

Supporting Information for

A gold-triggered dearomative spirocarbocyclization/Diels–Alder reaction cascade towards diverse bridged *N*-heterocycles

Yi He,^{a,†} Thomas Narmon,^{a,†} Danjun Wu,^b Zhenghua Li,^{*a} Luc Van Meervelt^c and Erik V. Van der Eycken^{*a,d}

^a Laboratory for Organic & Microwave-Assisted Chemistry (LOMAC), Department of Chemistry, KU Leuven, Celestijnenlaan 200F, B-3001 Leuven, Belgium

^b College of Pharmaceutical Science, Zhejiang University of Technology, 18 Chaowang Road, 310014 Hangzhou, China

^c Biomolecular Architecture, Department of Chemistry, KU Leuven, Celestijnenlaan 200F, B-3001 Leuven, Belgium

^d Peoples' Friendship University of Russia (RUDN University), 6 Miklukho-Maklaya Street, 117198 Moscow, Russia

[†]Both authors contributed equally to this manuscript.

Table of Contents

General Methods.....	S2
General procedure for the synthesis of Ugi products	S3
General procedure for the Microwave-assisted Intramolecular Diels-Alder Reaction.....	S14
Scale-up synthesis of bridged compound 2a	S16
Preliminary investigation on the cascade dearomative spirocarbocyclization/iodination process	S16
Crystallographic data for compound 2a and 2k	S17
Copies of NMR spectra (Post-Ugi products).....	S21
Copies of NMR spectra (Ugi products)	S42

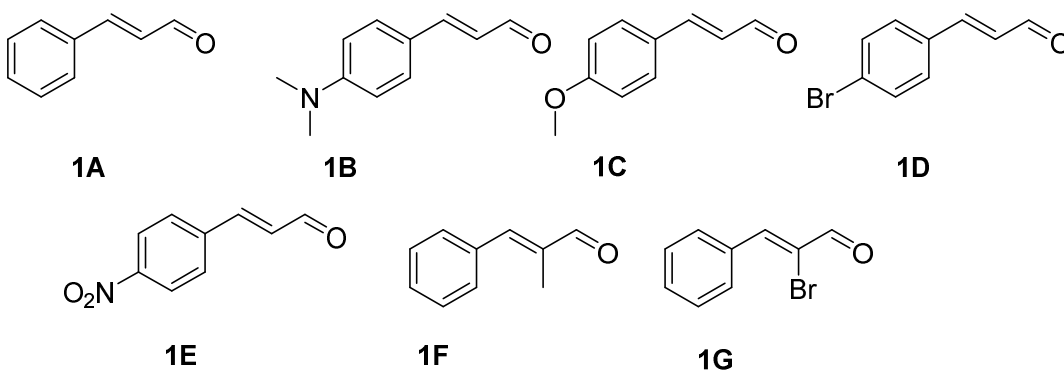
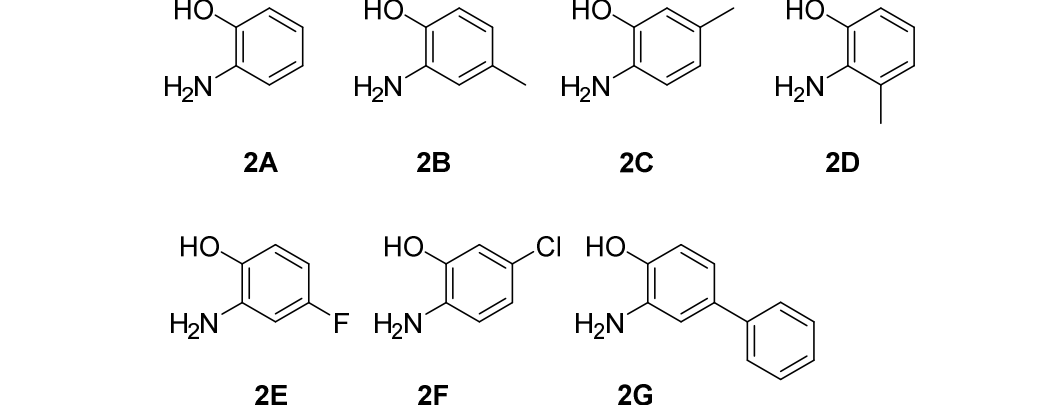
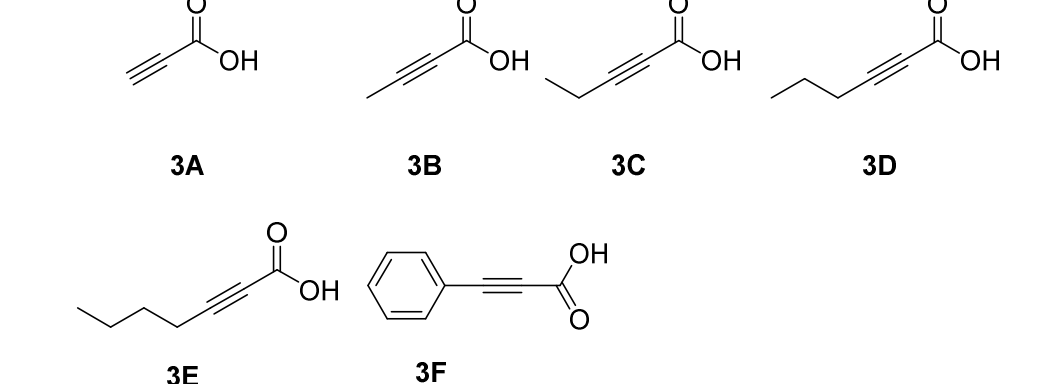
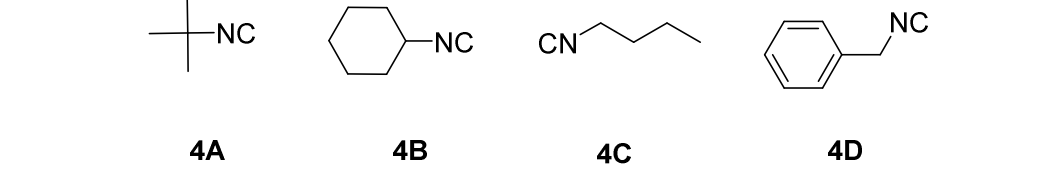
General Methods

