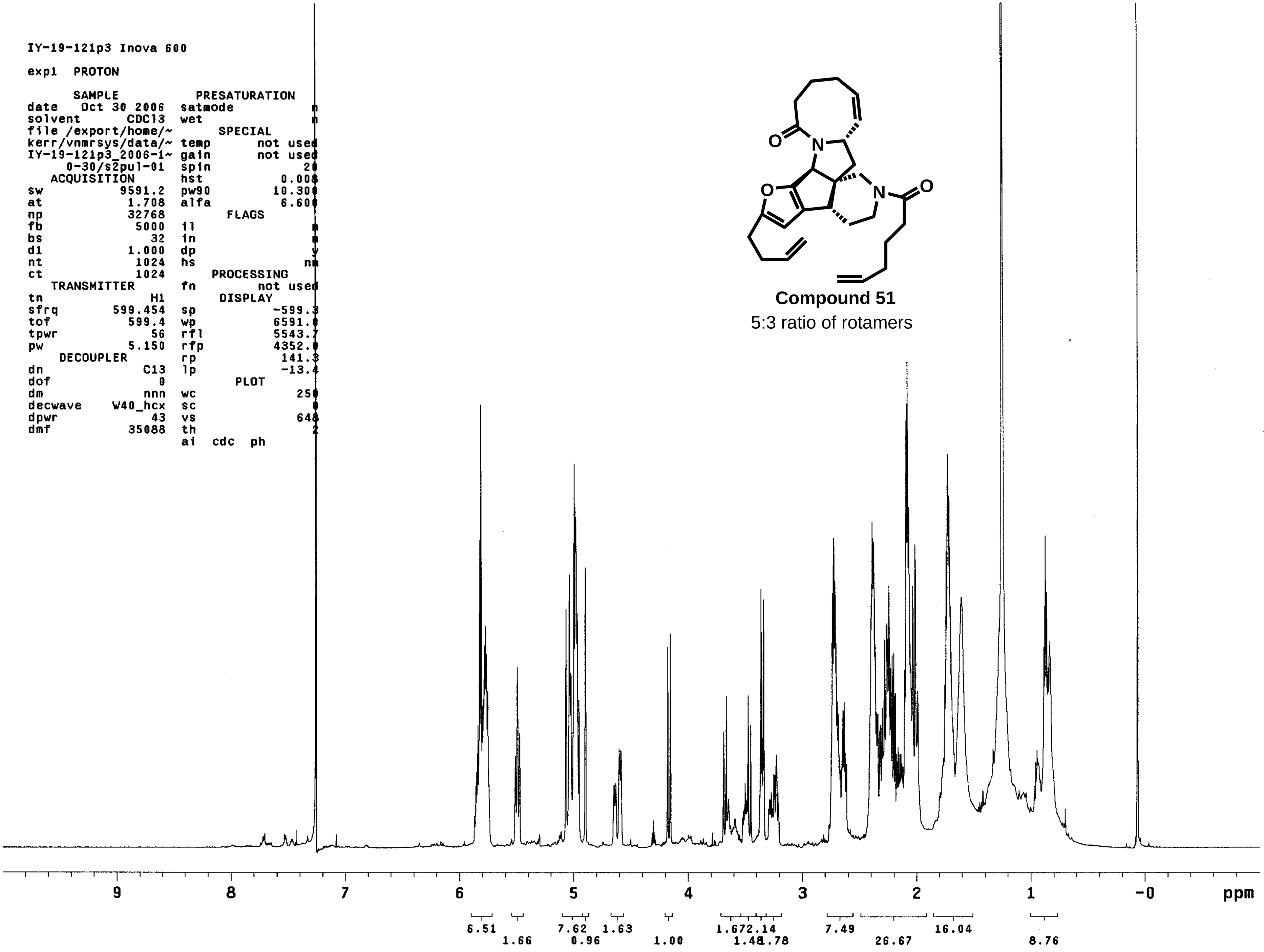
```
13C OBSERVE

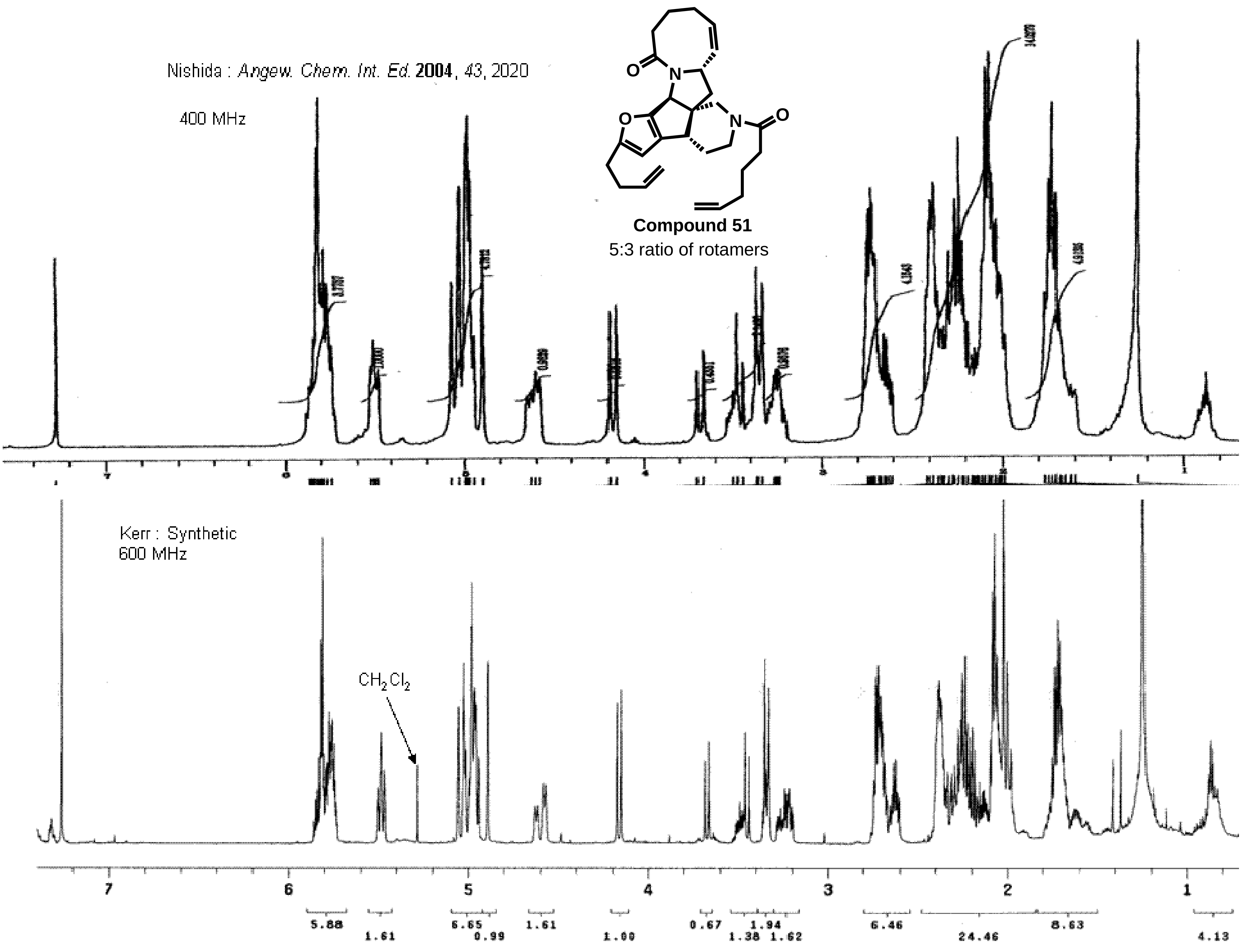
exp1  s2pul

      SAMPLE               SPECIAL
date   Oct 17 2006  temp      not used
solvent      CDCl3  gain      not used
file           exp  spin            20
   ACQUISITION      hst          0.008
sw         25133.5  pw90         8.100
at           1.199  alfa        20.000
np           60288         FLAGS
fb           14000  il               n
bs              64  in               n
d1           1.000  dp               y
nt           20000  hs              nn
ct            3264       PROCESSING
   TRANSMITTER      lb            1.00
tn             C13  fn        not used
sfrq       100.531         DISPLAY
tof         1545.3  sp           -15.5
tpwr            52  wp         22127.5
pw           4.050  rfl         9274.3
    DECOUPLER       rfp         7740.0
dn              H1  rp          -117.8
dof              0  lp          -334.5
dm             yyy           PLOT
dmm              w  wc             250
dpwr            39  sc               0
dmf           9174  vs            9806
                    th              16
                    ai  no   ph
```



