

Supporting Information
for
Synthesis of (–)-julocrotine and a diversity oriented Ugi-approach to analogues and probes

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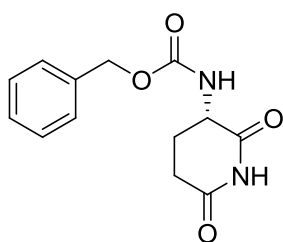
Experimental procedures and analytical data

General remarks

All commercially available chemicals were used without further purification. Dichloromethane and THF were dried before use, following conventional procedures. HPLC grade methanol was used in Ugi reactions. Analytical thin layer chromatography (TLC) was performed using silica gel 60 F₂₅₄ aluminum sheets and the visualization of the spots was done under UV light (254 nm) or by reaction with a solution of ninhydrin in *n*-butanol (3:1 w/v), 3% acetic acid and heating. Flash column chromatography was performed over silica gel (0.040–0.063 mm). Melting points are uncorrected. ¹H and ¹³C NMR were recorded in CDCl₃ solutions at 25 °C, at 400 MHz and 100 MHz,

respectively. Chemical shifts (δ) are reported in ppm relative to the TMS (^1H NMR) and to the solvent signal (^{13}C NMR). High resolution ESI mass spectra were obtained from a Bruker Apex III Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer equipped with an Infinity cell, a 7.0 Tesla superconducting magnet, an RF-only hexapole ion guide and an external electrospray ion source (off-axis spray).

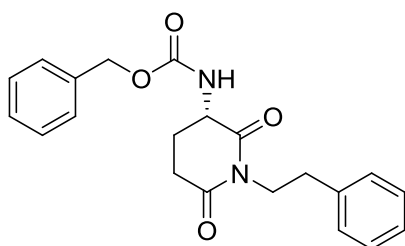
(*S*)-Benzyl (2,6-dioxopiperidin-3-yl)carbamate (**3**) [1].



To a stirred solution of Cbz-L-Glutamine (12.0 g, 42.9 mmol) in dry DMF (120 mL) was added DCC (9.75 g, 47.3 mmol) and *N*-hydroxysuccinimide (5.44 g, 47.3), and the mixture was heated at 80 °C for 18 h. The reaction mixture was cooled to r.t. and the precipitated DCU was filtered off. The filtrate was diluted with EtOAc (50 mL), washed with water (3 x 50 mL) and brine (50 mL), and dried over anhydrous Na_2SO_4 . The solvent was evaporated under reduced pressure and the crude material purified by silica gel isocratic column chromatography, with (3:7) ethyl acetate:dichloromethane as eluents, to afford 8.53 g of **3** as a white solid.

Yield: 76%, mp 111–112 °C (lit. [2]: mp 113.2 °C; $[\alpha]_D^{20}$ -46.6 (*c* 1.0, MeOH), (lit. [2]: $[\alpha]_D^{20}$ -42.7 (*c* 1.0, MeOH)); ^1H NMR δ 1.89 (dq, *J* = 5.2, 13.6 Hz, 1H), 2.58 (m, 1H), 2.69 (m, 1H), 2.79 (m, 1H), 4.35 (q, *J* = 5.2 Hz, 1H), 5.11 (s, 2H), 5.82 (d, *J* = 6.4 Hz, 1H), 7.29–7.38 (m, 5H), 8.93 (s, 1H); ^{13}C NMR δ 25.0, 31.1, 51.9, 67.2, 128.09, 128.5, 135.9, 156.1, 171.7, 172.1; ESI-MS *m/z* 263.2 [*M* + 1], 285.3 [*M* + 23].

(*S*)-Benzyl (2,6-dioxo-1-phenethylpiperidin-3-yl)carbamate (**4**) [3].

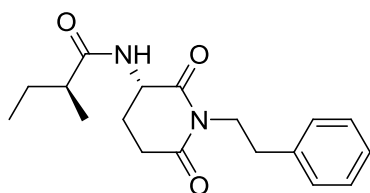


To a stirred solution of **3** (7.54 g, 28.8 mmol), 2-phenylethanol (2.67 mL, 22.2 mmol) and triphenylphosphine (7.54 g, 28.8 mmol) in anhydrous THF (240 mL) was added dropwise DIAD (6.09 mL, 31.0 mmol) at r.t. After the mixture had been stirred for 20 h, the solvent was removed under reduced pressure. The crude material was purified by silica gel isocratic column chromatography, with (3:7) ethyl acetate:hexanes as eluents, to afford 7.29 g of **4** as colorless crystals.

Yield: 90%; mp 122–123 °C (lit. [4]: mp 122–123 °C); $[\alpha]_D^{20} -29.2$ (*c* 1.0, CHCl₃) (lit. [4]: $[\alpha]_D^{20} -30.6$ (*c* 1.12, CHCl₃)); ¹H NMR δ 1.74 (dq, *J* = 4.8, 13.2 Hz, 1H), 2.48 (m, 1H), 2.67 (m, 1H), 2.81 (m, 3H), 4.02 (m, 2H), 4.27 (m, 1H), 5.15 (s, 2H), 5.64 (br, 1H), 7.20–7.33 (m, 10H); ¹³C NMR δ 25.5, 32.1, 35.4, 41.4, 52.6, 69.3, 126.3, 128.1, 128.3, 128.5, 128.9, 136.0, 138.9, 158.5, 171.4, 172.9; ESI-MS *m/z* 367.3 [M + 1], 389.5 [M + 23].

(*S*)-*N*-[(*S*)-2,6-Dioxo-1-phenethylpiperidin-3-yl]-2-methylbutanamide,

(-)-julocrotine (**1**).



To a stirred solution of compound **4** (0.37 g, 1.0 mmol) in MeOH (10 mL) was added Pd/C (34.0 mg, 10% w/w). The reaction vessel was evacuated, purged with hydrogen and kept under H₂ atmosphere (balloon). The suspension was stirred for 4 h at r.t. After filtration through Celite, the solvent was removed under reduced pressure to yield an oily product **5**, which was used in the next step without further purification [5].

To a solution of crude intermediate **5** in CH₂Cl₂ (2 mL) were added (*S*)-2-methylbutanoic acid (0.12 mL, 1.1 mmol), EDCI (0.23 g, 1.2 mmol) and HOBT (0.15 g, 1.1 mmol). After the mixture had been stirred for 16 h, the solvent was removed under reduced pressure. The crude material was purified by silica gel gradient column chromatography, with (3:7–1:1) ethyl acetate:hexanes as eluents, to afford 0.24 g of **1** as a white solid.

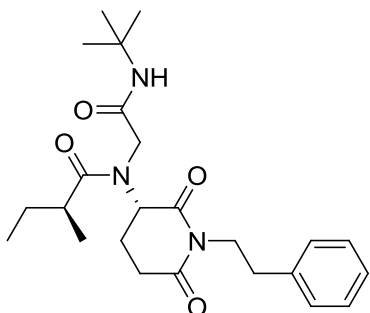
Yield: 73%; mp 107–108 °C (lit. [4]: mp 106–107 °C); $[\alpha]_D^{20}$ –44.02 (*c* 0.88, MeOH) (lit. [4]: $[\alpha]_D^{20}$ –46.0 (*c* 0.88, MeOH)); ¹H NMR δ 0.93 (t, *J* = 7.4 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H), 1.47 (m, 1H), 1.68 (m, 2H), 2.22 (m, 1H), 2.50 (m, 1H), 2.68, 2.76 (d, *J* = 5.2, 3.2 Hz, 2H), 2.80 (t, *J* = 7.6 Hz, 2H), 4.00 (m, 2H), 4.49 (ddd, *J* = 5.2, 5.2, 13.2 Hz, 1H), 6.35 (d, *J* = 5.2 Hz, 1H), 7.18–7.29 (m, 5H); ¹³C NMR δ 11.7, 17.2, 24.3, 27.1, 31.6, 33.8, 41.5, 42.8, 51.1, 126.5, 128.4, 128.9, 138.0, 170.9, 171.8, 176.8.

General procedure for the synthesis of compounds 6a–g.

To a solution of compound **5** (0.23 g, 1.0 mmol) in MeOH (5.0 mL) was added paraformaldehyde (30 mg, 1.0 mmol), and the contents were stirred for 2 h [6]. After this time the suitable carboxylic acid (1.0 mmol) and *tert*-butyl isonitrile (0.11 mL, 1.0 mmol) were added, and the stirring was continued for 18 h. The solvent was removed under reduced pressure and the crude material purified by silica gel column

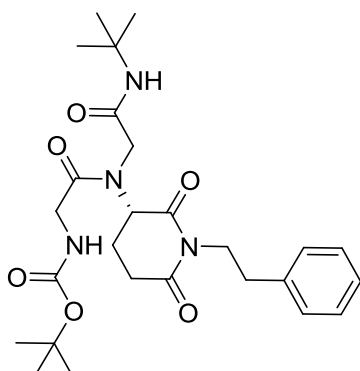
chromatography to afford the desired products. The details for the purification of the individual products are given below.

(*S*)-*N*-(2-(*tert*-Butylamino)-2-oxoethyl)-*N*-((*S*)-2,6-dioxo-1-phenethylpiperidin-3-yl)-2-methylbutanamide (**6a**).



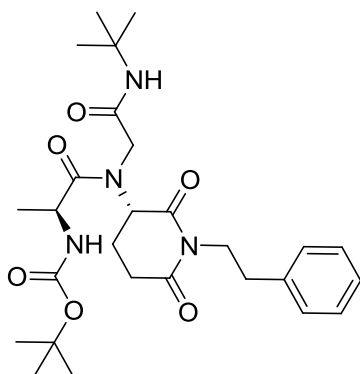
Purified by silica gel isocratic column chromatography with (3:7) ethyl acetate:hexanes as eluents. Yield: 61%; $[\alpha]_D^{20} -3.5$ (*c* 1.0, MeOH); $^1\text{H NMR}$ δ 0.85 (t, $J = 7.6$ Hz, 3H), 1.08 (d, $J = 6.4$ Hz, 2H), 1.38 (m, 10H), 1.58 (m, 1H), 1.96 (m, $J = 6.4$ Hz, 1H), 2.44 (m, 3H), 2.83 (m, 3H), 3.65 (m, 2H), 4.01 (m, 2H), 4.21(1H, m), 7.16–7.28 (m, 5H), 8.41 (bs, 1H); $^{13}\text{C NMR}$ δ 11.5, 17.1, 20.7, 27.3, 28.5, 31.3, 33.5, 37.3, 41.5, 51.6, 126.3, 128.3, 128.43, 138.5, 167.4, 170.4, 171.0; HRMS m/z calcd for $\text{C}_{24}\text{H}_{35}\text{N}_3\text{NaO}_4$, 452.2525; found, 452.2519.

(*S*)-*tert*-Butyl 2-((2-(*tert*-butylamino)-2-oxoethyl) (2,6-dioxo-1-phenethylpiperidin-3-yl)amino)-2-oxoethylcarbamate (**6b**).



Purified by silica gel isocratic column chromatography with (1:1) ethyl acetate:hexanes as eluents. Yield: 58%; $[\alpha]_D^{20} -16.4$ (*c* 1.0 MeOH); $^1\text{H NMR}$ δ 1.33 (m, 18H), 1.97 (m, 1H), 2.37 (m, 1H), 2.50 (m, 1H), 2.70–2.77 (m, 3H), 3.69 (m, 2H), 3.87–3.98 (m, 5H), 5.31 (bs, 1H), 7.08–7.23 (m, 5H), 8.00 (bs, 1H); $^{13}\text{C NMR}$ δ 20.5, 28.1, 28.3, 31.2, 33.5, 40.5, 41.4, 42.1, 51.6, 60.1, 79.6, 126.3, 128.3, 128.7, 138.2, 155.4, 166.3, 170.3, 170.7; HRMS *m/z* calcd for $\text{C}_{26}\text{H}_{38}\text{N}_4\text{NaO}_6$, 525.2689; found, 525.2684.

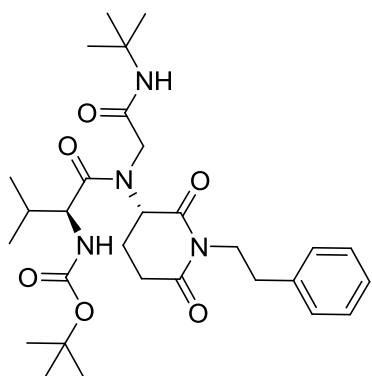
tert-Butyl (*S*)-1-((2-(*tert*-butylamino)-2-oxoethyl) ((*S*)-2,6-dioxo-1-phenethylpiperidin-3-yl)amino)-1-oxopropan-2-yl carbamate (**6c**).



Purified by silica gel isocratic column chromatography with (1:1) ethyl acetate:hexanes as eluent. Yield: 56%; mp 149–150°C; $[\alpha]_D^{20} -55.6$ (*c* 1.0 MeOH); $^1\text{H NMR}$ δ 1.26 (m, 3H), 1.35 (m, 18H), 1.98 (m, 1H), 2.38 (m, 1H), 2.54 (m, 1H), 2.75–2.79 (m, 3H), 3.69

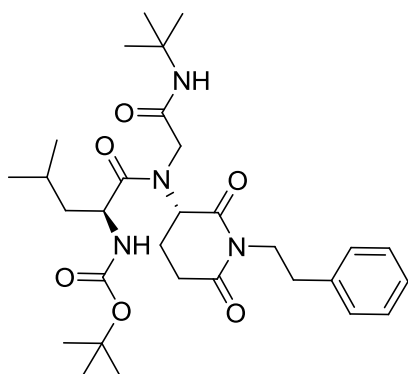
(m, 1H), 3.94–4.03 (m, 4H), 4.33 (m, 4H), 5.20 (bd, 1H), 7.13–7.25 (m, 5H), 7.92 (bs, 1H); ^{13}C NMR δ 17.6, 20.4, 28.1, 28.3, 31.3, 33.5, 40.5, 41.4, 46.8, 51.8, 60.2, 79.7, 126.3, 128.3, 128.8, 138.3, 155.0, 166.6, 167.0, 170.4; HRMS m/z calcd for $\text{C}_{27}\text{H}_{40}\text{N}_4\text{NaO}_6$, 539.2846; found, 539.2827.

tert-Butyl (*S*)-1-((2-(*tert*-butylamino)-2-oxoethyl) ((*S*)-2,6-dioxo-1-phenethylpiperidin-3-yl)amino)-3-methyl-1-oxobutan-2-yl carbamate (**6d**).



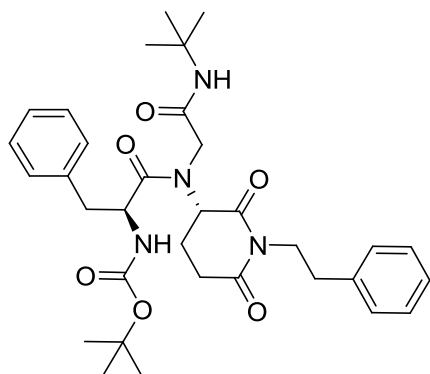
Purified by silica gel isocratic column chromatography with (3:7) ethyl acetate:hexanes as eluent. Yield: 63%; $[\alpha]_D^{20}$ -41.6 (c 1.0 MeOH); ^1H NMR δ 0.91–1.00 (m, 6H), 1.44 (m, 18H), 1.83–2.07 (m, 2H), 2.38–2.60 (m, 2H), 2.82 (m, 3H), 3.62–3.75 (m, 2H), 3.98–4.02 (m, 3H), 4.22 (m, 1H), 5.01 (d, $J = 9.2$ Hz, 1H), 7.18–7.28 (m, 5H), 8.08 (bs, 1H); ^{13}C NMR δ 17.5, 19.5, 20.5, 25.6, 28.3, 28.5, 31.2, 31.5, 33.7, 41.7, 52.6, 55.5, 60.2, 67.9, 79.9, 126.5, 128.5, 128.9, 138.6, 155.7, 170.0, 170.5; HRMS m/z calcd for $\text{C}_{29}\text{H}_{44}\text{N}_4\text{NaO}_6$, 567.3159; found, 567.3153.

tert-Butyl (*S*)-1-((2-(*tert*-butylamino)-2-oxoethyl) ((*S*)-2,6-dioxo-1-phenethylpiperidin-3-yl)amino)-4-methyl-1-oxopentan-2-ylcarbamate (**6e**).



Purified by silica gel isocratic column chromatography with (3:7) ethyl acetate:hexanes as eluent. Yield: 63%; $[\alpha]_D^{20} -52.1$ (*c* 1.0 MeOH); $^1\text{H NMR}$ δ 0.86–0.91 (m, 6H), 1.34 (m, 20H), 1.66 (m, 1H), 1.96 (m, 1H), 2.29 (m, 1H), 2.50 (m, 1H), 2.74 (m, 3H) 3.71 (m, 1H), 3.92 (t, *J* = 8.4 Hz, 2H), 4.01 (m, 2H), 4.29 (m, 1H), 4.96 (d, *J* = 8.4 Hz, 1H), 7.11–7.22 (m, 5H), 7.95 (bs, 1H); $^{13}\text{C NMR}$ δ 20.4, 21.4, 23.3, 24.5, 28.1, 28.3, 28.5, 31.4, 33.6, 41.2, 41.5, 49.5, 51.9, 60.2, 79.8, 126.3, 128.3, 128.8, 138.4, 155.5, 166.6, 169.8, 170.5; HRMS *m/z* calcd for $\text{C}_{30}\text{H}_{46}\text{N}_4\text{NaO}_6$, 581.3315; found, 581.3309.

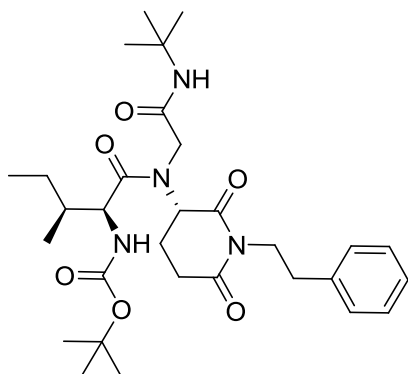
tert-Butyl (*S*)-1-((2-(*tert*-butylamino)-2-oxoethyl) ((*S*)-2,6-dioxo-1-phenethylpiperidin-3-yl)amino)-1-oxo-3-phenylpropan-2-yl carbamate (**6f**).



