Supporting Information

Reduced-Amide Inhibitor of Pin1 Binds in a Conformation Resembling a Twisted-Amide Transition State[†]

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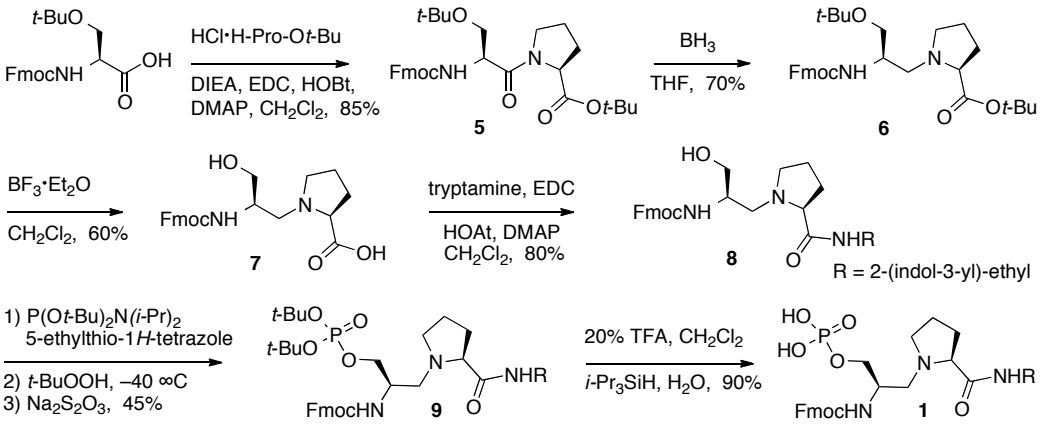
Synthesis of Reduced Amide Inhibitors. The key step in the synthesis of **1** was selective reduction of the amide in the presence of both an ester and a carbamate (Scheme S1).(*1, 2*) Fmoc–Ser(*t*-Bu)–OH was coupled to H–Pro–O*t*-Bu to form amide **5** using1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC) (Scheme 1). Amide **5** was reduced selectively with borane to form the reduced amide **6**. Both *t*-Bu groups were removed with $BF_3{\cdot}Et_2O$ to form intermediate **7**, although the deprotection has only been reported for a *t*-Bu ester.(*3*) Acid **7**, with the unprotected alcohol side chain, was coupled selectively to tryptamine using EDC, 1-hydroxyl-7-azabenzo-triazole (HOAt),(*4*) and DMAP to give amide **8** in 80% yield.

[†] *Accession Codes:* Coordinates and structure factors have been deposited in the Protein Data Bank. PDB accession code: Pin1–inhibitor **2** complex, 3NTP. We thank the NIH for financial support from Grant No. R01 CA110940 (FAE), S10 RR16658 (FAE) for the LC-MSMS, and the Welch Foundation for Grant F-1778 (YZ).

Phosphorylation to give **9** was accomplished with di-*tert*-butyl diisopropyl phosphoramidite, followed by oxidation with *tert*-butyl hydroperoxide.(*5, 6*) Deprotection with TFA released the final phosphorylated Pin1 inhibitor **1**. Inhibitors **2**, **3**, **4a**, and **4b** were synthesized by similar procedures (Schemes S2, S3, and S4).

Scheme 1. Synthesis of reduced amide **1**.



General Procedures. Unless otherwise indicated, all reactions were carried out under N_2 in flame-dried glassware. THF was distilled from Na-benzophenone, and CH_2Cl_2 was dried by passage through dry alumina. Anhydrous DMF (99.8%), MeOH, and DIEA were used directly from sealed bottles. Trifluoroethanol (TFE, 99+%) was distilled from Na before use. LiCl (99+%) was dried under vacuum at 150 °C for 24 h. $NaHCO_3$, NH_4Cl, and brine (NaCl) refer to saturated aqueous solutions unless otherwise noted. Chromatography refers to the flash method of Still et al.(*7*) performed on 230–400 mesh silica gel with reagent grade solvents as % (v/v). ^1H, ^{13}C, and ^{31}P NMR spectra were obtained at 500, 125, and 162 MHz, respectively, at ambient temperature in $CDCl_3$ unless otherwise noted. Chemical shifts are reported in parts per million

(ppm) downfield from tetramethylsilane (TMS). Data are reported as follows: chemical shift, multiplicity: singlet (s), doublet (d), triplet (t), quadruplet (q), quintuplet (qt), multiplet (m), coupling constants *J* in Hz, and integration. In ^{13}C NMR spectral listings, minor rotamers are labeled (m). Analytical HPLC (Anal. HPLC): normal phase (NP-HPLC) were obtained on a MetaSil AQ 5μ SiO_2, 4.6 × 50 mm column, 5% *i*-PrOH/hexanes (v/v) isocratic, flow rate 1.0 mL min^{-1}, unless otherwise noted. Reverse phase (RP-HPLC) were obtained on a C18 4.6 × 50 mm column, with 10% CH_3CN/H_2O for 3 min, then 10 to 90% CH_3CN/H_2O gradient over 6 min, held at 90% for 9 min, flow rate 1.0 mL min^{-1}, with UV detection, unless otherwise noted. Anal. HPLC results are listed as: retention time (min), purity (%).

Fmoc–Ser(O*t*Bu)–Pro–O*t*Bu, 5. A solution of DIEA (1.0 g, 7.8 mmol) and HCl·H–Pro–O*t*Bu (1.3 g, 5.3 mmol) in DMF (5 mL) was added to a solution of Fmoc–Ser(O*t*Bu)–OH (2.0 g, 5.2 mmol), EDC (1.2 g, 6.3 mmol), and HOBt (1.0 g, 6.3 mmol) in DMF (15 mL). The mixture was stirred at rt for 14 h, then diluted with EtOAc (80 mL), and washed with 1 M HCl (30 mL), and 5% aq $NaHCO_3$ (20 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated. The crude product was purified by chromatography with 30 to 50% EtOAc/hexanes to yield **5** (2.0 g, 80%) as a colorless oil. Anal. HPLC: 254 nm, 2.0 min, 98%. $[\alpha]^{25}_D = -48.6$ (*c* 1, MeOH). ^1H NMR: δ 7.74 (d, *J* = 7.2, 2H), 7.59 (d, *J* = 6.9, 2H), 7.38 (t, *J* = 7.6, 2H), 7.27 (m, 2H), 5.74 (d, *J* = 7.7, 0.4H), 5.71 (d, *J* = 8.0, 0.6H), 4.92 (dd, *J* = 1.6, 8.3, 0.4H), 4.65 (dt, *J* = 6.4, 8.2, 0.6H), 4.51 (ddd, *J* = 4.9, 7.8, 10.1, 0.4H), 4.35 (m, 2.4H), 4.19 (dd, *J* = 7.7, 15.9, 1H), 3.85 (ddd, *J* = 5.2, 7.5, 9.7, 0.6H), 3.65 (m, 1.4H), 3.58 (dd, *J* = 4.7, 6.4, 1H), 3.52 (m, 0.6H), 3.36 (dd, *J* = 8.4,

10.0, 0.6H), 2.23 (m, 1H), 2.12 (m, 2H), 1.90 (m, 2H), 1.46 (s, 5H), 1.42 (s, 4H), 1.20 (s, 5H), 1.13 (s, 4H). ^{13}C NMR: δ 171.1 (m), 170.9, 170.2 (m), 169.3, 156.0, 155.3 (m), 144.01 (m), 143.99, 143.90, 143.87 (m), 141.31 (m), 141.30, 127.7, 127.1 (m), 125.24, 125.21 (m), 119.99 (m), 119.98, 82.5 (m), 81.1, 73.7 (m), 73.6, 67.1, 67.0 (m), 64.0 (m), 62.8, 59.93 (m), 59.89, 53.1, 52.7 (m), 47.3, 47.17 (m), 47.16, 46.3 (m), 30.7 (m), 29.1, 28.0, 27.9 (m), 27.4 (m), 27.3, 24.8 (m), 22.5. HRMS (FAB$^+$): calcd for $C_{31}H_{41}N_2O_6$ $[M + H]^+$ m/z =537.2965, found m/z = 537.2979.

Fmoc–Ser(O*t*Bu)–Ψ[CH$_2$N]-Pro–O*t*Bu, 6. Fmoc–Ser(O*t*Bu)–Pro–O*t*Bu **5** (1.27 g, 2.37 mmol) in dry THF (10 mL) was added to a solution of borane (1.00 M in THF, 3.94 mL, 3.94 mmol) at 0 °C over a period of 15 min. The mixture was stirred at rt for 24 h, cooled to 0 °C, and MeOH (5 mL) was added slowly. The solvents were evaporated, and the residue was purified by chromatography (step gradient: 0 then 25% EtOAc/hexanes) to yield **6** (1.26 g, 65%) as a colorless oil. Anal. HPLC: 210 nm, 2.0 min, 95%. $[\alpha]^{25}_D$ = –27.0 (*c* 1, MeOH). ^{1}H NMR: δ 7.75 (d, *J* = 7.5, 2H), 7.66 (t, *J* = 6.6, 2H), 7.39 (t, *J* = 7.4, 2H), 7.29 (tt, *J* = 1.4, 7.4, 2H), 5.96 (d, *J* = 6.0, 1H), 4.34 (m, 2H), 4.24 (t, *J* = 7.1, 1H), 3.74 (m, 1H), 3.59 (m, 1H), 3.41 (m, 1H), 3.21 (m, 2H), 2.80 (m, 2H), 2.59 (d, *J* = 6.5, 1H), 2.06 (m, 1H), 1.85 (m, 3H), 1.47 (s, 9H), 1.19 (s, 9H). ^{13}C NMR: δ 174.2, 156.3, 144.2, 141.3, 127.6, 127.0, 125.3, 120.0, 80.7, 73.0, 67.5, 66.6, 61.2, 55.5, 54.7, 51.0, 47.4, 29.6, 28.1, 27.6, 23.9. HRMS (FAB$^+$): calcd for $C_{31}H_{43}N_2O_5$ $[M + H]^+$ m/z = 523.3172, found m/z = 523.3169.

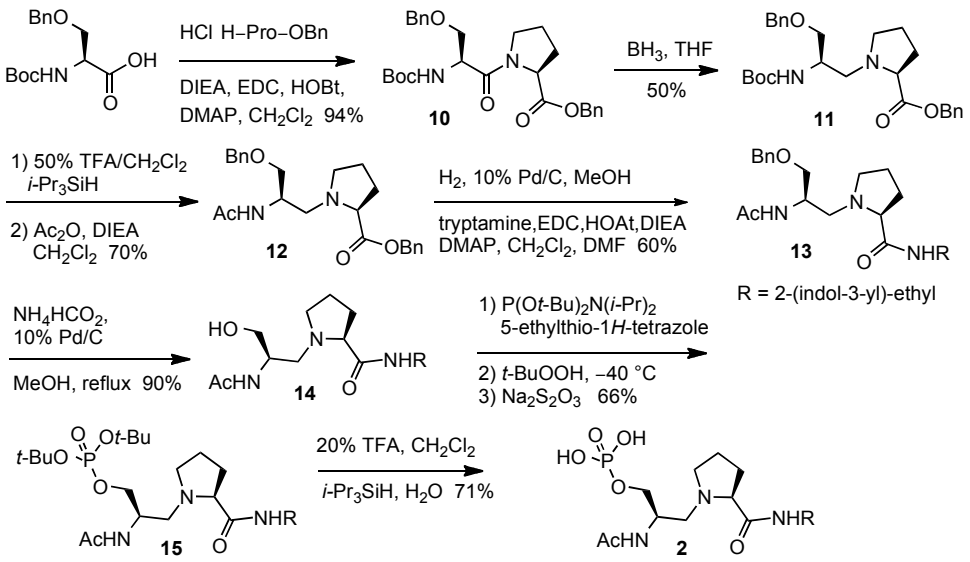
Fmoc–Ser–Ψ[CH_2N]-Pro–2-(indol-3-yl)-ethylamine, 8. Fmoc–Ser(O*t*Bu)–Ψ[CH_2N]-Pro–O*t*Bu **6** (250 mg, 4.78 mmol) was dissolved in CH_2Cl_2 (8 mL), and $BF_3{\cdot}Et_2O$ (0.8 mL, 6.3 mmol) was added. The reaction mixture was stirred at rt for 20 min. After evaporation, the residue was purified by chromatography (gradient: 10 to 25% of MeOH/CH_2Cl_2) to yield **7** (108 mg, 55%) as a colorless oil. HRMS: calcd for $C_{23}H_{27}N_2O_5$ $[M + H]^+$ m/z = 411.1920, found m/z = 411.1932. Fmoc–Ser–Ψ[CH_2N]–Pro–OH **7** (55 mg, 0.13 mmol), tryptamine (26 mg, 0.16 mmol), HOAt (25 mg, 0.16 mmol), and DMAP (5.0 mg, 0.04 mmol) were dissolved in DMF (3 mL), and EDC (31 mg, 0.16 mmol) was added. The reaction mixture was stirred at rt for 14 h, then diluted with EtOAc (50 mL) and washed with water (25 mL × 3), followed by brine (15 mL). The organic layer was dried over Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography using 9% MeOH/EtOAc to yield **8** as a colorless oil (35 mg, 47%). $[\alpha]^{25}_D$ = –28.7 (*c* 1, MeOH). ^{1}H NMR: δ 8.10 (br s, 1H), 7.78 (d, *J* = 7.6, 2H), 7.58 (m, 3H), 7.41 (t, *J* = 7.4, 2H), 7.33 (t, *J* = 7.6, 2H), 7.15 (d, *J* = 8.1, 1H), 7.08 (qt, *J* = 7.0, 2H), 6.94 (d, *J* = 2.3, 1H), 4.67 (d, *J* = 8.8, 1H), 4.46 (t, *J* = 5.7, 2H), 4.19 (t, *J* = 6.1, 1H), 3.57 (m, 2H), 3.47 (m, 1H), 3.18 (m, 2H), 3.05 (m, 1H), 2.90 (m, 2H), 2.86 (m, 1H), 2.25 (m, 1H), 2.17, (m, 2H), 2.10 (m, 1H), 1.71 (m, 4H), 1.63 (m, 1H). ^{13}C NMR: δ 174.5, 156.3, 144.0, 141.5, 136.3, 127.9, 127.7, 127.3, 125.0, 122.4, 122.3, 120.2, 119.6, 119.0, 113.4, 111.5, 68.4, 66.3, 62.2, 55.3, 53.7, 51.2, 47.4, 39.4, 30.2, 24.9, 24.1. MS (ESI^+): calcd for $C_{33}H_{37}N_4O_4$ $[M + H]^+$ m/z = 553.28, found m/z = 553.32.

Fmoc–Ser(PO(O*t*Bu)$_2$)–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine, 9. To a solution of **8** (85 mg, 0.15 mmol) in THF (4 mL) was added 5-ethylthio–H–tetrazole (60 mg, 0.46 mmol) and di-*tert*-butyl diisopropylphosphoramidite (85 mg, 0.31 mmol) at rt. The mixture was stirred at rt for 17 h, and cooled to –40 °C. A solution of 5–6 M *tert*-butyl hydroperoxide in decane (0.11 mL, 0.61 mmol) was added slowly, and the mixture was stirred at –40 °C for 1 h, then at rt for 30 min. The reaction was cooled to –40 °C, and quenched by addition of saturated aq $Na_2S_2O_3$. The mixture was extracted with EtOAc (20 mL × 2), and the combined organic extracts were washed with water (20 mL), brine (20 mL), and dried over Na_2SO_4. Concentration under vacuum provided a residue, which was purified by chromatography to give **9** as a colorless oil (51 mg, 45%). Anal. HPLC: 210 nm, 4.0 min, 81%. ^{1}H NMR (400 MHz): δ 9.03 (br, 1H), 7.77 (d, *J* = 7.6, 2H), 7.59 (m, 3H), 7.41 (t, *J* = 7.4, 2H), 7.31 (m, 3H), 7.12 (t, *J* = 7.1, 1H), 7.06 (t, *J* = 7.2, 1H & s, 1H), 5.07 (d, *J* = 8.3, 1H), 4.38 (ddd, *J* = 6,6, 10.8, 15.0, 2H), 4.19 (t, *J* = 6.7, 1H), 3.81 (tt, *J* = 3.6, 7.2, 1H), 3.67 (dt, 2H), 3.56 (m, 1H), 3.38 (ddd, *J* = 5.2, 8.5, 10.6, 1H), 3.02 (m, 2H), 2.95 (m, 2H), 2.43 (dd, *J* = 5.6, 12.4, 1H), 2.33 (m, 2H), 2.09 (m, 1H), 1.80 (m, 1H), 1.71 (m, 1H), 1.56 (m, 1H), 1.48 (d, *J* = 2.0, 18H). ^{13}C NMR (100 MHz): δ 174.3, 156.1, 143.9, 141.4, 136.5, 127.8, 127.2, 125.15, 125.11, 122.3, 122.0, 120.1, 119.3, 119.0, 113.0, 111.6, 83.4, 69.2, 66.7, 66.2, 56.8, 54.2, 50.7, 47.3, 39.2, 30.3, 29.9, 24.8, 24.3. ^{31}P NMR: δ -8.43. HRMS (FAB$^+$): calcd for $C_{41}H_{54}N_4O_7P$ $[M + H]^+$ m/z = 745.3730, found m/z = 745.3751.

Fmoc–Ser(PO(OH)$_2$)–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine, 1. To a solution of **9** (43 mg, 0.058 mmol) in anhydrous CH_2Cl_2 (2 mL) was added a mixture of TFA (0.5 mL), H_2O (0.1 mL)

and TIPSH (0.02 mL), and the reaction was stirred at rt for 1 h. The solvent was removed under vacuum, and the residue was purified by semi-preparative HPLC on an XBridge C18 4.6 × 50 mm column with 10% B for 3 min, then 10% to 90% B gradient over 10 min, at 15 mL/min (A: 0.1% TFA/H_2O (v/v), B: 0.1% TFA/CH_3CN (v/v)) to provide **1** at 11.2 min as a white solid after lyophilization (35 mg, 95%). Anal. HPLC: C18 4.6 × 50 mm column, gradient: 10% B for 3 min, then 10 to 90% B over 6 min, held 90% B for 9 min, 254 nm, 8.7 min, 97%. $[\alpha]^{25}_{D} = -4.4$ (*c* 1, MeOH). ^{1}H NMR (CD_3OD): δ 7.74 (dd, *J* = 2.8, 7.3, 2H), 7.62 (d, *J* = 7.3, 1H), 7.52 (dd, *J* = 7.7, 13.5, 2H), 7.34 (m, 3H), 7.26 (t, *J* = 7.5, 1H), 7.22(t, *J* = 7.6, 1H), 7.05 (m, 2H), 6.94 (t, *J* = 7.4, 1H), 4.44 (dd, *J* = 6.4, 10.6, 1H), 4.31 (dd, *J* = 7.1, 10.5, 1H), 4.15 (m, 2H), 4.08 (m, 1H), 3.94 (m, 1H), 3.89 (m, 1H), 3.68 (m, 1H), 3.52 (m, 2H), 3.39 (d, *J* = 11.5, 1H), 3.28 (d, *J* = 13.0, 1H), 3.16 (m, 1H), 2.95 (m, 2H), 2.36 (m, 1H), 2.04 (m, 1H), 1.86 (m, 2H). ^{13}C NMR (CD_3OD): δ 168.6, 158.0, 145.3, 145.0, 142.6, 138.1, 128.8, 128.2, 126.2, 126.1, 123.7, 122.4, 120.9, 119.7, 119.3, 112.8, 112.4, 68.7, 68.0, 66.6, 57.6, 56.7, 41.8, 30.8, 26.0, 24.2. ^{31}P NMR (CD_3OD): δ 0.29. MS (ESI^+) calcd for $C_{33}H_{37}N_4O_7P$ $[M]^+$ m/z =632.24 found m/z = 632.27.

Scheme S2. Synthesis of Ac–pSer–Ψ[CH_2N]–Pro–2-(indol-3-yl)-ethylamine inhibitor **2**.



Boc–Ser(OBn)–Pro–OBn, 10. Boc–L–Ser(OBn)–OH (2.00 g, 6.77 mmol), HCl·H–Pro–OBn (1.80 g, 7.45 mmol), and DIEA (2.63 g, 20.3 mmol) were dissolved in CH_2Cl_2 (100 mL) and cooled to 0 °C. EDC (1.55 g, 8.12 mmol), HOBt (1.24 g, 8.12 mmol) and DMAP (227 mg, 2.03 mmol) were added, and the mixture was stirred at rt for 48 h. The mixture was diluted with 20 mL CH_2Cl_2, washed with 1N HCl (50 mL × 2), $NaHCO_3$ (50 mL × 2), and brine (50 mL). The organic layer was dried over Na_2SO_4, filtered and evaporated. The crude product was purified by chromatography (step gradient: 25 then 50% EtOAc/hexanes) to yield **10** (3.0 g, 94%) as a colorless oil. Anal. HPLC: 210 nM, 10.4 min, 99%. $[\alpha]^{25}_{D} = -56.9$ (*c* 1, MeOH). ^{1}H NMR δ 7.32 (m, 10H), 5.41 (d, *J* = 8.6, 0.82H), 5.37 (d, *J* = 8.5, 0.18H), 5.21 (d, *J* = 12.1, 1H), 5.10 (d, *J* = 12.5, 1H), 4.84 (dd, *J* = 2.1, 8.2, 0.18H), 4.70 (m, 0.82H), 4.58 (dd, *J* = 3.8, 8.4, 1H), 4.51 (d, *J* = 11.7, 1H), 4.44 (d, *J* = 11.9, 1H), 3.69 (m, 2H), 3.61 (m, 2H), 2.19 (m, 1H), 1.97 (m, 3H), 1.42 (s, 7.4H), 1.40 (s, 1.6H). ^{13}C NMR δ 171.8 (m), 171.7, 170.2 (m), 169.5, 155.4, 154.8 (m), 138.0, 137.9 (m), 135.7, 135.5(m), 128.7 (m), 128.6, 128.43(m), 128.39, 128.32, 128.26 (m), 128.2,

127.8(m), 127.71, 127.66, 127.5(m), 79.8, 79.7 (m), 73.4 (m), 73.2, 71.7 (m), 70.5, 67.5 (m), 66.9, 59.3 (m), 59.2, 52.1, 51.5 (m), 47.1, 46.5 (m), 30.8 (m), 29.1, 28.40, 28.37 (m), 24.9, 22.3 (m). HRMS (FAB$^+$) calcd for $C_{27}H_{35}N_2O_6$ [M + H]$^+$ *m*/*z* = 483.24951, found *m*/*z* = 483.24969.

Boc–Ser(OBn)–Ψ[CH_2N]–Pro–OBn, 11. Boc–Ser(OBn)–Pro–OBn **10** (3.00 g, 6.22 mmol) was dissolved in dry THF (14 mL), and BH_3 (1 M in THF, 12.4 mL, 12.4 mmol) was added dropwise at 0 °C. After the addition was complete, the resulting mixture was stirred at 0 °C for 2 h, then at rt for 24 h. The reaction was cooled to 0 °C, and MeOH (10 mL) was added slowly. The solvent was evaporated, and the residue was purified by chromatography with 25% EtOAc/hexanes to yield **11** (1.4 g, 50%) as a colorless oil. Anal. HPLC: 254 nm, 11.2 min, 97%. $[\alpha]^{25}_D = -34.4$ (*c* 1, MeOH). ^{1}H NMR δ 7.31 (m, 10H), 5.15 (m, 1H), 5.13 (d, *J* = 12.3, 1H), 5.09 (d, *J* = 12.3, 1H), 4.51 (d, *J* = 11.8, 1H), 4.46 (d, *J* = 11.7, 1H), 3.79 (m, 1H), 3.67 (m, 1H), 3.55 (dd, *J* = 5.0, 9.2, 1H), 3.32 (dd, *J* = 5.6, 8.6, 1H), 3.17 (dt, *J* = 4.1, 8.0, 1H), 2.86 (dd, *J* = 8.0, 12.4, 1H), 2.65 (m, 1H), 2.52 (m, 1H), 2.08 (m, 1H), 1.90 (m, 2H), 1.80 (m, 1H), 1.43 (s, 9H). ^{13}C NMR δ 174.3, 155.7, 138.5, 136.1, 128.6, 128.4, 128.2, 127.7, 127.6, 79.1, 73.2, 70.0, 66.6, 66.3, 55.7, 54.1, 49.7, 29.5, 28.5, 23.9. HRMS (FAB$^+$) calcd for $C_{27}H_{37}N_2O_5$ [M + H]$^+$ *m*/*z* = 469.2702, found *m*/*z* = 469.2709.

Ac–Ser(OBn)–Ψ[CH_2N]–Pro–OBn, 12. Boc–Ser(OBn)–Ψ[CH_2N]–Pro–OBn **11** (500 mg, 1.07 mmol) was dissolved in CH_2Cl_2 (10 mL) and a solution of TFA (10 mL) and *i*-Pr_3SiH (0.1 mL) was added. The mixture was stir at rt for 2 h, and concentrated under reduced pressure. The ammonium salt obtained was dissolved in CH_2Cl_2 (5 mL) with DIEA (0.6 mL), and Ac_2O (0.6

mL) was added. The mixture was stir at rt for 14 h. After concentration, the residue was purified by chromatography with EtOAc to yield **12** (0.30 g, 70%) as a colorless oil. Anal. HPLC: 210 nM, 9.4 min, 99%. $[\alpha]^{25}_{D} = -27.4$ (*c* 1, MeOH). ^{1}H NMR δ 7.34 (m, 10H), 6.67 (d, *J* = 7.3, 1H), 5.15 (d, *J* = 12.1, 1H), 5.10 (d, *J* = 12.2, 1H), 4.54 (d, *J* = 11.9, 1H), 4.46 (d, *J* = 11.9, 1H), 4.07 (m, 1H), 3.68 (dd, *J* = 4.4, 9.2, 1H), 3.48 (dd, *J* = 7.0, 9.2, 1H), 3.37 (m, 1H), 3.17 (m, 1H), 2.86 (dd, *J* = 4.0, 13.0, 1H), 2.74 (dd, *J* = 6.0, 12.8, 1H), 2.54 (m, 1H), 2.17 (m, 1H), 1.94 (s, 3H), 1.86 (m, 3H). ^{13}C NMR δ 175.1, 170.1, 138.4, 135.9, 128.7, 128.5, 128.4, 128.3, 127.9, 127.8, 73.3, 69.4, 67.2, 66.6, 55.6, 55.5, 48.7, 30.0, 24.3, 23.4. HRMS (FAB^{+}) calcd for $C_{24}H_{31}N_2O_4$ [M + H]$^{+}$ *m*/*z* = 411.2284, found *m*/*z* = 411.2273.

Ac–Ser(OBn)–Ψ[CH_2N]–Pro–2-(indol-3-yl)-ethylamine, 13. Ac–Ser(OBn)–Ψ[CH_2N]–Pro–OBn **12** (0.15 g, 0.36 mmol) was dissolved in MeOH (5 mL), and 10% Pd/C (30 mg) was added. The reaction was stirred at rt under H_2 at 1 atm for 2 h. The solution was filtered through Celite, washed with MeOH, and the solvent was evaporated. The crude oil and tryptamine (60 mg, 0.38 mmol) were dissolved in a mixture of CH_2Cl_2 (10 mL), and DMF (5 mL), and HOAt (58 mg, 0.38 mmol), DMAP (10 mg, 0.09 mmol), and EDC (72 mg, 0.38 mmol) were added. The mixture was stirred at rt for 24 h, diluted with CH_2Cl_2 (30 mL), washed with water (20 mL), and brine (25 mL). The organic layer was dried over Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography (step gradient: 6% to 17% MeOH/EtOAc) to yield **13** as a light yellow oil (85 mg; 60%). Anal. HPLC: 210 nM, 8.5 min, 96%. ^{1}H NMR δ 8.43 (br s, 1H), 7.56 (m, 2H), 7.32 (m, 4H), 7.16 (m, 3H), 7.08 (dt, *J* = 0.9, 7.4, 1H), 6.97 (d, *J* = 2.4, 1H), 5.60

(d, J = 8.1, 1H), 4.18 (d, J = 11.8, 1H), 4.13 (d, J = 11.9, 1H), 3.96 (dtt, J = 3.0, 6.0, 9.0, 1H), 3.65 (dq, J = 6.6, 13.2, 1H), 3.40 (m, 1H), 3.15 (dd, J = 3.0, 9.6, 1H), 3.13 (dd, J = 3.4, 9.6, 1H), 3.05 (m, 2H), 3.01 (dt, J = 6.2, 14.4, 1H), 2.88 (dt, J = 7.2, 14.4, 1H), 2.56 (dd, J = 8.7, 12.1, 1H), 2.37 (dd, J = 6.2, 12.1, 1H), 2.34 (dt, J = 6.8, 9.5, 1H), 2.12 (m, 1H), 1.87 (s, 3H), 1.82 (m, 1H), 1.75 (m, 1H), 1.64 (m, 1H). ^{13}C NMR δ 174.6, 169.8, 137.9, 136.5, 128.6, 128.0, 127.6, 122.2, 122.1, 119.4, 113.3, 111.4, 73.1, 69.2, 68.9, 56.7, 54.4, 48.5, 39.4, 30.4, 25.4, 24.5, 23.5. HRMS (FAB$^+$) calcd for $C_{27}H_{35}N_4O_3$ [M + H]$^+$ m/z = 463.27092, found m/z = 463.27051.

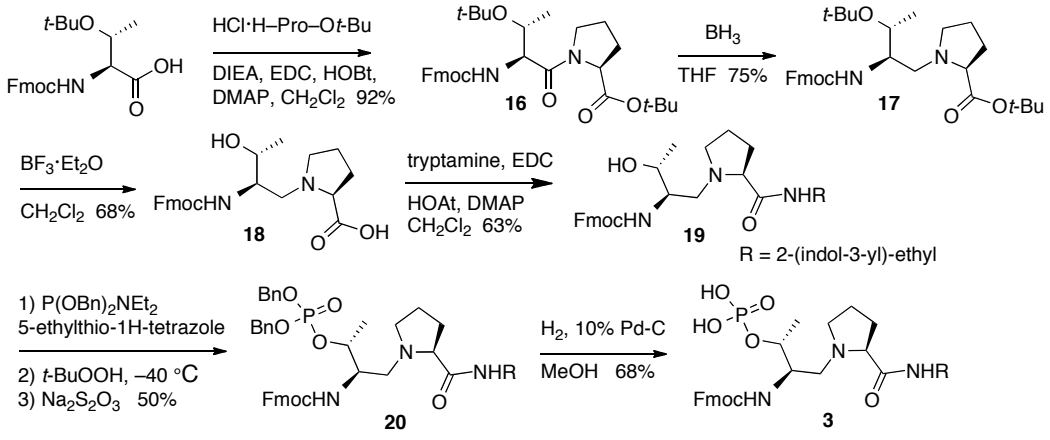
Ac–Ser–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine, 14. Ac–Ser(OBn)–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine **13** (125 mg, 0.270 mmol) was dissolved in MeOH (8 mL), and 10% Pd/C (50 mg) and ammonium formate (120 mg) were added. The reaction mixture was heated at reflux for 8 h. After cooling to rt, the mixture was filtered through Celite, washed with MeOH, and purified by chromatography with 17% MeOH/EtOAc to give **14** as a lightly yellow oil (100 mg, 100%). Anal. HPLC: 210 nM, 7.0 min, 94%. ^{1}H NMR δ 8.58 (br, 1H), 7.60 (d, J = 8.1, 1H), 7.37 (d, J = 8.1, 1H), 7.35 (m, 1H), 7.20 (t, J = 7.6, 1H), 7.10 (t, J = 7.4, 1H), 7.00 (s, 1H), 5.97 (br, 1H), 3.84 (m, 1H), 3.65 (m, 1H), 3.53 (m, 1H), 3.28 (m, 2H), 3.03 (m, 2H), 2.93 (m, 2H), 2.45 (m, 1H), 2.24 (m, 2H), 2.09 (m, 1H), 1.91 (s, 3H), 1.74 (m, 3H). ^{13}C NMR (CD_3OD, 100MHz) δ 177.2, 173.1, 138.1, 128.8, 123.5, 122.4, 119.6, 119.4, 113.1, 112.2, 69.6, 62.9, 57.1, 55.4, 51.9, 41.0, 31.3, 26.1, 25.0, 22.7. HRMS (FAB$^+$) calcd for $C_{20}H_{29}N_4O_3$ [M + H]$^+$ m/z = 373.22397, found m/z = 373.22684.

Ac–Ser(PO(O*t*Bu)$_2$)–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine, 15. To a solution of **14** (70 mg, 0.19 mmol) in THF (8 mL) was added 5-ethylthio–H–tetrazole (98 mg, 0.75 mmol) and di-*tert*-butyl diisopropylphosphoramidite (0.12 mL, 0.38 mmol), and the mixture was stirred at rt for 15 h. The mixture was cooled to –40 °C, *t*-BuOOH (5–6 M in decane, 0.15 mL, 0.75 mmol) was added slowly, and the mixture was stirred at rt for 30 min. The mixture was cooled to –40 °C, and quenched with saturated aq $Na_2S_2O_3$. The mixture was extracted with CH_2Cl_2 (20 mL × 2), and the combined organic extracts were dried over Na_2SO_4. Concentration under vacuum provided a residue, that was purified by chromatography (step gradient: 9 then 17% EtOAc/MeOH) to give **15** as a colorless oil (70 mg, 66%). Anal. HPLC: gradient 10% B for 3 min, then 10 to 90% B over 6 min, 254 nm, 8.5 min, 98%. $[\alpha]^{25}_{D}$ = +21.6 (*c* 1, MeOH). ^{1}H NMR δ 9.01 (s, 1H), 7.64 (d, *J* = 8.0, 1H), 7.38 (m, 2H), 7.19 (m, 1H), 7.10 (m, 2H), 6.07 (d, *J* = 7.9, 1H), 3.90 (m, 1H), 3.79 (m, 1H), 3.63 (m, 2H), 3.47 (dt, *J* = 5.2, 10.4, 1H), 3.10 (m, 1H), 3.01 (m, 3H), 2.47 (dd, *J* = 5.8, 12.2, 1H), 2.37 (m, 2H), 2.09 (m, 1H), 1.84 (s, 3H), 1.80 (m, 1H), 1.73 (m, 1H), 1.57 (m, 1H), 1.50 (d, *J* = 6.4, 18H). ^{13}C NMR δ 174.5, 170.1, 136.6, 127.8, 122.4, 122.1, 119.4, 119.0, 113.1, 111.5, 83.53 (d, $^2J_{P\text{-}C}$ = 4.2), 83.47 (d, $^2J_{P\text{-}C}$ = 4.2), 69.2, 66.4 (d, $^2J_{P\text{-}C}$ = 5.7), 56.4, 54.4, 49.1 (d, $^3J_{P\text{-}C}$ = 4.8), 39.2, 30.4, 30.03 (d, $^3J_{P\text{-}C}$ = 4.3), 29.99 (d, $^3J_{P\text{-}C}$ = 4.3), 25.0, 24.5, 23.4. ^{31}P NMR δ –7.86. MS (ESI$^+$) calcd for $C_{28}H_{45}N_4O_6P$ [M + H]$^+$ *m*/*z* = 565.3, found *m*/*z* = 565.3.