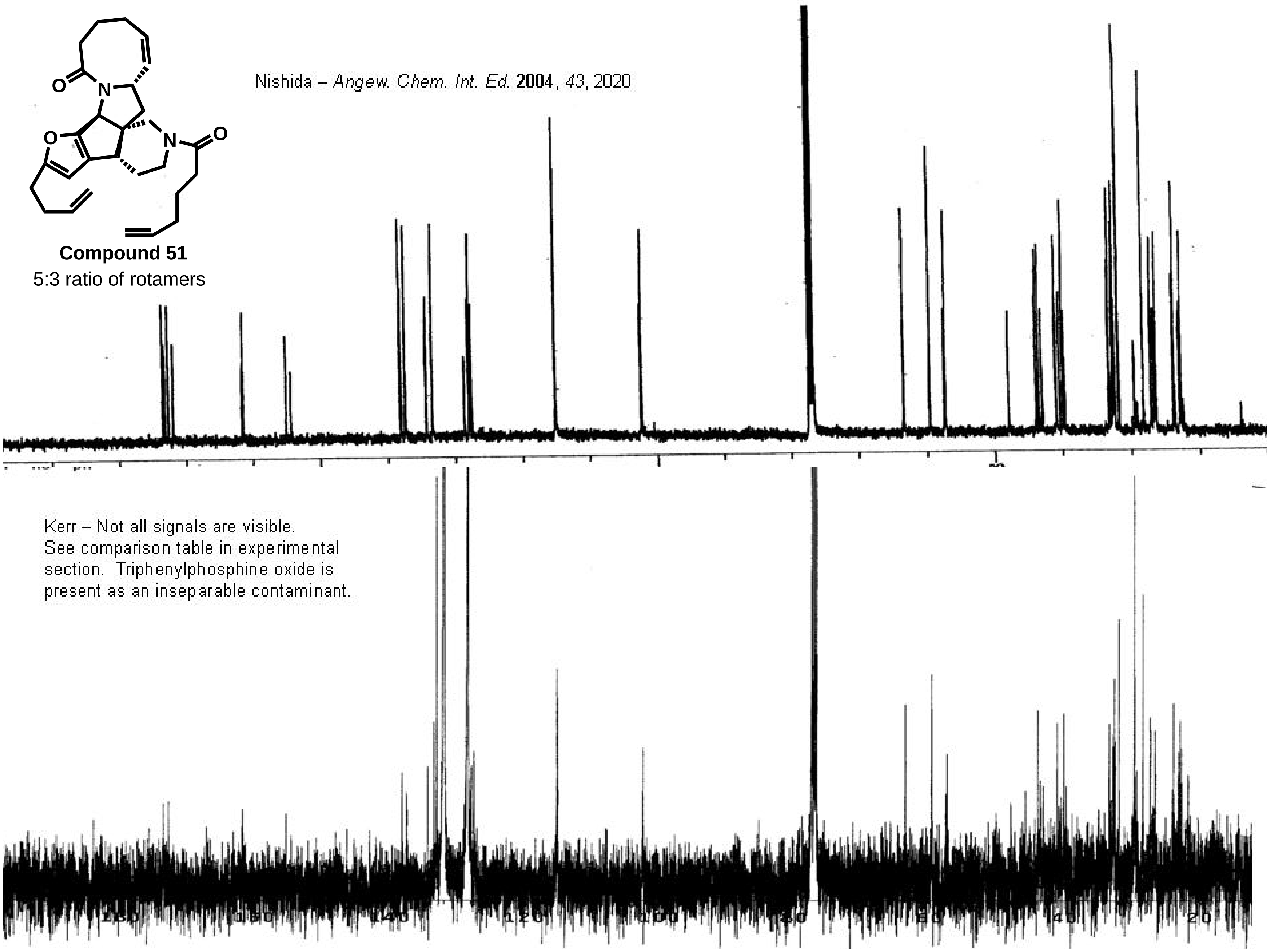
Compound 59
5:3 ratio of rotamers





Compound 51

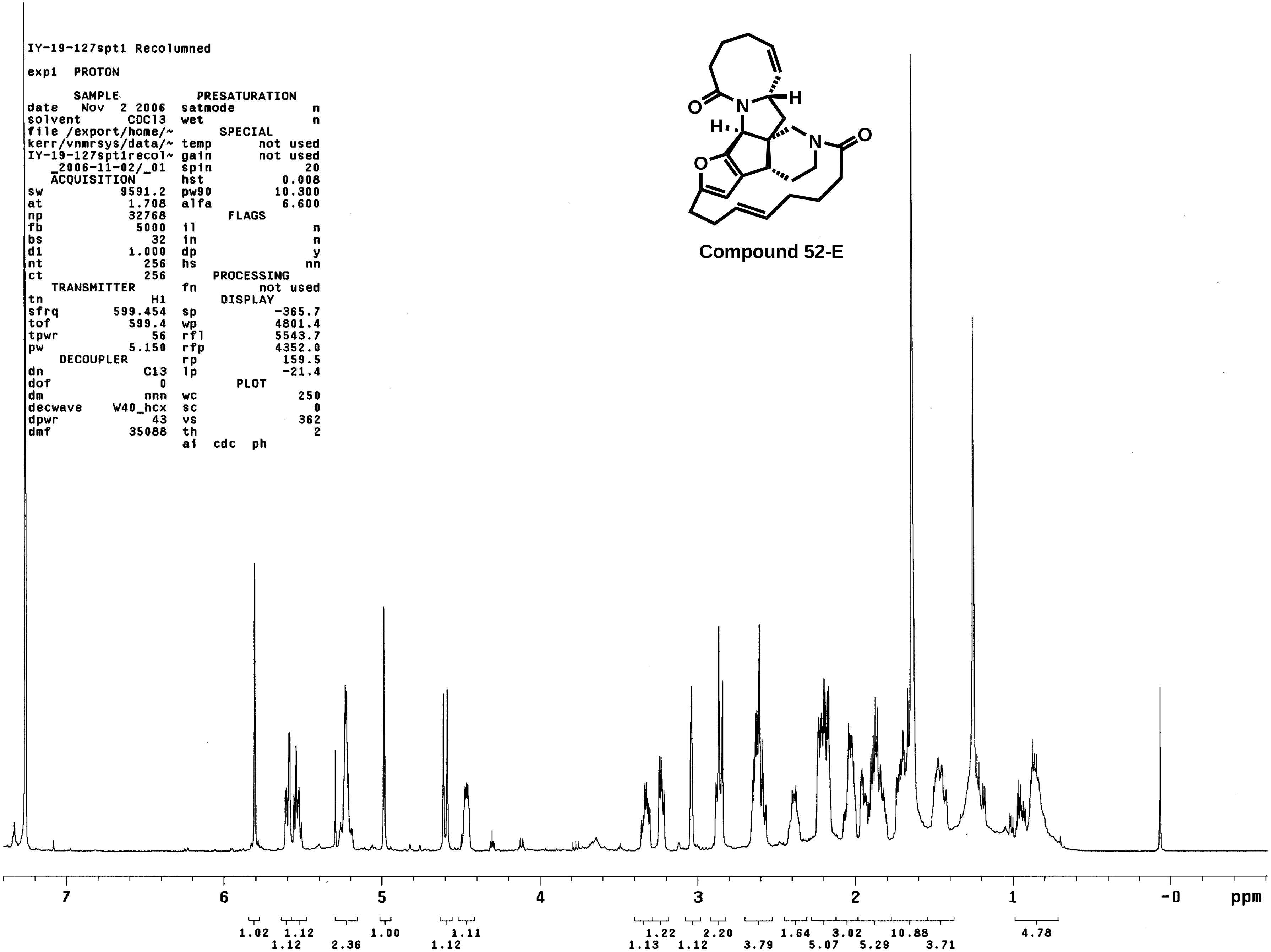
5:3 ratio of rotamers



Compound 51
5:3 ratio of rotamers

Nishida – *Angew. Chem. Int. Ed.* **2004**, *43*, 2020

Kerr – Not all signals are visible.
See comparison table in experimental section. Triphenylphosphine oxide is present as an inseparable contaminant.



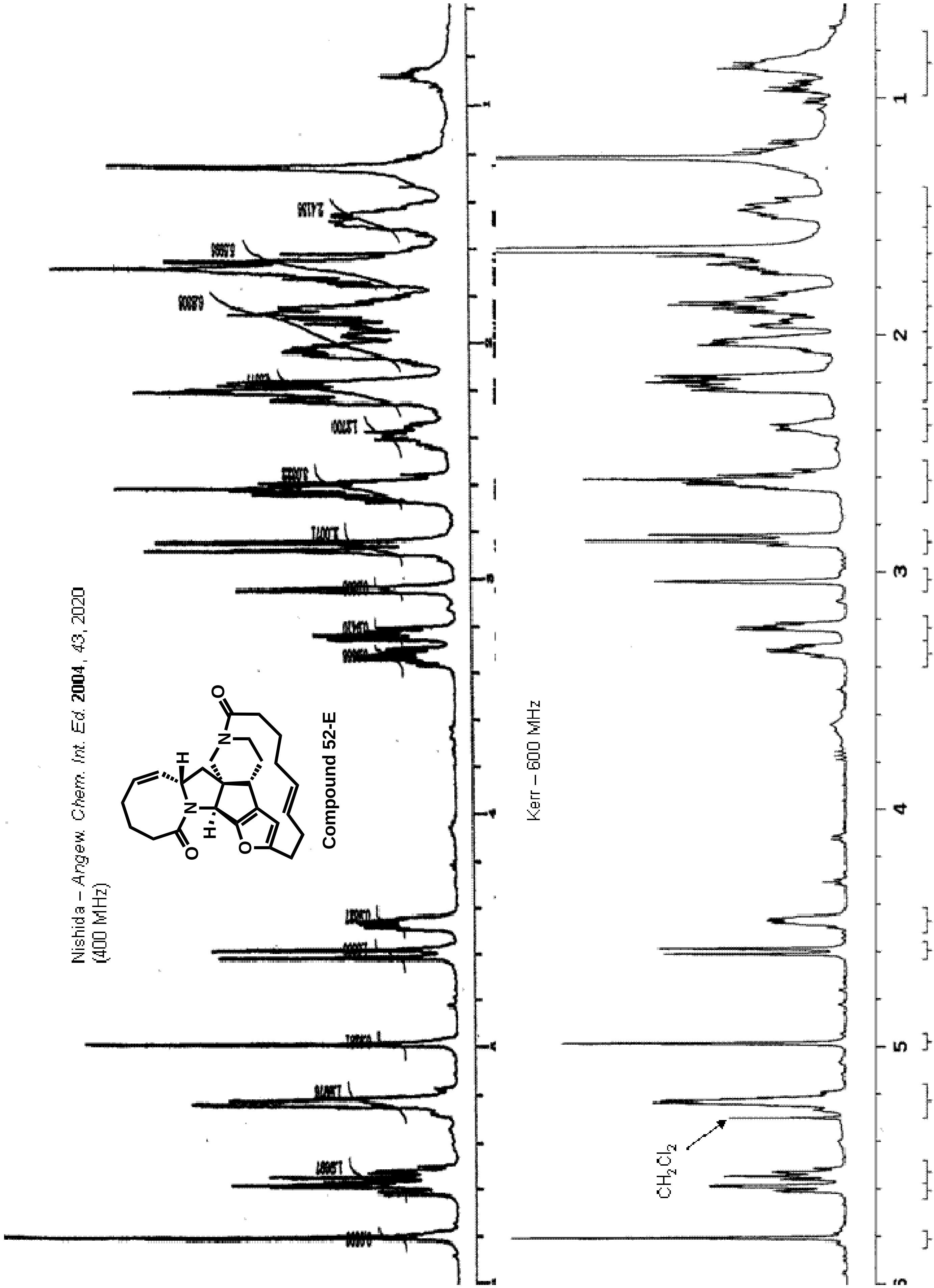
```
IY-19-127spt1 Recolumned

exp1  PROTON

      SAMPLE               PRESATURATION
date   Nov  2 2006  satmode             n
solvent      CDCl3  wet                 n
file /export/home/~        SPECIAL
kerr/vnmrsys/data/~ temp         not used
IY-19-127spt1recol~ gain         not used
   _2006-11-02/_01  spin               20
   ACQUISITION      hst             0.008
sw          9591.2  pw90           10.300
at           1.708  alfa            6.600
np           32768          FLAGS
fb            5000  il                  n
bs              32  in                  n
d1           1.000  dp                  y
nt             256  hs                 nn
ct             256       PROCESSING
   TRANSMITTER      fn           not used
tn              H1         DISPLAY
sfrq       599.454  sp             -365.7
tof          599.4  wp             4801.4
tpwr            56  rfl            5543.7
pw           5.150  rfp            4352.0
     DECOUPLER      rp              159.5
dn             C13  lp              -21.4
dof              0            PLOT
dm             nnn  wc                250
decwave    W40_hcx  sc                  0
dpwr            43  vs                362
dmf          35088  th                  2
                    ai   cdc  ph
```

