Supporting Information

Binaphthyl-1,2,3-Triazole Peptidomimetics with Activity Against *Clostridium difficile* and Other Pathogenic Bacteria

Steven M. Wales,[a] Katherine A. Hammer,[b] Amy M. King,[c] Andrew J. Tague,[a] Dena Lyras,[c] Thomas V. Riley,[b] 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*

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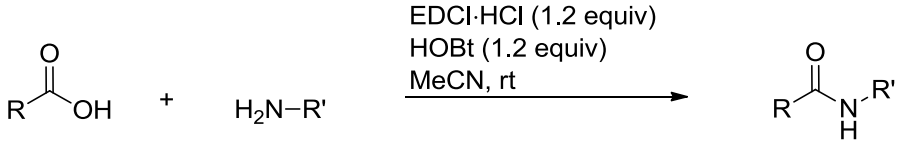
Synthesis and Characterization Methods. All reactions were carried out in standard laboratory glassware with magnetic stirring. Thin layer chromatography (TLC) was performed on aluminum-backed 0.20 mm silica gel plates. Visualization was accomplished with UV light, a ninhydrin staining solution in *n*-butanol 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 (^1H: δ = 0.00 ppm) and solvent resonance (^{13}C: δ = 77.0 ppm). Spectra acquired in CD_3OD are reported relative to solvent resonance (^1H: δ = 3.31 ppm; ^{13}C: δ = 49.0 ppm). ^1H 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, 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. For ^{13}C NMR spectra, resonances are given to 1 decimal place, except where more information is needed to distinguish resolved signals. Infrared (IR) spectra were obtained on a Shimadzu IRAffinity-1 FTIR Spectrometer in combination with a MIRacle 10 Single Reflection Attenuated Total Reflectance accessory outfitted with a 1.5 mm round diamond crystal. IR samples were analyzed as neat solids or oils. Low resolution mass spectrometry (MS) was performed on a Shimadzu LC-2010 Electrospray Ionization (ESI) Mass Spectrometer. All samples were prepared in HPLC grade methanol with a trace of formic acid. 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 hydrochloride 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 Synergi 4u Fusion-RP 80Å column (φ = 4.6 × 150 mm) at a wavelength (λ) of 280 nm using water/acetonitrile (both containing 0.1% TFA) as the mobile phase. All samples were injected at a concentration of ~1 mg mL^{-1} in HPLC grade MeOH (injection volume = 20 μL).

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. Known reagents and alkynes that were not commercially available were prepared according to literature procedures cited within. All other reagents were purchased reagent grade and used as received.

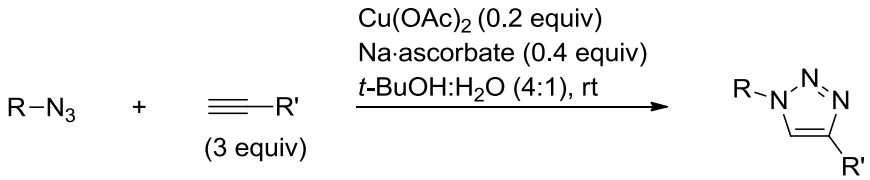
General Synthetic Procedures 1−5

General Procedure 1 for Peptide Coupling



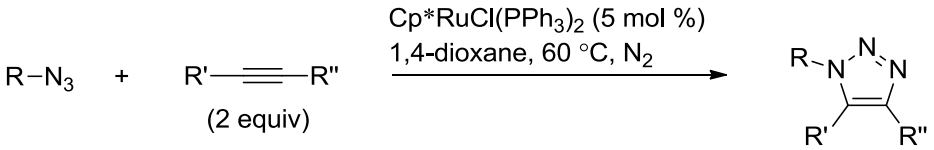
A reaction vessel was charged in air with the carboxylic acid (1.0 equiv), EDCI·HCl (1.2 equiv), HOBt (1.2 equiv) and the specified equivalents of the amine. If the latter was an ammonium salt, a slight excess of $(i\text{-Pr})_2NEt$ was also added as noted. To this was added the specified volume of HPLC grade MeCN (not pre-dried) and the resulting mixture was stirred at rt in an air atmosphere for the time specified. 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, yielding in most cases the analytically pure peptide. Purification was carried out by flash chromatography with the indicated eluent if required.

General Procedure 2 for Copper Catalyzed Azide−Alkyne Cycloaddition



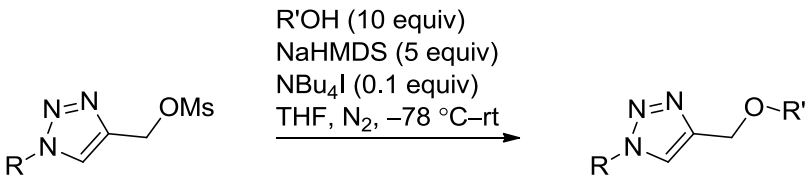
A reaction vessel was charged in air with the azide (1.0 equiv), $Cu(OAc)_2 \cdot H_2O$ (0.2 equiv), Na·ascorbate (0.4 equiv), and the neat alkyne (3.0 equiv). To this was added *t*-BuOH (20 mL/mmol of azide) and H_2O (5 mL/mmol of azide). The mixture was sonicated briefly (<1 min) and the resulting suspension stirred at rt in an air atmosphere for the time specified. The mixture was diluted with EtOAc (20 mL for reactions with ≤1 mmol of azide; or 20 mL/mmol of azide for larger scale) and shaken with a 1:1 mixture of 32% aqueous NH_3:brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. If required, the residue was purified using either a small silica pipette plug or conventional flash chromatography as specified, to give the desired 1,4-substituted triazole.

General Procedure 3 for Ruthenium Catalyzed Azide−Alkyne Cycloaddition



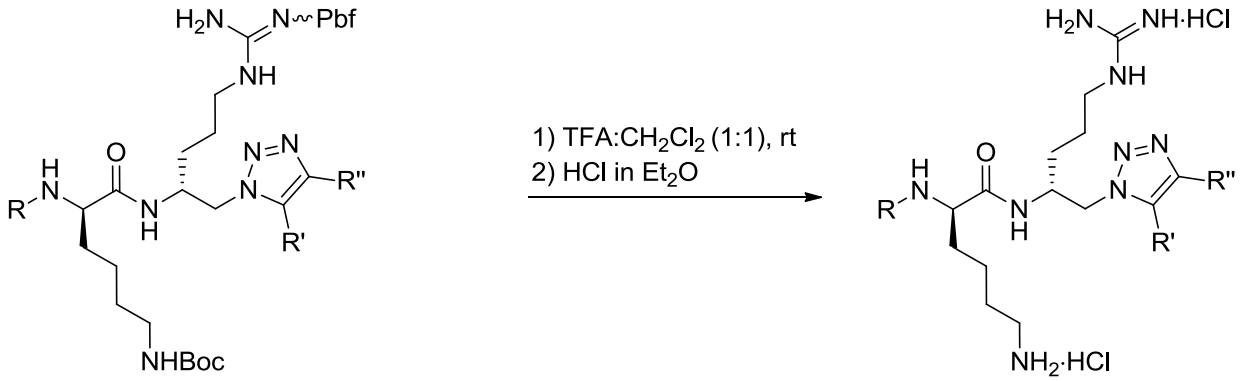
An oven-dried vial was charged in air with the azide (1.0 equiv), $Cp^*RuCl(PPh_3)_2$ (5 mol %) and the neat alkyne (2.0 equiv). The vial was fitted with a rubber septum, evacuated and refilled with N_2 (single cycle), then anhydrous 1,4-dioxane (10 mL/mmol of azide) was added. The sealed vessel was heated at 60 °C under N_2 for the specified time. After cooling to rt, the reaction mixture (with solvent) was directly subjected to flash chromatography with the specified eluent to provide the desired 1,5-disubstituted- or 1,4,5-trisubstituted triazole.

General Procedure 4 for the Preparation of Alkyl Ethers



To the neat alkyl alcohol (R'OH, 10 equiv) under N_2 at −78 °C was added a solution of NaHMDS (1 M in THF, 5 equiv) and the solution was stirred at −78 °C for 15 min to generate the sodium alkoxide. To this was added a solution of the mesylate (1 equiv) and NBu_4I (0.1 equiv) in THF and the external cooling batch was allowed to warm to rt with stirring for the indicated time. 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. If required, purification was carried out by flash chromatography to provide the desired alkyl ether.

General Procedure 5 for TFA Mediated Deprotection on Small Scale (<0.1 mmol)



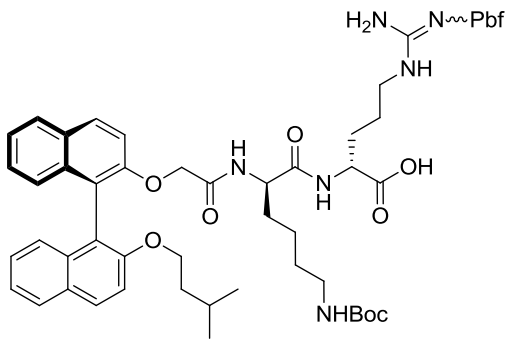
To a solution of the *N*-protected peptide in reagent grade CH_2Cl_2 (3.3 mL/0.1 mmol of substrate) was added TFA (3.3 mL/0.1 mmol of substrate) and the solution was stirred at rt in an air atmosphere for the time specified. The solvents were removed under reduced pressure and the residue dried under 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 as thin films which routinely gave easily-handled powders upon scratching with a spatula.

Note 1: The above procedure was utilized for all compound classes in this study, regardless of the number of protecting groups present.

Note 2: For larger scale deprotection reactions (>0.1 mmol) 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). 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 and Characterization of Class A Triazoles

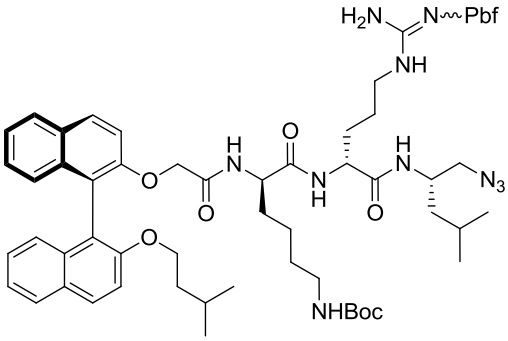
(*R*)-2-((*R*)-6-((tert-Butoxycarbonyl)amino)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamido)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentanoic acid (4)



This compound was prepared in two steps from acid **2**[S1] via peptide coupling with amine **3**[S2] and subsequent saponification. Thus, the intermediate terminal ester was prepared according to *General Procedure 1* using the known acid **2**[S1] (1.313 g, 2.04 mmol), EDCI·HCl (470 mg, 2.45 mmol), HOBt (331 mg, 2.45 mmol), amine **3**[S2] (900 mg, 2.04 mmol) and MeCN (20 mL) with a 19.5 h reaction time. Work-up as described gave the ester (2.228 g, 102%

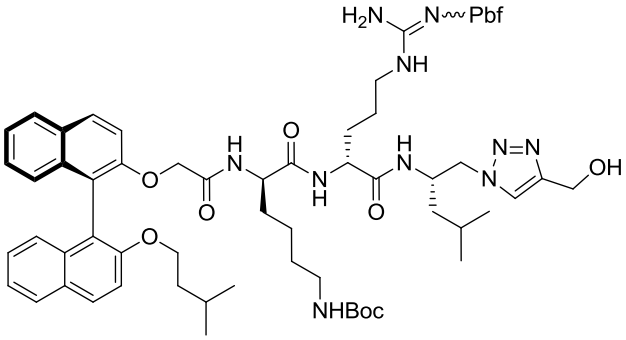
of theoretical yield) as a pale yellow solid. To this was added LiOH (489 mg, 20.40 mmol), reagent grade THF (20 mL) and H_2O (20 mL) and the mixture was stirred at rt in an air atmosphere for 3.5 h. The mixture was diluted with CH_2Cl_2 (40 mL) and 1 M HCl (30 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give **4** (1.980 g, 92% over two steps) as a white solid. TLC (5% MeOH/CH_2Cl_2) R_F = 0.39; $[\alpha]_D^{25}$ −31.9 (*c* 2.43, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.88 (m, 2H), 7.87 – 7.80 (m, 2H), 7.46 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.26 (m, 3H), 7.26 – 7.13 (m, 3H), 7.10 (d, *J* = 8.4 Hz, 1H), 6.61 – 6.16 (bm, 3H), 4.82 (bs, 1H), 4.52 (d, *J* = 14.3 Hz, 1H), 4.47 – 4.35 (m, 2H), 4.19 – 4.10 (m, 1H), 4.10 – 4.02 (m, 1H), 3.95 – 3.86 (m, 1H), 3.23 – 3.04 (m, 2H), 3.01 – 2.79 (m, 4H), 2.53 (s, 3H), 2.47 (s, 3H), 2.05 (s, 3H), 1.89 – 1.76 (m, 1H), 1.74 – 1.63 (m, 1H), 1.57 – 1.33 (m, 18H), 1.31 – 1.08 (m, 5H), 1.04 – 0.93 (m, 1H), 0.89 – 0.77 (m, 2H), 0.54 (d, *J* = 6.3 Hz, 3H), 0.49 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 171.2, 169.1, 158.7, 156.2, 154.4, 152.2, 138.4, 133.8, 133.6, 132.3, 129.74, 129.70, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.6, 124.1, 123.7, 120.4, 119.3, 117.4, 115.9, 114.3, 86.3, 79.1, 68.3, 67.9, 52.5, 51.9, 43.1, 40.5, 40.1, 37.9, 31.0, 29.1, 28.8, 28.5, 28.4, 25.0, 24.5, 22.3, 22.2, 22.0, 19.2, 17.8, 12.4; IR (cm^{-1}) υ 2961, 1684, 1507, 1241, 1088, 808, 747; MS (ES$^-$) *m/z* 1050 (100%, M−H); HRMS (ES$^-$) Calcd. for $C_{57}H_{73}N_6O_{11}S$: 1049.5058, Found: 1049.5015.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-azido-4-methylpentan-2-yl)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 (6)**



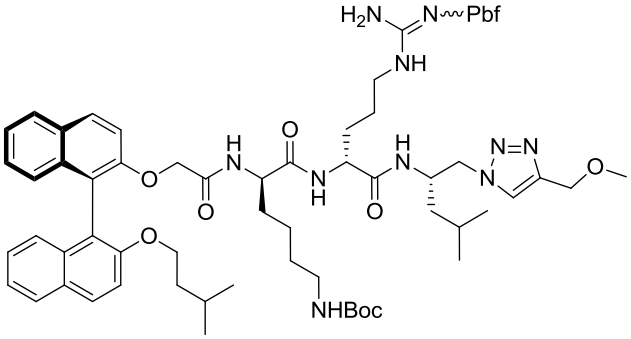
This compound was prepared according to *General Procedure 1* using acid **4** (210.3 mg, 0.20 mmol), EDCI·HCl (46.0 mg, 0.24 mmol), HOBt (32.4 mg, 0.24 mmol), ammonium salt **5**[S3] (102.5 mg, 0.40 mmol), (*i*-Pr)$_2$NEt (0.10 mL, 0.60 mmol) and MeCN (1.0 mL) with a 24 h reaction time. Work-up as described gave **6** (230.8 mg, 98%) as an off-white solid. TLC (7.5% MeOH/CH_2Cl_2) R_F = 0.52; $[\alpha]_D^{25}$ −41.8 (*c* 1.08, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.89 (m, 2H), 7.85 (app. t, *J* = 7.2 Hz, 2H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.28 (m, 3H), 7.28 – 7.18 (m, 3H), 7.15 (d, *J* = 8.6 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 1H), 7.07 (bs, 1H), 6.27 (bs, 2H), 6.19 (d, *J* = 6.4 Hz, 1H), 4.89 – 4.78 (m, 1H), 4.54 (d, *J* = 13.8 Hz, 1H), 4.47 – 4.34 (m, 2H), 4.15 – 3.98 (m, 3H), 3.95 – 3.81 (m, 1H), 3.39 – 3.26 (m, 2H), 3.27 – 3.08 (m, 2H), 3.02 – 2.83 (m, 4H), 2.59 (s, 3H), 2.50 (s, 3H), 2.08 (s, 3H), 1.90 – 1.74 (m, 1H), 1.67 – 1.33 (m, 20H), 1.32 – 1.05 (m, 7H), 1.05 – 0.73 (m, 9H), 0.53 (d, *J* = 6.2 Hz, 3H), 0.48 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 171.3, 169.1, 158.7, 156.4, 156.0, 154.3, 152.1, 138.1, 133.8, 133.5, 132.8, 132.0, 129.7, 129.6, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.8, 124.6, 124.1, 123.8, 120.4, 119.3, 117.5, 115.8, 114.2, 86.3, 78.8, 68.2, 68.1, 54.7, 52.8, 47.5, 43.2, 40.7, 40.2, 40.0, 37.9, 31.1, 29.3, 29.0, 28.50, 28.48, 28.4, 25.6, 24.7, 24.4, 23.1, 22.4, 22.2, 22.0, 21.9, 21.8, 19.3, 17.9, 12.4; IR (cm^{-1}) υ 3317, 2960, 2100, 1660, 1545, 1457, 1367, 1243, 1168, 1091, 807, 747; MS (ES$^+$) *m/z* 1198 (100%, M+Na), 1176 (56%, M+H); HRMS (ES$^+$) Calcd. for $C_{63}H_{87}N_{10}O_{10}S$: 1175.6327, Found: 1175.6321.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)-4-methylpentan-2-yl)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 (7)**



This compound was prepared according to *General Procedure 2* using azide **6** (80.0 mg, 0.068 mmol), $Cu(OAc)_2 \cdot H_2O$ (2.7 mg, 0.014 mmol), Na·ascorbate (5.4 mg, 0.027 mmol), propargyl alcohol (11.4 mg, 0.20 mmol), *t*-BuOH (1.36 mL) and H_2O (0.34 mL). After stirring at rt for 27.5 h, TLC analysis (75% EtOAc/pet. ether) indicated the presence of some unreacted azide. Additional portions of $Cu(OAc)_2 \cdot H_2O$ (2.7 mg, 0.014 mmol) and Na·ascorbate (5.4 mg, 0.027 mmol) were added and stirring was continued for a further 3 h. Work-up as described and purification by flash chromatography (2.3 g silica, 100% EtOAc to 5% MeOH/EtOAc) gave **7** (53.0 mg, 63%) as an off-white solid. TLC (4% MeOH/EtOAc) R_F = 0.13; $[\alpha]_D^{25}$ −24.6 (*c* 2.38, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (app. t, *J* = 7.8 Hz, 2H), 7.86 (app. t, *J* = 6.3 Hz, 2H), 7.75 (bs, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.44 – 7.17 (m, 6H), 7.17 – 7.08 (m, 2H), 6.41 (bs, 2H), 6.27 (bs, 1H), 6.05 (bs, 1H), 4.98 (bs, 1H), 4.63 (s, 2H), 4.53 (d, *J* = 14.6 Hz, 1H), 4.47 – 4.26 (m, 4H), 4.26 – 4.16 (m, 1H), 4.09 – 4.01 (m, 1H), 3.98 – 3.84 (m, 2H), 3.24 – 3.04 (m, 2H), 3.03 – 2.81 (m, 4H), 2.57 (s, 3H), 2.49 (s, 3H), 2.07 (s, 3H), 1.74 – 1.35 (m, 20H), 1.36 – 1.06 (m, 8H), 1.05 – 0.75 (m, 9H), 0.54 (d, *J* = 6.3 Hz, 3H), 0.48 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 171.9, 169.3, 158.7, 156.5, 156.1, 154.4, 152.2, 147.6, 138.1, 133.8, 133.6, 132.7, 132.1, 129.7, 129.6, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.6, 124.1, 123.8, 123.6, 120.3, 119.5, 117.5, 116.0, 114.3, 86.3, 78.9, 68.3, 68.0, 56.0, 53.3, 53.2, 53.0, 48.1, 43.1, 40.6, 40.0, 37.9, 30.8, 29.1, 28.9, 28.5, 28.4, 25.5, 24.6, 24.4, 23.1, 22.4, 22.2, 22.0, 21.7, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1254 (100%, M+Na), 1232 (94%, M+H); HRMS (ES^+) Calcd. for $C_{66}H_{90}N_{10}NaO_{11}S$: 1253.6409, Found: 1253.6443.

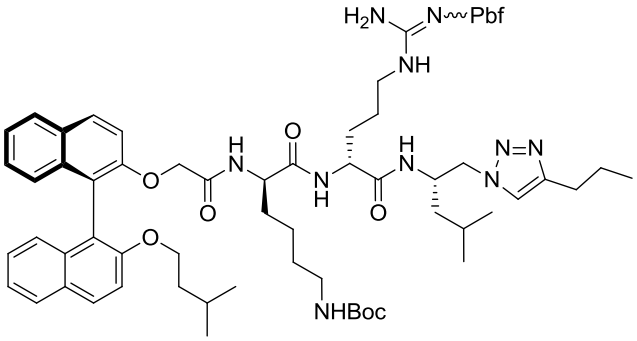
***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(((*R*)-1-(((*S*)-1-(4-(methoxymethyl)-1*H*-1,2,3-triazol-1-yl)-4-methylpentan-2-yl)amino)-1-oxo-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-6-oxohexyl)carbamate (10)**



This compound was prepared in two steps from alcohol **7** via mesylation and subsequent etherification with methoxide. Thus, to a solution of alcohol **7** (45.4 mg, 0.037 mmol) and NEt_3 (5.6 mg, 0.055 mmol) in CH_2Cl_2 (0.17 mL) at 0 °C in air was added a solution of MsCl (8.4 mg, 0.074 mmol) in CH_2Cl_2 (0.20 mL). The mixture was stirred for 5 min, then diluted with cold 1 M HCl (20 mL) and EtOAc (20 mL). The organic layer was washed with saturated $NaHCO_3$ (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give the mesylate ester derivative (49.7 mg, 103% of theoretical yield) as a pale yellow gum. TLC (4% MeOH/EtOAc) R_F = 0.56. This intermediate was then utilized in the preparation of ether **10** according to *General Procedure 4* using MeOH (11.8 mg, 0.37 mmol), NaHMDS (1 M in THF, 0.18 mL, 0.18 mmol) and a solution of the

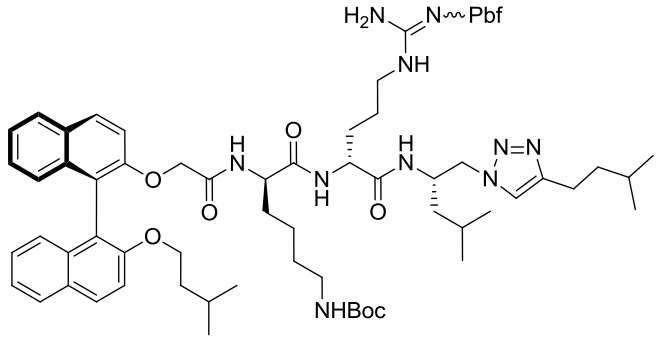
mesylate (49.7 mg, 0.037 mmol) and NBu_4I (1.4 mg, 0.0037 mmol) in THF (1.0 mL) with a 2 h reaction time. Flash chromatography (2.5 g silica, 100% CH_2Cl_2 to 4% MeOH/CH_2Cl_2) gave **10** (28.8 mg, 63% over two steps) as a white solid. TLC (4% MeOH/EtOAc) R_F = 0.28, (7.5% MeOH/CH_2Cl_2) R_F = 0.47; $[\alpha]_D^{25}$ −26.4 (*c* 1.29, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 – 7.91 (m, 2H), 7.91 – 7.81 (m, 2H), 7.72 (s, 1H), 7.53 – 7.43 (m, 1H), 7.42 – 7.07 (m, 8H), 6.33 (bs, 2H), 6.22 (bs, 1H), 4.85 (bs, 1H), 4.66 – 4.21 (m, 8H), 4.11 – 4.00 (m, 1H), 3.98 – 3.82 (m, 2H), 3.32 (s, 3H), 3.26 – 3.02 (m, 2H), 3.03 – 2.84 (m, 4H), 2.57 (s, 3H), 2.49 (s, 3H), 2.08 (s, 3H), 1.81 – 1.06 (m, 27H), 1.06 – 0.76 (m, 10H), 0.59 – 0.44 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 171.3, 169.5, 158.7, 156.4, 156.1, 154.4, 152.3, 144.6, 138.2, 133.9, 133.7, 133.0, 132.2, 129.84, 129.80, 129.7, 129.3, 128.0, 127.9, 126.7, 126.6, 125.5, 125.0, 124.6, 124.2, 123.9, 123.8, 120.4, 119.7, 117.5, 116.1, 114.4, 86.3, 79.0, 68.5, 68.2, 65.6, 58.1, 53.6, 53.4, 52.9, 48.0, 43.2, 40.5, 40.4, 40.1, 38.0, 30.8, 29.2, 29.1, 28.5, 28.4, 25.4, 24.6, 24.5, 23.1, 22.5, 22.3, 22.0, 21.7, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1268 (100%, M+Na), 1246 (50%, M+H); HRMS (ES^+) Calcd. for $C_{67}H_{92}N_{10}NaO_{11}S$: 1267.6565, Found: 1267.6598.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(((*R*)-1-(((*S*)-4-methyl-1-(4-propyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)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 (8)**



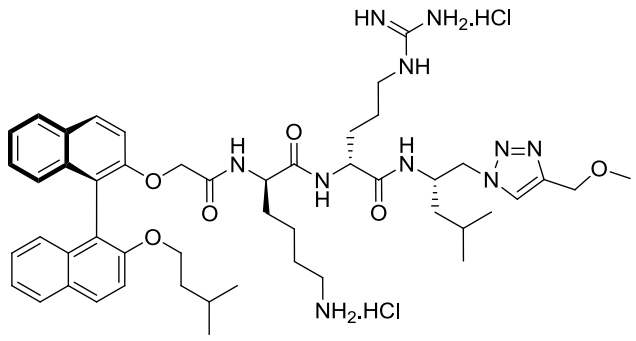
This compound was prepared according to *General Procedure 2* using azide **6** (65.0 mg, 0.055 mmol), $Cu(OAc)_2{\cdot}H_2O$ (2.2 mg, 0.011 mmol), Na·ascorbate (4.4 mg, 0.022 mmol), 1-pentyne (11.2 mg, 0.17 mmol), *t*-BuOH (1.16 mL) and H_2O (0.29 mL) with a 48 h reaction time. Purification by a pipette silica plug (1.2 cm silica, 100% EtOAc) gave **8** (63.8 mg, 93%) as an off-white solid. TLC (75% EtOAc/pet. ether) R_F = 0.10; $[\alpha]_D^{25}$ −27.0 (*c* 3.05, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.91 (m, 2H), 7.89 – 7.82 (m, 2H), 7.49 – 7.43 (m, 2H), 7.38 – 7.19 (m, 5H), 7.19 – 7.10 (m, 3H), 6.41 (bs, 2H), 6.22 (bd, *J* = 5.4 Hz, 1H), 5.98 (bs, 1H), 4.85 (bs, 1H), 4.56 (d, *J* = 14.6 Hz, 1H), 4.48 – 4.37 (m, 2H), 4.37 – 4.24 (m, 3H), 4.08 – 4.02 (m, 1H), 4.01 – 3.94 (m, 1H), 3.92 – 3.84 (m, 1H), 3.23 – 3.07 (m, 2H), 2.98 – 2.87 (m, 4H), 2.67 – 2.55 (m, 5H), 2.50 (s, 3H), 2.07 (s, 3H), 1.82 – 1.73 (m, 1H), 1.69 – 1.57 (m, 3H), 1.54 – 1.33 (m, 17H), 1.32 – 1.07 (m, 8H), 1.06 – 0.97 (m, 1H), 0.96 – 0.78 (m, 12H), 0.54 (d, *J* = 6.5 Hz, 3H), 0.48 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 171.2, 169.3, 158.6, 156.5, 156.0, 154.4, 152.2, 147.9, 138.1, 133.8, 133.6, 133.0, 132.1, 129.8, 129.7, 129.6, 129.2, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.8, 122.0, 120.3, 119.6, 117.4, 116.0, 114.3, 86.3, 78.9, 68.4, 68.1, 53.5, 53.2, 52.9, 47.9, 43.2, 40.5, 40.3, 40.1, 37.9, 30.8, 29.1, 28.5, 28.4, 27.5, 25.4, 24.6, 24.4, 23.1, 22.5, 22.2, 22.0, 21.6, 19.2, 17.9, 13.6, 12.4; MS (ES^+) *m/z* 1266 (90%, M+Na), 1244 (100%, M+H); HRMS (ES^+) Calcd. for $C_{68}H_{94}N_{10}NaO_{10}S$: 1265.6773, Found: 1265.6819.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*S*)-1-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)-4-methylpentan-2-yl)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 (9)**



This compound was prepared according to *General Procedure 2* using azide **6** (65.0 mg, 0.055 mmol), $Cu(OAc)_2 \cdot H_2O$ (2.2 mg, 0.011 mmol), Na·ascorbate (4.4 mg, 0.022 mmol), 5-methyl-1-hexyne (15.9 mg, 0.17 mmol), *t*-BuOH (1.16 mL) and H_2O (0.29 mL) with a 48 h reaction time. Purification by a pipette silica plug (1.2 cm silica, 100% EtOAc) gave **9** (65.1 mg, 93%) as an off-white solid. TLC (75% EtOAc/pet. ether) R_F = 0.10; $[\alpha]_D^{25}$ −24.2 (*c* 3.09, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.92 (m, 2H), 7.89 – 7.83 (m, 2H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.44 (s, 1H), 7.38 – 7.20 (m, 5H), 7.19 – 7.10 (m, 3H), 6.42 (bs, 2H), 6.23 (bd, *J* = 5.5 Hz, 1H), 6.07 – 5.99 (bm, 1H), 4.86 (bs, 1H), 4.58 (d, *J* = 14.5 Hz, 1H), 4.47 – 4.38 (m, 2H), 4.36 – 4.25 (m, 3H), 4.09 – 4.02 (m, 1H), 4.00 – 3.94 (m, 1H), 3.92 – 3.85 (m, 1H), 3.23 – 3.09 (m, 2H), 2.99 – 2.87 (m, 4H), 2.64 (t, *J* = 7.9 Hz, 2H), 2.58 (s, 3H), 2.50 (s, 3H), 2.08 (s, 3H), 1.83 – 1.72 (m, 1H), 1.68 – 1.33 (m, 21H), 1.33 – 1.07 (m, 8H), 1.06 – 0.96 (m, 1H), 0.96 – 0.77 (m, 15H), 0.54 (d, *J* = 6.5 Hz, 3H), 0.48 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 171.5, 169.3, 158.6, 156.5, 156.0, 154.3, 152.2, 148.3, 138.1, 133.8, 133.6, 133.0, 132.1, 129.7, 129.6, 129.2, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.8, 121.8, 120.3, 119.6, 117.4, 116.0, 114.2, 86.2, 78.9, 68.4, 68.1, 53.5, 53.2, 52.8, 47.9, 43.2, 40.4, 40.2, 40.0, 38.3, 37.9, 30.8, 29.1, 28.5, 28.4, 27.5, 25.4, 24.6, 24.4, 23.4, 23.1, 22.5, 22.3, 22.2, 22.0, 21.6, 19.2, 17.9, 12.4; MS (ES^+) *m/z* 1294 (100%, M+Na), 1272 (48%, M+H); HRMS (ES^+) Calcd. for $C_{70}H_{99}N_{10}O_{10}S$: 1271.7266, Found: 1271.7239.

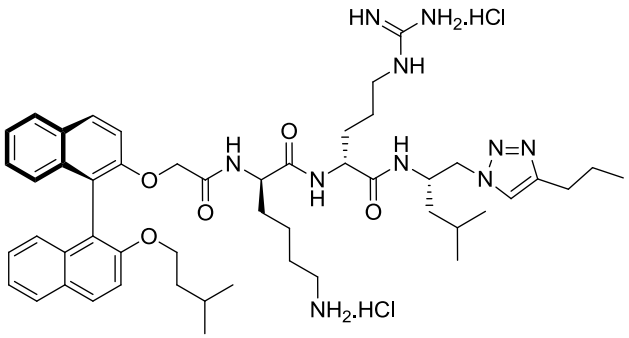
(*R*)-6-Amino-N-((*R*)-5-guanidino-1-(((*S*)-1-(4-(methoxymethyl)-1*H*-1,2,3-triazol-1-yl)-4-methylpentan-2-yl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (11)



This compound was prepared according to *General Procedure 5* using **10** (25.3 mg, 0.020 mmol), CH_2Cl_2 (0.66 mL) and TFA (0.66 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.33 mL) as described gave **11** (14.8 mg, 76%) as an off-white solid. $[\alpha]_D^{25}$ −10.3 (*c* 0.57, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.10 – 7.98 (m, 3H), 7.97 – 7.87 (m, 2H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.50 (d, *J* = 8.9 Hz, 1H), 7.42 – 7.30 (m, 2H), 7.29 – 7.19 (m, 2H), 7.14 – 7.02 (m, 2H), 4.63 – 4.43 (m, 5H), 4.43 – 4.29 (m, 2H), 4.22 – 4.04 (m, 3H), 4.00 – 3.90 (m, 1H), 3.34 (s, 3H), 3.22 – 3.10 (m, 2H), 2.92 – 2.78 (m, 2H), 1.79 – 1.40 (m, 9H), 1.38 – 1.12 (m, 5H), 1.08 – 0.98 (m, 2H), 0.95 (d, *J* = 6.3 Hz, 3H), 0.90 (d, *J* = 6.1 Hz, 3H), 0.58 (d, *J* = 6.2 Hz, 3H), 0.52 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.7, 173.2, 171.1, 158.5, 156.0, 154.2, 145.1, 135.2, 135.1, 131.5, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.5, 126.4, 126.0, 125.3, 124.8, 121.8, 120.6, 116.9, 116.1, 69.4, 69.0, 66.0, 58.5, 55.1, 54.5, 54.0, 49.0, 41.9, 41.5, 40.4, 39.3, 32.1, 30.0, 27.9, 26.3, 25.8, 25.6, 23.7, 23.3, 22.8, 22.5,

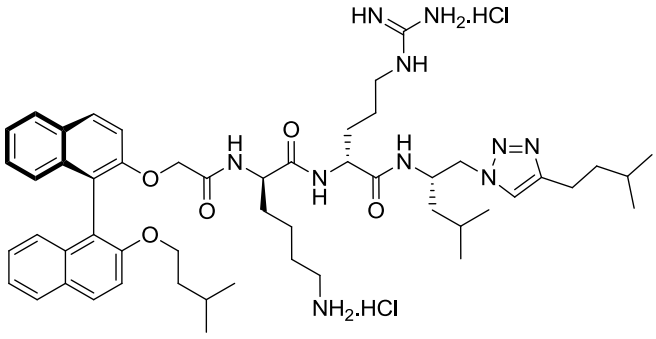
21.8; IR (cm^{-1}) υ 2957, 1653, 1559, 1507, 1212, 1049, 809, 745; MS (ES^+) *m/z* 893 (<5%, M+H), 447 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{49}H_{69}N_{10}O_6$: 893.5402, Found: 893.5415.

(*R*)-6-Amino-N-((*R*)-5-guanidino-1-(((*S*)-1-(4-propyl-1*H*-1,2,3-triazol-1-yl)-4-methylpentan-2-yl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (12)



This compound was prepared according to *General Procedure 5* using **8** (60.2 mg, 0.048 mmol), CH_2Cl_2 (1.59 mL) and TFA (1.59 mL) with a 39.5 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.80 mL) as described gave **12** (42.4 mg, 91%) as an off-white solid. $[\alpha]_D^{25}$ −11.5 (*c* 1.55, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.18 (s, 1H), 8.04 (app. d, *J* = 9.0 Hz, 2H), 7.92 (app. t, *J* = 7.0 Hz, 2H), 7.59 – 7.49 (m, 2H), 7.39 – 7.31 (m, 2H), 7.27 – 7.18 (m, 2H), 7.11 – 7.00 (m, 2H), 4.60 (s, 2H), 4.52 – 4.43 (m, 1H), 4.43 – 4.28 (m, 2H), 4.18 – 4.06 (m, 3H), 4.00 – 3.90 (m, 1H), 3.24 – 3.11 (m, 2H), 2.92 – 2.76 (m, 2H), 2.72 (t, *J* = 7.5 Hz, 2H), 1.80 – 1.48 (m, 11H), 1.36 – 1.03 (m, 7H), 1.01 – 0.86 (m, 9H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.9, 173.5, 171.3, 158.5, 155.9, 154.3, 145.9, 135.2, 135.1, 131.4, 130.9, 130.7, 129.3, 129.1, 128.2, 127.55, 127.47, 126.4, 126.0, 125.2, 124.8, 121.8, 120.6, 116.8, 116.3, 69.5, 69.0, 57.0, 54.7, 54.4, 49.1, 41.8, 41.2, 40.4, 39.3, 31.9, 29.5, 27.8, 26.5, 26.4, 25.7, 25.6, 23.7, 23.4, 22.8, 22.7, 22.5, 21.7, 13.9; IR (cm^{-1}) υ 2956, 1654, 1559, 1507, 1217, 1149, 1047, 805, 746, 668; MS (ES^+) *m/z* 892 (<5%, M+H), 446 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{50}H_{71}N_{10}O_5$: 891.5609, Found: 891.5649.

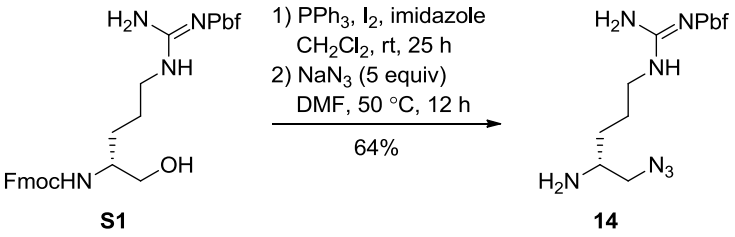
(*R*)-6-Amino-N-((*R*)-5-guanidino-1-(((*S*)-1-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)-4-methylpentan-2-yl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (13)



This compound was prepared according to *General Procedure 5* using **9** (60.2 mg, 0.047 mmol), CH_2Cl_2 (1.55 mL) and TFA (1.55 mL) with a 39.5 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.78 mL) as described gave **13** (39.5 mg, 84%) as an off-white solid. $[\alpha]_D^{25}$ −10.6 (*c* 1.37, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.13 (s, 1H), 8.04 (app. d, *J* = 9.0 Hz, 2H), 7.96 – 7.87 (m, 2H), 7.59 – 7.47 (m, 2H), 7.40 – 7.30 (m, 2H), 7.27 – 7.18 (m, 2H), 7.12 – 6.99 (m, 2H), 4.60 (s, 2H), 4.48 – 4.26 (m, 3H), 4.19 – 4.04 (m, 3H), 4.01 – 3.89 (m, 1H), 3.24 – 3.09 (m, 2H), 2.91 – 2.77 (m, 2H), 2.74 (t, *J* = 8.4 Hz, 2H), 1.79 – 1.70 (m, 1H), 1.70 – 1.46 (m, 11H), 1.35 – 1.03 (m, 7H), 1.02 – 0.85 (m, 12H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.9, 173.6, 171.3, 158.5, 155.9, 154.3, 146.6, 135.2, 135.1, 131.4, 130.9, 130.7, 129.3, 129.1, 127.7, 127.54, 127.49, 126.4, 126.0, 125.2, 124.8, 121.8, 120.6, 116.9, 116.3, 69.5, 69.0, 56.7, 54.6, 54.4, 49.1, 41.8, 41.2, 40.4, 39.3, 38.4, 31.9, 29.5, 28.7, 27.8, 26.5, 25.7, 25.6, 23.7, 23.4, 22.85, 22.76, 22.6, 22.5, 21.8; IR (cm^{-1}) υ 2957, 1654, 1560, 1507,

1212, 1170, 1047, 808, 748; MS (ES^+) *m/z* 920 (<5%, M+H), 460 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{52}H_{75}N_{10}O_5$: 919.5922, Found: 919.5953.

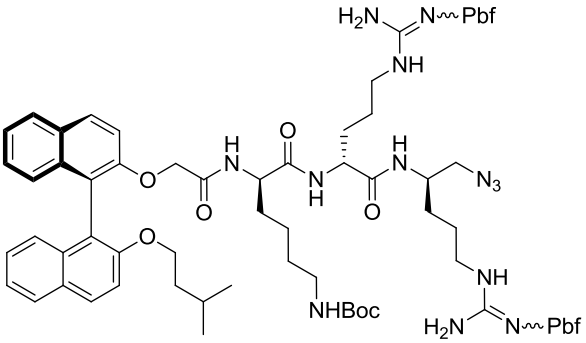
(*R*)-*N*-(Amino((4-amino-5-azidopentyl)amino)methylene)-2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-sulfonamide (14)



S1 **14**

A mixture of PPh_3 (957 mg, 3.65 mmol), I_2 (926 mg, 3.65 mmol) and imidazole (414 mg, 6.08 mmol) in CH_2Cl_2 (25 mL) was stirred at rt under N_2 for 10 min. To the bright yellow mixture was added a solution of the known amino alcohol **S1**[S4] (1.544 g, 2.43 mmol) in CH_2Cl_2 (10 mL) and the mixture was stirred at rt for 25 h. The resulting white suspension was gravity filtered to remove the imidazole salts and the filtrate was concentrated under reduced pressure. The residue was subjected to flash chromatography (33.6 g silica, 100% CH_2Cl_2 to 4% MeOH/CH_2Cl_2) giving a mixture of the iodinated intermediate and PPh_3O (2.600 g). This mixture was dissolved in DMF (10 mL) and NaN_3 (791 mg, 12.16 mmol) was added. The suspension was then heated under N_2 at 50 °C for 10 h. The mixture was diluted with EtOAc/Et_2O (1:1, 60 mL) and washed with H_2O (5×20 mL) to remove the DMF, then brine (20 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography (26 g silica, 100% CH_2Cl_2 to 10% MeOH/CH_2Cl_2) gave amino azide **14** (682 mg, 64% over two steps) as a white foam. TLC (10% MeOH/CH_2Cl_2) R_F = 0.21; $[\alpha]_D^{25}$ +0.61 (*c* 8.23, THF); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.43 – 6.20 (bm, 3H), 3.33 (dd, *J* = 12.0, 4.1 Hz, 1H), 3.26 – 3.05 (m, 3H), 2.96 (s, 2H), 2.92 – 2.80 (m, 1H), 2.57 (s, 3H), 2.51 (s, 3H), 2.10 (s, 3H), 1.71 – 1.55 (m, 4H), 1.55 – 1.39 (m, 7H), 1.38 – 1.21 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 156.3, 138.1, 132.7, 132.0, 124.6, 117.5, 86.4, 58.0, 50.6, 43.1, 40.8, 31.5, 28.5, 25.7, 19.2, 17.9, 12.4; IR (cm^{-1}) υ 3343, 2971, 2101, 1550, 1252, 1047, 994, 734, 659; MS (ES^+) *m/z* 438 (100%, M+H); HRMS (ES^+) Calcd. for $C_{19}H_{32}N_7O_3S$: 438.2287, Found: 438.2277.

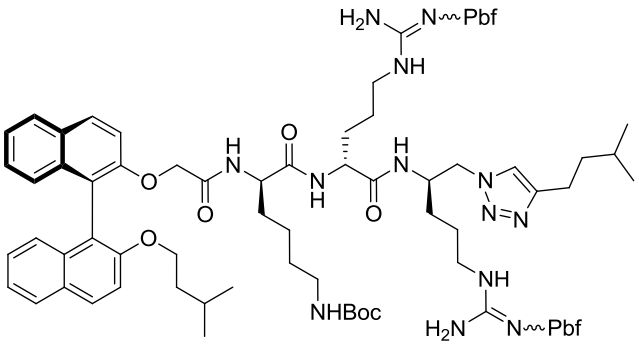
***tert*-Butyl ((*R*)-6-(((*R*)-1-(((*R*)-1-azido-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-1-oxo-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (15)**



This compound was prepared according to *General Procedure 1* using acid **4** (83.1 mg, 0.079 mmol), EDCI·HCl (18.2 mg, 0.095 mmol), HOBt (12.8 mg, 0.095 mmol), amine **14** (51.9 mg, 0.12 mmol) and MeCN (0.4 mL) with a 23 h reaction time. Work-up as described gave **15** (115.5 mg, 99%) as a pale yellow solid. TLC (10% MeOH/CH_2Cl_2) R_F = 0.65; $[\alpha]_D^{25}$ −19.7 (*c* 0.92, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 – 7.88 (m, 2H), 7.84 (app. t, *J* = 8.7 Hz, 2H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.17 (m, 6H), 7.17 – 7.09 (m, 2H), 6.48 – 6.08 (bm, 6H), 4.83 (bs, 1H), 4.50 (d, *J* = 14.6 Hz, 1H), 4.46 – 4.35 (m, 2H), 4.07 – 3.91 (m, 3H), 3.90 – 3.81 (m, 1H), 3.40 – 3.06 (m, 6H), 3.00 – 2.81 (m, 6H), 2.56 (s, 6H), 2.48 (s, 6H), 2.06 (s, 6H), 1.92 – 1.79 (m, 1H), 1.72 – 1.58 (m, 1H), 1.58 – 1.32 (m, 28H), 1.32 – 1.04 (m, 5H), 1.04 – 0.91 (m, 1H), 0.92 – 0.72 (m, 2H), 0.52 (d, *J* = 6.5 Hz, 3H), 0.47 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 171.5, 169.1, 158.7, 158.6, 156.5, 156.3, 156.1,

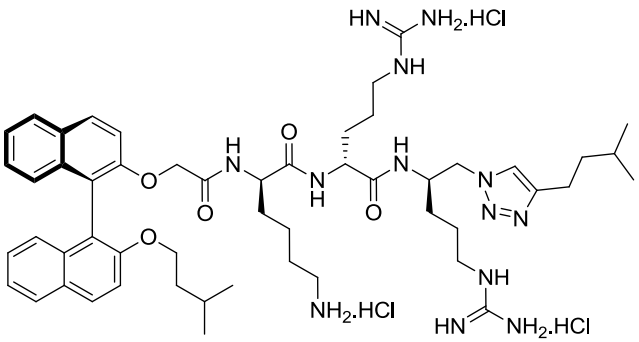
154.4, 152.2, 138.2, 138.1, 133.8, 133.6, 132.9, 132.6, 132.1, 129.8, 129.7, 129.6, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.6, 124.5, 124.1, 123.8, 120.4, 119.4, 117.5, 117.4, 115.9, 114.3, 86.33, 86.27, 78.9, 68.2, 68.0, 54.5, 53.1, 53.0, 49.0, 43.1, 40.7, 40.1, 37.9, 30.9, 29.3, 29.1, 29.0, 28.5, 28.4, 25.7, 25.4, 24.4, 22.5, 22.2, 22.0, 19.23, 19.19, 17.91, 17.87, 12.38, 12.36; IR (cm^{-1}) υ 3321, 2922, 2103, 1550, 1242, 1090, 807; MS (ES^+) *m/z* 1493 (100%, M+Na), 1471 (94%, M+H).

tert-Butyl ((*R*)-6-(((*R*)-1-(((*R*)-1-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)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 (16)



This compound was prepared according to *General Procedure 2* using azide **15** (55.0 mg, 0.037 mmol), $Cu(OAc)_2{\cdot}H_2O$ (1.5 mg, 0.0074 mmol), Na·ascorbate (2.9 mg, 0.015 mmol), 5-methyl-1-hexyne (10.7 mg, 0.11 mmol), *t*-BuOH (0.8 mL) and H_2O (0.2 mL) with a 21 h reaction time. Purification by a pipette silica plug (1.2 cm silica, 100% EtOAc) gave **16** (51.0 mg, 87%) as a pale yellow solid. TLC (100% EtOAc) R_F = 0.21; $[\alpha]_D^{25}$ −19.6 (*c* 2.47, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (app. d, *J* = 8.2 Hz, 2H), 7.88 – 7.79 (m, 2H), 7.54 – 7.38 (m, 3H), 7.38 – 7.17 (m, 5H), 7.17 – 7.07 (m, 2H), 6.59 – 6.16 (bm, 6H), 4.88 (bs, 1H), 4.52 (d, *J* = 14.3 Hz, 1H), 4.45 – 4.19 (m, 5H), 4.06 – 3.96 (m, 1H), 3.95 – 3.79 (m, 2H), 3.30 – 3.07 (m, 4H), 2.98 – 2.85 (m, 6H), 2.67 – 2.60 (m, 2H), 2.57 (s, 6H), 2.49 (s, 6H), 2.06 (s, 6H), 1.74 – 1.63 (m, 1H), 1.62 – 1.32 (m, 32H), 1.32 – 1.04 (m, 5H), 1.04 – 0.95 (m, 1H), 0.95 – 0.79 (m, 8H), 0.52 (d, *J* = 6.1 Hz, 3H), 0.46 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 171.4, 169.4, 158.7, 158.6, 156.6, 156.3, 156.1, 154.4, 152.2, 148.2, 138.20, 138.16, 133.8, 133.6, 133.0, 132.8, 132.15, 132.11, 129.8, 129.72, 129.68, 129.2, 128.0, 127.9, 126.7, 126.5, 125.5, 124.9, 124.6, 124.5, 124.2, 123.8, 122.4, 120.4, 119.5, 117.5, 117.4, 115.9, 114.4, 86.30, 86.27, 78.9, 68.3, 68.1, 53.4, 53.1, 52.6, 49.5, 43.2, 40.5, 40.1, 38.3, 37.9, 30.8, 29.1, 28.9, 28.52, 28.50, 28.4, 27.5, 25.6, 25.3, 24.4, 23.3, 22.5, 22.33, 22.32, 22.2, 22.0, 19.3, 19.2, 18.0, 17.9, 12.4; MS (ES^+) *m/z* 1589 (18%, M+Na), 1567 (100%, M+H); HRMS (ES^+) Calcd. for $C_{83}H_{115}N_{13}NaO_{13}S_2$: 1588.8076, Found: 1588.8105.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(((*R*)-5-guanidino-1-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)amino)-1-oxopentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·trihydrochloride (17)

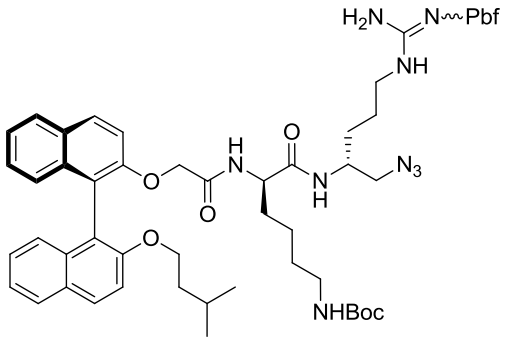


This compound was prepared according to *General Procedure 5* using **16** (48.0 mg, 0.031 mmol), CH_2Cl_2 (1.00 mL) and TFA (1.00 mL) with a 39.5 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.50 mL) as described gave **17** (27.5 mg, 84%) as a tan solid. $[\alpha]_D^{25}$ −1.5 (*c* 0.67, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.15 (s, 1H), 8.04 (app. d, *J* = 8.4 Hz, 2H), 7.97 – 7.89 (m, 2H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.51 (d, *J* = 8.9 Hz, 1H), 7.41 – 7.32 (m, 2H), 7.28 – 7.20 (m, 2H), 7.09 (d, *J* = 8.5 Hz, 1H), 7.04 (d, *J* = 8.5 Hz, 1H), 4.65 – 4.51 (m, 3H), 4.48

– 4.39 (m, 1H), 4.34 – 4.24 (m, 1H), 4.20 – 4.08 (m, 2H), 4.05 (t, *J* = 7.2 Hz, 1H), 3.99 – 3.91 (m, 1H), 3.26 – 3.10 (m, 4H), 2.87 – 2.75 (m, 4H), 1.82 – 1.47 (m, 12H), 1.35 – 1.03 (m, 6H), 0.97 (d, *J* = 5.3 Hz, 6H), 0.93 – 0.83 (m, 2H), 0.58 (d, *J* = 6.4 Hz, 3H), 0.52 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 174.3, 173.7, 171.4, 158.5, 155.9, 154.3, 146.5, 135.2, 135.1, 131.4, 130.9, 130.7, 129.3, 129.1, 128.0, 127.6, 127.5, 126.4, 126.0, 125.2, 124.8, 121.8, 120.7, 116.9, 116.3, 69.4, 69.0, 56.7, 54.7, 54.5, 50.6, 41.9, 41.8, 40.5, 39.3, 38.4, 31.8, 29.7, 29.6, 28.7, 27.9, 26.4, 26.1, 25.6, 23.4, 22.8, 22.62, 22.60, 22.5; IR (cm^{-1}) υ 3174, 2959, 1653, 1507, 1213, 1170, 1046, 1006, 810, 745; MS (ES^+) *m/z* 482 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{52}H_{76}N_{13}O_5$: 962.6092, Found: 962.6122.

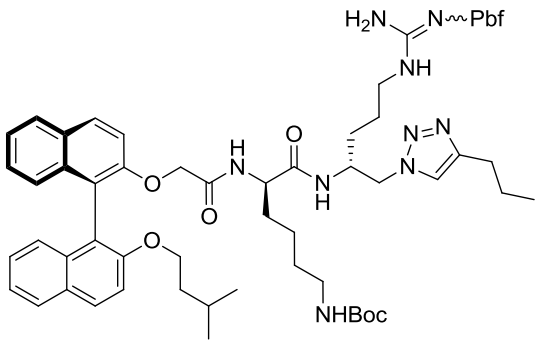
Synthesis and Characterization of Class B Triazoles

***tert*-Butyl ((*R*)-6-(((*R*)-1-azido-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 (18)**



This compound was prepared according to *General Procedure 1* using the known acid **2**[S1] (1.806 g, 2.81 mmol), EDCI·HCl (646 mg, 3.37 mmol), HOBt (455 mg, 3.37 mmol), amine **14** (1.266 g, 2.89 mmol) and MeCN (28 mL) with a 4.5 h reaction time. Work-up as described gave **18** (2.899 g, 97%) as an off-white solid. TLC (10% MeOH/CH_2Cl_2) R_F = 0.60, (75% EtOAc/pet. ether) R_F = 0.68; $[\alpha]_D^{25}$ −24.0 (*c* 5.31, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (app. t, *J* = 9.4 Hz, 2H), 7.92 – 7.83 (m, 2H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.41 – 7.20 (m, 5H), 7.18 – 7.09 (m, 2H), 6.72 (d, *J* = 8.5 Hz, 1H), 6.17 (d, *J* = 7.6 Hz, 1H), 6.07 (bs, 2H), 4.59 (t, *J* = 5.7 Hz, 1H), 4.45 (ABq, $\Delta\delta_{AB}$ = 0.06, *J* = 14.5 Hz, 2H), 4.09 – 3.96 (m, 2H), 3.96 – 3.85 (m, 2H), 3.30 (dd, *J* = 12.4, 4.5 Hz, 1H), 3.23 (dd, *J* = 12.4, 5.8 Hz, 1H), 3.17 – 3.02 (m, 2H), 3.03 – 2.84 (m, 4H), 2.56 (s, 3H), 2.50 (s, 3H), 2.08 (s, 3H), 1.51 – 1.31 (m, 20H), 1.31 – 1.06 (m, 5H), 0.97 – 0.75 (m, 3H), 0.55 (d, *J* = 6.5 Hz, 3H), 0.50 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 168.8, 158.6, 156.1, 155.9, 154.4, 152.1, 138.2, 133.8, 133.6, 133.2, 132.1, 129.8, 129.75, 129.68, 129.2, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.4, 124.1, 123.7, 120.4, 119.3, 117.3, 115.9, 114.2, 86.2, 78.9, 68.3, 67.9, 54.6, 52.6, 48.8, 43.2, 40.5, 40.0, 37.9, 31.1, 29.1, 28.5, 28.4, 25.6, 24.5, 22.4, 22.20, 22.16, 22.0, 19.2, 17.9, 12.4; IR (cm^{-1}) υ 3330, 2929, 2097, 1653, 1507, 1244, 1087, 808; MS (ES^+) *m/z* 1085 (24%, M+Na), 1063 (100%, M+H); HRMS (ES^+) Calcd. for $C_{57}H_{75}N_9NaO_9S$: 1084.5306, Found: 1084.5342.

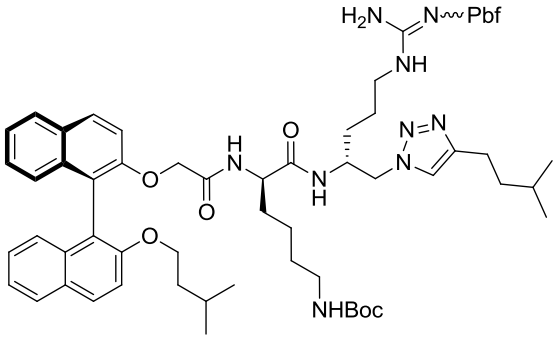
***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxo-6-(((*R*)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)-1-(4-propyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)amino)hexyl)carbamate (19)**



This compound was prepared according to *General Procedure 2* using azide **18** (45.0 mg, 0.042 mmol), $Cu(OAc)_2{\cdot}H_2O$ (1.7 mg, 0.0085 mmol), Na·ascorbate (3.3 mg, 0.017 mmol), 1-pentyne (8.6 mg, 0.13 mmol), *t*-BuOH (0.89 mL) and H_2O (0.21 mL) with a 14 h reaction time. Flash chromatography (2.4 g silica, 100% EtOAc) gave **19** (43.3 mg, 90%) as a pale yellow solid. TLC (2% MeOH/EtOAc) R_F = 0.53; $[\alpha]_D^{25}$ −23.5 (*c* 1.97, CH_2Cl_2);

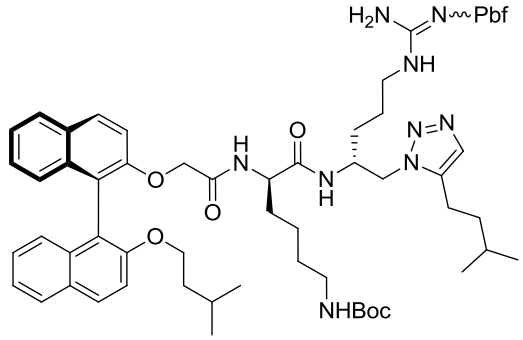
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (app. t, *J* = 9.5 Hz, 2H), 7.84 (app. t, *J* = 7.7 Hz, 2H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.38 (s, 1H), 7.36 – 7.17 (m, 5H), 7.16 – 7.07 (m, 3H), 6.24 (bs, 2H), 6.18 (bd, *J* = 6.9 Hz, 1H), 4.88 (bs, 1H), 4.48 (d, *J* = 14.5 Hz, 1H), 4.41 – 4.27 (m, 3H), 4.26 – 4.16 (m, 1H), 4.07 – 3.92 (m, 2H), 3.92 – 3.84 (m, 1H), 3.15 – 3.05 (m, 2H), 2.98 – 2.84 (m, 4H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.67 (sex, *J* = 7.3 Hz, 2H), 1.56 – 1.34 (m, 19H), 1.34 – 1.09 (m, 6H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.86 – 0.78 (m, 1H), 0.77 – 0.64 (m, 2H), 0.53 (d, *J* = 6.4 Hz, 3H), 0.49 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 168.9, 158.6, 156.2, 156.1, 154.3, 152.1, 147.9, 138.2, 133.7, 133.5, 132.9, 132.1, 129.7, 129.72, 129.69, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.7, 122.1, 120.2, 119.3, 117.4, 115.8, 114.1, 86.3, 78.9, 68.2, 67.8, 52.9, 52.6, 49.2, 43.1, 40.5, 39.9, 37.8, 30.9, 29.6, 29.0, 28.5, 28.4, 27.5, 25.3, 24.4, 22.6, 22.3, 22.2, 22.0, 19.3, 17.9, 13.8, 12.4; MS (ES$^+$) *m/z* 1153 (57%, M+Na), 1131 (100%, M+H); HRMS (ES$^+$) Calcd. for $C_{62}H_{84}N_9O_9S$: 1130.6113, Found: 1130.6077.

tert-Butyl ((*R*)-6-(((*R*)-1-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)-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 (20)



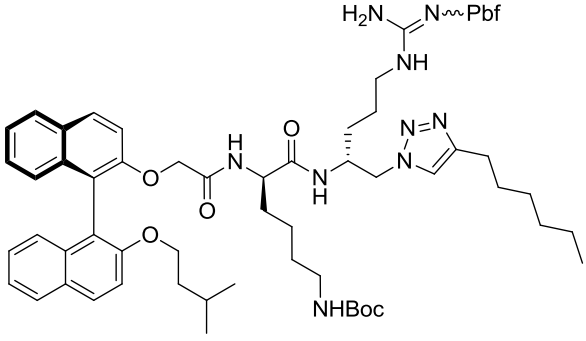
This compound was prepared according to *General Procedure 2* using azide **18** (100 mg, 0.094 mmol), $Cu(OAc)_2{\cdot}H_2O$ (3.8 mg, 0.019 mmol), Na·ascorbate (7.5 mg, 0.038 mmol), 5-methyl-1-hexyne (27.2 mg, 0.28 mmol), *t*-BuOH (2.0 mL) and H_2O (0.5 mL) with a 20 h reaction time. Flash chromatography (3.5 g silica, 100% EtOAc) gave **20** (73.4 mg, 67%) as a white solid. TLC (2% MeOH/EtOAc) R_F = 0.42, (75% EtOAc/ pet. ether) R_F = 0.15; $[\alpha]_D^{25}$ −25.1 (*c* 0.72, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.90 (m, 2H), 7.85 (app. t, *J* = 7.7 Hz, 2H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.38 (s, 1H), 7.37 – 7.27 (m, 3H), 7.26 – 7.17 (m, 2H), 7.17 – 7.07 (m, 3H), 6.25 (bs, 2H), 6.19 (bd, *J* = 6.1 Hz, 1H), 4.91 – 4.84 (m, 1H), 4.48 (d, *J* = 14.5 Hz, 1H), 4.41 – 4.27 (m, 3H), 4.26 – 4.15 (m, 1H), 4.06 – 3.95 (m, 2H), 3.92 – 3.85 (m, 1H), 3.15 – 3.04 (m, 2H), 2.98 – 2.84 (m, 4H), 2.69 (t, *J* = 8.0 Hz, 2H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.65 – 1.51 (m, 3H), 1.43 (t, *J* = 11.8 Hz, 19H), 1.29 – 1.09 (m, 6H), 0.94 (d, *J* = 6.5 Hz, 6H), 0.86 – 0.78 (m, 1H), 0.76 – 0.62 (m, 2H), 0.53 (d, *J* = 6.4 Hz, 3H), 0.49 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 168.8, 158.6, 156.2, 156.0, 154.3, 152.1, 148.3, 138.1, 133.8, 133.6, 133.0, 132.1, 129.7, 129.6, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.7, 121.9, 120.3, 119.3, 117.4, 115.8, 114.2, 86.3, 78.8, 68.2, 67.9, 52.8, 52.6, 49.2, 43.2, 40.5, 39.9, 38.4, 37.9, 31.0, 29.0, 28.5, 28.4, 27.7, 25.3, 24.5, 23.5, 22.4, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES$^+$) *m/z* 1197 (11%, M+K), 1181 (26%, M+Na), 1159 (100%, M+H); HRMS (ES$^+$) Calcd. for $C_{64}H_{87}N_9NaO_9S$: 1180.6245, Found: 1180.6309.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(5-isopentyl-1*H*-1,2,3-triazol-1-yl)-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 (21)**



This compound was prepared according to *General Procedure 3* using azide **18** (50.0 mg, 0.047 mmol), Cp*RuCl(PPh$_3$)$_2$ (1.9 mg, 0.0024 mmol), 5-methyl-1-hexyne (9.0 mg, 0.094 mmol) and 1,4-dioxane (0.47 mL) with a 20 h reaction time. Flash chromatography (3.0 g silica, 80% EtOAc/pet. ether to 100% EtOAc) gave **21** (40.2 mg, 74%) as a pale yellow solid. TLC (100% EtOAc) R_F = 0.11; $[\alpha]_D^{25}$ −23.0 (*c* 1.88, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.89 (m, 2H), 7.89 – 7.81 (m, 2H), 7.48 – 7.40 (m, 2H), 7.38 – 7.17 (m, 6H), 7.13 (d, *J* = 8.5 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 1H), 6.27 – 6.13 (bm, 3H), 5.02 – 4.92 (m, 1H), 4.48 (d, *J* = 14.5 Hz, 1H), 4.37 (d, *J* = 14.5 Hz, 1H), 4.31 – 4.16 (m, 3H), 4.08 – 3.99 (m, 1H), 3.99 – 3.85 (m, 2H), 3.21 – 3.07 (m, 2H), 2.99 – 2.85 (m, 4H), 2.71 – 2.60 (m, 2H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.66 – 1.51 (m, 3H), 1.51 – 1.37 (m, 19H), 1.35 – 1.09 (m, 6H), 0.95 (d, *J* = 6.3 Hz, 6H), 0.91 – 0.79 (m, 1H), 0.77 – 0.62 (m, 2H), 0.54 (d, *J* = 6.4 Hz, 3H), 0.49 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 168.9, 158.6, 156.2, 156.0, 154.3, 152.2, 138.2, 135.1, 133.8, 133.6, 133.1, 132.2, 131.6, 129.8, 129.72, 129.67, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.5, 124.1, 123.7, 120.4, 119.3, 117.4, 115.9, 114.2, 86.3, 78.8, 68.2, 68.0, 52.7, 50.8, 48.7, 43.2, 40.6, 40.1, 37.9, 36.9, 30.9, 29.2, 28.5, 28.4, 27.6, 25.3, 24.5, 23.4, 22.5, 22.32, 22.29, 22.2, 22.1, 21.0, 19.3, 17.9, 12.4; MS (ES$^+$) *m/z* 1181 (73%, M+Na), 1159 (100%, M+H); HRMS (ES$^-$) Calcd. for $C_{64}H_{86}N_9O_9S$: 1156.6269, Found: 1156.6318.

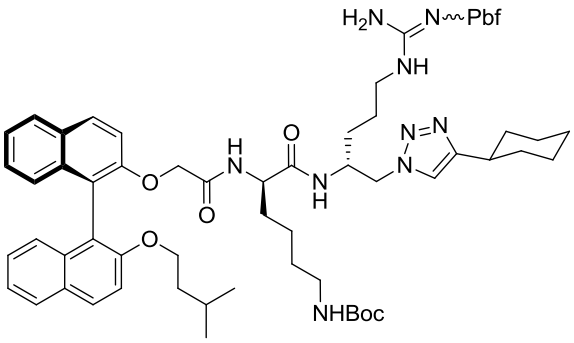
***tert*-Butyl ((*R*)-6-(((*R*)-1-(4-hexyl-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (22)**



This compound was prepared according to *General Procedure 2* using azide **18** (50.0 mg, 0.047 mmol), Cu(OAc)$_2$·H$_2$O (1.9 mg, 0.0094 mmol), Na·ascorbate (3.7 mg, 0.019 mmol), 1-octyne (15.6 mg, 0.14 mmol), *t*-BuOH (1.0 mL) and H$_2$O (0.25 mL) with a 24 h reaction time. Work-up as described gave **22** (52.0 mg, 94%) as an off-white solid. TLC (100% EtOAc) R_F = 0.10; $[\alpha]_D^{25}$ −21.9 (*c* 2.45, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.90 (m, 2H), 7.85 (app. t, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.38 (s, 1H), 7.37 – 7.26 (m, 3H), 7.26 – 7.17 (m, 3H), 7.14 (d, *J* = 8.5 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 1H), 6.27 (bs, 2H), 6.18 (bd, *J* = 5.7 Hz, 1H), 4.90 (bs, 1H), 4.48 (d, *J* = 14.5 Hz, 1H), 4.41 – 4.27 (m, 3H), 4.25 – 4.16 (m, 1H), 4.07 – 3.95 (m, 2H), 3.93 – 3.85 (m, 1H), 3.15 – 3.04 (m, 2H), 2.97 – 2.84 (m, 4H), 2.67 (t, *J* = 7.5 Hz, 2H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.69 – 1.59 (m, 2H), 1.52 – 1.08 (m, 29H), 0.94 – 0.76 (m, 4H), 0.75 – 0.63 (m, 2H), 0.53 (d, *J* = 6.3 Hz, 3H), 0.49 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.8, 158.6, 156.2, 156.0, 154.3, 152.1, 148.1, 138.1, 133.8, 133.6, 133.0, 132.1, 129.7, 129.6, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.7, 121.9, 120.3, 119.3, 117.4, 115.9, 114.2, 86.3, 78.8, 68.2, 67.9, 52.8, 52.6, 49.2, 43.2, 40.5, 39.9, 37.9, 31.5, 31.0, 29.4, 29.02, 28.95, 28.5, 28.4, 25.6, 25.3, 24.5, 22.5, 22.4, 22.2,

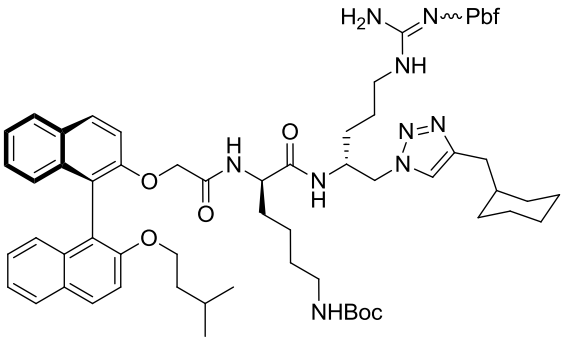
22.0, 19.2, 17.9, 14.0, 12.4; MS (ES^+) *m/z* 1195 (100%, M+Na), 1173 (92%, M+H); HRMS (ES^+) Calcd. for $C_{65}H_{89}N_9NaO_9S$: 1194.6402, Found: 1194.6436.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(4-cyclohexyl-1*H*-1,2,3-triazol-1-yl)-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 (23)**



This compound was prepared according to *General Procedure 2* using azide **18** (45.0 mg, 0.042 mmol), $Cu(OAc)_2{\cdot}H_2O$ (1.7 mg, 0.0085 mmol), Na·ascorbate (3.3 mg, 0.017 mmol), cyclohexylacetylene (14.1 mg, 0.13 mmol), *t*-BuOH (0.89 mL) and H_2O (0.21 mL) with a 3.5 h reaction time. Purification by a pipette silica plug (3 cm silica, 100% pet. ether then 100% EtOAc) gave **23** (40.9 mg, 82%) as a white solid. TLC (2% MeOH/EtOAc) R_F = 0.42, (75% EtOAc/ pet. ether) R_F = 0.15; $[\alpha]_D^{25}$ −22.5 (*c* 0.75, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (app. t, *J* = 8.7 Hz, 2H), 7.88 – 7.81 (m, 2H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.12 (m, 8H), 7.10 (d, *J* = 8.5 Hz, 1H), 6.34 – 6.24 (bm, 3H), 6.18 (bd, *J* = 5.7 Hz, 1H), 4.87 (bs, 1H), 4.48 (d, *J* = 14.4 Hz, 1H), 4.41 – 4.27 (m, 3H), 4.26 – 4.16 (m, 1H), 4.07 – 3.95 (m, 2H), 3.93 – 3.85 (m, 1H), 3.17 – 3.03 (m, 2H), 2.96 – 2.83 (m, 4H), 2.77 – 2.67 (m, 1H), 2.55 (s, 3H), 2.48 (s, 3H), 2.12 – 1.98 (m, 5H), 1.87 – 1.70 (m, 3H), 1.52 – 1.32 (m, 23H), 1.31 – 1.08 (m, 7H), 0.87 – 0.75 (m, 1H), 0.75 – 0.62 (m, 2H), 0.53 (d, *J* = 6.4 Hz, 3H), 0.49 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.8, 158.6, 156.2, 156.0, 154.3, 153.3, 152.1, 138.2, 133.8, 133.6, 133.0, 132.1, 129.7, 129.6, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.7, 120.7, 120.3, 119.3, 117.4, 115.8, 114.2, 86.3, 78.8, 68.2, 67.9, 52.8, 52.6, 49.2, 43.2, 40.5, 39.9, 37.9, 35.2, 32.9, 31.1, 29.1, 29.0, 28.5, 28.4, 26.1, 26.0, 25.3, 24.5, 22.4, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1209 (25%, M+K), 1193 (100%, M+Na), 1170 (48%, M+H); HRMS (ES^+) Calcd. for $C_{65}H_{87}N_9NaO_9S$: 1192.6245, Found: 1192.6278.

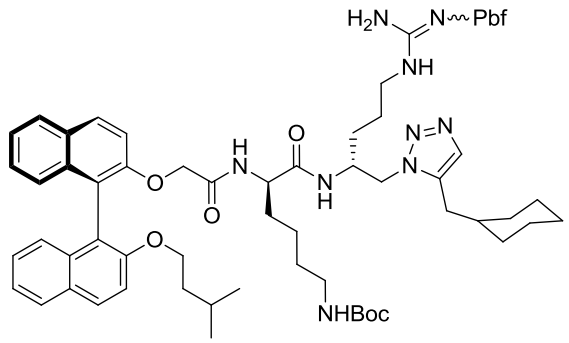
***tert*-Butyl ((*R*)-6-(((*R*)-1-(4-(cyclohexylmethyl)-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (24)**



This compound was prepared according to *General Procedure 2* using azide **18** (45.0 mg, 0.042 mmol), $Cu(OAc)_2{\cdot}H_2O$ (1.7 mg, 0.0085 mmol), Na·ascorbate (3.3 mg, 0.017 mmol), 3-cyclohexyl-1-propyne (15.9 mg, 0.13 mmol), *t*-BuOH (0.89 mL) and H_2O (0.21 mL) with a 14 h reaction time. Flash chromatography (2.4 g silica, 100% EtOAc) gave **24** (46.5 mg, 93%) as an off-white solid. TLC (2% MeOH/EtOAc) R_F = 0.33; $[\alpha]_D^{25}$ −23.3 (*c* 2.17, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.89 (m, 2H), 7.84 (app. t, *J* = 7.1 Hz, 2H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.26 (m, 4H), 7.26 – 7.16 (m, 2H), 7.13 (d, *J* = 8.5 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 1H), 7.02 (bs, 1H), 6.25 – 6.14 (bm, 3H), 4.84 (bs, 1H), 4.47 (d, *J* = 14.6 Hz, 1H), 4.41 – 4.27 (m, 3H), 4.26 – 4.16 (m, 1H), 4.06 – 3.99 (m, 1H), 3.99 – 3.92 (m, 1H), 3.92 – 3.85 (m, 1H), 3.16 – 3.05 (m, 2H), 2.98 – 2.84 (m, 4H), 2.63 – 2.52 (m, 5H), 2.49 (s, 3H), 2.07 (s, 3H), 1.74 – 1.57 (m, 5H), 1.52 – 1.34 (m, 19H), 1.33 – 1.10 (m, 9H), 1.01 – 0.80 (m, 4H), 0.79 – 0.66 (m, 2H),

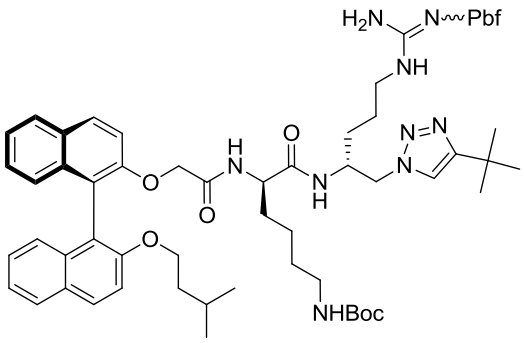
0.54 (d, J = 6.4 Hz, 3H), 0.49 (d, J = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.9, 158.7, 156.2, 156.1, 154.4, 152.2, 146.7, 138.2, 133.9, 133.7, 133.1, 132.1, 129.81, 129.75, 129.7, 129.2, 128.0, 127.9, 126.6, 126.5, 125.5, 125.0, 124.5, 124.1, 123.8, 122.6, 120.4, 119.5, 117.4, 116.0, 114.3, 86.3, 78.9, 68.4, 68.0, 52.9, 52.7, 49.2, 43.2, 40.6, 40.0, 38.0, 37.9, 33.3, 33.02, 32.99, 30.9, 29.1, 28.5, 28.4, 26.4, 26.1, 25.3, 24.5, 22.4, 22.2, 22.1, 19.2, 17.9, 12.4; MS (ES^+) *m/z* 1207 (100%, M+Na), 1185 (83%, M+H); HRMS (ES^+) Calcd. for $C_{66}H_{90}N_9O_9S$: 1184.6582, Found: 1184.6550.

tert-Butyl ((_R_)-6-(((_R_)-1-(5-(cyclohexylmethyl)-1_H_-1,2,3-triazol-1-yl)-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 (25)



This compound was prepared according to *General Procedure 3* using azide **18** (75.0 mg, 0.071 mmol), Cp*RuCl(PPh_3)$_2$ (2.8 mg, 0.0035 mmol), 3-cyclohexyl-1-propyne (17.3 mg, 0.14 mmol) and 1,4-dioxane (0.71 mL) with a 24 h reaction time. Flash chromatography (3.0 g silica, 100% EtOAc) gave **25** (58.2 mg, 70%) as a tan solid. TLC (100% EtOAc) R_F = 0.15; $[\alpha]_D^{25}$ −25.9 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (app. t, J = 9.4 Hz, 2H), 7.89 – 7.83 (m, 2H), 7.47 – 7.40 (m, 2H), 7.38 – 7.07 (m, 8H), 6.20 – 6.13 (bm, 3H), 4.94 (bs, 1H), 4.49 (d, J = 14.6 Hz, 1H), 4.37 (d, J = 14.5 Hz, 1H), 4.29 – 4.24 (m, 2H), 4.23 – 4.15 (m, 1H), 4.08 – 3.99 (m, 1H), 3.97 – 3.85 (m, 2H), 3.16 – 3.10 (m, 2H), 3.00 – 2.86 (m, 4H), 2.63 – 2.53 (m, 4H), 2.53 – 2.45 (m, 4H), 2.07 (s, 3H), 1.74 – 1.65 (m, 6H), 1.60 – 1.36 (m, 21H), 1.32 – 1.07 (m, 8H), 1.04 – 0.80 (m, 3H), 0.80 – 0.64 (m, 2H), 0.54 (d, J = 6.5 Hz, 3H), 0.49 (d, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 168.9, 158.6, 156.15, 156.06, 154.3, 152.1, 138.2, 136.8, 133.8, 133.6, 133.0, 132.5, 132.1, 129.8, 129.70, 129.67, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.5, 124.1, 123.8, 120.2, 119.3, 117.4, 115.8, 114.1, 86.3, 78.9, 68.2, 67.8, 52.7, 50.7, 48.8, 43.2, 40.6, 40.0, 37.9, 37.4, 33.1, 32.9, 30.8, 30.5, 29.2, 29.1, 28.6, 28.4, 26.1, 26.0, 25.9, 25.1, 24.5, 22.5, 22.3, 22.1, 19.3, 18.0, 12.5; MS (ES^+) *m/z* 1207 (64%, M+Na), 1185 (100%, M+H).

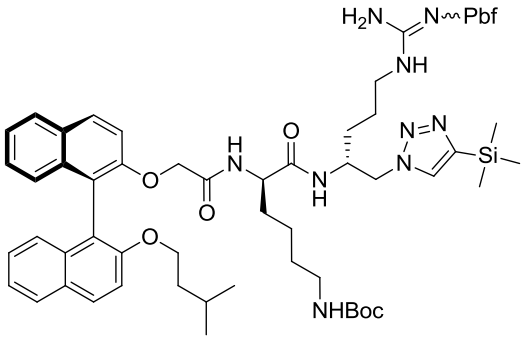
tert-Butyl ((_R_)-6-(((_R_)-1-(4-(_tert_-butyl)-1_H_-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((_S_)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (26)



This compound was prepared according to *General Procedure 2* using azide **18** (50.0 mg, 0.047 mmol), $Cu(OAc)_2{\cdot}H_2O$ (1.9 mg, 0.0094 mmol), Na·ascorbate (3.7 mg, 0.019 mmol), *tert*-butylacetylene (11.5 mg, 0.14 mmol), *t*-BuOH (1.0 mL) and H_2O (0.25 mL) with a 7 h reaction time. Work-up as described gave **26** (53.1 mg, 99%) as an off-white solid. TLC (100% EtOAc) R_F = 0.09; $[\alpha]_D^{25}$ −17.0 (*c* 2.57, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 – 7.90 (m, 2H), 7.88 – 7.81 (m, 2H), 7.44 (d, J = 8.9 Hz, 1H), 7.39 – 7.26 (m, 4H), 7.25 – 7.17 (m, 2H), 7.17 – 7.12 (m, 2H), 7.10 (d, J = 8.5 Hz, 1H), 6.28 (bs, 2H), 6.18 (bd, J = 6.5 Hz, 1H), 4.87 (bs, 1H), 4.49 (d, J = 14.5 Hz, 1H), 4.42 – 4.27 (m, 3H), 4.26 – 4.18 (m, 1H), 4.08 – 4.00 (m, 1H), 4.00 – 3.93 (m,

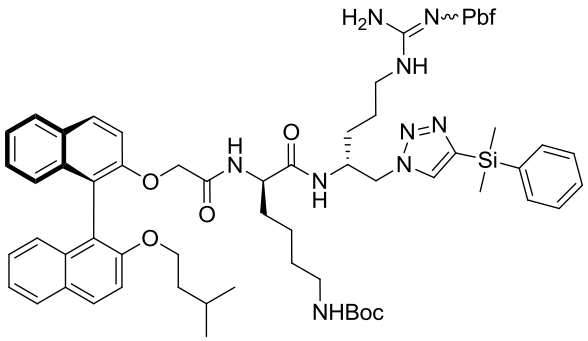
1H), 3.93 – 3.86 (m, 1H), 3.16 – 3.06 (m, 2H), 2.97 – 2.82 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.06 (s, 3H), 1.52 – 1.38 (m, 19H), 1.33 (s, 9H), 1.29 – 1.09 (m, 6H), 0.87 – 0.76 (m, 1H), 0.76 – 0.66 (m, 2H), 0.54 (d, *J* = 6.4 Hz, 3H), 0.49 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.8, 158.6, 157.4, 156.2, 156.0, 154.3, 152.1, 138.2, 133.8, 133.6, 133.1, 132.1, 129.74, 129.73, 129.6, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.8, 120.3, 119.9, 119.4, 117.4, 115.9, 114.2, 86.3, 78.9, 68.3, 67.9, 52.8, 52.6, 49.1, 43.2, 40.5, 39.9, 37.9, 30.9, 30.4, 29.1, 28.9, 28.5, 28.40, 28.38, 25.2, 24.5, 22.4, 22.2, 22.1, 19.2, 17.9, 12.4; MS (ES^+) *m/z* 1167 (100%, M+Na), 1145 (67%, M+H); HRMS (ES^+) Calcd. for $C_{63}H_{86}N_9O_9S$: 1144.6269, Found: 1144.6288.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxo-6-(((*R*)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)-1-(4-(trimethylsilyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)amino)hexyl)carbamate (27)**



A solution of azide **18** (200 mg, 0.19 mmol) and TMS-acetylene (0.28 mL, 1.88 mmol) in toluene (1.9 mL) was heated at 100 °C in a sealed tube under N_2 for 24 h. The solvent was removed under reduced pressure and the residue was subjected to flash chromatography (6.0 g silica, 80% EtOAc/pet. ether to 100% EtOAc) to give **27** (203 mg, 93%) as a white solid. TLC (100% EtOAc) R_F = 0.54; $[\alpha]_D^{25}$ −23.6 (*c* 0.64, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (app. t, *J* = 9.3 Hz, 2H), 7.85 (app. t, *J* = 8.8 Hz, 2H), 7.62 (s, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.12 (m, 6H), 7.10 (d, *J* = 8.5 Hz, 1H), 7.04 (bs, 1H), 6.23 (bs, 2H), 6.17 (bd, *J* = 5.7 Hz, 1H), 4.86 – 4.79 (m, 1H), 4.49 (d, *J* = 14.5 Hz, 1H), 4.44 – 4.34 (m, 3H), 4.29 – 4.18 (m, 1H), 4.06 – 3.99 (m, 1H), 3.99 – 3.93 (m, 1H), 3.92 – 3.85 (m, 1H), 3.16 – 3.05 (m, 2H), 2.96 – 2.83 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.06 (s, 3H), 1.53 – 1.33 (m, 19H), 1.27 – 1.08 (m, 6H), 0.91 – 0.63 (m, 3H), 0.53 (d, *J* = 6.4 Hz, 3H), 0.49 (d, *J* = 6.3 Hz, 3H), 0.32 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.9, 158.6, 156.2, 156.0, 154.3, 152.1, 146.3, 138.2, 133.8, 133.6, 133.0, 132.1, 130.3, 129.7, 129.6, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.8, 120.3, 119.4, 117.4, 115.9, 114.2, 86.3, 78.9, 68.3, 67.9, 52.6, 52.4, 49.2, 43.2, 40.5, 39.9, 37.9, 30.8, 29.1, 28.9, 28.5, 28.4, 25.2, 24.5, 22.4, 22.2, 22.1, 19.3, 17.9, 12.4, −1.1; MS (ES^+) *m/z* 1182 (10%, M+Na), 1160 (100%, M+H); HRMS (ES^+) Calcd. for $C_{62}H_{86}N_9O_9SSi$: 1160.6039, Found: 1160.6083.

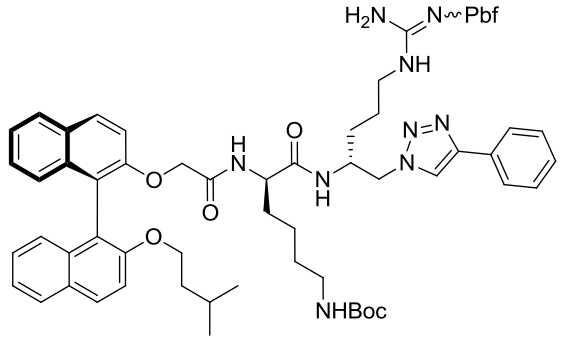
***tert*-Butyl ((*R*)-6-(((*R*)-1-(4-(dimethyl(phenyl)silyl)-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (28)**



A solution of azide **18** (63.7 mg, 0.060 mmol) and dimethylphenylsilylacetylene (0.053 mL, 0.30 mmol) in toluene (0.6 mL) was heated at 100 °C in a sealed tube under N_2 for 40 h. The solvent was removed under reduced pressure and the residue was subjected to flash chromatography (3.0 g silica, 100% EtOAc) to give **28** (70.8 mg, 96%) as a white solid. TLC (2% MeOH/EtOAc) R_F = 0.32; $[\alpha]_D^{25}$ −22.8 (*c* 3.26, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 – 7.88 (m, 2H), 7.87 – 7.79 (m, 2H), 7.61 (s, 1H), 7.58 (app. d, *J* = 6.3 Hz, 2H), 7.42 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.16 (m, 8H), 7.14 (d, *J* = 8.5 Hz, 1H), 7.09 (d, *J*

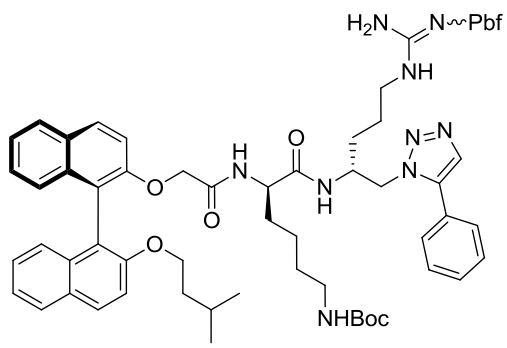
= 8.4 Hz, 1H), 6.24 (bs, 2H), 6.16 (bd, *J* = 5.1 Hz, 1H), 4.82 – 4.73 (m, 1H), 4.46 (d, *J* = 14.3 Hz, 1H), 4.40 – 4.31 (m, 3H), 4.27 – 4.16 (m, 1H), 4.06 – 3.98 (m, 1H), 3.98 – 3.92 (m, 1H), 3.91 – 3.84 (m, 1H), 3.15 – 3.02 (m, 2H), 2.89 (s, 2H), 2.87 – 2.78 (m, 2H), 2.53 (s, 3H), 2.46 (s, 3H), 2.05 (s, 3H), 1.51 – 1.31 (m, 19H), 1.28 – 1.07 (m, 6H), 0.85 – 0.73 (m, 1H), 0.72 – 0.62 (m, 2H), 0.59 (s, 6H), 0.53 (d, *J* = 6.4 Hz, 3H), 0.48 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.8, 158.6, 156.2, 156.0, 154.3, 152.1, 144.7, 138.2, 136.9, 133.9, 133.8, 133.6, 133.0, 132.1, 131.2, 129.7, 129.6, 129.4, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.7, 120.3, 119.3, 117.4, 115.8, 114.2, 86.3, 78.8, 68.2, 67.9, 52.6, 52.4, 49.1, 43.2, 40.5, 39.9, 37.9, 30.8, 29.0, 28.9, 28.5, 28.4, 25.1, 24.5, 22.3, 22.2, 22.0, 19.3, 17.9, 12.4, −2.3; MS (ES^+) *m/z* 1244 (16%, M+Na), 1222 (100%, M+H); HRMS (ES^+) Calcd. for $C_{67}H_{88}N_9O_9SSi$: 1222.6195, Found: 1222.6223.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxo-6-(((*R*)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)-1-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)amino)hexyl)carbamate (29)**



This compound was prepared according to *General Procedure 2* using azide **18** (100 mg, 0.094 mmol), $Cu(OAc)_2{\cdot}H_2O$ (3.8 mg, 0.019 mmol), Na·ascorbate (7.5 mg, 0.038 mmol), phenylacetylene (28.8 mg, 0.28 mmol), *t*-BuOH (2.0 mL) and H_2O (0.5 mL) with a 4.5 h reaction time. Flash chromatography (3.3 g silica, 100% CH_2Cl_2 to 10% MeOH/CH_2Cl_2) gave **29** (98.2 mg, 90%) as a white solid. TLC (10% MeOH/CH_2Cl_2) R_F = 0.60, (75% EtOAc/ pet. ether) R_F = 0.10; $[\alpha]_D^{25}$ −19.0 (*c* 4.57, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.96 – 7.80 (m, 4H), 7.77 (d, *J* = 8.6 Hz, 1H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.49 – 7.41 (m, 2H), 7.40 – 7.29 (m, 2H), 7.29 – 7.17 (m, 4H), 7.17 – 7.07 (m, 3H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.30 (bs, 2H), 6.11 (bs, 1H), 4.85 (bs, 1H), 4.46 (d, *J* = 10.9 Hz, 1H), 4.41 – 4.23 (m, 3H), 4.07 – 4.00 (m, 1H), 3.96 – 3.86 (m, 1H), 3.83 – 3.72 (m, 1H), 3.17 – 3.06 (m, 2H), 2.87 (s, 2H), 2.84 – 2.75 (m, 2H), 2.56 (s, 3H), 2.47 (s, 3H), 2.06 (s, 3H), 1.57 – 1.29 (m, 19H), 1.29 – 1.21 (m, 1H), 1.16 – 1.00 (m, 5H), 0.78 – 0.62 (m, 1H), 0.61 – 0.49 (m, 2H), 0.47 (d, *J* = 5.9 Hz, 3H), 0.43 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 168.6, 158.6, 156.0, 155.9, 154.1, 151.9, 147.1, 138.1, 133.6, 133.4, 132.9, 132.0, 130.5, 129.63, 129.59, 129.0, 128.9, 128.1, 127.9, 127.8, 126.43, 126.37, 125.5, 125.4, 124.7, 124.5, 124.0, 123.6, 121.4, 120.1, 118.9, 117.3, 115.6, 114.1, 86.2, 78.6, 67.9, 67.7, 53.3, 52.2, 49.1, 43.0, 40.2, 39.7, 37.7, 31.4, 29.1, 28.6, 28.4, 28.3, 26.0, 24.3, 22.2, 22.1, 21.9, 19.2, 17.9, 12.4; MS (ES^+) *m/z* 1165 (100%, M+H); HRMS (ES^+) Calcd. for $C_{65}H_{82}N_9O_9S$: 1164.5956, Found: 1164.5991.