Ac–Ser(PO(OH)$_2$)–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine, 2. To a solution of **15** (30 mg, 0.053 mmol) in CH_2Cl_2 (2 mL) was added a mixture of TFA (0.5 mL), H_2O (0.01 mL) and *i*-

Pr_3SiH (0.01 mL), and the reaction was stirred at rt for 1 h. The solvent was removed under vacuum, and the residue was purified by semi-preparative HPLC with 10% B for 2 min, then 10% to 90% CH_3CN/H_2O gradient over 9 min, at 15 mL/min (A: 0.1% TFA/H_2O, B, 0.1% TFA in CH_3CN) to provide **2**, ret. time 5.4 min, as a white solid after lyophilization (17 mg, 71%). Anal. HPLC: gradient 10% B for 3 min, then 10 to 90% B over 6 min (A: 0.1% TFA/H_2O, B: 0.1% TFA/CH_3CN), 254 nm, 6.4 min, 97%. $[\alpha]^{25}_D = -12.3$ (*c* 1, MeOH). ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.9 (s, 1H), 8.38 (br, 1H), 8.04 (d, *J* = 6.0, 1H), 7.56 (d, *J* = 7.6, 1H), 7.33 (d, *J* = 8.0, 1H), 7.15 (s, 1H), 7.05 (t, *J* = 7.4, 1H), 6.97 (t, *J* = 7.4, 1H), 4.11 (m, 1H), 3.80 (m, 2H), 3.62 (m, 1H), 3.39 (m, 3H), 3.07 (m, 1H), 2.85 (m, 4H), 2.18 (m, 1H), 1.83 (s, 3H), 1.71 (m, 3H). ^{13}C NMR (CD_3OD) δ 173.8, 168.7, 138.2, 128.8, 123.8, 122.4, 119.6, 119.3, 112.8, 112.4, 68.8, 66.2, 57.4, 56.8, 48.2, 41.7, 30.8, 26.0, 24.2, 22.8. ^{31}P NMR (DMSO-d_6) δ –0.78. HRMS (FAB$^+$) calcd for $C_{20}H_{30}N_4O_6P$ $[M + H]^+$ *m/z* = 453.1903, found *m/z* = 453.1912.

Scheme S3. Synthesis of Fmoc–pThr–Ψ[CH_2N]–Pro–2-(indol-3-yl)-ethylamine inhibitor **3**.



Fmoc–Thr(O*t*Bu)–Pro–O*t*Bu, 16. A solution of DIEA (0.49 g, 3.8 mmol) and HCl·H–Pro–O*t*Bu (0.52 g, 2.5 mmol) in CH_2Cl_2 (25 mL) was added to a solution of Fmoc–Thr(O*t*Bu)–OH (1.0 g, 2.5 mmol), EDC (0.58g, 3.0 mmol), and HOBt (0.46 g, 3.0 mmol) in CH_2Cl_2 (25 mL). The mixture was stirred at rt for 13 h, washed with 1 M HCl (30 mL), 5% aq $NaHCO_3$ (30 mL), and brine (30 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated. The crude product was purified by chromatography with 20% EtOAc/hexanes to give **16** (1.3 g, 92%) as a colorless oil. ^{1}H NMR δ 7.75 (d, *J* = 7.7, 2H), 7.59 (m, 2H), 7.38 (m, 2H), 7.29 (m, 2H), 5.95 (d, *J* = 6.9, 0.4H), 5.75 (d, *J* = 7.8, 0.6H), 5.21 (dd, *J* = 3.4, 7.0, 0.4H), 4.45 (dd, *J* = 5.2, 7.8, 0.6H), 4.35 (m, 3H), 4.20 (t, *J* = 7.2, 1H), 3.92 (m, 1.6H), 3.72 (m, 1H), 3.54 (dt, *J* = 8.2, 16.6, 0.4H), 2.19 (m, 1H), 2.05-1.84 (m, 3H), 1.47 (s, 5.4H), 1.42 (s, 3.6H), 1.27 (s, 3.6H), 1.23 (s, 5.4H), 1.21 (d, *J* = 6.2, 1.8H), 1.07 (d, *J* = 6.6, 1.2H). ^{13}C NMR δ 171.5 (m), 171.2, 169.0, 168.3 (m), 155.9, 155.3 (m), 144.1, 143.9 (m), 127.7, 127.1, 125.31, 125.26 (m), 120.0, 82.5 (m), 81.3, 75.1 (m), 74.6, 70.9 (m), 69.2, 67.0, 66.9 (m), 60.14 (m), 60.06, 57.6, 57.3 (m), 48.0, 47.2, 46.6 (m), 30.7, 30.5 (m), 29.2 (m), 28.4, 28.0, 27.9 (m), 25.0, 22.3(m), 19.2, 17.6 (m). HRMS (ESI$^+$) calcd for $C_{32}H_{43}N_2O_6$ $[M + H]^+$ *m/z* = 551.3121, found *m/z* = 551.3134.

Fmoc–Thr(O*t*Bu)–Ψ[CH_2N]–Pro–O*t*Bu, 17. Fmoc–Thr(O*t*Bu)–Pro–O*t*Bu **16** (1.14 g, 2.08 mmol) in dry THF (15 mL) was added to a solution of BH_3 (1.00 M in THF, 4.15 mL, 4.15 mmol) at 0 °C over a period of 15 min. The resulting mixture was stirred at rt for 13 h, cooled to 0 °C, and MeOH (5 mL) was added slowly. After evaporation, the residue was purified by chromatography with 12% EtOAc/hexanes to yield **17** (0.44 g, 40%) as a colorless oil, and 0.54

g (47%) of the starting material was recovered. ^{1}H NMR δ 7.76 (m, 2H), 7.61 (m, 2H), 7.39 (m, 2H), 7.31 (m, 2H), 5.28 (d, *J* = 8.3, 1H), 4.36 (d, *J* = 7.3, 2H), 4.25 (t, *J* = 7.2, 1H), 3.99 (m, 1H), 3.62 (m, 1H), 3.25 (dd, *J* = 4.1, 8.7, 1H), 3.06 (m, 1H), 2.85 (dd, *J* = 6.0, 12.4, 1H), 2.67 (q, *J* = 7.5, 1H), 2.55 (dd, *J* = 7.3, 12.3, 1H), 2.04 (m, 1H), 1.83 (m, 3H), 1.44 (s, 9H), 1.20 (s, 9H), 1.13 (d, *J* = 6.4, 3H). ^{13}C NMR δ 174.0, 156.9, 144.5, 141.5, 127.8, 127.2, 125.4, 124.8, 120.2, 66.7, 66.6, 66.3, 65.3, 55.5, 55.4, 53.2, 50.5, 47.5, 29.7, 29.0, 28.3, 23.5, 20.1. HRMS (ESI^{+}) calcd for $C_{32}H_{45}N_2O_5$ $[M + H]^+$ *m/z* = 537.3328, found *m/z* = 537.3325.

Fmoc–Thr–Ψ[CH_2N]–Pro–2-(indol-3-yl)-ethylamine, 19.

Fmoc–Thr(O*t*Bu)–Ψ[CH_2N]–Pro–O*t*Bu **17** (240 mg, 4.47 mmol) was dissolved in CH_2Cl_2 (8 mL), and $BF_3{\cdot}Et_2O$ (0.8 mL, 6.3 mmol), iPr_3SiH (10 μL), and H_2O (10 μL) were added. The reaction mixture was stirred at rt for 1 h. After evaporation, the residue was purified by chromatography (step gradient: 10% then 25% MeOH/CH_2Cl_2) to yield **18** (130 mg, 68%) as a colorless oil. Fmoc–Thr–Ψ[CH_2N]–Pro–OH **18** (130 mg, 0.31 mmol) was dissolved in DMF (10 mL). EDC (72 mg, 0.37 mmol), HOAt (58 mg, 0.37 mmol), DMAP (10.0 mg, 0.092 mmol) and tryptamine (60 mg, 0.37 mmol) were added in order. The reaction mixture was stirred at rt for 12 h, diluted with EtOAc (60 mL), and washed with water (40 mL). The aqueous solution was extracted with EtOAc (30 mL), and the combined organic extracts were washed with $NaHCO_3$ (30 mL), water (30 mL), and brine (30 mL). The organic layer was dried over Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography with EtOAc to give **19** as a colorless oil (110 mg, 63%). ^{1}H NMR δ 7.92 (s, 1H), 7.78 (d, *J* = 7.5, 2H), 7.59 (app. t, *J* = 6.4,

3H), 7.41 (t, *J* = 7.1, 2H), 7.33 (app. t, *J* = 7.4, 3H), 7.13 (m, 3H), 6.94 (s, 1H), 4.55 (d, *J* = 8.2, 1H), 4.49 (d, *J* = 6.0, 2H), 4.20 (t, *J* = 6.0, 1H), 3.64 (app. sextet, *J* = 6.5, 1H), 3.55 (m, 2H), 3.36 (m, 1H), 3.07 (dt, *J* = 6.2, 14.8, 1H), 2.93 (m, 2H), 2.88 (dt, *J* = 6.3, 15.1, 1H), 2.34 (t, *J* = 10.8, 1H), 2.18 (m, 2H), 2.12 (m, 1H), 1.81-1.65 (m, 6H), 0.83 (d, *J* = 6.4, 3H). ^{13}C NMR δ 156.6, 144.1, 144.0, 141.5, 136.3, 127.9, 127.6, 127.3, 125.0, 122.6, 122.4, 120.2, 119.7, 119.0, 113.7, 111.6, 68.4, 66.2, 65.2, 56.2, 54.3, 53.6, 47.5, 39.0, 30.1, 25.2, 24.0, 19.9. HRMS (ESI$^+$) calcd for $C_{34}H_{39}N_4O_4$ $[M + H]^+$ *m/z* = 567.2971, found *m/z* = 567.2981.

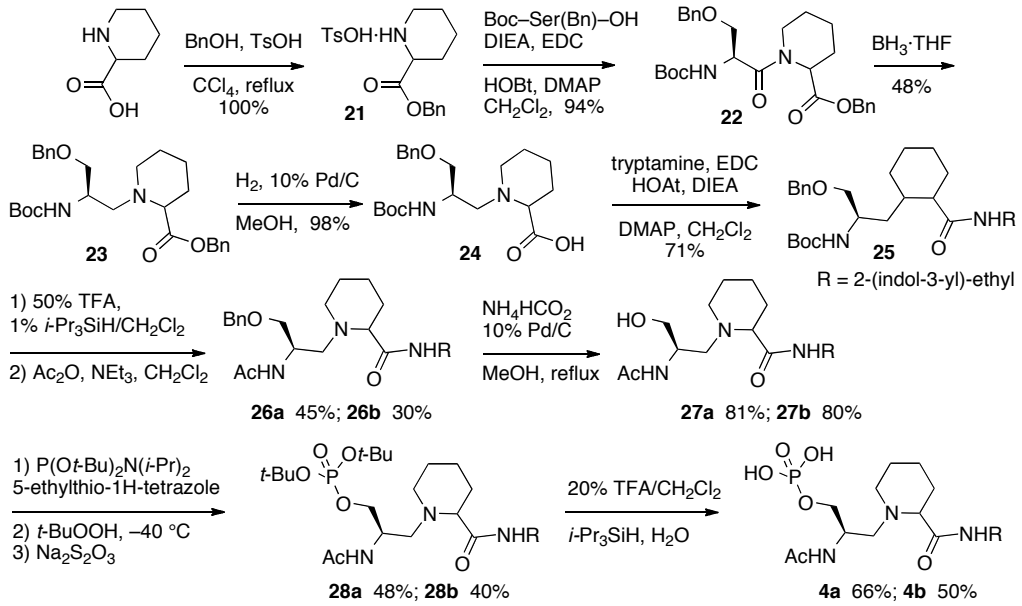
Fmoc–Thr(PO(OBn)$_2$)–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine, 20. To a solution of **19** (60 mg, 0.11 mmol) in THF (3 mL) was added 5-ethylthio–1*H*–tetrazole (41 mg, 0.32 mmol) and dibenzyl diethylphosphoramidite (67 mg, 0.21 mmol), and the mixture was stirred at rt for 16 h. The mixture was cooled to –40 °C, *t*-BuOOH (5–6 M in decane, 0.077 mL, 0.42 mmol) was added slowly, and the mixture was stirred at –40 °C for 10 min, then at rt for 30 min. The mixture was cooled to –40 °C, and quenched by addition of saturated aq $Na_2S_2O_3$. The mixture was diluted with EtOAc (60 mL), washed with water (20 mL × 2), brine (20 mL), and dried over Na_2SO_4. Concentration under vacuum provided a residue, which was purified by chromatography with EtOAc to give **20** as a colorless oil (44 mg, 50%). ^{1}H NMR δ 8.37 (s, 1H), 7.77 (d, *J* = 7.4, 1H), 7.65 (d, *J* = 7.7, 1H), 7.58 (d, *J* = 7.4, 1H), 7.56 (d, *J* = 7.4, 1H), 7.40 (t, *J* = 7.6, 2H), 7.36-7.24 (m, 13H), 7.12 (t, *J* = 7.4, 1H), 7.05 (t, *J* = 7.4, 1H), 6.98 (d, *J* = 2.0, 1H), 5.06 (dd, *J* = 9.0, 11.6, 1H), 5.01 (dd, *J* = 8.5, 11.8, 1H), 4.97 (dd, *J* = 10.4, 11.9, 1H), 4.92 (dd, *J* = 9.9, 11.8, 1H), 4.50 (d, *J* = 9.6, 1H), 4.46 (d, *J* = 6.3, 2H), 4.35 (m, 1H), 4.18 (t, *J* = 6.3, 1H), 3.67 (app. Sextet,

J = 6.7, 1H), 3.58 (m, 1H), 3.48 (m, 1H), 3.06-2.94 (m, 3H), 2.81 (t, J = 7.0, 1H), 2.38 (dd, J = 6.8, 12.6, 1H), 2.18 (m, 2H), 2.03 (m, 1H), 1.78 (m, 2H), 1.64 (m, 1H), 1.50 (m, 1H), 1.08 (d, J = 6.3, 3H). ^{13}C NMR δ 174.5, 156.6, 144.0, 143.9, 141.5, 136.4, 135.8 (d, $^{3}J_{P\text{-}C}$ = 5.1), 135.7 (d, $^{3}J_{P\text{-}C}$ = 6.4), 129.0, 128.9, 128.2, 128.0, 127.9, 127.7, 127.2, 125.01, 124.95, 122.2, 122.0, 120.2, 119.3, 119.0, 113.4, 111.3, 75.5 (d, $^{2}J_{P\text{-}C}$ = 5.8), 69.68 (d, $^{2}J_{P\text{-}C}$ = 5.3), 69.64(d, $^{2}J_{P\text{-}C}$ = 5.0), 69.4, 66.5, 58.0, 55.2, 54.6, 47.5, 39.2, 30.5, 25.2, 24.6, 18.6. ^{31}P NMR (202 MHz) δ 0.22. HRMS (ESI^{+}) calcd for $C_{48}H_{52}N_4O_7P$ $[M + H]^+$ m/z =827.3574, found m/z = 827.3579.

Fmoc–Thr(PO(OH)$_2$)–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine, 3. Dibenzyl phosphate **20** (15 mg, 0.018 mmol), and 10% Pd/C (13 mg) were dissolved in MeOH (2 mL). The reaction was stirred under H_2 (1 atm) at rt for 2 h. The mixture was filtered through Celite, and washed with MeOH. After evaporation, the residue was purified by semi-preparative HPLC (10% CH_3CN/H_2O for 3 min, then 10% to 90% CH_3CN/H_2O gradient over 7 min, 12 mL/min) to give **3**, ret. time 9.5 min, as a white solid after lyophilization (8.0 mg, 68%). Anal. HPLC: gradient 10% B for 3 min, then 10–90% B over 6 min (A: 0.1% HCO_2H/H_2O, B: 0.1% HCO_2H/CH_3CN), 254 nm, 8.3 min, 99%. ^{1}H NMR (CD_3OD) δ 7.77 (dd, J = 4.2, 7.6, 2H), 7.65 (d, J = 7.7, 1H), 7.56 (t, J = 6.8, 2H), 7.35 (m, 3H), 7.27 (t, J = 7.6, 1H), 7.24 (t, J = 7.5, 1H), 7.07 (t, J = 7.6, 1H), 7.06 (s, 1H), 6.96 (t, J = 7.4, 1H), 4.46 (d, J = 6.3, 2H), 4.28 (m, 1H), 4.20 (t, J = 6.2, 1H), 4.05 (m, 1H), 3.92 (m, 1H), 3.54 (m, 3H), 3.23 (m, 1H), 3.10 (m, 1H), 2.98 (m, 2H), 2.32 (m, 1H), 1.98 (m, 1H), 1.83 (m, 2H), 1.17 (d, J = 4.8, 3H). ^{13}C NMR (CD_3OD) δ 158.7, 145.5, 145.0, 142.6, 138.2, 128.8, 128.7, 128.1, 126.2, 126.1, 123.7, 122.4, 120.9, 119.6, 119.3, 112.9, 112.3,

72.61, 72.57, 68.2, 67.7, 57.6, 57.4, 54.0, 41.6, 31.0, 26.0, 24.4, 18.5. HRMS (ESI^+) calcd for $C_{34}H_{40}N_4O_7P$ $[M + H]^+$ m/z = 647.2635, found m/z = 647.2639.

Scheme S4. Synthesis of inhibitors **4a** and **4b**.



Boc–Ser(OBn)–(∗)Pip–OBn, 22. Racemic H–(∗)Pip–OH (6.25 g, 48.4 mmol) was suspended in CCl_4 (80 mL), and TsOH (11.0 g, 96.8 mmol) and BnOH (40 mL) were added. The reaction was heated at reflux for 24 h. Evaporation of solvent and precipitation with Et_2O (500 mL) yielded TsOH·H–(∗)Pip–OBn **21** (17.4 g, 100%) as a white solid. TsOH·H–(∗)Pip–OBn **21** (3.50 g, 8.82 mmol) and DIEA (2.64 g, 20.3 mmol) were dissolved in CH_2Cl_2 (80 mL). Boc–L-Ser(OBn)–OH (2.00 g, 6.78 mmol), EDC (1.55 g, 8.12 mmol), HOBt (1.25 g, 8.12 mmol) and DMAP (0.25 mg, 2.03 mmol) were added. The mixture was stirred at rt for 15 h, washed with water (30 mL), 1M HCl (30 mL × 2), $NaHCO_3$ (30 mL × 2), and brine (30 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated. The crude product was purified by chromatography with

25% EtOAc/hexanes to yield **22** (3.1 g, 94%) as a colorless oil. ^{1}H NMR (50 °C) δ 7.27 (m, 10H), 5.49 (br s 1H), 5.40 (m, 1H), 5.15 (m, 2H), 4.90 (m, 1H), 4.48 (m, 2H), 3.87 (m, 1H), 3.63-3.51 (m, 2H), 3.20 (m, 1H), 2.25 (m, 1H), 1.72-1.46 (m, 4H), 1.43 (br s, 9H), 1.26 (m, 1H). ^{13}C NMR δ 170.8, 170.5, 170.2 (d), 138.0 (d), 137.7, 135.7, 135.6 (d), 128.6, 128.4 (d), 128.33, 128.29 (d), 128.2, 128.06 (d), 127.99, 127.97 (d), 127.89, 127.8, 127.6, 79.67, 77.36 (d), 73.3, 73.1 (d), 71.2, 70.4 (d), 67.0 (d), 66.9, 52.6, 52.4 (d), 50.5 (d), 50.2, 43.7 (d), 43.6, 28.4, 26.6, 25.2 (d), 24.8, 21.0, 20.8 (d). HRMS (ESI^{+}) calcd for $C_{28}H_{37}N_2O_6$ $[M + H]^{+}$ m/z = 497.2652, found m/z = 497.2655.

Boc–Ser(OBn)–Ψ[CH$_2$N]–(∗)Pip–OBn, 23. Boc–Ser(OBn)–(∗)Pip–OBn **22** (2.80 g, 5.78 mmol) was dissolved in dry THF (12 mL), and BH_3 (1 M in THF, 11.6 mL, 11.6 mmol) was added dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 3 h and at rt for 11 h. the reaction was cooled to 0 °C, and MeOH (9 mL) was added slowly. The resulting mixture was evaporated and purified by chromatography with 9% EtOAc/hexane to yield **23** (1.3 g, 48%) as a colorless oil. ^{1}H NMR δ 7.35-7.27 (m, 10H), 5.14 (m, 2.5H), 4.92 (br, 0.5H), 4.47 (m, 2H), 3.76 (m, 1H), 3.60 (m, 1H), 3.54 (m, 0.5H), 3.42 (m, 0.5H), 3.24 (m, 1H), 3.08 (m, 0.5H), 3.02 (m, 0.5H), 2.64 (m, 1H), 2.50 (m, 1H), 2.32 (m, 1H), 1.81-1.38 (m, 6H), 1.46 (s, 4.5H), 1.44 (s, 4.5H). ^{13}C NMR δ 173.9, 173.7 (d), 156.0 (d), 155.7, 138.4, 136.1, 128.70, 128.67 (d), 128.48, 128.46 (d), 128.39, 128.36 (d), 128.30 (d), 128.26, 127.8, 127.74, 127.71 (d), 79.2 (d), 79.1, 73.4, 73.2 (d), 70.3, 70.0 (d), 66.2, 66.1 (d), 64.7, 64.2 (d), 57.2 (d), 57.1, 50.6 (d), 50.1, 48.7,

48.4 (d), 29.54, 29.52 (d), 28.58, 28.56 (d), 25.6, 25.5 (d), 22.2, 22.1 (d). HRMS (ESI^+) calcd for $C_{28}H_{39}N_2O_5$ $[M + H]^+$ m/z = 483.2859, found m/z = 483.2772.

Boc–Ser(OBn)–Ψ[CH_2N]–(∗)Pip–2-(indol-3-yl)-ethylamine, 25. Boc–Ser(OBn)–Ψ[CH_2N]–(∗)Pip–OBn **23** (1.0 g, 2.1 mmol) was dissolved in MeOH (50 mL), and 10% Pd/C (200 mg) was added. The reaction was stirred at rt under H_2 (1 atm) for 2 h. After filtration through Celite and washing with MeOH, evaporation gave Boc–Ser(OBn)–Ψ[CH_2N]–(∗)Pip–OH **24** (0.8 g, 98%) as a slightly yellow oil. Without further purification, the crude Boc–Ser(OBn)–Ψ[CH_2N]–(∗)Pip–OH was dissolved in CH_2Cl_2 (400 mL); tryptamine (0.40 g, 2.5 mmol), EDC (0.48 g, 2.5 mmol), HOAt (0.39 g, 2.5 mmol), and DMAP (0.07 mg, 0.63 mmol) were added. The mixture was stirred at rt for 18 h, washed with water (150 mL), and brine (150 mL). The organic layer was dried over Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography with 33% EtOAc/hexanes to yield **25** as a light yellow oil (0.8 g, 71%). ^1H NMR δ 8.25 (br, 0.6H), 8.11 (br, 0.4H), 7.59 (t, J = 7.5, 1H), 7.33-7.15 (m, 7.8H), 7.09 (m, 1H), 7.99 (m, 0.8H), 6.86 (br, 0.4H), 4.66 (d, J = 8.9, 0.4H), 4.32 (m, 2.6H), 3.80 (m, 1.6), 3.60 (m, 0.4H), 3.48 (m, 1H), 3.28-2.88 (m, 5H), 2.73 (m, 1H), 2.50 (m, 0.4H), 2.41 (m, 0.6H), 2.28 (dd, J = 6.6, 12.8, 0.4H), 2.17 (dd, J = 3.8, 13.0, 0.6H), 2.08 (m, 0.4H), 1.88 (m, 1.6H), 1.64-1.24 (m, 15H). ^{13}C NMR (100 mHz) δ 174.8 (d), 174.2, 158.82, 155.78 (d), 138.1, 137.9 (d), 136.45 (d), 136.46, 128.5, 127.91 (d), 127.88, 127.8, 127.7 (d), 127.6, 127.4 (d), 122.2, 122.1 (d), 122.0, 118.93, 119.5, 119.4 (d), 118.88 (d), 113.4 (d), 113.0, 111.4, 111.3 (d), 79.5, 77.4 (d), 73.2, 70.6 (d), 69.6 (d), 67.9, 58.9 (d), 57.1, 52.3, 51.8, 48.7, 47.8 (d), 39.3, 38.9 (d), 30.2 (d), 29.4, 28.6, 28.5 (d),

25.4, 25.2 9 (d), 24.6 (d), 24.3, 23.4 (d), 23.3. HRMS (FAB$^+$) calcd for $C_{31}H_{43}N_4O_4$ [M + H]$^+$ *m/z* = 535.3284, found *m/z* = 535.3285.

Ac–Ser(OBn)–Ψ[CH$_2$N]–(*R/S*)Pip–2-(indol-3-yl)-ethylamine, 26a and **26b.** Boc–Ser(OBn)–Ψ[CH$_2$N]–(∗)Pip–2-(indol-3-yl)-ethylamine **25** (120 mg, 0.22 mmol) was dissolved in CH_2Cl_2 (4 mL) and a solution of TFA (4 mL), and *i*-Pr_3SiH (0.01 mL) was added at 0 °C. The mixture was stirred at 0 °C for 30 min, and at rt for 2 h. The crude mixture was concentrated under reduced pressure. The ammonium salt obtained was dissolved in CH_2Cl_2, and basified with $NaHCO_3$ (40 mL). After separation, the aqueous layer was extracted with CH_2Cl_2 (20 mL × 3). The combined organic layers were washed with brine (20 mL), and dried over Na_2SO_4. After filtration and evaporation, the residue was dissolved in CH_2Cl_2 (5 mL). Ac_2O (46 mg, 0.45 mmol) and Et_3N (46 mg, 0.45 mmol) were added. The reaction mixture was stirred at rt for 14 h. After dilution with CH_2Cl_2 (50 mL), the mixture was washed with 0.1 M NaOH (20 mL × 2), and brine (20 mL), and dried over Na_2SO_4. After filtration and concentration, the residue was purified by chromatography with EtOAc to yield two diastereomers: **26a** (48 mg, 45%), and **26b** (32 mg, 30%). **26a**: ^{1}H NMR δ 8.17 (s, 1H), 7.58 (d, *J* = 7.4, 1H), 7.31 (m, 4H), 7.23 (m, 2H), 7.18 (app. dt, *J* = 1.0, 7.9, 1H), 7.10 (t, *J* = 7.4, 2H), 7.02 (d, *J* = 2.3, 1H), 5.59 (d, *J* = 8.9, 1H), 4.34 (d, *J* = 12.1, 1H), 4.30 (d, *J* = 12.0, 1H), 4.07 (m, 1H), 3.62 (m, 1H), 3.54 (m, 1H), 3.23 (dd, *J* = 3.0, 9.6, 1H), 3.14 (dd, *J* = 3.8, 9.6, 1H), 2.97 (m, 2H), 2.88 (dt, *J* = 3.8, 7.9, 1H), 2.70 (dd, *J* = 3.5, 9.6, 1H), 2.40 (dd, *J* = 8.4, 12.9, 1H), 2.24 (dd, *J* = 6.2, 13.0, 1H), 2.08 (m, 1H), 1.86 (m, 1H), 1.84 (s, 3H), 1.64 (m, 1H), 1.53 (m, 2H), 1.31 (m, 2H). ^{13}C NMR δ 174.3, 170.0, 137.8, 136.5,

128.6, 128.1, 127.9, 127.6, 122.2, 122.1, 119.5, 118.9, 113.2, 111.4, 69.2, 68.1, 56.4, 52.6, 47.3, 47.2, 38.9, 38.8, 29.6, 25.3, 24.5, 23.3. HRMS (FAB$^+$) calcd for $C_{28}H_{37}N_4O_3$ [M + H]$^+$ *m/z* = 477.2866, found *m/z* = 477.2841. **26b**: ^{1}H NMR δ 8.05 (br, 1H), 7.57 (d, *J* = 7.9, 1H), 7.38 (m, 2H), 7.32 (m, 3H), 7.28 (dd, *J* = 0.6, 8.0, 1H), 7.17 (dt, *J* = 1.0, 7.2, 1H), 7.09 (dt, *J* = 0.7, 7.4, 1H), 6.92 (d, *J* = 1.8, 1H), 6.62 (t, *J* = 5.2, 1H), 5.43 (br, 1H), 4.45 (d, *J* =11.4, 1H), 4.42 (d, *J* = 12.0, 1H), 4.14 (m, 1H), 3.72 (m, 1H), 3.53 (m, 1H), 3.32 (dd, *J* = 3.0, 9.6, 1H), 3.30 (dd, *J* = 4.4, 9.3, 1H), 3.04 (m, 2H), 2.94 (m, 1H), 2.73 (dd, *J* = 3.6, 9.8, 1H), 2.58 (dd, *J* = 10.6, 12.9, 1H), 2.26 (dd, *J* = 3.8, 13.2, 1H), 1.85 (m, 1H), 1.82 (m, 1H), 1.62 (m, 1H), 1.54 (s, 3H), 1.52 (m, 1H), 1.30 (m, 2H). ^{13}C NMR δ 174.6, 170.3, 138.0, 136.4, 128.7, 128.2, 128.1, 127.2, 122.4, 122.3, 119.6, 118.7, 113.0, 111.5, 73.5, 70.9, 67.7, 57.9, 51.5, 46.8, 39.2, 29.6, 25.2, 24.3, 23.3, 23.0. HRMS (ESI$^+$) calcd for $C_{28}H_{37}N_4O_3$ [M + H]$^+$ *m/z* = 477.2866, found *m/z* = 477.2848.

Ac–L-Ser(PO(O*t*Bu)$_2$)–Ψ[CH$_2$N]–(*R/S*)Pip–2-(indol-3-yl)-ethylamine, 28a and **28b.** Ac–L-Ser(OBn)–Ψ[CH$_2$N]–(∗)Pip–2-(indol-3-yl)-ethylamine **26a** (38 mg, 0.080 mmol) was dissolved in MeOH (5 mL), and 10% Pd/C (20 mg) and ammonium formate (150 mg) were added. The reaction was heated at reflux for 5 h. After filtration through Celite and washing with MeOH, evaporation yielded **27a** (25 mg, 81%) as a slightly yellow oil. To the crude **27a** (25 mg, 0.065 mmol) in THF (5 mL) was added 5-ethylthio–H–tetrazole (34 mg, 0.26 mmol) and di-*tert*-butyl diisopropylphosphoramidite (72 mg, 0.26 mmol) at rt, and the mixture was stirred at rt for 8 h. The mixture was cooled to –40 °C and *t*-BuOOH (5–6 M in decane, 47 μL, 0.26 mmol) was added slowly and the mixture was stirred at rt for 30 min. The reaction was cooled to –40 °C,

and quenched by addition of saturated aq $Na_2S_2O_3$. The mixture was extracted with CH_2Cl_2 (20 mL × 2), and the combined organic extracts were dried over Na_2SO_4. Concentration under vacuum provided a residue, which was purified by chromatography (step gradient: 0% then 9% *i*-PrOH/EtOAc) to give **28a** as a colorless oil (18 mg, 48%). ^{1}H NMR δ 9.00 (br, 1H), 7.64 (d, *J* = 7.9, 1H), 7.38 (d, *J* = 7.8, 1H), 7.17 (dt, *J* = 1.2, 7.6, 1H), 7.10 (dt, *J* = 0.8, 7.4, 1H), 6.92 (m, 1H), 5.83 (d, *J* = 8.0 1H), 4.05 (m, 1H), 3.75 (m, 2H), 3.62 (m, 1H), 3.42 (m, 1H), 3.05 (m, 2H), 2.84 (m, 1H), 2.75 (dd, J = 3.4, 8.7, 1H), 2.33 (dd, 1H), 2.27 (dd, 1H), 2.15 (t, 1H), 1.82 (s, 3H), 1.79 (m, 1H), 1.59 (m, 2H), 1.49 (s, 18H), 1.46 (m, 1H), 1.31 (m, 2H). ^{13}C NMR δ 173.8, 170.2, 136.6, 127.6, 122.4, 122.1, 119.4, 119.0, 113.0, 111.6, 83.4, 67.9, 66.3, 55.7, 51.8, 47.4, 38.8, 30.0, 28.8, 25.2, 24.0, 23.3, 23.1. ^{31}P: δ -8.53. ^{31}P NMR δ –8.53. HRMS (FAB$^+$) calcd for $C_{29}H_{48}N_4O_6P$ $[M + H]^+$ *m/z* = 579.3311, found *m/z* = 579.3265. By a similar procedure, **28b** was obtained as a colorless oil (12 mg, 40%). ^{1}H NMR δ 10.22 (s, 1H), 7.58 (d, *J* = 7.9, 1H), 7.41 (d, *J* = 8.4, 1H), 7.17 (m, 1H), 7.10 (m, 1H), 7.06 (br, 1H), 6.43 (br, 1H), 5.01 (d, *J* = 5.9, 1H), 4.22 (br, 1H), 3,86 (m, 2H), 3.78 (m, 1H), 3.56 (m, 1H), 3.18 (m, 1H), 3.13 (m, 1H), 3.05 (m, 1H), 2.67 (dd, *J* = 3.4, 10.8, 1H), 2.58 (m, 1H), 2.05 (dd, *J* = 3.3, 13.0, 1H), 1.92 (m, 1H), 1.82 (m, 2H), 1.67 (m, 1H), 1.52 (m, 21H), 1.48 (m, 1H), 1.37 (m, 1H), 1.22 (m, 1H). ^{13}C NMR δ 174.8, 170.6, 136.8, 127.1, 122.6, 122.2, 119.4, 118.7, 112.5, 112.1, 83.5, 68.3, 67.5, 58.1, 52.0, 46.1, 39.2, 30.8, 30.0, 25.0, 24.8, 23.4, 22.3. ^{31}P-NMR δ -9.26. HRMS (FAB$^+$) calcd for $C_{29}H_{48}N_4O_6P$ $[M + H]^+$ *m/z* = 579.3311, found *m/z* = 579.3351.

Ac–L-Ser(PO(OH)$_2$)–Ψ[CH$_2$N]–(*R/S*)Pip–2-(indol-3-yl)-ethylamine, 4a and **4b.** To a solution of **28a** (15 mg, 0.026 mmol) in CH_2Cl_2 (4 mL) was added a mixture of TFA (1 mL), H_2O (0.04 mL), and *i*-Pr_3SiH (0.04 mL), and the reaction was stirred at rt for 1h. The solvent was removed under vacuum, and the residue was purified by semi-preparative HPLC (5% CH_3CN/H_2O for 5 min, then 5% to 30% CH_3CN/H_2O gradient over 10 min, 12 mL/min) to provide **4a** at 9.5 min, as a white solid after lyophilization (8.0 mg, 66%). Anal. HPLC: gradient 10% B for 3 min, then 10–90% B over 6 min (A: 0.1% HCO_2H/H_2O, B: 0.1% HCO_2H/CH_3CN), 254 nm, 6.5 min, 97%. ^{1}H NMR (CD_3OD) δ 7.56 (d, *J* = 7.7, 1H), 7.35 (d, *J* = 8.3, 1H), 7.10 (s, 1H), 7.08 (t, *J* = 7.2, 1H), 7.00 (t, *J* = 7.5, 1H), 4.35 (m, 1H), 3.90 (m, 2H), 3.74 (m, 2H), 3.60 (m, 2H), 3.12 (m, 3H), 2.99 (t, *J* = 6.8, 2H), 2.00 (m, 1H), 1.97 (s, 3H), 1.78 (m, 4H), 1.52 (m, 1H). ^{13}C NMR (CD_3OD) δ 174.1, 168.9, 138.2, 128.8, 123.7, 122.4, 120.0, 119.3, 112.7, 112.4, 65.8, 58.5, 57.5, 54.3, 48.2, 41.2, 29.5, 26.0, 23.7, 22.5, 21.6. ^{31}P NMR (CD_3OD) δ 0.69. HRMS (ESI$^+$) calcd for $C_{21}H_{32}N_4O_6P$ $[M + H]^+$ *m/z* = 467.2059, found *m/z* = 467.2062. By a similar procedure, **4b** at 9.5 min, was obtained as a white solid (4 mg, 50%). Anal. HPLC: 6.5 min, 95%. ^{1}H NMR (400 mHz, CD_3OD) δ 7.57 (d, *J* = 7.9, 1H), 7.37 (d, *J* = 8.1, 1H), 7.10 (m, 2H), 7.00 (t, *J* = 7.4, 1H), 4.39 (m, 1H), 3.90 (m, 3H), 3.58 (m, 3H), 3.12 (m, 1H), 2.94 (m, 4H), 2.00 (s, 3H), 1.92 (m, 2H), 1.80 (m, 1H), 1.69 (m, 2H), 1.51 (m, 1H). ^{13}C NMR (CD_3OD) δ 176.1, 169.7, 138.2, 128.7, 123.9, 122.4, 119.6, 119.3, 112.6, 112.5, 67.9, 65.6, 60.7, 53.6, 47.8, 41.0, 30.3, 26.1, 24.2, 22.5, 22.4. ^{31}P NMR (202 MHz, CD_3OD) δ 1.64. HRMS (ESI$^+$) calcd for $C_{21}H_{32}N_4O_6P$ $[M + H]^+$ *m/z* = 467.2059, found *m/z* = 467.2060.

