Electronic Supplementary Material (ESI) for Green Chemistry.

A pot-economy and diastereoselective synthesis involving catalyst-free click reaction for fused-triazolobenzodiazepines

Xiaofeng Zhang,[a] Sanjun Zhi,[b] Wei Wang,[c] Shuai Liu,[a]

Jerry P. Jasinski,[d] Wei Zhang[a*]

[a] *Center for Green Chemistry and Department of Chemistry, University of Massachusetts Boston, 100 Morrissey Boulevard, Boston, MA 02125, USA, E-mail: wei2.zhang@umb.edu.*

[b] *Jiangsu Key Laboratory for the Chemistry of Low-Dimensional Materials, Huaiyin Normal University, Huaian, Jiangsu 223300, PR China*

[c] *School of Chemistry and Chemical Engineering, Shaanxi Normal University, Xi'an, 710062, PR China*

[d] *Department of Chemistry, Keene State College, 220 Main Street, Keene, NH 03435-2001 USA*

Contents

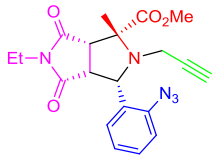
1. General Information

Chemicals and solvents were purchased from commercial suppliers and used as received. ^{1}H NMR (300 or 400 MHz) and ^{13}C NMR spectra (75 or 101 MHz) were recorded on Agilent NMR spectrometers. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26; acetonitrile δ 1.94; DMSO δ 2.50), carbon (chloroform δ 77.0; acetonitrile δ 1.32 and 118.26; DMSO δ 39.5). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants were reported in Hertz (Hz). The high resolution mass (HRMS) spectra were obtained on a Waters Micromass GCT Premier. LC-MS were performed on an Agilent 2100 LC with a 6130 quadrupole MS spectrometer. A C_{18} column (5.0 μm, 6.0 x 50 mm) was used for the separation. The mobile phases were MeOH and H_2O both containing 0.05% CF_3CO_2H. A linear gradient was used to increase from 25:75 v/v MeOH/H_2O to 100% MeOH over 7.0 min at a flow rate of 0.7 mL/min. UV detections were conducted at 210 nm, 254 nm and 365 nm. Low resolution mass spectra were recorded in APCI (atmospheric pressure chemical ionization). Final products were purified on Angela HP-100 pre-LC system with a Venusil PrepG C_{18} column (10 μm, 120 Å, 21.2 mm x 250 mm).

Synthesis of intermediate 6a

To a solution of alanine methyl ester hydrochloride **2a** (1.2 mmol), 2-azidebenzaldehyde **3a** (1.1 mmol), and N-Ethylmaleimide **4a** (1.0 mmol) in 2.0 mL of CH_3CN was added Et_3N (2.0 mmol). After stirred at 25 ^{o}C for 5 min, the reaction mixture was heated under microwaves at 115 ^{o}C for 25 min. Upon the completion of the reaction as monitored by LC-MS, propargyl bromide solution (80% in toluene, 5.0 mmol) and K_2CO_3 (1.5 mmol) were added to the reaction mixture and then heated by microwaves at 120 ^{o}C for 40 min. The concentrated reaction mixture was isolated on a semi prep-HPLC with C18 column to afford **a** light yellow solid **6a** (71% yield).

*methyl(1R,3S,3aR,6aS)-3-(2-azidophenyl)-5-ethyl-1-methyl-4,6-dioxo-2-(prop-2-yn-1-yl)octahydropyrrolo[3,4-c]pyrrole-1-carboxylate (**6a**):*



6a

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.16 (m, 3H), 7.11 – 6.99 (m, 1H), 4.96 (d, J = 10.0 Hz, 1H), 3.87 – 3.82 (m, 3H), 3.70 (dd, J = 18.7, 2.4 Hz, 1H), 3.60 (dd, J = 10.0, 8.0 Hz, 1H), 3.44 – 3.12 (m, 4H), 2.20 (t, J = 2.5 Hz, 1H), 1.66 (s, 3H), 0.95 (t, J = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.2, 174.3, 172.2, 138.9, 129.1, 127.7, 127.3, 124.8, 118.2, 79.2, 74.6, 70.1, 57.8, 54.6, 52.3, 46.0, 35.4, 33.7, 18.8, 12.8.

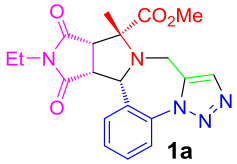
General procedure for one-pot synthesis of triazolobenzodiazepines 1

To a solution of an amino ester **2** (1.2 mmol), 2-azidebenzaldehyde **3** (1.1 mmol), and maleimide **4** (1.0 mmol) in 2.0 mL of CH_3CN was added Et_3N (2.0 mmol). After stirred at 25 ^{o}C for 5 min, the reaction mixture was heated under microwaves at 115 ^{o}C for 25 min. Upon the completion of the reaction as monitored by LC-MS, propargyl bromide solution (80% in toluene, 5.0 mmol) and K_2CO_3 (1.5 mmol) were added to the reaction mixture and then heated by microwaves at 150 ^{o}C for 50 min. The

concentrated reaction mixture was isolated on a semi prep-HPLC with C_{18} column to afford purified product **1** as a single diastereomer.

2. Analytical data for Intermediate 6a and Final Products 1

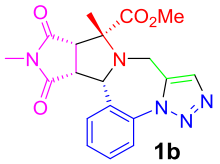
*methyl(11R,11aS,14aR,14bS)-13-ethyl-11-methyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1a**):*



1a

Following the general procedure, the title compound **1a** was obtained as a white solid (69% yield).
^{1}H NMR (400 MHz, CD_3CN) δ 8.12 (dd, *J* = 5.6, 4.0 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.50 – 7.42 (m, 3H), 5.13 (d, *J* = 7.1 Hz, 1H), 4.02 (d, *J* = 15.2 Hz, 1H), 3.72 – 3.57 (m, 5H), 3.16 (dd, *J* = 14.3, 7.4 Hz, 3H), 1.52 (s, 3H), 0.74 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (101 MHz, CD_3CN) δ 175.3, 174.6, 171.5, 137.5, 134.5, 132.1, 130.5, 128.2, 127.2, 126.9, 123.8, 70.5, 67.2, 53.5, 51.7, 47.6, 39.0, 33.1, 14.8, 11.7.
HRMS (EI, m/z): calcd. for $C_{20}H_{21}N_5O_4$: 395.1594, Found: 395.1622.

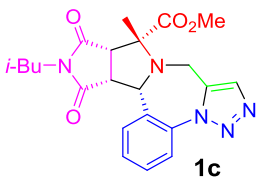
*methyl(11R,11aS,14aR,14bS)-11,13-dimethyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1b**):*



1b

Following the general procedure, the title compound **1b** was obtained as a white solid (63% yield).
^{1}H NMR^{1}H NMR (400 MHz, CD_3CN) δ 8.20 – 8.12 (m, 1H), 7.71 – 7.63 (m, 1H), 7.50 – 7.42 (m, 3H), 5.11 (d, *J* = 7.1 Hz, 1H), 4.03 (d, *J* = 15.2 Hz, 1H), 3.75 (t, *J* = 7.5 Hz, 1H), 3.66 – 3.57 (m, 4H), 3.18 (d, *J* = 7.8 Hz, 1H), 2.62 (s, 3H), 1.52 (s, 3H).
^{13}C NMR (101 MHz, CD_3CN) δ 175.6, 174.9, 171.5, 137.2, 134.3, 132.1, 130.7, 128.2, 127.2, 126.6, 123.6, 70.6, 67.2, 53.5, 51.9, 47.7, 39.4, 24.1, 14.7.
HRMS (EI, m/z): calcd. for $C_{19}H_{19}N_5O_4$: 381.1437, Found: 381.1511.

*methyl(11R,11aS,14aR,14bS)-13-isobutyl-11-methyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1c**):*

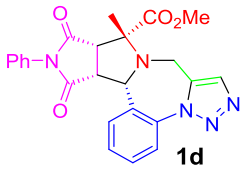


1c

Following the general procedure, the title compound **1c** was obtained as a white solid (63% yield).
^{1}H NMR (400 MHz, CD_3CN) δ 8.13 – 8.05 (m, 1H), 7.64 (ddd, *J* = 12.8, 6.5, 5.0 Hz, 1H), 7.49 – 7.41 (m, 3H), 5.16 (d, *J* = 7.4 Hz, 1H), 4.04 (d, *J* = 15.1 Hz, 1H), 3.72 – 3.57 (m, 6H), 3.13 (d, *J* = 7.6 Hz, 1H),

2.96 (dd, *J* = 13.1, 7.5 Hz, 2H), 1.52 (s, 3H), 0.56 (d, *J* = 6.7 Hz, 3H), 0.34 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, CD_3CN) δ 175.7, 174.8, 171.4, 132.2, 128.2, 127.1, 126.8, 123.8, 70.5, 67.4, 53.3, 51.5, 47.4, 45.2, 39.0, 26.3, 18.8, 18.2, 14.5.
HRMS (EI, m/z): calcd. for $C_{22}H_{25}N_5O_4$: 423.1907, Found: 423.2022.

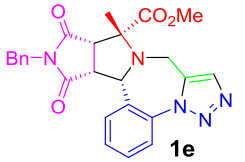
*methyl(11R,11aS,14aR,14bS)-11-methyl-12,14-dioxo-13-phenyl-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1d**):*



1d

Following the general procedure, the title compound **1d** was obtained as a white solid (46% yield).
1H NMR (300 MHz, CD_3CN) δ 8.13-8.05 (m, 3.5 Hz, 1H), 7.73-7.66 (m, 1H), 7.52 – 7.10 (m, 6H), 6.89 – 6.72 (m, 2H), 5.19 (d, J = 6.9 Hz, 1H), 4.05 (d, J = 15.2 Hz, 1H), 3.83 (t, J = 7.3 Hz, 1H), 3.73 – 3.50 (m, 4H), 3.29 (d, J = 7.7 Hz,1), 1.55 (s, 3H).
^{13}C NMR (75 MHz, CD_3CN) δ 175.8, 175.2, 172.5, 138.5, 135.5, 133.1, 133.1, 131.5, 129.9, 129.3, 128.2, 127.8, 127.4, 124.7, 71.9, 68.3, 54.7, 52.8, 49.1, 39.9, 15.9.
HRMS (EI, m/z): calcd. for $C_{24}H_{21}N_5O_4$: 443.1594, Found: 443.1684.

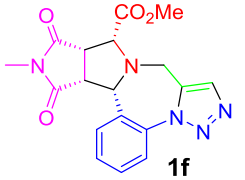
*methyl(11R,11aS,14aR,14bS)-13-benzyl-11-methyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1e**):*



1e

Following the general procedure, the title compound **1e** was obtained as a white solid (66% yield).
1H NMR (300 MHz, CD_3CN) δ 8.14–7.93 (m, 1H), 7.70–7.48 (m, 2H), 7.48–7.22 (m, 2H), 7.13-7.00 (m, 3H), 6.72 (d, J = 7.0 Hz, 2H), 5.19 (d, J = 7.3 Hz, 1H), 4.36 (s, 2H), 4.05 (d, J = 15.1 Hz, 1H), 3.77 (t, J = 7.5 Hz, 1H), 3.72 – 3.56 (m, 1H), 3.30 (s, 3H), 3.21 (d, J = 7.7 Hz, 1H), 1.52 (s, 3H).
^{13}C NMR (75 MHz, CD_3CN) δ 176.3, 175.7, 172.2, 138.5, 136.1, 135.4, 133.2, 131.5, 129.2, 128.8, 128.1, 127.6, 126.6, 124.7, 71.6, 68.4, 54.5, 52.3, 48.5, 42.1, 40.1, 15.4.
HRMS (EI, m/z): calcd. for $C_{25}H_{23}N_5O_4$: 457.1750, Found: 457.1872.

*methyl(11R,11aS,14aR,14bS)-13-methyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1f**):*

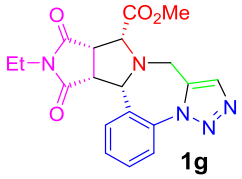


1f

Following the general procedure, the title compound **1f** was obtained as a white solid (58% yield).
^{1}H NMR (400 MHz, CD_3CN) δ 8.18 (d, *J* = 9.7 Hz, 1H), 7.80 (dd, J = 6.9, 2.5 Hz, 1H), 7.54 (d, *J* = 0.5 Hz, 1H),7.52 – 7.44 (m, 2H), 4.53 (d, *J* = 6.9 Hz, 1H), 4.15 (d, *J* = 15.1 Hz, 1H), 3.82 – 3.72 (m, 3H),

3.66 (d, *J* = 15.1 Hz, 1H), 3.55 (t, *J* = 8.1 Hz, 1H), 3.29 (d, *J* = 5.3 Hz, 3H).
^{13}C NMR (101 MHz, DMSO) δ 176.0, 175.6, 169.4, 136.3, 134.3, 132.3, 132.1, 128.7, 127.7, 126.3, 123.3, 118.5, 70.2, 66.8, 52.2, 47.4, 46.0, 42.5, 25.1, 1.6, 0.5.