Purified by silica gel isocratic column chromatography with (3:7) ethyl acetate:hexanes as eluents. Yield: 60%; $[\alpha]_D^{20} -63.5$ (*c* 1.0 MeOH); $^1\text{H NMR}$ δ 1.35 (m, 18H), 1.79 (m,

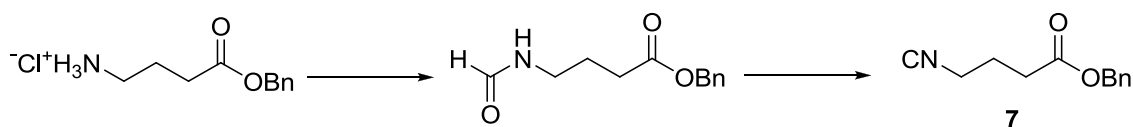
1H), 2.46 (m, 2H), 2.82 (m, 3H), 2.87–3.01 (m, 2H), 1.69 (m, 2H), 3.96 (m, 3H), 4.57 (m, 1H), 5.15 (br, 1H), 7.17–7.28 (m, 10H), 7.99 (bs, 1H); ¹³C NMR δ 20.1, 28.2, 28.3, 31.4, 33.6, 39.3, 41.5, 51.8, 60.3, 80.0, 126.4, 127.3, 128.4, 128.5, 128.8, 129.4, 135.4, 138.5, 154.9, 166.4, 169.7, 170.4, 172.1; HRMS *m/z* calcd for C₃₃H₄₄N₄NaO₆, 615.3159; found, 615.3153.

tert-Butyl (2*S*,3*S*)-1-((2-((*tert*-butylamino)-2-oxoethyl) ((*S*)-2,6-dioxo-1-phenethyl piperidin-3-yl)amino)-3-methyl-1-oxopentan-2-yl carbamate (**6g**).

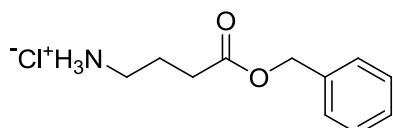


Purified by silica gel isocratic column chromatography with (3:7) ethyl acetate:hexanes as eluent. Yield: 55%; $[\alpha]_D^{20} -52.77$ (*c* 1.0 MeOH); ¹H NMR δ 0.84–0.93 (m, 6H), 1.48 (m, 1H), 1.37 (m, 19H), 1.55–1.64 (m, 1H), 2.03 (m, 1H), 2.49 (m, 2H), 2.79 (m, 3H), 3.79 (m, 1H), 3.98 (m, 3H), 4.23 (m, 2H), 5.01 (d, *J* = 8.4 Hz, 1H), 7.15–7.27 (m, 5H), 7.98 (bs, 1H); ¹³C NMR δ 11.2, 15.5, 20.3, 24.1, 28.2, 28.3, 28.4, 31.4, 33.6, 37.8, 41.5, 51.9, 54.7, 60.2, 79.8, 126.3, 128.3, 128.8, 138.5, 155.6, 166.6, 169.7, 170.5, 172.6; HRMS *m/z* calcd for C₃₀H₄₆N₄NaO₆, 581.3315; found, 581.3309.

Preparation of isocyanide 7 from γ -aminobutyric acid



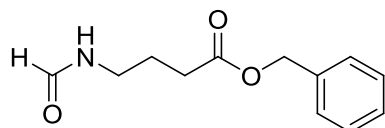
Benzyl 4-aminobutyrate, HCl salt



To a stirred suspension of γ -aminobutyric acid (10.3 g, 0.1 mol) in benzyl alcohol (150 mL) at 0 °C was added dropwise thionyl chloride (73 mL, 1.0 mol) over 1 h. The resulting solution was heated at 80 °C for 4 h and then allowed to cool down overnight. The contents were poured into diethyl ether (1.5 L) and then stored at -30 °C to allow for complete precipitation. The precipitated solid was filtered off, washed with diethyl ether, and recrystallized from cold diethyl ether/ethanol (9:1) to afford 13.3 g of the product as colorless needles.

Yield: 58%; mp 108–109 °C (lit. [7]: mp 109–110 °C); ^1H NMR δ 2.03 (q, $J = 7.6$ Hz, 2H), 2.45 (t, $J = 7.6$ Hz, 2H), 3.03 (m, 2H), 4.25 (s, 3H), 5.01 (s, 2H), 7.24 (m, 5H); ^{13}C NMR δ 22.4, 30.9, 39.1, 66.5, 126.9, 128.2, 128.5, 135.6, 172.9.

Benzyl 4-formamidobutanoate

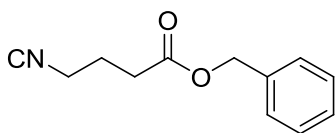


To benzyl 4-aminobutyrate HCl salt (13.3 g, 57.9 mmol) was added trimethyl orthoformate (150 mL) at r.t. and the mixture was stirred under reflux for 18 h. The contents were then allowed to cool down to r.t. and the solvent was removed under

reduced pressure. Further co-evaporations with toluene (25 mL, 2 times) were performed in order to remove remaining traces of trimethyl orthoformate. The product was obtained as a colorless oil and used in the next step without further purification.

Yield: quant.; $^1\text{H NMR}$ δ 1.87 (q, $J = 6.8$ Hz, 2H), 2.42 (t, $J = 6.8$ Hz, 2H), 3.32 (q, $J = 6.8$ Hz, 2H), 5.01 (s, 2H), 6.20 (bs, 1H), 7.34 (5H, m), 8.11 (s, 1H); $^{13}\text{C NMR}$ δ 24.3, 31.6, 37.6, 66.4, 126.9, 128.2, 128.4, 135.6, 161.7, 173.1; HRMS m/z calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_3\text{Na}$, 244.0950; found, 244.0944.

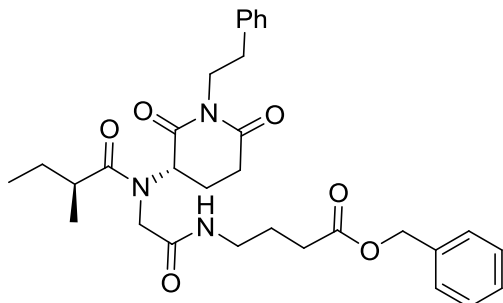
Benzyl 4-isocyanobutanoate (7)



To a solution of benzyl 4-formamidobutanoate (12.2 g, 55.0 mmol) and diisopropylamine (23.3 mL, 165.0 mmol) in dichloromethane (200 mL) at 0 °C was added phosphoryl chloride (6.13 mL, 66.0 mmol) dropwise for 1 h under a nitrogen atmosphere. The solution was allowed to warm to r.t. and stirred for 4 h. Aqueous NaHCO_3 solution (100 mL) was added to the reaction and the contents transferred to a separatory funnel. The organic layer was successively washed with concentrated NaHCO_3 (two times, 100 mL), brine (once, 100 mL) and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the crude product purified by isocratic column chromatography on silica gel, with (3:7) ethyl acetate:hexanes as eluent, to give 8.0 g of the title compound as light-yellow oil.

Yield: 72%; $^1\text{H NMR}$ δ 2.01 (m, 2H), 2.56 (t, $J = 7.2$ Hz, 2H), 3.32 (tt, $J = 6.8, 1.6$ Hz, 2H), 5.14 (s, 2H), 7.36 (5H, m); $^{13}\text{C NMR}$ δ 24.1, 30.4, 40.7, 66.6, 128.2, 128.3, 128.5, 135.5, 156.7, 171.9; HRMS m/z calcd for $\text{C}_{12}\text{H}_{13}\text{NO}_2\text{Na}$, 226.0844; found, 226.0838.

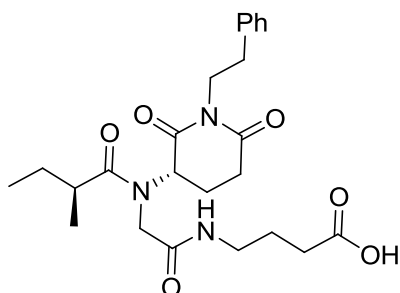
Benzyl 4-(2-((*S*)-*N*-((*S*)-2,6-dioxo-1-phenethylpiperidin-3-yl)-2-methylbutanamido) acetamido) butanoate (**8**).



To a stirred solution of compound **5** (0.37 g, 1.0 mmol) in MeOH (10 mL), paraformaldehyde (30 mg, 1.0 mmol) was added, and the contents were stirred for 2 h. Then (*S*)-2-methylbutanoic acid (0.11 mL, 1.0 mmol) and isonitrile **7** (0.20 g, 1.0 mmol) were added and the stirring was continued for 18 h. The solvent was removed under reduced pressure and the crude material purified by gradient silica gel column chromatography with (100:0–95:5) ethyl acetate:MeOH as eluent. The obtained material was dissolved in ethyl acetate (10 mL), filtered through a syringe filter (0.45 micron pore size) and evaporated to afford 0.34 g of the target compound **8** as a light-yellow oil.

Yield:61%; $[\alpha]_D^{20} -3.02$ (*c* 1.0, CHCl₃); ¹H NMR δ 0.87 (t, *J* = 7.4 Hz, 3H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.41 (m, 1H), 1.59 (m, 1H), 1.95 (m, 3H), 2.45 (m, 6H), 2.83 (t, *J* = 7.6 Hz, 2H), 3.36 (q, *J* = 6.8 Hz, 2H), 3.73 (m, 2H), 4.01 (t, *J* = 7.6 Hz, 2H), 4.6 (s, 1H), 5.09 (s, 2H), 7.17–7.35 (m, 10H), 8.83 (bs, 1H); ¹³C NMR δ 11.4, 16.8, 20.5, 24.4, 27.2, 31.2, 31.4, 33.5, 36.9, 38.7, 41.6, 52.6, 60.2, 66.1, 126.2, 128.0, 128.1, 128.4, 128.6, 128.8, 135.6, 138.3, 168.4, 170.3, 171.6, 172.5; HRMS *m/z* calcd for C₃₁H₃₉N₃NaO₆, 572.2737; found, 572.2731.

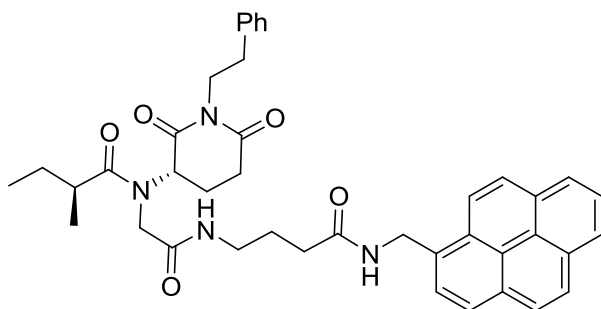
4-(2-((*S*)-*N*-((*S*)-2,6-Dioxo-1-phenethylpiperidin-3-yl)-2-methylbutanamido) acetamido) butanoic acid (**9**).



To a stirred solution of **8** (0.27 g, 0.5 mmol) in MeOH (5 mL) was added Pd/C (26 mg, 10% w/w). The reaction vessel was evacuated, purged with hydrogen and kept under H₂ atmosphere (balloon). The suspension was stirred for 4 h at r.t. and filtered through Celite to remove the heterogeneous catalyst. The solvent was evaporated under reduced pressure to yield 0.23 g of a colorless oil, which was used in the next step without further purification.

Yield: quant.; [α]_D²⁰ -7.02 (*c* 1.0, CHCl₃); ¹H NMR δ 0.86 (t, *J* = 7.4 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H), 1.42 (m, 1H), 1.59 (m, 1H), 1.85 (m, 2H), 1.93 (m, 1H), 2.47 (m, 6H), 2.85 (t, *J* = 7.6 Hz, 2H), 3.37 (q, *J* = 6.8 Hz, 2H), 3.73 (m, 2H), 4.05 (t, *J* = 7.6 Hz, 2H), 4.6 (s, 1H), 7.25 (m, 5H), 8.93 (bs, 1H); ¹³C NMR δ 11.5, 16.9, 20.6, 24.2, 27.3, 31.2, 31.3, 33.5, 37.1, 38.9, 41.7, 52.8, 60.2, 126.3, 128.4, 128.7, 138.5, 169.3, 170.5, 171.9, 176.5; HRMS *m/z* calcd for C₂₄H₃₃N₃NaO₆, 482.2267; found, 482.2261.

(*S*)-*N*-((*S*)-2,6-Dioxo-1-phenethylpiperidin-3-yl)-2-methyl-*N*-(2-oxo-2-(4-oxo-4-(pyren-1-ylmethylamino) butylamino) ethyl) butanamide (**10**).



To a solution of **9** (60 mg, 0.13 mmol) in dry dichloromethane (5.0 mL) were added 1-pyrenemethylamine hydrochloride (17 mg, 0.14 mmol), EDCI (26 mg, 0.14 mmol), DMAP (2 mg, 10 mol %) and triethylamine (0.1 mL, 0.39 mmol) at r.t. The reaction mixture was stirred at r.t. for 24 h. The contents were transferred to a separatory funnel and successively washed with 10% v/v HCl (two times, 20 mL), water (once, 10 mL), and brine (once, 10 mL), and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the crude product purified by gradient silica gel column chromatography with (1:0–8:2) ethyl acetate:methanol as eluent. The obtained material was dissolved in ethyl acetate (10 mL), filtered through a syringe filter (0.45 micron pore size) and evaporated to afford 70 mg of **10** as a light-yellow oil.

Yield: 80%.; $[\alpha]_D^{20} -7.0$ (*c* 1.0, CHCl₃); UV (MeOH) λ_{\max} (log ϵ): 199 (5.49), 233 (5.19), 242 (5.34), 255 (4.72), 265 (4.96), 275 (5.17), 312 (4.68), 326 (4.98), 341 (5.13); ¹H NMR δ 0.88 (t, *J* = 7.4 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.32 (m, 1H), 1.52 (m, 1H), 1.88 (m, 2H), 2.03 (m, 1H), 2.47 (m, 6H), 3.31–3.65 (m, 6H), 3.91–4.61 (m, 3H), 4.90–5.25 (m, 2H), 7.06–7.26 (m, 5H), 7.61 (bs, 1H), 7.86–8.19 (m, 9H), 8.76 (bs, 1H); ¹³C NMR δ 11.6, 16.9, 20.3, 25.9, 27.3, 30.7, 32.5, 33.5, 36.9, 37.1, 38.2, 41.4, 42.6, 52.8, 60.9, 122.8, 124.4, 124.8, 124.9, 125.4, 125.6, 126.1, 126.3, 127.3, 128.2, 128.6,

128.8, 128.9, 130.2, 130.6, 131.2, 131.3, 138.4, 169.4, 169.9, 172.1, 172.9; HRMS *m/z* calcd for C₄₁H₄₄N₄NaO₅, 695.3209; found, 695.3204.

References

- 1 Kaldor, S. W.; Hammond, M.; Dressman, B. A.; Labus, J. M.; Chadwell, F. W.; Kline, A. D.; Heinz, B. A. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 2021-2026.
- 2 Lee, J.; Son, K.; Kim, M.; Jung, G.; Choi, J.; Lee, E. S.; Park, M. *Arch. Pharm. Res.* **1999**, *22*, 491-495.
- 3 Sen, S. E.; Roach, S. L. *Synthesis* **1995**, 756-758.
- 4 Silva, L. L.; Joussef, A. C. *J. Nat. Prod.* **2011**, *74*, 1531-1534.
- 5 The formation of a colored pigment during the hydrogenation of the intermediate **4** has already been reported. For more details see: Sondheimer, E.; Holley, R. W. *J. Am. Chem. Soc.* **1957**, *79*, 3767-3770.
- 6 After addition of formaldehyde initially a methanolic suspension is formed, that after approximately 2 h becomes clear as the oligomeric starting material is consumed. It indicates that imine formation is completed as can be easily confirmed by ESI-MS. It is important not to add the carboxylic acid and isonitrile components to a solution still containing unreacted formaldehyde as otherwise the yields of desired products decrease and the competing Passerini reaction is observed.
- 7 Evans, R.L.; Irreverre, F. *J. Org. Chem.* **1959**, *24*, 863-864.

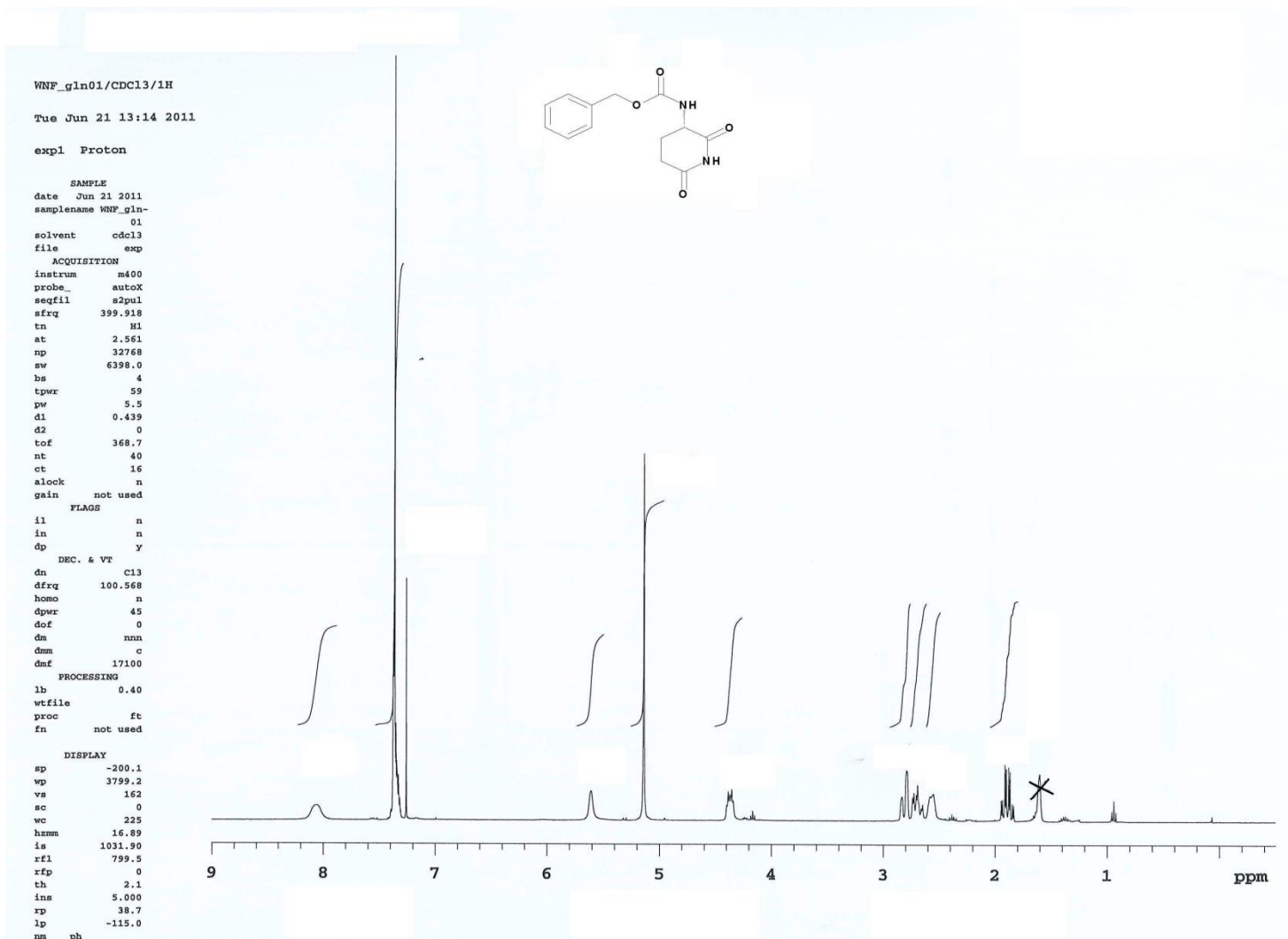


Figure S1: ¹H NMR spectrum of compound 3.

