Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Expedient Synthesis of Imino-C-Nucleoside Fleximers Featuring a One-Pot Procedure to Prepare Aryl Triazoles

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Supporting Information

General Details

Reactions requiring anhydrous conditions were carried out in oven-dried glassware under a positive pressure of argon or nitrogen in anhydrous solvents using standard Schlenk techniques. Anhydrous tetrahydrofuran over 3 Å molecular sieves was purchased from Acros Organics and used as received. Solvents used for extraction and purification by flash chromatography were used as received unless otherwise noted. Commercially available starting materials and reagents were used as received unless otherwise noted. Reactions performed at low temperature were cooled with a water/ice bath to reach 0 °C. Reaction progress was monitored by thin layer chromatography (TLC) on Merck Aluminum-backed silica gel coated TLC plates (60 Å, F254 indicator). TLC plates were visualised by exposure to ultraviolet light (254 nm), followed by staining with either $KMnO_4$ solution or Cerium Molybdate solution (Hanessian's Stain) or ninhydrin solution. For the detection of boronic acids, TLC was performed with visualisation by staining with alizarin solution, followed by exposure to ultraviolet light (365 nm). Monitoring by LCMS analysis was performed on an Agilent 1260 Infinity II Series LC System with an Agilent 6120B Single Quadrupole LC/MS (ESI), equipped with an Agilent 1100 Multi Wavelength Detector and an Agilent Infinity II 1290 Evaporative Light Scattering Detector using a C18 Kinetex column (50 × 3 mm, 2.6 µm) with a linear gradient system (solvent A: 0.1% (v/v) formic acid in water, solvent B: MeOH, 30% - 100% B over 6 min) at a flow rate of 1 $mL \cdot min^{-1}$. Flash column chromatography was performed using silica gel (60, 230–400 mesh) with the denoted solvent system or with a Büchi Pure C815 Flash automated flash chromatography system using prepacked FlashPure cartridges containing silica gel (50 µm irregular) using ACS grade solvents. Preparative thin layer chromatography (TLC) was performed on pre-coated silica gel plates (Merck/UV254) and products were visualised by UV fluorescence. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogenous materials, unless otherwise stated. NMR spectra were recorded at 293 K unless otherwise noted, on a Bruker® DRX400 spectrometer operating at 400 MHz for ^{1}H nuclei, 100 MHz for ^{13}C nuclei and 376 MHz for ^{19}F nuclei or a Bruker® DRX500 spectrometer operating at 500 MHz for ^{1}H nuclei and 126 MHz for ^{13}C nuclei in either deuterated chloroform, methanol or DMSO. All chemical shifts (δ) are reported in parts per million (ppm) and referenced to residual protium or the carbon resonance of the NMR solvent, respectively. Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, td = triplet of doublets, ddd = doublet of doublet of doublets, m = multiplet), coupling constants (*J*) in Hertz (Hz) where applicable, integration. Optical rotations of chiral compounds were measured on a Rudolph Research Analytical Autopol IV automatic polarimeter or a PerkinElmer® 341 polarimeter, using sodium-D line (589 nm) at the indicated temperature in the indicated solvent. Concentrations are quoted in grams per 100 mL. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer using a diamond ATR sampling accessory. Absorption peaks are reported as wavenumbers (v, cm^{-1}). High resolution mass spectroscopy (HRMS) was performed on a Waters Q-TOF Premier Tandem Mass spectrometer fitted with a Waters 2795 HPLC or a VG-70SE spectrometer at a nominal accelerating voltage of 70 eV or on a Bruker micrOTOF-Q II mass spectrometer.

Safety Note on Handling Azido Compounds[1–3]

Handling Sodium Azide

Sodium azide is highly toxic (LC_{50} Inhalation = 37 mg/m^3 for rats, LD_{50} Dermal = 20mg/kg for rabbits) and highly soluble in water (>30 g/100 mL at 0 °C). Sodium azide can be absorbed dermally and therefore must be handled with appropriate personal protection equipment. Sodium azide decomposes above 275 °C, generating highly reactive sodium metal. Sodium azide is not compatible with any acid as it forms highly explosive hydrazoic acid on contact, even in dilute solution. Sodium azide is not compatible with halogenated solvents. For instance, sodium azide readily reacts with dichloromethane to form the highly explosive diazidomethane that cannot be removed from the reaction during workup.

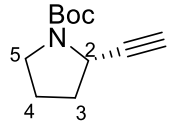
Low Molecular Weight Organic Azides

Low molecular weight organic azides are potentially explosive substances that can decompose with a slight input of external energy (heat, friction, pressure etc). Although we have not experienced any explosions thus far, any organic azides where the weight attributed to the azido group exceeds 25% of the molecular weight should be handled with caution. Use of a blast shield and avoidance of very large-scale reactions when dealing with these substances is highly recommended.

Chan-Lam/CuAAC Model Study

Preparation of Model Alkyne **2**

***tert*-Butyl (*S*)-2-ethynylpyrrolidine-1-carboxylate (2)**



To a mixture of powdered K_2CO_3 (6.25 g, 45.2 mmol) and tosyl azide (2.57 g, 13.0 mmol) in MeCN (85 mL) was added dimethyl-2-oxopropylphosphonate (1.65 mL, 12.0 mmol), and the colourless suspension was stirred at rt for 2 h. Then a solution of Boc-L-prolinal (1.90 mL, 10.0 mmol) in MeOH (85 mL) was added dropwise over 30 min to the suspension and the mixture was stirred at rt for 15 h. The reaction mixture was filtered over Celite®, then the filter cake was washed with Et_2O (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude residue was purified *via* flash chromatography (pentane/Et_2O, 9:1) to afford the *title compound* **2** (1.49 g, 76%) as a colourless oil.

$[\alpha]_D^{23.4}$ –81.1 (*c* 0.7, $CHCl_3$); lit **2** $[\alpha]_D^{20.0}$ –63.7 (c 0.67, $CHCl_3$);

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 4.49 – 4.34 (m, 1H, H-2), 3.44 – 3.29 (m, 2H, H-5), 2.20 (s, 1H, C≡CH), 2.03 – 1.79 (m, 4H, H-3 and H-4), 1.46 (s, 9H, $OC(CH_3)_3$);

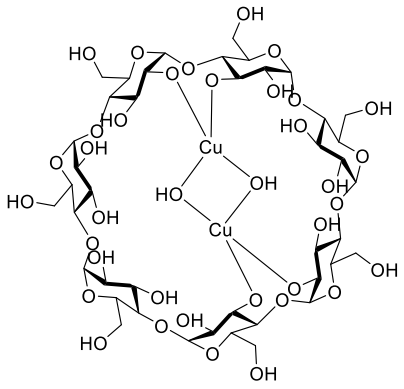
^{13}C NMR (100 MHz, $CDCl_3$): δ 154.1 (C, C=O), 84.3 (C, *C*≡CH), 79.8 (C, O*C*$(CH_3)_3$), 69.8 (CH, C≡*C*H*), 69.4 (CH, C≡*C*H), 48.0 (CH, C-2), 47.8 (CH, C-2*), 45.6 (CH_2, C-5*), 45.5 (CH_2, C-5), 33.7 (CH_2, C-3), 33.0 (CH_2, C-3*), 28.5 (3 × CH_3, $OC(CH_3)_3$), 24.4 (CH_2, C-4*), 23.6 (CH_2, C-4);

*denotes minor rotamer

The spectroscopic data were in agreement with that reported in the literature.[4]

Preparation of Copper Cyclodextrin Catalyst **4**

[μ-[β-Cyclodextrinato(4-)-κ*O*^{2A},κ*O*^{3G},κ*O*^{2D},κ*O*^{3C}]]di-μ-hydroxydicuprate(2-) (4)



$[Cu_2(\mu\text{-}OH)_2(\beta\text{-CD})]^{2-}$ was prepared according to the procedure by Matsui *et al*.[5] To a stirred solution of β-cyclodextrin (1.14 g, 1.0 mmol) in 0.50 M aq. NaOH (50 mL) was added a solution of 0.04 M aq. $CuSO_4 \cdot 5(H_2O)$ (75 mL, 3.0 mmol). After stirring at rt for 6 h, the resultant solution was filtered to remove excess copper (II) hydroxide. Ethanol (*ca* 400 mL) was added to the filtrate until a light blue

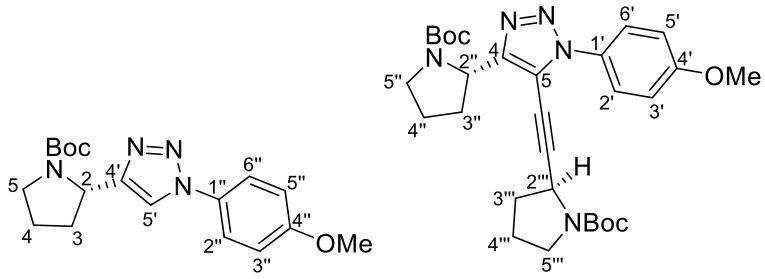
suspension was formed. After standing at rt for 16 h, the precipitate was filtered, washed with cold ethanol and water respectively, then dried *in vacuo* to afford the *title compound* **4** (1.10 g, 84%) as a light blue solid.

IR ν_{max} (neat): 3305, 1646, 1445, 1371, 875 cm^{-1};

The spectroscopic data were in agreement with that reported in the literature.[6]

Characterisation for Compounds **6** and **7**

***tert*-Butyl (*S*)-2-(1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)pyrrolidine-1-carboxylate (6)** and ***N*,*N*'-Di-*tert*-butoxycarbonyl-1-(4-methoxyphenyl)-4-((*S*)-pyrrolidin-2-yl)-5-(((*S*)-pyrrolidin-2-yl)ethynyl)-1*H*-1,2,3-triazole (7)**



Method A: Chan-Lam/CuAAC without additives

To a suspension of $[Cu_2(\mu\text{-}OH)_2(\beta\text{-}CD)]^{2-}$ (5 mol%, 17 mg, 13 μmol) in MeOH (0.75 mL) was added sequentially 4-methoxyphenyl boronic acid (58 mg, 0.38 mmol) and aq. NaN_3 (0.25 mL, 0.77 mmol, 3M in H_2O), and the mixture stirred, while exposed to air, at 50 °C for 16 h. After cooling to rt, alkyne **2** (52 mg, 0.27 mmol) was added to the reaction and the resultant mixture was stirred at rt for 16 h. EtOAc (5 mL) and water (1 mL) was added to the reaction, then was subsequently extracted with EtOAc (5 mL) and washed with brine (5 mL). The aqueous layer was further extracted with EtOAc (2 × 5 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by preparative thin layer chromatography (pet. ether/EtOAc, 17:3 v/v) to afford the *title compounds* **6** (34 mg, 37%) as an off-white solid and **7** (13 mg, 12%) as a colourless oil.

Method B: Optimised Chan-Lam/CuAAC

To a suspension of $[Cu_2(\mu\text{-}OH)_2(\beta\text{-}CD)]^{2-}$ (5 mol%, 17 mg, 13 μmol) in MeOH (0.75 mL) was added sequentially 4-methoxyphenyl boronic acid (58 mg, 0.38 mmol) and aq. NaN_3 (0.25 mL, 0.77 mmol, 3 Min H_2O), and the mixture stirred, while exposed to air, at 50 °C for 16 h. After cooling to rt, H_2O (0.5 mL) was added to the reaction followed by sodium ascorbate (10 mg, 50 μmol) and alkyne **2** (50 mg, 0.25 mmol). The resultant mixture was stirred at rt for 3 h then EtOAc (2 mL) and 2 M aq. $(NH_4)_2CO_3$ (0.5 mL) were added. Upon complete dissolution of the solute, the reaction mixture was extracted with EtOAc (5 mL) and washed with brine (5 mL). The aqueous layer was further extracted with EtOAc (2 × 5 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered

and concentrated *in vacuo*. The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 7:3) to afford the *title compound* **6** (67 mg, 76%) as an off-white solid.

Triazole **6**

$[\alpha]_D^{22.4}$ –40.0 (*c* 1.05, MeOH);

IR ν_{max} (neat): 2974, 1687, 1513, 1391, 1252, 1159, 1113, 1036, 833 cm^{-1};

^1H NMR (400 MHz, CD_3OD): *δ* 8.26 – 8.18 (m, 1H, H-5′), 7.71 (d, *J* = 9.0 Hz, 2H, H-2″ and H-6″), 7.10 (d, *J* = 8.7 Hz, 2H, H-3″ and H-5″), 5.05 (m, 1H, H-2), 3.86 (s, 3H, OCH_3), 3.68 – 3.60 (m, 1H, H_a-5), 3.52 – 3.45 (m, 1H, H_b-5), 2.36 – 2.32 (m, 1H, H_a-3), 2.15 – 2.07 (m, 2H, H_b-3 and H_a-4), 2.01 – 1.95 (m, 1H, H_b-4), 1.46 – 1.29 (m, 9H, $OC(CH_3)_3$);

^{13}C NMR (100 MHz, CD_3OD): δ 161.6 (C, C-4″), 156.3 (C, C=O*), 156.1 (C, C=O), 152.7 (C, C-4′), 152.6 (C, C-4′*), 131.7 (C, C-1″), 123.2 (CH, C-2″), 123.1 (CH, C-6″), 121.8 (CH, C-5′*), 121.2 (CH, C-5′), 116.0 (2 × CH, C-3″ and C-5″), 81.1 (C, $OC(CH_3)_3$), 56.1 (CH_3, OCH_3), 55.0 (CH, C-2), 54.5 (CH, C-2*), 48.0 (CH_2, C-5*), 47.5 (CH_2, C-5), 34.8 (CH_2, C-3), 33.5 (CH_2, C-3*), 30.9 (3 × CH_3, $OC(CH_3)_3$*) , 28.6 (3 × CH_3, $OC(CH_3)_3$), 24.9 (CH_2, C-4*), 24.2 (CH_2, C-4);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{24}N_4NaO_3$, 367.1741; found, 367.1740.

Bis-pyrrolidine **7**

$[\alpha]_D^{17.4}$ –56.0 (*c* 1.5, MeOH);

IR ν_{max} (neat): 2975, 1693, 1516, 1392, 1366, 1254, 1162, 1118 cm^{-1};

^1H NMR (400 MHz, CD_3OD): *δ* 7.64 – 7.58 (m, 2H, H-2′ and H-6′), 7.13 – 7.11 (m, 2H, H-3′ and H-5′), 5.10 – 5.00 (m, 1H, H-2″), 4.72 – 4.67 (m, 1H, H-2‴), 3.88 (s, 3H, OCH_3), 3.62 – 3.35 (m, 4H, H-5″ and H-5‴), 2.41 –2.38 (m, 1H, H_a-3″), 2.21 – 1.97 (m, 7H, H_b-3″ and H-4″ and H-3‴ and H-4‴), 1.46 – 1.26 (m, 18H, 2 × $OC(CH_3)_3$);

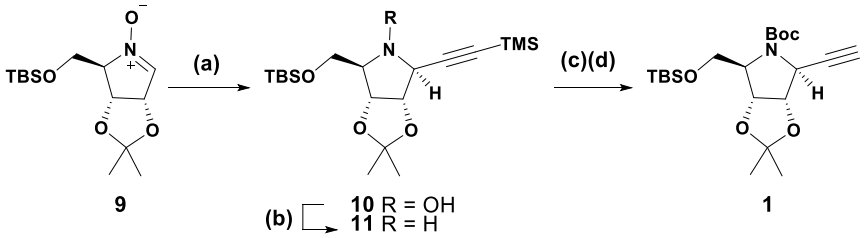
^{13}C NMR (100 MHz, CD_3OD): δ 162.0 (C, C-4′), 156.0 (C, C=O*), 155.6 (2 × C, 2 × C=O), 154.3 (C, C-4), 130.5 (C, C-1′), 126.4 (CH, C-2′), 126.3 (CH, C-6′), 126.1 (C, C-5), 119.1 (2 × CH, C-3′* and C-5′*), 115.7 (2 × CH, C-3′ and C-5′), 104.5 (C, 2‴-*C*≡C), 104.0 (C, 2‴-*C*≡C*), 81.5 (C, $OC(CH_3)_3$*), 81.4 (C, $OC(CH_3)_3$*), 81.1 (C, $OC(CH_3)_3$), 80.9 (C, $OC(CH_3)_3$), 68.3 (C, 5-*C*≡C*), 66.9 (C, 5-*C*≡C), 56.2 (CH_3, OCH_3), 55.1 (CH, C-2″), 50.3 (CH, C-2‴), 49.9 (CH, C-2‴*), 48.0 (CH_2, C-5″), 47.2 (CH_2, C-5‴*), 46.7 (CH_2, C-5‴), 35.2 (CH_2, C-3″), 34.4 (CH_2, C-3‴), 33.6 (CH_2, C-3‴*), 30.9 (3 × CH_3, $OC(CH_3)_3$*), 28.8 (3 × CH_3, $OC(CH_3)_3$), 28.7 (3 × CH_3, $OC(CH_3)_3$), 25.5 (CH_2, C-4‴), 25.1 (CH_2, C-4‴*), 24.6 (CH_2, C-4″);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{29}H_{39}N_5NaO_5$, 560.2843; found, 560.2830.

*denotes minor rotamer

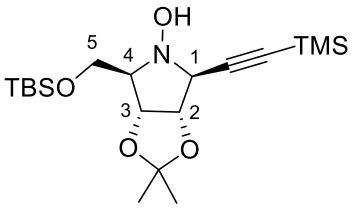
Synthesis of Flex-Imino-C-Nucleosides

Preparation of Alkyne Intermediate **1**



Reagents and Conditions: a) *n*-BuLi (2.2 equiv.), TMS-acetylene (2.5 equiv.), THF, 0 ˚C, quant.; b) Zn (28 equiv.), AcOH, rt, 51%; c) Boc_2O (1.3 equiv), MeOH, rt, 16 h; d) K_2CO_3 (5 equiv.), MeOH, 50 ˚C, 40 min, 95% over 2 steps.

(1*S*)-1-(Trimethylsilyl)ethynyl)-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-*N*-hydroxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (10)



n-Butyllithium (10 mL, 1.9 M in cyclohexane, 19 mmol) was added dropwise to a solution of ethynyltrimethylsilane (3 mL, 21.7 mmol) in THF (20 mL) at 0 °C. After five minutes, the light-yellow solution was added dropwise, by syringe, to a stirred solution of nitrone **9** (2.58 g, 8.6 mmol) in THF (80 mL) at 0 °C over two minutes. After 30 minutes, the reaction was quenched with sat. aq. NH_4Cl (20 mL), then diluted with EtOAc (50 mL). The organic phase was separated, and the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to afford the *title compound* **10** as a light amber oil (3.42 g, quant.).

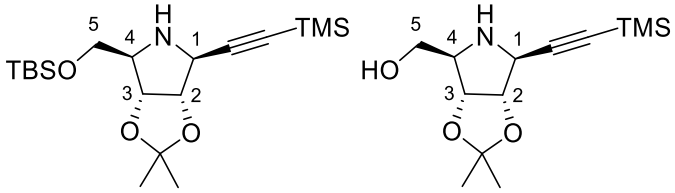
$[\alpha]_D^{23}$ –19.5 (*c* 0.2, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.34 (s, 1H, N-O*H*), 4.50 – 4.43 (m, 1H, H-2), 4.37 (dd, *J* = 7.0, 4.7 Hz, 1H, H-3), 3.93 – 3.79 (m, 2H, H-5), 3.70 (d, *J* = 6.2 Hz, 1H, H-1), 3.06 (q, *J* = 5.1 Hz, 1H, H-4), 1.53 (s, 3H, C*CH*$_3$CH$_3$), 1.31 (s, 3H, CCH$_3$*CH*$_3$), 0.90 (s, 9H, (CH$_3$)$_3$C-Si), 0.18 (s, 9H, Si(CH$_3$)$_3$), 0.09 (s, 3H, *t*-Bu-SiCH$_3$), 0.08 (s, 3H, *t*-Bu-SiCH$_3$);

^{13}C NMR (126 MHz, $CDCl_3$): δ 113.9 (C, *C*(CH$_3$)$_2$), 102.7 (C, *C*≡C-TMS), 89.7 (C, C≡*C*-TMS), 81.2 (CH, C-2), 77.8 (CH, C-3), 73.3 (CH, C-4), 65.8 (CH$_2$, C-5), 62.8 (CH, C-1), 27.2 (CH$_3$, C*C*H$_3$CH$_3$), 25.9 (CH$_3$, CCH$_3$*C*H$_3$), 25.1 (3 × CH$_3$, (*C*H$_3$)$_3$C-Si), 18.3 (C, (CH$_3$)$_3$*C*-Si), –0.1 (3 × CH$_3$, (*C*H$_3$)$_3$Si), –5.31 (CH$_3$, (CH$_3$)$_3$CSi-(*C*H$_3$)$_2$), –5.32 (CH$_3$, (CH$_3$)$_3$CSi-(*C*H$_3$)$_2$);

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{38}NO_4Si_2$, 400.2334; found, 400.2343.

(1*S*)-1-(Trimethylsilyl)ethynyl)-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (11) and **(1*S*)-1-(Trimethylsilyl)ethynyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (S11)**



Zinc dust (15.7 g, 240 mmol) was added to a solution of hydroxylamine **10** (3.4 g, 8.5 mmol) in glacial acetic acid (85 mL) and left to stir vigorously overnight. The reaction mixture was filtered through Celite® and concentrated *in vacuo* to afford a 3:2 mixture of TBS-protected amino ether **11** and amino-alcohol **11a**. The products were separated and purified by automated flash column chromatography (linear gradient 10-100% EtOAc in pet. ether on silica gel) to afford the *title compounds* **11** (1.67 g, 51%) as a colourless oil; and **11a** (0.65 g, 28%) as a colourless solid.

11-5-O-TBS

$[\alpha]_D^{23}$ –24.5 (*c* 0.6, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.65 (dd, *J* = 6.3, 3.2 Hz, 1H, H-2), 4.59 (dd, *J* = 6.3, 2.7 Hz, 1H, H-3), 3.86 (d, *J* = 3.2 Hz, 1H, H-1), 3.79 (dd, *J* = 10.3, 6.5 Hz, 1H, H-5), 3.70 (dd, *J* = 10.2, 5.5 Hz, 1H, H-5), 3.24 (td, *J* = 6.0, 2.7 Hz, 1H, H-4), 1.49 (s, 3H, C*CH*$_3$CH$_3$), 1.32 (s, 3H, C*C*H$_3$C*H*$_3$), 0.90 (s, 9H, (CH$_3$)$_3$C-Si), 0.14 (s, 9H, Si(CH$_3$)$_3$), 0.07 (s, 3H × 2, *t*-Bu-Si(CH$_3$)$_2$);

^{13}C NMR (126 MHz, $CDCl_3$) δ 112.9 (C, *C*(CH$_3$)$_2$), 105.5 (C, *C*≡C-TMS), 89.0 (C, C≡*C*-TMS), 87.1 (CH, C-2), 82.8 (CH, C-3), 66.9 (CH, C-4), 63.2 (CH$_2$, C-5), 56.4 (CH, C-1), 27.0 (CH$_3$, C*C*H$_3$CH$_3$), 25.9 (3 × CH$_3$, (*C*H$_3$)$_3$C-Si), 24.9 (CH$_3$, CCH$_3$*C*H$_3$), 18.3 (C, (CH$_3$)$_3$*C*-Si), –0.2 (3 × CH$_3$, (*C*H$_3$)$_3$Si), –5.3 (CH$_3$, (CH$_3$)$_3$CSi-(*C*H$_3$)$_2$), –5.4 (CH$_3$, (CH$_3$)$_3$CSi-(*C*H$_3$)$_2$);

HRMS (ESI/QTOF) *m/z*: [M + H]$^+$ calcd for $C_{19}H_{38}NO_3Si_2$, 384.2385; found 384.2399.

S11-5-OH: (ethyl acetate impurity present; see spectral images)

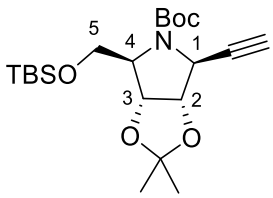
$[\alpha]_D^{23}$ –5.2 (*c* 0.9, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.72 (dd, *J* = 5.8, 2.2 Hz, 1H, H-2), 4.56 (dd, *J* = 5.9, 1.7 Hz, 1H, H-3), 3.95 (d, *J* = 2.2 Hz, 1H, H-1), 3.73 – 3.61 (m, 2H, H-5), 3.38 (ddd, *J* = 7.6, 5.5, 1.8 Hz, 1H, H-4), 1.47 (s, 3H, C*CH*$_3$CH$_3$), 1.30 (s, 3H, CCH$_3$C*H*$_3$), 0.15 (s, 9H, Si(CH$_3$)$_3$);

^{13}C NMR (126 MHz, $CDCl_3$) δ 112.2 (C, *C*(CH$_3$)$_2$), 105.4 (C, *C*≡C-TMS), 89.3 (C, C≡*C*-TMS), 87.2 (CH, C-2), 83.1 (CH, C-3), 66.9 (CH, C-4), 62.2 (CH$_2$, C-5), 56.3 (CH, C-1), 26.7 (CH$_3$, C*C*H$_3$CH$_3$), 24.4 (CH$_3$, CCH$_3$*C*H$_3$), –0.3 (3 × CH$_3$, (CH$_3$)$_3$Si);

HRMS (ESI/QTOF) *m/z*: [M + H]$^+$ calcd for $C_{13}H_{24}NO_3Si$, 270.1520; found 270.1527.

(1*S*)-1-Ethynyl-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-*N*-*tert*-butoxycarbonyl-1,4-imino-2,3-*O*-isopropylidene-D-ribitol (1)



To a solution of pyrrolidine **11** (1.00 g, 2.61 mmol) in methanol (50 mL) was added di-*tert*-butyl dicarbonate (0.74 g, 3.39 mmol) portion-wise at 0 °C. After stirring at rt for 16 h, the reaction mixture was concentrated *in vacuo*. The crude residue was redissolved in methanol (30 mL), then powdered K_2CO_3 (1.8 g, 13.0 mmol) was added and the resultant suspension was stirred at 50 °C for 40 min. After cooling to rt, the reaction was diluted with CH_2Cl_2 (100 mL), quenched with sat. aq. NH_4Cl (20 mL) and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic extracts were washed with brine (50 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1) to afford the *title compound* **1** (1.07 g, 95% over 2 steps) as a colourless oil.

$[\alpha]_D^{25.3}$ –4.3 (*c* 1.0, $CHCl_3$);

IR ν_{max} (neat): 2931, 2858, 1699, 1381, 1252, 1162, 1122, 1055, 834, 776 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6, 343 K): δ 4.76 – 4.71 (m, 2H, H-2 and H-3), 4.50 (br s, 1H, H-1), 3.93 (dd, *J* = 8.3, 4.9 Hz, 1H, H-4), 3.76 – 3.63 (m, 2H, H-5), 3.26 – 3.25 (m, 1H, C≡CH), 1.43 (s, 9H, $OC(CH_3)_3$), 1.36 (s, 3H, CCH_3CH_3), 1.28 (s, 3H, CCH_3CH_3), 0.90 (s, 9H, $SiC(CH_3)_3$), 0.08 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, DMSO-d_6, 343 K): δ 152.7 (C, C=O), 111.1 (C, $C(CH_3)_2$), 84.4 (CH, C-2), 81.7 (C, C≡CH), 81.4 (CH, C-3), 79.5 (C, $OC(CH_3)_3$), 74.5 (CH, C≡CH), 65.5 (CH, C-4), 61.4 (CH_2, C-5), 54.7 (CH, C-1), 27.7 (3 × CH_3, $OC(CH_3)_3$), 26.5 (CH_3, CCH_3CH_3), 25.5 (3 × CH_3, $SiC(CH_3)_3$), 24.7 (CH_3, CCH_3CH_3), 17.6 (C, $SiC(CH_3)_3$), –5.7 (CH_3, $SiCH_3$), –5.8 (CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{21}H_{38}NO_5Si$, 412.2514; found, 412.2513.

General Procedures and Characterisation for Compounds **(S)12a-12x**

General Procedure A: One-pot Chan-Lam/CuAAC Sequence

To a suspension of $[Cu_2(\mu\text{-}OH)_2(\beta\text{-}CD)]^{2-}$ (6.0 μmol) in MeOH (0.35 mL) was added sequentially; water (0.15 mL), aryl boronic acid (240 μmol), and NaN_3 (730 μmol). The mixture was stirred, exposed to air, at 50 °C for 16 h. After cooling to rt, H_2O (0.2 mL) was added to the reaction followed by sodium ascorbate (12 μmol) and alkyne **1** (120 μmol). The resultant mixture was stirred at rt for 16h then EtOAc and 2 M aq. $(NH_4)_2CO_3$ were added. Upon complete dissolution of the solute, the reaction mixture was extracted with EtOAc and washed with brine. The aqueous layer was further extracted with EtOAc (×2). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compounds* **S12a** – **S12x**.

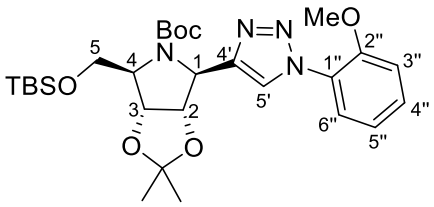
General Procedure B: Global Deprotection with HCl

A solution of protected nucleoside **S12a** – **S12p**, **S12r or S12u** – **S12x** in 6 M aq. HCl (1.0 mL) was stirred vigorously at rt for 16 h. The reaction was concentrated *in vacuo* and the crude residue was triturated with cold Et_2O (1.0 mL). The resultant solid was dissolved in 0.1 M aq. HCl (3.0 mL) and lyophilised to afford the *title compounds* **12a** – **12p**, **12r**, or **12u** – **12x**. Analytical samples were prepared by trituration of the solid with cold MeCN followed by lyophilisation.

General Procedure C: Global Deprotection with TFA

A solution of protected nucleoside **S12q** or **S12s** – **S12t** in aq. TFA (25% v/v, 1.0 mL) was stirred at rt for 6 h. Water (3.0 mL) was added and the aqueous layer was washed with CH_2Cl_2 (2 × 1.0 mL), then lyophilised to afford the *title compounds* **12q** or **12s** – **12t**. Analytical samples were prepared by trituration of the solid with cold MeCN followed by lyophilisation.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(2-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12a)



General procedure A was followed using alkyne **1** (48 mg, 120 μmol) and 2-methoxyphenylboronic acid (35 mg, 230 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12a** (32 mg, 52%) as an off-white solid.

$[\alpha]_D^{20.5}$ –15.8 (*c* 0.24, $CHCl_3$);

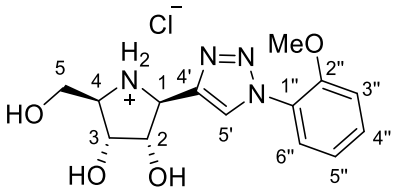
IR ν_{max} (neat): 2932, 2858, 1694, 1507, 1391, 1367, 1250, 1124, 1049, 835, 730 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.12 – 7.96 (m, 1H, H-5′), 7.75 (dd, *J* = 7.9, 1.9 Hz, H-6″), 7.40 – 7.38 (m, 1H, H-4″), 7.07 – 7.05 (m, 2H, H-3″ and H-5″), 5.38 – 5.17 (m, 2H, H-1 and H-2), 4.93 – 4.85 (m, 1H, H-3), 4.21 – 4.08 (m, 1H, H-4), 3.85 (s, 3H, OCH_3), 3.71 – 3.58 (m, 2H, H-5), 1.53 (s, 3H, $_{C\text{-}CH3}$), 1.44 (s, 9H, $OC(CH_3)_3$), 1.37 (s, 3H, CCH_3CH_3), 0.85 – 0.80 (m, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3 (C, C=O), 154.0 (C, C=O*), 151.1 (C, C-2″), 147.4 (C, C-4′*), 146.1 (C, C-4′), 130.0 (CH, C-4″), 126.4 (C, C-1″), 125.6 (CH, C-6″*), 125.4 (CH, C-6″), 125.1 (CH, C-5′), 124.0 (CH, C-5′*), 121.3 (CH, C-5″*), 121.2 (CH, C-5″), 112.3 (CH, C-3″), 111.7 (C, $C(CH_3)_2$), 84.6 (CH, C-2*), 83.2 (CH, C-2), 82.8 (CH, C-3), 81.8 (CH, C-3*), 80.2 (C, $OC(CH_3)_3$), 66.4 (CH, C-4), 66.0 (CH, C-4*), 62.3 (CH_2, C-5), 61.1 (CH, C-1*), 60.1 (CH, C-1), 55.9 (CH_3, OCH_3), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.3 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{44}N_4NaO_6Si$, 583.2922; found, 583.2991.

(1*S*)-1-(1-(2-Methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12a·HCl)



Following general procedure B, nucleoside **S12a** (30 mg, 53 μmol) was deprotected to afford the *title compound* **12a·HCl** (15 mg, 87%) as a white solid.

$[\alpha]_D^{19.4}$ –9.5 (*c* 0.4, MeOH);

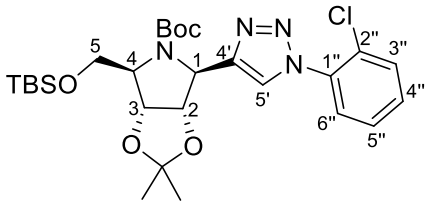
IR ν_{max} (film): 1635, 1508, 1288, 1255, 1124, 1016 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6): *δ* 10.67 – 10.65 (m, 1H, NH), 8.89 – 8.87 (m, 1H, NH), 8.70 (s, 1H, H-5′), 7.62 (dd, *J* = 7.8, 2.0 Hz, 1H, H-6″), 7.58 – 7.53 (m, 1H, H-4″), 7.35 (dd, *J* = 8.5, 1.0 Hz, 1H, H-3″), 7.16 (td, *J* = 7.8, 1.0 Hz, H-5″), 4.68 – 4.64 (m, 1H, H-1), 4.45 – 4.42 (m, 1H, H-2), 4.22 – 4.20 (m, 1H, H-3), 3.74 (d, *J* = 5.5 Hz, 2H, H-5), 3.58 – 3.54 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-d_6): δ 151.5 (CH, C-2″), 140.6 (C, C-4′), 131.0 (C, C-4″), 126.7 (CH, C-5′), 125.6 (CH, C-6″), 125.4 (C, C-1″), 121.0 (CH, C-5″), 113.2 (CH, C-3″), 73.9 (CH, C-2), 70.4 (CH, C-3), 65.4 (CH, C-4), 58.6 (CH_2, C-5), 56.7 (CH, C-1) 56.2 (CH_3, OCH_3);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{19}N_4O_4$, 307.1401; found, 307.1402

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(2-chlorophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12b)



General procedure A was followed using alkyne **1** (46 mg, 110 μmol) and 2-chlorophenylboronic acid (35 mg, 220 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford *the title compound* **S12b** (52 mg, 51%) as an off-white solid.

$[\alpha]_D^{19.9}$ –16.0 (*c* 0.5, $CHCl_3$);

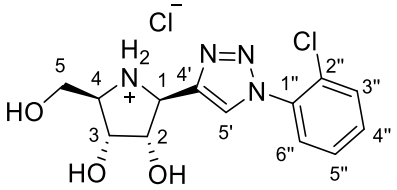
IR ν_{max} (neat): 2932, 2858, 1694, 1496, 1382, 1367, 1252, 1169, 1124, 1052, 834, 776, 779 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6, 343 K): δ 8.27 (s, 1H, H-5′), 7.76 – 7.73 (m, 1H, H-3″), 7.65 – 7.57 (m, 3H, H-4″, H-5″ and H-6″), 5.14 (s, 1H, H-1), 5.10 (d, J = 5.6 Hz, 1H, H-2), 4.79 (d, J = 5.6 Hz, 1H, H-3), 4.04 (dd, J = 8.9, 4.9 Hz, 1H, H-4), 3.59 (ABX, $\Delta\delta_{AB}$ = 0.17, J_{AB} = 9.8 Hz, J_{AX} = 8.9 Hz, J_{BX} = 4.9 Hz, 2H, H-5), 1.46 (s, 3H, CC$H_3$$CH_3$), 1.40 (s, 9H, OC$(CH_3)_3$), 1.34 (s, 3H, $CCH_3C$$H_3$), 0.85 (s, 9H, SiC$(CH_3)_3$), 0.02 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, DMSO-d_6, 343 K): 153.1 (C, C=O), 146.3 (C, C-4′), 134.2 (C, C-1″), 131.2 (CH, C-4″), 130.2 (CH, C-3″), 128.06 (CH, C-5″ or C-6″), 128.04 (C, C-2″), 127.8 (CH, C-5″ or C-6″), 124.4 (CH, C-5′), 110.9 (C, $C(CH_3)_2$), 83.5 (CH, C-2), 81.6 (CH, C-3), 79.3 (C, O$C(CH_3)_3$), 65.5 (CH, C-4), 61.9 (CH_2, C-5), 59.9 (CH, C-1), 27.7 (3 × CH_3, OC$(CH_3)_3$, 26.8 (CH_3, CCH_3CH_3), 25.4 (3 × CH_3, SiC$(CH_3)_3$), 24.8 (CH_3, CCH_3CH_3), 17.5 (C, Si$C(CH_3)_3$), –5.7 (CH_3, $SiCH_3$), –5.8 (CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{41}ClN_4NaO_3Si$, 587.2427; found, 587.2424.

(1*S*)-1-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12b·HCl)



Following general procedure B, nucleoside **S12b** (26.0 mg, 46.0 μmol) was deprotected to afford the *title compound* **12b·HCl** (15.4 mg, 96%) as a cream solid.

$[\alpha]_D^{21.4}$ –12.5 (*c* 0.2, MeOH);

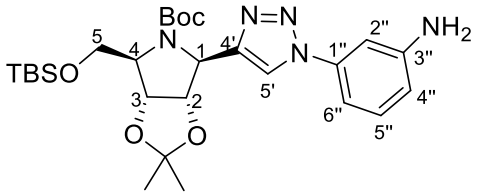
IR ν_{max} (film): 1627, 1498, 1239, 1130, 1077, 1050, 761 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD): *δ* 8.57 (s, 1H, H-5′), 7.73 – 7.70 (m, 1H, H-3″), 7.66 – 7.55 (m, 3H, H-6″, H-4″ and H-5″), 4.91 (d, *J* = 6.4 Hz, 1H, H-1), 4.60 (dd, *J* = 6.4, 4.8 Hz, 1H, H-2), 4.43 (dd, *J* = 4.9, 4.4 Hz, 1H, H-3), 3.98 – 3.93 (m, 2H, H-5), 3.81 – 3.77 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 141.9 (C, C-4′), 135.8 (C, C-1″), 132.9 (CH, C-4″), 131.9 (CH, C-3″), 130.3 (C, C-2″), 129.4 (CH, C-5″ or C-6″), 129.2 (CH, C-5″ or C-6″), 127.9 (CH, C-5′), 75.8 (CH, C-2), 72.5 (CH, C-3), 67.0 (CH, C-4), 60.0 (CH_2, C-5), 58.8 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{16}ClN_4O_3$, 311.0905; found, 311.0910.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(3-aminophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12c)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and 3-aminophenylboronic acid (38 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12c** (43 mg, 65%) as a yellow solid.

$[\alpha]_D^{20.1}$ –18.9 (*c* 1.1, $CHCl_3$);

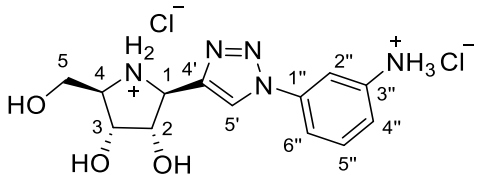
IR ν_{max} (neat): 2931, 1685, 1392, 1255, 1161, 1052, 835, 775 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.95 – 7.77 (m, 1H, H-5′), 7.23 (t, *J* = 7.9 Hz, 1H, H-5″), 7.08 (s, 1H, H-2″), 6.99 – 6.93 (m, 1H, H-4″), 6.69 (d, J = 7.6 Hz, 1H, H-6″), 5.39 – 5.15 (m, 2H, H-1 and H-2), 4.93 – 4.82 (m, 1H, H-3), 4.22 – 4.08 (m, 1H, H-4), 3.92 (br s, 2H, NH_2), 3.71 – 3.56 (m, 2H, H-5), 1.53 (s, 3H, CCH_3CH_3), 1.45 (s, 9H, $OC(CH_3)_3$), 1.37 (s, 3H, CCH_3CH_3), 0.84 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4 (C, C=O), 147.9 (C, C-3″), 147.2 (C, C-4′), 138.0 (C, C-1″), 130.5 (CH, C-5″), 121.2 (CH, C-5′), 120.0 (CH, C-5′*), 115.1 (CH, C-6″), 111.8 (C, $C(CH_3)_2$), 110.0 (CH, C-4″), 106.9 (CH, C-2″), 84.7 (CH, C-2*), 83.0 (CH, C-2), 82.7 (CH, C-3), 81.8 (CH, C-3*), 80.4 (C, $OC(CH_3)_3$), 66.4 (CH, C-4), 66.0 (CH, C-4*), 62.4 (CH_2, C-5), 61.3 (CH, C-1*), 60.1 (CH, C-1), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.3 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.2 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{43}N_5NaO_5Si$, 568.2926; found, 568.2926.

(1*S*)-1-(1-(3-aminophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol dihydrochloride (12c·2HCl)



Following general procedure B, nucleoside **S12c** (21 mg, 38 μmol) was deprotected to afford the *title compound* **12c·2HCl** (14 mg, 96%) as a yellow solid.

$[\alpha]_D^{20.9}$ –2.7 (*c* 0.3, MeOH);

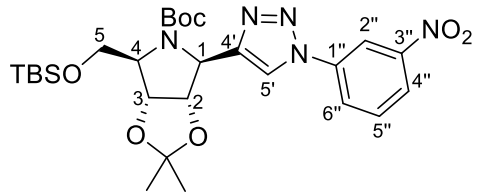
IR ν_{max} (film): 3058, 2892, 1575, 1484, 1122, 1062, 804 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6): *δ* 10.72 (br s, 1H, NH), 9.10 (s, 1H, H-5′), 8.93 (br s, 1H, NH), 7.87 (s, 1H, H-2″), 7.77 (d, *J* = 8.3 Hz, 1H, H-4″), 7.69 – 7.65 (m, 1H, H-5″), 7.43 (d, *J* = 7.6 Hz, 1H, H-6″), 4.66 – 4.65 (m, 1H, H-1), 4.44 (dd, *J* = 6.9, 4.9 Hz, 1H, H-2), 4.21 – 4.19 (m, 1H, H-3), 3.74 (d, *J* = 4.9 Hz, 2H, H-5) 3.55 – 3.54 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-d_6): δ 142.0 (C, C-4′), 137.0 (C, C-3″), 136.4 (C, C-1″), 131.3 (CH, C-5″), 123.5 (CH, C-5′), 122.3 (CH, C-6″), 117.4 (CH, C-4″), 113.6 (CH, C-2″), 73.8 (CH, C-2), 70.5 (CH, C-3), 65.4 (CH, C-4), 58.6 (CH_2, C-5), 56.5 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{13}H_{17}N_5NaO_3$, 314.1224; found, 314.1223.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12d)



General procedure A was followed using alkyne **1** (49 mg, 120 μmol) and 3-nitrophenylboronic acid (40 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12d** (28 mg, 41%) as a tan solid.

$[\alpha]_D^{19.2}$ –35.8 (*c* 1.4, $CHCl_3$);

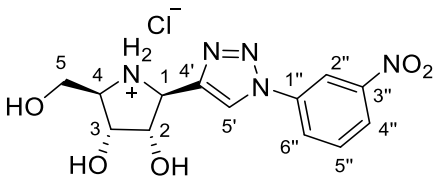
IR ν_{max} (neat): 2932, 1690, 1538, 1392, 1350, 1254, 1161, 1124, 1054, 834, 776 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.59 (s, 1H, H-2″), 8.29 (d, *J* = 7.2 Hz, 1H, H-4″), 8.14 – 7.94 (m, 2H, H-5′ and H-6″), 7.73 (t, *J* = 7.2 Hz, 1H, H-5″), 5.37 – 5.11 (m, 2H, H-1 and H-2), 4.92 – 4.80 (m, 1H, H-3), 4.28 – 4.10 (m, 1H, H-4), 3.73 – 3.63 (m, 2H, H-5), 1.54 (s, 3H, CCH_3CH_3), 1.46 (s, 9H, $OC(CH_3)_3$), 1.38 (s, 3H, CCH_3CH_3), 0.83 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4 (C, C=O), 149.0 (C, C-3″), 148.4 (C, C-4′), 137.8 (C, C-1″), 131.0 (CH, C-5″), 125.8 (CH, C-6″), 123.2 (CH, C-4″), 121.1 (CH, C-5′), 115.3 (CH, C-2″), 112.0 (C, $C(CH_3)_2$), 83.0 (CH, C-2), 82.6 (CH, C-3), 80.7 (C, $OC(CH_3)_3$), 66.3 (CH, C-4), 62.5 (CH_2, C-5), 60.3 (CH, C-1), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.4 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.2 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{41}N_5NaO_7Si$, 598.2667; found, 598.2669.

(1*S*)-1-(1-(3-Nitrophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12d·HCl)



Following general procedure B, nucleoside **S12d** (20 mg, 34 μmol) was deprotected to afford the *title compound* **12d·HCl** (9.0 mg, 73%) as a tan solid.

$[\alpha]_D^{21.5}$ –4.0 (*c* 0.1, MeOH);

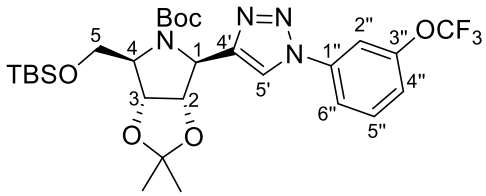
IR ν_{max} (film): 1533, 1352, 1048, 737 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD): *δ* 8.97 (s, 1H, H-5′), 8.78 (dd, *J* = 2.0, 1.9 Hz, 1H, H-2″), 8.40 – 8.34 (m, 2H, H-4″ and H-6″), 7.89 (dd, *J* = 8.50, 8.0 Hz, 1H, H-5″), 4.92 (d, *J* = 6.3 Hz, 1H, H-1), 4.60 (dd, *J* = 6.3, 4.6 Hz, 1H, H-2), 4.43 (dd, *J* = 4.9, 4.6 Hz, 1H, H-3), 3.98 – 3.90 (m, 2H, H-5), 3.81 – 3.78 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 150.4 (C, C-3″), 143.2 (C, C-4′), 138.8 (C, C-1″), 132.5 (CH, C-5″), 127.3 (CH, C-6″), 124.6 (CH, C-5′ or C-4″), 124.4 (CH, C-5′ or C-4″), 116.5 (CH, C-2″), 75.8 (CH, C-2), 72.6 (CH, C-3), 67.1 (CH, C-4), 60.0 (CH_2, C-5), 58.8 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{16}N_5O_5$, 322.1146; found, 322.1147.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(3-trifluoromethoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12e)



General procedure A was followed using alkyne **1** (49 mg, 120 μmol) and 3-trifluoromethoxyphenylboronic acid (40 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12e** (53 mg, 73%) as an off-white solid.

$[\alpha]_D^{19.2}$ –22.1 (*c* 1.3, $CHCl_3$);

IR ν_{max} (neat): 2932, 2859, 1693, 1392, 1253, 1213, 1162, 1123, 1054, 835, 777 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.02 – 7.83 (m, 1H, H-5′), 7.65 – 7.63 (m, 2H, H-2″ and H-6″), 7.54 (t, *J* = 8.3 Hz, H-5″), 7.29 – 7.27 (m, 1H, H-4″), 5.37 – 5.15 (m, 2H, H-1 and H-2), 4.92 – 4.80 (m, 1H, H-3), 4.26 – 4.09 (m, 1H, H-4), 3.72 – 3.62 (m, 2H, H-5), 1.53 (s, 3H, $CC\mathit{H}_3CH_3$), 1.45 (s, 9H, $OC(CH_3)_3$), 1.37 (s, 3H, $CCH_3C\mathit{H}_3$), 0.83 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

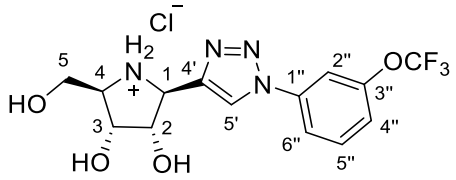
^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3 (C, C=O), 149.9 (C, C-3″), 147.9 (C, C-4′), 138.1 (C, C-1″), 131.0 (CH, C-5″), 121.0 (CH, C-5′), 120.3 (q, *J* = 258 Hz, C, OCF_3), 120.7 (CH, C-4″), 119.7 (CH, C-5′*), 118.3 (CH, C-2″), 113.3 (CH, C-6″), 111.8 (C, $\mathit{C}(CH_3)_2$), 84.7 (CH, C-2*), 82.9 (CH, C-2), 82.5 (CH, C-3), 81.6 (CH, C-3*), 80.4 (C, $O\mathit{C}(CH_3)_3$), 66.2 (CH, C-4), 65.9 (CH, C-4), 62.4 (CH_2, C-5), 61.4 (CH, C-1*), 60.1 (CH, C-1), 28.4 (3 × CH_3, $OC(\mathit{C}H_3)_3$, 27.2 (CH_3, $C\mathit{C}H_3CH_3$), 25.8 (3 × CH_3, $SiC(\mathit{C}H_3)_3$), 25.3 (CH_3, $CCH_3\mathit{C}H_3$), 18.2 (C, $Si\mathit{C}(CH_3)_3$), –5.4 (2 × CH_3, $SiCH_3$);

^{19}F NMR (376 MHz, $CDCl_3$): –57.9;

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$calcd for $C_{28}H_{41}F_3N_4NaO_6Si$, 637.2640; found, 637.2641.

*denotes minor rotamer

(1*S*)-1-(1-(3-Trifluoromethoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12e·HCl)



Following general procedure B, nucleoside **S12e** (53 mg, 89 μmol) was deprotected to afford the *title compound* **12e·HCl** (33 mg, 97%) as a tan solid.

$[\boldsymbol{\alpha}]_D^{20.5}$ –5.1 (*c* 0.9, MeOH);

IR ν_{max} (film): 1608, 1501, 1259, 1214, 1171, 1049 cm^{-1};

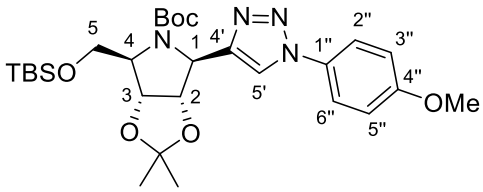
^{1}H NMR (400 MHz, CD_3OD): *δ* 8.81 (s, 1H, H-5′), 7.93 – 7.89 (m, 2H, H-2″ and H-6″), 7.73 (t, *J* = 8.3 Hz, H-5″), 7.49 – 7.46 (m, 1H, H-4″), 4.88 (d, *J* = 6.3 Hz, 1H, H-1), 4.58 (dd, *J* = 6.3, 4.5 Hz, 1H, H-2), 4.42 (dd, *J* = 5.0, 4.5 Hz, 1H, H-3), 3.97 – 3.89 (m, 2H, H-5), 3.79 – 3.76 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 151.1 (q, *J* = 1 Hz, C, C-3″), 142.9 (C, C-4′), 139.3 (C, C-1′), 132.9 (CH, C-5″), 124.3 (CH, C-5′), 122.5 (CH, C-4″), 121.8 (q, *J* = 258 Hz, C, OCF_3), 120.2 (CH, C-2″), 114.6 (CH, C-6″), 75.7 (CH, C-2), 72.5 (CH, C-3), 67.0 (CH, C-4), 60.0 (CH_2, C-5), 58.9 (CH, C-1);

^{19}F NMR (376 MHz, CD_3OD): –59.5

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{15}F_3N_4NaO_4$, 383.0938; found, 383.0936.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12f)



General procedure A was followed using alkyne **1** (99 mg, 240 μmol) and 4-methoxyphenylboronic acid (73 mg, 480 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 9:1) to afford the *title compound* **S12f** (78 mg, 61%) as an off-white solid.

$[\alpha]_D^{19.6}$ –31.5 (*c* 1.1, $CHCl_3$);

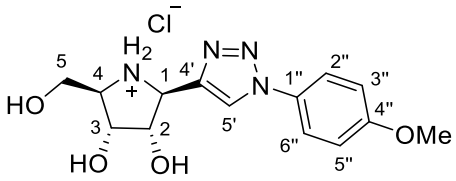
IR ν_{max} (neat): 2931, 2857, 1692, 1518, 1392, 1367, 1252, 1169, 1124, 1039, 834, 778 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.92 – 7.73 (m, 1H, H-5′), 7.61 – 7.59 (m, 2H, Ar-H), 7.01 – 6.99 (m, 2H, Ar-H), 5.40 – 5.16 (m, 2H, H-1 and H-2), 4.93 – 4.82 (m, 1H, H-3), 4.24 – 4.08 (m, 1H, H-4), 3.85 (s, 3H, OCH_3), 3.74 – 3.61 (m, 2H, H-5), 1.53 (s, 3H, CCH_3CH_3), 1.46 (s, 9H, $OC(CH_3)_3$), 1.38 (s, 3H, CCH_3CH_3), 0.84 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7 (C, C-4″), 154.3 (C, C=O), 147.3 (C, C-4′), 130.5 (C, C-1″), 122.1 (2 × CH, C-2″ or C-3″), 121.2 (CH, C-5′), 114.7 (2 × CH, C-2″ or C-3″), 111.7 (C, $C(CH_3)_2$), 83.0 (CH, C-2), 82.6 (CH, C-3), 80.3 (C, $OC(CH_3)_3$), 66.3 (CH, C-4), 62.3 (CH_2, C-5), 60.0 (CH, C-1), 55.6 (CH_3, OCH_3), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.2 (CH_3, CCH_3CH_3), 25.8 (3 × CH_3, $SiC(CH_3)_3$), 25.3 (CH_3, CCH_3CH_3), 18.2 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{44}N_4NaO_6Si$, 583.2992; found, 583.2992.

(1*S*)-1-(1-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12f·HCl)



Following general procedure B, nucleoside **S12f** (34 mg, 61 μmol) was deprotected to afford the *title compound* **12f·HCl** (19 mg, 91%) as a white solid.

$[\alpha]_D^{20.2}$ –6.4 (*c* 0.13, MeOH);

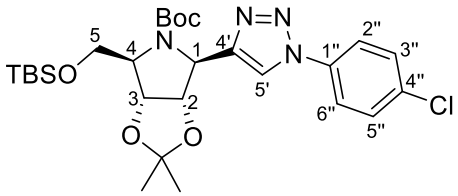
IR ν_{max} (neat): 3309, 3088, 2861, 2709, 1520, 1230, 1060, 830 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6): *δ* 8.95 – 8.91 (m, 1H, H-5′), 7.81 (d, *J* = 9.0 Hz, 2H, H-2″), 7.17 (d, *J* = 9.0 Hz, 2H, H-3″), 5.78 – 5.76 (m, 1H, 2-OH), 5.60 (d, *J* = 5.3 Hz, 1H, 3-OH), 5.37 – 5.36 (m, 1H, 5-OH), 4.63 (d, *J* = 7.1 Hz, 1H, H-1), 4.43 – 4.39 (m, 1H, H-2), 4.21 – 4.18 (m, 1H, H-3), 3.84 (s, 3H, OCH_3), 3.75 – 3.73 (m, 2H, H-5), 3.54 – 3.53 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-d_6): δ 159.5 (C, C-4″), 141.6 (C, C-4′), 129.8 (C, C-1″), 123.2 (CH, C-5′), 121.8 (2 × CH, C-2″), 115.0 (2 × CH, C-3″), 73.9 (CH, C-2), 70.6 (CH, C-3), 65.3 (CH, C-4), 58.7 (CH_2, C-5), 56.8 (CH, C-1), 55.6 (CH_3, OCH_3);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{19}N_4O_4$, 307.1401; found, 307.1400.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(4-chlorophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12g)



General procedure A was followed using alkyne **1** (45 mg, 110 μmol) and 4-chlorophenylboronic acid (35 mg, 220 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12g** (43 mg, 69%) as an off-white solid.

$[\alpha]_D^{20.3}$ –27.5 (*c* 1.0, $CHCl_3$);

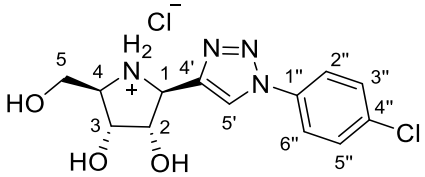
IR ν_{max} (neat): 2931, 1691, 1502, 1367, 1123, 1053, 832, 776 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.99 – 7.80 (m, 1H, H-5′), 7.66 (d, *J* = 8.4 Hz, 2H, H-2″ and H-6″), 7.48 (d, *J* = 8.4 Hz, 2H, H-3″ and H-5″), 6.99 – 6.93 (m, 1H, H-4″), 6.69 (d, J = 7.6 Hz, 1H, H-6″), 5.38 – 5.15 (m, 2H, H-1 and H-2), 4.92 – 4.80 (m, 1H, H-3), 4.22 – 4.08 (m, 1H, H-4), 3.72 – 3.61 (m, 2H, H-5), 1.53 (s, 3H, CC*H*$_3$CH$_3$), 1.46 (s, 9H, OC(CH$_3$)$_3$), 1.38 (s, 3H, CCH$_3$C*H*$_3$), 0.84 (s, 9H, SiC(CH$_3$)$_3$), 0.00 (s, 6H, 2 × SiCH$_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4 (C, C=O), 147.9 (C, C-4′), 135.6 (C, C-1″), 134.5 (C, C-4″), 130.0 (2 × CH, C-3″ and C-5″), 121.7 (2 × CH, C-2″ and C-6″), 121.1 (CH, C-5′), 111.9 (C, *C*(CH$_3$)$_2$), 83.0 (CH, C-2), 82.6 (CH, C-3), 80.5 (C, O*C*(CH$_3$)$_3$), 66.4 (CH, C-4), 62.5 (CH_2, C-5), 60.2 (CH, C-1), 28.5 (3 × CH$_3$, OC(*C*H$_3$)$_3$, 27.4 (CH$_3$, C*C*H$_3$CH$_3$), 25.9 (3 × CH$_3$, SiC(*C*H$_3$)$_3$), 25.4 (CH$_3$, CCH$_3$*C*H$_3$), 18.3 (C, Si*C*(CH$_3$)$_3$), –5.2 (2 × CH$_3$, SiCH$_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{41}ClN_4NaO_5Si$, 587.2427; found, 587.2426.

(1*S*)-1-(1-(4-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12g·HCl)



Following general procedure B, nucleoside **S12g** (20 mg, 36 μmol) was deprotected to afford the *title compound* **12g·HCl** (10 mg, 82%) as a white solid.

$[\alpha]_D^{21.1}$ –8.0 (*c* 0.1, MeOH);

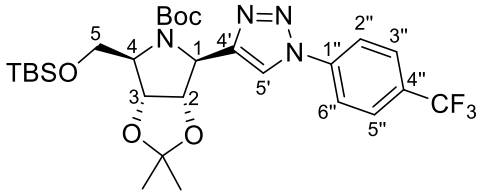
IR ν_{max} (neat): 3253, 2928, 2470, 1504, 1239, 1094, 1017, 986, 831 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.08 (s, 1H, H-5′), 7.98 – 7.94 (m, 2H, H-2″), 7.74 – 7.70 (m, 2H, H-3″), 5.77 (d, J = 6.0 Hz, 1H, 2-OH), 5.60 (d, J = 4.9 Hz, 1H, 3-OH), 5.37 – 5.34 (m, 1H, 5-OH), 4.64 (d, J = 7.0 Hz, 1H, H-1), 4.44 – 4.40 (m, 1H, H-2), 4.21 – 4.18 (m, 1H, H-3), 3.74 – 3.72 (m, 2H, H-5), 3.56 – 3.52 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-d_6): δ 142.1 (C, C-4′), 135.1 (C, C-1″), 133.3 (C, C-4″), 130.0 (2 × CH, C-3″), 123.3 (CH, C-5′), 121.8 (2 × CH, C-2″), 73.9 (CH, C-2), 70.5 (CH, C-3), 65.3 (CH, C-4), 58.7 (CH_2, C-5), 56.6 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{16}ClN_4O_3$, 311.0905; found, 311.0905.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(4-trifluoromethylphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol S12h



General procedure A was followed using alkyne **1** (47 mg, 110 μmol) and 4-trifluoromethylphenylboronic acid (43 mg, 230 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12h** (51 mg, 75%) as an off-white solid.

$[\alpha]_D^{19.2}$ –30.5 (*c* 0.4, $CHCl_3$);

IR ν_{max} (neat): 2933, 2859, 1692, 1618, 1392, 1323, 1252, 1167. 1125, 1069, 835, 776 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H, H-5″), 7.86 (d, J = 8.3 Hz, 2H, H-3″ and H-5″), 7.77 (d, J = 8.3 Hz, 2H, H-2″ and H-6″), 5.38 – 5.15 (m, 2H, H-1 and H-2), 4.92 – 4.80 (m, 1H, H-3), 4.27 – 4.09 (m, 1H, H-4), 3.73 – 3.62 (m, 2H, H-5), 1.53 (s, 3H, CCH_3CH_3), 1.45 (s, 9H, $OC(CH_3)_3$), 1.37 (s, 3H, CCH_3CH_3), 0.83 (s, 9H, $SiC(CH_3)_3$), –0.01 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4 (C, C=O), 148.1 (C, C-4′), 139.5 (C, C-1″), 130.8 (q, J = 33 Hz, C, C-4″), 127.1 (2 × CH, C-2″ and C-6″), 123.6 (q, J = 272 Hz, C, CF_3), 121.0 (CH, C-5′), 120.4(2 × CH, C-3″ and C-5″), 119.6 (CH, C-5′*),

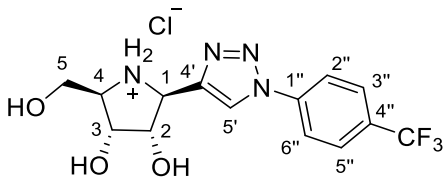
112.0 (C, $C(CH_3)_2$), 84.8 (CH, C-2*), 83.0 (CH, C-2), 82.6 (CH, C-3), 81.8 (CH, C-3*), 80.5 (C, $OC(CH_3)_3$), 66.3 (CH, C-4), 65.9 (CH, C-4*), 62.5 (CH_2, C-5), 61.5 (CH, C-1*), 60.2 (CH, C-1), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.3 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

^{19}F NMR (376 MHz, $CDCl_3$): –62.6;

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{41}F_3N_4NaO_5Si$, 621.2691; found, 621.2693.

*denotes minor rotamer

(1*S*)-1-(1-(4-Trifluoromethylphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12h·HCl)



Following general procedure B, nucleoside **S12h** (30.0 mg, 51 μmol) was deprotected to afford the *title compound* **12h·HCl** (18.6 mg, 97%) as a white solid.

$[\alpha]_D^{20.9}$ –6.0 (*c* 0.1, MeOH);

IR ν_{max} (neat): 3337, 2902, 1616, 1400, 1325, 1161, 1112, 1069, 856 cm^{-1};

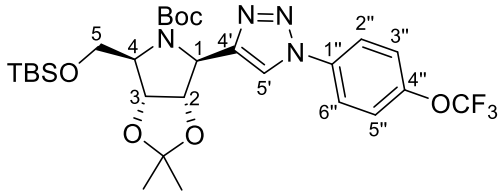
^{1}H NMR (400 MHz, CD_3OD): *δ* 8.91 (s, 1H, H-5′), 8.14 (d, *J* = 8.4 Hz, 2H, H-2″), 7.93 (d, *J* = 8.4 Hz, 2H, H-3″), 4.91 (d, *J* = 6.5 Hz, 1H, H-1), 4.62 (dd, *J* = 6.5, 4.5 Hz, 1H, H-2), 4.44 (dd, *J* = 4.8, 4.5 Hz, 1H, H-3), 3.98 – 3.90 (m, 2H, H-5), 3.82 – 3.78 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 143.1 (C, C-4′), 140.8 (C, C-1′), 131.9 (q, *J* = 33 Hz, C, C-4″), 128.3 (q, *J* = 3 Hz, 2 × CH, C-3''), 125.1 (q, *J* = 271 Hz, C, CF_3), 124.2 (CH, C-5′), 122.0 (2 × CH, C-2''), 75.7 (CH, C-2), 72.6 (CH, C-3), 67.1 (CH, C-4), 60.0 (CH_2, C-5), 58.8 (CH, C-1);

^{19}F NMR (376 MHz, CD_3OD): –64.2;

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{16}F_3N_4O_3$, 345.1169; found, 345.1169.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(4-trifluoromethoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol S12i



General procedure A was followed using alkyne **1** (51 mg, 120 μmol) and 4-trifluoromethoxyphenylboronic acid (51 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12i** (50 mg, 66%) as an off-white solid.