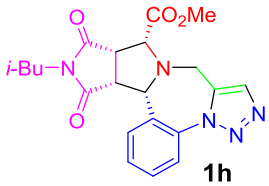
*methyl(11R,11aS,14aR,14bS)-13-ethyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1g**):*



1g

Following the general procedure, the title compound **1g** was obtained as a white solid (65% yield).
^{1}H NMR (400 MHz, CD_3CN) δ 8.15 (dd, *J* = 5.2, 4.5 Hz, 1H), 7.78 (s, 1H), 7.56 – 7.44 (m, 3H), 4.54 (d, *J* = 6.8 Hz, 1H), 4.20 – 4.02 (m, 2H), 3.80 – 3.62 (m, 5H), 3.56 – 3.47 (m, 1H), 3.34 – 3.19 (m, 2H), 0.82 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (101 MHz, CD_3CN) δ 175.4, 174.7, 169.0, 131.6, 131.2, 128.5, 127.4, 126.1, 123.5, 70.2, 66.6, 51.6, 47.2, 45.8, 41.7, 33.3, 11.8.

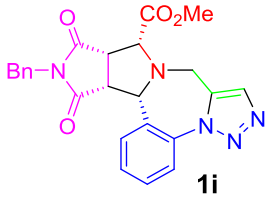
*methyl(11R,11aS,14aR,14bS)-13-isobutyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1h**):*



1h

Following the general procedure, the title compound **1h** was obtained as a white solid (61% yield).
^{1}H NMR (400 MHz, , CD_3CN) δ 8.14 – 8.08 (m, 1H), 7.76 – 7.65 (m, 1H), 7.57 – 7.32 (m, 3H), 4.63 (d, *J* = 7.0 Hz, 1H), 4.20 (d, *J* = 14.9 Hz, 1H), 3.82 – 3.61 (m, 5H), 3.50 (t, *J* = 7.8 Hz, 1H), 3.01 (dd, *J* = 13.1, 7.4 Hz, 3H), 1.66 – 1.50 (m, 1H), 0.58 (d, *J* = 6.8 Hz,3 H), 0.44 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, , CD_3CN) δ 175.8, 175.0, 168.9, 136.6, 134.5, 131.7, 130.9, 128.4, 127.3, 126.1, 123.6, 70.6, 66.7, 51.5, 47.2, 45.9, 45.4, 41.4, 26.5, 18.8, 18.5.

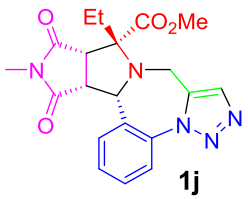
*methyl(11R,11aS,14aR,14bS)-13-benzyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1i**):*



1i

Following the general procedure, the title compound **1i** was obtained as a white solid (63% yield).
^{1}H NMR (400 MHz, CD_3CN) δ 8.12 (dd, *J* = 6.0, 3.7 Hz, 1H), 7.70 (dd, *J* = 5.8, 3.8 Hz, 1H), 7.62 (d, *J* = 0.7 Hz, 1H), 7.44 (dd, *J* = 6.1, 3.5 Hz, 2H), 7.14 (d, *J* = 7.4 Hz, 1H), 7.04 (dd, *J* = 10.7, 4.5 Hz, 2H), 6.88 – 6.80 (m, 2H), 4.71 (d, *J* = 7.1 Hz, 1H), 4.52 – 4.23 (m, 4H), 3.88 – 3.76 (m, 2H), 3.73 – 3.58 (m, 4H).
^{13}C NMR (101 MHz, CD_3CN) δ 175.5, 174.7, 168.8, 136.8, 135.1, 131.7, 131.0, 128.4, 128.2, 127.3, 126.8, 125.8, 123.5, 70.8, 66.8, 51.5, 47.3, 46.2, 41.7, 41.3.

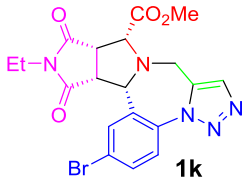
*methyl(11R,11aS,14aR,14bS)-11-ethyl-13-methyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1j**):*



1j

Following the general procedure, the title compound 1a was obtained as a white solid (61% yield).
^{1}H NMR (400 MHz, CD_3CN) δ 8.18 – 7.99 (m, 1H), 7.72 – 7.55 (m, 1H), 7.55 – 7.35 (m, 3H), 5.21 (d, J = 7.4 Hz, 1H), 4.32 (d, J = 15.2 Hz, 1H), 3.86 (d, J = 15.1 Hz, 1H), 3.75 – 3.53 (m, 4H), 3.20 (d, J = 7.8 Hz, 1H), 2.58 (s, 3H), 2.07 – 1.96 (m, 2H), 1.09 (t, J = 7.4 Hz, 3H).
^{13}C NMR (101 MHz, CD_3CN) δ 175.7, 174.8, 170.9, 137.8, 134.6, 132.1, 130.4, 128.3, 127.3, 127.0, 123.8, 73.3, 66.8, 52.5, 51.6, 48.0, 39.5, 24.5, 24.0, 9.5.

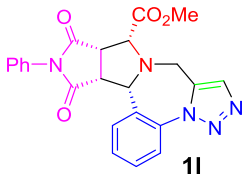
*methyl(11R,11aS,14aR,14bS)-2-bromo-13-ethyl-12,14-dioxo-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1k**):*



1k

Following the general procedure, the title compound **1k** was obtained as a white solid (60% yield).
^{1}H NMR (400 MHz, CD_3CN) δ 8.08 (d, J = 8.9 Hz, 1H), 8.00 (d, J = 2.1 Hz, 1H), 7.63 (dd, J = 8.9, 2.3 Hz, 1H), 7.53 (s, 1H), 4.52 (d, J = 6.8 Hz, 1H), 4.15 (d, J = 15.1 Hz, 1H), 3.81 – 3.62 (m, 6H), 3.52 (t, J = 8.0 Hz, 1H), 3.25 (q, J = 7.2 Hz, 2H), 0.83 (t, J = 7.2 Hz, 3H).
^{13}C NMR (101 MHz CD_3CN) δ 175.2, 174.8, 168.9, 136.3, 134.2, 134.0, 131.4, 128.3, 125.3, 120.4, 69.7, 66.5, 51.7, 47.1, 45.8, 41.7, 33.3, 11.8.

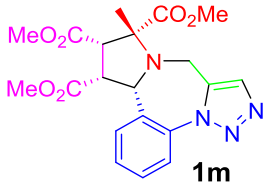
*methyl(11R,11aS,14aR,14bS)-12,14-dioxo-13-phenyl-11a,12,13,14,14a,14b-hexahydro-9H,11H-benzo[f]pyrrolo[3',4':3,4]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11-carboxylate (**1l**):*



1l

Following the general procedure, the title compound 1a was obtained as a white solid (33% yield).
^{1}H NMR (400 MHz, CH_3CN) δ 8.19 – 8.11 (m, 1H), 7.85 – 7.77 (m, 1H), 7.60 – 7.55 (m, 1H), 7.52 – 7.32 (m, 5H), 6.98 – 6.90 (m, 2H), 4.64 (d, *J* = 6.5 Hz, 1H), 4.21 (d, *J* = 15.1 Hz, 1H), 3.93 – 3.85 (m, 2H), 3.78 – 3.65 (m, 5H).
^{13}C NMR (101 MHz, CH_3CN) δ 175.0, 174.3, 169.2, 136.3, 134.7, 132.1, 131.5, 131.2, 128.9, 128.5, 127.5, 126.4, 126.1, 123.6, 70.3, 67.0, 51.8, 47.8, 46.2, 41.6.

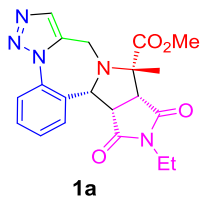
*trimethyl(11R,12S,13R,13aS)-11-methyl-11,12,13,13a-tetrahydro-9H-benzo[f]pyrrolo[1,2-d][1,2,3]triazolo[1,5-a][1,4]diazepine-11,12,13-tricarboxylate (**1m**):*



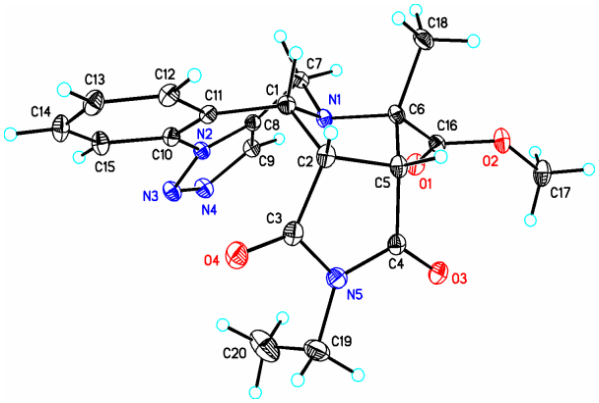
1m

Following the general procedure, the title compound 1a was obtained as a off-white solid (55% yield).
^{1}H NMR (300 MHz, CD_3CN) δ 7.82 – 7.67 (m, 3H), 7.63 – 7.54 (m, 2H), 4.28 – 4.15 (m, 3H), 3.68 (s, 3H), 3.52 (s, 3H), 3.45 – 3.28 (m, 4H), 3.28 (s, 1H), 1.60 (s, 3H).
^{13}C NMR (75 MHz, CD_3CN) δ 173.1, 172.8, 171.6, 145.2, 137.2, 134.7, 132.4, 130.1, 128.9, 124.4, 70.0, 62.6, 56.7, 52.9, 52.2, 45.7, 37.1, 22.1.