WNF_gln01/CDC13/13C

Sample: WNF_gln01

File: exp

Pulse Sequence: s2pu1

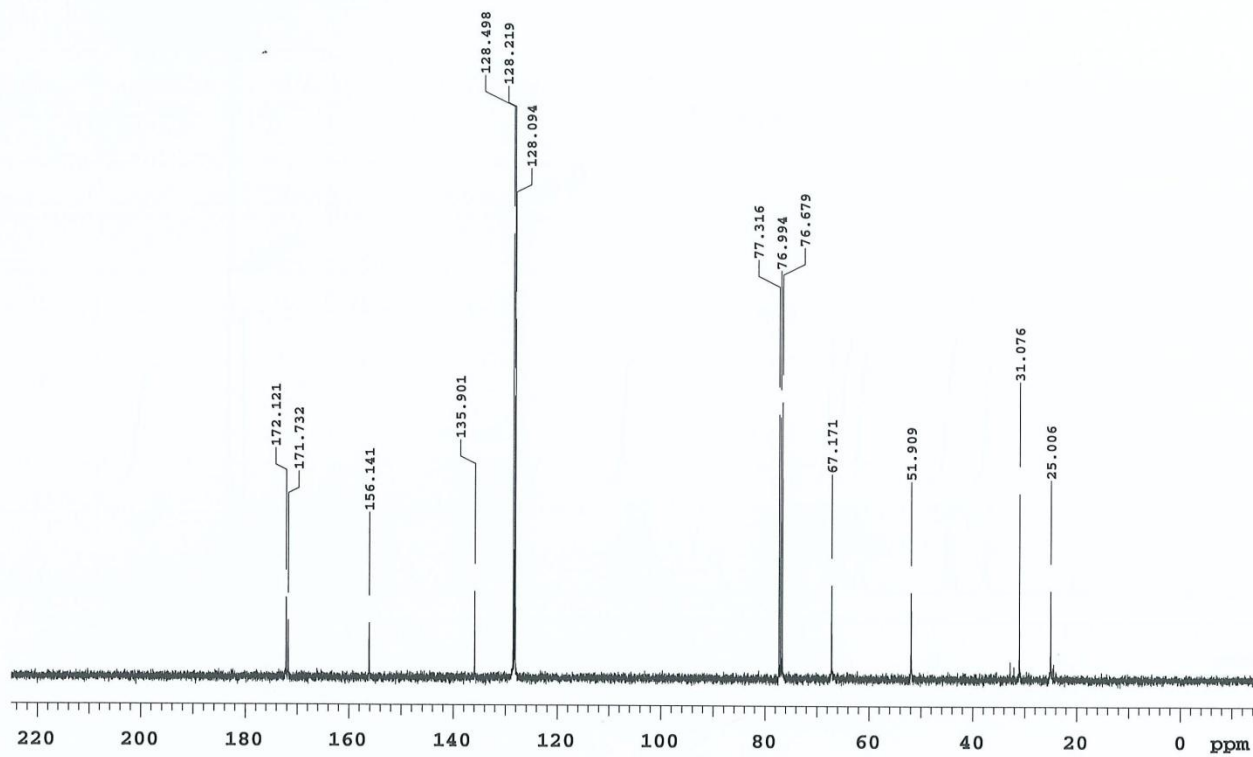
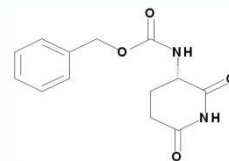


Figure S2: ^{13}C NMR spectrum of compound 3.

WNF_gln02/CDCl3/1H
Fri Jun 17 15:12 2011
exp6 Proton

SAMPLE
date Jun 17 2011
samplename WNF_gln-
02
solvent cdcl3
file exp

ACQUISITION
instrum M400
probe autoX
seqfil s2pul
sfrq 399.918
tn H1
at 2.561
np 32768
sw 6398.0
bs 4
tpwr 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 20
alock n
gain not used

FLAGS
il n
in n
dp y

DEC. & VT
dn Cl3
dfrq 100.568
homo n
dpr 45
dof 0
dm nnn
dnn c
dmf 17100

PROCESSING
lb 0.40
wtfile
proc ft
fn not used

DISPLAY
sp -102.4
wp 3366.9
vs 162
sc 0
wc 225
hzmm 14.96
is 569.41
xfl 799.5
xlp 0
th 2.1
ins 2.000
xp 42.8
lp -120.0
nm ph

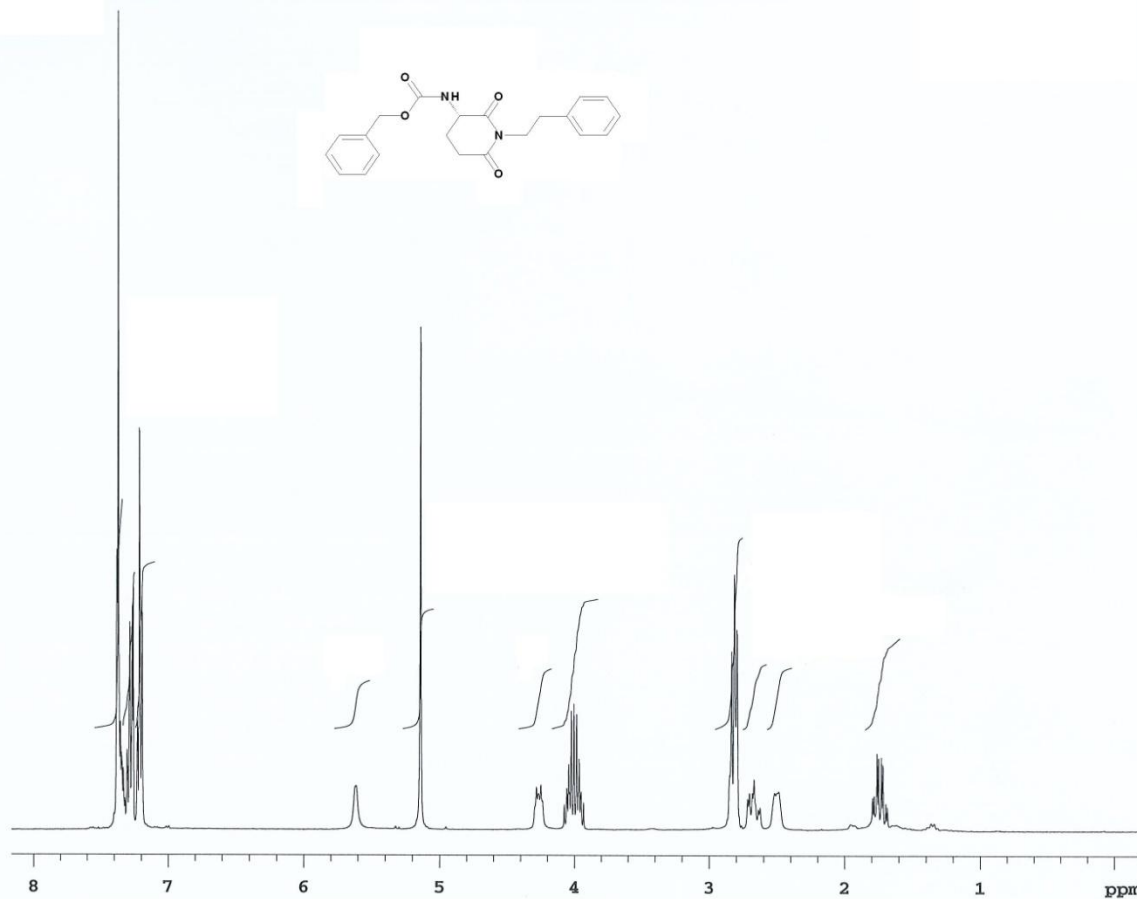
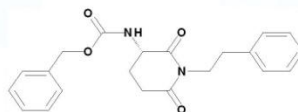


Figure S3: ¹H NMR spectrum of compound 4.

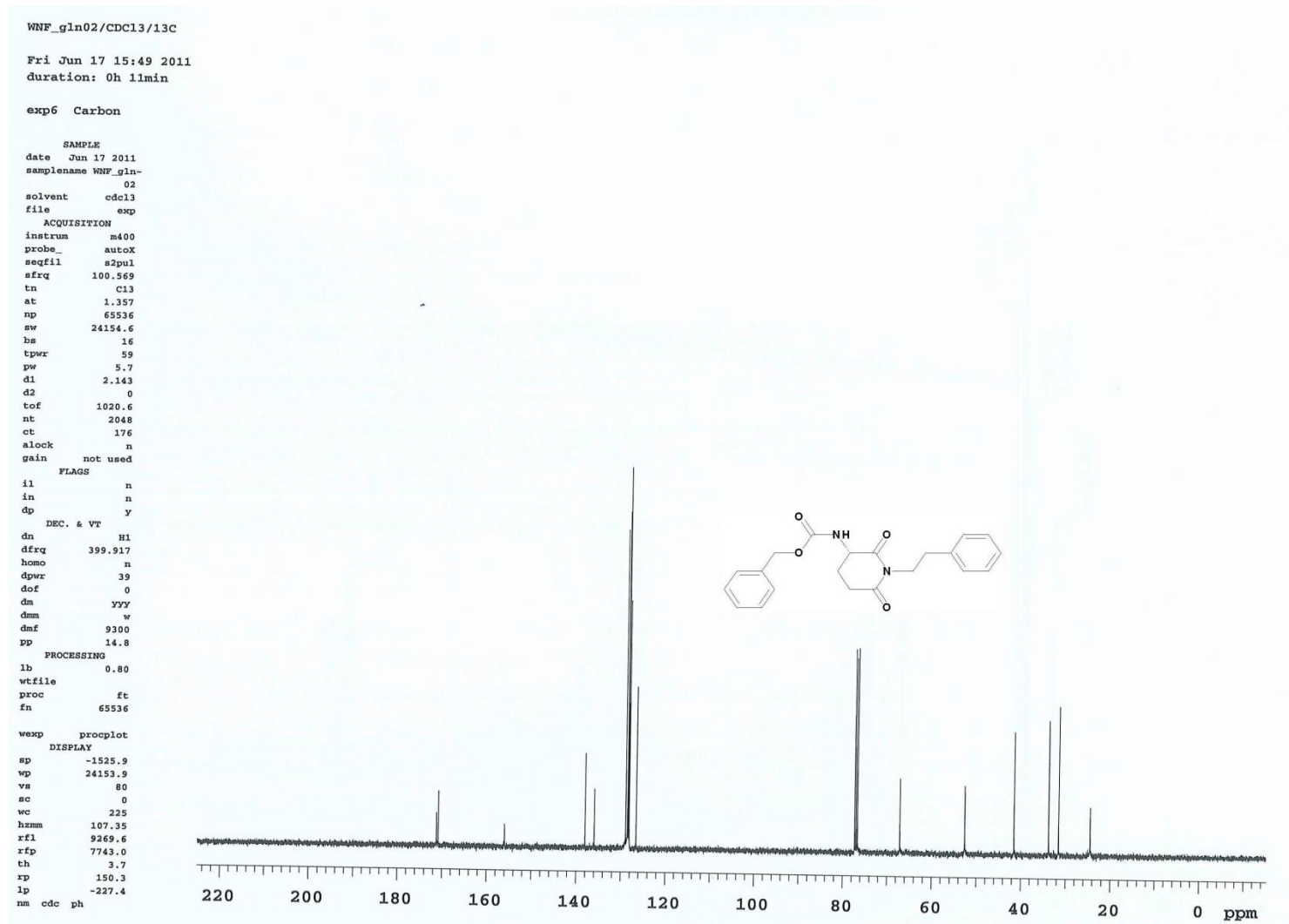


Figure S4: ¹³C NMR spectrum of compound 4.

WNF_gln03/CHCl3/1H
(-)-Julocrotine

Wed Jun 22 18:12 2011

expl Proton

SAMPLE
date Jun 22 2011
samplename WNF_gln-
03
solvent cdcl3
file exp

ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 399.918
tn H1
at 2.561
np 32768
sw 6398.0
bs 4
tpwr 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 32
alock n
gain not used

FLAGS
il n
in n
dp Y

DEC. & VT
dn C13
dfrq 100.568
homo n
dpwr 45
dof 0
dm nnn
dmm c
dmf 17100

PROCESSING
lb 0.40
wtfile
proc ft
fn not used

DISPLAY
sp -200.1
wp 3399.3
vs 162
sc 0
wc 225
hzmm 15.11
is 573.86
rfl 799.5
rfp 0
th 5.8
ins 3.000
fp 9.9
lp -97.3
nm ph

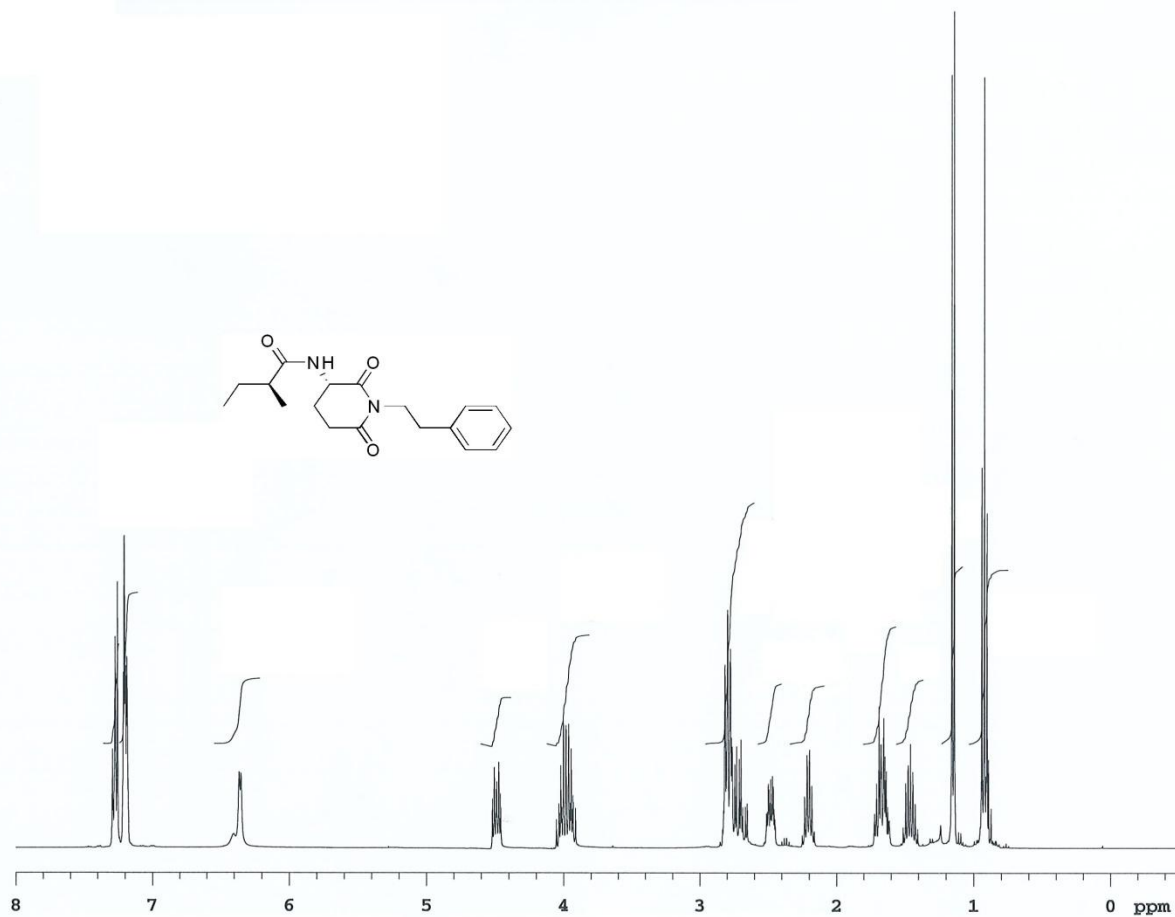


Figure S5: ¹H NMR spectrum of compound 1.

WNF_gln03/CHCl3/13C

Wed Jun 22 18:14 2011

duration: 0h 3min

exp2 Carbon

```
SAMPLE
date      Jun 22 2011
samplname WNF_gln-
          03
solvent   cdcl3
file      exp
ACQUISITION
instrum   m400
probe_    autoX
seqfil    s2pul
sfrq      100.569
tn        C13
at        1.357
np        65536
sw        24154.6
hs        16
tpwr      59
pw        5.7
d1        2.143
d2        0
tof       1020.6
nt        2048
ct        48
alock     n
gain      not used
FLAGS
il        n
in        n
dp        y
DEC. & VT
dn        H1
dfrq      399.917
homo      n
dprv      39
dof       0
dm        yyy
dwm       w
dnf       9300
pp        14.8
PROCESSING
lb        0.80
wtfile
proc      ft
fn        65536
wexp      procplot
DISPLAY
sp        -1517.9
vp        24153.9
va        80
sc        0
wc        225
hzmm      107.35
rf1       1518.6
rfp       0
th        6.8
xp        133.6
lp        -217.4
--
```

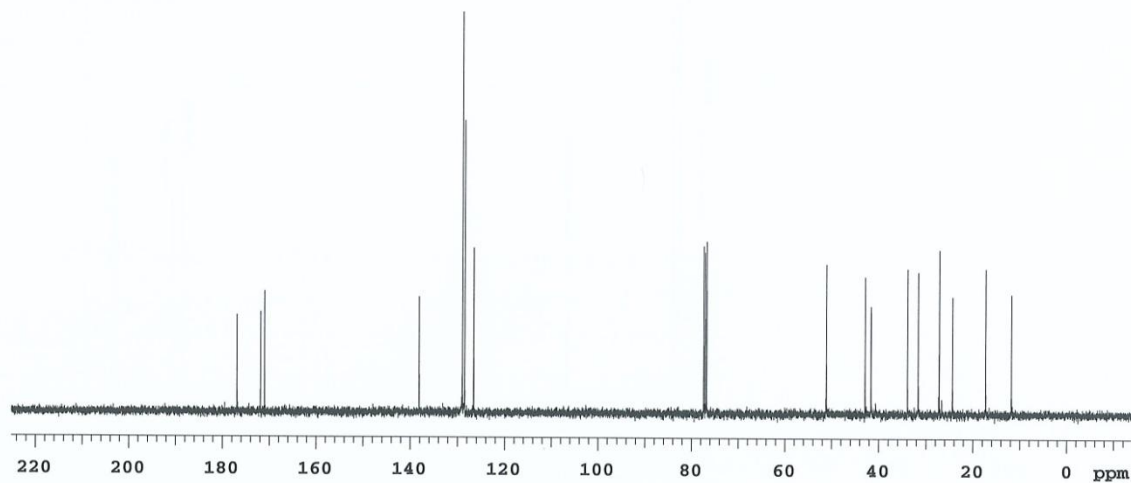
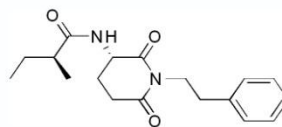


Figure S6: ^{13}C NMR spectrum of compound **1**.

