Supporting Information

Thermodynamic and Structural Effects of Macrocyclic Constraints in Protein-Ligand Interactions

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MATERIALS AND EXPERIMENTAL METHODS

General for Synthetic Experiments. Solvents and reagents were reagent grade and were used without purification, unless otherwise noted. *N*, *N*-dimethylformamide (DMF) was dried by passage through two columns of activated molecular sieves. Dichloromethane (CH_2Cl_2), triethylamine (Et_3N), 2,6-lutidine, and *N*-methylmorpholine (NMM) were distilled from calcium hydride. Removal of solvent or concentration under reduced pressure was performed using a rotary evaporator at 25–30 °C. Flash chromatography was preformed with the indicated solvents and Merck 250-400 mesh silica gel. HPLC was conducted using a binary solvent system, where solvent system A was 0.1% aqueous TFA and solvent system B was 0.1% TFA in acetonitrile, with a C18 column (10 mm particle size, 300 Å pore size), 22 mm diameter 250 mm (flow rate of 8 mL/min), being used for preparative work and a C18 column (10 mm particle size, 300 Å pore size), 4.6 mm diameter 250 (flow rate of 1 mL/min), being used for analytical work. Analytical TLC was preformed with Merck-60 TLC plates and the indicated solvents.

Melting points were determined on a melting point apparatus and are uncorrected. Proton (^{1}H) nuclear magnetic resonance (NMR) spectra were obtained at the indicated field strength as solutions in the indicated solvent. Chemical shifts are reported in parts per million (ppm, δ) referenced relative to the center of the residual ^{1}H resonance of the solvent (CD_3OD: 3.30 ppm; DMSO-d_6: 2.49 ppm; D_2O: 4.67 ppm; $CDCl_3$: 7.24 ppm). Coupling constants are reported in hertz (Hz). Splitting patterns are designated as: s = singlet; d = doublet; dd = doublet of doublet; ddd = doublet of doublet of doublets; t = triplet; q = quartet; p = pentuplet; hep = heptet; m = multiplet; comp = overlapping multiplets of non-magnetically equivalent protons; br = broad; app = apparent. Carbon 13 (^{13}C) NMR spectra were obtained at the field indicated strength as solutions in the indicated solvent. Resonances are reported in ppm referenced from the center of the ^{13}C multiplet of the solvent (CD_3OD: 49.0 ppm; DMSO-d_6: 39.5 ppm, $CDCl_3$: 77.0 ppm). Spectra taken in D_2O were referenced utilizing an external standard. Isothermal titration calorimetry was performed as previously described.[1]

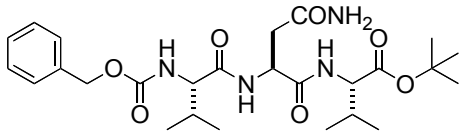
General procedure for the coupling of amino acids and peptides. Preparation of 9, 11, 15, 17, 19, 22, 26, 28, 29, 31, 32, 33, 35, 37, 39, 42, 44, 46, 48, 50.

Method A: *N*-Methylmorpholine (NMM) (42 mg, 46 μL, 0.417 mmol) was added to a solution of *N*-protected amino acid (0.139 mmol) and *C*-protected amino acid (0.153 mmol) in DMF

(2 mL) at –10 ºC. 1-(3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDCI) (30 mg, 0.153 mmol) and 1-hydroxybenzotriazole hydrate (HOBt) (38 mg, 0.278 mmol) were added, and the reaction was warmed to room temperature over 2 h and stirring continued at room temperature for 15 h. The reaction was concentrated to dryness under reduced pressure. The residue was triturated with saturated $NaHCO_3$ (5 mL), and the resultant solid was isolated by vacuum filtration and washed sequentially with H_2O (3 mL), 1 M HCl (3 x 3 mL) and H_2O (5 mL). If the material was not >90% pure by ^1H NMR, the crude product was purified using flash chromatography or preparative RP HPLC using a binary gradient of solvents, A and B (given).

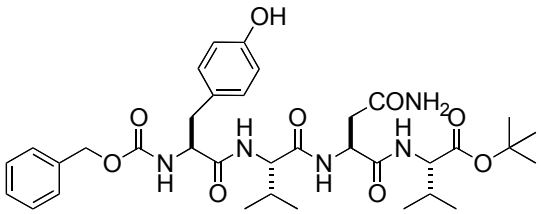
Method B: NMM (464 mg, 505 µL, 4.59 mmol) was added to a solution of *N*-protected amino acid (1.53 mmol) and *C*-protected amino acid (1.68 mmol) in DMF (15 mL) at –10 ºC. EDCI (323 mg, 1.68 mmol) and HOBt (413 mg, 3.06 mmol) were added, the mixture was warmed to room temperature over 2 h and stirring continued for 14 h. The mixture was concentrated to dryness under reduced pressure. Saturated $NaHCO_3$ (15 mL) was added, and the aqueous phase was extracted with CH_2Cl_2 (3 x 15 mL). The combined organics were washed with 1 M HCl (3 x 15 mL), H_2O (25 mL), dried (Na_2SO_4) and concentrated to dryness under reduced pressure. If the material was not >90% pure by ^1H NMR, the crude product was purified using flash chromatography or preparative RP HPLC using a binary gradient of solvents, A and B (given).

Method C: A solution of *N*-protected amino acid (51 mg, 0.149 mmol) and *C*-protected amino acid (72 mg, 0.149 mmol) in DMF (2.0 mL) was cooled to –10 ºC, whereupon 2,6-lutidine (48 mg, 0.446 mmol, 52 µL) and *O*-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU) (56 mg, 0.149 mmol) were added. The reaction was warmed to room temperature over 2 h, and stirring was continued at room temperature for 15 h. The reaction was concentrated to dryness under reduced pressure. The residue was triturated with saturated $NaHCO_3$ (5 mL), and the resultant solid was isolated by vacuum filtration and washed sequentially with H_2O (3 mL), 1 M HCl (3 x 3 mL) and H_2O (5 mL) to yield. If the material was not >90% pure by ^1H NMR, the crude product was purified using flash chromatography or preparative RP HPLC using a binary gradient of solvents, A and B (given).



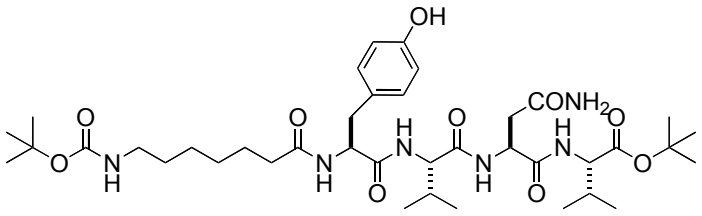
15

(*N*-Cbz-valyl)-aspargyl-valyl-O^{t}Bu (15). Prepared from Cbz-Val and H_2N-Asn-Val-O-tBu[2] according to the general procedure (method A) to yield 655 mg (93%) of the title compound as a white solid: mp 195-196 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.38-7.26 (comp, 5 H), 5.13 (d, *J* = 12.3 Hz, 1 H), 5.07 (d, *J* = 12.3 Hz, 1 H), 4.80 (app t, *J* = 6.5 Hz, 1 H), 4.18 (d, *J* = 5.5 Hz, 1 H), 3.98 (d, *J* = 6.5 Hz, 1 H), 2.80-2.67 (comp, 2 H), 2.18-2.05 (comp, 2 H), 1.47 (s, 9 H), 1.00-0.90 (comp, 12 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.0, 174.0, 172.9, 171.9, 158.7, 138.1, 129.5, 129.0, 128.8, 82.9, 67.8, 62.2, 60.0, 51.4, 37.7, 31.9, 31.8, 28.3, 19.8, 19.5, 18.5, 18.4; mass spectrum (ESI) m/z [$C_{35}H_{50}N_5O_9$ (M+H) requires].



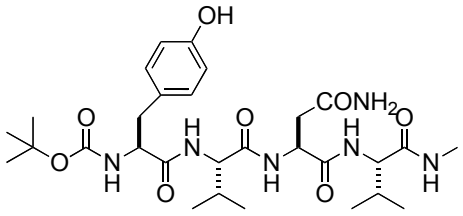
17

(*N*-Cbz-tyrosyl)-valyl-aspargyl-valyl-O^{t}Bu (17). Prepared from Cbz-Tyr and **16** according to the general procedure (method A) to yield 337 mg (72%) of the title compound as a white solid. The white solid was purified by flash column chromatography eluting with CH_2CL_2/MeOH (9:1): mp 215-217 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.33-7.22 (comp, 5 H), 7.06-7.02 (comp, 2 H), 6.70-6.66 (comp, 2 H), 5.04 (d, *J* = 12.8 Hz, 1 H), 4.99 (d, *J* = 12.8 Hz, 1 H), 4.76 (app t, *J* = 6.7 Hz, 1 H), 4.34 (dd, *J* = 9.5, 5.0 Hz, 1 H), 4.20-4.14 (comp, 2 H), 3.04 (dd, *J* = 13.9, 5.0 Hz, 1 H), 2.79-2.68 (comp, 2 H), 2.64 (dd, *J* = 15.7, 6.7 Hz, 1 H), 2.17-2.02 (comp, 2 H), 1.46 (s, 9 H), 0.96-0.88 (comp, 12 H); ^{13}C NMR (125 MHz, CD_3OD) δ 174.9, 174.4, 173.1, 172.8, 171.9, 158.4, 157.2, 138.2, 131.3, 129.5, 129.2, 128.9, 128.7, 116.3, 83.0, 67.6, 60.1, 60.0, 58.1, 51.3, 38.1, 37.9, 32.1, 31.9, 28.3, 19.8, 19.5, 18.5, 18.4; mass spectrum (ESI) m/z 684.3607 [$C_{35}H_{50}N_5O_9$ (M+H) requires 684.3609].



19

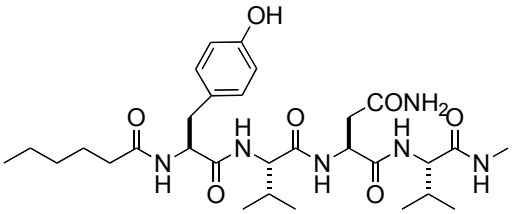
(6-*N*-Boc-hexylcarbonyl)-tyrosyl-valyl-aspargyl-valyl-O^{t}Bu (19). Prepared from 7-(*tert*-butoxycarbonylamino)heptanoic acid and **18** according to the general procedure (method A) to yield 236 mg (92%) of the title compound as a white solid. The crude material was purified by preparative RP HPLC with a gradient of 0% B to 60% B over 30 min: mp 194-196 ºC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.10 (br s, 1 H), 8.19 (d, J = 7.6 Hz, 1 H), 7.94 (d, J = 8.5 Hz, 1 H), 7.77 (d, J = 8.3 Hz, 1 H), 7.72 (d, J = 8.9 Hz, 1 H), 7.33 (s, 1 H), 7.03-6.99 (comp, 2 H), 6.92 (s, 1 H), 6.69 (app t, J = 5.1 Hz, 1 H), 6.62-6.58 (comp, 2 H), 4.62 (dd, J = 13.3, 7.5 Hz, 1 H), 4.46 (ddd, J = 10.5, 8.5, 4.0 Hz, 1 H), 4.21 (dd, J = 8.9, 6.2 Hz, 1 H), 4.01 (dd, J = 8.3, 5.5 Hz, 1 H), 2.92-2.82 (comp, 3 H), 2.62 (dd, J = 14.1, 10.5 Hz, 1 H), 2.54-2.48 (m, 1 H), 2.42 (dd, J = 15.8, 7.5 Hz, 1 H), 2.05-1.93 (comp, 4 H), 1.39 (s, 9 H), 1.35 (s, 9 H), 1.36-1.24 (comp, 4 H), 1.17-1.04 (comp, 4 H), 0.87-0.77 (comp, 12 H); ^{13}C NMR (125 MHz) δ 172.2, 171.5 171.4, 170.9, 170.6, 170.2, 155.6, 155.5, 129.9, 128.2, 114.7, 80.6, 77.2, 57.8, 57.2, 54.0, 49.3, 40.1, 36.9, 36.1, 35.1, 30.8, 30.0, 29.3, 28.2, 28.2, 26.0, 25.2, 19.2, 18.8, 17.8, 17.7; mass spectrum (ESI) m/z 777.4759 [$C_{26}H_{38}N_6O_7$ (M+H) requires 777.4762].



29

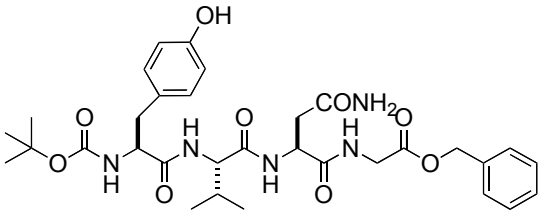
(*N*-Boc-tyrosyl)-valyl-aspargyl-valyl-NHMe (29). Prepared from Boc-Tyr and H_2N-Val-Asn-Val-NHMe[3] according to the general procedure (method A) to yield 206 mg (95%) of the title compound as a white solid. The crude material was purified by preparative RP HPLC with a gradient of 0% B to 60% B over 30 min: mp 235-237 ºC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.10 (br s, 1 H), 8.25 (d, J = 7.6 Hz, 1 H), 7.86-7.81 (m, 1 H), 7.69-7.62 (comp, 2 H), 4.60 (app dd, J = 13.9, 7.5 Hz, 1 H), 4.24 (dd, J = 8.9, 6.2 Hz, 1 H), 4.08 (ddd, J = 10.6, 8.9, 4.9 Hz, 1 H), 4.04 (dd, J = 8.8,

5.8 Hz, 1 H), 2.84 (dd, *J* = 14.0, 4.0 Hz, 1 H), 2.63-2.53 (comp, 5 H), 2.40 (dd, *J* = 15.5, 6.2 Hz, 1 H), 2.06-1.98 (m, 1 H), 1.98-1.89 (m, 1 H), 1.29 (s, 8 H), 1.23 (s, 1 H), 0.87-0.76 (comp, 12 H); ^{13}C NMR (125 MHz) δ 171.8, 171.6, 170.9, 170.7, 170.6, 155.6, 155.2, 130.0, 128.3, 114.8, 78.0, 57.7, 56.9, 56.1, 49.5, 36.8, 36.3, 31.2, 29.9, 28.1, 27.8, 25.4, 19.1, 19.1, 17.8, 17.6; mass spectrum (ESI) m/z 607.3450 [$C_{29}H_{47}N_6O_8$ (M+H) requires 607.3455].



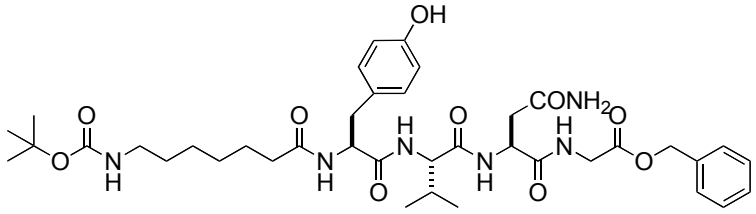
31

Pentylcarbonyl-tyrosyl-valyl-aspargyl-valyl-NHMe (31). Prepared from hexanoic acid and **30** according to the general procedure (method A) to yield 130 mg (91%) of the title compound as a white solid. The crude material was purified by preparative RP HPLC with a gradient of 0% B to 55% B over 30 min: mp 281-283 ºC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.20 (d, *J* = 7.6 Hz, 1 H), 7.94 (d, *J* = 8.5 Hz, 1 H), 7.87-7.82 (m, 1 H), 7.71 (d, *J* = 8.8 Hz, 1 H), 7.67 (d, *J* = 8.9 Hz, 1 H), 7.42 (br s, 1 H), 7.03-6.99 (comp, 2 H), 6.96 (br s, 1 H), m 6.63-6.59 (comp, 2 H), 4.61 (app dd, *J* = 13.8, 7.5 Hz, 1 H), 4.45 (ddd, *J* = 10.6, 8.5, 4.0 Hz, 1 H), 4.20 (dd, *J* = 8.9, 6.4 Hz, 1 H), 4.04 (dd, *J* = 8.8, 5.8 Hz, 1 H), 2.87 (dd, *J* = 14.0, 4.0 Hz, 1 H), 2.64-2.53 (comp, 5 H), 2.41 (dd, *J* = 15.4, 6.2 Hz, 1 H), 2.07-1.96 (comp, 3 H), 1.96-1.88 (m, 1 H), 1.39-1.31 (comp, 2 H), 1.22-1.13 (comp, 2 H), 1.10-1.01 (comp, 2 H), 0.85-0.75 (comp, 15 H); ^{13}C NMR (125 MHz) δ 172.2, 171.8, 171.5, 170.9, 170.7, 170.5, 155.6, 130.0, 128.1, 114.7, 57.7, 57.1, 54.0, 49.6, 36.8, 36.2, 35.1, 30.9, 30.6, 29.9, 25.4, 24.9, 21.8, 19.11, 19.10, 17.8, 17.6, 13.8; mass spectrum (ESI) m/z 627.3477 [$C_{30}H_{48}N_6O_7Na$ (M+Na) requires 627.3510].



9

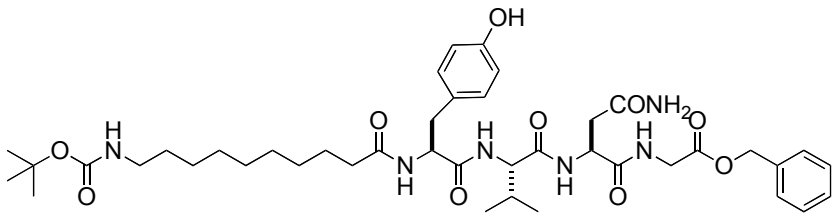
(*N*-Boc-tyrosyl)-valyl-aspargyl-glycyl-OBn (9). Prepared from Boc-Tyr and H_2N-Val-Asn-Gly-OBn[4] according to the general procedure (method A) to yield 25 mg (89%) of the title compound as a white solid. The crude material was purified by preparative RP HPLC using a gradient of 0% B to 65% B over 30 min: mp 177-181 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.36-7.27 (comp, 5 H), 7.06-7.02 (comp, 2 H), 6.71-6.67 (comp, 2 H), 5.15 (s, 2 H), 4.75 (dd, *J* = 7.2, 6.0 Hz, 1 H), 4.27 (dd, *J* = 9.5, 5.1 Hz, 1 H), 4.13 (d, *J* = 6.8 Hz, 1 H), 4.01 (d, *J* = 17.7 Hz, 1 H), 3.60 (d, *J* = 17.7 Hz, 1 H), 3.01 (dd, *J* = 14.1, 5.1 Hz, 1 H), 2.77 (dd, *J* = 15.7, 6.0 Hz, 1 H), 2.73-2.68 (m, 1 H), 2.67 (dd, *J* = 15.7, 7.2 Hz, 1 H), 2.12-2.04 (m, 1 H), 1.35 (s, 9 H), 1.00-0.90 (comp, 6 H); ^{13}C NMR (125 MHz) δ 175.1, 174.8, 173.4, 173.2, 170.9, 157.8, 157.2, 137.2, 131.4, 129.6, 129.4, 129.3, 129.2, 116.2, 80.7, 67.9, 60.5, 57.5, 51.4, 42.2, 37.9, 37.6, 31.9, 28.7, 19.7, 18.6; mass spectrum (ESI) m/z 664.2953 [$C_{32}H_{43}N_5O_9Na$ (M+Na) requires 664.2981].



11

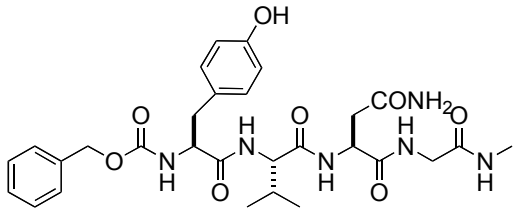
(6-*N*-Boc-hexylcarbonyl)-tyrosyl-valyl-aspargyl-glycyl-OBn (11). Prepared from 7-(*tert*-butoxycarbonylamino)heptanoic acid and **10** according to the general procedure (method A) to yield 186 mg (97%) of the title compound as a white solid. The crude material was purified by preparative RP HPLC with a gradient of 0% B to 60% B over 30 min: mp 198-200 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.35-7.27 (comp, 5 H), 7.08-7.04 (comp, 2 H), 6.71-6.67 (comp, 2 H), 5.14 (s, 2 H), 4.75 (dd, *J* = 7.2, 6.0 Hz, 1 H), 4.63 (dd, *J* = 10.1, 5.0 Hz, 1 H), 4.13 (d, *J* = 6.6 Hz, 1 H), 4.02 (d, *J* = 17.5 Hz, 1 H), 3.96 (d, *J* = 17.5 Hz, 1 H), 3.07 (dd, *J* = 14.2, 5.0 Hz, 1 H), 2.98 (t, *J* = 7.0 Hz, 2 H), 2.76 (dd, *J* = 15.7, 6.0 Hz, 1 H), 2.75 (dd, *J* = 14.2, 10.1 Hz, 1 H), 2.68 (dd, *J* = 15.7, 7.2 Hz, 1 H), 2.15-2.05 (comp, 3 H), 1.50-1.41 (comp, 11 H), 1.41-1.35 (comp, 2 H), 1.26-1.18 (comp, 2 H),

1.18-1.10 (comp, 2 H), 0.95 (d, J = 3.8 Hz, 3 H), 0.93 (d, J = 3.8 Hz, 3 H); ^{13}C NMR (125 MHz) δ 176.3, 174.8, 174.6, 173.4, 173.2, 170.9, 158.6, 157.2, 137.2, 131.3, 129.6, 129.3, 129.3, 116.2, 79.8, 67.9, 60.5, 56.0, 51.4, 42.2, 41.3, 37.6, 36.8, 31.8, 30.8, 29.7, 28.8, 27.5, 26.9, 19.7, 18.6; mass spectrum (ESI) m/z 769.4119 [$C_{39}H_{57}N_6O_{10}$ (M+H) requires 769.4136].



22

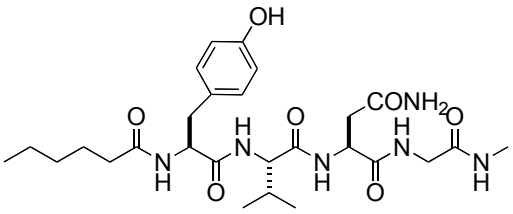
(9-*N*-Boc-nonylcarbonyl)-tyrosyl-valyl-aspargyl-glycyl-OBn (22). Prepared from 10-(*tert*-butoxycarbonylamino)decanoic acid and **21** according to the general procedure (method A) to yield 97 mg (97%) of the title compound as a white solid. The crude material was purified by preparative RP HPLC with a gradient of 0% B to 70% B over 30 min: mp 201-204 ºC (dec); ^{1}H NMR (500 MHz, CD_3OD) δ 7.36-7.26 (comp, 5 H), 7.05 (d, J = 8.5 Hz, 2 H), 6.68 (d, J = 8.5 Hz, 2 H), 5.15 (s, 2 H), 4.75 (dd, J = 7.1, 6.0 Hz, 1 H), 4.62 (dd, J = 10.0, 5.0 Hz, 1 H), 4.12 (d, J = 6.6 Hz, 1 H), 4.02 (d, J = 17.7 Hz, 1 H), 3.97 (d, J = 17.7 Hz, 1 H), 3.06 (dd, J = 14.1, 5.0 Hz, 1 H), 3.00 (app t, J = 7.1 Hz, 2 H), 2.80-2.72 (comp, 2 H), 2.68 (dd, J = 15.7, 7.1 Hz, 1 H), 2.17-2.04 (comp, 3 H), 1.50-1.39 (comp, 13 H), 1.32-1.10 (comp, 10 H), 0.97-0.90 (comp, 6 H); ^{13}C NMR (125 MHz) δ 176.4, 174.8, 174.6, 173.3, 173.2, 170.9, 158.6, 157.2, 137.2, 131.2, 129.6, 129.3, 129.2, 116.2, 79.8, 67.9, 60.6, 56.0, 51.4, 42.2, 41.4, 37.6, 36.9, 31.8, 31.0, 30.5, 30.4, 30.1, 28.8, 27.8, 26.9, 19.7, 18.6; mass spectrum (ESI) m/z 811.4600 [$C_{42}H_{63}N_6O_{10}$ (M+H) requires 811.4593] 777, 765.



26

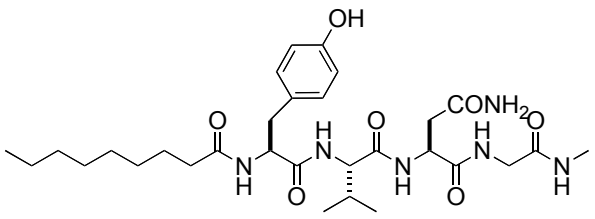
(*N*-Cbz-tyrosyl)-valyl-aspargyl-glycyl-NHMe (26). Prepared from Cbz-Tyr and H_2N-Val-Asn-Val-NHMe[4] according to the general procedure (method A) to yield 137 mg (92%) of the title compound as a white solid. The crude material was purified by preparative RP HPLC with a

gradient of 0% B to 55% B over 30 min: mp 223-224 ºC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.15 (br s, 1 H), 8.28 (d, J = 7.0 Hz, 1 H), 8.17 (t, J = 5.9 Hz, 1 H), 7.89 (d, J = 8.3 Hz, 1 H), 7.68-7.61 (m, 1 H), 7.49-7.42 (comp, 2 H), 7.35-7.18 (comp, 5 H), 7.07-7.03 (comp, 2 H), 7.01 (br s, 1 H), 6.65-6.60 (comp, 2 H), 4.98-4.88 (comp, 2 H), 4.40 (dd, J = 13.4, 7.0 Hz, 1 H), 4.25 (ddd, J = 14.6, 9.0, 3.6 Hz, 1 H), 4.17 (dd, J = 8.3, 6.8 Hz, 1 H), 3.64 (dd, J = 16.8, 6.0 Hz, 1 H), 3.58 (dd, J = 16.8, 6.0 Hz, 1 H), 2.88 (dd, J = 14.0, 3.6 Hz, 1 H), 2.63-2.51 (comp, 6 H), 2.02-1.90 (m, 1 H), 0.87-0.76 (comp, 6 H); ^{13}C NMR (125 MHz) δ 172.0, 171.8, 171.1, 170.9, 169.0, 155.8, 155.7, 137.0,130.1, 128.2, 128.1, 127.6, 127.3, 114.8, 65.1, 57.6, 56.3, 49.9, 42.5, 36.7, 36.5, 30.6, 25.4, 19.0, 18.0; mass spectrum (ESI) m/z 621.2643 [$C_{29}H_{38}N_6O_8Na$ (M+Na) requires 621.2640].



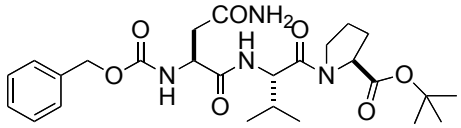
28

Pentylcarbonyl-tyrosyl-valyl-aspargyl-glycyl-NHMe (28). Prepared from hexanoic acid and **27** according to the general procedure (method C) to yield 38 mg (62%) of the title compound as a white solid. The crude material was purified by preparative RP HPLC with a gradient of 0% B to 60% B over 30 min: mp 227-230 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.08-7.03 (comp, 2 H), 6.70-6.66 (comp, 2 H), 4.62 (dd, J = 10.0, 5.0 Hz, 1 H), 4.59 (t, J = 6.5 Hz, 1 H), 4.09 (d, J = 6.9 Hz, 1 H), 3.85 (d, J = 16.9 Hz, 1 H), 3.79 (d, J = 16.9 Hz, 1 H), 3.03 (dd, J = 14.0, 5.0 Hz, 1 H), 2.82 (dd, J = 15.8, 6.5 Hz, 1 H), 2.76 (dd, J = 15.8, 6.5 Hz, 1 H), 2.74 (dd, J = 14.0, 10.0 Hz, 1 H), 2.71 (s, 3 H), 2.13 (t, J = 7.5 Hz, 2 H), 2.11-2.04 (m, 1 H), 1.46 (p, J = 15.3, 7.5 Hz, 2 H), 1.30-1.21 (comp, 2 H), 1.18-1.09 (comp, 2 H), 0.97-0.92 (comp, 6 H), 0.85 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz) δ 176.4, 175.0, 174.7, 173.7, 173.4, 172.2, 157.2, 131.2, 129.2, 116.2, 60.6, 56.0, 52.0, 43.8, 37.7, 37.3, 36.8, 32.3, 31.8, 26.6, 26.3, 23.4, 19.6, 18.7, 14.2; mass spectrum (ESI) m/z 563.3190 [$C_{26}H_{38}N_6O_7$ (M+H) requires 563.3193].



32

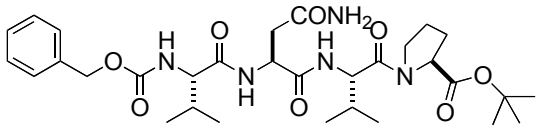
Octylcarbonyl-tyrosyl-valyl-asparagyl-glycl-NHMe (32). Prepared from nonanoic acid and **31** according to the general procedure (method A) to yield 62 mg (85%) of the title compound as a white solid. The crude material was purified using RP HPLC with a gradient of 0% B to 70% B over 30 min: mp 232-233 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.08-7.03 (comp, 2 H), 6.71-6.66 (comp, 2 H), 4.62 (dd, *J* = 10.0, 5.1 Hz, 1 H), 4.59 (app t, *J* = 6.5 Hz, 1 H), 4.09 (d, *J* = 6.9 Hz, 1 H), 3.85 (d, *J* = 16.7 Hz, 1 H), 3.80 (d, *J* = 16.7 Hz, 1 H), 3.03 (dd, *J* = 14.1, 5.1 Hz, 1 H), 2.81 (dd, *J* = 15.8, 6.5 Hz, 1 H), 2.75 (dd, *J* = 15.8, 6.5 Hz, 1 H), 2.74 (dd, *J* = 14.1, 10.0 Hz, 1 H), 2.71 (s, 3 H), 2.13 (app t, *J* = 7.3 Hz, 2 H), 2.10-2.04 (m, 1 H), 1.50-1.42 (comp, 2 H), 1.34-1.11 (comp, 10 H), 0.98-0.92 (comp, 6 H), 0.88 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz) δ 176.4, 175.0, 174.7, 173.7, 173.4, 172.2, 157.2, 131.2, 129.2, 116.2, 60.6, 56.0, 52.0, 43.8, 37.7, 37.3, 36.8, 33.0, 31.8, 30.4, 30.2, 30.1, 27.0, 26.3, 23.7, 19.6, 18.7, 14.4; mass spectrum (ESI) m/z 605.3665 [$C_{30}H_{49}N_6O_7$ (M+H) requires 605.3663].



33

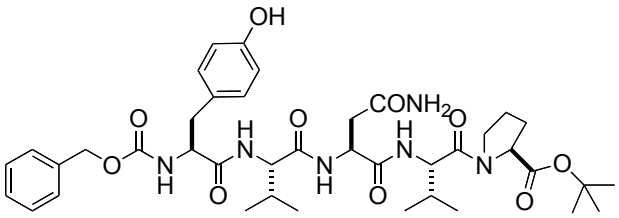
(*N*-Cbz-asparagyl)-valyl-prolyl-O^{t}Bu (33). Prepared from Cbz-Asn and H_2N-Val-Pro-O-*t*Bu[5] according to the general procedure (method B) to yield 785 mg (98%) of the title compound as a white solid. The crude product was purified by flash chromatography, eluting with CH_2Cl_2/CH_3OH (95:5): mp 48-51 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.7 Hz, 1 H), 7.37-7.28 (comp, 5 H), 6.42 (d, *J* = 8.5 Hz, 1 H), 6.10 (br s, 1 H), 5.76 (br s, 1 H), 5.14-5.09 (comp, 2 H), 4.58-4.50 (comp, 2 H), 4.36 (dd, *J* = 8.2, 4.9 Hz, 1 H), 3.79-3.72 (m, 1 H), 3.66-3.59 (m, 1 H), 2.90 (dd, *J* = 15.6, 3.9 Hz, 1 H), 2.59 (dd, *J* = 15.6, 5.7 Hz, 1 H), 2.22-2.12 (m, 1 H), 2.12-2.05 (m, 1 H), 2.05-1.98 (m, 1 H), 1.98-1.87 (comp, 2 H), 1.44 (s, 9 H), 1.01 (d, *J* = 6.8 Hz, 3 H), 0.93 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz) δ 173.3, 171.2, 170.7, 170.1, 156.2, 136.2, 128.5, 128.2, 81.4, 67.2,

59.8, 55.9, 51.7, 47.3, 36.9, 31.2, 29.1, 28.0, 24.9, 19.4, 17.7; mass spectrum (ESI) *m/z* 519.2814 [$C_{26}H_{39}N_4O_7$ (M+H) requires 519.2813].



35

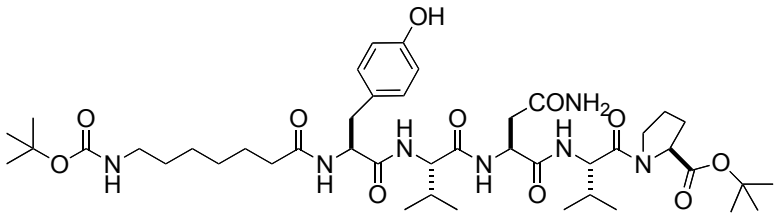
(*N*-Cbz-valyl)-asparagyl-valyl-prolyl-O^{t}Bu (35). Prepared from Cbz-Val and **34** according to the general procedure (method B) to yield 571 mg (89%) of the title compound as a white solid. The crude product was purified by flash chromatography, eluting with CH_2Cl_2/CH_3OH (95:5): mp 183-184 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.8 Hz, 1 H), 7.70 (d, *J* = 8.6 Hz, 1 H), 7.38-7.24 (comp, 5 H), 6.40 (br s, 1 H), 6.02 (br s, 1 H), 5.91 (d, *J* = 8.6 Hz, 1 H), 5.12 (d, *J* = 12.1 Hz, 1 H), 4.99 (d, *J* = 12.1 Hz, 1 H), 4.92-4.84 (m, 1 H), 4.53 (app t, *J* = 7.6 Hz, 1 H), 4.35 (dd, *J* = 8.4, 4.9 Hz, 1 H), 4.14 (dd, *J* = 8.2, 8.1 Hz, 1 H), 3.80-3.72 (m, 1 H), 3.66-3.58 (m, 1 H), 2.78 (dd, *J* = 15.3, 5.3 Hz, 1 H), 2.57 (dd, *J* = 15.3, 6.1 Hz, 1 H), 2.20-1.84 (comp, 6 H), 1.42 (s, 9 H), 1.04-0.86 (comp, 12 H); ^{13}C NMR (100 MHz) δ 173.3, 171.6, 171.3, 170.6, 170.0, 156.7, 136.4, 128.5, 128.0, 81.3, 66.9, 60.3, 59.8, 56.0, 49.9, 47.2, 37.1, 31.3, 30.9, 29.1, 28.0, 24.9, 19.4, 19.3 17.7; mass spectrum (ESI) *m/z* 618.3498 [$C_{31}H_{48}N_5O_8$ (M+H) requires 618.3497].



37

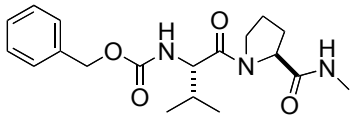
(*N*-Cbz-tyrosyl)-valyl-asparagyl-valyl-prolyl-O^{t}Bu (37). Prepared from Cbz-Tyr and **36** according to the general procedure (method A) to yield 423 mg (97%) of the title compound as a white solid. The crude product was found to be >95% pure by ^{1}H NMR and used without further purification: mp 193-194 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.32-7.19 (comp, 5 H), 7.04 (d, *J* = 8.6 Hz, 2 H), 6.68 (d, *J* = 8.6 Hz, 2 H), 5.05 (d, *J* = 12.7 Hz, 1 H), 4.98 (d, *J* = 12.7 Hz, 1 H), 4.75 (app t, *J* = 6.7 Hz, 1 H), 4.45 (d, *J* = 7.6 Hz, 1 H), 4.41 (dd, *J* = 9.8, 4.7 Hz, 1 H), 4.30 (dd, *J* = 8.4, 4.9 Hz, 1 H), 4.22 (d, *J* = 6.8 Hz, 1 H), 3.84-3.76 (m, 1 H), 3.67-3.59 (m, 1 H), 3.05 (dd, *J* = 14.1, 4.7 Hz, 1

H), 2.74 (dd, *J* = 14.1, 9.8 Hz, 1 H), 2.71 (dd, *J* = 15.4, 6.7 Hz, 1 H), 2.63 (dd, *J* = 15.4, 6.7 Hz, 1 H), 2.24-1.84 (comp, 6 H), 1.48-1.41 (s, 9 H), 1.03 (d, *J* = 6.8 Hz, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 0.93 (d, *J* = 7.6 Hz, 3 H), 0.91 (d, *J* = 7.6 Hz, 3 H); ^{13}C NMR (100 MHz) δ 174.7, 174.4, 173.1, 172.8, 172.7, 171.9, 158.3, 157.2, 138.2, 131.4, 129.4, 129.3, 128.9, 128.6, 116.2, 82.6, 67.5, 61.4, 60.0, 58.0, 57.7, 51.5, 38.2, 37.9, 32.1, 31.8, 30.2, 28.2, 25.8, 19.8, 18.7, 18.6; mass spectrum (ESI) *m/z* 781.4129 [$C_{40}H_{57}N_6O_{10}$ (M+H) requires 781.4131].



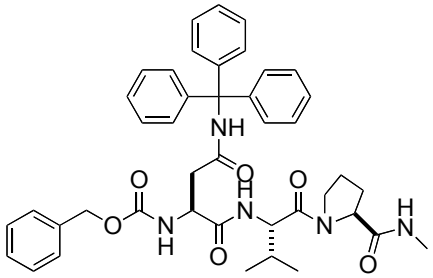
39

(6-*N*-Boc-hexylcarbonyl)-tyrosyl-valyl-asparagyl-valyl-prolyl-O^{t}Bu (39). Prepared from 7-(*tert*-butoxycarbonylamino)heptanoic acid and **38** according to the general procedure (method A) to yield 106 mg (97%) of the title compound as a white solid. The crude product was purified using RP HPLC with a gradient of 0% B to 60% B over 30 min: mp 180-182 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.07-7.03 (comp, 2 H), 6.70-6.66 (comp, 2 H), 4.70 (app t, *J* = 6.7 Hz, 1 H), 4.63 (dd, *J* = 10.2, 4.9 Hz, 1 H), 4.44 (d, *J* = 7.8 Hz, 1 H), 4.30 (dd, *J* = 8.5, 5.1 Hz, 1 H), 4.18 (d, *J* = 6.8 Hz, 1 H), 3.84-3.77 (m, 1 H), 3.67-3.60 (m, 1 H), 3.06 (dd, *J* = 14.1, 4.9 Hz, 1 H), 2.98 (t, *J* = 7.0 Hz, 2 H), 2.75 (dd, *J* = 14.1, 10.2 Hz, 1 H), 2.71 (dd, *J* = 15.6, 6.7 Hz, 1 H), 2.65 (dd, *J* = 15.6, 6.7 Hz, 1 H), 2.24-2.16 (m, 1 H), 2.15-2.04 (comp, 4 H), 2.04-1.86 (comp, 3 H), 1.50-1.34 (comp, 22 H), 1.26-1.19 (comp, 2 H), 1.18-1.10 (comp, 2 H), 1.03 (d, *J* = 6.8 Hz, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 0.94 (d, *J* = 6.8 Hz, 3 H), 0.92 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz) δ 176.2, 174.8, 174.2, 173.1, 172.8, 172.7, 171.9, 158.6, 157.2, 131.3, 129.3, 116.2, 82.6, 79.8, 61.4, 60.1, 57.8, 56.0, 51.5, 41.3, 37.8, 37.7, 36.8, 32.0, 31.8, 30.8, 30.2, 29.7, 28.8, 28.2, 27.6, 26.9, 25.8, 19.8, 18.7, 18.5; mass spectrum (ESI) *m/z* 874.5286 [$C_{44}H_{72}N_7O_{11}$ (M+H) requires 874.5284].



42

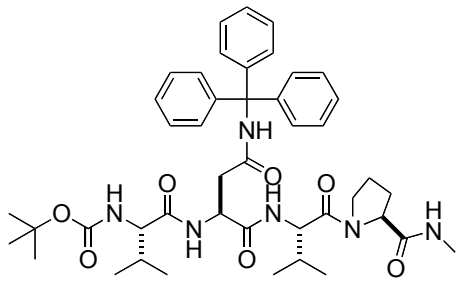
(*N*-Cbz-valyl)-prolyl-NHMe (42). Prepared from Cbz-Val and Pro-NHMe according to the general procedure (method B) to yield 1.95 g (70%) of the title compound as a white solid. The crude product was purified by flash chromatography, eluting with EtOAc/hexane (4:1): mp 41-43 ºC; ^{1}H NMR (400 MHz, CD_3OD) (rotamers 15:85) δ 7.37-726 (comp, 5 H), 6.89 (br s, 1 H), 5.68 (d, *J* = 8.9 Hz, 1 H), 5.10 (d, *J* = 12.3 Hz, 1 H), 5.04 (d, *J* = 12.3 Hz, 1 H), 4.51 (dd, *J* = 8.2, 3.1 Hz, 0.85 H), 4.44-4.38 (m, 0.15 H), 4.35-4.28 (m, 0.85 H), 4.00-3.95 (m, 0.15 H), 3.76-3.67 (m, 0.85 H), 3.62-3.54 (m, 0.85 H), 3.44 (br s, 0.15 H), 3.35 (br s, 0.15 H), 2.78-2.65 (comp, 3 H), 2.50-2.43 (m, 0.15 H), 2.36-2.27 (m, 0.85 H), 2.18-1.78 (comp, 4 H), 0.96 (d, *J* = 6.5 Hz, 3 H), 0.90 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (100 MHz, CD_3OD) δ 172.3, 171.7, 171.6, 156.7, 156.6, 136.5, 128.7, 128.4, 128.3, 67.2, 59.9, 59.8, 57.8, 57.7, 47.9, 31.7, 27.3, 26.3, 26.1, 25.3, 19.7, 19.5, 18.1, 17.8; mass spectrum (ESI) *m/z* 362.2077 [$C_{19}H_{28}N_3O_4$ (M+H) requires 362.2080].



44

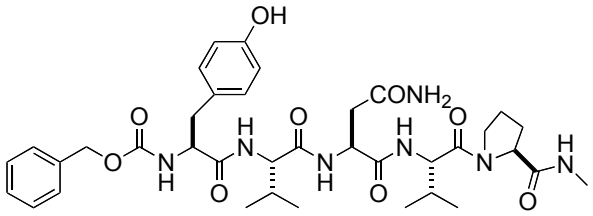
[*N*-Cbz-*N*-(trityl)-glutamyl]-valyl-prolyl-NHMe (44). Prepared from Cbz-Asn(Trt) and **43** according to the general procedure (method A) to yield 250 mg (87%) of the title compound as a white solid. The crude product was purified by flash chromatography, eluting with CH_2Cl_2/MeOH (95:5): mp 126-128 ºC; ^{1}H NMR (400 MHz, CD_3OD) (rotamers 5:1) δ 7.40-7.11 (comp, 20 H), 5.14 (d, *J* = 12.3 Hz, 1 H), 5.00 (d, *J* = 12.3 Hz, 1 H), 4.59 (dd, *J* = 8.6, 4.3 Hz, 1 H), 4.53 (d, *J* = 6.8 Hz, 1 H), 4.15 (app t, *J* = 6.5 Hz, 1 H), 3.63-3.51 (comp, 2 H), 2.78 (dd, *J* = 15.1, 8.6 Hz, 1 H), 2.66 (dd, *J* = 15.1, 4.3 Hz, 1 H), 2.57 (s, 2.5 H), 2.49 (s, 0.5 H), 2.14-1.60 (comp, 5 H), 1.02-0.80 (comp, 6 H); ^{13}C NMR (100 MHz) δ 173.7, 172.2, 170.9, 170.2, 156.9, 144.7, 136.8, 128.8, 128.4, 128.0, 127.6,

126.7, 70.6, 66.8, 60.6, 56.4, 52.2, 38.6, 30.9, 29.4, 25.2, 24.8, 18.7, 17.3; mass spectrum (ESI) *m/z* 718.3607 [$C_{42}H_{48}N_5O_6$ (M+H) requires 718.3605].