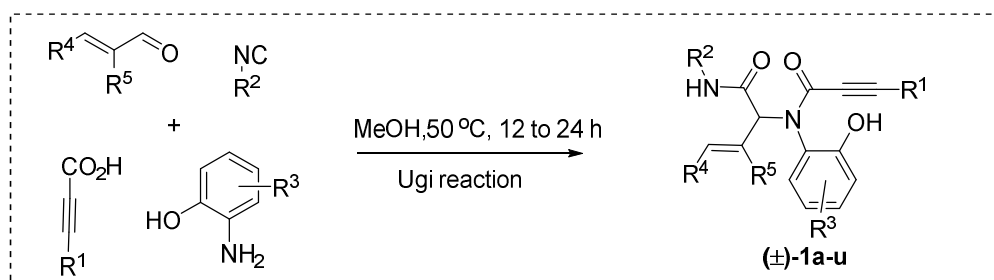
NMR spectra were recorded on a 300, 400 or 600 MHz instrument using CDCl_3 or $\text{DMSO-}d_6$ as solvent. The mixture of CDCl_3 and $\text{DMSO-}d_6$ was applied as solvent wherever was necessary. The ^1H and ^{13}C chemical shifts are reported in parts per million relative to tetramethylsilane as an internal standard. Spectra were acquired on a quadrupole orthogonal acceleration time-of-flight mass spectrometer (Synapt G2 HDMS, Waters, Milford, MA). Samples were infused at 3 $\mu\text{L}/\text{min}$ and spectra were obtained in positive (or: negative) ionization mode with a resolution of 15000 (FWHM) using leucine enkephalin as lock mass. For chromatography, analytical TLC plates and 70-230 mesh silica gel were used. All the solvents and chemicals were purchased and used as available. Data for ^1H NMR are recorded as follows: chemical shift (δ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, coupling constant (s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ , ppm).

The microwave irradiation experiments were carried out in a dedicated CEM-Discover monomode microwave apparatus, operating at a frequency of 2.45GHz with continuous irradiation power from 0 to 300 W and utilization of the standard absorbance level of 100 W. The reactions were carried out in 10 mL glass tubes, sealed with Teflon septum and placed in the microwave cavity. The reactions were irradiated at the required set temperature for the stipulated time and then cooled to the ambient temperature with air jet cooling.

General procedure for the synthesis of Ugi products

Table S1: Starting materials for Ugi reaction

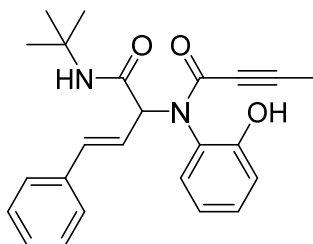
Aldehydes	 <p>1A: <chem>C=CC=O</chem> 1B: <chem>C=CC=O</chem> 1C: <chem>C=CC=O</chem> 1D: <chem>C=CC=O</chem> 1E: <chem>C=CC=O</chem> 1F: <chem>C=CC=O</chem> 1G: <chem>C=CC=O</chem></p>
Amines	 <p>2A: <chem>Nc1ccc(O)cc1</chem> 2B: <chem>Nc1ccc(O)c(C)c1</chem> 2C: <chem>Nc1ccc(O)c(C)c1</chem> 2D: <chem>Nc1ccc(O)c(C)c1</chem> 2E: <chem>Nc1ccc(O)c(F)c1</chem> 2F: <chem>Nc1ccc(O)c(Cl)c1</chem> 2G: <chem>Nc1ccc(O)c(Cc2ccccc2)c1</chem></p>
Acids	 <p>3A: <chem>CC#CC(=O)O</chem> 3B: <chem>CC#CC(=O)O</chem> 3C: <chem>CC#CC(=O)O</chem> 3D: <chem>CC#CC(=O)O</chem> 3E: <chem>CCCC#CC(=O)O</chem> 3F: <chem>c1ccc(cc1)C#CC(=O)O</chem></p>
Isonitriles	 <p>4A: <chem>CC(C)(C)C#N</chem> 4B: <chem>C1CCCCC1C#N</chem> 4C: <chem>CCCC#N</chem> 4D: <chem>c1ccc(cc1)CC#N</chem></p>



A screw-cap vial equipped with a magnetic stir bar was charged with aldehyde (0.8 mmol, 1.0 equiv.), amine (0.88 mmol, 1.1 equiv.), alkynoic acid (0.88 mmol, 1.1 equiv.), isonitrile (0.88 mmol, 1.1 equiv.), and methanol (3 mL). The reaction mixture was stirred at 50 °C for 12-24 h. The reaction solution was then concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel with EtOAc/Heptane (v/v, 1/2) to provide the desired Ugi products **1a-u** as solid.