$[\alpha]_D^{20.4}$ –20.4 (*c* 1.0, $CHCl_3$);

IR ν_{max} (neat): 2931, 2858, 1690, 1517, 1392, 1368, 1254, 1213, 1162, 1054, 834, 757 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.01 (s, 1H, H-5′), 7.81 – 7.74 (m, 2H, H-2″ and H-6″), 7.37 – 7.35 (m, 2H, H-3″ and H-5″), 5.37 – 5.15 (m, 2H, H-1 and H-2), 4.92 – 4.80 (m, 1H, H-3), 4.25 – 4.09 (m, 1H,

H-4), 3.72 – 3.60 (m, 2H, H-5), 1.53 (s, 3H, CC*H*$_3$CH$_3$), 1.45 (s, 9H, OC(CH$_3$)$_3$), 1.37 (s, 3H, CCH$_3$C*H*$_3$), 0.83 (s, 9H, SiC(CH$_3$)$_3$), –0.01 (s, 6H, 2 × SiCH$_3$);

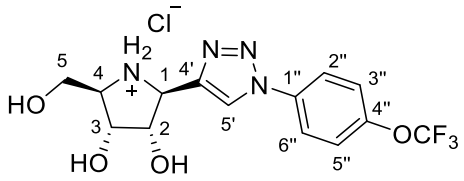
^{13}C NMR (100 MHz, CDCl$_3$): δ 154.3 (C, C=O), 149.0 (C, C-4″), 147.8 (C, C-4′), 135.5 (C, C-1″), 122.3 (2× CH, C-3″ and C-5″), 121.9 (2 × CH, C-2″ and C-6″), 121.2 (CH, C-5″), 120.4 (q, *J* = 258 Hz, C, OCF$_3$), 119.9 (CH, C-5″*), 111.9 (C, *C*(CH$_3$)$_2$), 84.7 (CH, C-2*), 83.0 (CH, C-2), 82.6 (CH, C-3), 81.7 (CH, C-3*), 80.5 (C, O*C*(CH$_3$)$_3$), 66.3 (CH, C-4), 66.0 (CH, C-4*), 62.5 (CH$_2$, C-5), 61.4 (CH, C-1*), 60.2 (CH, C-1), 28.5 (3 × CH$_3$, OC(*C*H$_3$)$_3$, 27.3 (CH$_3$, C*C*H$_3$CH$_3$), 25.9 (3 × CH$_3$, SiC(*C*H$_3$)$_3$), 25.4 (CH$_3$, CCH$_3$*C*H$_3$), 18.3 (C, Si*C*(CH$_3$)$_3$), –5.3 (2 × CH$_3$, SiCH$_3$);

^{19}F NMR (376 MHz, CDCl$_3$): –58.0

HRMS (ESI/Q-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{28}H_{41}F_3N_4NaO_6Si$, 637.2640; found, 637.2641.

*denotes minor rotamer

(1*S*)-1-(1-(4-Trifluoromethoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12i·HCl)



Following general procedure B, nucleoside **S12i** (44.0 mg, 72.0 μmol) was deprotected to afford the *title compound* **12i·HCl** (22.5 mg, 79%) as a cream solid.

$[\alpha]_D^{20.5}$ –6.0 (*c* 0.1, MeOH);

IR ν_{max} (film): 3339, 2922, 1517, 1397, 1207, 1162, 1056, 1033 cm^{-1};

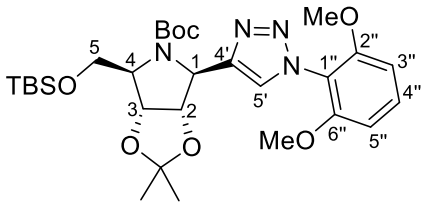
^{1}H NMR (400 MHz, DMSO-*d*$_6$): *δ* 10.53 – 10.50 (m, 1H, NH), 9.10 (s, 1H, H-5′), 8.84 – 8.79 (m, 1H, NH), 8.07 – 8.05 (m, 2H, H-2″), 7.67 (d, *J* = 8.6 Hz, 1H, H-3″), 5.79 – 5.75 (m, 1H, 2-OH), 5.62 – 5.61 (m, 1H, 3-OH), 5.36 – 5.35 (m, 1H, 5-OH), 4.65 (d, *J* = 6.7 Hz, 1H, H-1), 4.44 – 4.42 (m, 1H, H-2), 4.21 – 4.20 (m, 1H, H-3), 3.75 – 3.70 (m, 2H, H-5), 3.57 – 3.53 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 148.1 (C, C-4″), 141.9 (C, C-4′), 135.2 (C, C-1″), 123.6 (CH, C-5′), 122.7 (2 × CH, C-3″), 122.1 (2 × CH, C-2″), 120.0 (q, *J* = 256 Hz, C, CF$_3$), 73.8 (CH, C-2), 70.5 (CH, C-3), 65.4 (CH, C-4), 58.6 (CH$_2$, C-5), 56.5 (CH, C-1);

^{19}F NMR (376 MHz, DMSO-*d*$_6$): –56.9;

HRMS (ESI/Q-TOF) *m/z*: [M+H]$^+$ calcd for $C_{14}H_{15}F_3N_4NaO_4$, 383.0938; found, 383.0942.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(2,6-dimethoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12j)



General procedure A was followed using alkyne **1** (49.5 mg, 120 μmol) and 2,6-dimethoxyphenylboronic acid (37 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12j** (32 mg, 45%) as an off-white solid.

$[\alpha]_D^{19.5}$ –3.7 (*c* 1.1, $CHCl_3$);

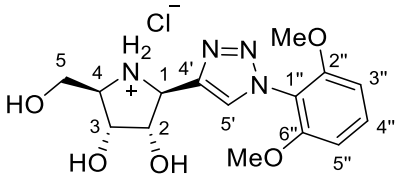
IR ν_{max} (neat): 2932, 1694, 1484, 1392, 1258, 1112, 1053, 1033, 835, 777 cm^{-1};

^{1}H NMR (400 MHz, DMSO-*d*$_6$, 343 K): *δ* 7.86 (s, 1H, H-5′), 7.50 (t, *J* = 8.6 Hz, 1H, H-4″), 6.87 (d, *J* = 8.6 Hz, 2H, H-3″ and H-5″), 5.09 – 5.05 (m, 2H, H-1 and H-2), 4.79 – 4.77 (m, 1H, H-3), 4.00 (dd, *J* = 9.2, 5.0 Hz, 1H, H-4), 3.72 – 3.66 (m, 7H, 2 × OCH_3 and H-5$_a$), 3.55 – 3.52 (m, 1H, H-5$_b$), 1.45 (s, 9H, $OC(CH_3)_3$), 1.38 (s, 3H, CCH_3CH_3), 0.87 (s, 9H, $SiC(CH_3)_3$), 0.04 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, DMSO-*d*$_6$, 343 K): δ 155.2 (2 × C, C-2″ and C-6″), 153.1 (C, C=O), 131.2 (CH, C-4″), 125.2 (CH, C-5′), 114.8 (C, C-1″), 110.9 (C, $C(CH_3)_2$), 104.7 (2 × CH, C-3″ and C-5″), 83.6 (CH, C-2), 81.5 (CH, C-3), 79.1 (C, $OC(CH_3)_3$), 65.4 (CH, C-4), 61.7 (CH_2, C-5), 59.9 (CH, C-1), 56.0 (2 × CH_3, OCH_3), 27.6 (3 × CH_3, $OC(CH_3)_3$), 26.8 (CH_3, CCH_3CH_3), 25.4 (3 × CH_3, $SiC(CH_3)_3$), 24.8 (CH_3, CCH_3CH_3), 17.5 (C, $SiC(CH_3)_3$), –5.7 (CH_3, $SiCH_3$), –5.8 (CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{29}H_{46}N_4NaO_7Si$, 613.3028; found, 613.3027.

(1*S*)-1-(1-(2,6-Dimethoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12j·HCl)



Following general procedure B, nucleoside **S12j** (21 mg, 36 μmol) was deprotected to afford the *title compound* **12j** (12 mg, 95%) as a white solid.

$[\alpha]_D^{21.2}$ –10.0 (*c* 0.1, MeOH);

IR ν_{max} (neat): 3306, 2916, 1600, 1483, 1261, 1106, 1051, 1033, 777 cm^{-1};

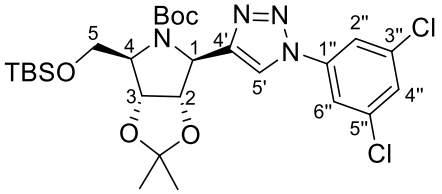
^{1}H NMR (400 MHz, DMSO-*d*$_6$): *δ* 10.70 – 10.67 (m, 1H, NH), 8.84 – 8.82 (m, 1H, NH), 8.39 (s, 1H, H-5′), 7.87 (s, 1H, H-2″), 7.53 (t, *J* = 8.5 Hz, 1H, H-4″), 6.90 (d, *J* = 8.5 Hz, 2H, H-3″ and H-5″), 4.65 –

4.59 (m, 1H, H-1), 4.36 (dd, *J* = 7.2, 4.8 Hz, 1H, H-2), 4.14 (dd, *J* = 4.8, 4.8 Hz, 1H, H-3), 3.75 – 3.73 (m, 8H, H-5 and 2 × OCH_3) 3.55 – 3.53 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-d_6): δ 155.3 (2 × C, C-2″ and C-6″), 139.9 (C, C-4′), 131.9 (CH, C-4″), 127.8 (CH, C-5′), 114.3 (C, C-1′), 104.8 (2 × CH, C-3″ and C-5″), 73.8 (CH, C-2), 70.2 (CH, C-3), 65.4 (CH, C-4), 58.6 (CH_2, C-5), 56.6 (CH, C-1), 56.3 (2 × CH_3, OCH_3);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{20}N_4NaO_5$, 359.1326; found, 359.1324.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(3,5-dichlorophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12k)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and 3,5-dichlorophenylboronic acid (46 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12k** (38 mg, 52%) as an off-white solid.

$[\alpha]_D^{21.3}$ –37.7 (*c* 0.3, $CHCl_3$);

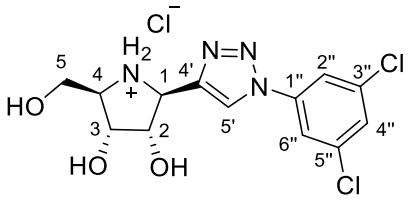
IR ν_{max} (neat): 2932, 1686, 1591, 1392, 1253, 1162, 1116, 1040, 836, 777 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.00 (s, 1H, H-5′), 7.66 (s, 2H, H-2″ and H-6″), 7.44 (s, 1H, H-4″), 5.36 – 5.07 (m, 2H, H-1 and H-2), 4.91 – 4.78 (m, 1H, H-3), 4.26 – 4.09 (m, 1H, H-4), 3.76 – 3.57 (m, 2H, H-5), 1.53 (s, 3H, CC*H*$_3$CH$_3$), 1.46 (s, 9H, OC(CH$_3$)$_3$), 1.37 (s, 3H, CCH$_3$C*H*$_3$), 0.84 (s, 9H, SiC(CH$_3$)$_3$), 0.00 (s, 6H, 2 × SiCH$_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4 (C, C=O), 148.1 (C, C-4′), 138.2 (C, C-1″), 136.3 (2 × C, C-3″ and C-5″), 128.6 (CH, C-4″), 121.0 (CH, C-5′), 118.9 (2 × CH, C-2″ and C-6″), 112.0 (C, *C*(CH$_3$)$_2$), 82.9 (CH, C-2), 82.6 (CH, C-3), 80.6 (C, O*C*(CH$_3$)$_3$), 66.3 (CH, C-4), 62.5 (CH_2, C-5), 60.2 (CH, C-1), 28.5 (3 × CH_3, OC(*C*H$_3$)$_3$, 27.3 (CH_3, C*C*H$_3$CH$_3$), 25.9 (3 × CH_3, SiC(*C*H$_3$)$_3$), 25.4 (CH_3, CCH$_3$*C*H$_3$), 18.3 (C, Si*C*(CH$_3$)$_3$), –5.2 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{40}Cl_2N_4NaO_5Si$, 621.2037; found, 621.2038.

(1*S*)-1-(1-(3,5-Dichlorophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12k·HCl)



Following general procedure B, nucleoside **S12k** (35 mg, 58 μmol) was deprotected to afford the *title compound* **12k·HCl** (22 mg, quant.) as a white solid.

$[\alpha]_D^{23.0}$ –6.8 (*c* 1.0, MeOH);

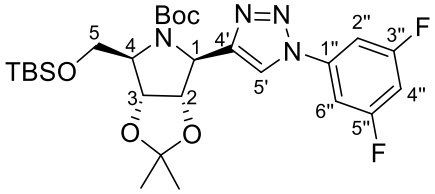
IR ν_{max} (neat): 3326, 2943, 2496, 1588, 1437, 1117, 1047, 1016, 807, 667 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD): *δ* 8.85 (s, 1H, H-5′), 7.97 (d, *J* = 1.9 Hz, 2H, H-2″ and H-6″), 7.62 (t, J = 1.9 Hz, 1H, H-4″), 4.88 (d, *J* = 6.5 Hz, 1H, H-1), 4.59 (dd, *J* = 6.3, 4.4 Hz, 1H, H-2), 4.42 (dd, *J* = 4.9, 4.4 Hz, 1H, H-3), 3.97 – 3.89 (m, 2H, H-5), 3.80 – 3.76 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 143.1 (C, C-4″), 139.7 (C, C-1″), 137.5 (2 × C, C-3″ and C-5″), 130.0 (CH, C-4″), 124.2 (CH, C-5′), 120.2 (2 × CH, C-2″ and C-6″), 75.8 (CH, C-2), 72.6 (CH, C-3), 67.1 (CH, C-4), 60.0 (CH_2, C-5), 58.8 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{15}Cl_2N_4O_3$, 345.0516; found, 345.0516.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(3,5-difluorophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12l)



General procedure A was followed using alkyne **1** (47 mg, 110 μmol) and 3,5-difluorophenylboronic acid (44 mg, 290 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12l** (31 mg, 48%) as an off-white solid.

$[\alpha]_D^{20.8}$ –24.5 (*c* 0.3, $CHCl_3$);

IR ν_{max} (neat): 2932, 2858, 1694, 1623, 1393, 1368, 1253, 1160, 1123, 1042, 989, 835, 776 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.99 – 7.80 (m, 1H, H-5′), 7.31 (d, *J* = 5.2 Hz, H-2″ and H-6″), 6.87 (t, *J* = 7.9 Hz, H-4″), 5.36 – 5.12 (m, 2H, H-1 and H-2), 4.91 – 4.78 (m, 1H, H-3), 4.26 – 4.09 (m, 1H, H-4), 3.72 – 3.58 (m, 2H, H-5), 1.53 (s, 3H, CCH_3CH_3), 1.45 (s, 9H, $OC(CH_3)_3$), 1.37 (s, 3H, CCH_3CH_3), 0.83 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5 (dd, *J* = 250, 14 Hz, 2 × C, C-3″ and C-5″), 154.4 (C, C=O), 154.0 (C, C=O*), 149.7 (C, C-4′*), 148.2 (C, C-4′), 138.7 (t, *J* = 13 Hz, C, C-1″), 121.0 (CH, C-5′),

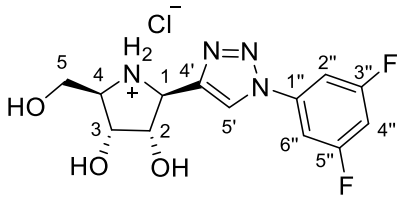
119.6 (CH, C-5′*), 112.0 (C, *C*(CH_3)$_2$), 104.1 – 103.8 (m, 3 × CH, C-2′, C-4′ and C-6′), 84.8 (CH, C-2*), 82.9 (CH, C-2), 82.6 (CH, C-3), 81.7 (CH, C-3*), 80.6 (C, O*C*(CH_3)$_3$), 66.3 (CH, C-4), 66.0 (CH, C-4*), 62.5 (CH_2, C-5), 61.5 (CH, C-1*), 60.2 (CH, C-1), 28.5 (3 × CH_3, OC(*C*H_3)$_3$, 27.3 (CH_3, C*C*H_3CH$_3$), 25.9 (3 × CH_3, SiC(*C*H_3)$_3$), 25.4 (CH_3, CCH$_3$*C*H_3), 18.3 (C, Si*C*(CH_3)$_3$), –5.3 (2 × CH_3, SiCH$_3$);

^{19}F NMR (376 MHz, $CDCl_3$): –105.9(*), –106.2;

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{40}F_2N_4NaO_5Si$, 589.2628; found, 589.2623.

*denotes minor rotamer

(1*S*)-1-(1-(3,5-Difluorophenyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12l·HCl)



Following general procedure B, nucleoside **S12l** (26.0 mg, 43.3 μmol) was deprotected to afford the *title compound* **12l·HCl** (16.4 mg, quant.) as a white solid.

$[\alpha]_D^{21.8}$ –6.4 (*c* 0.5, MeOH);

IR ν_{max} (neat): 2906, 1623, 1475, 1129, 1057, 992, 854 cm^{-1};

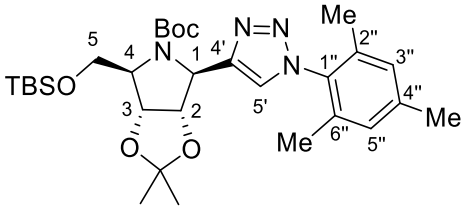
^{1}H NMR (400 MHz, CD_3OD): *δ* 8.81 (s, 1H, H-5′), 7.67 – 7.62 (m, 2H, H-2′ and H-6′), 7.21 – 7.15 (m, 1H, H-4′), 4.86 (d, *J* = 6.6 Hz, 1H, H-1), 4.56 (dd, *J* = 6.0, 4.5 Hz, 1H, H-2), 4.42 (dd, *J* = 5.0, 4.5 Hz, 1H, H-3), 3.96 – 3.88 (m, 2H, H-5), 3.80 – 3.75 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 164.9 (dd, *J* = 249, 14 Hz, 2 × C, C-3′ and C-5′), 143.0 (C, C-4′), 139.9 (t, *J* = 13 Hz, C, C-1′), 124.3 (CH, C-5′), 105.2 (t, *J* = 26 Hz, CH, C-4′), 105.3 – 105.0 (m, 2 × CH, C-2′ and C-6′), 75.7 (CH, C-2), 72.7 (CH, C-3), 67.1 (CH, C-4), 60.0 (CH_2, C-5), 58.8 (CH, C-1);

^{19}F NMR (376 MHz, DMSO-*d*$_6$): 106.7;

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{15}F_2N_4O_3$, 313.1107; found, 313.1105.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-mesityl-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12m)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and 2,4,6-trimethylphenylboronic acid (40 mg, 240 μmol). The crude residue was purified *via* flash

chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12m** (46 mg, 67%) as an off-white solid.

$[\alpha]_D^{19.4}$ –3.3 (*c* 0.3, $CHCl_3$);

IR ν_{max} (neat): 2955, 2929, 2858, 1694, 1391, 1367, 1254, 1161, 1122, 1053, 836, 777 cm^{-1};

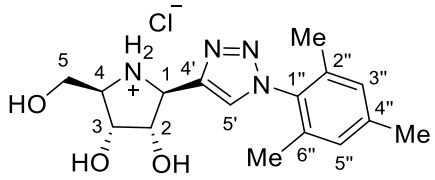
^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.64 – 7.49 (m, 1H, H-5′), 6.96 (s, 2H, H-3″ and H-5″), 5.53 – 5.18 (m, 2H, H-1 and H-2), 4.93 – 4.88 (m, 1H, H-3), 4.22 – 4.07 (m, 1H, H-4), 3.71 – 3.41 (m, 2H, H-5), 2.33 (s, 3H, 4″-CH_3), 1.91 (s, 6H, 2″-CH_3 and 6″-CH_3), 1.53 (s, 3H, C*C*$H_3$$CH_3$), 1.42 – 1.38 (m, 12H, $OC(CH_3)_3$ and CCH_3C*H*$_3$), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.02 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.2 (C, C=O), 153.9 (C, C=O*), 148.0 (C, C-4′), 146.7 (C, C-4′*), 140.0 (C, C-4″), 135.0 (2 × C, C-2″ and C-6″), 133.5 (C, C-1″), 130.9 (2 × CH, C-3″* and C-5″*), 129.1 (2 × CH, C-3″ and C-5″), 125.2 (CH, C-5′), 123.7 (CH, C-5′), 111.8 (C, *C*$(CH_3)_2$), 84.6 (CH, C-2*), 82.7 (CH, C-2), 82.5 (CH, C-3), 81.8 (CH, C-3*), 80.2 (C, O*C*$(CH_3)_3$), 66.2 (CH, C-4), 65.9 (CH, C-4*), 62.5 (CH_2, C-5), 60.9 (CH, C-1*), 60.0 (CH, C-1), 28.4 (3 × CH_3, OC(*C*H_3)$_3$, 27.2 (CH_3, C*C*H_3CH_3), 25.9 (3 × CH_3, SiC(*C*H_3)$_3$), 25.2 (CH_3, CCH_3*C*H_3), 21.1 (CH_3, 4″-CH_3), 18.3 (C, Si*C*$(CH_3)_3$), 17.2 (2 × CH_3, 2″-CH_3 and 6″-CH_3), –5.2 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{48}N_4NaO_5Si$, 595.3286; found, 595.3286.

*denotes minor rotamer

(1*S*)-1-(1-Mesityl-1*H*-1,2,3-triazol-4-yl)-1,4-dideox-1,4-imino-D-ribitol hydrochloride (12m·HCl)



Following general procedure B, nucleoside **S12m** (43 mg, 89 μmol) was deprotected to afford the *title compound* **12m·HCl** (24 mg, 97%) as a white solid.

$[\alpha]_D^{20.9}$ –12.2 (*c* 0.5, MeOH);

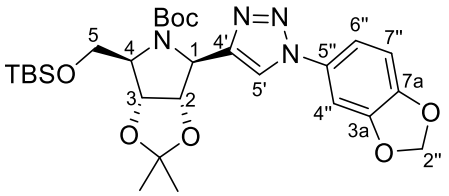
IR ν_{max} (neat): 3274, 2921, 1597, 1112, 1048, 1037, 849 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD): *δ* 8.30 (s, 1H, H-5′), 7.09 (s, 1H, H-3″), 4.91 (d, *J* = 6.1 Hz, 1H, H-1), 4.60 (dd, *J* = 6.1, 4.6 Hz, 1H, H-2), 4.41 (dd, *J* = 4.6, 4.6 Hz, 1H, H-3), 3.98 – 3.89 (m, 2H, H-5), 3.80 – 3.77 (m, 1H, H-4), 2.37 (s, 3H, 4″-CH_3), 1.97 (s, 6H, 2 × 2″-CH_3);

^{13}C NMR (100 MHz, CD_3OD): δ 142.0 (C, C-4′ or C-4″), 141.9 (C, C-4′ or C-4″), 136.2 (2 × C, C-2″), 134.4 (C, C-1″), 130.2 (2 × CH, C-3″), 128.0 (CH, C-5′), 75.8 (CH, C-2), 72.5 (CH, C-3), 67.0 (CH, C-4), 59.9 (CH_2, C-5), 59.0 (CH, C-1), 21.2 (CH_3, 4″-CH_3), 17.3 (2 × CH_3, 2″-CH_3);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{16}H_{23}N_4O_3$, 319.1765; found, 319.1764.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(5-benzo[*d*][1,3]dioxolyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12n)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and 3,4-methylenedioxyphenylboronic acid (41 mg, 250 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12n** (48 mg, 68%) as an off-white solid.

$[\alpha]_D^{19.0}$ –32.2 (*c* 0.9, $CHCl_3$);

IR ν_{max} (neat): 2931, 2858, 1693, 1507, 1471, 1392, 1244, 1162, 1123, 1036, 836, 777 cm^{-1};

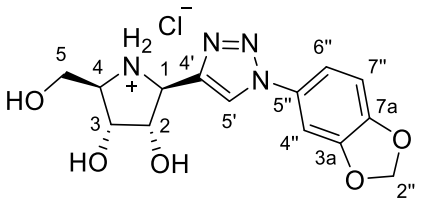
^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.90 – 7.72 (m, 1H, H-5′), 7.22 (s, 1H, H-4″), 7.12 – 7.10 (m, 1H, H-6″), 6.88 (d, *J* = 8.1 Hz, 1H, H-7″), 6.06 (s, 2H, H-2″), 5.39 – 5.15 (m, 2H, H-1 and H-2), 4.92 – 4.82 (m, 1H, H-3), 4.24 – 4.09 (m, 1H, H-4), 3.72 – 3.61 (m, 2H, H-5), 1.53 (s, 3H, $CC\mathit{H}_3CH_3$), 1.46 (s, 9H, $OC(CH_3)_3$), 1.38 (s, 3H, $CCH_3C\mathit{H}_3$), 0.84 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3 (C, C=O), 148.7 (C, C-3a″), 148.0 (C, C-7a″), 147.4 (C, C-4′), 131.7 (C, C-5″), 121.4 (CH, C-5′), 120.2 (CH, C-5′*), 114.2 (CH, C-6″), 111.9 (C, $C(CH_3)_2$), 108.5 (CH, C-7″), 102.8 (CH, C-4″), 102.2 (CH_2, C-2″), 84.7 (CH, C-2*), 83.0 (CH, C-2), 82.7 (CH, C-3), 81.8 (CH, C-3*), 80.4 (C, $OC(CH_3)_3$), 66.4 (CH, C-4), 66.0 (CH, C-4*), 62.5 (CH_2, C-5), 61.3 (CH, C-1*), 60.2 (CH, C-1), 28.6 (3 × CH_3, $OC(CH_3)_3$), 27.4 (CH_3, CCH_3CH_3), 26.0 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.2 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{42}N_4NaO_7Si$, 597.2715; found, 597.2715.

*denotes minor rotamer

(1*S*)-1-(1-(5-Benzo[*d*][1,3]dioxolyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12n·HCl)



Following general procedure B, nucleoside **S12n** (34.5 mg, 56.5 μmol) was deprotected to afford the *title compound* **12n·HCl** (20.0 mg, quant.) as a white solid.

$[\alpha]_D^{20.6}$ –12.0 (*c* 0.1, MeOH);

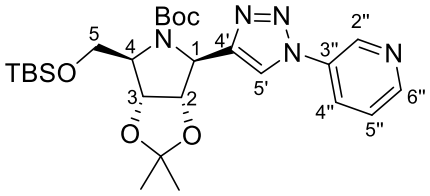
IR ν_{max} (neat): 3256, 2923, 2691, 1584, 1505, 1413, 1243, 1080, 1033, 927, 815 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.61 (s, 1H, NH), 8.95 (s, 1H, H-5′), 8.83 (s, 1H, NH), 7.50 (d, *J* = 2.5 Hz, 1H, H-4″), 7.37 (dd, *J* = 8.4, 2.5 Hz, H-6″), 7.13 (d, *J* = 8.4 Hz, 1H, H-7″), 6.17 (s, 2H, H-2″), 5.79 – 5.60 (m, 3H, 3 × OH), 4.62 – 4.10 (m, 1H, H-1), 4.41 (dd, *J* = 7.0, 4.8 Hz, 1H, H-2), 4.20 (dd, *J* = 4.8, 4.8 Hz, 1H, H-3), 3.73 (d, *J* = 4.9 Hz, 2H, H-5), 3.55 – 3.50 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-d_6): δ 148.3 (C, C-3a), 147.7 (C, C-7a), 141.5 (C, C-4′), 130.7 (C, C-5″), 123.4 (CH, C-5′), 113.9 (CH, C-6″), 108.7 (CH, C-7″), 102.2 (CH_2, C-2″), 101.9 (CH, C-4″), 73.8 (CH, C-2), 70.5 (CH, C-3), 65.3 (CH, C-4), 58.6 (CH_2, C-5), 56.7 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{16}N_4NaO_5$, 343.1013; found, 343.1014.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(3-pyridyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12o)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and pyridine-3-boronic acid (30 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12o** (9.0 mg, 14%) as an off-white solid.

$[\alpha]_D^{18.8}$ –26.2 (*c* 0.9, $CHCl_3$);

IR ν_{max} (neat): 2956, 1646, 1395, 1258, 1123, 1014 cm^{-1};

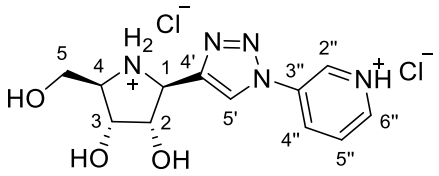
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.99 (m, 1H, H-2″), 8.69 (d, *J* = 3.5 Hz, 1H, H-6″), 8.11 – 7.88 (m, 2H, H-4″ and H-5′), 7.50 – 7.47 (m, 1H, H-5″), 5.38 – 5.17 (m, 2H, H-1 and H-2), 4.92 – 4.81 (m, 1H, H-3), 4.27 – 4.09 (m, 1H, H-4), 3.73 – 3.60 (m, 2H, H-5), 1.54 (s, 3H, CCH_3CH_3), 1.46 (s, 9H, $OC(CH_3)_3$), 1.38 (s, 3H, CCH_3CH_3), 0.83 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4 (C, C=O), 149.9 (CH, C-6″), 148.2 (C, C-4′), 141.7 (CH, C-2″), 133.7 (C, C-3″), 128.0 (CH, C-4″), 124.3 (CH, C-5″), 121.1 (CH, C-5′), 119.7 (CH, C-5″*), 112.0 (C, $C(CH_3)_2$), 84.8 (CH, C-2*), 83.0 (CH, C-2), 82.6 (CH, C-3), 81.7 (CH, C-3*), 80.6 (C, $OC(CH_3)_3$), 66.3 (CH, C-4), 66.0 (CH, C-4*), 62.5 (CH_2, C-5), 61.4 (CH, C-1*), 60.3 (CH, C-1), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.4 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{41}N_5NaO_5Si$, 554.2769; found, 554.2770.

*denotes minor rotamer

(1*S*)-1-(1-(3-Pyridyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol dihydrochloride (12o·2HCl)



Following general procedure B, nucleoside S**12o** (41.7 mg, 78 μmol) was deprotected to afford the *title compound* **12o·2HCl** (27.5 mg, quant.) as a yellow solid.

$[\alpha]_D^{22.1}$ –23.0 (*c* 0.1, H_2O);

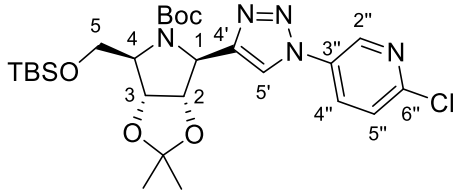
IR ν_{max} (film): 3313, 2920, 2850, 1633, 1411, 1113, 1015 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD): *δ* 9.49 (s, 1H, H-2″), 9.03 (s, 1H, H-5′), 8.93 – 8.90 (m, 2H, H-4″ and H-6″), 8.13 (dd, *J* = 8.3, 5.5 Hz, 1H, H-5″), 4.92 (d, *J* = 6.6 Hz, 1H, H-1), 4.61 (dd, *J* = 6.6, 4.5 Hz, 1H, H-2), 4.42 (dd, *J* = 4.9, 4.5 Hz, 1H, H-3), 3.97 – 3.89 (m, 2H, H-5), 3.80 – 3.76 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 149.5 (CH, C-6″), 142.1 (C, C-4′), 140.8 (CH, C-2″), 133.3 (C, C-3″), 129.8 (CH, C-4″), 125.1 (CH, C-5″), 123.9 (CH, C-5′), 73.9 (CH, C-2), 70.5 (CH, C-3), 65.5 (CH, C-4), 58.6 (CH_2, C-5), 56.5 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{16}N_5O_3$, 278.1248; found, 278.1245.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(6-chloropyridin-3-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12p)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and 6-chloro-3-pyridinylboronic acid (38 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12p** (52 mg, 76%) as an off-white solid.

$[\alpha]_D^{19.0}$ –30.3 (*c* 0.9, $CHCl_3$);

IR ν_{max} (neat): 2932, 1690, 1481, 1382, 1112, 1053, 833, 777 cm^{-1};

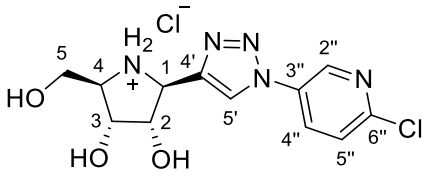
^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.76 – 8.73 (m, 1H, H-2″), 8.09 (dd, *J* = 8.5, 2.1 Hz, H-4″), 8.04 – 7.85 (m, 1H, H-5′), 7.51 (d, *J* = 8.5 Hz, 1H, H-5″), 5.36 – 5.15 (m, 2H, H-1 and H-2), 4.91 – 4.79 (m, 1H, H-3), 4.27 – 4.10 (m, 1H, H-4), 3.72 – 3.60 (m, 2H, H-5), 1.54 (s, 3H, CCH_3CH_3), 1.46 (m, 9H, $OC(CH_3)_3$), 1.38 (s, 3H, CCH_3CH_3), 0.83 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.5 (C, C=O), 151.2 (C, C-6″), 148.5 (C, C-4′), 141.1 (CH, C-2″), 132.8 (C, C-3″), 130.7 (CH, C-4″), 125.2 (CH, C-5″), 121.1 (CH, C-5′), 112.0 (C, $C(CH_3)_2$), 83.0 (CH,

C-2), 82.6 (CH, C-3), 80.7 (C, O*C*(CH$_3$)$_3$), 66.3 (CH, C-4), 62.5 (CH$_2$, C-5), 60.3 (CH, C-1), 28.5 (3 × CH$_3$, OC(*C*H$_3$)$_3$, 27.4 (CH$_3$, C*C*H$_3$CH$_3$), 25.9 (3 × CH$_3$, SiC(*C*H$_3$)$_3$), 25.4 (CH$_3$, CCH$_3$*C*H$_3$), 18.3 (C, Si*C*(CH$_3$)$_3$), –5.3 (2 × CH$_3$, SiCH$_3$);

HRMS (ESI/Q-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{40}ClN_5NaO_5Si$, 588.2379; found, 588.2383.

(1*S*)-1-(1-(6-Chloropyridin-3-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12p·HCl)



Following general procedure B, nucleoside **S12p** (50 mg, 88 µmol) was deprotected to afford the *title compound* **12p·HCl** (25 mg, 84%) as a cream solid.

$[\alpha]_D^{20.3}$ –24.1 (*c* 0.24, H$_2$O);

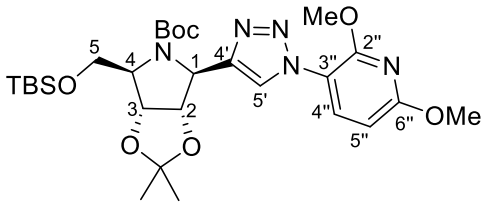
IR ν_{max} (neat): 3313, 2863, 2715, 1567, 1623, 1488, 1390, 1360, 1113, 1022 cm^{-1};

^{1}H NMR (400 MHz, CD$_3$OD): *δ* 8.94 (d, *J* = 2.0 Hz, 1H, H-2″), 8.84 (s, 1H, H-5′), 8.36 – 8.33 (m, 1H, H-4″), 7.71 (d, *J* = 8.6 Hz, 1H, H-5″), 4.88 (d, *J* = 6.5 Hz, 1H, H-1), 4.58 (dd, *J* = 6.0, 4.5 Hz, 1H, H-2), 4.42 (dd, *J* = 4.6, 4.5 Hz, 1H, H-3), 3.97 – 3.89 (m, 2H, H-5), 3.80 – 3.76 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD$_3$OD): δ 152.4 (C, C-6″), 143.2 (C, C-4″), 142.7 (CH, C-2″), 134.3 (C, C-3″), 132.8 (CH, C-4″), 126.6 (CH, C-5″), 124.5 (CH, C-5′), 75.8 (CH, C-2), 72.6 (CH, C-3), 67.1 (CH, C-4), 60.0 (CH$_2$, C-5), 58.8 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{12}H_{14}ClN_5NaO_3$, 334.0677; found, 334.0684.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(2,6-dimethoxypyridin-3-yl)-1H-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-O-isopropylidene-5-O-tert-butyldimethylsilyl-D-ribitol (S12q)



General procedure A was followed using alkyne **1** (47 mg, 110 µmol) and 2,6-dimethoxypyridin-3-ylboronic acid (42 mg, 230 µmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12q** (30 mg, 44%) as an off-white solid.

$[\alpha]_D^{21.6}$ –25.0 (*c* 0.1, CHCl$_3$);

IR ν_{max} (neat): 2933, 1697, 1594, 1496, 1390, 1322, 1254, 1170, 1110, 1039, 835, 776 cm^{-1};

^{1}H NMR (400 MHz, CDCl$_3$): *δ* 8.09 – 7.94 (m, 2H, H-4″ and H-5′), 6.44 – 6.37 (m, 1H, H-5″), 5.35 – 5.14 (m, 2H, H-1 and H-2), 4.92 – 4.84 (m, 1H, H-3), 4.21 – 4.07 (m, 1H, H-4), 3.99 (s, 3H, 2″-OCH$_3$),

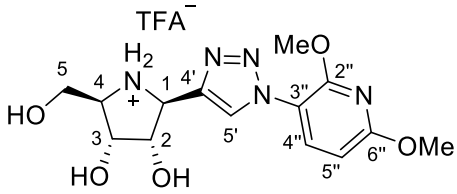
3.96 (s, 3H, 6″-OCH_3), 3.71 – 3.62 (m, 2H, H-5), 1.53 (s, 3H, CCH_3CH_3), 1.45 (s, 9H, $OC(CH_3)_3$), 1.37 (s, 3H, CCH_3CH_3), 0.85 – 0.80 (m, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5 (C, C-6″), 154.3 (C, C=O), 153.8 (C, C-2″), 147.6 (C, C-4′), 146.4 (C, C-4′*), 136.2 (CH, C-4″), 124.4 (CH, C-5′), 123.5 (CH, C-5′*), 114.0 (C, C-3″), 111.8 (C, $C(CH_3)_2$), 102.3 (CH, C-5″*), 102.0 (CH, C-5″), 84.6 (CH, C-2*), 83.2 (CH, C-2), 82.8 (CH, C-3), 81.8 (CH, C-3*), 80.2 (C, $OC(CH_3)_3$), 66.4 (CH, C-4), 66.0 (CH, C-4*), 62.4 (CH_2, C-5), 61.2 (CH, C-1*), 60.1 (CH, C-1), 54.1 (CH_3, 2″-OCH_3 or 6″-OCH_3), 54.0 (CH_3, 2″-OCH_3 or 6″-OCH_3), 28.5 (3 × CH_3, $OC(CH_3)_3$), 27.3 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{45}N_5NaO_7Si$, 614.2980; found, 614.2984.

*denotes minor rotamer

(1*S*)-1-(1-(2,6-Dimethoxypyridin-3-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol trifluoroacetate salt (12q·TFA)



Following general procedure C, nucleoside **S12q** (25 mg, 42 μmol) was deprotected to afford the *title compound* **12q·TFA** (18 mg, quant.) as a white solid.

$[\alpha]_D^{23.8}$ –12.0 (*c* 0.2, H_2O);

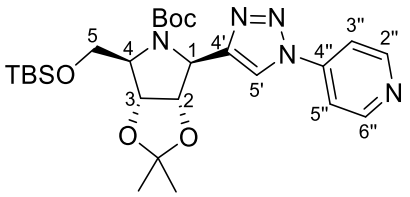
IR ν_{max} (neat): 3229, 1661, 1593, 1411, 1205, 1120, 1046 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD): *δ* 8.50 (s, 1H, H-5′), 7.96 (d, *J* = 8.5 Hz, 1H, H-4″), 6.52 (d, *J* = 8.5 Hz, 1H, H-5″), 4.86 (d, *J* = 6.4 Hz, 1H, H-1), 4.56 (dd, *J* = 6.4, 4.6 Hz, 1H, H-2), 4.42 (dd, *J* = 4.8, 4.6 Hz, 1H, H-3), 4.03 (s, 3H, 2″-OCH_3), 3.99 (s, 3H, 6″-OCH_3), 3.95 – 3.87 (m, 2H, H-5), 3.78 – 3.74 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 164.8 (C, C-6″), 156.1 (C, C-2″), 141.8 (C, C-4′), 138.1 (CH, C-4″), 127.2 (CH, C-5′), 114.5 (C, C-3″), 103.3 (CH, C-5″), 75.9 (CH, C-2), 72.6 (CH, C-3), 66.9 (CH, C-4), 60.0 (CH_2, C-5), 59.0 (CH, C-1), 54.65 (CH_3, 2″-OCH_3 or 6″-OCH_3), 54.60 (CH_3, CH_3, 2″-OCH_3 or 6″-OCH_3);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{20}N_5O_5$, 338.1459; found, 338.1458.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(4-pyridyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12r)



General procedure A was followed using alkyne **1** (49 mg, 120 μmol) and pyridine-4-boronic acid (30 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12r** (28 mg, 41%) as an off-white solid.

$[\alpha]_D^{20.1}$ –27.4 (*c* 1.0, $CHCl_3$);

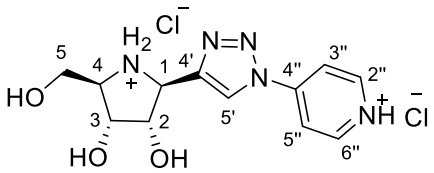
IR ν_{max} (neat): 2931, 1691, 1590, 1391, 1254, 1161, 1124, 1053, 834, 776 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.77 (s, 2H, H-2″ and H-6″), 8.11 – 7.91 (m, 1H, H-5′), 7.69 (s, 2H, H-3 and H-5″), 5.36 – 5.15 (m, 2H, H-1 and H-2), 4.91 – 4.78 (m, 1H, H-3), 4.27 – 4.10 (m, 1H, H-4), 3.72 – 3.59 (m, 2H, H-5), 1.53 (s, 3H, CCH_3CH_3), 1.45 (s, 9H, $OC(CH_3)_3$), 1.37 (s, 3H, CCH_3CH_3), 0.82 (s, 9H, $SiC(CH_3)_3$), –0.01 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4 (C, C=O), 151.7 (2 × CH, C-2″ and C-6″), 148.4 (C, C-4′), 143.1 (C, C-4″), 120.5 (CH, C-5′), 113.7 (2 × CH, C-3″ and C-5″), 112.0 (C, $C(CH_3)_2$), 82.9 (CH, C-2), 82.6 (CH, C-3), 80.6 (C, $OC(CH_3)_3$), 66.3 (CH, C-4), 62.5 (CH_2, C-5), 60.2 (CH, C-1), 28.5 (3 × CH_3, $OC(CH_3)_3$), 27.4 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{41}N_5NaO_5Si$, 554.2769; found, 554.2771.

(1*S*)-1-(1-(4-Pyridyl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol dihydrochloride (12r·2HCl)



Following general procedure B, nucleoside **S12r** (16.6 mg, 31.2 μmol) was deprotected to afford the *title compound* **12r·2HCl** (10.9 mg, quant) as a yellow solid.

$[\alpha]_D^{21.2}$ –45.5 (*c* 0.2, H_2O);

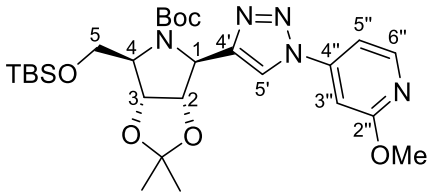
IR ν_{max} (film): 3361, 1636, 1520, 1048 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD): *δ* 9.30 (s, 1H, H-5′), 9.14 (m, 2H, H-2″ and H-5″), 8.72 – 8.71 (m, 2H, H-3″ and H-5″), 4.94 (d, *J* = 6.9 Hz, 1H, H-1), 4.64 (dd, *J* = 6.9, 4.9 Hz, 1H, H-2), 4.42 (dd, *J* = 4.9, 4.5 Hz, 1H, H-3), 3.98 – 3.89 (m, 2H, H-5), 3.83 – 3.79 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 150.4 (2 × CH, C-2″ and C-6″), 146.0 (C, C-4″), 144.4 (C, C-4′), 125.2 (CH, C-5′), 118.2 (2 × CH, C-3″ and C-5″), 75.7 (CH, C-2), 72.5 (CH, C-3), 67.4 (CH, C-4), 60.0 (CH_2, C-5), 58.4 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{16}N_5O_3$, 278.1248; found, 278.1246.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(2-methoxypyridin-4-yl)-1H-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-O-isopropylidene-5-O-tert-butyldimethylsilyl-D-ribitol (S12s)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and 2-methoxypyridin-4-ylboronic acid (37 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12s** (41 mg, 60%) as an off-white solid.

$[\alpha]_D^{21.5}$ –52.7 (*c* 0.3, $CHCl_3$);

IR ν_{max} (neat): 2932, 2858, 1694, 1607, 1473, 1390, 1367, 1160, 1129, 1040, 834, 776 cm^{-1};

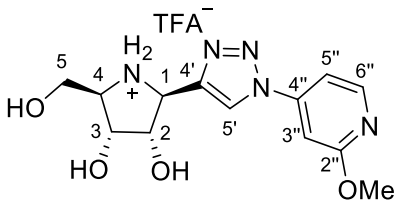
^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.26 (d, *J* = 5.8 Hz, 1H, H-6″), 8.05 – 7.85 (m, 1H, H-5′), 7.28 (dd, *J* = 5.8, 1.2 Hz, 1H, H-5″), 7.07 (s, 1H, H-3″), 5.34 – 5.12 (m, 2H, H-1 and H-2), 4.90 – 4.78 (m, 1H, H-3), 4.25 – 4.08 (m, 1H, H-4), 3.98m (s, 3H, OCH_3), 3.72 – 3.57 (m, 2H, H-5), 1.52 (s, 3H, CCH_3CH_3), 1.44 (s, 9H, $OC(CH_3)_3$), 1.36 (s, 3H, CCH_3CH_3), 0.81 (s, 9H, $SiC(CH_3)_3$), –0.03 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6 (C, C-2″), 154.4 (C, C=O), 148.9 (CH, C-6″), 148.1 (C, C-4′), 145.2 (C, C-4″), 120.7 (CH, C-5′), 119.3 (CH, C-5′*), 112.0 (C, $C(CH_3)_2$), 107.8 (CH, C-5″), 100.7 (CH, C-3″), 84.8 (CH, C-2*), 82.9 (CH, C-2), 82.6 (CH, C-3), 81.7 (CH, C-3*), 80.6 (C, $OC(CH_3)_3$), 66.3 (CH, C-4), 66.0 (CH, C-4*), 62.5 (CH_2, C-5), 61.5 (CH, C-1*), 60.4 (CH, C-1), 54.1 (CH_3, OCH_3), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.3 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{43}N_5NaO_6Si$, 584.2875; found, 584.2873.

*denotes minor rotamer

(1*S*)-1-(1-(2-Methoxypyridin-4-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol trifluoroacetate salt (12s·TFA)



Following general procedure C, nucleoside **s12s** (6.5 mg, 12.0 μmol) was deprotected to afford the *title compound* **12s·TFA** (5.0 mg, quant.) as a tan solid.

$[\alpha]_D^{21.4}$ –4.0 (*c* 0.1, MeOH);

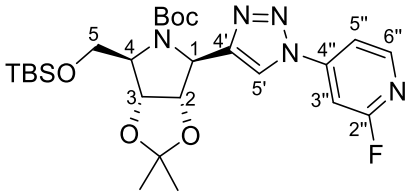
IR ν_{max} (neat): 3261, 1634, 1508, 1371, 1240, 985 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6): *δ* 9.13 (s, 1H, H-5′), 8.39 (d, J = 6.0 Hz, 1H, H-6″), 7.63 (dd, *J* = 6.0, 1.5 Hz, 1H, H-5″), 7.41 (d, *J* = 1.5 Hz, 1H, H-3″), 5.59 – 5.56 (m, 1H, 2-OH), 5.47 – 5.46 (m, 1H, 3-OH), 5.25 – 5.19 (m, 1H, 5-OH), 4.53 (br s, 1H, H-1), 4.32 (br s, 1H, H-2), 4.11 (br s, 1H, H-3), 3.95 (s, OCH_3), 3.67 (br s, 2H, H-5), 3.45 (br s, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-d_6): δ 164.9 (C, C-2″), 149.3 (CH, C-6″), 144.8 (C, C-4″), 142.2 (C, C-4′), 123.6 (CH, C-5′), 107.7 (CH, C-5″), 99.9 (C, C-3″), 73.7 (CH, C-2), 70.4 (CH, C-3), 65.4 (CH, C-4), 58.5 (CH_2, C-5), 56.4 (CH, C-1), 53.9 (CH_3, OCH_3);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{13}H_{17}N_5NaO_4$, 330.1173; found, 330.1166.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(2-fluoropyridin-4-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12t)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and 2-fluoropyridin-4-ylboronic acid (34 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12t** (12 mg, 18%) as an off-white solid.

$[\alpha]_D^{20.3}$ –26.5 (*c* 0.2, $CHCl_3$);

IR ν_{max} (neat): 2931, 2858, 1691, 1607, 1392, 1252, 1161, 1124, 1055, 834, 777 cm^{-1};

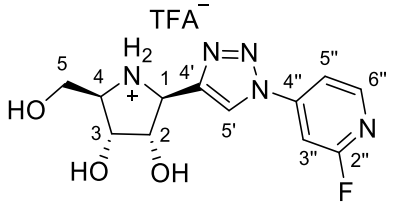
^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.34 (d, *J* = 5.4 Hz, 1H, H-6″), 8.12 – 7.91 (m, 1H, H-5′), 7.60 (d, *J* = 5.4 Hz, 1H, H-5″), 7.37 (s, 1H, H-3″), 5.36 – 5.09 (m, 2H, H-1 and H-2), 4.91 – 4.78 (m, 1H, H-3), 4.29 – 4.11 (m, 1H, H-4), 3.77 – 3.59 (m, 2H, H-5), 1.54 (s, 3H, CCH_3CH_3), 1.46 (s, 9H, $OC(CH_3)_3$), 1.38 (s, 3H, CCH_3CH_3), 0.83 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8 (d, *J* = 240 Hz, C, C-2″), 154.4 (C, C=O), 149.7 (d, *J* = 17 Hz, C-6″), 148.6 (C, C-4′), 147.0 (d, J = 11 Hz, C-4″), 120.8 (CH, C-5′), 112.1 (CH, C-5″), 111.7 (C, $C(CH_3)_2$), 99.9 (d, *J* = 42 Hz, C-3″), 82.9 (CH, C-2), 82.6 (CH, C-3), 80.8 (C, $OC(CH_3)_3$), 66.3 (CH, C-4), 62.5 (CH_2, C-5), 60.3 (CH, C-1), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.4 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

^{19}F NMR (376 MHz, $CDCl_3$): –63.6(*), –63.8;

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{40}FN_5NaO_5Si$, 572.2675; found, 572.2673.

(1*S*)-1-(1-(2-Fluoropyridin-4-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol trifluoroacetate salt (12t·TFA)



Following general procedure C, nucleoside **S12t** (5.0 mg, 9.0 μmol) was deprotected to afford the *title compound* **S12t·TFA** (2.0 mg, 54%) as a white solid.

$[\alpha]_D^{23.2}$ –52.0 (*c* 0.05, H_2O);

IR ν_{max} (neat): 3319, 2952, 1668, 1609, 1422, 1183, 1130, 1040, 837, 798, 721 cm^{-1};

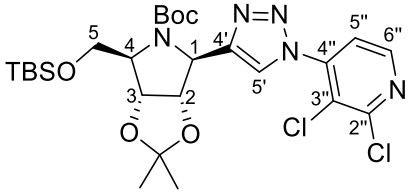
^{1}H NMR (400 MHz, CD_3OD): *δ* 8.96 (s, 1H, H-5′), 8.44 (d, *J* = 5.7 Hz, 1H, H-6″), 7.94 – 7.92 (m, 1H, H-5″), 7.71 (dd, *J* = 1.5, 1.4 Hz, 1H, H-3″), 4.88 (d, *J* = 6.4 Hz, 1H, H-1), 4.58 (dd, *J* = 6.4, 4.4 Hz, 1H, H-2), 4.42 (dd, *J* = 4.5, 4.4 Hz, 1H, H-3), 3.96 – 3.88 (m, 2H, H-5), 3.80 – 3.77 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 166.1 (d, *J* = 239 Hz, C, C-2″), 150.9 (d, *J* = 16 Hz, CH, C-6″), 148.5 (d, *J* = 10 Hz, C, C-4″), 143.5 (C, C-4″), 124.1 (CH, C-5″), 113.4 (d, *J* = 4 Hz, CH, C-5″), 101.2 (d, *J* = 45 Hz, CH, C-3″), 75.9 (CH, C-2), 72.6 (CH, C-3), 67.2 (CH, C-4), 60.0 (CH_2, C-5), 58.7 (CH, C-1);

^{19}F NMR (376 MHz, CD_3OD): –67.1, –77.3;

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{12}H_{14}FN_5NaO_3$, 318.0973; found, 318.0972.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(2,3-dichloropyridin-4-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12u)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and 2,3-dichloropyridin--4--ylboronic acid (47 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12u** (14 mg, 19%) as an off-white- solid.

$[\alpha]_D^{20.9}$ –28.0 (*c* 1.0, $CHCl_3$);

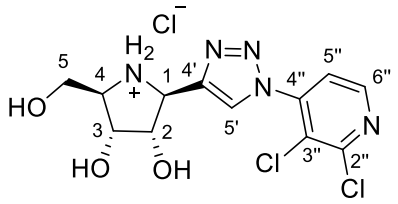
IR ν_{max} (neat): 2955, 2882, 1693, 1573, 1391, 1365, 1161, 1124, 1022, 834, 776, 508 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.47 (d, *J* = 5.0 Hz, 1H, H-6″), 8.27 – 8.11 (m, 1H, H-5′), 7.67 (d, *J* = 5.4 Hz, 1H, H-5″), 5.38 – 5.18 (m, 2H, H-1 and H-2), 4.90 – 4.82 (m, 1H, H-3), 4.27 – 4.11 (m, 1H, H-4), 3.72 – 3.54 (m, 2H, H-5), 1.55 (s, 3H, $CC\mathit{H}_3CH_3$), 1.45 (s, 9H, $OC(CH_3)_3$), 1.39 (s, 3H, $CCH_3C\mathit{H}_3$), 0.84 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4 (C, C=O), 151.9 (C, C-2″), 147.9 (CH, C-6″), 147.6 (C, C-4′), 143.4 (C, C-4″), 124.5 (CH, C-5′), 123.1 (C, C-3″), 119.8 (CH, C-5″), 112.1 (C, $\mathit{C}(CH_3)_2$), 83.0 (CH, C-2), 82.6 (CH, C-3), 80.7 (C, $O\mathit{C}(CH_3)_3$), 66.2 (CH, C-4), 62.5 (CH_2, C-5), 60.3 (CH, C-1), 28.5 (3 × CH_3, $OC(\mathit{C}H_3)_3$, 27.4 (CH_3, $C\mathit{C}H_3CH_3$), 25.9 (3 × CH_3, $SiC(\mathit{C}H_3)_3$), 25.4 (CH_3, $CCH_3\mathit{C}H_3$), 18.4 (C, $Si\mathit{C}(CH_3)_3$), –5.2 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{39}Cl_2N_5NaO_5Si$, 622.1990; found, 622.1986.

(1*S*)-1-(1-(2,3-Dichloropyridin-4-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12u·HCl)



Following general procedure B, nucleoside **S12u** (12 mg, 20 μmol) was deprotected to afford the *title compound* **12u·HCl** (7.8 mg, 93%) as a white solid.

$[\alpha]_D^{24.6}$ –21.0 (*c* 0.1, H_2O);

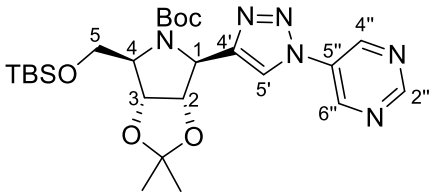
IR ν_{max} (neat): 3376, 2868, 2498, 1578, 1363, 1142, 1059, 1041, 856, 788 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD): *δ* 8.79 (s, 1H, H-5′), 8.57 (d, *J* = 5.0 Hz, 1H, H-6″), 7.76 (d, *J* = 5.0 Hz, 1H, H-5″), 4.91 (d, *J* = 6.5 Hz, 1H, H-1), 4.58 (dd, *J* = 6.5, 4.7 Hz, 1H, H-2), 4.42 (dd, *J* = 4.7, 4.5 Hz, 1H, H-3), 3.97 – 3.89 (m, 2H, H-5), 3.80 – 3.77 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 152.4 (C, C-2″), 149.7 (CH, C-6″), 144.8 (C, C-4″), 142.6 (C, C-4′), 127.5 (CH, C-5′), 125.6 (C, C-3″), 122.0 (CH, C-5″), 76.0 (CH, C-2), 72.7 (CH, C-3), 67.2 (CH, C-4), 60.0 (CH_2, C-5), 58.7 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{14}Cl_2N_5O_3$, 346.0468; found, 346.0467.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(pyrimidin-5-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12v)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and pyrimidine-5-boronic acid (30 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12v** (34 mg, 54%) as an off-white solid.

$[\alpha]_D^{21.1}$ –45.7 (*c* 0.3, $CHCl_3$);

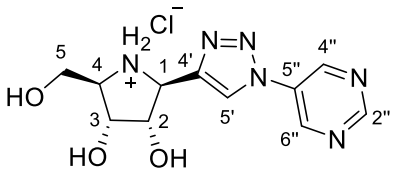
IR ν_{max} (neat): 2931, 1690, 1472, 1393, 1255, 1163, 1125, 1056, 836, 777, 718 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 9.27 (s, 1H, H-2″), 9.15 (s, 2H, H-4″ and H-6″), 8.10 (s, 1H, C-5′), 5.36 – 5.09 (m, 2H, H-1 and H-2), 4.90 – 4.79 (m, 1H, H-3), 4.27 – 4.10 (m, 1H, H-4), 3.71 – 3.57 (m, 2H, H-5), 1.53 (s, 3H, CCH_3CH_3), 1.45 (s, 9H, $OC(CH_3)_3$), 1.37 (s, 3H, CCH_3CH_3), 0.82 (s, 9H, $SiC(CH_3)_3$), –0.02 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4 (CH, C-2″), 154.4 (C, C=O), 148.8 (C, C-4′), 148.4 (2 × CH, C-4″ and C-6″), 132.2 (C, C-5″), 121.0 (CH, C-5′), 112.1 (C, $C(CH_3)_2$), 83.0 (CH, C-2), 82.5 (CH, C-3), 80.7 (C, $OC(CH_3)_3$), 66.2 (CH, C-4), 62.5 (CH_2, C-5), 60.3 (CH, C-1), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.4 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{25}H_{40}N_6NaO_5Si$, 555.2722; found, 555.2722.

(1*S*)-1-(1-(Pyrimidin-5-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12v·HCl)



Following general procedure B, nucleoside S**12v** (34 mg, 64 μmol) was deprotected to afford the *title compound* **12v·HCl** (20 mg, quant) as a white solid.

$[\alpha]_D^{20.5}$ –19.0 (*c* 0.2, H_2O);

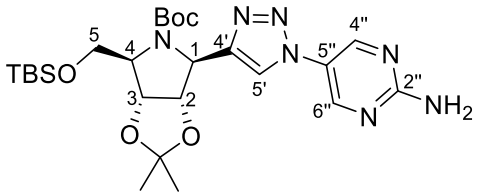
IR ν_{max} (neat): 3278, 1592, 1438, 1147, 1032, 857, 804, 667 cm^{-1};

^{1}H NMR (400 MHz, CD_3OD): *δ* 8.82 (s, 1H, H-5′), 7.98 (d, *J* = 1.5 Hz, 2H, H-4″ and H-6″), 7.65 – 7.64 (m, 1H, H-2″), 4.87 (d, *J* = 6.4 Hz, 1H, H-1), 4.57 (dd, *J* = 6.4, 4.5 Hz, 1H, H-2), 4.42 (dd, *J* = 5.0, 4.5 Hz, 1H, H-3), 3.97 – 3.88 (m, 2H, H-5), 3.79 – 3.75 (m, 1H, H-4);

^{13}C NMR (100 MHz, CD_3OD): δ 143.1 (C, C-4″), 137.5 (C, C-5″), 130.0 (CH, C-2″), 124.1 (CH, C-5′), 120.2 (2 × CH, C-4″ and C-6″), 75.9 (CH, C-2), 72.6 (CH, C-3), 67.0 (CH, C-4), 60.1 (CH_2, C-5), 58.8 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{11}H_{14}N_6NaO_3$, 301.1020; found, 301.1020.

(1*S*)-*N*-*tert*-Butoxycarbonyl-1-(1-(2-aminopyrimidin-5-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-D-ribitol (S12w)



General procedure A was followed using alkyne **1** (50 mg, 120 μmol) and 2-aminopyrimidin-5--ylboronic acid (34 mg, 240 μmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12w** (27 mg, 41%) as an off-white- solid.

$[\alpha]_D^{21.2}$ –24.0 (*c* 0.1, $CHCl_3$);

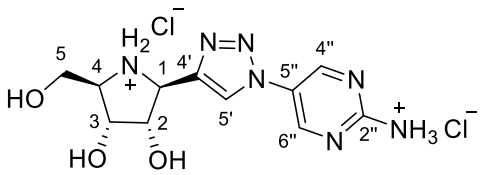
IR ν_{max} (neat): 2931, 1684, 1628, 1489, 1395, 1371, 1256, 1162, 1127, 1055, 835, 779 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.57 (s, 2H, H-6″ and C-6″), 7.90 (s, 1H, H-5′), 5.60 (s, 1H, NH_2), 5.35 – 5.13 (m, 2H, H-1 and H-2), 4.9 – 4.89 (m, 1H, H-3), 4.11 – 4.07 (m, 1H, H-4), 3.71 – 3.58 (m, 2H, H-5), 1.52 (s, 3H, CCH_3CH_3), 1.44 (s, 9H, $OC(CH_3)_3$), 1.36 (s, 3H, CCH_3CH_3), 0.83 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8 (C, C-2″), 154.4 (C, C=O), 151.5 (2 × CH, C-4″ and C-6″), 147.9 (C, C-4′), 124.6 (C, C-5″), 121.6 (CH, C-5′), 112.0 (C, $C(CH_3)_2$), 83.0 (CH, C-2), 82.6 (CH, C-3), 80.6 (C, $OC(CH_3)_3$), 66.3 (CH, C-4), 62.5 (CH_2, C-5), 60.3 (CH, C-1), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.3 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{25}H_{41}N_7NaO_5Si$, 570.2831; found, 570.2831.

(1*S*)-1-(1-(2-Aminopyrimidin-5-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol dihydrochloride (12w·2HCl)



Following general procedure B, nucleoside **S12w** (27 mg, 49 μmol) was deprotected to afford the *title compound* **12w·2HCl** (18 mg, quant) as a white solid.

$[\alpha]_D^{24.7}$ –40.0 (*c* 0.1, H_2O);

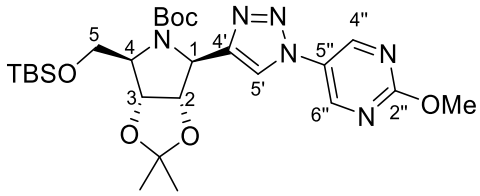
IR ν_{max} (film): 3339, 1681, 1637, 1404, 1041, 1016, 669 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.66 – 10.65 (m, 1H, NH), 8.88 – 8.82 (m, 2H, H-5′ and NH), 8.69 (s, 2H, H-4″ and H-6″), 4.66 – 4.61 (m, 1H, H-1), 4.39 (dd, J = 6.8, 4.4 Hz, 1H, H-2), 4.19 (dd J = 5.0, 4.4 Hz, 1H, H-3), 3 3.73 (d, J = 4.8 Hz, 2H, H-5), 3.56 – 3.52 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-d_6): δ 163.1 (C, C-2″), 151.3 (2 × CH, C-4″ and C-6″), 141.5 (C, C-4′), 123.7 (CH, C-5′), 122.7 (C,C-5″), 73.9 (CH, C-2), 70.5 (CH, C-3), 65.3 (CH, C-4), 58.6 (CH_2, C-5), 56.6 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{11}H_{15}N_7NaO_3$, 316.1129; found, 316.1130.

(1*S*)-*N-tert*-Butoxycarbonyl-1-(1-(2-methoxypyrimidin-5-yl)-1H-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-2,3-O-isopropylidene-5-O-tert-butyldimethylsilyl-D-ribitol (S12x)



General procedure A was followed using alkyne **1** (50 mg, 120 µmol) and 2-methoxypyrimidine-5-boronic acid (37 mg, 240 µmol). The crude residue was purified *via* flash chromatography (pet. ether/EtOAc, 19:1 → 4:1) to afford the *title compound* **S12x** (26 mg, 38%) as an off-white- solid.

$[\alpha]_D^{21.4}$ –29.0 (*c* 0.1, $CHCl_3$);

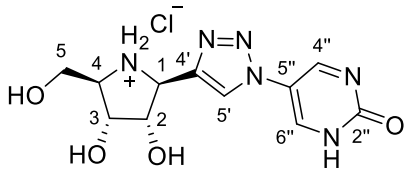
IR ν_{max} (neat): 2931, 1693, 1567, 1484, 1392, 1330, 1123, 1046, 835, 777 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.85 (s, 2H, H-4″ and H-6″), 7.97 – 7.78 (m, 1H, H-5′), 5.34 – 5.15 (m, 2H, H-1 and H-2), 4.90 – 4.80 (m, 1H, H-3), 4.27 – 4.08 (m, 4H, H-4 and OCH_3), 3.71 – 3.60 (m, 2H, H-5), 1.53 (s, 3H, CCH_3CH_3), 1.45 (s, 9H, $OC(CH_3)_3$), 1.37 (s, 3H, CCH_3CH_3), 0.82 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 6H, 2 × $SiCH_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.3 (C, C-2″), 154.4 (C, C=O), 151.9 (2 × CH, C-4″ and C-6″), 148.4 (C, C-4′), 127.5 (C, C-5″), 121.4 (CH, C-5′), 112.0 (C, $C(CH_3)_2$), 83.0 (CH, C-2), 82.5 (CH, C-3), 80.6 (C, $OC(CH_3)_3$), 66.3 (CH, C-4), 62.5 (CH_2, C-5), 60.3 (CH, C-1), 55.8 (CH_3, OCH_3), 28.5 (3 × CH_3, $OC(CH_3)_3$, 27.4 (CH_3, CCH_3CH_3), 25.9 (3 × CH_3, $SiC(CH_3)_3$), 25.4 (CH_3, CCH_3CH_3), 18.3 (C, $SiC(CH_3)_3$), –5.3 (2 × CH_3, $SiCH_3$);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{42}N_6NaO_6Si$, 585.2827; found, 585.2824.