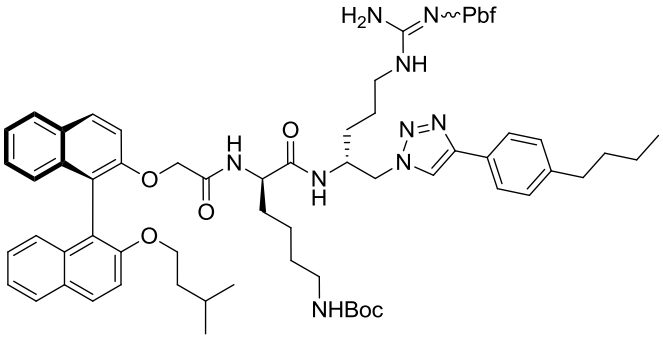
***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxo-6-(((*R*)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)-1-(5-phenyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)amino)hexyl)carbamate (30)**



This compound was prepared according to *General Procedure 3* using azide **18** (50.0 mg, 0.047 mmol), $Cp^*RuCl(PPh_3)_2$ (1.9 mg, 0.0024 mmol), phenylacetylene (9.0 mg, 0.094 mmol) and 1,4-dioxane (0.47 mL) with a 20 h reaction time. Flash chromatography (2.7 g silica, 80% EtOAc/pet. ether to 100% EtOAc) gave **30** (44.9 mg, 82%) as a pale yellow solid. TLC (100% EtOAc) R_F = 0.17; $[\alpha]_D^{25}$ −30.0 (*c* 2.13, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95

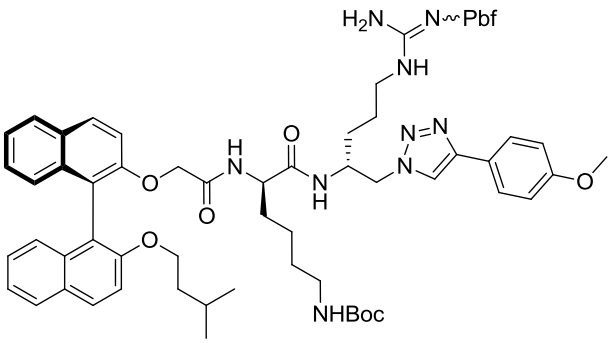
(app. t, *J* = 9.6 Hz, 2H), 7.90 – 7.81 (m, 2H), 7.69 (s, 1H), 7.51 – 7.12 (m, 13H), 7.10 (d, *J* = 8.4 Hz, 1H), 6.16 (bd, *J* = 6.7 Hz, 1H), 6.10 (bs, 2H), 5.04 (bs, 1H), 4.48 (d, *J* = 14.5 Hz, 1H), 4.41 – 4.28 (m, 3H), 4.10 – 3.96 (m, 2H), 3.96 – 3.83 (m, 2H), 3.07 – 2.83 (m, 6H), 2.53 (s, 3H), 2.47 (s, 3H), 2.06 (s, 3H), 1.49 – 1.36 (m, 15H), 1.36 – 1.04 (m, 10H), 0.98 – 0.59 (m, 3H), 0.52 (d, *J* = 6.3 Hz, 3H), 0.48 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 168.8, 158.5, 156.1, 156.0, 154.2, 152.0, 138.4, 138.2, 135.1, 133.7, 133.5, 133.1, 132.9, 132.1, 129.8, 129.72, 129.68, 129.2, 129.1, 128.9, 128.0, 127.9, 126.6, 126.53, 126.49, 125.4, 124.9, 124.4, 124.1, 123.7, 120.1, 119.2, 117.3, 115.8, 114.1, 86.2, 78.8, 68.1, 67.8, 52.5, 51.5, 48.7, 43.1, 40.3, 40.0, 37.8, 30.9, 29.3, 29.0, 28.5, 28.4, 25.2, 24.4, 22.4, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1186 (32%, M+Na), 1164 (100%, M+H); HRMS (ES^+) Calcd. for $C_{65}H_{82}N_9O_9S$: 1164.5956, Found: 1164.6000.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(4-(4-butylphenyl)-1*H*-1,2,3-triazol-1-yl)-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 (31)**



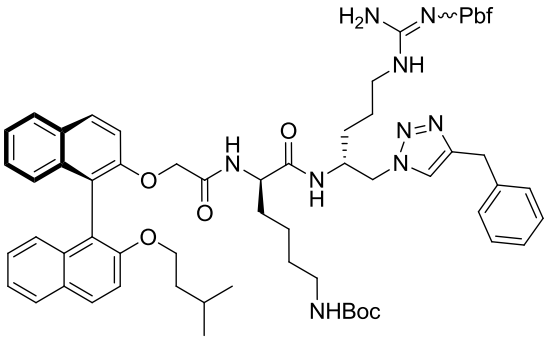
This compound was prepared according to *General Procedure 2* using azide **18** (50.0 mg, 0.047 mmol), $Cu(OAc)_2 \cdot H_2O$ (1.9 mg, 0.0094 mmol), Na·ascorbate (3.7 mg, 0.019 mmol), (4-butylphenyl)acetylene (22.2 mg, 0.14 mmol), *t*-BuOH (1.0 mL) and H_2O (0.25 mL) with a 7 h reaction time. Purification by a pipette silica plug (3 cm silica, 100% pet. ether then 100% EtOAc) gave **31** (49.9 mg, 87%) as a pale yellow solid. TLC (75% EtOAc/pet. ether) R_F = 0.06; $[\alpha]_D^{25}$ −29.7 (*c* 2.37, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.90 – 7.74 (m, 4H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.30 – 7.18 (m, 6H), 7.18 – 7.08 (m, 4H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.27 (bs, 2H), 6.09 (bd, *J* = 6.6 Hz, 1H), 4.81 (bs, 1H), 4.44 (d, *J* = 10.8 Hz, 1H), 4.41 – 4.23 (m, 4H), 4.06 – 3.97 (m, 1H), 3.96 – 3.89 (m, 1H), 3.82 – 3.74 (m, 1H), 3.16 – 3.05 (m, 2H), 2.89 (s, 2H), 2.85 – 2.76 (m, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 2.56 (s, 3H), 2.48 (s, 3H), 2.06 (s, 3H), 1.64 (quin, *J* = 7.7 Hz, 2H), 1.55 – 1.31 (m, 21H), 1.30 – 1.20 (m, 1H), 1.18 – 1.01 (m, 5H), 0.93 (t, *J* = 7.3 Hz, 3H), 0.72 – 0.62 (m, 1H), 0.59 – 0.50 (m, 2H), 0.48 (d, *J* = 6.3 Hz, 3H), 0.45 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 168.7, 158.6, 156.1, 156.0, 154.2, 152.0, 147.4, 143.0, 138.2, 133.7, 133.5, 133.0, 132.1, 129.73, 129.70, 129.66, 129.0, 128.9, 128.0, 127.94, 127.87, 126.5, 126.4, 125.5, 125.4, 124.8, 124.5, 124.1, 123.6, 120.9, 120.2, 119.0, 117.4, 115.7, 114.1, 86.3, 78.7, 68.1, 67.8, 53.3, 52.3, 49.2, 43.1, 40.4, 39.8, 37.8, 35.4, 33.5, 31.3, 29.1, 28.7, 28.5, 28.4, 25.9, 24.4, 22.5, 22.3, 22.2, 22.0, 19.3, 17.9, 13.9, 12.4; MS (ES^+) *m/z* 1243 (53%, M+Na), 1221 (100%, M+H); HRMS (ES^+) Calcd. for $C_{69}H_{89}N_9NaO_9S$: 1242.6402, Found: 1242.6389.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(((*R*)-1-(4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-6-oxohexyl)carbamate (32)**



This compound was prepared according to *General Procedure 2* using azide **18** (63.7 mg, 0.060 mmol), $Cu(OAc)_2 \cdot H_2O$ (2.4 mg, 0.012 mmol), Na·ascorbate (4.8 mg, 0.024 mmol), 4-methoxyphenylacetylene (23.8 mg, 0.18 mmol), *t*-BuOH (1.3 mL) and H_2O (0.3 mL) with a 4.5 h reaction time. Flash chromatography (2.6 g silica, 100% EtOAc) gave **32** (57.0 mg, 79%) as an off-white solid. TLC (100% EtOAc) R_F = 0.12; $[\alpha]_D^{25}$ −32.1 (*c* 2.55, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.90 – 7.78 (m, 5H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.31 – 7.06 (m, 6H), 7.04 (d, *J* = 8.5 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.24 (bs, 2H), 6.09 (bd, *J* = 7.2 Hz, 1H), 4.87 (bs, 1H), 4.44 (d, *J* = 11.2 Hz, 1H), 4.38 – 4.19 (m, 4H), 4.06 – 3.97 (m, 1H), 3.96 – 3.88 (m, 1H), 3.84 (s, 3H), 3.82 – 3.74 (m, 1H), 3.15 – 3.03 (m, 2H), 2.88 (s, 2H), 2.86 – 2.77 (m, 2H), 2.56 (s, 3H), 2.47 (s, 3H), 2.06 (s, 3H), 1.56 – 1.18 (m, 20H), 1.18 – 1.00 (m, 5H), 0.78 – 0.64 (m, 1H), 0.64 – 0.50 (m, 2H), 0.48 (d, *J* = 6.3 Hz, 3H), 0.44 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 168.7, 159.6, 158.6, 156.04, 155.99, 154.2, 151.9, 147.2, 138.2, 133.7, 133.5, 133.0, 132.1, 129.73, 129.67, 129.1, 128.0, 127.9, 126.9, 126.54, 126.46, 125.4, 124.8, 124.5, 124.1, 123.7, 123.3, 120.5, 120.2, 119.1, 117.4, 115.7, 114.3, 114.1, 86.3, 78.7, 68.1, 67.7, 55.3, 53.3, 52.3, 49.2, 43.1, 40.4, 39.8, 37.8, 31.3, 29.1, 28.7, 28.5, 28.4, 26.1, 24.4, 22.3, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1216 (19%, M+Na), 1194 (100%, M+H); HRMS (ES^+) Calcd. for $C_{66}H_{84}N_9O_{10}S$: 1194.6062, Found: 1194.6084.

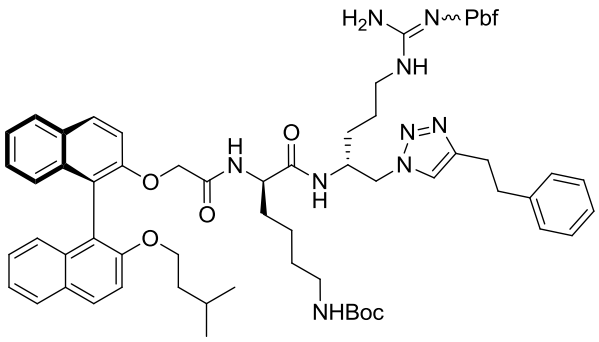
***tert*-Butyl ((*R*)-6-(((*R*)-1-(4-benzyl-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (33)**



This compound was prepared according to *General Procedure 2* using azide **18** (45.0 mg, 0.042 mmol), $Cu(OAc)_2 \cdot H_2O$ (1.7 mg, 0.0085 mmol), Na·ascorbate (3.3 mg, 0.017 mmol), 3-phenyl-1-propyne (15.1 mg, 0.13 mmol), *t*-BuOH (0.89 mL) and H_2O (0.21 mL) with a 8 h reaction time. Purification by a pipette silica plug (3 cm silica, 100% pet. ether then 100% EtOAc) gave **33** (42.4 mg, 85%) as an off-white solid. TLC (75% EtOAc/pet. ether) R_F = 0.16; $[\alpha]_D^{25}$ −22.1 (*c* 1.62, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ ^{1}H NMR (500 MHz, cdcl$_3$) δ 7.97 – 7.89 (m, 2H), 7.85 (t, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.07 (m, 14H), 6.27 – 6.13 (bm, 3H), 4.85 (bs, 1H), 4.45 (d, *J* = 14.5 Hz, 1H), 4.40 – 4.23 (m, 3H), 4.22 – 4.09 (m, 1H), 4.08 – 3.98 (m, 3H), 3.98 – 3.91 (m, 1H), 3.91 – 3.84 (m, 1H), 3.15 – 3.00 (m, 2H), 2.95 – 2.81 (m, 4H), 2.53 (s, 3H), 2.46 (s, 3H), 2.06 (s, 3H), 1.51 – 1.27 (m, 19H), 1.27 – 1.06 (m, 6H), 0.85 – 0.74 (m, 1H), 0.74 – 0.59 (m, 2H), 0.53 (d, *J* = 6.4 Hz, 3H), 0.48 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.9, 158.6, 156.2, 156.0, 154.3, 152.1, 147.2, 138.9, 138.2, 133.8, 133.6, 133.0, 132.1, 129.8, 129.7, 129.2, 128.63, 128.56, 128.0, 127.9, 126.6, 126.5, 126.4, 125.5, 124.9, 124.5, 124.1, 123.8, 122.8, 120.3, 119.4, 117.4, 115.9, 114.2, 86.3, 78.9, 68.3, 67.9, 52.9, 52.6, 49.2, 43.2, 40.5, 39.9, 37.9, 32.0, 30.9, 29.0, 28.5, 28.4, 25.3, 24.5, 22.4, 22.3, 22.1, 19.3, 17.9,

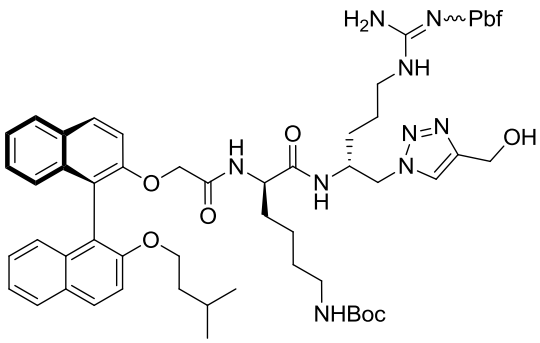
12.4; MS (ES^+) *m/z* 1201 (31%, M+Na), 1178 (100%, M+H); HRMS (ES^+) Calcd. for $C_{66}H_{83}N_9NaO_9S$: 1200.5932, Found: 1200.5975.

tert-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxo-6-(((*R*)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)-1-(4-phenethyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)amino)hexyl)carbamate (34)



This compound was prepared according to *General Procedure 2* using azide **18** (63.7 mg, 0.060 mmol), $Cu(OAc)_2{\cdot}H_2O$ (2.4 mg, 0.012 mmol), Na·ascorbate (4.8 mg, 0.024 mmol), 4-phenyl-1-butyne (23.4 mg, 0.18 mmol), *t*-BuOH (1.3 mL) and H_2O (0.3 mL) with a 4.5 h reaction time. Flash chromatography (2.5 g silica, 100% EtOAc) gave **34** (58.1 mg, 81%) as an off-white solid. TLC (100% EtOAc) R_F = 0.13; $[\alpha]_D^{25}$ −26.2 (*c* 2.66, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 – 7.88 (m, 2H), 7.88 – 7.79 (m, 2H), 7.42 (d, *J* = 9.0 Hz, 1H), 7.34 (t, *J* = 7.1 Hz, 1H), 7.32 – 7.07 (m, 13H), 6.24 (bs, 2H), 6.18 (bd, *J* = 5.8 Hz, 1H), 4.87 (bs, 1H), 4.47 (d, *J* = 14.4 Hz, 1H), 4.41 – 4.25 (m, 3H), 4.23 – 4.14 (m, 1H), 4.06 – 3.93 (m, 2H), 3.92 – 3.84 (m, 1H), 3.15 – 3.05 (m, 2H), 3.05 – 2.84 (m, 8H), 2.55 (s, 3H), 2.48 (s, 3H), 2.06 (s, 3H), 1.52 – 1.32 (m, 19H), 1.32 – 1.06 (m, 6H), 0.90 – 0.78 (m, 1H), 0.78 – 0.63 (m, 2H), 0.53 (d, *J* = 6.2 Hz, 3H), 0.48 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.8, 158.6, 156.2, 156.0, 154.3, 152.1, 147.1, 141.0, 138.2, 133.8, 133.6, 133.0, 132.1, 129.7, 129.6, 129.1, 128.37, 128.36, 128.0, 127.9, 126.6, 126.5, 126.1, 125.4, 124.9, 124.5, 124.1, 123.7, 122.3, 120.3, 119.3, 117.4, 115.8, 114.2, 86.3, 78.9, 68.2, 67.9, 52.9, 52.6, 49.2, 43.2, 40.5, 39.9, 37.9, 35.5, 31.0, 29.04, 28.95, 28.5, 28.4, 27.4, 25.3, 24.5, 22.4, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1214 (18%, M+Na), 1192 (100%, M+H); HRMS (ES^+) Calcd. for $C_{67}H_{86}N_9O_9S$: 1192.6269, Found: 1192.6289.

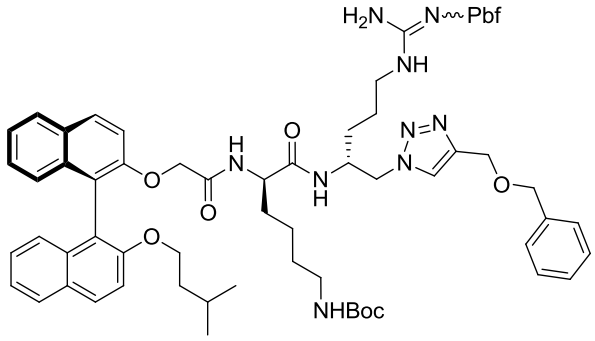
tert-Butyl ((*R*)-6-(((*R*)-1-(4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (35)



This compound was prepared according to *General Procedure 2* using azide **18** (400 mg, 0.38 mmol), $Cu(OAc)_2{\cdot}H_2O$ (15.0 mg, 0.075 mmol), Na·ascorbate (29.8 mg, 0.15 mmol), propargyl alcohol (63.3 mg, 1.13 mmol), *t*-BuOH (8.0 mL) and H_2O (2.0 mL) with a 5 h reaction time. Work-up as described gave **35** (387 mg, 92%) as an off-white solid. TLC (4% MeOH/EtOAc) R_F = 0.28; $[\alpha]_D^{25}$ −20.2 (*c* 2.37, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.89 (m, 2H), 7.88 – 7.80 (m, 2H), 7.63 (s, 1H), 7.46 (d, *J* = 9.2 Hz, 1H), 7.40 – 7.25 (m, 4H), 7.25 – 7.16 (m, 2H), 7.14 (d, *J* = 8.6 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.40 – 6.22 (bm, 3H), 4.97 (bs, 1H), 4.66 (s, 2H), 4.54 – 4.31 (m, 5H), 4.18 – 4.10 (m, 1H), 4.09 – 3.96 (m, 2H), 3.94 – 3.85 (m, 1H), 3.20 – 3.03 (m, 2H), 3.01 – 2.84 (m, 4H), 2.55 (s, 3H), 2.47 (s, 3H), 2.06 (s, 3H), 1.52 – 1.30 (m, 19H), 1.28 – 1.08 (m, 6H), 0.96 – 0.85 (m, 1H), 0.83 – 0.68 (m, 2H), 0.53 (d, *J* = 6.4 Hz, 3H), 0.49 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 168.9, 158.6, 156.3, 156.2, 154.3, 152.2, 147.7, 138.1, 133.8, 133.6, 132.8, 132.1, 129.7, 129.1, 128.0, 127.9, 126.6, 126.5,

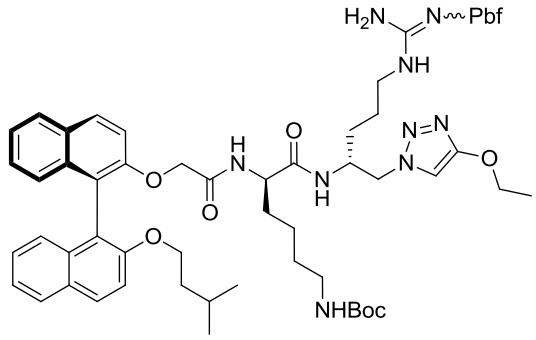
125.4, 124.9, 124.5, 124.1, 123.7, 123.5, 120.3, 119.3, 117.4, 115.9, 114.2, 86.3, 78.9, 68.2, 67.9, 55.8, 52.7, 49.5, 43.1, 40.4, 40.0, 37.9, 31.1, 29.0, 28.5, 28.4, 25.5, 24.4, 22.4, 22.2, 22.0, 19.2, 17.9, 12.4; MS (ES^+) *m/z* 1141 (100%, M+Na), 1119 (41%, M+H); HRMS (ES^+) Calcd. for $C_{60}H_{79}N_9NaO_{10}S$: 1140.5568, Found: 1140.5571.

tert-Butyl ((*R*)-6-(((*R*)-1-(4-((benzyloxy)methyl)-1*H*-1,2,3-triazol-1-yl)-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 (36)



This compound was prepared according to *General Procedure 2* using azide **18** (100 mg, 0.094 mmol), $Cu(OAc)_2{\cdot}H_2O$ (3.8 mg, 0.019 mmol), Na·ascorbate (7.5 mg, 0.038 mmol), 3-benzyloxy-1-propyne[S5] (41.3 mg, 0.28 mmol), *t*-BuOH (2.0 mL) and H_2O (0.5 mL) with a 19 h reaction time. Flash chromatography (3.4 g silica, 100% EtOAc to 2% MeOH/EtOAc) gave **36** (84.8 mg, 75%) as a pale yellow solid. TLC (75% EtOAc/pet. ether) R_F = 0.14; $[\alpha]_D^{25}$ −26.4 (*c* 0.80, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 – 7.88 (m, 2H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.66 (s, 1H), 7.41 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.16 (m, 10H), 7.16 – 7.06 (m, 3H), 6.26 – 6.11 (bm, 3H), 4.82 (bs, 1H), 4.64 (s, 2H), 4.59 (s, 2H), 4.46 (d, *J* = 14.6 Hz, 1H), 4.41 – 4.32 (m, 3H), 4.26 – 4.16 (m, 1H), 4.05 – 3.93 (m, 2H), 3.91 – 3.83 (m, 1H), 3.13 – 3.03 (m, 2H), 2.95 – 2.81 (m, 4H), 2.54 (s, 3H), 2.47 (s, 3H), 2.06 (s, 3H), 1.52 – 1.33 (m, 19H), 1.31 – 1.05 (m, 6H), 0.87 – 0.75 (m, 1H), 0.74 – 0.60 (m, 2H), 0.52 (d, *J* = 6.4 Hz, 3H), 0.48 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.9, 158.6, 156.2, 156.0, 154.3, 152.1, 144.8, 138.2, 137.7, 133.8, 133.6, 133.0, 132.1, 129.7, 129.1, 128.4, 128.0, 127.92, 127.88, 127.8, 126.6, 126.5, 125.5, 124.9, 124.5, 124.1, 124.0, 123.8, 120.3, 119.3, 117.4, 115.9, 114.2, 86.3, 78.9, 72.5, 68.3, 67.9, 63.4, 53.0, 52.7, 49.2, 43.2, 40.5, 39.9, 37.9, 30.9, 29.0, 28.5, 28.4, 25.3, 24.5, 22.4, 22.3, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1230 (26%, M+Na), 1209 (100%, M+H); HRMS (ES^+) Calcd. for $C_{67}H_{85}N_9NaO_{10}S$: 1230.6038, Found: 1230.6003.

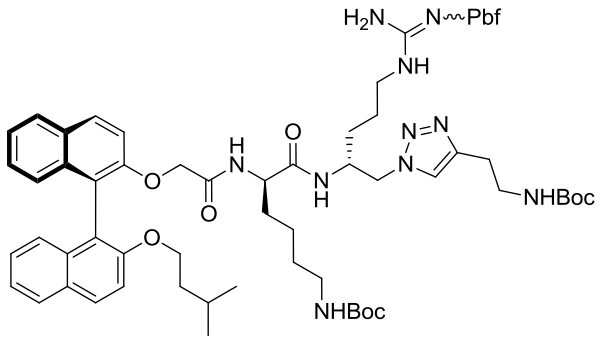
tert-Butyl ((*R*)-6-(((*R*)-1-(4-ethoxy-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (37)



This compound was prepared according to *General Procedure 2* using azide **18** (63.7 mg, 0.060 mmol), $Cu(OAc)_2{\cdot}H_2O$ (2.4 mg, 0.012 mmol), Na·ascorbate (4.8 mg, 0.024 mmol), ethoxyacetylene (40 wt % in hexane, 31.5 mg of solution, 12.6 mg of alkyne, 0.18 mmol), *t*-BuOH (1.3 mL) and H_2O (0.3 mL) with a 4.5 h reaction time. Flash chromatography (2.4 g silica, 50% EtOAc/pet. ether to 100% EtOAc) gave **37** (59.2 mg, 87%) as a brown solid. TLC (100% EtOAc) R_F = 0.10; $[\alpha]_D^{25}$ −4.3 (*c* 2.68, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.90 (m, 2H), 7.89 – 7.82 (m, 2H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.38 – 7.07 (m, 9H), 6.24 (bs, 2H), 6.17 (bd, *J* = 6.4 Hz, 1H), 4.87 (bs, 1H), 4.46 (d, *J* = 14.5 Hz, 1H), 4.37 (d, *J* = 14.5 Hz, 1H), 4.34 – 4.15 (m,

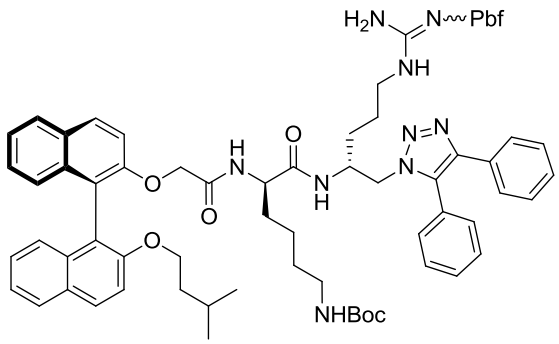
4H), 4.07 – 3.96 (m, 2H), 3.93 – 3.85 (m, 1H), 3.17 – 3.01 (m, 2H), 3.00 – 2.84 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.63 – 1.05 (m, 28H), 0.90 – 0.76 (m, 1H), 0.75 – 0.59 (m, 2H), 0.53 (d, *J* = 6.3 Hz, 3H), 0.48 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.8, 160.7, 158.6, 156.1, 156.0, 154.3, 152.1, 138.2, 133.8, 133.6, 133.0, 132.1, 129.7, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.5, 124.1, 123.7, 120.3, 119.2, 117.4, 115.8, 114.2, 107.3, 86.3, 78.8, 68.2, 67.9, 66.4, 53.8, 52.5, 49.1, 43.2, 40.4, 39.9, 37.8, 31.1, 29.0, 28.9, 28.5, 28.4, 25.5, 24.5, 22.3, 22.2, 22.0, 19.2, 17.9, 14.8, 12.4; MS (ES^+) *m/z* 1154 (25%, M+Na), 1132 (100%, M+H); HRMS (ES^+) Calcd. for $C_{61}H_{82}N_9O_{10}S$: 1132.5905, Found: 1132.5929.

tert-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxo-6-(((*R*)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)-1-(4-(2-*tert*-butoxycarbonylaminoethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)amino)hexyl)carbamate (39)



This compound was prepared according to *General Procedure 2* using azide **18** (50.0 mg, 0.047 mmol), $Cu(OAc)_2 \cdot H_2O$ (1.9 mg, 0.0094 mmol), Na·ascorbate (3.7 mg, 0.019 mmol), 4-(*tert*-butoxycarbonylamino)-1-butyne[S6] (15.6 mg, 0.14 mmol), *t*-BuOH (1.0 mL) and H_2O (0.25 mL) with a 5 h reaction time. Purification by a pipette silica plug (3 cm silica, 10% EtOAc/pet. ether to 100% EtOAc) gave **39** (45.4 mg, 78%) as a white solid. TLC (100% EtOAc) R_F = 0.08; $[\alpha]_D^{25}$ −15.9 (*c* 2.16, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.91 (m, 2H), 7.89 – 7.81 (m, 2H), 7.53 (s, 1H), 7.46 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.28 (m, 4H), 7.26 – 7.17 (m, 2H), 7.14 (d, *J* = 8.5 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 6.19 (bs, 1H), 5.42 (bs, 1H), 4.99 (bs, 1H), 4.51 (d, *J* = 14.5 Hz, 1H), 4.44 – 4.31 (m, 3H), 4.25 – 4.15 (m, 1H), 4.08 – 4.01 (m, 1H), 4.00 – 3.86 (m, 2H), 3.47 – 3.32 (m, 2H), 3.24 – 3.07 (m, 2H), 3.00 – 2.82 (m, 6H), 2.54 (s, 3H), 2.47 (s, 3H), 2.07 (s, 3H), 1.58 – 1.35 (m, 28H), 1.32 – 1.09 (m, 6H), 0.93 – 0.64 (m, 3H), 0.55 (d, *J* = 6.4 Hz, 3H), 0.50 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 171.7, 168.9, 159.4, 156.1, 154.4, 152.2, 145.1, 138.8, 133.8, 133.6, 132.6, 129.75, 129.72, 129.67, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.1, 123.8, 123.0, 120.3, 119.4, 117.7, 115.9, 114.3, 86.6, 79.1, 78.9, 68.3, 68.0, 53.0, 52.8, 49.3, 43.1, 41.0, 40.7, 40.0, 37.9, 30.9, 29.1, 28.8, 28.5, 28.42, 28.40, 26.1, 25.1, 24.5, 22.4, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1254 (67%, M+Na), 1232 (100%, M+H); HRMS (ES^+) Calcd. for $C_{66}H_{90}N_{10}NaO_{11}S$: 1253.6409, Found: 1253.6443.

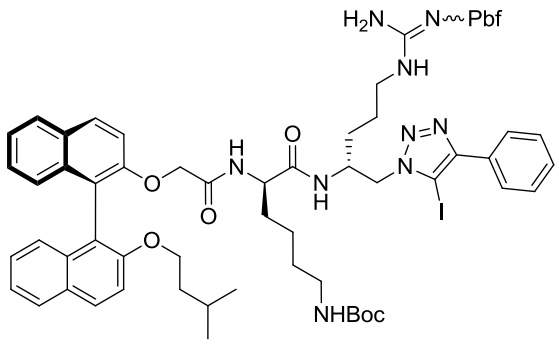
tert-Butyl ((*R*)-6-(((*R*)-1-(4,5-diphenyl-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxohexyl)carbamate (40)



This compound was prepared according to *General Procedure 3* using azide **18** (1.00 g, 0.94 mmol), $Cp^*RuCl(PPh_3)_2$ (37.5 mg, 0.047 mmol), diphenylacetylene (335.5 mg, 1.88 mmol) and 1,4-dioxane (9.4 mL) with a 45 h reaction time. Removal of the solvent under reduced pressure, followed by flash chromatography (10.3 g silica, 50% EtOAc/pet. ether to 100% EtOAc) gave **40** (1.099 g, 94%) as a brown solid. TLC (100% EtOAc) R_F = 0.18; $[\alpha]_D^{25}$ −39.4 (*c* 1.88,

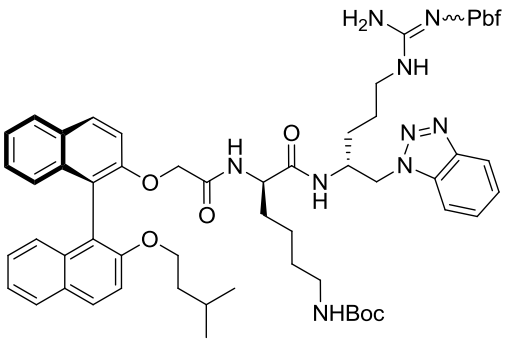
CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.9 Hz, 1H), 7.85 (app. d, *J* = 8.3 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.61 (app. d, *J* = 7.0 Hz, 2H), 7.56 – 7.48 (m, 3H), 7.43 – 7.37 (m, 2H), 7.36 – 7.13 (m, 10H), 7.11 (d, *J* = 8.5 Hz, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 6.15 – 6.03 (bm, 3H), 4.86 (bs, 1H), 4.48 (d, *J* = 14.2 Hz, 1H), 4.40 (d, *J* = 14.4 Hz, 1H), 4.24 – 4.09 (m, 2H), 4.08 – 3.90 (m, 3H), 3.82 – 3.73 (m, 1H), 3.05 – 2.93 (m, 2H), 2.90 (s, 2H), 2.88 – 2.81 (m, 2H), 2.53 (s, 3H), 2.47 (s, 3H), 2.05 (s, 3H), 1.49 – 1.36 (m, 15H), 1.36 – 1.00 (m, 8H), 0.95 – 0.81 (m, 1H), 0.79 – 0.69 (m, 1H), 0.68 – 0.61 (m, 1H), 0.60 – 0.51 (m, 2H), 0.48 (d, *J* = 6.3 Hz, 3H), 0.44 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 168.9, 158.5, 156.0, 155.9, 154.2, 152.0, 144.0, 138.2, 135.1, 134.2, 133.9, 133.8, 133.5, 133.3, 132.1, 130.8, 130.1, 129.8, 129.7, 129.5, 129.1, 128.6, 128.0, 127.93, 127.87, 127.6, 126.6, 126.5, 125.4, 124.9, 124.4, 124.1, 123.7, 120.2, 119.1, 117.3, 115.8, 114.1, 86.2, 78.8, 68.1, 67.8, 52.4, 51.7, 48.6, 43.2, 40.3, 39.9, 37.8, 31.0, 29.6, 28.8, 28.52, 28.51, 28.4, 25.5, 24.4, 22.4, 22.2, 22.0, 19.2, 17.9, 12.4; MS (ES^+) *m/z* 1263 (100%, M+Na), 1241 (22%, M+H); HRMS (ES^+) Calcd. for $C_{71}H_{85}N_9NaO_9S$: 1262.6089, Found: 1262.6136.

tert-Butyl ((*R*)-6-(((*R*)-1-(5-iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)-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 (41)



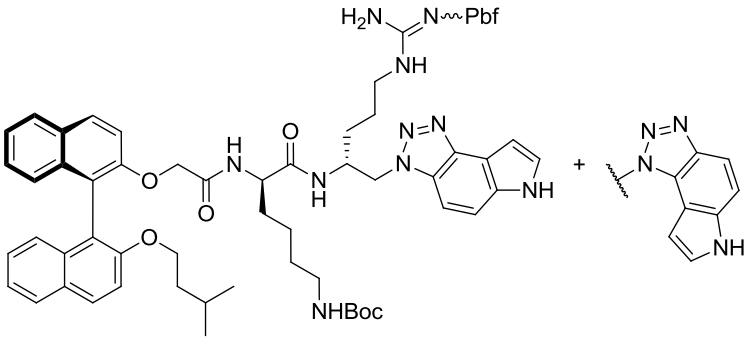
An oven-dried vial was charged in air with azide **18** (63.7 mg, 0.060 mmol), CuI (0.6 mg, 0.0030 mmol), 1-iodo-2-phenylethyne[S7] (25.0 mg, 0.11 mmol) and NEt_3 (12.1 mg, 0.12 mmol). The vial was evacuated and refilled with N_2 (single cycle), then THF (0.6 mL) was added. The mixture was stirred at rt under N_2 for 18 h after which time TLC analysis (100% EtOAc) indicated the presence of some unreacted azide. Additional CuI (0.6 mg, 0.0030 mmol), NEt_3 (10 mg, 0.10 mmol) and THF (0.6 mL) were added and stirring was continued for a further 22.5 h. The mixture was diluted with EtOAc (20 mL) and shaken with a 1:1 mixture of 32% aqueous NH_3:brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (2.5 g silica, 75% EtOAc/pet. ether to 100% EtOAc) gave **41** (65.9 mg, 85%) as an off-white solid. TLC (100% EtOAc) R_F = 0.27; $[\alpha]_D^{25}$ −41.6 (*c* 1.18, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.4 Hz, 2H), 7.91 (d, *J* = 9.0 Hz, 1H), 7.87 – 7.79 (m, 2H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.45 – 7.40 (m, 1H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.30 – 7.18 (m, 5H), 7.16 (t, *J* = 8.1 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.19 (bs, 2H), 6.10 (d, *J* = 7.7 Hz, 1H), 4.81 (bs, 1H), 4.51 – 4.31 (m, 5H), 4.05 – 3.97 (m, 1H), 3.96 – 3.88 (m, 1H), 3.82 – 3.73 (m, 1H), 3.22 – 3.07 (m, 2H), 2.90 (s, 2H), 2.89 – 2.79 (m, 2H), 2.58 (s, 3H), 2.50 (s, 3H), 2.07 (s, 3H), 1.60 – 1.23 (m, 20H), 1.20 – 0.99 (m, 5H), 0.76 – 0.53 (m, 3H), 0.48 (d, *J* = 6.3 Hz, 3H), 0.44 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.7, 158.5, 156.0, 155.9, 154.2, 152.0, 149.0, 138.2, 133.7, 133.4, 133.2, 132.1, 130.1, 129.7, 129.6, 129.0, 128.6, 128.5, 128.0, 127.8, 127.1, 126.5, 126.4, 125.4, 124.8, 124.4, 124.0, 123.6, 120.2, 119.0, 117.3, 115.7, 114.1, 86.2, 78.7, 77.4, 68.0, 67.8, 53.8, 52.2, 48.7, 43.1, 40.4, 39.8, 37.7, 31.1, 29.4, 28.8, 28.5, 28.4, 25.7, 24.3, 22.3, 22.2, 21.9, 19.2, 17.9, 12.4; MS (ES^+) *m/z* 1312 (20%, M+Na), 1290 (100%, M+H); HRMS (ES^+) Calcd. for $C_{65}H_{81}IN_9O_9S$: 1290.4923, Found: 1290.4974.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)-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 (42)**



An oven-dried vial was charged in air with azide **18** (63.7 mg, 0.060 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (19.7 mg, 0.066 mmol) and CsF (18.2 mg, 0.12 mmol). The vial was evacuated and refilled with N_2 (single cycle), then MeCN (0.6 mL) was added. The mixture was stirred at rt under N_2 for 23 h after which time TLC analysis (75% EtOAc/pet. ether) indicated the presence of some unreacted azide. A solution containing additional 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (26.9 mg, 0.090 mmol) in MeCN (0.2 mL) was added, followed by CsF (18.2 mg, 0.12 mmol) and stirring was continued for a further 16 h. The mixture was diluted with EtOAc (20 mL) and washed with saturated $NaHCO_3$ (20 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (2.4 g silica, 80% EtOAc/pet. ether to 100% EtOAc) gave **42** (55.6 mg, 81%) as an off-white solid. TLC (100% EtOAc) R_F = 0.72; $[\alpha]_D^{25}$ −22.6 (*c* 2.62, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.3 Hz, 1H), 7.91 (d, *J* = 9.0 Hz, 1H), 7.89 – 7.82 (m, 2H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.49 – 7.42 (m, 1H), 7.42 – 7.19 (m, 7H), 7.19 – 7.10 (m, 2H), 7.06 (d, *J* = 8.5 Hz, 1H), 6.20 (bs, 2H), 6.10 (bd, *J* = 6.1 Hz, 1H), 4.81 (bs, 1H), 4.70 – 4.58 (m, 2H), 4.42 – 4.26 (m, 3H), 4.02 – 3.89 (m, 2H), 3.86 – 3.78 (m, 1H), 3.15 – 3.03 (m, 2H), 2.90 (s, 2H), 2.88 – 2.77 (m, 2H), 2.55 (s, 3H), 2.48 (s, 3H), 2.06 (s, 3H), 1.64 – 1.55 (m, 1H), 1.53 – 1.36 (m, 18H), 1.31 – 1.23 (m, 1H), 1.21 – 1.04 (m, 5H), 0.94 – 0.82 (m, 1H), 0.64 – 0.48 (m, 5H), 0.46 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.7, 158.6, 156.1, 156.0, 154.2, 152.0, 145.5, 138.2, 133.8, 133.5, 133.0, 132.1, 129.71, 129.66, 129.0, 128.0, 127.9, 127.5, 126.53, 126.49, 125.5, 124.8, 124.5, 124.1, 124.0, 123.7, 120.3, 119.6, 119.1, 117.4, 115.7, 114.2, 110.1, 86.3, 78.9, 68.1, 67.8, 52.2, 51.2, 49.3, 43.2, 40.5, 40.0, 37.8, 31.0, 29.2, 28.9, 28.5, 28.4, 25.7, 24.4, 22.3, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1160 (37%, M+Na), 1138 (100%, M+H); HRMS (ES^+) Calcd. for $C_{63}H_{79}N_9NaO_9S$: 1160.5619, Found: 1160.5660.

***tert*-Butyl ((*R*)-6-(((*R*)-1-([1,2,3]triazolo[4,5-*e*]indol-1/3(6*H*)-yl)-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 (43)**

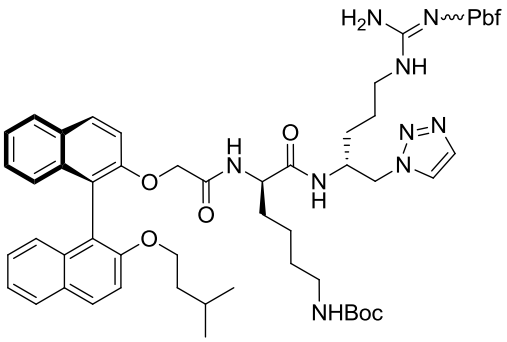


~2:1 (major isomer not determined)

An oven-dried vial was charged in air with azide **18** (41.0 mg, 0.039 mmol), 4-(trimethylsilyl)-1*H*-indol-5-yl trifluoromethanesulfonate (26.0 mg, 0.077 mmol) and CsF (11.7 mg, 0.077 mmol). The vial was evacuated and refilled with N_2 (single cycle), then MeCN (0.4 mL) was added. The mixture was stirred at rt under N_2 for 25 h after which time TLC analysis (75% EtOAc/pet. ether) indicated the presence of some unreacted azide. Additional portions of 4-(trimethylsilyl)-1*H*-indol-5-yl trifluoromethanesulfonate (10 mg, 0.030 mmol) and CsF (10 mg, 0.066 mmol) were added and

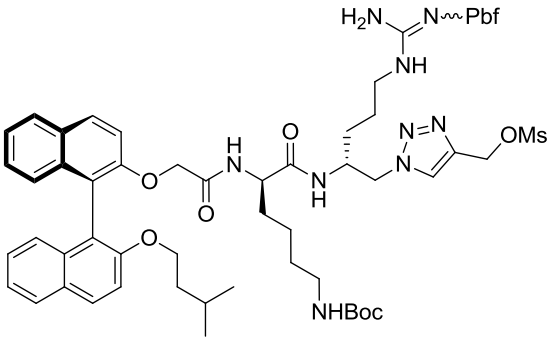
stirring was continued for a further 45 h. The mixture was diluted with CH_2Cl_2 (20 mL) and gravity filtered to remove insoluble salts. The filtrate was concentrated under reduced pressure and the residue subjected to flash chromatography (2.5 g silica, 100% EtOAc) giving **43** (26.4 mg, 58%) as a pale grey solid. This material was an approximate 2:1 mixture of regioisomers as determined by ^{1}H NMR analysis. TLC (2% MeOH/EtOAc) R_F = 0.34; MS (ES^+) *m/z* 1200 (100%, M+Na), 1178 (48%, M+H); HRMS (ES^+) Calcd. for $C_{65}H_{80}N_{10}NaO_9S$: 1199.5728, Found: 1199.5757. This mixture was characterized by NMR spectroscopy after deprotection. See the data for compound **67** on page S49.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxo-6-(((*R*)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)-1-(1*H*-1,2,3-triazol-1-yl)pentan-2-yl)amino)hexyl)carbamate (68)**



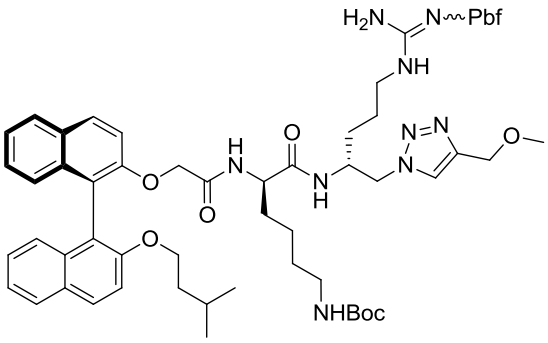
To the neat TMS-substituted triazole **27** (85.5 mg, 0.074 mmol) was added a commercial solution of TBAF (1 M in THF, 0.74 mL, 0.74 mmol) and the solution was stirred at rt in an air atmosphere for 7 d. The solution was diluted with EtOAc (25 mL) and washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (2.9 g silica, 2% MeOH/EtOAc) gave **68** (73.0 mg, 91%) as a white solid. TLC (2% MeOH/EtOAc) R_F = 0.13; $[\alpha]_D^{25}$ −26.2 (*c* 0.68, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.90 (m, 2H), 7.85 (app. t, *J* = 7.4 Hz, 2H), 7.68 (s, 1H), 7.65 (s, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.32 – 7.17 (m, 5H), 7.14 (d, *J* = 8.5 Hz, 1H), 7.09 (d, *J* = 8.5 Hz, 1H), 6.25 (bs, 2H), 6.18 (bd, *J* = 6.1 Hz, 1H), 4.97 – 4.89 (m, 1H), 4.50 – 4.32 (m, 4H), 4.29 – 4.17 (m, 1H), 4.05 – 3.93 (m, 2H), 3.92 – 3.84 (m, 1H), 3.16 – 3.04 (m, 2H), 2.99 – 2.84 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.56 – 1.36 (m, 19H), 1.28 – 1.07 (m, 6H), 0.85 – 0.74 (m, 1H), 0.73 – 0.59 (m, 2H), 0.53 (d, *J* = 6.4 Hz, 3H), 0.48 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.8, 158.6, 156.2, 156.1, 154.3, 152.1, 138.2, 133.8, 133.6, 133.5, 132.9, 132.1, 129.73, 129.70, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.89, 124.87, 124.6, 124.1, 123.7, 120.3, 119.3, 117.4, 115.8, 114.2, 86.3, 78.9, 68.2, 67.9, 52.9, 52.6, 49.3, 43.2, 40.4, 40.0, 37.9, 31.0, 29.0, 28.5, 28.4, 25.4, 24.5, 22.3, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1111 (100%, M+Na), 1088 (45%, M+H); HRMS (ES^+) Calcd. for $C_{59}H_{77}N_9NaO_9S$: 1110.5463, Found: 1110.5491.

(1-((*R*)-2-((*R*)-6-((tert-Butoxycarbonyl)amino)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamido)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentyl)-1*H*-1,2,3-triazol-4-yl)methyl methanesulfonate (S2)



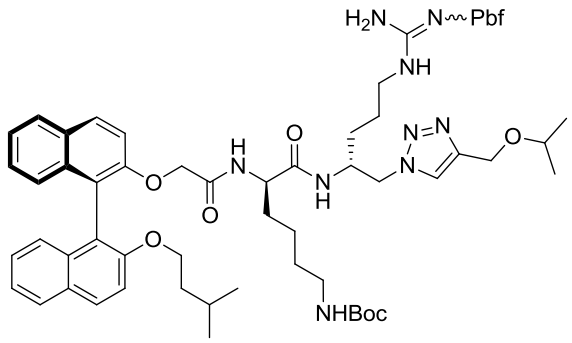
To a solution of alcohol **35** (256 mg, 0.23 mmol) in CH_2Cl_2 (2 mL) at 0 °C in air was added NEt_3 (0.13 mL, 0.92 mmol) and MsCl (0.053 mL, 0.69 mmol). The mixture was stirred for 5 min, then diluted with cold 1 M HCl (20 mL) and CH_2Cl_2 (20 mL). The organic layer was washed with saturated $NaHCO_3$ (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give mesylate **S2** (265 mg, 97%) as a pale yellow solid. TLC (4% MeOH/EtOAc) R_F = 0.63. This intermediate was stored in a freezer and used for the synthesis of ethers **70**−**76** according to *General Procedure 4*.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(((*R*)-1-(4-(methoxymethyl)-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-6-oxohexyl)carbamate (70)**



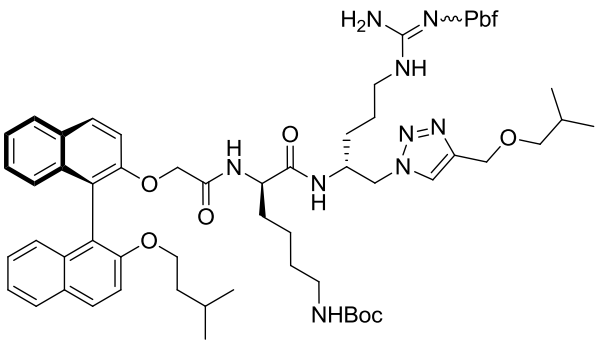
This compound was prepared according to *General Procedure 4* using MeOH (17.6 mg, 0.55 mmol), NaHMDS (1 M in THF, 0.28 mL, 0.28 mmol) and a solution of mesylate **S2** (66.3 mg, 0.055 mmol) and NBu_4I (2.0 mg, 0.0055 mmol) in THF (1.5 mL) with a 19 h reaction time. Work-up as described gave **70** (51.5 mg, 82%) as a pale yellow solid. TLC (2% MeOH/EtOAc) R_F = 0.18; $[\alpha]_D^{25}$ −17.4 (*c* 2.44, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.89 (m, 2H), 7.89 – 7.80 (m, 2H), 7.64 (s, 1H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.39 – 7.06 (m, 8H), 6.30 – 6.13 (bm, 3H), 4.87 (bs, 1H), 4.61 – 4.44 (m, 3H), 4.44 – 4.30 (m, 3H), 4.27 – 4.13 (m, 1H), 4.10 – 3.94 (m, 2H), 3.94 – 3.85 (m, 1H), 3.39 (s, 3H), 3.16 – 3.03 (m, 2H), 2.99 – 2.84 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.53 – 1.33 (m, 19H), 1.32 – 1.07 (m, 6H), 0.95 – 0.78 (m, 1H), 0.77 – 0.62 (m, 2H), 0.53 (d, *J* = 6.2 Hz, 3H), 0.49 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.9, 158.6, 156.2, 156.0, 154.3, 152.1, 144.7, 138.2, 133.8, 133.6, 133.0, 132.1, 129.73, 129.69, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.5, 124.1, 123.9, 123.7, 120.3, 119.3, 117.4, 115.9, 114.2, 86.3, 78.9, 68.3, 67.9, 65.7, 58.2, 52.9, 52.7, 49.2, 43.2, 40.5, 39.9, 37.9, 30.9, 29.01, 28.95, 28.5, 28.4, 25.3, 24.5, 22.4, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1154 (100%, M+Na), 1133 (30%, M+H); HRMS (ES^+) Calcd. for $C_{61}H_{81}N_9NaO_{10}S$: 1154.5725, Found: 1154.5748.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(((*R*)-1-(4-(isopropoxymethyl)-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-6-oxohexyl)carbamate (71)**



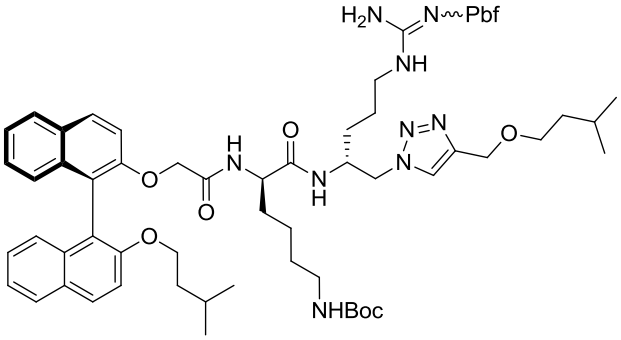
This compound was prepared according to *General Procedure 4* using *i*-PrOH (33.1 mg, 0.55 mmol), NaHMDS (1 M in THF, 0.28 mL, 0.28 mmol) and a solution of mesylate **S2** (66.3 mg, 0.055 mmol) and NBu_4I (2.0 mg, 0.0055 mmol) in THF (1.5 mL) with a 19 h reaction time. Work-up as described gave **71** (54.5 mg, 85%) as a pale yellow solid. TLC (2% MeOH/EtOAc) R_F = 0.54; $[\alpha]_D^{25}$ −20.2 (*c* 2.60, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.89 (m, 2H), 7.89 – 7.81 (m, 2H), 7.62 (s, 1H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.38 – 7.05 (m, 8H), 6.30 – 6.15 (bm, 3H), 4.88 (bs, 1H), 4.59 (s, 2H), 4.49 (d, *J* = 14.7 Hz, 1H), 4.44 – 4.31 (m, 3H), 4.26 – 4.15 (m, 1H), 4.09 – 3.94 (m, 2H), 3.94 – 3.85 (m, 1H), 3.73 (sep, *J* = 5.9 Hz, 1H), 3.15 – 3.05 (m, 2H), 2.97 – 2.84 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.58 – 1.33 (m, 19H), 1.32 – 1.08 (m, 12H), 0.94 – 0.63 (m, 3H), 0.54 (d, *J* = 6.1 Hz, 3H), 0.49 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 168.9, 158.6, 156.2, 156.0, 154.3, 152.1, 145.7, 138.2, 133.8, 133.6, 133.0, 132.1, 129.71, 129.68, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.5, 124.1, 123.7, 123.6, 120.3, 119.3, 117.4, 115.9, 114.2, 86.3, 78.9, 71.5, 68.3, 67.9, 61.5, 52.9, 52.6, 49.2, 43.2, 40.5, 39.9, 37.9, 30.9, 29.0, 28.9, 28.5, 28.4, 25.2, 24.5, 22.3, 22.2, 22.05, 22.01, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1182 (100%, M+Na), 1160 (39%, M+H); HRMS (ES^+) Calcd. for $C_{63}H_{85}N_9NaO_{10}S$: 1182.6038, Found: 1182.6078.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(4-(isobutoxymethyl)-1*H*-1,2,3-triazol-1-yl)-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 (72)**



This compound was prepared according to *General Procedure 4* using *i*-BuOH (40.8 mg, 0.55 mmol), NaHMDS (1 M in THF, 0.28 mL, 0.28 mmol) and a solution of mesylate **S2** (66.3 mg, 0.055 mmol) and NBu_4I (2.0 mg, 0.0055 mmol) in THF (1.5 mL) with a 19 h reaction time. Work-up as described gave **72** (51.5 mg, 79%) as a pale yellow solid. TLC (2% MeOH/EtOAc) R_F = 0.56; $[\alpha]_D^{25}$ −18.2 (*c* 2.32, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.89 (m, 2H), 7.89 – 7.80 (m, 2H), 7.63 (s, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.05 (m, 8H), 6.31 – 6.14 (bm, 3H), 4.88 (bs, 1H), 4.58 (s, 2H), 4.48 (d, *J* = 14.5 Hz, 1H), 4.44 – 4.31 (m, 3H), 4.27 – 4.17 (m, 1H), 4.09 – 3.94 (m, 2H), 3.94 – 3.86 (m, 1H), 3.28 (d, *J* = 6.5 Hz, 2H), 3.16 – 3.04 (m, 2H), 2.98 – 2.84 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.92 – 1.82 (m, 1H), 1.53 – 1.33 (m, 19H), 1.32 – 1.08 (m, 6H), 0.93 – 0.81 (m, 7H), 0.77 – 0.63 (m, 2H), 0.54 (d, *J* = 6.3 Hz, 3H), 0.49 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 168.8, 158.6, 156.2, 156.0, 154.3, 152.1, 145.3, 138.2, 133.8, 133.6, 133.0, 132.1, 129.71, 129.66, 129.1, 128.0, 127.9, 126.6, 126.5, 125.4, 124.9, 124.5, 124.1, 123.7, 123.6, 120.3, 119.3, 117.4, 115.9, 114.2, 86.3, 78.9, 77.6, 68.2, 67.9, 64.3, 52.9, 52.6, 49.2, 43.2, 40.5, 39.9, 37.9, 30.9, 29.0, 28.5, 28.4, 28.3, 25.3, 24.5, 22.3, 22.2, 22.0, 19.33, 19.26, 17.9, 12.4; MS (ES^+) *m/z* 1196 (100%, M+Na), 1174 (36%, M+H); HRMS (ES^+) Calcd. for $C_{64}H_{87}N_9NaO_{10}S$: 1196.6194, Found: 1196.6229.

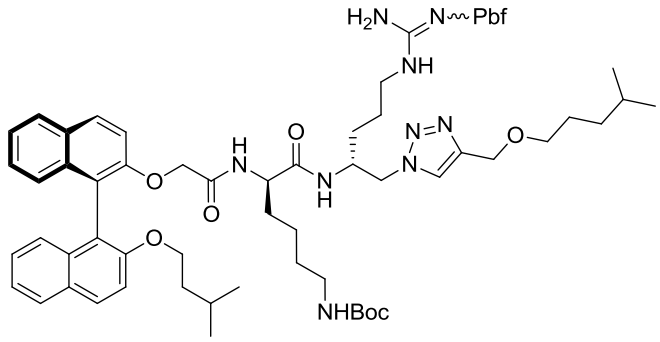
***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(((*R*)-1-(4-((isopentyloxy)methyl)-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-6-oxohexyl)carbamate (73)**



This compound was prepared according to *General Procedure 4* using *i*-pentyl-OH (48.5 mg, 0.55 mmol), NaHMDS (1 M in THF, 0.28 mL, 0.28 mmol) and a solution of mesylate **S2** (66.3 mg, 0.055 mmol) and NBu_4I (2.0 mg, 0.0055 mmol) in THF (1.5 mL) with a 19 h reaction time. Flash chromatography (3.6 g silica, 100% CH_2Cl_2 to 4% MeOH/CH_2Cl_2) gave **73** (35.3 mg, 54%) as a white solid. TLC (2% MeOH/EtOAc) R_F = 0.56; $[\alpha]_D^{25}$ −19.6 (*c* 1.63, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.90 (m, 2H), 7.89 – 7.81 (m, 2H), 7.63 (s, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.17 (m, 5H), 7.17 – 7.07 (m, 3H), 6.26 – 6.14 (bm, 3H), 4.86 (bs, 1H), 4.58 (s, 2H), 4.49 (d, *J* = 14.5 Hz, 1H), 4.44 – 4.32 (m, 3H), 4.26 – 4.16 (m, 1H), 4.07 – 4.00 (m, 1H), 4.00 – 3.94 (m, 1H), 3.93 – 3.85 (m, 1H), 3.54 (t, *J* = 6.7 Hz, 2H), 3.16 – 3.04 (m, 2H), 3.01 – 2.85 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.74 – 1.64 (m, 1H), 1.57 – 1.34 (m, 21H), 1.32 – 1.07 (m, 6H), 0.94 – 0.79 (m, 7H), 0.78 – 0.64 (m, 2H), 0.54 (d, *J* = 6.3 Hz, 3H), 0.49 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.9, 158.6, 156.2, 156.0, 154.3, 152.1, 145.2, 138.2, 133.8, 133.6, 133.0, 132.1, 129.73, 129.70, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.5, 124.1, 123.8, 123.7, 120.3, 119.4, 117.4, 115.9, 114.2, 86.3, 78.9, 69.3, 68.3, 67.9, 64.1, 53.0, 52.7, 49.2, 43.2, 40.5, 40.0, 38.4, 37.9,

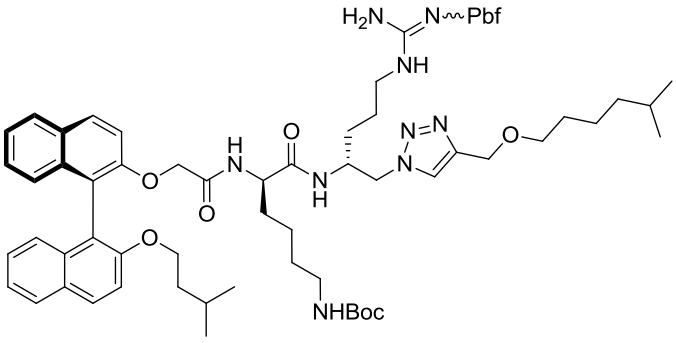
30.9, 29.01, 28.95, 28.5, 28.4, 25.3, 25.0, 24.5, 22.6, 22.4, 22.3, 22.1, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1210 (100%, M+Na), 1188 (31%, M+H); HRMS (ES^+) Calcd. for $C_{65}H_{89}N_9NaO_{10}S$: 1210.6351, Found: 1210.6379.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(((*R*)-1-(4-(((4-methylpentyl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-6-oxohexyl)carbamate (74)**



This compound was prepared according to *General Procedure 4* using *i*-hexyl-OH (46.0 mg, 0.45 mmol), NaHMDS (1 M in THF, 0.23 mL, 0.23 mmol) and a solution of mesylate **S2** (54.0 mg, 0.045 mmol) and NBu_4I (1.7 mg, 0.0045 mmol) in THF (1.5 mL) with a 15 h reaction time. Flash chromatography (2.7 g silica, 100% EtOAc) gave **74** (27.3 mg, 50%) as an off-white solid. TLC (2% MeOH/EtOAc) R_F = 0.33; $[\alpha]_D^{25}$ −20.9 (*c* 1.23, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.90 (m, 2H), 7.89 – 7.81 (m, 2H), 7.63 (s, 1H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.39 – 7.17 (m, 5H), 7.17 – 7.06 (m, 3H), 6.25 – 6.12 (bm, 3H), 4.86 (bs, 1H), 4.59 (s, 2H), 4.49 (d, *J* = 14.6 Hz, 1H), 4.44 – 4.32 (m, 3H), 4.27 – 4.16 (m, 1H), 4.08 – 3.93 (m, 2H), 3.93 – 3.85 (m, 1H), 3.50 (t, *J* = 6.6 Hz, 2H), 3.16 – 3.03 (m, 2H), 3.00 – 2.84 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.65 – 1.34 (m, 22H), 1.34 – 1.07 (m, 8H), 0.94 – 0.79 (m, 7H), 0.77 – 0.63 (m, 2H), 0.53 (d, *J* = 6.2 Hz, 3H), 0.49 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 168.9, 158.6, 156.2, 156.1, 154.3, 152.1, 145.2, 138.2, 133.8, 133.6, 133.0, 132.1, 129.8, 129.2, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.5, 124.1, 123.79, 123.76, 120.3, 119.4, 117.4, 115.9, 114.2, 86.3, 78.9, 71.3, 68.3, 67.9, 64.1, 53.0, 52.7, 49.2, 43.2, 40.5, 40.0, 37.9, 35.1, 30.8, 29.02, 28.98, 28.5, 28.4, 27.8, 27.5, 25.3, 24.5, 22.5, 22.4, 22.3, 22.1, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1225 (100%, M+Na), 1203 (99%, M+H); HRMS (ES^+) Calcd. for $C_{66}H_{92}N_9O_{10}S$: 1202.6688, Found: 1202.6636.

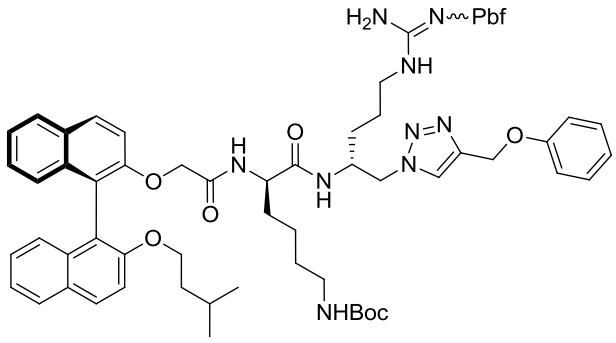
***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(((*R*)-1-(4-(((5-methylhexyl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)amino)-6-oxohexyl)carbamate (75)**



This compound was prepared according to *General Procedure 4* using *i*-heptyl-OH (52.3 mg, 0.45 mmol), NaHMDS (1 M in THF, 0.23 mL, 0.23 mmol) and a solution of mesylate **S2** (54.0 mg, 0.045 mmol) and NBu_4I (1.7 mg, 0.0045 mmol) in THF (1.5 mL) with a 15 h reaction time. Flash chromatography (2.7 g silica, 100% EtOAc) gave **75** (22.7 mg, 41%) as an off-white solid. TLC (2% MeOH/EtOAc) R_F = 0.45; $[\alpha]_D^{25}$ −19.7 (*c* 1.05, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.90 (m, 2H), 7.90 – 7.80 (m, 2H), 7.62 (s, 1H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.38 – 7.18 (m, 5H), 7.17 – 7.01 (m, 3H), 6.26 – 6.10 (bm, 3H), 4.85 (bs, 1H), 4.59 (s, 2H), 4.48 (d, *J* = 14.7 Hz, 1H), 4.44 – 4.30 (m, 3H), 4.27 – 4.16 (m, 1H), 4.07 – 3.93 (m, 2H), 3.93 – 3.84 (m, 1H), 3.51 (t, *J* = 6.5 Hz, 2H), 3.17 – 3.02 (m, 2H), 3.00 – 2.84 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.62 – 1.08 (m, 32H), 0.93 – 0.79 (m, 7H), 0.78 – 0.64 (m, 2H), 0.53

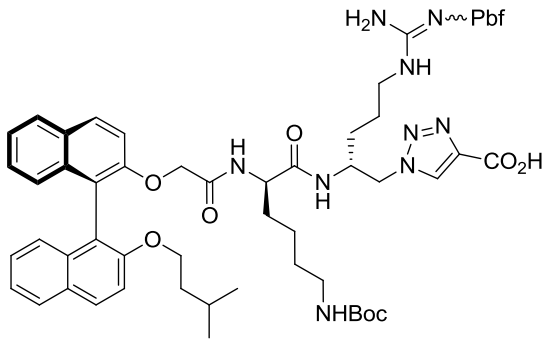
(d, J = 6.2 Hz, 3H), 0.49 (d, J = 6.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 168.9, 158.6, 156.1, 156.0, 154.3, 152.1, 145.2, 138.2, 133.8, 133.6, 132.9, 132.1, 129.8, 129.7, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.5, 124.1, 123.8, 120.2, 119.3, 117.4, 115.9, 114.1, 86.3, 78.9, 71.0, 68.3, 67.8, 64.1, 53.0, 52.7, 49.2, 43.2, 40.5, 39.9, 38.8, 37.8, 30.8, 29.9, 29.0, 28.9, 28.5, 28.4, 27.9, 25.3, 24.5, 23.9, 22.6, 22.4, 22.3, 22.1, 19.3, 18.0, 12.5; MS (ES^+) *m/z* 1239 (100%, M+Na), 1217 (66%, M+H); HRMS (ES^+) Calcd. for $C_{67}H_{94}N_9O_{10}S$: 1216.6844, Found: 1216.6801.

tert-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-oxo-6-(((*R*)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)-1-(4-(phenoxymethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)amino)hexyl)carbamate (76)



A suspension of PhOH (27.3 mg, 0.29 mmol) and Cs_2CO_3 (94.5 mg, 0.29 mmol) in MeCN (0.5 mL) was stirred under N_2 at rt for 40 min. To this was added a solution of mesylate **S2** (68.5 mg, 0.057 mmol) in MeCN (0.5 mL) and the mixture was stirred at rt for 17 h. The mixture was diluted with CH_2Cl_2 (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 (3.6 g silica, 100% CH_2Cl_2 to 4% MeOH/CH_2Cl_2) gave **76** (32.8 mg, 48%) as a white solid. TLC (2% MeOH/EtOAc) R_F = 0.59; $[\alpha]_D^{25}$ −23.2 (*c* 1.53, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.87 (m, 2H), 7.87 – 7.79 (m, 2H), 7.74 (s, 1H), 7.42 (d, J = 8.8 Hz, 1H), 7.38 – 7.06 (m, 10H), 7.01 – 6.93 (m, 3H), 6.23 (bs, 2H), 6.17 (bs, 1H), 5.15 (s, 2H), 4.76 (bs, 1H), 4.51 – 4.32 (m, 4H), 4.28 – 4.17 (m, 1H), 4.07 – 3.93 (m, 2H), 3.92 – 3.83 (m, 1H), 3.15 – 3.04 (m, 2H), 2.97 – 2.81 (m, 4H), 2.55 (s, 3H), 2.47 (s, 3H), 2.06 (s, 3H), 1.61 – 1.32 (m, 19H), 1.30 – 1.06 (m, 6H), 0.89 – 0.76 (m, 1H), 0.76 – 0.60 (m, 2H), 0.52 (d, J = 5.5 Hz, 3H), 0.47 (d, J = 5.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 168.9, 158.6, 158.2, 156.2, 156.0, 154.3, 152.1, 143.8, 138.2, 133.8, 133.6, 132.9, 132.1, 129.7, 129.5, 129.1, 128.0, 127.9, 126.6, 126.5, 125.5, 124.9, 124.6, 124.2, 124.1, 123.8, 121.3, 120.3, 119.3, 117.4, 115.9, 114.8, 114.2, 86.3, 78.9, 68.3, 67.9, 61.8, 53.0, 52.7, 49.3, 43.2, 40.5, 39.9, 37.9, 30.9, 28.99, 28.95, 28.5, 28.4, 25.4, 24.5, 22.4, 22.3, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 1217 (100%, M+Na), 1195 (95%, M+H); HRMS (ES^+) Calcd. for $C_{66}H_{83}N_9NaO_{10}S$: 1216.5881, Found: 1216.5919.

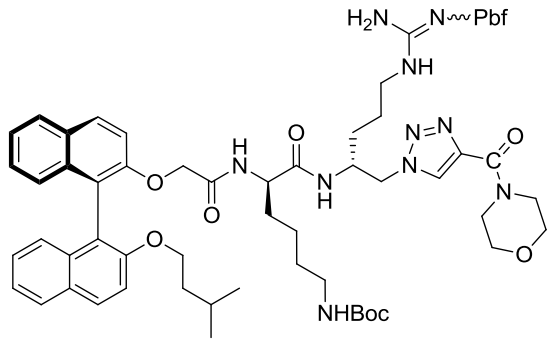
1-((*R*)-2-((*R*)-6-((tert-Butoxycarbonyl)amino)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamido)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentyl)-1*H*-1,2,3-triazole-4-carboxylic acid (84)



This compound was prepared in two steps from azide **18** via cycloaddition with methyl propiolate and subsequent saponification. Thus, the triazole ester intermediate **38** was prepared according to *General Procedure 2* using azide **18** (300 mg, 0.28 mmol), $Cu(OAc)_2{\cdot}H_2O$ (11.3 mg, 0.056 mmol), Na·ascorbate (22.4 mg, 0.11 mmol), methyl propiolate (71.2 mg, 0.85 mmol), *t*-BuOH (5.6 mL) and H_2O (1.4 mL) with a 7 h reaction time. Flash chromatography (10 g silica, 100% EtOAc to 4% MeOH/EtOAc) gave **38** (181.4 mg, 56%) as a pale yellow solid. TLC (2% MeOH/EtOAc) R_F = 0.45. To this intermediate (177.4 mg, 0.15 mmol) was

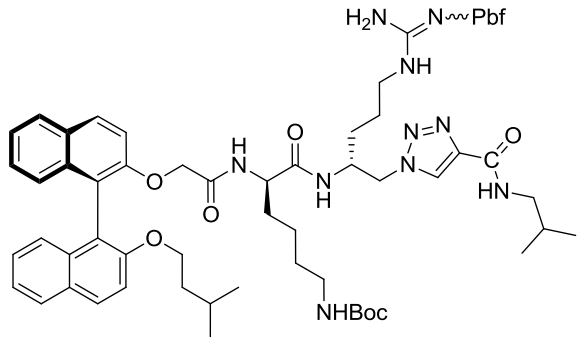
added LiOH (37.1 mg, 1.55 mmol), reagent grade THF (1.5 mL) and H_2O (1.5 mL) and the mixture was stirred at rt in an air atmosphere for 2 h. The mixture was diluted with CH_2Cl_2 (20 mL) and 1 M HCl (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give **84** (165.6 mg, 95% from the ester) as a pale yellow solid. TLC (10% MeOH/CH_2Cl_2) R_F = 0.53; $[\alpha]_D^{25}$ −14.1 (*c* 2.19, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, major rotamer only) δ 8.30 (bs, 1H), 7.95 (d, *J* = 7.4 Hz, 1H), 7.89 (d, *J* = 8.7 Hz, 1H), 7.83 (app. d, *J* = 7.7 Hz, 2H), 7.46 (d, *J* = 8.9 Hz, 1H), 7.37 – 7.24 (m, 3H), 7.24 – 7.10 (m, 3H), 7.07 (d, *J* = 8.3 Hz, 1H), 6.63 – 6.20 (bm, 4H), 4.97 (bs, 1H), 4.66 – 4.32 (m, 3H), 4.32 – 4.15 (m, 1H), 4.15 – 3.96 (m, 2H), 3.96 – 3.82 (m, 2H), 3.31 – 3.08 (m, 2H), 3.04 – 2.78 (m, 4H), 2.53 (s, 3H), 2.46 (s, 3H), 2.05 (s, 3H), 1.67 – 1.06 (m, 25H), 0.95 – 0.80 (m, 2H), 0.74 – 0.63 (m, 1H), 0.56 – 0.51 (m, 3H), 0.50 – 0.46 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, most signals broad) δ 171.9, 169.1, 162.2, 161.2, 156.3, 154.4, 152.9, 152.2, 140.7, 139.2, 135.1, 134.8, 133.8, 133.5, 129.7, 129.0, 128.0, 127.8, 126.5, 126.4, 125.8, 125.5, 124.9, 124.8, 124.0, 123.6, 120.3, 119.1, 118.7, 115.8, 114.4, 87.5, 79.1, 68.1, 67.9, 53.4, 52.9, 49.3, 42.7, 41.9, 40.1, 37.8, 31.0, 29.1, 28.5, 28.4, 24.8, 24.5, 22.2, 22.1, 19.6, 18.1, 12.4; MS (ES^+) *m/z* 1154 (23%, M+Na), 1133 (100%, M+H); HRMS (ES^+) Calcd. for $C_{60}H_{78}N_9O_{11}S$: 1132.5542, Found: 1132.5558.

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



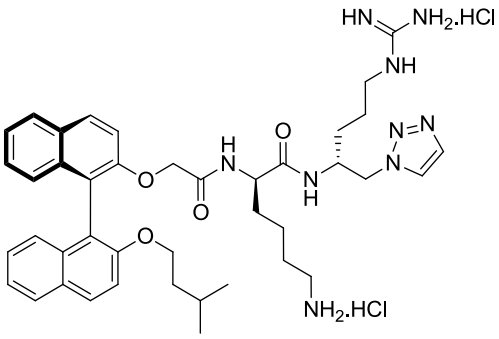
To a suspension of acid **84** (38.0 mg, 0.034 mmol) in THF (0.17 mL) at 0 °C in an air atmosphere (capped vial) was added NEt_3 (10.2 mg, 0.10 mmol) and a solution of isobutyl chloroformate (13.7 mg, 0.10 mmol) in THF (0.17 mL). The cloudy mixture was stirred at 0 °C for 2.5 h, then morpholine (23.4 mg, 0.27 mmol) was added. The mixture was allowed to warm to rt with stirring over a further 21.5 h. EtOAc (20 mL) was added and the solution was washed sequentially with 1 M HCl (2×15 mL), saturated $NaHCO_3$ (15 mL), 1 M HCl again (15 mL) and brine (15 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (2.4 g silica, 100% CH_2Cl_2 to 4% MeOH/CH_2Cl_2) gave **85** (18.4 mg, 46%) as a white solid. TLC (10% MeOH/CH_2Cl_2) R_F = 0.46; $[\alpha]_D^{25}$ −24.4 (*c* 0.36, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.98 – 7.89 (m, 2H), 7.85 (app. t, *J* = 7.5 Hz, 2H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.06 (m, 8H), 6.22 (bs, 2H), 6.13 (bd, *J* = 6.3 Hz, 1H), 4.94 (bs, 1H), 4.54 – 4.34 (m, 4H), 4.32 – 4.18 (m, 3H), 4.06 – 3.98 (m, 1H), 3.97 – 3.84 (m, 2H), 3.83 – 3.72 (m, 6H), 3.15 – 3.03 (m, 2H), 2.99 – 2.86 (m, 4H), 2.55 (s, 3H), 2.48 (s, 3H), 2.07 (s, 3H), 1.57 – 1.34 (m, 19H), 1.32 – 1.06 (m, 6H), 0.85 – 0.76 (m, 1H), 0.75 – 0.61 (m, 2H), 0.52 (d, *J* = 6.4 Hz, 3H), 0.48 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 169.1, 159.9, 158.7, 156.2, 154.3, 152.0, 143.6, 138.2, 133.8, 133.6, 132.9, 132.2, 129.8, 129.5, 129.2, 128.1, 128.0, 126.7, 126.6, 125.5, 124.9, 124.6, 124.2, 123.9, 120.2, 119.3, 117.5, 115.9, 114.1, 86.4, 79.0, 68.3, 67.8, 67.2, 66.9, 53.2, 52.7, 49.2, 47.3, 43.2, 43.0, 40.5, 39.9, 37.9, 30.8, 29.0, 28.9, 28.6, 28.4, 25.4, 24.5, 22.35, 22.29, 22.1, 19.3, 18.0, 12.5; MS (ES^+) *m/z* 1224 (100%, M+Na), 1202 (35%, M+H); HRMS (ES^+) Calcd. for $C_{64}H_{85}N_{10}O_{11}S$: 1201.6120, Found: 1201.6119.

***tert*-Butyl ((*R*)-6-(((*R*)-1-(4-(isobutylcarbamoyl)-1*H*-1,2,3-triazol-1-yl)-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)**



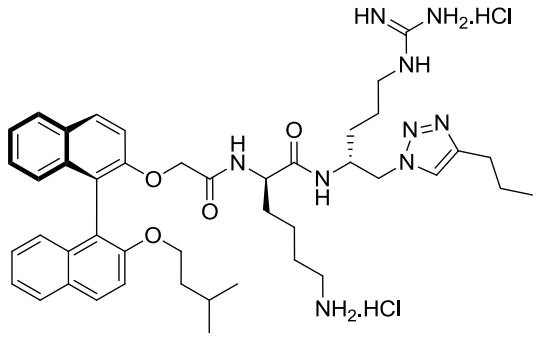
To a suspension of acid **84** (40.3 mg, 0.036 mmol) in THF (0.18 mL) at 0 °C in an air atmosphere (capped vial) was added NEt_3 (10.8 mg, 0.11 mmol) and a solution of isobutyl chloroformate (14.6 mg, 0.11 mmol) in THF (0.18 mL). The cloudy mixture was stirred at 0 °C for 2.5 h, then isobutylamine (20.8 mg, 0.29 mmol) was added. The mixture was allowed to warm to rt with stirring over a further 17 h. EtOAc (20 mL) was added and the solution was washed sequentially with 1 M HCl (2×15 mL), saturated $NaHCO_3$ (15 mL), 1 M HCl again (15 mL) and brine (15 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (2.4 g silica, 100% CH_2Cl_2 to 4% MeOH/CH_2Cl_2) gave **86** (17.5 mg, 41%) as a white solid. TLC (10% MeOH/CH_2Cl_2) R_F = 0.67; $[\alpha]_D^{25}$ −24.6 (*c* 0.77, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.93 (app. t, *J* = 9.2 Hz, 2H), 7.88 – 7.80 (m, 2H), 7.46 – 7.05 (m, 10H), 6.22 (bs, 2H), 6.16 (bs, 1H), 4.92 (bs, 1H), 4.53 – 4.32 (m, 4H), 4.30 – 4.18 (m, 1H), 4.05 – 3.84 (m, 3H), 3.28 (t, *J* = 5.8 Hz, 2H), 3.16 – 3.02 (m, 2H), 3.00 – 2.86 (m, 4H), 2.54 (s, 3H), 2.48 (s, 3H), 2.06 (s, 3H), 1.96 – 1.86 (m, 1H), 1.57 – 1.35 (m, 19H), 1.29 – 1.06 (m, 6H), 0.98 (d, *J* = 6.4 Hz, 6H), 0.82 – 0.59 (m, 3H), 0.52 (d, *J* = 6.4 Hz, 3H), 0.48 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 169.0, 160.1, 158.7, 157.0, 156.2, 156.1, 154.3, 152.1, 143.1, 138.2, 133.8, 133.6, 132.9, 132.1, 129.8, 129.1, 128.1, 127.9, 126.6, 126.5, 125.5, 124.9, 124.6, 124.2, 123.8, 120.3, 119.3, 117.5, 115.9, 114.2, 86.3, 78.9, 68.3, 67.9, 53.3, 52.7, 49.3, 46.5, 43.2, 40.5, 39.9, 37.9, 31.0, 29.1, 29.0, 28.7, 28.6, 28.5, 25.4, 24.5, 22.4, 22.3, 22.1, 20.2, 19.3, 18.0, 12.5; MS (ES^+) *m/z* 1210 (100%, M+Na), 1188 (84%, M+H); HRMS (ES^+) Calcd. for $C_{64}H_{86}N_{10}NaO_{10}S$: 1209.6147, Found: 1209.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (69)



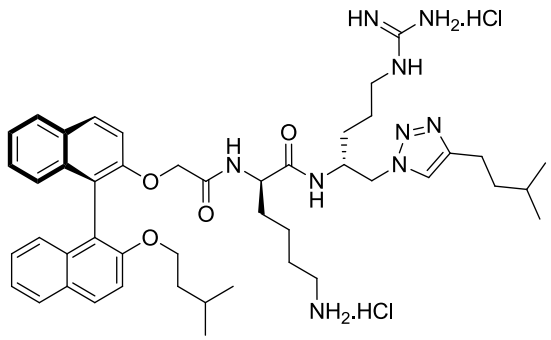
This compound was prepared according to *General Procedure 5* using **68** (68.4 mg, 0.063 mmol), CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) with a 20 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 1.0 mL) as described gave **69** (40.7 mg, 80%) as a white solid. $[\alpha]_D^{25}$ −17.6 (*c* 1.49, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.10 – 8.00 (m, 3H), 7.96 – 7.88 (m, 2H), 7.83 (s, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.27 – 7.19 (m, 2H), 7.06 (app. t, *J* = 7.5 Hz, 2H), 4.64 – 4.39 (m, 4H), 4.39 – 4.28 (m, 1H), 4.19 – 4.07 (m, 1H), 4.03 – 3.90 (m, 2H), 3.24 – 3.10 (m, 2H), 2.82 – 2.72 (m, 2H), 1.78 – 1.40 (m, 6H), 1.34 – 1.11 (m, 4H), 0.93 – 0.82 (m, 1H), 0.80 – 0.64 (m, 2H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.53 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.2, 170.6, 158.5, 155.9, 154.0, 135.2, 135.0, 134.3, 131.4, 130.9, 130.8, 130.7, 129.3, 129.1, 127.54, 127.49, 127.1, 126.4, 125.9, 125.2, 124.8, 121.8, 120.4, 116.9, 115.9, 69.2, 69.0, 54.6, 53.6, 50.5, 41.9, 40.4, 39.3, 32.3, 30.0, 27.8, 26.1, 25.6, 23.1, 22.8, 22.6; IR (cm^{-1}) υ 3179, 2954, 1654, 1507, 1213, 1049, 807, 745, 617; MS (ES^+) *m/z* 736 (<5%, M+H), 369 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{41}H_{54}N_9O_4$: 736.4299, Found: 736.4320.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-propyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((S)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (44)



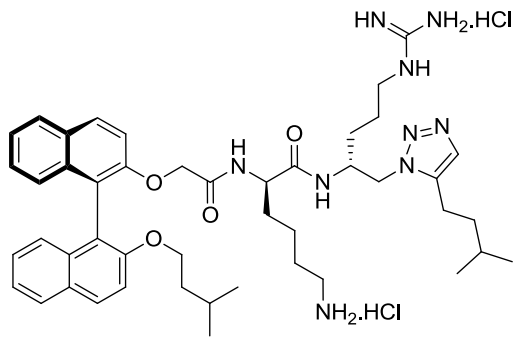
This compound was prepared according to *General Procedure 5* using **19** (38.8 mg, 0.034 mmol), CH_2Cl_2 (1.11 mL) and TFA (1.11 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.56 mL) as described gave **44** (23.2 mg, 79%) as an off-white solid. $[\alpha]_D^{25}$ −14.0 (*c* 0.63, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.15 (s, 1H), 8.03 (app. d, *J* = 9.0 Hz, 2H), 7.96 – 7.88 (m, 2H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.23 (app. t, *J* = 7.4 Hz, 2H), 7.10 – 7.02 (m, 2H), 4.65 (d, *J* = 10.8 Hz, 1H), 4.59 – 4.42 (m, 3H), 4.35 – 4.26 (m, 1H), 4.17 – 4.08 (m, 1H), 4.02 – 3.91 (m, 2H), 3.25 – 3.11 (m, 2H), 2.85 – 2.70 (m, 4H), 1.81 – 1.47 (m, 8H), 1.41 – 1.11 (m, 4H), 1.07 – 0.95 (m, 4H), 0.91 – 0.79 (m, 2H), 0.58 (d, *J* = 6.4 Hz, 3H), 0.52 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.7, 170.8, 158.5, 155.9, 154.1, 146.6, 135.2, 135.1, 131.4, 130.8, 130.7, 129.3, 129.1, 127.6, 127.5, 127.1, 126.3, 126.0, 125.2, 124.8, 121.7, 120.6, 116.8, 116.0, 69.3, 69.0, 56.5, 53.8, 50.5, 41.8, 40.4, 39.3, 32.3, 29.6, 27.7, 26.8, 26.1, 25.6, 23.5, 23.1, 22.8, 22.5, 13.9; IR (cm^{-1}) υ 2959, 1653, 1507, 1213, 1048, 808, 745; MS (ES^+) *m/z* 778 (<5%, M+H), 390 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{44}H_{60}N_9O_4$: 778.4768, Found: 778.4767.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (45)



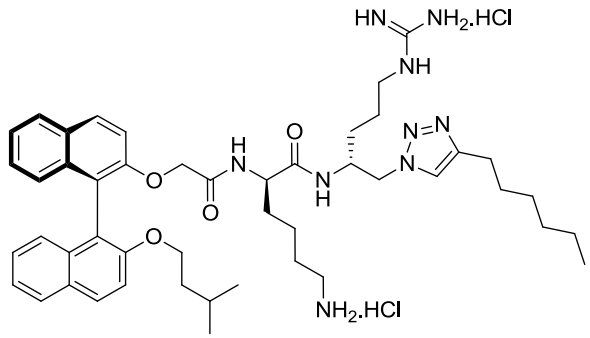
This compound was prepared according to *General Procedure 5* using **20** (71.9 mg, 0.062 mmol), CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) with a 20 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 1.0 mL) as described gave **45** (53.1 mg, 97%) as a white solid. $[\alpha]_D^{25}$ −16.4 (*c* 2.06, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.09 – 8.00 (m, 2H), 7.98 – 7.88 (m, 3H), 7.54 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 8.8 Hz, 1H), 7.41 – 7.31 (m, 2H), 7.30 – 7.20 (m, 2H), 7.13 – 7.01 (m, 2H), 4.63 – 4.50 (m, 2H), 4.50 – 4.37 (m, 2H), 4.94 – 4.24 (m, 1H), 4.19 – 4.09 (m, 1H), 4.04 – 3.92 (m, 2H), 3.24 – 3.10 (m, 2H), 2.87 – 2.71 (m, 4H), 1.77 – 1.45 (m, 9H), 1.36 – 1.11 (m, 4H), 1.07 – 0.90 (m, 7H), 0.90 – 0.75 (m, 2H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.5, 170.7, 158.5, 155.9, 154.0, 148.0, 135.2, 135.0, 131.4, 130.9, 130.8, 130.7, 129.3, 129.1, 127.6, 127.5, 126.3, 125.9, 125.8, 125.2, 124.8, 121.7, 120.6, 116.9, 116.0, 69.3, 69.0, 55.7, 53.8, 50.5, 41.9, 40.4, 39.3, 39.1, 32.3, 29.7, 28.7, 27.7, 26.1, 25.6, 23.5, 23.3, 22.8, 22.74, 22.72, 22.6; IR (cm^{-1}) υ 2960, 1653, 1507, 1212, 1049, 808, 745; MS (ES^+) *m/z* 806 (<5%, M+H), 404 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{46}H_{64}N_9O_4$: 806.5081, Found: 806.5092.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(5-isopentyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (46)



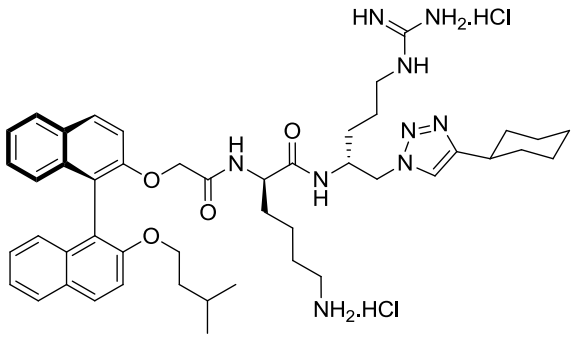
This compound was prepared according to *General Procedure 5* using **21** (37.1 mg, 0.032 mmol), CH_2Cl_2 (1.05 mL) and TFA (1.05 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.52 mL) as described gave **46** (21.5 mg, 77%) as a tan solid. $[\alpha]_D^{25}$ −19.3 (*c* 0.53, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.08 – 7.99 (m, 3H), 7.97 – 7.88 (m, 2H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.41 – 7.31 (m, 2H), 7.23 (app. t, *J* = 7.4 Hz, 2H), 7.11 – 7.02 (m, 2H), 4.63 – 4.39 (m, 4H), 4.38 – 4.26 (m, 1H), 4.19 – 4.08 (m, 1H), 4.06 – 3.91 (m, 2H), 3.24 – 3.12 (m, 2H), 2.86 (t, *J* = 8.0 Hz, 2H), 2.83 – 2.69 (m, 2H), 1.82 – 1.46 (m, 9H), 1.39 – 1.11 (m, 4H), 1.03 (d, *J* = 6.0 Hz, 6H), 0.95 – 0.85 (m, 1H), 0.83 – 0.72 (m, 2H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.4, 170.7, 158.5, 155.9, 154.0, 142.8, 135.2, 135.1, 131.4, 130.9, 130.8, 130.7, 130.3, 129.3, 129.1, 127.6, 127.5, 126.4, 126.0, 125.2, 124.8, 121.8, 120.5, 116.8, 115.9, 69.2, 68.9, 53.6, 53.5, 49.5, 42.0, 40.4, 39.3, 37.6, 32.3, 29.8, 29.0, 27.8, 26.2, 25.6, 23.3, 22.8, 22.7, 22.6, 22.2; IR (cm^{-1}) υ 2957, 1654, 1507, 1217, 1047, 808, 743; MS (ES^+) *m/z* 807 (<5%, M+H), 404 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{46}H_{64}N_9O_4$: 806.5081, Found: 806.5118.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-hexyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (47)



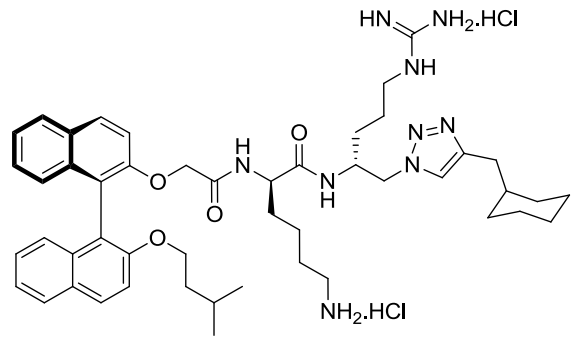
This compound was prepared according to *General Procedure 5* using **22** (47.8 mg, 0.041 mmol), CH_2Cl_2 (1.34 mL) and TFA (1.34 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.67 mL) as described gave **47** (34.2 mg, 94%) as a tan solid. $[\alpha]_D^{25}$ −15.1 (*c* 0.95, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.18 (s, 1H), 8.03 (app. d, *J* = 9.0 Hz, 2H), 7.96 – 7.89 (m, 2H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.49 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.23 (app. t, *J* = 7.5 Hz, 2H), 7.12 – 7.02 (m, 2H), 4.70 – 4.41 (m, 4H), 4.34 – 4.25 (m, 1H), 4.18 – 4.08 (m, 1H), 4.02 – 3.91 (m, 2H), 3.23 – 3.11 (m, 2H), 2.86 – 2.70 (m, 4H), 1.80 – 1.47 (m, 8H), 1.46 – 1.10 (m, 10H), 1.07 – 0.97 (m, 1H), 0.96 – 0.79 (m, 5H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.7, 170.9, 158.5, 155.9, 154.1, 146.5, 135.2, 135.1, 131.4, 130.8, 130.7, 129.3, 129.1, 127.6, 127.5, 126.3, 126.0, 125.2, 124.8, 121.7, 120.6, 116.8, 116.0, 69.3, 69.0, 56.8, 53.9, 50.5, 41.8, 40.4, 39.3, 32.5, 32.2, 29.8, 29.6, 29.5, 27.7, 26.1, 25.6, 24.7, 23.6, 23.5, 22.8, 22.5, 14.4; IR (cm^{-1}) υ 2923, 1653, 1506, 1214, 1149, 1048, 811, 747; MS (ES^+) *m/z* 821 (<5%, M+H), 411 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{47}H_{66}N_9O_4$: 820.5238, Found: 820.5256.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-cyclohexyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (48)



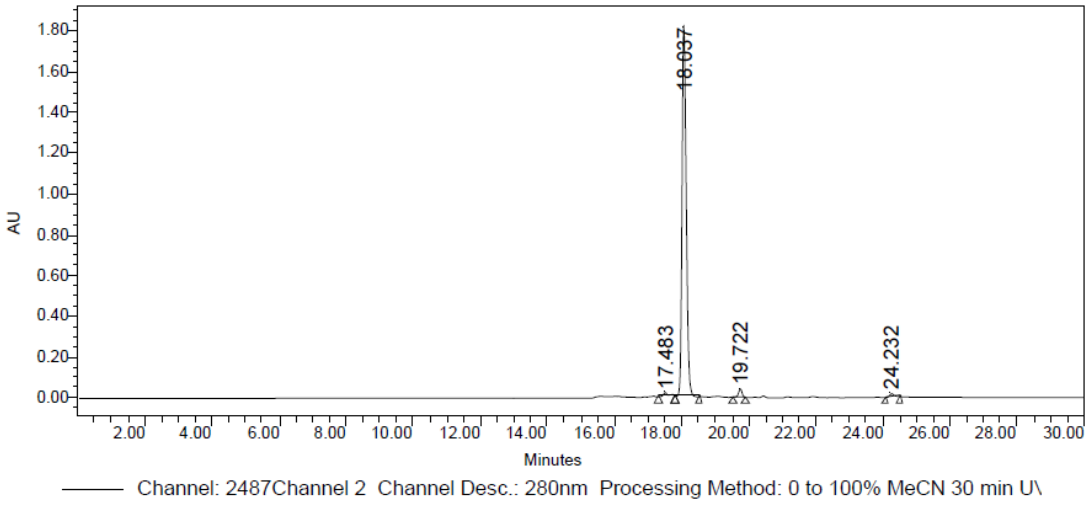
This compound was prepared according to *General Procedure 5* using **23** (74.5 mg, 0.064 mmol), CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) with a 20 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 1.0 mL) as described gave **48** (52.6 mg, 93%) as a white solid. $[\alpha]_D^{25}$ −14.1 (*c* 2.18, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ ^{1}H NMR (500 MHz, CD_3OD) δ 8.09 – 7.97 (m, 3H), 7.95 – 7.89 (m, 2H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 7.41 – 7.31 (m, 2H), 7.24 (app. t, *J* = 7.7 Hz, 2H), 7.13 – 7.02 (m, 2H), 4.62 – 4.51 (m, 2H), 4.49 – 4.38 (m, 2H), 4.35 – 4.25 (m, 1H), 4.18 – 4.09 (m, 1H), 4.02 – 3.92 (m, 2H), 3.23 – 3.11 (m, 2H), 2.91 – 2.69 (m, 3H), 2.12 – 2.00 (m, 2H), 1.96 – 1.84 (m, 2H), 1.84 – 1.09 (m, 16H), 1.00 – 0.87 (m, 1H), 0.87 – 0.76 (m, 2H), 0.58 (d, *J* = 6.3 Hz, 3H), 0.53 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.4, 170.7, 158.4, 155.8, 154.0, 135.1, 135.0, 131.3, 130.83, 130.78, 130.6, 129.2, 129.1, 127.6, 127.5, 126.3, 125.9, 125.1, 124.8, 124.2, 121.6, 120.5, 116.8, 115.9, 69.2, 68.9, 55.3, 53.7, 50.5, 41.8, 40.4, 39.2, 36.0, 33.8, 32.3, 29.8, 27.7, 27.0, 26.9, 26.1, 25.6, 23.3, 22.8, 22.6; IR (cm^{-1}) υ 292, 1654, 1507, 1213, 1169, 1048, 810, 747; MS (ES^+) *m/z* 818 (<5%, M+H), 410 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{47}H_{64}N_9O_4$: 818.5081, Found: 818.5110.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(cyclohexylmethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (49)



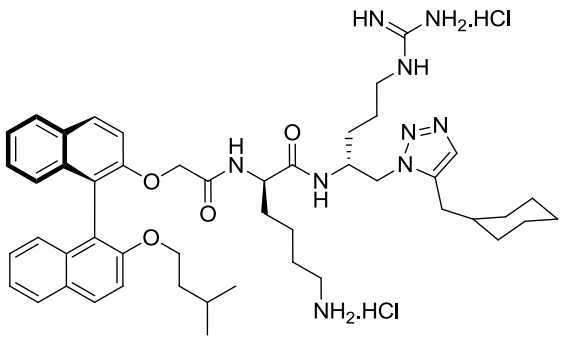
This compound was prepared according to *General Procedure 5* (larger scale modification, see *Note 2*) using **24** (777.2 mg, 0.66 mmol), CH_2Cl_2 (11.0 mL), TFA (11.0 mL) and H_2O (0.24 mL, 13.12 mmol, 20 equiv) with a 17.5 h reaction time. Work-up as described, followed by treatment with HCl (2 M in Et_2O, 7.0 mL) and double precipitation of the product from MeOH with Et_2O gave **49** (557.1 mg, 94%) as an off-white solid. $[\alpha]_D^{25}$ −14.7 (*c* 0.76, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.16 (s, 1H), 8.03 (app. d, *J* = 9.0 Hz, 2H), 7.96 – 7.88 (m, 2H), 7.54 (d, *J* = 8.9 Hz, 1H), 7.49 (d, *J* = 8.9 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.24 (app. t, *J* = 7.0 Hz, 2H), 7.12 – 7.02 (m, 2H), 4.66 (d, *J* = 10.9 Hz, 1H), 4.60 – 4.42 (m, 3H), 4.36 – 4.26 (m, 1H), 4.17 – 4.07 (m, 1H), 4.03 – 3.90 (m, 2H), 3.24 – 3.11 (m, 2H), 2.85 – 2.72 (m, 2H), 2.70 (d, *J* = 6.8 Hz, 2H), 1.80 – 1.47 (m, 11H), 1.44 – 1.10 (m, 8H), 1.08 – 0.95 (m, 3H), 0.93 – 0.80 (m, 2H), 0.58 (d, *J* = 6.4 Hz, 3H), 0.52 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.6, 170.9, 158.5, 155.9, 154.1, 145.4, 135.2, 135.1, 131.4, 130.8, 130.7, 129.3, 129.1, 127.62, 127.59, 127.5, 126.4, 126.0, 125.2, 124.8, 121.8, 120.7, 116.9, 116.0, 69.4, 69.1, 56.5, 53.9, 50.6, 41.9, 40.4, 39.3, 38.9, 33.8, 33.7, 32.5, 32.2, 29.6, 27.7, 27.2, 27.1, 26.1, 25.6, 23.5, 22.8, 22.5; IR (cm^{-1}) υ 2925, 1654, 1507, 1215, 1047, 807, 747; MS (ES^+) *m/z* 832 (<5%, M+H), 417 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{48}H_{66}N_9O_4$: 832.5238, Found: 832.5273; HPLC phenomenex Synergi 4u Fusion-RP 80Å column, Flow rate = 1.0 $mLmin^{-1}$, Eluent profile: 100% H_2O for 2 min, then linear gradient to 100% MeCN over 20 min, then 100% MeCN for 8 min (both solvents containing 0.1% TFA), λ = 280 nm, t_R = 18.0 min (96.0% peak area).

