**Supporting Information**

# Synthesis and Antimicrobial Activity of Binaphthyl-Based, Functionalized Oxazole and Thiazole Peptidomimetics

Steven M. Wales,[a] Katherine A. Hammer,[b] Kittiya Somphol,[a] Isabell Kemker,[a] David C. Schröder,[a] Andrew J. Tague,[a] Zinka Brkic,[a] Amy M. King,[c] Dena Lyras,[c] Thomas V. Riley,[b] John B. Bremner,[a] Paul A. Keller*[a] and Stephen G. Pyne*[a]

[a] *School of Chemistry, University of Wollongong, Wollongong, NSW 2522, Australia*
keller@uow.edu.au
spyne@uow.edu.au

[b] *School of Pathology and Laboratory Medicine, The University of Western Australia, Crawley, WA 6009, Australia*

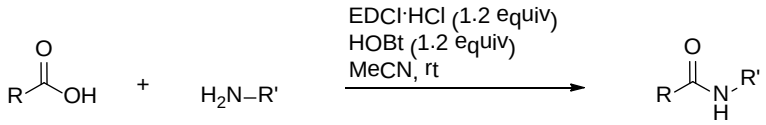
[c] *Department of Microbiology, Monash University, Clayton, VIC 3800, Australia*

## Table of Contents

**Synthesis and Characterization Methods.** All reactions were carried out in standard laboratory glassware with magnetic stirring. Thin layer chromatography (TLC) was performed on aluminum-backed 0.20 mm silica gel plates. Visualization was accomplished with UV light, a ninhydrin staining solution in *n*-butanol and/or an aqueous ceric ammonium molybdate solution. Flash chromatography and silica pipette plugs were performed under positive air pressure using Silica Gel 60 of 230−400 mesh (40−63 μm). Optical Rotations were measured at 25 °C in the specified solvent with a path length of 1.0 dm on a Jasco P-2000 Digital Polarimeter (λ = 589 nm). Concentrations (*c*) are given in g/100 mL. Proton and carbon magnetic resonance spectra ($^1$H NMR and $^{13}$C NMR) were recorded on a Varian Mercury 300 MHz spectrometer, a Varian Inova 500 MHz spectrometer or a Varian VNMRS PS54 500 MHz spectrometer. Spectra aquired in $CDCl_3$ are reported relative to tetramethylsilane ($^1$H: δ = 0.00 ppm) and solvent resonance ($^{13}$C: δ = 77.0 ppm). Spectra acquired in $CD_3OD$ are reported relative to solvent resonance ($^1$H: δ = 3.31 ppm; $^{13}$C: δ = 49.0 ppm). $^1$H NMR data are reported as follows: chemical shift, multiplicity (abbreviations: s = singlet, bs = broad singlet, d = doublet, bd = broad doublet, app. d = apparent doublet, dd = doublet of doublets, ddd = doublet of doublets of doublets, t = triplet, app. t = apparent triplet, q = quartet, ABq = AB quartet, quin = quintet, sex = sextet, sep = septet, m = multiplet and bm = broad multiplet), coupling constant (Hz) and integration. Infrared (IR) spectra were obtained on a Shimadzu IRAffinity-1 FTIR Spectrometer with neat samples. Low resolution mass spectrometry (MS) was performed on a Shimadzu LC-2010 Electrospray Ionization (ESI) Mass Spectrometer. High resolution mass spectrometry (HRMS) was performed on a Waters Quadrupole-Time of Flight (QTOF) Xevo Spectrometer via ESI with Leucine-Enkephalin as an internal standard. For isolated ammonium salts of basic amino compounds, "M" refers to the mass of the corresponding *neutral* molecule. High performance liquid chromatography (HPLC) was performed on a reverse-phase Phenomenex C18 column (φ = 4.6 × 150 mm) using water/acetonitrile (both containing 0.1% TFA) as the mobile phase at a flow rate of 1.0 mL/min, with a detection wavelength (λ) of 254 nm.

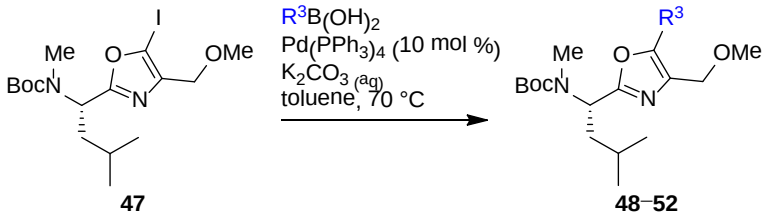
**Synthesis Materials.** Nitrogen ($N_2$) was dried by passage through self-indicating silica gel (2−4 mm bead size). Unless otherwise noted, anhydrous solvents (obtained from commercial sources) were utilized. Carboxylic acid **A** was prepared according to a published procedure.[S1] Other known reagents that were not obtained commercially were prepared according to literature procedures cited within. All other reagents were purchased reagent grade and used as received.

**General Synthetic Procedures 1−4**

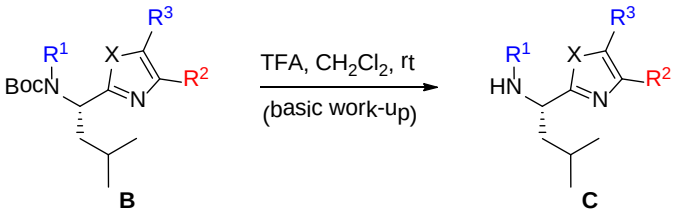



***General Procedure 1 for Amide Bond Formation:*** A reaction vessel was charged in air with the carboxylic acid (1.0 equiv), EDCI·HCl (1.2 equiv), HOBt (1.2 equiv) and the amine (1.0−1.3 equiv). If the latter was an ammonium salt, a slight excess of $NEt(i\text{-}Pr)_2$ was also added. To this was added HPLC grade MeCN to a concentration of 0.2−0.3 M in the carboxylic acid (unless otherwise specified) and the resulting mixture was stirred at rt in an air atmosphere until TLC analysis indicated complete consumption of the carboxylic acid. After removal of the solvent under reduced pressure (for reactions with less than 5 mL of MeCN this is not necessary), the residue was dissolved in EtOAc (20 mL for reactions with ≤1 mmol of acid; or 20 mL/mmol of acid for larger scale) and washed sequentially with 1 M HCl (2×20 mL; to remove any excess amine, EDCI and the urea by-product), saturated $NaHCO_3$ (2×20 mL; to remove HOBt) and brine (20 mL). The organic layer was

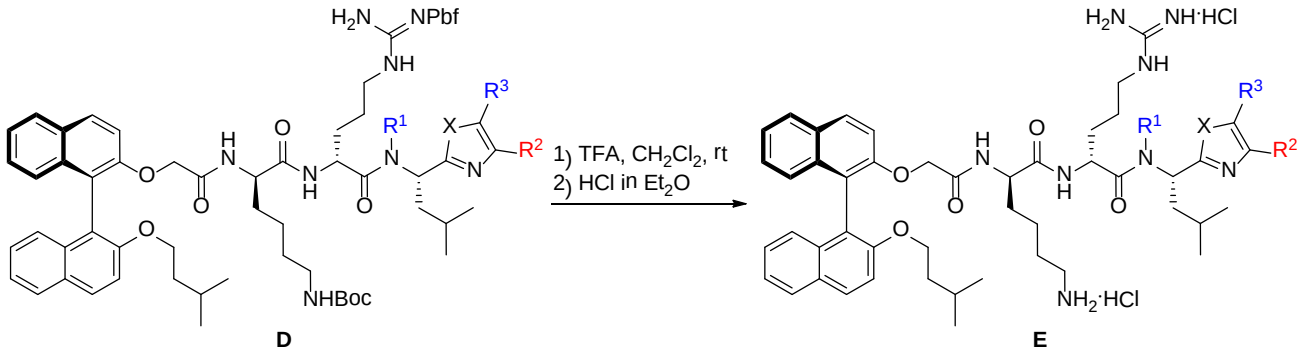
dried ($MgSO_4$) and concentrated under reduced pressure. If required, purification was carried out by flash chromatography with the indicated eluent.




***General Procedure 2 for Suzuki Coupling of Oxazole 47:*** A mixture of iodinated compound **47** (1.0 equiv), a boronic acid (1.0 equiv), aqueous $K_2CO_3$ (2 M, 2.0 equiv), $Pd(PPh_3)_4$ (10 mol %) and toluene (20 mL/mmol of **47**) was heated at 70 ºC under $N_2$ for 7−72 h. After cooling to rt, EtOAc (20 mL) was added, followed by 1 M NaOH (20 mL). The organic layer was separated and the aqueous layer further extracted with EtOAc (20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated. Flash chromatography gave the desired C−C coupling product.




***General Procedure 3 for Boc Deprotection of Type B Oxa(thia)zoles:*** To a solution of the Boc-protected compound **B** (1.0 equiv) in reagent grade $CH_2Cl_2$ (1.0 mL/0.10 mmol of substrate) was added neat TFA (15.0 equiv) and the solution was stirred at rt in an air atmosphere until TLC analysis (ninhydrin staining solution) indicated complete consumption of the starting material (reaction times typically 2−6 h). The mixture was diluted with $CH_2Cl_2$ (15 mL) and 1 M NaOH (15 mL). The organic layer was separated and the aqueous layer further extracted with $CH_2Cl_2$ (15 mL). The combined organic layers were dried ($Na_2SO_4$) and concentrated under reduced pressure to provide the desired amine **C** with no further purification necessary. In cases where an aqueous work-up was not performed (noted within), at the completion of the reaction, the $CH_2Cl_2$ and excess TFA were removed under reduced pressure. Further drying under high vacuum for several hours provided the corresponding amine·TFA salts, with a small amount of persistent residual TFA in most cases (obtained masses were ≤120% of theoretical). This was inconsequential for analytical characterization (NMR, MS) and subsequent use in peptide coupling reactions.



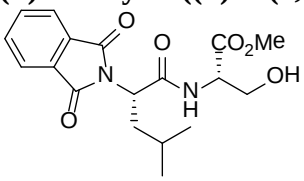

D E

***General Procedure 4 for Pbf/Boc Deprotection of Type D Peptidomimetics:*** To a solution of the *N*-protected peptide **D** in reagent grade $CH_2Cl_2$ (3.3 mL/0.1 mmol of substrate) was added TFA (3.3 mL/0.1 mmol of substrate) and, where specified, $H_2O$ (20 equiv, see the *Note* below), and the solution was stirred at rt in an air atmosphere for 16 h. The solvents were removed under reduced pressure and the residue dried under high vacuum. This was taken up in $CH_2Cl_2$ (~0.5 mL) and an aliquot of excess ethereal HCl (2 M in $Et_2O$, 1.6 mL/0.1 mmol of substrate) was added to exchange the TFA anion with chloride. The mixture was again concentrated and dried under reduced pressure. The remaining sticky solid was dissolved in minimal MeOH (≤10 drops from a Pasteur pipette for ≤0.05 mmol of product) and reagent grade $Et_2O$ (5 mL) was rapidly added, resulting in instantaneous precipitation of the product. The precipitate was collected via vacuum filtration and the original vessel (containing significant product deposited on the glass) and filter cake were washed with $Et_2O$ (3×10 mL). The filter cake was transferred back into the original vessel (containing the remainder of the product) via dissolution with MeOH (~10 mL). Concentration and drying under reduced pressure provided the desired hydrochloride salts **E** as thin films which routinely gave easily-handled powders upon scratching with a spatula.

***Note:*** For larger scale deprotection reactions (>0.1 mmol) and certain substrates (e.g., alcohol **90**), it was *necessary* to add $H_2O$ (20 equiv) from the outset to avoid side reactions resulting from sulfonation of the substrate (net addition of $SO_3H$ at nucleophilic sites). For larger scale reactions, the same work-up and isolation procedure was utilized as described above, except that a second precipitation of the HCl salt from MeOH/$Et_2O$ was required to completely remove the non-volatile by-product: 2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran.

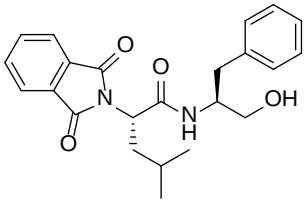
***Synthesis of Type B Protected Amino Oxazoles and Thiazoles***

**(*S*)-Methyl 2-((*S*)-2-(1,3-dioxoisoindolin-2-yl)-4-methylpentanamido)-3-hydroxypropanoate (5)**



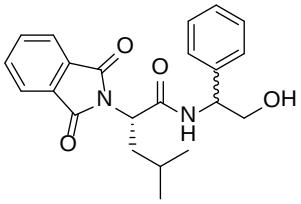
This compound was prepared according to *General Procedure 1* using carboxylic acid **4**[S2] (1.568 g, 6.00 mmol), HCl·H-Ser(L)-OMe (933 mg, 6.00 mmol) and MeCN (60 mL), with added $NEt(i\text{-}Pr)_2$ (1.25 mL, 7.20 mmol). Flash chromatography (100% $CH_2Cl_2$ to 2% MeOH/$CH_2Cl_2$) gave **5** (1.793 g, 82%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.48. This compound was used directly in the next step without further analysis.

**(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-((*S*)-1-hydroxy-3-phenylpropan-2-yl)-4-methylpentanamide (6)**



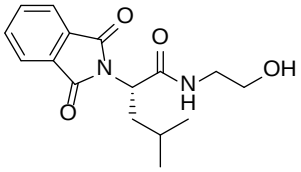
This compound was prepared according to *General Procedure 1* using carboxylic acid **4**[S2] (1.00 g, 3.825 mmol) and (*S*)-2-amino-3-phenylpropan-1-ol[S3] (580 mg, 3.825 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) gave **6** (1.10 g, 73%) as a solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 0.87-0.89 (m, 6H), 1.35-1.40 (m, 1H), 1.70-1.75 (m, 1H), 2.17-2.23 (m, 1H), 2.81-2.91 (m, 3H), 3.57-3.59 (m, 1H), 3.65-3.58 (m, 1H), 4.12-4.16 (m, 1H), 4.83 (dd, $J_1$ = 5.5 Hz, $J_2$ = 11.0 Hz, 1H), 6.46-6.48 (m, 1H, NH), 7.08-7.17 (m, 5H), 7.73-7.75 (m, 2H), 7.81-7.84 (m, 2H).

**(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-(2-hydroxy-1-phenylethyl)-4-methylpentanamide (7)**



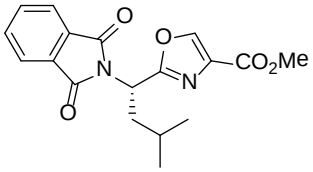
This compound was prepared according to *General Procedure 1* using carboxylic acid **4**[S2] (1.00g, 3.825 mmol) and (±)-2-amino-2-phenylethan-1-ol[S3] (520 mg, 3.825 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) gave **7** (1.00 g, 69%) as a solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 0.91-0.95 (m, 6H), 1.39-1.52 (m, 1H), 1.85-1.94 (m, 1H), 2.33-2.45 (m, 1H), 2.54 (br s, 1H, OH), 3.77-3.91 (m, 2H), 4.93-5.00 (m, 1H), 5.03-5.09 (m, 1H, NH), 7.26-7.28 (m, 5H), 7.72-7.77 (m, 2H), 7.82-7.87 (m, 2H).

**(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-*N*-(2-hydroxyethyl)-4-methylpentanamide (8)**



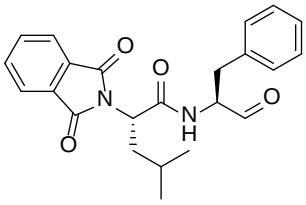
This compound was prepared according to *General Procedure 1* using carboxylic acid **4**[S2] (159.0 mg, 0.61 mmol) and ethanolamine (37.2 mg, 0.61 mmol) to yield **8** (159.0 mg, 86%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.34; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.88 – 7.83 (m, 2H), 7.78 – 7.72 (m, 2H), 6.89 (t, *J* = 5.6 Hz, 1H), 4.89 (dd, *J* = 11.6, 4.6 Hz, 1H), 3.64 (t, *J* = 5.0 Hz, 2H), 3.36 (q, *J* = 5.3 Hz, 2H), 3.31 (bs, 1H), 2.35 (ddd, *J* = 14.9, 11.6, 4.1 Hz, 1H), 1.83 (ddd, *J* = 14.2, 9.9, 4.7 Hz, 1H), 1.53 – 1.34 (m, 1H), 0.91 (d, *J* = 6.5 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 170.1, 168.2, 134.2, 131.5, 123.5, 61.4, 52.6, 42.4, 37.3, 25.1, 23.1, 21.0. MS ($ES^+$) *m/z* 327 (100%, M+Na); HRMS ($ES^+$) Calcd. for $C_{16}H_{20}N_2NaO_4$: 327.1321 (M+Na), Found: 327.1318.

**(*S*)-Methyl 2-(1-(1,3-dioxoisoindolin-2-yl)-3-methylbutyl)oxazole-4-carboxylate (9)**



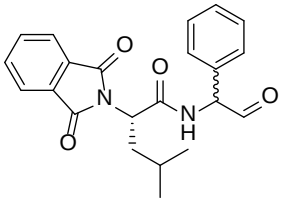
To a solution of **5** (1.793 g, 4.95 mmol) in $CH_2Cl_2$ (50 mL) at −10 °C (ice/salt bath) under $N_2$ was added Deoxo-Fluor® (0.91 mL, 4.95 mmol) dropwise and the mixture was allowed to warm to rt with stirring over 27 h. After re-cooling to −10 °C, a second aliquot of Deoxo-Fluor® (0.10 mL, 0.49 mmol) was added and the mixture was stirred at 0 °C for a further 4 h, before quenching with saturated $NaHCO_3$ (20 mL). The organic phase was separated and washed with brine (20 mL), then dried ($MgSO_4$) and concentrated under reduced pressure to give the intermediate dihydrooxazole (1.813 g) as a pale yellow gum. TLC (25% EtOAc/pet. ether) $R_F$ = 0.22. This was dissolved in MeCN (20 mL) and the solution was cooled to −10 °C under $N_2$, then $CCl_4$ (0.96 mL, 9.90 mmol) and DBU (1.48 mL, 9.90 mmol) were added and the solution was allowed to warm to rt and stirred for 4 h. After removing the solvent under reduced pressure, the residue was dissolved in $CH_2Cl_2$ (50 mL) and washed sequentially with 1 M HCl (30 mL) and saturated $NaHCO_3$ (25 mL), before being dried ($MgSO_4$) and concentrated. Flash chromatography (5% EtOAc/pet. ether to 20% EtOAc/pet. ether) gave **9** (1.025 g, 61% over two steps) as a white solid. TLC (25% EtOAc/pet. ether) $R_F$ = 0.53; $[\alpha]_D^{25}$ −26.5 (*c* 1.53, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.88 − 7.86 (m, 2H), 7.78 − 7.75 (m, 2H), 5.59 (dd, *J* = 11.1, 4.6 Hz, 1H), 3.90 (s, 3H), 2.55 (ddd, *J* = 14.9, 11.1, 4.2 Hz, 1H), 2.25 (ddd, *J* = 14.4, 9.9, 4.6 Hz, 1H), 1.65 – 1.54 (m, 1H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.3, 162.5, 161.4, 144.2, 134.3, 133.5, 131.6, 123.6, 52.1, 46.2, 38.1, 24.7, 23.0, 21.2; MS ($ES^+$) *m/z* 365 (26%, M+Na), 343 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{18}H_{18}N_2NaO_5$: 365.1113 (M+Na), Found: 365.1115.

**(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-4-methyl-*N*-((*S*)-1-oxo-3-phenylpropan-2-yl)pentanamide (10)**



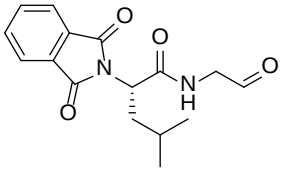
To a solution of **6** (500 mg, 1.27 mmol) in $CH_2Cl_2$ (30 mL) at 0 °C was added Dess-Martin periodinane (600 mg, 1.41 mmol) and the mixture was allowed to warm to rt over 2 h. A solution of 1 M NaOH (20 mL) was added and after continued stirring for 15 min the layers were separated. The aqeous phase was extracted with $CH_2Cl_2$ (3×20 mL) and the combined organic layers were washed with water (30 mL), dried ($MgSO_4$) and concentrated to give the aldehyde **10** (450 mg, 91%). $^1$H NMR (300 MHz, $CDCl_3$) δ 0.92-0.93 (m, 6H), 1.39-1.49 (m, 1H), 1.76-1.86 (m, 1H), 2.25-2.35 (m, 1H), 3.16 (d, *J* = 6.9 Hz, 2H), 4.67 (ABq, *J* = 6.6 Hz, 1H), 4.92 (dd, $J_1$ = 5.1 Hz, $J_2$ = 11.1 Hz, 1H), 6.71 (d, J = 6.3 Hz, 1H, NH), 7.11-7.21 (m, 5H), 7.76-7.83 (m, 2H), 7.85-7.89 (m, 2H), 9.62 (s, 1H). This compound was used in the next step without further purification.

**(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-4-methyl-*N*-(2-oxo-1-phenylethyl)pentanamide (11)**



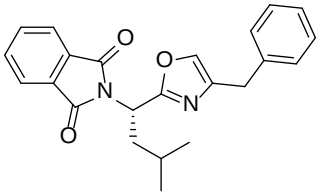
To a solution of **7** (500 mg, 1.31 mmol) in $CH_2Cl_2$ (30 mL) at 0 °C was added Dess-Martin periodinane (600 mg, 1.41 mmol) and the mixture was allowed to warm to rt over 2 h. A solution of 1 M NaOH (20 mL) was added and after continued stirring for 15 min the layers were separated. The aqeous phase was extracted with $CH_2Cl_2$ (3×20 mL) and the combined organic layers were washed with water (30 mL), dried ($MgSO_4$) and concentrated to give the aldehyde **11** (400 mg, 81%). $^1$H NMR (300 MHz, $CDCl_3$) δ 0.90-0.98 (m, 6H), 1.41-1.54 (m, 1H), 1.82-1.96 (m, 1H), 2.39-2.49 (m, 1H), 4.96-5.03 (m, 1H), 5.20-5.45 (m, 1H), 7.27-7.42 (m, 5H), 7.71-7.77 (m, 2H), 7.83-7.88 (m, 2H), 9.25 (s, 1H). This compound was used in the next step without further purification.

**(*S*)-2-(1,3-Dioxoisoindolin-2-yl)-4-methyl-*N*-(2-oxoethyl)pentanamide (12)**



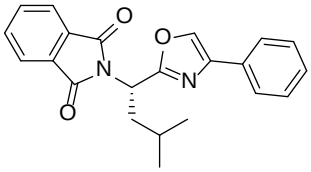
To a solution of **8** (46.0 mg, 0.15 mmol) in $CH_2Cl_2$ (0.75 mL) at 0 °C was added Dess-Martin periodinane (66.0 mg, 0.16 mmol) and the mixture was allowed to warm to rt over 1 h. The mixture was diluted with EtOAc (15 mL) and washed with saturated $NaHCO_3$ (2×15 mL) and brine (15 mL), then dried ($Na_2SO_4$) and concentrated to give the aldehyde **12** (48.4 mg, quant.) as a white foam. TLC (50% EtOAc/pet. ether) $R_F$ = 0.36; $^1$H NMR (300 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.98 – 7.67 (m, 4H), 6.90 (bs, 1H), 5.04 – 4.93 (m, 1H), 4.27 – 4.18 (m, 2H), 2.40 (t, $J$ = 12.7 Hz, 1H), 1.94 – 1.81 (m, 1H), 1.56 – 1.41 (m, 1H), 0.95 (d, $J$ = 5.4 Hz, 6H). This compound was used in the next step without further purification.

**(*S*)-2-(1-(4-Benzyloxazol-2-yl)-3-methylbutyl)isoindoline-1,3-dione (13)**



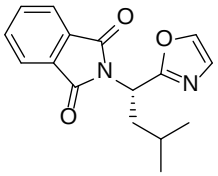
Hexachloroethane (625 mg, 2.64 mmol) and $PPh_3$ (700 mg, 2.67 mmol) were stirred in THF (5 mL) for 10 min, then a solution of aldehyde **10** (380 mg, 0.97 mmol) in THF (5 mL) was added. The reaction mixture was stirred at rt for 10 min, then pyridine (500 µL, 6.21 mmol) was added dropwise by syringe during 15 min. After heating at reflux for 2.5 d the reaction mixture was concentrated and purified by column chromatography (5% EtOAc/pet. ether to 20% EtOAc/pet. ether) yielded oxazole **13** (140 mg, 34%). $^1$H NMR (300 MHz, $CDCl_3$) δ 1.00 (d, $J$ = 6.0 Hz, 3H), 1.03 (d, $J$ = 6.0 Hz, 3H), 1.58-1.67 (m, 1H), 2.16-2.26 (m, 1H), 2.53-2.63 (m, 1H), 3.89 (s, 2H), 5.57 (dd, $J_1$ = 4.8 Hz, $J_2$ = 11.1 Hz, 1H), 7.13-7.14 (m, 1H), 7.24-7.35 (m, 5H), 7.75-7.88 (m, 2H), 7.86-7.90 (m, 2H).

**(*S*)-2-(3-Methyl-1-(4-phenyloxazol-2-yl)butyl)isoindoline-1,3-dione (14)**



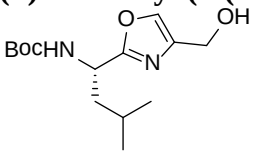
Hexachloroethane (600 mg, 2.53 mmol) and $PPh_3$ (700 mg, 2.67 mmol) were stirred in THF (5 mL) for 10 min, then a solution of aldehyde **11** (380 mg, 1.00 mmol) in THF (5 mL) was added. The reaction mixture was stirred at rt for 10 min, then pyridine (500 µL, 6.21 mmol) was added dropwise by syringe during 15 min. After heating at reflux for 2.5 d the reaction mixture was concentrated and purified by column chromatography (5% EtOAc/pet. ether to 20% EtOAc/pet. ether) yielded oxazole **14** (180 mg, 50%). $^1$H NMR (300 MHz, $CDCl_3$) δ 1.03 (d, $J$ = 6.3 Hz, 3H), 1.07 (d, $J$ = 6.3 Hz, 3H), 1.60-1.78 (m, 1H), 2.27-2.36 (m, 1H), 2.56-2.66 (m, 1H), 5.65 (dd, $J_1$ = 4.8, $J_2$ = 10.5 Hz, 1H), 7.29-7.41 (m, 3H), 7.71-7.79 (m, 4H), 7.85 (s, 1H), 7.89 (d, $J$ = 5.4 Hz, 1H), 7.90 (d, $J$ = 5.4 Hz, 1H).

**(*S*)-2-(3-Methyl-1-(oxazol-2-yl)butyl)isoindoline-1,3-dione (15)**



To a solution of $PPh_3O$ (78.1 mg, 0.28 mmol) in $CH_2Cl_2$ (3.0 mL) at 0 °C under $N_2$ was added dropwise a solution of $Tf_2O$ (39.5 mg, 0.14 mmol) in $CH_2Cl_2$ (1.0 mL). After 5 min at 0 °C, the mixture was cooled to −78 °C (EtOAc/liquid $N_2$ slush bath) and a solution of **12** (42.4 mg, 0.14 mmol) in $CH_2Cl_2$ (1.6 mL) was added. The mixture was allowed to warm to rt and stirred for 19 h. Saturated $NaHCO_3$ (5 mL) and $CH_2Cl_2$ (5 mL) were added, and the organic layer was dried ($MgSO_4$) and concentrated. Flash chromatography (5% EtOAc/pet. ether to 15% EtOAc/pet. ether) gave **15** (17.8 mg, 45%) as a colorless gum. TLC (20% EtOAc/pet. ether) $R_F$ = 0.36; $[\alpha]_D^{25}$ −37.4 (*c* 0.89, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.89 − 7.85 (m, 2H), 7.76 − 7.72 (m, 2H), 7.58 (s, 1H), 7.08 (s, 1H), 5.57 (dd, $J$ = 10.8, 5.0 Hz, 1H), 2.54 (ddd, $J$ = 14.9, 10.9, 4.5 Hz, 1H), 2.20 (ddd, $J$ = 14.4, 9.7, 5.0 Hz, 1H), 1.68 – 1.58 (m, 1H), 1.02 (d, $J$ = 6.6 Hz, 3H), 0.98 (d, $J$ = 6.7 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 167.6, 161.7, 139.0, 134.2, 131.7, 127.3, 123.5, 46.4, 38.2, 24.9, 23.1, 21.4; MS ($ES^+$) *m/z* 285 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{16}H_{16}N_2NaO_3$: 307.1059 (M+Na), Found: 307.1069.

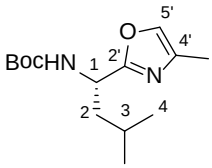
**(*S*)-*tert*-Butyl (1-(4-(hydroxymethyl)oxazol-2-yl)-3-methylbutyl)carbamate (17)**



To a solution of the known oxazole ester **16**[S4] (1.08 g, 3.46 mmol) in THF (10 mL) at 0 °C under $N_2$ was added a solution of $LiBH_4$ (2.0 M in THF, 5.2 mL, 10.4 mmol) followed by dropwise addition of absolute EtOH (1.0 mL, 17.1 mmol). The mixture was allowed to warm to rt with stirring over 3 h, then EtOAc (5 mL) was added. After an additional 30 min, the reaction mixture was re-cooled to 0 °C and quenched by the dropwise addition of 1 M HCl (10 mL) until the evolution of $H_2$ had ceased. The mixture was poured into water (20 mL) and the product extracted with EtOAc (3×15 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and concentrated to give **17** (870 mg, 88%) as a pale yellow gum. TLC (50% EtOAc/pet. ether) $R_F$ = 0.49; TLC (5%

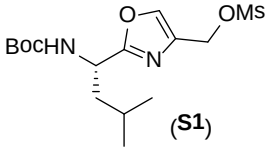
MeOH/$CH_2Cl_2$) $R_F$ = 0.48; $[\alpha]_D^{25}$ −57.9 (*c* 1.94, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 5.09 (bm, 1H), 4.98 – 4.89 (m, 1H), 4.58 (d, *J* = 5.8 Hz, 2H), 2.48 (t, *J* = 6.1 Hz, 1H), 1.78 – 1.59 (m, 3H), 1.44 (s, 9H), 0.95 (d, *J* = 5.8 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 165.7, 155.1, 140.2, 134.9, 79.9, 56.1, 47.3, 43.5, 28.3, 24.6, 22.5, 22.1; MS ($ES^+$) *m/z* 307 (100%, M+Na), 285 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{14}H_{25}N_2O_4$: 285.1814 (M+H), Found: 285.1811.

**(*S*)-*tert*-Butyl (3-methyl-1-(4-methyloxazol-2-yl)butyl)carbamate (18)**




A reaction vessel was charged with $PPh_3$ (1.5 equiv, 55.3 mg, 0.21 mmol), $I_2$ (1.5 equiv, 53.3 mg, 0.21 mmol) and imidazole (1.5 equiv, 14.3 mg, 0.21 mmol) and a solution of the alcohol **17** (1 equiv, 40.0 mg, 0.14 mmol) in $CH_2Cl_2$ (3 mL) was added dropwise. The mixture was stirred for 1.5 h at rt. Additional poritions of $I_2$ (1 equiv, 35.5 mg, 0.14 mmol), $PPh_3$ (1 equiv, 36.7 mg, 0.14 mmol) and imidazole (1 equiv, 9.5 mg, 0.14 mmol) was then added and the mixture was stirred for a further 1 h. The solvents were removed under reduced pressure. To the residue, containing the iodinated intermediate, was added Mg powder (20 equiv, 68.0 mg, 2.80 mmol) and MeOH (3 mL) and the suspension was sonicated for 20 min. The mixture was diluted with EtOAc (10 mL) and brine (10 mL) and extracted with EtOAc (3×10 mL). The combined organic layers were dried ($MgSO_4$) and the solvent removed under reduced pressure. Flash chromatography (100 mL of 5% EtOAc/pet. ether, then 100 mL of 7.5% EtOAc/pet. ether) yielding the methyl-oxazole derivative **18** as a colorless oil (21.7 mg, 58 %). TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.59. $^1$H NMR (500 MHz, $CDCl_3$) δ 0.94 (6H, d, *J* = 6.1 Hz, H4 and H3-C$\underline{H}_3$), 1.44 (9H, s, $(CH_3)_3$), 1.58 - 1.77 (1H, m, H3), 1.89 - 1.93 (2H, m, H2), 2.15 (3H, s, H4'-C$\underline{H}_3$), 4.56 (1H, bd, *J* = 7.2 Hz, H1), 4.90 - 5.04 (2H, m, NH), 7.28 (1H, s, H5'). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 11.6 (C4'-$\underline{C}H_3$), 21.9 (C4/C3-$\underline{C}H_3$), 22.3 (C4/C3-$\underline{C}H_3$), 22.7 (C3), 28.4 C($\underline{C}H_3)_3$), 43.8 (C2), 47.5 (C1), 79.9 ($\underline{C}(CH_3)_3$), 134.1 (C4'), 136.4 (C5'), 155.4 (CO), 164.6 (C2'). MS ($ESI^+$) *m/z* = 269 (100 %, $[M+H]^+$), 291 (15 %, $[M+Na]^+$). HRMS ($ESI^+$) $[M+Na]^+$ Calcd. for $C_{14}H_{24}N_2NaO_3$: 291.1685, Found: 291.1685.

**(*S*)-(2-(1-((*tert*-Butoxycarbonyl)amino)-3-methylbutyl)oxazol-4-yl)methyl methanesulfonate (S1)**



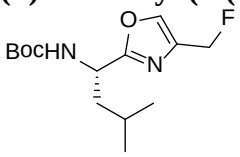

(**S1**)

The following is a general procedure used for the preparation of mesylate **S1** as an intermediate in the synthesis of compounds **19**, **27** and **29**−**32**. Note that this compound is relatively unstable, and thus was always prepared freshly before use.

To a solution of alcohol **17** (1.0 equiv) and $NEt_3$ (1.3−1.6 equiv) in reagent grade $CH_2Cl_2$ ([**17**] = 0.1 M) at 0 °C in an air atmosphere was added MsCl (1.3−1.6 equiv) and the mixture was allowed to warm to rt with stirring over 45 min. The mixture was diluted with $CH_2Cl_2$ (20 mL) and washed with saturated $NaHCO_3$ (20 mL) and brine (20 mL), then dried ($MgSO_4$). The solvent was removed under reduced pressure to give **S1** as a yellow gum (essentially quantitative yield) which could be used without further purification. In one case, the product was further purified for analytical purposes by flash column chromatography (15% EtOAc/pet. ether) to yield **S1** (99 mg, 96%) as a colorless oil. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.63; TLC (25% EtOAc/pet. ether) $R_F$ = 0.18; $^1$H NMR (500 MHz,

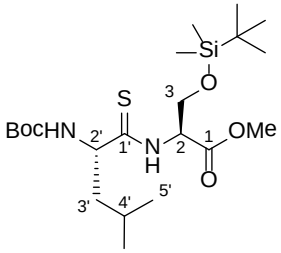
$CDCl_3$): δ 0.95 (2 x d, $J$ = 6.5 Hz, 6H, 2 x $CH_3$), 1.43 (s, 9H, $^t$Bu), 1.63-1.74 (m, 3H, CH and $CH_2$), 3.04 (s, 3H, OMs), 4.89-4.98 (m, 1H, CH), 4.99-5.08 (m, 1H, NH), 5.16 (s, 2H, $CH_2O$), 7.71 (s, 1H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.3 ($CH_3$), 22.8 ($CH_3$), 24.9 (CH), 28.5 (C($\underline{C}H_3)_3$), 43.5 ($CH_2$), 47.7 (CH), 63.2 ($CH_2O$), 80.3 ($\underline{C}(CH_3)_3$), 134.3, 166.1 (ArC), 138.4(ArCH), 155.3 (C=O). MS (ESI, +ve) *m/z* 363 (100%) $[M+H]^+$.

**(*S*)-*tert*-Butyl (1-(4-(fluoromethyl)oxazol-2-yl)-3-methylbutyl)carbamate (19)**




To the neat mesylate **S1** (36.2 mg, 0.10 mmol, prepared from **17** as described above) cooled to 0 °C was added a solution of TBAF (1.0 M in THF, 1.0 mL, 1.0 mmol) and the solution was allowed to warm to rt over 2 h. The mixture was diluted with $Et_2O$ (15 mL) and washed sequentially with 1 M HCl (20 mL), saturated $NaHCO_3$ (20 mL) and brine (20 mL), then dried ($MgSO_4$) and concentrated. Flash chromatography (6% EtOAc/pet. ether) gave **19** (18.1 mg, 63%) as a pale yellow gum. TLC (20% EtOAc/pet. ether) $R_F$ = 0.55; $[\alpha]_D^{25}$ −45.6 (*c* 0.74, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, $J_{C-F}$ = 4.7 Hz, 1H), 5.28 (d, $J_{C-F}$ = 47.9 Hz, 2H), 5.07 – 4.89 (m, 2H), 1.81 – 1.61 (m, 3H), 1.44 (s, 9H), 0.95 (d, $J$ = 6.3 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.7, 155.1, 137.3 (d, $J_{C-F}$ = 8.2 Hz), 136.2 (d, $J_{C-F}$ = 19.8 Hz), 80.0, 76.1 (d, $J_{C-F}$ = 164.8 Hz), 47.4, 43.4, 28.3, 24.6, 22.6, 22.1; MS ($ES^+$) *m/z* 309 (100%, M+Na), 231 (78%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{14}H_{23}FN_2NaO_3$: 309.1590 (M+Na), Found: 309.1598.

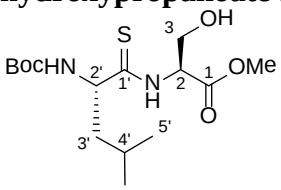
**(*S*)-Methyl 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-4-methylpentanethioamido)-3-((*tert*-butyldimethylsilyl)oxy)propanoate (21)**




A suspension of TBS-protected dipeptide **20**[S5] (2.18 g, 4.88 mmol) and Lawesson's reagent (98.8 mg, 2.44 mmol) in toluene (49.0 mL) was heated to 80 °C and stirred at this temperature for 20 min. Analysis by mass spectrometry showed full conversion. After evaporation of the solvent, flash column chromatography (*d* = 3.5 cm, *h* = 20 cm, 10% EtOAc/pet. ether) provided **21** (1.89 g, 84%) as a colourless oil. TLC (10% EtOAc/pet. ether) $R_F$ = 0.43. $[\alpha]_D^{25}$ = +40,9 (c 1.6, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.02 (3H, s, Si($CH_{a3}$)$_2$), 0.03 (3H, s, Si($CH_{b3}$)$_2$), 0.86 (9H, s, SiC($CH_3$)$_3$), 0.95 (3H, d, $J$ = 2.3 Hz, H5' or 4'-$CH_3$), 0.96 (3H, d, $J$ = 2.3 Hz, H5' or 4'-$CH_3$), 1.43 (9H, s, OC($CH_3$)$_3$), 1.51 - 1.63 (1H, m, $H3_a$'), 1.65 - 1.84 (2H, m, $H3_b$', H4'), 3.76 (3H, s, $OCH_3$), 4.03 (1H, dd, $J$ = 10.3, 2.8 Hz, $H3_a$), 4.11 (1H, dd, $J$ = 10.7, 2.2 Hz, $H3_b$), 4.37 - 4.48 (1H, m, H2'), 5.08 - 5.24 (2H, m, H2a, 2'-NH), 8.36 (1H, bd, $J$ = 6.0 Hz, 2-NH). $^{13}$C NMR (126 MHz, $CDCl_3$) δ -5.6 (Si($C_aH_3$)$_2$), -5.4 (Si($C_bH_3$)$_2$), 18.3 (Si$\underline{C}$($CH_3$)$_2$), 22.3 (C5' or 4'-$CH_3$), 23.0 (C5' or 4'-$CH_3$), 25.0 (C4'), 25.8 (SiC($\underline{C}H_3$)$_2$), 28.4 (OC($\underline{C}H_3$)$_3$), 45.3 (C3'), 52.7 ($OCH_3$), 59.5 (C2), 60.5 (C2'), 62.4 (C3), 80.2 (O$\underline{C}$($CH_3$)$_3$), 155.3 ($\underline{C}$=O(OC($CH_3$)$_3$)), 169.7 (C1), 205.9 (C1'). IR (neat) $\nu$ [$cm^{-1}$] = 3315 (w), 2956 (m), 2930 (m), 2858 (w), 2358 (w), 2327(w), 1705 (s), 1506 (s), 1367 (s), 1251 (s), 1163 (s), 1112 (s), 1044 (m), 834 (s), 777 (s). MS ($ESI^+$) *m/z* = 363 (62%, $[M\text{-Boc}]^+$), 407 (100%, [M-

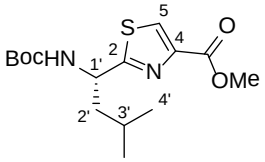
Boc+$HCO_2H$]$^+$), 463 (10%, [M+H]$^+$), 485 (66%, [M+Na]$^+$). HRMS (ESI$^+$) [M+Na]$^+$ Calcd. for $C_{21}H_{42}N_2O_5SiSNa$: 485.2481, Found: 485.2493.

**(*S*)-Methyl 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-4-methylpentanethioamido)-3-hydroxypropanoate (22)**




To a solution of TBS-protected peptide **21** (1.79 g, 3.87 mmol) in THF (31.0 mL) TBAF (1 M in THF, 7.75 mL, 7.75 mmol) was added and the mixture stirred at rt for 30 min. TLC analysis (5:95 MeOH/$CH_2Cl_2$, ninhydrin stain) indicated the reaction being finished after 20 min. After concentration the resulting yellow oil was re-dissolved in EtOAc (40 mL) and the organic layer washed with $H_2O$ (3 x 40 mL), brine (2 x 40 mL), dried ($MgSO_4$) and the solvent evaporated. The product was purified by flash chromatography (*d* = 3.5 cm, *h* = 12 cm, 10% EtOAc/pet. ether to 40% EtOAc/pet. ether) to yield compound **22** (1.05 g, 78%) as a highly viscous pale yellow oil. TLC (50% EtOAc/pet. ether) $R_F$ = 0.57. $[\alpha]_D^{25}$ = +14,8 (*c* 1.6, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.94 (3H, d, *J* = 4.1 Hz, H5' or 4'-$CH_3$), 0.96 (3H, d, *J* = 4.2 Hz, H5' or 4'-$CH_3$), 1.41 (9H, s, $(CH_3)_3$), 1.56 - 1.66 (1H, m, H3$_a$'), 1.65 - 1.80 (2H, m, H3$_b$', H4'), 3.47 (1H, bs, OH), 3.80 (3H, s, $OCH_3$), 3.96 - 4.05 (1H, m, H3$_a$), 4.07 - 4.18 (1H, m, H3$_b$), 4.34 - 4.44 (1H, m, H2'), 5.17 - 5.33 (2H, m, H2, 2'-NH), 8.75 (1H, bd, *J* = 5.8 Hz, 2-NH). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 22.3 (C5' or 4'-$CH_3$), 22.9 (C5' or 4'-$CH_3$), 24.9 (C4'), 28.4 ($(CH_3)_3$), 44.2 (C3'), 53.0 ($OCH_3$), 59.8 (C2), 60.0 (C2'), 61.4 (C3), 80.8 ($\underline{C}(CH_3)_3$), 156.3 ($\underline{C}$=O($OC(CH_3)_3$)), 170.2 (C1), 206.5 (C1'). IR (neat) *ν* [cm$^{-1}$] = 3311 (w), 2958 (m), 2360 (w), 1734 (m), 1684 (s), 1507 (s), 1436 (m), 1368 (s), 1247 (m), 1161 (s), 1066 (m), 1046 (m), 1023 (m), 911 (m), 731 (s). MS (ESI$^+$) *m/z* = 249 (16%, [M-Boc+H]$^+$), 293 (37%, [M-Boc+$HCO_2H$]), 349 (3%, [M+H]$^+$), 371 (100%, [M+Na]$^+$) HRMS (ESI$^+$) [M+Na]$^+$ Calcd. for $C_{15}H_{28}N_2O_5SNa$: 371.1617, Found: 371,1624.

**Methyl 2-((*S*)-1-((*tert*-butoxycarbonyl)amino)-3-methylbutyl)-thiazole-4-carboxylate (23)**

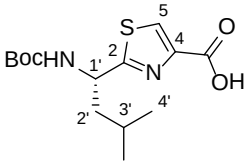



Step I: To a solution of peptide **22** (1.00 g, 2.87 mmol) in $CH_2Cl_2$ (29.0 mL) at -15 °C under nitrogen atmosphere, was added dropwise Deoxo-Fluor® (0.64 mL, 3.47 mmol) over 2 min. TLC analysis (5:95 MeOH/$CH_2Cl_2$, ninhydrin stain) showed the reaction to be finished after *ca.* 40 min. Saturated $NaHCO_3$ (30 mL) was added before the organic layer was separated, dried ($MgSO_4$) and the solvent evaporated. The dihydrothiazole intermediate (0.67 g) was obtained as an amber solid and used for the next step without further purification.

Step II: To a solution of the dihydrothiazole (0.67 g, 2.02 mmol) and $CCl_4$ (0.40 mL, 4.11 mmol) in MeCN (8.1 mL) under nitrogen atmosphere at −10 °C, DBU (0.61 mL, 4.09 mmol) was added dropwise over 1 min. The reaction mixture was then stirred for further 20 min at 0 °C. TLC analysis (25% EtOAc/pet. ether, ninhydrin stain) showed the reaction to be finished after 10 min. After the solvent was evaporated, EtOAc (40 mL) and 1M HCl (40 mL) were added and the seperated organic phase washed with 1M HCl (40 mL), saturated $NaHCO_3$ (2 x 40 mL), brine (2 x 40 mL) and dried ($MgSO_4$). Evaporation of the solvent provided the thiazole ester **23** (0.58 g, 78% over two steps) as a pale yellow oil. NMR data for **23** was in good agreement with that reported previously for the *R*-

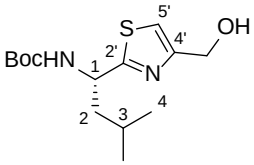
enantiomer prepared by an alternative route (*ent*-**23**).[S6] TLC (25% EtOAc/pet. ether) $R_F$ = 0.63. $[\alpha]_D^{25}$ = −46.5 (*c* 1.68, $CH_2Cl_2$). Lit. (*R*-enantiomer)[S6a] $[\alpha]_D^{20}$ = +50.4 (*c* 1.46, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.96 – 0.99 (6H, m), 1.42 (9H, s, $(CH_3)_3$), 1.63 - 1.82 (2H, m, $H2_a$', H3'), 1.85 - 1.99 (1H, m, $H2_b$'), 3.93 (3H, s, $OCH_3$), 4.97 - 5.09 (1H, m, H1'), 5.09 - 5.19 (1H, m, NH), 8.08 (1H, s, H5). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 21.8 (C4' or 3'-$CH_3$), 23.1 (C4' or 3'-$CH_3$), 25.1 (C3'), 28.4 ($(CH_3)$), 44.5 (C2'), 51.5 (C1'), 52.6 ($OCH_3$), 80.3 ($\underline{C}(CH_3)_3$), 127.3 (C5), 147.1 (C4), 155.2 ($\underline{C}$=O(C$(CH_3)_3$)), 162.0 ($\underline{C}$=O($OCH_3$)), 174.9 (C2). IR (neat) *ν* [$cm^{-1}$] = 3346 (w), 2958 (m), 2358 (w), 1700 (s), 1506 (m), 1367 (m), 1243 (s), 1212 (s), 1164 (s), 1094 (m), 1045 (m), 1024 (m), 990 (m), 916 (m), 867 (m), 779 (m), 752 (m), 732 (m). MS ($ESI^+$) *m/z* = 273 (44%, $[M\text{-}Boc+HCO_2H]^+$), 329 (32%, $[M+H]^+$), 351 (100%, $[M+Na]^+$). HRMS ($ESI^+$) $[M+Na]^+$ Calcd. for $C_{15}H_{24}N_2O_4SNa$: 351.1354, Found: 351.1361.

**2-((*S*)-1'-((*tert*-Butoxycarbonyl)amino)-3-methylbutyl)-thiazole-4-carboxylic acid (24)**




A suspension of thiazole ester **23** (0.63 g, 2.00 mmol) and $LiOH{\cdot}H_2O$ (0.85 g, 20.14 mmol) in THF (20.0 mL) and $H_2O$ (20.0 mL) was stirred at rt for 1 h, after which time TLC analysis (25:75 EtOAc/pet. ether, ninhydrin) showed no remaining starting material. The reaction mixture was diluted with $CH_2Cl_2$ (40 mL), acidified to pH 1-2 with 1 M HCl (40 mL) and the phases separated. The aqueous layer was further extracted with $CH_2Cl_2$ (40 mL), the combined organic phases washed with brine (2 x 40 mL), dried ($MgSO_4$) and the solvent evaporated. The known thiazole carboxylic acid **24** (0.58 g, 92%) was obtained as a pale yellow solid. NMR data was in good agreement with that reported previously for **24** prepared by an alternative route.[S7] mp 120−122 °C. $[\alpha]_D^{25}$ = −41.2 (c 1.4, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.91 - 1.01 (6H, m, H4' and 4'-$CH_3$), 1.43 (9H, s, $(CH_3)_3$), 1.63 - 1.83 (2H, m, $H2_a$' and H3'), 1.84 - 1.97 (1H, m, $H2_b$'), 4.97 (0H, bs, H1' rotamer), 5.06 (1H, bs, H1'), 5.22 (1H, bs, NH), 6.32 (0H, bs, NH rotamer), 8.18 (1H, s, H5). $^{13}$C NMR (126 MHz, $CDCl_3$) δ [ppm] = 21.9 (C4' or 3'-$CH_3$), 23.1 (C4' or 3'-$CH_3$), 25.0 (C3'), 28.4 ($(CH_3)_3$), 44.5 (C2'), 51.4 (C1'), 80.5 ($\underline{C}(CH_3)_3$), 128.3 (C5), 146.7 (C4), 155.3 ($\underline{C}$=O(OC$(CH_3)_3$)), 164.1(C=O(OH)), 175.1(C2). IR (neat) *ν* [$cm^{-1}$] = 3110 (w), 2956 (w), 1706 (s), 1684 (s), 1653 (m), 1506 (m), 1489 (m), 1404 (m), 1367 (m), 1216 (s), 1168 (s), 1099 (m), 1020 (m), 917 (m), 777 (m), 735 (m). MS ($ESI^-$) *m/z* = 313 (100%, $[M-H]^-$). HRMS ($ESI^-$) $[M-H]^-$ Calcd. for $C_{14}H_{21}N_2O_4S$: 313.1222, Found: 313.1220.

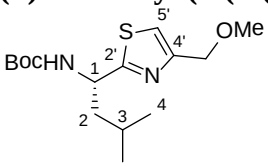
***tert*-Butyl (*S*)-(1-(4-(hydroxymethyl)thiazol-2-yl)-3-methylbutyl)carbamate (25)**




To a solution of acid **24** (57.4 mg, 0.18 mmol) and $NEt_3$ (27.7 mg, 0.27 mmol) in THF (1.80 mL) at 0 °C was added isobutyl chloroformate (0.036 mL, 0.27 mmol) and the resulting suspension was stirred in a capped vial (air atmosphere) on ice for 45 min. The suspension (filtration not required) was then added dropwise to an ice cold solution of $NaBH_4$ (69.1 mg, 1.83 mmol) in water (1.8 mL) in the air (open vessel to vent $CO_2$ and $H_2$). After stirring for 1.5 h on ice, the excess $NaBH_4$ was quenched by the dropwise addition of 1 M HCl. After $H_2$ evolution had ceased, the mixture was futher diluted with 1 M HCl (20 mL) and EtOAc (30 mL). The organic layer was washed with

saturated $NaHCO_3$ (20 mL) and brine (20 mL), then dried ($MgSO_4$) and concentrated. Flash chromatography (100% $CH_2Cl_2$ to 2.5% MeOH/$CH_2Cl_2$) gave **25** (49.5 mg, 90%) as a colorless gum. TLC (50% EtOAc/pet. ether) $R_F$ = 0.49, or TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.44. $[\alpha]_D^{25} = -44.7$ (c 1.7, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.95 (6H, d, $J$ = 5.7 Hz, H4 and 3-$CH_3$), 1.43 (9H, s, $(CH_3)_3$), 1.58 - 1.75 (2H, m, $H2_a$, H3), 1.75 - 1.96 (1H, m, $H2_b$), 3.10 (1H, bs, OH), 4.71 (2H, s, C$H_2$OH), 4.82 - 5.11 (1H, m, H1), 5.18 (1H, bd, $J$ = 8.2 Hz, NH), 7.07 (1H, s, H5'). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 22.1 (C4 or 3-$CH_3$), 23.0 (C4 or 3-$CH_3$), 25.0 (C3), 28.5 ($(CH_3)_3$), 45.2 (C2), 51.3 (C1), 60.9 ($CH_2OH$), 80.1 (C$(CH_3)_3$), 114.3 (C5'), 155.2 (C=O), 156.4 (C4'), 174.3 (C2'). IR (neat) $\nu$ [$cm^{-1}$] = 3314 (w), 2958 (m), 2870 (w), 1688 (s), 1521 (m), 1470 (m), 1391 (m), 1367 (s), 1251 (s), 1165 (s), 1045 (s), 1024 (s). MS ($ESI^+$) $m/z$ = 245 (24%, $[M\text{-Boc}+HCO_2H]^+$), 301 (75%, $[M+H]^+$), 323 (100%, $[M+Na]^+$). HRMS ($ESI^+$) $[M+H]^+$ Calcd. for $C_{14}H_{25}N_2O_3S$: 301.1586, Found: 301.1575.

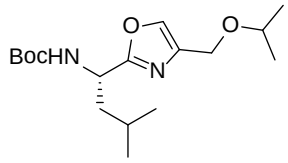
**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)thiazol-2-yl)-3-methylbutyl)carbamate (26)**




Step I: To a solution of thiazole alcohol **25** (75.8 mg, 0.25 mmol) in $CH_2Cl_2$ (1.3 mL) at 0 °C, $NEt_3$ (46 µL, 0.33 mmol) was added followed by dropwise addition of MsCl (30 µL, 0.39 mmol). TLC analysis (25% EtOAc/pet. ether, ninhydrin stain) showed the reaction to be finished after 15 min. The reaction mixture was then diluted with EtOAc (30 mL), the organic layer washed with 1 M HCl (2 x 30 mL), saturated $NaHCO_3$ (2 x 30 mL), brine (2 x 30 mL), dried ($MgSO_4$) and the solvent evaporated. The resulting mesylate was used without further purification.

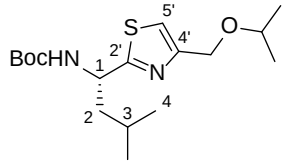
Step II: To a solution of MeOH (0.21 mL, 5.18 mmol) in THF (0.63 mL) in an oven dried vial under nitrogen atmosphere at −78 °C, NaHMDS (1 M in THF, 1.55 mL, 1.55 mmol) was added. After 20 min, a solution of the mesylate (from Step I) and $NBu_4I$ (13.8 mg, 0.04 mmol) in THF (2.5 mL) was added dropwise over 2 min. The reaction mixture was stirred overnight at rt. A TLC analysis (25% EtOAc/pet. ether) showed no remaining starting material after 12 h and analysis by mass spectrometry indicated the formation of the desired product. The reaction mixture was diluted with EtOAc (30 mL), the organic layer washed with 1 M HCl (2 x 30 mL), $H_2O$ (2 x 30 mL), saturated $NaHCO_3$ (2 x 30 mL), brine (2 x 30 mL), dried ($MgSO_4$) and the solvent evaporated. Re-evaporation from $CH_2Cl_2$ yielded the methyl ether derivative **26** (58.3 mg, 73% over two steps) as a viscous yellow oil. TLC (25% EtOAc/pet. ether) $R_F$ = 0.51. $[\alpha]_D^{25} = -14.8$ (c 2.9, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.94 (3H, d, $J$ = 4.0 Hz, H4 or 3-$CH_3$), 0.95 (3H, d, $J$ = 4.2 Hz, H4 or 3-$CH_3$), 1.42 (9H, s, $(CH_3)_3$), 1.60 - 1.77 (2H, m, $H2_a$ and H3), 1.77 - 1.95 (1H, m, $H2_b$), 3.43 (3H, s, $OCH_3$), 4.52 (2H, s, C$H_2$$OCH_3$), 4.88 (0H, bs, H1 rotamer), 5.01 (1H, bs, H1), 5.10 (1H, bs, NH), 5.33 (0H, bs, NH rotamer), 7.09 (1H, s, H5'). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 22.0 (C4 or 3-$CH_3$), 23.0 (C4 or 3-$CH_3$), 25.0 (C3), 28.5 ($(CH_3)_3$), 45.1 (C2), 51.3 (C1), 58.7 ($OCH_3$), 70.5 (C$H_2$$OCH_3$), 80.0 (C$(CH_3)_3$), 115.4 (C5'), 153.9 (C4'), 155.2 (C=O), 173.8 (C2'). IR (neat) $\nu$ [$cm^{-1}$] = 3322 (w), 2957 (m), 1699 (s), 1518 (m), 1470 (m), 1391(m), 1367 (s), 1250 (s), 1166 (s), 1098 (s), 1045 (m), 1024 (m), 978 (w), 952 (w), 911 (w), 876 (w), 733 (s). MS ($ESI^+$) $m/z$ = 259 (23%, $[M\text{-Boc}+HCO_2H]^+$), 315 (93%, $[M+H]^+$), 337 (100%, $[M+Na]^+$). HRMS ($ESI^+$) $[M+Na]^+$ Calcd. for $C_{15}H_{26}N_2O_3NaS$: 337.1562, Found: 337.1578.

**(*S*)-*tert*-Butyl (1-(4-(isopropoxymethyl)oxazol-2-yl)-3-methylbutyl)carbamate (27)**



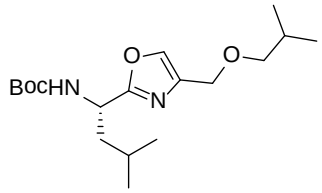

To an ice cold solution of dry i-PrOH (0.1 mL, excess) in dry THF (1.0 mL) was added NaHMDS (1 M in THF, 0.5 mL), and then the mixture was stirred in the ice bath for 15 min. A solution of mesylate **S1** (30 mg, 0.083 mmol, prepared from **17** as described above) in dry THF (0.5 mL) was added, followed by TBAI, and then the mixture was warmed up to rt and stirred overnight. Upon the completion, brine was added, and then the mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine (3 x 5 mL), dried over $MgSO_4$ and concentrated. The crude residue was purified by flash column chromatography (13% EtOAc/pet. ether) to give **27** (22 mg, 81%) as a colorless oil. $[\alpha]_D^{25}$ −41.95 (*c* 1.1, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$): δ 0.94 (d, *J* = 5.5 Hz, 6H, 2 x $CH_3$ (Leu)), 1.21 (d, *J* = 6.5 Hz, 6H, 2 x $CH_3$), 1.44 (s, 9H, $^t$Bu), 1.63-1.72 (m, 3H, CH and $CH_2$), 3.72 (septet *J* = 6.0 Hz, 1H, OCH), 4.41 (s, 2H, $CH_2O$), 4.83-4.99 (m, 1H, CH), 4.99-5.10 (m, 1H, NH), 7.51 (s, 1H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.3 (OCH($\underline{C}H_3)_2$) 22.4 ($CH_3$), 22.9 ($CH_3$), 24.9 (CH), 28.6 (C($\underline{C}H_3)_3$), 43.9 ($CH_2$), 47.6 (CH), 62.5 ($CH_2O$), 71.9 (OCH), 80.0 ($\underline{C}(CH_3)_3$), 135.9 (ArCH), 138.9, 165.2 (ArC), 155.3 (C=O). MS (ESI, +ve) *m/z* 327 (30%) $[M+H]^+$; 349 (100) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{17}H_{31}N_2O_4$ 327.2284, found 327.2269.

**(*S*)-*tert*-Butyl (1-(4-(isopropoxymethyl)thiazol-2-yl)-3-methylbutyl)carbamate (28)**



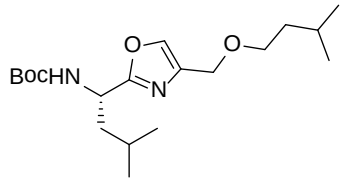

A solution of dry THF (1 mL) and i-PrOH (20 equiv, 0.27 mL, 3.8 mmol) under $N_2$ was cooled to −78° C and NaHDMS (6 equiv, 0.21 mL, 1.1 mmol) was added. A solution of the mesylate ester derivative of alcohol **25** (1 equiv, 72.1 mg, 0.19 mmol, prepared as in Step I for compound **26**) and TBAI (0.1 equiv, 7 mg, 0.02 mmol) in dry THF (1 mL) was added at once to the mixture. This was stirred overnight at rt. The mixture was diluted with EtOAc (20 mL) and washed with HCl (1 M, 2×10 mL), saturated $NaHCO_3$ (2×10 mL) and brine (2×10 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified with pipette flash chromatography (10 % EtOAc/pet. ether) yielding **28** (31.2 mg, 48 %) as a yellow oil. TLC (10% EtOAc/pet. ether) $R_F$ = 0.85. $[\alpha]_D^{25}$ = −24.3 (*c* 1.77, $CH_2Cl_2$). $^1$H NMR (300 MHz, $CDCl_3$) δ 0.95 (6H, d, *J* = 6.0 Hz, H4 and H3-$CH_3$), 1.20 – 1.26 (6H, m, OCH($C\underline{H}_3)_2$), 1.41 (9H, s, $(CH_3)_3$), 1.64 - 1.70 (2H, m, H3), 1.79 - 1.84 (1H, m, H2), 3.68 - 3.77 (1H, m, OC$\underline{H}(CH_3)_2$), 4.11 (1H, dd, *J* = 7.1 Hz, H1), 4.59 (2H, s, $C\underline{H}_2OCH(CH_3)_2$), 4.69 (bs, 1H, rotamer), 5.01 - 5.10 (1H, bd, NH), 5.28 (1H, bs, NH rotamer), 7.09 (1H, s, H5'). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 21.9 (C4 or C3-$CH_3$), 22.1 (C4 or C3-$CH_3$), 22.8 ($CH_2OCH(\underline{C}H_3)_2$), 24.8 (C3), 28.3 ($(CH_3)_3$), 45.0 (C2), 51.1 (C1), 52.1 (C1, rotamer), 66.3 ($\underline{C}H_2OCH(CH_3)_2$), 71.6 ($CH_2O\underline{C}H(CH_3)_2$), 79.8 ($\underline{C}(CH_3)_3$), 116.4 (C5'), 153.2 (C=O), 157.2 (C4'), 173.3 (C2'). MS ($ESI^+$) *m/z* = 343 (100 %, $[M+H]^+$), 365 (30 %, $[M+Na]^+$). HRMS ($ESI^+$) $[M+Na]^+$ Calcd. for $C_{17}H_{30}N_2O_3NaS$: 365.1875, Found: 365.1875.

**(*S*)-*tert*-Butyl (1-(4-(isobutoxymethyl)oxazol-2-yl)-3-methylbutyl)carbamate (29)**



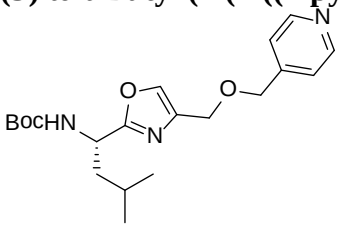

To a solution of i-BuOH (0.37 mL, 4.00 mmol) in THF (0.5 mL) under $N_2$ at −78 °C was added a solution of NaHMDS (1.0 M in THF, 1.2 mL, 1.2 mmol) and the solution was stirred at −78 °C for 15 min to generate the sodium alkoxide. To this was added a solution of mesylate **S1** (72.5 mg, 0.20 mmol, prepared from **17** as described above) and TBAI (7.4 mg, 0.020 mmol) in THF (2.0 mL) and the mixture was allowed to warm to rt with stirring for 24 h. The mixture was diluted with $Et_2O$ (20 mL) and washed with 1 M HCl (20 mL) and saturated $NaHCO_3$ (20 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (6% EtOAc/pet. ether) gave **29** (54.4 mg, 80%) as a colorless gum. TLC (10% EtOAc/pet. ether) $R_F$ = 0.23; $[\alpha]_D^{25}$ −43.9 (*c* 0.15, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.51 (s, 1H), 5.07 (bm, 1H), 4.98 – 4.88 (bm, 1H), 4.40 (s, 2H), 3.27 (d, *J* = 6.7 Hz, 2H), 1.89 (sep, *J* = 6.7 Hz, 1H), 1.77 – 1.60 (m, 3H), 1.43 (s, 9H), 0.94 (d, *J* = 6.4 Hz, 6H), 0.91 (d, *J* = 6.7 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 164.9, 155.0, 138.2, 135.7, 79.7, 77.7, 64.9, 47.4, 43.6, 28.33, 28.26, 24.6, 22.6, 22.1, 19.3; MS ($ES^+$) *m/z* 379 (18%, M+K), 363 (100%, M+Na), 341 (49%, M+H), 285 (58%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{18}H_{32}N_2NaO_4$: 363.2260 (M+Na), Found: 363.2256.

**(*S*)-*tert*-Butyl (1-(4-(isopentoxymethyl)oxazol-2-yl)-3-methylbutyl)carbamate (30)**



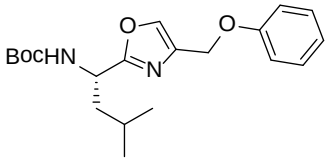

To a solution of i-PentylOH (0.44 mL, 4.00 mmol) in THF (0.5 mL) under $N_2$ at −78 °C was added a solution of NaHMDS (1.0 M in THF, 1.2 mL, 1.2 mmol) and the solution was stirred at −78 °C for 15 min to generate the sodium alkoxide. To this was added a solution of mesylate **S1** (72.5 mg, 0.20 mmol, prepared from **17** as described above) and TBAI (7.4 mg, 0.020 mmol) in THF (2.0 mL) and the mixture was allowed to warm to rt with stirring for 14 h. The mixture was diluted with $Et_2O$ (20 mL) and washed with 1 M HCl (20 mL) and saturated $NaHCO_3$ (20 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (5% EtOAc/pet. ether) gave **30** (49.9 mg, 70%) as a pale yellow gum. TLC (10% EtOAc/pet. ether) $R_F$ = 0.25; $[\alpha]_D^{25}$ −44.1 (*c* 2.14, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 5.07 (bm, 1H), 5.00 – 4.88 (m, 1H), 4.40 (s, 2H), 3.54 (t, *J* = 6.9 Hz, 2H), 1.79 – 1.61 (m, 4H), 1.50 (q, *J* = 6.9 Hz, 2H), 1.43 (s, 9H), 0.94 (d, *J* = 6.4 Hz, 6H), 0.90 (d, *J* = 6.7 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.0, 155.0, 138.1, 135.8, 79.8, 69.4, 64.7, 47.4, 43.6, 38.4, 28.3, 25.0, 24.6, 22.6, 22.1; MS ($ES^+$) *m/z* 377 (45%, M+Na), 355 (100%, M+H), 299 (52%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{19}H_{34}N_2NaO_4$: 377.2416 (M+Na), Found: 377.2418.

**(*S*)-*tert*-Butyl (1-(4-((4-pyridylmethoxy)methyl)oxazol-2-yl)-3-methylbutyl)carbamate (31)**



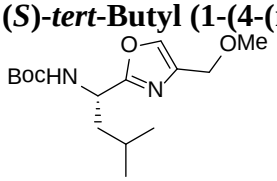
To an ice cold solution of 4-pyridine carbinol (9 mg, 0.082 mmol) in dry THF (0.5 mL) was added NaHMDS (1 M in THF, 0.123 mL), and then the mixture was stirred in the ice bath for 15 min. A solution of mesylate **S1** (29 mg, 0.080 mmol, prepared from **17** as described above) in dry THF (0.5 mL) was added, and then the mixture was warmed up to rt and stirred overnight. Upon the completion, brine was added, and then the mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine (3 x 5 mL), dried over $MgSO_4$ and concentrated. The crude residue was purified by flash column chromatography (2% MeOH/$CH_2Cl_2$) to give **31** (15 mg, 50%) as a colorless oil. $[\alpha]_D^{25}$ −43.8 (*c* 0.7, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$): δ 0.95 (d, *J* = 6.5 Hz, 6H, 2 x $CH_3$), 1.44 (s, 9H, $^t$Bu), 1.64-1.75 (m, 3H, CH and $CH_2$), 4.50 (s, 2H, $CH_2O$), 4.62 (s, 2H, C$\underline{H}_2$Py), 4.94-4.95 (m, 1H, CH), 5.03 (br s, 1H, NH), 7.29 (s, 2H, ArH), 7.57 (s, 1H, ArH (oxazole)), 8.60 (s, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.4 ($CH_3$), 22.9 ($CH_3$), 24.9 (CH), 28.5 (C($\underline{C}H_3)_3$), 43.8 ($CH_2$), 47.7 (CH), 63.7 ($CH_2O$), 71.0 ($\underline{C}H_2$Py), 80.2 ($\underline{C}(CH_3)_3$), 122.2, 150.1 (ArCH), 136.5 (ArCH (oxazole)), 137.6, 147.3, 165.6 (ArC), 155.4 (C=O). MS (ESI, +ve) *m/z* 376 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{20}H_{30}N_3O_4$ 376.2236, found 376.2241.

**(*S*)-*tert*-Butyl (3-methyl-1-(4-(phenoxymethyl)oxazol-2-yl)butyl)carbamate (32)**



A mixture of mesylate **S1** (30 mg, 0.083 mmol, prepared from **17** as described above), phenol (9 mg, 0.091 mmol), caesium carbonate (68 mg, 0.21 mmol) and dry acetone (4 mL) was stirred under nitrogen atmosphere at rt for 15 h. The solvent was evaporated, then the residue was taken up in $CH_2Cl_2$ and washed with brine, before being dried over $MgSO_4$ and concentrated. The crude was purified by flash column chromatography (1% MeOH/$CH_2Cl_2$) to yield **32** (27 mg, 90%) as a colorless oil. $[\alpha]_D^{25}$ −47.5 (*c* 1.4, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$): δ 0.95 (d, *J* = 6.0 Hz, 6H, 2 x $CH_3$), 1.44 (s, 9H, $^t$Bu), 1.64-1.78 (m, 3H, CH and $CH_2$), 4.90-5.02 (m, 1H, CH), 4.98 (s, 2H, $CH_2O$), 4.99-5.10 (m, 1H, NH), 6.96-6.97 (m, 3H, ArH), 7.29 (t, *J* = 8.0 Hz, 2H, ArH), 7.60 (s, 1H, ArH (oxazole)); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.4 ($CH_3$), 22.9 ($CH_3$), 24.9 (CH), 28.5 (C($\underline{C}H_3)_3$), 43.8 ($CH_2$), 47.7 (CH), 62.7 ($CH_2O$), 80.1 ($\underline{C}(CH_3)_3$), 115.0, 121.5, 129.7 (ArCH), 136.4 (ArCH (oxazole)), 137.2, 158.5, 165.5 (ArC), 155.3 (C=O). MS (ESI, +ve) *m/z* 361 (40%) $[M+H]^+$; 383 (100) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{20}H_{29}N_2O_4$ 361.2127, found 361.2123.

**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)carbamate (33)**

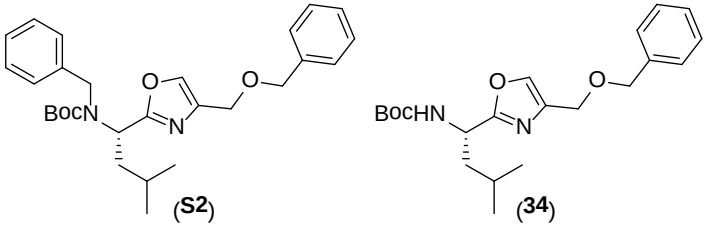


To a solution of **17** (78 mg, 0.27 mmol) in dry THF (2 mL) at −78 ºC was slowly added NaHMDS (1.0 M in THF, 0.54 mL, 2.0 equiv), and then the mixture was stirred at this temperature for 30 min. Methyl iodide (15 µL, 0.24 mmol) and TBAI (10.0 mg, 0.027 mmol) were added and the resulting

mixture was then slowly warmed up to rt and stirred for 15 h. Upon completion, brine (5 mL) was added, and the mixture was extracted with EtOAC (3 x 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated. The residue was subjected to flash chromatography (14% EtOAc/pet. ether to 16% EtOAc/pet. ether). The first compound eluted was the *N*,*O*-dimethylated product **45** (8 mg, 10%, see below for an optimized synthesis of this compound and characterization data).

The second compound eluted from the column was the desired *O*-methylated product **33** (47 mg, 59%). $[\alpha]_D^{25}$ −51.81 (*c* 2.0, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$): δ 0.94 (d, *J* = 6.0 Hz, 6H, 2 x $CH_3$), 1.43 (s, 9H, $^t$Bu), 1.63-1.75 (m, 3H, CH and $CH_2$), 3.42 (s, 3H, $OCH_3$), 4.36 (s, 2H, $CH_2O$), 4.94 (d, *J* = 6.5 Hz, 1H, CH), 5.07 (d, *J* = 14.0 Hz, 1H, NH), 7.53 (s, 1H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.2 ($CH_3$), 22.6 ($CH_3$), 24.7 (CH), 28.3 (C($\underline{C}H_3)_3$), 43.6 ($CH_2$), 47.4 (CH), 58.5 ($OCH_3$), 66.3 ($CH_2O$), 79.9 ($\underline{C}(CH_3)_3$), 136.0 (ArCH), 137.7, 165.3 (ArC), 155.1 (C=O). MS (ESI, +ve) *m/z* 299 (75%) $[M+H]^+$; 321 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{15}H_{27}N_2O_4$ 299.1971, found 299.1956.

**(*S*)-*tert*-Butyl benzyl(1-(4-((benzyloxy)methyl)oxazol-2-yl)-3-methylbutyl)carbamate (S2) and (*S*)-*tert*-butyl (1-(4-((benzyloxy)methyl)oxazol-2-yl)-3-methylbutyl)carbamate (34)**

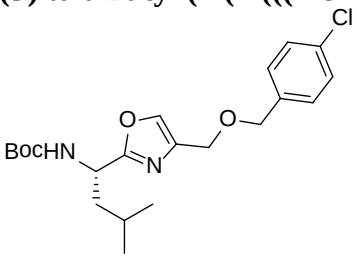


(**S2**) (**34**)

These compounds were synthesized using the synthetic procedure described for **33** from **17** (57 mg, 0.20 mmol), benzyl bromide (24 µL, 0.20 mmol), NaHMDS (1 M in THF, 0.40 mL, 2.0 equiv), TBAI (catalytic) and THF (1.5 mL). The first compound collected from the chromatography column was the *N*,*O*-dibenzylated product **S2** (45 mg, 48%). $^1$H NMR (500 MHz, $CDCl_3$): δ 0.70-1.00 (m, 6H, 2 x $CH_3$), 1.29-1.60 (m, 10H, CH and $^t$Bu), 1.72-1.97 (m, 2H, $CH_2$), 4.25-4.45 (m, 2H, $NC\underline{H}_2Ph$), 4.34 (s, 2H, $CH_2O$), 4.51 (s, 2H, $OC\underline{H}_2Ph$), 5.15-5.30 (m, 0.5H, CH), 5.58-5.71 (m, 0.5H, CH), 6.99-7.45 (m, 10H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.4 ($CH_3$), 22.7 ($CH_3$), 24.6 (CH), 28.3 (C($\underline{C}H_3)_3$), 39.2 ($CH_2$), rotamers 47.1/47.5 ($N\underline{C}H_2Ph$), rotamers 50.9/52.2 (CH), 63.9 ($CH_2O$), 73.4 ($O\underline{C}H_2Ph$), 80.5 ($\underline{C}(CH_3)_3$), 126.6, 127.7, 127.8, 128.0, 128.3, 128.5 (ArCH), 136.1 (ArCH (oxazole)), 137.7, 137.8, 139.1, 163.4 (ArC), 155.8 (C=O). MS (ESI, +ve) *m/z* 465 (100%) $[M+H]^+$; 487 (80) $[M+Na]^+$.

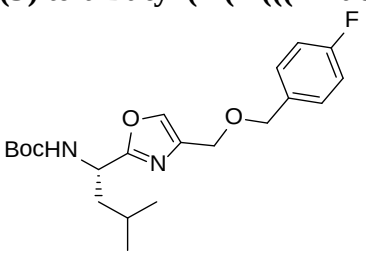
The second compound collected from the column chromatography was the *O*-benzylated product **34** (19 mg, 25%). $^1$H NMR (500 MHz, $CDCl_3$): δ 0.94 (d, *J* = 6.0 Hz, 6H, 2 x $CH_3$), 1.43 (s, 9H, $^t$Bu), 1.63-1.74 (m, 3H, CH and $CH_2$), 4.45 (s, 2H, $CH_2O$), 4.60 (s, 2H, $C\underline{H}_2Ph$), 4.93-4.95 (m, 1H, CH), 5.08-5.09 (m, 1H, NH), 7.29-7.53 (m, 5H, ArH), 7.53 (s, 1H, ArH (oxazole)); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.1 ($CH_3$), 22.6 ($CH_3$), 24.6 (CH), 28.3 (C($\underline{C}H_3)_3$), 43.6 ($CH_2$), 47.4 (CH), 63.9 ($CH_2O$), 72.7 ($OCH_2Ph$), 79.8 ($\underline{C}(CH_3)_3$), 127.7, 127.9, 128.4 (ArCH), 136.0 (ArCH (oxazole)), 137.8, 165.2 (ArC), 155.1 (C=O). MS (ESI, +ve) *m/z* 375 (100%) $[M+H]^+$.

**(*S*)-*tert*-Butyl (1-(4-(((4-chlorobenzyl)oxy)methyl)oxazol-2-yl)-3-methylbutyl)carbamate (35)**



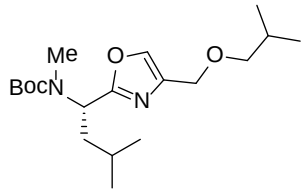

This was synthesised using the synthetic procedure described for **33** from **17** (61 mg, 0.21 mmol), *p*-chlorobenzyl bromide (44 mg, 0.21 mmol), NaHMDS (1 M in THF, 0.42 mL) and THF (2 mL) to yield **35** (37 mg, 43%) as an oil. $^1$H NMR (300 MHz, $CDCl_3$): δ 0.94 (d, $J$ = 6.6 Hz, 6H, 2 x $CH_3$), 1.43 (s, 9H, $^t$Bu), 1.62-1.75 (m, 3H, CH and $CH_2$), 4.44 (s, 2H, $CH_2O$), 4.56 (s, 2H, C$\underline{H}_2$ArCl), 4.93-4.95 (m, 1H, CH), 5.04-5.07 (m, 1H, NH), 7.29-7.33 (m, 4H, ArH), 7.53 (s, 1H, ArH (oxazole)); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 22.1 ($CH_3$), 22.6 ($CH_3$), 24.6 (CH), 28.3 (C($\underline{C}H_3)_3$), 43.5 ($CH_2$), 47.3 (CH), 63.9 ($CH_2O$), 71.8 ($\underline{C}H_2$ArCl), 79.9 ($\underline{C}(CH_3)_3$), 128.5, 129.1 (ArCH), 136.1 (ArCH (oxazole)), 133.5, 136.2, 137.5, 165.2 (ArC), 155.1 (C=O). MS (ESI, +ve) *m/z* 409 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{21}H_{30}N_2O_4Cl$ 409.1894, found 409.1885.

**(*S*)-*tert*-Butyl (1-(4-(((4-fluorobenzyl)oxy)methyl)oxazol-2-yl)-3-methylbutyl)carbamate (36)**



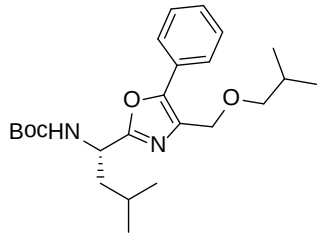

To a solution of **17** (56.9 mg, 0.20 mmol) in THF (2.0 mL) under $N_2$ at −78 °C was added a solution of NaHMDS (1.0 M in THF, 0.22 mL, 0.22 mmol) and the solution was stirred at −78 °C for 25 min. To this was added a solution of 4-fluorobenzyl chloride (31.8 mg, 0.22 mmol) and TBAI (3.7 mg, 0.010 mmol) in THF (1.0 mL) and the mixture was allowed to warm to rt with stirring for 6 h. The mixture was re-cooled to −78 °C and a further aliquot of NaHMDS (1.0 M in THF, 0.40 mL, 0.40 mmol) was added and stirring continued, allowing to warm to rt, over 29 h. A solution containing additional 4-fluorobenzyl chloride (31.8 mg, 0.22 mmol) and TBAI (7.4 mg, 0.020 mmol) in THF (0.5 mL) was added and stirring was continued for a further 72 h. The mixture was diluted with $Et_2O$ (20 mL) and washed with 1 M HCl (20 mL) and saturated $NaHCO_3$ (20 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (12% EtOAc/pet. ether) gave **36** (26.6 mg, 34%) as a colorless oil. TLC (20% EtOAc/pet. ether) $R_F$ = 0.48; $[\alpha]_D^{25}$ −44.4 (*c* 0.22, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.32 (app. t, $J$ = 6.6 Hz, 2H), 7.03 (app. t, $J$ = 8.5 Hz, 2H), 5.09 – 5.01 (bm, 1H), 4.99 – 4.90 (bm, 1H), 4.56 (s, 2H), 4.44 (s, 2H), 1.77 – 1.60 (m, 3H), 1.44 (s, 9H), 0.95 (d, $J$ = 6.2 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.2, 162.4 (d, $J_{C-F}$ = 245.6 Hz), 155.1, 137.7, 136.1, 133.5 (d, $J_{C-F}$ = 3.3 Hz), 129.6 (d, $J_{C-F}$ = 8.1 Hz), 115.2 (d, $J_{C-F}$ = 21.4 Hz), 79.8, 71.9, 63.9, 47.4, 43.6, 28.3, 24.6, 22.6, 22.1; MS ($ES^+$) *m/z* 431 (22%, M+K), 415 (100%, M+Na), 393 (60%, M+H), 337 (55%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{21}H_{29}FN_2NaO_4$: 415.2009 (M+Na), Found: 415.2009.

**(*S*)-*tert*-Butyl (1-(4-(isobutoxymethyl)oxazol-2-yl)-3-methylbutyl)(methyl)carbamate (37)**



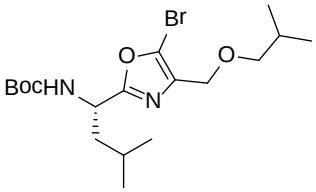

To a solution of **29** (27.2 mg, 0.080 mmol) and TBAI (3.0 mg, 0.008 mmol) in THF (0.8 mL) under $N_2$ at −78 °C was added a solution of KHMDS (1.0 M in THF, 0.096 mL, 0.096 mmol) and the solution was stirred at −78 °C for 1 h. To this was added MeI (0.025 mL, 0.40 mmol) and the mixture was allowed to warm to rt with stirring for 18 h. The mixture was quenched with saturated $NH_4Cl$ (3 mL), then diluted with $Et_2O$ (15 mL), washed with brine (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (3.5% EtOAc/pet. ether) gave **37** (21.2 mg, 75%) as a colorless gum. TLC (10% EtOAc/pet. ether) $R_F$ = 0.65; $[\alpha]_D^{25}$ −65.4 (*c* 0.92, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 5.62 – 5.50 (bm, $H_\alpha$, rotamer A, 1H), 5.38 – 5.25 (bm, $H_\alpha$, rotamer B, 1H), 4.41 (s, 2H), 3.28 (d, *J* = 6.7 Hz, 2H), 2.69 (bs, 3H), 1.99 – 1.76 (m, 3H), 1.66 – 1.54 (m, 1H), 1.48 (s, 9H), 0.97 (d, *J* = 6.1 Hz, 6H), 0.91 (d, *J* = 6.7 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, major rotamer only, Boc carbonyl was not observed) δ 163.6, 138.2, 136.1, 80.3, 77.8, 65.1, 51.8, 50.5, 38.6, 28.38, 28.36, 24.3, 23.2, 21.6, 19.3; MS ($ES^+$) *m/z* 377 (100%, M+Na), 355 (45%, M+H), 299 (23%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{19}H_{34}N_2NaO_4$: 377.2416 (M+Na), Found: 377.2419.

**(*S*)-*tert*-Butyl (1-(4-(isobutoxymethyl)-5-phenyloxazol-2-yl)-3-methylbutyl)carbamate (38)**



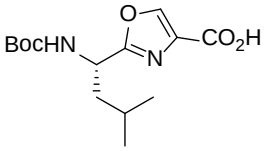

Based on a literature C−H arylation method,[S8] a 15 mL glass vial equipped with a stir bar was charged in the air with **29** (40.9 mg, 0.12 mmol), $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$ (4.9 mg, 0.0060 mmol), $PPh_3$ (3.1 mg, 0.012 mmol), $Ag_2CO_3$ (66.2 mg, 0.24 mmol), PhI (29.4 mg, 0.14 mmol) and water (1.2 mL). The vial was fitted with a rubber septum, evacuated and refilled with $N_2$ (two cycles), then heated at 70 °C with rapid stirring for 40 h during which time a silver mirror formed on the reaction vial. After cooling to rt, the mixture was filtered through celite with the aid of $CH_2Cl_2$ (30 mL), then concentrated under reduced pressure. Flash chromatography (5% EtOAc/pet. ether) gave **38** (32.1 mg, 64%) as a colorless gum. TLC (10% EtOAc/pet. ether) $R_F$ = 0.38; $[\alpha]_D^{25}$ −44.3 (*c* 1.53, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.5 Hz, 2H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 7.3 Hz, 1H), 5.17 – 4.94 (m, 2H), 4.53 (s, 2H), 3.33 (d, *J* = 6.7 Hz, 2H), 1.93 (sep, *J* = 6.7 Hz, 1H), 1.84 – 1.65 (m, 3H), 1.45 (s, 9H), 0.98 (d, *J* = 5.7 Hz, 6H), 0.92 (d, *J* = 6.7 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 162.7, 155.1, 148.8, 132.5, 128.7, 128.4, 128.1, 126.1, 79.8, 77.5, 65.1, 47.4, 43.7, 28.4, 28.3, 24.7, 22.6, 22.2, 19.5; MS ($ES^+$) *m/z* 439 (19%, M+Na), 417 (100%, M+H), 361 (11%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{24}H_{36}N_2NaO_4$: 439.2573 (M+Na), Found: 439.2590.

**(*S*)-*tert*-Butyl (1-(5-bromo-4-(isobutoxymethyl)oxazol-2-yl)-3-methylbutyl)carbamate (39)**



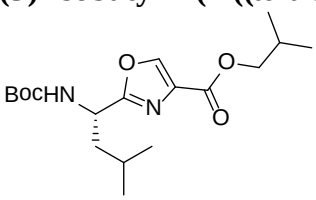

To a solution of **29** (54.0 mg, 0.16 mmol) in THF (1.6 mL) at −78 ºC under $N_2$ was added dropwise a solution of LDA (1.55 M in THF, 0.215 mL, 0.33 mmol) and the mixture was stirred at −78 ºC for 1.25 h. To this was added a solution of NBS (62.1 mg, 0.35 mmol) in THF (1.0 mL) and the mixture was allowed to warm to 10 ºC over 1.25 h, before quenching with saturated $NH_4Cl$ (2 mL) and stirring for a further 15 min. The mixture was diluted with $Et_2O$ (20 mL), washed with brine (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (3.5% EtOAc/pet. ether) gave **39** (26.8 mg, 40%) as a pale yellow gum. TLC (10% EtOAc/pet. ether) $R_F$ = 0.42; $[\alpha]_D^{25}$ −38.3 (*c* 1.21, $CH_2Cl_2$); $^1$H NMR (300 MHz, $CDCl_3$) δ 5.06 – 4.86 (m, 2H), 4.33 (s, 2H), 3.24 (d, *J* = 6.7 Hz, 2H), 1.89 (sep, *J* = 6.6 Hz, 1H), 1.77 – 1.59 (m, 3H), 1.44 (s, 9H), 0.95 (d, *J* = 5.2 Hz, 6H), 0.90 (d, *J* = 6.7 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 165.8, 155.0, 135.7, 120.2, 80.0, 77.6, 63.5, 47.5, 43.3, 28.3, 24.6, 22.7, 22.0, 19.3; MS ($ES^+$) *m/z* 443 (100%, M+Na, $^{81}$Br), 441 (99%, M+Na, $^{79}$Br), 421 (26%, M+H, $^{81}$Br), 419 (23%, M+H, $^{79}$Br); HRMS ($ES^+$) Calcd. for $C_{18}H_{31}{}^{79}BrN_2NaO_4$: 441.1365 (M+Na), Found: 441.1381. Continued elution (3.5% EtOAc/pet. ether) returned the starting material **29** (22.1 mg, 41% recovery).

**(*S*)-2-(1-((*tert*-Butoxycarbonyl)amino)-3-methylbutyl)oxazole-4-carboxylic acid (40)**




A mixture of ester **16**[S4] (187.4 mg, 0.60 mmol) and LiOH (143.7 mg, 6.00 mmol) in THF (6 mL) and water (6 mL) was stirred at rt in an air atmosphere for 3.5 h. The mixture was diluted with EtOAc (20 mL) and 1 M HCl (20 mL) and the organic phase was washed with water (15 mL) and brine (15 mL), then dried ($MgSO_4$) and concentrated to give the known acid **40** (176.4 mg, 99%) as a white solid. NMR data was in good agreement with that reported previously for **40** prepared by saponification with NaOH in dioxane.[S4] TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.24; $[\alpha]_D^{25}$ −70.8 (*c* 2.26, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 10.01 (bs, 1H), 8.27 (s, 1H), 6.06 (bm, 1H), 5.09 − 4.96 (m, 1H), 1.76 (t, *J* = 7.0 Hz, 2H), 1.66 (sep, *J* = 6.6 Hz, 1H), 1.40 (s, 9H), 0.95 (app. t, *J* = 6.9 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.5, 163.9, 155.5, 144.5, 133.2, 80.0, 47.4, 43.2, 28.2, 24.7, 22.5, 22.0; MS ($ES^-$) *m/z* 297 (100%, M−H); HRMS ($ES^+$) Calcd. for $C_{14}H_{21}N_2O_5$: 297.1450 (M−H), Found: 297.1461.

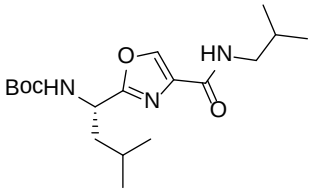
**(*S*)-Isobutyl 2-(1-((*tert*-butoxycarbonyl)amino)-3-methylbutyl)oxazole-4-carboxylate (41)**




This ester was prepared according to *General Procedure 1* using carboxylic acid **40** (29.8 mg, 0.10 mmol) and i-BuOH (74.1 mg, 1.00 mmol), with a 42 h reaction time. Flash chromatography (5% EtOAc/pet. ether) gave **41** (17.4 mg, 49%) as a pale yellow gum. TLC (10% EtOAc/pet. ether) $R_F$ = 0.25; $[\alpha]_D^{25}$ −46.1 (*c* 0.87, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.13 (s, 1H), 5.11 (bm, 1H), 5.04 –

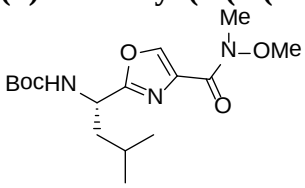
4.92 (m, 1H), 4.11 (d, *J* = 6.8 Hz, 2H), 2.06 (sep, *J* = 6.8 Hz, 1H), 1.82 – 1.59 (m, 3H), 1.43 (s, 9H), 0.98 (d, *J* = 6.8 Hz, 6H), 0.95 (d, *J* = 6.5 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.0, 161.2, 155.1, 143.4, 133.4, 80.0, 71.1, 47.4, 43.5, 28.3, 27.8, 24.6, 22.6, 22.0, 19.0; MS ($ES^+$) *m/z* 377 (100%, M+Na), 299 (49%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{18}H_{30}N_2NaO_5$: 377.2052 (M+Na), Found: 377.2057.

**(*S*)-*tert*-Butyl (1-(4-(isobutylcarbamoyl)oxazol-2-yl)-3-methylbutyl)carbamate (42)**



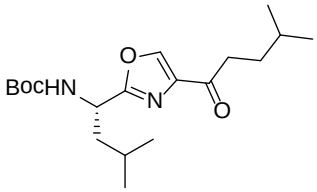

This compound was prepared according to *General Procedure 1* using carboxylic acid **40** (29.8 mg, 0.10) and i-Bu$NH_2$ (8.8 mg, 0.12 mmol) with a 24 h reaction time to give **42** (30.6 mg, 87%) as a pale yellow gum. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.58; $[\alpha]_D^{25}$ −48.9 (*c* 1.26, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 6.97 (bs, 1H), 5.13 – 4.85 (m, 2H), 3.23 (t, *J* = 6.9 Hz, 2H), 1.88 (sep, *J* = 6.8 Hz, 1H), 1.79 – 1.60 (m, 3H), 1.44 (s, 9H), 1.02 – 0.92 (m, 12H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 164.4, 160.5, 155.0, 140.7, 136.2, 80.1, 47.4, 46.3, 43.1, 28.6, 28.3, 24.6, 22.5, 22.0, 20.1; MS ($ES^+$) *m/z* 376 (100%, M+Na), 298 (90%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{18}H_{31}N_3NaO_4$: 376.2212 (M+Na), Found: 376.2199.

**(*S*)-*tert*-Butyl (1-(4-(methoxy(methyl)carbamoyl)oxazol-2-yl)-3-methylbutyl)carbamate (43)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **40** (89.5 mg, 0.30 mmol) and *N*,*O*-dimethylhydroxylamine·HCl (35.1 mg, 0.36 mmol), with added $NEt(i\text{-}Pr)_2$ (46.5 mg, 0.36 mmol) and a 16 h reaction time to give **43** (98.2 mg, 96%) as a pale yellow gum. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.59; $[\alpha]_D^{25}$ −48.5 (*c* 3.49, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 5.20 – 5.13 (m, 1H), 5.03 – 4.94 (m, 1H), 3.75 (s, 3H), 3.38 (s, 3H), 1.83 – 1.60 (m, 3H), 1.43 (s, 9H), 0.95 (d, *J* = 6.7 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 164.7, 161.0, 155.1, 142.2, 133.4, 79.9, 61.3, 47.2, 43.5, 33.2, 28.2, 24.6, 22.5, 22.1; MS ($ES^+$) *m/z* 364 (100%, M+Na), 342 (16%, M+H), 286 (41%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{16}H_{27}N_3NaO_5$: 364.1848 (M+Na), Found: 364.1851.

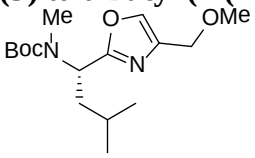
**(*S*)-*tert*-Butyl (3-methyl-1-(4-(4-methylpentanoyl)oxazol-2-yl)butyl)carbamate (44)**




*Preparation of (i-pentyl)MgBr:* To a suspension of acid-washed Mg flakes (48.6 mg, 2.00 mmol) in THF (2.0 mL) under $N_2$ was added in a single aliquot (i-pentyl)Br (0.25 mL, 2.00 mmol) and the suspension was stirred at rt for 2 h. The resulting supernatant was titrated with a standard solution of 2-butanol in toluene (1.00 M) with 1,10-phenanthroline (*ca.* 3 mg) as indicator[S9] to determine the concentration of the Grignard reagent (0.61 M, 61% of theoretical).

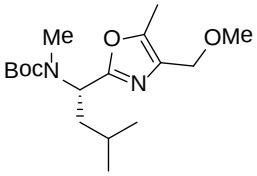
To a solution of **43** (21.0 mg, 0.062 mmol) in THF (0.22 mL) under $N_2$ at −10 °C (ice/salt bath) was added a solution of (i-pentyl)MgBr (prepared as described above, 0.61 M in THF, 0.40 mL, 0.25 mmol) and the mixture was allowed to warm to rt and stirred for 19 h. After quenching with saturated $NH_4Cl$ (3 mL), the mixture was diluted with EtOAc (15 mL) and the organic layer washed with saturated $NaHCO_3$ (15 mL) and brine (15 mL), then dried ($MgSO_4$) and concentrated. Flash chromatography (5% EtOAc/pet. ether) gave **44** (16.3 mg, 75%) as a pale yellow gum. TLC (10% EtOAc/pet. ether) $R_F$ = 0.38; $[\alpha]_D^{25}$ −46.8 (*c* 1.00, $CH_2Cl_2$); $^1$H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 5.12 – 4.89 (m, 2H), 2.87 (t, *J* = 7.4 Hz, 2H), 1.81 – 1.55 (m, 6H), 1.44 (s, 9H), 0.98 – 0.91 (m, 12H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 195.4, 165.3, 155.1, 141.8, 140.6, 80.1, 47.4, 43.3, 37.9, 32.6, 28.3, 27.7, 24.7, 22.6, 22.4, 22.1; MS ($ES^+$) *m/z* 375 (100%, M+Na), 297 (82%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{19}H_{32}N_2NaO_4$: 375.2260 (M+Na), Found: 375.2267.

**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)(methyl)carbamate (45)**




To a solution of **17** (260 mg, 0.91 mmol) in THF (9.0 mL) under $N_2$ at −78 °C was added a solution of NaHMDS (1.0 M in THF, 2.00 mL, 2.00 mmol) and the solution was stirred at −78 °C for 25 min. To this was added a solution of MeI (1.292 g, 9.10 mmol) and TBAI (33.2 mg, 0.09 mmol) in THF (5.0 mL) and the mixture was allowed to warm to rt with stirring for 16 h. The mixture was diluted with EtOAc (20 mL) and washed with 1 M HCl (20 mL) and saturated $NaHCO_3$ (20 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (14% EtOAc/pet. ether) gave **45** (216 mg, 76%) as a colorless gum. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.97 (d, *J* = 7.0 Hz, 6H, 2 x $CH_3$), 1.48 (s, 9H, $^t$Bu), 1.49-1.69 (m, 1H, CH), 1.79-2.00 (m, 2H, $CH_2$), 2.69 (s, 3H, $NCH_3$), 3.42 (s, 3H, $OCH_3$), 4.37 (s, 2H, $CH_2O$), 5.28-5.40 (m, 0.5H, CH), 5.50-5.65 (m, 0.5H, CH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ rotamers 21.5/21.7 ($CH_3$), 23.2 ($CH_3$), rotamers 24.3/24.6 (CH), 28.3 ($C(\underline{C}H_3)_3$), rotamers 28.9/29.2 ($NCH_3$), rotamers 38.2/38.5 ($CH_2$), rotamers 50.5/51.8 (CH), 58.5 ($OCH_3$), 66.3 ($CH_2O$), rotamers 80.0/80.3 ($\underline{C}(CH_3)_3$), 136.3 (ArH), 137.6, 163.9 (ArC), rotamers 155.5/156.0 (C=O). MS (ESI, +ve) *m/z* 313 (100%) $[M+H]^+$; 335 (50%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{16}H_{29}N_2O_4$ 313.2127, found 313.2126.

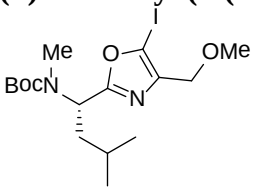
**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)-5-methyloxazol-2-yl)-3-methylbutyl)(methyl)carbamate (46)**




To a solution of **45** (49 mg, 0.16 mmol) in dry THF (0.5 mL) at -78 ºC was slowly added *n*-BuLi (2.5 M in hexane, 0.13 mL, 2.0 equiv.). After stirring at -78 ºC for 30 min, methyl iodide (1 mL, excess) was added dropwise. The mixture was stirred at this temperature for additional 30 min, and then was quenched with saturated aqueous $NH_4Cl$ (3 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated. The yellowish crude was purified by column flash chromatography (0.5% MeOH/$CH_2Cl_2$) to yield **46** (23 mg, 45%) as a yellowish compound. $^1$H NMR (300 MHz, $CDCl_3$): δ 0.96 (d, *J* = 6.6 Hz, 6H, $CH_3$), 0.97 (d, *J* = 6.6 Hz, 6H, $CH_3$), 1.49 (s, 9H, $^t$Bu), 1.51-1.66 (m, 1H, CH), 1.73-1.99 (m, 2H, $CH_2$), 2.30 (s, 3H, Ar$C\underline{H}_3$), 2.68 (s, 3H, $NCH_3$), 3.39 (s, 3H, $OCH_3$), 4.29 (s, 2H, $CH_2O$), 5.21-5.31 (m, 0.5H, CH), 5.44-

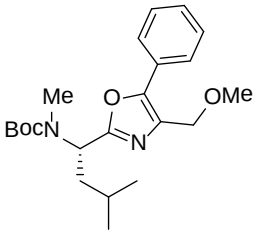
5.56 (m, 0.5H, CH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 10.23 (Ar<u>C</u>$H_3$), rotamers 21.6/21.8 ($CH_3$), 23.3 ($CH_3$), rotamers 24.3/24.7 (CH), 28.4 (C(<u>C</u>$H_3$)$_3$), rotamers 28.9/29.2 ($NCH_3$), 38.5 ($CH_2$), rotamers 50.4/51.7 (CH), 58.5 ($OCH_3$), 65.9 ($CH_2O$), rotamers 80.0/80.2 (<u>C</u>($CH_3$)$_3$), 131.5, 134.4, 146.7, 161.5 (ArC), rotamers 155.6/156.0 (C=O). MS (ESI, +ve) *m/z* 327 (100%) $[M+H]^+$; 349 (40%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{17}H_{31}N_2O_4$ 327.2284, found 327.2272. Further elution (0.5% MeOH/$CH_2Cl_2$) returned the starting material **45** (7 mg, 14% recovery).

**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)-5-iodooxazol-2-yl)-3-methylbutyl)(methyl)carbamate (47)**



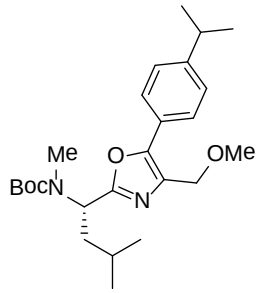

To a solution of **45** (216 mg, 0.69 mmol) in dry THF (1 mL) at -78 ºC was slowly added *n*-BuLi (2.5 M in hexane, 0.33 mL, 1.2 equiv.). After stirring at -78 ºC for 30 min, a solution of iodine (200 mL, 0.79 mmol) in dry THF (1 mL) was alowly added. The mixture was stirred at this temperature for additional 30 min, and then was quenched with saturated aqueous $NH_4Cl$ (3 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated. The yellowish crude was purified by column flash chromatography (10% EtOAc/pet. ether) to yield **47** (181 mg, 60%) as a colorless oil. $[\alpha]_D^{25}$ −62.95 (*c* 1.0, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): δ 0.97 (2 x d, *J* = 6.6 Hz, 6H, 2 x $CH_3$), 1.48 (s, 9H, $^t$Bu), 1.51-1.67 (m, 1H, CH), 1.72-2.01 (m, 2H, $CH_2$), 2.71 (s, 3H, $NCH_3$), 3.40 (s, 3H, $OCH_3$), 4.29 (s, 2H, $CH_2O$), 5.26-5.38 (m, 0.5H, CH), 5.52-5.65 (m, 0.5H, CH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ rotamers 21.5/21.7 ($CH_3$), 23.2 ($CH_3$), rotamers 24.3/24.6 (CH), 28.4 (C(<u>C</u>$H_3$)$_3$), rotamers 29.1/29.3 ($NCH_3$), 38.3 ($CH_2$), rotamers 50.8/52.0 (CH), 58.5 ($OCH_3$), 65.8 ($CH_2O$), rotamers 80.2/80.5 (<u>C</u>($CH_3$)$_3$), 88.4, 142.6, 168.4 (ArC), rotamers 155.4/156.0 (C=O). MS (ESI, +ve) *m/z* 435 (35%) $[M+H]^+$; 461 (100) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{16}H_{28}N_2O_4I$ 439.1094, found 439.1113. Further elution (14% EtOAc/pet. ether) returned the starting material **45** (43 mg, 20% recovery).

**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)-5-phenyloxazol-2-yl)-3-methylbutyl)(methyl)carbamate (48)**



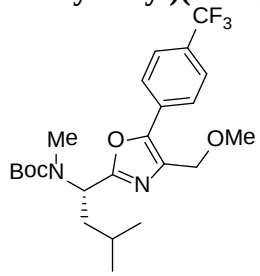

This compound was prepared according to *General Procedure 2* using **47** (20 mg, 0.046 mmol) and phenylboronic acid (6 mg, 0.049 mmol). Purification by flash column chromatography (7% EtOAc/pet. ether) afforded **48** (17 mg, 95%) as a yellow oil. $[\alpha]_D^{25}$ −50.7 (*c* 1.0, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.10 (d, *J* = 6.9 Hz, 6H, 2 x $CH_3$), 1.50 (s, 9H, $^t$Bu), 1.63-1.71 (m, 1H, CH), 1.84-2.05 (m, 2H, $CH_2$), 2.17 (s, 3H, $NCH_3$), 3.47 (s, 3H, $OCH_3$), 4.51 (s, 2H, $CH_2O$), 5.31-5.45 (m, 0.5H, CH), 5.56-5.70 (m, 0.5H, CH), 7.37 (d, *J* = 6.9 Hz, 1H, ArH), 7.42-7.47 (m, 2H, ArH), 7.63-7.66 (m, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ rotamers 21.8/22.1 ($CH_3$), 23.5 ($CH_3$), rotamers 24.6/24.9 (CH), 28.6 (C(<u>C</u>$H_3$)$_3$), rotamers 29.3/29.6 ($NCH_3$), 38.7 ($CH_2$), rotamers 50.9/52.1 (CH), 58.4 ($OCH_3$), 66.8 ($CH_2O$), rotamers 80.2/80.6 (<u>C</u>($CH_3$)$_3$), 126.4, 128.9, 129.1 (ArCH), 128.3, 132.4, 149.3, 161.9 (ArC), 155.8 (C=O). MS (ESI, +ve) *m/z* 389 (60%) $[M+H]^+$; 411 (100) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{22}H_{33}N_2O_4$ 389.2440, found 389.2443.

**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)-5-(4-isopropylphenyl)oxazol-2-yl)-3-methylbutyl)(methyl)carbamate (49)**



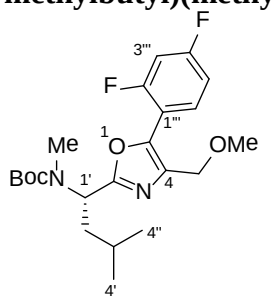

This compound was prepared according to *General Procedure 2* using **47** (19 mg, 0.043 mmol) and (4-isopropylphenyl)boronic acid (8 mg, 0.049 mmol). Purification by flash column chromatography (7% EtOAc/pet. ether) afforded **49** (14 mg, 76%) as a yellow oil. $[\alpha]_D^{25}$ −53.5 (*c* 0.7, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$): δ 0.99 (d, *J* = 6.5 Hz, 6H, 2 x $CH_3$), 1.27 (d, *J* = 6.5 Hz, 6H, 2 x $CH_3$Ar), 1.50 (s, 9H, $^t$Bu), 1.58-1.69 (m, 1H, CH), 1.81-2.03 (m, 2H, $CH_2$), 2.72-2.76 (m, 3H, $NCH_3$), 2.94 (septet, *J* = 7.0 Hz, 1H, $C_6H_4C\underline{H}(CH_3)_2$), 3.46 (s, 3H, $OCH_3$), 4.50 (s, 2H, $CH_2O$), 5.31-5.42 (m, 0.5H, CH), 5.55-5.69 (m, 0.5H, CH), 7.30 (d, *J* = 7.5 Hz, 2H, ArH), 7.56 (d, *J* = 6.5 Hz, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ rotamers 21.8/22.1 ($CH_3$), 23.5 ($CH_3$), 24.1 (($\underline{C}H_3)_2$CHAr), rotamers 24.7/25.0 (CH), 28.7 (C($\underline{C}H_3)_3$), rotamers 29.3/29.6 ($NCH_3$), 34.2 (($CH_3)_2\underline{C}$HAr), 38.8 ($CH_2$), rotamers 50.9/52.1 (CH), 58.4 ($OCH_3$), 66.9 ($CH_2O$), rotamers 80.2/80.6 ($\underline{C}(CH_3)_3$), 126.5, 127.2 (ArCH), 125.9, 131.4, 149.5, 149.9, 161.9 (ArC), 155.8 (C=O). MS (ESI, +ve) *m/z* 431 (100%) $[M+H]^+$; 453 (90) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{25}H_{39}N_2O_4$ 431.2910, found 431.2930.

**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)-5-(4-trifluoromethylphenyl)oxazol-2-yl)-3-methylbutyl)(methyl)carbamate (50)**



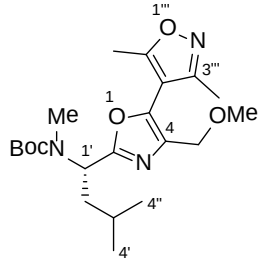

This compound was prepared according to *General Procedure 2* using **47** (24 mg, 0.055 mmol) and (4-(trifluoromethyl)phenyl)boronic acid (6 mg, 0.049 mmol). Purification by flash column chromatography (10% EtOAc/pet. ether) afforded **50** (21 mg, 84%) as a yellow oil. $[\alpha]_D^{25}$ −49.06 (*c* 1.1, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$): δ 1.04 (d, *J* = 6.5 Hz, 6H, 2 x $CH_3$), 1.53 (s, 9H, $^t$Bu), 1.59-1.78 (m, 1H, CH), 1.82-2.10 (m, 2H, $CH_2$), 2.79-2.80 (m, 3H, $NCH_3$), 3.50 (s, 3H, $OCH_3$), 4.56 (s, 2H, $CH_2O$), 5.35-5.50 (m, 0.5H, CH), 5.61-5.71 (m, 0.5H, CH), 7.73 (d, *J* = 6.5 Hz, 2H, ArH), 7.78 (d, *J* = 6.5 Hz, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ rotamers 21.5/21.8 ($CH_3$), 23.3 ($CH_3$), rotamers 24.4/24.7 (CH), 28.4 (C($\underline{C}H_3)_3$), rotamers 29.1/29.4 ($NCH_3$), rotamers 38.4/38.6 ($CH_2$), rotamers 50.7/51.9 (CH), 58.3 ($OCH_3$), 66.6 ($CH_2O$), rotamers 80.2/80.5 ($\underline{C}(CH_3)_3$), 124.0 (q, *J* = 273 Hz, $CF_3$), 125.9, 126.2 (ArCH), 130.3 (q, *J* = 30 Hz, $\underline{C}CF_3$), 131.3, 134.0, 147.7, rotamers 162.5/162.4 (ArC), rotamers 155.5/156.0 (C=O). MS (ESI, +ve) *m/z* 457 (50%) $[M+H]^+$; 479 (100) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{23}H_{32}N_2O_4F_3$ 457.2314, found 457.2336.

**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)-5-(2,4-difluorophenyl)oxazol-2-yl)-3-methylbutyl)(methyl)carbamate (51)**




This compound was prepared according to *General Procedure 2* using **47** (25 mg, 0.057 mmol) and (2,4-difluorophenyl)boronic acid (10 mg, 0.062 mmol). Purification by flash column chromatography (12% EtOAc/pet. ether) afforded **51** (22 mg, 91%) as a yellow oil. $[\alpha]_D^{25}$ −62.96 (*c* 1.1, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): δ 0.99 (d, *J* = 6.9 Hz, 6H, 2 x $CH_3$), 1.48 (s, 9H, $^t$Bu), 1.55-1.69 (m, 1H, CH), 1.81-2.05 (m, 2H, $CH_2$), 2.76 (s, 3H, $NCH_3$), 3.41 (s, 3H, $OCH_3$), 4.40 (d, *J* = 9 Hz, 2H, $CH_2O$), 5.33-5.45 (m, 0.5H, CH), 5.56-5.69 (m, 0.5H, CH), 6.89-7.00 (m, 2H, ArH), 7.49-7.56 (m, 1H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ rotamers 21.5/21.8 ($CH_3$), 23.2 ($CH_3$), rotamers 24.4/24.7 (CH), 28.4 ($C(\underline{C}H_3)_3$), rotamers 29.0/29.3 ($NCH_3$), 38.5 ($CH_2$), rotamers 50.7/51.9 (CH), 58.5 ($OCH_3$), rotamers 66.1/66.2 ($CH_2O$), rotamers 80.0/80.4 ($\underline{C}(CH_3)_3$), 104.8 (t, *J* = 26 Hz, C3'''), 111.9 (d, *J* = 21 Hz, C5'''), 112.7 (d, *J* = 11 Hz, C1'''), 131.2 (C6'''), 134.4 (C4), 143.0 (C3), rotamers 155.5/156.0 (C=O), 159.5 (dd, $J_1$ = 253 Hz, $J_2$ = 12 Hz, C2'''), 163.1 (C2), 163.4 (dd, $J_1$ = 251 Hz, $J_2$ = 12 Hz, C4'''); MS (ESI, +ve) *m/z* 425 (50%) $[M+H]^+$; 447 (100) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{22}H_{31}N_2O_4F_2$ 425.2252, found 425.2243.

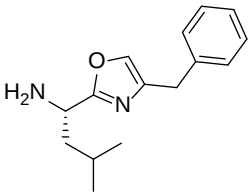
**(*S*)-*tert*-Butyl (1-(4-(methoxymethyl)-5-(3,5-dimethylisoxazol-4-yl)oxazol-2-yl)-3-methylbutyl)(methyl)carbamate (52)**




This compound was prepared according to *General Procedure 2* using **47** (20 mg, 0.046 mmol) and (3,5-dimethylisoxazol-4-yl)boronic acid (7 mg, 0.051 mmol). Purification by flash column chromatography (13% EtOAc/pet. ether) afforded **52** (16 mg, 85%) as a yellow oil. $[\alpha]_D^{25}$ −60.48 (*c* 0.8, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): δ 0.99 (d, *J* = 6.6 Hz, 3H, $CH_3$), 1.00 (d, *J* = 6.9 Hz, 3H, $CH_3$), 1.48 (s, 9H, $^t$Bu), 1.59-1.71 (m, 1H, CH), 1.79-2.04 (m, 2H, $CH_2$), 2.26 (s, 3H, $CH_3$), 2.43 (s, 3H, $CH_3$), 2.73 (s, 3H, $NCH_3$), 3.42 (s, 3H, $OCH_3$), 4.25 (ABq, *J* = 11.4 Hz, 2H, $CH_2O$), 5.34-5.40 (m, 0.5H, CH), 5.56-5.61 (m, 0.5H, CH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 10.6 ($CH_3$), 11.4 ($CH_3$), rotamers 21.4/21.6 and 23.3 (C4' and C4''), rotamers 24.3/24.6 (C3'), 28.4 ($C(\underline{C}H_3)_3$), rotamers 28.9/29.4 ($NCH_3$), 38.2 (C2'), rotamers 50.7/51.8 (C1'), 58.9 ($OCH_3$), 65.8 ($CH_2O$), rotamers 80.1/80.6 ($\underline{C}(CH_3)_3$), 104.9 (C3'''), 134.7 (C5), 139.3 (C4), rotamers 155.4/155.9 (C=O), 159.1 (C4'''), rotamers 163.8/164.0 (C2), 168.4 (C2'''). MS (ESI, +ve) *m/z* 408 (90%) $[M+H]^+$; 430 (100) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{21}H_{34}N_3O_5$ 408.2498, found 408.2505.

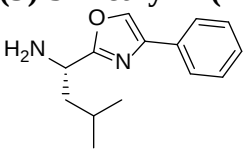
***Synthesis of Type C Amino Oxazoles and Thiazoles***

**(*S*)-1-(4-Benzyloxazol-2-yl)-3-methylbutan-1-amine (53)**



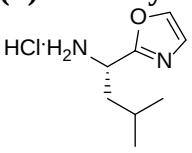
A solution of Type **B** protected amine **13** (140 mg, 0.37 mmol) and ethylenediamine (0.10 mL, 1.50 mmol) in ethanol (5 mL) was heated at reflux for 18 h. The ethanol was removed in vacuo and the remaining mixture was dissolved in $CH_2Cl_2$ and acidified with 1 M HCl. The organic layer was separated and the aqeous phase was made basic with 1M NaOH, then extracted with $CH_2Cl_2$ (3×30 mL). The combined organic layers were dried ($Na_2SO_4$) and concentrated to give amine **53** (70 mg, 78%). $^1$H NMR (300 MHz, $CDCl_3$) δ 0.92-0.97 (m, 6H), 1.60-1.75 (m, 5H/$NH_2$), 3.86 (s, 2H), 4.03-4.08 (m, 1H), 7.17 (s, 1H), 7.22-7.35 (m, 5H). Subsequent coupling to commercially obtained Fmoc-D-Arg(Pbf)-OH (see Scheme S7) revealed that amine **53** had been formed with minor amounts of the (*R*)-enantiomer (due to the formation of chromatographically separable epimers), presumably as a consequence of partial racemization during this deprotection protocol.

**(*S*)-3-Methyl-1-(4-phenyloxazol-2-yl)butan-1-amine (54)**



A solution of Type **B** protected amine **14** (160 mg, 0.44 mmol) and ethylenediamine (0.10 mL, 1.50 mmol) in ethanol (5 mL) was heated at reflux for 18 h. The ethanol was removed in vacuo and the remaining mixture was dissolved in $CH_2Cl_2$ and acidified with 1 M HCl. The organic layer was separated and the aqeous phase was made basic with 1M NaOH, then extracted with $CH_2Cl_2$ (3×30 mL). The combined organic layers were dried ($Na_2SO_4$) and concentrated to give **54** (90 mg, 87%). $^1$H NMR (300 MHz, $CDCl_3$) δ 0.72-1.00 (m, 6H), 1.68-1.86 (m, 5H/$NH_2$), 4.11-4.19 (m, 1H), 7.27-7.34 (m, 1H), 7.38-7.42 (m, 2H), 7.70-7.74 (m, 2H), 7.84 (s, 1H). Subsequent coupling to commercially obtained Fmoc-D-Arg(Pbf)-OH (see Scheme S7) revealed that amine **54** had been formed with minor amounts of the (*R*)-enantiomer (due to the formation of chromatographically separable epimers), presumably as a consequence of partial racemization during this deprotection protocol.