(1*S*)-1-(1-(2-Oxo-1,2-dihydropyrimidin-5-yl)-1*H*-1,2,3-triazol-4-yl)-1,4-dideoxy-1,4-imino-D-ribitol hydrochloride (12x·HCl)



Following general procedure B, nucleoside **S12x** (4.0 mg, 7.1 μmol) was deprotected to afford the *title compound* **12x·HCl** (2.3 mg, quant) as a white solid.

$[\alpha]_D^{24.9}$ –16.5 (*c* 0.2, H_2O);

IR ν_{max} (neat): 3289, 2695, 1768, 1738, 1591, 1280, 1216, 1047, 658 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.80 (s, 1H, NH), 8.92 – 8.88 (m, 4H, NH, H-5′, H-4′ and H-6′), 4.63 – 4.62 (m, 1H, H-1), 4.37 (dd, *J* = 6.6, 4.8 Hz, 1H, H-2), 4.18 – 4.16 (m, 1H, H-3), 3.72 – 3.71 (m, 2H, H-5), 3.54 – 3.53 (m, 1H, H-4);

^{13}C NMR (100 MHz, DMSO-d_6): δ 155.3 (C, C-2″), 151.4 (2 × CH, C-4″ and C-6″), 141.5 (C, C-4′), 124.6 (CH, C-5′), 118.1 (C, C-5″), 73.9 (CH, C-2), 70.4 (CH, C-3), 65.5 (CH, C-4), 58.5 (CH_2, C-5), 56.5 (CH, C-1);

HRMS (ESI/Q-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{11}H_{14}N_6NaO_4$, 317.0969; found, 317.0963.

Antiviral Assessment of Nucleosides

Antiviral testing was carried out under the non-clinical and pre-clinical services program offered by the National Institute of Allergy and Infectious Diseases (NIAID). Nucleosides **12a**-**12x** were tested against a panel of RNA viruses including viruses including Dengue virus (DENV-2, virus strain New Guinea C), Influenza A virus (H1N1, virus strain California/07/2009), Middle East respiratory syndrome−related coronavirus (MERS-CoV, virus strain EMC), Respiratory syncytial virus (RSV, virus strain A2), Rift Valley fever virus (RVFV, virus strain MP-12), Yellow fever virus (YFV, virus strain 17D) and Zika virus (ZIKV, virus strain MR766). Notable antiviral activity from the flex-imino-C-nucleoside series is summarised in Table S1. Briefly, compounds were added to cells prior to addition of virus at an appropriate multiplicity of infection to cause visible cytopathic effect (CPE). When maximal CPE was observed in virus controls, cells were stained with neutral red dye for a dye-uptake assay. These data were used to calculate EC_{50}, CC_{50} and selective index (SI_{50} = CC_{50}/EC_{50}) for the compounds.

Table S1: Antiviral Screening Against RNA Viruses

Entry	Virus	Cell-Line	Compound	EC_{50} (μM)	CC_{50} (μM)	SI_{50}
1	DENV-2	Huh7	12c	>32	>32	0
			12i	>32	>32	0
			12t	>32	>32	0
2	H1N1	MDCK	12c	>32	>32	0
			12i	23	>32	>1.4
			12t	86	>100	>1.2
3	MERS-COV	Vero 76	12c	>6.2	6.2	0
			12i	>32	>32	0
			12t	>32	>32	0
4	RSV	RD MA-104 RD	12c	>100	>100	0
			12i	>32	>32	0
			12t	>100	>100	0
5	RVFV	Vero 76	12c	>32	>32	0
			12i	>32	>32	0
			12t	>32	>32	0
6	YFV	Huh7	12c	>32	>32	0
			12i	>32	>32	0
			12t	>32	>32	0
7	ZIKV	Vero 76	12c	>32	>32	0
			12i	>32	>32	0
			12t	ND	ND	0

EC_{50} and CC_{50} were determined by CPE, as measured by neutral red dye uptake. Tested drug concentration range from 0.01–32 μM (vehicle, DMSO) or 0.01–100 μM (vehicle, DMSO) for entry 4.

References

1 Sodium Azide| Sigma-Aldrich, https://www.sigmaaldrich.com/NZ/en/substance/sodiumazide650126628228, (accessed May 31, 2023).

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5 Y. Matsui, T. Kurita and Y. Date, *BCSJ*, 1972, **45**, 3229–3229.

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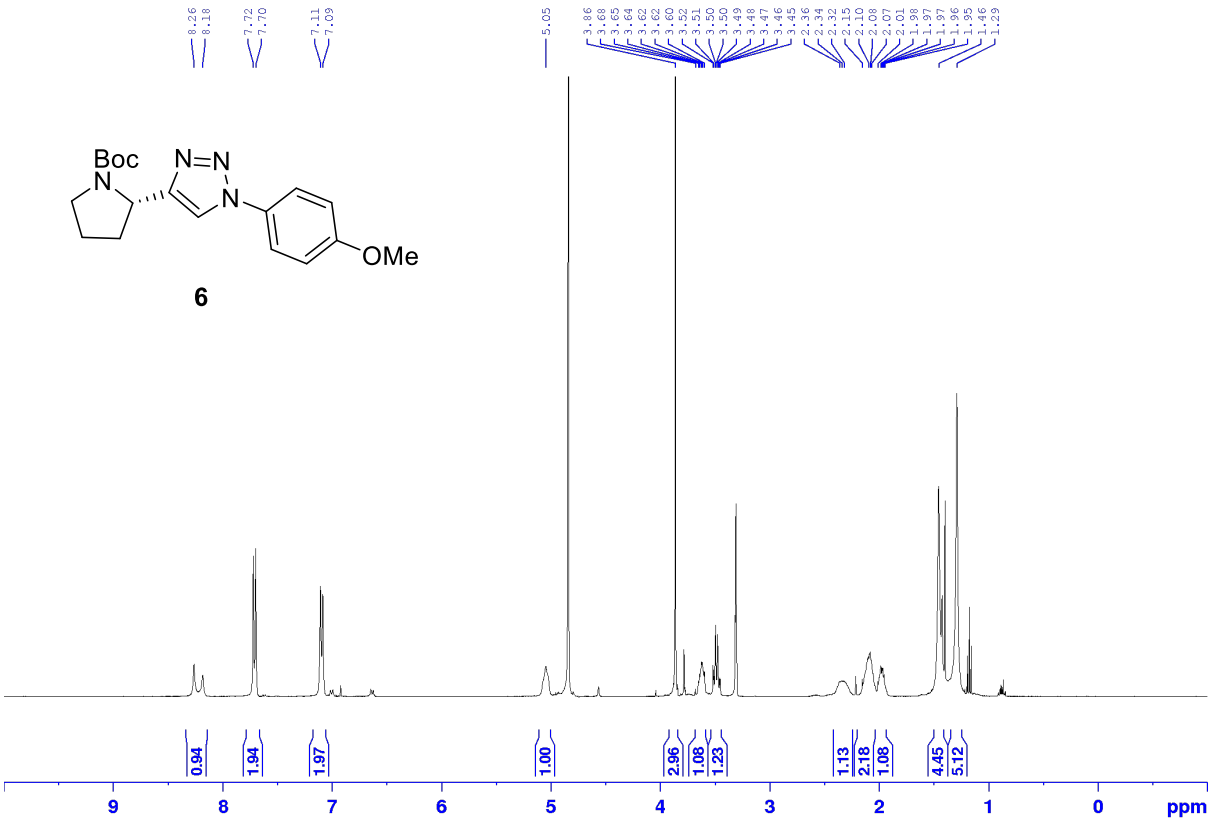
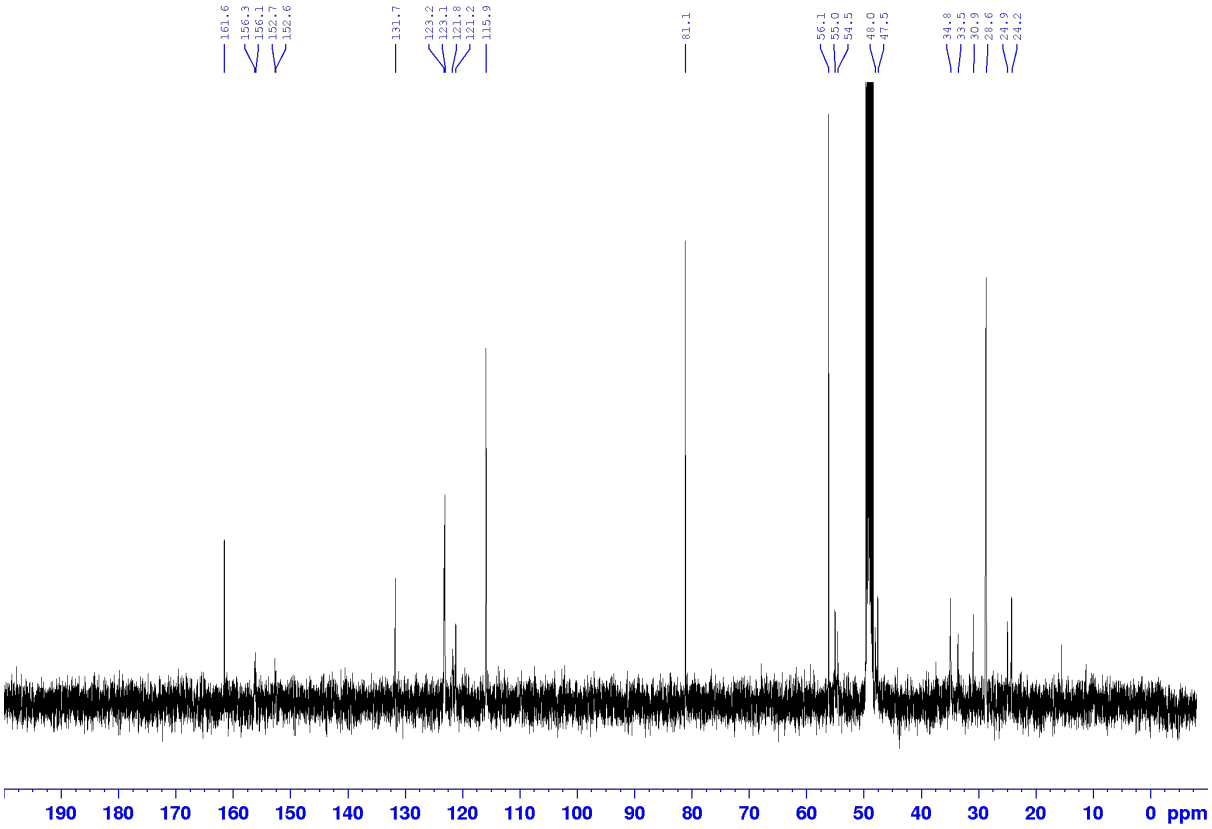
NMR Spectra of Novel Compounds

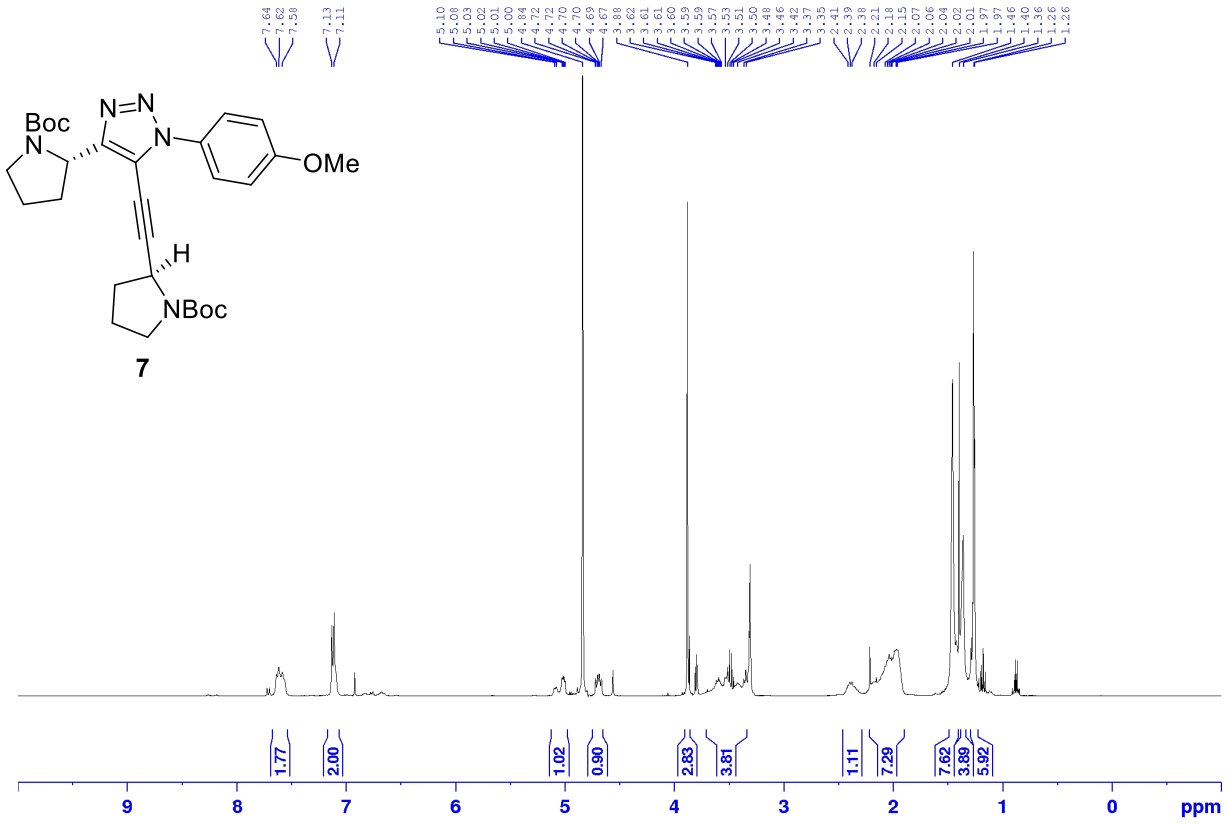
^{1}H NMR (400 MHz, CD_3OD)



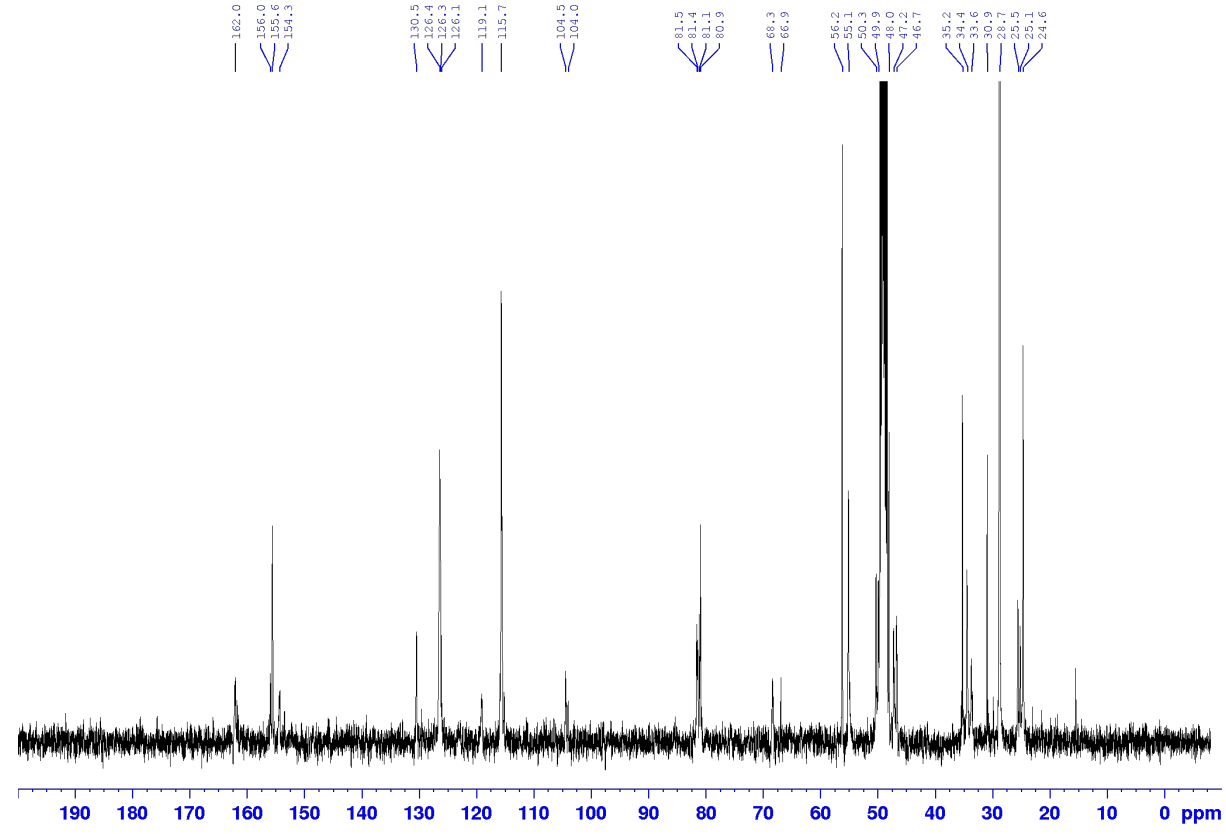
^{13}C NMR (100 MHz, CD_3OD)



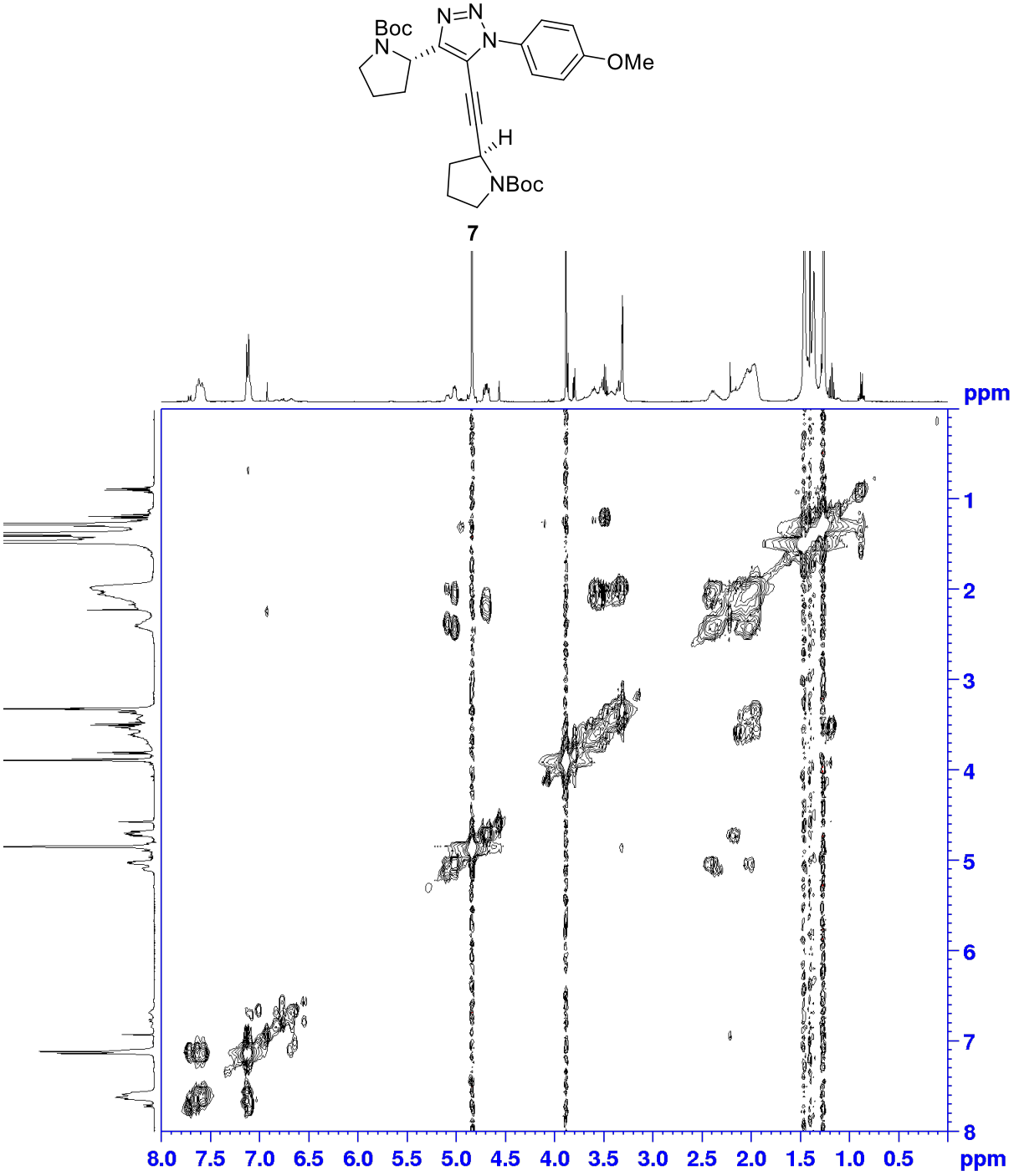
^{1}H NMR (400 MHz, CD_3OD)



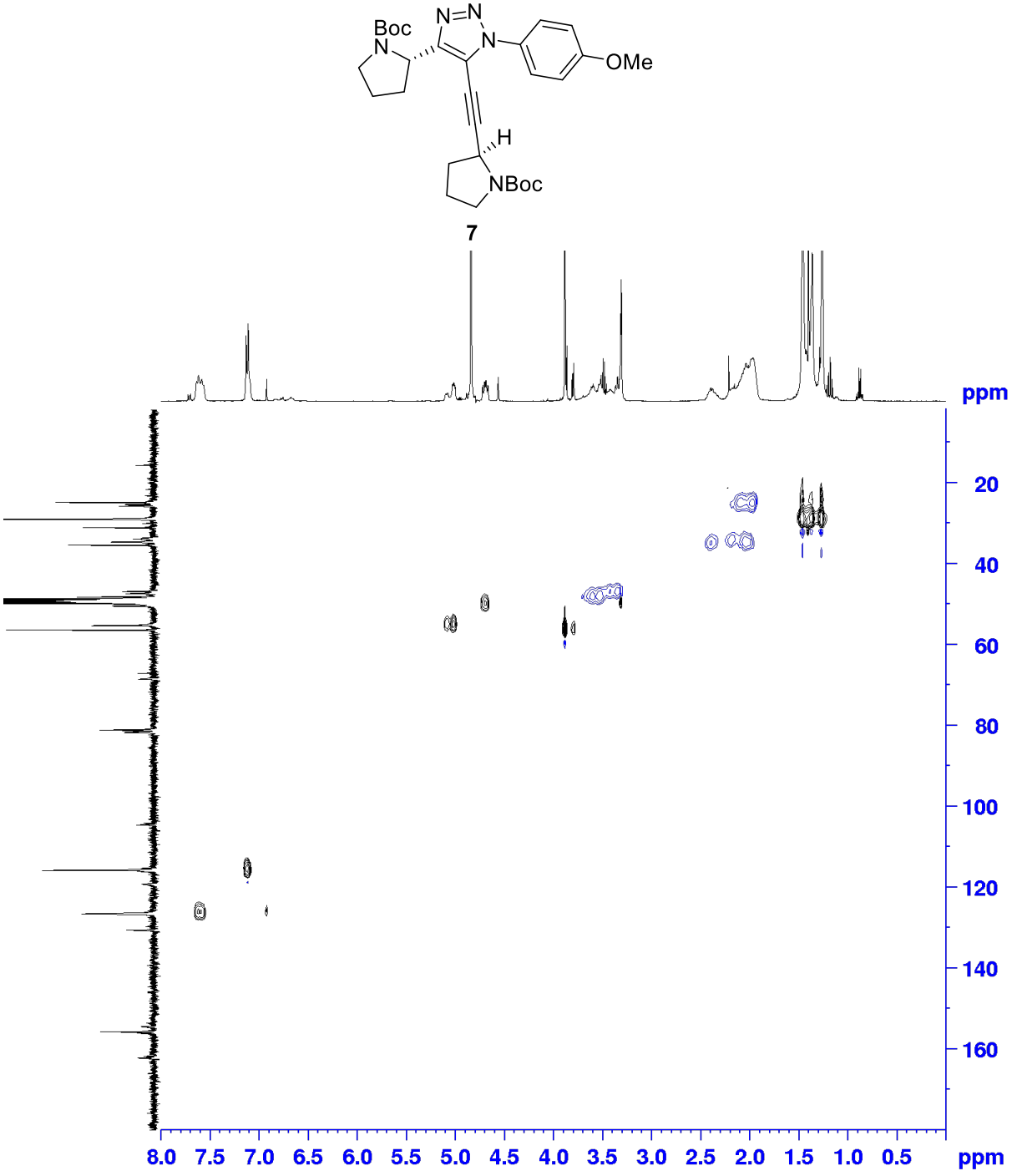
^{13}C NMR (100 MHz, CD_3OD)



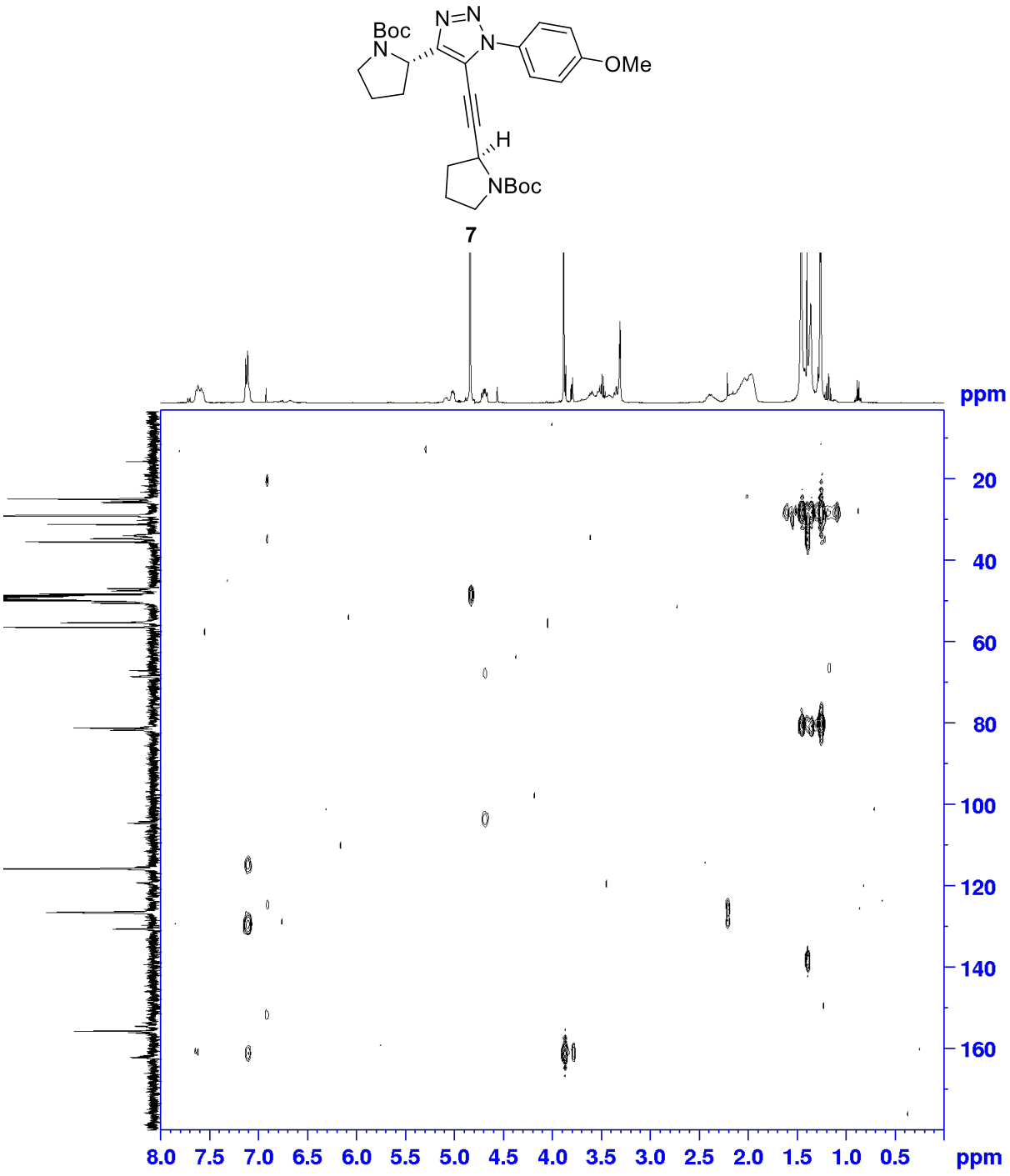
COSY (CD_3OD, 400 MHz, 298 K) of **7**:



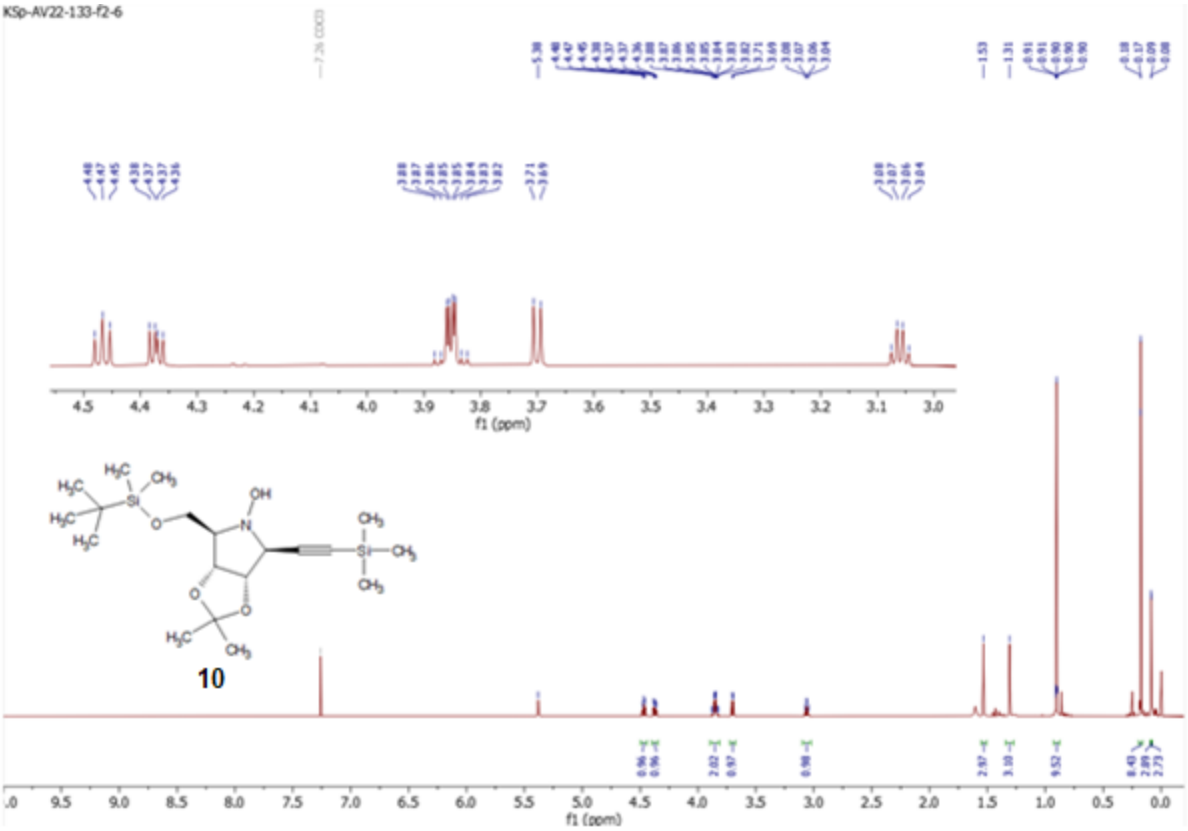
EDITED HSQC (CD_3OD, 400 MHz, 298 K) of **7**:



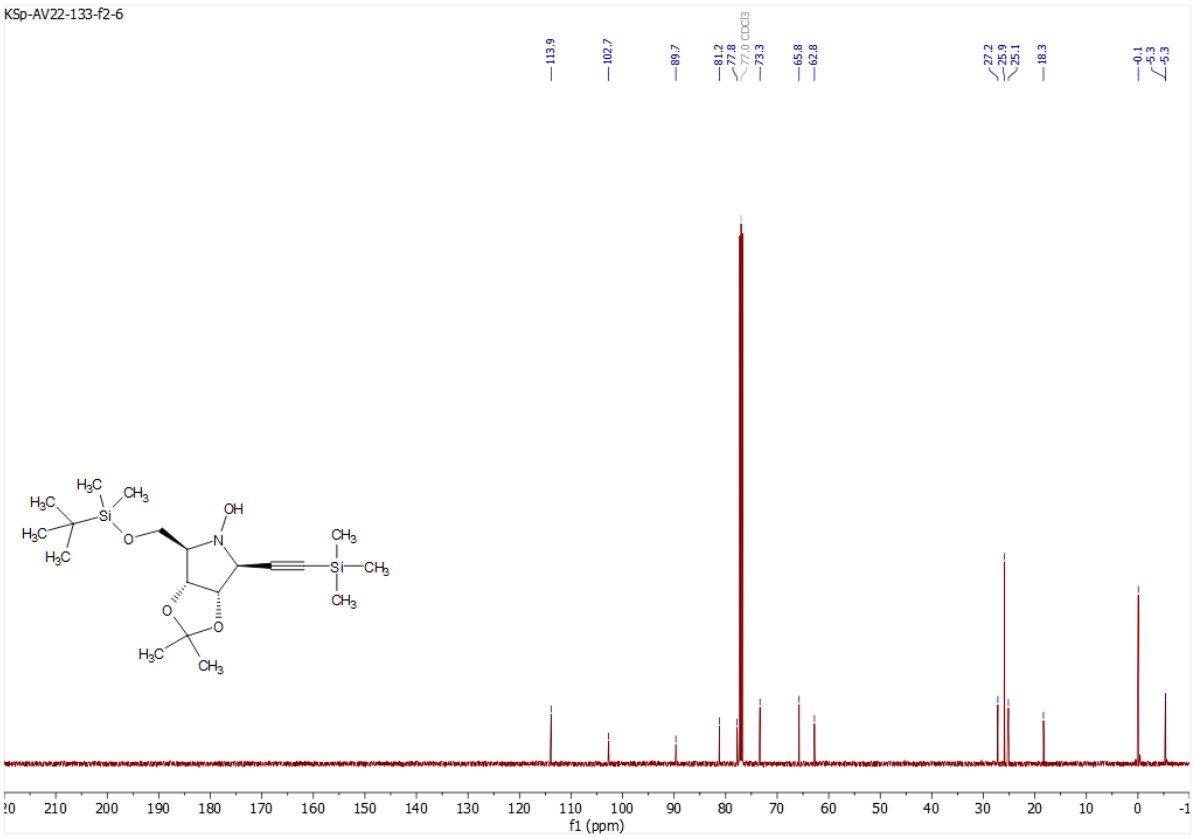
HMBC (CD_3OD, 400 MHz, 298 K) of **7**:



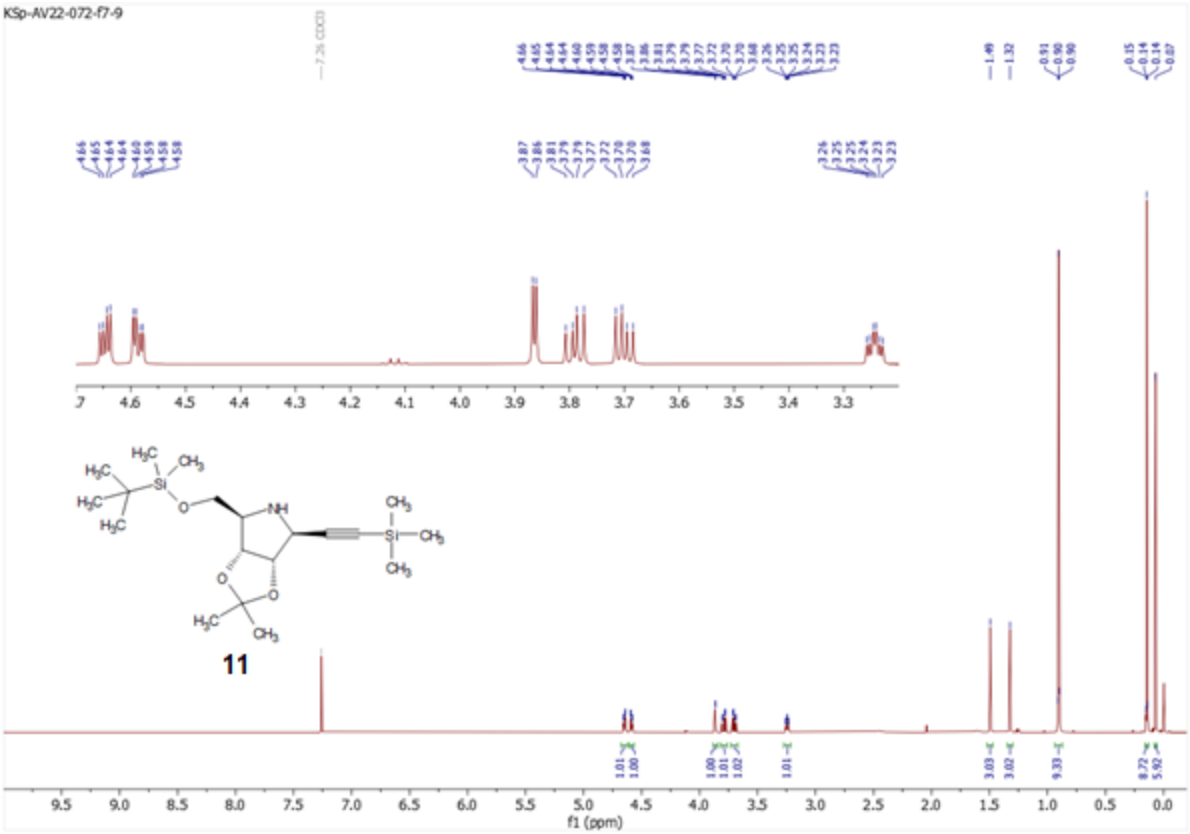
^{1}H NMR (500 MHz, $CDCl_3$)



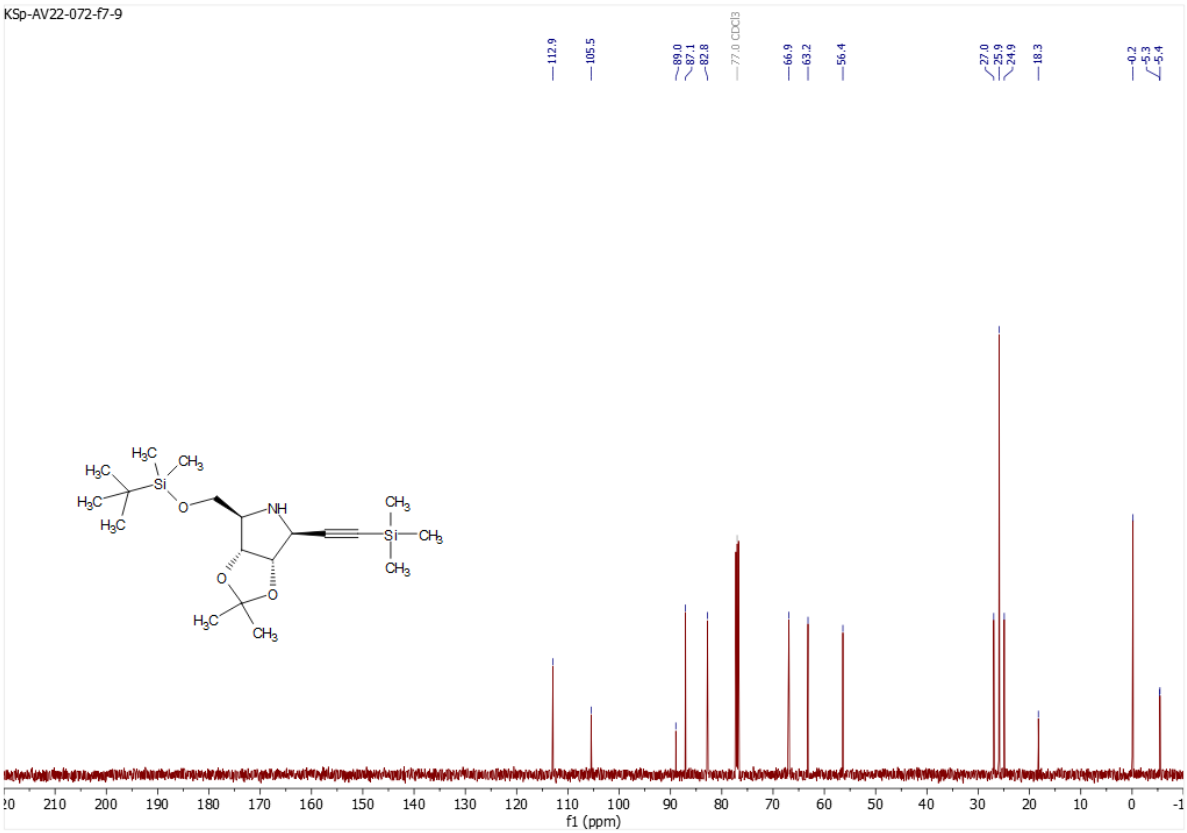
^{13}C NMR (126 MHz, $CDCl_3$)



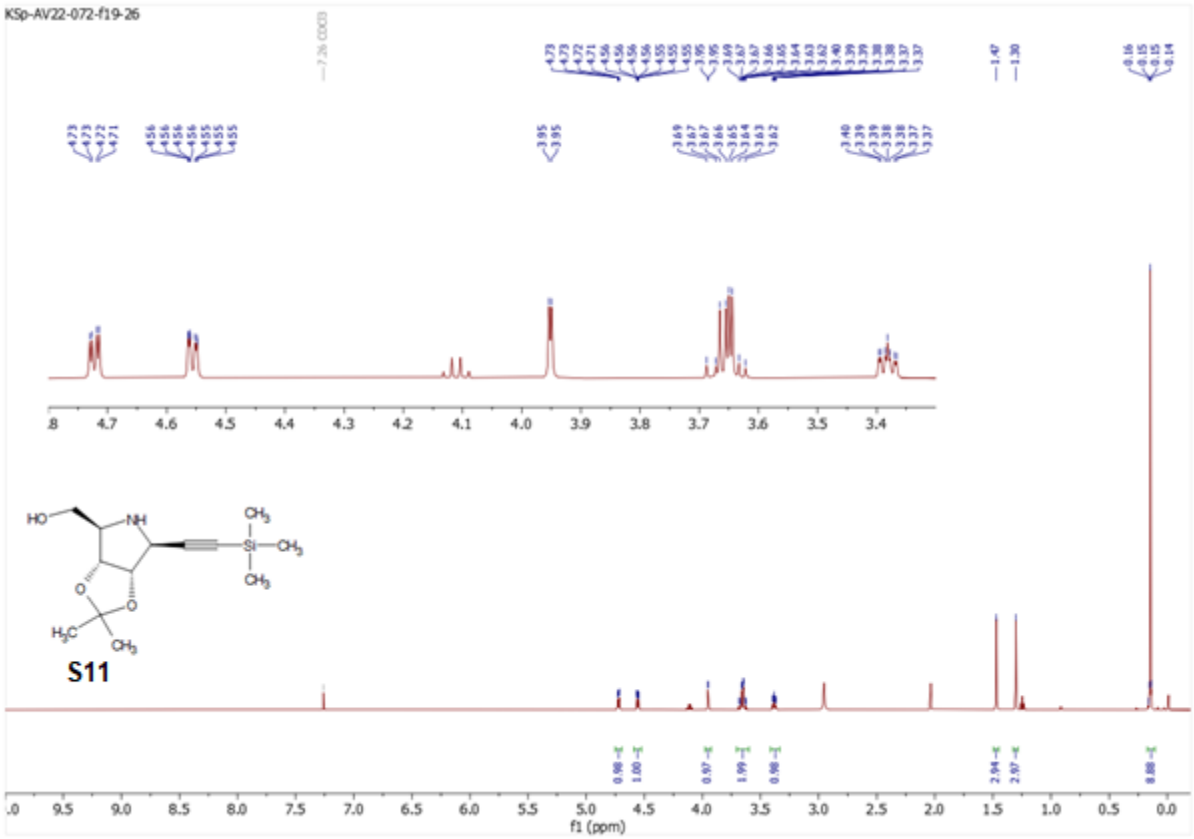
^{1}H NMR (500 MHz, $CDCl_3$)



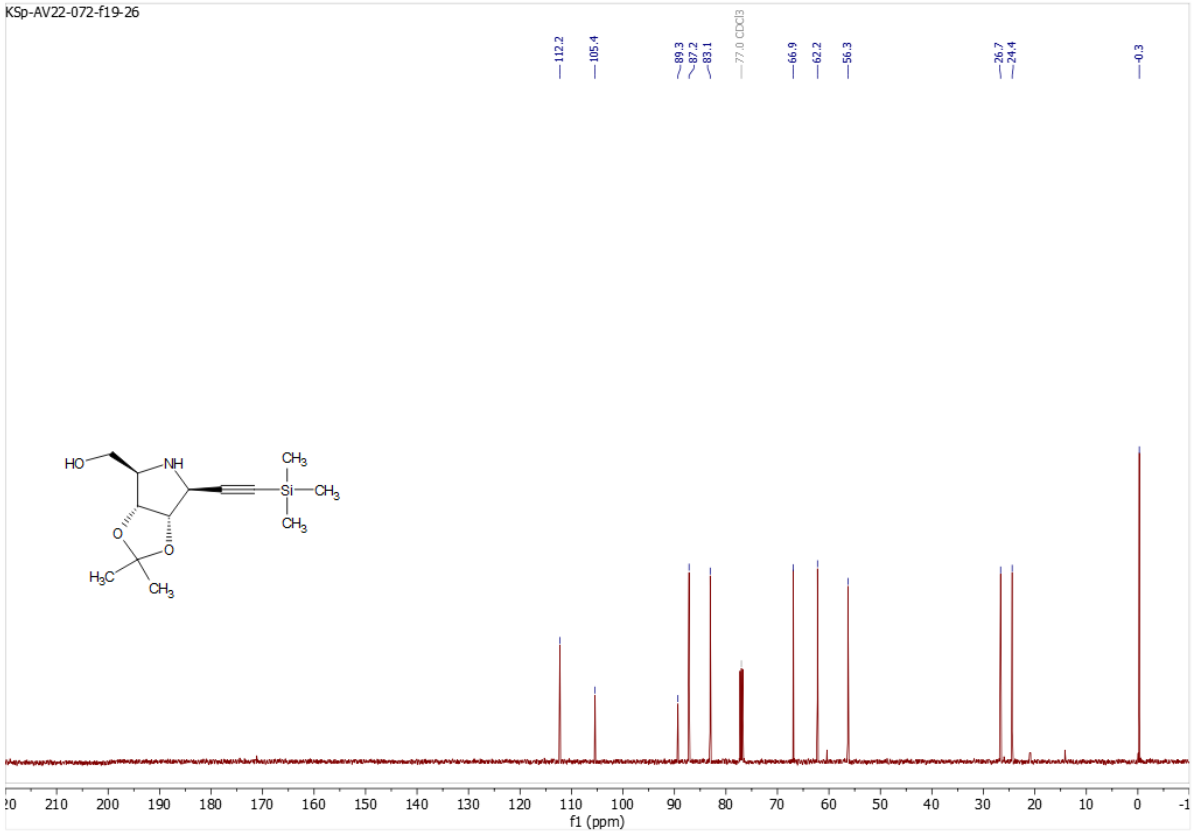
^{13}C NMR (126 MHz, $CDCl_3$)



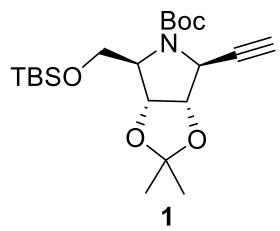
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, DMSO-d_6, 343 K)



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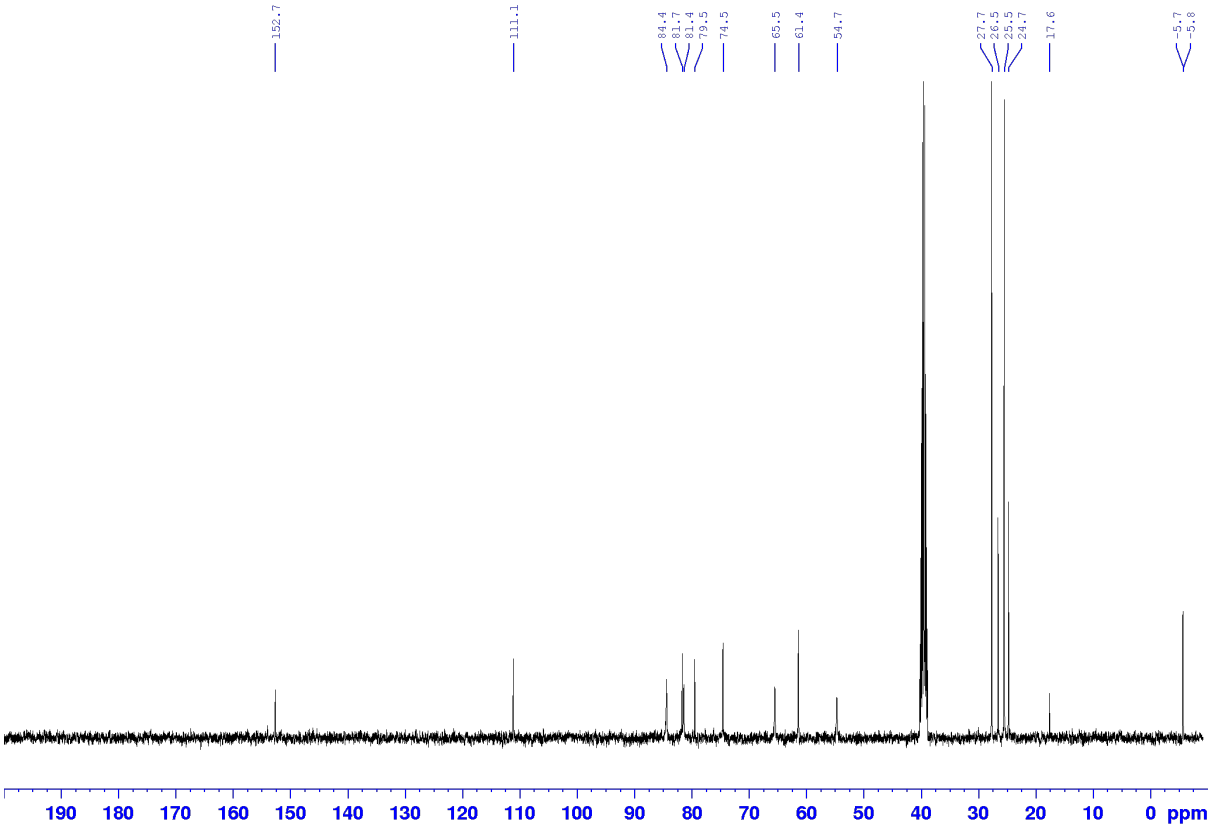
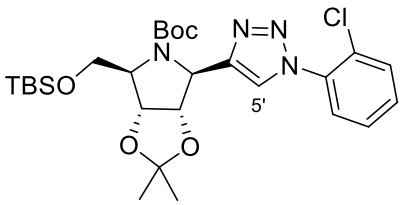
^{13}C NMR (100 MHz, DMSO-d_6, 343 K)



Note from the Authors

Isolated nucleoside products from the tandem Chan-Lam/CuAAC reaction display broad resonances in the ^{1}H NMR spectra which likely arises from rotational isomerism exerted by the presence of the Boc protecting group (Figure 1, blue). This has the effect of broadening the diagnostic H-5′ singlet such that it appears as a multiplet. To show that the isolated product is homogenous and that the developed tandem sequence is regioselective, a high temperature NMR experiment was carried out in deuterated DMSO at 343 K (Figure 1, black). Indeed, line shape improved under these conditions. Given that the NMR spectra of the protected nucleosides **S12a-x** appear similar to that of **S12b** and the NMR spectra of the final nucleoside analogues are well-resolved, it is reasonable to assume that **S12a-x** are pure single products. Since variable temperature NMR is a time-consuming practice, its use was limited to the sterically hindered compounds in the series, for the purpose of observing quaternary carbons.



S12b

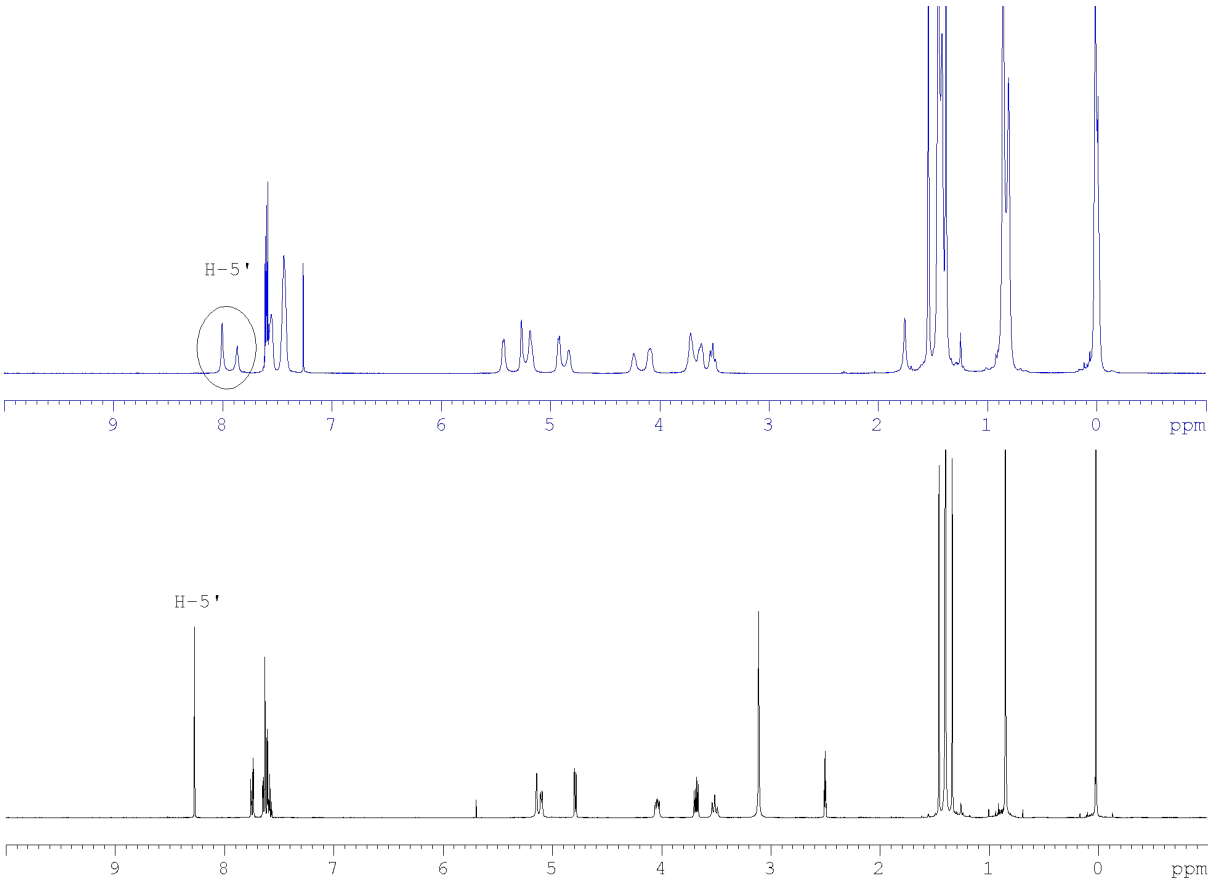
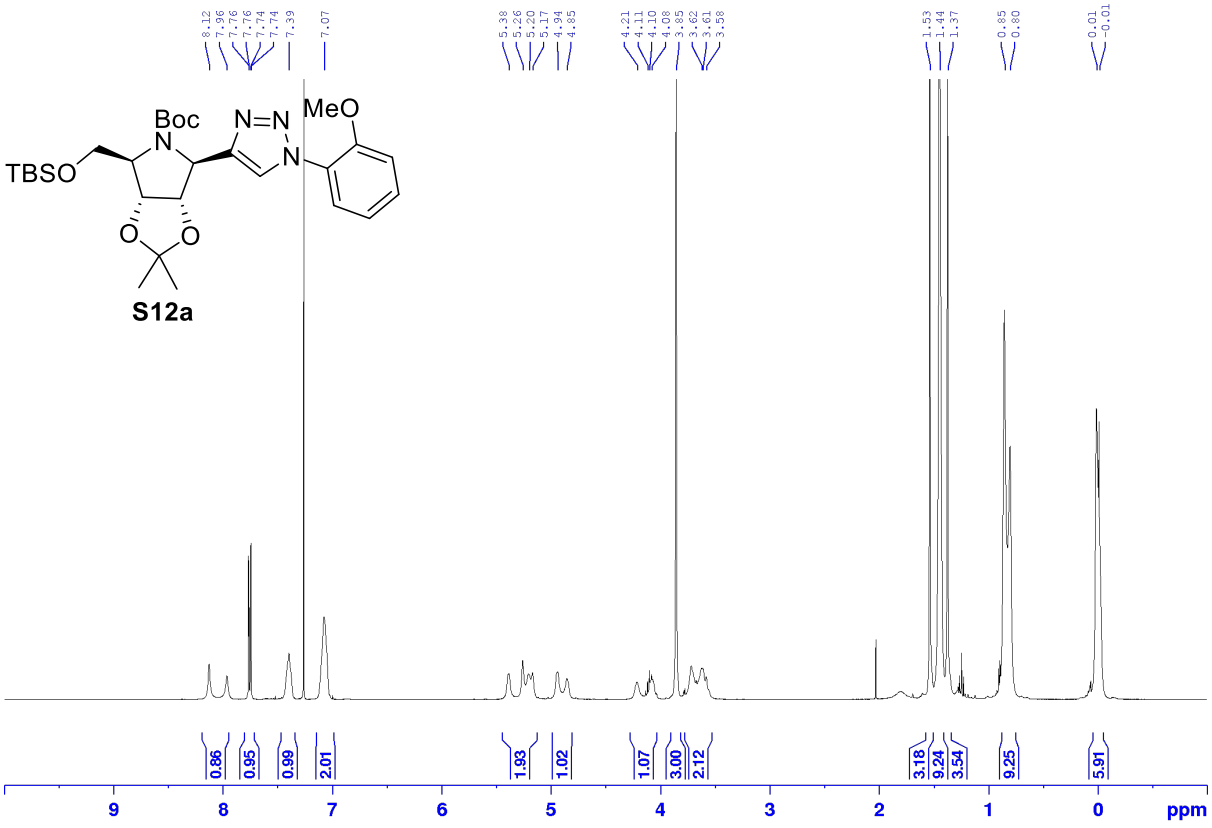
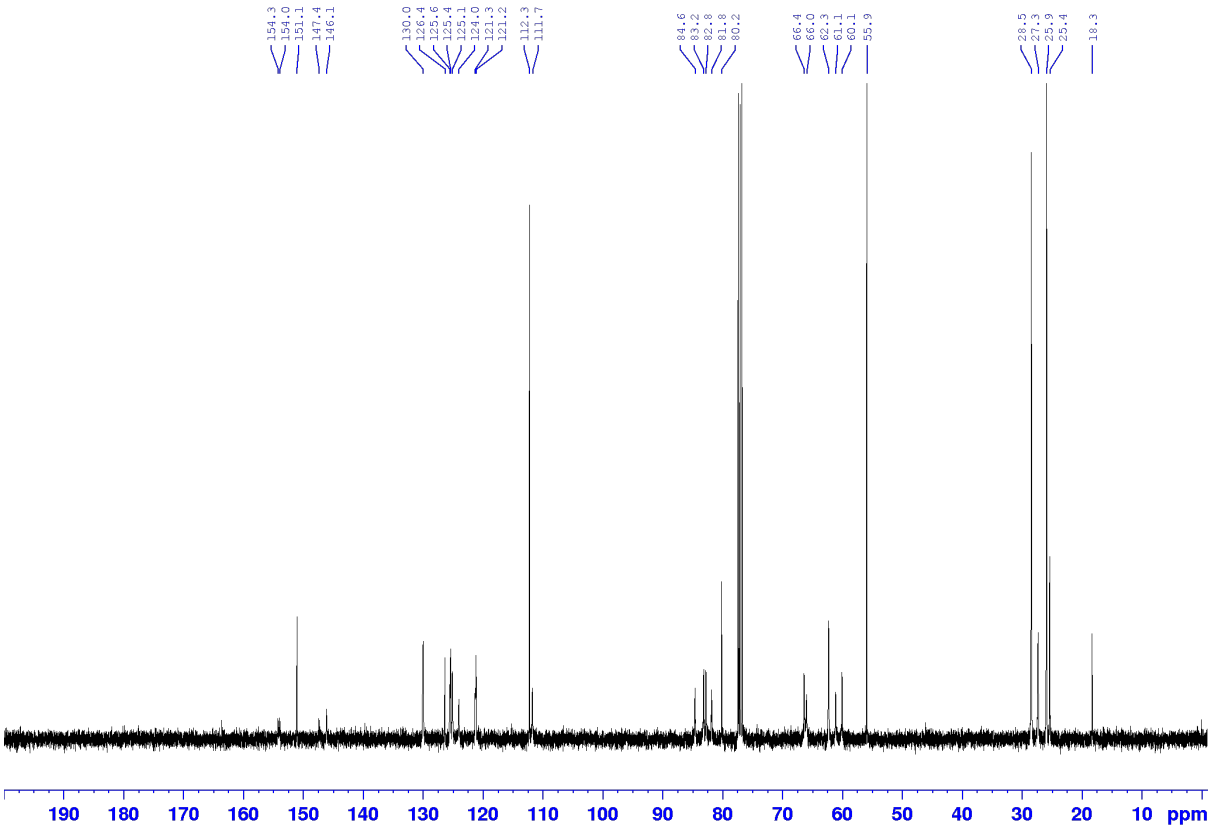


Figure 1: *Comparative ^{1}H NMR Spectra of **S12b**. Blue was recorded at 400 MHz in $CDCl_3$ at 298 K and black was recorded at 400 MHz in DMSO-d_6 at 343 K.*

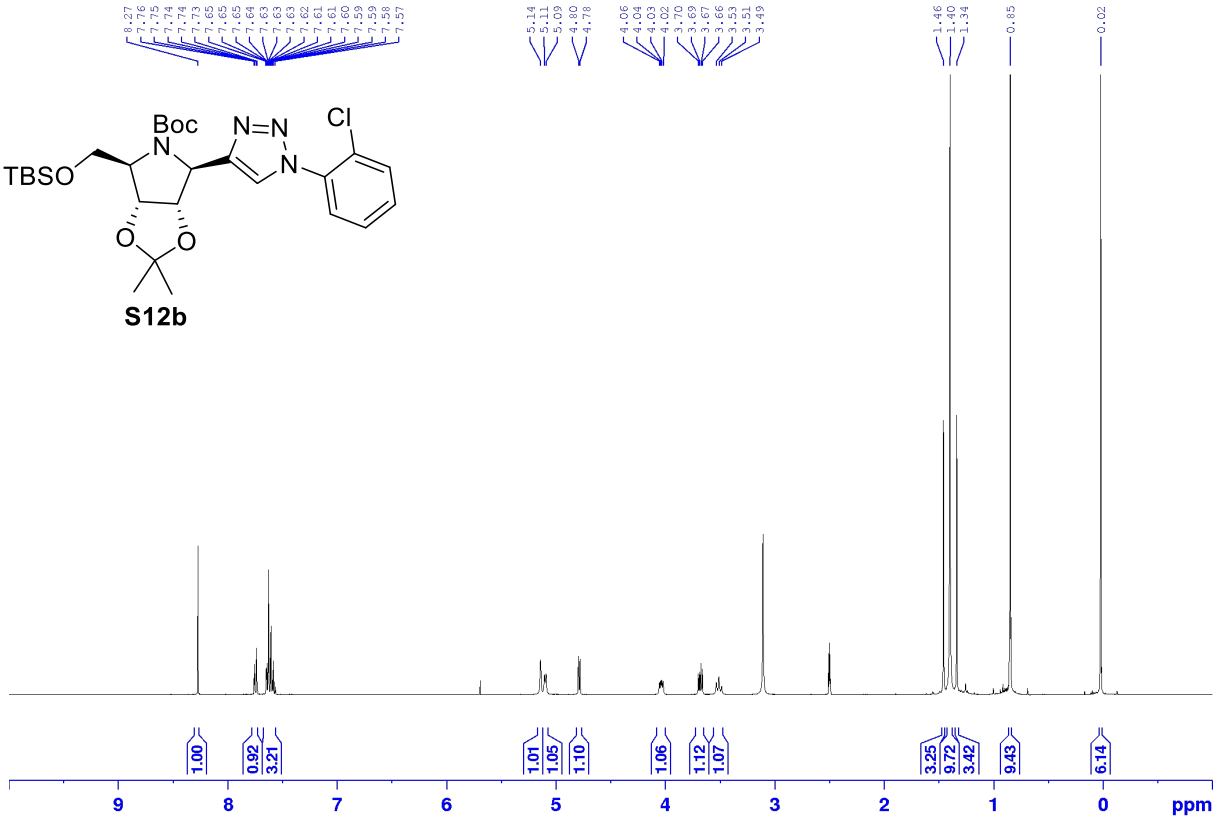
^{1}H NMR (400 MHz, $CDCl_3$)