46

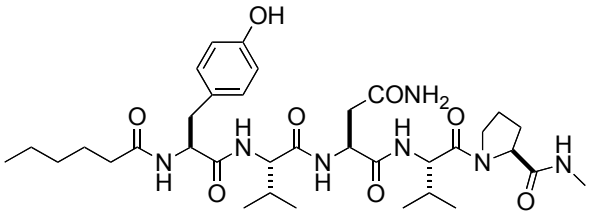
(*N*-Boc-valyl)-[*N*-(trityl)-glutamyl]-valyl-prolyl-NHMe (46). Prepared from Boc-Val and **45** according to the general procedure (method A) to yield 112 mg (87%) of the title compound as a white solid. The crude product was purified by flash chromatography, eluting with CH_2Cl_2/MeOH (95:5): mp 149-150 ºC; ^{1}H NMR (400 MHz, CD_3OD) (rotamers 20:80) δ 7.28-7.16 (comp, 15 H), 4.78 (app t, *J* = 7.0 Hz, 1 H), 4.51-4.44 (m, 1 H), 4.29 (dd, *J* = 7.8, 5.7 Hz, 0.8 H), 4.23 (d, *J* = 7.6 Hz, 0.2 H), 4.02-3.93 (comp, 1.2 H), 3.78-3.72 (m, 0.8 H), 3.66-3.58 (m, 0.8 H), 3.49-3.44 (m, 0.2 H), 2.78-2.62 (comp, 5 H), 2.15-1.72 (comp, 6 H), 1.41 (s, 9 H), 1.01-0.85 (comp, 12 H); ^{13}C NMR (100 MHz) δ 173.7, 173.0, 171.6, 171.0, 170.2, 156.7, 144.7, 128.8, 127.6, 126.6, 79.4, 70.6, 60.6, 59.9, 56.8, 50.3, 38.3, 31.4, 30.6, 29.4, 27.6, 25.2, 24.8, 18.7, 17.4, 17.0; mass spectrum (ESI) *m/z* 783.4451 [$C_{44}H_{59}N_6O_7$ (M+H) requires 783.4445].



48

(*N*-Cbz-tyrosyl)-valyl-glutamyl-valyl-prolyl-NHMe (48). Prepared from Cbz-Tyr and **47** according to the general procedure (method A) to yield 600 mg (88%) of the title compound as a white solid. The crude product was purified by flash chromatography, eluting with CH_2Cl_2/MeOH (9:1): mp 204-205 ºC; ^{1}H NMR (500 MHz, DMSO-d_6, 363 K) δ 8.82 (s, 1 H), 8.00 (d, *J* = 7.4 Hz, 1 H), 7.56 (d, *J* = 8.2 Hz, 1 H), 7.41-7.20 (comp, 7 H), 7.23 (d, *J* = 8.5 Hz, 2 H), 6.65 (d, *J* = 8.5 Hz, 2 H), 4.99 (s, 2 H), 4.62 (app dd, *J* = 14.0, 6.6 Hz, 1 H), 4.42-4.33 (m, 1 H), 4.31-4.18 (comp, 3 H),

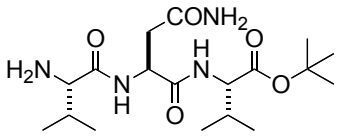
3.70-3.50 (comp, 2 H), 2.96 (dd, *J* = 14.2. 4.2 Hz, 1 H), 2.70 (dd, *J* = 14.2, 10.0 Hz, 1 H), 2.61-2.53 (comp, 4 H), 2.51-2.41 (comp, 2 H), 2.07-1.87 (comp, 4 H), 1.86-1.73 (comp, 2 H), 0.95-0.81 (comp, 12 H); ^{13}C NMR (125 MHz) δ 171.4, 171.1, 171.0, 170.3, 170.0, 169.2, 155.4, 155.3, 136.6, 129.5, 127.8, 127.7, 127.1, 126.8, 114.6, 65.0, 59.2, 57.3, 56.1, 55.3, 49.4, 46.6, 36.7, 36.3, 30.2, 29.9, 28.5, 25.0, 24.0, 18.7, 17.4; mass spectrum (ESI) *m/z* 738.3824 [$C_{37}H_{52}N_9O_7$ (M+H) requires 738.3821].



50

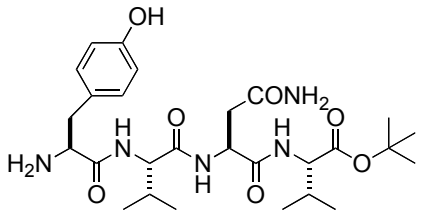
Pentylcarbonyl-*O*-phosphotyrosyl-valyl-asparagyl-valyl-prolyl-NHMe (50). Prepared from hexanoic acid and **49** according to the general procedure (method A) to yield 95 mg (89%) of the title compound as a white solid. The crude product was found to be >95% pure by ^{1}H NMR and used without further purification: mp 240-241 ºC; ^{1}H NMR (500 MHz, DMSO-d_6, 403 K) δ 8.56 (br s, 1 H), 7.80 (d, *J* = 7.4 Hz, 1 H), 7.42 (br s, 1 H), 7.30 (d, *J* = 7.9 Hz, 1 H), 7.26-7.14 (comp, 2 H), 7.00 (dd, *J* = 6.4, 1.8 Hz, 2 H), 6.64 (comp, 3 H), 4.61 (app dd, *J* = 14.0, 6.4 Hz, 1 H), 4.53-4.45 (m, 1 H), 4.42-4.31 (comp, 2 H), 4.19 (dd, *J* = 8.6, 6.1 Hz, 1 H), 3.70-3.50 (comp, 2 H), 2.98 (dd, *J* = 14.4. 4.8 Hz, 1 H), 2.74 (dd, *J* = 14.4, 9.3 Hz, 1 H), 2.62-2.55 (comp, 4 H), 2.52-2.44 (m, 1 H), 2.10-1.78 (comp, 8 H), 1.5-1.42 (comp, 2 H), 1.30-1.15 (comp, 4 H), 0.94-0.82 (comp, 15 H); ^{13}C NMR (125 MHz) δ 171.7, 171.0, 170.9, 170.8, 170.0, 169.7, 169.1, 155.1, 129.1, 127.7, 114.4, 59.1, 57.3, 55.1, 53.7, 49.4, 46.2, 36.5, 35.6, 34.7, 30.1, 29.8, 24.7, 24.0, 20.9, 18.4, 17.03, 17.01, 12.7; mass spectrum (ESI) *m/z* 724.4004 [$C_{35}H_{55}N_7O_8Na$ (M+Na) requires 724.4004].

Representative procedure for hydrogenolysis of *N*-Cbz protected peptides. Preparation of 16, 18, 27, 34, 36, 38, 43, 45, 49.



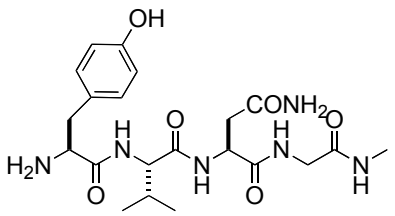
16

Valyl-aspargyl-valyl-O^{t}Bu (16). The benzyl carbamate **15** (526 mg, 1.01 mmol) was dissolved in MeOH (10 mL) containing 10% Pd/C (108 mg, 10 mol %). The resulting mixture was purged four times with H_2, and the suspension was stirred under H_2 (1 atm) for 7 h. The mixture was filtered through a pad of celite, and the pad was washed with MeOH (5 mL). The combined filtrate and washings were concentrated to dryness under reduced pressure to yield 390 mg (99%) of **16** as a white solid. This material was found to be >90% pure by ^{1}H NMR and used without further purification: mp 64-66 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 4.82 (dd, *J* = 7.5, 5.8 Hz, 1 H), 4.19 (d, *J* = 5.5 Hz, 1 H), 3.20 (d, *J* = 5.1 Hz, 1 H), 2.73 (dd, *J* = 15.7, 5.8 Hz, 1 H), 2.67 (dd, *J* = 15.7, 7.5 Hz, 1 H), 2.19-2.09 (m, 1 H), 2.06-1.96 (m, 1 H), 1.47 (s, 9 H), 1.00-0.90 (comp, 12 H); ^{13}C NMR (75 MHz, CD_3OD) δ 176.5, 174.8, 173.1, 172.0, 83.0, 61.3, 59.8, 51.1, 38.1, 33.1, 31.9, 28.3, 19.8, 19.5, 18.3, 17.6; mass spectrum (ESI) m/z [$C_{35}H_{50}N_5O_9$ (M+H) requires].



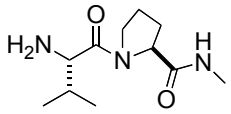
18

Tyrosyl-valyl-aspargyl-valyl-O^{t}Bu (18). Prepared in 89% yield by hydrogenolysis of **17** (43 mg, 0.062 mmol) in MeOH (15 mL) as a white solid. This material was shown to be >95% pure by ^{1}H NMR and was used without further purification: mp 93-96 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.06-7.01 (comp, 2 H), 6.74-6.69 (comp, 2 H), 4.77 (t, *J* = 6.5 Hz, 1 H), 4.18 (d, *J* = 6.8 Hz, 1 H), 4.15 (d, *J* = 5.5 Hz, 1 H), 3.64 (dd, *J* = 8.2, 5.1 Hz, 1 H), 2.98 (dd, *J* = 13.3, 5.1 Hz, 1 H), 2.79-2.61 (comp, 3 H), 2.18-2.02 (comp, 2 H), 1.46 (s, 9 H), 0.97-0.89 (comp, 12 H); ^{13}C NMR (100 MHz, CD_3OD) δ 176.4, 174.8, 173.2, 172.8, 171.9, 157.4, 131.5, 129.0, 116.4, 82.9, 59.9, 57.4, 51.3, 41.0, 37.9, 32.0, 31.9, 28.3, 19.8, 19.5, 18.6, 18.4; mass spectrum (ESI) *m/z* 550.3236 [$C_{27}H_{44}N_5O_7$ (M+H) requires 550.3235].



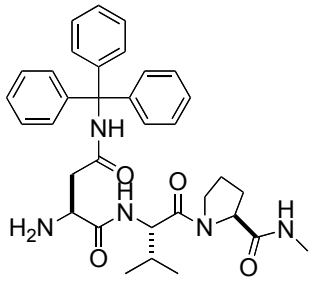
27

Tyrosyl-valyl-aspargyl-glycyl-NHM3 (27). Prepared in 99% yield by hydrogenolysis of **26** (80 mg, 0.134 mmol) in MeOH (25 mL) as a white solid. This material was shown to be >95% pure by ^{1}H NMR and was used without further purification: mp 98-100 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (d, *J* = 8.5 Hz, 2 H), 6.74 (d, *J* = 8.5 Hz, 2 H), 4.64 (app t, *J* = 6.5 Hz, 1 H), 4.13 (d, *J* = 6.8 Hz, 1 H), 3.87 (d, *J* = 17.1 Hz, 1 H), 3.81 (d, *J* = 17.1 Hz, 1 H), 3.76 (dd, *J* = 8.5, 5.1 Hz, 1 H), 3.03 (dd, *J* = 14.0, 5.1 Hz, 1 H), 2.86-2.70 (comp, 6 H), 2.11-2.03 (m, 1 H), 0.94 (app d, *J* = 6.8 Hz, 6 H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.7, 174.9, 173.6, 173.4, 172.1, 157.6, 131.5, 128.4, 116.5, 60.5, 57.0, 52.0, 43.7, 40.4, 37.3, 31.8, 26.3, 19.6, 18.8; mass spectrum (ESI) *m/z* 465.2456 [$C_{21}H_{33}N_6O_6$ (M+H) requires 465.2456].



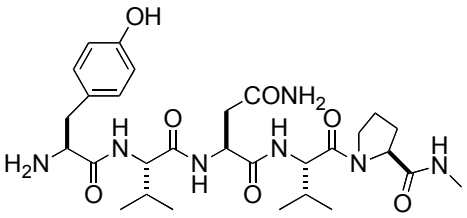
43

Valyl-prolyl-NHMe (43). Prepared in 85% yield by hydrogenolysis of **42** (75 mg, 0.208 mmol) in MeOH (2 mL) as a clear glass. This material was found to be >95% pure by ^{1}H NMR and used without further purification. ^{1}H NMR (400 MHz, CD_3OD) (rotamers 20:80) δ 4.45 (dd, *J* = 8.5, 3.1 Hz, 0.2 H), 4.36 (dd, *J* = 8.2, 5.1 Hz, 0.8 H), 3.76-3.59 (comp, 1.8 H), 3.57-3.46 (m, 0.2 H), 3.40 (d, *J* = 5.8 Hz, 0.8 H), 2.95 (d, *J* = 7.2 Hz, 0.2 H), 2.77 (s, 0.5 H), 2.72 (s, 2.5 H), 2.32-1.80 (comp, 5 H), 1.02-0.90 (comp, 6 H); ^{13}C NMR (100 MHz) δ 175.3, 174.2, 173.9, 173.6, 60.6, 60.5, 58.5, 57.8, 33.3, 33.1, 33.08, 30.6, 26.6, 26.3, 26.0, 23.4, 20.04, 19.95, 18.2, 17.5; mass spectrum (ESI) *m/z* 228.1717 [$C_{11}H_{22}N_3O_2$ (M+H) requires 228.1712].



45

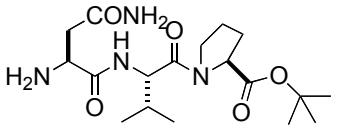
***N*-(Trityl)-asparagyl-valyl-prolyl-NHMe (45).** Prepared in 99% yield by hydrogenolysis of **44** (1.50 g, 2.09 mmol) in MeOH (30 mL) as a white solid. This material was found to be >90% pure by ^{1}H NMR and used without further purification: mp 114-116 ºC; ^{1}H NMR (400 MHz, CD_3OD) (rotamers 20:80) δ 7.30-7.16 (comp, 15 H), 4.52 (dd, *J* = 8.5, 3.1 Hz, 0.2 H), 4.46 (d, *J* = 7.4 Hz, 0.8 H), 4.33-4.25 (comp, 1 H), 3.88-3.80 (m, 0.8 H), 3.71-3.62 (comp, 1.8 H), 3.61-3.55 (m, 0.2 H), 3.52-3.45 (m, 0.2 H), 2.74-2.65 (comp, 4 H), 2.55 (dd, *J* = 15.5, 8.8 Hz, 1 H), 2.22-1.94 (comp, 3 H), 1.92-1.80 (comp, 2 H), 1.07-0.88 (comp, 6 H), ^{13}C NMR (100 MHz) δ 175.2, 174.6, 173.6, 172.9, 171.6, 171.4, 171.2, 144.9, 128.9, 127.6, 126.7, 70.5, 60.9, 60.6, 56.6, 56.3, 52.2, 52.1, 41.2, 41.2, 35.8, 32.0, 31.7, 30.7, 29.5, 25.7, 25.2, 24.9, 22.1, 18.7, 18.4, 17.5, 17.4; mass spectrum (ESI) *m/z* 584.3254 [$C_{34}H_{42}N_5O_4$ (M+H) requires 584.3231].



49

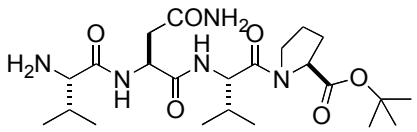
Tyrosyl-valyl-asparagyl-valyl-prolyl-NHMe (49). Prepared in 92% yield by hydrogenolysis of **48** (60 mg, 0.081 mmol) in MeOH (3 mL) as a white solid. This material was found to be >95% pure by ^{1}H NMR and used without further purification: mp 139-142 ºC; ^{1}H NMR (400 MHz, CD_3OD) (rotamers 20:80) δ 7.03 (d, *J* = 8.2 Hz, 2 H), 6.71 (d, *J* = 8.2 Hz, 2 H), 4.99-4.84 (app t, *J* = 6.8 Hz, 1 H), 4.54-4.49 (m, 0.2 H), 4.45 (d, *J* = 7.5 Hz, 0.8 H), 4.34 (dd, *J* = 8.2, 5.5 Hz, 0.8 H), 4.28 (d, *J* = 7.5 Hz, 0.2 H), 4.22-4.15 (m, 1 H), 3.87-3.77 (m, 0.8 H), 3.71-3.62 (m, 1 H), 3.59 (dd, *J* = 7.9, 4.8 Hz, 1 H), 3.53-3.44 (m, 0.2 H), 2.96 (dd, *J* = 13.7, 4.8 Hz, 1 H), 2.75-2.60 (comp, 6 H), 2.28-1.98 (comp, 4 H), 1.98-1.82 (comp, 2 H), 1.03-0.86 (comp, 12 H); ^{13}C NMR (100 MHz) δ 176.9, 174.9, 174.7, 173.2, 172.7, 172.1, 157.3, 131.5, 129.3, 116.4, 61.7, 59.8, 58.0, 57.5,

51.5, 41.2, 37.8, 32.1, 31.7, 30.7, 26.3, 26.0, 19.83, 19.81, 18.7, 18.6; mass spectrum (ESI) *m/z* 604.34532 [$C_{29}H_{46}N_7O_7$ (M+H) requires 604.347].



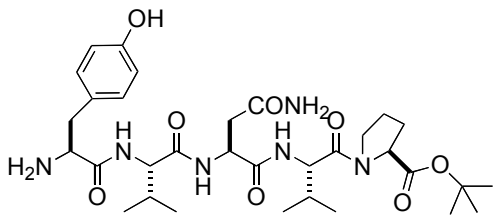
34

Asparagyl-valyl-prolyl-O^{t}Bu (34). Prepared in 94% yield by hydrogenolysis of **33** (740 mg, 1.43 mmol) in MeOH (25 mL) as a white solid. The crude product was purified by flash chromatography, eluting with CH_2Cl_2/CH_3OH (9:1): mp 37-39 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 9.2 Hz, 1 H), 6.33 (br s, 1 H), 5.74 (br s, 1 H), 4.55 (dd, *J* = 9.2, 6.7 Hz, 1 H), 4.36 (dd, *J* = 8.8, 5.3 Hz, 1 H), 3.85-3.78 (m, 1 H), 3.70 (m, 1 H), 3.67-3.62 (m, 1 H), 2.67 (dd, *J* = 15.1, 4.2 Hz, 1 H), 2.59 (dd, *J* = 15.1, 7.5 Hz, 1 H), 2.24-2.17 (m, 1 H), 2.15-2.08 (m, 1 H), 2.07-2.01 (m, 1 H), 2.01-1.87 (comp, 4 H), 1.45 (s, 9 H), 1.04 (d, *J* = 6.7 Hz, 3 H), 0.93 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz) δ 174.1, 173.6, 171.4, 170.6, 81.6, 60.0, 55.7, 52.8, 47.5, 40.6, 31.4, 29.3, 28.2, 25.2, 19.7, 18.0; mass spectrum (ESI) *m/z* 385.2442 [$C_{18}H_{33}N_4O_5$ (M+H) requires 385.2446].



36

Valyl-asparagyl-valyl-prolyl-O^{t}Bu (36). Prepared in 95% yield by hydrogenolysis of **35** (513 mg, 0.830 mmol) in MeOH (15 mL) as a white solid. This material was found to be >95% pure by ^{1}H NMR and used without further purification: mp 81-83 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 4.76 (dd, *J* = 7.2, 5.9 Hz, 1 H), 4.46 (d, *J* = 7.4 Hz, 1 H), 4.30 (dd, *J* = 8.6, 5.3 Hz, 1 H), 3.88-3.80 (m, 1 H), 3.70-3.62 (m, 1 H), 3.24 (d, *J* = 5.3 Hz, 1 H), 2.70 (dd, *J* = 15.5, 5.9 Hz, 1 H), 2.65 (dd, *J* = 15.5, 7.2 Hz, 1 H), 2.28-2.17 (m, 1 H), 2.15-1.86 (comp, 5 H), 1.45 (s, 9 H), 1.06-0.90 (comp, 12 H); ^{13}C NMR (125 MHz) δ 174.8, 173.6, 171.7, 171.6, 170.9, 81.4, 60.3, 60.0, 56.5, 50.2, 36.7, 31.7, 30.7, 29.0, 27.0, 24.7, 18.6, 18.5, 17.4, 16.5; mass spectrum (ESI) *m/z* 484.3130 [$C_{23}H_{42}N_5O_6$ (M+H) requires 484.3130].

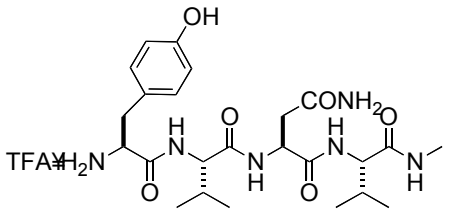


38

Tyrosyl-valyl-asparagyl-valyl-prolyl-O^{t}Bu (38). Prepared in 81% yield by hydrogenolysis of **37** (104 mg, 0.133 mmol) in MeOH (10 mL) as a white solid. The crude product was purified by flash chromatography, eluting with CH_2Cl_2/CH_3OH (9:1): mp 132-134 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.06-7.02 (comp, 2 H), 6.74-6.70 (comp, 2 H), 4.73 (app t, *J* = 6.8 Hz, 1 H), 4.44 (d, *J* = 7.6 Hz, 1 H), 4.29 (dd, *J* = 8.5, 5.1 Hz, 1 H), 4.18 (d, *J* = 6.8 Hz, 1 H), 3.85-3.78 (m, 1 H), 3.67-3.61 (comp, 2 H), 2.99 (dd, *J* = 13.8, 4.9 Hz, 1 H), 2.71 (dd, *J* = 13.8, 8.0 Hz, 1 H), 2.70 (dd, *J* = 15.6, 6.8 Hz, 1 H), 2.64 (dd, *J* = 15.6, 6.8 Hz, 1 H), 2.24-2.16 (m, 1 H), 2.14-1.86 (comp, 5 H), 1.44 (s, 9 H), 1.03 (d, *J* = 6.8 Hz, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 0.93 (d, *J* = 6.8 Hz, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H) ; ^{13}C NMR (125 MHz) δ 176.0, 174.7, 173.2, 172.8, 172.7, 171.9, 157.5, 131.5, 128.9, 116.5, 82.6, 61.4, 59.9, 57.7, 57.3, 51.5, 40.8, 37.7, 32.1, 31.8, 30.2, 28.2, 25.8, 19.8, 18.7, 18.6; mass spectrum (ESI) *m/z* 647.3767 [$C_{32}H_{51}N_6O_8$ (M+H) requires 647.3763].

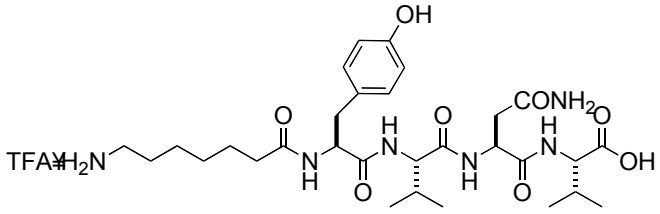
General Procedure for removal of *tert*-butyl carbamate from peptides. Preparation of 10, 13, 20, 24, 30, 40, 47.

Trifluoroacetic acid (TFA) (422 μL, 648 mg, 5.68 mmol) was added to a solution of *tert*-butyl carbamate (0.142 mmol) in CH_2Cl_2 (1.5 mL) with stirring. The resulting solution was stirred at room temperature for 4 h, whereupon the volatiles were removed under reduced pressure. The residue was triturated with Et_2O (4 x 2 mL) to produce a white solid, which was dried *in vacuo* to yield the trifluoroacetate (TFA) salt of the title compound. This material was shown to be >95% pure by ^{1}H NMR and was used without further purification.



30

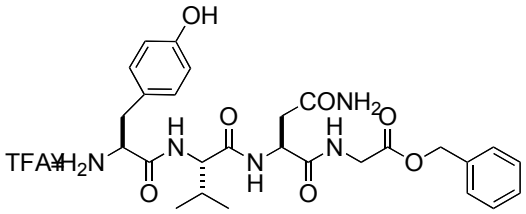
Tyrosyl-valyl-aspargyl-valyl-NHMe (30). Prepared from **29** according to the general procedure to yield 170 mg (99%) of the TFA salt of the title compound as a white solid. This material was shown to be >95% pure by ^{1}H NMR and was used without further purification: mp 259-260 ºC; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.31 (s, 1 H), 8.50 (d, 9.1 Hz, 1 H), 8.35 (d, J = 7.4 Hz, 1 H), 7.87-7.82 (m, 1 H), 7.69 (d, J = 8.9 Hz, 1 H), 7.43 (br s, 1 H), 7.05-7.01 (comp, 2 H), 6.98 (br s, 1 H), 6.71-6.67 (comp, 2 H), 4.63 (app dd, J = 14.1, 7.4 Hz, 1 H), 4.28 (dd, J = 9.1, 6.4 Hz, 1 H), 4.08-3.98 (comp, 2 H), 2.97 (dd, J = 14.4, 4.5 Hz, 1 H), 2.76 (dd, J = 14.4, 8.3 Hz, 1 H), 2.62-2.54 (comp, 4 H), 2.42 (dd, J = 15.5, 6.5 Hz, 1 H), 2.04-1.91 (comp, 2 H), 0.89-0.83 (comp, 6 H), 0.82-0.75 (comp, 6 H); ^{13}C NMR (125 MHz) δ 171.7, 170.9, 170.7, 170.2, 156.5, 130.4, 124.8, 115.3, 78.0, 57.6, 57.3, 53.4, 49.6, 36.8, 36.4, 31.1, 30.0, 25.4, 19.1, 19.1, 17.8, 17.6; mass spectrum (ESI) *m/z* 507.2926 [$C_{24}H_{39}N_6O_6$ (M+H) requires 507.2950].



20

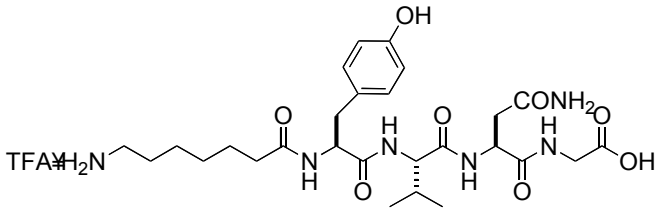
6-Amino hexylcarbonyl-tyrosyl-valyl-aspargyl-valyl-NHMe (20). Prepared from **19** according to the general procedure to yield 161 mg (96%) of the TFA salt of the title compound as a white solid. This material was shown to be >95% pure by ^{1}H NMR and was used without further purification: mp 226-227 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.09-7.05 (comp, 2 H), 6.72-6.67 (comp, 2 H), 4.81-4.76 (m, 1 H), 4.62 (dd, J = 10.3, 5.0 Hz, 1 H), 4.30 (d, J = 5.1 Hz, 1 H), 4.22 (d, J = 6.8 Hz, 1 H), 3.07 (dd, J = 14.4, 5.0 Hz, 1 H), 2.92-2.85 (comp, 2 H), 2.78-2.70 (comp, 2 H), 2.65 (dd, J = 15.7, 7.2 Hz, 1 H), 2.24-2.03 (comp, 4 H), 1.63-1.55 (comp, 2 H), 1.53-1.46 (comp, 2 H), 1.37-1.27 (comp, 2 H), 1.23-1.15 (comp, 2 H), 1.01-0.88 (comp, 12 H); ^{13}C NMR (125 MHz) δ 176.1, 174.9, 174.4, 174.1, 173.1, 172.9, 157.1, 131.3, 129.4, 116.2, 59.9, 59.1, 56.2, 51.4, 40.7,

37.9, 37.8, 36.5, 32.3, 31.8, 29.3, 28.3, 27.0, 26.5, 19.9, 19.6, 18.5, 18.3; mass spectrum (ESI) *m/z* 619.3460 [$C_{30}H_{47}N_6O_8$ (M–H) requires 619.3461].



10

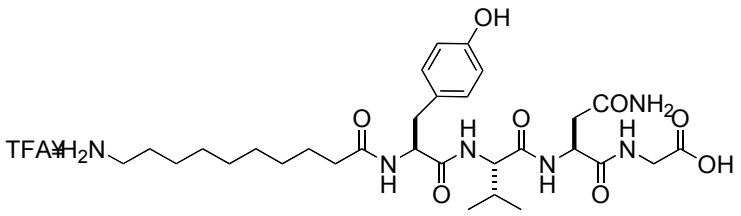
Tyrosyl-valyl-aspargyl-glycyl-OBn (10). Prepared from **9** according to the general procedure to yield 179 mg (90%) of the TFA salt of the title compound as a white solid. This material was shown to be >90% pure by ^{1}H NMR and was used without further purification: mp 187-190 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.38-7.26 (comp, 5 H), 7.13-7.08 (comp, 2 H), 6.81-6.76 (comp, 2 H), 5.15 (s, 2 H), 4.77 (dd, *J* = 7.2, 6.2 Hz, 1 H), 4.20 (d, *J* = 7.2 Hz, 1 H), 4.12 (dd, *J* = 8.9, 5.1 Hz, 1 H), 4.04 (d, *J* = 17.6 Hz, 1 H), 3.96 (d, *J* = 17.6 Hz, 1 H), 3.20 (dd, *J* = 14.5, 5.1 Hz, 1 H), 2.92 (dd, *J* = 14.5, 8.9 Hz, 1 H), 2.78 (dd, *J* = 15.7, 6.2 Hz, 1 H), 2.69 (dd, *J* = 15.7, 7.2 Hz, 1 H), 2.16-2.03 (m, 1 H), 1.03-0.93 (comp, 6 H); ^{13}C NMR (125 MHz) δ 174.7, 173.3, 172.8, 170.9, 170.2, 158.3, 137.2, 129.6, 129.3, 129.3, 126.0, 117.0, 67.9, 60.7, 55.7, 51.4, 42.2, 37.8, 37.8, 31.9, 19.7, 18.7; mass spectrum (ESI) *m/z* 542.2609 [$C_{27}H_{36}N_5O_7$ (M+H) requires 542.2627].



13

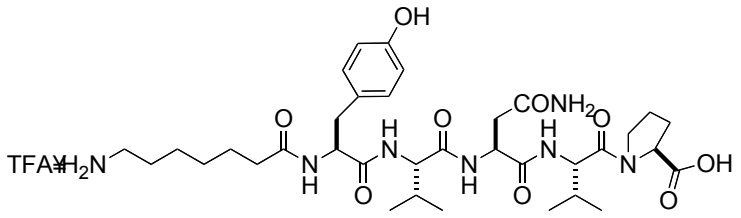
6-Amino hexylcarbonyl-tyrosyl-valyl-aspargyl-glycyl-OH (13). Prepared from **12** according to the general procedure to yield 108 mg (100%) of the TFA salt of the title compound as a white solid. This material was shown to be >90% pure by ^{1}H NMR and was used without further purification: mp 168-172 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.11-7.05 (comp, 2 H), 6.72-6.67 (comp, 2 H), 4.76 (app t, *J* = 7.1 Hz, 1 H), 4.63 (dd, *J* = 10.3, 4.8 Hz, 1 H), 4.15 (d, *J* = 6.5 Hz, 1 H), 3.95 (d, *J* = 17.8 Hz, 1 H), 3.87 (d, *J* = 17.8 Hz, 1 H), 3.08 (dd, *J* = 14.4, 4.8 Hz, 1 H), 2.93-2.73 (comp, 4 H), 2.69 (dd, *J* = 15.8, 7.1 Hz, 1 H), 2.20-2.04 (comp, 3 H), 1.63-1.54 (comp, 2 H), 1.53-

1.45 (comp, 2 H), 1.36-1.26 (comp, 2 H), 1.25-1.17 (comp, 2 H), 0.98-0.90 (comp, 6 H); ^{13}C NMR (100 MHz, CD_3OD) δ 176.1, 174.9, 174.5, 173.3, 173.2, 172.7, 157.1, 131.3, 129.3, 116.2, 60.4, 56.1, 51.4, 42.0, 40.6, 37.7, 36.5, 31.9, 29.3, 28.3, 27.0, 26.5, 19.7, 18.6; mass spectrum (ESI) *m/z* 579.3137 [$C_{27}H_{43}N_6O_8$ (M+H) requires 579.3157].



24

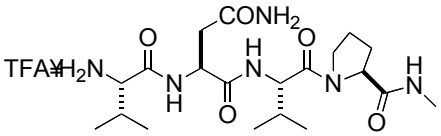
9-Amino nonylcarbonyl-tyrosyl-valyl-aspargyl-glycyl-OH (24). Prepared from **23** according to the general procedure to yield 85 mg (99%) of the TFA salt of the title compound as a white solid. This material was shown to be >90% pure by ^{1}H NMR and was used without further purification: mp 177-180 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, *J* = 8.5 Hz, 2 H), 6.68 (d, *J* = 8.5 Hz, 2 H), 4.77 (app t, *J* = 6.2 Hz, 1 H), 4.63 (dd, *J* = 9.9, 4.8 Hz, 1 H), 4.14 (d, *J* = 6.5 Hz, 1 H), 3.93 (d, *J* = 17.8 Hz, 1 H), 3.87 (d, *J* = 17.8 Hz, 1 H), 3.07 (dd, *J* = 14.4, 4.8 Hz, 1 H), 2.94-2.86 (comp, 3 H), 2.78 (dd, *J* = 15.8, 6.2 Hz, 1 H), 2.68 (dd, *J* = 15.7, 6.2 Hz, 1 H), 2.19-2.05 (comp, 3 H), 1.68-1.58 (comp, 2 H), 1.53-1.42 (comp, 2 H), 1.41-1.11 (comp, 10 H), 0.97 (d, *J* = 6.5 Hz, 3 H), 0.93 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (150 MHz, CD_3OD) δ 176.3, 174.9, 174.6, 173.2, 173.1, 173.0, 157.2, 131.3, 129.3, 116.2, 60.5, 56.1, 51.4, 42.3, 40.8, 37.7, 37.6, 36.8, 31.9, 30.21, 30.17, 30.1, 29.9, 28.6, 27.4, 26.8, 19.7, 18.6; mass spectrum (ESI) *m/z* 621.3608 [$C_{30}H_{49}N_6O_8$ (M+H) requires 621.3606].



40

6-Amino hexylcarbonyl-tyrosyl-valyl-aspargyl-valyl-prolyl-OH (40). Prepared from **39** according to the general procedure to yield 97 mg (98%) of the TFA salt of the title compound as a

white solid. This material was shown to be >90% pure by ^{1}H NMR and was used without further purification: mp 138-141 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, *J* = 8.5 Hz, 2 H), 6.70 (d, *J* = 8.5 Hz, 2 H), 4.74 (app t, *J* = 6.5 Hz, 1 H), 4.66 (dd, *J* = 10.3, 4.8 Hz, 1 H), 4.46 (d, *J* = 7.9 Hz, 1 H), 4.44-4.38 (m, 1 H), 4.19 (d, *J* = 6.8 Hz, 1 H), 3.88-3.80 (m, 1 H), 3.73-3.65 (m, 1 H), 3.09 (dd, *J* = 14.0, 4.8 Hz, 1 H), 2.92-2.85 (comp, 2 H), 2.80-2.70 (comp, 2 H), 2.66 (dd, *J* = 15.4, 6.5 Hz, 1 H), 2.29-1.94 (comp, 8 H), 1.65-1.56 (comp, 2 H), 1.54-1.46 (comp, 2 H), 1.37-1.28 (comp, 2 H), 1.24-1.15 (comp, 2 H), 1.03 (d, *J* = 6.8 Hz, 3 H), 1.00-0.90 (comp, 9 H); ^{13}C NMR (125 MHz, CD_3OD) δ 176.0, 175.2, 174.8, 174.3, 173.1, 172.6, 172.1, 157.1, 131.3, 129.4, 116.2, 60.5, 60.1, 57.8, 56.1, 51.5, 40.7, 37.9, 37.7, 36.5, 32.1, 31.9, 30.2, 29.3, 28.3, 27.0, 26.5, 25.9, 19.8, 19.6, 18.8, 18.6; mass spectrum (ESI) *m/z* 718.4136 [$C_{35}H_{56}N_7O_9$ (M+H) requires 718.4134].



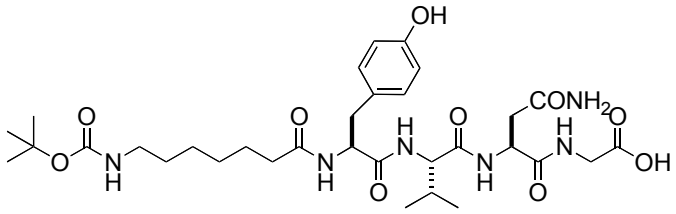
47

Valyl-asparagyl-valyl-prolyl-NHMe (47). Prepared from **46** according to the general procedure to yield 87 mg (88%) of the TFA salt of the title compound as a white solid. This material was shown to be >90% pure by ^{1}H NMR and was used without further purification: mp 148-150 ºC; ^{1}H NMR (400 MHz, CD_3OD) (rotamers 20:80) δ 4.96-4.90 (m, 1 H), 4.53 (d, *J* = 7.0 Hz, 1 H), 4.36-4.28 (m, 1 H), 3.87-3.79 (m, 1 H), 3.73-3.61 (comp, 1.8 H), 3.54-3.46 (m, 1 H), 2.81-2.67 (comp, 4 H), 2.60 (dd, *J* = 15.5, 7.6 Hz, 1 H), 2.30-2.01 (comp, 4 H), 2.00-1.83 (comp, 2 H), 1.10-0.90 (comp, 12 H); ^{13}C NMR (100 MHz, CD_3OD) δ 173.7, 173.2, 171.4, 171.1, 168.4, 60.7, 58.4, 56.5, 50.5, 36.6, 30.7, 30.4, 29.5, 25.2, 24.9, 18.7, 17.6, 17.3, 16.9; mass spectrum (ESI) *m/z* 441.2820 [$C_{20}H_{37}N_6O_5$ (M+H) requires 441.2837].

General procedure for the deprotection of *C*-terminal benzyl ester protected macrocycle precursors. Preparation of 12, 23.

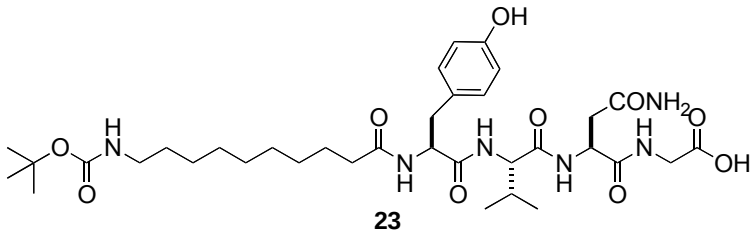
The benzyl ester (0.012 mmol) was dissolved in MeOH/H_2O (4 mL, 3:1) containing 10% Pd/C (1 mg, 10 mol %). The resulting mixture was purged four times with H_2, and the suspension as stirred under H_2 (1 atm) for 6 h. The mixture was filtered through a pad of celite, and the pad was washed with MeOH (5 mL) and H_2O (2 mL). The combined filtrate and washings were concentrated to dryness under reduced pressure. If the material was not found to be >95 % pure by

^{1}H NMR, the crude product was purified using flash chromatography, or preparative RP HPLC using a binary gradient of solvents, A and B (given).



12

(6-*N*-Boc-hexylcarbonyl)-tyrosyl-valyl-asparagyl-glycyl-OH (12). Prepared from **11** according to the general procedure to yield 106 mg (92%) of the title compound as a white solid. The crude material was purified by preparative RP HPLC with a gradient of 0% B to 55% B over 30 min: mp 212-214 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.11-7.05 (comp, 2 H), 6.72-6.66 (comp, 2 H), 4.75 (app t, *J* = 7.0 Hz, 1 H), 4.64 (dd, *J* = 9.9, 5.0 Hz, 1 H), 4.17-4.12 (m, 1 H), 3.95 (d, *J* = 18.5 Hz, 1 H), 3.86 (d, *J* = 18.5 Hz, 1 H), 3.06 (dd, *J* = 14.0, 5.0 Hz, 1 H), 3.01-2.85 (comp, 2 H), 2.82-2.74 (comp, 2 H), 2.68 (dd, *J* = 15.8, 7.0 Hz, 1 H), 2.20-2.04 (comp, 3 H), 1.63-1.08 (comp, 17 H), 0.98-0.91 (comp, 6 H); ^{13}C NMR (125 MHz, CD_3OD) δ 176.3, 174.9, 174.5, 173.2, 173.1, 172.7, 158.6, 157.2, 131.3, 129.3, 116.2, 79.8, 60.5, 56.0, 51.4, 42.0, 41.3, 37.7, 37.6, 36.8, 31.9, 30.8, 29.7, 28.8, 27.5, 26.9, 19.7, 18.6; mass spectrum (ESI) *m/z* 677.3516 [$C_{32}H_{49}N_6O_{10}$ (M–1) requires 677.3516].



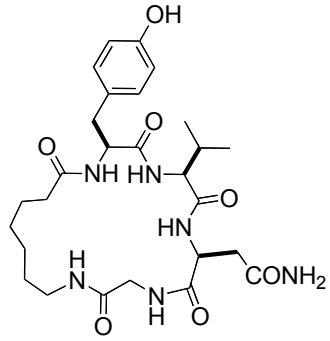
23

(9-*N*-Boc-nonylcarbonyl)-tyrosyl-valyl-asparagyl-glycyl-OH (23). Prepared from **22** according to the general procedure to yield 7 mg (78%) of the title compound as a white solid. It was found to be > 95% pure by ^{1}H NMR and used without further purification: mp 200-202 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.06 (d, *J* = 8.5 Hz, 2 H), 6.68 (d, *J* = 8.5 Hz, 2 H), 4.76 (app t, *J* = 6.1 Hz, 1 H), 4.63 (dd, *J* = 9.9, 4.9 Hz, 1 H), 4.14 (d, *J* = 6.8 Hz, 1 H), 3.92 (d, *J* = 17.8 Hz, 1 H), 3.86 (d, *J* = 17.8 Hz, 1 H), 3.06 (dd, *J* = 14.1, 4.9 Hz, 1 H), 3.00 (app t, *J* = 7.1 Hz, 1 H), 2.82-2.73

(comp, 2 H), 2.68 (dd, *J* = 15.5, 7.1 Hz, 1 H), 2.17-2.04 (comp, 3 H), 1.51-1.38 (comp, 13 H), 1.32-1.10 (comp, 10 H), 0.94 (app t, *J* = 6.8 Hz, 6 H); ^{13}C NMR (125 MHz) δ 176.4, 174.9, 174.6, 173.2, 173.0, 158.6, 157.2, 131.2, 129.3, 116.2, 79.8, 60.5, 56.0, 51.4, 42.4, 41.4, 37.7, 37.6, 36.9, 31.9, 31.0, 30.5, 30.4, 30.3, 30.1, 28.8, 27.9, 26.9, 19.7, 18.6; mass spectrum (ESI) *m/z* 719.3974 [$C_{35}H_{55}N_6O_{10}$ (M–H) requires 719.3974].

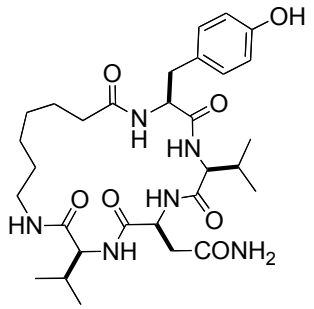
General procedure for macrocyclization of the free amino acid. Preparation of 14, 21, 25, 41.

A solution of the free amino acid (0.0386 mmol), pentafluorphenyl diphenylphosphinate (FDPP) (30 mg, 0.077 mmol), and NMM (20 mg, 21 μL, 0.193 mmol), in DMF (38 mL) was stirred at room temperature for 48 h. The volatiles were removed under reduced pressure, and the residue was purified via preparative RP HPLC with a binary gradient of solvents, A and B (given).