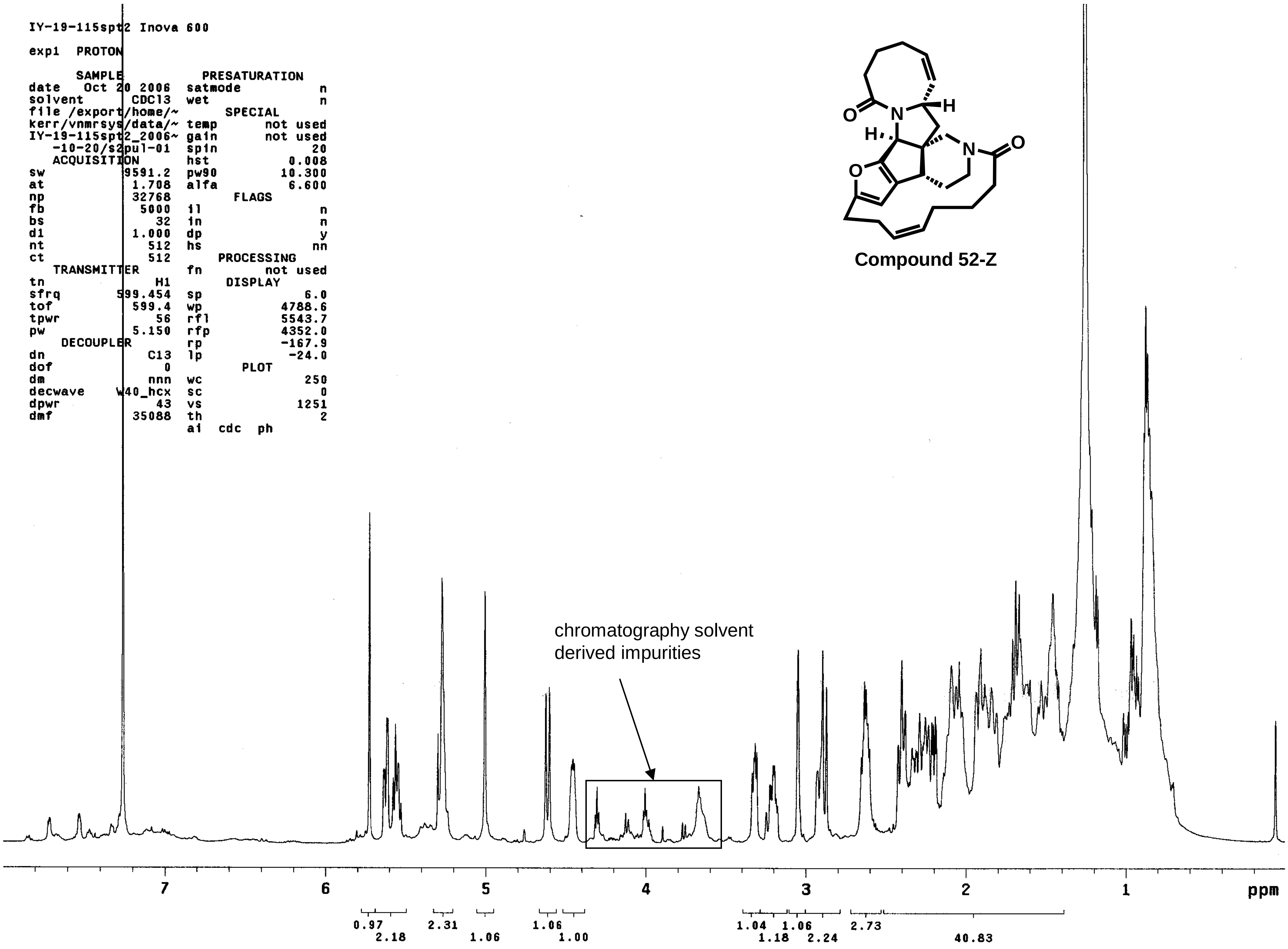
Compound 52-E

Nishida – *Angew. Chem. Int. Ed.* **2004**, 43, 2020
(400 MHz)