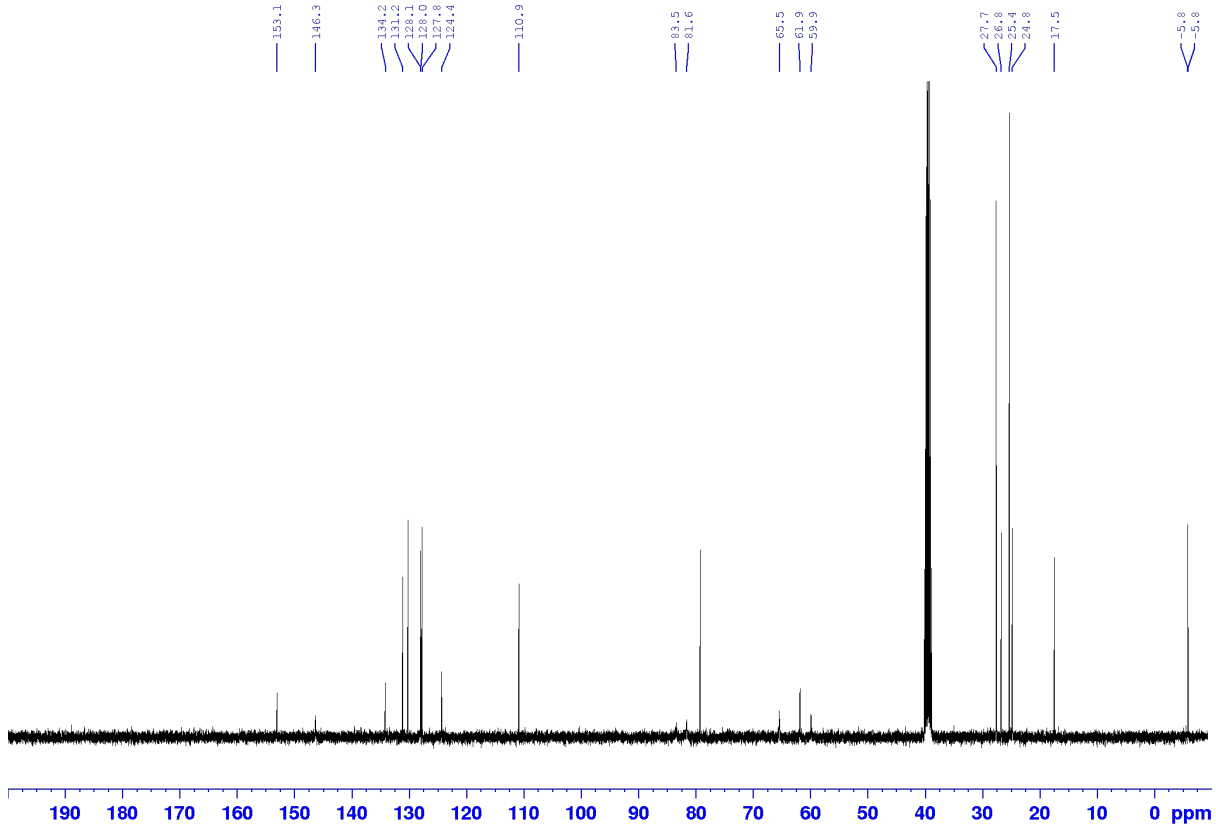
^{13}C NMR (100 MHz, $CDCl_3$)



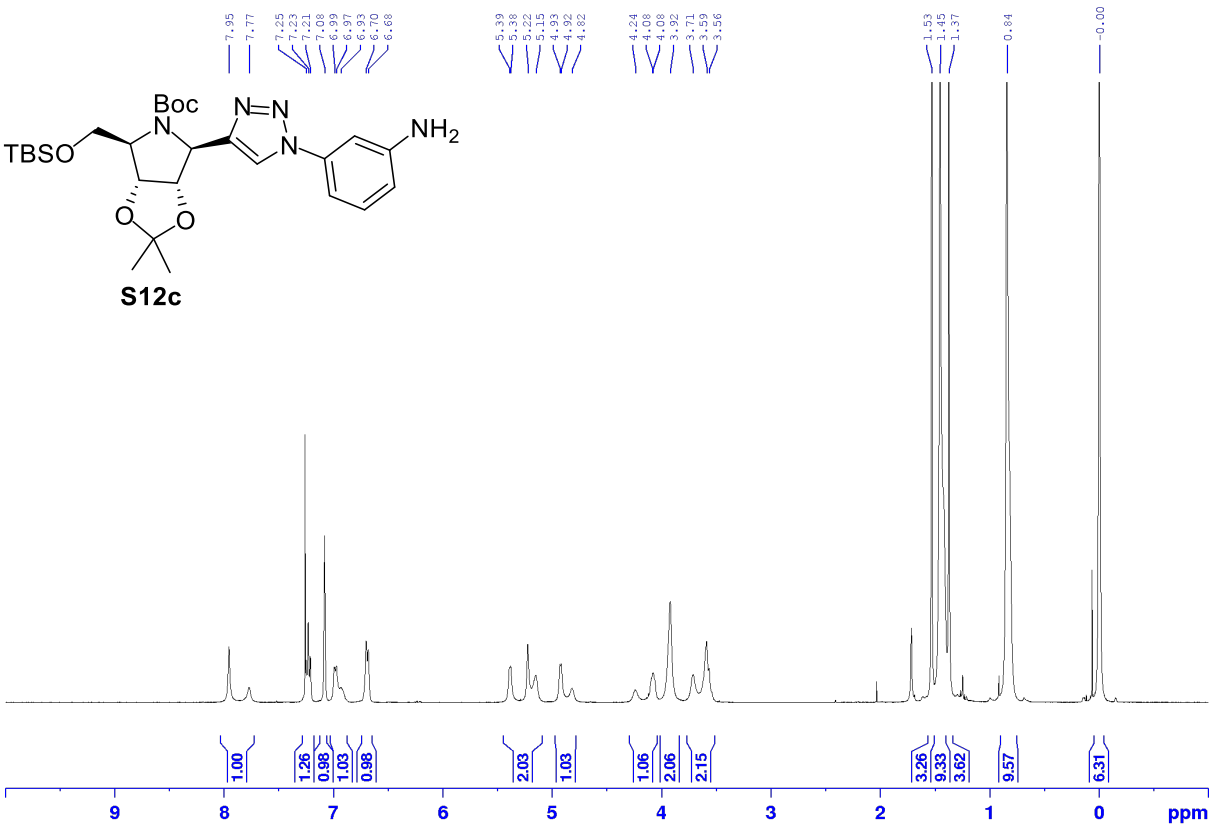
^{1}H NMR (400 MHz, DMSO-d_6, 343 K)



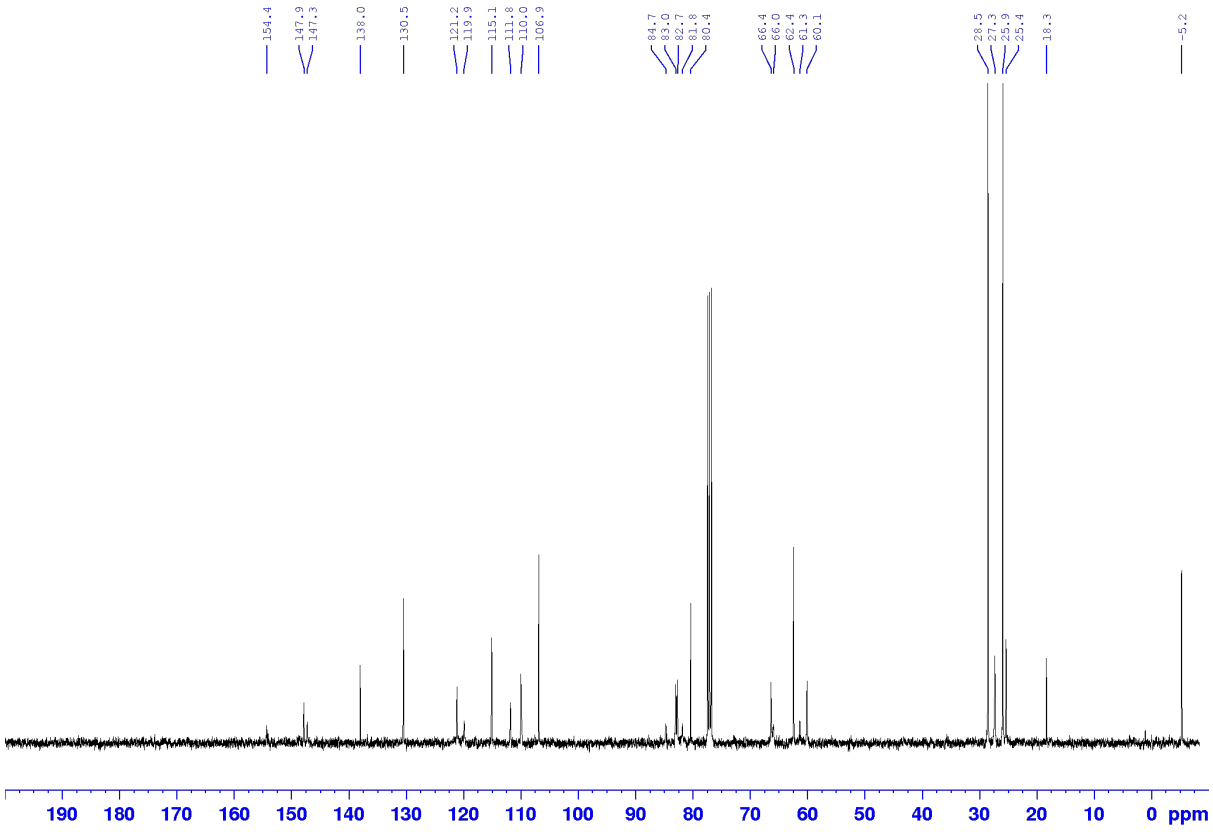
^{13}C NMR (100 MHz, DMSO-d_6, 343 K)



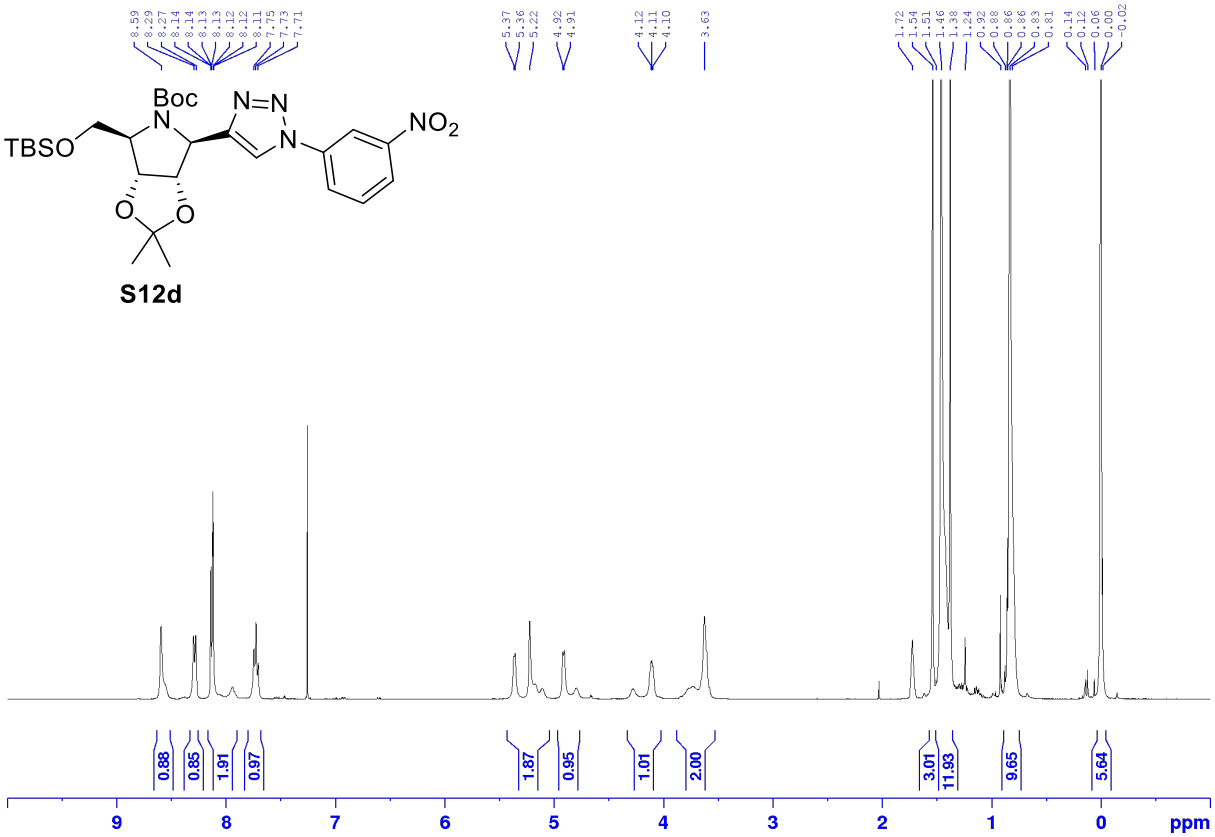
^{1}H NMR (400 MHz, $CDCl_3$)



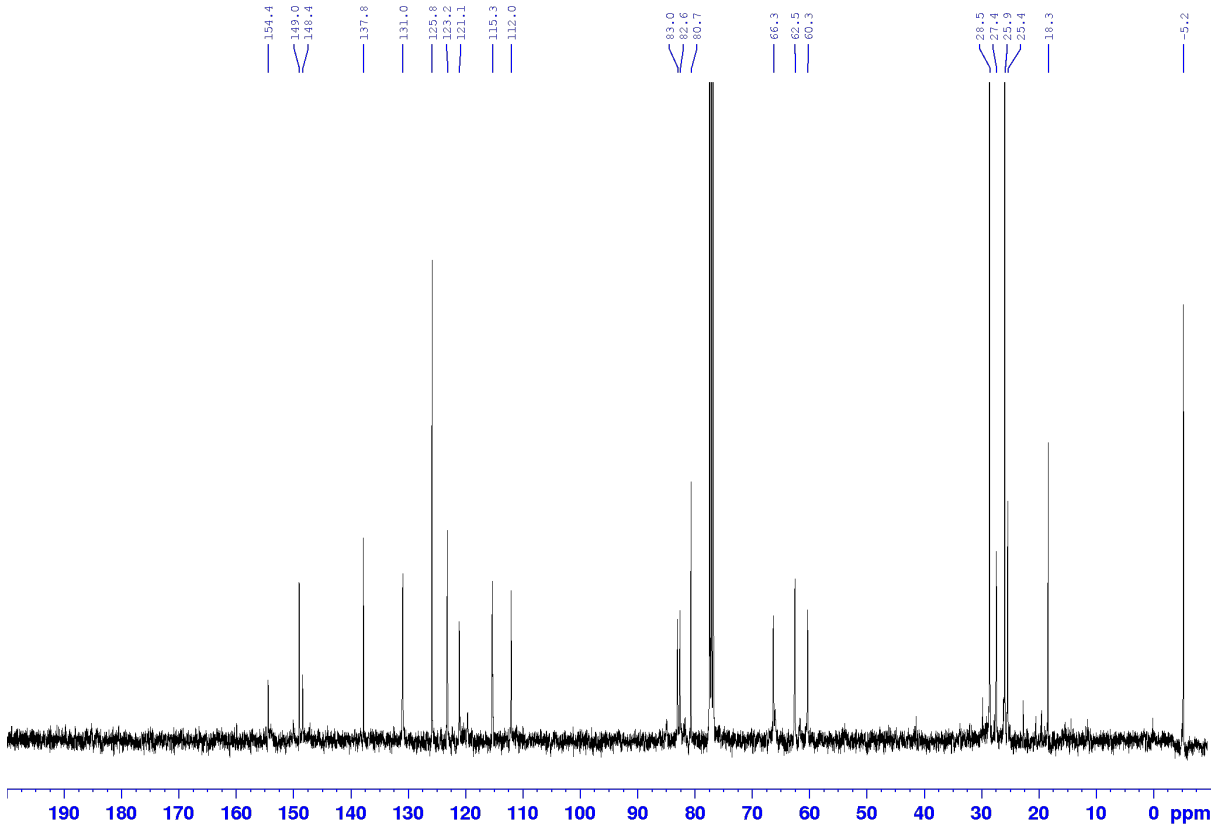
^{13}C NMR (100 MHz, $CDCl_3$)



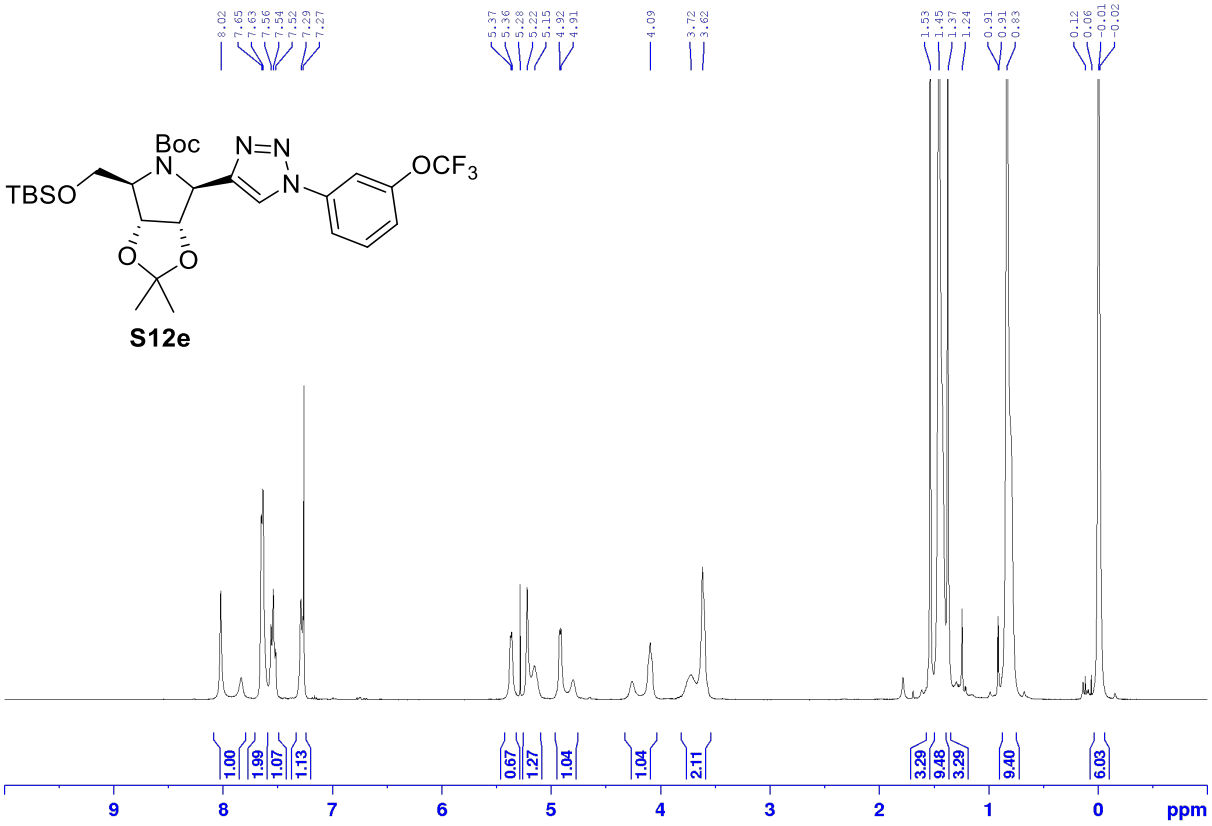
^{1}H NMR (400 MHz, $CDCl_3$)



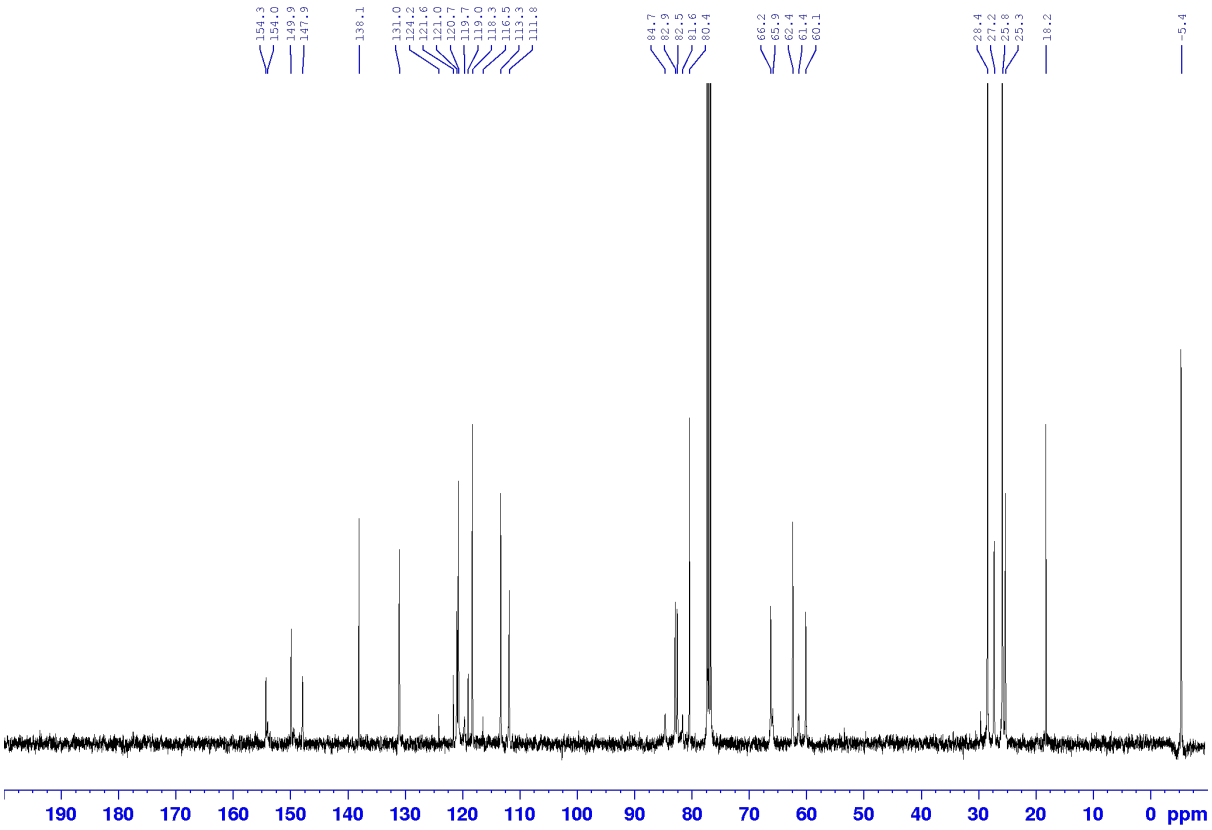
^{13}C NMR (100 MHz, $CDCl_3$)



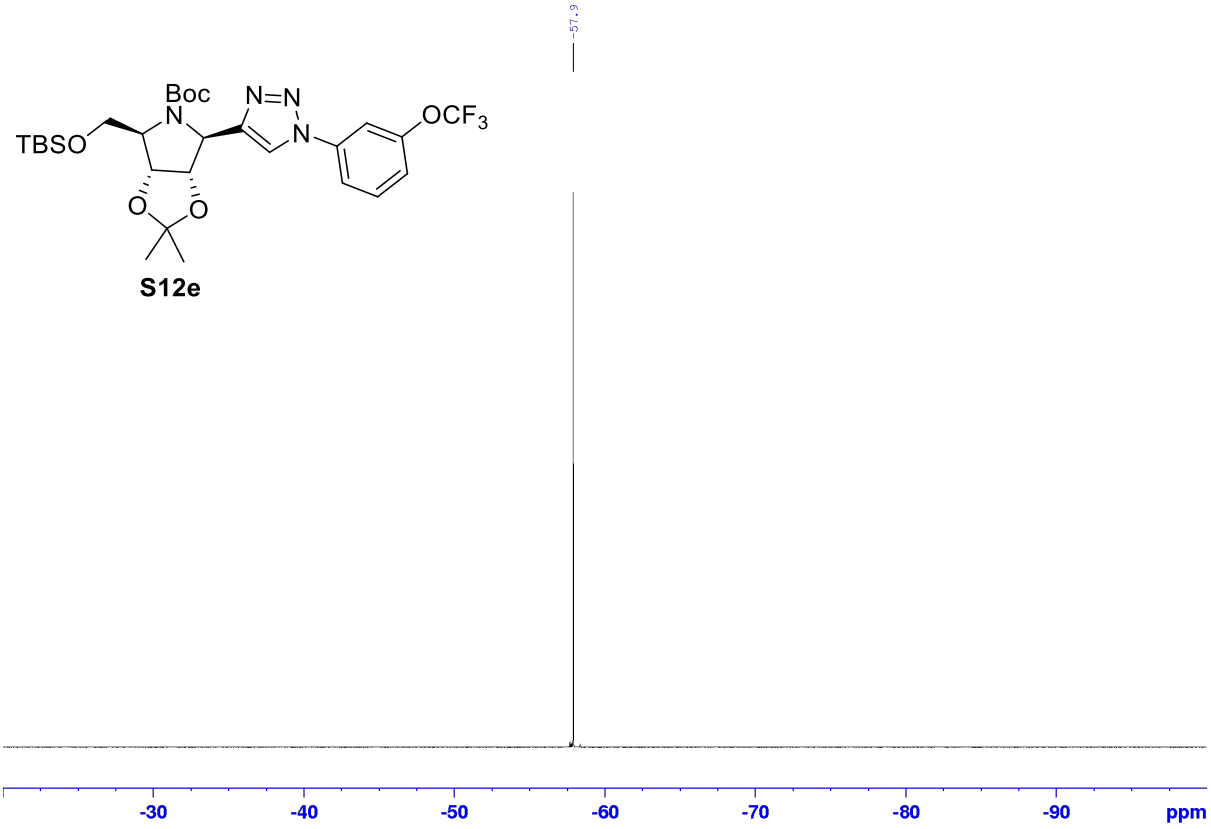
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

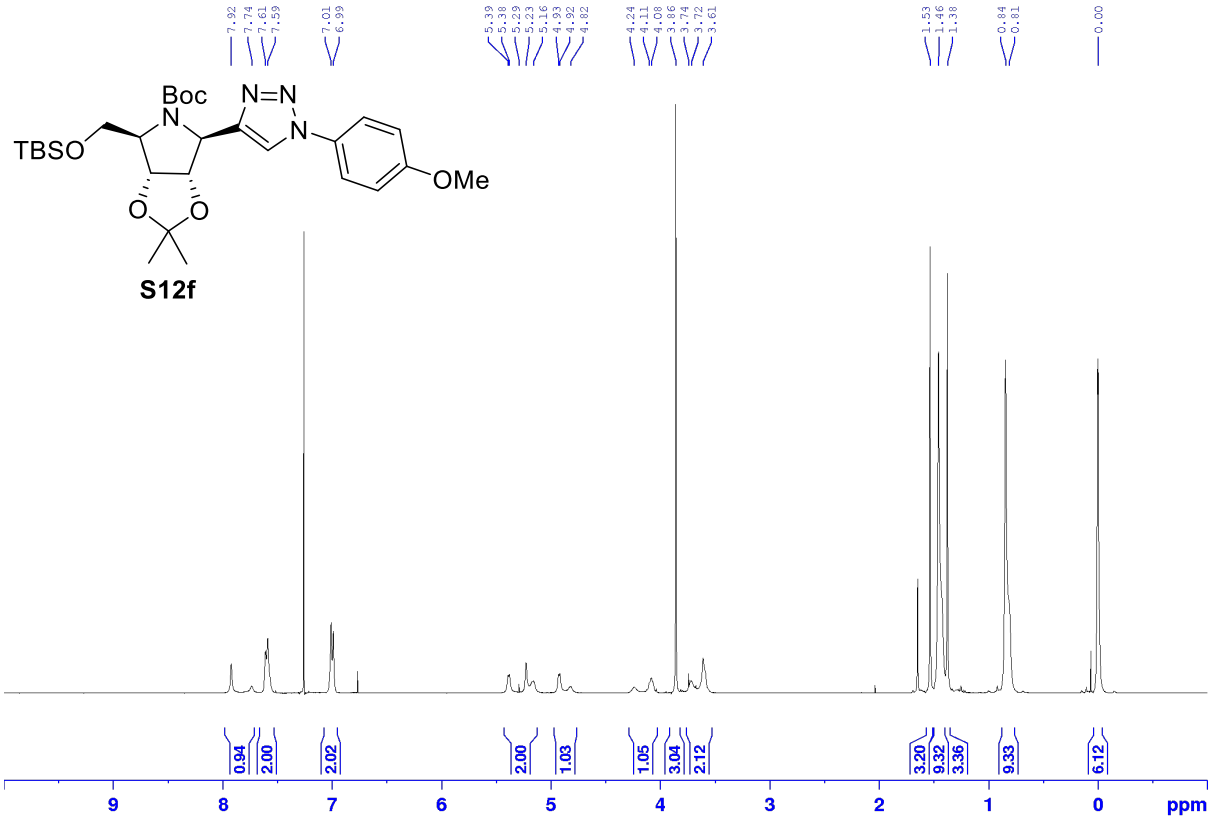


^{19}F NMR (376 MHz, $CDCl_3$)

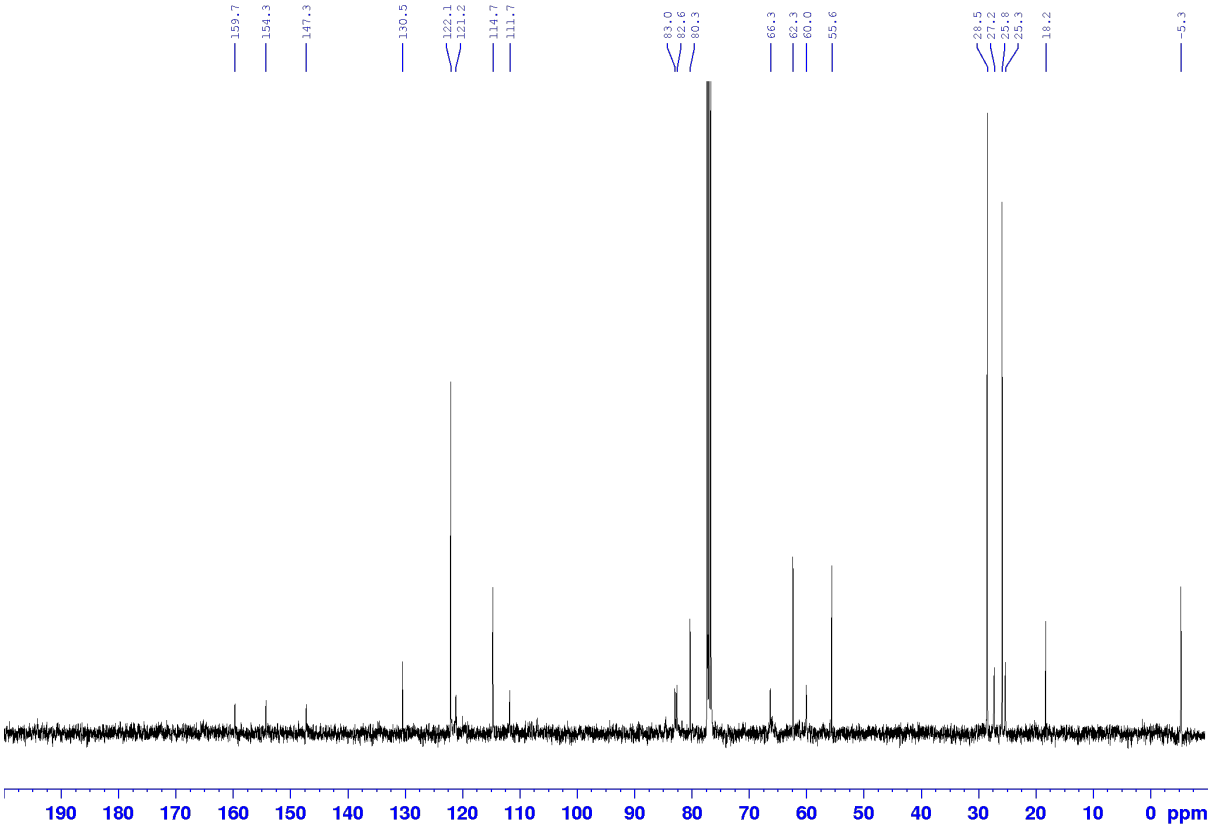


S12e

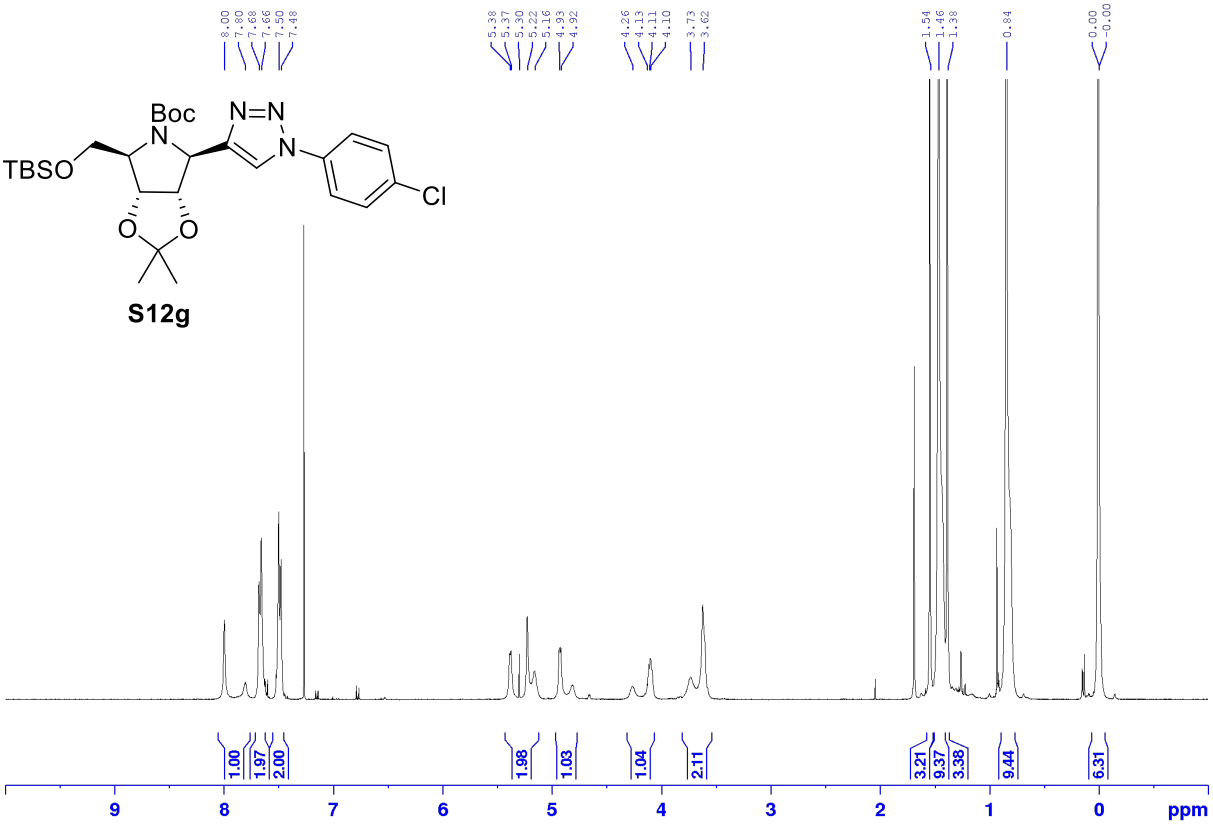
^{1}H NMR (400 MHz, $CDCl_3$)



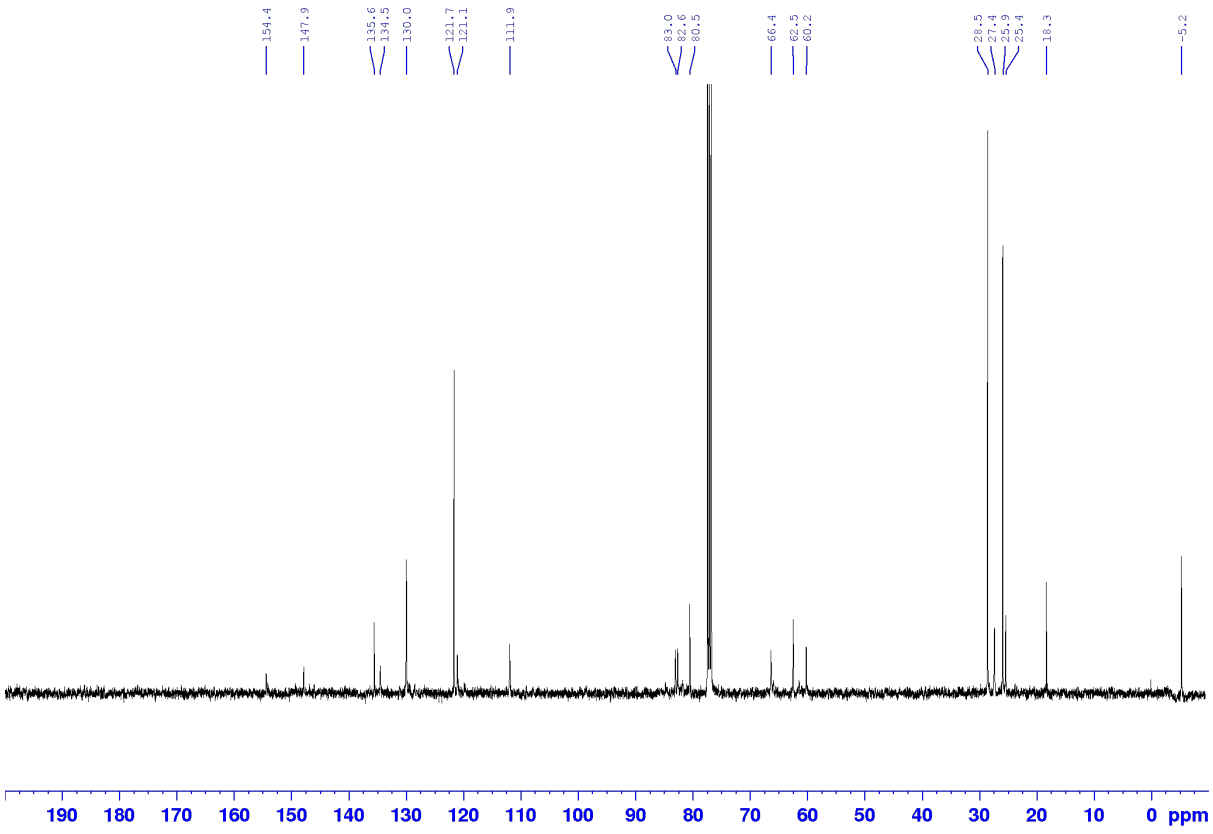
^{13}C NMR (100 MHz, $CDCl_3$)



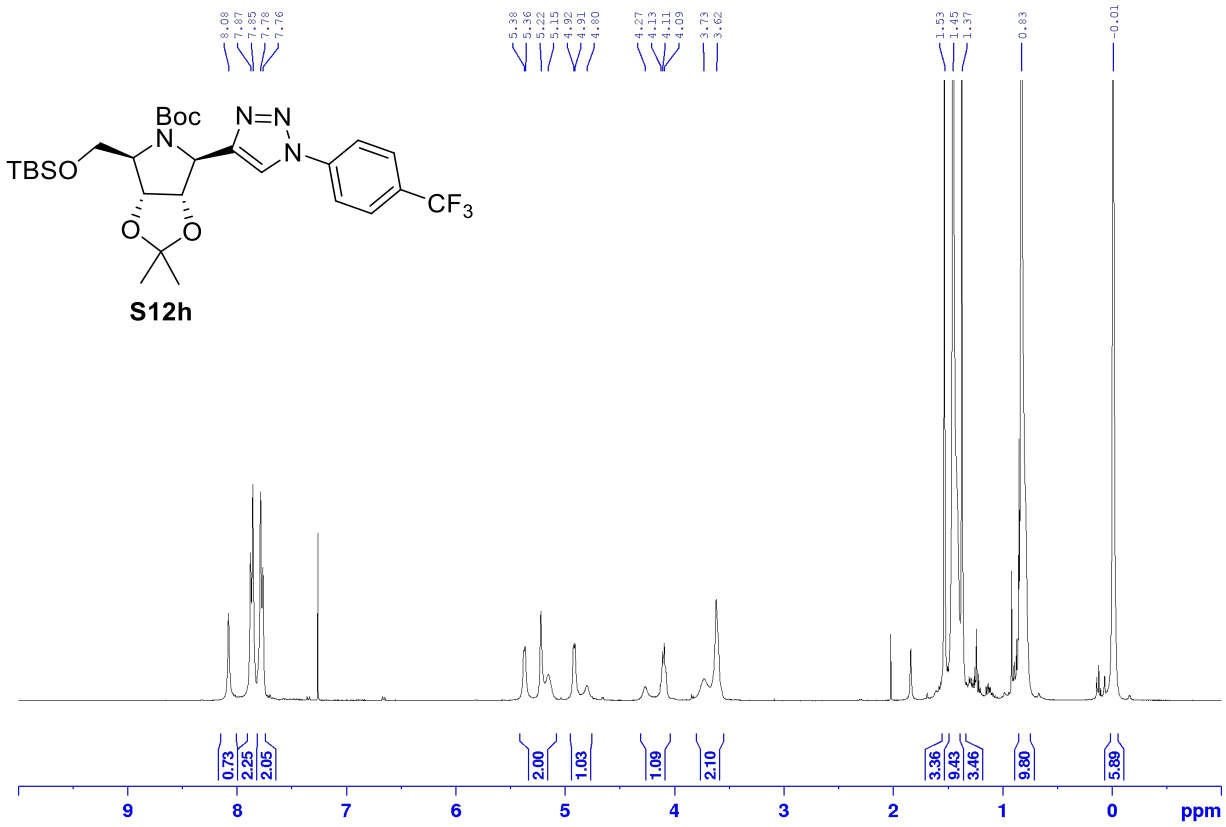
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

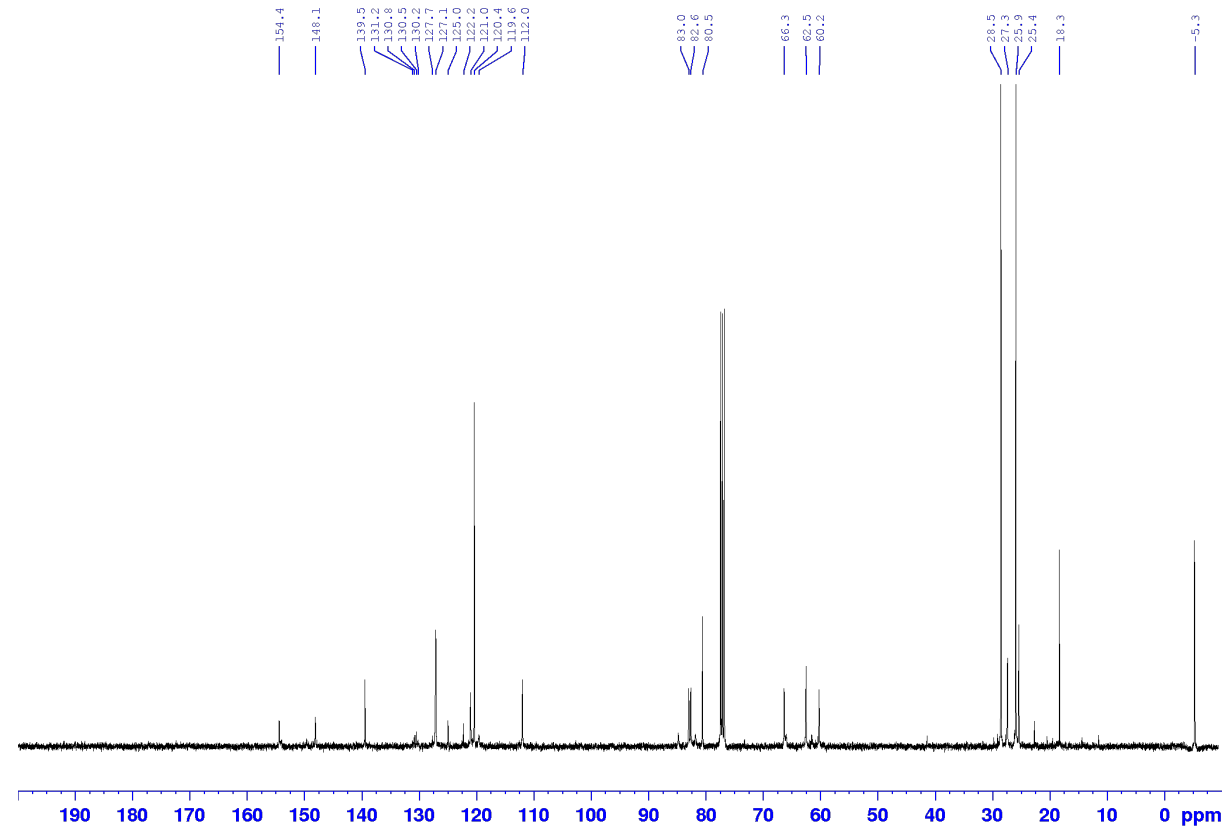


^{1}H NMR (400 MHz, $CDCl_3$)



S12h

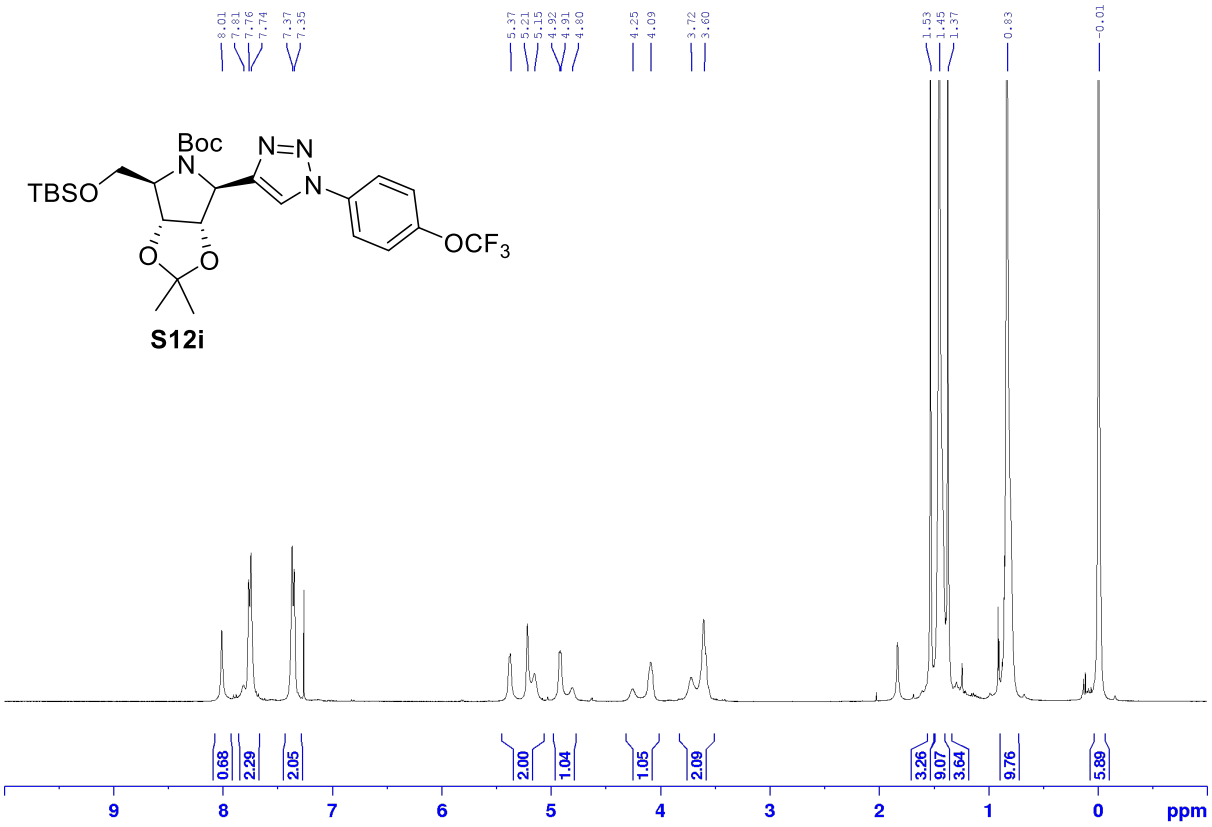
^{13}C NMR (100 MHz, $CDCl_3$)



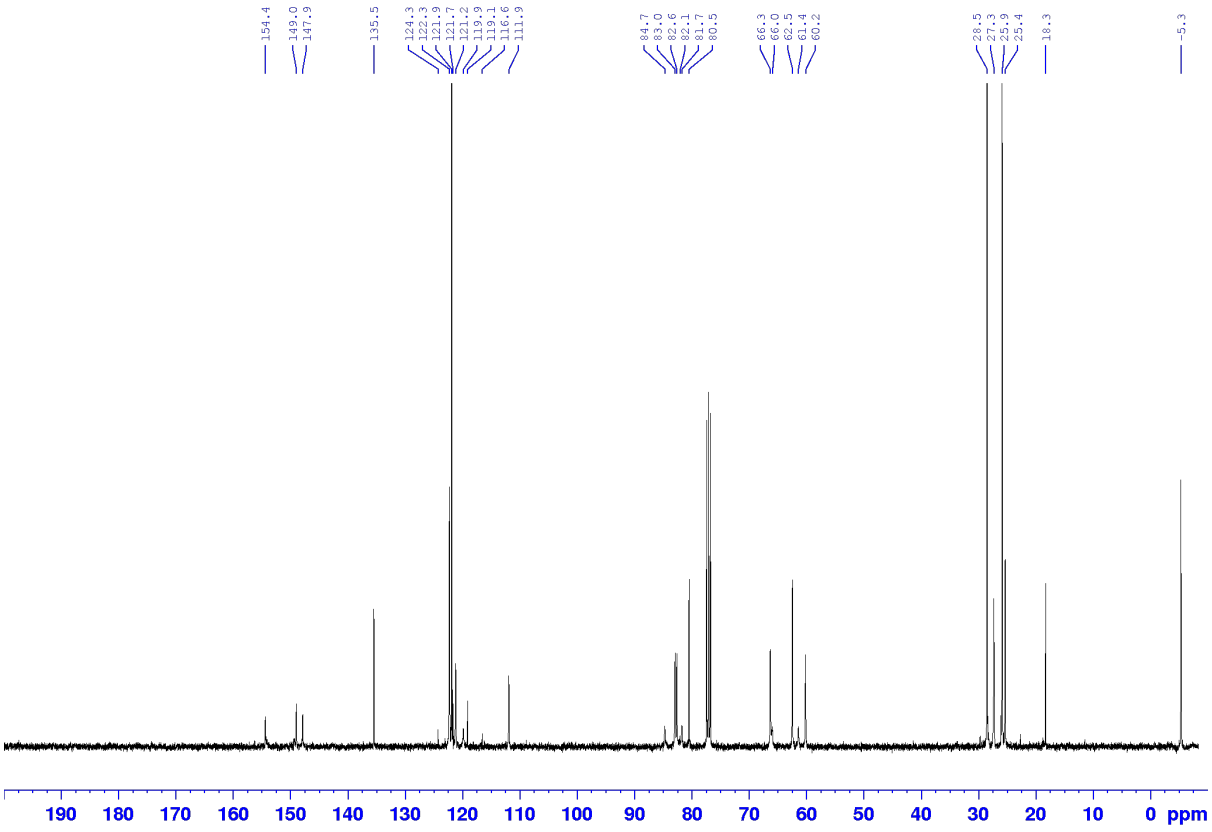
^{19}F NMR (376 MHz, $CDCl_3$)

S12h

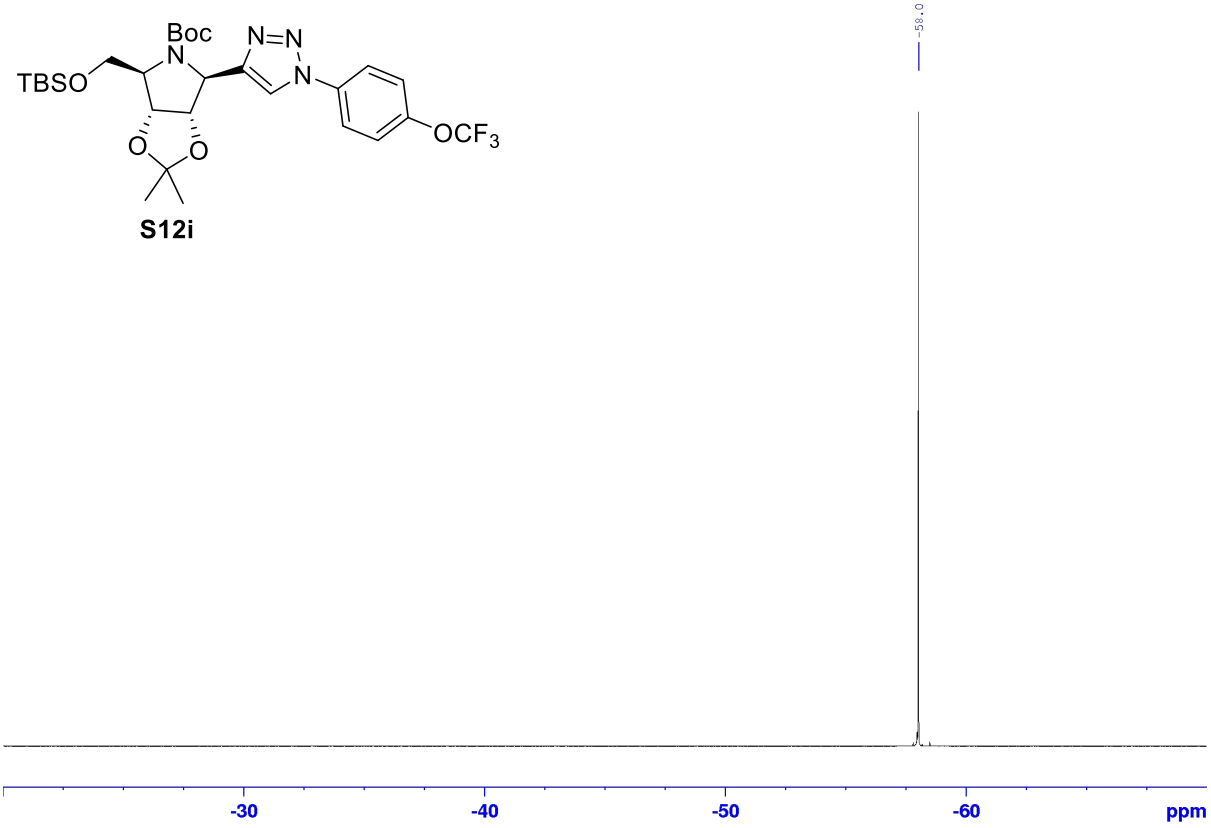
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

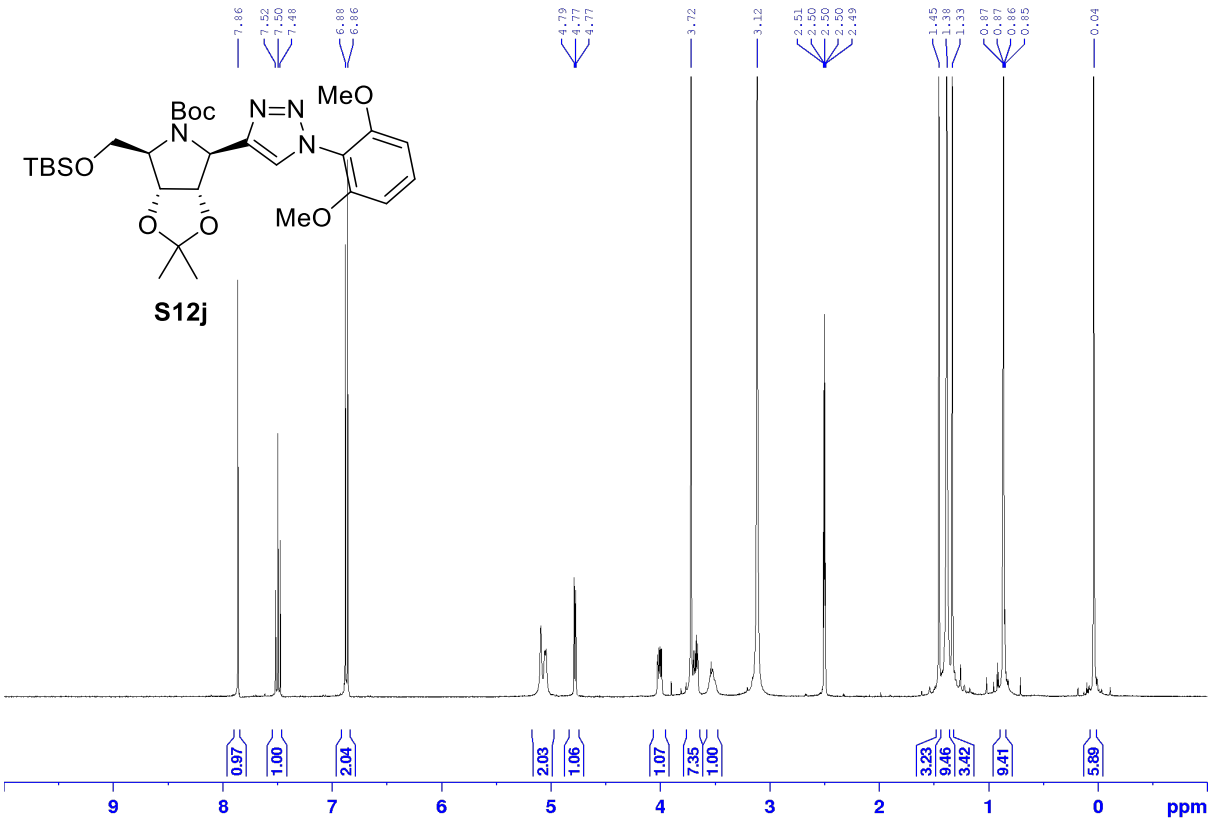


^{19}F NMR (376 MHz, $CDCl_3$)

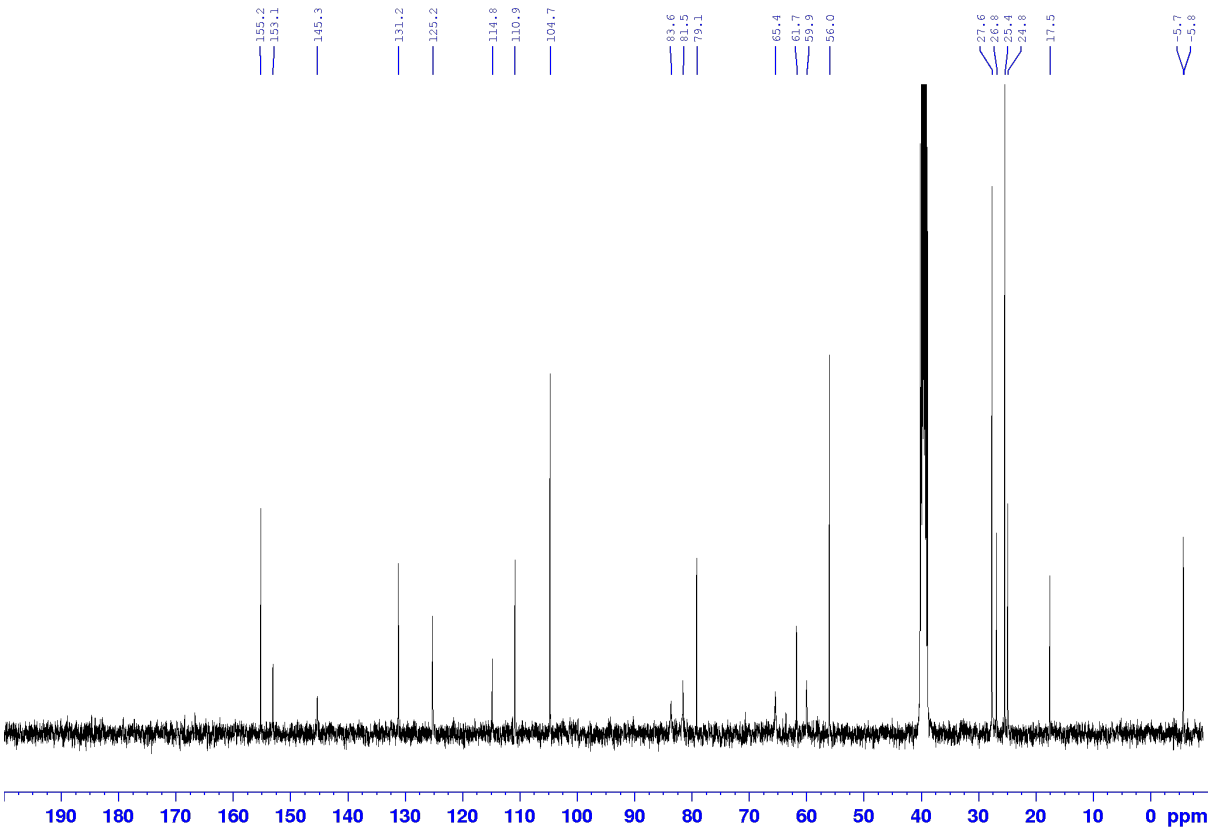


S12i

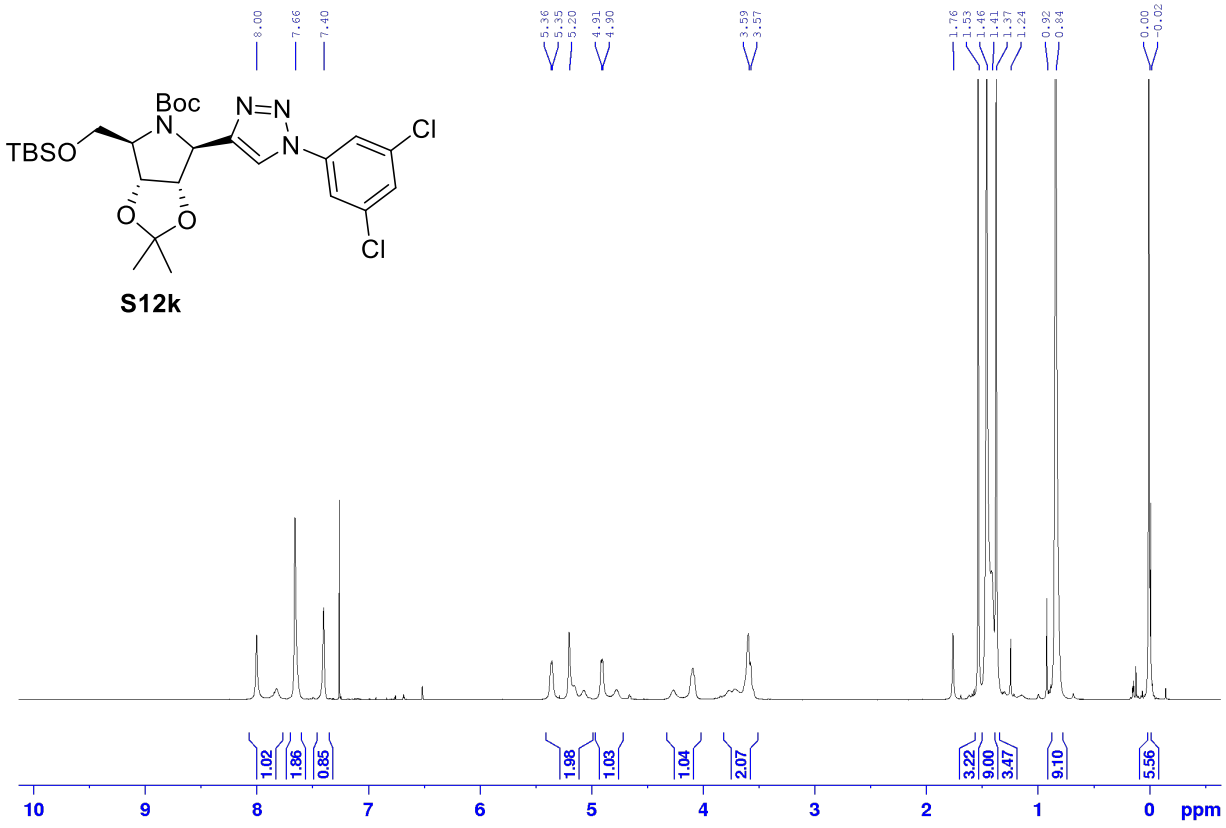
^{1}H NMR (400 MHz, DMSO-d_6, 343 K)