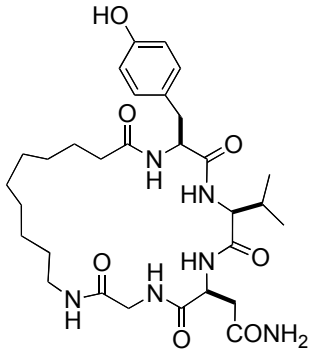
14

Cyclo-[6-amino-(hexylcarbonyl)-tyrosyl-valyl-asparagyl-glycyl] (14). Prepared from **13** according to the general procedure to yield 45 mg (53%) of the title compound as a white solid. The residue was purified via preparative RP HPLC with a gradient of 0% B to 50% B over 30 min: mp 160-164 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.08-7.04 (comp, 2 H), 6.71-6.67 (comp, 2 H), 4.46 (dd, *J* = 10.9, 4.0 Hz, 1 H), 4.40 (t, *J* = 6.9 Hz, 1 H), 4.33 (d, *J* = 5.9 Hz, 1 H), 4.08 (d, *J* = 17.1 Hz, 1 H), 3.53 (d, *J* = 17.1 Hz, 1 H), 3.34-3.28 (m, 1 H), 3.23 (dd, *J* = 14.4, 4.0 Hz, 1 H), 3.06 (ddd, *J* = 12.7, 7.9, 4.4 Hz, 1 H), 2.81 (dd, *J* = 14.4, 10.9 Hz, 1 H), 2.72-2.63 (comp, 2 H), 2.21-2.10 (comp, 2 H), 2.08-1.99 (m, 1 H), 1.73-1.43 (comp, 6 H), 1.40-1.31 (comp, 2 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 0.93 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz) δ 171.1, 174.0, 173.9, 173.7, 173.5, 171.8, 157.3, 131.0, 129.5, 116.3, 58.9, 57.5, 53.4, 43.8, 39.4, 37.4, 36.9, 36.8, 33.4, 29.1, 29.0, 26.6, 26.4, 19.6, 18.4; mass spectrum (ESI) *m/z* 559.2875 [$C_{27}H_{39}N_6O_7$ (M–H) requires 559.2870].



21

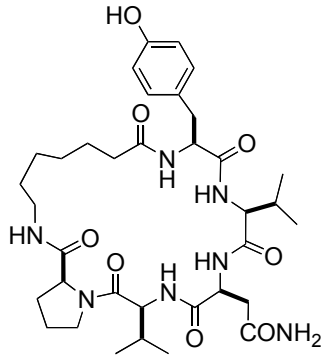
Cyclo-[6-amino-(hexylcarbonyl)-tyrosyl-valyl-asparagyl-valyl] (21). Prepared from **20** according to the general procedure to yield 39 mg (48%) of the title compound as a white solid. The residue was purified via preparative RP HPLC with a gradient of 0% B to 60% B over 30 min: mp 162-165 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.17-7.13 (comp, 2 H), 6.76-6.72 (comp, 2 H), 4.64 (dd, *J* =11.3, 3.8 Hz, 1 H), 4.49 (t, *J* = 5.3 Hz, 1 H), 4.17 (d, *J* = 8.5 Hz, 1 H), 3.95 (d, *J* = 5.0 Hz, 1 H), 3.54 (ddd, *J* = 13.5, 6.3, 3.2 Hz, 1 H), 3.35-3.30 (m, 1 H), 2.94 (dd, *J* = 16.0, 5.3 Hz, 1 H), 2.87 (ddd, *J* = 13.5, 9.1, 2.6 Hz, 1 H), 2.81 (dd, *J* = 14.9, 11.3 Hz, 1 H), 2.66 (dd, *J* = 16.0, 5.3 Hz, 1 H), 2.28 (ddd, *J* = 14.9, 10.9, 4.2 Hz, 1 H), 2.23-2.11 (comp, 3 H), 1.86-1.77 (m, 1 H), 1.61-1.49 (comp, 2 H), 1.46-1.38 (comp, 1 H), 1.38-1.26 (comp, 4 H), 1.07-1.02 (comp, 6 H), 1.00-0.95 (comp, 6 H); ^{13}C NMR (125 MHz) δ 177.4, 176.9, 175.1, 173.5, 173.3, 172.5, 157.4, 130.9, 129.3, 116.3, 62.8, 61.9, 56.5, 53.1, 39.9, 37.3, 35.7, 35.1, 32.5, 31.2, 30.4, 29.1, 27.1, 26.2, 19.9, 19.4, 19.3, 18.9; mass spectrum (ESI) *m/z* 603.3509 [$C_{30}H_{47}N_6O_7$ (M+H) requires 603.3506].



25

Cyclo-[9-amino-(nonylcarbonyl)-tyrosyl-valyl-asparagyl-glycyl] (25). Prepared in approximately 50% yield as a white solid from **24** according to the general procedure; purified via preparative RP HPLC with a gradient of 0% B to 65% B over 30 min. Could not remove the by-

product produced by FDPP, so the yield is not accurate and clean spectra could not be obtained. Carried on for phosphorylation so separation could be carried out at that stage.



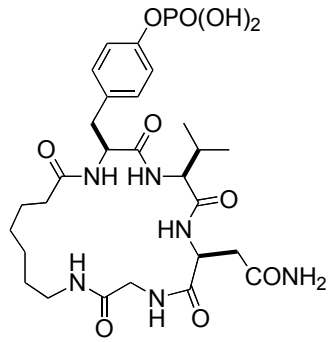
41

Cyclo-[6-amino-(hexylcarbonyl)-tyrosyl-valyl-asparagyl-valyl-prolyl] (41). Prepared from **40** according to the general procedure to yield 70 mg (84%) of the title compound as a white solid. The residue was purified via preparative RP HPLC with a gradient of 0% B to 60% B over 30 min: mp 171-172 ºC; ^{1}H NMR (500 MHz, CD_3OD) (rotamers 1:9) δ 7.10 (d, *J* = 8.6 Hz, 1.8 H), 7.05 (d, *J* = 8.6 Hz, 0.2 H), 6.69 (d, *J* = 8.6 Hz, 2 H), 4.68 (dd, *J* = 9.6, 5.6 Hz, 0.9 H), 4.56 (d, *J* = 8.7 Hz, 0.9 H), 4.53-4.49 (comp, 1 H), 4.43-4.39 (m, 0.1 H), 4.35 (dd, *J* = 8.2, 5.9 Hz, 0.9 H), 4.25 (d, *J* = 5.4 Hz, 0.1 H), 4.15 (d, *J* = 6.9 Hz, 0.1 H), 3.78-3.66 (comp, 3 H), 3.57-3.52 (m, 1 H), 3.15-3.09 (comp, 1 H), 3.02 (dd, *J* = 16.1, 7.2 Hz, 1 H), 2.92-2.76 (comp, 3 H), 2.28-2.00 (comp, 6 H), 1.96-1.84 (comp, 2 H), 1.64-1.22 (comp, 8 H), 1.94-0.88 (comp, 12 H); ^{13}C NMR (500 MHz, DMSO-d_6, 403 K) δ 171.9, 171.2, 171.1, 170.4, 170.0, 169.5, 169.0, 155.2, 129.1, 127.7, 114.5, 59.5, 55.2, 50.2, 46.3, 38.0, 36.0, 35.1, 30.2, 29.4, 27.9, 27.7, 24.9, 24.3, 18.6, 18.5, 17.1, 17.0; mass spectrum (ESI) *m/z* 698.3872 [$C_{35}H_{52}N_7O_8$ (M+H) requires 698.3884].

General procedure for *O*-phosphorylation of tyrosine. Preparation of 1–8.

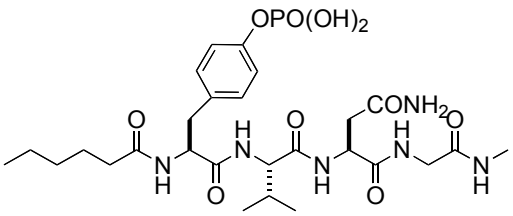
1-*H*-Tetrazole (11 mg, 0.155 mmol) and dibenzyl diisopropylphosphoramidite (**75**) (43 mg, 42 μL, 0.124 mmol) were added to a solution of the tyrosine-peptide (0.031 mmol) in DMF (10 mL) at 0 ºC, and the solution was stirred at 0 ºC for 1 h and at room temperature for 15 h. The solution was cooled to 0 ºC, and 6 M *tert*-butyl hydroperoxide in decane (119 μL) was added. The resulting solution was stirred at 0 ºC for 30 min and then at room temperature for 5 h, whereupon it was cooled to 0 ºC and 5% aqueous $NaHSO_3$ (1.4 mL) added. The solution was stirred at 0 ºC for 30 min and at room temperature for 2 h. The mixture was transferred to a separatory funnel containing H_2O

(10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL). DMF (5 mL) was added to the aqueous layer, which was again extracted with CH_2Cl_2 (15 mL); this was repeated one more time, whereupon a final extraction of the aqueous layer with CH_2Cl_2 (15 mL) was performed. The organic layers were combined and concentrated to dryness under reduced pressure. The residue was triturated with Et_2O (4 x 3 mL) to yield 24 mg of the crude benzyl protected phosphotyrosine ligand as a white solid. The crude product (24 mg, 0.0265 mmol) was dissolved in MeOH/H_2O (18 mL, 15:3) containing 10% Pd/C (3 mg), and the mixture was purged four times with H_2. The suspension was stirred under H_2 (1 atm) for 14 h. The mixture was filtered through a pad of celite, and the pad was washed with MeOH (10 mL). The combined filtrate and washings were concentrated under reduced pressure to give a solid that was purified via preparative RP HPLC using a binary gradient of solvents, A and B (given).



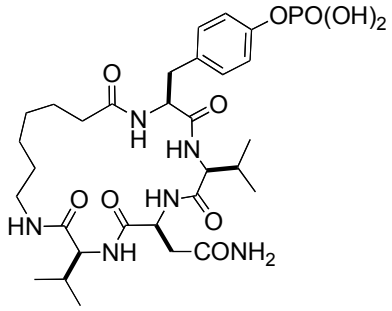
1

Cyclo-[6-amino-(hexylcarbonyl)-*O*-phosphotyrosyl-valyl-asparagyl-glycyl] (1). Prepared from **14** according to the general procedure to yield 16 mg (50%) of the title compound as a white solid over two-steps. The crude material was purified via preparative RP HPLC using a gradient of 0% B to 50% B over 30 min: mp 178-182 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.25-7.21 (comp, 2 H), 7.14-7.10 (comp, 2 H), 4.52 (dd, *J* = 11.1, 3.8 Hz, 1 H), 4.40 (t, *J* = 7.0 Hz, 1 H), 4.34 (d, *J* = 6.0 Hz, 1 H), 4.07 (d, *J* = 17.1 Hz, 1 H), 3.54 (d, *J* = 17.1 Hz, 1 H), 3.36-3.27 (comp, 2 H), 3.07 (ddd, *J* = 12.9, 7.8, 4.4 Hz, 1 H), 2.88 (dd, *J* = 14.4, 11.1 Hz, 1 H), 2.70-2.60 (comp, 2 H), 2.20-2.08 (comp, 2 H), 2.07-2.00 (m, 1 H), 1.73-1.45 (comp, 6 H), 1.40-1.32 (comp, 2 H), 0.98 (d, *J* = 6.8 Hz, 3 H), 0.94 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz) δ 177.1, 174.0, 173.5, 173.5, 171.8, 151.7, 135.3, 131.2, 121.4, 121.3, 59.0, 57.2, 53.4, 43.8, 39.5, 37.4, 36.9, 36.8, 33.5, 29.2, 29.0, 26.6, 26.4, 19.6, 18.5; mass spectrum (ESI) *m/z* 639.2538 [$C_{27}H_{40}N_6O_{10}P$ (M–H) requires 639.2550].



4

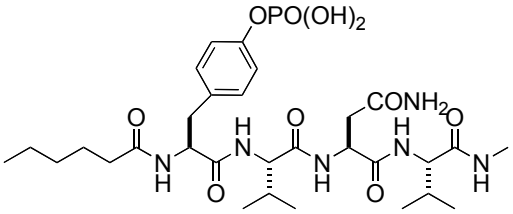
Pentylcarbonyl-*O*-phosphotyrosyl-valyl-asparagyl-glycl-NHMe (4). Prepared from **28** according to the general procedure to yield 10 mg (24%) of the title compound as a white solid over two-steps. The crude material was purified via preparative RP HPLC using a gradient of 0% B to 60% B over 30 min: mp 205-208 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.24-7.20 (comp, 2 H), 7.14-7.10 (comp, 2 H), 4.66 (dd, *J* 9.9, 5.2 Hz, 1 H), 4.60 (t, *J* = 6.5 Hz, 1 H), 4.10 (d, *J* = 6.9 Hz, 1 H), 3.85 (d, *J* = 17.0 Hz, 1 H), 3.79 (d, *J* = 17.0 Hz, 1 H), 3.10 (dd, *J* = 14.0, 5.2 Hz, 1 H), 2.86-2.72 (comp, 3 H), 2.70 (s, 3 H), 2.13 (td, *J* = 7.5, 1.6 Hz, 2 H), 2.09-2.02 (m, 1 H), 1.48 (p, *J* = 15.3, 7.5 Hz, 2 H), 1.31-1.23 (comp, 2 H), 1.21-1.14 (comp, 2 H), 0.98-0.92 (comp, 6 H), 0.86 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz) δ 176.4, 175.0, 174.4, 173.7, 173.5, 172.2, 151.7, 134.8, 131.4, 121.3, 121.2, 60.6, 55.7, 52.0, 43.8, 37.7, 37.3, 36.7, 32.4, 31.8, 26.6, 26.3, 23.4, 19.6, 18.7, 14.2; mass spectrum (ESI) *m/z* 643.2858 [$C_{27}H_{44}N_6O_{10}P$ (M+H) requires 643.2857].



2

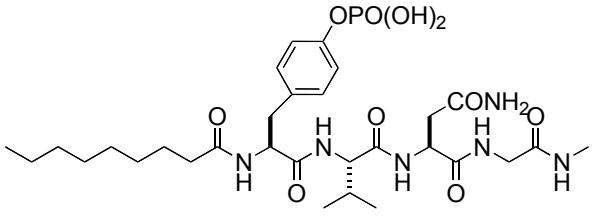
Cyclo-[6-amino-(hexylcarbonyl)-*O*-phosphotyrosyl-valyl-asparagyl-valyl] (2). Prepared from **21** according to the general procedure to yield 12 mg (37%) of the title compound as a white solid over two-steps. The crude material was purified via preparative RP HPLC using a gradient of 0% B to 50% B over 30 min: mp 199-202 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.35-7.30 (comp, 2 H), 7.18-7.13 (comp, 2 H), 4.69 (dd, *J* = 11.4, 3.3 Hz, 1 H), 4.48 (t, *J* = 5.1 Hz, 1 H), 4.17 (d, *J* = 8.5 Hz, 1 H), 3.96 (d, *J* = 5.1 Hz, 1 H), 3.54 (ddd, *J* = 13.4, 6.6, 3.5 Hz, 1 H), 3.42 (dd, *J* = 15.3, 3.3 Hz, 1 H), 2.96 (dd, *J* = 16.0, 5.1 Hz, 1 H), 2.92-2.84 (comp, 2 H), 2.66 (dd, *J* = 16.0, 5.1 Hz, 1 H), 2.28

(ddd, *J* = 14.4, 10.6, 4.1 Hz, 1 H), 2.22-2.09 (comp, 3 H), 1.87-1.77 (m, 1 H), 1.62-1.49 (comp, 2 H), 1.47-1.38 (comp, 1 H), 1.38-1.26 (comp, 4 H), 1.09-1.03 (comp, 6 H), 1.01-0.95 (comp, 6 H); ^{13}C NMR (125 MHz) δ 177.2, 177.0, 175.2, 173.5, 173.3, 172.5, 151.8, 135.0, 131.0, 121.4, 62.8, 61.9, 56.3, 53.1, 39.9, 37.4, 35.6, 35.1, 32.5, 31.2, 30.4, 29.1, 27.1, 26.2, 20.0, 19.4, 19.4, 18.9; mass spectrum (ESI) *m/z* 681.3044 [$C_{30}H_{46}N_6O_{10}P$ (M–H) requires 681.3013].



5

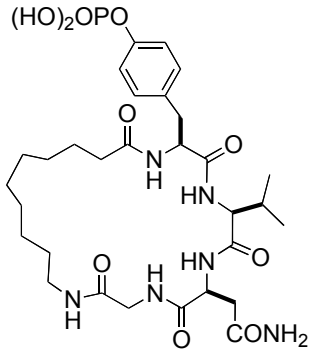
Pentylcarbonyl-*O*-phosphotyrosyl-valyl-asparagyl-valyl-NHMe (5). Prepared from **31** according to the general procedure to yield 4 mg (11%) of the title compound as a white solid over two-steps. The crude material was purified via preparative RP HPLC using a gradient of 0% B to 50% B over 30 min: mp 199-202 ºC; ^{1}H NMR (500 MHz, D_2O) δ 7.14-7.10 (comp, 2 H), 7.06-7.02 (comp, 2 H), 4.63 (app t, *J* = 7.0 Hz, 1 H), 4.53 (dd, *J* = 8.6, 6.4 Hz, 1 H), 3.99 (d, *J* = 7.8 Hz, 1 H), 3.95 (d, *J* = 7.0 Hz, 1 H), 3.00 (dd, *J* = 14.0, 6.4 Hz, 1 H), 2.87 (dd, *J* = 14.0, 8.6 Hz, 1 H), 2.74 (dd, *J* = 15.3, 7.0 Hz, 1 H), 2.67-2.61 (comp, 4 H), 2.12 (t, *J* = 7.2 Hz, 2 H), 2.06-1.98 (m, 1 H), 1.94-1.87 (m, 1 H), 1.44-1.37 (comp, 2 H), 1.18-1.12 (comp, 2 H), 1.08-1.02 (comp, 2 H), 0.85-0.77 (comp, 12 H), 0.74 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 172.3, 171.8, 171.3, 171.1, 170.8, 170.6, 150.2, 133.3, 130.0, 119.51, 119.47, 57.7, 57.2, 53.7, 49.6, 36.9, 36.2, 35.1, 31.0, 30.7, 29.9, 25.5, 24.9, 21.8, 19.2, 19.1, 17.8, 17.6, 13.8; mass spectrum (ESI) *m/z* 683.3152 [$C_{30}H_{48}N_6O_{10}P$ (M–H) requires 683.3170].



6

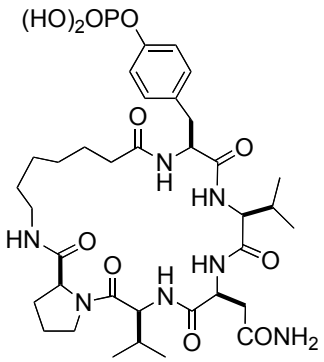
Octylcarbonyl-*O*-phosphotyrosyl-valyl-asparagyl-glycyl-NHMe (6). Prepared from **32** according to the general procedure to yield 8 mg (37%) of the title compound as a white solid over

two-steps. The crude material was purified via preparative RP HPLC using a gradient of 10% B to 70% B over 30 min: mp 220-221 ºC (dec); ^{1}H NMR (500 MHz, CD_3OD) δ 7.24-7.20 (comp, 2 H), 7.14-7.10 (comp, 2 H), 4.66 (dd, *J* = 9.6, 5.2 Hz, 1 H), 4.60 (app t, *J* = 6.5 Hz, 1 H), 4.10 (d, *J* = 6.9 Hz, 1 H), 3.86 (d, *J* = 17.0 Hz, 1 H), 3.79 (d, *J* = 17.0 Hz, 1 H), 3.10 (dd, *J* = 14.2, 5.1 Hz, 1 H), 2.83 (dd, *J* = 14.2, 9.6 Hz, 1 H), 2.81 (dd, *J* = 15.7, 6.5 Hz, 1 H), 2.76 (dd, *J* = 15.7, 6.5 Hz, 1 H), 2.70 (s, 3 H), 2.17-2.11 (comp, 2 H), 2.10-2.03 (m, 1 H), 1.52-1.44 (comp, 2 H), 1.34-1.16 (comp, 10 H), 0.98-0.92 (comp, 6 H), 0.88 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz) δ 176.4, 175.0, 174.3, 173.7, 173.4, 172.2, 151.7, 134.8, 131.4, 121.3, 121.2, 60.6, 56.0, 52.0, 43.8, 37.7, 37.3, 36.8, 33.0, 31.8, 30.4, 30.3, 30.2, 26.9, 26.3, 23.7, 19.6, 18.7, 14.4; mass spectrum (ESI) *m/z* 685.3326 [$C_{30}H_{50}N_6O_{10}P$ (M+H) requires 685.3326].



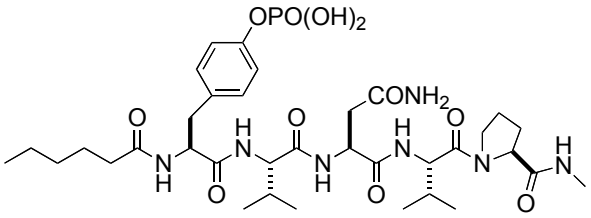
3

Cyclo-[9-amino-(nonylcarbonyl)-*O*-phosphotyrosyl-valyl-asparagyl-glycyl] (3). Prepared from **25** according to the general procedure to yield 9 mg (22%) of the title compound as a white solid over two-steps. The crude material was purified via preparative RP HPLC using a gradient of 0% B to 60% B over 30 min: mp 190-192 ºC; ^{1}H NMR (500 MHz, CD_3OD) δ 7.24 (d, *J* = 8.4 Hz, 2 H), 7.11 (dd, *J* = 8.4, 1.0 Hz, 2 H), 4.66 (dd, *J* = 10.0, 5.1 Hz, 1 H), 4.50 (app t, *J* = 6.6 Hz, 1 H), 4.07 (d, *J* = 7.3 Hz, 1 H), 3.89 (d, *J* = 17.1 Hz, 1 H), 3.75 (d, *J* = 17.1 Hz, 1 H), 3.30-3.20 (comp, 2 H), 3.14-3.06 (m, 1 H), 2.88 (dd, *J* = 14.2, 10.0 Hz, 1 H), 2.70 (d, *J* = 6.6 Hz, 2 H), 2.22-2.16 (m, 1 H), 2.13-2.00 (comp, 2 H), 1.70-1.62 (m, 1 H), 1.56-1.46 (comp, 3 H), 1.37-1.22 (comp, 10 H), 0.98 (d, *J* = 2.7 Hz, 3 H), 0.97 (d, *J* = 2.7 Hz, 3 H); ^{13}C NMR (125 MHz) δ 176.7, 174.4, 174.1, 173.9, 173.7, 171.4, 151.6, 135.3, 131.4, 121.3, 61.0, 55.8, 52.8, 43.8, 40.3, 36.8, 36.6, 36.2, 32.4, 29.6, 29.3, 29.1, 29.0, 27.0, 26.2, 19.5, 19.2; mass spectrum (ESI) *m/z* 681.3011 [$C_{30}H_{46}N_6O_{10}P$ (M–H) requires 681.3018].



7

Cyclo-[6-amino-(hexanylcarbonyl)-*O*-phosphotyrosyl-valyl-asparagyl-valyl-prolyl] (7). Prepared from **41** according to the general procedure to yield 9 mg (64%) of the title compound as a white solid over two-steps. The crude material was purified via preparative RP HPLC using a gradient of 0% B to 60% B over 30 min: mp 207-210 ºC; ^{1}H NMR (500 MHz, D_2O) (rotamers 20:80) δ 7.16 (d, *J* = 8.5 Hz, 1.6 H), 7.12 (d, *J* = 8.5 Hz, 0.4 H) 7.03 (comp, 2 H), 4.62 (comp, 1 H), 4.50-4.39 (comp, 2 H), 4.21 (app t, *J* = 7.3 Hz, 0.8 H), 4.14 (d, *J* = 6.2 Hz, 0.2 H), 4.02 (d, *J* = 6.8 Hz, 0.2 H), 3.86 (d, *J* = 6.2 Hz, 0.8 H) 3.72-3.66 (m, 0.8 H), 3.63-3.57 (m, 0.8 H), 3.52-3.46 (m, 0.2 H), 3.43-3.37 (m, 0.2 H), 3.31-3.24 (m, 0.8 H), 3.18 (dd, *J* = 14.5, 5.1 Hz, 0.8 H), 3.14-3.09 (comp, 0.4 H), 3.04-2.98 (m, 0.2 H), 2.96-2.84 (comp, 2.6 H), 2.79 (dd, *J* = 14.4, 10.4 Hz, 0.8 H), 2.73 (dd, *J* = 15.7, 5.2 Hz, 0.2 H), 2.67 (dd, *J* = 15.7, 8.7 Hz, 0.2 H), 2.20-1.90 (comp, 6 H), 1.87-1.70 (comp, 2 H), 1.50-1.34 (comp, 4 H), 1.24-1.08 (comp, 4 H), 0.91-0.76 (comp, 12 H) ; ^{13}C NMR (125 MHz) δ 177.3, 175.2, 174.0, 173.22, 173.19, 171.7, 171.0, 150.9, 132.2, 130.1, 120.4, 61.2, 60.8, 60.7, 60.4, 58.8, 53.8, 51.4, 48.2, 40.0, 39.7, 38.9, 36.8, 36.0, 35.3, 35.0, 30.8, 30.5, 29.2, 29.1, 28.2, 28.1, 27.9, 27.6, 26.3, 25.4, 25.2, 24.9, 24.7, 18.5, 18.42, 18.39, 18.1, 17.9, 17.5, 17.11, 16.99; mass spectrum (ESI) *m/z* 778.3546 [$C_{35}H_{53}N_7O_1P$ (M–H) requires 778.3552].



8

Pentylcarbonyl-*O*-phosphotyrosyl-valyl-asparagyl-valyl-prolyl-NHMe (8). Prepared from **50** according to the general procedure to yield 10 mg (47%) of the title compound as a white solid

over two-steps. The crude material was purified via preparative RP HPLC using a gradient of 10% B to 70% B over 30 min: mp 215-216 ºC (dec); ^{1}H NMR (500 MHz, D_2O) δ 7.07 (dd, *J* = 8.5 Hz, 2 H), 6.99 (d, *J* = 8.5 Hz, 2 H), 4.56 (app t, *J* = 7.3 Hz, 1 H), 4.52-4.45 (m, 1 H), 4.29 (d, *J* = 7.8 Hz, 1 H), 4.18 (app t, *J* = 7.6 Hz, 1 H), 3.96 (d, *J* = 7.8 Hz, 1 H), 3.74-3.65 (m, 1 H), 3.60-3.52 (m, 1 H), 3.00-2.92 (m, 1 H), 2.84-2.77 (m, 1 H), 2.67-2.53 (comp, 5 H), 2.16-1.70 (comp, 8 H), 1.38-1.29 (comp, 2 H), 1.14-1.05 (comp, 2 H), 1.02-9.95 (comp, 2 H), 0.86-0.66 (comp, 15 H); ^{13}C NMR (500 MHz, D_2O) δ 177.4, 174.8, 174.4, 173.4, 172.7, 172.0, 171.9, 151.0, 132.2, 130.7, 120.6, 61.1, 59.3, 57.3, 54.9, 50.6, 48.4, 36.4, 36.3, 35.5, 30.6, 30.5, 30.0, 29.6, 26.0, 25.1, 24.7, 21.8, 18.52, 18.50, 17.7, 17.6, 13.3; mass spectrum (ESI) *m/z* 780.3703 [$C_{35}H_{55}N_7O_{11}P$ (M–H) requires 780.3689].

Table S1. X-ray diffraction data and refinement statistics for the Grb2 SH2 domain in complex with **7** and **8**.

Data Set	Grb2 SH2/ **2**	Grb2 SH2/ **7**	Grb2 SH2/ **8**
Data Collection			
Total reflections[a]	145812 / 145072	429544 / 428917	208429 / 208411
Unique reflections[a]	25618 / 23689	73832 / 70926	9451 / 9416
Resolution range (Å) (outer shell)	50.00–2.02 (2.09–2.02)	50.00–1.7 (1.75–1.69)	50.00–1.9 (1.93–1.86)
Completeness, % (outer shell)	99.7 (99.8)	91.3 (69.4)	99.6 (97.0)
Data redundancy (outer shell)	5.7 (5.4)	5.8 (4.1)	22.1 (19.5)
R_{sym}[b] (outer shell)	0.098 (0.355)	0.066 (0.275)	0.066 (0.152)
I/ σ(I)	9.9 (2.4)	24.5 (3.7)	60.6 (21.1)
Refinement			
No. reflections[c]	23058 / 2529	43604 / 2376	7251 / 385
R_{cryst}[d] / R_{free}, %	18.0 / 22.2	18.0 / 22.3	18.7 / 22.4
RMS dev. from ideal values			
Bond lengths (Å)	0.0057	0.0173	0.0158
Bond angles (deg)	1.24	1.74	1.65
B-factor restraints (Å^2)			
Backbone bonds (RMS / σ)	1.34 / 1.5	1.18 / 1.5	1.26 / 1.5
Side-chain bonds (RMS / σ)	1.99 / 2.0	1.97 / 2.0	1.99 / 2.0
Backbone angles (RMS / σ)	2.10 / 2.0	1.80 / 2.0	1.93 / 2.0
Side-chain angles (RMS / σ)	2.83 / 2.5	2.69 / 2.5	2.97 / 2.5
Crystal			
Space group	$P3_221$	C_2	$P4_12_12$
Cell dimensions			
a, b, c (Å)	83.16, 83.16, 96.01	83.22, 141.32, 62.45	49.24, 49.24, 86.13
α, β, γ (deg.)	90.0, 90.0, 120.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0
No. complexes in asym. unit	3	6	1
Solvent content, %	46.8	47.7	38.7
Matthews Coef; V_m (Å^3/Da)	2.31	2.35	2.01
Bulk solvent b-factor (Å^2)	68.4	23.9	24.6
Final Model			
No. protein residues	294	628	99
No. protein atoms	2430	5185	819
No. ligand atoms	141	324	54
No. water molecules	372	728	107
No. solvent molecules	0	10	1
No. res. in alt. conformations	0	0	0

[a] no. reflections / no. for which $I/\sigma(I) \geq 1.0$

[b] $R_{sym} = \sum |I_i - \langle I \rangle| / \sum I_i$, where I_i is the scaled intensity of the *i*th observation and $\langle I \rangle$ is the mean intensity for that reflection.

[c] no. reflections used in refinement; working set / free R set

[d] $R_{cryst} = \sum ||F_{calc}| - |F_{obs}|| / \sum |F_{obs}|$, where F_{calc} and F_{obs} are the calculated and observed structure factor amplitudes, respectively.

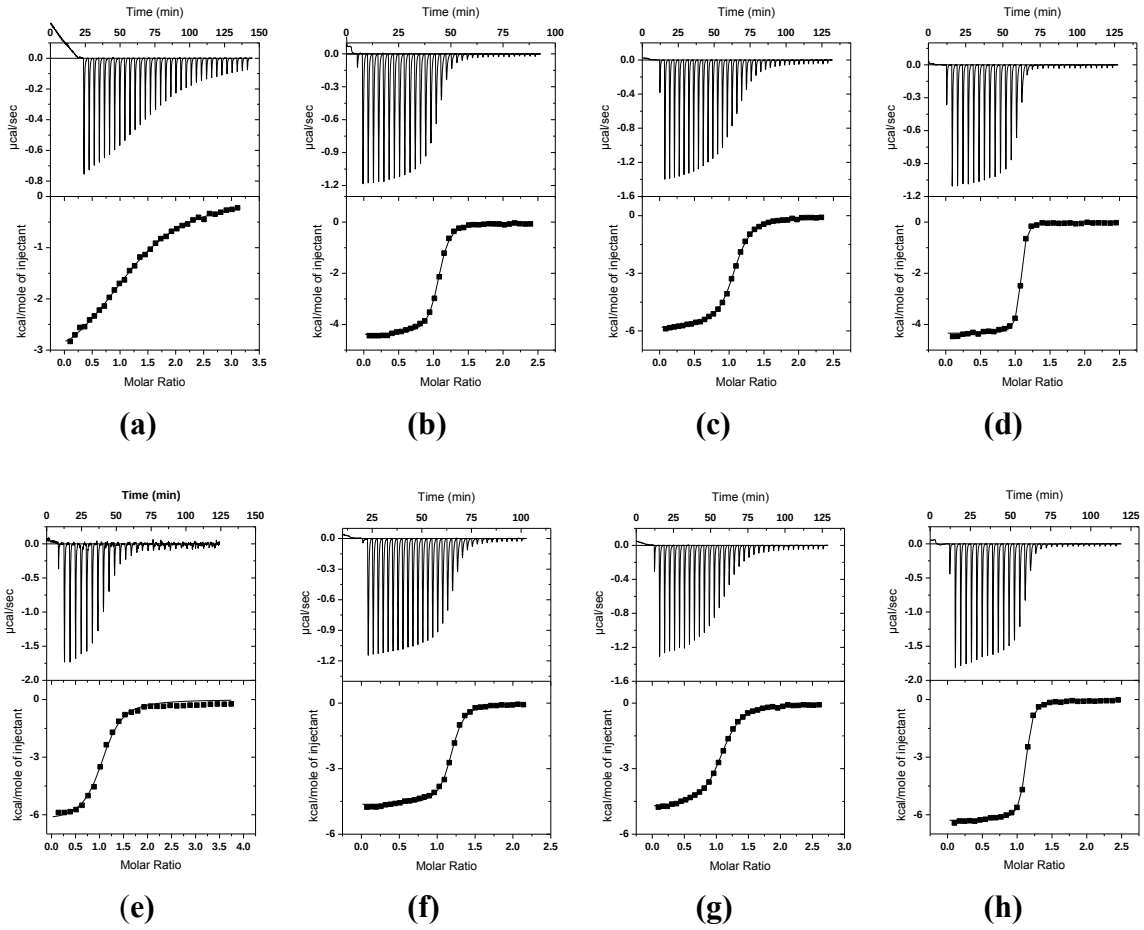
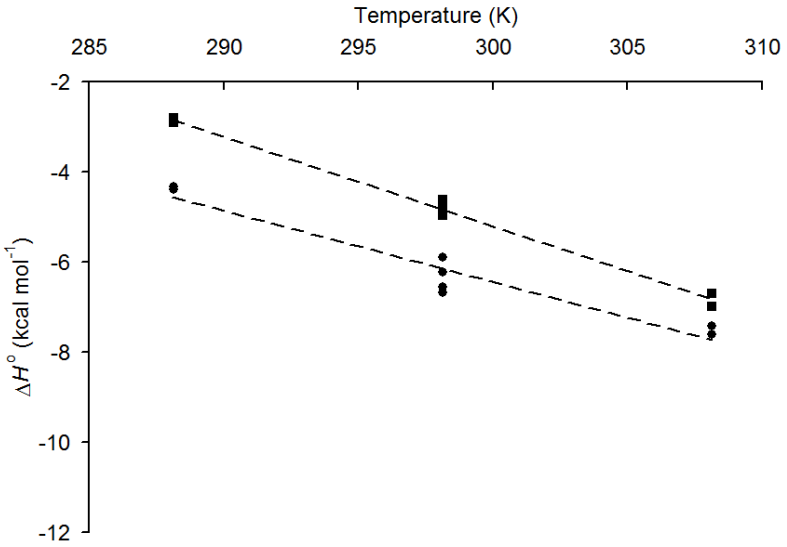
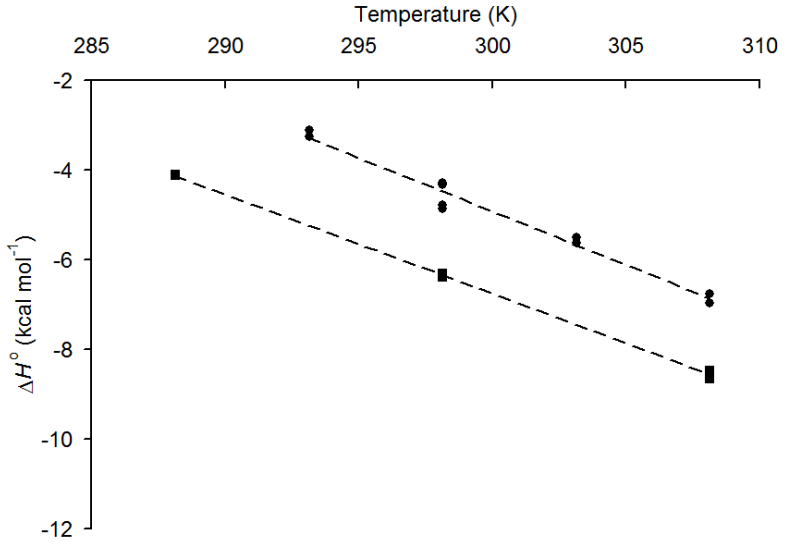


Figure S1. Typical ITC traces obtained for the interactions between phosphotyrosine-derived ligands and monomeric Grb2 SH2 domain in HEPES buffer (50 mM) (pH = 7.45±0.05) and NaCl (150 mM). **Top of Graph:** Titration data obtained from 30–35 x 7–9 µL injections of ligand, giving the exothermic heats of complexation (µcal/s). The baseline at 0.0 µcal/s was obtained from the raw data by subtracting pre- and post-injection data. **Bottom of Graph:** Integrated ITC data, giving heats of complexation per mol of ligand injected. Data were corrected for heats of dilution by subtracting a blank titration, acquired by injecting an equal amount of ligand into buffer. The solid line was obtained by applying a nonlinear least squares fit to solve for the thermodynamic parameters n, (number of binding sites), K_a and $\Delta H°$. (a) Data for ligand **1**. (b) Data for ligand **2**. (c) Data for ligand **3**. (d) Data for ligand **7**. (e) Data for ligand **4**. (f) Data for ligand **5**. (g) Data for ligand **6**. (h) Data for ligand **8**.

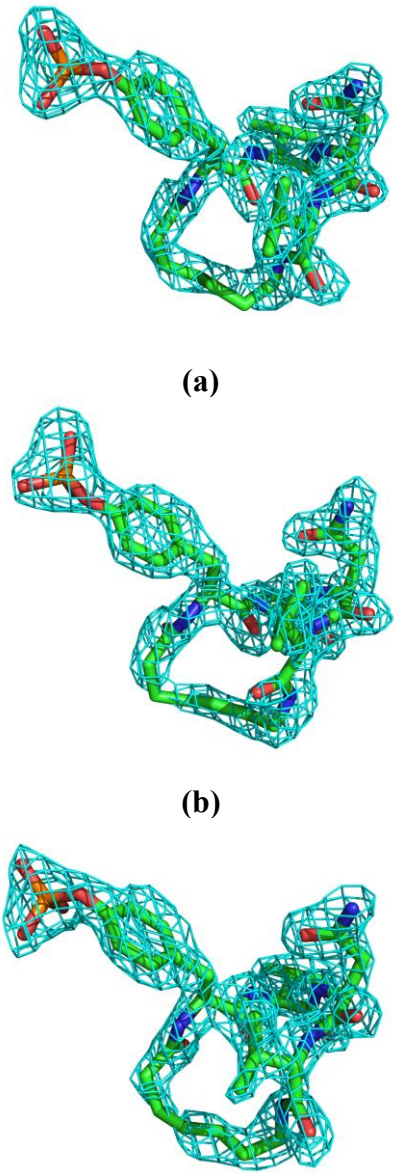


(a)



(b)

Figure S2. ΔH^0 of binding as a function of temperature for macrocyclic (circles) and acyclic (squares) ligand pairs **3**/**6** (a) and **7**/**8** (b) in which the slope of the lines is the change in heat capacity, ΔC_p, on binding.



(a)

(b)

(c)

Figure S3. Electron density difference omit maps showing the structure of **2** bound to the Grb2 SH2 domain. The maps, indicated by the cyan wire mesh, are unweighted F_o-F_c omit maps contoured at +3 σ, showing only the portion within 1.0–1.5 Å of each ligand atom in the complexes for clarity a) Complex **a** of the domain with **2**. b) Complex **b** of the domain with **2**. c) Complex **c** of the domain with **2**.

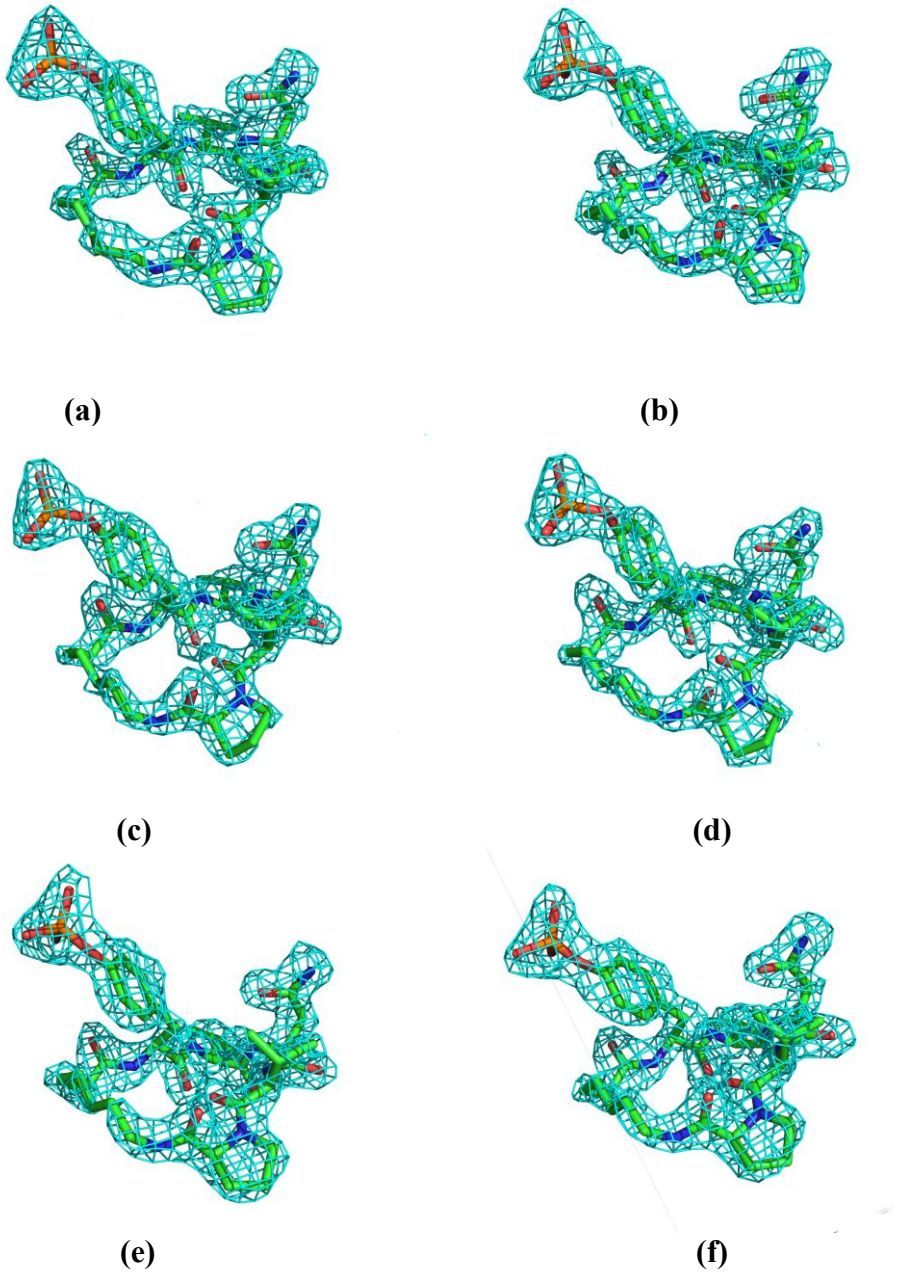


Figure S4. Electron density difference omit maps showing the structure of **7** bound to the Grb2 SH2 domain. The maps, indicated by the cyan wire mesh, are unweighted F_o-F_c omit maps contoured at +3 σ, showing only the portion within 1.0–1.5 Å of each ligand atom in the complexes for clarity a) Complex **a** of the domain with **7**. b) Complex **b** of the domain with **7**. c) Complex **c** of the domain with **7**. d) Complex **d** of the domain with **7**. e) Complex **e** of the domain with **7**. f) Complex **f** of the domain with **7**.