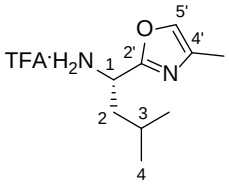
**(*S*)-3-Methyl-1-(oxazol-2-yl)butan-1-ammonium chloride (55)**



To a solution of Type **B** protected amine **15** (16.9 mg, 0.059 mmol) in i-PrOH (0.50 mL) and $H_2O$ (0.09 mL) was added $NaBH_4$ (11.2 mg, 0.30 mmol) and the mixture was stirred at rt in a capped vial (air atmosphere) for 20 h. To this was added AcOH (0.08 mL) and the mixture was heated at 80 °C for 2 h. An additional aliquot of AcOH (0.06 mL) was added and heating continued at 80 °C for a further 6 h to complete the amide hydrolysis. The mixture was diluted with 1 M HCl (10 mL) and EtOAc (10 mL). The aqueous phase was separated and basified to pH ≥10 with 25% $K_2CO_3$ and the free amine was extracted with $CH_2Cl_2$ (3×10 mL). The combined organic layers were dried ($Na_2SO_4$)

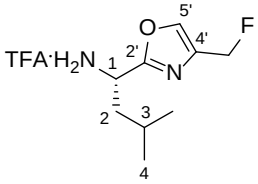
and filtered, and then an aliquot of ethereal HCl (2 M in $Et_2O$, 0.20 mL) was added to convert the amine to the non-volatile HCl salt. Removal of the solvents under reduced pressure gave **55** (8.5 mg, 75%) as a white solid. $^1$H NMR (500 MHz, $CD_3OD$) δ 8.02 (s, 1H), 7.26 (s, 1H), 4.63 (dd, *J* = 9.2, 6.0 Hz, 1H), 2.06 – 1.97 (m, 1H), 1.87 – 1.79 (m, 1H), 1.60 (sep, *J* = 6.8 Hz, 1H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H); $^{13}$C NMR (125 MHz, $CD_3OD$) δ 161.2, 142.1, 128.7, 48.5, 42.1, 25.8, 22.8, 22.0; MS ($ES^+$) *m/z* 155 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_8H_{14}N_2NaO$: 177.1004 (M+Na), Found: 177.1005. Subsequent coupling to the stereochemically pure carboxylic acid **A** (with formation of ~90:10 inseparable epimers) revealed that amine **55** had contained *ca.* 10% of the minor (*R*)-enantiomer, presumably as a consequence of partial racemization during this deprotection protocol.

**(*S*)-1-(4-methyloxazol-2-yl)-3-methylbutan-1-ammonium trifluoroacetate (56)**



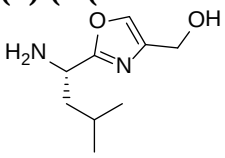

This compound was prepared according to *General Procedure 3* using Type **B** protected amine **18** (21.7 mg, 0.08 mmol) and omitting the aqueous work-up to yield amine·TFA salt **56** (27.4 mg, 120% of theoretical due to residual TFA) as a yellow oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 0.89 - 0.96 (6H, m, H4 and H3-C$\underline{H}_3$), 1.26 - 1.57 (3H, m, H3 and H2), 2.00 (2H, bm, NH), 2.17 (3H, s, H4'-C$\underline{H}_3$), 4.68 - 4.84 (1H, bm, H1), 7.47 (1H, s, H5'). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 10.3 (C4'-$\underline{C}H_3$), 21.3 (C4/3-$CH_3$), 22.4 (C4/3-$CH_3$), 24.7 (C3), 40.9 (C2), 47.9 (C1), 136.5 (C4'), 136.7 (C5'), 159.7 (C2'). MS ($ESI^+$) *m/z* = 169 (100 %, $[M+H]^+$).

**(*S*)-1-(4-(fluoromethyl)oxazol-2-yl)-3-methylbutan-1-ammonium trifluoroacetate (57)**




This compound was prepared according to *General Procedure 3* using Type **B** protected amine **19** (26 mg, 0.09 mmol) and omitting the aqueous work-up to yield amine·TFA salt **57** (27.1 mg, quant.) as a yellow oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 0.92 (6H, t, *J* = 6.8 Hz H4 and H3-C$\underline{H}_3$), 1.27 - 1.60 (3H, m, H2 and H3), 1.90 - 1.99 (2H, bm, NH), 4.56 - 4.70 (1H, bm, H1), 5.18 (2H, d, $J_{H\text{-}F}$ = 47.4 Hz, $CH_2F$), 7.66 (1H, s, H5'). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 21.5 (C4/C3-$\underline{C}H_3$), 22.3 (C4/C3-$\underline{C}H_3$), 24.7 (C3), 41.1 (C2), 48.2 (C1), 75.5 ($J_{C\text{-}F}$ = 164.5 Hz), 136.4 (C5'), 136.7 (C5'), 139.2 (C4'), 139.3 (C4'), 160.7 (C2'). MS ($ESI^+$) *m/z* = 187 (100 %, $[M+H]^+$).

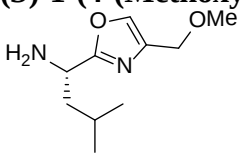
**(*S*)-(2-(1-Amino-3-methylbutyl)oxazol-4-yl)methanol (58)**




This compound was prepared according to *General Procedure 3* using Type **B** protected amine **17** (22.2 mg, 0.078 mmol) to give **58** (11.2 mg, 78%) as a pale yellow gum. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.51 (s, 1H), 4.57 (s, 2H), 4.06 (t, *J* = 7.0 Hz, 1H), 2.19 (bs, 3H), 1.76 – 1.56 (m, 3H), 0.94 (d, *J* = 6.2 Hz, 3H), 0.92 (d, *J* = 6.1 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.4, 140.0, 134.7, 56.4, 48.3,

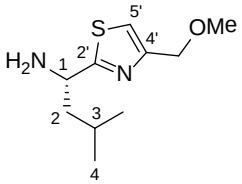
45.1, 24.7, 22.7, 22.1; MS ($ES^+$) *m/z* 185 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_9H_{17}N_2O_2$: 185.1290 (M+H), Found: 185.1284.

**(*S*)-1-(4-(Methoxymethyl)oxazol-2-yl)-3-methylbutan-1-amine (59)**



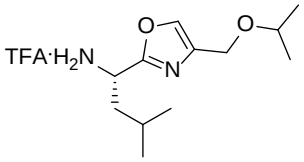
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **33** (45 mg, 0.15 mmol) to yield **59** (25 mg, 84%) as an oil. $^1$H NMR (300 MHz, $CDCl_3$): δ 0.92 (d, *J* = 6.3 Hz, 3H, $CH_3$), 0.94 (d, *J* = 6.3 Hz, 3H, $CH_3$), 1.60-1.76 (m, 5H, CH, $CH_2$ and $NH_2$), 3.43 (s, 3H, $OCH_3$), 4.00-4.15 (m, 1H, CH), 4.36 (s, 2H, $CH_2O$), 7.54 (s, 1H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 22.0 ($CH_3$), 22.8 ($CH_3$), 24.7 (CH), 45.0 ($CH_2$), 48.2 (CH), 58.5 ($OCH_3$), 66.2 ($CH_2O$), 135.9 (ArCH), 137.3, 168.4 (ArC). MS (ESI, +ve) *m/z* 199 (100%) $[M+H]^+$; HRMS ($ES^+$) Calcd. for $C_{10}H_{19}N_2O_2$: 199.1447 $[M+H]^+$, Found: 199.1445.

**(*S*)-1-(4-(Methoxymethyl)thiazol-2-yl)-3-methylbutan-1-amine (60)**



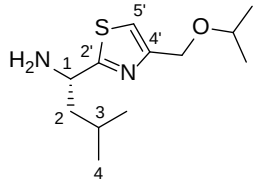
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **26** (58.3 mg, 0.18 mmol) to yield **60** (33.8 mg, 85%) as a viscous yellow oil. $[\alpha]_D^{25} = -5.7$ (c 1.7, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.94 (6H, t, *J* = 6.8 Hz, H4 and 3-$CH_3$), 1.56 - 1.66 (1H, m, $H2_a$), 1.69 - 1.83 (4H, m, $H2_a$ and H3 and $NH_2$), 3.43 (3H, s, $OCH_3$), 4.29 (1H, dd, *J* = 8.8, 4.8 Hz, H1), 4.52 (2H, s, $C\underline{H_2}OCH_3$), 7.11 (1H, s, H5'). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 21.9 (C4 or 3-$CH_3$), 23.3 (C4 or 3-$CH_3$), 25.0 (C3), 47.9 (C2), 52.5 (C1), 58.7 ($OCH_3$), 70.6 ($\underline{C}H_2OCH_3$), 115.5 (C5'), 153.4 (C4'), 178.8 (C2'). IR (neat) *ν* [$cm^{-1}$] = 3374 (w), 2955 (m), 2927 (m), 2870 (m), 1719 (w), 1664 (w), 1612 (w), 1533 (w), 1468 (m), 1368 (m), 1259 (m), 1195 (m), 1138 (m), 1094 (s), 985 (w), 953 (w), 907 (w), 861 (w), 803 (m), 746 (m). MS ($ESI^+$) *m/z* = 215 (100%, $[M+H]^+$). HRMS ($ESI^+$) $[M+H]^+$ Calcd. for $C_{10}H_{19}N_2OS$: 215.1218, Found: 215.1216.

**(*S*)-1-(4-(Isopropoxymethyl)oxazol-2-yl)-3-methylbutan-1-ammonium trifluoroacetate (61)**



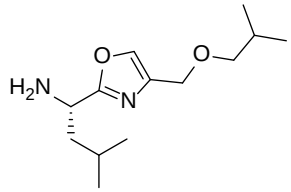
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **27** (22 mg, 0.067 mmol) and omitting the aqueous work-up to yield amine·TFA salt **61** (22 mg, 96%) as an oil. $^1$H NMR (500 MHz, $CD_3OD$): δ 0.92 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.96 (d, *J* = 7.0 Hz, 3H, $CH_3$), 1.16 (d, *J* = 6.5 Hz, 3H, 2 x $CH_3$), 1.55-1.61 (m, 1H, CH), 1.75-1.80 (m, 1H, $CH_2$ ($H_a$)), 1.95-2.01 (m, 1H, $CH_2$ ($H_b$)), 3.72 (septet, *J* = 6.0 Hz, 1H, OCH), 4.42 (s, 2H, $CH_2O$), 4.56 (dd, $J_1$ = 6.5, $J_2$ = 9.0 Hz, 1H, CH), 7.90 (s, 1H, ArH (oxazole)); $^{13}$C NMR (126 MHz, $CD_3OD$): δ 22.0, 22.2, 22.3, 22.8 (4 x $CH_3$), 25.7 (CH), 42.0 ($CH_2$), 48.5 (CH), 65.6 ($CH_2O$), 70.9 (CHO), 140.4 (ArCH), 140.6, 161.3 (ArC). MS (ESI, +ve) *m/z* 227 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{12}H_{23}N_2O_2$ 227.1760, found 227.1754.

**(*S*)-1-(4-(Isopropoxymethyl)thiazol-2-yl)-3-methylbutan-1-amine (62)**



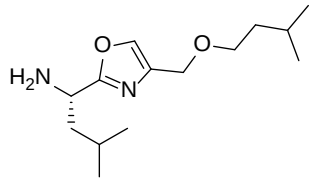
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **28** (53.2 mg, 0.16 mmol) to yield **62** (27.4 mg, 71%) as a yellow oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 0.96 (6H, t, *J* = 10.0 Hz, H4 and 3-$CH_3$), 1.22 - 1.26 (6H, m, $CH_2OCH(C\underline{H}_3)_2$), 1.59 - 1.68 (1H, m, H3), 1.71 - 1.80 (2H, m, H2), 1.86 (1H, bs, NH), 3.73 - 3.77 (1H, m, $CH_2OC\underline{H}(CH_3)_2$), 4.29 (1H, dd, *J* = 8.8, 4.9 Hz H1), 4.60 (2H, s, $C\underline{H}_2OCH(CH_3)_2$), 7.12 (1H, s, H5'). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 21.9 (C4 or 3-$CH_3$), 22.1 (C4 or 3-$CH_3$), 23.1 ($CH_2OCH(\underline{C}H_3)_2$), 24.8 (C3), 47.7 (C2), 52.3 (C1), 66.3 ($\underline{C}H_2OCH(CH_3)_2$), 71.6 ($CH_2O\underline{C}H(CH_3)_2$), 114.5 (C5'), 154.3 (C4'), 178.1 (C2'). MS ($ESI^+$) *m/z* = 243 (100 %, $[M+H]^+$). HRMS ($ESI^+$) $[M+H]^+$ Calcd. for $C_{12}H_{22}N_2NaOS$: 243.1531, Found: 243.1531.

**(*S*)-1-(4-(Isobutoxymethyl)oxazol-2-yl)-3-methylbutan-1-amine (63)**



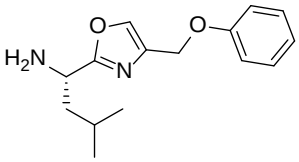
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **29** (34.0 mg, 0.10 mmol) to give **63** (24.2 mg, 100%) as a pale yellow oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.50 (s, 1H), 4.38 (s, 2H), 4.04 (t, *J* = 7.0 Hz, 1H), 3.26 (d, *J* = 6.5 Hz, 2H), 1.88 (sep, *J* = 6.5 Hz, 1H), 1.73 – 1.58 (m, 5H), 0.93 – 0.87 (m, 12H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.0, 138.0, 135.5, 77.8, 65.0, 48.3, 45.1, 28.3, 24.7, 22.8, 22.0, 19.3; MS ($ES^+$) *m/z* 241 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{13}H_{25}N_2O_2$: 241.1916 (M+H), Found: 241.1928.

**(*S*)-1-(4-((Isopentyloxy)methyl)oxazol-2-yl)-3-methylbutan-1-amine (64)**



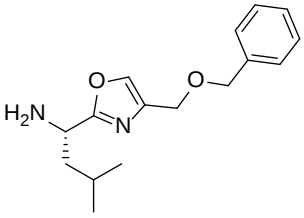
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **30** (42.7 mg, 0.12 mmol) to give **64** (27.1 mg, 89%) as a pale yellow gum. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 4.40 (s, 2H), 4.06 (t, *J* = 6.9 Hz, 1H), 3.55 (t, *J* = 7.0 Hz, 2H), 1.77 – 1.58 (m, 6H), 1.51 (q, *J* = 7.0 Hz, 2H), 0.99 – 0.85 (m, 12H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.1, 137.8, 135.6, 69.4, 64.7, 48.3, 45.1, 38.4, 25.0, 24.7, 22.8, 22.6, 22.0; MS ($ES^+$) *m/z* 255 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{14}H_{27}N_2O_2$: 255.2073 (M+H), Found: 255.2075.

**(*S*)-3-Methyl-1-(4-(phenoxymethyl)oxazol-2-yl)butan-1-amine (65)**



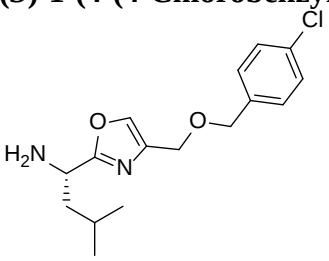
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **32** (27 mg, 0.075 mmol) to yield **65** (19 mg, 97%) as an oil. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 0.91 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.94 (d, *J* = 6.0 Hz, 3H, $CH_3$), 1.71-1.76 (m, 1H, CH), 1.98-2.08 (m, 2H, $CH_2$), 4.59 (t, *J* = 7.0 Hz, 1H, CH), 4.96 (ABq, *J* = 13.5 Hz, 2H, $CH_2O$), 6.93-6.97 (m, 3H, ArH), 7.26 (d, *J* = 9.2 Hz, 2H, ArH), 7.65 (s, 1H, ArH (oxazole)), 9.07 (br s, 2H, $NH_2$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 21.9 ($CH_3$), 22.3 ($CH_3$), 24.5 (CH), 41.0 ($CH_2$), 47.8 (CH), 62.5 ($CH_2O$), 115.0, 151.5, 129.6 (ArCH), 137.6, 158.1, 159.9 (ArC). MS (ESI, +ve) *m/z* 261 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{15}H_{21}N_2O_2$ 261.1603, found 261.1607.

**(*S*)-1-(4-(Benzyloxymethyl)oxazol-2-yl)-3-methylbutan-1-amine (66)**



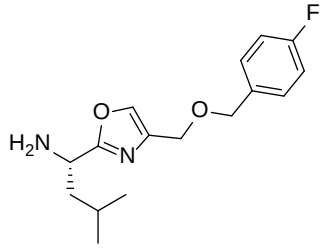
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **34** (19 mg, 0.050 mmol) to yield **66** (10 mg, 73%) as an oil. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 0.91-0.95 (m, 6H, 2 x $CH_3$), 1.62-1.72 (m, 3H, CH and $CH_2$), 1.85-2.04 (m, 2H, $NH_2$), 4.02-4.17 (m, 1H, CH), 4.45 (s, 2H, $CH_2O$), 4.62 (s, 2H, C$\underline{H}_2$Ph), 7.26-7.36 (m, 5H, ArH), 7.53 (s, 1H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 22.0 ($CH_3$), 22.8 ($CH_3$), 24.7 (CH), 45.0 ($CH_2$), 48.3 (CH), 63.9 ($CH_2O$), 72.7 ($\underline{C}H_2$Ph), 127.7, 127.9, 128.4 (ArCH), 135.9 (ArCH (oxazole)), 137.5, 137.7, 168.2. MS (ESI, +ve) *m/z* 275 (100%) $[M+H]^+$.

**(*S*)-1-(4-(4-Chlorobenzyloxymethyl)oxazol-2-yl)-3-methylbutan-1-amine (67)**



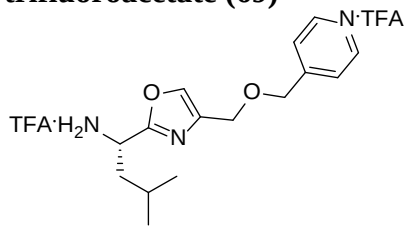
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **35** (37 mg, 0.090 mmol) to yield **67** (27 mg, 97%) as an oil. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 0.92 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.95 (d, *J* = 6.0 Hz, 3H, $CH_3$), 1.61-1.76 (m, 5H, CH, $CH_2$ and $NH_2$), 4.02-4.12 (m, 1H, CH), 4.44 (s, 2H, $CH_2O$), 4.58 (s, 2H, C$\underline{H}_2$ArCl), 7.27-7.34 (m, 4H, ArH), 7.54 (s, 1H, ArH (oxazole)); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.0 ($CH_3$), 22.8 ($CH_3$), 24.7 (CH), 45.1 ($CH_2$), 48.3 (CH), 64.0 ($CH_2O$), 71.8 ($\underline{C}H_2$ArCl), 128.5, 129.1 (ArCH), 135.9 (ArCH (oxazole)), 133.5, 136.3, 137.3; MS (ESI, +ve) *m/z* 309 (100%) $[M+H]^+$.

**(*S*)-1-(4-(((4-Fluorobenzyl)oxy)methyl)oxazol-2-yl)-3-methylbutan-1-amine (68)**



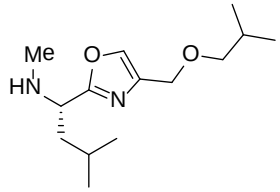
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **36** (22.2 mg, 0.057 mmol) to give **68** (13.5 mg, 82%) as a colorless gum. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.38 − 7.29 (m, 2H), 7.03 (app. t, *J* = 8.5 Hz, 2H), 4.57 (s, 2H), 4.44 (s, 2H), 4.07 (t, *J* = 6.8 Hz, 1H), 1.81 – 1.57 (m, 5H), 0.95 (d, *J* = 6.0 Hz, 3H), 0.92 (d, *J* = 5.8 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.3, 162.4 (d, $J_{C–F}$ = 245.6 Hz), 137.4, 135.9, 133.6 (d, $J_{C–F}$ = 3.0 Hz), 129.7 (d, $J_{C–F}$ = 8.0 Hz), 115.3 (d, $J_{C–F}$ = 21.4 Hz), 72.0, 63.9, 48.3, 45.1, 24.7, 22.8, 22.0; MS (ES$^+$) *m/z* 293 (100%, M+H); HRMS (ES$^+$) Calcd. for $C_{16}H_{22}FN_2O_2$: 293.1665 (M+H), Found: 293.1653.

**(*S*)-4-(((2-(1-Ammonio-3-methylbutyl)oxazol-4-yl)methoxy)methyl)pyridin-1-ium trifluoroacetate (69)**



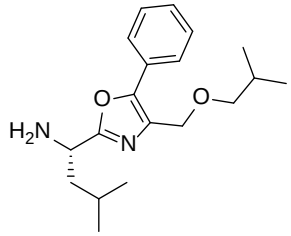
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **31** (13 mg, 0.035 mmol) and omitting the aqueous work-up to yield amine·TFA salt **69** (13 mg, 96%) as an oil. $^{1}$H NMR (300 MHz, $CD_3OD$): δ 0.85 (d, *J* = 6.6 Hz, 3H, $CH_3$), 0.89 (d, *J* = 6.6 Hz, 3H, $CH_3$), 1.45-1.58 (m, 1H, CH), 1.67-1.77 (m, 1H, $CH_2$ ($H_a$)), 1.84-1.96 (m, 1H, $CH_2$ ($H_b$)), 4.52 (dd, $J_1$ = 6.3, $J_2$ = 9.0 Hz, 1H, CH), 4.58 (d, *J* = 3.9 Hz, 2H, $CH_2O$), 4.81 (s, 2H, C$\underline{H}_2$Py), 7.94-7.99 (m, 2H, ArH), 7.98 (s, 1H, ArH (oxazole)), 8.71 (d, *J* = 3.9 Hz, 2H, ArH); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 22.0 ($CH_3$), 22.8 ($CH_3$), 25.8 (CH), 42.0 ($CH_2$), 48.5 (CH), 65.4 ($CH_2O$), 70.7 ($\underline{C}H_2$Py), 125.8, 143.0 (ArCH), 139.2, 161.4, 161.7 (ArC). MS (ESI, +ve) *m/z* 276 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{15}H_{22}N_3O_2$ 276.1712, found 276.1708.

**(*S*)-1-(4-(Isobutoxymethyl)oxazol-2-yl)-*N*,3-dimethylbutan-1-amine (70)**



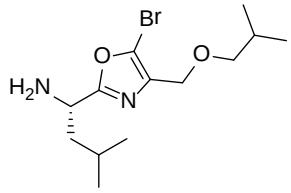
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **37** (18.4 mg, 0.052 mmol) to give **70** (8.6 mg, 65%) as a pale yellow gum. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.55 (s, 1H), 4.43 (s, 2H), 3.79 (t, *J* = 7.5 Hz, 1H), 3.29 (d, *J* = 6.7 Hz, 2H), 2.32 (s, 3H), 1.90 (sep, *J* = 6.5 Hz, 1H), 1.72 – 1.48 (m, 4H), 0.99 – 0.82 (m, 12H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 166.5, 138.0, 135.7, 77.7, 65.1, 56.7, 43.5, 34.2, 28.4, 24.9, 22.52, 22.48, 19.4; MS (ES$^+$) *m/z* 255 (100%, M+H); HRMS (ES$^+$) Calcd. for $C_{14}H_{27}N_2O_2$: 255.2073 (M+H), Found: 255.2072.

**(*S*)-1-(4-(Isobutoxymethyl)-5-phenyloxazol-2-yl)-3-methylbutan-1-amine (71)**



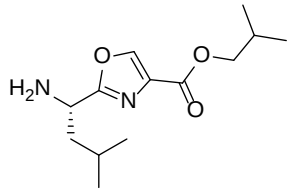
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **38** (30.6 mg, 0.073 mmol) to give **71** (21.0 mg, 91%) as a pale yellow gum. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.6 Hz, 2H), 7.50 – 7.31 (m, 3H), 4.53 (s, 2H), 4.12 (t, *J* = 6.8 Hz, 1H), 3.35 (d, *J* = 6.3 Hz, 2H), 1.94 (sep, *J* = 6.5 Hz, 1H), 1.86 – 1.63 (m, 5H), 1.03 – 0.88 (m, 12H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 165.9, 148.5, 132.4, 128.7, 128.3, 128.2, 126.0, 77.5, 65.2, 48.3, 45.1, 28.4, 24.8, 22.9, 22.1, 19.5; MS ($ES^+$) *m/z* 317 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{19}H_{29}N_2O_2$: 317.2229 (M+H), Found: 317.2226.

**(*S*)-1-(5-Bromo-4-(isobutoxymethyl)oxazol-2-yl)-3-methylbutan-1-amine (72)**



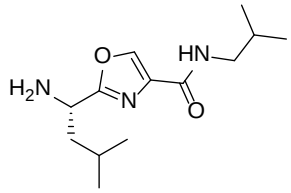
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **39** (24.2 mg, 0.058 mmol) to give **72** (16.1 mg, 88%) as a pale yellow gum. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 4.32 (s, 2H), 4.04 (t, *J* = 6.9 Hz, 1H), 3.25 (d, *J* = 6.8 Hz, 2H), 1.91 (sep, *J* = 6.8 Hz, 1H), 1.80 – 1.56 (m, 5H), 1.04 – 0.85 (m, 12H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 168.9, 135.5, 120.0, 77.7, 63.5, 48.5, 44.7, 28.3, 24.7, 22.8, 21.9, 19.3; MS ($ES^+$) *m/z* 321 (94%, M+H, $^{81}$Br), 319 (100%, M+H, $^{79}$Br); HRMS ($ES^+$) Calcd. for $C_{13}H_{24}{}^{79}BrN_2O_2$: 319.1021 (M+H), Found: 319.1037.

**(*S*)-Isobutyl 2-(1-amino-3-methylbutyl)oxazole-4-carboxylate (73)**



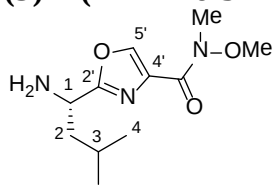
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **41** (17.4 mg, 0.049 mmol) to give **73** (10.3 mg, 82%) as a pale yellow gum. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 4.18 – 4.08 (m, 3H), 2.08 (sep, *J* = 6.6 Hz, 1H), 1.82 – 1.59 (m, 5H), 1.04 – 0.87 (m, 12H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 168.9, 161.3, 143.4, 133.2, 71.0, 48.4, 44.9, 27.8, 24.7, 22.8, 22.0, 19.1; MS ($ES^+$) *m/z* 255 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{13}H_{23}N_2O_3$: 255.1709 (M+H), Found: 255. 1700.

**(*S*)-2-(1-Amino-3-methylbutyl)-*N*-isobutyloxazole-4-carboxamide (74)**



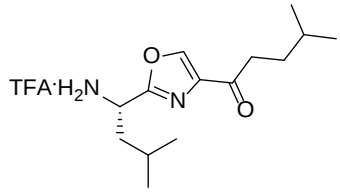
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **42** (25.2 mg, 0.071 mmol) to give **74** (17.1 mg, 94%) as an off-white solid. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 6.98 (bs, 1H), 4.09 (t, *J* = 6.8 Hz, 1H), 3.24 (t, *J* = 6.9 Hz, 2H), 1.89 (sep, *J* = 6.7 Hz, 1H), 1.78 – 1.59 (m, 5H), 1.04 – 0.88 (m, 12H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.6, 160.6, 140.4, 136.1, 48.2, 46.3, 45.1, 28.6, 24.7, 22.7, 22.0, 20.1; MS ($ES^+$) *m/z* 254 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{13}H_{24}N_3O_2$: 254.1869 (M+H), Found: 254.1870.

**(*S*)-2-(1-Amino-3-methylbutyl)-*N*-methoxy-*N*-methyloxazole-4-carboxamide (75)**



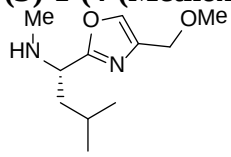
This compound was prepared according to *General Procedure 3* using Type **B** protected amine **43** (29.5 mg, 0.09 mmol) to give **75** (16.8 mg, 81%) as a yellow oil. TLC (5% $MeOH/CH_2Cl_2$) $R_F$ = 0.48. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 0.92 - 0.96 (6H, m, H4 and H3-C$\underline{H}_3$), 1.64 - 1.77 (4H, m, H3/H2/NH), 3.38 (3H, s, N-$CH_3$), 3.76 (3H, s, O-$CH_3$), 4.14 (1H, t, *J* = 6.9 Hz, H1), 8.11 (1H, s, H5'). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 22.2 (C4/3-$\underline{C}H_3$), 22.9 (C4/3-$\underline{C}H_3$), 24.9 (C3), 33.4 (N-$CH_3$), 45.1 (C2), 48.5 (C1), 61.5 (O-$CH_3$), 133.4 (C4'), 142.4 (C5'), 159.7 (C2'), 167.8 (CO). MS ($ESI^+$) *m/z* = 242 (100 %, $[M+H]^+$).

**(*S*)-3-Methyl-1-(4-(4-methylpentanoyl)oxazol-2-yl)butan-1-ammonium trifluoroacetate (76)**



This compound was prepared according to *General Procedure 3* using Type **B** protected amine **44** (19.9 mg, 0.056 mmol) and omitting the aqueous work-up to give amine·TFA salt **76** (22.5 mg, 109% of theoretical due to residual TFA) as a yellow gum. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 8.29 (s, 1H), 4.74 (t, *J* = 7.5 Hz, 1H), 2.80 (t, *J* = 7.1 Hz, 2H), 1.99 (t, *J* = 7.6 Hz, 2H), 1.80 – 1.48 (m, 4H), 1.07 – 0.82 (m, 12H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 195.4, 161.6, 144.4, 139.8, 47.7, 41.0, 37.7, 32.5, 27.6, 24.4, 22.2, 21.5; MS ($ES^+$) *m/z* 253 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{14}H_{25}N_2O_2$: 253.1916 (M+H), Found: 253.1919.

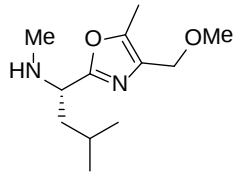
**(*S*)-1-(4-(Methoxymethyl)oxazol-2-yl)-*N*,3-dimethylbutan-1-amine (77)**



This compound was prepared according to *General Procedure 3* using Type **B** protected amine **45** (16 mg, 0.051 mmol) to yield **77** (9 mg, 82%) as an oil. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 0.88 (d, *J* =

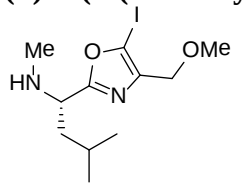
6.5 Hz, 3H, $CH_3$), 0.93 (d, *J* = 6.5 Hz, 3H, $CH_3$), 1.55-1.59 (m, 1H, CH), 1.68-1.72 (m, 2H, $CH_2$), 2.04 (br s, 1H, NH), 2.34 (s, 3H, $NCH_3$), 3.43 (s, 3H, $OCH_3$), 3.83 (t, *J* = 7.5 Hz, 1H, CH), 4.39 (s, 2H, $CH_2O$), 7.57 (s, 1H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.4 ($CH_3$), 22.5 ($CH_3$), 24.9 (CH), 34.0 ($NCH_3$), 43.3 ($CH_2$), 56.6 (CH), 58.5 ($OCH_3$), 66.4 ($CH_2O$), 136.0 (ArCH), 137.5, 166.3 (ArC). MS (ESI, +ve) *m/z* 213 (100%) $[M+H]^+$.

**(*S*)-1-(4-(Methoxymethyl)-5-methyloxazol-2-yl)-*N*,3-dimethylbutan-1-amine (78)**



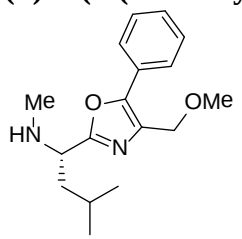

This compound was prepared according to *General Procedure 3* using Type **B** protected amine **46** (23 mg, 0.070 mmol) to yield **78** (11 mg, 69%) as an oil. $^1$H NMR (300 MHz, $CDCl_3$): δ 0.88 (d, *J* = 6.3 Hz, 3H, $CH_3$), 0.93 (d, *J* = 6.0 Hz, 3H, $CH_3$), 1.54-1.68 (m, 1H, CH, $CH_2$ and NH), 2.32 and 2.33 (2 x s, 3H each, Ar$C\underline{H}_3$ and $NCH_3$), 3.40 (s, 3H, $OCH_3$), 3.73 (t, *J* = 7.5 Hz, 1H, CH), 4.30 (s, 2H, $CH_2O$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 10.5 (Ar$\underline{C}H_3$) 22.7 ($CH_3$), 22.8 ($CH_3$), 25.2 (CH), 34.5 ($NCH_3$), 43.7 ($CH_2$), 56.8 (CH), 58.4 ($OCH_3$), 66.1 ($CH_2O$), 131.4, 146.4, 164.4 (ArC). MS (ESI, +ve) *m/z* 227 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{12}H_{23}N_4O_2$ 227.1760, found 227.1756.

**(*S*)-1-(4-(Methoxymethyl)-5-iodooxazol-2-yl)-*N*,3-dimethylbutan-1-amine (79)**




This compound was prepared according to *General Procedure 3* using Type **B** protected amine **47** (19.2 mg, 0.05 mmol) to yield **79** (13.3 mg, 90%) as a colorless oil. TLC (5% $MeOH/CH_2Cl_2$) $R_F$ = 0.31. $^1$H NMR (500 MHz, $CDCl_3$) δ 0.88 - 0.94 (6H, q, H4 and H3-C$\underline{H}_3$), 1.56 - 1.67 (4H, m, H3/H2/NH), 2.34 (3H, s, N-$CH_3$), 3.40 (3H, s, O-$CH_3$), 3.80 (1H, t, *J* = 7.2 Hz, H1), 4.31 (3H, s, H4'-C$\underline{H}_2$). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 22.5 (C4/C3-$\underline{C}H_3$), 22.7 (C4/C3-$\underline{C}H_3$), 25.0 (C3), 34.4 (N-$CH_3$), 43.5 (C2), 56.9 (C1), 58.5 (O-$CH_3$), 65.9 (H4'-$\underline{C}H_2$), 87.7 (C4'), 142.5 (C5'), 171.4 (C2'). MS ($ESI^+$) *m/z* = 339 (100 %, $[M+H]^+$). HRMS ($ESI^+$) $[M+Na]^+$ Calcd. for $C_{11}H_{19}IN_2NaO_2$: 361.0389, Found: 361.0377.

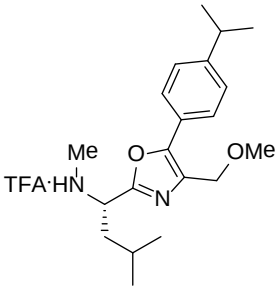
**(*S*)-1-(4-(Methoxymethyl)-5-phenyloxazol-2-yl)-*N*,3-dimethylbutan-1-amine (80)**




This compound was prepared according to *General Procedure 3* using Type **B** protected amine **48** (16 mg, 0.041 mmol) to yield **80** (9 mg, 80%) as an oil. $^1$H NMR (300 MHz, $CDCl_3$): δ 0.91 (d, *J* = 6.6 Hz, 3H, $CH_3$), 0.96 (d, *J* = 6.3 Hz, 3H, $CH_3$), 1.63-1.77 (m, 1H, CH), 2.39 (s, 3H, $NCH_3$), 3.47 (s, 3H, $OCH_3$), 3.85 (t, *J* = 7.5 Hz, 1H, CH), 4.53 (s, 2H, $CH_2O$), 7.37 (d, *J* = 7.2 Hz, 2H, ArH), 7.43-7.48 (m, 2H, ArH), 7.67 (dd, $J_1$ = 1.5, $J_2$ = 6.9 Hz, 1H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 22.6 (2 x $CH_3$), 25.0 (CH), 34.3 ($NCH_3$), 43.6 ($CH_2$), 56.7 (CH), 58.2 ($OCH_3$), 66.7 ($CH_2O$), 126.1, 128.5,

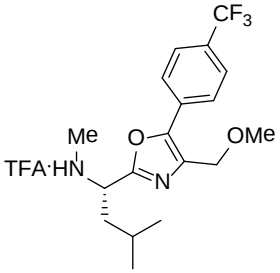
128.8 (ArCH), 128.2, 132.1, 148.7, 164.5 (ArC). MS (ESI, +ve) *m/z* 289 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{17}H_{25}N_2O_2$ 289.1916, found 289.1921.

**(*S*)-1-(5-(4-Isopropylphenyl)-4-(methoxymethyl)oxazol-2-yl)-*N*,3-dimethylbutan-1-ammonium trifluoroacetate (81)**



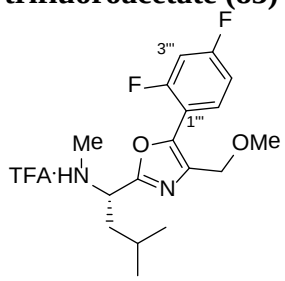

This compound was prepared according to *General Procedure 3* using Type **B** protected amine **49** (19 mg, 0.0.043 mmol) and omitting the aqueous work-up to yield amine·TFA salt **81** (18 mg, 94%) as an oil. $^1$H NMR (500 MHz, $CD_3OD$): δ 0.88 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.93 (d, *J* = 6.5 Hz, 3H, $CH_3$), 1.20 (d, *J* = 7.0 Hz, 3H, 2 x $CH_3$), 1.45-1.54 (m, 1H, CH), 1.78-1.83 (m, 1H, $CH_2$ ($H_a$)), 2.04-2.10 (m, 1H, $CH_2$ ($H_b$)), 2.63 (s, 3H, $NCH_3$), 2.89 (septet, *J* = 7.0 Hz, 1H, $C_6H_4C\underline{H}(CH_3)_2$), 3.38 (s, 3H, $OCH_3$), 4.47 (s, 2H, $CH_2O$), 4.51 (dd, $J_1$ = 4.5, $J_2$ = 11.0 Hz, 1H, CH), 7.30 (d, *J* = 8.0 Hz, 2H, ArH), 7.54 (d, *J* = 8.0 Hz, 2H, ArH); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 22.5, 23.1, 24.1 (4 x $CH_3$), 25.8 (CH), 31.6 ($NCH_3$), 35.0 (CH), 42.2 ($CH_2$), 56.0, ($OCH_3$), 58.5 (CH), 66.9 ($CH_2O$), 127.3, 128.0 (ArCH), 125.5, 133.2, 151.7, 156.7 (ArC). MS (ESI, +ve) *m/z* 331 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{20}H_{31}N_2O_2$ 331.2386, found 231.2398.

**(*S*)-1-(5-(4-Trifluoromethylphenyl)-4-(methoxymethyl)oxazol-2-yl)-*N*,3-dimethylbutan-1-ammonium trifluoroacetate (82)**



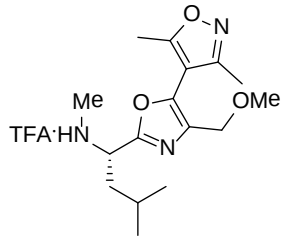

This compound was prepared according to *General Procedure 3* using Type **B** protected amine **50** (21 mg, 0.046 mmol) and omitting the aqueous work-up to yield amine·TFA salt **82** (21 mg, 97%) as an oil. $^1$H NMR (500 MHz, $CD_3OD$): δ 0.97 (d, *J* = 6.5 Hz, 3H, $CH_3$), 1.02 (d, *J* = 6.5 Hz, 3H, $CH_3$), 1.57-1.61 (m, 1H, CH), 1.90-1.96 (m, 1H, $CH_2$ ($H_a$)), 2.14-2.20 (m, 2H, $CH_2$ ($H_b$)), 2.76 (s, 3H, $NCH_3$), 3.46 (s, 3H, $OCH_3$), 4.61 (s, 2H, $CH_2O$), 4.71 (dd, $J_1$ = 5.0, $J_2$ = 11.0 Hz, 1H, CH), 7.83 (d, *J* = 8.0 Hz, 2H, ArH), 7.94 (d, *J* = 8.0 Hz, 2H, ArH); $^{13}$C NMR (126 MHz, $CD_3OD$): δ 21.7 ($CH_3$), 23.2 ($CH_3$), 26.2 (CH), 31.8 ($NCH_3$), 40.5 ($CH_2$), 56.3, ($OCH_3$), 58.6 (CH), 67.1 ($CH_2O$), 125.4 (q, *J* = 272 Hz, $CF_3$), 1.27.1 (t, *J* = 3.8 Hz, ArCH), 127.9 (ArCH), 132.0 (q, *J* = 33 Hz, $\underline{C}CF_3$), 132.0, 136.3, 150.5, 158.3 (ArC). MS (ESI, +ve) *m/z* 357 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{18}H_{24}N_2O_2F_3$ 357.1790, found 357.1801.

**(*S*)-1-(5-(2,4-Difluorophenyl)-4-(methoxymethyl)oxazol-2-yl)-*N*,3-dimethylbutan-1-ammonium trifluoroacetate (83)**




This compound was prepared according to *General Procedure 3* using Type **B** protected amine **51** (22 mg, 0.052 mmol) and omitting the aqueous work-up to yield amine·TFA salt **83** (22 mg, 97%) as an oil. $^{1}$H NMR (500 MHz, $CD_3OD$): δ 0.94 (d, $J$ = 6.5 Hz, 3H, $CH_3$), 0.99 (d, $J$ = 7.0 Hz, 3H, $CH_3$), 1.53-1.59 (m, 1H, CH), 1.90 (ddd, $J_1$ = 4.5, $J_2$ = 9.0, $J_3$ = 13.5 Hz, 1H, $CH_2$ ($H_a$)), 2.12 (ddd, $J_1$ = 5.0, $J_2$ = 10.5, $J_3$ = 13.0 Hz, 1H, $CH_2$ ($H_b$)), 2.73 (s, 3H, $NCH_3$), 3.34 (s, 3H, $OCH_3$), 4.44 (s, 2H, $CH_2O$), 4.66 (dd, $J_1$ = 6.0, $J_2$ = 11.5 Hz, 1H, CH), 7.13-7.20 (m, 2H, ArH), 7.65-7.69 (m, 1H, ArH); $^{13}$C NMR (126 MHz, $CD_3OD$): δ 21.6 ($CH_3$), 23.2 ($CH_3$), 26.1 (CH), 31.8 ($NCH_3$), 40.5 ($CH_2$), 56.3, ($OCH_3$), 58.6 (CH), 66.7 ($CH_2O$), 105.8 (t, $J$ = 26 Hz, C3'''), 113.0 (d, $J$ = 11 Hz, C5'''), 113.3 (dd, $J_1$ = 3 Hz, $J_2$ = 22 Hz, C5'''), 133.0 (dd, $J_1$ = 3 Hz, $J_2$ = 10 Hz, C6'''), 136.8 (C4), 146.1 (C3), 159.0 (C2), 161.3 (dd, $J_1$ = 3 Hz, $J_2$ = 253 Hz, C2'''), 165.6 (dd, $J_1$ = 12 Hz, $J_2$ = 252 Hz, C4'''). MS (ESI, +ve) *m/z* 325 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{17}H_{23}N_2O_2F_2$ 325.1728, found 325.1741.

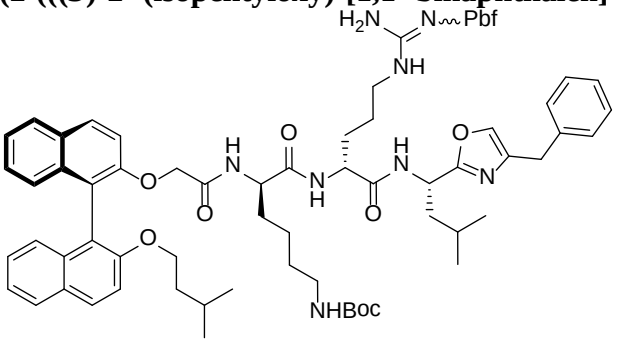
**(*S*)-1-(4-(Methoxymethyl)-5-(3,5-dimethylisoxazol-4-yl)oxazol-2-yl)-*N*,3-dimethylbutan-1-ammonium trifluoroacetate (84)**




This compound was prepared according to *General Procedure 3* using Type **B** protected amine **52** (16 mg, 0.039 mmol) and omitting the aqueous work-up to yield amine·TFA salt **84** (15 mg, 94%) as an oil. $^{1}$H NMR (300 MHz, $CD_3OD$): δ 0.95 (d, $J$ = 6.9 Hz, 3H, $CH_3$), 0.99 (d, $J$ = 6.6 Hz, 3H, $CH_3$), 1.46-1.59 (m, 1H, CH), 1.89 (ddd, $J_1$ = 4.8, $J_2$ = 9.0, $J_3$ = 13.2 Hz, 1H, $CH_2$ ($H_a$)), 2.10 (ddd, $J_1$ = 5.1, $J_2$ = 10.8, $J_3$ = 15.9 Hz, 1H, $CH_2$ ($H_b$)), 2.24 (s, 3H, $CH_3$), 2.43 (s, 3H, $CH_3$), 2.73 (s, 3H, $NCH_3$), 3.38 (s, 3H, $OCH_3$), 4.33 (s, 2H, $CH_2O$), 4.65 (dd, $J_1$ = 4.8, $J_2$ = 10.8 Hz, 1H, CH); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 10.5, 11.6, 21.6, 23.2 (4 x $CH_3$), 26.2 (CH), 31.8 ($NCH_3$), 40.5 ($CH_2$), 56.3, ($OCH_3$), 59.0 (CH), 66.5 ($CH_2O$), 105.4, 137.6, 142.2, 159.8, 160.4, 171.1 (ArC). MS (ESI, +ve) *m/z* 308 (100%) $[M+H]^+$. HRMS (ESI, +ve) calcd for $C_{16}H_{26}N_3O_3$ 308.1974, found 308.1988.

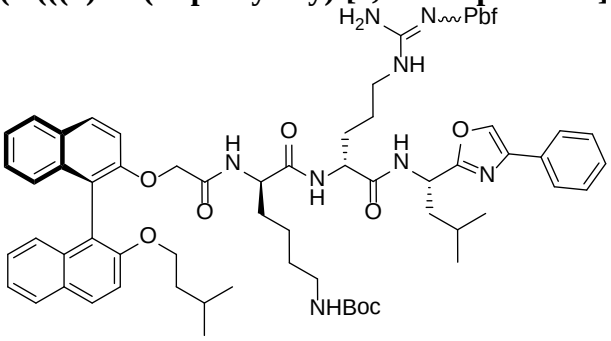
***Synthesis of Type D Protected Peptidomimetics***

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-benzyloxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (85)**




This compound was prepared according to *General Procedure 1* using the known carboxylic acid **S11**[S10] (50 mg, 0.12 mmol, structure drawn in Scheme S7) and amine **S10** (53 mg, 0.06 mmol, structure drawn in Scheme S7). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) gave **85** (80 mg, 100% based on **S10**, 21% over five steps from amine **53**, see Scheme S7) as a solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 0.49 (d, *J* = 6.3 Hz, 3H), 0.52 (d, *J* = 6.3 Hz, 3H), 0.74-0.89 (m, 2H), 0.92 (d, *J* = 6.3 Hz, 3H), 0.95 (d, *J* = 6.3 Hz, 3H), 1.05-1.98 (m, 16H), 1.45-1.46 (m, 15H, $^t$Bu and 2 x $CH_3$ (Pbf)), 2.10 (s, 3H, $CH_3$ (Pbf)), 2.52 (s, 3H, $CH_3$ (Pbf)), 2.59 (s, 3H, $CH_3$ (Pbf)), 2.90-2.99 (m, 2H), 2.96 (s, 2H, $CH_2$ (Pbf)), 3.05-3.24 (m, 2H), 3.76 (s, 2H), 3.86-3.92 (m, 1H), 4.01-4.08 (m, 2H), 4.40-4.56 (m, 3H), 4.81-4.85 (m, 1H), 5.13-5.21 (m, 1H), 6.15 (d, J = 6.9 Hz, NH), 6.30 (br s, NH), 7.12-7.43 (m, 12H), 7.46 (d, *J* = 9.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 8.03 (s, 1H). MS (ESI +ve) *m/z* 1277 ($[M+H]^+$, 30%), 1299 ($[M+H]^+$, 100%).

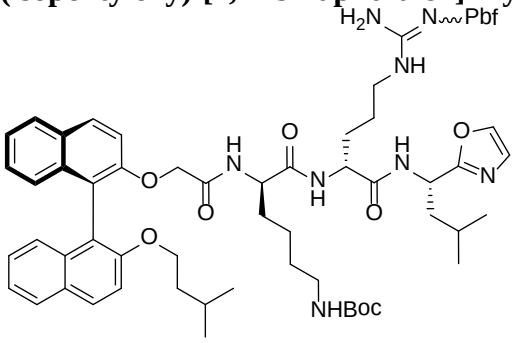
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-phenyloxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (86)**




This compound was prepared according to *General Procedure 1* using the known carboxylic acid **S12**[S10] (40 mg, 0.062 mmol, structure drawn in Scheme S7) and amine **S9** (40 mg, 0.063 mmol, structure drawn in Scheme S7). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) gave **86** (60 mg, 76%, 12% over three steps from amine **54**, see Scheme S7) as a solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 0.45 (d, *J* = 6.3 Hz, 3H), 0.49 (d, *J* = 6.3 Hz, 3H), 0.67-0.82 (m, 2H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.96 (d, *J* = 6.6 Hz, 3H), 1.02-1.48 (m, 11H), 1.42 (s, 15H, $^t$Bu and 2 x $CH_3$ (Pbf)), 1.78-1.92 (m, 3H), 2.04 (s, 3H, $CH_3$ (Pbf)), 2.48 (s, 3H, $CH_3$ (Pbf)), 2.55 (s, 3H, $CH_3$ (Pbf)), 2.79-2.96 (m, 2H), 2.87 (s, 2H, $CH_2$ (Pbf)), 3.00-3.22 (m, 2H), 3.77-3.84 (m, 1H), 3.92-4.02 (m, 2H), 4.37-4.52 (m, 3H), 4.70-4.82 (m, 1H, NH), 5.20-5.28 (m, 1H), 6.08 (d, *J* = 6.9 Hz, 1H, NH), 6.27 (br s, 2H, NH), 7.09-

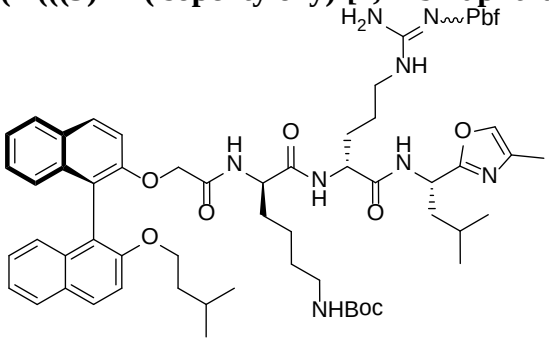
7.43 (m, 13H), 7.60-7.63 (m, 1H), 7.79-7.90 (m, 4H); MS (ESI +ve) *m/z* 1263 ($[M+H]^+$, 30%), 1285 ($[M+Na]^+$, 100%).

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (87)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (39.1 mg, 0.037 mmol) and Type **C** amine·HCl salt **55** (8.5 mg, 0.045 mmol), with added $NEt(i\text{-}Pr)_2$ (8.7 mg, 0.067 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% $MeOH/CH_2Cl_2$) gave **87** (32.4 mg, 73%) as a white solid, which was revealed by NMR analysis to be a *ca.* 90:10 mixture of diastereomers, epimeric at leucine, presumably due to partial racemization of amine **55** in the phthalimide deprotection step. TLC (5% $MeOH/CH_2Cl_2$) $R_F$ = 0.42 (both diastereomers); $[\alpha]_D^{25}$ −33.3 (*c* 1.62, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$, major diastereomer only) δ 7.96 (t, *J* = 8.4 Hz, 2H), 7.87 (t, *J* = 6.9 Hz, 2H), 7.60 – 7.10 (m, 11H), 6.92 (s, 1H), 6.27 (bs, 2H), 6.13 (bd, *J* = 5.5 Hz, 1H), 5.17 (dd, *J* = 15.0, 7.9 Hz, 1H), 4.82 (bs, 1H), 4.56 – 4.35 (m, 3H), 4.12 – 3.81 (m, 3H), 3.26 – 3.04 (m, 2H), 3.02 – 2.86 (m, 4H), 2.56 (s, 3H), 2.49 (s, 3H), 2.07 (s, 3H), 1.98 – 1.85 (m, 1H), 1.84 – 1.71 (m, 2H), 1.69 – 1.02 (m, 26H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.84 – 0.69 (m, 2H), 0.52 (d, *J* = 6.5 Hz, 3H), 0.46 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$, major diastereomer only) δ 171.6, 171.3, 169.5, 164.7, 158.6, 156.2, 156.1, 154.3, 152.1, 138.7, 138.3, 133.8, 133.6, 133.1, 132.2, 129.8, 129.3, 128.1, 127.9, 126.7, 126.6, 126.5, 125.4, 125.0, 124.5, 124.2, 124.0, 123.8, 120.2, 119.7, 117.4, 116.1, 114.0, 86.3, 79.0, 68.6, 68.0, 53.3, 52.5, 46.1, 43.2, 42.1, 40.5, 40.1, 38.0, 31.0, 29.0, 28.5, 28.4, 25.5, 24.7, 24.5, 22.7, 22.5, 22.3, 22.04, 21.97, 21.8, 19.2, 17.9, 12.4; MS ($ES^+$) *m/z* 1210 (100%, M+Na), 1188 (97%, M+H).

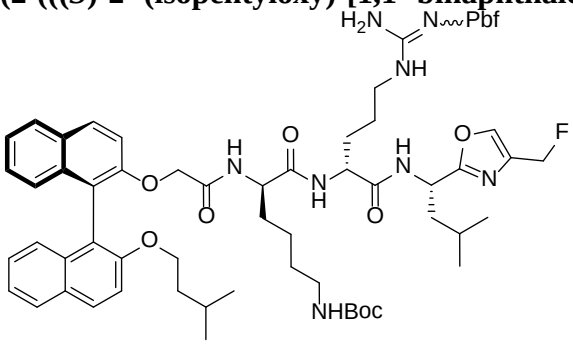
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(methyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (88)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (115.6 mg, 0.11 mmol) and Type **C** amine·TFA salt **56** (22.6 mg, 0.08 mmol, limiting reagent in this case), with added $NEt(i\text{-}Pr)_2$ (28 µL, 0.16 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% $MeOH/CH_2Cl_2$)

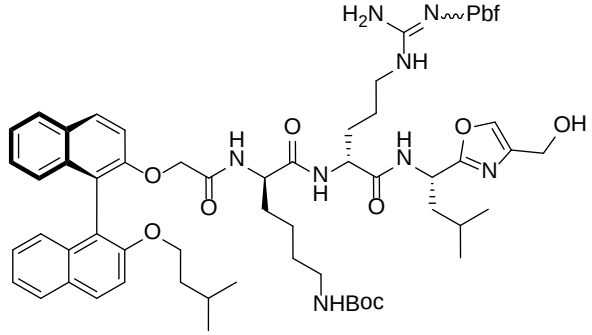
gave **88** as a white solid (the yield of this analogue was determined after deprotection, see the experimental procedure for compound **120**). TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.39. $[\alpha]_D^{25} = -86.5$ (*c* 0.68, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.48 (3H, d, *J* = 6.5 Hz), 0.52 (3H, d, *J* = 6.5 Hz), 0.71 - 0.84 (4H, m), 0.89 - 0.93 (6H, q, *J* = 6.5 Hz), 1.05 - 1.11 (2H, m), 1.15 - 1.19 (3H, m), 1.24 - 1.27 (3H, m), 1.42 (16H, d, *J* = 9.6 Hz), 1.54 - 1.62 (3H, m), 1.71 - 1.81 (2H, m), 1.82 - 1.92 (2H, m), 2.04 (3H, s), 2.07 (3H, s), 2.49 (3H, s), 2.55 (3H, s), 2.92 (2H, bs), 3.10 - 3.17 (4H, bm), 3.84 - 3.88 (2H, m), 4.02 - 4.06 (3H, m), 4.40 - 4.52 (4H, m), 4.82 (1H, bs), 5.14 (2H, m), 5.29 (1H, s), 6.12 (2H, d, *J* = 6.5 Hz ), 6.27 (3H, bs), 7.15 (3H, m), 7.22 - 7.26 (5H, m), 7.31 - 7.37 (4H, m), 7.86 (2H, t, *J* = 8.2 Hz) , 7.95 (2H, t, *J* = 8.1 Hz). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 11.4, 12.6, 18.0, 19.4, 21.9, 22.2, 22.4, 22.9, 24.6, 24.8, 28.6, 28.7, 29.2, 31.5, 38.1, 40.6, 42.3, 43.4, 46.2, 53.2, 53.5, 68.2, 68.6, 86.4, 105.1, 114.2, 115.9, 117.5, 119.7, 120.4, 124.0, 124.3, 124.6, 125.6, 126.8, 126.9, 128.1, 128.2, 129.4, 129.9, 132.4, 133.2, 133.7, 134.0, 134.4, 136.0, 138.4, 152.2, 154.5, 156.4, 158.8, 164.1, 169.5, 171.3. IR (neat) *v* [$cm^{-1}$] = 3852 (s), 3331 (s), 2300 (m), 1653 (s), 1559 (s), 1244 (w), 1074 (w). MS ($ESI^+$) *m/z* = 1201 (75 %, $[M+H]^+$), 1223 (100 %, $[M+Na]^+$).

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(fluoromethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (89)**



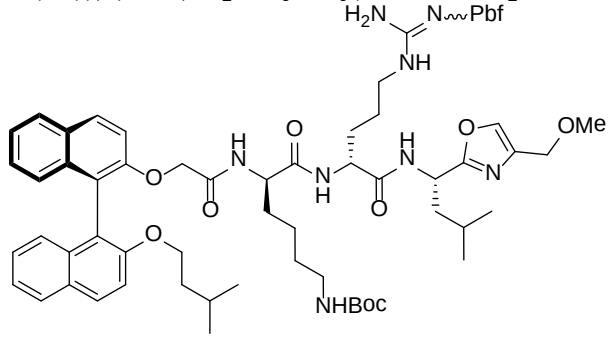

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (73.0 mg, 0.07 mmol) and Type **C** amine·TFA salt **57** (27.1 mg, 0.09 mmol), with added $NEt(i\text{-}Pr)_2$ (19.2 µL, 0.11 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) gave **89** (73.0 mg, 86%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.38. $[\alpha]_D^{25} = -31.9$ (*c* 0.037, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.46 - 0.56 (6H,m), 0.71 - 0.81 (2H, m), 0.90 - 0.95 (7H, m), 1.03 - 1.19 (7H, m), 1.42 (16H, d, *J* = 5.4 Hz), 1.61 - 1.92 (6H, m), 2.07 (3H, s), 2.49 (3H, s), 2.56 (3H, s), 2.84 - 3.00 (4H, bm), 3.10 - 3.16 (2H, bm), 3.84 - 3.93 (1H, m), 4.02 - 4.09 (2H, m), 4.39 - 4.55 (4H, m), 4.76 (1H, bs), 5.18 (2H, d, $J_{H\text{-}F}$ = 48.0 Hz), 5.29 (1H, s), 6.09 - 6.15 (3H, m), 6.20 - 6.30 (3H, m), 7.13 - 7.64 (m), 7.85 - 7.89 (2H, m) , 7.94 - 7.98 (2H, m). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 12.6, 18.1, 19.4, 21.9, 22.2, 22.5, 23.0, 24.6, 24.8, 28.6, 28.7, 29.2, 31.4, 38.1, 40.6, 42.1, 43.4, 46.2, 53.6, 53.8, 68.2, 68.8, 75.9 ($J_{C\text{-}F}$ = 166.3 Hz), 86.5, 105.1, 114.2, 116.3, 117.6, 124.2, 124.4, 124.7, 125.2, 125.6, 126.8, 127.0, 128.2, 128.3, 129.5, 130.0, 132.4, 133.2, 133.7, 134.0, 138.5, 152.2, 154.5, 156.4, 169.8, 171.5. IR (neat) *v* [$cm^{-1}$] = 3865 (s), 3726 (s), 3634 (s), 2963 (w), 2321 (w), 1706 (s), 1558 (s), 1505 (s), 1268 (m), 1171 (m), 803 (w). MS ($ESI^+$) *m/z* = 1220 (75 %, $[M+H]^+$), 1242 (100 %, $[M+Na]^+$).

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(hydroxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (90)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (53.3 mg, 0.051 mmol) and Type **C** amine **58** (11.2 mg, 0.061 mmol) to give **90** (58.3 mg, 94%) as an off-white solid. TLC (2% MeOH/EtOAc) $R_F$ = 0.34; $[\alpha]_D^{25}$ −55.9 (*c* 2.17, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.04 (bd, *J* = 7.9 Hz, 1H), 7.95 (d, *J* = 9.0 Hz, 1H), 7.88 (t, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.47 – 7.40 (m, 3H), 7.39 – 7.32 (m, 2H), 7.31 – 7.21 (m, 2H), 7.15 (d, *J* = 8.3 Hz, 2H), 6.37 – 6.06 (bm, 3H), 5.00 – 4.80 (m, 2H), 4.56 (d, *J* = 14.4 Hz, 1H), 4.48 – 4.27 (m, 4H), 4.05 – 3.98 (m, 1H), 3.92 – 3.83 (m, 2H), 3.05 – 2.84 (m, 4H), 2.56 (s, 3H), 2.51 – 2.47 (m, 5H), 2.07 (s, 3H), 1.82 – 1.69 (m, 2H), 1.68 – 1.55 (m, 2H), 1.52 – 1.39 (m, 15H), 1.38 – 0.98 (m, 12H), 0.92 (d, *J* = 4.9 Hz, 3H), 0.88 (d, *J* = 4.9 Hz, 3H), 0.53 (d, *J* = 6.4 Hz, 3H), 0.47 (d, *J* = 6.3 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 172.0, 171.3, 170.0, 165.9, 158.6, 156.2, 156.1, 154.4, 151.9, 139.7, 138.2, 135.6, 133.8, 133.5, 133.1, 132.2, 129.9, 129.8, 129.7, 129.2, 128.2, 127.9, 126.8, 126.7, 125.4, 124.9, 124.5, 124.2, 124.0, 120.1, 119.5, 117.3, 116.0, 113.7, 86.2, 79.0, 68.4, 67.9, 55.1, 53.8, 46.5, 43.2, 41.9, 40.3, 40.2, 37.9, 30.7, 29.3, 28.6, 28.4, 25.5, 24.6, 24.4, 22.7, 22.3, 22.0, 21.6, 19.2, 17.9, 12.4; MS ($ES^+$) *m/z* 1239 (79%, M+Na), 1217 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{66}H_{89}N_8O_{12}S$: 1217.6321 (M+H), Found: 1217.6342.

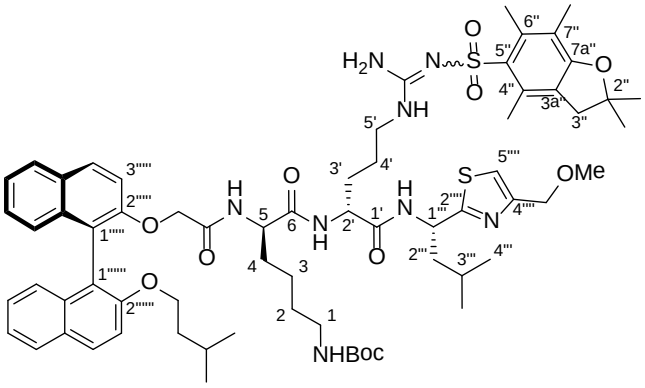
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (91)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (117 mg, 0.11 mmol) and Type **C** amine **59** (22 mg, 0.11 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **91** (90 mg, 66%) as an off-white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.49 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.53 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.70-0.85 (m, 2H, $CH_2$), 0.86-0.96 (m, 1H, $CH_2$ ($H_a^*$)), 0.90 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 0.93 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.07-1.15 (m, 1H, CH), 1.16-1.20 (m, 2H, $CH_2$), 1.21-1.29 (m, 2H, $CH_2$), 1.26-1.36 (m, 1H, $CH_2$ ($H_b^*$)), 1.41-1.53 (m, 2H, $CH_2$), 1.42 (s, 9H, $^t$Bu), 1.44 (s, 6H, 2 x $CH_3$ (Pbf)), 1.53-1.67 (m, 1H, $CH_2$ ($H_a^\#$)), 1.56-1.69 (m, 1H, CH), 1.74-1.80 (m, 2H, $CH_2$), 1.86-1.92 (m, 1H, $CH_2$ ($H_b^\#$)), 2.07 (s, 3H, $CH_3$ (Pbf)), 2.50 (s, 3H,

$CH_3$ (Pbf)), 2.56 (s, 3H, $CH_3$ (Pbf)), 2.86-2.98 (m, 2H, $CH_2N$ (Lys)), 2.92 (s, 2H, $CH_2$ (Pbf)), 3.04-3.23 (m, 2H, $CH_2N$ (Arg)), 3.47 (s, 3H, $OCH_3$), 3.85-3.90 (m, 1H $CH_2O$ ($H_a$)), 3.94-4.03 (m, 1H, CH), 4.02-4.07 (m, 1H $CH_2O$ ($H_b$)), 4.23 (s, 2H, oxazole-C$\underline{H}_2$), 4.42-4.48 (m, 1H, CH), 4.47 (ABq, *J* = 14.5 Hz, 2H, $OCH_2CO$), 4.76-4.82 (m, 1H, N$\underline{H}$Boc), 5.13-5.18 (m, 1H, CH), 6.10 (d, *J* = 6.0 Hz, 1H, NH), 6.26 (br s, 2H , 2 x NH), 7.13-1.17 (m, 2H, ArH), 7.22-7.29 (m, 2H, ArH), 7.32-7.37 (m, 2H, ArH), 7.46 (d, *J* = 9.0 Hz, 2H, ArH), 7.50 (s, 1H, ArH (oxazole)), 7.86-7.88 (m, 2H, ArH), 7.95-7.98 (m, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 12.4, 17.9, 19.2 ($CH_3$ (Pbf)), 21.7, 22.0, 22.3, 22.8 ($CH_3$), 22.5, 25.4, 29.1, 30.9, 37.9, 42.0 ($CH_2$), 24.4, 24.6, 46.0, 52.4, 53.2 (CH), 28.4 (C($\underline{C}H_3)_3$), 28.5 (2 x $CH_3$ (Pbf)), 40.1 ($CH_2N$ (Lys)), 40.5 ($CH_2N$ (Arg)), 43.2 ($CH_2$ (Pbf)), 58.3 ($OCH_3$), 66.1 (oxazole-$\underline{C}H_2$), 68.0 ($O\underline{C}H_2CO$), 68.5 ($CH_2O$), 79.0 ($\underline{C}(CH_3)_3$), 86.3 (C (Pbf)), 114.1, 116.0, 124.0, 124.2, 125.0, 125.4, 126.6, 126.8, 127.9, 128.1, 129.8 (ArCH), 117.3, 119.6, 120.2, 124.5, 129.3, 129.7, 132.2, 133.1, 133.6, 133.8, 137.3, 138.3, 152.1, 154.3, 156.2, 164.9 (ArC), 156.0 (C=O (Boc)), 158.6 (C=N), 169.5, 171.2, 171.8 (C=O). MS (ESI, +ve) *m/z* 1232 (5%) $[M+H]^+$; 1253 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{67}H_{91}N_8O_{12}S$ 1231.6477, found 1231.6493.

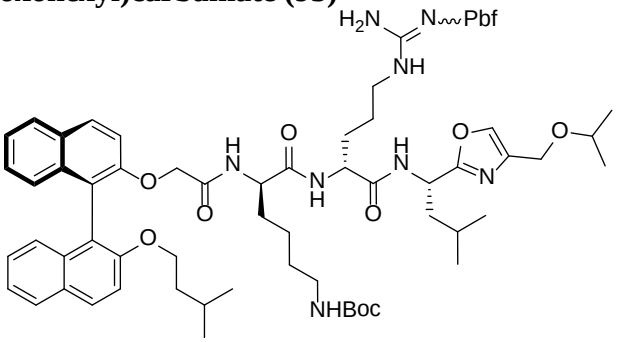
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(methoxymethyl)thiazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (92)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (124 mg, 0.12 mmol) and Type **C** amine **60** (33.8 mg, 0.16 mmol). Flash chromatography (100% $CH_2Cl_2$ to 6% MeOH/$CH_2Cl_2$) gave **92** (101 mg, 69%) as a light yellow solid. mp 82−90 °C. TLC (10% MeOH/$CH_2Cl_2$) $R_F$ = 0.68. $[\alpha]_D^{25}$ = −32.37 (c 5.0, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$, major rotamer only) δ 0.48 (3H, d, *J* = 6.2 Hz, $CH_{3a}$ ($^i$Pent)), 0.52 (3H, d, *J* = 6.4 Hz, $CH_{3b}$ ($^i$Pent)), 0.72 - 0.84 (2H, m, $CH_2$ (Lys)), 0.88 - 1.01 (7H, m, 3'''-$CH_3$, H4''', CH), 1.03 - 1.15 (1H, m, CH ($^i$Pent)), 1.14 - 1.40 (6H, m, $\underline{CH_2}CH(CH_3)_2$ ($^i$Pent)), 1.30 - 1.50 (16H, m, $(CH_3)_3$, 2''$(CH_3)_2$), 1.52 - 1.96 (7H, m, H3', H4', H2''', H3'''), 2.07 (3H, s, H7''), 2.48 (3H, s, H6''), 2.56 (3H, s, H4''), 2.74 - 2.96 (2H, $CH_2N$ (Lys)), 2.88 - 2.92 (H3''), 3.13 (2H, bs, H5'), 3.40 (3H, s, $OCH_3$), 3.82 - 3.92 (1H, m, $CH_{2a}$, ($^i$Pent)), 3.98 - 4.20 (2H, m, $CH_{2b}$ ($^i$Pent), H5), 4.33 - 4.56 (3H, $O\underline{CH_2}C$=O, H2'), 4.49 (2H, 4''''-$CH_2$) 4.84 (1H, s), 1-NH), 5.24 - 5.39 (1H, m, H1'''), 6.16 - 6.21 (1H, m, NH (Lys)), 6.21 - 6.37 (3H, m, guanidino), 7.10 (2H, t, *J* = 10.3, Hz, ArH), 7.16 (1H, s, H5''''), 7.18 - 7.27 (3H, m, ArH, NH(Arg)), 7.30 (1H, t, *J* = 7.5 Hz, ArH), 7.35 (2H, t, *J* = 7.4 Hz, ArH), 7.40 - 7.46 (1H, m, ArH), 7.54 - 7.65 (1H, m, NH (Leu)), 7.85 (2H, t, *J* = 9.3 Hz, ArH), 7.89 - 7.97 (2H, m, ArH). $^{13}$C NMR (126 MHz, $CDCl_3$, major rotamer only) δ 12.4 (7''-$CH_3$), 17.9 (4''-$CH_3$), 19.2 (6''-$CH_3$), 21.4, 21.6, 22.0, 22.2, 22.4, 23.0, 24.4, 24.8, 25.5 (C4'), 28.4 ($(CH_3)_3$), 28.5 (2''-$(CH_3)_2$), 29.0 (C4), 31.2 (C3'), 37.9 ($OCH_2\underline{C}H_2$), 38.4, 40.0 (C5'), 40.3 (C1), 43.1 (C3''), 43.7 (C2'''), 50.0 (C1'''), 52.7 (C5, C2'), 58.4 ($OCH_3$), 68.1 ($O\underline{C}H_2C$=O), 68.2 ($OCH_2$ ($^i$Pent)), 70.3 (4''''-$CH_2$), 78.8 ($\underline{C}(CH_3)_3$), 86.2 (C2''), 114.2, 115.5, 115.8, 117.3, 119.3, 120.3, 123.8, 124.1, 124.5, 124.8, 125.4, 126.5, 126.6, 127.9, 128.0, 129.1, 129.6, 129.7, 129.7, 132.1, 132.9, 133.5, 133.7, 138.1, 152.1 (C2'''''' or C2''''''), 153.4 (C4''''),

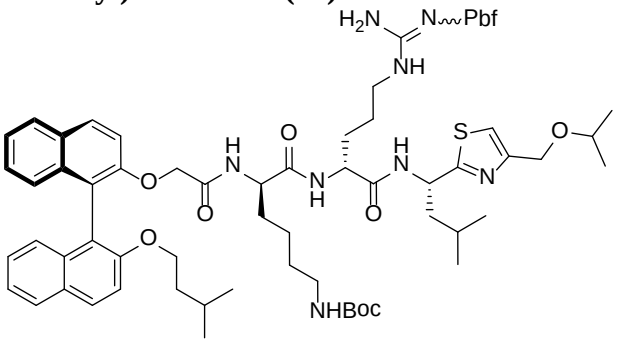
154.3 (C2"'" or C2""), 155.9 (guanidino), 156.3 (C=O(OC(CH$_3$)$_3$), 158.6 (C7a"), 169.1 (C=O), 171.4 (C=O), 173.5 (C=O). IR (neat) $\nu$ [cm$^{-1}$] = 3340 (w), 2934 (w), 2369 (w), 1673 (m), 1658 (m), 1548 (s), 1514 (s), 1462 (w), 1365 (w), 1246 (m), 1162 (m), 1094 (s), 906 (w), 809 (m), 745 (m), 665 (m), 611 (m). MS (ESI$^+$) *m/z* = 1247 (100%, [M+H]$^+$), 1270 (48%, [M+Na]$^+$). HRMS (ESI$^+$) [M+H]$^+$ Calcd. for $C_{67}H_{91}N_8O_{11}S_2$: 1247.6249, Found: 1247.6283.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(isopropoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (93)**



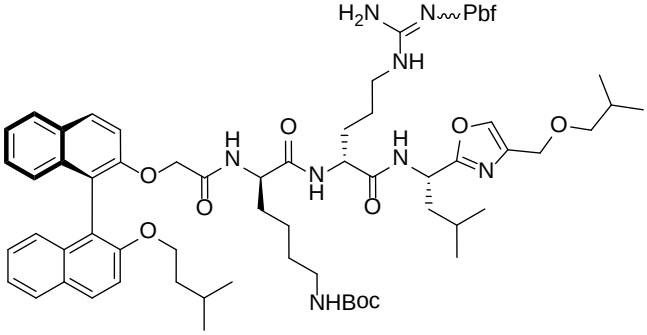

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (68 mg, 0.065 mmol) and Type **C** amine·TFA salt **61** (22 mg, 0.065 mmol), with added NEt(i-Pr)$_2$ (10.1 mg, 0.078 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **93** (70 mg, 85%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.48 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.53 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.71-0.83 (m, 2H, $CH_2$), 0.89-0.94 (m, 1H, $CH_2$ ($H_a^*$)), 0.90 (d, *J* = 6.0 Hz, 3H, $CH_3$ (Leu)), 0.93 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.06-1.15 (m, 1H, CH), 1.12-1.20 (m, 2H, $CH_2$), 1.15 (d, *J* = 6.0 Hz, 3H, $CH_3$), 1.16 (d, *J* = 6.5 Hz, 3H, $CH_3$), 1.21-1.30 (m, 2H, $CH_2$), 1.30-1.42 (m, 1H, $CH_2$ ($H_b^*$)), 1.42-1.52 (m, 2H, $CH_2$), 1.43 (s, 9H, $^t$Bu), 1.44 (s, 6H, 2 x $CH_3$ (Pbf)), 1.52-1.67 (m, 2H, CH and $CH_2$ ($H_a^\#$)), 1.72-1.82 (m, 2H, $CH_2$), 1.79-1.89 (m, 1H, $CH_2$ ($H_b^\#$)), 2.07 (s, 3H, $CH_3$ (Pbf)), 2.49 (s, 3H, $CH_3$ (Pbf)), 2.55 (s, 3H, $CH_3$ (Pbf)), 2.76-2.98 (m, 2H, $CH_2$N (Lys)), 2.92 (s, 2H, $CH_2$ (Pbf)), 3.00-3.12 (m, 1H, $CH_2$N (Arg, $H_a$)), 3.12-3.24 (m, 1H, $CH_2$N (Arg, $H_b$)), 3.63-3.68 (m, 1H, OCH), 3.85-3.89 (m, 1H $CH_2$O ($H_a$)), 4.01-4.06 (m, 2H, CH and $CH_2$O ($H_b$)), 4.33 (s, 2H, oxazole-C$\underline{H}_2$), 4.36-4.48 (m, 1H, CH), 4.47 (ABq, *J* = 14.5 Hz, 2H, OCH$_2$CO), 4.77-4.86 (m, 1H, N$\underline{H}$Boc), 5.15-5.19 (m, 1H, CH), 6.14 (d, *J* = 6.0 Hz, 1H, NH), 6.28 (br s, 2H , 2 x NH), 7.13 (d, *J* = 9.0 Hz, 1H, ArH), 7.16 (d, *J* = 9.0 Hz, 1H, ArH), 7.21-7.37 (m, 5H, ArH), 7.45 (d, *J* = 9.0 Hz, 1H, ArH), 7.49 (s, 1H, ArH (oxazole)), 7.85-7.87 (m, 2H, ArH), 7.94-7.97 (m, 2H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.5, 17.9, 19.3 ($CH_3$ (Pbf)), 21.8, 22.01, 22.03, 22.1, 22.3, 22.8 ($CH_3$), 22.5, 25.5, 29.1, 29.3, 31.1, 38.0, 42.1 ($CH_2$), 24.5, 24.7, 46.1, 52.6, 53.0 (CH), 28.5 (C($\underline{C}H_3$)$_3$), 28.6 (2 x $CH_3$ (Pbf)), 40.1 ($CH_2$N (Lys)), 40.5 ($CH_2$N (Arg)), 43.3 ($CH_2$ (Pbf)), 62.3 (oxazole-$\underline{C}H_2$), 68.1 (O$\underline{C}H_2$CO), 68.4 ($CH_2$O), 71.7 (OCH), 78.9 ($\underline{C}$(CH$_3$)$_3$), 86.3 (C (Pbf)), 114.2, 116.0, 124.0, 124.2, 125.0, 125.5, 126.6, 126.8, 128.0, 128.1, 129.79, 129.8 (ArCH), 117.4, 119.5, 120.4, 124.5, 129.2, 132.2, 133.1, 133.6, 133.9, 138.3, 138.5, 152.2, 154.4, 156.3, 164.5 (ArC), 135.9 (ArCH (oxazole)), 156.1 (C=O (Boc)), 158.6 (C=N), 169.4, 171.2, 171.5 (C=O). MS (ESI, +ve) *m/z* 1259 (5%) [M+H]$^+$; 1281 (100%) [M+Na]$^+$. HRMS (ESI, +ve) calcd for $C_{69}H_{95}N_8O_{12}S$ 1259.6790, found 1259.6852 [M+H]$^+$; calcd for $C_{69}H_{94}N_8O_{12}SNa$ 1281.6610, found 1281.6605 [M+Na]$^+$.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(isopropoxymethyl)thiazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (94)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (87 mg, 0.08 mmol) and Type **C** amine **62** (26 mg, 0.11 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) gave **94** (64.4 mg, 63%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.35. $[\alpha]_D^{25}$ = −35.1 (*c* 0.19, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.48 (3H, d, *J* = 6.2 Hz), 0.52 (3H, d, *J* = 6.0 Hz), 0.70 - 0.84 (2H, m), 0.91 - 0.95 (6H, m), 1.03 - 1.19 (1H, m), 1.19 - 1.25 (8H, m), 1.42 (16H, d, *J* = 6.3 Hz), 1.52 - 1.86 (7H, m), 2.06 (3H, s), 2.48 (3H, s), 2.56 (3H, s), 2.84 - 2.98 (2H, bm), 3.19 (2H, bs), 3.66 - 3.74 (1H, m), 3.85 - 3.88 (1H, m), 3.98 - 4.20 (1H, m), 4.43 - 4.48 (3H, m), 4.56 (2H, s) 4.79 (1H, bs), 5.28 - 5.31 (1H, m), 6.13 - 6.23 (3H, m), 6.23 (3H, m), 7.11- 7.51 (m), 7.88 (2H, t, *J* = 7.5 Hz) , 7.94 (2H, d, *J* = 8.9 Hz). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 13.1, 18.6, 19.9, 22.2, 22.7, 22.9, 23.1, 23.6, 25.1, 25.5, 29.0, 29.2, 29.7, 31.2, 38.5, 40.0, 40.6, 43.8, 44.6, 50.6, 53.3, 66.9, 68.6, 69.0, 72.3, 78.8, 86.9, 114.8, 115.3, 116.6, 118.0, 120.9, 124.5, 124.8, 125.1, 125.6, 126.1, 127.2, 127.4, 128.6, 128.7, 129.8, 130.4, 132.8, 133.6, 134.2, 134.4, 138.9, 152.7, 154.9, 155.2, 156.9, 159.3, 158.6, 169.9, 171.9, 172.1, 173.5. IR (neat) *ν* [$cm^{-1}$] = 3409 (s), 2957 (m), 1654 (s), 1549 (s), 1459 (m), 1366 (m), 1246, 1087 (s), 806 (m), 668 (m). MS ($ESI^+$) *m/z* = 1297 (100 %, $[M+Na]^+$). HRMS ($ESI^+$) $[M+H]^+$ Calcd. for $C_{69}H_{94}N_8NaO_{11}S_2$: 1297.6381, Found: 1297.6381.

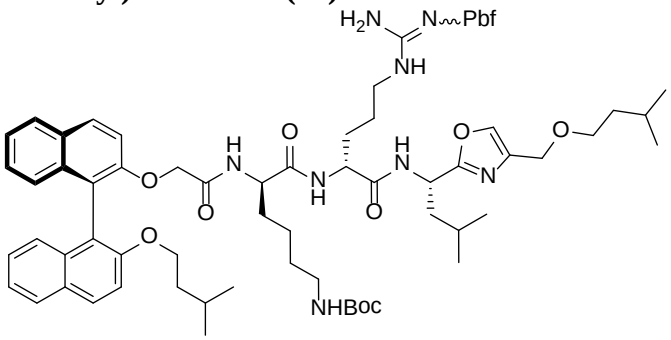
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(isobutoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (95)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (84.1 mg, 0.080 mmol) and Type **C** amine **63** (24.0 mg, 0.10 mmol). Flash chromatography (100% $CH_2Cl_2$ to 1.5% MeOH/$CH_2Cl_2$) gave **95** (83.8 mg, 82%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.45; $[\alpha]_D^{25}$ −42.1 (*c* 0.77, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.96 (t, *J* = 8.6 Hz, 2H), 7.88 – 7.83 (m, 2H), 7.54 – 7.19 (m, 9H), 7.18 – 7.11 (m, 2H), 6.28 (bs, 2H), 6.13 (bd, *J* = 6.1 Hz, 1H), 5.17 (dd, *J* = 14.7, 7.8 Hz, 1H), 4.82 (bs, 1H), 4.57 – 4.38 (m, 3H), 4.31 (s, 2H), 4.11 – 3.96 (m, 2H), 3.87 (dd, *J* = 15.4, 6.8 Hz, 1H), 3.25 – 3.00 (m, 4H), 2.92 (s, 2H), 2.87 – 2.78 (m, 2H), 2.56 (s, 3H), 2.49 (s, 3H),

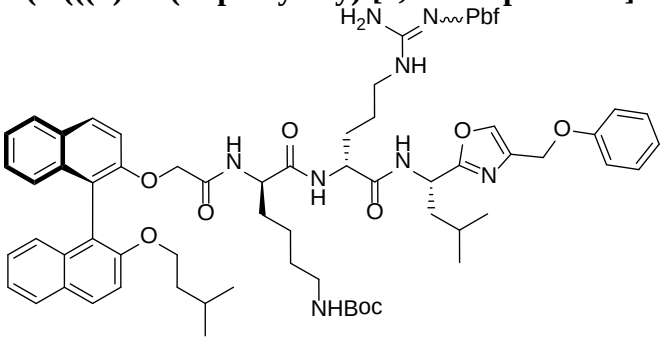
2.07 (s, 3H), 1.92 – 1.70 (m, 4H), 1.68 – 1.53 (m, 2H), 1.51 – 1.35 (m, 15H), 1.30 – 1.05 (m, 8H), 0.99 – 0.83 (m, 13H), 0.83 – 0.70 (m, 2H), 0.53 (d, *J* = 6.3 Hz, 3H), 0.48 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.5, 171.2, 169.4, 164.5, 158.6, 156.2, 156.0, 154.3, 152.1, 138.2, 138.0, 135.8, 133.8, 133.5, 133.1, 132.1, 129.74, 129.72, 129.2, 128.0, 127.9, 126.7, 126.5, 125.4, 124.9, 124.4, 124.2, 123.9, 120.2, 119.5, 117.3, 116.0, 114.1, 86.2, 78.9, 77.7, 68.5, 68.0, 64.9, 53.0, 52.5, 46.0, 43.2, 42.1, 40.4, 40.0, 37.9, 31.0, 29.2, 29.0, 28.5, 28.4, 28.3, 25.4, 24.6, 24.4, 22.8, 22.5, 22.3, 22.0, 21.7, 19.3, 19.2, 17.9, 12.4; MS ($ES^+$) *m/z* 1312 (25%, M+K), 1296 (98%, M+Na), 1274 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{70}H_{97}N_8O_{12}S$: 1273.6947 (M+H), Found: 1273.6965.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(isopentoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (96)**



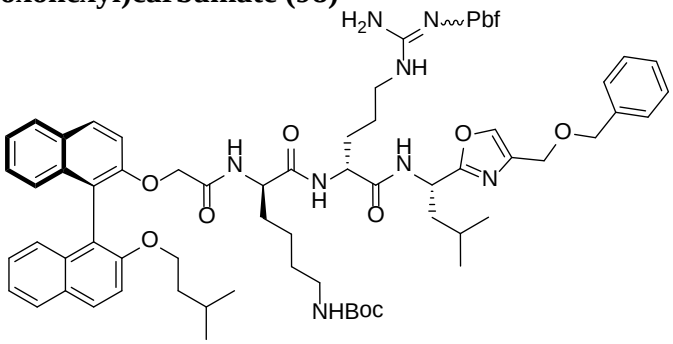

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (84.1 mg, 0.080 mmol) and Type **C** amine **64** (27.1 mg, 0.11 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) gave **96** (87.7 mg, 85%) as an off-white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.47; $[\alpha]_D^{25}$ −39.1 (*c* 3.95, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.91 (m, 2H), 7.89 – 7.82 (m, 2H), 7.52 – 7.41 (m, 2H), 7.42 – 7.19 (m, 7H), 7.18 – 7.10 (m, 2H), 6.29 (bs, 2H), 6.16 (bd, *J* = 6.6 Hz, 1H), 5.18 (dd, *J* = 15.1, 7.7 Hz, 1H), 4.83 (bs, 1H), 4.58 – 4.27 (m, 5H), 4.14 – 3.98 (m, 2H), 3.87 (dd, *J* = 15.5, 6.7 Hz, 1H), 3.49 (t, *J* = 6.7 Hz, 2H), 3.23 – 2.81 (m, 6H), 2.54 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.89 – 1.72 (m, 3H), 1.71 – 1.31 (m, 23H), 1.30 – 1.04 (m, 5H), 1.03 – 0.71 (m, 15H), 0.52 (d, *J* = 6.4 Hz, 3H), 0.48 (d, *J* = 6.3 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.4, 171.1, 169.2, 164.2, 158.6, 156.2, 156.0, 154.3, 152.1, 138.2, 138.0, 135.9, 133.8, 133.5, 133.0, 132.1, 129.7, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.4, 124.1, 123.8, 120.3, 119.4, 117.3, 115.9, 114.2, 86.2, 78.8, 69.4, 68.3, 68.0, 64.7, 52.8, 45.9, 43.2, 42.0, 40.4, 40.0, 38.3, 37.9, 31.1, 29.3, 29.0, 28.5, 28.4, 25.4, 25.0, 24.6, 24.4, 22.7, 22.57, 22.55, 22.4, 22.2, 22.0, 21.7, 19.2, 17.9, 12.4; MS ($ES^+$) *m/z* 1309 (100%, M+Na), 1288 (98%, M+H); HRMS ($ES^+$) Calcd. for $C_{71}H_{99}N_8O_{12}S$: 1287.7103 (M+H), Found: 1287.7087.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(phenoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (97)**



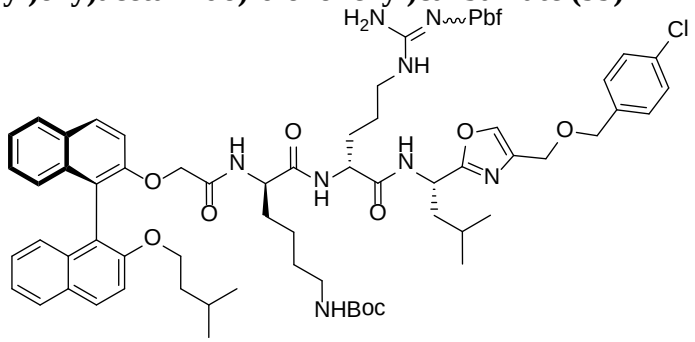

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (77 mg, 0.073 mmol) and Type **C** amine **65** (77 mg, 0.073 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **97** (50 mg, 53%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.46 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.50 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.72-0.86 (m, 2H, $CH_2$), 0.89-0.96 (m, 7H, $CH_2$ ($H_a^*$) and 2 x $CH_3$ (Leu)), 1.05-1.11 (m, 1H, CH), 1.12-1.37 (m, 2H, $CH_2$), 1.23-1.37 (m, 3H, $CH_2$ and $CH_2$ ($H_b^*$)), 1.40-1.53 (m, 2H, $CH_2$), 1.42-1.43 (s, 15H, 2 x $CH_3$ (Pbf) and $^t$Bu), 1.57-1.66 (m, 2H, CH and $CH_2$ ($H_a^\#$)), 1.76-1.95 (m, 3H, $CH_2$ and $CH_2$ ($H_b^\#$)), 2.07 (s, 3H, $CH_3$ (Pbf)), 2.48 (s, 3H, $CH_3$ (Pbf)), 2.55 (s, 3H, $CH_3$ (Pbf)), 2.87-2.94 (m, 2H, $CH_2$N (Lys)), 2.90 (s, 2H, $CH_2$ (Pbf)), 3.01-3.12 (m, 1H, $CH_2$N (Arg, $H_a$)), 3.13-3.24 (m, 1H, $CH_2$N (Arg, $H_b$)), 3.82-3.86 (m, 1H $CH_2$O ($H_a$)), 3.95-4.05 (m, 2H, CH and $CH_2$O ($H_b$)), 4.43-4.52 (m, 1H, CH), 4.47 (ABq, *J* = 14.5 Hz, 2H, $OCH_2CO$), 4.74-4.82 (m, 1H, N<u>H</u>Boc), 4.85 (s, 1H, oxazole-C<u>H</u>$_2$ ($H_a$)), 4.98 (s, 1H, oxazole-C<u>H</u>$_2$ ($H_b$)), 5.20 (dd, $J_1$ = 9.0, $J_2$ = 15.0 Hz, 1H, CH), 6.10 (d, *J* = 6.5 Hz, 1H, NH), 6.24 (br s, 2H , 2 x NH), 6.85 (d, *J* = 8.5 Hz, 1H, ArH), 6.94-6.99 (m, 3H, ArH), 7.12 (d, *J* = 8.5 Hz, 1H, ArH), 7.15 (d, *J* = 8.5 Hz, 1H, ArH), 7.20-7.38 (m, 6H, ArH), 7.44 (d, *J* = 9.0 Hz, 1H, ArH), 7.59 (s, 1H, ArH (oxazole)), 7.85 (d, *J* = 8.0 Hz, 2H, ArH), 7.89 (d, *J* = 9.0 Hz, 1H, ArH), 7.96 (d, *J* = 9.0 Hz, 1H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.5, 17.9, 19.3 ($CH_3$ (Pbf)), 21.8, 22.0, 22.3, 22.9 ($CH_3$), 22.6, 25.5, 29.1, 29.2, 31.0, 37.9, 42.1 ($CH_2$), 24.5, 24.7, 46.1, 53.2 (CH), 28.5 (C(<u>C</u>H$_3$)$_3$), 28.6 (2 x $CH_3$ (Pbf)), 40.1 ($CH_2$N (Lys)), 40.5 ($CH_2$N (Arg)), 43.2 ($CH_2$ (Pbf)), 62.4 (oxazole-<u>C</u>H$_2$), 68.0 (O<u>C</u>H$_2$CO), 68.5 ($CH_2$O), 79.0 (<u>C</u>(CH$_3$)$_3$), 86.3 (C (Pbf)), 114.1, 114.7, 114.8, 116.0, 121.26, 121.32, 124.0, 124.2, 125.0, 125.5, 126.7, 126.8, 128.0, 128.1, 129.49, 129.52, 129.9 (ArCH), 117.4, 119.6, 120.3, 124.5, 129.3, 129.8, 132.3, 133.1, 133.6, 133.9, 136.8, 138.3, 152.1, 154.3, 156.3, 158.2, 164.9 (ArC), 156.1 (C=O (Boc)), 158.7 (C=N), 169.5, 171.3, 171.6 (C=O). MS (ESI, +ve) *m/z* 1294 (5%) $[M+H]^+$, 1316 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{72}H_{93}N_8O_{12}S$ 1293.6634, found 1293.6641 $[M+H]^+$, calcd for $C_{72}H_{92}N_8O_{12}NaS$ 1315.6453, found 1315.6473 $[M+Na]^+$.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(benzyloxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (98)**



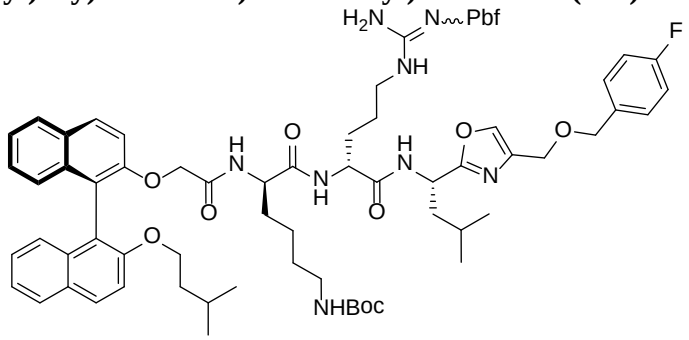

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (38 mg, 0.036 mmol) and Type **C** amine **66** (10 mg, 0.036 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **98** (17 mg, 36%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.48 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.52 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.75-0.82 (m, 2H, $CH_2$), 0.90-0.94 (m, 1H, $CH_2$ ($H_a^*$)), 0.91 (d, *J* = 7.0 Hz, 3H, $CH_3$ (Leu)), 0.93 (d, *J* = 6.0 Hz, 3H, $CH_3$ (Leu)), 1.08-1.14 (m, 1H, CH), 1.15-1.20 (m, 2H, $CH_2$), 1.22-1.30 (m, 3H, $CH_2$ and $CH_2$ ($H_b^*$)), 1.40-1.52 (m, 2H, $CH_2$), 1.42 (s, 9H, $^t$Bu), 1.43 (s, 6H, 2 x $CH_3$ (Pbf)), 1.54-1.64 (m, 2H, CH and $CH_2$ ($H_a^\#$)), 1.76-1.80 (m, 2H, $CH_2$), 1.86-1.92 (m, 1H, $CH_2$ ($H_b^\#$)), 2.07 (s, 3H, $CH_3$ (Pbf)), 2.49 (s, 3H, $CH_3$ (Pbf)), 2.56 (s, 3H, $CH_3$ (Pbf)), 2.85-3.00 (m, 2H, $CH_2$N (Lys)), 2.91 (s, 2H, $CH_2$ (Pbf)), 3.00-3.24 (m, 2H, $CH_2$N (Arg)), 3.84-3.88 (m, 1H $CH_2$O ($H_a$)), 3.93-4.02 (m, 1H, CH), 4.00-4.04 (m, 1H $CH_2$O ($H_b$)), 4.36 (s, 2H, oxazole-C$\underline{H}_2$), 4.41-4.48 (m, 1H, CH), 4.47 (ABq, *J* = 15.0 Hz, 2H, OC$H_2$CO), 4.50 (s, 2H, C$\underline{H}_2$Ph), 4.71-4.79 (m, 1H, N$\underline{H}$Boc), 5.15-5.20 (m, 1H, CH), 6.10 (d, *J* = 6.5 Hz, 1H, NH), 6.21 (br s, 2H , 2 x NH), 7.12-7.16 (m, 2H, ArH), 7.21-7.37 (m, 10H, ArH), 7.44 (d, *J* = 9.0 Hz, 1H, ArH), 7.50 (s, 1H, ArH (oxazole)), 7.84-7.87 (m, 2H, ArH), 7.92 (d, *J* = 9.0 Hz, 1H, ArH), 7.96 (d, *J* = 9.0 Hz, 1H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 12.5, 17.9, 19.3 ($CH_3$ (Pbf)), 21.8, 22.0, 22.3, 22.8 ($CH_3$), 22.5, 25.3, 29.1, 30.8, 37.9, 42.2 ($CH_2$), 24.5, 24.7, 46.1, 52.4, 53.2 (CH), 28.6 (C($\underline{C}H_3)_3$), 29.1 (2 x $CH_3$ (Pbf)), 40.1 ($CH_2$N (Lys)), 40.5 ($CH_2$N (Arg)), 43.2 ($CH_2$ (Pbf)), 63.8 (oxazole-$\underline{C}H_2$), 68.0 (O$\underline{C}H_2$CO), 68.5 ($CH_2$O), 72.5 ($\underline{C}H_2$Ph), 79.0 ($\underline{C}(CH_3)_3$), 86.3 (C (Pbf)), 114.1, 116.0, 124.0, 124.2, 125.0, 125.5, 126.6, 126.8, 127.8, 128.0, 128.1, 128.4, 129.7, 129.8 (ArCH), 117.4, 119.6, 120.2, 124.5, 129.3, 132.2, 133.1, 133.6, 133.8, 137.6, 138.3, 152.1, 154.3, 156.2, 164.8 (ArC), 156.0 (C=O (Boc)), 158.6 (C=N), 169.5, 171.1, 171.5 (C=O). MS (ESI, +ve) *m/z* 1307 (5%) $[M+H]^+$; 1329 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{73}H_{95}N_8O_{12}S$ 1307.6790, found 1307.6843.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(4-chlorobenzyloxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (99)**



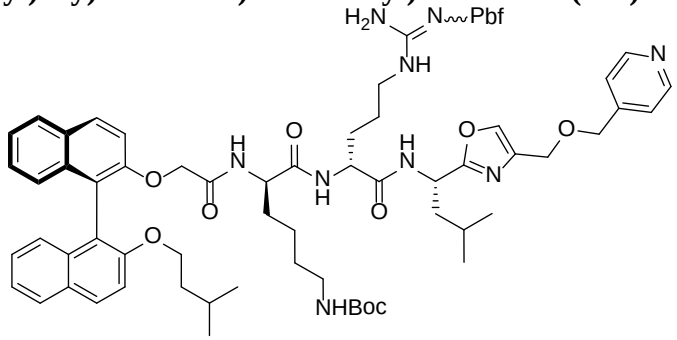

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (85 mg, 0.081 mmol) and Type **C** amine **67** (25 mg, 0.081 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **99** (89 mg, 82%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.48 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.52 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.76-0.83 (m, 2H, $CH_2$), 0.90-0.94 (m, 1H, $CH_2$ ($H_a^*$)), 0.91 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 0.93 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.07-1.13 (m, 1H, CH), 1.15-1.20 (m, 2H, $CH_2$), 1.21-1.38 (m, 3H, $CH_2$ and $CH_2$ ($H_b^*$)), 1.40-1.52 (m, 2H, $CH_2$), 1.42 (s, 9H, $^t$Bu), 1.43 (s, 6H, 2 x $CH_3$ (Pbf)), 1.54-1.64 (m, 2H, CH and $CH_2$ ($H_a^\#$)), 1.74-1.82 (m, 2H, $CH_2$), 1.81-1.92 (m, 1H, $CH_2$ ($H_b^\#$)), 2.07 (s, 3H, $CH_3$ (Pbf)), 2.49 (s, 3H, $CH_3$ (Pbf)), 2.55 (s, 3H, $CH_3$ (Pbf)), 2.86-2.98 (m, 2H, $CH_2$N (Lys)), 2.91 (s, 2H, $CH_2$ (Pbf)), 3.00-3.12 (m, 1H, $CH_2$N (Arg, $H_a$)), 3.12-3.23 (m, 1H, $CH_2$N (Arg, $H_b$)), 3.84-3.88 (m, 1H $CH_2$O ($H_a$)), 3.95-4.05 (m, 2H, CH and $CH_2$O ($H_b$)), 4.35 (s, 2H, oxazole-C$\underline{H}_2$), 4.41-4.49 (m, 1H, CH), 4.47 (ABq, *J* = 15.0 Hz, 2H, $OCH_2CO$), 4.45 (s, 2H, C$\underline{H}_2$ArCl), 4.73-4.99 (m, 1H, N$\underline{H}$Boc), 5.15-5.20 (m, 1H, CH), 6.11 (d, *J* = 7.0 Hz, 1H, NH), 6.22 (br s, 2H , 2 x NH), 7.13 (d, *J* = 8.5 Hz, 1H, ArH), 7.15 (d, *J* = 9.0 Hz, 1H, ArH), 7.20-7.38 (m, 9H, ArH), 7.44 (d, *J* = 9.0 Hz, 2H, ArH), 7.51 (s, 1H, ArH (oxazole)), 7.84-7.87 (m, 2H, ArH), 7.92 (d, *J* = 9.0 Hz, 1H, ArH), 7.95 (d, *J* = 9.0 Hz, 1H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.4, 17.9, 19.2 ($CH_3$ (Pbf)), 21.7, 22.0, 22.2, 22.8 ($CH_3$), 22.4, 25.4, 29.0, 29.2, 31.0, 37.8, 41.9 ($CH_2$), 24.4, 24.6, 45.9, 52.5, 52.9 (CH), 28.4 (C($\underline{C}H_3)_3$), 28.5 (2 x $CH_3$ (Pbf)), 40.0 ($CH_2$N (Lys)), 40.3 ($CH_2$N (Arg)), 43.1 ($CH_2$ (Pbf)), 63.9 (oxazole-$\underline{C}H_2$), 68.0 (O$\underline{C}H_2CO$), 68.3 ($CH_2$O), 71.6 ($\underline{C}H_2$ArCl), 78.9 ($\underline{C}(CH_3)_3$), 86.2 (C (Pbf)), 114.1, 115.8, 123.9, 124.1, 124.9, 125.4, 126.5, 126.7, 127.9, 128.0, 128.5, 129.0, 129.7, 136.2 (ArCH), 117.3, 119.4, 120.2, 124.5, 129.1, 132.1, 132.9, 133.4, 133.5, 133.7, 136.2, 137.3, 138.2, 152.0, 154.3, 156.2, 164.6 (ArC), 156.0 (C=O (Boc)), 158.6 (C=N), 169.3, 171.3, 171.5 (C=O). MS (ESI, +ve) *m/z* 1363 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{73}H_{94}N_8O_{12}SCl$ 1341.6400, found 1341.6428.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(4-fluorobenzyloxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (100)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (38.8 mg, 0.037 mmol) and Type **C** amine **68** (13.5 mg, 0.046 mmol). Flash chromatography (100% $CH_2Cl_2$ to 2% MeOH/$CH_2Cl_2$) gave **100** (38.4 mg, 79%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.38; $[\alpha]_D^{25}$ −41.2 (*c* 1.82, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.90 (m, 2H), 7.85 (t, *J* = 7.1 Hz, 2H), 7.50 (s, 1H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.39 – 7.19 (m, 9H), 7.18 – 7.10 (m, 2H), 6.99 (t, *J* = 8.3 Hz, 2H), 6.24 (bs, 2H), 6.12 (bd, *J* = 6.0 Hz, 1H), 5.17 (q, *J* = 6.6 Hz, 1H), 4.82 – 4.72 (bm, 1H), 4.60 – 4.28 (m, 7H), 4.06 – 3.95 (m, 2H), 3.86 (q, *J* = 8.0 Hz, 1H), 3.24 – 2.99 (m, 2H), 2.92 – 2.88 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.06 (s, 3H), 1.94 – 1.52 (m, 6H), 1.51 – 1.36 (m, 15H), 1.36 – 1.04 (m, 8H), 0.93 (d, *J* = 6.3 Hz, 3H), 0.90 (d, *J* = 6.2 Hz, 3H), 0.84 – 0.71 (m, 2H), 0.52 (d, *J* = 6.2 Hz, 3H), 0.47 (d, *J* = 6.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.5, 171.2, 169.4, 164.7, 162.4 (d, $J_{C-F}$ = 245.8 Hz), 158.6, 156.2, 156.0, 154.3, 152.1, 138.3, 137.5, 136.2, 133.8, 133.6, 133.5 (d, $J_{C-F}$ = 3.1 Hz), 133.0, 132.2, 129.8, 129.7, 129.6 (d, $J_{C-F}$ = 8.1 Hz), 129.2, 128.1, 127.9, 126.7, 126.6, 125.5, 124.9, 124.5, 124.2, 123.9, 120.3, 119.5, 117.4, 115.9, 115.2 (d, $J_{C-F}$ = 21.4 Hz), 114.1, 86.3, 79.0, 71.8, 68.4, 68.0, 63.8, 53.1, 52.5, 46.0, 43.2, 42.1, 40.4, 40.1, 37.9, 30.9, 29.3, 29.1, 28.5, 28.4, 25.4, 24.6, 24.5, 22.8, 22.5, 22.3, 22.0, 21.7, 19.2, 17.9, 12.4; MS (ES$^+$) *m/z* 1347 (16%, M+Na), 1325 (100%, M+H); HRMS (ES$^+$) Calcd. for $C_{73}H_{94}FN_8O_{12}S$: 1325.6696 (M+H), Found: 1325.6704.

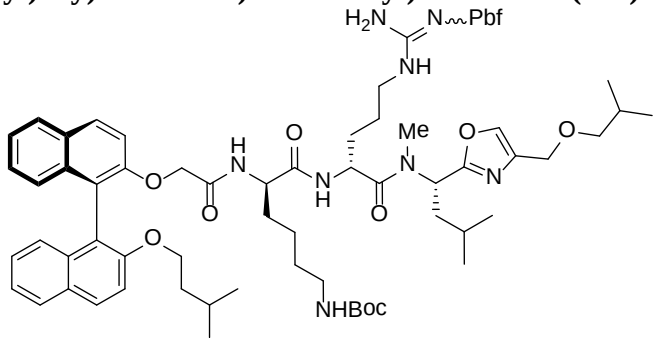
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-((4-(pyridin-4-ylmethoxy)methyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (101)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (35 mg, 0.033 mmol) and Type **C** amine·TFA salt **69** (13 mg, 0.033 mmol), with added NEt(i-Pr)$_2$ (5.1 mg, 0.040 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **101** (81 mg, 81%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.48 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.52 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.73-0.86 (m, 2H, $CH_2$), 0.90-1.01 (m, 1H, $CH_2$ ($H_a^*$)), 0.91 (d, *J* = 6.5 Hz, 3H, $CH_3$

(Leu)), 0.94 (d, $J$ = 6.0 Hz, 3H, $CH_3$ (Leu)), 08-1.13 (m, 1H, CH), 1.15-1.20 (m, 2H, $CH_2$), 1.21-1.29 (m, 2H, $CH_2$), 1.30-1.40 (m, 2H, $CH_2$ ($H_b$*)), 1.41 (s, 9H, $^t$Bu), 1.42-1.52 (m, 2H, $CH_2$), 1.43 (s, 6H, 2 x $CH_3$ (Pbf)), 1.56-1.63 (m, 2H, CH and $CH_2$ ($H_a$#)), 1.73-1.93 (m, 3H, $CH_2$ and $CH_2$ ($H_b$#)), 2.06 (s, 3H, $CH_3$ (Pbf)), 2.48 (s, 3H, $CH_3$ (Pbf)), 2.54 (s, 3H, $CH_3$ (Pbf)), 2.84-2.98 (m, 2H, $CH_2$N (Lys)), 2.90 (s, 2H, $CH_2$ (Pbf)), 2.99-3.23 (m, 2H, $CH_2$N (Arg)), 3.84-3.89 (m, 1H $CH_2$O ($H_a$)), 4.01-4.02 (m, 2H, CH and $CH_2$O ($H_b$)), 4.35-4.58 (m, 3H, CH and $OCH_2CO$), 4.42 (s, 2H, oxazole-C$\underline{H}_2$), 4.53 (s, 2H, C$\underline{H}_2$-Py), 4.78-4.85 (m, 1H, N$\underline{H}$Boc), 5.19 (dd, $J_1$ = 8.5, $J_2$ = 14.5 Hz, 1H, CH CH), 6.14 (d, $J$ = 6.0 Hz, 1H, NH), 6.23 (br s, 2H , 2 x NH), 7.12 (d, $J$ = 9.0 Hz, 1H, ArH), 7.15 (d, $J$ = 9.0 Hz, 1H, ArH), 7.21-7.26 (m, 5H, ArH), 7.30-7.37 (m, 2H, ArH), 7.43 (d, $J$ = 9.0 Hz, 1H, ArH), 7.54 (s, 1H, ArH (oxazole)), 7.83-7.87 (m, 2H, ArH), 7.91-7.96 (m, 2H, ArH), 8.54 (d, $J$ = 5.5 Hz, 2H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.5, 17.9, 19.3 ($CH_3$ (Pbf)), 21.8, 22.1, 22.3, 22.8 ($CH_3$), 22.6, 25.5, 29.2, 29.4, 31.0, 38.0, 42.1 ($CH_2$), 24.5, 24.7, 46.1, 52.6, 53.1 (CH), 28.5 (C($\underline{C}H_3)_3$), 28.6 (2 x $CH_3$ (Pbf)), 40.1 ($CH_2$N (Lys)), 40.5 ($CH_2$N (Arg)), 43.3 ($CH_2$ (Pbf)), 64.5 (oxazole-$\underline{C}H_2$), 68.1 (O$\underline{C}H_2$CO), 68.4 ($CH_2$O), 70.7 ($\underline{C}H_2$Py), 79.0 ($\underline{C}(CH_3)_3$), 86.3 (C (Pbf)), 114.2, 116.0, 121.8, 124.0, 124.3, 125.0, 125.5, 126.7, 126.8, 128.0, 128.1, 129.78, 129.83, 149.8 (ArCH), 117.4, 119.5, 120.4, 124.6, 129.3, 129.81, 132.2, 133.1, 133.6, 133.9, 137.2, 138.3, 147.1, 152.2, 154.4, 156.3, 164.8 (ArC), 136.4 (ArCH (oxazole)), 156.1 (C=O (Boc)), 158.7 (C=N), 169.4, 171.3, 171.5 (C=O). MS (ESI, +ve) *m/z* 1308 (100%) $[M+H]^+$; 1330 (25%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{72}H_{94}N_9O_{12}S$ 1308.6743, found 1308.6744.

