

Supporting Information (SI) for:

**Conformational promiscuity in triazolamers derived from quaternary amino acids
mimics peptide behaviour**

Jordi Solà,^{a,*} Michael Bolte,^b and Ignacio Alfonso^{a,*}

Dr. J. Solà. Dr. I. Alfonso
Department of Biological Chemistry and Molecular Modelling. Institute of Advanced
Chemistry of Catalonia, IQAC-CSIC
Jordi Girona 18-26, 08034. Barcelona, Spain.
Fax: (+34)932045904
E-mail: jordi.sola@iqac.csic.es; ignacio.alfonso@iqac.csic.es.

Dr. M. Bolte Institut für Anorganische Chemie, J.-W.-Goethe-Universität
Max-von-Laue-Str.7, D-60438
Frankfurt/Main (Germany)

1. General Methods.....	S3
2. Synthesis of oligomers	S4
3. ¹ H and ¹³ C NMR spectra	S23
4. Figures	S45

GENERAL METHODS

Reagents and solvents were purchased from commercial suppliers (Aldrich, Fluka or Merck) and were used without further purification. Flash chromatographic purifications and were performed using Silica 60 Å 35-70 µm Chromagel (SDS). TLCs were performed using 6x3 cm SiO₂ pre-coated aluminium plates (ALUGRAM® SIL G/UV254).

Nuclear Magnetic Resonance (NMR) spectroscopic experiments were carried out on a Varian INOVA 500 spectrometer or in a Varian Mercury 400 instrument. The chemical shifts are reported in ppm relative to trimethylsilane (TMS), and coupling constants (*J*) are reported in Hertz (Hz).

High Resolution Mass Spectrometry (HRMS) analyses were carried out at the IQAC Mass Spectrometry Facility, using a UPLC-ESI-TOF equipment: [Acquity UPLC® BEH C18 1.7 mm, 2.1x100 mm, LCT Premier Xe, Waters]. (CH₃CN + 20 mM HCOOH and H₂O + 20 mM HCOOH) mixtures at 0.3 mL/min were used as mobile phase.

Optical rotation data were recorded on Perkin-Elmer Polarimeter-341

X-ray crystallographic analysis Crystal Structure Analyses: Data were collected on a STOE IPDS II two-circle diffractometer with a Genix Microfocus tube with mirror optics using MoK α radiation ($\lambda = 0.71073$ Å). The data were scaled using the frame scaling procedure in the X-AREA program system.¹ The structure was solved by direct methods using the program SHELXL.²

CCDC numbers for the crystal structures: CCDC 1406855 (**8a**), 1406856 (**10c**)

¹ Stoe & Cie. X-AREA. *Diffractometer control program system*; Stoe & Cie: Darmstadt. Germany, 2002.

² G. M. Sheldrick, *Acta Crystallogr., Sect. A* 2008, **64**, 112-122.

Synthesis of oligomers.

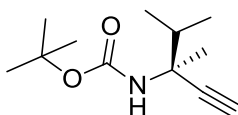
Synthesis of *tert*-butyl N-(2-methylbut-3-yn-2-yl)carbamate 1a.

This compound was synthesised from commercially available 2-Methyl-3-butyn-2-amine and Boc₂O according to a known procedure.³

¹H-NMR (400 MHz, CDCl₃): δ 4.68 (brs, 1H), 2.29 (s, 1H), 1.58 (s, 6H), 1.45 (s, 9H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 146.9 (CO), 87.6 (C), 85.3 (C), 68.8 (CH), 47.1 (C), 28.5 (CH₃), 27.6 (CH₃) ppm.

Synthesis of alkyne 1b.



a) *Synthesis of N-Boc (L)-Methylvalinol.* To an ice-cooled solution of methylvalinol⁴ (250 mg, 2.13 mmol) in 15 mL of dry dichloromethane, 700 mg (3.2 mmol) of Di-*tert*-butyl-dicarbonate were added followed by 0.45 mL (3.2 mmol) of trimethylamine. The mixture was stirred overnight diluted with 25 mL of dichloromethane and washed with a saturated solution of NaHCO₃ (2x10 mL). The organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:Hexane 20:80) to yield 325 mg (1.50 mmol, 70%) of the title compound as pale yellow oil.

¹H-NMR (400 MHz, CDCl₃): δ 4.60 (brs, 1H), 3.73 (dd, *J*= 11.8, 7.9 Hz, 1H), 3.63 (dd, *J*= 11.8, 4.7 Hz, 1H), 2.32 (hept, *J*= 6.9 Hz, 1H), 1.43 (s, 9H), 1.00 (s, 3H), 0.93 (d, *J*= 7.0 Hz, 3H), 0.90 (d, *J*= 7.1 Hz, 3H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 156.7 (C), 80.0 (C), 68.9 (CH₂), 60.1 (C), 31.1 (CH), 28.5 (CH₃), 18.5 (CH₃), 17.4 (CH₃), 16.9 (CH₃) ppm.

MS (ESI⁺) *m/z*= 457 ([2M+Na]⁺, 100%); 240 ([M+Na]⁺, 50%).

HRMS: Calc. for C₁₁H₂₃NO₃ + Na⁺: 240.1576, found 240.1495.

³ C. Francavilla, E.Low, S.Nair, B. Kim, T. P. Shiau, D. Debabov, C. Celeri, N. Alvarez, A. Houchin, P. Xu, R. Najafi, R. Jain. *Bioorg. Med. Chem. Lett.* 2009, **19**, 2731–2734

⁴ WO2010019203A1, 2010

b) *Synthesis of N-Boc (L)-Methylvalinal*

430 mg (1.97 mmol) of N-Boc (L)-Methylvalinol were dissolved in 30 mL of dry dichloromethane. 1.0 g (2.36 mg) of Dess-Martin periodinane was added dropwise and the mixture stirred for 6h. Upon completion (TLC monitoring) the sample was diluted to 60 mL of dichloromethane, washed with saturated NaHCO₃ (2x10 mL) and brine (10 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:Hexane 10:90 to 20:80) to yield 400 mg (1.86 mmol, 95%) of the aldehyde as a pale yellow oil that crystallises on standing.

¹H-NMR (400 MHz, CDCl₃): δ 9.49 (s, 1H), 4.97 (s, 1H), 2.10 (brm, 1H), 1.44 (s, 9H), 1.34 (s, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 201.8 (CHO), 155.1 (C), 80.2 (C), 64.5 (C), 33.2 (CH), 28.4 (CH₃), 17.2 (CH₃), 17.0 (CH₃), 16.8 (CH₃) ppm.

MS (ESI⁺) *m/z* = 453 ([2M+Na]⁺, 100%); 238 ([M+Na]⁺, 30%).

HRMS: Calc. for C₁₁H₂₁NO₃ + Na⁺: 238.1419, found 238.1404.

c) *Synthesis of 1b*.

200 mg of N-Boc (L)-Methylvalinal (0.93 mmol) were dissolved in 2.5 mL of methanol. 255 mg of K₂CO₃ were then added followed by 170 μL of Bestman-Ohira reagent (1.12 mmol). The mixture was stirred at room T until no SM could be detected (TLC monitoring, 22h). The reaction was quenched with 1 mL of water and diluted with 40 mL of ethyl acetate, washed with saturated NaHCO₃ (10 mL) and brine (10 mL). The organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:Hexane 5:95 to 10:90) to yield 190 mg (0.90 mmol, 97%) of the alkyne as yellowish oil.

[α]²⁰_D = +0.80 (c = 1.0, CHCl₃)

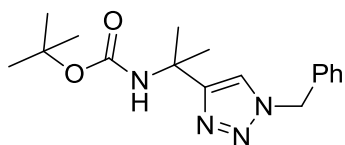
¹H-NMR (400 MHz, CDCl₃): δ 4.68 (s, 1H), 2.30 (s, 1H), 2.27 (hep, *J* = 6.8 Hz, 1H), 1.53 (s, 3H), 1.43 (s, 9H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 154.2 (C), 85.5 (C), 79.6 (C), 70.9 (CH), 55.2 (C), 35.4 (CH), 28.5 (CH₃), 24.3 (CH₃), 17.9 (CH₃), 17.4 (CH₃) ppm.

MS (ESI⁺) *m/z* = 445 ([2M+Na]⁺, 100%); 234 ([M+Na]⁺, 40%).

HRMS: Calc. for C₁₂H₂₁NO₂ + Na⁺: 234.1417, found 234.1459.

Synthesis of triazole monomer 3a



tert-butyl N-(2-methylbut-3-yn-2-yl)carbamate (530 mg, 2.89 mmol) was dissolved in 10 mL of H₂O.THF (1:1). 420 mg (3 mmol) of benzyl azide were added followed by 90 mg (0.6 mmol) of CuSO₄·5H₂O and 1.2 g (6 mmol) of sodium ascorbate. The resulting solution was stirred at room temperature overnight under a nitrogen atmosphere. Upon completion (TLC monitoring) 30 mL of brine were added and the mixture extracted with dichloromethane (3x30 mL). The organic extracts were combined and dried with Na₂SO₄, filtered and concentrated *in vacuo*. The resulting crude was purified by column chromatography (SiO₂, EtOAc:hexane 2:8 to 1:1) to yield 890 mg (2.81 mmol, 97%) of the title compound as white solid.

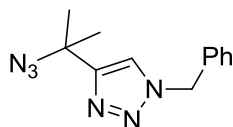
¹H-NMR (400 MHz, CDCl₃): δ 7.40 – 7.31 (m, 3H), 7.26 – 7.21 (m, 2H), 5.49 (s, 2H), 5.15 (s, 1H), 1.67 (s, 6H), 1.34 (s, 9H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 154.4 (CO +C), 134.9 (C), 129.2 (CH), 128.8 (CH), 128.15 (CH), 120.3 (CH) 54.2 (CH₂), 50.7 (C), 28.5 (2xCH₃) ppm.

MS (ESI⁺) *m/z*= 655 ([2M+Na]⁺, 100%); 317 ([M+H]⁺, 50%).

HRMS: Calc. for C₁₇H₂₄N₄O₂ + H⁺: 317.1978, found 317.1985.

Azide monomer **4a**



400 mg (1.26 mmol) of **3a** were dissolved in 2.0 mL of dichloromethane. TFA (2 mL) was then added and the mixture stirred for 2 h (TLC monitoring). The resulting solution was concentrated *in vacuo*. The traces of TFA were eliminated by co-evaporation with chloroform (3x5 mL) under reduced pressure. The crude amine was then dissolved in 10 mL of MeOH and 550 mg (4 mmol) of K₂CO₃ were added followed by 400 mg (1.90 mmol) of 1H-Imidazole-1-sulfonyl azide hydrochloride and 2.5 mg (0.01 mmol) of CuSO₄·5H₂O. The mixture was stirred overnight, diluted with 20 mL of water, acidified to pH=2 with 4 M HCl solution, and extracted with dichloromethane (3x15 mL). The organic extracts were washed with 10 mL of saturated NaHCO₃, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 2:8 to 4:6) to yield 305 mg (1.26 mmol, quantitative) of **4a** as a colourless oil that crystallised on standing.

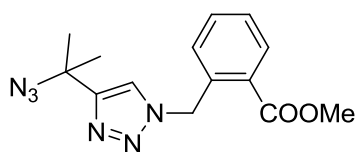
¹H-NMR (400 MHz, CDCl₃): δ 7.33 – 7.24 (m, 4H), 7.20 – 7.12 (m, 2H), 5.40 (s, 2H), 1.56 (s, 6H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 152.4 (C), 134.5 (C), 129.3 (CH), 128.9 (CH), 128.2 (CH), 120.1 (CH), 59.1 (C), 54.4 (CH₂), 27.3 (CH₃) ppm.

MS (ESI⁺) m/z= 243 ([M+H]⁺, 100%).

HRMS: Calc. for C₁₂H₁₄N₆ + H⁺: 243.1358, found 243.1359.

Azide monomer 4b



Following the procedure described for 4a, 510 mg (1.36 mmol) of **3b** in 4 mL of CHCl_3 :TFA 1:1 were used. After solvent elimination the crude amine TFA salt was dissolved in 10 mL of methanol and 660 mg (4.76 mmol) of K_2CO_3 were added followed by 430 mg (2.04 mmol) of 1H-imidazole-1-sulfonyl azide hydrochloride and 2.5 mg (0.01 mmol) of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. The mixture was stirred overnight, diluted with 20 mL of water, acidified to pH=2 with 4 M HCl solution, and extracted with dichloromethane (3x20 mL). The organic extracts were washed with 10 mL of saturated NaHCO_3 , dried over Na_2SO_4 , filtered and concentrated *in vacuo*. The crude product was used without further purification (yellowish oil), 405 mg (1.36, quantitative yield).

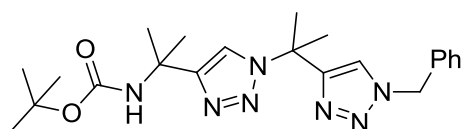
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.67 (dd, J = 7.8, 1.4 Hz, 1H), 7.15 (ddd, J = 7.6, 7.6, 1.5 Hz, 1H), 7.05 (ddd, J = 7.7, 7.7, 1.3 Hz, 1H), 6.88 (s, 1H), 6.87 – 6.80 (m, 1H), 5.57 (s, 2H), 4.91 (s, 1H), 3.55 (s, 3H), 1.30 (s, 6H) ppm.

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ 167.3 (CO), 151.8 (C), 136.3 (C), 133.3 (CH), 131.3 (CH), 130.5 (CH), 128.9 (CH), 128.7 (C), 121.1 (CH), 59.1 (C), 52.6 (CH_3), 52.1 (CH_2), 27.4 (CH_3) ppm.

MS (ESI⁺) m/z = 623 ($[\text{2M}+\text{Na}]^+$, 100%), 323 ($[\text{M}+\text{Na}]^+$, 50%), 301 ($[\text{M}+\text{H}]^+$, 25%).

HRMS: Calc. for $\text{C}_{14}\text{H}_{16}\text{N}_6\text{O}_2 + \text{H}^+$: 301.1413, found 301.1375.

Synthesis of dimer 5a



350 mg (1.44 mmol) of azide **4a** were dissolved in 10 mL of a 1:1 mixture THF: H_2O . *tert*-butyl N-(2-methylbut-3-yn-2-yl)carbamate (320 mg, 1.72 mmol) was added followed by 570 mg (2.88 mmol) of sodium ascorbate and 70 mg (0.28 mmol) of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. The mixture was stirred under nitrogen atmosphere for 16 h (TLC monitoring). Upon completion 10 mL of brine were added and the mixture was

extracted with dichloromethane (3x15 mL). The organic extracts were combined, washed with brine (10 mL), dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 1:1) to yield 470 mg (1.10 mmol, 78%) of the title compound as white solid.

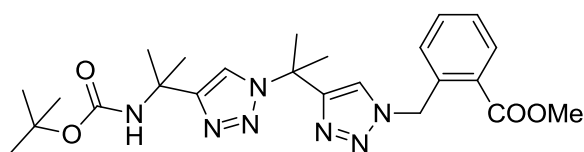
¹H-NMR (400 MHz, CDCl₃): δ 7.52 (s, 1H), 7.40 – 7.32 (m, 3H), 7.30 – 7.22 (m, 3H), 5.46 (s, 2H), 5.16 (s, 1H), 2.09 (s, 6H), 1.66 (s, 6H), 1.35 (s, 9H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 154.5 (C), 153.5 (C), 152.1 (C), 134.4 (C), 129.3 (CH), 129.0 (CH), 128.3 (CH), 121.0 (CH), 118.7 (CH), 79.2 (C), 59.4 (C), 54.4 (CH₂), 50.8 (C), 28.7 (CH₃), 28.5 (2xCH₃) ppm.

MS (ESI⁺) m/z= 448 ([M+Na]⁺, 100%); 426 ([M+H]⁺, 50%).

HRMS: Calc. for C₂₂H₃₁N₇O₂ + H⁺: 426.2617, found 426.2623.

Synthesis of dimer 5b



455 mg (1.51 mmol) of azide **4b** were dissolved in 10 mL of a 1:1 mixture THF:H₂O. *tert*-butyl N-(2-methylbut-3-yn-2-yl)carbamate (280 mg, 1.51 mmol) was added followed by 600 mg (3.00 mmol) of sodium ascorbate and 75 mg (0.30 mmol) of CuSO₄·5H₂O. The mixture was stirred under nitrogen atmosphere for 16 h (TLC monitoring). Upon completion 10 mL of brine were added and the mixture was extracted with dichloromethane (3x15 mL). The organic extracts were combined, washed with brine (10 mL), dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 1:1) to yield 470 mg (1.10 mmol, 78%) of the title compound as white solid.

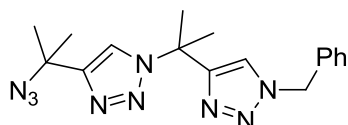
¹H-NMR (400 MHz, CDCl₃): δ 8.02 (dd, *J*= 7.9, 1.4 Hz, 1H), 7.59 – 7.45 (m, 3H), 7.41 (dd, *J*= 7.6, 1.3 Hz, 1H), 7.15 (d, *J*= 7.7 Hz, 1H), 5.91 (s, 2H), 5.17 (brs, 1H), 3.91 (s, 3H), 2.10 (s, 6H), 1.66 (s, 6H), 1.34 (s, 9H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 167.2 (CO), 154.5 (CO), 153.6 (C), 151.6 (C), 136.4 (C), 133.3 (CH), 131.3 (CH), 130.3 (CH), 128.8 (CH), 128.6 (C), 122.0 (CH), 118.7 (CH), 79.1 (C), 59.4 (C), 52.5 (CH₃), 52.1 (CH₂), 50.9 (C), 28.7 5 (CH₃), 28.5 (2xCH₃) ppm.

MS (ESI⁺) m/z= 989 ([2M+Na]⁺, 55%); 484 ([M+H]⁺, 100%).

HRMS: Calc. for C₂₄H₃₃N₇O₄ + H⁺: 484.2672, found 484.2576.

Azide dimer 6a



Following the procedure described for 4a, 420 mg (1.26 mmol) of **5a** in 4 mL of CHCl₃:TFA 1:1 were used. After solvent elimination the crude amine TFA salt was dissolved in 10 mL of methanol and 485 mg (3.5 mmol) of K₂CO₃ were added followed by 310 mg (1.48 mmol) of 1H-Imidazole-1-sulfonyl azide hydrochloride and 2.5 mg (0.01 mmol) of CuSO₄·5H₂O. The mixture was stirred overnight, diluted with 20 mL of water, acidified to pH=2 with 4 M HCl solution, and extracted with dichloromethane (3x20 mL). The organic extracts were washed with 10 mL of saturated NaHCO₃, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 1:1) to yield 310 mg (0.88 mmol, 90%) of **6a** as white solid.

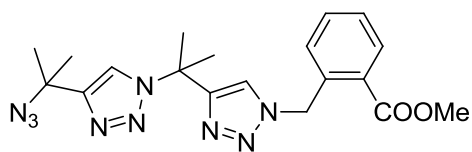
¹H-NMR (400 MHz, CDCl₃): δ 7.59 (s, 1H), 7.46 – 7.31 (m, 4H), 7.31 – 7.21 (m, 2H), 5.49 (s, 2H), 2.11 (s, 6H), 1.66 (s, 6H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 151.7 (C), 151.4 (C), 134.2 (C), 129.3 (CH), 129.1 (CH), 128.3 (CH), 121.1 (CH), 118.7 (CH), 59.6 (C), 59.1 (C), 54.5 4 (CH₂), 28.6 (CH₃), 27.3 (CH₃) ppm.

MS (ESI⁺) m/z= 703 ([2M+H]⁺, 100%), 352 ([M+H]⁺, 74%).

HRMS: Calc. for C₁₇H₂₁N₉ + H⁺: 352.1998, found 352.1985.

Azide dimer **6b**



Following the procedure described for **4a**, 655 mg (135 mmol) of **5b** in 5 mL of CHCl_3 :TFA 1:1 were used. After solvent elimination the crude amine TFA salt was dissolved in 10 mL of methanol and 650 mg (4.7 mmol) of K_2CO_3 were added followed by 425 mg (2.03 mmol) of 1H-Imidazole-1-sulfonyl azide hydrochloride and 2.5 mg (0.01 mmol) of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. The mixture was stirred overnight, diluted with 20 mL of water, acidified to pH=2 with 4 M HCl solution, and extracted with dichloromethane (3x20 mL). The organic extracts were washed with 10 mL of saturated NaHCO_3 , dried over Na_2SO_4 , filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO_2 , EtOAc:hexane 1:1) to yield 507 mg (1.24 mmol, 92%) of **6b** as white solid.