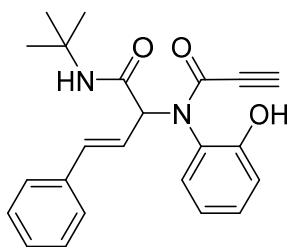
Ugi products were in many cases found to appear as mixture of two rotamers, so it should be noted that in this case, the ^1H and ^{13}C NMR spectra are not very characteristic.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)-4-phenylbut-3-enamide (**1a**)



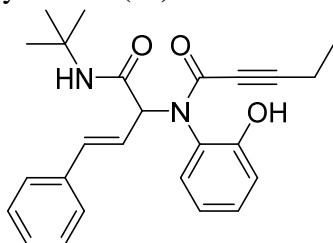
Pale yellow solid, Yield 78% (Mixture of rotamers \approx 1.2: 1), Melting point: 86-88 °C. ^1H NMR (400 MHz, CDCl_3) δ = 10.92 (s, 0.52H), 10.81 (s, 0.47H), 7.47 (d, J = 6.9 Hz, 0.98H), 7.41 – 7.32 (m, 1.62H), 7.26 (d, J = 3.5 Hz, 0.52H), 7.23 – 7.18 (m, 1.86H), 7.14 (dd, J = 7.0, 2.7 Hz, 1.14H), 7.03 (m, 1.53H), 6.94 – 6.87 (m, 0.76H), 6.86 – 6.80 (m, 0.55H), 6.79 – 6.70 (m, 1.06H), 6.64 (d, J = 15.7 Hz, 0.55H), 6.58 (d, J = 16.1 Hz, 0.51H), 5.86 (s, 0.53H), 5.83 (s, 0.54H), 5.73 (dd, J = 15.7, 9.5 Hz, 0.59H), 5.30 (d, J = 9.5 Hz, 0.55H), 4.19 (d, J = 9.0 Hz, 0.48H), 1.70 (s, 1.47H), 1.69 (s, 1.55H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ = 171.6, 170.0, 156.0, 155.7, 154.8, 154.6, 138.6, 136.9, 135.5, 135.2, 132.1, 130.6, 130.6, 129.6, 129.1, 129.0, 128.8, 128.6, 128.6, 127.0, 126.8, 125.1, 121.4, 120.7, 119.1, 119.1, 118.0, 118.0, 90.4, 90.1, 69.6, 64.2, 52.7, 52.6, 28.5, 28.5, 3.9, 3.9. HRMS (ESI) calculated for $\text{C}_{24}\text{H}_{27}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 391.2021, found 391.2020.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxyphenyl)propiolamido)-4-phenylbut-3-enamide (**1b**)



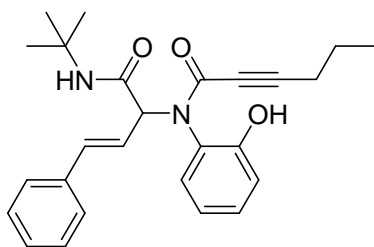
Pale yellow solid, Yield 66% (Mixture of rotamers \approx 3: 1), Melting point: 79-81 °C. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ = 11.39 (s, 1H), 8.58 (s, 1H), 7.48 – 7.18 (m, 6H), 7.17 – 7.04 (m, 2H), 6.88 (d, J = 8.2 Hz, 1H), 6.84 (t, J = 7.5 Hz, 0.32H), 6.77 (t, J = 7.5 Hz, 0.72H), 6.61 (d, J = 15.8 Hz, 0.75H), 6.55 (d, J = 16.0 Hz, 0.24H), 6.05 (dd, J = 15.8, 8.4 Hz, 0.22H), 5.72 (dd, J = 15.8, 8.5 Hz, 0.80H), 5.41 (d, J = 8.5 Hz, 0.76H), 5.08 (d, J = 8.3 Hz, 0.22H), 1.99 (s, 1H), 1.32 (s, 6.86H), 1.29 (s, 2.10H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ = 171.9, 168.7, 156.1, 153.9, 136.6, 136.0, 135.7, 134.5, 132.9, 131.2, 129.2, 129.1, 129.0, 129.0, 129.0, 128.9, 128.8, 128.4, 126.8, 126.7, 125.6, 122.3, 119.4, 117.6, 82.7, 76.5, 63.2, 60.2, 51.8, 51.5, 51.0, 28.9, 28.7, 28.7, 21.2, 14.6. **HRMS** (ESI) calculated for $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 377.1865, found 377.1863.

(*E*)-*N*-(1-(*tert*-butylamino)-1-oxo-4-phenylbut-3-en-2-yl)-*N*-(2-hydroxyphenyl)pent-2-ynamide (**1c**)