HPLC Trace of Compound **49**:



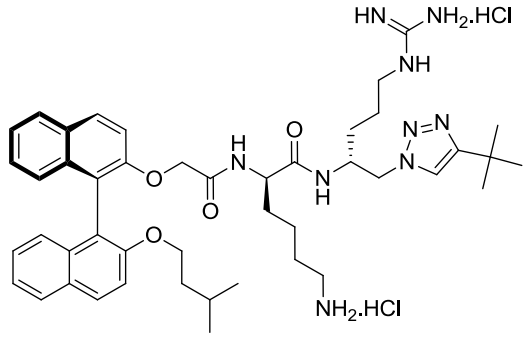
	Channel Description	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	280nm	17.483	211840	1.28	18822
2	280nm	18.037	15863499	95.99	1827064
3	280nm	19.722	286247	1.73	40355
4	280nm	24.232	164188	0.99	16781

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(5-(cyclohexylmethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (50)



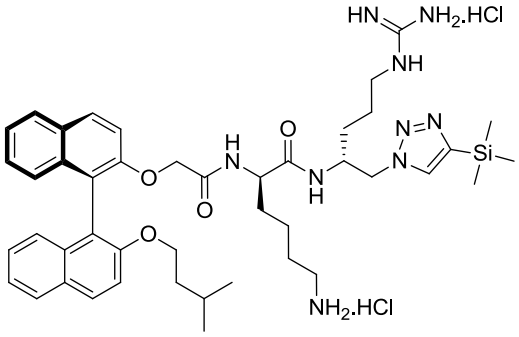
This compound was prepared according to *General Procedure 5* using **25** (37.8 mg, 0.032 mmol), CH_2Cl_2 (1.02 mL) and TFA (1.02 mL) with a 16 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.51 mL) as described gave **50** (27.5 mg, 95%) as a pale green solid. $[\alpha]_D^{25}$ −26.2 (*c* 0.67, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.04 (app. d, *J* = 8.9 Hz, 2H), 7.97 (s, 1H), 7.93 (app. t, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.23 (app. t, *J* = 7.4 Hz, 2H), 7.06 (app. t, *J* = 8.1 Hz, 2H), 4.57 – 4.51 (m, 2H), 4.48 – 4.40 (m, 2H), 4.32 – 4.25 (m, 1H), 4.17 – 4.10 (m, 1H), 4.05 – 3.93 (m, 2H), 3.23 – 3.10 (m, 2H), 2.84 – 2.66 (m, 4H), 1.85 – 1.46 (m, 12H), 1.40 – 1.02 (m, 9H), 0.98 – 0.87 (m, 1H), 0.84 – 0.73 (m, 2H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.53 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.5, 170.7, 158.5, 155.9, 154.0, 141.8, 135.2, 135.1, 131.4, 130.8, 130.7, 130.3, 129.3, 129.1, 127.6, 127.5, 126.4, 126.0, 125.2, 124.8, 121.8, 120.5, 116.8, 115.9, 69.2, 68.9, 53.9, 53.5, 49.8, 41.9, 40.4, 39.3, 38.2, 34.2, 33.8, 32.3, 31.4, 29.7, 27.7, 27.2, 27.12, 27.05, 26.2, 25.6, 23.4, 22.8, 22.6; IR (cm^{-1}) υ 3387, 2925, 1654, 1540, 1507, 1458, 1214, 1048, 807, 745; MS (ES^+) *m/z* 832 (<5%, M+H), 417 (100%, M+2H).

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(*tert*-butyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (51)



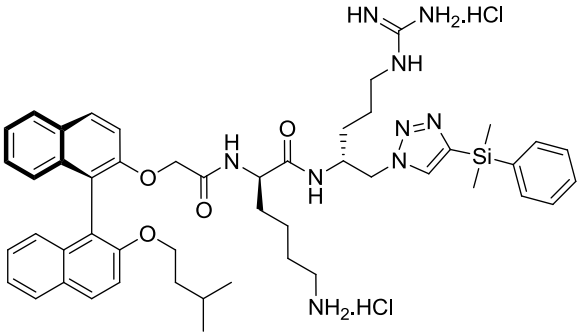
This compound was prepared according to *General Procedure 5* using **26** (48.6 mg, 0.042 mmol), CH_2Cl_2 (1.38 mL) and TFA (1.38 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.69 mL) as described gave **51** (34.5 mg, 94%) as a tan solid. $[\alpha]_D^{25}$ −10.1 (*c* 1.05, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ ^{1}H NMR δ 8.17 (s, 1H), 8.07 – 7.99 (m, 2H), 7.92 (app. d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.31 (m, 2H), 7.23 (app. t, *J* = 7.5 Hz, 2H), 7.11 – 7.01 (m, 2H), 4.63 (dd, *J* = 13.7, 3.2 Hz, 1H), 4.55 (d, *J* = 14.7 Hz, 1H), 4.51 – 4.41 (m, 2H), 4.36 – 4.26 (m, 1H), 4.17 – 4.08 (m, 1H), 4.02 – 3.91 (m, 2H), 3.24 – 3.11 (m, 2H), 2.85 – 2.69 (m, 2H), 1.80 – 1.56 (m, 4H), 1.51 (quin, *J* = 7.6 Hz, 2H), 1.42 (s, 9H), 1.36 – 1.11 (m, 4H), 1.02 – 0.79 (m, 3H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.7, 170.8, 158.5, 155.9, 155.6, 154.1, 135.2, 135.1, 131.4, 130.85, 130.83, 130.7, 129.3, 129.1, 127.6, 127.5, 126.3, 126.0, 125.6, 125.2, 124.8, 121.7, 120.7, 116.9, 116.0, 69.3, 69.1, 56.6, 53.8, 50.5, 41.8, 40.4, 39.3, 32.3, 31.8, 30.1, 29.5, 27.7, 26.1, 25.6, 23.5, 22.8, 22.5; IR (cm^{-1}) υ 2960, 1653, 1507, 1212, 1168, 1048, 807, 747; MS (ES^+) *m/z* 792 (<5%, M+H), 397 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{45}H_{62}N_9O_4$: 792.4925, Found: 792.4964.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-trimethylsilyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (52)



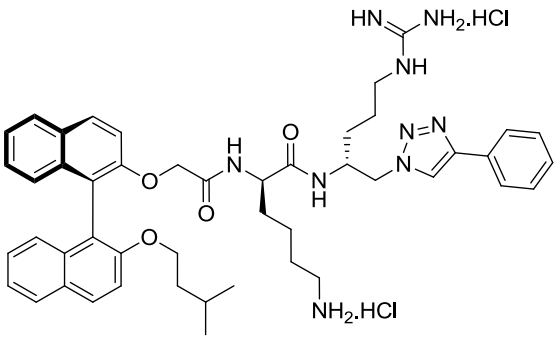
This compound was prepared according to *General Procedure 5* using **27** (60.0 mg, 0.052 mmol), CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) with a 21.5 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 1.0 mL) as described gave **52** (29.3 mg, 64%) as an off-white solid. $[\alpha]_D^{25}$ −11.0 (*c* 1.11, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.46 (s, 1H), 8.08 – 8.00 (m, 2H), 7.92 (app. d, *J* = 7.9 Hz, 2H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.49 (d, *J* = 9.2 Hz, 1H), 7.43 – 7.31 (m, 2H), 7.24 (app. t, *J* = 7.4 Hz, 2H), 7.12 – 7.01 (m, 2H), 4.73 (d, *J* = 11.2 Hz, 1H), 4.62 – 4.52 (m, 2H), 4.47 (d, *J* = 14.7 Hz, 1H), 4.38 – 4.26 (m, 1H), 4.13 (dd, *J* = 14.8, 6.2 Hz, 1H), 4.04 – 3.91 (m, 2H), 3.24 – 3.11 (m, 2H), 2.83 – 2.68 (m, 2H), 1.81 – 1.56 (m, 4H), 1.52 (quint, *J* = 7.5 Hz, 2H), 1.41 – 1.10 (m, 4H), 1.06 – 0.94 (m, 1H), 0.94 – 0.77 (m, 2H), 0.58 (d, *J* = 6.2 Hz, 3H), 0.52 (d, *J* = 6.1 Hz, 3H), 0.44 (s, 9H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.5, 170.8, 158.5, 155.9, 154.0, 145.9, 135.2, 135.0, 134.0, 131.3, 130.8, 130.7, 129.3, 129.1, 127.6, 127.5, 126.3, 125.9, 125.2, 124.8, 121.7, 120.6, 116.8, 115.9, 69.2, 69.0, 55.3, 53.7, 50.6, 41.8, 40.4, 39.2, 32.2, 29.7, 27.7, 26.1, 25.6, 23.4, 22.8, 22.6, −1.3; IR (cm^{-1}) υ 2955, 1653, 1559, 1212, 1148, 1049, 848, 804, 748; MS (ES^+) *m/z* 808 (<5%, M+H), 405 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{44}H_{62}N_9O_4Si$: 808.4694, Found: 808.4708.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-dimethylphenylsilyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (53)



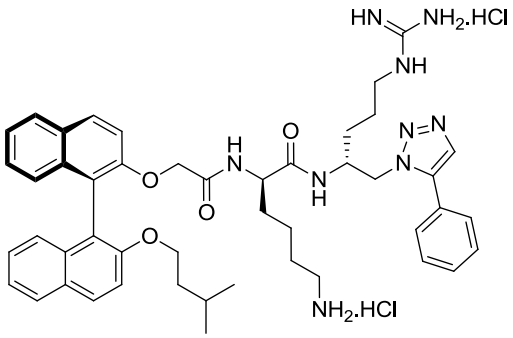
This compound was prepared according to *General Procedure 5* using **28** (65.2 mg, 0.053 mmol), CH_2Cl_2 (1.70 mL) and TFA (1.70 mL) with a 17 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.85 mL) as described gave **53** (47.7 mg, 95%) as an off-white solid. $[\alpha]_D^{25}$ −9.9 (*c* 1.78, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.43 (s, 1H), 8.03 (app. t, *J* = 9.6 Hz, 2H), 7.92 (app. d, *J* = 6.0 Hz, 2H), 7.60 (app. d, *J* = 7.3 Hz, 2H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 9.0 Hz, 1H), 7.45 – 7.30 (m, 5H), 7.23 (app. t, *J* = 9.1 Hz, 2H), 7.12 – 7.01 (m, 2H), 4.75 – 4.68 (m, 1H), 4.60 – 4.50 (m, 2H), 4.45 (d, *J* = 14.8 Hz, 1H), 4.36 – 4.25 (m, 1H), 4.17 – 4.07 (m, 1H), 4.00 – 3.89 (m, 2H), 3.24 – 3.11 (m, 2H), 2.81 – 2.62 (m, 2H), 1.80 – 1.55 (m, 4H), 1.47 (quin, *J* = 7.6 Hz, 2H), 1.35 – 1.09 (m, 4H), 1.02 – 0.91 (m, 1H), 0.88 – 0.77 (m, 2H), 0.71 (s, 3H), 0.70 (s, 3H), 0.57 (d, *J* = 6.5 Hz, 3H), 0.51 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.7, 170.8, 158.5, 155.9, 154.1, 143.6, 141.8, 136.2, 135.2, 135.1, 134.9, 131.5, 131.4, 130.9, 130.7, 129.5, 129.3, 129.1, 127.6, 127.5, 126.3, 125.9, 125.2, 124.8, 121.8, 120.7, 116.9, 116.1, 69.4, 69.1, 56.5, 53.8, 50.6, 41.8, 40.4, 39.3, 32.2, 29.5, 27.6, 26.1, 25.6, 23.5, 22.8, 22.5, −2.78, −2.84; IR (cm^{-1}) υ 2954, 1653, 1559, 1212, 1148, 1049, 812, 741; MS (ES^+) *m/z* 870 (<5%, M+H), 436 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{49}H_{64}N_9O_4Si$: 870.4851, Found: 870.4884.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (54)



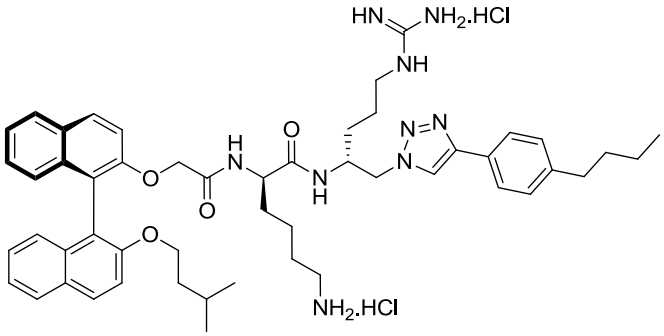
This compound was prepared according to *General Procedure 5* using **29** (161.5 mg, 0.14 mmol), CH_2Cl_2 (4.6 mL) and TFA (4.6 mL) with a 30 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 2.3 mL) as described gave **54** (114.8 mg, 94%) as an off-white solid. $[\alpha]_D^{25}$ −26.1 (*c* 0.54, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.45 (s, 1H), 8.01 (d, *J* = 8.9 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.74 (app. t, *J* = 8.9 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 2H), 7.45 (app. t, *J* = 8.6 Hz, 2H), 7.39 – 7.29 (m, 2H), 7.28 – 7.13 (m, 3H), 7.01 (app. d, *J* = 8.3 Hz, 2H), 4.63 (d, *J* = 11.8 Hz, 1H), 4.55 – 4.35 (m, 4H), 4.11 – 3.96 (m, 2H), 3.86 (q, *J* = 7.9 Hz, 1H), 3.26 – 3.12 (m, 2H), 2.72 – 2.56 (m, 2H), 1.84 – 1.54 (m, 4H), 1.40 (quin, *J* = 7.6 Hz, 2H), 1.32 – 1.06 (m, 4H), 0.83 – 0.70 (m, 1H), 0.69 – 0.45 (m, 8H); ^{13}C NMR (125 MHz, CD_3OD) δ 172.8, 170.6, 158.1, 155.3, 153.4, 147.7, 134.7, 134.5, 130.9, 130.7, 130.6, 130.3, 130.1, 129.9, 129.1, 128.8, 127.3, 127.1, 126.9, 125.9, 125.5, 124.8, 124.6, 121.3, 119.8, 116.8, 115.7, 69.3, 68.9, 56.4, 53.2, 50.5, 42.3, 41.0, 38.9, 32.5, 30.2, 27.7, 26.2, 25.2, 23.2, 22.6, 22.4; IR (cm^{-1}) υ 2960, 1653, 1559, 1212, 1049, 804, 745; MS (ES^+) *m/z* 812 (5%, M+H), 407 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{47}H_{58}N_9O_4$: 812.4612, Found: 812.4591.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(5-phenyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (55)



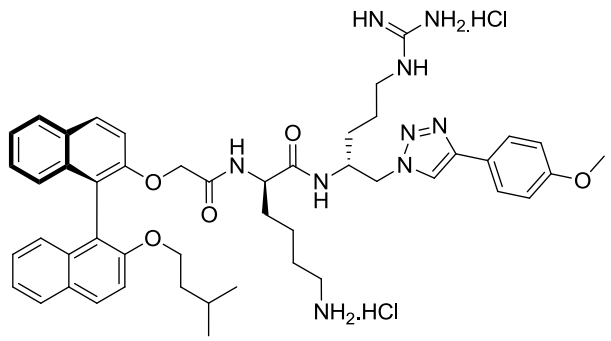
This compound was prepared according to *General Procedure 5* using **30** (40.8 mg, 0.035 mmol), CH_2Cl_2 (1.15 mL) and TFA (1.15 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.57 mL) as described gave **55** (20.4 mg, 66%) as an off-white solid. $[\alpha]_D^{25}$ −43.5 (*c* 0.47, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.10 – 8.01 (m, 2H), 7.99 (s, 1H), 7.97 – 7.88 (m, 2H), 7.63 – 7.53 (m, 6H), 7.46 (d, *J* = 9.0 Hz, 1H), 7.35 (app. t, *J* = 7.3 Hz, 2H), 7.22 (app. t, *J* = 7.5 Hz, 2H), 7.06 (app. d, *J* = 8.3 Hz, 2H), 4.64 – 4.37 (m, 4H), 4.19 – 4.11 (m, 1H), 4.11 – 4.03 (m, 1H), 4.02 – 3.94 (m, 2H), 3.07 – 2.94 (m, 2H), 2.88 – 2.75 (m, 2H), 1.61 – 1.37 (m, 6H), 1.37 – 1.11 (m, 4H), 0.96 – 0.85 (m, 1H), 0.79 (quin, *J* = 7.5 Hz, 2H), 0.57 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.0, 170.6, 158.4, 155.9, 154.0, 140.5, 135.2, 135.1, 133.4, 131.4, 131.2, 130.9, 130.7, 130.4, 129.3, 129.1, 127.6, 127.52, 127.49, 126.4, 125.9, 125.2, 124.8, 121.8, 120.5, 116.9, 115.8, 69.1, 68.9, 53.6, 53.5, 49.6, 41.8, 40.5, 39.3, 32.4, 30.0, 27.9, 26.0, 25.6, 23.2, 22.8, 22.6; IR (cm^{-1}) υ 2953, 1654, 1507, 1212, 1147, 1046, 808, 747, 695; MS (ES^+) *m/z* 812 (<5%, M+H), 407 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{47}H_{58}N_9O_4$: 812.4612, Found: 812.4636.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(4-butylphenyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (56)



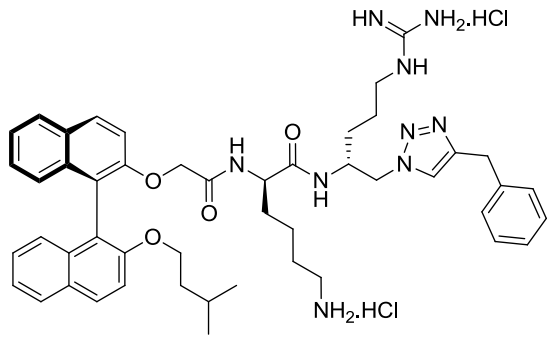
This compound was prepared according to *General Procedure 5* using **31** (46.4 mg, 0.038 mmol), CH_2Cl_2 (1.25 mL) and TFA (1.25 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.62 mL) as described gave **56** (28.7 mg, 80%) as an off-white solid. $[\alpha]_D^{25}$ −25.0 (*c* 0.84, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.45 (s, 1H), 8.01 (d, *J* = 9.1 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 7.2 Hz, 2H), 7.75 – 7.68 (m, 2H), 7.44 (d, *J* = 8.7 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.13 (m, 4H), 7.00 (app. d, *J* = 8.3 Hz, 2H), 4.63 (d, *J* = 11.9 Hz, 1H), 4.54 – 4.36 (m, 4H), 4.11 – 3.97 (m, 2H), 3.84 (q, *J* = 6.2 Hz, 1H), 3.26 – 3.12 (m, 2H), 2.77 – 2.59 (m, 4H), 1.84 – 1.54 (m, 6H), 1.46 – 1.32 (m, 4H), 1.32 – 1.07 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H), 0.81 – 0.70 (m, 1H), 0.69 – 0.57 (m, 2H), 0.55 (d, *J* = 6.3 Hz, 3H), 0.50 (d, *J* = 5.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.3, 170.6, 158.5, 155.7, 153.9, 147.8, 145.6, 135.1, 135.0, 131.3, 130.8, 130.7, 130.51, 130.46, 129.2, 129.1, 127.6, 127.5, 127.4, 126.9, 126.3, 125.9, 125.1, 124.6, 123.7, 121.7, 120.2, 116.7, 115.8, 69.1, 68.8, 55.7, 53.4, 50.5, 41.9, 40.4, 39.2, 36.4, 34.9, 32.6, 29.8, 27.7, 26.2, 25.6, 23.31, 23.27, 22.8, 22.6, 14.3; IR (cm^{-1}) υ 2923, 1653, 1506, 1214, 1172, 1047, 809, 747; MS (ES^+) *m/z* 869 (<5%, M+H), 435 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{51}H_{66}N_9O_4$: 868.5238, Found: 868.5265.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (57)



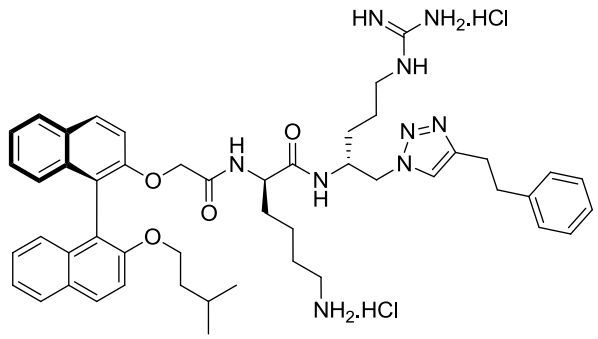
This compound was prepared according to *General Procedure 5* using **32** (51.0 mg, 0.043 mmol), CH_2Cl_2 (1.40 mL) and TFA (1.40 mL) with a 17 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.69 mL) as described gave **57** (38.1 mg, 97%) as an off-white solid. $[\alpha]_D^{25}$ −16.7 (*c* 1.47, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.40 (s, 1H), 8.01 (d, *J* = 8.9 Hz, 1H), 7.94 – 7.84 (m, 3H), 7.77 (app. t, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 9.0 Hz, 1H), 7.34 (app. t, *J* = 8.1 Hz, 2H), 7.30 – 7.15 (m, 3H), 7.12 (d, *J* = 7.5 Hz, 2H), 7.01 (app. d, *J* = 8.4 Hz, 2H), 4.64 (d, *J* = 12.3 Hz, 1H), 4.55 – 4.35 (m, 4H), 4.11 – 3.97 (m, 2H), 3.93 – 3.81 (m, 4H), 3.26 – 3.12 (m, 2H), 2.75 – 2.60 (m, 2H), 1.83 – 1.55 (m, 4H), 1.42 (quin, *J* = 7.4 Hz, 2H), 1.34 – 1.07 (m, 4H), 0.85 – 0.74 (m, 1H), 0.72 – 0.60 (m, 2H), 0.55 (d, *J* = 6.3 Hz, 3H), 0.50 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.4, 170.6, 162.4, 158.5, 155.8, 153.9, 146.8, 135.2, 135.0, 131.3, 130.79, 130.77, 130.5, 129.2, 129.1, 128.7, 127.5, 126.3, 125.9, 125.1, 124.7, 124.0, 121.7, 121.3, 120.3, 116.7, 115.9, 115.8, 69.1, 68.9, 56.15, 56.05, 53.5, 50.6, 41.9, 40.4, 39.2, 32.5, 29.7, 27.7, 26.2, 25.6, 23.3, 22.8, 22.5; IR (cm^{-1}) υ 2958, 1653, 1559, 1212, 1175, 1049, 809, 746; MS (ES^+) *m/z* 842 (<5%, M+H), 422 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{48}H_{60}N_9O_5$: 842.4717, Found: 842.4733.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-benzyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (58)



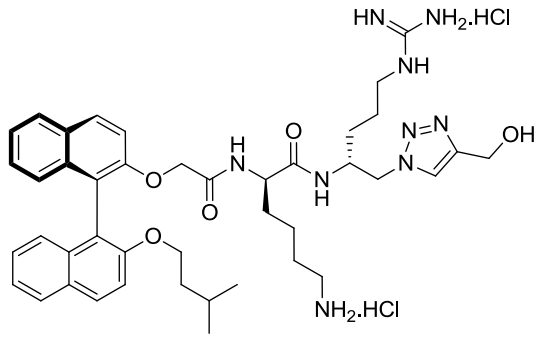
This compound was prepared according to *General Procedure 5* using **33** (42.4 mg, 0.036 mmol), CH_2Cl_2 (1.18 mL) and TFA (1.18 mL) with a 18.5 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.59 mL) as described gave **58** (29.9 mg, 93%) as a tan solid. $[\alpha]_D^{25}$ −14.0 (*c* 2.07, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.07 – 8.00 (m, 2H), 7.99 (s, 1H), 7.92 (app. t, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 7.39 – 7.18 (m, 9H), 7.06 (app. t, *J* = 9.8 Hz, 2H), 4.64 – 4.49 (m, 2H), 4.49 – 4.38 (m, 2H), 4.34 – 4.24 (m, 1H), 4.18 – 4.06 (m, 3H), 4.02 – 3.90 (m, 2H), 3.24 – 3.09 (m, 2H), 2.82 – 2.67 (m, 2H), 1.77 – 1.40 (m, 6H), 1.36 – 1.10 (m, 4H), 0.97 – 0.86 (m, 1H), 0.86 – 0.72 (m, 2H), 0.57 (d, *J* = 6.4 Hz, 3H), 0.52 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.3, 170.6, 158.5, 155.9, 154.0, 146.9, 140.3, 135.2, 135.0, 131.3, 130.9, 130.6, 129.7, 129.3, 129.1, 127.6, 127.53, 127.49, 126.4, 125.9, 125.2, 124.8, 121.7, 120.5, 116.8, 116.0, 69.2, 68.9, 54.6, 53.6, 50.6, 41.9, 40.3, 39.2, 32.5, 32.2, 29.9, 27.7, 26.0, 25.6, 23.1, 22.8, 22.6; IR (cm^{-1}) υ 2953, 1653, 1507, 1212, 1148, 1047, 809, 746; MS (ES^+) *m/z* 826 (1%, M+H), 414 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{48}H_{60}N_9O_4$: 826.4768, Found: 826.4763.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-phenethyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (59)



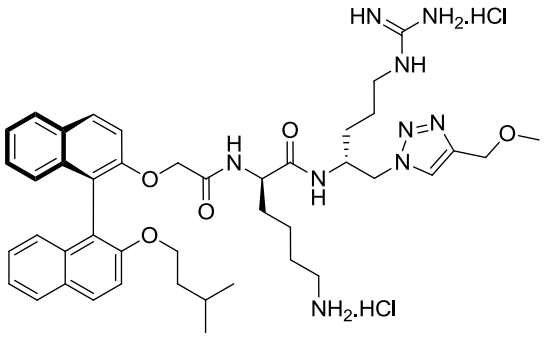
This compound was prepared according to *General Procedure 5* using **34** (53.2 mg, 0.045 mmol), CH_2Cl_2 (1.45 mL) and TFA (1.45 mL) with a 17 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.73 mL) as described gave **59** (36.1 mg, 89%) as an off-white solid. $[\alpha]_D^{25}$ −12.7 (*c* 1.36, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.06 – 7.96 (m, 3H), 7.90 (app. t, *J* = 7.7 Hz, 2H), 7.54 – 7.46 (m, 2H), 7.39 – 7.26 (m, 4H), 7.26 – 7.17 (m, 5H), 7.10 – 7.01 (m, 2H), 4.63 – 4.52 (m, 2H), 4.50 – 4.39 (m, 2H), 4.31 – 4.23 (m, 1H), 4.14 – 4.06 (m, 1H), 4.02 – 3.89 (m, 2H), 3.23 – 2.97 (m, 6H), 2.84 – 2.69 (m, 2H), 1.74 – 1.46 (m, 6H), 1.39 – 1.09 (m, 4H), 1.03 – 0.91 (m, 1H), 0.88 – 0.76 (m, 2H), 0.57 (d, *J* = 6.3 Hz, 3H), 0.51 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.6, 170.8, 158.5, 155.9, 154.1, 146.1, 141.8, 141.2, 135.2, 135.0, 131.4, 130.8, 130.7, 129.7, 129.5, 129.3, 129.1, 127.58, 127.57, 127.5, 127.3, 126.3, 125.9, 125.2, 124.8, 121.7, 120.6, 116.9, 116.0, 69.3, 69.0, 56.4, 53.9, 50.6, 41.9, 40.4, 39.2, 35.8, 32.3, 29.5, 27.7, 27.1, 26.1, 25.6, 23.4, 22.8, 22.5; IR (cm^{-1}) υ 2948, 1653, 1559, 1212, 1168, 1048, 809, 746; MS (ES^+) *m/z* 840 (<5%, M+H), 421 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{49}H_{62}N_9O_4$: 840.4925, Found: 840.4964.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (60)



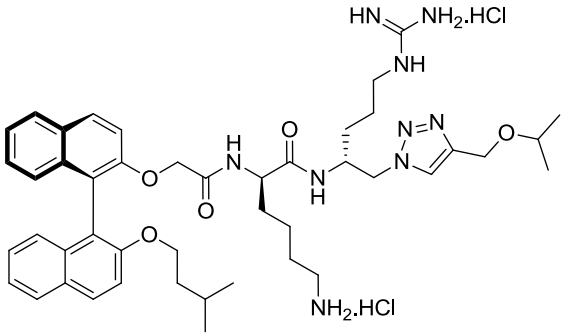
This compound was prepared according to *General Procedure 5* using **35** (65.8 mg, 0.059 mmol), CH_2Cl_2 (1.93 mL) and TFA (1.93 mL) with a 22 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.97 mL) as described gave **60** (43.5 mg, 88%) as an off-white solid. $[\alpha]_D^{25}$ −12.6 (*c* 1.67, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.07 – 7.99 (m, 3H), 7.92 (app. t, *J* = 7.6 Hz, 2H), 7.56 (d, *J* = 9.0 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.23 (app. t, *J* = 7.3 Hz, 2H), 7.06 (app. t, *J* = 8.1 Hz, 2H), 4.74 (s, 2H), 4.64 – 4.50 (m, 2H), 4.50 – 4.37 (m, 2H), 4.37 – 4.26 (m, 1H), 4.13 (dd, *J* = 15.2, 6.1 Hz, 1H), 4.03 – 3.91 (m, 2H), 3.25 – 3.09 (m, 2H), 2.86 – 2.72 (m, 2H), 1.77 – 1.43 (m, 6H), 1.35 – 1.09 (m, 4H), 0.99 – 0.86 (m, 1H), 0.85 – 0.68 (m, 2H), 0.58 (d, *J* = 6.4 Hz, 3H), 0.52 (d, *J* = 5.8 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.5, 170.7, 158.4, 155.8, 153.9, 147.8, 135.1, 135.0, 131.3, 130.9, 130.8, 130.6, 129.3, 129.1, 127.5, 127.4, 126.3, 125.8, 125.1, 124.8, 121.7, 120.4, 116.8, 115.9, 69.2, 68.9, 55.7, 55.5, 53.7, 50.5, 41.8, 40.4, 39.2, 32.2, 29.7, 27.7, 26.0, 25.5, 23.2, 22.8, 22.5; IR (cm^{-1}) υ 3189, 2950, 1653, 1559, 1212, 1148, 1046, 808, 746; MS (ES^+) *m/z* 766 (<5%, M+H), 384 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{42}H_{56}N_9O_5$: 766.4404, Found: 766.4435.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(methoxymethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (77)



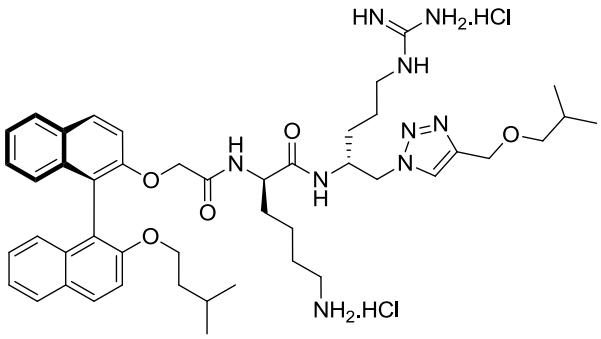
This compound was prepared according to *General Procedure 5* using **70** (47.7 mg, 0.042 mmol), CH_2Cl_2 (1.38 mL) and TFA (1.38 mL) with a 22 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.69 mL) as described gave **77** (35.0 mg, 97%) as an off-white solid. $[\alpha]_D^{25}$ −16.9 (*c* 0.71, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.11 – 7.98 (m, 3H), 7.92 (app. d, *J* = 7.3 Hz, 2H), 7.55 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.41 – 7.29 (m, 2H), 7.23 (app. t, *J* = 7.2 Hz, 2H), 7.06 (app. t, *J* = 8.3 Hz, 2H), 4.65 – 4.50 (m, 4H), 4.50 – 4.38 (m, 2H), 4.37 – 4.26 (m, 1H), 4.18 – 4.07 (m, 1H), 4.03 – 3.90 (m, 2H), 3.24 – 3.09 (m, 2H), 2.88 – 2.72 (m, 2H), 1.78 – 1.43 (m, 6H), 1.33 – 1.10 (m, 4H), 0.98 – 0.86 (m, 1H), 0.83 – 0.69 (m, 2H), 0.58 (d, *J* = 6.4 Hz, 3H), 0.53 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.3, 170.7, 158.5, 155.9, 154.0, 145.2, 135.2, 135.1, 131.4, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.3, 125.9, 125.2, 124.8, 121.8, 120.5, 116.9, 115.9, 69.2, 69.0, 65.9, 58.7, 55.0, 53.7, 50.5, 41.9, 40.4, 39.3, 32.3, 29.9, 27.8, 26.1, 25.6, 23.2, 22.8, 22.6; IR (cm^{-1}) υ 3193, 2946, 1653, 1559, 1506, 1213, 1148, 1049, 808, 746; MS (ES^+) *m/z* 780 (<5%, M+H), 391 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{43}H_{58}N_9O_5$: 780.4561, Found: 780.4597.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(isopropoxymethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (78)



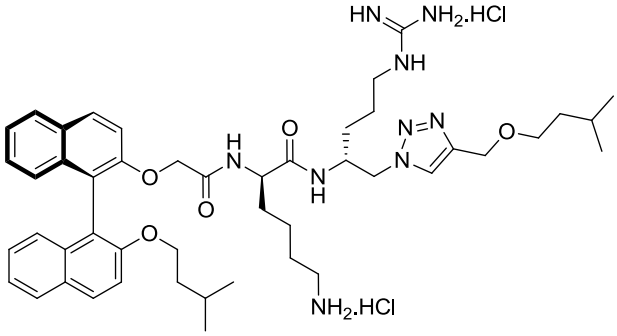
This compound was prepared according to *General Procedure 5* using **71** (51.2 mg, 0.044 mmol), CH_2Cl_2 (1.44 mL) and TFA (1.44 mL) with a 22 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.72 mL) as described gave **78** (34.9 mg, 90%) as an off-white solid. $[\alpha]_D^{25}$ −17.5 (*c* 1.16, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.11 – 7.97 (m, 3H), 7.92 (app. d, *J* = 6.8 Hz, 2H), 7.55 (d, *J* = 9.1 Hz, 1H), 7.47 (d, *J* = 8.9 Hz, 1H), 7.41 – 7.29 (m, 2H), 7.23 (app t., *J* = 8.2 Hz, 2H), 7.06 (app. t, *J* = 9.3 Hz, 2H), 4.69 – 4.36 (m, 6H), 4.35 – 4.24 (m, 1H), 4.18 – 4.07 (m, 1H), 4.04 – 3.89 (m, 2H), 3.78 (sep, *J* = 6.4 Hz, 1H), 3.26 – 3.08 (m, 2H), 2.87 – 2.73 (m, 2H), 1.77 – 1.43 (m, 6H), 1.36 – 1.09 (m, 10H), 1.01 – 0.87 (m, 1H), 0.87 – 0.71 (m, 2H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.53 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.4, 170.7, 158.5, 155.9, 154.0, 145.5, 135.2, 135.0, 131.3, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.6, 126.3, 125.9, 125.2, 124.8, 121.7, 120.5, 116.8, 115.9, 73.2, 69.2, 68.9, 61.4, 55.4, 53.7, 50.5, 41.9, 40.4, 39.2, 32.2, 29.7, 27.8, 26.1, 25.6, 23.3, 22.8, 22.5, 22.4, 22.3; IR (cm^{-1}) υ 2950, 1653, 1559, 1506, 1212, 1148, 1048, 808, 746; MS (ES^+) *m/z* 808 (<5%, M+H), 405 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{45}H_{62}N_9O_5$: 808.4874, Found: 808.4910.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(isobutoxymethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (79)



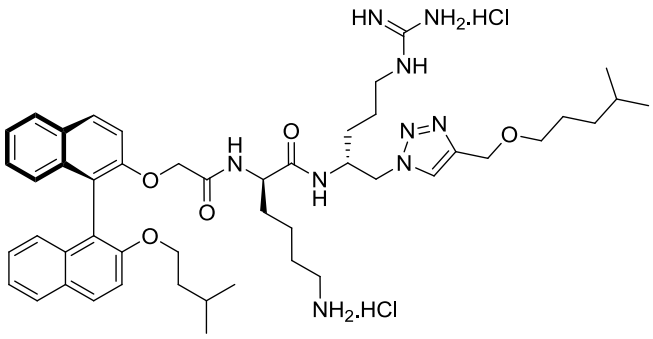
This compound was prepared according to *General Procedure 5* using **72** (46.1 mg, 0.039 mmol), CH_2Cl_2 (1.28 mL) and TFA (1.28 mL) with a 22 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.64 mL) as described gave **79** (28.4 mg, 81%) as an off-white solid. $[\alpha]_D^{25}$ −16.3 (*c* 1.10, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.08 – 7.98 (m, 3H), 7.92 (app. d, *J* = 7.9 Hz, 2H), 7.54 (d, *J* = 9.1 Hz, 1H), 7.47 (d, *J* = 9.1 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.23 (app. t, *J* = 7.6 Hz, 2H), 7.06 (app. t, *J* = 8.7 Hz, 2H), 4.68 – 4.38 (m, 6H), 4.36 – 4.25 (m, 1H), 4.18 – 4.07 (m, 1H), 4.03 – 3.90 (m, 2H), 3.33 – 3.28 (m, 2H), 3.24 – 3.10 (m, 2H), 2.88 – 2.73 (m, 2H), 1.88 (sep, *J* = 6.7 Hz, 1H), 1.78 – 1.43 (m, 6H), 1.36 – 1.10 (m, 4H), 1.02 – 0.85 (m, 7H), 0.85 – 0.72 (m, 2H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.2, 170.6, 158.4, 155.8, 153.9, 145.7, 135.1, 135.0, 131.3, 130.8, 130.6, 129.2, 129.1, 127.6, 127.5, 126.3, 126.1, 125.9, 125.2, 124.8, 121.7, 120.5, 116.8, 115.9, 78.6, 69.2, 69.0, 64.5, 54.9, 53.7, 50.5, 41.9, 40.4, 39.2, 32.2, 29.9, 29.5, 27.8, 26.0, 25.5, 23.1, 22.8, 22.5, 19.7; IR (cm^{-1}) υ 2954, 1653, 1559, 1506, 1212, 1046, 807, 745; MS (ES^+) *m/z* 822 (<5%, M+H), 412 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{46}H_{64}N_9O_5$: 822.5030, Found: 822.5067.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(isopentoxymethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (80)



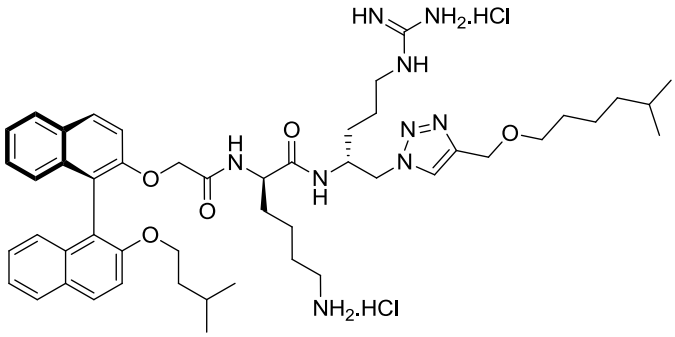
This compound was prepared according to *General Procedure 5* using **73** (32.5 mg, 0.027 mmol), CH_2Cl_2 (0.89 mL) and TFA (0.89 mL) with a 22 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.44 mL) as described gave **80** (20.1 mg, 81%) as an off-white solid. $[\alpha]_D^{25}$ −11.1 (*c* 0.66, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.07 – 7.99 (m, 3H), 7.92 (app. d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.47 (d, *J* = 9.1 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.23 (app. t, *J* = 7.3 Hz, 2H), 7.06 (app. t, *J* = 8.4 Hz, 2H), 4.66 – 4.49 (m, 4H), 4.49 – 4.38 (m, 2H), 4.35 – 4.25 (m, 1H), 4.17 – 4.09 (m, 1H), 4.02 – 3.91 (m, 2H), 3.57 (t, *J* = 6.8 Hz, 2H), 3.22 – 3.10 (m, 2H), 2.88 – 2.73 (m, 2H), 1.78 – 1.38 (m, 9H), 1.34 – 1.11 (m, 4H), 0.99 – 0.85 (m, 7H), 0.85 – 0.71 (m, 2H), 0.58 (d, *J* = 6.5 Hz, 3H), 0.53 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.3, 170.7, 158.5, 155.9, 154.0, 145.8, 135.2, 135.0, 131.4, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.0, 125.9, 125.2, 124.8, 121.8, 120.5, 116.9, 115.9, 70.2, 69.2, 69.0, 64.4, 54.8, 53.7, 50.5, 41.9, 40.4, 39.6, 39.3, 32.3, 29.9, 27.8, 26.2, 26.1, 25.6, 23.2, 23.0, 22.8, 22.6; IR (cm^{-1}) υ 2955, 1653, 1559, 1507, 1216, 1148, 1049, 808, 746; MS (ES^+) *m/z* 836 (<5%, M+H), 419 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{47}H_{66}N_9O_5$: 836.5187, Found: 836.5200.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(((4-methylpentyl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (81)



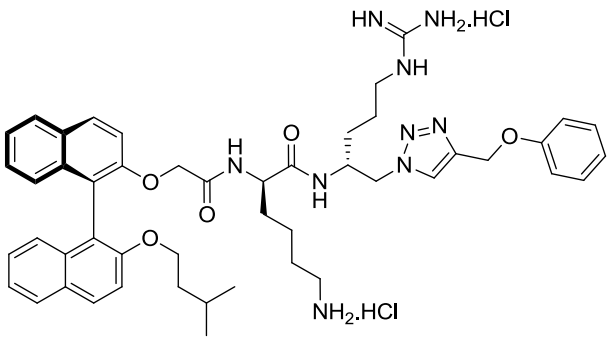
This compound was prepared according to *General Procedure 5* using **74** (24.0 mg, 0.020 mmol), CH_2Cl_2 (0.66 mL) and TFA (0.66 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.33 mL) as described gave **81** (15.1 mg, 82%) as an off-white solid. $[\alpha]_D^{25}$ −11.6 (*c* 0.44, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.07 – 7.98 (m, 3H), 7.92 (app. d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.28 – 7.19 (m, 2H), 7.06 (app. t, *J* = 8.0 Hz, 2H), 4.61 (s, 2H), 4.59 – 4.50 (m, 2H), 4.49 – 4.38 (m, 2H), 4.34 – 4.25 (m, 1H), 4.17 – 4.09 (m, 1H), 4.02 – 3.91 (m, 2H), 3.53 (t, *J* = 6.5 Hz, 2H), 3.23 – 3.10 (m, 2H), 2.87 – 2.74 (m, 2H), 1.75 – 1.44 (m, 9H), 1.34 – 1.11 (m, 6H), 0.99 – 0.85 (m, 7H), 0.85 – 0.72 (m, 2H), 0.58 (d, *J* = 6.4 Hz, 3H), 0.53 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.3, 170.7, 158.5, 155.9, 154.0, 145.9, 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, 121.8, 120.5, 116.9, 115.9, 72.2, 69.2, 69.0, 64.4, 54.8, 53.7, 50.5, 41.9, 40.4, 39.3, 36.4, 32.3, 30.0, 29.1, 28.6, 27.9, 26.1, 25.6, 23.2, 23.0, 22.8, 22.6; IR (cm^{-1}) υ 2960, 1653, 1559, 1507, 1212, 1049, 808, 745; MS (ES^+) *m/z* 850 (<5%, M+H), 426 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{48}H_{68}N_9O_5$: 850.5343, Found: 850.5358.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(((5-methylhexyl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (82)



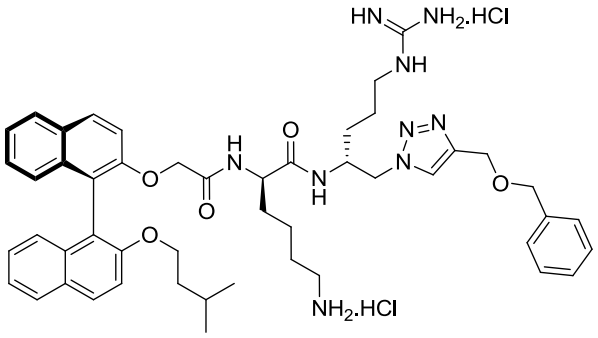
This compound was prepared according to *General Procedure 5* using **75** (40.9 mg, 0.034 mmol), CH_2Cl_2 (1.10 mL) and TFA (1.10 mL) with a 22 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.55 mL) as described gave **82** (26.9 mg, 85%) as a tan solid. $[\alpha]_D^{25}$ −15.6 (*c* 0.31, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.09 – 7.98 (m, 3H), 7.91 (app. d, *J* = 7.8 Hz, 2H), 7.53 (d, *J* = 8.7 Hz, 1H), 7.46 (d, *J* = 8.9 Hz, 1H), 7.40 – 7.29 (m, 2H), 7.22 (app. t, *J* = 7.4 Hz, 2H), 7.06 (app. t, *J* = 8.0 Hz, 2H), 4.66 – 4.49 (m, 4H), 4.48 – 4.38 (m, 2H), 4.35 – 4.24 (m, 1H), 4.16 – 4.08 (m, 1H), 4.03 – 3.91 (m, 2H), 3.54 (t, *J* = 6.1 Hz, 2H), 3.23 – 3.09 (m, 2H), 2.89 – 2.73 (m, 2H), 1.76 – 1.43 (m, 9H), 1.43 – 1.10 (m, 8H), 1.00 – 0.72 (m, 9H), 0.57 (d, *J* = 6.4 Hz, 3H), 0.52 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.3, 170.7, 158.5, 155.9, 154.0, 135.2, 135.1, 131.4, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.1, 126.0, 125.2, 124.8, 121.8, 120.5, 116.9, 115.9, 72.0, 69.2, 69.0, 64.4, 54.9, 53.7, 50.5, 41.9, 40.4, 40.0, 39.3, 32.3, 31.0, 30.0, 29.1, 27.9, 26.1, 25.6, 25.1, 23.2, 23.0, 22.8, 22.6; IR (cm^{-1}) υ 2954, 1653, 1559, 1507, 1218, 1148, 1048, 807, 746; MS (ES^+) *m/z* 865 (<5%, M+H), 433 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{49}H_{70}N_9O_5$: 864.5500, Found: 864.5536.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(phenoxymethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (83)



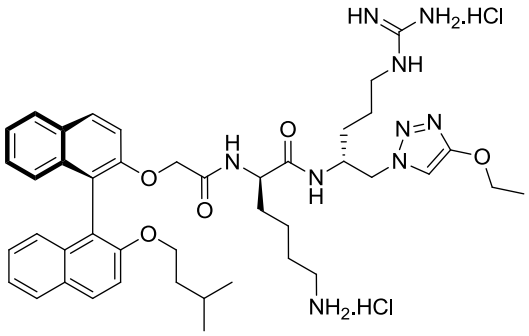
This compound was prepared according to *General Procedure 5* using **76** (29.9 mg, 0.025 mmol), CH_2Cl_2 (0.82 mL) and TFA (0.82 mL) with a 22 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.41 mL) as described gave **83** (15.0 mg, 66%) as an off-white solid. $[\alpha]_D^{25}$ −19.4 (*c* 0.43, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.10 (s, 1H), 8.02 (app. t, *J* = 9.4 Hz, 2H), 7.90 (app. t, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.9 Hz, 1H), 7.46 (d, *J* = 8.9 Hz, 1H), 7.39 – 7.27 (m, 4H), 7.27 – 7.18 (m, 2H), 7.10 – 7.01 (m, 4H), 6.98 (t, *J* = 7.1 Hz, 1H), 5.19 (s, 2H), 4.61 – 4.49 (m, 2H), 4.49 – 4.37 (m, 2H), 4.36 – 4.26 (m, 1H), 4.16 – 4.07 (m, 1H), 4.02 – 3.90 (m, 2H), 3.24 – 3.09 (m, 2H), 2.85 – 2.70 (m, 2H), 1.76 – 1.42 (m, 6H), 1.33 – 1.10 (m, 4H), 0.96 – 0.85 (m, 1H), 0.83 – 0.67 (m, 2H), 0.57 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.3, 170.7, 159.7, 158.5, 155.9, 154.0, 145.0, 135.2, 135.0, 131.4, 130.9, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.1, 125.9, 125.2, 124.8, 122.4, 121.8, 120.5, 116.8, 115.9, 69.2, 68.9, 62.3, 54.6, 53.7, 50.5, 41.9, 40.4, 39.2, 32.3, 30.0, 27.8, 26.1, 25.6, 23.2, 22.8, 22.5; IR (cm^{-1}) υ 2960, 1653, 1559, 1507, 1212, 1148, 1049, 808, 746; MS (ES^+) *m/z* 842 (<5%, M+H), 422 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{48}H_{60}N_9O_5$: 842.4717, Found: 842.4714.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(benzyloxymethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (61)



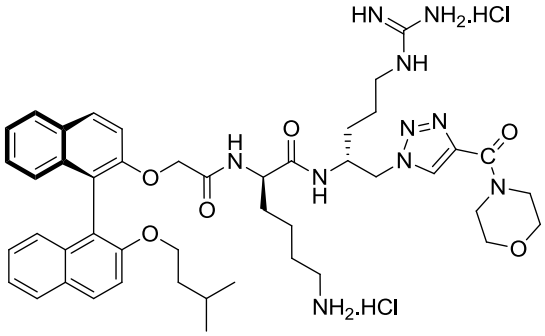
This compound was prepared according to *General Procedure 5* using **36** (80.3 mg, 0.066 mmol), CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) with a 20 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 1.0 mL) as described gave **61** (57.3 mg, 93%) as a white solid. $[\alpha]_D^{25}$ −20.6 (*c* 1.76, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.07 – 7.99 (m, 3H), 7.97 (d, *J* = 9.0 Hz, 1H), 7.94 – 7.85 (m, 2H), 7.51 – 7.42 (m, 2H), 7.42 – 7.27 (m, 6H), 7.27 – 7.17 (m, 2H), 7.05 (app. t, *J* = 7.6 Hz, 2H), 4.72 – 4.48 (m, 6H), 4.47 – 4.37 (m, 2H), 4.37 – 4.27 (m, 1H), 4.13 – 4.04 (m, 1H), 4.00 – 3.87 (m, 2H), 3.22 – 3.10 (m, 2H), 2.82 – 2.68 (m, 2H), 1.76 – 1.37 (m, 5H), 1.35 – 1.08 (m, 4H), 0.96 – 0.83 (m, 1H), 0.81 – 0.65 (m, 2H), 0.57 (d, *J* = 6.5 Hz, 3H), 0.51 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.2, 170.6, 158.5, 155.9, 154.0, 139.2, 135.2, 135.0, 131.4, 130.9, 130.8, 130.6, 129.5, 129.3, 129.2, 129.1, 128.9, 127.6, 127.5, 126.4, 125.9, 125.2, 124.8, 121.8, 120.4, 116.8, 115.9, 73.4, 69.2, 69.0, 63.9, 54.7, 53.7, 50.5, 41.9, 40.4, 39.2, 32.2, 30.0, 27.8, 26.1, 25.6, 23.1, 22.8, 22.6; IR (cm^{-1}) υ 2957, 1653, 1507, 1457, 1328, 1213, 1046, 807, 746; MS (ES^+) *m/z* 856 (<5%, M+H), 429 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{49}H_{62}N_9O_5$: 856.4874, Found: 856.4869.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-ethoxy-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (62)



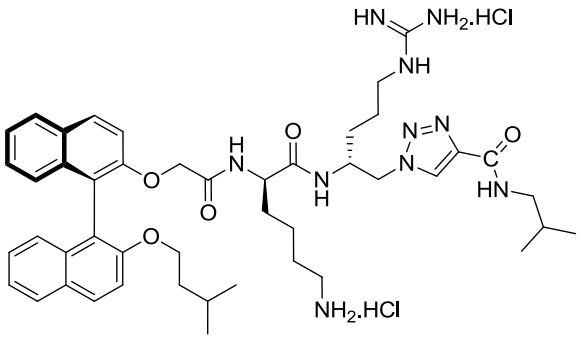
This compound was prepared according to *General Procedure 5* using **37** (53.5 mg, 0.047 mmol), CH_2Cl_2 (1.5 mL) and TFA (1.5 mL) with a 17 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.75 mL) as described gave **62** (34.1 mg, 85%) as a light brown solid. $[\alpha]_D^{25}$ −13.2 (*c* 1.15, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.03 (app. d, *J* = 8.9 Hz, 2H), 7.92 (app. d, *J* = 7.1 Hz, 2H), 7.59 (s, 1H), 7.55 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.27 – 7.19 (m, 2H), 7.10 – 7.02 (m, 2H), 4.58 – 4.40 (m, 3H), 4.37 – 4.25 (m, 2H), 4.21 (q, *J* = 6.8 Hz, 2H), 4.17 – 4.10 (m, 1H), 4.02 – 3.93 (m, 2H), 3.24 – 3.11 (m, 2H), 2.84 – 2.72 (m, 2H), 1.76 – 1.41 (m, 9H), 1.33 – 1.12 (m, 4H), 0.97 – 0.86 (m, 1H), 0.80 – 0.67 (m, 2H), 0.58 (d, *J* = 6.2 Hz, 3H), 0.53 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.3, 170.7, 160.9, 158.5, 155.9, 154.0, 135.2, 135.0, 131.4, 130.9, 130.8, 130.7, 129.3, 129.1, 127.55, 127.48, 126.4, 125.9, 125.2, 124.8, 121.8, 120.5, 116.9, 115.9, 109.6, 69.2, 69.04, 69.00, 56.1, 53.7, 50.4, 41.9, 40.4, 39.3, 32.4, 29.9, 27.8, 26.1, 25.6, 23.2, 22.8, 22.6, 15.1; IR (cm^{-1}) υ 2955, 1653, 1559, 1507, 1213, 1170, 1047, 808, 746; MS (ES^+) *m/z* 780 (<5%, M+H), 391 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{43}H_{58}N_9O_5$: 780.4561, Found: 780.4575.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(morpholine-4-carbonyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (87)



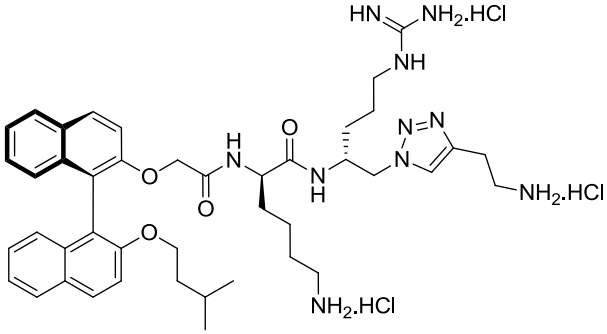
This compound was prepared according to *General Procedure 5* using **85** (24.7 mg, 0.021 mmol), CH_2Cl_2 (0.68 mL) and TFA (0.68 mL) with a 23 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.34 mL) as described gave **87** (16.3 mg, 86%) as an off-white solid. $[\alpha]_D^{25}$ −20.1 (*c* 0.60, MeOH); ^{1}H NMR (500 MHz, CD_3OD, major rotamer only) δ 8.39 (s, 1H), 8.02 (app. t, *J* = 8.3 Hz, 2H), 7.91 (app. d, *J* = 7.8 Hz, 2H), 7.54 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 8.9 Hz, 1H), 7.41 – 7.29 (m, 2H), 7.28 – 7.18 (m, 2H), 7.06 (app. d, *J* = 8.1 Hz, 2H), 4.66 – 4.50 (m, 2H), 4.50 – 4.38 (m, 2H), 4.38 – 4.29 (m, 1H), 4.22 – 4.02 (m, 3H), 4.02 – 3.91 (m, 2H), 3.90 – 3.62 (m, 6H), 3.25 – 3.10 (m, 2H), 2.88 – 2.74 (m, 2H), 1.79 – 1.41 (m, 6H), 1.36 – 1.10 (m, 4H), 0.93 – 0.82 (m, 1H), 0.82 – 0.67 (m, 2H), 0.58 (d, *J* = 6.4 Hz, 3H), 0.53 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD, major rotamer only) δ 173.3, 170.7, 162.2, 158.5, 155.9, 154.0, 143.5, 135.2, 135.0, 131.4, 130.9, 130.6, 130.1, 129.8, 129.3, 129.1, 127.6, 127.5, 126.4, 125.9, 125.2, 124.8, 121.7, 120.4, 116.9, 115.8, 69.1, 69.0, 68.1, 67.8, 54.8, 53.6, 50.5, 48.9, 44.3, 41.9, 40.3, 39.2, 32.4, 29.9, 27.8, 26.1, 25.6, 23.2, 22.8, 22.6; IR (cm^{-1}) υ 1653, 1559, 1506, 1235, 1067, 809, 749; MS (ES^+) *m/z* 849 (<5%, M+H), 425 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{46}H_{60}N_{10}NaO_6$: 871.4595, Found: 871.4623.

1-((*R*)-2-((*R*)-6-Amino-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamido)-5-guanidinopentyl)-*N*-isobutyl-1*H*-1,2,3-triazole-4-carboxamide·dihydrochloride (88)



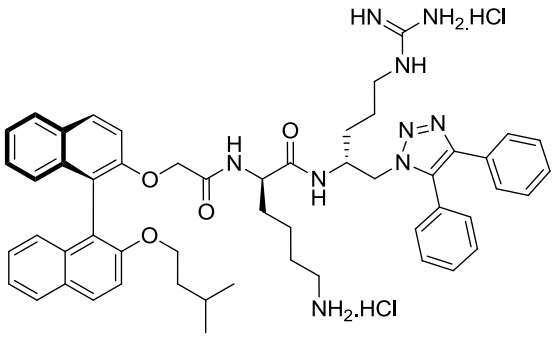
This compound was prepared according to *General Procedure 5* using **86** (14.1 mg, 0.012 mmol), CH_2Cl_2 (0.39 mL) and TFA (0.39 mL) with a 23 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.20 mL) as described gave **88** (8.7 mg, 81%) as an off-white solid. $[\alpha]_D^{25}$ −15.9 (*c* 0.42, MeOH); ^{1}H NMR (500 MHz, CD_3OD, major rotamer only) δ 8.41 (s, 1H), 8.11 – 7.95 (m, 2H), 7.90 (app. t, *J* = 7.6 Hz, 2H), 7.57 – 7.41 (m, 2H), 7.41 – 7.27 (m, 2H), 7.27 – 7.15 (m, 2H), 7.12 – 6.98 (m, 2H), 4.67 – 4.50 (m, 2H), 4.50 – 4.38 (m, 2H), 4.37 – 4.27 (m, 1H), 4.17 – 4.07 (m, 1H), 4.07 – 3.99 (m, 1H), 3.99 – 3.91 (m, 1H), 3.34 – 3.24 (m, 2H), 3.23 – 3.08 (m, 2H), 2.90 – 2.73 (m, 2H), 2.03 – 1.91 (m, 1H), 1.79 – 1.41 (m, 6H), 1.37 – 1.09 (m, 4H), 1.04 – 0.97 (m, 6H), 0.89 – 0.78 (m, 1H), 0.78 – 0.68 (m, 2H), 0.57 (d, *J* = 6.4 Hz, 3H), 0.52 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD, major rotamer only) δ 173.2, 170.6, 162.5, 158.6, 155.9, 154.0, 143.8, 135.2, 135.0, 131.4, 131.0, 130.8, 130.6, 129.2, 129.1, 127.9, 127.8, 127.5, 126.4, 125.9, 125.2, 124.7, 121.8, 120.4, 116.9, 115.9, 69.2, 69.0, 54.8, 53.5, 50.6, 47.8, 41.9, 40.4, 39.3, 32.5, 29.9, 29.4, 27.7, 26.1, 25.6, 23.1, 22.8, 22.6, 20.6; IR (cm^{-1}) υ 2960, 1653, 1559, 1507, 1240, 1049, 805, 745; MS (ES^+) *m/z* 836 (<5%, M+H), 418 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{46}H_{63}N_{10}O_5$: 835.4983, Found: 835.5023.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4-(2-aminoethyl)-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·trihydrochloride (63)



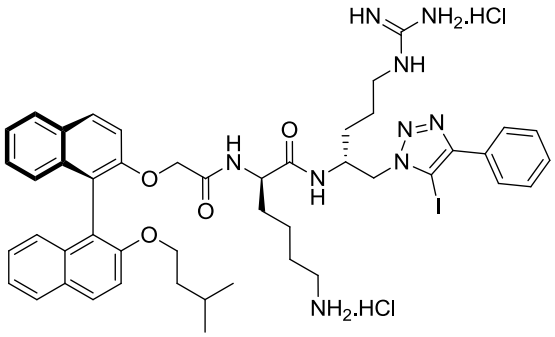
This compound was prepared according to *General Procedure 5* using **39** (42.5 mg, 0.035 mmol), CH_2Cl_2 (1.13 mL) and TFA (1.13 mL) with a 23 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.57 mL) as described gave **63** (28.6 mg, 93%) as a tan solid. $[\alpha]_D^{25}$ −14.2 (*c* 0.77, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.05 (app. t, *J* = 7.7 Hz, 2H), 7.99 – 7.89 (m, 3H), 7.57 (d, *J* = 9.0 Hz, 1H), 7.50 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.24 (app. t, *J* = 7.5 Hz, 2H), 7.12 – 7.02 (m, 2H), 4.63 – 4.51 (m, 2H), 4.50 – 4.35 (m, 2H), 4.30 – 4.21 (m, 1H), 4.18 – 4.10 (m, 1H), 4.01 – 3.91 (m, 2H), 3.34 – 3.25 (m, 2H), 3.24 – 3.14 (m, 2H), 3.12 (t, *J* = 7.1 Hz, 2H), 2.88 – 2.74 (m, 2H), 1.76 – 1.49 (m, 6H), 1.41 – 1.32 (m, 1H), 1.32 – 1.20 (m, 2H), 1.16 (sep, *J* = 6.5 Hz, 1H), 1.08 – 0.97 (m, 1H), 0.95 – 0.82 (m, 2H), 0.58 (d, *J* = 6.6 Hz, 3H), 0.52 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 173.6, 170.9, 158.5, 155.9, 154.1, 143.5, 135.2, 135.0, 131.4, 130.90, 130.86, 130.7, 129.3, 129.1, 127.6, 127.5, 126.4, 126.0, 125.9, 125.2, 124.8, 121.8, 120.6, 116.9, 116.1, 69.3, 69.0, 55.0, 54.1, 50.7, 41.9, 40.4, 40.0, 39.3, 32.1, 29.7, 27.8, 26.2, 25.6, 24.2, 23.4, 22.8, 22.5; IR (cm^{-1}) υ 2956, 1654, 1507, 1214, 1148, 1047, 862, 808, 745; MS (ES^+) *m/z* 390 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{43}H_{59}N_{10}O_4$: 779.4721, Found: 779.4707.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(4,5-diphenyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (64)



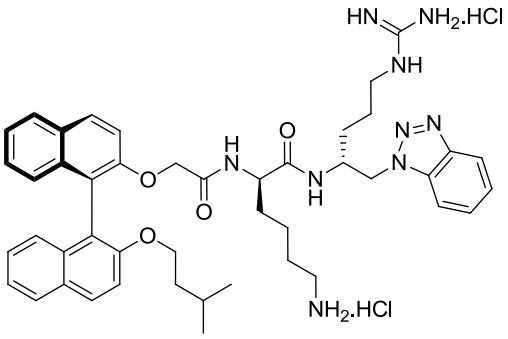
This compound was prepared according to *General Procedure 5* (larger scale modification, see *Note 2*) using **40** (1.096 g, 0.88 mmol), CH_2Cl_2 (15.0 mL), TFA (15.0 mL) and H_2O (0.32 mL, 17.67 mmol, 20 equiv) with a 17.5 h reaction time. Work-up as described, followed by treatment with HCl (2 M in Et_2O, 10.0 mL) and double precipitation of the product from MeOH with Et_2O gave **64** (780.6 mg, 92%) as a light brown solid. $[\alpha]_D^{25}$ −60.6 (*c* 0.40, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.01 (d, *J* = 8.9 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.82 (d, *J* = 8.9 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.66 – 7.54 (m, 7H), 7.45 (d, *J* = 8.9 Hz, 1H), 7.41 – 7.31 (m, 5H), 7.28 (t, *J* = 7.3 Hz, 1H), 7.24 – 7.14 (m, 2H), 7.04 – 6.97 (m, 2H), 4.52 (d, *J* = 14.6 Hz, 1H), 4.44 – 4.27 (m, 3H), 4.13 – 4.00 (m, 3H), 3.85 (q, *J* = 7.6 Hz, 1H), 3.07 – 2.92 (m, 2H), 2.84 – 2.70 (m, 2H), 1.61 – 1.33 (m, 7H), 1.33 – 1.07 (m, 3H), 0.93 – 0.82 (m, 1H), 0.82 – 0.67 (m, 2H), 0.54 (d, *J* = 6.3 Hz, 3H), 0.49 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 172.9, 170.5, 158.5, 155.8, 153.9, 145.3, 135.9, 135.2, 135.0, 131.70, 131.67, 131.44, 131.37, 130.8, 130.7, 130.6, 130.5, 129.8, 129.5, 129.2, 129.1, 128.7, 127.7, 127.5, 126.3, 125.9, 125.2, 124.7, 121.7, 120.3, 116.7, 115.7, 69.1, 68.9, 53.7, 53.3, 49.6, 41.8, 40.5, 39.3, 32.6, 30.0, 27.9, 26.1, 25.6, 23.3, 22.8, 22.6; IR (cm^{-1}) υ 2958, 1653, 1507, 1215, 1171, 1046, 863, 809, 751, 693; MS (ES^+) *m/z* 888 (<5%, M+H), 445 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{53}H_{62}N_9O_4$: 888.4925, Found: 888.4959.

(*R*)-6-Amino-*N*-((*R*)-5-guanidino-1-(5-iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (65)



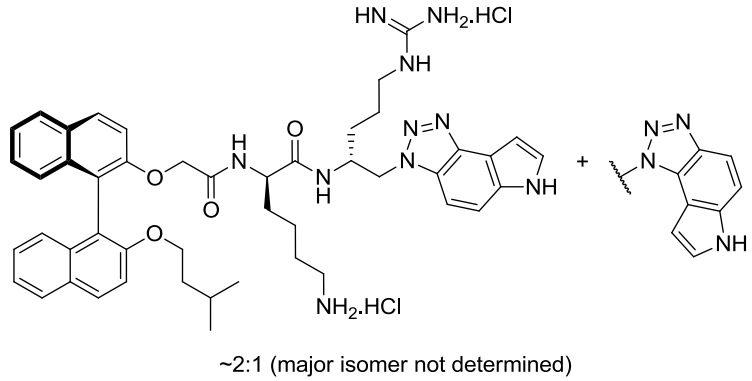
This compound was prepared according to *General Procedure 5* using **41** (45.5 mg, 0.035 mmol), CH_2Cl_2 (1.10 mL) and TFA (1.10 mL) with a 17 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.56 mL) as described gave **65** (36.2 mg, 100%) as an off-white solid. $[\alpha]_D^{25}$ −17.0 (*c* 1.23, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.02 (app. d, *J* = 7.1 Hz, 3H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.82 (d, *J* = 9.0 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.57 (app. t, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.45 (d, *J* = 9.0 Hz, 1H), 7.41 – 7.32 (m, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.24 – 7.15 (m, 2H), 7.01 (app. d, *J* = 8.4 Hz, 2H), 4.65 – 4.46 (m, 4H), 4.40 (d, *J* = 14.6 Hz, 1H), 4.13 – 4.00 (m, 2H), 3.91 – 3.82 (m, 1H), 3.26 – 3.13 (m, 2H), 2.76 – 2.63 (m, 2H), 1.85 – 1.57 (m, 4H), 1.53 – 1.41 (m, 2H), 1.41 – 1.31 (m, 1H), 1.31 – 1.09 (m, 3H), 0.93 – 0.81 (m, 1H), 0.78 – 0.64 (m, 2H), 0.55 (d, *J* = 6.4 Hz, 3H), 0.51 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 172.9, 170.6, 158.5, 155.8, 153.9, 150.7, 135.1, 135.0, 131.6, 131.3, 130.8, 130.7, 130.5, 130.0, 129.9, 129.2, 129.1, 128.5, 127.5, 126.4, 125.8, 125.1, 124.6, 121.7, 120.2, 116.7, 115.8, 80.8, 69.1, 68.8, 55.7, 53.3, 49.7, 42.0, 40.4, 39.2, 32.5, 30.0, 27.8, 26.3, 25.6, 23.2, 22.8, 22.6; IR (cm^{-1}) υ 1653, 1559, 1506, 1213, 1168, 1046, 807, 745; MS (ES^+) *m/z* 938 (<5%, M+H), 470 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{47}H_{57}IN_9O_4$: 938.3578, Found: 938.3593.

(*R*)-*N*-((*R*)-1-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)-5-guanidinopentan-2-yl)-6-amino-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (66)



This compound was prepared according to *General Procedure 5* using **42** (52.4 mg, 0.046 mmol), CH_2Cl_2 (1.50 mL) and TFA (1.50 mL) with a 17 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.74 mL) as described gave **66** (24.5 mg, 62%) as an off-white solid. $[\alpha]_D^{25}$ −18.4 (*c* 0.63, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.11 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 9.0 Hz, 1H), 7.95 – 7.88 (m, 3H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.27 (m, 3H), 7.26 – 7.14 (m, 2H), 7.01 (app. t, *J* = 9.5 Hz, 2H), 4.92 – 4.79 (m, 1H), 4.78 – 4.70 (m, 1H), 4.54 – 4.42 (m, 2H), 4.37 (d, *J* = 14.7 Hz, 1H), 4.05 – 3.98 (m, 1H), 3.98 – 3.92 (m, 1H), 3.92 – 3.83 (m, 1H), 3.25 – 3.10 (m, 2H), 2.76 – 2.62 (m, 2H), 1.90 – 1.78 (m, 1H), 1.76 – 1.56 (m, 3H), 1.46 – 1.33 (m, 2H), 1.31 – 1.03 (m, 4H), 1.01 – 0.88 (m, 1H), 0.67 – 0.47 (m, 8H); ^{13}C NMR (75 MHz, CD_3OD) δ 172.9, 170.5, 158.5, 155.8, 153.9, 146.3, 135.2, 134.9, 131.3, 130.8, 130.5, 129.2, 129.1, 129.0, 127.5, 126.3, 126.0, 125.8, 125.2, 124.6, 121.8, 120.2, 119.8, 116.7, 115.8, 112.0, 69.1, 68.8, 53.2, 52.9, 50.0, 41.9, 40.4, 39.2, 32.3, 30.1, 27.8, 26.2, 25.6, 23.1, 22.8, 22.6; IR (cm^{-1}) υ 2954, 1653, 1559, 1507, 1212, 1166, 1049, 807, 746; MS (ES^+) *m/z* 786 (<5%, M+H), 394 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{45}H_{56}N_9O_4$: 786.4455, Found: 786.4484.

(*R*)-*N*-((*R*)-1-([1,2,3]Triazolo[4,5-*e*]indol-1/3(6*H*)-yl)-5-guanidinopentan-2-yl)-6-amino-2-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexanamide·dihydrochloride (67)



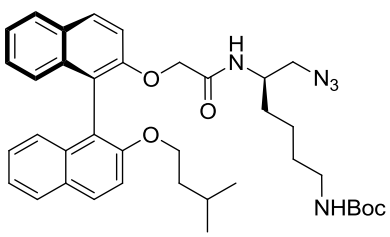
~2:1 (major isomer not determined)

This compound was prepared according to *General Procedure 5* using **43** (24.8 mg, 0.021 mmol), CH_2Cl_2 (0.69 mL) and TFA (0.69 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.35 mL) as described gave **67** (12.3 mg, 65%) as a dark grey solid. This material was an approximate 2:1 mixture of regioisomers as determined by ^{1}H NMR analysis. $[\alpha]_D^{25}$ −28.9 (*c* 0.39, MeOH); ^{1}H NMR (500 MHz, CD_3OD, signals denoted with an asterisk* have been assigned as the resolved minor isomer) δ 8.01 – 7.92 (m, 2H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.85 – 7.79 (m, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.57* (s, 1H), 7.43 – 7.37 (m, 1H), 7.37 – 7.30 (m, 1H), 7.30 – 7.09 (m, 4H), 7.06 – 6.92 (m, 3H), 5.11 – 4.99 (m, 1H), 4.99 – 4.91* (m, 1H), 4.91 – 4.77 (m, 1H), 4.67 – 4.60* (m, 1H), 4.60 – 4.52 (m, 1H), 4.48 – 4.39 (m, 1H), 4.38 – 4.29 (m, 1H), 4.01 – 3.92 (m, 1H), 3.90 – 3.78 (m, 1H), 3.78 – 3.72* (m, 1H), 3.69 – 3.62 (m, 1H), 3.28 – 3.11 (m, 2H), 2.74 – 2.51 (m, 2H), 1.99 – 1.86 (m, 1H), 1.82 – 1.58 (m, 3H), 1.45 – 1.24 (m, 3H), 1.23 – 1.00 (m, 4H), 0.63 – 0.41 (m, 8H), 0.41 – 0.31* (m, 2H); ^{13}C NMR (75 MHz, CD_3OD, signals denoted with an asterisk* have been assigned as the resolved minor isomer) δ 172.9, 170.5*, 170.4, 158.54, 158.51*, 155.8*, 155.7, 153.9*, 153.8, 136.4*, 136.0, 135.7, 135.15*, 135.12, 135.0*, 134.9, 131.6, 131.3, 130.8, 130.7, 130.6, 130.42, 130.36, 130.0*, 129.13, 129.07, 127.5, 127.42, 127.36, 126.6*, 126.3, 125.8, 125.2, 124.6*, 124.5, 121.79*, 121.76, 120.00*, 119.96, 117.6, 116.6*, 116.4, 115.8*, 115.7, 115.3*, 114.6*, 111.2*,

110.5*, 105.2, 69.0, 68.6*, 68.4, 54.9*, 54.8, 53.1*, 52.9, 50.0, 41.9, 40.4, 39.2*, 39.1, 32.5, 32.2*, 29.93*, 29.91, 27.8*, 27.7, 26.4, 26.3*, 25.6, 23.14, 23.07*, 22.8, 22.6; IR (cm^{-1}) υ 3198, 2924, 1654, 1507, 1243, 1147, 1002, 807, 742; MS (ES^+) *m/z* 825 (<5%, M+H), 413 (100%, M+2H); HRMS (ES^+) Calcd. for $C_{47}H_{57}N_{10}O_4$: 825.4564, Found: 825.4600.

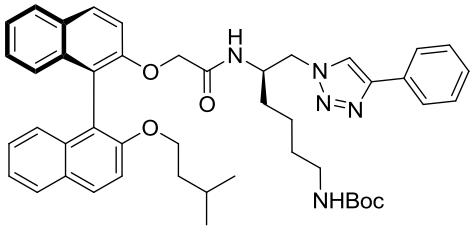
Synthesis and Characterization of Class C Triazoles

***tert*-Butyl ((*R*)-6-azido-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexyl)carbamate (91)**



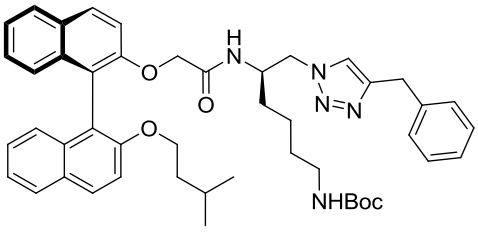
This compound was prepared according to *General Procedure 1* using the known acid **89**[S1] (207 mg, 0.50 mmol), EDCI·HCl (115 mg, 0.60 mmol), HOBt (81 mg, 0.60 mmol), known amine **90**[S8] (142 mg, 0.55 mmol) and MeCN (5.0 mL) with a 24 h reaction time. Work-up as described gave **91** (309 mg, 94%) as a pale yellow gum. TLC (5% MeOH/CH_2Cl_2) R_F = 0.45, (30% EtOAc/ pet. ether) R_F = 0.17; $[\alpha]_D^{25}$ −28.7 (*c* 0.73, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 9.1 Hz, 1H), 7.99 (d, *J* = 8.9 Hz, 1H), 7.89 (app. t, *J* = 6.7 Hz, 2H), 7.48 (d, *J* = 9.1 Hz, 1H), 7.39 – 7.29 (m, 3H), 7.28 – 7.22 (m, 2H), 7.18 (app. t, *J* = 9.2 Hz, 2H), 5.60 (d, *J* = 9.1 Hz, 1H), 4.48 (s, 2H), 4.42 (br s, 1H), 4.01 (dt, *J* = 9.4, 6.3 Hz, 1H), 3.94 (dt, *J* = 9.5, 6.4 Hz, 1H), 3.79 – 3.72 (m, 1H), 3.06 (dd, *J* = 12.3, 4.7 Hz, 1H), 2.99 – 2.88 (m, 4H), 1.44 (s, 9H), 1.33 – 1.15 (m, 8H), 1.11 – 1.02 (m, 1H), 0.60 (d, *J* = 6.5 Hz, 3H), 0.56 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 155.8, 154.5, 151.9, 133.8, 133.6, 129.7, 129.6, 129.4, 129.1, 127.86, 127.92, 126.6, 126.5, 125.3, 124.9, 124.0, 123.8, 120.1, 119.5, 115.7, 113.8, 78.9, 68.1, 67.7, 54.2, 47.6, 40.1, 37.9, 31.0, 29.3, 28.3, 24.5, 22.6, 22.1, 22.0; IR (cm^{-1}) υ 3385, 2930, 2101, 1683, 1506, 1457, 1363, 1243, 1168, 1094, 807, 747; MS (ES^+) *m/z* 676 (100%, M+Na); HRMS (ES^+) Calcd. for $C_{38}H_{48}N_5O_5$: 654.3655, Found: 654.3657.

***tert*-Butyl ((*R*)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)-6-(4-phenyl-1*H*-1,2,3-triazol-1-yl)hexyl)carbamate (92)**



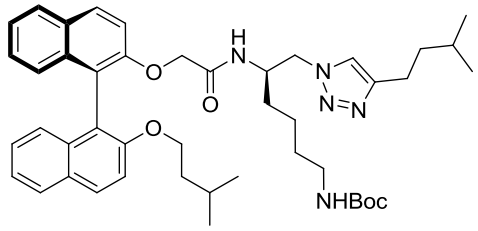
This compound was prepared according to *General Procedure 2* using azide **91** (52.0 mg, 0.080 mmol), $Cu(OAc)_2·H_2O$ (3.0 mg, 0.015 mmol), Na·ascorbate (6.0 mg, 0.030 mmol), phenylacetylene (23.5 mg, 0.230 mmol), *t*-BuOH (1.50 mL) and H_2O (0.40 mL) with a 19.5 h reaction time. Flash chromatography (3.0 g silica, 100% pet. ether to 100% EtOAc) gave **92** (55.0 mg, 92%) as a tan solid. TLC (40% EtOAc/pet. ether) R_F = 0.18; $[\alpha]_D^{25}$ −46.1 (*c* 0.35, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 – 7.93 (m, 2H), 7.92 – 7.85 (m, 2H), 7.76 (d, *J* = 7.6 Hz, 2H), 7.45 (s, 1H), 7.41 – 7.22 (m, 9H), 7.22 – 7.14 (m, 2H), 5.58 (d, *J* = 8.6 Hz, 1H), 4.54 – 4.38 (m, 3H), 4.22 (dd, *J* = 13.7, 5.2 Hz, 1H), 3.99 (br s, 1H), 3.93 – 3.75 (m, 3H), 1.43 (s, 9H), 1.35 – 1.03 (m, 6H), 0.95 – 0.80 (m, 2H), 0.73 – 0.64 (m, 1H), 0.52 (d, *J* = 6.5 Hz, 3H), 0.48 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 155.9, 154.6, 151.9, 147.7, 133.8, 133.6, 130.5, 129.9, 129.8, 129.6, 129.1, 128.8, 128.11, 128.05, 128.0, 126.9, 126.6, 125.7, 125.4, 125.0, 124.2, 124.1, 120.2, 119.9, 119.7, 116.0, 113.9, 79.1, 68.3, 67.8, 52.7, 48.7, 40.1, 37.9, 29.7, 29.3, 28.4, 24.5, 22.5, 22.2, 22.0; MS (ES^+) *m/z* 778 (100%, M+Na); HRMS (ES^+) Calcd. for $C_{46}H_{53}N_5NaO_5$: 778.3944, Found: 778.3974.

***tert*-Butyl ((*R*)-6-(4-benzyl-1*H*-1,2,3-triazol-1-yl)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexyl)carbamate (93)**



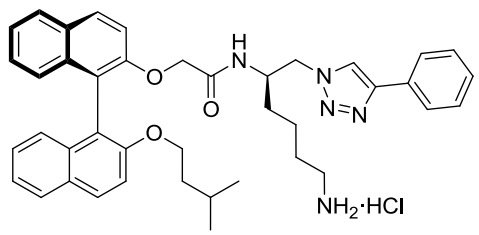
This compound was prepared according to *General Procedure 2* using azide **91** (50.0 mg, 0.076 mmol), $Cu(OAc)_2 \cdot H_2O$ (3.0 mg, 0.015 mmol), Na·ascorbate (6.0 mg, 0.030 mmol), 3-phenyl-1-propyne (26.7 mg, 0.23 mmol), *t*-BuOH (1.50 mL) and H_2O (0.40 mL) with a 46 h reaction time and a 35 °C temperature (obtained *via* oil bath). Flash chromatography (3.0 g silica, 30% EtOAc/pet. ether to 100% EtOAc) gave **93** (46.0 mg, 79%) as a tan solid. TLC (2.5% MeOH/CH_2Cl_2) R_F = 0.25; $[\alpha]_D^{25}$ −26.7 (*c* 0.32, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (app. t, *J* = 8.4 Hz, 2H), 7.90 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.34 (m, 2H), 7.30 – 7.12 (m, 10H), 6.91 (s, 1H), 5.55 (d, *J* = 8.6 Hz, 1H), 4.43 – 4.37 (m, 2H), 4.26 (d, *J* = 14.3 Hz, 1H), 4.09 – 4.02 (m, 1H), 4.02 – 3.93 (m, 3H), 3.93 – 3.75 (m, 3H), 2.90 (s, 2H), 1.43 (s, 9H), 1.35 – 1.04 (m, 6H), 0.86 – 0.75 (m, 2H), 0.74 – 0.64 (m, 1H), 0.56 (d, *J* = 6.6 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H; ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 156.0, 154.7, 152.0, 147.6, 139.2, 134.0, 133.7, 130.0, 129.9, 129.8, 129.3, 128.7, 128.2, 128.1, 127.1, 126.8, 126.5, 125.6, 125.1, 124.4, 124.2, 121.9, 120.3, 119.9, 116.1, 114.1, 79.2, 68.5, 67.8, 52.8, 49.0, 40.2, 38.1, 32.2, 29.8, 29.4, 28.5, 24.6, 22.6, 22.4, 22.2; MS (ES^+) *m/z* 792 (100%, M+Na).