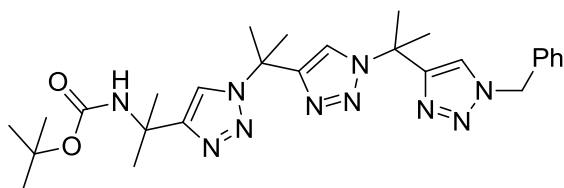
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 8.03 (dd, $J = 7.9, 1.4$ Hz, 1H), 7.59 (s, 1H), 7.56 (s, 1H), 7.52 (ddd, $J = 7.6, 7.6, 1.5$ Hz, 1H), 7.43 (dd, $J = 7.5, 7.5$ Hz, 1H), 7.22 (d, $J = 7.8$ Hz, 1H), 5.92 (s, 2H), 3.91 (d, $J = 0.7$ Hz, 3H), 2.12 (s, 6H), 1.66 (d, $J = 0.7$ Hz, 6H) ppm.

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ 167.2 (CO), 151.3 (C), 151.2 (C), 136.2 (C), 133.3 (CH), 131.4 (CH), 130.6 (CH), 129.0 (CH), 128.8 (C), 122.0 (CH), 118.7 (CH), 59.6 (C), 59.1 (C), 52.6 (CH_3), 52.1 (CH_3), 28.6 (CH_3), 27.3 (CH_3) ppm.

MS (ESI^+) $m/z = 841$ ($[\text{2M}+\text{Na}]^+$, 30%), 819 ($[\text{2M}+\text{H}]^+$, 100%), 410 ($[\text{M}+\text{H}]^+$, 55%).

HRMS: Calc. for $\text{C}_{19}\text{H}_{23}\text{N}_9\text{O}_2 + \text{H}^+$: 410.2053, found 410.2012.

Synthesis of trimer 7a



255 mg (0.73 mmol) of azide **6a** were dissolved in 8 mL of a 1:1 mixture THF:H₂O. *tert*-butyl N-(2-methylbut-3-yn-2-yl)carbamate (160 mg, 0.87 mmol) was added followed by 290 mg (1.46 mmol) of sodium ascorbate and 35 mg (0.14 mmol) of CuSO₄·5H₂O. The mixture was stirred under nitrogen atmosphere for 16 h (TLC monitoring). Upon completion 10 mL of brine were added and the mixture was extracted with dichloromethane (3x15 mL). The organic extracts were combined, washed with brine (10 mL), dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 50:50 to 100% EtOAc) to yield 310 mg (0.58 mmol, 80%) of the title compound as white solid.

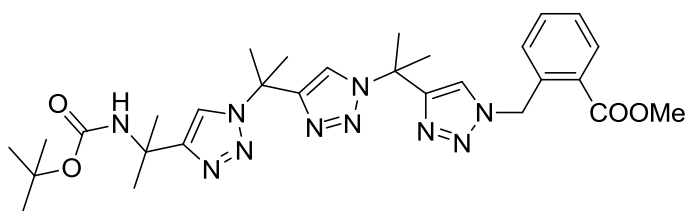
¹H-NMR (400 MHz, CDCl₃): δ 7.53 (s, 1H), 7.50 (s, 1H), 7.44 – 7.32 (m, 4H), 7.32 – 7.17 (m, 2H), 5.48 (s, 2H), 2.08 (s, 6H), 2.07 (s, 6H), 1.66 (s, 6H), 1.35 (s, 9H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 154.6 (C) 154.5 (C), 153.5 (C), 152.1 (C), 134.4 (C), 129.3 (CH), 129.0 (CH), 128.3 (CH), 121.0 (CH), 118.7 (CH), 79.2 (C), 59.4 (C), 54.4 (CH₂), 50.8 (C), 28.7 (CH₃), 28.5 (2xCH₃) ppm.

MS (ESI⁺) *m/z*= 458 ([M+Na]⁺, 100%); 436 ([M+H]⁺, 50%).

HRMS: Calc. for C₂₇H₃₈N₁₀O₂ + H⁺: 435.3257, found 435.3154.

Synthesis of trimer 7b



450 mg (1.10 mmol) of azide **6b** were dissolved in 20 mL of a 2:1 mixture THF:H₂O. *tert*-butyl N-(2-methylbut-3-yn-2-yl)carbamate (202 mg, 1.10 mmol) was added followed by 130 mg (0.66 mmol) of sodium ascorbate and 54 mg (0.21 mmol) of CuSO₄·5H₂O. The mixture was stirred under nitrogen atmosphere for 16 h (TLC monitoring). Upon completion 10 mL of brine were added and the mixture was extracted with dichloromethane (3x15 mL). The organic extracts were combined, washed with brine (10 mL), dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 50:50 to 100% EtOAc) to yield 642 mg (1.08 mmol, 98%) of the title compound as white solid.

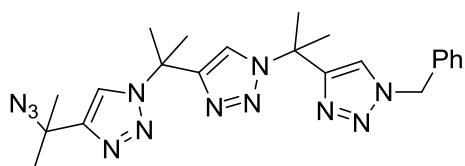
¹H-NMR (400 MHz, CDCl₃): δ 8.02 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.61 (s, 1H), 7.58 – 7.47 (m, 3H), 7.42 (ddd, *J* = 7.7, 7.6, 1.3 Hz, 1H), 7.25 – 7.17 (m, 1H), 5.91 (s, 2H), 5.19 (s, 1H), 3.90 (s, 3H), 2.08 (s, 6H), 2.07 (s, 6H), 1.65 (s, 6H), 1.35 (s, 9H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 167.0 (CO), 154.4 (CO), 153.4 (C), 150.8 (C), 150.7 (C), 136.0 (C), 133.1 (CH), 131.2 (CH), 130.4 (CH), 128.8 (CH), 128.6 (C), 121.9 (CH), 119.5 (CH), 118.5 (CH), 79.0 (C), 59.5 (C), 59.1 (C), 52.4 (C), 51.9 (CH₂), 50.7 (CH₃), 28.5 (CH₃), 28.3 (CH₃), 28.2 (CH₃) ppm.

MS (ESI⁺) *m/z* = 1185 ([2M+H]⁺, 20%); 593 ([M+H]⁺, 100%).

HRMS: Calc. for C₂₉H₄₀N₁₀O₄ + H⁺: 593.3312, found 593.3243.

Synthesis of trimer 8a



Following the procedure described for 4a, 225 mg (0.42 mmol) of **7a** in 4 mL of CHCl_3 :TFA 1:1 were used. After solvent elimination the crude amine TFA salt was dissolved in 5 mL of methanol and 200 mg (1.47 mmol) of K_2CO_3 were added followed by 135 mg (0.64 mmol) of 1H-Imidazole-1-sulfonyl azide hydrochloride and 2.0 mg (0.01 mmol) of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. The mixture was stirred overnight, diluted with 20 mL of water, acidified to pH=2 with 4 M HCl solution, and extracted with dichloromethane (3x15 mL). The organic extracts were washed with 10 mL of saturated NaHCO_3 , dried over Na_2SO_4 , filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO_2 , EtOAc:hexane 1:1) to yield 175 mg (0.38 mmol, 90%) of **8a** as white solid.

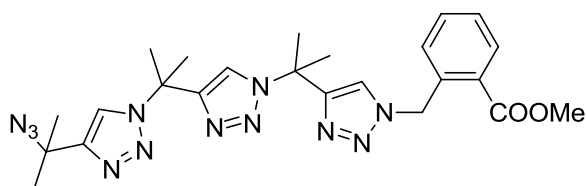
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.59 (s, 1H), 7.53 (s, 1H), 7.42 – 7.37 (m, 3H), 7.36 (s, 1H), 7.30 – 7.27 (m, 2H), 2.10 (s, 6H), 2.08 (s, 6H), 1.66 (s, 6H) ppm.

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ 151.3 (C), 151.2 (C), 150.6 (C), 134.2 (C), 129.4 (CH), 129.1 (CH), 128.4 (CH), 121.1 (CH), 119.7 (CH), 118.7 (CH), 59.7 (C), 59.5 (C), 59.1 (C), 54.5 (CH₂), 28.7 (CH₃), 27.3 (CH₃) ppm.

MS (ESI^+) m/z = 921 ($[\text{2M}+\text{H}]^+$, 90%); 461 ($[\text{M}+\text{H}]^+$, 100%).

HRMS: Calc. for $\text{C}_{22}\text{H}_{28}\text{N}_{12} + \text{H}^+$: 461.2638, found 461.2576.

Synthesis of trimer 8b



Following the procedure described for 4a, 620 mg (1.05 mmol) of **7b** in 8 mL of CHCl_3 :TFA 1:1 were used. After solvent elimination the crude amine TFA salt was dissolved in 10 mL of methanol and 505 mg (3.70 mmol) of K_2CO_3 were added followed by 330 mg (1.57 mmol) of 1H-imidazole-1-sulfonyl azide hydrochloride and 2.0 mg (0.01 mmol) of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. The mixture was stirred overnight, diluted with 20 mL of water, acidified to pH=2 with 4 M HCl solution, and extracted with dichloromethane (3x15 mL). The organic extracts were washed with 10 mL of saturated NaHCO_3 , dried over Na_2SO_4 , filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO_2 , EtOAc:hexane 60:40) to yield 460 mg (0.88 mmol, 85%) of **8a** as white solid.

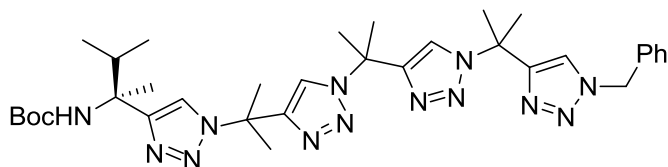
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 1H 8.01 (dd, $J = 7.7, 1.4$ Hz, 1H), 7.61 (s, 1H), 7.57 (s, 1H), 7.55 – 7.47 (m, 2H), 7.45 – 7.35 (m, 1H), 7.22 (dd, $J = 7.5, 1.4$ Hz, 1H), 5.90 (s, 2H), 3.89 (s, 3H), 2.07 (s, 12H), 1.64 (s, 6H) ppm.

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ 167.2 (CO), 151.2 (C), 150.8 (C), 150.5 (C), 136.1 (C), 133.3 (CH), 131.4 (CH), 130.7 (CH), 129.0 (CH), 128.8 (C), 122.1 (CH), 119.8 (CH), 118.8 (CH), 59.7 (C), 59.5 (C), 59.1 (C), 52.6 (CH_3), 52.1 (CH_2), 28.6 (CH_3), 27.3 (CH_3) ppm.

MS (ESI⁺) $m/z = 1037$ ($[\text{2M}+\text{H}]^+$, 100%); 519 ($[\text{M}+\text{H}]^+$, 65%).

HRMS: Calc. for $\text{C}_{22}\text{H}_{30}\text{N}_{12}\text{O}_2 + \text{H}^+$: 519.2693, found 519.2911.

Synthesis of tetramer 9a



60 mg (0.13 mmol) of azide 8a were dissolved in 4 mL of a 2:1 mixture THF:H₂O. Alkyne **1b** (30 mg, 0.14 mmol) was added followed by 51 mg (0.26 mmol) of sodium ascorbate and 8 mg (0.032 mmol) of CuSO₄·5H₂O. The mixture was stirred under nitrogen atmosphere for 16 h (TLC monitoring). Upon completion 10 mL of brine were added and the mixture was extracted with dichloromethane (3x15 mL). The organic extracts were combined, washed with brine (10 mL), dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 50:50 to 80:20) to yield 80 mg (0.12 mmol, 92%) of the title compound as white solid.

$[\alpha]_D^{20} = -14.0$ (c = 0.2, CHCl₃)

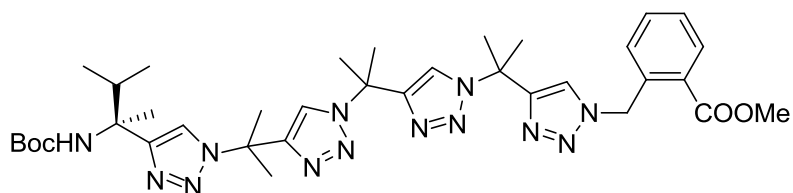
¹H-NMR (400 MHz, CDCl₃): δ 7.56 (s, 1H), 7.51 (s, 1H), 7.45 (s, 1H), 7.41 – 7.35 (m, 4H), 7.31 – 7.27 (m, 2H), 5.51 (s, 2H), 5.43 (brs, 1H), 2.46 (m, 1H), 2.08 (2xs, 12 H), 2.06 (s, 6H), 2.05 (s, 4H), 1.67 (s, 3H), 1.36 (s, 9H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.77 (d, *J* = 6.8 Hz, 3H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 151.3 (C), 151.0 (2xC), 150.4 (C), 149.5 (C), 134.3 (C), 129.4 (CH), 129.1 (CH), 128.4 (CH), 121.1 (CH), 119.82 (CH), 119.78 (CH), 119.6 (CH), 59.7 (C), 59.7 (C), 59.4 (C), 57.2 (C), 54.5 (CH₂), 35.8 (CH) 28.8 (CH₃), 28.75 (CH₃), 28.71 (CH₃), 28.6 (CH₃), 28.5 (CH₃), 21.9 (CH₃), 17.6 (CH₃), 17.5 (CH₃) ppm.

MS (ESI⁺) *m/z* = 672 ([M+H]⁺, 100%).

HRMS: Calc. for C₃₄H₄₉N₁₃O₂ + H⁺: 672.4210, found 672.3945.

Synthesis of tetramer 9b



104 mg (0.20 mmol) of azide 8b were dissolved in 4 mL of a 2:1 mixture THF:H₂O. Alkyne **1b** (42 mg, 0.20 mmol) was added followed by 25 mg (0.06 mmol) of sodium ascorbate and 10 mg (0.04 mmol) of CuSO₄·5H₂O. The mixture was stirred under nitrogen atmosphere for 2 h (TLC monitoring). Upon completion 10 mL of brine were added and the mixture was extracted with dichloromethane (3x15 mL). The organic extracts were combined, washed with brine (10 mL), dried over Na₂SO₄, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 50:50 to 80:20) to yield 105 mg (0.14 mmol, 72%) of the title compound as white solid.

$[\alpha]_D^{20} = -24.5$ (c = 0.2, CHCl₃)

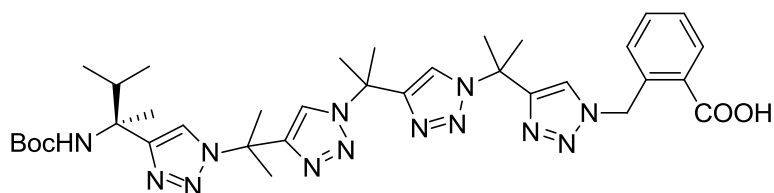
¹H-NMR (400 MHz, CDCl₃): δ 8.03 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.65 (s, 1H), 7.57 (s, 1H), 7.54 (ddd, *J* = 7.6, 1.5 Hz, 1H), 7.50 (s, 1H), 7.48 (s, 1H), 7.43 (ddd, *J* = 7.7, 1.3 Hz, 1H), 7.24 (dd, *J* = 7.6, 1.3 Hz, 1H), 5.93 (s, 2H), 5.46 (s, 1H), 3.91 (s, 3H), 2.54 – 2.39 (m, 1H), 2.09 (s, 6H), 2.08 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 2.05 (s, 3H), 1.67 (s, 3H), 1.36 (s, 9H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.76 (d, *J* = 6.8 Hz, 3H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 167.3 (CO), 154.8 (CO), 150.9 (2xC), 150.8 (C), 150.3 (C), 136.1 (C), 133.3 (CH), 131.4 (CH), 130.7 (CH), 129.0 (CH), 128.8 (C), 122.1 (CH), 119.9 (CH), 119.8 (CH), 119.7 (CH), 78.9 (C), 59.7 (C), 59.7 (C), 59.4 (C), 57.2 (C), 52.6 (CH₃), 52.1 (CH₂), 35.8 (CH), 28.76 (CH₃), 28.73 (CH₃), 28.69 (CH₃), 28.66 (overlapping, (CH₃)), 28.5 (CH₃), 22.0 (CH₃), 17.64 (CH₃), 17.56 (CH₃) ppm.

MS (ESI⁺) *m/z* = 1459 ([2M+H]⁺, 15%); 730 ([M+H]⁺, 100%).

HRMS: Calc. for C₃₆H₅₁N₁₃O₄ + H⁺: 730.4265, found 730.4158.

Synthesis of tetramer 9c



50 mg (0.07 mmol) of ester 9b were dissolved in 4 mL of a 3:1 mixture THF:H₂O. LiOH (4 mg, 0.1 mmol) was then added and the mixture stirred until no starting material could be detected (TLC monitoring). The solution was then acidified with KHSO₄ 2.0 M and extracted with DCM (3x15 mL). The organic extracts were dried over Na₂SO₄, filtered and concentrated in vacuo. The crude product was purified by column chromatography (SiO₂, DCM:EtOH 95:5) to yield 46 mg (0.06 mmol, 86%) of the title compound as white solid.

$[\alpha]_D^{20} = -4.5$ (c = 0.2, CHCl₃)

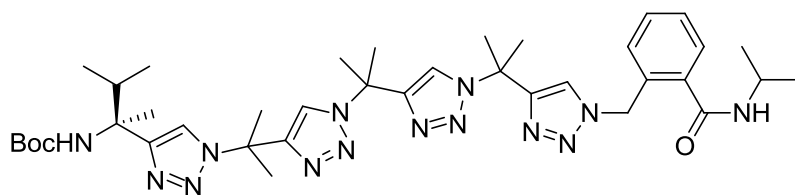
¹H-NMR (400 MHz, CDCl₃): δ 8.14 (d, $J = 7.7$ Hz, 1H), 7.71 – 7.52 (m, 3H), 7.34 – 7.48 (m, 4H), 5.90 (A of AB, $J = 14.0$ Hz, 1H), 5.86 (B of AB, $J = 14.0$ Hz, 1H) 5.54 (s, 1H), 2.55 – 2.36 (m, 1H), 2.14 (s, 3H), 2.12 (s, 3H), 2.07 (m, 12H), 1.69 (s, 3H), 1.32 (s, 9H), 0.88 (d, $J = 6.7$ Hz, 3H), 0.77 (d, $J = 6.8$ Hz, 3H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 167.5 (CO), 150.8 (2xC), 150.1 (C), 135.4 (C), 133.0 (CH), 132.6 (CH), 132.1 (CH + C), 129.3 (C), 122.0 (CH), 120.3 (CH), 119.9 (CH), 119.8 (CH), 60.6 (C), 60.1 (C), 59.8 (C), 57.1 (C), 52.5 (CH₂), 31.1 (CH), 29.0 (CH₃), 28.9 (CH₃), 28.7 (CH₃), 28.6 (CH₃), 28.5 (CH₃), 17.6 (CH₃), 17.3 (CH₃) ppm.

MS (ESI⁺) $m/z = 716$ ([M+H]⁺, 100%).

HRMS: Calc. for C₃₅H₄₉N₁₃O₄ + H⁺: 716.4109, found 716.7062.

Synthesis of tetramer 9d



20 mg (0.03 mmol) of acid tetramer **9c** were dissolved in 2 mL of dry DMF. Hobt (5.6 mg, 0.04 mmol) and EDCI (8.6 mg, 0.05 mmol) were added followed by 10 μ L (0.06 mmol) of DIPEA and 10 μ L (0.12 mmol) of isopropylamine. The mixture was stirred overnight and then diluted with 30 mL of EtOAc and washed with HCL 0.1 M (2 x 5 mL), NaHCO₃ sat (2x5 mL) and brine (2x5mL). The organic layer was dried over Na₂SO₄, filtered and concentrated by evaporation under reduced pressure. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 80:20) to yield 16 mg (0.02 mmol, 76%) of the **9d** as pale yellow solid.