3. X-Ray Report of 1a



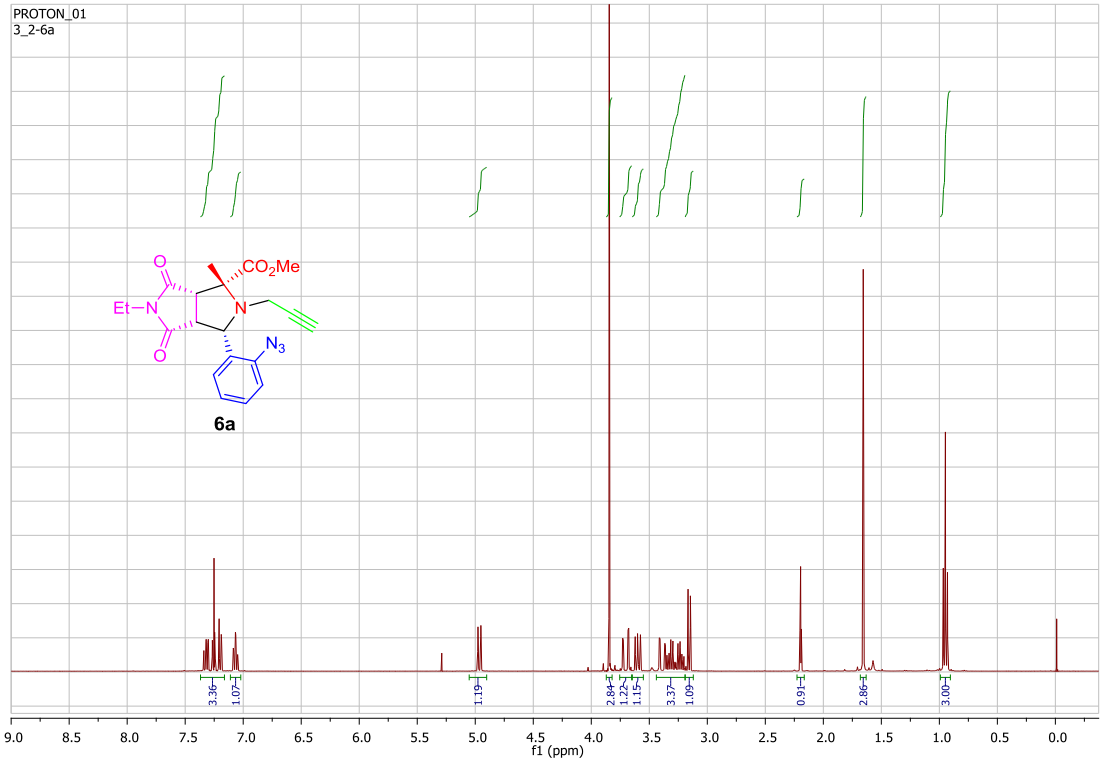
1a

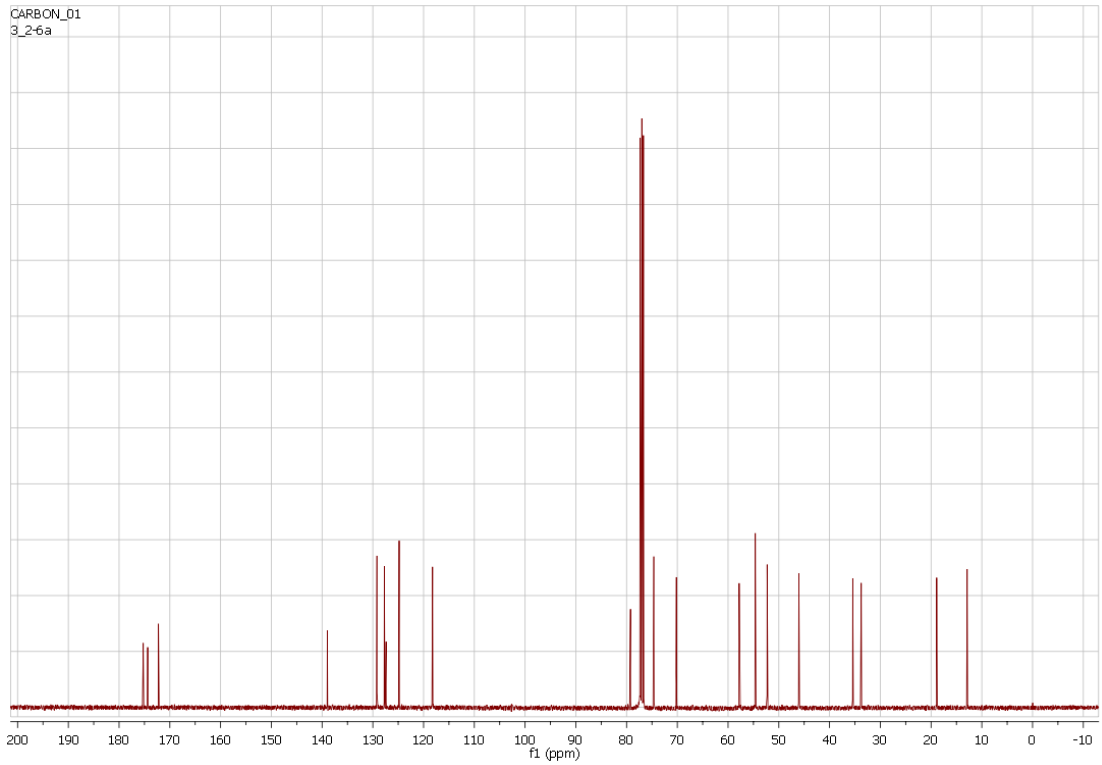


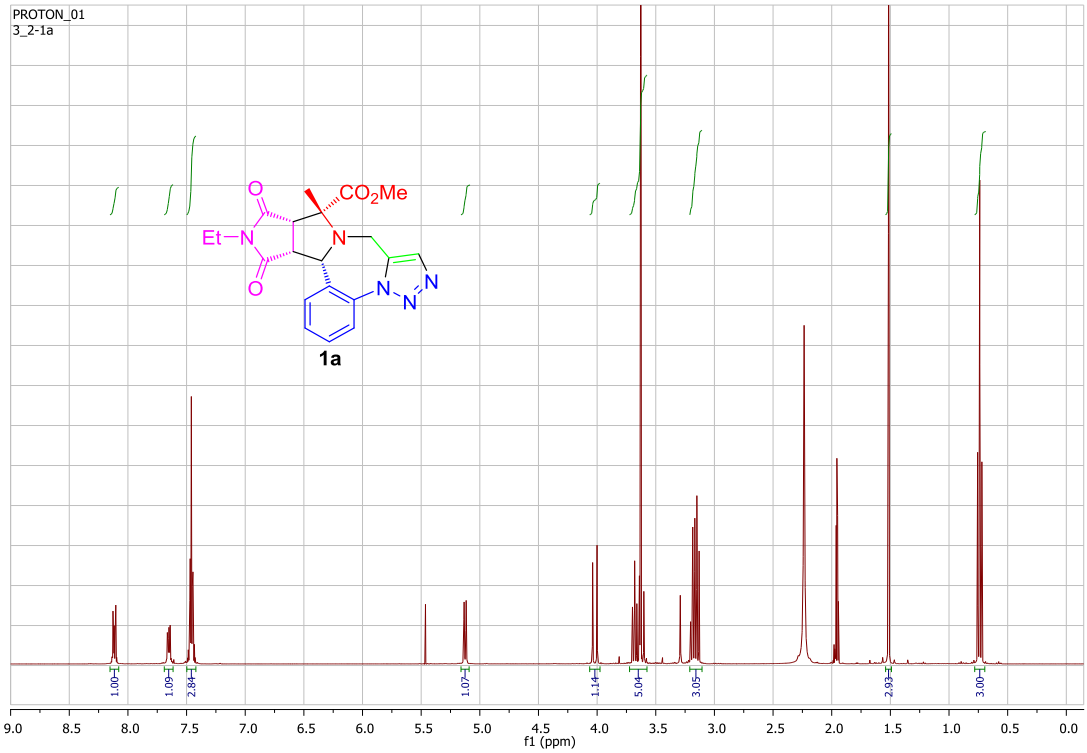
Bond precision	c-c=0.0020 Å	Wavelength=1.54184
Cell	a=9.9263 (3) b=15.4568(5) c=12.4445(4)	
	α=90 β=96.737(3) γ=90	
Temperature	173K	
	Calculated	Reported
Volumn	1896.16(10)	1896.11(11)
Space group	-P 2yn	P 1 21/n 1
Hall group	P 2yb	-P 2yn
Moiety formula	C_{20} H_{21} N_5 O_4	C_{20} H_{21} N_5 O_4
Sum formula	C_{20} H_{21} N_5 O_4	C_{20} H_{21} N_5 O_4
Mr	395.42	395.42
Dx,g cm^{-3}	1.385	1.1.385
Z	4	4
Mu (mm^{-1})	0.821	0.821
F000	832.0	832.0
F000’	834.67	
h,k,lmax	12, 19, 15	12, 18, 15
Nref	3689	3613
Tmin,Tmax	0.759, 0.877	0.841, 1.000
Tmin’	0.732	
Correction method= Multi-scan		
AbsCorr = MULTI-SCAN		
Data completeness= 0.979 Theta(max)= 71.390		
R(reflections)= 0.0416(3265) wR2(reflections)= 0.1141(3613)		
S = 1.043 Npar= 266		

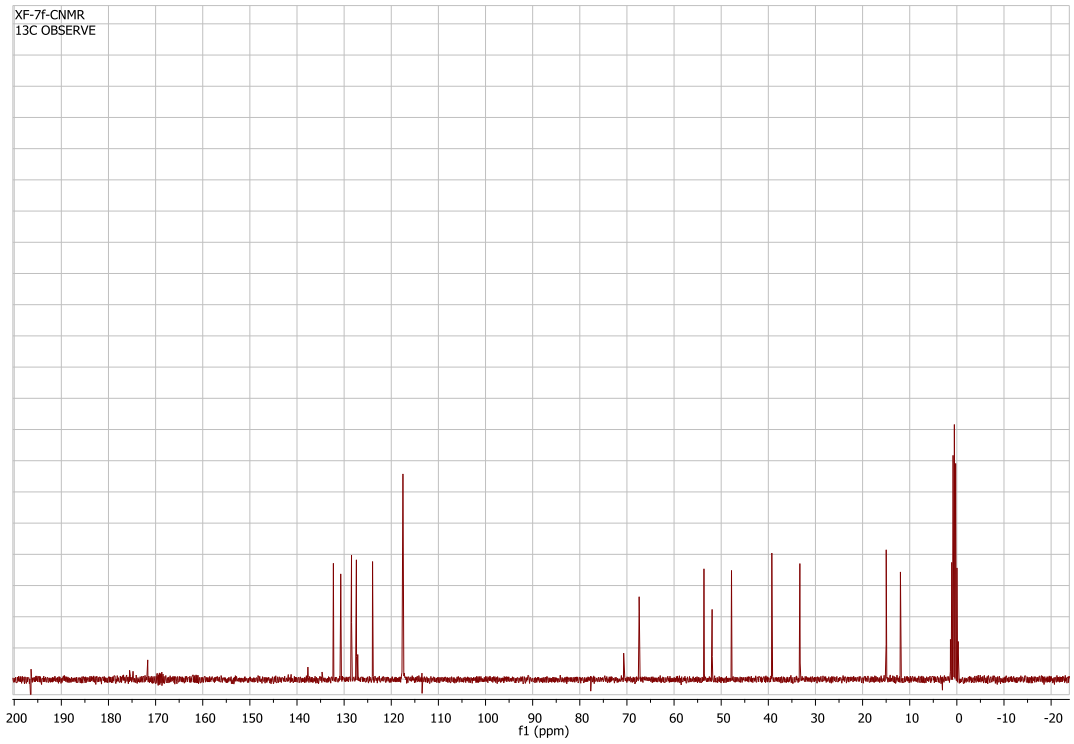
Crystallographic data (excluding structural factors) for compound **1a** has been deposited at the Cambridge Crystallographic Data Centre under the deposition number CCDC1454972.

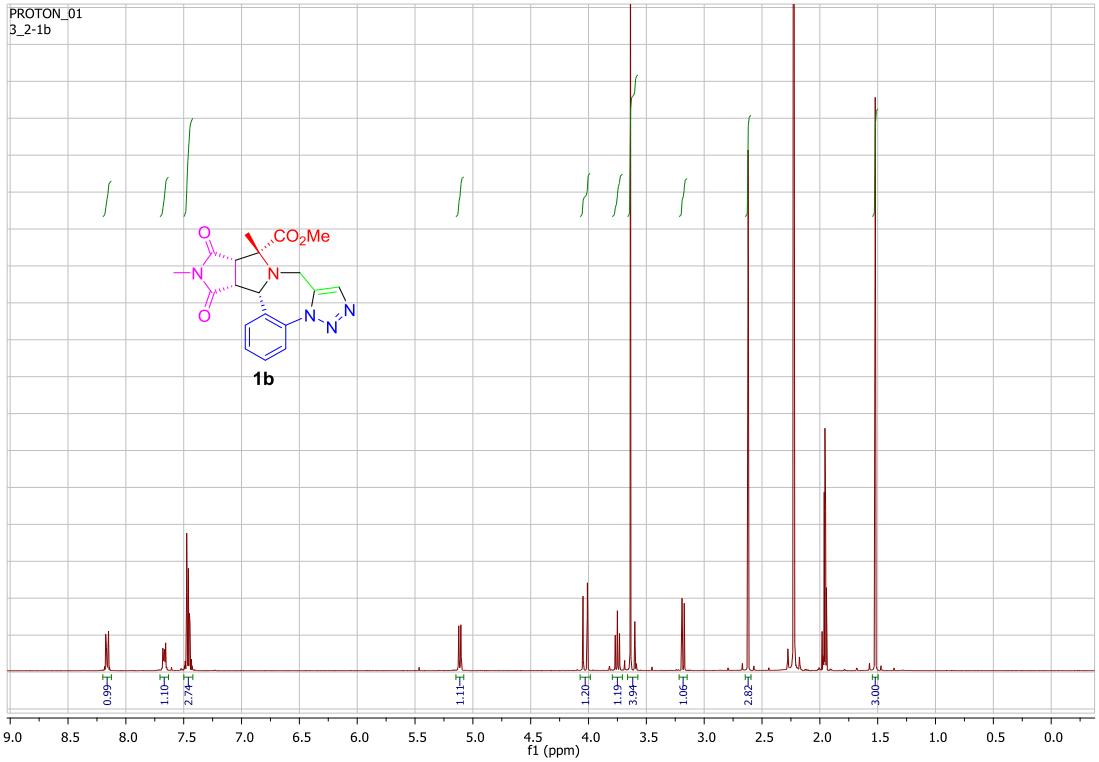
4. NMR Spectra of Intermediate 6a and Products 1