References

1. Roeske, R. W., Weitl, F. L., Prasad, K. U., and Thompson, R. M. (1976) Selective Reduction of the Amide Carbonyl Group in Dipeptides by Borane, *J. Org. Chem. 41*, 1260-1261.

2. Cushman, M., and Oh, Y.-I. (1991) Development of Methodology for the Synthesis of Stereochemically Pure Phe[CH_2N]Pro Linkages in HIV Protease Inhibitors, *J. Org. Chem. 56*, 4161-4167.

3. Papanikos, A., and Meldal, M. (2004) α-Keto Amide Peptides: A Synthetic Strategy to Resin-Bound Peptide Isosteres for Protease Inhibitor Screening on Solid Support, *J. Comb. Chem. 6*, 181-195.

4. Carpino, L. A. (1993) 1-Hydroxy-7-azabenzotriazole: an efficient coupling additive, *J. Am. Chem. Soc. 115*, 4397-4398.

5. Perich, J. W., and Johns, R. B. (1988) Di-*t*-butyl *N,N*-diethylphosphoramidite and dibenzyl *N,N*-diethylphosphoramidite. Highly reactive reagents for the 'phosphite-triester' phosporylation of serine-containing peptides, *Tetrahedron Lett. 29*, 2369-2372.

6. Zhao, S., and Etzkorn, F. A. (2007) A phosphorylated prodrug for the inhibition of Pin1, *Bioorg. Med. Chem. Lett. 17*, 6615-6618.

7. Still, W. C., Kahn, M., and Mitra, A. (1978) Rapid Chromatographic Technique for Preparative Separations with Moderate Resolution, *J. Org. Chem. 43*, 2923-2925.

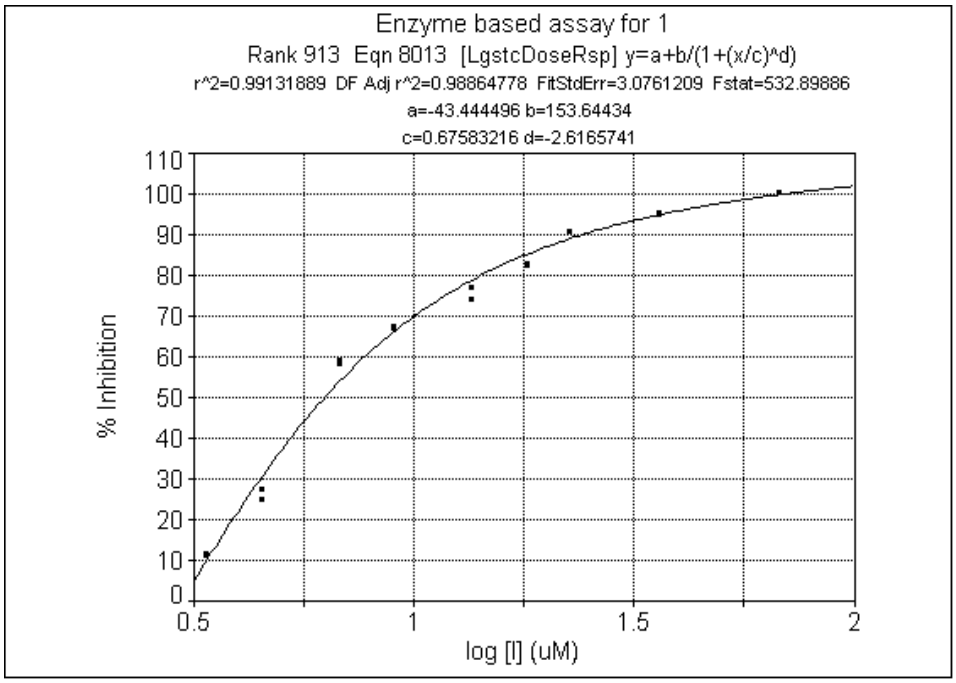


Figure S1. Dose response curve for inhibition of Pin1 by Fmoc–Ser(PO(OH)$_2$)–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine **1** (IC_{50} = 6.3 ± 0.4 μM).

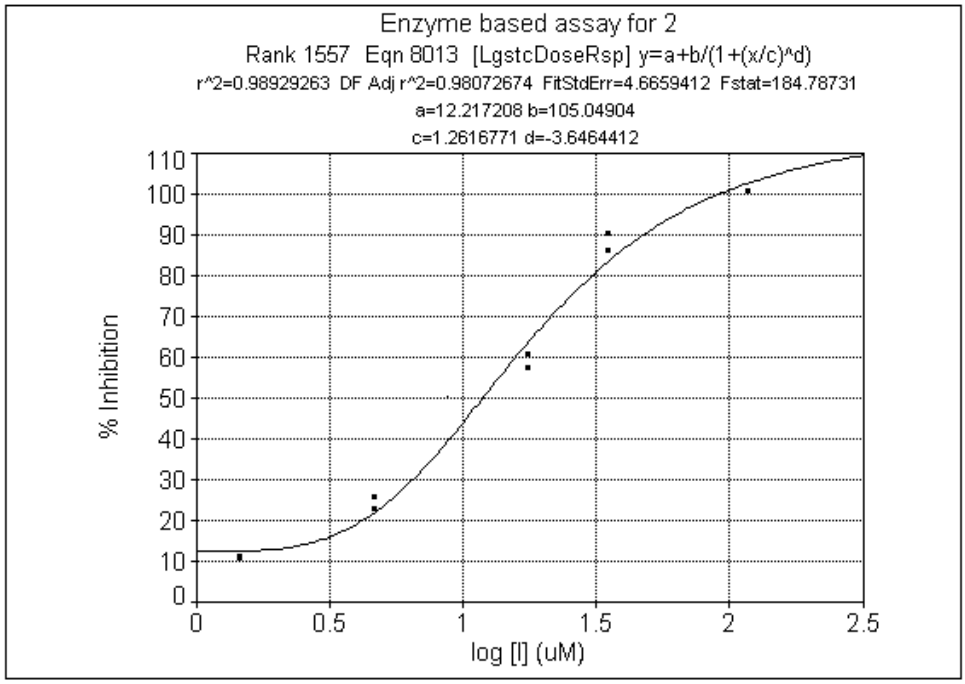


Figure S2. Dose response curve for inhibition of Pin1 by Ac–Ser(PO(OH)$_2$)–Ψ[CH$_2$N]–Pro–2-(indol-3-yl)-ethylamine **2** (IC_{50} = 12 ± 2 μM).

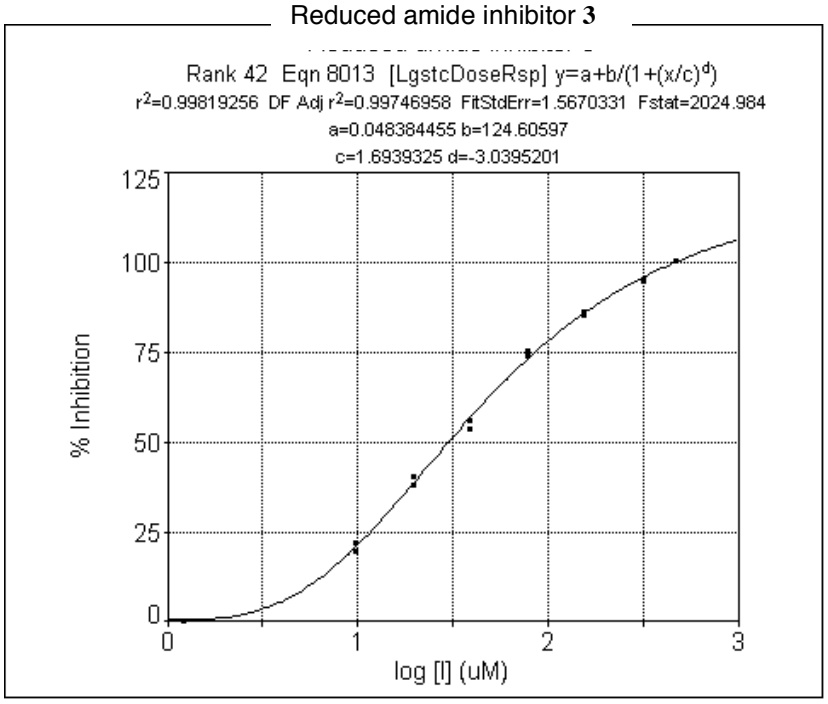


Figure S3. Dose response curve for inhibition of Pin1 by Fmoc–Thr($PO(OH)_2$)–Ψ[CH_2N]–Pro–2-(indol-3-yl)-ethylamine **3** (IC_{50} = 30 ± 2 μM).

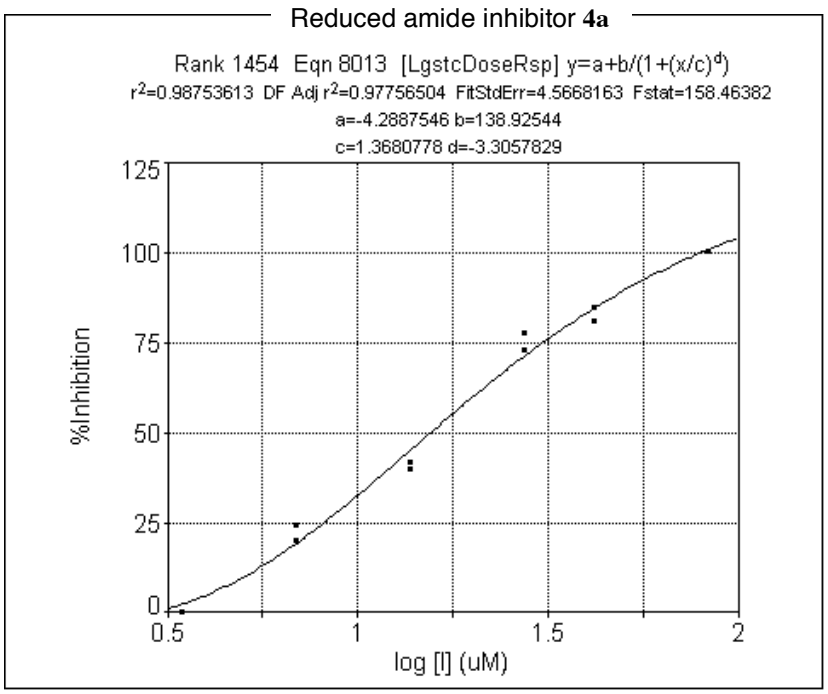


Figure S4. Dose response curve for inhibition of Pin1 by Ac–Ser($PO(OH)_2$)–Ψ[CH_2N]-(∗)Pip–2-(indol-3-yl)-ethylamine **4a** (IC_{50} = 16 ± 2 μM).

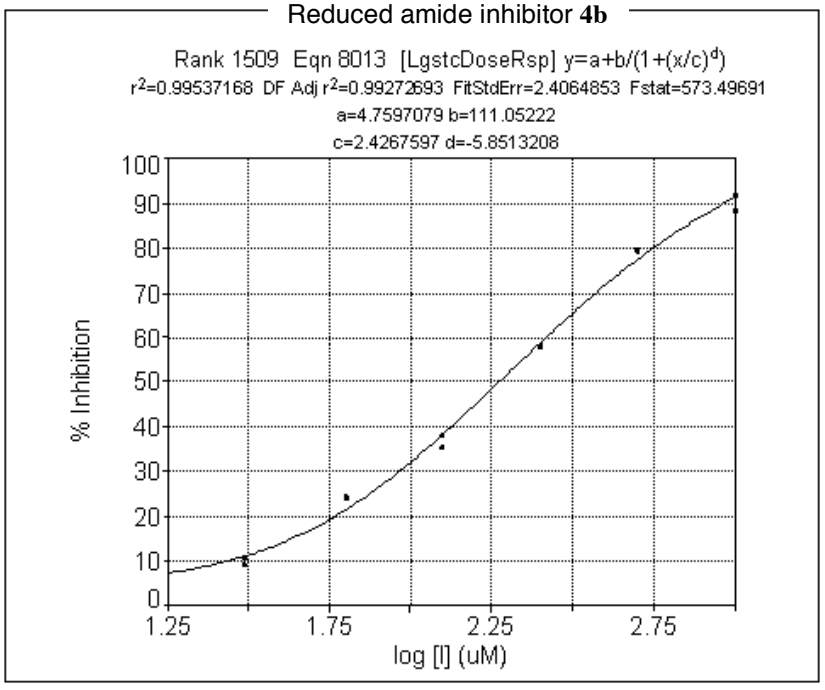
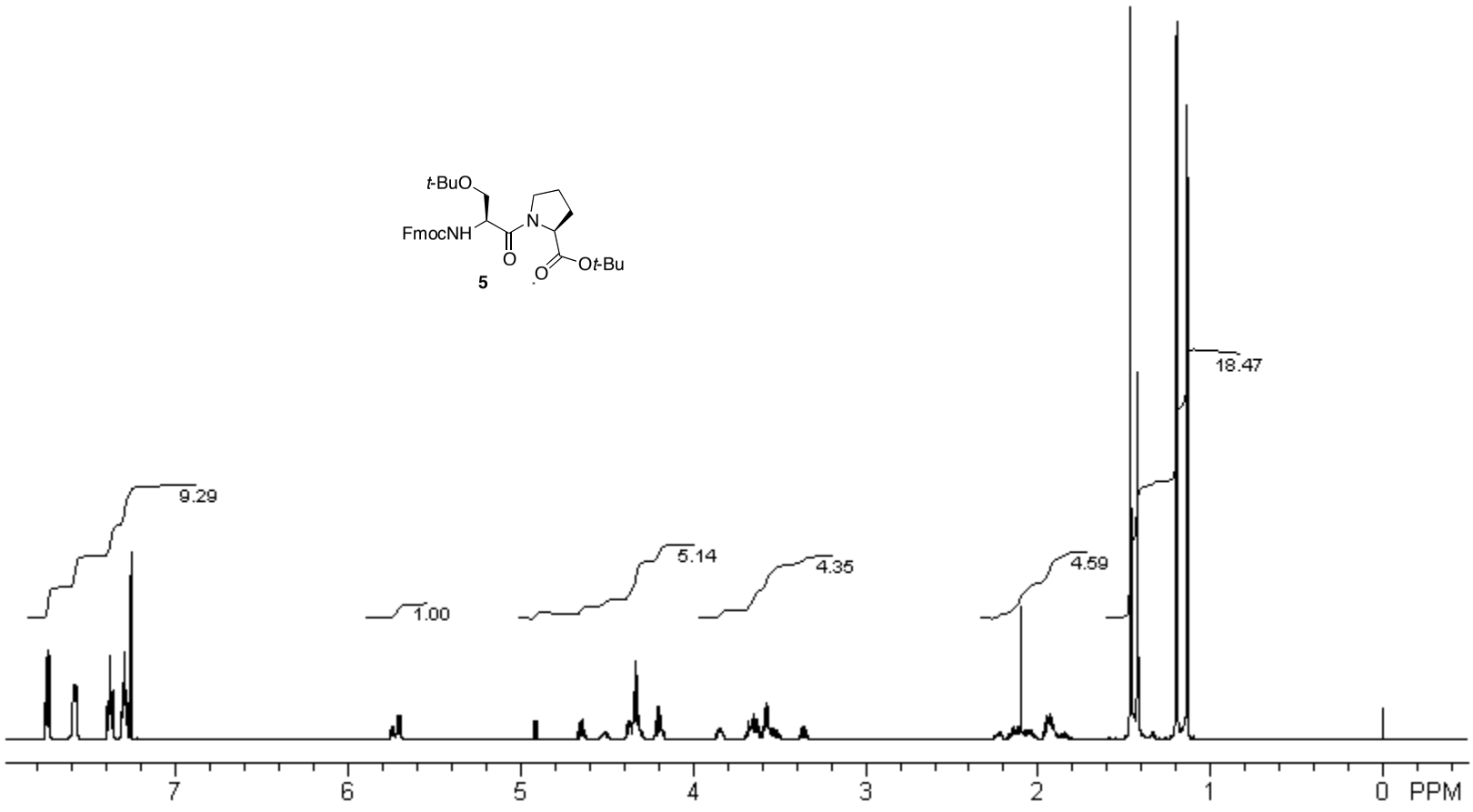


Figure S5. Dose response curve for inhibition of Pin1 by Ac–Ser($PO(OH)_2$)–Ψ[CH_2N]-(∗)Pip–2-(indol-3-yl)-ethylamine **4b** (IC_{50} = 190 ± 20 μM).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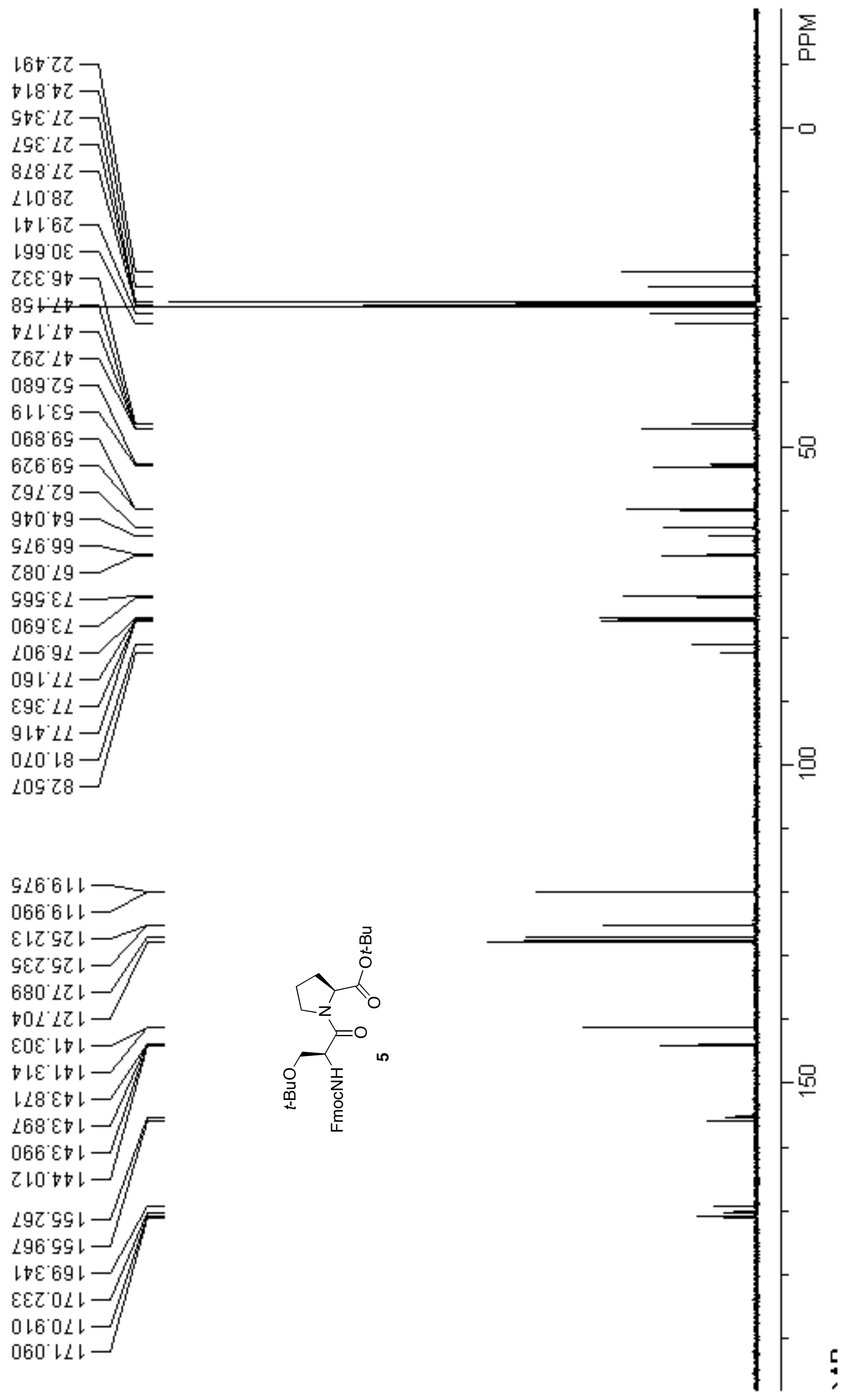
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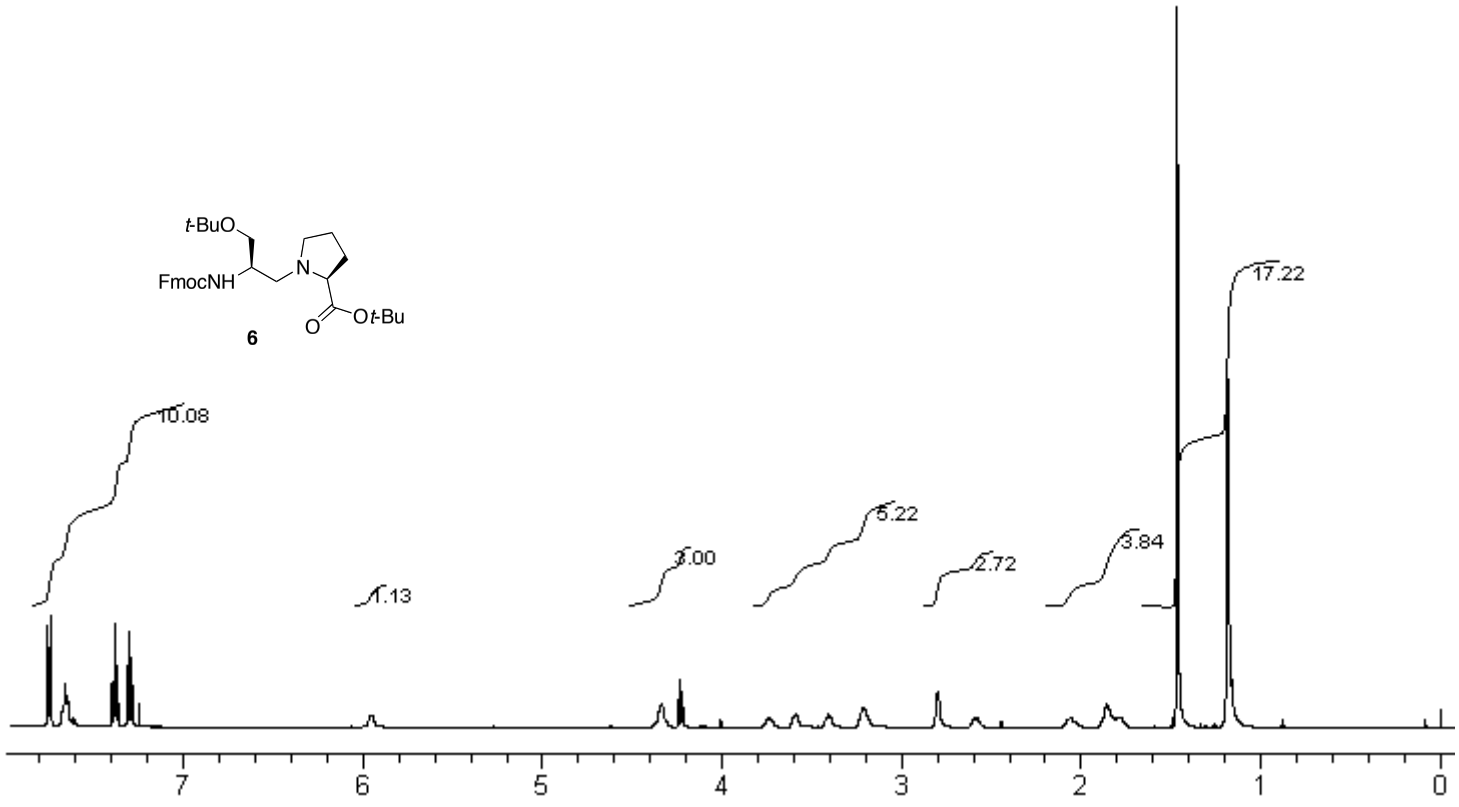
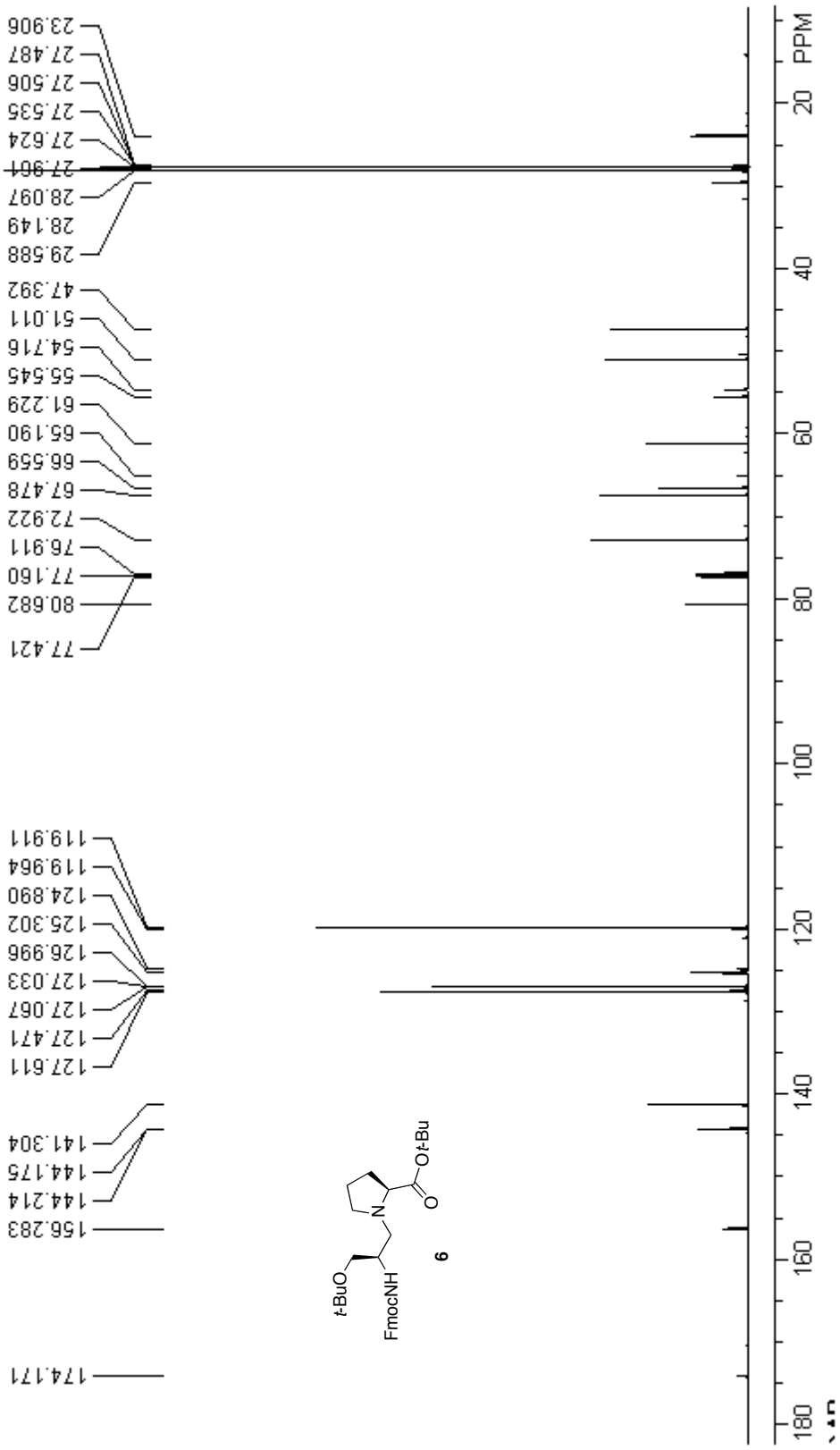
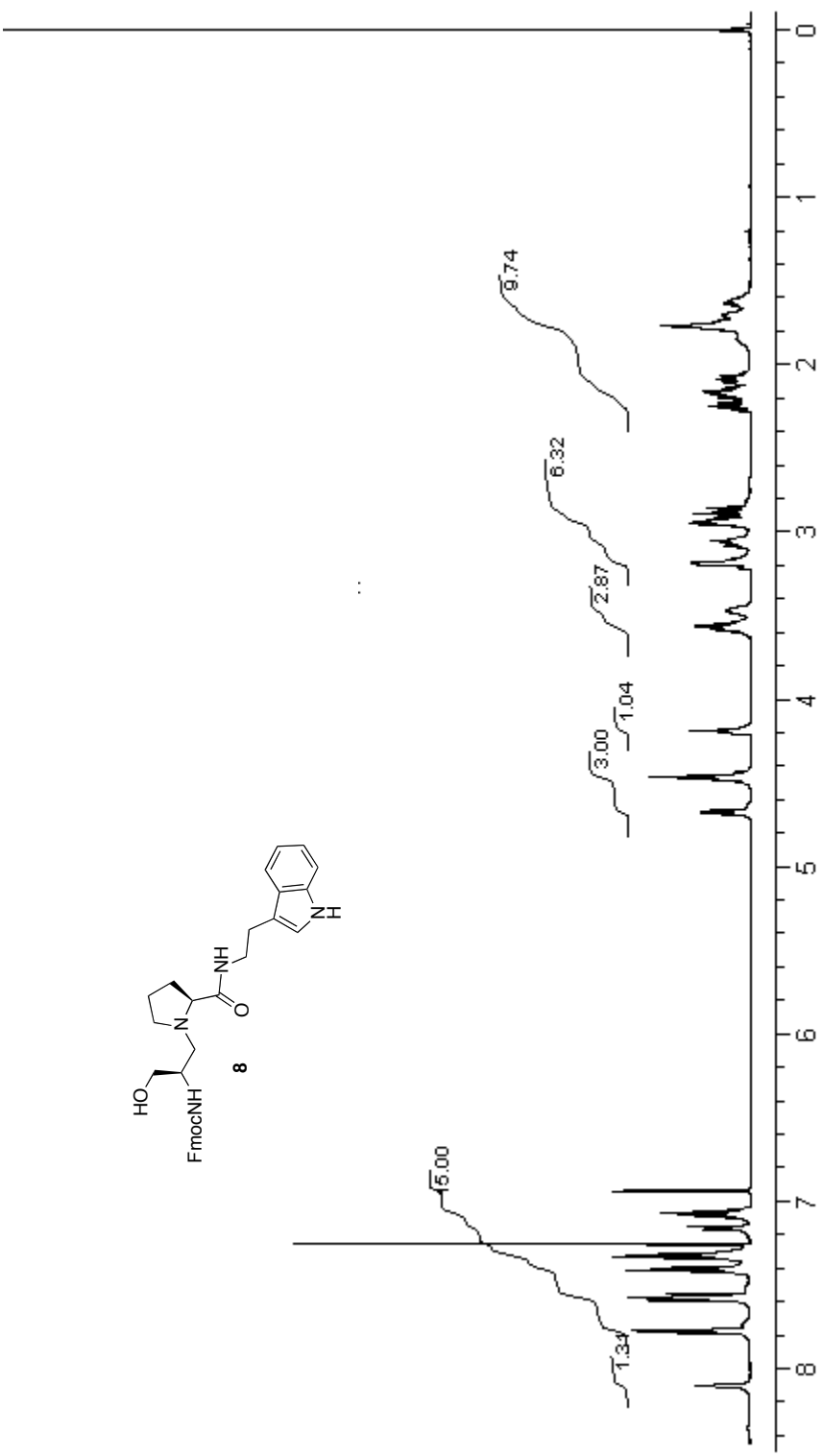
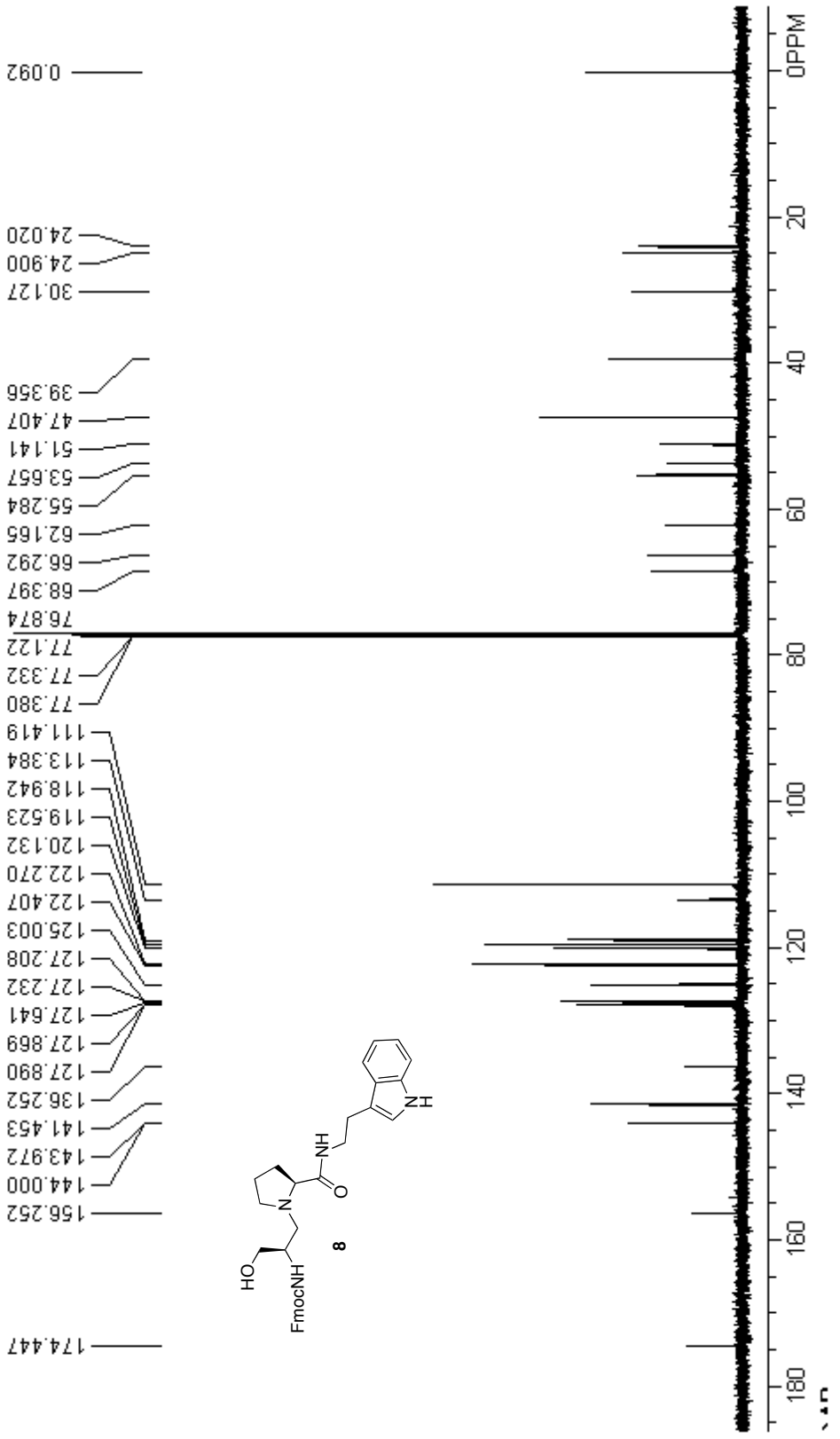
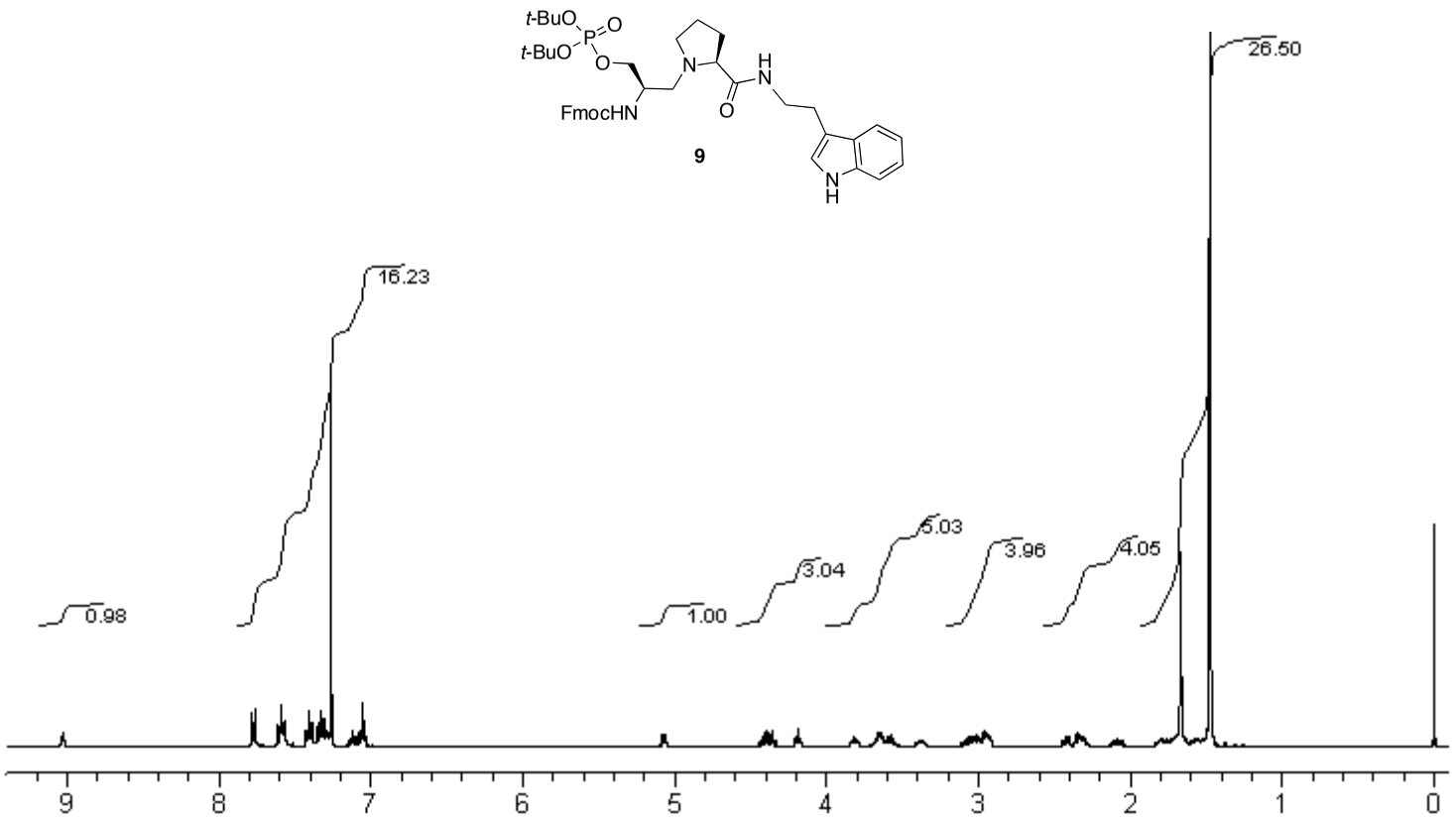
119.990
125.213
125.235
127.089
127.704
141.303
141.314
143.871
143.897
143.990
144.012
155.267
155.967
169.341
170.233
170.910
171.090
t-BuO
FmocNH
O
N
O
Ot-Bu
5
PPM
0
50
100
150