$[\alpha]_D^{20} = -14.8$ (c =0.2, CHCl₃)

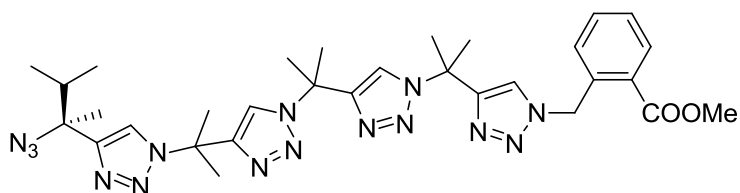
¹H-NMR (400 MHz, CDCl₃): δ 7.80 (s, 1H), 7.51 (s, 1H), 7.47 (s, 1H), 7.46 – 7.30 (m, 5H), 6.06 (d, $J = 7.9$ Hz, 1H), 5.69 (A and B of AB, $J=14.0$ Hz, 2H), 5.43 (s, 1H), 4.20 (m, 1H) 2.45 (m, 1H), 2.05 (s, 6H), 2.04 (s, 6H), 2.02 (overlapping peaks, 6H), 1.64 (s, 3H), 1.33 (s, 9H), 1.27 – 1.13 (m, 6H), 0.79 (d, $J = 6.9$ Hz, 3H), 0.74 (d, $J = 6.8$ Hz, 3H) ppm.

¹³C-NMR (101 MHz, CDCl₃): δ 168.1 (CO), 167.5 (CO), 150.9 (C), 150.7 (C), 150.2 (C), 136.0 (C), 133.3 (C), 131.1 (2xCH), 129.2 (CH), 127.4 (CH), 122.3 (CH), 120.0 (CH), 119.9 (CH), 119.7 (CH), 81.7 (C), 59.7 (2xC), 59.4 (2xC), 57.2 (C), 51.5 42.4 (CH),, 28.8 (CH₃), 28.7 (overlapping signals, CH₃), 28.5 (CH₃), 22.8 (CH₃), 22.0 (CH₃), 21.2 (CH₃), 17.6 (CH₃), 17.5 (CH₃) ppm.

MS (ESI⁺) $m/z = 1513$ ([2M+H]⁺, 10%), 757 ([M+H]⁺, 100%)

HRMS: Calc. for C₃₈H₅₆N₁₄O₃ + H⁺:757.4738, found 757.4609.

Synthesis of azide 10b



70 mg (0.095 mmol) of Boc-protected 9b were dissolved in 4 mL of a 2:1 mixture CHCl_3 :TFA. The mixture was stirred at r.t. for 2h and then the solvent removed *in vacuo*. The residue was evaporated two more times with 5 mL of CHCl_3 and then redissolved in 5 mL of methanol. K_2CO_3 (45 mg, 0.33 mmol), 1H-Imidazole-1-sulfonyl azide hydrochloride (33 mg, 0.16 mmol) and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. (1.0 mg, 0.01 mmol) were then added and the mixture stirred overnight. The mixture was then acidified with HCl 2.0 M and extracted with CH_2Cl_2 (3x 15 mL). The organic extracts were combined, washed with NaHCO_3 sat (10 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO_2 , EtOAc:hexane 80:20) to yield 38 mg (0.06 mmol, 61%) of the title compound as white foam.

$[\alpha]_D^{20} = -20.12$ (c = 0.2, CHCl_3)

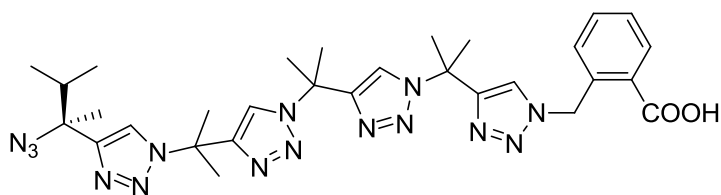
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 8.03 (dd, $J = 7.8, 1.5$ Hz, 1H), 7.66 (s, 1H), 7.58 (s, 1H), 7.56 (s, 1H), 7.54 (ddd, $J = 7.6, 7.6, 1.5$ Hz, 1H), 7.50 (s, 1H), 7.44 (ddd, $J = 7.6, 7.6, 1.3$ Hz, 1H), 7.24 (d, $J = 1.5$ Hz, 1H), 5.93 (s, 2H), 3.92 (s, 3H), 2.22 (hept, $J = 6.8$ Hz, 1H), 2.09 (s, 12H), 2.06 (s, 6H), 1.64 (s, 3H), 1.62 – 1.55 (s, 9H), 0.91 (d, $J = 6.8$ Hz, 3H), 0.82 (d, $J = 6.8$ Hz, 3H), ppm.

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ 167.5 (CO), 150.8 (C), 150.7 (C), 150.2 (C), 150.0 (C), 136.1 (C), 133.3 (CH), 131.4 (CH), 130.8 (CH), 129.0 (CH), 128.8 (C), 122.1 (CH), 119.9 (CH), 119.8 (CH), 65.9 (C), 59.7 (C), 59.7 (C), 59.6 (C), 52.6 (CH_3), 52.1 (CH_2), 37.1 (CH), 29.9 (CH_3), 28.7 (overlapping peaks, CH_3), 28.7, 28.7, 20.5 (CH_3), 17.8 (CH_3), 17.5 (CH_3) ppm.

MS (ESI⁺) $m/z = 1334$ ($[\text{2M}+\text{Na}]^+$, 45%); 1311 ($[\text{2M}+\text{H}]^+$, 47%); 678 ($[\text{M}+\text{Na}]^+$, 58%); 656 ($[\text{M}+\text{H}]^+$, 100%).

HRMS: Calc. $\text{C}_{31}\text{H}_{41}\text{N}_{15}\text{O}_2 + \text{H}^+$: 656.3646, found 656.3416.

Synthesis of azide 10c



30 mg (0.045 mmol) of azide 10b were dissolved in 4 mL of a 3:1 mixture THF:H₂O. LiOH (3.5 mg, 0.09 mmol) was added and the mixture stirred at r.t. for 2h and then the solvent removed *in vacuo*. The residue was evaporated two more times with 5 mL of CHCl₃ and then redissolved in 5 mL of methanol. K₂CO₃ (45 mg, 0.33 mmol), 1H-imidazole-1-sulfonyl azide hydrochloride (33 mg, 0.16 mmol) and CuSO₄·5H₂O. (1.0 mg, 0.01 mmol) were then added and the mixture stirred overnight. The mixture was then acidified with HCl 2.0 M and extracted with CH₂Cl₂ (3x 15 mL). The organic extracts were combined, washed with NaHCO₃ sat (10 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO₂, EtOAc:hexane 80:20) to yield 38 mg (0.06 mmol, 61%) of the title compound as white foam.

$[\alpha]_D^{20} = -1.25$ (c = 0.2, CHCl₃)

¹H-NMR (400 MHz, CDCl₃): δ 8.14 (d, $J = 7.3$ Hz, 1H), 7.67 (s, 1H), 7.60 – 7.55 (m, 2H), 7.53 (s, 1H), 7.46 (s, 1H), 7.50 – 7.41 (m, 1H), 7.33 (s, 1H), 5.85 (s, 2H), 2.22 (hept, $J = 6.9$ Hz, 1H), 2.15 (s, 6H), 2.07 (s, 12H), 1.67 (s, 3H), 0.89 (d, $J = 6.8$ Hz, 3H), 0.83 (d, $J = 6.8$ Hz, 4H) ppm.

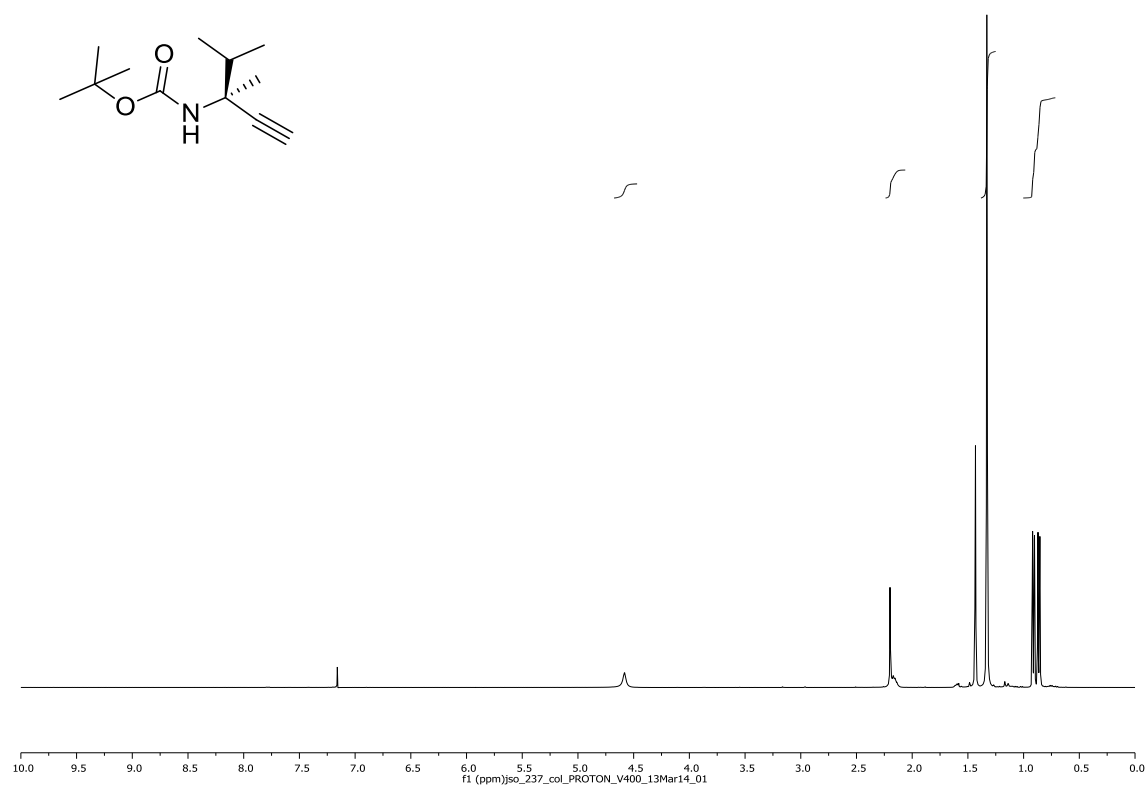
¹³C-NMR (101 MHz, CDCl₃): δ 168.0 (CO), 150.7 (C), 150.1 (C), 149.93 (C), 149.85 (C), 135.5 (C), 133.0 (CH), 132.6 (CH), 132.0 (CH), 129.2 (CH), 121.9 (CH), 120.3 (CH), 119.7 (CH), 119.5 (CH), 65.7 (CH₂), 60.6 (C), 60.1 (C), 59.6 (C), 52.5 (C), 37.1 (CH), 28.8 (CH₃), 28.50 (CH₃), 28.48 (CH₃), 28.4 (CH₃), 28.4 (CH₃), 20.3 (CH₃), 17.6 (CH₃), 17.3 (CH₃) ppm.

MS (ESI⁺) $m/z = 1283$ ([2M+H]⁺, 20%); 642 ([M+H]⁺, 100%).

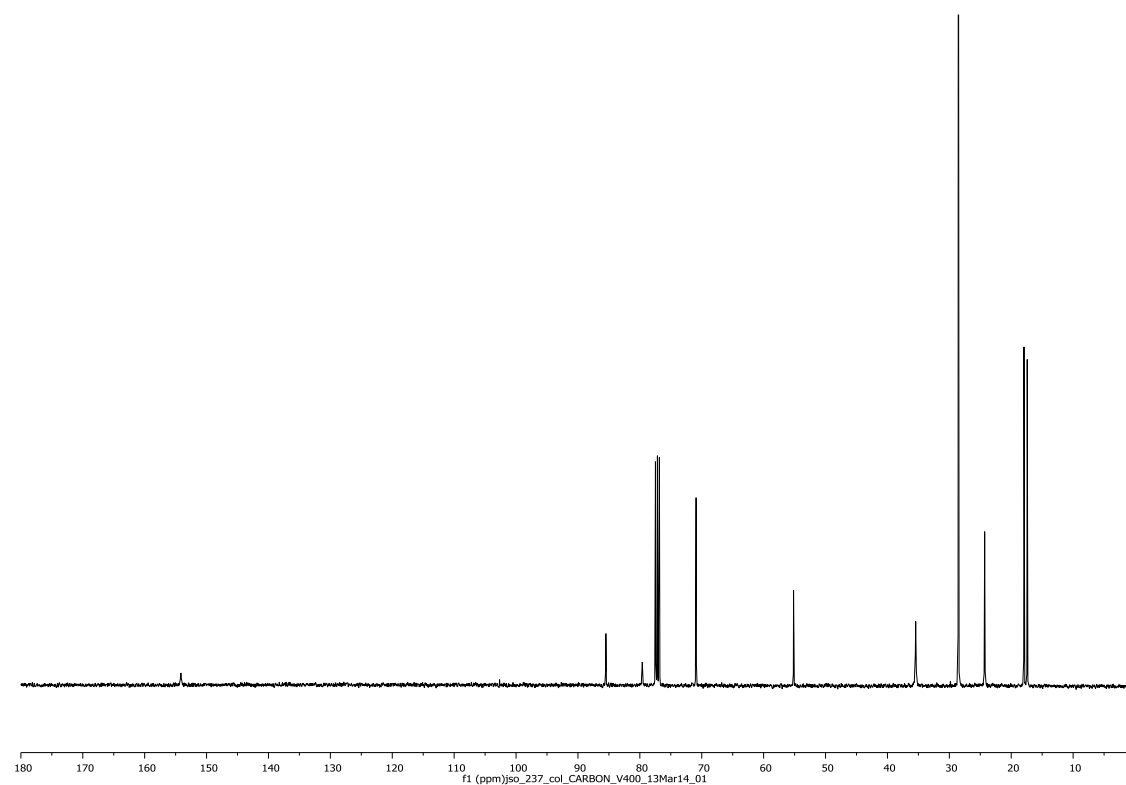
HRMS: Calc. C₃₀H₃₉N₁₅O₂+ H⁺:642.3489, found 642.3514.

Supplementary figures: ^1H and ^{13}C NMR spectra

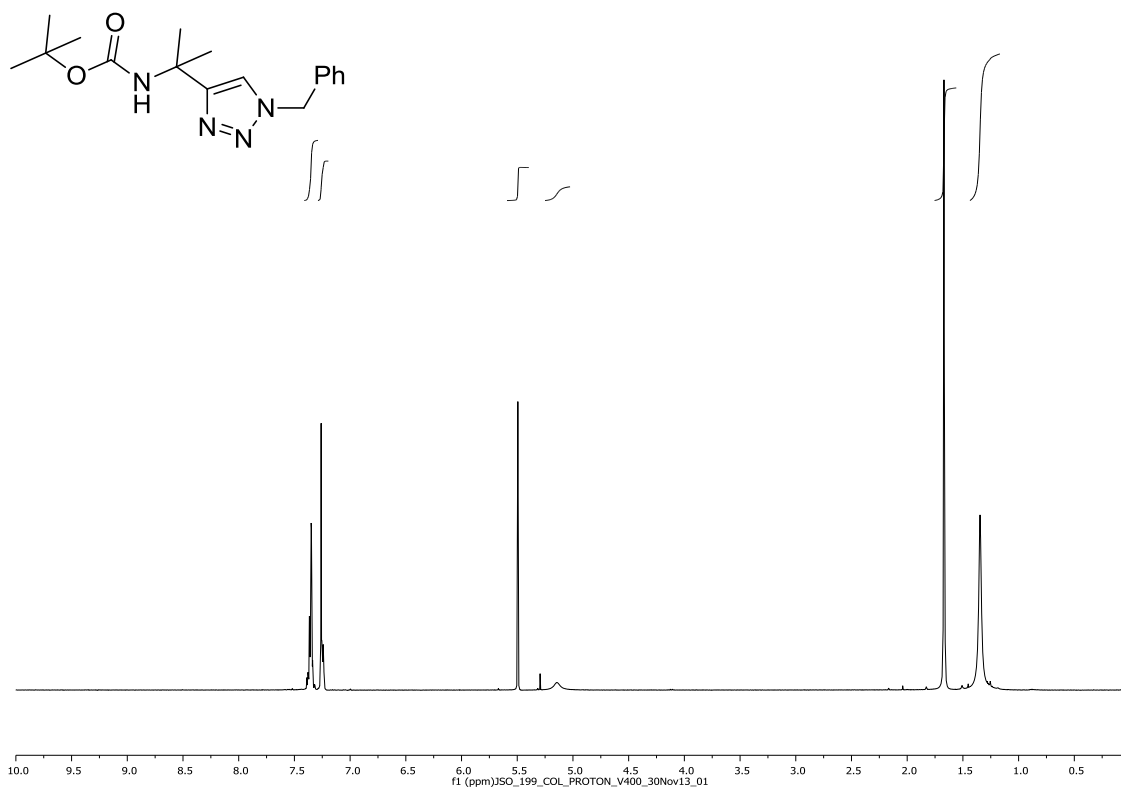
1b ^1H -NMR (400 MHz, CDCl_3)



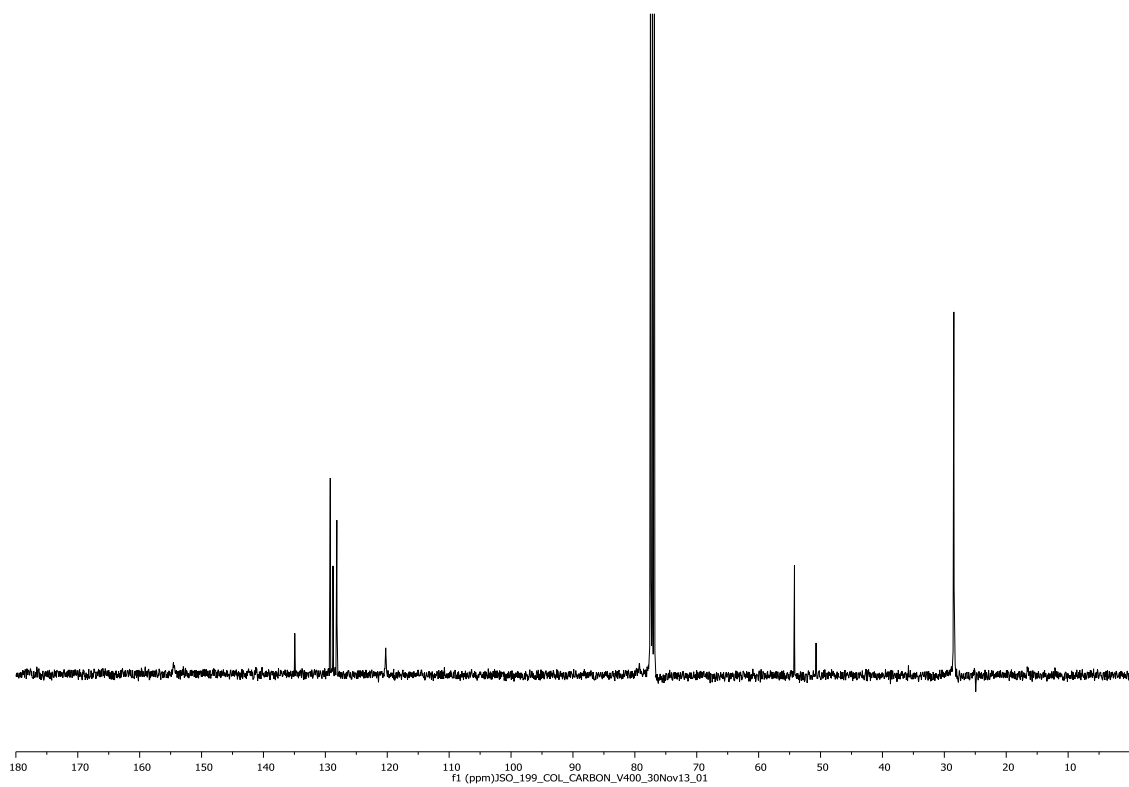
1b ^{13}C -NMR (100 MHz, CDCl_3)