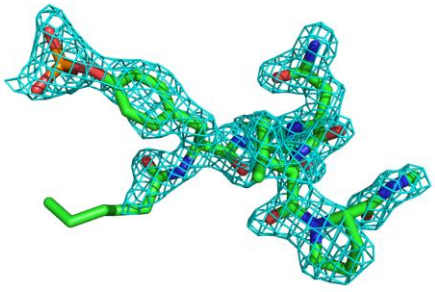
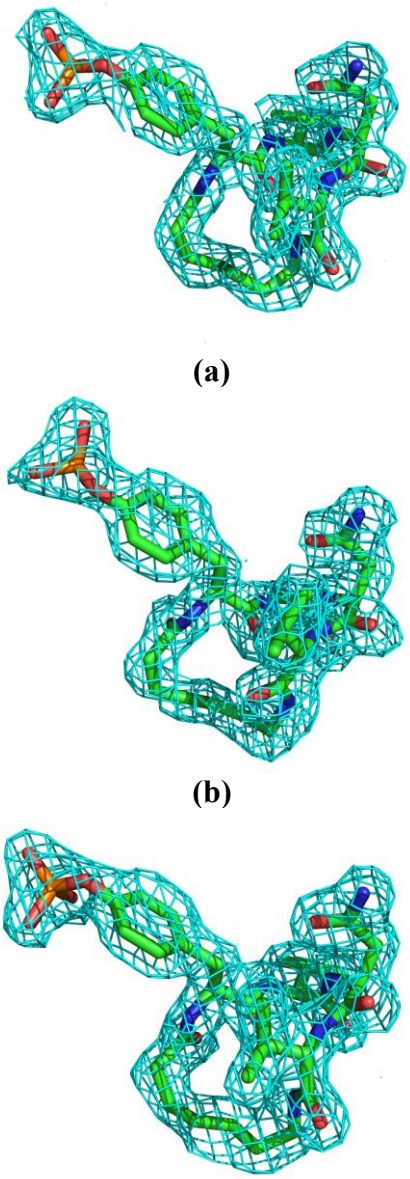


Figure S5. Electron density difference omit map showing the structure of **8** bound to the Grb2 SH2 domain. The map, indicated by the cyan wire mesh, is an unweighted F_o-F_c omit map contoured at +3 σ, showing only the portion within 1.0–1.5 Å of each ligand atom in the complexes for clarity.



(a)

(b)

(c)

Figure S6. Electron density difference maps showing the structure of **2** bound to the Grb2 SH2 domain. The maps, indicated by the cyan wire mesh, are unweighted $2F_o$-F_c maps contoured at +1 σ, showing only the portion within 1.0–1.5 Å of each ligand atom in the complexes for clarity a) Complex **a** of the domain with **2**. b) Complex **b** of the domain with **2**. c) Complex **c** of the domain with **2**.

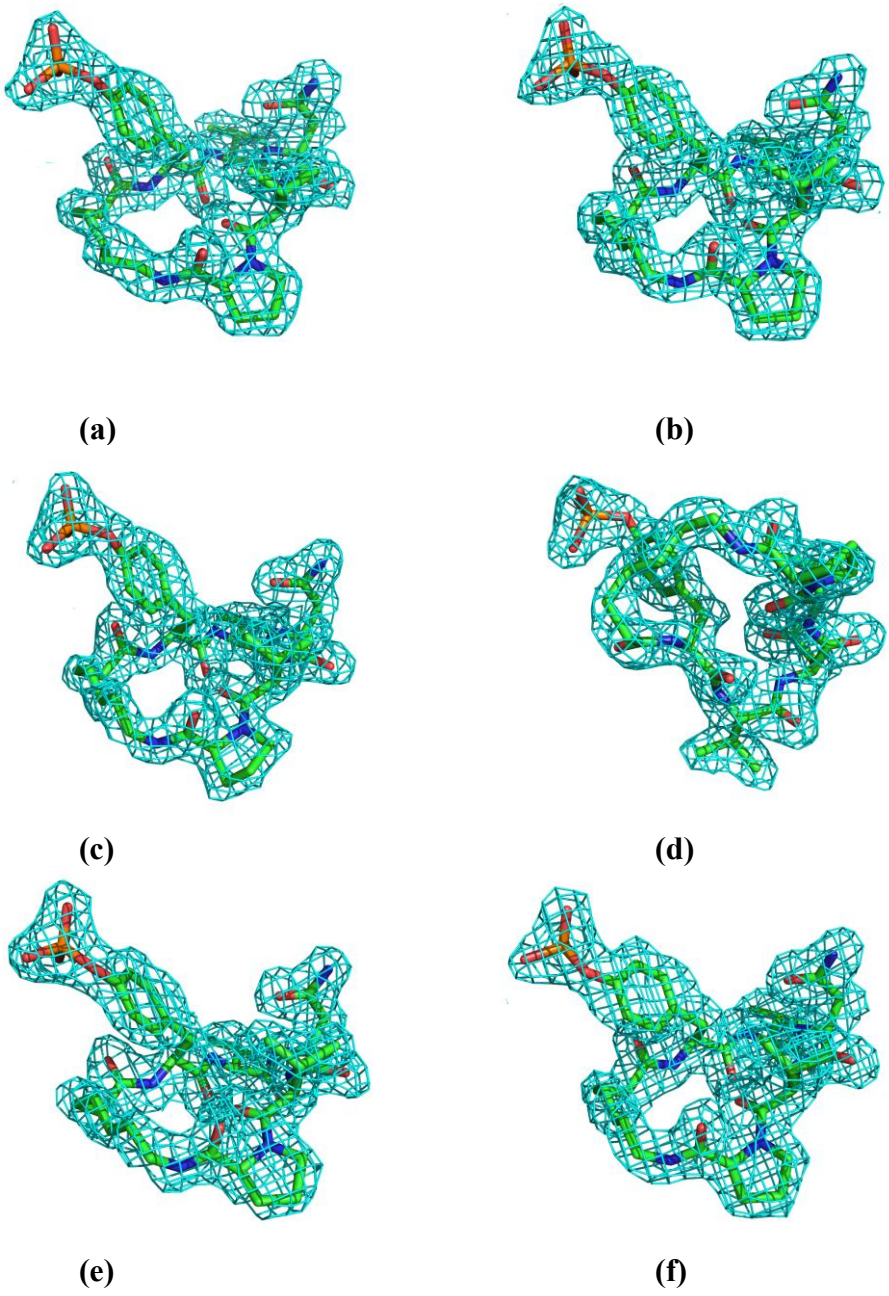


Figure S7. Electron density difference maps showing the structure of **7** bound to the Grb2 SH2 domain. The maps, indicated by the cyan wire mesh, are unweighted $2F_o$-F_c maps contoured at +1 σ, showing only the portion within 1.0–1.5 Å of each ligand atom in the complexes for clarity a) Complex **a** of the domain with **7**. b) Complex **b** of the domain with **7**. c) Complex **c** of the domain with **7**. d) Complex **d** of the domain with **7**. e) Complex **e** of the domain with **7**. f) Complex **f** of the domain with **7**.

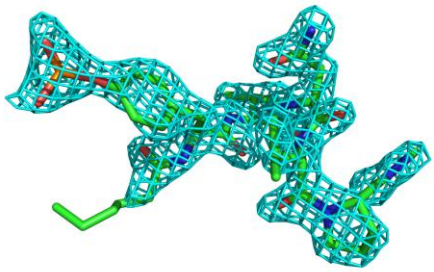


Figure S8. Electron density difference map showing the structure of **8** bound to the Grb2 SH2 domain. The map, indicated by the cyan wire mesh, is an unweighted $2F_o$-F_c maps contoured at +1 σ, showing only the portion within 1.0–1.5 Å of each ligand atom in the complexes for clarity.

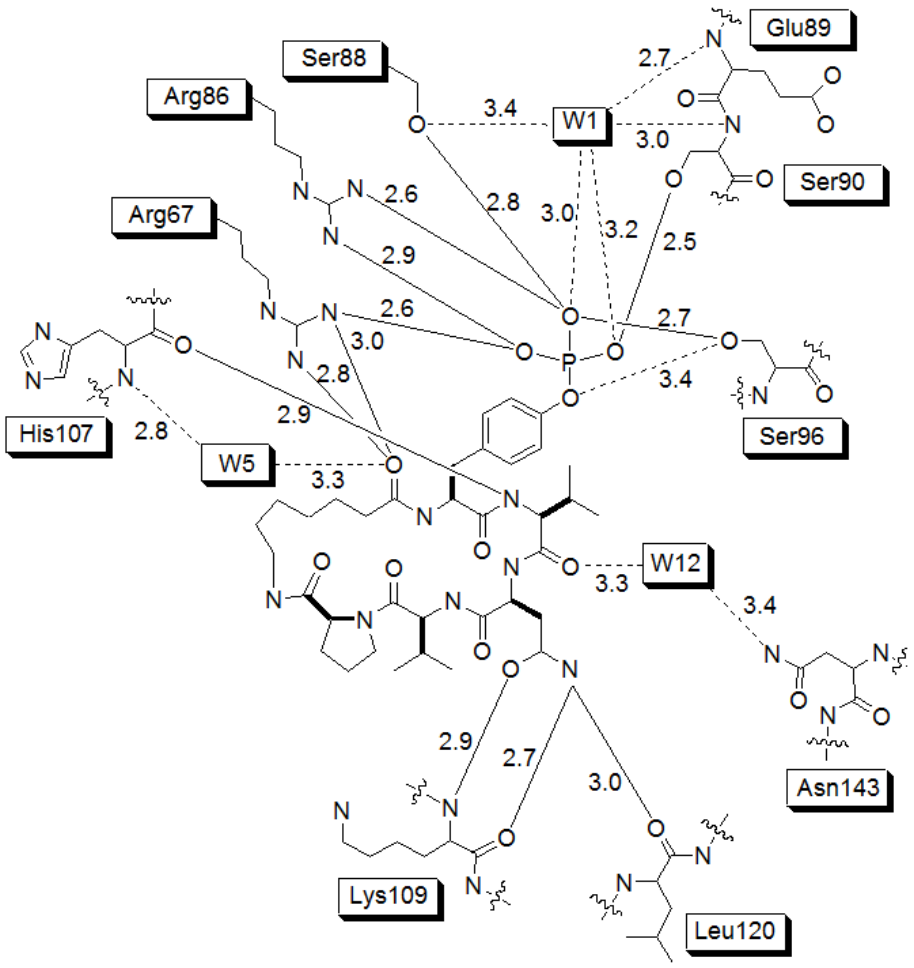


Figure S9. Contact diagram of the **a** complex of **7** bound to the Grb2 SH2 domain showing all direct and single water-mediated polar protein-ligand contacts.

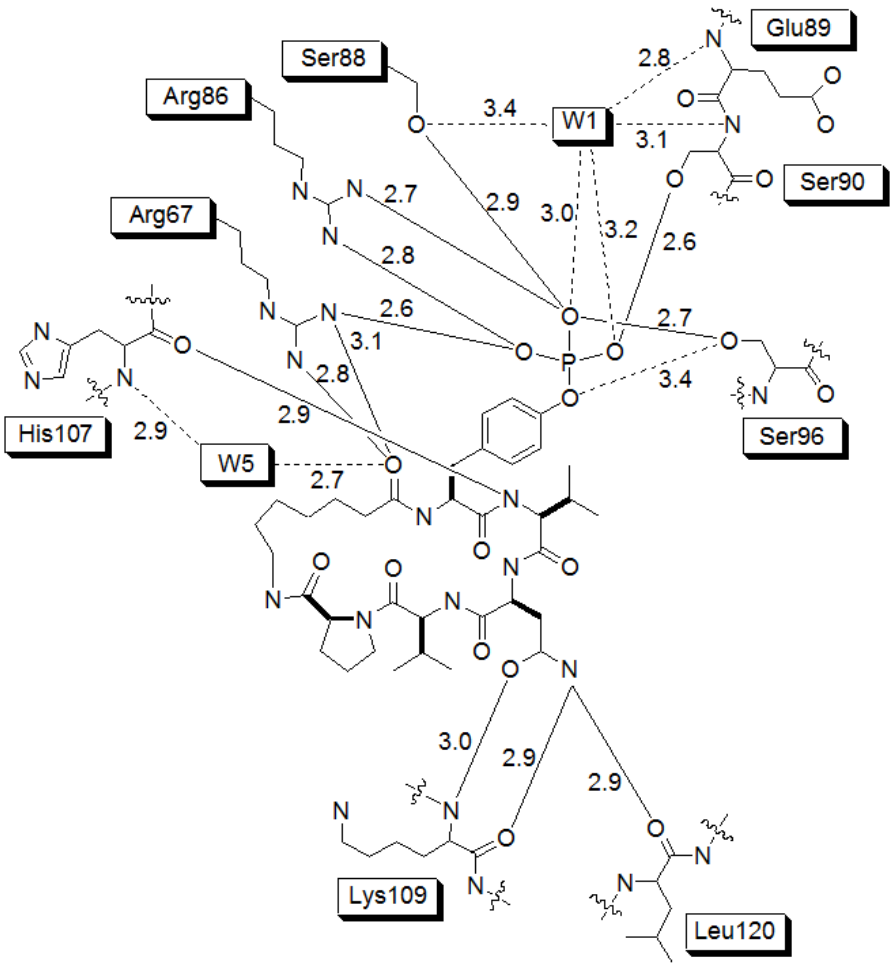


Figure S10. Contact diagram of the **b** complex of **7** bound to the Grb2 SH2 domain showing all direct and single water-mediated polar protein-ligand contacts.

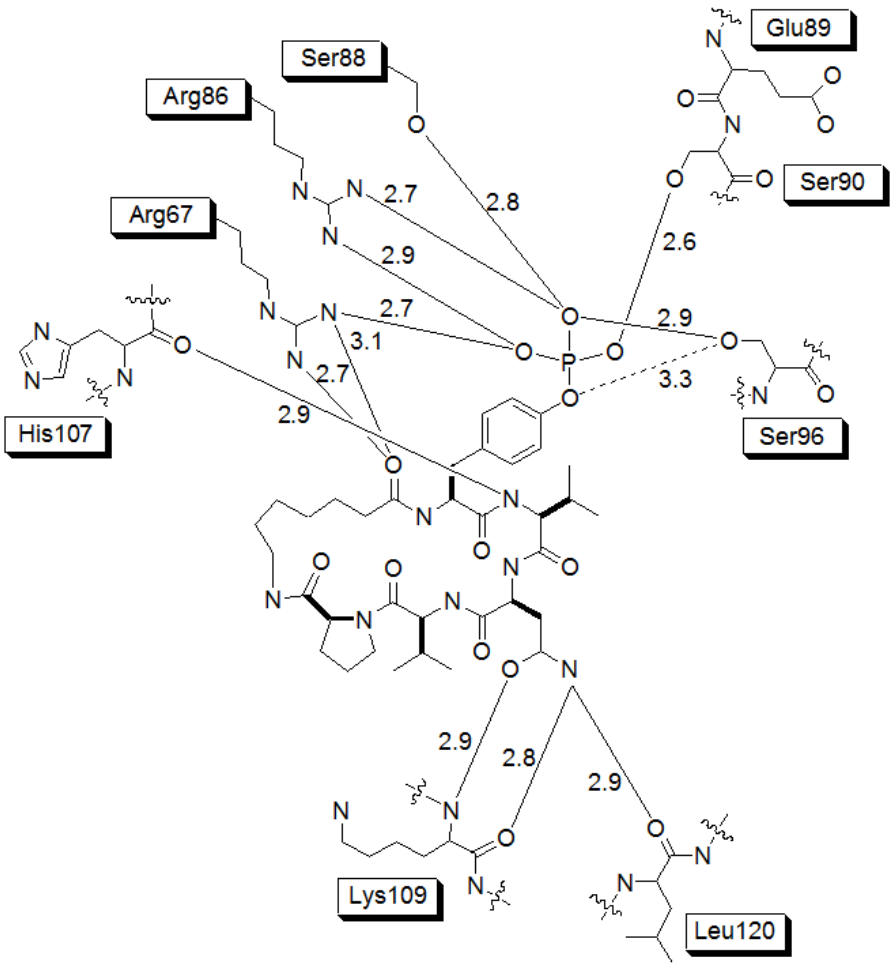


Figure S11. Contact diagram of the **c** complex of **7** bound to the Grb2 SH2 domain showing all direct and single water-mediated polar protein-ligand contacts.

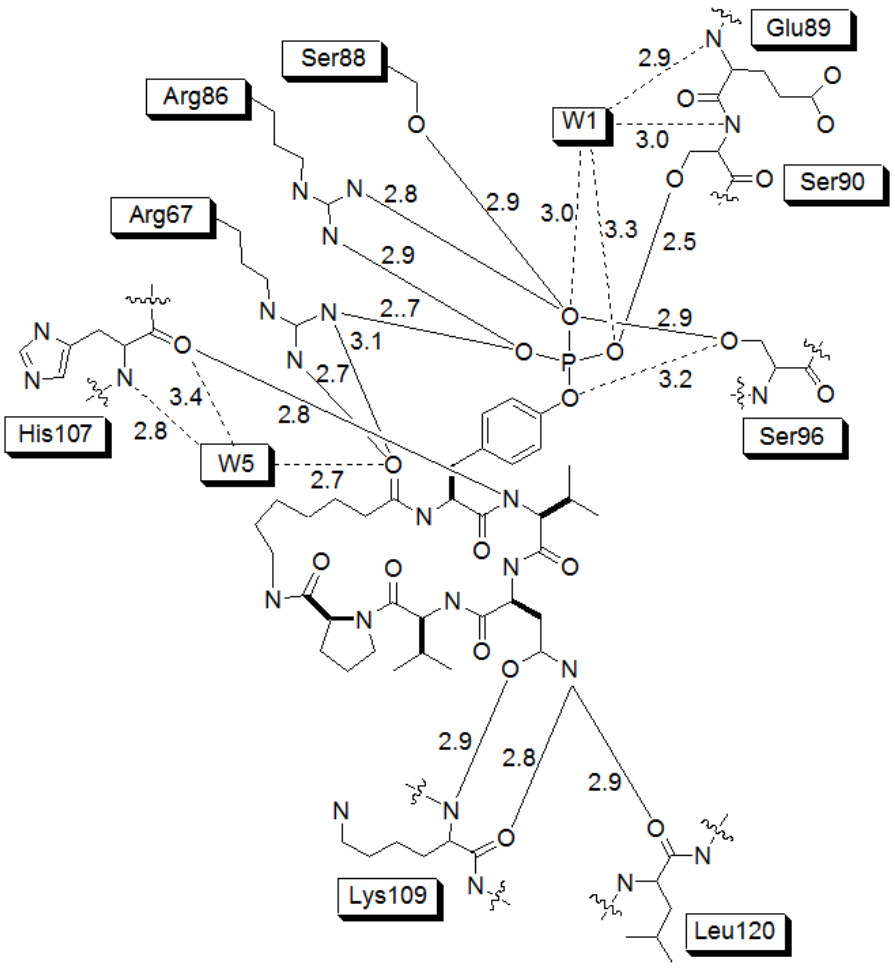


Figure S12. Contact diagram of the **d** complex of **7** bound to the Grb2 SH2 domain showing all direct and single water-mediated polar protein-ligand contacts.

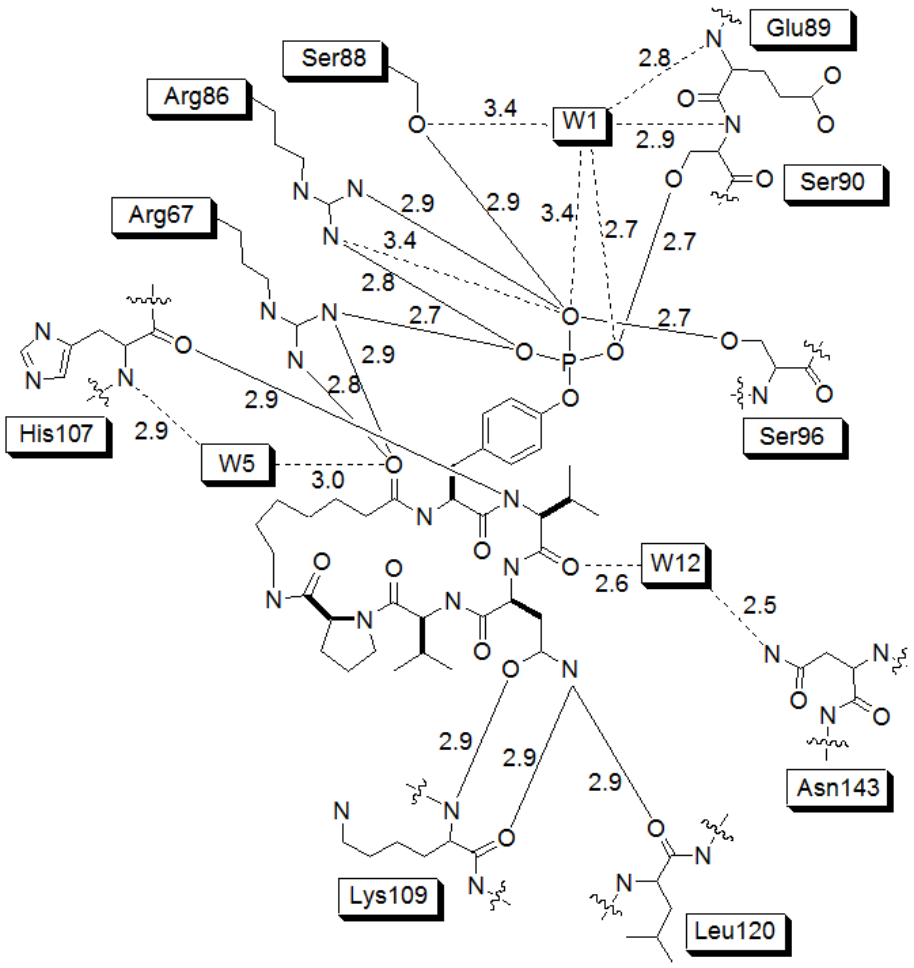


Figure S13. Contact diagram of the **e** complex of **7** bound to the Grb2 SH2 domain showing all direct and single water-mediated polar protein-ligand contacts.

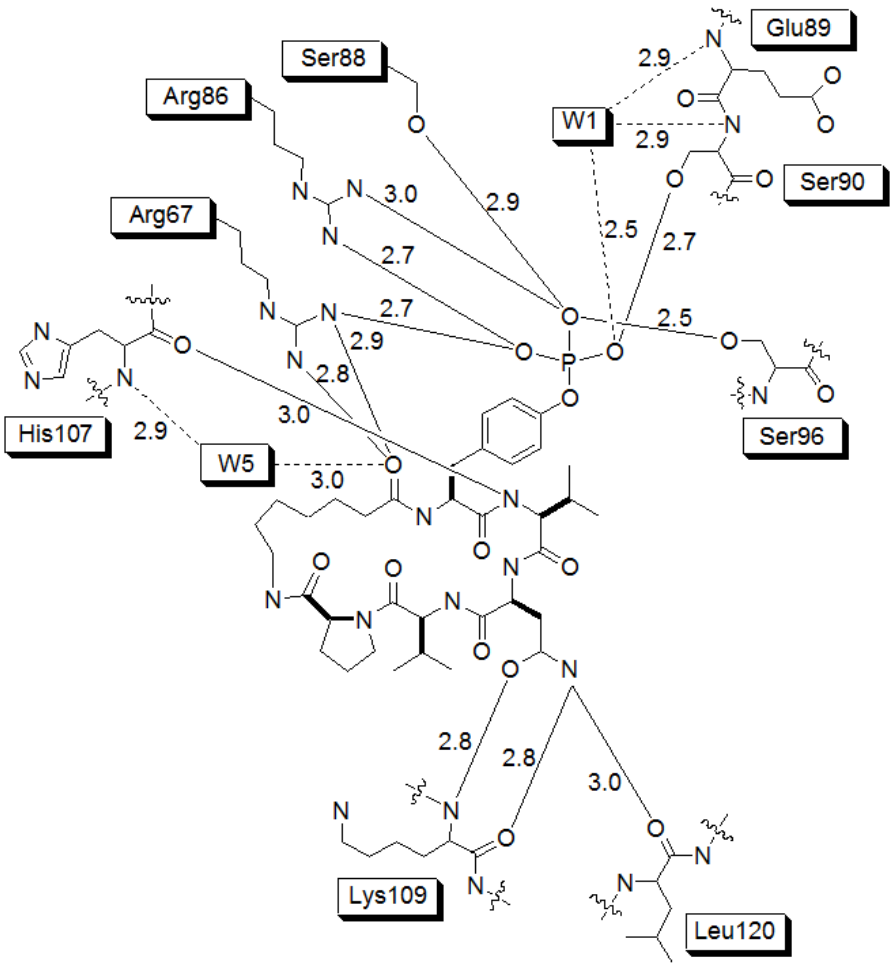


Figure S14. Contact diagram of the **f** complex of **7** bound to the Grb2 SH2 domain showing all direct and single water-mediated polar protein-ligand contacts.

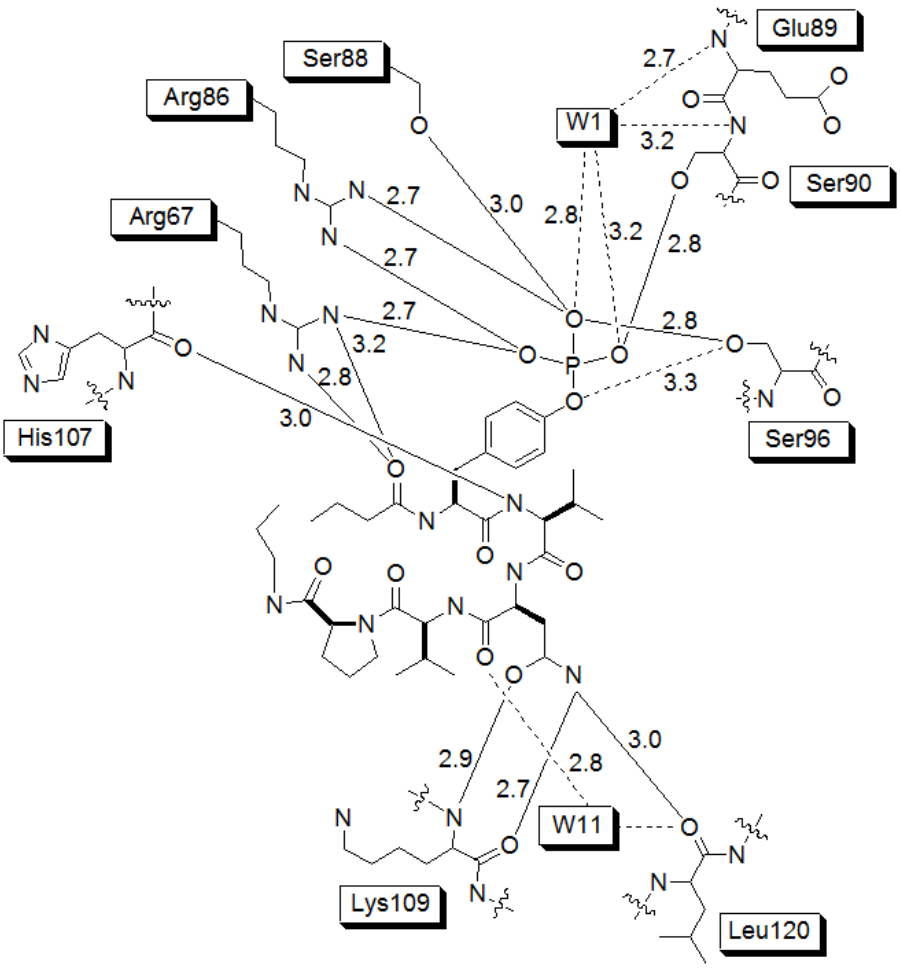
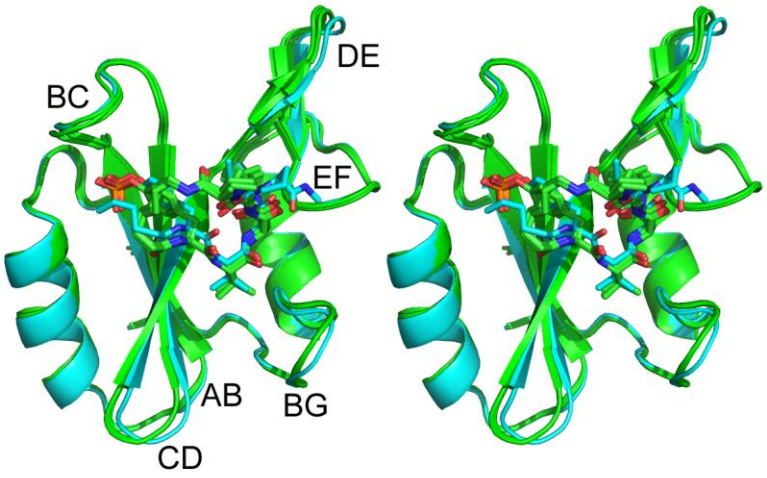


Figure S15. Contact diagram of the complex of **8** bound to the Grb2 SH2 domain showing all direct and single water-mediated polar protein-ligand contacts.

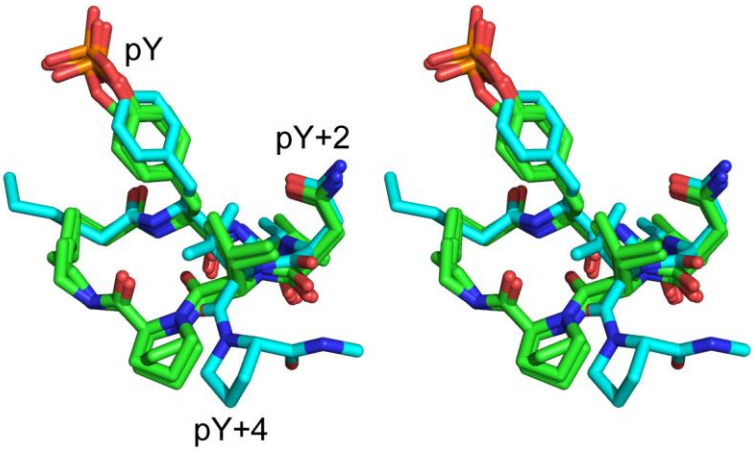
Table S2. Direct and single water-mediated contacts in the complexes of **7** and **8**.[a]

Ligand	CO–pY Contacts		Other Contacts		Total		
	Direct	Water-mediated	Direct	Water-mediated	Direct	Water-mediated	Grand Total
7a	9	3	4	1	13	4	17
7b	9	3	4	0	13	3	16
7c	9	0	4	0	13	0	13
7d	9	3	4	0	13	3	16
7e	9	3	4	1	13	4	17
7f	9	2	4	0	13	2	15
8	9	2	4	1	13	3	16

[a] Only contacts between polar non-hydrogen atoms with atom-atom distances in the range 2.5–3.4 Å were counted with the exception of the **f** complex of **7** for which one direct between the domain and the CO-pY region of the ligand with a distance of 3.5 Å was included. Contacts mediated by a single, ordered water molecule conforming to the same distance criterion were also counted. Contacts between multiple non-hydrogen atoms of the domain to the same non-hydrogen atom of the ligand mediated by the same ordered water molecule were counted only once. Contacts between the same non-hydrogen atom of the domain to *x* non-hydrogen atoms of the ligand mediated by the same ordered water molecule were counted *x* times. No attempt was made to characterize the contacts based on the orientation of donor/acceptor dipole moments. Entries for the **a** and **b**, **c** and **d**, and **e** and **f** complexes of **7**, for which the domain adopts different conformations, are delineated by the grey highlighting.



(a)



(b)

Figure S16. Stereo images of **7** and **8** bound to the Grb2 SH2 domain following domain alignment. Oxygen, nitrogen, and phosphorous atoms are colored red, blue, and orange, respectively. Carbon atoms belonging to the complexes of **7** are colored green while those belonging to the complex of **8** are colored cyan. Only the **a**, **c**,and **e** complexes of **7**, which are representative of the three conformations of the domain in the six complexes, are shown for clarity. a) Image showing the complete domain (ribbons) and the bound ligands (sticks). b) Image showing only the ligands (sticks).

References

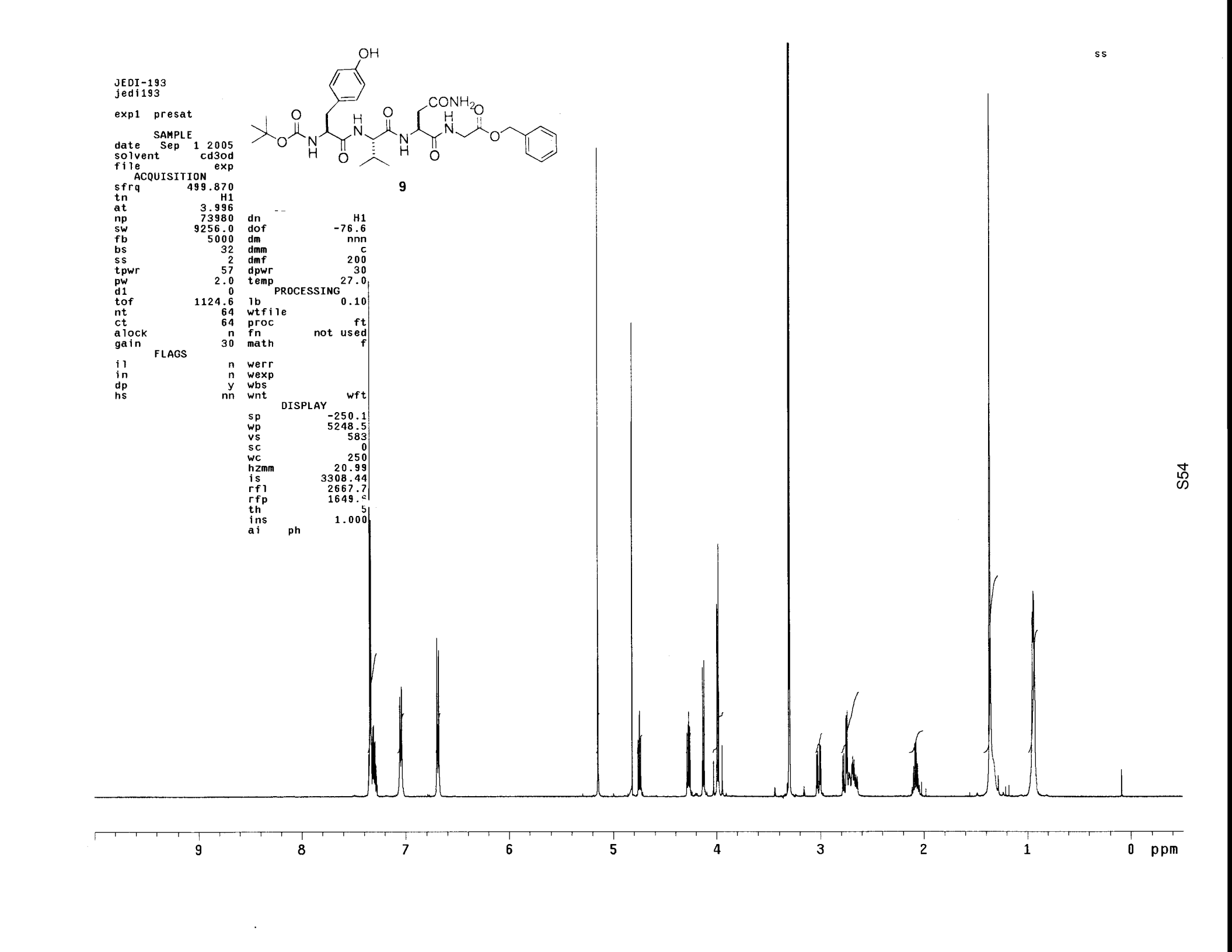
1) DeLorbe, J. E.; Clements, J. H.; Teresk, M. G.; Benfield, A. P.; Plake, H. R.; Millspaugh, L. E.; Martin, S. F. "Thermodynamic and Structural Effects of Conformational Constraints in Protein−Ligand Interactions. Entropic Paradoxy Associated with Ligand Preorganization" *J. Am. Chem. Soc.* **2009**, *131*, 16758-16770.

2) Miroshnikov, A. I.; Kiryushkin, A. A.; Ovchinnikov, Y. A. "Mass-Spectrometric Determination of the Amino Acid Sequence in Peptides. XII. Synthesis of Derivatives of Peptides Containing Asparagine and Glutamine Residues" *Zhurnal Obshchei Khimii* **1970**, *40*, 223-235.

3) Teresk, M. G. Design, Synthesis, and Thermodynamic Evaluation of Conformationally-Constrained Pseudopeptides and Synthetic Approaches to Sieboldine A. Dissertation, University of Texas at Austin, 2008.

4) Millspaugh, L. E. Synthesis and Evaluation of Macrocyclic and Conformationally Constrained Peptide Replacements for the Grb2-SH2 Domain. Dissertation, University of Texas at Austin, 2005.

5) Muir, J. C.; Pattenden, G.; Thomas, R. M. "Total Synthesis of (–)-muscoride A. A Novel Bis-oxazole Based Alkaloid from the Cyanobacterium Nostoc muscorum" *Synthesis* **1998**, 613-618.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pw 2.0
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ct 64
alock n
gain 30
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in n
dp y
hs nn
dn H1
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dmm c
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dpwr 30
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werr
wexp
wbs
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ins 1.000
ai ph
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ss
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JEDI-193
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hs	nn		
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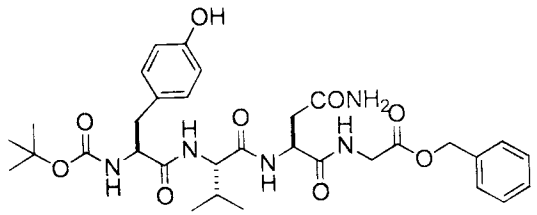

9

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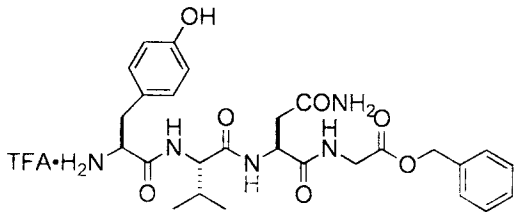

10

JEDII-48

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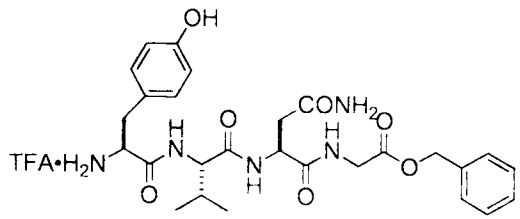

10

JEDI-245

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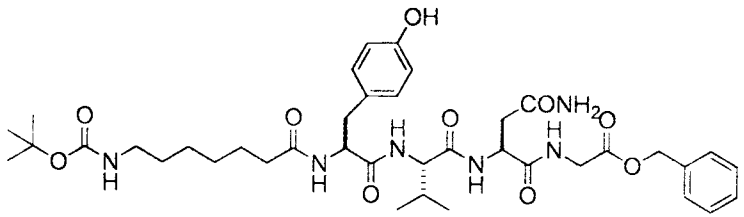

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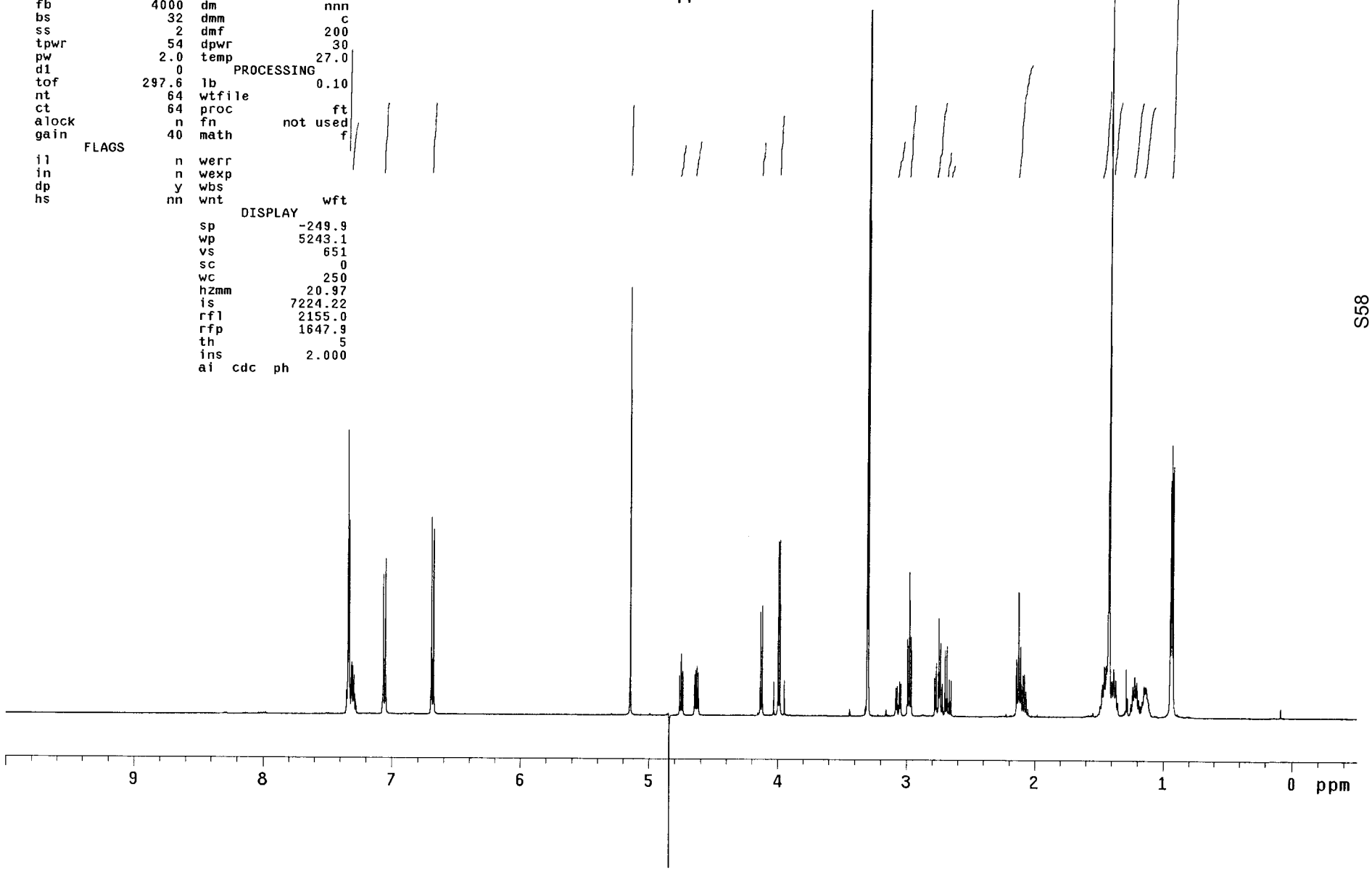

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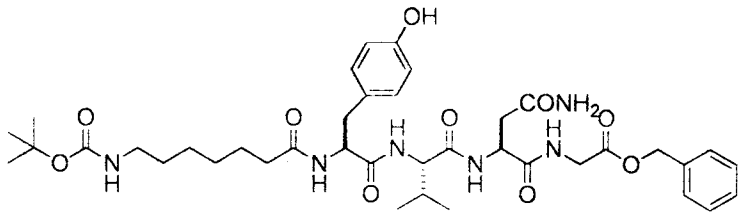