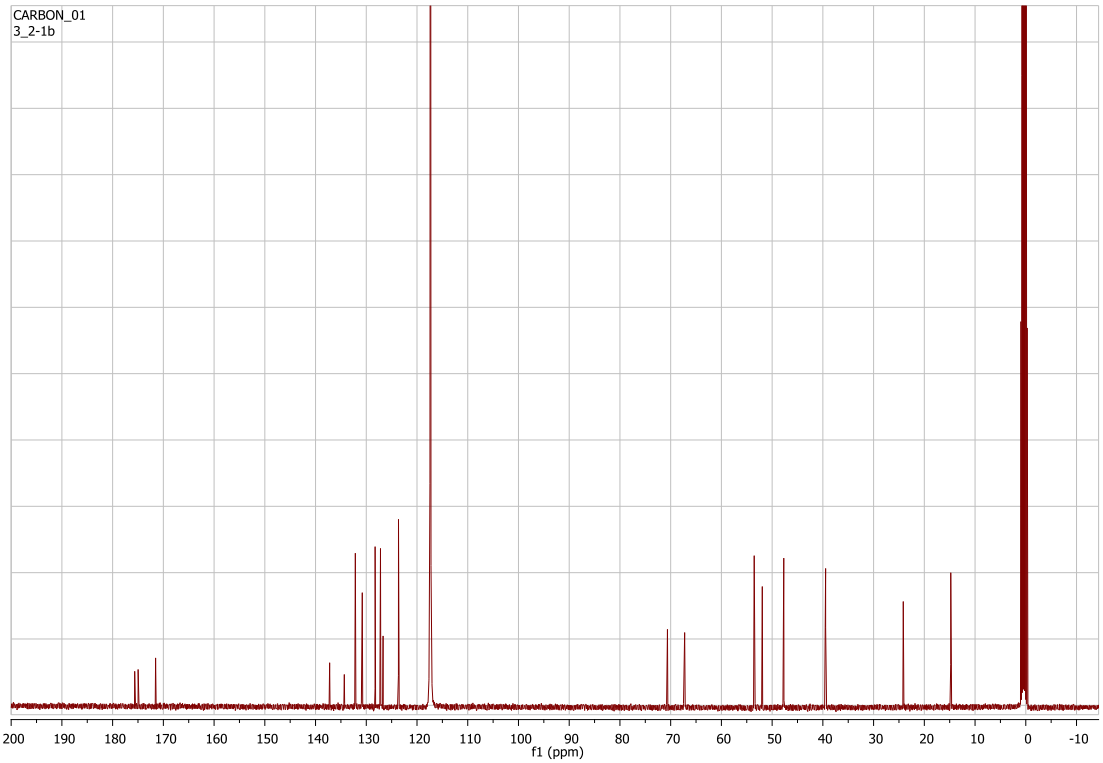


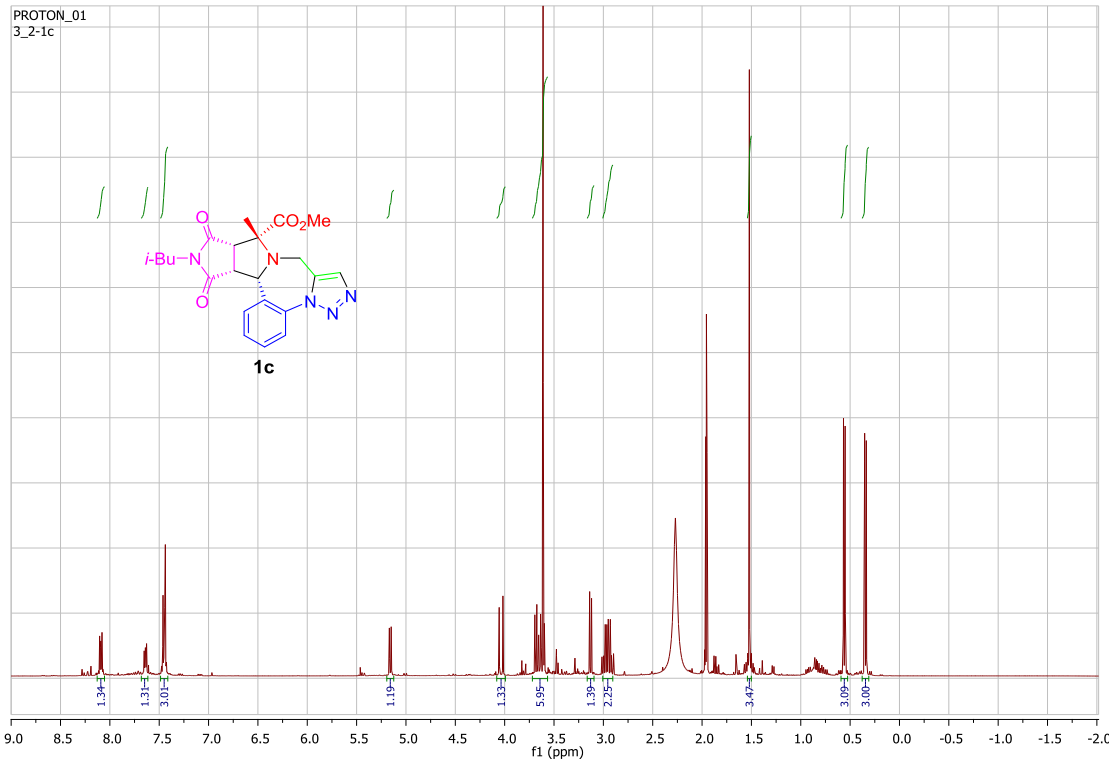


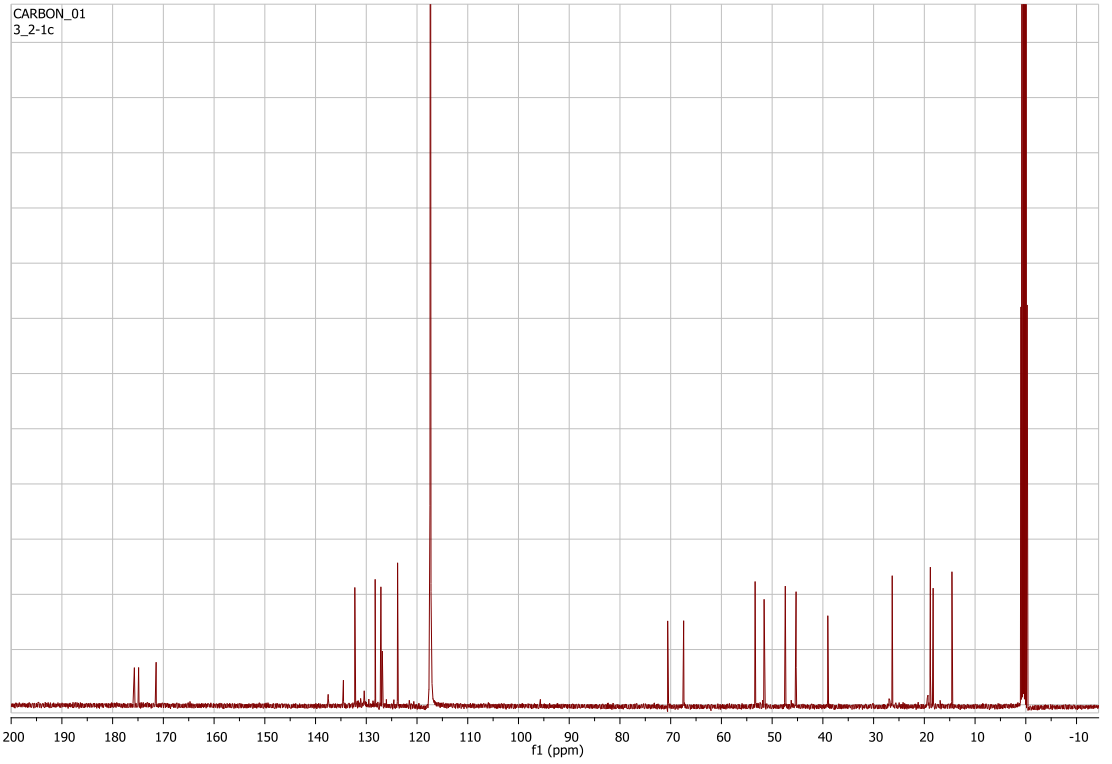

PROTON_01
3_2-1a
O
CO2Me
Et−N
N
O
N
N
N
1a
1.00
1.09
2.84
1.07
1.14
5.04
3.05
2.93
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

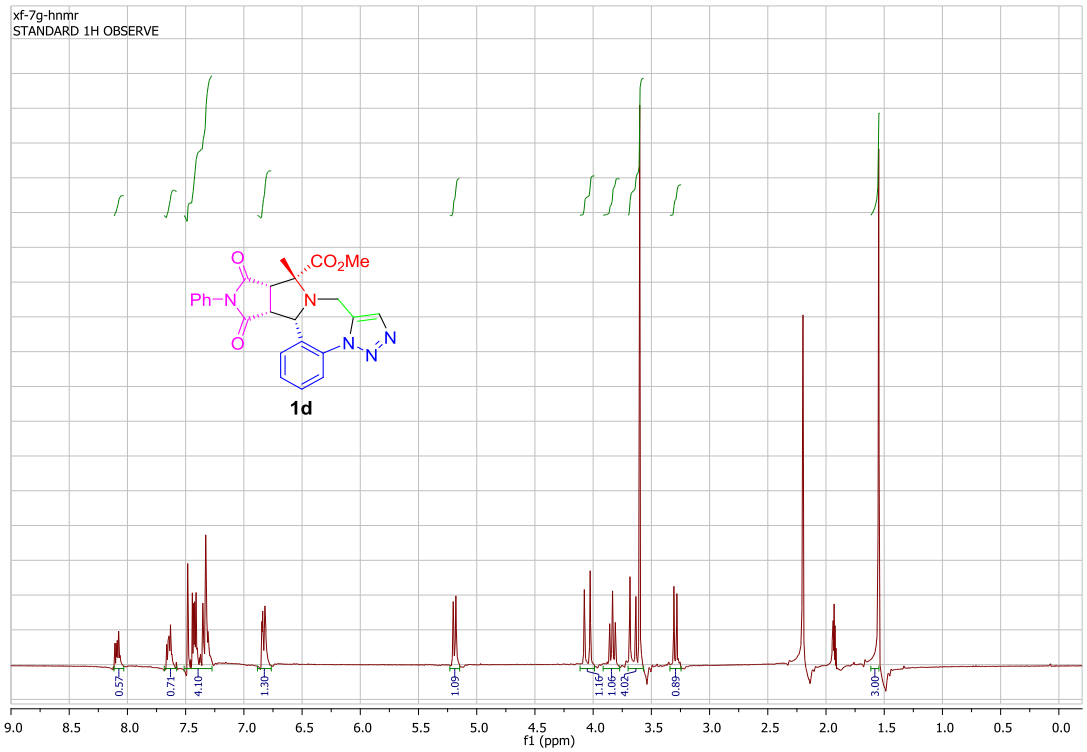

XF-7f-CNMR
13C OBSERVE
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

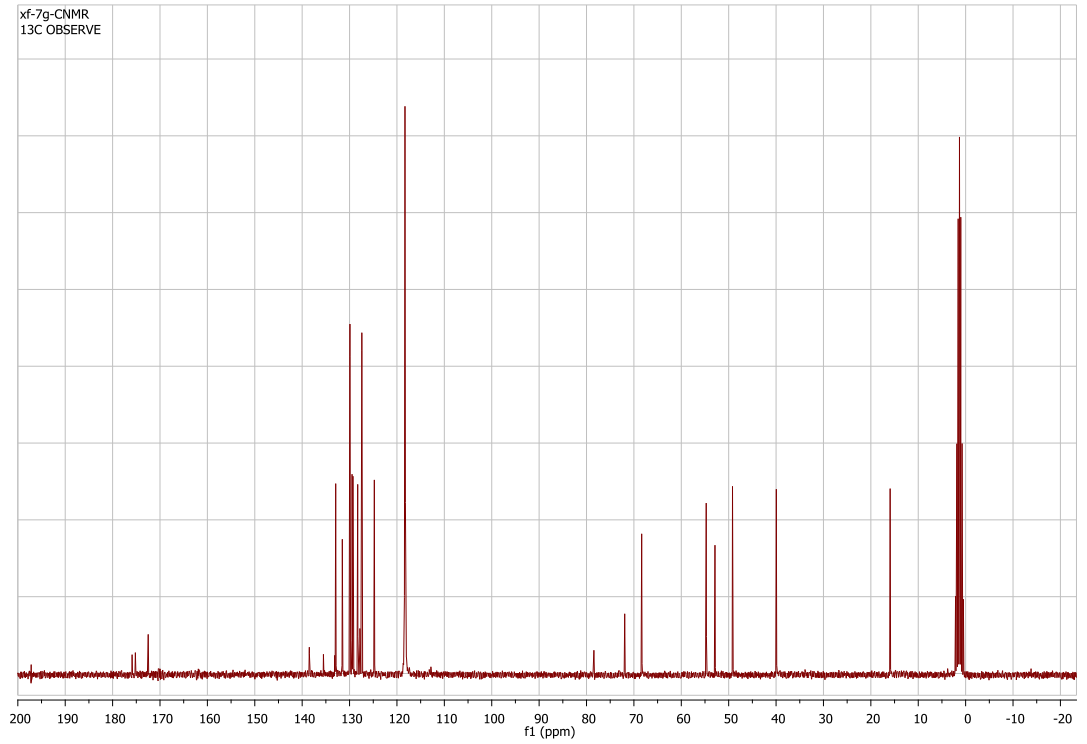

PROTON_01
3_2-1b
CO2Me
1b
0.99
1.10
2.74
1.11
1.20
1.19
3.94
1.06
2.82
3.00
f1 (ppm)