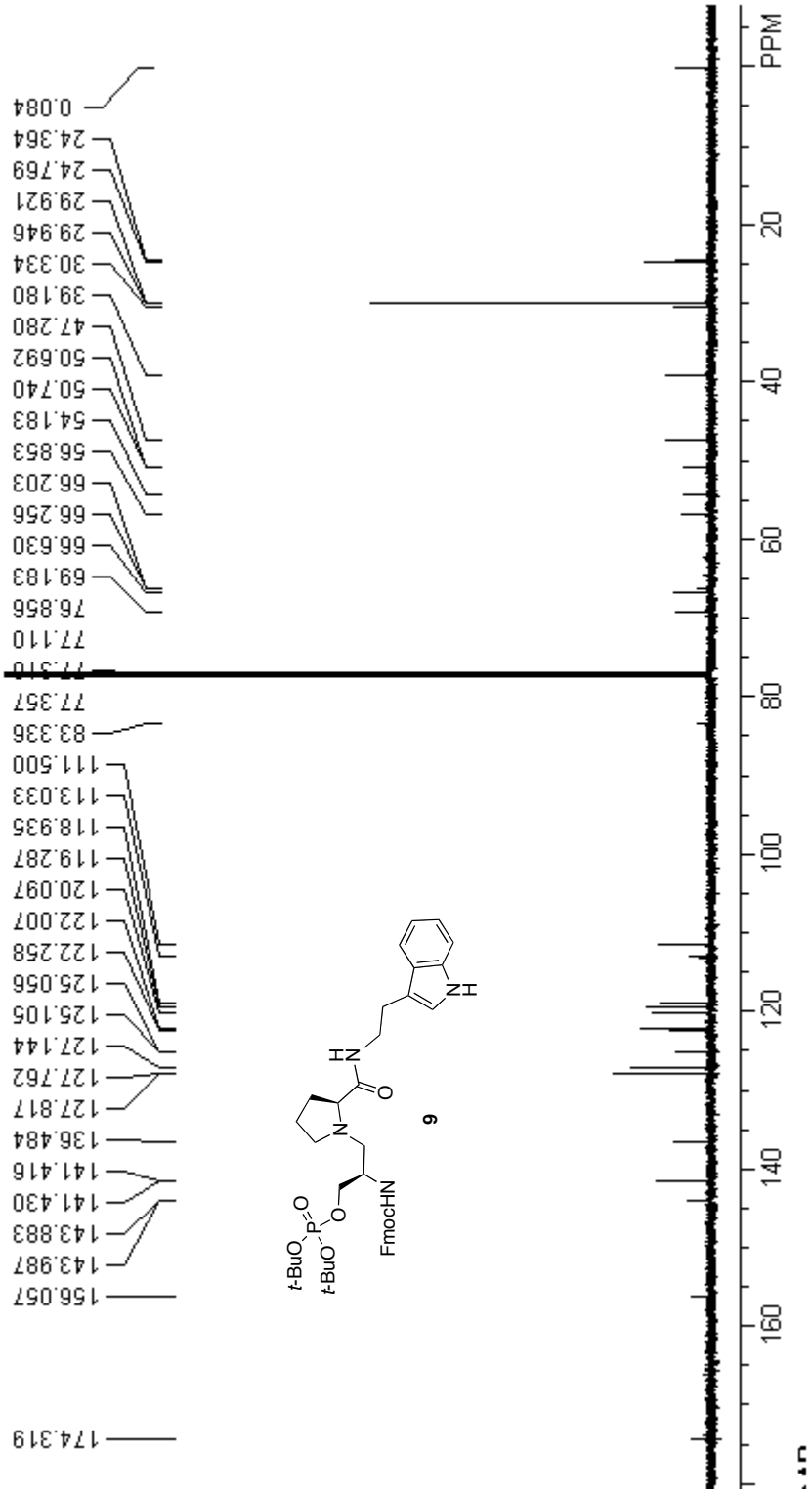

t-BuO
FmocNH
N
O
Ot-Bu
6
10.08
1.13
3.00
6.22
2.72
3.84
17.22
7
6
5
4
3
2
1
0


23.906
27.487
27.506
27.535
27.624
27.961
28.097
28.149
29.588
47.392
51.011
54.716
55.545
61.229
65.190
66.559
67.478
72.922
76.911
77.160
80.682
77.421
119.911
119.964
124.890
125.302
126.996
127.033
127.067
127.471
127.611
141.304
144.175
144.214
156.283
174.171
t-BuO
FmocNHN
O
Ot-Bu
6
PPM
20
40
60
80
100
120
140
160
180

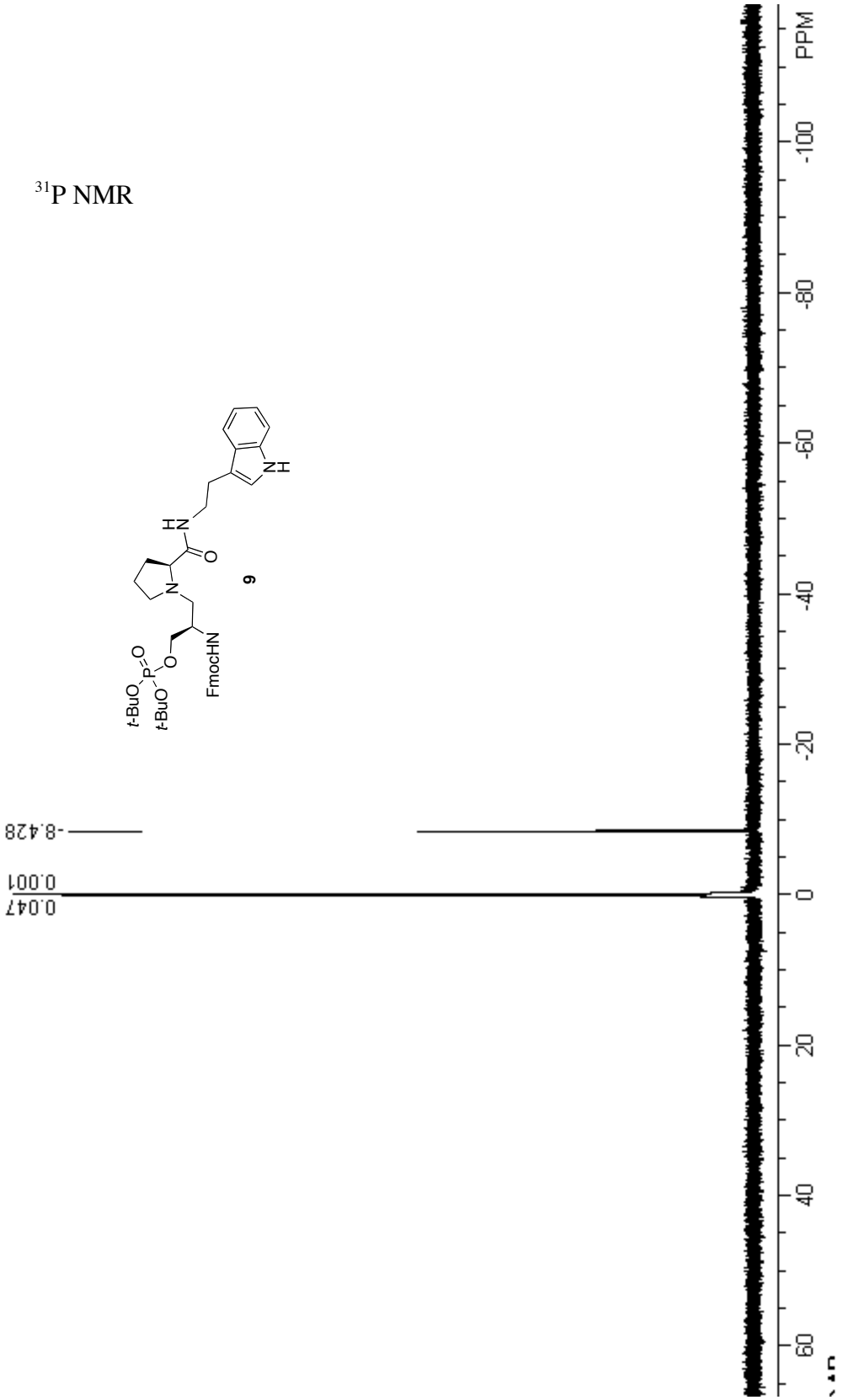

HO
FmocNH
N
NH
O
NH
8
5.00
1.34
3.00
1.04
2.87
6.32
9.74
0
1
2
3
4
5
6
7
8

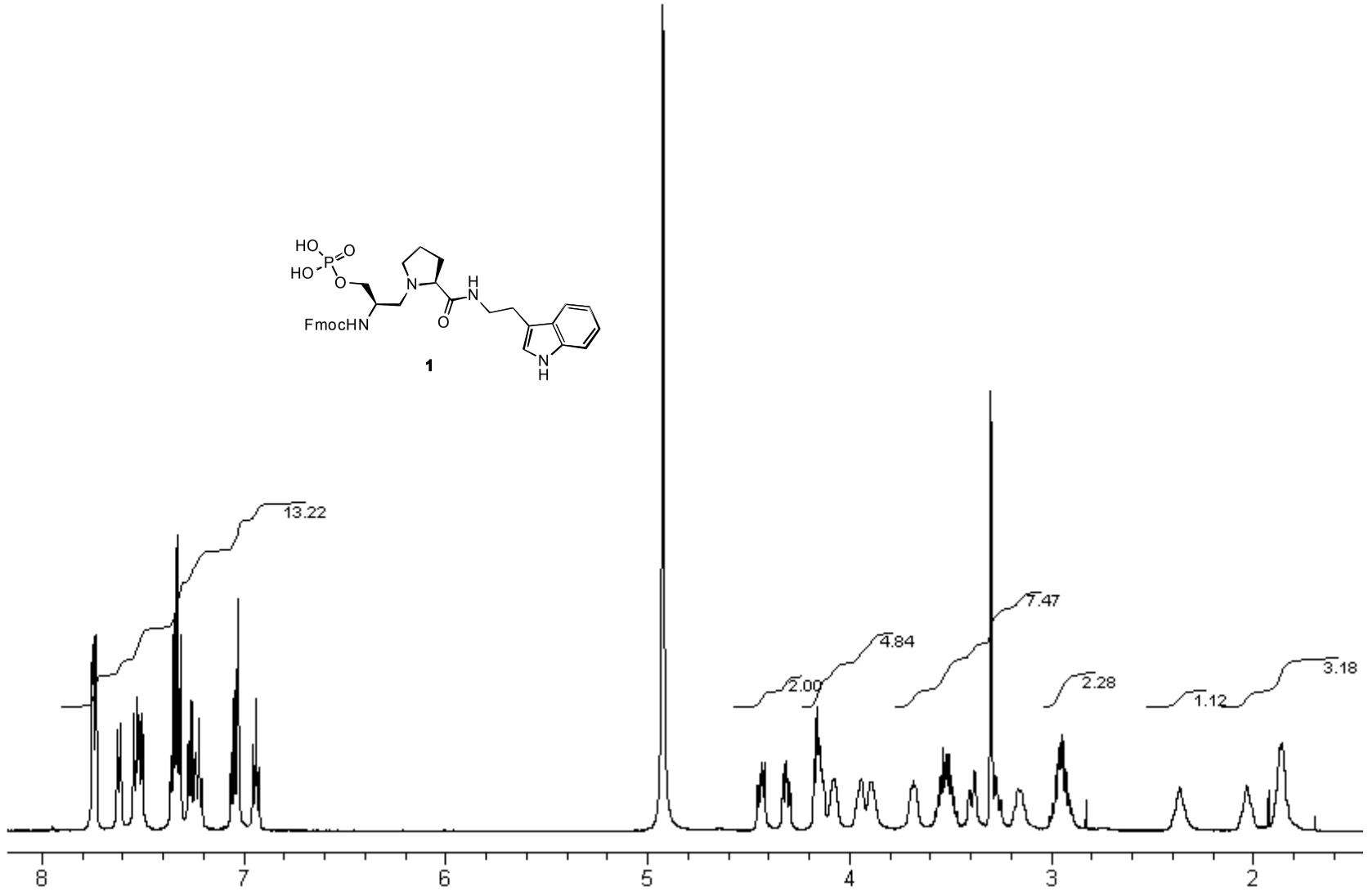

0.092
24.020
24.900
30.127
39.356
47.407
51.141
53.657
55.284
62.165
66.292
68.397
76.874
77.122
77.332
77.380
111.419
113.384
118.942
119.523
120.132
122.270
122.407
125.003
127.208
127.232
127.641
127.869
127.890
136.252
141.453
143.972
144.000
156.252
174.447
HO
FmocNH
8
NH
NH
O
N
N
H
0PPM
20
40
60
80
100
120
140
160
180

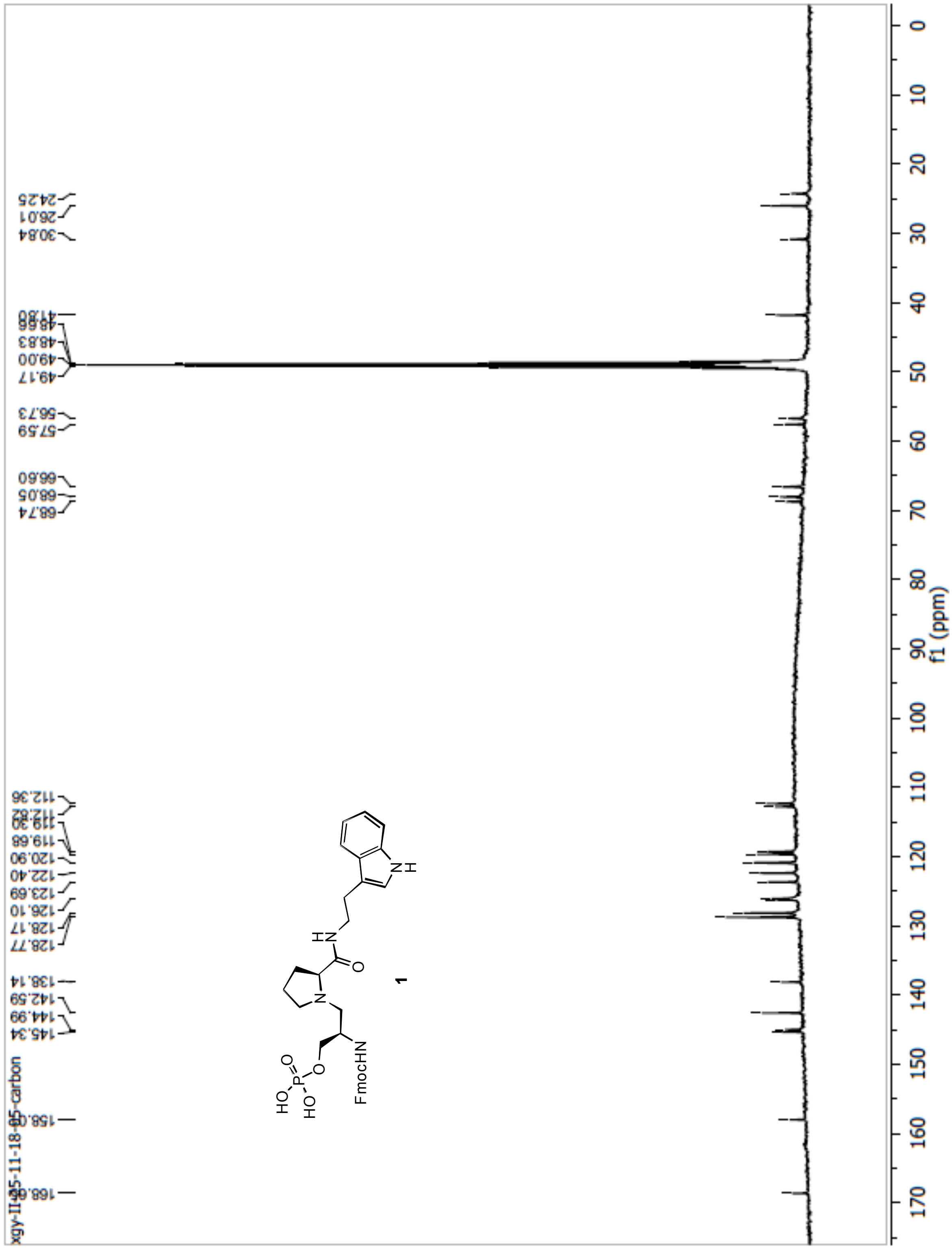

t-BuO
t-BuO
P
O
O
N
H
N
O
FmocHN
N
H
9
26.50
16.23
6.03
3.96
4.05
3.04
0.98
1.00
9
8
7
6
5
4
3
2
1
0


0.084
24.364
24.769
29.921
29.946
30.334
39.180
47.280
50.692
50.740
54.183
56.853
66.203
66.256
66.630
69.183
76.856
77.110
77.310
77.357
83.336
111.500
113.033
118.935
119.287
120.097
122.007
122.258
125.056
125.105
127.144
127.762
127.817
136.484
141.416
141.430
143.883
143.987
156.057
174.319
PPM
20
40
60
80
100
120
140
160
t-BuO
t-BuO
FmocHN
9

^{31}P NMR

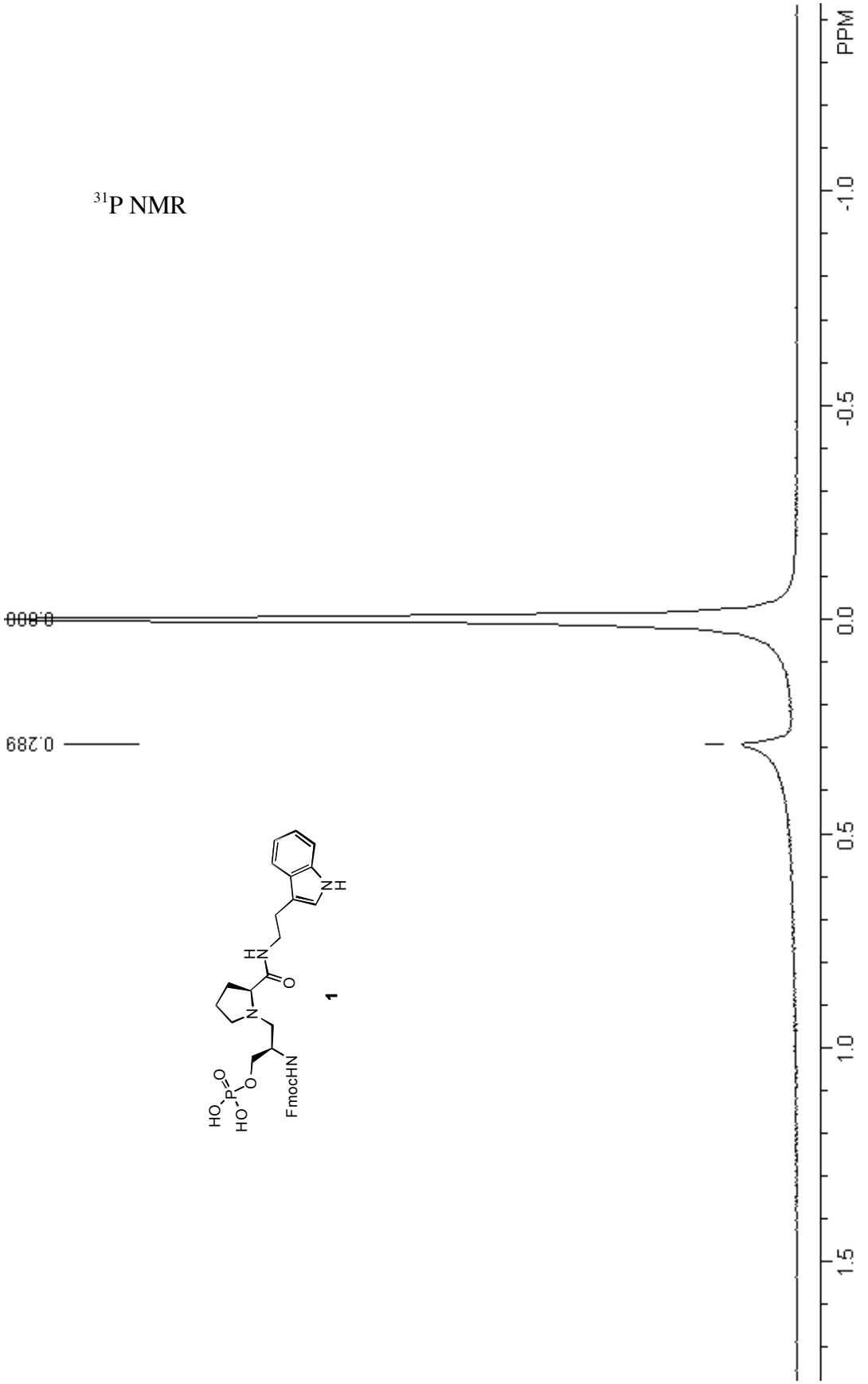


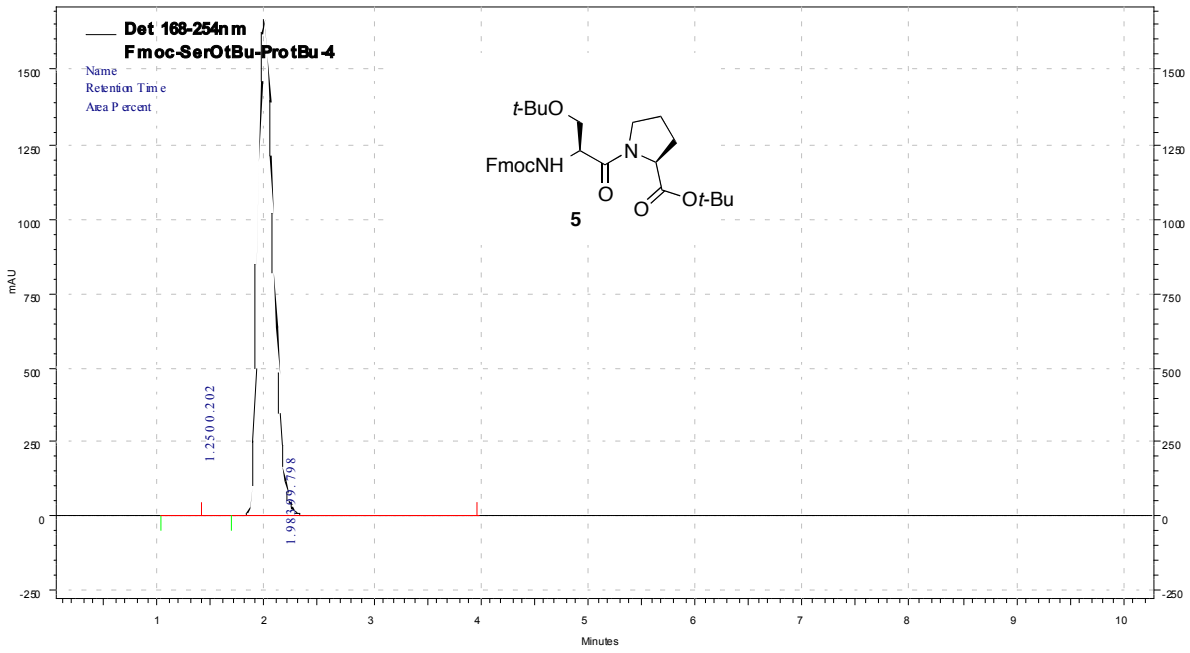

HO
HO
P
O
O
N
H
N
FmocHN
O
1
13.22
2.00
4.84
7.47
2.28
1.12
3.18
8
7
6
5
4
3
2

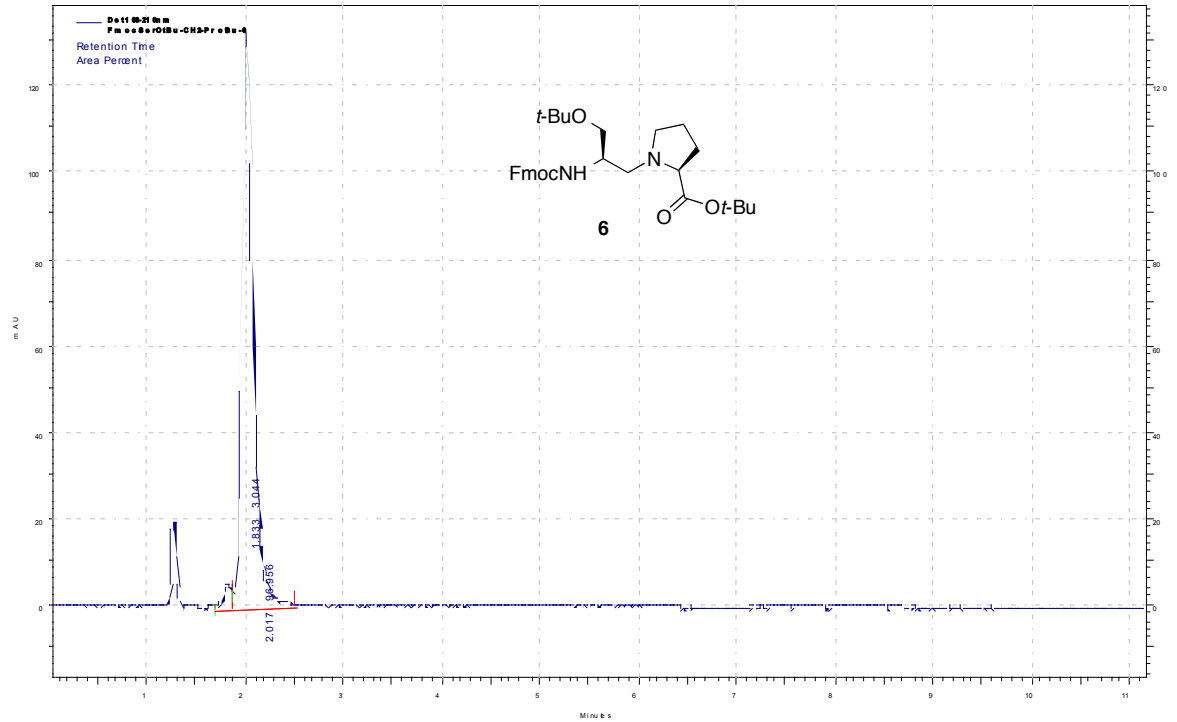

f1 (ppm)
24.25
26.01
30.84
41.80
48.66
48.83
49.00
49.17
56.73
57.59
66.60
68.05
68.74
112.36
112.82
119.30
119.68
120.90
122.40
123.69
126.10
128.17
128.77
138.14
142.59
144.99
145.34
FmocHN
HO
O
P
NH

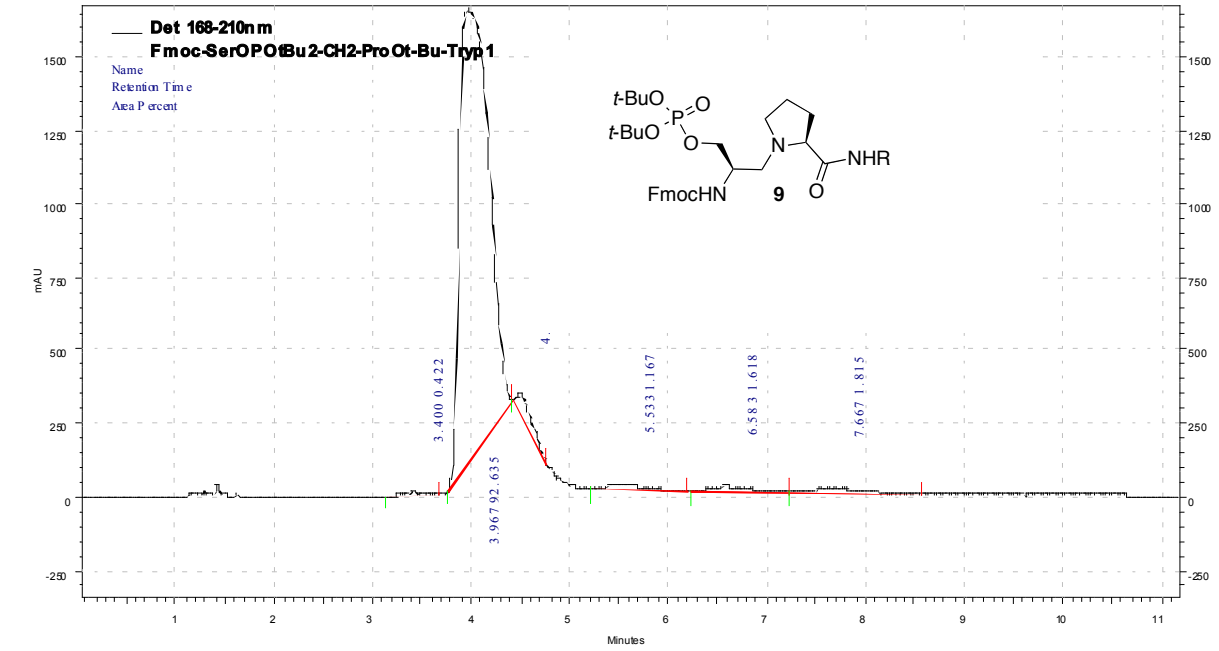
1

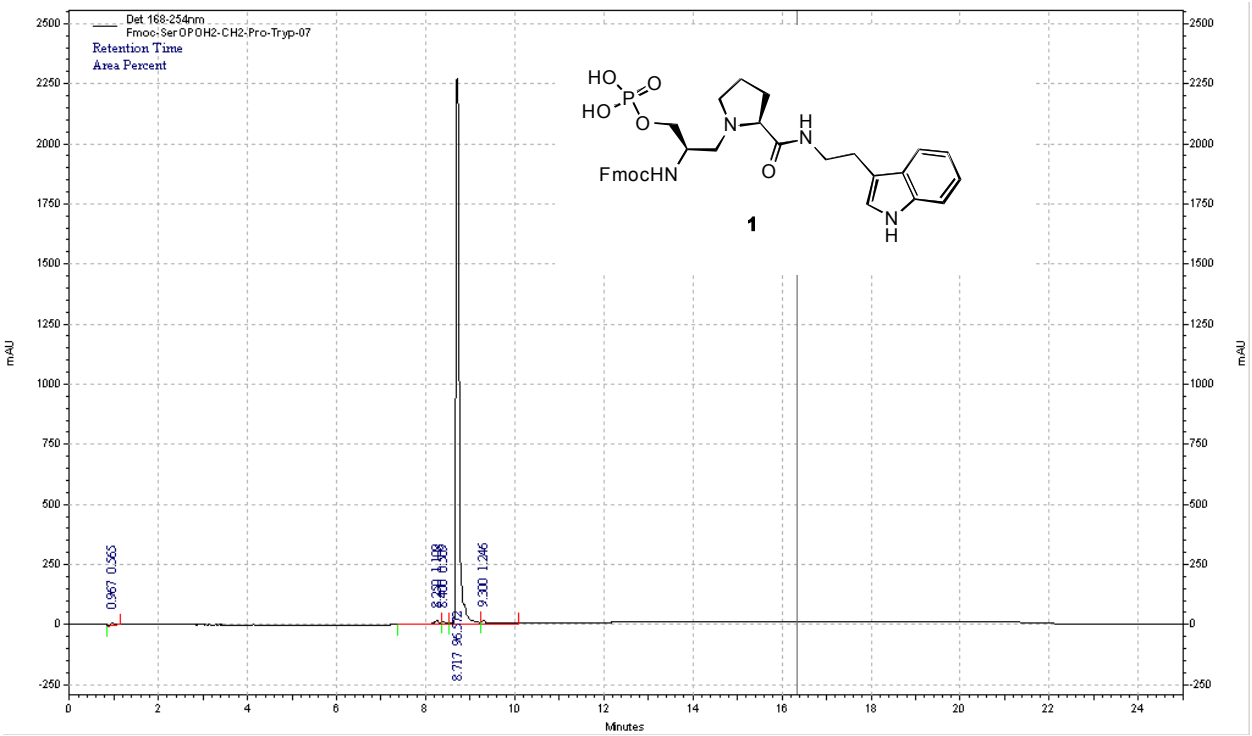
^{31}P NMR



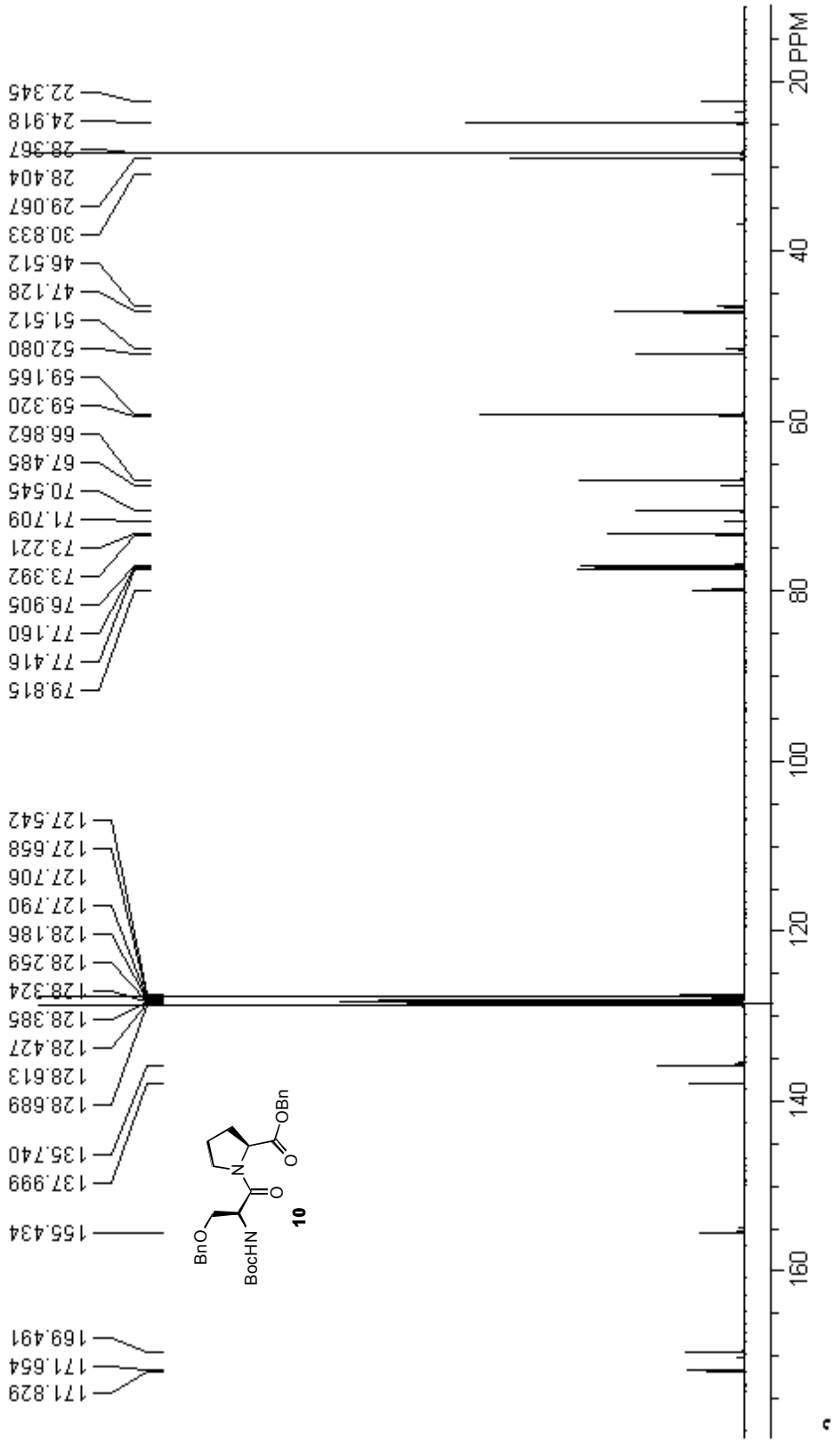

Det 168-254nm
Fmoc-SerOtBu-ProtBu-4
Name
Retention Time
Area Percent
t-BuO
FmocNH
N
O
O
Ot-Bu
5
mAU
Minutes