WNF_gln04/CDC13/1H
Wed Jun 29 10:29 2011
expl Proton

SAMPLE
date Jun 29 2011
samplename WNF_gln-
04
solvent cdc13
file exp

ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 399.918
tn HL
at 2.561
np 32768
sw 6398.0
bs 4
tper 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 16
slock n
gain not used

FLAGS
fl n
in n
dp Y

DEC. & VT
dn C13
dfrq 100.568
homo n
dper 45
dof 0
dm nnn
dms c
dnt 17100

PROCESSING
lb 0.40
wtfile
proc ft
fn not used

DISPLAY
sp -158.7
vp 3783.2
vs 392
sc 0
wc 225
hzmm 16.81
is 142.71
rfi 799.5
rfp 0
th 2.9
ina 3.000
xp 0.5
lp -96.6
ms ph

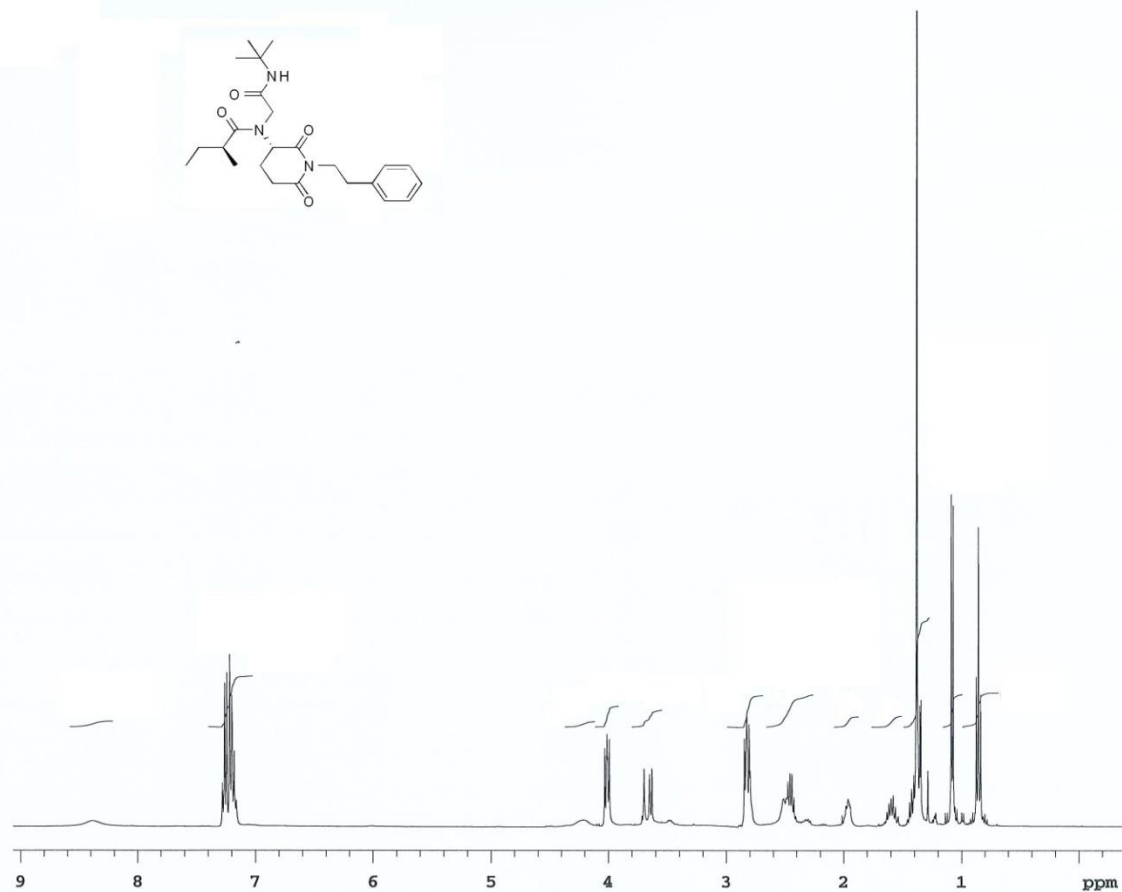
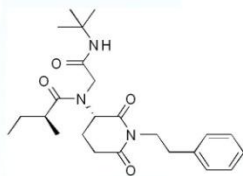


Figure S7: ^1H NMR spectrum of compound **6a**.

WNF_gln04/CDC13/13C

Wed Jun 29 10:30 2011
duration: 0h 5min

exp2 Carbon

```
SAMPLE
date Jun 29 2011
samplename WNF_gln-
04
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.569
tn C13
at 1.357
np 65536
sw 24154.6
bs 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 2048
ot 80
alock n
gain not used
FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dfrq 399.917
homo n
dpwr 39
dof 0
dm yyy
dmm w
dmf 9300
pp 14.8
PROCESSING
lb 0.80
wtfile
proc ft
fn 65536
wexp procploc
DISPLAY
sp -1520.3
wp 24153.9
vs 80
sc 0
wc 225
lsmm 107.35
rf1 9272.1
rfp 7743.0
th 3.1
xp 154.9
lp -236.0
nm cdc ph
```

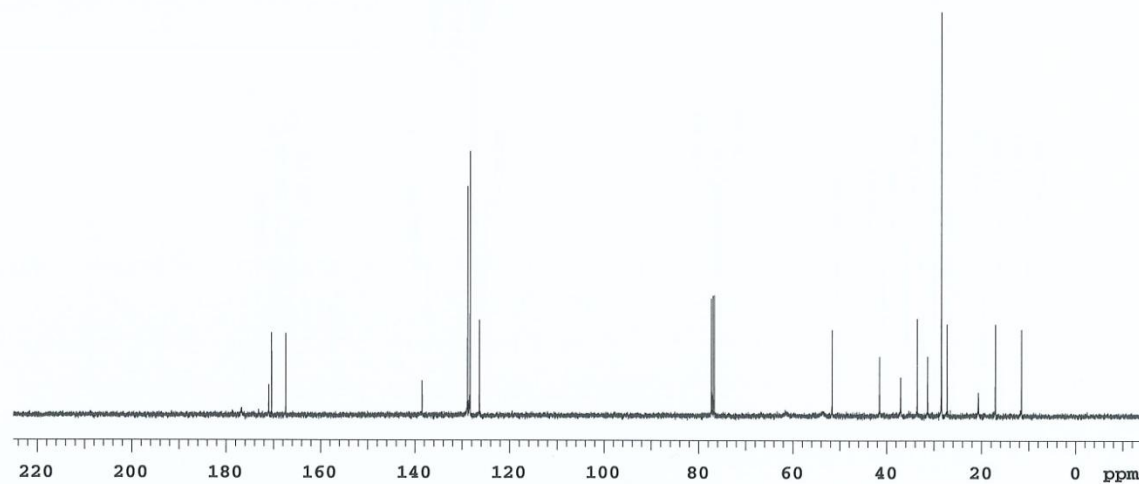
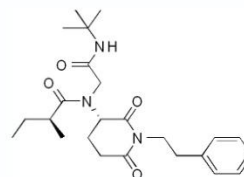


Figure S8: ^{13}C NMR spectrum of compound **6a**.

WNF_gln05/CDCl3/1H

Wed Jun 29 10:41 2011

exp1 Proton

```
SAMPLE
date      Jun 29 2011
samplname WNF_gln-
          05
solvent   cdcl3
file      exp
ACQUISITION
instrum   m400
probe     autoX
seqfil    s2pu1
sfrq      399.918
tn        H1
at        2.561
np        32768
sw        6398.0
bs        4
tpwr      59
pw        5.5
dl        0.439
d2        0
tof       368.7
nt        40
ct        24
alock     n
gain      not used
          FLAGS
il        n
in        n
dp        y
          DEC. & VT
dn        C13
dfrq      100.568
homo      n
dpwr      45
dof       0
dm        nnn
dmm       c
dmf       17100
PROCESSING
lb        0.40
wtfile
proc      ft
fn        not used
```

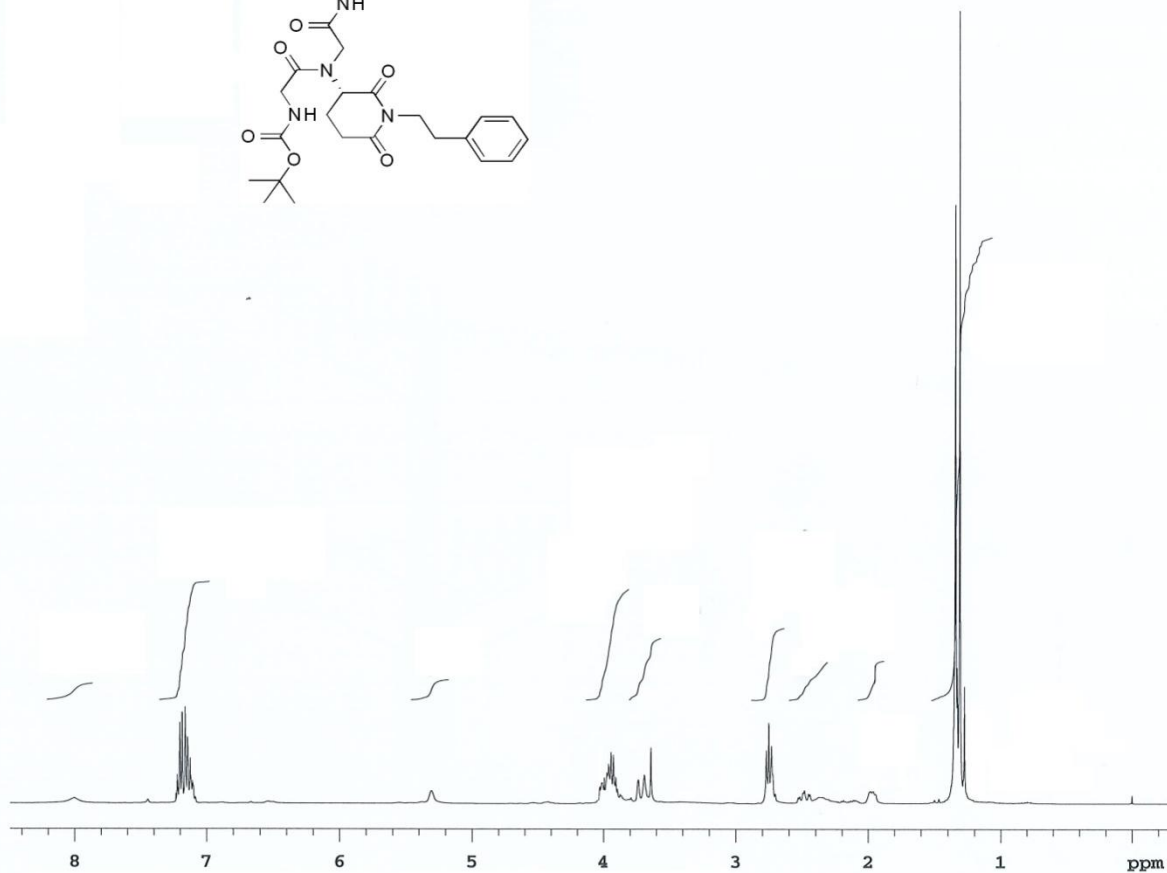
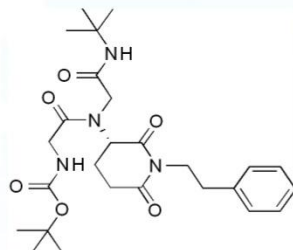


Figure S9: ^1H NMR spectrum of compound **6b**.

WNF_gln05/CDC13/13C

Wed Jun 29 10:42 2011
duration: 0h 7min

exp2 Carbon

```
SAMPLE
date Jun 29 2011
samplename WNF_gln-
04
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoK
seqfil s2pul
sfrq 100.569
tn C13
at 1.357
np 65536
sw 24154.6
bs 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 2048
ct 112
alock n
gain not used
FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dfrq 399.917
homo n
dpr 39
dof 0
dm YYY
dmm w
dmf 9300
pp 14.8
PROCESSING
lb 0.80
wtfile
proc ft
fn 65536
wexp procplot
DISPLAY
sp -1536.9
vp 24153.9
vs 153
sc 0
wc 225
hmm 107.35
rf1 9280.7
rfp 7743.0
th 5.2
rp 157.2
lp -238.9
nm cdc ph
```

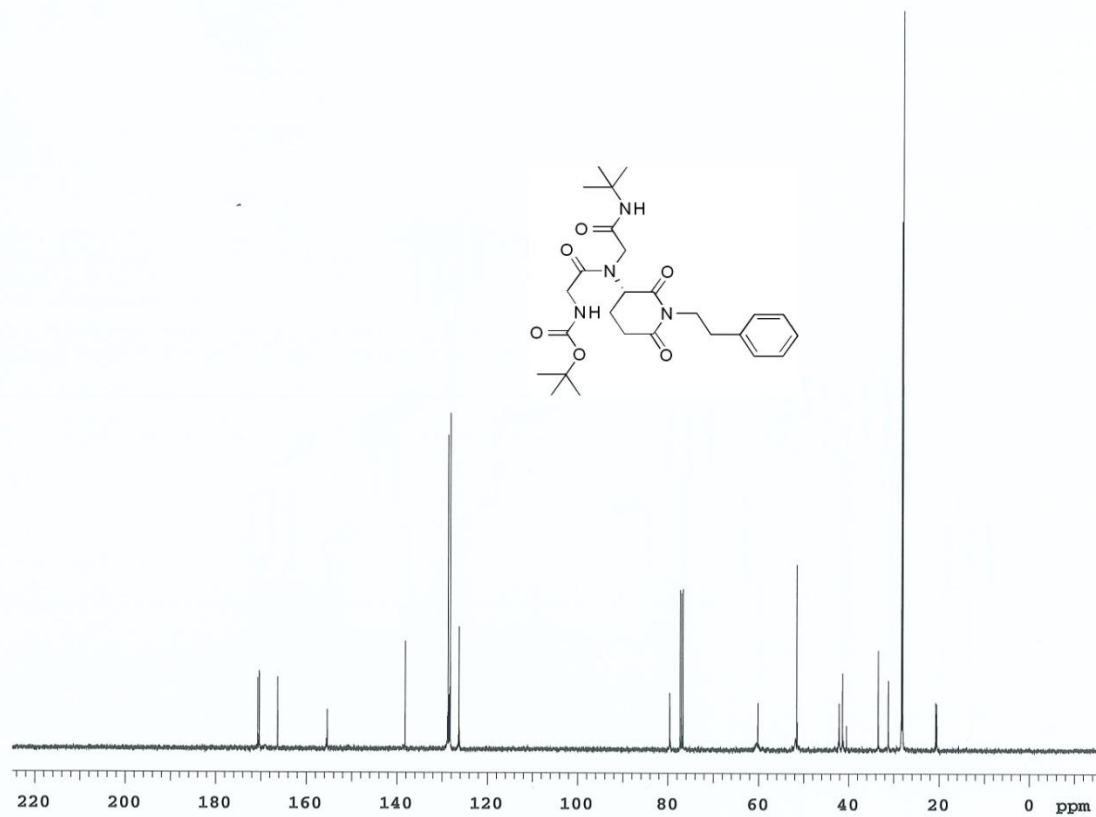
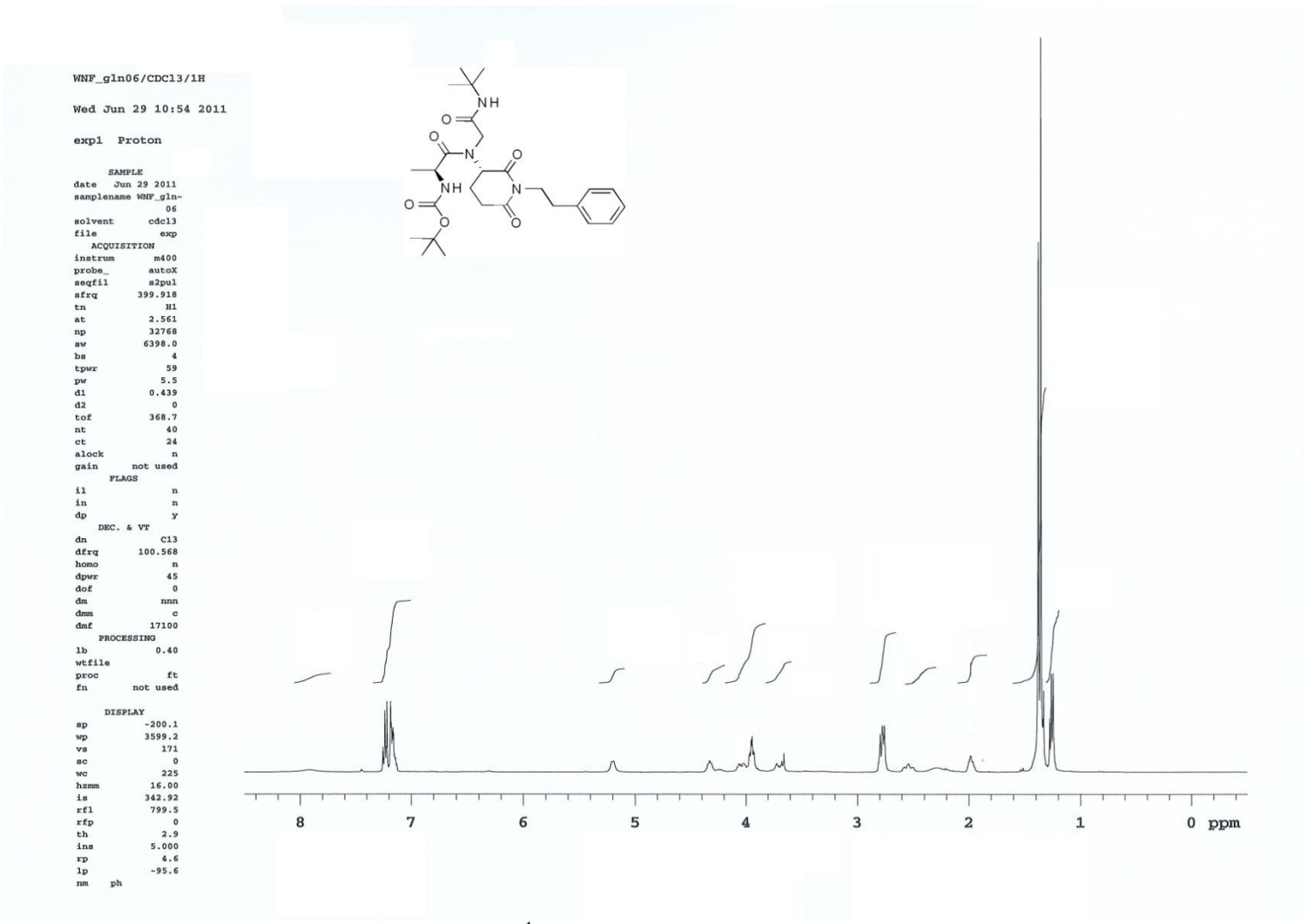


Figure S10: ^{13}C NMR spectrum of compound **6b**.