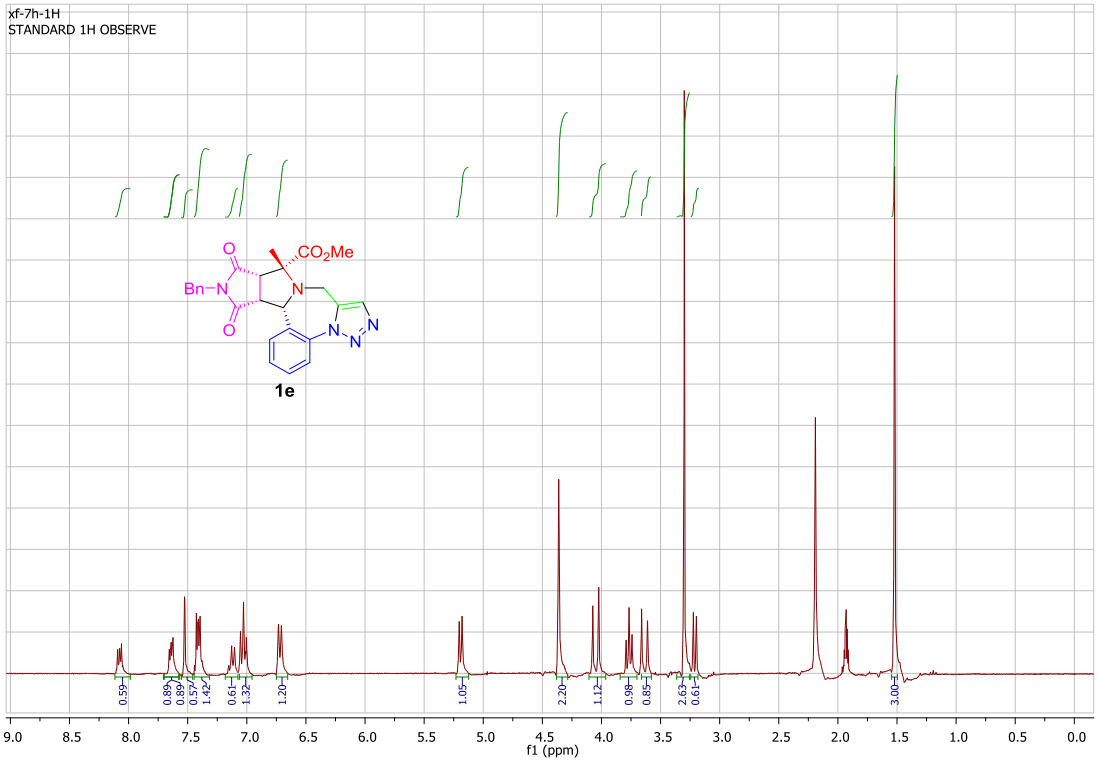

CARBON_01
3_2-1b
f1 (ppm)

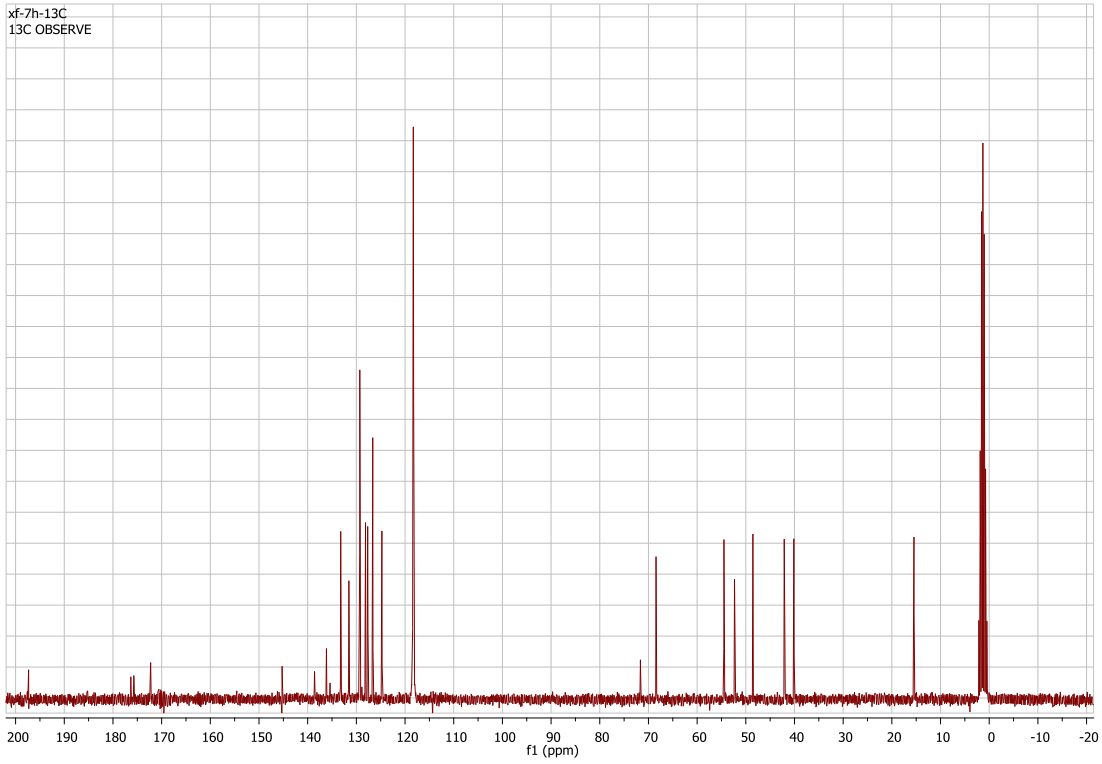

PROTON_01
3_2-1c
CO2Me
i-Bu
N
O
O
N
N
N
1c
1.34
1.31
3.01
1.19
1.33
5.95
1.39
2.25
3.47
3.09
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)

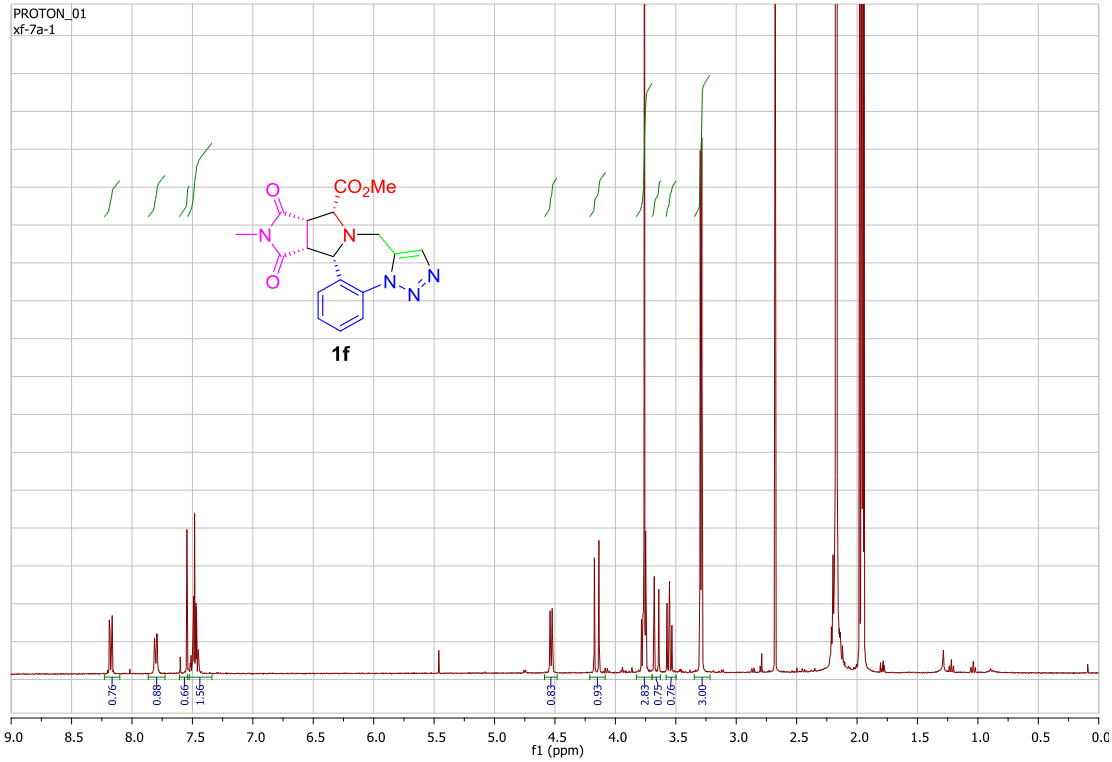

CARBON_01
3_2-1c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

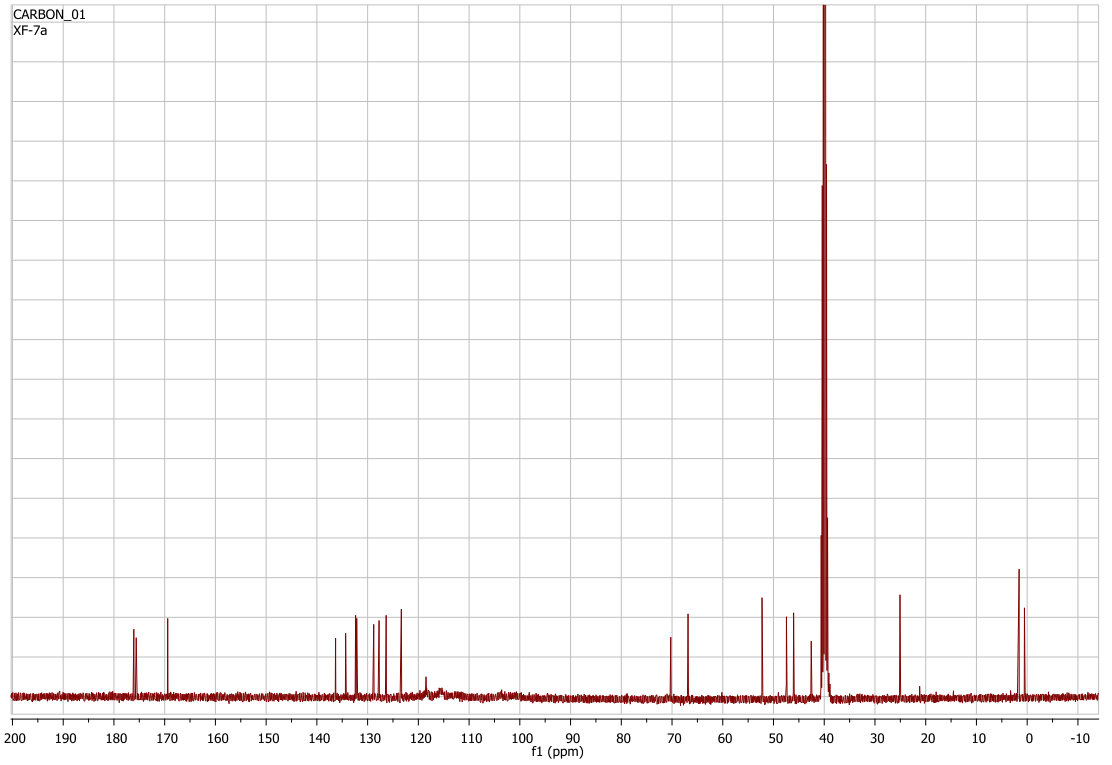

xf-7g-hnmr
STANDARD 1H OBSERVE
O
CO2Me
Ph–N
N
O
N
N
N
1d
0.57
0.71
4.10
1.30
1.09
1.16
1.06
4.02
0.89
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