Retention Time
Area Percent
t-BuO
FmocNH
N
O
Ot-Bu
6
m A U
Minutes

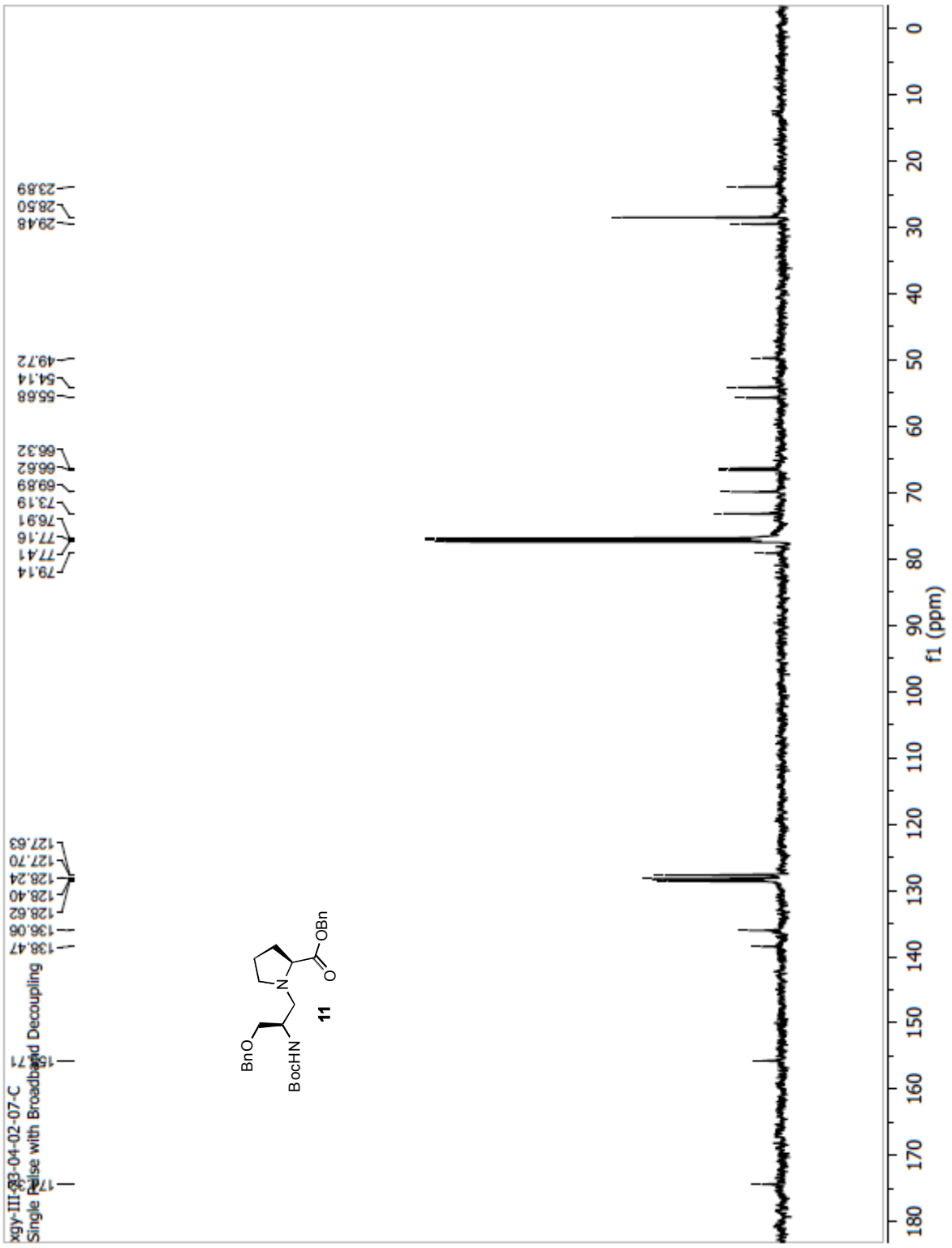

Det 168-210nm
Fmoc-SerOPOtBu2-CH2-ProOt-Bu-Tryp1
Name
Retention Time
Area Percent
t-BuO
t-BuO
P
O
O
N
NHR
FmocHN
9
O
mAU
Minutes
3.400 0.422
3.967 92.635
5.533 1.167
6.583 1.618
7.667 1.815


Det 168-254nm
Fmoc-SerOPOH2-CH2-Pro-Tryp-07
Retention Time
Area Percent
HO
HO
P
O
O
N
H
N
FmocHN
O
N
H
1
mAU
Minutes
0.967 0.565
8.717 96.572
9.300 1.246

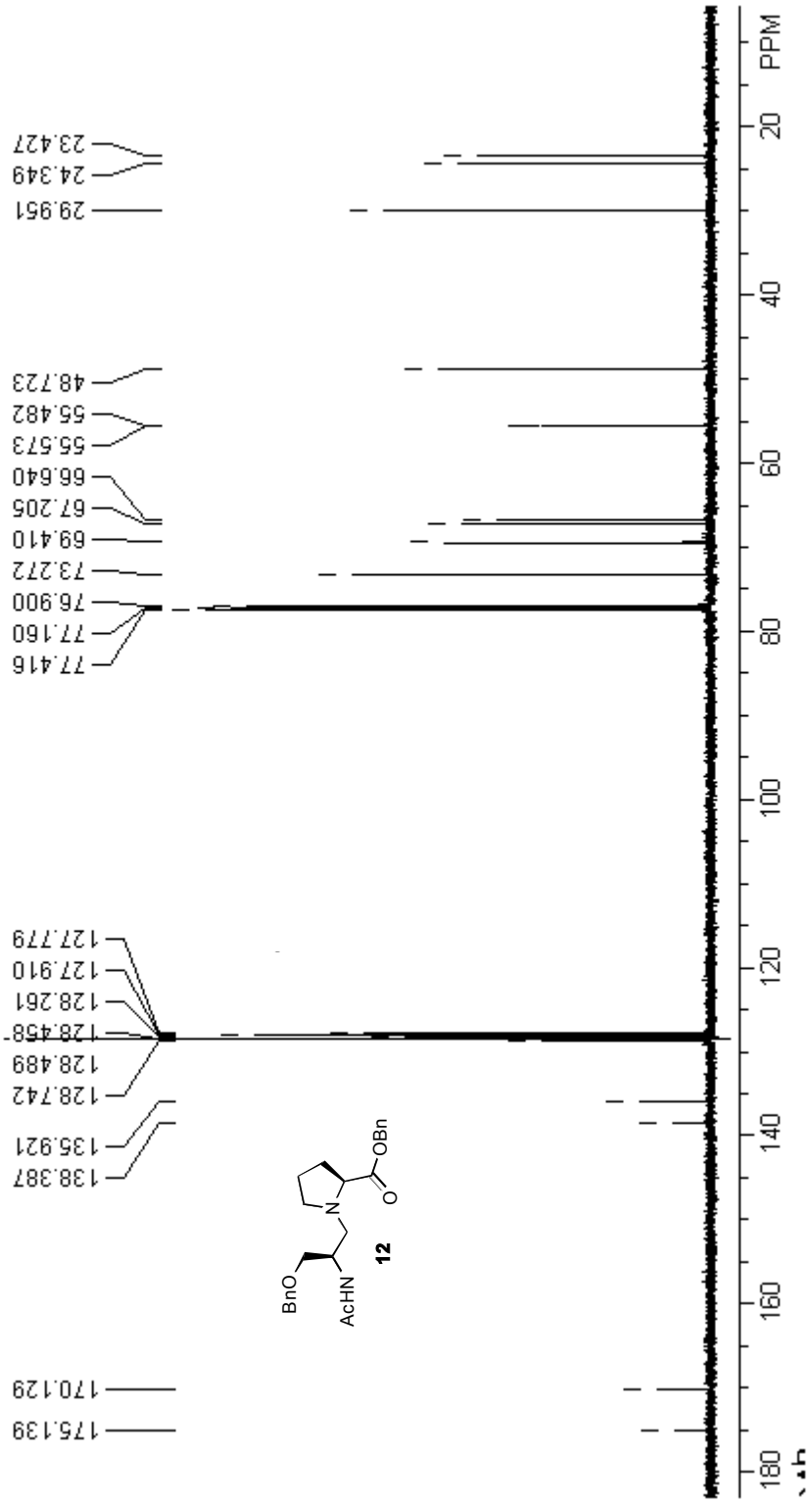
1.403
1.425
1.958
1.968
1.982
1.986
3.608
3.620
3.713
4.434
4.457
4.497
4.520
4.573
4.581
4.597
5.090
5.115
5.169
5.193
7.260
7.272
7.292
7.294
7.309
7.313
7.320
7.323
7.329
7.338
7.339
7.341
7.343
7.345
7.345
7.356
7.357
9.67
6.89
7.09
4.04
4.12
4.37
9.00
PPM
BnO
BocHN
OBn
10


22.345
24.918
28.367
28.404
29.067
30.833
46.512
47.128
51.512
52.080
59.165
59.320
66.862
67.485
70.545
71.709
73.221
73.392
76.905
77.160
77.416
79.815
127.542
127.658
127.706
127.790
128.186
128.259
128.324
128.385
128.427
128.613
128.689
135.740
137.999
155.434
169.491
171.654
171.829
20 PPM
40
60
80
100
120
140
160
OBn
O
N
O
BnO
BocHN
10

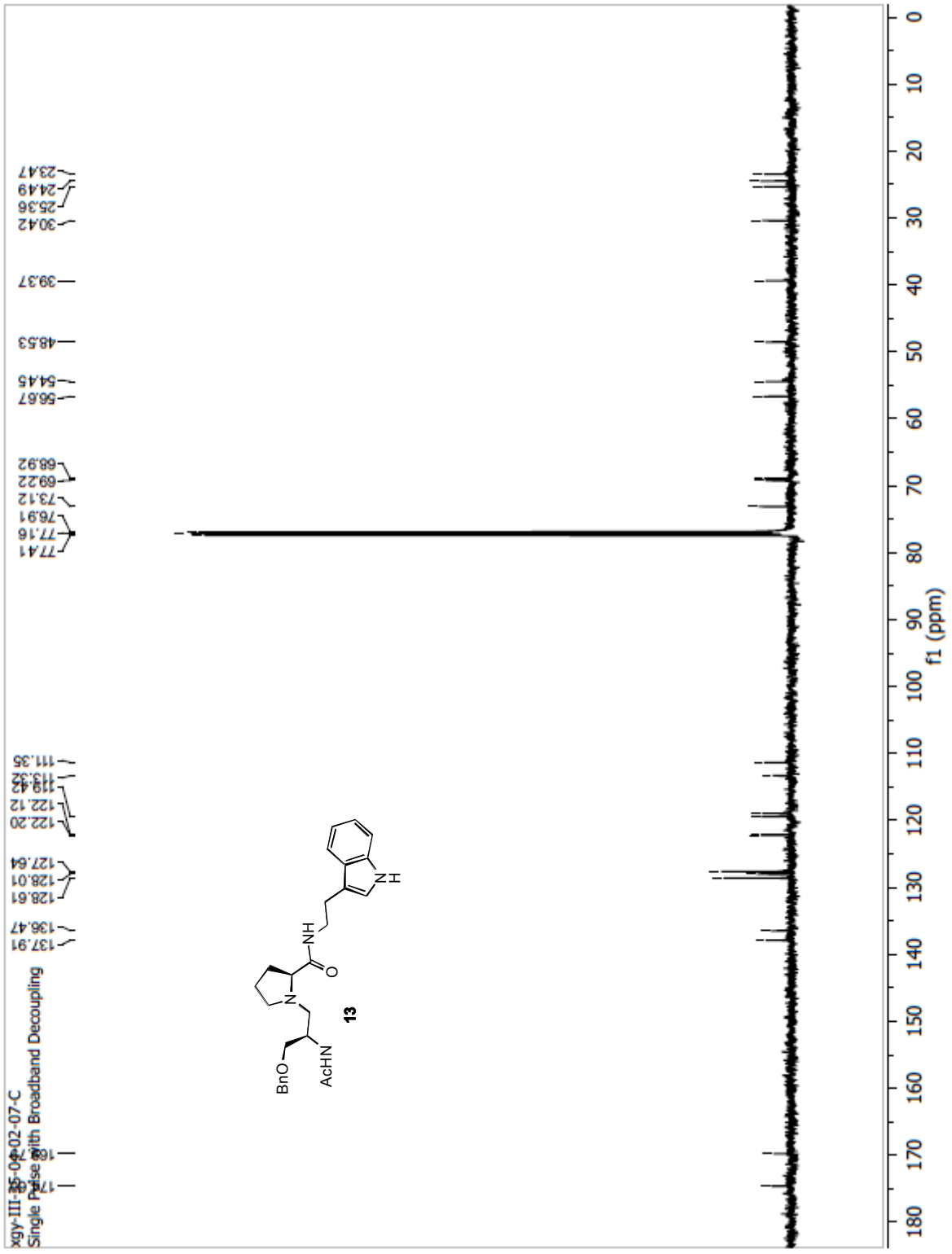
1.433
8.77
1.891
4.30
2.16
1.00
2.09
3.01
2.09
3.00
2.839
2.855
3.304
3.315
3.321
4.451
4.474
4.502
4.526
5.076
5.101
5.119
5.143
10.08
7.277
7.282
7.297
7.305
7.313
7.322
7.331
7.334
BnO
BocHN
OBn
11
1 PPM


xgy-III-83-04-02-07-C
Single Pulse with Broadband Decoupling
BnO
BocHN
OBn
O
11
f1 (ppm)

7.349
7.347
7.339
7.338
7.335
7.330
7.321
7.319
7.312
7.307
7.294
7.290
7.277
7.260
5.163
5.138
5.114
5.089
4.549
4.525
4.473
4.449
3.697
3.689
3.679
3.670
3.489
3.475
3.471
2.852
2.767
2.755
1.940
1.868
10.52
1.01
2.10
2.11
1.00
1.04
2.10
1.02
3.11
7.88
PPM
BnO
AcHN
OBn
12

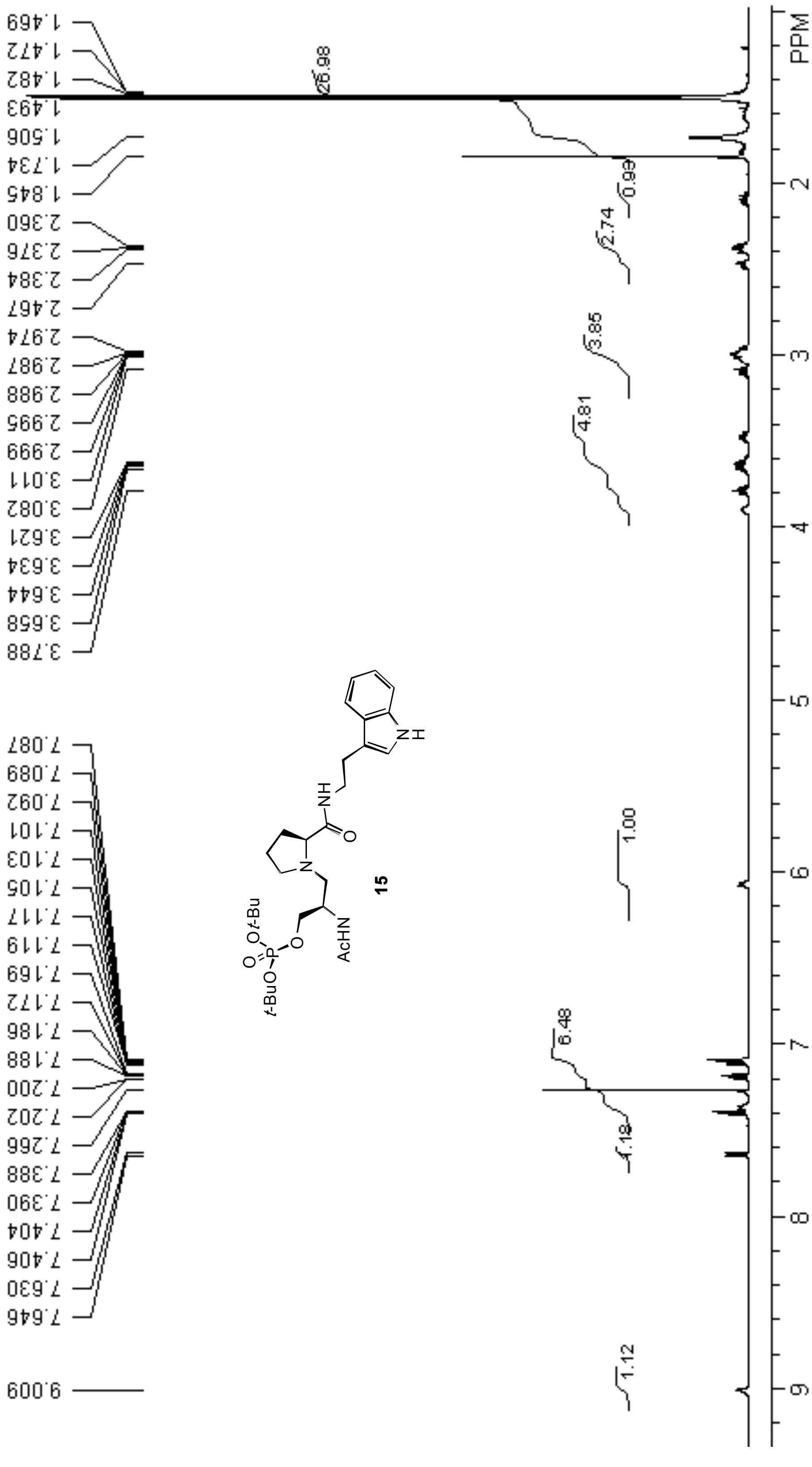

23.427
24.349
29.951
48.723
55.482
55.573
66.640
67.205
69.410
73.272
76.900
77.160
77.416
127.779
127.910
128.261
128.458
128.489
128.742
135.921
138.387
170.129
175.139
PPM
20
40
60
80
100
120
140
160
180
OBn
O
N
BnO
AcHN
12

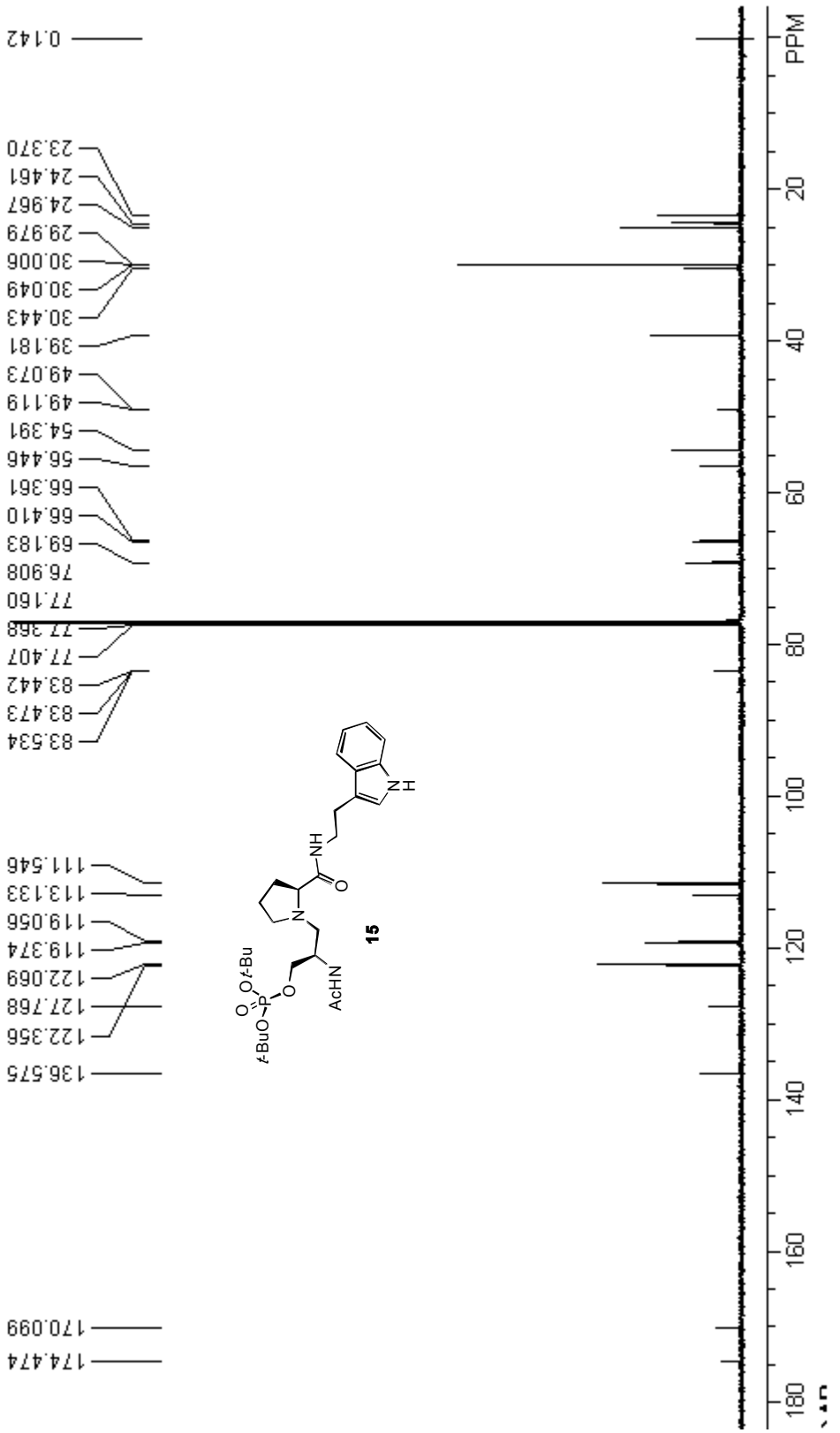
7.567
7.552
7.350
7.348
7.345
7.334
7.330
7.327
7.319
7.315
7.300
7.285
7.261
7.189
7.187
7.173
7.092
7.091
7.077
7.075
6.970
6.965
4.169
4.143
4.119
3.146
3.139
3.133
3.067
3.056
3.051
3.047
3.037
2.985
2.556
2.539
1.872
11.36
7.58
6.04
2.96
1.92
0.98
1.00
0.99
1.00
1.13
PPM
BnO
AcHN
NH
NH
13


xgy-III-35-04-02-07-C
Single Pulse with Broadband Decoupling
13
BnO
AcHN
NH
O
N
H
f1 (ppm)

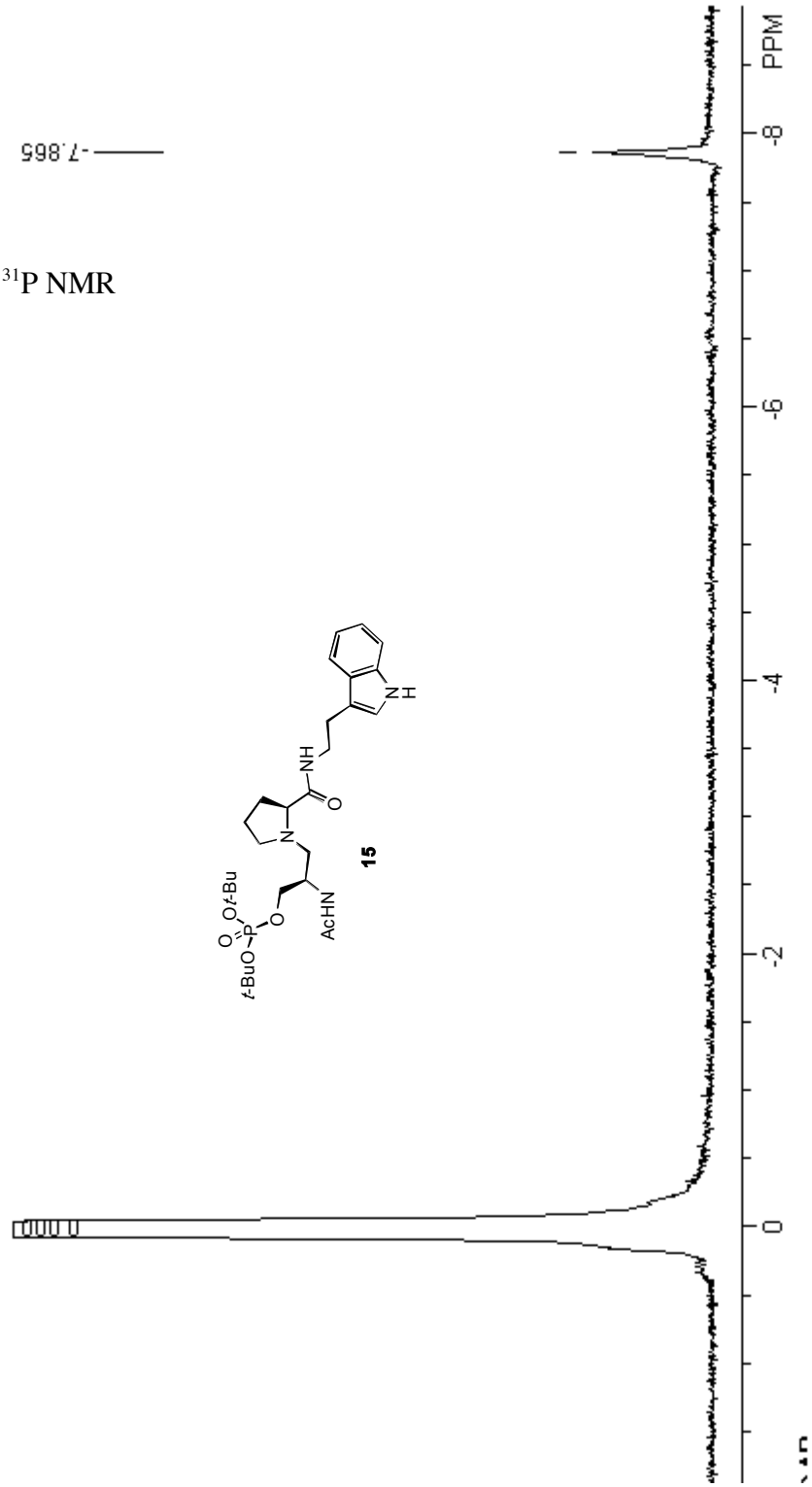
7.605
7.588
7.382
7.366
7.260
7.256
7.196
7.180
7.120
7.105
7.004
3.286
3.280
3.272
3.028
3.024
3.017
2.954
2.946
2.934
2.920
2.905
2.447
2.253
2.241
2.229
2.219
1.906
1.12
8.77
1.00
2.55
1.00
7.43
12.19
PPM
14

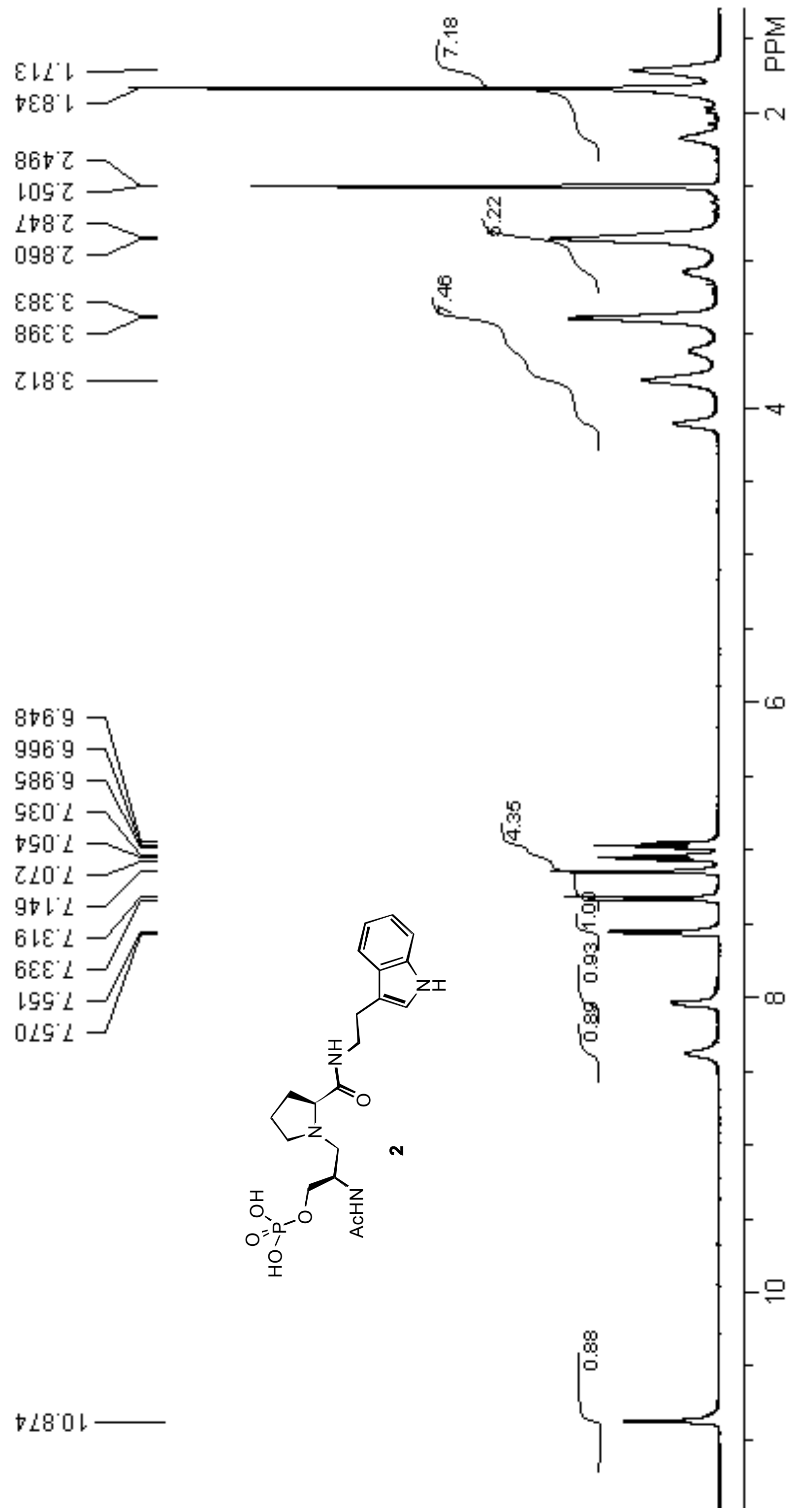
22.747
25.058
26.072
31.332
40.954
48.364
48.576
48.789
49.000
49.212
49.422
49.633
51.870
55.382
62.912
57.123
69.558
112.257
113.144
119.363
119.616
119.653
122.358
123.497
128.843
138.126
173.131
177.237
14
AcHN
HO
NH
O
N
NH
20
40
60
80
100
120
140
160
180
PPM

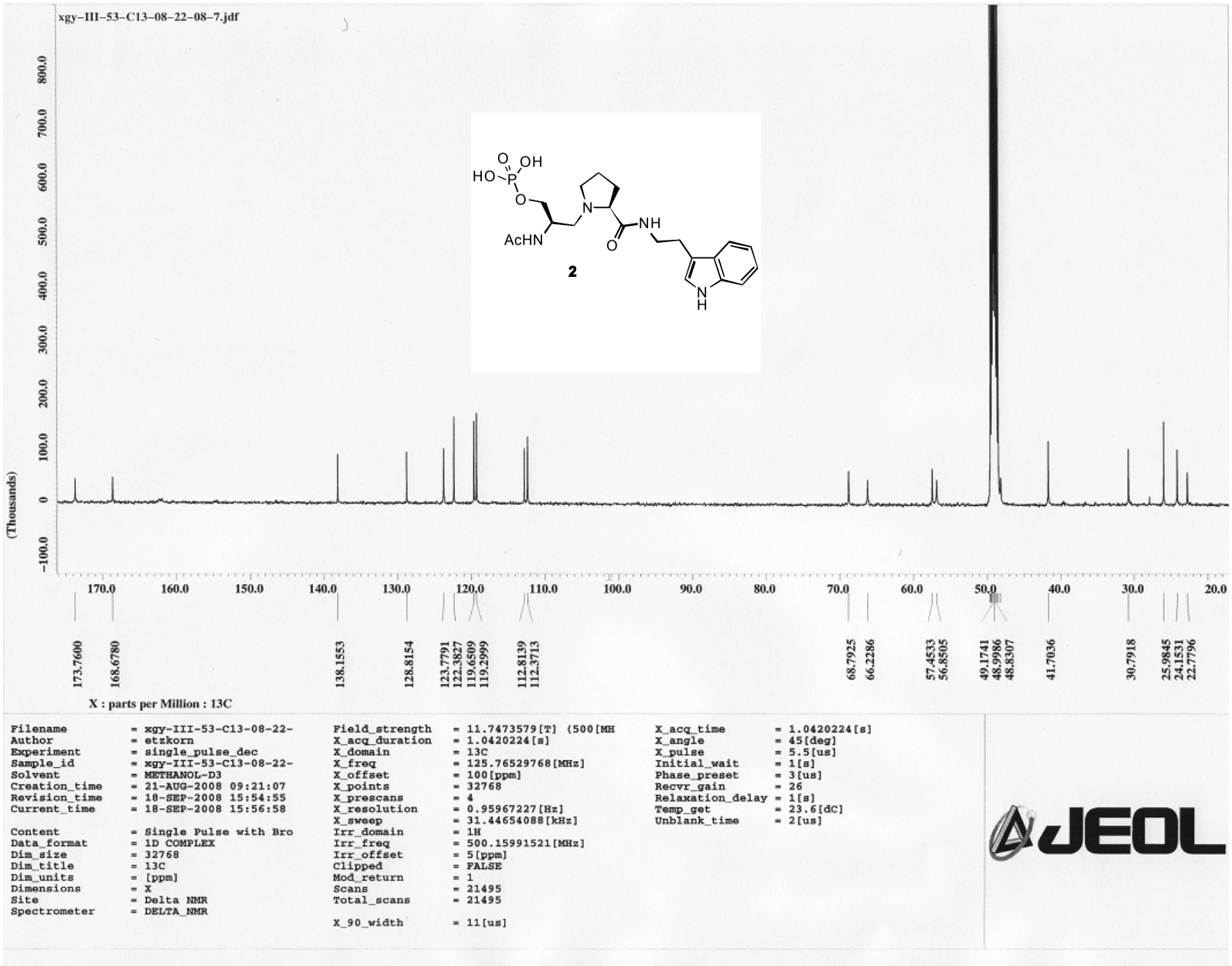

1.469
1.472
1.482
1.493
1.506
1.734
1.845
2.360
2.376
2.384
2.467
2.974
2.987
2.988
2.995
2.999
3.011
3.082
3.621
3.634
3.644
3.658
3.788
7.087
7.089
7.092
7.101
7.103
7.105
7.117
7.119
7.169
7.172
7.186
7.188
7.200
7.202
7.266
7.388
7.390
7.404
7.406
7.630
7.646
9.009
26.98
0.99
2.74
3.85
4.81
1.00
6.48
1.18
1.12
t-BuO
Ot-Bu
AcHN
NH
15
PPM