^{13}C NMR (100 MHz, DMSO-d_6, 343 K)

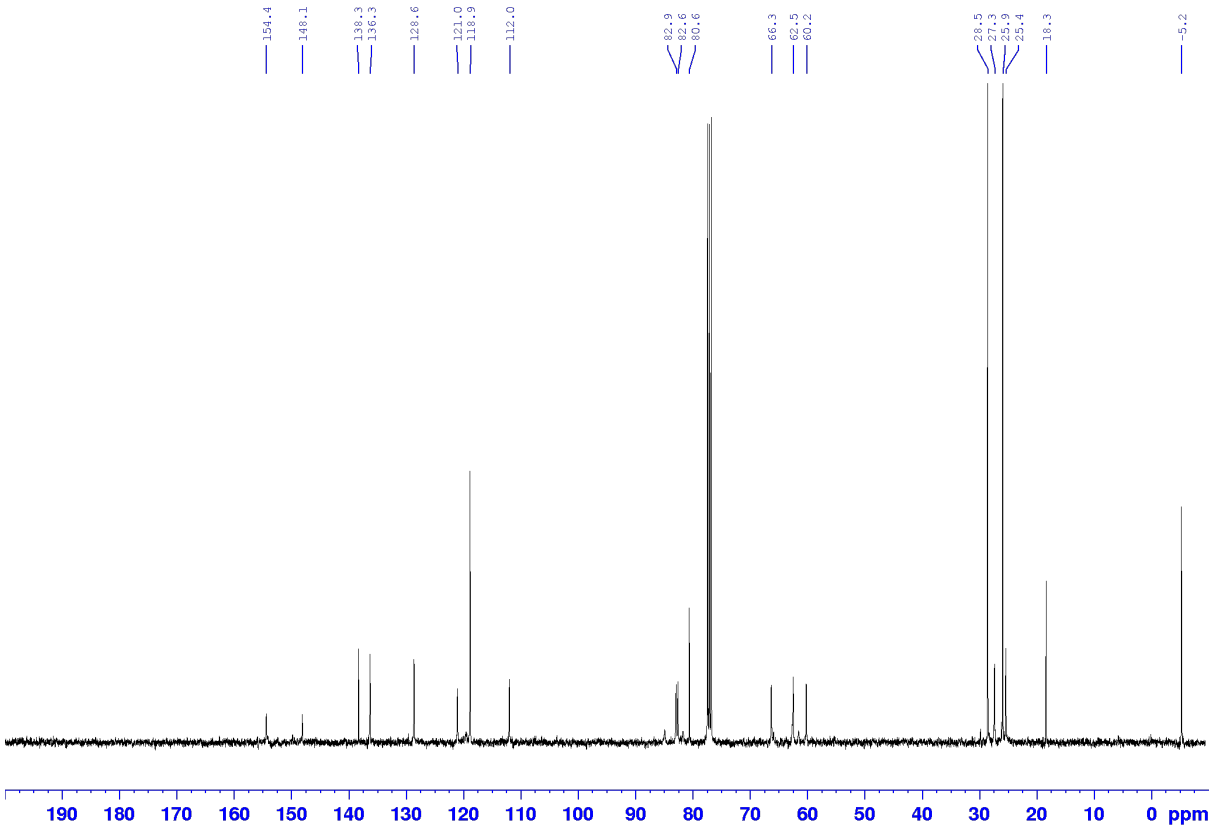


^{1}H NMR (400 MHz, $CDCl_3$)

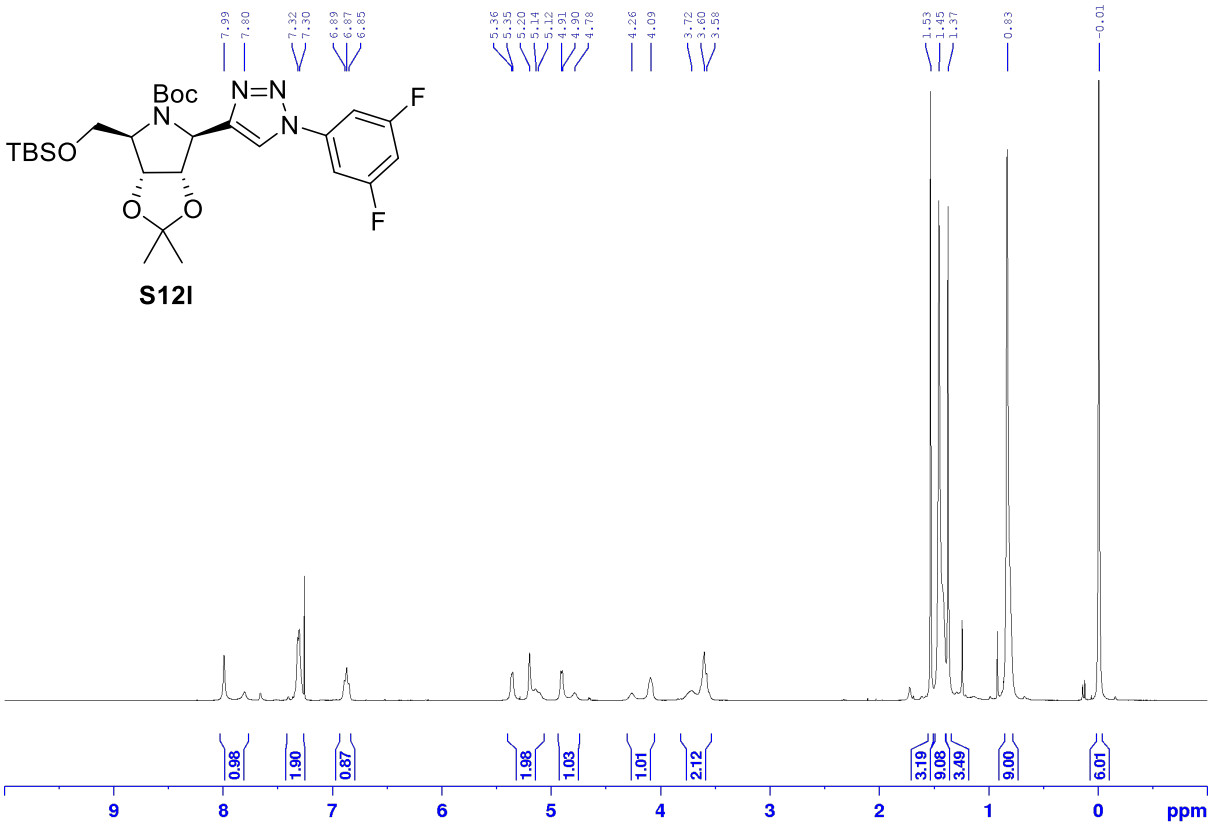


S12k

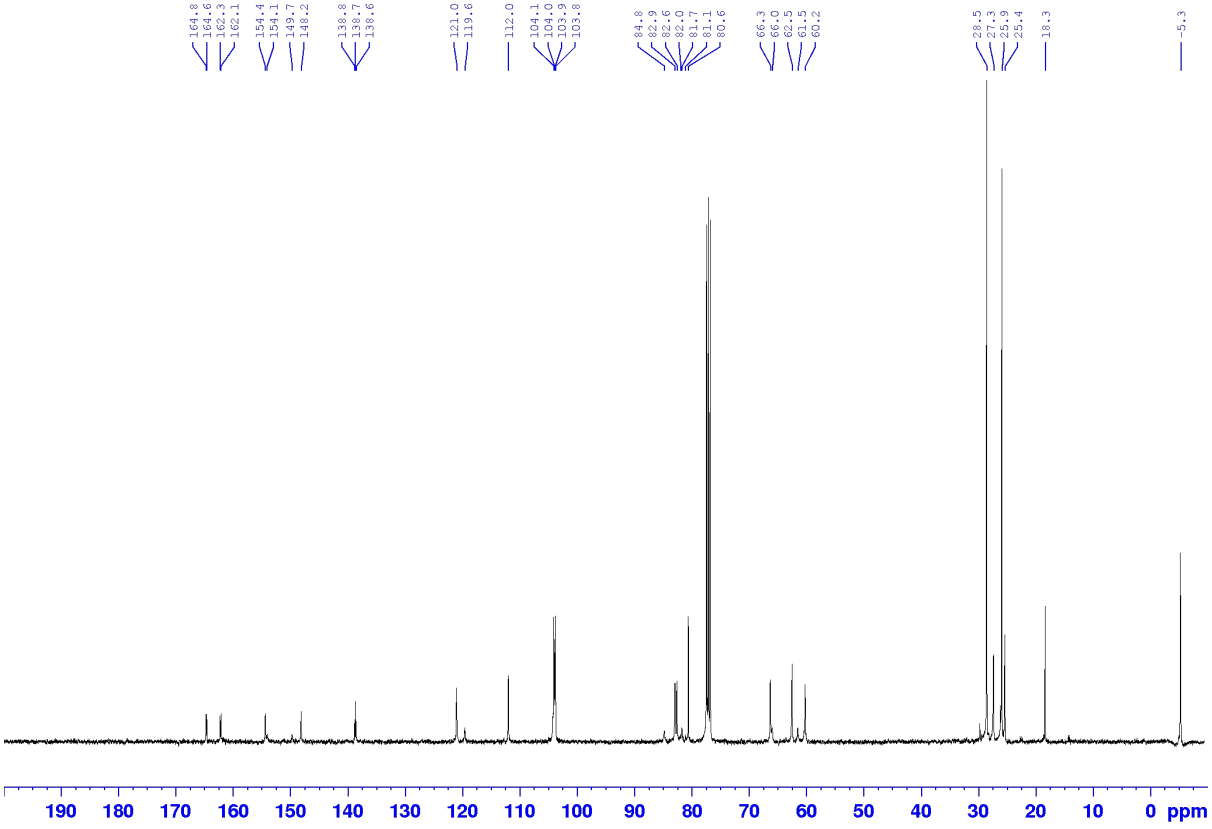
^{13}C NMR (100 MHz, $CDCl_3$)



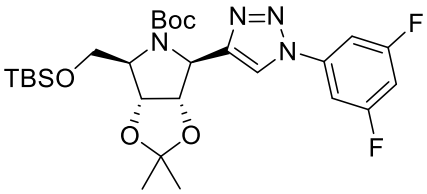
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

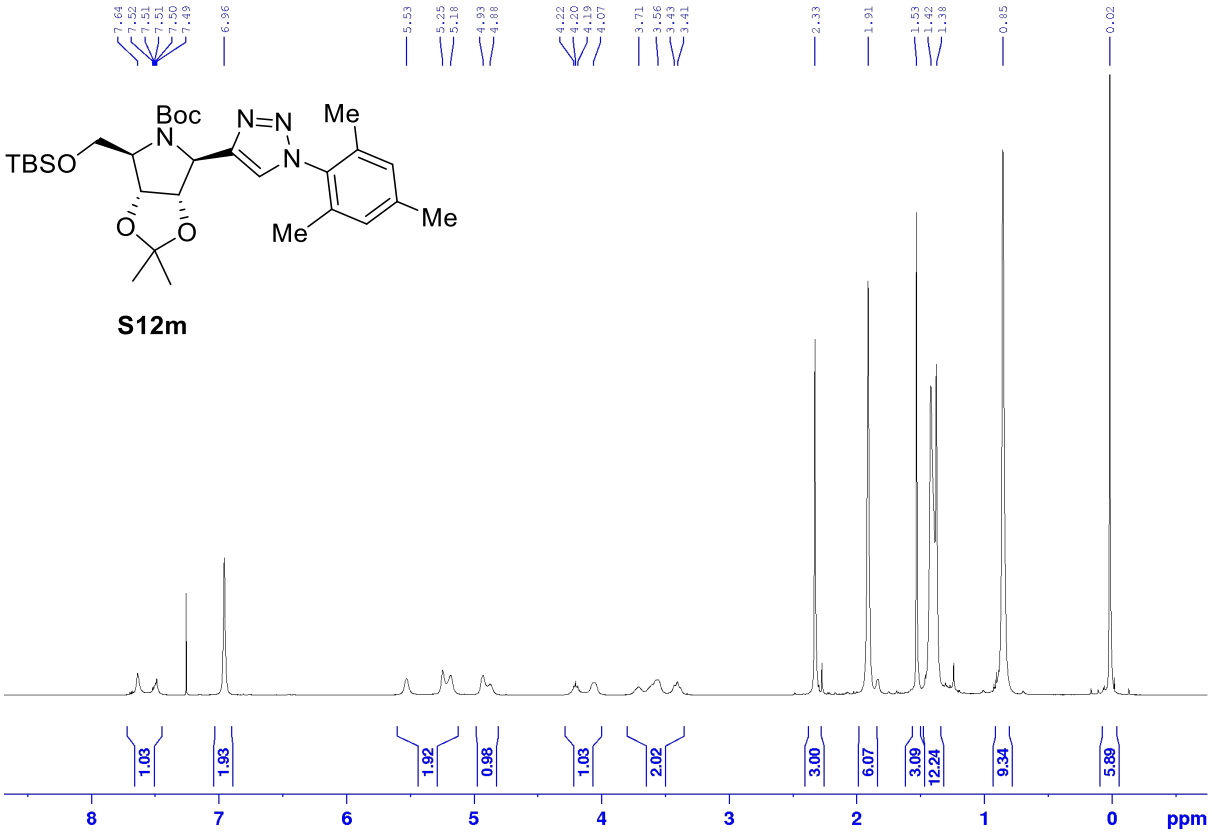


^{19}F NMR (376 MHz, $CDCl_3$)



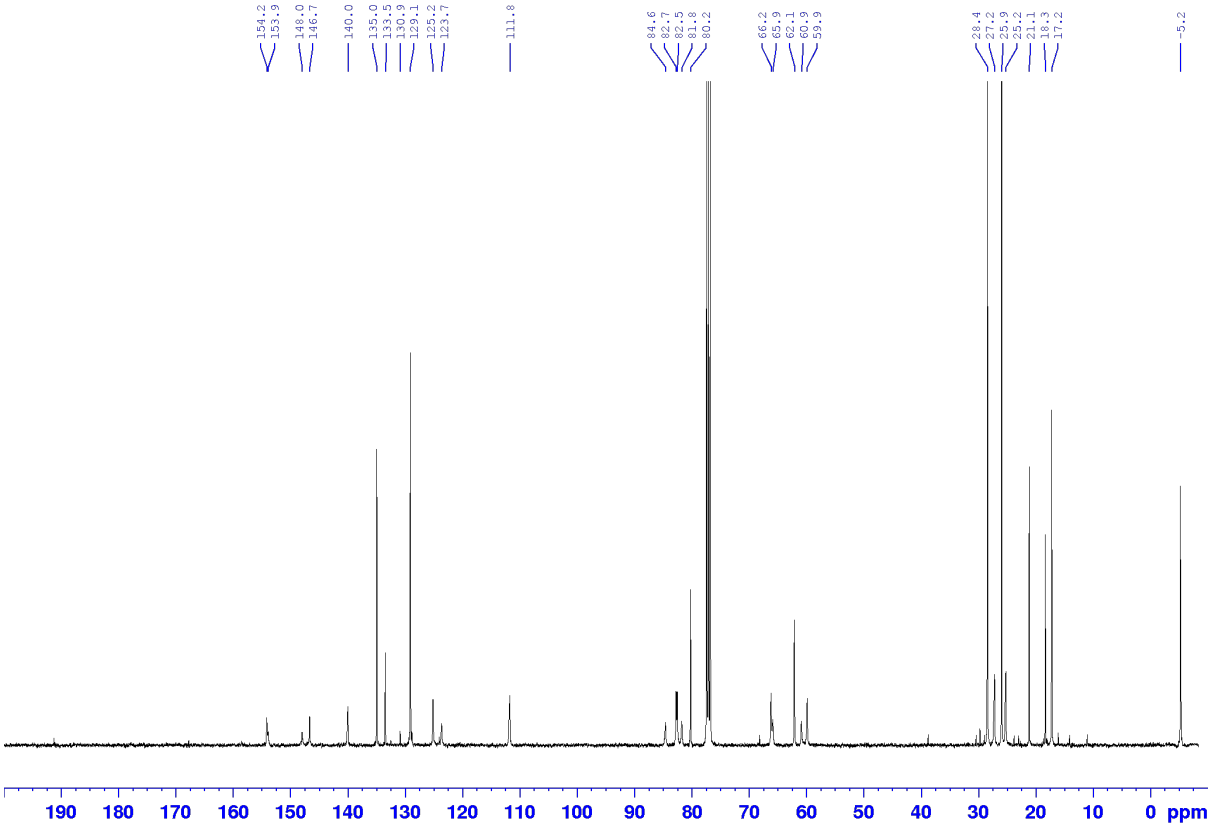
S12l

^{1}H NMR (400 MHz, $CDCl_3$)

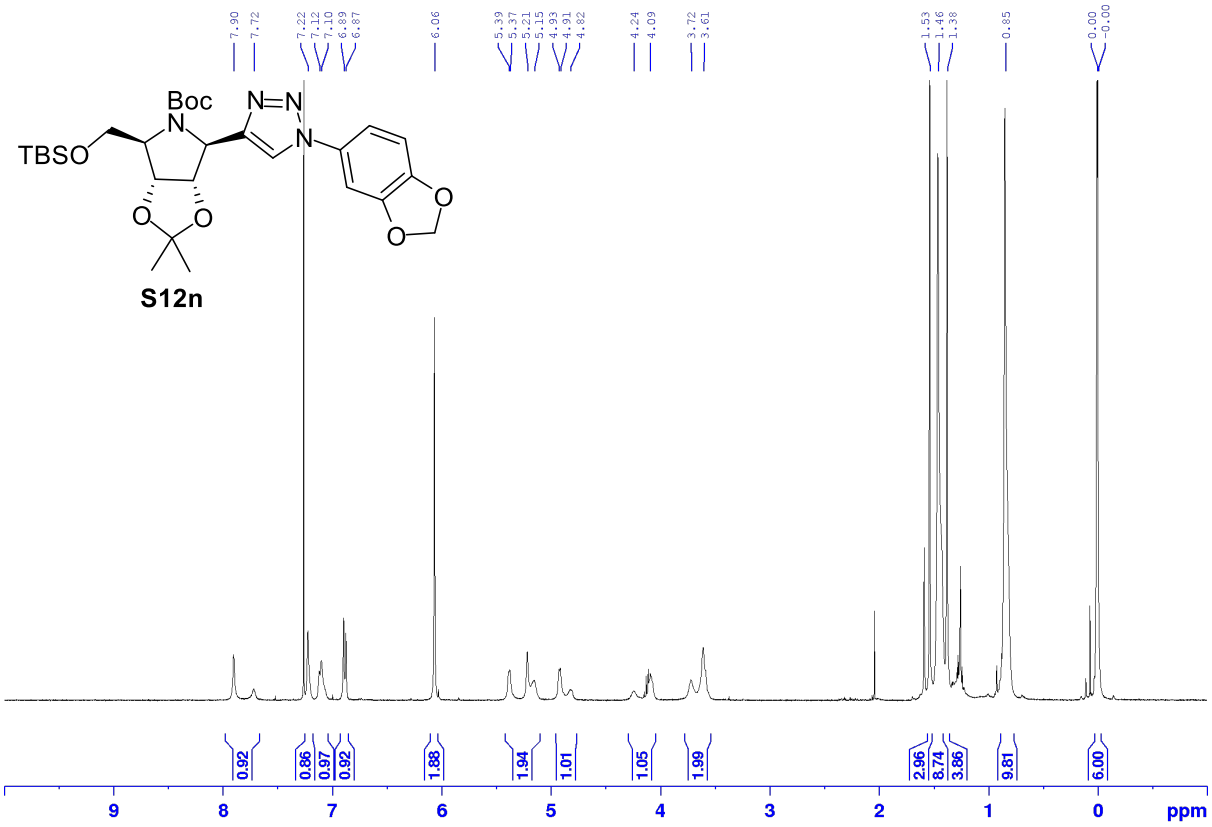


S12m

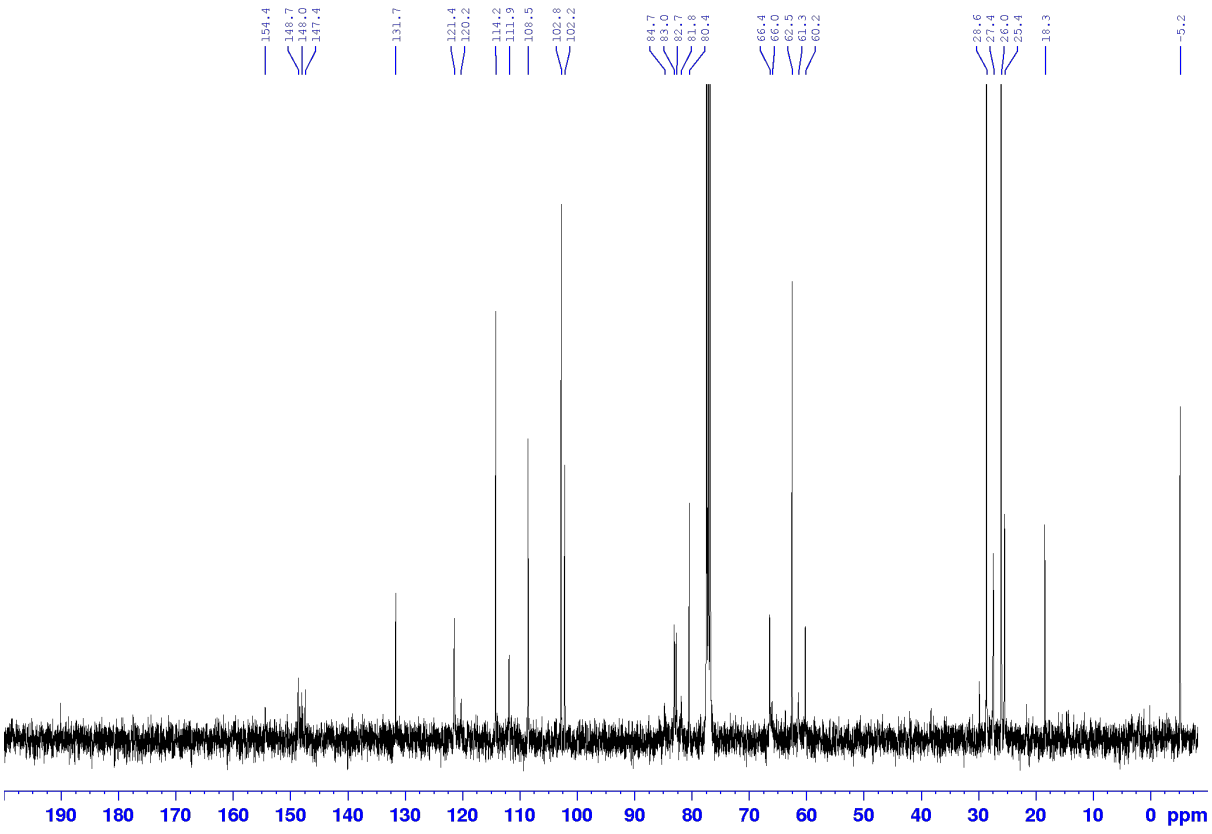
^{13}C NMR (100 MHz, $CDCl_3$)



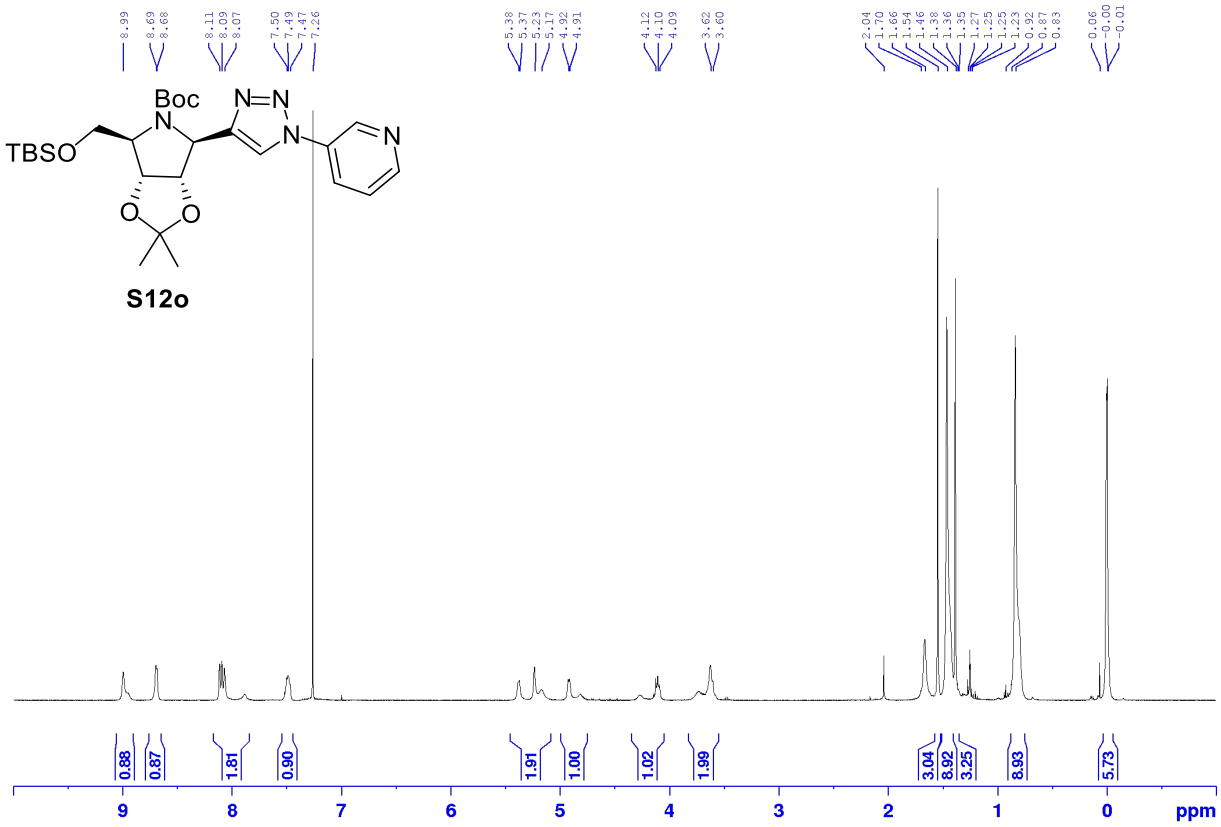
^{1}H NMR (400 MHz, $CDCl_3$)



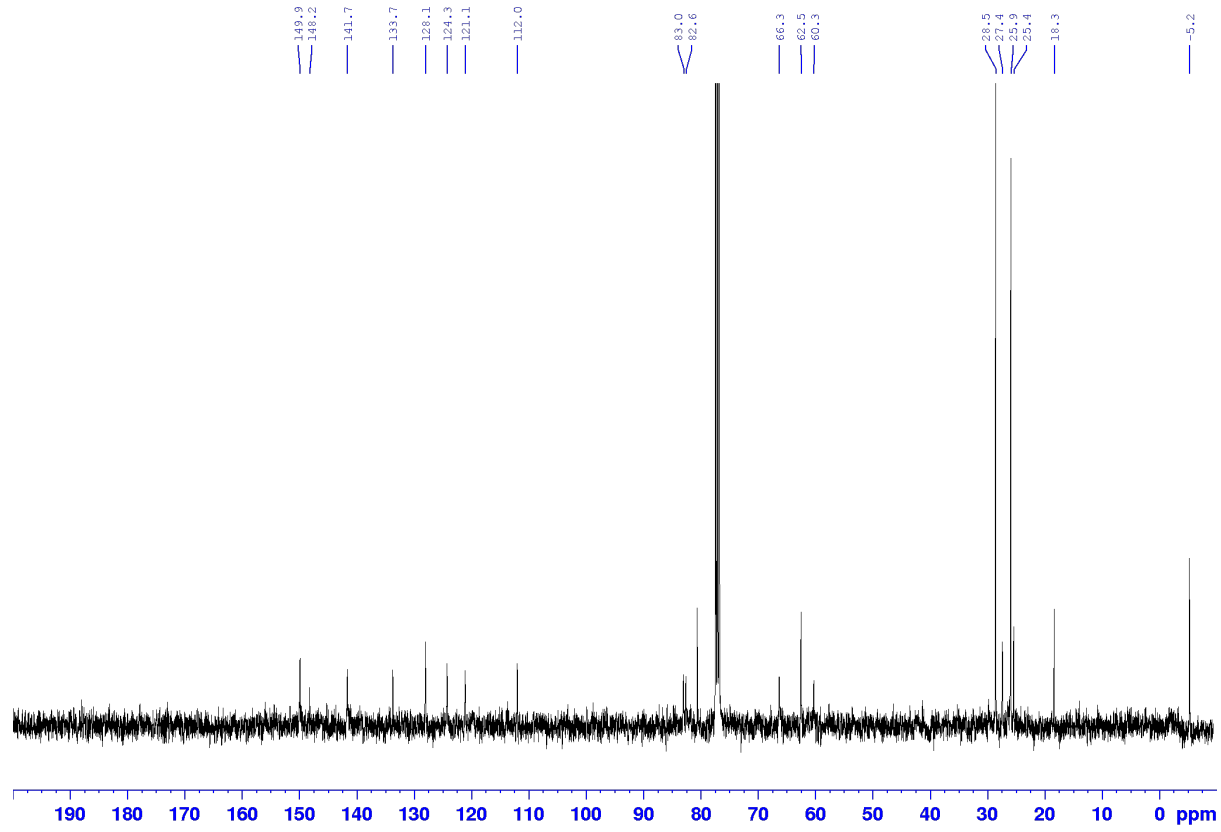
^{13}C NMR (100 MHz, $CDCl_3$)



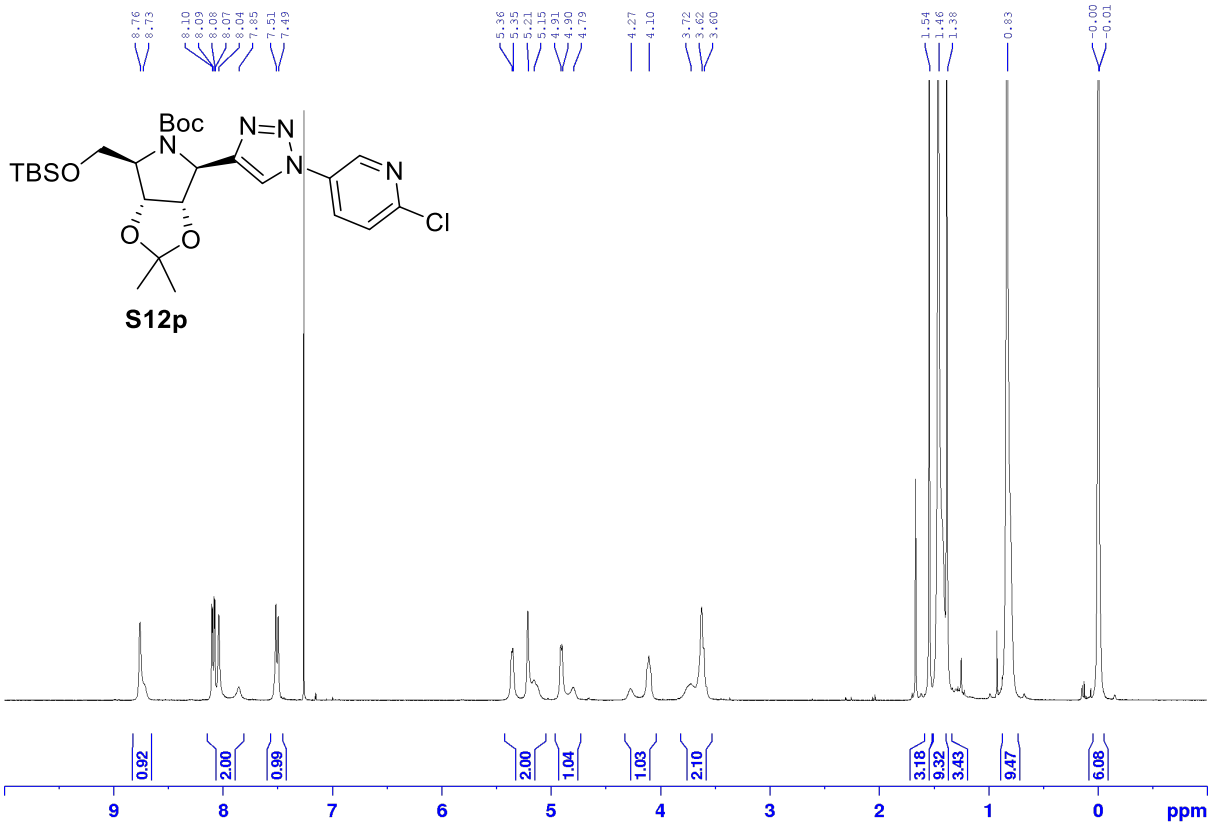
^{1}H NMR (400 MHz, $CDCl_3$)



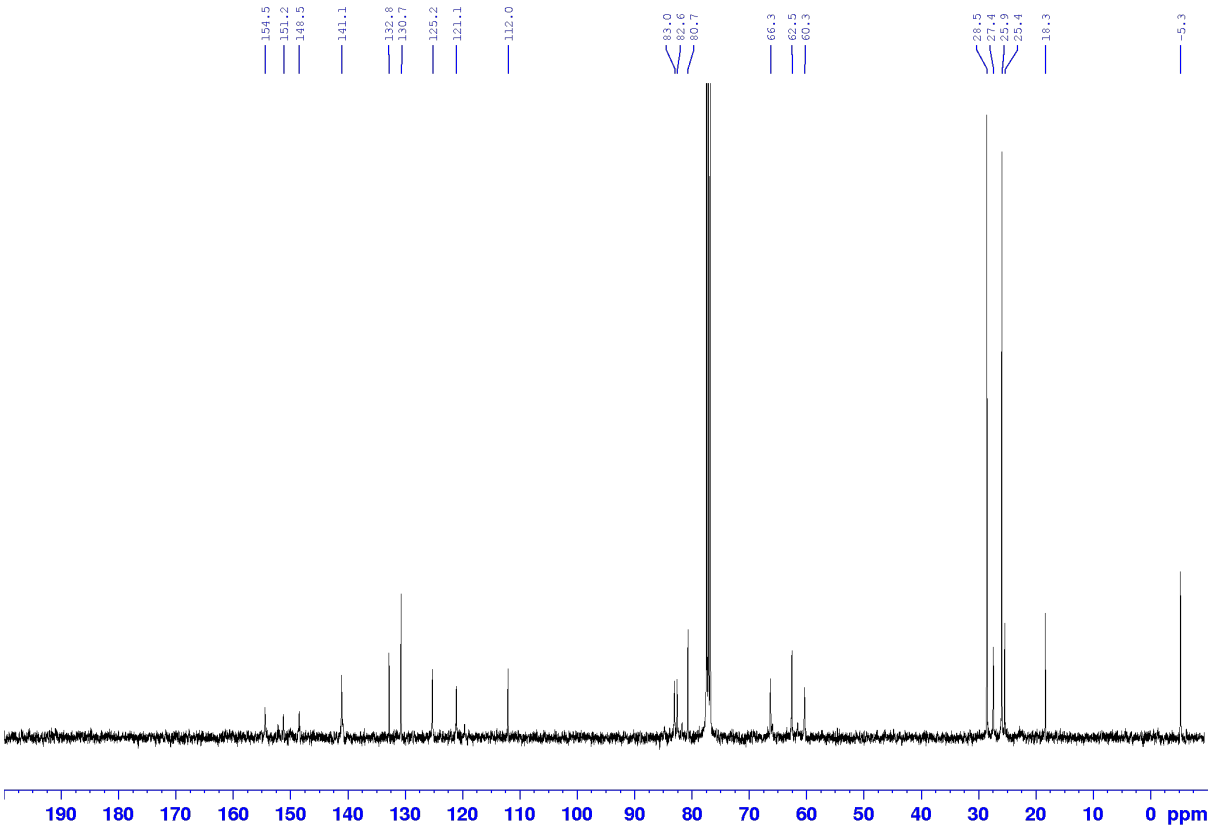
^{13}C NMR (100 MHz, $CDCl_3$)



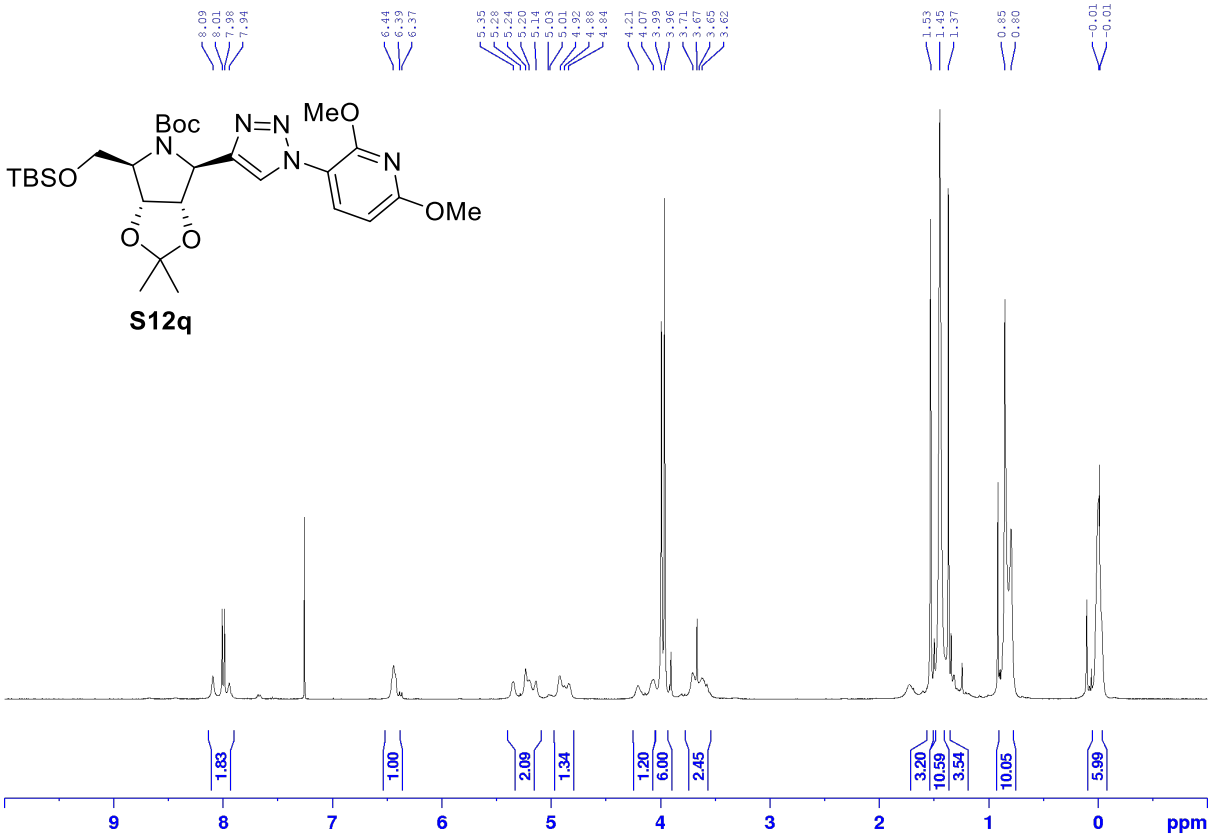
^{1}H NMR (400 MHz, $CDCl_3$)



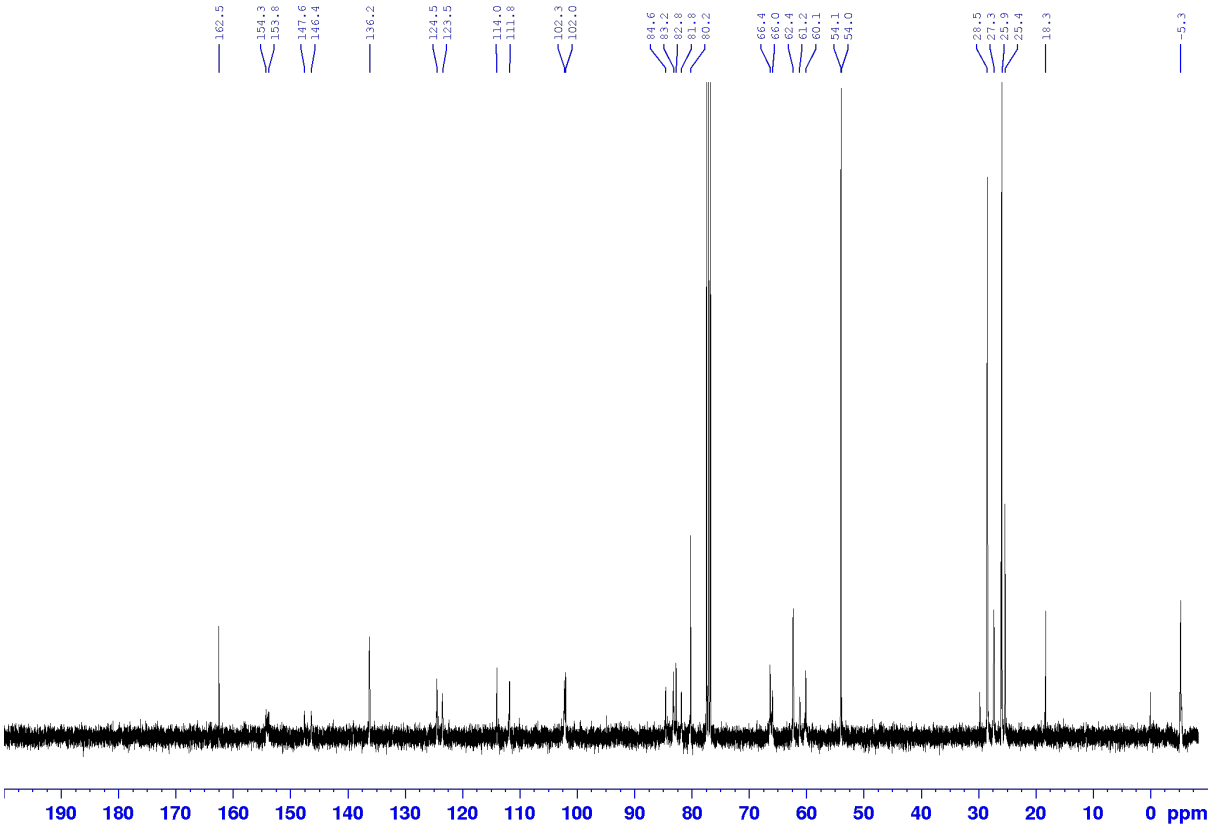
^{13}C NMR (100 MHz, $CDCl_3$)



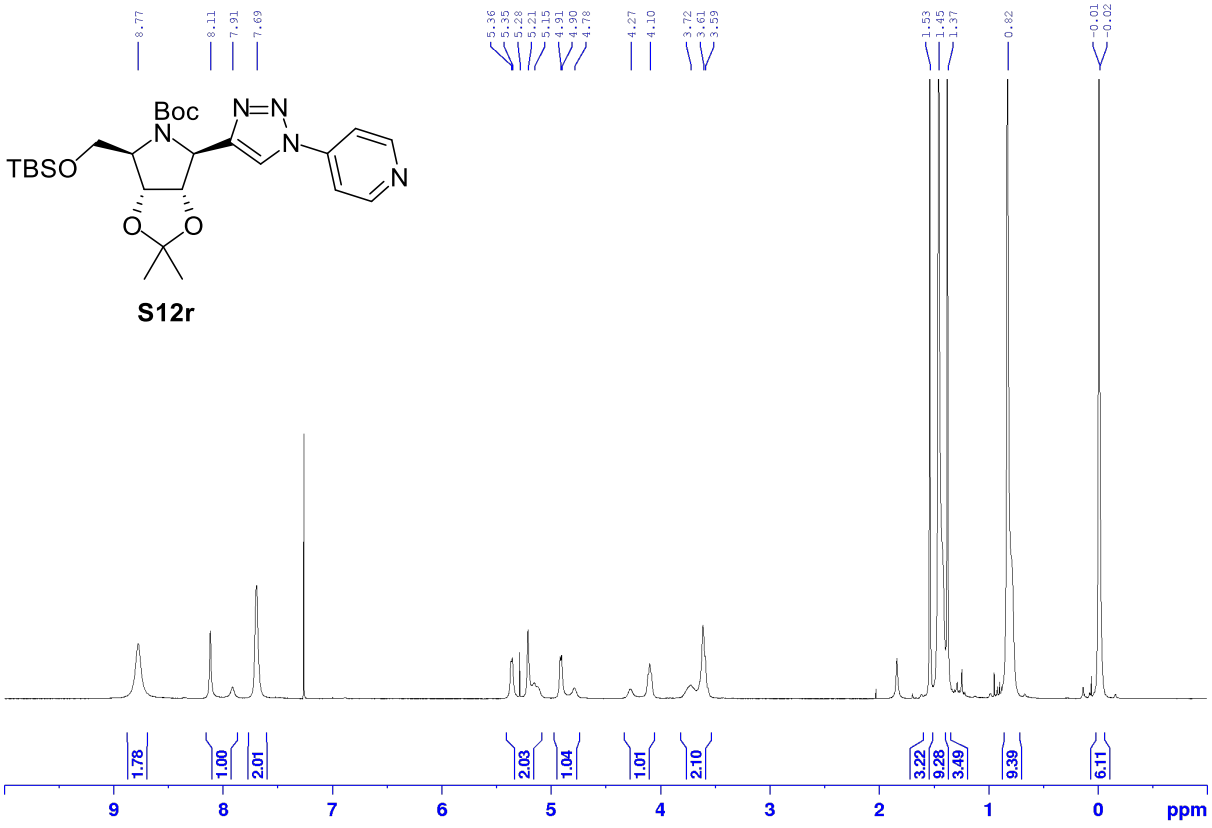
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

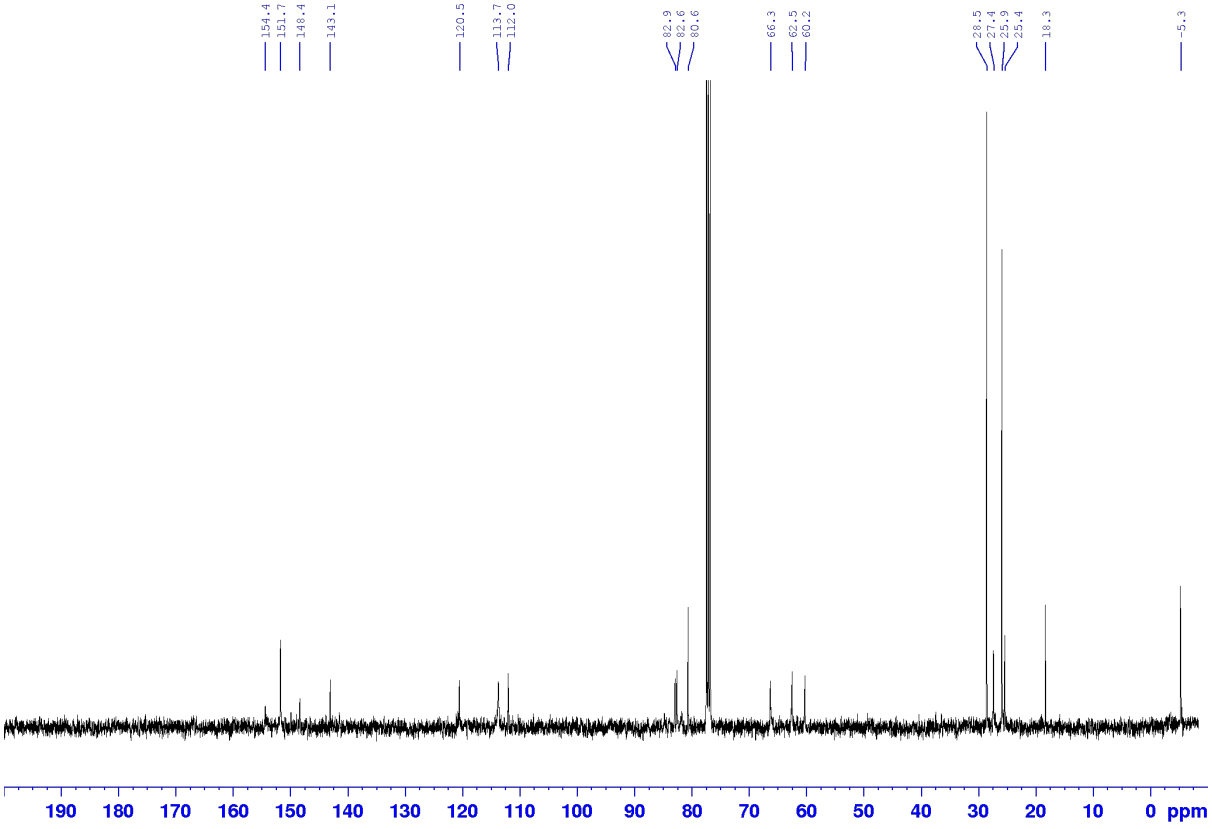


^{1}H NMR (400 MHz, $CDCl_3$)

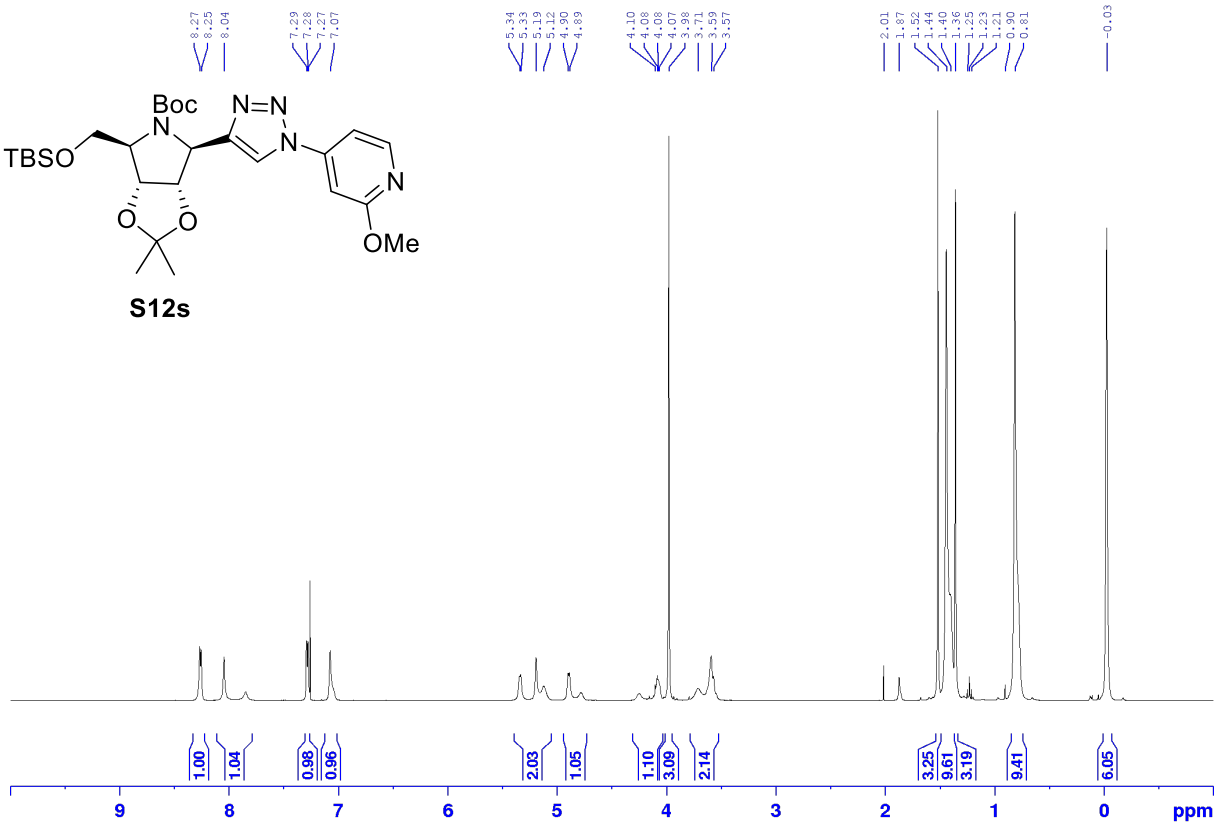


S12r

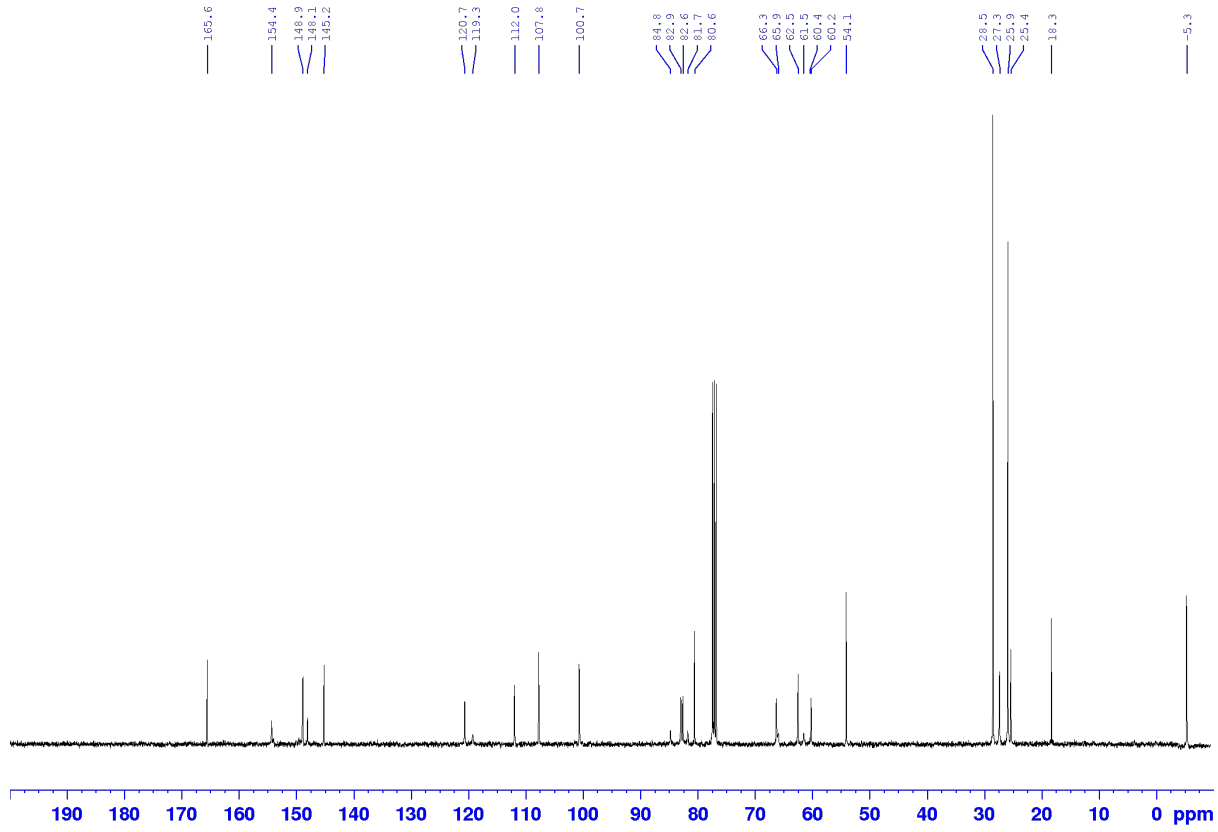
^{13}C NMR (100 MHz, $CDCl_3$)



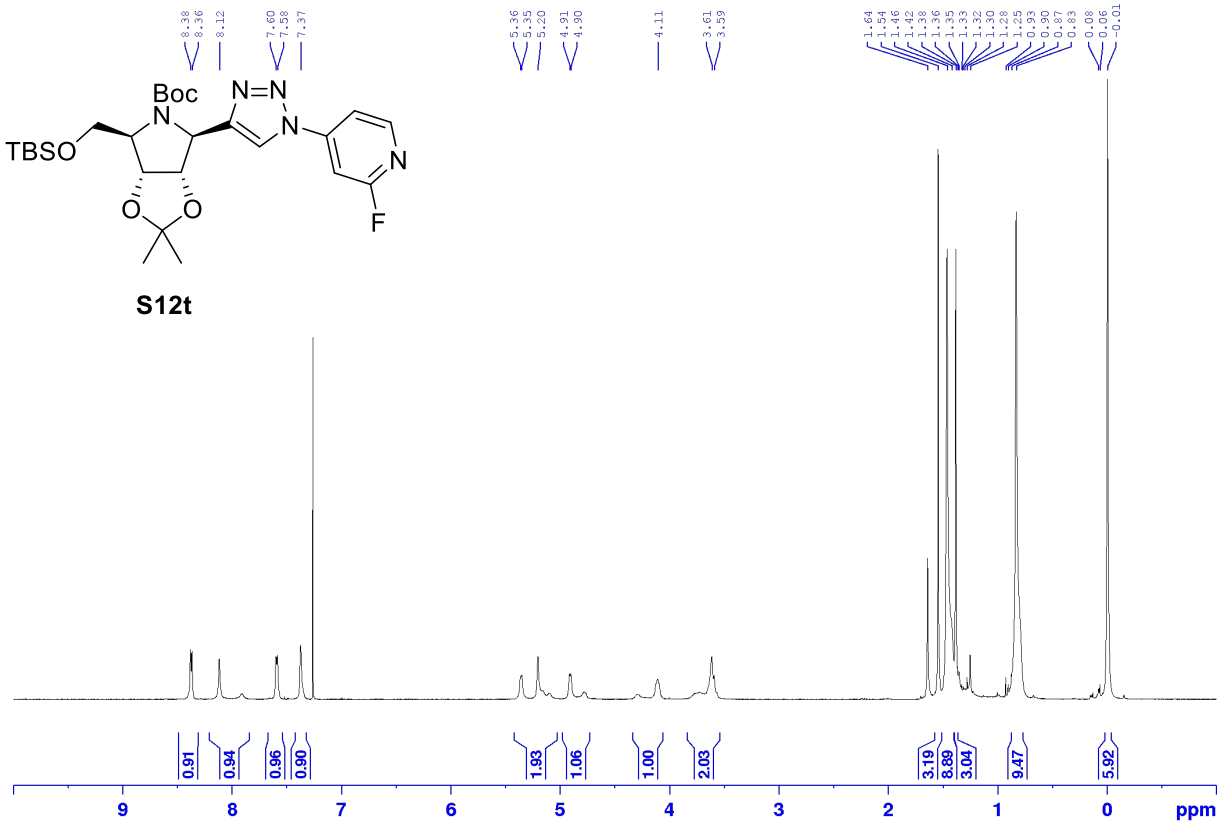
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

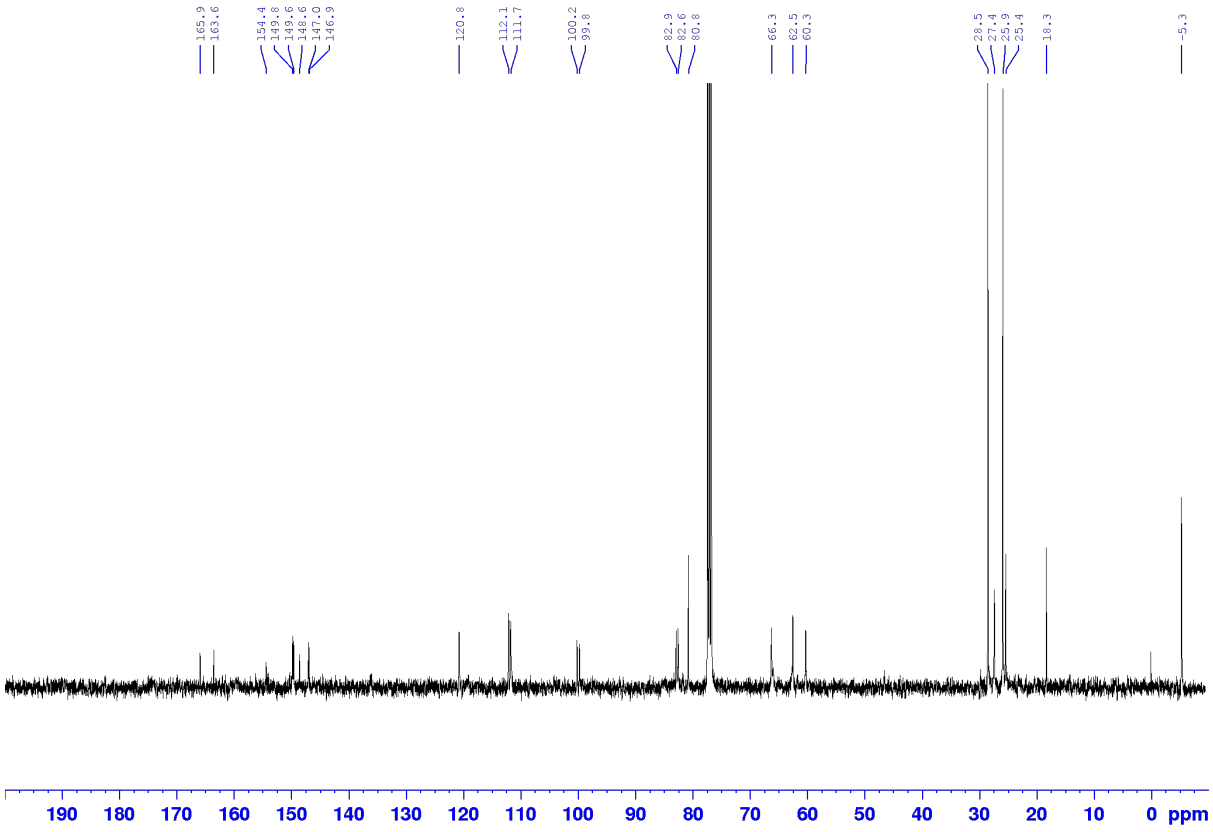


^{1}H NMR (400 MHz, $CDCl_3$)

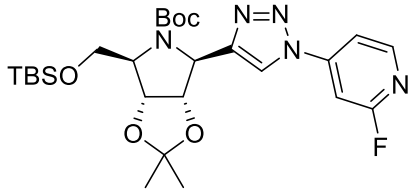


S12t

^{13}C NMR (100 MHz, $CDCl_3$)

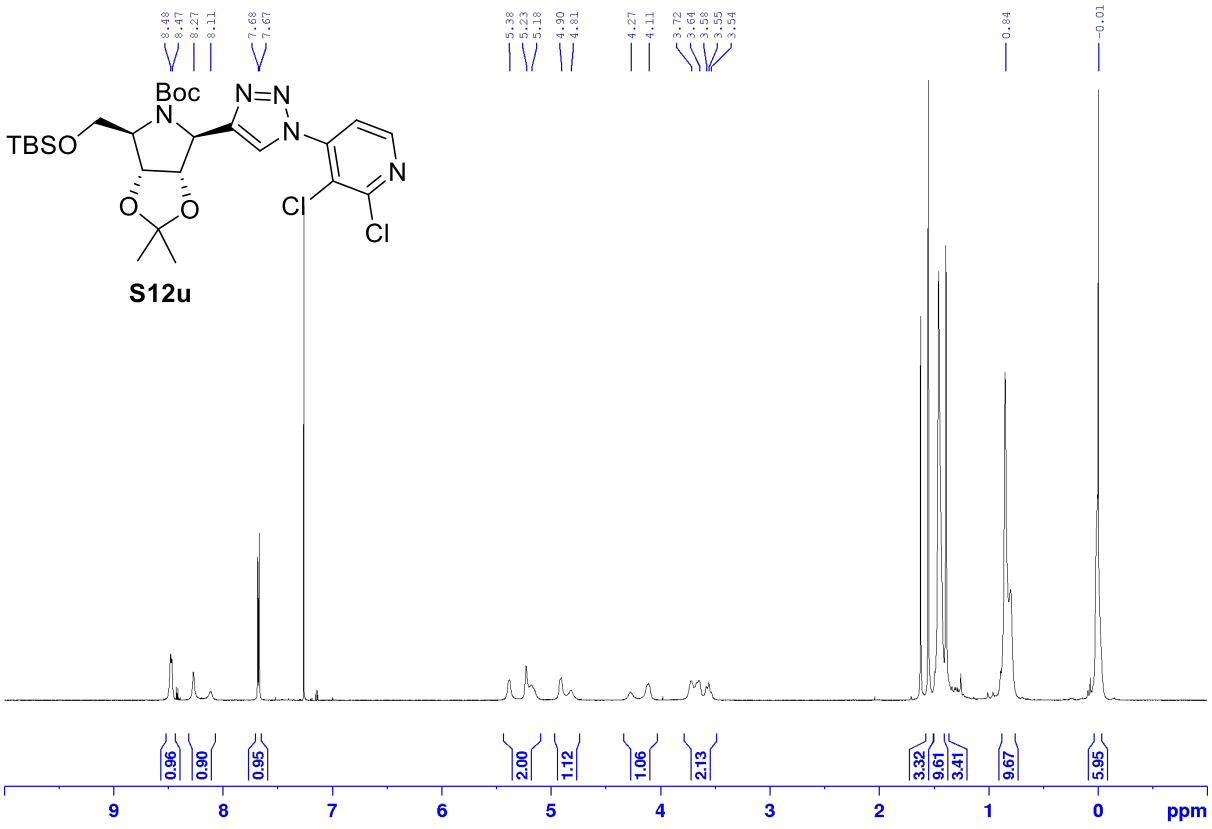


^{19}F NMR (376 MHz, $CDCl_3$)