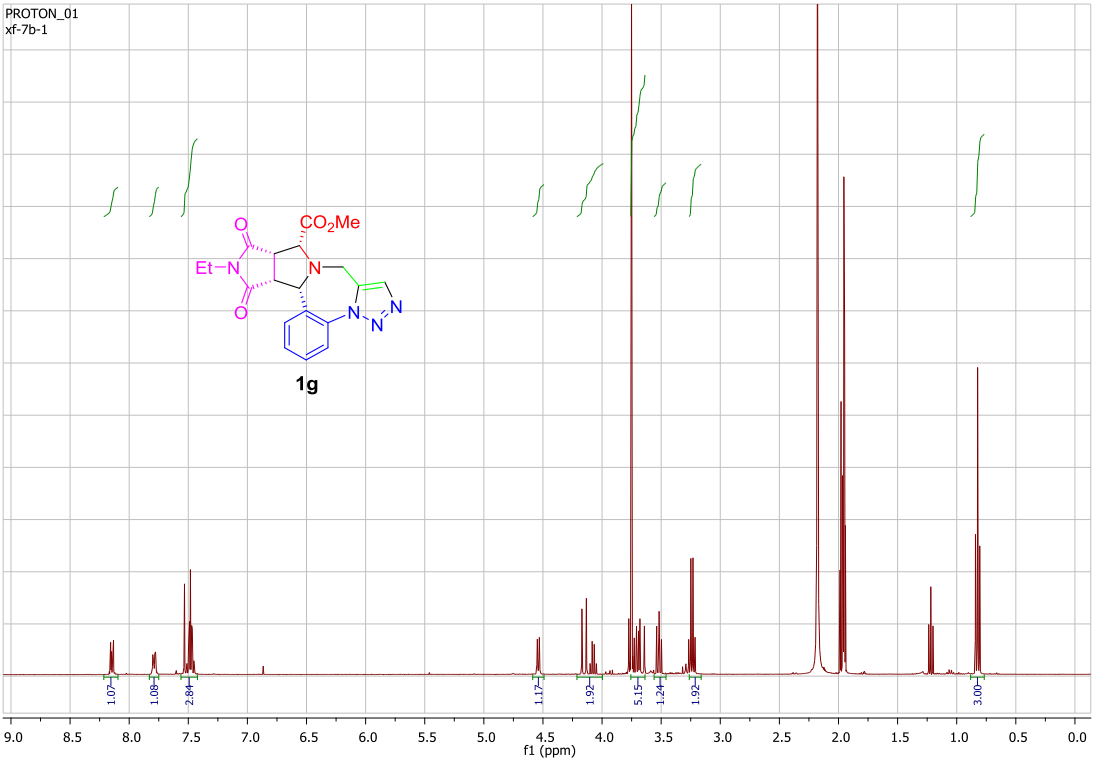

xf-7g-CNMR
13C OBSERVE
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

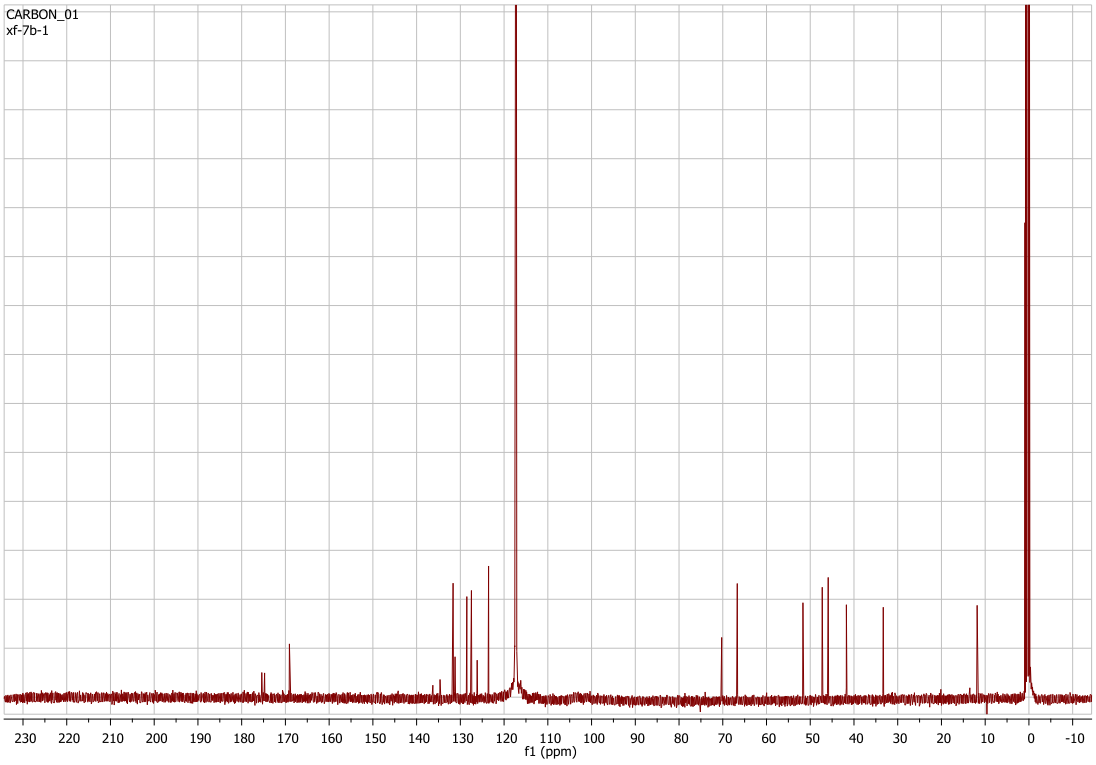

xf-7h-1H
STANDARD 1H OBSERVE
CO2Me
Bn–N
O
O
N
N
N
N
1e
0.59
0.89
0.89
0.57
1.42
0.61
1.32
1.20
1.05
2.20
1.12
0.98
0.85
2.63
0.61
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

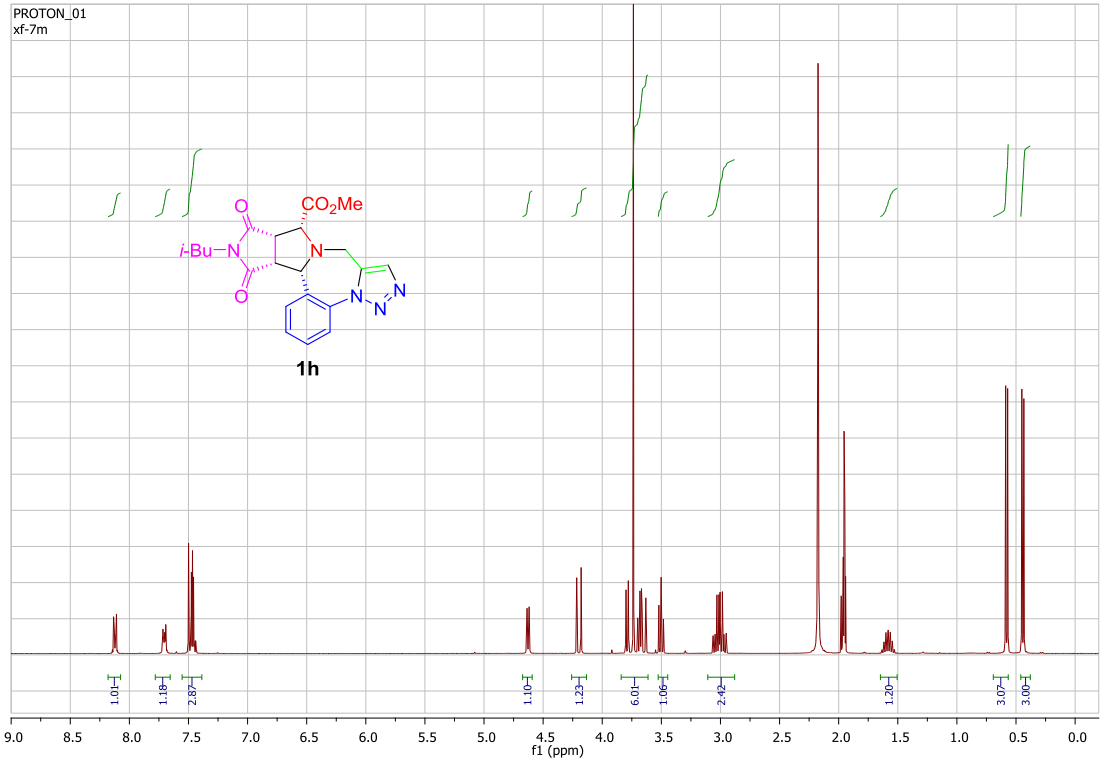

xf-7h-13C
13C OBSERVE
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

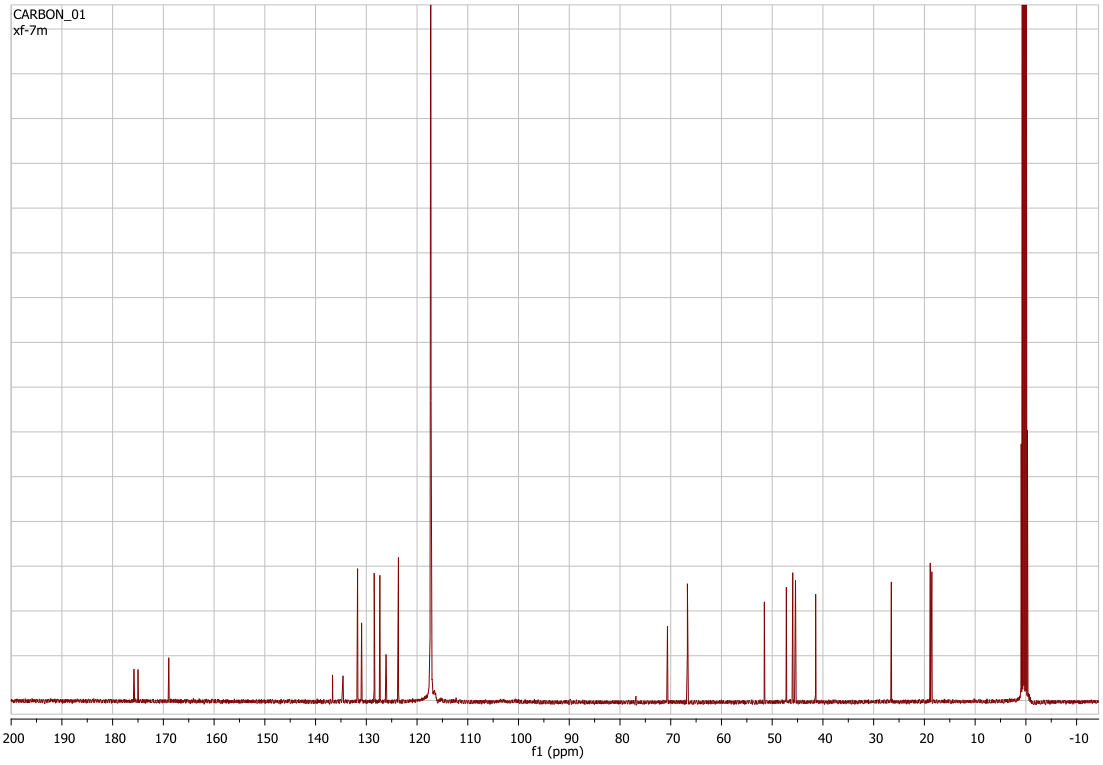

PROTON_01
xf-7a-1
CO2Me
1f
0.76
0.88
0.66
1.56
0.83
0.93
2.83
0.75
0.76
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