WNF_gln06/CDC13/13C

Wed Jun 29 10:55 2011
duration: 0h 7min

exp2 Carbon

```
SAMPLE
date Jun 29 2011
samplename WNF_gln-
06
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.569
tn c13
at 1.357
mp 65536
sv 24154.6
hs 16
tpwr 59
pw 5.7
d1 2.143
d3 0
tof 1020.6
nt 2048
ct 112
alock n
gain not used
PLAGE
il n
in n
dp y
dn DEC. & VT H1
dfrq 399.917
homo n
dprw 39
dof 0
dm yyy
dmm w
dmf 9300
pp 14.8
PROCESSING
lb 0.80
wfile
proc Ft
fn 65536
wexp procpilot
DISPLAY
sp -1533.7
wp 24153.9
vs 151
sc 0
wc 225
hzmm 107.35
rfl 9277.5
zfp 7743.0
th 5.7
rp 154.3
lp -236.3
nm edc ph
```

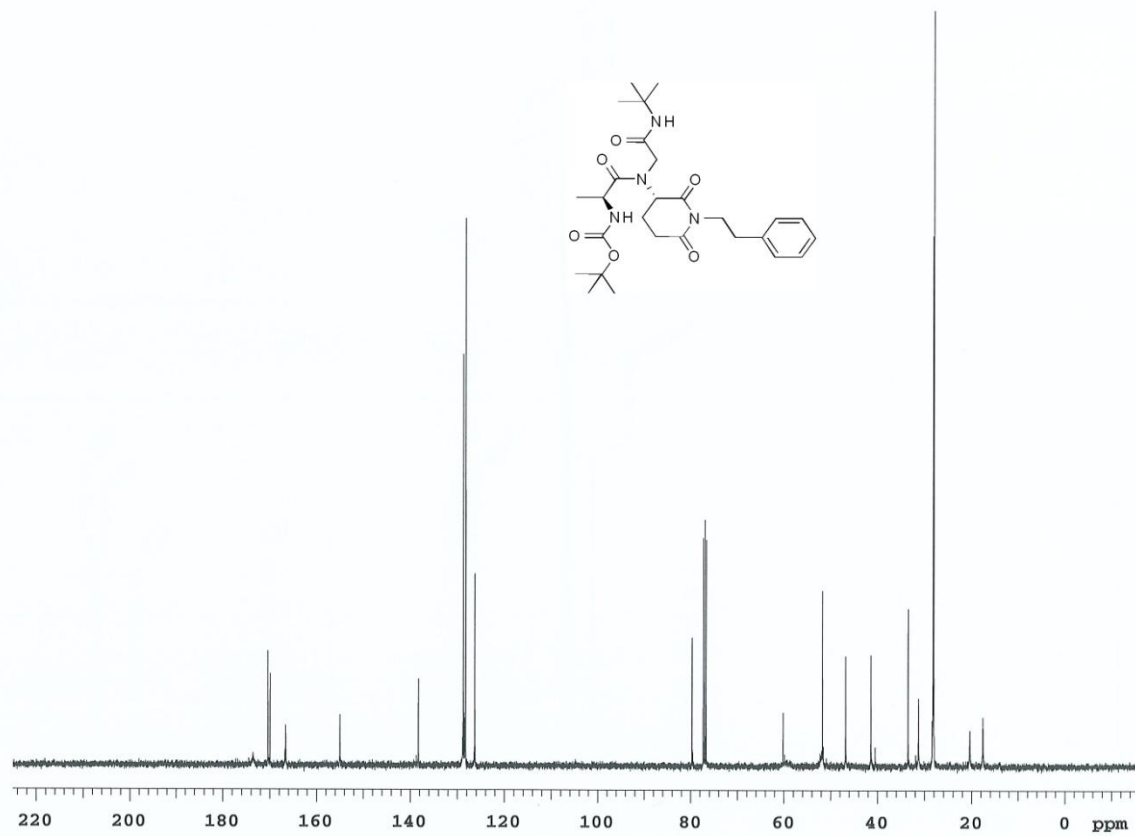


Figure S12: ^{13}C NMR spectrum of compound **6c**.

WNF_gln10/CDC13/1H
Wed Jun 29 11:49 2011

expl Proton

SAMPLE
date Jun 29 2011
samplename WNF_gln-
10
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 399.918
tn H1
at 2.561
np 32768
sw 6398.0
bs 4
tpwr 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 8
alock n
gain not used

FLAGS
il n
in n
dp y
DEC. & VT
dn C13
dfrq 100.568
homo n
dpwr 45
dof 0
dm nmn
dmm c
dmf 17100
PROCESSING
lb 0.40
wtfile
proc ft
fn not used

DISPLAY
sp -200.1
wp 3799.2
va 162
sc 0
wc 225
hmm 16.89
is 377.06
rfl 799.5
rfp 0
th 2.9
ins 5.000
rp 4.6
lp -99.9
nm ph

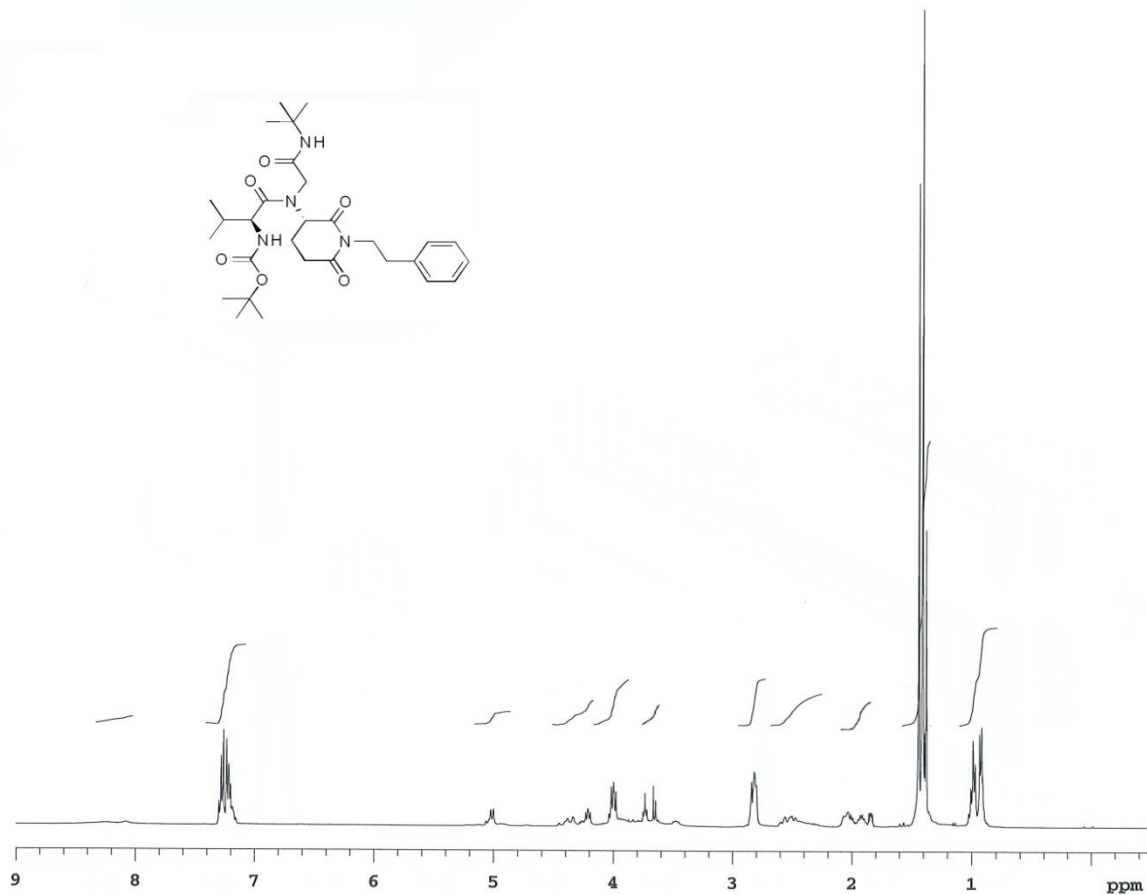
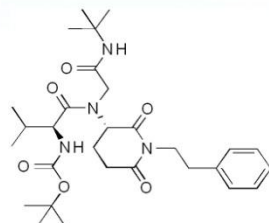


Figure S13: ¹H NMR spectrum of compound 6d.

WNF_gln10/CDC13/13C

Wed Jun 29 11:50 2011
duration: 1h 3min

exp2 Carbon

```
SAMPLE
date Jun 29 2011
samplename WNF_gln-
09
solvent cdc13
file exp
ACQUISITION
instrum m400
probe autoX
seqfil s2pul
sfrq 100.569
tn C13
at 1.357
np 65536
sw 24154.6
hs 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 2048
ct 1008
alock n
gain not used
FLAGS
il n
in n
dp y
dn DEC. & Vr H1
dfrq 399.917
homo n
dpwr 39
dof 0
dm yyy
dum w
dmf 9300
pp 14.8
PROCESSING
lb 0.80
wtfile
proc ft
fn 65536
wexp procp1ot
DISPLAY
sp -1517.9
wp 24153.9
vs 146
sc 0
wc 225
hzsm 107.35
rf1 1518.6
rfp 0
th 68.3
rp 164.8
lp -275.9
nm cdc ph
```

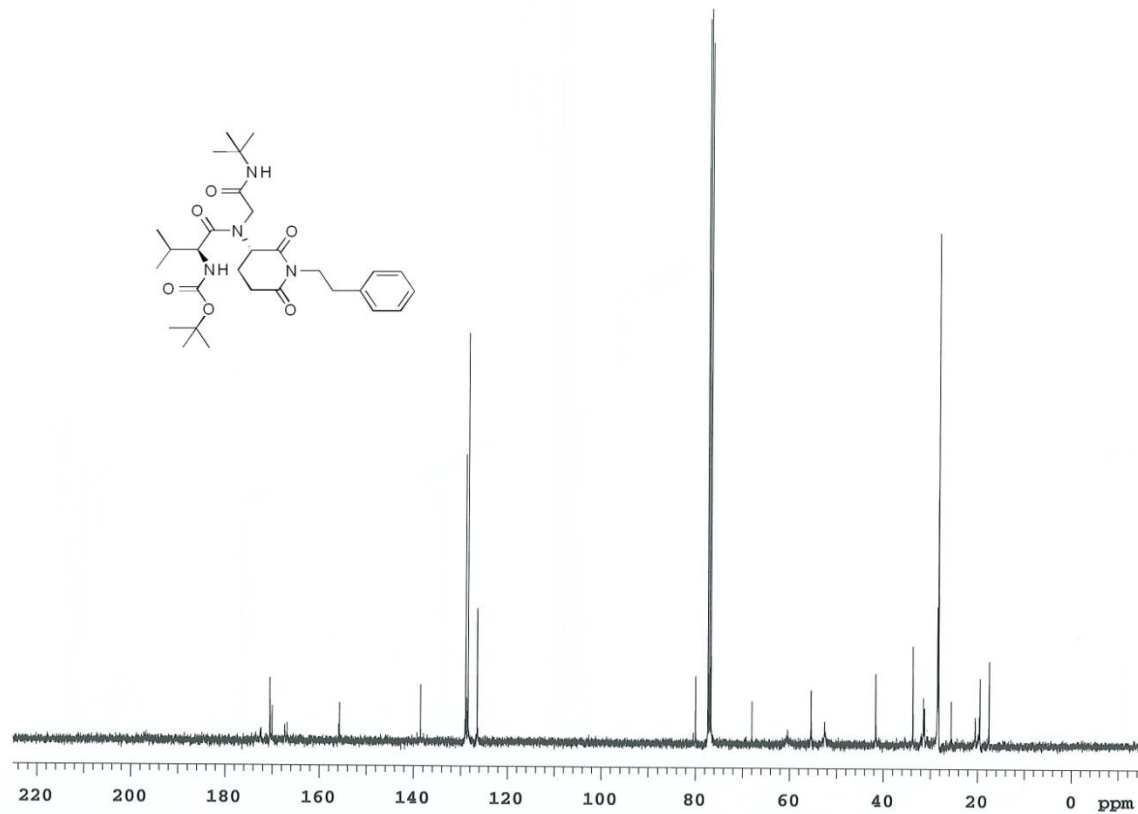


Figure S14: ^{13}C NMR spectrum of compound **6d**.

WNF_gln08/CDC13/1H
Wed Jun 29 11:24 2011
exp1 Proton

SAMPLE
date Jun 29 2011
samplename WNF_gln-
08
solvent cdcl3
file exp

ACQUISITION
instrum m400
probe autoX
seqfil s2pul
sfrq 399.918
tn H1
at 2.561
np 32768
sw 6398.0
ds 4
tpwr 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 12
slock n
gain not used

FLAGS
il n
in n
dp y

DEC. & VT
dn C13
dfrq 100.568
homo n
dpwr 45
dof 0
dm nnn
dms c
dmf 17100

PROCESSING
lb 0.40
wtfile
proc ft
fn not used

DISPLAY
sp -91.1
vp 3446.6
vs 168
sc 0
wc 225
hzm 15.32
is 347.71
xfl 816.2
xrp 0
th 2.9
ins 5.000
rp 2.9
lp -89.6
rm ph

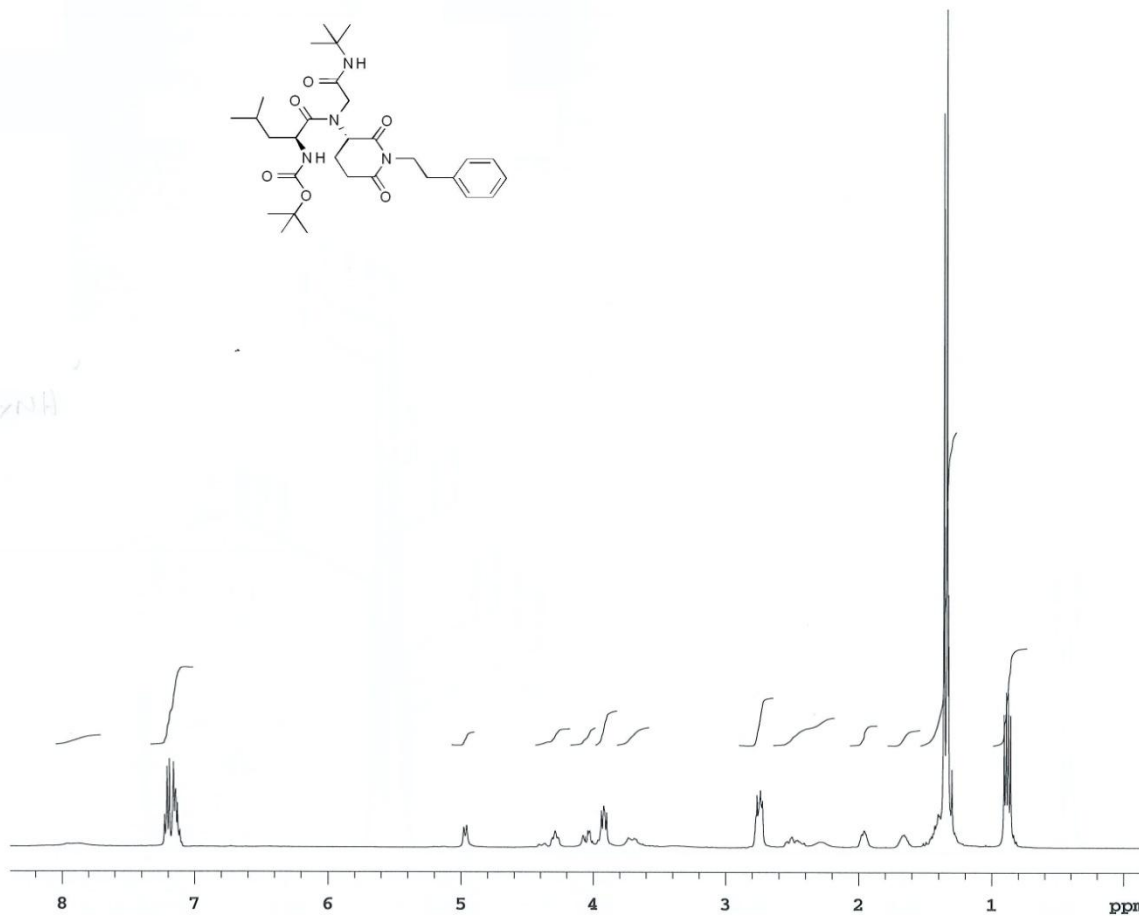
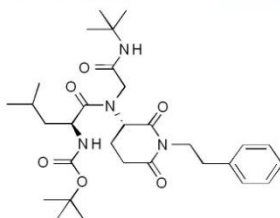


Figure S15: ^1H NMR spectrum of compound **6e**.