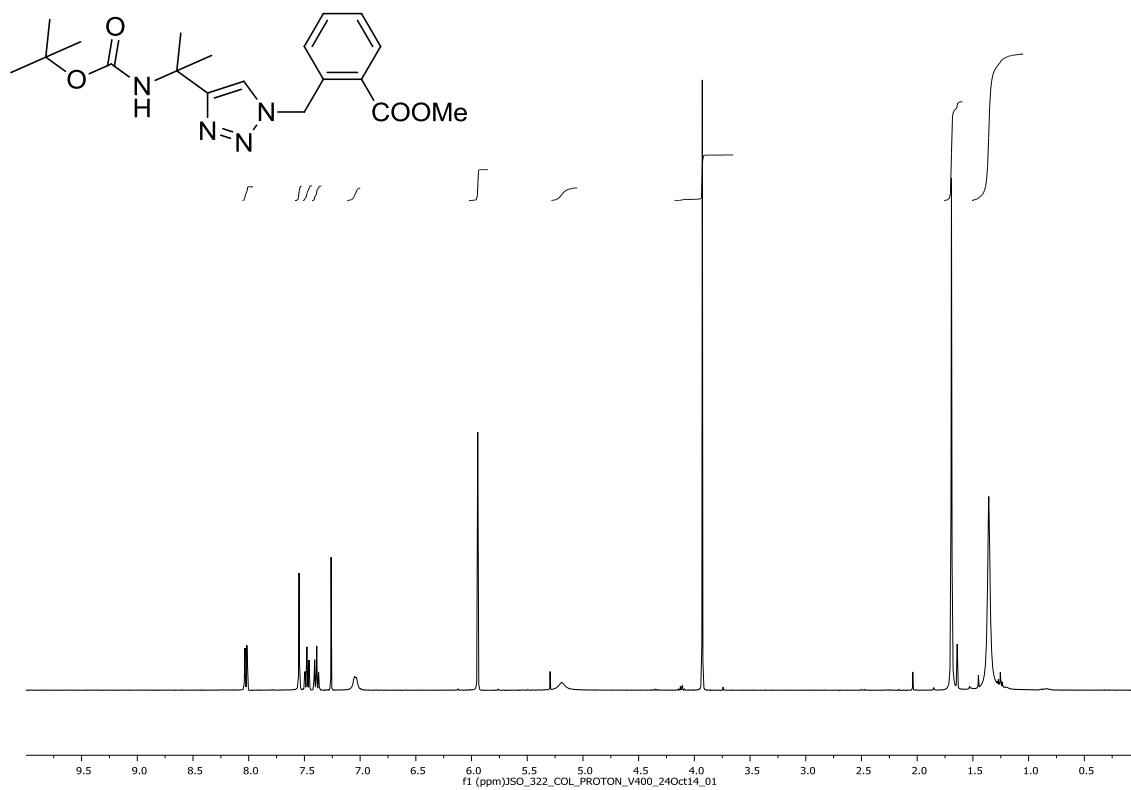
3a $^1\text{H-NMR}$ (400 MHz, CDCl_3)



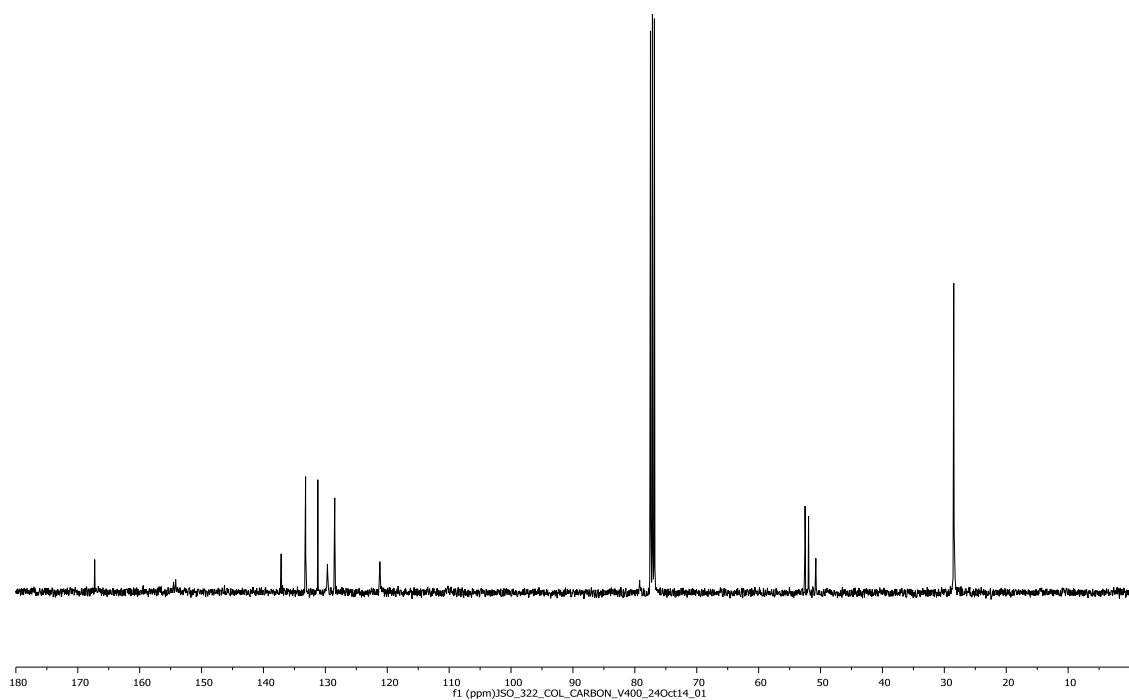
3a $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



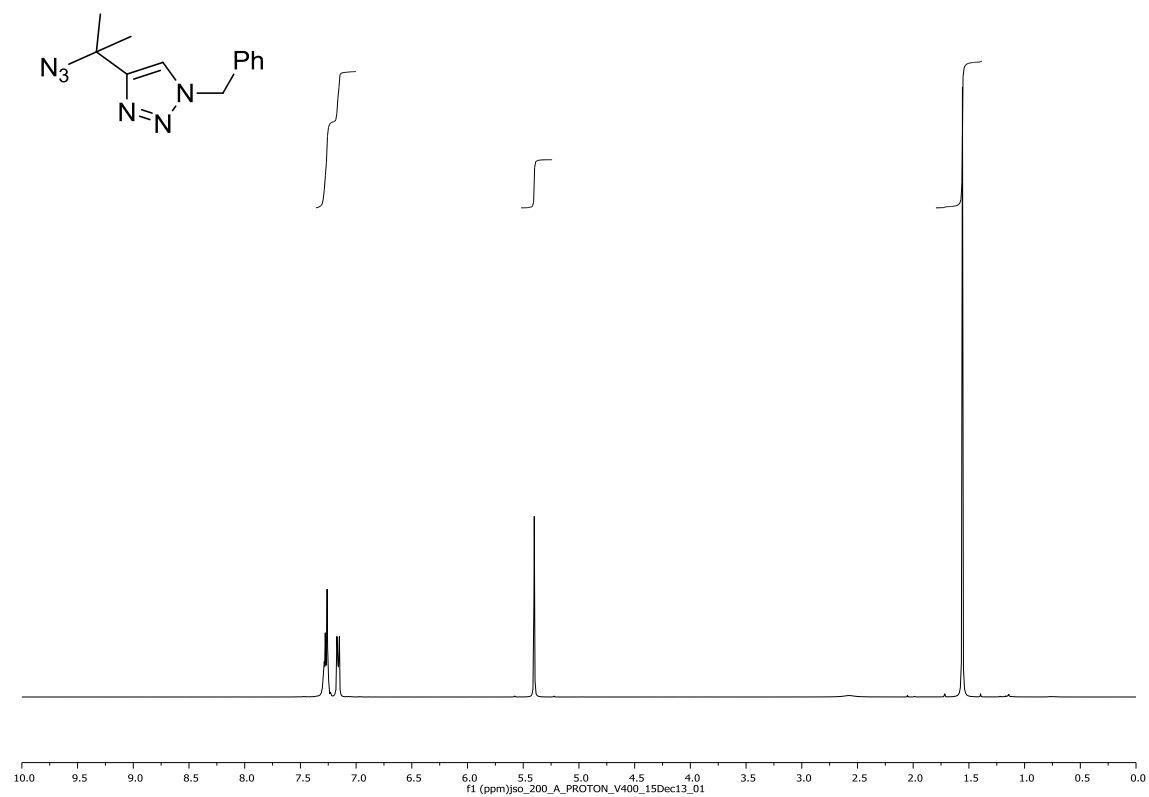
3b $^1\text{H-NMR}$ (400 MHz, CDCl_3)



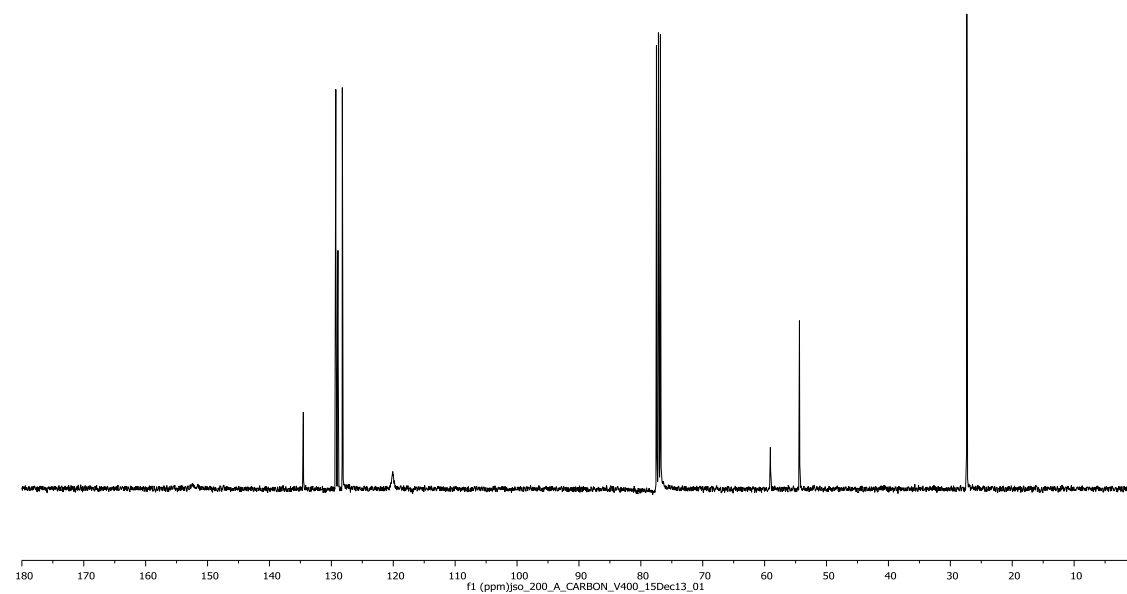
3b $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



4a $^1\text{H-NMR}$ (400 MHz, CDCl_3)



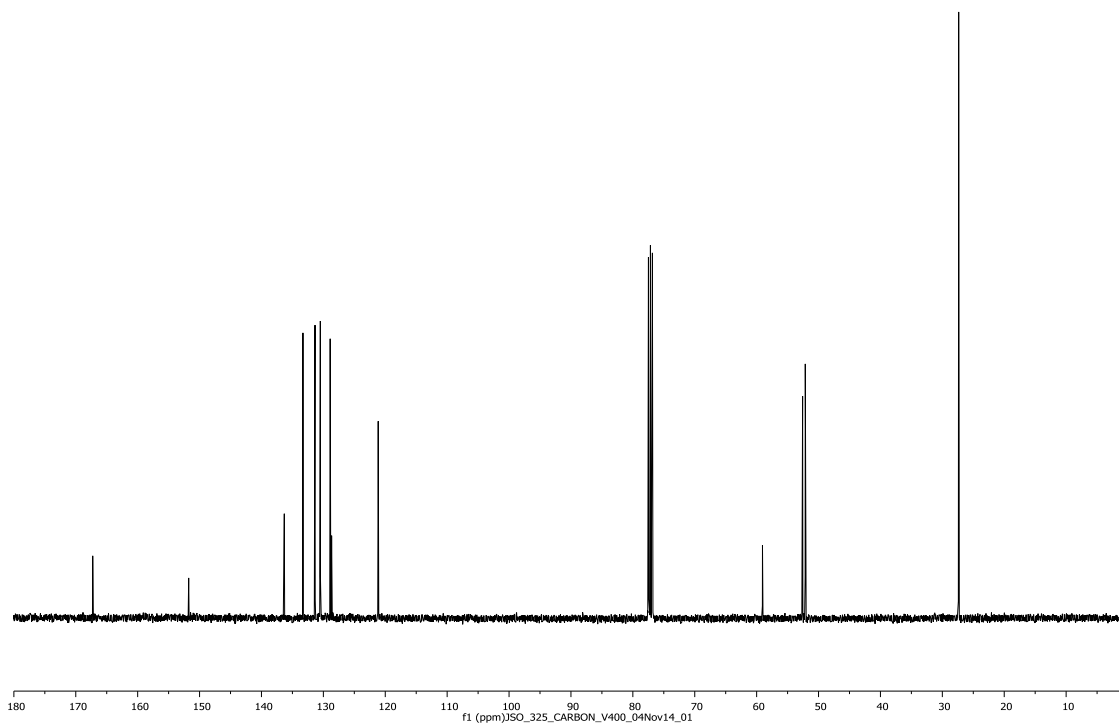
4a $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



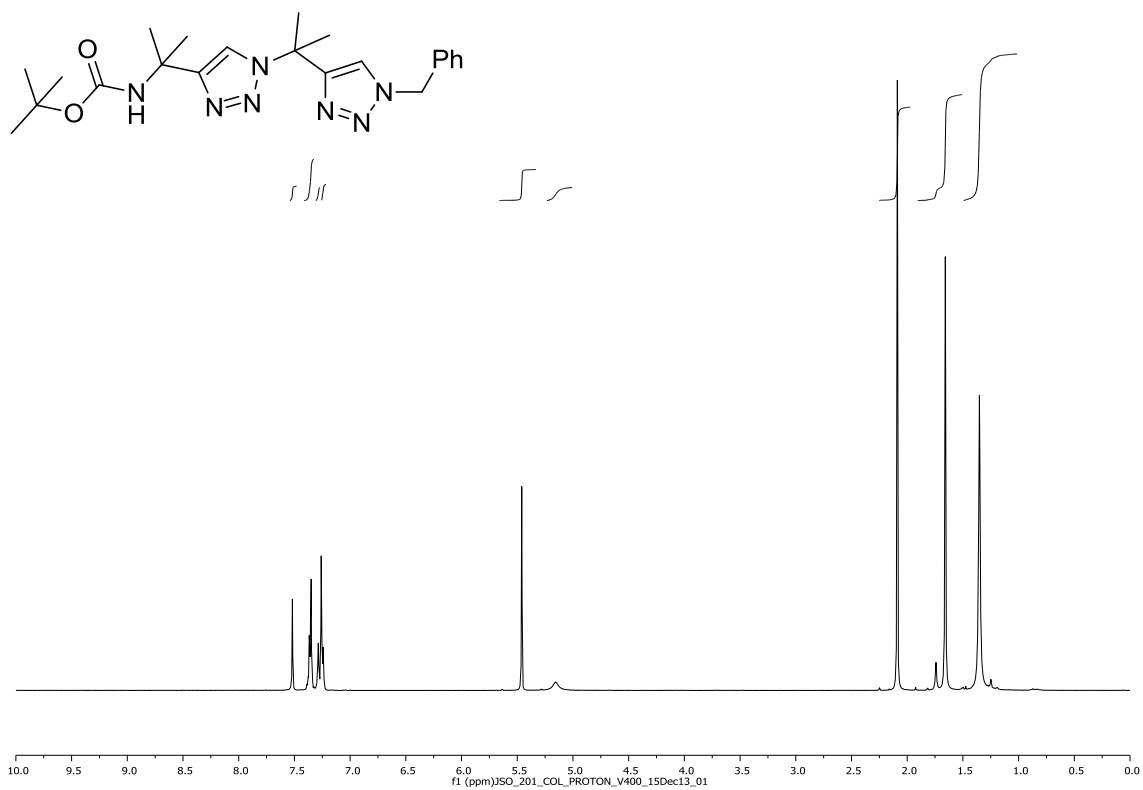
4b $^1\text{H-NMR}$ (400 MHz, CDCl_3)



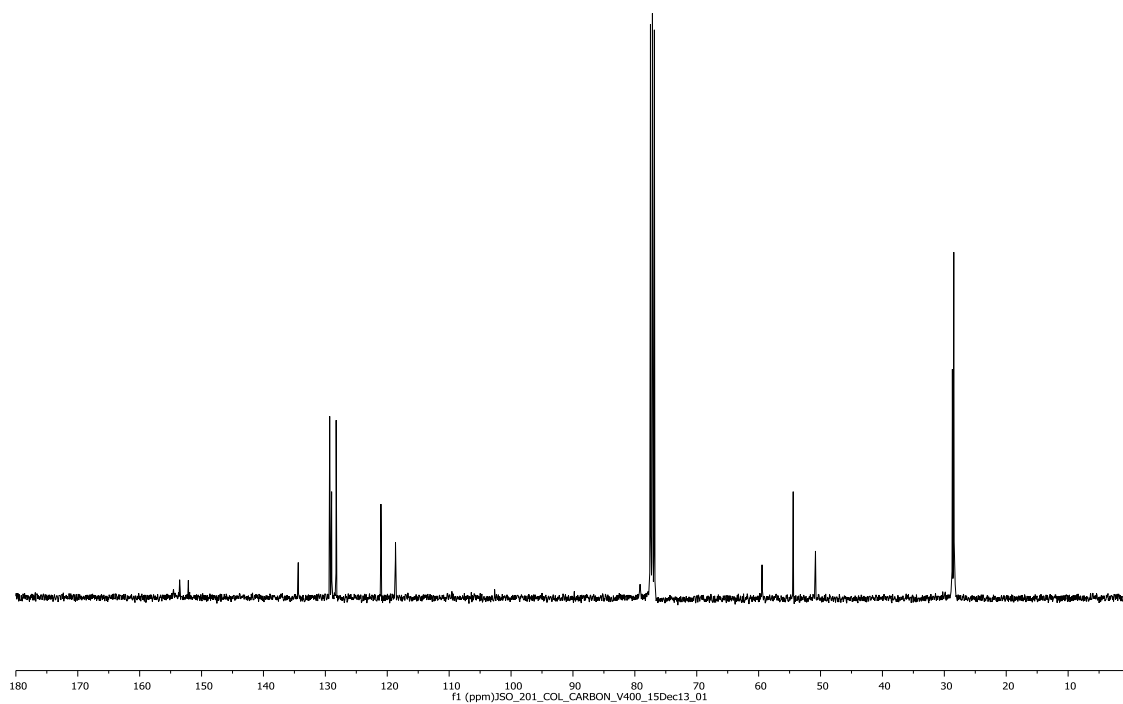
4b $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



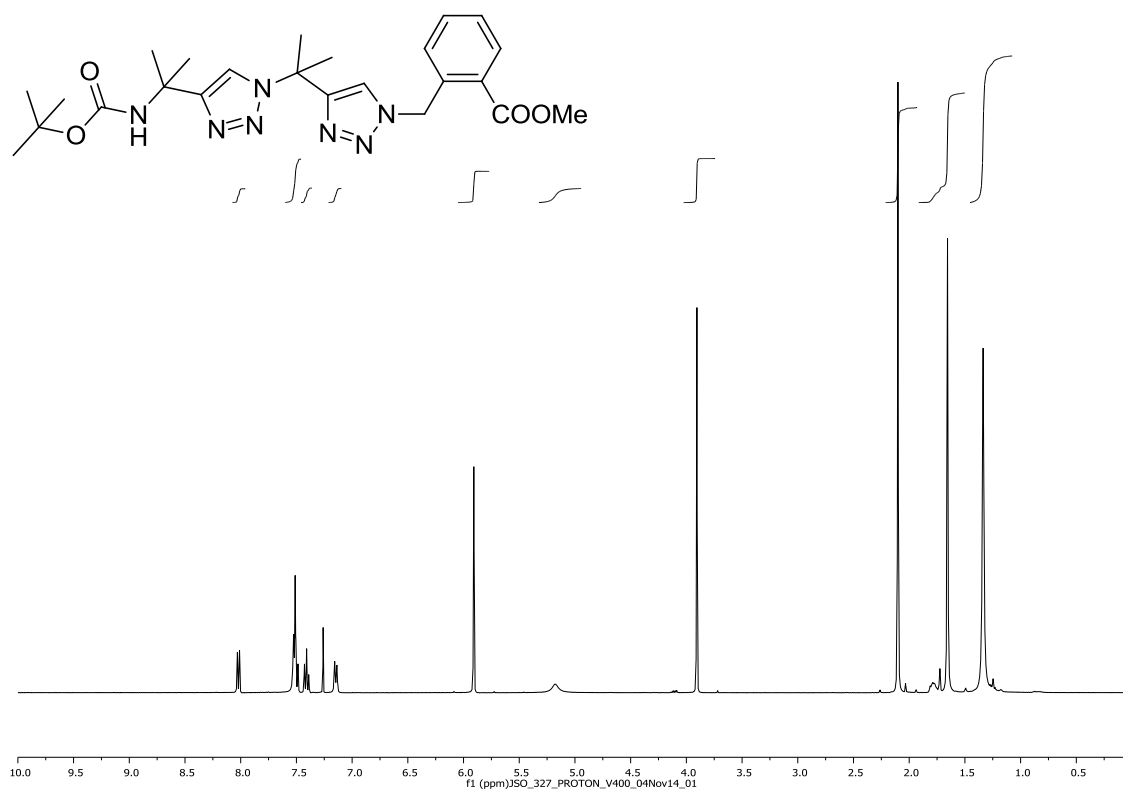
5a ¹H-NMR (400 MHz, CDCl₃)