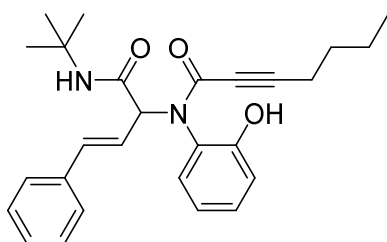
Pale yellow solid, Yield 63%, Melting point: 72-74 °C. $^1\text{H NMR}$ (300 MHz, $\text{DMSO-}d_6$) δ = 11.38 (s, 1H), 8.53 (s, 1H), 7.32 – 7.15 (m, 5H), 7.14 – 7.04 (m, 2H), 6.86 (d, J = 8.1 Hz, 1H), 6.75 (t, J = 7.5 Hz, 1H), 6.60 (d, J = 15.9 Hz, 1H), 5.73 (dd, J = 15.9, 8.5 Hz, 1H), 5.39 (d, J = 8.5 Hz, 1H), 2.04 (q, J = 7.4 Hz, 2H), 1.31 (s, 9H), 0.73 (t, J = 7.4 Hz, 3H). $^{13}\text{C NMR}$ (75 MHz, $\text{DMSO-}d_6$) δ = 171.7, 155.7, 154.2, 135.8, 135.0, 132.4, 130.1, 128.6, 128.4, 128.1, 126.2, 125.8, 122.4, 118.6, 116.9, 94.3, 74.1, 62.6, 59.6, 51.3, 28.4, 28.3, 14.0, 12.4, 11.4. **HRMS** (ESI) calculated for $\text{C}_{25}\text{H}_{29}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 405.2178, found 405.2181.

(*E*)-*N*-(1-(*tert*-butylamino)-1-oxo-4-phenylbut-3-en-2-yl)-*N*-(2-hydroxyphenyl)hex-2-ynamide (**1d**)



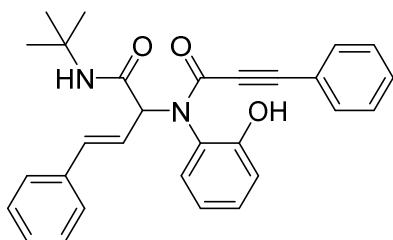
Pale yellow solid, Yield 49%, Melting point: 79-81 °C. $^1\text{H NMR}$ (300 MHz, $\text{DMSO-}d_6$) δ = 11.39 (s, 1H), 8.56 (s, 1H), 7.30 – 7.16 (m, 5H), 7.14 – 7.05 (m, 2H), 6.86 (d, J = 8.2 Hz, 1H), 6.74 (t, J = 7.5 Hz, 1H), 6.59 (d, J = 15.9 Hz, 1H), 5.72 (dd, J = 15.9, 8.5 Hz, 1H), 5.39 (d, J = 8.5 Hz, 1H), 2.06 (t, J = 6.6 Hz, 2H), 1.31 (s, 9H), 1.17 – 1.04 (m, 2H), 0.62 (t, J = 7.1 Hz, 3H). $^{13}\text{C NMR}$ (75 MHz, $\text{DMSO-}d_6$) δ = 171.7, 155.7, 154.2, 135.8, 135.0, 132.4, 130.1, 128.6, 128.4, 128.1, 126.2, 125.8, 122.4, 118.6, 116.9, 92.9, 62.7, 51.3, 28.3, 20.5, 19.7, 12.7. **HRMS** (ESI) calculated for $\text{C}_{26}\text{H}_{31}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 419.2334, found 419.2338.

(*E*)-*N*-(1-(*tert*-butylamino)-1-oxo-4-phenylbut-3-en-2-yl)-*N*-(2-hydroxyphenyl)hept-2-ynamide (**1e**)



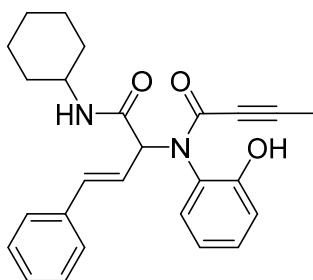
Pale yellow solid, Yield 39%, Melting point: 94-95 °C. $^1\text{H NMR}$ (300 MHz, $\text{DMSO-}d_6$) δ = 11.38 (s, 1H), 8.55 (s, 1H), 7.30 – 7.15 (m, 5H), 7.13 – 7.05 (m, 2H), 6.86 (d, J = 8.2 Hz, 1H), 6.74 (t, J = 7.6 Hz, 1H), 6.59 (d, J = 15.9 Hz, 1H), 5.72 (dd, J = 15.9, 8.5 Hz, 1H), 5.39 (d, J = 8.5 Hz, 1H), 2.08 (t, J = 6.4 Hz, 2H), 1.31 (s, 9H), 1.14 – 0.86 (m, 4H), 0.70 (t, J = 7.0 Hz, 3H). $^{13}\text{C NMR}$ (75 MHz, $\text{DMSO-}d_6$) δ = 171.7, 155.7, 154.2, 135.8, 135.0, 132.3, 130.1, 128.6, 128.4, 128.1, 126.2, 125.7, 122.4, 118.6, 116.9, 93.0, 74.7, 62.6, 51.3, 29.0, 28.3, 20.7, 17.4, 13.1. **HRMS** (ESI) calculated for $\text{C}_{27}\text{H}_{33}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 433.2491, found 433.2483.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxyphenyl)-3-phenylpropiolamido)-4-phenylbut-3-enamide (**1f**)