0.142
23.370
24.461
24.967
29.979
30.006
30.049
30.443
39.181
49.073
49.119
54.391
56.446
66.361
66.410
69.183
76.908
77.160
77.368
77.407
83.442
83.473
83.534
111.546
113.133
119.056
119.374
122.069
127.768
122.356
136.575
170.099
174.474
PPM
20
40
60
80
100
120
140
160
180
15

^{31}P NMR



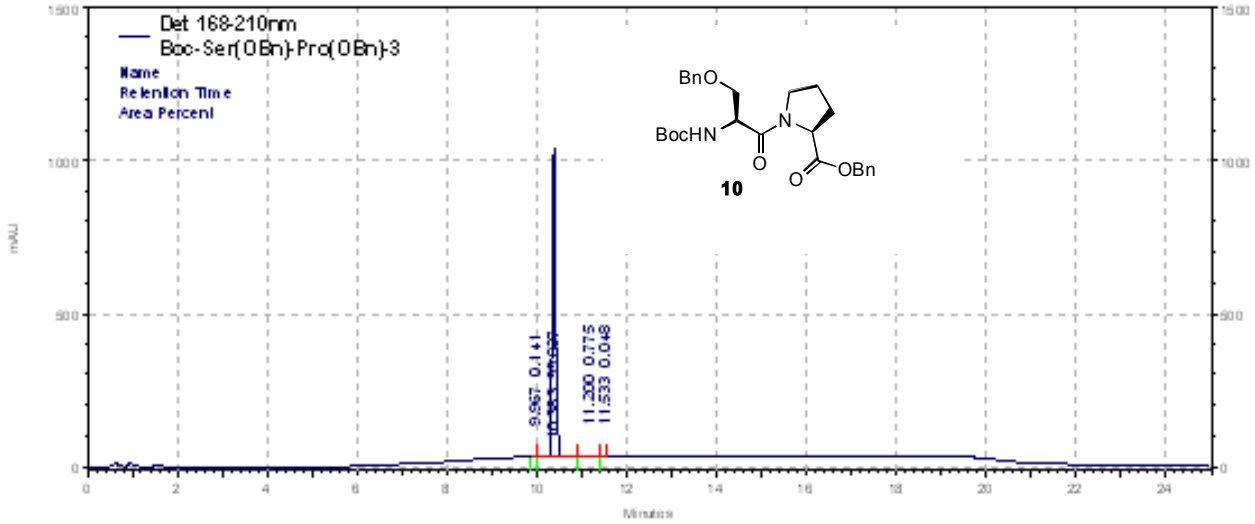

1.713
1.834
2.498
2.501
2.847
2.860
3.383
3.398
3.812
6.948
6.966
6.985
7.035
7.054
7.072
7.146
7.319
7.339
7.551
7.570
10.874
7.18
5.22
7.46
4.35
1.00
0.93
0.89
0.88
PPM
2
4
6
8
10
AcHN
NH
N
HO
OH
2

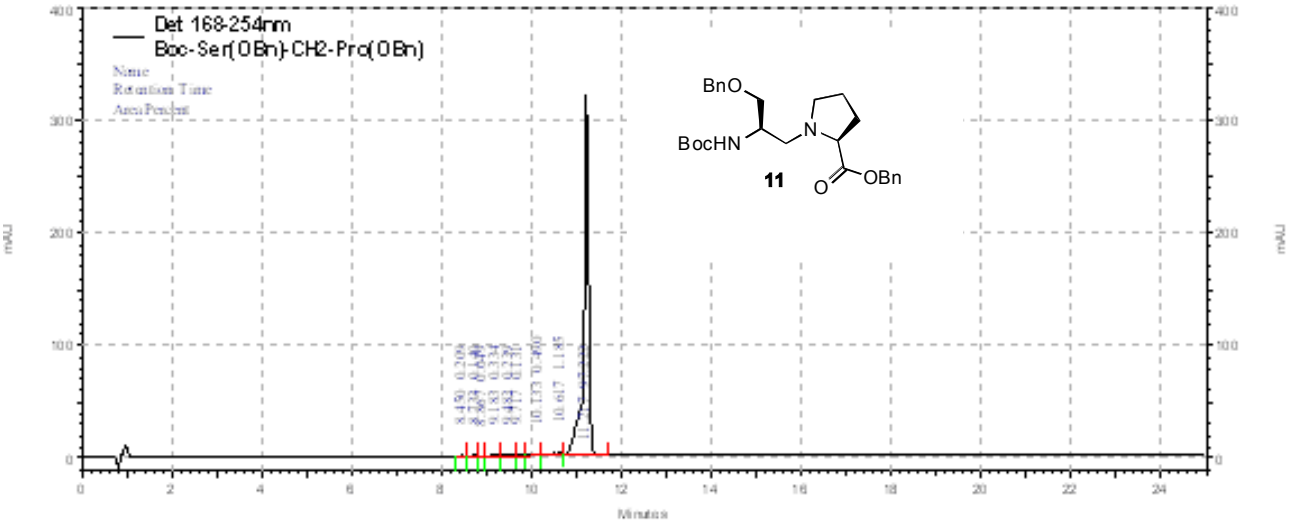

xgy-III-53-C13-08-22-08-7.jdf
(Thousands)
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0
-100.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
173.7600
168.6780
138.1553
128.8154
123.7791
122.3827
119.6509
119.2999
112.8139
112.3713
68.7925
66.2286
57.4533
56.8505
49.1741
48.9986
48.8307
41.7036
30.7918
25.9845
24.1531
22.7796
X : parts per Million : 13C
2
Filename = xgy-III-53-C13-08-22-
Author = etzkorn
Experiment = single_pulse_dec
Sample_id = xgy-III-53-C13-08-22-
Solvent = METHANOL-D3
Creation_time = 21-AUG-2008 09:21:07
Revision_time = 18-SEP-2008 15:54:55
Current_time = 18-SEP-2008 15:56:58
Content = Single Pulse with Bro
Data_format = 1D COMPLEX
Dim_size = 32768
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = Delta NMR
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.0420224[s]
X_domain = 13C
X_freq = 125.76529768[MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 0.95967227[Hz]
X_sweep = 31.44654088[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 21495
Total_scans = 21495
X_90_width = 11[us]
X_acq_time = 1.0420224[s]
X_angle = 45[deg]
X_pulse = 5.5[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 26
Relaxation_delay = 1[s]
Temp_get = 23.6[dC]
Unblank_time = 2[us]
JEOL

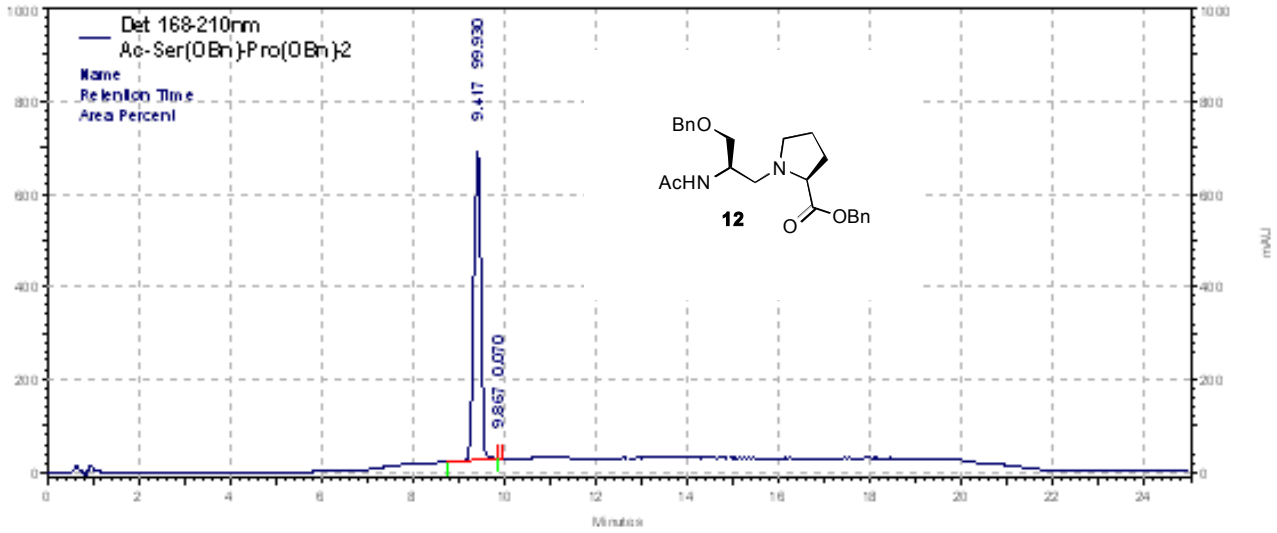
^{31}P NMR

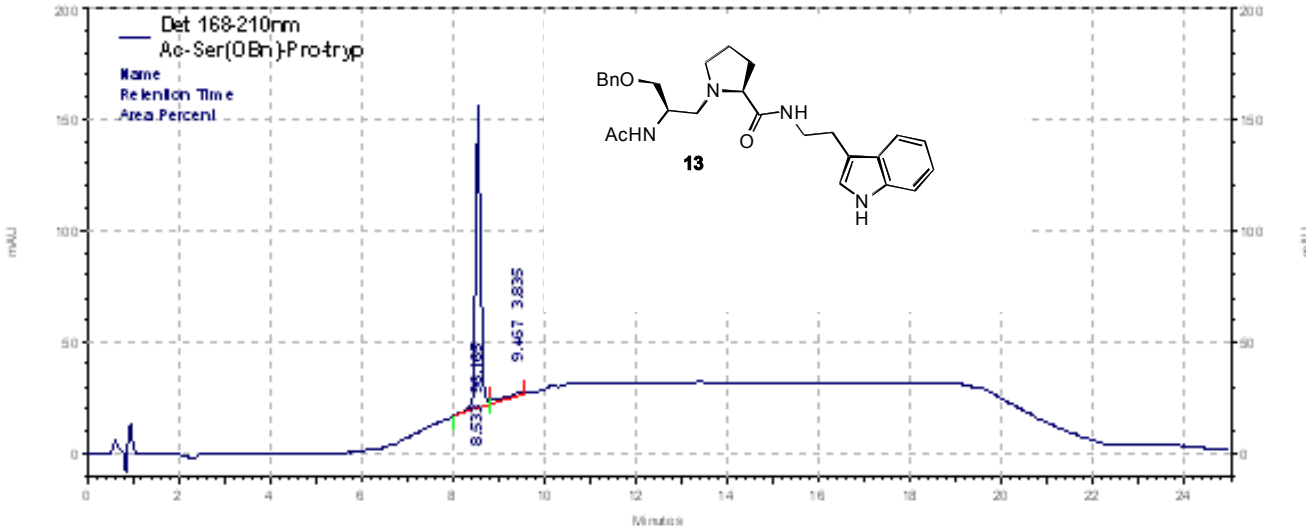
2
AcHN
NH
O
N
H
HO
OH
P

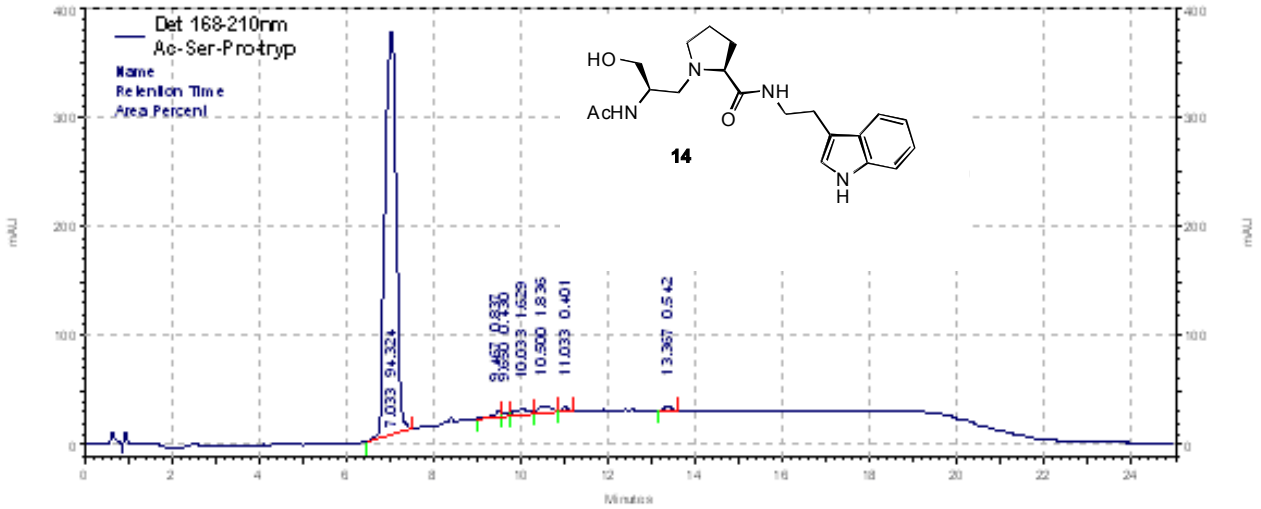
PHOSPHORUS OBSERVE
STANDARD PARAMETERS
PHOSPHATE REGION
Pulse Sequence: s2pul
Solvent: DMSO
Ambient temperature
File: xgy-III-53-P-H3PO4-DMSO
INOVA-400 "inova400a1t"
Relax. delay 1.000 sec
Pulse 70.0 degrees
Acq. time 2.000 sec
Width 29996.3 Hz
1000 repetitions
OBSERVE P31, 161.9011158 MHz
DECOUPLE H1, 399.9480181 MHz
Power 41 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 50 min, 8 sec
Mar 20 2007
VA Tech Chemistry NMR Lab
0.093
0.785
ppm

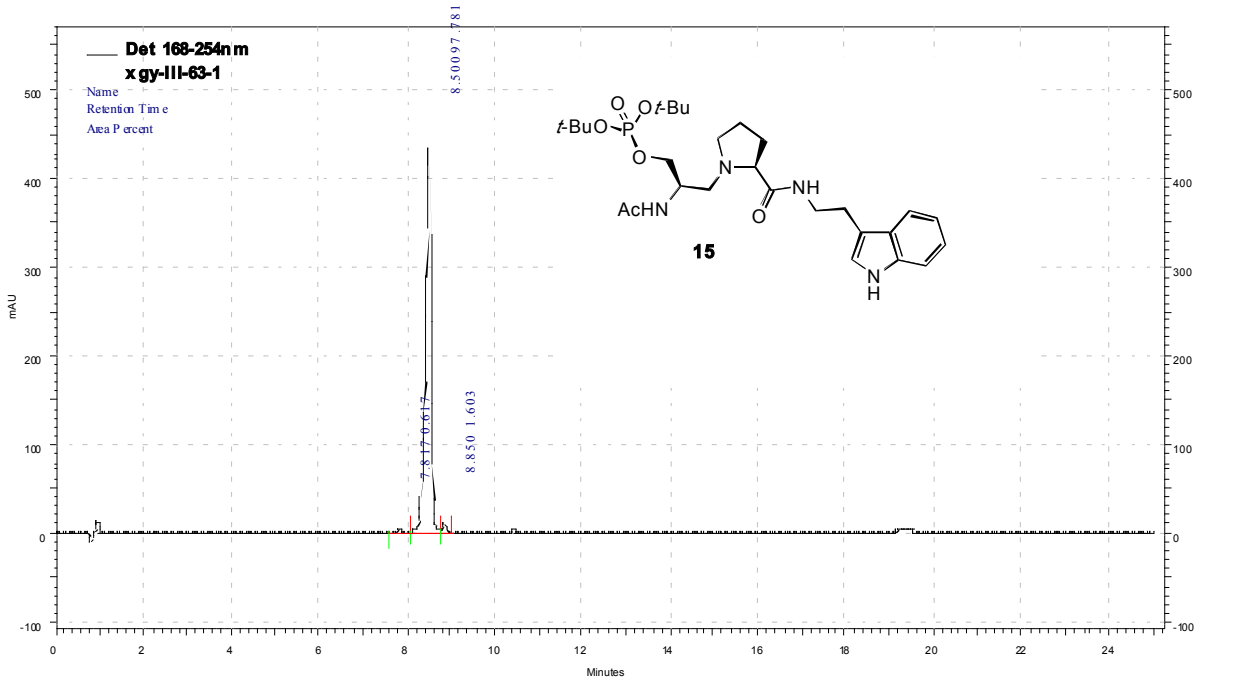

Det 168-210nm
Boc-Ser(OBn)-Pro(OBn)-3
Name
Retention Time
Area Percent
BnO
BocHN
N
O
O
OBn
10
mAU
Minutes

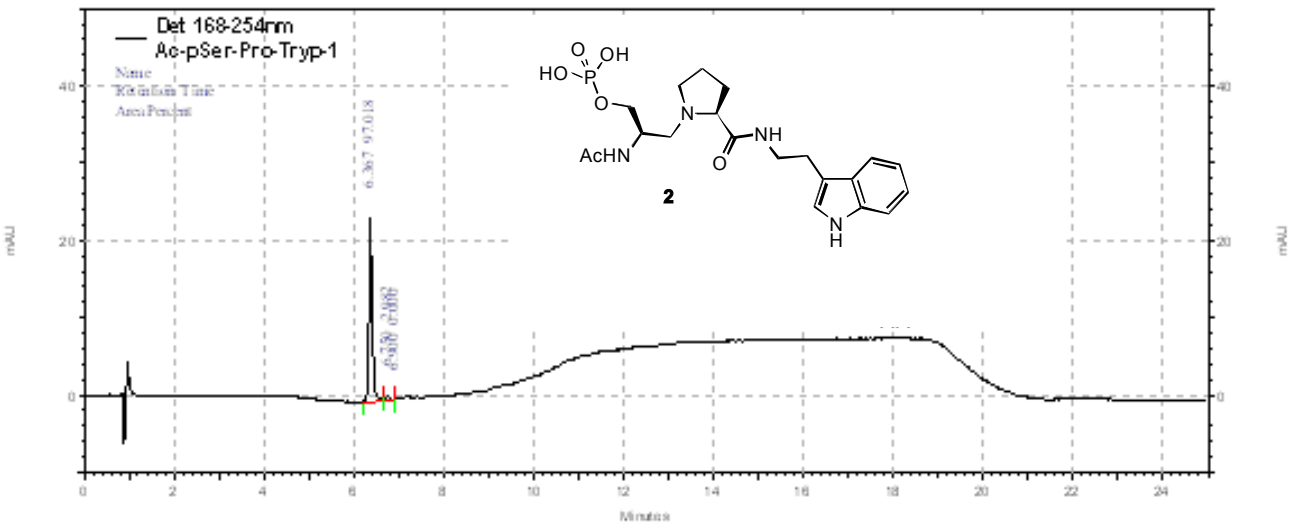

Det 168-254nm
Boc-Ser(OBn)-CH2-Pro(OBn)
Name
Retention Time
Area Percent
BnO
BocHN
N
O
OBn
11
mAU
Minutes

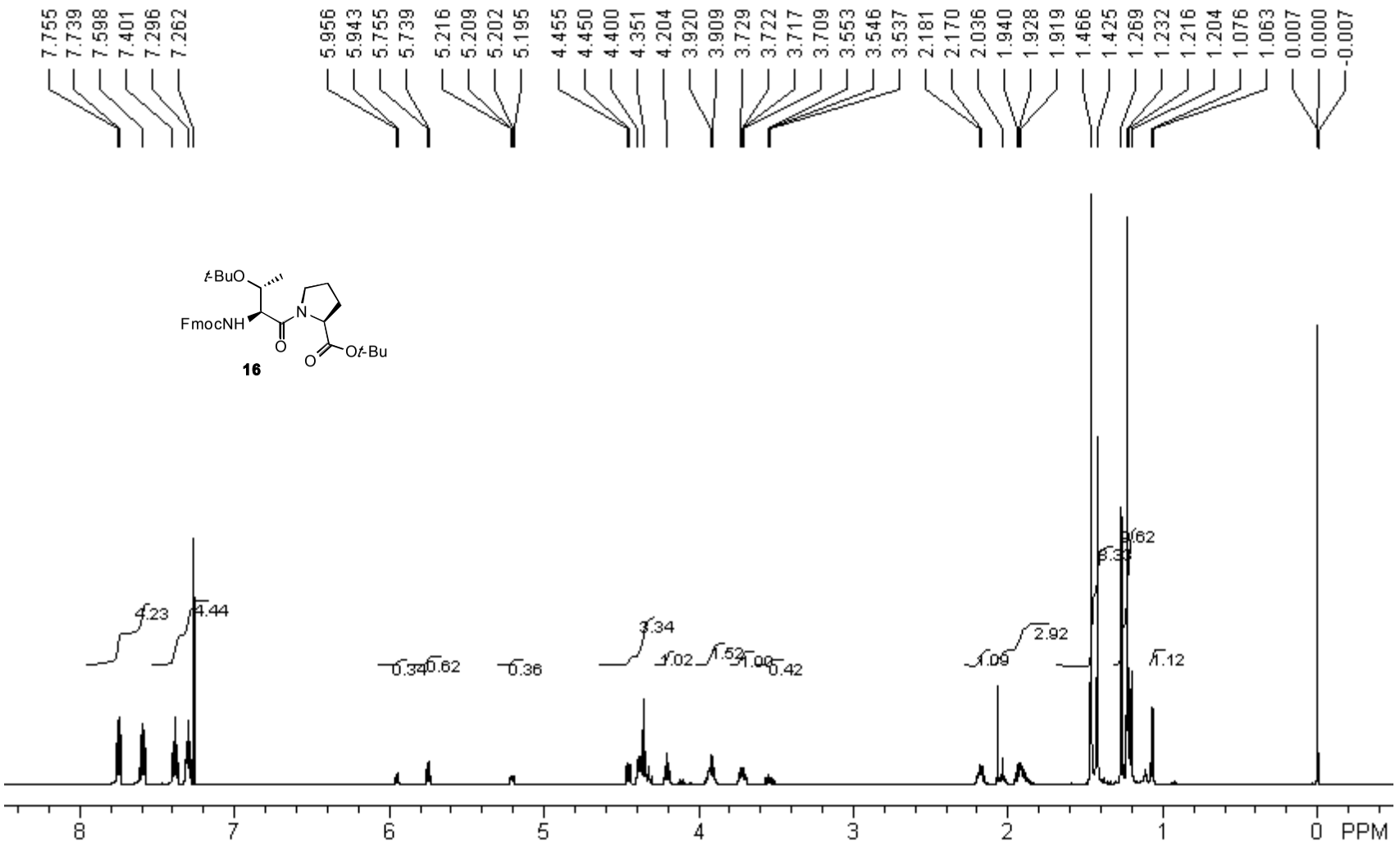

Det 168-210nm
Ac-Ser(OBn)-Pro(OBn)-2
Name
Retention Time
Area Percent
9.417 99.930
9.867 0.070
BnO
AcHN
N
O
OBn
12
mAU
Minutes

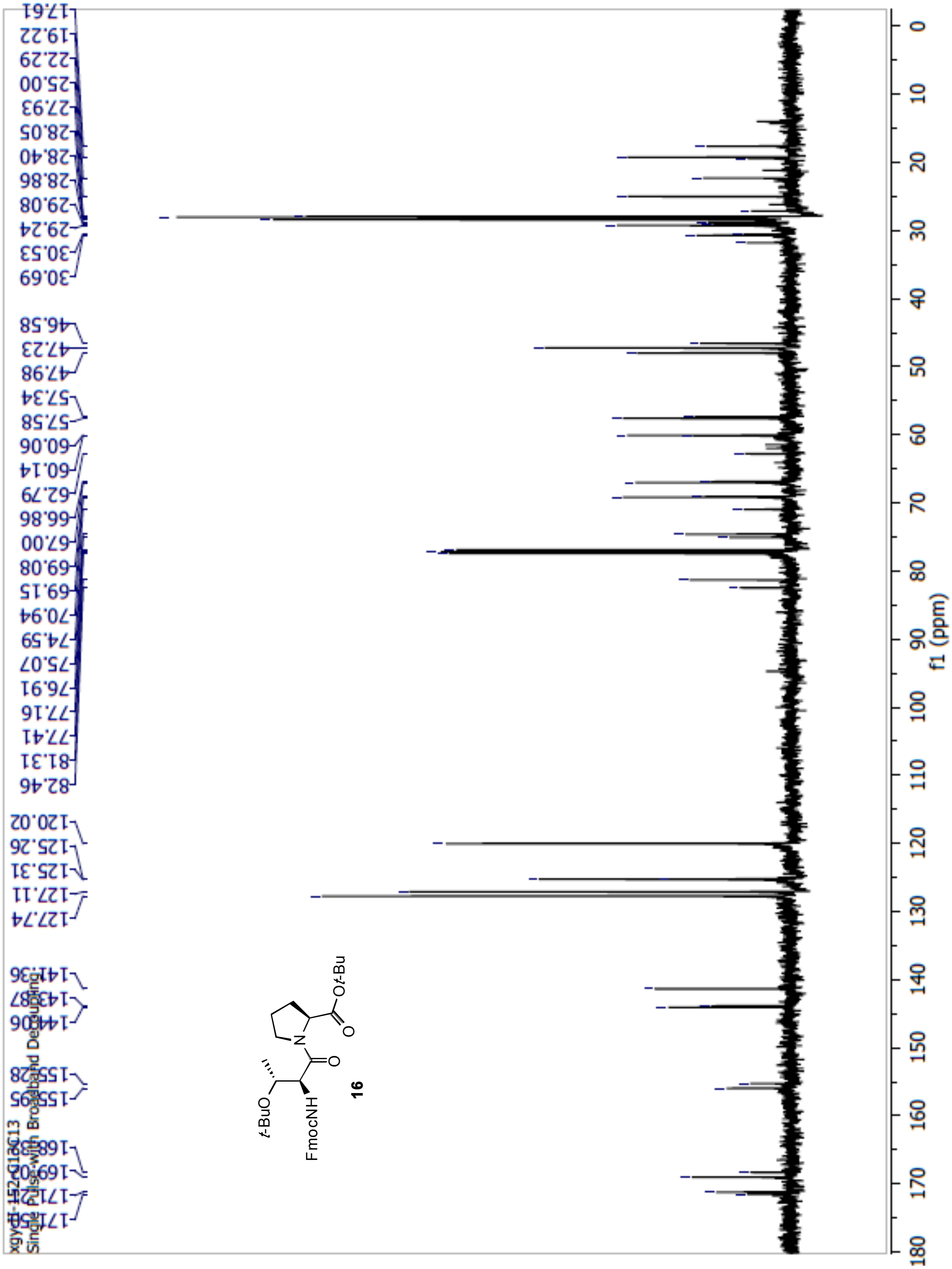

Det 168-210nm
Ac-Ser(OBn)-Pro-tryp
Name
Retention Time
Area Percent
8.533 36.165
9.467 3.835
BnO
AcHN
N
O
NH
N
H
13
mAU
Minutes


Det 168-210nm
Ac-Ser-Pro-tryp
Name
Retention Time
Area Percent
HO
AcHN
N
O
NH
N
H
14
mAU
Minutes


Det 168-254nm
xgy-III-63-1
Name
Retention Time
Area Percent
t-BuO
O
P
O
O
t-Bu
AcHN
N
O
NH
N
H
15
mAU
Minutes

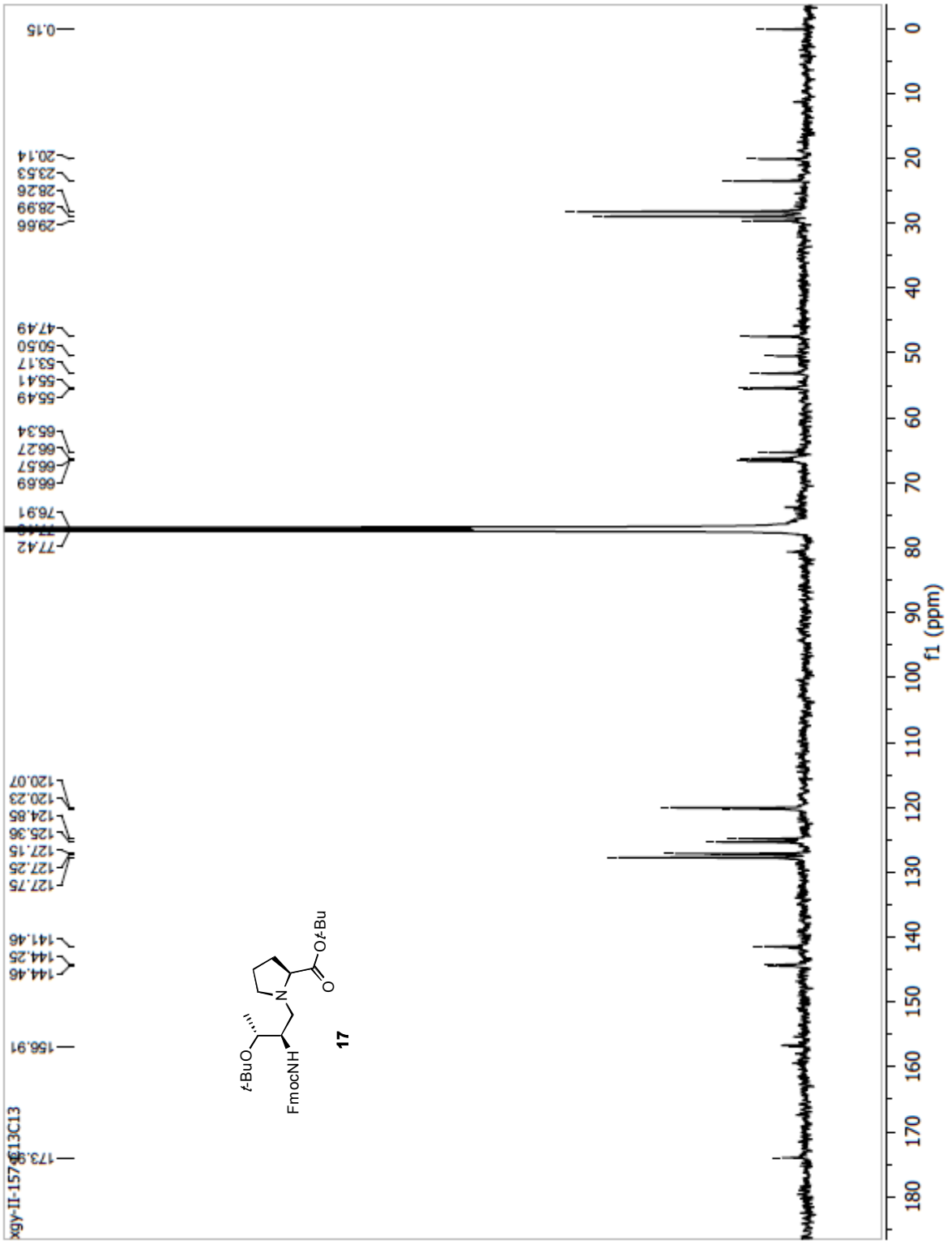

Det 168-254nm
Ac-pSer-Pro-Tryp-1
mAU
Minutes
2


7.755
7.739
7.598
7.401
7.296
7.262
5.956
5.943
5.755
5.739
5.216
5.209
5.202
5.195
4.455
4.450
4.400
4.351
4.204
3.920
3.909
3.729
3.722
3.717
3.709
3.553
3.546
3.537
2.181
2.170
2.036
1.940
1.928
1.919
1.466
1.425
1.269
1.232
1.216
1.204
1.076
1.063
0.007
0.000
-0.007
t-BuO
FmocNH
O
N
O
Ot-Bu
16
4.23
4.44
0.34
0.62
0.36
3.34
1.02
1.52
1.08
0.42
1.09
2.92
3.62
3.32
1.12
8
7
6
5
4
3
2
1
0
PPM

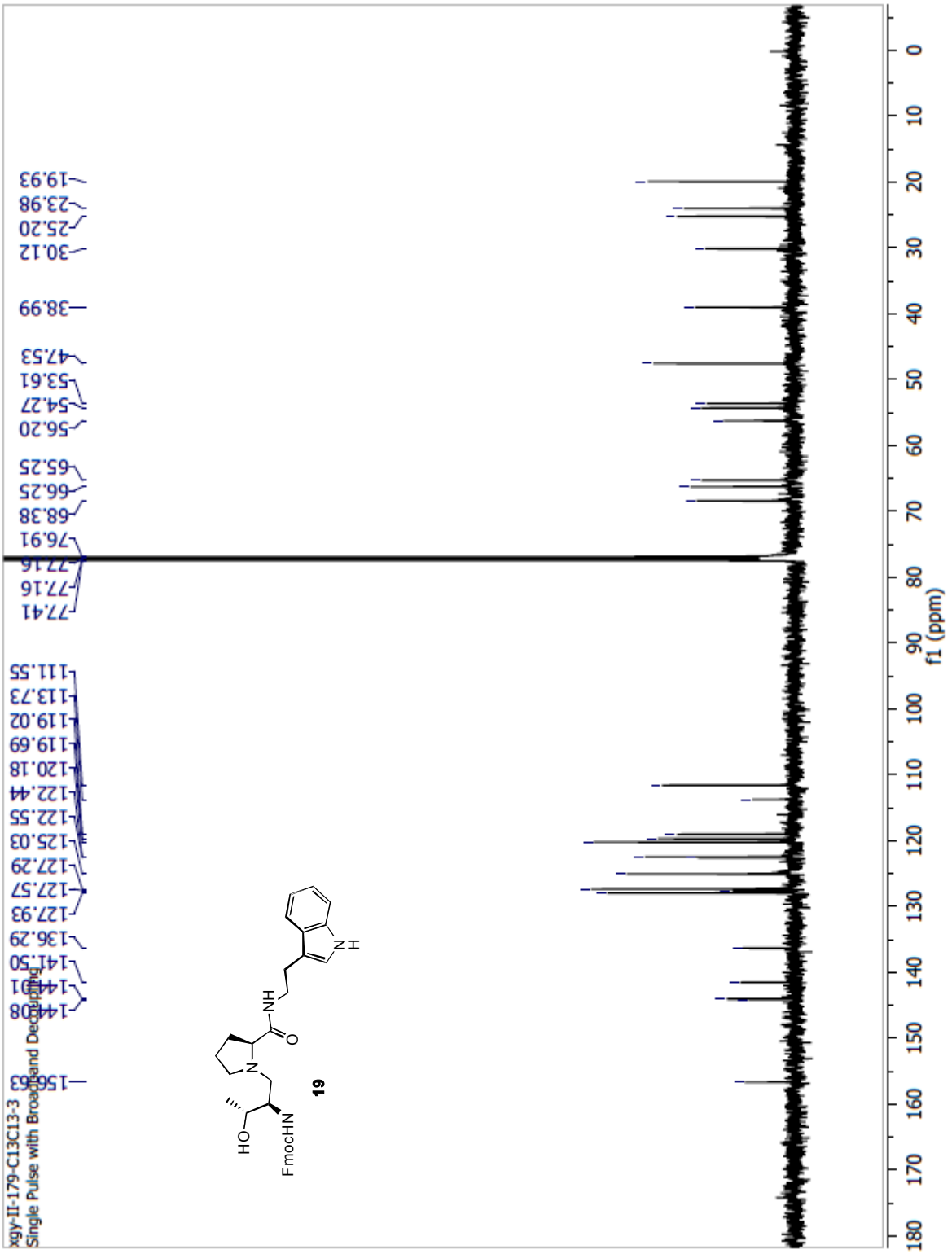

Single Pulse with Broadband Decoupling
t-BuO
FmocNH
N
O
Ot-Bu
16
17.61
19.22
22.29
25.00
27.93
28.05
28.40
28.86
29.08
29.24
30.53
30.69
46.58
47.23
47.98
57.34
57.58
60.06
60.14
62.79
66.86
67.00
69.08
69.15
70.94
74.59
75.07
76.91
77.16
77.41
81.31
82.46
120.02
125.26
125.31
127.11
127.74
f1 (ppm)