***tert*-Butyl ((*R*)-6-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)-5-(2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamido)hexyl)carbamate (94)**



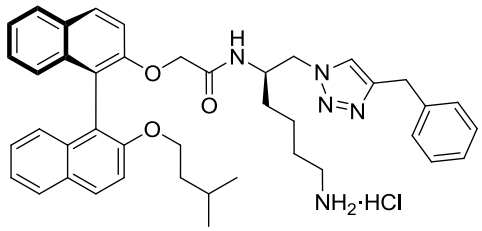
This compound was prepared according to *General Procedure 2* using azide **91** (50.0 mg, 0.076 mmol), $Cu(OAc)_2 \cdot H_2O$ (3.0 mg, 0.015 mmol), Na·ascorbate (6.0 mg, 0.030 mmol), 5-methyl-1-hexyne (21.9 mg, 0.228 mmol), *t*-BuOH (1.60 mL) and H_2O (0.40 mL) with a 48 h reaction time and a 35 °C temperature (obtained *via* oil bath). Flash chromatography (3.0 g silica, 30% EtOAc/pet. ether to 100% EtOAc) gave **94** (41.0 mg, 72%) as a tan solid. TLC (2.5% MeOH/CH_2Cl_2) R_F = 0.16; $[\alpha]_D^{25}$ −18.7 (*c* 0.60, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 6.8 Hz, 1H), 7.99 (d, *J* = 6.7 Hz, 1H), 7.90 (app. t, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 9.1 Hz, 1H), 7.40 – 7.24 (m, 5H), 7.22 – 7.15 (m, 2H), 7.00 (s, 1H), 5.60 (d, *J* = 8.7 Hz, 1H), 4.51 – 4.36 (m, 3H), 4.06 (dd, *J* = 13.6, 5.9 Hz, 1H), 3.98 (dt, *J* = 9.4, 6.3 Hz, 1H), 3.94 – 3.87 (m, 2H), 3.81 (dd, *J* = 13.6, 7.0 Hz, 1H), 2.98 – 2.85 (m, 2H), 2.66 – 2.60 (m, 2H), 1.59 – 1.53 (m, 1H), 1.53 – 1.47 (m, 2H), 1.43 (s, 9H), 1.33 – 1.06 (m, 6H), 0.91 (d, *J* = 1.3 Hz, 3H), 0.90 (d, *J* = 1.4 Hz, 3H), 0.86 – 0.77 (m, 2H), 0.72 – 0.64 (m, 1H), 0.57 (d, *J* = 6.6 Hz, 3H), 0.53 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ168.3, 155.9, 154.5, 152.0, 148.6, 133.8, 133.6, 129.9, 129.8, 129.7, 129.1, 128.1, 128.0, 126.9, 126.7, 125.4, 125.0, 124.2, 124.1, 120.7, 120.3, 119.8, 116.0, 114.0, 79.1, 68.4, 67.9, 52.7, 48.7, 40.0, 38.4, 38.0, 29.6, 29.2, 28.4, 27.6, 24.5, 23.5, 22.4, 22.4, 22.36, 22.33, 22.1; MS (ES^+) *m/z* 772 (100%, M+Na); HRMS (ES^+) Calcd. for $C_{45}H_{59}N_5O_5$: 749.4516, Found: 749.4504.

***N*-((*R*)-6-Amino-1-(4-phenyl-1*H*-1,2,3-triazol-1-yl)hexan-2-yl)-2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide·hydrochloride (95)**



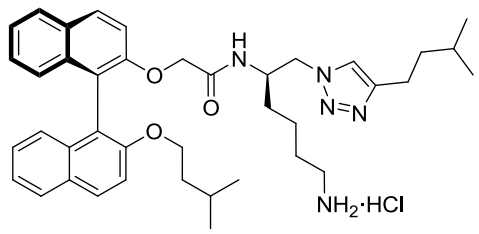
This compound was prepared according to *General Procedure 5* using **92** (47.0 mg, 0.062 mmol), CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 1.0 mL) as described gave **95** (37.0 mg, 86%) as a tan solid. $[\alpha]_D^{25}$ −19.7 (*c* 1.22, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.10 – 7.82 (m, 6H), 7.74 (d, *J* = 7.5 Hz, 2H), 7.51 (d, *J* = 9.0 Hz, 1H), 7.46 – 7.18 (m, 7H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.09 (d, *J* = 8.6 Hz, 1H), 4.54 – 4.29 (m, 3H), 4.12 (br s, 1H), 4.00 – 3.80 (m, 3H), 2.86 – 2.64 (m, 2H), 1.59 – 1.39 (m, 2H), 1.35 – 1.22 (m, 1H), 1.22 – 1.08 (m, 2H), 1.08 – 0.93 (m, 3H), 0.93 – 0.74 (m, 1H), 0.50 (d, *J* = 6.6 Hz, 3H), 0.46 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 171.0, 156.1, 153.8, 150.3, 135.2, 135.0, 131.6, 131.4, 131.1, 131.0, 130.8, 130.0, 129.44, 129.42, 129.2, 127.9, 127.6, 126.7, 126.3, 126.1, 125.3, 125.2, 122.7, 121.5, 121.0, 117.3, 115.6, 69.4, 69.0, 54.2, 50.0, 40.5, 39.2, 31.9, 27.9, 25.5, 23.5, 22.7, 22.4; IR (cm^{-1}) υ 3373, 2954, 1683, 1653, 1558, 1506, 1244, 1147, 809, 765; MS (ES^+) *m/z* 656 (100%, M+H); HRMS (ES^+) Calcd. for $C_{41}H_{45}N_5NaO_3$: 678.3420, Found: 678.3448.

***N*-((*R*)-6-Amino-1-(4-benzyl-1*H*-1,2,3-triazol-1-yl)hexan-2-yl)-2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide·hydrochloride (96)**



This compound was prepared according to *General Procedure 5* using **93** (36.0 mg, 0.047 mmol), CH_2Cl_2 (1.5 mL) and TFA (1.5 mL) with a 20 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 1.0 mL) as described gave **96** (27.0 mg, 82%) as a tan solid. $[\alpha]_D^{25}$ −14.5 (*c* 0.58, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.08 (d, *J* = 9.1 Hz, 1H), 8.04 (d, *J* = 9.1 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.44 – 7.34 (m, 3H), 7.31 – 7.22 (m, 2H), 7.22 – 7.08 (m, 8H), 4.38 (d, *J* = 14.6 Hz, 1H), 4.31 (dd, *J* = 14.0, 4.3 Hz, 1H), 4.11 (d, *J* = 14.6 Hz, 1H), 4.10 – 3.98 (m, 2H), 3.99 – 3.87 (m, 3H), 3.67 (dd, *J* = 14.0, 9.2 Hz, 1H), 2.81 – 2.66 (m, 2H), 1.53 – 1.40 (m, 2H), 1.36 – 1.25 (m, 1H), 1.27 – 1.11 (m, 2H), 1.14 – 1.02 (m, 1H), 1.03 – 0.93 (m, 2H), 0.88 – 0.76 (m, 1H), 0.52 (d, *J* = 6.6 Hz, 3H), 0.48 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 170.7, 156.1, 153.7, 148.2, 140.4, 135.2, 135.1, 131.5, 131.1, 130.8, 129.7, 129.5, 129.2, 128.0, 127.7, 127.5, 126.3, 126.1, 125.3, 125.2, 124.3, 121.5, 121.1, 117.3, 115.7, 69.4, 68.9, 54.3, 50.0, 49.5, 49.3, 40.5, 39.3, 32.5, 32.0, 27.8, 25.5, 23.4, 22.8, 22.4; IR (cm^{-1}) υ 3650, 2957, 1734, 1683, 1653, 1558, 1506, 1457, 1244, 1073, 809, 750; MS (ES^+) *m/z* 670 (100%, M+H), 692 (10%, M+Na); HRMS (ES^+) Calcd. for $C_{42}H_{47}N_5NaO_3$: 692.3577, Found: 692.3611.

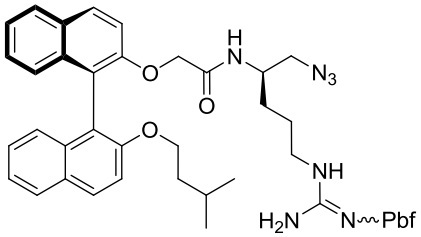
***N*-((*R*)-6-Amino-1-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)hexan-2-yl)-2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide·hydrochloride (97)**



This compound was prepared according to *General Procedure 5* using **94** (25.0 mg, 0.033 mmol), CH_2Cl_2 (1.0 mL) and TFA (1.0 mL) with a 24 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.5 mL) as described gave **97** (22.0 mg, 97%) as a tan solid. $[\alpha]_D^{25}$ −21.2 (*c* 0.49, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.10 (d, *J* = 8.9 Hz, 1H), 8.04 (d,

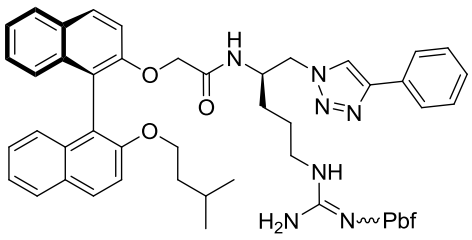
J = 9.0 Hz, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.62 (d, *J* = 9.0 Hz, 1H), 7.44 – 7.33 (m, 3H), 7.27 (q, *J* = 8.5 Hz, 2H), 7.20 (s, 1H), 7.15 (d, *J* = 8.6 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 1H), 4.45 and 4.34 (ABq, *J* = 14.6 Hz, 2H), 4.27 (dd, *J* = 13.9, 4.5 Hz, 1H), 4.13 – 4.01 (m, 2H), 4.01 – 3.90 (m, 1H), 3.74 (dd, *J* = 13.9, 8.7 Hz, 1H), 2.80 – 2.66 (m, 2H), 2.65 – 2.53 (m, 2H), 1.54 – 1.37 (m, 4H), 1.37 – 1.06 (m, 6H), 1.02 – 0.76 (m, 8H), 0.56 (d, *J* = 6.5 Hz, 3H), 0.51 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 170.8, 156.1, 153.8, 149.2, 135.2, 135.1, 131.5, 131.09, 131.05, 130.8, 129.5, 129.2, 127.9, 127.7, 126.3, 126.1, 125.3, 125.2, 123.4, 121.6, 121.1, 117.3, 115.8, 69.4, 69.1, 54.2, 49.9, 40.4, 39.7, 39.3, 32.0, 28.6, 27.8, 25.6, 24.2, 23.4, 22.8, 22.7, 22.5; IR (cm^{-1}) υ 3363, 2956, 2361, 1680, 1653, 1507, 1272, 1203, 1136, 810; MS (ES^+) *m/z* 650 (100%, M+H); HRMS (ES^+) Calcd. for $C_{40}H_{52}N_5O_3$: 650.4070, Found: 650.4043.

_N_-((_R_)-1-Azido-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)-2-(((_S_)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide (98)



This compound was prepared according to *General Procedure 1* using the known acid **89**[S1] (92.0 mg, 0.22 mmol), EDCI·HCl (51.1 mg, 0.27 mmol), HOBt (36.0 mg, 0.27 mmol), amine **14** (100 mg, 0.23 mmol) and MeCN (2.2 mL) with a 4.5 h reaction time. Work-up as described gave **98** (176.5 mg, 95%) as an off-white solid. TLC (5% MeOH/CH_2Cl_2) R_F = 0.41; $[\alpha]_D^{25}$ −23.6 (*c* 0.85, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.30 – 7.21 (m, 3H), 7.21 – 7.10 (m, 3H), 6.25 (bs, 2H), 6.04 (bs, 1H), 5.58 (d, *J* = 9.4 Hz, 1H), 4.44 (ABq, $\Delta\delta_{AB}$ = 0.04, *J* = 14.4 Hz, 2H), 4.02 – 3.95 (m, 1H), 3.95 – 3.89 (m, 1H), 3.74 – 3.65 (m, 1H), 3.06 – 2.83 (m, 5H), 2.72 (dd, *J* = 12.4, 5.8 Hz, 1H), 2.58 (s, 3H), 2.50 (s, 3H), 2.08 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H), 1.29 – 1.20 (m, 2H), 1.17 (sep, *J* = 6.5 Hz, 1H), 1.09 – 1.00 (m, 1H), 1.00 – 0.86 (m, 2H), 0.57 (d, *J* = 6.5 Hz, 3H), 0.56 – 0.47 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 158.6, 156.1, 154.5, 151.8, 138.1, 133.8, 133.4, 133.0, 132.1, 129.71, 129.66, 129.4, 129.0, 128.0, 127.9, 126.7, 126.5, 125.4, 124.7, 124.5, 124.1, 123.8, 120.1, 119.3, 117.4, 115.6, 113.8, 86.3, 68.1, 67.6, 54.1, 47.3, 43.1, 40.4, 37.8, 28.8, 28.5, 28.4, 24.9, 24.4, 22.2, 22.0, 19.2, 17.9, 12.4; IR (cm^{-1}) υ 3349, 2944, 2101, 1550, 1242, 1094, 807, 746; MS (ES^+) *m/z* 856 (100%, M+Na), 834 (41%, M+H); HRMS (ES^+) Calcd. for $C_{46}H_{55}N_7NaO_6S$: 856.3832, Found: 856.3862.

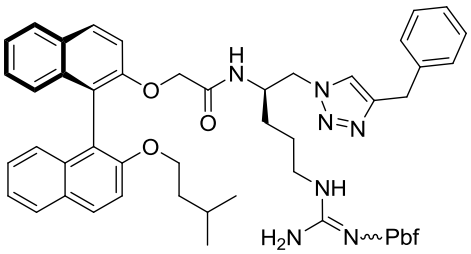
2-(((_S_)-2'-(Isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)-_N_-((_R_)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)-1-(4-phenyl-1_H_-1,2,3-triazol-1-yl)pentan-2-yl)acetamide (99)



This compound was prepared according to *General Procedure 2* using azide **98** (40.0 mg, 0.048 mmol), $Cu(OAc)_2·H_2O$ (1.9 mg, 0.0096 mmol), Na·ascorbate (3.8 mg, 0.019 mmol), phenylacetylene (14.3 mg, 0.14 mmol), *t*-BuOH (1.0 mL) and H_2O (0.25 mL) with a 24 h reaction time. Work-up as described gave **99** (44.0 mg, 98%) as an off-white solid. TLC (75% EtOAc/pet. ether) R_F = 0.33; $[\alpha]_D^{25}$ −28.7 (*c* 2.07, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 9.0 Hz, 1H), 7.89 – 7.84 (m, 2H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.38 – 7.12 (m, 11H), 6.32 (bs, 2H), 6.06 (bs, 1H), 5.52 (d, *J* = 9.1 Hz, 1H), 4.34 (ABq, $\Delta\delta_{AB}$ = 0.08, *J* = 14.3 Hz, 2H), 4.20 (dd, *J* = 14.0, 3.5 Hz, 1H), 4.02 – 3.92 (m, 1H), 3.90 – 3.77 (m, 1H), 3.61 (dd, *J* = 13.9, 7.9 Hz, 1H), 3.05 – 2.93

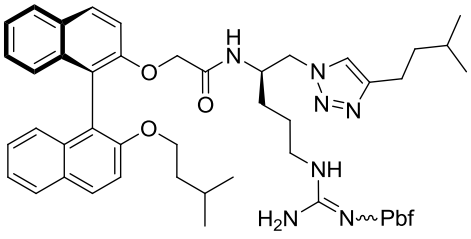
(m, 2H), 2.88 (s, 2H), 2.61 (s, 3H), 2.51 (s, 3H), 2.07 (s, 3H), 1.38 (s, 6H), 1.20 – 0.98 (m, 6H), 0.64 – 0.53 (m, 1H), 0.51 (d, *J* = 6.5 Hz, 3H), 0.47 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 158.6, 156.2, 154.6, 151.8, 147.4, 138.2, 133.8, 133.5, 132.2, 130.4, 129.9, 129.7, 129.6, 129.0, 128.8, 128.2, 128.1, 128.0, 127.0, 126.6, 125.6, 125.4, 124.9, 124.6, 124.2, 124.1, 120.5, 120.0, 119.6, 117.4, 115.9, 113.8, 86.3, 68.3, 67.6, 52.7, 48.3, 43.1, 40.3, 37.9, 28.5, 28.4, 24.8, 24.4, 22.2, 22.0, 19.3, 17.9, 12.4; MS (ES^+) *m/z* 958 (99%, M+Na), 936 (100%, M+H); HRMS (ES^+) Calcd. for $C_{54}H_{61}N_7NaO_6S$: 958.4302, Found: 958.4330.

_N_-((_R_)-1-(4-Benzyl-1_H_-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)-2-(((_S_)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide (100)



This compound was prepared according to *General Procedure 2* using azide **98** (40.0 mg, 0.048 mmol), $Cu(OAc)_2{\cdot}H_2O$ (1.9 mg, 0.0096 mmol), Na·ascorbate (3.8 mg, 0.019 mmol), 3-phenyl-1-propyne (16.3 mg, 0.14 mmol), *t*-BuOH (1.0 mL) and H_2O (0.25 mL) with a 24 h reaction time. Purification by a pipette silica plug (3 cm silica, 100% pet. ether then 100% EtOAc) gave **100** (38.9 mg, 85%) as an off-white solid. TLC (75% EtOAc/pet. ether) R_F = 0.35; $[\alpha]_D^{25}$ −29.1 (*c* 1.89, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 9.0 Hz, 1H), 7.92 – 7.86 (m, 2H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.32 – 7.23 (m, 2H), 7.22 – 7.12 (m, 7H), 7.10 (app. d, *J* = 7.1 Hz, 2H), 6.75 (s, 1H), 6.22 (bs, 2H), 5.95 (bs, 1H), 5.47 (d, *J* = 9.2 Hz, 1H), 4.30 (d, *J* = 14.3 Hz, 1H), 4.12 – 4.02 (m, 2H), 3.99 – 3.82 (m, 5H), 3.46 (dd, *J* = 13.8, 8.5 Hz, 1H), 3.05 – 2.95 (m, 2H), 2.90 (s, 2H), 2.60 (s, 3H), 2.51 (s, 3H), 2.08 (s, 3H), 1.40 (s, 6H), 1.29 – 1.01 (m, 5H), 1.00 – 0.91 (m, 1H), 0.64 – 0.52 (m, 4H), 0.50 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 158.6, 156.1, 154.5, 151.8, 147.0, 139.0, 138.2, 133.8, 133.5, 133.2, 132.2, 129.8, 129.75, 129.67, 129.1, 128.5, 128.4, 128.2, 128.0, 127.0, 126.6, 126.4, 125.4, 124.9, 124.5, 124.2, 122.3, 120.0, 119.7, 117.4, 115.9, 113.9, 86.3, 68.3, 67.4, 52.7, 48.4, 43.2, 40.2, 37.9, 31.9, 28.5, 24.8, 24.4, 22.3, 22.0, 19.2, 17.9, 12.4; MS (ES^+) *m/z* 972 (96%, M+Na), 950 (100%, M+H); HRMS (ES^+) Calcd. for $C_{55}H_{63}N_7NaO_6S$: 972.4458, Found: 972.4495.

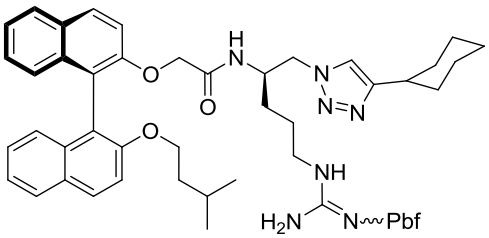
_N_-((_R_)-1-(4-Isopentyl-1_H_-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)-2-(((_S_)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide (101)



This compound was prepared according to *General Procedure 2* using azide **98** (40.0 mg, 0.048 mmol), $Cu(OAc)_2{\cdot}H_2O$ (1.9 mg, 0.0096 mmol), Na·ascorbate (3.8 mg, 0.019 mmol), 5-methyl-1-hexyne (13.8 mg, 0.14 mmol), *t*-BuOH (1.0 mL) and H_2O (0.25 mL) with a 24 h reaction time. Work-up as described gave **101** (43.7 mg, 98%) as an off-white solid. TLC (75% EtOAc/pet. ether) R_F = 0.34; $[\alpha]_D^{25}$ −30.9 (*c* 2.09, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.90 (m, 2H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.32 – 7.22 (m, 3H), 7.21 – 7.12 (m, 3H), 6.85 (s, 1H), 6.30 (bs, 2H), 6.03 (bs, 1H), 5.54 (d, *J* = 8.8 Hz, 1H), 4.40 (d, *J* = 14.2 Hz, 1H), 4.30 (d, *J* = 14.0 Hz, 1H), 4.12 – 4.03 (m, 1H), 4.03 – 3.85 (m, 3H), 3.55 (dd, *J* = 13.6, 8.0 Hz, 1H), 3.06 – 2.97 (m, 2H), 2.91 (s, 2H), 2.64 – 2.54 (m, 5H), 2.52 (s, 3H), 2.08 (s, 3H), 1.55 – 1.36 (m, 9H), 1.29 – 1.03 (m, 5H), 1.03 – 0.94 (m, 1H), 0.87 (d, *J* = 6.1 Hz, 6H), 0.64 – 0.54 (m, 4H), 0.52 (d, *J* = 6.5

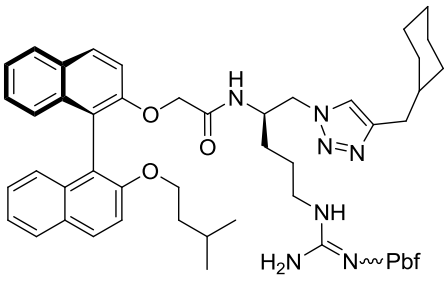
Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 158.6, 156.1, 154.6, 151.9, 148.2, 138.2, 133.8, 133.5, 133.2, 132.1, 129.9, 129.8, 129.7, 129.1, 128.1, 128.0, 127.0, 126.6, 125.4, 124.9, 124.5, 124.2, 121.3, 120.1, 119.7, 117.4, 115.9, 113.9, 86.2, 68.4, 67.7, 52.5, 48.3, 43.2, 40.3, 38.4, 37.9, 28.5, 27.5, 24.7, 24.5, 23.4, 22.29, 22.26, 22.2, 22.0, 19.2, 17.9, 12.4; MS (ES^+) *m/z* 952 (100%, M+Na), 930 (84%, M+H); HRMS (ES^+) Calcd. for $C_{53}H_{67}N_7NaO_6S$: 952.4771, Found: 952.4803.

_N_-((_R_)-1-(4-Cyclohexyl-1_H_-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)-2-(((_S_)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide (102)



This compound was prepared according to *General Procedure 2* using azide **98** (70.0 mg, 0.084 mmol), $Cu(OAc)_2{\cdot}H_2O$ (3.4 mg, 0.017 mmol), Na·ascorbate (6.7 mg, 0.034 mmol), cyclohexylacetylene (27.2 mg, 0.25 mmol), *t*-BuOH (1.68 mL) and H_2O (0.42 mL) with a 16 h reaction time. Purification by a pipette silica plug (3 cm silica, 100% pet. ether then 100% EtOAc) gave **102** (62.4 mg, 79%) as a white solid. TLC (75% EtOAc/pet. ether) R_F = 0.23; $[\alpha]_D^{25}$ −30.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.92 (m, 2H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.12 (m, 7H), 6.82 (s, 1H), 6.23 (bs, 2H), 5.90 (bs, 1H), 5.54 (d, *J* = 9.0 Hz, 1H), 4.36 (ABq, $\Delta\delta_{AB}$ = 0.09, *J* = 14.3 Hz, 2H), 4.07 (dd, *J* = 13.8, 4.8 Hz, 1H), 4.03 – 3.95 (m, 1H), 3.95 – 3.84 (m, 2H), 3.54 (dd, *J* = 13.7, 7.9 Hz, 1H), 3.09 – 2.98 (m, 1H), 2.99 – 2.86 (m, 4H), 2.67 – 2.57 (m, 4H), 2.53 (s, 3H), 2.08 (s, 3H), 1.96 – 1.87 (m, 2H), 1.80 – 1.64 (m, 3H), 1.41 (s, 6H), 1.38 – 0.91 (m, 12H), 0.56 (d, *J* = 6.5 Hz, 3H), 0.53 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 158.6, 156.1, 154.6, 153.5, 151.9, 138.3, 133.8, 133.6, 133.3, 132.2, 129.9, 129.8, 129.7, 129.1, 128.2, 128.0, 127.1, 126.7, 125.4, 124.9, 124.5, 124.3, 124.2, 120.2, 119.7, 117.4, 116.0, 114.0, 86.3, 68.5, 67.8, 52.5, 48.3, 43.2, 40.3, 38.0, 35.1, 32.9, 32.8, 28.5, 28.4, 26.0, 25.9, 24.5, 22.3, 22.1, 19.3, 17.9, 12.5; MS (ES^+) *m/z* 964 (64%, M+Na), 943 (100%, M+H).

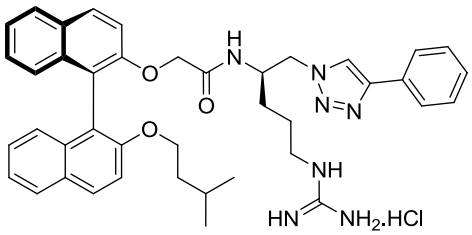
_N_-((_R_)-1-(4-(Cyclohexylmethyl)-1_H_-1,2,3-triazol-1-yl)-5-(2-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)pentan-2-yl)-2-(((_S_)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide (103)



This compound was prepared according to *General Procedure 2* using azide **98** (70.0 mg, 0.084 mmol), $Cu(OAc)_2{\cdot}H_2O$ (3.4 mg, 0.017 mmol), Na·ascorbate (6.7 mg, 0.034 mmol), 3-cyclohexyl-1-propyne (30.8 mg, 0.25 mmol), *t*-BuOH (1.68 mL) and H_2O (0.42 mL) with a 16 h reaction time. Purification by a pipette silica plug (3 cm silica, 100% pet. ether then 100% EtOAc) gave **103** (71.3 mg, 89%) as a white solid. TLC (75% EtOAc/pet. ether) R_F = 0.31; $[\alpha]_D^{25}$ −36.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.92 (m, 2H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 9.0 Hz, 1H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.35 – 7.13 (m, 6H), 6.74 (s, 1H), 6.23 (bs, 2H), 5.95 (bs, 1H), 5.52 (d, *J* = 9.2 Hz, 1H), 4.35 (ABq, $\Delta\delta_{AB}$ = 0.11, *J* = 14.3 Hz, 2H), 4.09 (dd, *J* = 13.8, 4.5 Hz, 1H), 4.04 – 3.83 (m, 3H), 3.52 (dd, *J* = 13.7, 8.2 Hz, 1H), 3.09 – 2.99 (m, 1H), 2.99 – 2.86 (m, 3H), 2.61 (s, 3H), 2.56 – 2.44 (m, 4H), 2.40 (dd, *J* = 14.2, 7.1 Hz, 1H), 2.09 (s, 3H), 1.69 – 1.52 (m, 5H), 1.53 – 1.44 (m, 1H), 1.41 (s, 6H), 1.29 – 0.94 (m, 10H), 0.85 (quin, *J* = 10.7 Hz, 2H), 0.57 (d, *J* = 6.5 Hz, 3H), 0.53 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 158.6, 156.1, 154.6, 151.8, 146.6, 138.3, 133.8, 133.5, 133.3, 132.2, 129.9, 129.8, 129.7, 129.1, 128.2, 128.0, 127.1, 126.7,

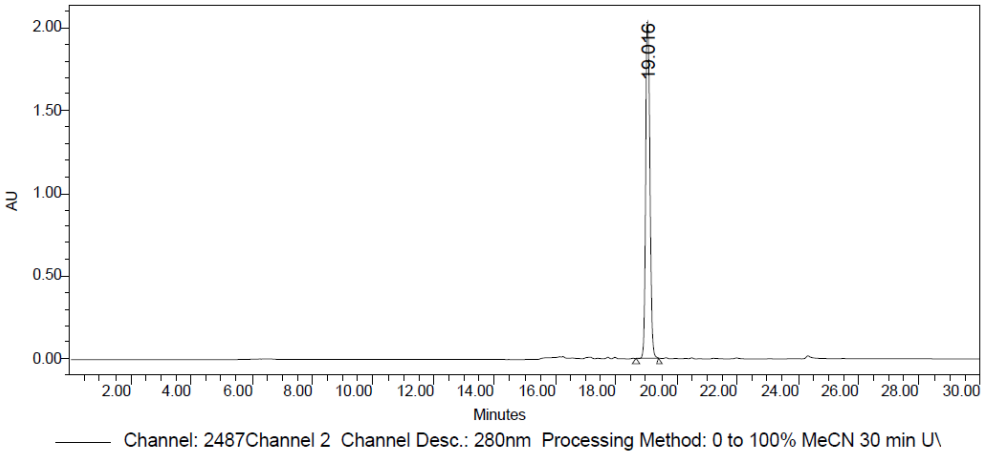
125.4, 124.9, 124.5, 124.3, 124.2, 122.0, 120.1, 119.7, 117.4, 115.9, 113.9, 86.3, 68.4, 67.7, 52.5, 48.3, 43.2, 40.3, 37.98, 37.96, 33.2, 32.9, 32.8, 28.5, 26.3, 26.07, 26.05, 24.5, 22.6, 22.3, 22.1, 19.3, 17.9, 12.5; MS (ES^+) *m/z* 978 (78%, M+Na), 956 (100%, M+H).

_N_-((_R_)-5-Guanidino-1-(4-phenyl-1_H_-1,2,3-triazol-1-yl)pentan-2-yl)-2-(((_S_)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide·hydrochloride (104)



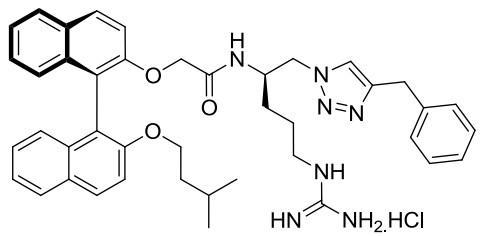
This compound was prepared according to *General Procedure 5* (larger scale modification, see *Note 2*) using **99** (844.4 mg, 0.90 mmol), CH_2Cl_2 (15.0 mL), TFA (15.0 mL) and H_2O (0.33 mL, 18.04 mmol, 20 equiv) with a 16 h reaction time. Work-up as described, followed by treatment with HCl (2 M in Et_2O, 10.0 mL) and double precipitation of the product from MeOH with Et_2O gave **104** (650.0 mg, 100%) as an off-white solid. $[\alpha]_D^{25}$ −28.5 (*c* 0.70, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.06 (d, *J* = 9.0 Hz, 1H), 8.03 – 7.87 (m, 4H), 7.75 (d, *J* = 7.7 Hz, 2H), 7.52 (d, *J* = 9.0 Hz, 1H), 7.45 – 7.33 (m, 6H), 7.30 – 7.21 (m, 2H), 7.14 (d, *J* = 8.5 Hz, 1H), 7.09 (d, *J* = 8.5 Hz, 1H), 4.51 – 4.36 (m, 3H), 4.19 – 4.10 (m, 1H), 4.01 – 3.91 (m, 2H), 3.91 – 3.84 (m, 1H), 3.09 – 2.96 (m, 2H), 1.45 – 1.34 (m, 1H), 1.28 – 1.11 (m, 4H), 1.07 (sep, *J* = 6.7 Hz, 1H), 0.93 – 0.82 (m, 1H), 0.51 (d, *J* = 6.5 Hz, 3H), 0.47 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 171.1, 158.4, 156.0, 153.8, 147.9, 135.1, 135.0, 131.4, 131.0, 130.7, 130.3, 130.2, 130.0, 129.4, 129.2, 127.9, 127.6, 126.9, 126.3, 126.0, 125.3, 125.2, 123.5, 121.5, 120.8, 117.1, 115.8, 69.2, 69.1, 54.8, 49.8, 41.7, 39.2, 29.5, 25.8, 25.5, 22.8, 22.4; IR (cm^{-1}) υ 3366, 2949, 1654, 1560, 1507, 1218, 1045, 808, 749, 693; MS (ES^+) *m/z* 684 (100%, M+H); HRMS (ES^+) Calcd. for $C_{41}H_{46}N_7O_3$: 684.3662, Found: 684.3677; HPLC phenomenex Synergi 4u Fusion-RP 80Å column, Flow rate = 1.0 $mLmin^{-1}$, Eluent profile: 100% H_2O for 2 min, then linear gradient to 100% MeCN over 20 min, then 100% MeCN for 8 min (both solvents containing 0.1% TFA), λ = 280 nm, t_R = 19.0 min (100% peak area).

HPLC Trace of Compound **104**:



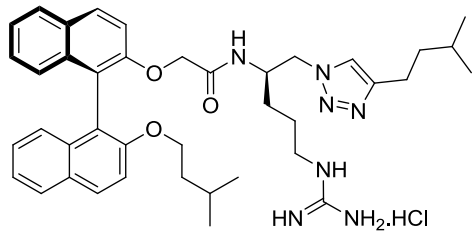
	Channel Description	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	280nm	19.016	20010837	100.00	2037425

***N*-((*R*)-5-Guanidino-1-(4-benzyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide·hydrochloride (105)**



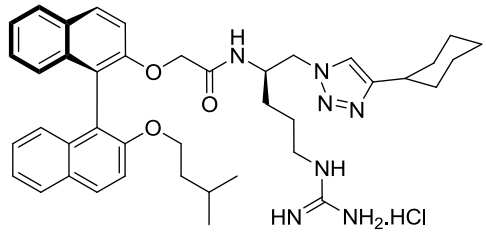
This compound was prepared according to *General Procedure 5* using **100** (36.6 mg, 0.039 mmol), CH_2Cl_2 (1.26 mL) and TFA (1.26 mL) with a 39.5 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.63 mL) as described gave **105** (21.7 mg, 77%) as a tan solid. $[\alpha]_D^{25}$ −28.3 (*c* 0.50, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.10 (d, *J* = 9.0 Hz, 1H), 8.05 (d, *J* = 9.0 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 8.9 Hz, 1H), 7.43 – 7.36 (m, 3H), 7.35 (s, 1H), 7.31 – 7.09 (m, 9H), 4.45 – 4.36 (m, 2H), 4.14 (d, *J* = 14.6 Hz, 1H), 4.11 – 4.02 (m, 2H), 3.99 (s, 2H), 3.98 – 3.91 (m, 1H), 3.77 (dd, *J* = 13.6, 9.6 Hz, 1H), 3.08 – 2.94 (m, 2H), 1.46 – 1.37 (m, 1H), 1.28 – 1.15 (m, 4H), 1.09 (sep, *J* = 6.4 Hz, 1H), 0.95 – 0.85 (m, 1H), 0.53 (d, *J* = 6.5 Hz, 3H), 0.49 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 171.0, 158.5, 156.0, 153.8, 146.7, 138.7, 135.2, 135.0, 131.5, 131.13, 131.05, 130.7, 129.9, 129.6, 129.5, 129.2, 128.01, 127.98, 127.7, 126.3, 126.1, 125.3, 125.2, 121.6, 120.9, 117.1, 116.0, 69.2, 69.1, 55.7, 49.9, 41.6, 39.2, 31.4, 29.4, 25.8, 25.5, 22.8, 22.4; IR (cm^{-1}) υ 3365, 2957, 1653, 1507, 1213, 1147, 1046, 807, 750; MS (ES^+) *m/z* 698 (100%, M+H); HRMS (ES^+) Calcd. for $C_{42}H_{47}N_7O_3$: 698.3819, Found: 698.3835.

***N*-((*R*)-5-Guanidino-1-(4-isopentyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide·hydrochloride (106)**



This compound was prepared according to *General Procedure 5* using **101** (40.5 mg, 0.044 mmol), CH_2Cl_2 (1.43 mL) and TFA (1.43 mL) with a 39.5 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.71 mL) as described gave **106** (24.8 mg, 80%) as an off-white solid. $[\alpha]_D^{25}$ −22.9 (*c* 0.78, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.12 (d, *J* = 9.0 Hz, 1H), 8.05 (d, *J* = 9.0 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.75 (s, 1H), 7.64 (d, *J* = 9.0 Hz, 1H), 7.47 – 7.34 (m, 3H), 7.32 – 7.23 (m, 2H), 7.15 (d, *J* = 8.5 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 1H), 4.56 – 4.40 (m, 2H), 4.32 (d, *J* = 14.7 Hz, 1H), 4.19 – 4.07 (m, 2H), 4.02 – 3.87 (m, 2H), 3.10 – 2.95 (m, 2H), 2.75 – 2.66 (m, 2H), 1.60 – 1.43 (m, 4H), 1.33 – 1.17 (m, 4H), 1.13 (sep, *J* = 6.6 Hz, 1H), 1.01 – 0.87 (m, 7H), 0.57 (d, *J* = 6.6 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 171.1, 158.5, 156.0, 154.0, 147.3, 135.2, 135.0, 131.5, 131.14, 131.05, 130.8, 129.4, 129.2, 127.9, 127.6, 126.5, 126.3, 126.1, 125.4, 125.2, 121.8, 120.9, 117.1, 116.1, 69.34, 69.31, 56.2, 49.9, 41.6, 39.3, 38.7, 29.4, 28.6, 25.8, 25.5, 23.0, 22.8, 22.6, 22.4; IR (cm^{-1}) υ 3365, 2955, 1653, 1507, 1216, 1147, 1047, 807, 745; MS (ES^+) *m/z* 678 (100%, M+H); HRMS (ES^+) Calcd. for $C_{40}H_{52}N_7O_3$: 678.4132, Found: 678.4154.

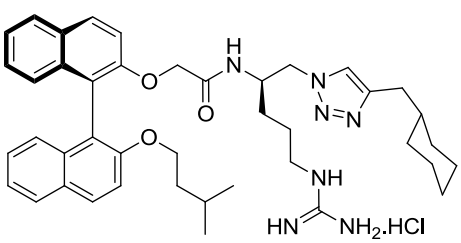
***N*-((*R*)-5-Guanidino-1-(4-cyclohexyl-1*H*-1,2,3-triazol-1-yl)pentan-2-yl)-2-(((*S*)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide·hydrochloride (107)**



This compound was prepared according to *General Procedure 5* using **102** (40.9 mg, 0.043 mmol), CH_2Cl_2 (1.38 mL) and TFA (1.38 mL) with a 14.5 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.69 mL) as described gave **107** (30.7 mg, 97%) as an off-white solid. $[\alpha]_D^{25}$ −34.1 (*c* 0.93, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ

8.13 (d, *J* = 9.0 Hz, 1H), 8.05 (d, *J* = 8.9 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.88 (s, 1H), 7.65 (d, *J* = 9.0 Hz, 1H), 7.46 – 7.35 (m, 3H), 7.33 – 7.24 (m, 2H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 1H), 4.56 (dd, *J* = 13.6, 3.0 Hz, 1H), 4.44 (d, *J* = 14.8 Hz, 1H), 4.31 (d, *J* = 14.8 Hz, 1H), 4.19 – 4.08 (m, 2H), 4.01 – 3.90 (m, 2H), 3.10 – 2.97 (m, 2H), 2.83 – 2.74 (m, 1H), 2.01 – 1.91 (m, 2H), 1.85 – 1.70 (m, 3H), 1.56 – 1.06 (m, 11H), 1.04 – 0.93 (m, 1H), 0.57 (d, *J* = 6.6 Hz, 3H), 0.51 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 171.2, 158.5, 156.0, 154.1, 151.1, 135.2, 135.0, 131.5, 131.2, 131.1, 130.8, 129.4, 129.2, 127.9, 127.7, 126.34, 126.29, 126.1, 125.4, 125.2, 121.8, 120.9, 117.2, 116.2, 69.4, 69.3, 56.9, 50.0, 41.6, 39.3, 34.8, 33.02, 32.99, 29.3, 26.6, 26.5, 25.8, 25.5, 22.9, 22.4; IR (cm^{-1}) υ 3368, 2929, 1653, 1506, 1457, 1214, 1168, 1048, 809, 747; MS (ES^+) *m/z* 690 (100%, M+H).

_N_-((_R_)-5-Guanidino-1-(4-(cyclohexylmethyl)-1_H_-1,2,3-triazol-1-yl)pentan-2-yl)-2-(((_S_)-2'-(isopentyloxy)-[1,1'-binaphthalen]-2-yl)oxy)acetamide·hydrochloride (108)



This compound was prepared according to *General Procedure 5* using **103** (50.3 mg, 0.053 mmol), CH_2Cl_2 (1.67 mL) and TFA (1.67 mL) with a 14.5 h reaction time. Work-up and treatment with HCl (2 M in Et_2O, 0.83 mL) as described gave **108** (31.2 mg, 80%) as an off-white solid. $[\alpha]_D^{25}$ −45.2 (*c* 0.93, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 8.13 (d, *J* = 9.0 Hz, 1H), 8.05 (d, *J* = 8.9 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.73 (s, 1H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.46 – 7.35 (m, 3H), 7.34 – 7.24 (m, 2H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.12 (d, *J* = 8.5 Hz, 1H), 4.58 (d, *J* = 10.9 Hz, 1H), 4.45 (d, *J* = 14.7 Hz, 1H), 4.27 (d, *J* = 14.7 Hz, 1H), 4.19 – 4.09 (m, 2H), 4.02 – 3.94 (m, 1H), 3.93 – 3.84 (m, 1H), 3.11 – 2.98 (m, 2H), 2.66 – 2.54 (m, 2H), 1.73 – 1.45 (m, 7H), 1.33 – 1.06 (m, 8H), 1.04 – 0.83 (m, 3H), 0.57 (d, *J* = 6.5 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 171.1, 158.5, 156.0, 154.0, 144.8, 135.1, 135.0, 131.5, 131.2, 131.1, 130.7, 129.5, 129.2, 128.0, 127.9, 127.7, 126.3, 126.1, 125.4, 125.2, 121.8, 120.9, 117.1, 116.1, 69.4, 69.3, 56.9, 49.9, 41.6, 39.3, 38.8, 33.6, 33.5, 32.0, 29.4, 27.1, 27.0, 25.8, 25.5, 22.9, 22.4; IR (cm^{-1}) υ 3364, 2924, 1654, 1507, 1458, 1215, 1049, 808, 747; MS (ES^+) *m/z* 704 (100%, M+H). HRMS (ES^+) Calcd. for $C_{42}H_{54}N_7O_3$: 704.4288, Found: 704.4315.

Antibacterial Testing Methods

C. difficile

Compounds were tested for their minimum inhibitory concentration (MIC) against three *Clostridium difficile* strains (Table S2). All strains are human isolates.[S9]

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.[S10] 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.

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

The test organisms for all compounds were *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, *Staphylococcus aureus* NCTC 10442, *Enterococcus faecalis* ATCC 29212 and *Streptococcus pneumoniae* ATCC 49619. The test organisms for selected Class B compounds were *Acinetobacter baumannii* ATCC 19606, *Acinetobacter baumannii* ATCC 15308, *Staphylococcus aureus* Mu50 (VISA), *Staphylococcus epidermidis* ATCC 11047, *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.[S10] 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.

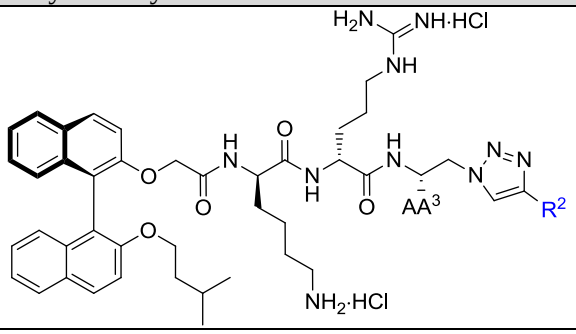
Organism(s)	Growth medium	Incubation conditions
E. coli , S. aureus, E. faecalis, A. baumannii, S. epidermidis	Mueller Hinton broth	24 h at 35 °C in ambient air
S. pneumoniae	Mueller Hinton broth supplemented with 2.5% lysed horse blood	24 h at 35 °C with 5% CO_2

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 was included in tests with Gram positive organisms as a positive control. Concentrations of ≤5% DMSO were not inhibitory to growth. MICs for vancomycin were within acceptable QC ranges.

Hemolysis Data

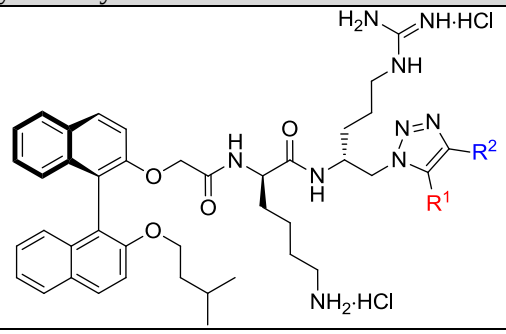
The hemolytic activity of each compound was assessed by the lysis of sheep erythrocytes. Briefly, 500 μL volumes of each compound in phosphate buffered saline (PBS) was combined with 480 μL PBS and 20 μL washed sheep erythrocytes (100%) in microcentrifuge tubes. The final concentration of erythrocytes 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 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. Hemolysis data for triazole classes A−C are shown in Tables S3−S5, respectively.

Table S3. Hemolysis assay for Class A triazoles.



entry	compound	AA^3	R^2	% hemolysis (control = 100%) 5 µg ml^{-1} mean	SD	50 µg ml^{-1} mean	SD
1	**11**	Leu	CH_2OMe	1.1	0.3	52.8	0.3
2	**12**	Leu	propyl	1.8	0.2	81.7	15.5
3	**13**	Leu	*i*-pentyl	1.5	0.2	84.7	18.1
4	**17**	D-Arg·HCl	*i*-pentyl	1.5	0.0	38.1	3.3

Table S4. Hemolysis assay for Class B triazoles.



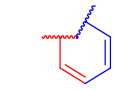
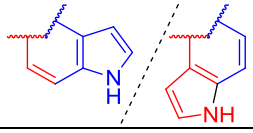
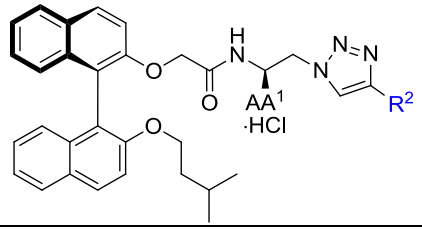
entry	compound	R^1	R^2	% hemolysis (control = 100%) 5 µg ml^{-1} mean	SD	50 µg ml^{-1} mean	SD
1	**69**	H	H	0.1	1.3	5.6	2.5
2	**44**	H	Propyl	0.0	0.0	44.2	2.1
3	**45**	H	*i*-Pentyl	1.3	1.6	93.7	11.7
4	**46**	*i*-Pentyl	H	2.7	0.0	73.7	0.2
5	**47**	H	*n*-Hexyl	1.6	0.1	86.2	0.7
6	**48**	H	Cy	1.3	0.2	90.1	13.1
7	**49**	H	CH_2Cy	1.8	0.0	82.7	0.2
8	**50**	CH_2Cy	H	2.5	0.6	90.0	9.9
9	**51**	H	*t*-Bu	1.1	0.1	59.9	0.4
10	**52**	H	$SiMe_3$	1.2	1.6	89.5	13.0
11	**53**	H	$SiMe_2Ph$	1.1	0.6	97.9	14.3
12	**54**	H	Ph	0.4	1.3	81.5	16.7
13	**55**	Ph	H	2.1	0.0	63.2	0.0
14	**56**	H	4-(*n*-Bu)-Ph	1.5	0.0	73.6	0.2
15	**57**	H	4-OMe-Ph	1.9	0.9	83.0	6.6
16	**58**	H	Bn	2.8	0.0	77.2	0.3
17	**59**	H	CH_2CH_2Ph	0.9	1.3	90.0	22.5
18	**60**	H	CH_2OH	0.8	0.3	4.4	1.6
19	**77**	H	CH_2OMe	0.8	0.3	7.0	1.9
20	**78**	H	CH_2O(*i*-Pr)	0.9	0.7	37.7	2.8
21	**79**	H	CH_2O(*i*-Bu)	1.5	0.1	69.6	6.7
22	**80**	H	CH_2O(*i*-Pent)	1.4	0.8	76.0	0.8
23	**81**	H	CH_2O(*i*-Hex)	2.2	0.6	82.4	15.3
24	**82**	H	CH_2O(*i*-Hept)	1.6	0.1	76.0	9.8
25	**83**	H	CH_2OPh	1.8	0.4	59.1	1.8
26	**61**	H	CH_2OBn	1.3	1.1	92.5	13.0
27	**62**	H	OEt	1.0	0.4	36.4	12.6
28	**87**	H	CO(Morph)	0.9	0.4	47.3	5.4
29	**88**	H	CONH(*i*-Bu)	1.6	0.5	91.1	5.9
30	**63**	H	$(CH_2)_2NH_2$·HCl	0.8	0.0	5.6	0.1
31	**64**	Ph	Ph	2.1	0.0	85.4	0.1
32	**65**	I	Ph	0.9	0.2	92.2	12.3
33	**66**			1.1	0.7	54.1	4.3
34	**67**			1.3	0.1	47.3	6.1

Table S5. Hemolysis assay for Class C triazoles.



entry	compound	AA^1	R^2	% hemolysis (control = 100%) 5 µg ml^{-1} mean	SD	50 µg ml^{-1} mean	SD
1	**95**	Lys	Ph	0.0	0.0	87.9	0.4
2	**96**	Lys	Bn	0.4	0.1	90.5	0.3
3	**97**	Lys	*i*-Pentyl	0.0	0.0	89.8	0.1
4	**104**	Arg	Ph	1.9	0.2	86.3	17.4
5	**105**	Arg	Bn	1.2	0.2	85.9	20.3
6	**106**	Arg	*i*-Pentyl	1.1	0.5	87.0	20.8
7	**107**	Arg	Cy	1.2	0.0	97.6	17.3
8	**108**	Arg	CH_2Cy	1.0	0.3	90.4	8.3

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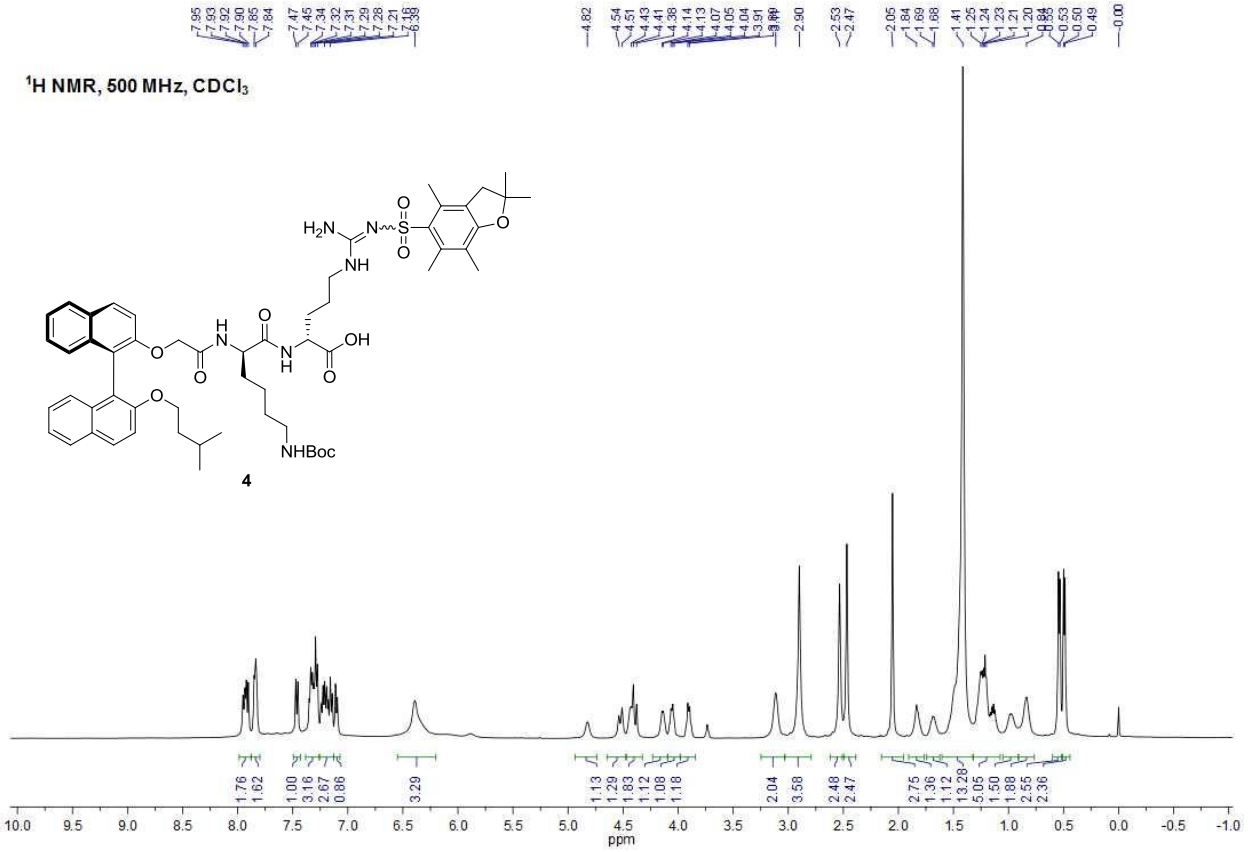
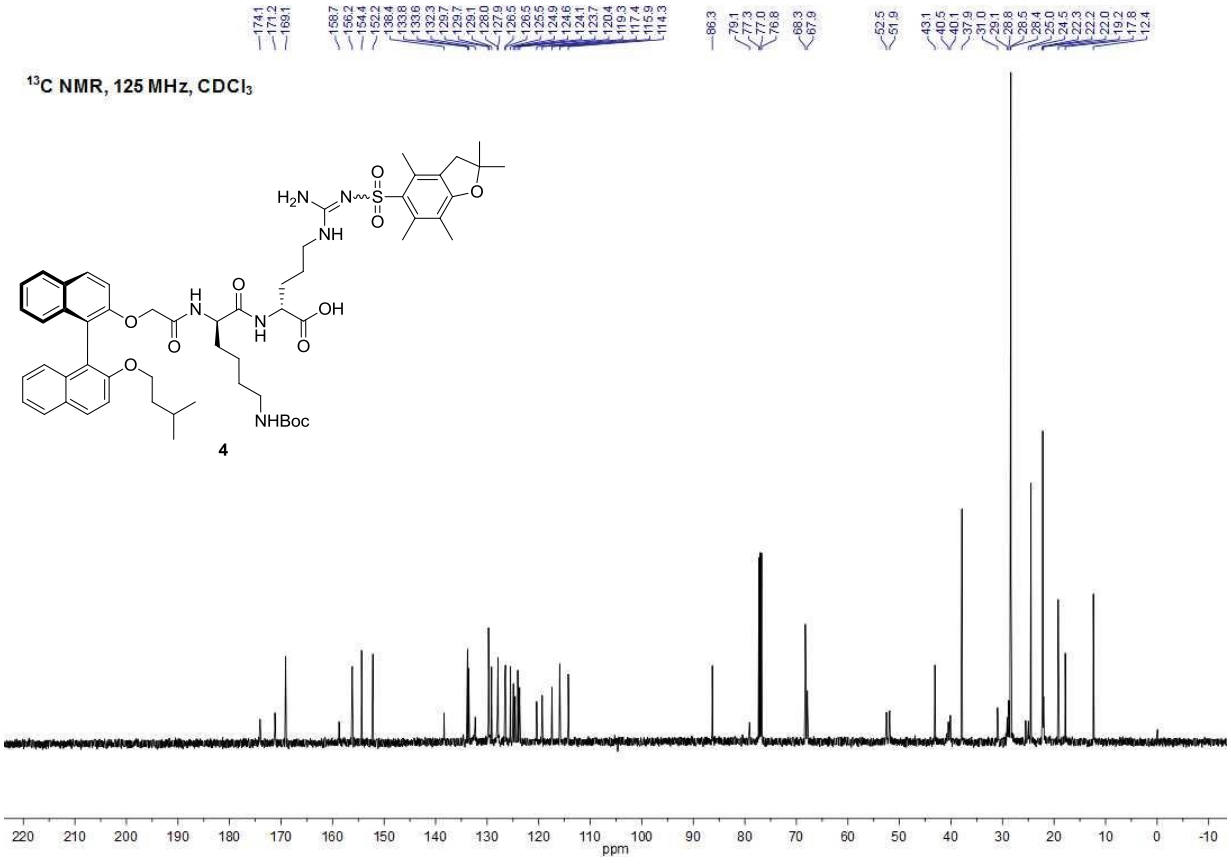
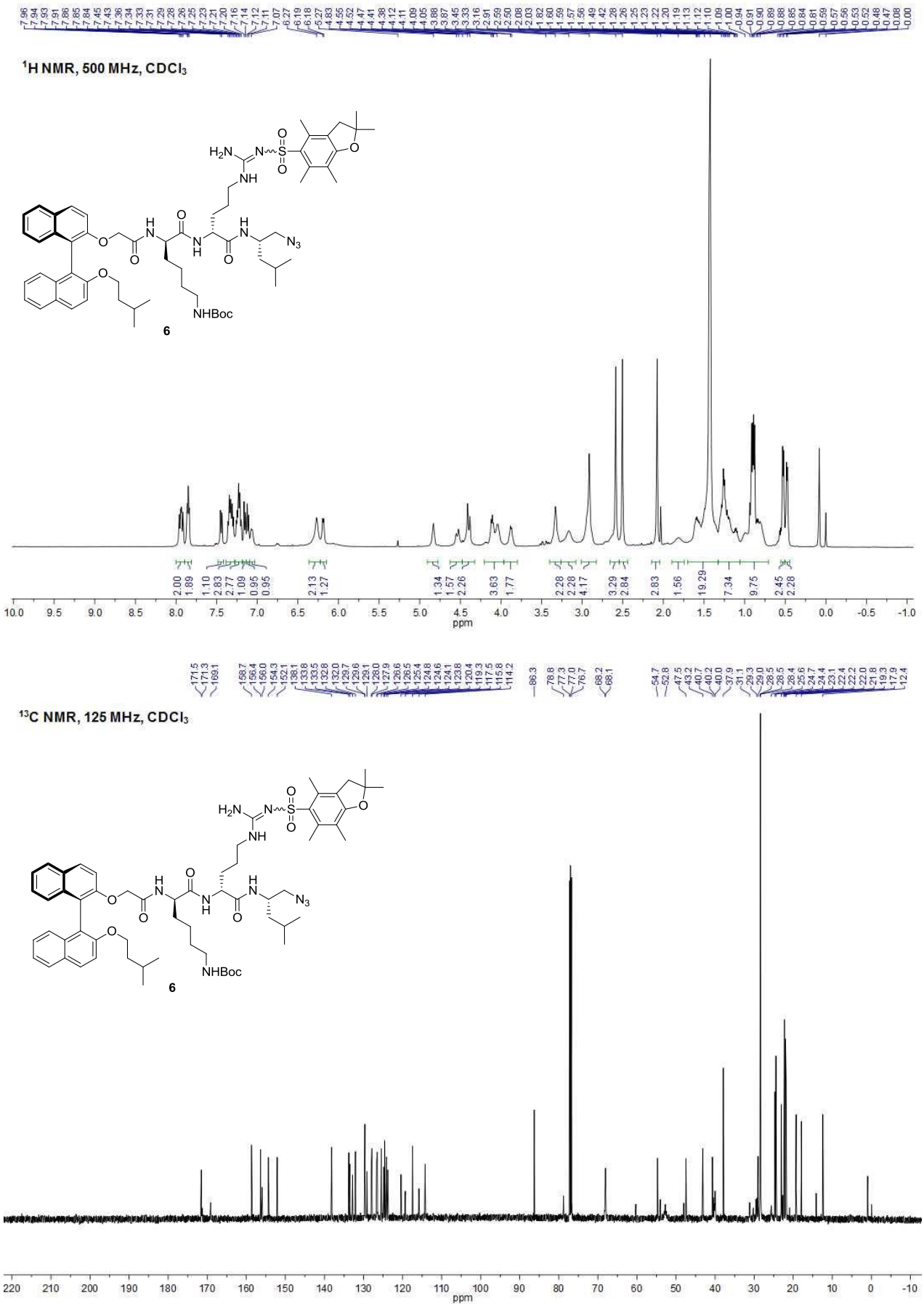
NMR Spectra of Key Intermediates and Final Compounds



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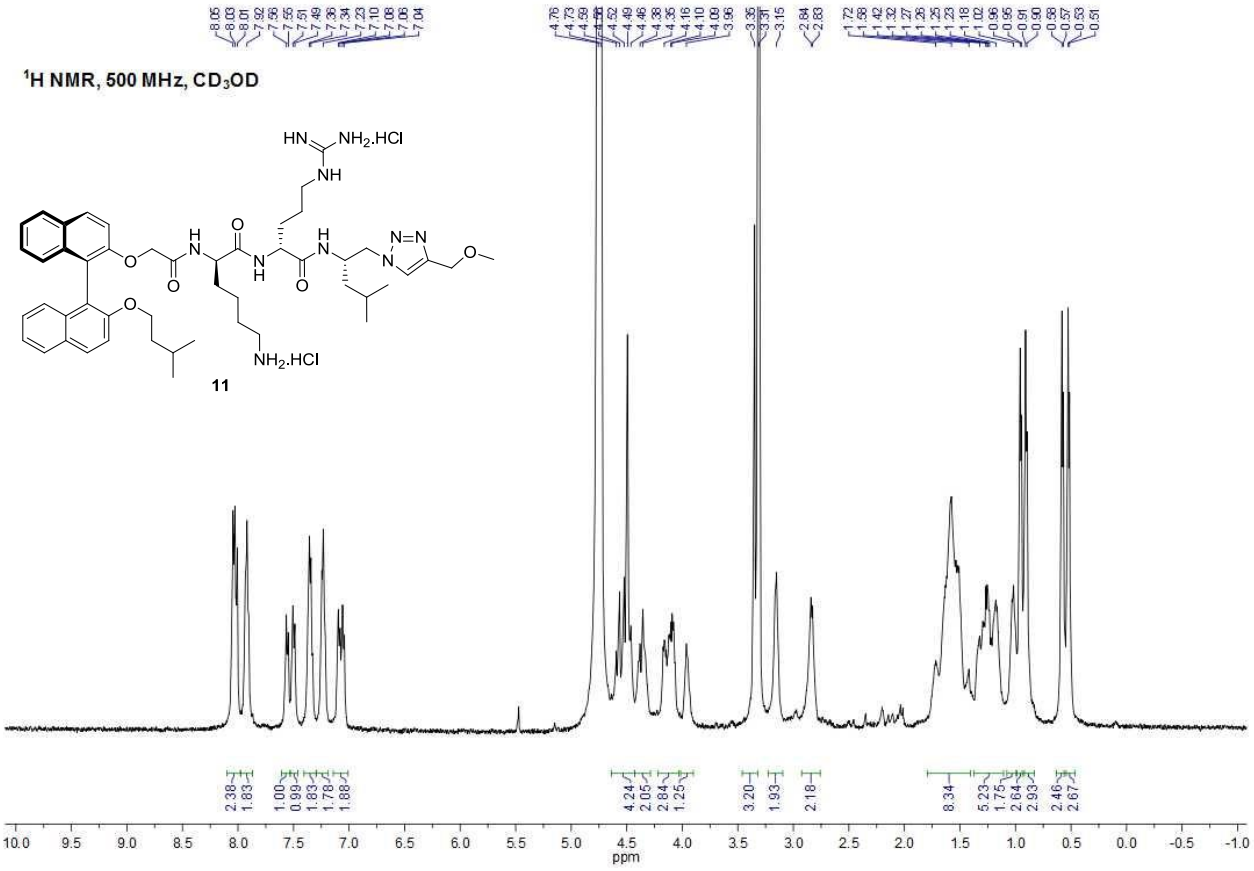
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11
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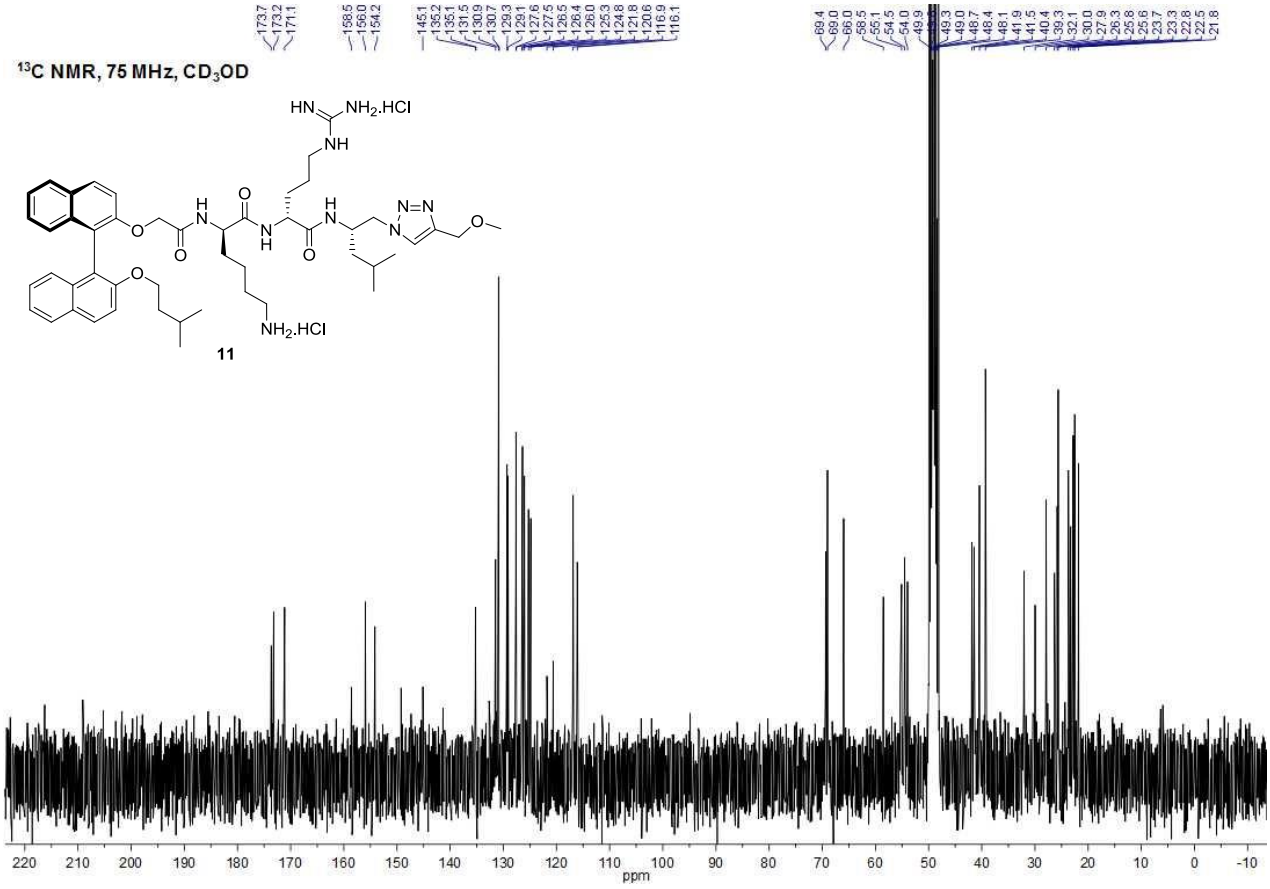
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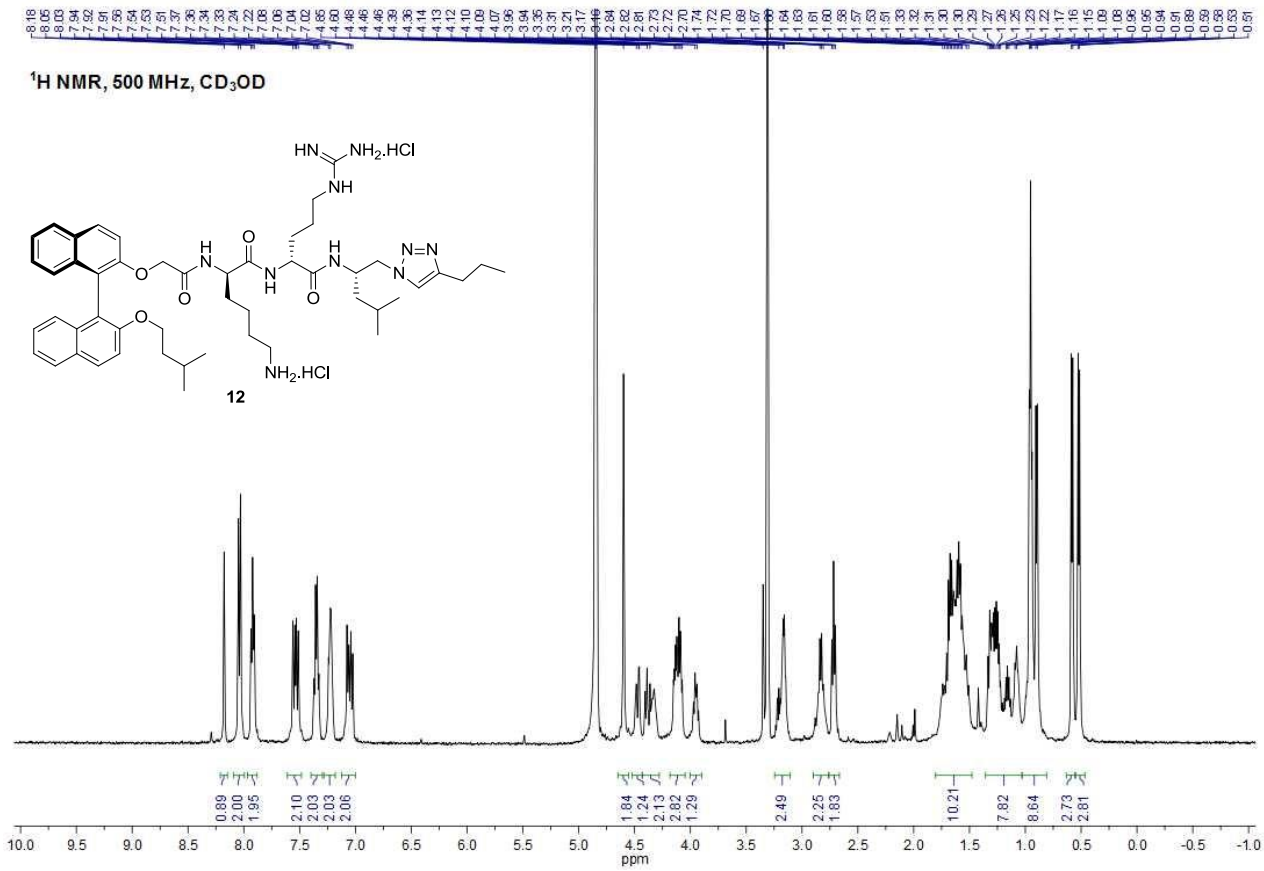
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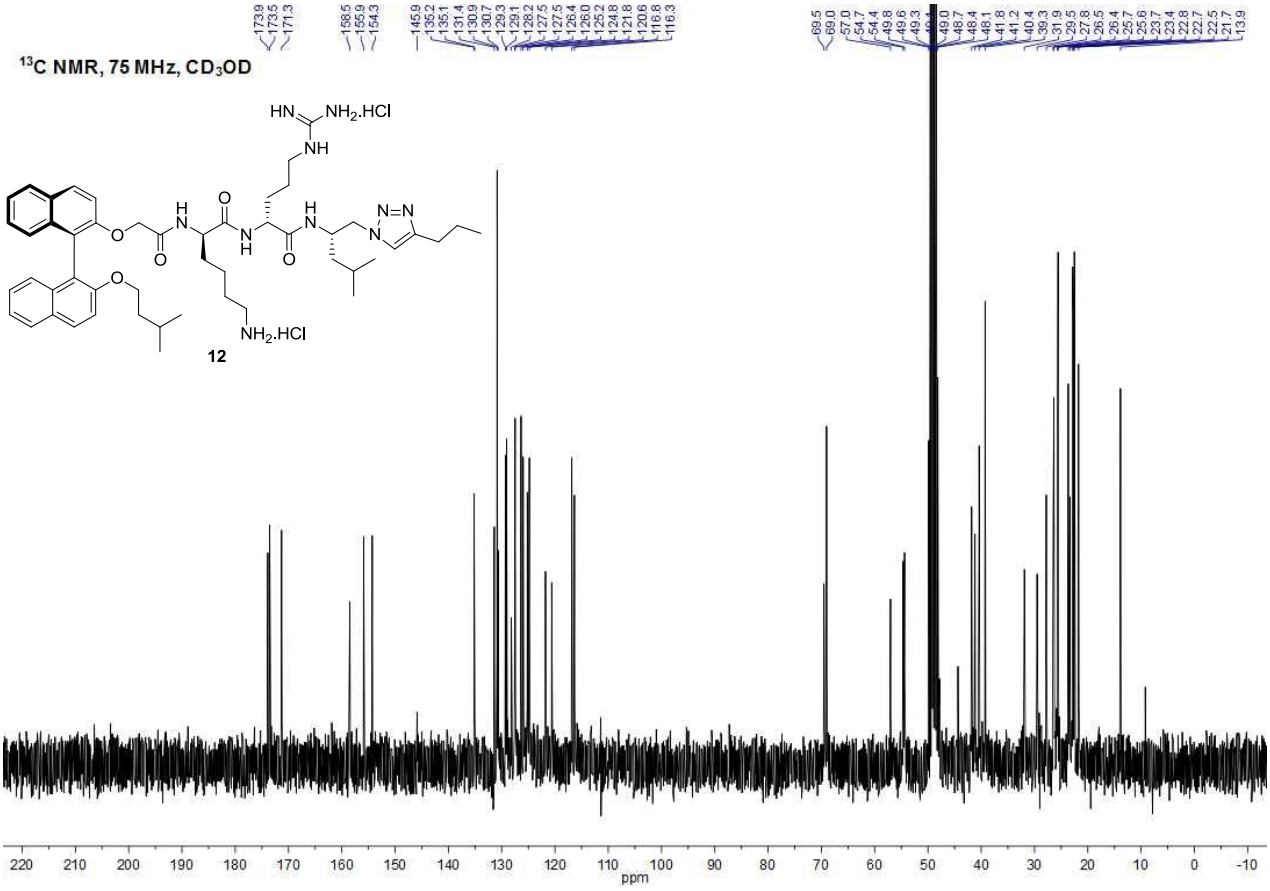
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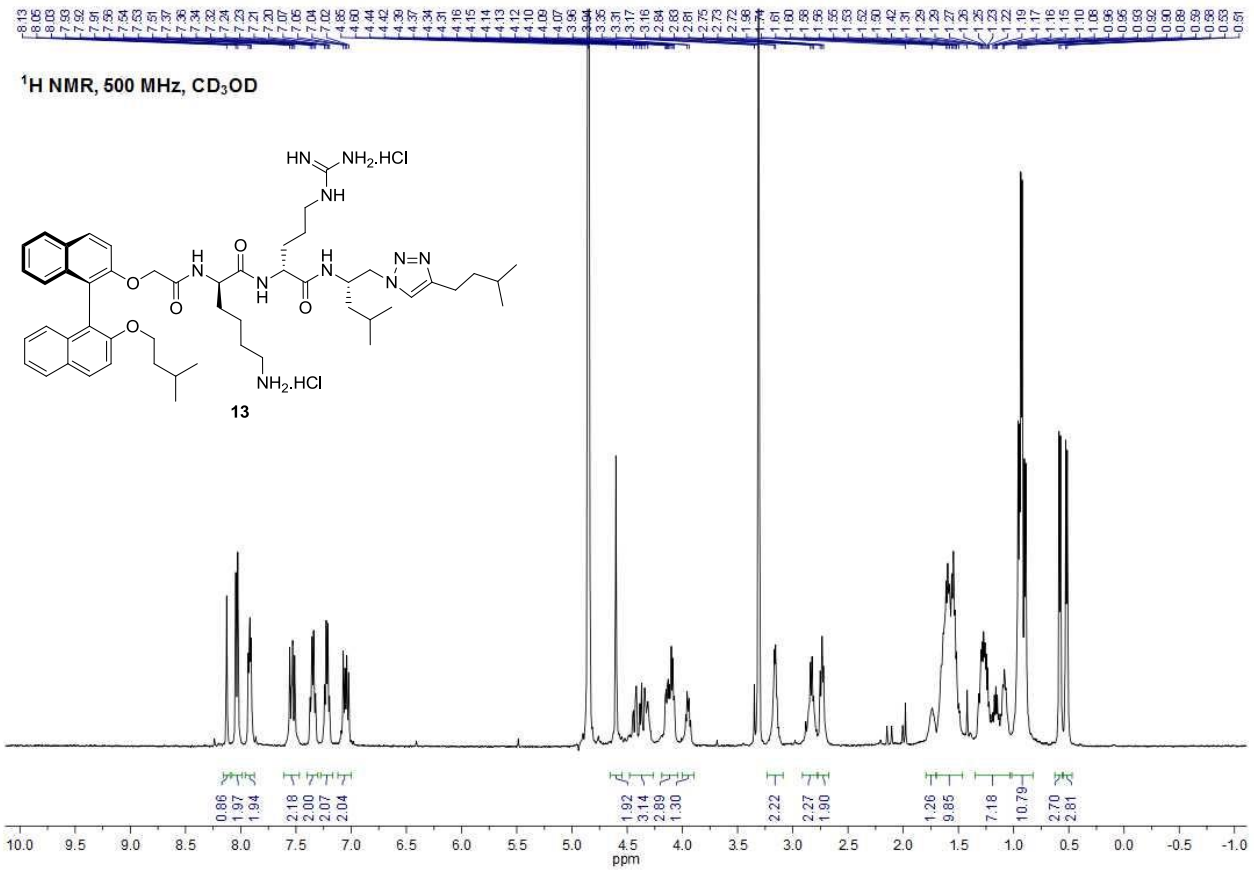
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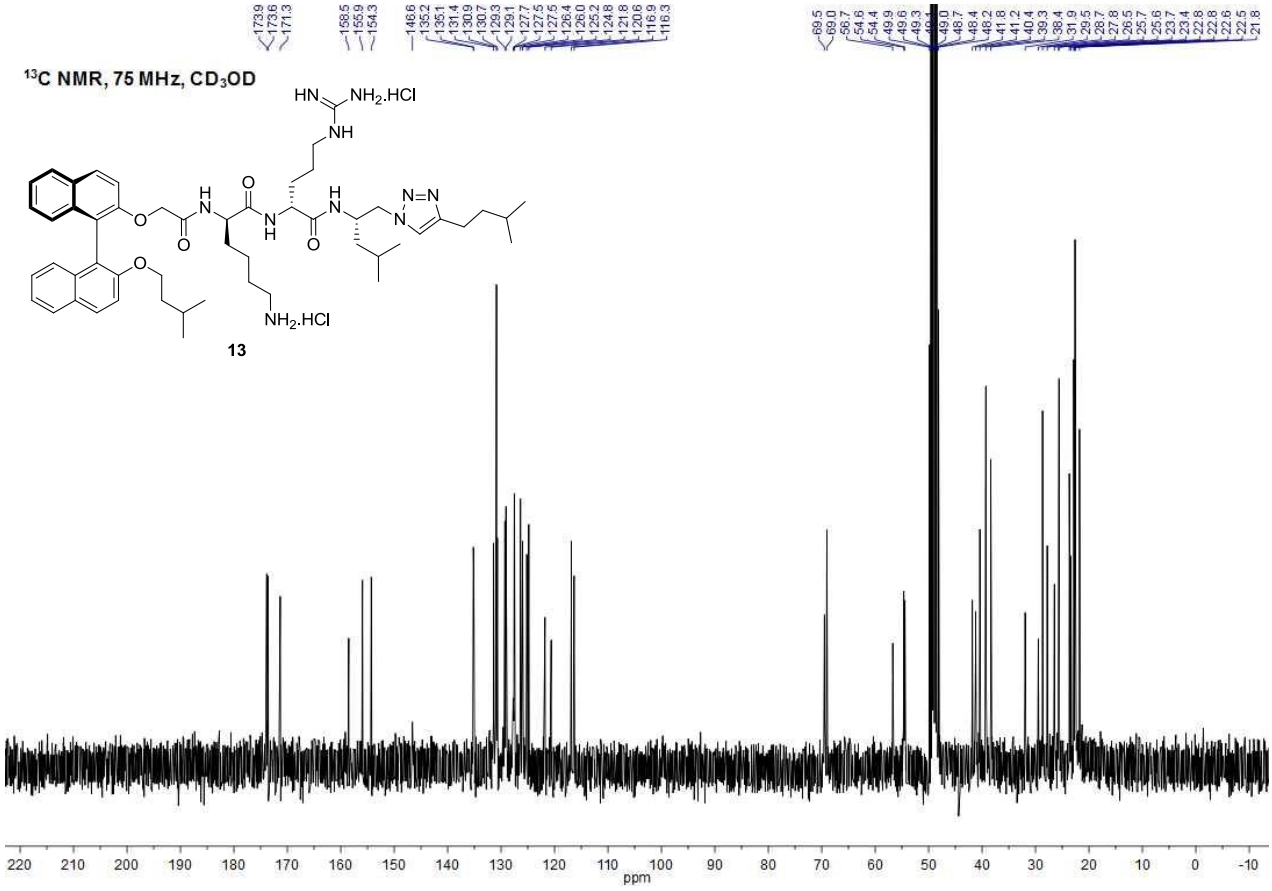
ppm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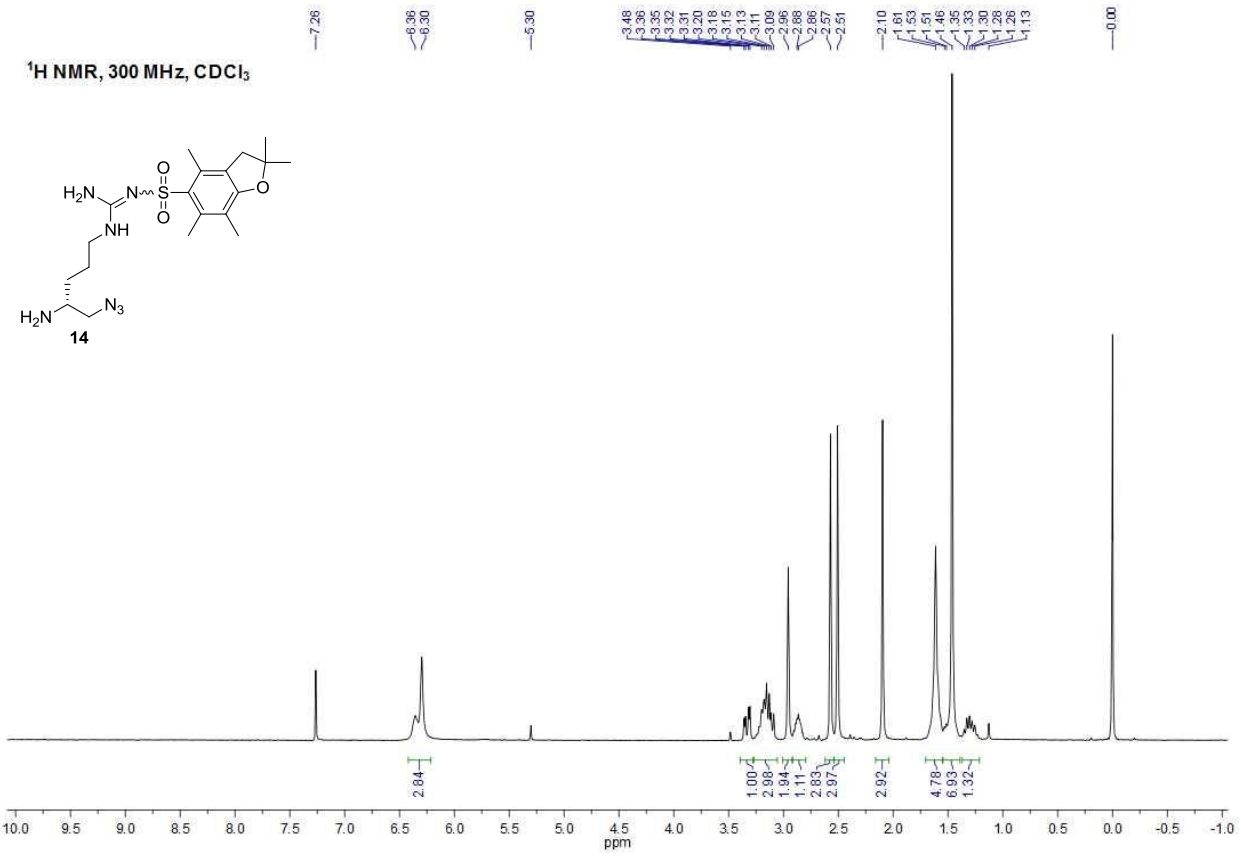
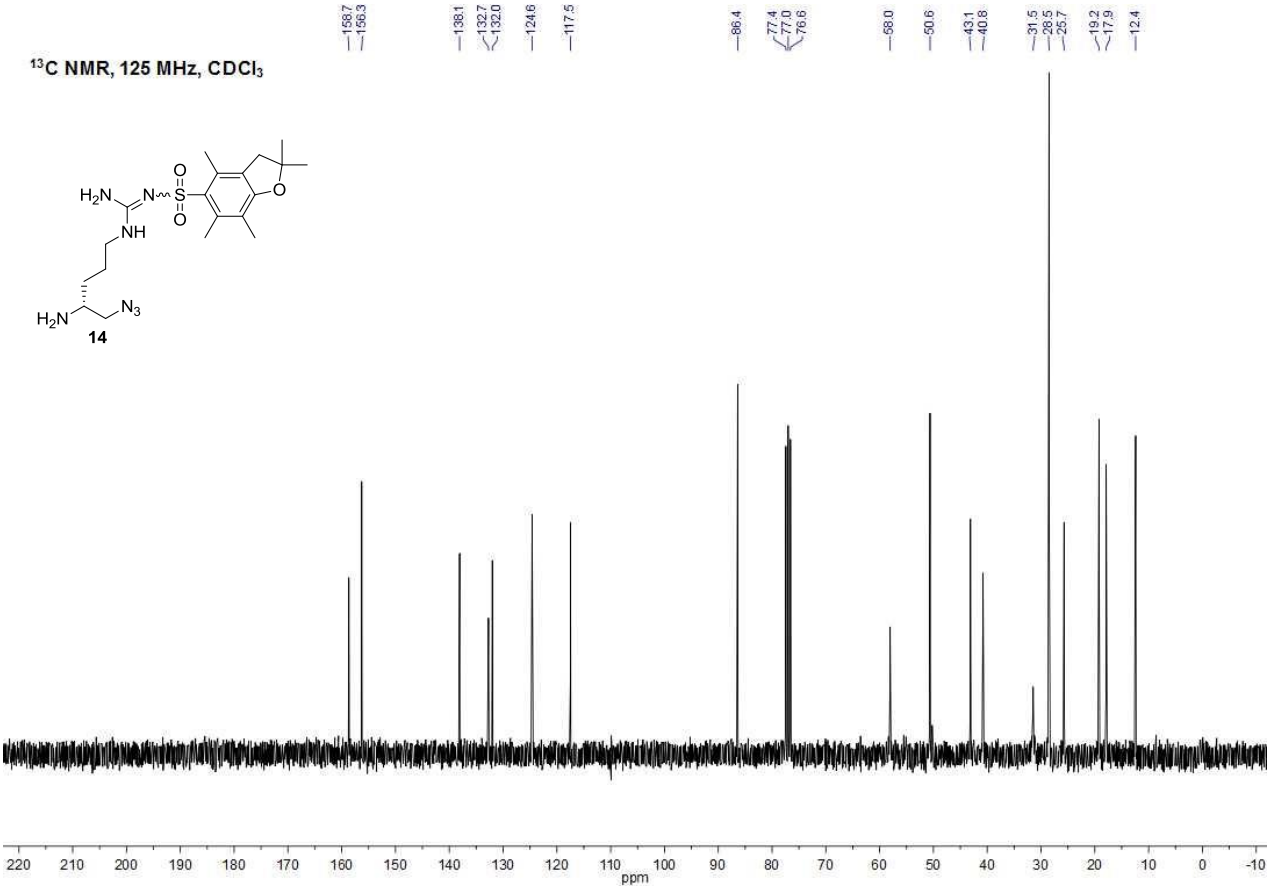
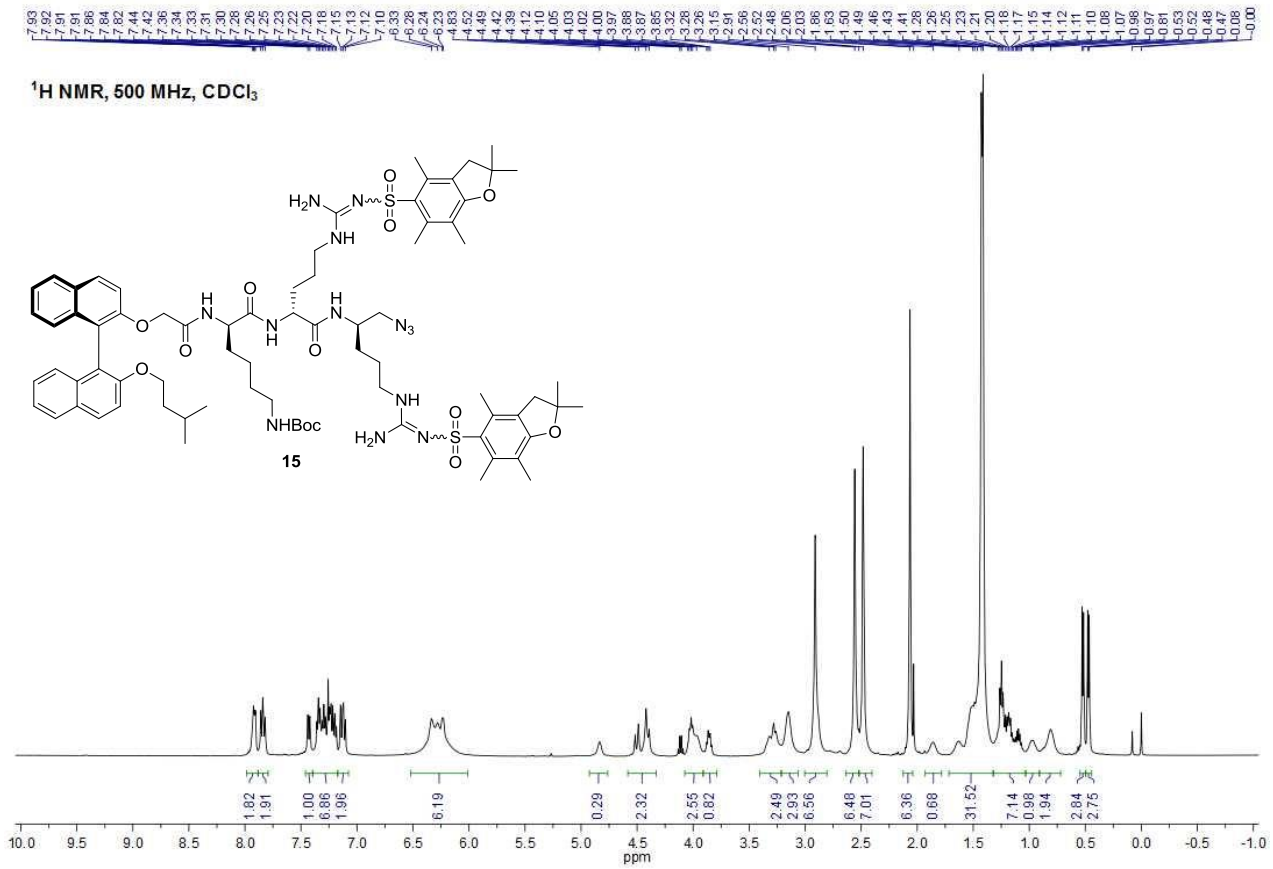
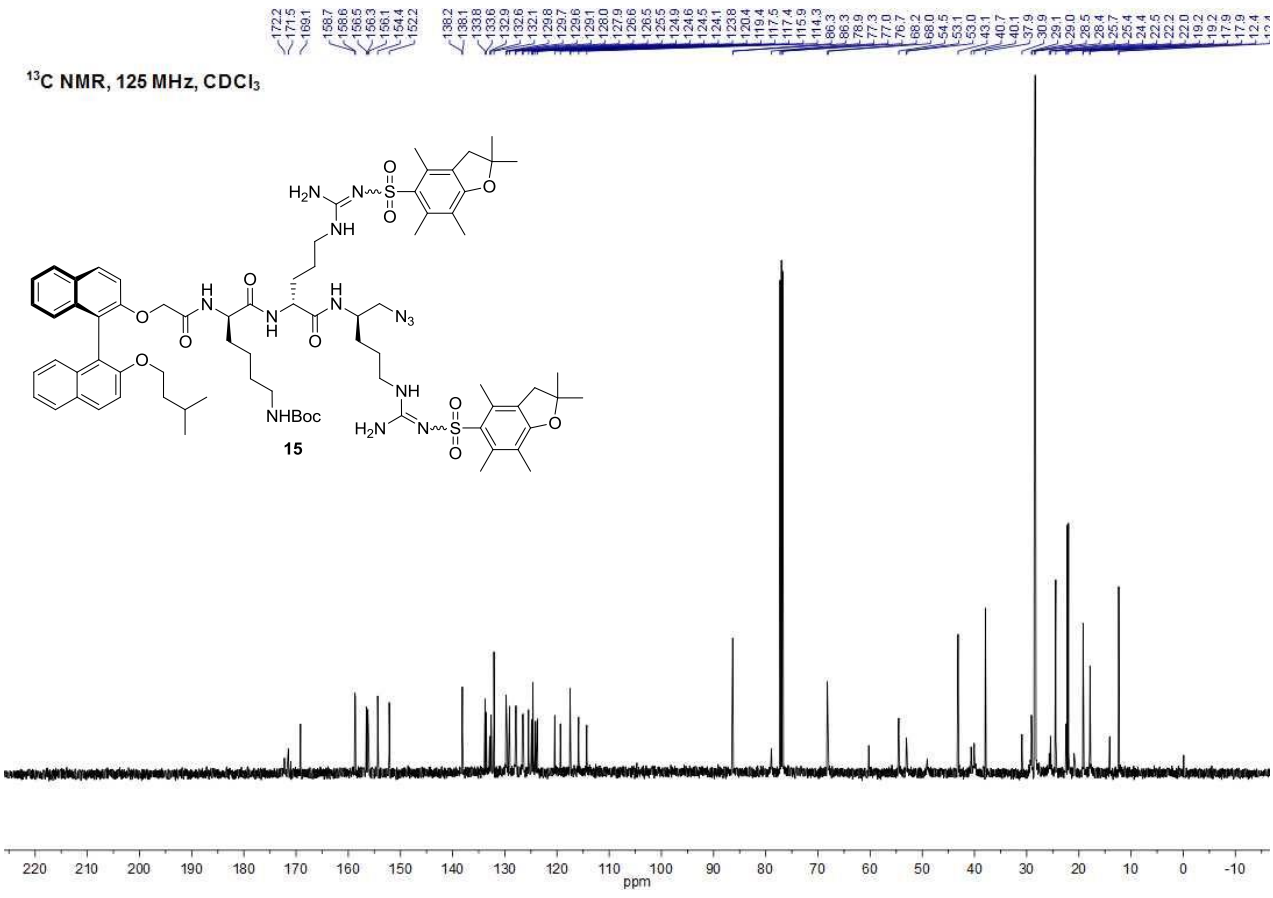
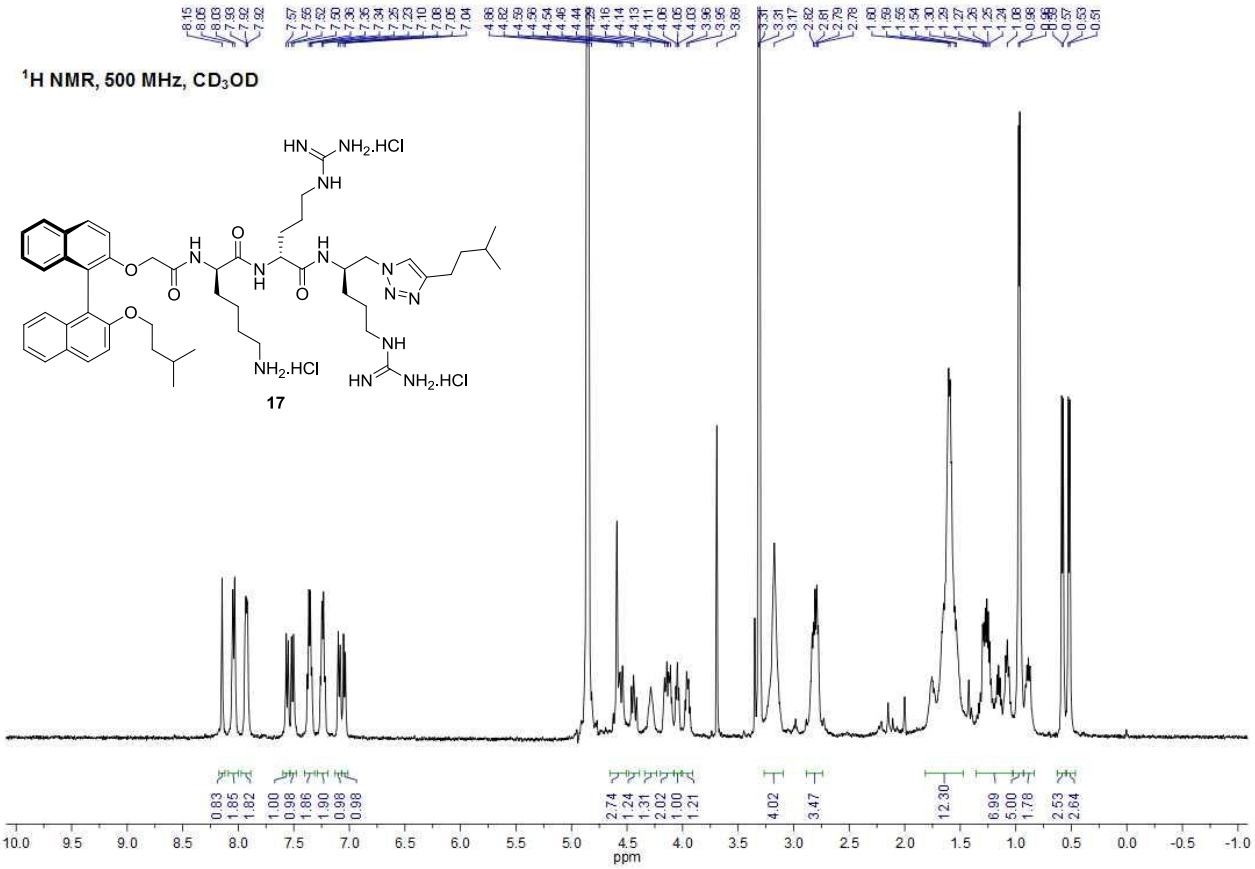
H
N
O
N=N
N
NH$_2$.HCl
13
ppm