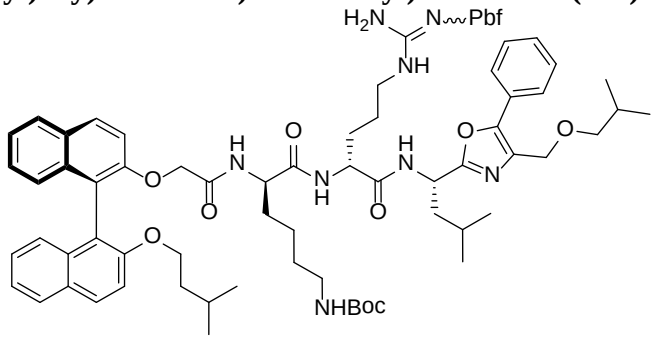
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(isobutoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (102)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (32.6 mg, 0.031 mmol) and Type **C** amine **70** (8.6 mg, 0.034 mmol). Flash chromatography (100% $CH_2Cl_2$ to 2.5% MeOH/$CH_2Cl_2$) gave **102** (15.6 mg, 39%) as an off-white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.44; $[\alpha]_D^{25}$ −41.6 (*c* 0.66, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$, major rotamer only) δ 8.01 – 7.94 (m, 2H), 7.87 (t, $J$ = 8.5 Hz, 2H), 7.55 (s, 1H), 7.47 (d, $J$ = 8.9 Hz, 1H), 7.39 – 7.21 (m, 5H), 7.18 – 7.12 (m, 2H), 6.91 (bd, $J$ = 8.0 Hz, 1H), 6.26 – 6.04 (bm, 3H), 5.90 (dd, $J$ = 8.9, 6.3 Hz, 1H), 4.86 – 4.79 (m, 1H), 4.62 – 4.42 (m, 3H), 4.40 (s, 2H), 4.11 – 4.03 (m, 1H), 3.95 – 3.80 (m, 2H), 3.33 – 3.23 (m, 3H), 3.19 – 3.08 (m, 1H), 2.99 – 2.88 (m, 4H), 2.83 (s, 3H), 2.59 (s, 3H), 2.53 (s, 3H), 2.09 (s, 3H), 1.98 – 1.67 (m, 5H), 1.66 – 1.07 (m, 24H), 1.01 – 0.71 (m, 15H), 0.56 (d, $J$ = 6.5 Hz, 3H), 0.51 (d, $J$ = 6.4 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.4, 170.8, 169.1, 162.1, 158.5, 156.1, 155.9, 154.4, 152.0, 138.4, 138.3, 136.4, 133.8, 133.6, 133.4, 132.3, 129.9, 129.8, 129.7, 129.2, 128.03, 127.99, 126.8, 126.6, 125.5, 125.0, 124.4, 124.2, 123.9, 120.2, 119.5, 117.3, 115.9, 114.1, 86.2, 79.1, 77.9, 68.4, 67.8, 65.0, 53.4, 53.1, 49.2, 43.3, 40.6, 40.1, 38.1, 37.9, 30.6, 30.0, 29.3, 28.6, 28.43, 28.36, 24.7, 24.5, 24.1, 23.2, 22.6, 22.3, 22.1, 21.5, 19.35, 19.30, 19.25, 17.9, 12.4; MS ($ES^+$) *m/z*

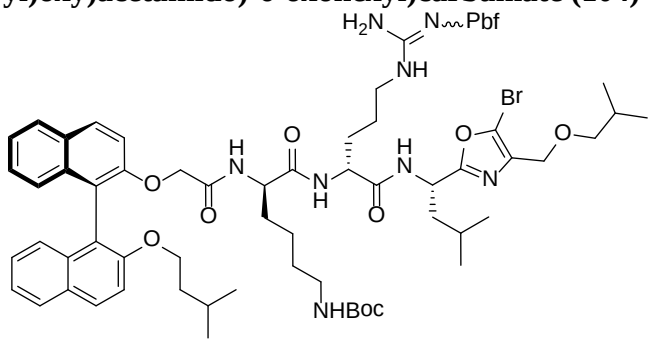
1309 (94%, M+Na), 1287 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{71}H_{98}N_8NaO_{12}S$: 1309.6923 (M+Na), Found: 1309.6969.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(isobutoxymethyl)-5-phenyloxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (103)**



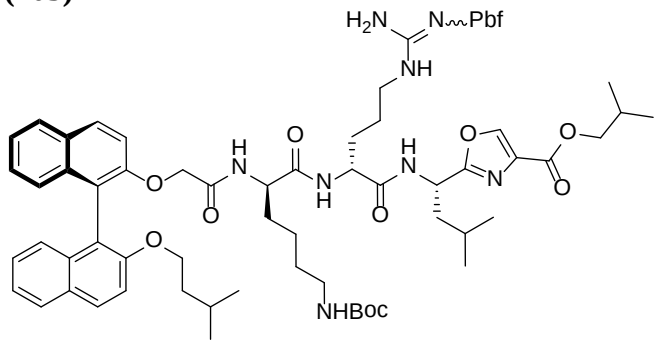
This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (63.1 mg, 0.060 mmol) and Type **C** amine **71** (21.0 mg, 0.066 mmol). Flash chromatography (100% $CH_2Cl_2$ to 2.5% MeOH/$CH_2Cl_2$) gave **103** (63.0 mg, 78%) as an off-white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.41; $[\alpha]_D^{25}$ −46.7 (*c* 2.29, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.9 Hz, 2H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.68 (d, *J* = 7.5 Hz, 2H), 7.53 – 7.17 (m, 11H), 7.15 (d, *J* = 8.5 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 1H), 6.27 (bs, 2H), 6.14 (bd, *J* = 6.8 Hz, 1H), 5.27 (dd, *J* = 14.8, 7.8 Hz, 1H), 4.77 (bs, 1H), 4.60 – 4.35 (m, 5H), 4.13 – 3.95 (m, 2H), 3.89 – 3.81 (m, 1H), 3.26 (d, *J* = 6.4 Hz, 2H), 3.21 – 3.10 (m, 1H), 2.96 – 2.76 (m, 5H), 2.54 (s, 3H), 2.47 (s, 3H), 2.03 (s, 3H), 1.95 – 1.77 (m, 4H), 1.70 – 1.04 (m, 26H), 0.96 (d, *J* = 6.4 Hz, 3H), 0.93 (d, *J* = 6.3 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 6H), 0.84 – 0.71 (m, 2H), 0.51 (d, *J* = 6.2 Hz, 3H), 0.46 (d, *J* = 6.1 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.4, 171.1, 169.3, 162.0, 158.6, 156.2, 156.0, 154.3, 152.1, 148.9, 138.2, 133.8, 133.5, 133.1, 132.3, 132.1, 129.7, 129.2, 128.6, 128.4, 128.02, 127.96, 127.9, 126.7, 126.5, 126.1, 125.5, 124.9, 124.4, 124.1, 123.8, 120.3, 119.4, 117.3, 115.9, 114.2, 86.2, 78.9, 77.5, 68.3, 68.1, 65.1, 52.7, 52.4, 46.0, 43.2, 42.3, 40.5, 40.0, 37.9, 29.6, 29.0, 28.5, 28.4, 28.3, 25.3, 24.7, 24.5, 22.8, 22.5, 22.3, 22.0, 21.9, 19.4, 19.2, 17.9, 12.4; MS ($ES^+$) *m/z* 1372 (56%, M+Na), 1349 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{76}H_{101}N_8O_{12}S$: 1349.7260 (M+H), Found: 1349.7295.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(5-bromo-4-(isobutoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (104)**



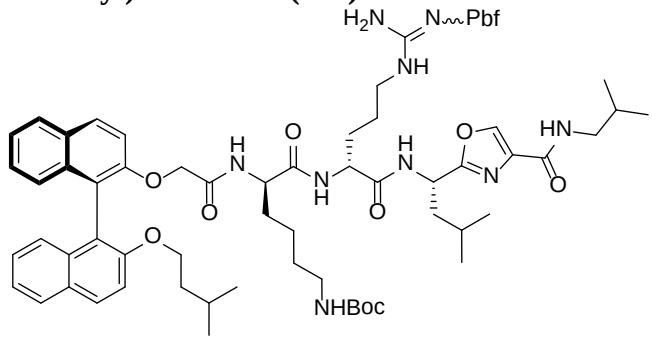
This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (48.4 mg, 0.046 mmol) and Type **C** amine **72** (16.1 mg, 0.050 mmol). Flash chromatography (100% $CH_2Cl_2$ to 2.5% MeOH/$CH_2Cl_2$) gave **104** (44.1 mg, 71%) as an off-white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.49; $[\alpha]_D^{25}$ −38.4 (*c* 1.89, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.96 (t, *J* = 8.5 Hz, 2H), 7.86 (t, *J* = 7.1 Hz, 2H), 7.48 – 7.39 (m, 2H), 7.39 – 7.20 (m, 6H), 7.18 – 7.11 (m, 2H), 6.26 (bs, 2H), 6.13 (bd, *J* = 6.2 Hz, 1H), 5.19 – 5.11 (m, 1H), 4.80 (bs, 1H), 4.60 – 4.38 (m, 3H), 4.25 (s, 2H), 4.12 – 3.95 (m, 2H), 3.91 – 3.82 (m, 1H), 3.18 (d, *J* = 6.5 Hz, 2H), 3.11 – 2.84 (m, 6H), 2.56 (s, 3H), 2.49 (s, 3H), 2.08 (s, 3H), 1.91 – 1.70 (m, 4H), 1.69 – 1.03 (m, 25H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.3 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 6H), 0.83 – 0.71 (m, 3H), 0.52 (d, *J* = 6.3 Hz, 3H), 0.47 (d, *J* = 6.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.5, 171.3, 169.4, 165.4, 158.6, 156.2, 156.0, 154.3, 152.1, 138.3, 135.6, 133.8, 133.6, 133.0, 132.2, 129.78, 129.76, 129.2, 128.1, 127.9, 126.7, 126.6, 125.4, 124.9, 124.5, 124.2, 123.9, 120.3, 119.6, 117.4, 116.0, 114.1, 86.3, 78.9, 77.5, 68.5, 68.0, 63.4, 52.9, 52.4, 46.2, 43.2, 41.8, 40.5, 40.0, 37.9, 31.0, 29.3, 29.0, 28.6, 28.4, 28.2, 25.4, 24.6, 24.5, 22.8, 22.5, 22.3, 22.0, 21.6, 19.31, 19.27, 17.9, 12.4; MS (ES$^+$) *m/z* 1375 (70%, M+Na, $^{81}$Br), 1373 (41%, M+Na, $^{79}$Br), 1353 (100%, M+H, $^{81}$Br), 1351 (84%, M+H, $^{79}$Br); HRMS (ES$^+$) Calcd. for $C_{70}H_{95}{}^{79}BrN_8Na_2O_{12}S$ (M+2Na): 698.2885, Found: 698.2852.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(isobutylcarboxy)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (105)**



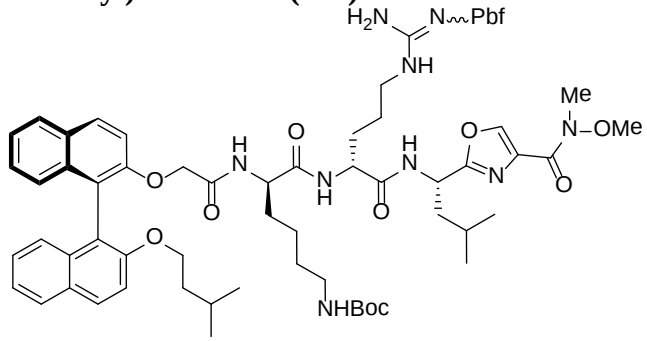

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (38.9 mg, 0.037 mmol) and Type **C** amine **73** (10.3 mg, 0.040 mmol). Flash chromatography (100% $CH_2Cl_2$ to 2.5% MeOH/$CH_2Cl_2$) gave **105** (30.5 mg, 64%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.45; $[\alpha]_D^{25}$ −37.1 (*c* 1.34, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 8.00 – 7.91 (m, 2H), 7.90 – 7.83 (m, 2H), 7.54 – 7.42 (m, 3H), 7.38 – 7.29 (m, 2H), 7.29 – 7.20 (m, 3H), 7.18 – 7.11 (m, 2H), 6.31 (bs, 2H), 6.13 (bd, *J* = 5.6 Hz, 1H), 5.18 (dd, *J* = 14.2, 8.6 Hz, 1H), 4.73 (bs, 1H), 4.55 (d, *J* = 14.3 Hz, 1H), 4.51 – 4.37 (m, 2H), 4.09 – 3.93 (m, 4H), 3.86 (dd, *J* = 15.8, 6.8 Hz, 1H), 3.27 – 3.03 (m, 2H), 3.01 – 2.84 (m, 4H), 2.56 (s, 3H), 2.49 (s, 3H), 2.07 (s, 3H), 2.00 (sep, *J* = 6.7 Hz, 1H), 1.94 – 1.70 (m, 3H), 1.70 – 1.58 (m, 2H), 1.57 – 1.37 (m, 17H), 1.37 – 1.03 (m, 6H), 1.02 – 0.87 (m, 13H), 0.84 – 0.69 (m, 2H), 0.52 (d, *J* = 6.4 Hz, 3H), 0.47 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.6, 171.5, 169.6, 165.9, 161.0, 158.6, 156.2, 156.0, 154.3, 152.1, 143.6, 138.3, 133.8, 133.6, 133.1, 132.9, 132.2, 129.74, 129.70, 129.3, 128.0, 127.9, 126.7, 126.5, 125.4, 125.0, 124.5, 124.1, 124.0, 120.2, 119.7, 117.3, 116.2, 114.2, 86.3, 79.0, 71.0, 68.6, 68.0, 53.3, 52.5, 46.1, 43.2, 41.8, 40.5, 40.1, 37.9, 30.9, 28.9, 28.5, 28.4, 27.7, 25.4, 24.6, 24.4, 22.8, 22.5, 22.3, 22.0, 21.6, 19.2, 19.0, 17.9, 12.4; MS (ES$^+$) *m/z* 1309 (91%, M+Na), 1287 (100%, M+H); HRMS (ES$^+$) Calcd. for $C_{70}H_{95}N_8O_{13}S$: 1287.6739 (M+H), Found: 1287.6810.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(isobutylcarbamoyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (106)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (58.9 mg, 0.056 mmol) and Type **C** amine **74** (17.1 mg, 0.067 mmol). Flash chromatography (100% $CH_2Cl_2$ to 2.5% MeOH/$CH_2Cl_2$) gave **106** (57.2 mg, 79%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.42; $[\alpha]_D^{25}$ −44.1 (*c* 2.63, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.93 (t, *J* = 7.7 Hz, 2H), 7.85 (t, *J* = 9.0 Hz, 2H), 7.57 (bs, 1H), 7.47 – 7.08 (m, 10H), 6.22 (bs, 2H), 6.14 (bd, *J* = 6.5 Hz, 1H), 5.22 (dd, *J* = 15.1, 8.0 Hz, 1H), 4.85 (bs, 1H), 4.57 – 4.32 (m, 3H), 4.11 – 3.95 (m, 2H), 3.92 – 3.82 (m, 1H), 3.24 – 3.12 (m, 2H), 3.05 – 2.81 (m, 6H), 2.52 (s, 3H), 2.45 (s, 3H), 2.06 (s, 3H), 1.91 – 1.72 (m, 4H), 1.68 – 1.04 (m, 26H), 1.02 – 0.87 (m, 12H), 0.85 – 0.70 (m, 2H), 0.52 (d, *J* = 6.2 Hz, 3H), 0.47 (d, *J* = 6.0 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.6, 171.4, 169.2, 163.7, 160.6, 158.7, 156.3, 156.0, 154.4, 152.1, 140.8, 138.2, 136.2, 133.8, 133.5, 132.8, 132.1, 129.8, 129.71, 129.68, 129.1, 128.0, 127.9, 126.7, 126.5, 125.5, 124.9, 124.6, 124.2, 123.9, 120.4, 119.3, 117.5, 115.8, 114.2, 86.3, 78.9, 68.2, 68.1, 52.8, 46.3, 45.8, 43.2, 41.8, 40.3, 40.0, 37.9, 31.1, 29.0, 28.6, 28.55, 28.52, 28.4, 25.7, 24.6, 24.5, 22.7, 22.4, 22.3, 22.0, 21.8, 20.1, 19.2, 17.9, 12.4; MS ($ES^+$) *m/z* 1308 (85%, M+Na), 1286 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{70}H_{95}N_9NaO_{12}S$: 1308.6719 (M+Na), Found: 1308.6738.

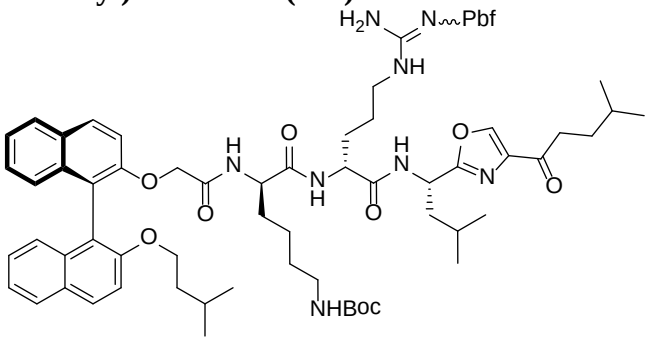
***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(((*R*)-1-(((*S*)-1-(4-(methoxy(methyl)carbamoyl) oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(3-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-6-oxohexyl)carbamate (107)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (55 mg, 0.05 mmol) and Type **C** amine **75** (16.5 mg, 0.07 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) gave **107** (27.5 mg, 43%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.41. $[\alpha]_D^{25}$ = −24.3 (*c* 0.92, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.46 (3H, d, *J* = 6.6 Hz), 0.51 (3H, d, *J* = 6.6 Hz), 0.69 - 0.83 (2H, m), 0.93 (6H, t, *J* = 6.4 Hz), 1.03 - 1.10 (2H, m), 1.13 - 1.26 (3H, m), 1.43 (16H, s, *J* = 9.6 Hz), 1.51 - 1.93 (6H, m), 2.07 (3H, s), 2.30 (3H, s), 2.51 (3H, s), 2.58 (3H, s),

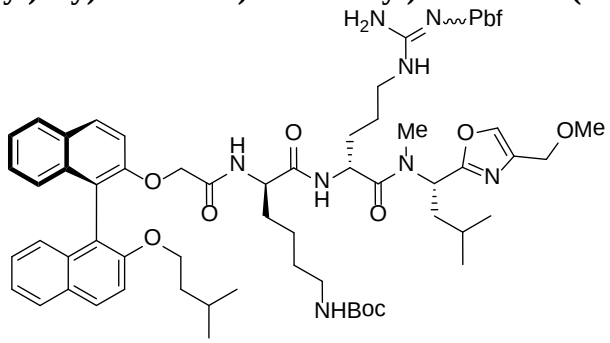
2.92 (4H, bs), 3.06 - 3.16 (1H, bm), 3.27 (3H, s), 3.73 (3H, s), 3.83 - 3.91 (2H, m), 4.02 - 4.06 (1H, m), 4.53 ($AB_q$, 4H, $\Delta\sigma_{AB}$ = 0.65, $J_{AB}$ = 14.5 Hz), 5.12 - 5.16 (1H, m), 5.30 (1H, s), 6.13 (2H, d, *J* = 6.5 Hz), 6.36 (2H, bs), 7.14 - 7.16 (2H, m), 7.23 - 7.26 (3H, m), 7.30 - 7.37 (4H, m), 7.47 (1H, d, *J* = 9.0 Hz), 7.87 (2H, t, *J* = 8.2 Hz) , 7.94 - 7.99 (2H, m), 8.09 (1H, s). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 12.7, 18.2, 19.5, 21.9, 22.2, 22.5, 23.0, 24.6, 24.9, 28.7, 28.8, 29.5, 33.1, 38.1, 40.8, 42.2, 43.5, 46.4, 53.7, 61.6, 68.2, 69.0, 86.5, 105.0, 114.6, 116.5, 117.5, 120.2, 120.4, 124.2, 124.4, 124.7, 125.3, 125.7, 126.8, 127.0, 128.1, 128.4, 129.6, 129.9, 130.0, 132.5, 133.9, 134.0, 138.5, 142.9, 152.4, 154.6, 156.5, 158.8, 165.3, 170.0, 171.8. IR (neat) *ν* [$cm^{-1}$] = 3852 (s), 3675 (s), 2966 (w), 2360 (m), 1684 (s), 1558 (s), 1507 (s), 1248 (w), 1089 (w), 667 (m). MS ($ESI^+$) *m/z* = 1275 (40 %, $[M+H]^+$), 1297 (100 %, $[M+Na]^+$).

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(4-methylpentanoyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (108)**



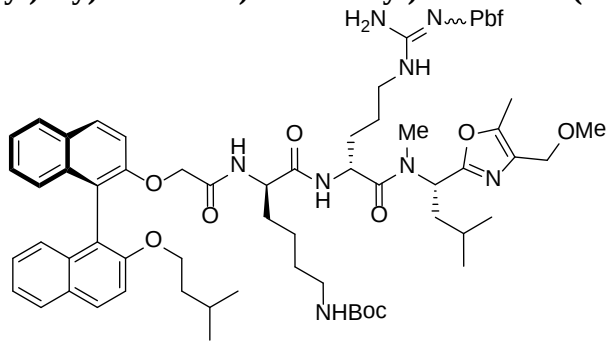

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (49.4 mg, 0.047 mmol) and Type **C** amine·TFA salt **76** (20.7 mg, 0.056 mmol), with added $NEt(i\text{-}Pr)_2$ (10.9 mg, 0.085 mmol). Flash chromatography (100% $CH_2Cl_2$ to 2.5% $MeOH/CH_2Cl_2$) gave **108** (45.2 mg, 75%) as an off-white solid. TLC (5% $MeOH/CH_2Cl_2$) $R_F$ = 0.49; $[\alpha]_D^{25}$ −40.2 (*c* 2.10, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.97 – 7.91 (m, 2H), 7.86 (t, *J* = 8.8 Hz, 2H), 7.52 (bs, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.41 – 7.29 (m, 3H), 7.29 – 7.19 (m, 3H), 7.17 – 7.10 (m, 2H), 6.31 (bs, 2H), 6.15 (bd, *J* = 6.7 Hz, 1H), 5.19 (dd, *J* = 15.0, 8.4 Hz, 1H), 4.80 – 4.71 (m, 1H), 4.58 – 4.34 (m, 3H), 4.11 – 3.96 (m, 2H), 3.93 – 3.81 (m, 1H), 3.26 – 3.02 (m, 2H), 2.97 – 2.86 (m, 4H), 2.80 (t, *J* = 7.6 Hz, 2H), 2.54 (s, 3H), 2.47 (s, 3H), 2.06 (s, 3H), 1.93 – 1.73 (m, 3H), 1.71 – 1.04 (m, 29H), 1.01 – 0.86 (m, 12H), 0.84 – 0.70 (m, 2H), 0.52 (d, *J* = 6.5 Hz, 3H), 0.47 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 194.8, 171.5, 169.4, 165.0, 158.6, 156.3, 156.0, 154.4, 152.1, 142.5, 140.2, 138.2, 133.8, 133.6, 133.0, 132.1, 129.8, 129.73, 129.67, 129.2, 128.0, 127.9, 126.7, 126.5, 125.4, 124.9, 124.5, 124.1, 123.9, 120.3, 119.6, 117.4, 116.0, 114.2, 86.3, 78.9, 68.4, 68.0, 53.0, 46.0, 43.2, 41.7, 40.4, 40.0, 37.9, 37.8, 32.5, 31.0, 29.2, 29.1, 28.5, 28.4, 27.6, 25.4, 24.6, 24.4, 22.7, 22.5, 22.36, 22.35, 22.3, 22.0, 21.7, 19.2, 17.9, 12.4; MS ($ES^+$) *m/z* 1307 (66%, M+Na), 1285 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_{71}H_{97}N_8O_{12}S$: 1285.6947 (M+H), Found: 1285.6956.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (109)**



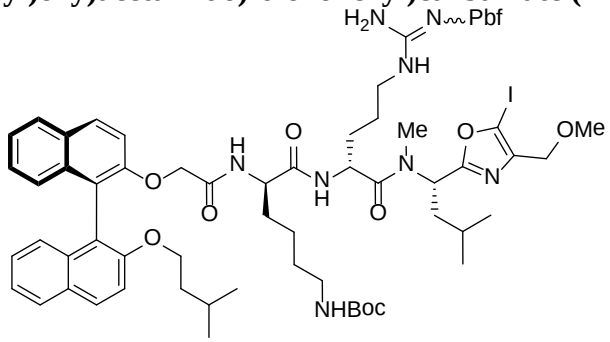

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (38 mg, 0.036 mmol) and Type **C** amine **77** (38 mg, 0.036 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **109** (17 mg, 47%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.51 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.56 (d, *J* = 7.0 Hz, 3H, $CH_3$), 0.75-0.86 (m, 2H, $CH_2$), 0.91-0.95 (m, 1H, $CH_2$ ($H_a^*$)), 0.92 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 0.97 (d, *J* = 7.0 Hz, 3H, $CH_3$ (Leu)), 1.12-1.17 (m, 1H, CH), 1.18-1.34 (m, 4H, 2 x $CH_2$), 1.30-1.41 (m, 1H, $CH_2$ ($H_b^*$)), 1.40-1.48 (m, 1H, CH), 1.44 (s, 15H, 2 x $CH_3$ (Pbf) and $^t$Bu), 1.46-1.54 (m, 2H, $CH_2$), 1.52-1.64 (m, 1H, $CH_2$ ($H_a^\#$)), 1.70-1.81 (m, 1H, $CH_2$ ($H_b^\#$)), 1.84-1.93 (m, 2H, $CH_2$), 2.08 (s, 3H, $CH_3$ (Pbf)), 2.53 (s, 3H, $CH_3$ (Pbf)), 2.59 (s, 3H, $CH_3$ (Pbf)), 2.83 (s, 3H, $NCH_3$), 2.88-3.00 (m, 2H, $CH_2N$ (Lys)), 2.94 (s, 2H, $CH_2$ (Pbf)), 3.07-3.19 (m, 1H, $CH_2N$ (Arg, $H_a$)), 3.23-3.32 (m, 1H, $CH_2N$ (Arg, $H_b$)), 3.42 (s, 3H, $OCH_3$), 3.80-3.88 (m, 1H, CH), 3.90-3.94 (m, 1H $CH_2O$ ($H_a$)), 4.05-4.09 (m, 1H $CH_2O$ ($H_b$)), 4.35 (s, 2H, oxazole-C<u>H</u>$_2$), 4.48 (ABq, *J* = 14.5 Hz, 2H, $OCH_2CO$), 4.54-4.61 (m, 1H, N<u>H</u>Boc), 4.81-4.84 (m, 0.7H, CH), 4.97-5.05 (m, 0.3H, CH), 5.90 (dd, $J_1$ = 6.0, $J_2$ = 10.0 Hz, 1H, CH), 6.08 (d, *J* = 6.0 Hz, 1H, NH), 6.13 (br s, 2H , 2 x NH), 6.89 (d, *J* = 8.0 Hz, 1H, NH), 7.14-7.16 (m, 2H, ArH), 7.23-7.26 (m, 2H, ArH), 7.29-7.38 (m, 2H, ArH), 7.47 (d, *J* = 9.0 Hz, 2H, ArH); 7.57 (s, 1H, ArH (oxazole)), 7.86-7.89 (m, 2H, ArH), 7.96-7.99 (m, 2H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.4, 17.9, 19.3 ($CH_3$ (Pbf)), 21.5, 22.1, 22.3, 23.2 ($CH_3$), 22.6, 24.0 29.2, 29.7, 30.6, 37.9, 38.0 ($CH_2$), 24.5, 24.7, 49.2, 53.4 (CH), 28.4 (C(<u>C</u>H$_3$)$_3$), 28.6 (2 x $CH_3$ (Pbf)), 40.1 ($CH_2N$ (Lys)), 40.5 ($CH_2N$ (Arg)), 43.2 ($CH_2$ (Pbf)), 58.5 ($OCH_3$), 66.2 (oxazole-<u>C</u>H$_2$), 67.8 (O<u>C</u>H$_2$CO), 68.3 ($CH_2O$), 79.1 (<u>C</u>(CH$_3$)$_3$), 86.2 (C (Pbf)), 114.0, 115.9, 123.9, 134.2, 125.0, 125.4, 126.6, 126.8, 128.0, 129.6, 129.9, 136.7, 137.3 (ArCH), 117.3, 119.5, 120.2, 124.4, 129.1, 129.8, 132.2, 133.4, 133.6, 133.8, 138.3, 152.0, 154.4, 156.1, 162.4 (ArC), 156.0 (C=O (Boc)), 158.5 (C=N), 169.1, 170.8, 171.1 (C=O). MS (ESI, +ve) *m/z* 1245 (5%) $[M+H]^+$; 1266 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{68}H_{93}N_8O_{12}S$ 1245.6643, found 1245.6696.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(methoxymethyl)-5-methyloxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (110)**



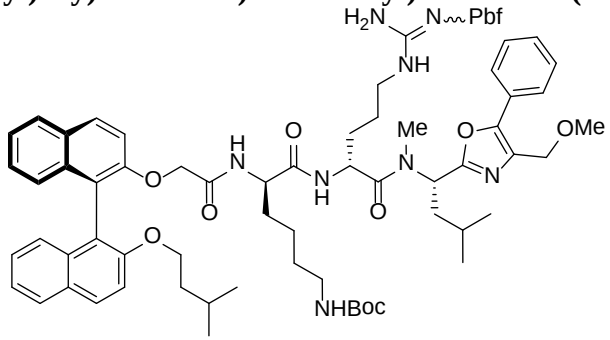

This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (51 mg, 0.048 mmol) and Type **C** amine **78** (10 mg, 0.044 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **110** (38 mg, 69%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.51 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.56 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.75-0.85 (m, 2H, $CH_2$), 0.88-1.00 (m, 1H, $CH_2$ ($H_a^*$)), 0.91 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 0.96 (d, *J* = 7.0 Hz, 3H, $CH_3$ (Leu)), 1.12-1.17 (m, 1H, CH), 1.18-1.30 (m, 4H, 2 x $CH_2$), 1.36-1.46 (m, 1H, $CH_2$ ($H_b^*$)), 1.43-1.44 (m, 16H, CH, 2 x $CH_3$ (Pbf) and $^t$Bu), 1.46-1.53 (m, 2H, $CH_2$), 1.50-1.61 (m, 1H, $CH_2$ ($H_a^\#$)), 1.68-1.78 (m, 1H, $CH_2$ ($H_b^\#$)), 1.81-1.91 (m, 2H, $CH_2$), 2.08 (s, 3H, $CH_3$ (Pbf)), 2.29 (s, 3H, oxazole-$CH_3$), 2.53 (s, 3H, $CH_3$ (Pbf)), 2.59 (s, 3H, $CH_3$ (Pbf)), 2.84 (s, 3H, $NCH_3$), 2.85-3.01 (m, 2H, $CH_2$N (Lys)), 2.94 (s, 2H, $CH_2$ (Pbf)), 3.06-3.20 (m, 1H, $CH_2$N (Arg, $H_a$)), 3.22-3.33 (m, 1H, $CH_2$N (Arg, $H_b$)), 3.38 (s, 3H, $OCH_3$), 3.88-3.94 (m, 2H, CH and $CH_2O$ ($H_a$)), 4.04-4.09 (m, 1H $CH_2O$ ($H_b$)), 4.27 (s, 2H, oxazole-C$\underline{H}_2$), 4.48 (ABq, *J* = 15.0 Hz, 2H, $OCH_2CO$), 4.58-4.66 (m, 1H, N$\underline{H}$Boc), 4.79-4.83 (m, 0.7H, CH), 4.96-5.00 (m, 0.3H, CH), 5.85 (dd, $J_1$ = 5.5, $J_2$ = 10.0 Hz, 1H, CH), 6.10 (d, *J* = 6.5 Hz, 1H, NH), 6.17 (br s, 2H , 2 x NH), 6.64 (d, *J* = 8.0 Hz, 1H, NH), 7.13-7.16 (m, 2H, ArH), 7.22-7.26 (m, 2H, ArH), 7.30-7.37 (m, 3H, ArH), 7.46 (d, *J* = 9.0 Hz, 1H, ArH), 7.85-7.89 (m, 2H, ArH), 7.97 (d, *J* = 8.5 Hz, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 10.5 (oxazole-$\underline{C}H_3$), 12.7, 18.2, 19.5 ($CH_3$ (Pbf)), 21.8, 22.3, 22.5, 23.4 ($CH_3$), 22.9, 24.5, 29.5, 29.9, 30.9, 38.2, 38.4 ($CH_2$), 24.8, 24.9, 49.3, 53.3, 53.6 (CH), 28.7 (C($\underline{C}H_3)_3$), 28.8 (2 x $CH_3$ (Pbf)), 30.2 ($NCH_3$), 40.3 ($CH_2$N (Lys)), 40.8 ($CH_2$N (Arg)), 43.5 ($CH_2$ (Pbf)), 58.5 ($OCH_3$), 66.0 (oxazole-$\underline{C}H_2$), 68.1 (O$\underline{C}H_2CO$), 68.6 ($CH_2O$), 79.3 ($\underline{C}(CH_3)_3$), 86.5 (C (Pbf)), 114.3, 116.1, 124.1, 124.4, 125.3, 125.7, 126.8, 127.0, 128.2, 128.3, 129.9, 130.1 (ArCH), 117.5, 119.7, 120.5, 124.7, 129.4, 130.1, 131.9, 132.5, 133.7, 133.9, 134.1, 138.5, 147.3, 152.3, 154.7, 156.4, 160.3 (ArC), 156.2 (C=O (Boc)), 158.8 (C=N), 169.3, 171.5 (C=O). MS (ESI, +ve) *m/z* 1260 (100%) $[M+H]^+$; 1282 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{69}H_{95}N_8O_{12}S$ 1259.6790, found 1259.6841.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(methoxymethyl)-5-iodooxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (111)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (32.6 mg, 0.03 mmol) and Type **C** amine **79** (13.3 mg, 0.04 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) gave **111** (15.7 mg, 37%) as a white solid. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.38. $[\alpha]_D^{25}$ = −44.2 (*c* 0.52, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CDCl_3$) δ 0.52 (3H, d, *J* = 6.5 Hz), 0.57 (3H, d, *J* = 6.5 Hz), 0.77 - 0.86 (2H, m), 0.92 - 0.97 (6H, m), 1.12 - 1.17 (2H, m), 1.22 - 1.31 (5H, m), 1.43 - 1.44 (16H, m), 1.55 - 1.63 (2H, m), 1.68 - 1.93 (7H, m), 2.09 (3H, s), 2.53 (3H, s), 2.59 (3H, s), 2.86 (4H, bs), 2.94 (3H, bs), 3.06 - 3.19 (1H, bm), 3.24 - 3.30 (1H, m), 3.40 (3H, s), 3.79 - 3.85 (1H, m), 3.88 - 3.95 (2H, m), 4.03 - 4.09 (1H, m), 4.27 (2H, s), 4.43 - 4.58 (4H, m), 4.82 - 4.84 (1H, m), 5.30 (1H, s), 5.88 - 5.92 (2H, m), 6.09 - 6.16 (3H, m), 6.88 (1H, d, *J* = 7.6 Hz), 7.14 - 7.16 (2H, d, *J* = 7.7 Hz), 7.24 - 7.26 (3H, m), 7.30 - 7.38 (3H, m), 7.47 (1H, d, *J* = 8.8 Hz), 7.88 (2H, t, *J* = 7.9 Hz) , 7.98 (2H, d, *J* = 9.0 Hz), 8.09 (1H, s). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 12.6, 18.1, 19.4, 21.6, 22.2, 22.4, 23.3, 24.7, 24.8, 28.6, 28.7, 29.4, 30.4, 38.1, 43.4, 49.6, 56.8, 58.7, 65.8, 68.0, 68.5, 86.4, 114.2, 116.1, 117.5, 119.7, 120.4, 124.0, 124.4, 125.2, 125.6, 126.8, 127.0, 128.1, 128.4, 129.3, 129.9, 130.0, 132.5, 133.8, 142.9, 152.2, 154.6, 156.2, 167.1, 171.6. IR (neat) *v* [$cm^{-1}$] = 3752 (s), 3342 (s), 2967 (m), 2334 (m), 1635 (s), 1558 (s), 1242 (m), 1090 (m), 809 (m), 667 (s). MS ($ESI^+$) *m/z* = 1371 (45 %, $[M+H]^+$), 1391 (100 %, $[M+Na]^+$).

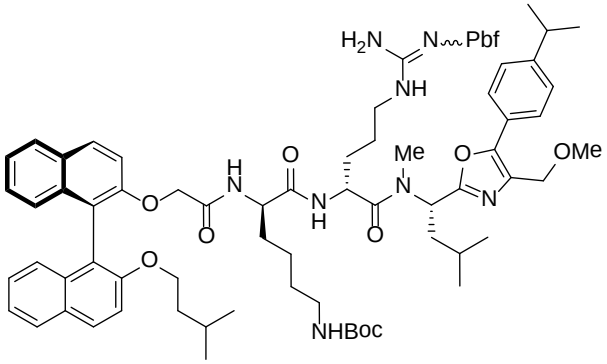
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(methoxymethyl)-5-phenyloxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (112)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (33 mg, 0.031 mmol) and Type **C** amine **80** (9 mg, 0.031 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **112** (33 mg, 81%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.45 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.55 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.72-0.84 (m, 2H, $CH_2$), 0.86-0.98 (m, 1H, $CH_2$ ($H_a^*$)), 0.95 (d, *J* = 6.0 Hz, 3H, $CH_3$ (Leu)), 0.99 (d, *J* = 6.0 Hz, 3H, $CH_3$ (Leu)), 1.12-1.17 (m, 1H,

CH), 1.19-1.26 (m, 4H, 2 x $CH_2$), 1.25-1.36 (m, 1H, $CH_2$ ($H_b^*$)), 1.38-1.50 (m, 1H, CH), 1.42 (s, 9H, $^t$Bu), 1.44 (s, 6H, 2 x $CH_3$ (Pbf)), 1.45-1.56 (m, 2H, $CH_2$), 1.55-1.65 (m, 1H, $CH_2$ ($H_a^\#$)), 1.70-1.80 (m, 1H, $CH_2$ ($H_b^\#$)), 1.86-2.00 (m, 2H, $CH_2$), 2.08 (s, 3H, $CH_3$ (Pbf)), 2.52 (s, 3H, $CH_3$ (Pbf)), 2.56 (s, 3H, $CH_3$ (Pbf)), 2.87-2.89 (m, 2H, $CH_2N$ (Lys)), 2.93 (s, 5H, $CH_2$ (Pbf) and $NCH_3$), 3.07-3.20 (m, 1H, $CH_2N$ (Arg, $H_a$)), 3.23-3.32 (m, 1H, $CH_2N$ (Arg, $H_b$)), 3.46 (s, 3H, $OCH_3$), 3.88-3.93 (m, 1H, CH and $CH_2O$ ($H_a$)), 4.03-4.07 (m, 1H $CH_2O$ ($H_b$)), 4.47 (ABq, $J$ = 14.5 Hz, 2H, $OCH_2CO$), 4.49 (s, 2H, oxazole-C$\underline{H}_2$), 4.55-4.64 (m, 1H, N$\underline{H}$Boc), 4.80-4.88 (m, 0.7H, CH), 5.02-5.12 (m, 0.3H, CH), 5.96-5.99 (m, 1H, CH), 6.10 (d, $J$ = 5.5 Hz, 1H, NH), 6.18 (br s, 2H , 2 x NH), 6.95 (d, $J$ = 7.5 Hz, 1H, NH), 7.12-7.1 (m, 2H, ArH), 7.23-7.26 (m, 2H, ArH), 7.28-7.38 (m, 5H, ArH), 7.42-7.44 (m, 3H, ArH), 7.62 (d, $J$ = 7.5 Hz, 1H, ArH), 7.84 (d, $J$ = 8.0 Hz, 1H, ArH), 7.87 (d, $J$ = 8.5 Hz, 1H, ArH), 7.94-7.97 (m, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 12.5, 17.9, 19.3 ($CH_3$ (Pbf)), 21.6, 22.1, 22.3, 23.2 ($CH_3$), 22.6, 24.2, 29.2, 29.7, 30.2, 38.0, 38.4 ($CH_2$), 24.5, 24.8, 49.3, 53.3 (CH), 28.4 (C(C$\underline{H}_3$)$_3$), 28.6 (2 x $CH_3$ (Pbf)), 30.7 ($NCH_3$), 40.1 ($CH_2N$ (Lys)), 40.6 ($CH_2N$ (Arg)), 43.3 ($CH_2$ (Pbf)), 58.3 ($OCH_3$), 66.5 (oxazole-$\underline{C}H_2$), 67.9 (O$\underline{C}H_2CO$), 68.3 ($CH_2O$), 79.6 ($\underline{C}(CH_3)_3$), 86.2 (C (Pbf)), 114.1, 115.9, 123.9, 124.2, 125.0, 125.5, 126.2, 126.3, 126.6, 126.8, 128.0, 128.8, 128.9, 129.7, 129.9 (ArCH), 117.3, 119.5, 120.3, 124.5, 127.8, 129.2, 132.27, 132.34, 133.4 133.7, 133.9, 138.3, 149.4, 152.1, 154.4, 156.2, 160.3 (ArC), 156.0 (C=O (Boc)), 158.6 (C=N), 169.1, 171.5 (C=O). MS (ESI, +ve) *m/z* 1322 (5%) $[M+H]^+$; 1344 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{74}H_{97}N_8O_{12}S$ 1321.6947, found 1321.6904 $[M+H]^+$; calcd for $C_{74}H_{96}N_8O_{12}SNa$ 1343.6766, found 1343.6729 $[M+Na]^+$.

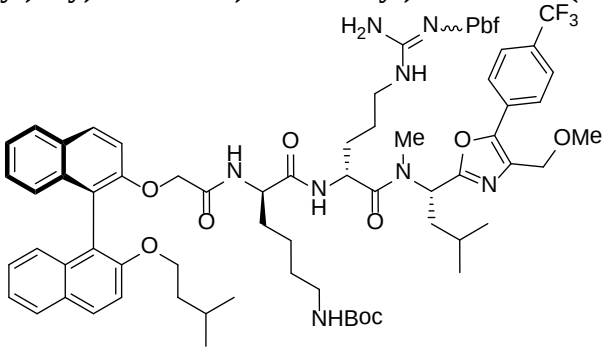
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(5-(4-isopropylphenyl)-4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (113)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (43 mg, 0.040 mmol) and Type **C** amine·TFA salt **81** (18 mg, 0.040 mmol), with added NEt(i-Pr)$_2$ (6.2 mg, 0.048 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **113** (36 mg, 65%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.50 (d, $J$ = 6.0 Hz, 3H, $CH_3$), 0.55 (d, $J$ = 6.5 Hz, 3H, $CH_3$), 0.52-0.84 (m, 2H, $CH_2$), 0.82-0.94 (m, 1H, $CH_2$ ($H_a^*$)), 0.94 (d, $J$ = 6.5 Hz, 3H, $CH_3$ (Leu)), 0.98 (d, $J$ = 6.0 Hz, 3H, $CH_3$ (Leu)), 1.11-1.18 (m, 1H, CH), 1.19-1.29 (m, 10H, 2 x $CH_2$, $C_6H_4CH(C\underline{H}_3)_2$), 1.32-1.41 (m, 1H, $CH_2$ ($H_b^*$)), 1.42-1.44 (m, 16H, CH, 2 x $CH_3$ (Pbf) and $^t$Bu), 1.44-1.56 (m, 2H, $CH_2$), 1.56-1.61 (m, 1H, $CH_2$ ($H_a^\#$)), 1.71-1.80 (m, 1H, $CH_2$ ($H_b^\#$)), 1.85-1.99 (m, 2H, $CH_2$), 2.08 (s, 3H, $CH_3$ (Pbf)), 2.53 (s, 3H, $CH_3$ (Pbf)), 2.59 (s, 3H, $CH_3$ (Pbf)), 2.87-2.98 (m, 3H, $CH_2$ (Lys) and $C_6H_4C\underline{H}(CH_3)_2$), 2.92 (s, 3H, $NCH_3$), 2.93 (s, 2H, $CH_2$ (Pbf)), 3.07-3.20 (m, 1H, $CH_2N$ (Arg, $H_a$)), 3.22-3.33 (m, 1H, $CH_2N$ (Arg, $H_b$)), 3.45 (s, 3H, $OCH_3$), 3.88-3.96 (m, 2H, CH and $CH_2O$ ($H_a$)), 4.05-4.07 (m, 1H $CH_2O$ ($H_b$)), 4.47 (ABq, $J$ = 14.0 Hz, 2H, $OCH_2CO$), 4.48 (s, 2H, oxazole-C$\underline{H}_2$), 4.55-4.65 (m, 1H, N$\underline{H}$Boc), 4.79-4.88 (m, 0.7H, CH), 5.05-5.10 (m, 0.3H, CH), 5.95-5.98 (m, 1H, CH), 6.10 (d, $J$ = 5.5 Hz, 1H, NH), 6.18-6.22 (m, 2H , 2 x NH), 6.98 (d, $J$ = 7.0 Hz, 1H,

NH), 7.13-7.16 (m, 2H, ArH), 7.23-7.26 (m, 2H, ArH), 7.29-7.37 (m, 5H, ArH), 7.45 (d, *J* = 9.5 Hz, 1H, ArH), 7.49 (d, *J* = 8.0 Hz, 1H, ArH), 7.55 (d, *J* = 8.0 Hz, 1H, ArH), 7.94-7.97 (m, 2H, ArH), 7.84-7.87 (m, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 12.5, 18.0, 19.3 ($CH_3$ (Pbf)), 21.7, 22.1, 22.3, 23.2 ($CH_3$), 22.6, 24.2, 29.2, 29.7, 30.7, 38.0, 38.4 ($CH_2$), 24.6, 24.8, 49.3, 53.3 (CH), 23.9 ($C_6H_4CH(\underline{C}H_3)_2$), 28.5 ($C(\underline{C}H_3)_3$), 28.6 (2 x $CH_3$ (Pbf)), 30.2 ($NCH_3$), 34.0 ($C_6H_4\underline{C}H(CH_3)_2$), 40.1 ($CH_2N$ (Lys)), 40.6 ($CH_2N$ (Arg)), 43.3 ($CH_2$ (Pbf)), 58.3 ($OCH_3$), 66.5 (oxazole-$\underline{C}H_2$), 67.9 ($O\underline{C}H_2CO$), 68.3 ($CH_2O$), 79.1 ($\underline{C}(CH_3)_3$), 86.2 (C (Pbf)), 114.1, 115.9, 123.9, 124.2, 125.0, 125.3, 126.4, 126.5, 126.6, 126.8, 127.0, 127.2, 128.0, 128.1, 129.7, 129.9 (ArCH), 117.3, 119.5, 120.3, 124.4, 125.5, 129.2, 129.8, 131.8, 132.3, 133.5, 133.7, 133.9, 138.3, 149.6, 149.9, 152.1, 154.4, 156.2, 160.0 (ArC), 156.0 (C=O (Boc)), 158.5 (C=N), 169.1, 170.8, 171.4 (C=O). MS (ESI, +ve) *m/z* 1364 (50%) $[M+H]^+$; 1386 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{77}H_{103}N_8O_{12}S$ 1363.7416, found 1363.7416; calcd for $C_{77}H_{102}N_8O_{12}SNa$ 1385.7236, found 1385.7175.

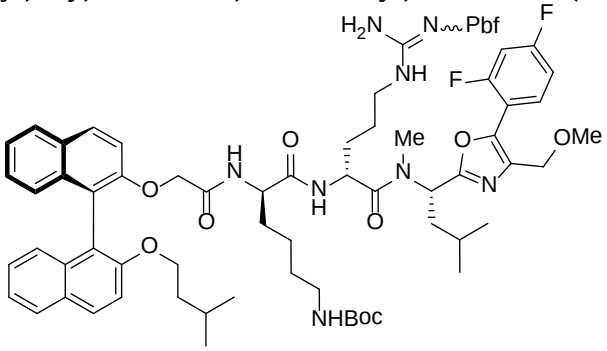
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(5-(4-trifluoromethylphenyl)-4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (114)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (47 mg, 0.045 mmol) and Type **C** amine·TFA salt **82** (21 mg, 0.045 mmol), with added $NEt(i\text{-}Pr)_2$ (7.0 mg, 0.054 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% $MeOH/CH_2Cl_2$) gave **114** (54 mg, 86%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.50 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.55 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.73-0.85 (m, 2H, $CH_2$), 0.86-0.96 (m, 1H, $CH_2$ ($H_a^*$)), 0.95 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.00 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.12-1.16 (m, 1H, CH), 1.18-1.31 (m, 4H, 2 x $CH_2$), 1.28-1.40 (m, 1H, $CH_2$ ($H_b^*$)), 1.38-1.50 (m, 1H, CH), 1.42 (s, 9H, $^t$Bu), 1.44 (s, 6H, 2 x $CH_3$ (Pbf)) 1.47-1.56 (m, 2H, $CH_2$), 1.54-1.65 (m, 1H, $CH_2$ ($H_a^\#$)), 1.71-1.81 (m, 1H, $CH_2$ ($H_b^\#$)), 1.87-1.97 (m, 2H, $CH_2$), 2.09 (s, 3H, $CH_3$ (Pbf)), 2.53 (s, 3H, $CH_3$ (Pbf)), 2.60 (s, 3H, $CH_3$ (Pbf)), 2.83-3.02 (m, 7H, $CH_2$ (Pbf), $CH_2N$ (Lys) and $NCH_3$), 3.08-3.21 (m, 1H, $CH_2N$ (Arg, $H_a$)), 3.22-3.39 (m, 1H, $CH_2N$ (Arg, $H_b$)), 3.47 (s, 3H, $OCH_3$), 3.80-3.90 (m, 1H, CH), 3.89-3.93 (m, 1H $CH_2O$ ($H_a$)), 4.00-4.08 (m, 1H $CH_2O$ ($H_b$)), 4.43-4.57 (m, 4H, CH, $OCH_2CO$ and N$\underline{H}$Boc), 4.51 (s, 2H, oxazole-$C\underline{H}_2$), 4.81-4.90 (m, 0.7H, CH), 5.06-5.12 (m, 0.3H, CH), 5.98 (dd, $J_1$ = 6.0, $J_2$ = 10.0 Hz, 1H, CH), 6.08 (d, *J* = 6.5 Hz, 1H, NH), 6.15 (br s, 2H , 2 x NH), 6.91 (d, *J* = 6.5 Hz, 1H, NH), 7.14-7.15 (m, 2H, ArH), 7.22-7.26 (m, 2H, ArH), 7.29-7.38 (m, 3H, ArH), 7.45 (d, *J* = 9.0 Hz, 2H, ArH), 7.69-7.72 (m, 2H, ArH), 7.76-7.78 (m, 2H, ArH), 7.84-7.89 (m, 2H, ArH), 7.95-7.98 (m, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 12.5, 18.0, 19.3 ($CH_3$ (Pbf)), 21.6, 22.1, 22.3, 23.2 ($CH_3$), 22.6, 24.2, 29.2, 29.7, 30.6, 38.0, 38.4 ($CH_2$), 24.6, 24.8, 49.2, 53.4 (CH), 28.4 ($C(\underline{C}H_3)_3$), 28.6 (2 x $CH_3$ (Pbf)), 30.2 ($NCH_3$), 40.1 ($CH_2N$ (Lys)), 40.6 ($CH_2N$ (Arg)), 43.3 ($CH_2$ (Pbf)), 58.4 ($OCH_3$), 66.5 (oxazole-$\underline{C}H_2$), 67.9 ($O\underline{C}H_2CO$), 68.4 ($CH_2O$), 79.2 ($\underline{C}(CH_3)_3$), 86.3 (C (Pbf)), 114.1, 115.9, 124.0, 124.3, 125.1, 125.5, 125.9, 126.2, 126.4, 126.7, 126.8, 128.0, 129.7, 129.9 (ArCH), 117.3, 119.6, 120.3, 124.5, 129.2, 129.9, 131.1, 132.3, 133.4, 133.7, 133.9, 134.1, 138.4, 148.0, 152.1, 154.4, 156.2, 161.0

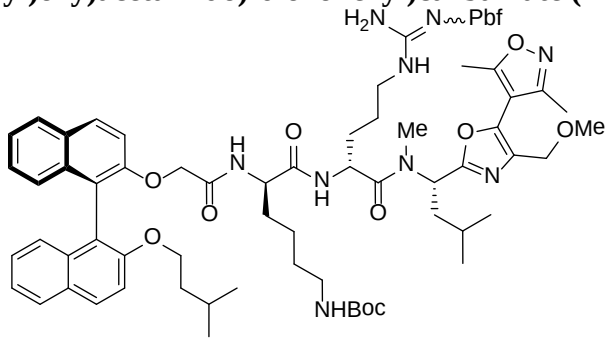
(ArC), 123.9 (q, $J$ = 273 Hz, $CF_3$), 130.4 (q, $J$ = 33 Hz, $\underline{C}CF_3$), 156.0 (C=O (Boc)), 158.6 (C=N), 169.1, 170.9, 171.6 (C=O). MS (ESI, +ve) *m/z* 1390 (5%) $[M+H]^+$; 1412 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{75}H_{95}N_8O_{12}F_3NaS$ 1411.6640, found 1411.6703 $[M+Na]^+$.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(5-(2,4-difluorophenyl)-4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (115)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (49 mg, 0.047 mmol) and Type **C** amine·TFA salt **83** (22 mg, 0.047 mmol), with added $NEt(i\text{-}Pr)_2$ (7.2 mg, 0.056 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% $MeOH/CH_2Cl_2$) gave **115** (55 mg, 86%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.50 (d, $J$ = 6.0 Hz, 3H, $CH_3$), 0.55 (d, $J$ = 6.0 Hz, 3H, $CH_3$), 0.70-0.90 (m, 2H, $CH_2$), 0.91-0.98 (m, 1H, $CH_2$ ($H_a^*$)), 0.94 (d, $J$ = 6.0 Hz, 3H, $CH_3$ (Leu)), 0.98 (d, $J$ = 6.0 Hz, 3H, $CH_3$ (Leu)), 1.11-1.17 (m, 1H, CH), 1.18-1.28 (m, 4H, 2 x $CH_2$), 1.29-1.36 (m, 1H, $CH_2$ ($H_b^*$)), 1.38-1.48 (m, 1H, CH), 1.42 (s, 9H, $^t$Bu), 1.44 (s, 6H, 2 x $CH_3$ (Pbf)), 1.45-1.55 (m, 2H, $CH_2$), 1.52-1.63 (m, 1H, $CH_2$ ($H_a^\#$)), 1.74-1.76 (m, 1H, $CH_2$ ($H_b^\#$)), 1.88-1.95 (m, 2H, $CH_2$), 2.08 (s, 3H, $CH_3$ (Pbf)), 2.53 (s, 3H, $CH_3$ (Pbf)), 2.59 (s, 3H, $CH_3$ (Pbf)), 2.87-2.99 (m, 2H, $CH_2N$ (Lys)), 2.926 (s, 3H, $NCH_3$), 2.93 (s, 2H, $CH_2$ (Pbf)), 3.07-3.19 (m, 1H, $CH_2N$ (Arg, $H_a$)), 3.20-3.33 (m, 1H, $CH_2N$ (Arg, $H_b$)), 3.40 (s, 3H, $OCH_3$), 3.89-3.93 (m, 2H, CH and $CH_2O$ ($H_a$)), 4.34-4.08 (m, 1H, $CH_2O$ ($H_b$)), 4.38 (s, 2H, oxazole-C$\underline{H}_2$), 4.47 (ABq, $J$ = 14.5 Hz, 2H, $OCH_2CO$), 4.57-4.66 (m, 1H, N$\underline{H}$Boc), 4.81-4.85 (m, 0.7H, CH), 5.01-5.12 (m, 0.3H, CH), 5.96 (dd, $J_1$ = 6.0, $J_2$ = 9.5 Hz, 1H, CH), 6.10 (d, $J$ = 6.5 Hz, 1H, NH), 6.14-6.23 (m, 3H , 3 x NH), 6.89-7.00 (m, 2H, ArH), 7.13-7.16 (m, 2H, ArH), 1.22-7.27 (m, 2H, ArH), 7.29-7.37 (m, 2H, ArH), 7.46 (d, $J$ = 8.5 Hz, 1H, ArH), 7.49-7.54 (m, 2H, ArH), 7.84-7.88 (m, 2H, ArH), 7.95-7.98 (m, 2H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.5, 17.9, 19.3 ($CH_3$ (Pbf)), 21.6, 22.1, 22.3, 23.2 ($CH_3$), 22.6, 24.3 29.2, 29.7, 30.7, 37.9, 38.3 ($CH_2$), 24.5, 24.8, 49.2, 49.4, 53.2 (CH), 28.4 (C($\underline{C}H_3)_3$), 28.6 (2 x $CH_3$ (Pbf)), 40.1 ($CH_2N$ (Lys)), 40.6 ($CH_2N$ (Arg)), 43.3 ($CH_2$ (Pbf)), 58.5 ($OCH_3$), 66.1 (oxazole-$\underline{C}H_2$), 67.9 (O$\underline{C}H_2CO$), 68.3 ($CH_2O$), 79.1 ($\underline{C}(CH_3)_3$), 86.2 (C (Pbf)), 104.8 (t, $J$ = 26 Hz, ArCH), 112.0 (dd, $J_1$ = 4, $J_2$ = 22 Hz, ArCH), 112.4 (d, $J$ = 4 Hz, ArC), 114.1, 115.9, 123.9, 124.2, 125.0, 125.5, 126.6, 126.8, 128.0, 128.1, 129.7, 129.9, (ArCH), 131.4 (dd, $J_1$ = 4, $J_2$ = 14 Hz, ArCH), 117.3, 119.5, 120.3, 124.5, 129.2, 129.8, 132.3, 133.4, 133.7, 134.6, 138.3, 143.2, 152.1, 154.4, 156.2, 161.8 (ArC), 156.0 (C=O (Boc)), 158.5 (C=N), 159.5 (dd, $J_1$ = 12, $J_2$ = 254 Hz, ArC), 163.5 (dd, $J_1$ = 12 $J_2$ = 253 Hz, ArC), 169.1, 170.8, 171.5 (C=O). MS (ESI, +ve) *m/z* 1358 (5%) $[M+H]^+$; 1380 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{74}H_{95}N_8O_{12}F_2S$ 1357.6758, found 1357.6742 $[M+H]^+$; $C_{74}H_{94}N_8O_{12}F_2SNa$ 1379.6578, found 1379.6573 $[M+Na]^+$.

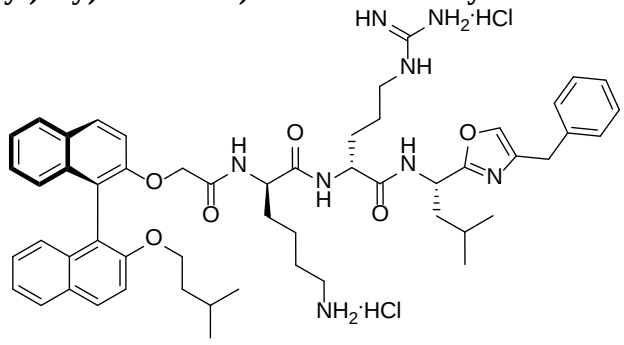
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(methoxymethyl)-5-(3,5-dimethylisoxazol-4-yl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (116)**




This compound was prepared according to *General Procedure 1* using carboxylic acid **A** (38 mg, 0.036 mmol) and Type **C** amine·TFA salt **84** (15 mg, 0.036 mmol), with added NEt(i-Pr)$_2$ (5.6 mg, 0.043 mmol). Flash chromatography (100% $CH_2Cl_2$ to 4% MeOH/$CH_2Cl_2$) gave **116** (36 mg, 75%) as an off white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.50 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.55 (d, *J* = 7.0 Hz, 3H, $CH_3$), 0.75-0.81 (m, 2H, $CH_2$), 0.92-0.99 (m, 1H, $CH_2$ ($H_a^*$)), 0.93 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 0.98 (d, *J* = 7.0 Hz, 3H, $CH_3$ (Leu)), 1.11-1.16 (m, 1H, CH), 1.18-1.26 (m, 4H, 2 x $CH_2$), 1.24-1.36 (m, 1H, $CH_2$ ($H_b^*$)), 1.36-1.48 (m, 16H, CH, 2 x $CH_3$ (Pbf) and $^t$Bu), 1.47-1.56 (m, 2H, $CH_2$), 1.56-1.60 (m, 1H, $CH_2$ ($H_a^\#$)), 1.69-1.78 (m, 1H, $CH_2$ ($H_b^\#$)), 1.87-1.95 (m, 2H, $CH_2$), 2.08 (s, 3H, $CH_3$ (Pbf)), 2.22 (s, 3H, isoxazole-C$\underline{H}_3$), 2.41 (s, 3H, isoxazole-C$\underline{H}_3$), 2.52 (s, 3H, $CH_3$ (Pbf)), 2.58 (s, 3H, $CH_3$ (Pbf)), 2.86-2.93 (m, 7H, $CH_2$ (Pbf), $CH_2$N (Lys) and $NCH_3$), 3.08-3.19 (m, 1H, $CH_2$N (Arg, $H_a$)), 3.22-3.32 (m, 1H, $CH_2$N (Arg, $H_b$)), 3.40 (s, 3H, $OCH_3$), 3.79-3.87 (m, 1H, CH), 3.89-3.94 (m, 1H $CH_2$O ($H_a$)), 4.04-4.08 (m, 1H $CH_2$O ($H_b$)), 4.23 (s, 2H, oxazole-C$\underline{H}_2$), 4.46 (ABq, *J* = 15.0 Hz, 2H, $OCH_2CO$), 4.60-4.62 (m, 1H, N$\underline{H}$Boc), 4.82-4.85 (m, 0.7H, CH), 5.01-5.08 (m, 0.3H, CH), 5.93 (dd, $J_1$ = 5.5, $J_2$ = 9.5 Hz, 1H, CH), 6.07 (d, *J* = 6.0 Hz, 1H, NH), 6.15 (br s, 2H , 2 x NH), 6.88 (d, *J* = 7.5 Hz, 1H, NH), 7.13-7.16 (m, 2H, ArH), 7.22-7.24 (m, 2H, ArH), 7.29-7.37 (m, 2H, ArH), 7.47 (d, *J* = 9.0 Hz, 2H, ArH), 7.86-7.88 (m, 2H, ArH), 7.96-7.99 (m, 2H, ArH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 10.6, 11.7, 12.5 ($CH_3$ (isoxazole)), 12.5, 17.9, 19.3 ($CH_3$ (Pbf)), 21.5, 22.1, 22.3, 23.2 ($CH_3$), 22.6, 24.2, 29.2, 30.1, 30.6, 38.0, 38.1 ($CH_2$), 24.6, 24.8, 49.4, 53.4 (CH), 28.5 (C($\underline{C}H_3)_3$), 28.6 (2 x $CH_3$ (Pbf)), 40.1 ($CH_2$N (Lys)), 40.6 ($CH_2$N (Arg)), 43.3 ($CH_2$ (Pbf)), 58.9 ($OCH_3$), 65.8 (oxazole-$\underline{C}H_2$), 67.8 (O$\underline{C}H_2CO$), 68.4 ($CH_2O$), 79.1 ($\underline{C}(CH_3)_3$), 86.3 (C (Pbf)), 114.1, 115.9, 124.0, 124.3, 125.0, 125.5, 126.7, 126.8, 128.0, 128.1, 129.7, 129.9 (ArCH), 104.8, 117.3, 119.5, 120.3, 124.5, 129.2, 129.9, 132.3, 133.4, 133.7, 133.9, 135.1, 138.3, 139.6, 152.1, 154.4, 156.2, 159.1, 162.5 (ArC), 156.0 (C=O (Boc)), 158.6 (C=N), 168.7, 169.1, 171.7 (C=O). MS (ESI, +ve) *m/z* 1340 (5%) $[M+H]^+$; 1362 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{73}H_{98}N_9O_{13}S$ 1340.7005, found 1340.7030 $[M+H]^+$; calcd for $C_{73}H_{97}N_9O_{13}SNa$ 1362.6824, found 1362.6810 $[M+Na]^+$.

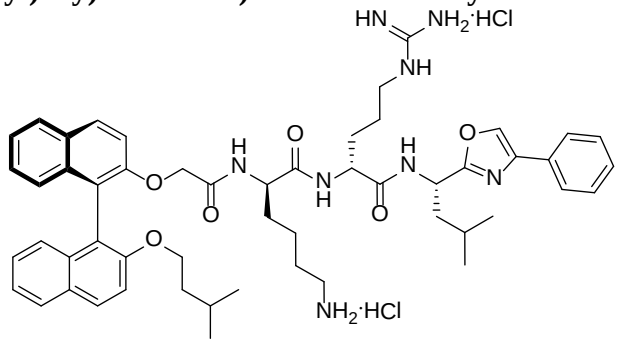
***Synthesis of Type E Final Compounds***

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-benzyloxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (117)**



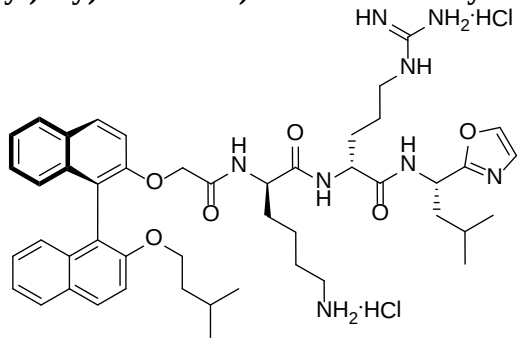
This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **85** (80 mg, 0.06 mmol) to give **117** (30 mg, 50%) as a white solid. $^1$H NMR (500 MHz, $CD_3OD$) δ 8.03 – 7.97 (m, 2H), 7.90 (d, *J* = 7.8 Hz, 2H), 7.53 – 7.46 (m, 2H), 7.40 – 7.16 (m, 10H), 7.11 – 7.03 (m, 2H), 5.14 – 5.06 (m, 1H), 4.51 (ABq, $\Delta\delta_{AB}$ = 0.05, *J* = 15.2 Hz, 2H), 4.31 – 4.23 (m, 1H), 4.17 – 4.05 (m, 2H), 4.01 – 3.90 (m, 1H), 3.80 (s, 2H), 3.23 – 3.06 (m, 2H), 2.90 – 2.76 (m, 2H), 1.89 – 1.44 (m, 11H), 1.32 – 1.10 (m, 3H), 1.07 – 0.87 (m, 8H), 0.56 (d, *J* = 6.7 Hz, 3H), 0.52 (d, *J* = 6.4 Hz, 3H); MS (ESI +ve) *m/z* 925 ($[M+H]^+$, <5%), 463 ($[M+2H]^{2+}$, 100%).

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-phenyloxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (118)**



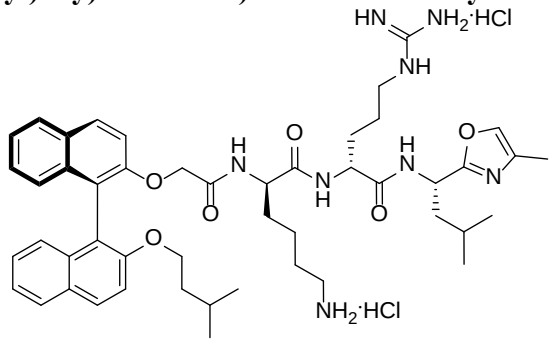
This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **86** (60 mg, 0.047 mmol) to give **118** (30 mg, 65%) as a white solid. $^1$H NMR (500 MHz, $CD_3OD$) δ 8.12 (s, 1H), 8.02 – 7.94 (m, 2H), 7.93 – 7.84 (m, 2H), 7.73 (d, *J* = 7.8 Hz, 2H), 7.50 (d, *J* = 9.0 Hz, 1H), 7.45 (d, *J* = 9.3 Hz, 1H), 7.42 – 7.27 (m, 5H), 7.23 (s, 2H), 7.11 – 7.01 (m, 2H), 5.24 – 5.17 (m, 1H), 4.52 (ABq, $\Delta\delta_{AB}$ = 0.07, *J* = 14.5 Hz, 2H), 4.35 – 4.27 (m, 1H), 4.16 – 4.04 (m, 2H), 3.97 – 3.88 (m, 1H), 3.27 – 3.08 (m, 2H), 2.88 – 2.72 (m, 2H), 1.93 – 1.41 (m, 11H), 1.33 – 1.09 (m, 5H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.96 (d, *J* = 6.2 Hz, 3H), 0.56 (d, *J* = 6.3 Hz, 3H), 0.51 (d, *J* = 6.2 Hz, 3H); MS (ESI +ve) *m/z* 911 ($[M+H]^+$, <5%), 456 ($[M+2H]^{2+}$, 100%). HRMS (ESI +ve) calcd for $C_{53}H_{67}N_8O_6$ 911.5184 $[M+H]^+$, found 911.5207.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (119)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **87** (31.1 mg, 0.026 mmol, a *ca.* 90:10 mixture of diastereomers, epimeric at leucine) to give **119** (15.2 mg, 64%, a *ca.* 90:10 mixture of diastereomers, epimeric at leucine) as a white solid. $[\alpha]_D^{25}$ −33.1 (*c* 0.48, MeOH); $^1$H NMR (500 MHz, $CD_3OD$, major diastereomer only) δ 8.07 – 8.00 (m, 2H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.90 (s, 1H), 7.56 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.17 (s, 1H), 7.10 – 7.04 (m, 2H), 5.21 – 5.15 (m, 1H), 4.51 (ABq, $\Delta\delta_{AB}$ = 0.09, *J* = 14.8 Hz, 2H), 4.37 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.19 – 4.07 (m, 2H), 4.01 – 3.93 (m, 1H), 3.23 – 3.13 (m, 2H), 2.83 – 2.73 (m, 2H), 1.91 – 1.37 (m, 11H), 1.33 – 1.07 (m, 5H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.58 (d, *J* = 6.4 Hz, 3H), 0.53 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (125 MHz, $CD_3OD$, major diastereomer only) δ 173.5, 173.1, 171.0, 165.9, 158.6, 156.0, 154.1, 141.1, 135.3, 135.1, 131.4, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 127.3, 126.4, 126.0, 125.2, 124.8, 121.9, 120.6, 117.0, 116.0, 69.3, 69.1, 54.0, 53.7, 47.2, 42.8, 41.9, 40.4, 39.3, 32.1, 30.3, 27.8, 26.3, 25.9, 25.6, 23.13, 23.07, 22.8, 22.5, 22.0; MS ($ES^+$) *m/z* 418 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{47}H_{63}N_8O_6$: 835.4871 (M+H), Found: 835.4872.

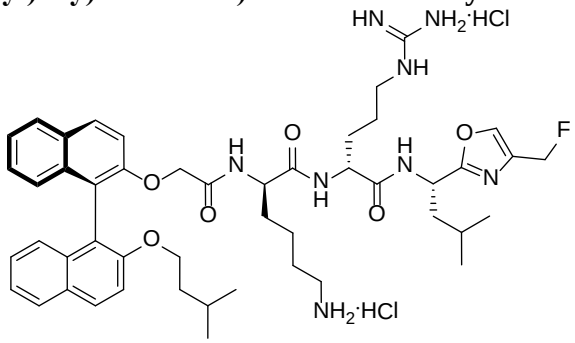
**(*R*)-6-Amino-*N*-((*R*)-1-(((*S*)-1-(4-(methyl)oxazol-2-yl)-3-methylbutyl)amino)-5-guanidino-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (120)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **88** (yield was not determined in the previous step) to give **120** (25.8 mg, 35% over three steps from Type **B** oxazole **18**) as a tan solid. $[\alpha]_D^{25}$ = −4.7 (*c* 0.86, MeOH). $^1$H NMR (500 MHz, $CD_3OD$) δ 0.51 (3H, d, *J* = 6.3 Hz), 0.56 (3H, d, *J* = 6.3 Hz), 0.94 (3H, d, *J* = 6.2 Hz), 0.99 (3H, d, *J* = 6.0 Hz), 1.09 - 1.24 (6H, m), 1.44 - 1.73 (10H, m), 1.80 - 1.96 (3H, m), 2.19 (3H, s), 2.77 (3H, bs), 3.16 (2H, bs), 3.27 (3H, s), 3.31 (3H, s), 3.91 - 3.94 (2H, bm), 4.09 (3H, bm), 4.30 - 4.32 (2H, m), 4.44 - 4.54 (2H, m),

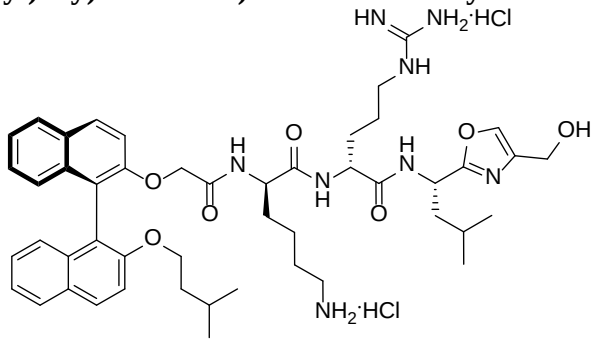
5.16 - 5.18 (1H, m), 7.00 - 7.04 (2H, m), 7.16 - 7.19 (3H, m), 7.31 (3H, t, *J* = 7.2 Hz), 7.45 (1H, d, *J* = 8.9 Hz), 7.51 (1H, d, *J* = 8.9 Hz), 7.83 - 7.90 (4H, m), 7.99 (3H, t, *J* = 8.3 Hz). $^{13}$C NMR (126 MHz, $CD_3OD$) 9.62, 21.6, 22.5, 22.8, 23.2, 25.6, 25.7, 26.3, 27.8, 30.0, 32.1, 39.3, 40.4, 41.5, 41.9, 47.1, 47.2, 53.8, 54.2, 69.1, 69.4, 116.1, 117.0, 120.7, 121.9, 124.8, 125.2, 125.9, 126.3, 127.5, 127.6, 129.1, 129.3, 130.7, 130.8, 131.4, 134.2 ,135.1, 135.2, 138.5, 154.1, 155.9, 158.6, 167.0, 171.0, 173.5, 173.8. IR (neat) *v* [$cm^{-1}$] = 3852 (s), 3735 (s), 2968 (m), 2307 (w), 1684 (s), 1505 (s), 1250 (m), 1042 (m), 608 (s). MS ($ESI^+$) *m/*2 = 425 (100 %, $[M+2H]^{2+}$), *m/z* = 849 (2 %, $[M+H]^+$). HRMS ($ESI^+$) $[M+H]^+$ Calcd. for $C_{48}H_{65}N_8O_6$: 849.5027, Found: 849.5037.

**(*R*)-6-Amino-*N*-((*R*)-1-(((*S*)-1-(4-(fluoromethyl)oxazol-2-yl)-3-methylbutyl)amino)-5-guanidino-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (121)**



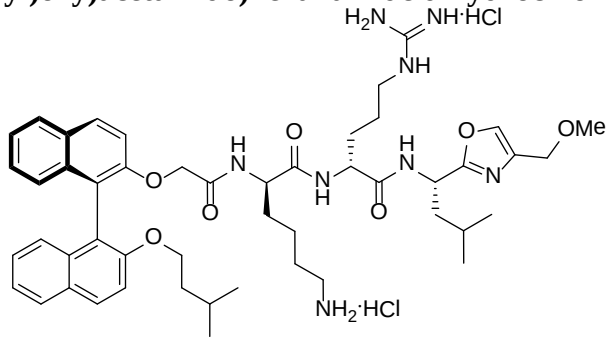

This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **89** (60.3 mg, 0.05 mmol) to give **121** (36.3 mg, 79%) as a tan solid. $[\alpha]_D^{25} = -4.7$ (*c* 0.083, MeOH). $^1$H NMR (500 MHz, $CD_3OD$) δ 0.53 (3H, d, *J* = 6.4 Hz), 0.59 (3H, d, *J* = 6.4 Hz), 0.94 - 1.00 (6H, m), 1.11 - 1.28 (4H, m), 1.43 - 1.86 (7H, m), 2.80 (2H, bs), 3.16 - 3.24 (2H, bm), 3.32 (1H, s), 3.36 (1H, s), 3.97 - 4.15 (3H, m), 4.43 - 4.59 (3H, m), 5.14 - 5.19 (1H, m), 5.27 (2H, d, $J_{H-F}$ = 47.5 Hz), 7.09 (2H, t), 7.24 (2H, t), 7.36 (2H, m), 7.48 - 7.56 (2H, d, *J* = 9.0 Hz), 7.60 (1H, bs), 7.93 (2H, t, *J* = 8.0 Hz), 8.01 - 8.03 (2H, m). $^{13}$C NMR (126 MHz, $CD_3OD$) δ 22.0, 22.5, 22.7, 23.0, 23.1, 25.6, 25.7, 25.9, 26.3, 27.7, 30.2, 32.1, 39.3, 40.4, 41.9, 42.5, 42.7, 47.1, 47.2, 53.7, 54.0, 69.1, 69.3, 71.9 ($J_{C-F}$ = 163.0 Hz), 116.0, 117.0, 120.6, 121.8, 124.8, 125.2, 125.9, 126.3, 126.5, 127.6, 129.1, 129.3, 130.7, 130.8, 131.4, 135.0, 135.2, 137.3, 137.4, 140.1, 154.0, 155.9, 158.5, 166.3, 171.0, 173.1, 173.4. IR (neat) *v* [$cm^{-1}$] = 3382 (s), 2955 (m), 2360 (m), 1653 (s), 1540 (s), 1230 (w), 1077 (m), 805 (w), 745 (w). MS ($ESI^+$) *m/*2< = 434 (100 %, $[M+2H]^{2+}$), *m/z* = 867 (2 %, $[M+H]^+$). HRMS ($ESI^+$) $[M+Na]^+$ Calcd. for $C_{48}H_{63}FN_8NaO_6$: 889.4752, Found: 889.4753.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(hydroxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (122)**



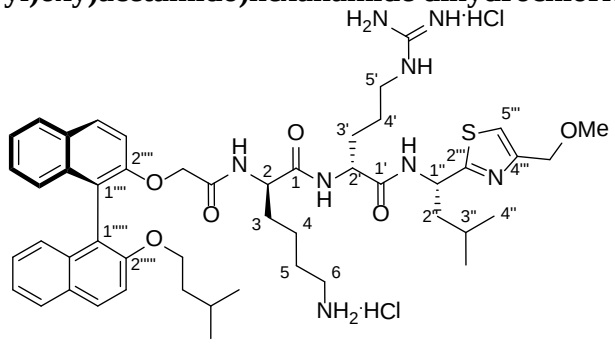
This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **90** (54.9 mg, 0.045 mmol), with added $H_2O$ (16.2 mg, 0.90 mmol) to prevent *O*-sulfonation (which occurred otherwise), giving **122** (39.3 mg, 93%) as a tan solid. $[\alpha]_D^{25}$ −21.3 (*c* 0.28, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.04 (d, *J* = 8.9 Hz, 2H), 7.92 (d, *J* = 7.9 Hz, 2H), 7.80 (s, 1H), 7.56 (d, *J* = 9.0 Hz, 1H), 7.49 (d, *J* = 8.9 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.11 – 7.03 (m, 2H), 5.17 – 5.11 (m, 1H), 4.61 – 4.43 (m, 4H), 4.38 (dd, *J* = 8.5, 5.0 Hz, 1H), 4.19 – 4.06 (m, 2H), 4.00 – 3.93 (m, 1H), 3.25 – 3.12 (m, 2H), 2.84 – 2.73 (m, 2H), 1.92 – 1.47 (m, 10H), 1.46 – 1.36 (m, 1H), 1.33 – 1.07 (m, 5H), 0.98 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 6.3 Hz, 3H), 0.58 (d, *J* = 6.4 Hz, 3H), 0.53 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (125 MHz, $CD_3OD$) δ 173.6, 173.2, 170.9, 166.5, 158.5, 155.9, 154.0, 140.5, 138.0, 137.9, 135.2, 135.0, 131.4, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 125.9, 125.2, 124.8, 121.8, 120.6, 117.0, 116.0, 69.3, 69.1, 56.2, 54.1, 53.7, 47.3, 42.3, 41.9, 40.4, 39.3, 32.1, 30.2, 27.7, 26.3, 25.8, 25.6, 23.11, 23.07, 22.8, 22.5, 21.9; MS ($ES^+$) *m/z* 866 (1%, M+H), 433 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{48}H_{65}N_8O_7$: 865.4976 (M+H), Found: 865.5018.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (123)**



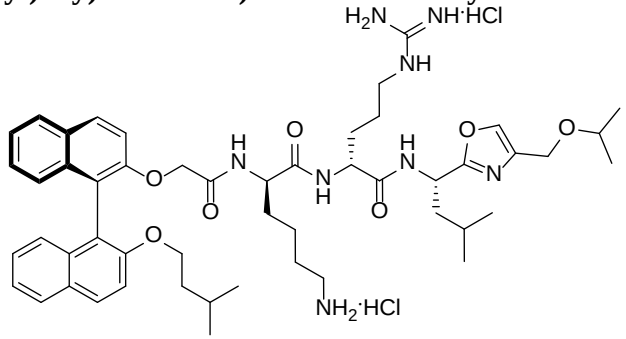

This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **91** (90 mg, 0.073 mmol) to yield **123** (66 mg, 95%) as an off-white solid. $[\alpha]_D^{25}$ −27.50 (*c* 3.1, MeOH). $^1$H NMR (300 MHz, $CD_3OD$): δ 0.48 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.53 (d, *J* = 6.3 Hz, 3H, $CH_3$), 0.88-0.95 (m, 2H, $CH_2$), 0.89 (d, *J* = 6.3 Hz, 3H, $CH_3$ (Leu)), 0.93 (d, *J* = 6.3 Hz, 3H, $CH_3$ (Leu)), 1.06-1.26 (m, 4H), 1.32-1.95 (m, 11H), 2.68-2.88 (m, 2H, $CH_2N$ (Lys)), 3.08-3.23 (m, 2H, $CH_2N$ (Arg)), 3.88-3.95 (m, 1H $CH_2O$ ($H_a$)), 4.06-4.11 (m, 2H, CH and $CH_2O$ ($H_b$)), 4.24-4.39 (m, 1H, CH), 4.30 (s, 2H, oxazole-C$\underline{H}_2$), 4.49 (ABq, *J* = 14.7 Hz, 2H, $OCH_2CO$), 5.05-5.17 (m, 1H, CH), 7.01-7.06 (m, 2H, ArH), 7.15-7.20 (m, 2H, ArH), 7.28-7.33 (m, 2H, ArH), 7.44 (d, *J* = 8.7 Hz, 1H, ArH), 7.52 (d, *J* = 8.7 Hz, 1H, ArH), 7.80 (s, 1H, ArH (oxazole)), 7.85-7.91 (m, 2H, ArH), 7.96-8.01 (m, 2H, ArH); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 22.0, 22.5, 22.8, 23.1 ($CH_3$), 23.0, 26.3, 27.7, 30.1, 32.0, 39.3, 40.4 ($CH_2$), 25.5, 25.8, 47.1, 53.8, 54.0 (CH), 41.9 ($CH_2N$ (Lys)), 42.7 ($CH_2N$ (Arg)), 58.5 ($OCH_3$), 66.6 (oxazole-$\underline{C}H_2$), 68.9 ($O\underline{C}H_2CO$), 69.2 ($CH_2O$), 115.9, 116.8, 124.8, 125.2, 125.9, 126.4, 127.5, 127.6, 129.1, 129.3, 130.8, 130.9 (ArCH), 120.4, 121.7, 130.7, 131.3, 135.0, 135.2, 138.5, 154.0, 155.9 (ArC), 158.5 (C=N), 171.0, 173.2, 173.5 (C=O). MS (ESI, +ve) *m/z* 879 (5%) $[M+H]^+$, 440 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{49}H_{67}N_8O_7$ 879.5133, found 879.5466.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(methoxymethyl)thiazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (124)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **92** (101 mg, 0.08 mmol) to give **124** (55.9 mg, 71%) as an off-white solid. mp 88−92 °C. $[\alpha]_D^{25} = -14.63$ (c 0.5, $CH_2Cl_2$). $^1$H NMR (500 MHz, $CD_3OD$, major rotamer only) δ 0.51 (3H, d, *J* = 6.5 Hz, ($CH_{3a}$ ($^i$Pent)), 0.51 (3H, d, *J* = 6.5 Hz, ($CH_{3b}$ ($^i$Pent)),) 0.92 - 1.07 (8H, m, H4", 3"-$CH_3$, $CH_2$ (Lys)), 1.09 - 2.15 (14H, m, $\underline{CH_2}\underline{CH}$($^i$Pent), H3"), 2.75 - 2.87 (2H, m, H6), 3.21 (2H, q, *J* = 6.7 Hz, H5'), 3.40 (1H, s, $OCH_3$), 3.89 - 4.02 (1H, m, $OCH_{2a}$ ($^i$Pent)), 4.06 - 4.23 (2H, m, $OCH_{2b}$ ($^i$Pent), H2), 4.36 (1H, dt, *J* = 8.9, 3.9 Hz, H2'), 4.44 - 4.65 (4H, m, $OCH_2CO$, 4'"-$CH_2$), 5.36 (1H, dd, *J* = 10.8, 3.9 Hz, H1"), 7.03 - 7.11 (2H, m, ArH), 7.17 - 7.24 (2H, m, ArH), 7.33 (2H, t, *J* = 7.5 Hz, ArH), 7.48 (1H, d, *J* = 9.0 Hz, ArH), 7.55 (1H, dd, *J* = 9.0, 5.6 Hz, ArH), 7.64 (1H, s, H5'"), 7.87 - 7.96 (2H, m, ArH), 7.98 - 8.07 (2H, m, ArH). $^{13}$C NMR (126 MHz, $CD_3OD$, major rotamer only) δ 21.4, 21.7, 22.5, 22.8, 23.1, 23.4, 25.6 (C4'), 26.1, 26.4, 27.7, 29.8, 32.1, 39.2, 40.4 (C5'), 41.8 (C6), 44.5 (C2"), 50.7 (C1"), 54.5 (C5, C2'), 58.9 ($OCH_3$), 68.9 ($O\underline{C}H_2CO$), 69.0 ($OCH_2$ ($^i$Pent)), 69.3 (4'"-$CH_2$), 116.1, 116.9, 119.7 (C5'"), 120.5, 121.8, 124.8, 125.2, 125.9, 126.3, 127.5, 127.6, 129.1, 129.3, 130.7, 130.8, 131.4, 135.0, 135.2, 150.9 (C2"" or C2""'), 154.1 (C4'"), 155.9 (C2"" or C2""'), 158.5 (guanidino),, 170.9 (C=O), 173.3 (C=O), 174.1 (C=O), 178.7. IR (neat) *v* [$cm^{-1}$] = 3179 (w), 3053 (w), 2953 (w), 2360 (w), 1654 (s), 1533 (m), 1507 (m), 1466 (m), 1431 (w), 1327 (w), 1215 (m), 1093 (m), 1047 (m), 1009 (w), 958 (w), 862 (w), 808 (m), 746 (m), 577 (w). MS ($ESI^+$) *m/*2 = 448 (100%, $[M+2H]^{2+}$), *m/z* = 895 (2%, $[M+H]^+$). HRMS ($ESI^+$) $[M+H]^+$ Calcd. for $C_{49}H_{67}N_8O_6S$: 895.4904, Found: 895.4935.

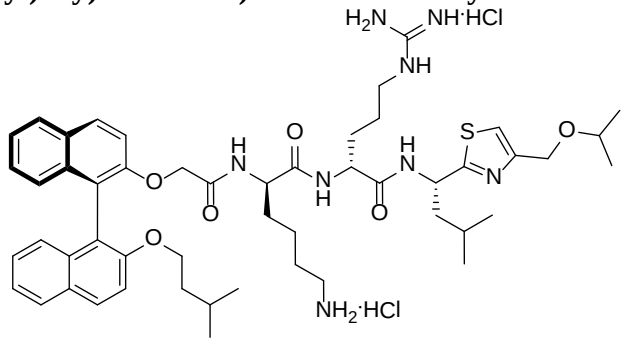
**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(isopropoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (125)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **93** (54 mg, 0.043 mmol) to yield **125** (40 mg, 95%) as an off-white solid. $[\alpha]_D^{25}$ −47.50 (*c* 1.9, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.51 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.56 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.91-0.97 (m, 2H, $CH_2$), 0.92 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 0.96 (d, *J* = 7.0 Hz, 3H, $CH_3$ (Leu)), 1.12-1.28 (m, 10H), 1.41-1.48 (m, 1H), 1.50-1.78 (m, 7H), 1.81-1.87 (m, 2H), 2.73-2.86 (m, 2H, $CH_2N$

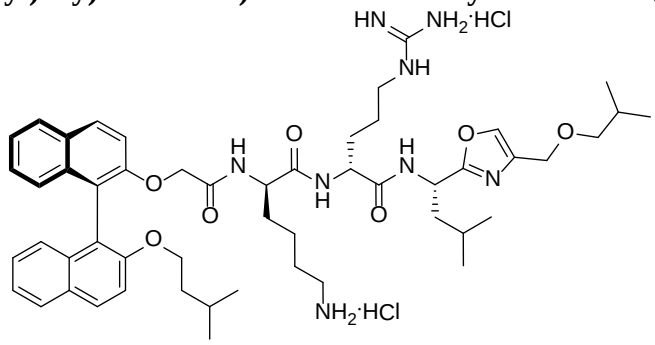
(Lys)), 3.13-3.23 (m, 2H, $CH_2N$ (Arg)), 3.71 (septet, $J$ = 6.0 Hz, 1H, OCH), 3.92-3.97 (m, 1H $CH_2O$ ($H_a$)), 4.08-4.14 (m, 2H, CH and $CH_2O$ ($H_b$)), 4.36 (dd, $J_1$ = 4.5, $J_2$ = 9.5 Hz, 1H, CH), 4.39 (s, 2H, oxazole-C$\underline{H}_2$), 4.50 (ABq, $J$ = 15.0 Hz, 2H, $OCH_2CO$), 5.14 (dd, $J_1$ = 6.5, $J_2$ = 9.5 Hz, 1H, CH), 7.04-7.08 (m, 2H, ArH), 7.19-7.23 (m, 2H, ArH), 7.32-7.35 (m, 2H, ArH), 7.47 (d, $J$ = 9.5 Hz, 1H, ArH), 7.53 (d, $J$ = 8.5 Hz, 1H, ArH), 7.81 (s, 1H, ArH (oxazole)), 7.89-7.92 (m, 2H, ArH), 8.00 (d, $J$ = 9.0 Hz, 1H, ArH), 8.01 (d, $J$ = 9.5 Hz, 1H, ArH); $^{13}$C NMR (126 MHz, $CD_3OD$): δ 22.0, 22.3, 22.4, 22.6, 22.8, 23.1 ($CH_3$), 23.06, 26.3, 27.7, 30.2, 32.0, 39.3, 40.4 ($CH_2$), 25.6, 25.9, 47.2, 53.7, 54.0 (CH), 41.9 ($CH_2N$ (Lys)), 42.7 ($CH_2N$ (Arg)), 64.4 (oxazole-$\underline{C}H_2$), 69.0 (O$\underline{C}H_2CO$), 69.3 ($CH_2O$), 72.9 (OCH), 116.0, 117.0, 124.8, 125.2, 126.0, 126.4, 127.5, 127.6, 129.1, 129.3, 130.85, 130.89, (ArCH), 120.5, 121.8, 130.7, 131.4, 135.1, 135.2, 139.1, 154.0, 155.9, 163.0 (ArC), 158.5 (C=N), 171.0, 173.1, 173.5 (C=O). MS (ESI, +ve) *m/z* 908 (5%) $[M+H]^+$, 455 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{51}H_{71}N_8O_7$ 907.5446, found 907.5490.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(isopropoxymethyl)thiazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (126)**



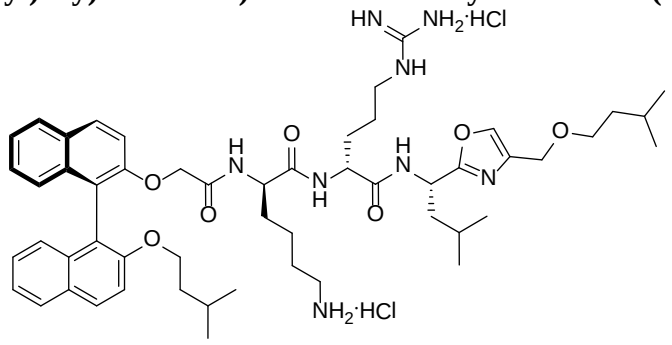

This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **94** (61.4 mg, 0.05 mmol) to give **126** (42.1 mg, 88%) as a tan solid. $[\alpha]_D^{25} = -13.1$ (*c* 0.11, MeOH). $^1$H NMR (500 MHz, $CD_3OD$) δ 0.50 (3H, d, $J$ = 6.5 Hz), 0.51 (3H, d, $J$ = 6.5 Hz), 0.96 - 1.00 (8H, m), 1.13 - 1.26 (6H, m), 1.51 - 1.87 (7H, m), 2.75 - 2.86 (2H, bm), 3.15 - 3.23 (2H, m), 3.34 (1H, s), 3.72 - 3.78 (1H, m), 3.96 - 4.12 (2H, m), 4.31 - 4.36 (1H, m), 4.47 - 4.60 (4H, m), 5.36 (1H, m), 7.04 (2H, t, $J$ = 9.2 Hz), 7.21 (2H, t, $J$ = 7.6 Hz), 7.33 (2H, q, $J$ = 7.2 Hz), 7.48 (1H, d, $J$ = 8.8 Hz),7.53 - 7.59 (1H,m), 7.65 (1H, bs), 7.91 (2H, t, $J$ = 7.7 Hz), 8.01 - 8.04 (2H, m). $^{13}$C NMR (126 MHz, $CD_3OD$) δ 21.4, 21.7, 22.5, 22.8, 23.1, 23.4, 25.6, 26.1, 26.4, 27.7, 29.8, 32.1, 39.2, 40.4, 41.8, 44.5, 50.7, 54.5, 58.9, 68.9, 69.0, 69.3, 116.1, 116.9, 119.7, 120.5, 121.8, 124.8, 125.2, 125.9, 126.3, 127.5, 127.6, 129.1, 129.3, 130.7, 130.8, 131.4, 135.0, 135.2, 150.9, 154.1, 155.9, 158.5, 170.9, 173.3, 174.1, 178.7. IR (neat) $\nu$ [$cm^{-1}$] = 3650 (s), 3446 (s), 1654 (s), 1507 (s), 1212 (m), 1048 (m), 804 (m), 668 (s). MS ($ESI^+$) *m/*2 = 462 (100 %, $[M+2H]^{2+}$), *m/z* = 996 (1 %, $[M+H]^+$). HRMS ($ESI^+$) $[M+H]^+$ Calcd. for $C_{51}H_{71}N_8O_6S$: 923.5217, Found: 923.5212.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(isobutoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (127)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **95** (77.4 mg, 0.061 mmol) to give **127** (60.2 mg, 100%) as a white solid. $[\alpha]_D^{25}$ −24.9 (*c* 2.51, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.06 – 7.99 (m, 2H), 7.91 (d, *J* = 8.1 Hz, 2H), 7.78 (s, 1H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.49 (d, *J* = 8.9 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.27 – 7.20 (m, 2H), 7.11 – 7.04 (m, 2H), 5.18 – 5.11 (m, 1H), 4.52 (ABq, $\Delta\delta_{AB}$ = 0.08, *J* = 14.8 Hz, 2H), 4.41 – 4.31 (m, 3H), 4.17 – 4.07 (m, 2H), 4.01 – 3.92 (m, 1H), 3.25 (d, *J* = 6.6 Hz, 2H), 3.22 – 3.11 (m, 2H), 2.85 – 2.75 (m, 2H), 1.91 – 1.40 (m, 12H), 1.33 – 1.09 (m, 5H), 0.97 (d, *J* = 6.4 Hz, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 6H), 0.57 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR (75 MHz, $CD_3OD$) δ 173.7, 173.3, 171.0, 165.8, 158.5, 155.9, 154.0, 138.9, 138.3, 135.2, 135.0, 131.3, 130.8, 130.6, 129.3, 129.1, 127.6, 127.5, 126.4, 125.9, 125.1, 124.8, 121.6, 120.5, 116.8, 115.9, 78.5, 69.2, 68.9, 65.2, 54.3, 53.9, 47.1, 42.8, 41.9, 40.3, 39.2, 32.0, 30.0, 29.5, 27.6, 26.4, 25.8, 25.6, 23.2, 23.0, 22.8, 22.6, 22.1, 19.7; MS ($ES^+$) *m/z* 921 (<5%, M+H), 461 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{52}H_{73}N_8O_7$: 921.5602 (M+H), Found: 921.5599.

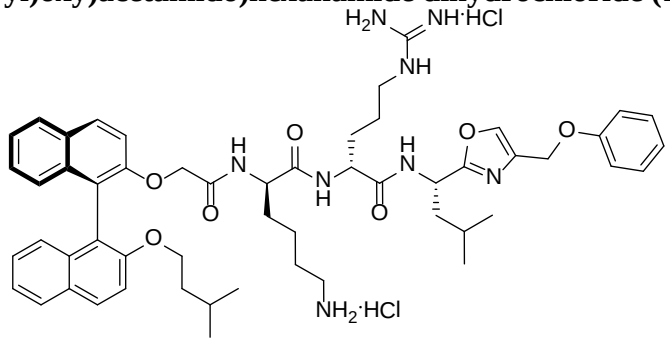
**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(isopentyloxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (128)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **96** (78.9 mg, 0.061 mmol) to give **128** (50.1 mg, 81%) as an off-white solid. $[\alpha]_D^{25}$ −17.5 (*c* 1.82, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.02 (t, *J* = 8.5 Hz, 2H), 7.92 (d, *J* = 8.1 Hz, 2H), 7.82 (s, 1H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.07 (t, *J* = 9.7 Hz, 2H), 5.18 – 5.12 (m, 1H), 4.52 (ABq, $\Delta\delta_{AB}$ = 0.10, *J* = 14.7 Hz, 2H), 4.41 – 4.34 (m, 3H), 4.18 – 4.06 (m, 2H), 4.01 – 3.92 (m, 1H), 3.52 (t, *J* = 6.3 Hz, 2H), 3.24 – 3.13 (m, 2H), 2.84 – 2.74 (m, 2H), 1.92 – 1.38 (m, 14H), 1.34 – 1.07 (m, 5H), 0.97 (d, *J* = 6.4 Hz, 3H), 0.93 (d, *J* = 6.0 Hz, 3H), 0.89 (d, *J* = 6.4 Hz, 6H), 0.58 (d, *J* = 5.9 Hz, 3H), 0.52 (d, *J* = 5.9 Hz, 3H); $^{13}$C NMR (125 MHz, $CD_3OD$) δ 173.5, 173.1, 170.9, 166.1, 158.5, 155.8, 154.0, 138.5, 135.2, 135.0, 131.3, 130.9, 130.8, 130.6, 129.3, 129.1, 127.6, 127.4, 126.3, 125.9, 125.1, 124.8, 121.7, 120.5, 116.9, 115.9, 70.1,

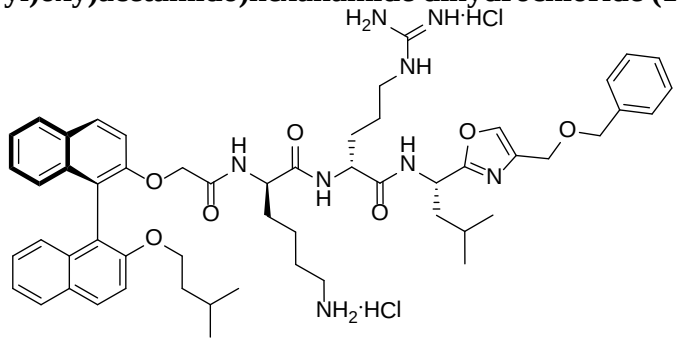
69.2, 69.0, 64.8, 54.1, 53.7, 47.1, 42.7, 41.9, 40.4, 39.5, 39.2, 32.0, 30.1, 27.7, 26.3, 26.1, 25.8, 25.6, 23.1, 23.0, 22.8, 22.6, 22.0; MS ($ES^+$) *m/z* 935 (<5%, M+H), 468 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{53}H_{75}N_8O_7$: 935.5759 (M+H), Found: 935.5788.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(phenoxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (129)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **97** (20 mg, 0.014 mmol) to yield **129** (14 mg, 92%) as an off-white solid. $[\alpha]_D^{25}$ +13.57 (*c* 0.6, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.52 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.57 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.95-1.02 (m, 8H, $CH_2$ and 2 x $CH_3$ (Leu)), 1.15-1.32 (m, 4H), 1.46-1.89 (m, 10H), 2.74-2.86 (m, 2H, $CH_2N$ (Lys)), 3.14-3.27 (m, 2H, $CH_2N$ (Arg)), 3.92-4.01 (m, 1H $CH_2O$ ($H_a$)), 4.06-4.18 (m, 2H, CH and $CH_2O$ ($H_b$)), 4.36-4.44 (m, 1H, CH), 4.53 (ABq, *J* = 14.5 Hz, 2H, $OCH_2CO$), 4.97 (s, 1H, oxazole-C$\underline{H}_2$ ($H_a$)), 5.05 (s, 1H, oxazole-C$\underline{H}_2$ ($H_b$)), 5.17-5.20 (m, 1H, CH), 6.95-7.01 (m, 3H, ArH), 7.06-7.10 (m, 2H, ArH), 7.23-7.29 (m, 4H, ArH), 7.34-7.38 (m, 2H, ArH), 7.48 (d, *J* = 9.0 Hz, 1H, ArH), 7.55 (d, *J* = 9.0 Hz, 1H, ArH), 7.92-7.94 (m, 2H, ArH), 8.02-8.03 (m, 2H, ArH); $^{13}$C NMR (126 MHz, $CD_3OD$): δ 22.0, 22.5, 22.8, 23.1 ($CH_3$), 23.1, 26.3, 27.8, 30.2, 32.1, 39.3, 40.4 ($CH_2$), 25.6, 25.9, 47.2, 53.8, 54.0 (CH), 41.9 ($CH_2N$ (Lys)), 42.8 ($CH_2N$ (Arg)), 62.8 (oxazole-$\underline{C}H_2$), 69.0 ($O\underline{C}H_2CO$), 69.3 ($CH_2O$), 115.9, 117.0, 122.3, 124.8, 125.2, 126.0, 126.4, 127.5, 127.6, 129.1, 129.3, 130.5, 130.6, 130.9 (ArCH), 120.6, 121.8, 130.7, 131.4, 135.1, 135.2, 138.0, 154.0, 155.9, 159.7, 166.1 (ArC), 158.6 (C=N), 171.1, 173.2, 173.5 (C=O). MS (ESI, +ve) *m/z* 942 (5%) $[M+H]^+$, 471 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{54}H_{69}N_8O_7$ 941.5289, found 941.5305.

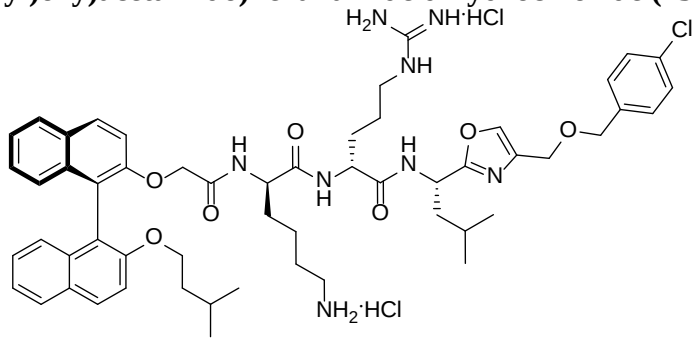
**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(benzyloxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (130)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **98** (17 mg, 0.013 mmol) to yield **130** (12 mg, 90%) as an off-white solid. $[\alpha]_D^{25}$ −28.44 (*c* 0.5, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.52-0.57 (m, 6H), 0.95-2.01 (m, 22H), 2.62-3.00 (m, 2H), 3.10-3.39 (m, 2H), 3.83-4.04 (m, 3H), 4.06-5.20 (m, 8H), 6.69-7.18 (m, 2H), 7.19-7.70 (m, 9H), 7.92-8.02

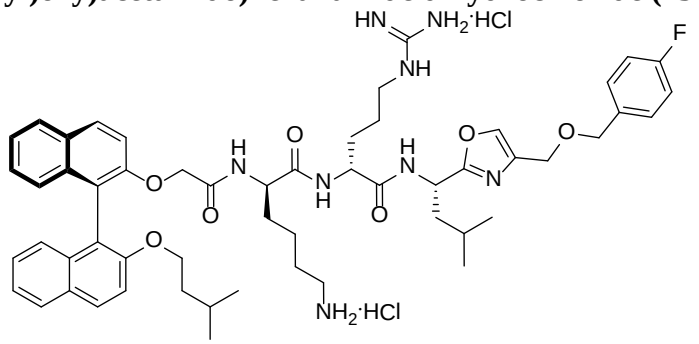
(m, 5H); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 22.1, 22.5, 22.8, 23.2, 25.4, 25.8, 39.2, 42.8, 47.0, 53.9, 64.8, 69.2, 73.7, 116.0, 117.2, 120.3, 121.5, 124.9, 125.1, 125.8, 126.2, 127.4, 127.6, 128.8, 129.0, 129.1, 129.4, 130.5, 130.9, 131.2, 134.9, 135.5, 138.6, 138.9, 153.8, 155.7, 158.4. MS (ESI, +ve) *m/z* 955 (5%) $[M+H]^+$, 478 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{55}H_{71}N_8O_7$ 955.5446, found 955.5489.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(4-chlorobenzyloxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (131)**



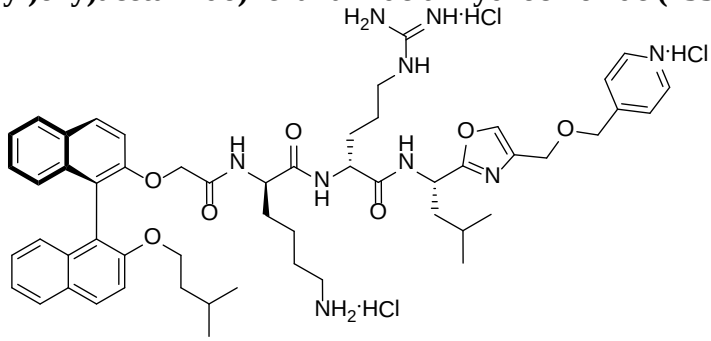

This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **99** (77 mg, 0.057 mmol) to yield **131** (60 mg, 97%) as an off-white solid. $[\alpha]_D^{25}$ −34.72 (*c* 2.0, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.50 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.55 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.88-1.02 (m, 2H, $CH_2$), 0.93 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 0.97 (d, *J* = 7.0 Hz, 3H, $CH_3$ (Leu)), 1.10-1.30 (m, 4H), 1.42-1.46 (m, 1H), 1.48-1.79 (m, 7H), 1.81-1.93 (m, 2H), 2.72-2.84 (m, 2H, $CH_2N$ (Lys)), 3.12-3.24 (m, 2H, $CH_2N$ (Arg)), 3.91-3.96 (m, 1H $CH_2O$ ($H_a$)), 4.06-4.13 (m, 2H, CH and $CH_2O$ ($H_b$)), 4.35-4.37 (m, 1H, CH), 4.44 (s, 2H, oxazole-C$\underline{H_2}$), 4.51 (ABq, *J* = 15.0 Hz, 2H, $OCH_2CO$), 4.52 (s, 2H, C$\underline{H_2}$ArCl), 5.13-5.16 (m, 1H, CH), 6.67 (d, *J* = 6.5 Hz, 1H, NH), 7.05-7.08 (m, 2H, ArH), 7.19-7.22 (m, 2H, ArH), 7.28-7.34 (m, 4H, ArH), 7.46 (d, *J* = 9.0 Hz, 1H, ArH), 7.52 (d, *J* = 9.0 Hz, 1H, ArH), 7.83 (s, 1H, ArH (oxazole)), 7.89-7.92 (m, 2H, ArH), 8.00 (d, *J* = 9.0 Hz, 2H, ArH), 8.15 (d, *J* = 7.5 Hz, 1H, NH), 8.45 (d, *J* = 8.0 Hz, 1H, NH); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 22.0, 22.5, 22.8, 23.1 ($CH_3$), 23.0, 26.3, 27.7, 30.2, 32.0, 39.3, 40.4 ($CH_2$), 25.6, 25.9, 47.2, 53.8, 54.0 (CH), 41.9 ($CH_2N$ (Lys)), 42.8 ($CH_2N$ (Arg)), 64.5 (oxazole-$\underline{C}H_2$), 69.0 ($O\underline{C}H_2CO$), 69.2 ($CH_2O$), 72.5 ($\underline{C}H_2$ArCl), 115.9, 116.9, 124.8, 125.2, 125.9, 126.4, 127.5, 127.6, 129.1, 129.3, 129.5, 130.5, 130.7, 130.9 (ArCH), 120.5, 121.8, 130.9, 131.4, 134.5, 135.1, 135.2, 138.1, 154.0, 155.9 (ArC), 158.5 (C=N), 171.0, 173.1, 173.5 (C=O). MS (ESI, +ve) *m/z* 989 (5%) $[M+H]^+$, 495 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{55}H_{70}N_8O_7Cl$ 989.5056, found 989.5065.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(4-fluorobenzyloxymethyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (132)**



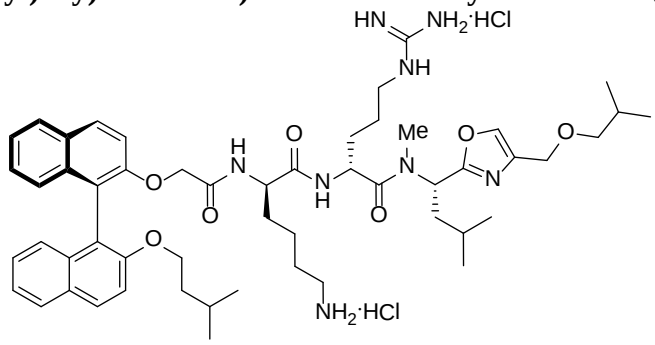
This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **100** (36.4 mg, 0.027 mmol) to give **132** (29.1 mg, 100%) as a white solid. $[\alpha]_D^{25}$ −23.3 (*c* 1.13, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.04 – 7.97 (m, 2H), 7.91 (d, *J* = 7.0 Hz, 2H), 7.80 (s, 1H), 7.52 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.39 – 7.30 (m, 4H), 7.27 – 7.19 (m, 2H), 7.11 – 7.00 (m, 4H), 5.14 (t, *J* = 6.9 Hz, 1H), 4.60 – 4.45 (m, 4H), 4.43 (s, 2H), 4.38 – 4.30 (m, 1H), 4.16 – 4.05 (m, 2H), 3.99 – 3.90 (m, 1H), 3.25 – 3.10 (m, 2H), 2.86 – 2.71 (m, 2H), 1.90 – 1.39 (m, 11H), 1.31 – 1.09 (m, 5H), 0.97 (d, *J* = 5.9 Hz, 3H), 0.93 (d, *J* = 6.0 Hz, 3H), 0.56 (d, *J* = 5.6 Hz, 3H), 0.51 (d, *J* = 5.4 Hz, 3H); $^{13}$C NMR (75 MHz, $CD_3OD$) δ 173.8, 173.5, 171.1, 166.0, 163.8 (d, $J_{C-F}$ = 244.1 Hz), 158.6, 155.9, 154.1, 138.6, 135.2, 135.0, 131.3, 131.08, 130.98, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.0, 125.2, 124.8, 121.7, 120.5, 116.9, 116.2, 116.0, 72.6, 69.2, 68.9, 64.4, 54.4, 53.9, 47.2, 42.8, 41.9, 40.2, 39.3, 32.0, 30.0, 27.6, 26.4, 25.9, 25.6, 23.2, 22.9, 22.8, 22.6, 22.0; MS ($ES^+$) *m/z* 973 (<5%, M+H), 487 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{55}H_{70}FN_8O_7$: 973.5352 (M+H), Found: 973.5367.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-((pyridin-4-ylmethoxy)methyl)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·trihydrochloride (133)**



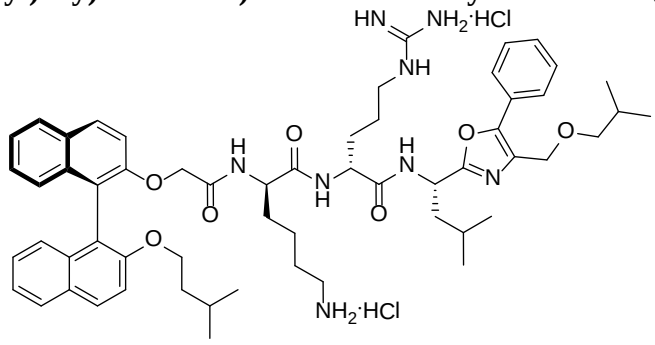

This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **101** (35 mg, 0.027 mmol) to yield **133** (21 mg, 76%) as an off white solid. $[\alpha]_D^{25}$ +14.85 (*c* 0.8, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.51 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.56 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.92-0.98 (m, 2H, $CH_2$), 0.93 (d, *J* = 6.0 Hz, 3H, $CH_3$ (Leu)), 0.97 (d, *J* = 6.0 Hz, 3H, $CH_3$ (Leu)), 1.14-1.33 (m, 4H), 1.44-1.80 (m, 8H), 1.81-1.94 (m, 2H), 2.75-2.86 (m, 2H, $CH_2N$ (Lys)), 3.14-3.25 (m, 2H, $CH_2N$ (Arg)), 3.93-3.97 (m, 1H $CH_2O$ ($H_a$)), 4.08-4.18 (m, 2H, CH and $CH_2O$ ($H_b$)), 4.33-4.42 (m, 1H, CH), 4.52 (ABq, *J* = 14.5 Hz, 2H, $OCH_2CO$), 4.62 (s, 2H, oxazole-C$\underline{H}_2$), 4.93 (s, 2H, C$\underline{H}_2$-Py), 5.14-5.17 (m, 1H, CH), 7.02-7.07 (m, 3H, ArH), 7.20-7.23 (m, 2H, ArH), 7.31-7.36 (m, 2H, ArH), 7.48 (d, *J* = 9.0 Hz, 1H, ArH), 7.53 (d, *J* = 8.5 Hz, 1H, ArH), 7.90-7.91 (m, 2H, ArH), 7.95 (s, 1H, ArH (oxazole)), 8.01-8.04 (m, 3H, ArH), 8.75-8.75 (m, 2H, ArH); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 22.0, 22.8, 23.2 ($CH_3$), 25.8, 27.8, 30.3, 32.1, 39.3, 40.4 ($CH_2$), 25.6, 25.9, 47.1, 53.8, 54.1 (CH), 41.9 ($CH_2N$ (Lys)), 42.8 ($CH_2N$ (Arg)), 65.5 (oxazole-$\underline{C}H_2$), 69.0 ($O\underline{C}H_2CO$), 69.3 ($CH_2O$), 70.7 ($\underline{C}H_2$-Py), 116.0, 117.0, 124.8, 125.2, 125.8, 126.0, 126.4, 127.5, 127.6, 129.1, 129.3, 130.88, 130.9, 140.3 (ArCH), 120.5, 121.8, 130.7, 131.4, 135.0, 135.2, 154.1, 155.9, 162.4 (ArC), 158.5 (C=N), 171.0, 173.2, 173.5 (C=O). MS (ESI, +ve) *m/z* 957 (<5%) $[M+H]^+$, 479 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{54}H_{70}N_9O_7$ 956.5398, found 956.5434.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(isobutoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (134)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **102** (13.2 mg, 0.010 mmol) to give **134** (9.0 mg, 87%) as an off-white solid. $[\alpha]_D^{25}$ −17.8 (*c* 0.25, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.06 – 7.98 (m, 2H), 7.91 (d, *J* = 8.1 Hz, 2H), 7.84 (s, 1H), 7.54 (d, *J* = 8.9 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.39 – 7.31 (m, 2H), 7.27 – 7.19 (m, 2H), 7.07 (t, *J* = 8.0 Hz, 2H), 5.93 – 5.87 (m, 1H), 4.81 – 4.74 (m, 1H), 4.50 (ABq, $\Delta\delta_{AB}$ = 0.09, *J* = 14.4 Hz, 2H), 4.41 (s, 2H), 4.23 – 4.09 (m, 2H), 4.02 – 3.92 (m, 1H), 3.27 (d, *J* = 6.2 Hz, 2H), 3.25 – 3.13 (m, 2H), 3.01 (s, 3H), 2.87 – 2.74 (m, 2H), 1.98 – 1.35 (m, 12H), 1.33 – 1.07 (m, 5H), 1.00 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.0 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 6H), 0.57 (d, *J* = 6.3 Hz, 3H), 0.52 (d, *J* = 6.0 Hz, 3H); $^{13}$C NMR (75 MHz, $CD_3OD$) δ 174.0, 172.9, 170.7, 164.2, 158.6, 155.9, 154.0, 139.3, 138.7, 135.2, 135.1, 131.4, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.0, 125.3, 124.8, 121.8, 120.5, 116.9, 116.0, 78.6, 69.3, 69.0, 65.3, 53.3, 50.9, 50.8, 41.9, 40.4, 39.3, 32.3, 31.0, 29.7, 29.6, 27.7, 26.2, 25.9, 25.6, 23.4, 23.0, 22.8, 22.6, 22.1, 19.7; MS ($ES^+$) *m/z* 935 (<5%, M+H), 468 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{53}H_{75}N_8O_7$: 935.5759 (M+H), Found: 935.5782.

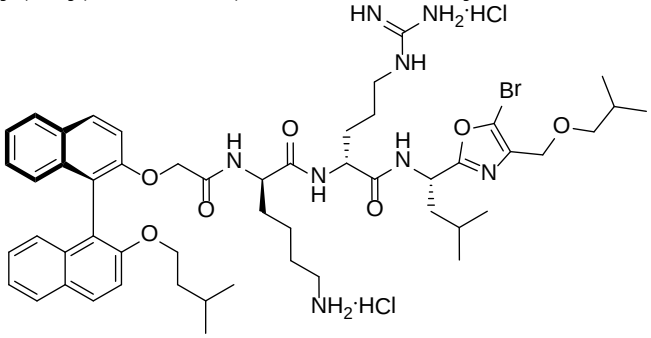
**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(isobutoxymethyl)-5-phenyloxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (135)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **103** (45.8 mg, 0.034 mmol) to give **135** (24.3 mg, 67%) as an off-white solid. $[\alpha]_D^{25}$ −30.5 (*c* 0.63, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.01 (d, *J* = 8.9 Hz, 1H), 7.95 (d, *J* = 9.0 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.74 (d, *J* = 7.6 Hz, 2H), 7.51 – 7.38 (m, 5H), 7.38 – 7.28 (m, 2H), 7.27 – 7.18 (m, 2H), 7.05 (t, *J* = 9.5 Hz, 2H), 5.24 – 5.19 (m, 1H), 4.58 – 4.41 (m, 4H), 4.41 – 4.35 (m, 1H), 4.14 – 4.05 (m, 2H), 3.93 – 3.85 (m, 1H), 3.36 – 3.33 (m, 2H), 3.24 – 3.13 (m, 2H), 2.81 – 2.69 (m, 2H), 1.96 – 1.05 (m, 17H), 1.01 (d, *J* = 6.0 Hz, 3H), 0.97 (d, *J* = 6.2 Hz, 3H), 0.91 (d, *J* = 6.0 Hz, 6H), 0.55 (d, *J* = 5.7 Hz, 3H), 0.49 (d, *J* = 5.6 Hz, 3H); $^{13}$C NMR (75 MHz, $CD_3OD$) δ 173.7, 173.2, 171.0, 163.6, 158.5, 155.9, 154.0, 150.5, 135.2, 135.0, 133.4, 131.4, 130.9, 130.6, 130.1, 129.3, 129.1, 129.0, 127.6, 127.5, 127.3, 126.4, 125.9, 125.2, 124.8, 121.7, 120.4, 116.9, 115.9, 78.5, 69.2, 68.9, 65.8,

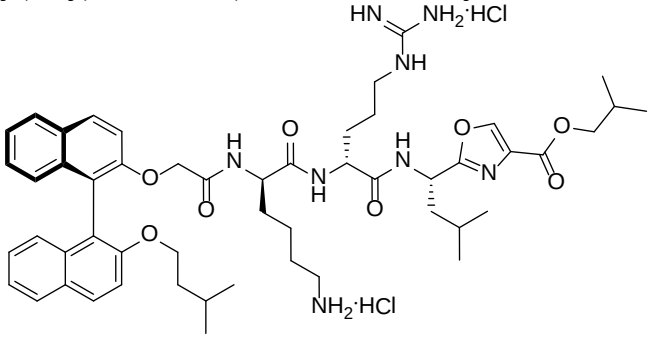
54.2, 53.7, 47.2, 42.9, 41.9, 40.3, 39.2, 32.1, 30.2, 29.7, 27.6, 26.4, 26.0, 25.6, 23.2, 23.0, 22.8, 22.5, 22.1, 19.8; MS ($ES^+$) *m/z* 997 (<5%, M+H), 499 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{58}H_{77}N_8O_7$: 997.5915 (M+H), Found: 997.5913.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(isobutoxymethyl)-5-bromooxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (136)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **104** (37.8 mg, 0.028 mmol) to give **136** (21.6 mg, 72%) as an off-white solid. $[\alpha]_D^{25}$ −29.3 (*c* 0.51, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.02 (t, *J* = 8.3 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.9 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 7.39 – 7.31 (m, 2H), 7.27 – 7.19 (m, 2H), 7.11 – 7.03 (m, 2H), 5.14 – 5.08 (m, 1H), 4.52 (ABq, $\Delta\delta_{AB}$ = 0.09, *J* = 14.7 Hz, 2H), 4.36 – 4.28 (m, 3H), 4.17 – 4.07 (m, 2H), 4.00 – 3.92 (m, 1H), 3.23 (d, *J* = 5.7 Hz, 2H), 3.21 – 3.12 (m, 2H), 2.86 – 2.75 (m, 2H), 1.90 – 1.39 (m, 12H), 1.33 – 1.09 (m, 5H), 0.97 (d, *J* = 5.8 Hz, 3H), 0.93 (d, *J* = 6.2 Hz, 3H), 0.89 (d, *J* = 6.1 Hz, 6H), 0.57 (d, *J* = 5.8 Hz, 3H), 0.52 (d, *J* = 5.7 Hz, 3H); $^{13}$C NMR (75 MHz, $CD_3OD$) δ 173.7, 173.3, 171.0, 166.6, 158.5, 155.9, 154.0, 137.0, 135.2, 135.1, 131.4, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.0, 125.2, 124.8, 122.3, 121.7, 120.5, 116.9, 115.9, 78.5, 69.2, 69.0, 64.3, 54.2, 53.8, 47.3, 42.5, 41.9, 40.4, 39.3, 32.1, 30.1, 29.5, 27.7, 26.3, 25.9, 25.6, 23.14, 23.07, 22.8, 22.6, 22.0, 19.7; MS ($ES^+$) *m/z* 1001 (<5%, M+H, $^{81}$Br), 999 (<5%, M+H, $^{79}$Br), 501 (100%, M+2H, $^{81}$Br), 500 (59%, M+2H, $^{79}$Br); HRMS ($ES^+$) Calcd. for $C_{52}H_{72}{}^{79}BrN_8O_7$: 999.4707 (M+H), Found: 999.4697.