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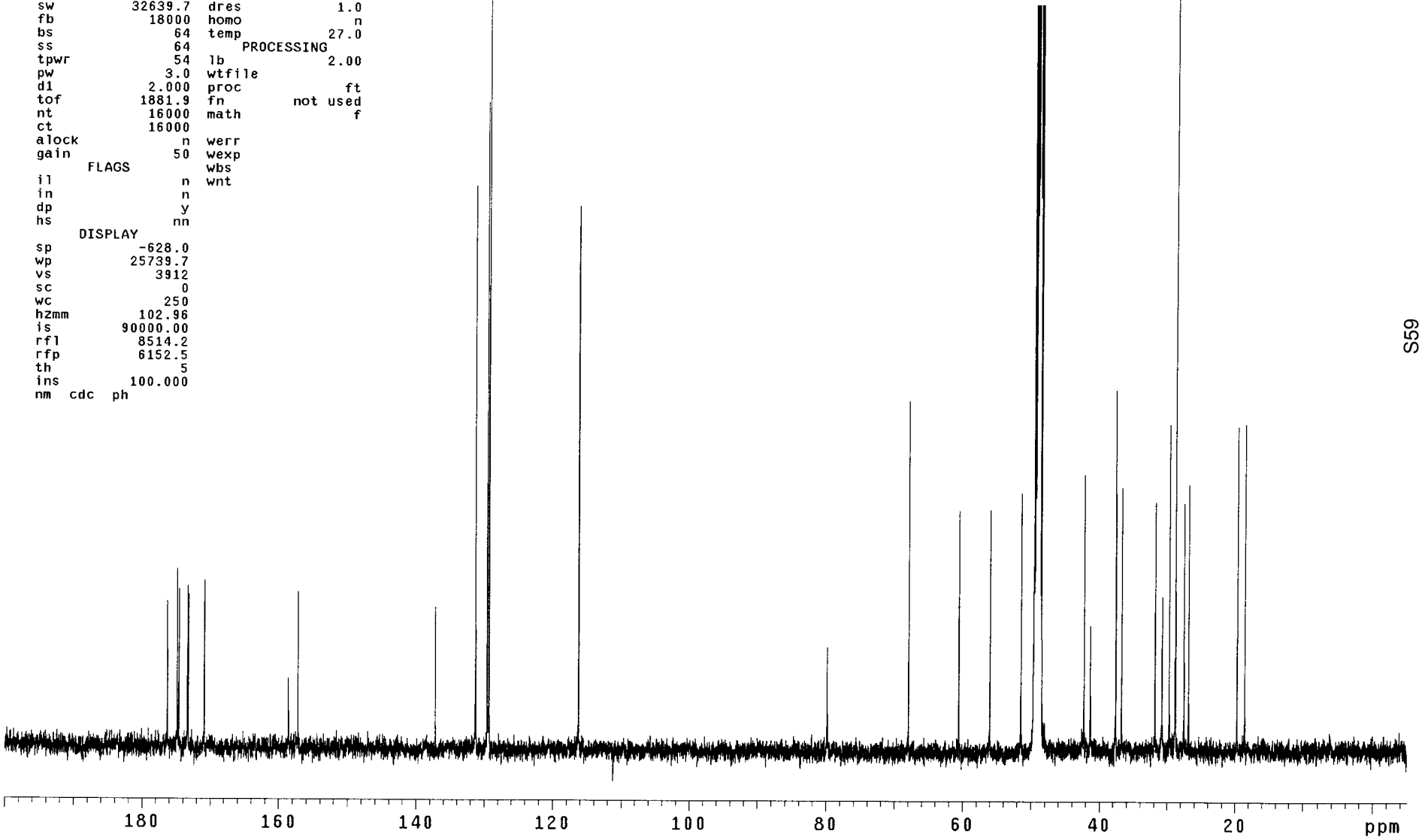

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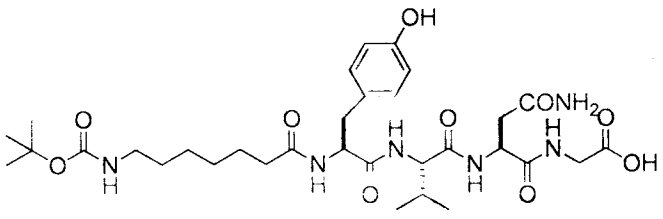

12

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JED7-44

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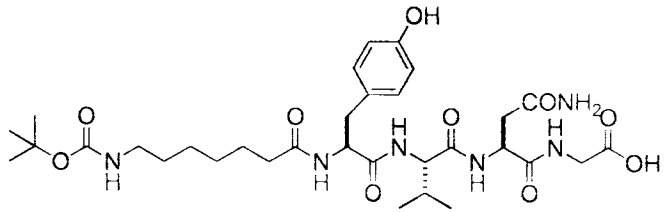

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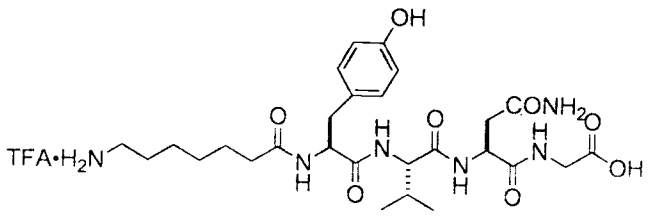

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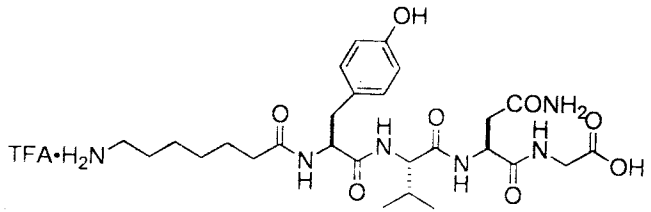

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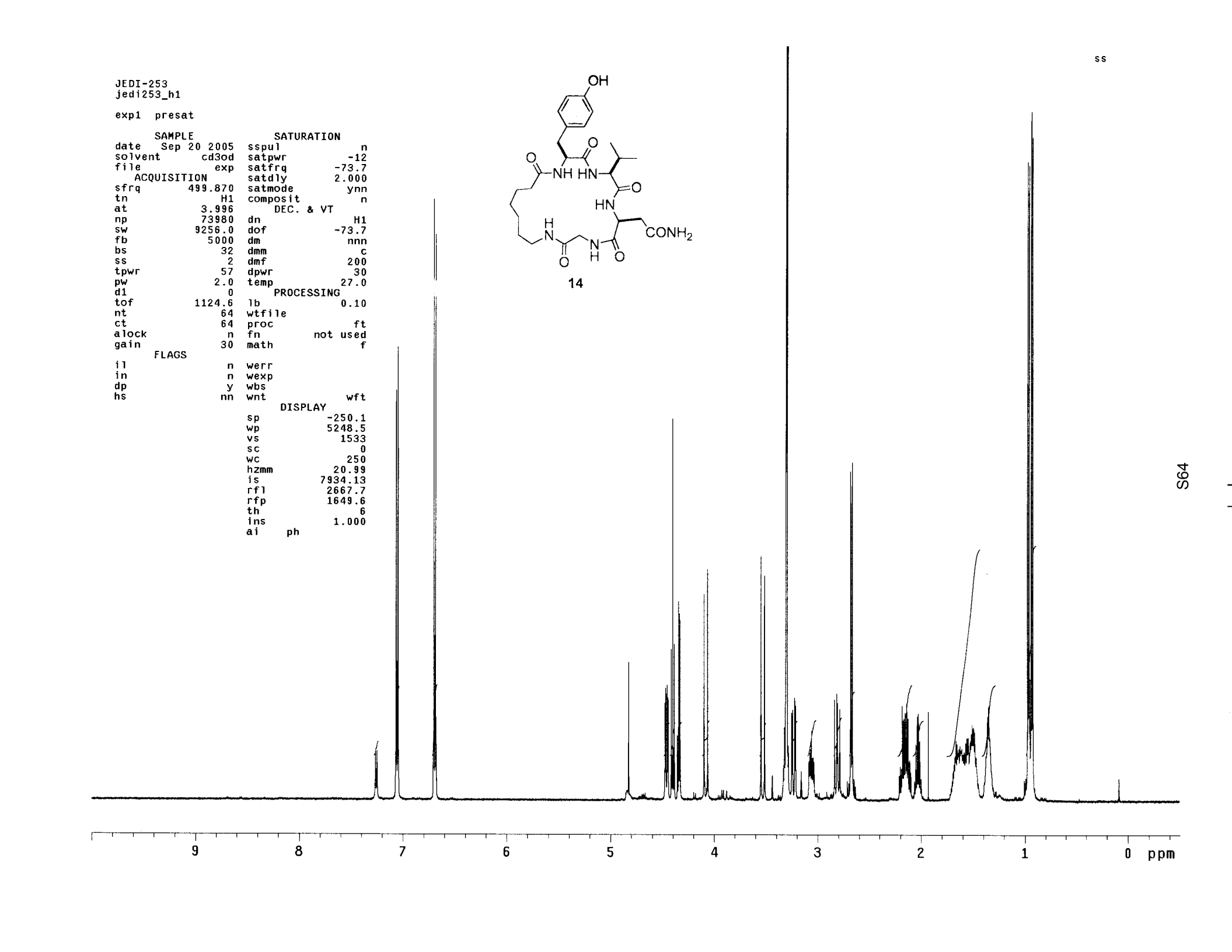
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gain 30
FLAGS
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dp y
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JEDI-253
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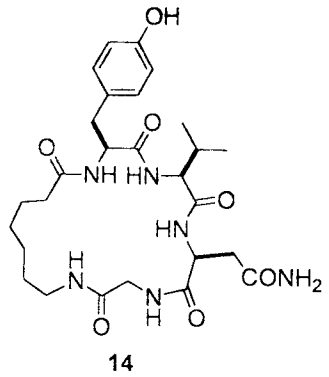
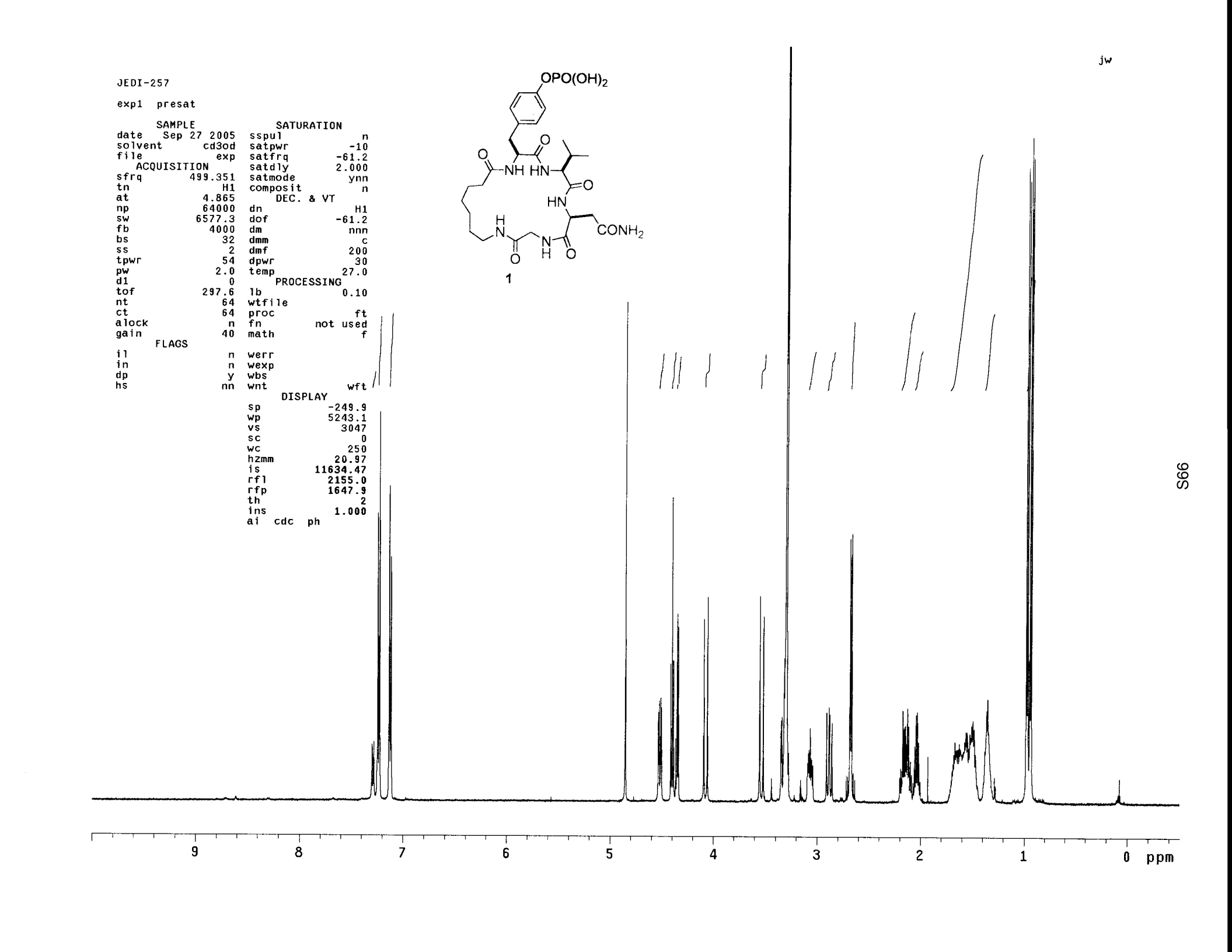
SAMPLE		DEC. & VT	
date	Sep 20 2005	dfrq	499.869
solvent	cd3od	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	10000	fn	not used
ct	10000	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.7		
wp	25766.5		
vs	6236		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	8538.8		
rfp	6158.9		
th	0		
ins	100.000		
ai cdc ph			



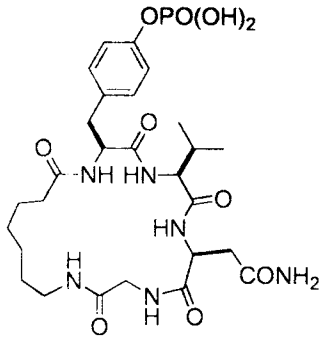
14


JEDI-257
exp1 presat
SAMPLE
date Sep 27 2005
solvent cd3od
file exp
ACQUISITION
sfrq 499.351
tn H1
at 4.865
np 64000
sw 6577.3
fb 4000
bs 32
ss 2
tpwr 54
pw 2.0
d1 0
tof 297.6
nt 64
ct 64
alock n
gain 40
FLAGS
il n
in n
dp y
hs nn
SATURATION
sspul n
satpwr -10
satfrq -61.2
satdly 2.000
satmode ynn
composit n
DEC. & VT
dn H1
dof -61.2
dm nnn
dmm c
dmf 200
dpwr 30
temp 27.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
DISPLAY
sp -249.9
wp 5243.1
vs 3047
sc 0
wc 250
hzmm 20.97
is 11634.47
rfl 2155.0
rfp 1647.9
th 2
ins 1.000
ai cdc ph
OPO(OH)2
NH HN
HN
CONH2
1
jw
9
8
7
6
5
4
3
2
1
0 ppm

JEDI-257

exp4 s2pul

SAMPLE		DEC. & VT	
date	Sep 27 2005	dfrq	499.351
solvent	cd3od	dn	H1
file	exp	dpwr	44
ACQUISITION		dof	-500.0
sfrq	125.575	dm	yyy
tn	C13	dmm	w
at	1.073	dmf	11000
np	70058	dseq	
sw	32639.7	dres	1.0
fb	18000	homo	n
bs	64	temp	27.0
ss	128	**PROCESSING**	
tpwr	54	lb	2.00
pw	3.0	wtfile	
d1	2.000	proc	ft
tof	1881.9	fn	not used
nt	14000	math	f
ct	14000		
alock	n	werr	
gain	50	wexp	
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-628.0		
wp	25739.7		
vs	9937		
sc	0		
wc	250		
hzmm	102.96		
is	90000.00		
rfl	8513.7		
rfp	6152.5		
th	10		
ins	100.000		
nm cdc ph			



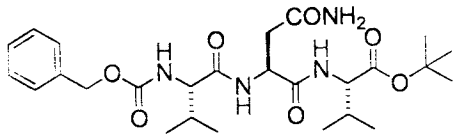
1

jw

JEDVII(68)

Pulse Sequence: s2pul
Solvent: cd3od
Ambient temperature
Mercury-400BB "nmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
24 repetitions
OBSERVE H1, 400.2685529 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 2 min, 48 sec

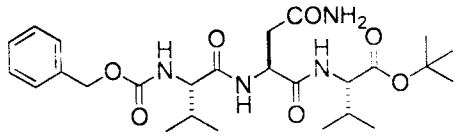


15

13C OBSERVE

Pulse Sequence: s2pul
 Solvent: cd3od
 Ambient temperature
File: jed7-68
INOVA-500 "nmrastro"

 Relax. delay 2.000 sec
 Pulse 36.0 degrees
 Acq. time 1.777 sec
 Width 18009.9 Hz
 304 repetitions
OBSERVE C13, 75.4700973 MHz
DECOUPLE H1, 300.1421085 MHz
 Power 40 dB
 continuously on
 WALTZ-16 modulated
Single precision data
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 17 hr, 52 min, 35 sec



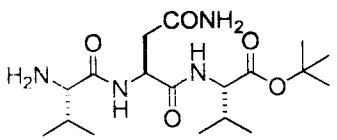
15

JEDVII(69)

Pulse Sequence: s2pul

Solvent: cd3od
Ambient temperature
Mercury-400BB "nmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
32 repetitions
OBSERVE H1, 400.2685529 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 0 sec

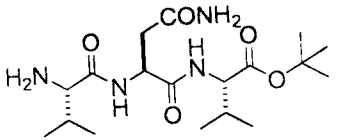


16

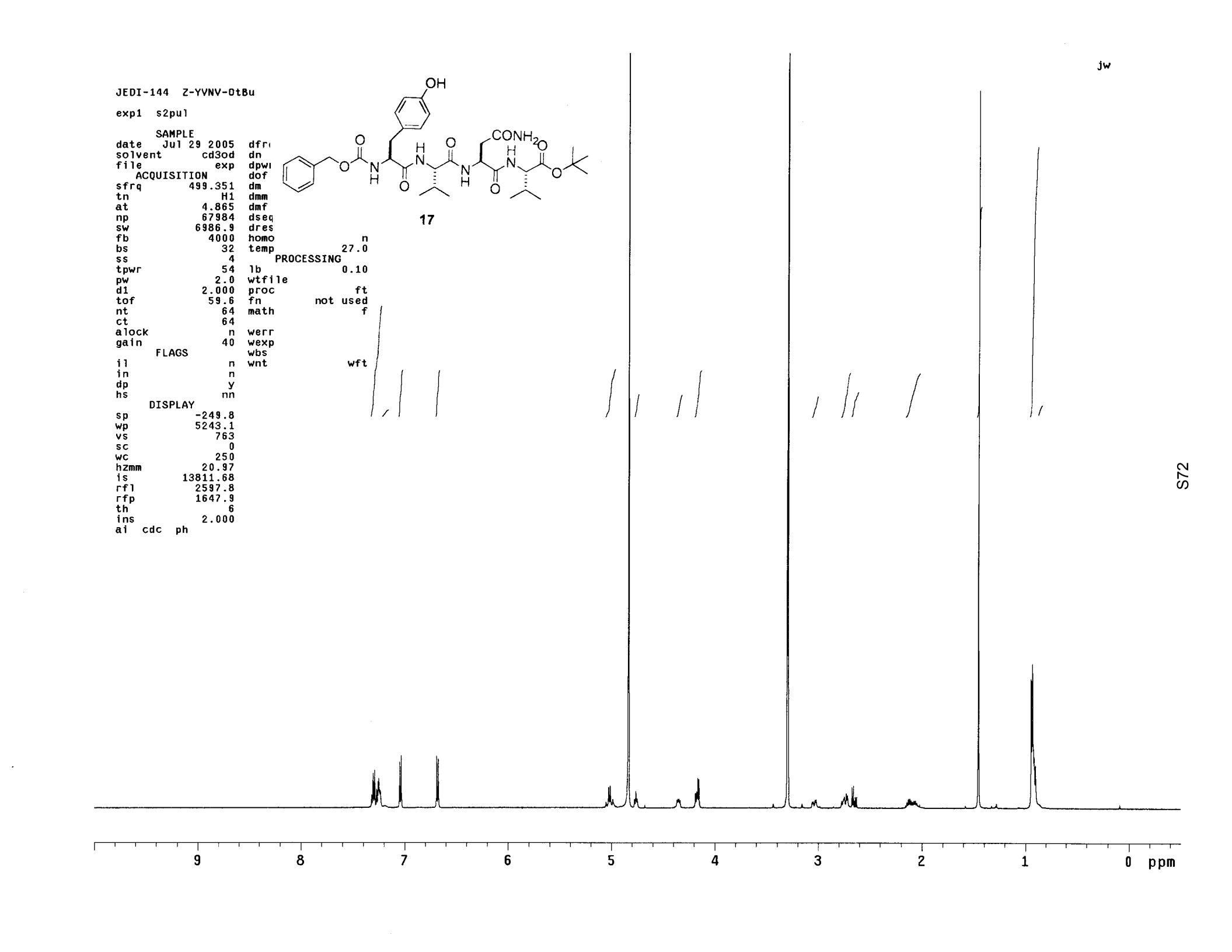
JEDVII(69)

Pulse Sequence: s2pul
Solvent: cd3od
Ambient temperature
UNITYplus-300 "nmr2"

Relax. delay 2.000 sec
Pulse 36.0 degrees
Acq. time 1.777 sec
Width 18009.9 Hz
735 repetitions
OBSERVE C13, 75.4702105 MHz
DECOUPLE H1, 300.1421085 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
Single precision data
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 17 hr, 53 min, 9 sec



16

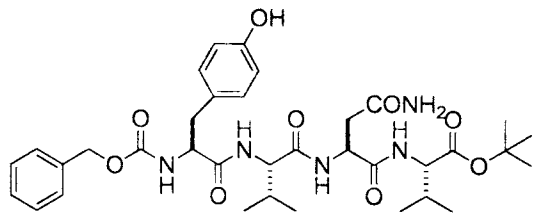

JEDI-144 Z-YVNV-OtBu
exp1 s2pul
SAMPLE
date Jul 29 2005
solvent cd3od
file exp
ACQUISITION
sfrq 499.351
tn H1
at 4.865
np 67984
sw 6986.9
fb 4000
bs 32
ss 4
tpwr 54
pw 2.0
d1 2.000
tof 59.6
nt 64
ct 64
alock n
gain 40
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -249.8
wp 5243.1
vs 763
sc 0
wc 250
hzmm 20.97
is 13811.68
rfl 2597.8
rfp 1647.9
th 6
ins 2.000
ai cdc ph
dfr
dn
dpwr
dof
dm
dmm
dmf
dseq
dres
homo n
temp 27.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
OH
CONH2
17
jw
S72
9
8
7
6
5
4
3
2
1
0 ppm

jw

JEDI-144 Z-YVNV-OtBu

exp4 s2pul

SAMPLE		DEC. & VT	
date	Jul 29 2005	dfrq	499.351
solvent	cd3od	dn	H1
file	exp	dpwr	44
ACQUISITION		dof	-500.0
sfrq	125.575	dm	yyy
tn	C13	dmm	w
at	1.073	dmf	11000
np	70058	dseq	
sw	32639.7	dres	1.0
fb	18000	homo	n
bs	64	temp	27.0
ss	64	PROCESSING	
tpwr	54	lb	2.00
pw	3.0	wtfile	
d1	2.000	proc	ft
tof	1881.9	fn	not used
nt	17000	math	f
ct	17000		
alock	n	werr	
gain	50	wexp	
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-628.0		
wp	25739.7		
vs	7678		
sc	0		
wc	250		
hzmm	102.96		
is	90000.00		
rfl	8513.7		
rfp	6152.5		
th	9		
ins	100.000		
nm cdc ph			

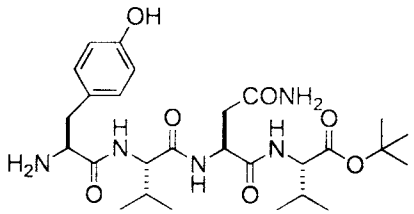


17

Archive directory:
Sample directory:

Pulse Sequence: s2pul
Solvent: cd3od
Ambient temperature
File: jed7-39_s2pul_H1
INOVA-500 "nmrastro"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 4.000 sec
Width 6410.3 Hz
16 repetitions
OBSERVE H1, 399.8062840 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 min, 48 sec



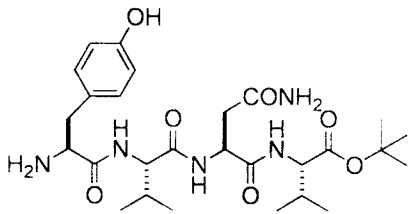
18

Archive directory:
Sample directory:

Pulse Sequence: s2pul

Solvent: cd3od
Ambient temperature
User: 1-14-87
File: jed7-39_s2pul_C13
INOVA-500 "nmrastro"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
256 repetitions
OBSERVE C13, 100.5312328 MHz
DECOUPLE H1, 399.8082857 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 14 min, 7 sec

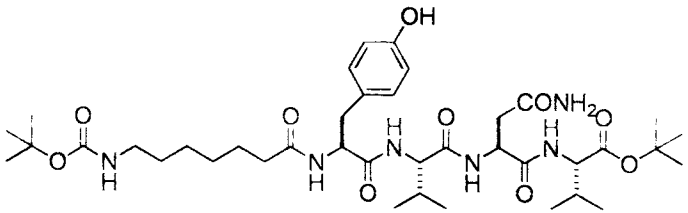


18

JEDI-282
jedI282_h1

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jan 13 2006	dfrq	499.8
solvent	DMSO	dn	
file	exp	dpwr	35
ACQUISITION		dof	0
sfrq	499.870	dm	nnn
tn	H1	dmm	c
at	3.996	dmf	20
np	73980	dseq	
sw	9256.0	dres	1.0
fb	not used	homo	n
bs	32	temp	27.0
tpwr	57	PROCESSING	
pw	2.0	lb	0.10
d1	2.000	wtfile	
tof	1124.6	proc	ft
nt	64	fn	not used
ct	64	math	f
alock	n		
gain	30	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	wft
dp	y		
hs	nn		
DISPLAY			
sp	-250.0		
wp	6248.3		
vs	578		
sc	0		
wc	250		
hzmm	24.99		
is	1438.12		
rfl	2256.5		
rfp	1244.7		
th	4		
ins	1.000		
ai	ph		



19

ss

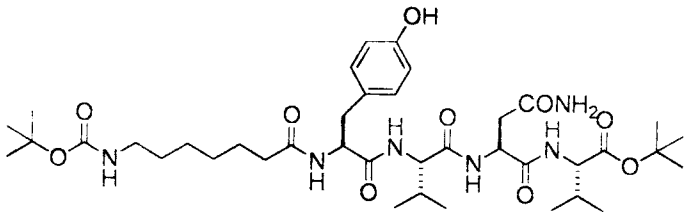
S76

11 10 9 8 7 6 5 4 3 2 1 ppm

JEDI-282
jedI282_c13

exp4 s2pul

SAMPLE		DEC. & VT	
date	Jan 13 2006	dfrq	499.869
solvent	DMSO	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	20000	fn	not used
ct	20000	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.5		
wp	25766.5		
vs	3486		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	7585.7		
rfp	4964.8		
th	3		
ins	100.000		
ai cdc ph			

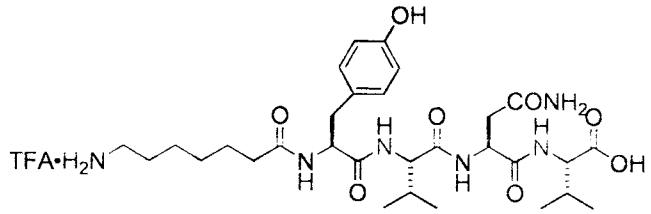


19

JEDVII(45)

Pulse Sequence: s2pul
Solvent: cd3od
Ambient temperature
Mercury-400BB "nmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
24 repetitions
OBSERVE H1, 400.2685529 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 0 sec

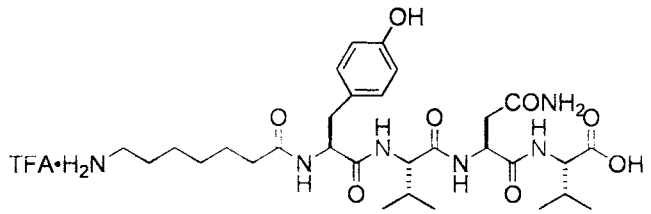


20

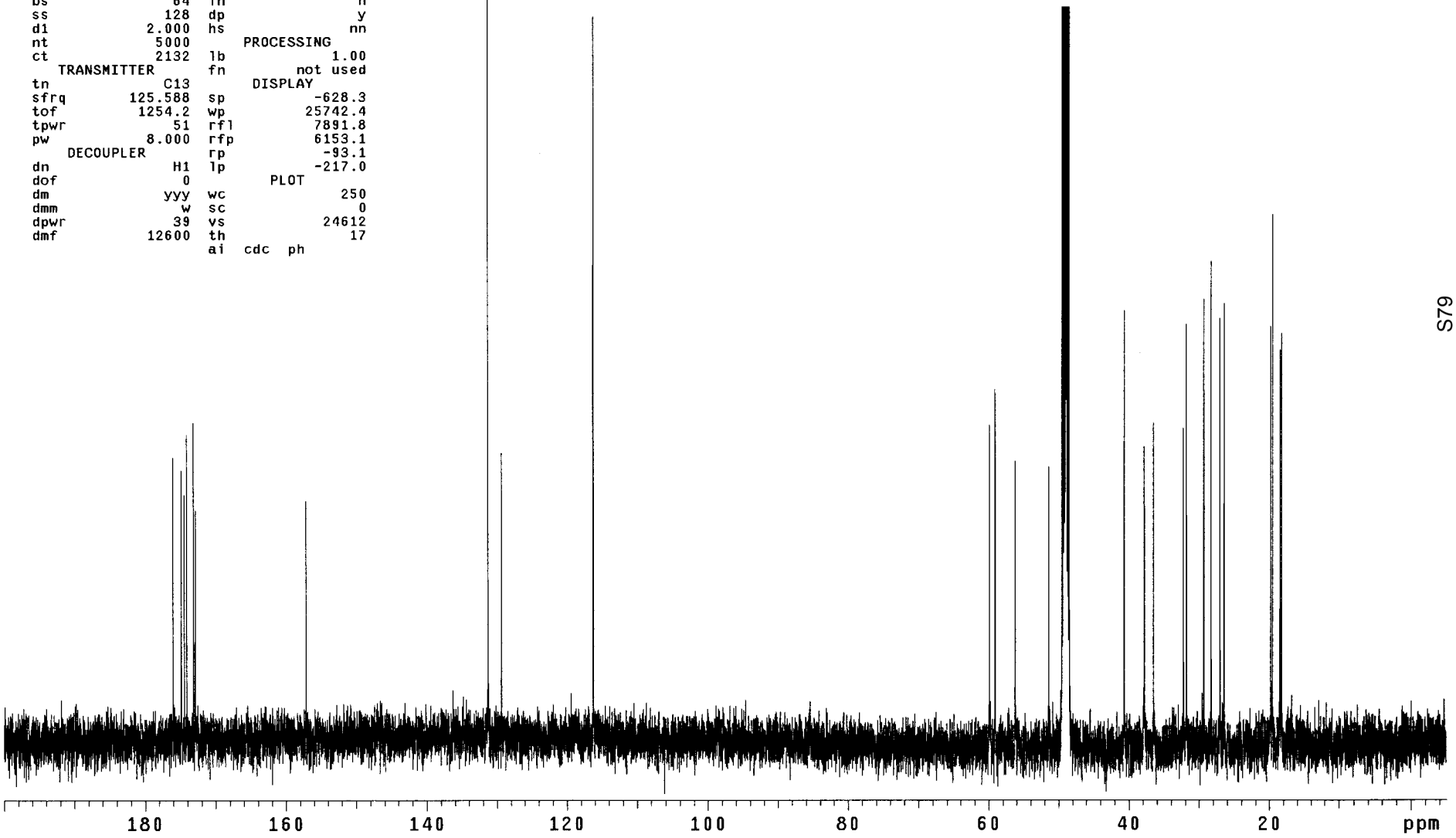
C13

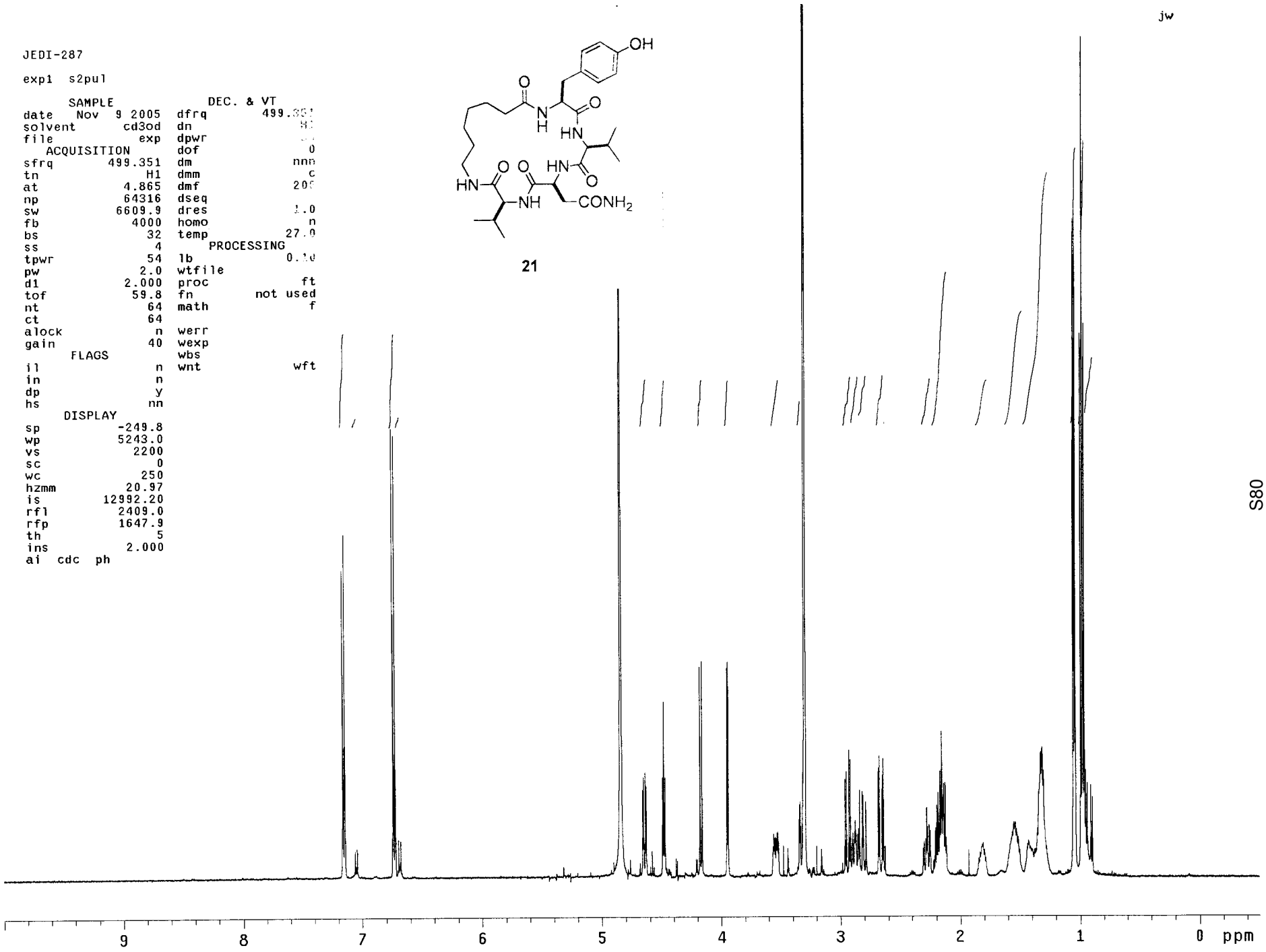
exp4 Carbon

SAMPLE		SPECIAL	
date	Apr 22 2010	temp	27.0
solvent	cd3od	gain	50
file	exp	spin	20
ACQUISITION		hst	0.008
sw	30143.2	pw90	15.500
at	1.062	alfa	10.000
np	64024	FLAGS	
fb	17000	il	n
bs	64	in	n
ss	128	dp	y
d1	2.000	hs	nn
nt	5000	PROCESSING	
ct	2132	lb	1.00
TRANSMITTER		fn	not used
tn	C13	DISPLAY	
sfrq	125.588	sp	-628.3
tof	1254.2	wp	25742.4
tpwr	51	rfl	7891.8
pw	8.000	rfp	6153.1
DECOUPLER		rp	-93.1
dn	H1	lp	-217.0
dof	0	PLOT	
dm	yyy	wc	250
dmm	w	sc	0
dpwr	39	vs	24612
dmf	12600	th	17
		ai	cdc ph



20

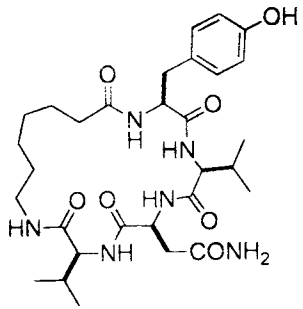



JEDI-287
exp1 s2pul
SAMPLE
date Nov 9 2005
solvent cd3od
file exp
ACQUISITION
sfrq 499.351
tn H1
at 4.865
np 64316
sw 6609.9
fb 4000
bs 32
ss 4
tpwr 54
pw 2.0
d1 2.000
tof 59.8
nt 64
ct 64
alock n
gain 40
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -249.8
wp 5243.0
vs 2200
sc 0
wc 250
hzmm 20.97
is 12992.20
rfl 2409.0
rfp 1647.9
th 5
ins 2.000
ai cdc ph
DEC. & VT
dfrq 499.35
dn H1
dpwr
dof 0
dm nnn
dmm c
dmf 20
dseq
dres 1.0
homo n
temp 27.0
PROCESSING
lb 0.1
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
21
jw
S80
9
8
7
6
5
4
3
2
1
0 ppm

JEDI-287

exp4 s2pul

SAMPLE		DEC. & VT	
date	Nov 8 2005	dfrq	499.351
solvent	cd3od	dn	H1
file	/export/home/~	dpwr	44
space	/data/jedi_28~	dof	-500.0
	7_c13bb.fid	dm	yyy
ACQUISITION		dmm	w
sfrq	125.575	dmf	11000
tn	C13	dseq	
at	1.073	dres	1.0
np	70058	homo	n
sw	32639.7	temp	27.0
fb	18000	PROCESSING	
bs	64	lb	2.00
ss	64	wtfile	
tpwr	54	proc	ft
pw	3.0	fn	not used
d1	2.000	math	f
tof	1881.9		
nt	16000	werr	
ct	16000	wexp	
alock	n	wbs	
gain	50	wnt	
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-628.0		
wp	25739.7		
vs	7798		
sc	0		
wc	250		
hzmm	102.96		
is	90000.00		
rfl	8513.7		
rfp	6152.5		
th	10		
ins	100.000		
nm cdc ph			



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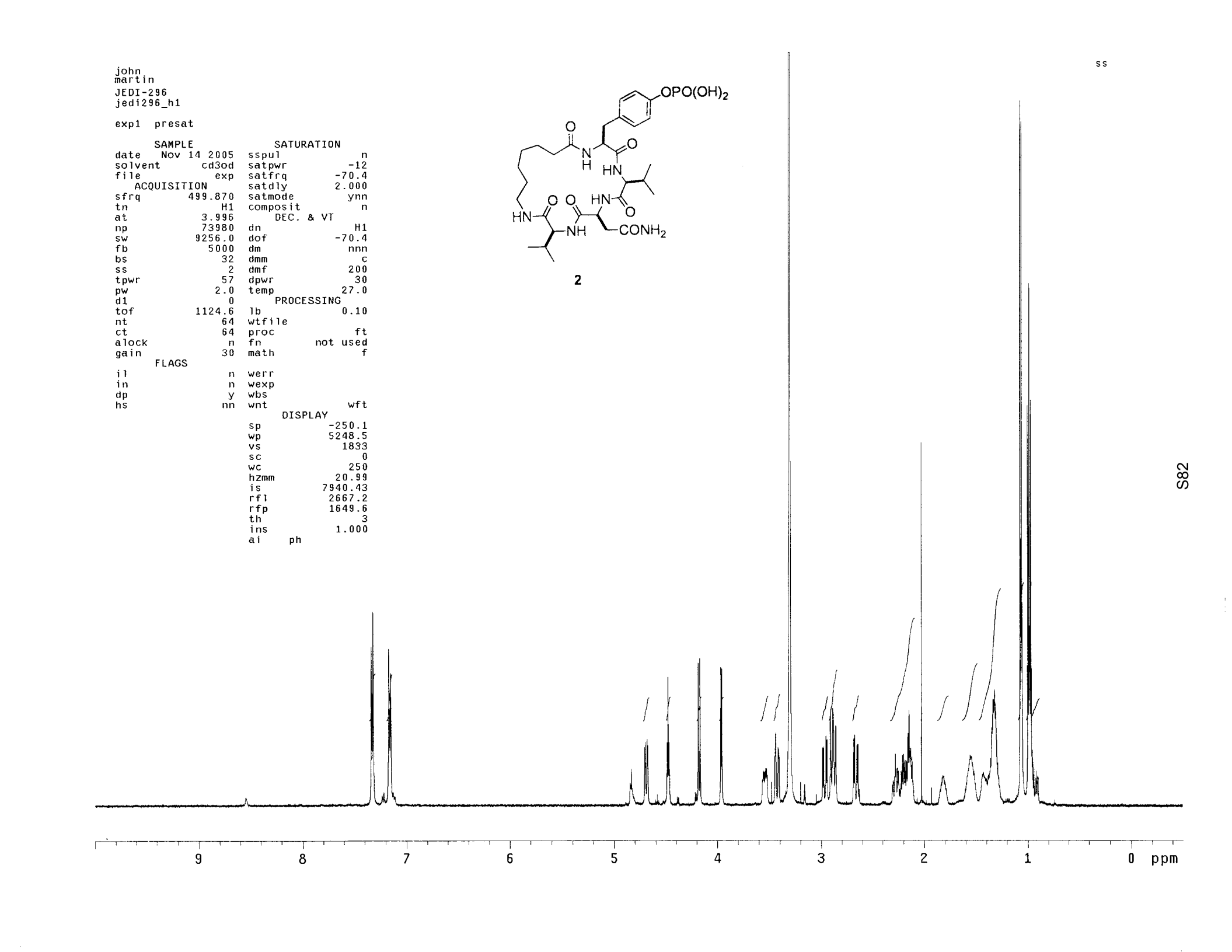
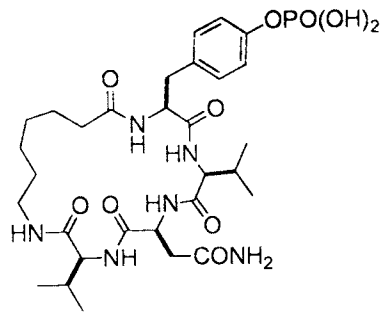

john
martin
JEDI-296
jedi296_h1
exp1 presat
SAMPLE
date Nov 14 2005
solvent cd3od
file exp
ACQUISITION
sfrq 499.870
tn H1
at 3.996
np 73980
sw 9256.0
fb 5000
bs 32
ss 2
tpwr 57
pw 2.0
d1 0
tof 1124.6
nt 64
ct 64
alock n
gain 30
FLAGS
il n
in n
dp y
hs nn
SATURATION
sspul n
satpwr -12
satfrq -70.4
satdly 2.000
satmode ynn
composit n
DEC. & VT
dn H1
dof -70.4
dm nnn
dmm c
dmf 200
dpwr 30
temp 27.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
DISPLAY
sp -250.1
wp 5248.5
vs 1833
sc 0
wc 250
hzmm 20.99
is 7940.43
rfl 2667.2
rfp 1649.6
th 3
ins 1.000
ai ph
OPO(OH)2
HN
NH
CONH2
2
ss
S82
9
8
7
6
5
4
3
2
1
0 ppm

john
martin
JEDI-296
jedi296_c13

exp4 s2pul

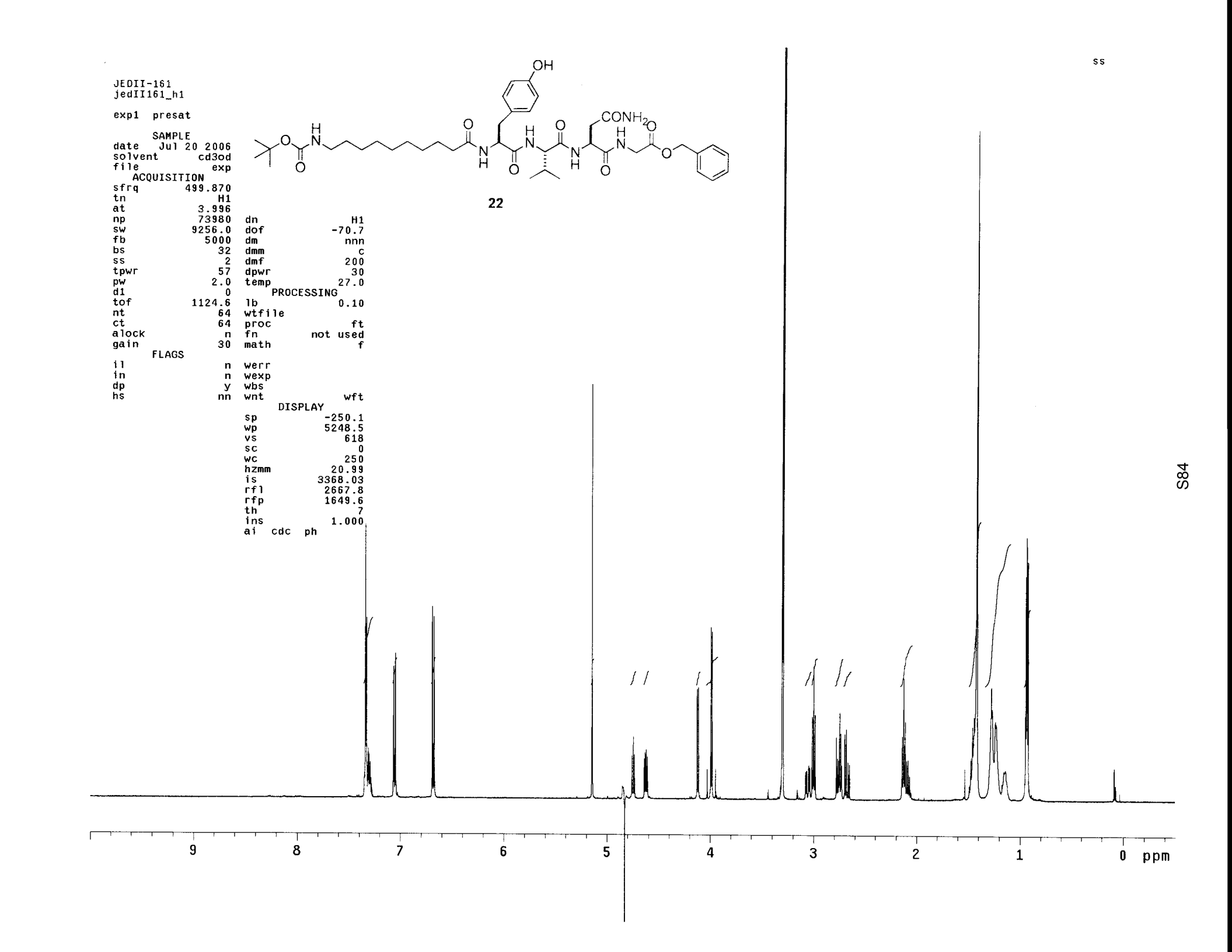
SAMPLE		DEC. & VT	
date	Nov 14 2005	dfrq	499.869
solvent	cd3od	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	10000	fn	not used
ct	10000	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.7		
wp	25766.5		
vs	15573		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	8538.8		
rfp	6158.9		
th	1		
ins	100.000		
ai cdc ph			