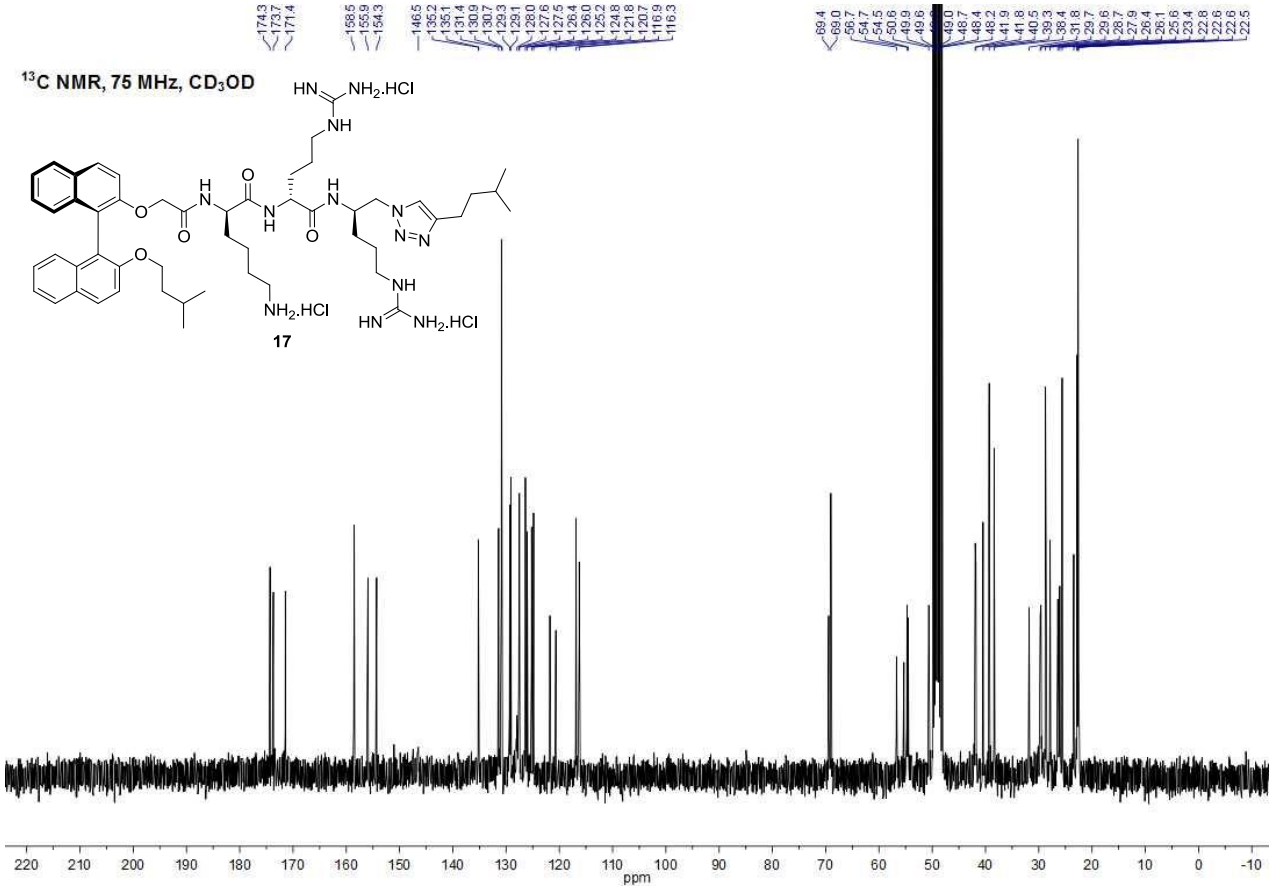

^{1}H NMR, 300 MHz, CDCl$_3$
14

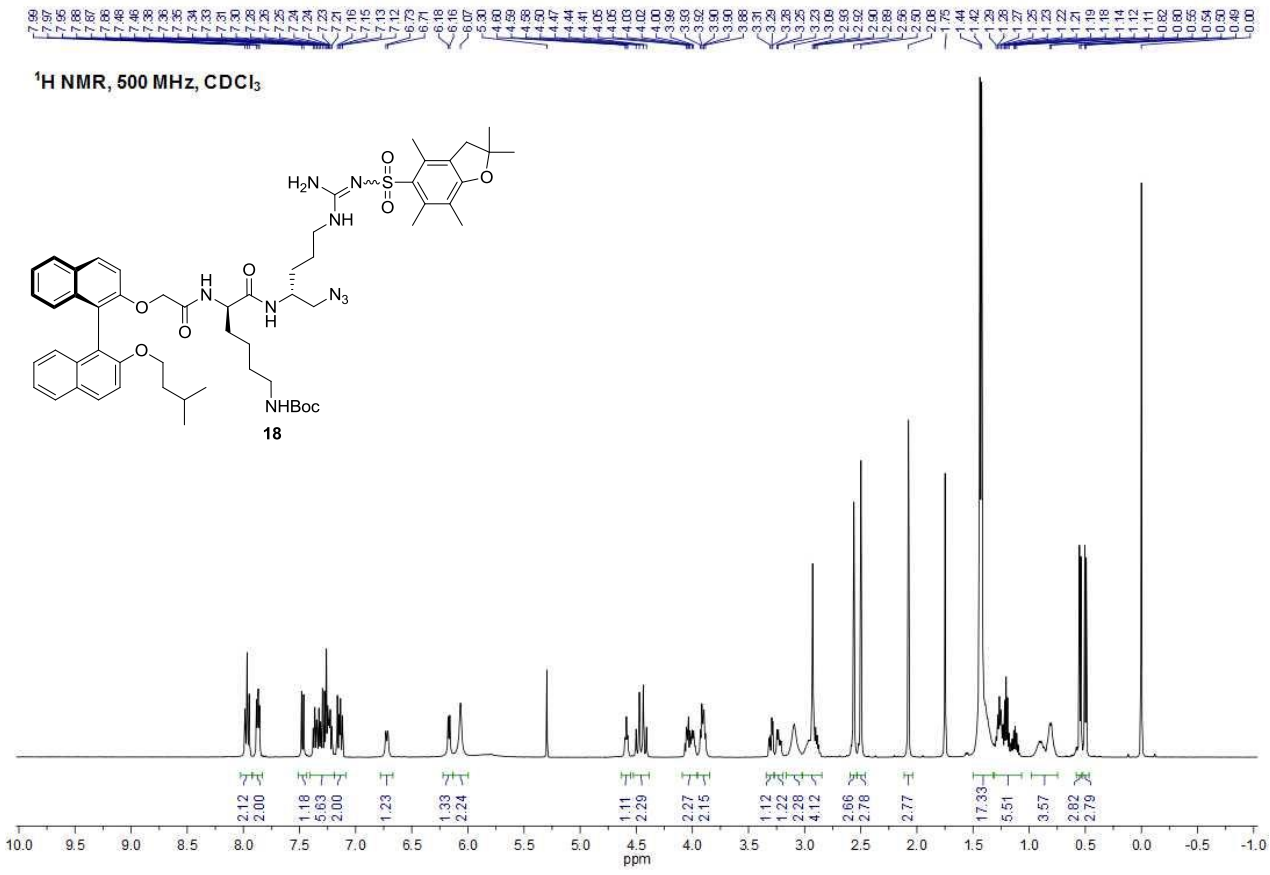

^{13}C NMR, 125 MHz, CDCl$_3$
14

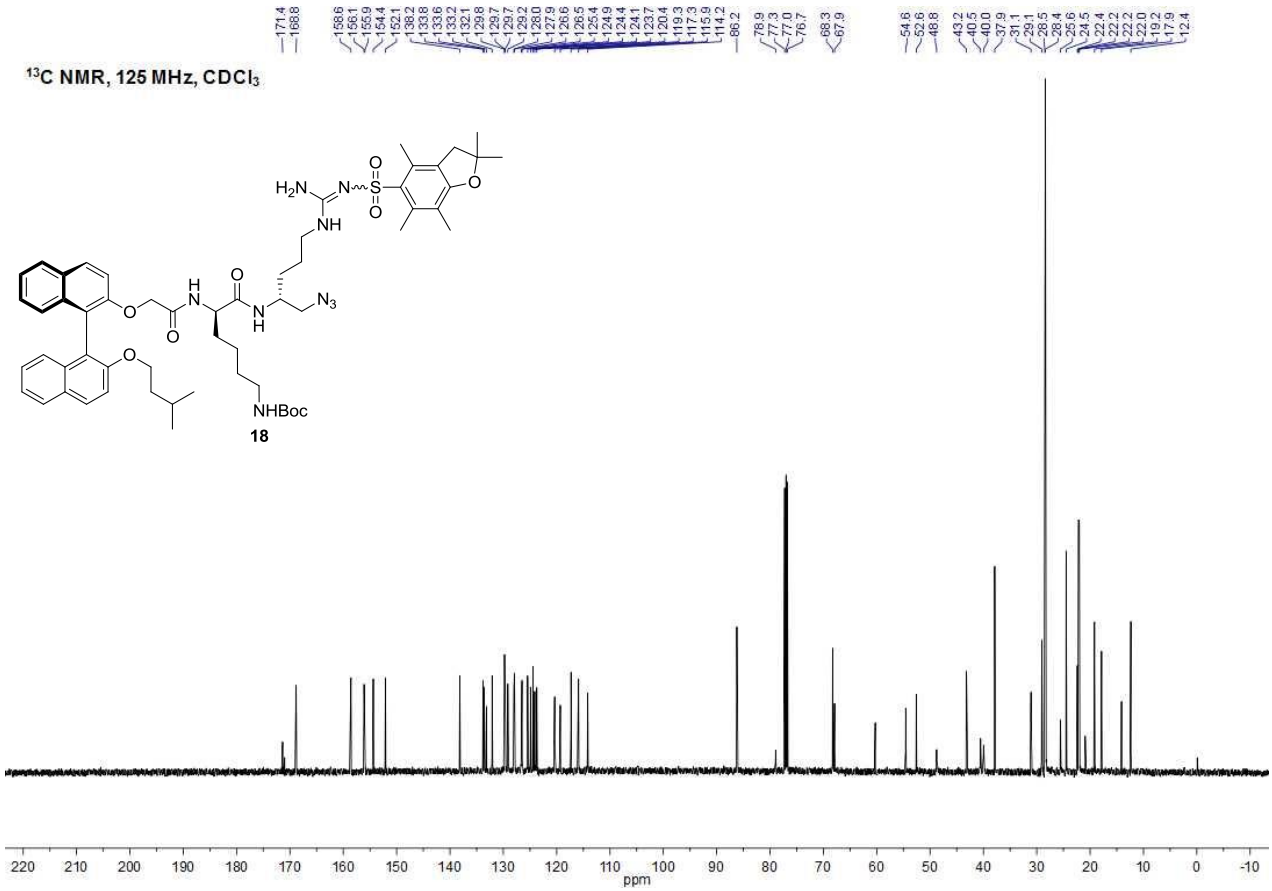

1H NMR, 500 MHz, CDCl3
15
ppm

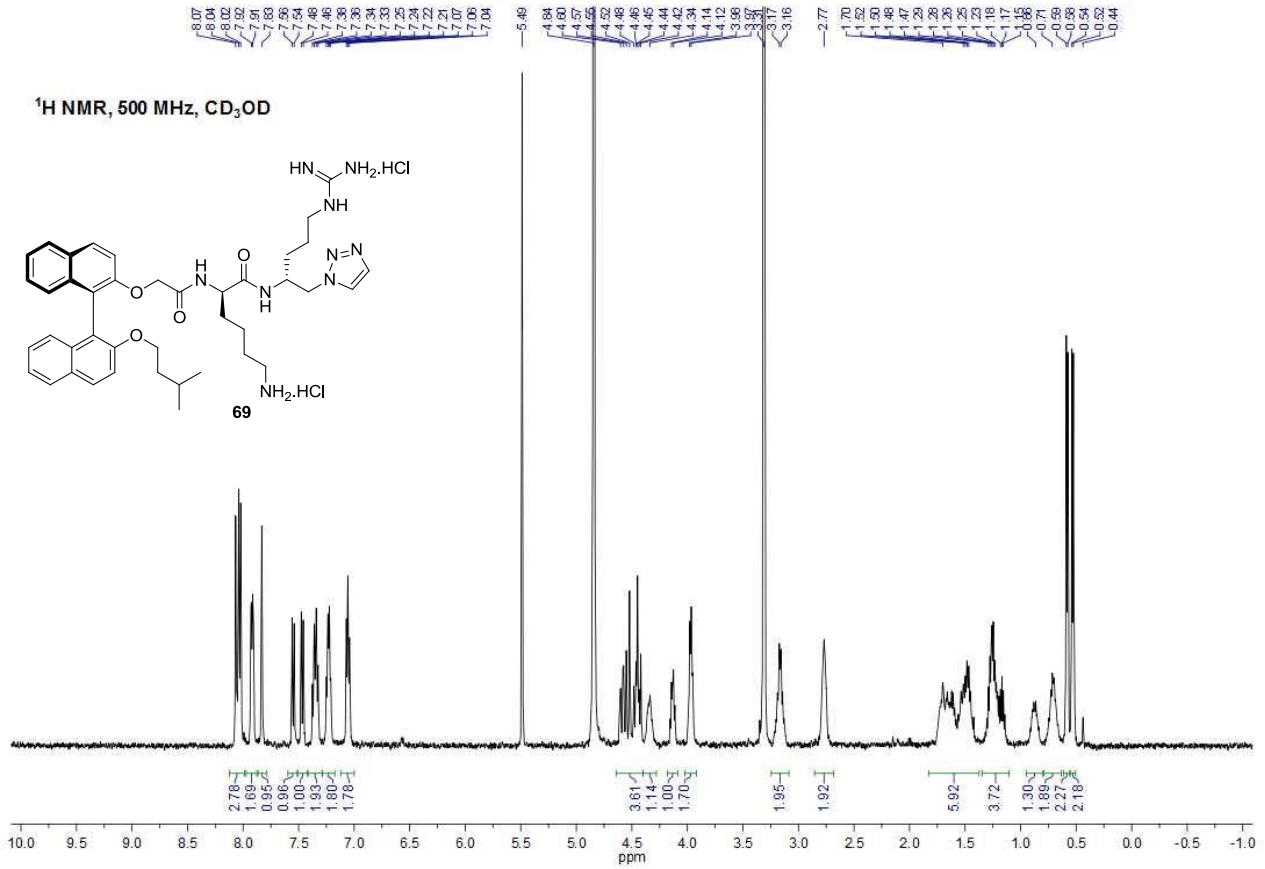

13C NMR, 125 MHz, CDCl3
15
ppm

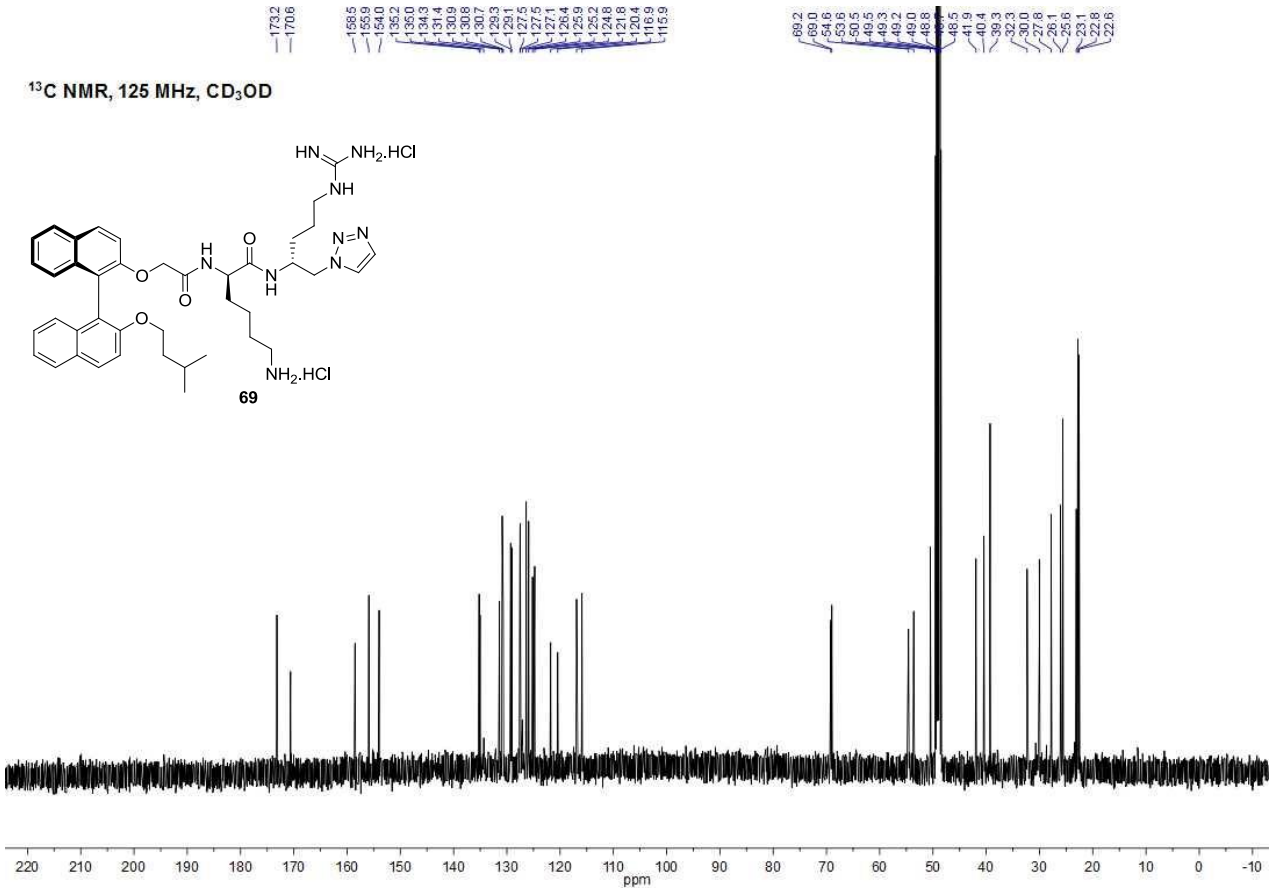

^{1}H NMR, 500 MHz, CD_3OD
17

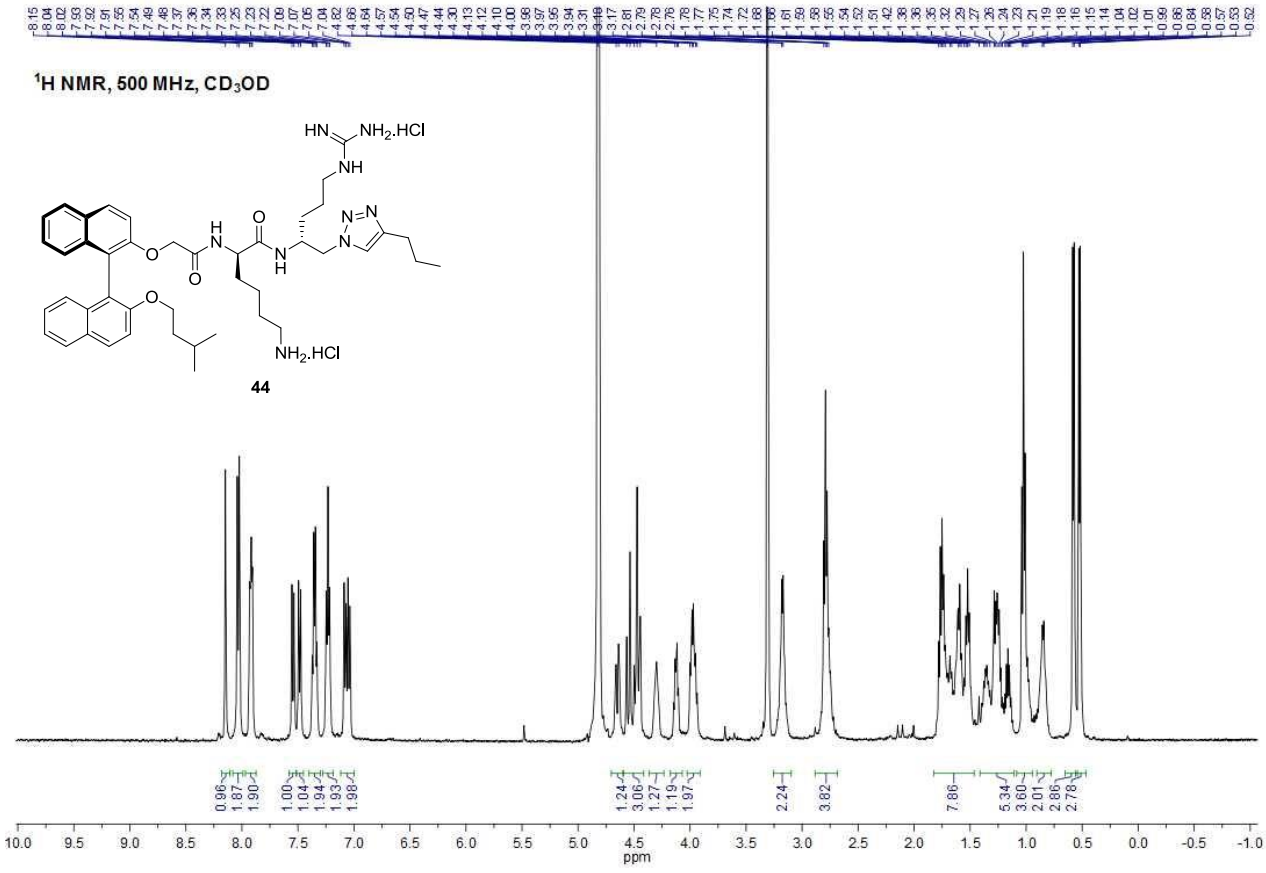

^{13}C NMR, 75 MHz, CD_3OD
17

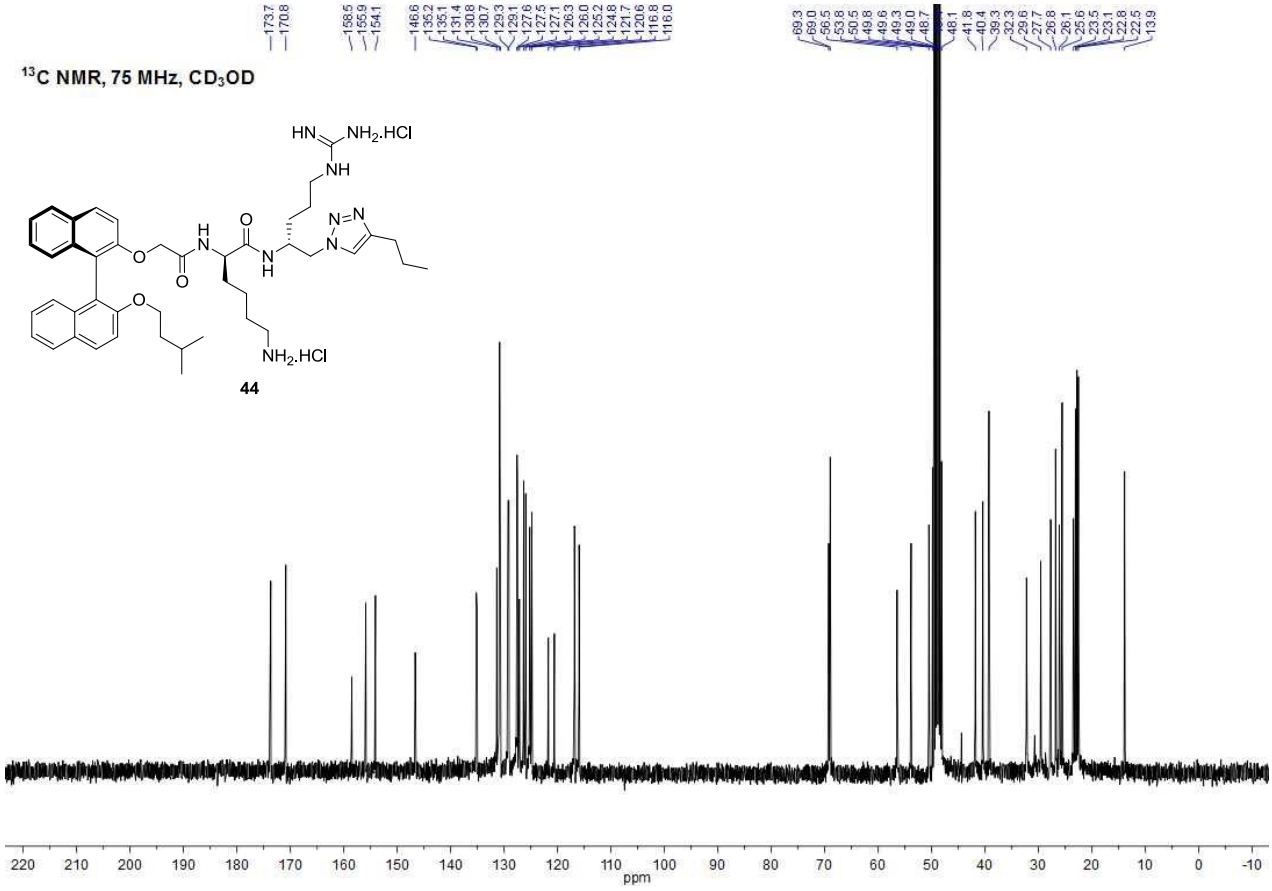

^{1}H NMR, 500 MHz, CDCl$_3$
18
ppm

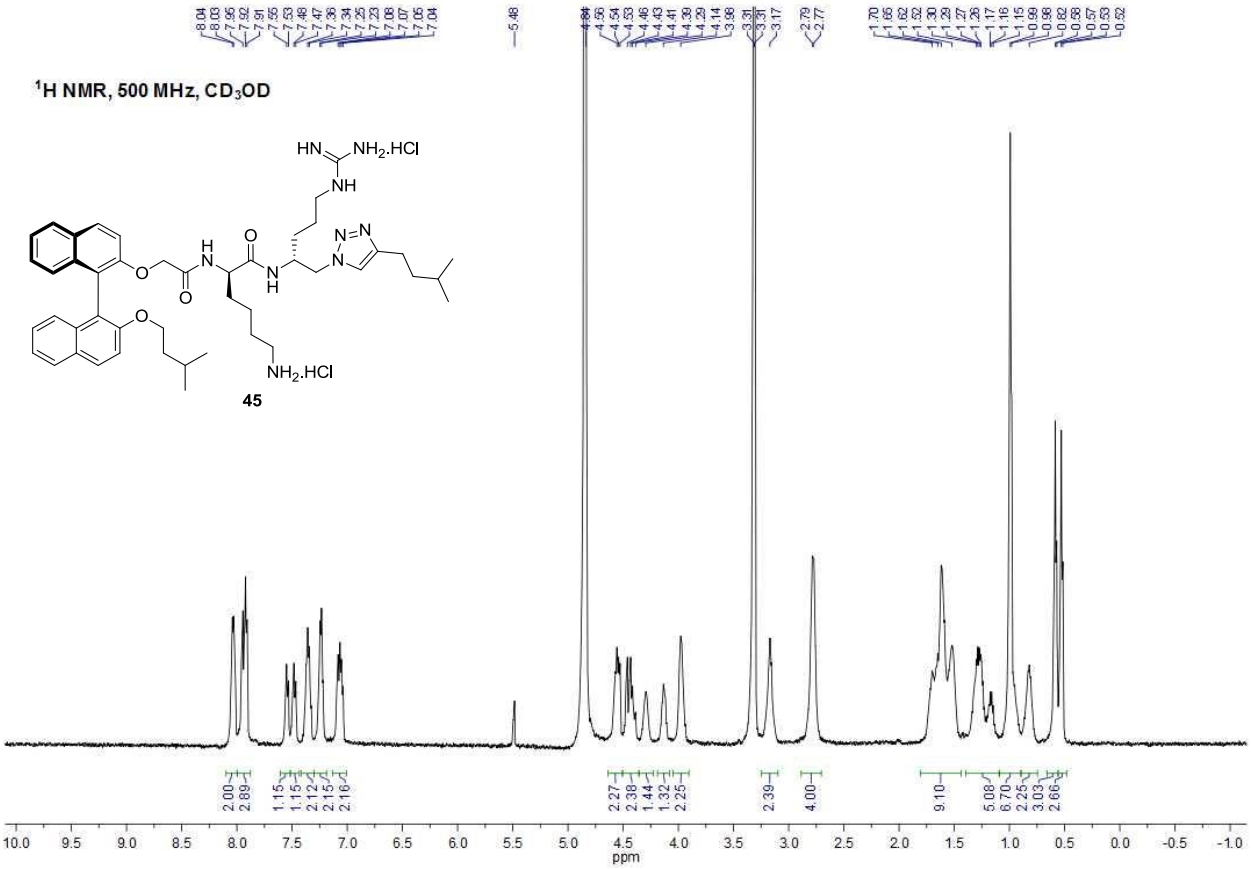

^{13}C NMR, 125 MHz, CDCl$_3$
18
ppm

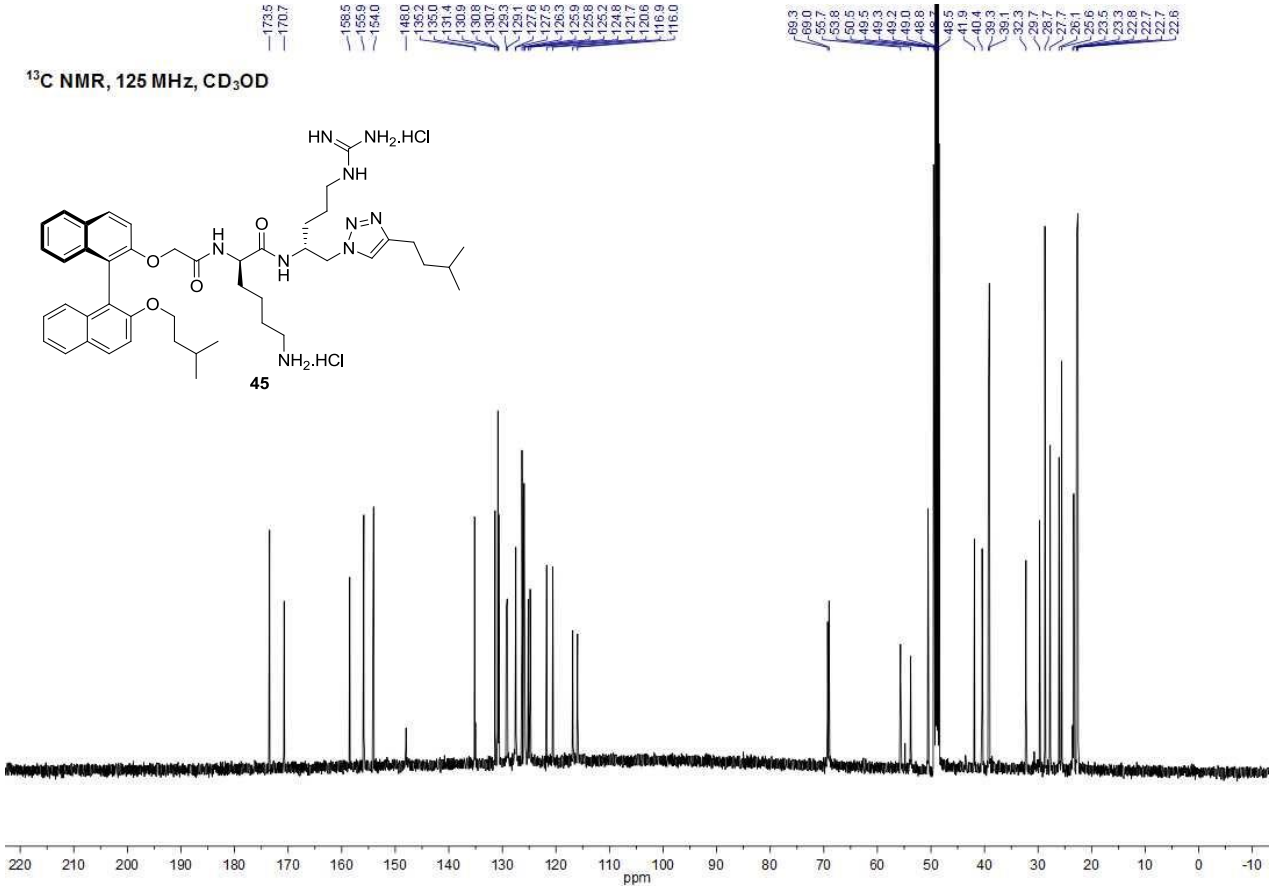

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
N
H
O
O
N
H
O
O
NH$_2$.HCl
69

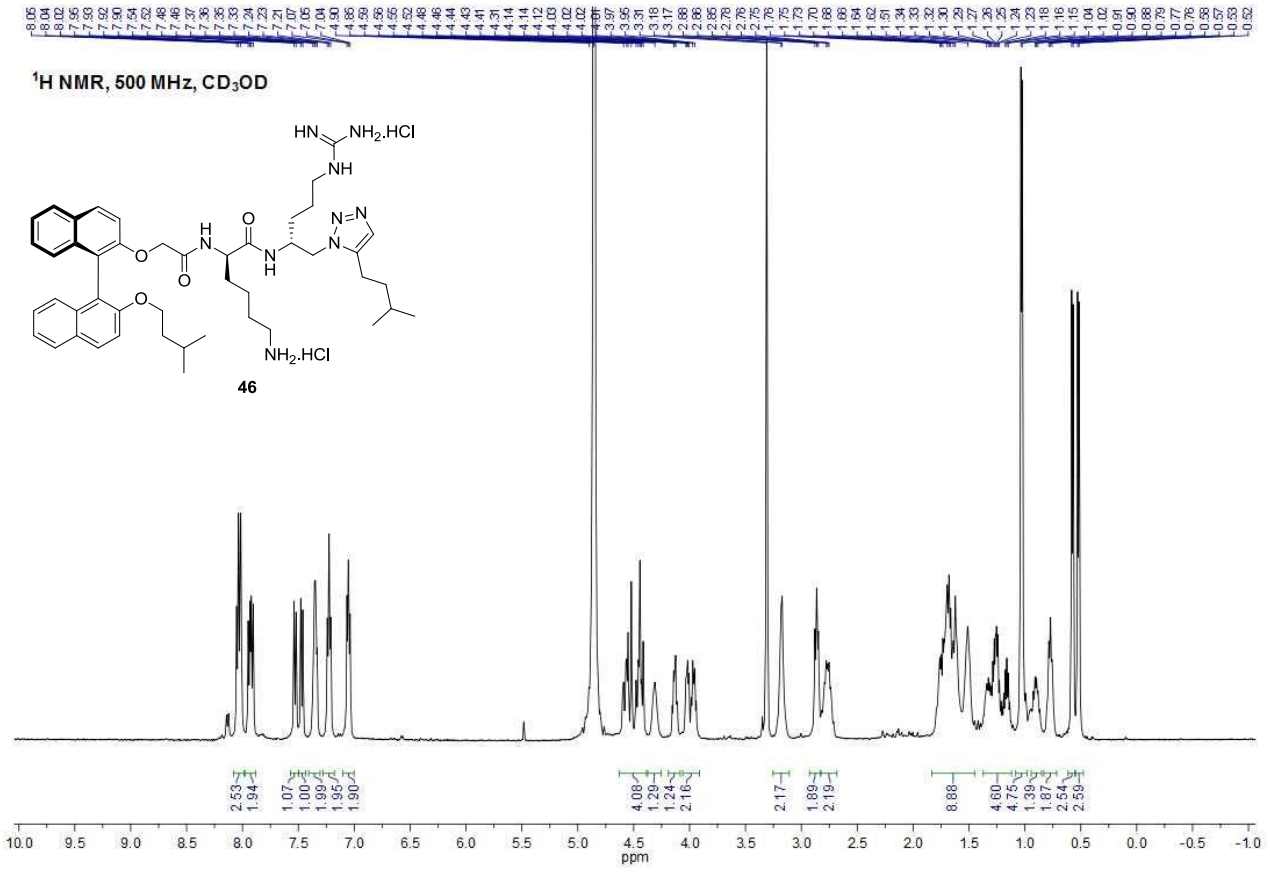

^{13}C NMR, 125 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
N
H
O
O
N
H
O
O
NH$_2$.HCl
69

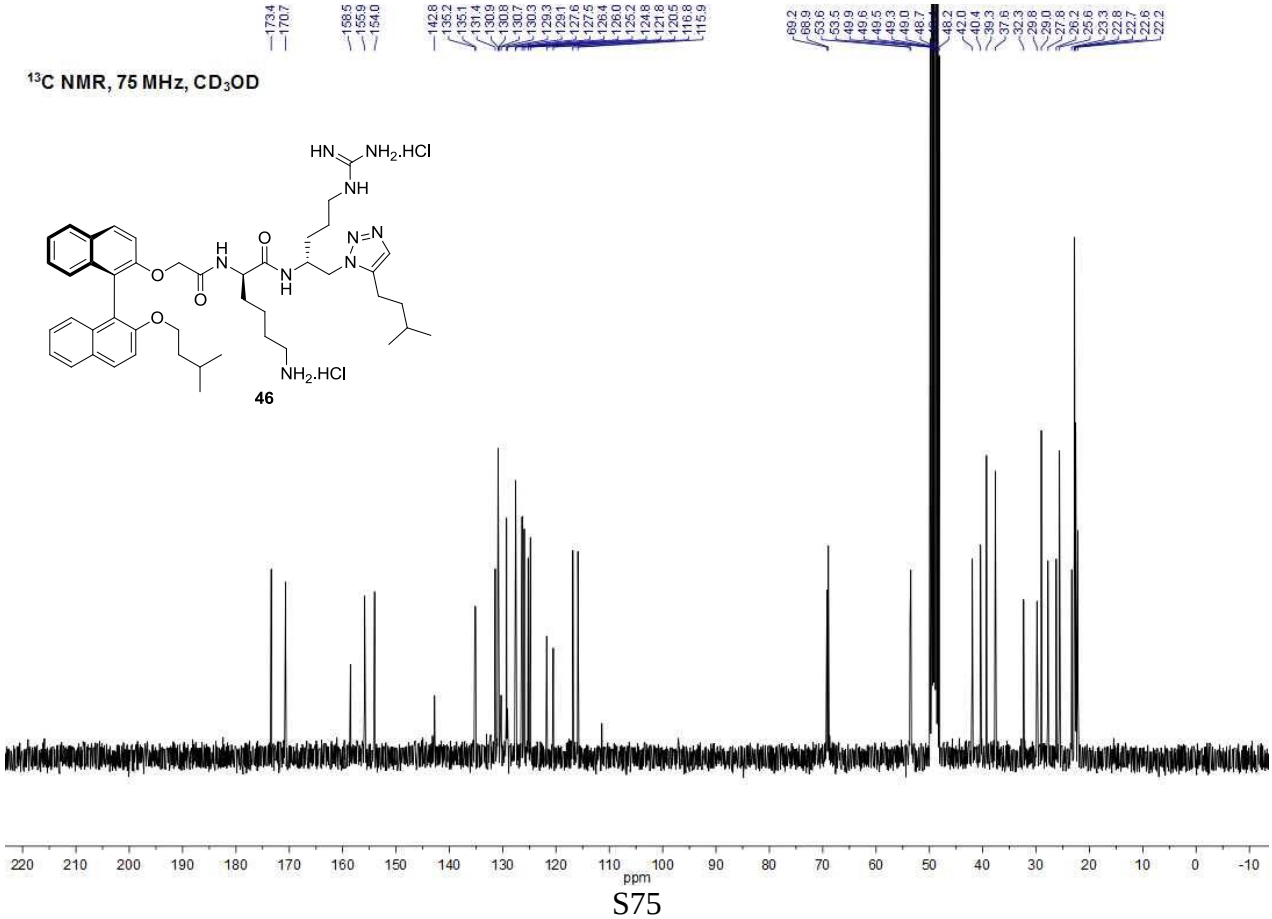

¹H NMR, 500 MHz, CD3OD
HN
NH2.HCl
NH
O
H
N
O
N=N
N
O
O
H
N
O
NH2.HCl
44
ppm

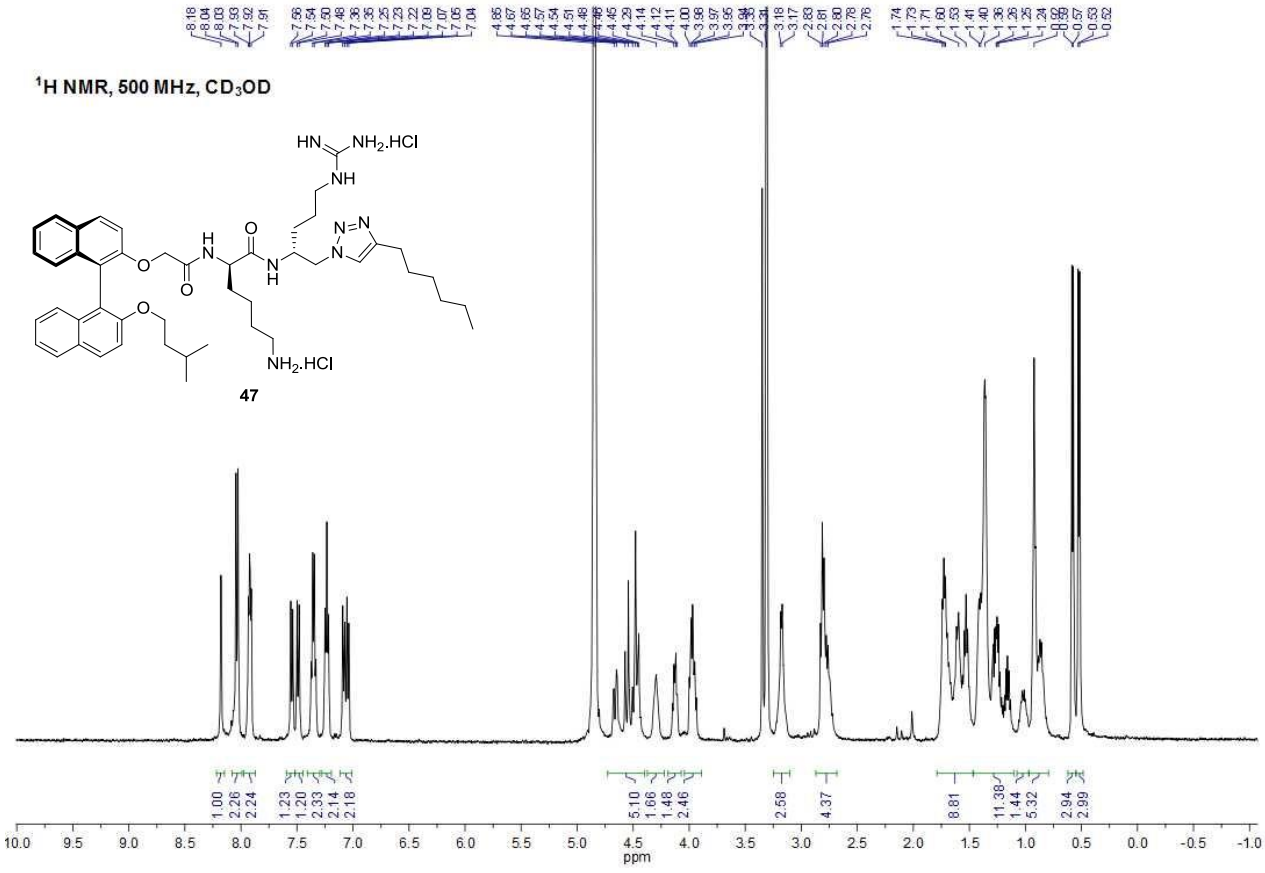

¹³C NMR, 75 MHz, CD3OD
HN
NH2.HCl
NH
O
H
N
O
N=N
N
O
O
H
N
O
NH2.HCl
44
ppm

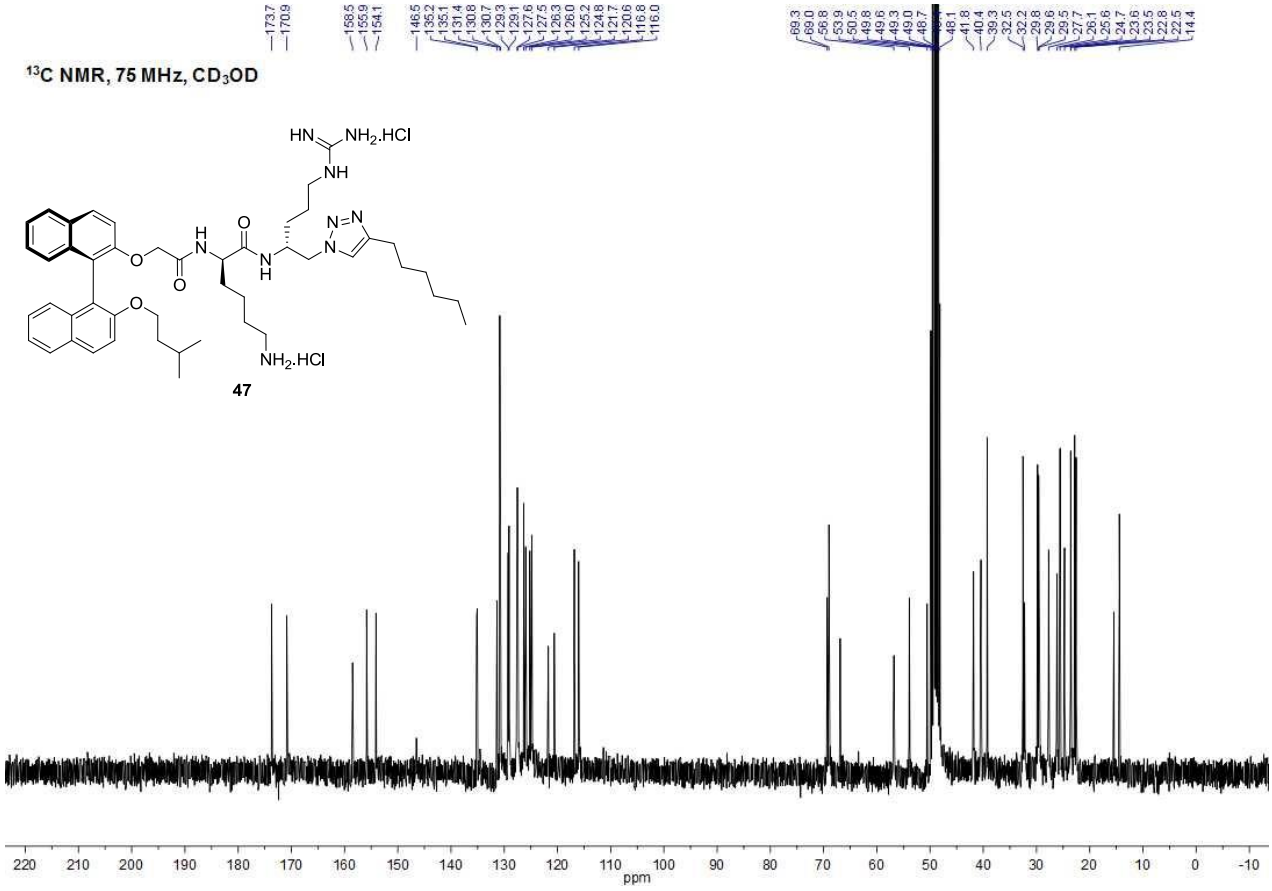

^{1}H NMR, 500 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
N=N
H
N
O
O
O
O
NH$_2$.HCl
45
ppm

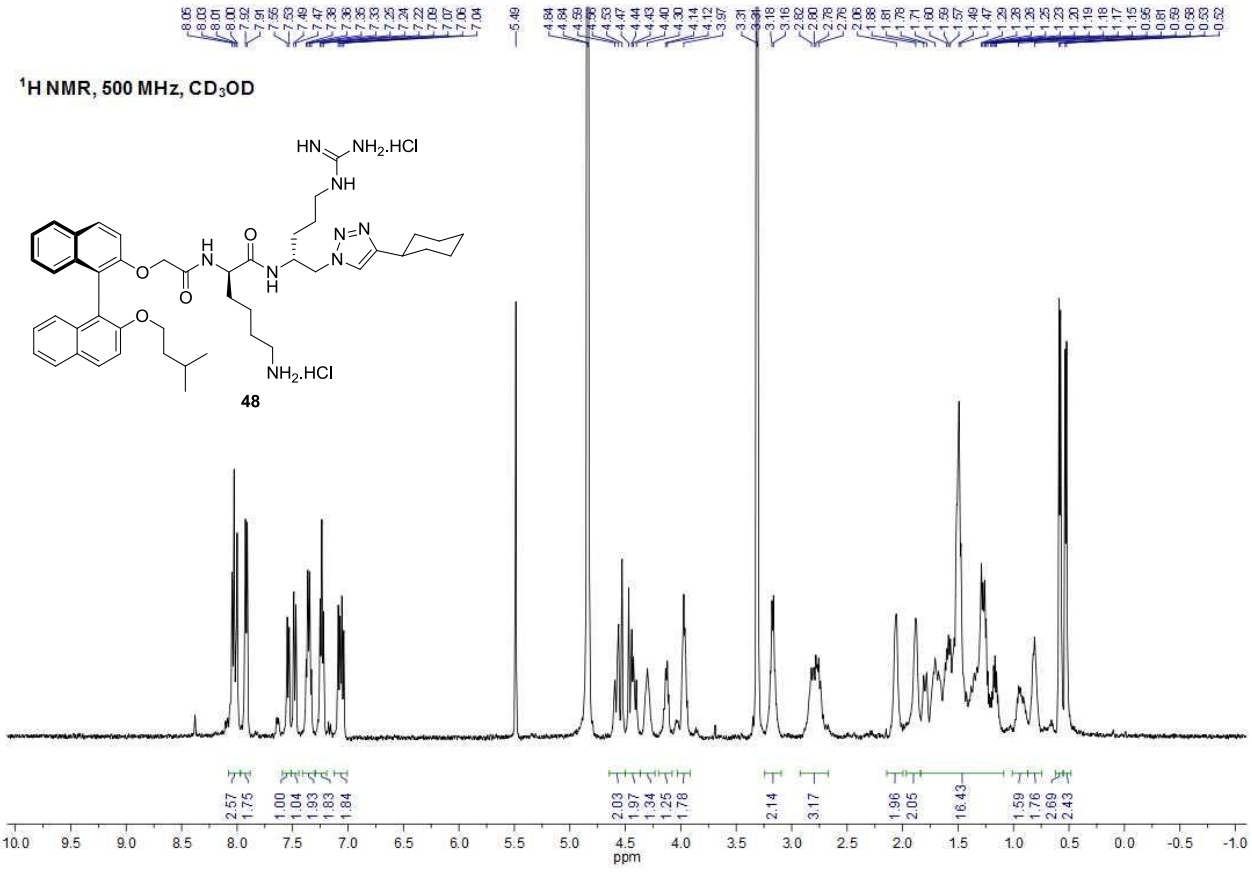

^{13}C NMR, 125 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
N=N
H
N
O
O
O
O
NH$_2$.HCl
45
ppm

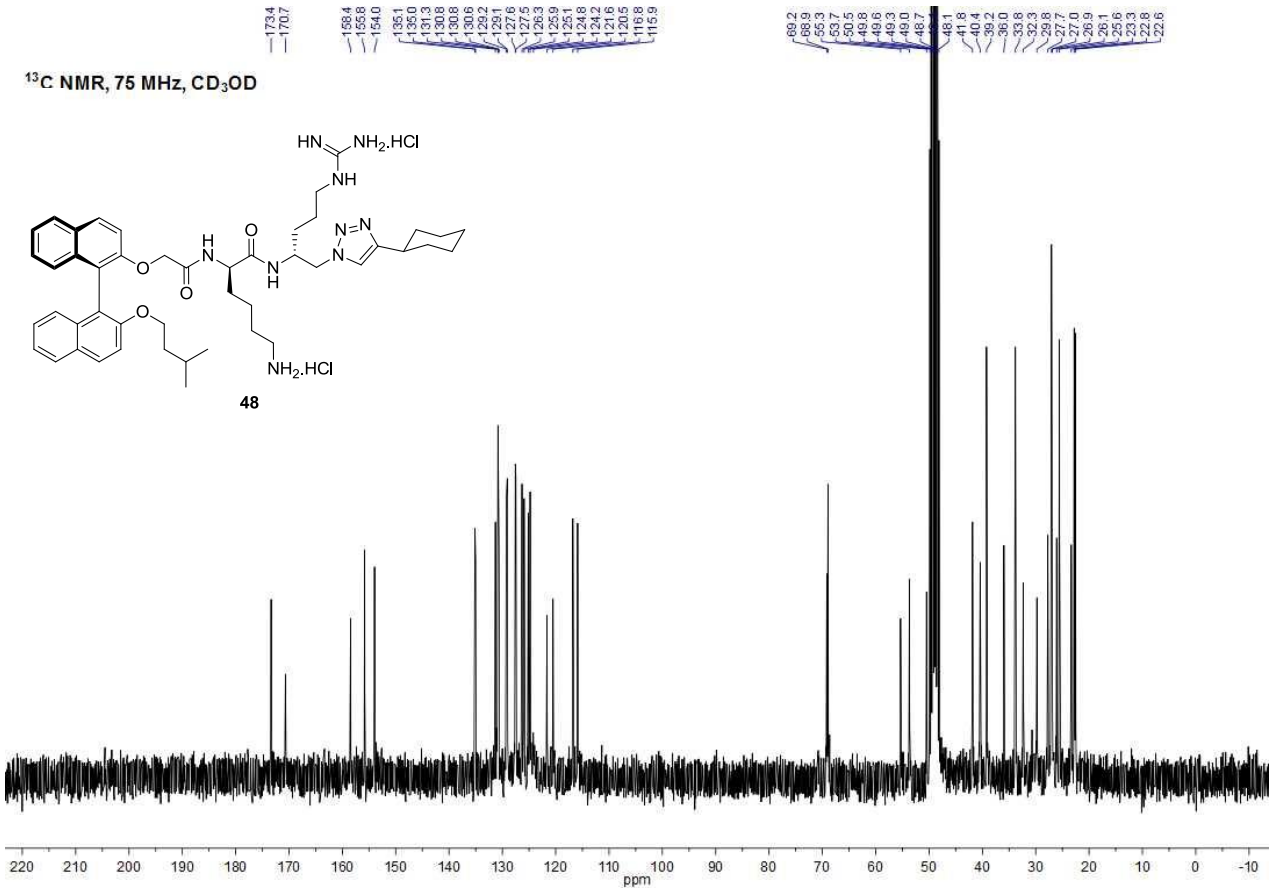

¹H NMR, 500 MHz, CD3OD
HN
NH2.HCl
NH
O
H
N
N
N=N
O
O
O
NH2.HCl
46
ppm

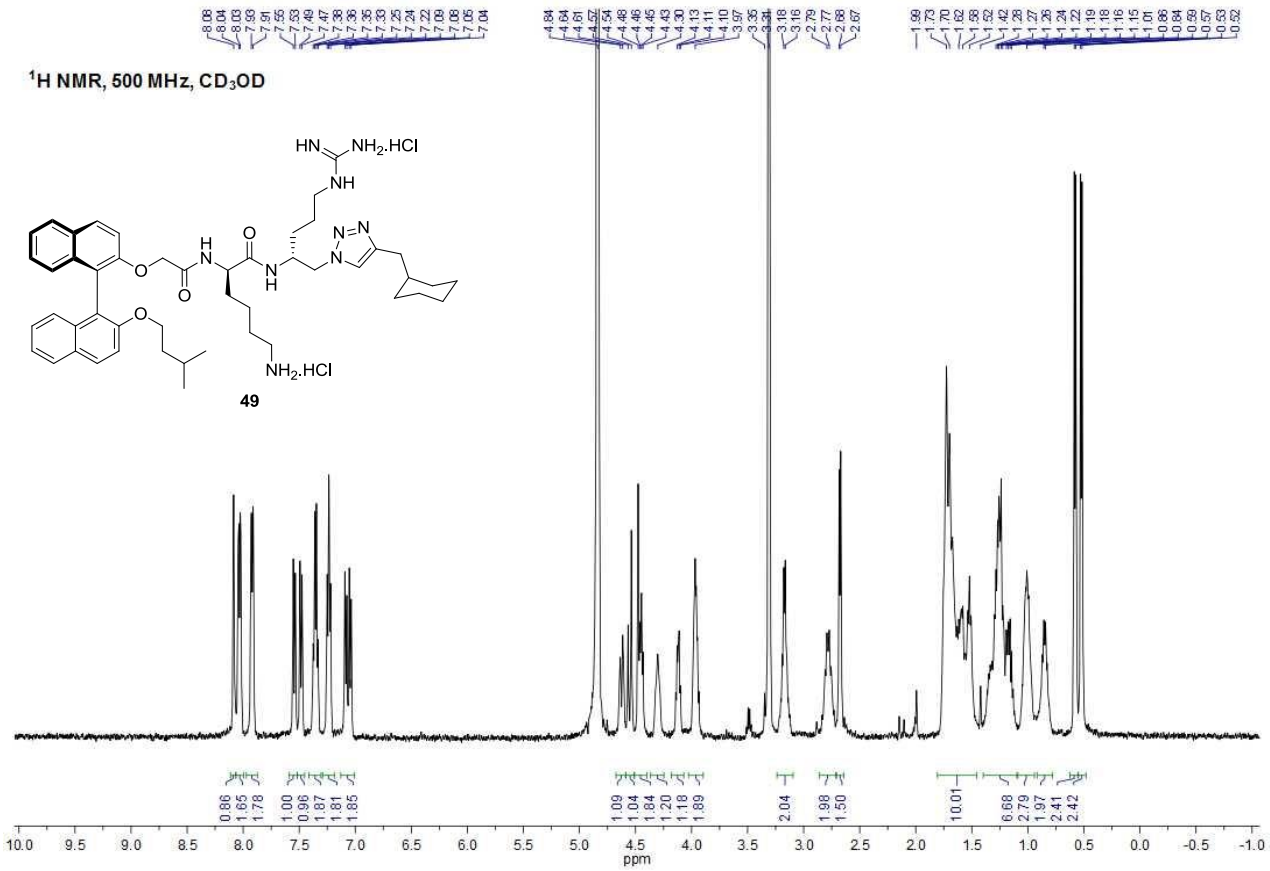

¹³C NMR, 75 MHz, CD3OD
HN
NH2.HCl
NH
O
H
N
N
N=N
O
O
O
NH2.HCl
46
ppm

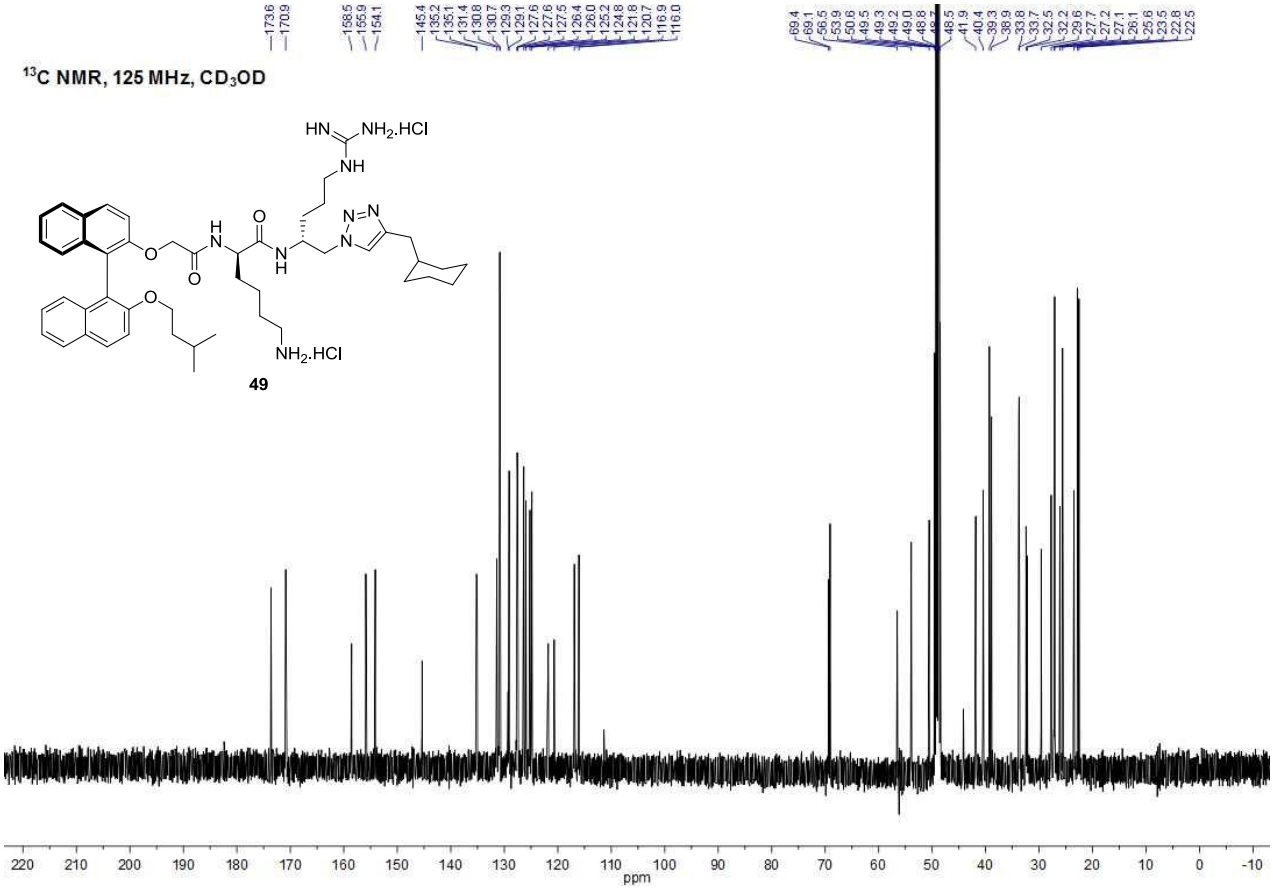

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
N
H
O
O
NH$_2$.HCl
47
ppm

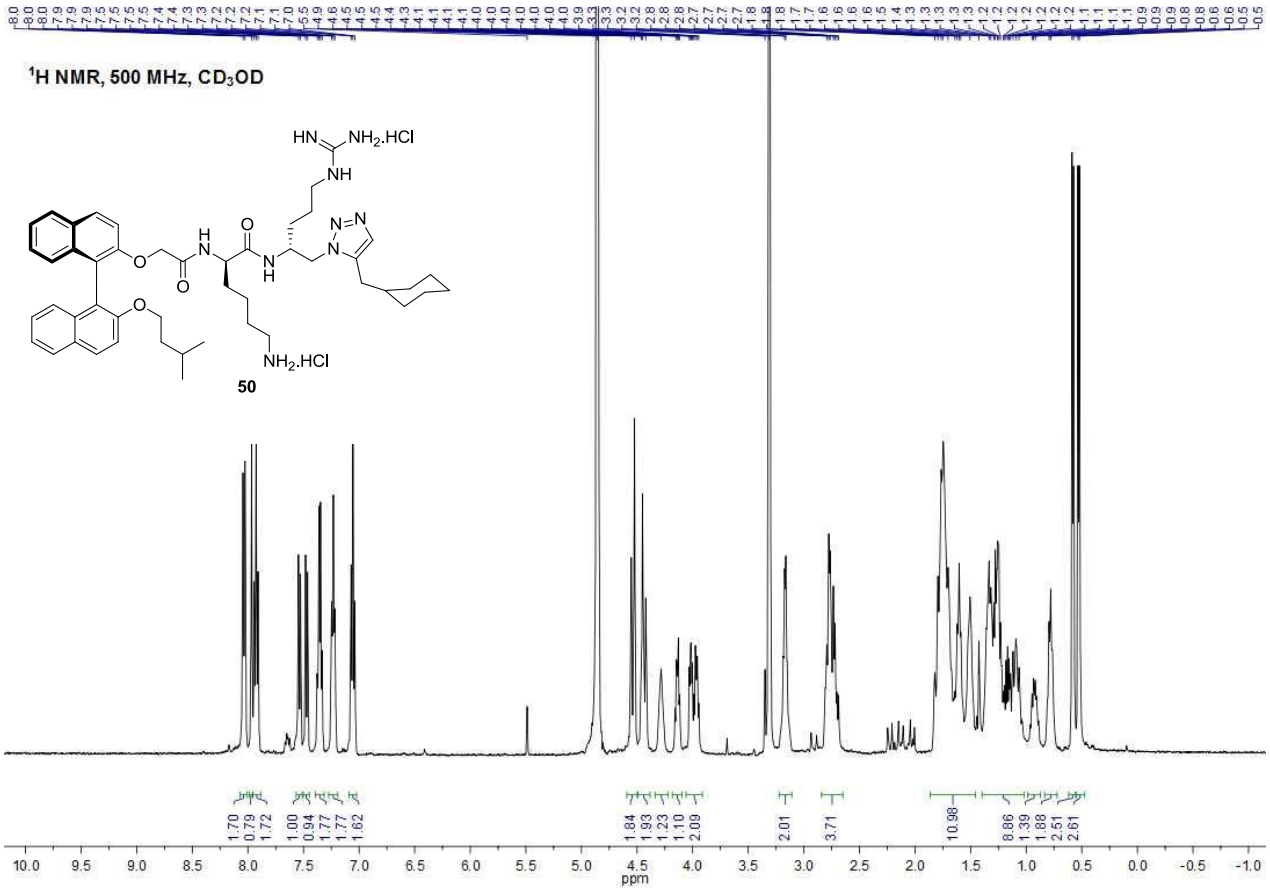

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
N
H
O
O
NH$_2$.HCl
47
ppm

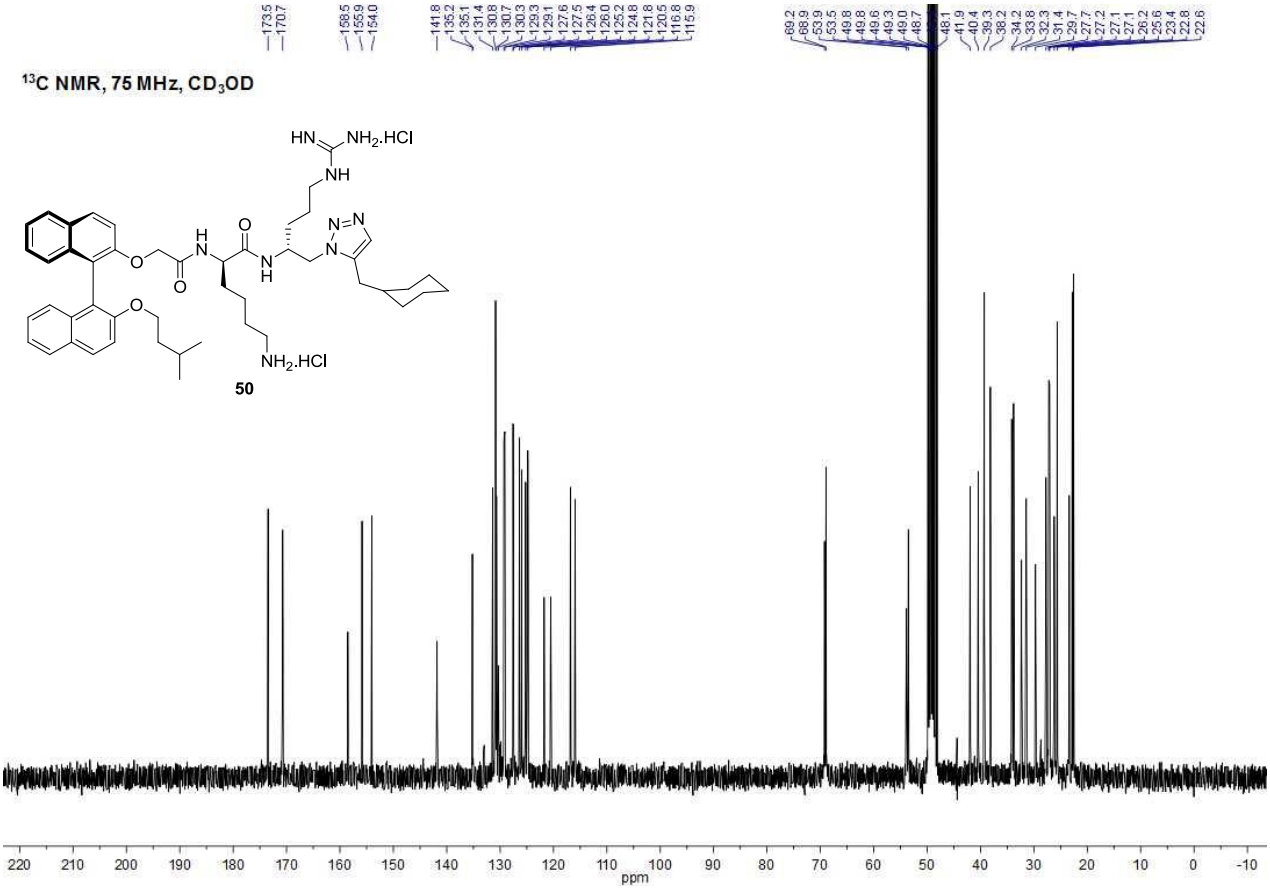

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
N
H
O
NH$_2$.HCl
48
ppm

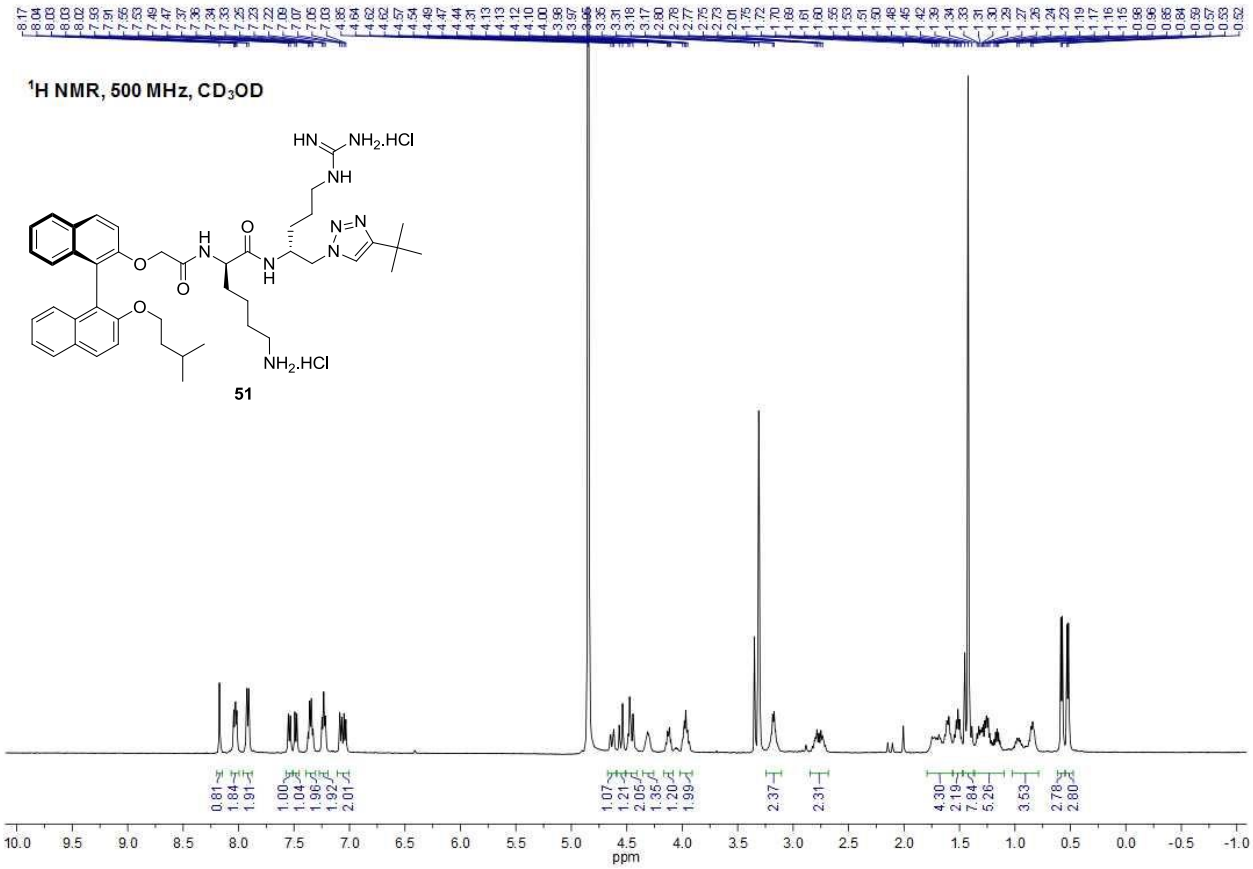

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
N
H
O
NH$_2$.HCl
48
ppm

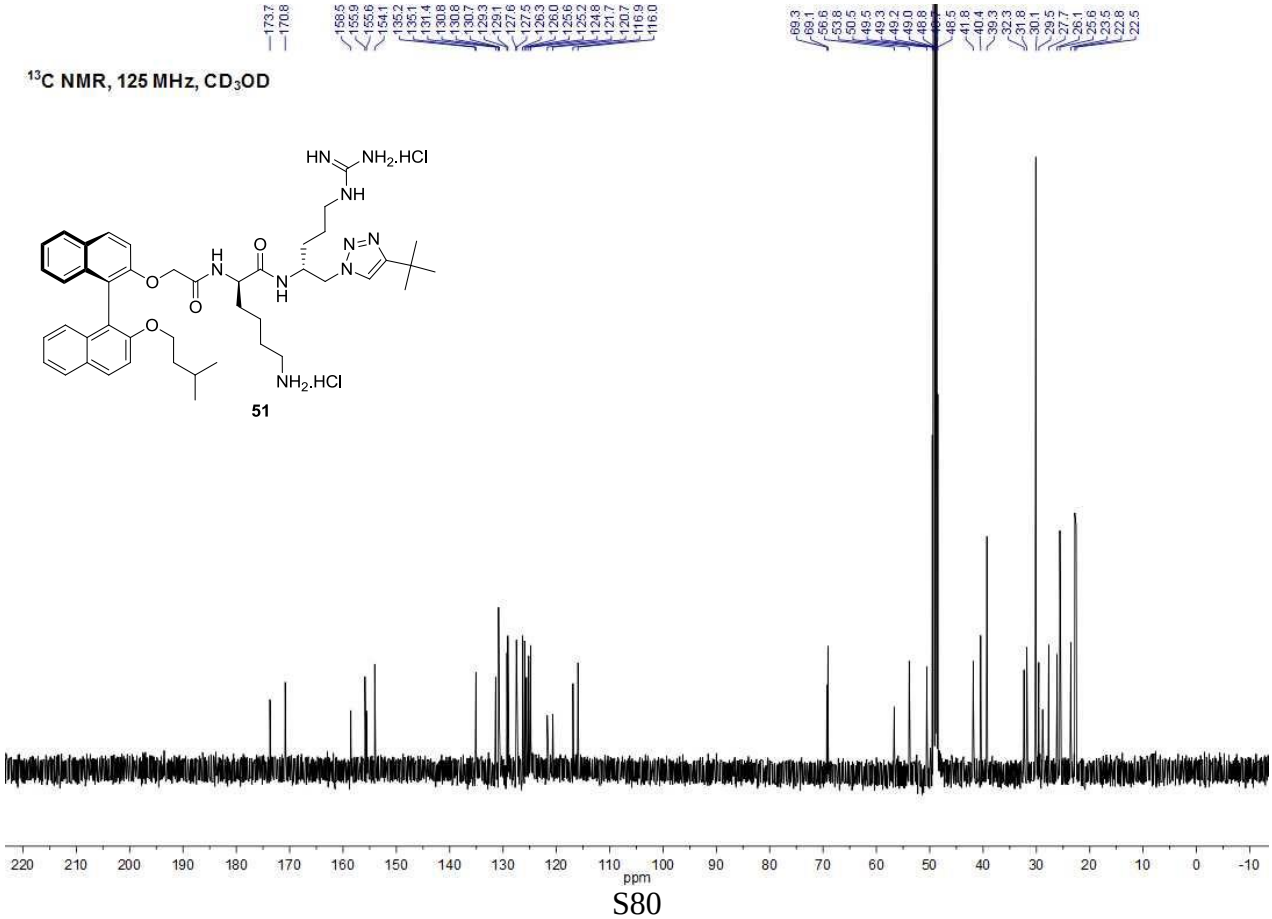

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
NH$_2$.HCl
49
ppm

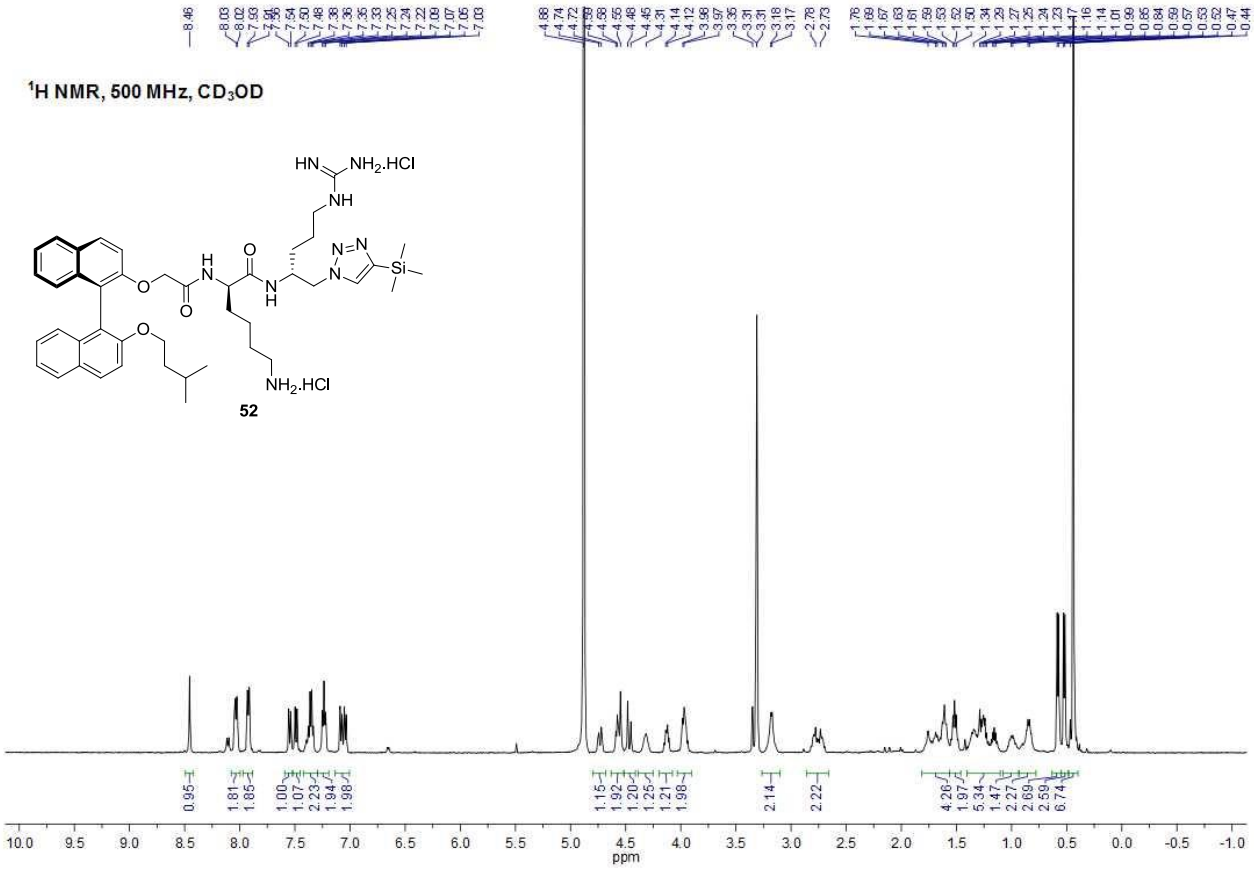

^{13}C NMR, 125 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
NH$_2$.HCl
49
ppm

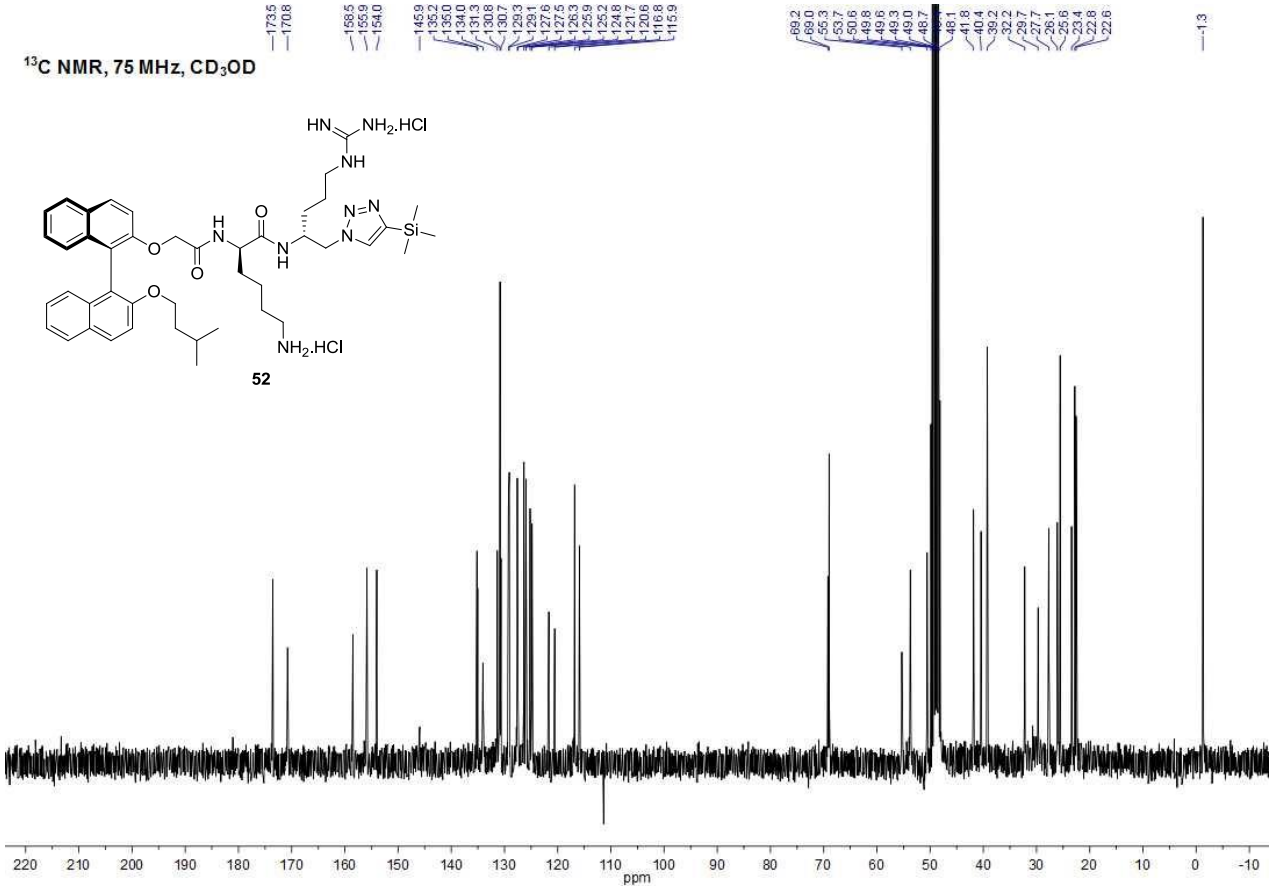

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
N
N=N
O
O
NH$_2$.HCl
50
1.70
0.79
1.72
1.00
0.94
1.77
1.77
1.62
1.84
1.93
1.23
1.10
2.09
2.01
3.71
10.98
8.86
1.39
1.88
2.51
2.61
ppm