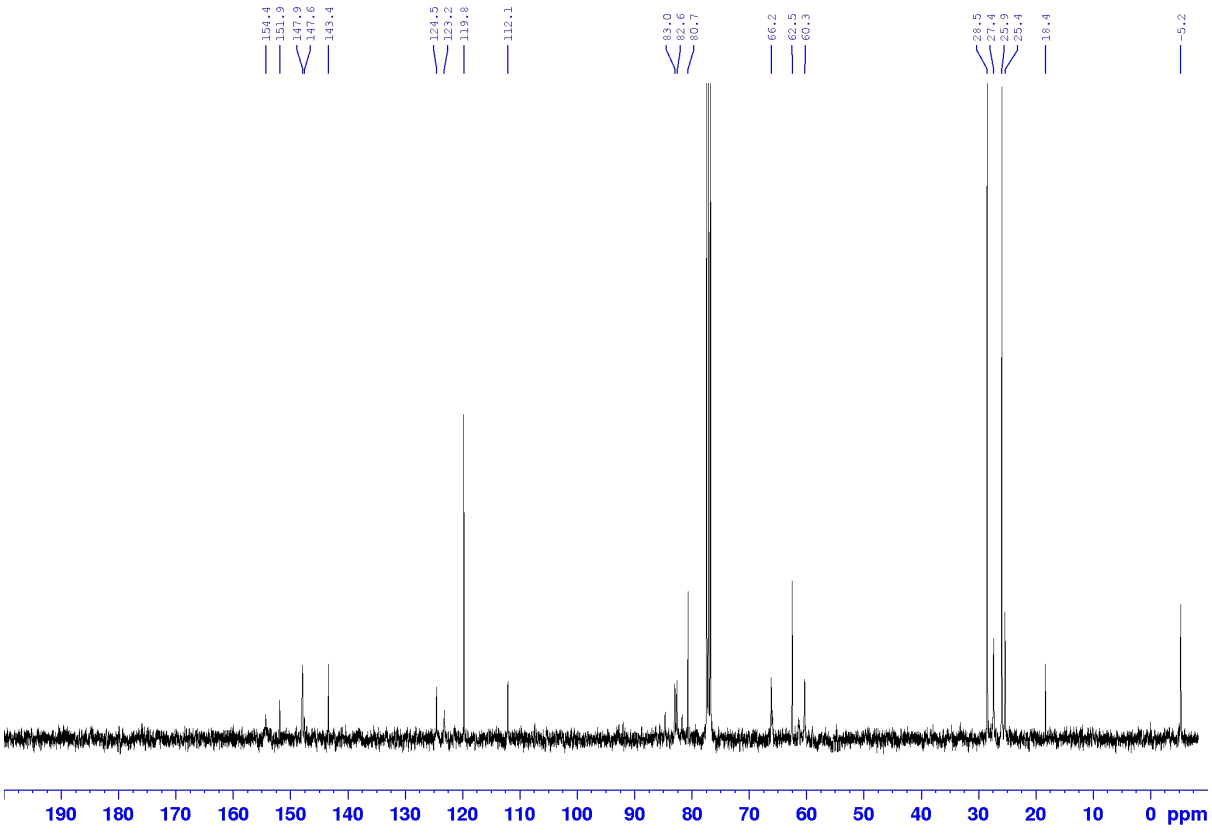


S12t

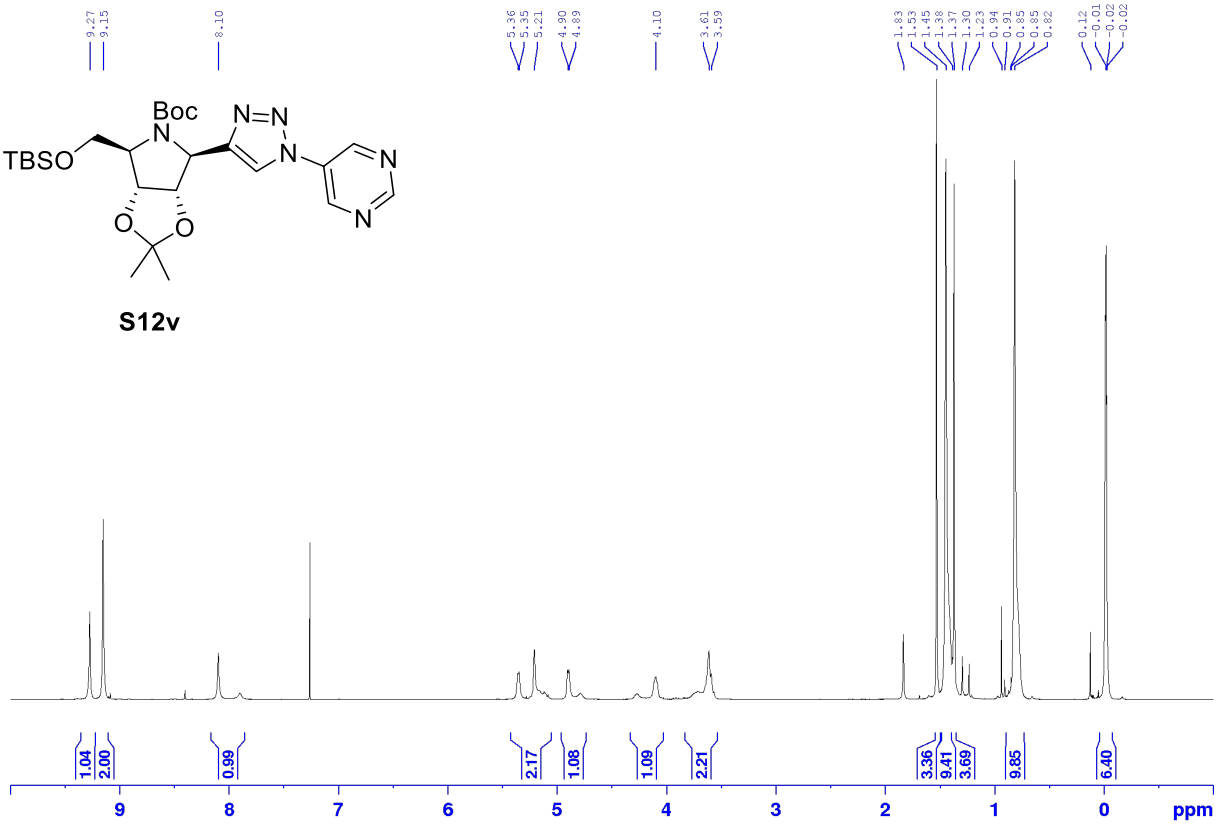
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

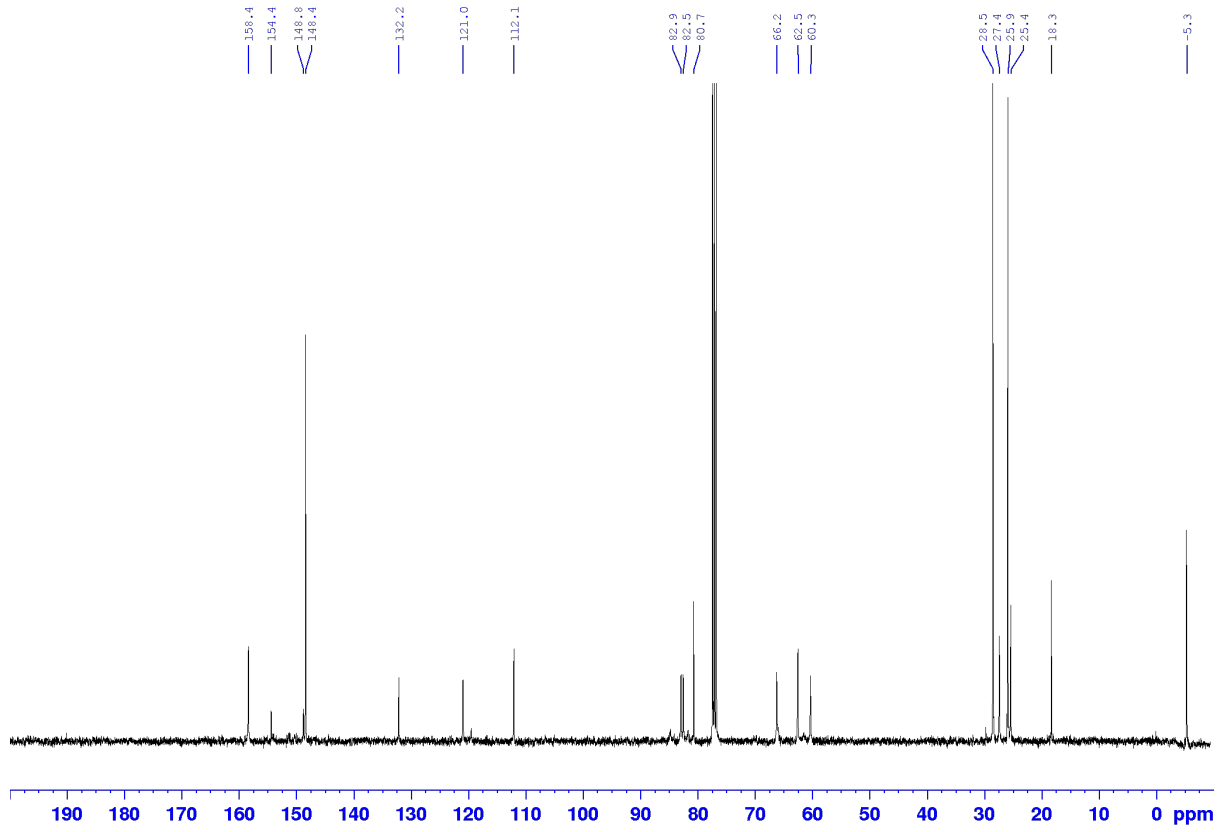


^{1}H NMR (400 MHz, $CDCl_3$)

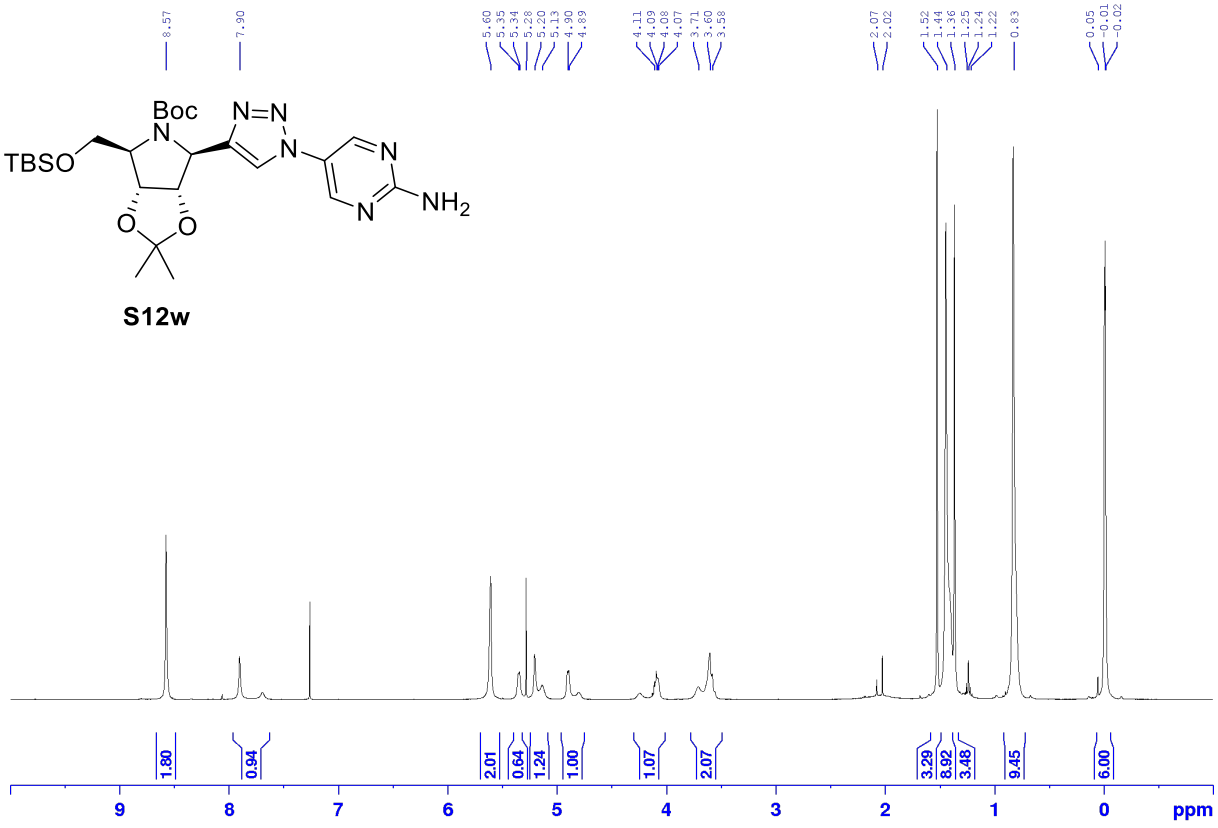


S12v

^{13}C NMR (100 MHz, $CDCl_3$)

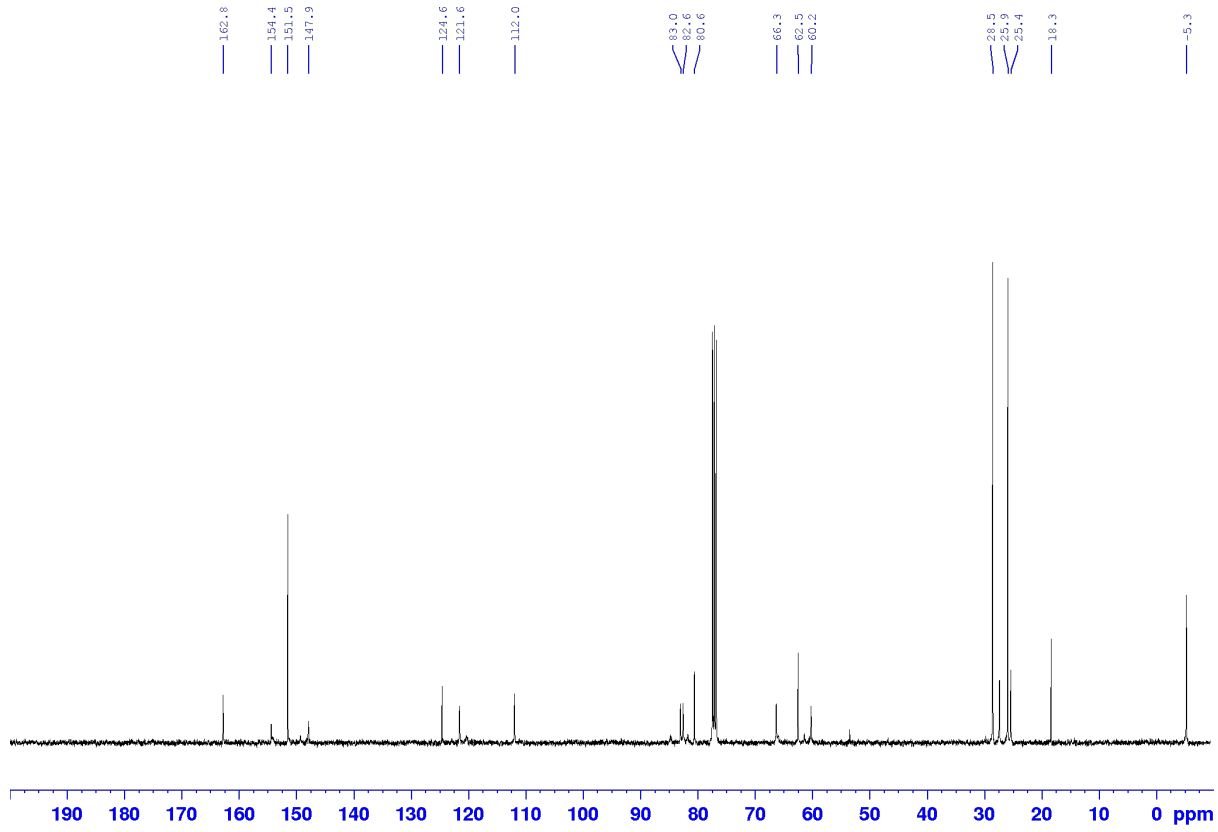


^{1}H NMR (400 MHz, $CDCl_3$)

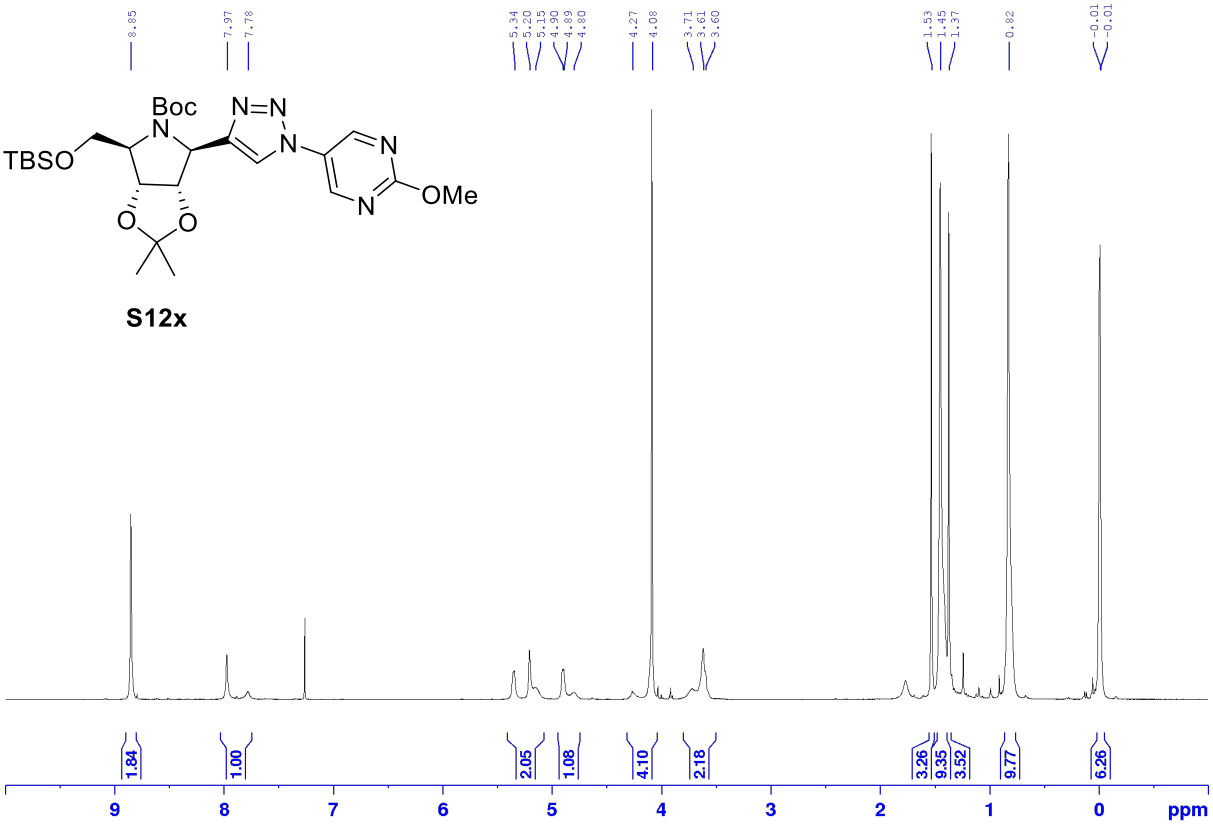


S12w

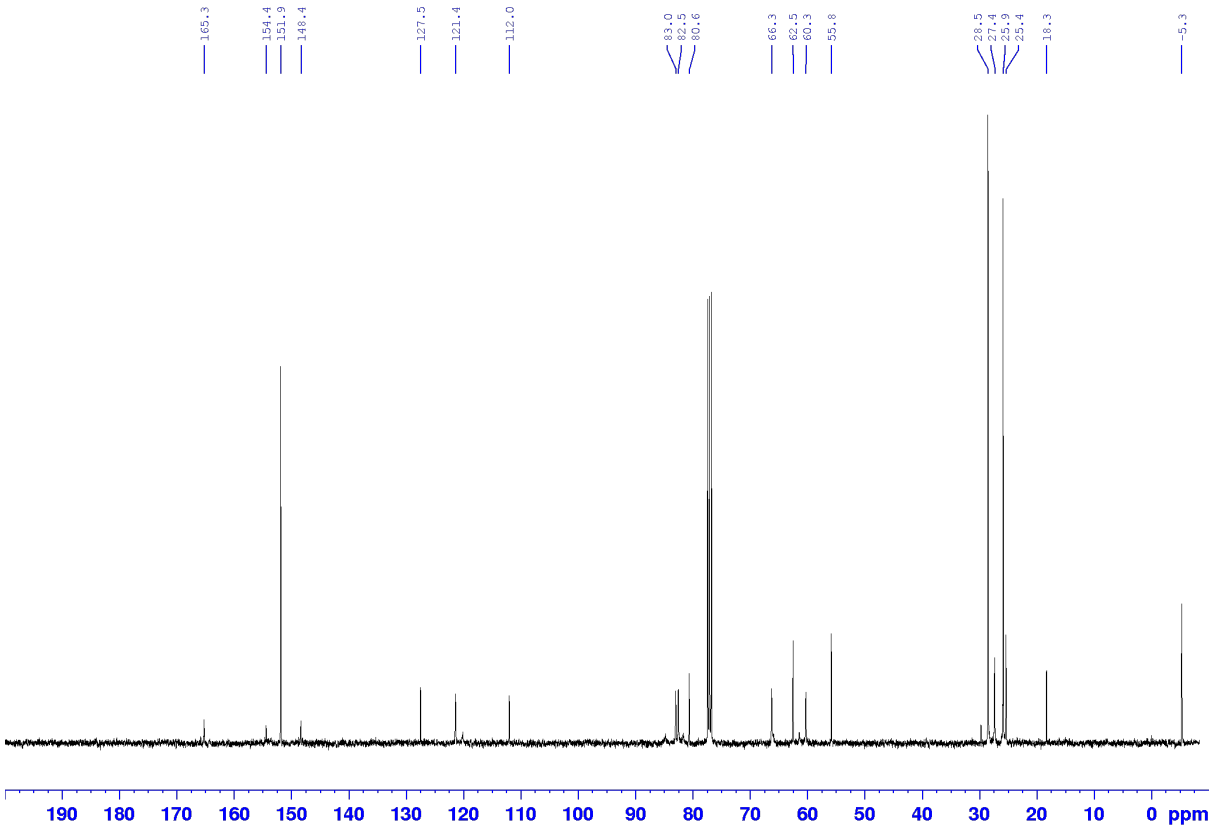
^{13}C NMR (100 MHz, $CDCl_3$)



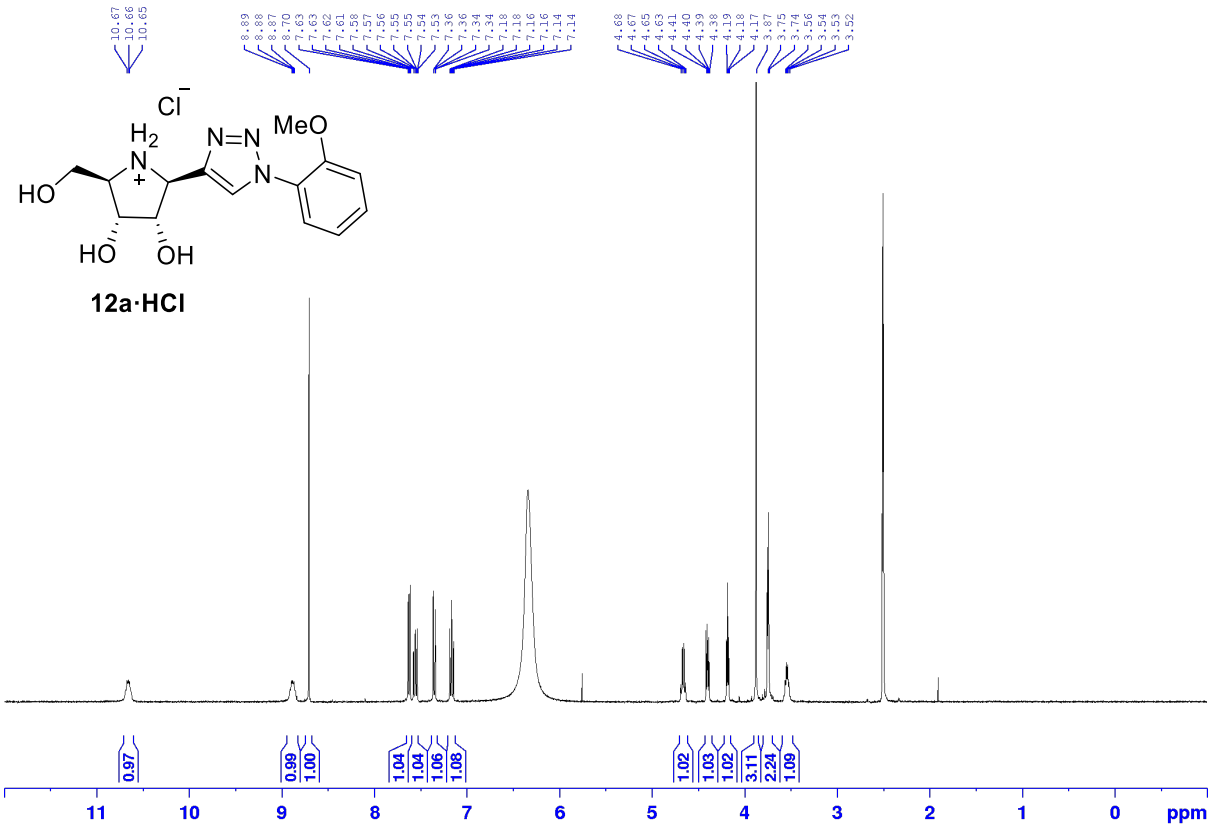
^{1}H NMR (400 MHz, $CDCl_3$)



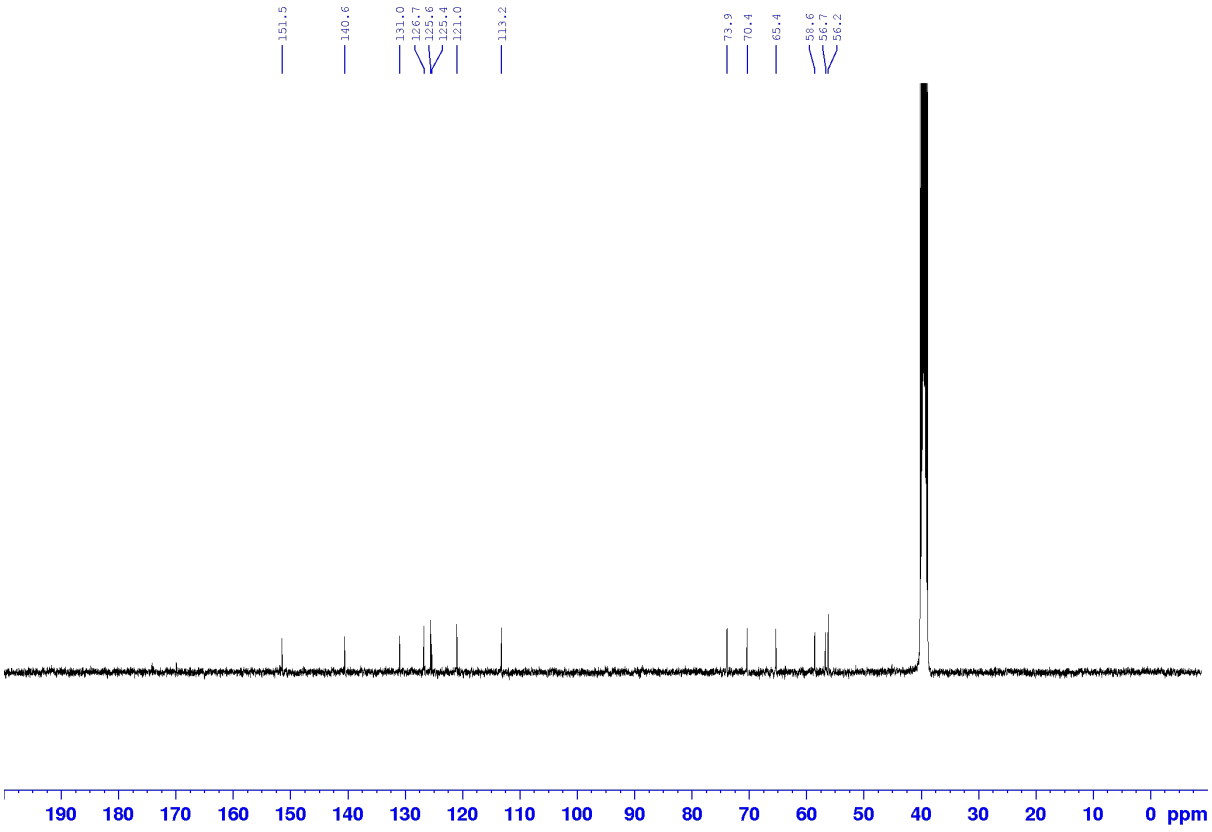
^{13}C NMR (100 MHz, $CDCl_3$)



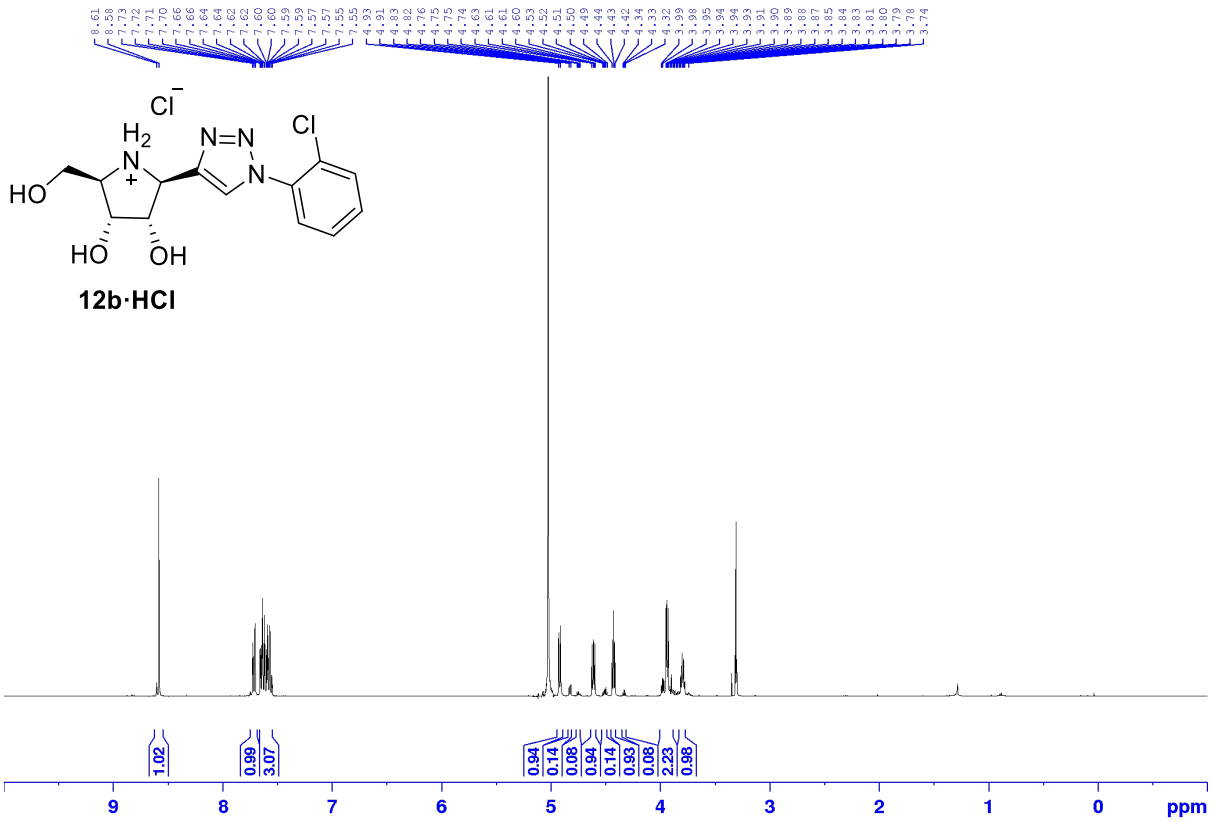
^{1}H NMR (400 MHz, DMSO-d_6)



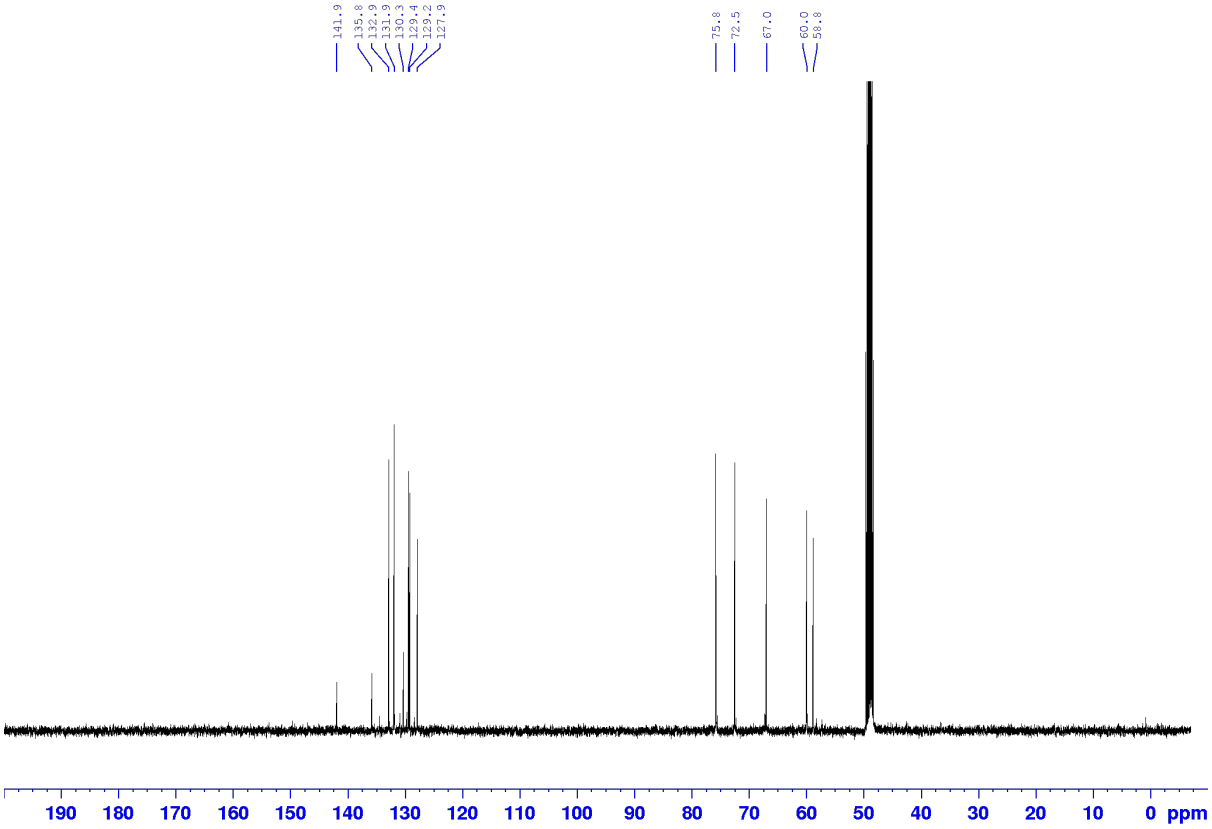
^{13}C NMR (100 MHz, DMSO-d_6)



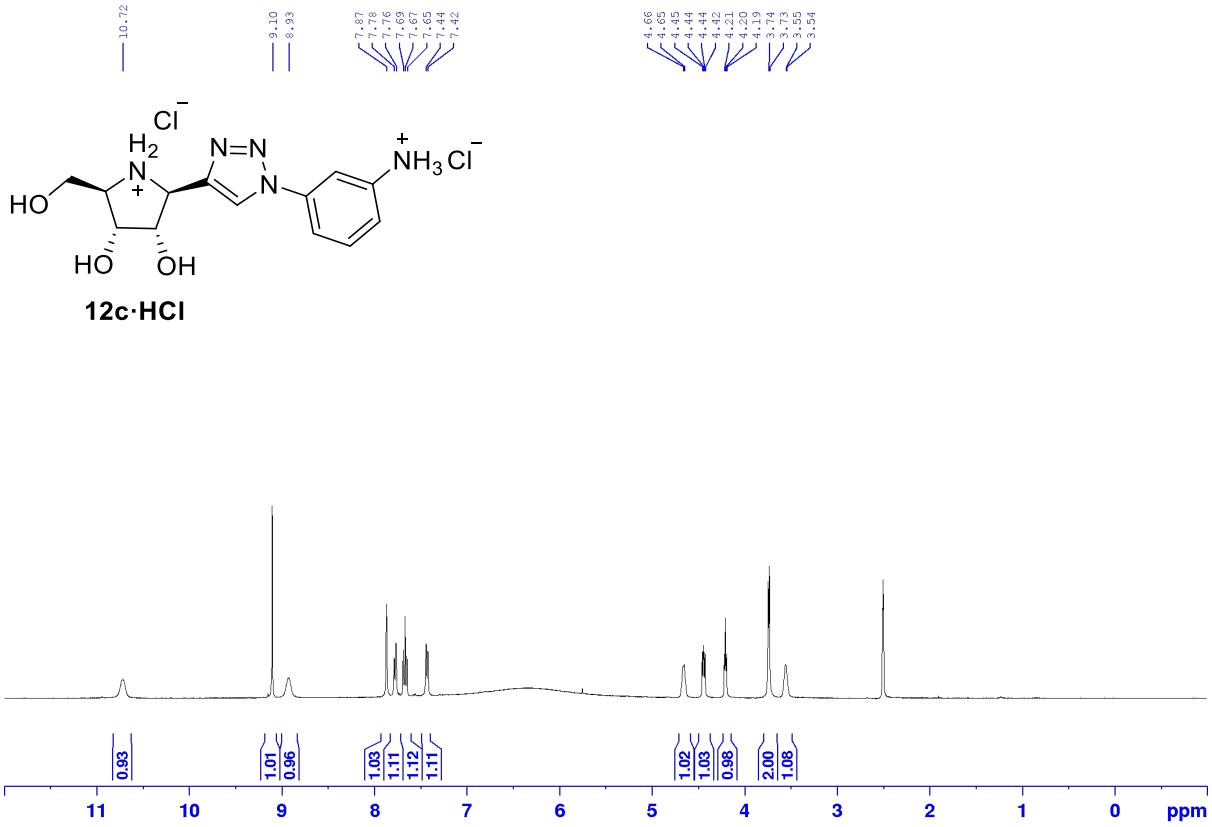
^{1}H NMR (400 MHz, CD_3OD)



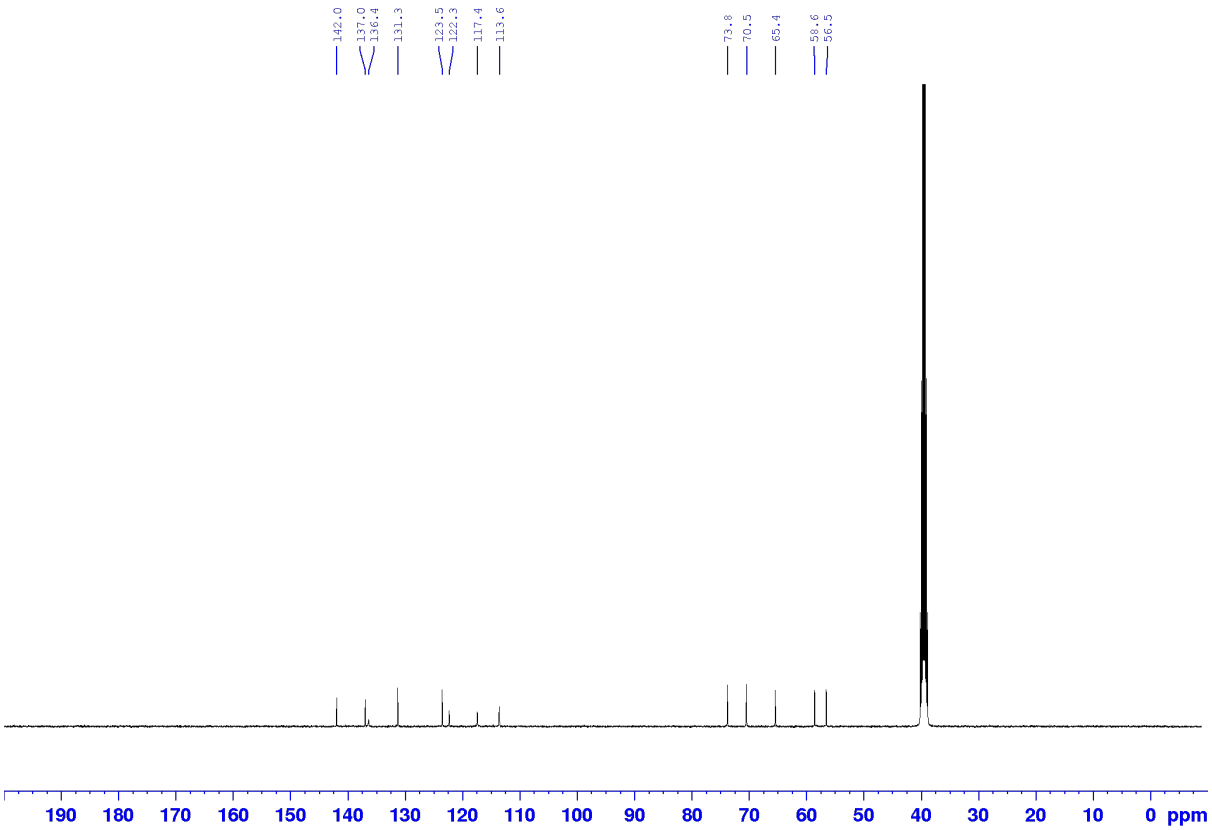
^{13}C NMR (100 MHz, CD_3OD)



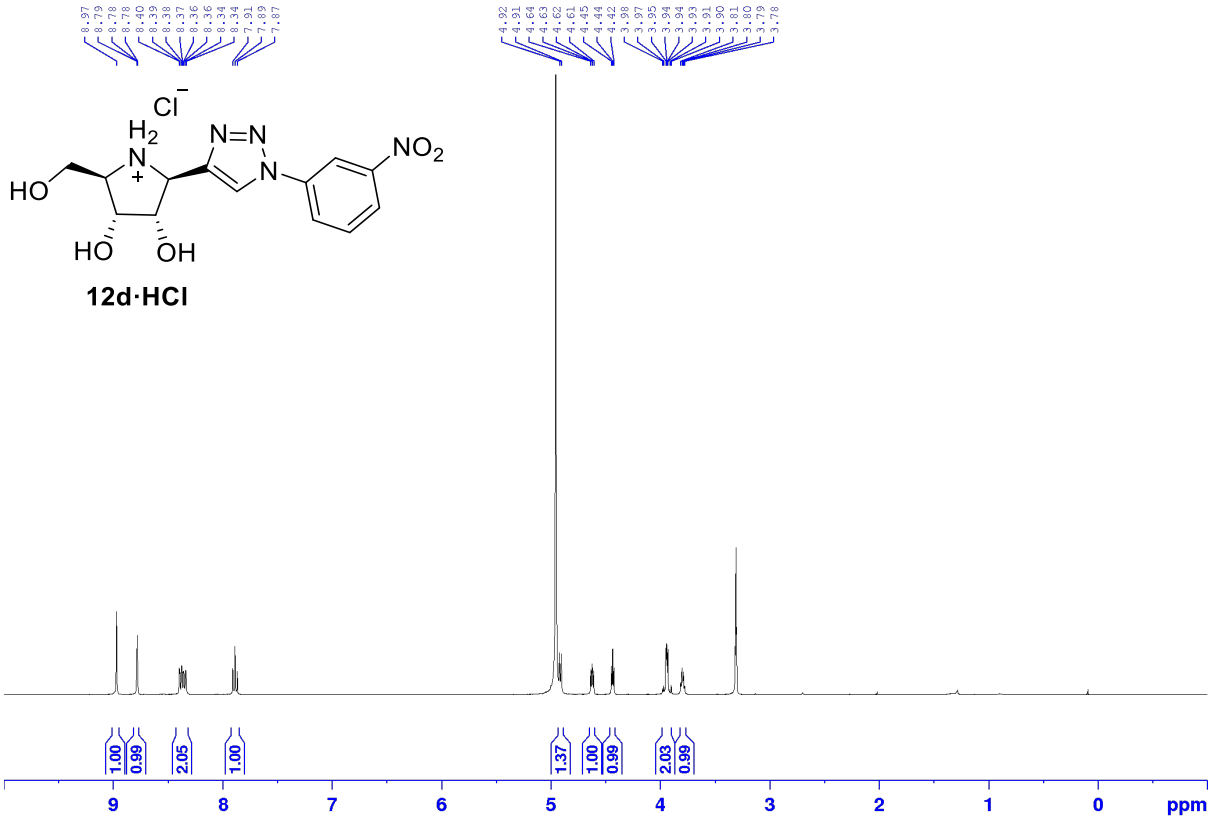
^{1}H NMR (400 MHz, DMSO-d_6)



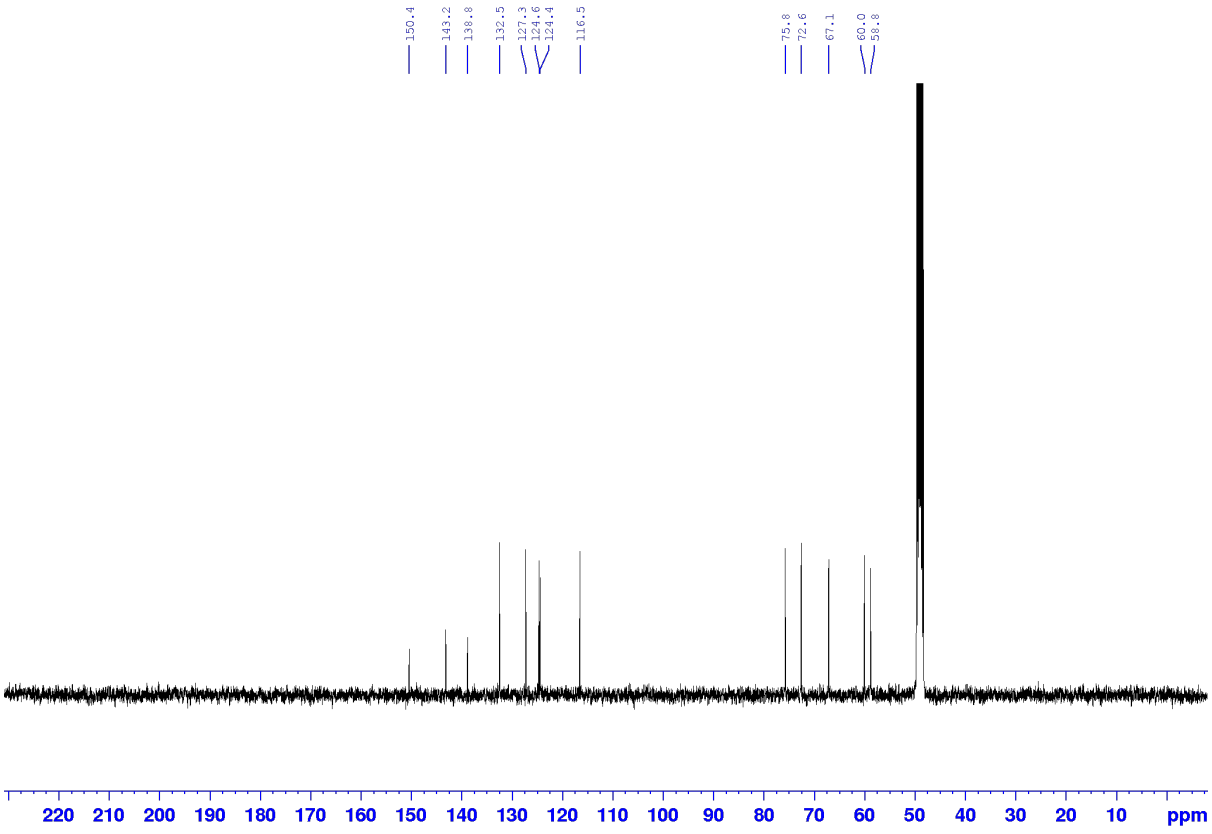
^{13}C NMR (100 MHz, DMSO-d_6)



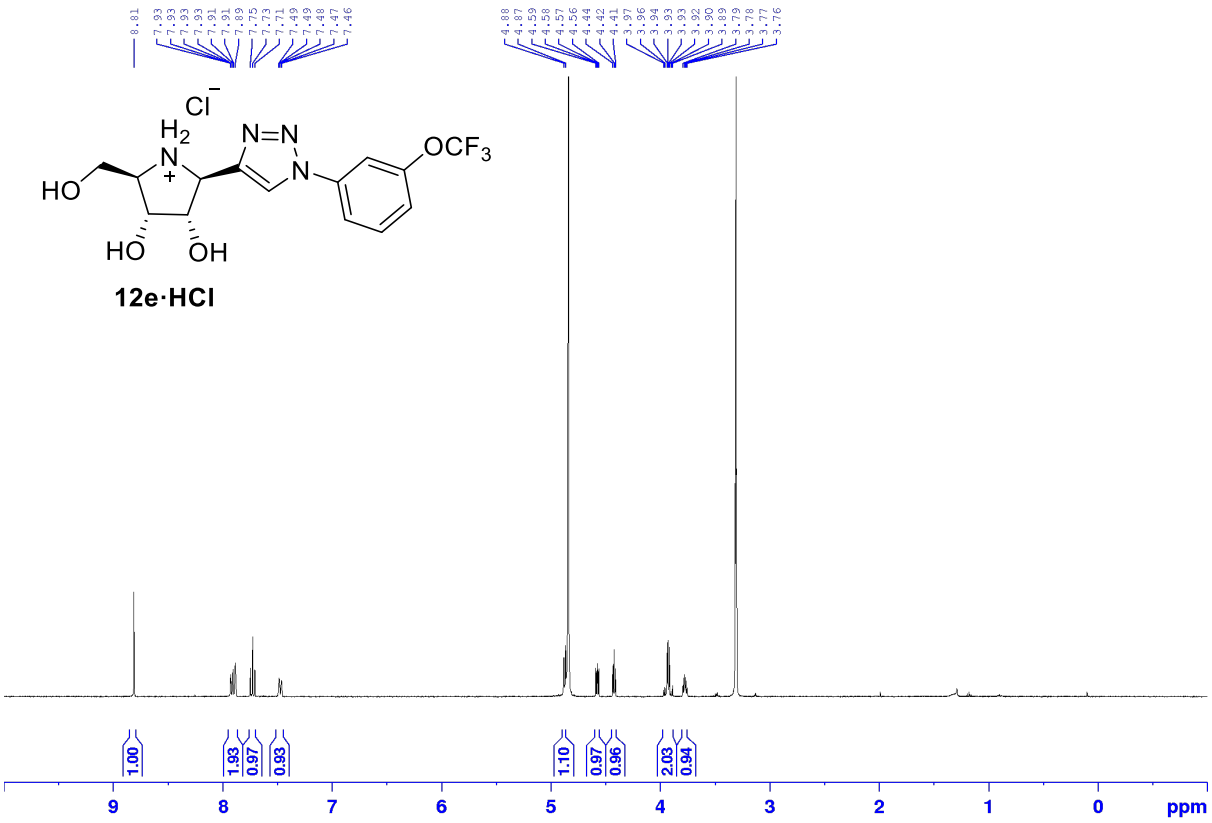
^{1}H NMR (400 MHz, CD_3OD)



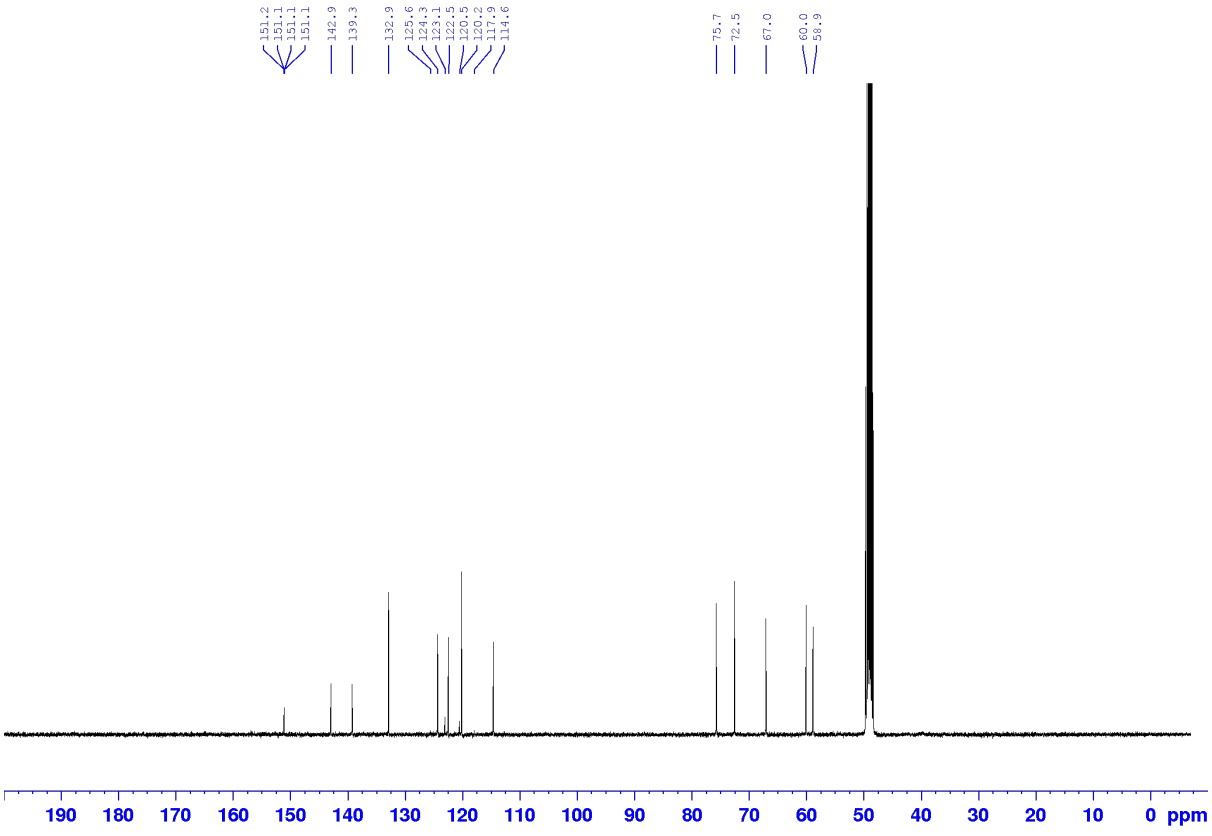
^{13}C NMR (100 MHz, CD_3OD)



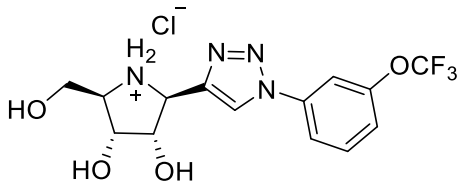
^{1}H NMR (400 MHz, CD_3OD)



^{13}C NMR (100 MHz, CD_3OD)

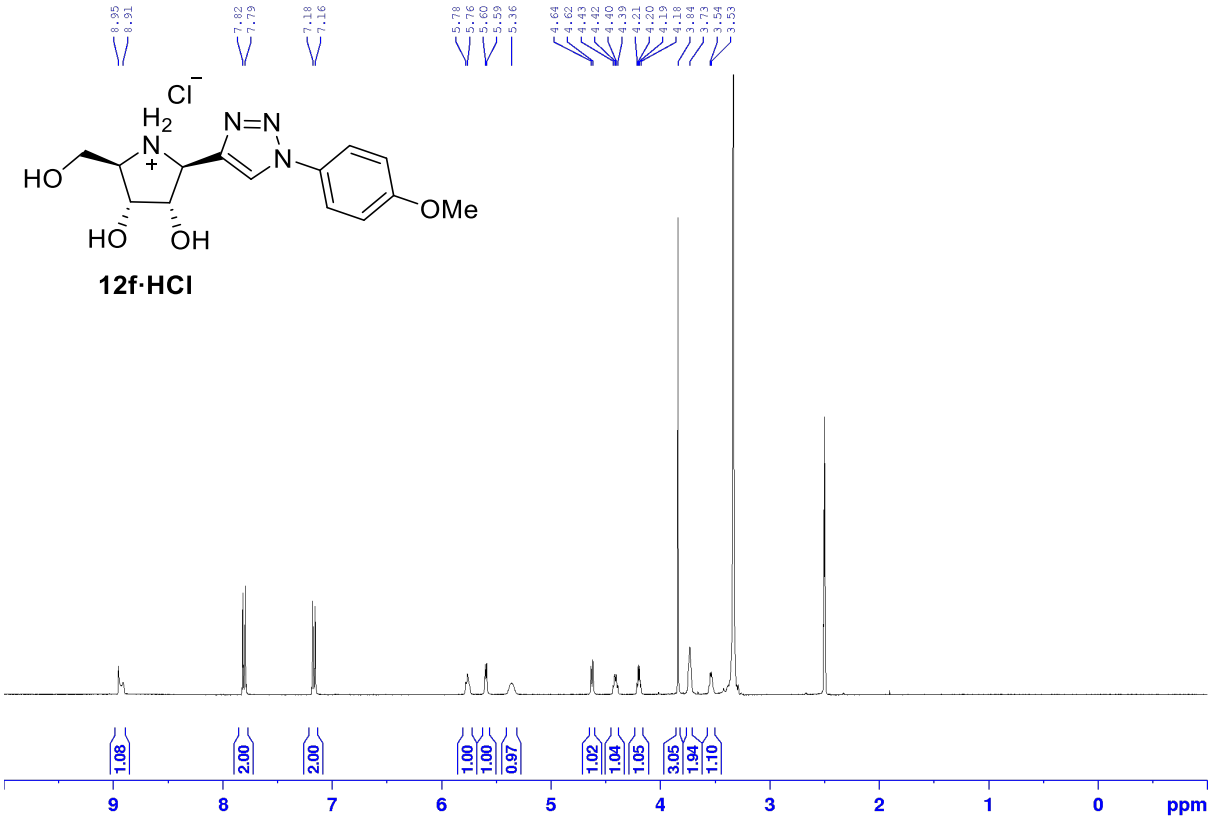


^{19}F NMR (376 MHz, CD_3OD)

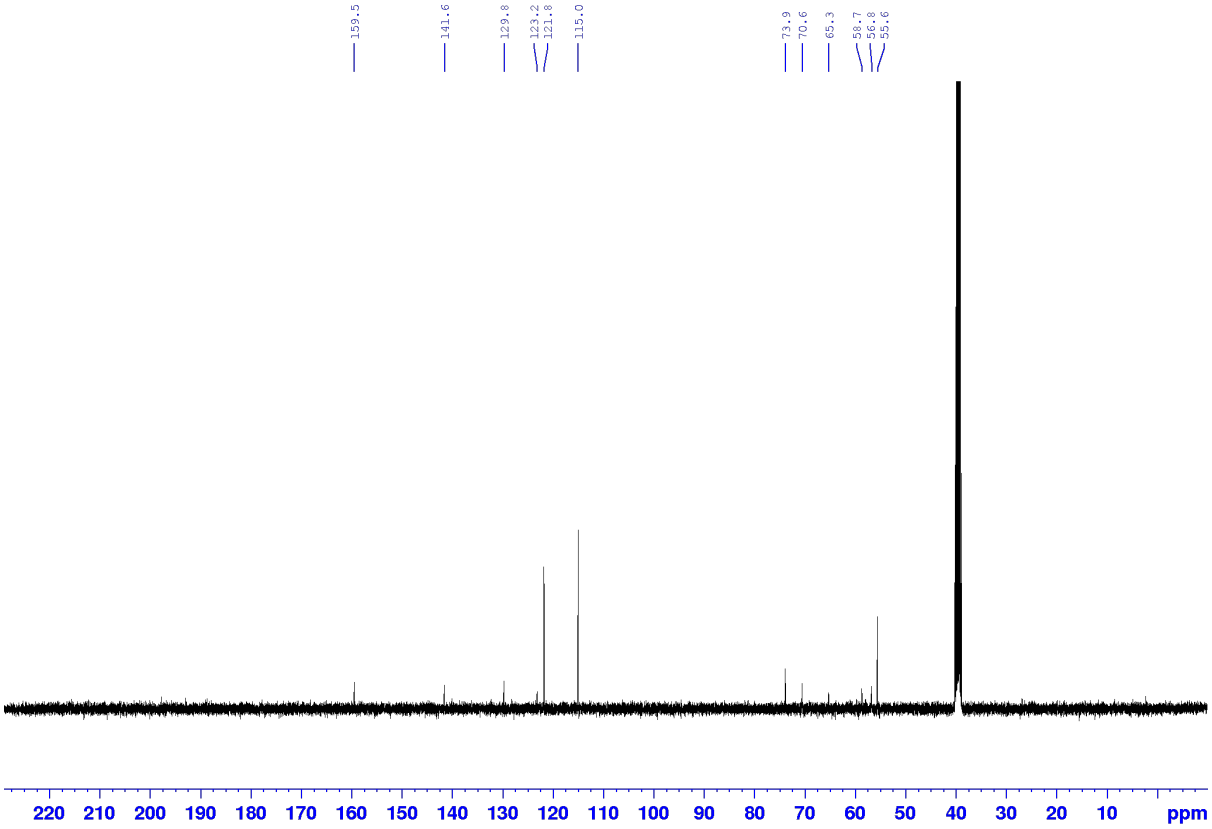


12e·HCl

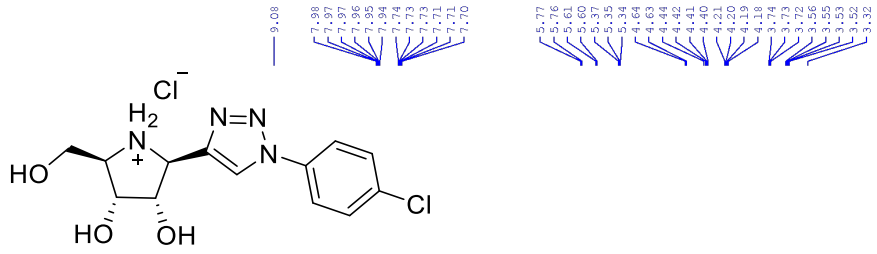
^{1}H NMR (400 MHz, DMSO-d_6)



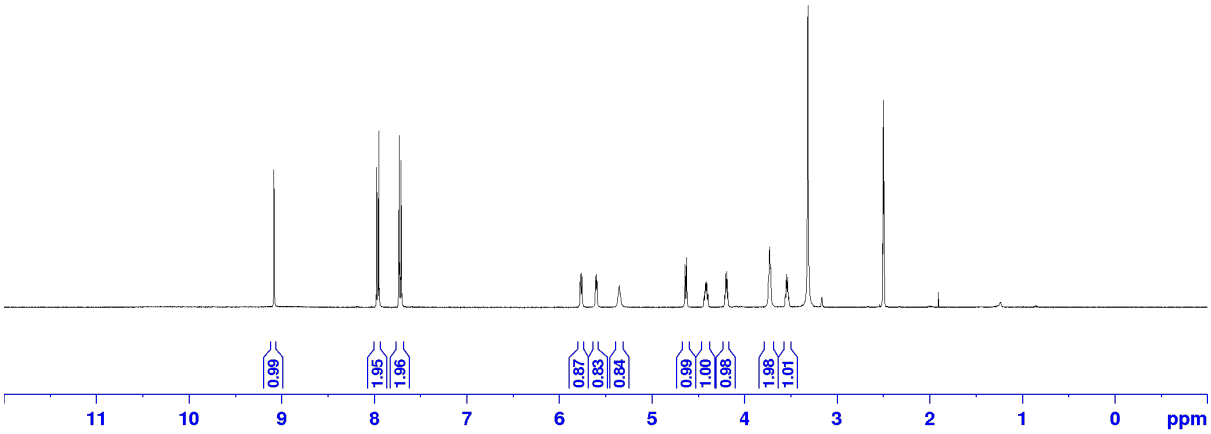
^{13}C NMR (100 MHz, DMSO-d_6)