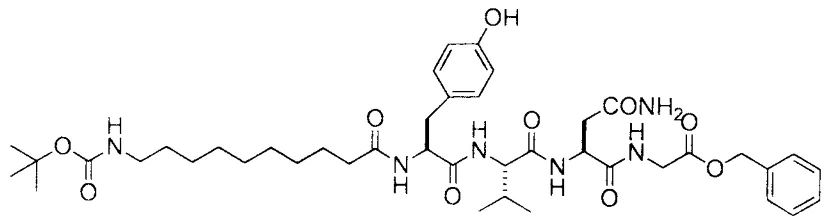
2

ss

S83

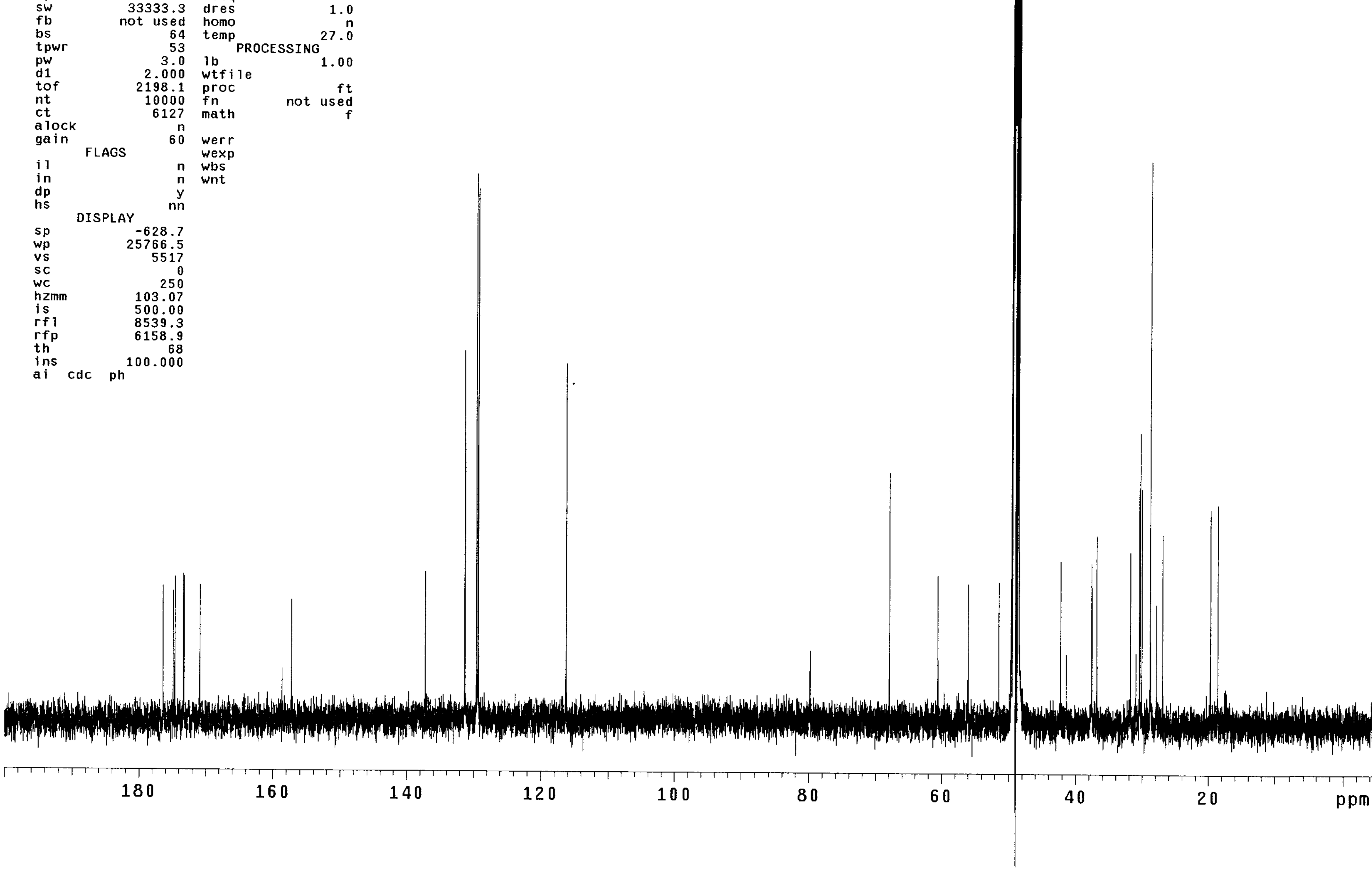

JEDII-161
jedII161_h1
exp1 presat
SAMPLE
date Jul 20 2006
solvent cd3od
file exp
ACQUISITION
sfrq 499.870
tn H1
at 3.996
np 73980
sw 9256.0
fb 5000
bs 32
ss 2
tpwr 57
pw 2.0
d1 0
tof 1124.6
nt 64
ct 64
alock n
gain 30
FLAGS
il n
in n
dp y
hs nn
dn H1
dof -70.7
dm nnn
dmm c
dmf 200
dpwr 30
temp 27.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
DISPLAY
sp -250.1
wp 5248.5
vs 618
sc 0
wc 250
hzmm 20.99
is 3368.03
rfl 2667.8
rfp 1649.6
th 7
ins 1.000
ai cdc ph
OH
CONH2
22
ss
9
8
7
6
5
4
3
2
1
0 ppm
S84

```
JEDII-161
jedII161_c13

exp4  s2pul

      SAMPLE                  DEC. & VT
date   Jul 21 2006    dfrq        499.869
solvent      cd3od    dn               H1
file           exp    dpwr             37
    ACQUISITION       dof               0
sfrq       125.706    dm              yyy
tn             C13    dmm               w
at           1.279    dmf           10582
np           85262    dseq
sw         33333.3    dres            1.0
fb        not used    homo              n
bs              64    temp           27.0
tpwr            53        PROCESSING
pw             3.0    lb             1.00
d1           2.000    wtfile
tof         2198.1    proc             ft
nt           10000    fn         not used
ct            6127    math              f
alock            n
gain            60    werr
     FLAGS            wexp
il               n    wbs
in               n    wnt
dp               y
hs              nn
     DISPLAY
sp          -628.7
wp         25766.5
vs            5517
sc               0
wc             250
hzmm        103.07
is          500.00
rfl         8539.3
rfp         6158.9
th              68
ins        100.000
ai   cdc   ph
```



22

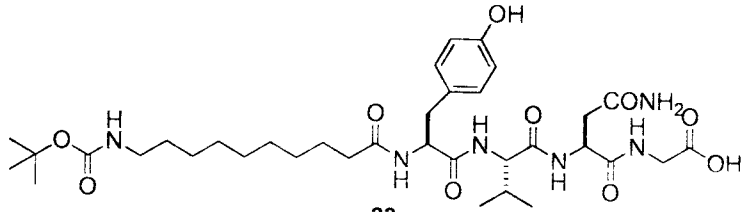
ss



jeq11196

exp1 presat

SAMPLE			
date	Jul 28 2006		
solvent	cd3od		
file	exp		
ACQUISITION			
sfrq	499.870	dn	H1
tn	H1	dof	-67.9
at	3.996	dm	nnn
np	73980	dmm	c
sw	9256.0	dmf	200
fb	5000	dpwr	30
bs	32	temp	27.0
ss	2	PROCESSING	
tpwr	57	lb	0.10
pw	2.0	wtfile	
d1	0	proc	ft
tof	1124.6	fn	not used
nt	64	math	f
ct	64		
alock	n		
gain	30		
FLAGS			
il	n	werr	
in	n	wexp	
dp	y	wbs	
hs	nn	wnt	wft
		DISPLAY	
		sp	-250.1
		wp	5248.5
		vs	285
		sc	0
		wc	250
		hzmm	20.99
		is	3130.23
		rfl	2667.8
		rfp	1649.6
		th	7
		ins	1.000
		ai cdc ph	

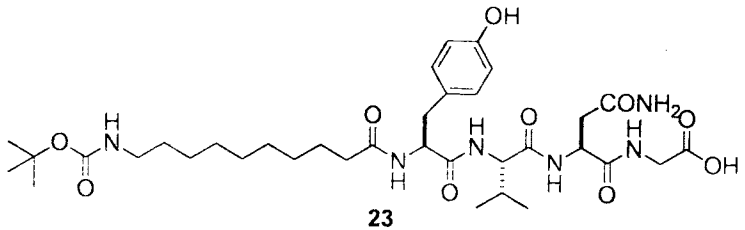


23

JEDII-196
jedII196

exp4 s2pul

SAMPLE		DEC. & VT	
date	Jul 28 2006	dfrq	499.869
solvent	cd3od	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	20000	fn	not used
ct	5975	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.7		
wp	25766.5		
vs	6099		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	8539.3		
rfp	6158.9		
th	68		
ins	100.000		
ai ph			

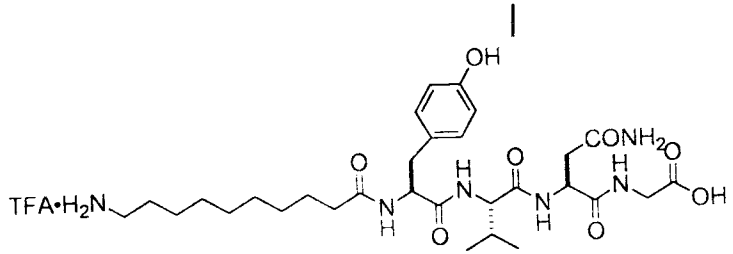


23

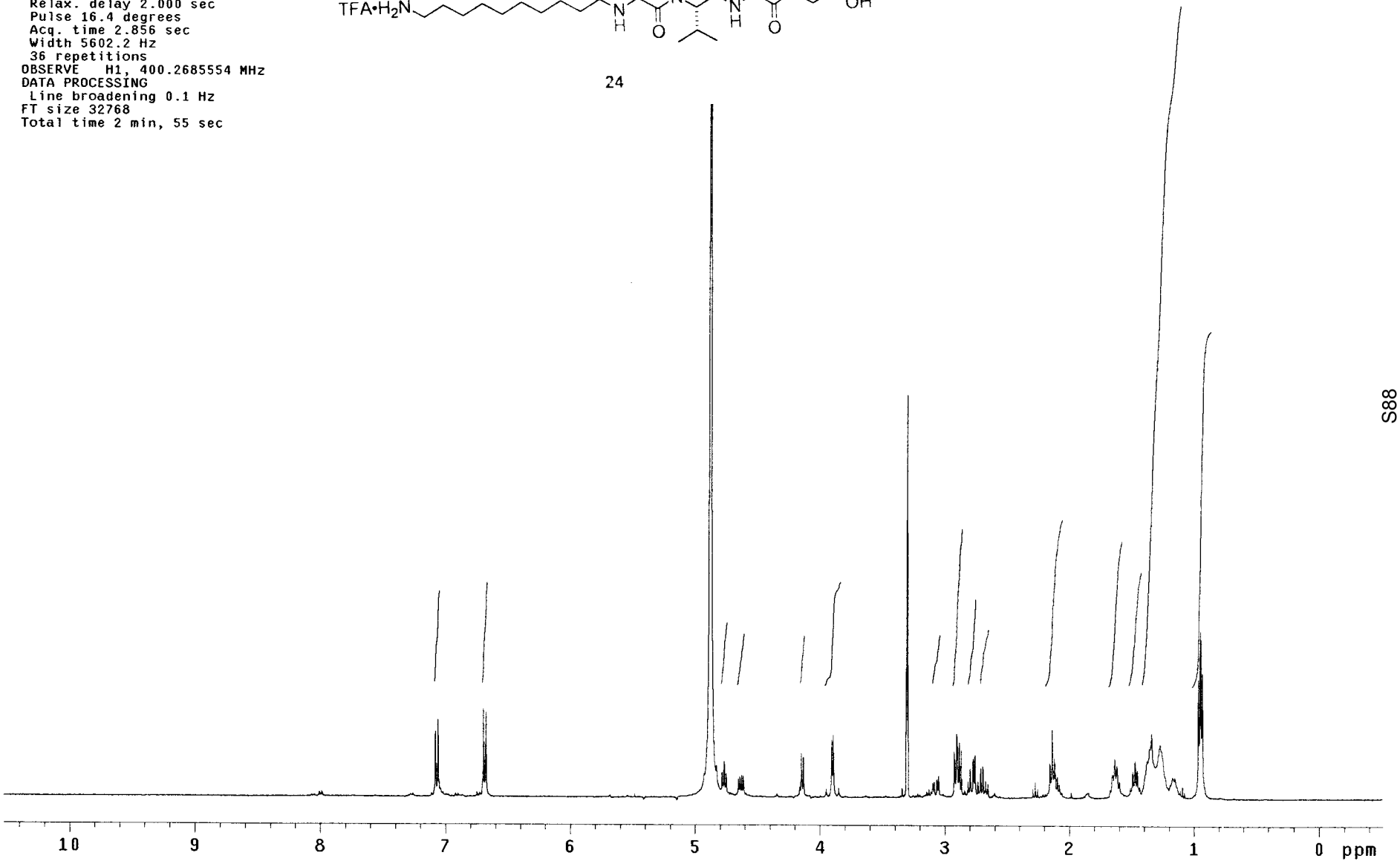
JEDII-278

Pulse Sequence: s2pul
Solvent: cd3od
Ambient temperature
File: jed2-278
INOVA-500 "nmrastro"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
36 repetitions
OBSERVE H1, 400.2685554 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 2 min, 55 sec



24

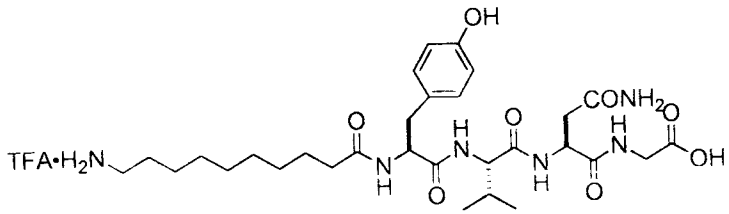


600 MHz nmrox

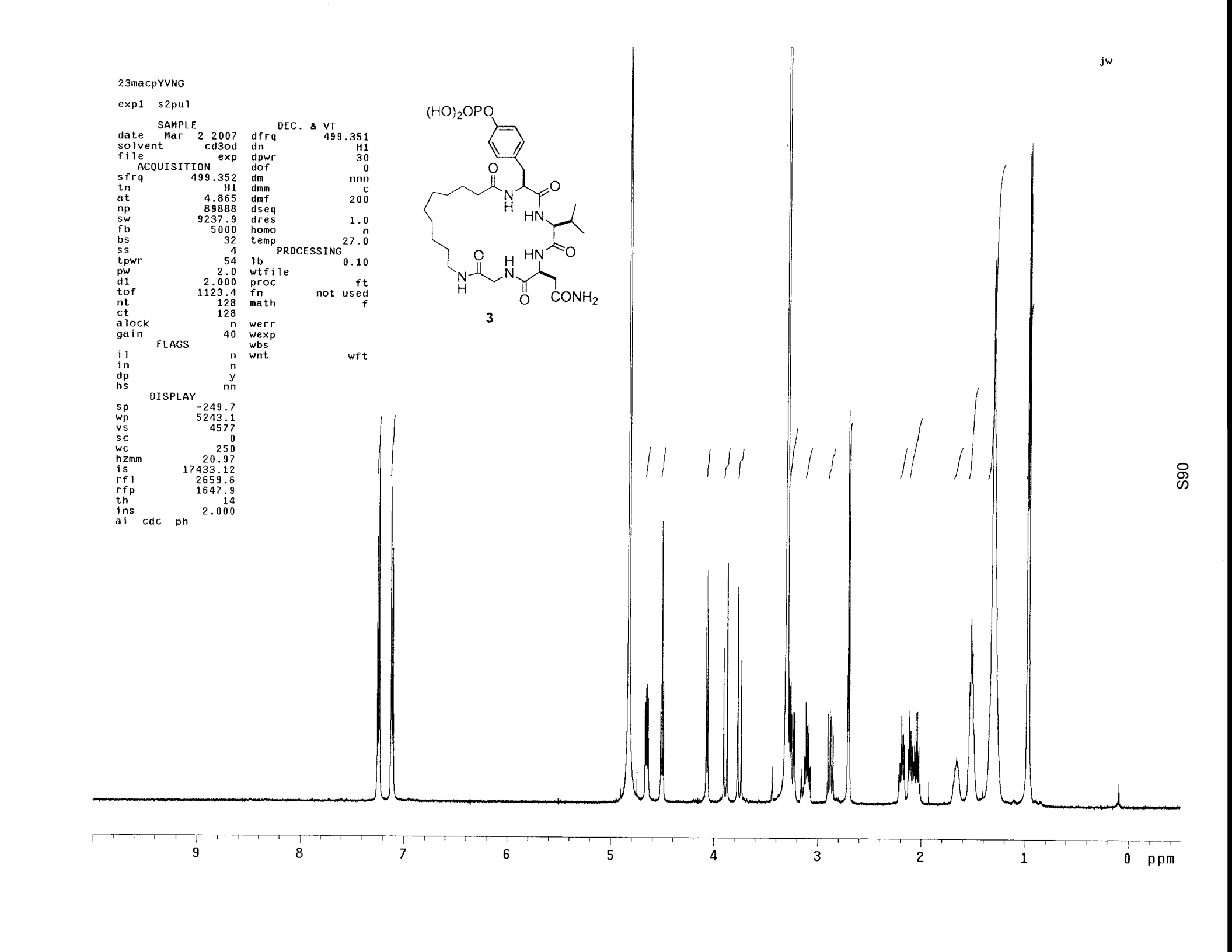
JEDII-278

exp4 Carbon

SAMPLE		SPECIAL	
date	Apr 28 2010	temp	27.0
solvent	cd3od	gain	30
file	exp	spin	20
ACQUISITION		hst	0.008
sw	40322.6	pw90	7.800
at	2.000	alfa	10.000
np	161290	FLAGS	
fb	17000	il	n
bs	64	in	n
d1	2.000	dp	y
nt	15000	hs	nn
ct	14976	PROCESSING	
TRANSMITTER		lb	0.50
tn	C13	fn	262144
sfrq	150.824	DISPLAY	
tof	2296.4	sp	-754.2
tpwr	58	wp	33931.4
pw	2.600	rfl	10745.8
DECOUPLER		rfp	7389.6
dn	H1	rp	211.4
dof	0	lp	32.3
dm	yyy	PLOT	
dmm	w	wc	250
dpwr	46	sc	0
dmf	15337	vs	296643
		th	7
		ai cdc ph	



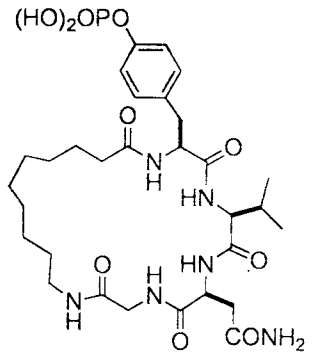
24


23macpYVNG
exp1 s2pul
SAMPLE
date Mar 2 2007
solvent cd3od
file exp
ACQUISITION
sfrq 499.352
tn H1
at 4.865
np 89888
sw 9237.9
fb 5000
bs 32
ss 4
tpwr 54
pw 2.0
d1 2.000
tof 1123.4
nt 128
ct 128
alock n
gain 40
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -249.7
wp 5243.1
vs 4577
sc 0
wc 250
hzmm 20.97
is 17433.12
rfl 2659.6
rfp 1647.9
th 14
ins 2.000
ai cdc ph
DEC. & VT
dfrq 499.351
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
temp 27.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
(HO)2OPO
HN
HN
CONH2
3
jw
S90
9
8
7
6
5
4
3
2
1
0 ppm

JEDIII-96
jedIII96_c13

exp4 s2pul

SAMPLE		DEC. & VT	
date	Feb 15 2007	dfrq	499.869
solvent	cd3od	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	14000	fn	not used
ct	14000	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.7		
wp	25766.5		
vs	7887		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	8539.3		
rfp	6158.9		
th	68		
ins	100.000		
ai cdc ph			



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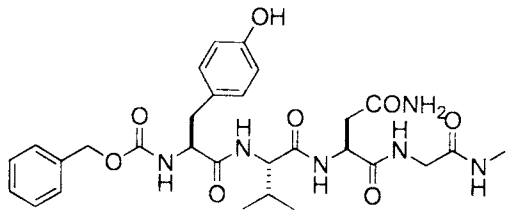
JEDI-286
jedi286_h1

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jan 26 2006	dfrq	499.869
solvent	DMSO	dn	H1
file	exp	dpwr	5
ACQUISITION		dof	
sfrq	499.870	dm	y
tn	H1	dmm	
at	3.996	dmf	20
np	73980	dseq	
sw	9256.0	dres	1.0
fb	not used	homo	n
bs	32	temp	27.0
tpwr	57	PROCESSING	
pw	2.0	lb	0.10
d1	2.000	wtfile	
tof	1124.6	proc	ft
nt	64	fn	not used
ct	64	math	f
alock	n		
gain	30	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	wft
dp	y		
hs	nn		
DISPLAY			
sp	-250.0		
wp	6248.3		
vs	579		
sc	0		
wc	250		
hzmm	24.99		
is	4492.40		
rfl	2257.0		
rfp	1244.7		
th	7		
ins	1.000		
ai	ph		



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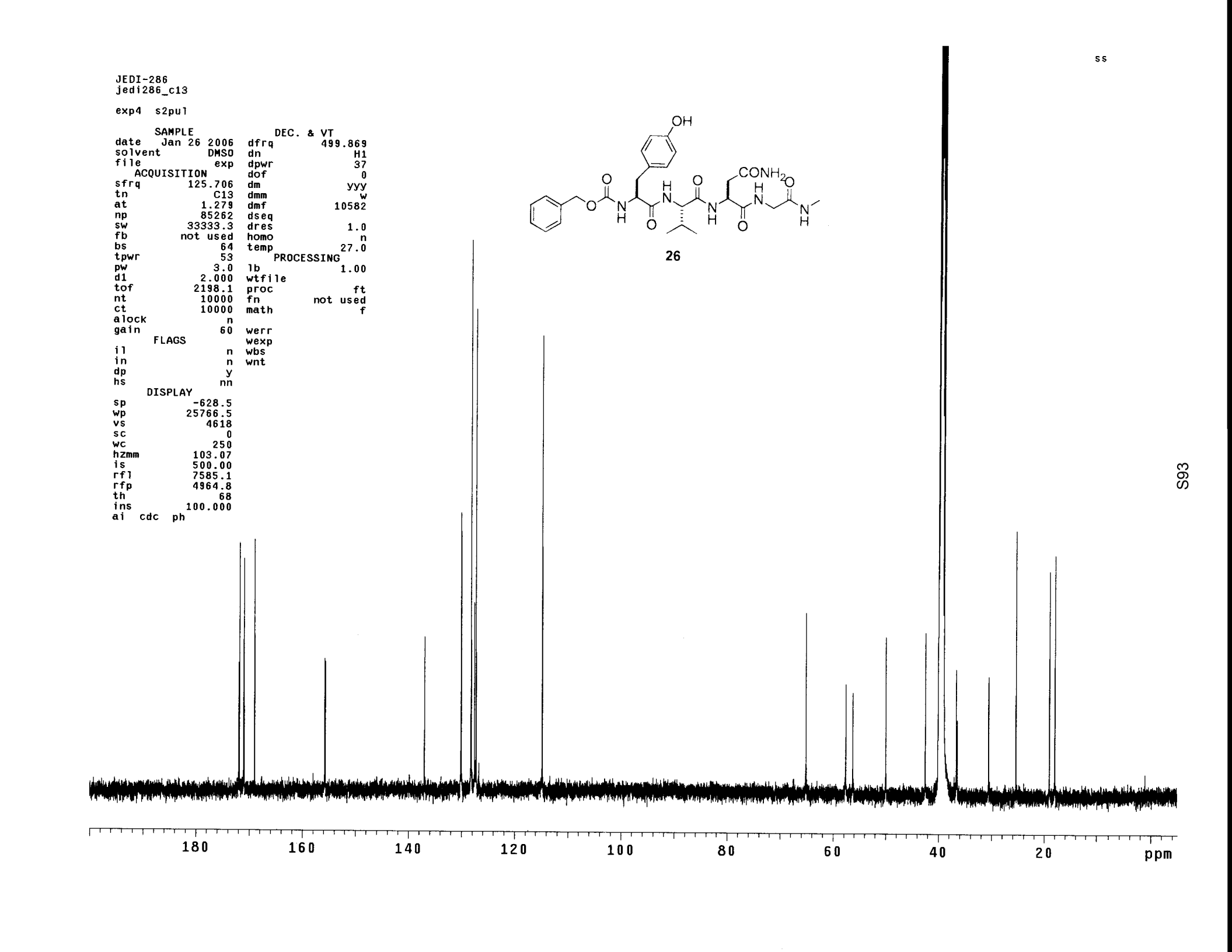
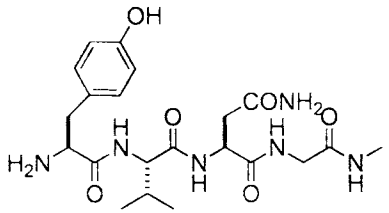
ss


JEDI-286
jedi286_c13
exp4 s2pul
SAMPLE
date Jan 26 2006
solvent DMSO
file exp
ACQUISITION
sfrq 125.706
tn C13
at 1.279
np 85262
sw 33333.3
fb not used
bs 64
tpwr 53
pw 3.0
d1 2.000
tof 2198.1
nt 10000
ct 10000
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -628.5
wp 25766.5
vs 4618
sc 0
wc 250
hzmm 103.07
is 500.00
rfl 7585.1
rfp 4964.8
th 68
ins 100.000
ai cdc ph
DEC. & VT
dfrq 499.869
dn H1
dpwr 37
dof 0
dm yyy
dmm w
dmf 10582
dseq
dres 1.0
homo n
temp 27.0
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
OH
CONH2
O
N
H
26
ss
S93
180
160
140
120
100
80
60
40
20
ppm

jed7-65

Pulse Sequence: s2pul
Solvent: cd3od
Ambient temperature
File: jed7-66
INOVA-500 "nmrastro"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
36 repetitions
OBSERVE H1, 400.2685529 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 2 min, 55 sec



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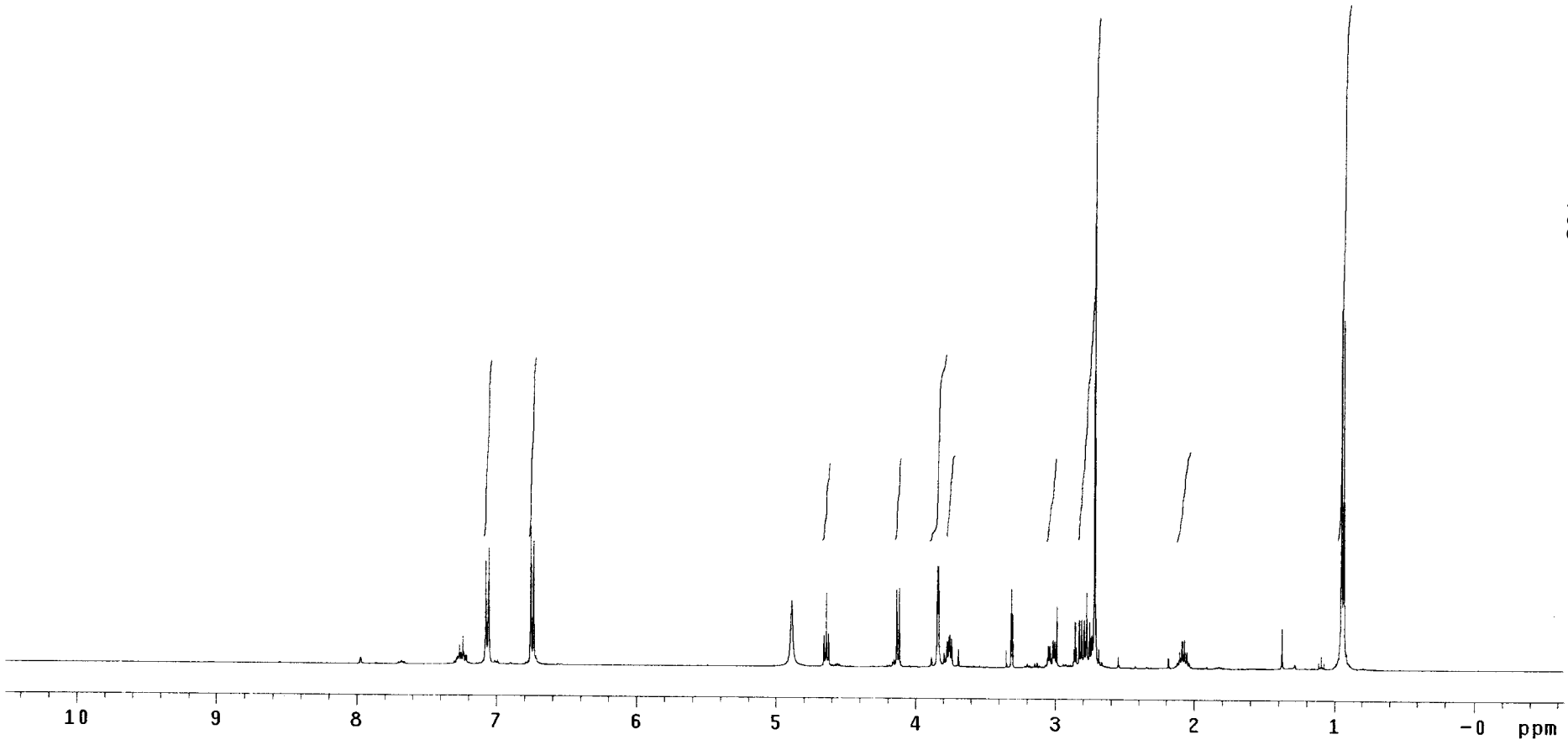
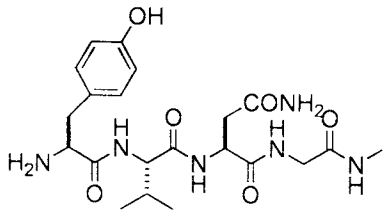


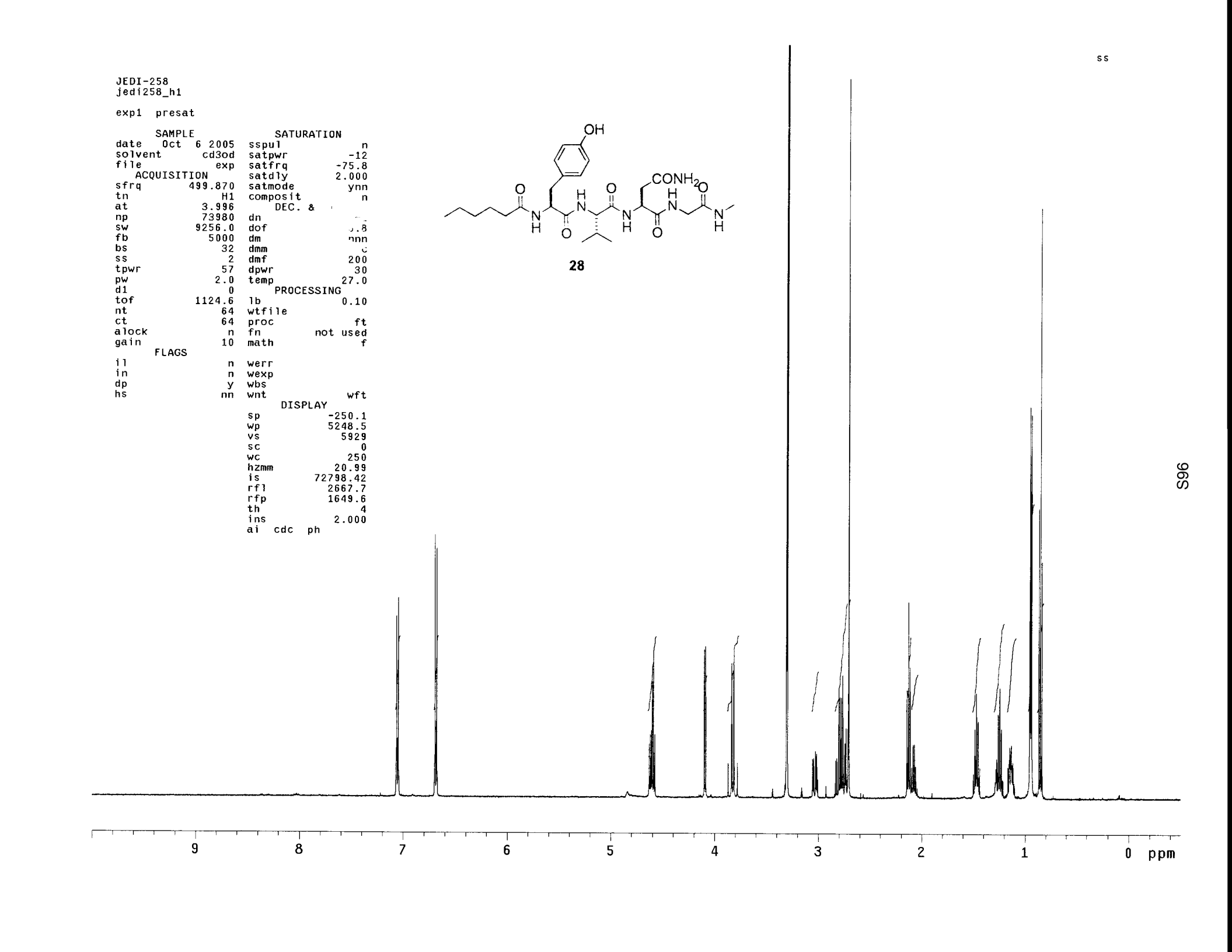
jed7-66

Pulse Sequence: s2pul
Solvent: cd3od
Ambient temperature
UNITYplus-300 "nmr2"

Relax. delay 2.000 sec
Pulse 36.0 degrees
Acq. time 1.777 sec
Width 18009.9 Hz
807 repetitions
OBSERVE C13, 75.4702116 MHz
DECOUPLE H1, 300.1421085 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
Single precision data
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 17 hr, 53 min, 9 sec



27

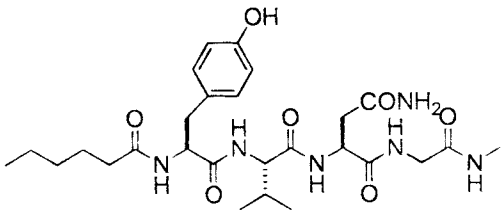

JEDI-258
jedi258_h1
exp1 presat
SAMPLE
date Oct 6 2005
solvent cd3od
file exp
ACQUISITION
sfrq 499.870
tn H1
at 3.996
np 73980
sw 9256.0
fb 5000
bs 32
ss 2
tpwr 57
pw 2.0
d1 0
tof 1124.6
nt 64
ct 64
alock n
gain 10
FLAGS
il n
in n
dp y
hs nn
SATURATION
sspul n
satpwr -12
satfrq -75.8
satdly 2.000
satmode ynn
composit n
DEC. &
dn
dof
dm nnn
dmm
dmf 200
dpwr 30
temp 27.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
DISPLAY
sp -250.1
wp 5248.5
vs 5929
sc 0
wc 250
hzmm 20.99
is 72798.42
rfl 2667.7
rfp 1649.6
th 4
ins 2.000
ai cdc ph
OH
CONH2
28
ss
S96
9
8
7
6
5
4
3
2
1
0 ppm

JEDI-258
jedi258_c13

exp4 s2pul

SAMPLE		DEC. & VT	
date	Oct 6 2005	dfrq	499.869
solvent	cd3od	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	10000	fn	not used
ct	10000	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.7		
wp	25766.5		
vs	8244		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	8538.8		
rfp	6158.9		
th	2		
ins	100.000		

ai cdc ph



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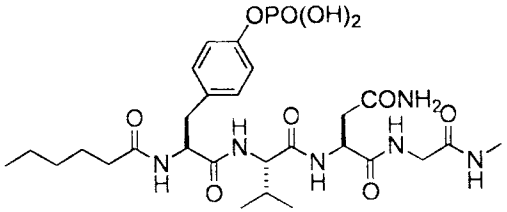
JEDI-267
jedi267_h1

exp1 presat

SAMPLE		SATURATION	
date	Oct 12 2005	sspul	n
solvent	cd3od	satpwr	-12
file	exp	satfrq	-73.0
ACQUISITION		satdly	2.000
sfrq	499.870	satmode	ynn
tn	H1	composit	n
at	3.996	DEC. & VT	
np	73980	dn	H1
sw	9256.0	dof	-73.0
fb	5000	dm	nnn
bs	32	dmm	c
ss	4	dmf	200
tpwr	57	dpwr	30
pw	2.0	temp	27.0
d1	0	PROCESSING	
tof	1124.6	lb	0.10
nt	64	wtfile	
ct	64	proc	ft
alock	n	fn	not used
gain	30	math	f
FLAGS			
il	n	werr	
in	n	wexp	
dp	y	wbs	
hs	nn	wnt	wft
		DISPLAY	
		sp	-250.1
		wp	5248.5
		vs	795
		sc	0
		wc	250
		hzmm	20.99
		is	7791.96
		rfl	2667.7
		rfp	1649.6
		th	3
		ins	2.000
		ai cdc ph	



4

ss

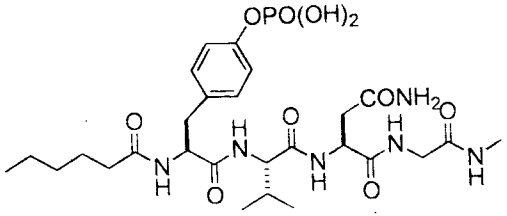
S98

9 8 7 6 5 4 3 2 1 0 ppm

JEDI-267
jedi267_c13

exp4 s2pul

SAMPLE		DEC. & VT	
date	Oct 12 2005	dfrq	499.869
solvent	cd3od	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
ss	32	PROCESSING	
tpwr	53	lb	1.00
pw	3.0	wtfile	
d1	2.000	proc	ft
tof	2198.1	fn	not used
nt	8000	math	f
ct	8000		
alock	n	werr	
gain	60	wexp	
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-628.7		
wp	25766.5		
vs	7759		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	8538.8		
rfp	6158.9		
th	1		
ins	100.000		
ai cdc ph			

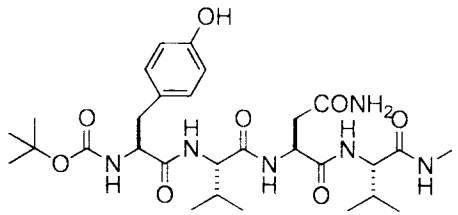


4

JEDII-35
jedII35_h1

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jan 12 2006	dfrq	499.869
solvent	DMSO	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.870	dm	nnn
tn	H1	dmm	c
at	3.996	dmf	200
np	73980	dseq	
sw	9256.0	dres	1.0
fb	not used	homo	n
bs	32	temp	27.0
tpwr	57	PROCESSING	
pw	2.0	lb	0.10
d1	2.000	wtfile	
tof	1124.6	proc	ft
nt	64	fn	not used
ct	64	math	f
alock	n		
gain	30	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	wft
dp	y		
hs	nn		
DISPLAY			
sp	-250.0		
wp	6248.3		
vs	212		
sc	0		
wc	250		
hzmm	24.99		
is	3045.21		
rfl	2256.5		
rfp	1244.7		
th	5		
ins	100.000		
ai	ph		

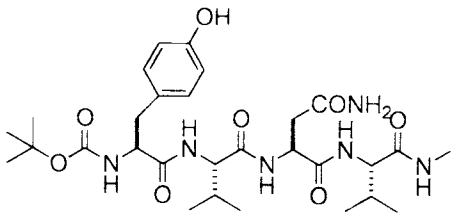


29

JEDII-35
jedII35_c13

exp4 s2pul

SAMPLE		DEC. & VT	
date	Jan 12 2006	dfrq	499.869
solvent	DMSO	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	10000	fn	not used
ct	10000	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.5		
wp	25766.5		
vs	3915		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	7585.1		
rfp	4964.8		
th	1		
ins	100.000		
ai cdc ph			