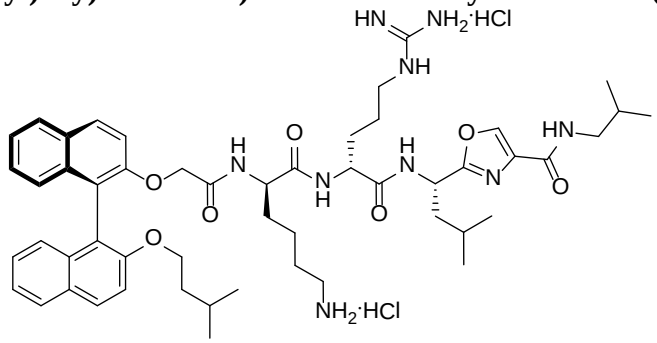
**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(isobutylcarboxy)oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (137)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **105** (26.7 mg, 0.021 mmol) to give **137** (19.1 mg, 91%) as an off-white solid. $[\alpha]_D^{25}$ −34.1 (*c* 0.40, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.48 (s, 1H), 8.00 (t, *J* = 9.4 Hz, 2H), 7.95 – 7.87 (m, 2H), 7.52 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.29 (m, 2H), 7.27 – 7.18 (m, 2H), 7.06 (t, *J* = 8.8 Hz, 2H), 5.17 (dd, *J* = 9.2, 6.0 Hz, 1H), 4.52 (ABq, $\Delta\delta_{AB}$ = 0.10, *J* = 14.7 Hz, 2H), 4.35 – 4.29

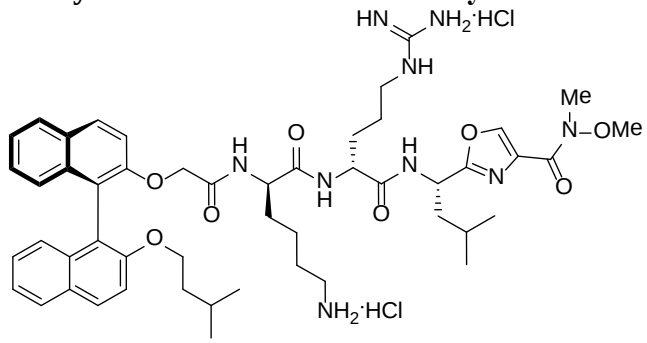
(m, 1H), 4.16 – 4.05 (m, 4H), 3.95 (dd, *J* = 15.3, 6.4 Hz, 1H), 3.24 – 3.11 (m, 2H), 2.91 – 2.79 (m, 2H), 2.02 (sep, *J* = 6.6 Hz, 1H), 1.92 – 1.36 (m, 11H), 1.32 – 1.09 (m, 5H), 1.03 – 0.91 (m, 12H), 0.57 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR (75 MHz, $CD_3OD$) δ 173.9, 173.4, 171.1, 166.7, 162.7, 158.6, 155.9, 154.0, 146.1, 135.2, 135.0, 134.0, 131.4, 130.8, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.0, 125.2, 124.8, 121.7, 120.5, 116.9, 115.9, 72.2, 69.2, 68.9, 54.4, 53.9, 47.1, 42.4, 41.9, 40.3, 39.3, 32.0, 29.9, 29.1, 27.6, 26.4, 25.9, 25.6, 23.2, 22.9, 22.8, 22.6, 21.9, 19.4; MS ($ES^+$) *m/z* 935 (<5%, M+H), 468 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{52}H_{72}N_8O_8$ (M+2H): 468.2737, Found: 468.2749.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(isobutylcarbamoyl)-oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (138)**



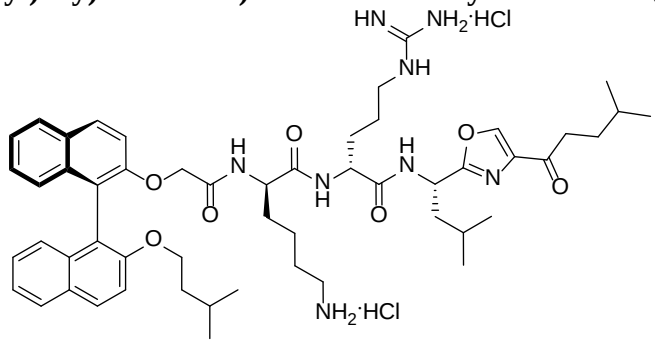
This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **106** (52.5 mg, 0.041 mmol) to give **138** (41.5 mg, 100%) as an off-white solid. $[\alpha]_D^{25}$ −22.9 (*c* 1.45, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.31 (s, 1H), 8.02 (t, *J* = 10.0 Hz, 2H), 7.91 (d, *J* = 7.9 Hz, 2H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.30 (m, 2H), 7.23 (t, *J* = 7.4 Hz, 2H), 7.11 – 7.03 (m, 2H), 5.21 – 5.13 (m, 1H), 4.50 (ABq, $\Delta\delta_{AB}$ = 0.09, *J* = 14.7 Hz, 2H), 4.38 – 4.30 (m, 1H), 4.18 – 4.07 (m, 2H), 3.95 (dd, *J* = 15.5, 6.4 Hz, 1H), 3.25 – 3.12 (m, 4H), 2.85 – 2.71 (m, 2H), 1.95 – 1.36 (m, 12H), 1.33 – 1.05 (m, 5H), 1.00 (d, *J* = 6.4 Hz, 3H), 0.98 – 0.87 (m, 9H), 0.57 (d, *J* = 6.4 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR (125 MHz, $CD_3OD$) δ 173.8, 173.1, 170.8, 165.6, 162.9, 158.5, 155.9, 154.0, 142.6, 137.2, 135.2, 135.0, 131.4, 130.8, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 125.9, 125.2, 124.8, 121.8, 120.5, 116.9, 116.0, 69.3, 69.0, 54.3, 53.6, 47.6, 47.1, 42.5, 41.9, 40.4, 39.3, 32.1, 30.2, 29.8, 27.7, 26.4, 25.9, 25.6, 23.2, 23.0, 22.8, 22.6, 22.0, 20.5; MS ($ES^+$) *m/z* 934 (<5%, M+H), 468 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{52}H_{72}N_9O_7$: 934.5555 (M+H), Found: 934.5567.

**2-((*S*)-1-((*R*)-2-((*R*)-6-Amino-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamido)-5-guanidinopentanamido)-3-methylbutyl)-*N*-methoxy-*N*-methyloxazole-4-carboxamide·dihydrochloride (139)**



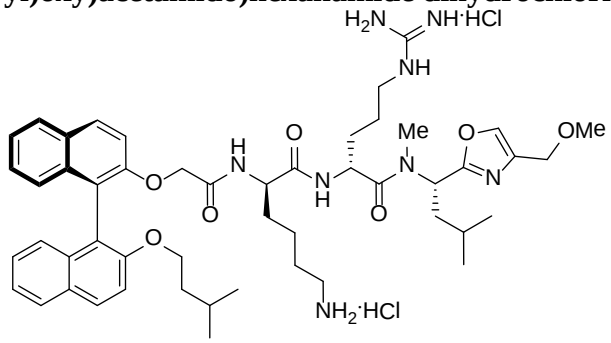
This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **107** (27.5 mg, 0.02 mmol) to give **139** (20.2 mg, 97%) as a tan solid. $[\alpha]_D^{25} = -24.4$ (*c* 0.67, MeOH). $^1$H NMR (500 MHz, $CD_3OD$) δ 0.54 (3H, d, *J* = 6.5 Hz), 0.59 (3H, d, *J* = 6.5 Hz), 0.96 (3H, d, *J* = 6.3 Hz), 1.01 (3H, d, *J* = 6.2 Hz), 1.15 - 1.35 (5H, m), 1.54 - 1.89 (9H, m), 2.89 (2H, t, *J* = 6.0 Hz), 3.22 (2H, bs), 3.33 (3H, s), 3.37 (3H, s), 3.41 (3H, s), 3.81 (3H, s), 3.94 - 3.99 (2H, bm), 4.09 - 4.14 (2H, m), 4.36 (1H, bs), 4.53 ($AB_q$, 4H, $\Delta\sigma_{AB}$ = 0.15, $J_{AB}$ = 14.7 Hz), 5.20 (1H, bs), 7.08 (2H, t, *J* = 7.8 Hz), 7.22 - 7.26 (2H, m), 7.34 - 7.39 (2H, m), 7.49 (1H, d, *J* = 8.9 Hz), 7.54 (1H, d, *J* = 8.9 Hz), 7.91 (2H, t, *J* = 7.8 Hz), 7.99 - 8.05 (2H, q), 8.53 (1H, bs). $^{13}$C NMR (126 MHz, $CD_3OD$) δ 22.0, 22.5, 22.8, 23.0, 25.6, 25.9, 26.4, 27.7, 30.0, 32.0, 39.3, 40.4, 41.9, 53.6, 54.1, 69.0, 69.2, 116.0, 116.9, 120.5, 121.8, 124.8, 125.3, 125.9, 126.4, 127.5, 127.6, 129.1, 129.2, 130.7, 130.8, 131.4, 135.0, 135.2, 154.0, 155.9, 158.6, 167.1, 170.8, 173.8. IR (neat) *ν* [$cm^{-1}$] = 3870 (s), 3336 (s), 3012 (m), 2296 (w), 1695 (s), 1505 (s), 1078 (w). MS ($ESI^+$) *m*/2 = 462 (100 %, $[M+2H]^{2+}$).

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(4-methylpentanoyl)-oxazol-2-yl)-3-methylbutyl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (140)**



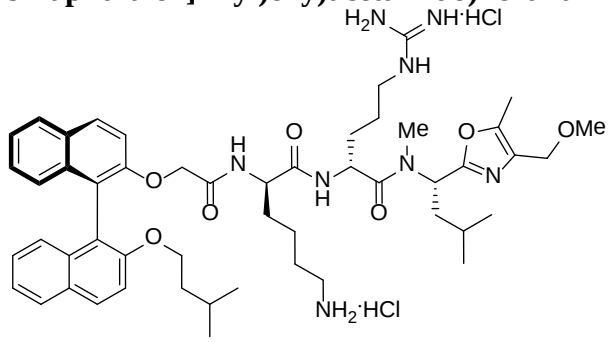

This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **108** (41.9 mg, 0.033 mmol) to give **140** (26.9 mg, 82%) as an off-white solid. $[\alpha]_D^{25}$ −19.9 (*c* 0.59, MeOH); $^1$H NMR (500 MHz, $CD_3OD$) δ 8.63 (s, 1H), 8.07 – 7.96 (m, 2H), 7.91 (d, *J* = 7.5 Hz, 2H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 7.41 – 7.30 (m, 2H), 7.28 – 7.18 (m, 2H), 7.07 (t, *J* = 8.8 Hz, 2H), 5.22 – 5.15 (m, 1H), 4.51 (ABq, $\Delta\delta_{AB}$ = 0.10, *J* = 14.8 Hz, 2H), 4.38 – 4.30 (m, 1H), 4.18 – 4.04 (m, 2H), 3.95 (dd, *J* = 15.4, 6.5 Hz, 1H), 3.25 – 3.12 (m, 2H), 2.91 – 2.75 (m, 4H), 1.93 – 1.36 (m, 14H), 1.34 – 1.08 (m, 5H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.97 – 0.87 (m, 9H), 0.57 (d, *J* = 6.4 Hz, 3H), 0.52 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (125 MHz, $CD_3OD$) δ 196.3, 173.7, 173.2, 171.0, 166.4, 158.6, 155.9, 154.1, 145.8, 141.2, 135.2, 135.1, 131.4, 130.8, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.0, 125.2, 124.8, 121.7, 120.6, 116.9, 116.0, 69.3, 69.0, 54.2, 53.8, 47.1, 42.4, 41.9, 40.4, 39.3, 38.7, 34.0, 32.0, 30.1, 28.9, 27.7, 26.4, 25.9, 25.6, 23.1, 23.0, 22.82, 22.79, 22.78, 22.6, 22.0; MS ($ES^+$) *m/z* 933 (<5%, M+H), 467 (100%, M+2H); HRMS ($ES^+$) Calcd. for $C_{53}H_{73}N_8O_7$: 933.5602 (M+H), Found: 933.5605.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (141)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **109** (17 mg, 0.014 mmol) to yield **141** (13 mg, 97%) as an off-white solid. $[\alpha]_D^{25}$ −39.32 (*c* 0.5, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.52 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.57 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.94-1.02 (m, 2H, $CH_2$), 0.95 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 0.99 (d, *J* = 7.0 Hz, 3H, $CH_3$ (Leu)), 1.07-1.21 (m, 2H), 1.22-1.30 (m, 2H), 1.38-1.83 (m, 8H), 1.83-1.98 (m, 2H), 2.76-2.87 (m, 2H, $CH_2N$ (Lys)), 3.01 (s, 3H, $NCH_3$), 3.11-3.26 (m, 2H, $CH_2N$ (Arg)), 3.38 (s, 3H, $OCH_3$), 3.94-3.98 (m, 1H $CH_2O$ ($H_a$)), 4.12-4.21 (m, 2H, CH and $CH_2O$ ($H_b$)), 4.36 (s, 2H, oxazole-C$\underline{H}_2$), 4.50 (ABq, *J* = 15.0 Hz, 2H, $OCH_2CO$), 4.74-4.82 (m, 1H, CH), 5.85-5.93 (m, 1H, CH), 7.05-7.08 (m, 2H, ArH), 7.22-7.24 (m, 2H, ArH), 7.32-7.37 (m, 2H, ArH), 7.47 (d, *J* = 8.5 Hz, 1H, ArH), 7.54 (d, *J* = 9.5 Hz, 1H, ArH), 7.86 (s, 1H, ArH (oxazole)), 7.90-7.92 (m, 2H, ArH), 8.00-8.04 (m, 2H, ArH); $^{13}$C NMR (126 MHz, $CD_3OD$): δ 22.1, 22.6, 22.8, 23.4 ($CH_3$), 23.0, 26.2, 27.7, 29.7, 32.3, 39.3 ($CH_2$), 25.7, 25.9, 50.8, 50.9, 53.3 (CH), 31.1 ($NCH_3$), 41.4 ($CH_2N$ (Lys)), 42.0 ($CH_2N$ (Arg)), 58.5 ($OCH_3$), 66.7 (oxazole-$\underline{C}H_2$), 69.0 (O$\underline{C}H_2CO$), 69.3 ($CH_2O$), 116.1, 117.0, 124.9, 125.3, 126.0, 126.4, 127.6, 129.1, 129.2, 129.3, 130.8, 130.9 (ArCH), 120.6, 121.9, 130.8, 131.5, 135.1, 135.3, 154.1, 156.0 (ArC), 158.6 (C=N), 172.9, 174.0 (C=O). MS (ESI, +ve) *m/z* 893 (5%) $[M+H]^+$, 447 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{50}H_{69}N_8O_7$ 893.5289, found 893.5322.

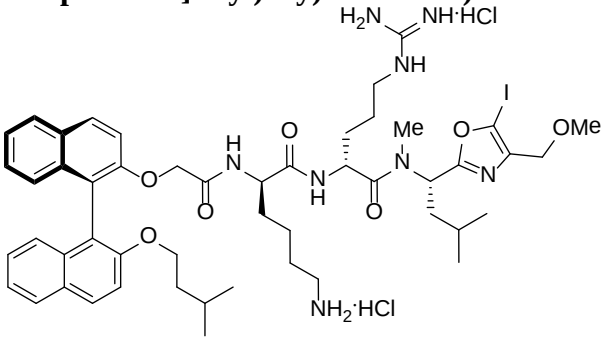
**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(methoxymethyl)-5-methyloxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (142)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **110** (37 mg, 0.029 mmol) to yield **142** (27 mg, 95%) as an off-white solid. $[\alpha]_D^{25}$ −74.29 (*c* 0.8, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.53 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.59 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.91-1.03 (m, 2H, $CH_2$), 0.96 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.00 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.15-1.31 (m, 4H), 1.43-1.83 (m, 8H), 1.77-1.98 (m, 2H), 2.33 (s, 3H, $CH_3$-oxazole), 2.76-2.88 (m, 2H, $CH_2N$ (Lys)), 3.03 (s, 3H, $NCH_3$), 3.13-3.28 (m, 2H, $CH_2N$ (Arg)), 3.36 (s, 3H, $OCH_3$), 3.96-3.99 (m, 1H $CH_2O$ ($H_a$)), 4.13-4.23 (m, 2H, CH and $CH_2O$ ($H_b$)), 4.31 (s, 2H, oxazole-C$\underline{H}_2$), 4.52 (ABq, *J* = 15.0 Hz, 2H, $OCH_2CO$), 4.75-4.84 (m, 1H, CH), 5.81-5.89 (m, 1H, CH), 7.06-7.10 (m, 2H, ArH),

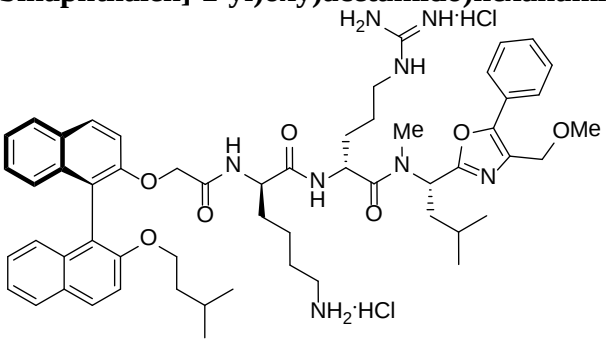
7.20-7.28 (m, 2H, ArH), 7.33-7.38 (m, 2H, ArH), 7.49 (d, *J* = 9.0 Hz, 1H, ArH), 7.55 (d, *J* = 9.0 Hz, 1H, ArH), 7.92-7.93 (m, 2H, ArH), 8.02-8.05 (m, 2H, ArH); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 22.1, 22.6, 22.8, 23.4 ($CH_3$), 23.0, 26.1, 27.8, 29.7, 32.3, 39.2, 39.3 ($CH_2$), 25.6, 25.9, 50.8, 53.3 (CH), 31.1 ($NCH_3$), 41.4 ($CH_2N$ (Lys)), 41.9 ($CH_2N$ (Arg)), 58.3 ($OCH_3$), 66.1 (oxazole-$\underline{C}H_2$), 69.0 ($O\underline{C}H_2CO$), 69.3 ($CH_2O$), 116.0, 116.9, 124.8, 125.2, 126.0, 126.4, 127.5, 127.6, 129.1, 129.3, 130.9 (ArCH), 120.6, 121.8, 130.7, 131.4, 132.5, 135.1, 135.2, 154.0, 155.9 (ArC), 158.6 (C=N), 170.7, 172.8, 174.0 (C=O). MS (ESI, +ve) *m/z* 908 (5%) $[M+H]^+$, 545 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{51}H_{71}N_8O_7$ 907.5446, found 907.5458.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(methoxymethyl)-5-iodooxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (143)**



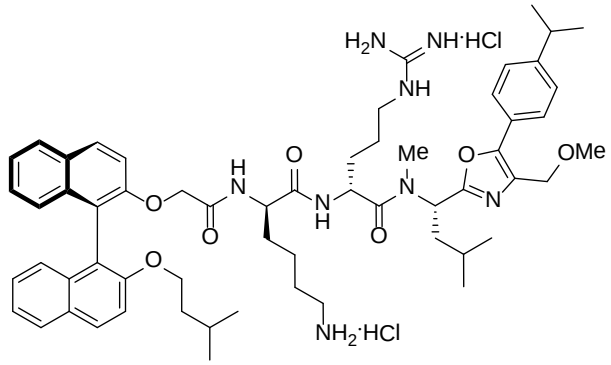
This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **111** (15.3 mg, 0.01 mmol) to yield **143** (6.8 mg, 52%) as a white solid. $[\alpha]_D^{25} = -21.4$ (*c* 0.21, MeOH). $^1$H NMR (500 MHz, $CD_3OD$) δ 0.56 (3H, d, *J* = 6.5 Hz), 0.62 (3H, d, *J* = 6.5 Hz), 0.98 - 1.04 (6H, ,m), 1.14 - 1.33 (5H, m), 1.47 - 2.04 (11H, m), 2.77 - 2.84 (2H, m), 3.06 (3H, s), 3.20 - 3.24 (2H, m), 3.34 - 3.35 (6H, m), 3.39 (3H, t, *J* = 10.0 Hz), 3.98 - 4.02 (1H, bm), 4.17 - 4.21 (2H, m), 4.32 (2H, s), 4.34 (1H, bs), 4.48 - 4.60 (3H, m), 5.90 - 5.93 (1H, m), 7.10 (2H, t, *J* = 7.7 Hz), 7.24 - 7.28 (2H, m), 7.35 - 7.41 (2H, m), 7.51 (1H, d, *J* = 9.0 Hz), 7.58 (1H, d, *J* = 8.2 Hz), 7.95 (2H, d, *J* = 8.2 Hz), 8.06 (2H, t, *J* = 9.2 Hz), 8.30 (1H, d, *J* = 7.9 Hz). $^{13}$C NMR (126 MHz, $CD_3OD$) δ 22.0, 22.6, 22.8, 23.1, 23.4, 25.7, 25.9, 26.1, 27.8, 29.7, 31.2, 32.4, 39.1, 40.5, 41.9, 50.7, 51.0, 58.6, 66.6, 69.1, 69.3, 103.4, 116.0, 117.0, 120.6, 121.9, 124.8, 125.2, 126.0, 126.4, 127.5, 127.6, 129.1, 129.3, 130.7, 130.8, 131.4, 135.1, 135.3, 143.8, 154.0, 155.9, 158.6, 161.4, 168.4, 171.0, 172.77 174.0. IR (neat) *ν* [$cm^{-1}$] = 3874 (s), 3752 (s), 2975 (w), 2289 (w), 1700 (s), 1587 (s), 1083 (w), 608 (s). MS ($ESI^+$) *m/2* = 510 (100 %, $[M+2H]^{2+}$), *m/z* = 1019 (2 %, $[M+H]^+$). HRMS ($ESI^+$) $[M+H]^+$ Calcd. for $C_{50}H_{68}IN_8O_7$: 1019.4256, Found: 1019.4280.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(methoxymethyl)-5-phenyloxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (144)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **112** (33 mg, 0.025 mmol) to yield **144** (25 mg, 96%) as an off-white solid. $[\alpha]_D^{25}$ −21.26 (*c* 1.0, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.48 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.54 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.88-0.97 (m, 2H, $CH_2$), 0.98 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.03 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.11-1.30 (m, 4H), 1.42-1.82 (m, 8H), 1.90-2.04 (m, 2H), 2.68-2.84 (m, 2H, $CH_2N$ (Lys)), 3.10 (s, 3H, $NCH_3$), 3.15-3.27 (m, 2H, $CH_2N$ (Arg)), 3.43 (s, 3H, $OCH_3$), 3.86-3.90 (m, 1H $CH_2O$ ($H_a$)), 4.05-4.09 (m, 1H, $CH_2O$ ($H_b$)), 4.13-4.22 (m, 1H, CH), 4.48 (ABq, *J* = 15.0 Hz, 2H, $OCH_2CO$), 4.51 (s, 2H, oxazole-C$\underline{H}_2$), 4.75-4.84 (m, 1H, CH), 5.94-5.97 (m, 1H, CH), 7.02-7.06 (m, 2H, ArH), 7.16-7.23 (m, 2H, ArH), 7.27-7.30 (m, 1H, ArH), 7.33-7.40 (m, 2H, ArH), 7.44-7.46 (m, 4H, ArH), 7.67-7.68 (m, 2H, ArH), 7.85 (d, *J* = 8.0 Hz, 1H, ArH), 7.90 (d, *J* = 8.0 Hz, 1H, ArH), 7.93 (d, *J* = 9.0 Hz, 1H, ArH), 8.01 (d, *J* = 9.5 Hz, 1H, ArH); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 22.1, 22.5, 22.8, 23.4 ($CH_3$), 23.0, 26.2, 27.7, 29.6, 32.3, 39.2 ($CH_2$), 25.6, 26.0, 50.9, 53.1 (CH), 31.2 ($NCH_3$), 40.4 ($CH_2N$ (Lys)), 42.0 ($CH_2N$ (Arg)), 58.5 ($OCH_3$), 67.3 (oxazole-$\underline{C}H_2$), 69.0 ($O\underline{C}H_2CO$), 69.4 ($CH_2O$), 116.0, 116.9, 124.8, 125.2, 125.9, 126.4, 127.4, 127.5, 127.6, 129.1, 129.2, 130.1, 130.2, 130.9 (ArCH), 120.5, 121.9, 128.9, 130.7, 131.4, 133.4, 135.1, 135.2, 154.1, 155.9 (ArC), 158.6 (C=N), 170.7, 172.8, 174.3 (C=O). MS (ESI, +ve) *m/z* 969 (5%) $[M+H]^+$, 485 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{56}H_{73}N_8O_7$ 969.5602, found 969.5620; HPLC $t_R$ = 28.4 min, see the HPLC trace provided for the specific gradient elution profile.

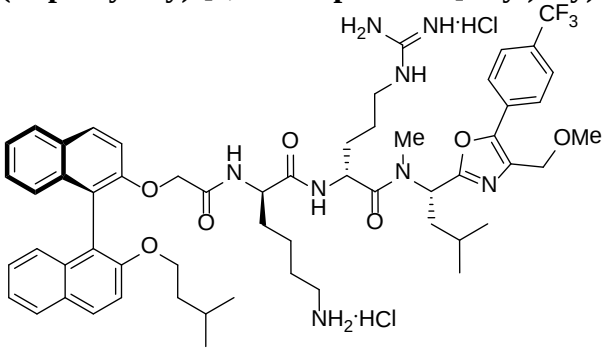
**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(5-(4-isopropylphenyl)-4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (145)**




This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **113** (36 mg, 0.026 mmol) to yield **145** (27 mg, 96%) as an off-white solid. $[\alpha]_D^{25}$ −3.78 (*c* 0.7, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.47 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.53 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.87-0.98 (m, 2H, $CH_2$), 0.98 (d, *J* = 6.0 Hz, 3H, $CH_3$ (Leu)), 1.03 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.10-1.30 (m, 10H), 1.40-1.87 (m, 8H), 1.88-2.06 (m, 2H), 2.69-2.84 (m, 2H, $CH_2N$ (Lys)), 2.86-3.74 (m, 1H, $C_6H_4C\underline{H}(CH_3)_2$), 3.12 (s, 3H, $NCH_3$), 3.14-3.27 (m, 2H, $CH_2N$ (Arg)), 3.43 (s, 3H, $OCH_3$), 3.83-3.87 (m, 1H $CH_2O$ ($H_a$)), 4.05-4.09 (m, 2H, $CH_2O$ ($H_b$)), 4.12-4.25 (m, 1H, CH), 4.48 (ABq, *J* = 15.0 Hz, 2H, $OCH_2CO$), 4.49 (s, 2H, oxazole-C$\underline{H}_2$), 4.74-4.84 (m, 1H, CH), 5.92-5.99 (m, 1H, CH), 7.02-7.04 (m, 2H, ArH), 7.14-7.28 (m, 3H, ArH), 7.32-7.34 (m, 3H, ArH), 7.43 (d, *J* = 9.0 Hz, 1H, ArH), 7.45 (d, *J* = 9.0 Hz, 1H, ArH), 7.58-7.59 (m, 2H, ArH), 7.83 (d, *J* = 7.5 Hz, 1H, ArH), 7.89 (d, *J* = 8.5 Hz, 1H, ArH), 7.92 (d, *J* = 9.0 Hz, 1H, ArH), 8.01 (d, *J* = 8.5 Hz, 1H, ArH); $^{13}$C NMR (75 MHz, $CD_3OD$): δ 22.1, 22.5, 22.8, 23.4 ($CH_3$), 22.9, 26.3, 27.6, 29.6, 32.3, 39.2, 39.4 ($CH_2$), 24.2, 24.3, 50.9, 51.0, 53.1 (CH), 31.2 ($NCH_3$), 40.4 ($CH_2N$ (Lys)), 42.0 ($CH_2N$ (Arg)), 58.5 ($OCH_3$), 67.3 (oxazole-$\underline{C}H_2$), 68.9 ($O\underline{C}H_2CO$), 69.4 ($CH_2O$), 116.1, 116.9, 124.7, 125.2, 126.0, 126.4, 127.6, 128.2, 129.1, 129.2, 130.8 (ArCH), 120.4, 122.0, 130.7, 131.4, 132.8, 135.1, 135.2, 151.4, 154.1, 155.9 (ArC), 158.6 (C=N), 170.7, 172.7, 174.3 (C=O). MS (ESI, +ve) *m/z* 1012 (5%) $[M+H]^+$, 506 (100%)

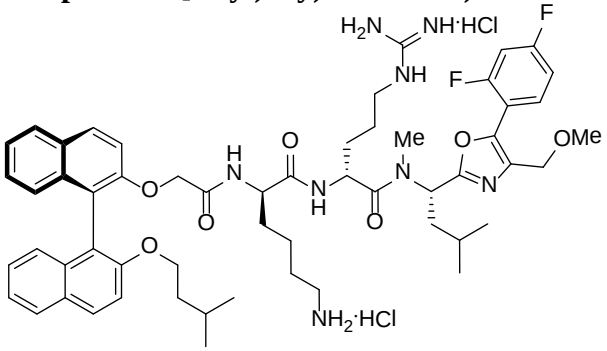
$[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{59}H_{79}N_8O_7$ 1011.6072, found 1011.6098; HPLC $t_R$ = 14.2 min, see the HPLC trace provided for the specific gradient elution profile.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(5-(4-trifluoromethylphenyl)-4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (146)**



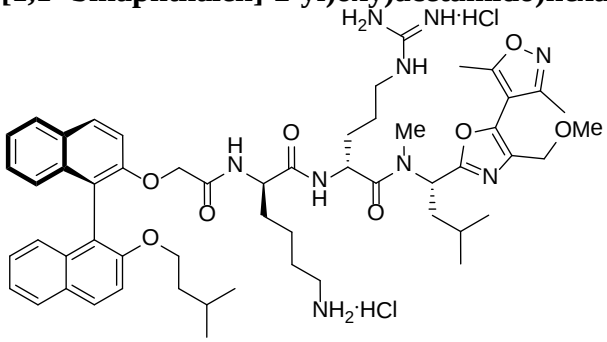
This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **114** (21 mg, 0.015 mmol) to yield **146** (14 mg, 86%) as an off-white solid. $[\alpha]_D^{25}$ +15.44 (*c* 0.7, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.51 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.57 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.96-0.98 (m, 2H, $CH_2$), 1.01 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.06 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.12-1.34 (m, 4H), 1.44-1.89 (m, 8H), 1.94-2.09 (m, 2H), 2.70-2.82 (m, 2H, $CH_2N$ (Lys)), 3.15 (s, 3H, $NCH_3$), 3.17-3.30 (m, 2H, $CH_2N$ (Arg)), 3.47 (s, 3H, $OCH_3$), 3.89-3.93 (m, 1H $CH_2O$ ($H_a$)), 4.08-4.13 (m, 1H, $CH_2O$ ($H_b$)), 4.15-4.24 (m, 1H, CH), 4.52 (ABq, *J* = 14.5 Hz, 2H, $OCH_2CO$), 4.55-4.59 (m, 2H, oxazole-C$\underline{H_2}$), 4.79-4.86 (m, 1H, CH), 5.97-5.99 (m, 1H, CH), 7.03-7.06 (m, 2H, ArH), 7.17-7.20 (m, 1H, ArH), 7.22-7.30 (m, 2H, ArH), 7.36-7.38 (m, 2H, ArH), 7.47-7.48 (m, 2H, ArH), 7.78-7.79 (m, 2H, ArH), 7.84-7.89 (m, 2H, ArH), 7.92 (d, *J* = 8.0 Hz, 1H, ArH), 7.95 (d, *J* = 9.0 Hz, 1H, ArH), 8.04 (d, *J* = 9.5 Hz, 1H, ArH); $^{13}$C NMR (126 MHz, $CD_3OD$): δ 22.1, 22.5, 22.8, 23.5 ($CH_3$), 23.0, 26.3, 27.7, 29.6, 32.3, 39.3 ($CH_2$), 25.6, 26.0, 51.1, 53.2 (CH), 31.3 ($NCH_3$), 40.4 ($CH_2N$ (Lys)), 42.0 ($CH_2N$ (Arg)), 58.6 ($OCH_3$), 67.3 (oxazole-$\underline{C}H_2$), 69.0 (O$\underline{C}H_2CO$), 69.5 ($CH_2O$), 116.1, 116.9, 124.8, 125.3, 126.0, 126.4, 126.4, 127.0, 127.6, 127.8, 129.1, 129.2, 130.8, 130.9 (ArCH), 120.6, 121.9, 130.7, 131.5, 132.5, 135.1, 135.2, 135.5, 154.1, 155.9 (ArC), 158.6 (C=N), 172.8, 174.4 (C=O). MS (ESI, +ve) *m/z* 1038 (5%) $[M+H]^+$, 520 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{57}H_{72}N_8O_7F_3$ 1037.5476, found 1037.5470; HPLC $t_R$ = 31.8 min, see the HPLC trace provided for the specific gradient elution profile.

**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(5-(2,4-difluorophenyl)-4-(methoxymethyl)oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (147)**



This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **115** (63 mg, 0.046 mmol) to yield **147** (48 mg, 97%) as an off-white solid. $[\alpha]_D^{25}$ −369.7 (*c* 0.88, MeOH); $^1$H NMR (500 MHz, $CD_3OD$): δ 0.49 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.54 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.90-1.04 (m, 2H, $CH_2$), 0.96 (d, *J* = 6.0 Hz, 3H, $CH_3$ (Leu)), 1.01 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.10-1.31 (m, 4H), 1.44-1.78 (m, 8H), 1.89-2.02 (m, 2H), 2.74-2.85 (m, 2H, $CH_2N$ (Lys)), 3.10 (s, 3H, $NCH_3$), 3.14-3.27 (m, 2H, $CH_2N$ (Arg)), 3.35 (s, 3H, $OCH_3$), 3.87-3.92 (m, 1H $CH_2O$ ($H_a$)), 4.07-4.12 (m, 1H, $CH_2O$ ($H_b$)), 4.11-4.26 (m, 1H, CH), 4.37-4.41 (m, 2H, oxazole-C$\underline{H}_2$), 4.49 (ABq, *J* = 14.5 Hz, 2H, $OCH_2CO$), 4.75-4.84 (m, 1H, CH), 5.92-5.95 (m, 1H, CH), 7.03-7.08 (m, 3H, ArH), 7.11-7.22 (m, 3H, ArH), 7.27-7.30 (m, 1H, ArH), 7.32-7.35 (m, 1H, ArH), 7.44-7.48 (m, 2H, ArH), 7.57-7.62 (m, 2H, ArH), 7.85 (d, *J* = 8.0 Hz, 1H, ArH), 7.89 (d, *J* = 8.0 Hz, 1H, ArH), 7.95 (d, *J* = 9.0 Hz, 1H, ArH), 8.00 (d, *J* = 9.0 Hz, 1H, ArH); $^{13}$C NMR (126 MHz, $CD_3OD$): δ 22.1, 22.5, 22.8, 23.4 ($CH_3$), 22.9, 26.2, 27.6, 29.6, 32.2, 39.3, 39.4 ($CH_2$), 25.6, 26.0, 51.0, 53.2 (CH), 31.3 ($NCH_3$), 40.4 ($CH_2N$ (Lys)), 42.0 ($CH_2N$ (Arg)), 58.6 ($OCH_3$), 66.8 (oxazole-$\underline{C}H_2$), 69.0 (O$\underline{C}H_2CO$), 69.4 ($CH_2O$), 105.7 (t, *J* = 26 Hz, ArCH), 113.2 (dd, $J_1$ = 4, $J_2$ = 22 Hz, ArCH), 116.1, 116.9, 125.2, 125.9, 126.4, 127.5, 127.6, 129.1, 129.2, 130.8, 130.9 (ArCH), 132.9 (dd, $J_1$ = 3, $J_2$ = 10 Hz, ArCH), 120.5, 121.9, 130.7, 131.4, 135.1, 135.2, 135.8, 154.1, 155.9 (ArC), 158.6 (C=N), 161.0 (d, *J* = 250 Hz, ArC), 165.1 (d, *J* = 250 Hz, ArC), 170.7, 172.8, 174.3 (C=O). MS (ESI, +ve) *m/z* 1006 (5%) $[M+H]^+$, 504 (100%) $[M+2H]^+$. HRMS (ESI, +ve) calcd for $C_{56}H_{71}N_8O_7F_2$ 1005.5414, found 1005.5453; HPLC $t_R$ = 29.1 min, see the HPLC trace provided for the specific gradient elution profile.

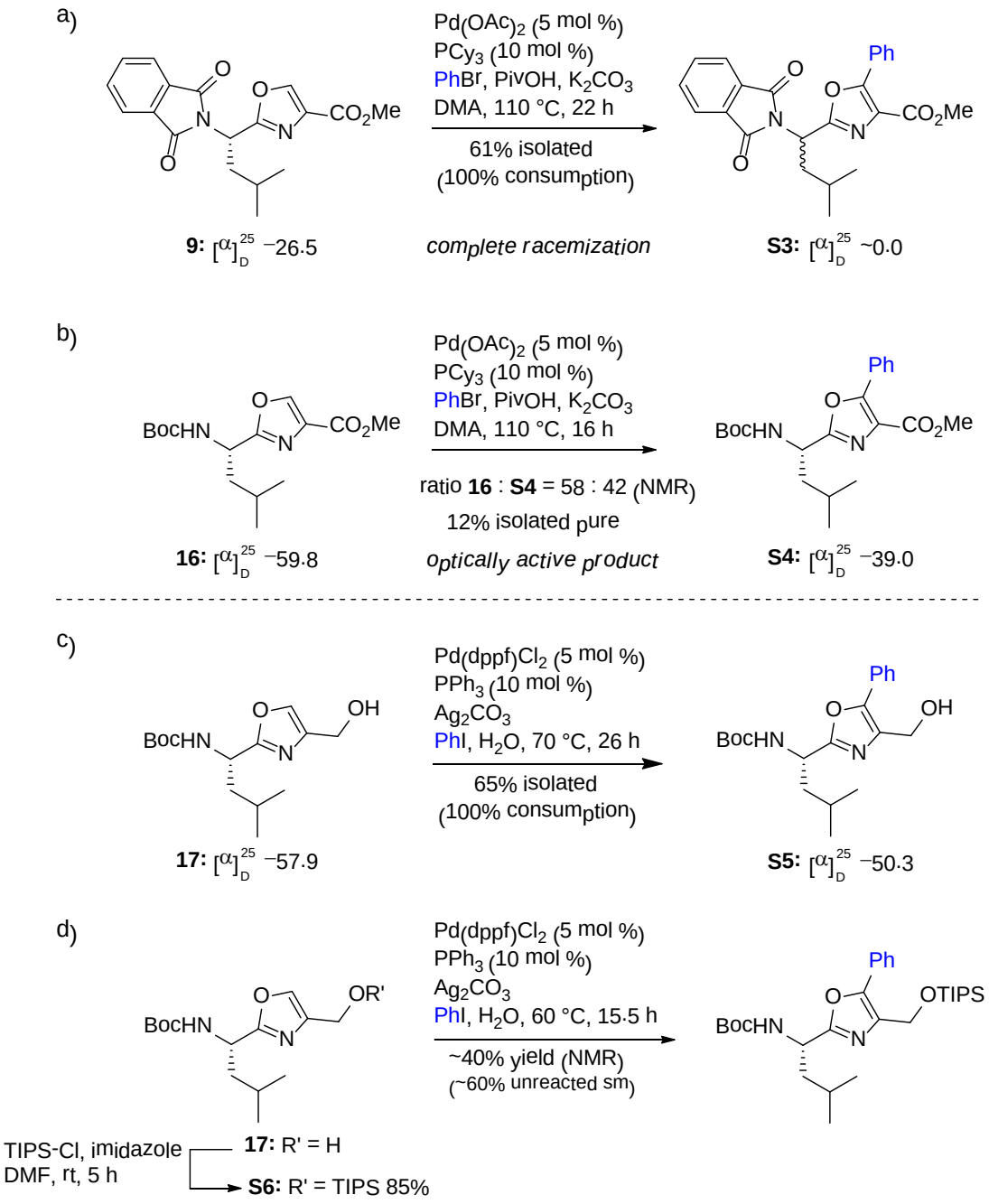
**(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*S*)-1-(4-(methoxymethyl)-5-(3,5-dimethylisoxazol-4-yl)-oxazol-2-yl)-3-methylbutyl)-*N*-methylamino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (148)**



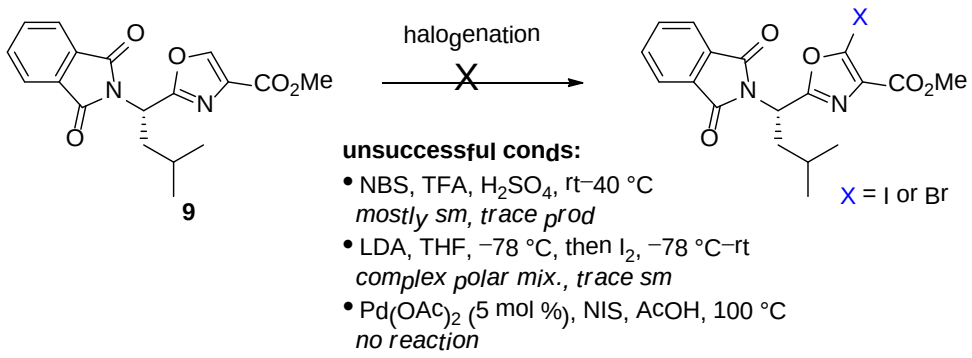

This compound was prepared according to *General Procedure 4* using Type **D** protected peptide **116** (32 mg, 0.024 mmol) to yield **148** (25 mg, 98%) as an off-white solid. $[\alpha]_D^{25}$ −61.35 (*c* 1.1, MeOH). $^1$H NMR (500 MHz, $CD_3OD$): δ 0.53 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.59 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.92-1.08 (m, 2H, $CH_2$), 0.99 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.04 (d, *J* = 6.5 Hz, 3H, $CH_3$ (Leu)), 1.14-1.33 (m, 4H), 1.37-1.83 (m, 8H), 1.86-2.06 (m, 2H), 2.24 (s, 3H, isoxazole-$CH_3$), 2.42 (s, 3H, isoxazole-$CH_3$), 2.75-2.86 (m, 2H, $CH_2N$ (Lys)), 3.08 (s, 3H, $NCH_3$), 3.16-3.28 (m, 2H, $CH_2N$ (Arg)), 3.39 (s, 3H, $OCH_3$), 3.94-3.99 (m, 1H $CH_2O$ ($H_a$)), 4.13-4.21 (m, 2H, CH and $CH_2O$ ($H_b$)), 4.30-4.33 (m, 2H, oxazole-C$\underline{H}_2$), 4.52 (ABq, *J* = 15.0 Hz, 2H, $OCH_2CO$), 4.73-4.85 (m, 1H, CH), 5.94 (dd, $J_1$ = 6.0, $J_2$ = 9.5 Hz, 1H, CH), 7.07-7.10 (m, 2H, ArH), 7.22-7.26 (m, 2H, ArH), 7.33-7.39 (m, 2H, ArH), 7.49 (d, *J* = 9.0 Hz, 1H, ArH), 7.55 (d, *J* = 8.5 Hz, 1H, ArH), 7.93 (d, *J* = 8.0 Hz, 2H, ArH), 8.02-8.06 (m, 2H, ArH); $^{13}$C NMR (126 MHz, $CD_3OD$): δ 10.8, 11.7 (2 x isoxazole-$\underline{C}H_3$), 22.0, 22.5, 22.8, 23.4 ($CH_3$), 23.1, 26.2, 27.7, 29.7, 32.3, 39.1, 39.3 ($CH_2$), 25.6, 29.9, 50.9, 51.0, 53.3 (CH), 31.2 ($NCH_3$), 40.4 ($CH_2N$ (Lys)), 41.9 ($CH_2N$ (Arg)), 58.9 ($OCH_3$), 66.6 (oxazole-$\underline{C}H_2$), 69.0 (O$\underline{C}H_2CO$), 69.3 ($CH_2O$), 116.0, 117.0, 124.8, 125.2, 126.0, 126.4, 127.5, 127.6, 129.1, 129.3, 130.9 (ArCH), 105.9, 120.6, 121.9, 130.7, 131.5, 135.1, 135.2, 136.5, 154.1, 155.9, 160.5 (ArC), 158.6 (C=N), 170.6, 172.8, 174.3 (C=O). MS (ESI, +ve) *m/z* 989 (5%) $[M+H]^+$, 495 (100%) $[M+2H]^+$.

HRMS (ESI, +ve) calcd for $C_{55}H_{74}N_9O_8$ 988.5660, found 988.5681; HPLC $t_R$ = 25.6 min, see the HPLC trace provided for the specific gradient elution profile.

## Additional Reaction Schemes

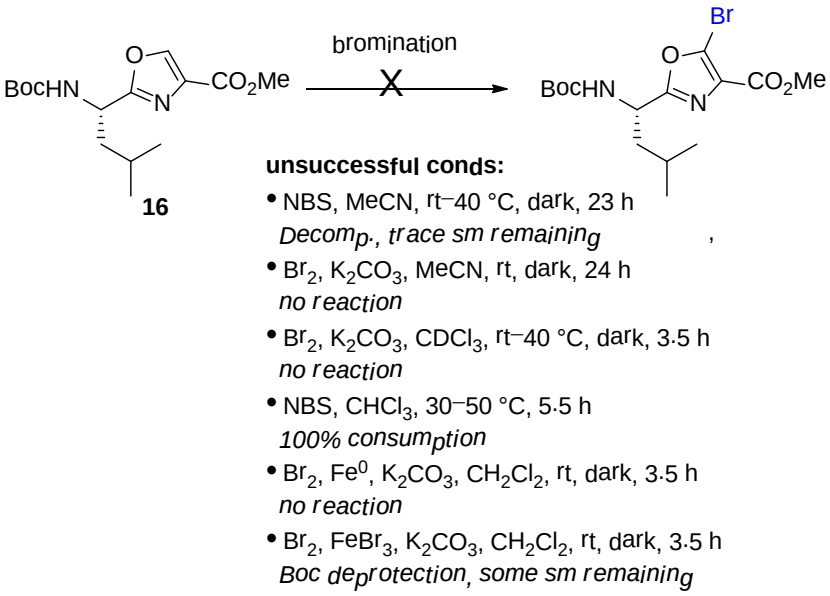



**Scheme S1** C-5-Arylation studies.



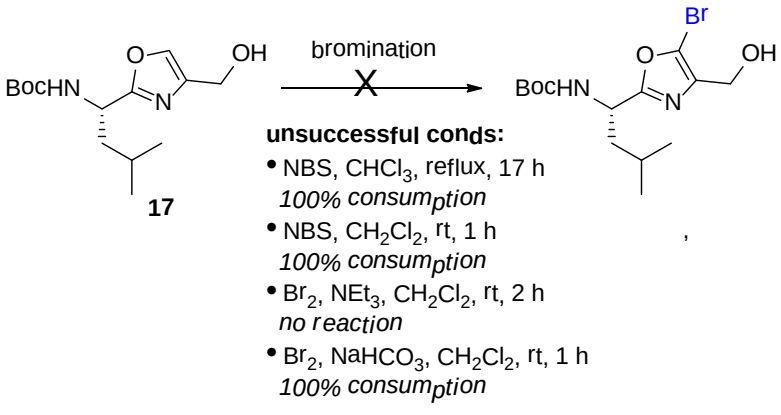

**Scheme S2** C-5-Halogenation studies with oxazole **9**.

---



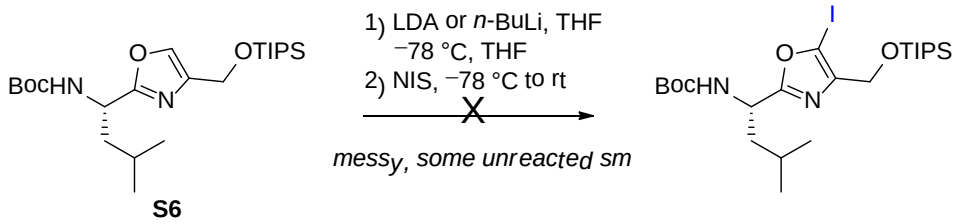

**Scheme S3** C-5-Bromination studies with oxazole **16**.

---

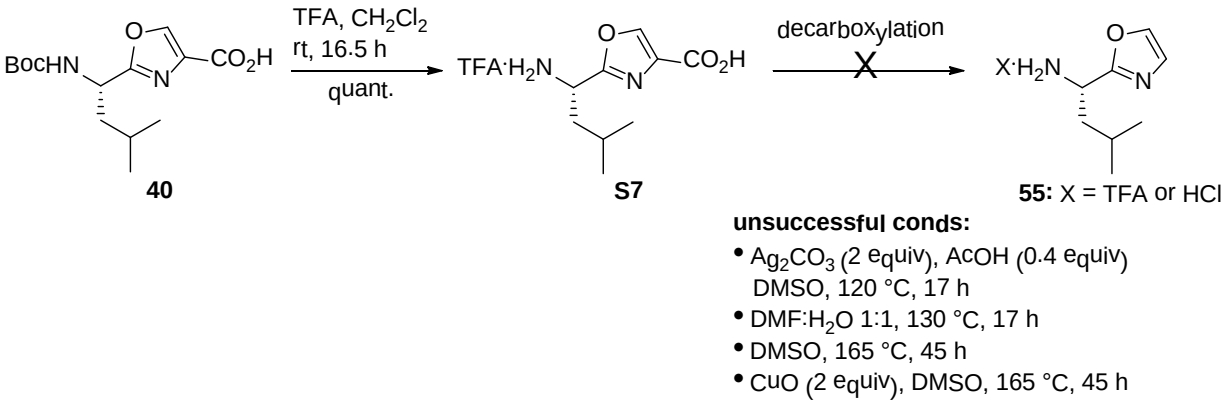



**Scheme S4** C-5-Bromination studies with oxazole **17**.

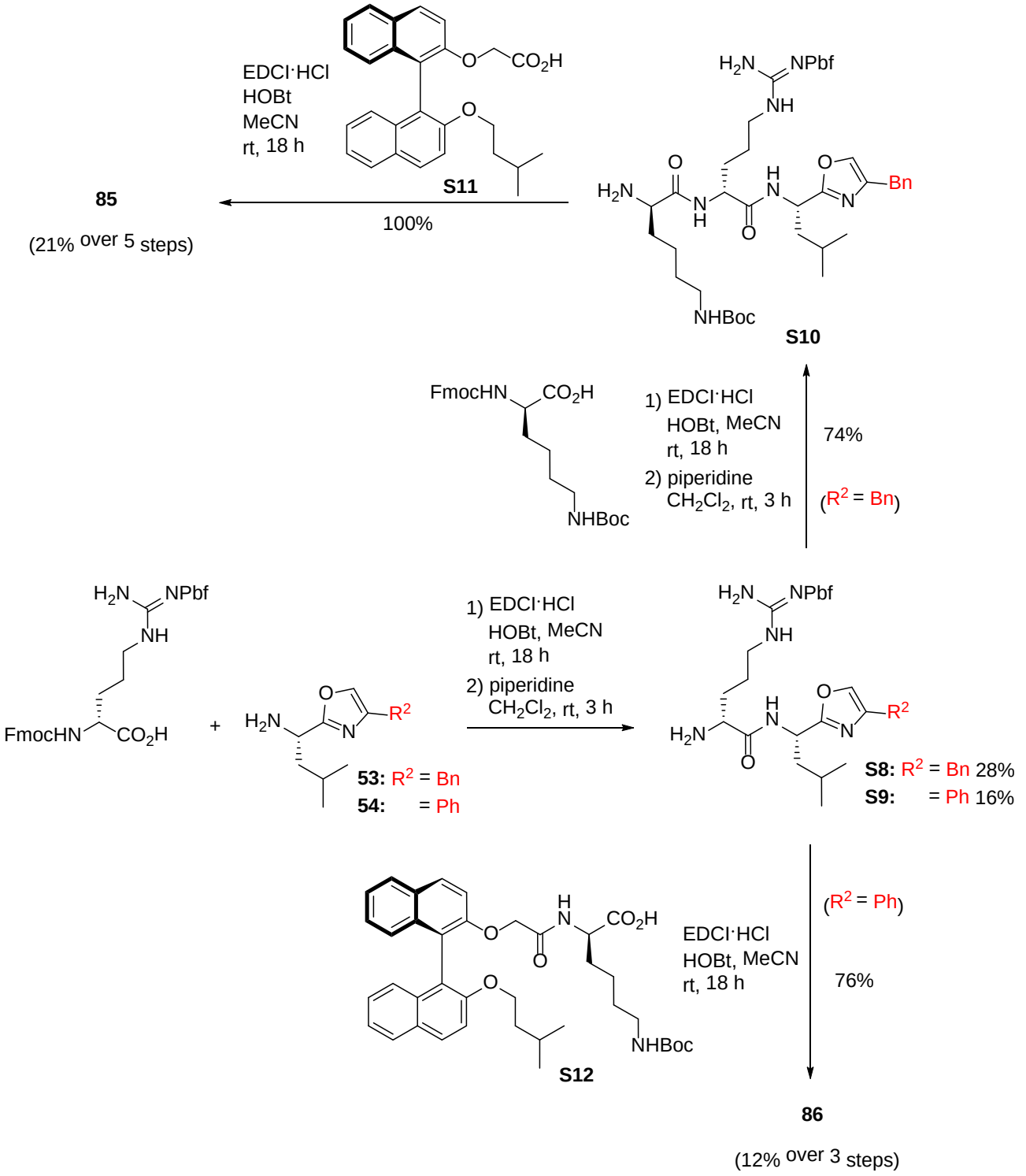
---



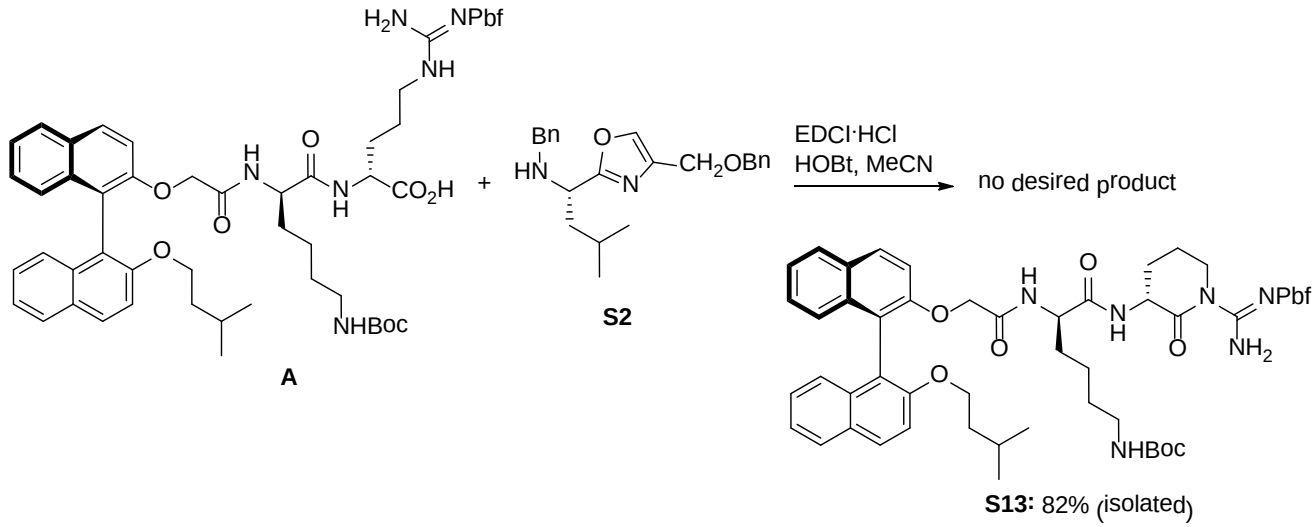

**Scheme S5** Attempted C-5-iodination of oxazole **S6**.




**Scheme S6** Decarboxylation studies with oxazole **S7**.




**Scheme S7** Synthesis of Type D protected peptidomimetics **85** and **86**.

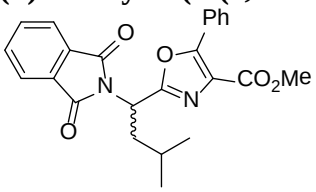



**Scheme S8** Synthesis of Arg-cyclized peptide **S13** from the attempted reaction of carboxylic acid A and *N*-Bn oxazole **S2**.

---

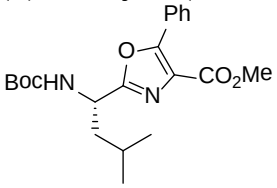
## Additional Experimental Procedures (for Schemes S1−S8)

### (±)-Methyl 2-(1-(1,3-dioxoisoindolin-2-yl)-3-methylbutyl)-5-phenyloxazole-4-carboxylate (S3)



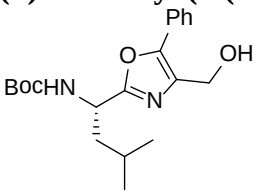

Based on a literature C−H arylation method,[S11] a dry 10 mL glass reaction tube equipped with a stir bar was charged in the air with **9** (51.4 mg, 0.15 mmol), $Pd(OAc)_2$ (1.7 mg, 0.0075 mmol), $PCy_3$ (4.2 mg, 0.015 mmol) and $K_2CO_3$ (62.2 mg, 0.45 mmol). The contents were dried under high vacuum for 1 h, then PhBr (28.3 mg, 0.18 mmol) and PivOH (6.1 mg, 0.060 mmol) were added. The tube was fitted with a rubber septum, evacuated and refilled with $N_2$ (two cycles), then DMA (0.75 mL) was introduced and the mixture heated at 110 °C for 22 h. After cooling to rt, the mixture was diluted with EtOAc (20 mL) and water (20 mL). The organic phase was washed with brine (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (15% EtOAc/pet. ether) gave **S3** (38.3 mg, 61%) as a pale yellow gum, which was found to be optically inactive, indicating that racemization had occurred under the basic reaction conditions. TLC (25% EtOAc/pet. ether) $R_F$ = 0.57; $[\alpha]_D^{25}$ 0.0 (*c* 1.47, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.93 (m, 2H), 7.90 – 7.85 (m, 2H), 7.78 – 7.73 (m, 2H), 7.46 – 7.40 (m, 3H), 5.66 (dd, *J* = 11.0, 4.5 Hz, 1H), 3.91 (s, 3H), 2.61 (ddd, *J* = 14.6, 10.9, 4.3 Hz, 1H), 2.26 (ddd, *J* = 14.1, 9.4, 4.6 Hz, 1H), 1.67 – 1.56 (m, 1H), 1.04 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.3, 162.4, 159.8, 155.8, 134.3, 131.6, 130.3, 128.5, 128.3, 126.9, 126.7, 123.6, 52.3, 46.3, 38.2, 24.8, 23.1, 21.3; MS ($ES^+$) *m/z* 441 (100%, M+Na), 419 (55%, M+H); HRMS ($ES^+$) Calcd. for $C_{24}H_{22}N_2NaO_5$: 441.1426 (M+Na), Found: 441.1405.

**(*S*)-Methyl 2-(1-amino-3-methylbutyl)-5-phenyloxazole-4-carboxylate (S4)**



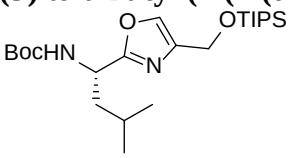

Based on a literature C−H arylation method,[S11] a dry 10 mL glass reaction tube equipped with a stir bar was charged in the air with **16**[S4] (46.9 mg, 0.15 mmol), $Pd(OAc)_2$ (1.7 mg, 0.0075 mmol), $PCy_3$ (4.2 mg, 0.015 mmol) and $K_2CO_3$ (62.2 mg, 0.45 mmol). The contents were dried under high vacuum for 1 h, then PhBr (28.3 mg, 0.18 mmol) and PivOH (6.1 mg, 0.060 mmol) were added. The tube was fitted with a rubber septum, evacuated and refilled with $N_2$ (two cycles), then DMA (0.75 mL) was introduced and the mixture heated at 110 °C for 16 h. After cooling to rt, the mixture was diluted with EtOAc (20 mL) and water (20 mL). The organic phase was washed with brine (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. $^1$H NMR analysis of the residue showed the starting material **16** and the desired product **S4** in a ratio of 58:42. A small amount of pure **S4** (7.2 mg, 12%, pale yellow gum) was isolated after partial separation from **16** via flash chromatography (10% EtOAc/pet. ether). This sample was found to be optically active, indicating that exchanging the phthalimide (see reaction above) for the Boc protecting group prevented racemization under the basic conditions. TLC (20% EtOAc/pet. ether) $R_F$ = 0.46; $[\alpha]_D^{25}$ −39.0 (*c* 0.36, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.06 – 8.00 (m, 2H), 7.50 – 7.44 (m, 3H), 5.16 – 4.99 (m, 2H), 3.93 (s, 3H), 1.85 – 1.66 (m, 3H), 1.44 (s, 9H), 1.00 – 0.95 (m, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 163.4, 162.5, 155.4, 155.1, 130.4, 128.4, 126.8, 126.6, 80.1, 52.3, 47.3, 43.5, 28.3, 24.7, 22.7, 22.0; MS ($ES^+$) *m/z* 411 (100%, M+Na), 389 (33%, M+H), 333 (33%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{21}H_{28}N_2NaO_5$: 411.1896 (M+Na), Found: 411.1884.

**(*S*)-*tert*-Butyl (1-(4-(hydroxymethyl)-5-phenyloxazol-2-yl)-3-methylbutyl)carbamate (S5)**



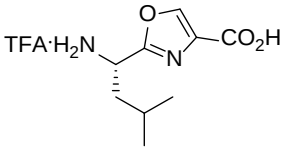

Based on a literature C−H arylation method,[S8] a 15 mL glass vial equipped with a stir bar was charged in the air with **17** (71.1 mg, 0.25 mmol), $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$ (10.2 mg, 0.013 mmol), $PPh_3$ (6.6 mg, 0.025 mmol), $Ag_2CO_3$ (137.8 mg, 0.50 mmol), PhI (61.2 mg, 0.30 mmol) and water (2.5 mL). The vial was fitted with a rubber septum, evacuated and refilled with $N_2$ (two cycles), then heated at 70 °C with rapid stirring for 26 h during which time a silver mirror formed on the reaction vial. After cooling to rt, the mixture was filtered through celite with the aid of $CH_2Cl_2$ (30 mL), then concentrated under reduced pressure. Flash chromatography (20% EtOAc/pet. ether) gave **S5** (58.8 mg, 65%) as a pale yellow gum. TLC (50% EtOAc/pet. ether) $R_F$ = 0.65; $[\alpha]_D^{25}$ −50.3 (*c* 1.15, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.7 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 5.33 (bm, 1H), 5.06 – 4.95 (m, 1H), 4.74 (d, *J* = 4.4 Hz, 2H), 3.67 (bs, 1H), 1.81 – 1.62 (m, 3H), 1.44 (s, 9H), 0.96 (d, *J* = 6.0 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 163.5, 155.1, 147.2, 134.6, 128.8, 128.6, 127.9, 126.1, 79.9, 56.7, 47.4, 43.7, 28.3, 24.7, 22.6, 22.1; MS ($ES^+$) *m/z* 383 (62%, M+Na), 361 (100%, M+H), 305 (32%, M+HCOOH−Boc); HRMS ($ES^+$) Calcd. for $C_{20}H_{28}N_2NaO_4$: 383.1947 (M+Na), Found: 383.1949.

**(*S*)-*tert*-Butyl (1-(4-(triisopropylsilyloxymethyl)oxazol-2-yl)-3-methylbutyl)carbamate (S6)**



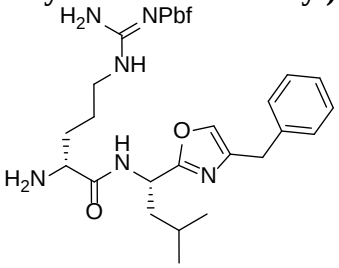
To a solution of alcohol **17** (284 mg, 1.00 mmol) and imidazole (245 mg, 2.50 mmol) in DMF (5.0 mL) under $N_2$ was stirred at rt for 10 min, then TIPS−Cl (0.25 mL, 1.20 mmol) was added and the mixture stirred at rt for 5 h. After dilution with water (20 mL) and $Et_2O$ (20 mL), the organic layer was washed sequentially with saturated $NaHCO_3$ (20 mL), water (20 mL) and brine (20 mL), then dried ($MgSO_4$) and concentrated. Flash chromatography (0.5% EtOAc/pet. ether to 4% EtOAc/pet. ether) gave **S6** (375 mg, 85%) as a colorless oil. TLC (5% EtOAc/pet. ether) $R_F$ = 0.44; $[\alpha]_D^{25}$ −40.3 (*c* 0.94, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.48 (s, 1H), 5.04 – 4.97 (m, 1H), 4.96 – 4.88 (m, 1H), 4.74 (s, 2H), 1.77 – 1.59 (m, 3H), 1.43 (s, 9H), 1.20 – 1.11 (m, 3H), 1.08 (d, *J* = 6.9 Hz, 18H), 0.94 (d, *J* = 6.0 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$ δ) δ 164.6, 155.0, 141.6, 134.6, 79.8, 59.3, 47.4, 43.6, 28.3, 24.6, 22.6, 22.2, 17.9, 11.9; MS ($ES^+$) *m/z* 463 (100%, M+Na), 441 (68%, M+H); HRMS ($ES^+$) Calcd. for $C_{23}H_{44}N_2NaO_4Si$: 463.2968 (M+Na), Found: 463.2993.

**(*S*)-3-Methyl-1-(4-carboxyoxazol-2-yl)butan-1-ammonium trifluoroacetate (S7)**



This compound was prepared according to *General Procedure 3* using Type **B** protected amine **40** (37.9 mg, 0.13 mmol) and omitting the aqueous work-up to give amine·TFA salt **S7** (43.7 mg, 110% of theoretical due to residual TFA) as a light brown gum. $^1$H NMR (300 MHz, $CD_3OD$) δ 8.58 (s, 1H), 4.68 (t, *J* = 6.5 Hz, 1H), 2.10 – 1.96 (m, 1H), 1.93 – 1.79 (m, 1H), 1.62 (sep, *J* = 6.5 Hz, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H); $^{13}$C NMR (75 MHz, $CD_3OD$) δ 163.7, 162.1, 147.1, 135.2, 48.3, 41.9, 25.7, 22.7, 22.0; MS ($ES^+$) *m/z* 199 (100%, M+H); HRMS ($ES^+$) Calcd. for $C_9H_{14}N_2NaO_3$: 221.0902 (M+Na), Found: 221.0900. Note that a similar synthetic route to the free amino acid form of **S7** (i.e., not the TFA salt) has been reported using different protecting groups.[S12]

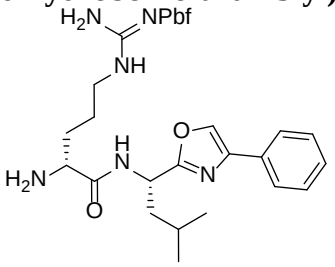
**(*R*)-2-Amino-*N*-((*S*)-1-(4-benzyloxazol-2-yl)-3-methylbutyl)-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentanamide (S8)**



This compound was prepared in two steps. The initial coupling reaction was performed according to *General Procedure 1* using amine **53** (70 mg, 0.29 mmol) and Fmoc-(*R*)-Arg(Pbf)-OH (186 mg, 0.29 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) yielded the Fmoc-protected precursor (100 mg, 40%). The protected amine was then stirred in 1% piperidine/$CH_2Cl_2$ for 3 h at rt. After removal of the solvent under reduce pressure, the residue was subjected to flash chromatography (2% MeOH/$CH_2Cl_2$ to 5% MeOH/$CH_2Cl_2$) to yield the free amine **S8** (50 mg, 69%, or 28% over two steps) as a solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 7.2 Hz, 3H), 1.47 (s, 6H, 2 x $CH_3$ (Pbf)), 1.49-1.63 (m, 4H), 1.72-1.77 (m, 3H), 2.08 (s, 3H, $CH_3$

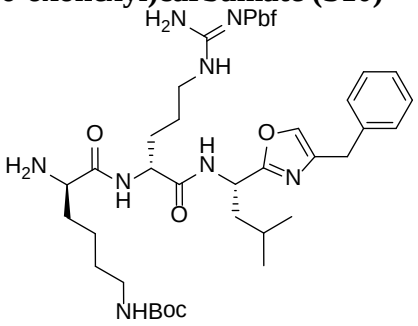
(Pbf)), 2.49 (s, 3H, $CH_3$ (Pbf)), 2.59 (s, 3H, $CH_3$ (Pbf)), 2.93 (s, 2H, $CH_2$ (Pbf)), 3.08-3.19 (m, 2H), 3.37-3.46 9m, 1H), 3.78 (s, 2H), 5.08-5.16 (m, 1H), 6.39 (br s, NH), 7.15-7.28 9m, 6H), 7.93 (d, *J* = 8.7 Hz, NH).

**(*R*)-2-Amino-*N*-((*S*)-1-(4-phenyloxazol-2-yl)-3-methylbutyl)-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentanamide (S9)**



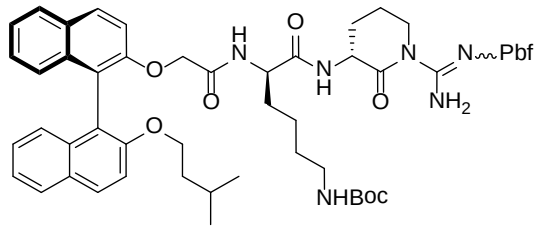
This compound was prepared in two steps. The initial coupling reaction was performed according to *General Procedure 1* using amine **54** (90 mg, 0.39 mmol) and Fmoc-(*R*)-Arg(Pbf)-OH (253 mg, 0.39 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) yielded the Fmoc-protected precursor (62 mg, 18%). The protected amine was then stirred in 1% piperidine/$CH_2Cl_2$ for 3 h at rt. After removal of the solvent under reduce pressure, the residue was subjected to flash chromatography (2% MeOH/$CH_2Cl_2$ to 5% MeOH/$CH_2Cl_2$) to yield the free amine **S9** (40 mg, 87%, or 16% over two steps) as a solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 0.96 (d, *J* = 6.3 Hz, 3H), 1.00 (d, *J* = 6.3 Hz, 3H), 1.49 (s, 6H, 2 x $CH_3$ (Pbf)), 1.57-1.78 (m, 4H), 1.86-1.91 (m, 3H), 2.11 (s, 3H, $CH_3$ (Pbf)), 2.53 (s, 3H, $CH_3$ (Pbf)), 2.60 (s, 3H, $CH_3$ (Pbf)), 2.77 (s, 2H, $CH_2$ (Pbf)), 3.17-3.31 (m, 2H), 3.73-3.82 (m, 1H), 5.20-5.28 (m, 1H), 6.58 (br s, 2H, NH), 6.82 (br s, 1H, NH), 7.28-7.41 (m, 3H), 7.69 (d, *J* = 7.2 Hz, 2H), 8.35 (d, *J* = 7.8 Hz, 1H, NH). See the section "*Synthesis of Type D Protected Peptidomimetics*" for the subsequent preparation of compound **86**.

***tert*-Butyl ((*R*)-5-amino-6-(((*R*)-1-(((*S*)-1-(4-benzyloxazol-2-yl)-3-methylbutyl)amino)-1-oxo-5-(-2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-6-oxohexyl)carbamate (S10)**



This compound was prepared in two steps. The initial coupling reaction was performed according to *General Procedure 1* using amine **S8** (50 mg, 0.077 mmol) and Fmoc-(*R*)-Lys(Boc)-OH (36 mg, 0.077 mmol). Flash chromatography (100% $CH_2Cl_2$ to 3% MeOH/$CH_2Cl_2$) yielded the Fmoc-protected precursor (70 mg, 82%). The protected amine was then stirred in 1% piperidine/$CH_2Cl_2$ for 3 h at rt. After removal of the solvent under reduce pressure, the residue was subjected to flash chromatography (2% MeOH/$CH_2Cl_2$ to 5% MeOH/$CH_2Cl_2$) to yield the free amine **S10** (50 mg, 90%, or 74% over two steps) as a solid. $^1$H NMR (300 MHz, $CDCl_3$) δ 0.87-0.92 (m, 6H), 1.33-1.86 (m, 13H), 1.40-1.45 (m, 15H, $^t$Bu and 2 x $CH_3$ (Pbf)), 2.07 (s, 3H, $CH_3$ (Pbf)), 2.49 (s, 3H, $CH_3$ (Pbf)), 2.56 (s, 3H, $CH_3$ (Pbf)), 2.93 (s, 2H, $CH_2$ (Pbf)), 3.05-3.24 (m, 4H), 3.78 (s, 2H), 4.16-4.55 (m, 2H), 5.04-5.12 (m, 2H), 6.51-6.46 (m, NH), 7.12-7.28 (m, 6H). See the section "*Synthesis of Type D Protected Peptidomimetics*" for the subsequent preparation of compound **85**.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxo-6-(((*R*)-2-oxo-1-(-*N*'-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)carbamimidoyl)piperidin-3-yl)amino)hexyl)carbamate (S13)**




This compound was formed as the major product in the attempted coupling of carboxylic acid **A** (89 mg, 0.085 mmol) and *N*,*O*-dibenzylated amine **S2** (45 mg, 0.097 mmol) according to *General Procedure 1*. Flash chromatography (100% $CH_2Cl_2$ to 1% MeOH/$CH_2Cl_2$) gave **S13** (72 mg, 82%) as a white solid. This compound was also a minor side product of most other coupling reactions with acid **A**. It has a slightly higher $R_F$ value than the desired peptidomimetic oxazoles in a MeOH/$CH_2Cl_2$ developing system, and is easily separated by flash chromatography from the desired products. TLC (5% MeOH/$CH_2Cl_2$) $R_F$ = 0.50; $^1$H NMR (500 MHz, $CDCl_3$): δ 0.52 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.57 (d, *J* = 6.5 Hz, 3H, $CH_3$), 0.84-1.02 (m, 4H), 1.13-1.35 (m, 6H), 1.38-1.59 (m, 2H), 1.43 (s, 9H, $^t$Bu), 1.47 (s, 6H, 2 x $CH_3$ (Pbf)), 1.65-1.51 (m, 3H), 2.11 (s, 3H, $CH_3$ (Pbf)), 2.28-2.35 (m, 1H), 2.52 (s, 3H, $CH_3$ (Pbf)), 2.57 (s, 3H, $CH_3$ (Pbf)), 2.89-3.01(m, 2H, $CH_2$N (Lys)), 2.97 (s, 2H, $CH_2$ (Pbf)), 3.37-3.42 (m, 1H), 3.88-3.93 (m, 1H), 3.99-4.04 (m, 1H), 4.08-4.12 (m, 1H), 4.44-4.60 (m, 5H), 6.19 (d, *J* = 8.0 Hz, 1H, NH), 6.75 (d, *J* = 6.0 Hz, 1H, NH), 7.13 (d, *J* = 8.5 Hz, 1H, ArH), 7.15 (d, *J* = 9.0 Hz, 1H, ArH), 7.22-7.26 (m, 2H, ArH), 7.31-7.38 (m, 3H, ArH), 7.46 (d, *J* = 9.5 Hz, 1H, ArH), 7.87-7.88 (m, 2H, ArH), 7.97 (d, *J* = 8.5 Hz, 1H, ArH), 7.98 (d, *J* = 8.5 Hz, 1H, ArH), 9.38 (br s, 1H, NH); $^{13}$C NMR (126 MHz, $CDCl_3$): δ 12.4, 17.9, 19.2, 19.7, 22.1, 22.3, 22.5, 24.6, 24.8, 28.4, 28.6, 29.2, 30.3, 38.0, 42.0, 43.1, 51.0, 52.4, 68.0, 68.5, 86.6, 114.0, 116.1, 117.7, 119.7, 120.5, 124.0, 124.3, 124.8, 125.1, 125.5, 126.7, 126.8, 128.0, 128.1, 129.3, 129.7, 129.8, 132.8, 133.7, 133.9, 138.9, 152.2, 153.8, 154.4, 155.9, 159.3, 168.8, 170.8, 175.2. MS (ESI, +ve) *m/z* 1034 (20%) $[M+H]^+$; 1056 (100%) $[M+Na]^+$. HRMS (ESI, +ve) calcd for $C_{57}H_{73}N_6O_{10}S$ 1033.5109, found 1033.5081.

**Antibacterial Testing Methods**

***S. aureus, E. faecalis, S. pneumoniae, E. coli, A. baumannii, VISA and VRE***

The test organisms for all compounds were *Staphylococcus aureus* ATCC 29213, *Staphylococcus aureus* NCTC 10442, *Enterococcus faecalis* ATCC 29212, *Streptococcus pneumoniae* ATCC 49619 and *Escherichia coli* ATCC 25922. The test organisms for selected compounds were *Acinetobacter baumannii* ATCC 19606, *Acinetobacter baumannii* ATCC 15308, *Staphylococcus aureus* Mu50 (VISA), *Enterococcus faecalis* ATCC 51299 (VRE) and *Enterococcus faecalis* clinical (VRE).

Each compound was dissolved in DMSO at a concentration of 5 mg $mL^{-1}$. These solutions were further diluted to 512 μg $mL^{-1}$ in sterile distilled water, resulting in a final DMSO concentration of 10.25%. The broth microdilution method was used to determine susceptibility.[S13] Briefly, each compound was serially diluted in 100 μL volumes of sterile distilled water in a 96-well microtiter tray. Wells were then inoculated with 100 μL volumes of each test organism in double-strength growth medium and incubated as described in Table S1. Final concentrations of compound ranged from 0.25−256 μg $mL^{-1}$. A positive growth control with no compound was included.

**Table S1.** Growth medium and incubation conditions for microorganisms tested in this study.

| Organism(s) | Growth medium | Incubation conditions |
|---|---|---|
| *S. aureus, E. faecalis, E. coli , A. baumannii* | Mueller Hinton broth | 24 h at 35 °C in ambient air |
| *S. pneumoniae* | Mueller Hinton broth supplemented with 2.5% lysed horse blood | 24 h at 35 °C with 5% $CO_2$ |

The entire assay was repeated 3−4 times per organism. MICs were determined visually as the lowest concentration of compound inhibiting growth. Modal MICs were then selected. A DMSO control was included with the first test to ensure that the solvent was not growth inhibitory. Vancomycin, chloramphenicol and ciprofloxacin were included when testing Gram positive organisms *E. coli* and *A. baumannii*, respectively, as positive controls. Concentrations of ≤5% DMSO were not inhibitory to growth. MICs for all antibiotics were within acceptable QC ranges.

***C. difficile***

Selected compounds were tested for their minimum inhibitory concentration (MIC) against three *Clostridium difficile* strains (Table S2). All strains are human isolates.[S14]

**Table S2.** *C. difficile* strains used in this study.

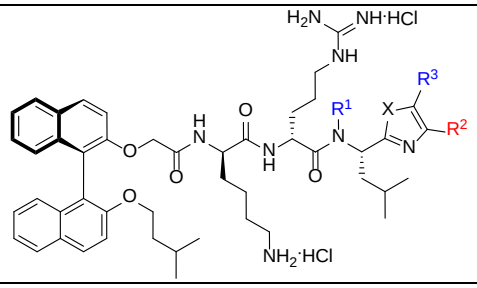
| *C. diff.* Strain | Description |
|---|---|
| M7404 | Canadian toxinotype III/ribotype 027 |
| R20291 | UK toxinotype III/ribotype 027 |
| 1470 | Toxinotype VIII/ribotype 017 |

The compounds were solubilized in DMSO at a concentration of 5 mg $mL^{-1}$. The MIC for each compound was determined utilizing the broth microdilution method described previously.[S13] Briefly, the compounds were diluted 1:2 in Heart Infusion (HI) medium (Oxiod) in 96-well polypropylene trays. The final concentration range was 1−128 μg $mL^{-1}$. The *C. difficile* strains were grown to mid-exponential growth phase, the cell number standardized by optical density and added to the microtiter trays. The cells were incubated anaerobically at 37 °C for 24 h. Each strain was tested in biological duplicate.

## Hemolysis Data

The hemolytic activity of each compound was assessed by the lysis of sheep erythrocytes (Table S3). Briefly, 500 μL volumes of each compound in phosphate buffered saline (PBS) was combined with 480 μL PBS and 20 μL washed sheep erythrocytes (100%) in microcentrifuge tubes. The final concentration of erythrocytes was 2% and of each compound was 50 μg $mL^{-1}$ and 5 μg $mL^{-1}$. Controls included a positive control (100% hemolysis) with 980 μL sterile distilled water and 20 μL erythrocytes and a negative control with 980 μL PBS and 20 μL erythrocytes. Tubes were incubated at 37 °C for 2 h on a rocker then centrifuged at 12 000 g for 5 min. Volumes of 100 μL of supernatant were transferred to the wells of a microtiter tray and the optical density was determined at 540 nm. The negative control value (blank) was subtracted from all other values and the resulting optical density values were expressed as a proportion of the positive control (100% hemolysis). This assay was repeated twice on separate occasions and the mean and standard deviation (SD) was calculated.

**Table S3.** Hemolysis assay for oxa(thia)zole peptidomimetics.




| | | | | | | % hemolysis (control = 100%) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 5 μg mL$^{-1}$ | | 50 μg mL$^{-1}$ | |
| entry | compound | X | $R^1$ | $R^2$ | $R^3$ | mean | SD | mean | SD |
| 1 | **1** | - | - | - | - | 2.8 | 0.6 | 107.1 | 2.7 |
| 2 | **2** | - | - | - | - | 1.5 | 0.2 | 84.7 | 18.1 |
| 3 | **3** | O | H | H | Bn | 1.4 | 0.4 | 50.4 | 7.6 |
| 4 | **117** | O | H | Bn | H | 2.3 | 0.1 | 99.2 | 2.4 |
| 5 | **118** | O | H | Ph | H | 1.6 | 0.7 | 66.1 | 1.7 |
| 6 | **119** | O | H | H | H | −0.1 | 0.2 | 65.8 | 2.2 |
| 7 | **120** | O | H | $CH_3$ | H | 0.0 | 0.4 | 60.0 | 0.9 |
| 8 | **121** | O | H | $CH_2F$ | H | 3.5 | 0.1 | 88.7 | 7.5 |
| 9 | **122** | O | H | $CH_2OH$ | H | 0.7 | 1.1 | 54.3 | 9.1 |
| 10 | **123** | O | H | $CH_2OMe$ | H | 1.2 | 1.2 | 72.7 | 13.9 |
| 11 | **124** | S | H | $CH_2OMe$ | H | 1.2 | 0.2 | 74.3 | 7.0 |
| 12 | **125** | O | H | $CH_2O$(i-Pr) | H | 2.2 | 1.3 | 95.5 | 3.4 |
| 13 | **126** | S | H | $CH_2O$(i-Pr) | H | 1.1 | 0.0 | 94.6 | 14.4 |
| 14 | **127** | O | H | $CH_2O$(i-Bu) | H | 4.1 | 3.7 | 106.1 | 0.2 |
| 15 | **128** | O | H | $CH_2O$(i-pent) | H | 1.6 | 1.1 | 98.6 | 4.8 |
| 16 | **129** | O | H | $CH_2OPh$ | H | 1.4 | 0.4 | 82.1 | 0.9 |
| 17 | **130** | O | H | $CH_2OBn$ | H | 2.2 | 1.8 | 101.6 | 6.6 |
| 18 | **131** | O | H | $CH_2O$(4-Cl-Bn) | H | 4.2 | 2.2 | 105.1 | 1.5 |
| 19 | **132** | O | H | $CH_2O$(4-F-Bn) | H | 0.9 | 1.2 | 101.9 | 6.9 |
| 20 | **133** | O | H | $CH_2O$(4-pyridyl-Me)·HCl | H | 0.8 | 0.2 | 56.1 | 10.0 |
| 21 | **134** | O | Me | $CH_2O$(i-Bu) | H | 0.1 | 0.5 | 89.2 | 10.2 |
| 22 | **135** | O | H | $CH_2O$(i-Bu) | Ph | 1.1 | 1.0 | 97.5 | 11.9 |
| 23 | **136** | O | H | $CH_2O$(i-Bu) | Br | 1.0 | 0.1 | 98.7 | 9.9 |
| 24 | **137** | O | H | $CO_2$(i-Bu) | H | 1.2 | 0.1 | 101.8 | 11.8 |
| 25 | **138** | O | H | CONH(i-Bu) | H | 0.8 | 0.6 | 98.8 | 12.5 |
| 26 | **139** | O | H | CONMe(OMe) | H | 0.0 | 0.0 | 39.0 | 4.7 |
| 27 | **140** | O | H | CO(i-pent) | H | 1.4 | 1.1 | 92.0 | 17.8 |
| 28 | **141** | O | Me | $CH_2OMe$ | H | 0.3 | 0.9 | 50.5 | 13.2 |
| 29 | **142** | O | Me | $CH_2OMe$ | Me | 1.4 | 0.2 | 56.4 | 8.0 |
| 30 | **143** | O | Me | $CH_2OMe$ | I | 0.2 | 0.0 | 68.0 | 3.7 |
| 31 | **144** | O | Me | $CH_2OMe$ | Ph | 2.6 | 2.9 | 103.6 | 2.4 |
| 32 | **145** | O | Me | $CH_2OMe$ | 4-(i-Pr)-Ph | 0.7 | 0.4 | 69.3 | 12.4 |
| 33 | **146** | O | Me | $CH_2OMe$ | 4-$CF_3$-Ph | 0.2 | 0.0 | 94.3 | 1.3 |
| 34 | **147** | O | Me | $CH_2OMe$ | 2,4-F,F-Ph | 0.7 | 0.1 | 87.8 | 2.0 |
| 35 | **148** | O | Me | $CH_2OMe$ | 4-(3,5-Me,Me)-isoxazolyl | 1.5 | 0.5 | 87.3 | 1.6 |

**References**


S1) S. M. Wales, K. A. Hammer, A. M. King, A. J. Tague, D. Lyras, T. V. Riley, P. A. Keller, S. G. Pyne, *Org. Biomol. Chem.* **2015**, *13*, 5743−5756.

S2) S. V. Pande, P. S. Utale, S. B. Gholse, P. V. Tekade, S. G. Patil, *Pharm. Chem. J.* **2014**, *48*, 29−33.

S3) M. J. McKennon, A. I. Meyers, *J. Org. Chem.* **1993**, *58*, 3568−3571.

S4) a) S. Murru, A. Nefzi, *ACS Comb. Sci.* **2014**, *16*, 39−45. b) S. Murru, C. T. Dooley, A. Nefzi, *Tetrahedron Lett.* **2013**, *54*, 7062−7064.

S5) F. Cavelier, C. Enjalbal, *Tetrahedron Lett.* **1996**, *37*, 5131−5134.

S6) a) U. Schmidt, P. Gleich, H. Griesser, R. Utz, *Synthesis* **1986**, *12*, 992−998. b) Y. Hamada, M. Shibata, T. Sugiura, S. Kato, T. Shioiri, *J. Org. Chem.* **1987**, *52*, 1252−1255.

S7) M. Stanchev, S. Tabakova, G. Videnov, E. Golovinsky, G. Jung, *Arch. Pharm. Pharm. Med. Chem.* **1999**, *332*, 297−304.

S8) S. A. Ohnmacht, P. Mamone, A. J. Culshaw, M. F. Greaney, *Chem. Commun.* **2008**, 1241−1243.

S9) S. C. Watson, J. F. Eastham, *J. Organomet. Chem.* **1967**, *9*, 165−168.

S10) J. B. Bremner, P. A. Keller, S. G. Pyne, T. P. Boyle, Z. Brkic, D. M. David, A. Garas, J. Morgan, M. Robertson, K. Somphol, M. H. Miller, A. S. Howe, P. Ambrose, S. Bhavnani, T. R. Fritsche, D. J. Biedenbach, R. N. Jones, R. W. Buckheit Jr., K. M. Watson, D. Baylis, J. A. Coates, J. Deadman, D. Jeevarajah, A. McCracken, D. I. Rhodes, *Angew. Chem. Int. Ed.* **2010**, *49*, 537−540.

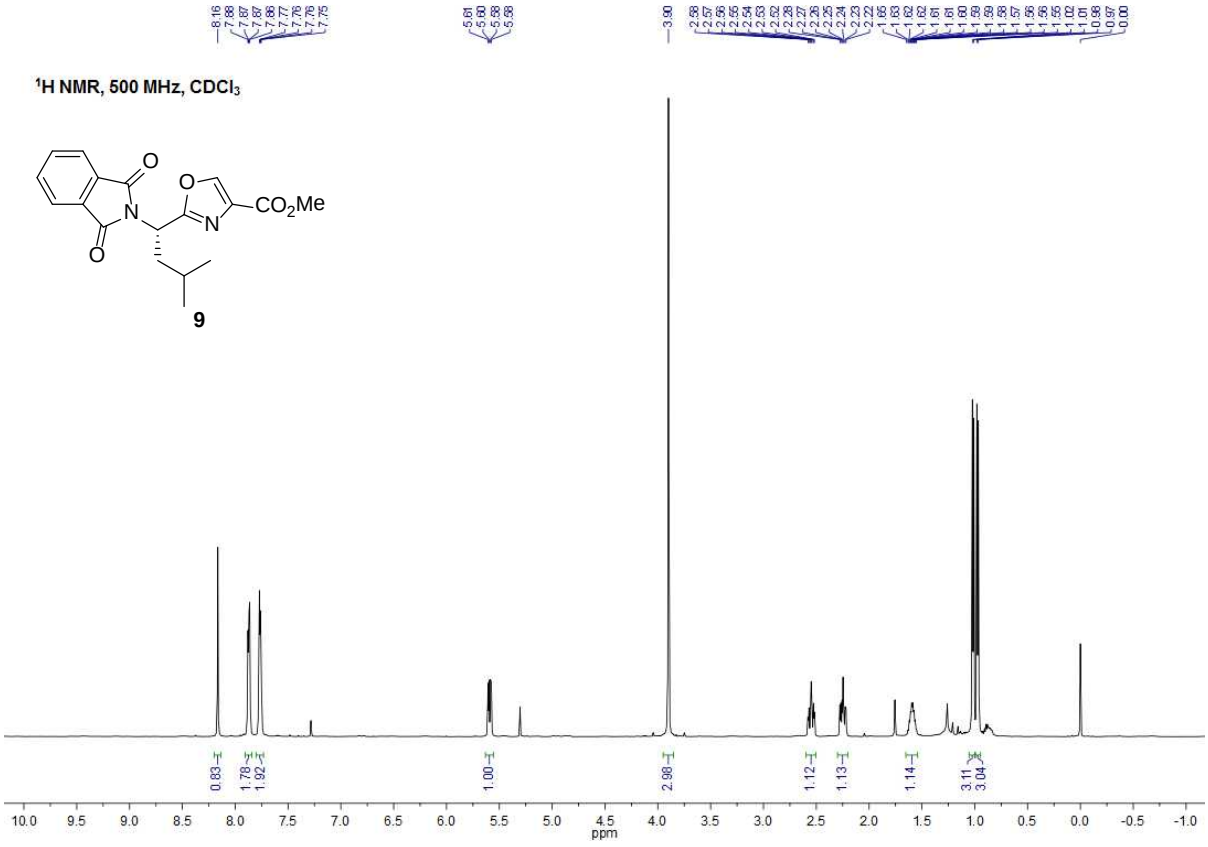
S11) N. A. Strotman, H. R. Chobanian, Y. Guo, J. He, J. E. Wilson, *Org. Lett.* **2010**, *12*, 3578−3581.

S12) S. J. Butler, K. A. Jolliffe, *Org. Biomol. Chem.* **2011**, *9*, 3471−3483.

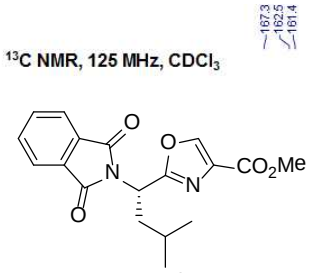
S13) Clinical and Laboratory Standards Institute. **2012**. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard–Ninth Edition. CLSI Document M07-A9. Clinical and Laboratory Standards Institute, Wayne, Pennsylvania.

S14) G. P. Carter, G. R. Douce, R. Govind, P. M. Howarth, K. E. Mackin, J. Spencer, A. M. Buckley, A. Antunes, D. Kotsanas, G. A. Jenkin, B. Dupuy, J. I. Rood, D. Lyras, *PLoS Pathog.* **2011**, *7*, e1002317.

## NMR Spectra of Selected Type B Oxa(thia)zoles



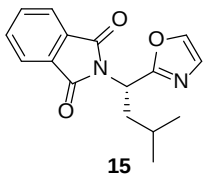
$^{13}$C NMR, 125 MHz, $CDCl_3$



9

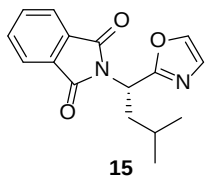


$^{1}$H NMR, 500 MHz, $CDCl_3$



15

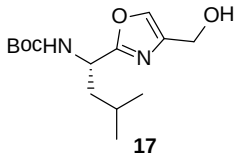
$^{13}$C NMR, 75 MHz, $CDCl_3$



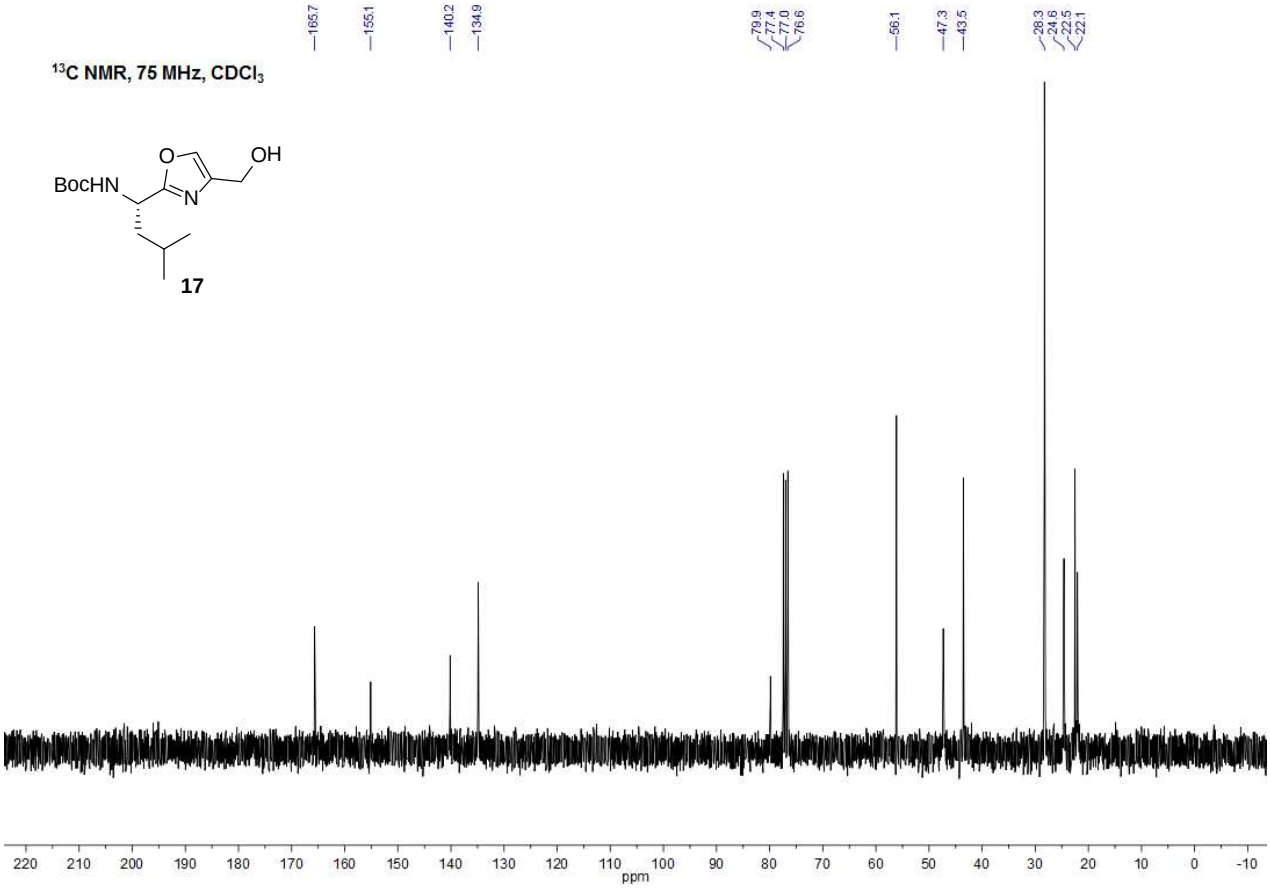
**15**

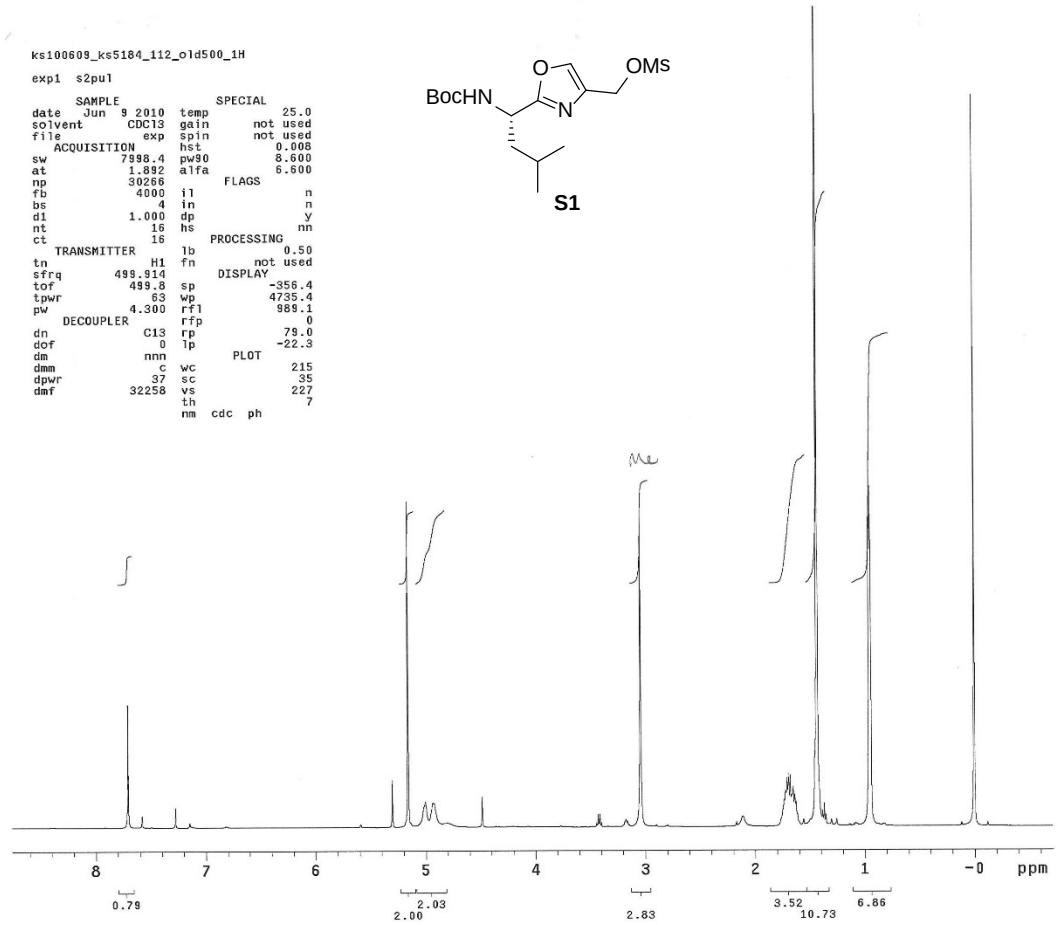


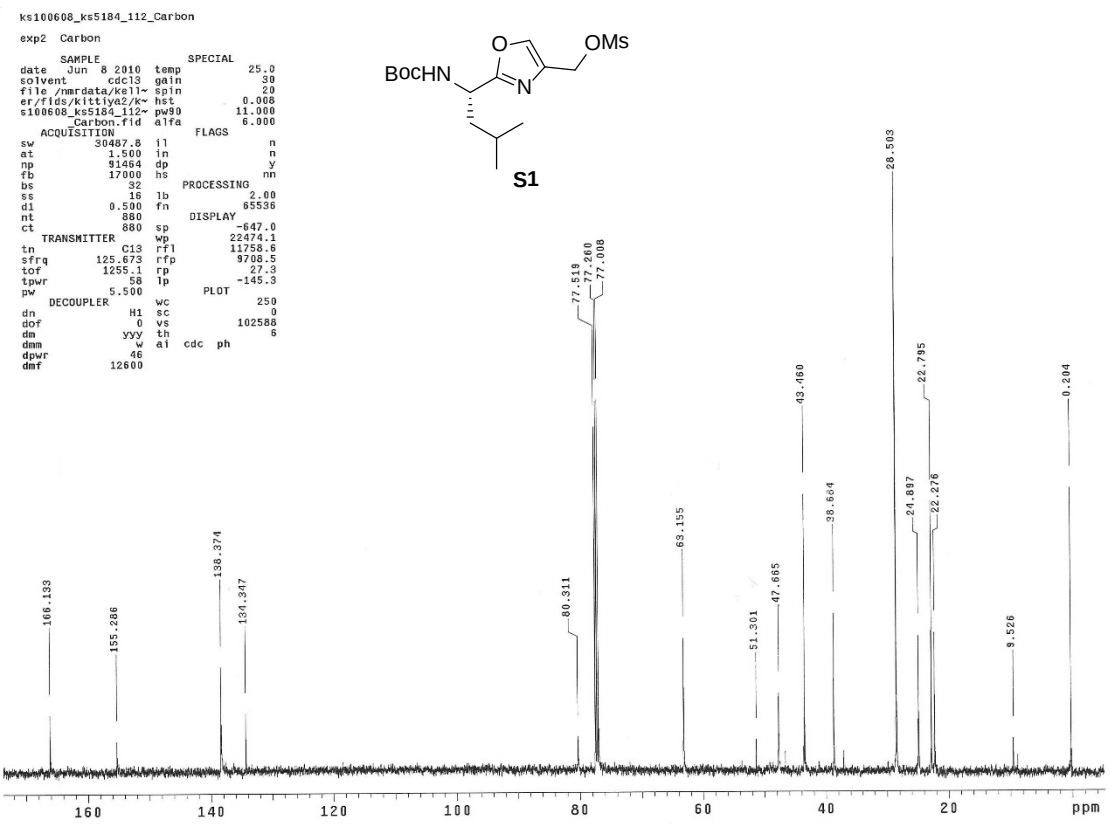

$^{1}$H NMR, 500 MHz, $CDCl_3$

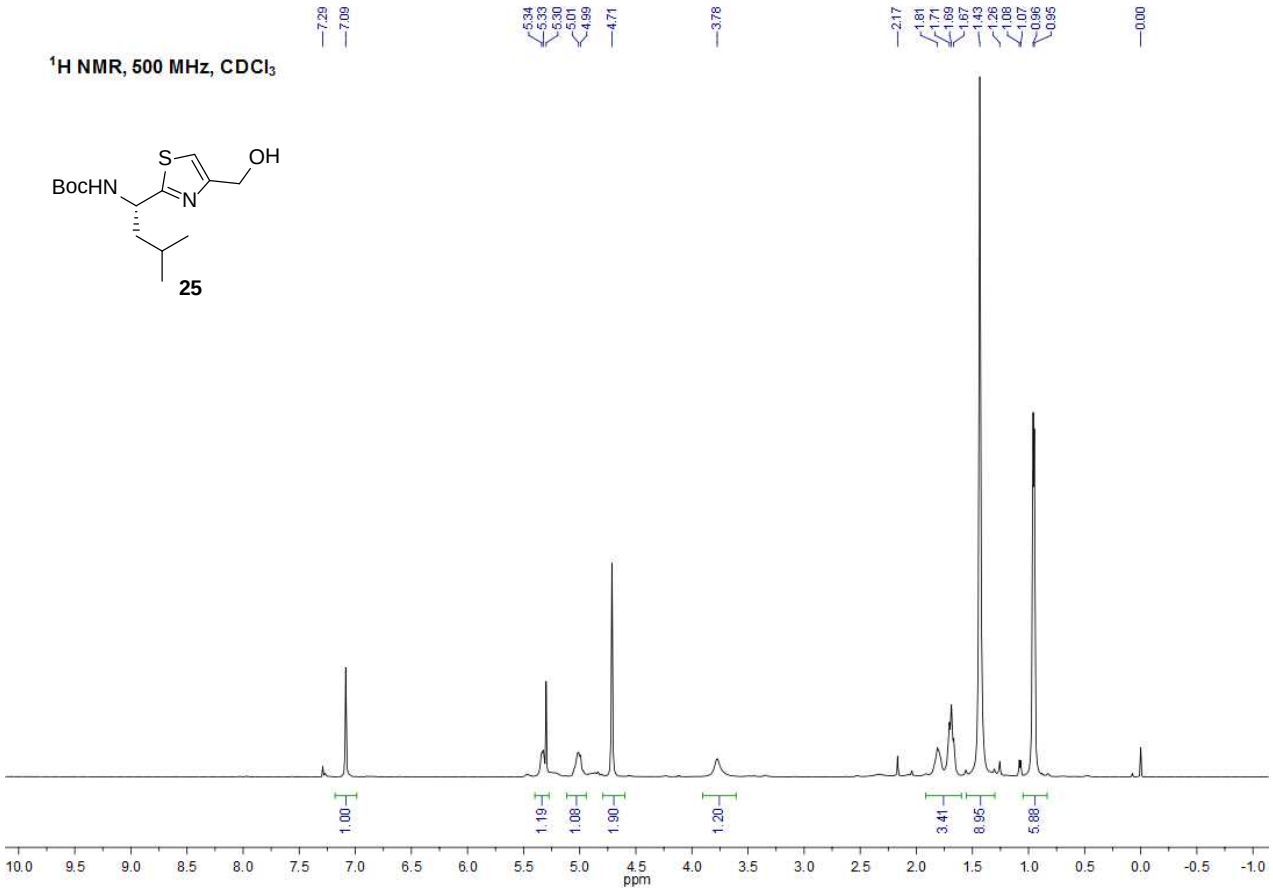


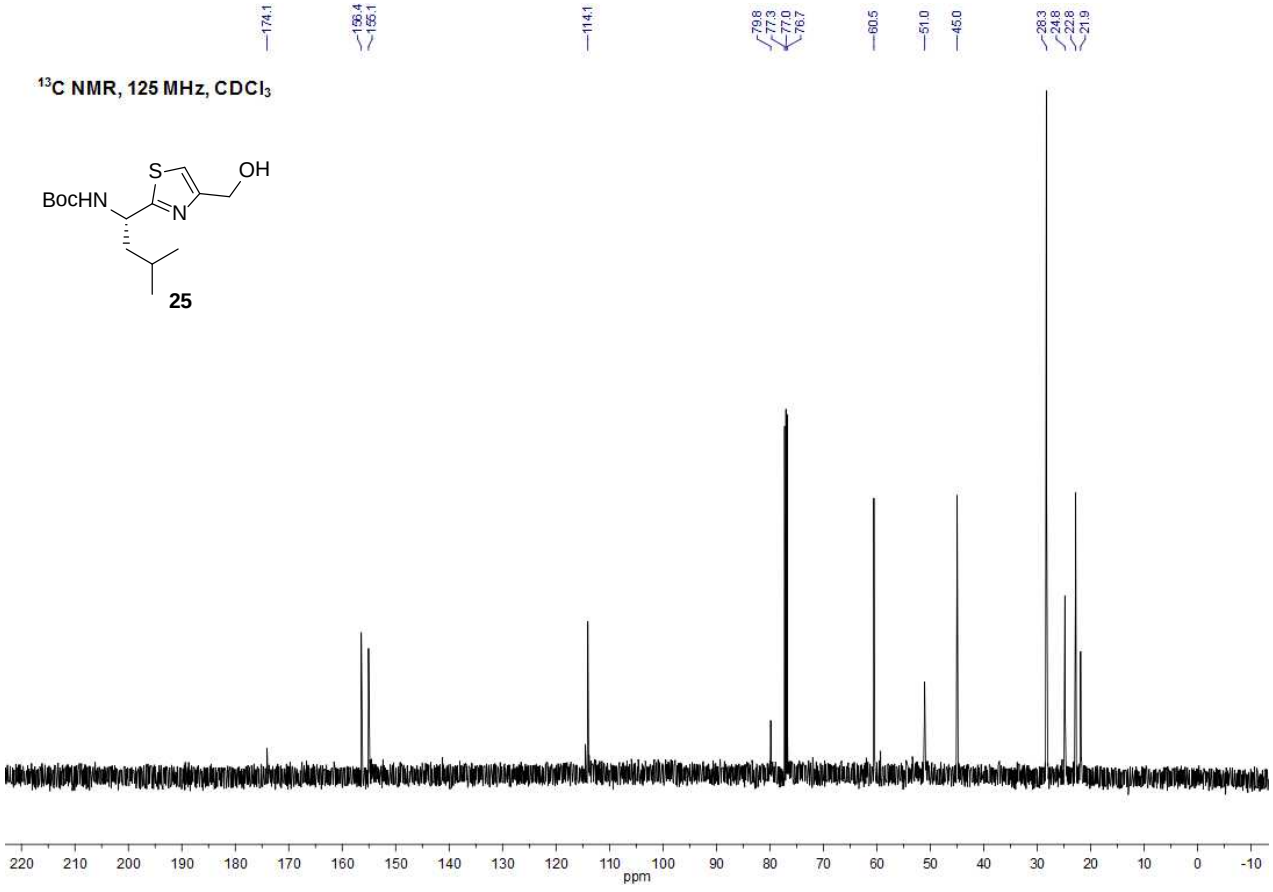
**17**


165.7
155.1
140.2
134.9
79.9
77.4
77.0
76.6
56.1
47.3
43.5
28.3
24.6
22.5
22.1
$^{13}$C NMR, 75 MHz, CDCl$_3$
BocHN
O
N
OH
17
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

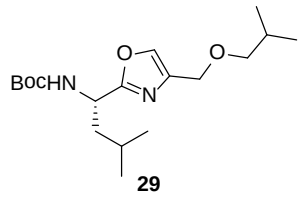

ks100609_ks5184_112_old500_1H
exp1 s2pul
SAMPLE
date Jun 8 2010
solvent CDCl3
file exp
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.914
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -356.4
wp 4735.4
rfl 989.1
rfp 0
rp 79.0
lp -22.3
PLOT
wc 215
sc 35
vs 227
th 7
nm cdc ph
BocHN
OMs
S1
8
7
6
5
4
3
2
1
-0
ppm
0.79
2.00
2.03
2.83
3.52
10.73
6.86


ks100608_ks5184_112_Carbon
exp2 Carbon
SAMPLE
date Jun 8 2010
solvent cdcl3
file /nmrdata/kell~
er/fids/kittiya2/k~
s100608_ks5184_112~
Carbon.fid
ACQUISITION
sw 30487.8
at 1.500
np 91464
fb 17000
bs 32
ss 16
d1 0.500
nt 880
ct 880
TRANSMITTER
tn C13
sfrq 125.673
tof 1255.1
tpwr 58
pw 5.500
DECOUPLER
dn H1
dof 0
dm yyy
dmm w
dpwr 46
dmf 12600
SPECIAL
temp 25.0
gain 30
spin 20
hst 0.008
pw90 11.000
alfa 6.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 2.00
fn 65536
DISPLAY
sp -647.0
wp 22474.1
rfl 11758.6
rfp 9708.5
rp 27.3
lp -145.3
PLOT
wc 250
sc 0
vs 102588
th 6
al cdc ph
BocHN
OMs
S1
166.133
155.286
136.374
134.347
80.311
77.519
77.260
77.008
63.155
51.301
47.685
43.460
38.664
28.503
24.887
22.795
22.276
9.526
0.204
160
140
120
100
80
60
40
20
ppm


7.29
7.09
5.34
5.33
5.30
5.01
4.99
4.71
3.78
2.17
1.81
1.71
1.69
1.67
1.43
1.26
1.08
1.07
0.96
0.95
0.00
1H NMR, 500 MHz, CDCl3
BocHN
S
N
OH
25
1.00
1.19
1.08
1.90
1.20
3.41
8.95
5.88
ppm


174.1
166.4
155.1
114.1
79.8
77.3
77.0
76.7
60.5
51.0
45.0
28.3
24.8
22.8
21.9
13C NMR, 125 MHz, CDCl3
BocHN
S
N
OH
25
ppm