WNF_gln08/CDC13/13C

Wed Jun 29 11:25 2011
duration: 0h 5min

exp2 Carbon

```
SAMPLE
date Jun 29 2011
samplename WNF_gln-
07
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.569
tn C13
at 1.357
np 65536
sw 24154.6
bs 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 2048
ct 80
alock n
gain not used
FLAGS
il n
in n
dp Y
DEC. & VT
dn H1
dfrq 399.917
homo n
dpwr 39
dof 0
dm YYY
dmm w
dmf 9300
dp 14.8
PROCESSING
lb 0.80
wefile
proc ft
fn 65536
wexp proplot
DISPLAY
sp -1530.6
vp 24153.9
vs 144
ac 0
vc 235
hnm 107.35
rfl 9274.4
rfd 7743.0
th 2.6
xp 153.9
lp -243.7
nm cdc ph
```

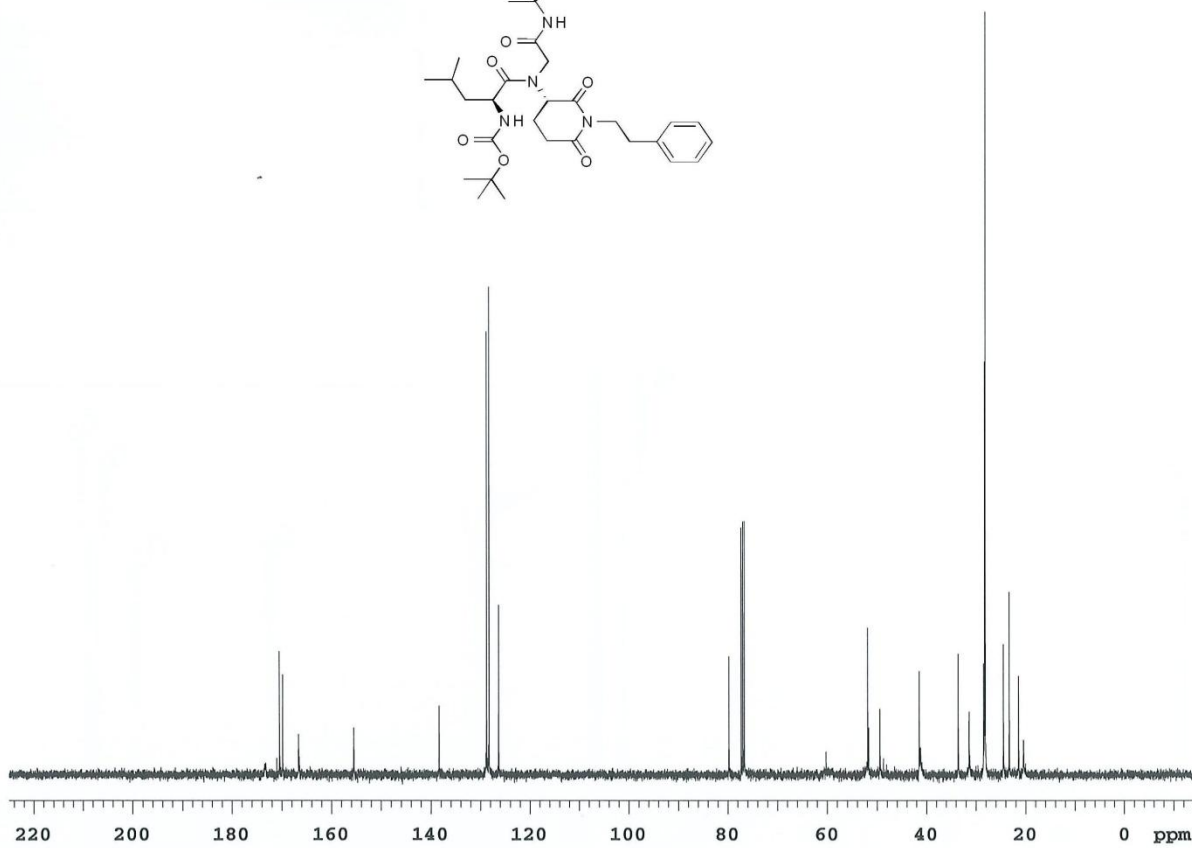
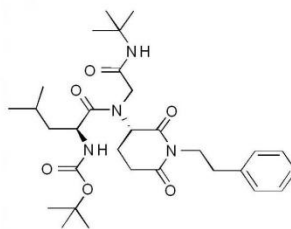


Figure S16: ^{13}C NMR spectrum of compound **6e**.

WNF_gln08/CDC13/13C

Wed Jun 29 11:25 2011
duration: 0h 5min

exp2 Carbon

```
SAMPLE
date Jun 29 2011
samplename WNF_gln-
07
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.629
tn C13
at 1.357
np 65536
sw 24154.6
bs 16
tpwr 59
pw 5.7
dl 2.143
d2 0
cof 1020.6
nt 2048
ct 80
alock n
gain not used
FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dfrq 399.917
homo n
dpwr 39
dof 0
dm yyy
dmm w
dmf 9300
dp 14.8
PROCESSING
lb 0.80
wtfile ft
proc 65536
fn
wexp procplot
DISPLAY
sp -1530.6
wp 24153.9
vs 144
sc 0
wc 225
hzmm 107.35
zfl 9274.4
zfp 7743.0
th 2.6
xp 153.9
lp -243.7
nm cdc ph
```

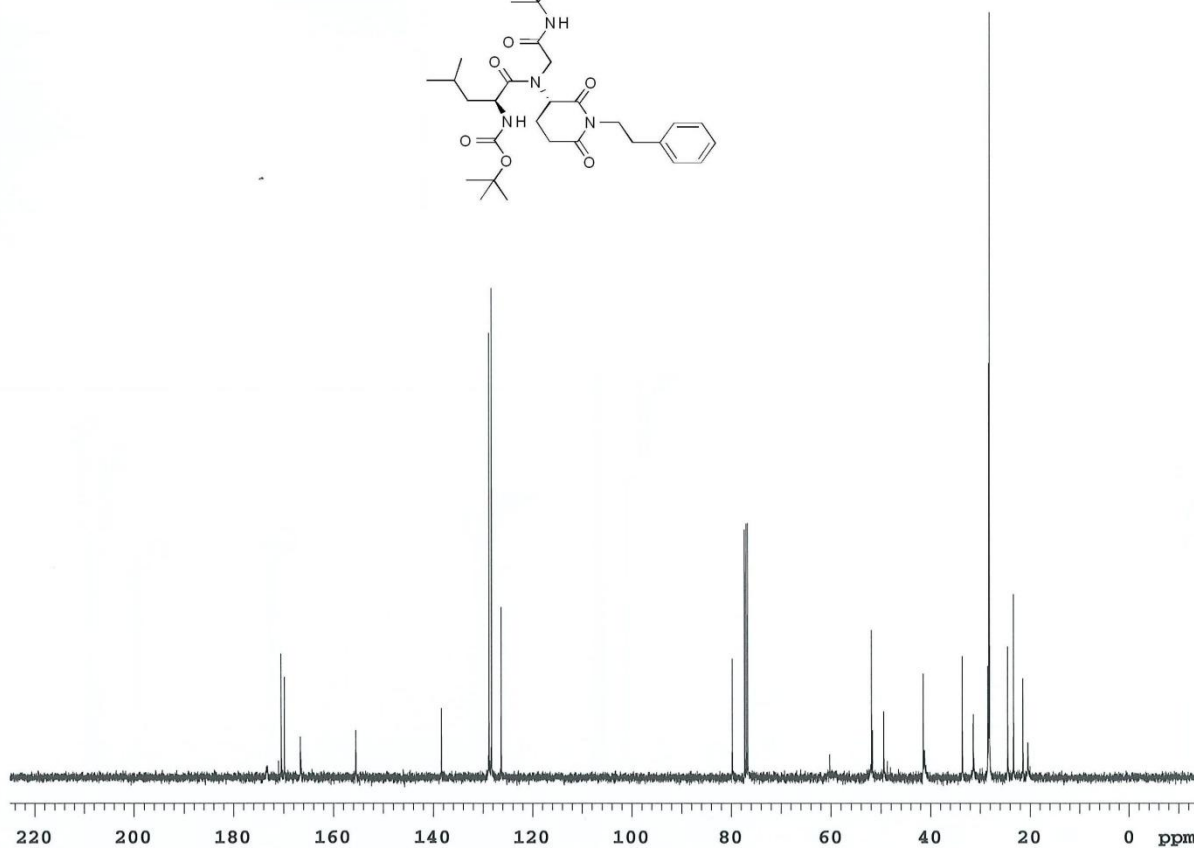
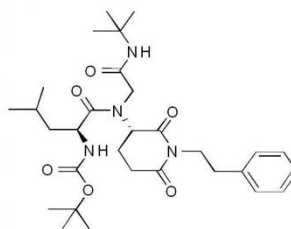


Figure S18: ^{13}C NMR spectrum of compound **6f**.

WNF_gln09/CDCl3/1H

Wed Jun 29 11:35 2011

exp1 Proton

SAMPLE
date Jun 29 2011
samplename WNF_gln-09
solvent cdcl3
file exp

ACQUISITION
instrum m400
probe_ autoX
seqfil #2p01
sfrq 399.916
tn H1
at 2.561
np 32768
sw 6398.0
bs 4
tpwr 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 16
alock n
gain not used

FLAGS
il n
in n
dp y

DEC. & VT
dn C13
dfrq 100.568
homo n
dpwr 45
dof 0
dm nnn
dmf 17100

PROCESSING
lb 0.40
wtfile
proc ft
fn not used

DISPLAY
sp -200.1
wd 3799.2
vs 162
sc 0
wc 225
hzmm 16.89
is 380.81
rf1 799.5
xfp 0
th 2.1
ins 5.000
rp 3.6
lp -97.3
nm ph

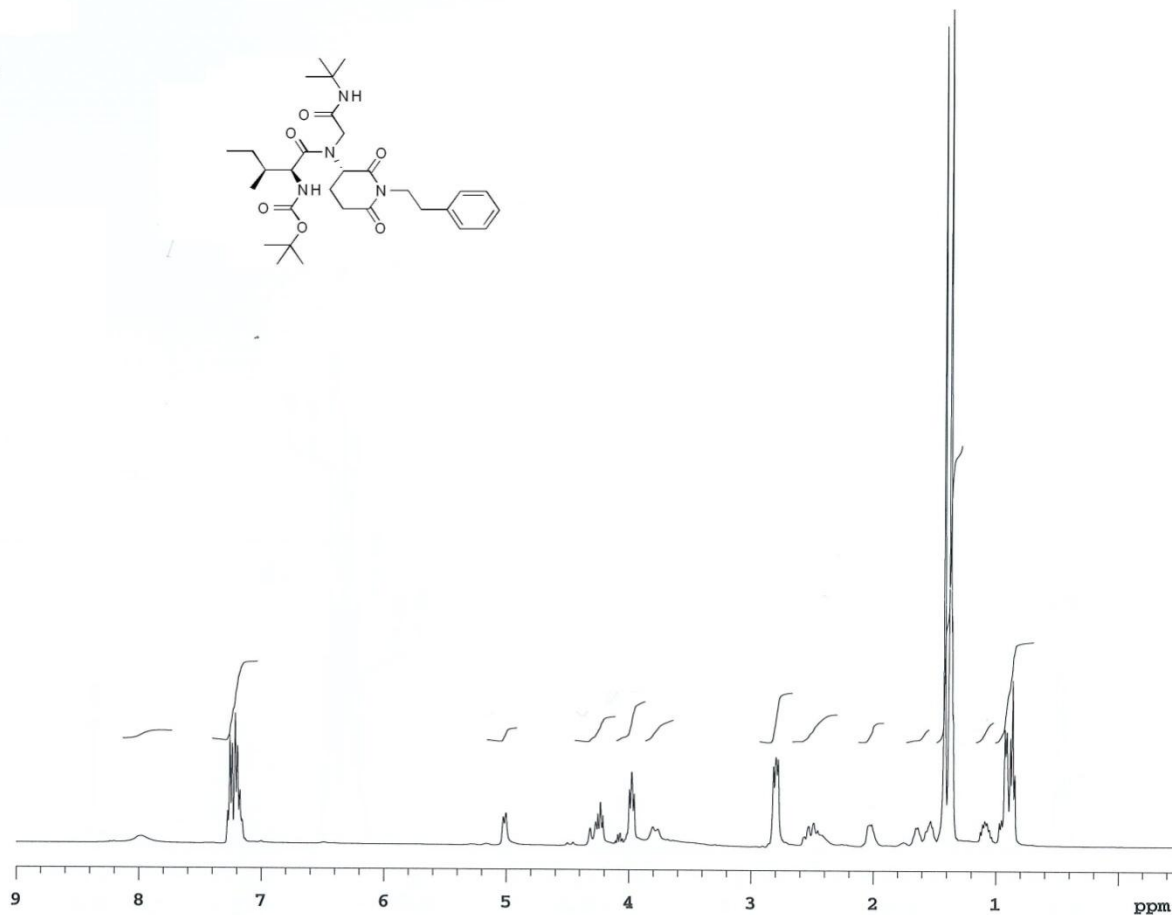


Figure S19: ¹H NMR spectrum of compound 6g.

WNF_gln09/CDC13/13C

Wed Jun 29 11:36 2011
duration: 0h 6min

exp2 Carbon

```
SAMPLE
date Jun 29 2011
samplename WNF_gln-
09
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.569
tn C13
at 1.357
np 65536
av 24154.6
ba 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 2048
ct 96
alock n
gain not used
FLAGS
ii n
in n
dp y
DEC. & VT
dn H1
dfrq 399.917
homo n
dpwr 39
dof 0
dm yyy
dmm w
dmf 9300
dp 14.8
PROCESSING
lb 0.80
wtfile
proc ft
fn 65536
wexp procplot
DISPLAY
sp -1528.3
vp 24153.9
vs 106
sc 0
wc 225
hzmm 107.35
rfl 9272.0
rfp 7743.0
th 6.2
xp 147.5
lp -235.8
nm cdc ph
```

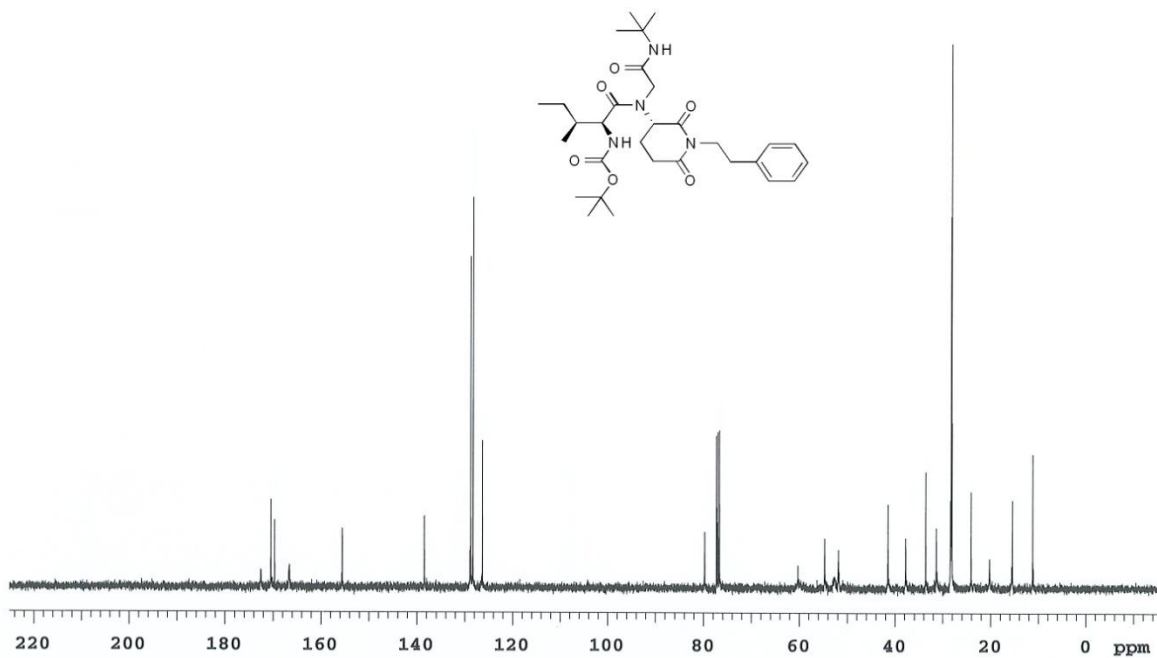
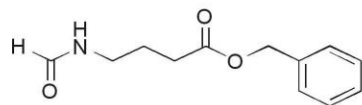


Figure S19: ^{13}C NMR spectrum of compound 6g.

WNF_gln016/CDC13/13C

Tue Aug 16 15:44 2011

exp1 Proton



```
SAMPLE
date Aug 16 2011
samplename WNF_gln-
016
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 399.918
tn H1
at 2.561
np 32768
sw 6398.0
bs 4
tpwr 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 28
alock n
gain not used
FLAGS
il n
in n
dp Y
DEC. & VT
dn C13
dfrq 100.568
homo n
dpwr 45
dof 0
dn nnn
dmm c
dmf 17100
PROCESSING
lb 0.40
wtfile
proc ft
fn not used
DISPLAY
sp -0.1
wp 3999.1
vs 88
sc 0
wc 225
hmm 17.77
is 531.09
rf1 799.5
rfp 0
th 2.9
ins 2.000
rp 9.5
lp -108.7
nm ph
```

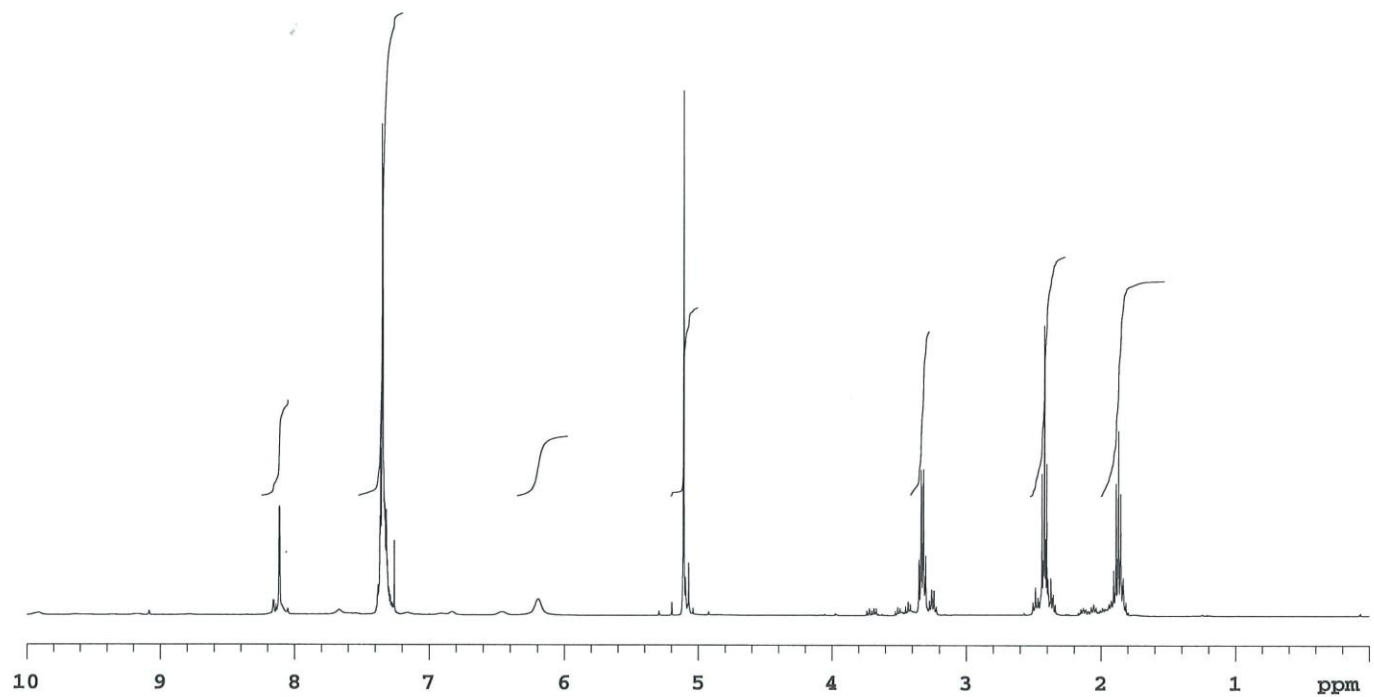


Figure S20: ¹H NMR spectrum of benzyl 4-formamidobutanoate.