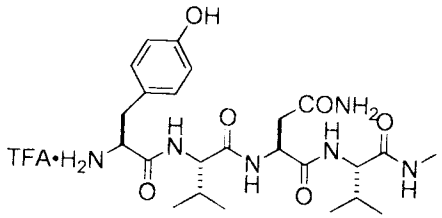
29

ss

JEDII-36
jedII36_h1

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jan 25 2006	dfrq	499.869
solvent	DMSO	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.870	dm	nnn
tn	H1	dmm	c
at	3.996	dmf	200
np	73980	dseq	
sw	9256.0	dres	1.0
fb	not used	homo	n
bs	32	temp	27.0
tpwr	57	PROCESSING	
pw	2.0	lb	0.10
d1	2.000	wtfile	
tof	1124.6	proc	ft
nt	64	fn	not used
ct	64	math	f
alock	n		
gain	30	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	wft
dp	y		
hs	nn		
DISPLAY			
sp	-250.0		
wp	6248.3		
vs	458		
sc	0		
wc	250		
hzmm	24.99		
is	20371.15		
rfl	2258.2		
rfp	1244.7		
th	7		
ins	1.000		
ai	ph		

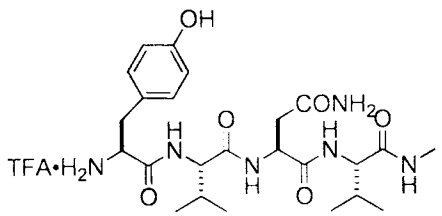


30

JEDII-36
jedII36_c13

exp4 s2pul

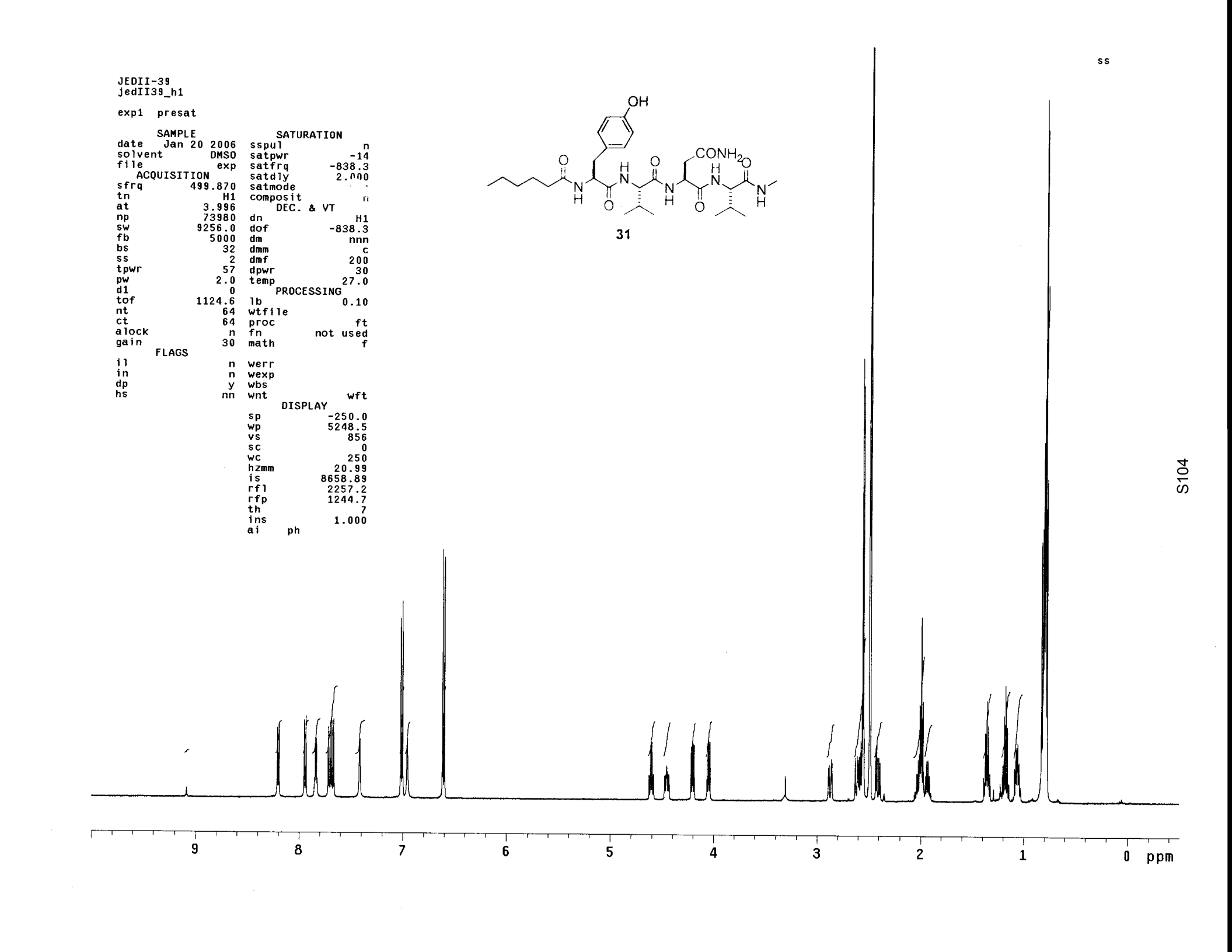
SAMPLE		DEC. & VT	
date	Jan 25 2006	dfrq	499.869
solvent	DMSO	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	10000	fn	not used
ct	10000	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.5		
wp	25766.5		
vs	11126		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	7586.2		
rfp	4964.8		
th	68		
ins	100.000		
ai cdc ph			

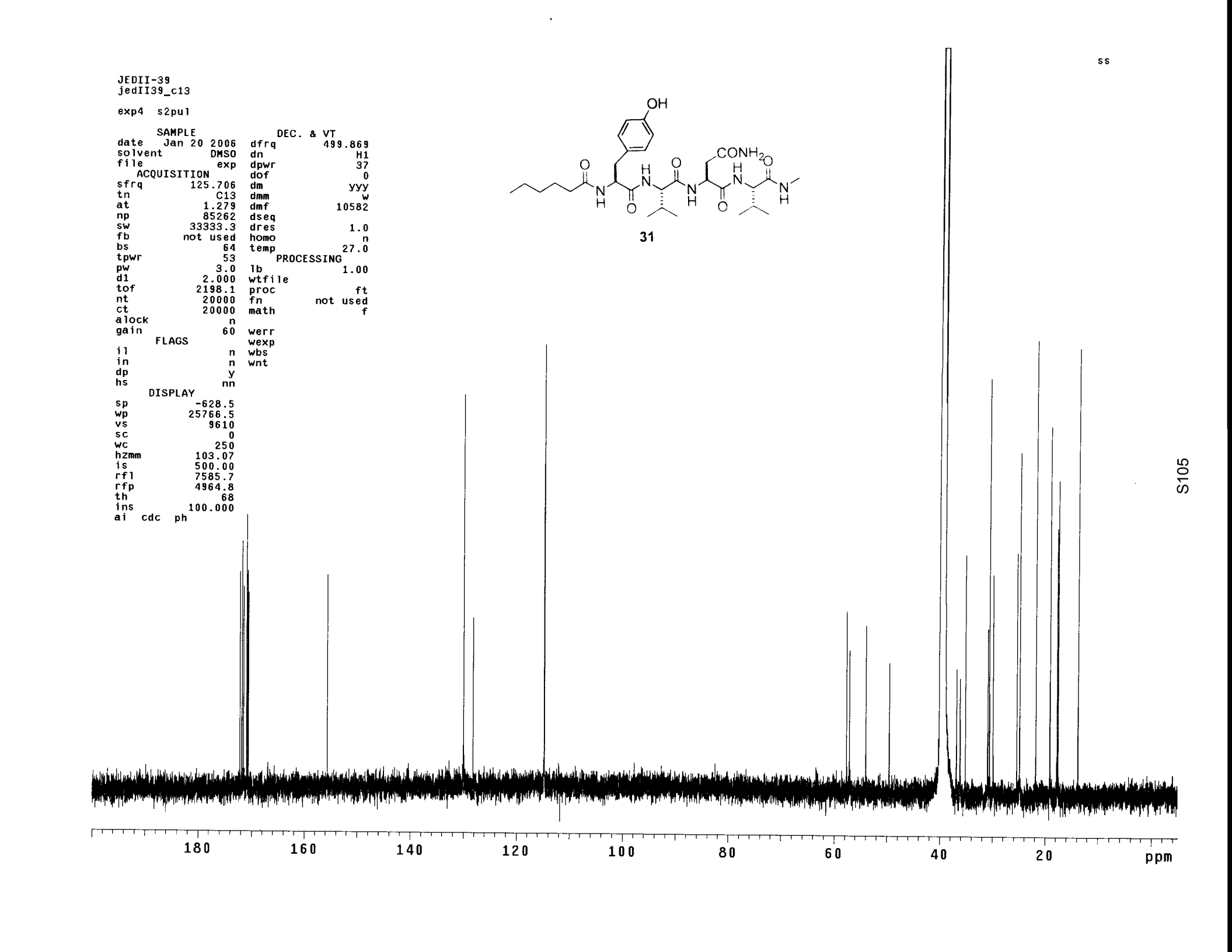


30

ss

S103

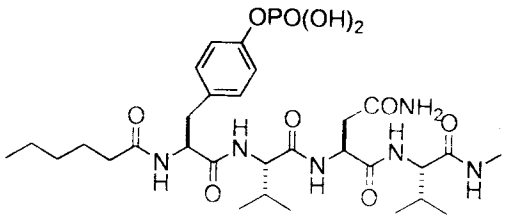

JEDII-39
jedII39_h1
exp1 presat
SAMPLE
date Jan 20 2006
solvent DMSO
file exp
ACQUISITION
sfrq 499.870
tn H1
at 3.996
np 73980
sw 9256.0
fb 5000
bs 32
ss 2
tpwr 57
pw 2.0
d1 0
tof 1124.6
nt 64
ct 64
alock n
gain 30
FLAGS
il n
in n
dp y
hs nn
SATURATION
sspul n
satpwr -14
satfrq -838.3
satdly 2.000
satmode
composit n
DEC. & VT
dn H1
dof -838.3
dm nnn
dmm c
dmf 200
dpwr 30
temp 27.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
DISPLAY
sp -250.0
wp 5248.5
vs 856
sc 0
wc 250
hzmm 20.99
is 8658.89
rfl 2257.2
rfp 1244.7
th 7
ins 1.000
ai ph
OH
CONH2
31
ss
S104
9
8
7
6
5
4
3
2
1
0 ppm


JEDII-39
jedII39_c13
exp4 s2pul
SAMPLE
date Jan 20 2006
solvent DMSO
file exp
ACQUISITION
sfrq 125.706
tn C13
at 1.279
np 85262
sw 33333.3
fb not used
bs 64
tpwr 53
pw 3.0
d1 2.000
tof 2198.1
nt 20000
ct 20000
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -628.5
wp 25766.5
vs 9610
sc 0
wc 250
hzmm 103.07
is 500.00
rfl 7585.7
rfp 4964.8
th 68
ins 100.000
ai cdc ph
DEC. & VT
dfrq 499.869
dn H1
dpwr 37
dof 0
dm yyy
dmm w
dmf 10582
dseq
dres 1.0
homo n
temp 27.0
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
OH
CONH2
31
ss
S105
180
160
140
120
100
80
60
40
20
ppm

JEDII-26-2

exp1 presat

SAMPLE		SATURATION	
date	Jan 2 2006	sspul	n
solvent	D2O	satpwr	-10
file	exp	satfrq	-165.8
ACQUISITION		satdly	2.000
sfrq	499.351	satmode	ynn
tn	H1	composit	n
at	4.865	DEC. & VT	
np	64000	dn	H1
sw	6577.3	dof	-165.8
fb	4000	dm	nnn
bs	32	dmm	c
ss	4	dmf	200
tpwr	54	dpwr	30
pw	2.0	temp	27.0
d1	0	PROCESSING	
tof	297.6	lb	0.10
nt	256	wtfile	
ct	256	proc	ft
alock	n	fn	not used
gain	40	math	f
FLAGS		werr	
il	n	wexp	
in	n	wbs	
dp	y	wnt	wft
hs	nn	DISPLAY	
		sp	-249.7
		wp	5243.1
		vs	40222
		sc	0
		wc	250
		hzmm	20.97
		is	934155.10
		rfl	494.2
		rfp	0
		th	7
		ins	10.000
		ai cdc ph	



5

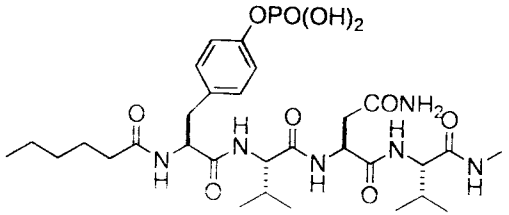
jw

S106

JED7-60

exp4 Carbon

SAMPLE		SPECIAL	
date	Apr 26 2010	temp	27.0
solvent	dmso	gain	50
file	exp	spin	20
ACQUISITION		hst	0.008
sw	30143.2	pw90	15.500
at	1.062	alfa	10.000
np	64024	FLAGS	
fb	17000	il	n
bs	64	in	n
ss	128	dp	y
d1	2.000	hs	nn
nt	17000	PROCESSING	
ct	17000	lb	1.00
TRANSMITTER		fn	not used
tn	C13	DISPLAY	
sfrq	125.588	sp	-628.2
tof	1254.3	wp	25742.4
tpwr	51	rfl	6934.2
pw	8.000	rfp	4960.2
DECOUPLER		rp	-93.0
dn	H1	lp	-212.5
dof	0	PLOT	
dm	yyy	wc	250
dmm	w	sc	0
dpwr	39	vs	58707
dmf	12600	th	8
		ai cdc ph	



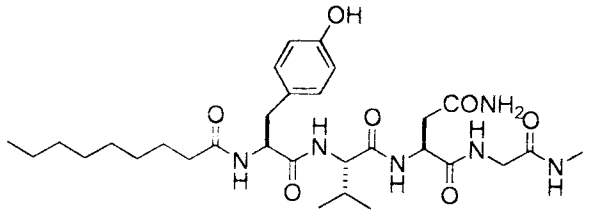
5

jw

JEDIII-34
jedIII34_h1

exp1 presat

SAMPLE		SATURATION	
date	Dec 5 2006	sspul	n
solvent	cd3od	satpwr	-12
file	exp	satfrq	-69.8
ACQUISITION		satdly	2.000
sfrq	499.870	satmode	ynn
tn	H1	composit	n
at	3.996	DEC. & VT	
np	73980	dn	H1
sw	9256.0	dof	-69.8
fb	5000	dm	nnn
bs	32	dmm	c
ss	2	dmf	200
tpwr	57	dpwr	30
pw	2.0	temp	27.0
d1	0	PROCESSING	
tof	1124.6	lb	0.10
nt	64	wtfile	
ct	64	proc	ft
alock	n	fn	not used
gain	30	math	f
FLAGS			
il	n	werr	
in	n	wexp	
dp	y	wbs	
hs	nn	wnt	wft
		DISPLAY	
		sp	-250.1
		wp	5248.5
		vs	477
		sc	0
		wc	250
		hzmm	20.99
		is	4384.62
		rfl	2667.5
		rfp	1649.6
		th	7
		ins	100.000
		ai cdc ph	



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ss

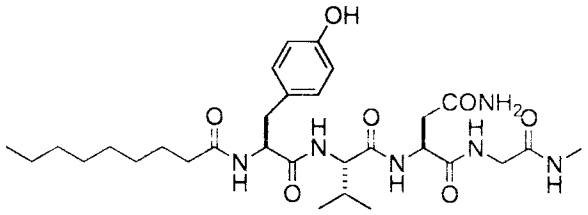
S108

JEDIII-34
jedIII34_c13

exp4 s2pul

SAMPLE		DEC. & VT	
date	Dec 5 2006	dfrq	499.869
solvent	cd3od	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	10000	fn	not used
ct	10000	math	f
alock	n		
gain	50	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.7		
wp	25766.5		
vs	11298		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	8538.8		
rfp	6158.9		
th	68		
ins	100.000		

ai cdc ph



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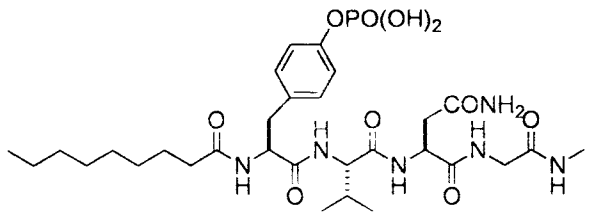
ss

JEDIII-41
jedIII41_h1

exp1 presat

SAMPLE		SATURATION	
date	Dec 6 2006	sspul	n
solvent	cd3od	satpwr	-12
file	exp	satfrq	-67.8
ACQUISITION		satdly	2.000
sfrq	499.870	satmode	ynn
tn	H1	composit	n
at	3.996	DEC. & VT	
np	73980	dn	H1
sw	9256.0	dof	-67.8
fb	5000	dm	nnn
bs	32	dmm	c
ss	2	dmf	200
tpwr	57	dpwr	30
pw	2.0	temp	27.0
d1	0	PROCESSING	
tof	1124.6	lb	0.10
nt	64	wtfile	
ct	64	proc	ft
alock	n	fn	not used
gain	30	math	f
FLAGS			
il	n	werr	
in	n	wexp	
dp	y	wbs	
hs	nn	wnt	wft
		DISPLAY	
		sp	-250.1
		wp	5248.5
		vs	1193
		sc	0
		wc	250
		hzmm	20.99
		is	4234.98
		rfl	1018.1
		rfp	0
		th	7
		ins	1.000
		ai cdc ph	



6

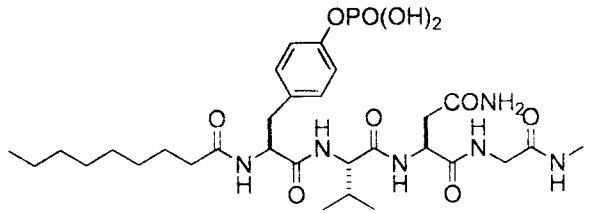
ss

S110

JEDIII-41
jedIII41_c13

exp4 s2pul

SAMPLE		DEC. & VT	
date	Dec 6 2006	dfrq	499.869
solvent	cd3od	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	27.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	7000	fn	not used
ct	7000	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.7		
wp	25766.5		
vs	12819		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	8538.8		
rfp	6158.9		
th	68		
ins	100.000		
ai cdc ph			



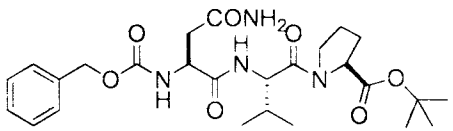
6

S111

JEDII-218

exp1 s2pul

SAMPLE		DEC. & VT	
date	Aug 18 2006	dfrq	499.349
solvent	CDCl3	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.350	dm	nnn
tn	H1	dmm	c
at	4.865	dmf	200
np	89888	dseq	
sw	9237.9	dres	1.0
fb	5000	homo	n
bs	32	temp	27.0
ss	4	PROCESSING	
tpwr	54	lb	0.10
pw	2.0	wtfile	
d1	2.000	proc	ft
tof	1123.4	fn	not used
nt	64	math	f
ct	64		
alock	n	werr	
gain	40	wexp	
FLAGS		wbs	
il	n	wnt	wft
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-249.8		
wp	5243.1		
vs	55		
sc	0		
wc	250		
hzmm	20.97		
is	1623.28		
rfl	1005.7		
rfp	0		
th	3		
ins	1.000		
ai cdc ph			



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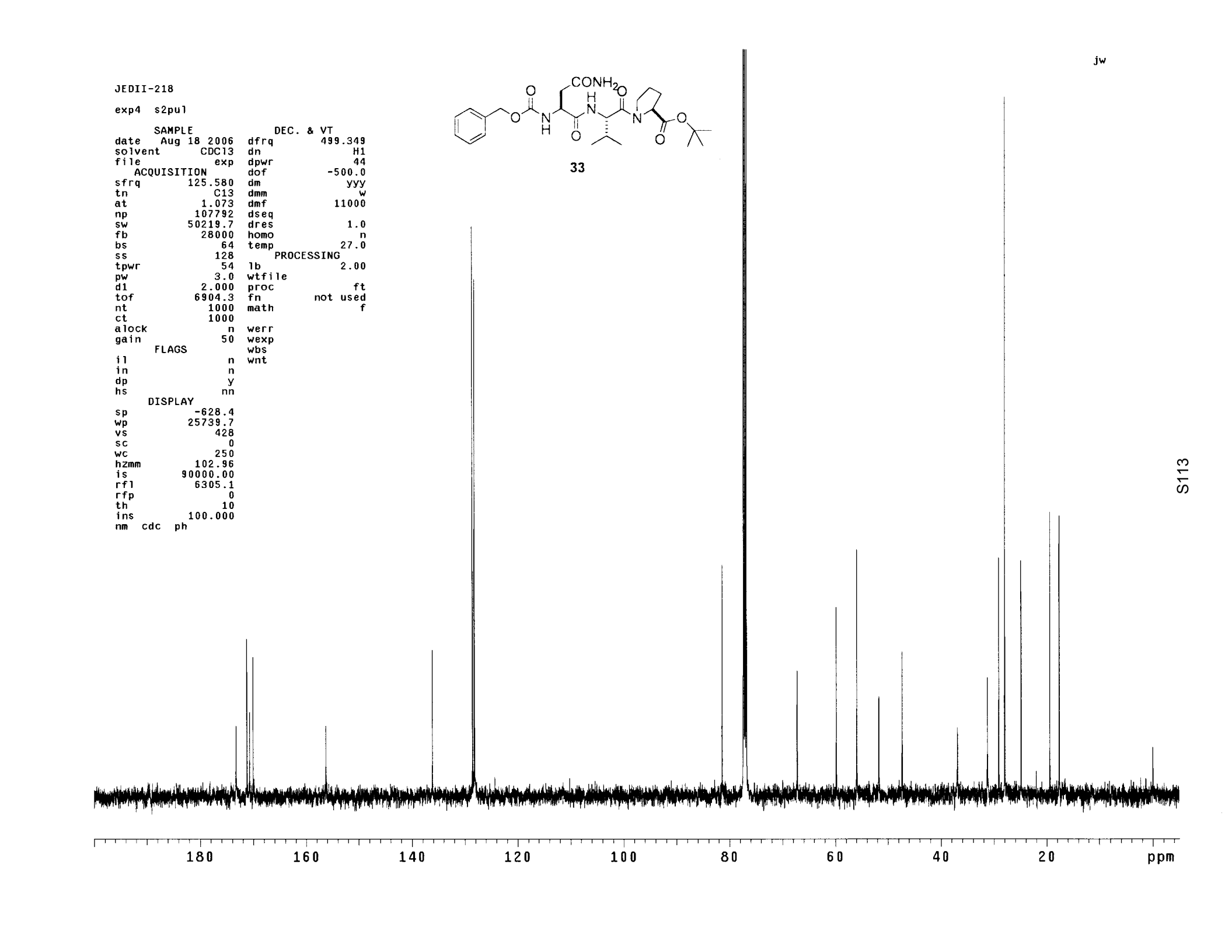
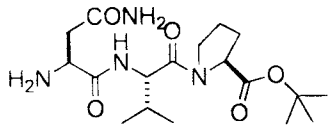

JEDII-218
exp4 s2pul
SAMPLE
date Aug 18 2006
solvent CDCl3
file exp
ACQUISITION
sfrq 125.580
tn C13
at 1.073
np 107792
sw 50219.7
fb 28000
bs 64
ss 128
tpwr 54
pw 3.0
d1 2.000
tof 6904.3
nt 1000
ct 1000
alock n
gain 50
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -628.4
wp 25739.7
vs 428
sc 0
wc 250
hzmm 102.96
is 90000.00
rfl 6305.1
rfp 0
th 10
ins 100.000
nm cdc ph
DEC. & VT
dfrq 499.349
dn H1
dpwr 44
dof -500.0
dm yyy
dmm w
dmf 11000
dseq
dres 1.0
homo n
temp 27.0
PROCESSING
lb 2.00
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
CONH2
33
jw
S113
180
160
140
120
100
80
60
40
20
ppm

Archive directory:
Sample directory:

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 27.0 C / 300.1 K
File: martin_jed2-220_s2pul_H1
INOVA-500 "nmrfred"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 4.049 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 399.8047051 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 min, 25 sec



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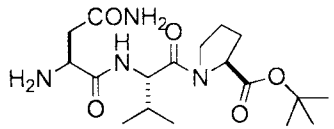
Automation directory: /export/home/staffw/vnmrsys/data/auto_2006.08.18
File : martin_jed2-220_s2pul_02
Sample id : s_20060818_47_01
Sample : jed2-220

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 27.0 C / 300.1 K
Sample #47, Operator: martin
File: martin_jed2-220_s2pul_02
VNMRS-400 "nmrrobo"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
512 repetitions
OBSERVE C13, 100.5309507 MHz
DECOUPLE H1, 399.8067108 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 28 min, 14 sec



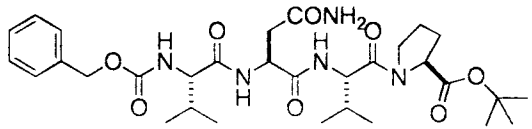
34

Archive directory:
Sample directory:

Pulse Sequence: s2pul

Solvent: cdcl3
Temp. 27.0 C / 300.1 K
File: martin_jed2-221_s2pul_H1
INOVA-500 "nmrfred"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 4.049 sec
Width 6410.3 Hz
64 repetitions
OBSERVE H1, 399.8047084 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 6 min, 39 sec

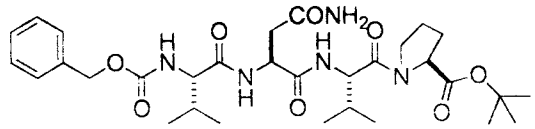


35

Automation directory: /export/home/staffw/vnmrsys/data/auto_2006.08.21
File : martin_jed2-221_s2pul_02
Sample id : s_20060821_4_01
Sample : jed2-221

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 27.0 C / 300.1 K
Sample #4, Operator: martin
File: martin_jed2-221_s2pul_02
VNMRS-400 "nmrrobo"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
1000 repetitions
OBSERVE C13, 100.5309733 MHz
DECOUPLE H1, 399.8067108 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 55 min, 9 sec

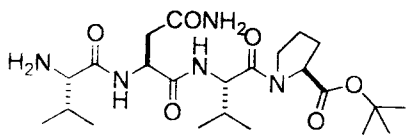


35

Archive directory:
Sample directory:

Pulse Sequence: s2pul
Solvent: cd3od
Temp. 27.0 C / 300.1 K
File: martin_jed2-223_1_s2pul_H1
INOVA-500 "nmrfred"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 4.049 sec
Width 6410.3 Hz
64 repetitions
OBSERVE H1, 399.8062867 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 6 min, 39 sec

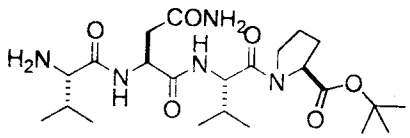


36

Automation directory: /export/home/staffw/vnmrsys/data/auto_2006.08.22
File : martin_jed2-223_1_s2pul_02
Sample id : s_20060822_7_02
Sample : jed2-223_1

Pulse Sequence: s2pul
Solvent: cd3od
Temp. 27.0 C / 300.1 K
Sample #7, Operator: martin
File: martin_jed2-223_1_s2pul_02
VNMRS-400 "nmrrobo"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
1000 repetitions
OBSERVE C13, 100.5313468 MHz
DECOUPLE H1, 399.8082860 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 55 min, 9 sec



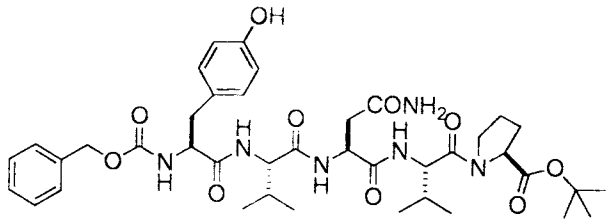
36

JEDII(225)-8/22/06

Pulse Sequence: s2pul

Solvent: CD3OD
Ambient temperature
Mercury-400BB "nmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
24 repetitions
OBSERVE H1, 400.2685554 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 0 sec



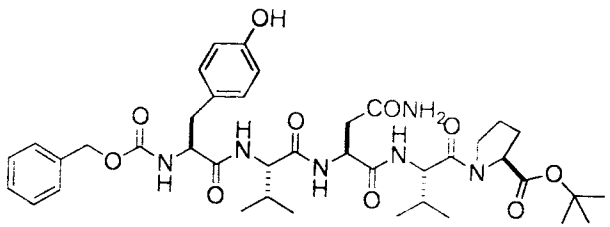
37

Archive directory:
Sample directory:

Pulse Sequence: s2pul

Solvent: cd3od
Temp. 27.0 C / 300.1 K
User: 1-14-87
File: martin_jed2-225_s2pul_C13
INOVA-500 "nmrfred"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
5000 repetitions
OBSERVE C13, 100.5312290 MHz
DECOUPLE H1, 399.8082860 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 4 hr, 35 min, 47 sec

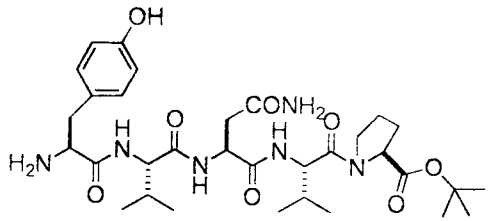


37

JEDII-227

exp1 s2pul

SAMPLE		DEC. & VT	
date	Aug 29 2006	dfrq	499.351
solvent	cd3od	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.352	dm	nnn
tn	H1	dmm	c
at	4.865	dmf	200
np	89888	dseq	
sw	9237.9	dres	1.0
fb	5000	homo	n
bs	32	temp	27.0
ss	4	PROCESSING	
tpwr	54	lb	0.10
pw	2.0	wtfile	
d1	2.000	proc	ft
tof	1123.4	fn	not used
nt	64	math	f
ct	64		
alock	n	werr	
gain	40	wexp	
FLAGS		wbs	
il	n	wnt	wft
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-249.7		
wp	5243.1		
vs	79		
sc	0		
wc	250		
hzmm	20.97		
is	2658.64		
rfl	2659.6		
rfp	1647.9		
th	3		
ins	1.000		
ai cdc ph			



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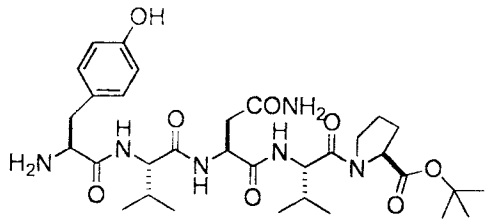
JEDII-227

exp4 s2pul

SAMPLE	
date	Aug 29 2006
solvent	cd3od
file	exp
ACQUISITION	
sfrq	125.575
tn	C13
at	1.073
np	70058
sw	32639.7
fb	18000
bs	64
ss	128
tpwr	60
pw	4.0
d1	2.000
tof	1881.9
nt	12000
ct	12000
alock	n
gain	50
FLAGS	
il	n
in	n
dp	y
hs	nn
DISPLAY	
sp	-627.9
wp	25739.9
vs	1449
sc	0
wc	250
hzmm	102.96
is	90000.00
rfl	8516.0
rfp	6152.5
th	8
ins	100.000
nm cdc ph	

DEC. & VT	
dfrq	499.351
dn	H1
dpwr	36
dof	-500.0
dm	yyy
dmm	w
dmf	14000
dseq	
dres	1.0
homo	n
temp	27.0
PROCESSING	
lb	2.00
wtfile	
proc	ft
fn	not used
math	f
werr	
wexp	
wbs	
wnt	



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jw

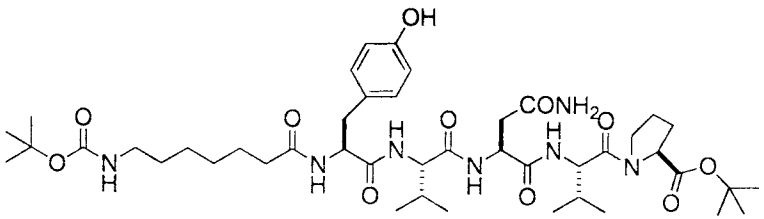
S123

180 160 140 120 100 80 60 40 20 ppm

JEDII-230

exp1 presat

SAMPLE		SATURATION	
date	Aug 30 2006	sspul	n
solvent	cd3od	satpwr	-10
file	exp	satfrq	-64.0
ACQUISITION		satdly	2.000
sfrq	499.352	satmode	ynn
tn	H1	composit	n
at	4.865	DEC. & VT	
np	89888	dn	H1
sw	9237.9	dof	-64.0
fb	5000	dm	nnn
bs	32	dmm	c
ss	4	dmf	200
tpwr	54	dpwr	30
pw	2.0	temp	27.0
d1	0	PROCESSING	
tof	1123.4	lb	0.10
nt	64	wtfile	
ct	64	proc	ft
alock	n	fn	not used
gain	40	math	f
FLAGS			
il	n	werr	
in	n	wexp	
dp	y	wbs	
hs	nn	wnt	wft
		DISPLAY	
		sp	-249.7
		wp	5243.1
		vs	194
		sc	0
		wc	250
		hzmm	20.97
		is	7536.10
		rfl	2659.6
		rfp	1647.9
		th	3
		ins	1.000
		ai cdc ph	



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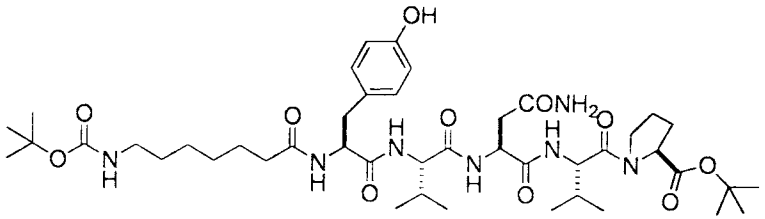
JEDII-230

exp4 s2pul

SAMPLE		DEC. & VT	
date	Aug 30 2006	dfrq	499.351
solvent	cd3od	dn	H1
file	exp	dpwr	36
ACQUISITION		dof	-500.0
sfrq	125.575	dm	yyy
tn	C13	dmm	w
at	1.073	dmf	14000
np	70058	dseq	
sw	32639.7	dres	1.0
fb	18000	homo	n
bs	64	temp	27.0
ss	128	PROCESSING	
tpwr	60	lb	2.00
pw	4.0	wtfile	
d1	2.000	proc	ft
tof	1881.9	fn	not used
nt	12000	math	f
ct	12000		
alock	n	werr	
gain	50	wexp	
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-627.9		
wp	25739.9		
vs	3399		
sc	0		
wc	250		
hzmm	102.96		
is	90000.00		
rfl	8514.5		
rfp	6152.5		
th	16		
ins	100.000		
nm cdc ph			



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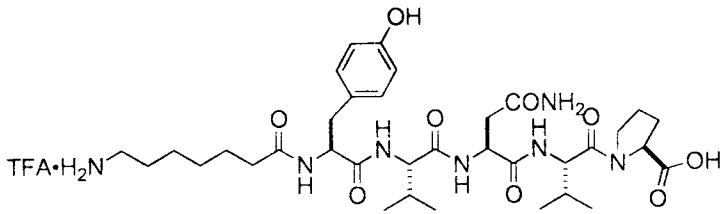
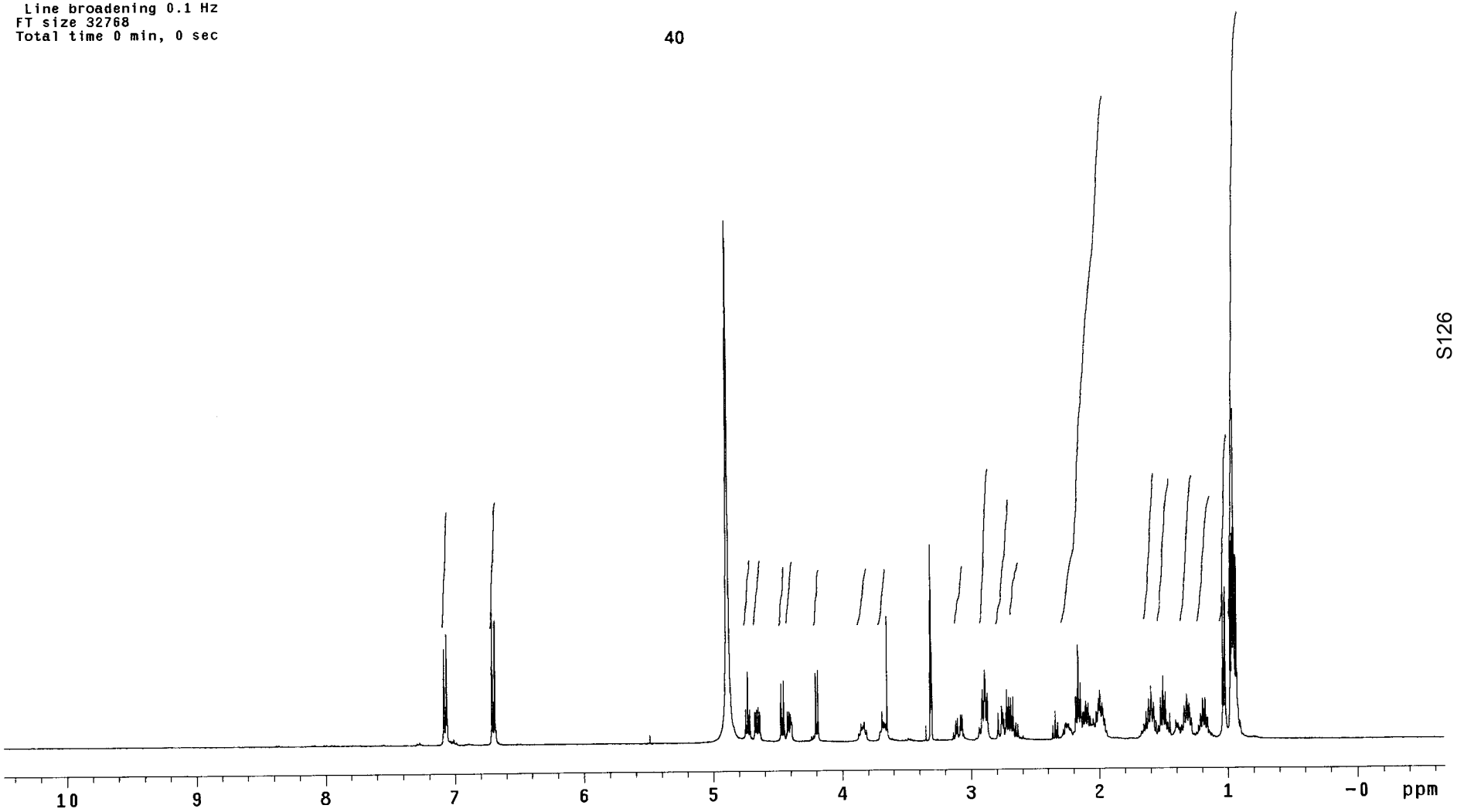
jed7-64

Pulse Sequence: s2pul
Solvent: cd3od
Ambient temperature
Mercury-400BB "nmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
48 repetitions
OBSERVE H1, 400.2685529 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 0 sec



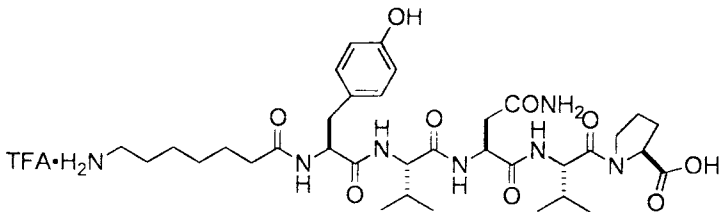
40



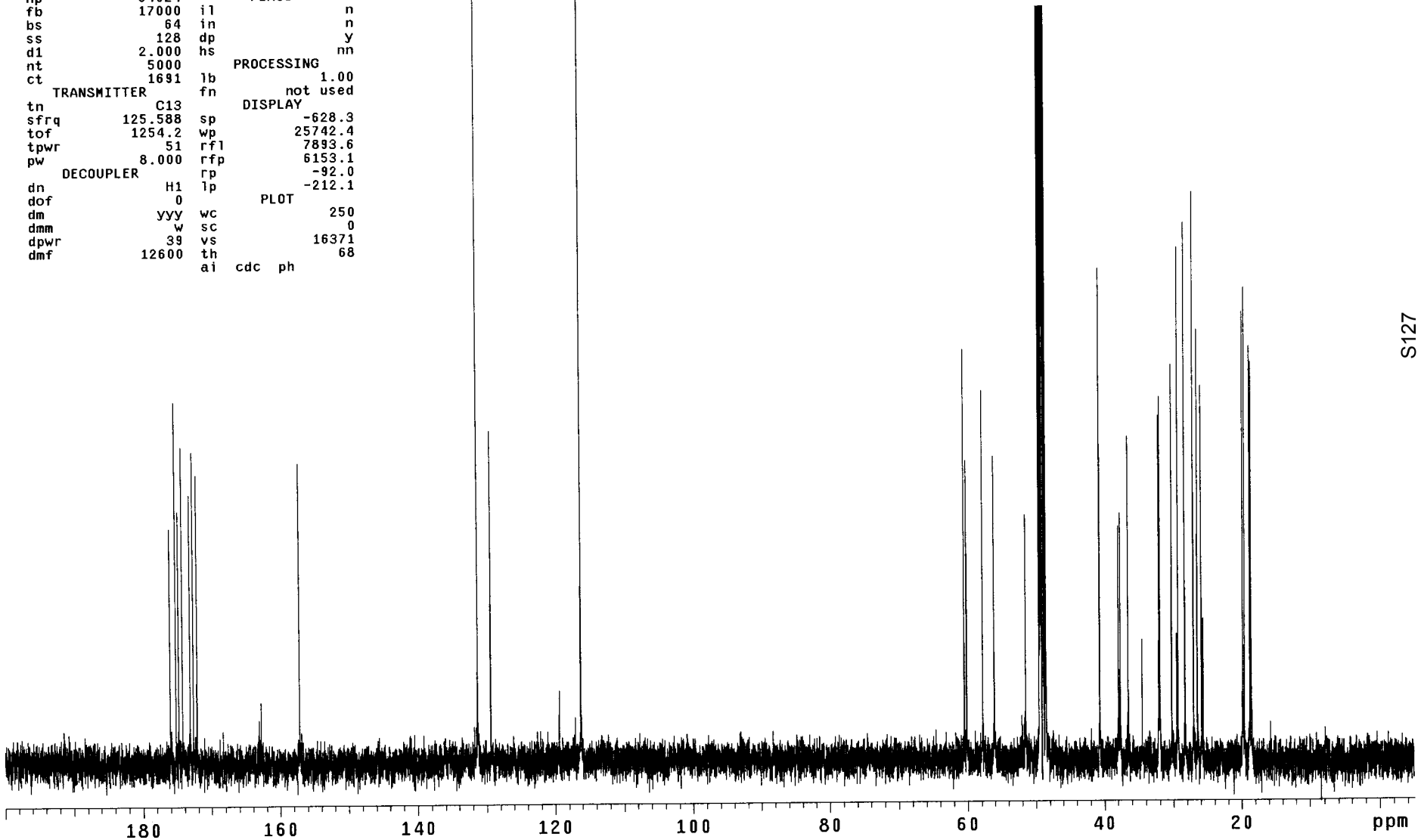
JED7-64

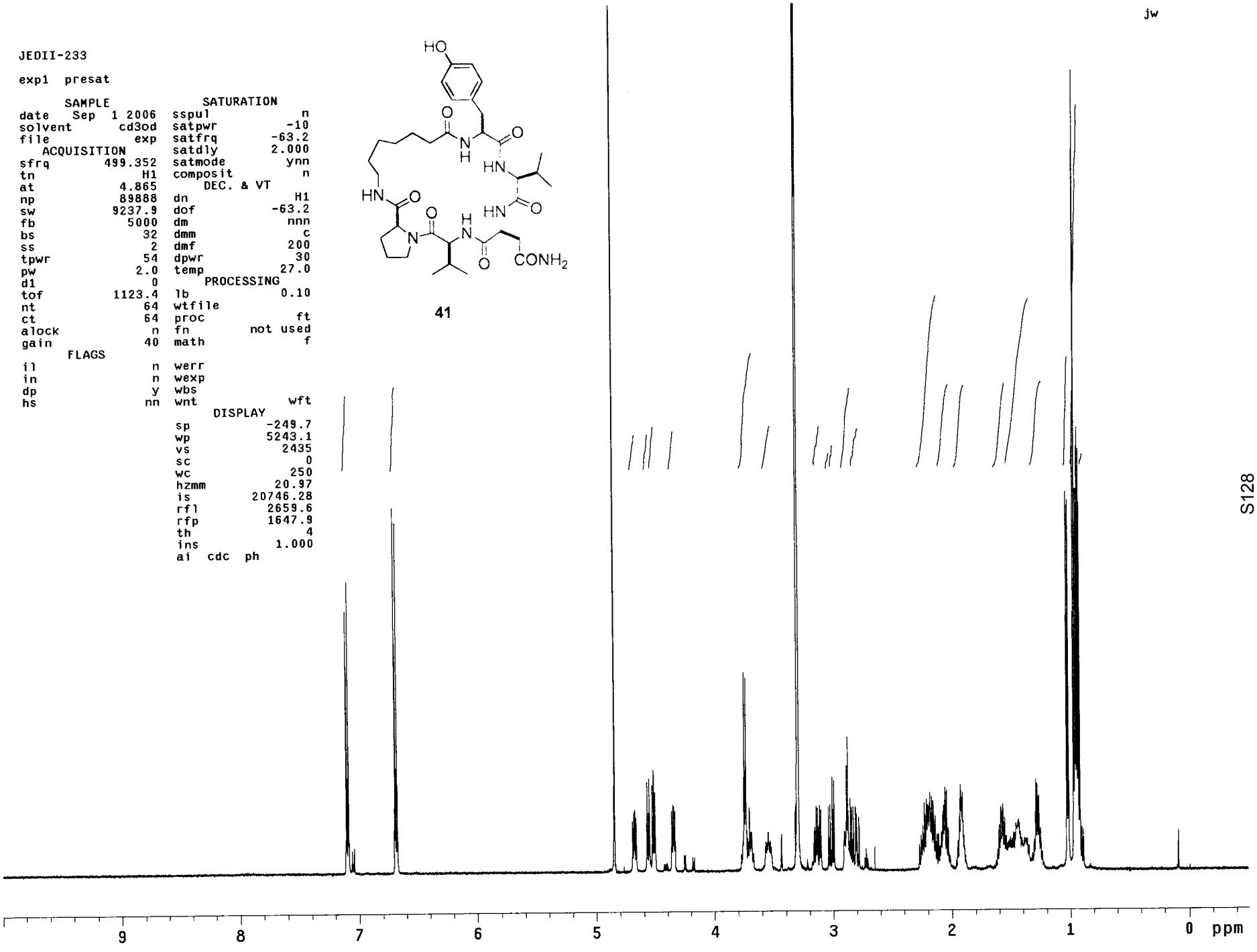
exp4 Carbon

SAMPLE		SPECIAL	
date	Apr 29 2010	temp	27.0
solvent	cd3od	gain	50
file	exp	spin	20
ACQUISITION		hst	0.008
sw	30143.2	pw90	15.500
at	1.062	alfa	10.000
np	64024	FLAGS	
fb	17000	il	n
bs	64	in	n
ss	128	dp	y
d1	2.000	hs	nn
nt	5000	PROCESSING	
ct	1691	lb	1.00
TRANSMITTER		fn	not used
tn	C13	DISPLAY	
sfrq	125.588	sp	-628.3
tof	1254.2	wp	25742.4
tpwr	51	rfl	7893.6
pw	8.000	rfp	6153.1
DECOUPLER		rp	-92.0
dn	H1	lp	-212.1
dof	0	PLOT	
dm	yyy	wc	250
dmm	w	sc	0
dpwr	39	vs	16371
dmf	12600	th	68
		ai cdc ph	