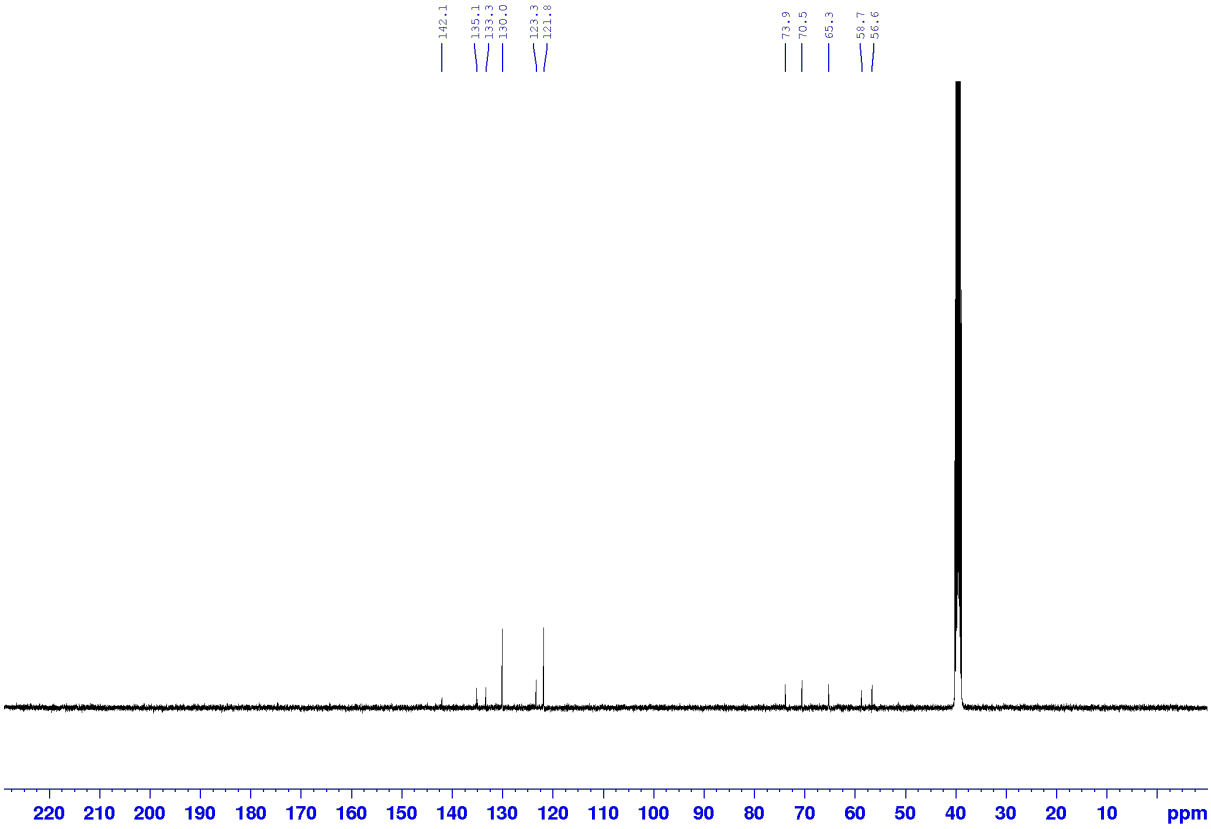
^{1}H NMR (400 MHz, DMSO-d_6)



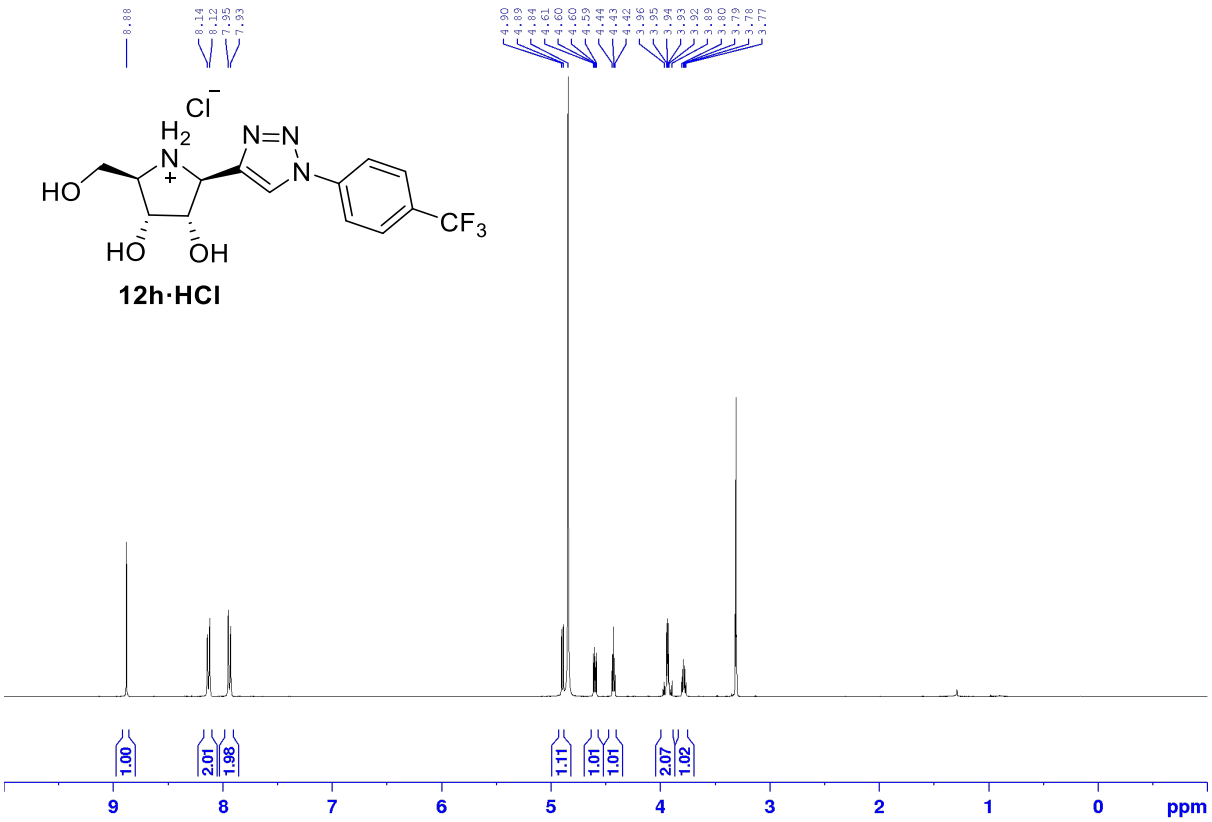
12g·HCl



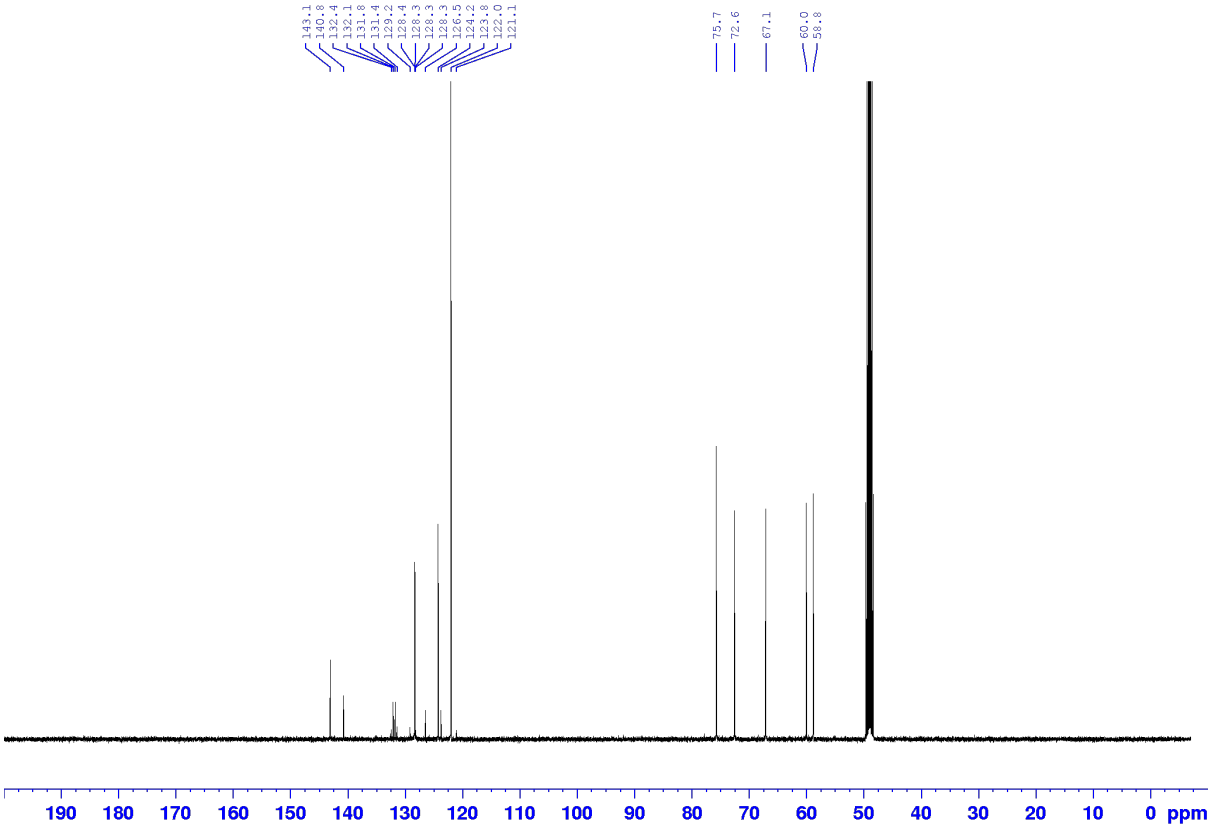
^{13}C NMR (100 MHz, DMSO-d_6)



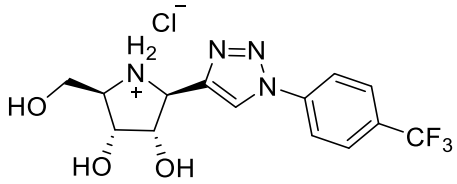
^{1}H NMR (400 MHz, CD_3OD)



^{13}C NMR (100 MHz, CD_3OD)

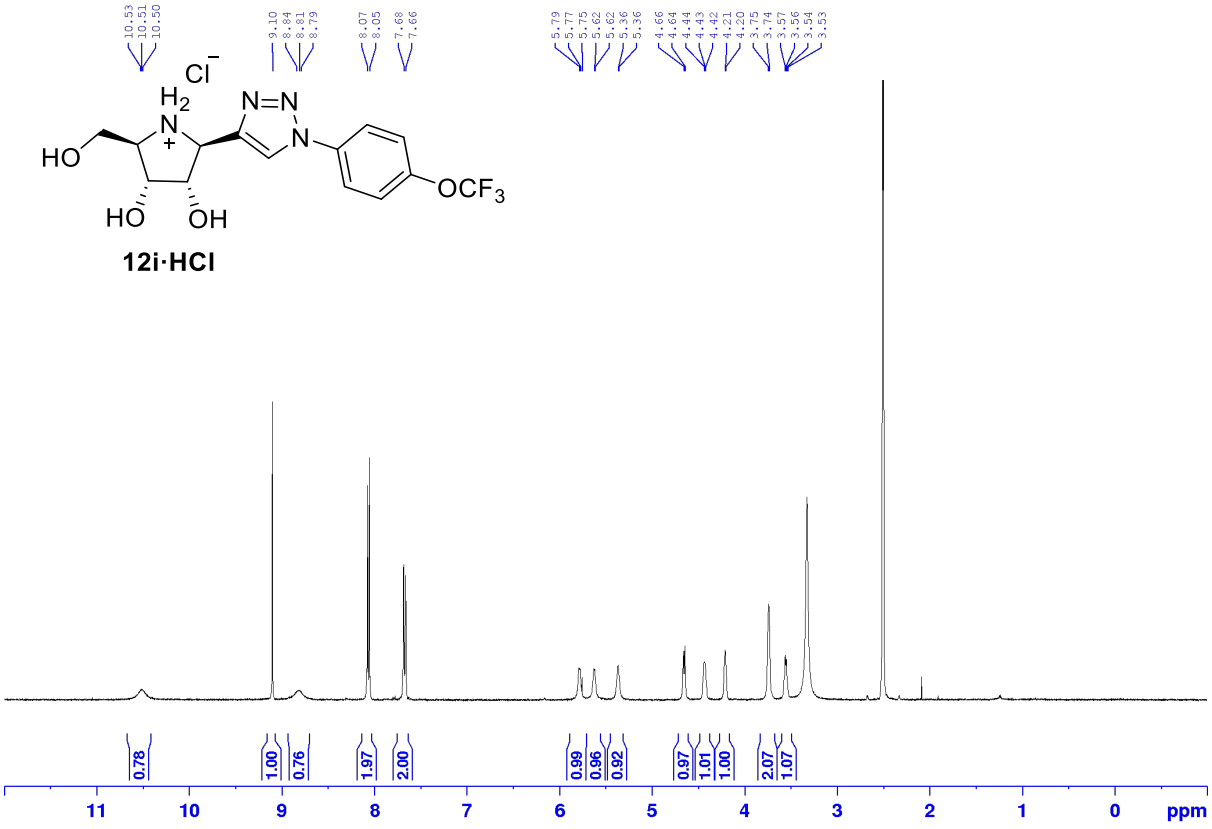


^{19}F NMR (376 MHz, CD_3OD)

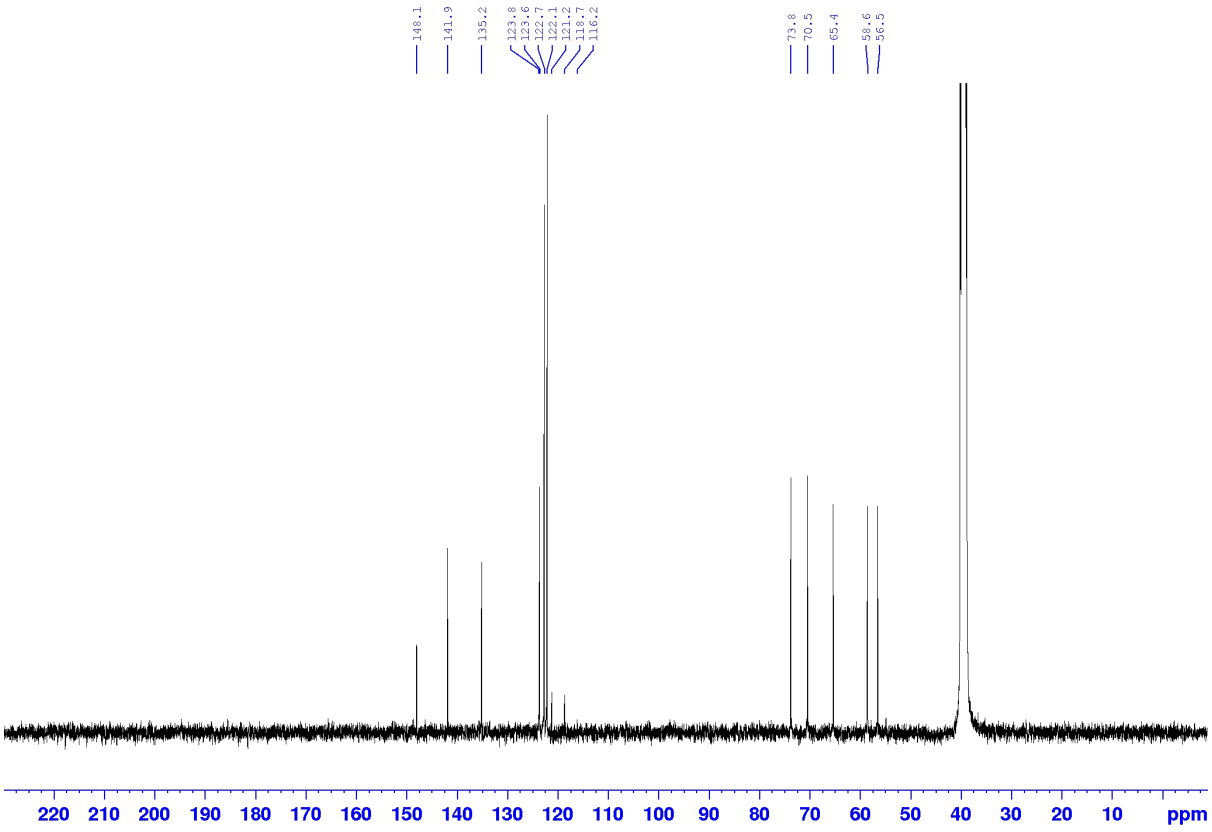


12h·HCl

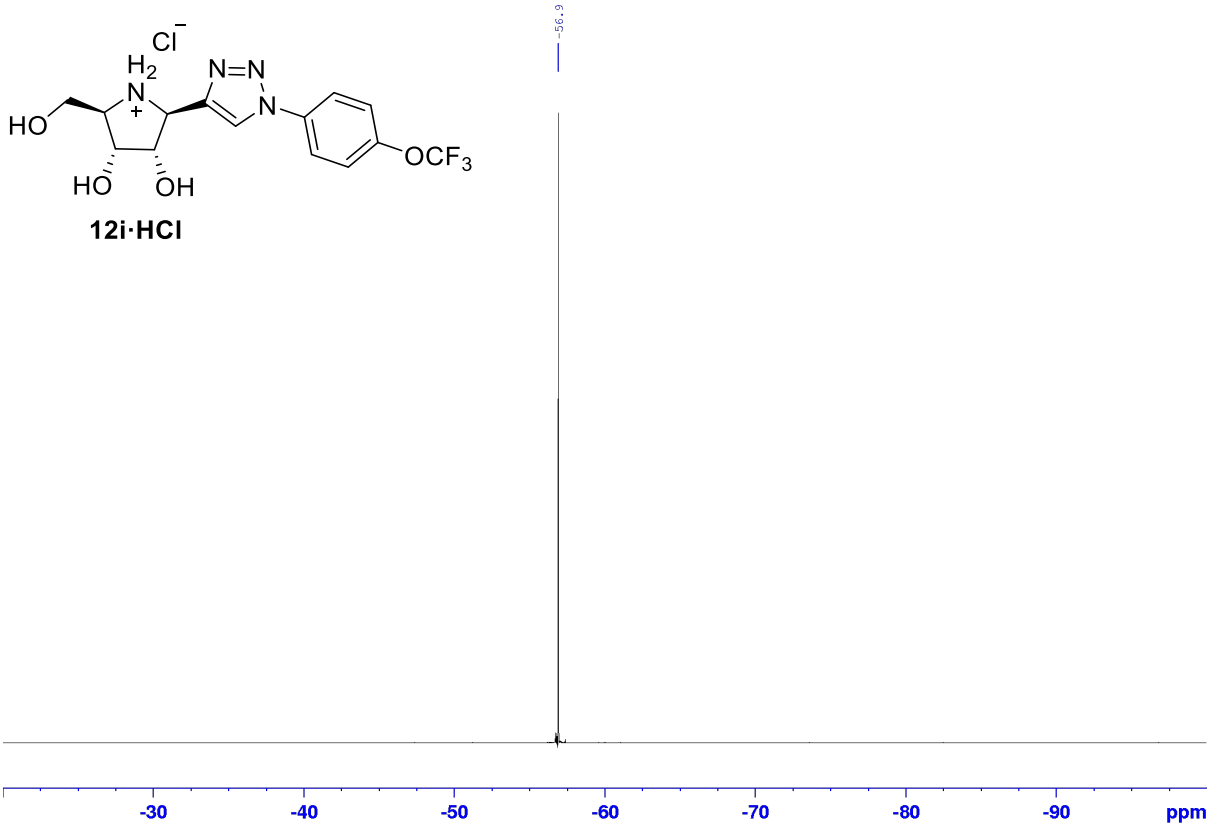
^{1}H NMR (400 MHz, DMSO-d_6)



^{13}C NMR (100 MHz, DMSO-d_6)

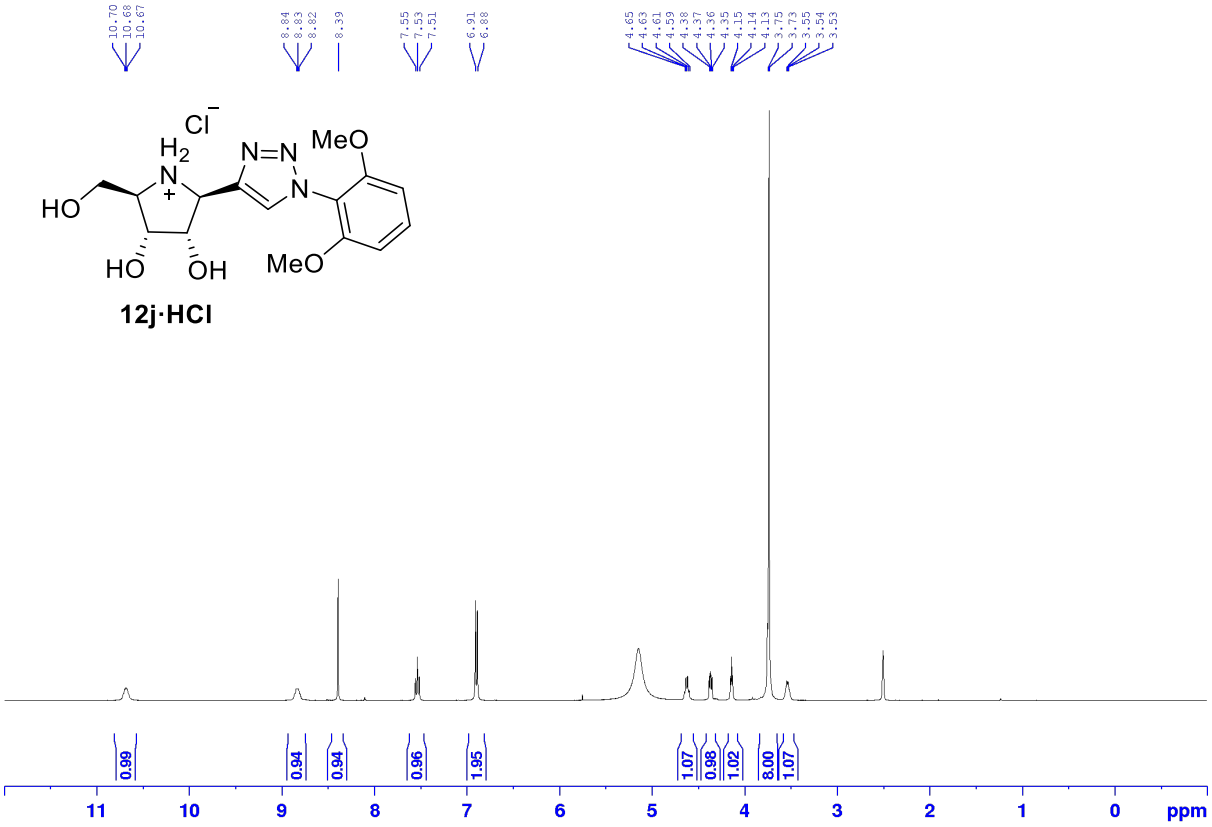


^{19}F NMR (376 MHz, CD_3OD)



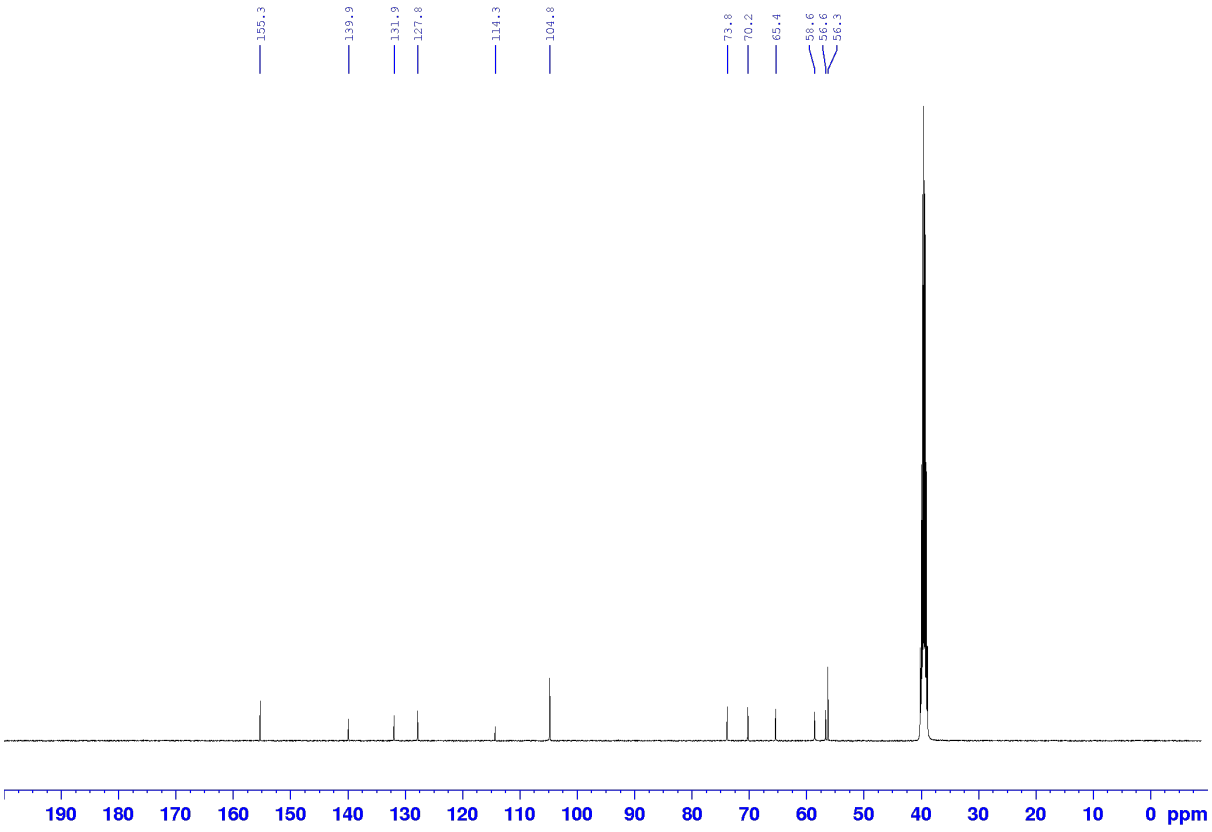
12i·HCl

^{1}H NMR (400 MHz, DMSO-d_6)

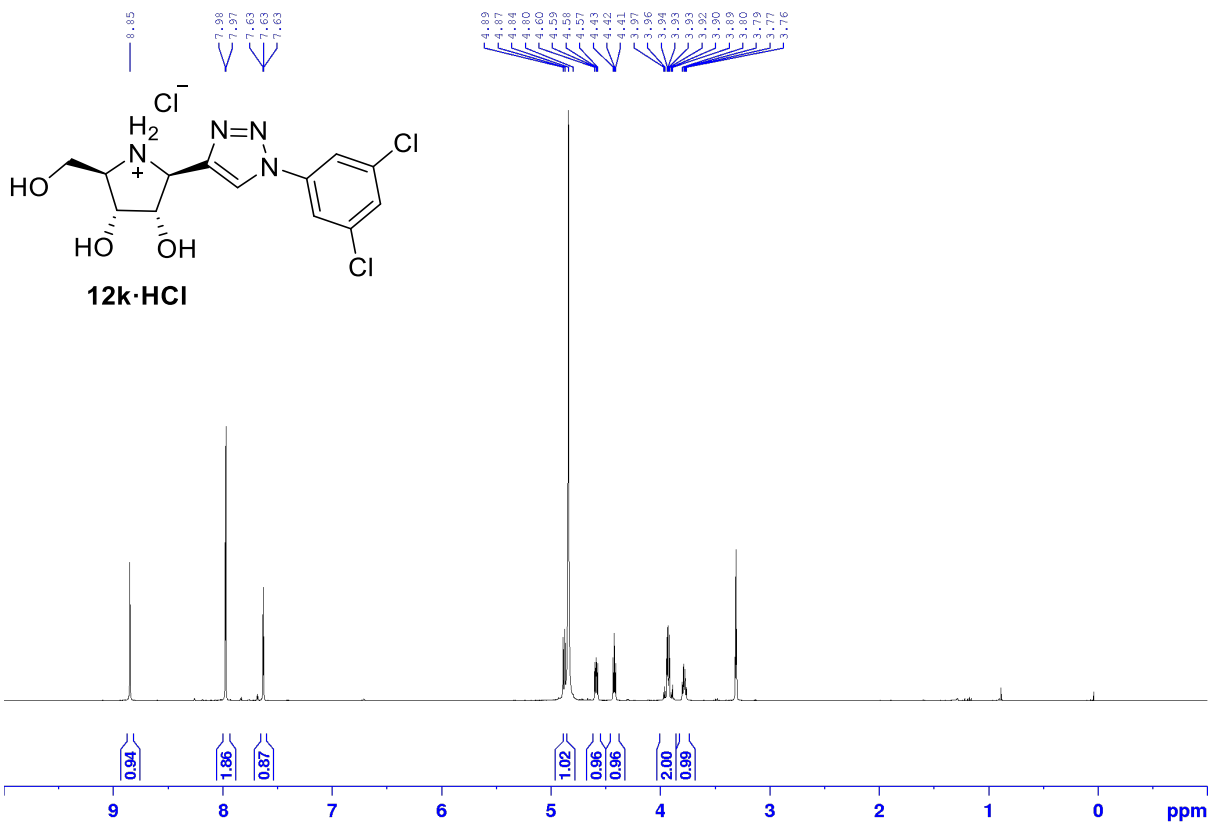


12j·HCl

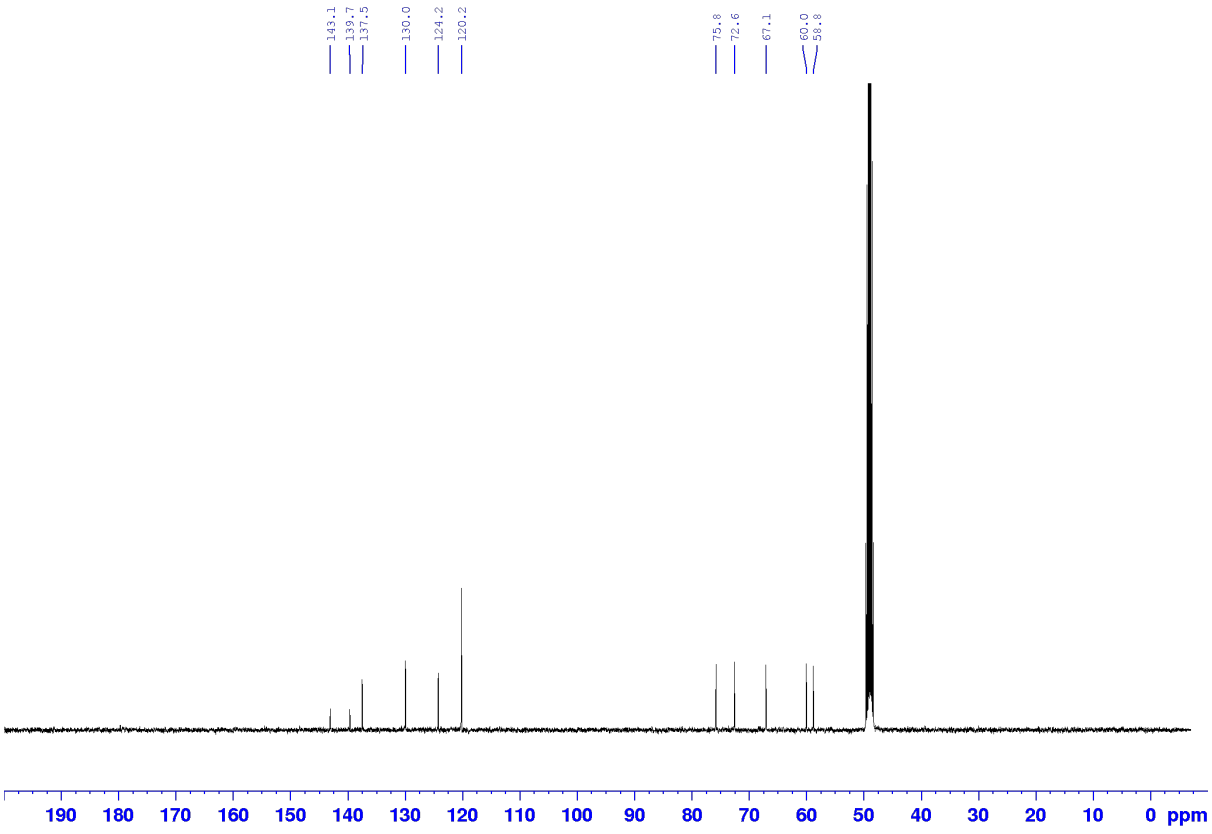
^{13}C NMR (100 MHz, DMSO-d_6)



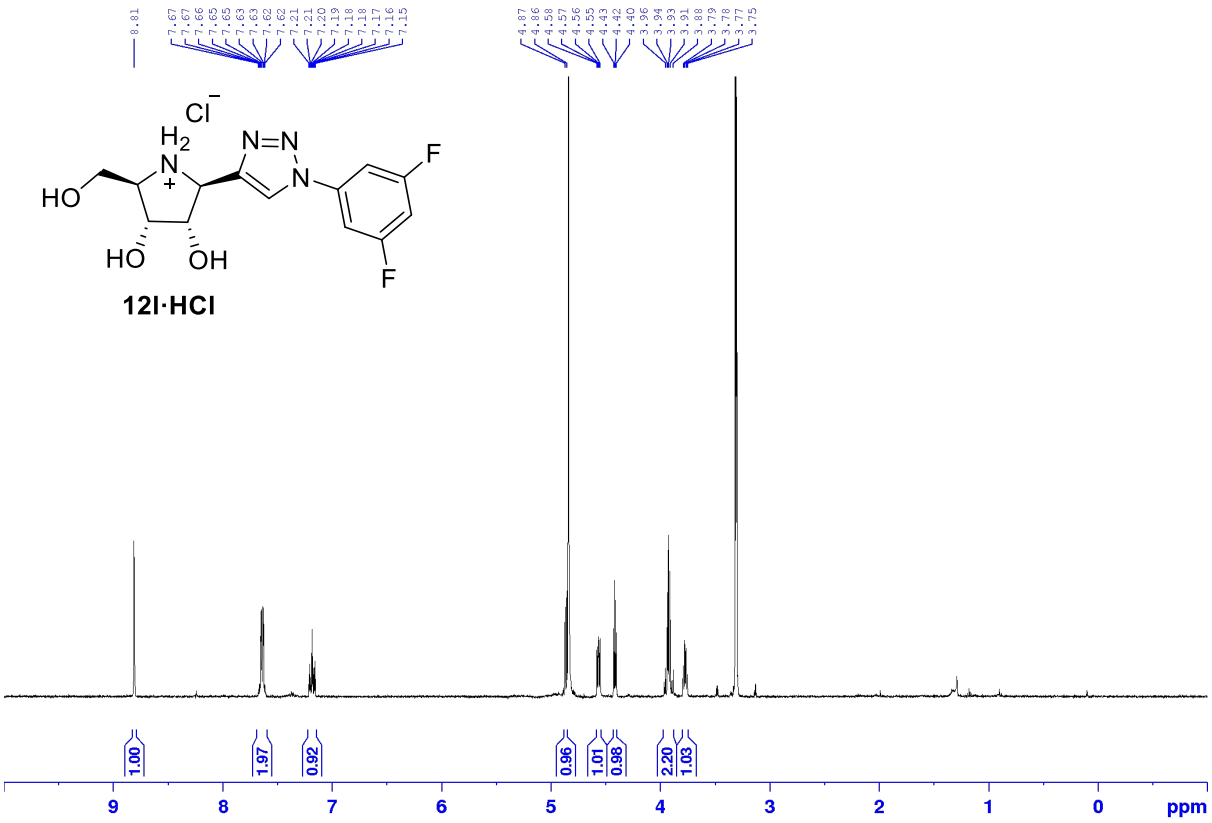
^{1}H NMR (400 MHz, CD_3OD)



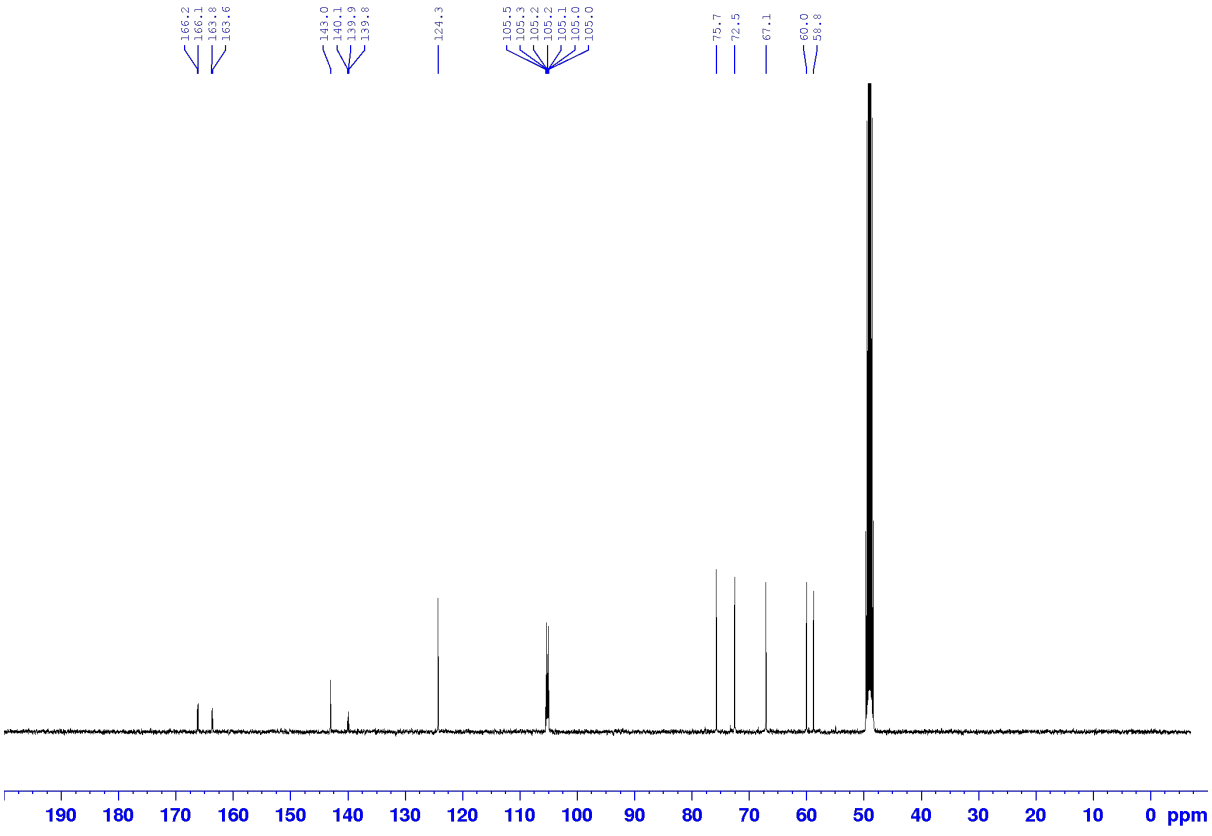
^{13}C NMR (100 MHz, CD_3OD)



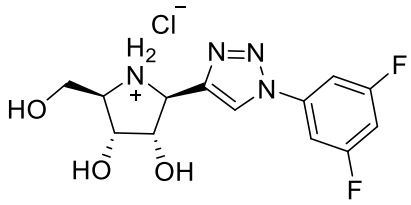
^{1}H NMR (400 MHz, CD_3OD)



^{13}C NMR (100 MHz, CD_3OD)

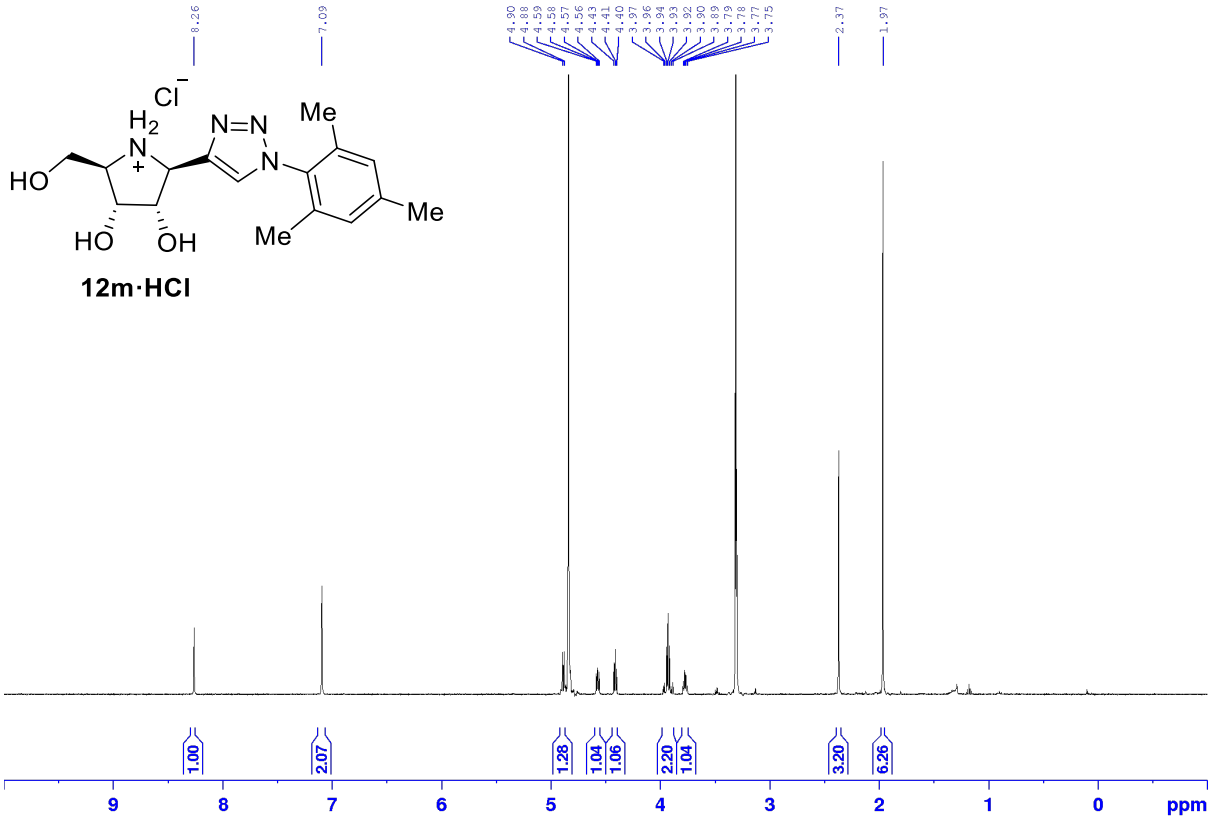


^{19}F NMR (376 MHz, DMSO-d_6)

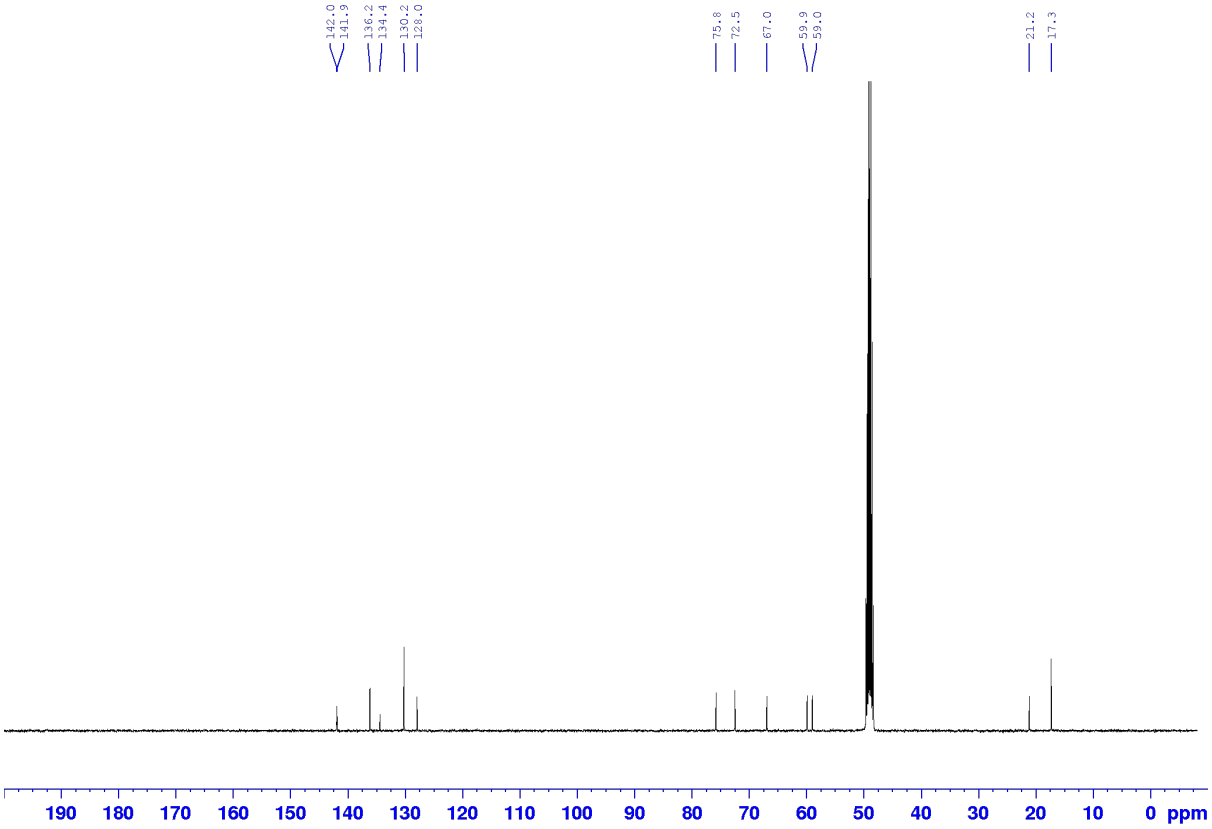


12l·HCl

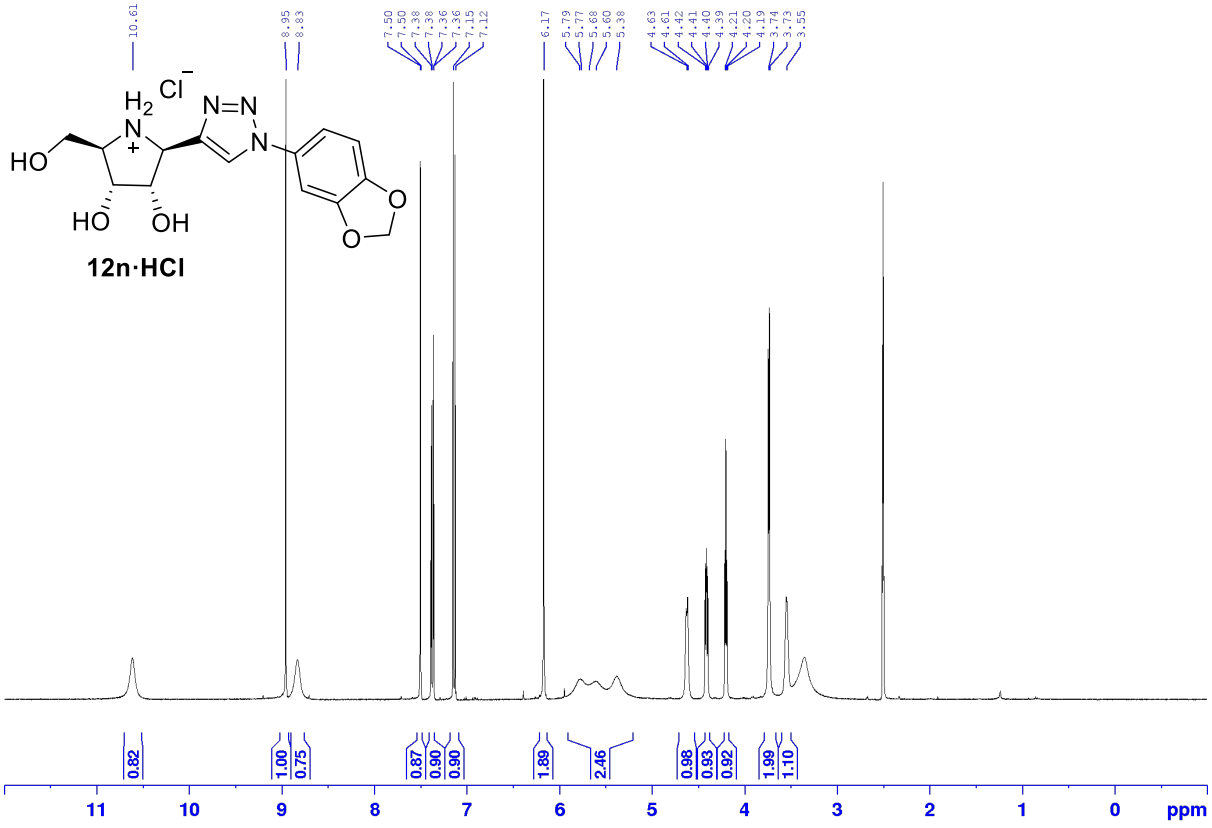
^{1}H NMR (400 MHz, CD_3OD)



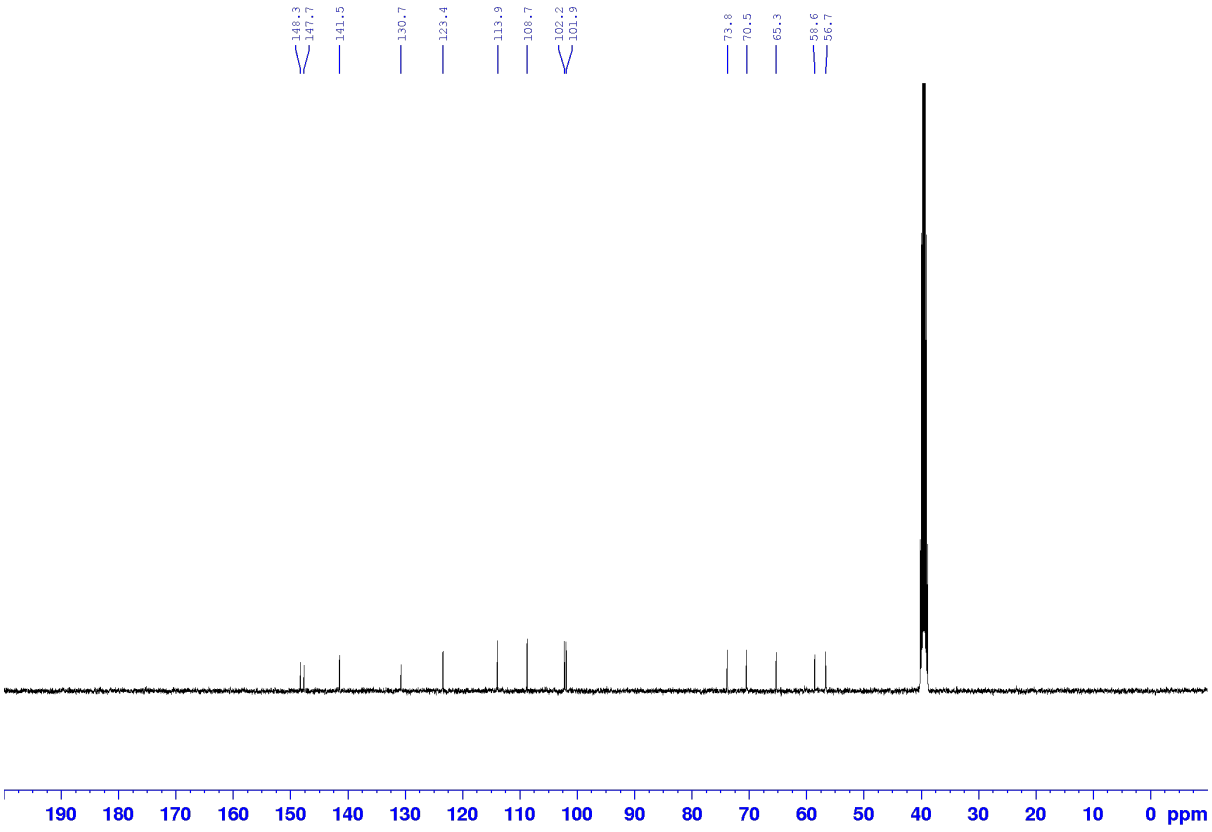
^{13}C NMR (100 MHz, CD_3OD)



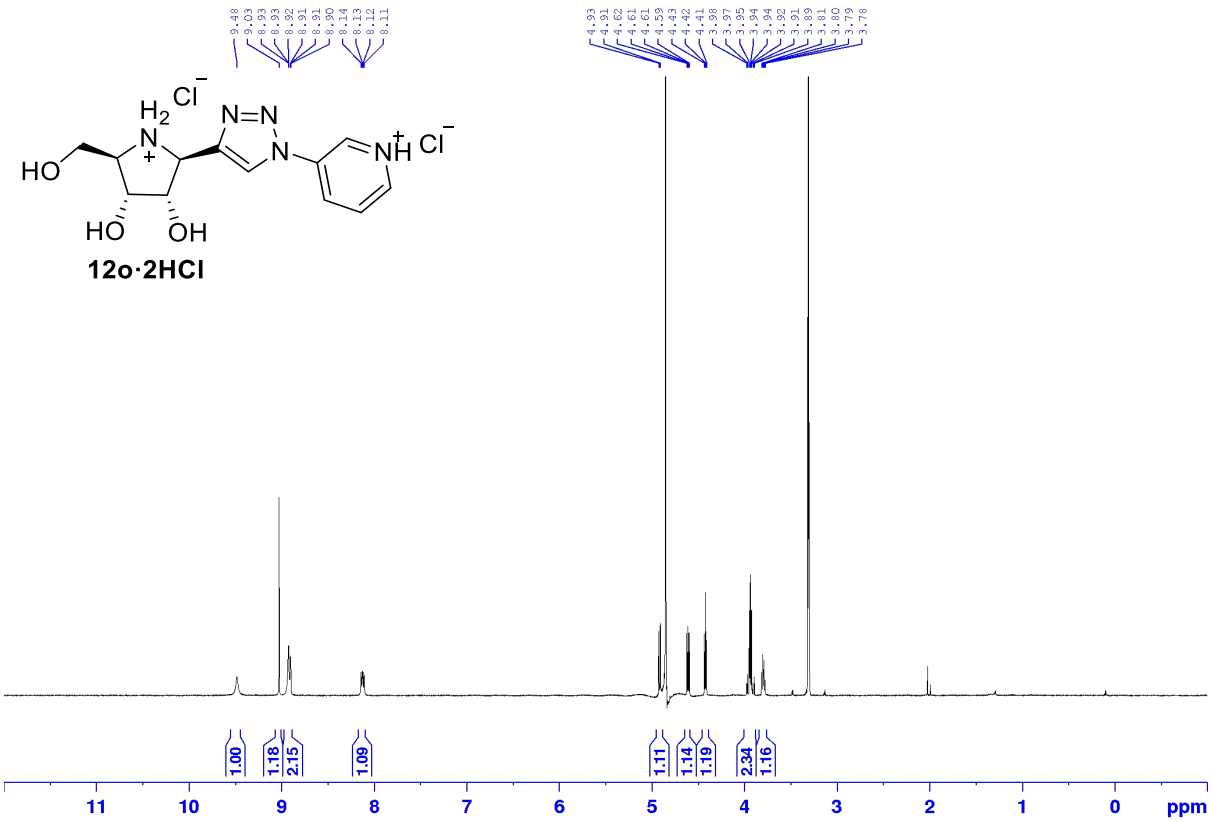
^{1}H NMR (400 MHz, DMSO-d_6)



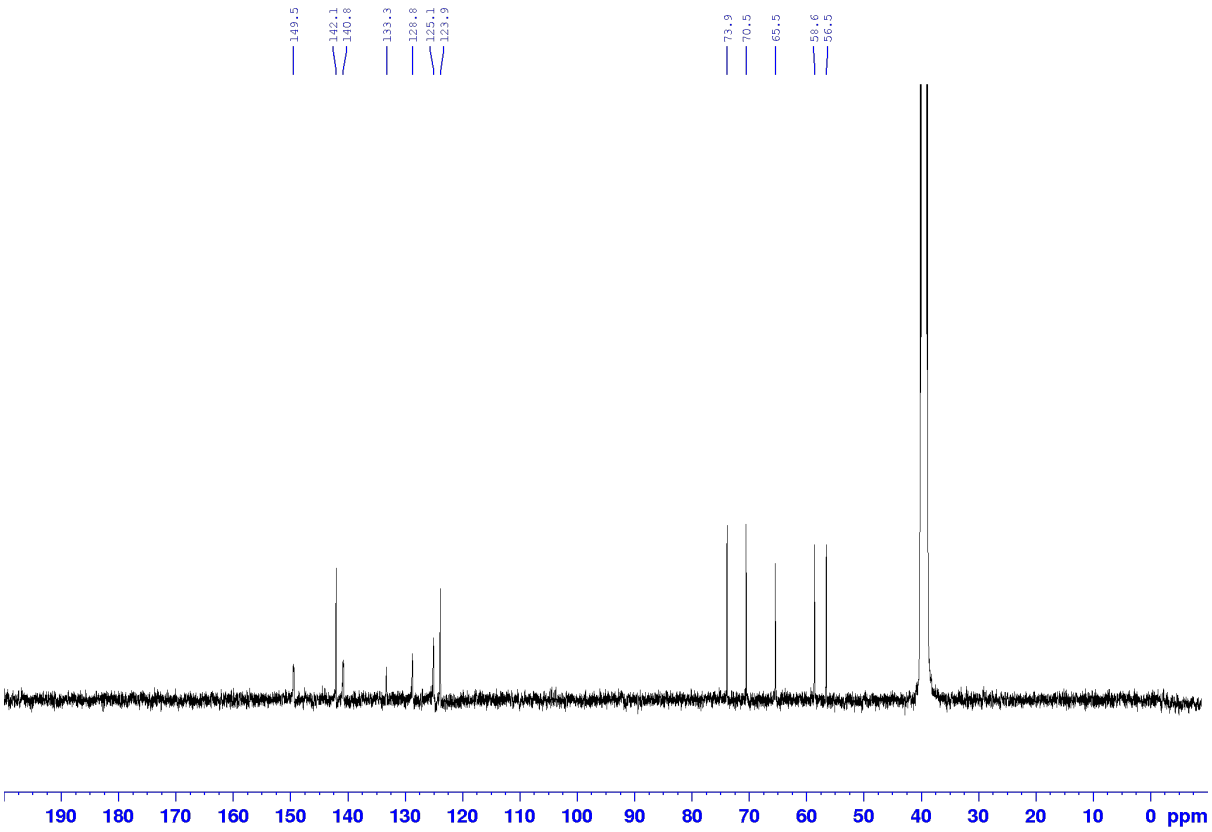
^{13}C NMR (100 MHz, DMSO-d_6)



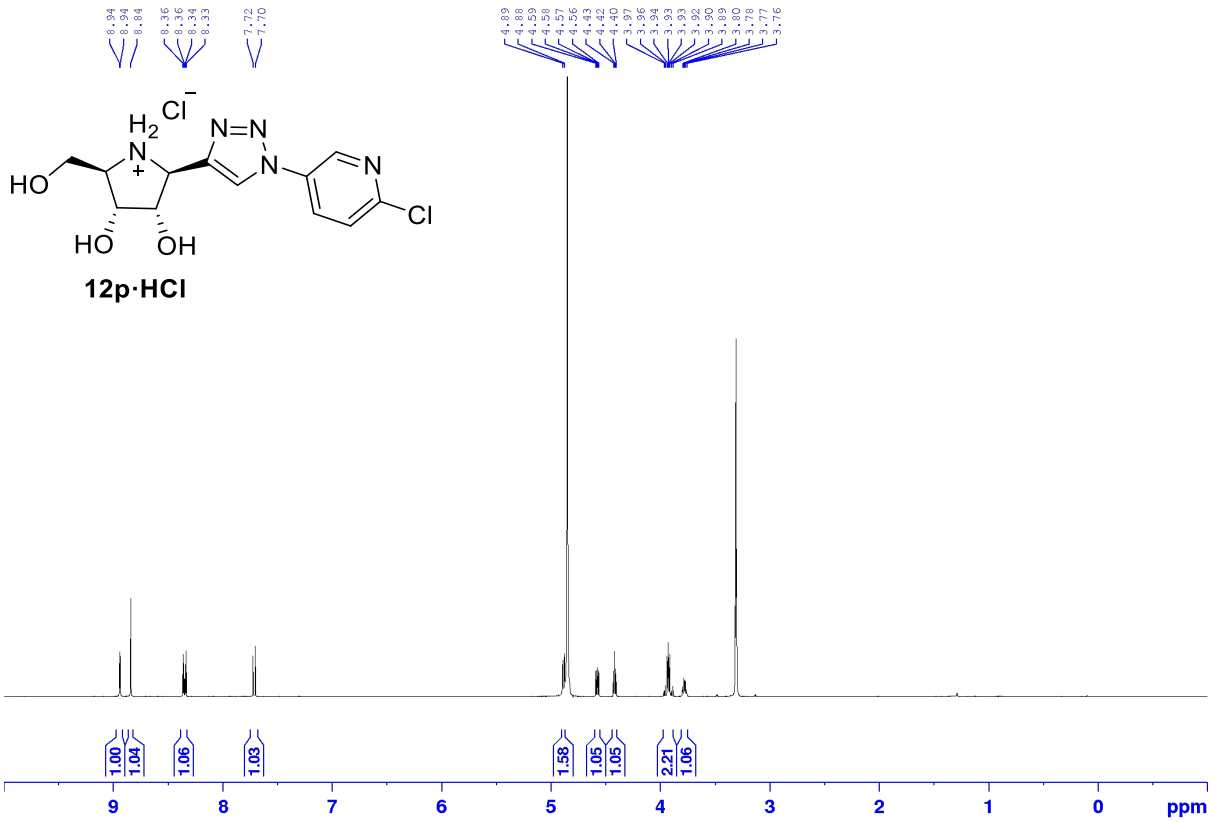
^{1}H NMR (400 MHz, CD_3OD)



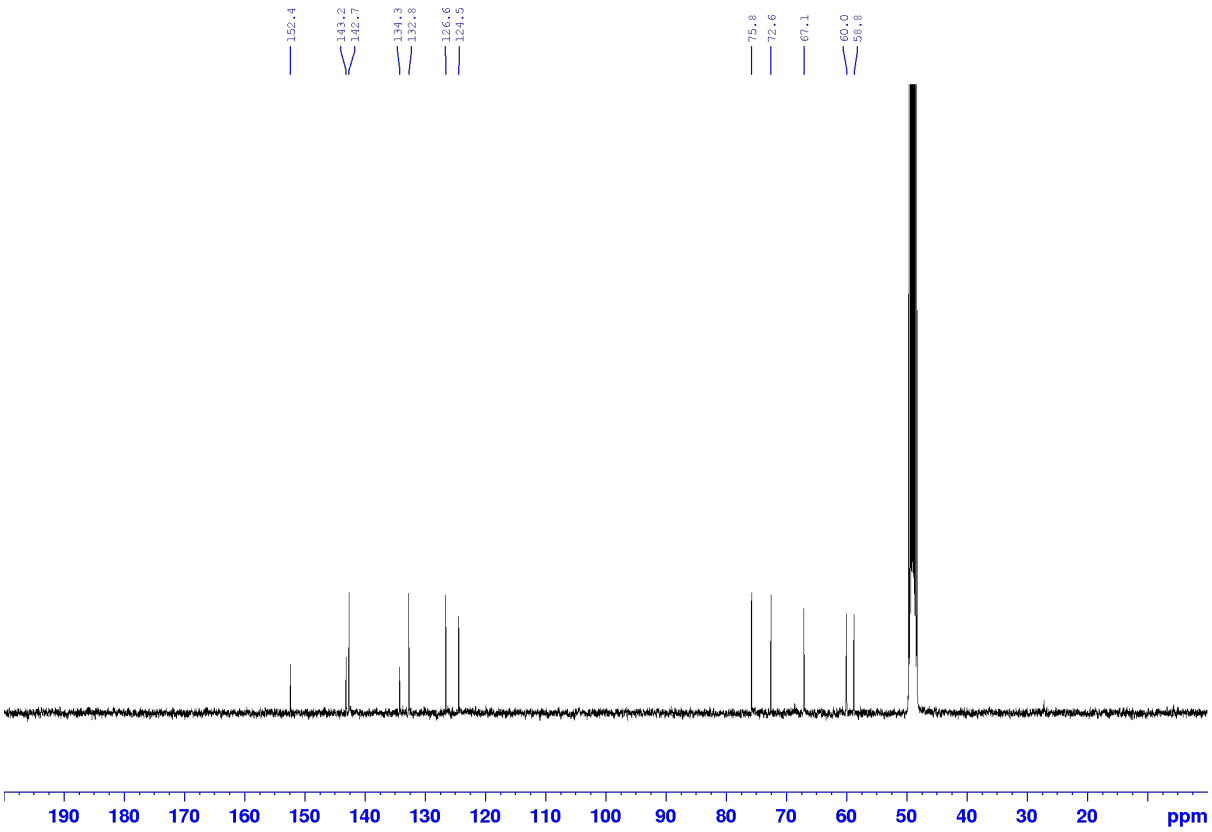
^{13}C NMR (100 MHz, DMSO-d_6)