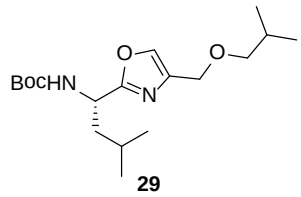
**$^1$H NMR, 500 MHz, $CDCl_3$**



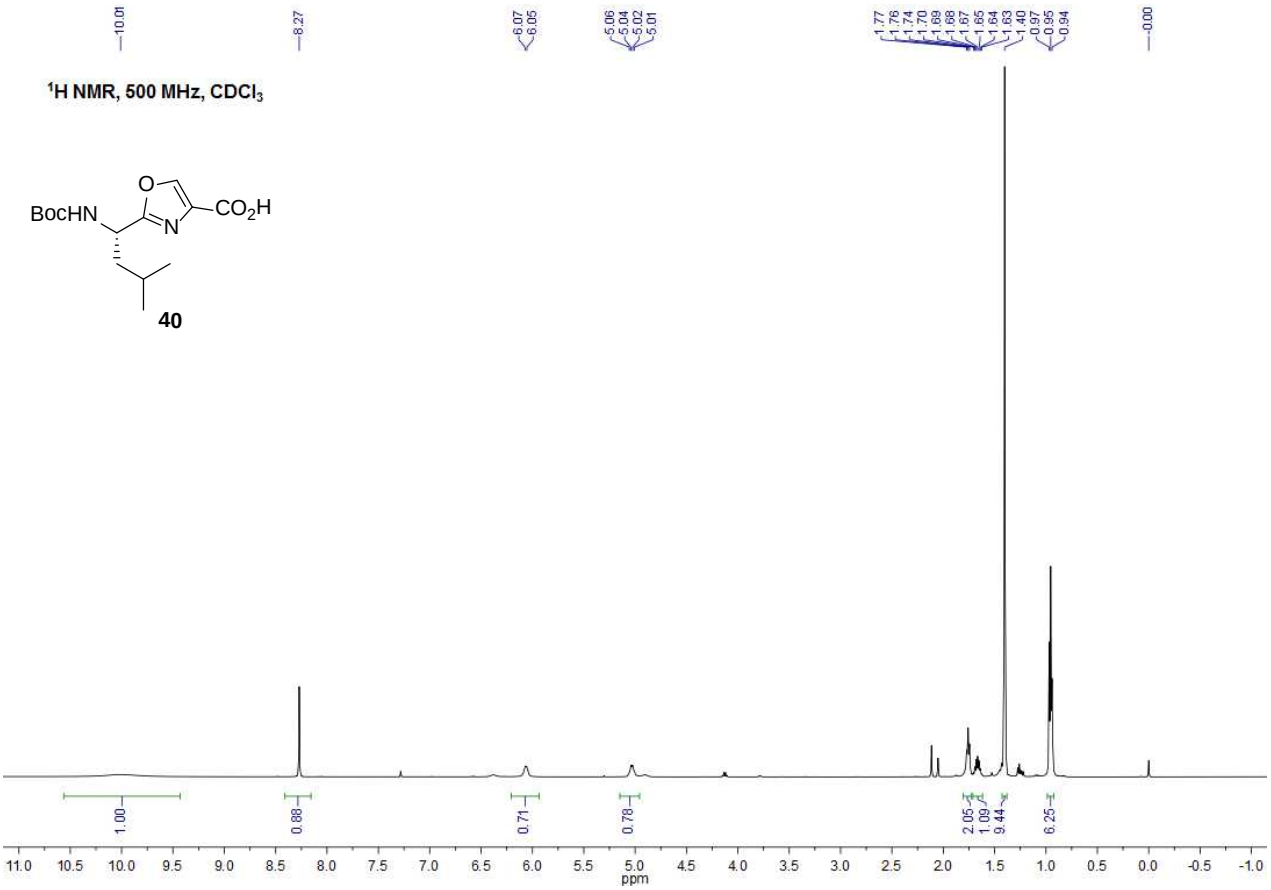

**29**




**$^{13}$C NMR, 125 MHz, $CDCl_3$**



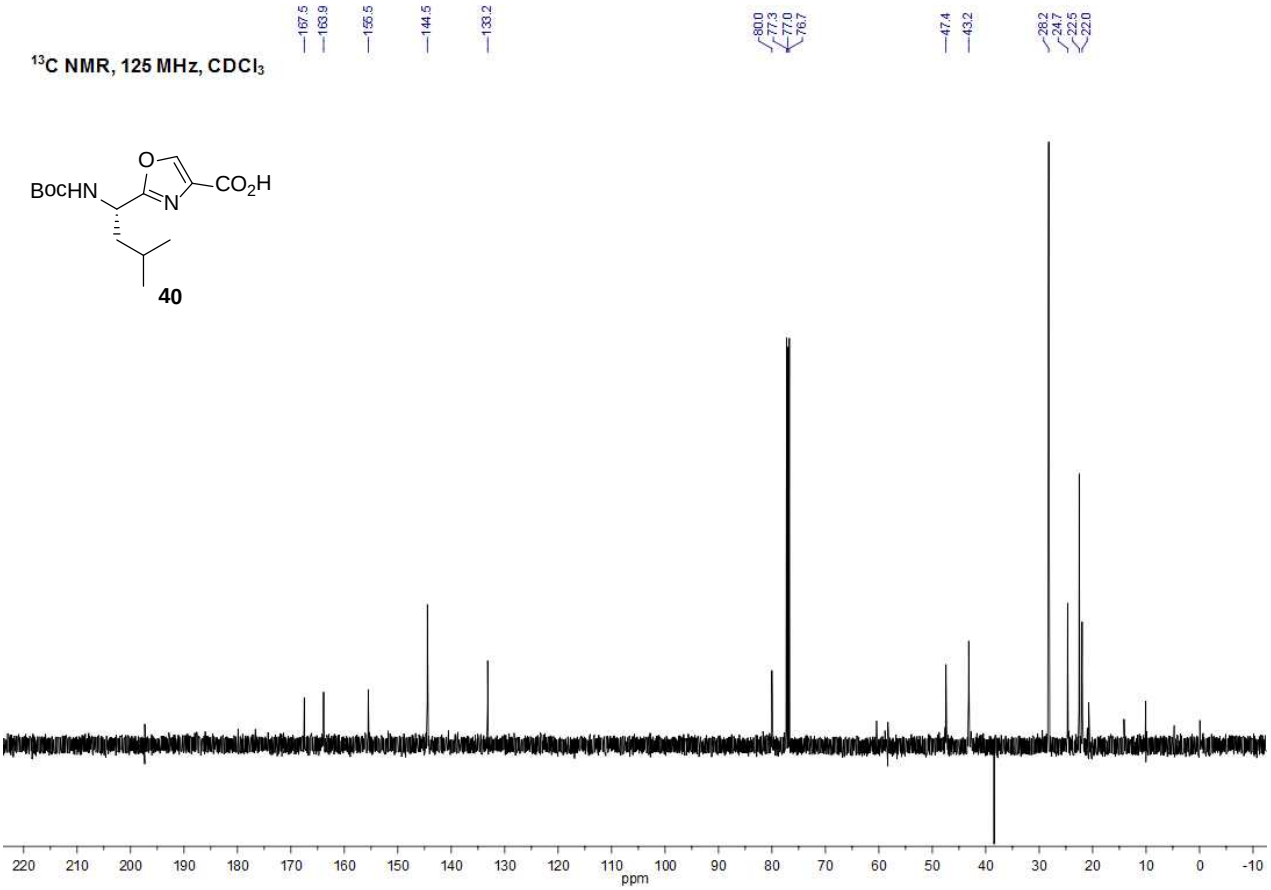

**29**




$^{1}$H NMR, 500 MHz, $CDCl_3$



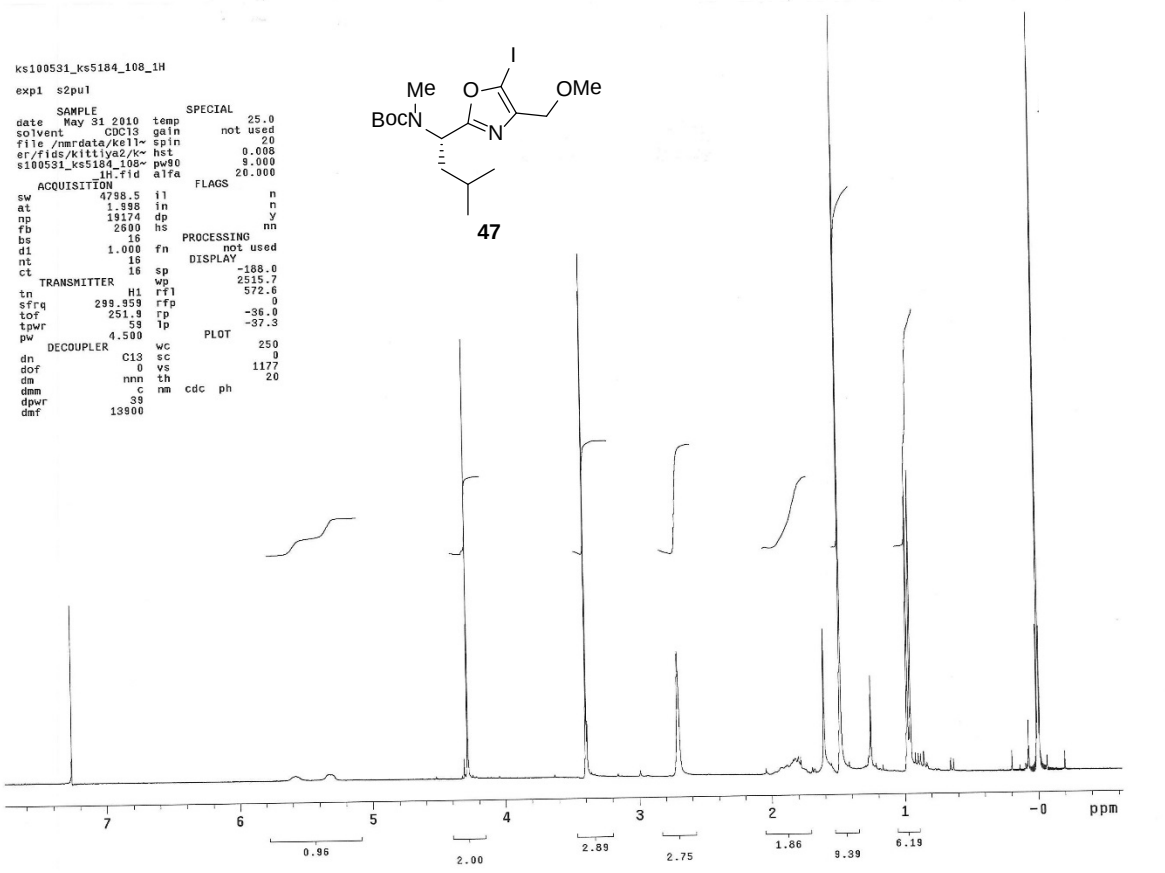

**40**

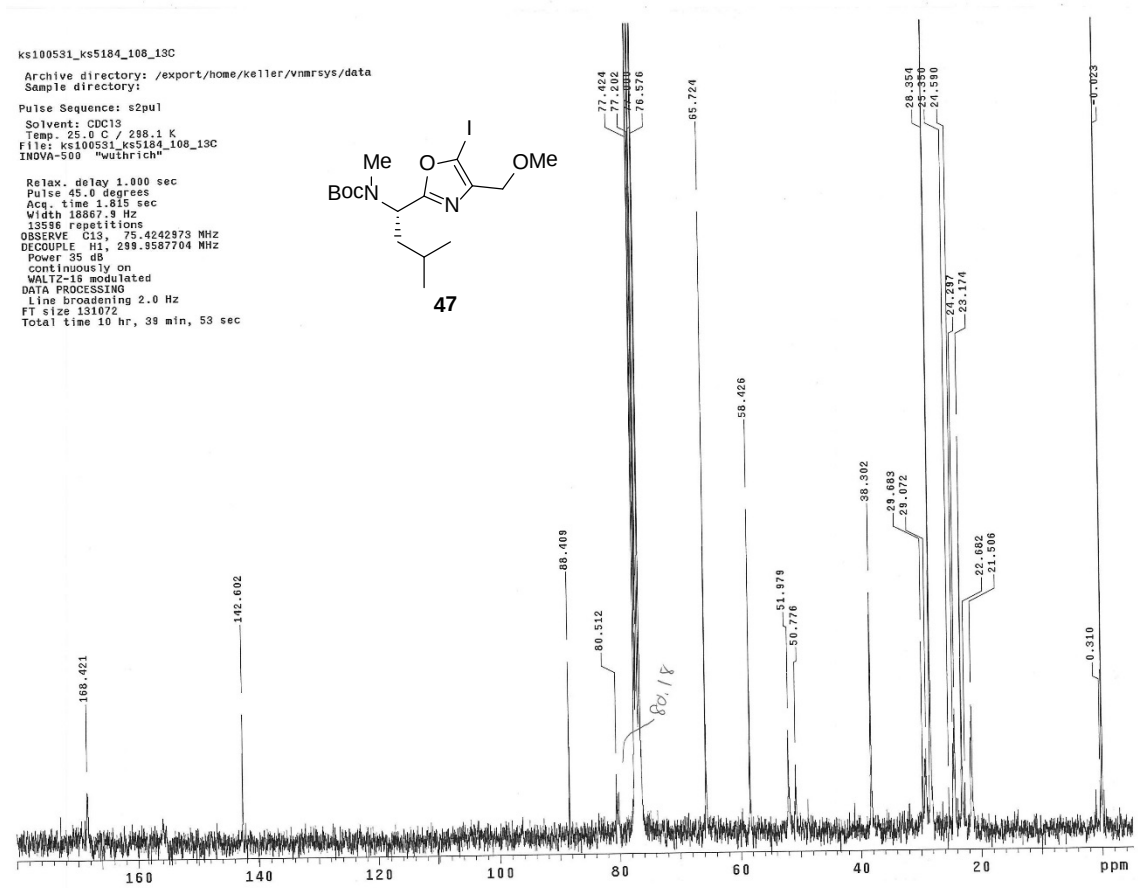



$^{13}$C NMR, 125 MHz, $CDCl_3$

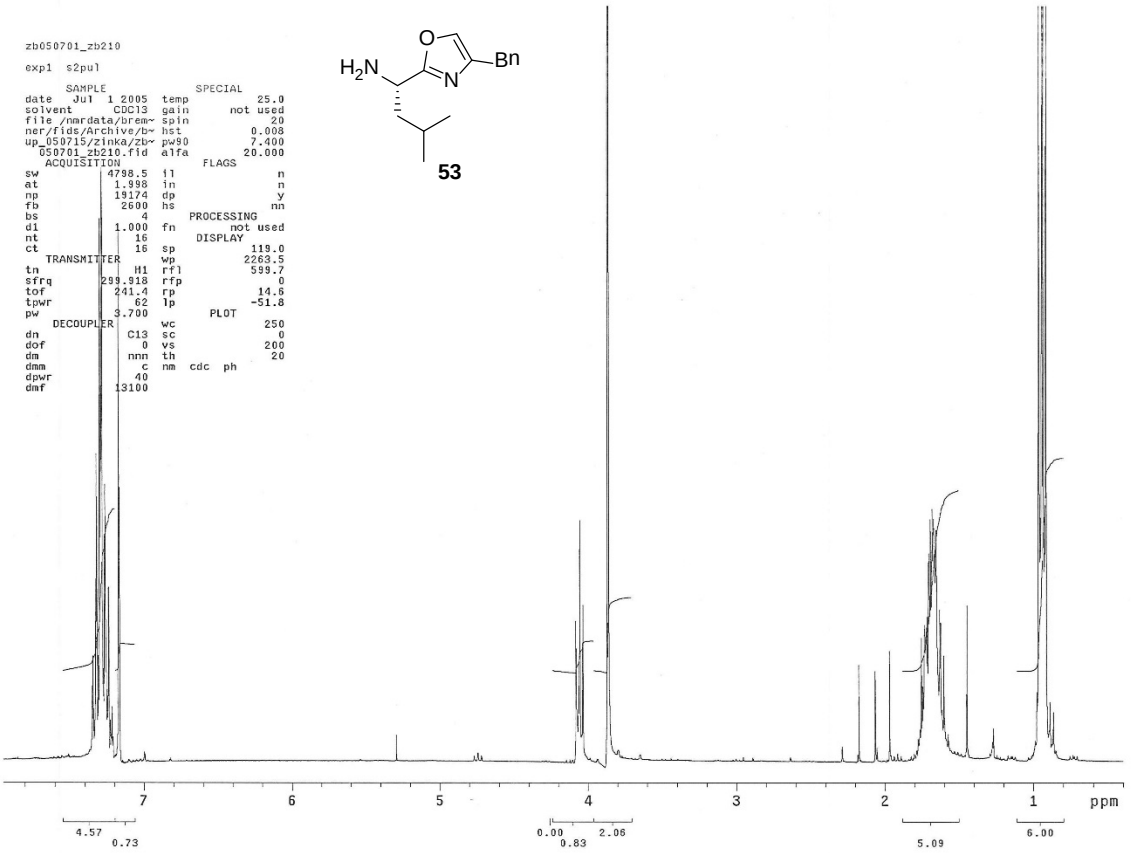


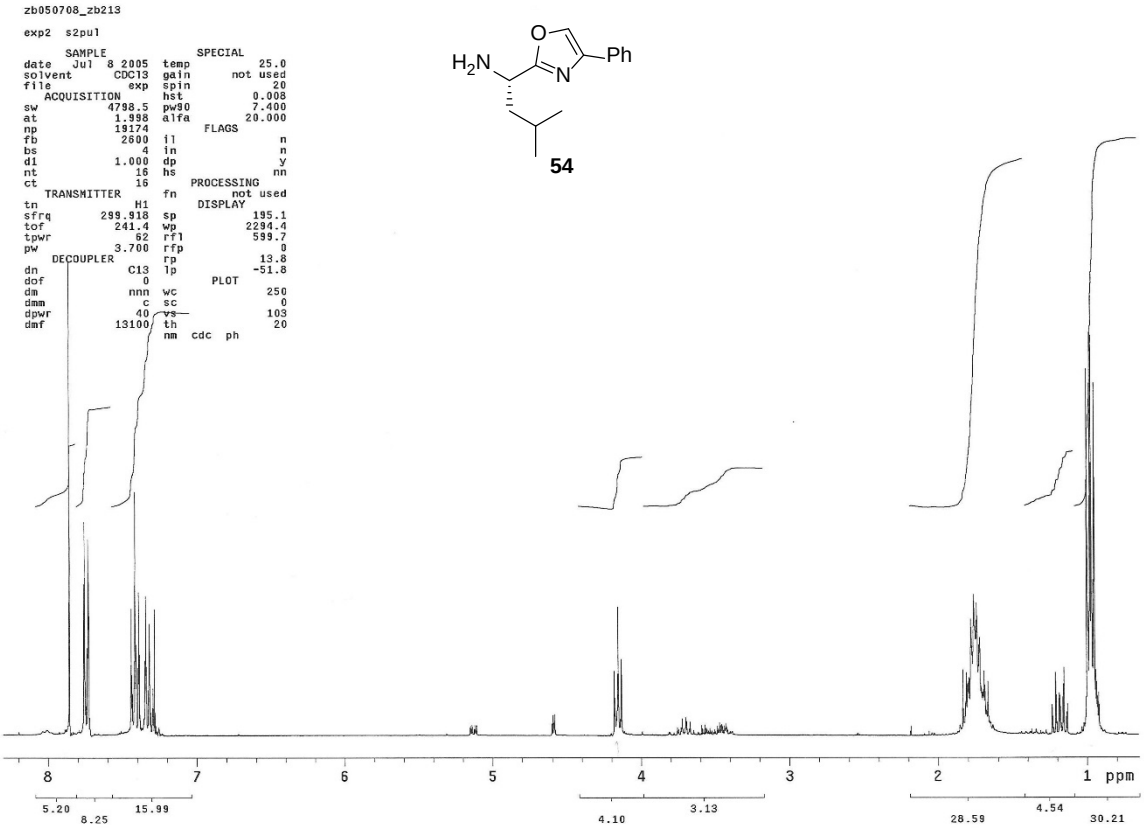

**40**

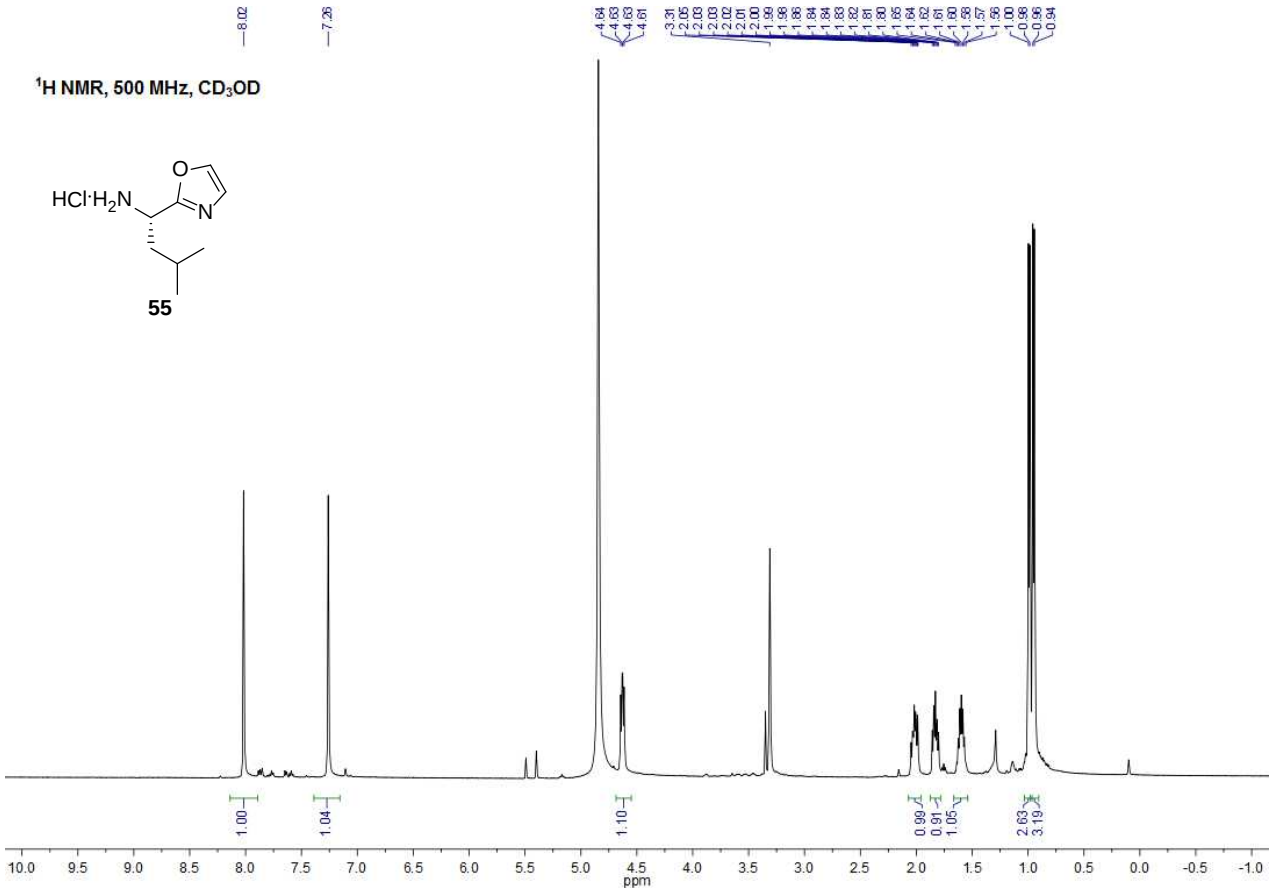

ks100531_ks5184_108_1H
exp1 s2pul
SAMPLE
date May 31 2010
solvent CDCl3
file /nmrdata/kell~
er/fids/kittiya2/K~
s100531_ks5184_108~
_1H.fid
ACQUISITION
sw 4798.5
at 1.998
np 19174
fb 2600
bs 16
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 299.959
tof 251.9
tpwr 59
pw 4.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 39
dmf 13900
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 9.000
alfa 20.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn not used
DISPLAY
sp -188.0
wp 2515.7
rfl 572.6
rfp 0
rp -36.0
lp -37.3
PLOT
wc 250
sc 0
vs 1177
th 20
cdc ph
I
Me
O
OMe
BocN
N
47
7
6
5
4
3
2
1
-0
ppm
0.96
2.00
2.89
2.75
1.86
9.39
6.19

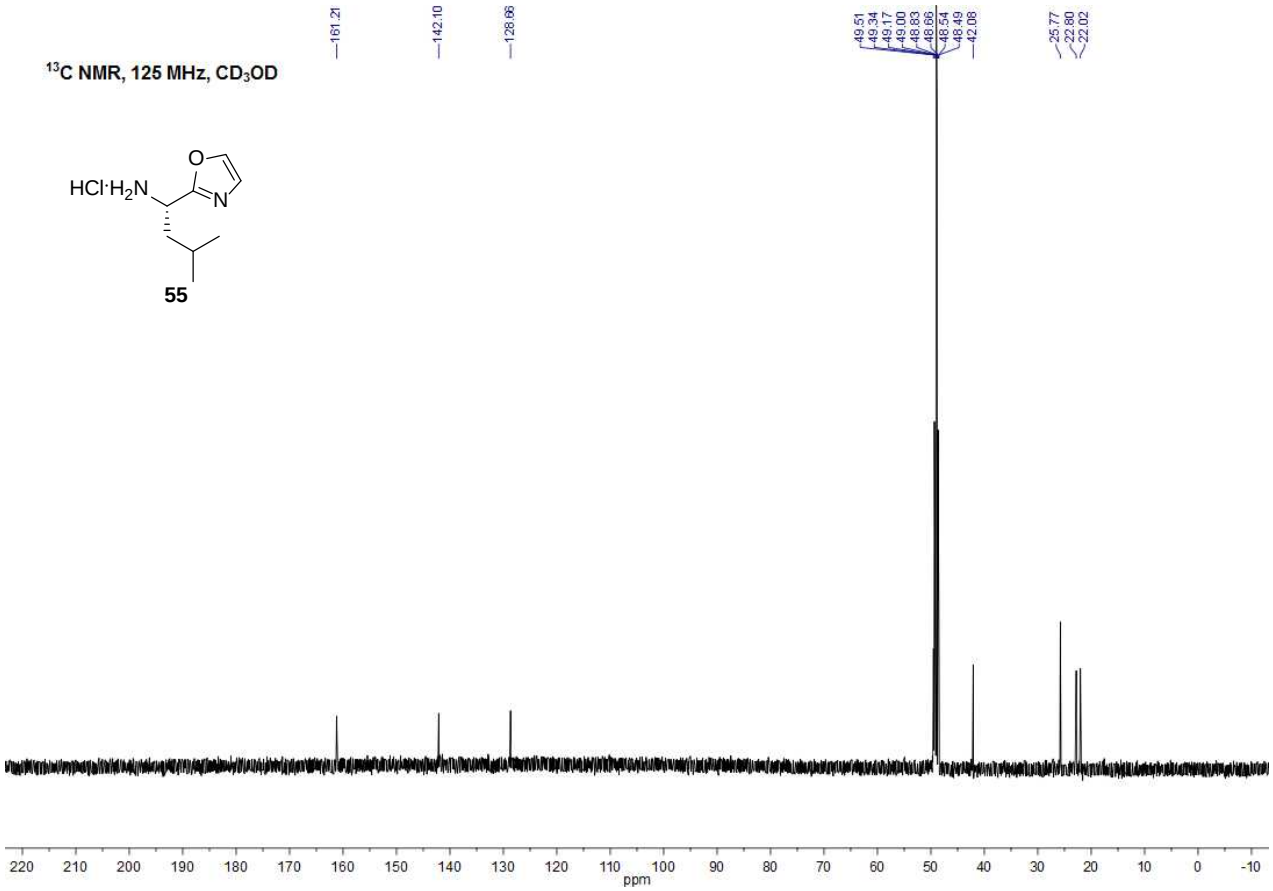

ks100531_ks5184_108_13C
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: ks100531_ks5184_108_13C
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.815 sec
Width 18867.9 Hz
13596 repetitions
OBSERVE C13, 75.4242973 MHz
DECOUPLE H1, 299.9587704 MHz
Power 35 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 10 hr, 39 min, 53 sec
I
Me
O
OMe
BocN
N
47
77.424
77.202
76.980
76.576
65.724
58.426
38.302
29.683
29.072
28.354
25.350
21.590
24.297
23.174
22.682
21.506
88.409
80.512
51.879
50.776
168.421
142.602
0.310
-0.023
160
140
120
100
80
60
40
20
ppm

## NMR Spectra of Type C Amino Oxa(thia)zoles 53−84

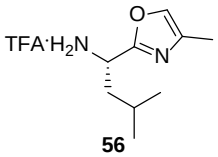



8.02
7.26
4.64
4.63
4.63
4.61
3.31
2.05
2.03
2.03
2.02
2.01
2.00
1.99
1.98
1.86
1.84
1.84
1.83
1.82
1.81
1.80
1.65
1.64
1.62
1.61
1.60
1.58
1.57
1.56
1.00
0.98
0.96
0.94
1H NMR, 500 MHz, CD3OD
HCl·H2N
O
N
55
1.00
1.04
1.10
0.99
0.91
1.05
2.63
3.19
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
ppm


161.21
142.10
128.66
49.51
49.34
49.17
49.00
48.83
48.66
48.54
48.49
42.08
25.77
22.80
22.02
13C NMR, 125 MHz, CD3OD
HCl·H2N
O
N
55
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

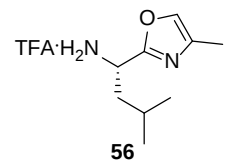
**$^1$H NMR, 500 MHz, $CDCl_3$**



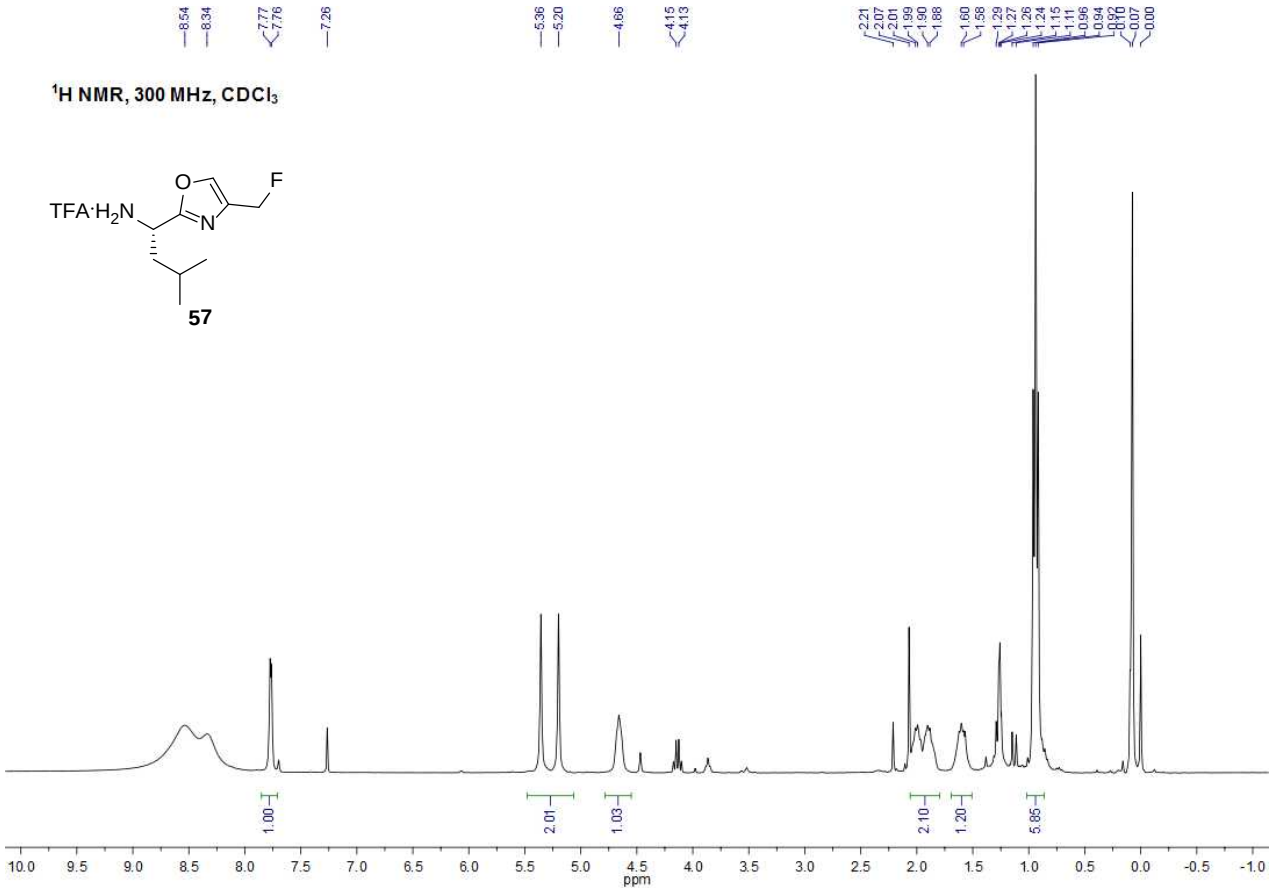

**56**

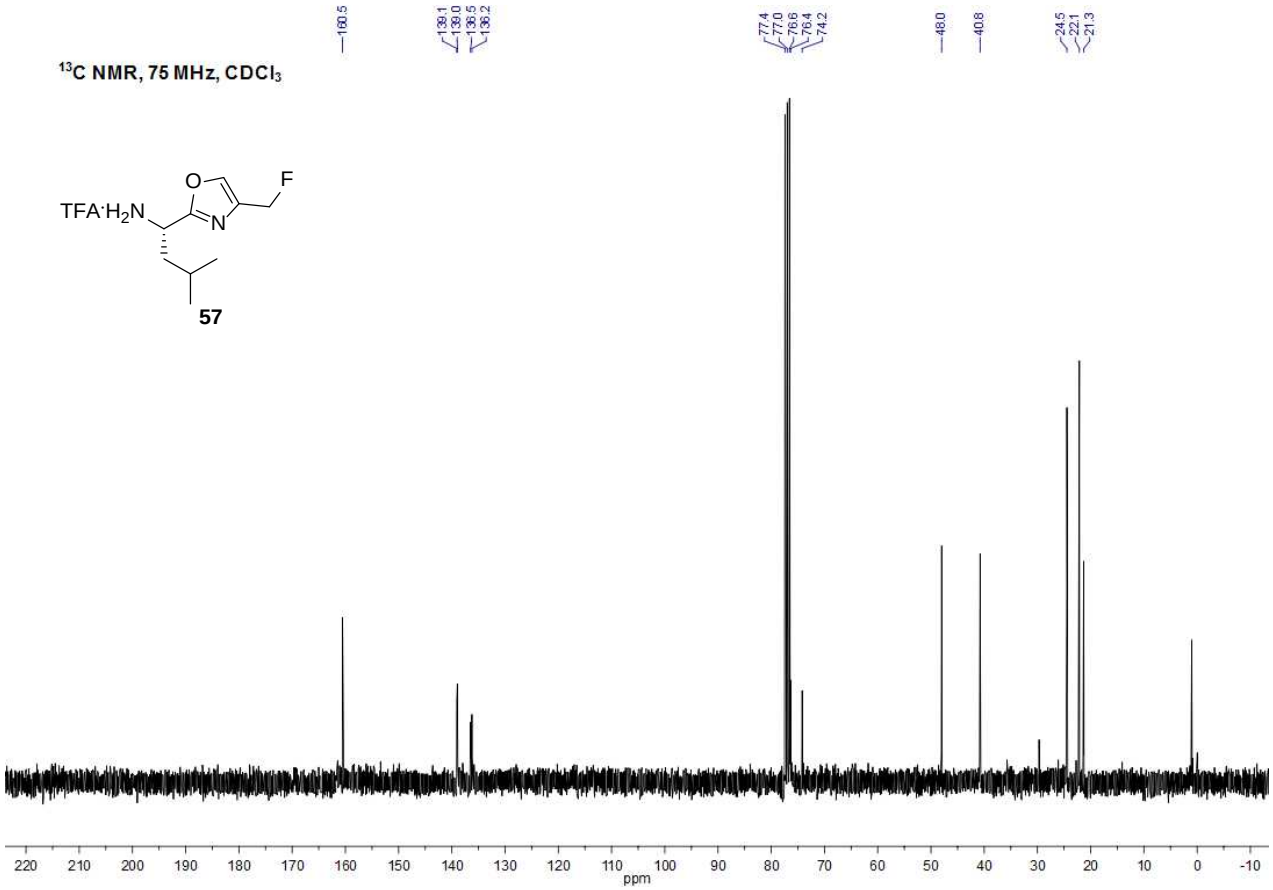


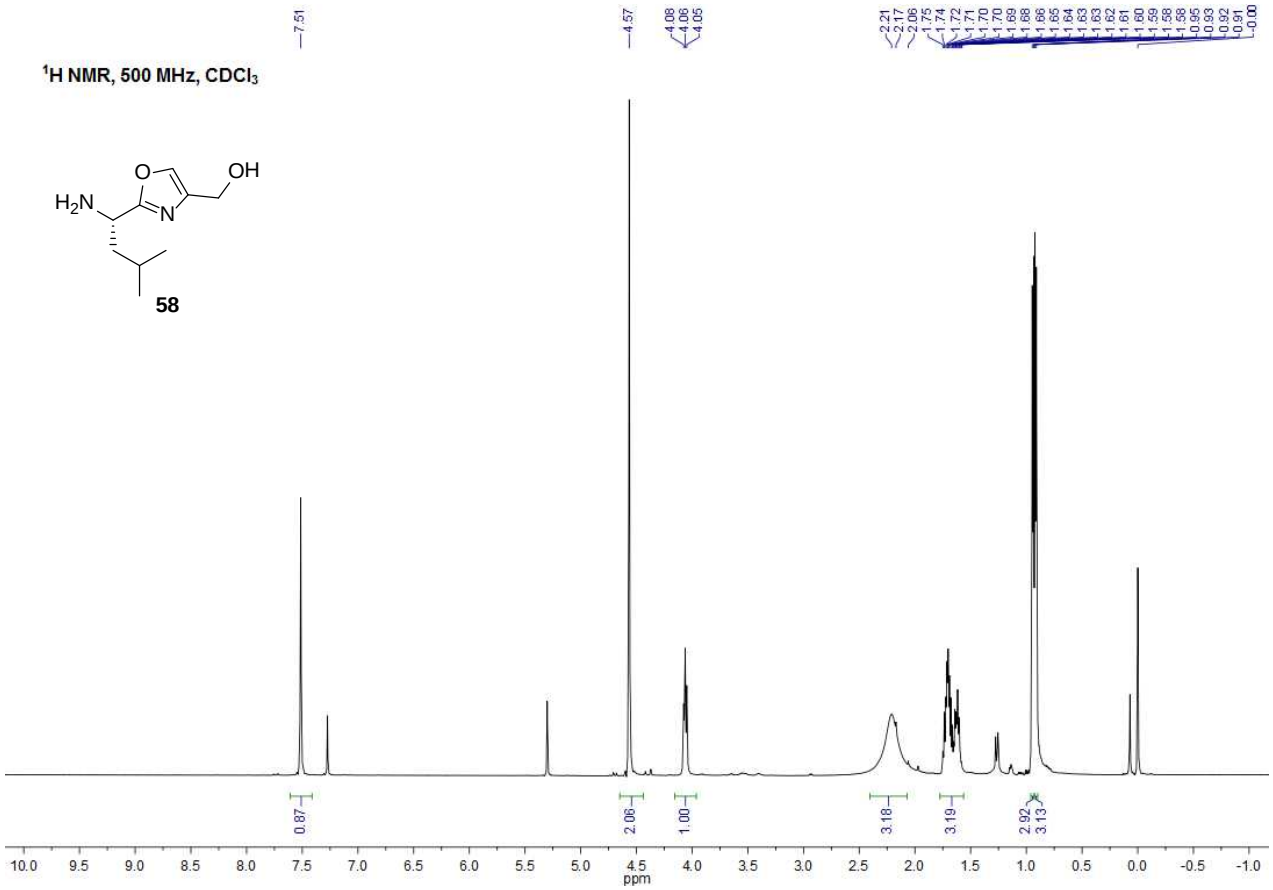

**$^{13}$C NMR, 125 MHz, $CDCl_3$**

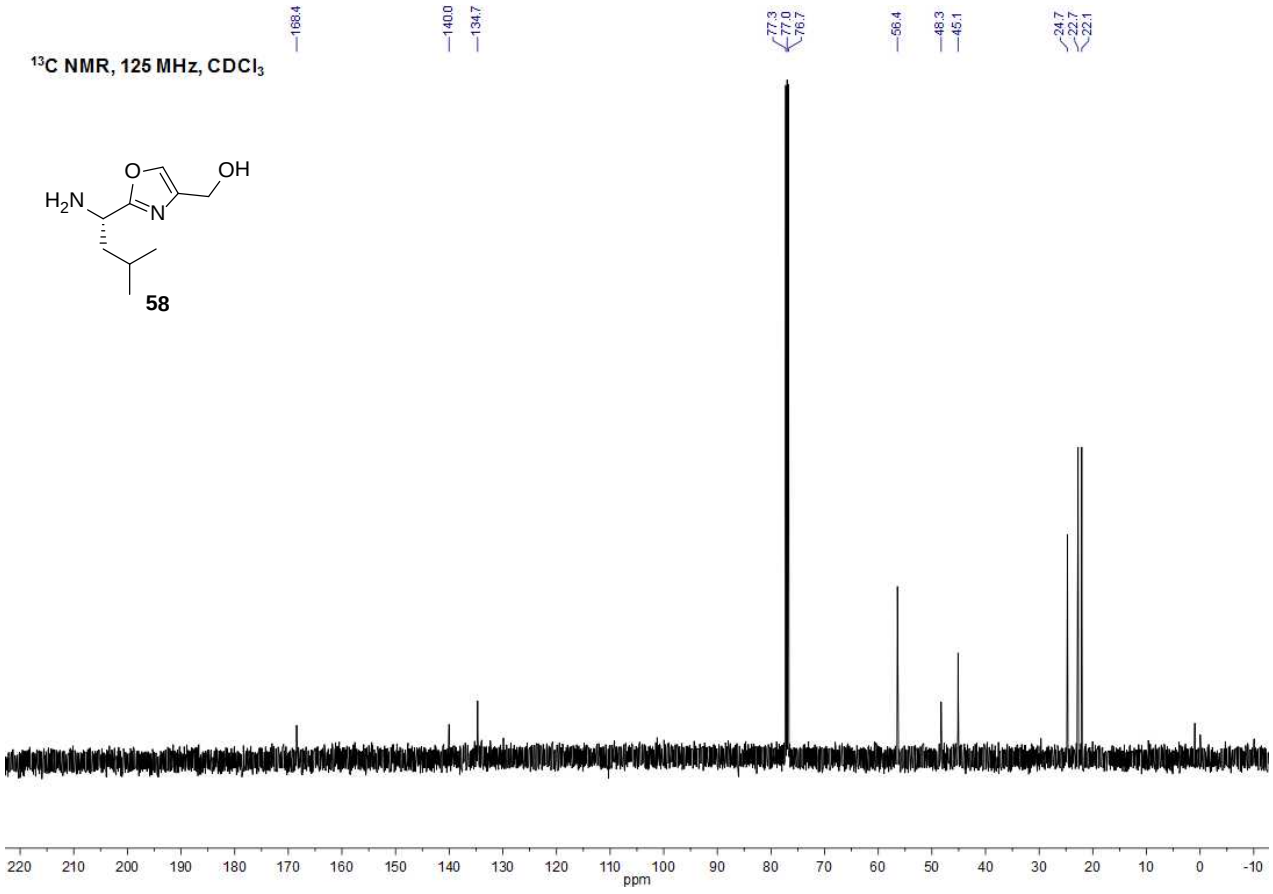


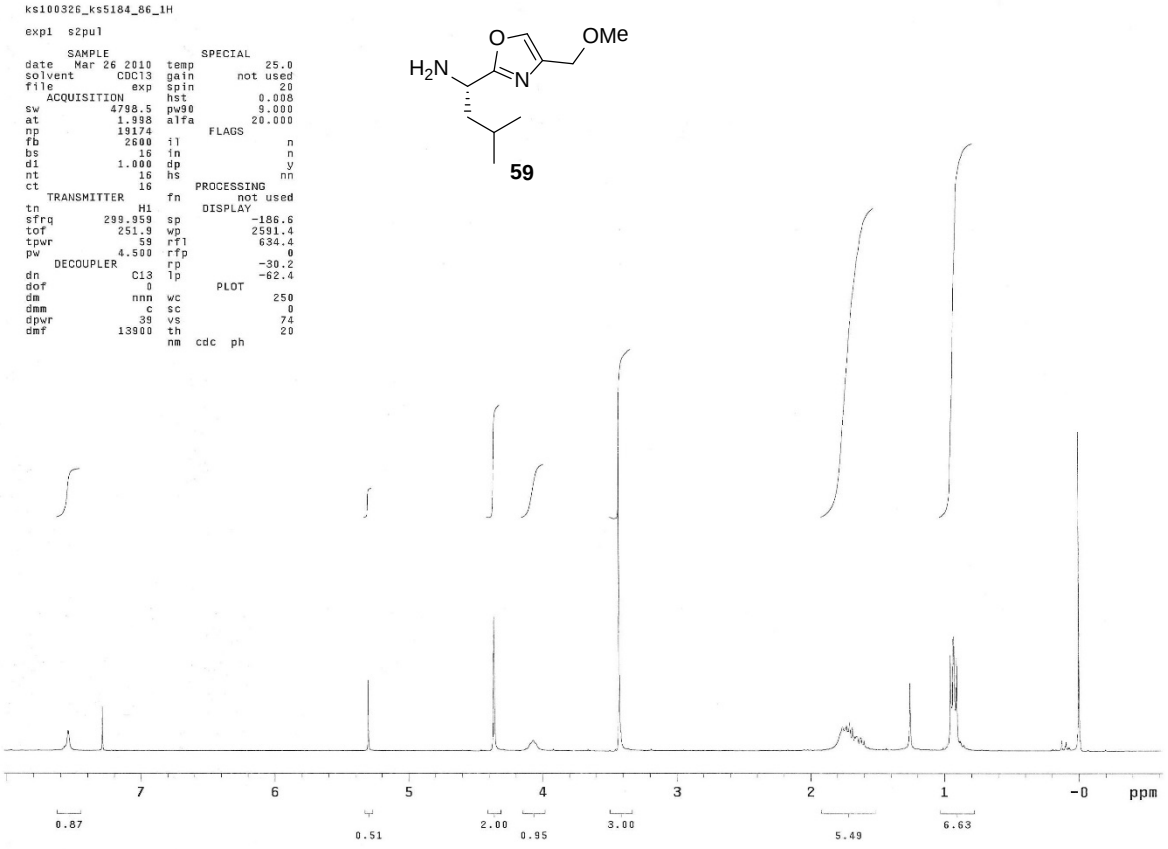

**56**

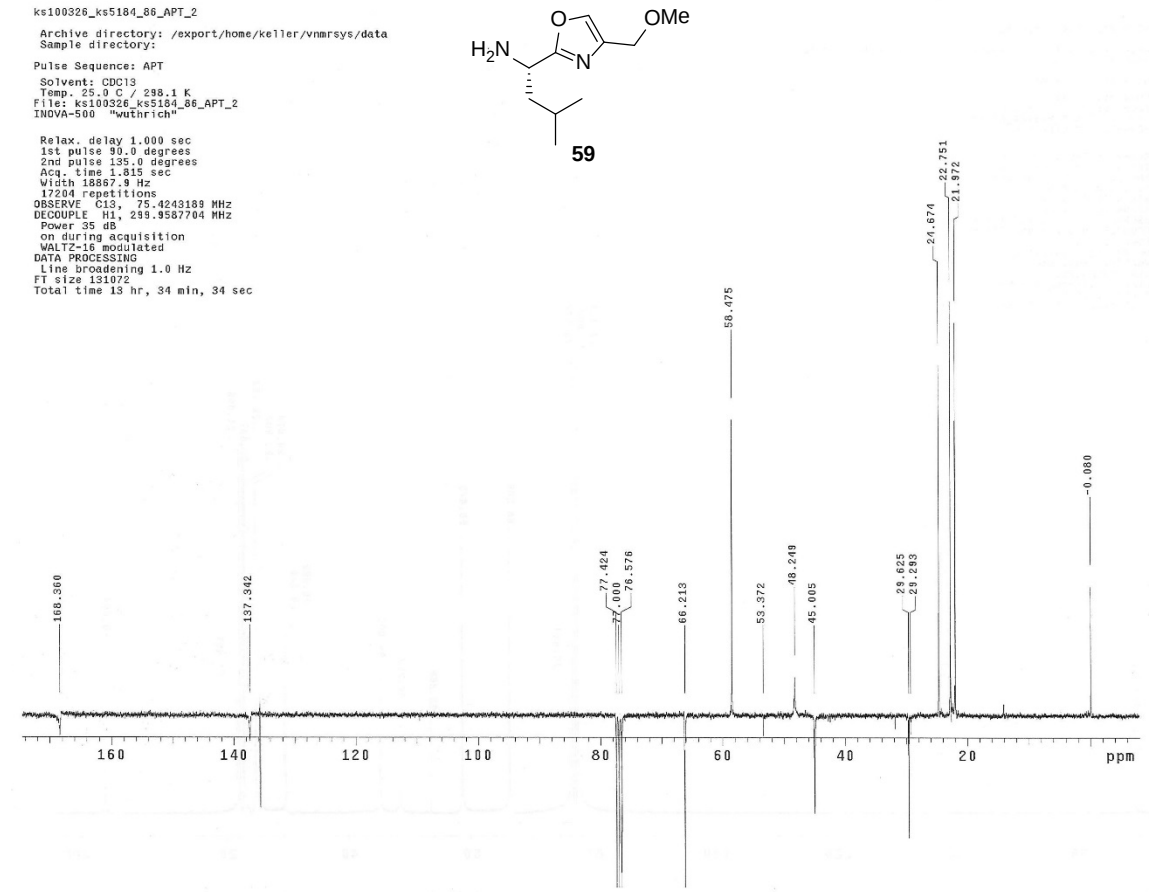

8.54
8.34
7.77
7.76
7.26
5.36
5.20
4.66
4.15
4.13
2.21
2.07
2.01
1.99
1.90
1.88
1.60
1.58
1.29
1.27
1.26
1.24
1.15
1.11
0.96
0.94
0.07
0.00
1H NMR, 300 MHz, CDCl3
TFA·H2N
O
N
F
57
1.00
2.01
1.03
2.10
1.20
5.85
ppm


160.5
139.1
139.0
136.5
136.2
77.4
77.0
76.6
76.4
74.2
48.0
40.8
24.5
22.1
21.3
13C NMR, 75 MHz, CDCl3
TFA·H2N
O
N
F
57
ppm

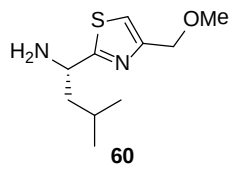

7.51
4.57
4.08
4.06
4.05
2.21
2.17
2.06
1.75
1.74
1.72
1.71
1.70
1.70
1.69
1.68
1.66
1.65
1.64
1.63
1.63
1.62
1.61
1.60
1.59
1.58
1.58
0.95
0.93
0.92
0.91
0.00
$^{1}$H NMR, 500 MHz, CDCl$_3$
OH
$H_2N$
O
N
58
0.87
2.06
1.00
3.18
3.19
2.92
3.13
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
ppm


168.4
140.0
134.7
77.3
77.0
76.7
56.4
48.3
45.1
24.7
22.7
22.1
$^{13}$C NMR, 125 MHz, CDCl$_3$
OH
$H_2N$
O
N
58
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm


ks100326_ks5184_86_1H
exp1 s2pul
SAMPLE
date Mar 26 2010
solvent CDCl3
file exp
ACQUISITION
sw 4798.5
at 1.998
np 19174
fb 2600
bs 16
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 299.959
tof 251.9
tpwr 59
pw 4.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 39
dmf 13900
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 9.000
alfa 20.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn not used
DISPLAY
sp -186.6
wp 2591.4
rfl 634.4
rfp 0
rp -30.2
lp -62.4
PLOT
wc 250
sc 0
vs 74
th 20
nm cdc ph
O
OMe
H2N
N
59
7
6
5
4
3
2
1
-0
ppm
0.87
0.51
2.00
0.95
3.00
5.49
6.63


ks100326_ks5184_86_APT_2
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: ks100326_ks5184_86_APT_2
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.815 sec
Width 18867.9 Hz
17204 repetitions
OBSERVE C13, 75.4243189 MHz
DECOUPLE H1, 299.9587704 MHz
Power 35 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 13 hr, 34 min, 34 sec
O
OMe
H2N
N
59
168.360
137.342
77.424
77.000
76.576
66.213
58.475
53.372
48.249
45.005
29.625
29.293
24.674
22.751
21.972
-0.080
160
140
120
100
80
60
40
20
ppm

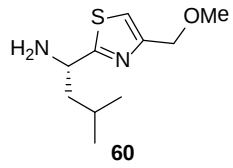
**$^{1}$H NMR, 500 MHz, $CDCl_3$**



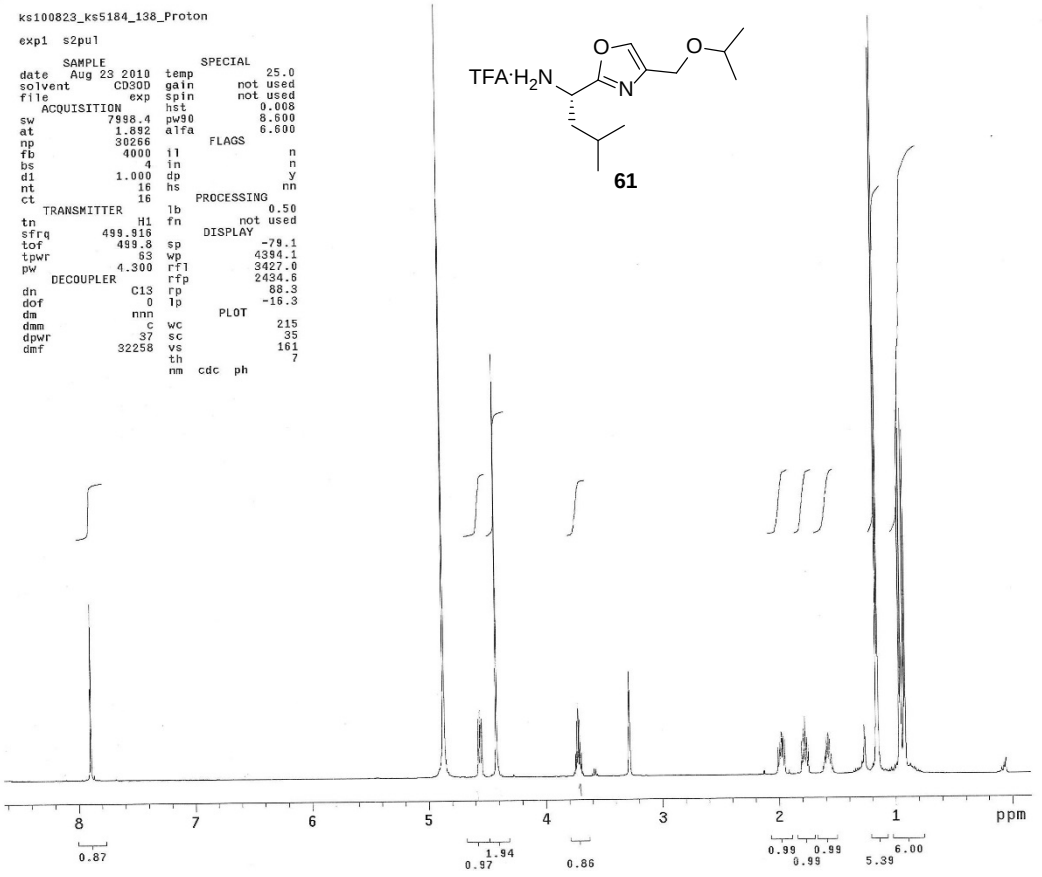

**60**

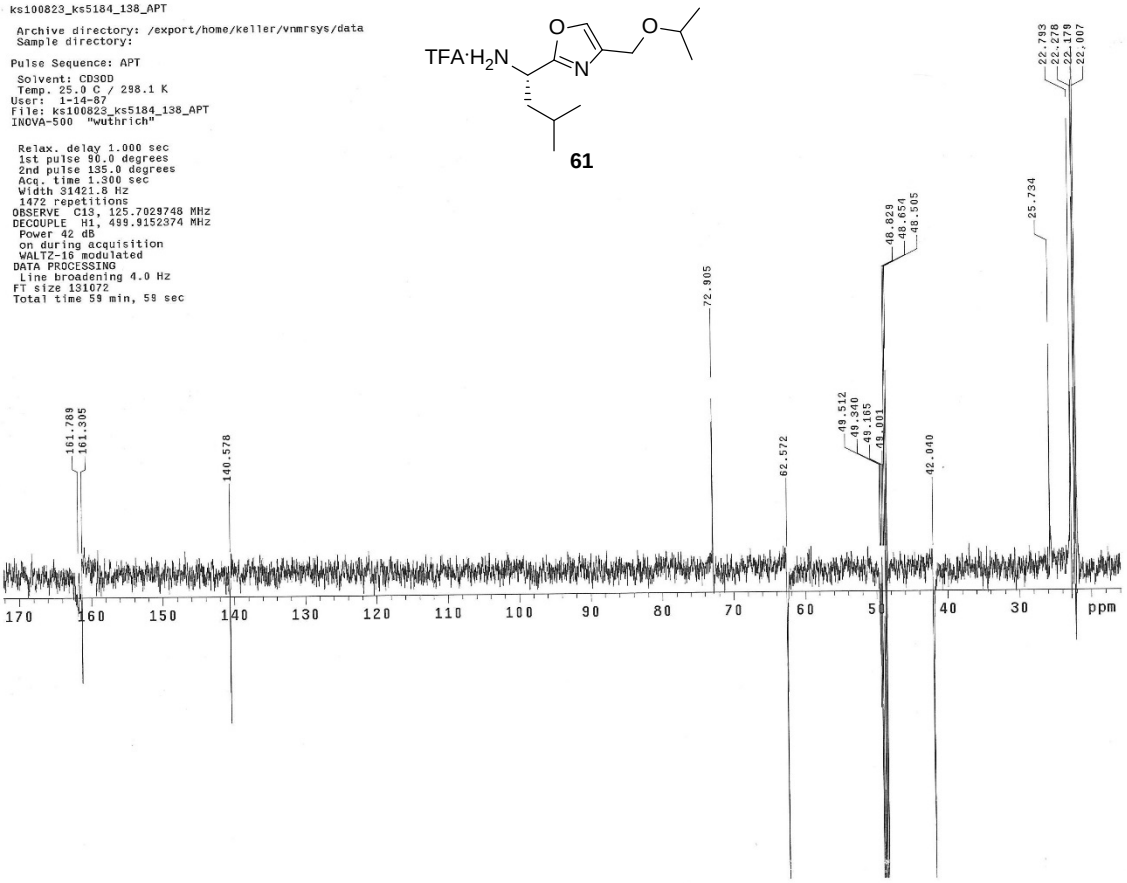


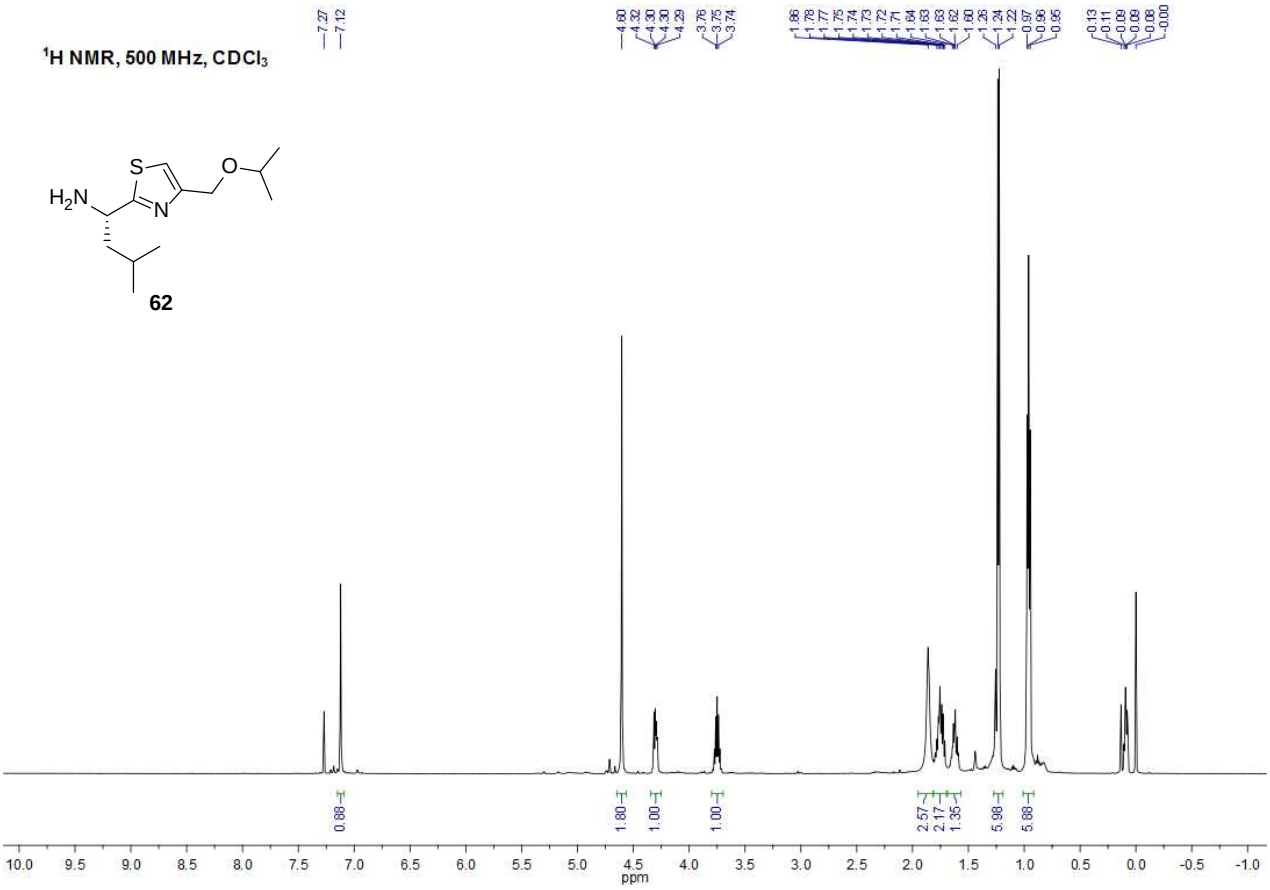

**$^{13}$C NMR, 125 MHz, $CDCl_3$**

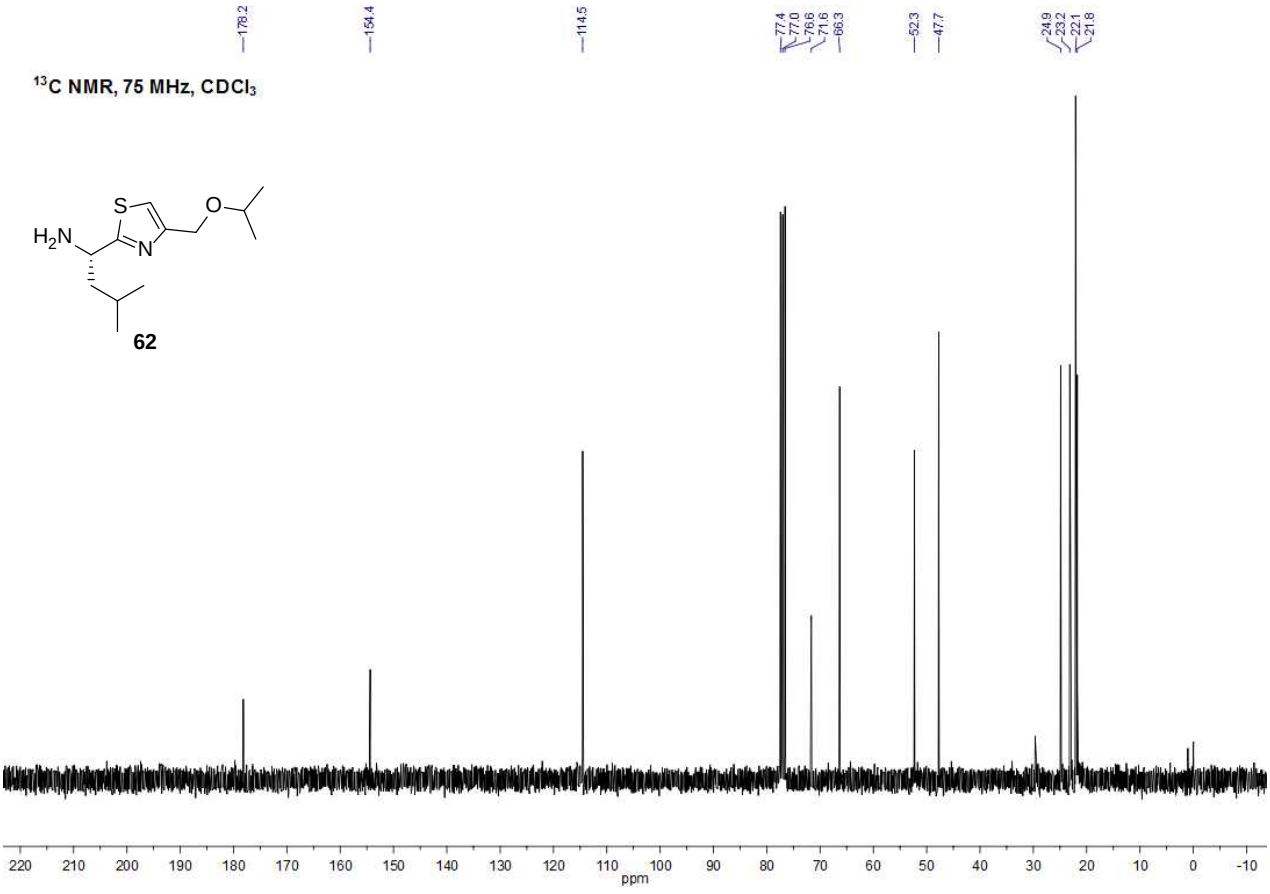


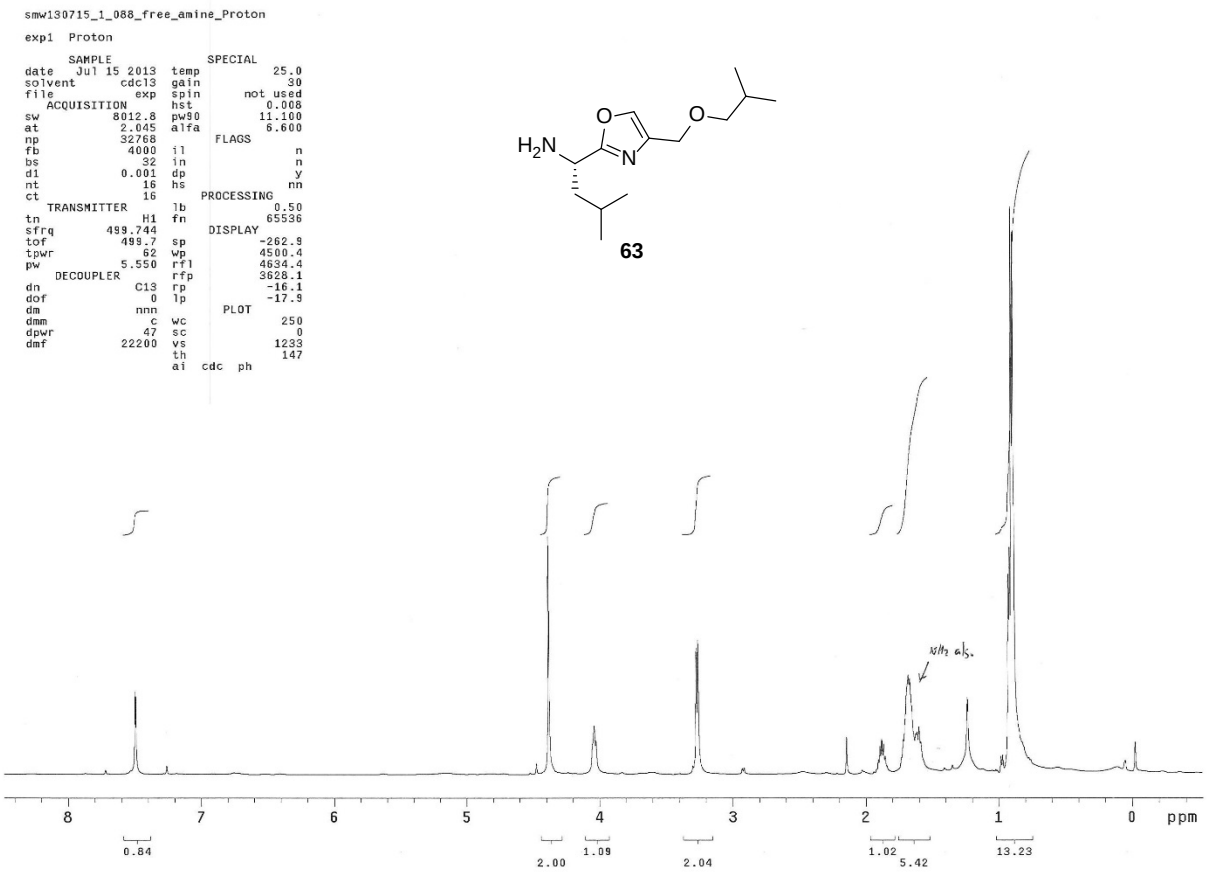

**60**

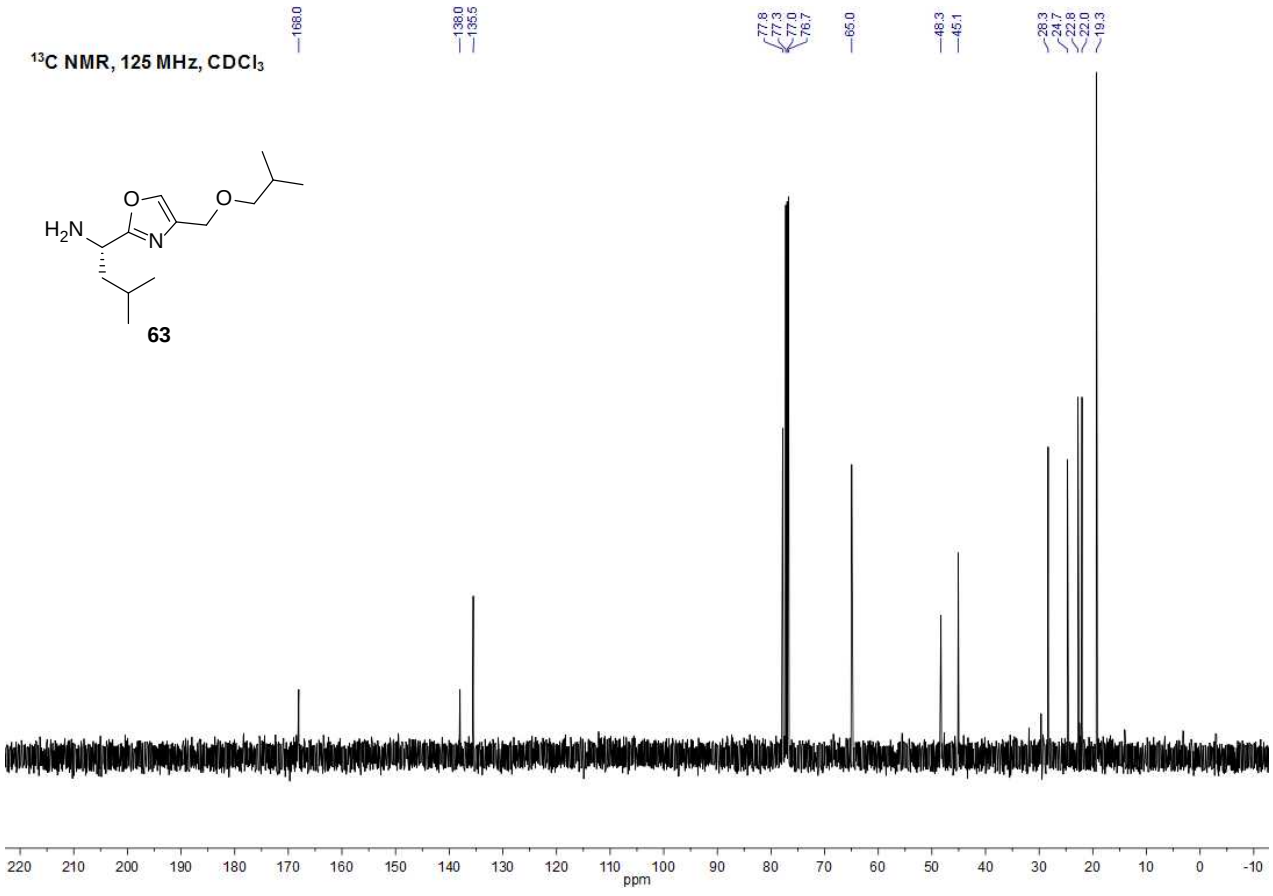

ks100823_ks5184_138_Proton
exp1 s2pul
SAMPLE
date Aug 23 2010
solvent CD3OD
file exp
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.916
tof 499.8
tpwr 53
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -79.1
wp 4394.1
rfl 3427.0
rfp 2434.6
rp 88.3
lp -16.3
PLOT
wc 215
sc 35
vs 161
th 7
nm cdc ph
TFA·H2N
O
N
O
61
8
7
6
5
4
3
2
1
ppm
0.87
1.94
0.97
0.86
0.99
0.99
0.99
6.00
5.39


ks100823_ks5184_138_APT
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100823_ks5184_138_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
1472 repetitions
OBSERVE C13, 125.7029748 MHz
DECOUPLE H1, 499.9152374 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 4.0 Hz
FT size 131072
Total time 59 min, 59 sec
TFA·H2N
O
N
O
61
161.789
161.305
140.578
72.905
62.572
49.512
49.340
49.165
48.991
48.829
48.654
48.505
42.040
25.734
22.793
22.278
22.179
22.007
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

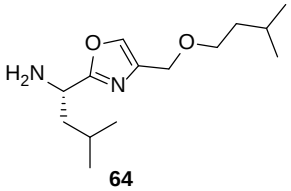

$^1$H NMR, 500 MHz, CDCl$_3$
62


$^{13}$C NMR, 75 MHz, CDCl$_3$
62


smw130715_1_088_free_amine_Proton
exp1 Proton
SAMPLE
date Jul 15 2013
solvent cdcl3
file exp
ACQUISITION
sw 8012.8
at 2.045
np 32768
fb 4000
bs 32
d1 0.001
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.744
tof 499.7
tpwr 62
pw 5.550
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 47
dmf 22200
SPECIAL
temp 25.0
gain 30
spin not used
hst 0.008
pw90 11.100
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn 65536
DISPLAY
sp -262.8
wp 4500.4
rfl 4634.4
rfp 3628.1
rp -16.1
lp -17.9
PLOT
wc 250
sc 0
vs 1233
th 147
ai cdc ph
63
8
7
6
5
4
3
2
1
0
ppm
0.84
2.00
1.09
2.04
1.02
5.42
13.23


13C NMR, 125 MHz, CDCl3
168.0
138.0
135.5
77.8
77.3
77.0
76.7
65.0
48.3
45.1
28.3
24.7
22.8
22.0
19.3
63
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

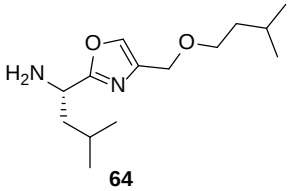
**$^1$H NMR, 500 MHz, $CDCl_3$**



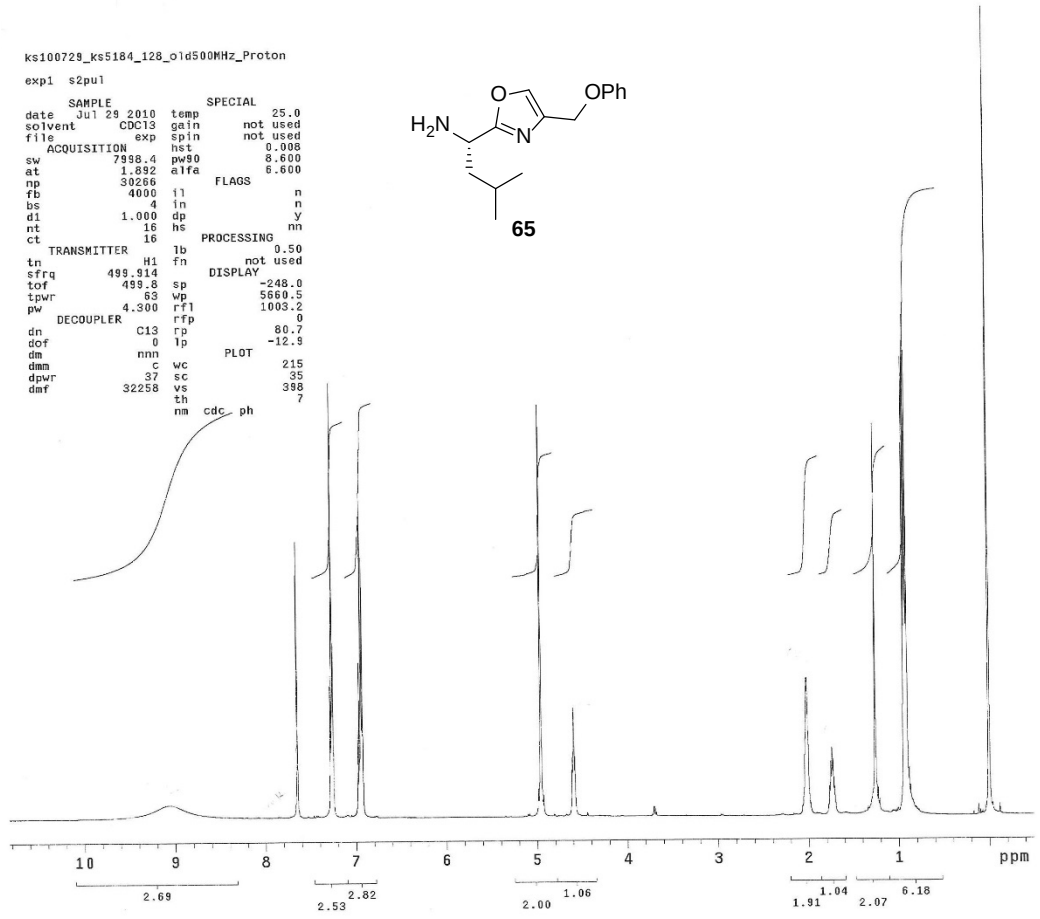
**64**

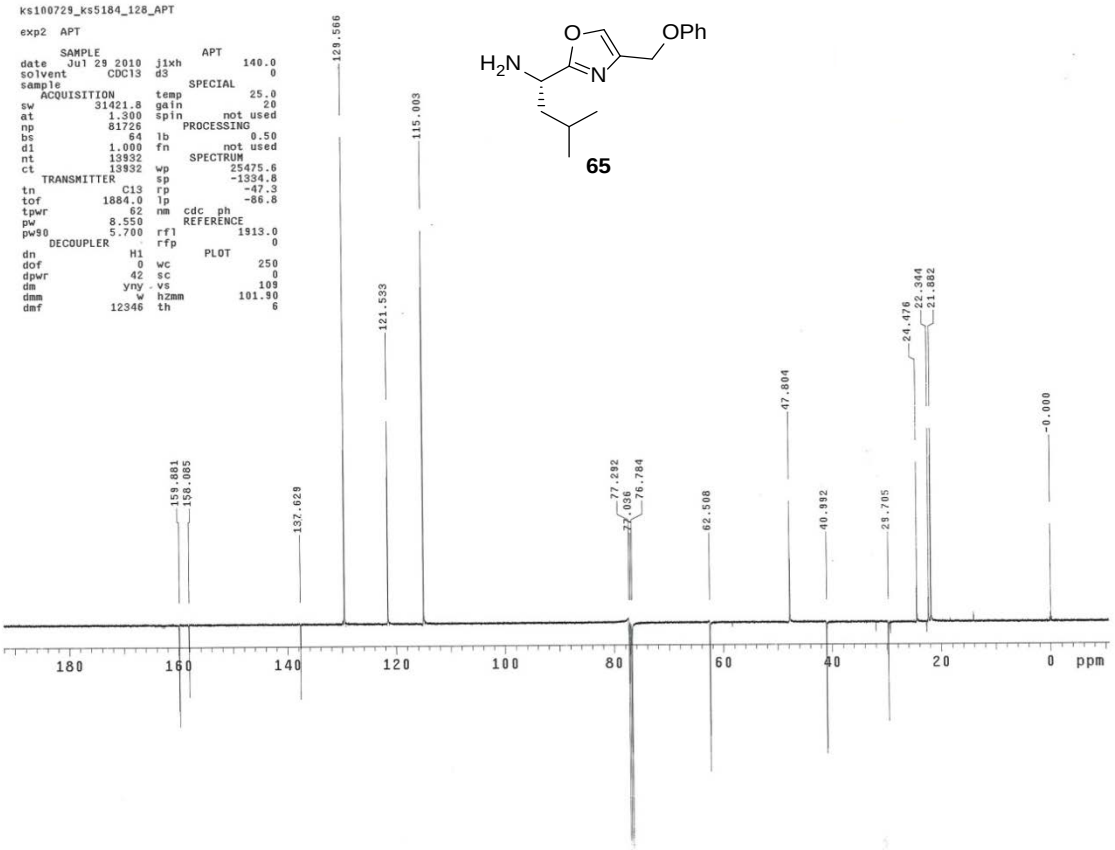


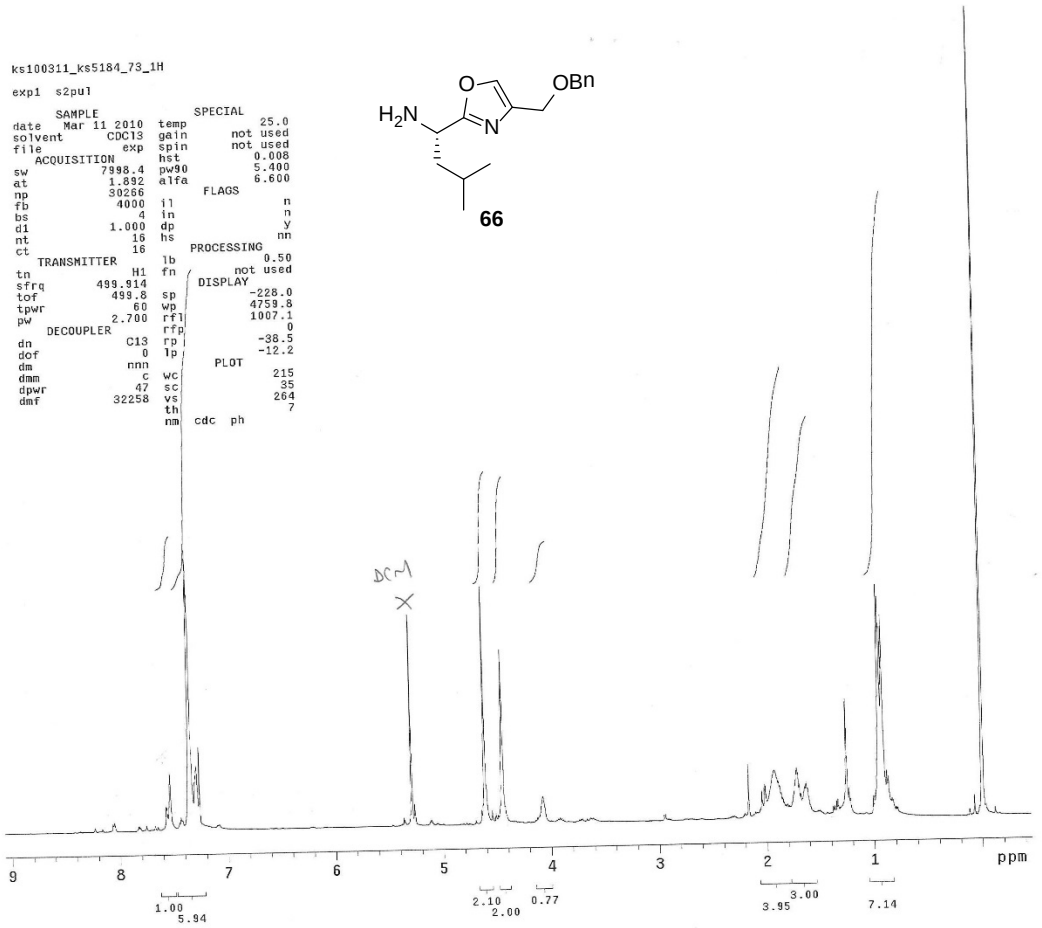

**$^{13}$C NMR, 125 MHz, $CDCl_3$**

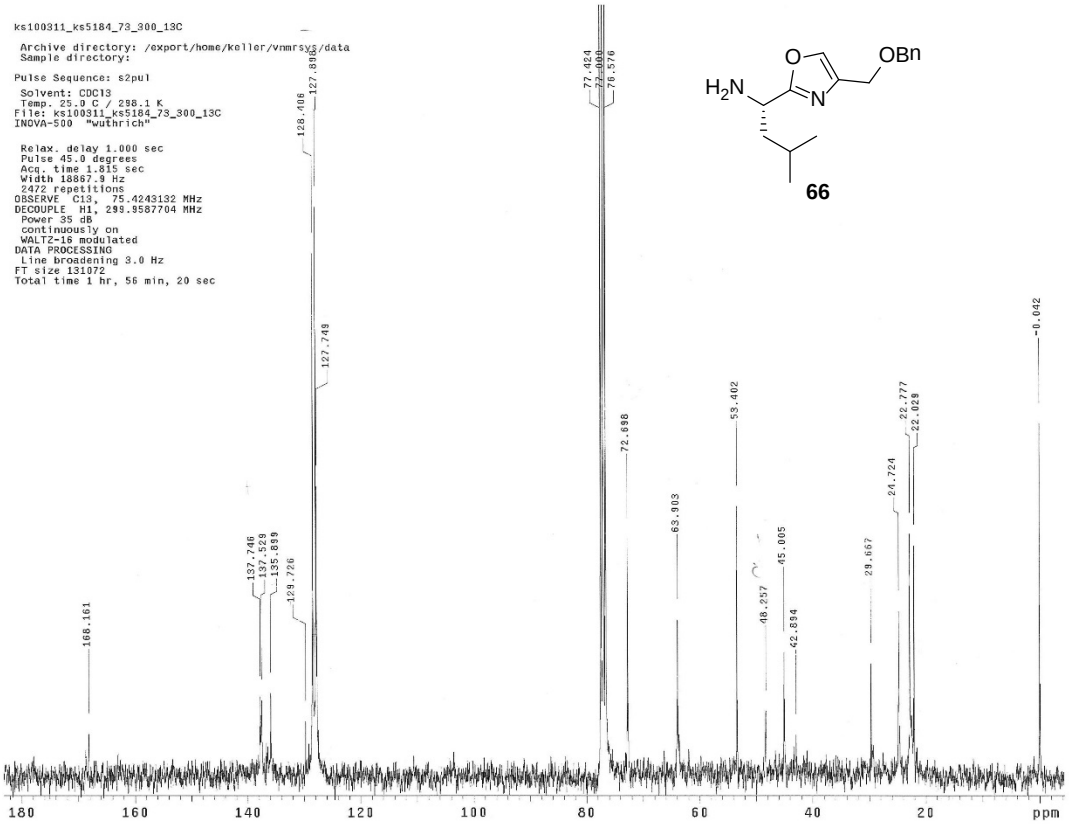


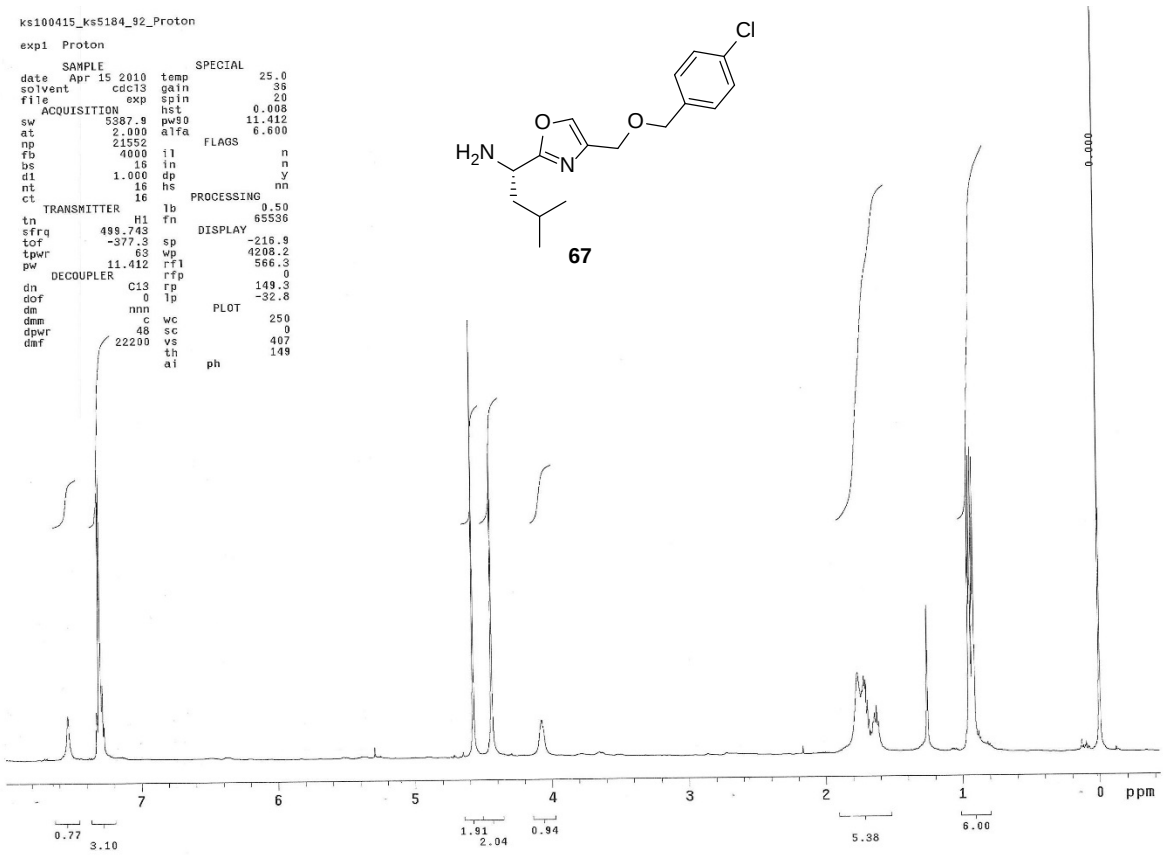
**64**

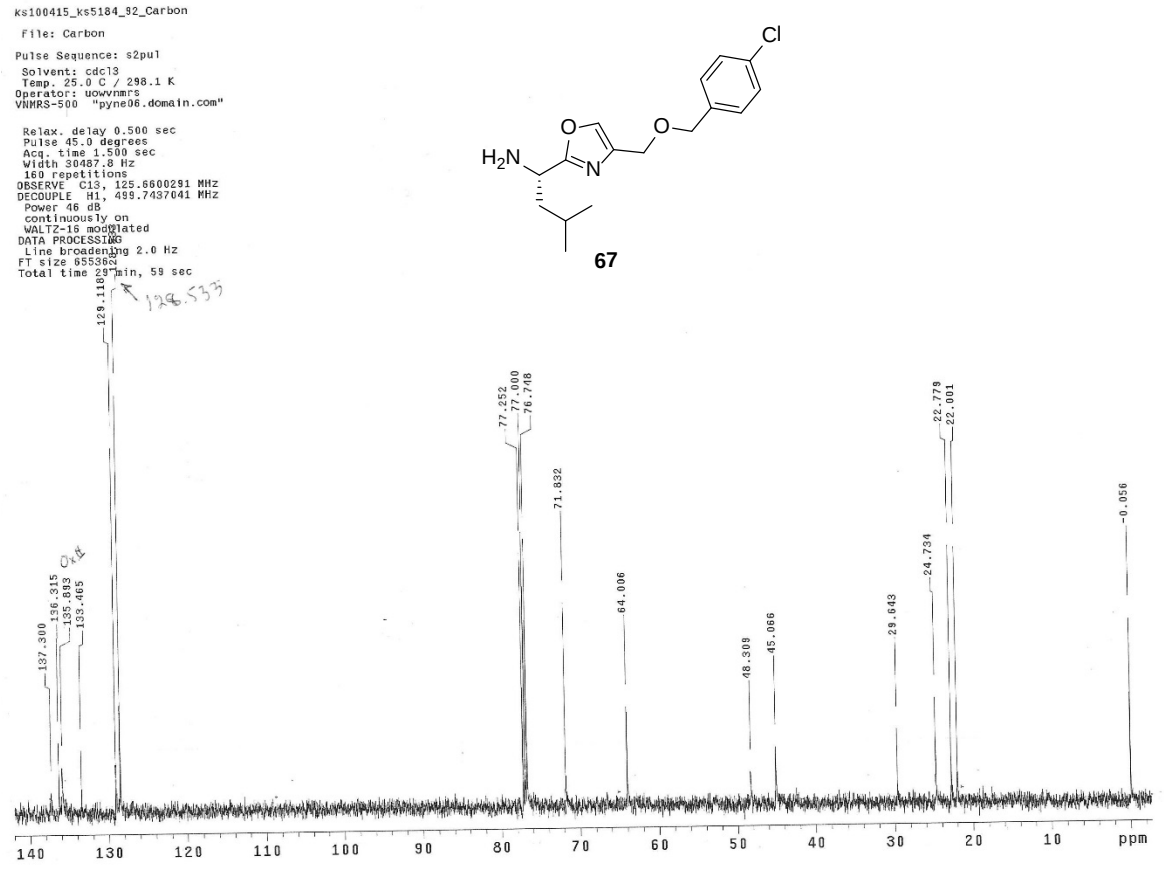

ks100729_ks5184_128_old500MHz_Proton
exp1 s2pul
SAMPLE
date Jul 29 2010
solvent CDCl3
file exp
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.914
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -248.0
wp 5660.5
rfl 1003.2
rfp 0
rp 80.7
lp -12.9
PLOT
wc 215
sc 35
vs 398
th 7
nm cdc_ph
O
OPh
H2N
N
65
10
9
8
7
6
5
4
3
2
1
ppm
2.69
2.53
2.82
2.00
1.06
1.91
1.04
2.07
6.18

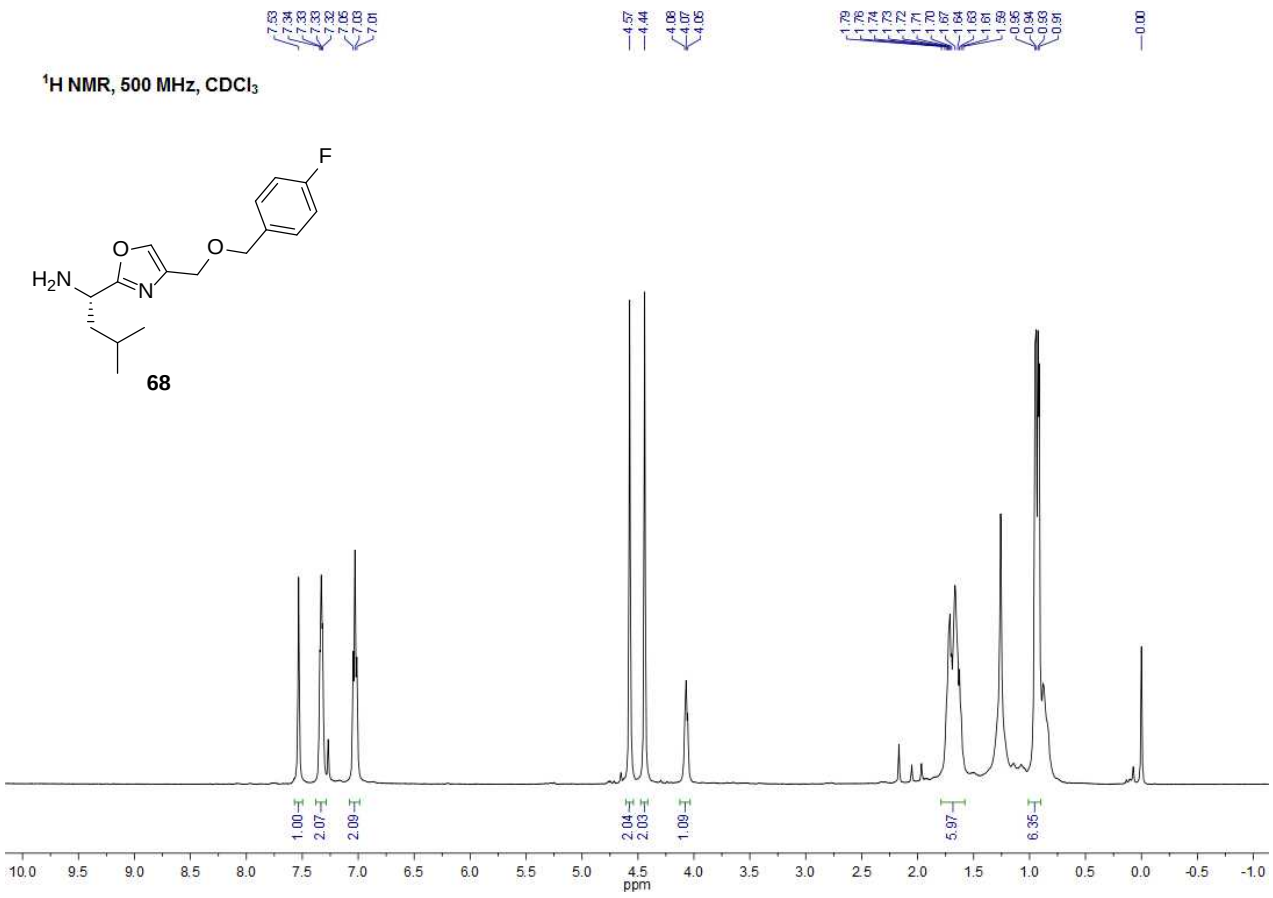

ks100729_ks5184_128_APT
exp2 APT
SAMPLE
date Jul 29 2010
solvent CDCl3
sample
ACQUISITION
sw 31421.8
at 1.300
np 81726
bs 64
d1 1.000
nt 13932
ct 13932
TRANSMITTER
tn C13
tof 1884.0
tpwr 62
pw 8.550
pw90 5.700
DECOUPLER
dn H1
dof 0
dpwr 42
dm yny
dmm w
dmf 12346
APT
j1xh 140.0
d3 0
SPECIAL
temp 25.0
gain 20
spin not used
PROCESSING
lb 0.50
fn not used
SPECTRUM
wp 25475.6
sp -1334.8
rp -47.3
lp -86.8
nm cdc_ph
REFERENCE
rfl 1913.0
rfp 0
PLOT
wc 250
sc 0
vs 109
hzmm 101.90
th 6
O
OPh
H2N
N
65
129.566
115.003
121.533
159.881
158.085
137.629
77.292
77.036
76.784
62.508
47.804
40.992
25.705
24.476
22.344
21.882
-0.000
180
160
140
120
100
80
60
40
20
0
ppm

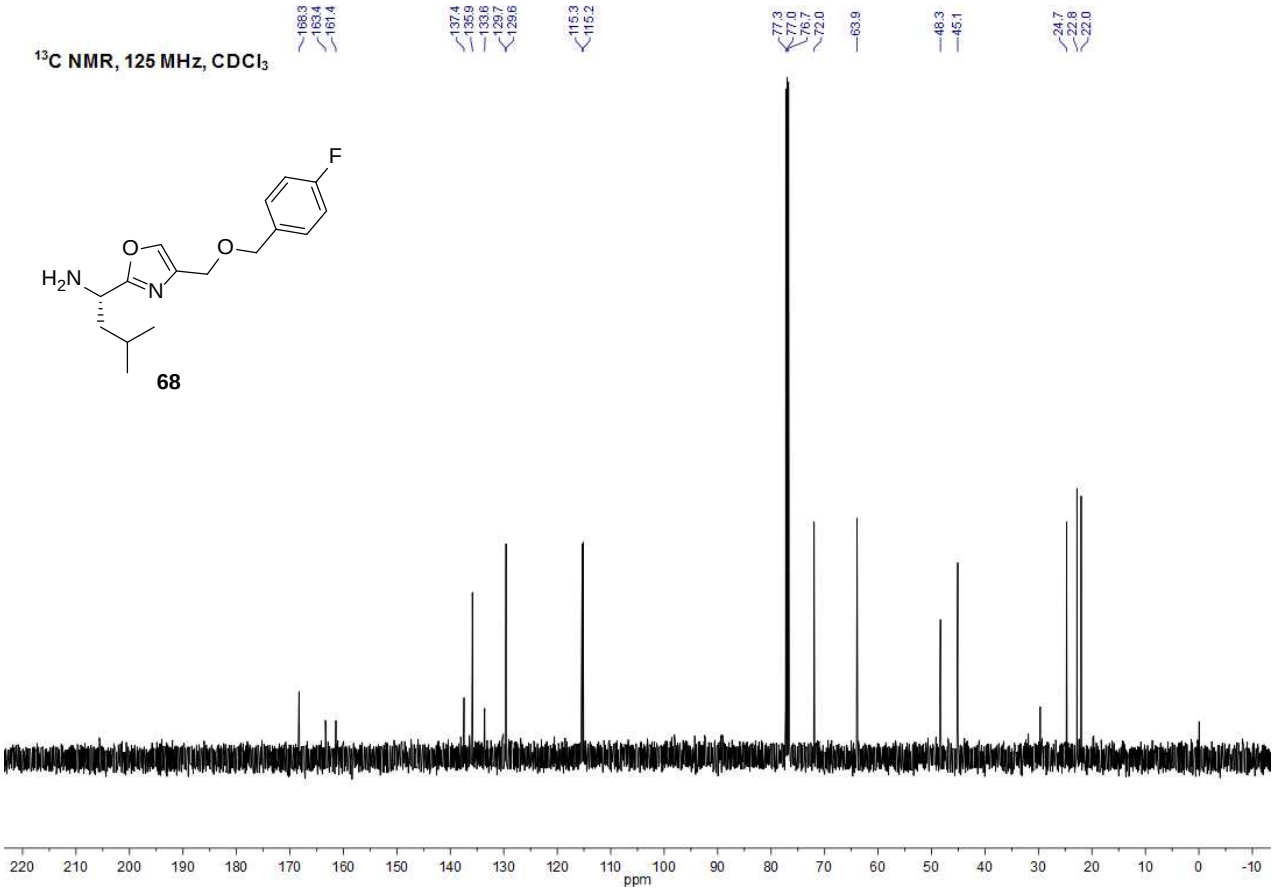

ks100311_ks5184_73_1H
expl s2pul
SAMPLE
date Mar 11 2010
solvent CDCl3
file exp
ACQUISITION
sw 7998.4
at 1.892
np 30286
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.914
tof 499.8
tpwr 60
pw 2.700
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 47
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 5.400
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -228.0
wp 4759.8
rfl 1007.1
rfp 0
rp -38.5
lp -12.2
PLOT
wc 215
sc 35
vs 264
th 7
nm cdc ph
O
OBn
H2N
N
66
9
8
7
6
5
4
3
2
1
ppm
1.00
5.94
2.10
2.00
0.77
3.95
3.00
7.14

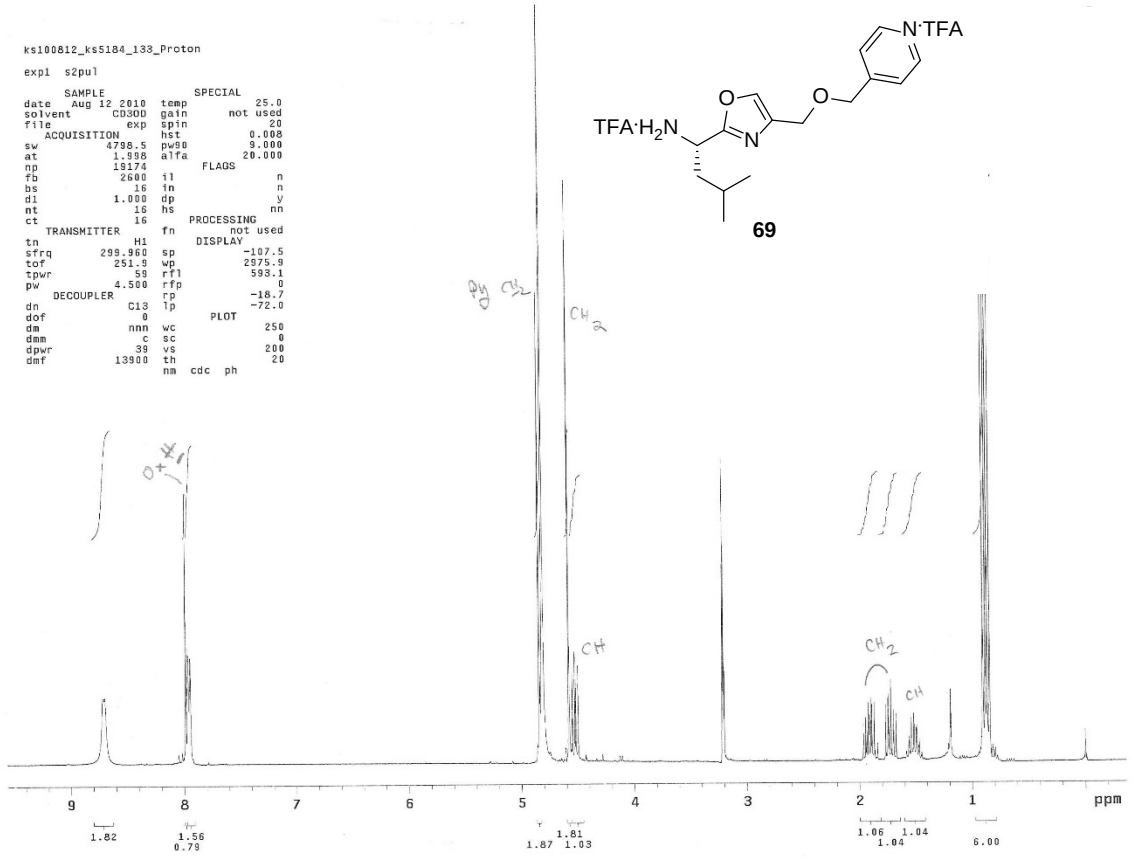

ks100311_ks5184_73_300_13C
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: ks100311_ks5184_73_300_13C
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.815 sec
Width 18867.9 Hz
2472 repetitions
OBSERVE C13, 75.4243132 MHz
DECOUPLE H1, 299.9587704 MHz
Power 35 dB
continuously ON
WALTZ-16 modulated
DATA PROCESSING
Line broadening 3.0 Hz
FT size 131072
Total time 1 hr, 56 min, 20 sec
O
OBn
H2N
N
66
168.161
137.746
137.529
135.859
129.726
128.408
127.896
127.749
77.464
77.040
76.616
72.688
63.903
53.402
48.257
45.005
42.884
29.667
24.724
22.777
22.029
-0.042
180
160
140
120
100
80
60
40
20
ppm

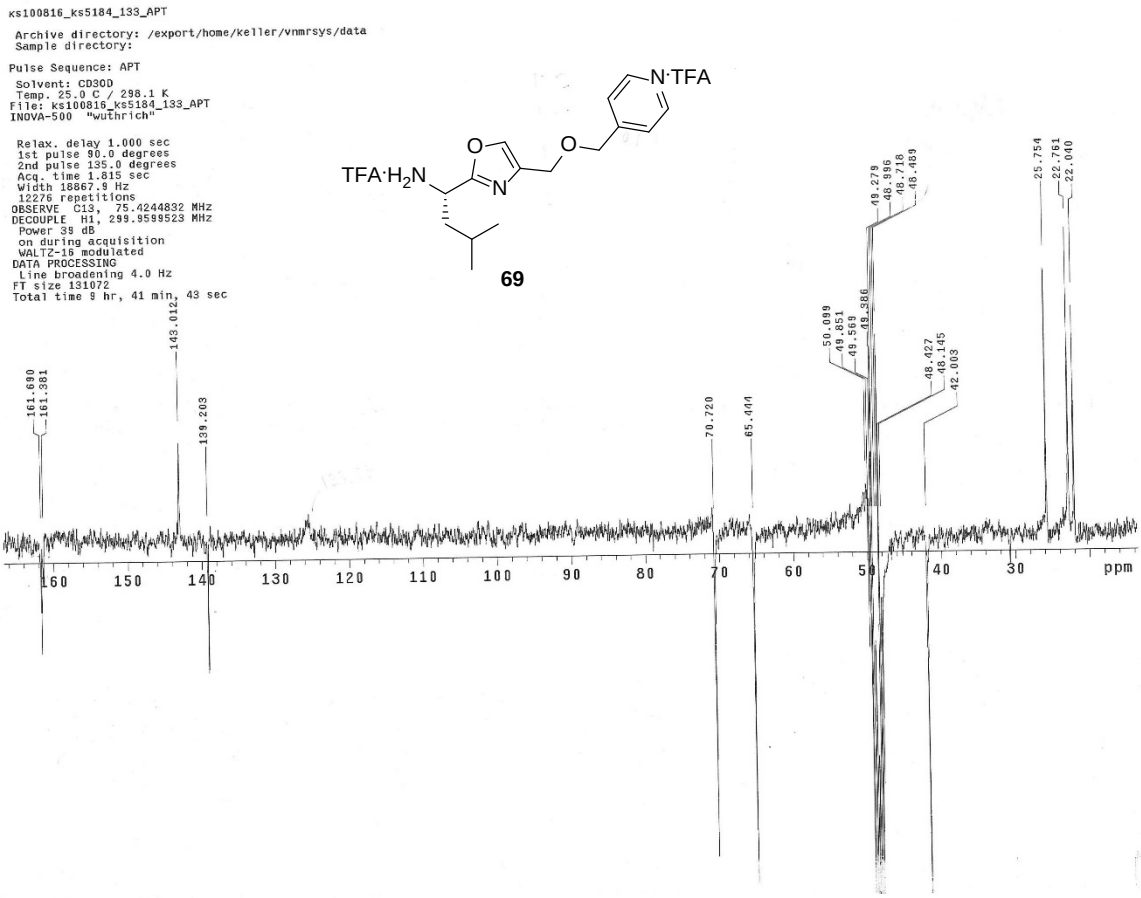

ks100415_ks5184_92_Proton
exp1 Proton
SAMPLE
date Apr 15 2010
solvent cdcl3
file exp
ACQUISITION
sw 5387.9
at 2.000
np 21552
fb 4000
bs 16
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.743
tof -377.3
tpwr 63
pw 11.412
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 48
dmf 22200
SPECIAL
temp 25.0
gain 36
spin 20
hst 0.008
pw90 11.412
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn 65536
DISPLAY
sp -216.9
wp 4208.2
rfl 566.3
rfp 0
rp 149.3
lp -32.8
PLOT
wc 250
sc 0
vs 407
th 149
ai ph
Cl
O
O
H2N
N
67
0.000
7
6
5
4
3
2
1
0 ppm
0.77
3.10
1.91
2.04
0.94
5.38
6.00

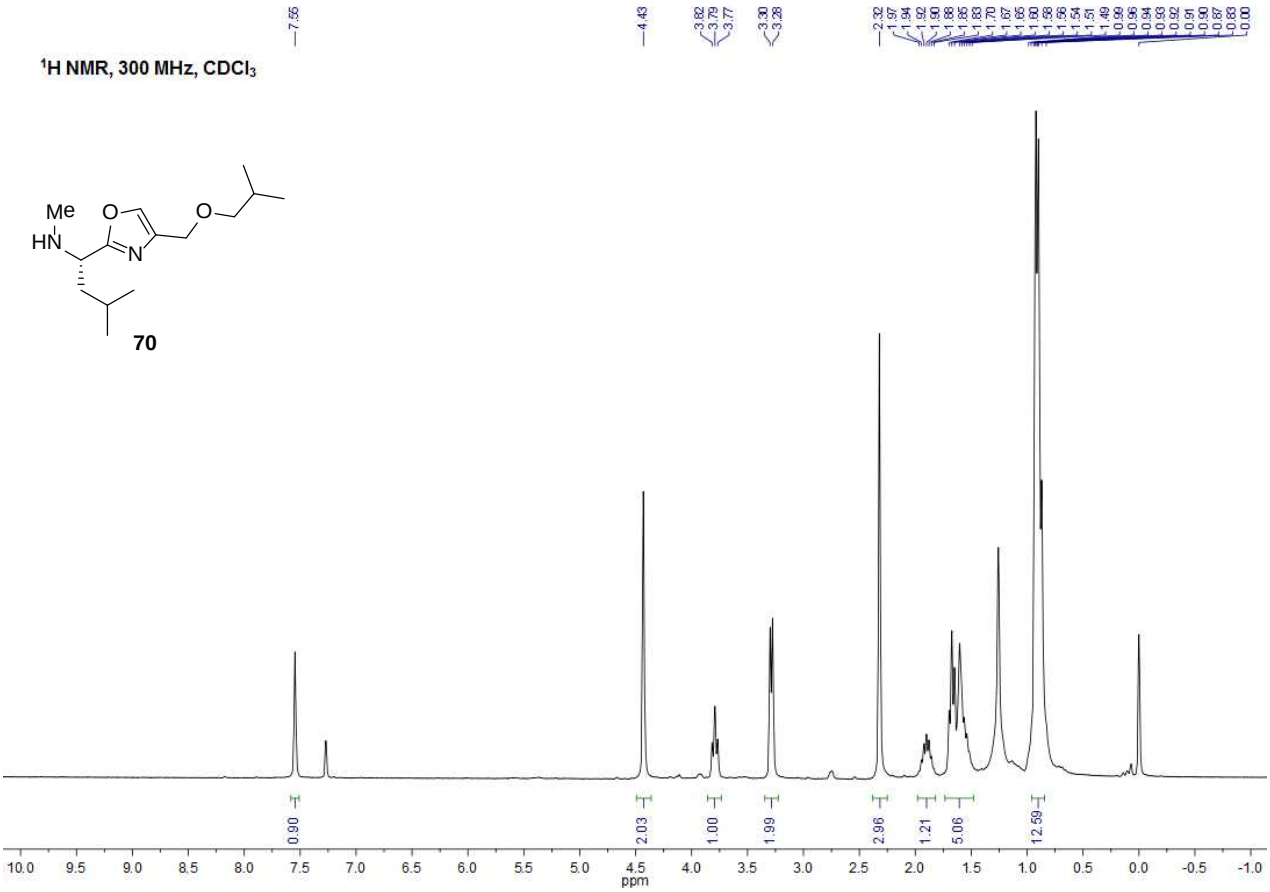

Ks100415_Ks5184_92_Carbon
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: uowvnmrs
VNMRS-500 "pyne06.domain.com"
Relax. delay 0.500 sec
Pulse 45.0 degrees
Acq. time 1.500 sec
Width 30487.8 Hz
160 repetitions
OBSERVE C13, 125.6600291 MHz
DECOUPLE H1, 499.7437041 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 29 min, 59 sec
Cl
O
O
H2N
N
67
137.300
136.315
135.893
133.465
129.118
77.252
77.000
76.748
71.832
64.006
48.309
45.066
29.643
24.734
22.779
22.001
-0.056
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

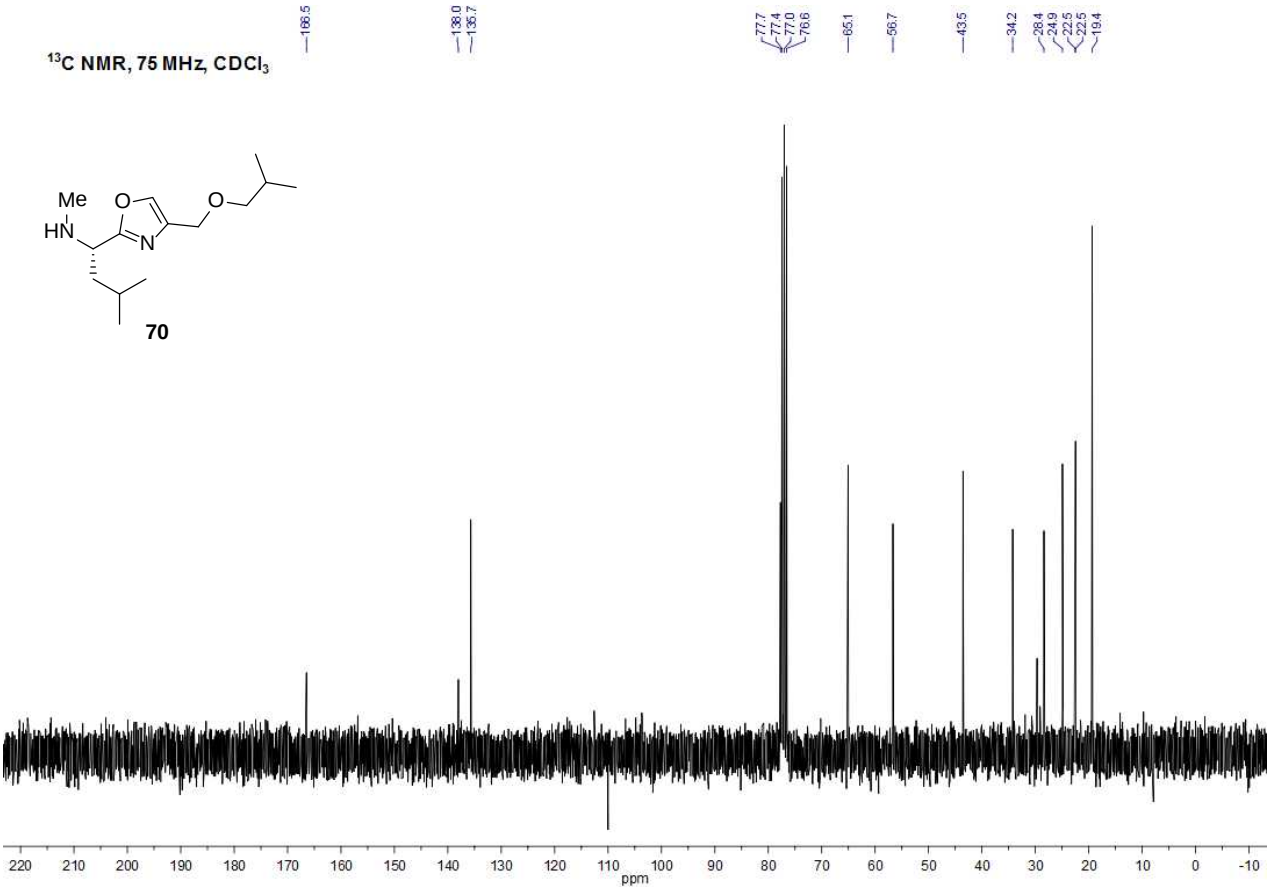

7.53
7.34
7.33
7.33
7.32
7.05
7.03
7.01
4.57
4.44
4.08
4.07
4.05
1.79
1.76
1.74
1.73
1.72
1.71
1.70
1.67
1.64
1.63
1.61
1.59
0.95
0.94
0.93
0.91
0.00
1H NMR, 500 MHz, CDCl3
F
O
O
H2N
N
68
1.00
2.07
2.09
2.04
2.03
1.09
5.97
6.35
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
ppm

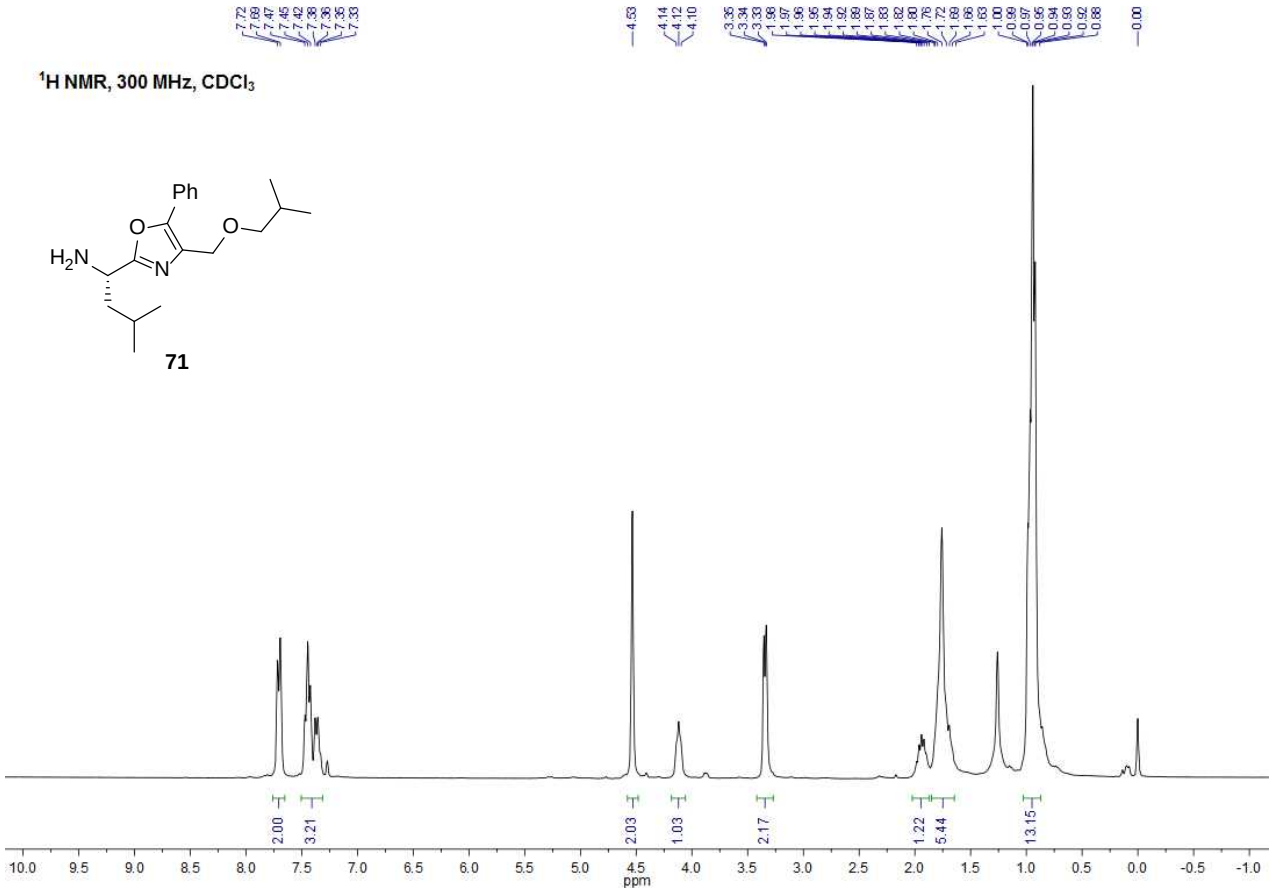

168.3
163.4
161.4
137.4
135.9
133.6
129.7
129.6
115.3
115.2
77.3
77.0
76.7
72.0
63.9
48.3
45.1
24.7
22.8
22.0
13C NMR, 125 MHz, CDCl3
F
O
O
H2N
N
68
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