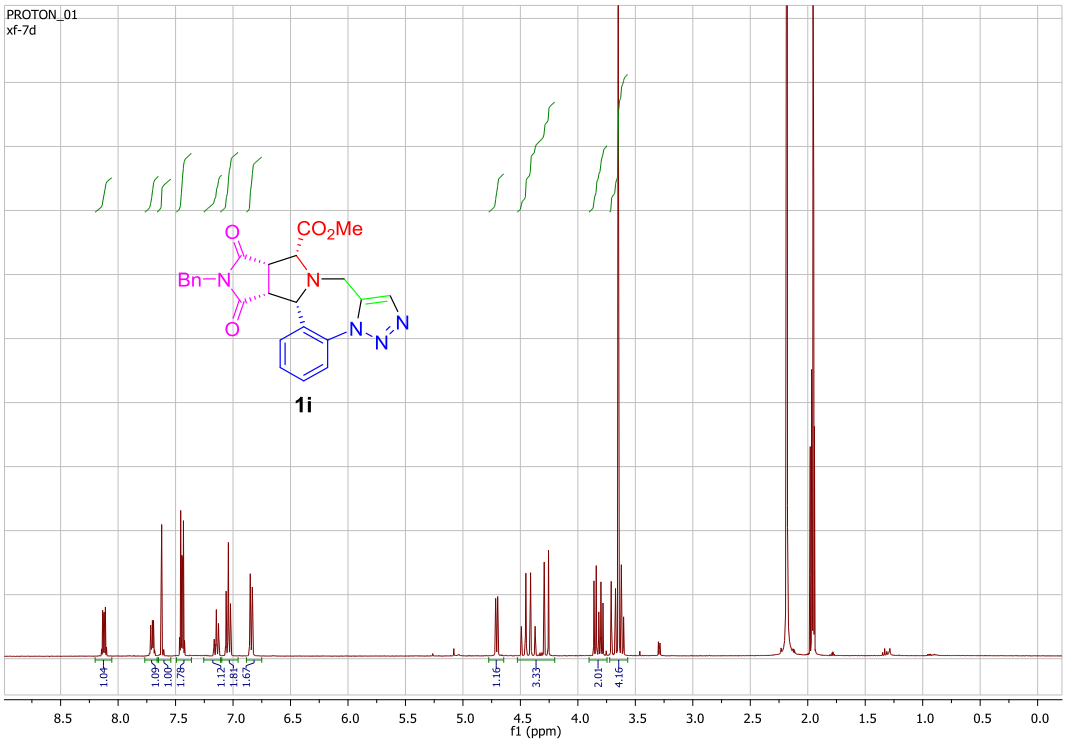

CARBON_01
XF-7a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

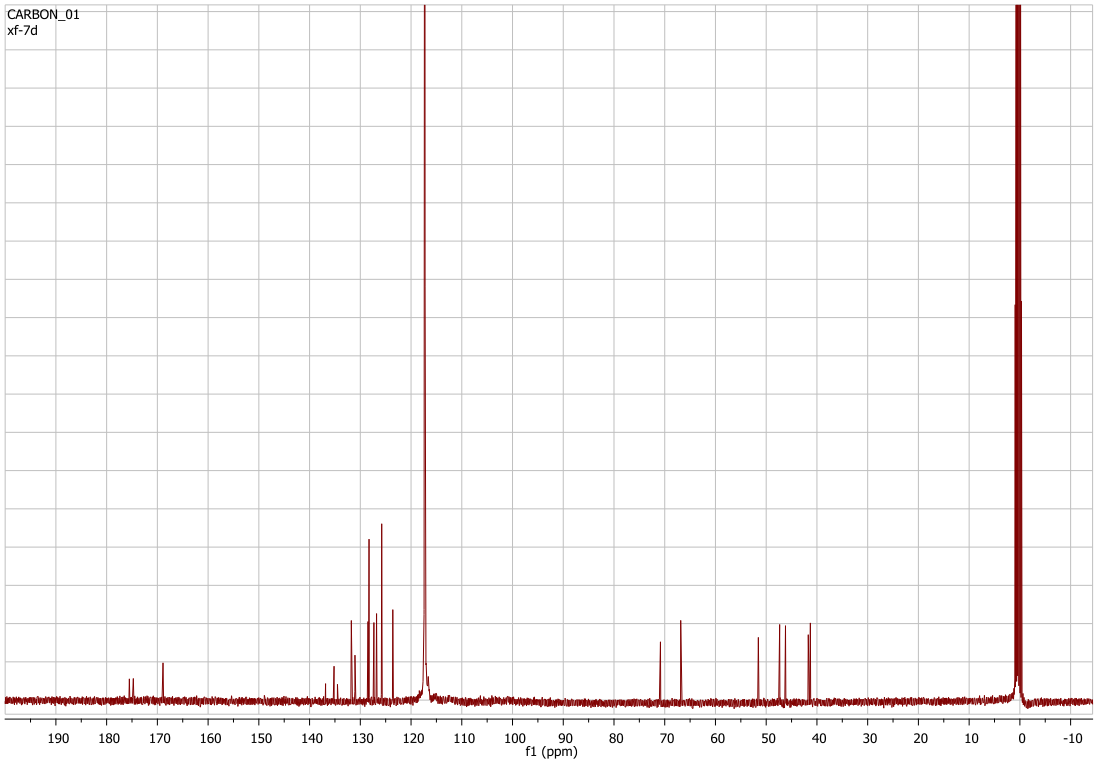

PROTON_01
xf-7b-1
CO2Me
Et−N
O
O
N
N
N
N
1g
1.07
1.08
2.84
1.17
1.92
5.15
1.24
1.92
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

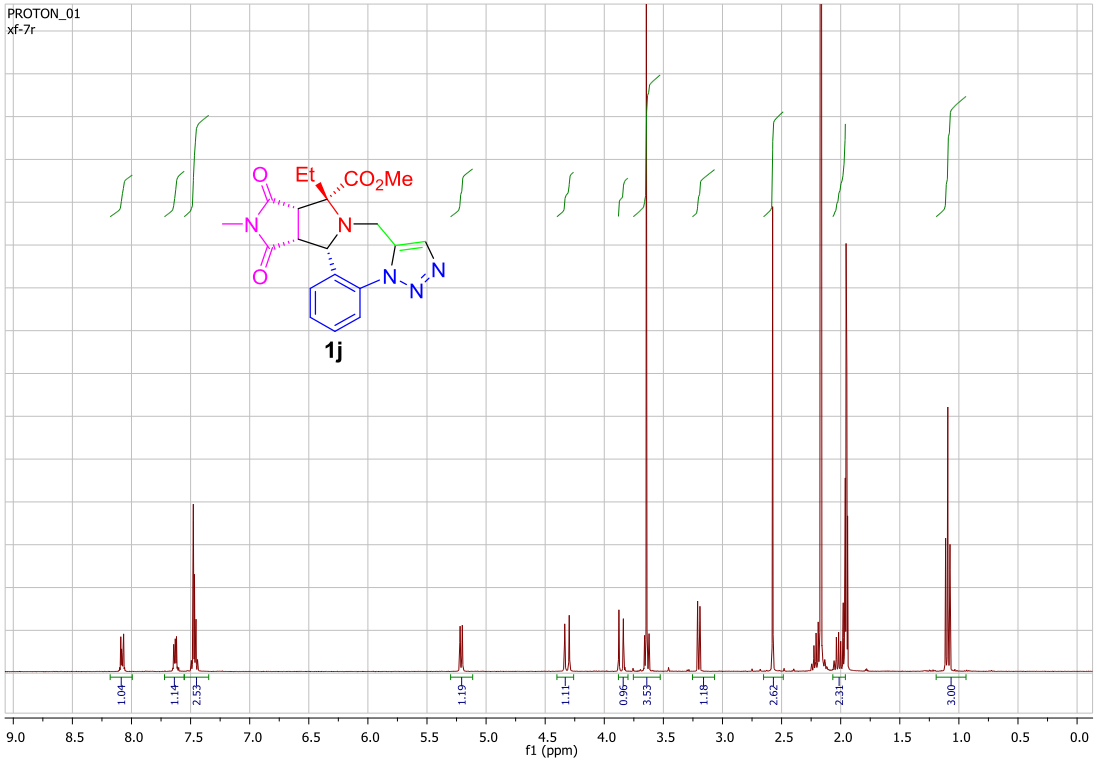

CARBON_01
xf-7b-1
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

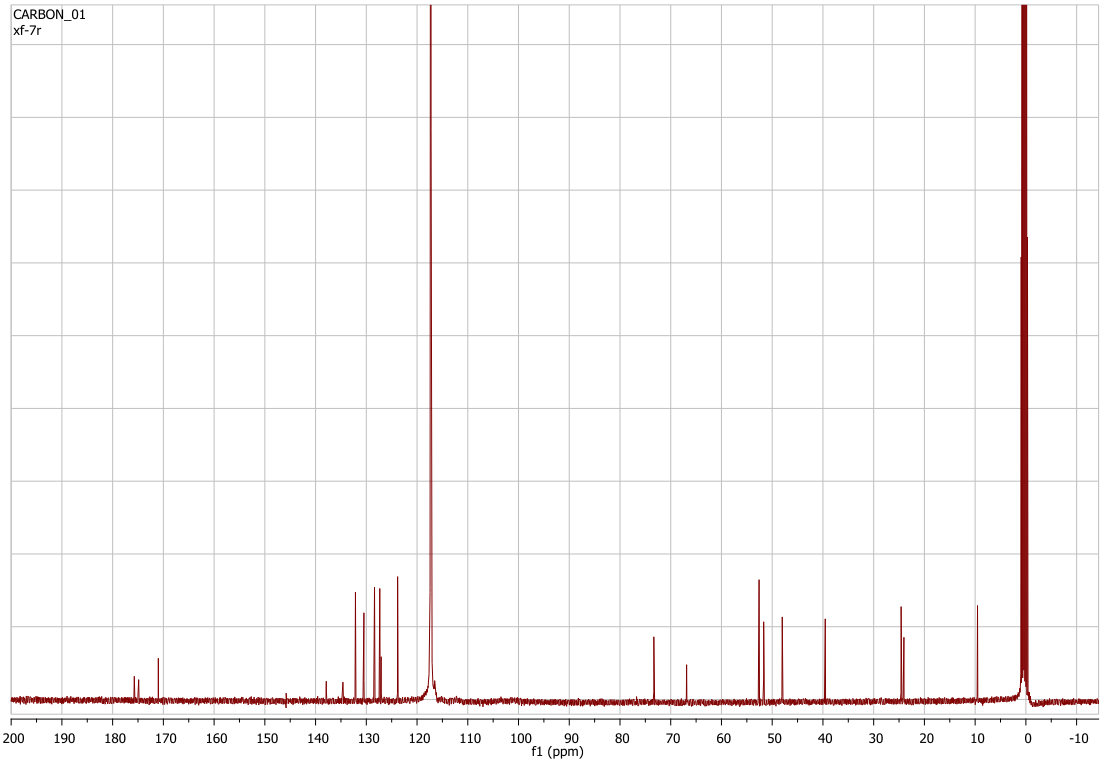

PROTON_01
xf-7m
CO2Me
i-Bu–N
1h
1.01
1.18
2.87
1.10
1.23
6.01
1.06
2.42
1.20
3.07
3.00
f1 (ppm)

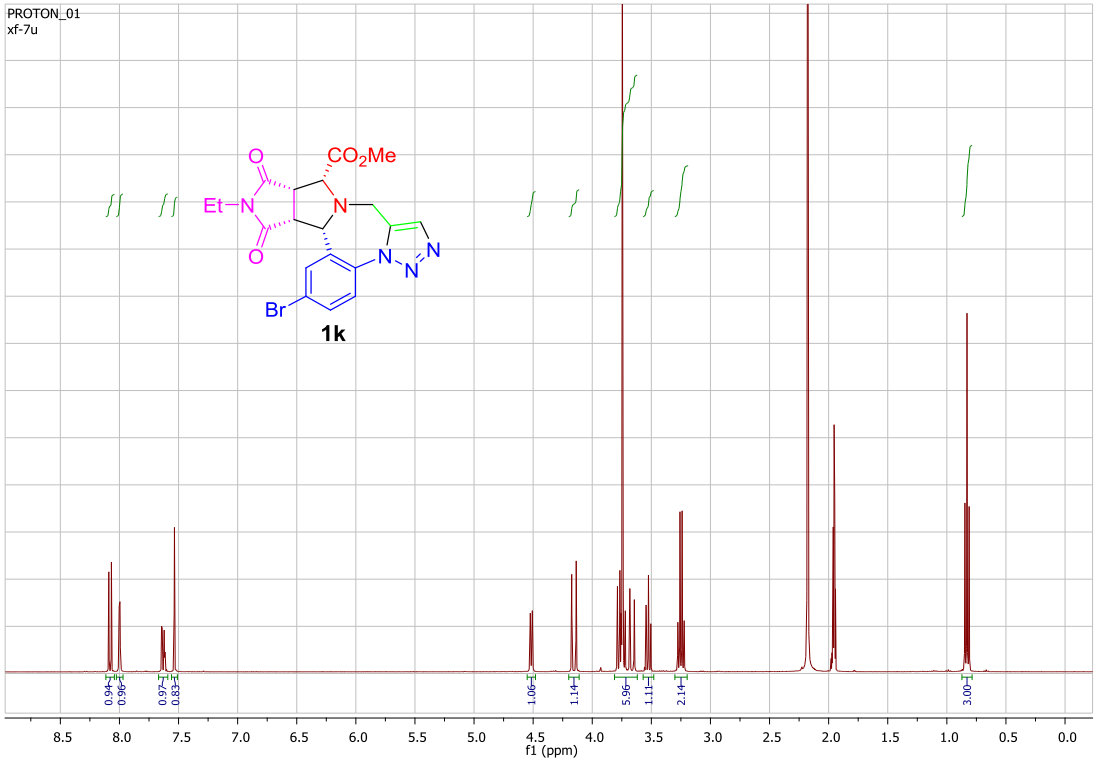

CARBON_01
xf-7m
f1 (ppm)

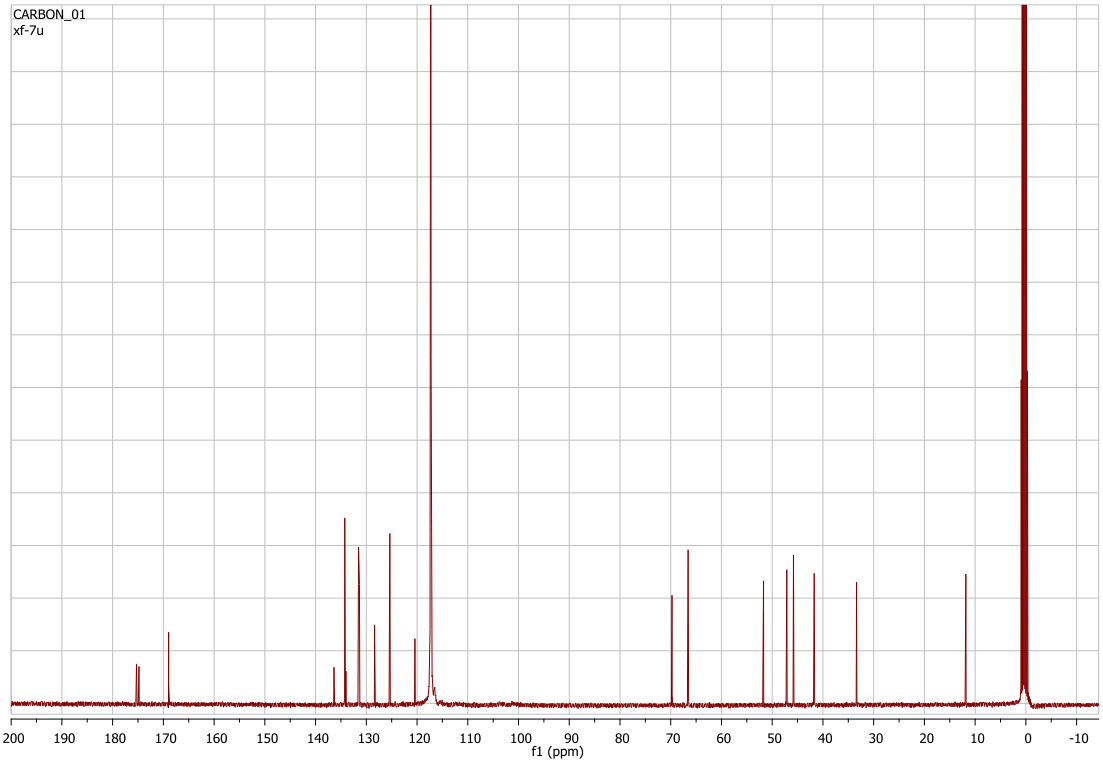

PROTON_01
xf-7d
CO2Me
Bn–N
O
O
N
N
N
N
1i
1.04
1.09
1.00
1.78
1.12
1.81
1.67
1.16
3.33
2.01
4.16
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