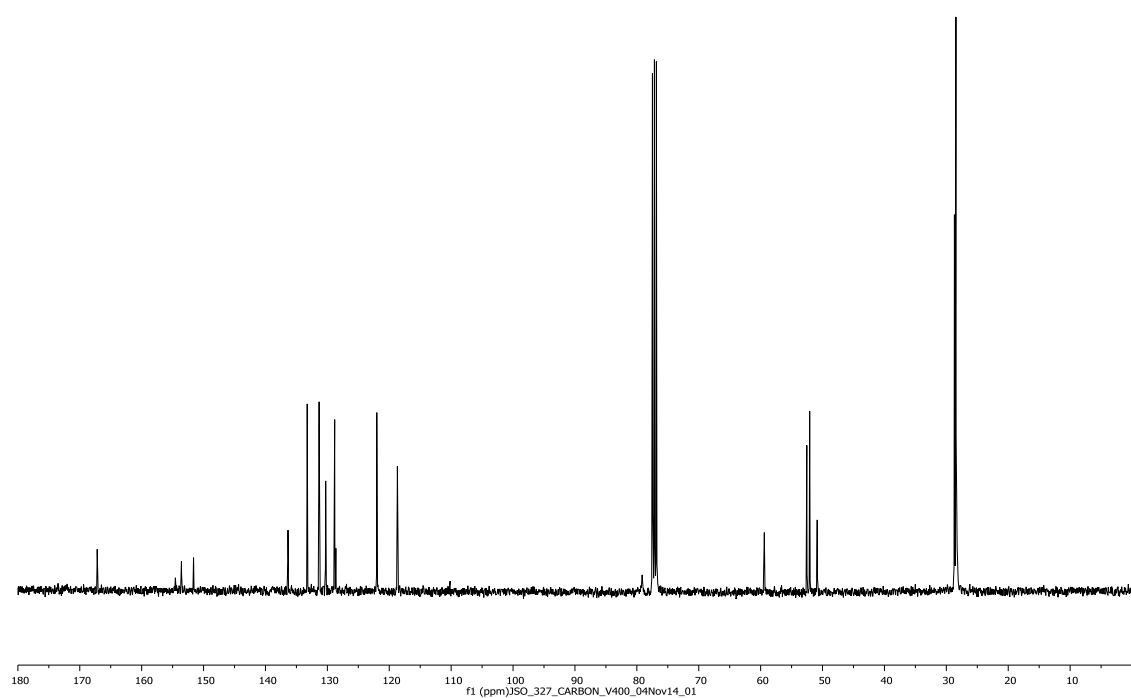
5a ¹³C-NMR (100 MHz, CDCl₃)



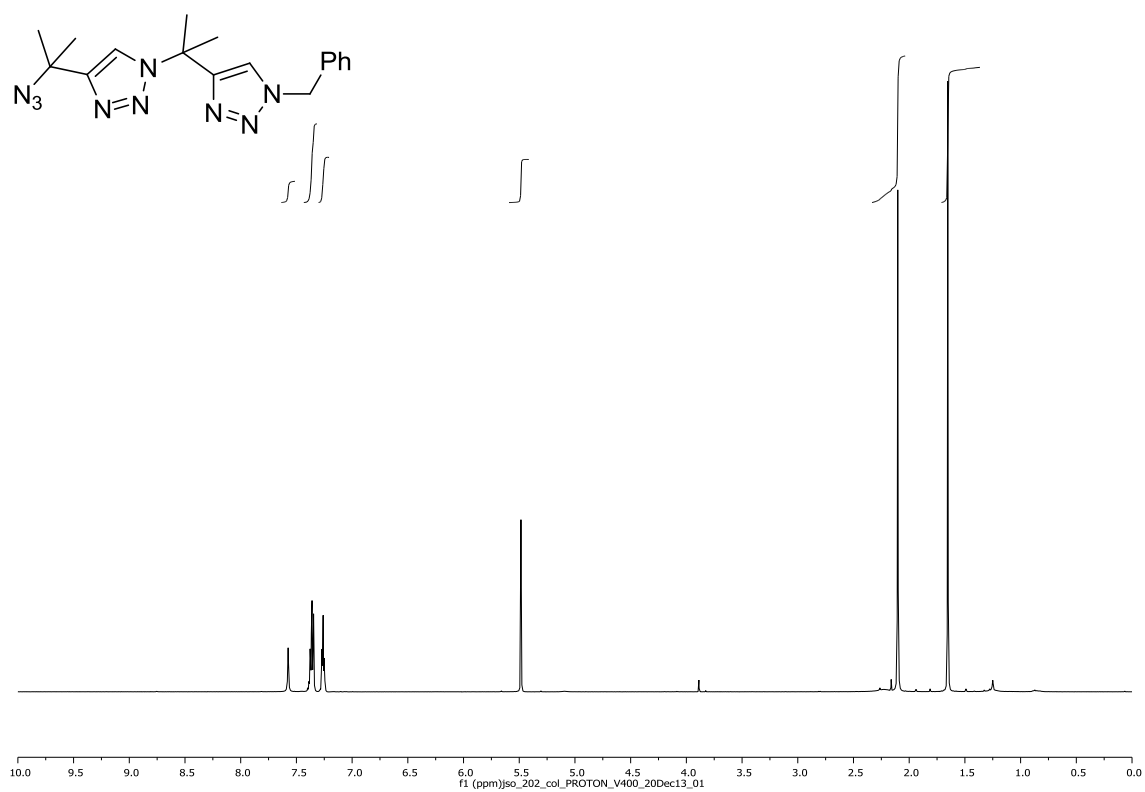
5b $^1\text{H-NMR}$ (400 MHz, CDCl_3)



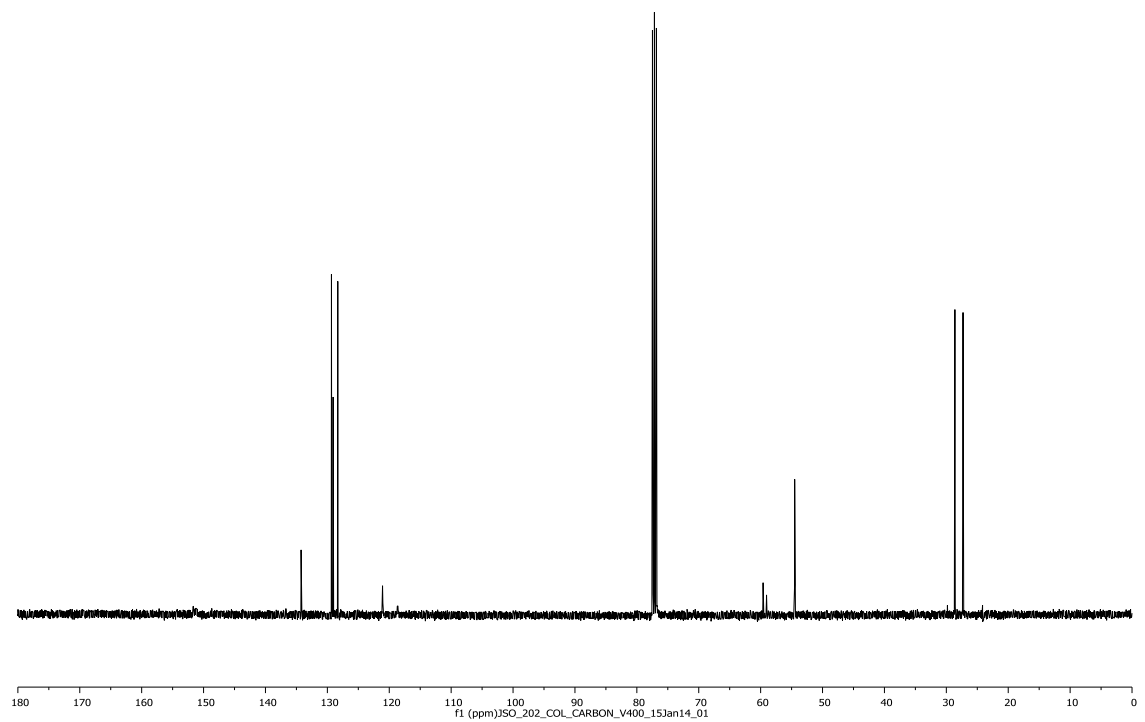
5b $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



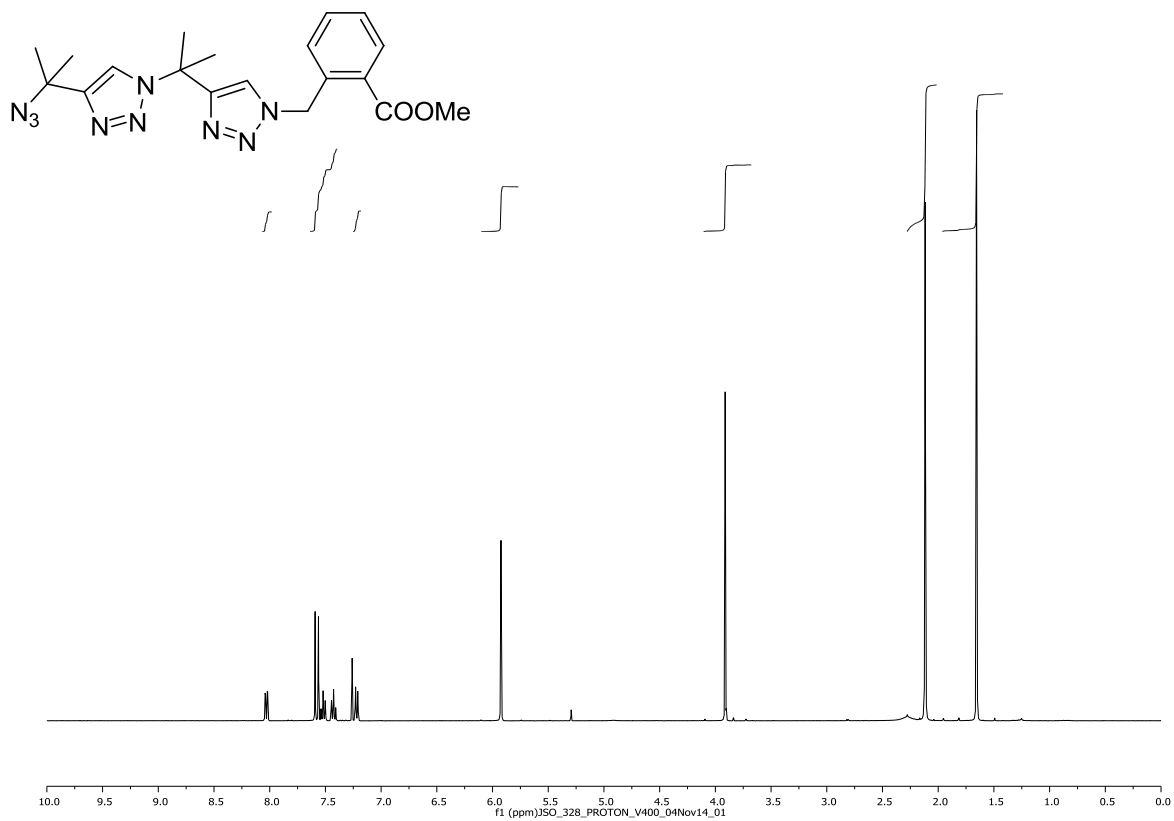
6a $^1\text{H-NMR}$ (400 MHz, CDCl_3)



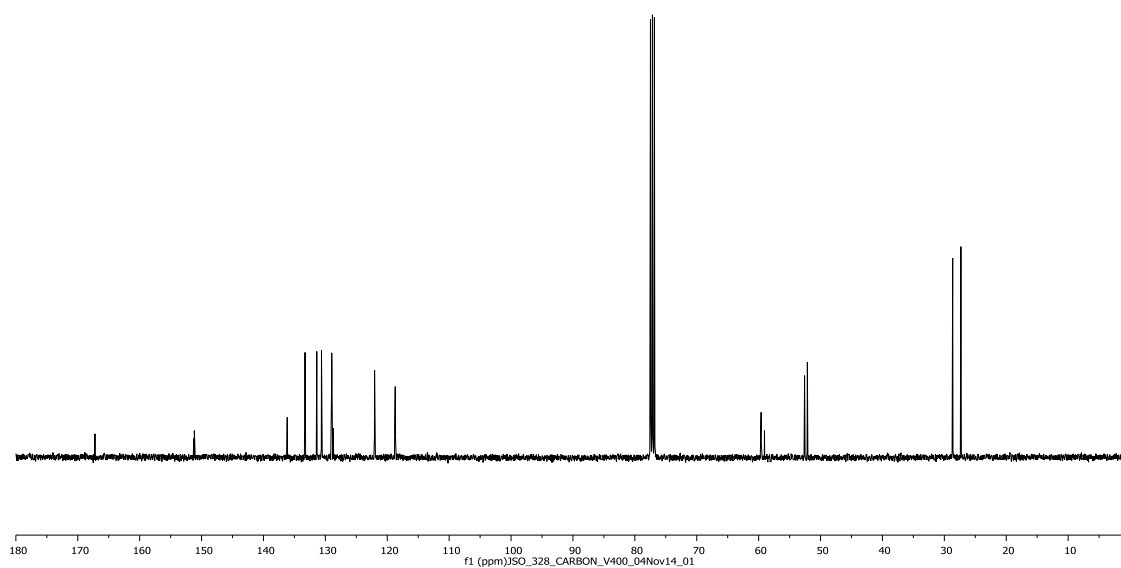
6a $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



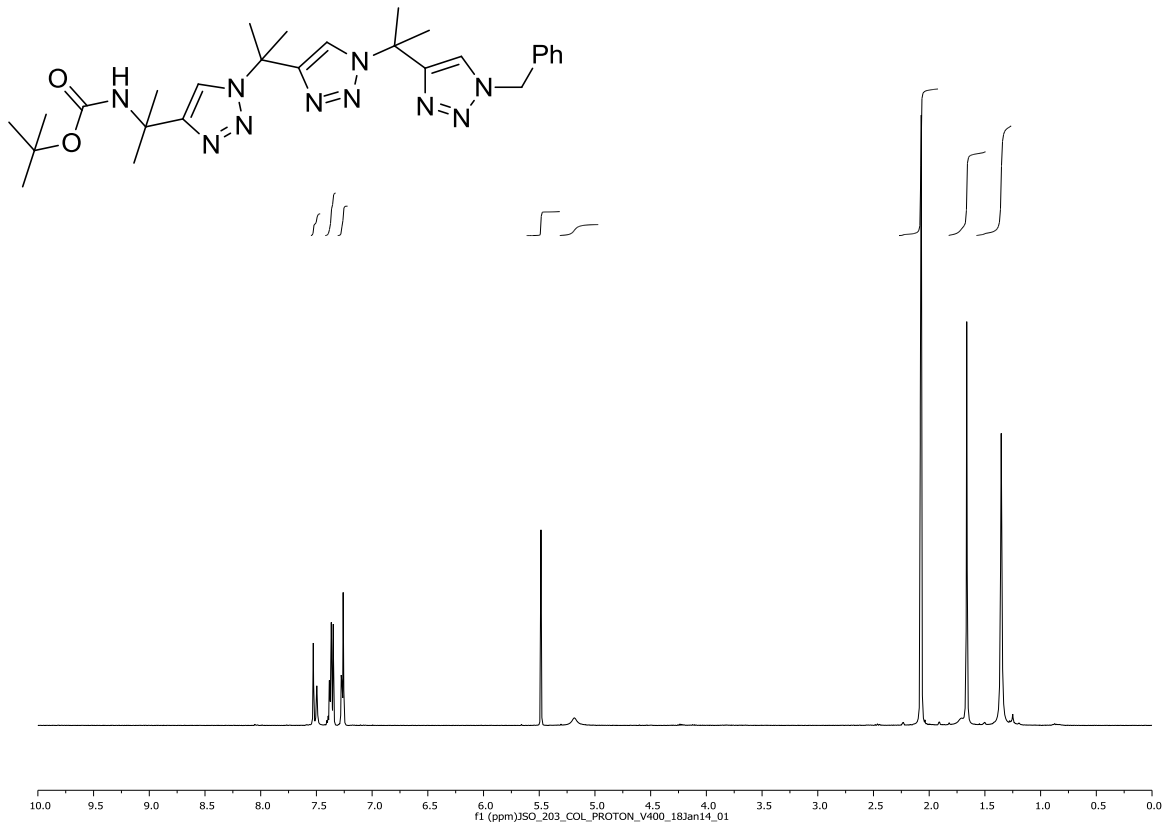
6b $^1\text{H-NMR}$ (400 MHz, CDCl_3)



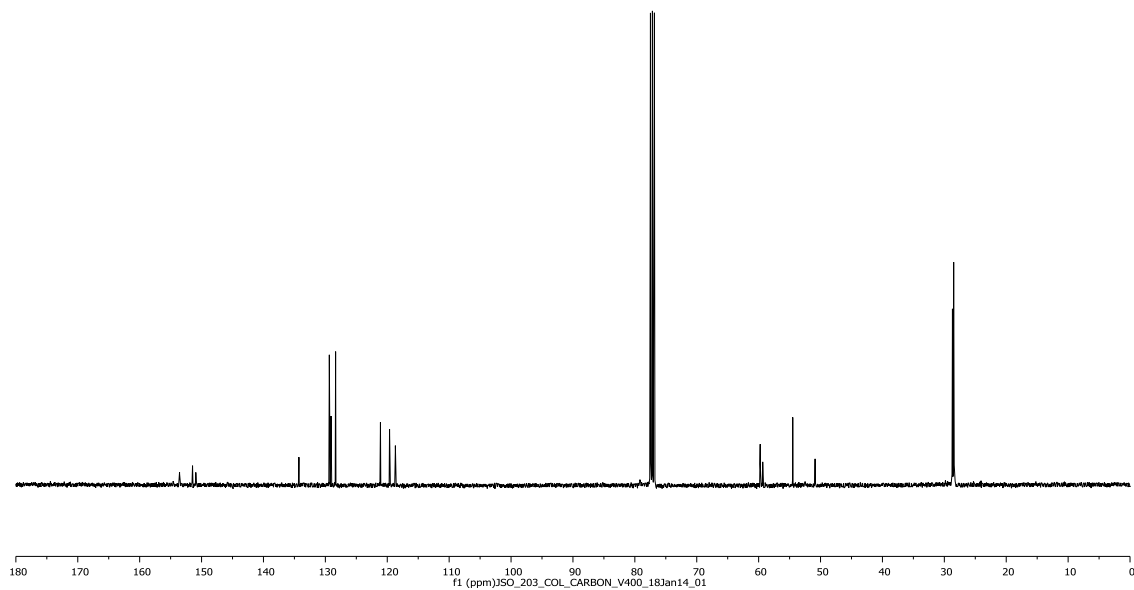
6b $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