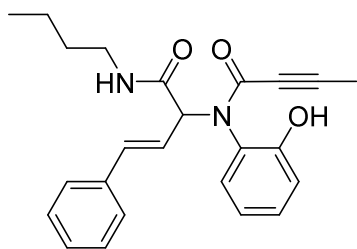
Pale yellow solid, Yield 59% (Mixture of rotamers \approx 1.2: 1), Melting point: 118-120 °C. **^1H NMR (300 MHz, DMSO- d_6)** δ = 11.51 (s, 0.57H), 9.56 (s, 0.52H), 8.63 (s, 0.49H), 7.68 (s, 0.56H), 7.48 – 7.14 (m, 10H), 7.12 – 7.03 (m, 2H), 6.97 – 6.85 (m, 1H), 6.81 – 6.73 (m, 1H), 6.65 (d, J = 15.9 Hz, 1H), 6.15 (dd, J = 15.9, 8.3 Hz, 0.22H), 5.81 (dd, J = 15.9, 8.3 Hz, 0.73H), 5.48 (d, J = 8.3 Hz, 0.68H), 5.15 (d, J = 8.3 Hz, 0.23H), 1.33 (s, 5H), 1.12 (s, 4H). **^{13}C NMR (75 MHz, DMSO- d_6)** δ = 171.5, 169.1, 165.6, 155.9, 152.8, 147.9, 140.3, 135.8, 135.4, 135.4, 135.2, 132.6, 132.1, 130.4, 129.8, 128.7, 128.6, 128.6, 128.3, 128.1, 127.5, 127.4, 127.3, 126.9, 126.3, 125.5, 122.2, 118.9, 118.7, 117.0, 116.7, 66.8, 51.4, 50.5, 32.5, 28.3, 28.2. **HRMS (ESI)** calculated for $\text{C}_{29}\text{H}_{29}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 453.2178, found 453.2176.

(*E*)-*N*-cyclohexyl-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)-4-phenylbut-3-enamide (**1g**)



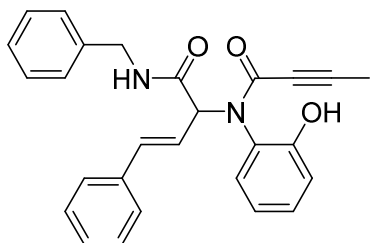
Pale yellow solid, Yield 60% (Mixture of rotamers \approx 3.5: 1), Melting point: 78-80 °C. **^1H NMR (400 MHz, DMSO- d_6)** δ = 11.41 (s, 1H), 8.79 (d, J = 7.9 Hz, 1H), 7.30 – 7.16 (m, 4H), 7.15 – 7.10 (m, 2H), 6.96 – 6.82 (m, 2H), 6.76 (t, J = 7.5 Hz, 1H), 6.60 (d, J = 15.6 Hz, 1H), 6.18 (dd, J = 15.9, 8.4 Hz, 0.22H), 5.73 (dd, J = 15.9, 8.5 Hz, 0.73H), 5.40 (d, J = 8.4 Hz, 0.67H), 4.98 (d, J = 8.3 Hz, 0.28H), 3.71 – 3.53 (m, 1H), 1.88 – 1.72 (m, 3H), 1.70 (s, 3H), 1.61 – 1.50 (m, 1H), 1.33 – 1.16 (m, 6H). **^{13}C NMR (101 MHz, DMSO- d_6)** δ = 171.7, 170.8, 156.0, 154.7, 136.7, 136.0, 135.7, 135.5, 132.9, 130.9, 129.2, 129.1, 129.0, 129.0, 128.9, 128.8, 128.4, 126.9, 126.8, 125.9, 123.2, 122.4, 119.2, 117.5, 90.1, 74.0, 62.7, 60.2, 49.1, 48.9, 48.7, 32.6, 32.4, 32.4, 25.6, 25.5, 25.0, 24.8, 21.2, 14.6, 3.9, 3.7, 3.6. **HRMS (ESI)** calculated for $\text{C}_{26}\text{H}_{29}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 417.2178, found 417.2179.

(*E*)-*N*-butyl-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)-4-phenylbut-3-enamide (**1h**)



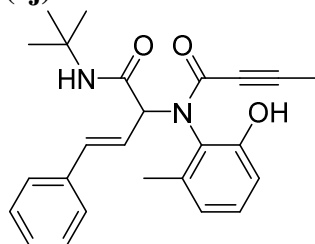
Pale yellow solid, Yield 38% (Mixture of rotamers \approx 2.5: 1), Melting point: 61-63 °C. ^1H NMR (400 MHz, DMSO- d_6) δ = 11.37 (s, 0.69H), 10.42 (s, 0.29H), 8.88 (t, J = 5.8 Hz, 0.75H), 8.08 (t, J = 5.8 Hz, 0.32H), 7.38 – 7.15 (m, 4H), 7.15 – 7.02 (m, 2H), 6.96 – 6.46 (m, 4H), 6.21 (dd, J = 15.8, 8.5 Hz, 0.29H), 5.70 (dd, J = 15.8, 8.7 Hz, 0.67H), 5.39 (d, J = 8.7 Hz, 0.61H), 4.94 (d, J = 8.5 Hz, 0.32H), 3.22 – 3.03 (m, 2H), 1.97 (s, 0.60H), 1.69 (s, 2.45H), 1.50 – 1.36 (m, 2H), 1.33 – 1.24 (m, 2H), 0.85 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, DMSO- d_6) δ = 172.7, 170.2, 156.0, 154.9, 154.7, 154.1, 144.4, 136.9, 136.6, 136.0, 135.8, 135.5, 132.9, 131.3, 130.9, 130.5, 129.2, 129.1, 128.8, 128.5, 128.4, 127.0, 126.8, 125.8, 122.6, 122.2, 119.9, 119.4, 119.3, 117.6, 117.0, 116.9, 114.9, 114.8, 90.1, 89.0, 74.6, 74.0, 65.2, 62.9, 31.5, 31.2, 19.9, 19.8, 14.2, 14.0, 3.6. HRMS (ESI) calculated for $\text{C}_{24}\text{H}_{27}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 391.2021, found 391.2015.