40



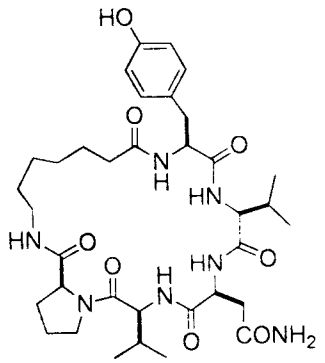

JEDII-233
exp1 presat
SAMPLE
date Sep 1 2006
solvent cd3od
file exp
ACQUISITION
sfrq 499.352
tn H1
at 4.865
np 89888
sw 9237.9
fb 5000
bs 32
ss 2
tpwr 54
pw 2.0
d1 0
tof 1123.4
nt 64
ct 64
alock n
gain 40
FLAGS
il n
in n
dp y
hs nn
SATURATION
sspul n
satpwr -10
satfrq -63.2
satdly 2.000
satmode ynn
composit n
DEC. & VT
dn H1
dof -63.2
dm nnn
dmm c
dmf 200
dpwr 30
temp 27.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
DISPLAY
sp -249.7
wp 5243.1
vs 2435
sc 0
wc 250
hzmm 20.97
is 20746.28
rfl 2659.6
rfp 1647.9
th 4
ins 1.000
ai cdc ph
HO
HN
CONH2
41
jw
S128
9
8
7
6
5
4
3
2
1
0 ppm

JEDII-242
temp=130c
jedII242_c13_130c

exp4 s2pul

SAMPLE		DEC. & VT	
date	Feb 13 2007	dfrq	499.869
solvent	DMSO	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	125.706	dm	yyy
tn	C13	dmm	w
at	1.279	dmf	10582
np	85262	dseq	
sw	33333.3	dres	1.0
fb	not used	homo	n
bs	64	temp	130.0
tpwr	53	PROCESSING	
pw	3.0	lb	1.00
d1	2.000	wtfile	
tof	2198.1	proc	ft
nt	18000	fn	not used
ct	18000	math	f
alock	n		
gain	60	werr	
FLAGS		wexp	
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-628.5		
wp	25766.5		
vs	11066		
sc	0		
wc	250		
hzmm	103.07		
is	500.00		
rfl	7667.5		
rfp	4964.8		
th	68		
ins	100.000		

ai cdc ph



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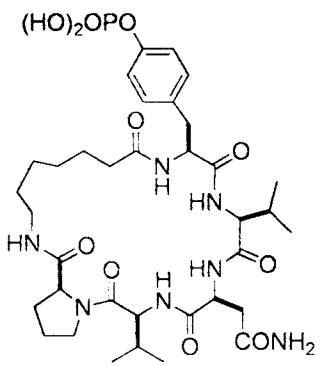
600 MHz nmrox

23macpYVNVP

exp1 Presat

SAMPLE		SPECIAL	
date	Mar 11 2010	temp	27.0
solvent	d2o	gain	40
file	exp	spin	20
ACQUISITION		hst	0.008
sw	9615.4	pw90	11.600
at	4.000	alfa	10.000
np	76924	FLAGS	
fb	4000	il	n
bs	8	in	n
ss	4	dp	y
d1	0.020	hs	nn
nt	128	PROCESSING	
ct	128	lb	0.10
TRANSMITTER		fn	262144
tn	H1	DISPLAY	
sfrq	599.755	sp	-299.9
tof	599.8	wp	6297.3
tpwr	61	rfl	1209.2
pw	11.600	rfp	0
DECOUPLER		rp	148.9
dn	C13	lp	-12.1
dof	0	PLOT	
dm	nnn	wc	250
dmm	c	sc	0
dpwr	37	vs	870
dmf	35088	th	45
		ai cdc ph	



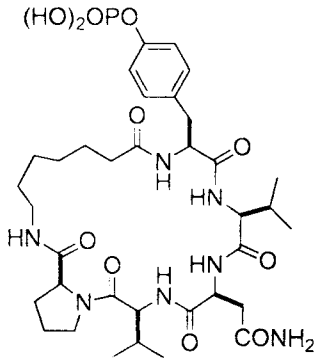
7

600 MHz nmrox

23macpYVNVP

exp4 Carbon

SAMPLE		SPECIAL	
date	Mar 11 2010	temp	27.0
solvent	d2o	gain	40
file	exp	spin	20
ACQUISITION		hst	0.008
sw	40322.6	pw90	7.800
at	2.000	alfa	10.000
np	161290	FLAGS	
fb	17000	il	n
bs	64	in	n
ss	32	dp	y
d1	2.000	hs	nn
nt	13000	PROCESSING	
ct	13000	lb	0.50
TRANSMITTER		fn	262144
tn	C13	DISPLAY	
sfrq	150.824	sp	-754.2
tof	2296.3	wp	30915.4
tpwr	58	rfl	3572.5
pw	3.900	rfp	0
DECOUPLER		rp	213.1
dn	H1	lp	0
dof	0	PLOT	
dm	yyy	wc	250
dmm	w	sc	0
dpwr	46	vs	267807
dmf	15337	th	68
		ai cdc ph	



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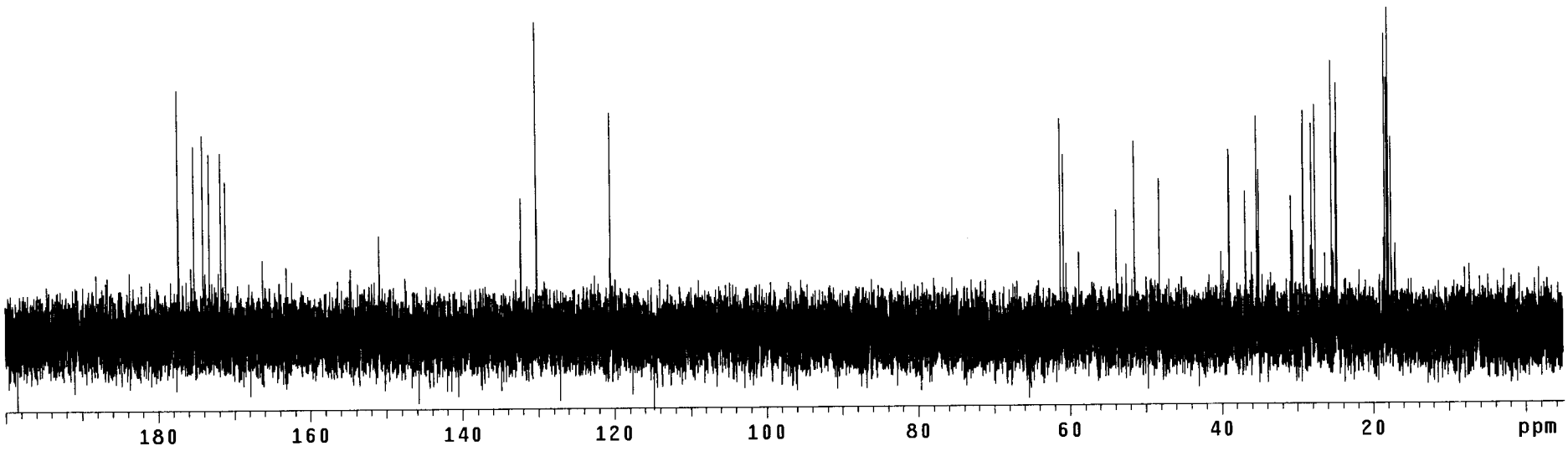
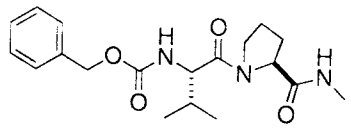


JEDII(291)-11/10/06

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "nmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
36 repetitions
OBSERVE H1, 400.2669784 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 34 sec



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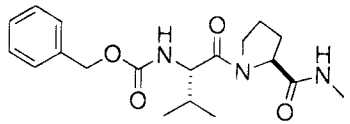
Archive directory:
Sample directory:

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 27.0 C / 300.1 K
User: 1-14-87
File: martin_jed2-291_s2pul_C13
INOVA-500 "nmrfred"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
1000 repetitions
OBSERVE C13, 100.5309507 MHz
DECOUPLE H1, 399.8067108 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 55 min, 9 sec



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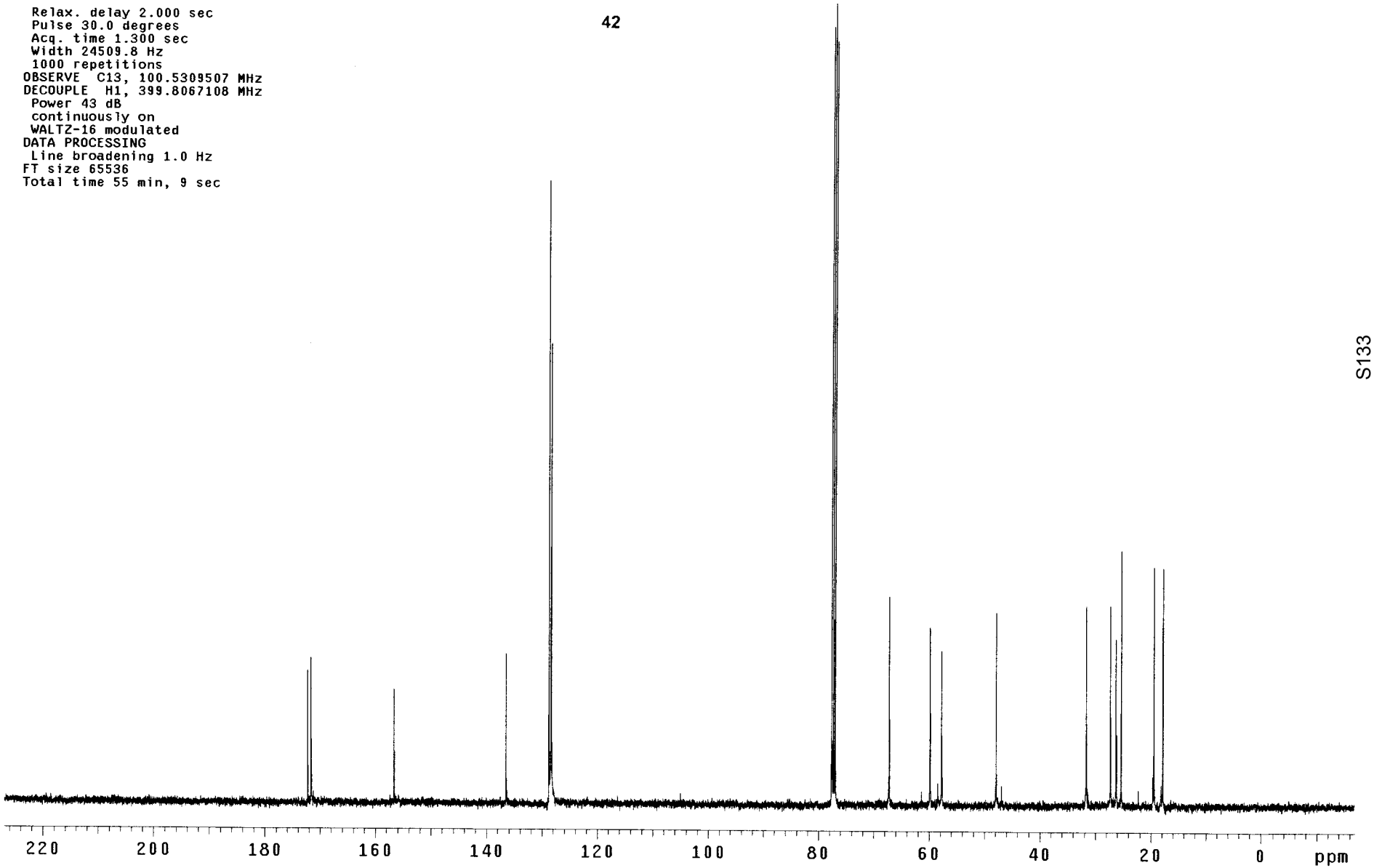
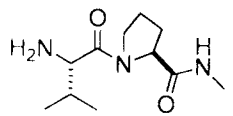


JEDIII(30)-1/30/07

Pulse Sequence: s2pul
Solvent: CD3OD
Ambient temperature
Mercury-400BB "nmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
34 repetitions
OBSERVE H1, 400.2685554 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 34 sec

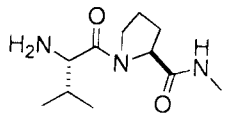


43

Archive directory:
Sample directory:

Pulse Sequence: s2pul
Solvent: cd3od
Temp. 27.0 C / 300.1 K
User: 1-14-87
File: martin_jed3-30carb_s2pul_C13
INOVA-500 "u5b"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
2000 repetitions
OBSERVE C13, 100.5312290 MHz
DECOUPLE H1, 399.8082860 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 50 min, 18 sec



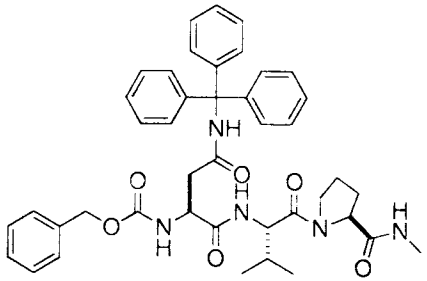
43

Archive directory:
Sample directory:

Pulse Sequence: s2pul

Solvent: cd3od
Temp. 27.0 C / 300.1 K
File: martin_jed2-295_s2pul_H1
INOVA-500 "u5b"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 4.049 sec
Width 6410.3 Hz
64 repetitions
OBSERVE H1, 399.8062867 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 6 min, 39 sec



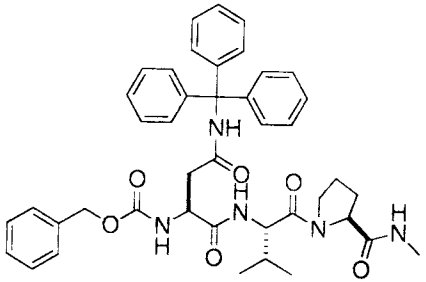
44

Archive directory:
Sample directory:

Pulse Sequence: s2pul

Solvent: cd3od
Temp. 27.0 C / 300.1 K
User: 1-14-87
File: martin_jed2-295a_s2pul_C13
INOVA-500 "u5b"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
5000 repetitions
OBSERVE C13, 100.5313468 MHz
DECOUPLE H1, 399.8082860 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 4 hr, 35 min, 47 sec

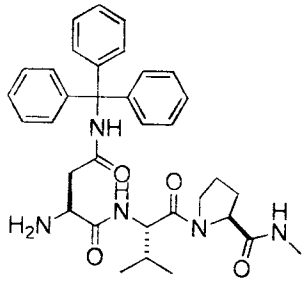


44

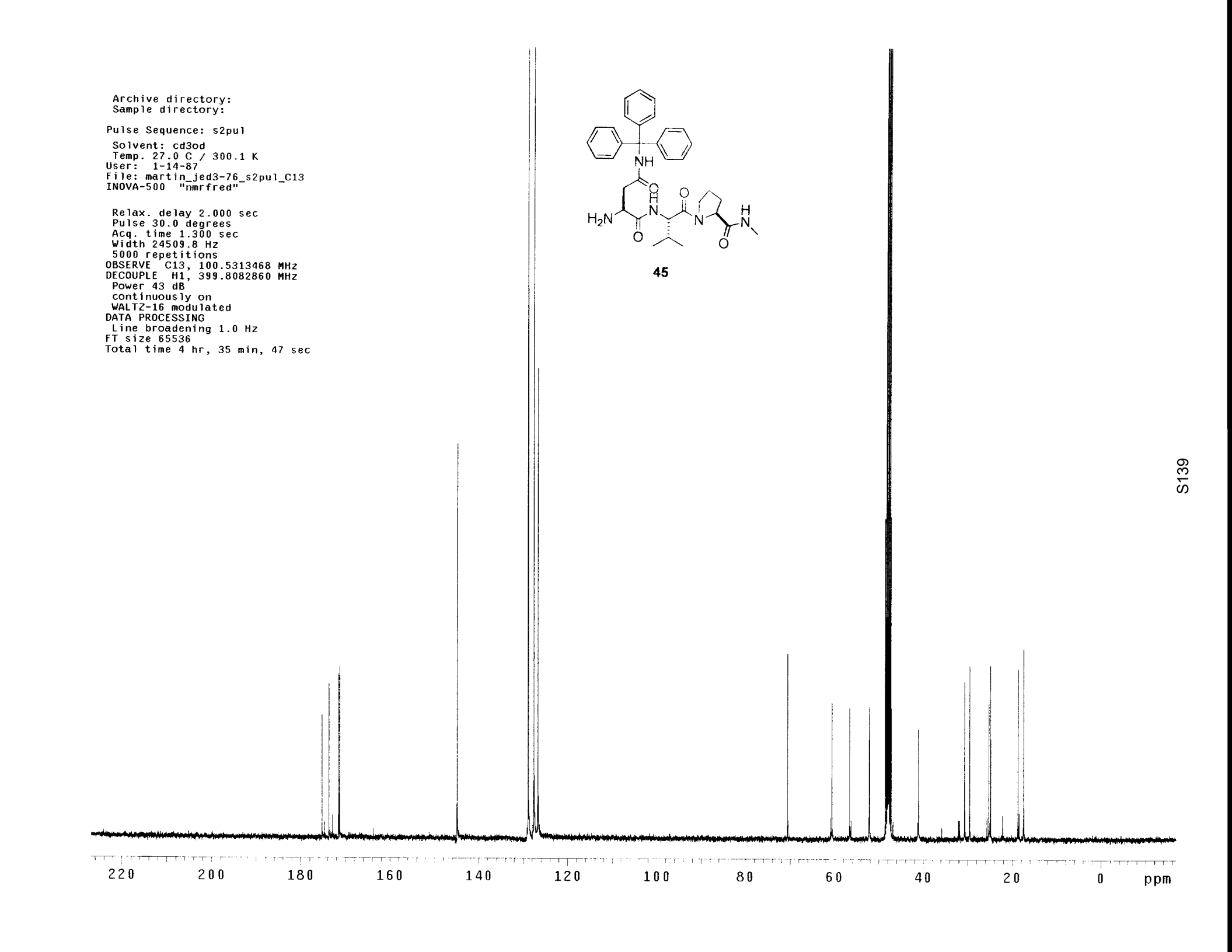
Archive directory:
Sample directory:

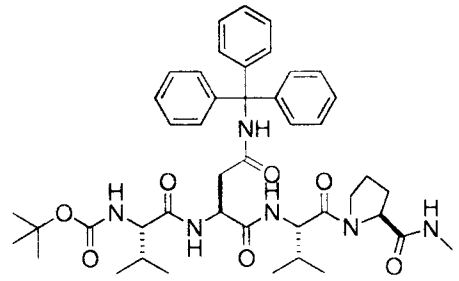
Pulse Sequence: s2pul
Solvent: cd3od
Temp. 27.0 C / 300.1 K
File: martin_jed3-76_s2pul_H1
INOVA-500 "nmrfred"

Relax. delay 5.000 sec
Pulse 30.0 degrees
Acq. time 4.049 sec
Width 6410.3 Hz
64 repetitions
OBSERVE H1, 399.8062867 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 9 min, 57 sec



45


Archive directory:
Sample directory:
Pulse Sequence: s2pul
Solvent: cd3od
Temp. 27.0 C / 300.1 K
User: 1-14-87
File: martin_jed3-76_s2pul_C13
INOVA-500 "nmrfred"
Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
5000 repetitions
OBSERVE C13, 100.5313468 MHz
DECOUPLE H1, 399.8082860 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 4 hr, 35 min, 47 sec
NH
OH
N
O
H_2N
O
N
O
H
N
45
220
200
180
160
140
120
100
80
60
40
20
0
ppm
S139



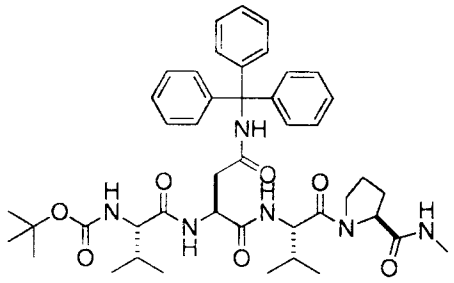
46

Archive directory:
Sample directory:

Pulse Sequence: s2pul

Solvent: cd3od
Temp. 27.0 C / 300.1 K
User: 1-14-87
File: martin_jed2-299_s2pul_C13
INOVA-500 "u5b"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
512 repetitions
OBSERVE C13, 100.5313468 MHz
DECOUPLE H1, 399.8082860 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 28 min, 14 sec



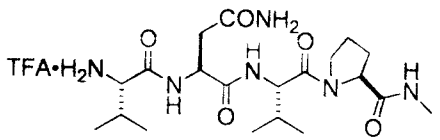
46

Archive directory:
Sample directory:

Pulse Sequence: s2pul

Solvent: cd3od
Temp. 27.0 C / 300.1 K
File: martin_jed3-71_s2pul_H1
INOVA-500 "u5b"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 4.049 sec
Width 6410.3 Hz
64 repetitions
OBSERVE H1, 399.8062867 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 6 min, 39 sec

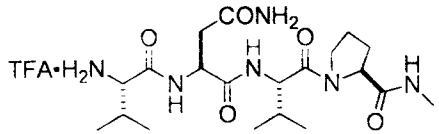


47

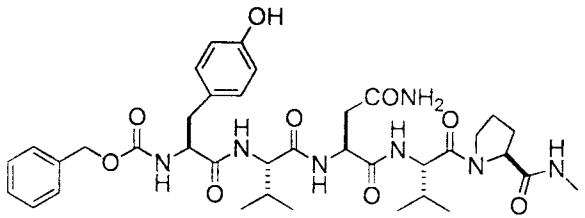
Archive directory:
Sample directory:

Pulse Sequence: s2pul
Solvent: cd3od
Temp. 27.0 C / 300.1 K
User: 1-14-87
File: martin_jed3-71_s2pul_C13
INOVA-500 "u5b"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
2000 repetitions
OBSERVE C13, 100.5313468 MHz
DECOUPLE H1, 399.8082860 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 50 min, 18 sec

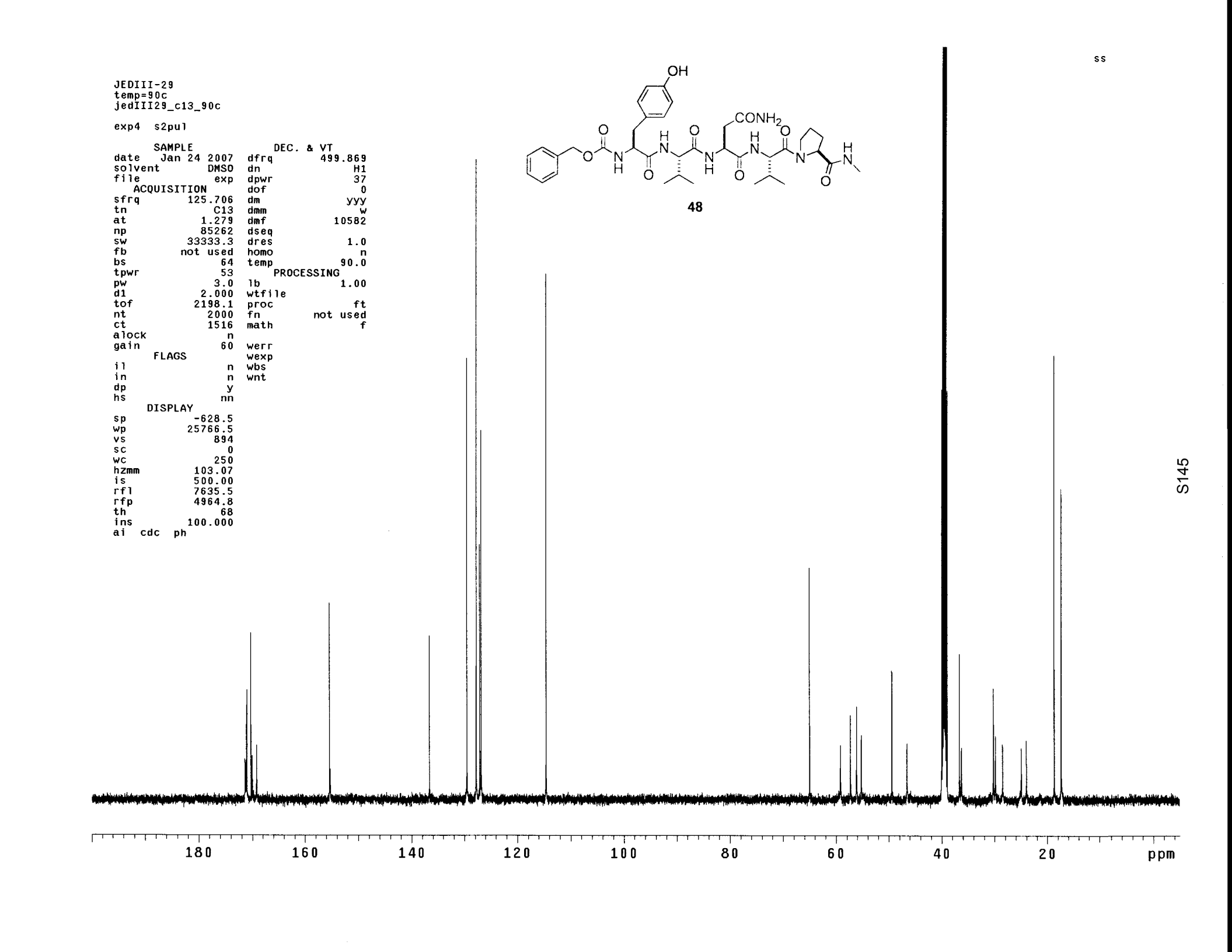


47



48

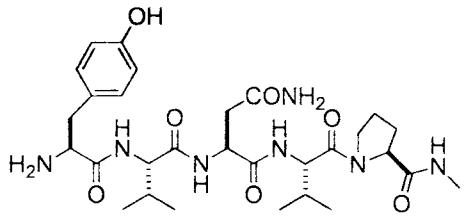
```
JEDIII-29
temp=90c
jedIII29_h1_90c

exp1  s2pul

      SAMPLE
date   Jan 24 2007
solvent       DMSO
file           exp
   ACQUISITION
sfrq       499.870
tn              H1
at             3.996
np             73980
sw            9256.0
fb         not used
bs                32
tpwr              57
pw               2.0
d1             2.000
tof           1124.6
nt                64
ct                64
alock              n
gain              60
      FLAGS
il                 n
in                 n
dp                 y
hs                nn
     DISPLAY
sp            -250.0
wp            5248.5
vs               476
sc                 0
wc               250
hzmm           20.99
is           2734.33
rfl          2256.4
rfp          1244.7
th                 7
ins            1.000
ai    ph

      DEC. & VT
dfrq       499.869
dn              H1
dpwr            30
dof              0
dm             nnn
dmm              c
dmf            200
dseq
dres           1.0
homo             n
temp          90.0
     PROCESSING
lb             0.10
wtfile
proc             ft
fn         not used
math             f
werr
wexp
wbs
wnt            wft
```


JEDIII-29
temp=90c
jedIII29_c13_90c
exp4 s2pul
SAMPLE
date Jan 24 2007
solvent DMSO
file exp
ACQUISITION
sfrq 125.706
tn C13
at 1.279
np 85262
sw 33333.3
fb not used
bs 64
tpwr 53
pw 3.0
d1 2.000
tof 2198.1
nt 2000
ct 1516
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -628.5
wp 25766.5
vs 894
sc 0
wc 250
hzmm 103.07
is 500.00
rfl 7635.5
rfp 4964.8
th 68
ins 100.000
ai cdc ph
DEC. & VT
dfrq 499.869
dn H1
dpwr 37
dof 0
dm yyy
dmm w
dmf 10582
dseq
dres 1.0
homo n
temp 90.0
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
OH
CONH2
48
ss
S145
180
160
140
120
100
80
60
40
20
ppm

JEDIII(91)-2/1/07

Pulse Sequence: s2pul
Solvent: CD3OD
Ambient temperature
Mercury-400BB "nmr6"

Relax. delay 2.000 sec
Pulse 16.4 degrees
Acq. time 2.856 sec
Width 5602.2 Hz
24 repetitions
OBSERVE H1, 400.2685554 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 0 sec

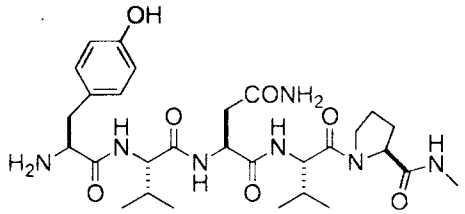


49

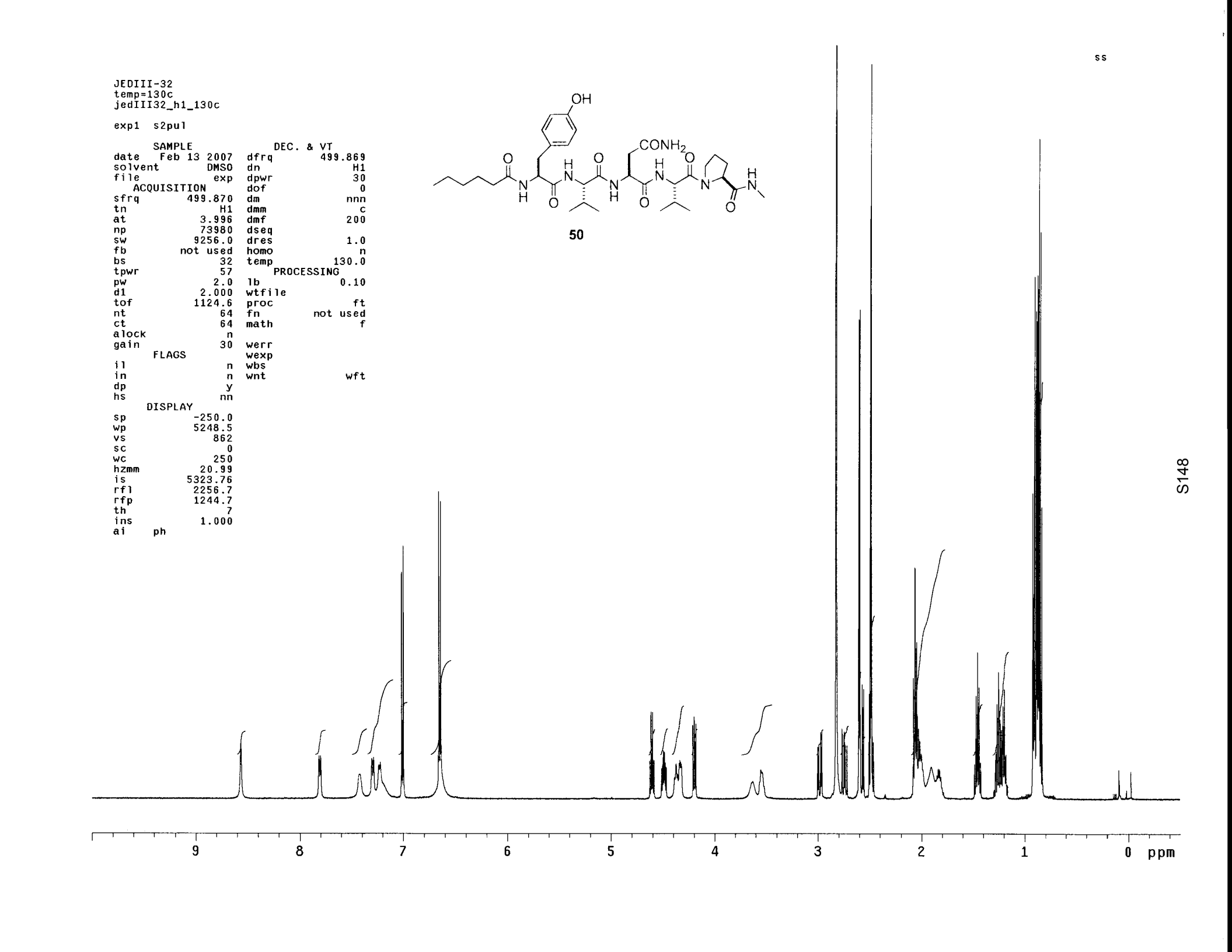
Archive directory:
Sample directory:

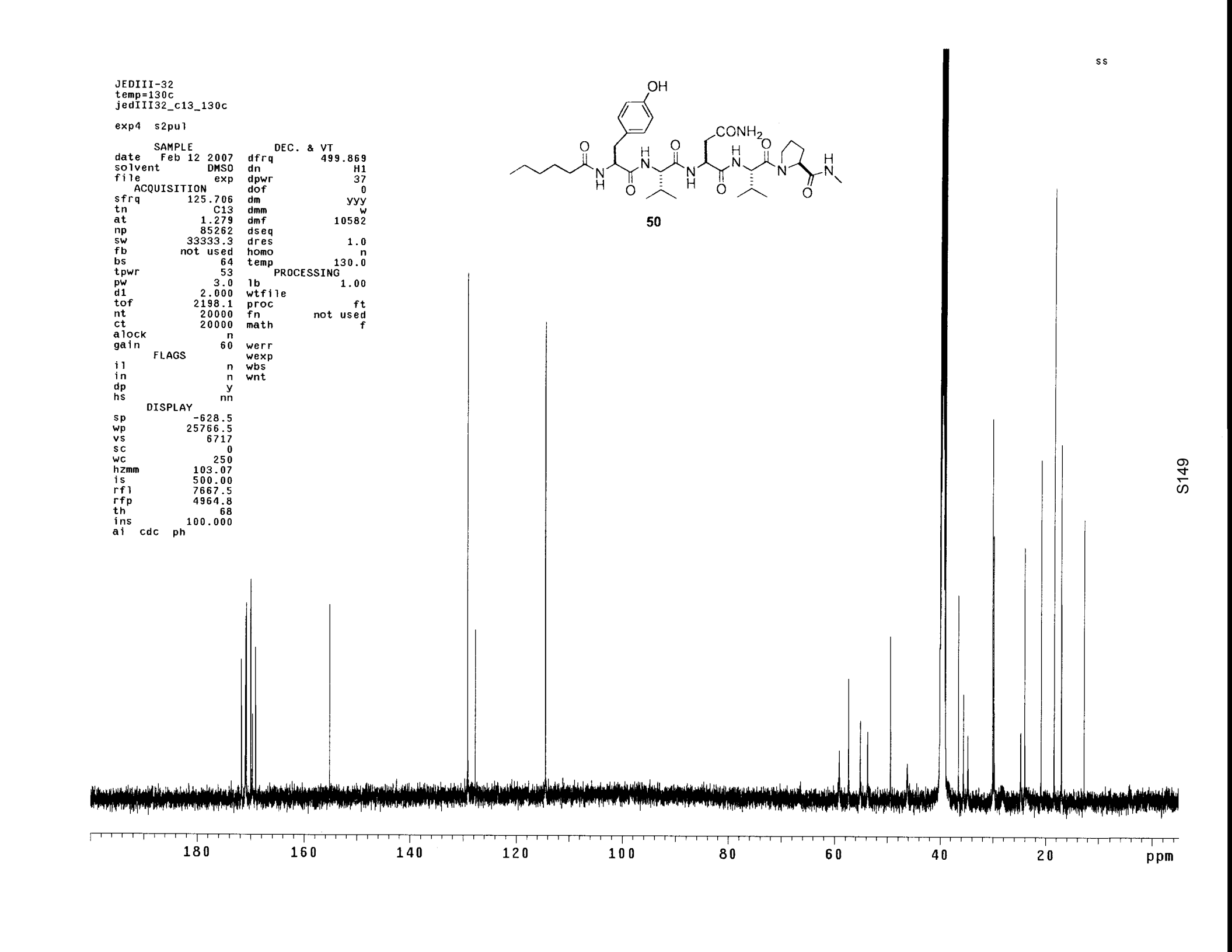
Pulse Sequence: s2pul
Solvent: cd3od
Temp. 27.0 C / 300.1 K
User: 1-14-87
File: martin_jed3-91_s2pul_C13
INOVA-500 "u5b"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
2000 repetitions
OBSERVE C13, 100.5312305 MHz
DECOUPLE H1, 399.8082860 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 50 min, 18 sec



49

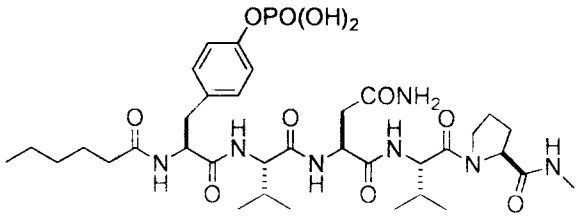

JEDIII-32
temp=130c
jedIII32_h1_130c
exp1 s2pul
SAMPLE
date Feb 13 2007
solvent DMSO
file exp
ACQUISITION
sfrq 499.870
tn H1
at 3.996
np 73980
sw 9256.0
fb not used
bs 32
tpwr 57
pw 2.0
d1 2.000
tof 1124.6
nt 64
ct 64
alock n
gain 30
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.0
wp 5248.5
vs 862
sc 0
wc 250
hzmm 20.99
is 5323.76
rfl 2256.7
rfp 1244.7
th 7
ins 1.000
ai ph
DEC. & VT
dfrq 499.869
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
temp 130.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
OH
CONH2
50
ss
S148
9
8
7
6
5
4
3
2
1
0 ppm


JEDIII-32
temp=130c
jedIII32_c13_130c
exp4 s2pul
SAMPLE
date Feb 12 2007
solvent DMSO
file exp
ACQUISITION
sfrq 125.706
tn C13
at 1.279
np 85262
sw 33333.3
fb not used
bs 64
tpwr 53
pw 3.0
d1 2.000
tof 2198.1
nt 20000
ct 20000
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -628.5
wp 25766.5
vs 6717
sc 0
wc 250
hzmm 103.07
is 500.00
rfl 7667.5
rfp 4964.8
th 68
ins 100.000
ai cdc ph
DEC. & VT
dfrq 499.869
dn H1
dpwr 37
dof 0
dm yyy
dmm w
dmf 10582
dseq
dres 1.0
homo n
temp 130.0
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
OH
CONH2
O
N
H
50
ss
S149
180
160
140
120
100
80
60
40
20
ppm

231inpYUNVP

exp1 Presat

SAMPLE		SPECIAL	
date	Mar 12 2010	temp	27.0
solvent	d2o	gain	50
file	exp	spin	0
ACQUISITION		hst	0.008
sw	7990.4	pw90	15.300
at	4.005	alfa	6.600
np	64000	FLAGS	
fb	4000	il	n
bs	32	in	n
ss	2	dp	y
d1	0.020	hs	nn
nt	64	PROCESSING	
ct	64	lb	0.20
TRANSMITTER		fn	65536
tn	H1	DISPLAY	
sfrq	499.403	sp	-249.7
tof	499.3	wp	5243.5
tpwr	55	rfl	998.8
pw	2.550	rfp	0
DECOUPLER		rp	106.7
dn	C13	lp	9[illegible]
dof	0	PLOT	
dm	nnn	wc	215
dmm	c	sc	35
dpwr	35	vs	9353
dmf	32258	th	45
		ai cdc ph	



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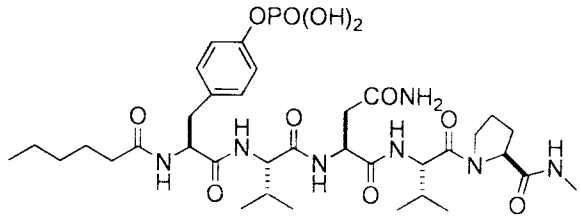
231inpYUNVP

exp4 s2pul

SAMPLE		SPECIAL	
date	Mar 12 2010	temp	27.0
solvent	d2o	gain	50
file	exp	spin	20
ACQUISITION		hst	0.008
sw	30143.2	pw90	15.500
at	1.062	alfa	10.000
np	64024	FLAGS	
fb	17000	il	n
bs	64	in	n
ss	128	dp	y
d1	2.000	hs	nn
nt	20000	PROCESSING	
ct	20000	lb	1.00
TRANSMITTER		fn	not used
tn	C13	DISPLAY	
sfrq	125.587	sp	-628.8
tof	1254.3	wp	25742.4
tpwr	51	rfl	1886.3
pw	8.000	rfp	0
DECOUPLER		rp	-3.7
dn	H1	lp	-219.5
dof	0	PLOT	
dm	yyy	wc	250
dmm	w	sc	0
dpwr	39	vs	119850
dmf	12600	th	19
		ai cdc ph	



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