0 PPM
1
2
3
4
5
6
7
8
17.67
12.69
6.07
1.25
2.53
0.96
2.68
7.04
1.16
1.00
8.23
8.88
-0.007
0.000
0.007
0.077
1.096
1.123
1.135
1.205
1.439
1.772
1.853
2.035
2.547
2.557
2.663
2.678
2.845
3.061
3.069
3.254
3.630
3.989
4.029
4.110
4.249
4.354
5.276
5.293
7.250
7.289
7.311
7.325
7.374
7.389
7.404
7.611
7.626
7.747
7.771
t-BuO
FmocNHN
Ot-Bu
O

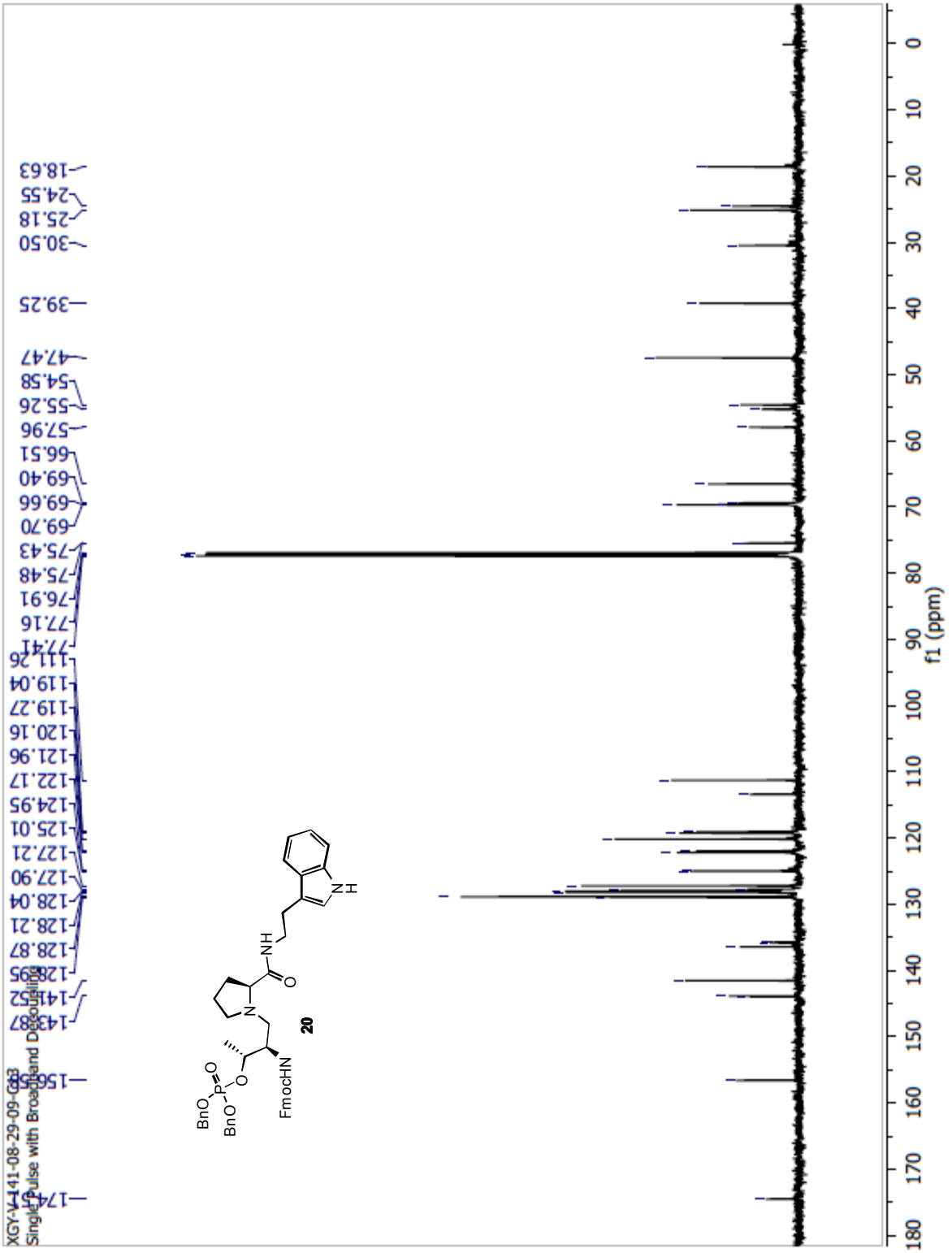
17


xgy-II-157-c13C13
0.15
20.14
23.53
28.26
28.99
29.66
47.49
50.50
53.17
55.41
55.49
65.34
66.27
66.57
66.69
76.91
77.16
77.42
120.07
120.23
124.85
125.36
127.15
127.25
127.75
141.46
144.25
144.46
156.91
173.98
FmocNH
t-BuO
O
Ot-Bu
17
f1 (ppm)

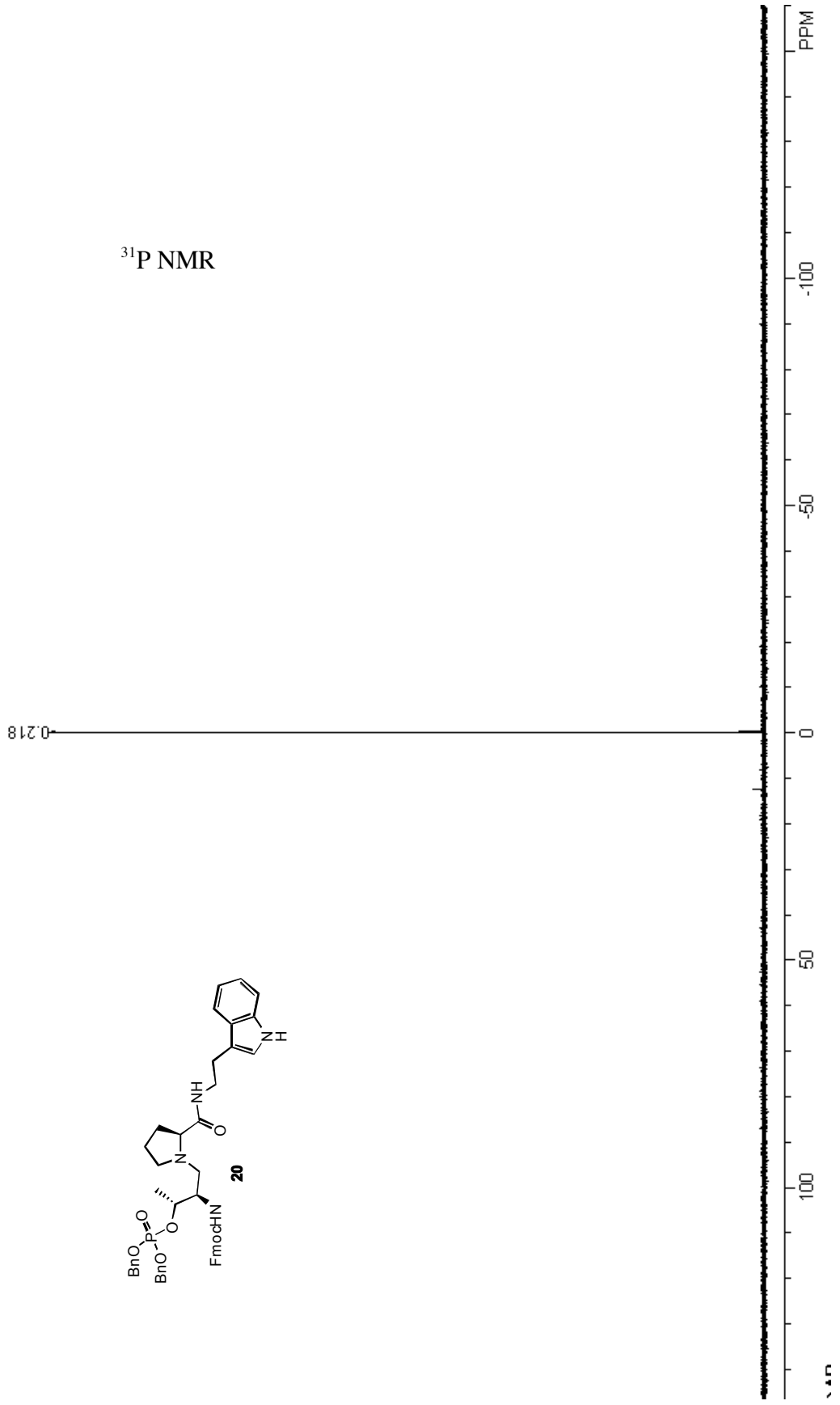
-0.002
0.001
0.826
0.839
1.666
1.684
1.748
1.752
1.785
1.793
2.122
2.178
2.197
2.314
2.335
2.865
2.919
2.952
3.053
3.067
3.352
3.366
3.553
3.566
3.650
3.663
4.205
4.217
4.487
4.489
4.499
4.501
4.542
4.558
6.944
7.086
7.152
7.259
7.262
7.264
7.333
7.396
7.411
7.586
7.769
7.784
7.915
6.49
3.21
1.17
3.14
2.07
0.86
3.00
1.30
4.18
4.35
4.33
6.59
2.88
0 1 2 3 4 5 6 7 8 PPM
NH
O
N
HO
FmocHN
19

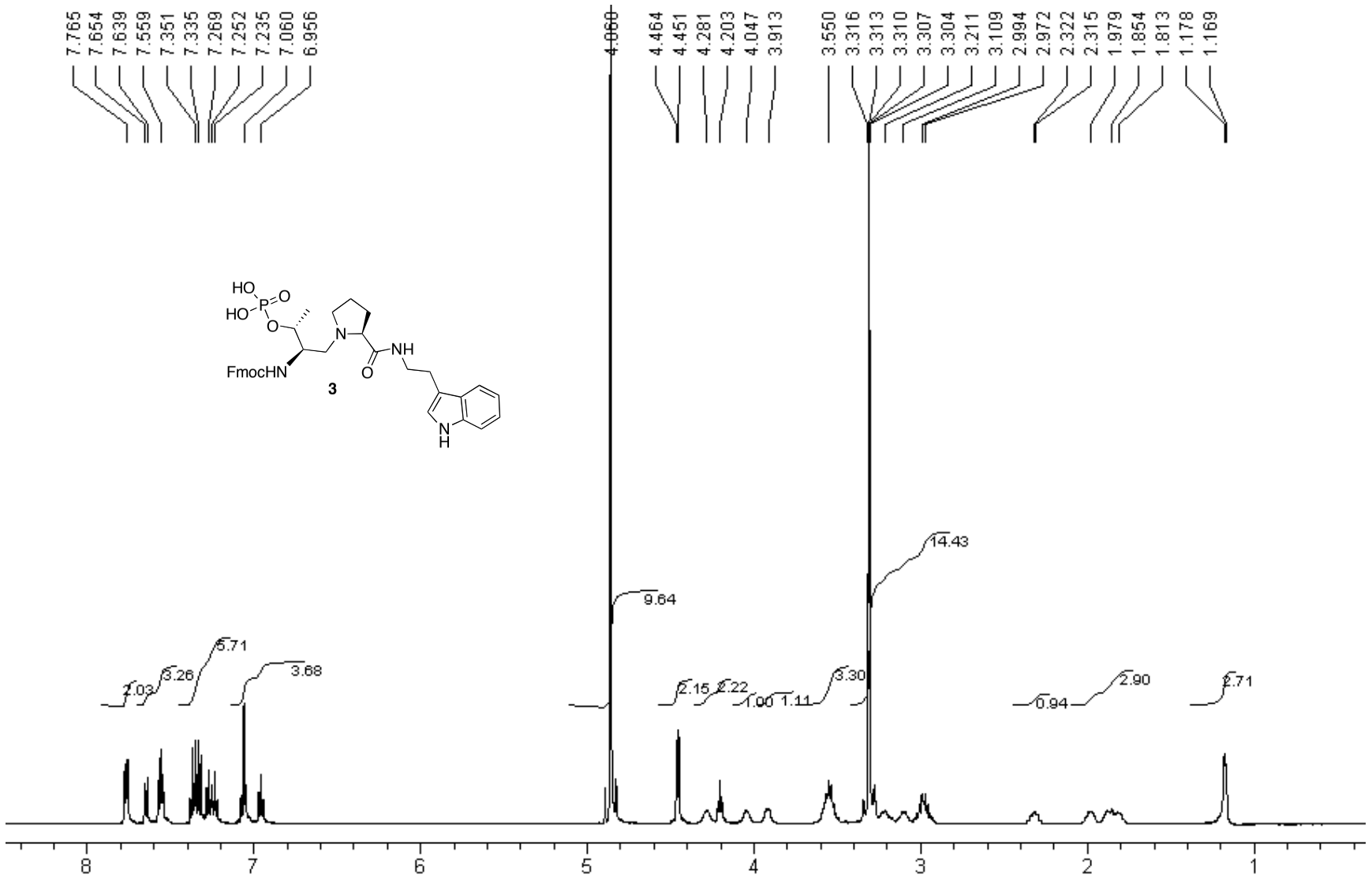

xgy-II-179-C13C13-3
Single Pulse with Broadband Decoupling
19
FmocHN
HO
NH
O
N
H
f1 (ppm)

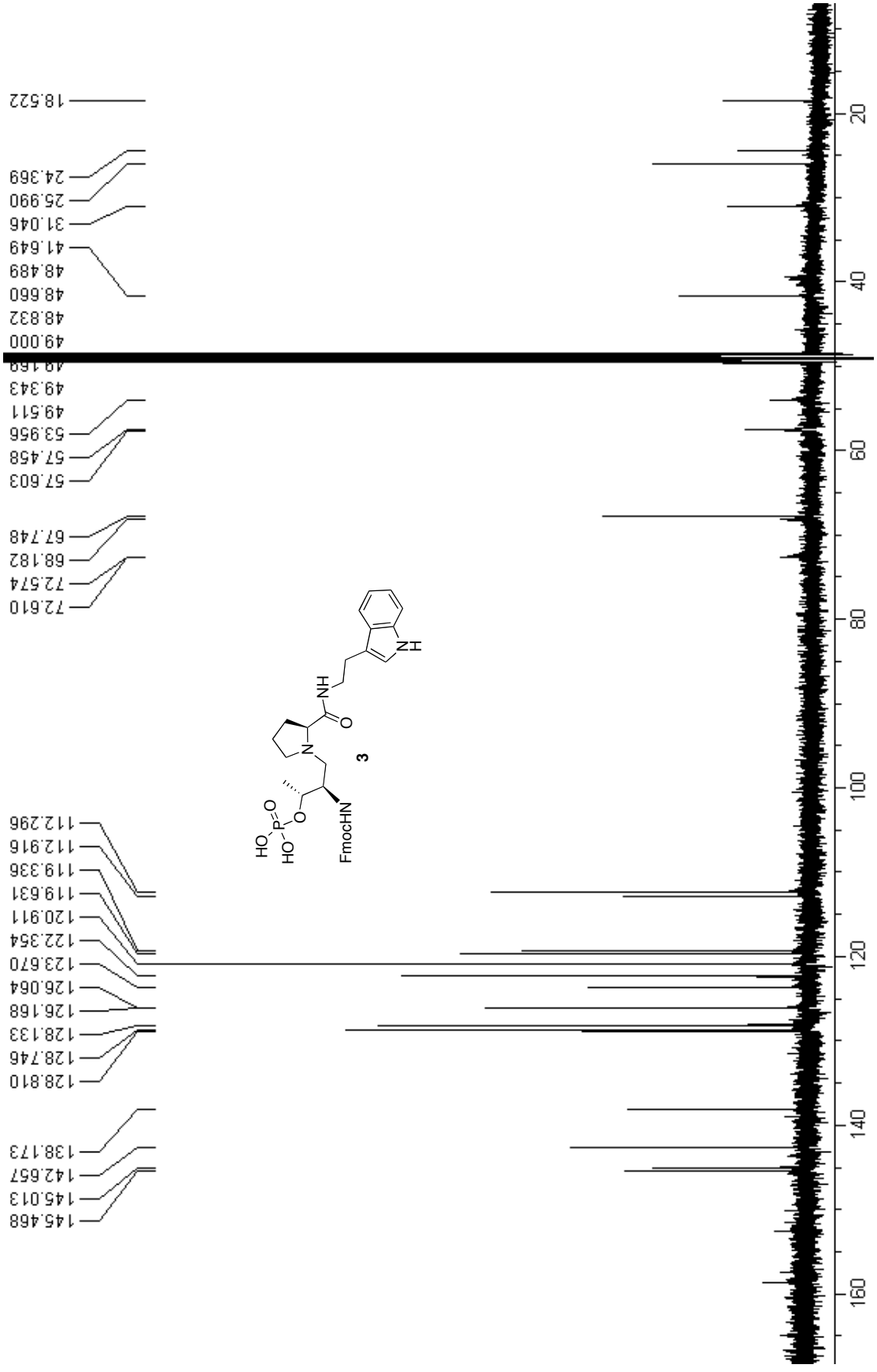
0.000
1.070
1.082
1.512
1.641
1.648
1.784
2.006
2.013
2.032
2.168
2.185
2.199
2.364
2.378
2.389
2.403
2.795
2.809
2.823
2.981
2.995
3.007
3.477
3.559
3.662
4.185
4.346
4.458
4.471
4.491
4.510
4.920
5.026
6.979
7.048
7.064
7.108
7.123
7.137
7.255
7.263
7.265
7.347
7.353
7.359
7.386
7.401
7.415
7.550
7.586
7.642
7.658
7.717
7.762
8.366
BnO
BnO
P
O
O
FmocHN
NH
O
N
N
H
20
26.88
1.09
4.52
5.41
3.52
4.56
1.08
1.09
1.57
1.64
2.37
3.26
PPM

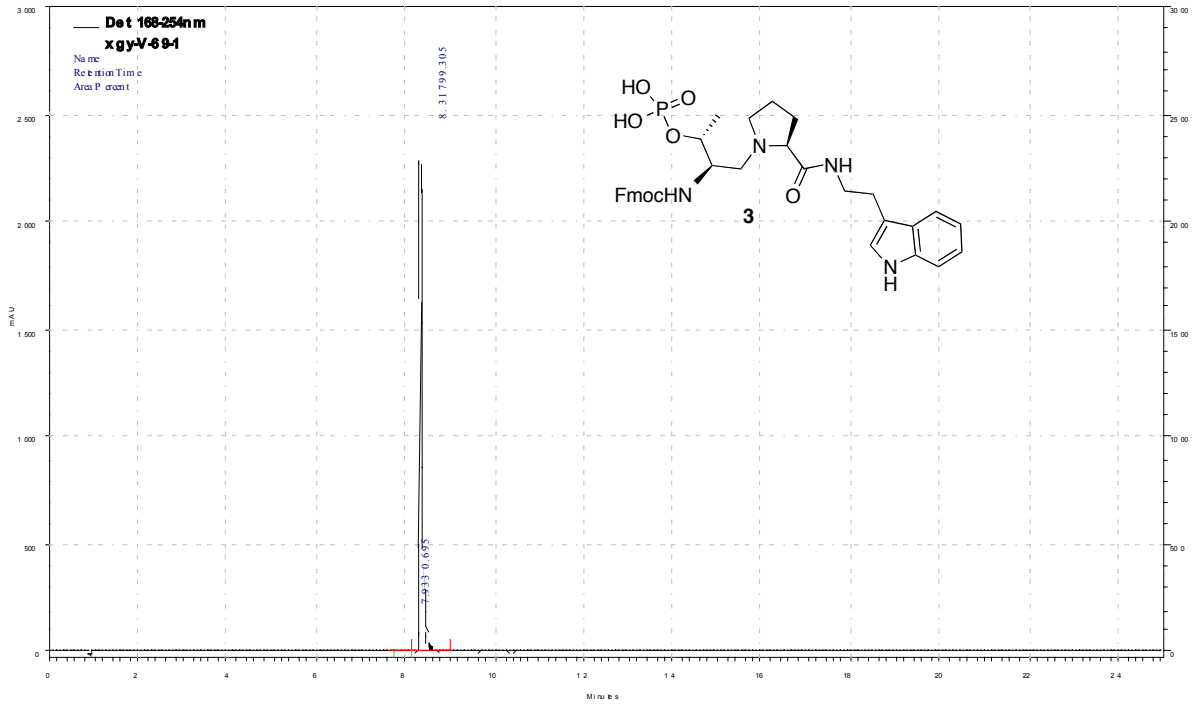

XGY-V-141-08-29-09-C13
Single Pulse with Broadband Decoupling
18.63
24.55
25.18
30.50
39.25
47.47
54.58
55.26
57.96
66.51
69.40
69.66
69.70
75.43
75.48
76.91
77.16
77.41
111.26
119.04
119.27
120.16
121.96
122.17
124.95
125.01
127.21
127.90
128.04
128.21
128.87
128.95
141.52
143.87
156.58
174.15
BnO
BnO
FmocHN
NH
NH
20
f1 (ppm)

^{31}P NMR




7.765
7.654
7.639
7.559
7.351
7.335
7.269
7.252
7.235
7.060
6.956
4.060
4.464
4.451
4.281
4.203
4.047
3.913
3.550
3.316
3.313
3.310
3.307
3.304
3.211
3.109
2.994
2.972
2.322
2.315
1.979
1.854
1.813
1.178
1.169
HO
HO
P
O
O
FmocHN
N
O
NH
N
H
3
14.43
9.64
6.71
3.68
3.26
2.03
2.15
2.22
1.00
1.11
3.30
0.94
2.90
2.71
8
7
6
5
4
3
2
1

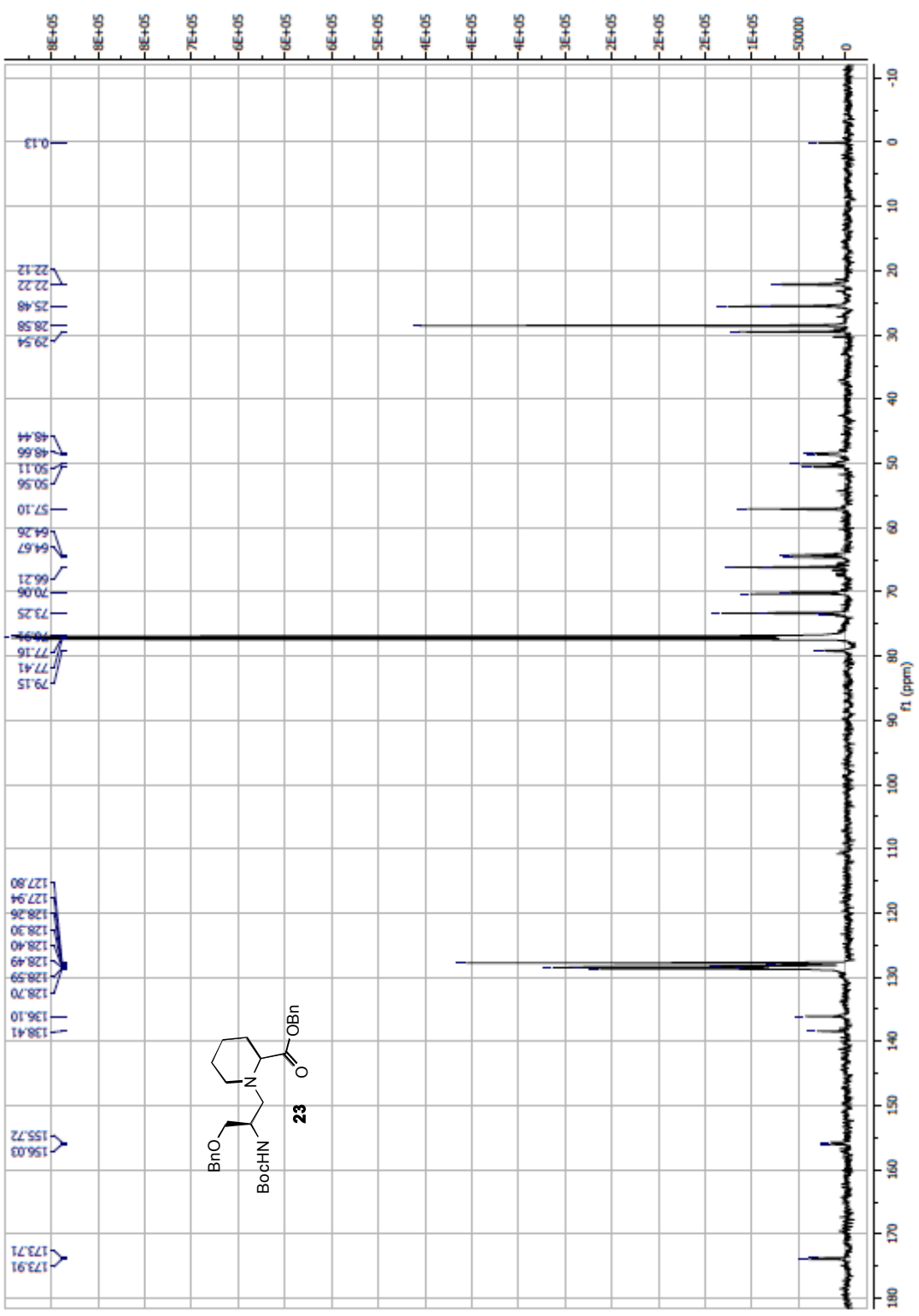

18.522
24.369
25.990
31.046
41.649
48.489
48.660
48.832
49.000
49.343
49.511
53.956
57.458
57.603
67.748
68.182
72.574
72.610
112.296
112.916
119.336
119.631
120.911
122.354
123.670
126.064
126.168
128.133
128.746
128.810
138.173
142.657
145.013
145.468
HO
HO
P
O
O
FmocHN
N
NH
O
NH
3
20
40
60
80
100
120
140
160


Det 168-254nm
xgy-V-69-1
Name
Retention Time
Area Percent
8.317 799.305
7.933 10.695
mAU
Minutes
HO
HO
P
O
O
N
NH
O
FmocHN
3
N
H

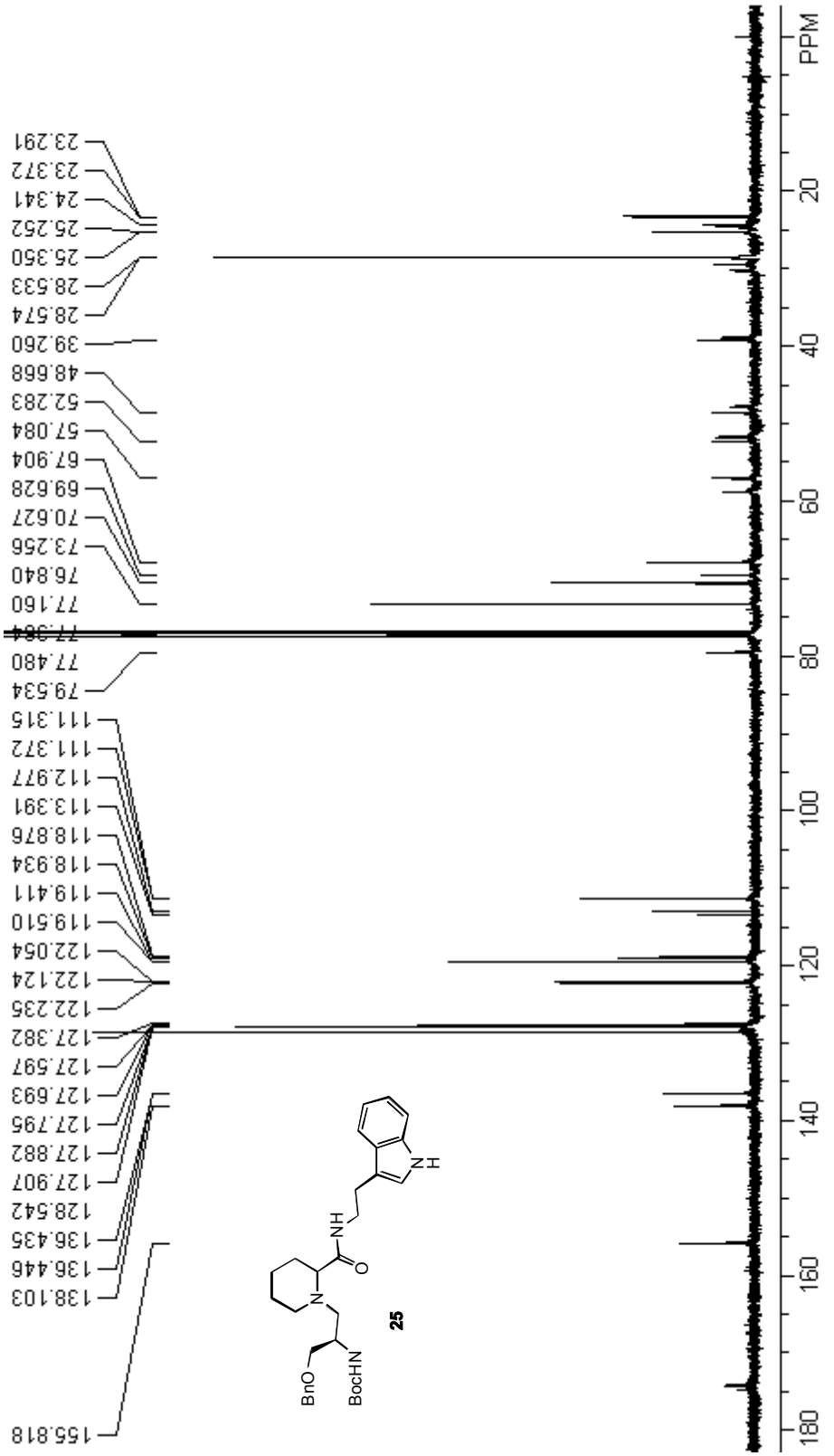
7.304
7.260
7.246
5.489
5.424
5.364
5.149
5.115
4.908
4.493
4.484
4.449
3.872
3.851
3.622
3.601
3.584
3.541
3.528
3.508
3.233
3.207
3.186
3.181
2.254
2.227
1.688
1.682
1.670
1.613
1.566
1.511
1.503
1.493
1.457
1.429
1.401
1.330
1.271
1.244
1.222
-0.000
17.62
13.61
1.00
0.88
2.56
0.88
2.96
1.56
2.77
2.08
BnO
BocHN
OBn
O
O
N
22

20.792
20.962
24.485
24.840
25.227
26.583
28.349
28.394
40.142
43.656
43.704
50.154
50.533
52.454
52.630
66.890
66.970
67.235
70.397
71.154
73.095
73.346
76.897
77.160
77.358
77.412
79.666
79.684
127.584
127.618
127.791
127.887
127.970
127.990
128.054
128.172
128.292
128.334
128.388
128.419
128.633
135.620
135.659
137.745
155.115
170.171
170.465
170.755
BnO
BocHN
OBn
22
0PPM

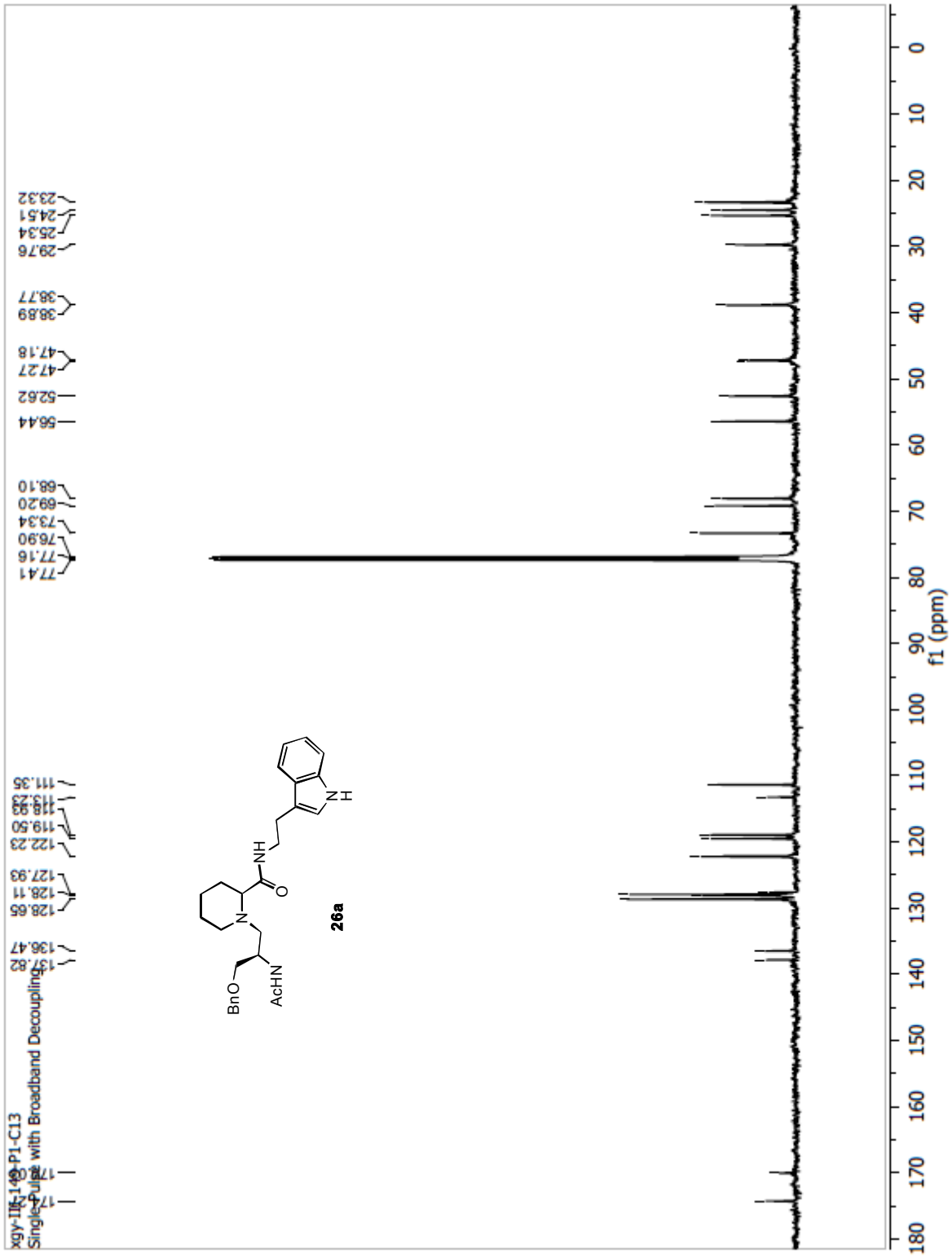
7.337
7.271
7.265
7.259
5.155
5.120
4.499
4.464
3.768
3.759
3.743
3.597
3.518
3.421
3.255
3.077
3.030
3.024
2.692
2.589
2.528
2.338
2.324
2.319
2.045
1.824
1.730
1.648
1.642
1.550
1.441
1.431
1.416
0.007
0.000
10.29
2.84
2.00
8.02
14.13
0 PPM
BnO
BocHN
OBn
O
N
23