Compound 52-E

Kerr – 600 MHz



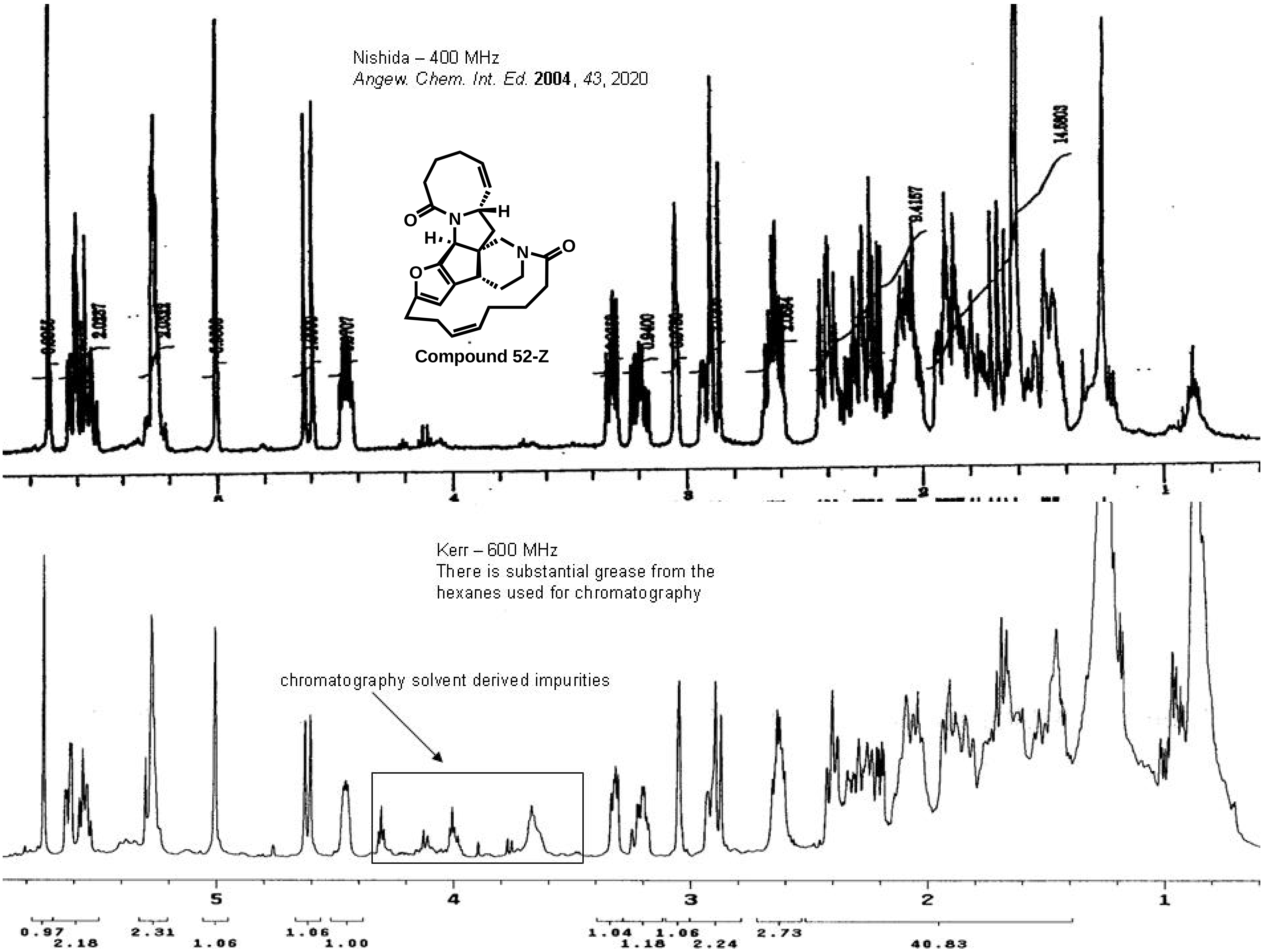
```
IY-19-115spt2 Inova 600

exp1  PROTON

       SAMPLE           PRESATURATION
date   Oct 20 2006   satmode            n
solvent       CDCl3   wet                n
file /export/home/~      SPECIAL
kerr/vnmrsys/data/~  temp        not used
IY-19-115spt2_2006~  gain        not used
   -10-20/s2pul-01   spin              20
    ACQUISITION      hst            0.008
sw           9591.2  pw90          10.300
at            1.708  alfa           6.600
np            32768         FLAGS
fb             5000  il                 n
bs               32  in                 n
d1            1.000  dp                 y
nt              512  hs                nn
ct              512        PROCESSING
    TRANSMITTER      fn          not used
tn               H1        DISPLAY
sfrq        599.454  sp               6.0
tof           599.4  wp            4788.6
tpwr             56  rfl           5543.7
pw            5.150  rfp           4352.0
     DECOUPLER       rp            -167.9
dn              C13  lp             -24.0
dof               0          PLOT
dm              nnn  wc               250
decwave     W40_hcx  sc                 0
dpwr             43  vs              1251
dmf           35088  th                 2
                     ai  cdc  ph
```