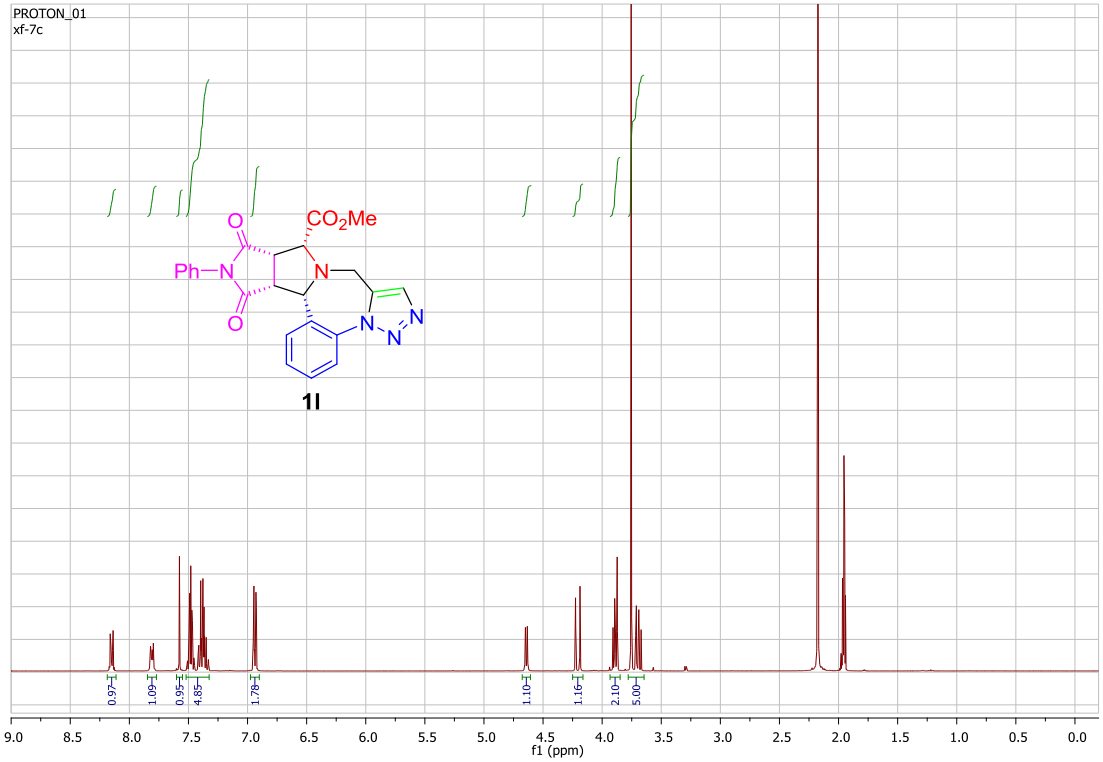

CARBON_01
xf-7d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

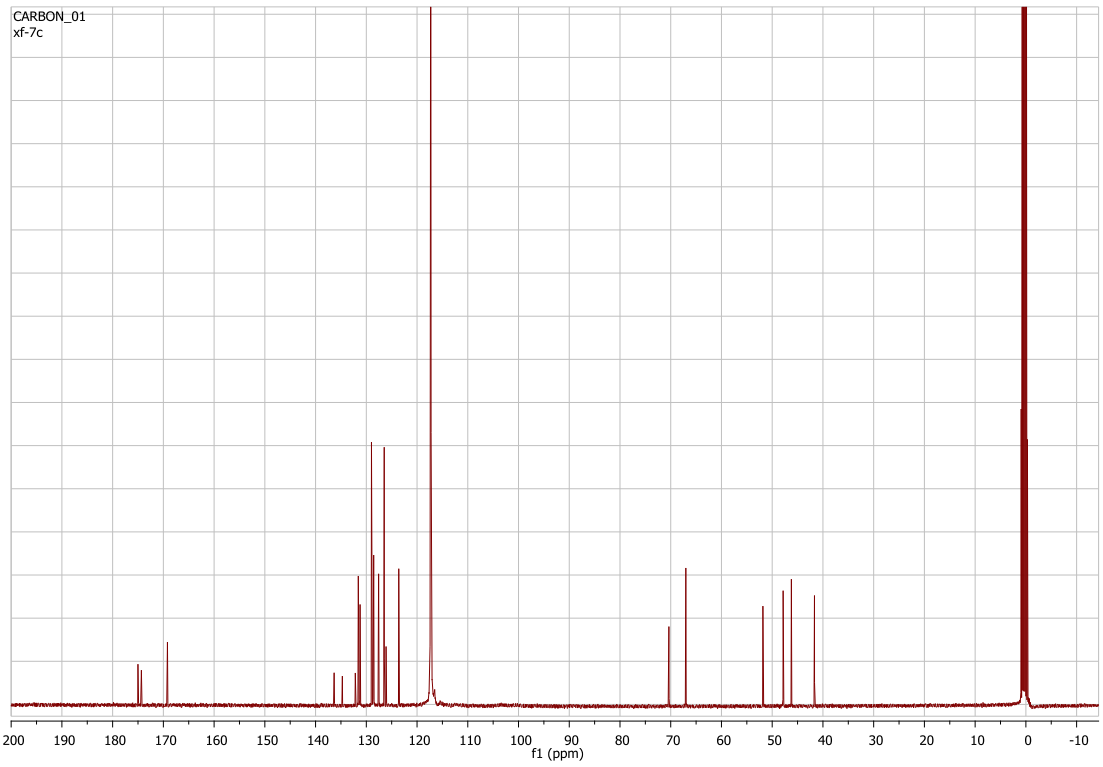

PROTON_01
xf-7r
Et
CO2Me
O
N
O
N
N
N
1j
1.04
1.14
2.53
1.19
1.11
0.96
3.53
1.18
2.62
2.31
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

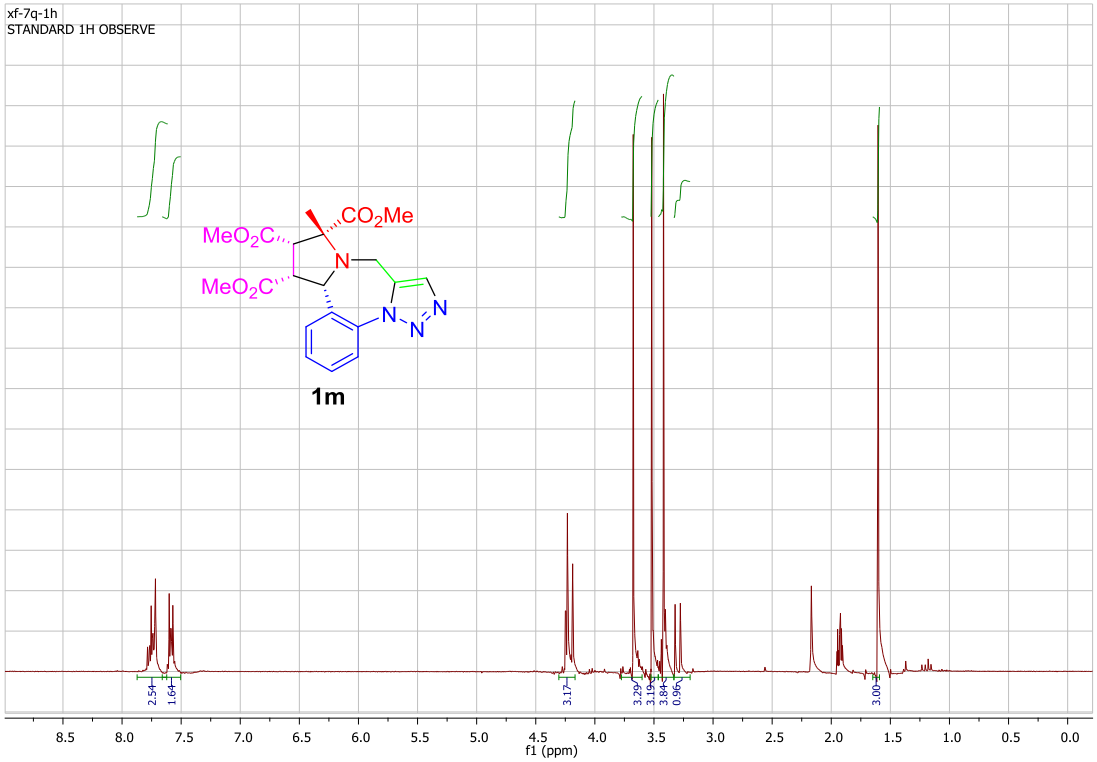

CARBON_01
xf-7r
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

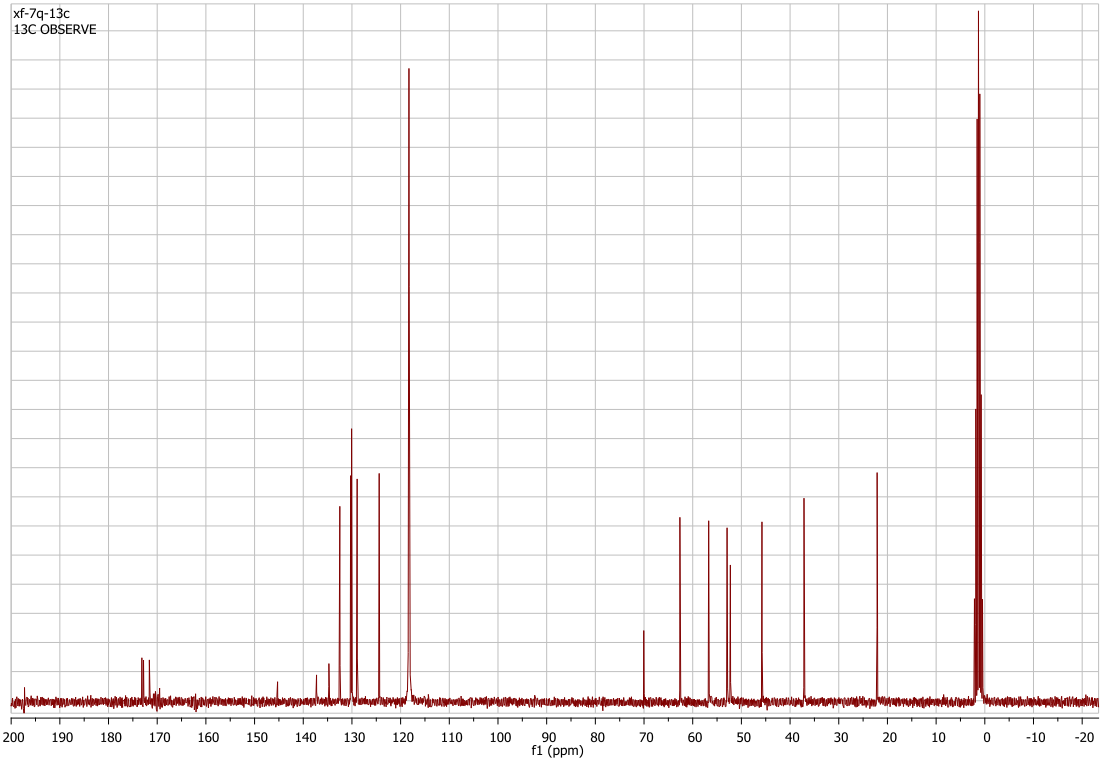

PROTON_01
xf-7u
O
CO2Me
Et
N
N
O
N
N
N
Br
1k
0.94
0.96
0.97
0.83
1.06
1.14
5.96
1.11
2.14
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


CARBON_01
xf-7u
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


PROTON_01
xf-7c
O
CO2Me
Ph—N
N
O
N
N
N
1l
0.97
1.09
0.95
4.85
1.78
1.10
1.16
2.10
5.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CARBON_01
xf-7c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


xf-7q-1h
STANDARD 1H OBSERVE
CO2Me
MeO2C
MeO2C
N
N
N
N
1m
2.54
1.64
3.17
3.39
3.19
3.84
0.96
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


xf-7q-13c
13C OBSERVE
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)