(*E*)-*N*-benzyl-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)-4-phenylbut-3-enamide (**1i**)



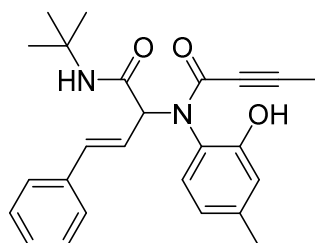
Pale yellow solid, Yield 53% (Mixture of rotamers \approx 2: 1), Melting point: 117-119 °C. ^1H NMR (400 MHz, DMSO- d_6) δ = 11.19 (s, 0.65H), 10.28 (s, 0.40H), 9.44 (t, J = 6.1 Hz, 0.67H), 8.67 (t, J = 6.1 Hz, 0.33H), 7.43 – 7.18 (m, 10H), 7.11 (t, J = 7.7 Hz, 2H), 6.92 – 6.74 (m, 2H), 6.66 – 6.59 (m, 1H), 6.20 (dd, J = 15.8, 8.6 Hz, 0.28H), 5.74 (dd, J = 15.8, 8.6 Hz, 0.65H), 5.48 (d, J = 8.6 Hz, 0.60H), 5.11 (d, J = 8.6 Hz, 0.31H), 4.53 – 4.29 (m, 2H), 1.99 (s, 0.72H), 1.70 (s, 2.24H). ^{13}C NMR (101 MHz, DMSO- d_6) δ = 173.1, 170.7, 155.9, 155.0, 154.8, 139.6, 138.8, 136.5, 136.0, 135.9, 135.6, 132.9, 131.5, 131.0, 130.5, 129.2, 129.1, 129.0, 129.0, 128.9, 128.8, 128.7, 128.7, 128.6, 128.5, 128.2, 127.7, 127.6, 127.5, 127.2, 127.0, 126.8, 126.1, 125.8, 122.5, 122.0, 119.4, 117.5, 90.3, 74.6, 74.0, 64.9, 63.0, 60.2, 43.2, 14.6, 3.8, 3.6. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 425.1865, found 425.1866.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxy-6-methylphenyl)but-2-ynamido)-4-phenylbut-3-enamide
(**1j**)



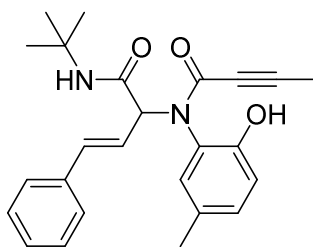
Pale yellow solid, Yield 31%, Melting point: 71-73 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 10.49 (s, 1H), 7.44 (s, 1H), 7.36 – 7.22 (m, 5H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.75 – 6.68 (m, 2H), 6.60 (d, *J* = 15.8 Hz, 1H), 6.30 (dd, *J* = 15.8, 9.2 Hz, 1H), 4.65 (d, *J* = 9.2 Hz, 1H), 2.25 (s, 3H), 1.70 (s, 3H), 1.29 (s, 9H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ = 169.5, 154.9, 154.4, 138.8, 136.6, 135.5, 129.8, 129.1, 129.0, 128.5, 128.2, 126.9, 126.8, 123.7, 121.1, 114.2, 87.5, 74.4, 66.8, 60.2, 51.2, 28.8, 28.7, 21.2, 18.7, 14.6, 3.6. HRMS (ESI) calculated for C₂₅H₂₉N₂O₃⁺ ([M+H]⁺): 405.2178, found 405.2170.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxy-4-methylphenyl)but-2-ynamido)-4-phenylbut-3-enamide
(**1k**)



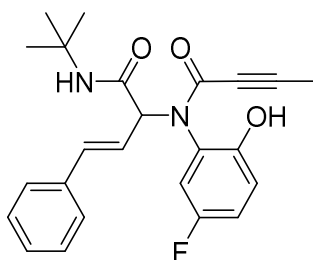
Pale yellow solid, Yield 89%, Melting point: 165-167 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ = 11.27 (s, 1H), 8.51 (s, 1H), 7.31 – 7.18 (m, 4H), 7.14 (d, *J* = 7.1 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.69 (s, 1H), 6.62 – 6.51 (m, 2H), 5.72 (dd, *J* = 15.8, 8.5 Hz, 1H), 5.36 (d, *J* = 8.5 Hz, 1H), 2.21 (s, 3H), 1.71 (s, 3H), 1.31 (s, 9H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ = 172.3, 155.6, 154.8, 140.3, 136.1, 135.3, 132.4, 129.2, 129.1, 129.0, 129.0, 128.9, 128.9, 128.7, 126.8, 123.3, 122.6, 120.1, 117.9, 90.0, 74.2, 63.2, 51.7, 28.9, 28.7, 28.7, 21.4, 3.7. HRMS (ESI) calculated for C₂₅H₂₉N₂O₃⁺ ([M+H]⁺): 405.2178, found 405.2182.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxy-5-methylphenyl)but-2-ynamido)-4-phenylbut-3-enamide
(**1l**)