WNF_gln016/CDC13/13C

Tue Aug 16 15:46 2011

duration: 2h 38min

exp2 Carbon

```
SAMPLE
date Aug 16 2011
samplename WNF_gln-
016
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.569
tn C13
at 1.357
np 65536
sw 24154.6
bs 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 2048
ct 1568
alock n
gain not used
FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dfrq 399.917
homo n
dpwr 39
dof 0
dm YYY
dmm w
dmf 9300
pp 14.8
PROCESSING
lb 0.80
wtfile
proc ft
fn 65536
wexp procpot
DISPLAY
sp -1523.8
wp 24153.9
vs 87
sc 0
wc 225
hzmm 107.35
rf1 9267.5
rfp 7743.0
th 68.3
rp 158.7
lp -220.1
nm cdc ph
```

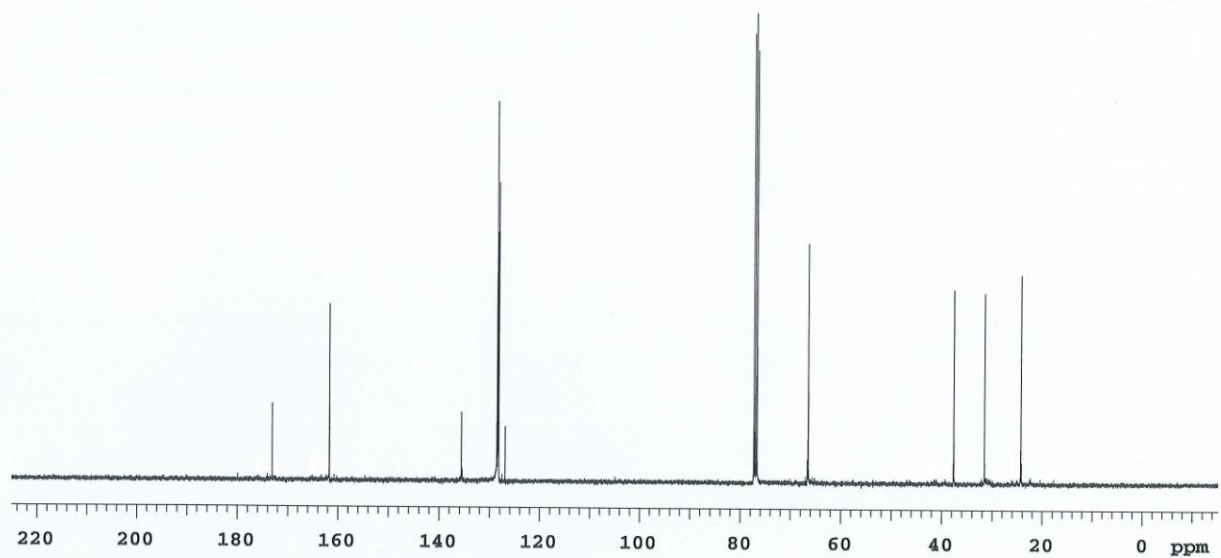
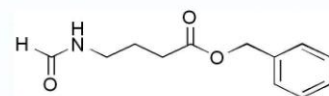


Figure S21: ^{13}C NMR spectrum of benzyl 4-formamidobutanoate.

WNF_gln016/CDCl3/13C

Tue Aug 16 17:33 2011

expt1 Proton

```
SAMPLE
date Aug 16 2011
samplename WNF_gln-
016
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 399.918
tn H1
at 2.561
np 32768
sw 6398.0
hs 4
tpwr 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 12
alock n
gain not used
FLAGS
il n
in n
dp y
DEC. & VT
dn C13
dfrq 100.568
homo n
dpr 45
dof 0
dm nnn
dmm c
dmf 17100
PROCESSING
lb 0.40
wtfile
proc ft
fn not used
DISPLAY
sp -200.1
wp 3599.2
vs 162
sc 0
wc 235
hmm 16.00
is 1312.28
sfl 799.5
sfp 0
th 2.1
ins 2.000
xp -4.7
lp -69.1
nm ph
```

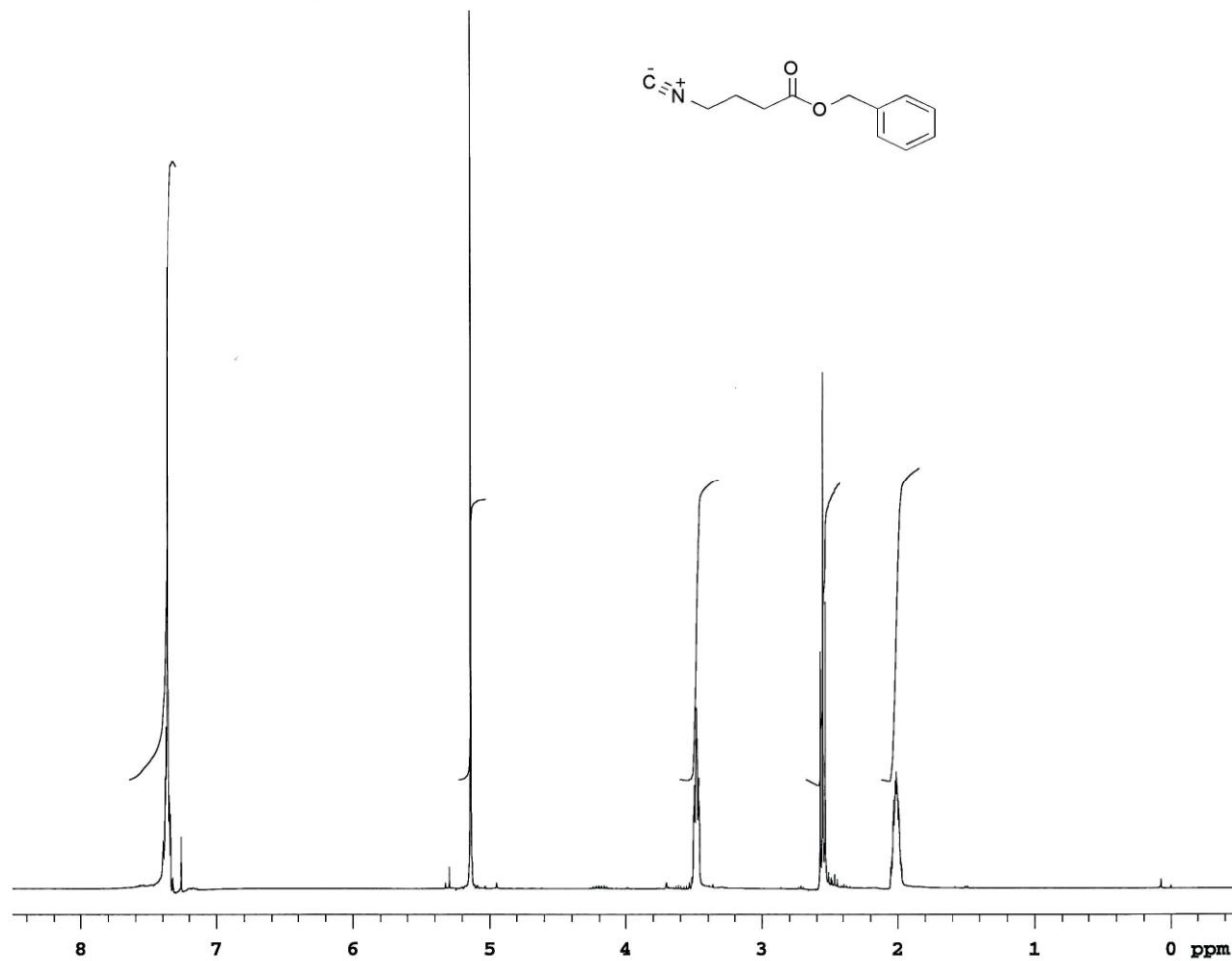


Figure S22: ^1H NMR spectrum of compound 7.

WNF_gln016/CDCl3/13C

Tue Aug 16 17:33 2011
duration: 2h 9min

exp2 Carbon

SAMPLE
date Aug 16 2011
samplename WNF_gln-016
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.569
tn C13
at 1.357
np 65536
sw 24154.6
bs 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 2048
ct 2048
alock n
gain not used
FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dfrq 399.917
homo n
dpr 39
dof 0
dm YYY
dmm w
dmf 9300
pp 14.8
PROCESSING
lb 0.80
wfile
proc ft
fn 65536
wexp procplot
DISPLAY
sp -1523.2
vp 24153.9
vs 80
sc 0
wc 225
hzm 107.35
xfl 9267.0
rfp 7743.0
th 2.1
xp 157.6
lp -219.2
nu cdc ph

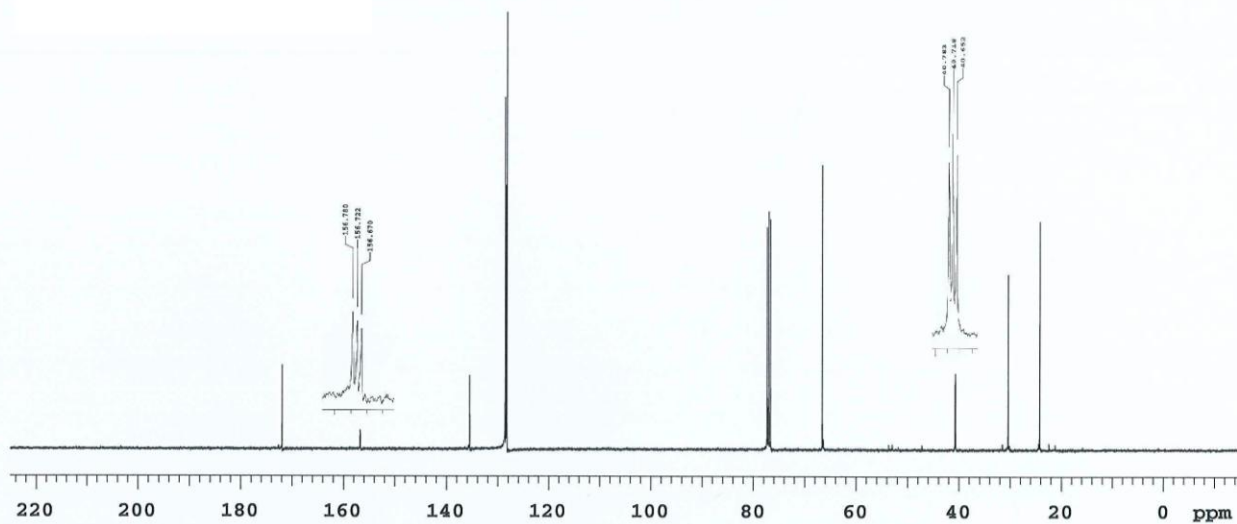
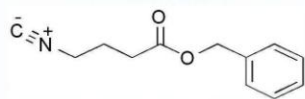


Figure S23: ¹³C NMR spectrum of compound 7.

WNF_gln_11/CDCl3/1H
 Fri Aug 5 10:34 2011
 expl Proton

SAMPLE
 date Aug 5 2011
 samplename WNF_gln-
 _11
 solvent cdcl3
 file exp

ACQUISITION
 instrum m400
 probe_ autoX
 seqfil s2pul
 srfq 399.918
 tn H1
 at 2.561
 np 32768
 sw 6398.0
 bs 4
 tpwr 59
 pw 5.5
 d1 0.439
 d2 0
 tof 368.7
 nt 40
 ct 16
 alock n
 gain not used

FLAGS
 il n
 in n
 dp y

DEC. & VT
 dn C13
 dfrq 100.568
 homo n
 dpwr 45
 dof 0
 dm nnn
 dmm c
 dmf 17100

PROCESSING
 lb 0.40
 wtfile
 proc ft
 fn not used

DISPLAY
 sp -200.1
 wp 3999.1
 vs 162
 sc 0
 wc 225
 hzmm 17.77
 ia 206.36
 rfl 789.7
 rfp 0
 th 5.8
 ina 2.000
 rp -14.0
 lp -95.2
 nm ph

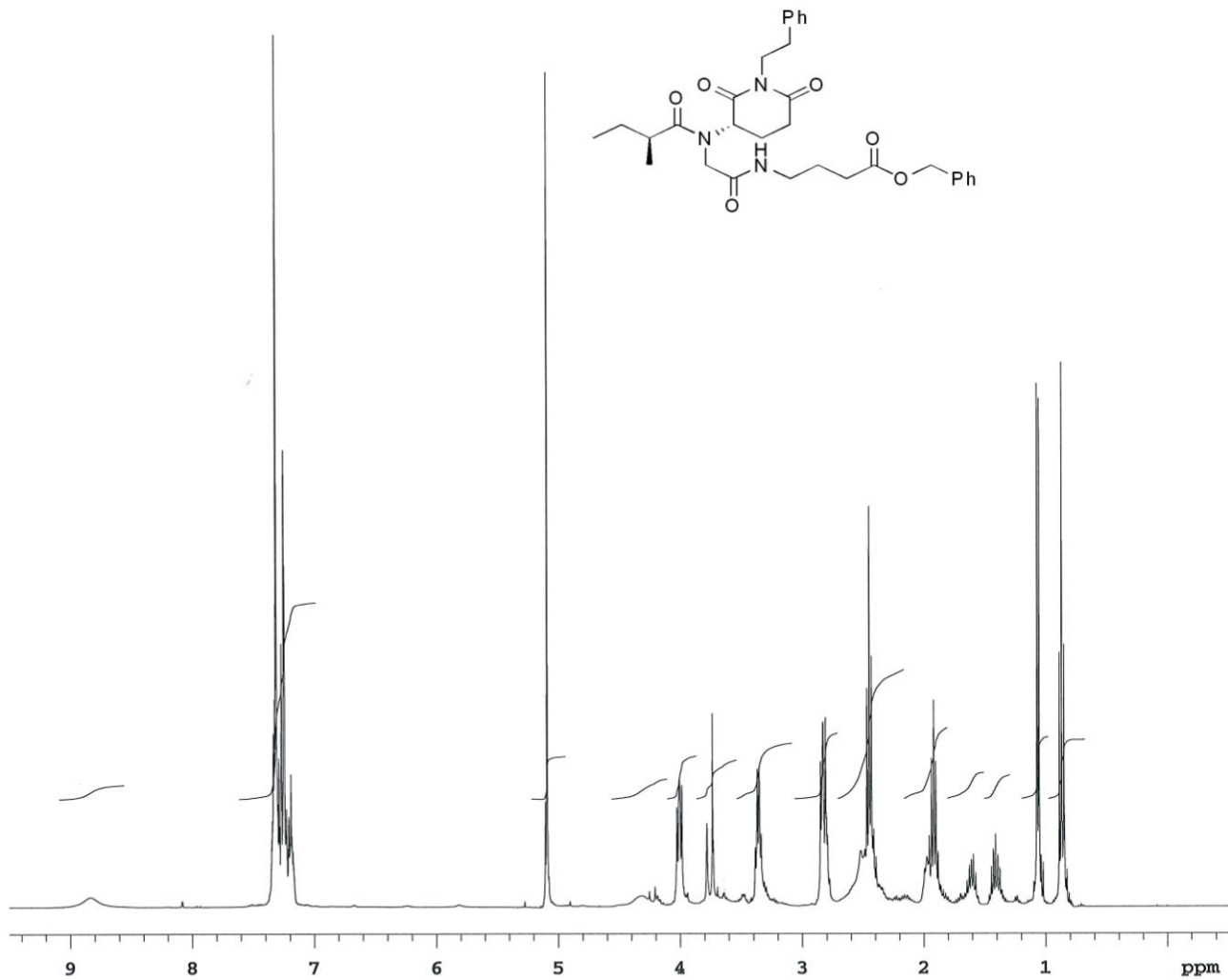


Figure S24: ¹H NMR spectrum of compound 8.

WNF_gln_11/CDC13/13C

Fri Aug 5 10:35 2011
duration: 0h 21min

exp2 Carbon

SAMPLE
date Aug 5 2011
samplename WNF_gln-
_11
solvent cdcl3
file exp

ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.569
tn C13
at 1.357
np 65536
sw 24154.6
bs 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 2048
ct 336
slock n
gain not used

FLAGS
il n
in n
dp y
DEC. & VT
dn H1
dfrq 399.917
homo n
dpwr 39
dof 0
dn YYY
dmm w
dmf 9300
pp 14.8

PROCESSING
lb 0.80
wtfile
proc ft
fn 65536

wexp procplot
DISPLAY
sp -1536.5
vp 24153.9
vs 103
sc 0
wc 225
hzmm 107.35
rfl 9280.3
rfp 7743.0
th 68.3
rp 140.0
lp -211.1
nm cdc ph

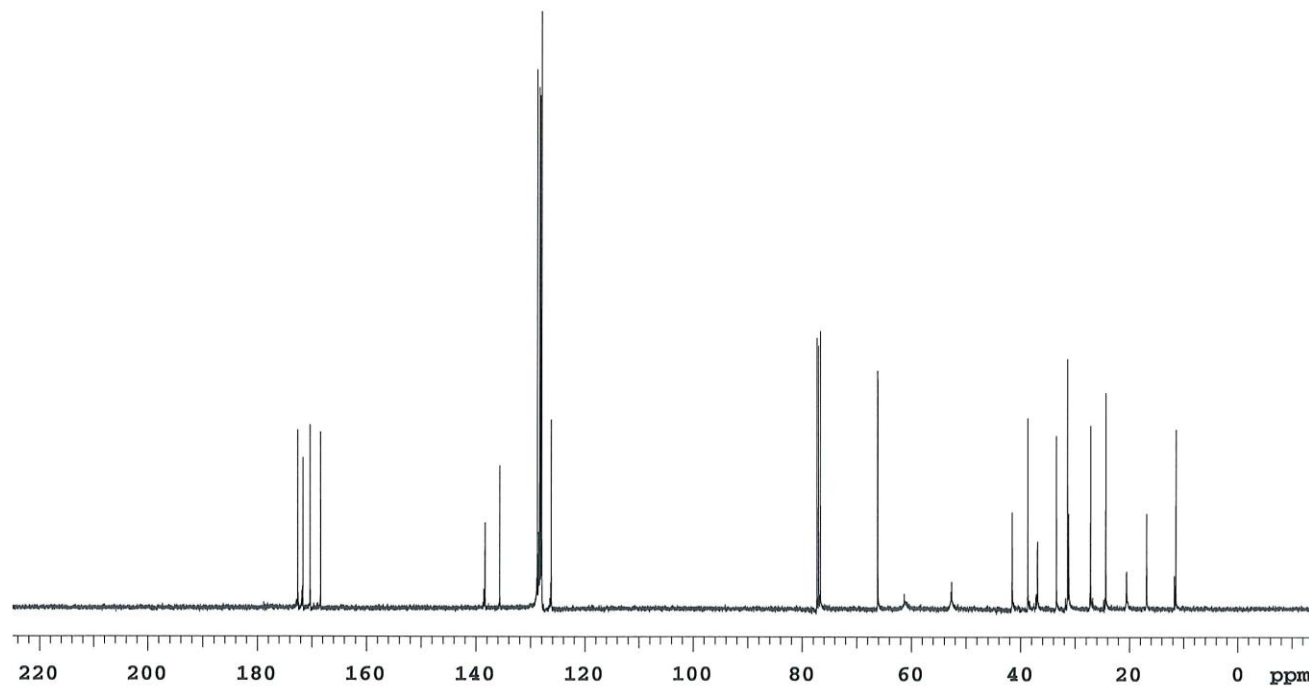
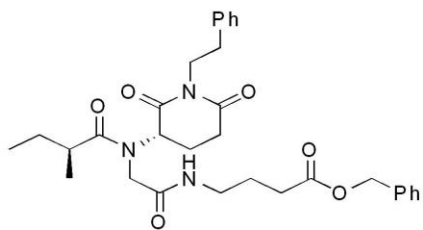


Figure S25: ^{13}C NMR spectrum of compound 8.