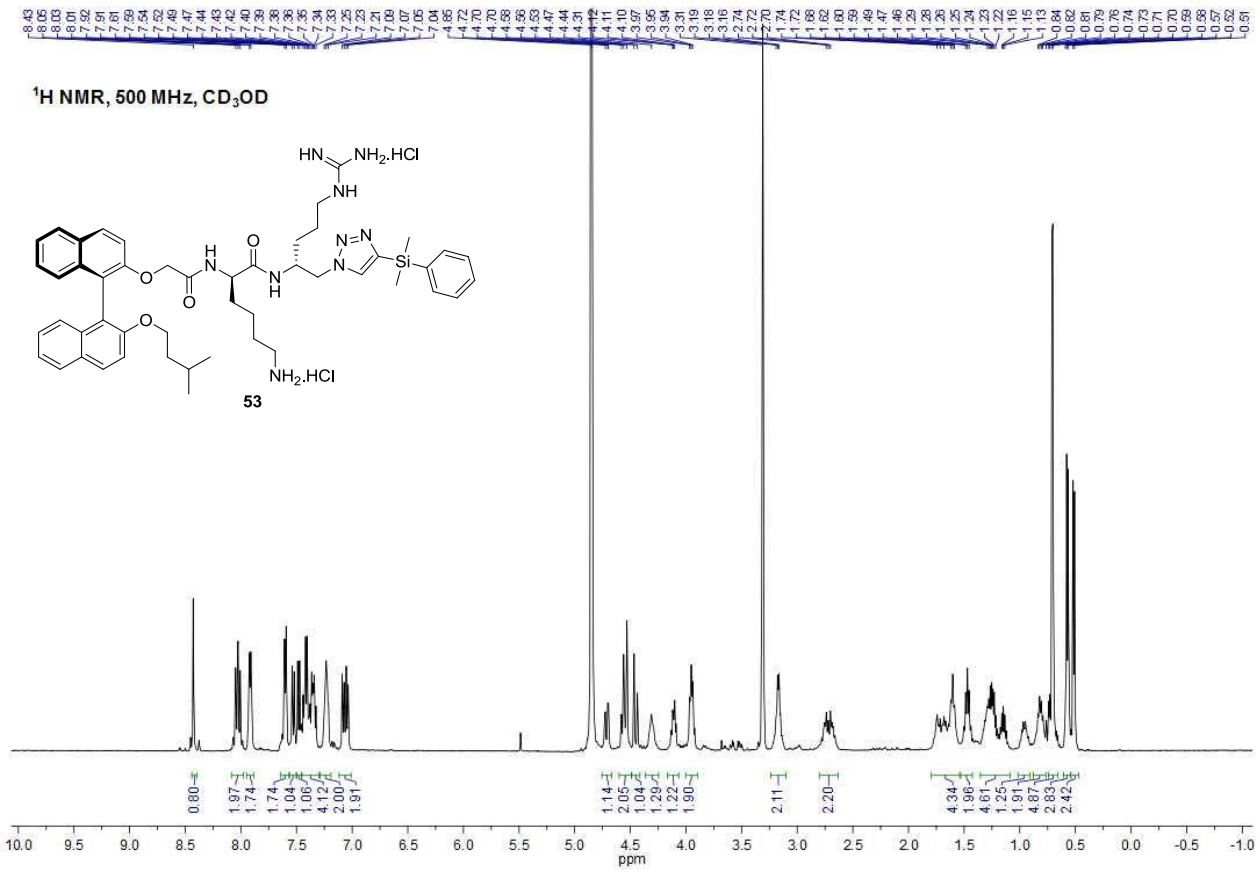

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
N
N=N
O
O
NH$_2$.HCl
50
173.5
170.7
158.5
155.9
154.0
141.8
135.2
135.1
131.4
130.8
130.7
130.3
129.3
129.1
127.6
127.5
126.4
126.0
125.2
124.8
121.8
120.5
116.8
115.9
69.2
68.9
53.9
53.5
49.8
49.8
49.6
49.3
49.0
48.7
48.1
41.9
40.4
39.3
38.2
34.2
33.8
32.3
31.4
29.7
27.7
27.2
27.1
27.1
26.2
25.6
23.4
22.8
22.6
ppm

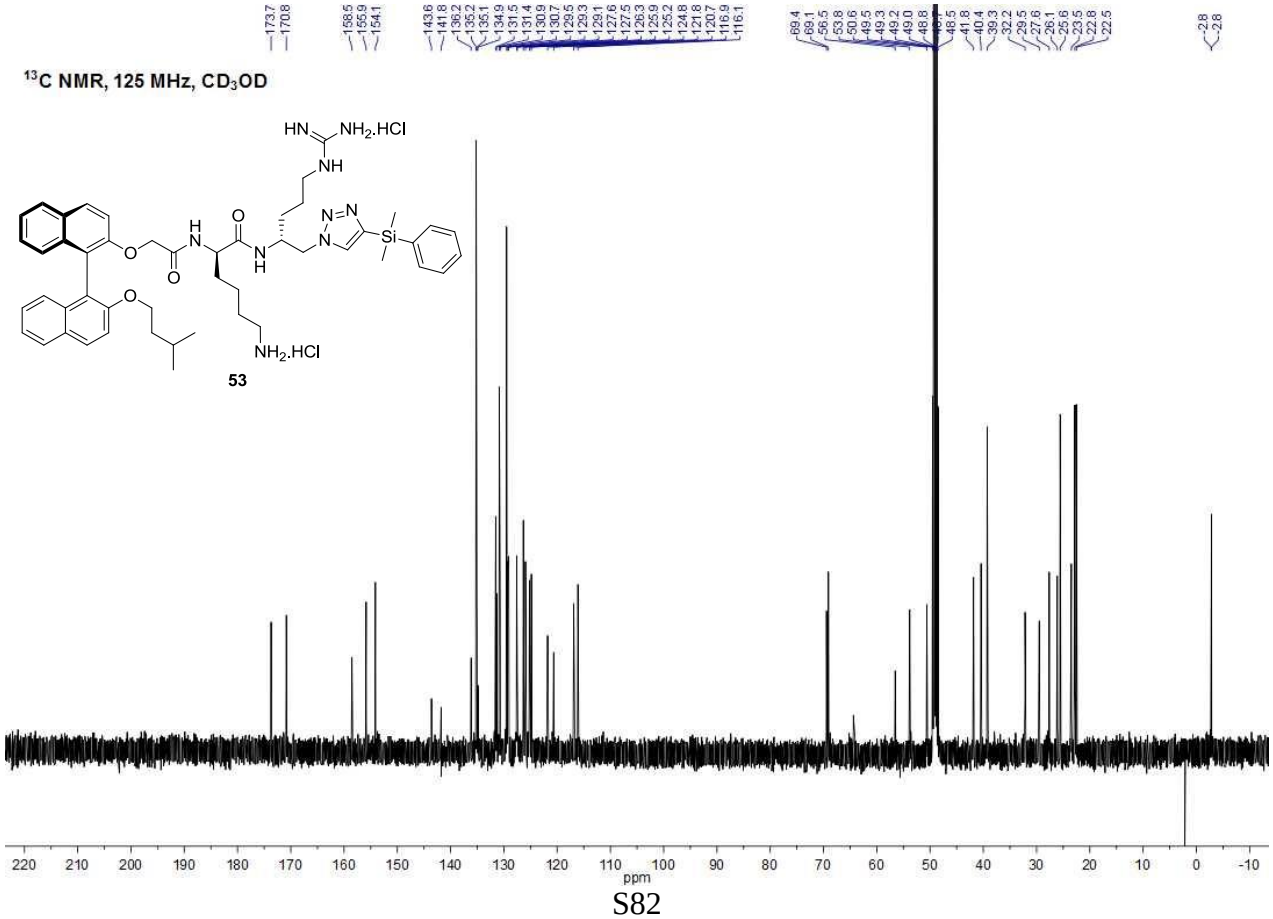

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
O
N
N
N
O
O
NH$_2$.HCl
51
ppm

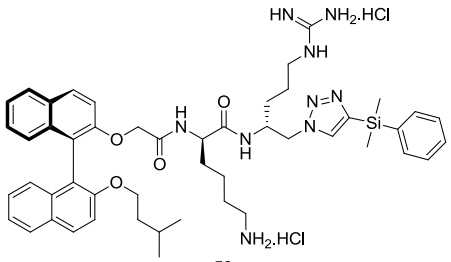

^{13}C NMR, 125 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
O
N
N
N
O
O
NH$_2$.HCl
51
ppm


^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
N
N
Si
O
O
O
NH$_2$.HCl
52
ppm


^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
N
N
Si
O
O
O
NH$_2$.HCl
52
ppm

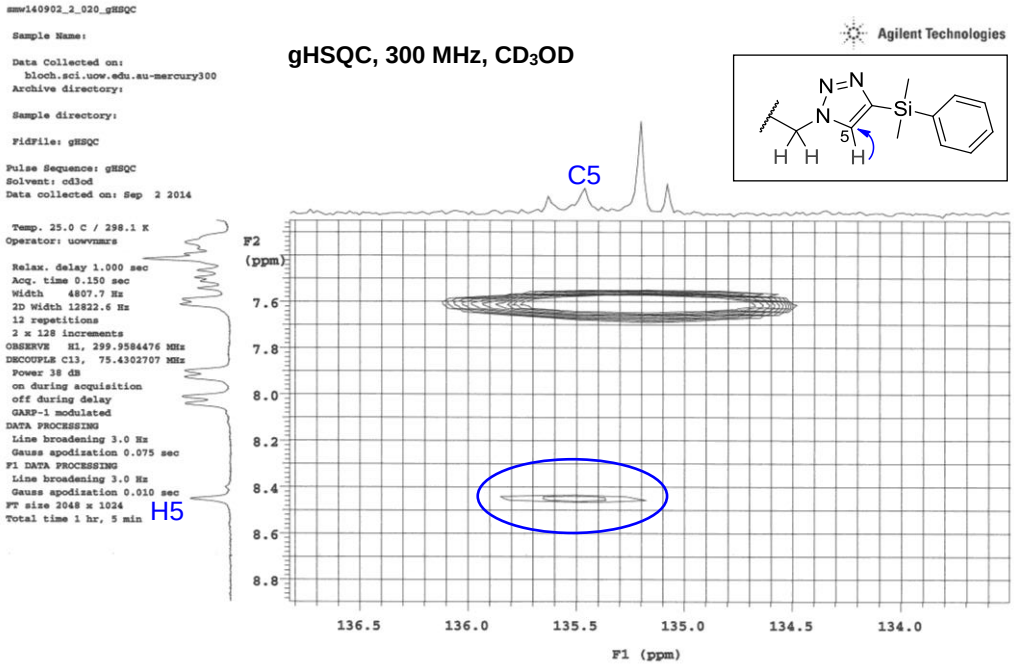

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
O
N
H
N=N
N
Si
O
O
NH$_2$.HCl
53
ppm


^{13}C NMR, 125 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
O
N
H
N=N
N
Si
O
O
NH$_2$.HCl
53
ppm

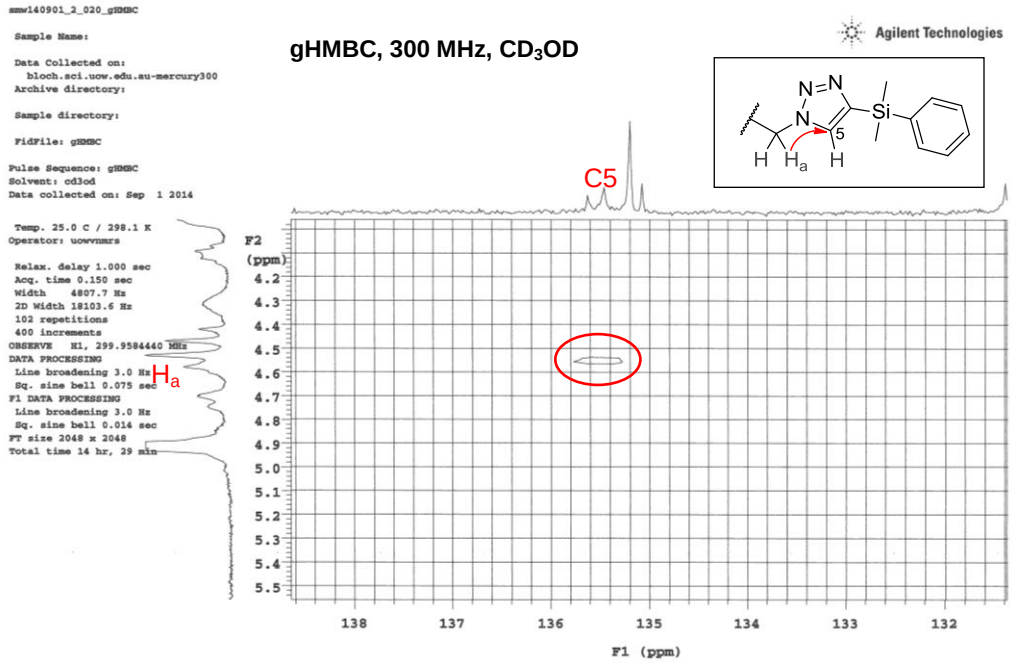


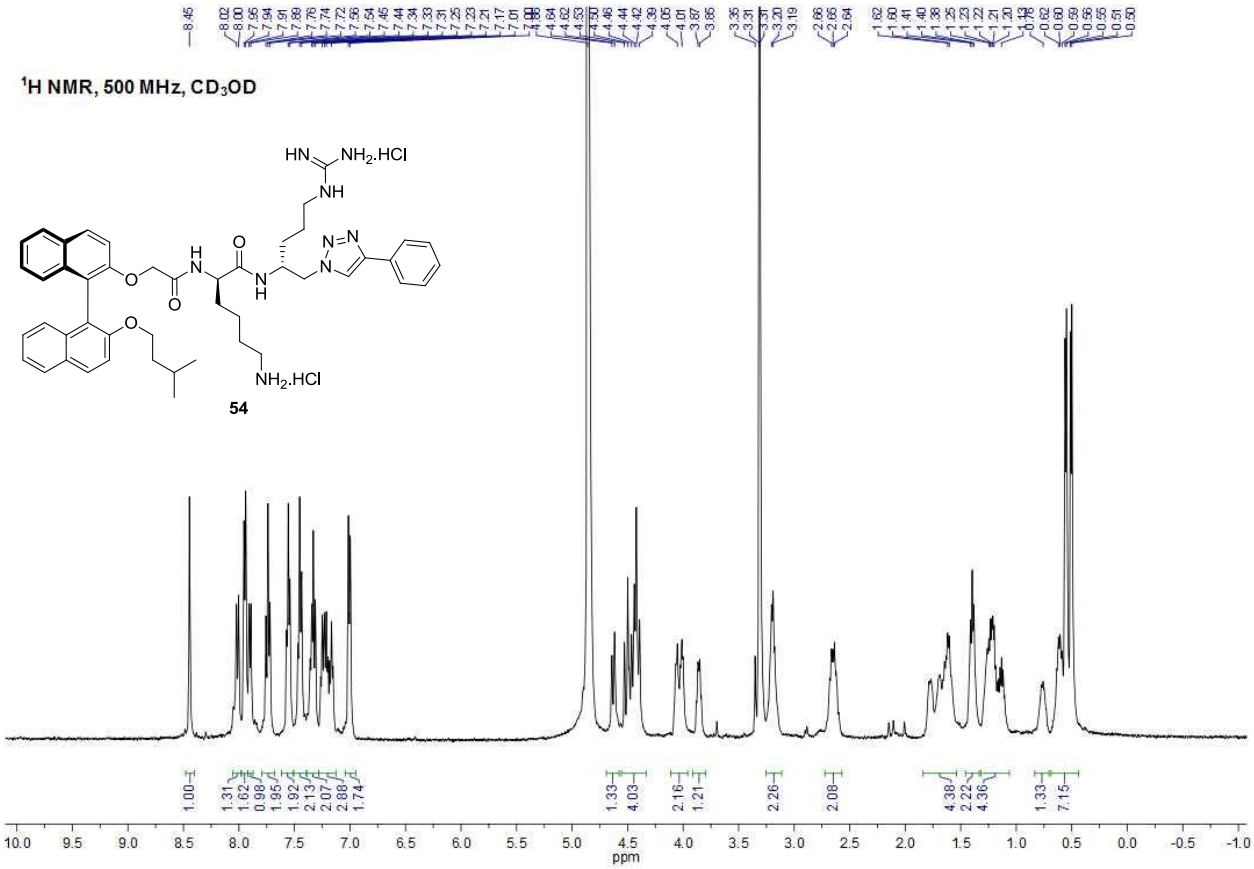
53

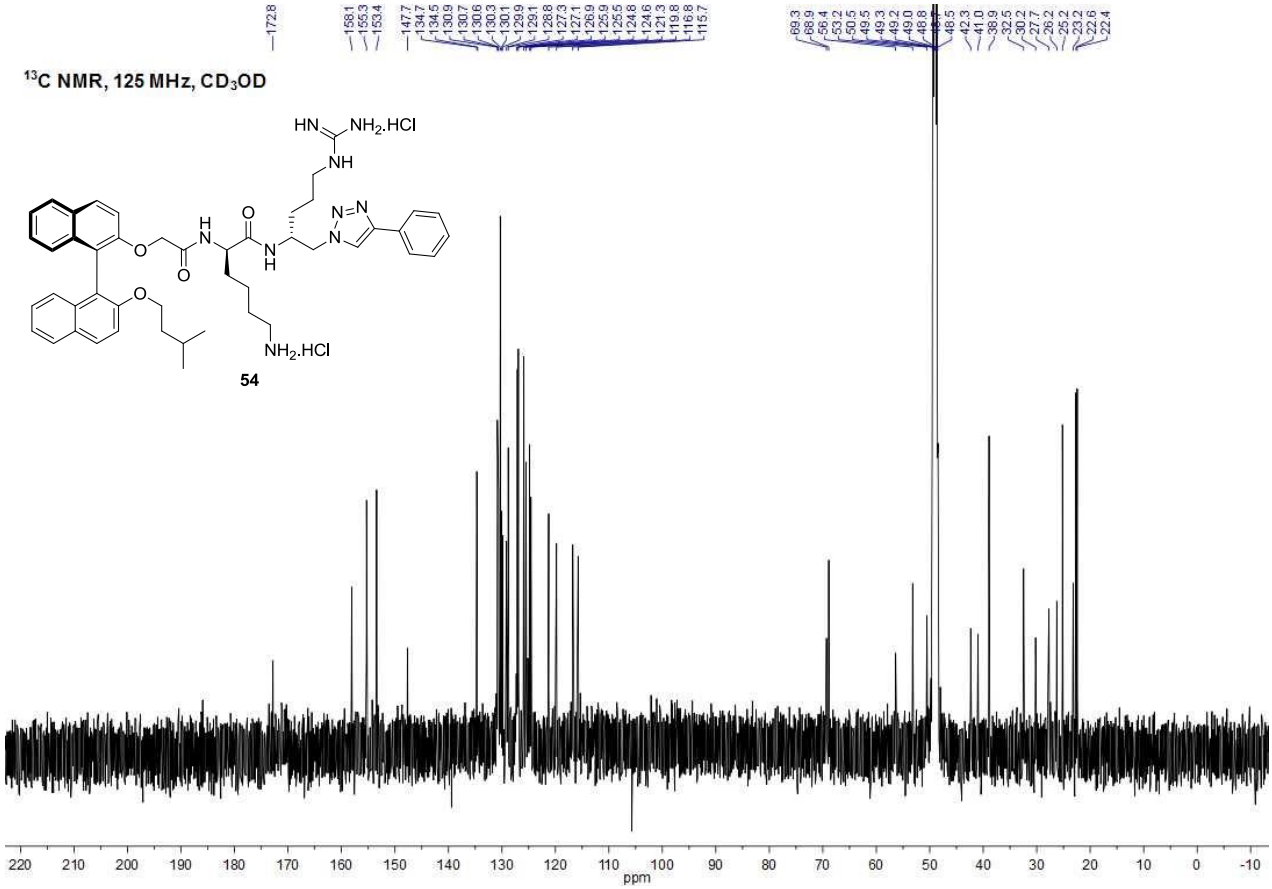
gHSQC, 300 MHz, CD_3OD

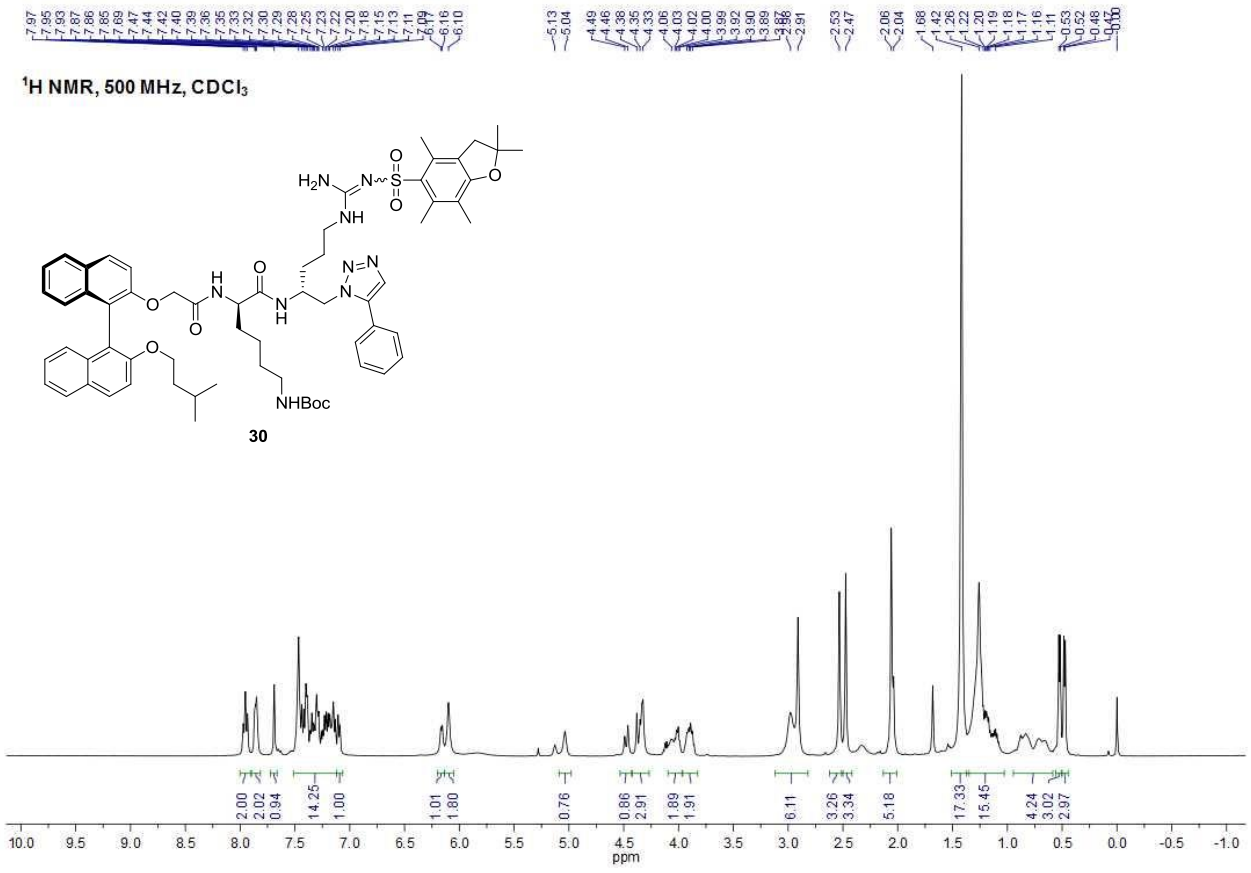


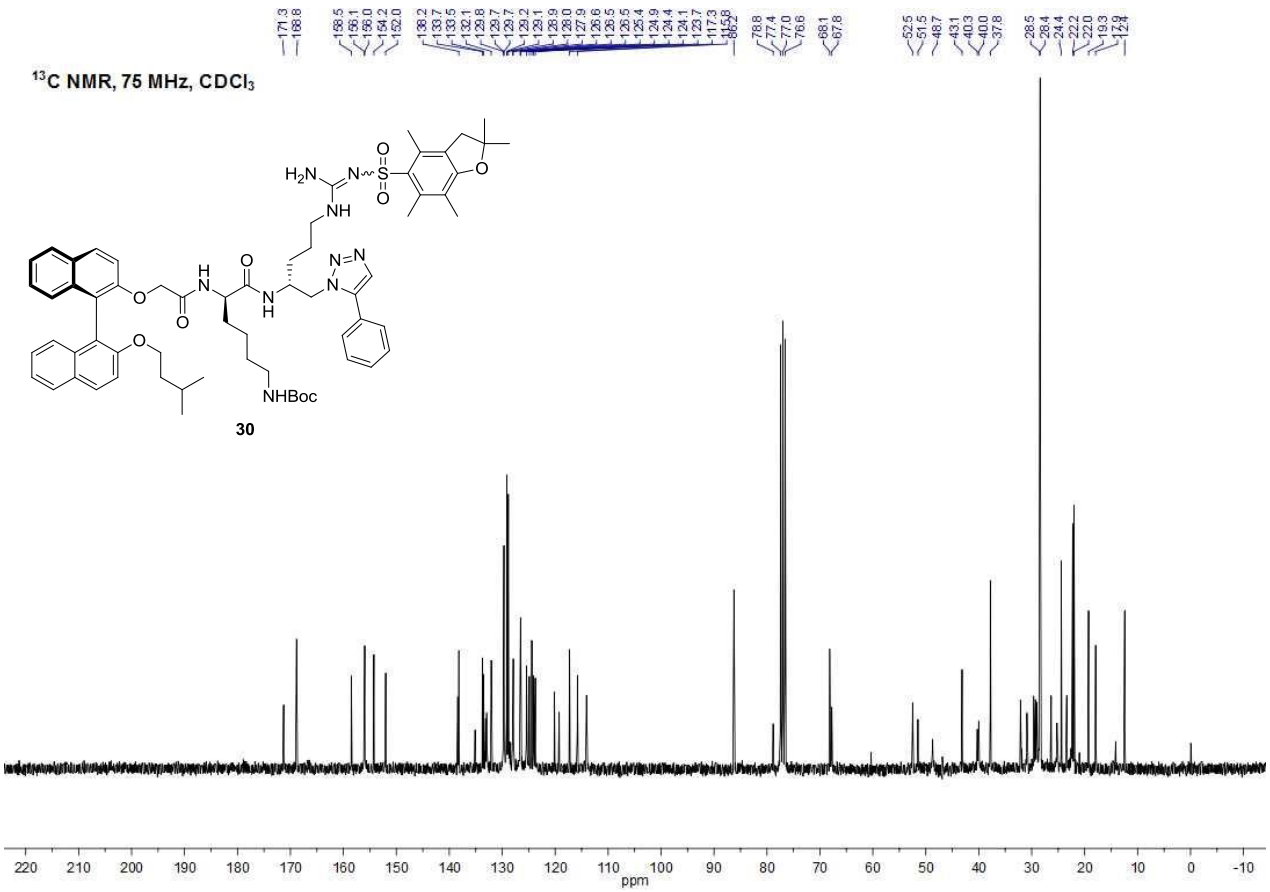
gHMBC, 300 MHz, CD_3OD

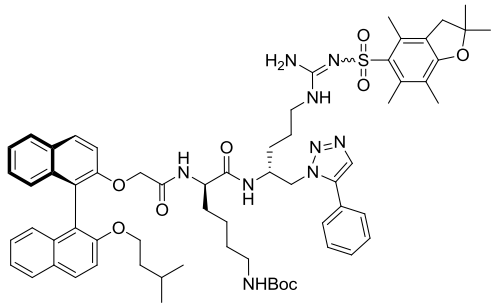



1H NMR, 500 MHz, CD3OD
HN
NH2.HCl
NH
N=N
O
H
N
O
N
H
O
O
NH2.HCl
54
ppm

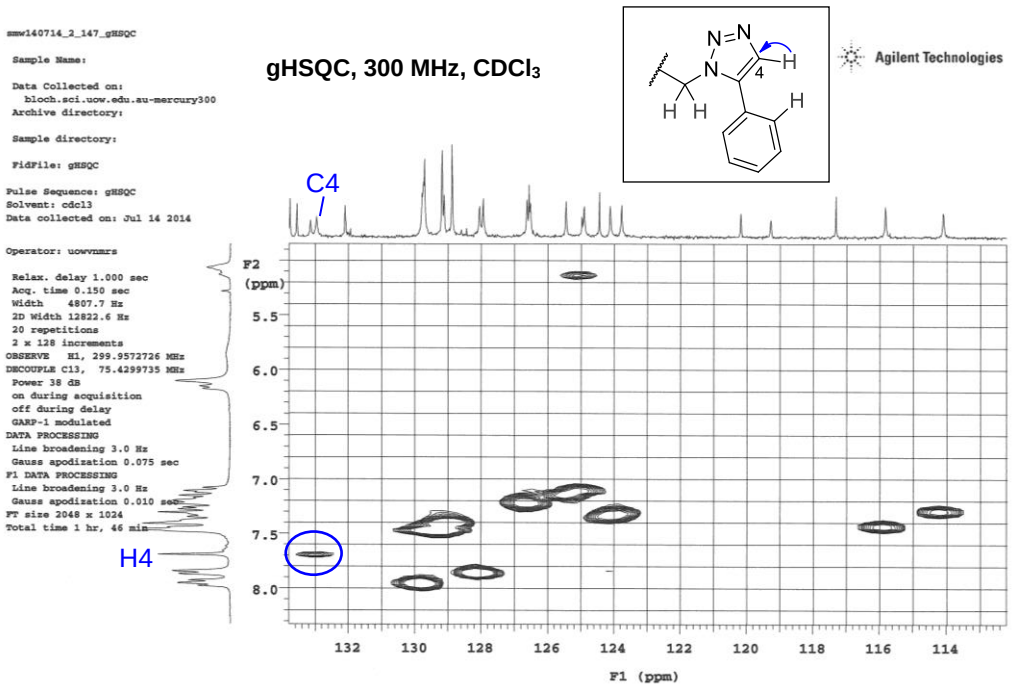

13C NMR, 125 MHz, CD3OD
HN
NH2.HCl
NH
N=N
O
H
N
O
N
H
O
O
NH2.HCl
54
ppm

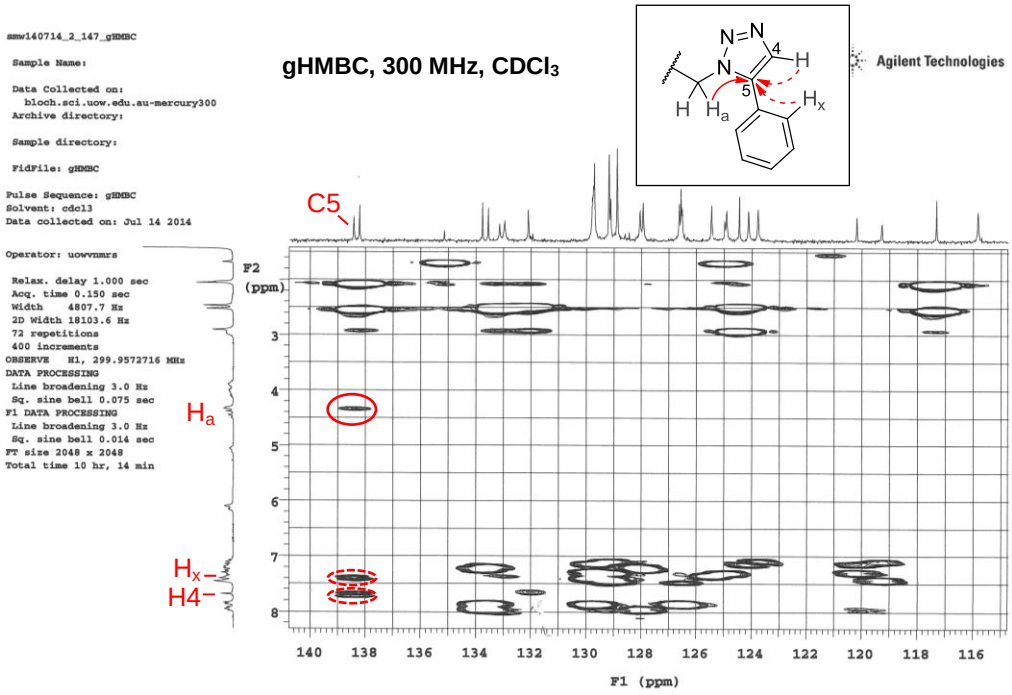

^{1}H NMR, 500 MHz, CDCl$_3$
30
ppm

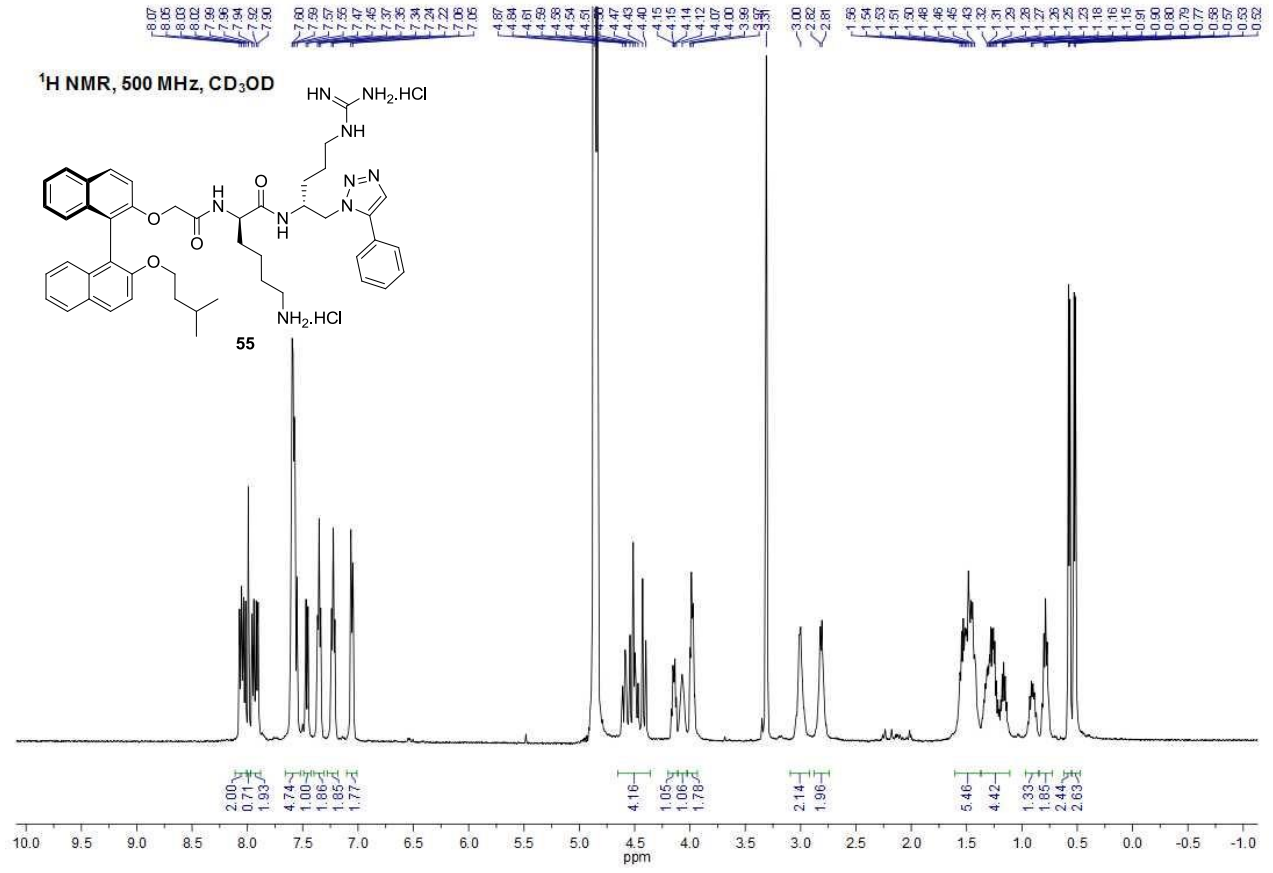

^{13}C NMR, 75 MHz, CDCl$_3$
30
ppm

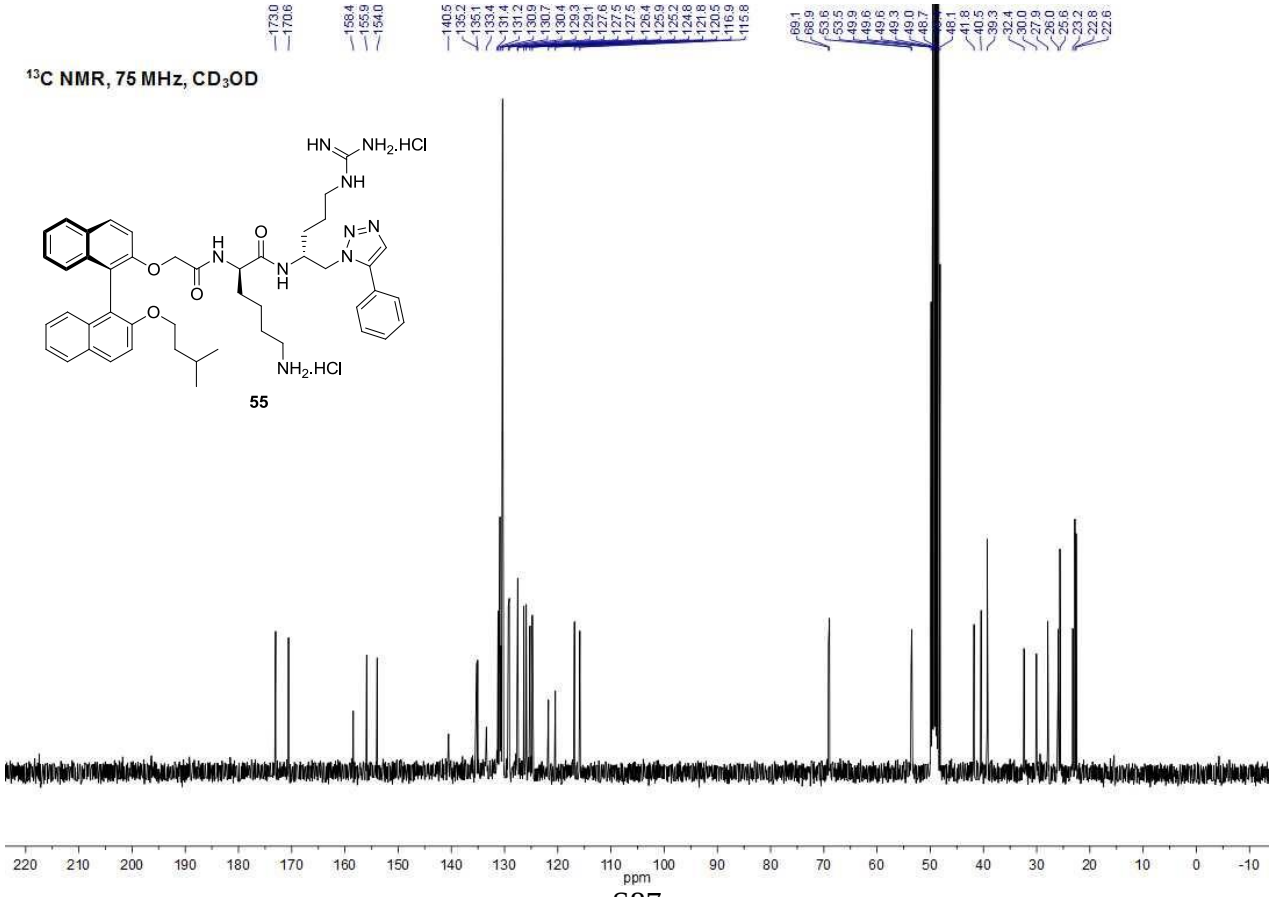


30

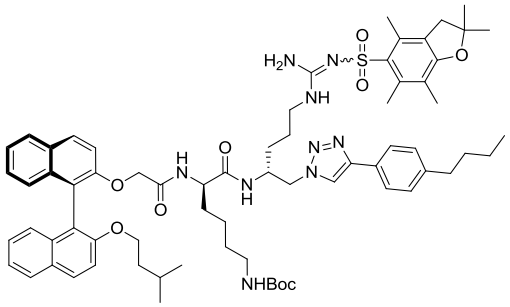

smw140714_2_147_gHSQC
Sample Name:
Data Collected on:
bloch.sci.uow.edu.au-mercury300
Archive directory:
Sample directory:
FidFile: gHSQC
Pulse Sequence: gHSQC
Solvent: cdcl3
Data collected on: Jul 14 2014
Operator: uowvnmrs
Relax. delay 1.000 sec
Acq. time 0.150 sec
Width 4807.7 Hz
2D Width 12822.6 Hz
20 repetitions
2 x 128 increments
OBSERVE H1, 299.9572726 MHz
DECOUPLE C13, 75.4299735 MHz
Power 38 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 3.0 Hz
Gauss apodization 0.075 sec
F1 DATA PROCESSING
Line broadening 3.0 Hz
Gauss apodization 0.010 sec
FT size 2048 x 1024
Total time 1 hr, 46 min
gHSQC, 300 MHz, CDCl3
Agilent Technologies
C4
H4
F2 (ppm)
F1 (ppm)


smw140714_2_147_gHMBC
Sample Name:
Data Collected on:
bloch.sci.uow.edu.au-mercury300
Archive directory:
Sample directory:
FidFile: gHMBC
Pulse Sequence: gHMBC
Solvent: cdcl3
Data collected on: Jul 14 2014
Operator: uowvnmrs
Relax. delay 1.000 sec
Acq. time 0.150 sec
Width 4807.7 Hz
2D Width 18103.6 Hz
72 repetitions
400 increments
OBSERVE H1, 299.9572716 MHz
DATA PROCESSING
Line broadening 3.0 Hz
Sq. sine bell 0.075 sec
F1 DATA PROCESSING
Line broadening 3.0 Hz
Sq. sine bell 0.014 sec
FT size 2048 x 2048
Total time 10 hr, 14 min
gHMBC, 300 MHz, CDCl3
Agilent Technologies
C5
Ha
Hx
H4
F2 (ppm)
F1 (ppm)


^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
N
H
N
O
O
O
O
O
NH$_2$.HCl
55
ppm

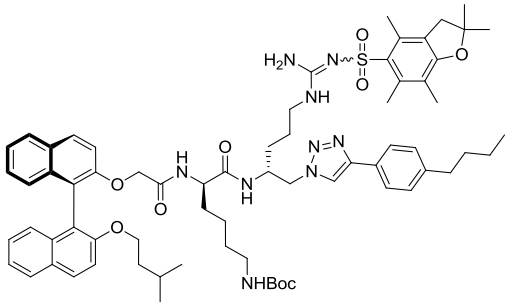

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
N
H
N
O
O
O
O
O
NH$_2$.HCl
55
ppm

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

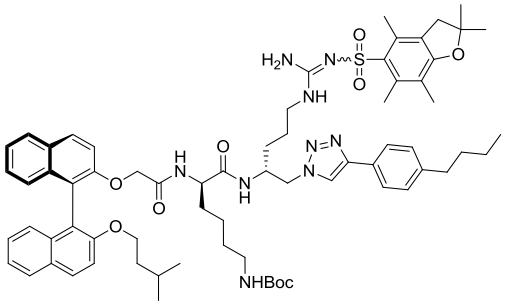


31

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

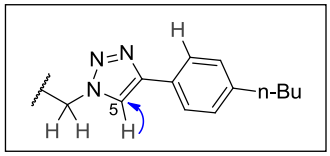


31



31

gHSQC, 500 MHz, $CDCl_3$



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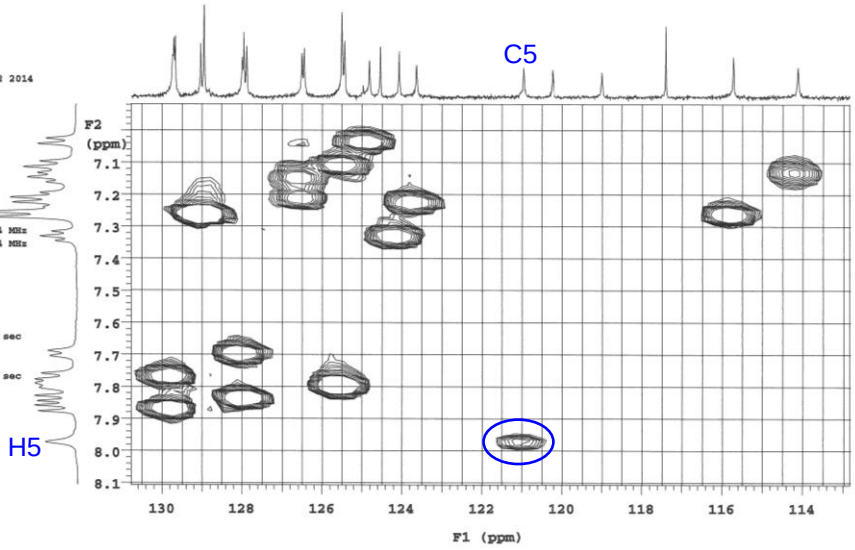
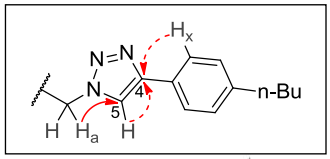
```
smw140702_2_137_gHSQC

 Sample Name:

 Data Collected on:
   ernst.sci.uow.edu.au-inova500
 Archive directory:

 Sample directory:

 FidFile: gHSQC

Pulse Sequence: gHSQC
Solvent: cdcl3
Data collected on: Jul  2 2014

 Temp. 25.0 C / 298.1 K
Operator: uowvnmrs

 Relax. delay 1.000 sec
 Acq. time 0.150 sec
 Width     7998.4 Hz
 2D Width 21367.5 Hz
 12 repetitions
 2 x 128 increments
OBSERVE   H1, 499.9049124 MHz
DECOUPLE C13, 125.7106134 MHz
 Power 37 dB
 on during acquisition
 off during delay
 W40_autoxdb modulated
DATA PROCESSING
 Line broadening 3.0 Hz
 Gauss apodization 0.075 sec
F1 DATA PROCESSING
 Line broadening 3.0 Hz
 Gauss apodization 0.006 sec
FT size 2048 x 1024
Total time 1 hr, 2 min
```

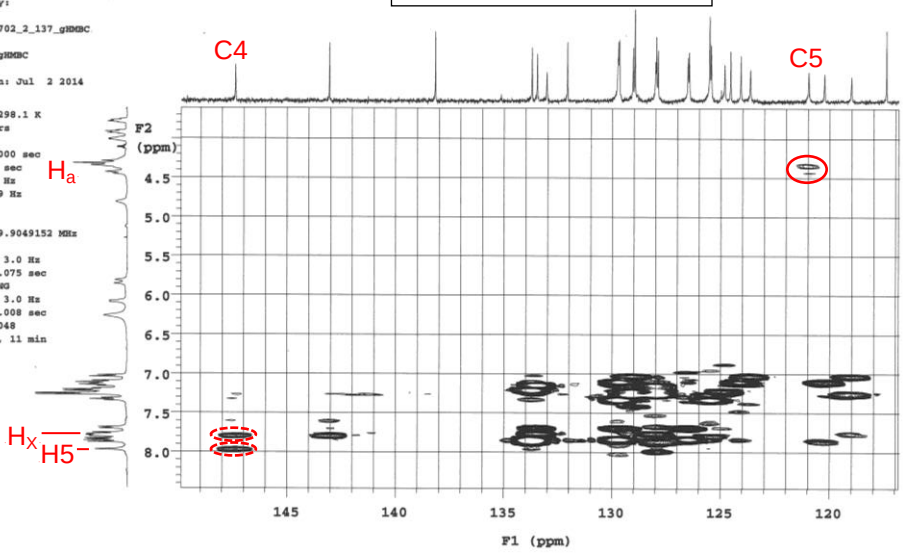


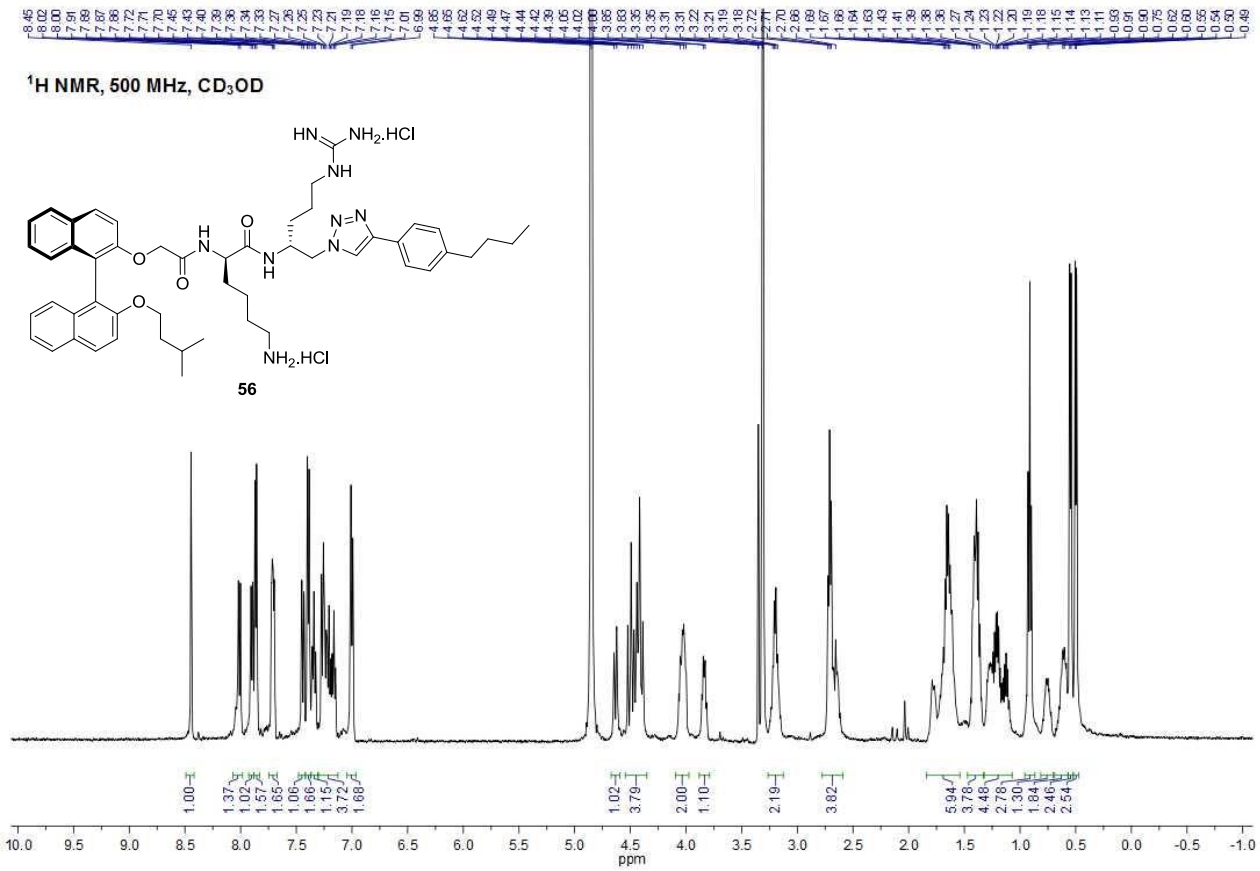
gHMBC, 500 MHz, $CDCl_3$

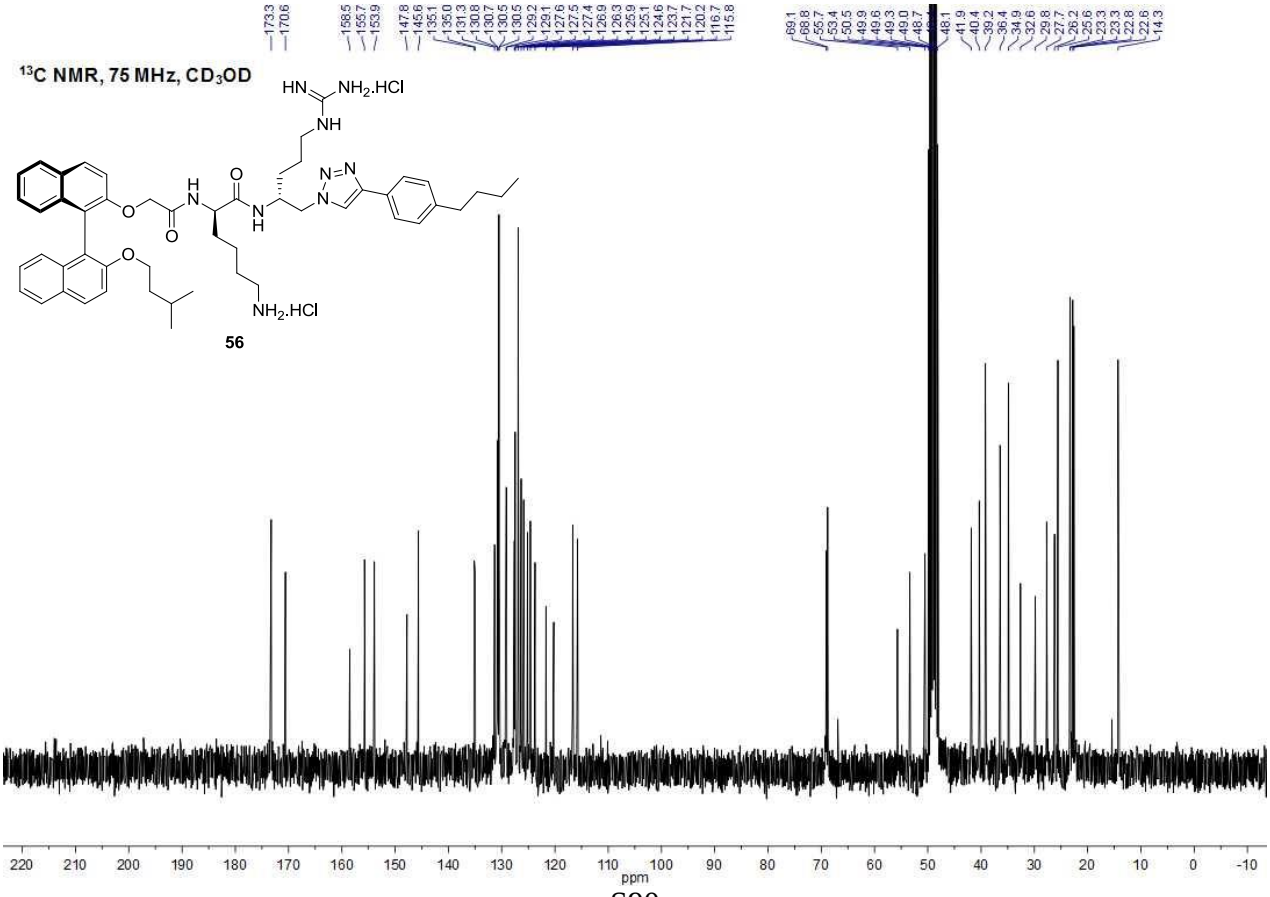


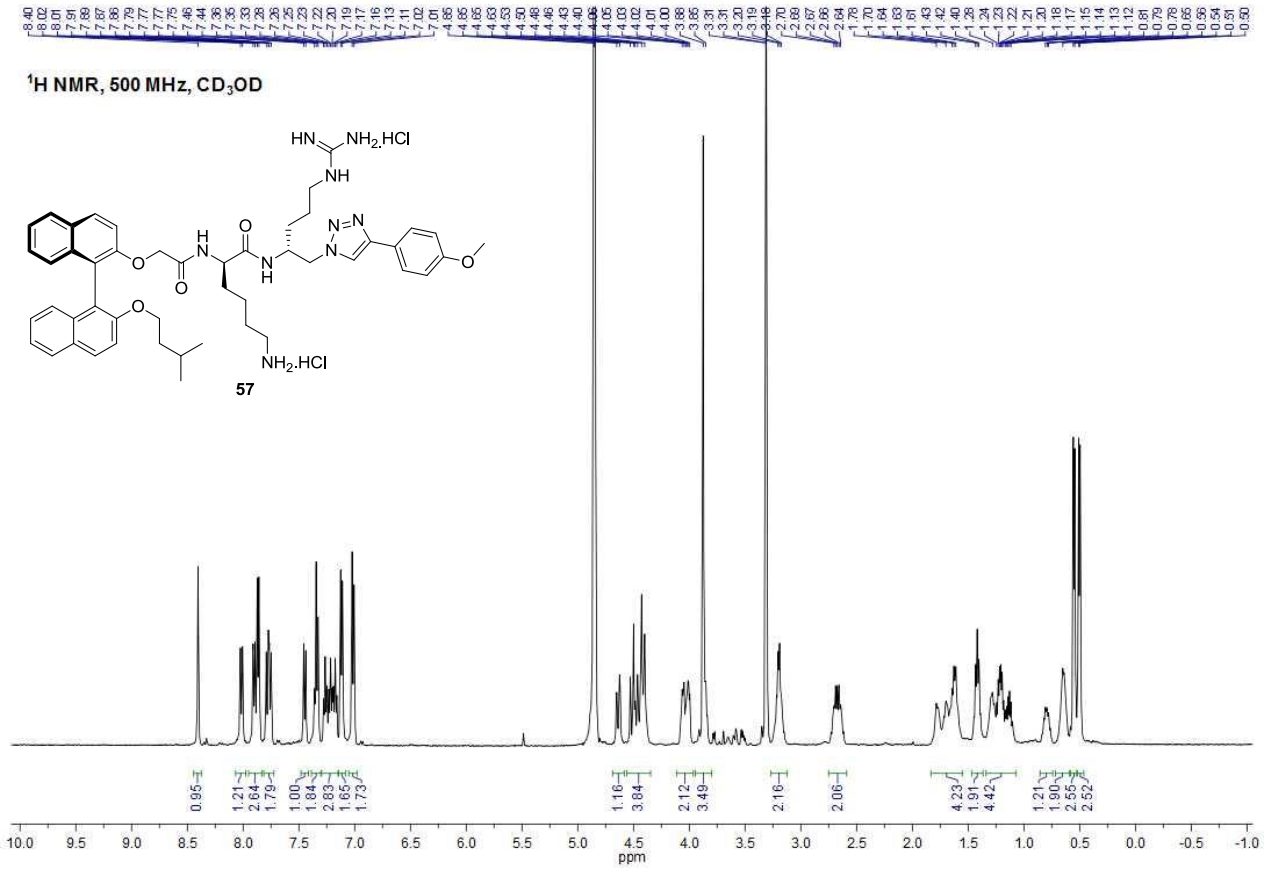
Agilent Technologies

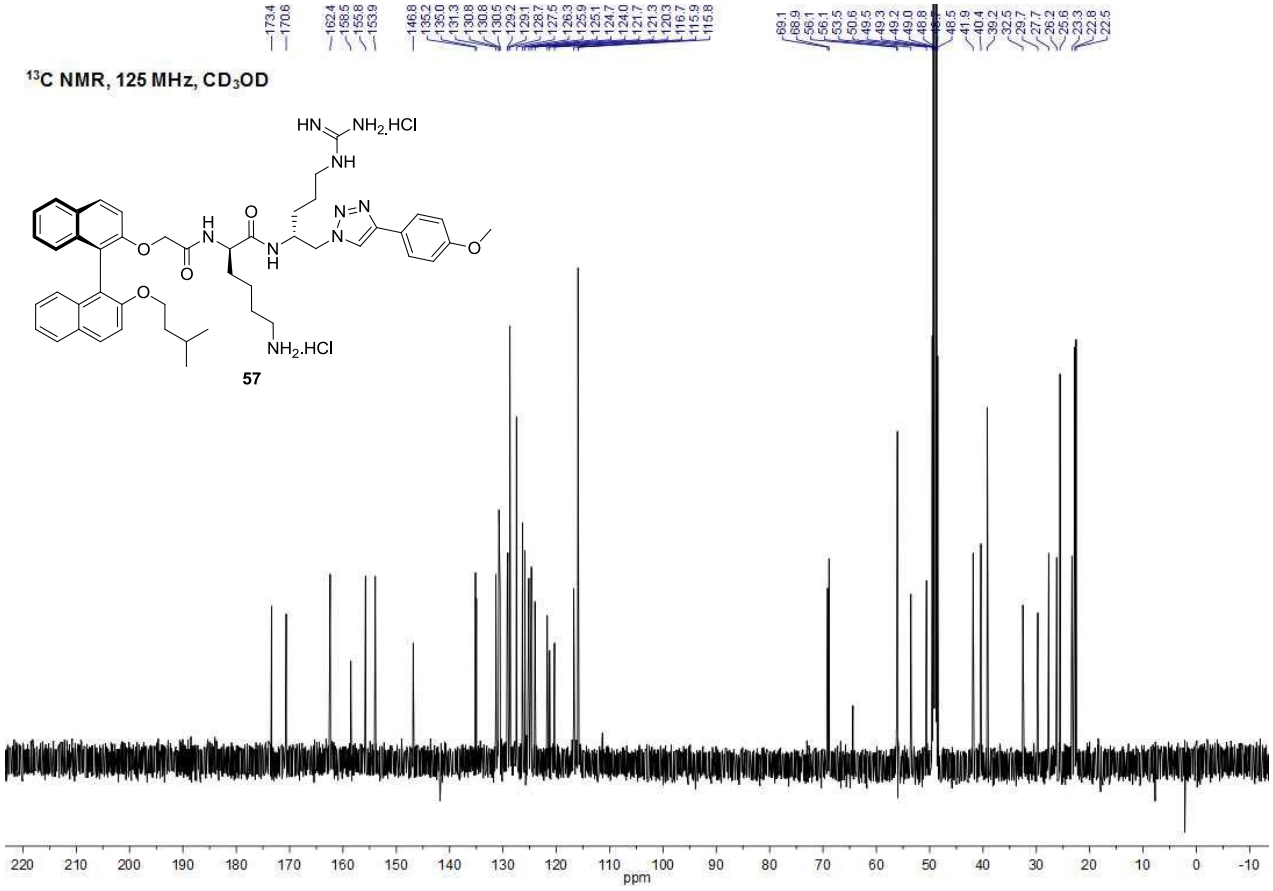
```
smw140702_2_137_gHMBC

 Sample Name:

 Data Collected on:
   ernst.sci.uow.edu.au-inova500
 Archive directory:

 Sample directory:

 FidFile: smw140702_2_137_gHMBC

Pulse Sequence: gHMBC
Solvent: cdcl3
Data collected on: Jul  2 2014

 Temp. 25.0 C / 298.1 K
Operator: uowvnmrs

 Relax. delay 1.000 sec
 Acq. time 0.150 sec
 Width     7998.4 Hz
 2D Width 30165.9 Hz
 86 repetitions
 400 increments
OBSERVE   H1, 499.9049152 MHz
DATA PROCESSING
 Line broadening 3.0 Hz
 Sq. sine bell 0.075 sec
F1 DATA PROCESSING
 Line broadening 3.0 Hz
 Sq. sine bell 0.008 sec
FT size 2048 x 2048
Total time 12 hr, 11 min
```

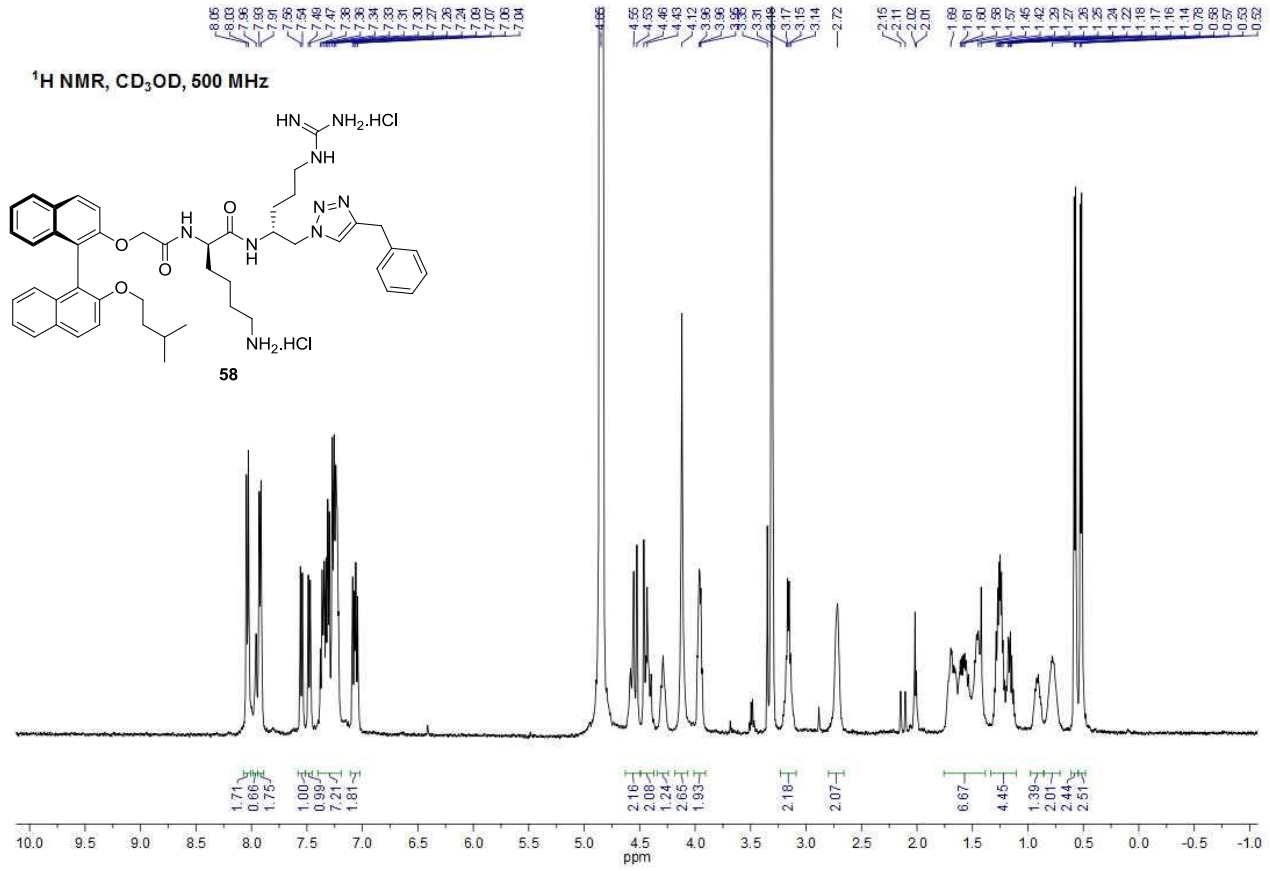


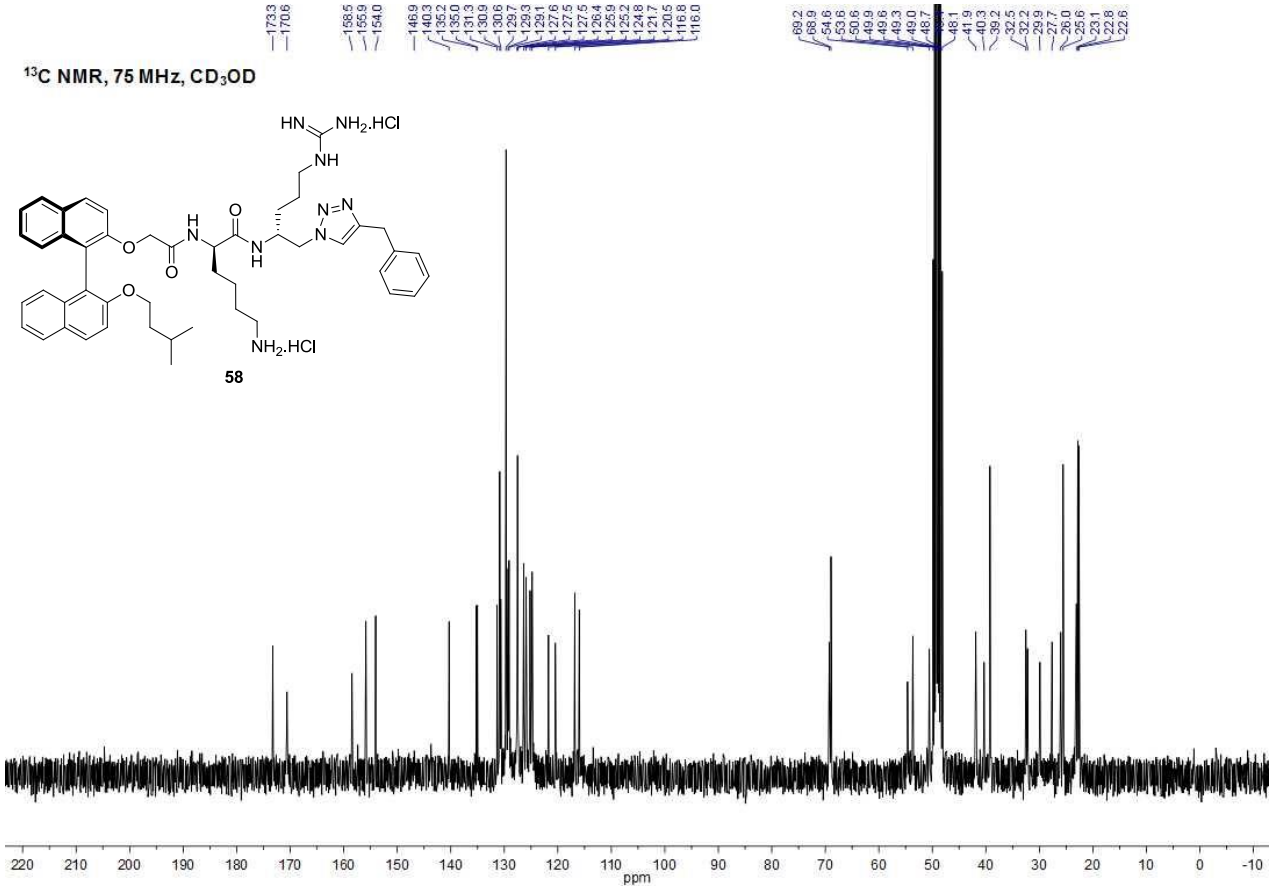

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
N
N=N
O
O
O
NH$_2$.HCl
56
ppm

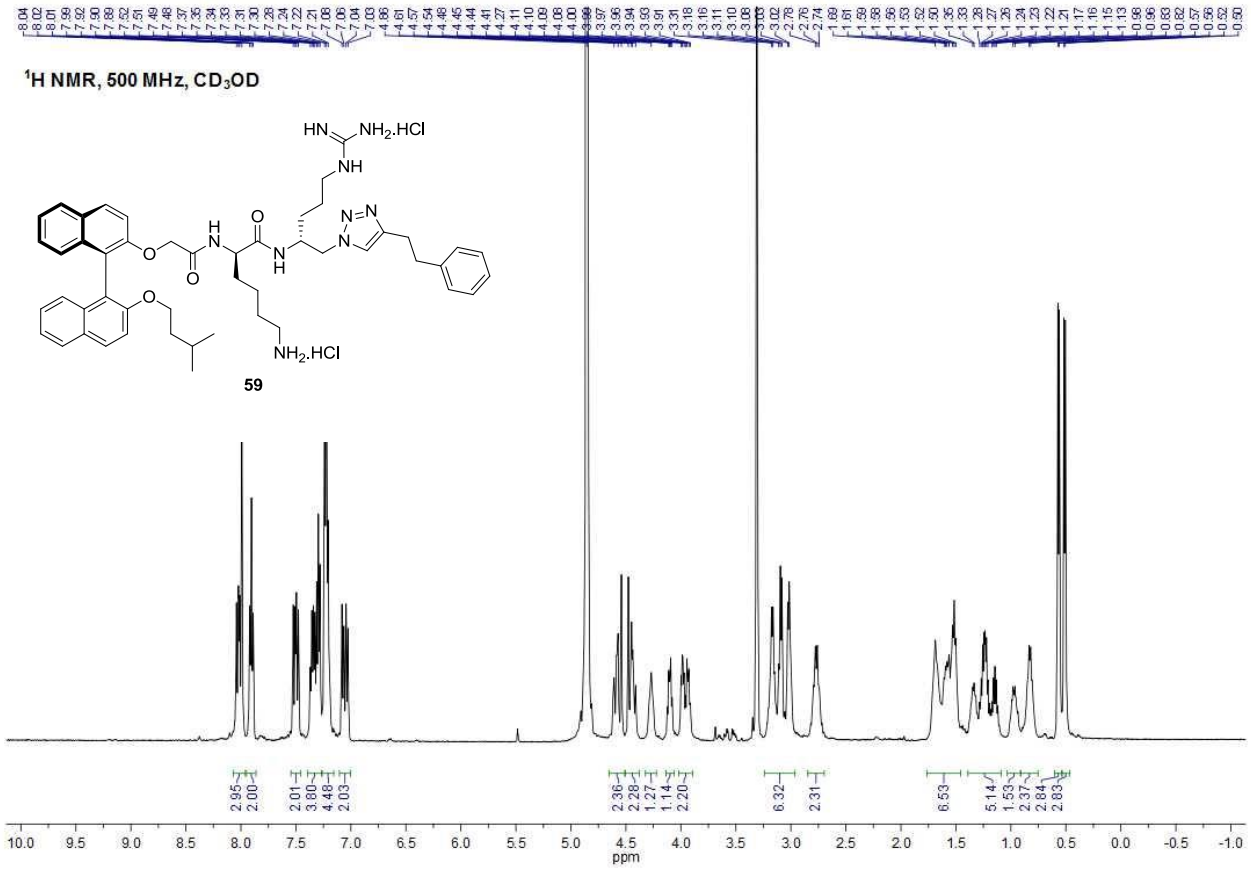

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
O
H
N
N
N=N
O
O
O
NH$_2$.HCl
56
ppm

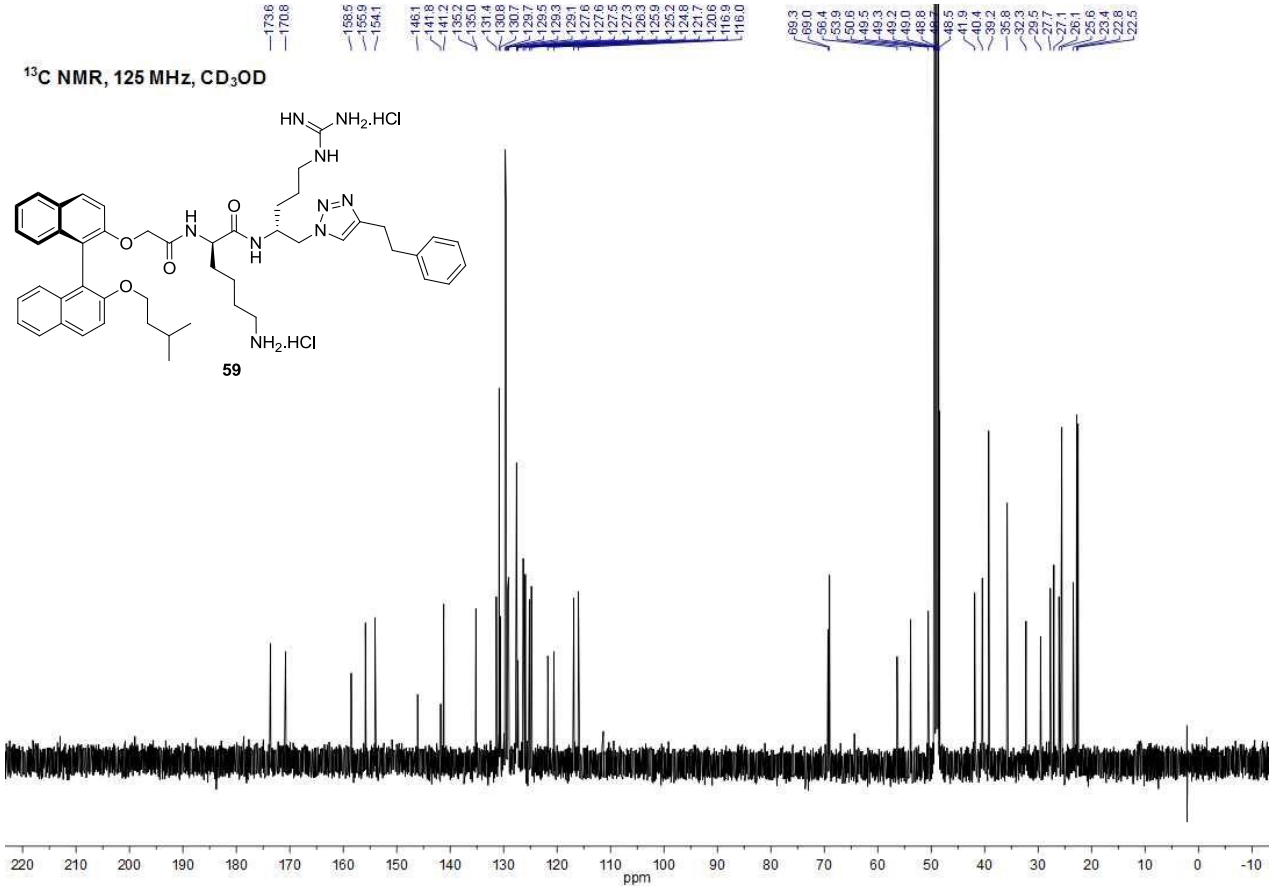

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
57
ppm

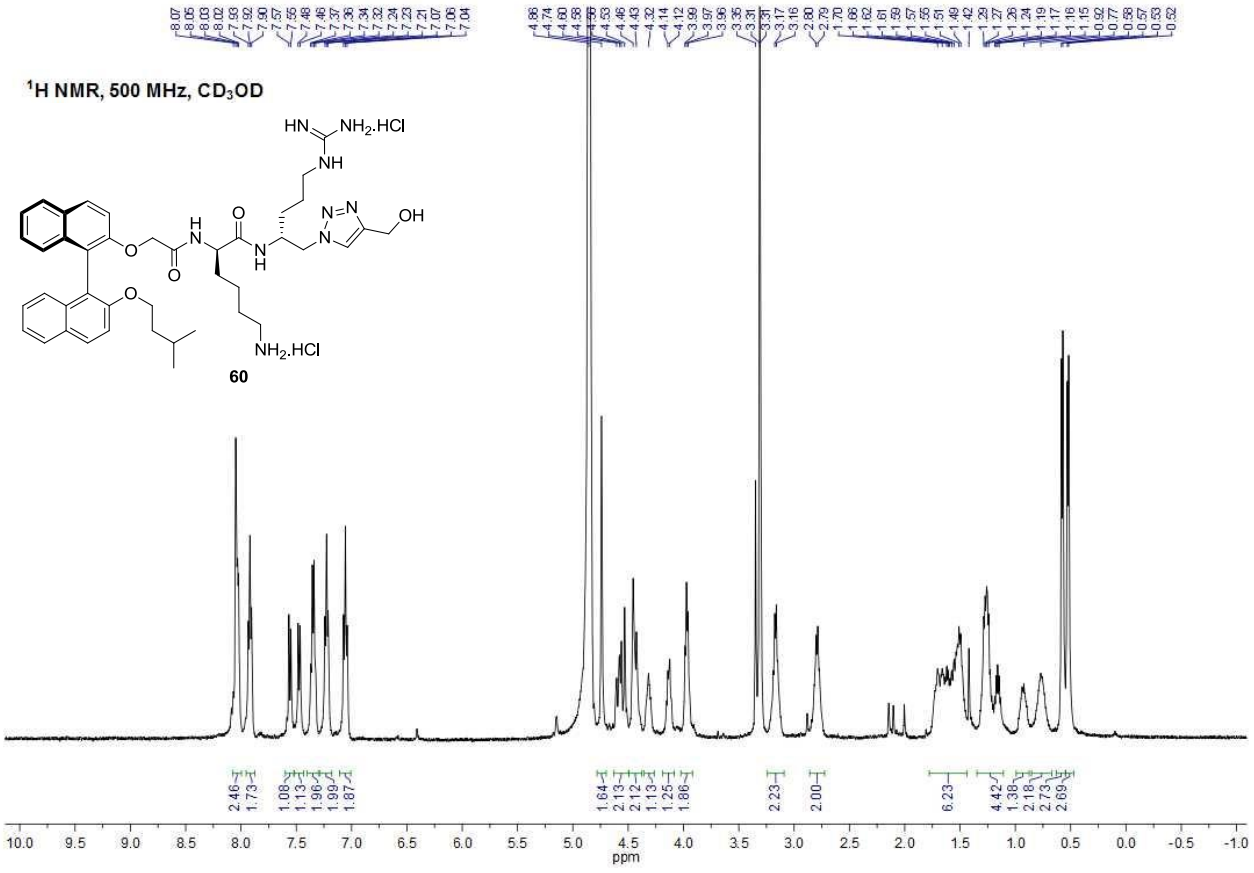

^{13}C NMR, 125 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
57
ppm

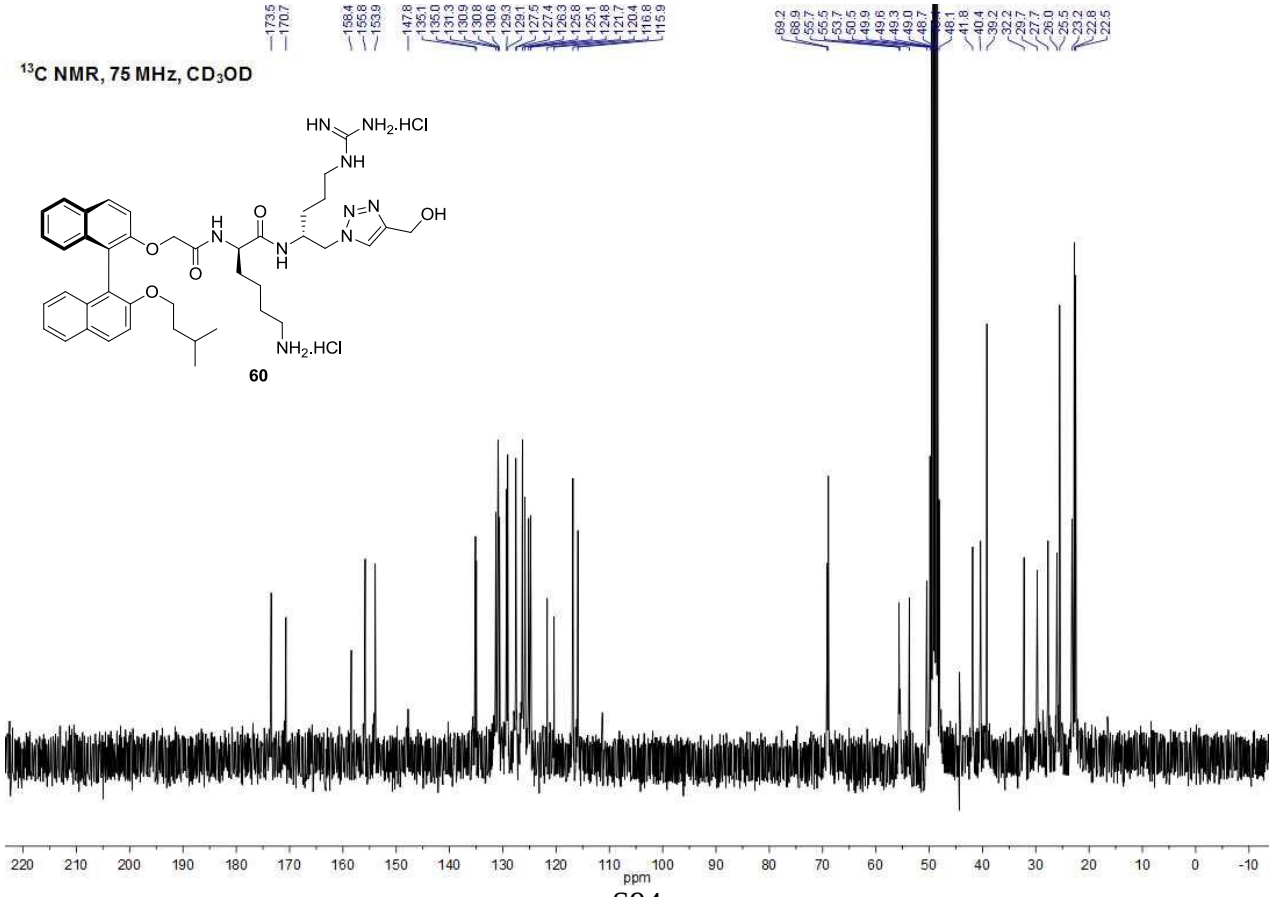

^{1}H NMR, CD$_3$OD, 500 MHz
HN
NH$_2$.HCl
NH
NH$_2$.HCl
58

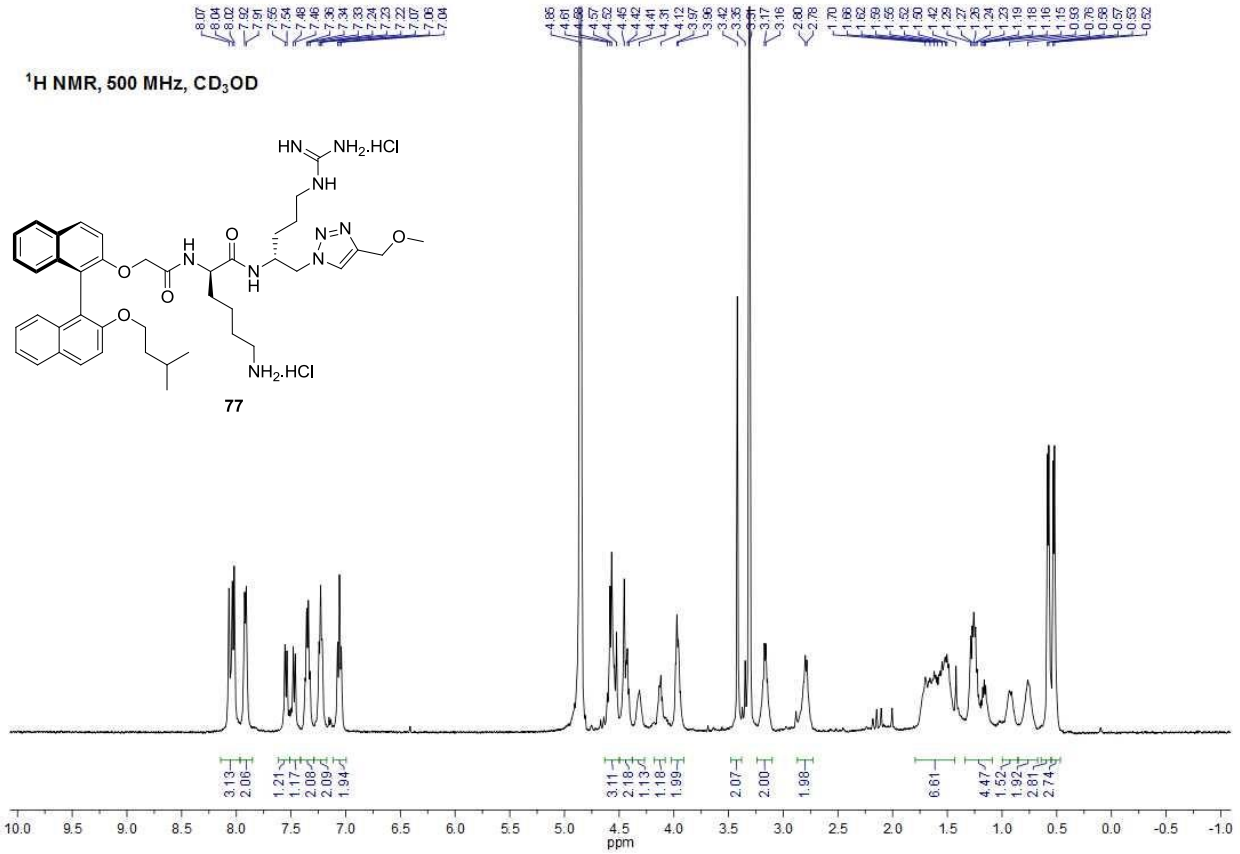

^{13}C NMR, 75 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
NH$_2$.HCl
58