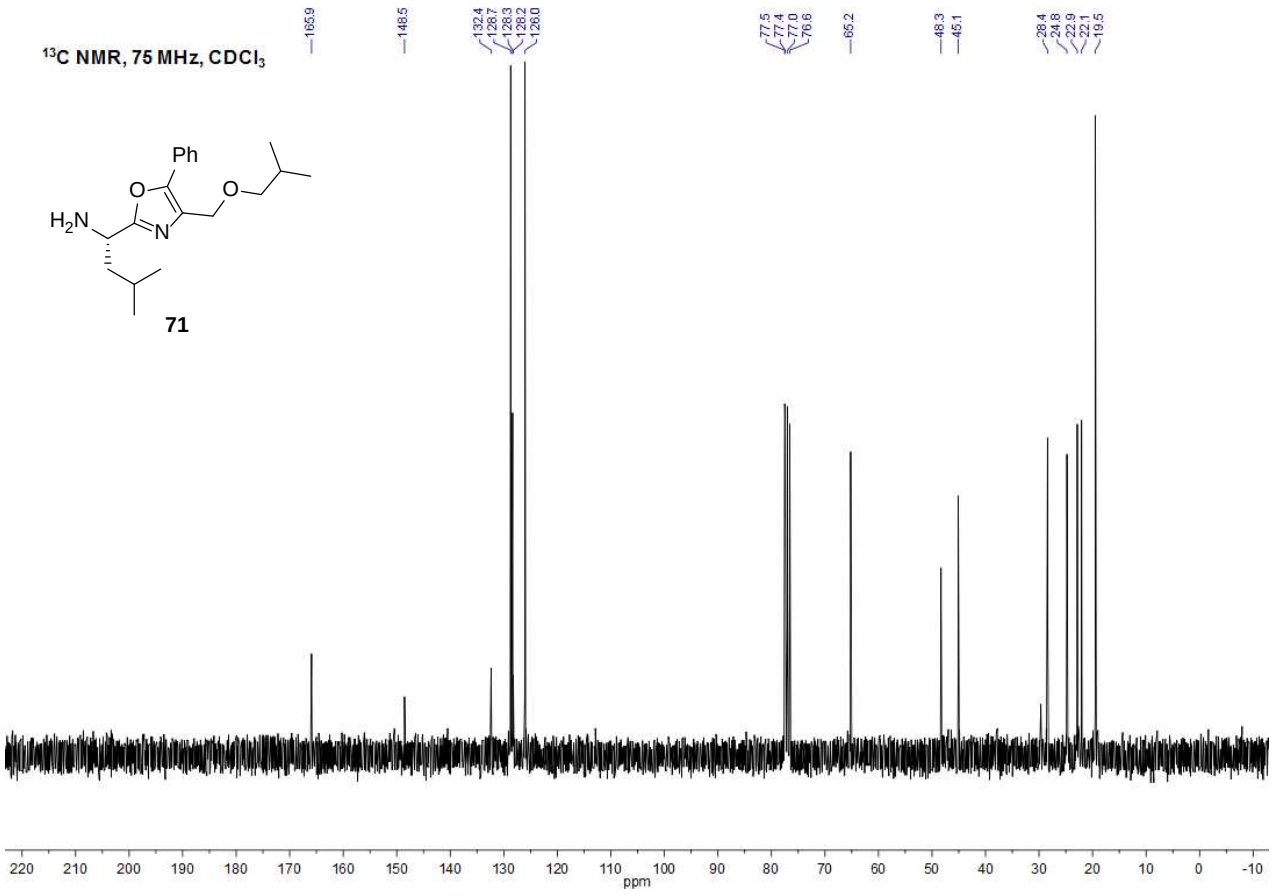

ks100812_ks5184_133_Proton
exp1 s2pul
SAMPLE
date Aug 12 2010
solvent CD3OD
file exp
ACQUISITION
sw 4798.5
at 1.598
np 19174
fb 2600
bs 16
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 299.960
tof 251.9
tpwr 59
pw 4.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 39
dmf 13900
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 9.000
alfa 20.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn not used
DISPLAY
sp -107.5
wp 2975.9
rfl 593.1
rfp 0
rp -18.7
lp -72.0
PLOT
wc 250
sc 0
vs 200
th 20
nm cdc ph
N·TFA
TFA·H2N
69
CH2
CH
CH2
CH
9
8
7
6
5
4
3
2
1
ppm
1.82
1.56
0.79
1.81
1.87 1.03
1.06 1.04
1.04
6.00


ks100816_ks5184_133_APT
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
File: ks100816_ks5184_133_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.815 sec
Width 18867.9 Hz
12276 repetitions
OBSERVE C13, 75.4244832 MHz
DECOUPLE H1, 299.9599523 MHz
Power 39 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 4.0 Hz
FT size 131072
Total time 9 hr, 41 min, 43 sec
N·TFA
TFA·H2N
69
161.690
161.381
143.012
139.203
70.720
65.444
50.099
49.851
49.569
49.279
48.986
48.718
48.489
48.386
48.427
48.145
42.003
25.754
22.761
22.040
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

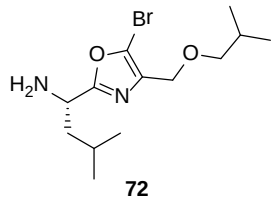

7.55
4.43
3.82
3.79
3.77
3.30
3.28
2.32
1.97
1.94
1.92
1.90
1.88
1.85
1.83
1.70
1.67
1.65
1.60
1.58
1.56
1.54
1.51
1.49
0.99
0.96
0.94
0.93
0.92
0.91
0.90
0.87
0.83
0.00
¹H NMR, 300 MHz, CDCl₃
Me
HN
O
N
O
70
0.90
2.03
1.00
1.99
2.96
1.21
5.06
12.59
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
ppm


166.5
138.0
135.7
77.7
77.4
77.0
76.6
65.1
56.7
43.5
34.2
28.4
24.9
22.5
22.5
19.4
¹³C NMR, 75 MHz, CDCl₃
Me
HN
O
N
O
70
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm


7.72
7.69
7.47
7.45
7.42
7.38
7.36
7.35
7.33
4.53
4.14
4.12
4.10
3.35
3.34
3.33
1.99
1.97
1.96
1.95
1.94
1.92
1.89
1.87
1.83
1.82
1.80
1.76
1.72
1.69
1.66
1.63
1.00
0.99
0.97
0.95
0.94
0.93
0.92
0.88
0.00
¹H NMR, 300 MHz, CDCl₃
Ph
O
O
H₂N
N
71
2.00
3.21
2.03
1.03
2.17
1.22
5.44
13.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
ppm


165.9
148.5
132.4
128.7
128.3
128.2
126.0
77.5
77.4
77.0
76.6
65.2
48.3
45.1
28.4
24.8
22.9
22.1
19.5
¹³C NMR, 75 MHz, CDCl₃
Ph
O
O
H₂N
N
71
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

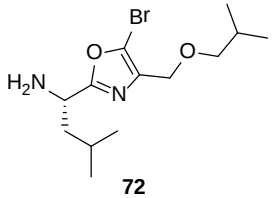
**$^1$H NMR, 300 MHz, $CDCl_3$**




**72**

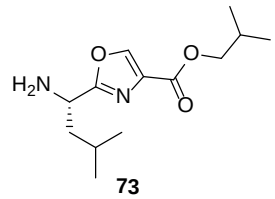



**$^{13}$C NMR, 75 MHz, $CDCl_3$**




**72**

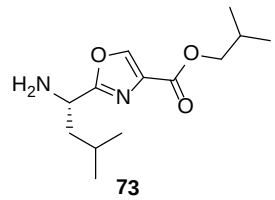
**$^1$H NMR, 300 MHz, $CDCl_3$**



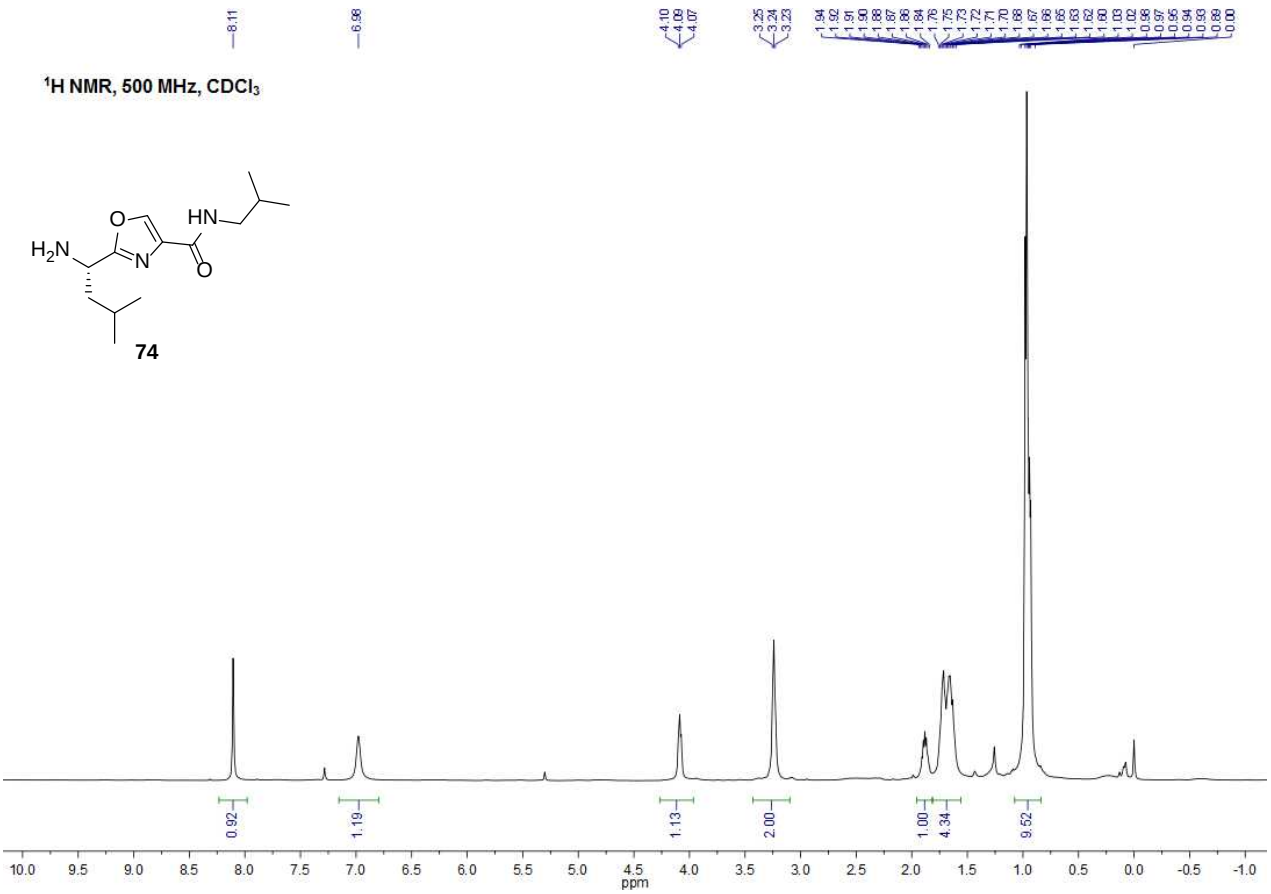
**73**

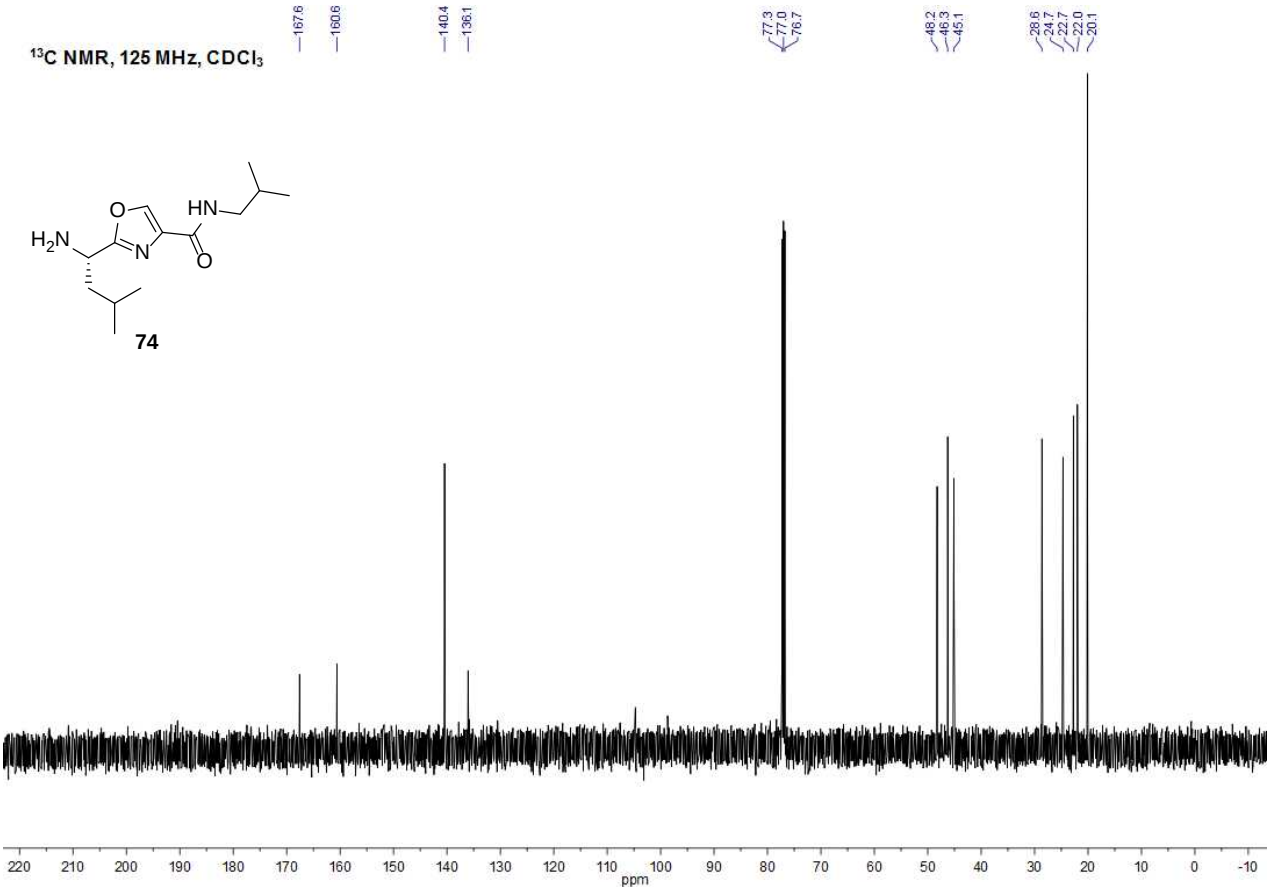


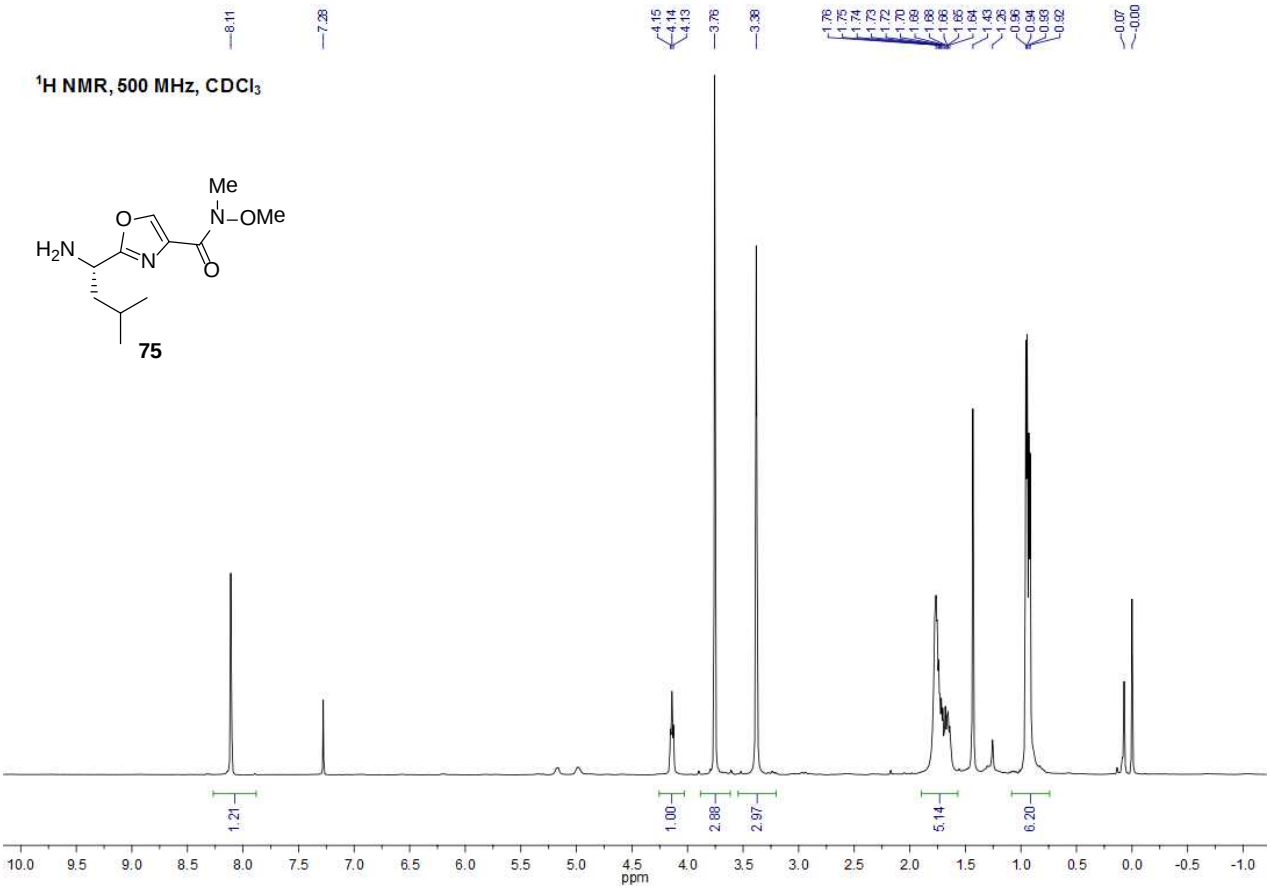

**$^{13}$C NMR, 75 MHz, $CDCl_3$**

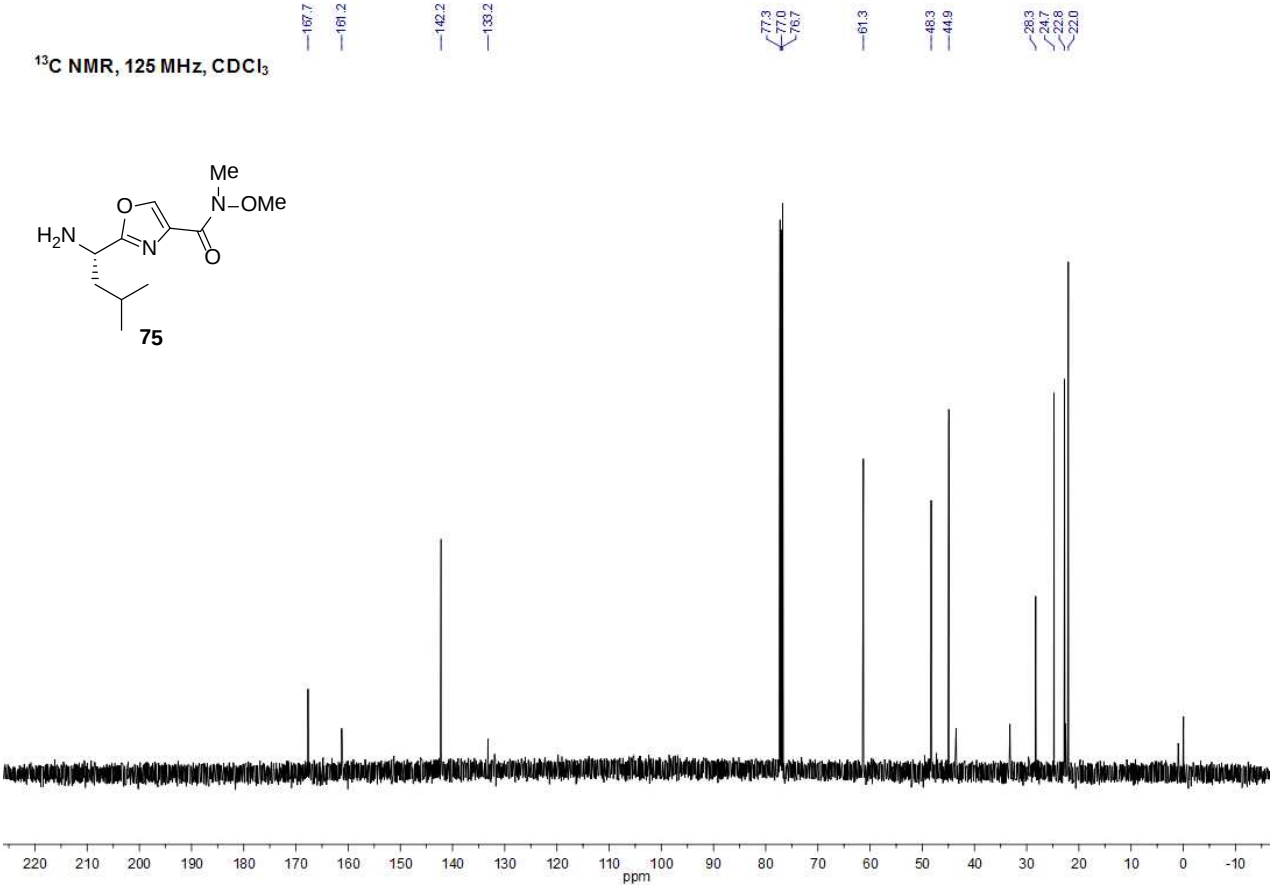


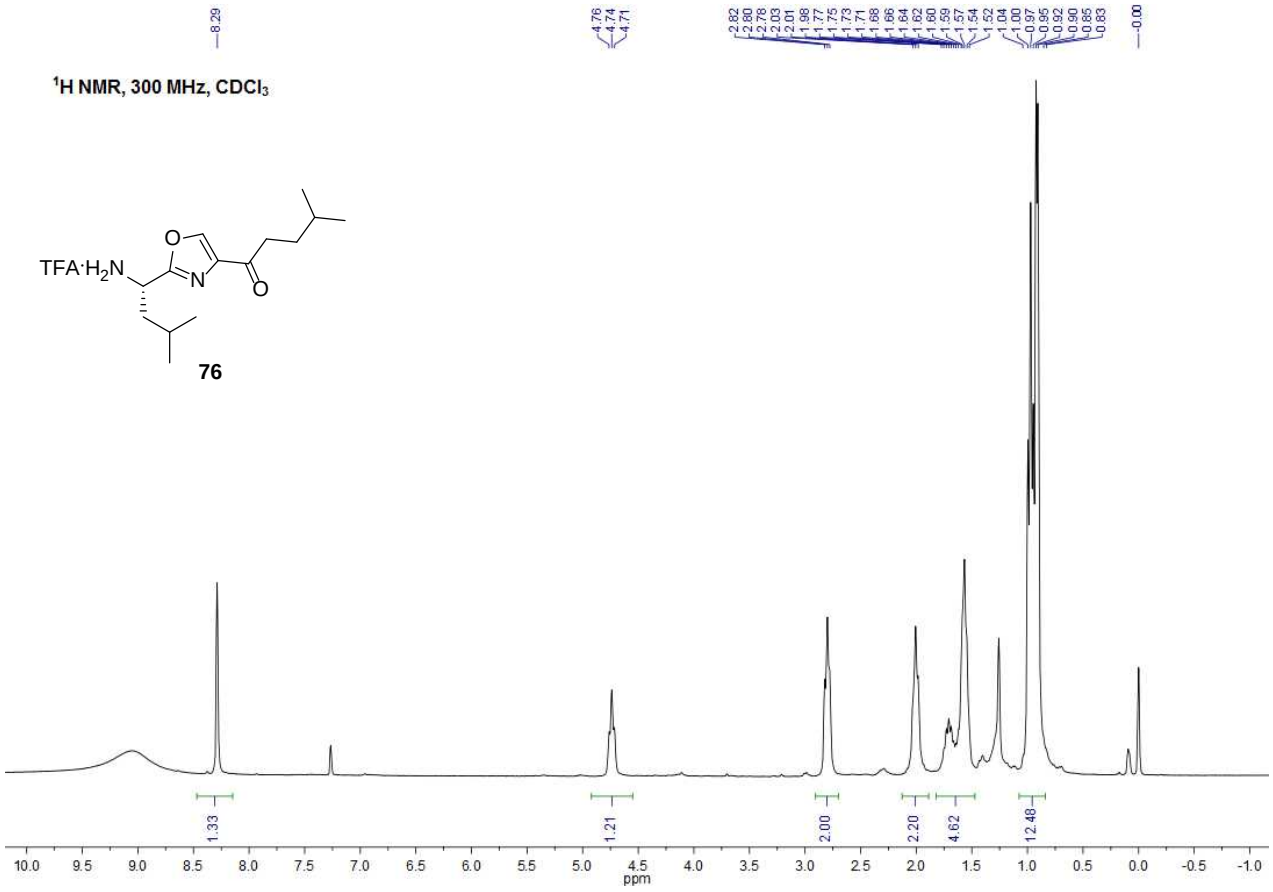
**73**

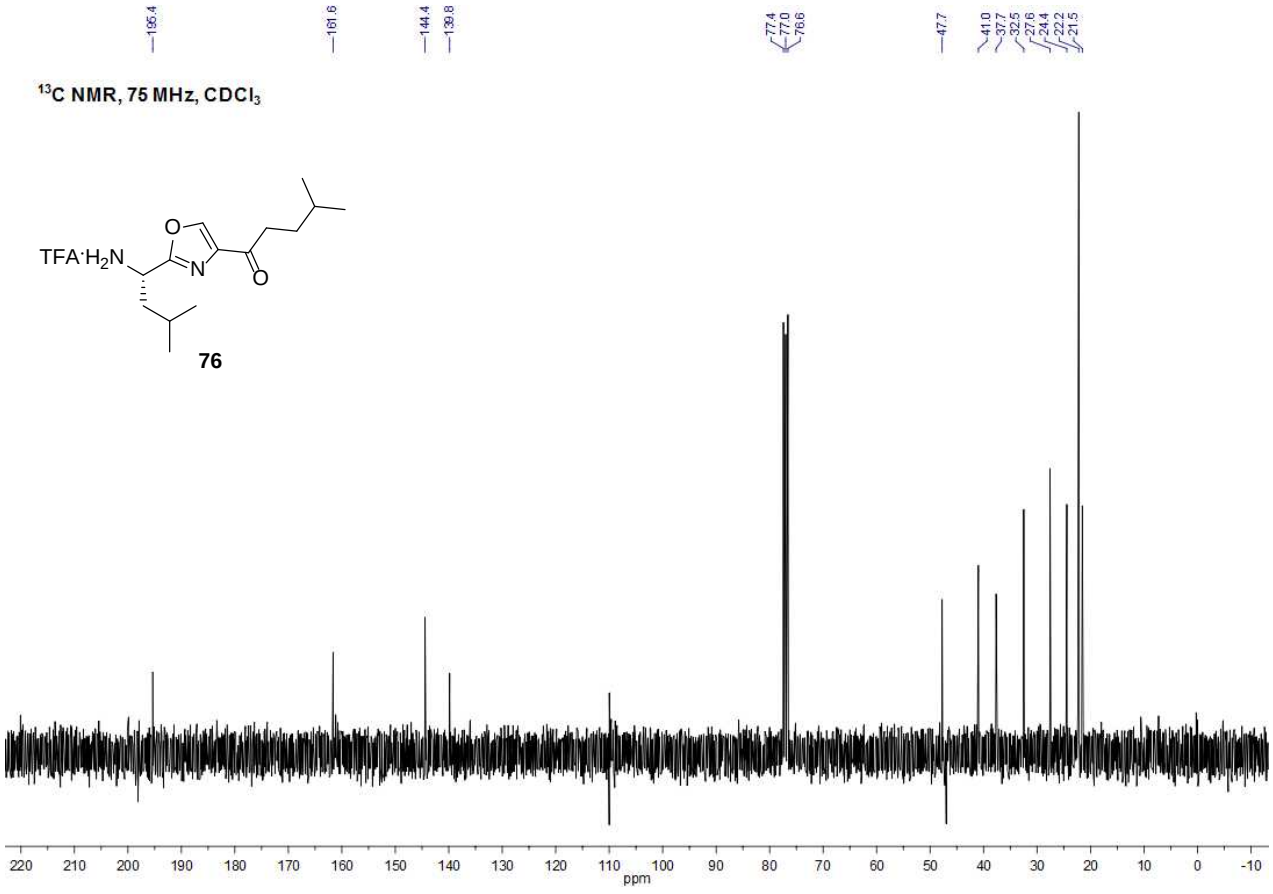

8.11
6.98
4.10
4.09
4.07
3.25
3.24
3.23
1.94
1.92
1.91
1.90
1.88
1.87
1.86
1.84
1.76
1.75
1.73
1.72
1.71
1.70
1.68
1.67
1.66
1.65
1.63
1.62
1.60
1.03
1.02
0.98
0.97
0.95
0.94
0.93
0.89
0.00
¹H NMR, 500 MHz, CDCl₃
O
HN
H₂N
N
O
74
0.92
1.19
1.13
2.00
1.00
4.34
9.52
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
ppm

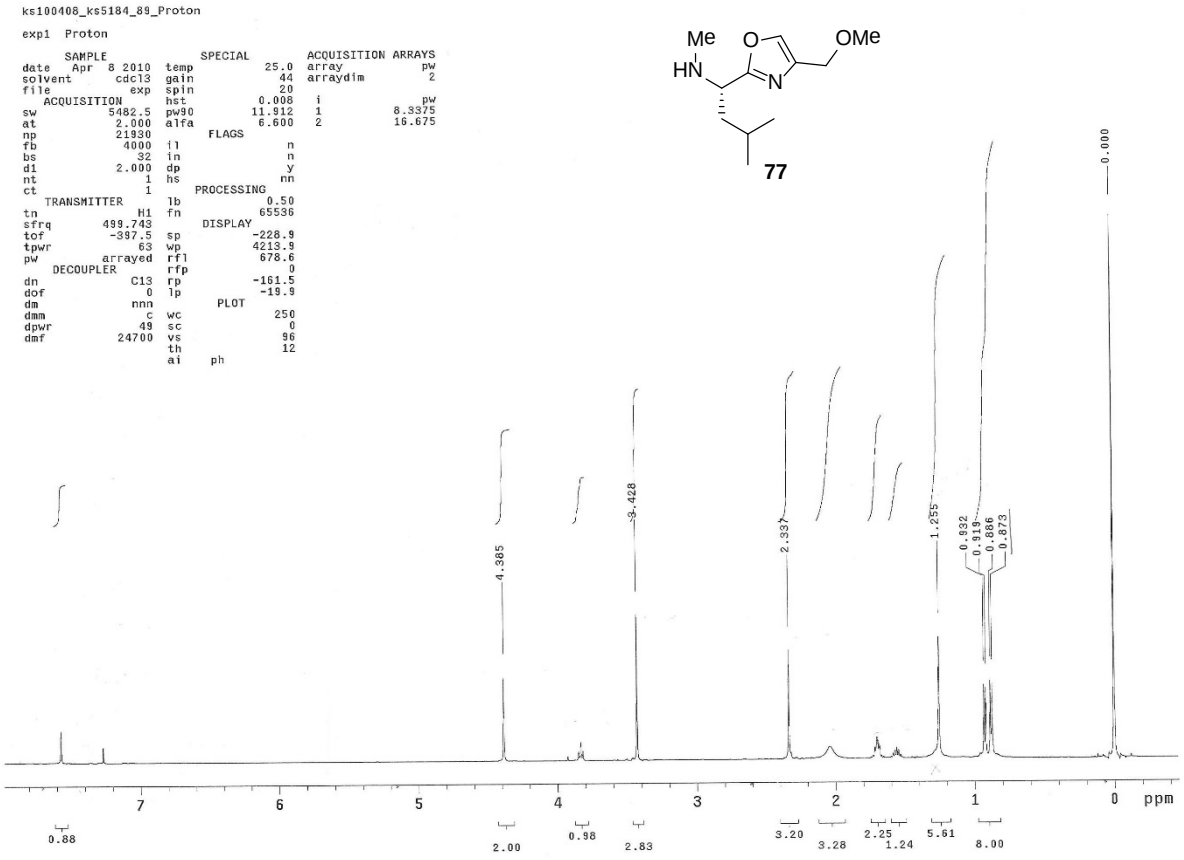

167.6
160.6
140.4
136.1
77.3
77.0
76.7
48.2
46.3
45.1
28.6
24.7
22.7
22.0
20.1
¹³C NMR, 125 MHz, CDCl₃
O
HN
H₂N
N
O
74
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

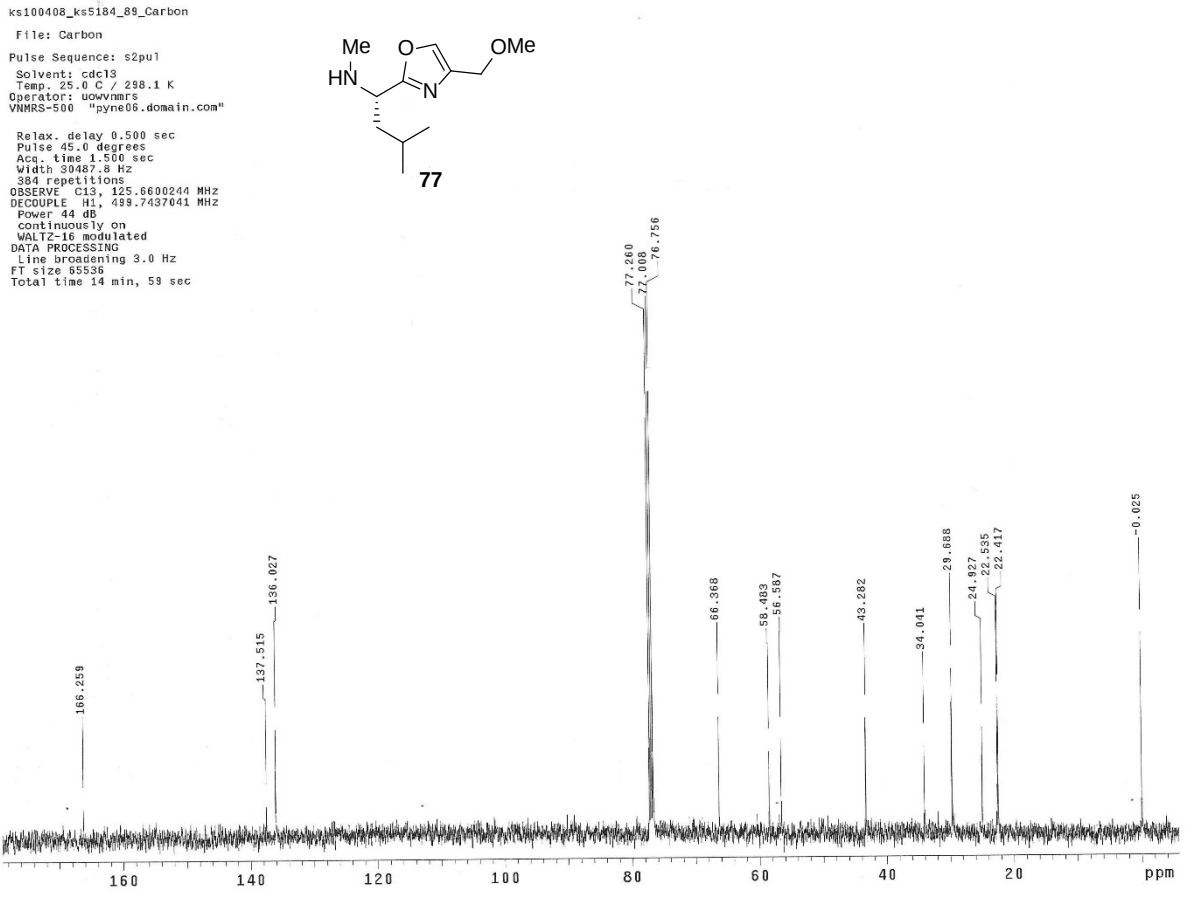

8.11
7.28
4.15
4.14
4.13
3.76
3.38
1.76
1.75
1.74
1.73
1.72
1.70
1.69
1.68
1.66
1.65
1.64
1.43
1.26
0.96
0.94
0.93
0.92
0.07
0.00
1H NMR, 500 MHz, CDCl3
Me
N–OMe
O
H2N
N
O
75
1.21
1.00
2.88
2.97
5.14
6.20
ppm

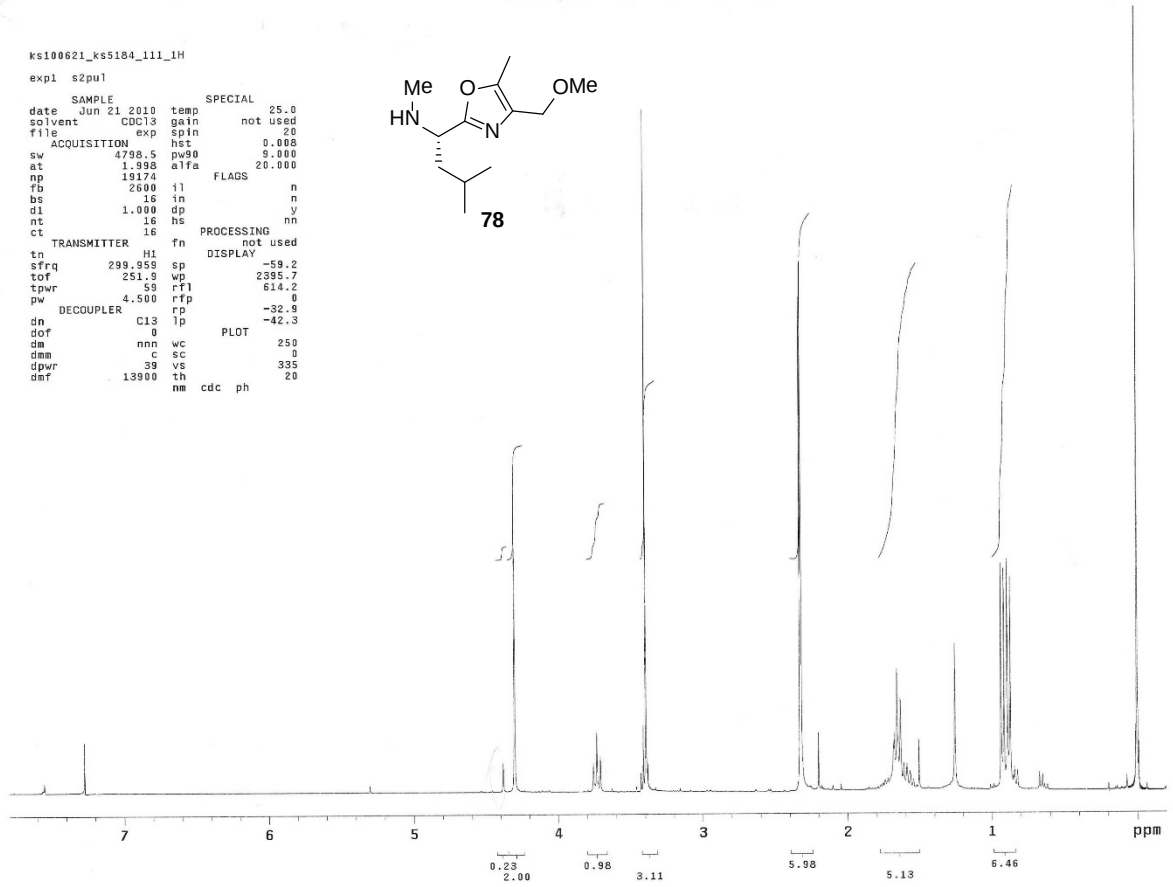

167.7
161.2
142.2
133.2
77.3
77.0
76.7
61.3
48.3
44.9
28.3
24.7
22.8
22.0
13C NMR, 125 MHz, CDCl3
Me
N–OMe
O
H2N
N
O
75
ppm

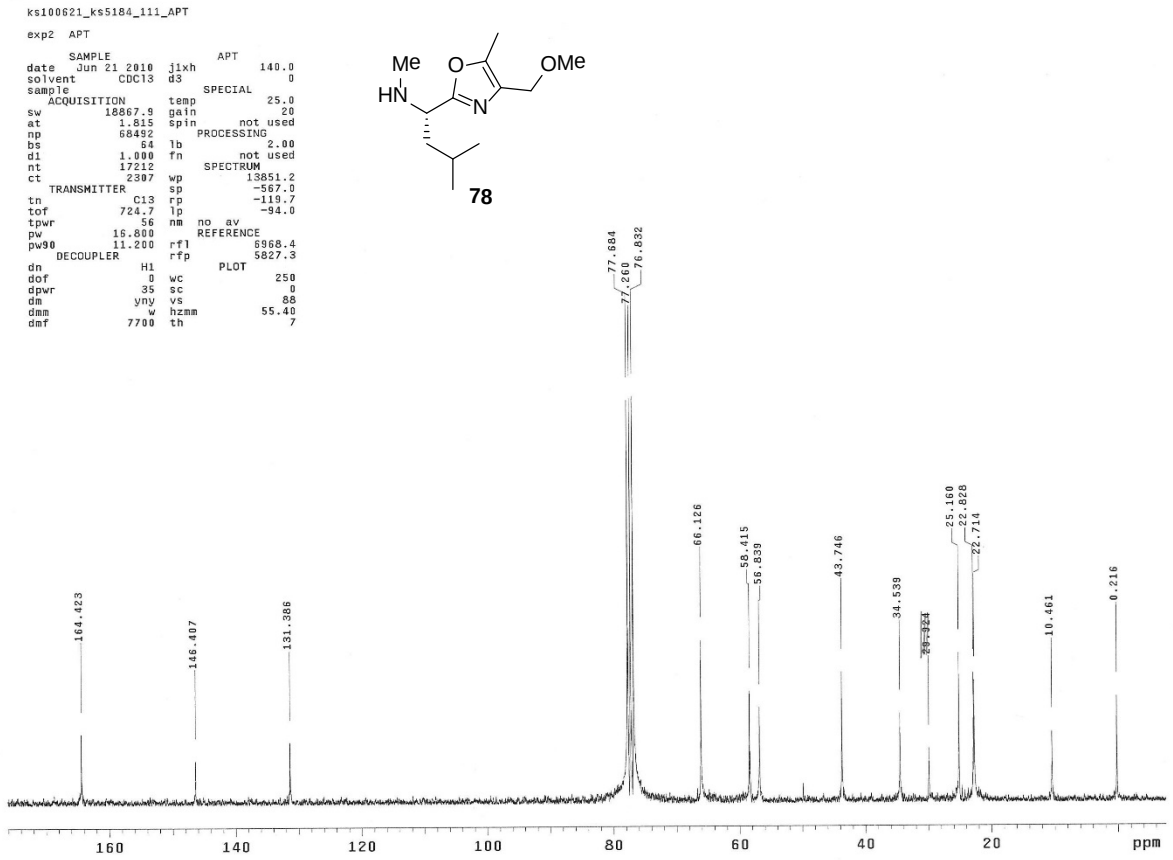

8.29
4.76
4.74
4.71
2.82
2.80
2.78
2.03
2.01
1.98
1.77
1.75
1.73
1.71
1.68
1.66
1.64
1.62
1.60
1.59
1.57
1.54
1.52
1.04
1.00
0.97
0.95
0.92
0.90
0.85
0.83
0.00
1H NMR, 300 MHz, CDCl3
TFA·H2N
O
N
O
76
1.33
1.21
2.00
2.20
4.62
12.48
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
ppm

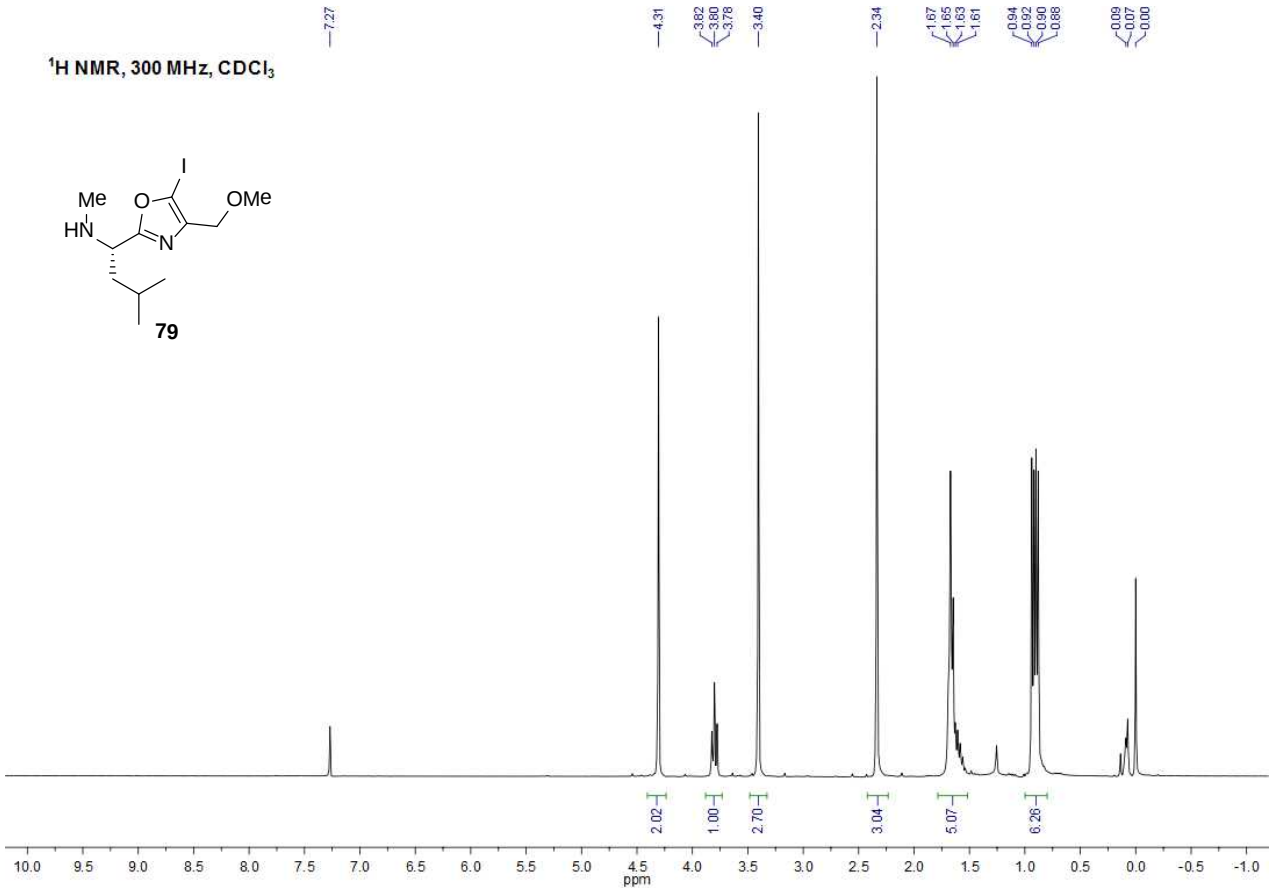

195.4
161.6
144.4
139.8
77.4
77.0
76.6
47.7
41.0
37.7
32.5
27.6
24.4
22.2
21.5
13C NMR, 75 MHz, CDCl3
TFA·H2N
O
N
O
76
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm


ks100408_ks5184_89_Proton
exp1 Proton
SAMPLE
date Apr 8 2010
solvent cdcl3
file exp
ACQUISITION
sw 5482.5
at 2.000
np 21930
fb 4000
bs 32
di 2.000
nt 1
ct 1
TRANSMITTER
tn H1
sfrq 499.743
tof -397.5
tpwr 63
pw arrayed
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 49
dmf 24700
SPECIAL
temp 25.0
gain 44
spin 20
hst 0.008
pw90 11.912
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn 65536
DISPLAY
sp -228.9
wp 4213.9
rfl 678.6
rfp 0
rp -161.5
lp -19.9
PLOT
wc 250
sc 0
vs 96
th 12
ai ph
ACQUISITION ARRAYS
array pw
arraydim 2
i pw
1 8.3375
2 16.675
Me
HN
O
N
OMe
77
4.385
3.428
2.337
1.255
0.932
0.919
0.886
0.873
0.000
7
6
5
4
3
2
1
0
ppm
0.88
2.00
0.98
2.83
3.20
3.28
2.25
1.24
5.61
8.00


ks100408_ks5184_89_Carbon
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: uowvnmrs
VNMRS-500 "pyne06.domain.com"
Relax. delay 0.500 sec
Pulse 45.0 degrees
Acq. time 1.500 sec
Width 30487.8 Hz
384 repetitions
OBSERVE C13, 125.6600244 MHz
DECOUPLE H1, 499.7437041 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 3.0 Hz
FT size 65536
Total time 14 min, 59 sec
Me
HN
O
N
OMe
77
166.259
137.515
136.027
77.260
77.008
76.756
66.368
58.483
56.587
43.282
34.041
29.688
24.927
22.535
22.417
0.025
160
140
120
100
80
60
40
20
ppm


ks100621_ks5184_111_1H
exp1 s2pul
SAMPLE
date Jun 21 2010
solvent CDCl3
file exp
ACQUISITION
sw 4798.5
at 1.998
np 19174
fb 2600
bs 16
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 299.959
tof 251.9
tpwr 59
pw 4.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 39
dmf 13900
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 9.000
alfa 20.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn not used
DISPLAY
sp -59.2
wp 2395.7
rfl 614.2
rfp 0
rp -32.9
lp -42.3
PLOT
wc 250
sc 0
vs 335
th 20
nm cdc ph
Me
O
OMe
HN
N
78
7
6
5
4
3
2
1
ppm
0.23
2.00
0.98
3.11
5.98
5.13
6.46

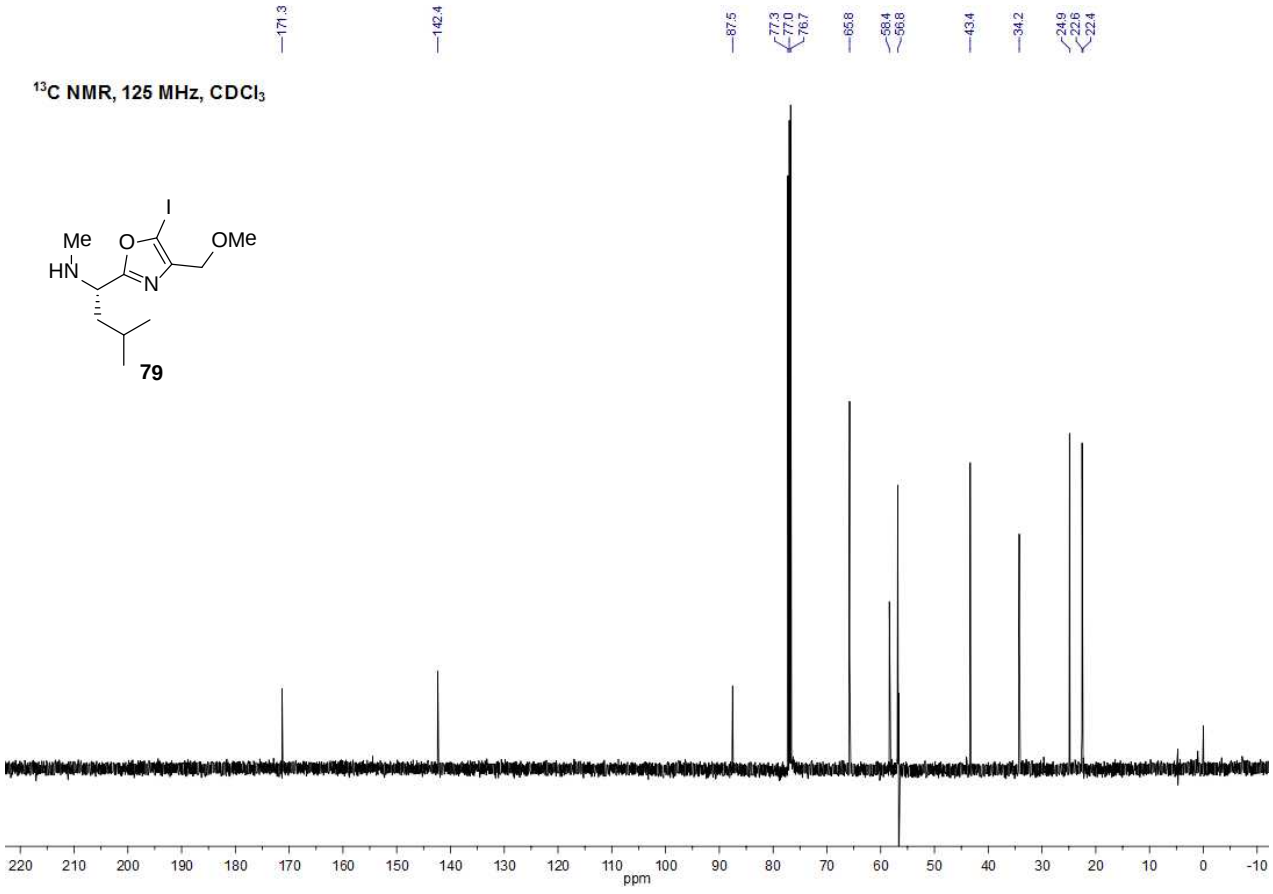

ks100621_ks5184_111_APT
exp2 APT
SAMPLE
date Jun 21 2010
solvent CDCl3
sample
ACQUISITION
sw 18867.9
at 1.815
np 68492
bs 64
d1 1.000
nt 17212
ct 2307
TRANSMITTER
tn C13
tof 724.7
tpwr 56
pw 16.800
pw90 11.200
DECOUPLER
dn H1
dof 0
dpwr 35
dm yny
dmm w
dmf 7700
APT
j1xh 140.0
d3 0
SPECIAL
temp 25.0
gain 20
spin not used
PROCESSING
lb 2.00
fn not used
SPECTRUM
wp 13851.2
sp -567.0
rp -119.7
lp -94.0
nm no av
REFERENCE
rfl 6968.4
rfp 5827.3
PLOT
wc 250
sc 0
vs 88
hzmm 55.40
th 7
Me
O
OMe
HN
N
78
77.684
77.260
76.832
66.126
58.415
56.839
43.746
34.539
28.321
25.160
22.828
22.714
10.461
0.216
164.423
146.407
131.386
160
140
120
100
80
60
40
20
ppm




**$^{1}$H NMR, 300 MHz, $CDCl_3$**



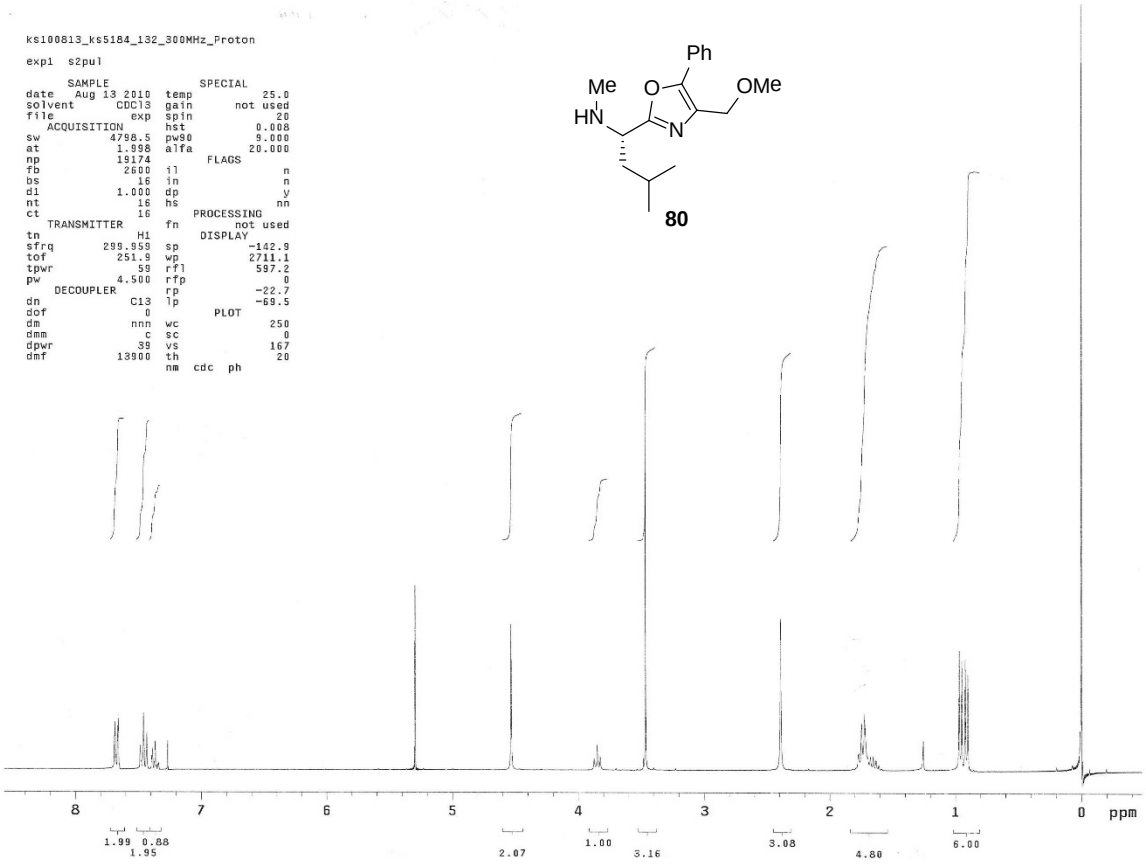

**79**

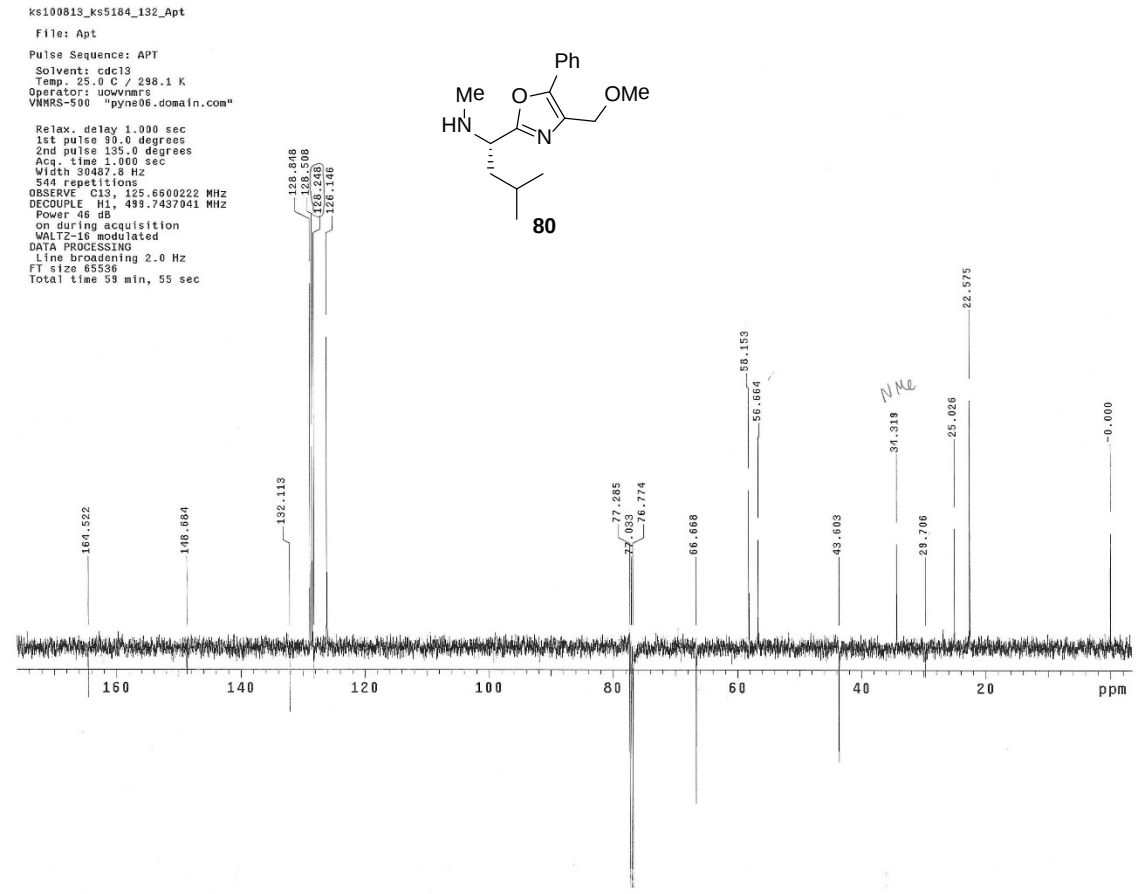



**$^{13}$C NMR, 125 MHz, $CDCl_3$**




**79**

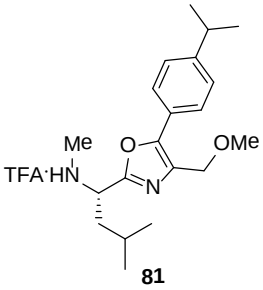

ks100813_ks5184_132_300MHz_Proton
expl s2pul
SAMPLE
date Aug 13 2010
solvent CDCl3
file exp
ACQUISITION
sw 4798.5
at 1.998
np 19174
fb 2600
bs 16
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 299.959
tof 251.8
tpwr 59
pw 4.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 39
dmf 13900
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 9.000
alfa 20.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn not used
DISPLAY
sp -142.9
wp 2711.1
rfl 597.2
rfp 0
rp -22.7
lp -69.5
PLOT
wc 250
sc 0
vs 167
th 20
nm cdc ph
Ph
Me
O
OMe
HN
N
80
8
7
6
5
4
3
2
1
0
ppm
1.99
0.88
1.95
2.07
1.00
3.16
3.08
4.80
6.00


ks100813_ks5184_132_Apt
File: Apt
Pulse Sequence: APT
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: uowvnmrs
VNMRS-500 "pyne06.domain.com"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.000 sec
Width 30487.8 Hz
544 repetitions
OBSERVE C13, 125.6600222 MHz
DECOUPLE H1, 499.7437041 MHz
Power 46 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 59 min, 55 sec
Ph
Me
O
OMe
HN
N
80
128.848
128.508
128.248
126.146
164.522
148.684
132.113
77.285
77.033
76.774
66.668
58.153
56.664
43.603
NMe
34.319
29.706
25.026
22.575
-0.000
160
140
120
100
80
60
40
20
ppm

ks100813_ks5184_134_Proton

exp1 Proton

| SAMPLE | | SPECIAL | |
|---|---|---|---|
| date | Aug 13 2010 | temp | 25.0 |
| solvent | cd3od | gain | 56 |
| file | exp | spin | 20 |
| ACQUISITION | | hst | 0.008 |
| sw | 4960.3 | pw90 | 18.288 |
| at | 2.000 | alfa | 6.600 |
| np | 19842 | FLAGS | |
| fb | 4000 | il | n |
| bs | 16 | in | n |
| d1 | 1.000 | dp | y |
| nt | 16 | hs | nn |
| ct | 16 | PROCESSING | |
| TRANSMITTER | | lb | 0.50 |
| tn | H1 | fn | 65536 |
| sfrq | 499.745 | DISPLAY | |
| tof | -485.5 | sp | -157.4 |
| tpwr | 63 | wp | 4237.8 |
| pw | 18.288 | rfl | 446.4 |
| DECOUPLER | | rfp | 0 |
| dn | C13 | rp | -42.8 |
| dof | 0 | lp | -39.4 |
| dm | nnn | PLOT | |
| dmm | c | wc | 250 |
| dpwr | 48 | sc | 0 |
| dmf | 22200 | vs | 188 |
| | | th | 158 |
| | | ai cdc ph | |



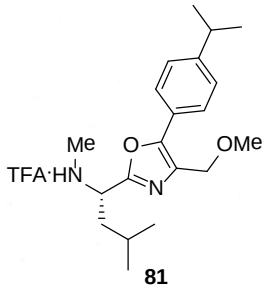

**81**



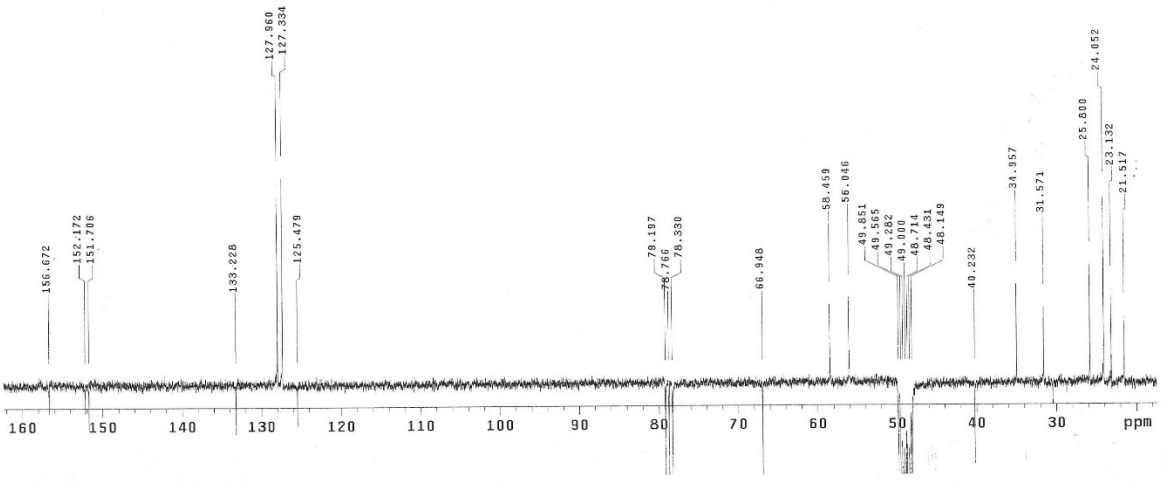

ks100816_ks5184_134_APT

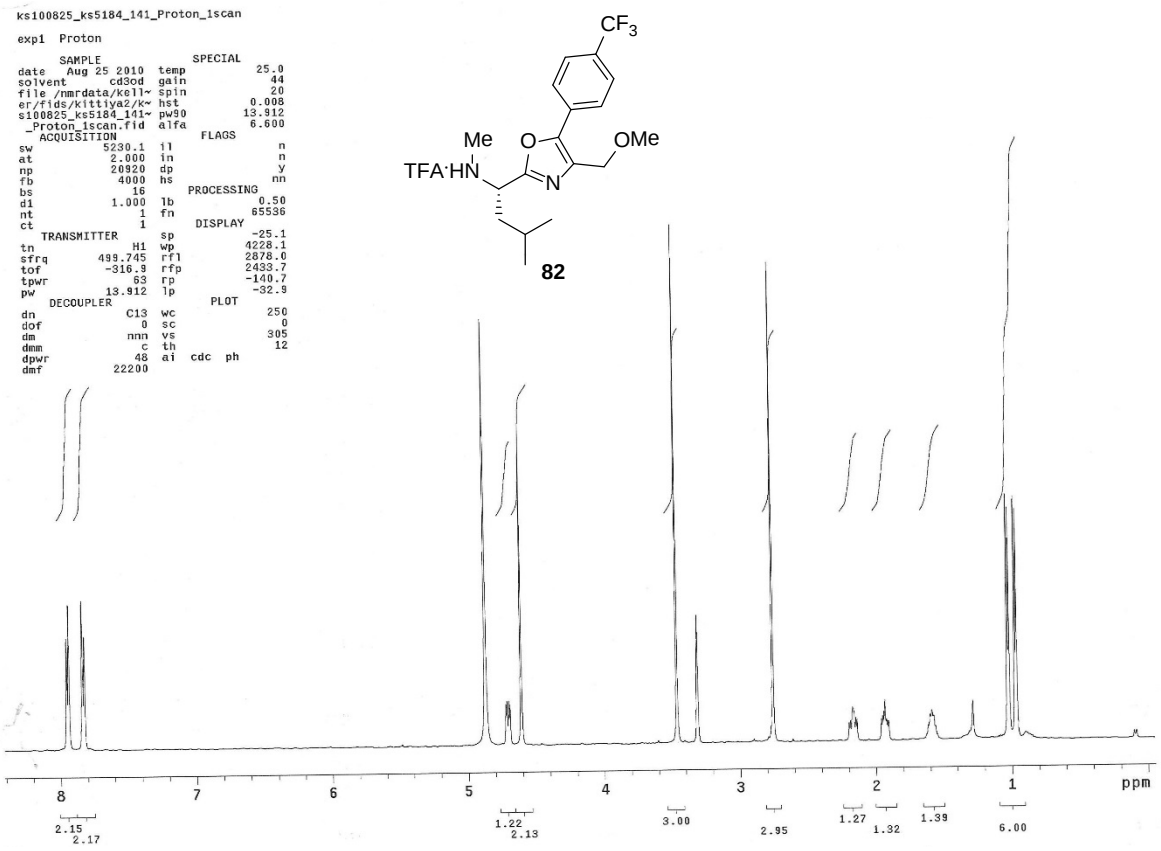
exp7 APT

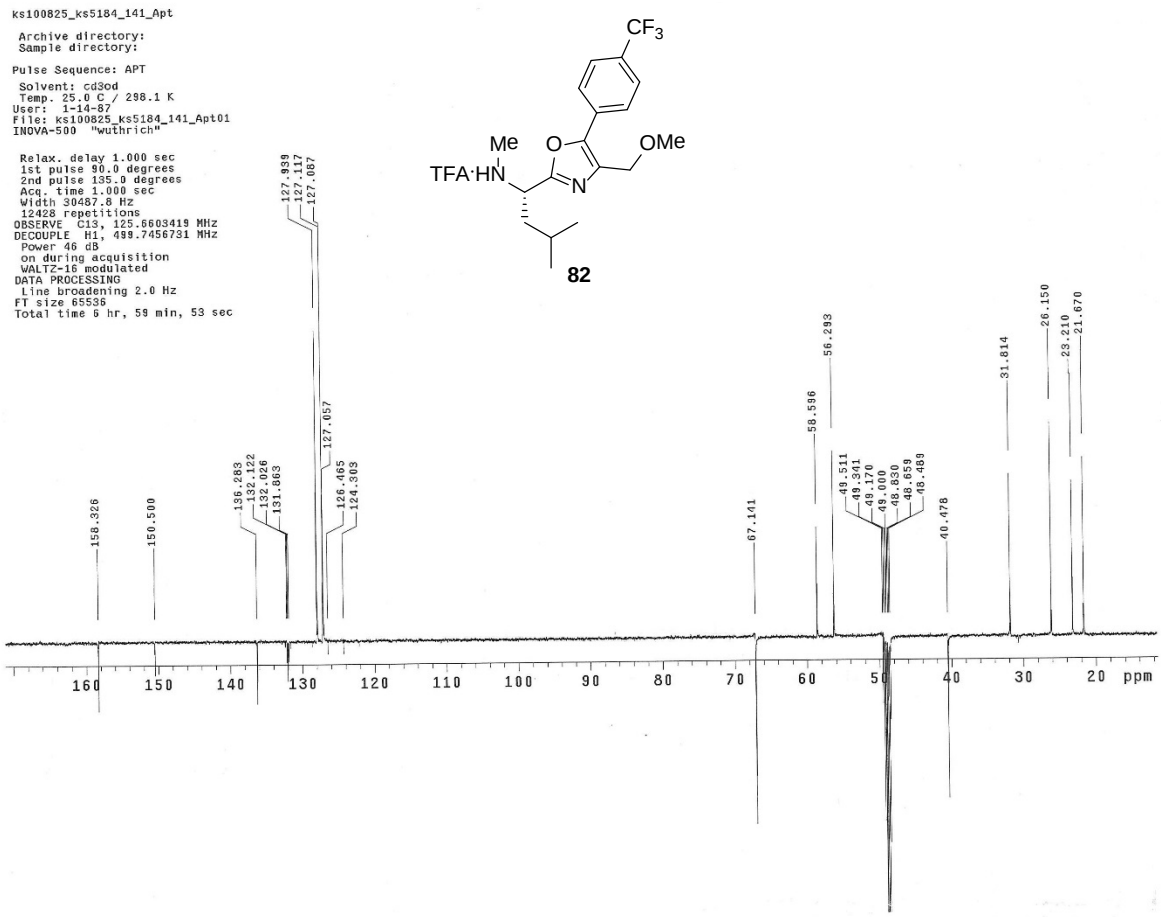
| SAMPLE | | APT | |
|---|---|---|---|
| date | Aug 16 2010 | j1xh | 140.0 |
| solvent | CD3OD | d3 | 0 |
| sample | | SPECIAL | |
| ACQUISITION | | temp | 25.0 |
| sw | 18867.9 | gain | 36 |
| at | 1.815 | spin | not used |
| np | 68492 | PROCESSING | |
| bs | 64 | lb | 1.00 |
| ss | 16 | fn | not used |
| d1 | 1.000 | SPECTRUM | |
| nt | 4900 | wp | 10928.7 |
| ct | 3586 | sp | 1316.9 |
| TRANSMITTER | | rp | -21.5 |
| tn | C13 | lp | -89.9 |
| tof | 724.7 | nm no ph | |
| tpwr | 56 | REFERENCE | |
| pw | 24.000 | rfl | 4774.8 |
| pw90 | 16.000 | rfp | 3695.8 |
| DECOUPLER | | PLOT | |
| dn | H1 | wc | 250 |
| dof | 0 | sc | 0 |
| dpwr | 39 | vs | 132 |
| dm | yny | hzmm | 43.71 |
| dmm | w | th | 6 |
| dmf | 11800 | | |

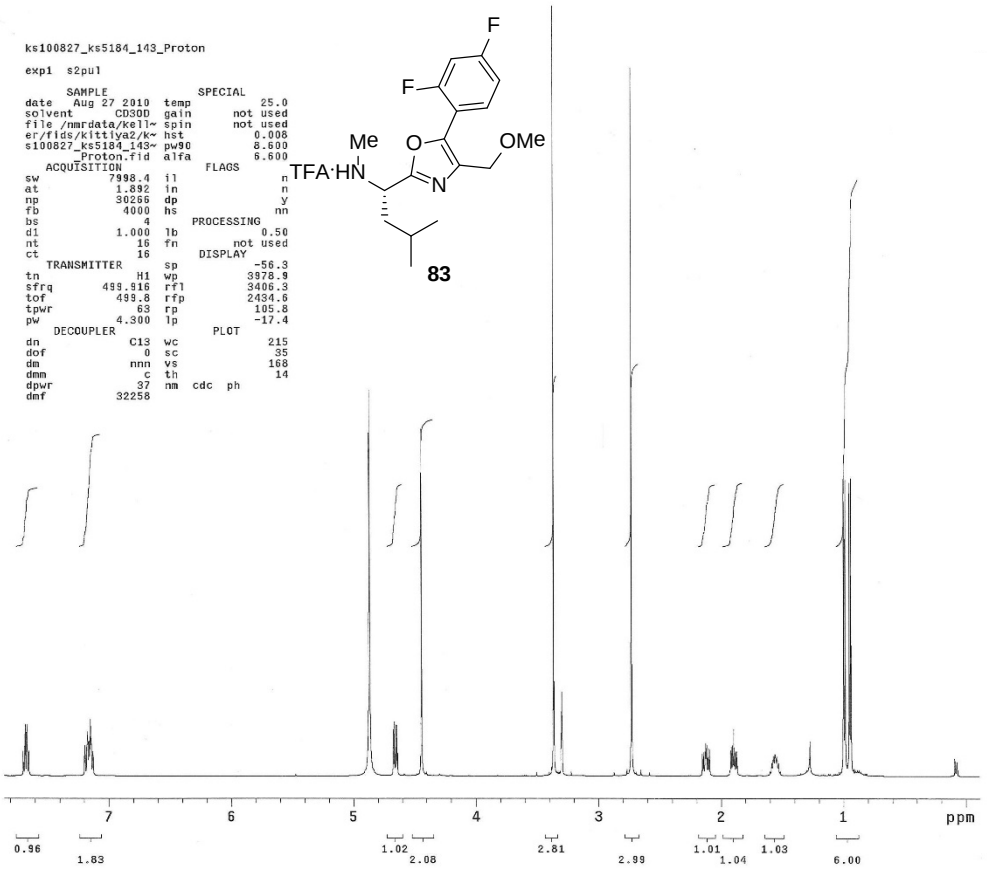


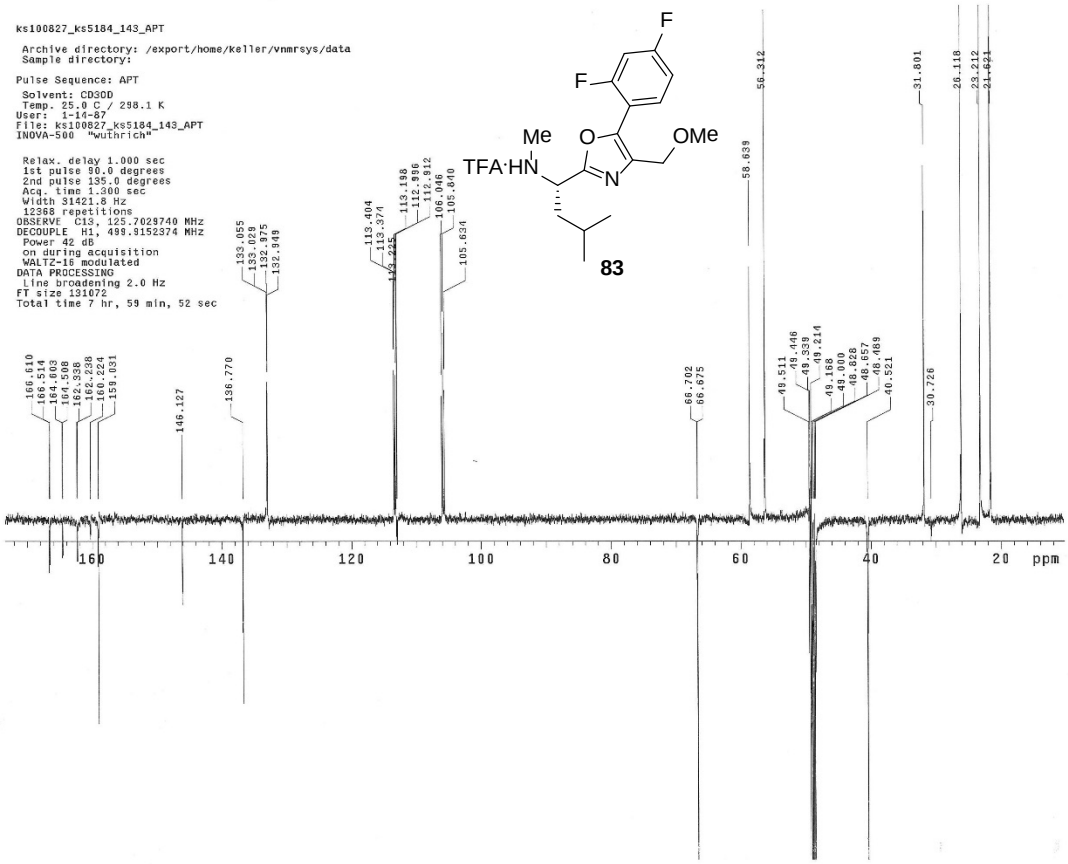

**81**

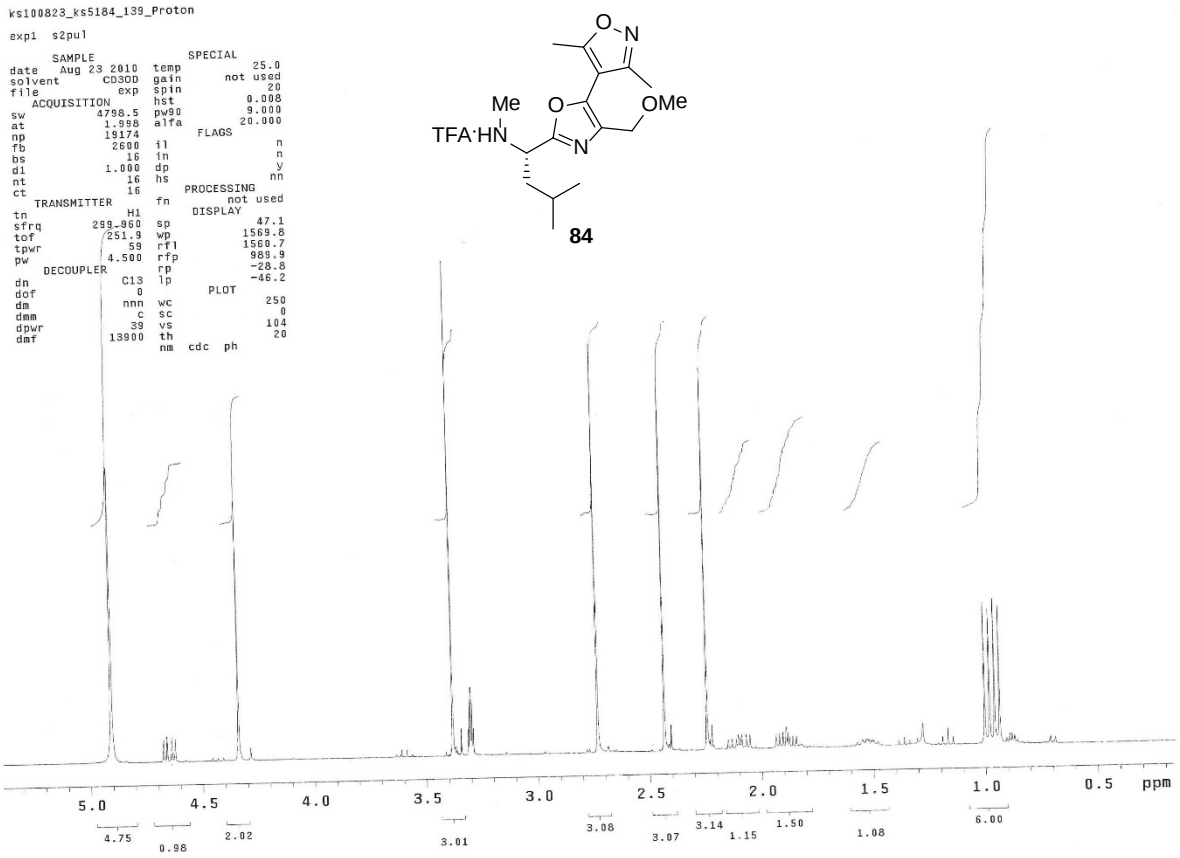


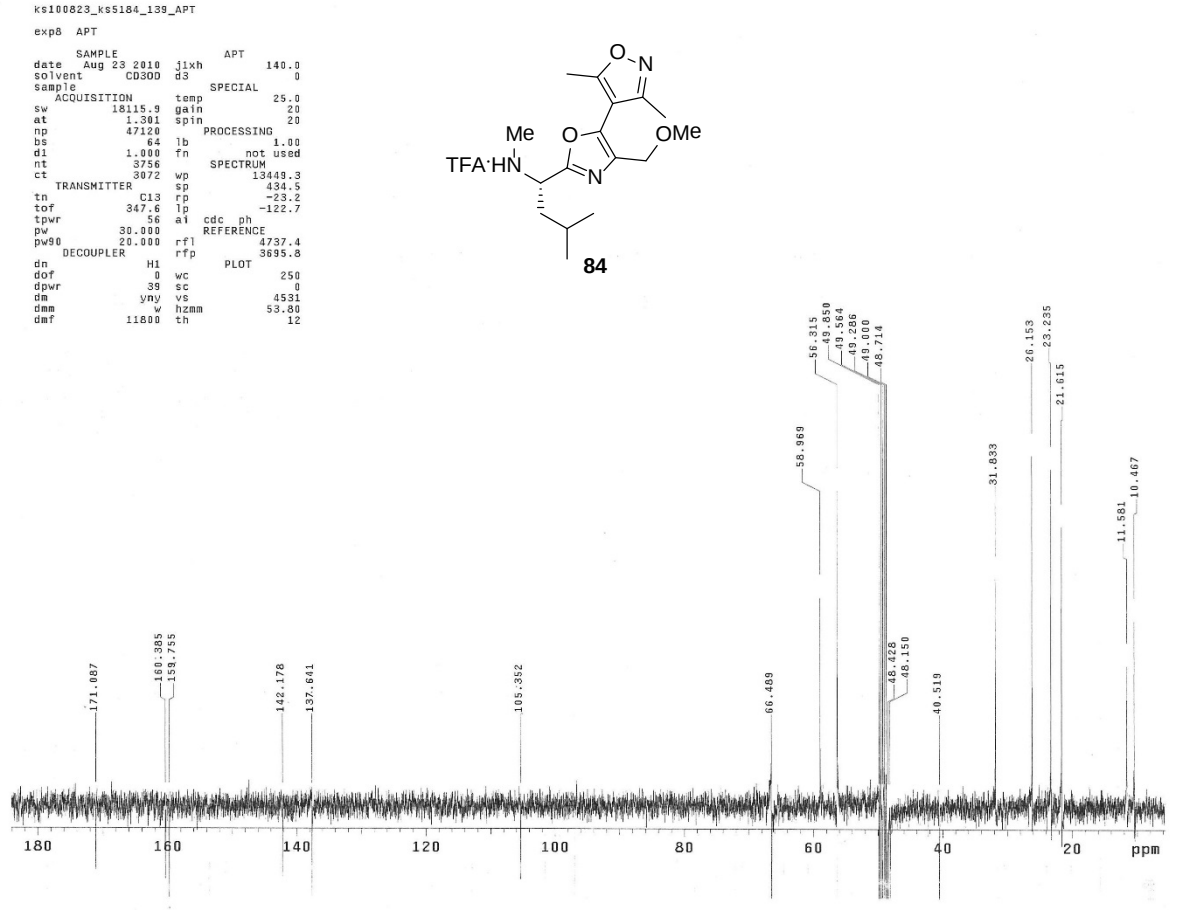

ks100825_ks5184_141_Proton_1scan
exp1 Proton
SAMPLE
date Aug 25 2010
solvent cd3od
file /nmrdata/kell~
er/fids/kittiya2/k~
s100825_ks5184_141~
_Proton_1scan.fid
ACQUISITION
sw 5230.1
at 2.000
np 20920
fb 4000
bs 16
d1 1.000
nt 1
ct 1
TRANSMITTER
tn H1
sfrq 499.745
tof -316.9
tpwr 63
pw 13.912
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 48
dmf 22200
SPECIAL
temp 25.0
gain 44
spin 20
hst 0.008
pw90 13.912
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn 65536
DISPLAY
sp -25.1
wp 4228.1
rf1 2878.0
rfp 2433.7
rp -140.7
lp -32.9
PLOT
wc 250
sc 0
vs 305
th 12
ai cdc ph
CF3
Me
O
OMe
TFA·HN
N
82
8
7
6
5
4
3
2
1
ppm
2.15
2.17
1.22
2.13
3.00
2.95
1.27
1.32
1.39
6.00


ks100825_ks5184_141_Apt
Archive directory:
Sample directory:
Pulse Sequence: APT
Solvent: cd3od
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100825_ks5184_141_Apt01
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.000 sec
Width 30487.8 Hz
12428 repetitions
OBSERVE C13, 125.6603419 MHz
DECOUPLE H1, 499.7456731 MHz
Power 46 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 6 hr, 59 min, 53 sec
CF3
Me
O
OMe
TFA·HN
N
82
158.326
150.500
136.283
132.122
132.026
131.863
127.939
127.117
127.087
127.057
126.465
124.303
67.141
58.596
56.293
49.511
49.341
49.170
49.000
48.830
48.659
48.489
40.478
31.814
26.150
23.210
21.670
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

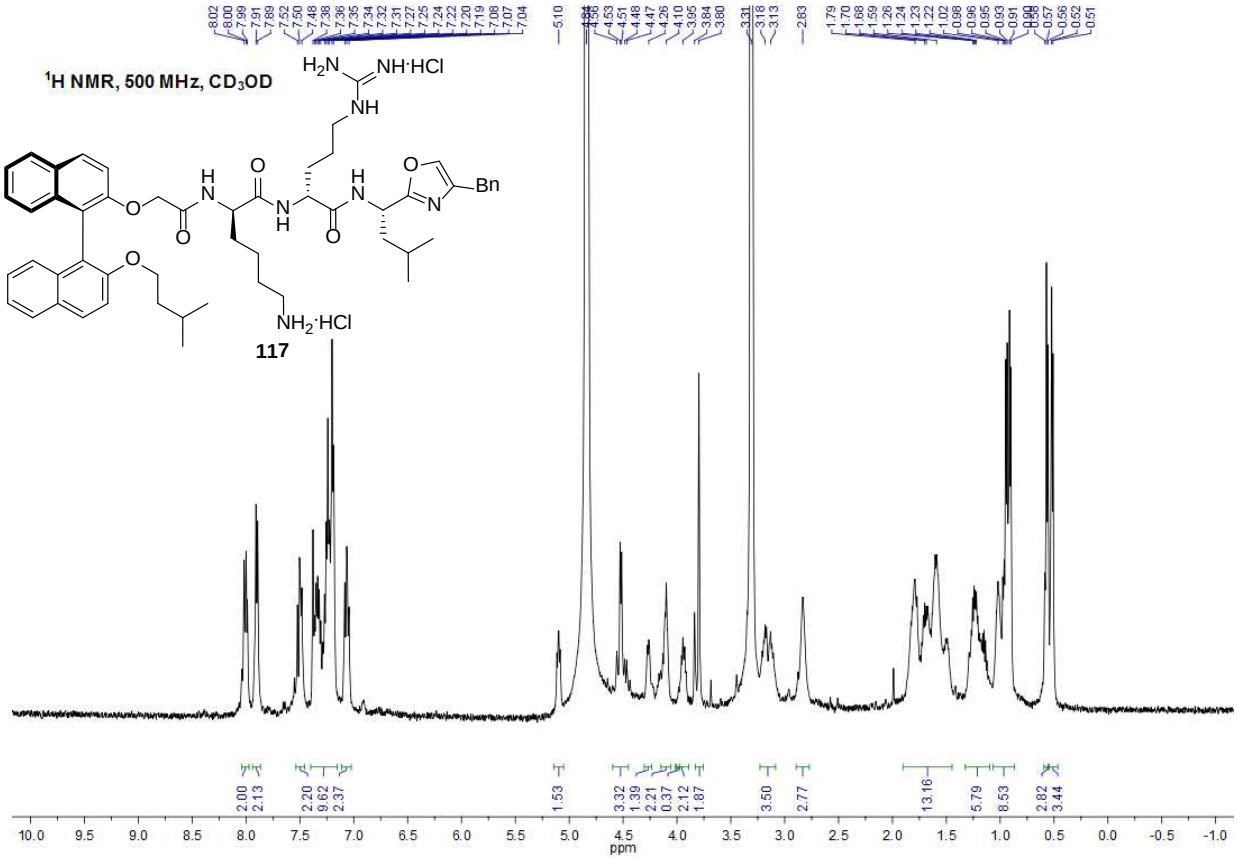

ks100827_ks5184_143_Proton
exp1 s2pul
SAMPLE
date Aug 27 2010
solvent CD3OD
file /nmrdata/kell~
er/fids/kittiya2/k~
s100827_ks5184_143~
_Proton.fid
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
dl 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.916
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -56.3
wp 3878.9
rfl 3406.3
rfp 2434.6
rp 105.8
lp -17.4
PLOT
wc 215
sc 35
vs 168
th 14
cdc ph
F
F
Me
O
OMe
TFA·HN
N
83
7
6
5
4
3
2
1
ppm
0.96
1.83
1.02
2.08
2.81
2.99
1.01
1.04
1.03
6.00

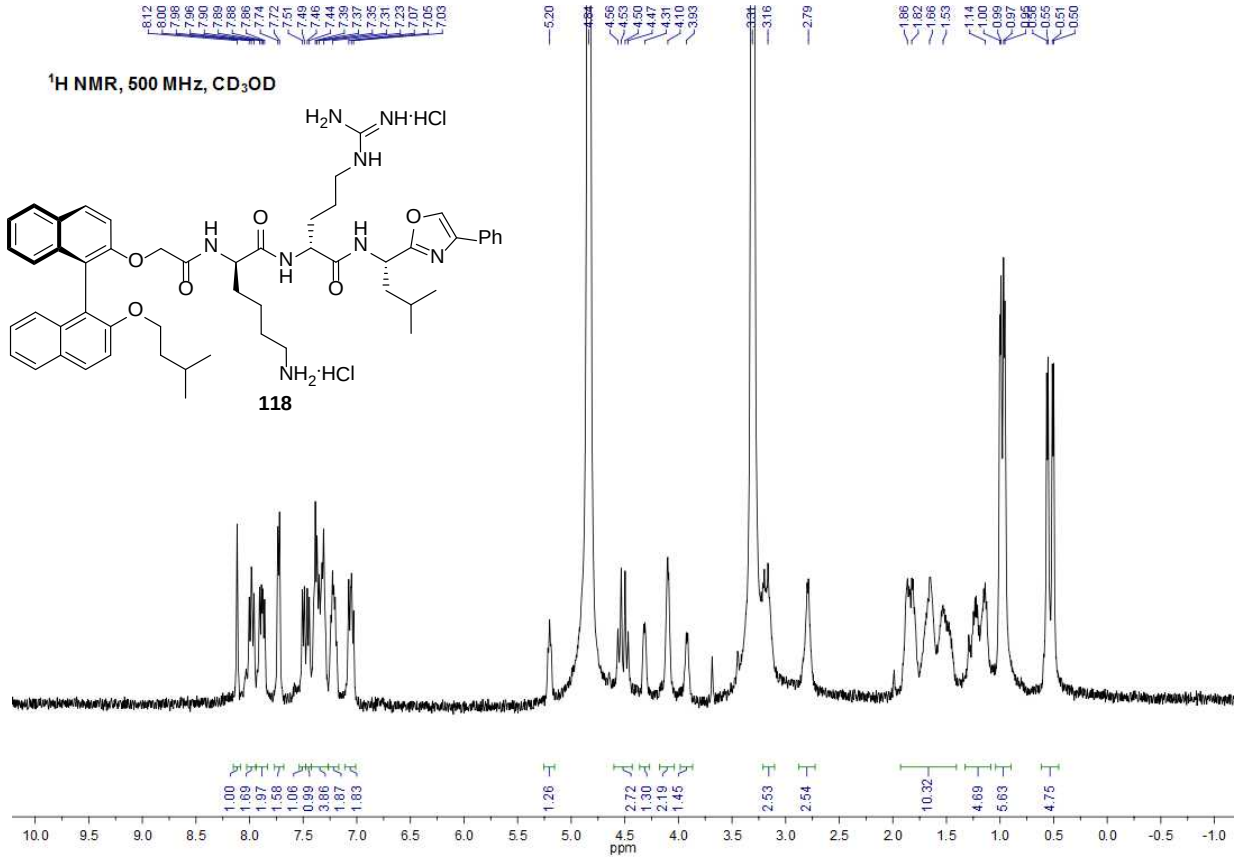

ks100827_ks5184_143_APT
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100827_ks5184_143_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
12368 repetitions
OBSERVE C13, 125.7029740 MHz
DECOUPLE H1, 499.9152374 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 7 hr, 59 min, 52 sec
F
F
Me
O
OMe
TFA·HN
N
83
160.610
160.514
160.408
160.308
160.238
160.224
159.031
146.127
136.770
133.055
133.029
132.975
132.949
113.404
113.374
113.225
113.198
112.996
112.812
106.046
105.840
105.634
66.702
66.675
58.639
56.312
49.511
49.446
49.339
49.214
49.168
49.000
48.829
48.657
48.489
40.521
31.801
30.726
26.118
23.212
21.621
160
140
120
100
80
60
40
20
ppm

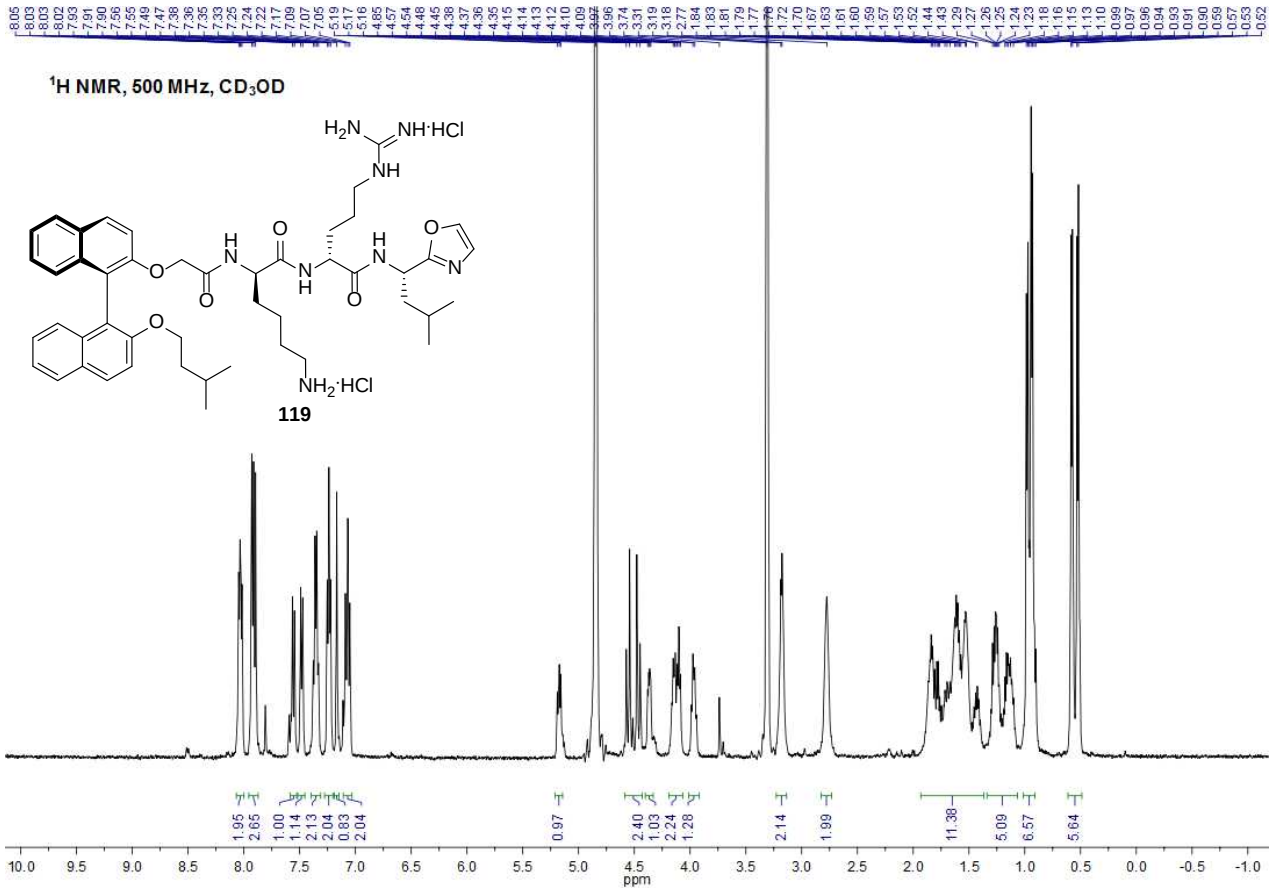

ks100823_ks5184_139_Proton
expl s2pul
SAMPLE
date Aug 23 2010
solvent CD3OD
file exp
ACQUISITION
sw 4798.5
at 1.998
np 19174
fb 2600
bs 16
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 299.960
tof 251.9
tpwr 59
pw 4.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 39
dmf 13900
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 9.000
alfa 20.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn not used
DISPLAY
sp 47.1
wp 1569.8
rfl 1560.7
rfp 989.9
rp -28.8
lp -46.2
PLOT
wc 250
sc 0
vs 104
th 20
nm cdc ph
Me
TFA·HN
O
N
OMe
84
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.75
0.98
2.02
3.01
3.08
3.07
3.14
1.15
1.50
1.08
6.00

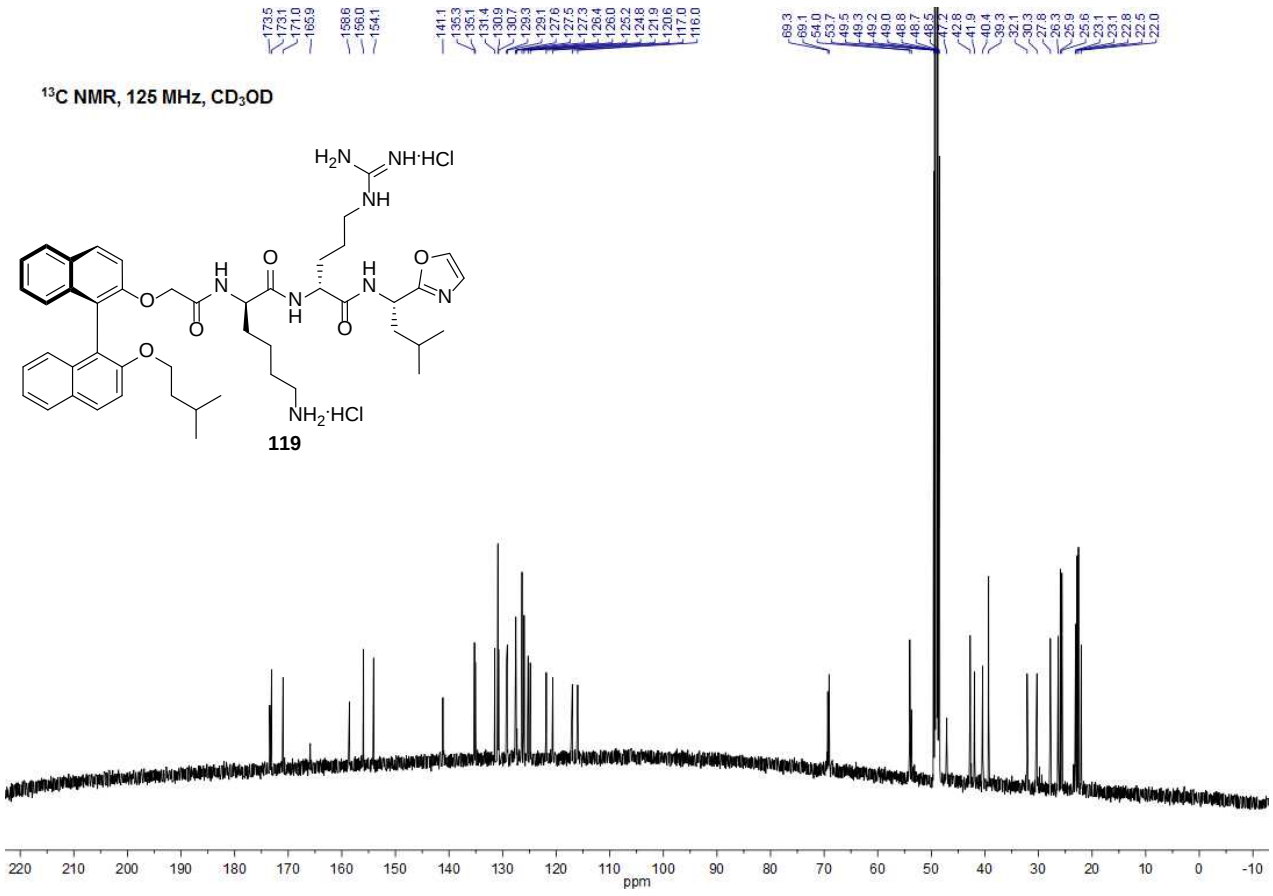

ks100823_ks5184_139_APT
exp8 APT
SAMPLE
date Aug 23 2010
solvent CD3OD
sample
ACQUISITION
sw 18115.9
at 1.301
np 47120
bs 64
d1 1.000
nt 3756
ct 3072
TRANSMITTER
tn C13
tof 347.6
tpwr 56
pw 30.000
pw90 20.000
DECOUPLER
dn H1
dof 0
dpwr 39
dm yny
dmm w
dmf 11800
APT
jlxh 140.0
d3 0
SPECIAL
temp 25.0
gain 20
spin 20
PROCESSING
lb 1.00
fn not used
SPECTRUM
wp 13449.3
sp 434.5
rp -23.2
lp -122.7
ai cdc ph
REFERENCE
rfl 4737.4
rfp 3695.8
PLOT
wc 250
sc 0
vs 4531
hzmm 53.80
th 12
Me
TFA·HN
O
N
OMe
84
171.087
160.385
159.755
142.178
137.641
105.352
66.409
58.969
56.315
49.850
49.564
49.286
49.000
48.714
48.428
48.150
40.519
31.833
26.153
23.235
21.615
11.581
10.467
180
160
140
120
100
80
60
40
20
ppm

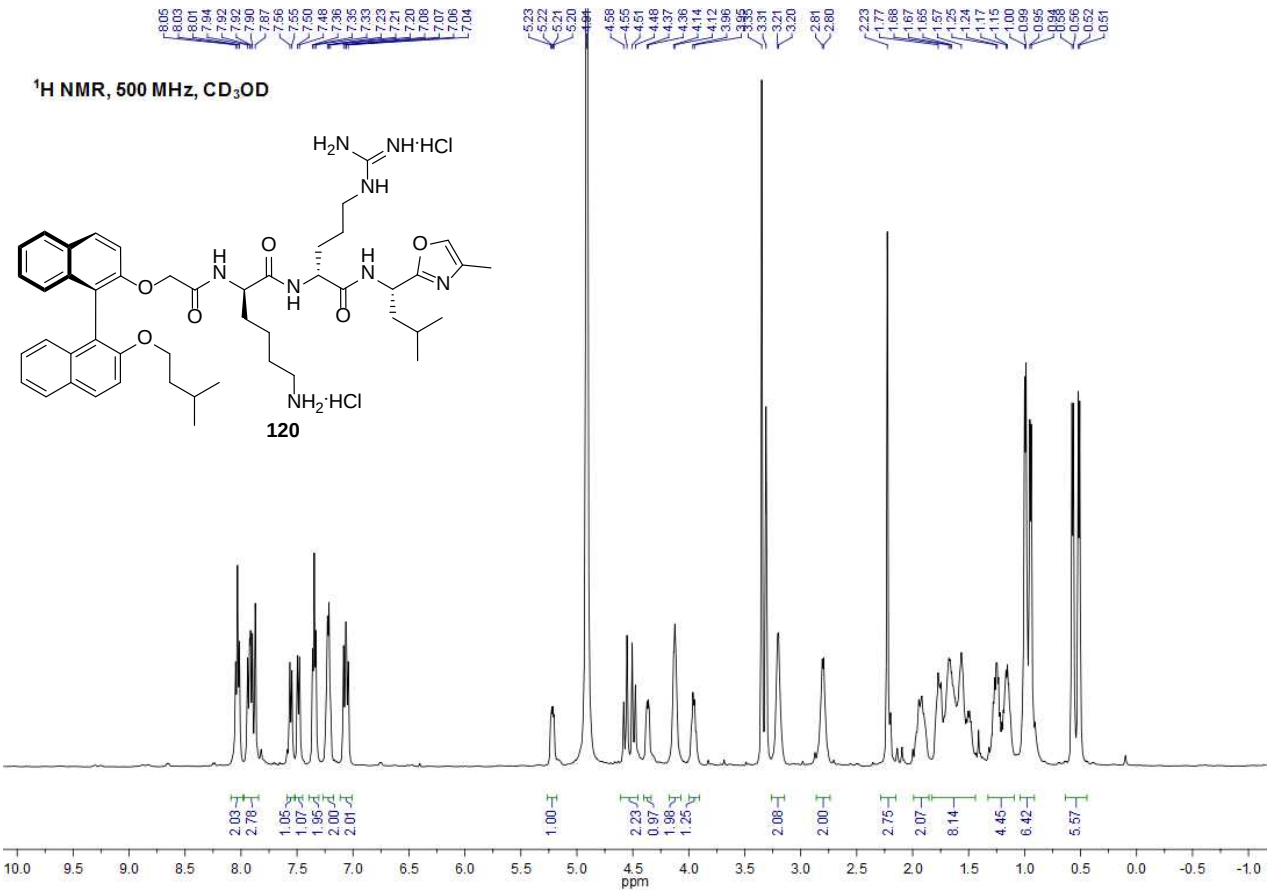
## NMR Spectra of Type E Final Compounds 117−148 and HPLC Traces of 144−148