Compound 52-Z

chromatography solvent derived impurities


Nishida – 400 MHz
Angew. Chem. Int. Ed. **2004**, *43*, 2020

Compound 52-Z

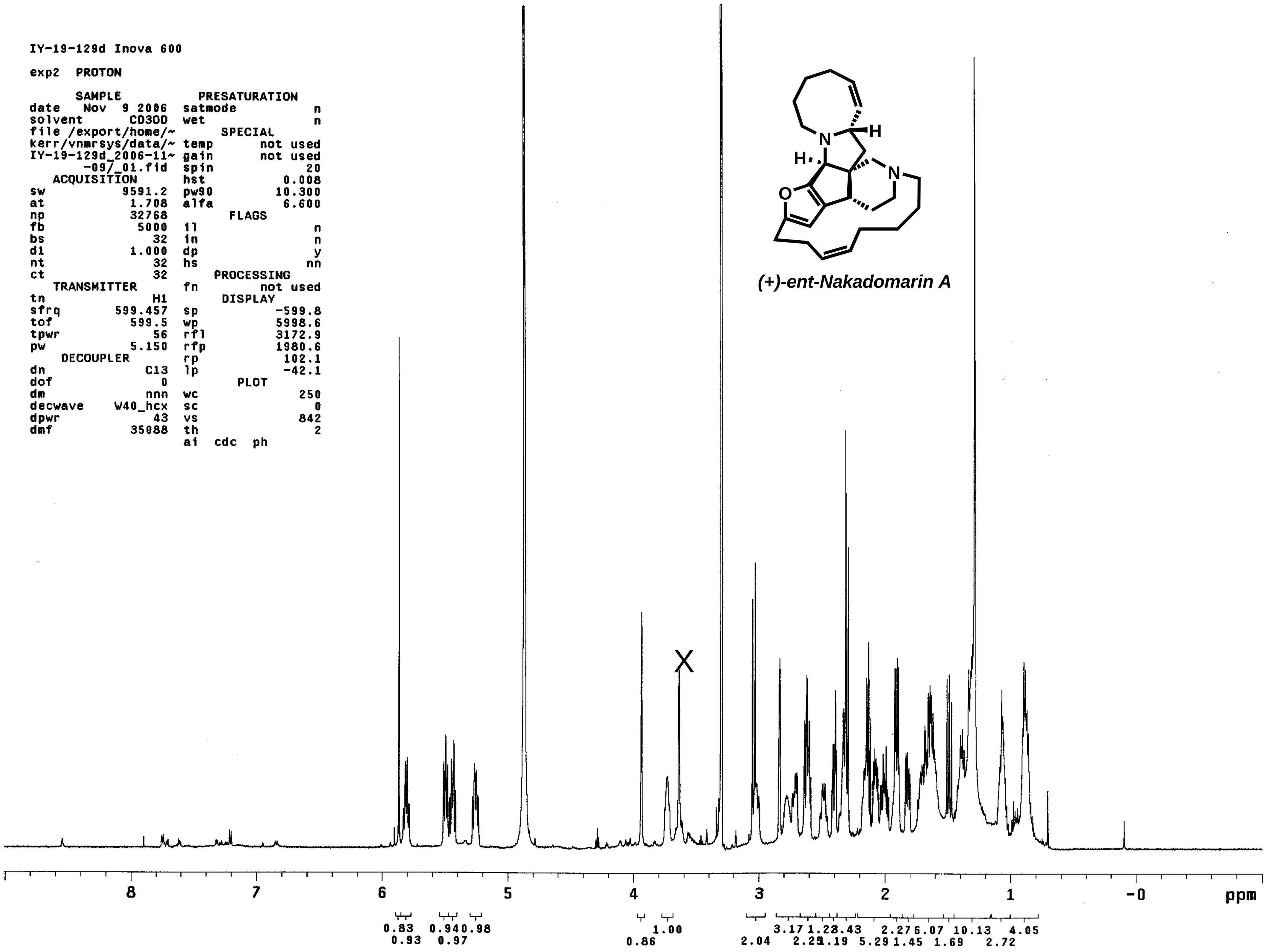
Kerr – 600 MHz
There is substantial grease from the hexanes used for chromatography