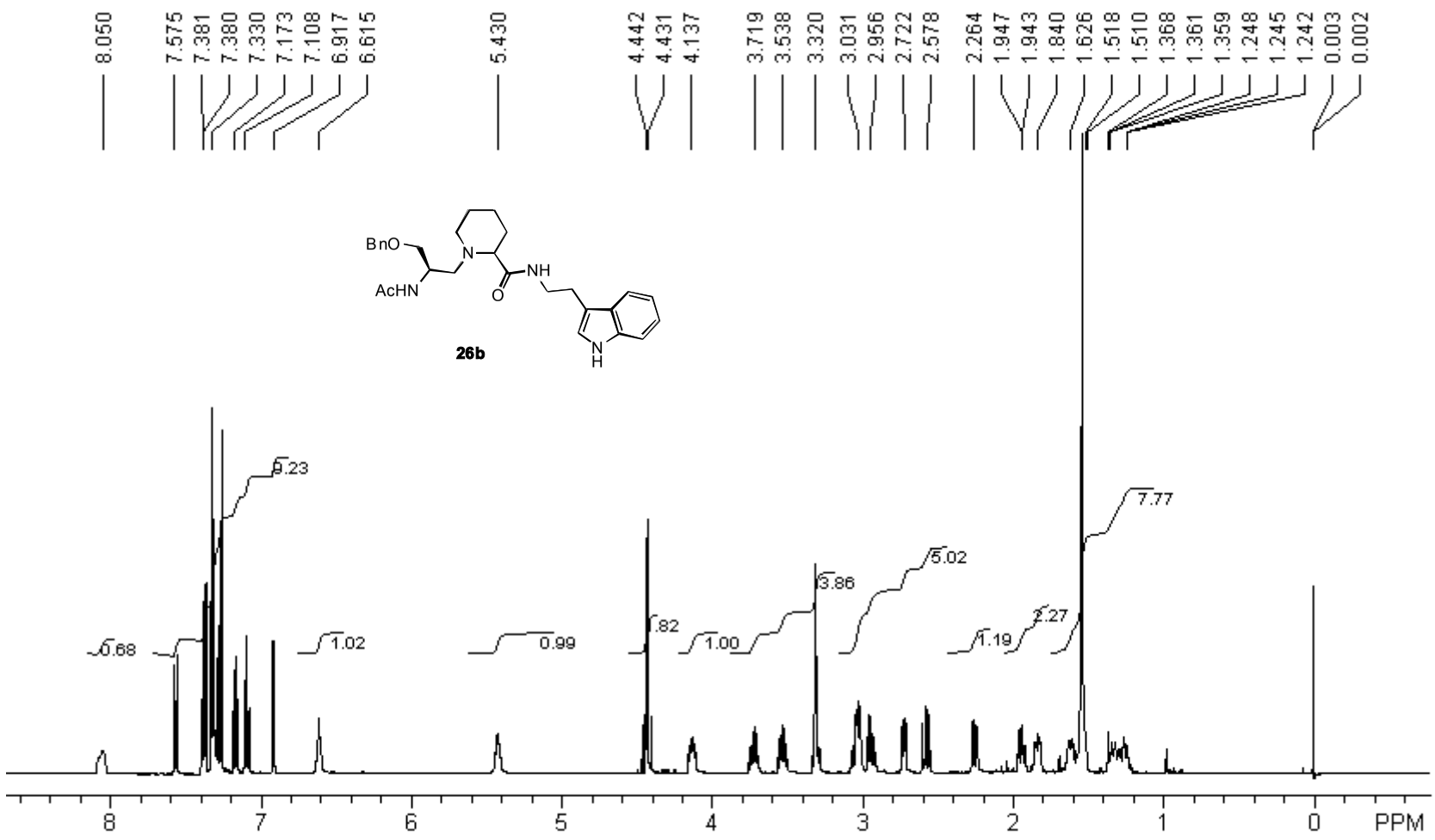

0.13
22.12
22.22
25.48
28.58
29.54
48.44
48.66
50.11
50.56
57.10
64.57
64.26
66.21
70.06
73.25
76.94
77.16
77.41
79.15
127.80
127.94
128.26
128.30
128.40
128.49
128.59
128.70
136.10
138.41
155.72
156.03
173.71
173.91
BnO
BocHN
23
OBn
O
N
f1 (ppm)

0.000
0.002
1.266
1.335
1.442
1.565
1.626
1.635
1.905
2.182
2.747
2.907
3.066
3.216
3.222
3.258
3.263
3.455
3.804
4.288
4.343
6.859
6.976
7.088
7.090
7.323
7.594
8.250
15.63
4.33
6.49
3.10
3.00
13.01
1.51
PPM
0
1
2
3
4
5
6
7
8
9
BnO
BocHN
NH
O
N
H
25


23.291
23.372
24.341
25.252
25.350
28.533
28.574
39.260
48.668
52.283
57.084
67.904
69.628
70.627
73.256
76.840
77.160
77.384
77.480
79.534
111.315
111.372
112.977
113.391
118.876
118.934
119.411
119.510
122.054
122.124
122.235
127.382
127.597
127.693
127.795
127.882
127.907
128.542
136.435
136.446
138.103
155.818
PPM
20
40
60
80
100
120
140
160
180
BnO
BocHN
NH
O
N
H
25

0.000
1.367
1.488
1.548
1.555
1.697
1.727
1.844
2.076
2.240
2.380
2.691
2.698
2.710
2.717
2.966
3.159
3.220
3.227
3.545
3.619
4.316
4.326
5.579
5.597
7.015
7.019
7.097
7.179
7.326
7.589
8.168
8.56
2.91
3.31
1.09
2.28
1.11
2.19
1.10
2.00
1.01
PPM
1
2
3
4
5
6
7
8
9
NH
O
N
N
H
BnO
AcHN
26a


xgy-III-140-P1-C13
Single Pulse with Broadband Decoupling
26a
BnO
AcHN
NH
HN
O
f1 (ppm)


8.050
7.575
7.381
7.380
7.330
7.173
7.108
6.917
6.615
5.430
4.442
4.431
4.137
3.719
3.538
3.320
3.031
2.956
2.722
2.578
2.264
1.947
1.943
1.840
1.626
1.518
1.510
1.368
1.361
1.359
1.248
1.245
1.242
0.003
0.002
BnO
N
NH
AcHN
O
N
H
26b
9.23
7.77
5.02
3.86
2.27
1.82
1.68
1.02
0.99
1.00
1.19
8
7
6
5
4
3
2
1
0
PPM

22.995
23.274
24.319
25.255
29.560
39.217
46.770
51.539
57.910
67.735
70.879
73.544
76.840
77.160
77.480
111.504
112.965
118.746
119.619
122.330
122.365
127.255
128.116
128.206
128.744
136.443
138.047
170.290
174.603
BnO
AcHN
NH
O
N
H
26b
PPM
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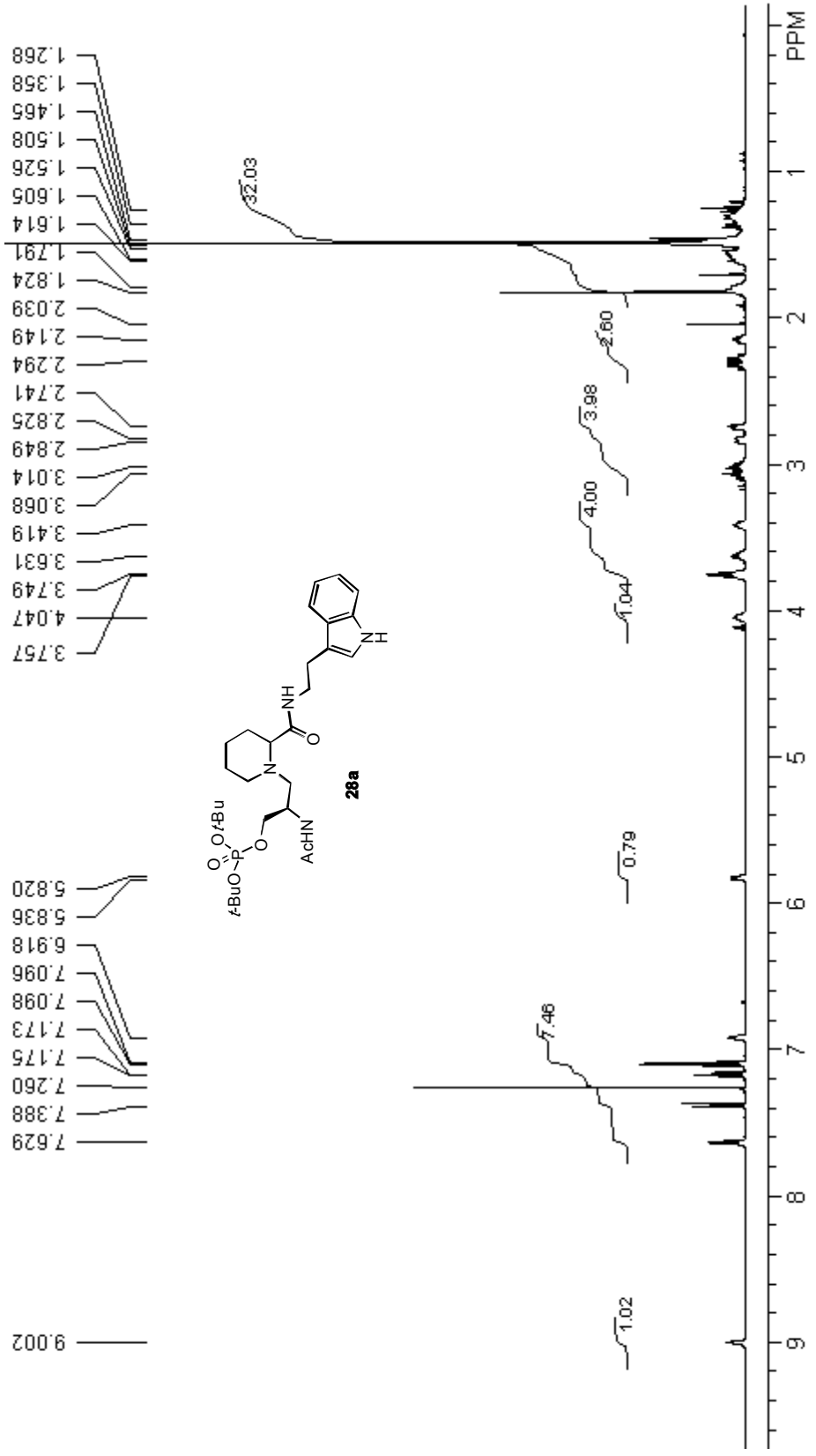
60
80
100
120
140
160
180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3.068
3.014
2.849
2.825
2.741
2.294
2.149
2.039
1.824
1.791
1.614
1.605
1.526
1.508
1.465
1.358
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32.03
2.60
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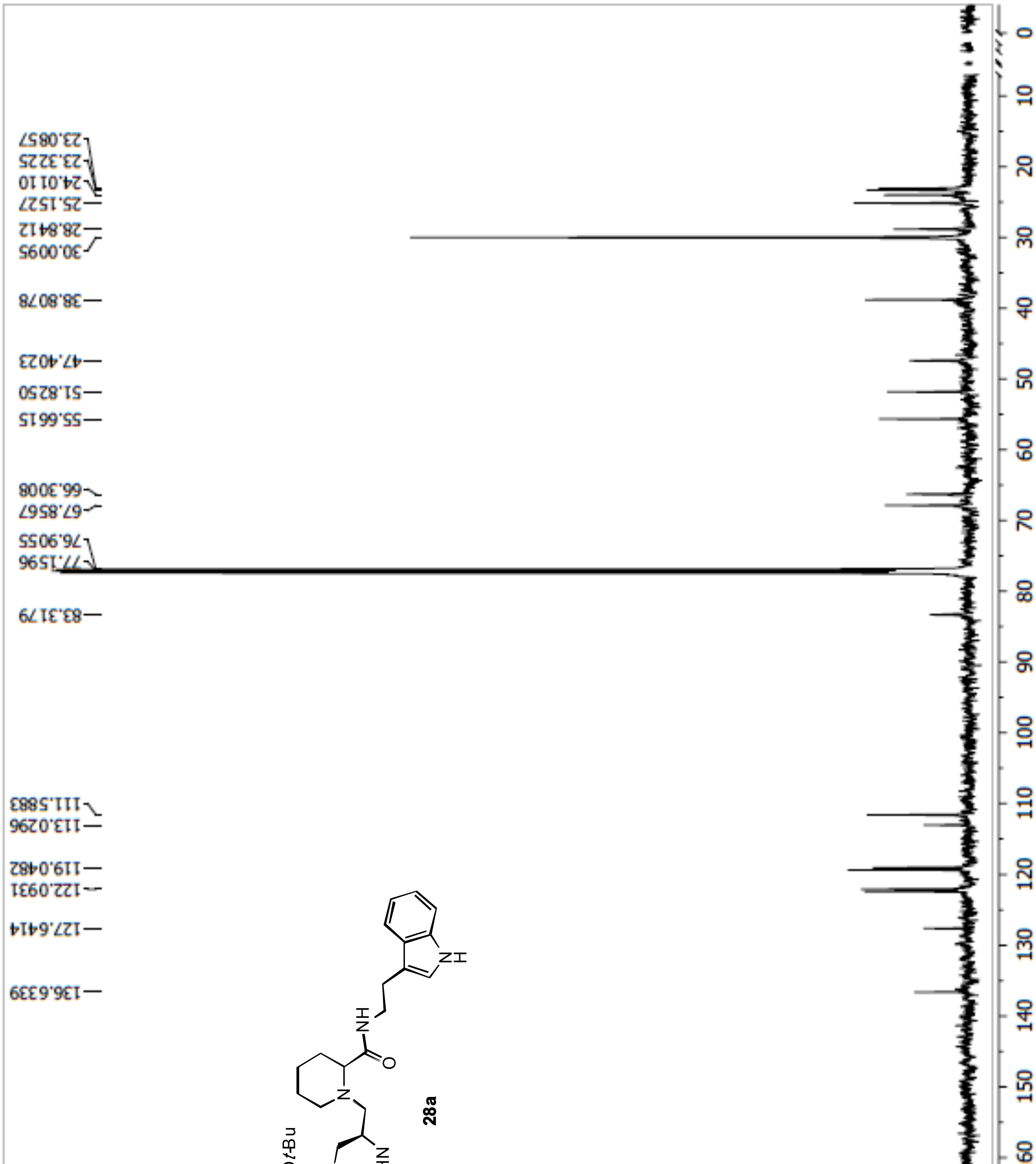
0.79
7.46
1.02
PPM
28a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66.3008
67.8567
76.9055
77.1596
83.3179
111.5883
113.0296
119.0482
122.0931
127.6414
136.6339
170.1671
173.7652
28a

^{31}P NMR

10.218
7.586
7.579
7.424
7.423
7.415
7.267
7.185
7.179
7.173
7.171
7.098
7.090
6.433
5.019
5.008
4.224
3.869
3.776
3.564
3.165
3.136
3.129
3.060
3.036
2.669
2.663
2.581
2.043
1.931
1.841
1.659
1.542
1.534
1.517
1.504
1.351
1.230
1.223
1.214
0.009
0.000
29.76
7.43
1.29
1.05
0.97
1.00
4.60
3.39
2.07
28b
PPM
0
2
4
6
8
10

22.326
23.445
24.835
24.980
29.945
29.986
30.035
30.063
30.847
39.203
46.109
46.179
52.020
58.117
67.454
67.509
68.273
76.899
77.160
77.415
83.428
83.634
112.127
112.462
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122.176
122.612
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174.855
PPM
20
40
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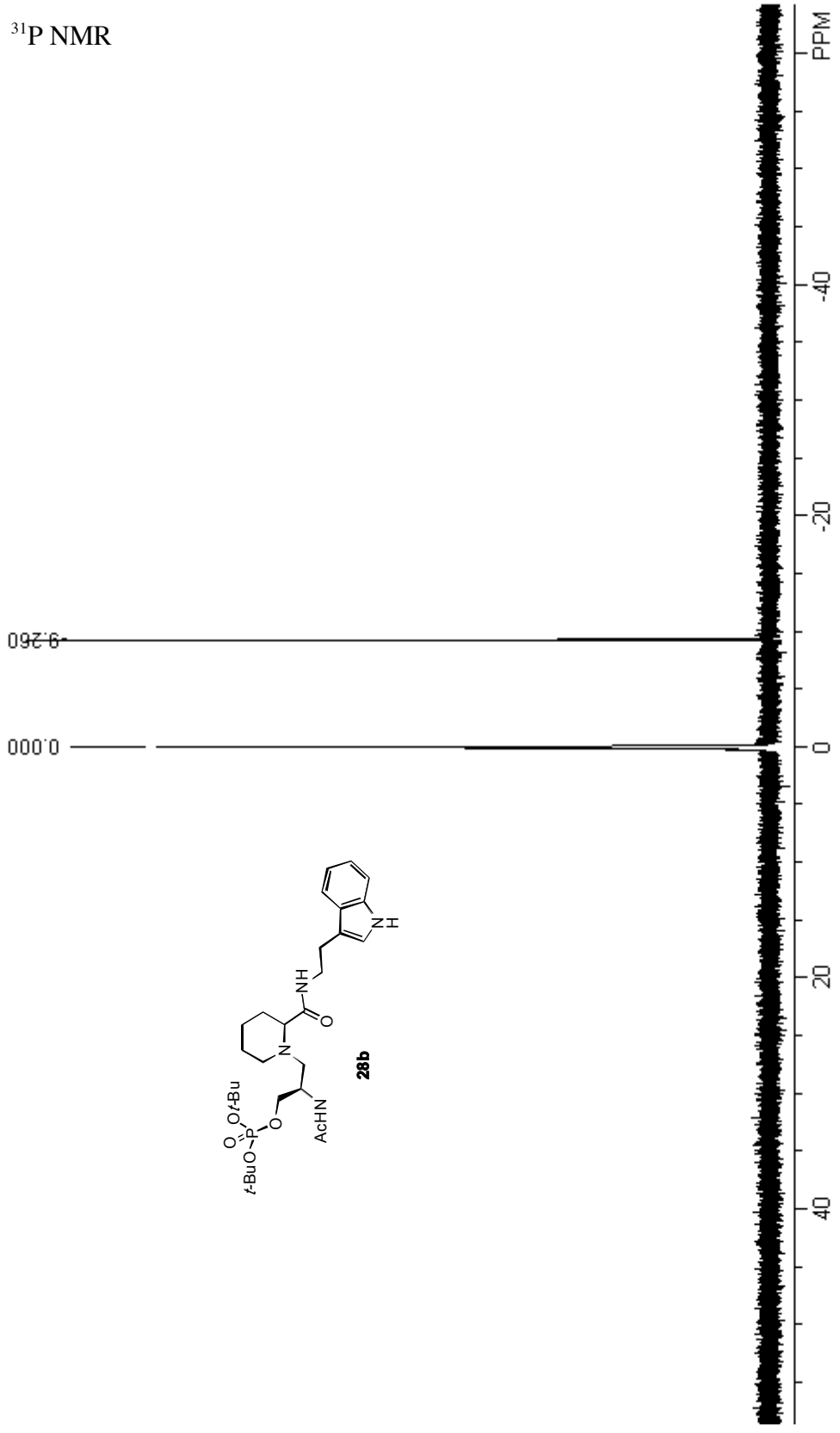
80
100
120
140
160
180
28b

^{31}P NMR



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7.359
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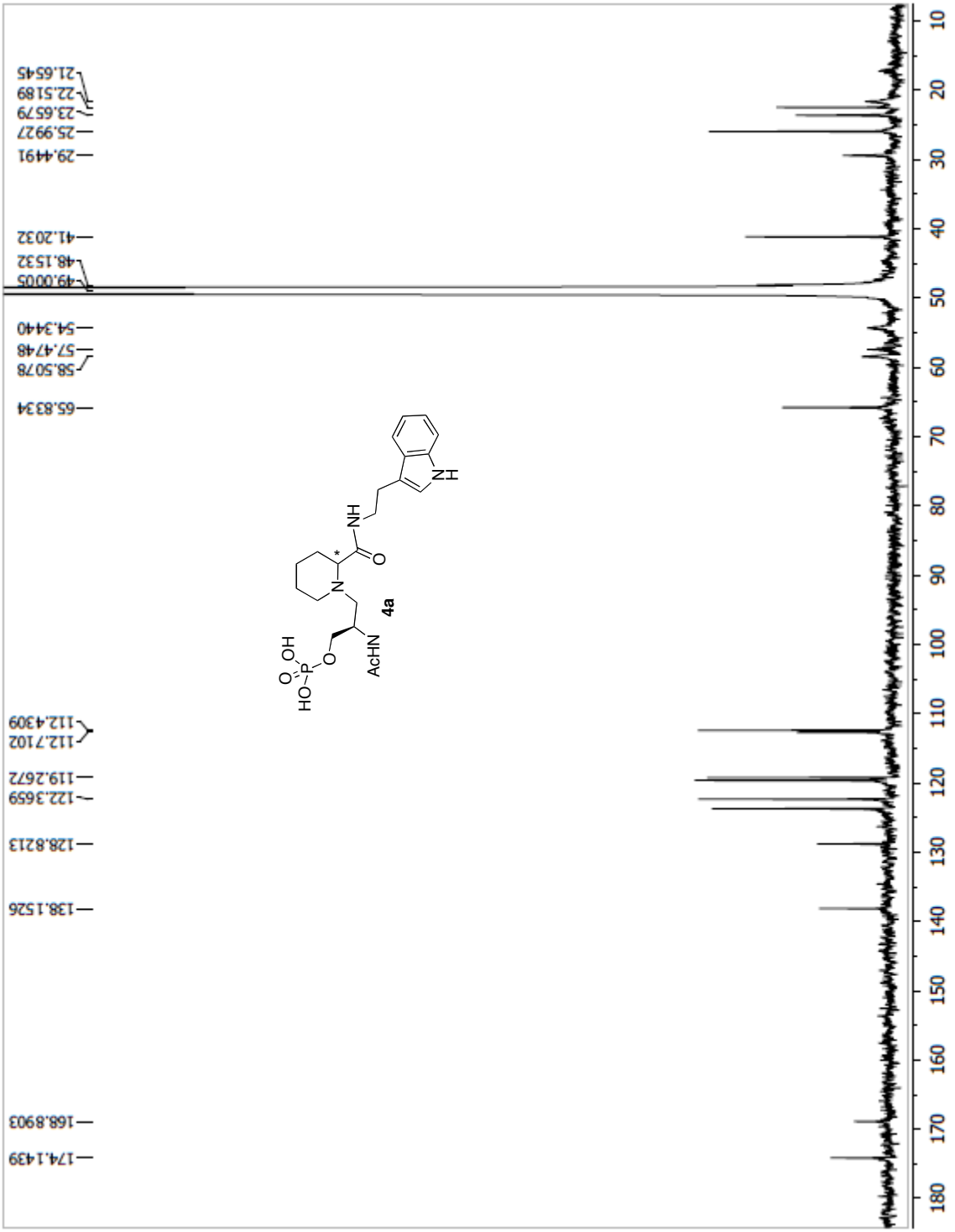
7.082
7.066
7.019
7.005
6.989
3.906
3.899
3.350
3.740
3.607
3.317
3.316
3.313
3.312
3.310
3.309
3.307
3.306
3.304
3.302
3.121
3.066
2.994
1.973
1.849
1.785
1.762
1.743
6.35
1.00
6.20
5.52
9.13
PPM
4a
AcHN
NH
O
N
H
HO
OH
P
O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128.8213
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4a
AcHN
NH
NH
O
OH
HO
P
O
10
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60
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80
90
100
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120
130
140
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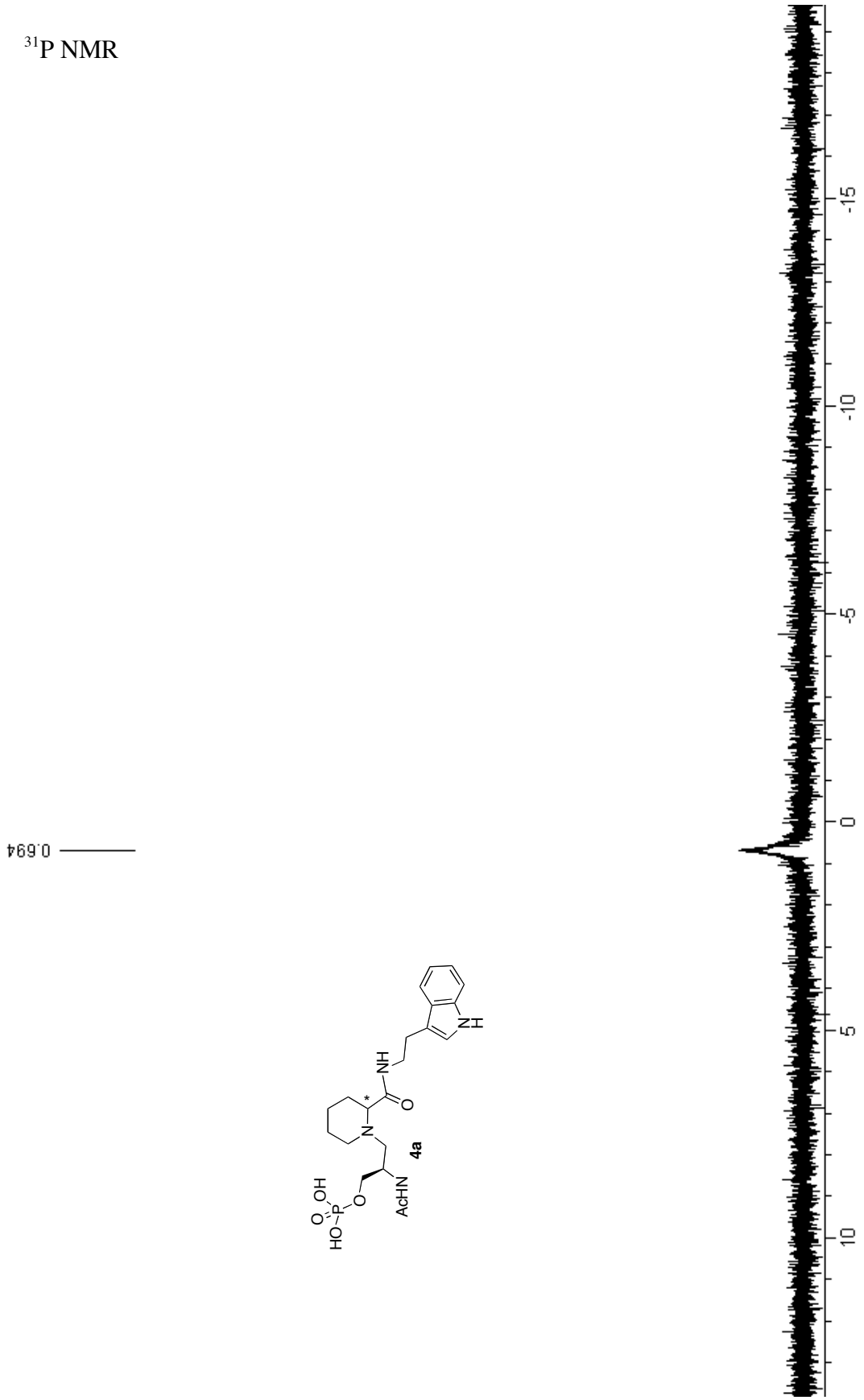
170
180

^{31}P NMR



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1.790
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1.882
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1.998
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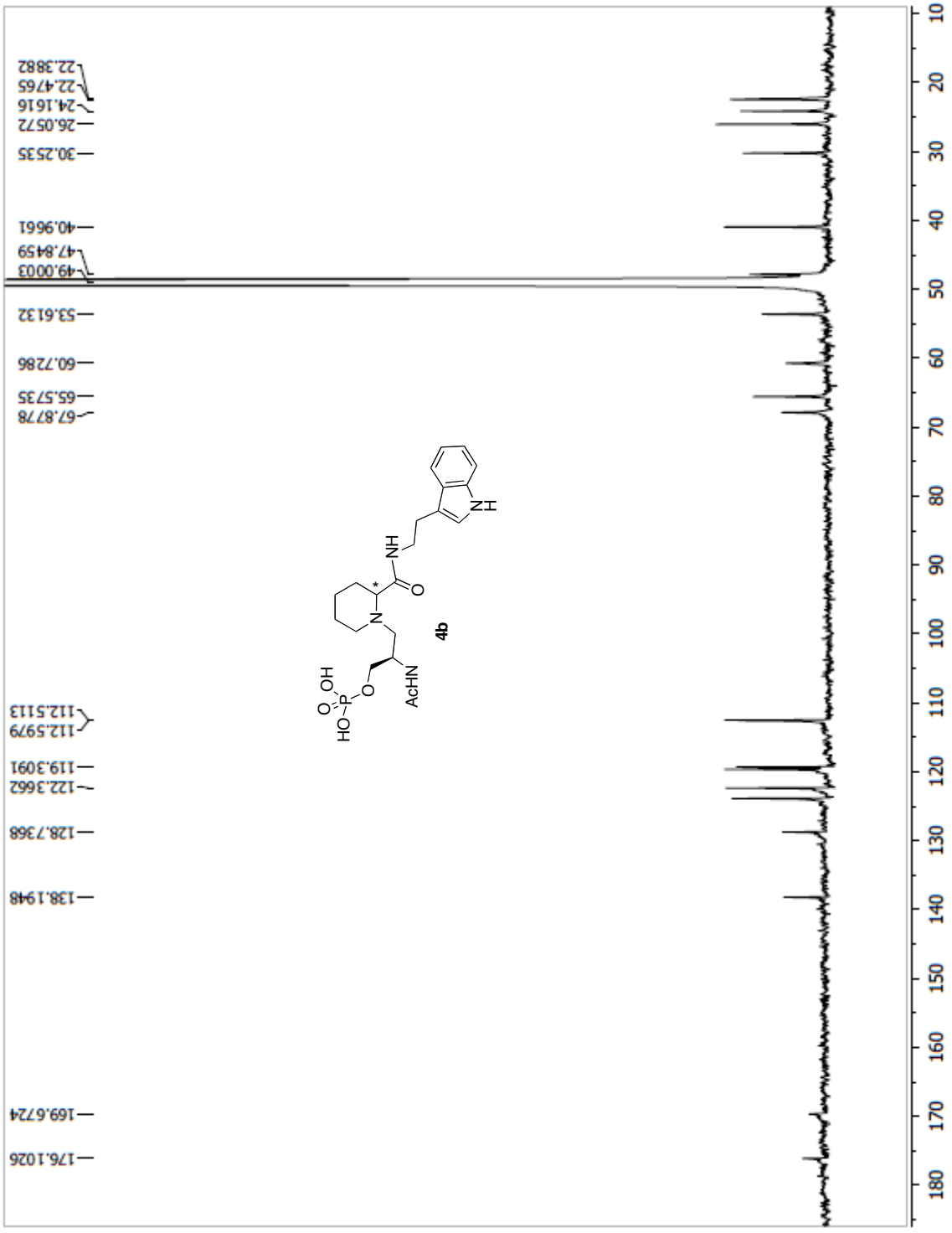
2.904
2.990
2.995
3.123
3.302
3.306
3.310
3.314
3.318
3.535
3.569
3.651
3.826
3.849
3.925
4.383
4.388
4.394
4.398
4.402
4.403
6.985
6.987
7.005
7.025
7.069
7.089
7.104
7.106
7.362
7.382
7.559
7.579
9.41
5.11
6.02
1.09
5.10
4b
AcHN
NH
HN
PPM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67.8778
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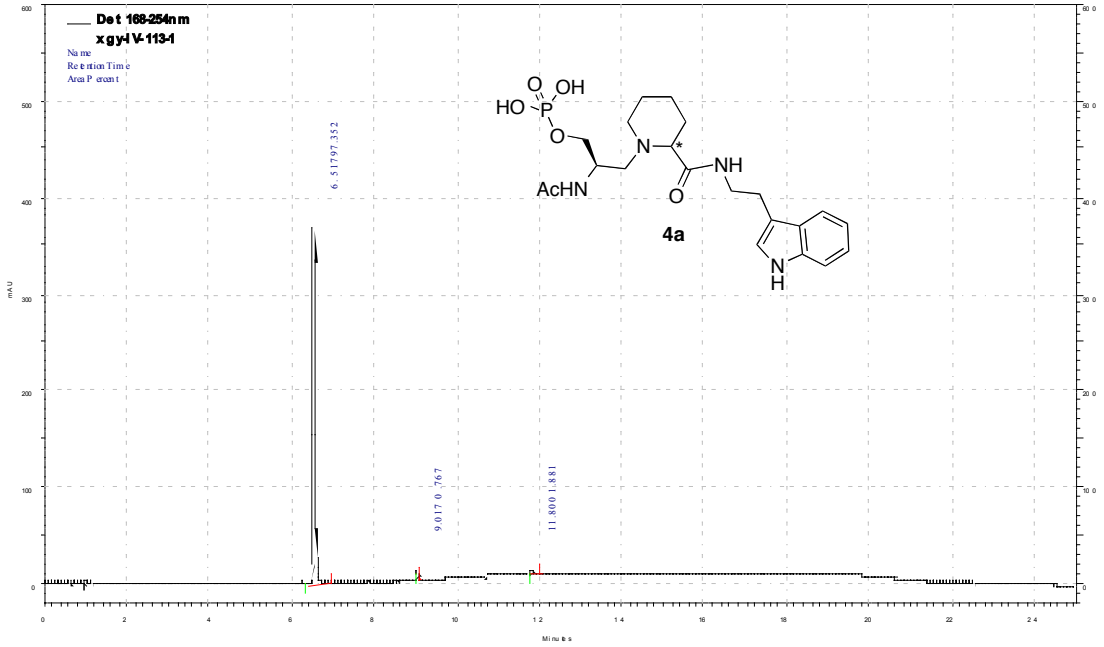
169.6724
176.1026
4b

^{31}P NMR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xgy-IV-113-1
Name
Retention Time
Area Percent
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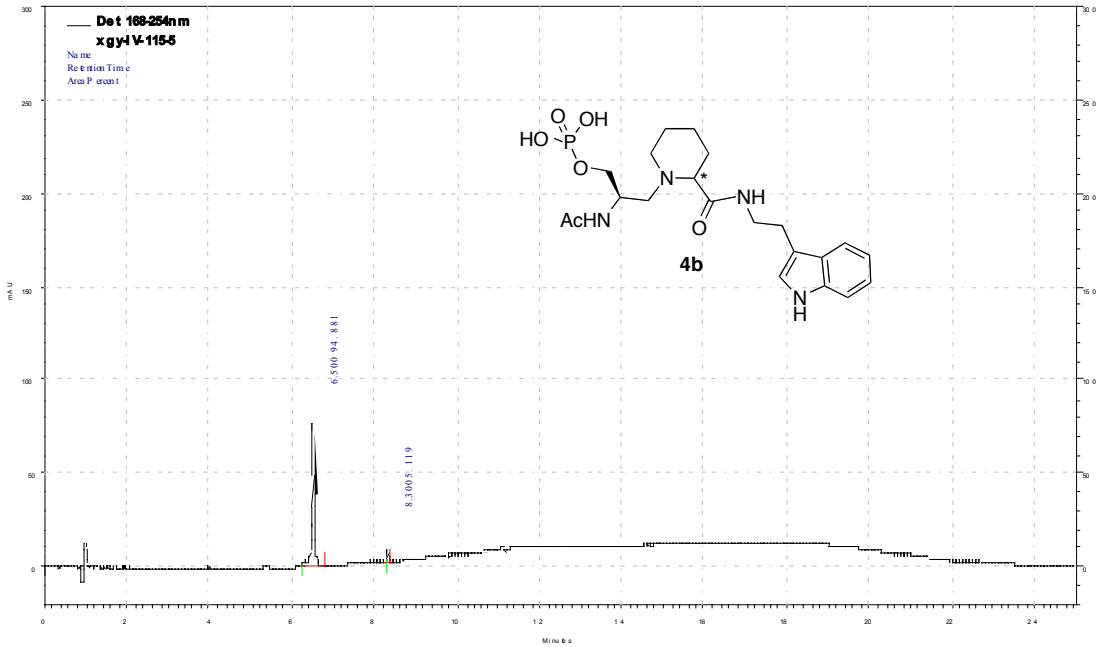
9.017 0.767
11.800 1.881
mAU
Minutes
4a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xgy-IV-115-5
Name
Retention Time
Area Percent
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mAU
Minutes
4b