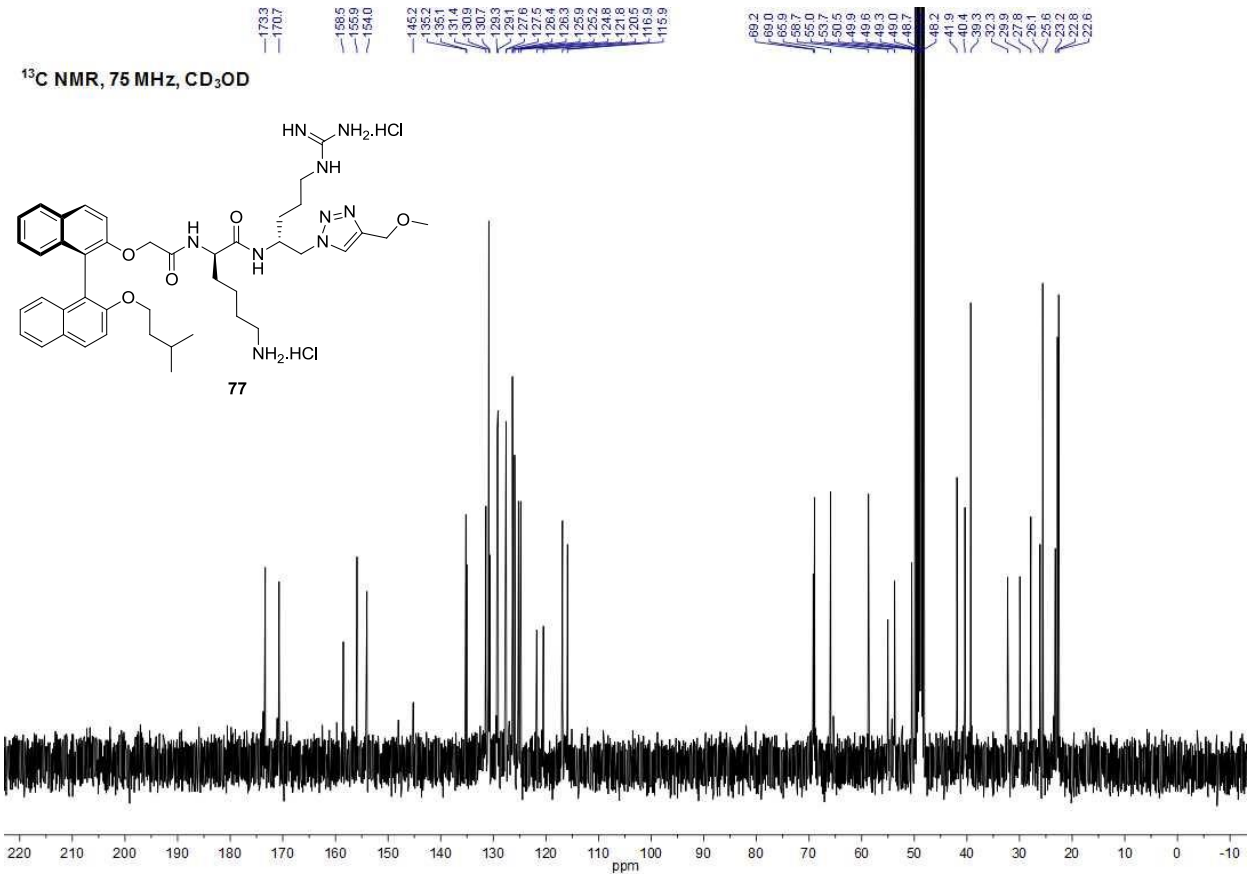

¹H NMR, 500 MHz, CD3OD
HN
NH2.HCl
NH
N=N
H
O
N
O
O
O
N
H
NH2.HCl
59
ppm

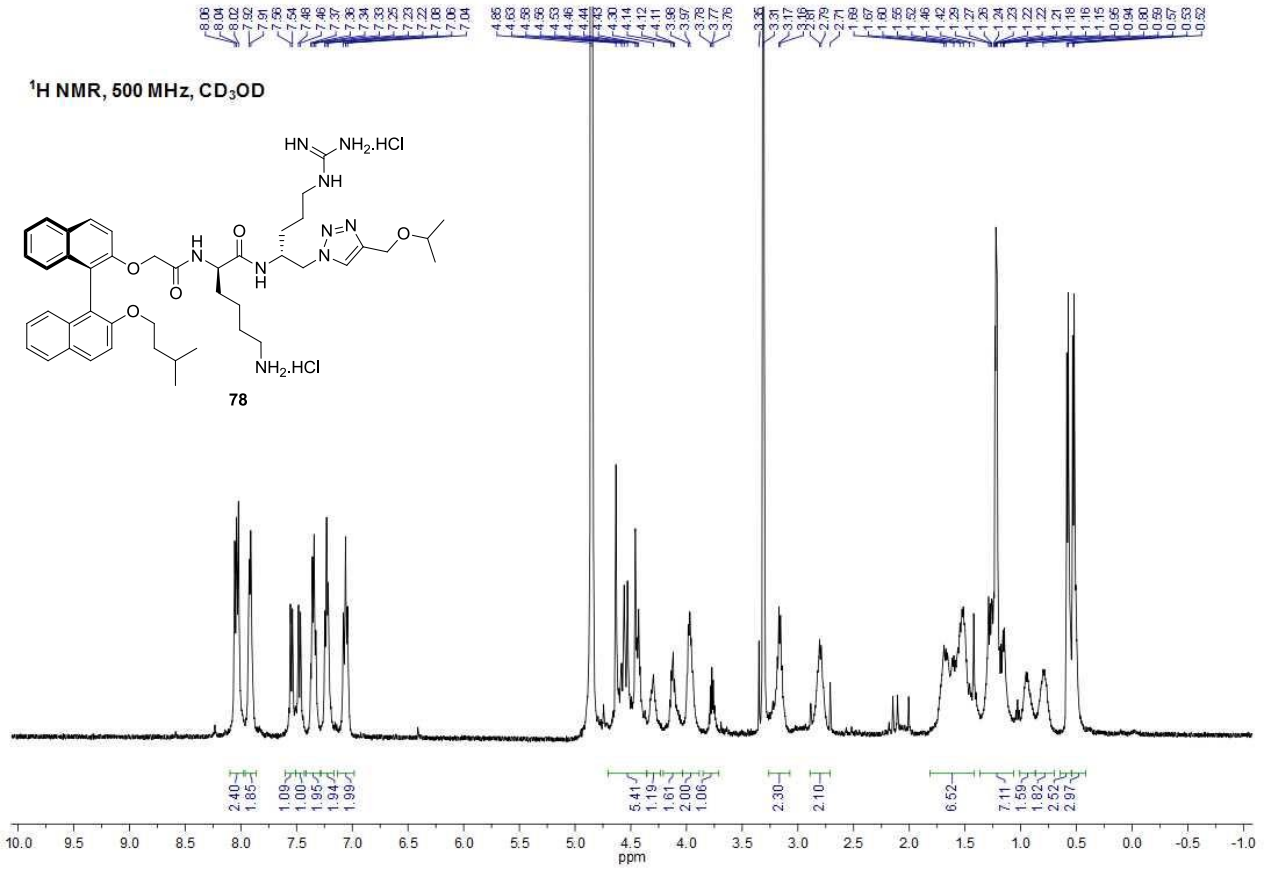

¹³C NMR, 125 MHz, CD3OD
HN
NH2.HCl
NH
N=N
H
O
N
O
O
O
N
H
NH2.HCl
59
ppm

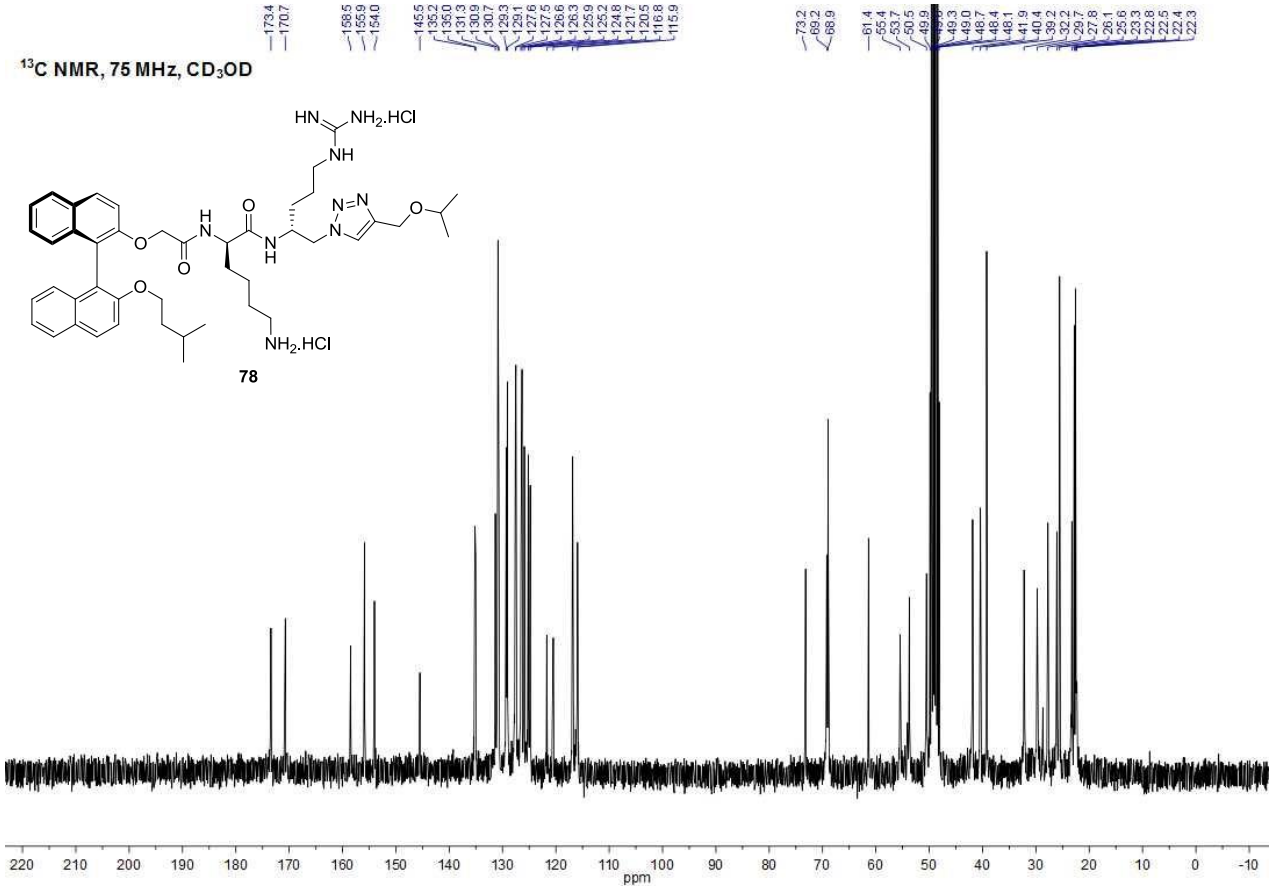

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
OH
O
H
N
O
N
H
O
O
NH$_2$.HCl
60
ppm

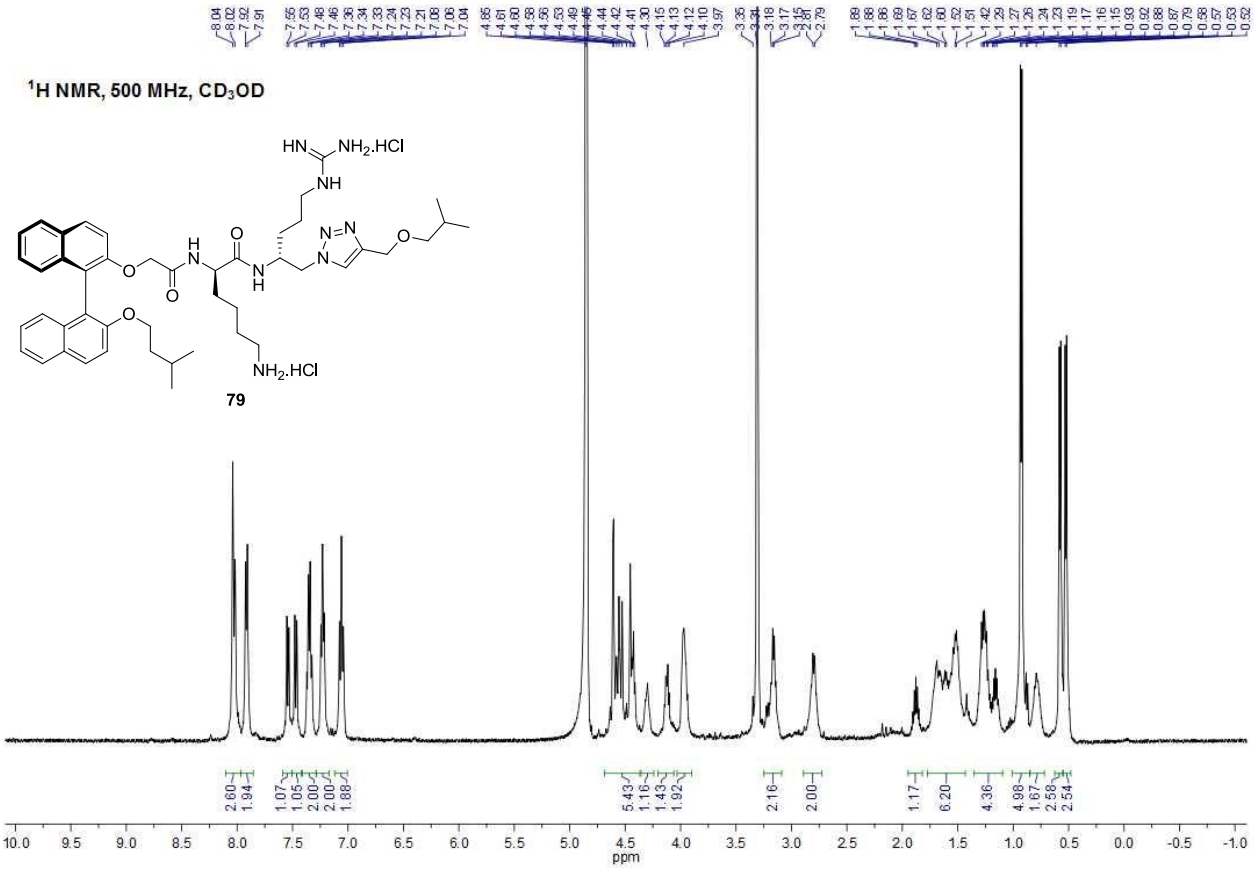

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
OH
O
H
N
O
N
H
O
O
NH$_2$.HCl
60
ppm

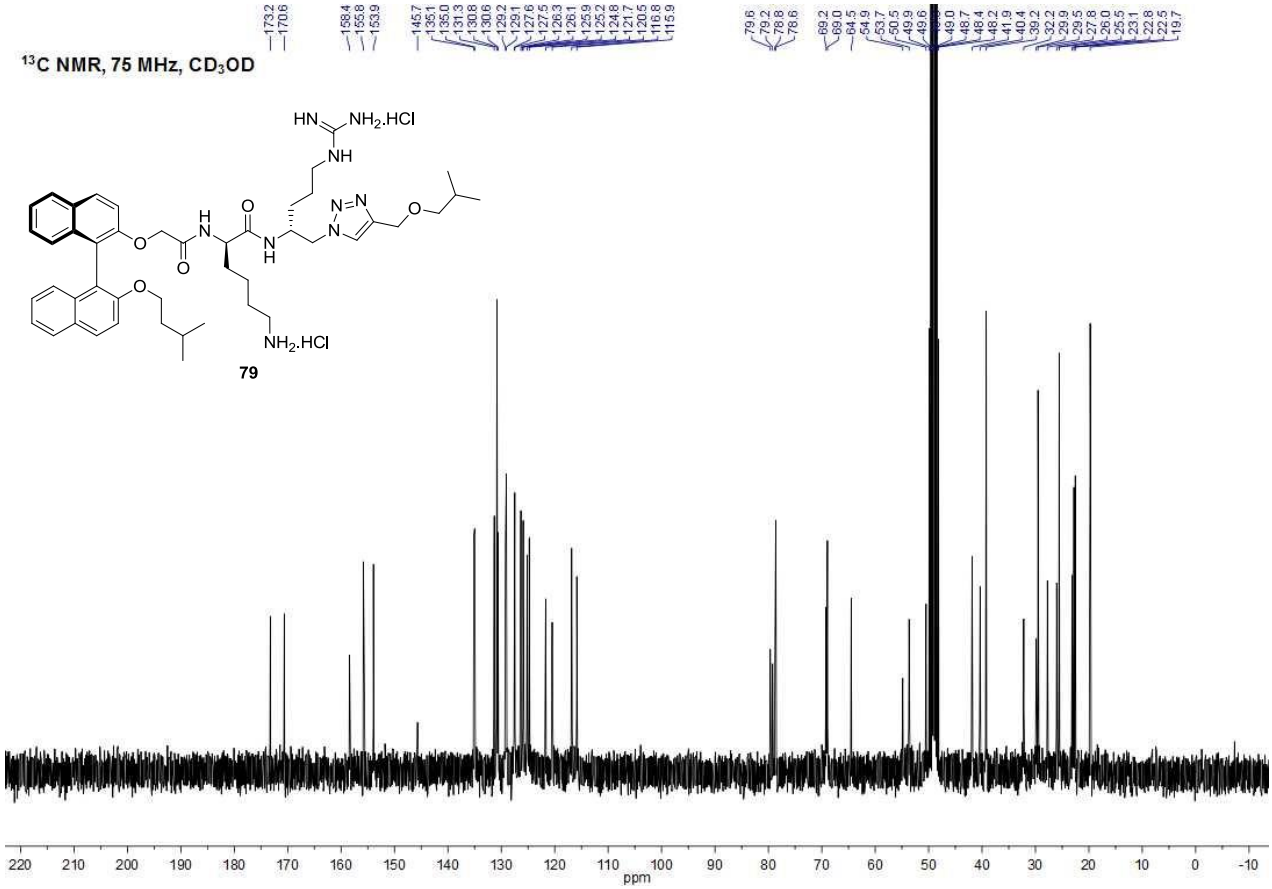

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
77
ppm

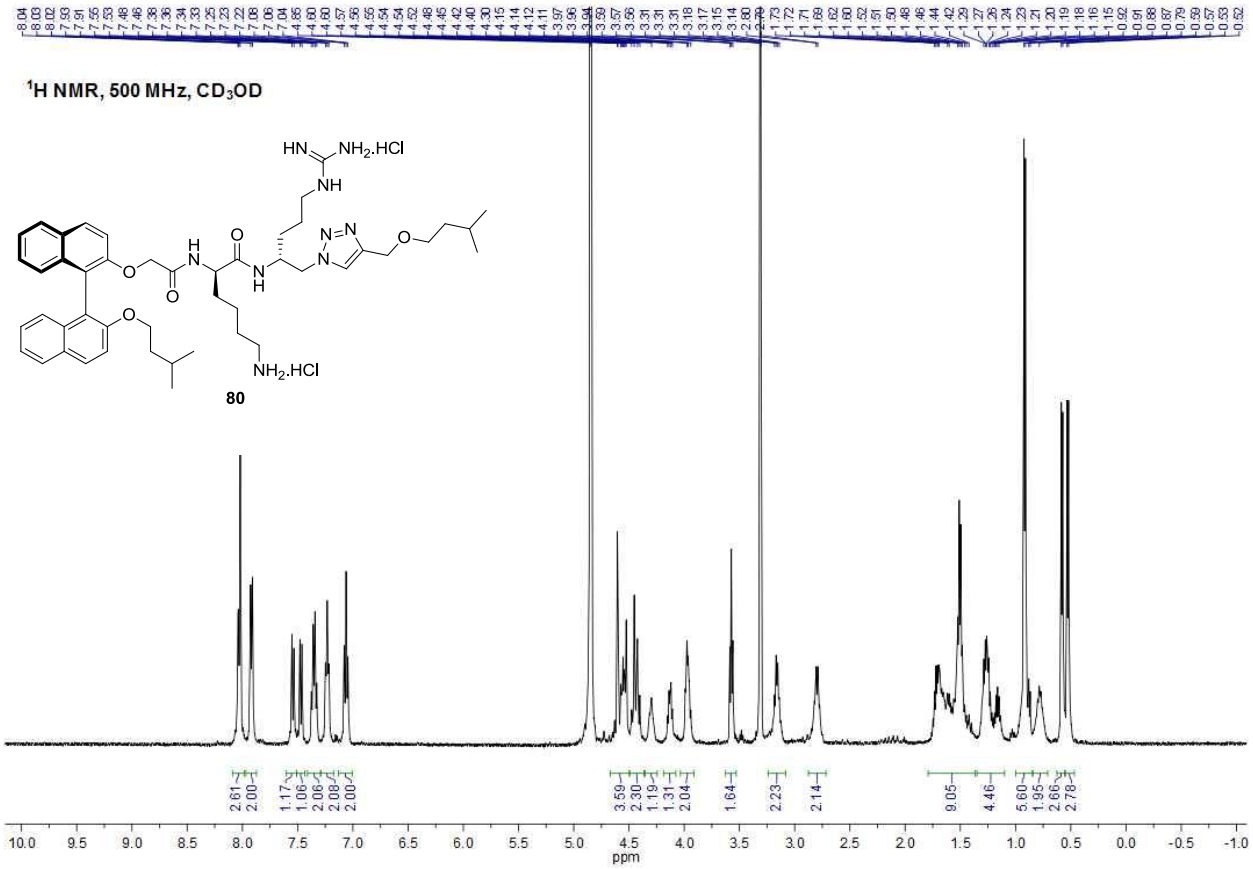

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
77
ppm

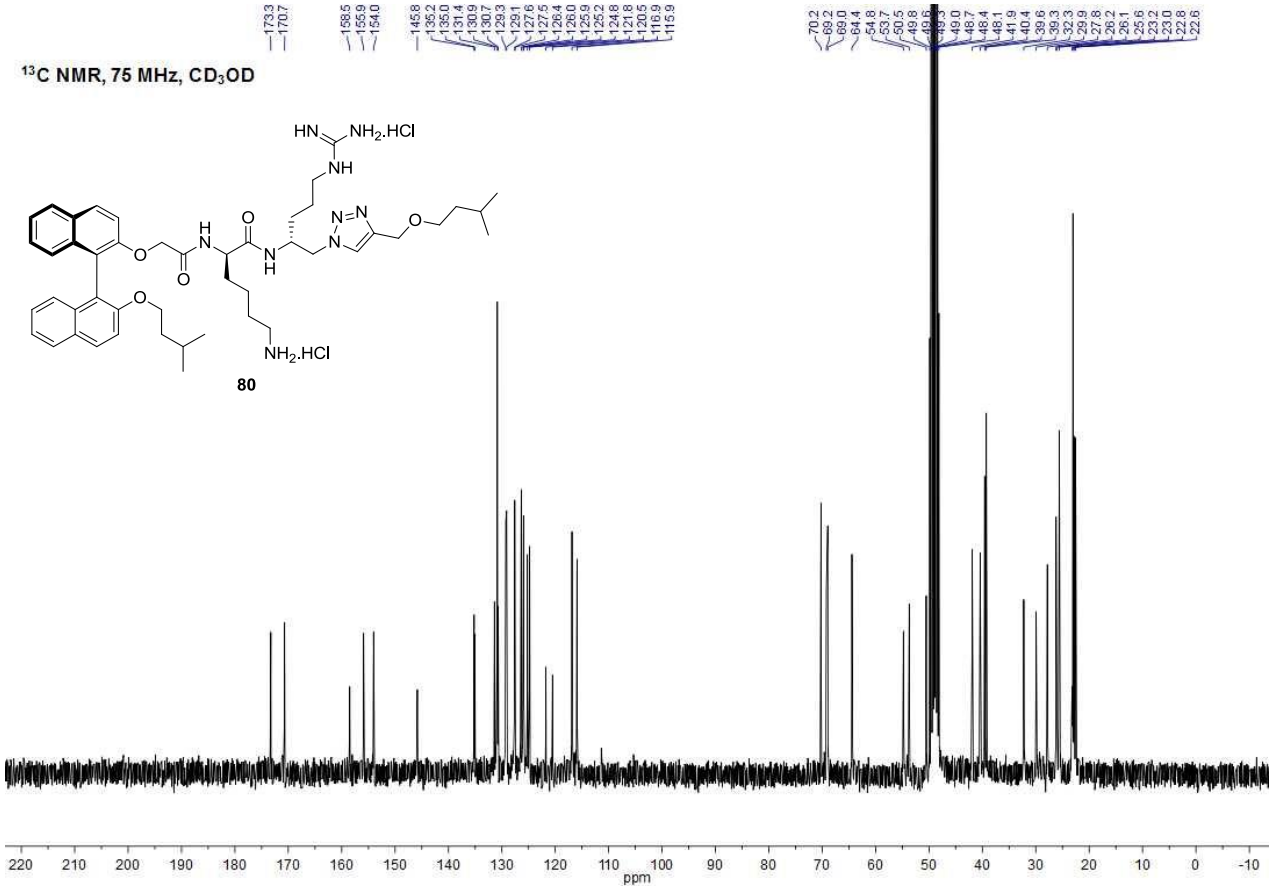

^{1}H NMR, 500 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
NH$_2$.HCl
78
ppm

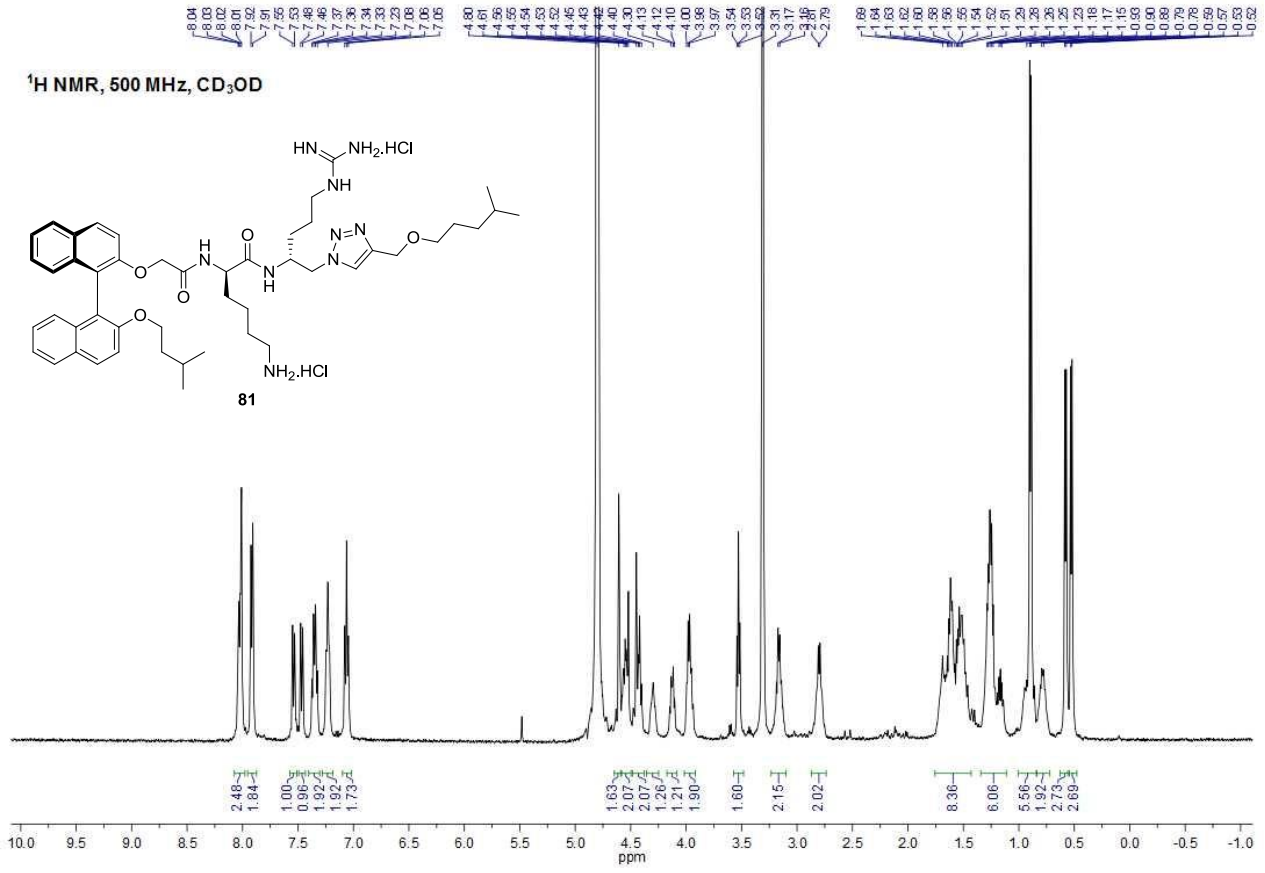

^{13}C NMR, 75 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
NH$_2$.HCl
78
ppm

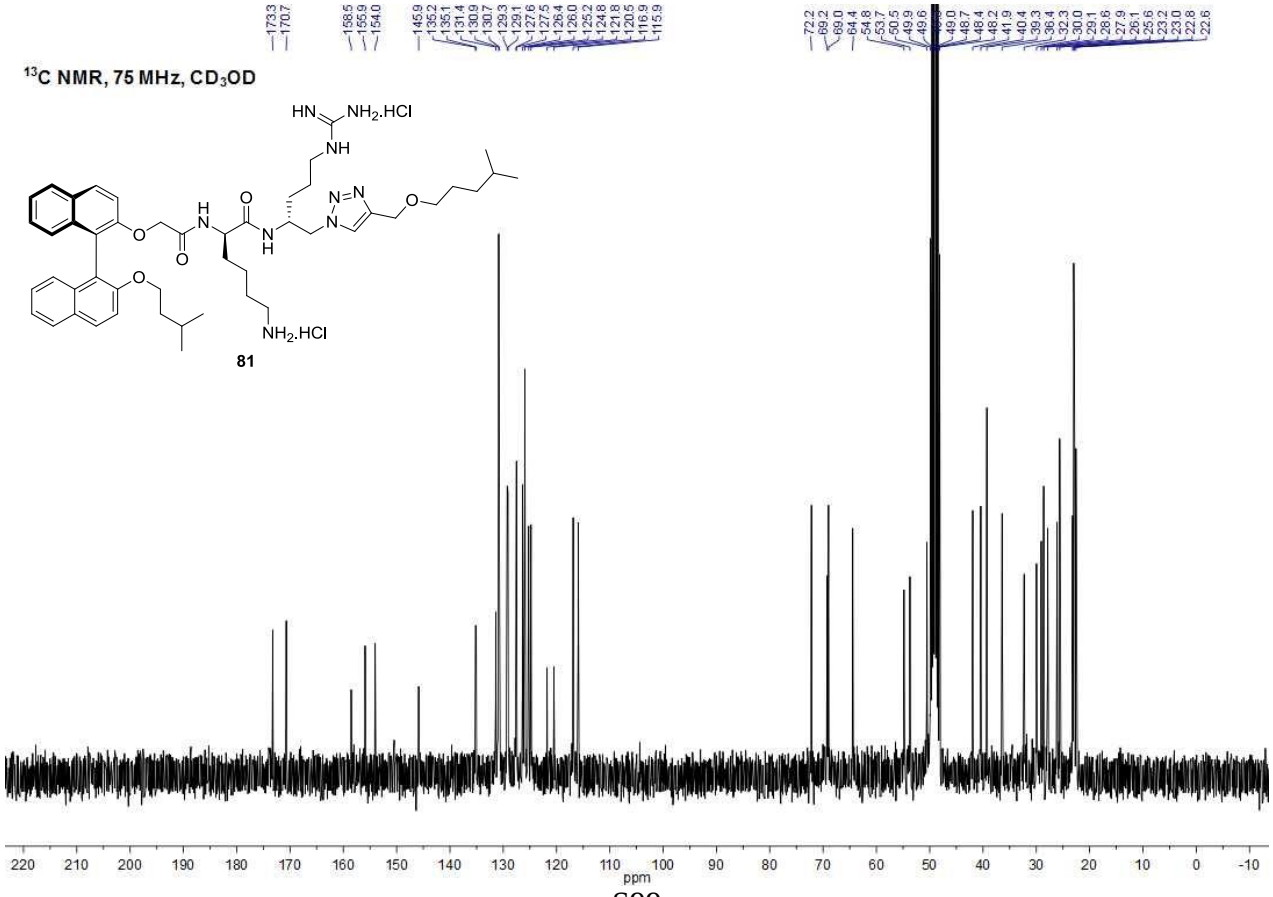

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
NH$_2$.HCl
79
ppm

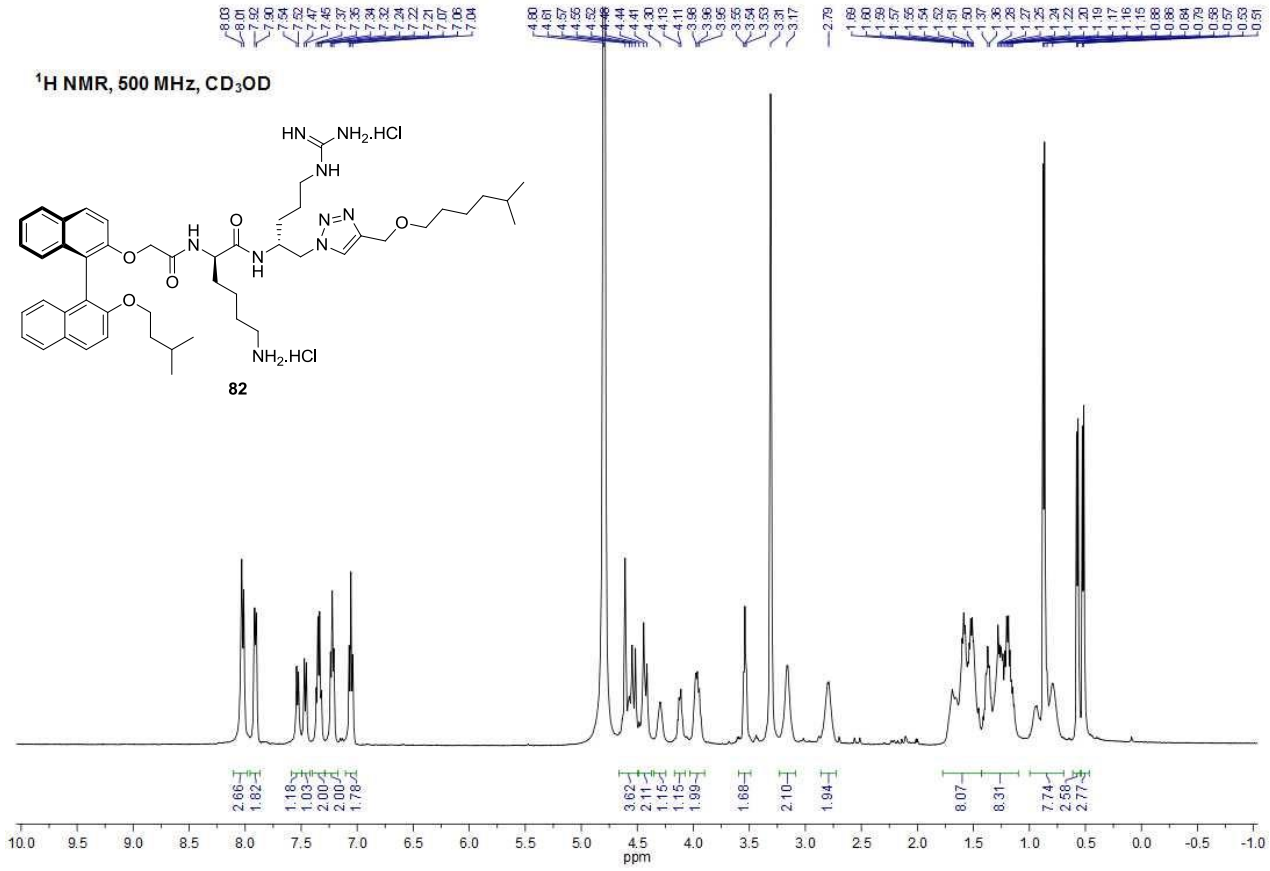

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
NH$_2$.HCl
79
ppm

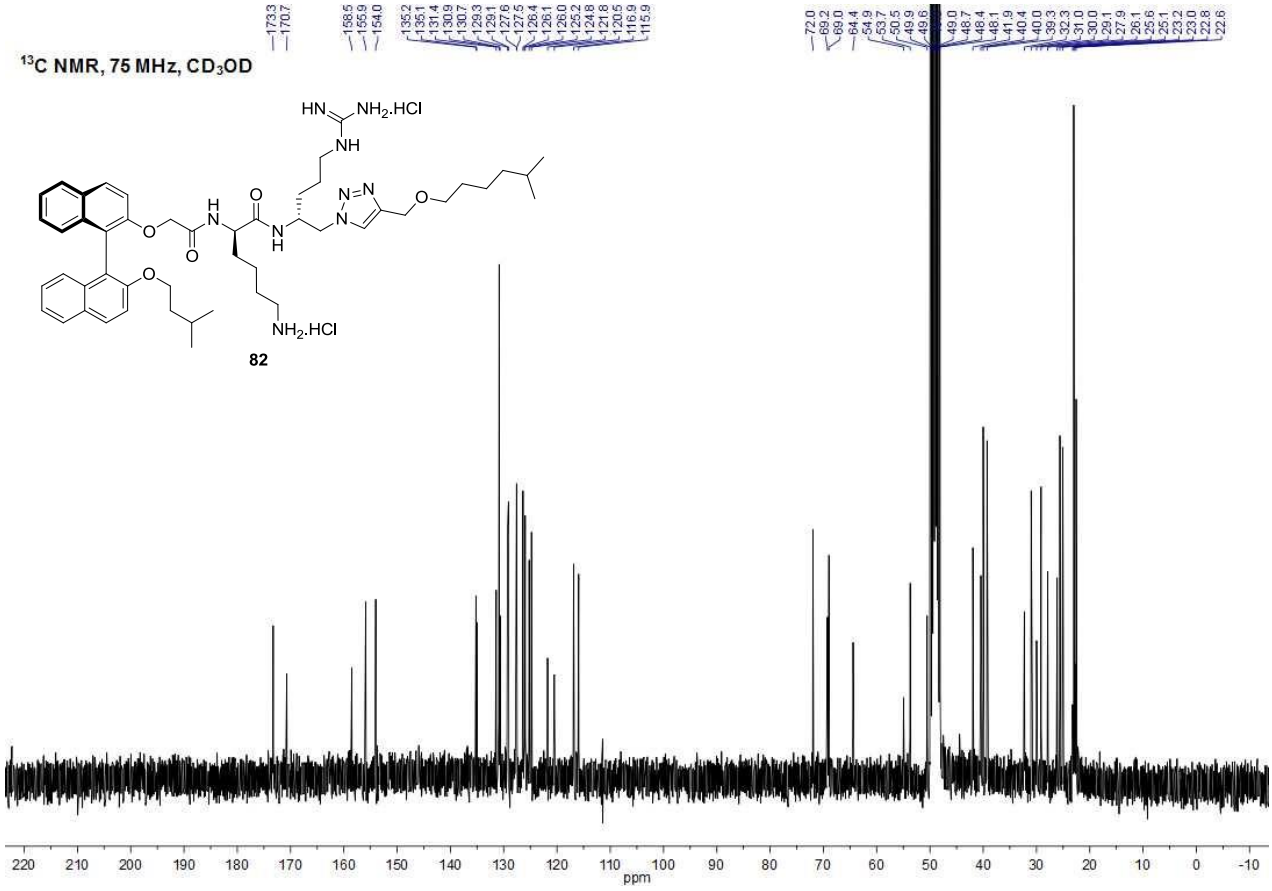

¹H NMR, 500 MHz, CD3OD
HN
NH2.HCl
NH
N=N
O
H
N
O
NH2.HCl
80
ppm

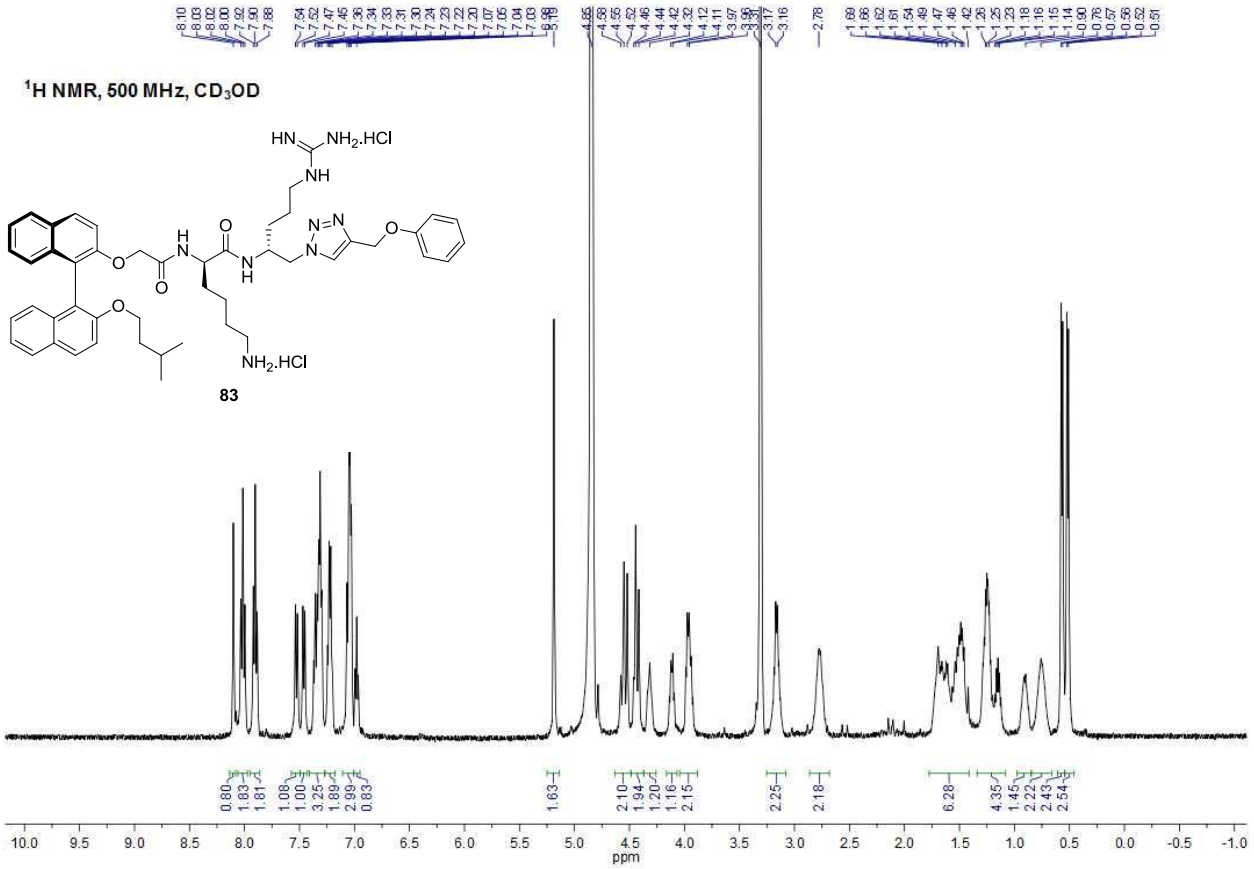

¹³C NMR, 75 MHz, CD3OD
HN
NH2.HCl
NH
N=N
O
H
N
O
NH2.HCl
80
ppm

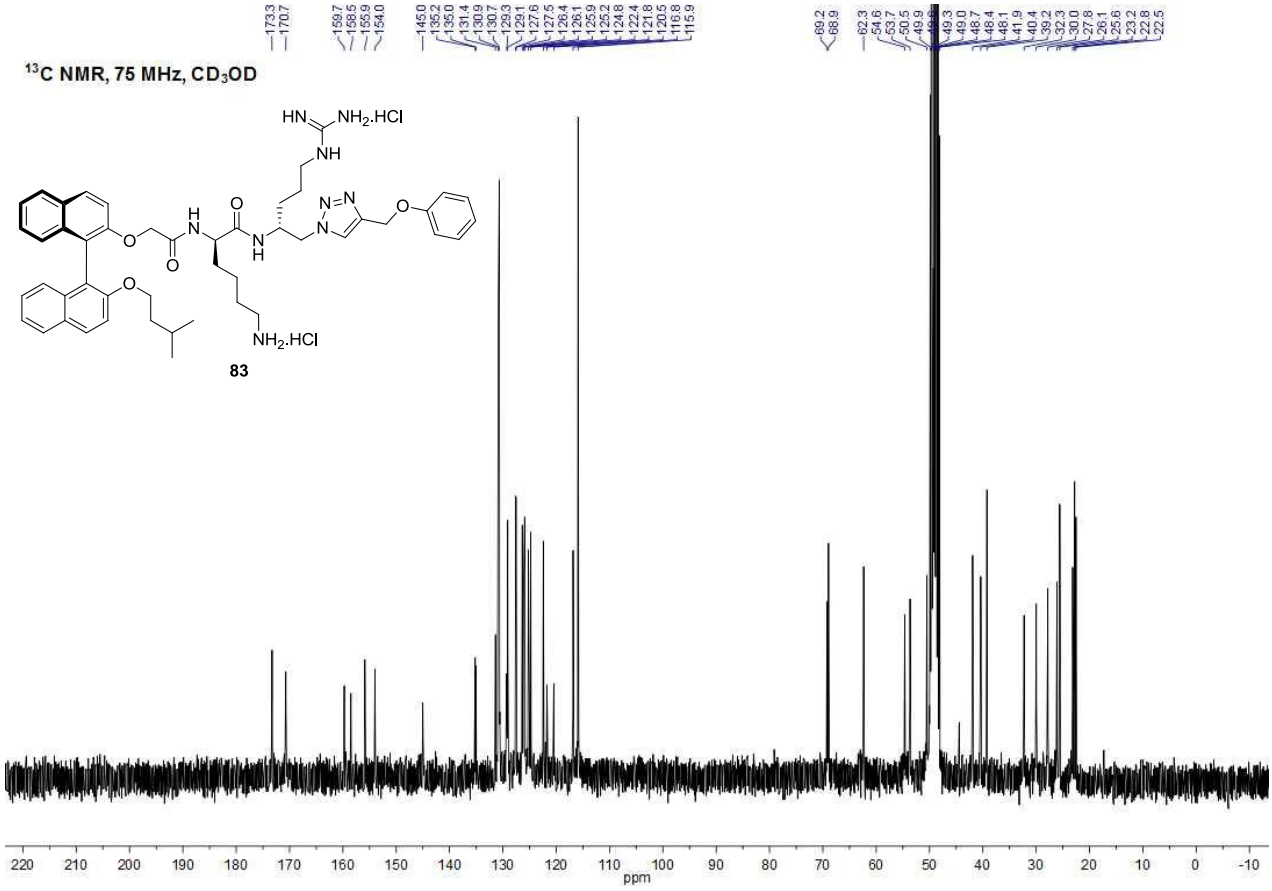

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
NH$_2$.HCl
81
ppm

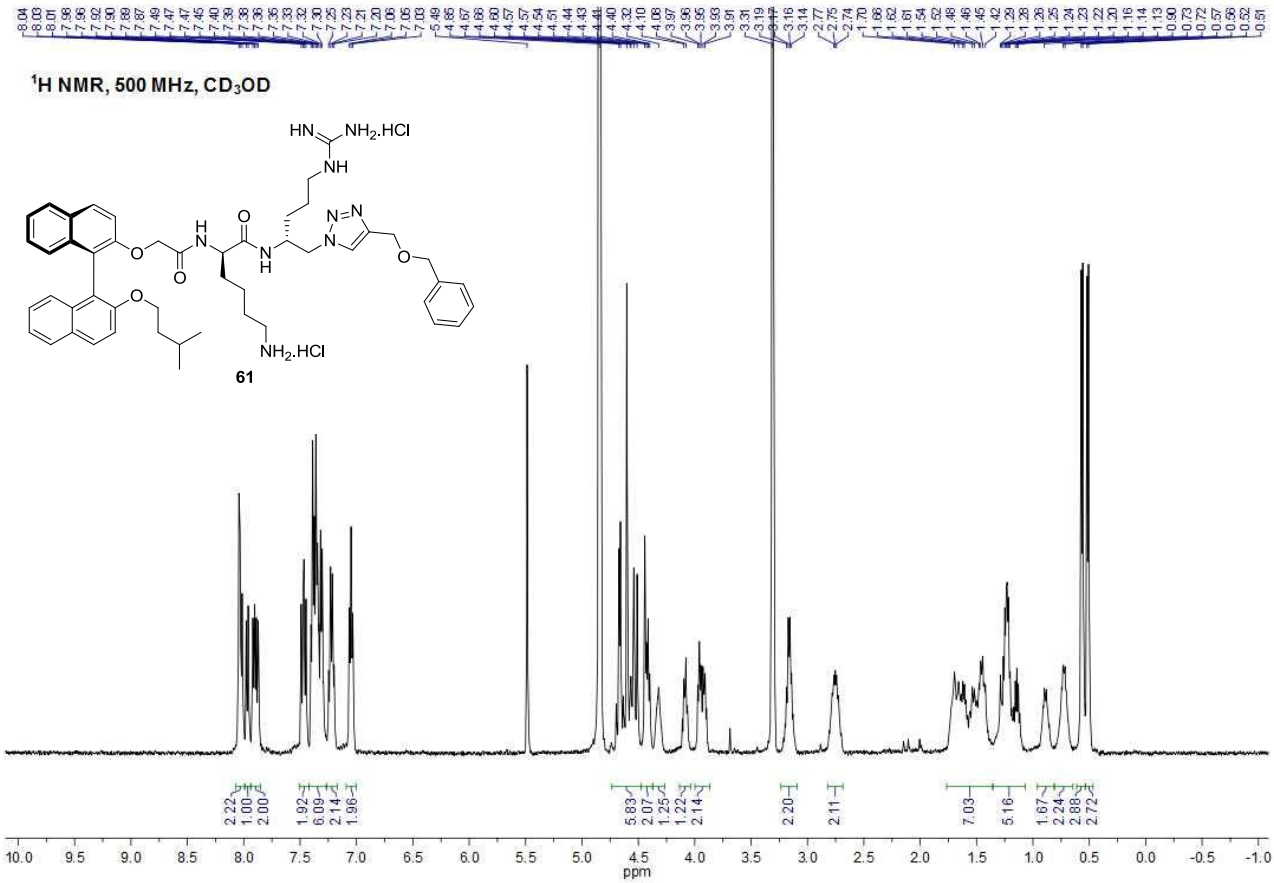

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
NH$_2$.HCl
81
ppm

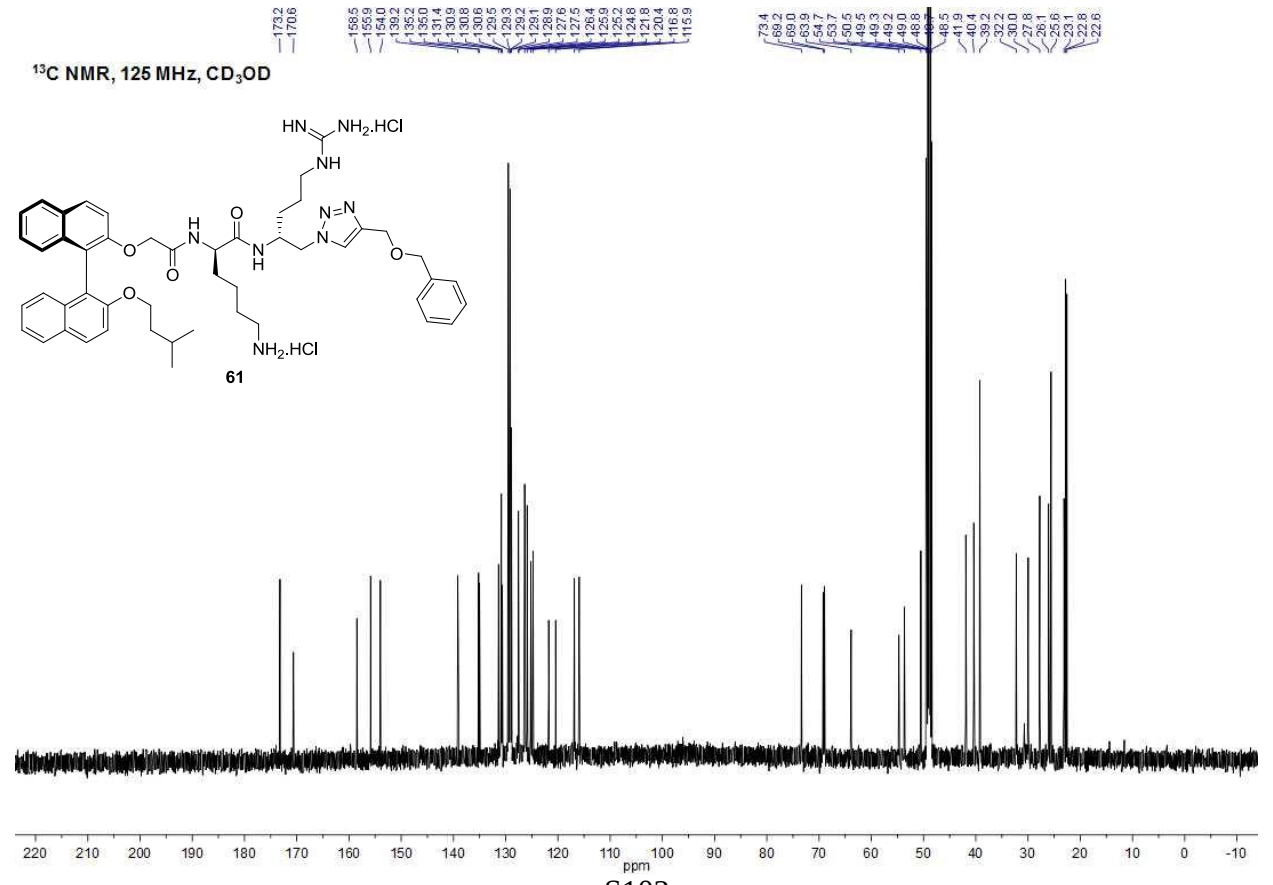

^{1}H NMR, 500 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
82
ppm

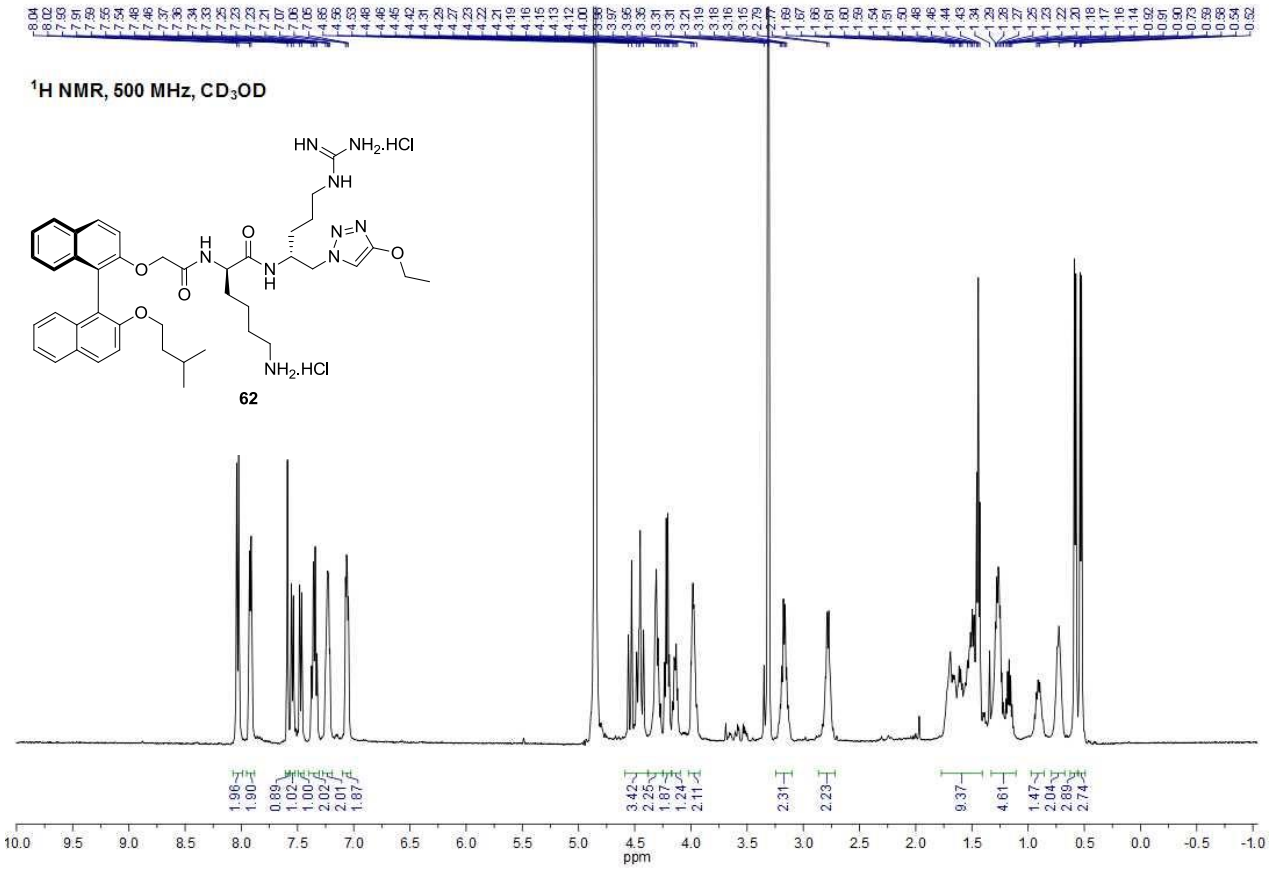

^{13}C NMR, 75 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
82
ppm

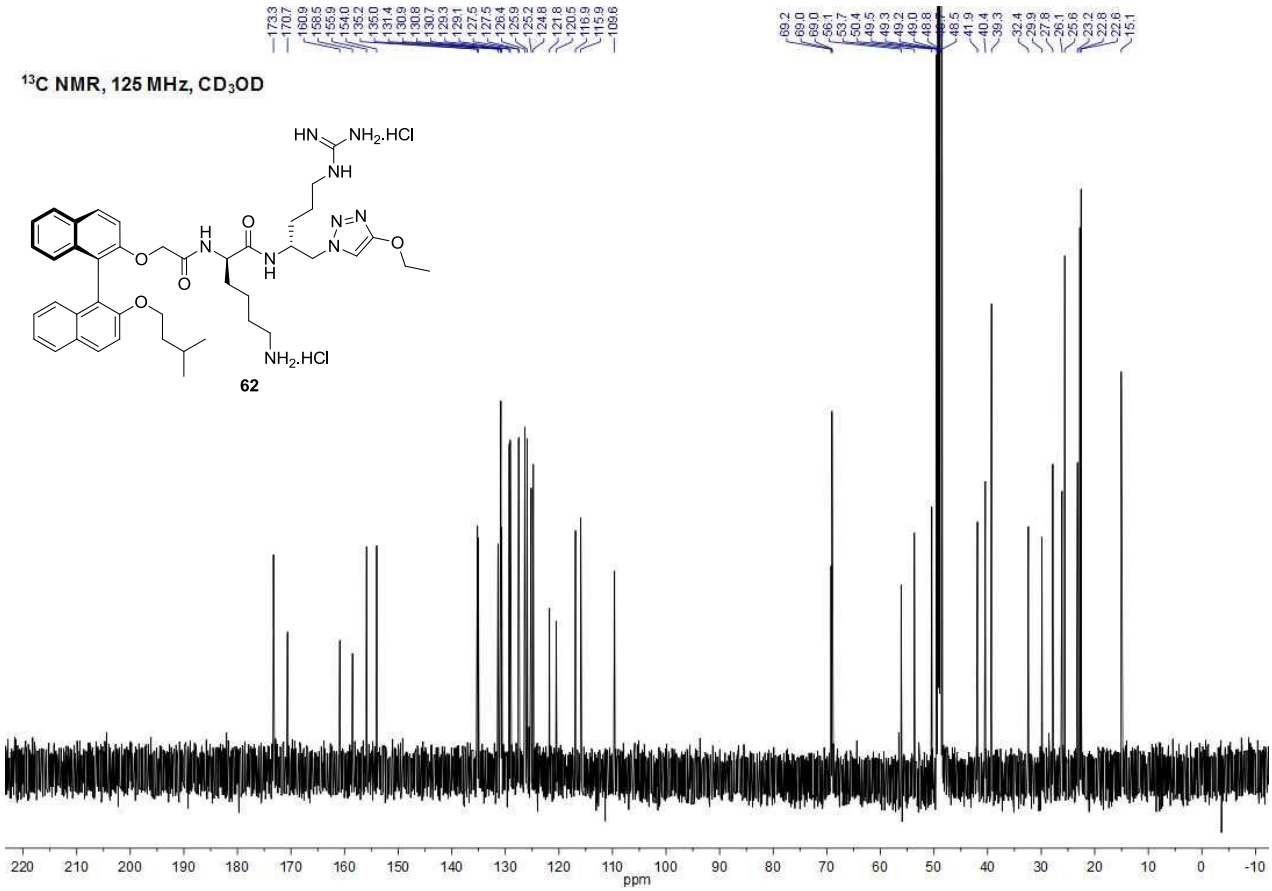

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
83
ppm

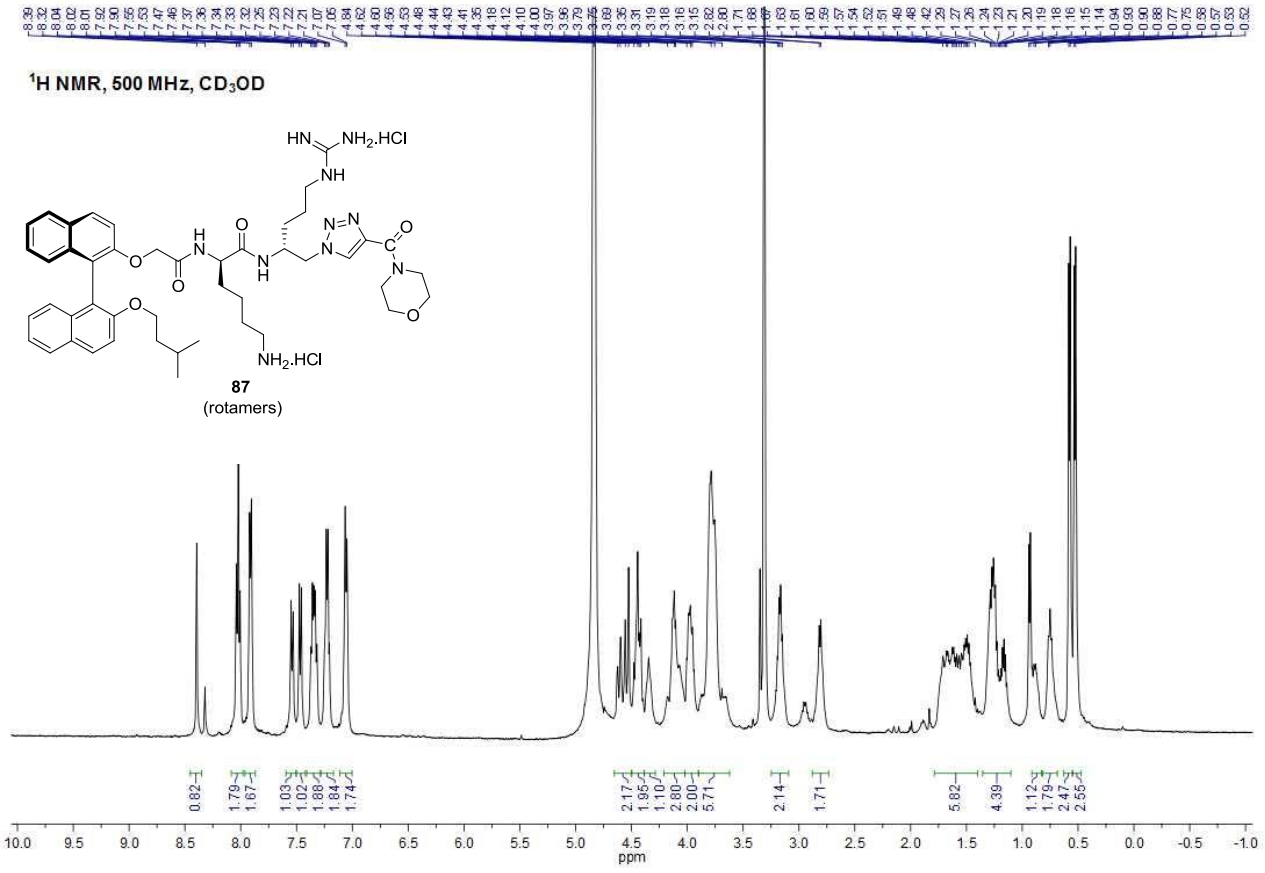

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
83
ppm

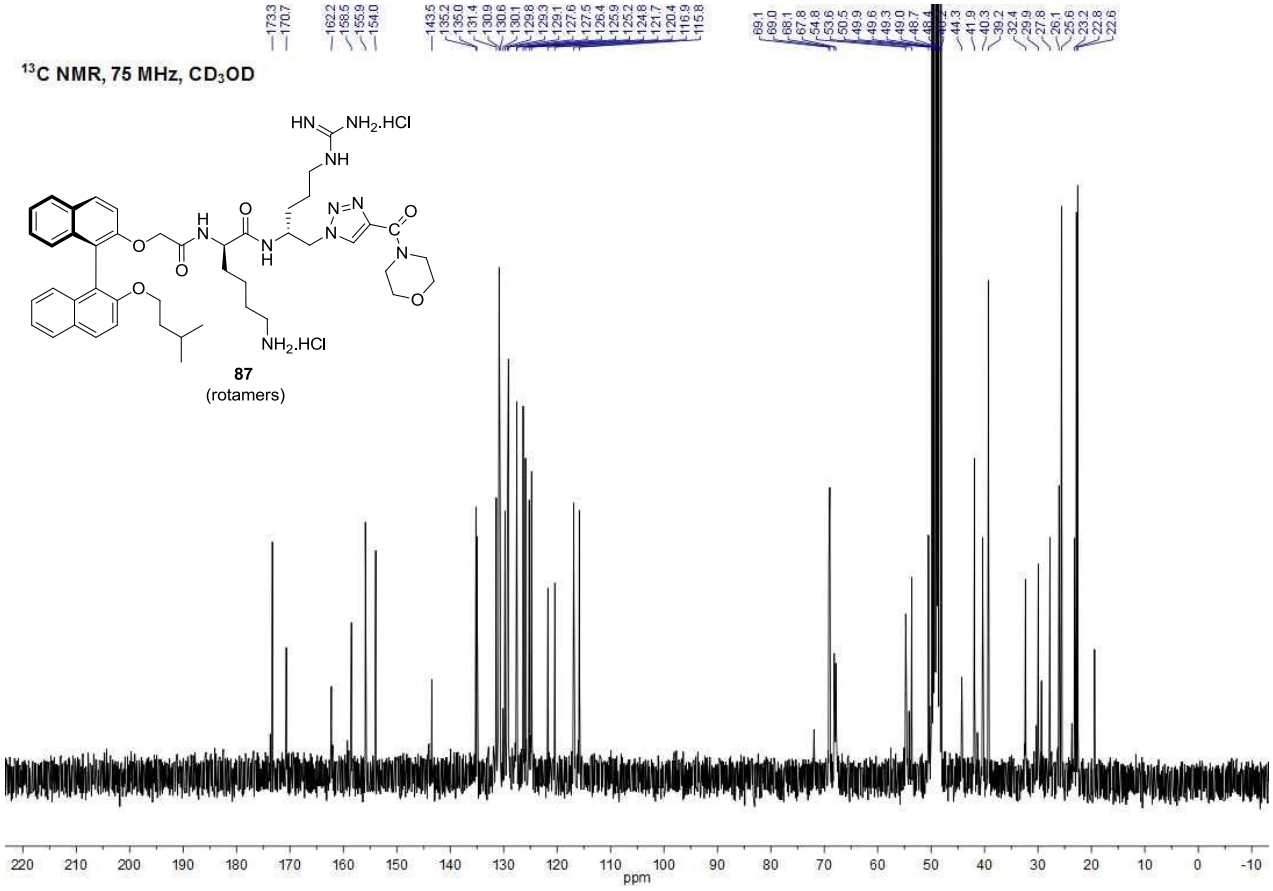

¹H NMR, 500 MHz, CD3OD
HN
NH2.HCl
NH
O
H
N
N
N
O
O
O
O
NH2.HCl
61
ppm

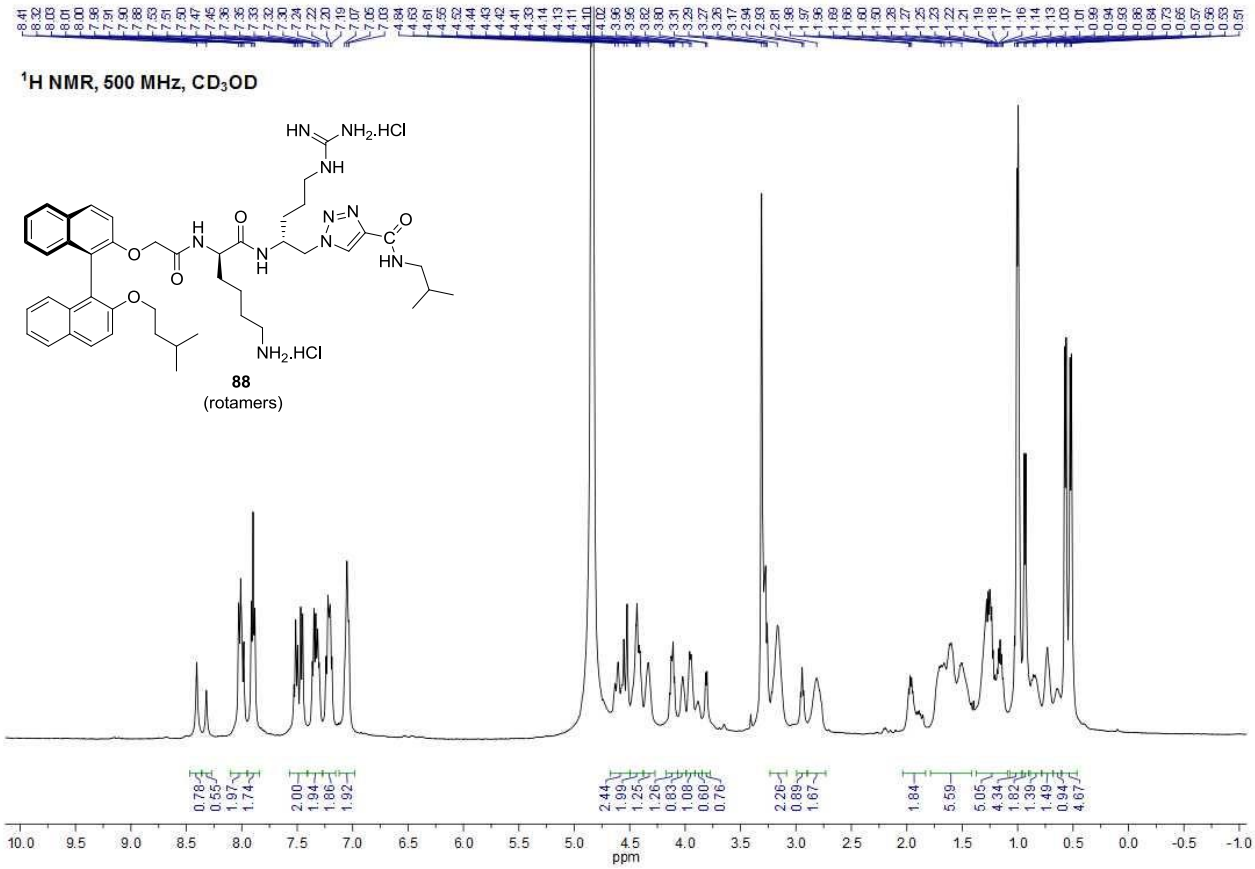

¹³C NMR, 125 MHz, CD3OD
HN
NH2.HCl
NH
O
H
N
N
N
O
O
O
O
NH2.HCl
61
ppm

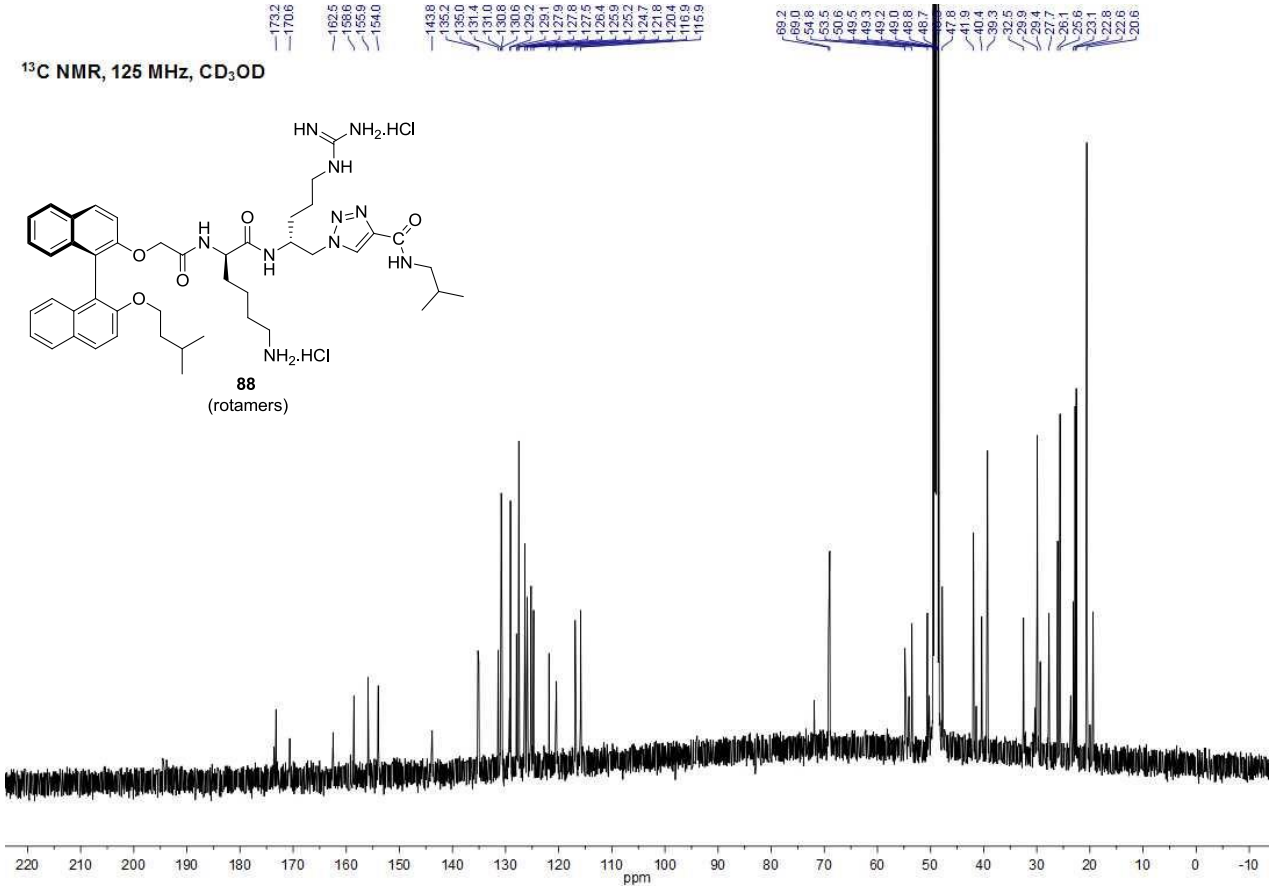

^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
62
ppm

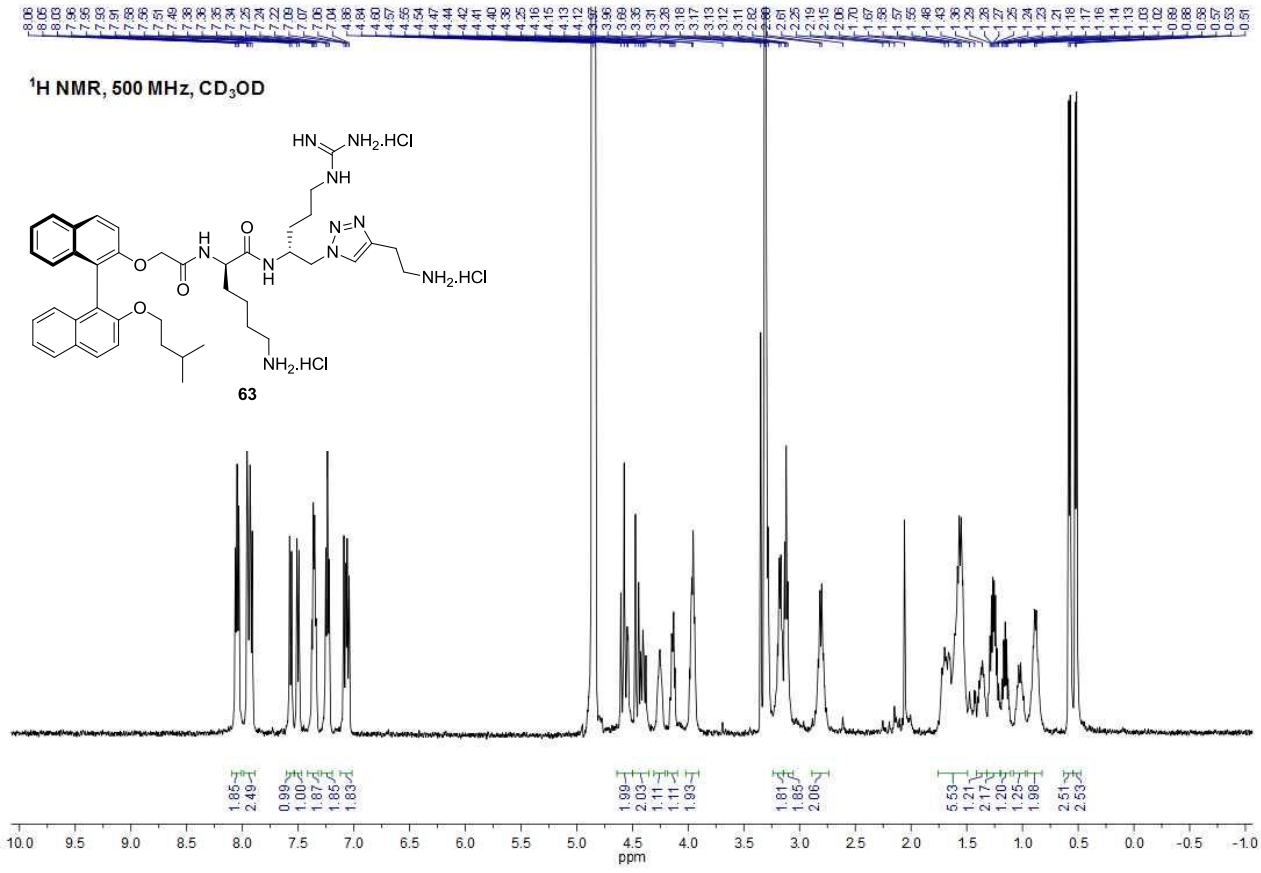

^{13}C NMR, 125 MHz, CD_3OD
HN
NH$_2$.HCl
NH
N=N
O
H
N
O
O
O
O
NH$_2$.HCl
62
ppm

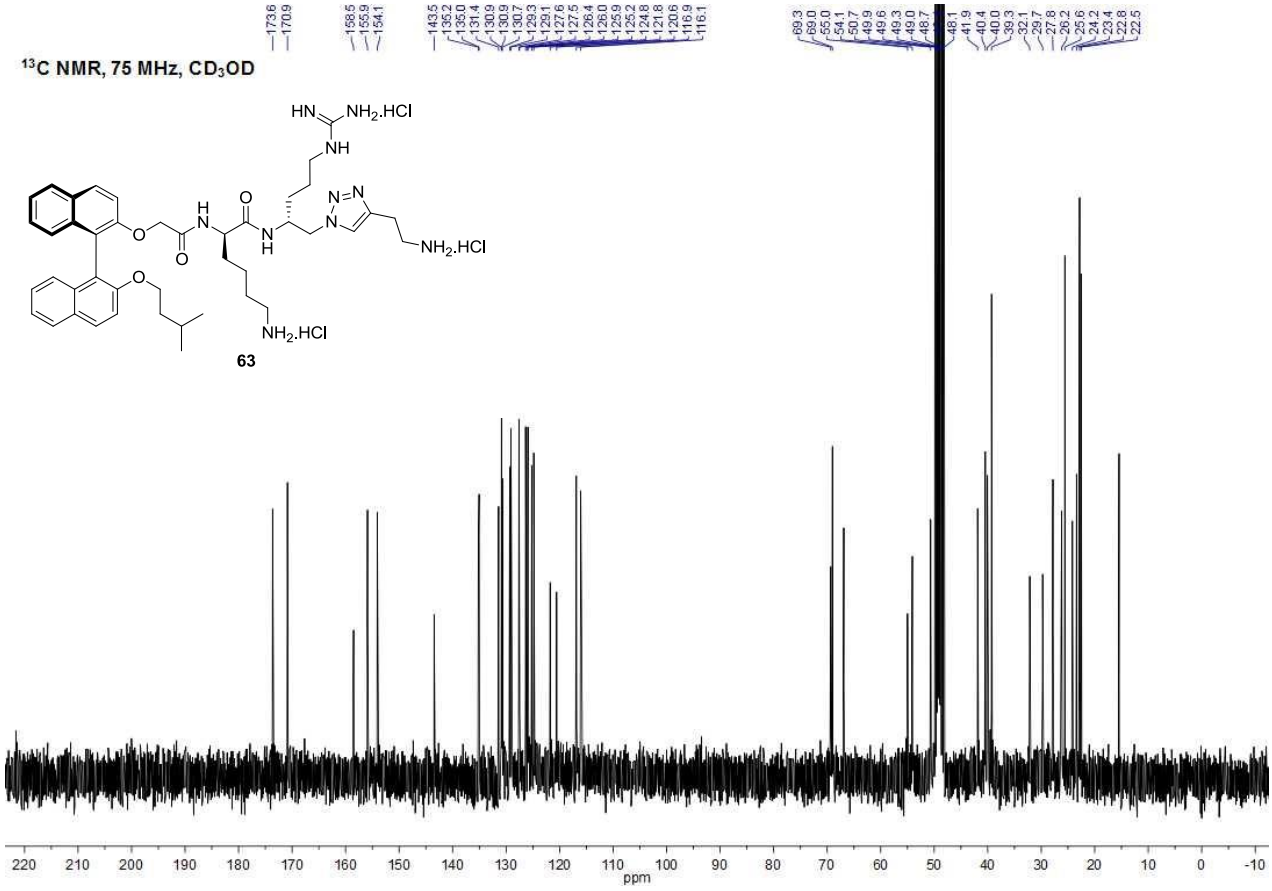

^{1}H NMR, 500 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
O
H
N
O
N
N
N
O
O
O
O
N
O
NH$_2$.HCl
87
(rotamers)
ppm

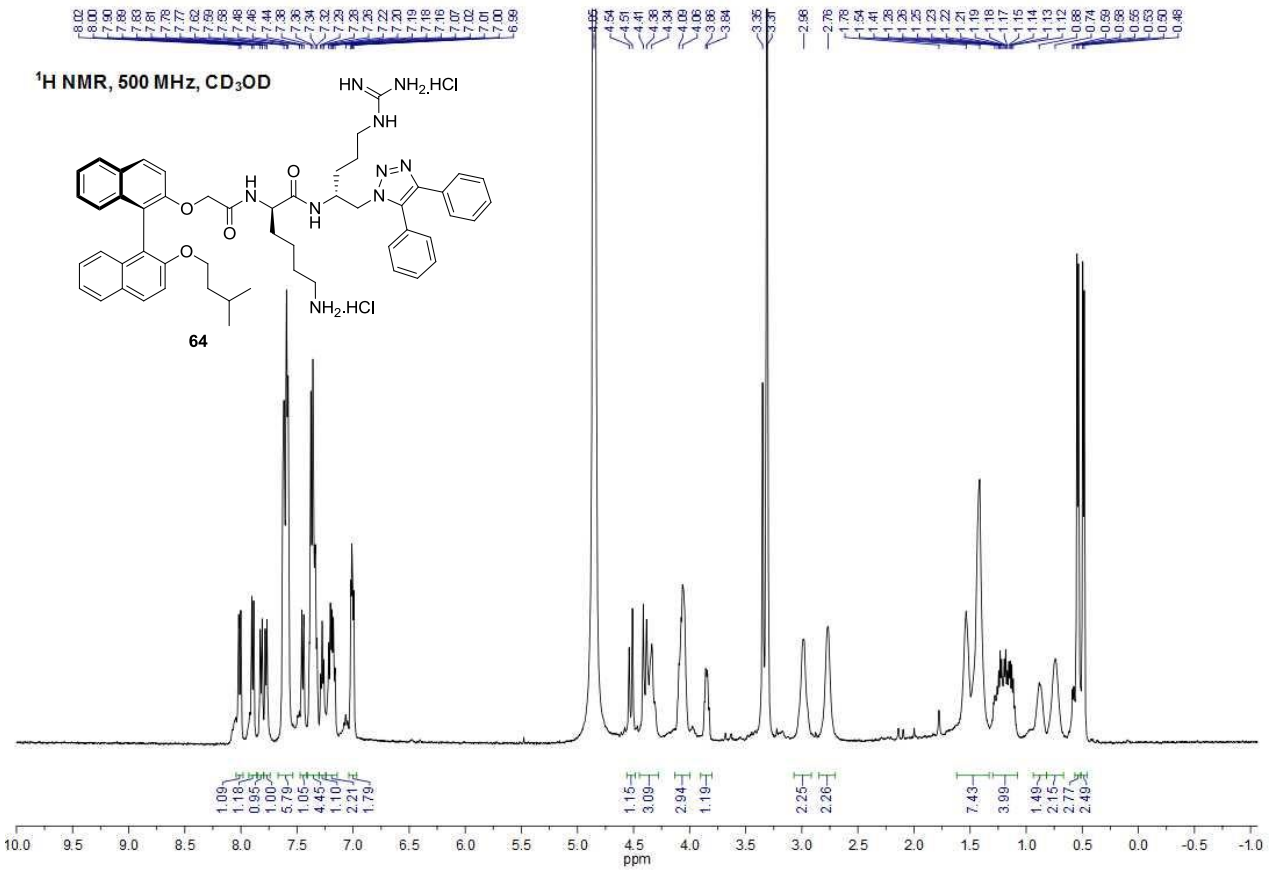

^{13}C NMR, 75 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
O
H
N
O
N
N
N
O
O
O
O
N
O
NH$_2$.HCl
87
(rotamers)
ppm

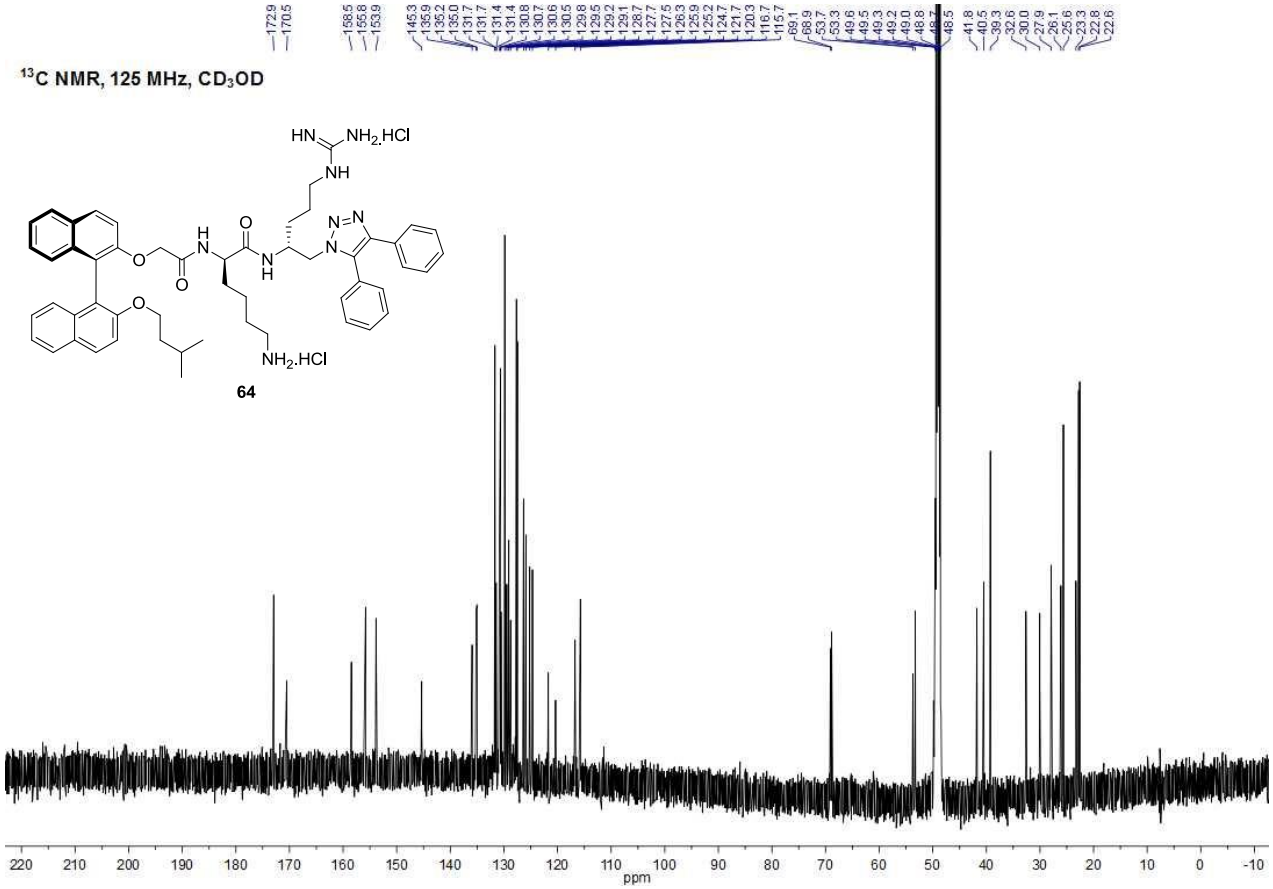

¹H NMR, 500 MHz, CD3OD
HN
NH2.HCl
NH
O
H
N
O
N
H
N=N
N
O
C
HN
O
O
O
NH2.HCl
88
(rotamers)
ppm

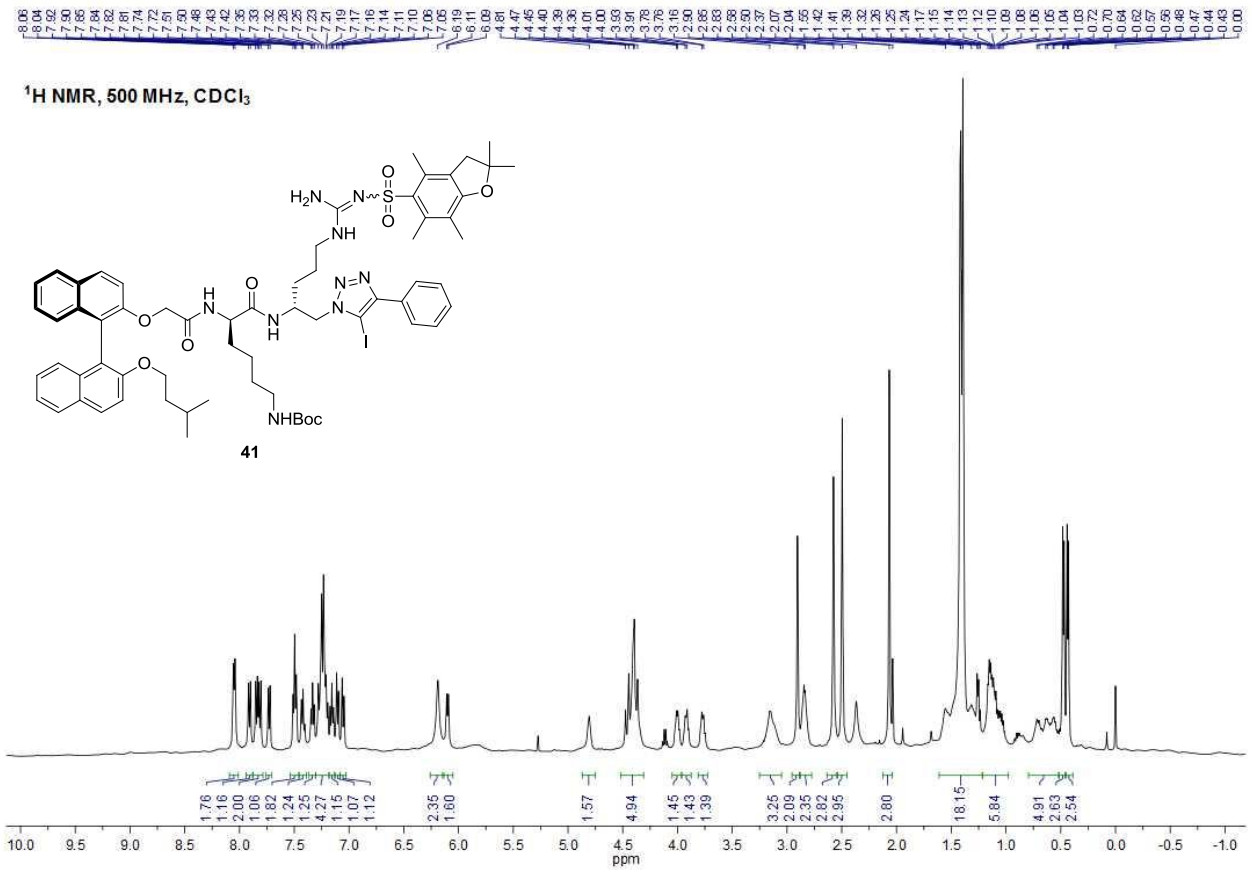

¹³C NMR, 125 MHz, CD3OD
HN
NH2.HCl
NH
O
H
N
O
N
H
N=N
N
O
C
HN
O
O
O
NH2.HCl
88
(rotamers)
ppm