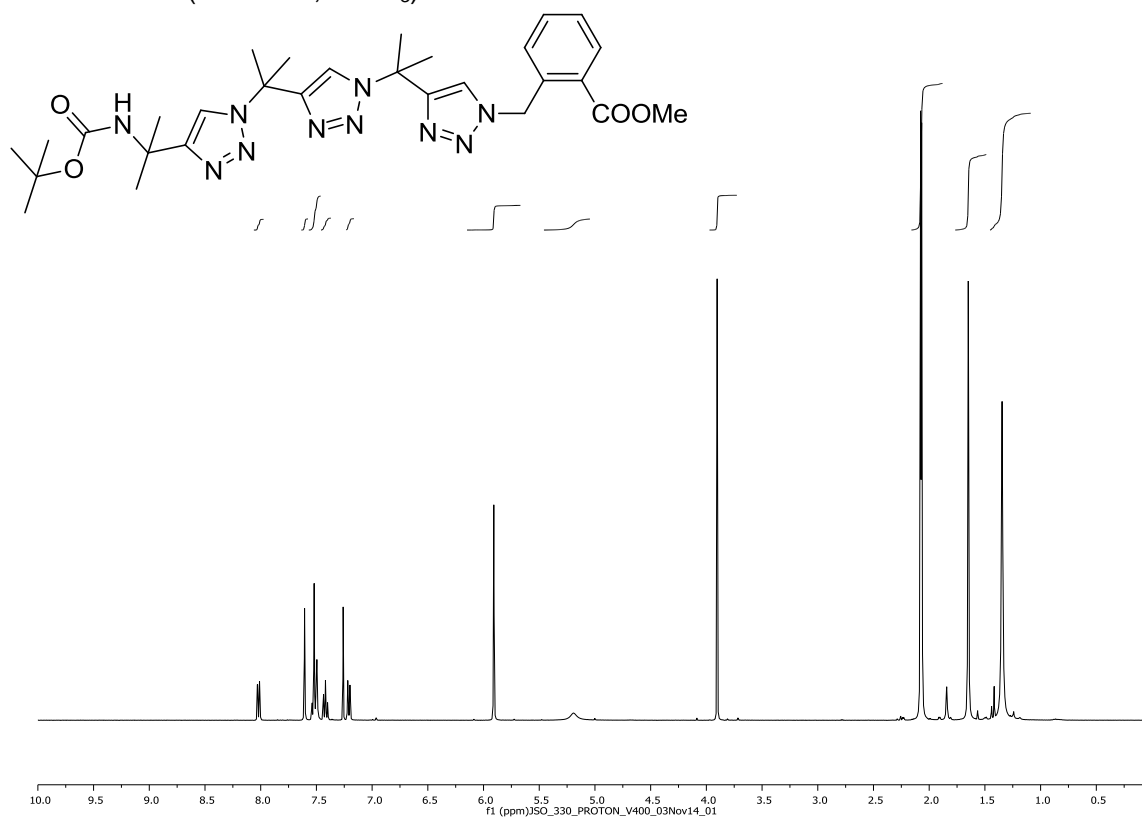
7a $^1\text{H-NMR}$ (400 MHz, CDCl_3)



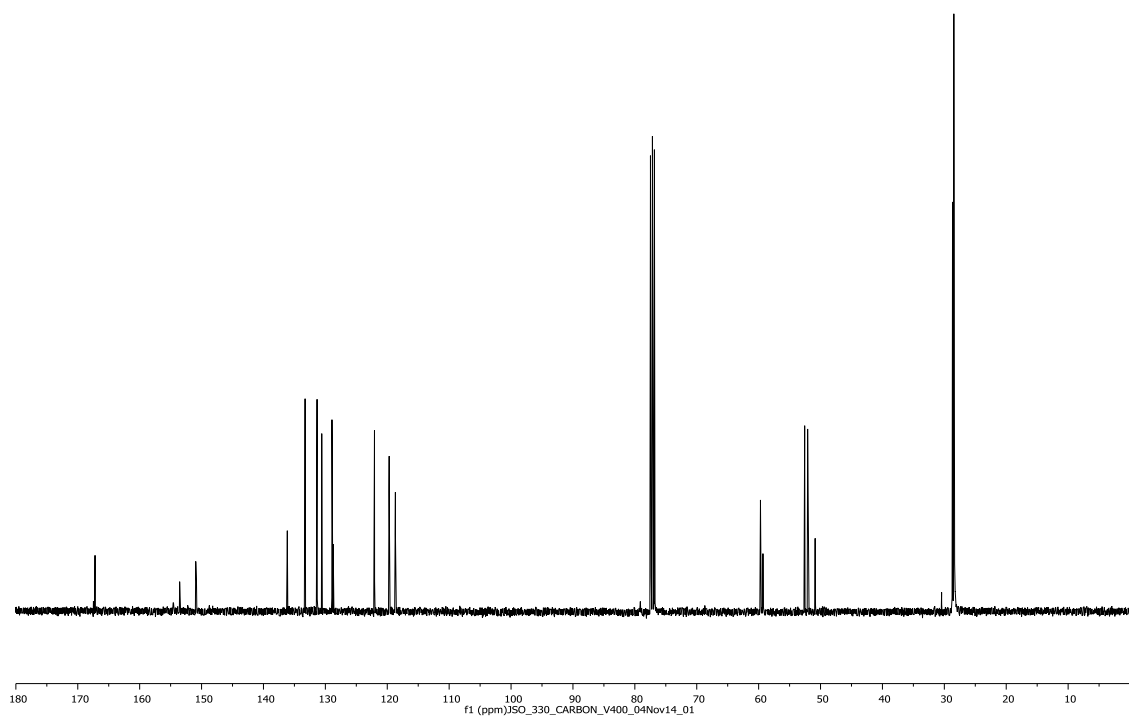
7a $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



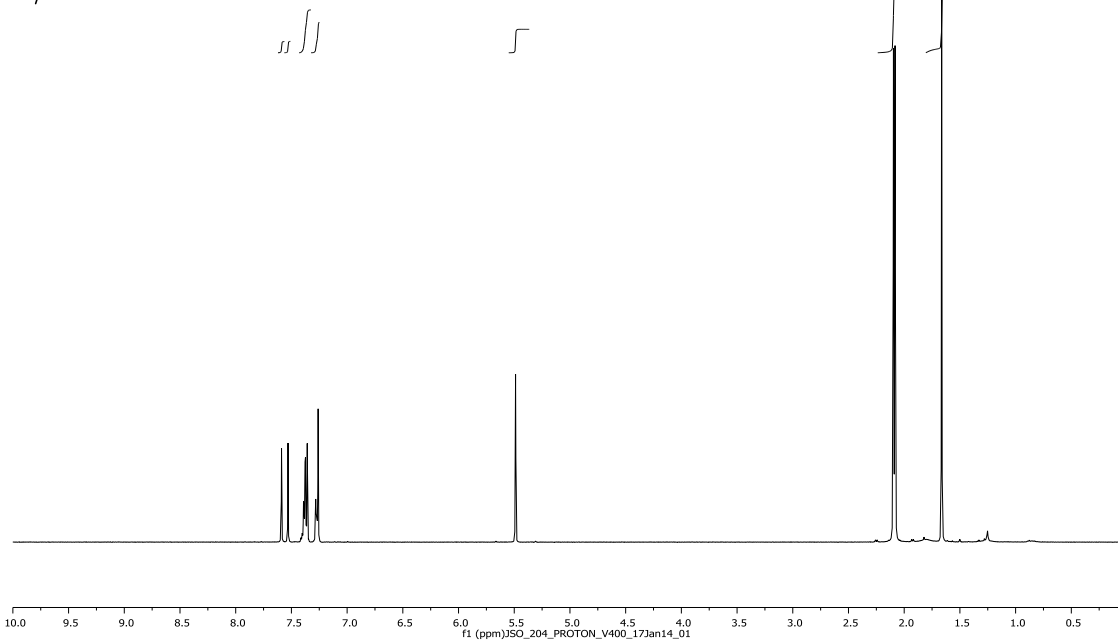
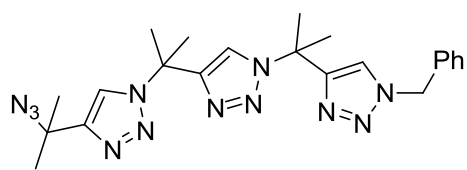
7b $^1\text{H-NMR}$ (400 MHz, CDCl_3)



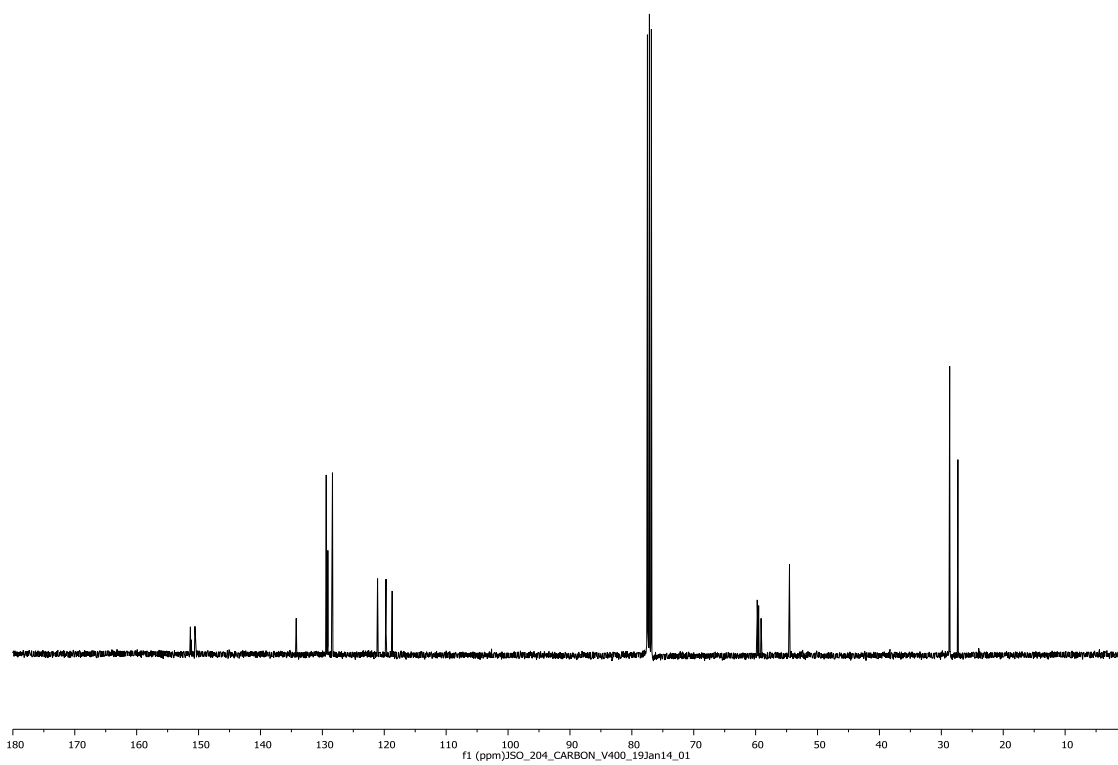
7b $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



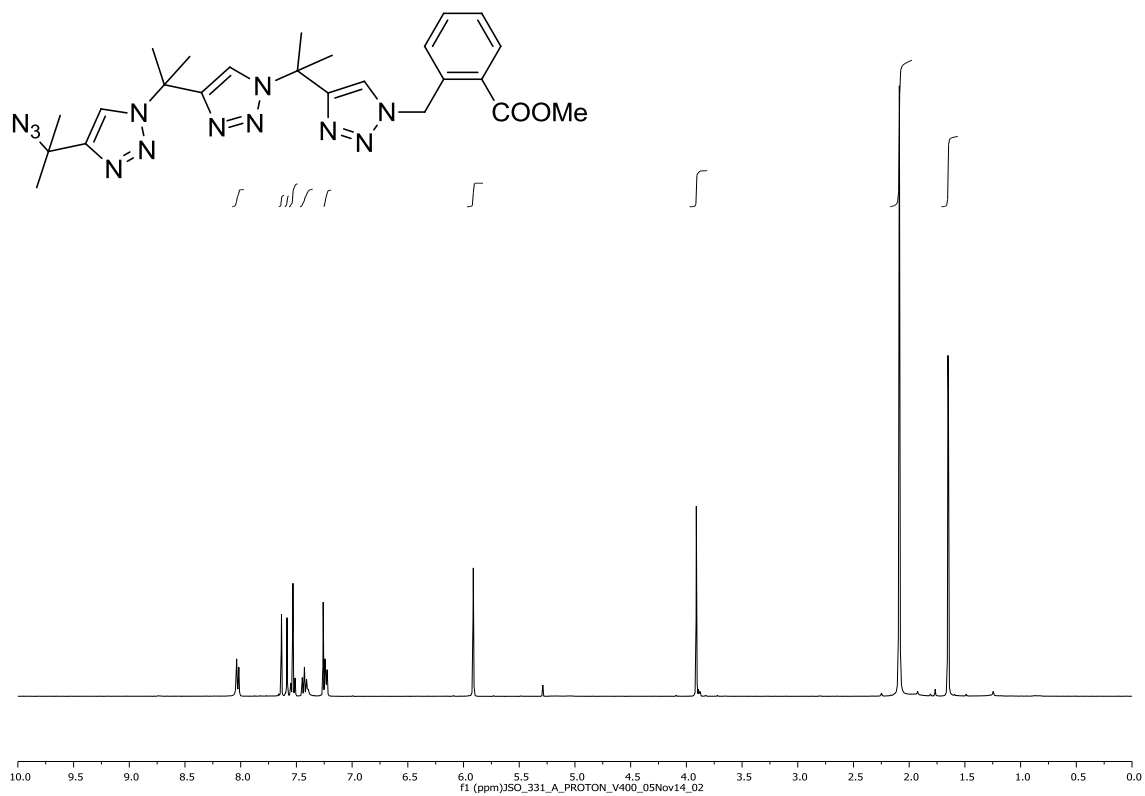
8a $^1\text{H-NMR}$ (400 MHz, CDCl_3)



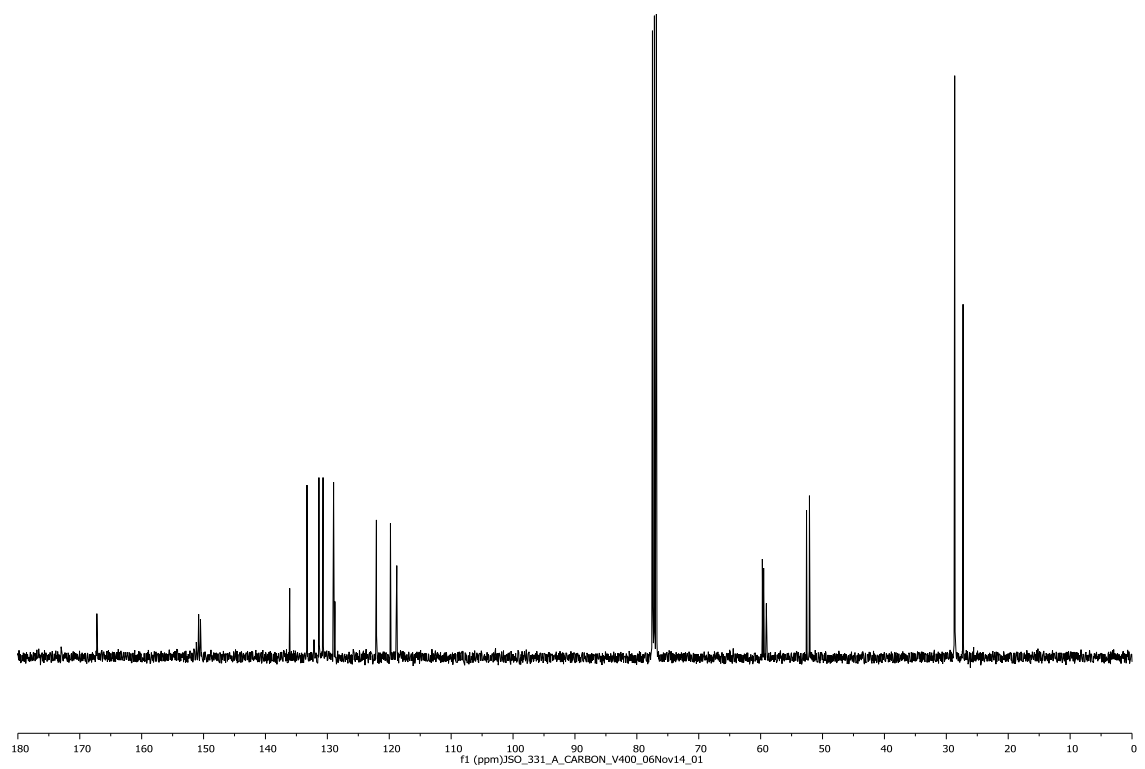
8a $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



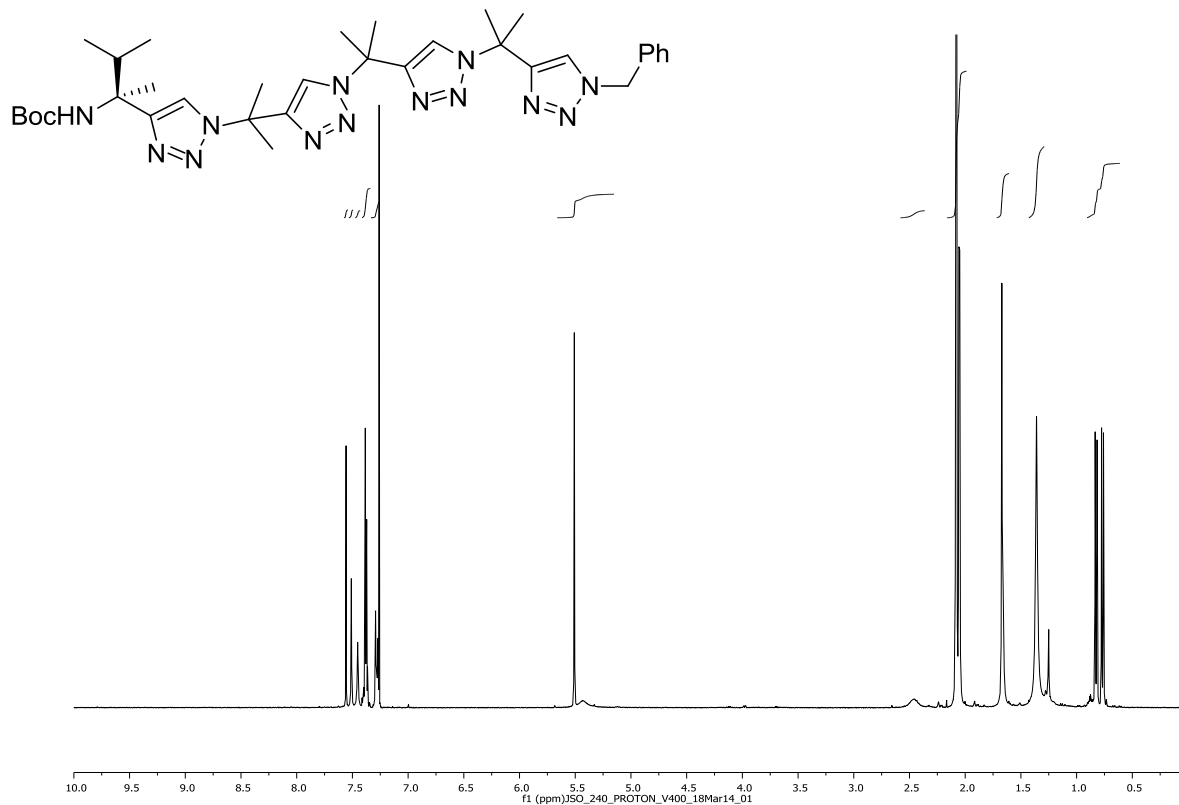
8b $^1\text{H-NMR}$ (400 MHz, CDCl_3)



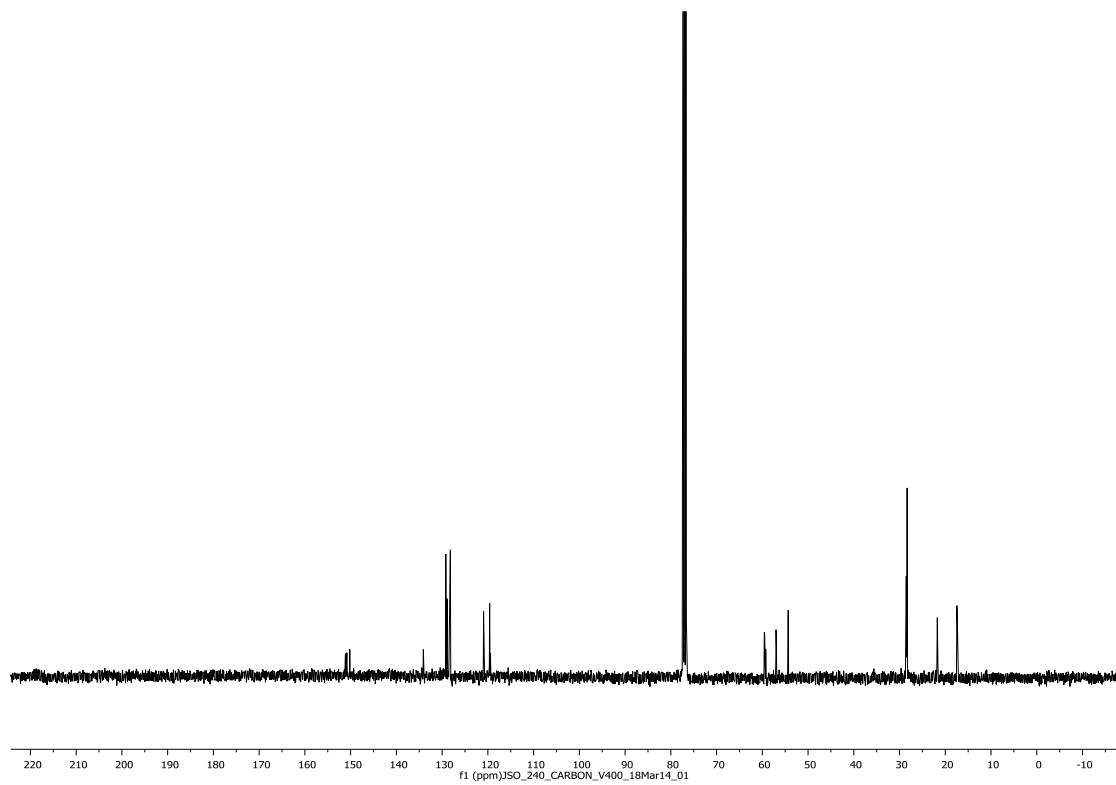
8b $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