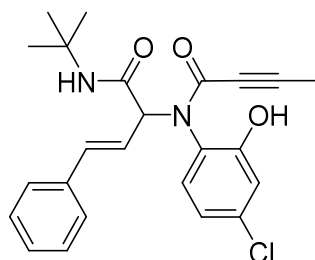
Pale yellow solid, Yield 67% (Mixture of rotamers \approx 4: 1), Melting point: 95-97 °C. $^1\text{H NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ = 11.10 (s, 1H), 8.50 (s, 1H), 7.34 – 7.21 (m, 3H), 7.15 – 7.08 (m, 2H), 7.01 (dd, J = 8.3, 2.1 Hz, 1H), 6.90 (s, 1H), 6.76 (d, J = 8.3 Hz, 1H), 6.60 (d, J = 15.8 Hz, 1H), 6.17 (dd, J = 16.0, 8.3 Hz, 0.19H), 5.72 (dd, J = 15.8, 8.5 Hz, 0.82H), 5.36 (d, J = 8.5 Hz, 0.75H), 4.93 (d, J = 8.3 Hz, 0.18H), 2.13 (s, 3H), 1.71 (s, 3H), 1.30 (s, 9H). $^{13}\text{C NMR}$ (151 MHz, $\text{DMSO-}d_6$) δ = 172.2, 154.6, 153.6, 136.1, 135.3, 132.8, 131.4, 129.2, 129.1, 129.0, 129.0, 128.9, 128.9, 128.7, 127.7, 126.8, 126.7, 125.5, 122.8, 117.1, 89.9, 74.2, 63.1, 51.7, 28.9, 28.7, 28.7, 20.3, 3.7. **HRMS** (ESI) calculated for $\text{C}_{25}\text{H}_{29}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 405.2178, found 405.2179.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(5-fluoro-2-hydroxyphenyl)but-2-ynamido)-4-phenylbut-3-enamide
(1m)



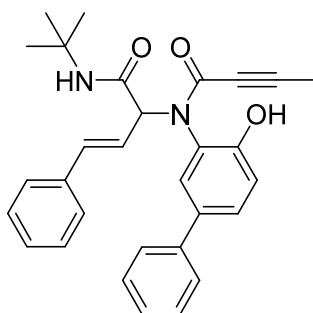
Pale yellow solid, Yield 49% (Mixture of rotamers \approx 4: 1), Melting point: 93-95 °C. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ = 11.38 (s, 1H), 8.58 (s, 1H), 7.37 – 7.21 (m, 4H), 7.18 – 6.95 (m, 3H), 6.95 – 6.80 (m, 1H), 6.58 (d, J = 16.1 Hz, 1H), 6.01 (dd, J = 15.9, 8.1 Hz, 0.20H), 5.78 (dd, J = 15.9, 8.3 Hz, 0.76H), 5.38 (d, J = 8.3 Hz, 0.72H), 5.16 (d, J = 8.1 Hz, 0.19H), 1.74 (s, 3H), 1.31 (s, 9H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ = 172.1, 169.0, 155.8, 154.4, 153.5, 152.9, 136.6, 136.0, 135.7, 134.6, 129.2, 129.1, 129.0, 128.9, 128.8, 128.4, 126.7, 126.7, 126.2, 126.1, 123.5, 122.3, 119.2, 119.0, 118.0, 117.9, 117.8, 117.6, 90.3, 73.9, 63.0, 51.8, 51.5, 51.0, 28.9, 28.7, 28.6, 3.6. **HRMS** (ESI) calculated for $\text{C}_{24}\text{H}_{26}\text{FN}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 409.1927, found 409.1926.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(4-chloro-2-hydroxyphenyl)but-2-ynamido)-4-phenylbut-3-enamide
(1n)



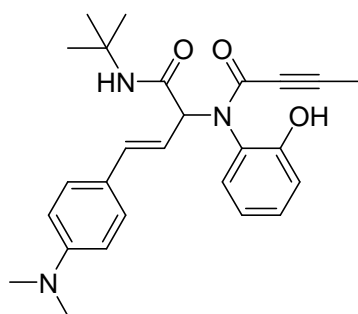
Pale yellow solid, Yield 52%, Melting point: 84-86 °C. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ = 11.96 (s, 1H), 8.62 (s, 1H), 7.26 (m, 3H), 7.18 – 7.15 (m, 2H), 6.96 – 6.87 (m, 2H), 6.82 (dd, J = 8.5, 2.4 Hz, 1H), 6.58 (d, J = 16.0 Hz, 1H), 5.76 (dd, J = 16.0, 8.3 Hz, 1H), 5.40 (d, J = 8.3 Hz, 1H), 1.75 (s, 3H), 1.31 (s, 9H). $^{13}\text{C NMR}$ (75 MHz, $\text{DMSO-}d_6$) δ = 171.7, 156.7, 154.0, 135.6, 135.4, 134.1, 133.7, 128.6, 128.3, 128.2, 126.3, 124.9, 121.9, 118.6, 116.8, 89.9, 78.5, 73.6, 62.5, 51.4, 28.5, 28.3, 28.2, 3.0. **HRMS** (ESI) calculated for $\text{C}_{24}\text{H}_{26}\text{ClN}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 425.1631, found 425.1633.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(4-hydroxy-[1,1'-biphenyl]-3-yl)but-2-ynamido)-4-phenylbut-3-enamide (**1o**)