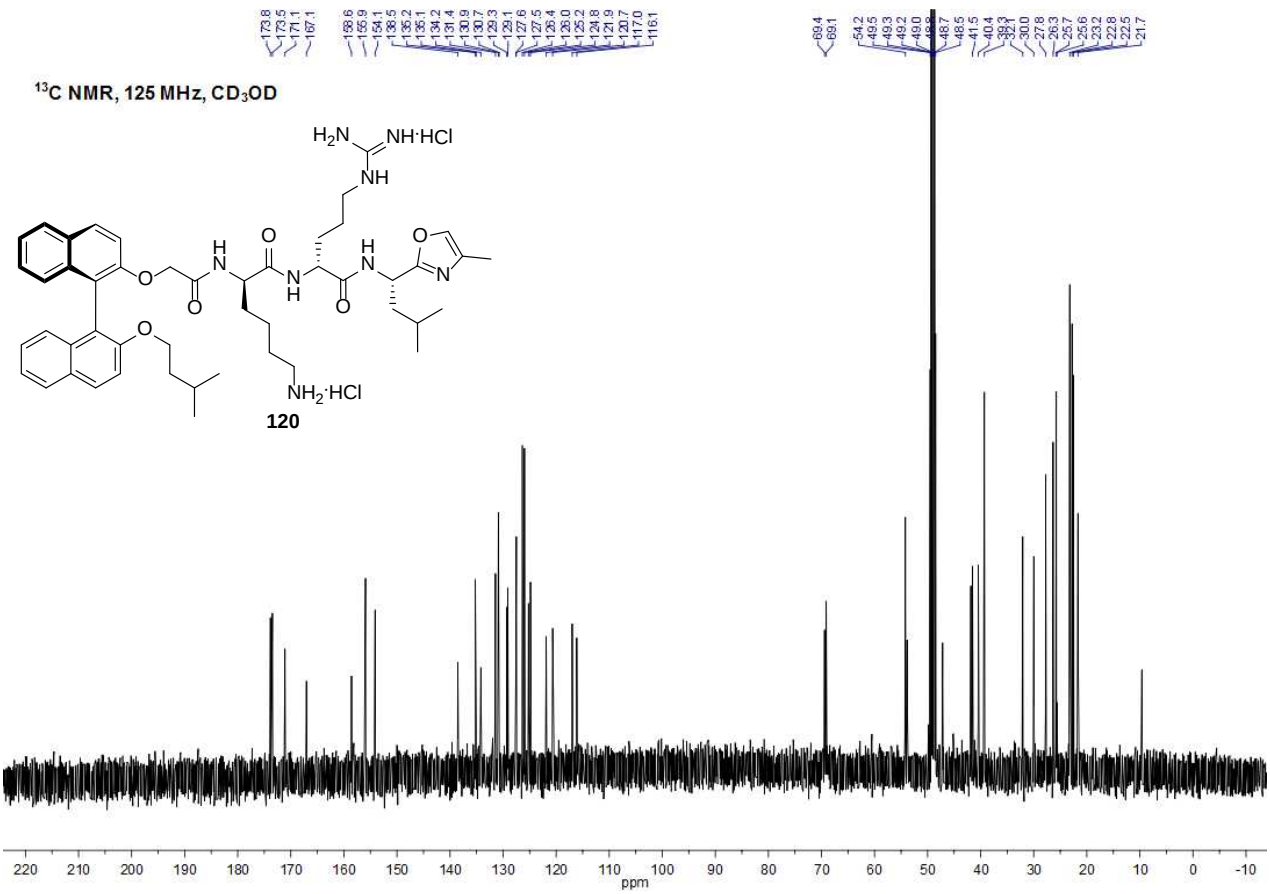


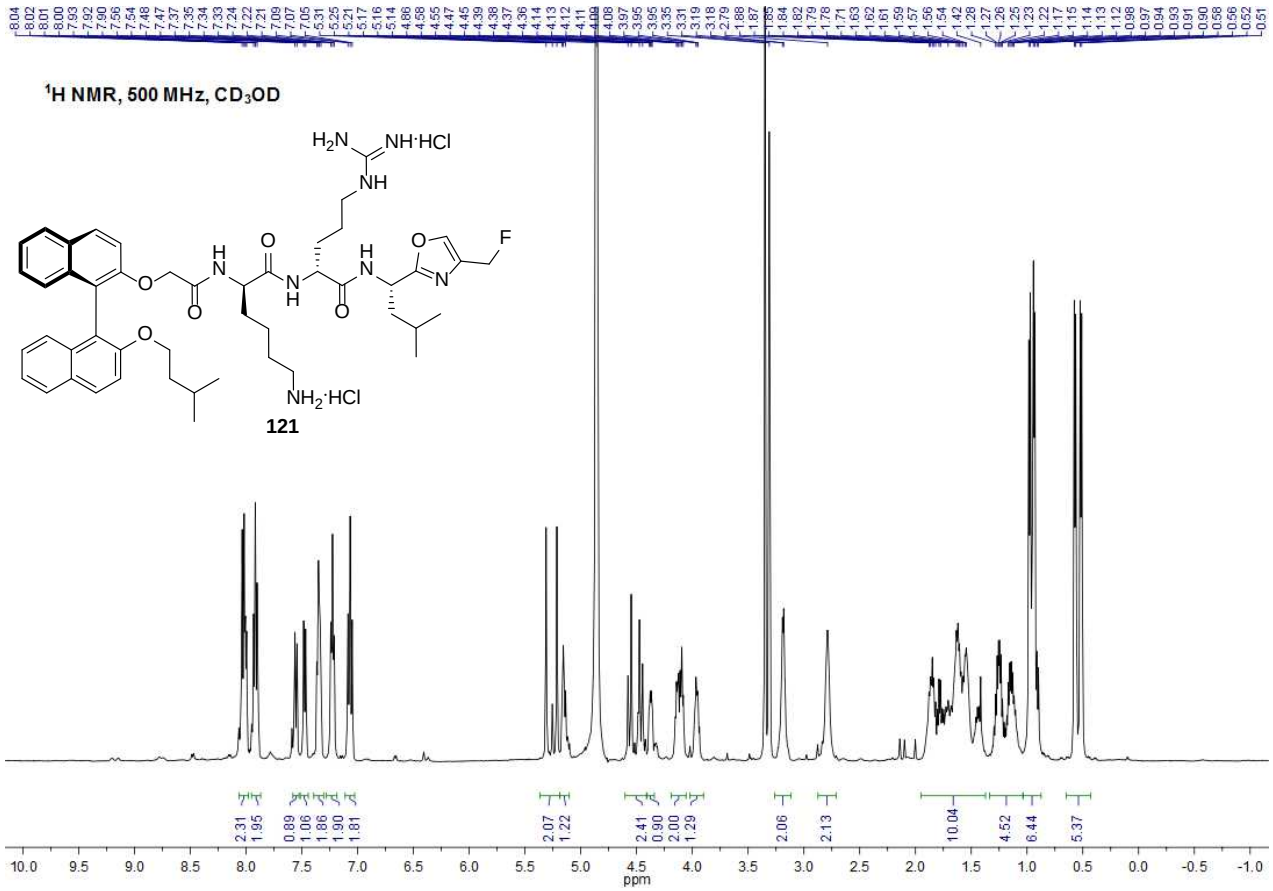



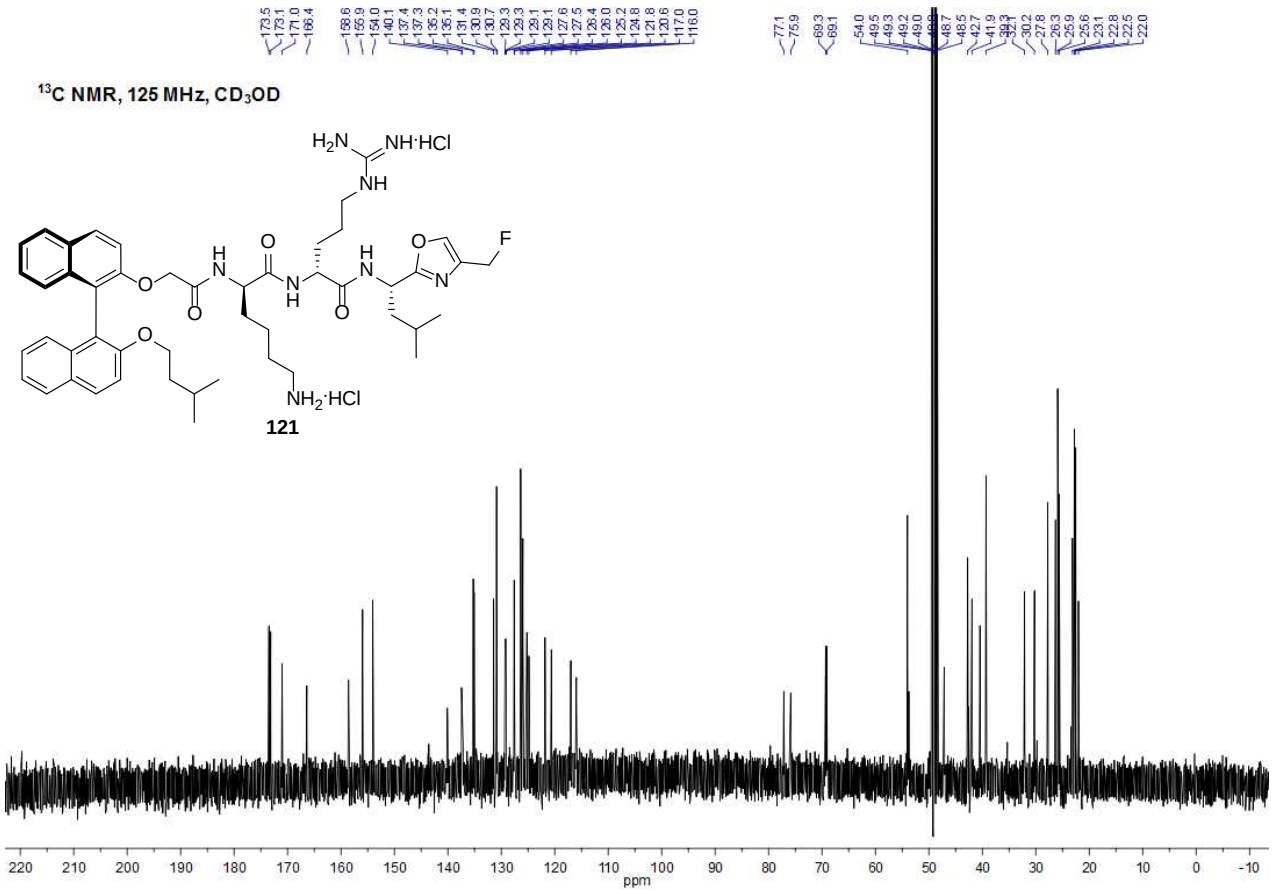

$^1$H NMR, 500 MHz, CD$_3$OD
119

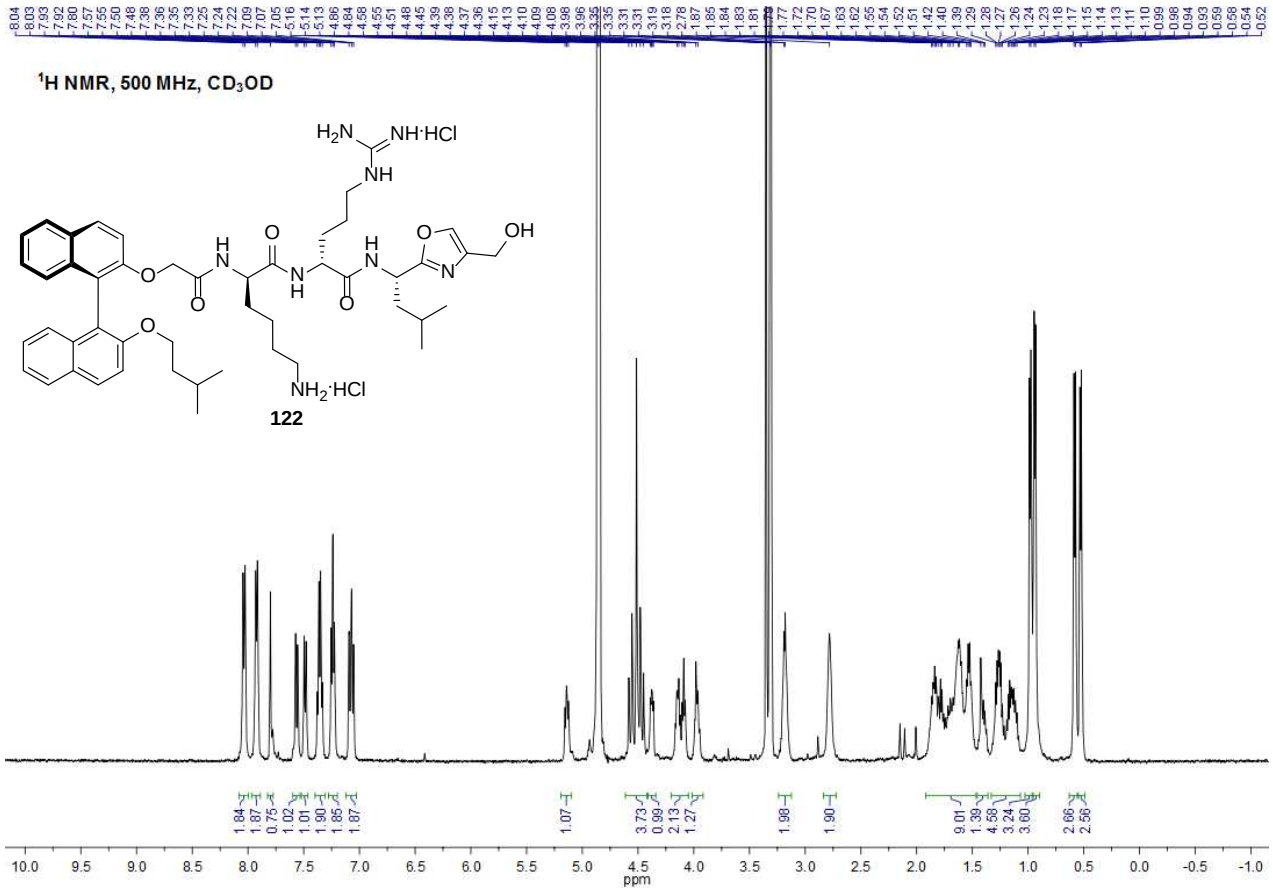

$^{13}$C NMR, 125 MHz, CD$_3$OD
119

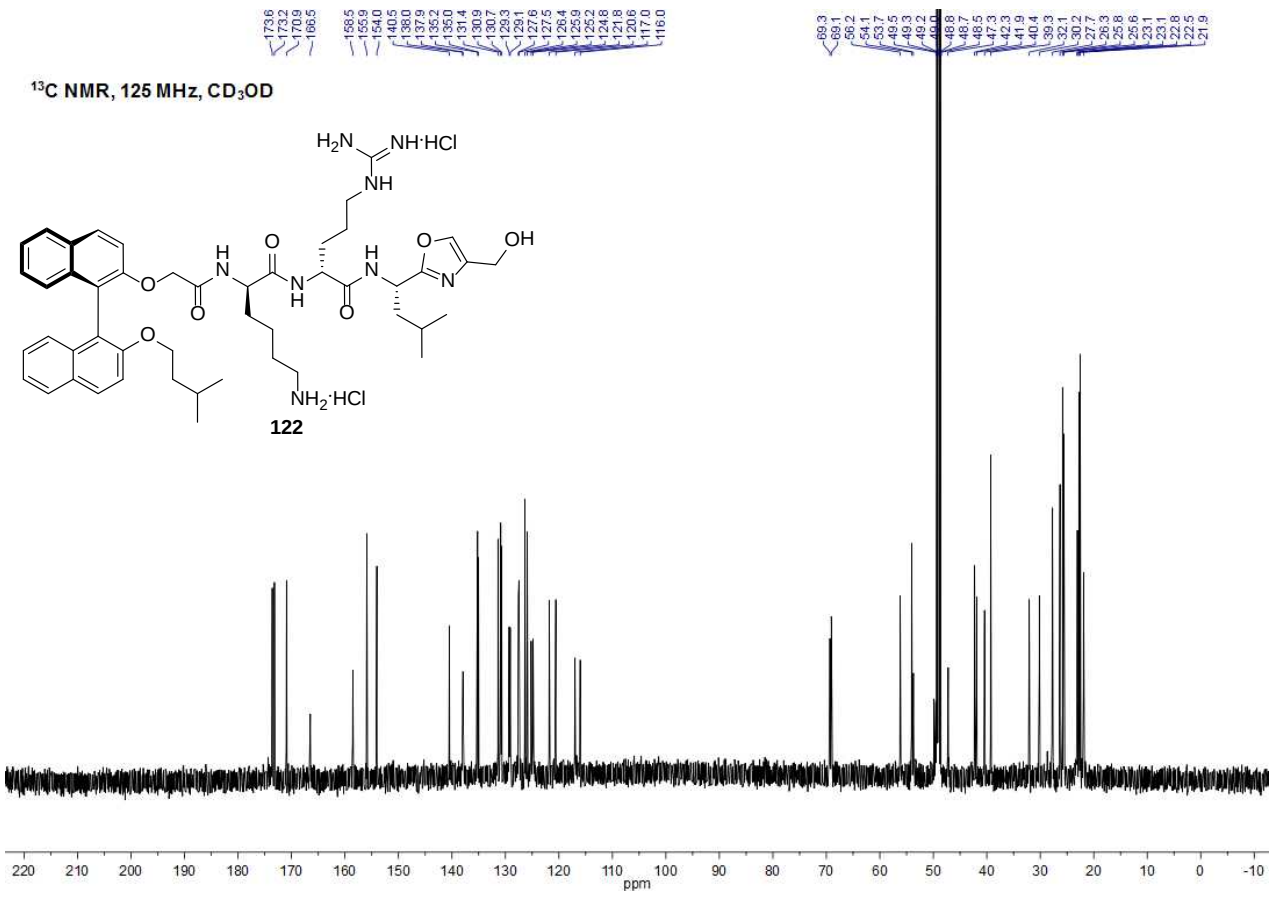

$^1$H NMR, 500 MHz, $CD_3OD$
120

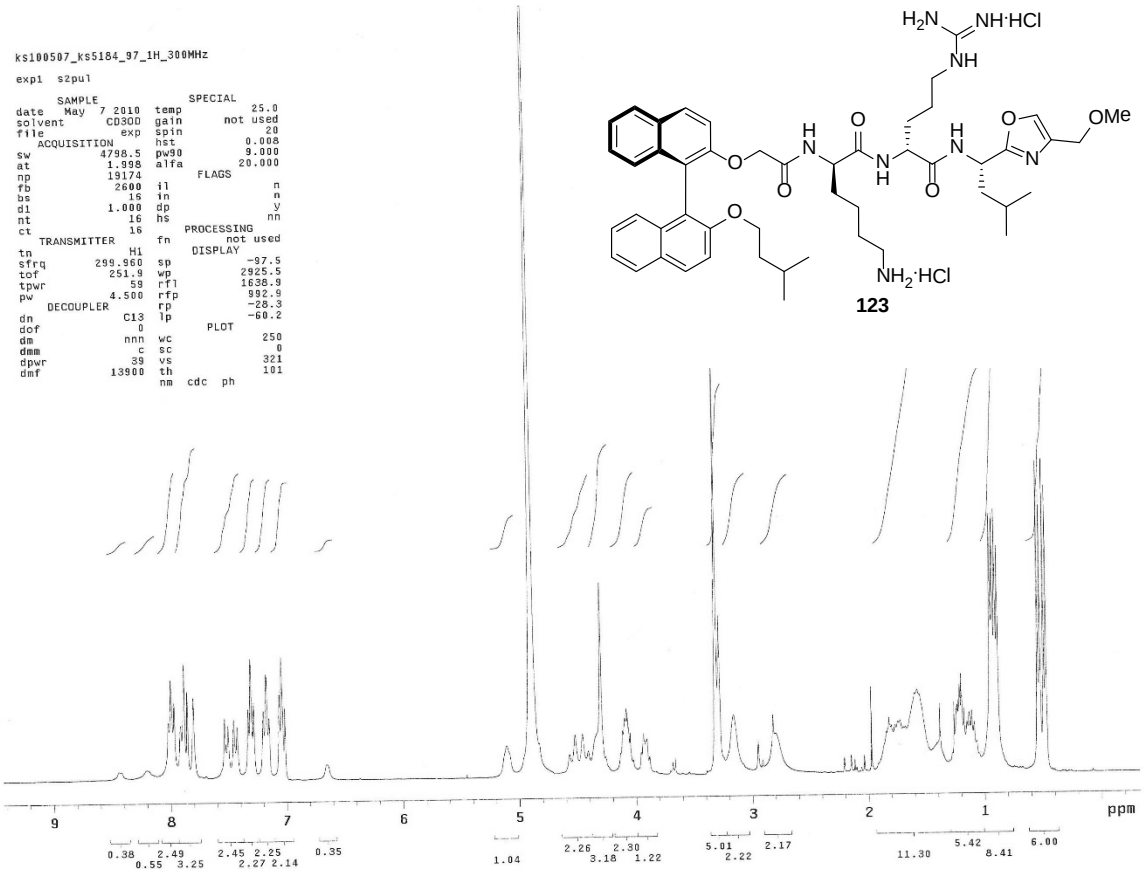

$^{13}$C NMR, 125 MHz, $CD_3OD$
120

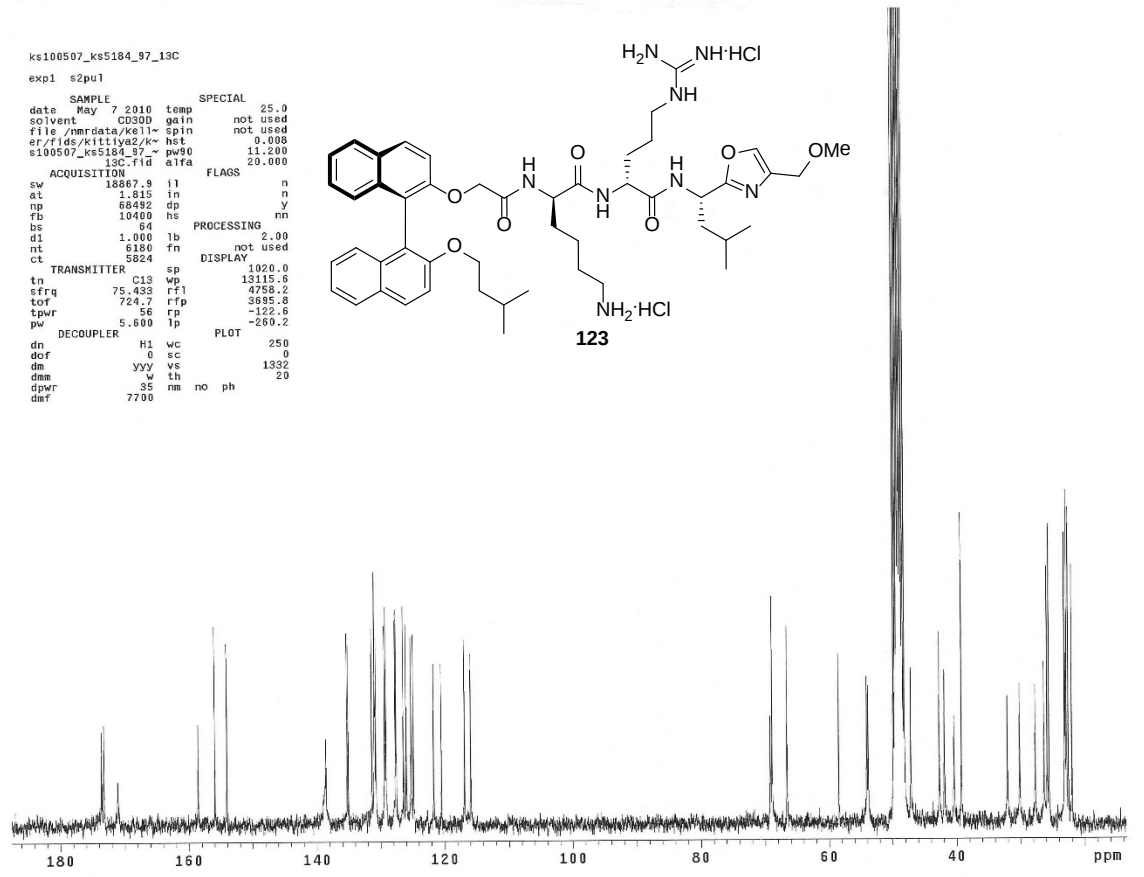

$^1$H NMR, 500 MHz, CD$_3$OD
121

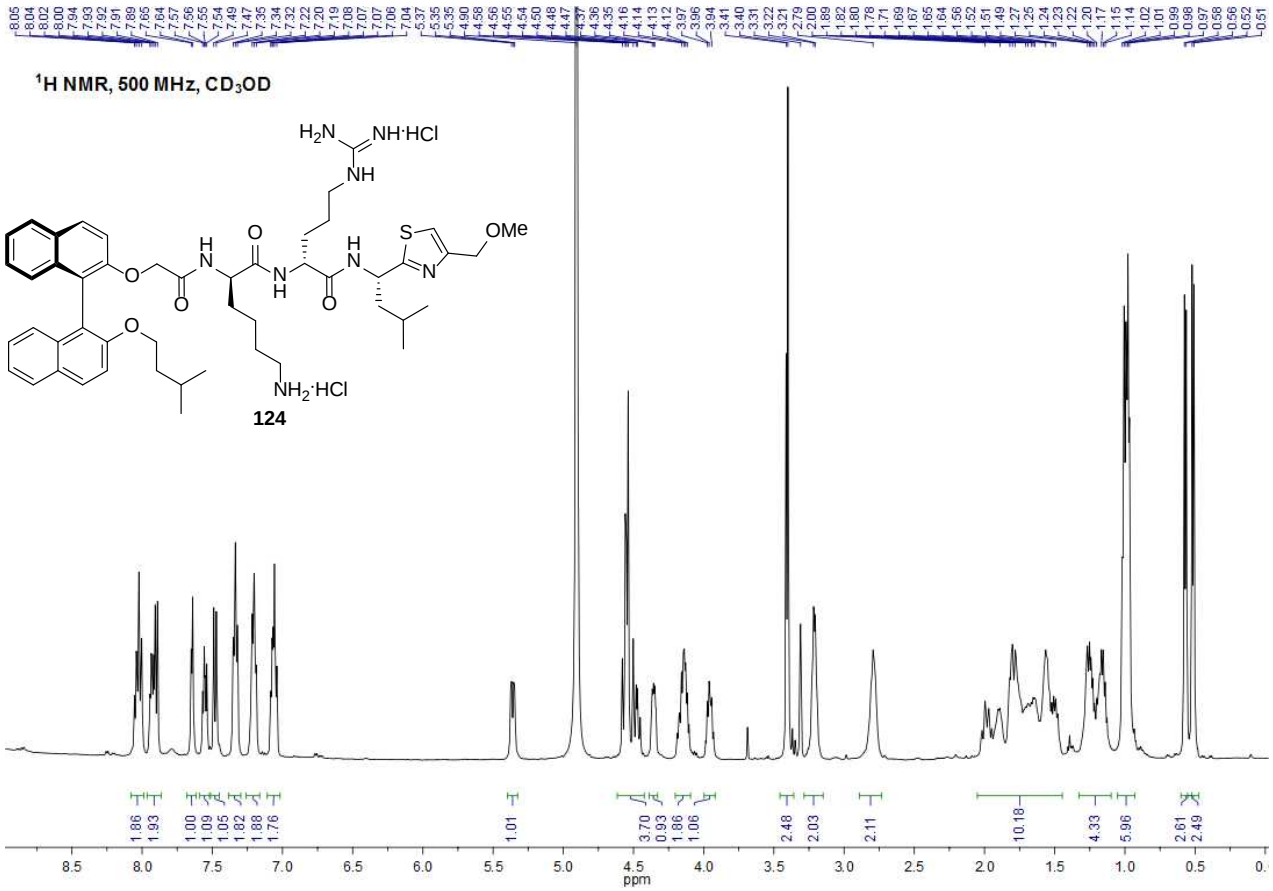

$^{13}$C NMR, 125 MHz, CD$_3$OD
121

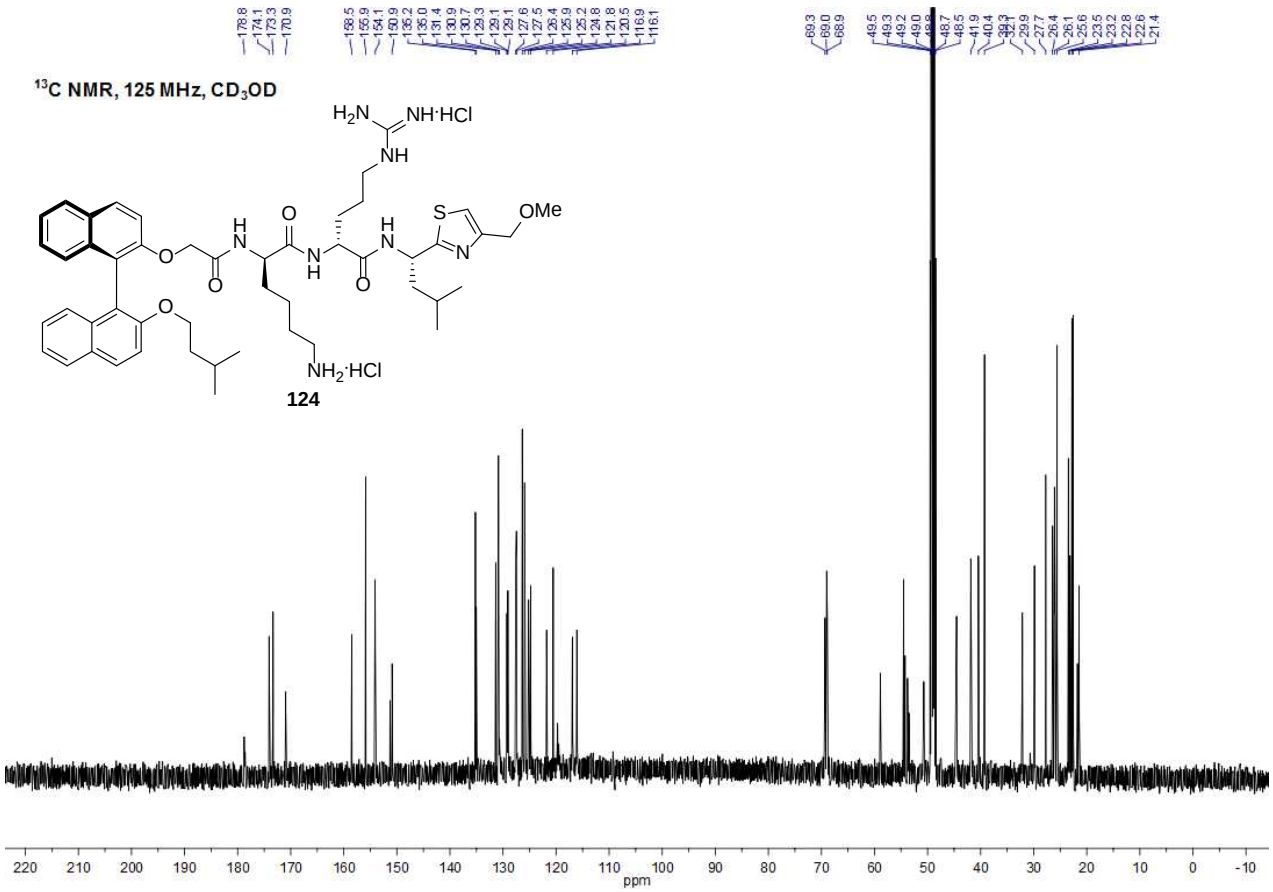

$^1$H NMR, 500 MHz, $CD_3OD$
122

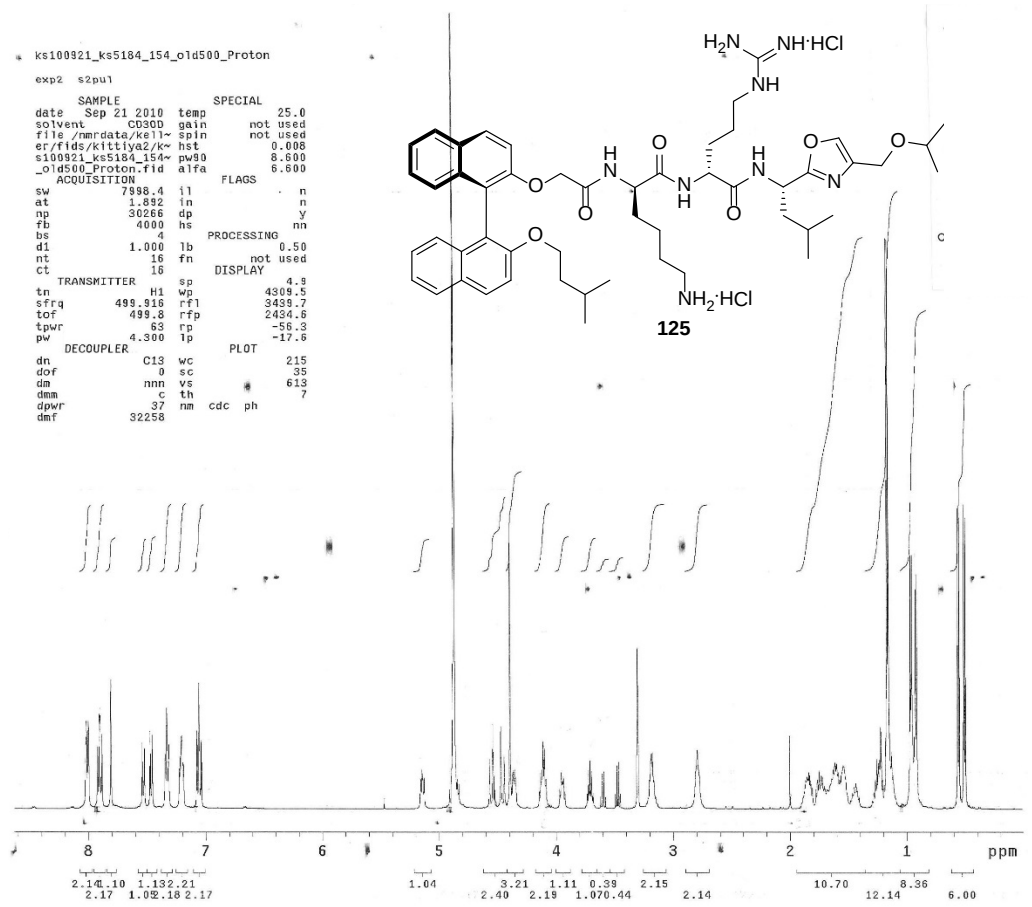

$^{13}$C NMR, 125 MHz, $CD_3OD$
122

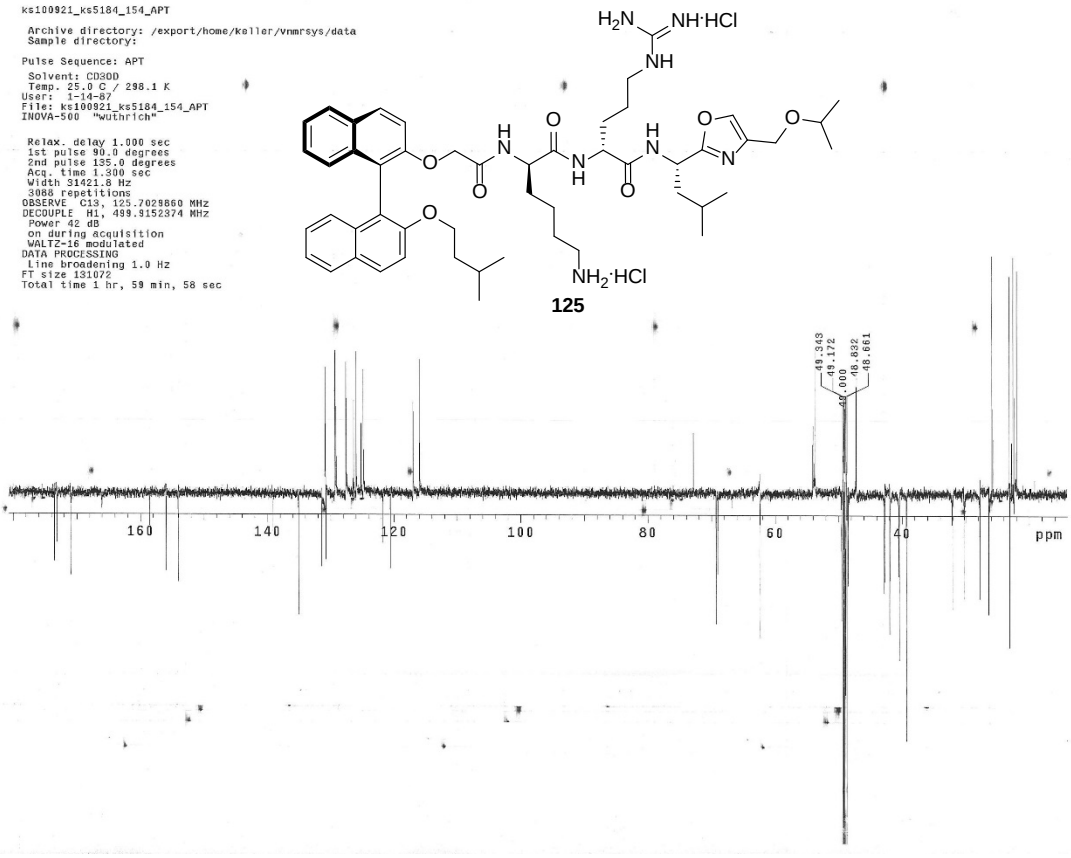

ks100507_ks5184_97_1H_300MHz
exp1 s2pul
SAMPLE
date May 7 2010
solvent CD3OD
file exp
ACQUISITION
sw 4798.5
at 1.998
np 19174
fb 2600
bs 16
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 299.960
tof 251.9
tpwr 59
pw 4.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 39
dmf 13900
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 9.000
alfa 20.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn not used
DISPLAY
sp -97.5
wp 2925.5
rfl 1638.9
rfp 992.9
rp -28.3
lp -60.2
PLOT
wc 250
sc 0
vs 321
th 101
nm cdc ph
H2N
NH·HCl
NH
OMe
NH2·HCl
123
ppm
0.38 2.49 0.55 3.25 2.45 2.25 2.27 2.14 0.35 1.04 2.26 2.30 3.18 1.22 5.01 2.22 2.17 11.30 5.42 8.41 6.00

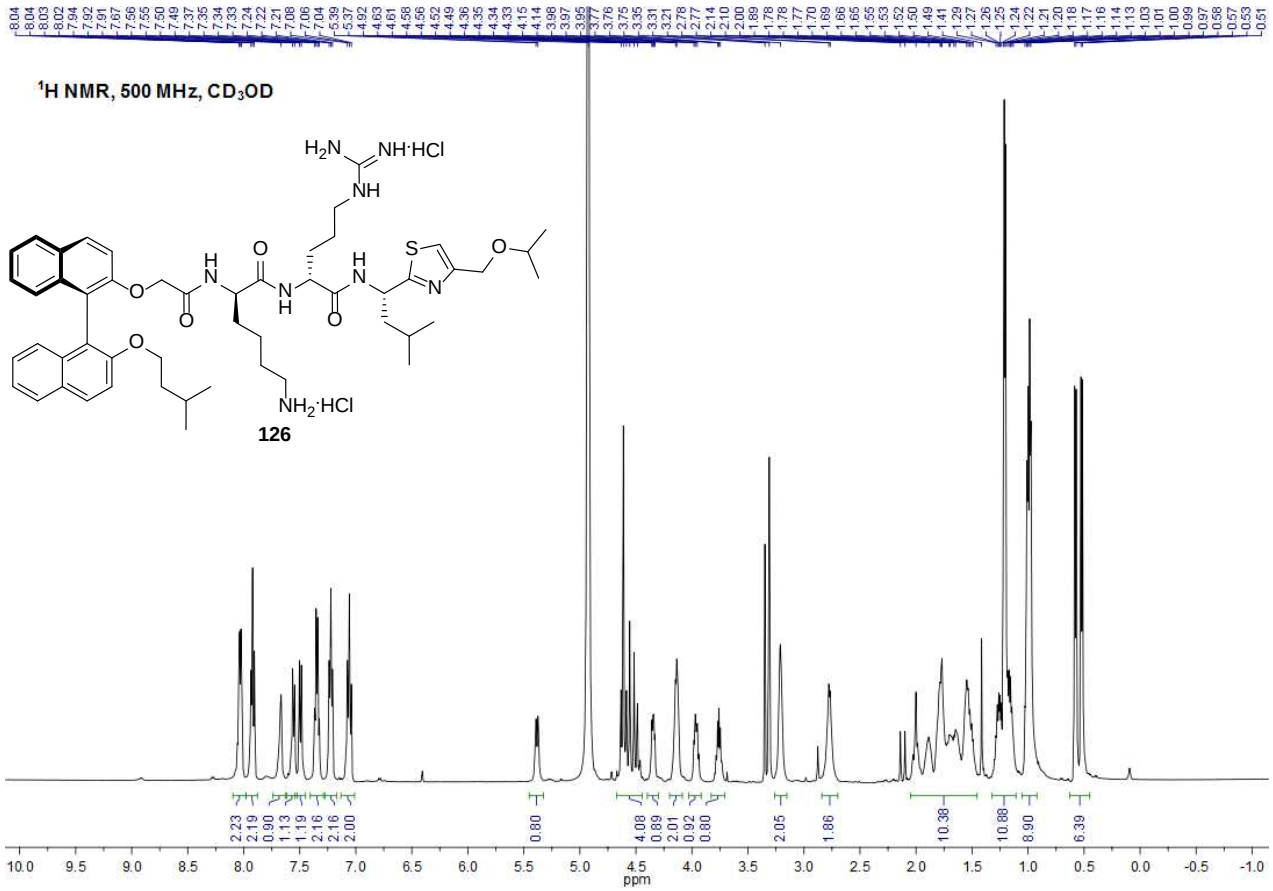

ks100507_ks5184_97_13C
exp1 s2pul
SAMPLE
date May 7 2010
solvent CD3OD
file /nmrdata/kell~
er/fids/kittiya2/k~
s100507_ks5184_97_~
13C.fid
ACQUISITION
sw 18867.9
at 1.815
np 68492
fb 10400
bs 64
d1 1.000
nt 6180
ct 5824
TRANSMITTER
tn C13
sfrq 75.433
tof 724.7
tpwr 56
pw 5.600
DECOUPLER
dn H1
dof 0
dm yyy
dmm w
dpwr 35
dmf 7700
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 11.200
alfa 20.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 2.00
fn not used
DISPLAY
sp 1020.0
wp 13115.6
rfl 4758.2
rfp 3695.8
rp -122.6
lp -260.2
PLOT
wc 250
sc 0
vs 1332
th 20
nm no ph
H2N
NH·HCl
NH
OMe
NH2·HCl
123
ppm

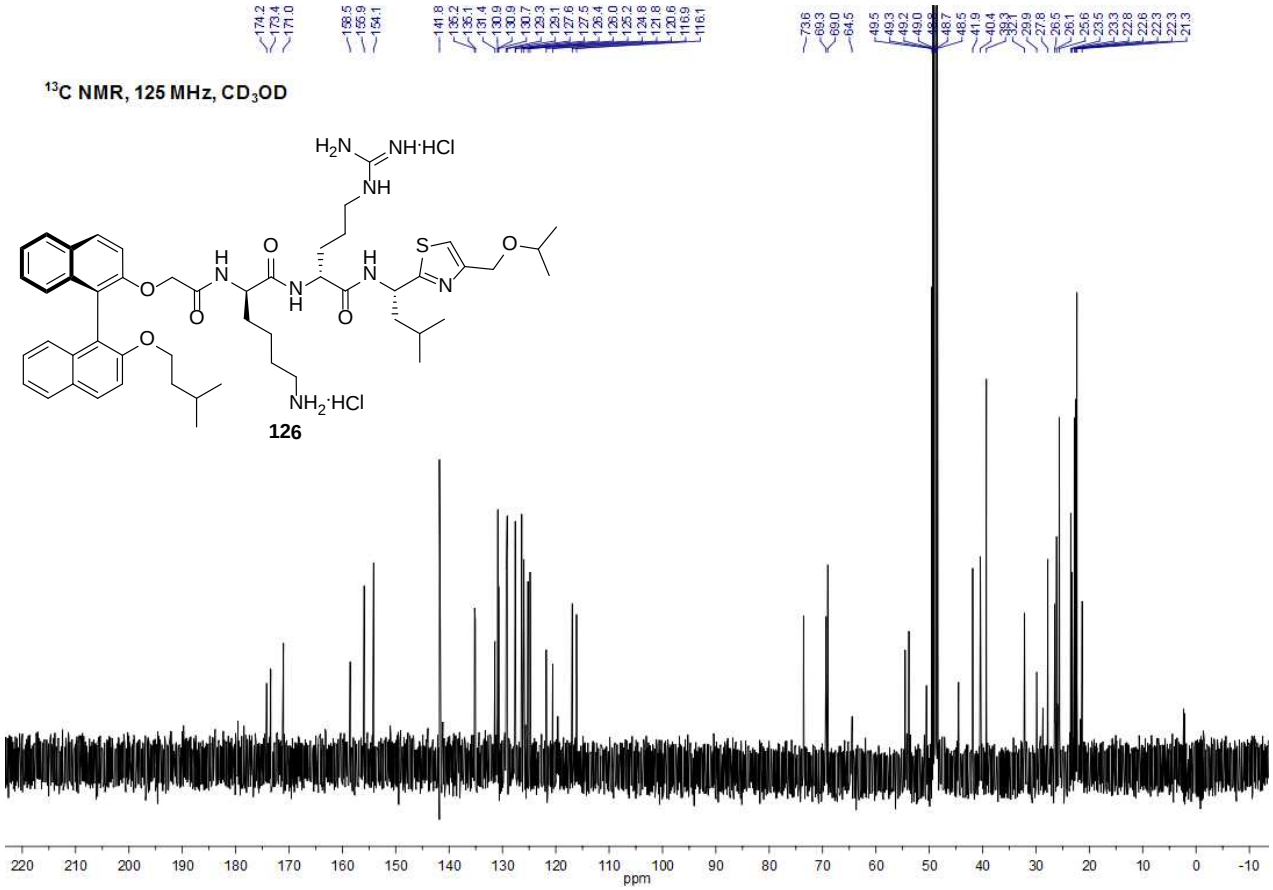

$^1$H NMR, 500 MHz, $CD_3OD$
124

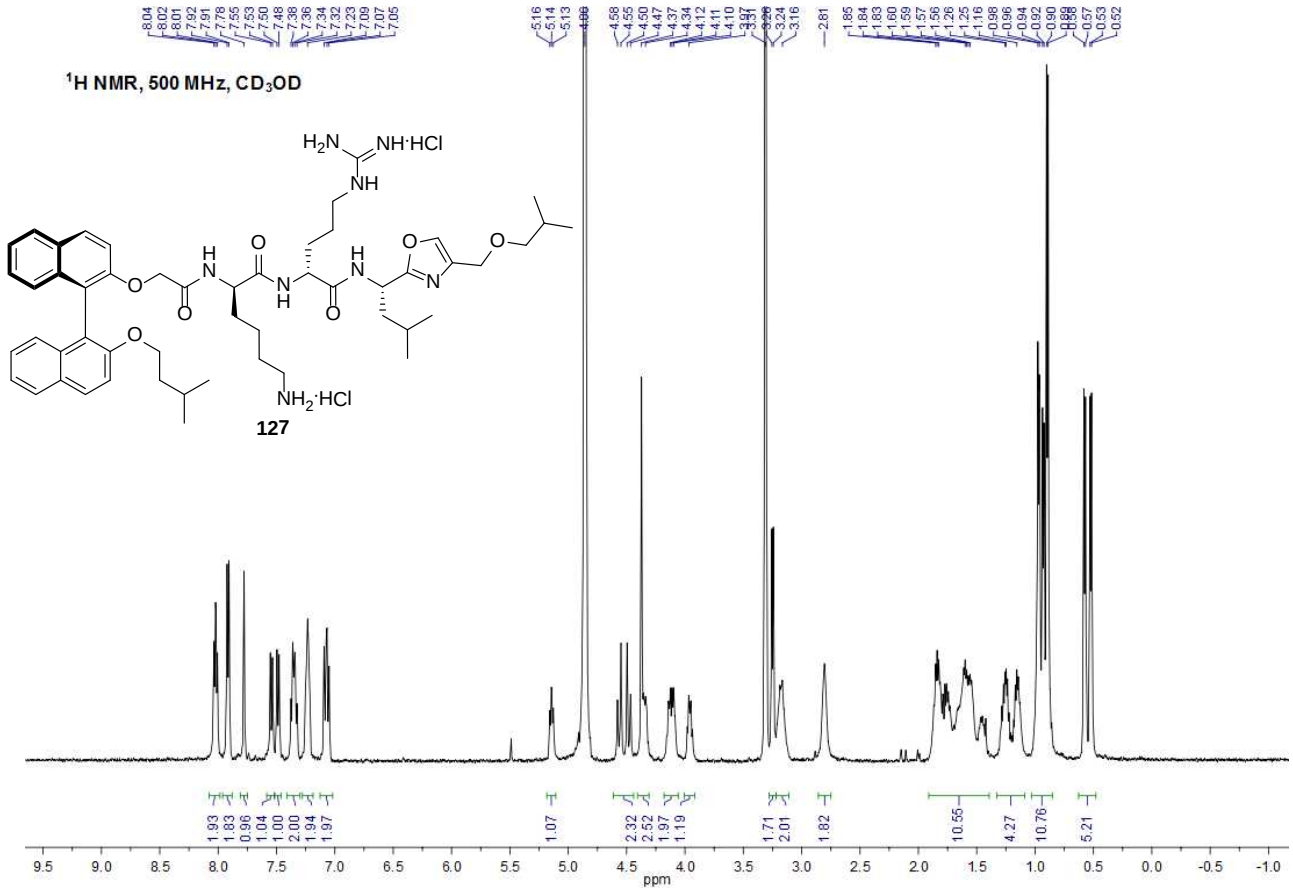

$^{13}$C NMR, 125 MHz, $CD_3OD$
124

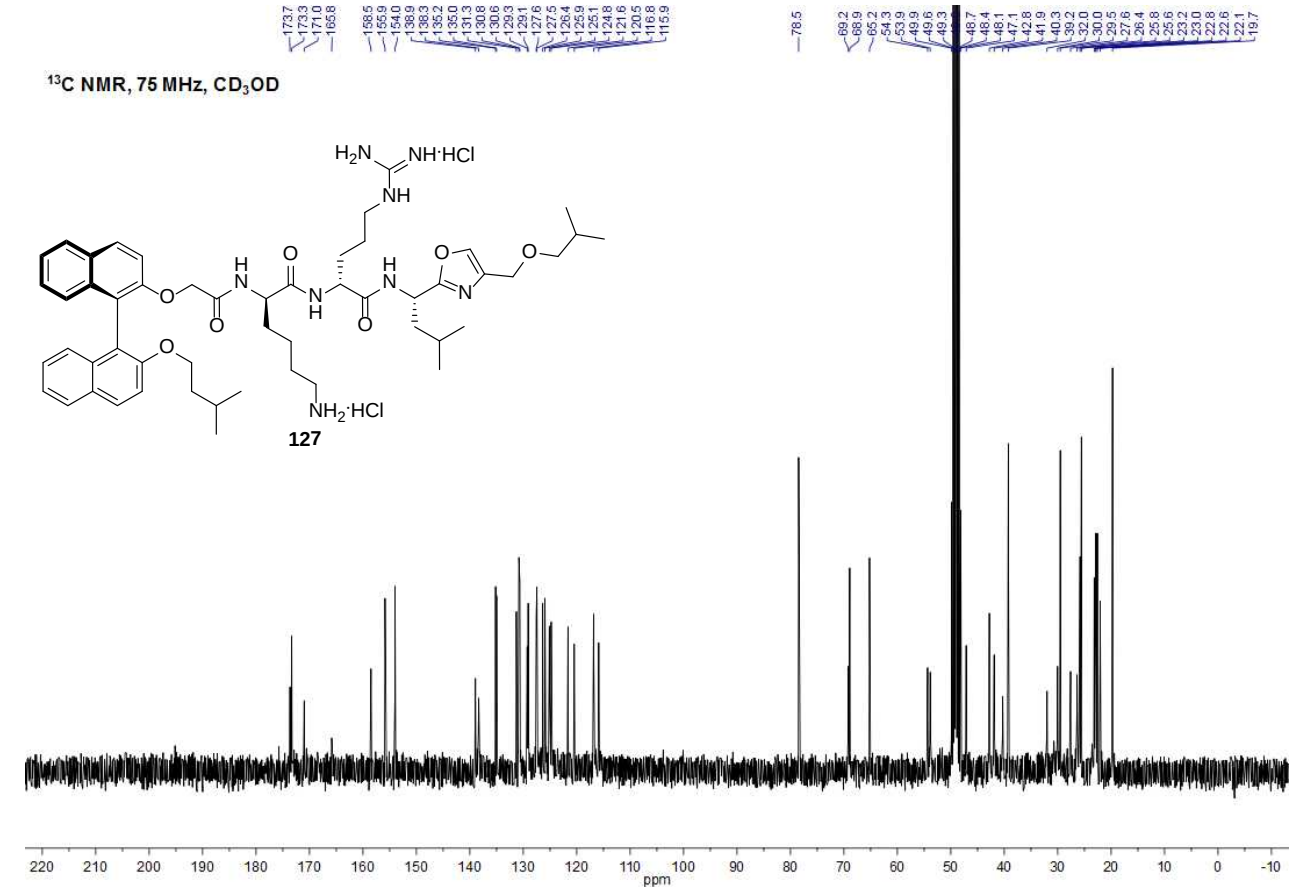

ks100921_ks5184_154_old500_Proton
exp2 s2pul
SAMPLE
date Sep 21 2010
solvent CD3OD
file /nmrdata/kell~
er/fids/kittiya2/k~
s100921_ks5184_154~
_old500_Proton.fid
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.916
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp 4.9
wp 4309.5
rfl 3439.7
rfp 2434.6
rp -56.3
lp -17.6
PLOT
wc 215
sc 35
vs 613
th 7
nm cdc ph
125
8
7
6
5
4
3
2
1
ppm
2.14 1.10 1.13 2.21 1.04 3.21 1.11 0.39 2.15 10.70 8.36
2.17 1.02 2.18 2.17 2.40 2.19 1.07 0.44 2.14 12.14 6.00

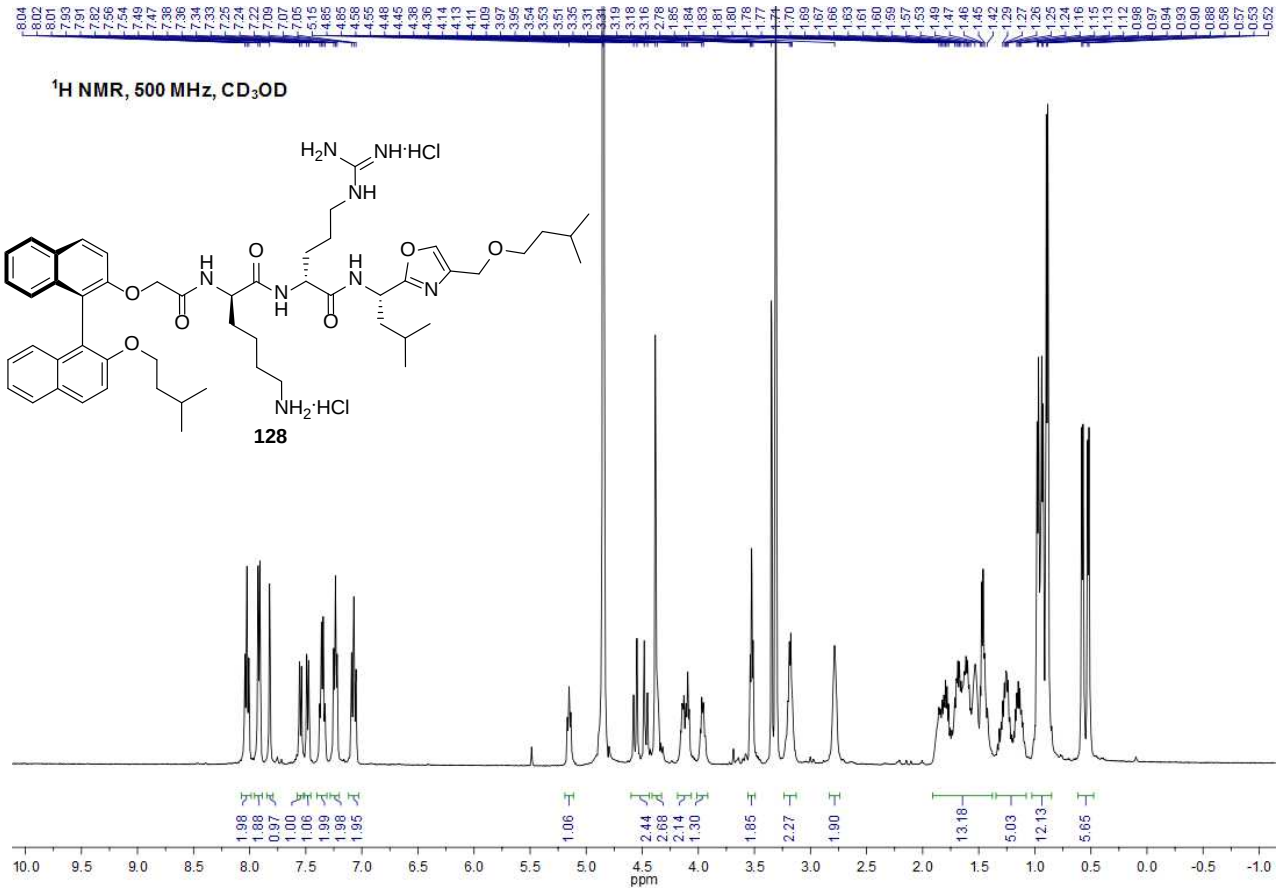

ks100921_ks5184_154_APT
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100921_ks5184_154_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
3088 repetitions
OBSERVE C13, 125.7029860 MHz
DECOUPLE H1, 499.8152374 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1 hr, 59 min, 58 sec
125
49.343
49.172
47.000
46.832
46.661
160
140
120
100
80
60
40
ppm

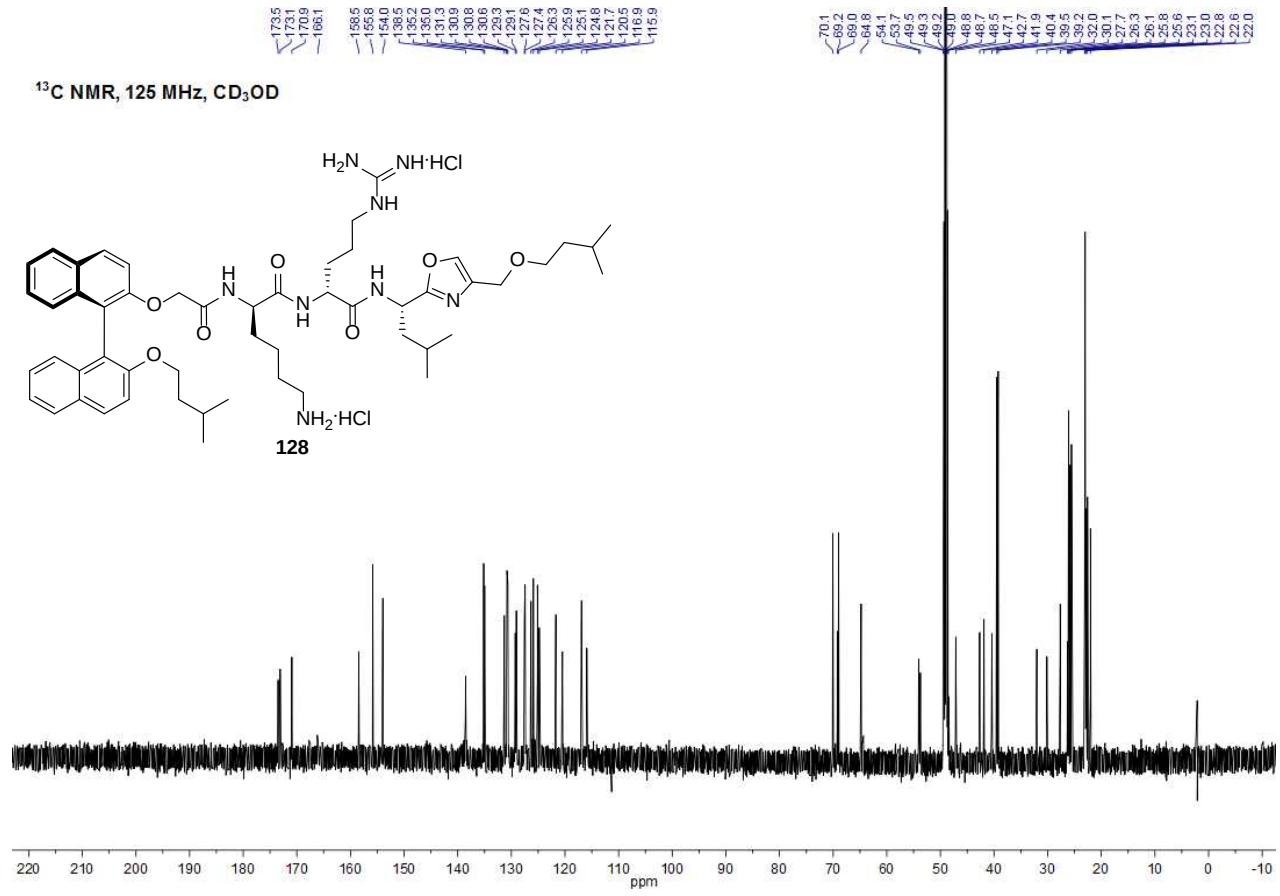

¹H NMR, 500 MHz, CD3OD
126

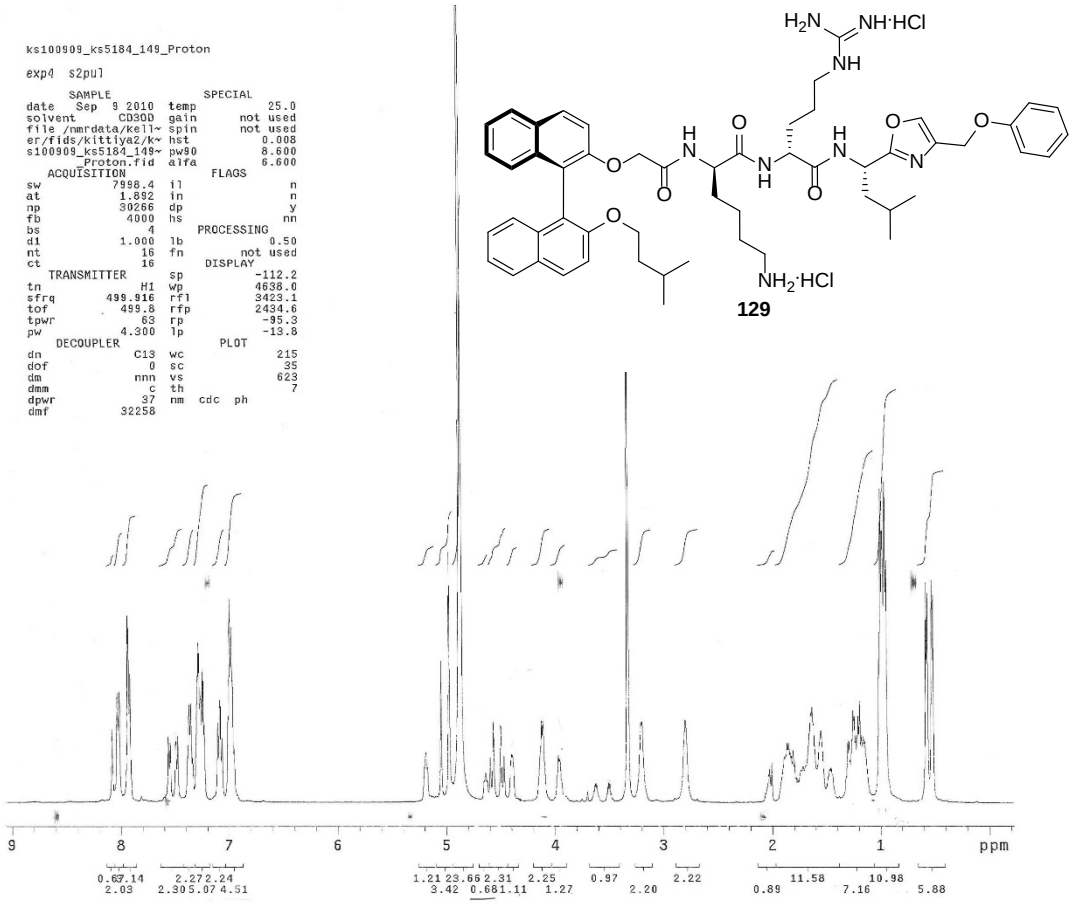

¹³C NMR, 125 MHz, CD3OD
126


$^1$H NMR, 500 MHz, CD$_3$OD
127


$^{13}$C NMR, 75 MHz, CD$_3$OD
127

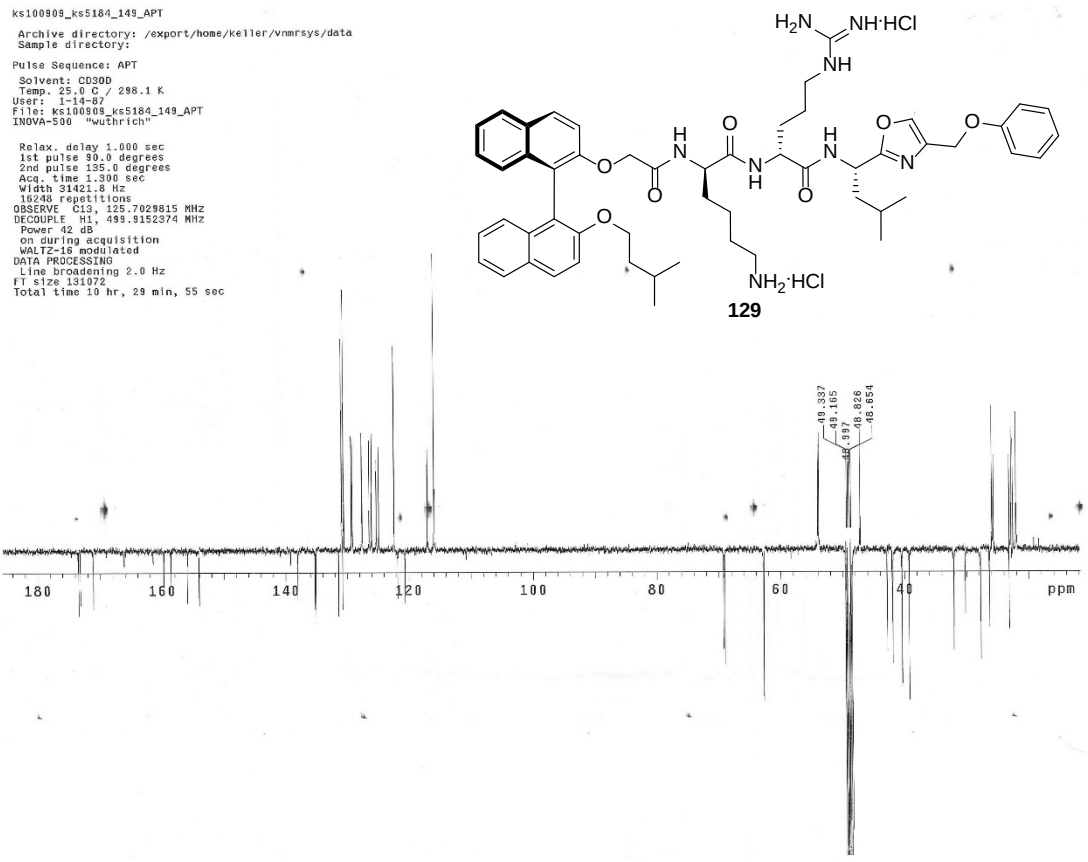

$^1$H NMR, 500 MHz, CD$_3$OD
128


$^{13}$C NMR, 125 MHz, CD$_3$OD
128


ks100909_ks5184_149_Proton
exp4 s2pul
SAMPLE
date Sep 9 2010
solvent CD3OD
file /nmrdata/kell~
er/fids/kittiya2/k~
s100909_ks5184_149~
_Proton.fid
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.916
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -112.2
wp 4638.0
rfl 3423.1
rfp 2434.6
rp -95.3
lp -13.8
PLOT
wc 215
sc 35
vs 623
th 7
nm cdc ph
9 8 7 6 5 4 3 2 1 ppm
0.67 7.14 2.27 2.24 1.21 23.66 2.31 2.25 0.97 2.22 11.58 10.98
2.03 2.30 5.07 4.51 3.42 0.68 1.11 1.27 2.20 0.89 7.16 5.88

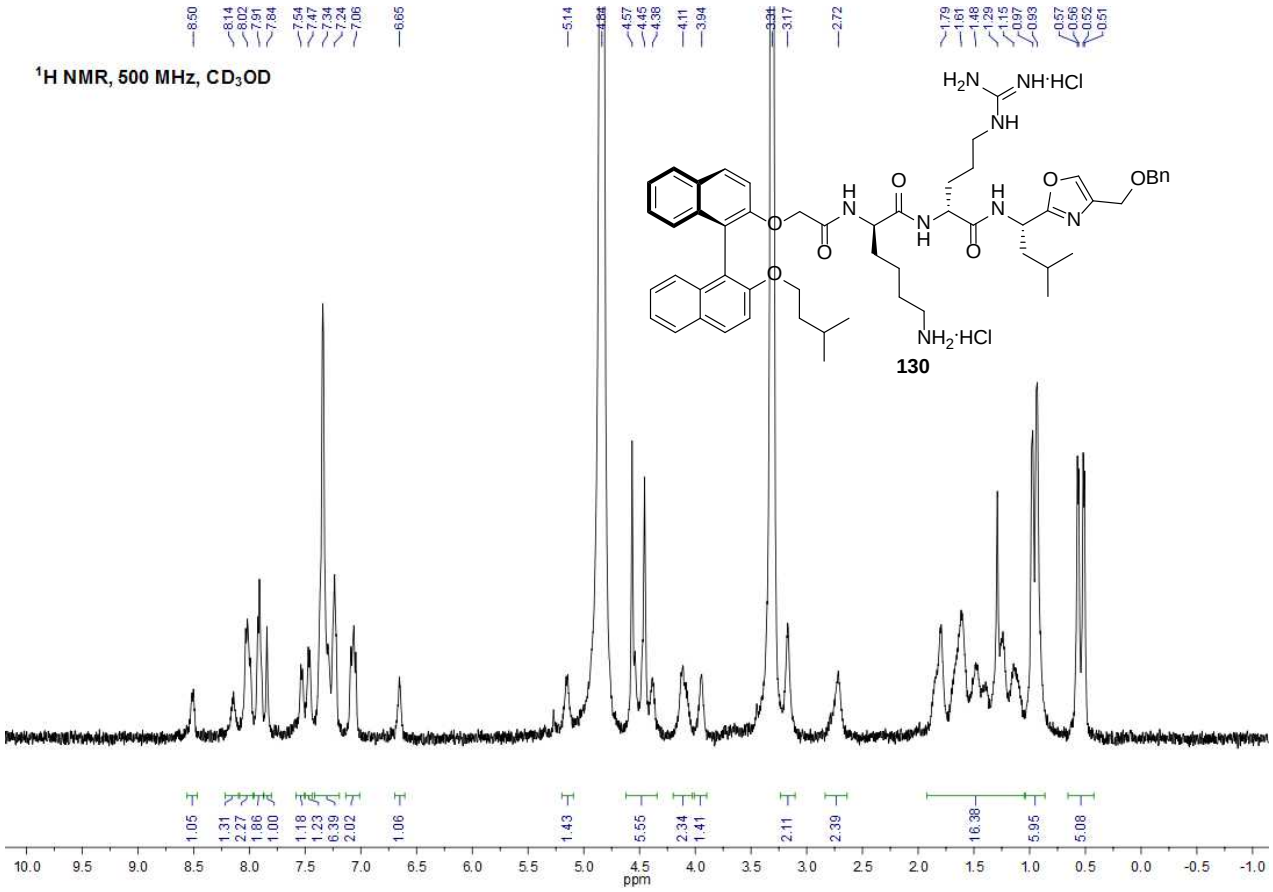

H2N
NH·HCl
NH
O
H
N
O
O
NH2·HCl

**129**


ks100909_ks5184_149_APT
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: i-14-87
File: ks100909_ks5184_149_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
16248 repetitions
OBSERVE C13, 125.7029815 MHz
DECOUPLE H1, 499.9152374 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 10 hr, 29 min, 55 sec
49.337
49.165
48.826
48.654
180 160 140 120 100 80 60 40 ppm

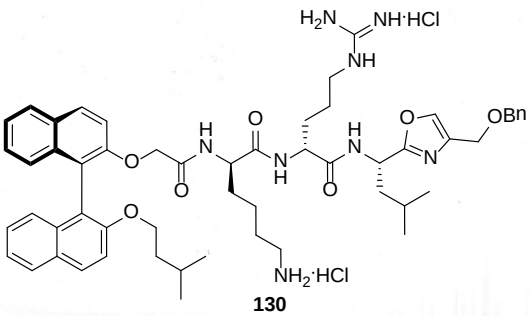

H2N
NH·HCl
NH
O
H
N
O
O
NH2·HCl

**129**

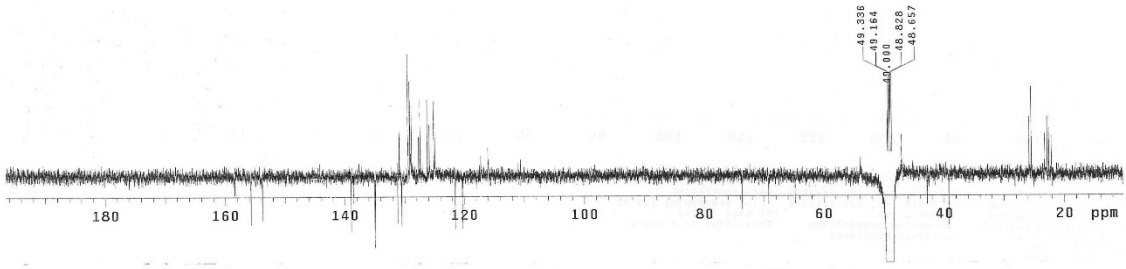


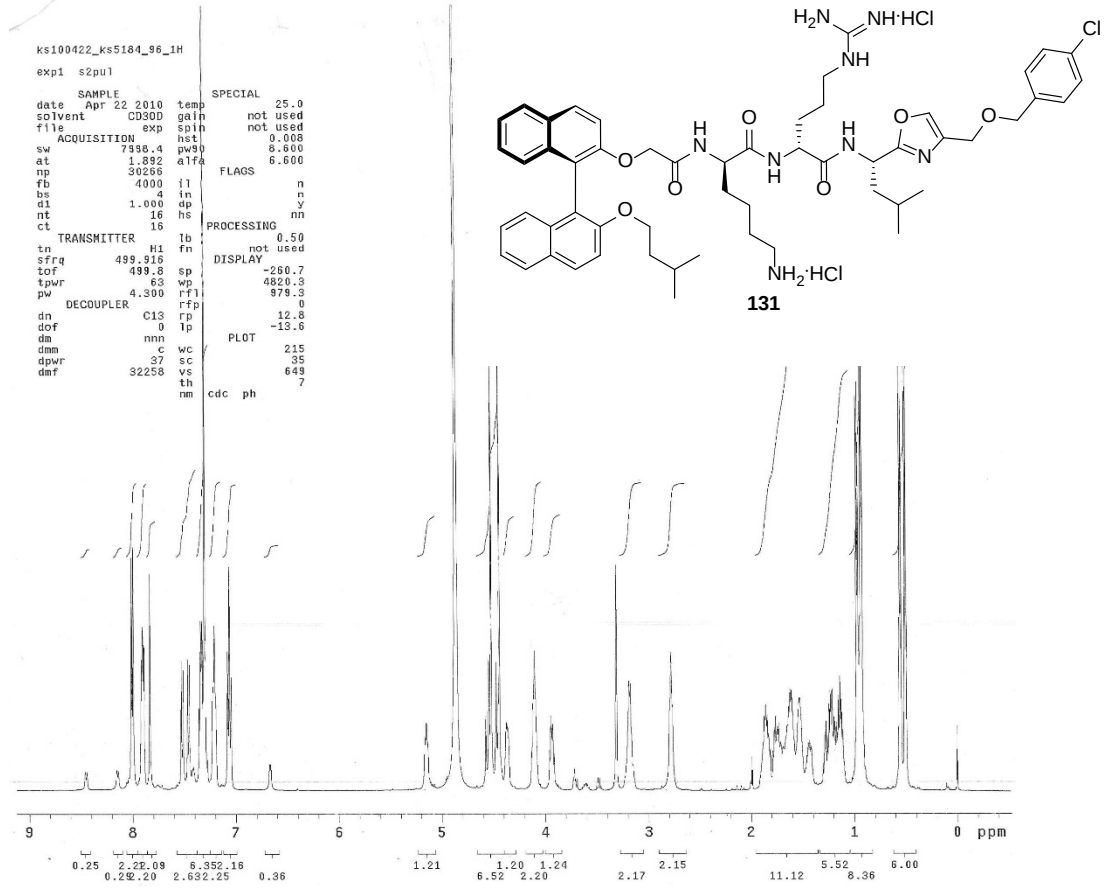

130

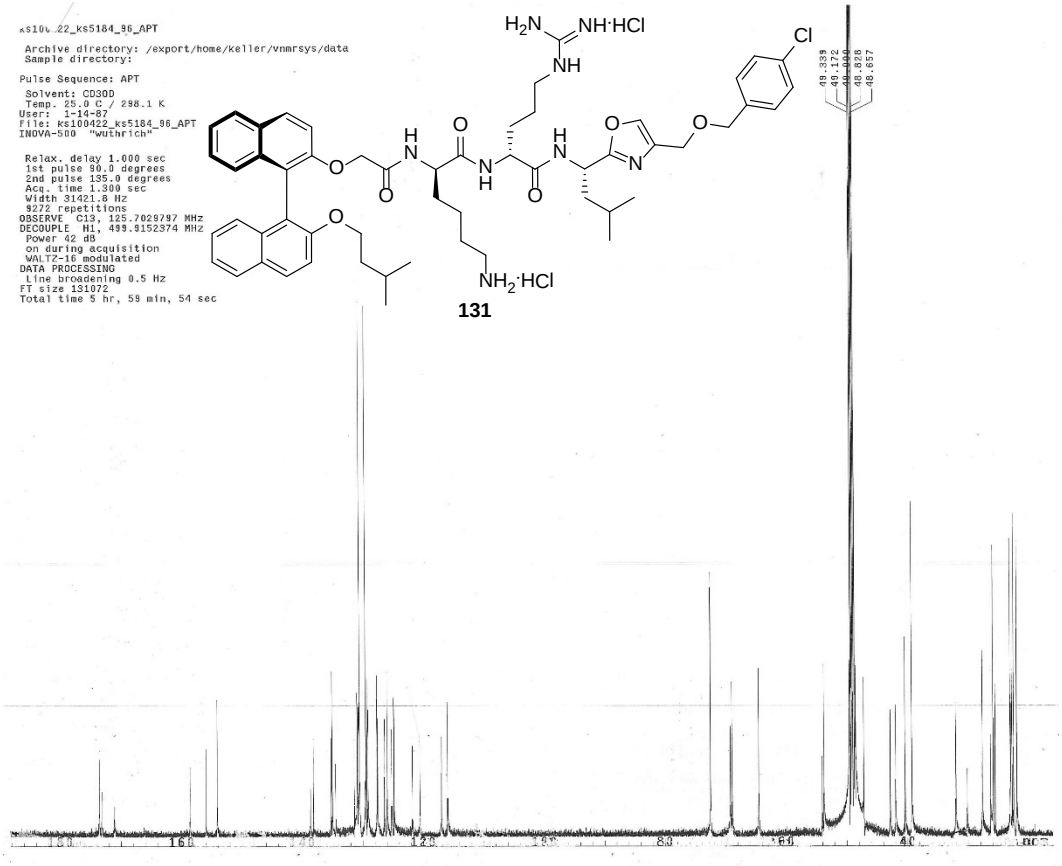
```
ks100325_ks5184_84_APT

exp2  APT

      SAMPLE                  APT
date    Mar 25 2010  jlxh          140.0
solvent       CD3OD  d3              0
sample                    SPECIAL
   ACQUISITION       temp          25.0
sw          31421.8  gain            20
at              1.300  spin       not used
np             81726       PROCESSING
bs                64  lb            1.00
ss                 8  fn         not used
di             1.000       SPECTRUM
nt             20120  wp         23411.0
ct             20120  sp          1294.4
   TRANSMITTER       rp           -76.5
tn                C13  lp           51.8
tof           1884.0  nm  cdc  ph
tpwr              63       REFERENCE
pw            24.000  rfl         7920.7
pw90          16.000  rfp         6159.4
   DECOUPLER                 PLOT
dn                H1  wc             250
dof                0  sc               0
dpwr              37  vs             344
dm               yny  hzmm         93.64
dmm                w  th             142
dmf           12821
```

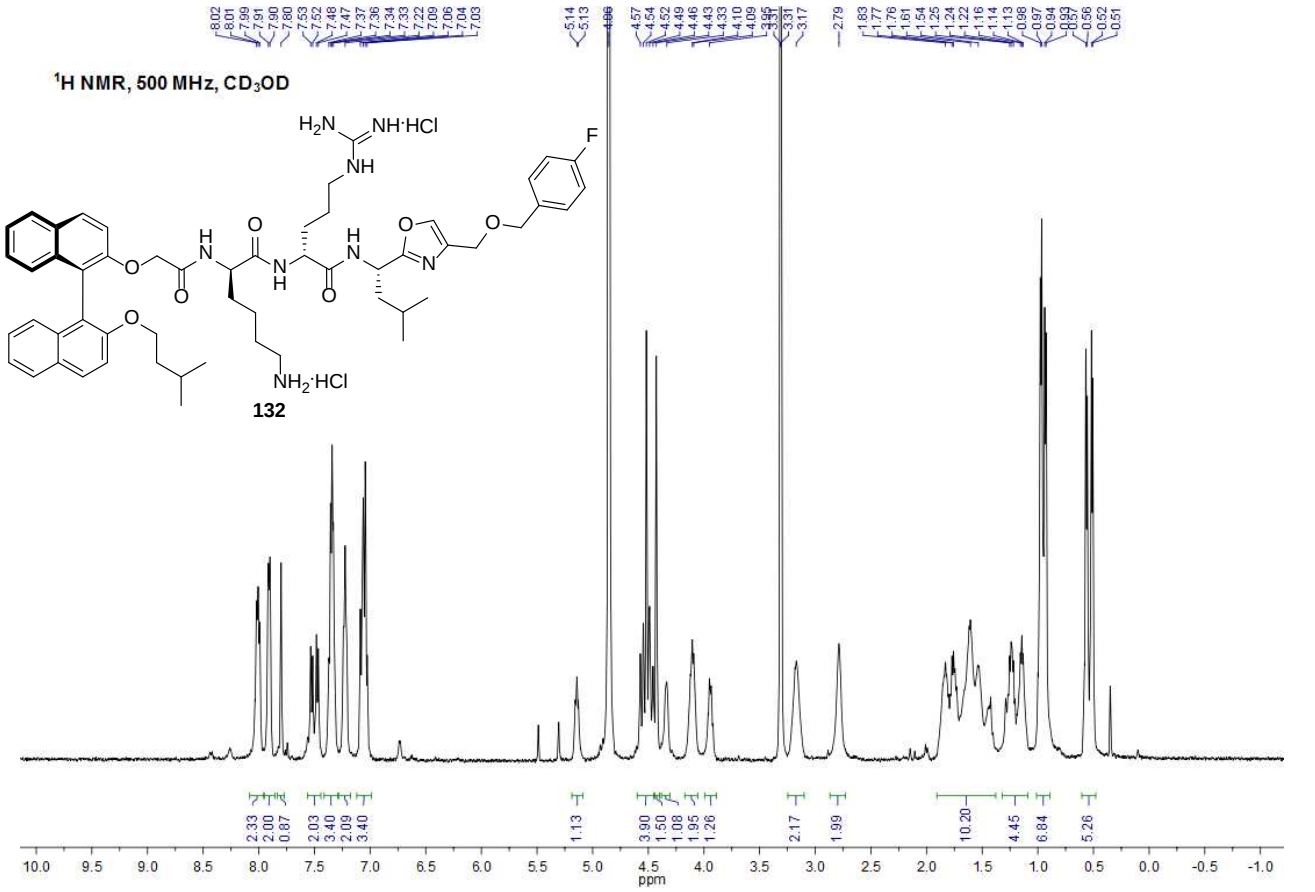


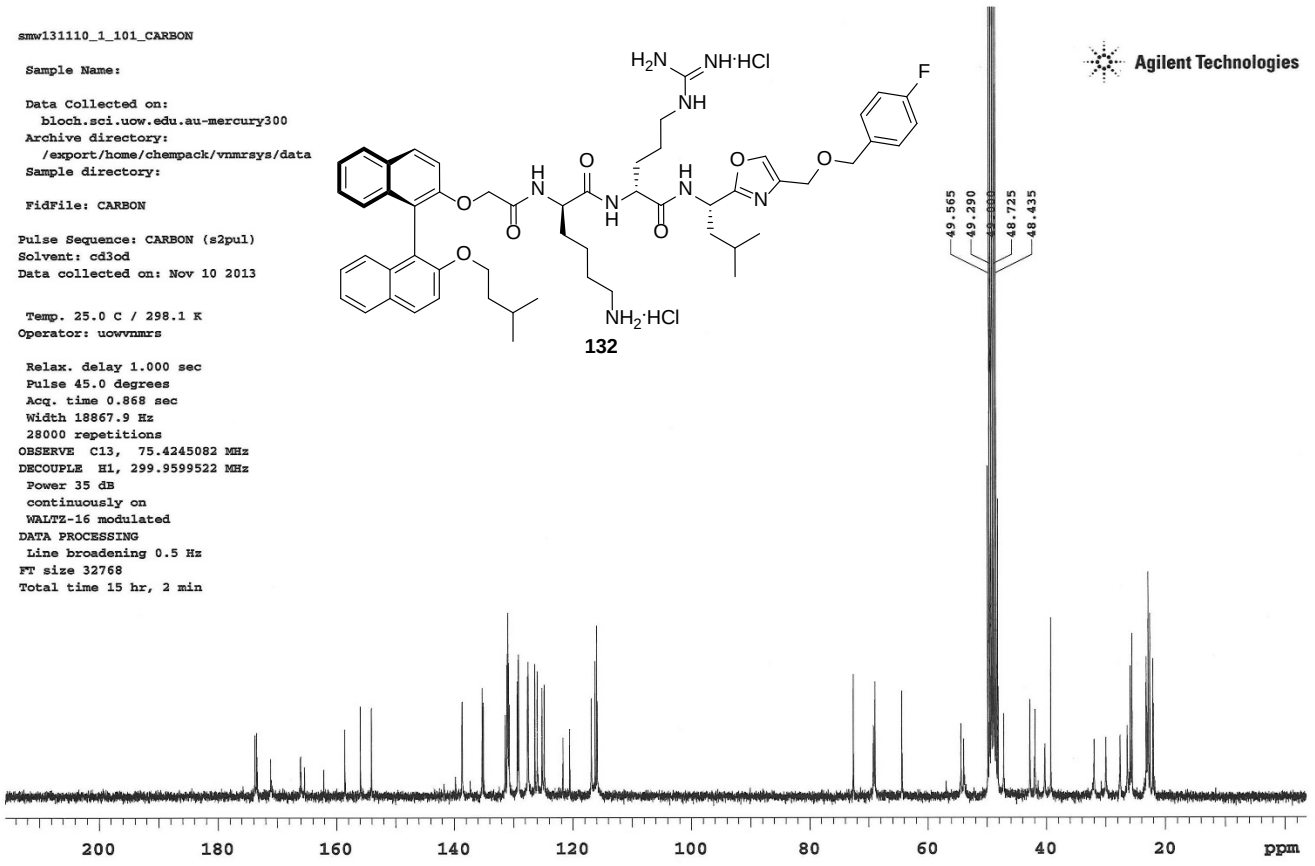
130

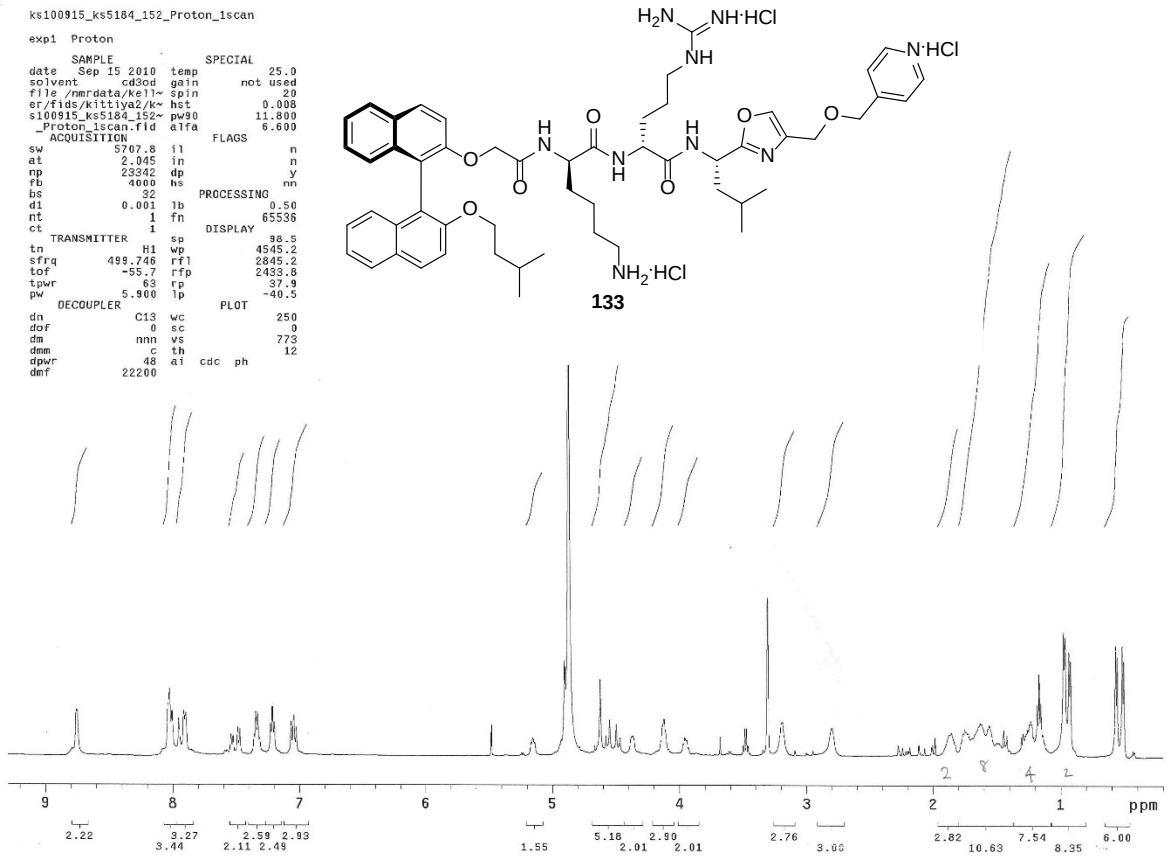


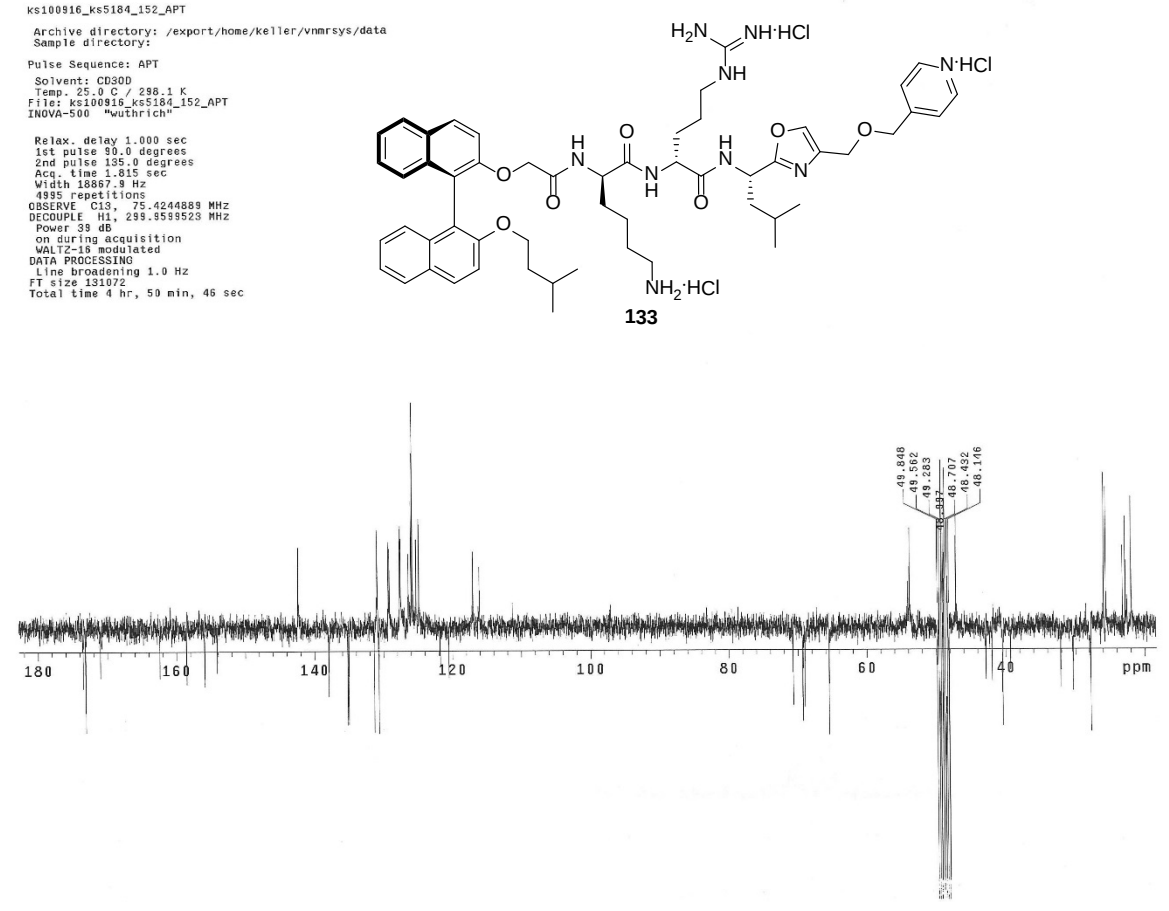

ks100422_ks5184_96_1H
exp1 s2pul
SAMPLE
date Apr 22 2010
solvent CD3OD
file exp
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.916
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -260.7
wp 4820.3
rfl 979.3
rfp 0
rp 12.8
lp -13.6
PLOT
wc 215
sc 35
vs 649
th 7
nm cdc ph
131
9 8 7 6 5 4 3 2 1 0 ppm
0.25 2.22 2.09 6.35 2.16
0.25 2.20 2.63 2.25 0.36
1.21
1.20 1.24
6.52 2.20
2.17
2.15
5.52
11.12 8.36
6.00

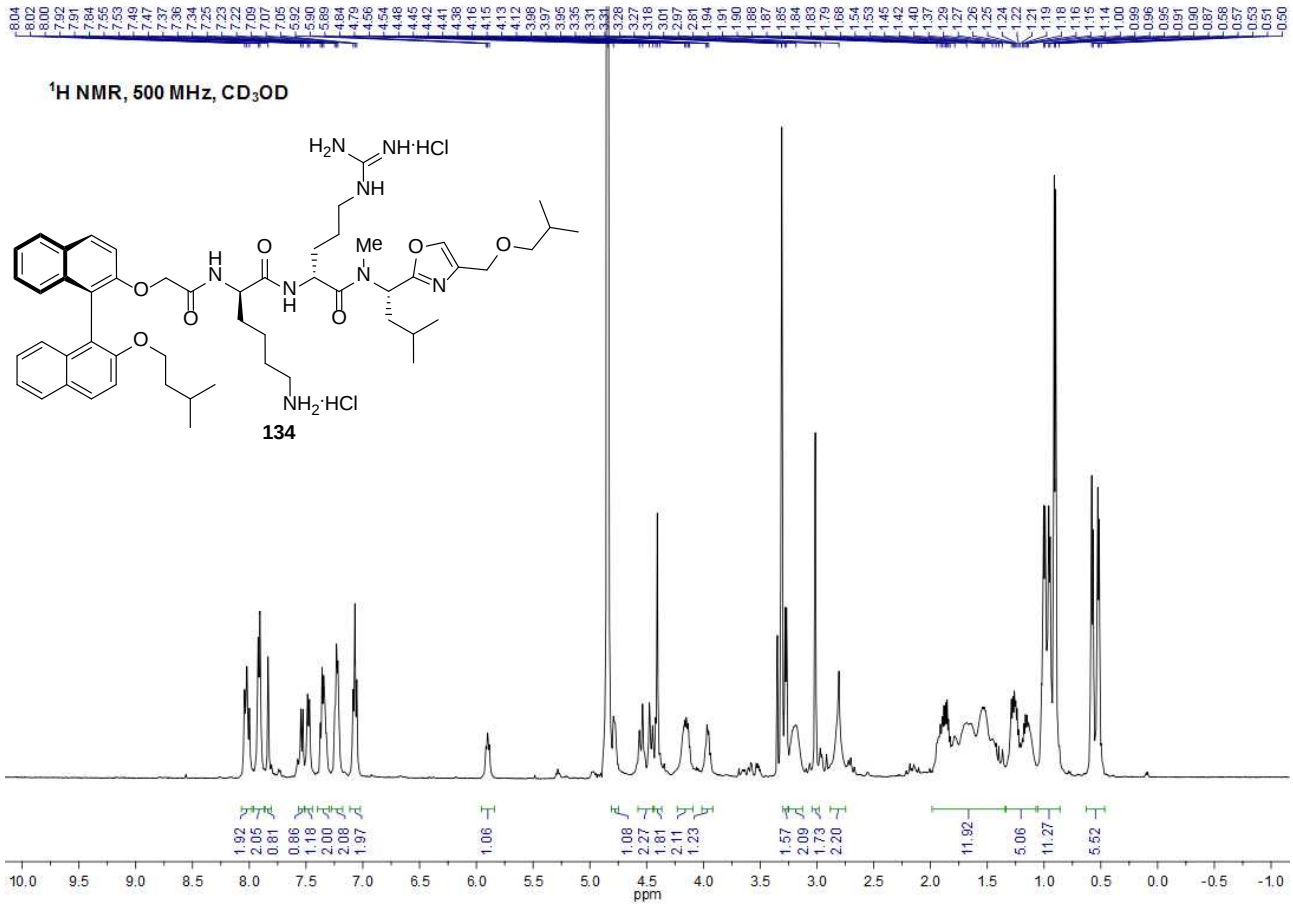

ks100422_ks5184_96_APT
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100422_ks5184_96_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
9272 repetitions
OBSERVE C13, 125.7029797 MHz
DECOUPLE H1, 499.9152374 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 5 hr, 59 min, 54 sec
131

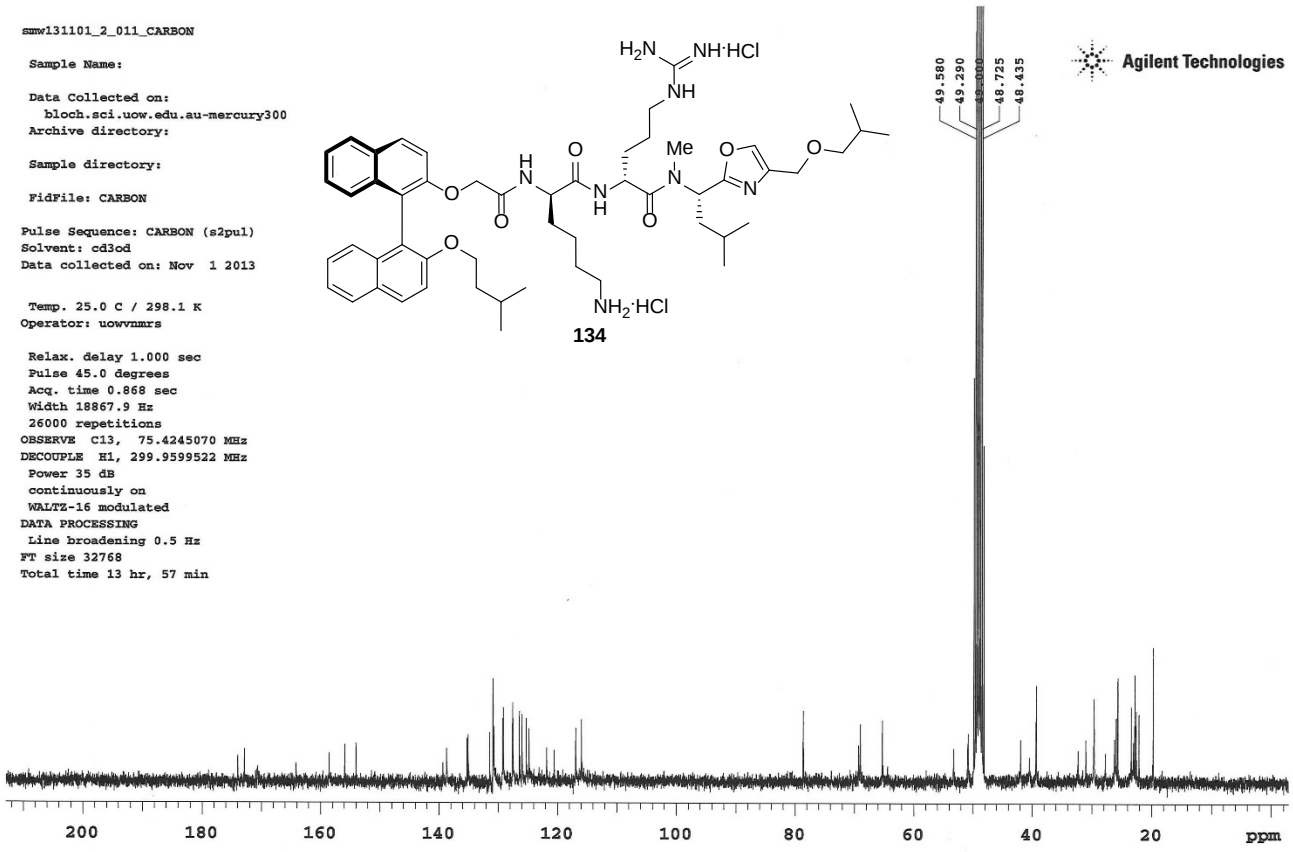

$^1$H NMR, 500 MHz, $CD_3OD$
132

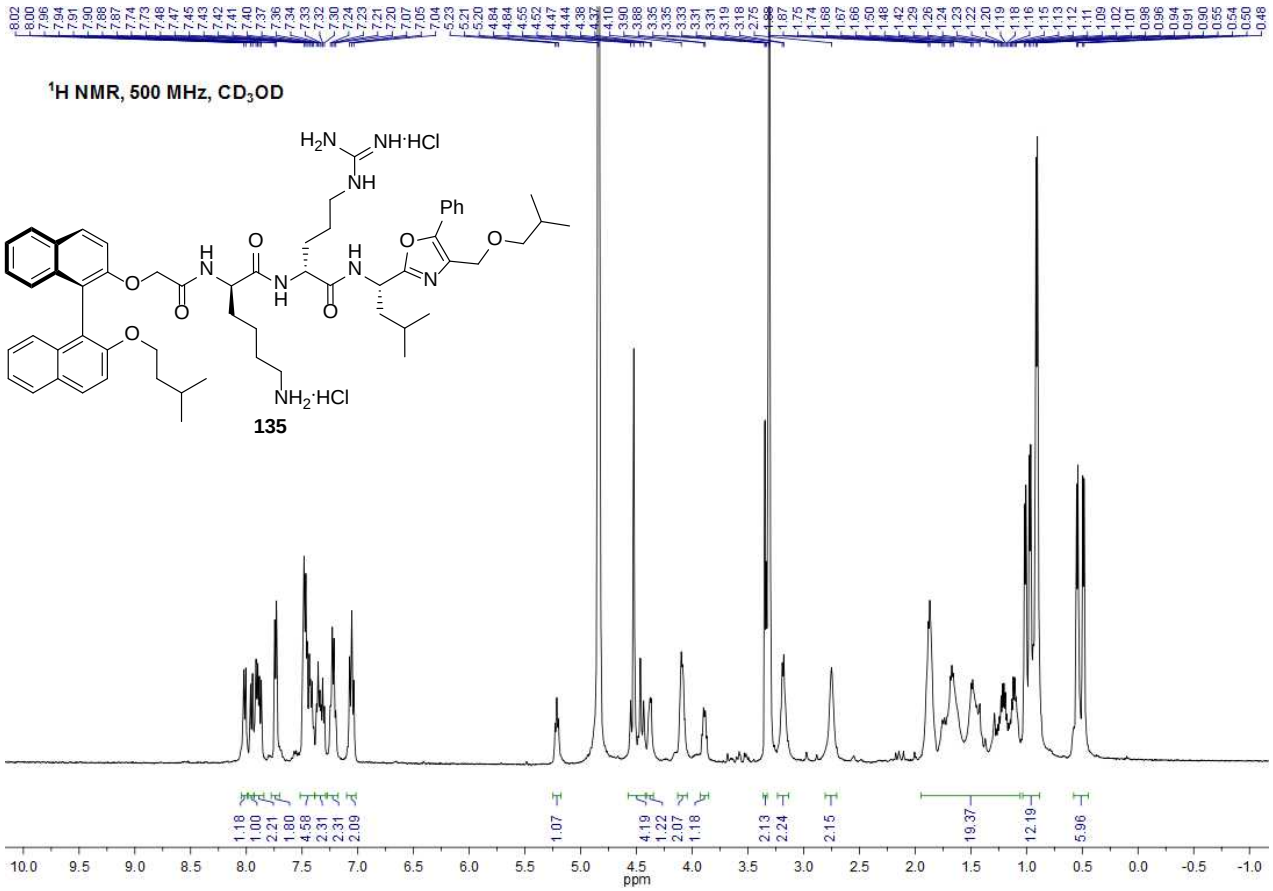

smw131110_1_101_CARBON
Sample Name:
Data Collected on:
bloch.sci.uow.edu.au-mercury300
Archive directory:
/export/home/chempack/vnmrsys/data
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Nov 10 2013
Temp. 25.0 C / 298.1 K
Operator: uowvnmrs
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.868 sec
Width 18867.9 Hz
28000 repetitions
OBSERVE C13, 75.4245082 MHz
DECOUPLE H1, 299.9599522 MHz
Power 35 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 32768
Total time 15 hr, 2 min
Agilent Technologies
132

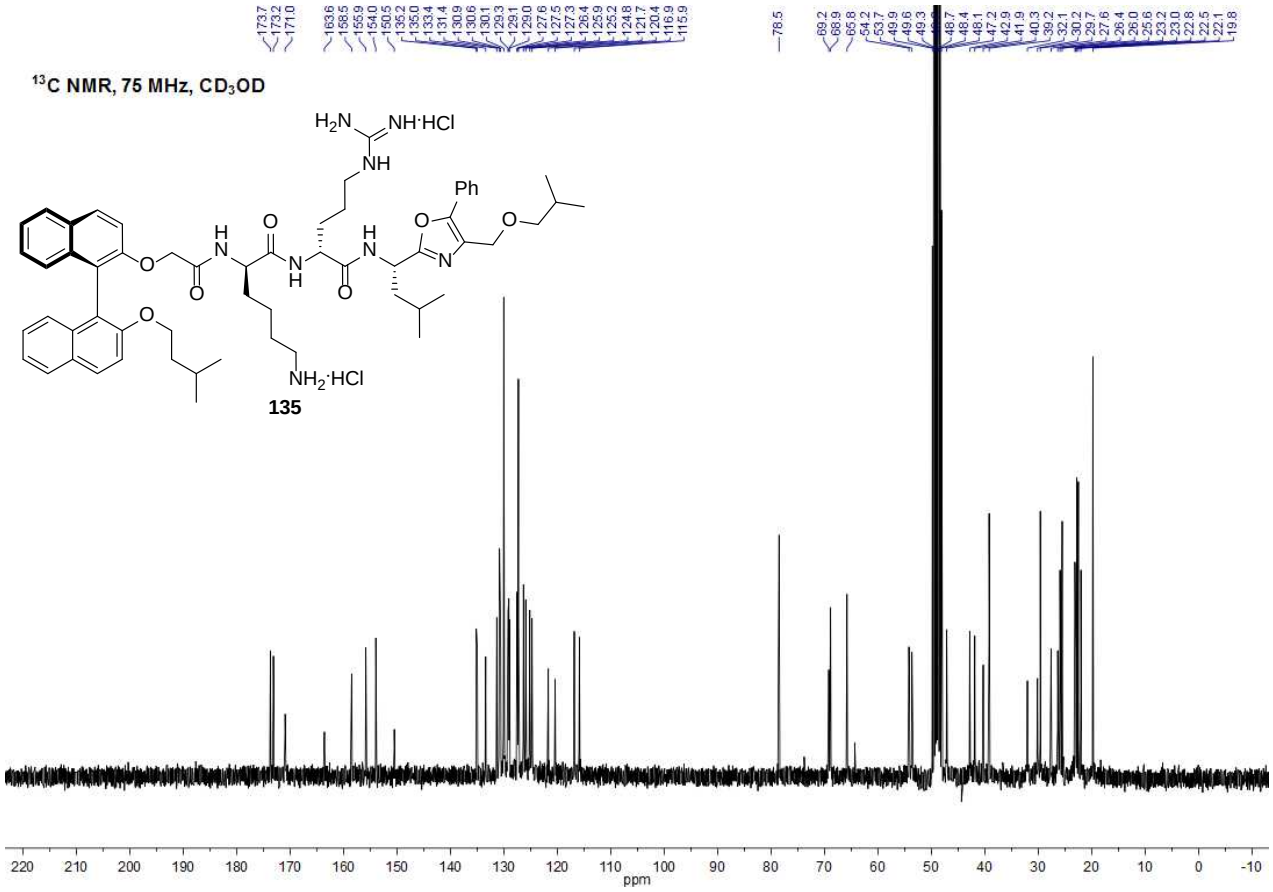

ks100915_ks5184_152_Proton_1scan
exp1 Proton
SAMPLE
date Sep 15 2010
solvent cd3od
file /nmrdata/kell~
er/fids/kittiya2/k~
s100915_ks5184_152~
_Proton_1scan.fid
ACQUISITION
sw 5707.8
at 2.045
np 23342
fb 4000
bs 32
d1 0.001
nt 1
ct 1
TRANSMITTER
tn H1
sfrq 498.746
tof -55.7
tpwr 63
pw 5.900
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 48
dmf 22200
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.800
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn 65536
DISPLAY
sp 98.5
wp 4545.2
rfl 2845.2
rfp 2433.8
rp 37.9
lp -40.5
PLOT
wc 250
sc 0
vs 773
th 12
ai cdc ph
H2N
NH·HCl
NH
N·HCl
NH2·HCl
133
9
8
7
6
5
4
3
2
1
ppm
2.22
3.27
3.44
2.59 2.93
2.11 2.49
1.55
5.18
2.01
2.80
2.01
2.76
3.00
2.82
10.63
7.54
8.35
6.00

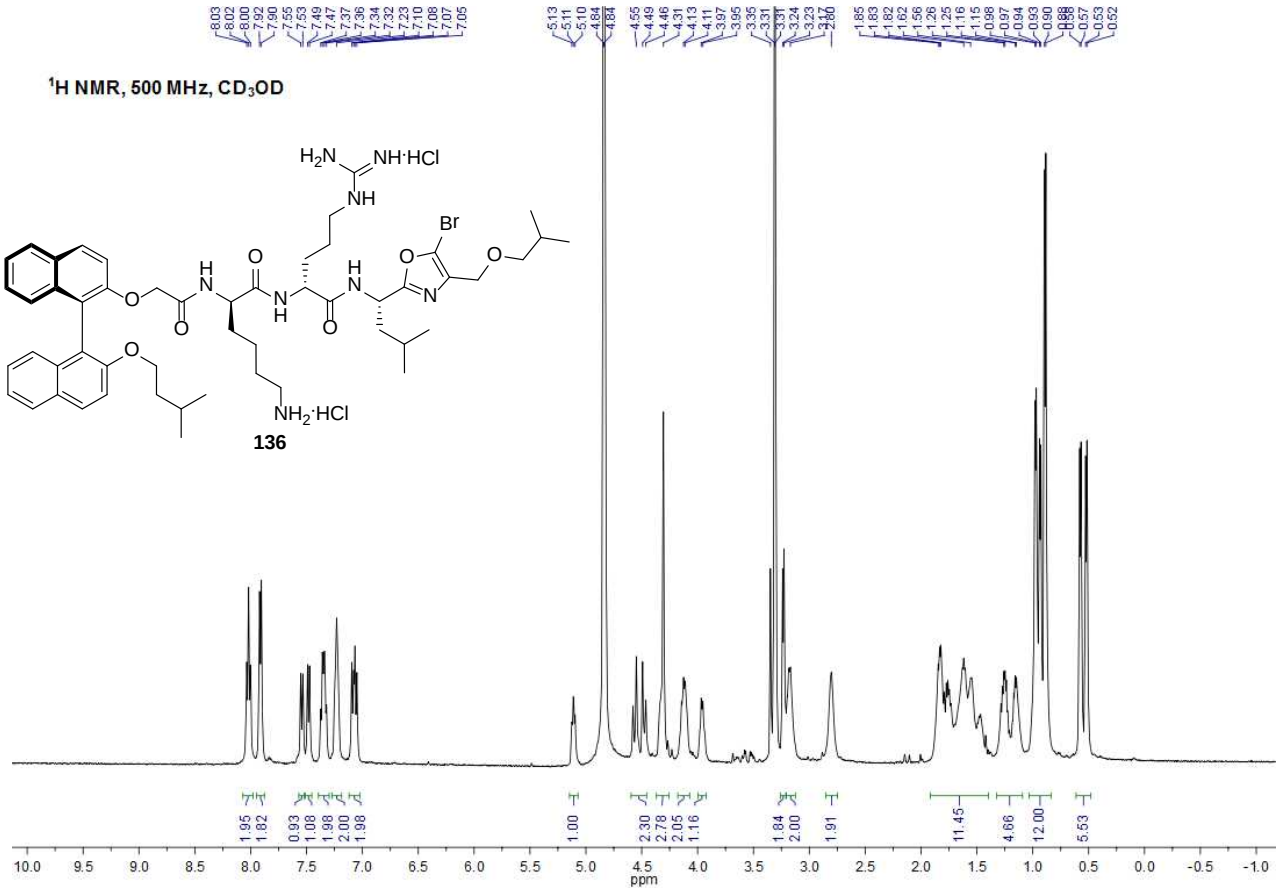

ks100916_ks5184_152_APT
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
File: ks100916_ks5184_152_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.815 sec
Width 18867.9 Hz
4995 repetitions
OBSERVE C13, 75.4244889 MHz
DECOUPLE H1, 299.9599523 MHz
Power 39 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 4 hr, 50 min, 46 sec
H2N
NH·HCl
NH
N·HCl
NH2·HCl
133
49.848
49.562
49.283
48.707
48.432
48.146
180
160
140
120
100
80
60
40
ppm

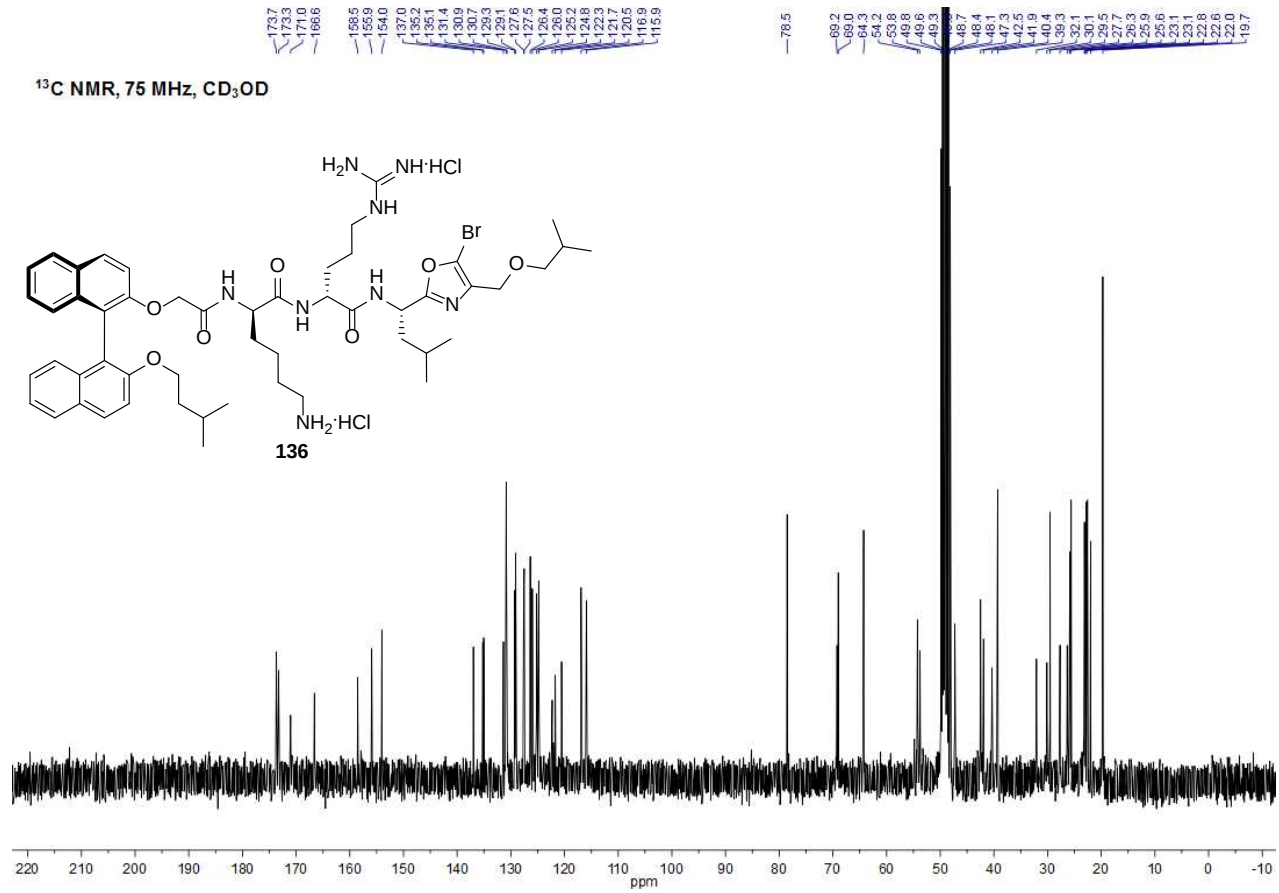

$^1$H NMR, 500 MHz, $CD_3OD$
134

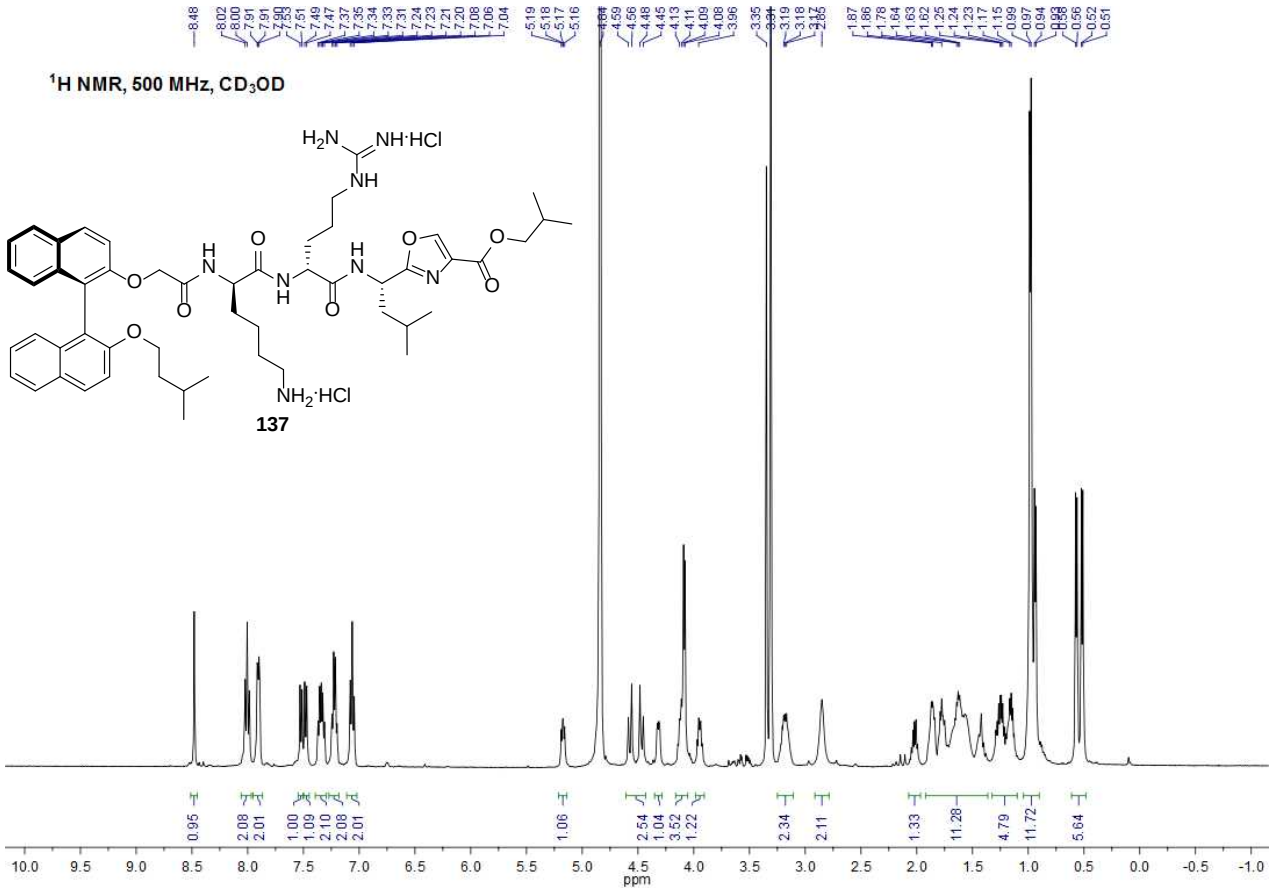

smw131101_2_011_CARBON
Sample Name:
Data Collected on:
bloch.sci.uow.edu.au-mercury300
Archive directory:
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Nov 1 2013
Temp. 25.0 C / 298.1 K
Operator: uowvnmrs
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.868 sec
Width 18867.9 Hz
26000 repetitions
OBSERVE C13, 75.4245070 MHz
DECOUPLE H1, 299.9599522 MHz
Power 35 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 32768
Total time 13 hr, 57 min
Agilent Technologies
134