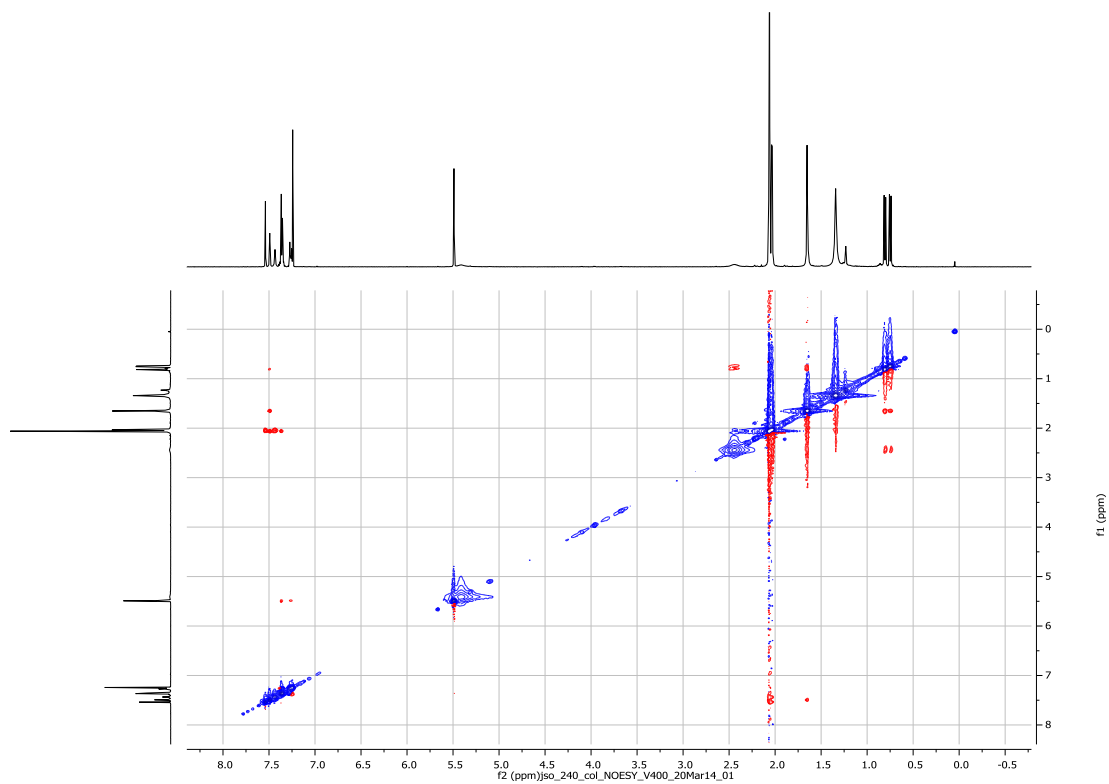
9a $^1\text{H-NMR}$ (400 MHz, CDCl_3)



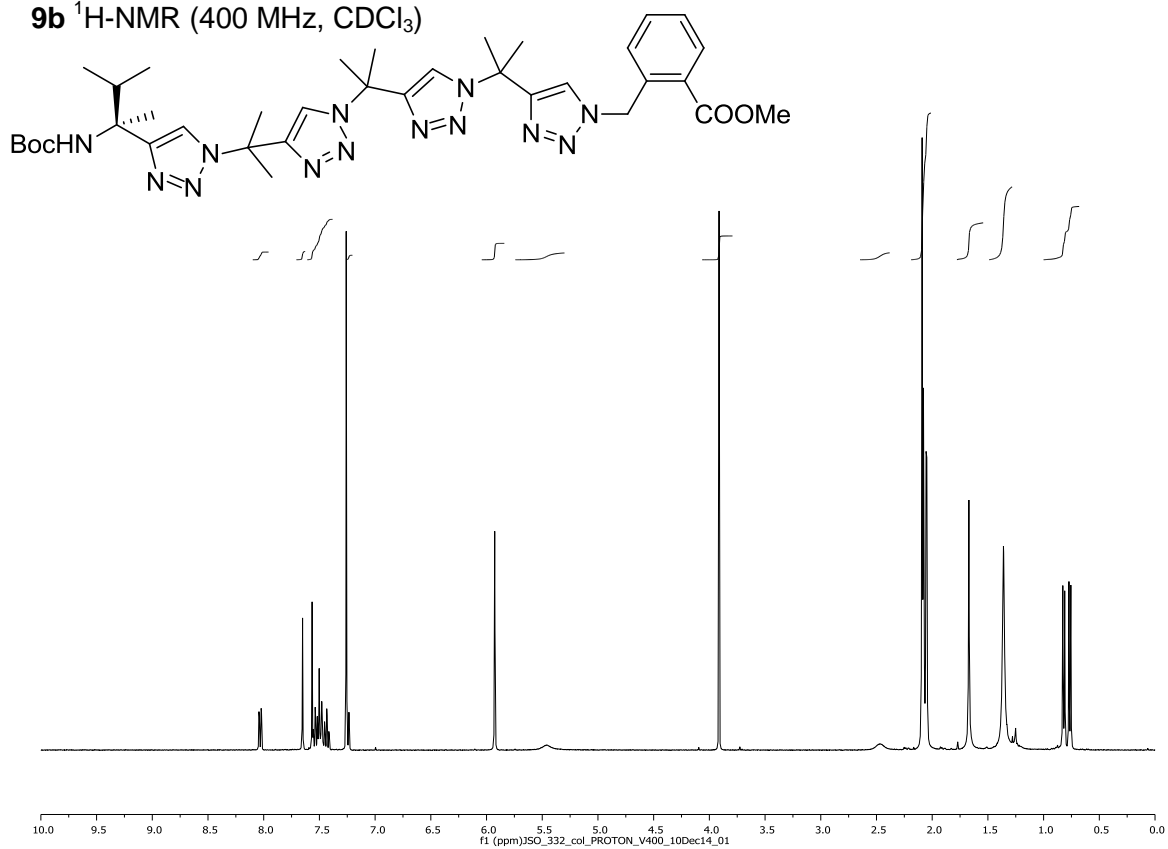
9a $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



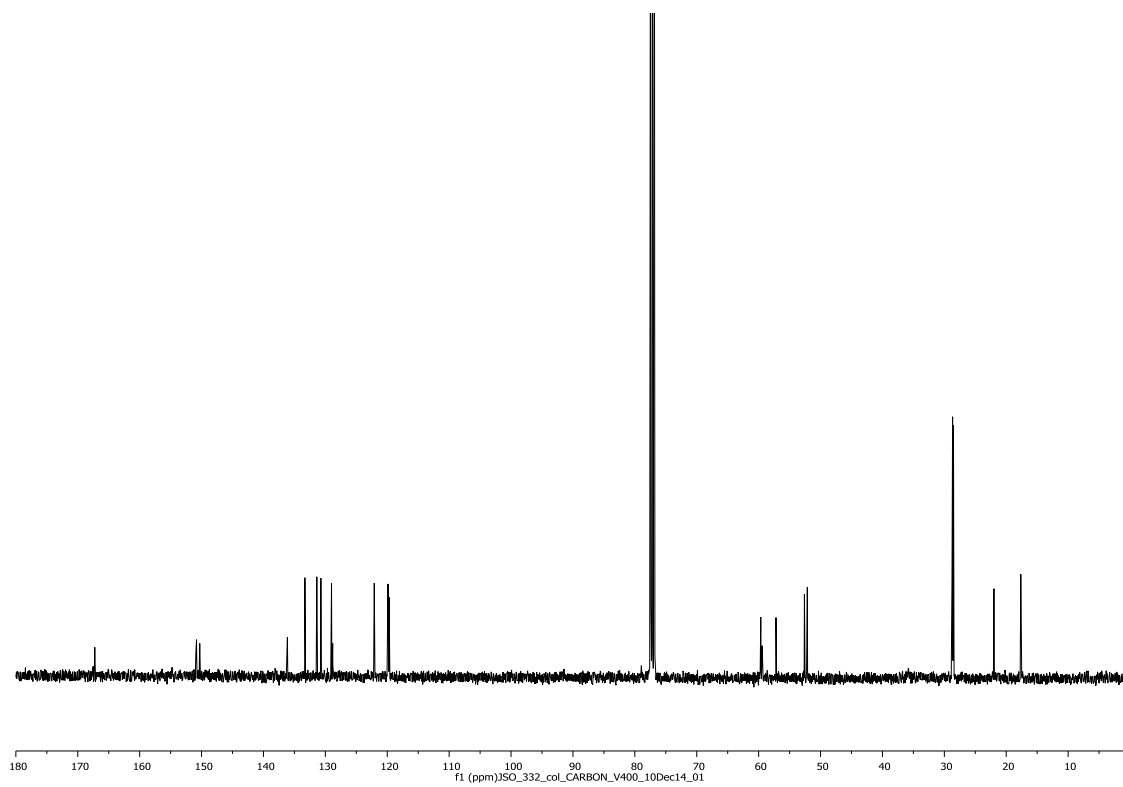
9a NOESY (400 MHz, CDCl₃)



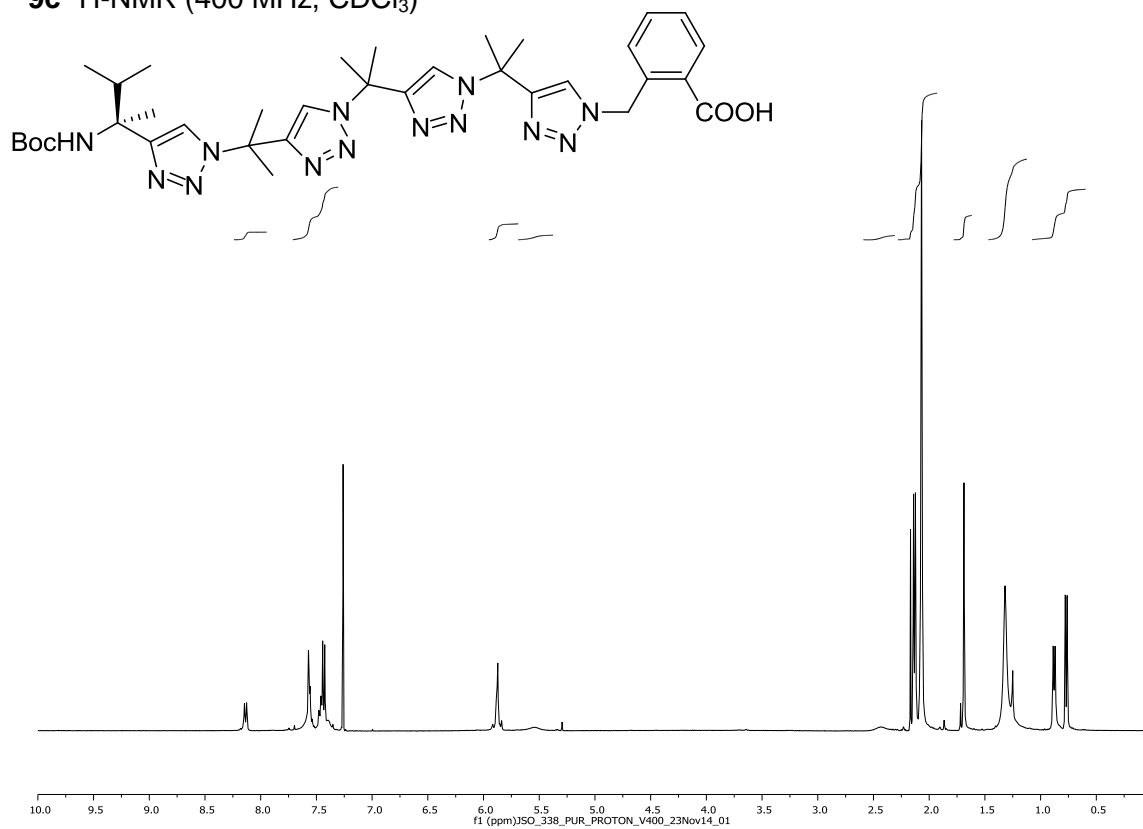
9b $^1\text{H-NMR}$ (400 MHz, CDCl_3)



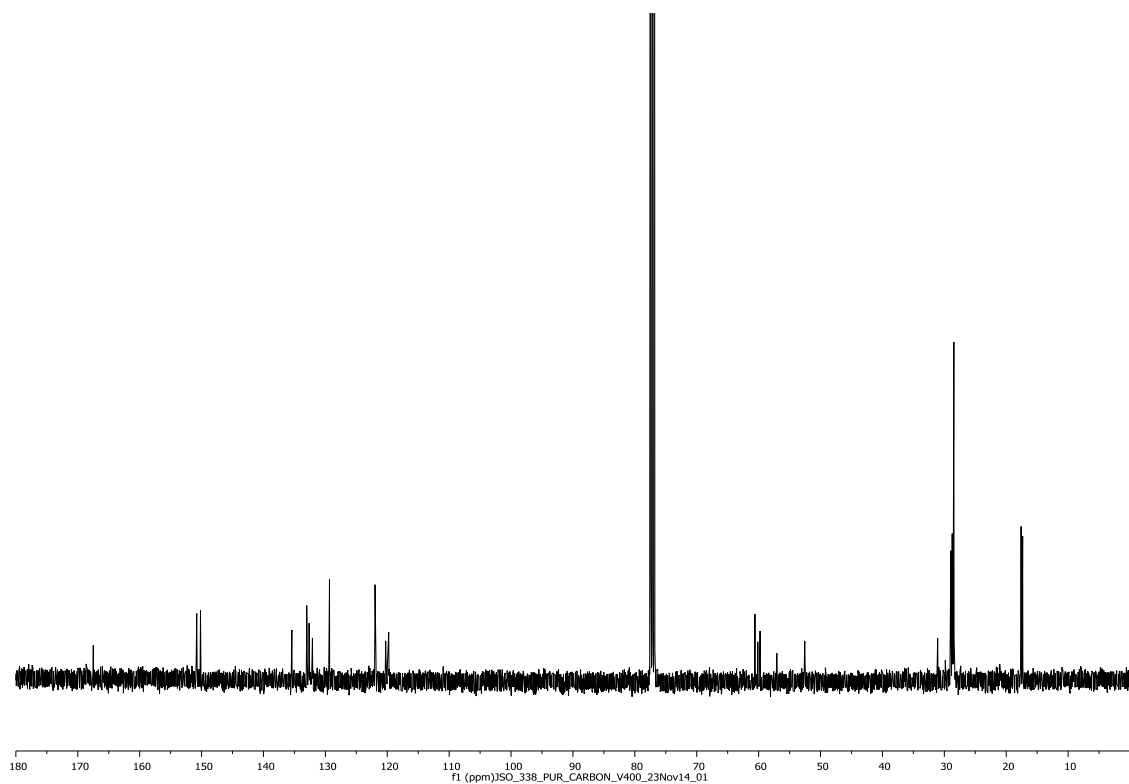
9b $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



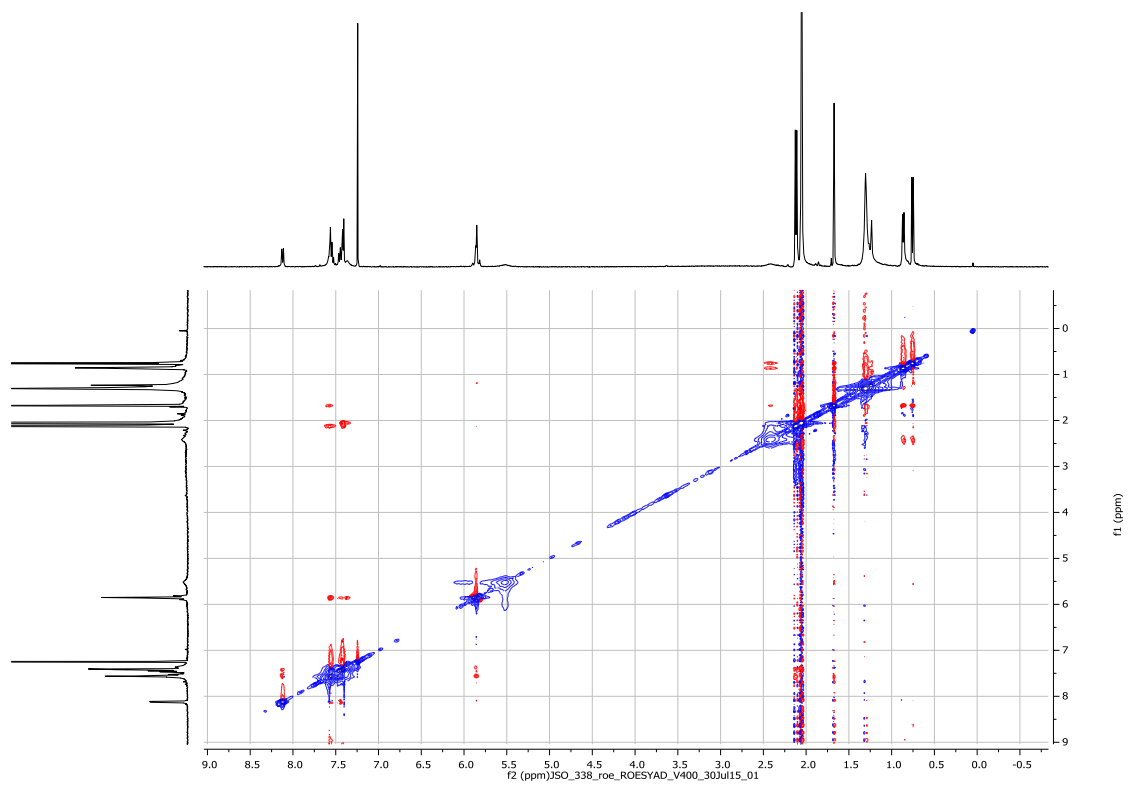
9c $^1\text{H-NMR}$ (400 MHz, CDCl_3)



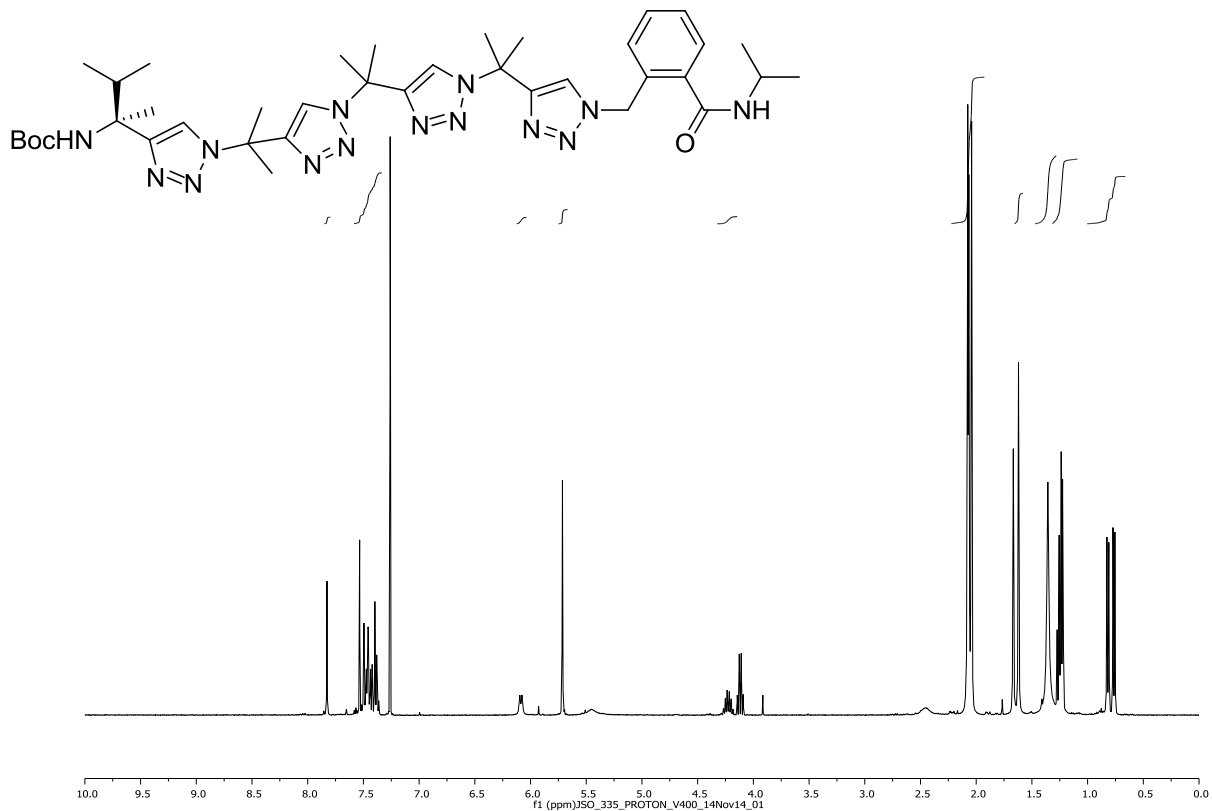
9c $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