WNF_gln014/CDC13/1H

Wed Aug 10 15:55 2011

expl Proton

SAMPLE
date Aug 10 2011
samplename WNF_gln-
014
solvent cdc13
file exp

ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 399.918
tn H1
at 2.561
np 32768
sw 6398.0
bs 4
tpwr 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 24
alock n
gain not used

FLAGS
il n
in n
dp y

DEC. & VT
dn C13
dfrq 100.568
homo n
dprw 45
dof 0
dn nnn
dmm c
dmf 17100

PROCESSING
lb 0.40
wtfile
proc ft
fn not used

DISPLAY
sp -200.3
vp 3999.1
vs 81
sc 0
wc 225
hzmm 17.77
is 399.01
rfl 821.2
rfd 0
th 5.8
ins 3.000
rp 33.1
lp -103.3
nm ph

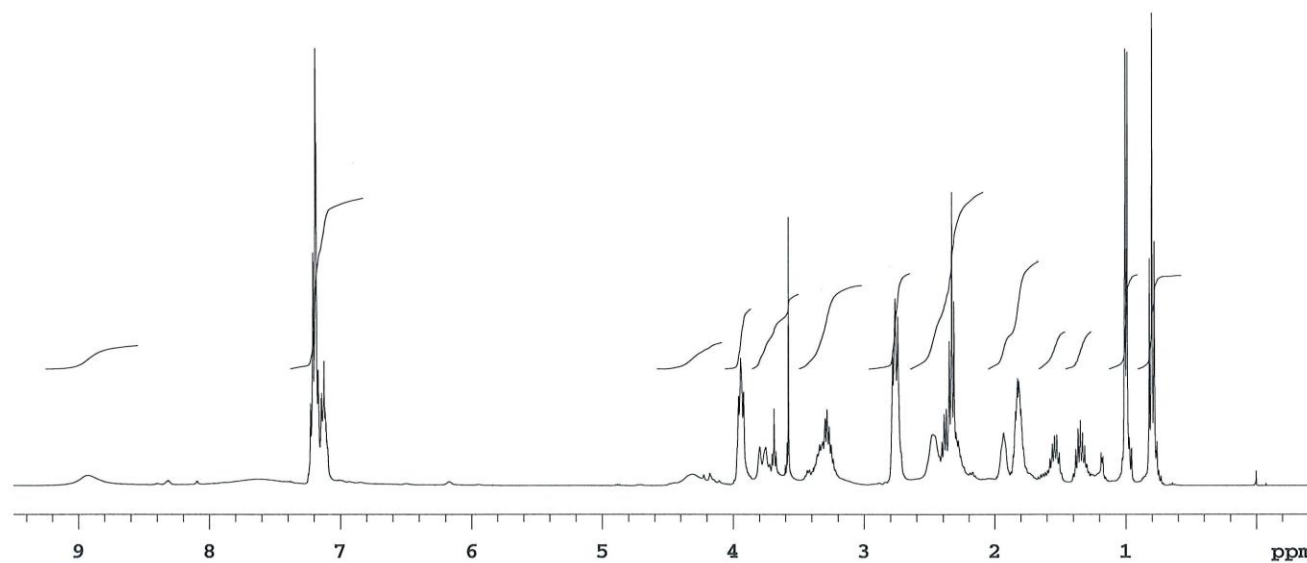
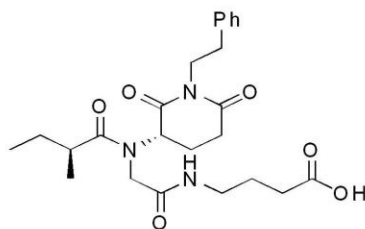


Figure S26: ^1H NMR spectrum of compound **9**.

WNF_gln014/CDC13/13C

Wed Aug 10 15:57 2011

duration: 1h 1min

exp2 Carbon

```
SAMPLE
date Aug 10 2011
samplename WNF_gln-
014
solvent cdcl3
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.569
tn C13
at 1.357
np 65536
sw 24154.6
hs 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 2048
ct 976
alock n
gain not used
FLAGS
il n
in n
dp Y
DEC. & VT
dn H1
dfrq 399.917
homo n
dpwr 39
dof 0
dm YY
dmm w
dmf 9300
pp 14.8
PROCESSING
lb 0.80
wfile
proc ft
fn 65536
wexp procplot
DISPLAY
sp -1524.8
wp 24153.9
vs 92
sc 0
wc 225
hzmm 107.35
rfl 9268.6
rfp 7743.0
th 68.3
rp -148.7
lp -258.0
nm cdc ph
```

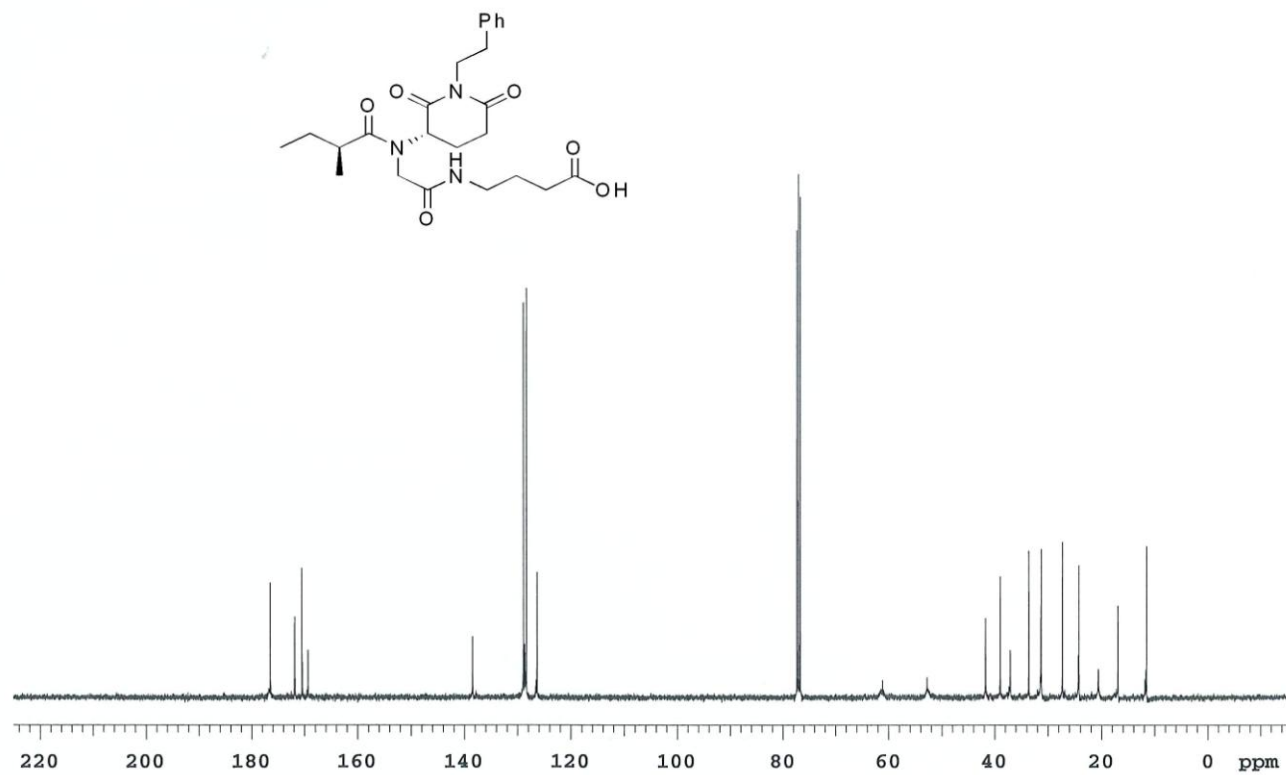


Figure S27: ^{13}C NMR spectrum of compound 9.

WNF_gln016/CDC13/13C

Tue Aug 16 22:09 2011

expl Proton

SAMPLE
date Aug 16 2011
samplename WNF000_-
gln016
solvent cdcl3
file exp

ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 399.918
tn H1
at 2.561
np 32768
sw 6398.0
bs 4
tpwr 59
pw 5.5
d1 0.439
d2 0
tof 368.7
nt 40
ct 40
alock n
gain not used

FLAGS
il n
in n
dp Y

DEC. & VT
dn C13
dfrq 100.568
homo n
dpwr 45
dof 0
dm nnn
dmm c
dmf 17100

PROCESSING
lb 0.40
wtfile
proc ft
fn not used

DISPLAY
sp -200.3
vp 4798.9
vs 91
sc 0
wc 225
hzmm 21.33
is 365.28
rfl 798.2
rfp 0
th 22.1
ins 3.000
rp -10.4
lp -75.6
nm ph

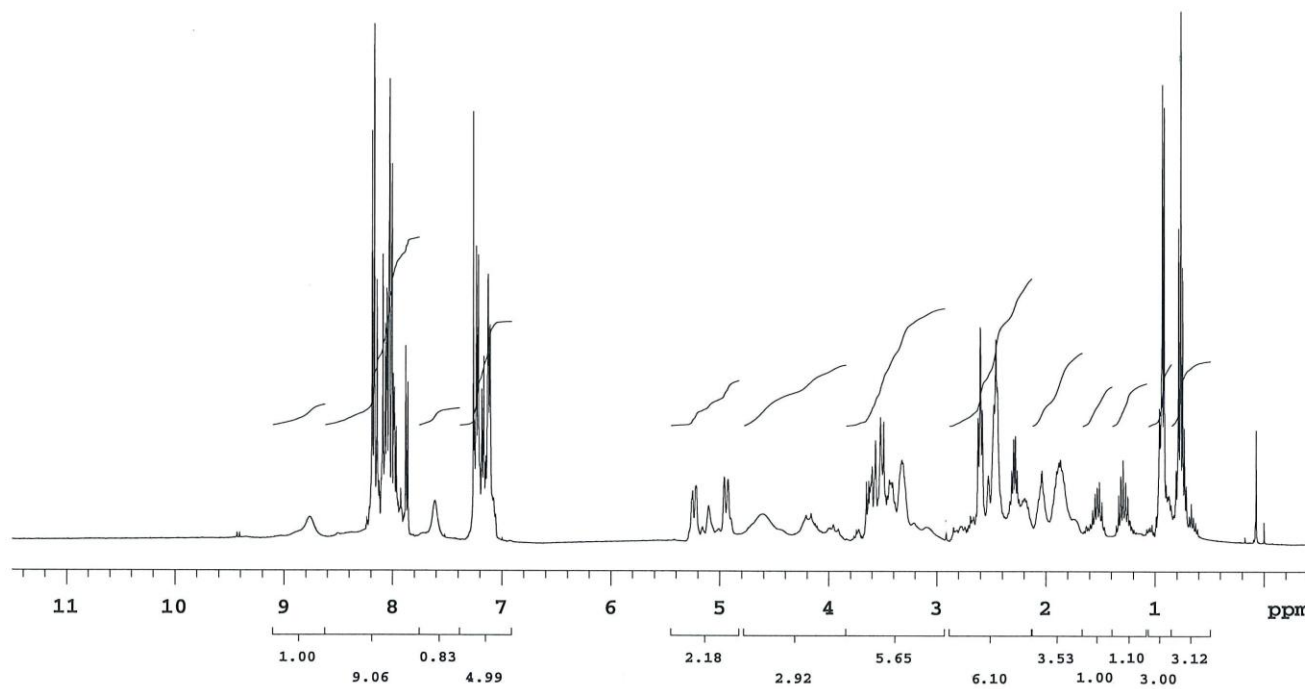
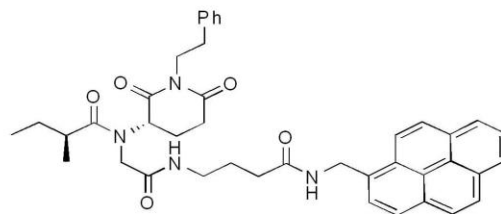


Figure S27: ¹H NMR spectrum of compound 10.

WNF_gln016/CDC13/13C

Tue Aug 16 22:12 2011
duration: 12h 40min

exp2 Carbon

SAMPLE
date Aug 16 2011
samplename WNF_gln-
016
solvent cdc13
file exp
ACQUISITION
instrum m400
probe_ autoX
seqfil s2pul
sfrq 100.569
tn C13
at 1.387
np 65536
sw 24154.6
ba 16
tpwr 59
pw 5.7
d1 2.143
d2 0
tof 1020.6
nt 12000
ct 11104
alock n
gain not used

FLAGS

il n
in n
dp y

DEC. & VT

dm H1
dfrq 399.917
homo n
dpr 39
dof 0
dm YYY
dmm w
dmf 9300
pp 14.8

PROCESSING

lb 0.80
wtfile
proc ft
fn 65536

wexp procp1ot

DISPLAY

sp -1517.9
wp 24153.9
vs 375
sc 0
vc 225
hzmm 107.35
rf1 1518.6
rfp 0
th 68.3
rp 148.5
lp -213.4
nm cdc ph

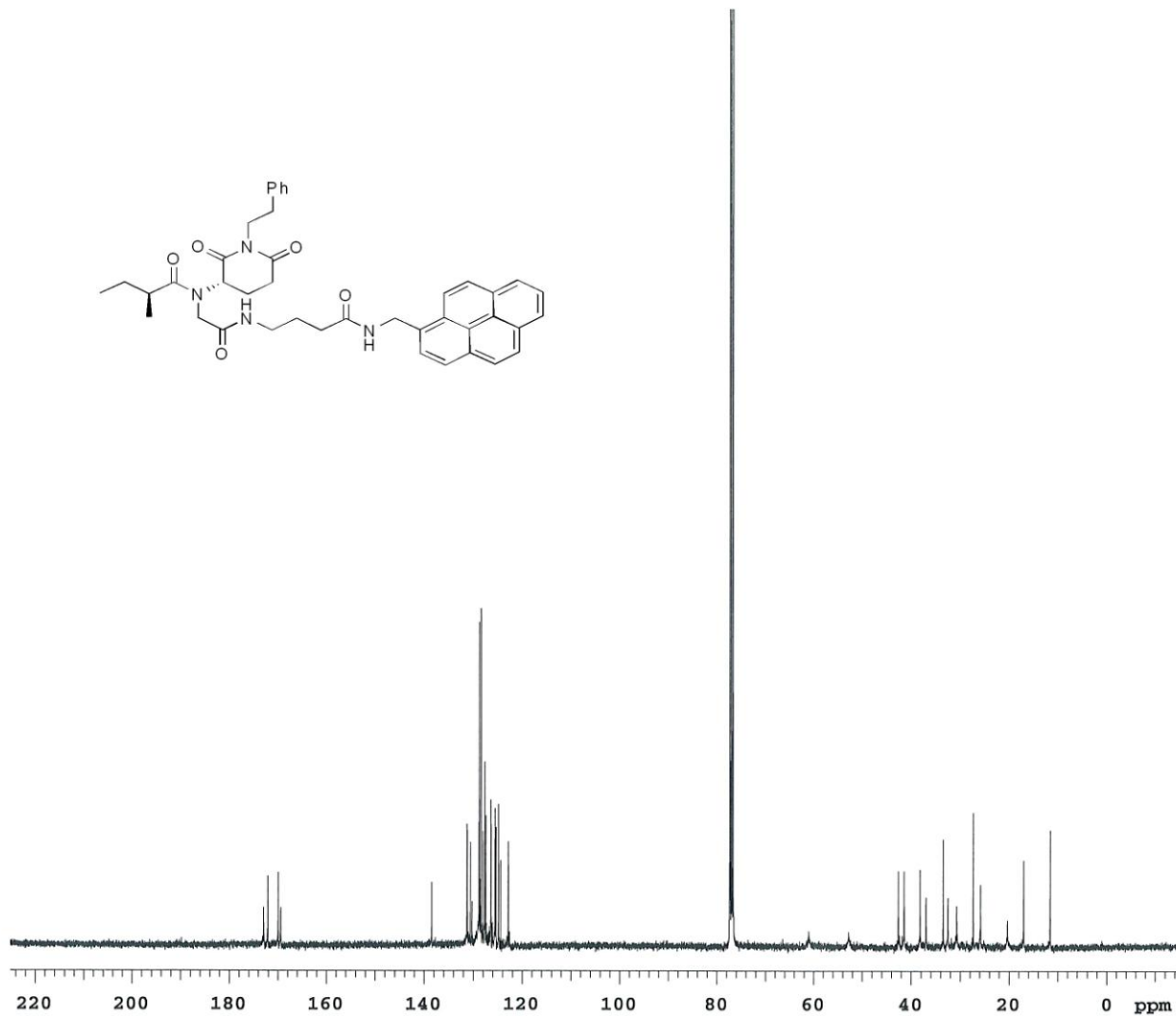


Figure S28: ¹³C NMR spectrum of compound 10.