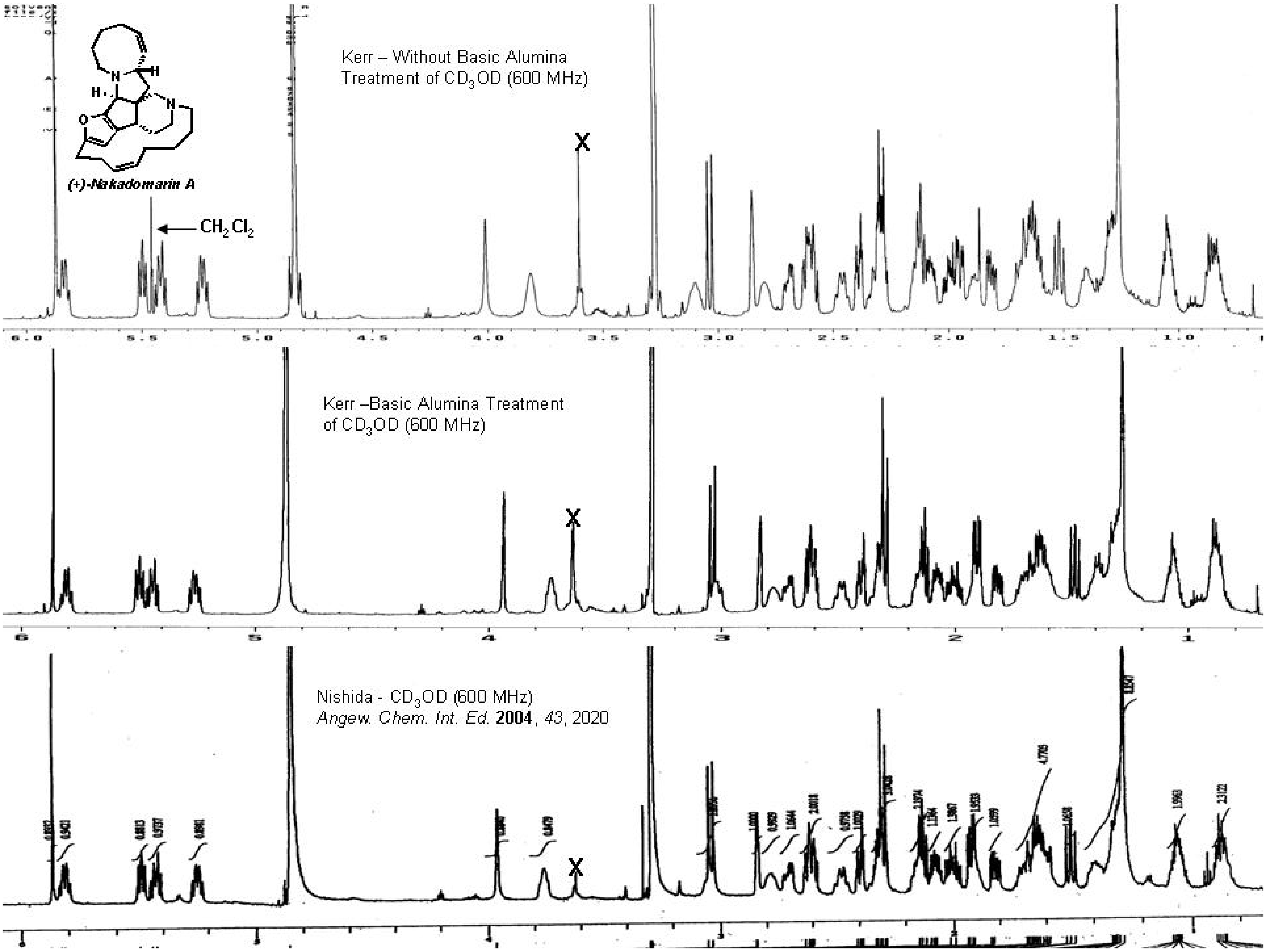
chromatography solvent derived impurities

```
IY-19-129d Inova 600

exp2  PROTON

      SAMPLE               PRESATURATION
date   Nov  9 2006   satmode            n
solvent      CD3OD   wet                n
file /export/home/~        SPECIAL
kerr/vnmrsys/data/~  temp       not used
IY-19-129d_2006-11~  gain       not used
     -09/_01.fid     spin             20
   ACQUISITION       hst           0.008
sw          9591.2   pw90         10.300
at           1.708   alfa          6.600
np           32768          FLAGS
fb            5000   il                n
bs              32   in                n
d1           1.000   dp                y
nt              32   hs               nn
ct              32        PROCESSING
   TRANSMITTER       fn         not used
tn              H1         DISPLAY
sfrq       599.457   sp           -599.8
tof          599.5   wp           5998.6
tpwr            56   rfl          3172.9
pw           5.150   rfp          1980.6
    DECOUPLER        rp            102.1
dn             C13   lp            -42.1
dof              0          PLOT
dm             nnn   wc              250
decwave    W40_hcx   sc                0
dpwr            43   vs              842
dmf          35088   th                2
                     ai   cdc   ph
```



(+)-Nakadomarin A
CH2Cl2
Kerr – Without Basic Alumina Treatment of CD3OD (600 MHz)
X
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Kerr –Basic Alumina Treatment of CD3OD (600 MHz)
X
6
5
4
3
2
1
Nishida - CD3OD (600 MHz)
Angew. Chem. Int. Ed. 2004, 43, 2020
X