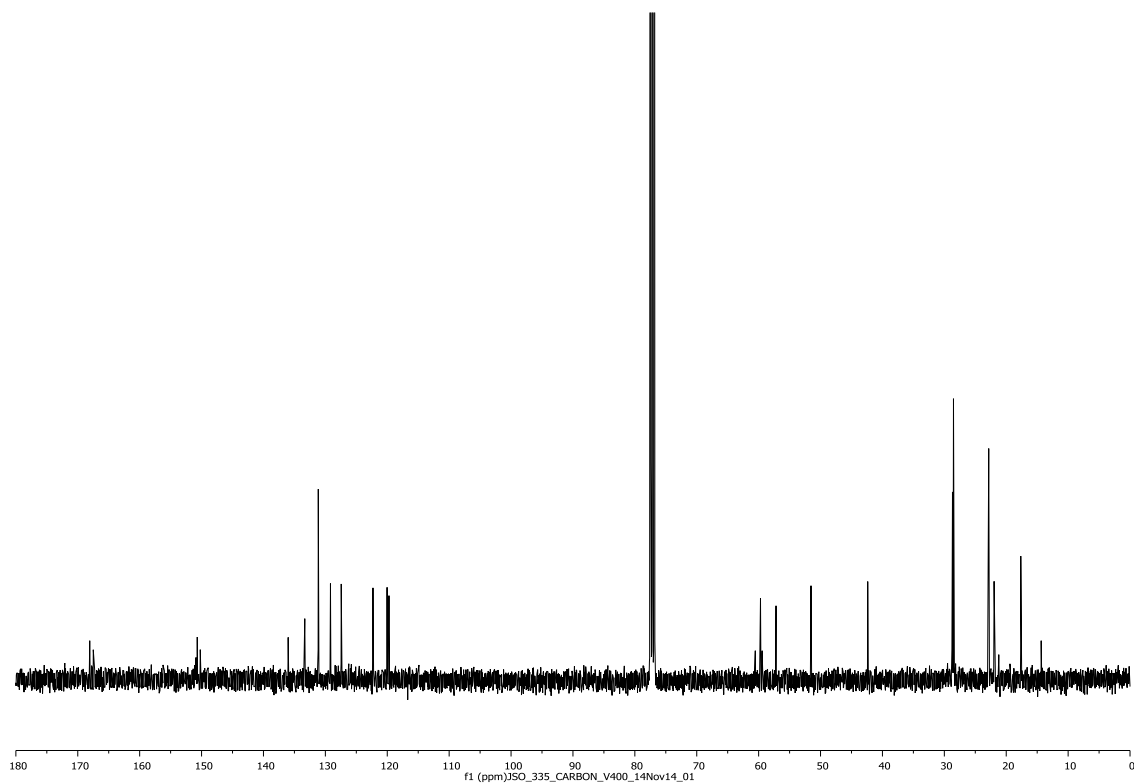
9c NOESY (400 MHz, CDCl₃)



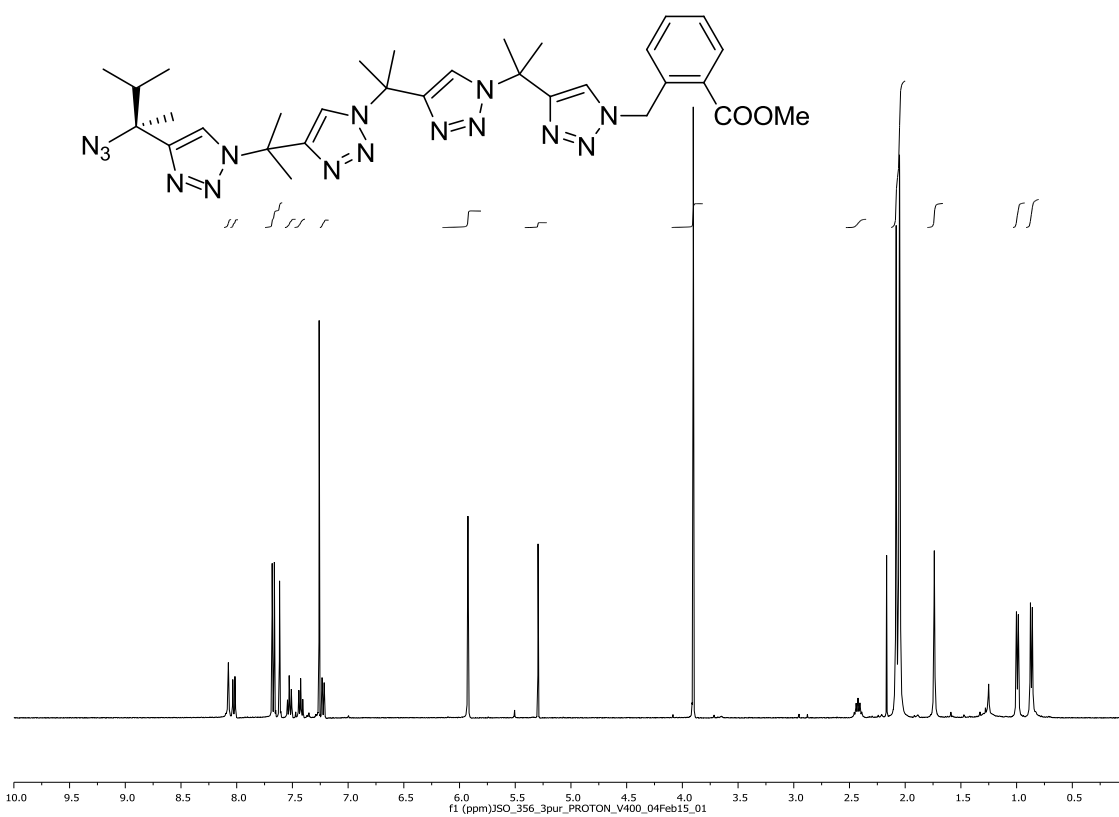
9d $^1\text{H-NMR}$ (400 MHz, CDCl_3)



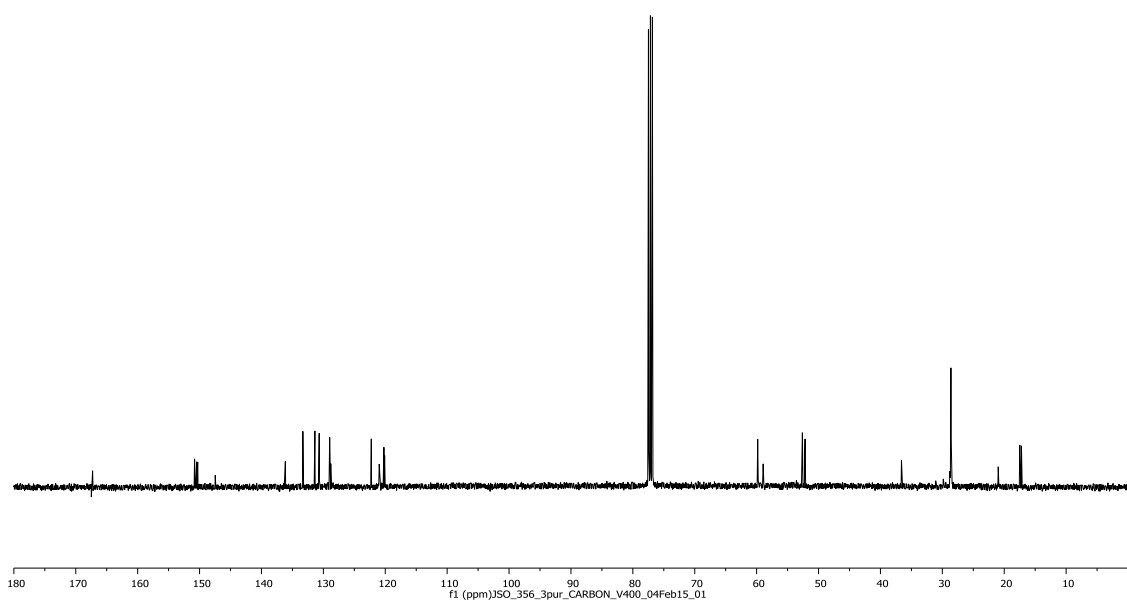
9d $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



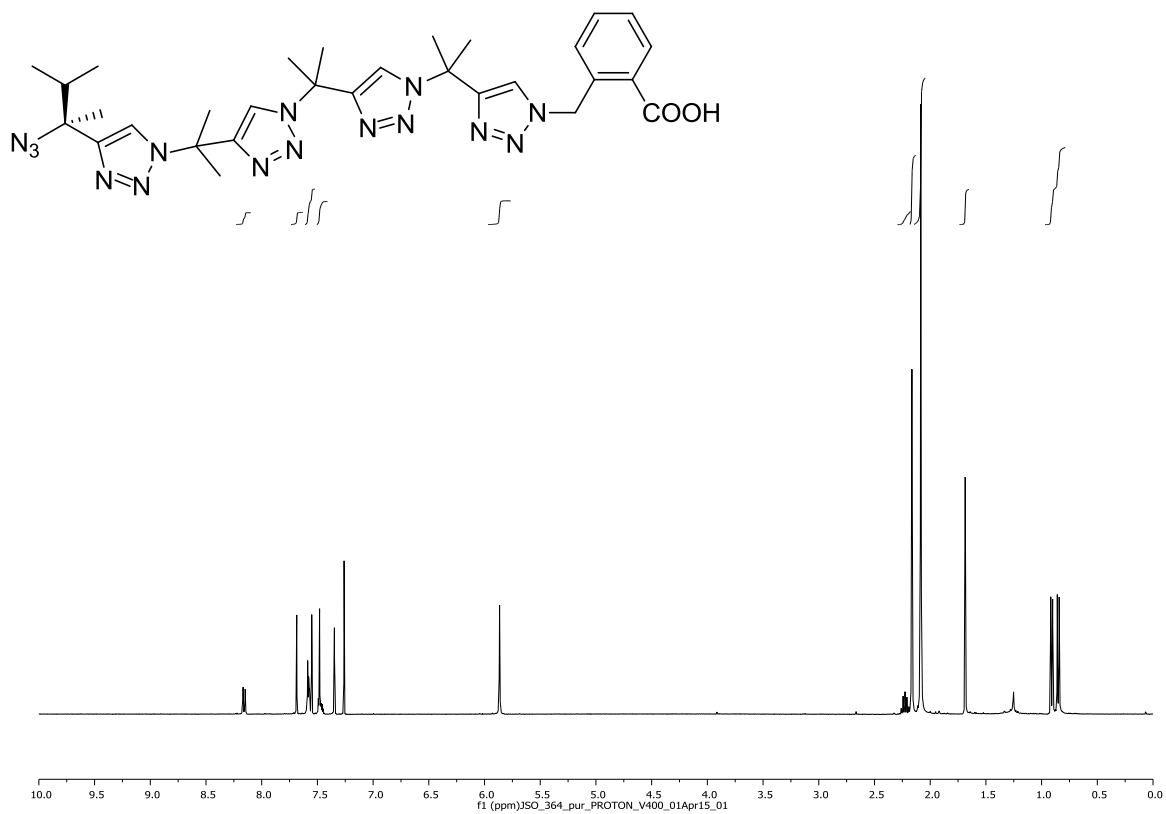
10b $^1\text{H-NMR}$ (400 MHz, CDCl_3)



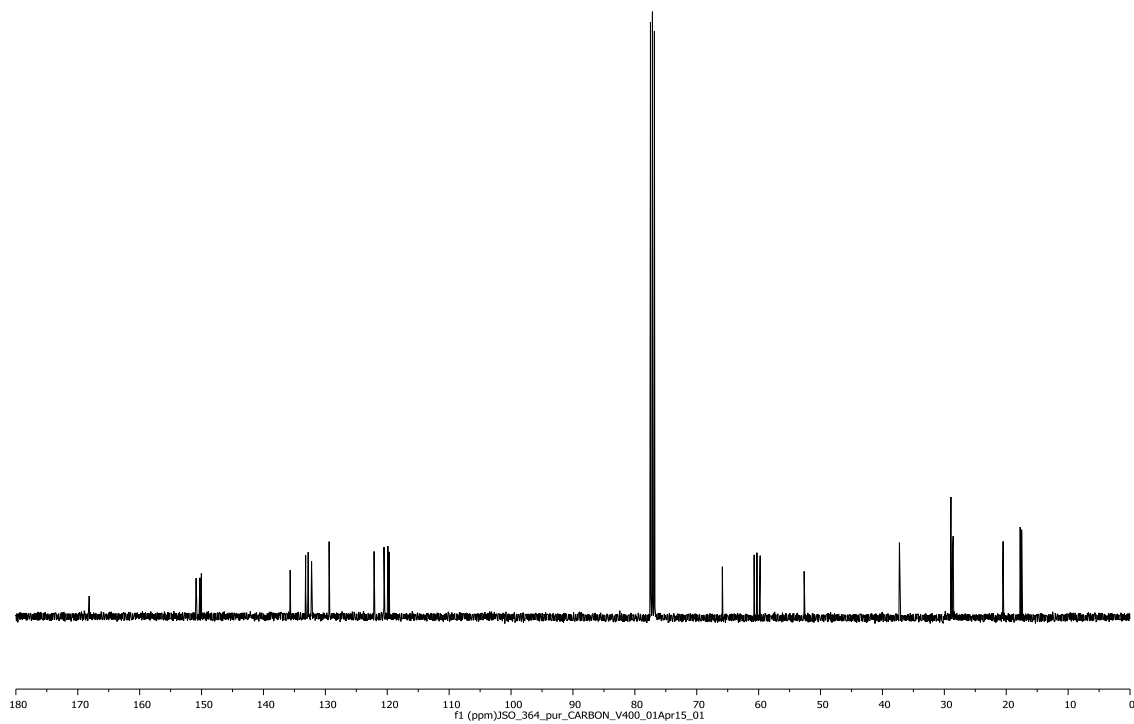
10b $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



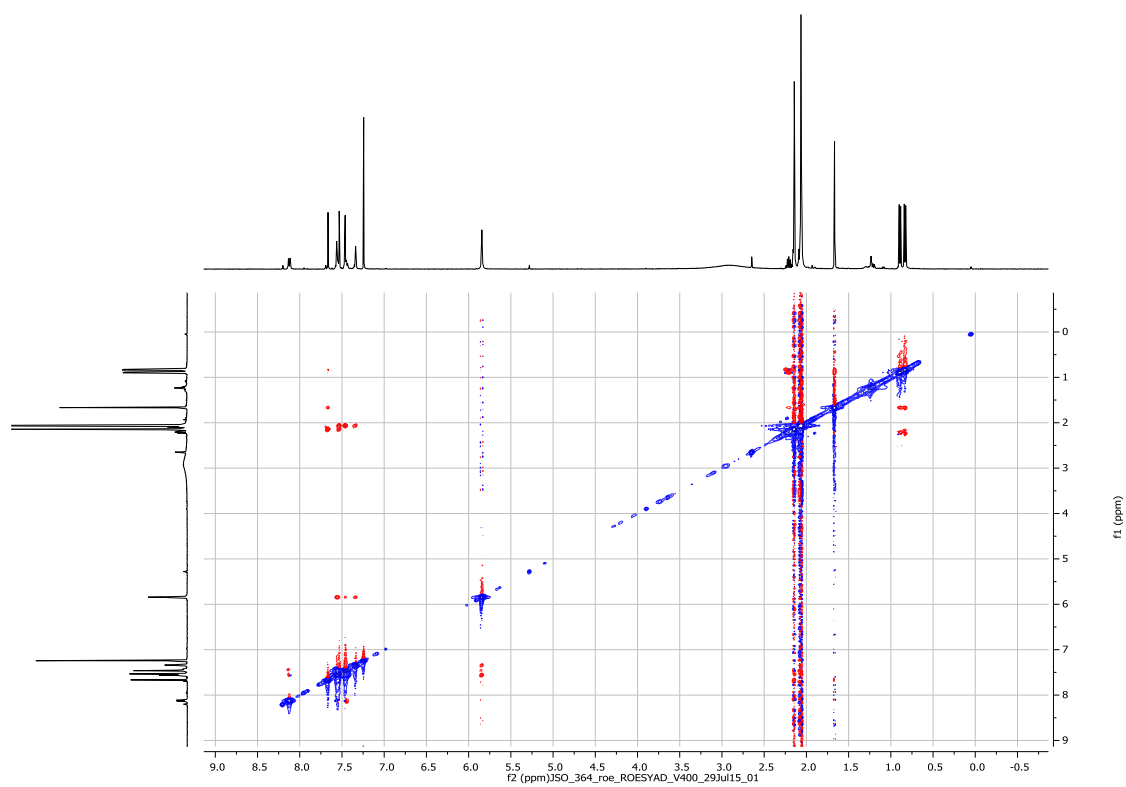
10c $^1\text{H-NMR}$ (400 MHz, CDCl_3)



10c $^{13}\text{C-NMR}$ (100 MHz, CDCl_3)



10c ROESY (400 MHz, CDCl₃)



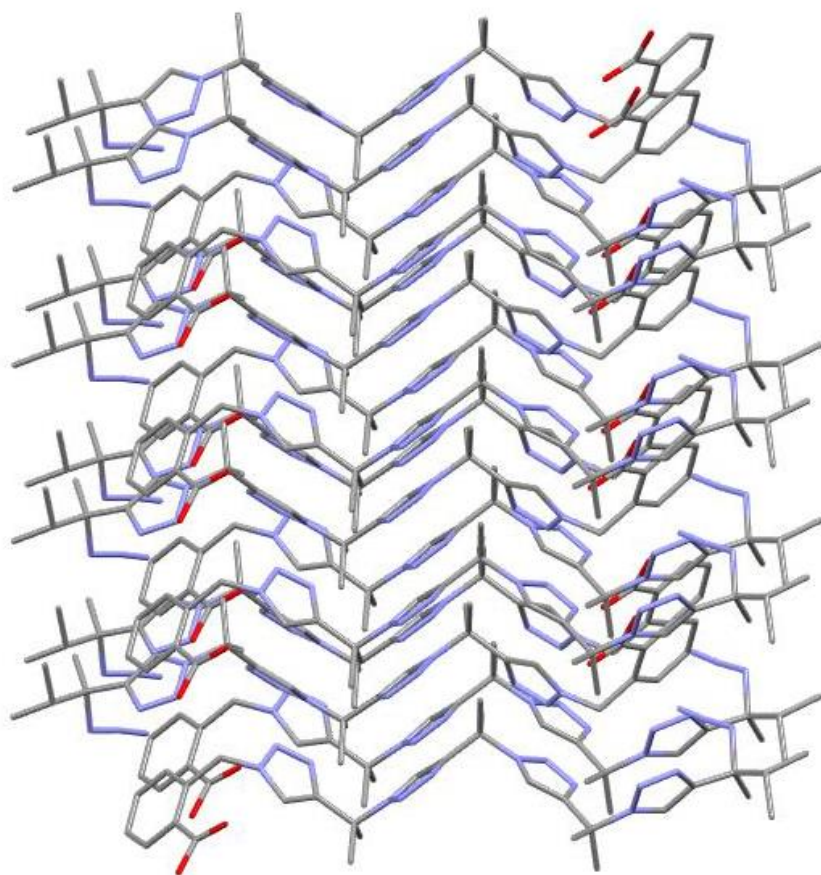


Figure ES11. Stacking of layers of product **10c** in the crystal cell