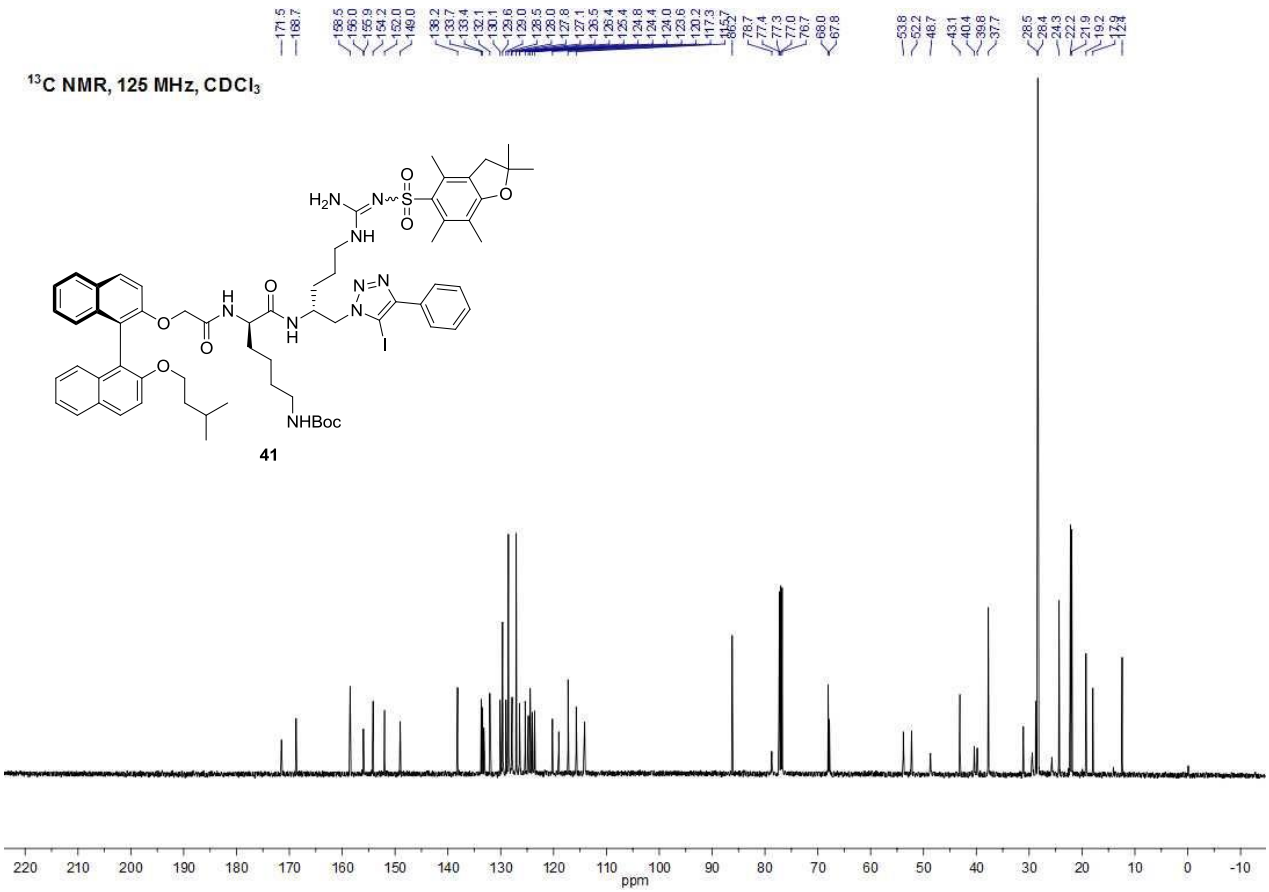

¹H NMR, 500 MHz, CD3OD
HN
NH2.HCl
NH
N=N
N
O
H
N
O
N
H
O
O
NH2.HCl
O
NH2.HCl
63
ppm

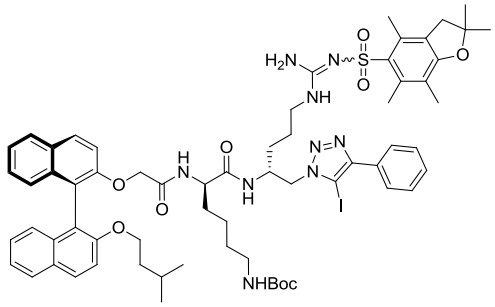

¹³C NMR, 75 MHz, CD3OD
HN
NH2.HCl
NH
N=N
N
O
H
N
O
N
H
O
O
NH2.HCl
O
NH2.HCl
63
ppm


^{1}H NMR, 500 MHz, CD_3OD
64
ppm

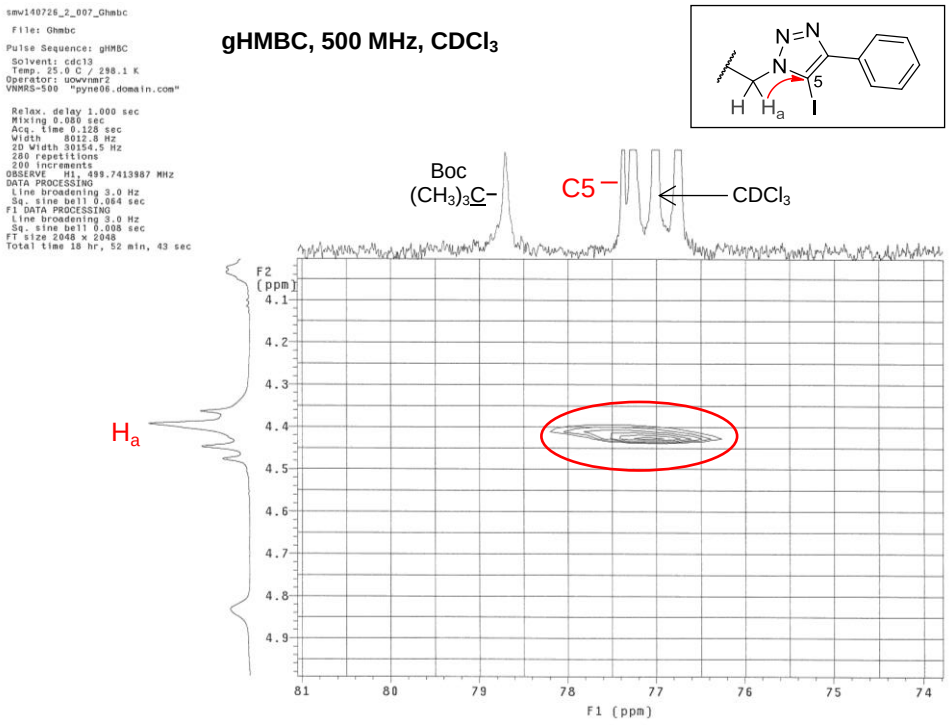

^{13}C NMR, 125 MHz, CD_3OD
64
ppm

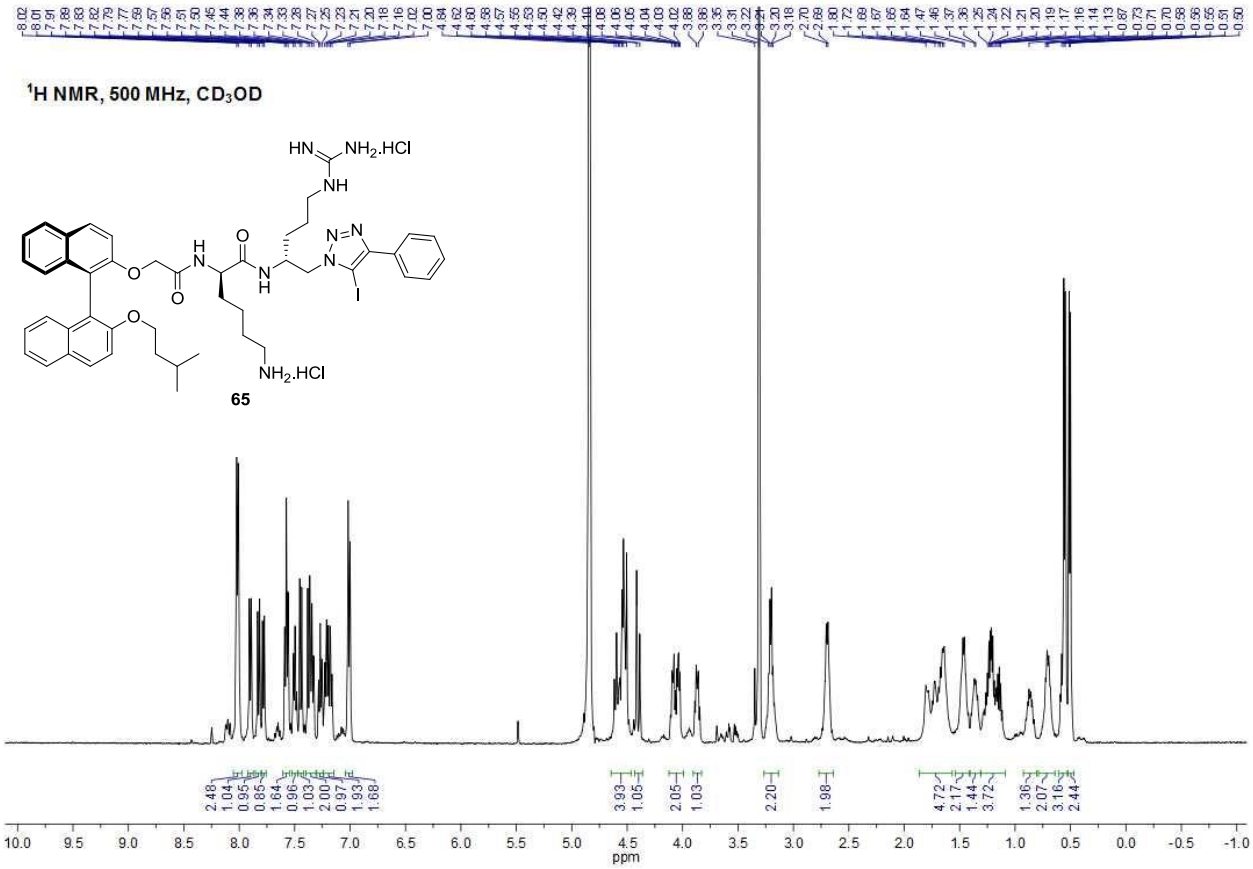

^{1}H NMR, 500 MHz, CDCl$_3$
41
ppm

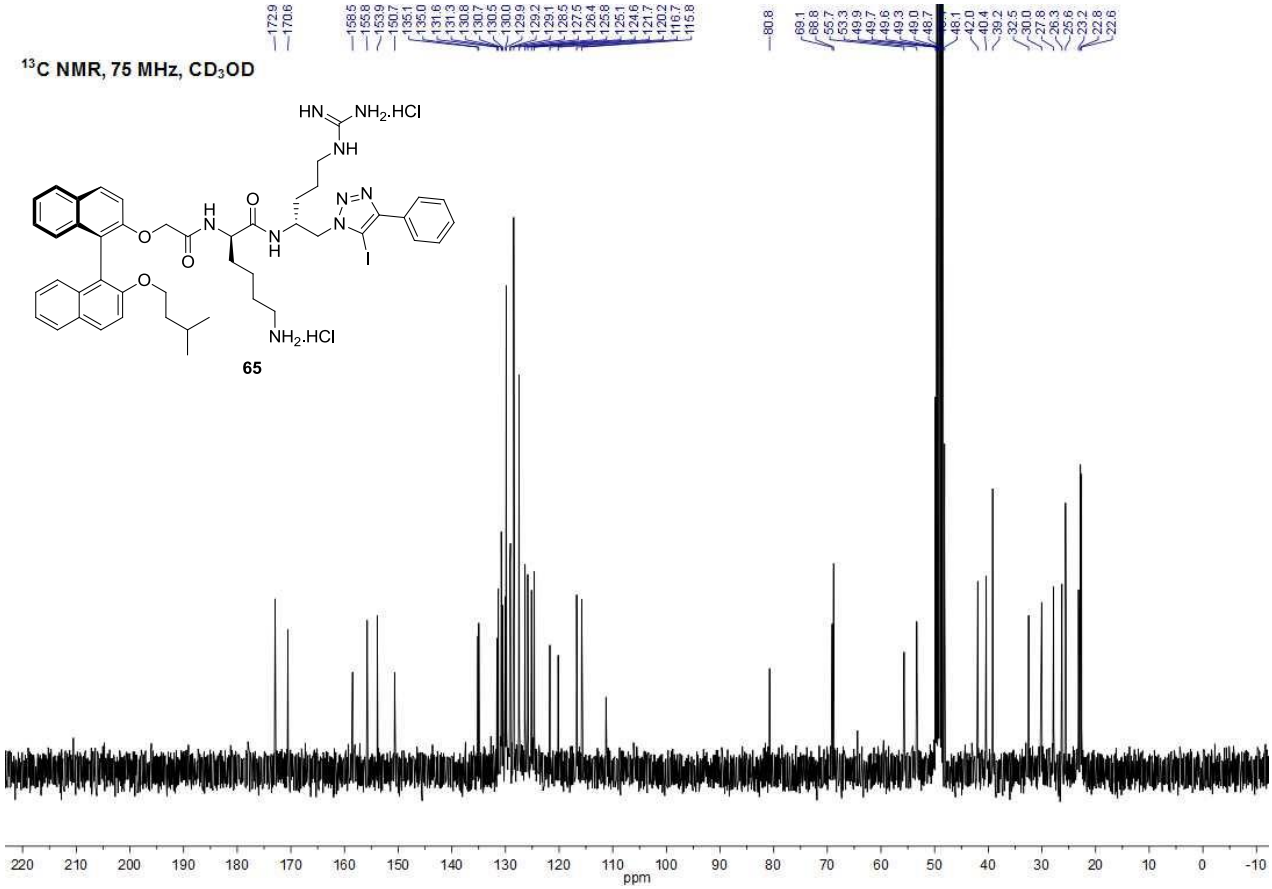

^{13}C NMR, 125 MHz, CDCl$_3$
41
ppm

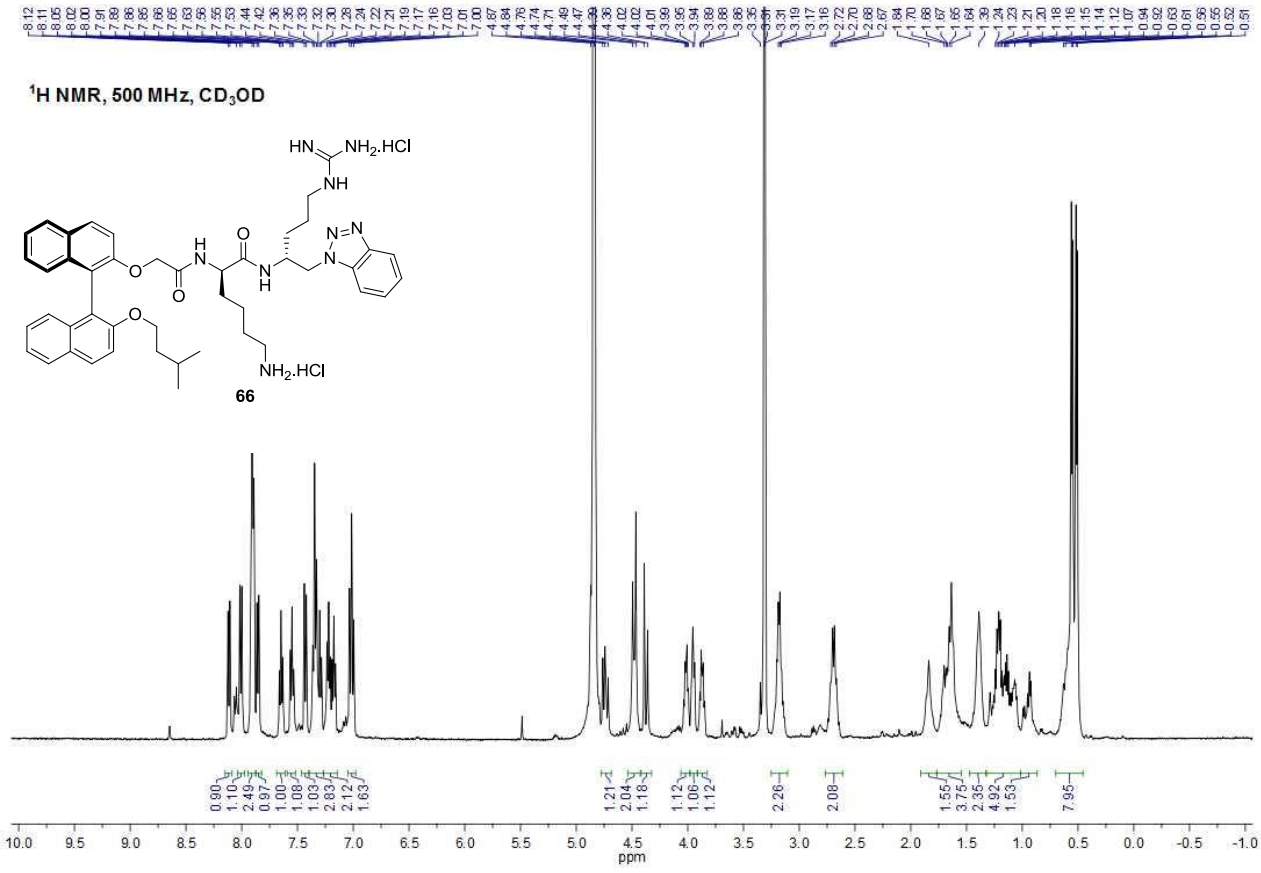


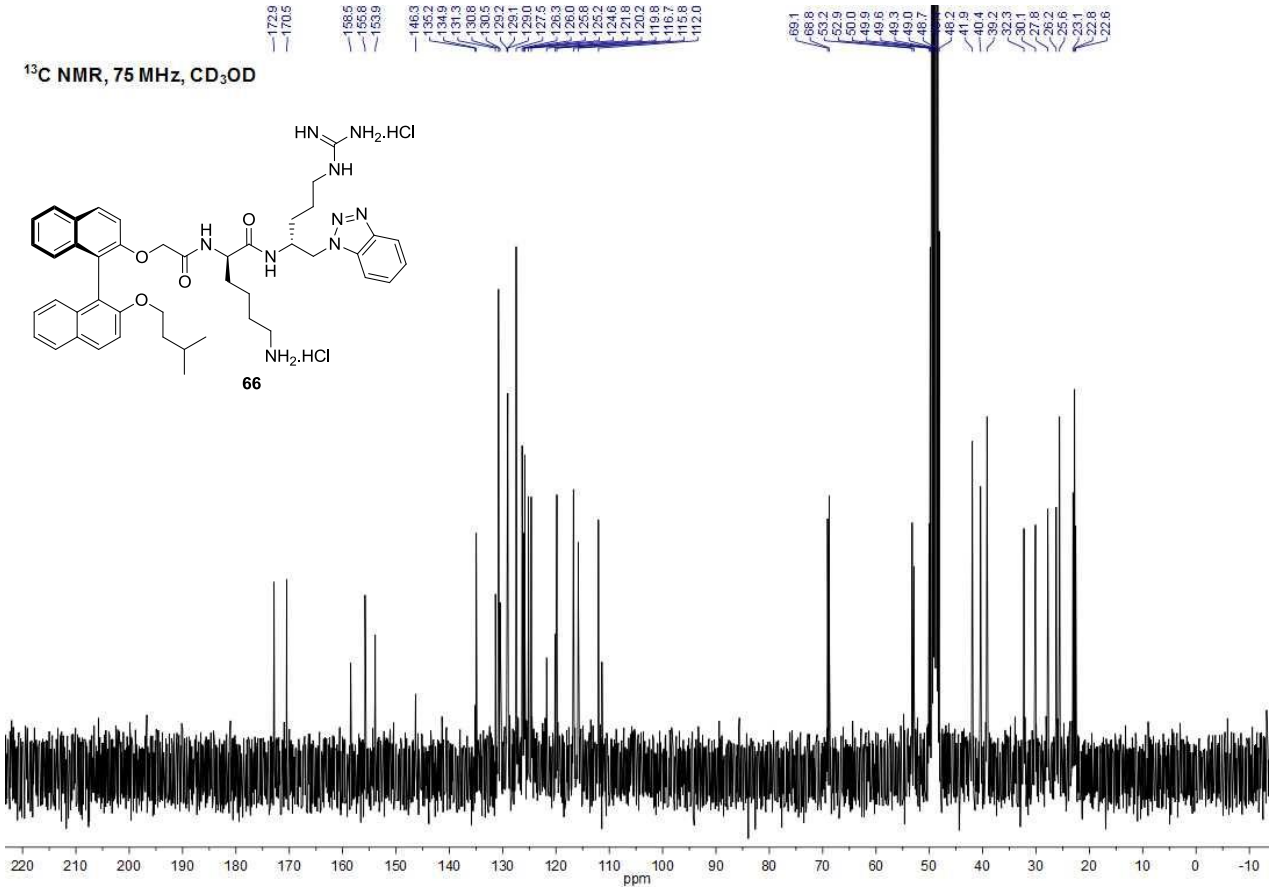
41

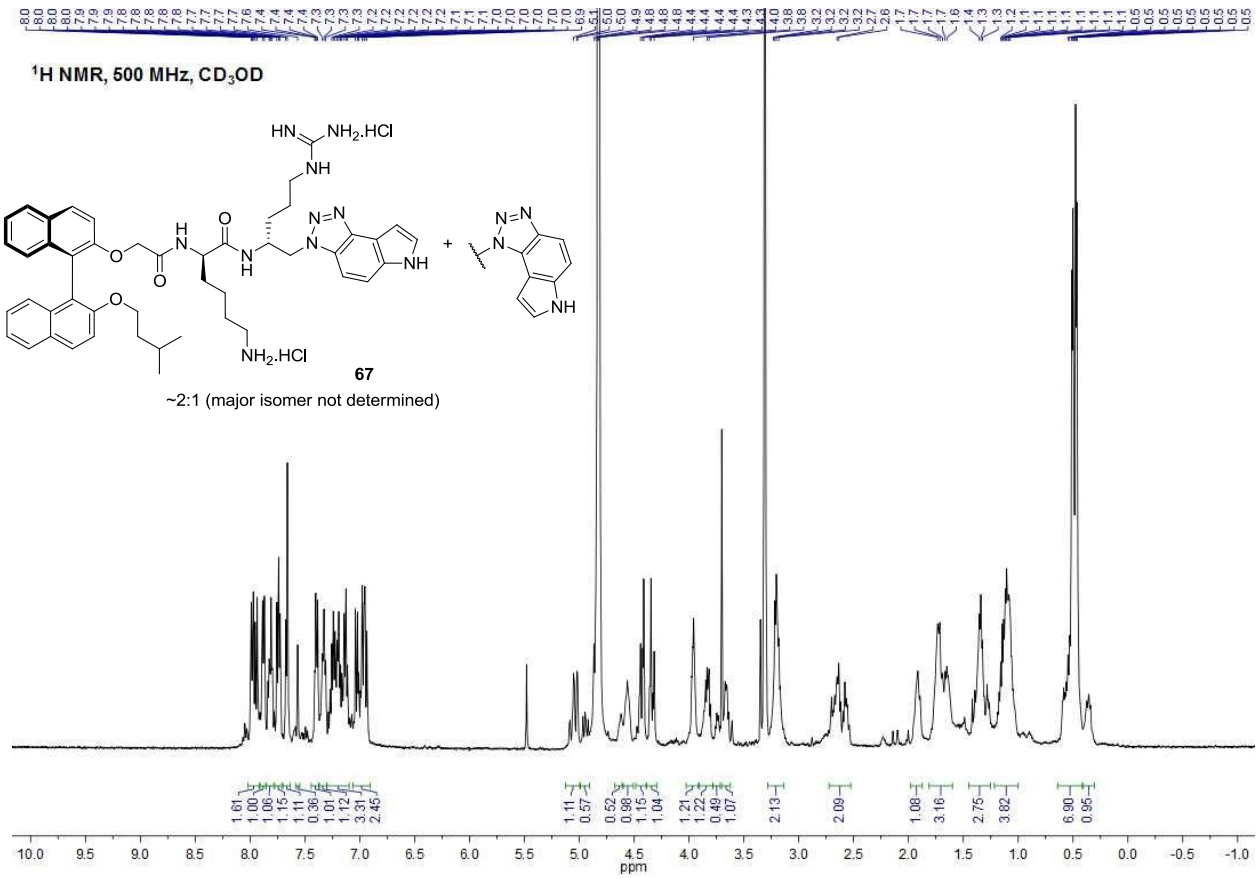

smw140726_2_007_Ghmbc
File: Ghmbc
Pulse Sequence: gHMBC
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: uowvnmr2
VNMRS-500 "pyne08.domain.com"
Relax. delay 1.000 sec
Mixing 0.080 sec
Acq. time 0.128 sec
Width 8012.8 Hz
2D Width 30154.5 Hz
280 repetitions
200 increments
OBSERVE H1, 499.7413987 MHz
DATA PROCESSING
Line broadening 3.0 Hz
Sq. sine bell 0.064 sec
F1 DATA PROCESSING
Line broadening 3.0 Hz
Sq. sine bell 0.008 sec
FT size 2048 x 2048
Total time 18 hr, 52 min, 43 sec
gHMBC, 500 MHz, CDCl3
H Ha
5
Boc
(CH3)3C
C5
CDCl3
Ha
F2 (ppm)
F1 (ppm)

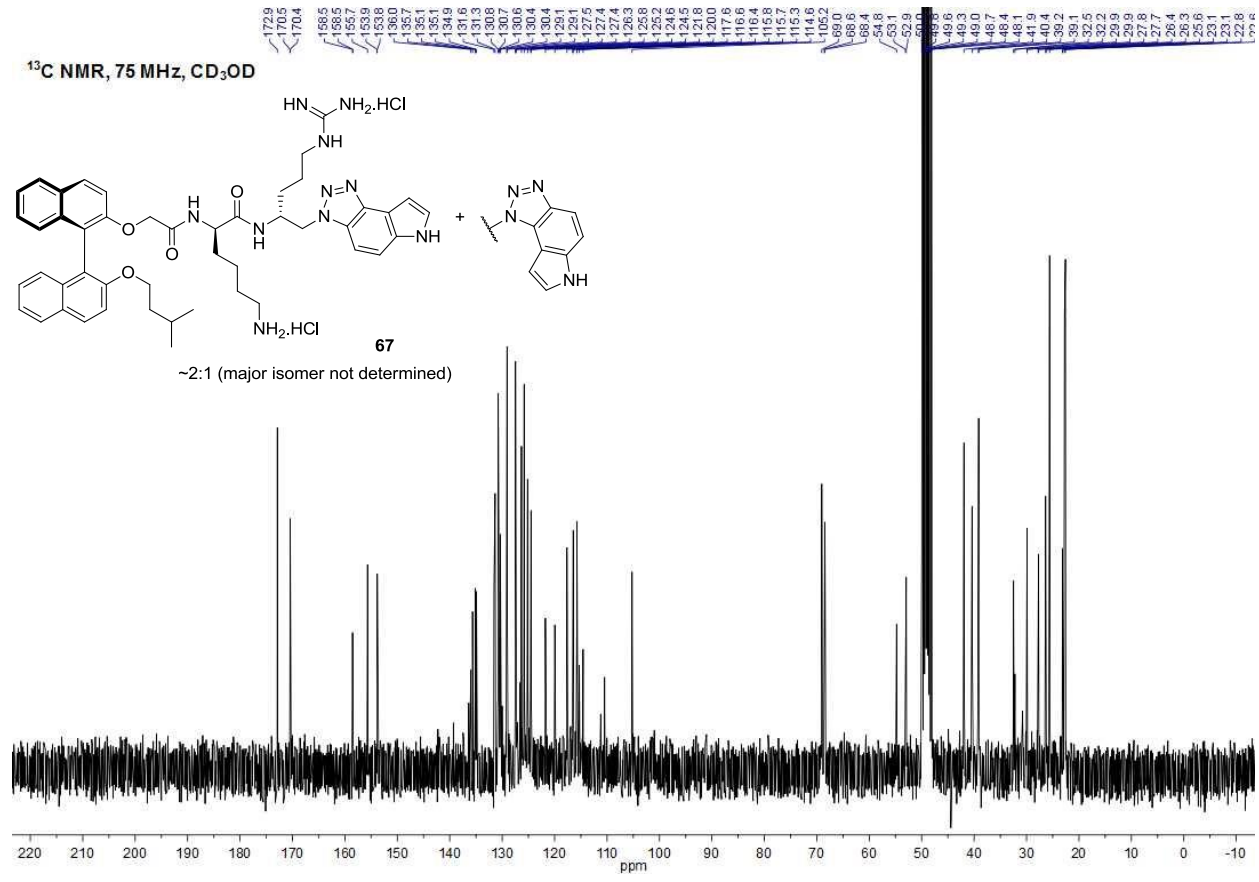

^{1}H NMR, 500 MHz, CD_3OD
65
ppm


^{13}C NMR, 75 MHz, CD_3OD
65
ppm

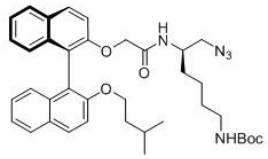

^{1}H NMR, 500 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
N=N
N
H
O
N
H
O
O
O
O
NH$_2$.HCl
66
ppm


^{13}C NMR, 75 MHz, CD$_3$OD
HN
NH$_2$.HCl
NH
N=N
N
H
O
N
H
O
O
O
O
NH$_2$.HCl
66
ppm


^{1}H NMR, 500 MHz, CD_3OD
HN
NH$_2$.HCl
NH
NH
NH$_2$.HCl
67
~2:1 (major isomer not determined)
ppm

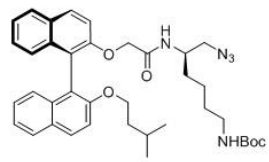

^{13}C NMR, 75 MHz, CD_3OD
HN
NH$_2$.HCl
NH
NH
NH$_2$.HCl
67
~2:1 (major isomer not determined)
ppm

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

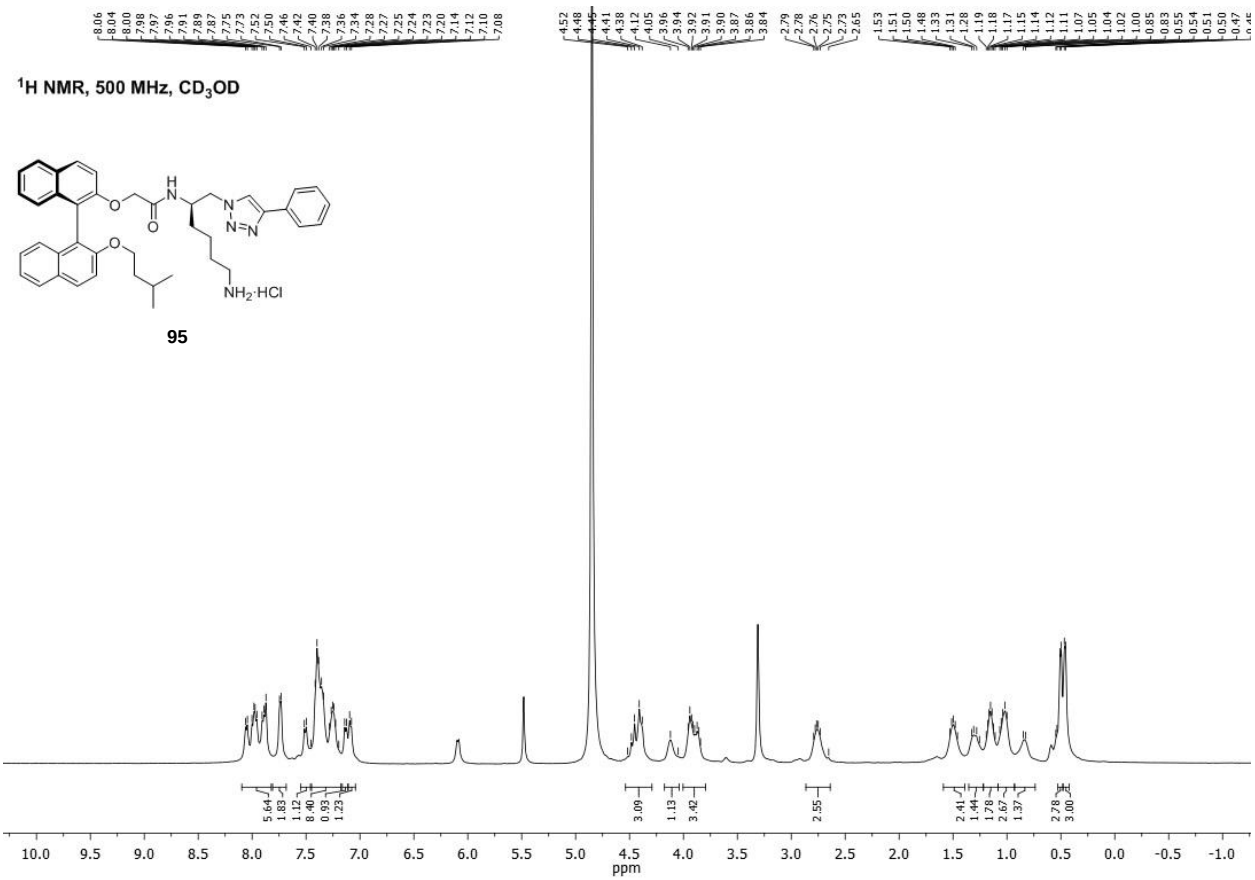


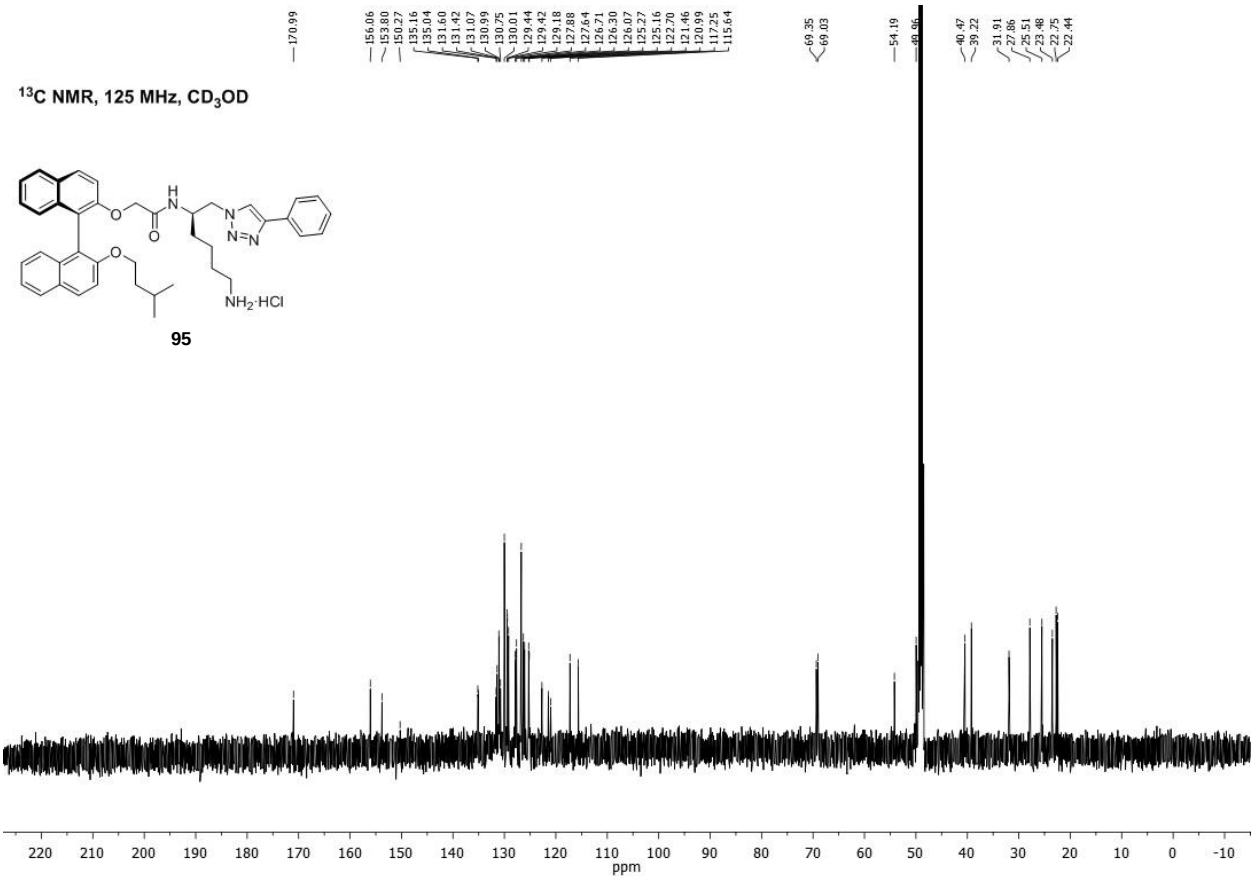
91

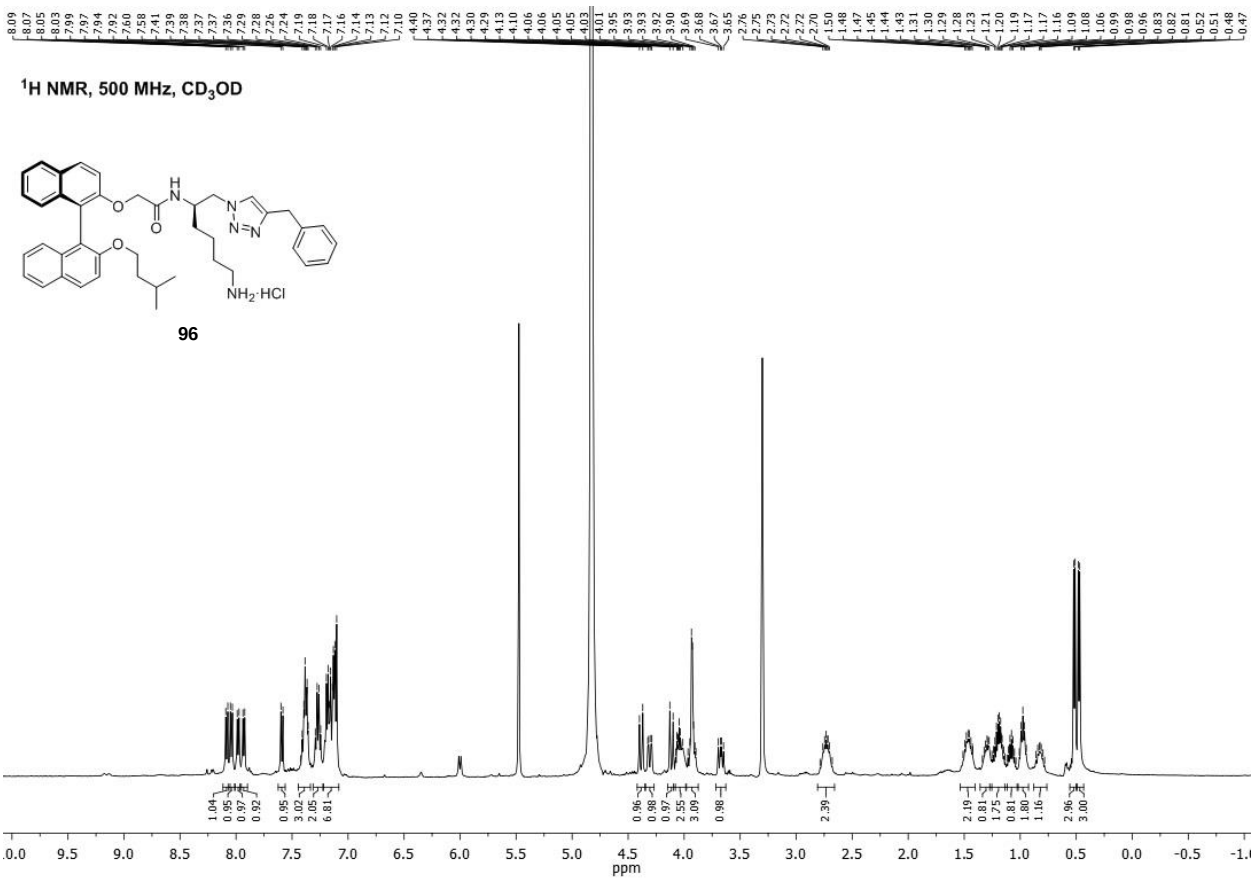
^{13}C NMR, 125 MHz, $CDCl_3$

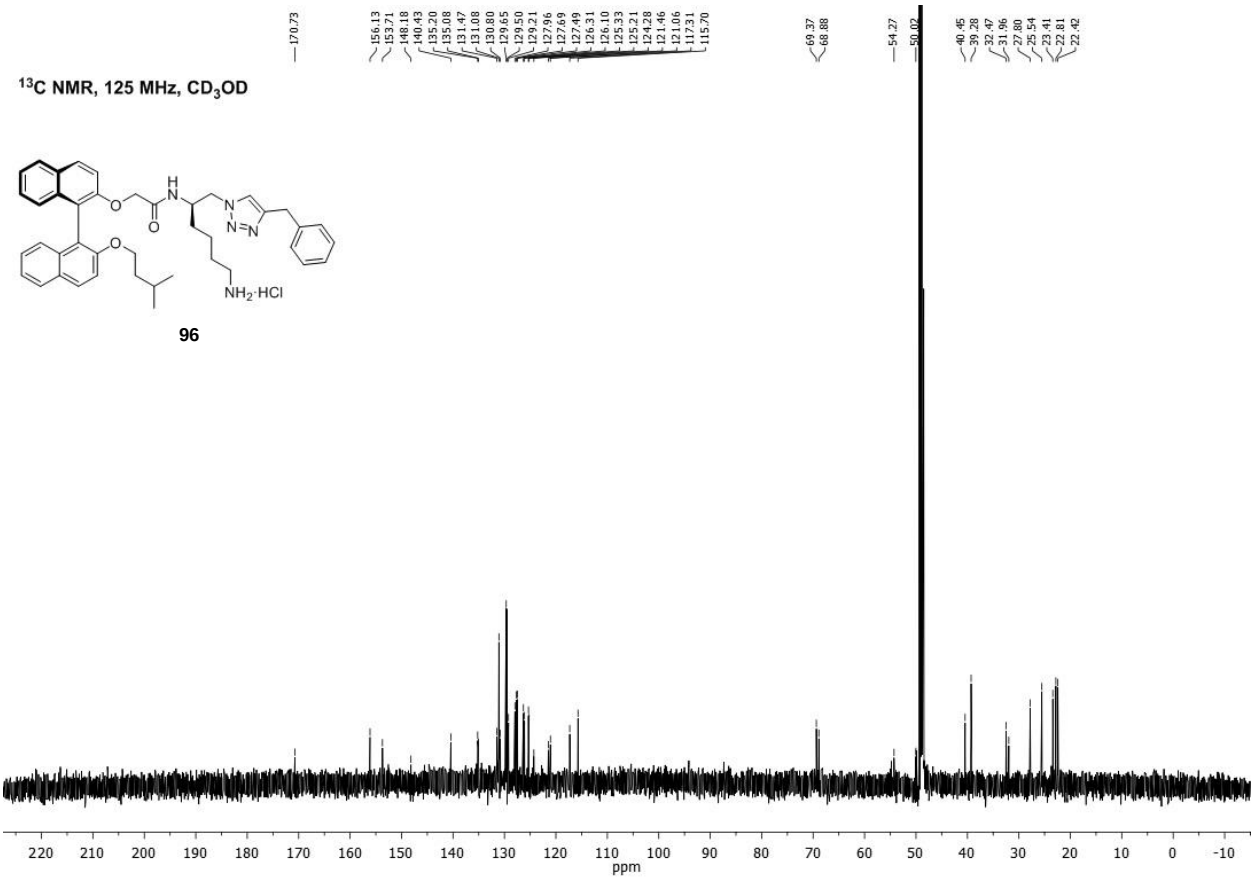


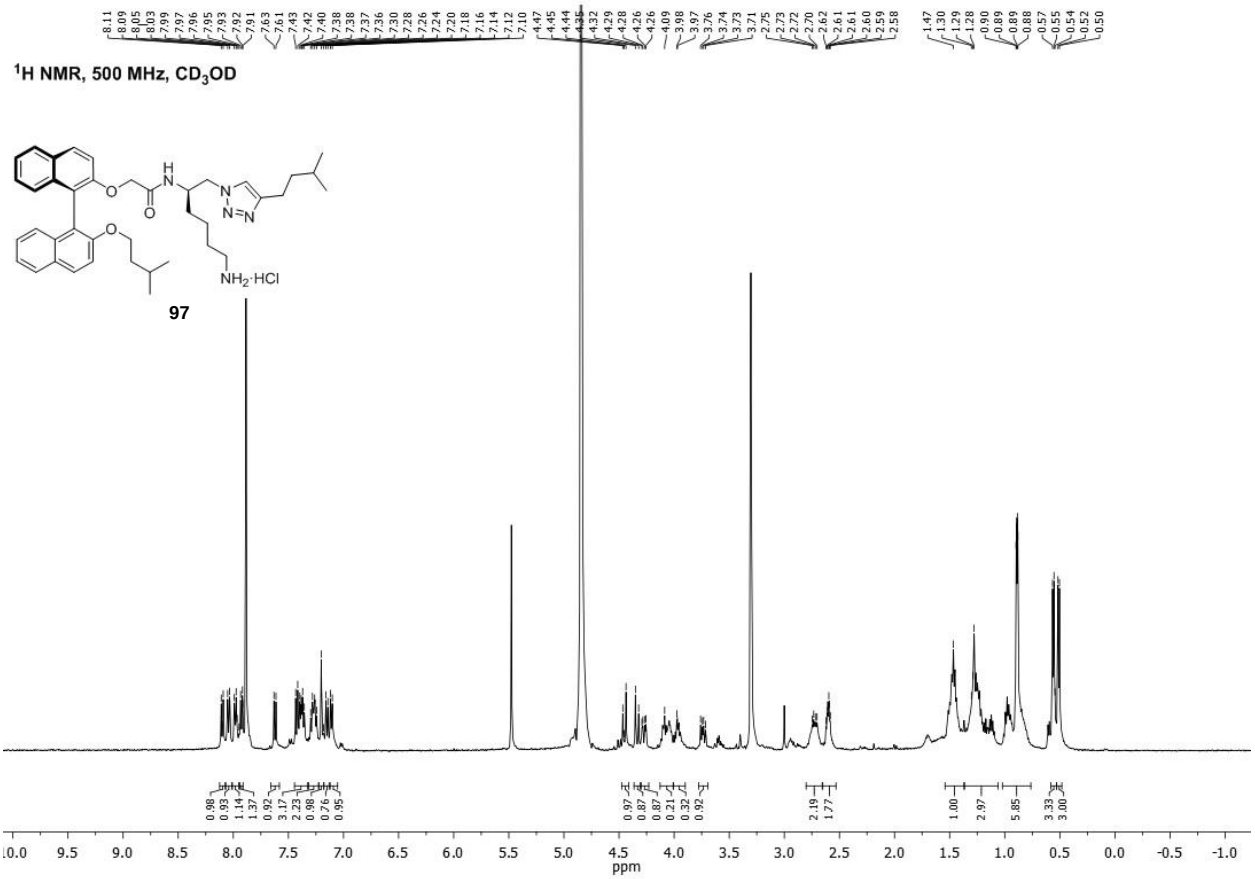
91

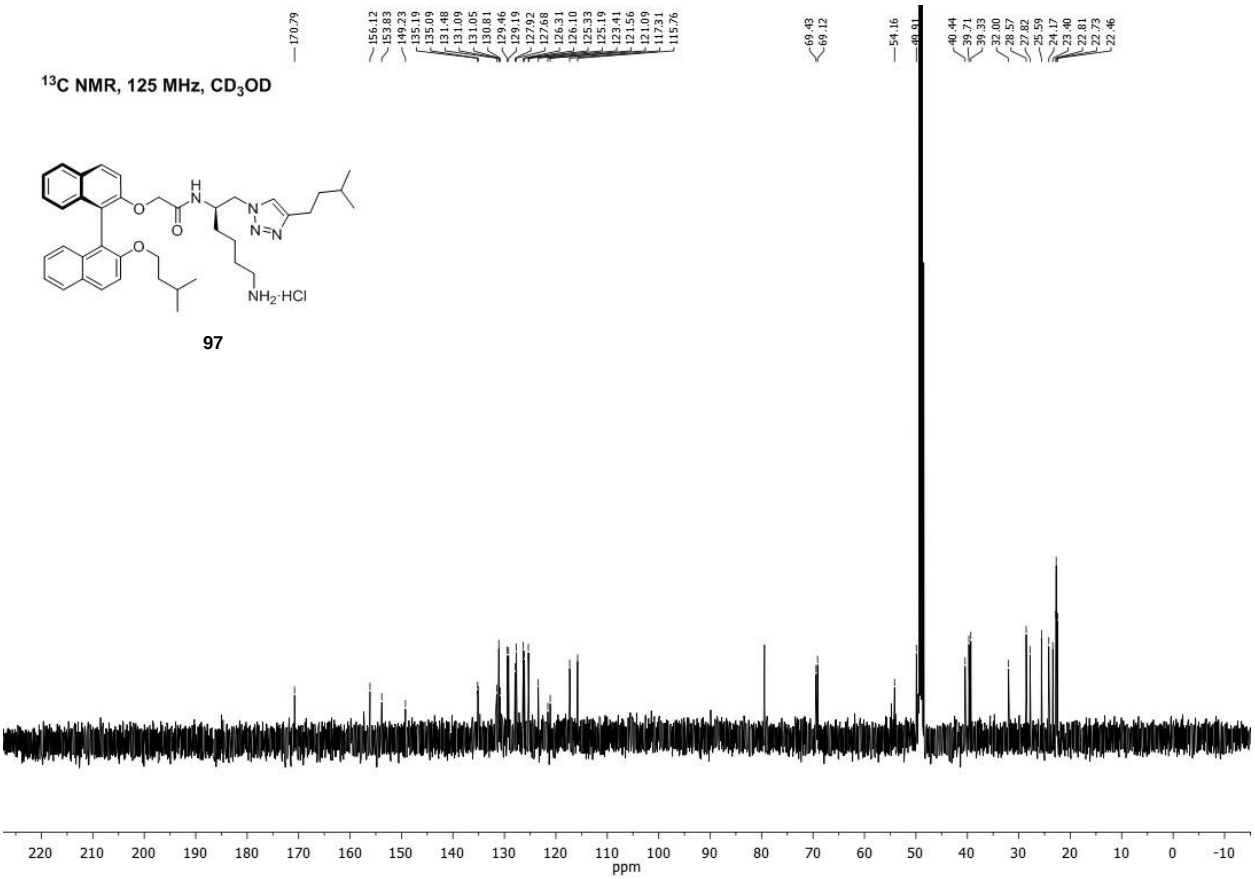

^{1}H NMR, 500 MHz, CD_3OD
NH$_2$·HCl
95
ppm

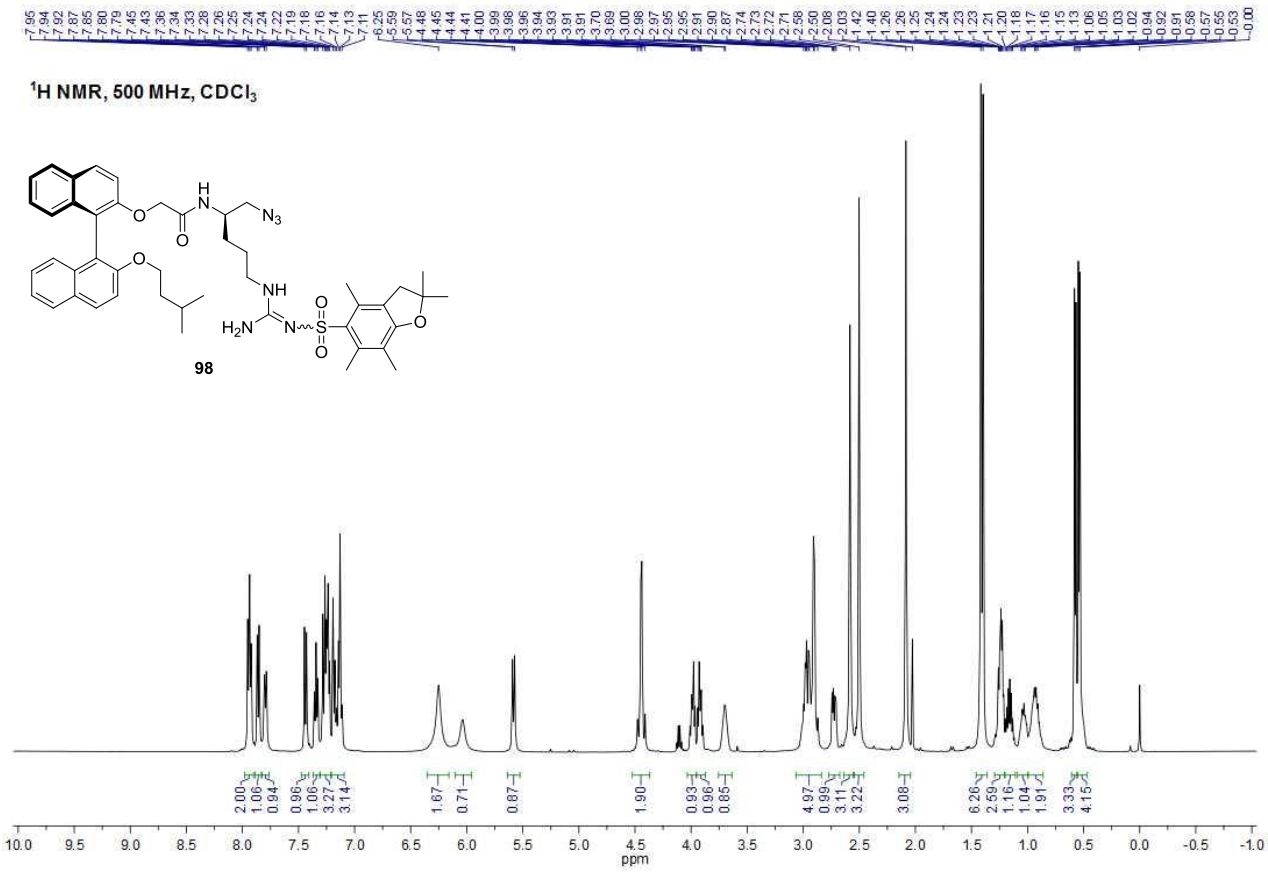

^{13}C NMR, 125 MHz, CD_3OD
NH$_2$·HCl
95
ppm

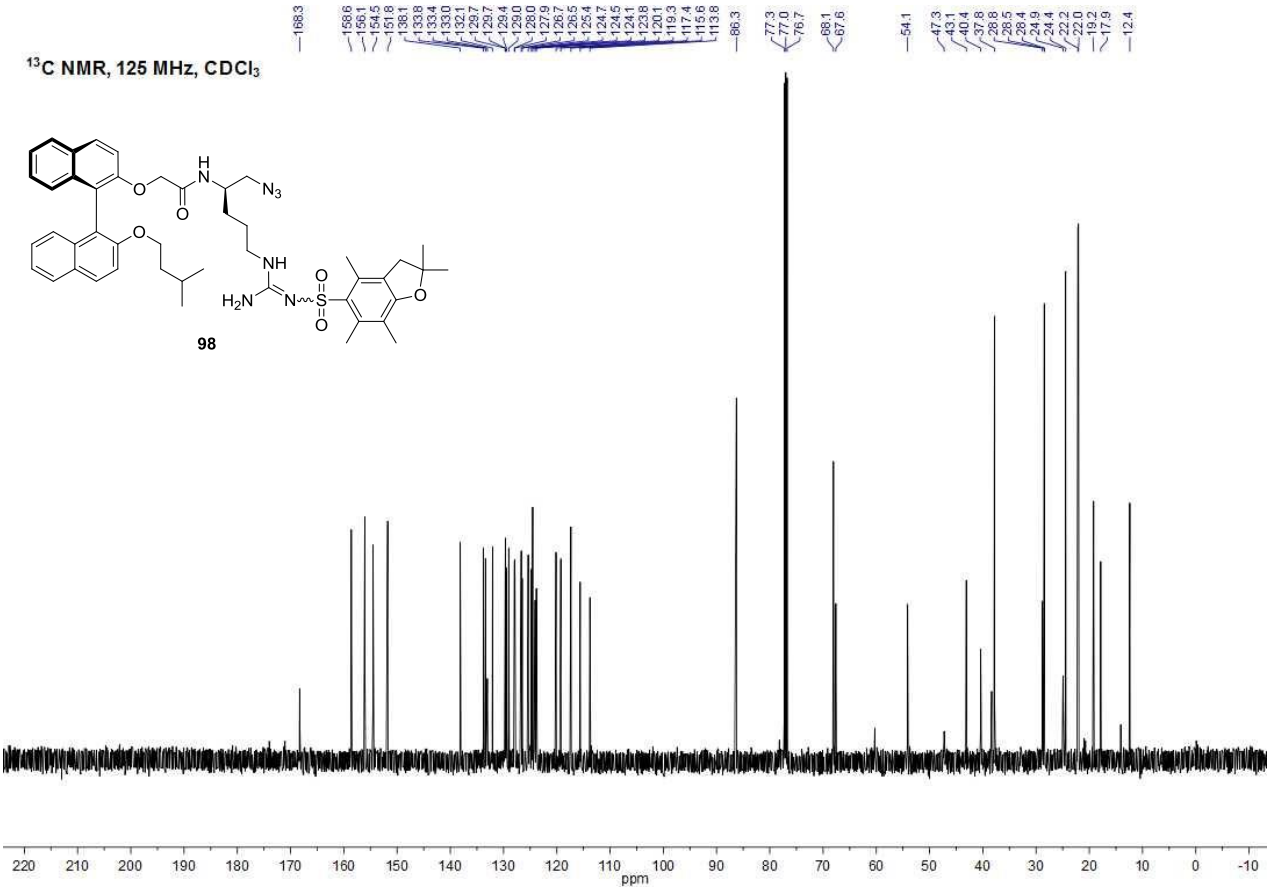

^{1}H NMR, 500 MHz, CD_3OD
$NH_2 \cdot HCl$
96
ppm

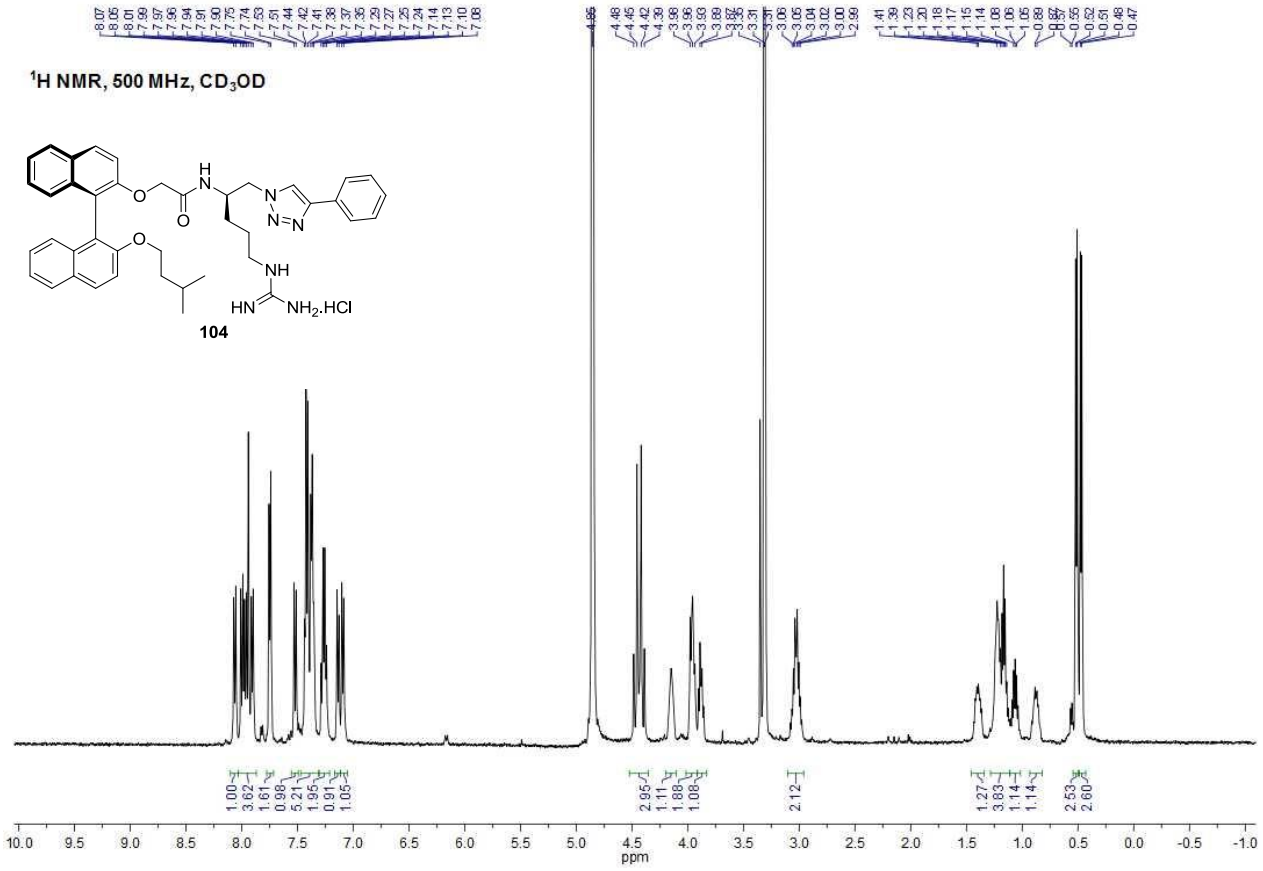

^{13}C NMR, 125 MHz, CD_3OD
$NH_2 \cdot HCl$
96
ppm

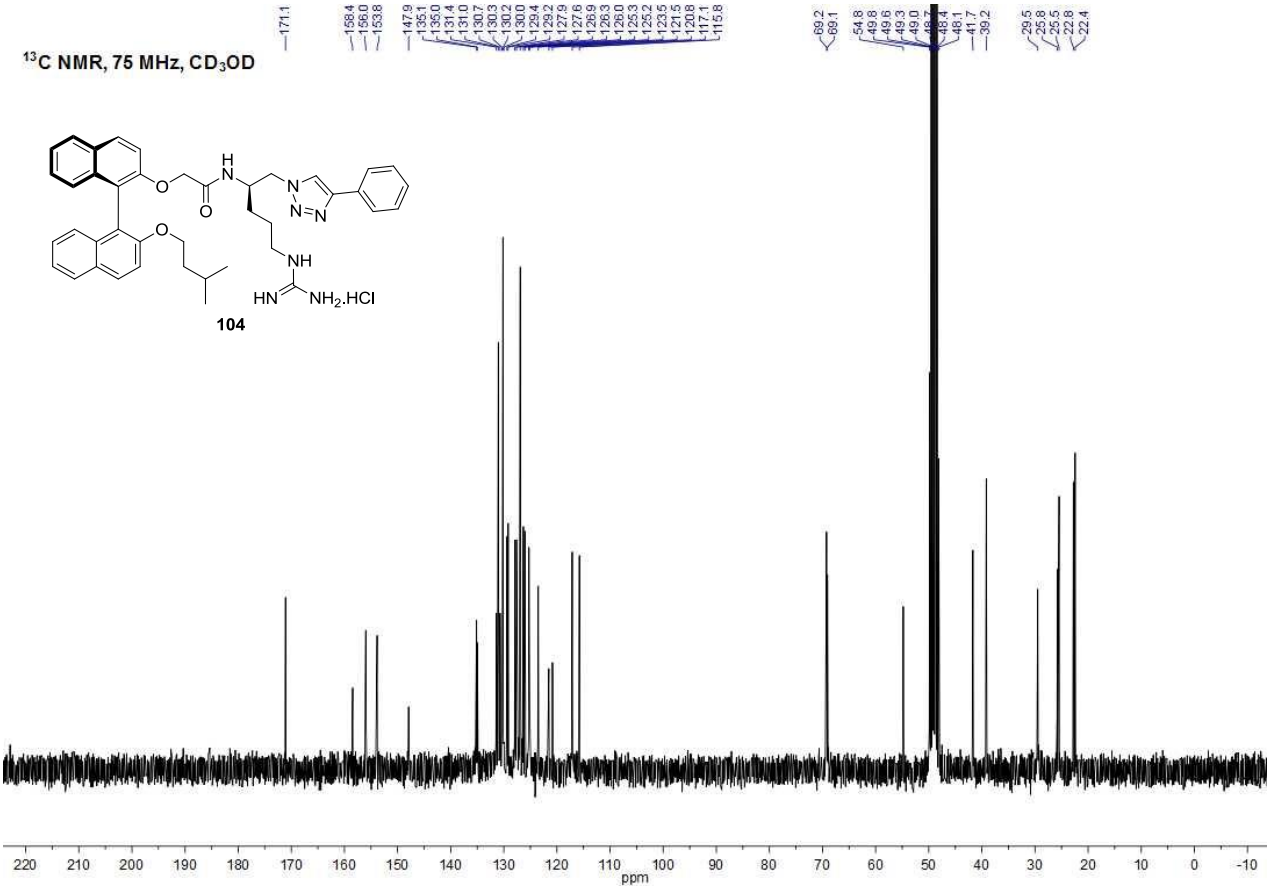

^{1}H NMR, 500 MHz, CD_3OD
97

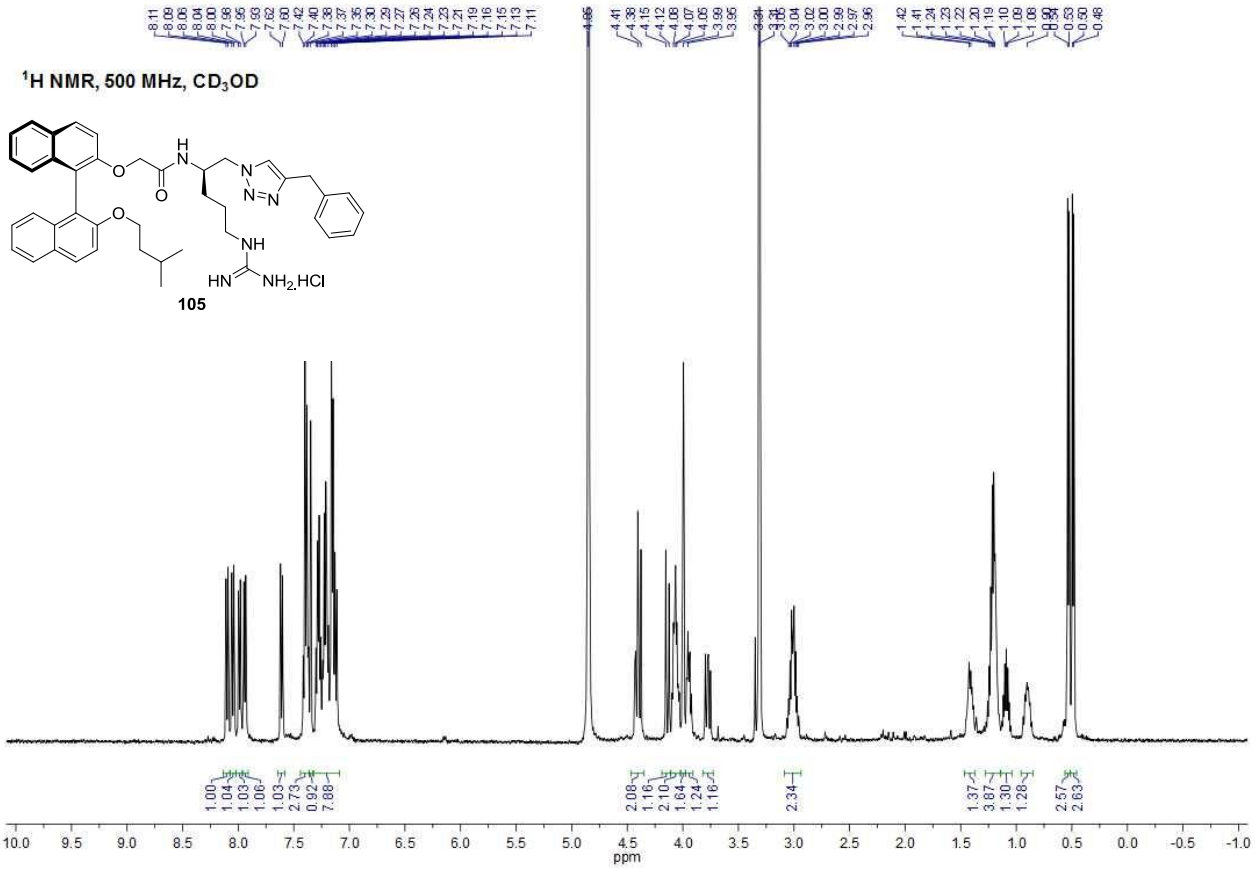

^{13}C NMR, 125 MHz, CD_3OD
97

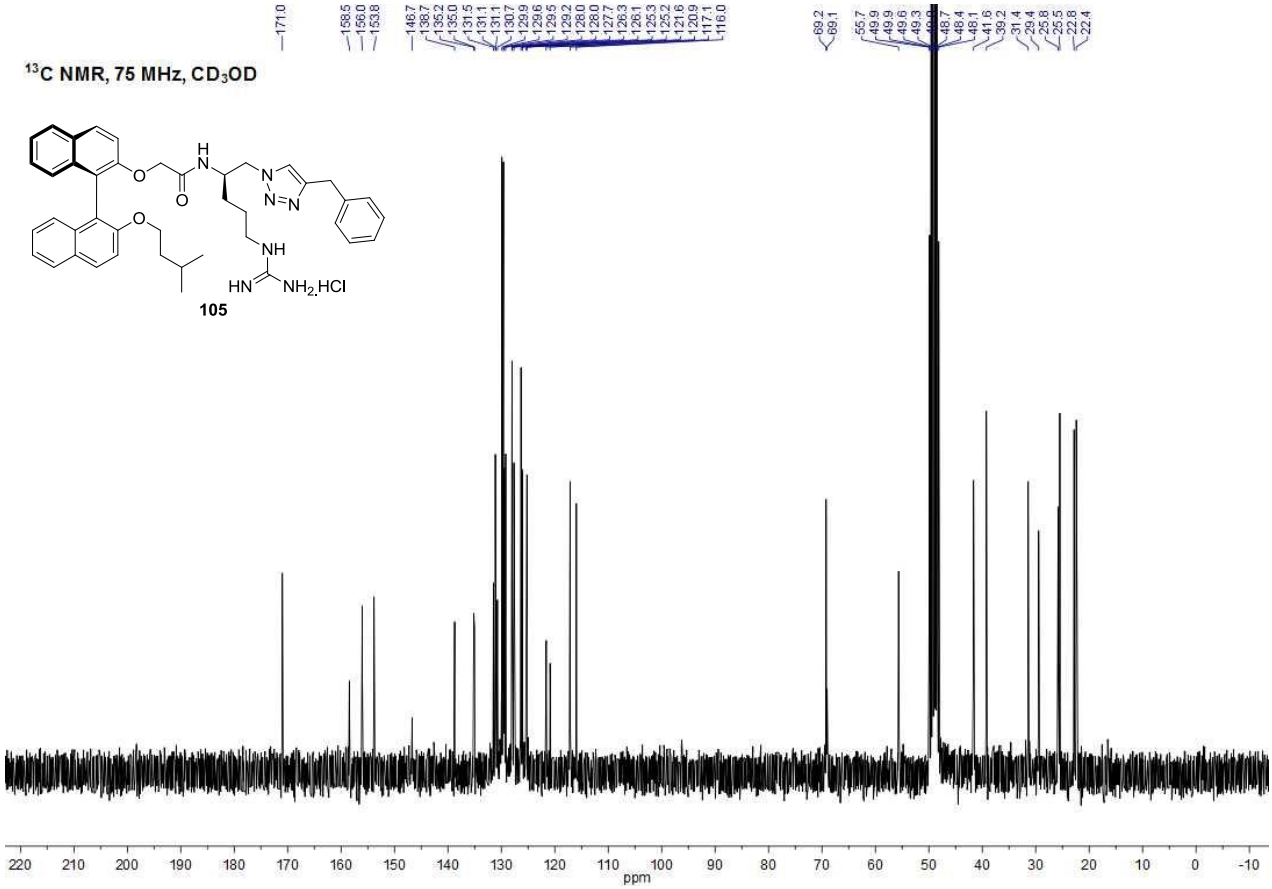

1H NMR, 500 MHz, CDCl3
98
ppm

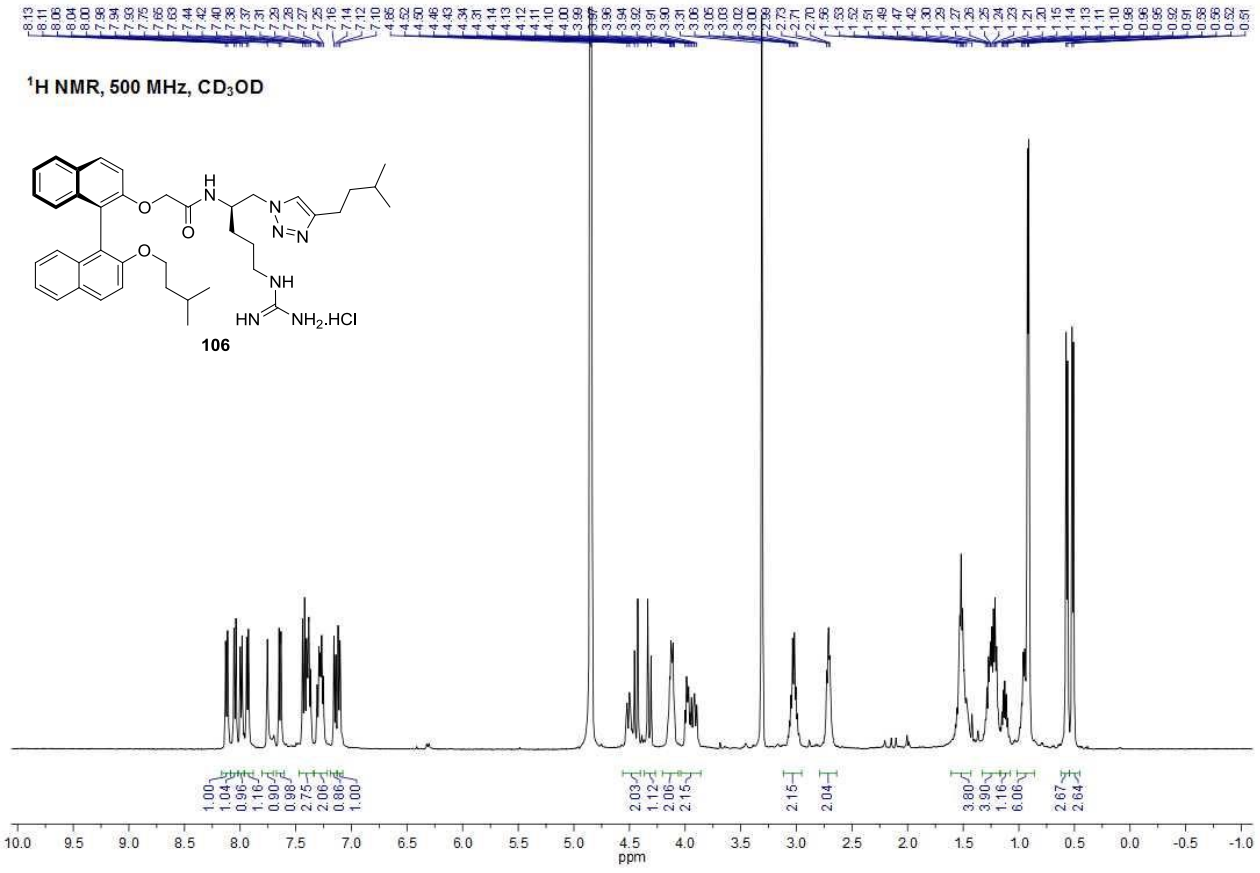

13C NMR, 125 MHz, CDCl3
98
ppm

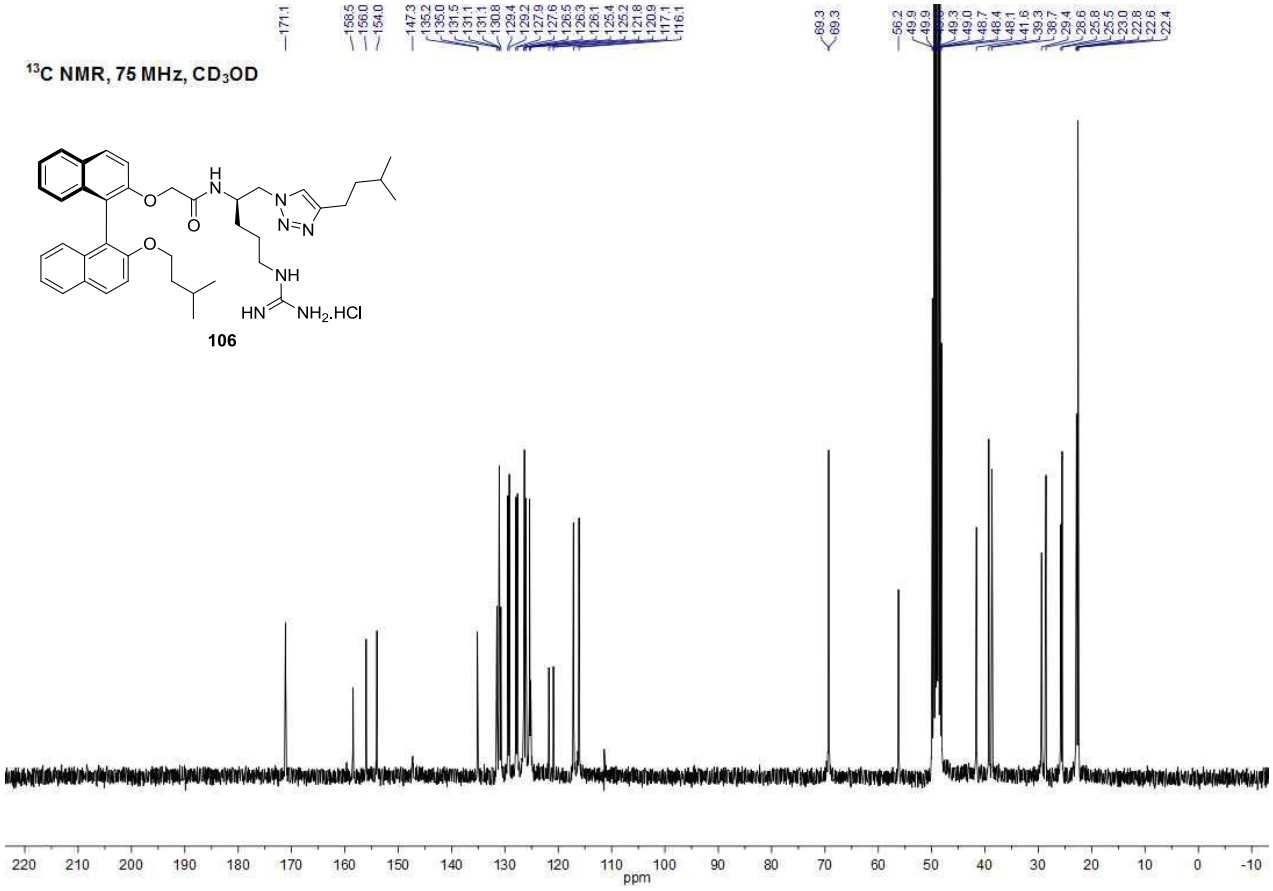

^{1}H NMR, 500 MHz, CD_3OD
104
ppm

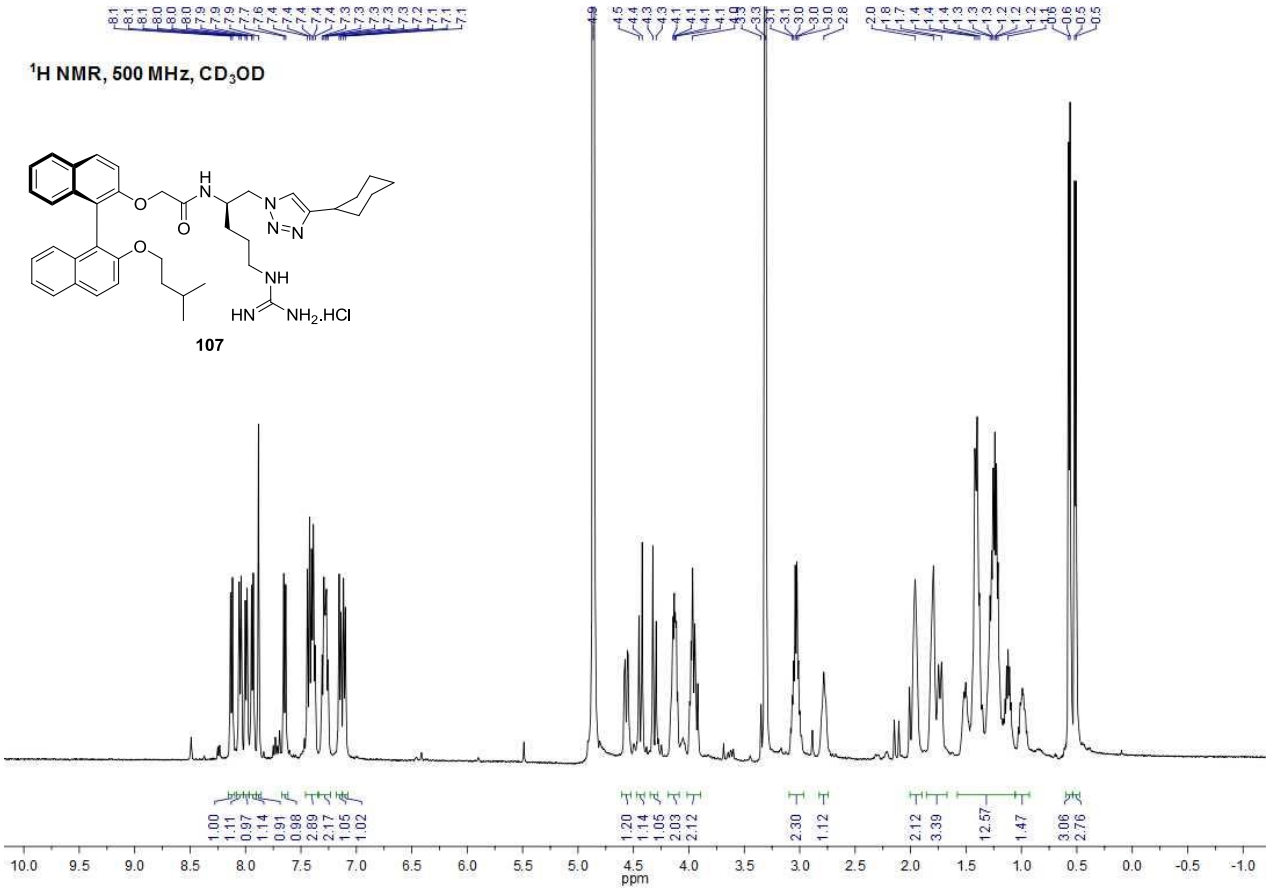

^{13}C NMR, 75 MHz, CD_3OD
104
ppm

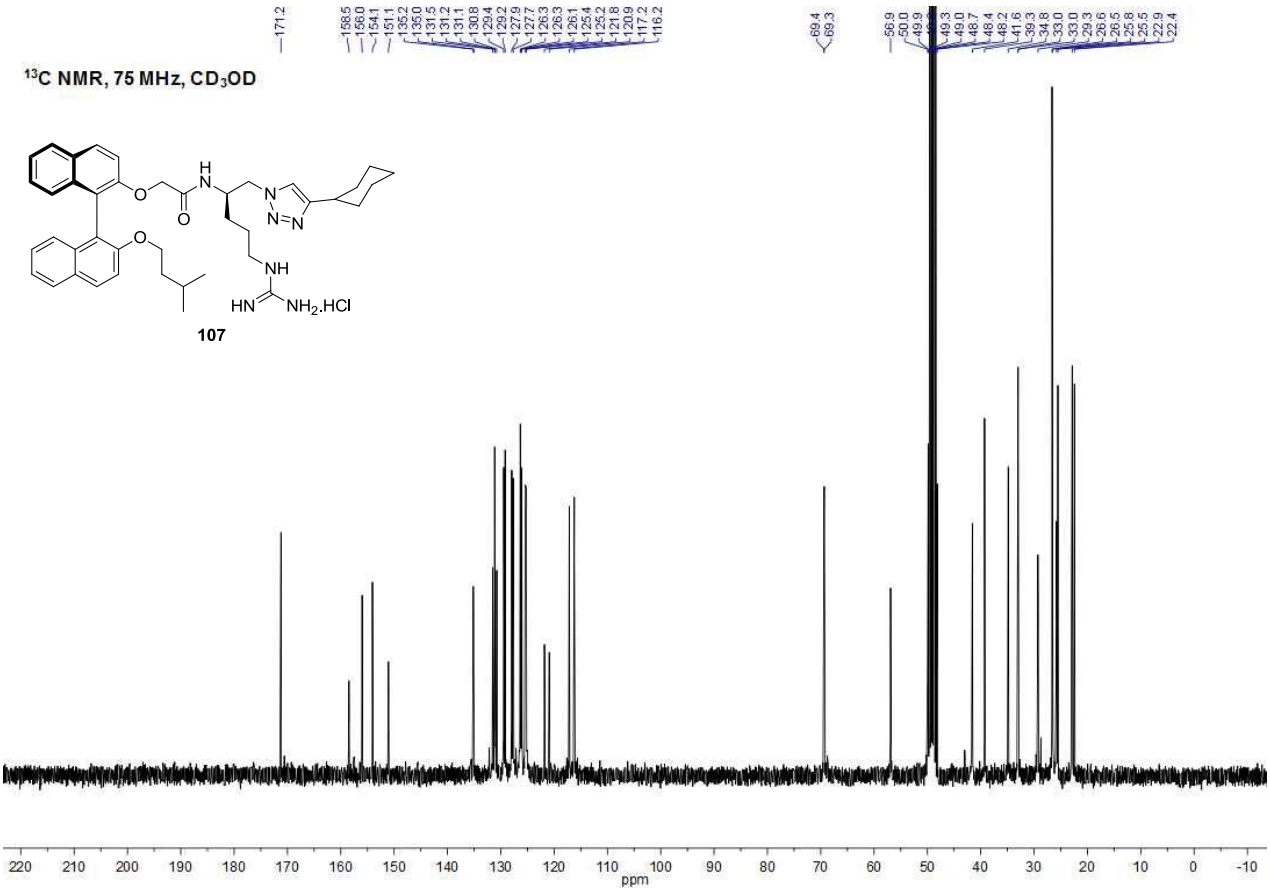

^{1}H NMR, 500 MHz, CD_3OD
105
ppm

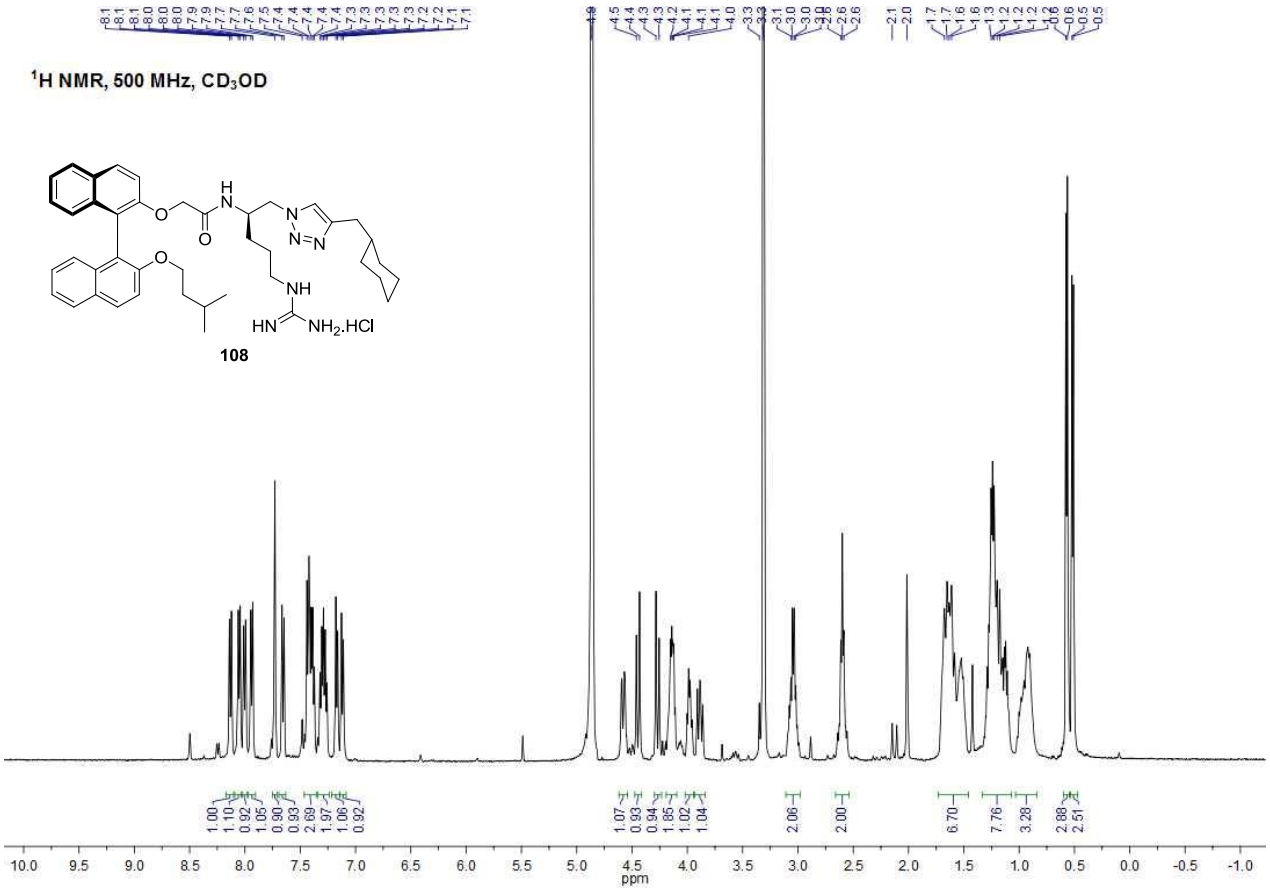

^{13}C NMR, 75 MHz, CD_3OD
105
ppm

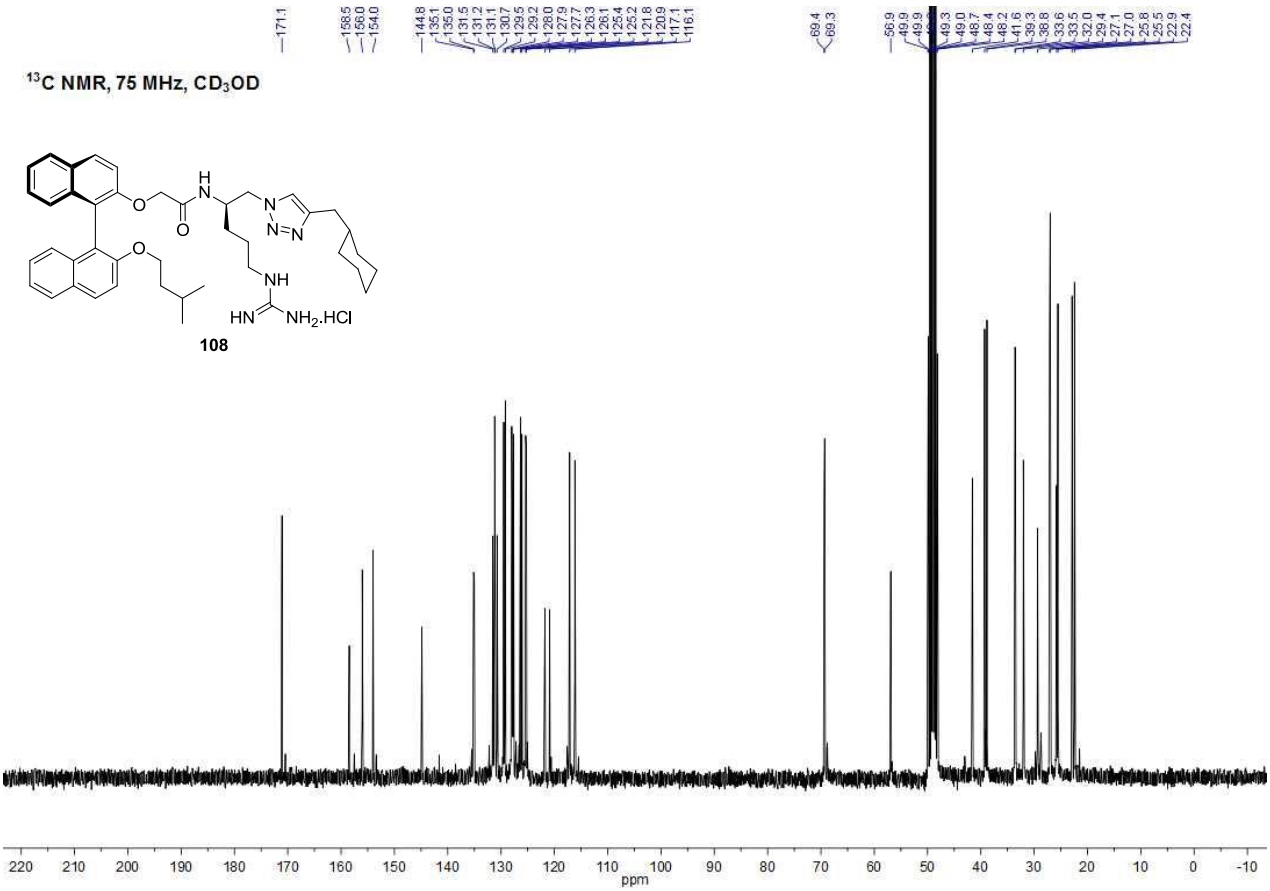

^{1}H NMR, 500 MHz, CD_3OD
106


^{13}C NMR, 75 MHz, CD_3OD
106


^{1}H NMR, 500 MHz, CD_3OD
107
ppm


^{13}C NMR, 75 MHz, CD_3OD
107
ppm


^{1}H NMR, 500 MHz, CD_3OD
108


^{13}C NMR, 75 MHz, CD_3OD
108