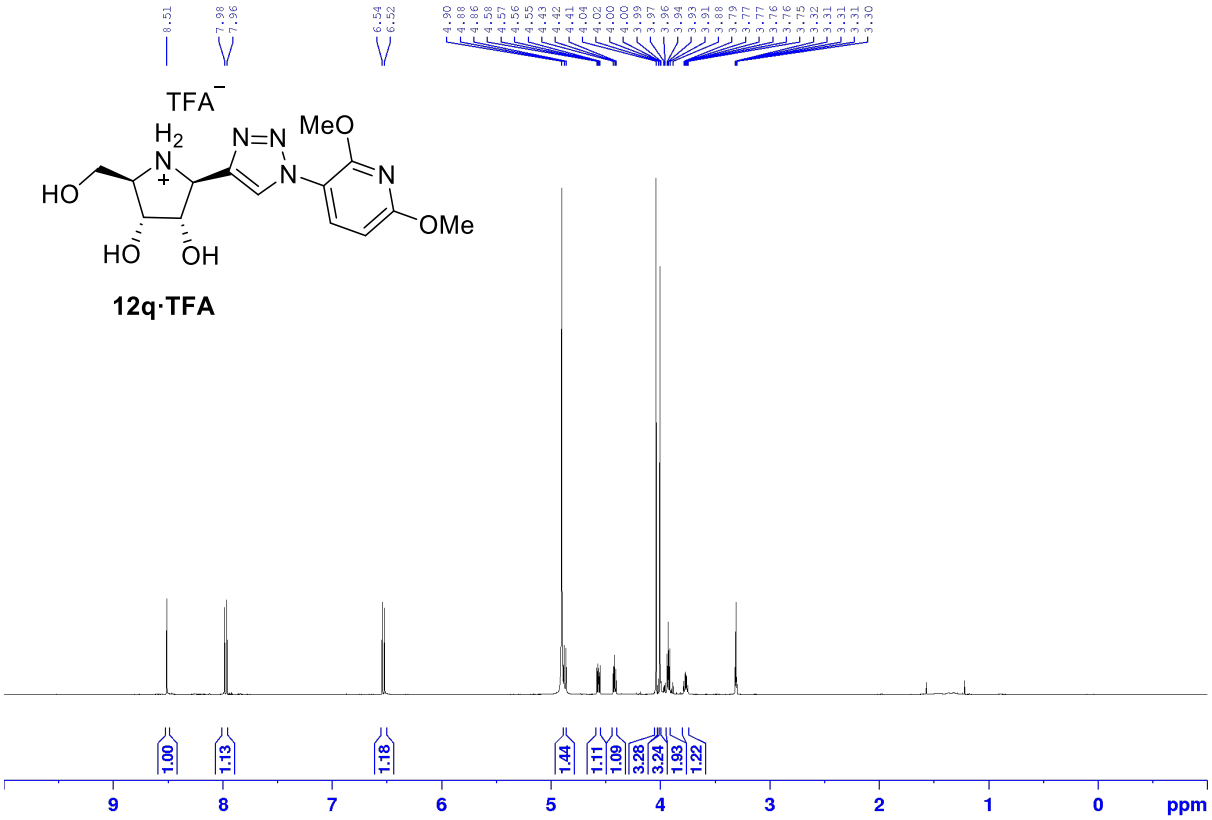
^{1}H NMR (400 MHz, CD_3OD)



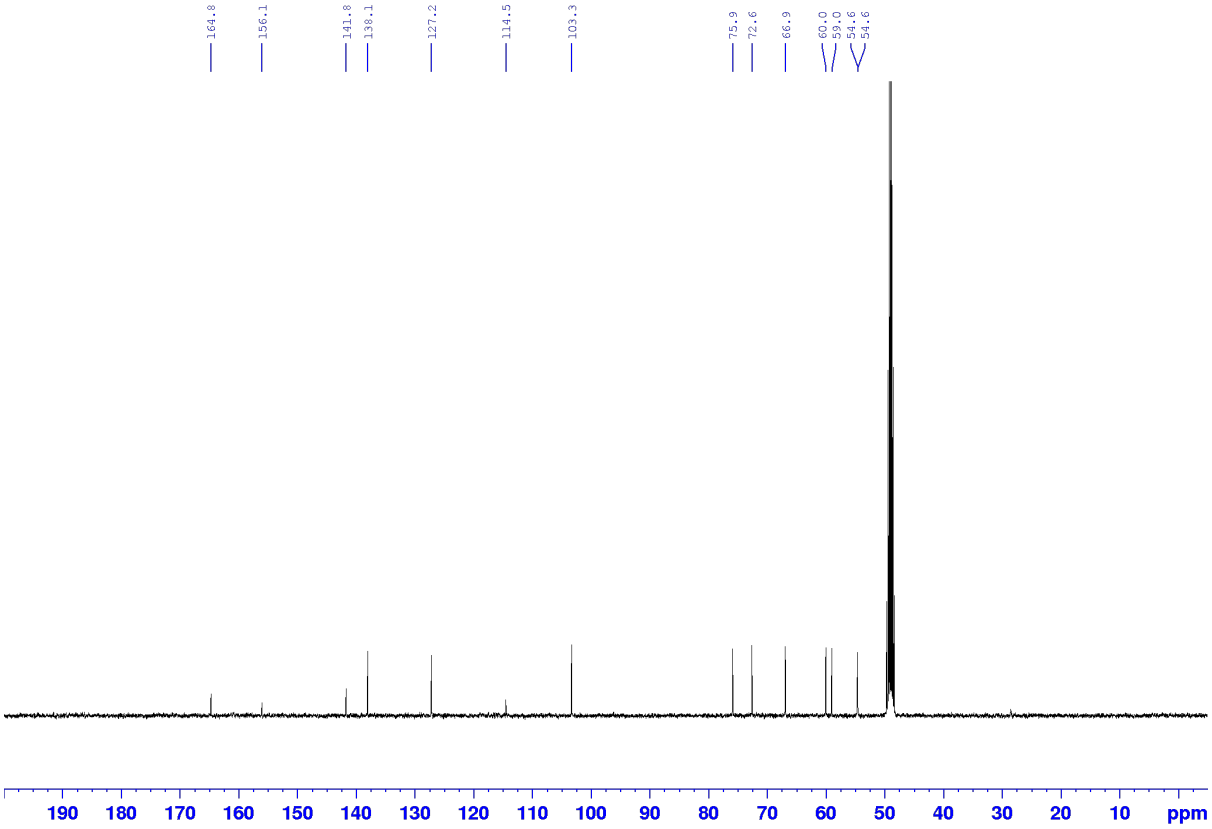
^{13}C NMR (100 MHz, CD_3OD)



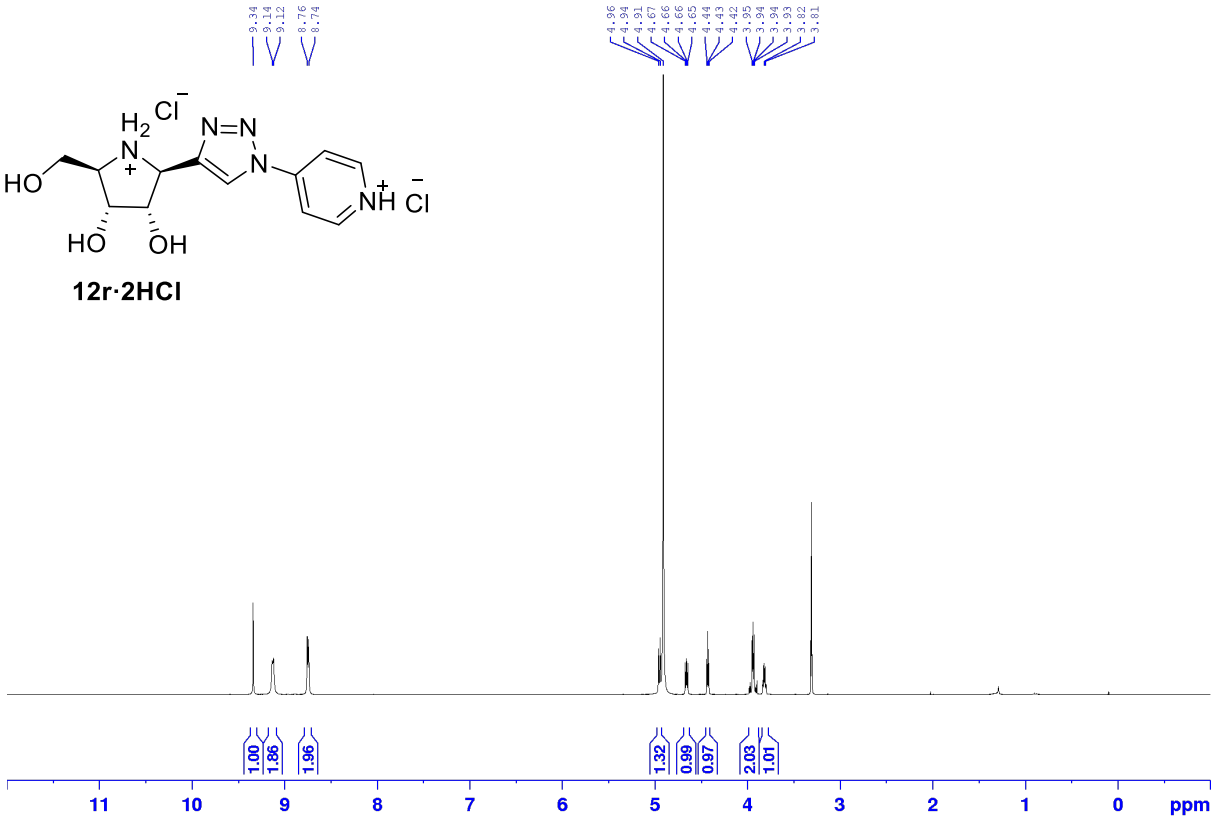
^{1}H NMR (400 MHz, CD_3OD)



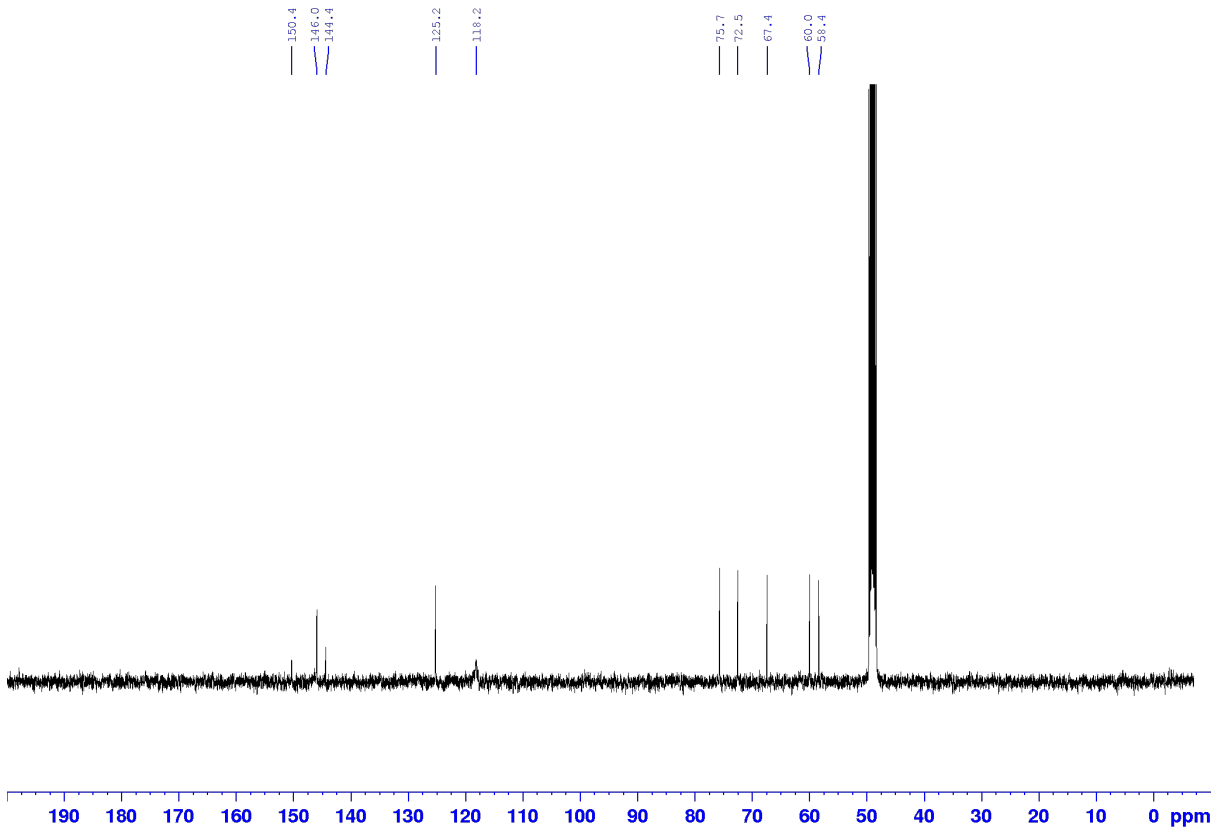
^{13}C NMR (100 MHz, CD_3OD)



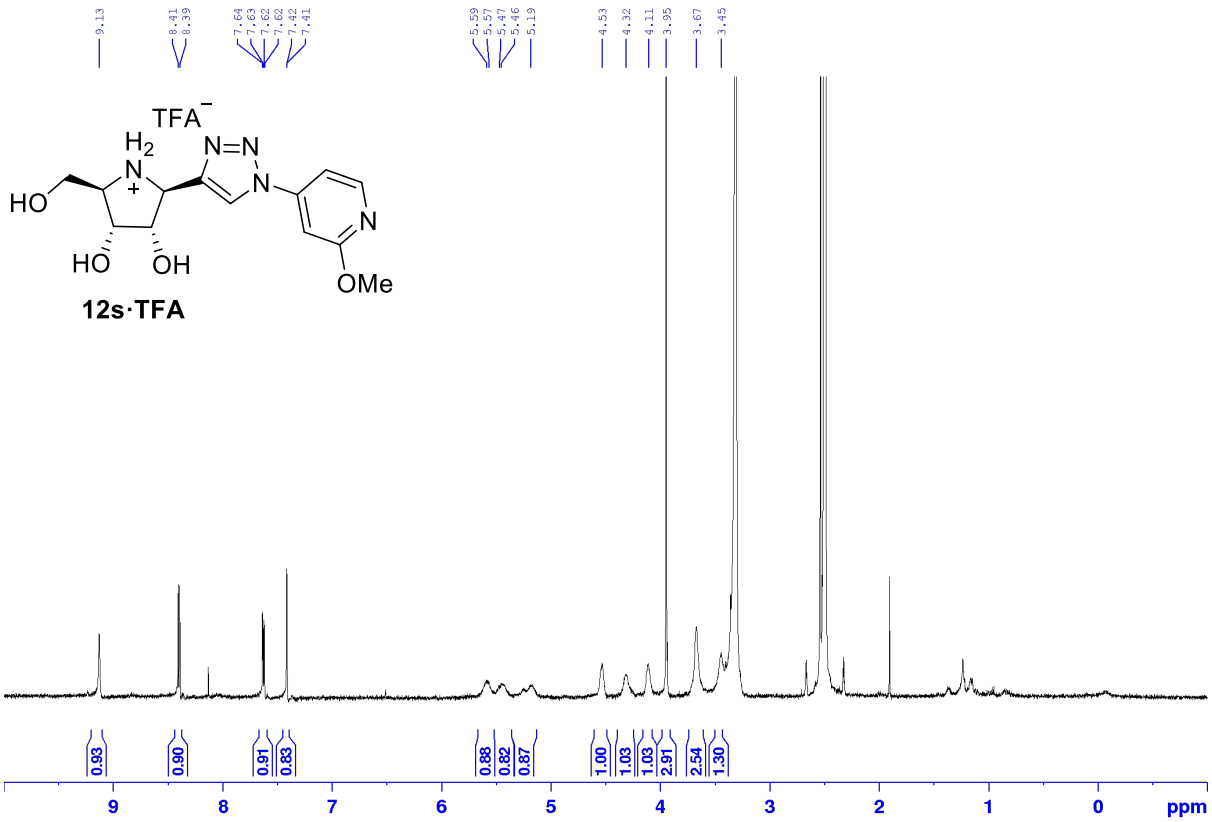
^{1}H NMR (400 MHz, CD_3OD)



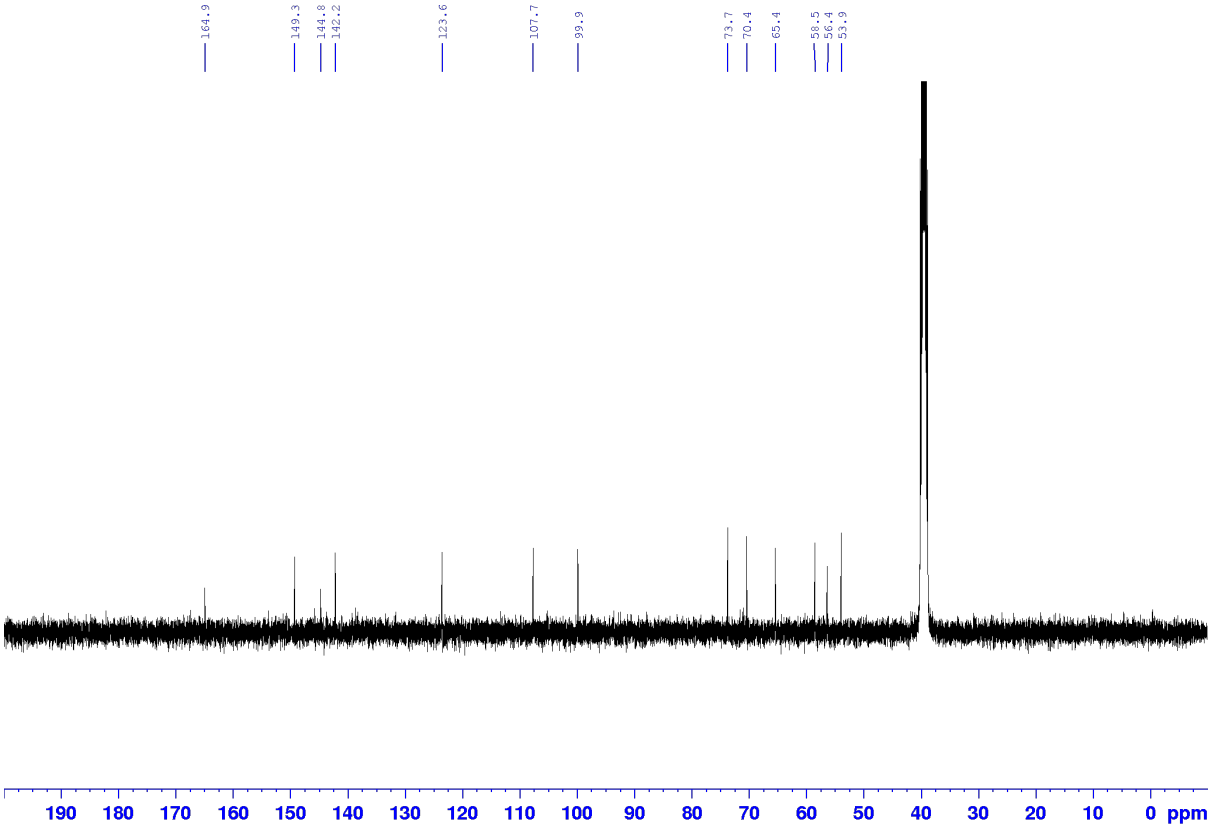
^{13}C NMR (100 MHz, CD_3OD)



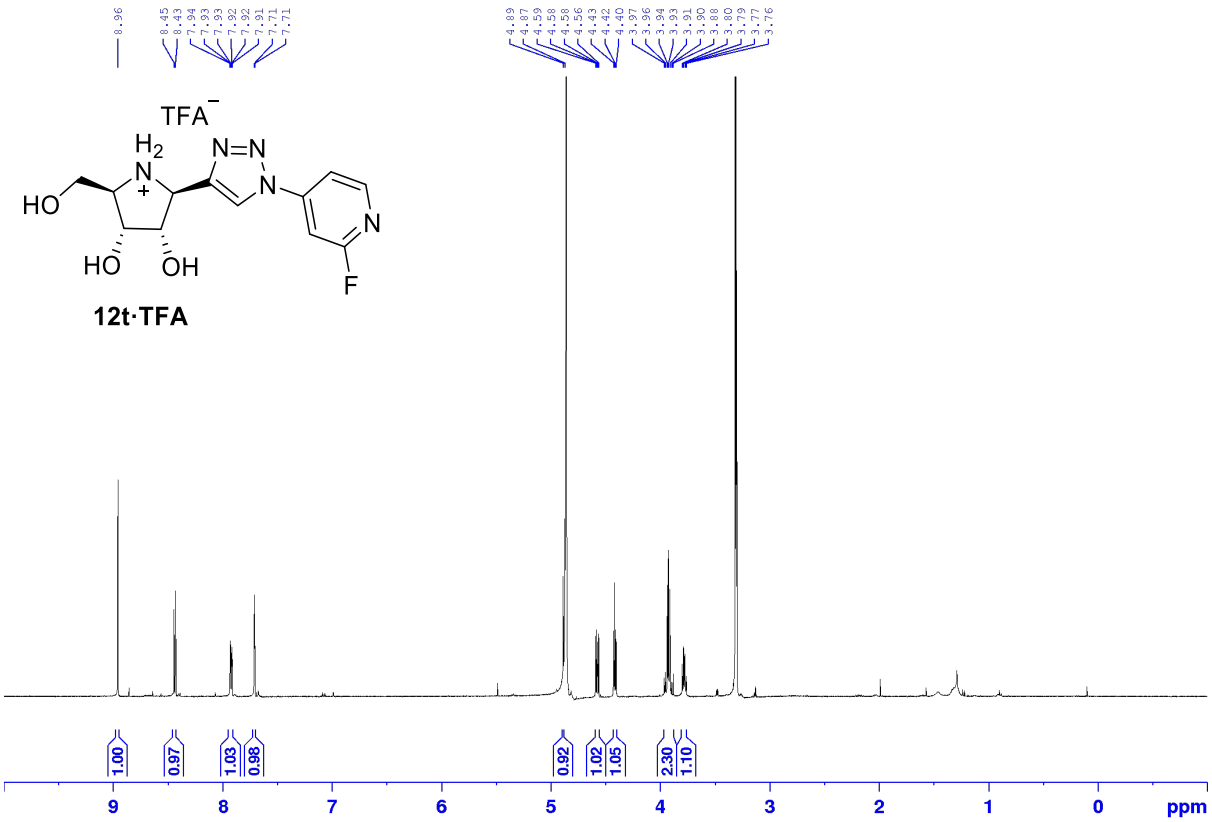
^{1}H NMR (400 MHz, DMSO-d_6)



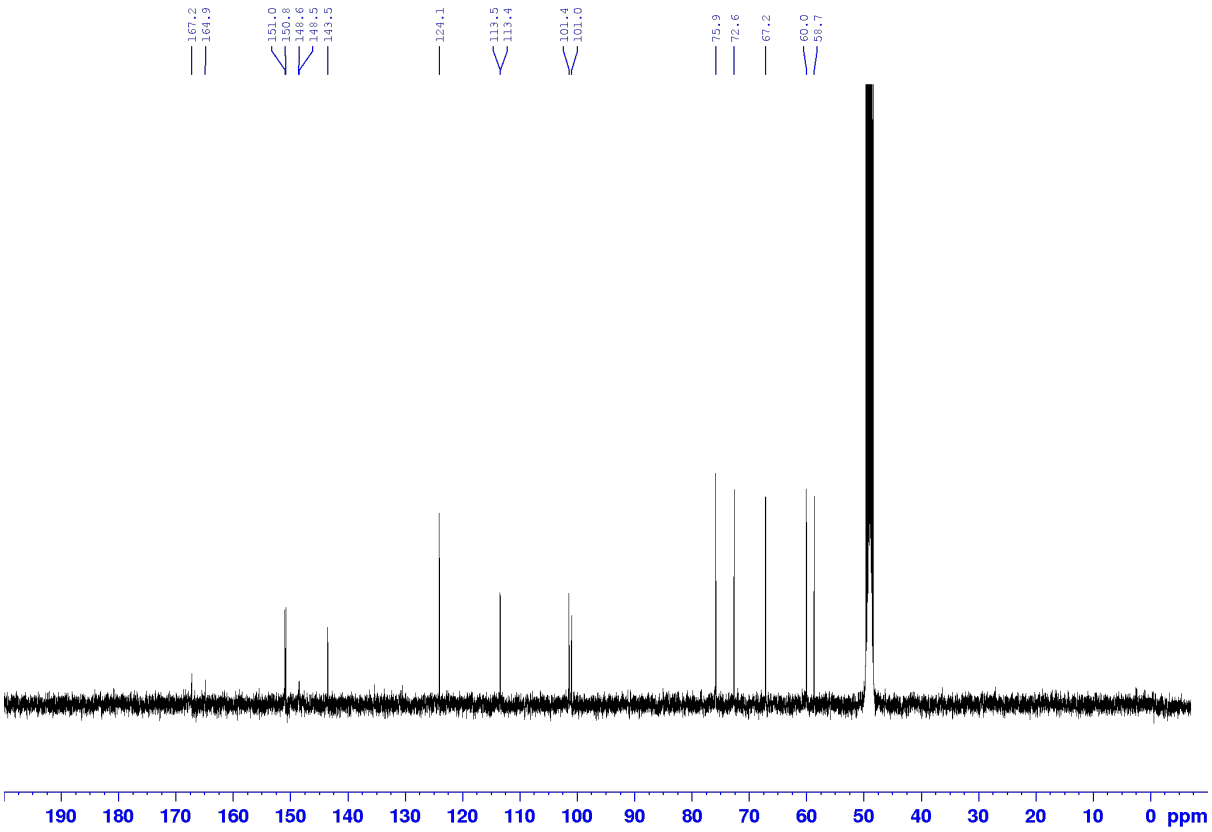
^{13}C NMR (100 MHz, DMSO-d_6)



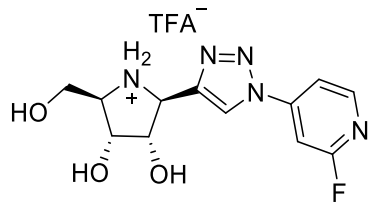
^{1}H NMR (400 MHz, CD_3OD)



^{13}C NMR (100 MHz, CD_3OD)

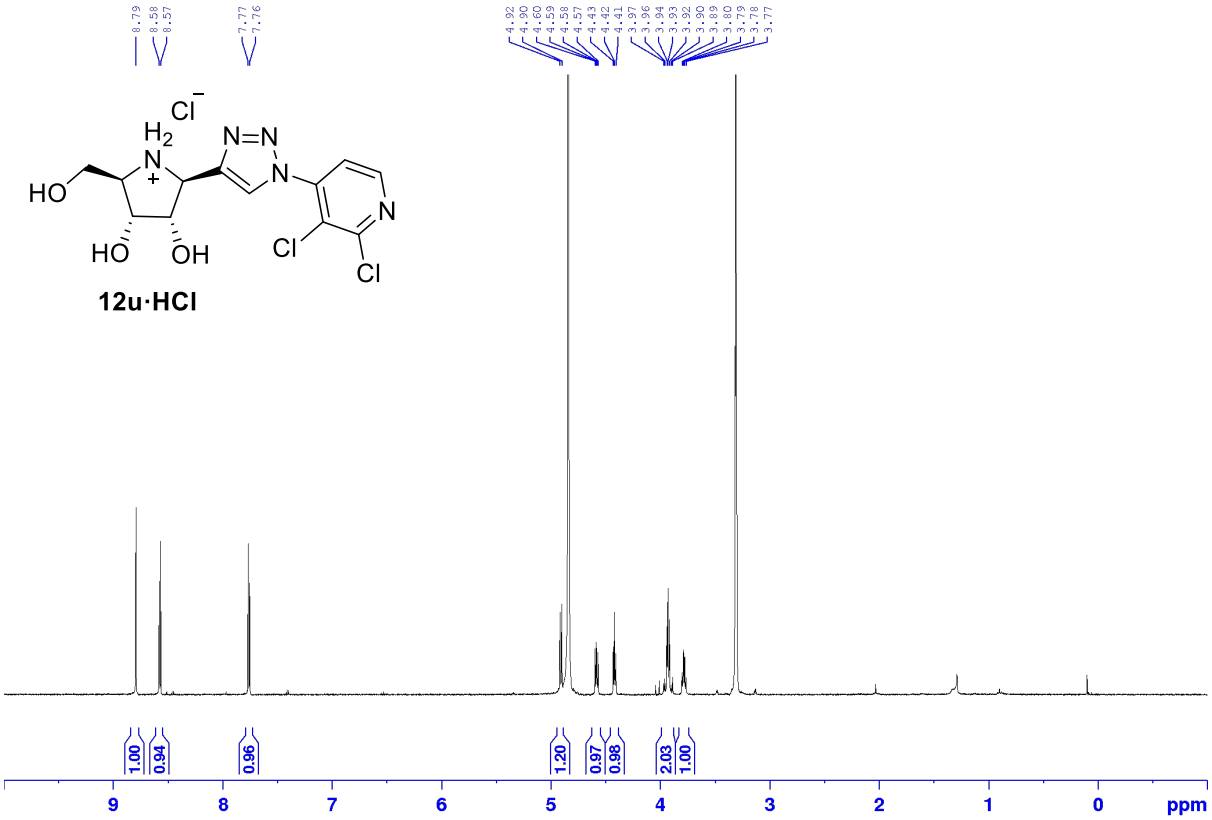


^{19}F NMR (376 MHz, CD_3OD)

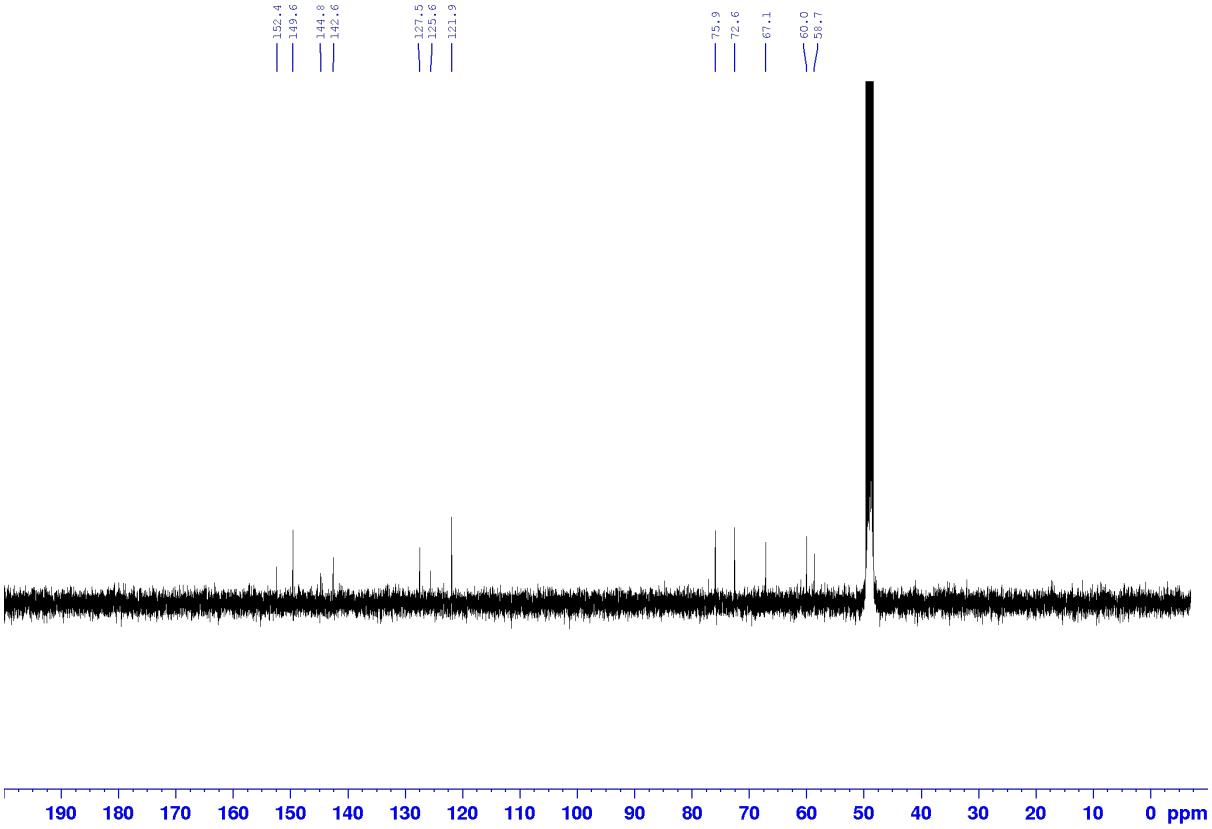


12t·TFA

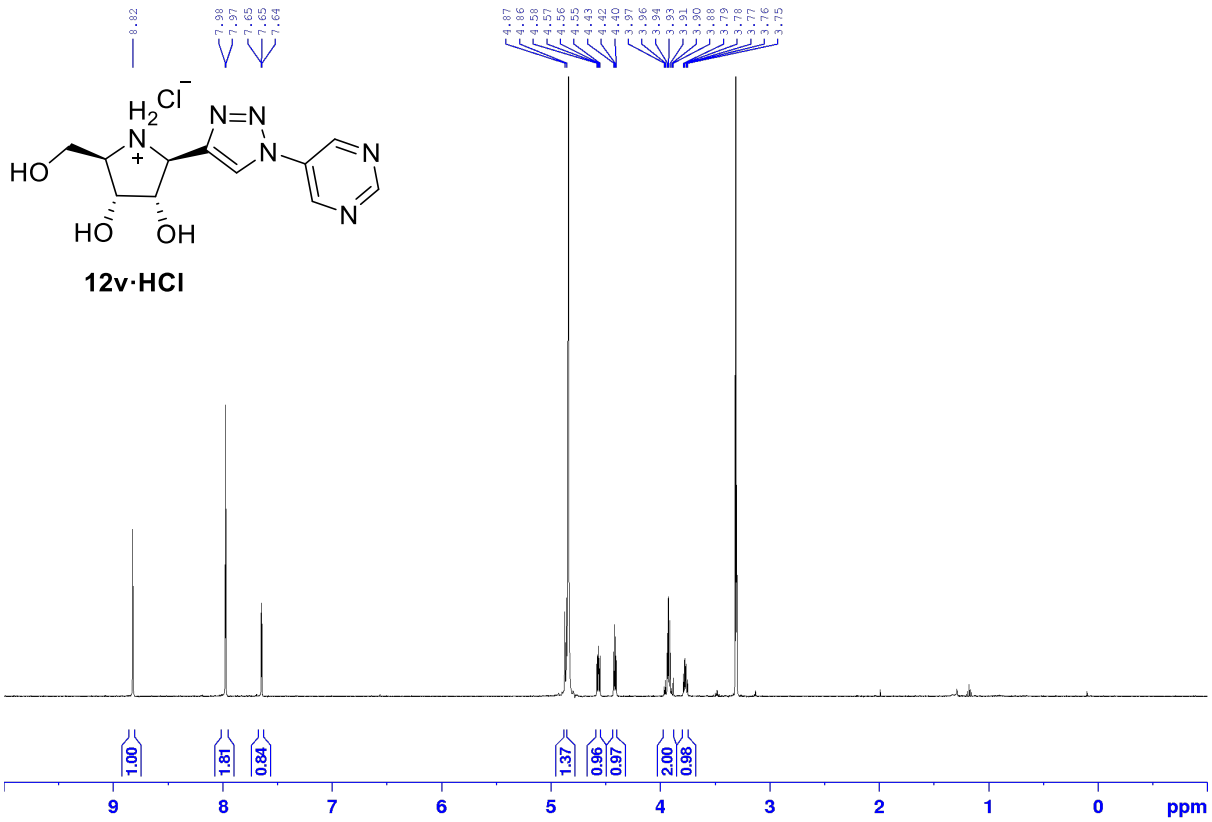
^{1}H NMR (400 MHz, CD_3OD)



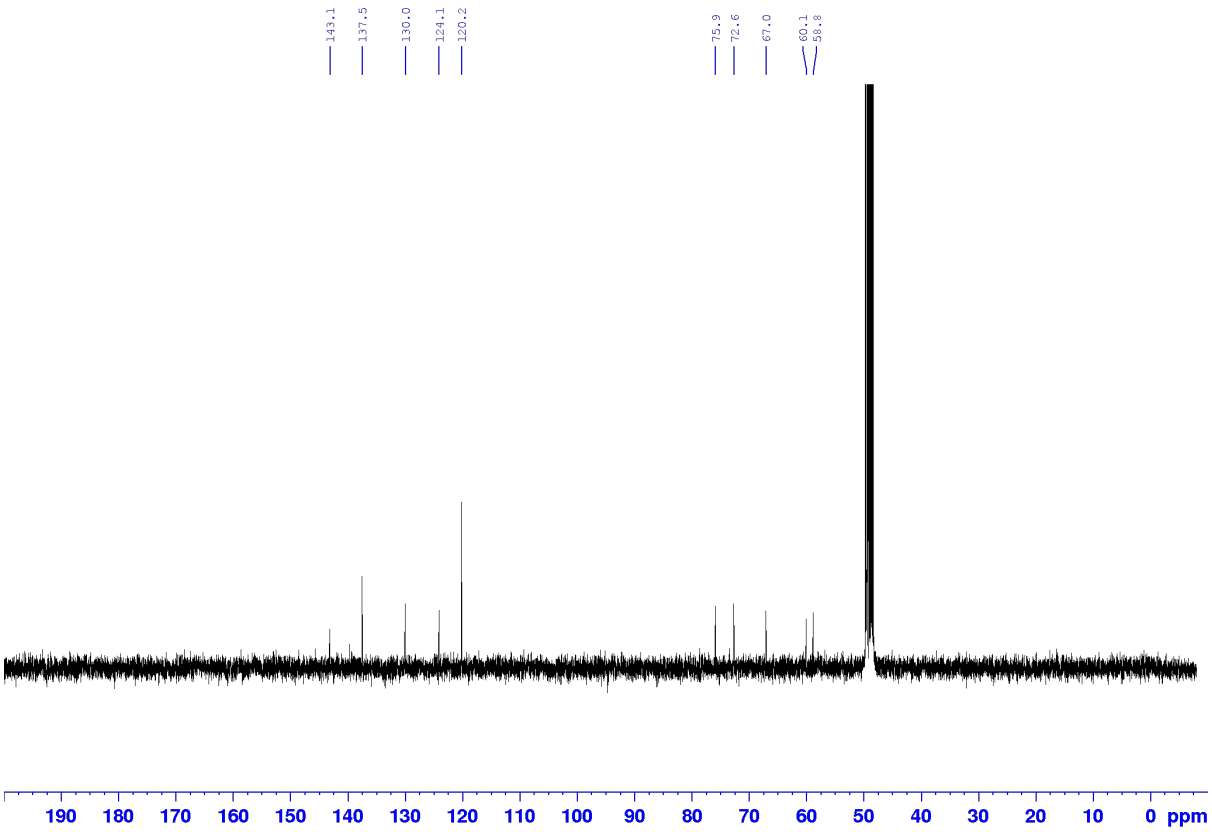
^{13}C NMR (100 MHz, CD_3OD)



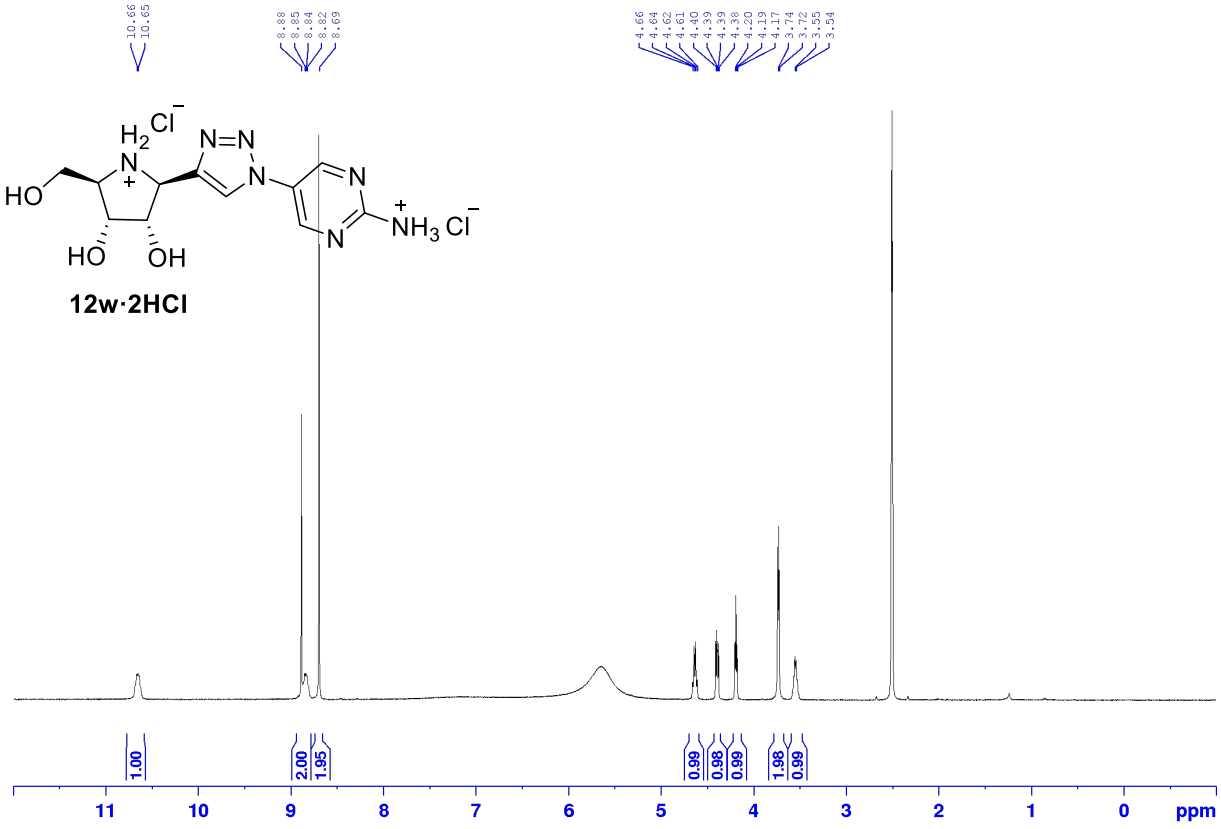
^{1}H NMR (400 MHz, CD_3OD)



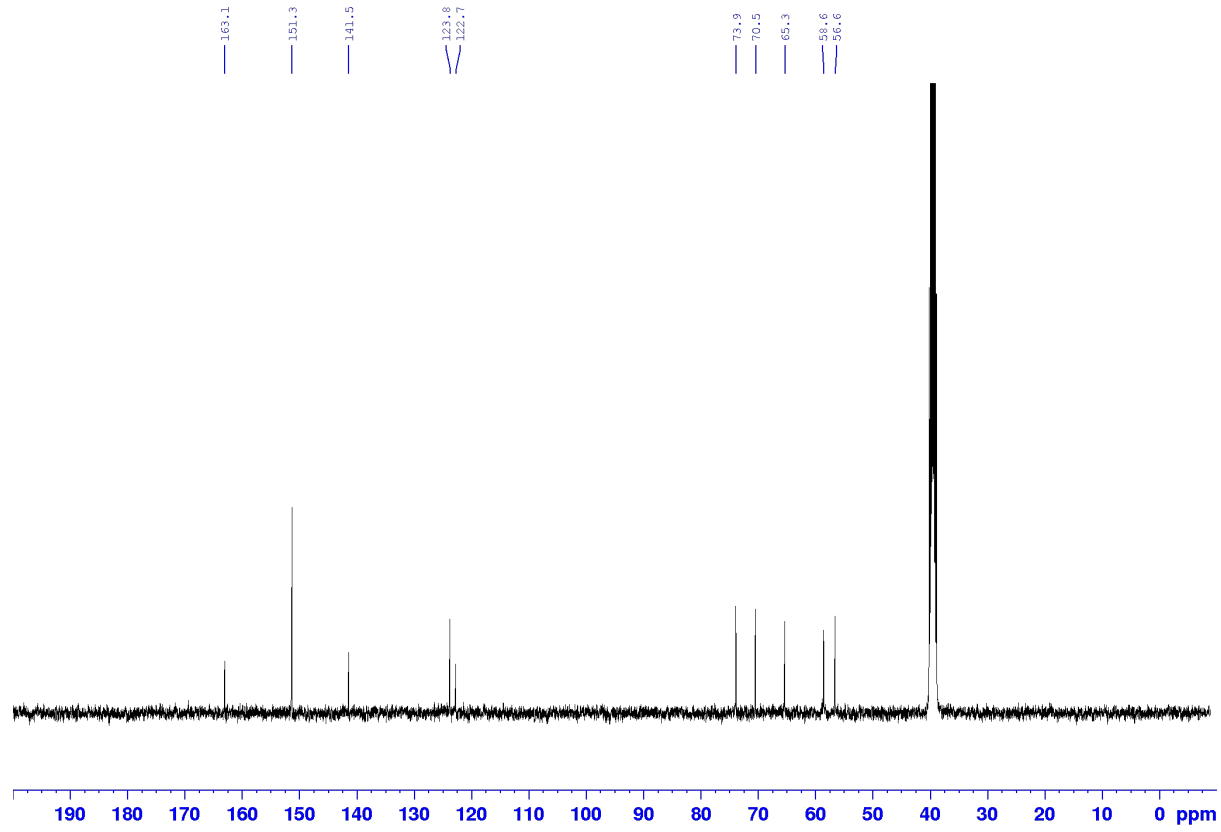
^{13}C NMR (100 MHz, CD_3OD)



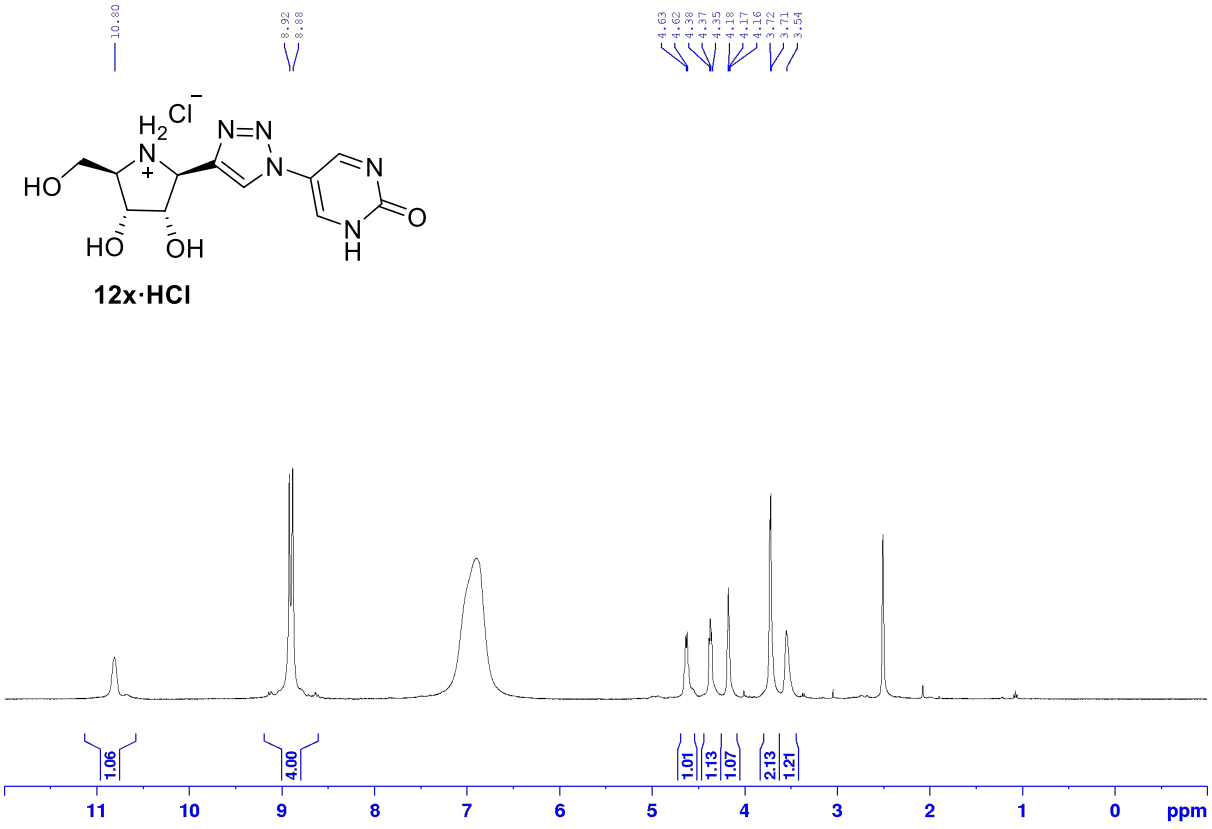
^{1}H NMR (400 MHz, DMSO-d_6)



^{13}C NMR (100 MHz, DMSO-d_6)

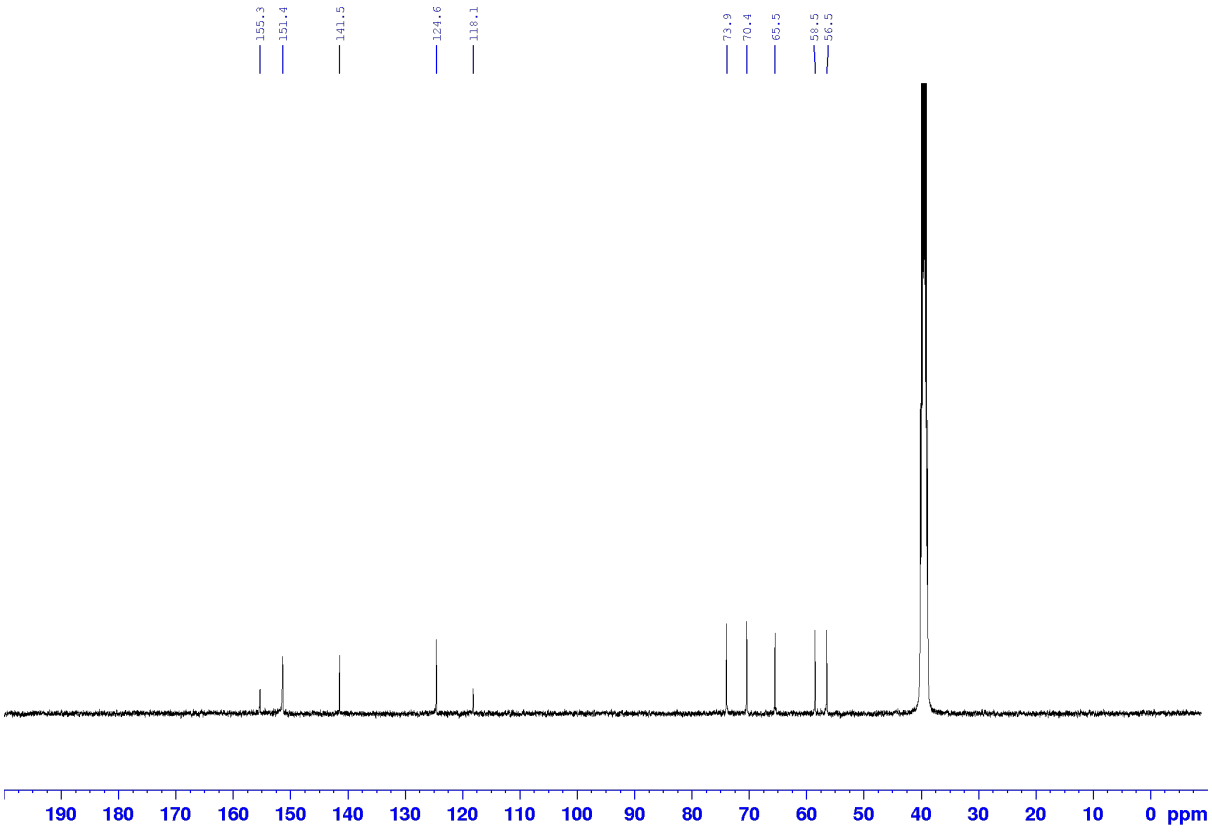


^{1}H NMR (400 MHz, DMSO-d_6)



12x·HCl

^{13}C NMR (100 MHz, DMSO-d_6)

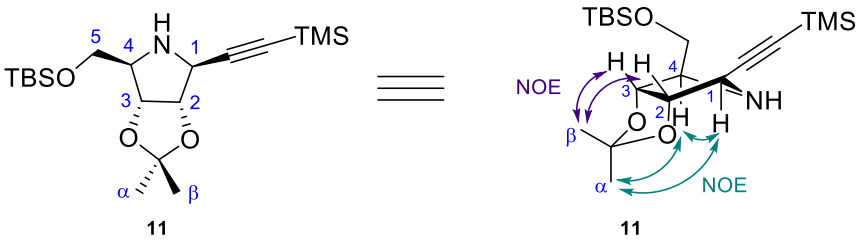


Assignment of the Pseudo-anomeric Position: Key NOESY correlations of **11**, **1** and **12f**

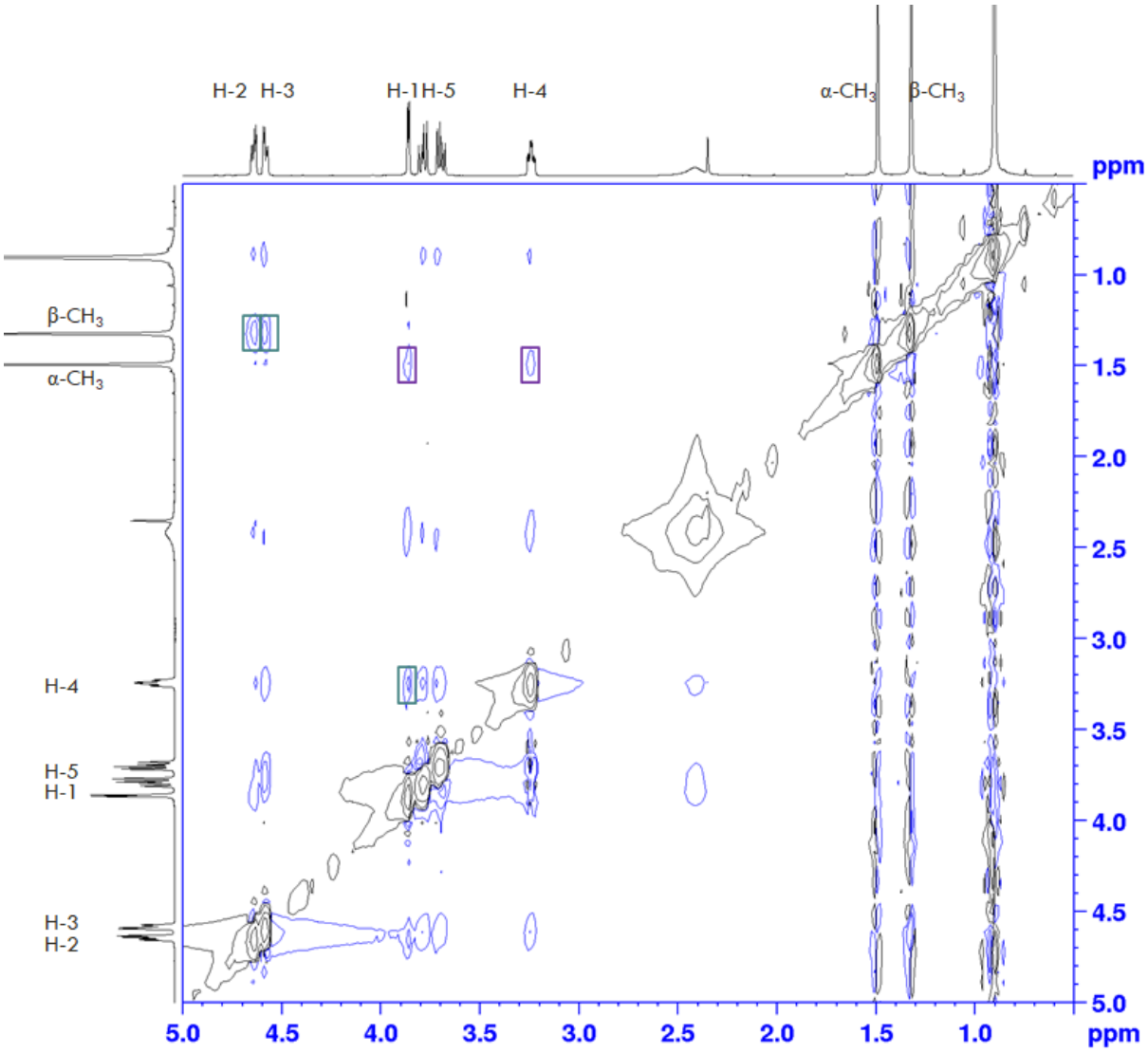
The relative stereochemistry of the key intermediates **11** and **1** were assigned by 2D NOESY experiments. Diagnostic NOE correlations reveal the 1,4-*cis* relationship of the iminoribitol scaffold, which corroborate with the formation of the β-pseudo-anomer.

Transformations to nucleoside analogue **12f** expectedly did not affect the previously set C-1 stereocentre. This was confirmed by observation of the H-1 to H-4 NOE correlation. By analogy, final nucleoside analogues **12a-12x** are also expected to possess the same stereochemistry.

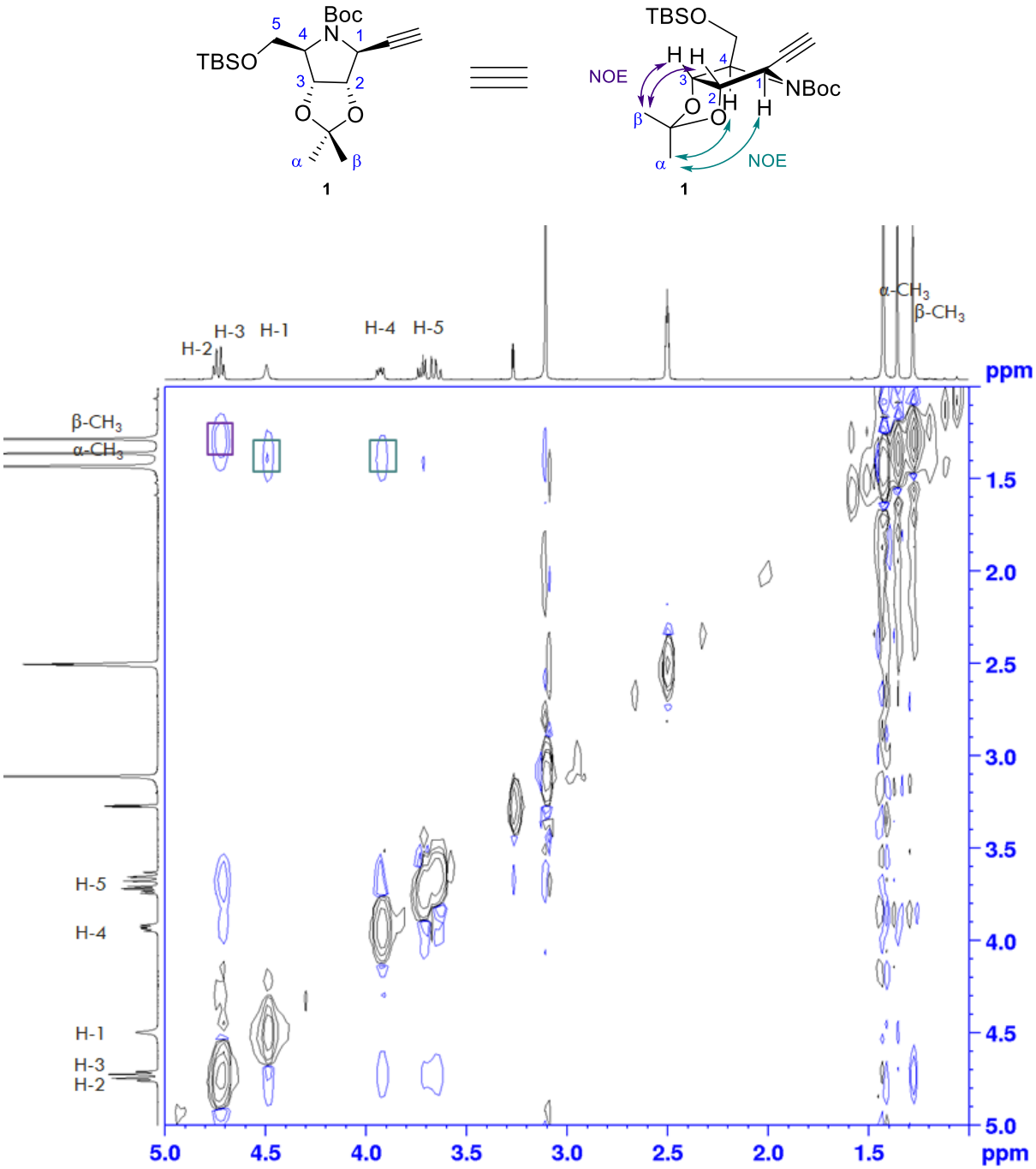
NOESY (CD_3Cl, 400 MHz, 298 K) of **11**:



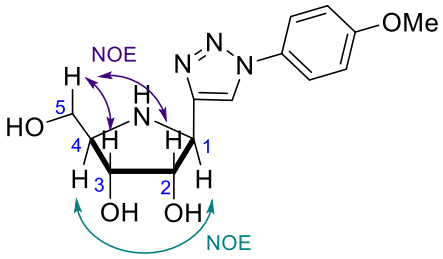
11 **11**



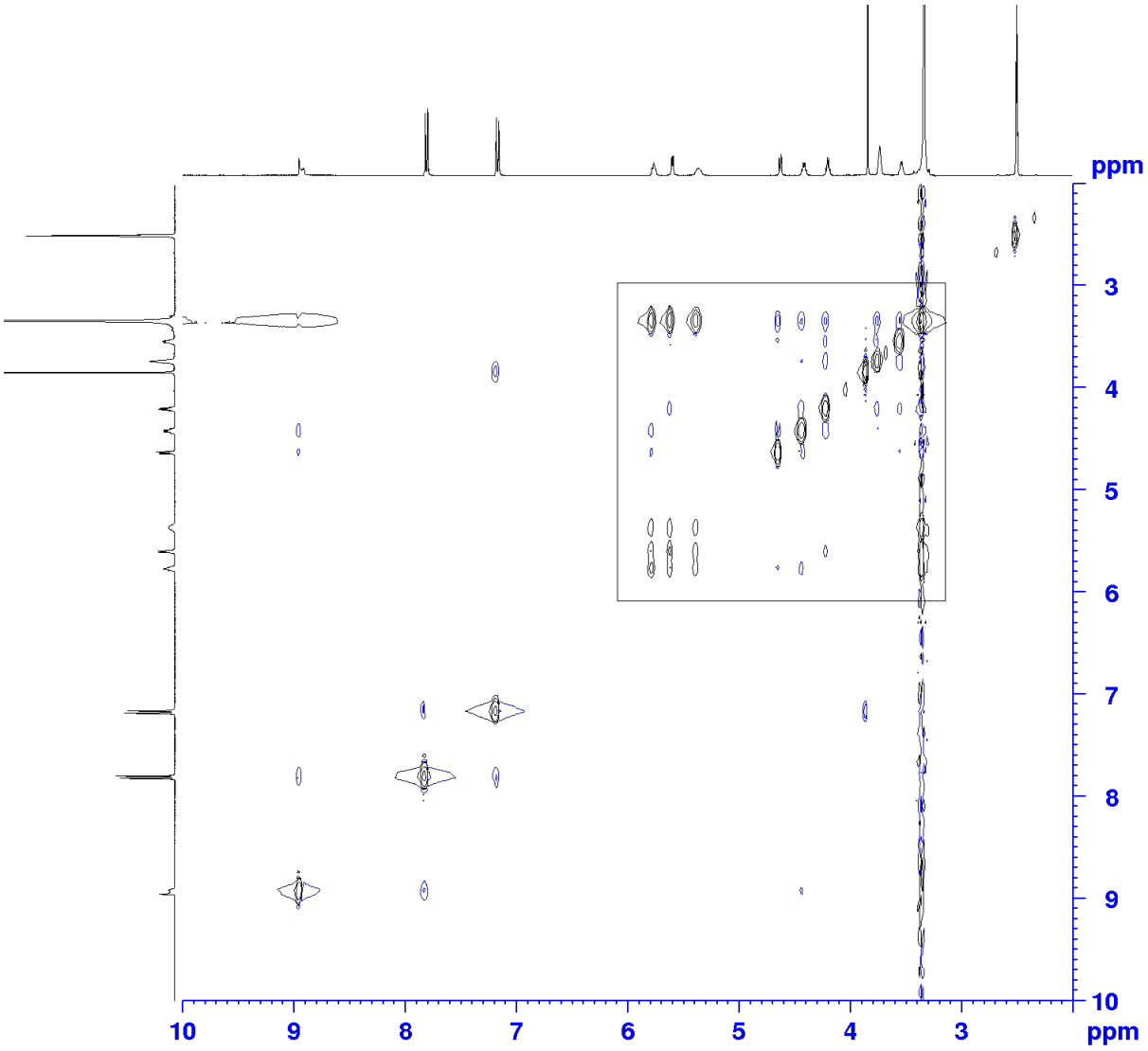
NOESY (DMSO-d_6, 400 MHz, 343 K) of **1**:



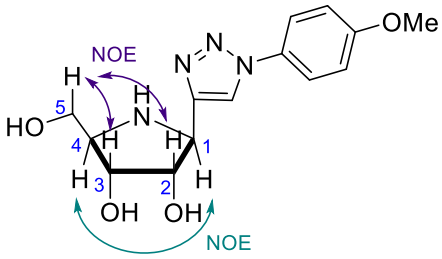
NOESY (DMSO-d_6, 400 MHz, 298 K) of **12f**:



12f



NOESY (DMSO-d_6, 400 MHz, 298 K) of **12f**:



12f