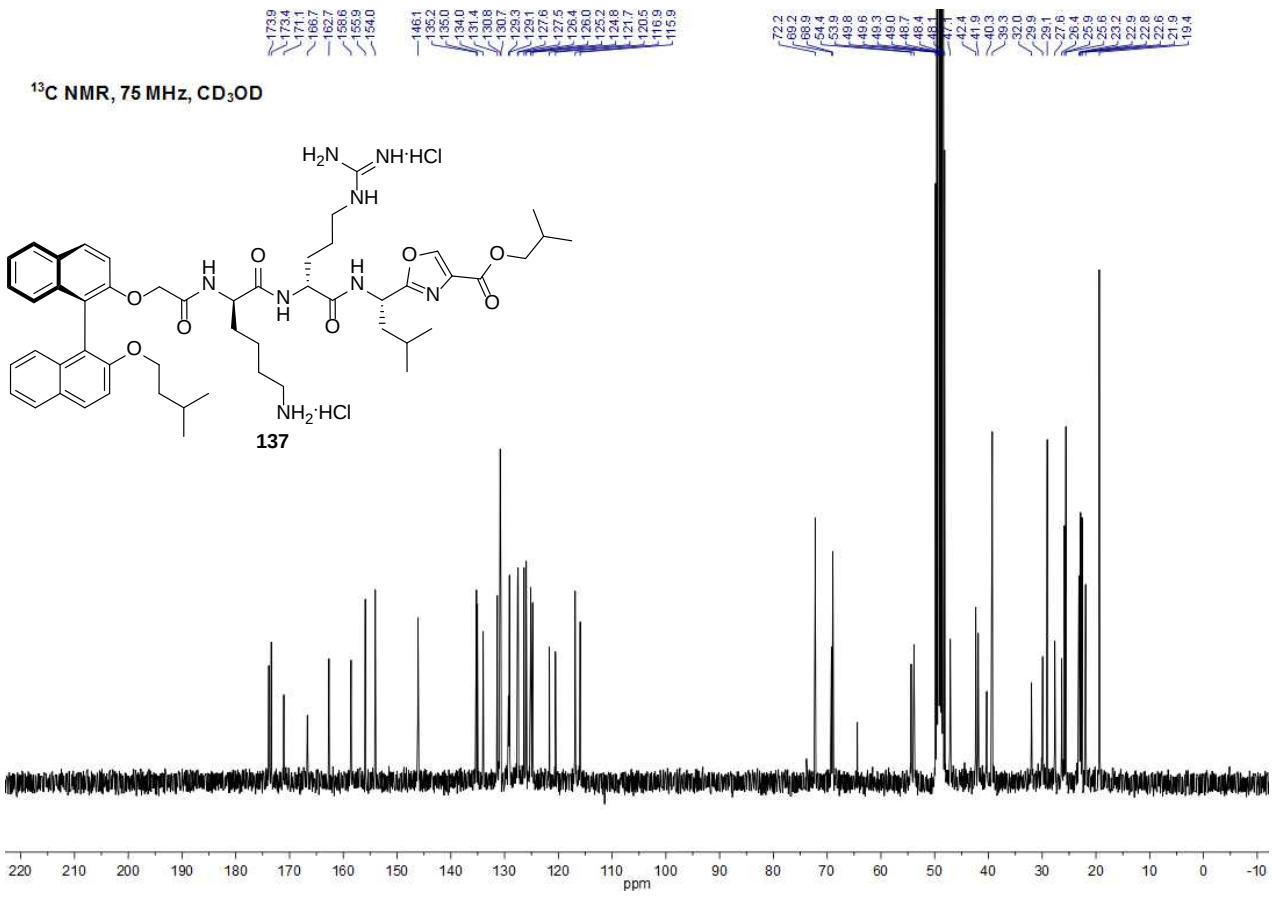

$^1$H NMR, 500 MHz, $CD_3OD$
135

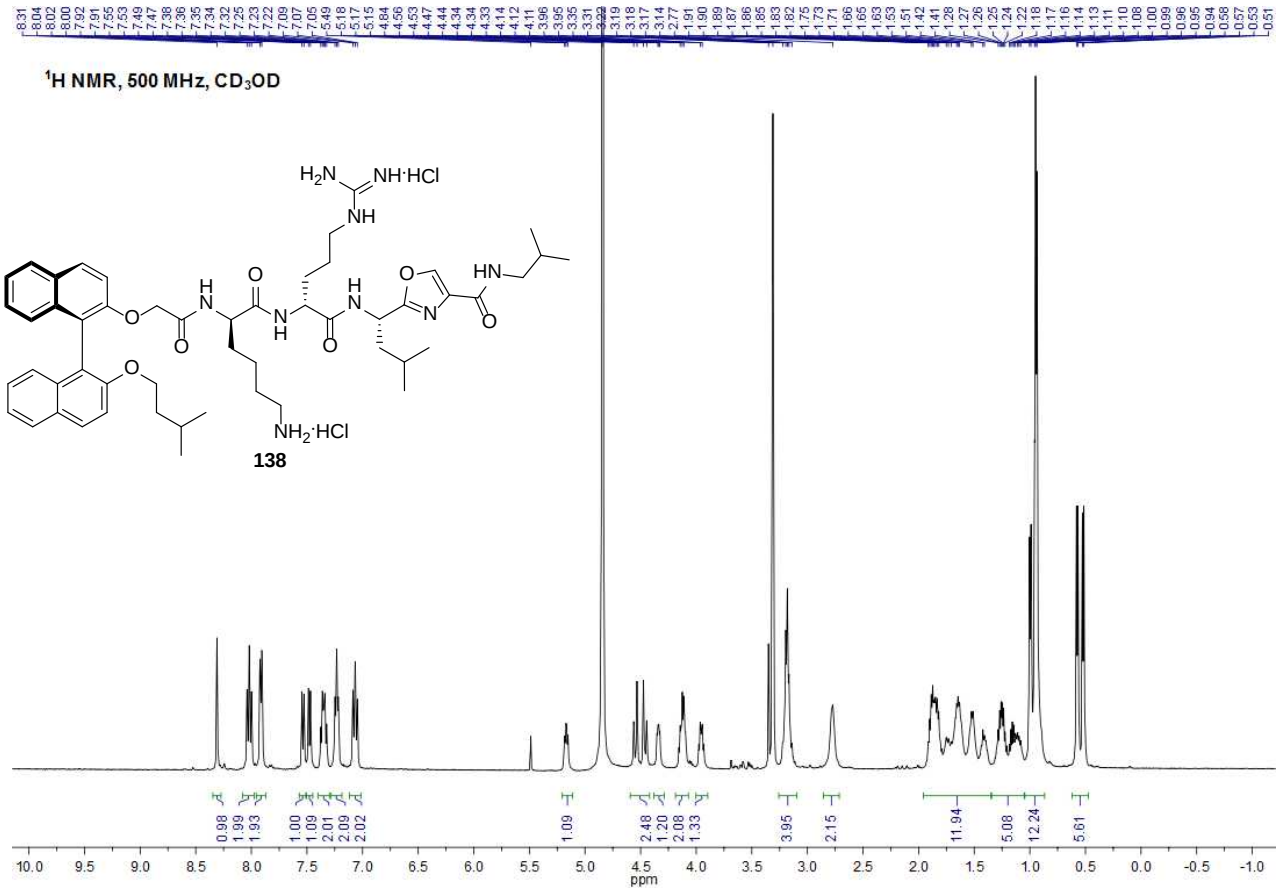

$^{13}$C NMR, 75 MHz, $CD_3OD$
135

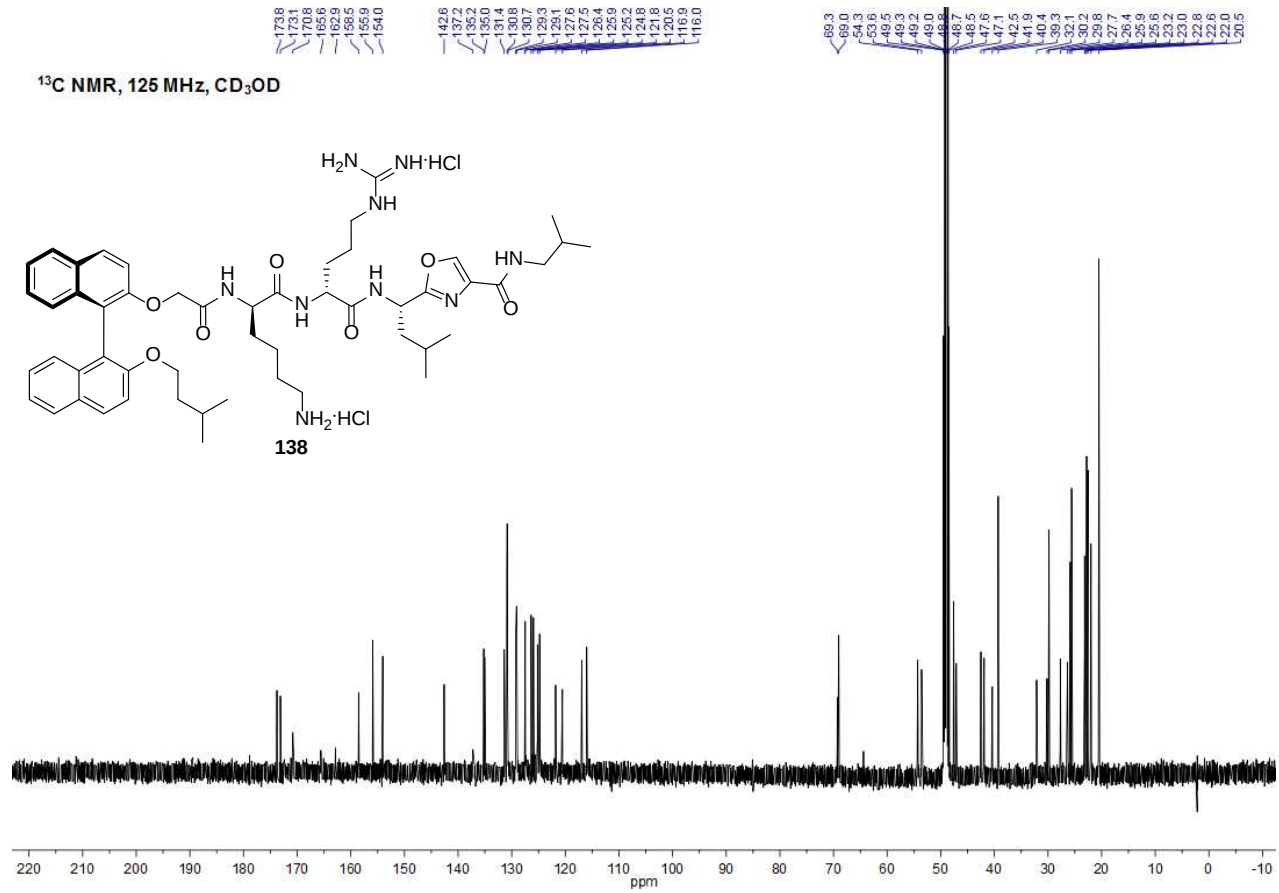

$^1$H NMR, 500 MHz, CD$_3$OD
136

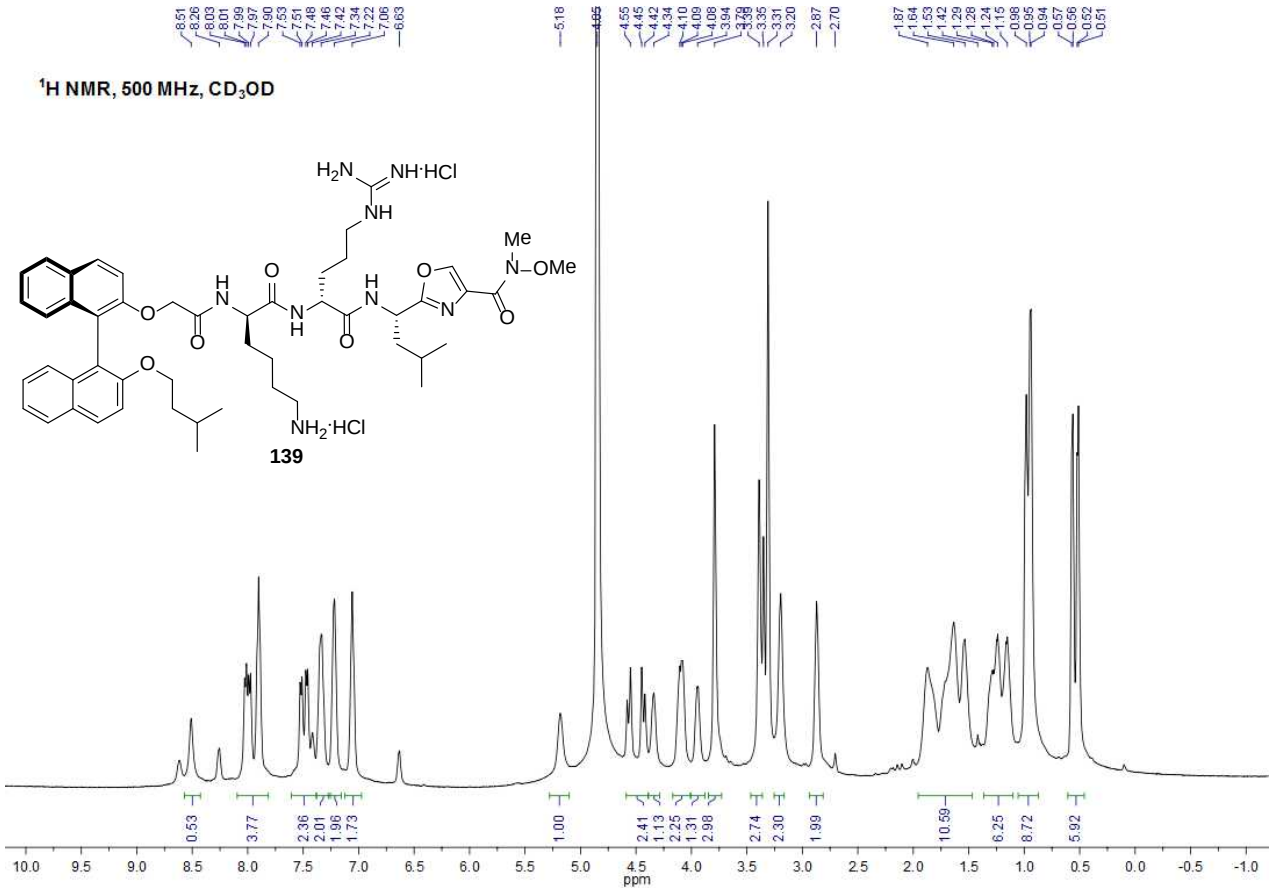

$^{13}$C NMR, 75 MHz, CD$_3$OD
136

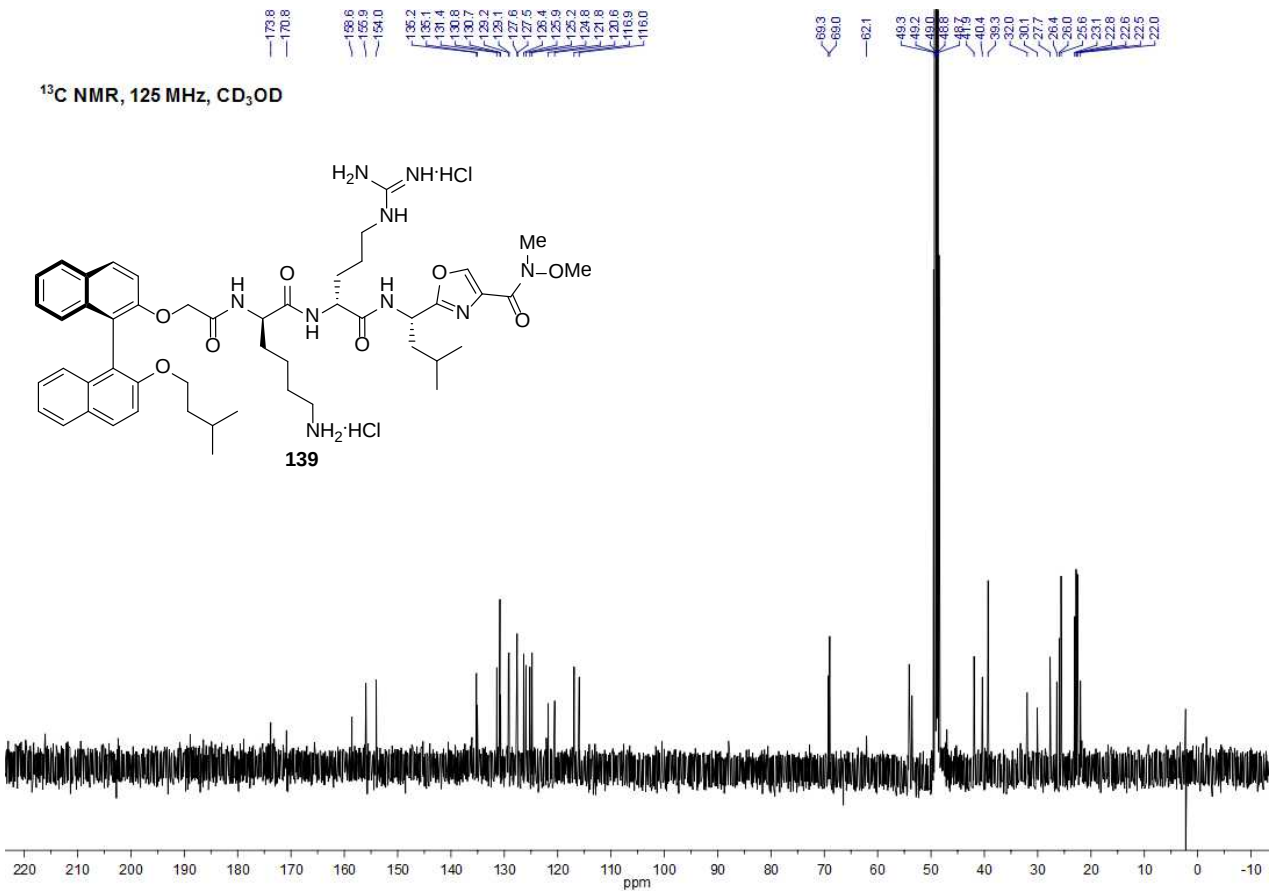

$^1$H NMR, 500 MHz, CD$_3$OD
137

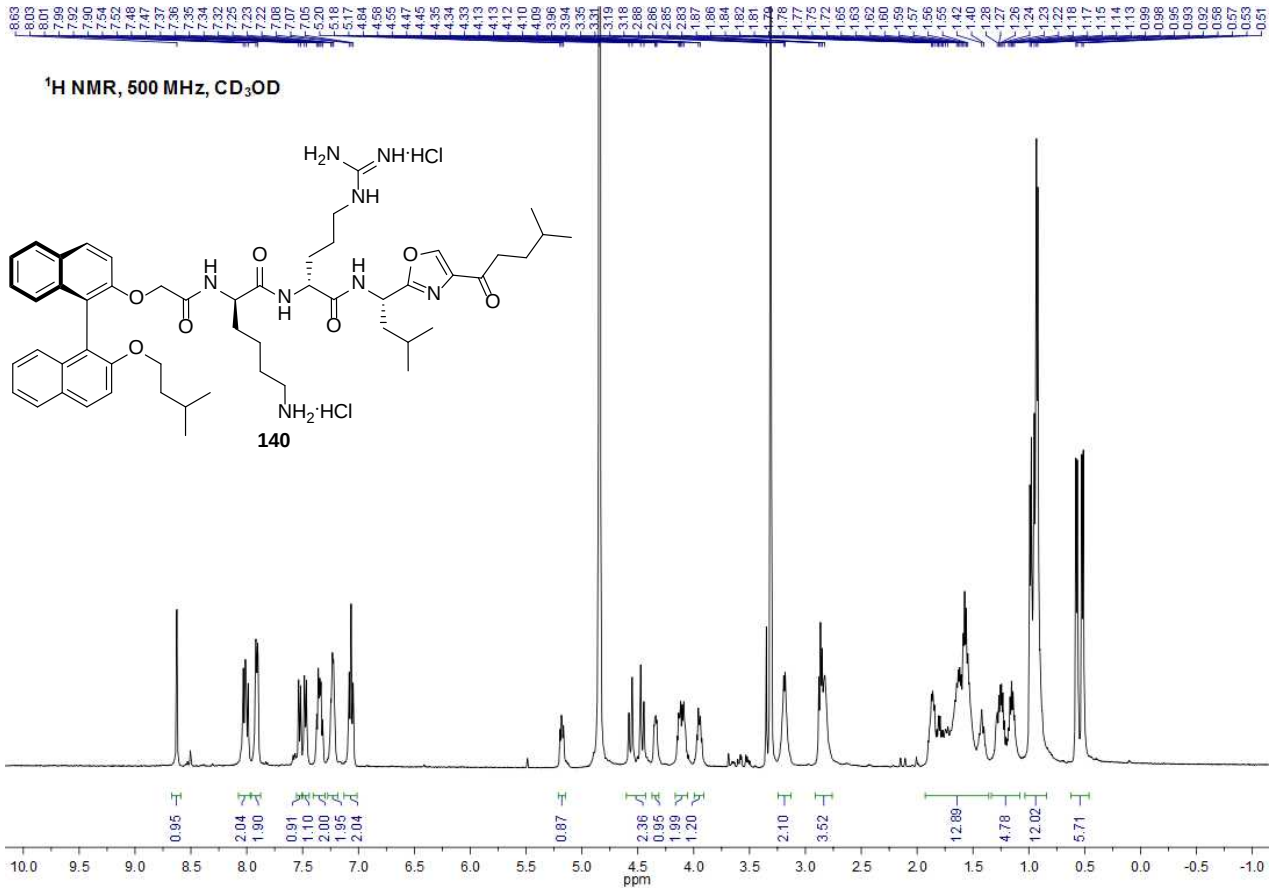

$^{13}$C NMR, 75 MHz, CD$_3$OD
137

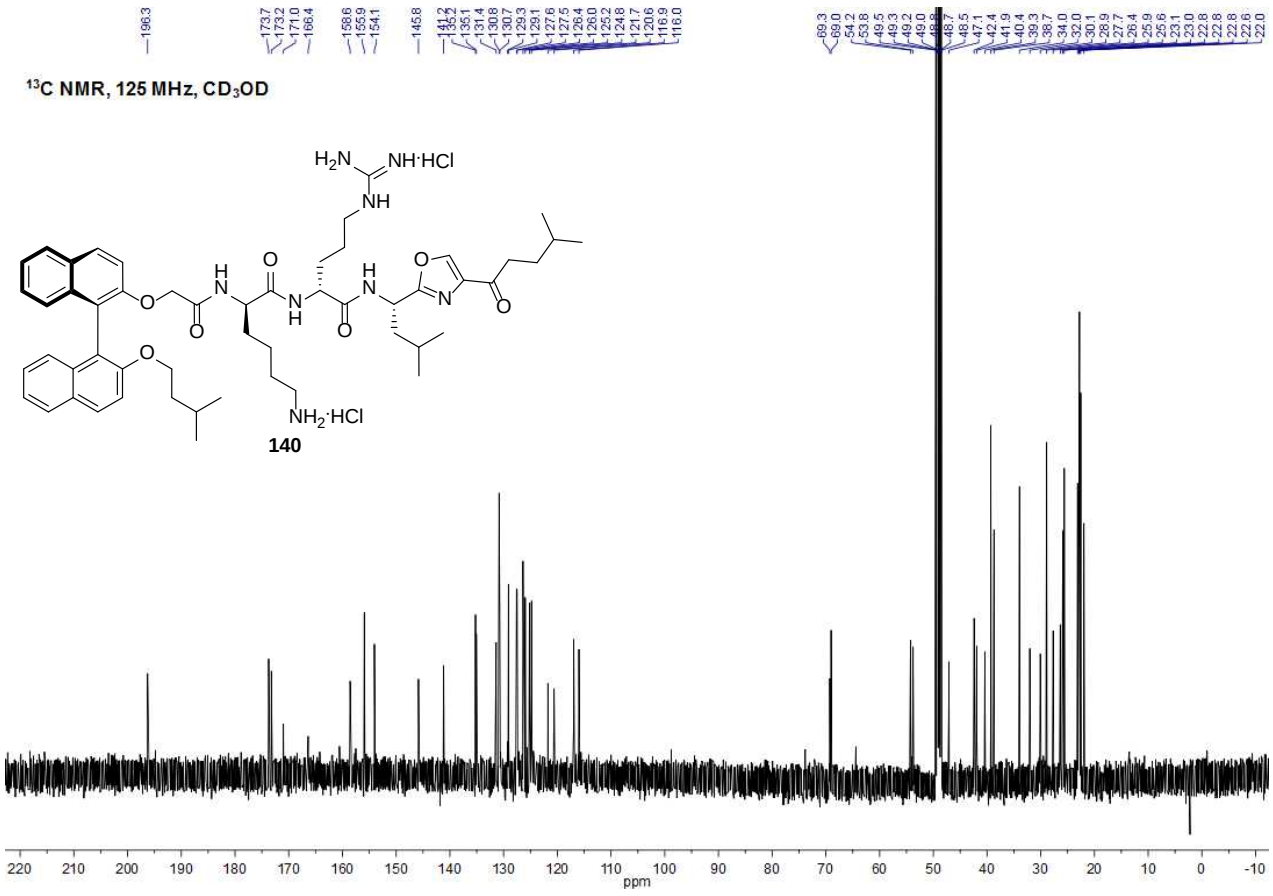

$^1$H NMR, 500 MHz, CD$_3$OD
138

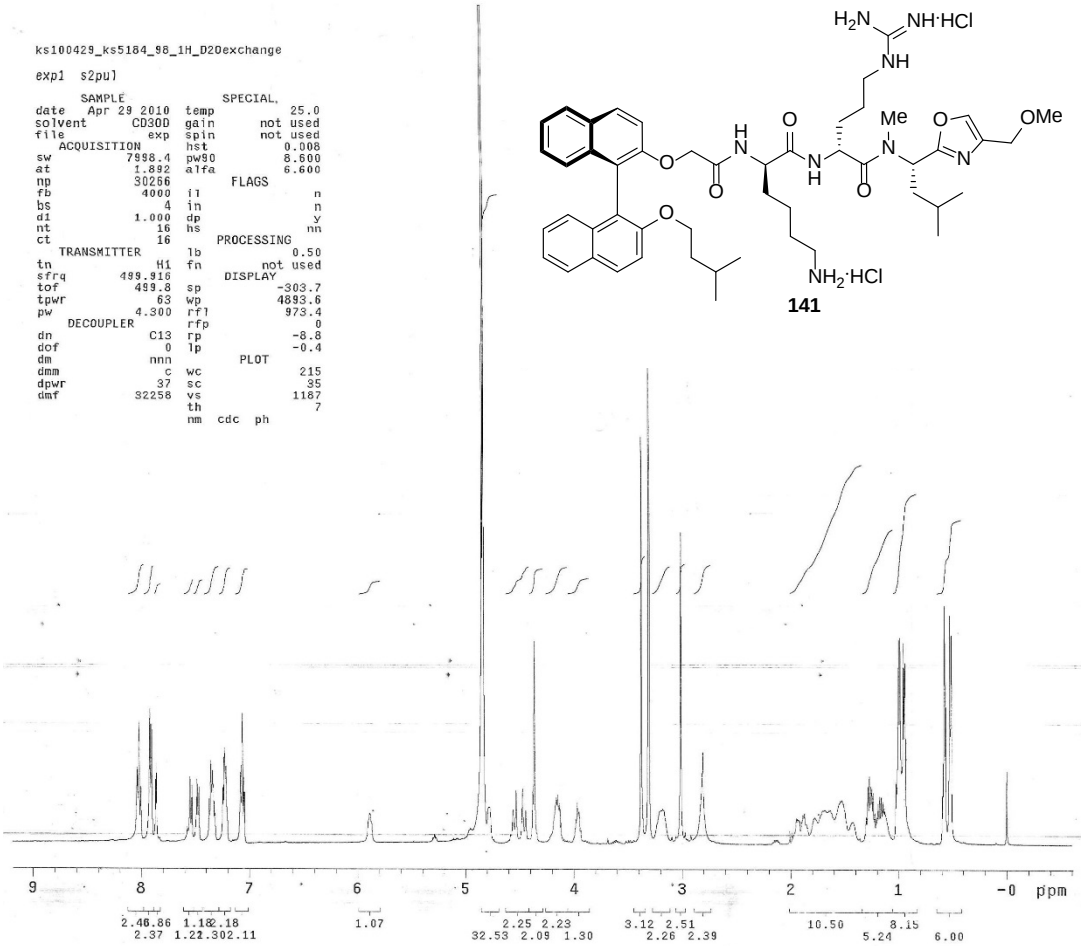

$^{13}$C NMR, 125 MHz, CD$_3$OD
138

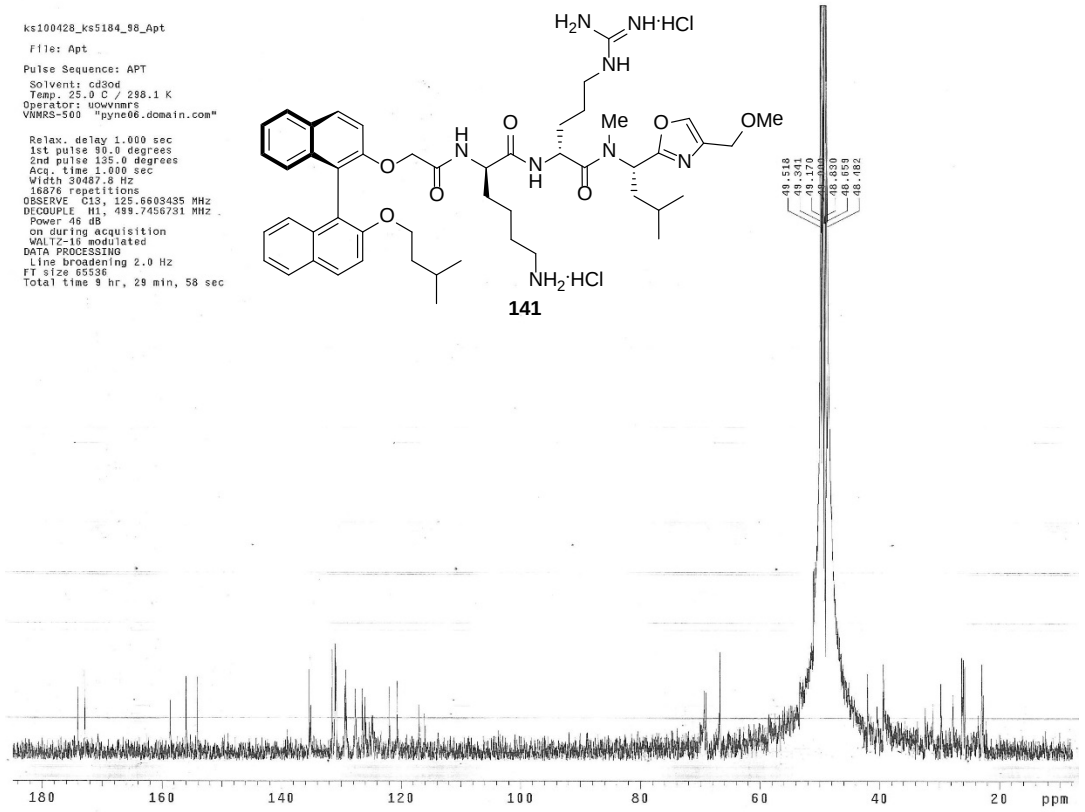

$^1$H NMR, 500 MHz, CD$_3$OD
139

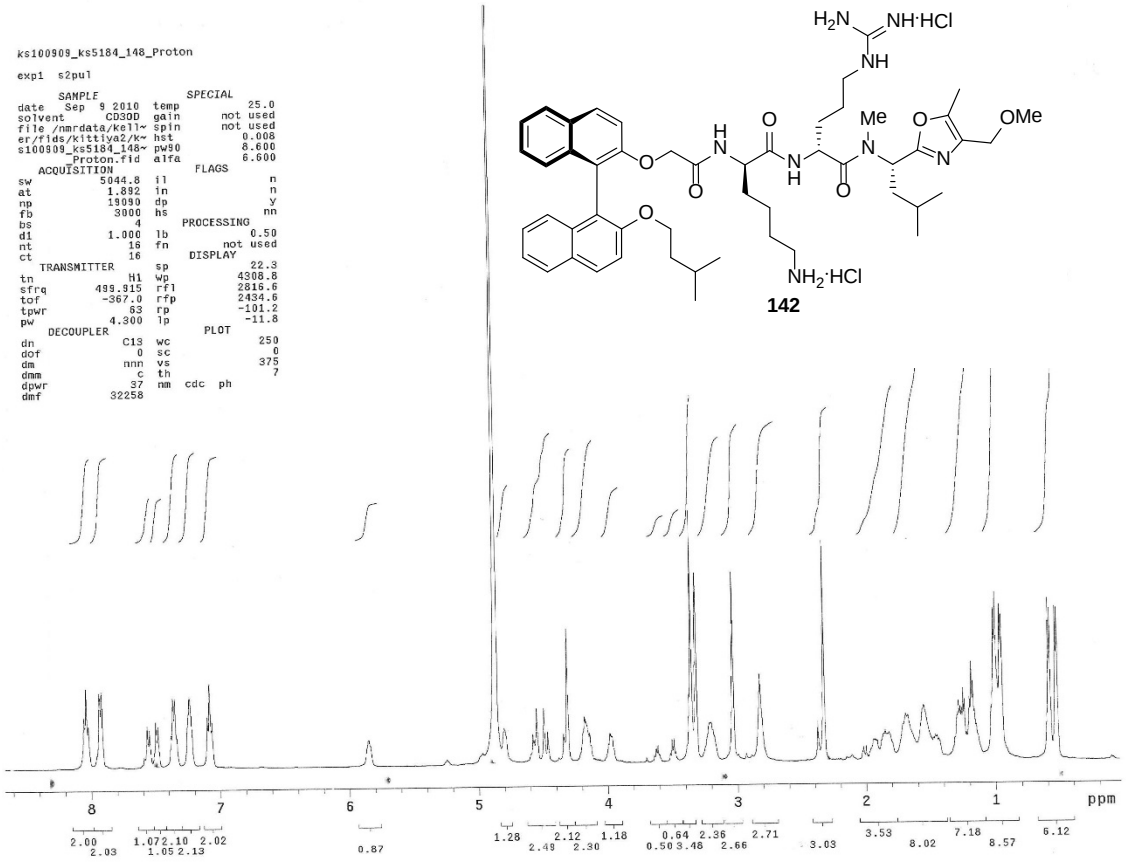

$^{13}$C NMR, 125 MHz, CD$_3$OD
139


$^1$H NMR, 500 MHz, CD$_3$OD
140


$^{13}$C NMR, 125 MHz, CD$_3$OD
140

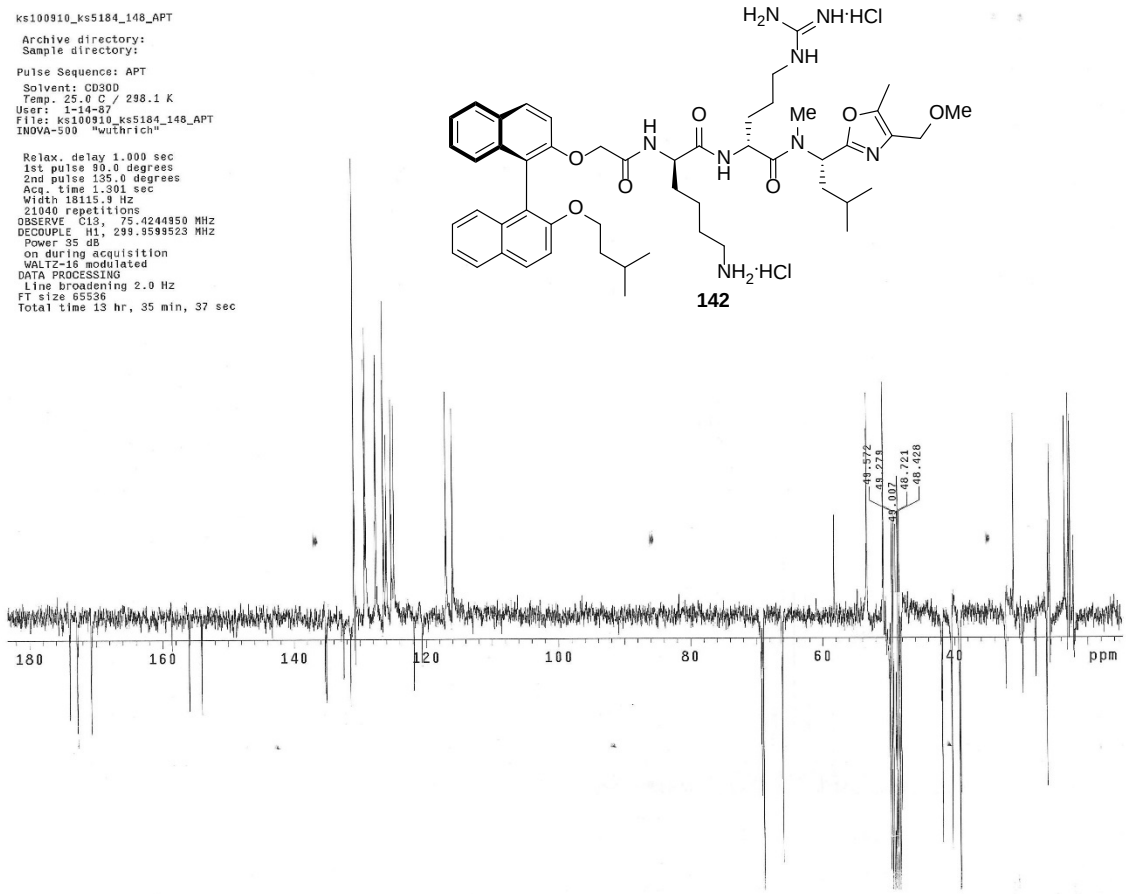

ks100429_ks5184_98_1H_D2Oexchange
exp1 s2pul
SAMPLE
date Apr 29 2010
solvent CD3OD
file exp
ACQUISITION
sw 7998.4
at 1.882
np 30256
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.916
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -303.7
wp 4893.6
rfl 973.4
rfp 0
rp -8.8
lp -0.4
PLOT
wc 215
sc 35
vs 1187
th 7
nm cdc ph
141
9 8 7 6 5 4 3 2 1 -0 ppm
2.46 0.86 1.18 2.18
2.37 1.22 1.30 2.11
1.07
2.25 2.23
32.53 2.09 1.30
3.12 2.51
2.26 2.39
10.50 8.15
5.24 6.00


ks100428_ks5184_98_Apt
File: Apt
Pulse Sequence: APT
Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: uowvnmrs
VNMRS-500 "pyne06.domain.com"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.000 sec
Width 30487.8 Hz
16876 repetitions
OBSERVE C13, 125.6603485 MHz
DECOUPLE H1, 499.7456731 MHz
Power 46 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 9 hr, 29 min, 58 sec
141
49.518
49.341
49.170
48.830
48.655
48.482
180 160 140 120 100 80 60 40 20 ppm


ks100909_ks5184_148_Proton
exp1 s2pul
SAMPLE
date Sep 9 2010
solvent CD3OD
file /nmrdata/kell~
er/fids/kittiya2/k~
s100909_ks5184_148~
Proton.fid
ACQUISITION
sw 5044.8
at 1.892
np 19090
fb 3000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.915
tof -367.0
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp 22.3
wp 4308.8
rfl 2816.6
rfp 2434.6
rp -101.2
lp -11.8
PLOT
wc 250
sc 0
vs 375
th 7
cdc ph
ppm
2.00 2.03 1.07 1.05 2.10 2.13 2.02 0.87 1.28 2.49 2.12 2.30 1.18 0.64 0.50 2.36 3.48 2.71 2.66 3.03 3.53 8.02 7.18 8.57 6.12

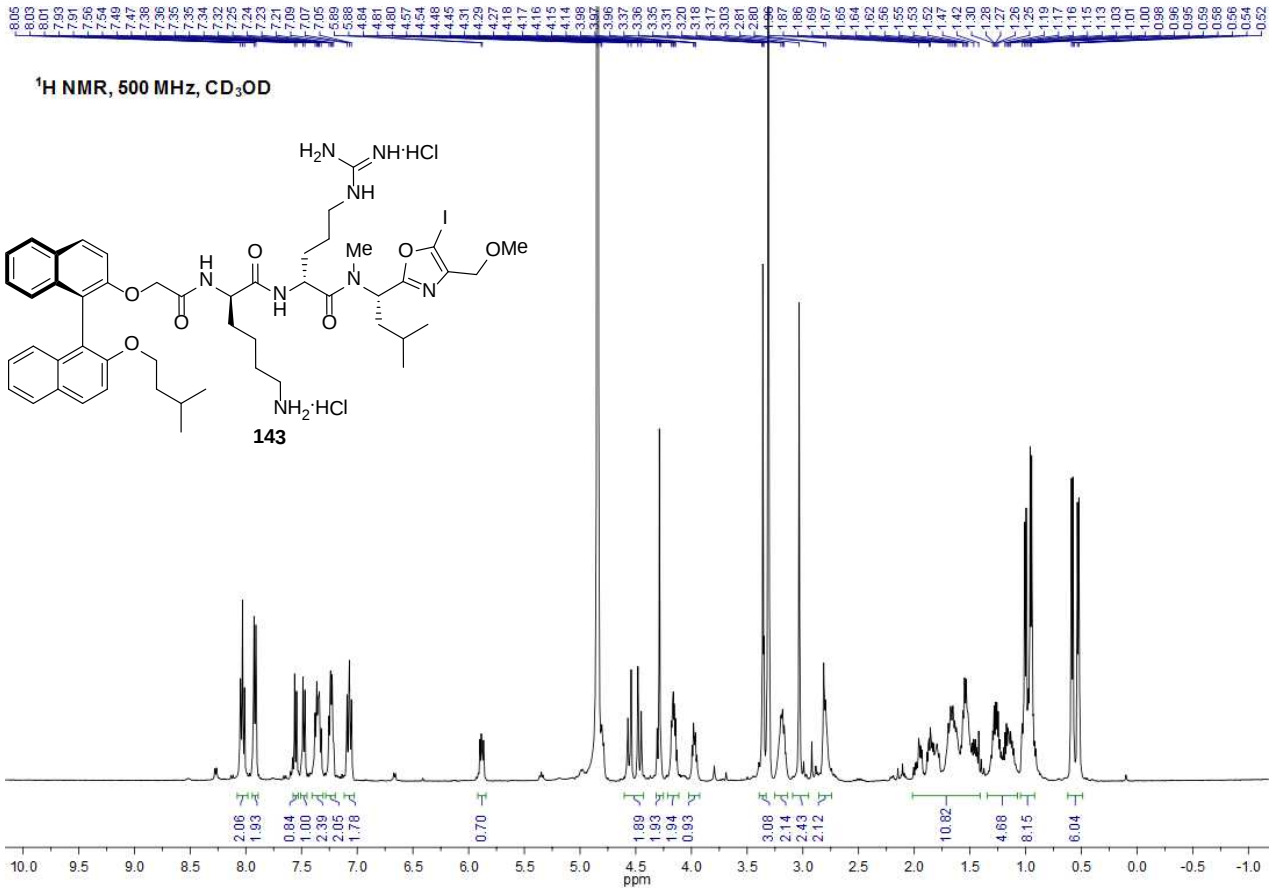


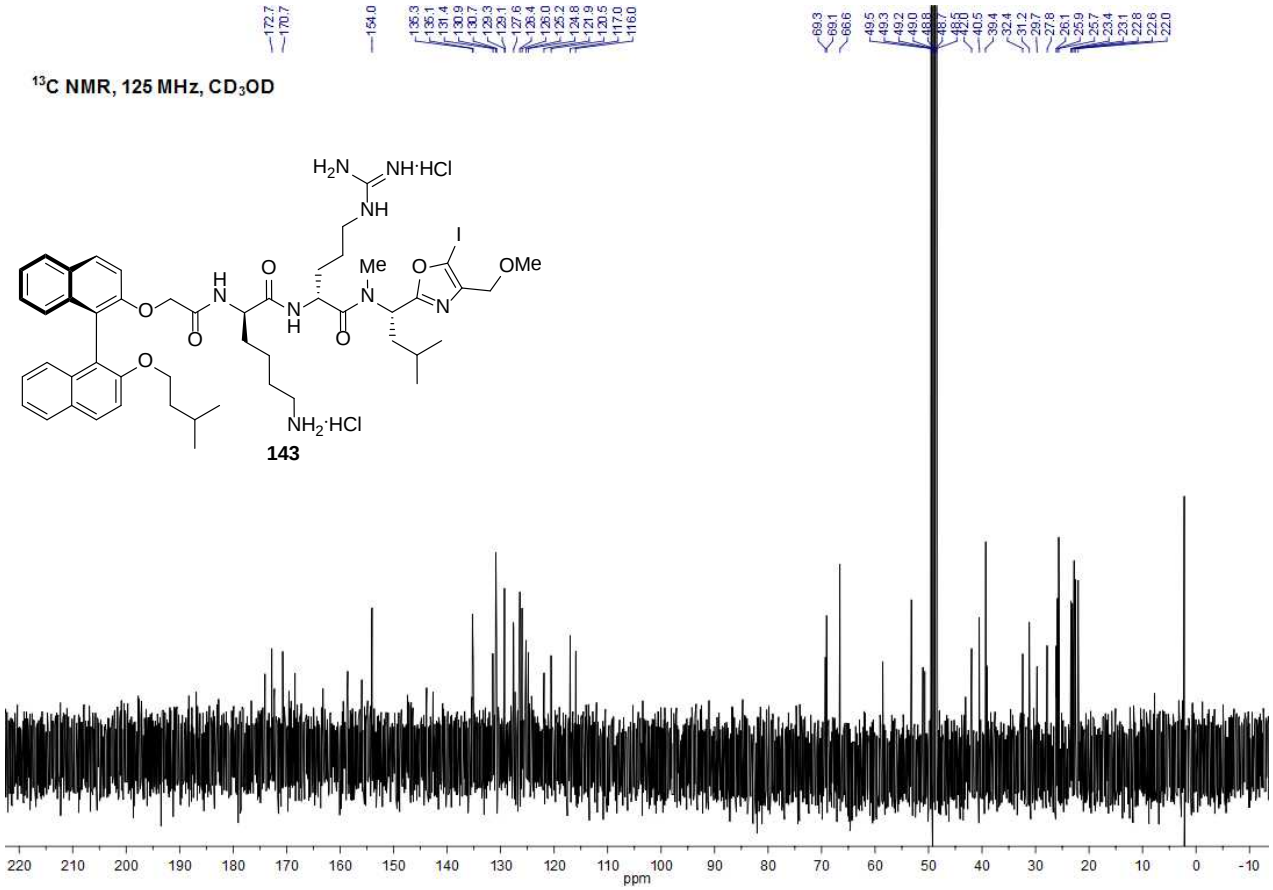
**142**

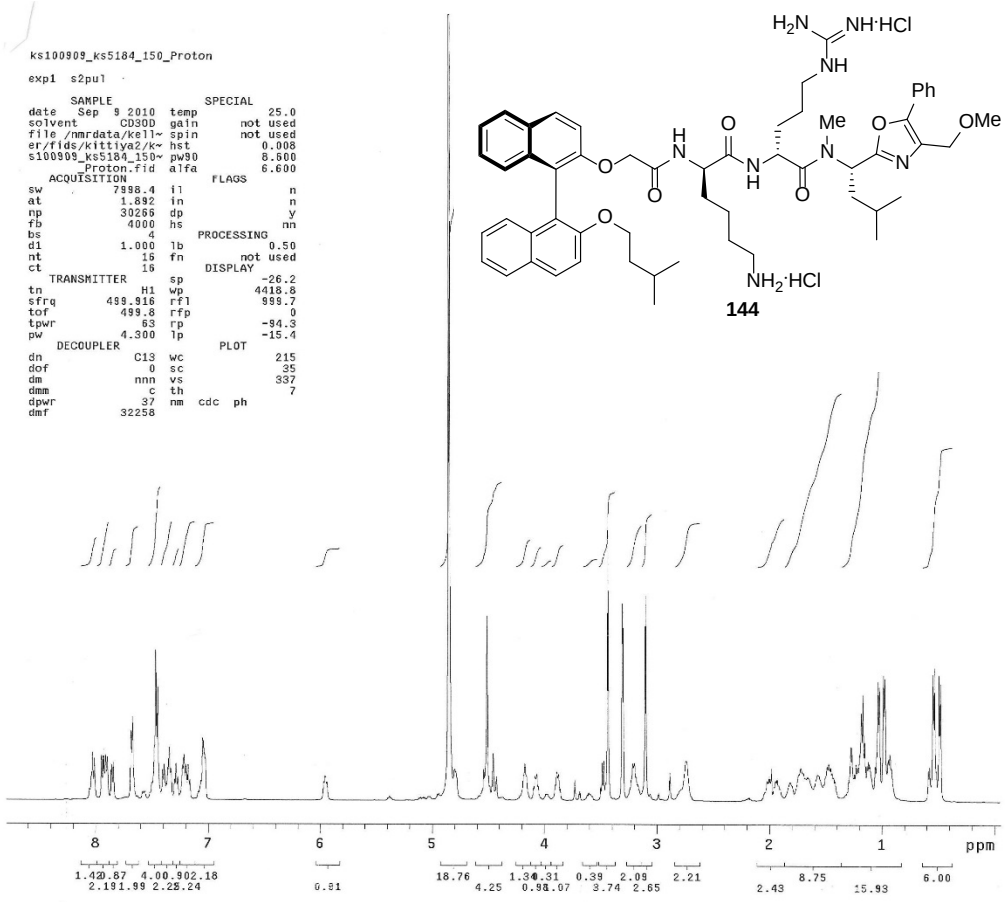

ks100910_ks5184_148_APT
Archive directory:
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100910_ks5184_148_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.301 sec
Width 18115.9 Hz
21040 repetitions
OBSERVE C13, 75.4244950 MHz
DECOUPLE H1, 299.9599523 MHz
Power 35 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 13 hr, 35 min, 37 sec
49.572
48.278
48.007
48.721
48.428
ppm

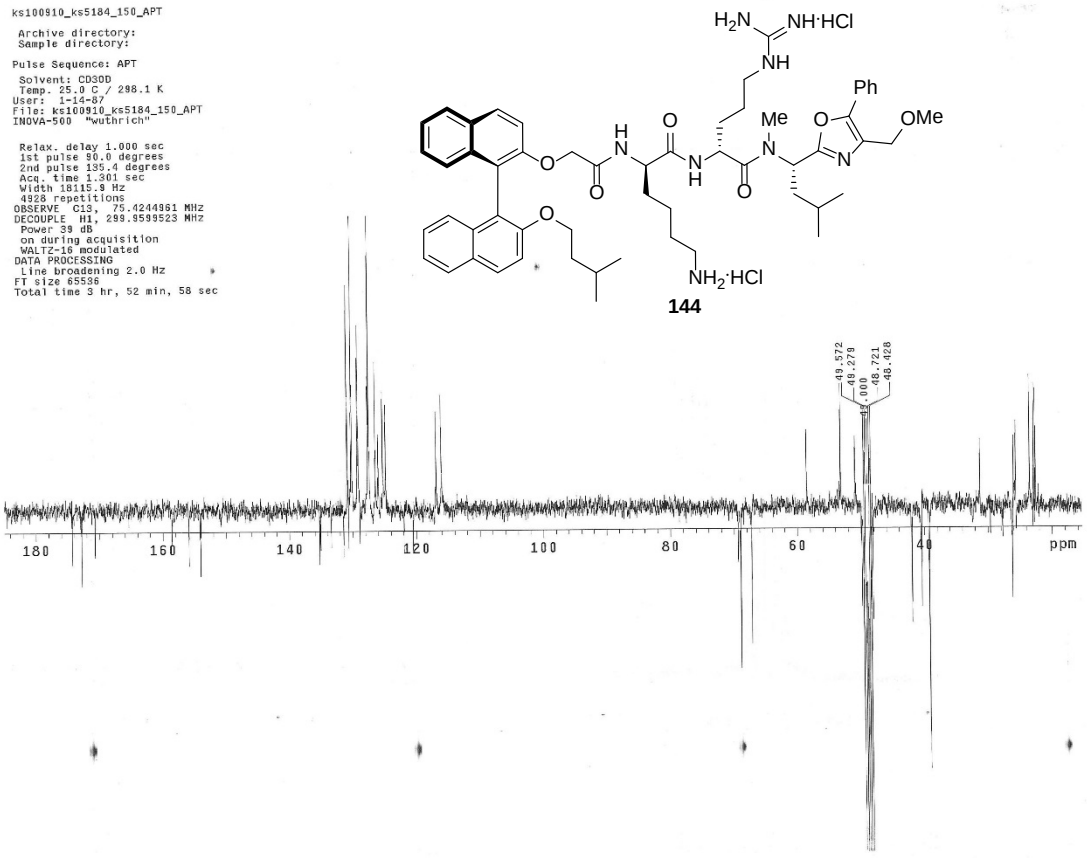


**142**


$^1$H NMR, 500 MHz, $CD_3OD$
143

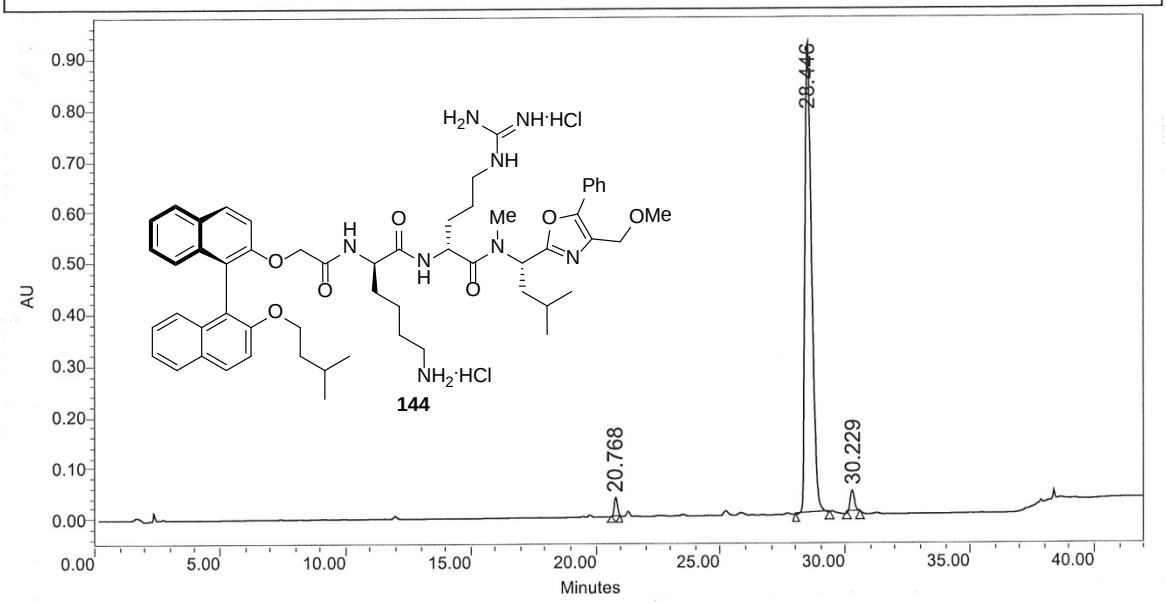

$^{13}$C NMR, 125 MHz, $CD_3OD$
143


ks100909_ks5184_150_Proton
exp1 s2pul
SAMPLE
date Sep 9 2010
solvent CD3OD
file /nmrdata/kell~
er/fids/kittiya2/k~
s100909_ks5184_150~
Proton.fid
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.916
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -26.2
wp 4418.8
rfl 999.7
rfp 0
rp -94.3
lp -15.4
PLOT
wc 215
sc 35
vs 337
th 7
nm cdc ph
144
ppm


ks100910_ks5184_150_APT
Archive directory:
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100910_ks5184_150_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.4 degrees
Acq. time 1.301 sec
Width 18115.9 Hz
4928 repetitions
OBSERVE C13, 75.4244861 MHz
DECOUPLE H1, 299.9599523 MHz
Power 39 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 3 hr, 52 min, 58 sec
144
ppm

## SAMPLE INFORMATION

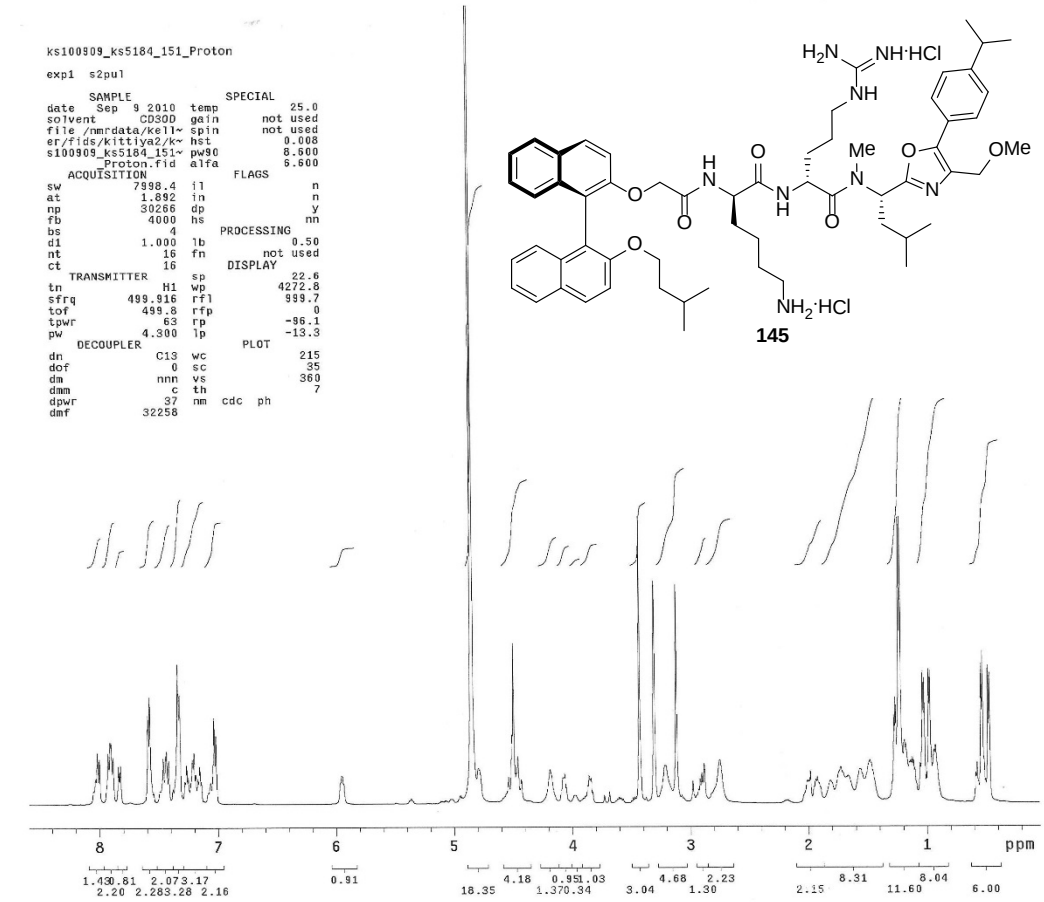
| | | | |
|---|---|---|---|
| Sample Name: | ks5184_150 | Acquired By: | Kittiya |
| Sample Type: | Unknown | Date Acquired: | 16/09/2010 3:13:58 PM |
| Vial: | 1 | Acq. Method: | ks ether2 |
| Injection #: | 3 | Date Processed: | 20/09/2010 12:00:04 PM |
| Injection Volume: | 20.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 42.00 Minutes | Channel Desc.: | 254 nm |
| | | Sample Set Name: | |

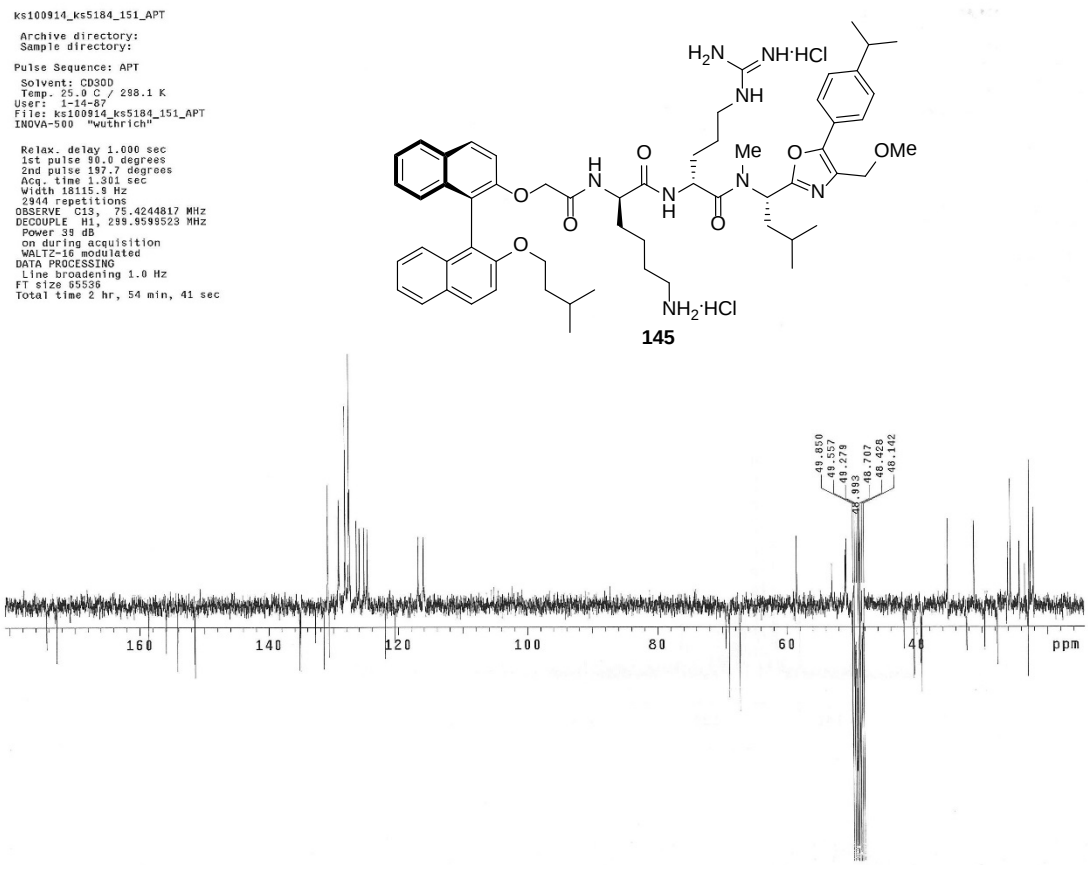



| | RT (min) | Area ( V*sec) | % Area | Height ( V) | % Height |
|---|---|---|---|---|---|
| 1 | 20.768 | 317585 | 1.74 | 36008 | 3.60 |
| 2 | 28.446 | 17429144 | 95.28 | 921781 | 92.07 |
| 3 | 30.229 | 545354 | 2.98 | 43429 | 4.34 |

| | Time | Flow | %A | %B | Curve |
|---|---|---|---|---|---|
| 1 | 0.01 | 1.00 | 85.0 | 15.0 | 6 |
| 2 | 2.00 | 1.00 | 85.0 | 15.0 | 1 |
| 3 | 35.00 | 1.00 | 40.0 | 60.0 | 6 |
| 4 | 36.00 | 1.00 | 40.0 | 60.0 | 1 |
| 5 | 37.00 | 1.00 | 0.0 | 100.0 | 1 |
| 6 | 42.00 | 1.00 | 0.0 | 100.0 | 1 |
| 7 | 43.00 | 0.00 | 0.0 | 100.0 | 1 |

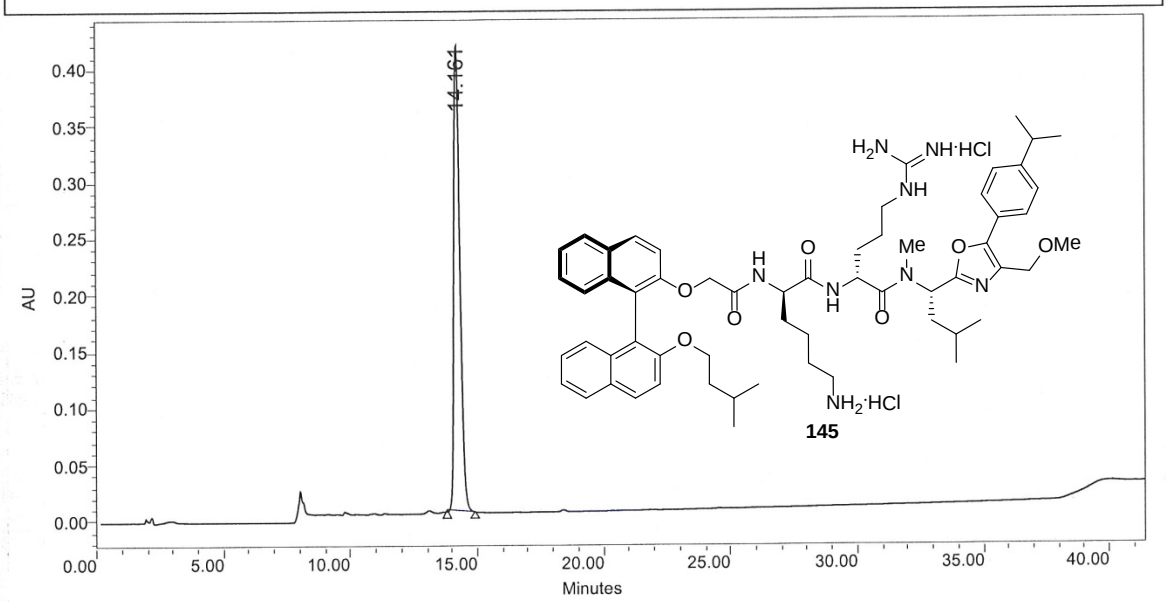
A = $H_2O$ + 0.1% TFA + 10% MeCN
B = MeCN + 0.1% TFA


ks100909_ks5184_151_Proton
exp1 s2pul
SAMPLE
date Sep 9 2010
solvent CD3OD
file /nmrdata/kell~
er/fids/kittiya2/k~
s100909_ks5184_151~
_Proton.fid
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.916
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp 22.6
wp 4272.8
rfl 999.7
rfp 0
rp -96.1
lp -13.3
PLOT
wc 215
sc 35
vs 360
th 7
cdc ph
145
8
7
6
5
4
3
2
1
ppm
1.43 0.81 2.07 3.17
2.20 2.28 3.28 2.16
0.91
18.35
4.18 0.95 1.03
1.37 0.34
3.04
4.68 2.23
1.30
2.15
8.31
11.60
8.04
6.00


ks100914_ks5184_151_APT
Archive directory:
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100914_ks5184_151_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 197.7 degrees
Acq. time 1.301 sec
Width 18115.8 Hz
2944 repetitions
OBSERVE C13, 75.4244817 MHz
DECOUPLE H1, 299.9599523 MHz
Power 39 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 2 hr, 54 min, 41 sec
145
49.850
49.557
49.279
48.993
48.707
48.428
48.142
160
140
120
100
80
60
40
ppm

## SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | ks5184_151 | Acquired By: | Kittiya |
| Sample Type: | Unknown | Date Acquired: | 27/09/2010 2:45:24 PM |
| Vial: | 1 | Acq. Method: | ks8 |
| Injection #: | 7 | Date Processed: | 27/09/2010 3:28:32 PM |
| Injection Volume: | 20.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 100.00 Minutes | Channel Desc.: | 254 nm |
| | | Sample Set Name: | |



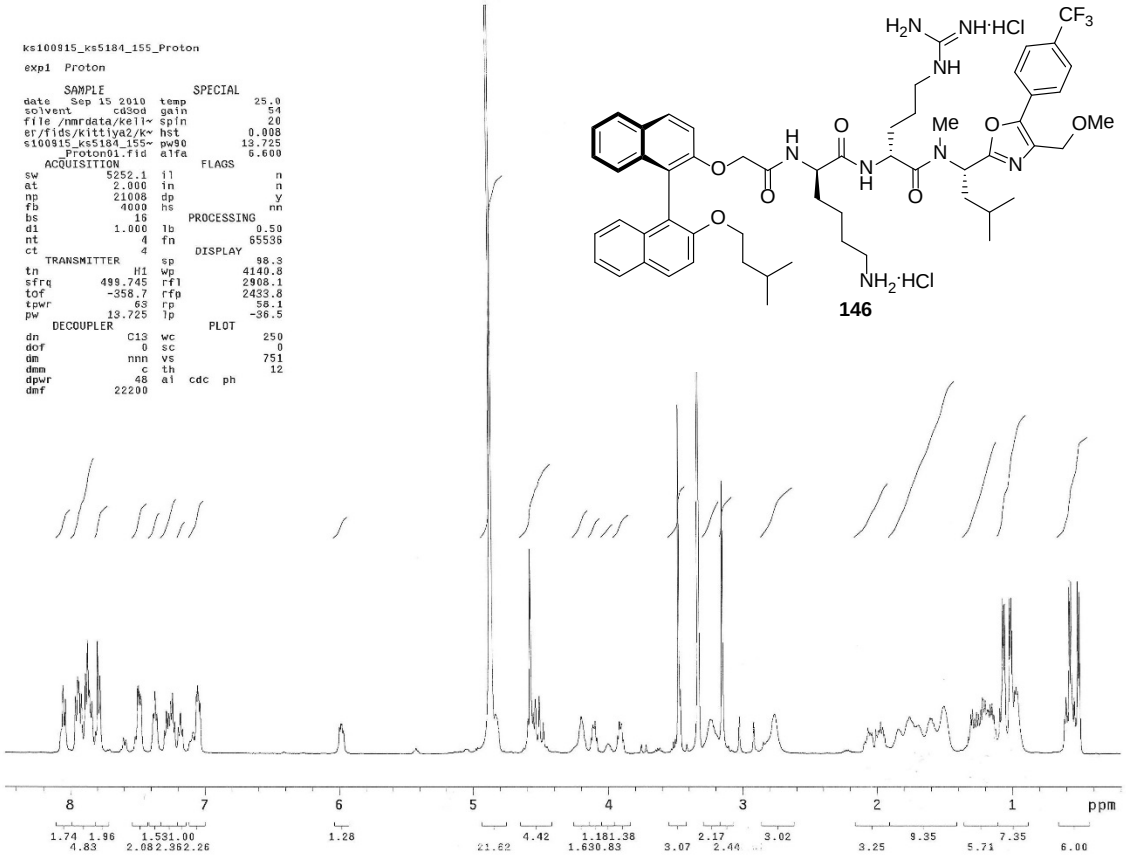

**145**

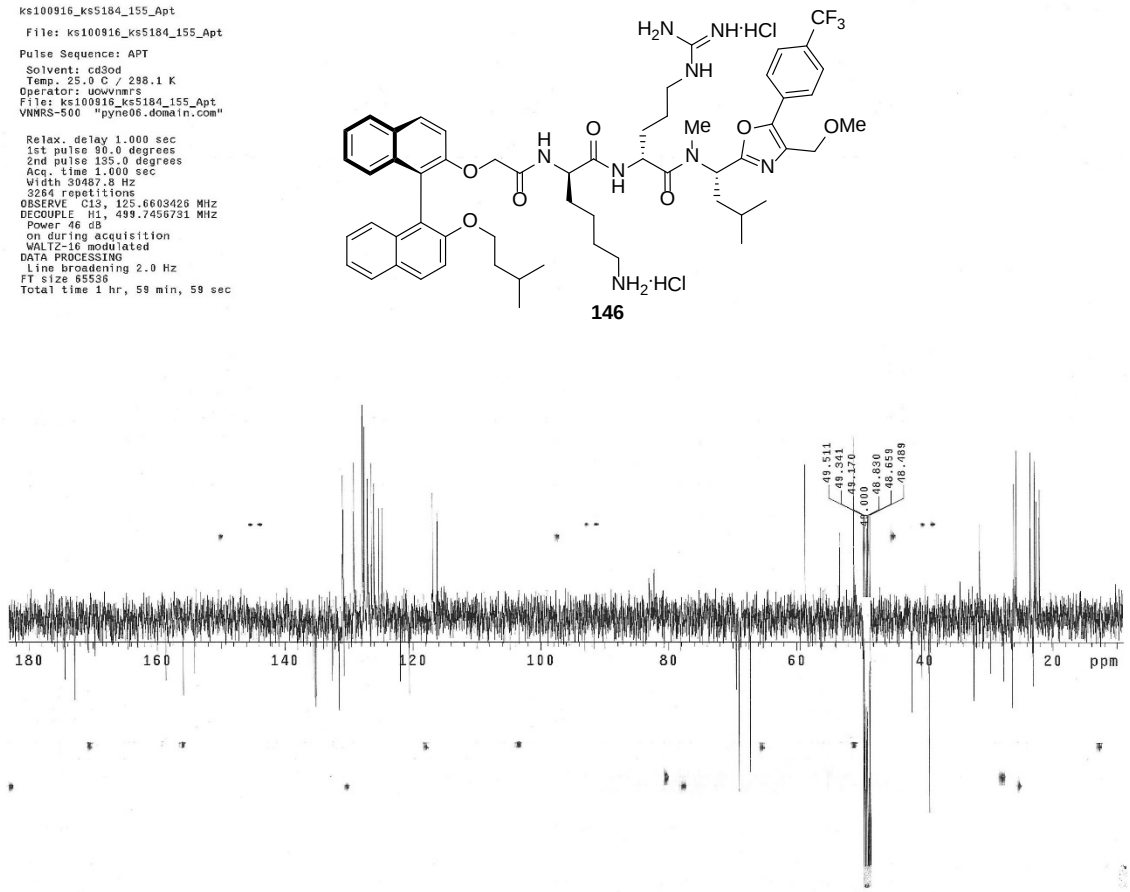
| | RT (min) | Area ( V*sec) | % Area | Height ( V) | % Height |
|---|---|---|---|---|---|
| 1 | 14.161 | 7005802 | 100.00 | 413058 | 100.00 |

KS8

| | Time | Flow | %A | %B | Curve |
|---|---|---|---|---|---|
| 1 | 0.01 | 1.00 | 100.0 | 0.0 | 6 |
| 2 | 5.00 | 1.00 | 100.0 | 0.0 | 1 |
| 3 | 6.00 | 1.00 | 50.0 | 50.0 | 6 |
| 4 | 36.00 | 1.00 | 20.0 | 80.0 | 6 |
| 5 | 37.00 | 1.00 | 0.0 | 100.0 | 6 |
| 6 | 42.00 | 1.00 | 0.0 | 100.0 | 1 |
| 7 | 42.01 | 0.00 | 0.0 | 100.0 | 1 |

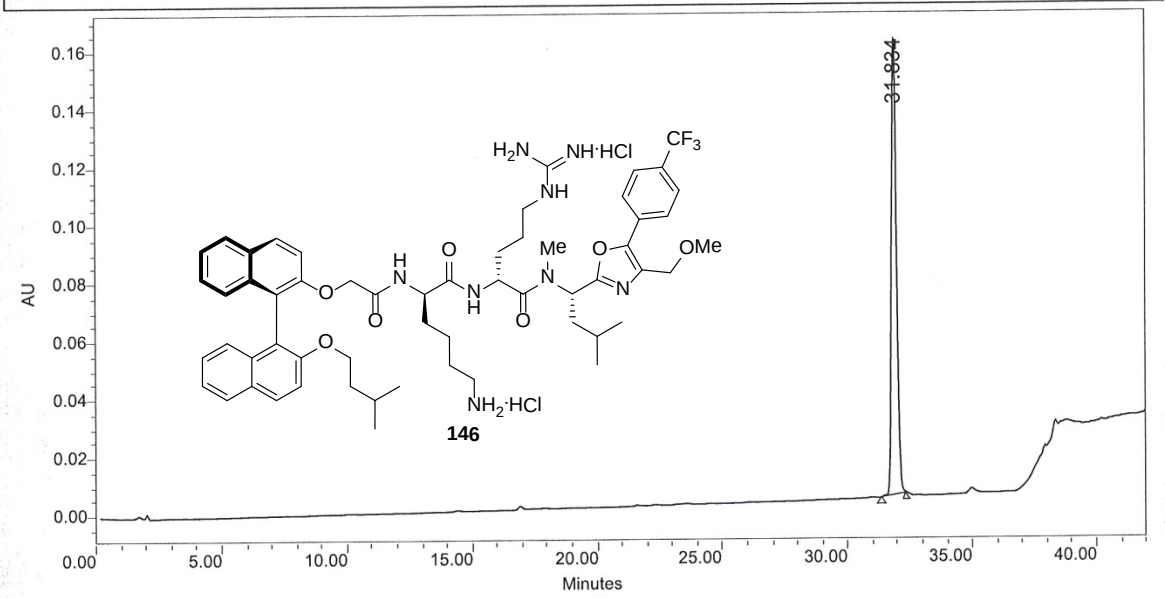
A = $H_2O$ + 0.1% TFA + 10% MeCN
B = MeCN + 0.1% TFA


ks100915_ks5184_155_Proton
exp1 Proton
SAMPLE
date Sep 15 2010
solvent cd3od
file /nmrdata/kell~
er/fids/kittiya2/k~
s100915_ks5184_155~
_Proton01.fid
ACQUISITION
sw 5252.1
at 2.000
np 21008
fb 4000
bs 16
d1 1.000
nt 4
ct 4
TRANSMITTER
tn H1
sfrq 499.745
tof -358.7
tpwr 63
pw 13.725
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 48
dmf 22200
SPECIAL
temp 25.0
gain 54
spin 20
hst 0.008
pw90 13.725
alfa 9.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn 65536
DISPLAY
sp 98.3
wp 4140.8
rfl 2908.1
rfp 2433.8
rp 58.1
lp -36.5
PLOT
wc 250
sc 0
vs 751
th 12
al cdc ph
146
8
7
6
5
4
3
2
1
ppm
1.74 1.96 1.531.00 1.28 21.82 4.42 1.181.38 2.17 3.02 9.35 7.35
4.83 2.082.362.26 1.630.83 3.07 2.44 3.25 5.71 6.00


ks100916_ks5184_155_Apt
File: ks100916_ks5184_155_Apt
Pulse Sequence: APT
Solvent: cd3od
Temp. 25.0 C / 298.1 K
Operator: uowvnmrs
File: ks100916_ks5184_155_Apt
VNMRS-500 "pyne06.domain.com"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.000 sec
Width 30487.8 Hz
3264 repetitions
OBSERVE C13, 125.6603426 MHz
DECOUPLE H1, 499.7456731 MHz
Power 46 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 1 hr, 59 min, 59 sec
146
49.511
49.341
49.170
49.000
48.830
48.659
48.489
180
160
140
120
100
80
60
40
20
ppm

## SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | ks5184_155 | Acquired By: | Kittiya |
| Sample Type: | Unknown | Date Acquired: | 27/09/2010 10:20:19 AM |
| Vial: | 1 | Acq. Method: | ks ether2 |
| Injection #: | 2 | Date Processed: | 27/09/2010 11:16:59 AM |
| Injection Volume: | 20.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 42.00 Minutes | Channel Desc.: | 254 nm |
| | | Sample Set Name: | |

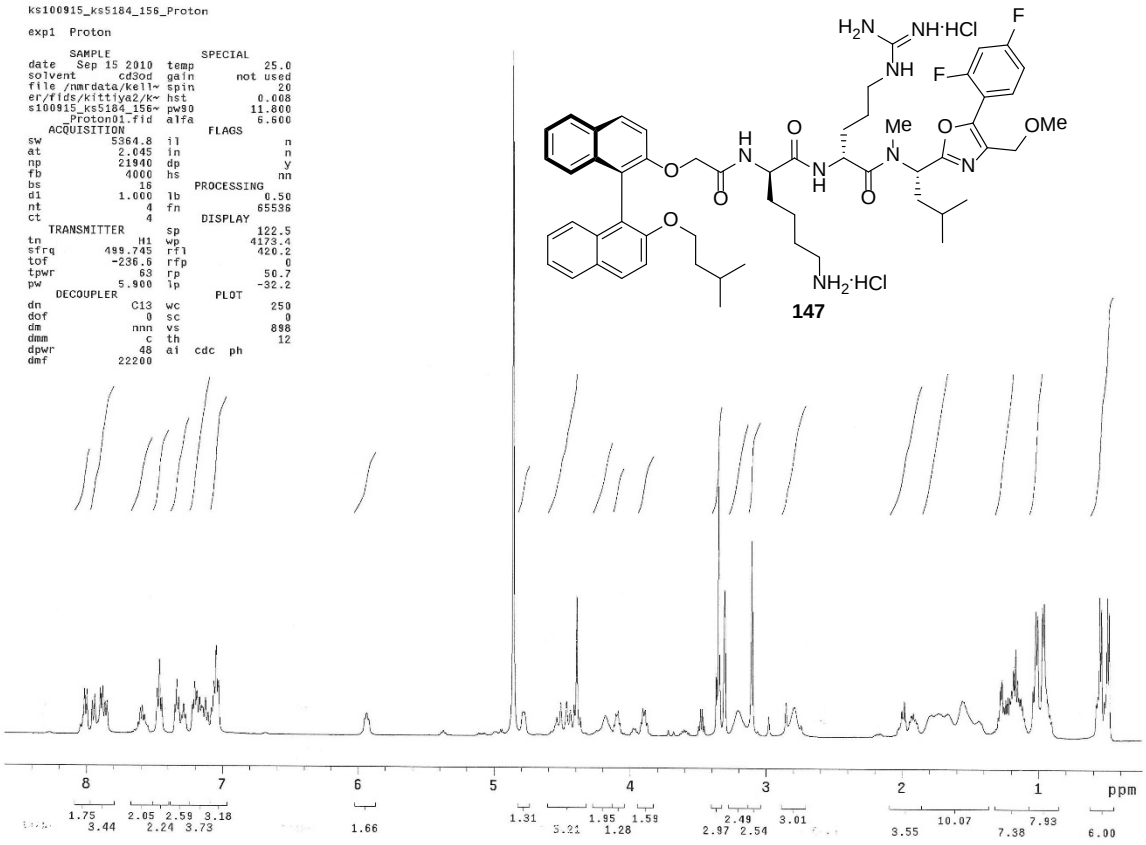


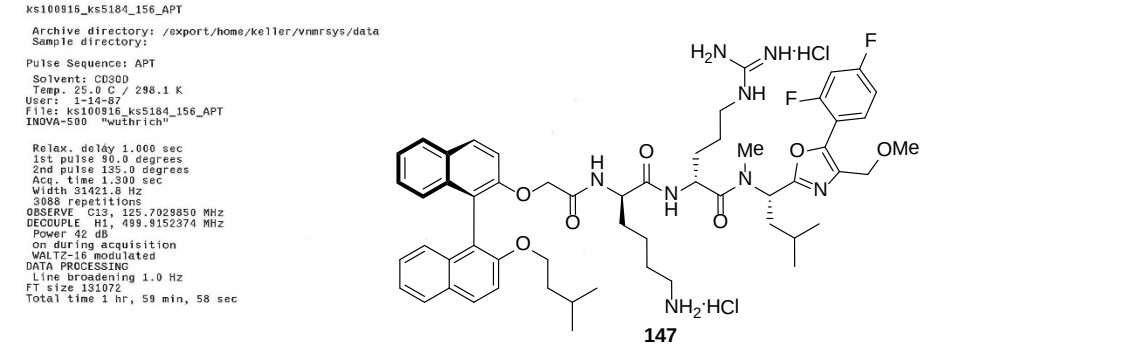

**146**

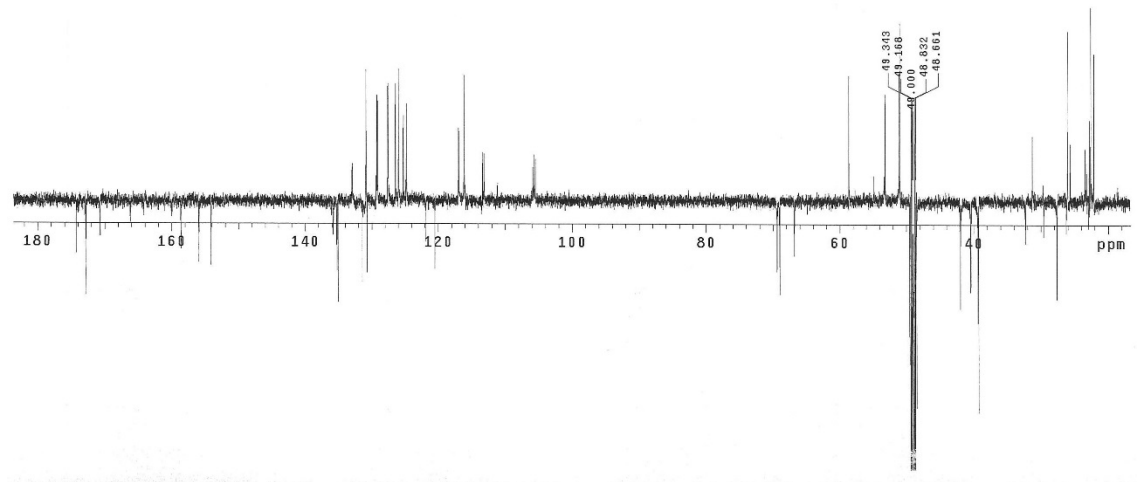
| | RT (min) | Area ( V*sec) | % Area | Height ( V) | % Height |
|---|---|---|---|---|---|
| 1 | 31.834 | 2237120 | 100.00 | 157893 | 100.00 |

| | Time | Flow | %A | %B | Curve |
|---|---|---|---|---|---|
| 1 | 0.01 | 1.00 | 85.0 | 15.0 | 6 |
| 2 | 2.00 | 1.00 | 85.0 | 15.0 | 1 |
| 3 | 35.00 | 1.00 | 40.0 | 60.0 | 6 |
| 4 | 36.00 | 1.00 | 40.0 | 60.0 | 1 |
| 5 | 37.00 | 1.00 | 0.0 | 100.0 | 1 |
| 6 | 42.00 | 1.00 | 0.0 | 100.0 | 1 |
| 7 | 43.00 | 0.00 | 0.0 | 100.0 | 1 |

A = $H_2O$ + 0.1% TFA + 10% MeCN
B = MeCN + 0.1% TFA

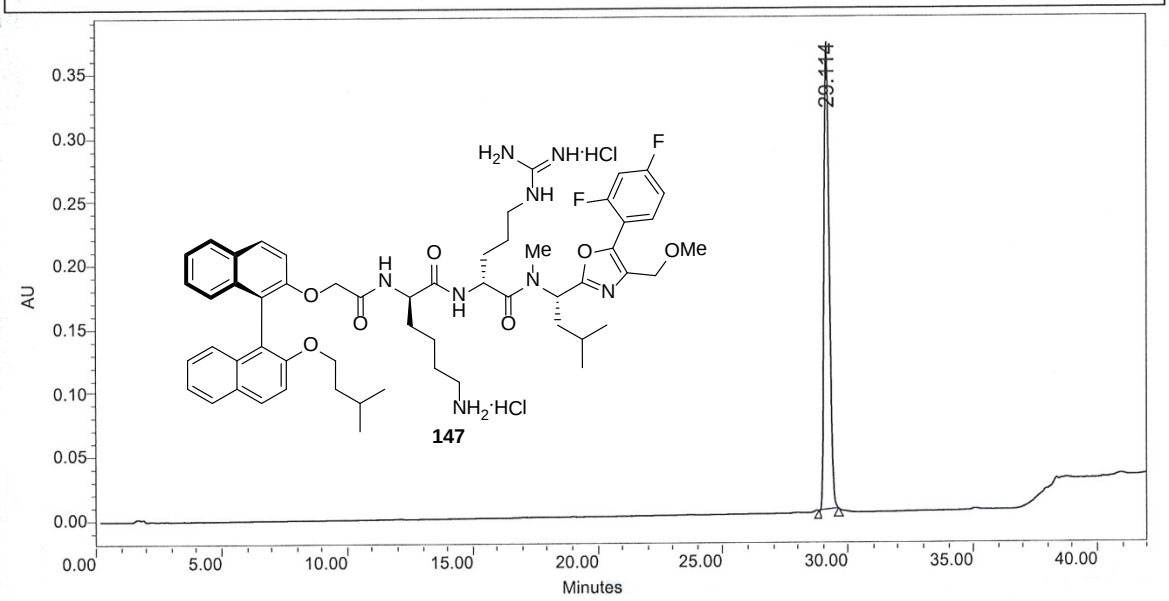

ks100915_ks5184_156_Proton
exp1 Proton
SAMPLE
date Sep 15 2010
solvent cd3od
file /nmrdata/kell~
er/fids/kittiya2/k~
s100915_ks5184_156~
_Proton01.fid
ACQUISITION
sw 5364.8
at 2.045
np 21940
fb 4000
bs 16
d1 1.000
nt 4
ct 4
TRANSMITTER
tn H1
sfrq 499.745
tof -236.6
tpwr 63
pw 5.900
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 48
dmf 22200
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.800
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn 65536
DISPLAY
sp 122.5
wp 4173.4
rf1 420.2
rfp 0
rp 50.7
lp -32.2
PLOT
wc 250
sc 0
vs 898
th 12
ai cdc ph
147
8
7
6
5
4
3
2
1
ppm
1.75
3.44
2.05
2.24
2.59
3.73
3.18
1.66
1.31
5.21
1.95
1.28
1.59
2.49
2.97
2.54
3.01
3.55
10.07
7.38
7.93
6.00


ks100916_ks5184_156_APT
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100916_ks5184_156_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
3088 repetitions
OBSERVE C13, 125.7029850 MHz
DECOUPLE H1, 499.9152374 MHz
Power 42 dB
On during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1 hr, 59 min, 58 sec
147


49.343
49.168
49.000
48.832
48.661
180
160
140
120
100
80
60
40
ppm

## SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | ks5184_156 | Acquired By: | Kittiya |
| Sample Type: | Unknown | Date Acquired: | 27/09/2010 12:04:18 PM |
| Vial: | 1 | Acq. Method: | ks ether2 |
| Injection #: | 4 | Date Processed: | 27/09/2010 1:46:27 PM |
| Injection Volume: | 20.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 42.00 Minutes | Channel Desc.: | 254 nm |
| | | Sample Set Name: | |

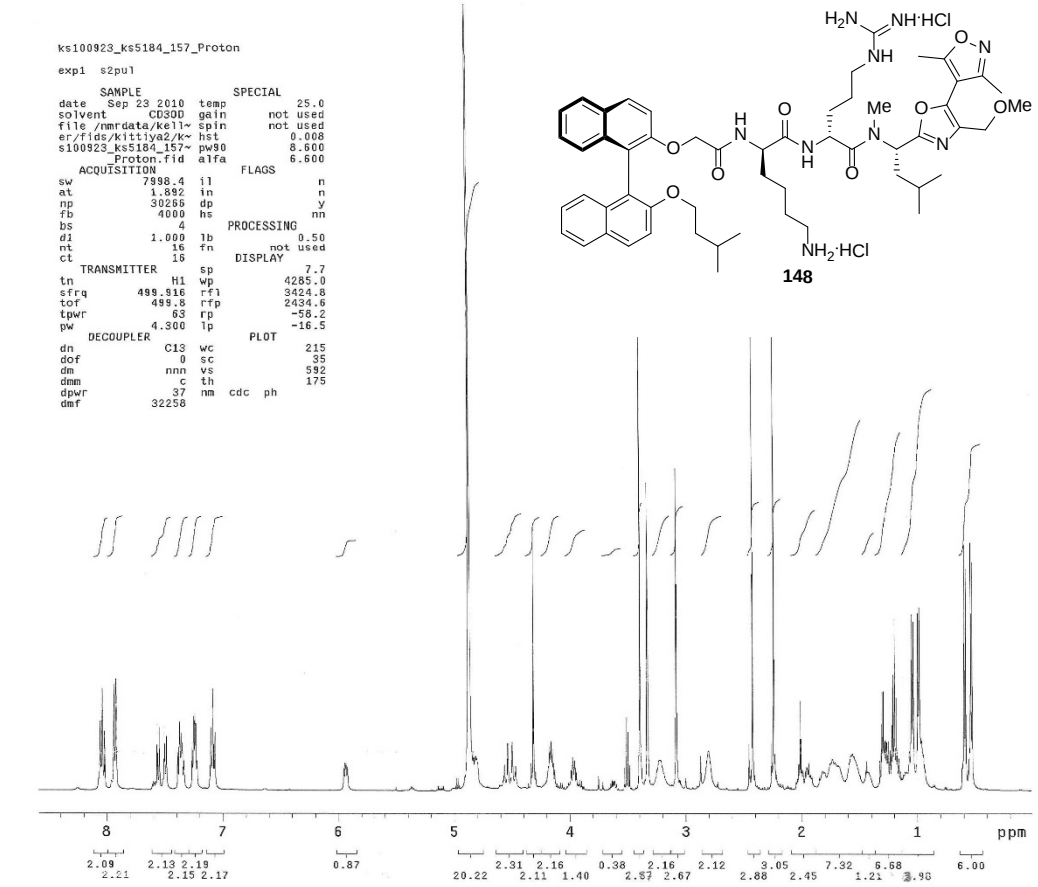


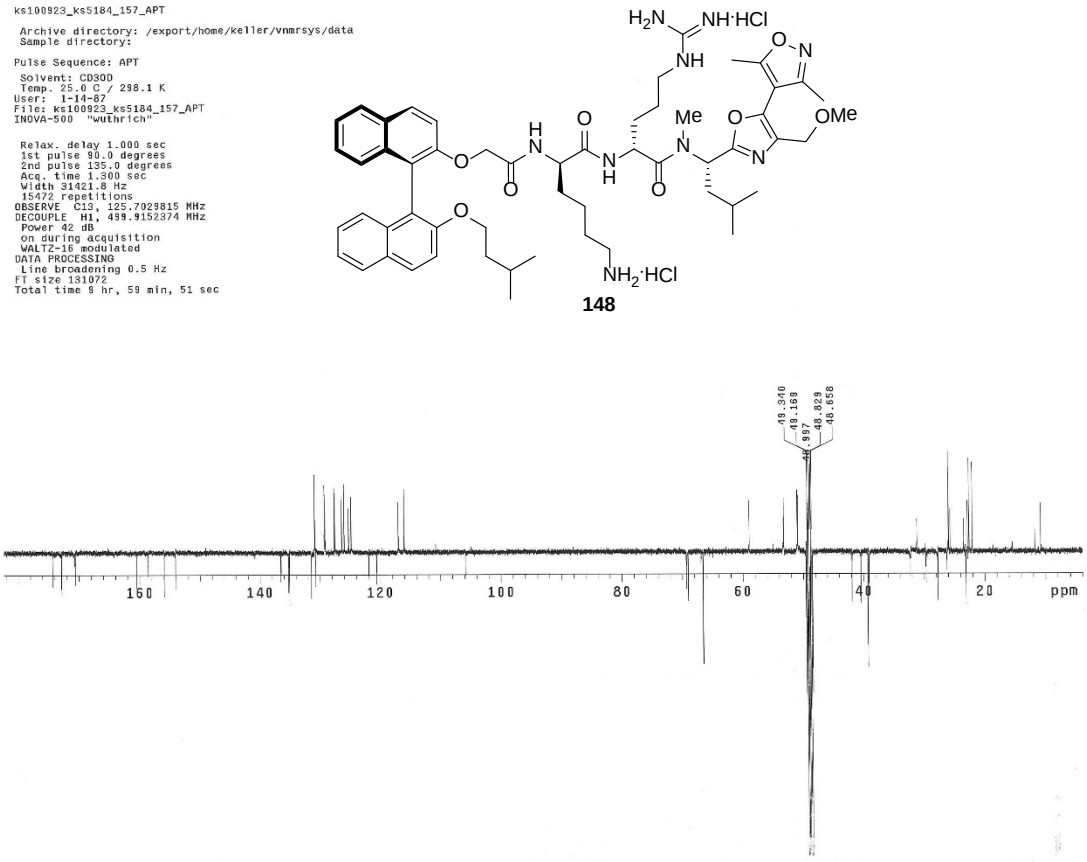

**147**

| | RT (min) | Area ( V*sec) | % Area | Height ( V) | % Height |
|---|---|---|---|---|---|
| 1 | 29.114 | 5323511 | 100.00 | 368085 | 100.00 |

| | Time | Flow | %A | %B | Curve |
|---|---|---|---|---|---|
| 1 | 0.01 | 1.00 | 85.0 | 15.0 | 6 |
| 2 | 2.00 | 1.00 | 85.0 | 15.0 | 1 |
| 3 | 35.00 | 1.00 | 40.0 | 60.0 | 6 |
| 4 | 36.00 | 1.00 | 40.0 | 60.0 | 1 |
| 5 | 37.00 | 1.00 | 0.0 | 100.0 | 1 |
| 6 | 42.00 | 1.00 | 0.0 | 100.0 | 1 |
| 7 | 43.00 | 0.00 | 0.0 | 100.0 | 1 |

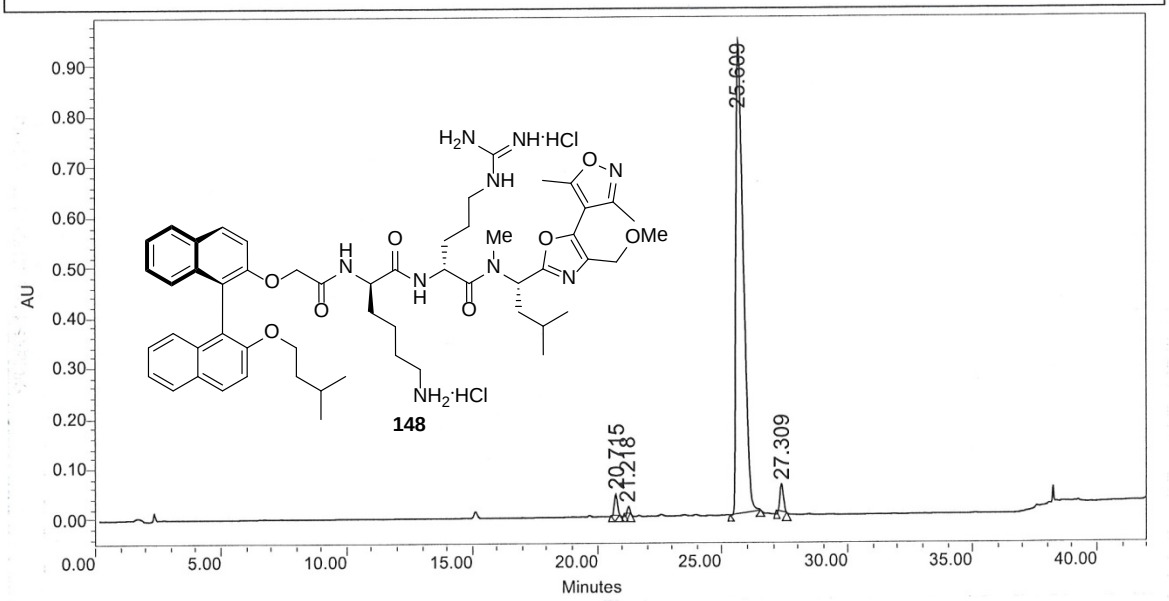
A = $H_2O$ + 0.1% TFA + 10% MeCN
B = MeCN + 0.1% TFA


ks100923_ks5184_157_Proton
exp1 s2pul
SAMPLE
date Sep 23 2010
solvent CD3OD
file /nmrdata/kell~
er/fids/kittiya2/k~
s100923_ks5184_157~
_Proton.fid
ACQUISITION
sw 7998.4
at 1.892
np 30266
fb 4000
bs 4
d1 1.000
nt 16
ct 16
TRANSMITTER
tn H1
sfrq 499.916
tof 499.8
tpwr 63
pw 4.300
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 37
dmf 32258
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 8.600
alfa 6.600
FLAGS
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp 7.7
wp 4285.0
rfl 3424.8
rfp 2434.6
rp -58.2
lp -16.5
PLOT
wc 215
sc 35
vs 592
th 175
nm cdc ph
148
8
7
6
5
4
3
2
1
ppm
2.09
2.21
2.13 2.19
2.15 2.17
0.87
20.22
2.31 2.16
2.11 1.40
0.38
2.57
2.16
2.67
2.12
3.05
2.88
7.32
2.45
6.68
1.21
6.00


ks100923_ks5184_157_APT
Archive directory: /export/home/keller/vnmrsys/data
Sample directory:
Pulse Sequence: APT
Solvent: CD3OD
Temp. 25.0 C / 298.1 K
User: 1-14-87
File: ks100923_ks5184_157_APT
INOVA-500 "wuthrich"
Relax. delay 1.000 sec
1st pulse 90.0 degrees
2nd pulse 135.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
15472 repetitions
OBSERVE C13, 125.7029815 MHz
DECOUPLE H1, 499.9152374 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 hr, 59 min, 51 sec
148
49.340
49.169
48.829
48.658
160
140
120
100
80
60
40
20
ppm

## SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | ks5184_157 | Acquired By: | Kittiya |
| Sample Type: | Unknown | Date Acquired: | 22/09/2010 11:29:52 AM |
| Vial: | 1 | Acq. Method: | ks ether2 |
| Injection #: | 13 | Date Processed: | 22/09/2010 1:22:33 PM |
| Injection Volume: | 20.00 ul | Channel Name: | 2487Channel 1 |
| Run Time: | 42.00 Minutes | Channel Desc.: | 254 nm |
| | | Sample Set Name: | |

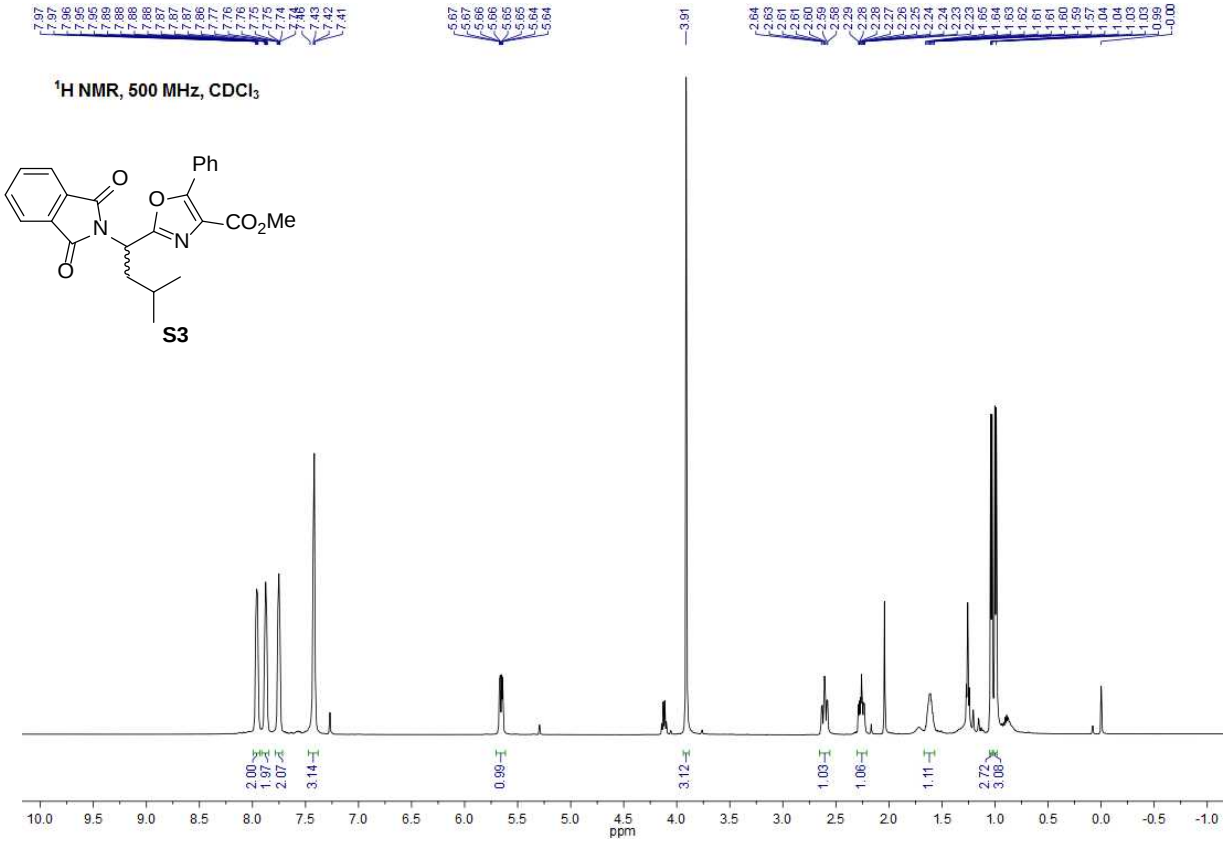


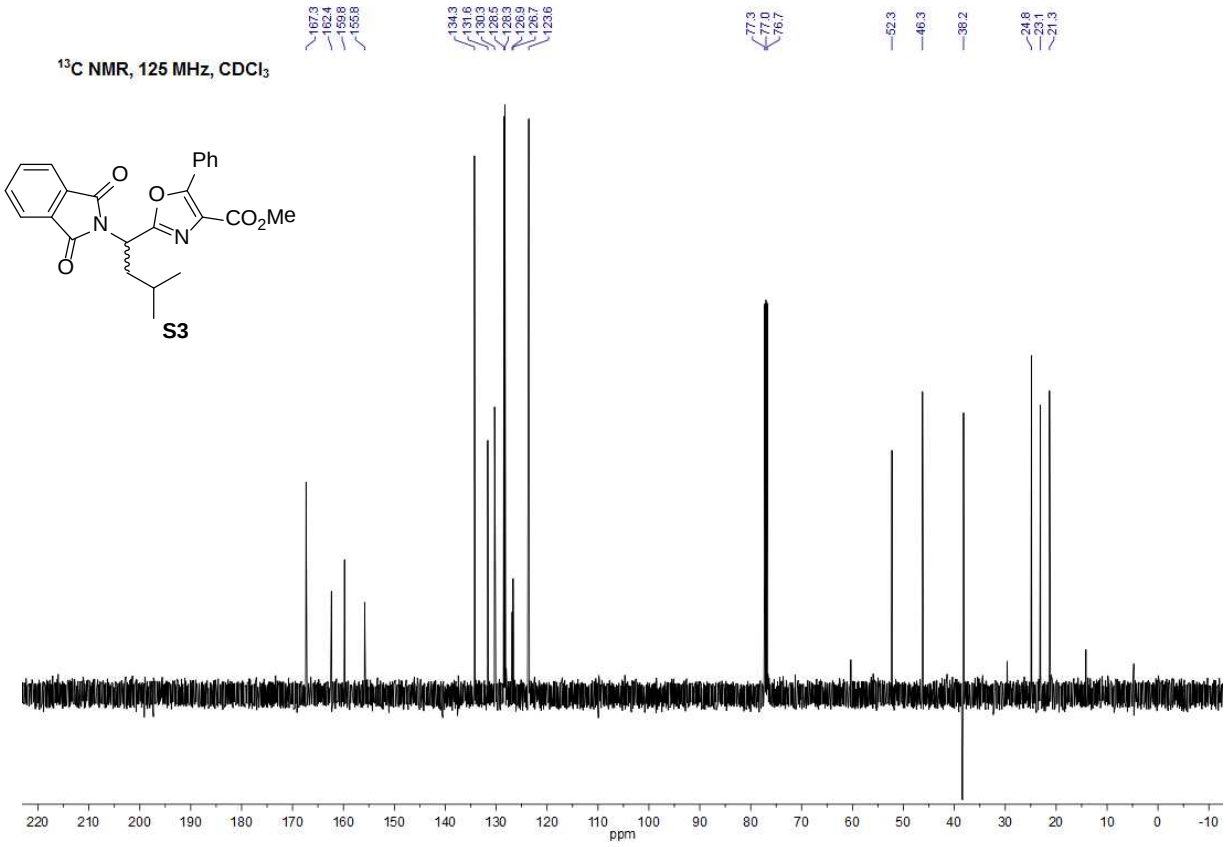

| | RT (min) | Area ( V*sec) | % Area | Height ( V) | % Height |
|---|---|---|---|---|---|
| 1 | 20.715 | 354335 | 1.76 | 42105 | 3.99 |
| 2 | 21.218 | 104809 | 0.52 | 15453 | 1.46 |
| 3 | 25.609 | 19087384 | 94.94 | 941383 | 89.21 |
| 4 | 27.309 | 558530 | 2.78 | 56289 | 5.33 |

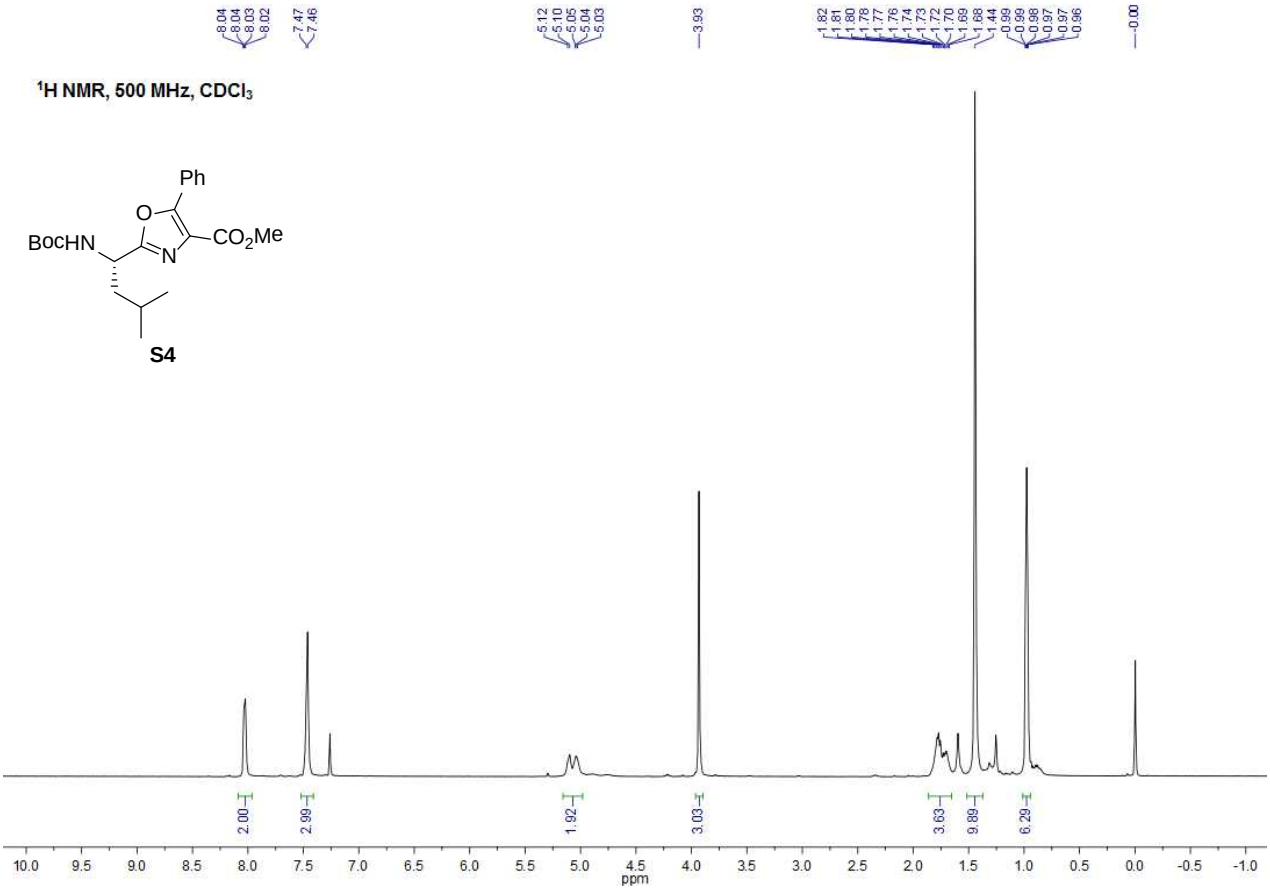
| | Time | Flow | %A | %B | Curve |
|---|---|---|---|---|---|
| 1 | 0.01 | 1.00 | 85.0 | 15.0 | 6 |
| 2 | 2.00 | 1.00 | 85.0 | 15.0 | 1 |
| 3 | 35.00 | 1.00 | 40.0 | 60.0 | 6 |
| 4 | 36.00 | 1.00 | 40.0 | 60.0 | 1 |
| 5 | 37.00 | 1.00 | 0.0 | 100.0 | 1 |
| 6 | 42.00 | 1.00 | 0.0 | 100.0 | 1 |
| 7 | 43.00 | 0.00 | 0.0 | 100.0 | 1 |

A = $H_2O$ + 0.1% TFA + 10% MeCN
B = MeCN + 0.1% TFA

## NMR Spectra of Oxazoles S3−S7



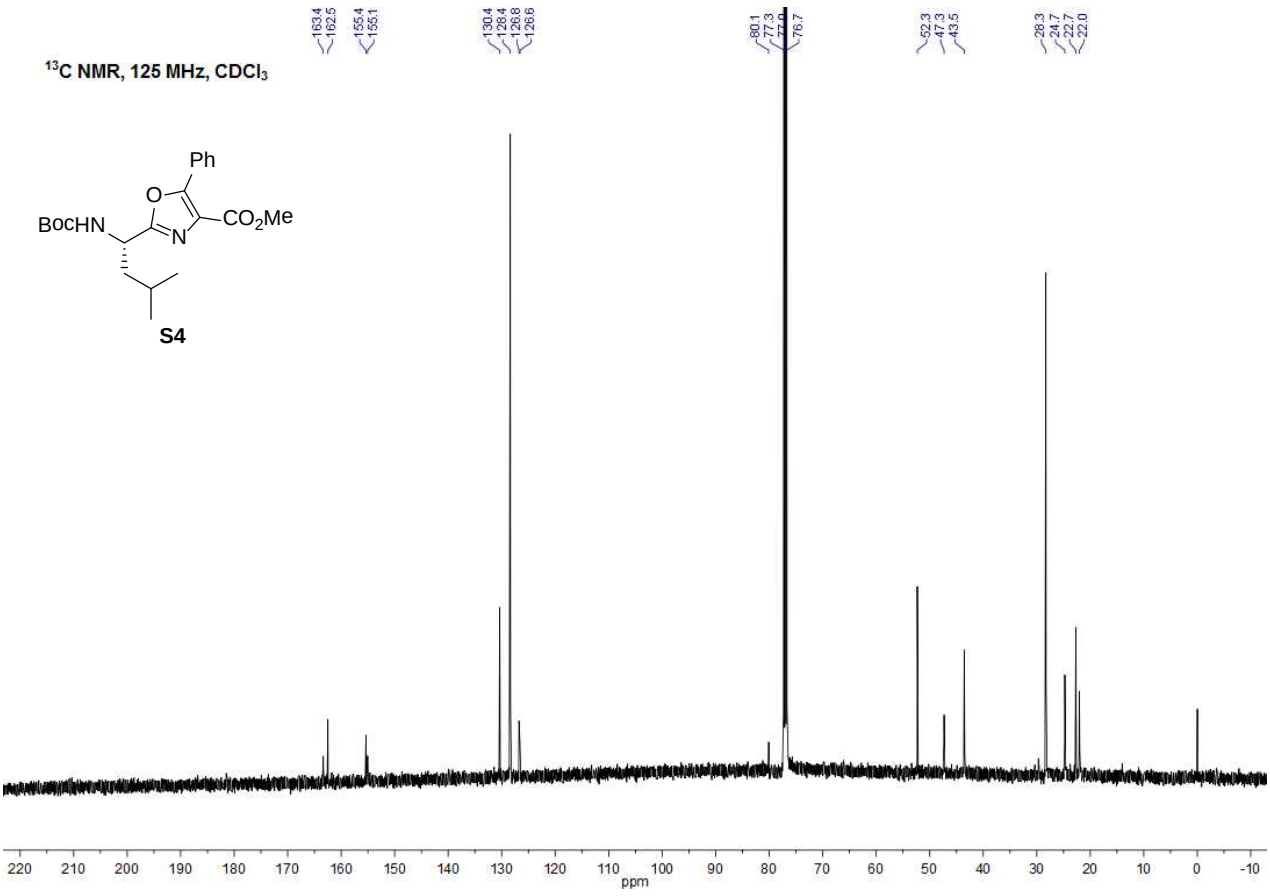






$^{1}$H NMR, 500 MHz, $CDCl_3$



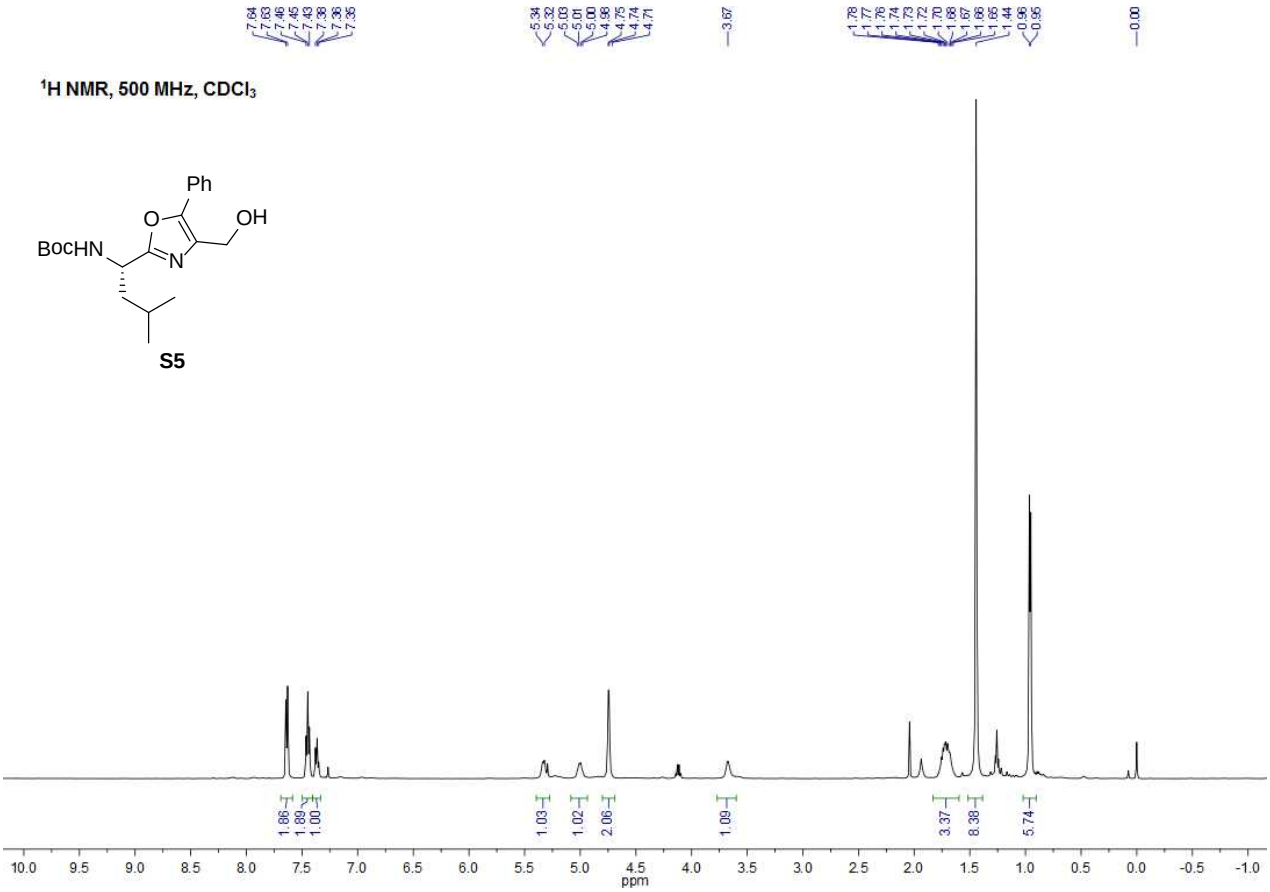

**S4**

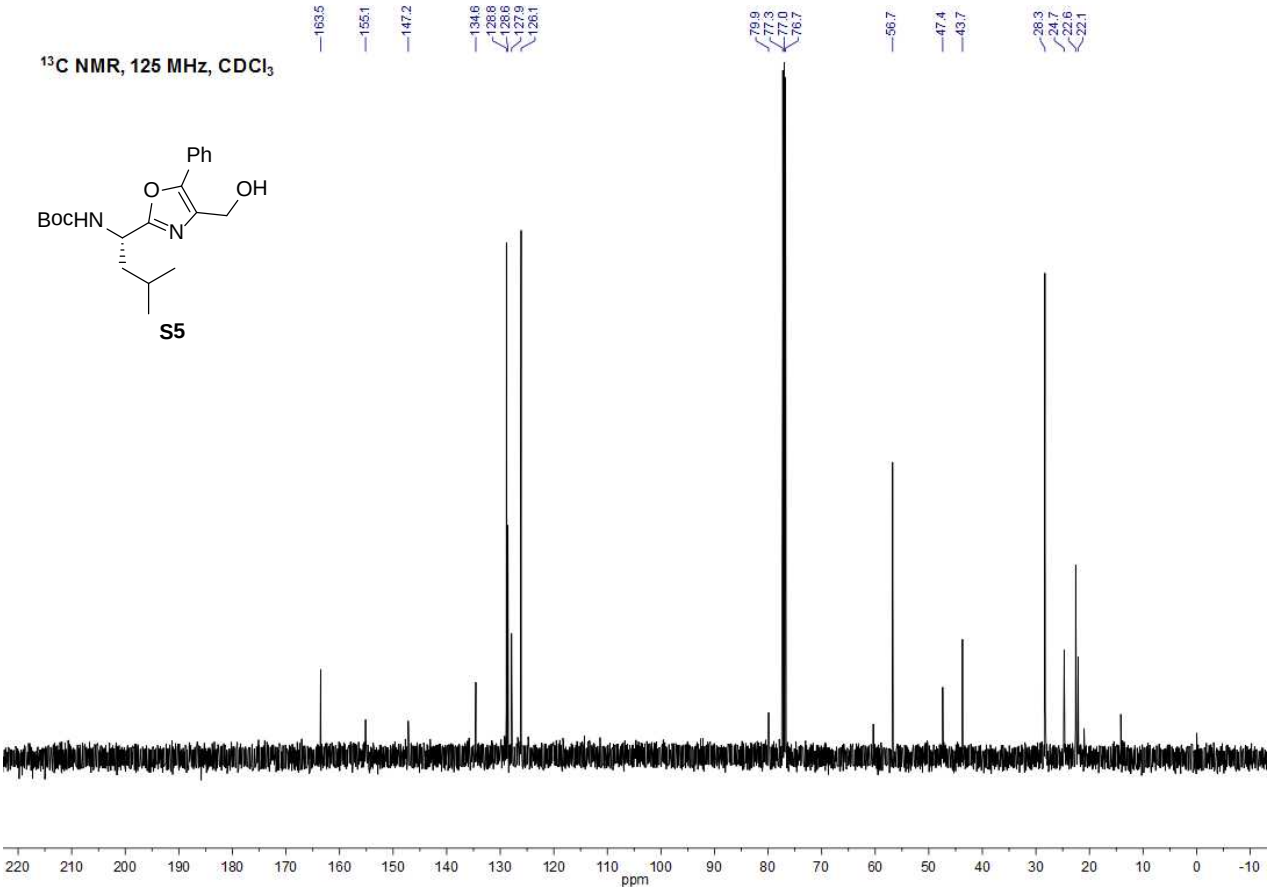



$^{13}$C NMR, 125 MHz, $CDCl_3$

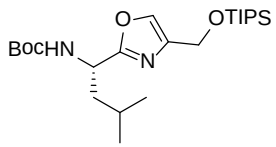



**S4**


7.64
7.63
7.46
7.45
7.43
7.38
7.36
7.35
5.34
5.32
5.03
5.01
5.00
4.98
4.75
4.74
4.71
3.67
1.78
1.77
1.76
1.74
1.73
1.72
1.70
1.68
1.67
1.66
1.65
1.44
0.96
0.95
0.00
1H NMR, 500 MHz, CDCl3
Ph
O
OH
BocHN
N
S5
1.86
1.89
1.00
1.03
1.02
2.06
1.09
3.37
8.38
5.74
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
ppm


163.5
155.1
147.2
134.6
128.8
128.6
127.9
126.1
79.9
77.3
77.0
76.7
56.7
47.4
43.7
28.3
24.7
22.6
22.1
13C NMR, 125 MHz, CDCl3
Ph
O
OH
BocHN
N
S5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

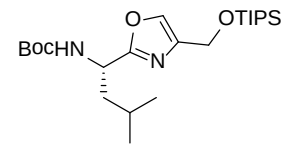
**$^1$H NMR, 500 MHz, $CDCl_3$**




**S6**

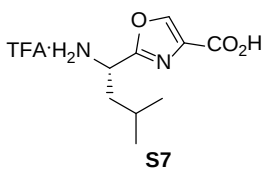



**$^{13}$C NMR, 125 MHz, $CDCl_3$**




**S6**

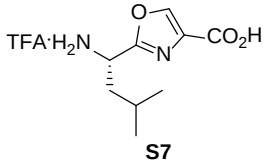
**$^1$H NMR, 300 MHz, $CD_3OD$**




**S7**




**$^{13}$C NMR, 75 MHz, $CD_3OD$**




**S7**