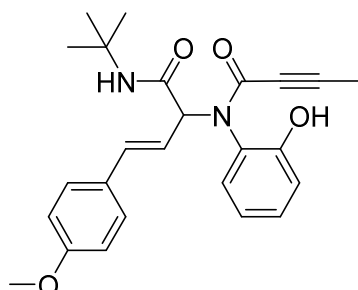
Pale yellow solid, Yield 54%, Melting point: 193-195 °C. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ = 11.55 (s, 1H), 8.60 (s, 1H), 7.57 – 7.46 (m, 4H), 7.36 (t, J = 7.5 Hz, 2H), 7.30 – 7.19 (m, 4H), 7.17 – 7.10 (m, 2H), 6.95 (d, J = 8.5 Hz, 1H), 6.62 (d, J = 15.8 Hz, 1H), 5.85 (dd, J = 15.8, 8.2 Hz, 1H), 5.45 (d, J = 8.2 Hz, 1H), 1.70 (s, 3H), 1.33 (s, 9H). $^{13}\text{C NMR}$ (75 MHz, $\text{DMSO-}d_6$) δ = 171.7, 155.2, 154.2, 139.4, 135.8, 135.2, 131.0, 130.6, 128.8, 128.7, 128.5, 128.3, 128.1, 126.5, 126.2, 126.1, 125.9, 125.8, 122.6, 117.4, 89.5, 62.6, 51.3, 28.3, 3.0. **HRMS** (ESI) calculated for $\text{C}_{30}\text{H}_{31}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 467.2334, found 467.2332.

(*E*)-*N*-(*tert*-butyl)-4-(4-(dimethylamino)phenyl)-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)but-3-enamide (**1p**)



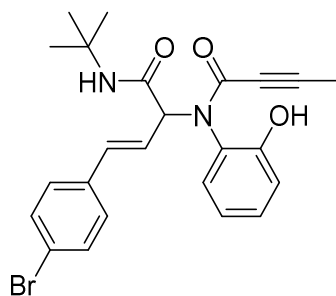
Pale yellow solid, Yield 50%, Melting point: 82-84 °C. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ = 11.43 (s, 1H), 8.47 (s, 1H), 7.18 (t, J = 7.7 Hz, 1H), 7.04 (d, J = 7.9 Hz, 1H), 6.93 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.1 Hz, 1H), 6.73 (t, J = 7.6 Hz, 1H), 6.56 (d, J = 8.4 Hz, 2H), 6.45 (d, J = 15.3 Hz, 1H), 5.49 – 5.20 (m, 1H), 5.31 (s, 1H), 2.85 (s, 6H), 1.68 (s, 3H), 1.30 (s, 9H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ = 172.8, 156.0, 154.6, 150.8, 135.7, 132.9, 130.7, 127.7, 126.1, 123.9, 119.1, 117.4, 117.2, 112.5, 89.8, 74.2, 63.5, 51.7, 28.7, 3.6. **HRMS** (ESI) calculated for $\text{C}_{26}\text{H}_{32}\text{N}_3\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 434.2443, found 434.2426.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)-4-(4-methoxyphenyl)but-3-enamide (**1q**)



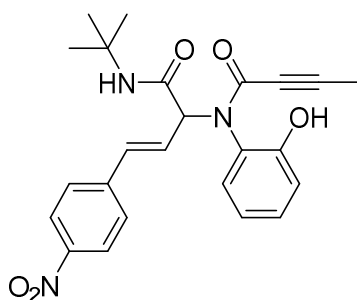
Pale yellow solid, Yield 28% (Mixture of rotamers \approx 1.3: 1), Melting point: 138-139 °C. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ = 8.09 – 7.81 (m, 2.55H), 7.40 – 7.17 (m, 3H), 7.16 – 6.93 (m, 2H), 6.92 – 6.81 (m, 1.32H), 6.81 – 6.49 (m, 2H), 4.41 (s, 0.54H), 3.47 (s, 0.43H), 2.43 (s, 1.75H), 2.05 (s, 1.22H), 2.02 (s, 1.74H), 1.73 (s, 1.25H), 1.40 (s, 4.46H), 1.31 (s, 3.50H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ = 167.4, 165.2, 155.3, 148.0, 144.5, 144.1, 134.4, 130.9, 130.1, 129.1, 129.0, 128.2, 126.9, 125.5, 121.9, 121.4, 120.6, 119.8, 119.3, 118.9, 118.7, 117.4, 115.5, 91.6, 67.1, 52.2, 52.2, 28.6, 28.5, 28.4, 28.3, 21.5, 3.6, 3.5. **HRMS** (ESI) calculated for $\text{C}_{25}\text{H}_{29}\text{N}_2\text{O}_4^+$ ($[\text{M}+\text{H}]^+$): 421.2127, found 421.2129.

(*E*)-4-(4-bromophenyl)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)but-3-enamide (**1r**)



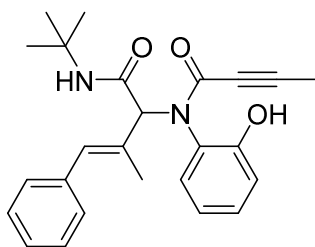
Pale yellow solid, Yield 62% (Mixture of rotamers \approx 3.5: 1), Melting point: 159-161 °C. ^1H NMR (300 MHz, DMSO- d_6) δ = 11.37 (s, 1H), 8.55 (s, 1H), 7.53 – 7.35 (m, 2.4H), 7.25 7.16 (m, 1.25H), 7.09 (d, J = 7.7 Hz, 2.26H), 6.94 – 6.69 (m, 2.06H), 6.63 – 6.47 (m, 1.07H), 6.18 (dd, J = 15.8, 8.2 Hz, 0.21H), 5.76 (dd, J = 15.8, 8.2 Hz, 0.74H), 5.37 (d, J = 8.4 Hz, 0.76H), 4.94 (d, J = 8.4 Hz, 0.20H), 1.70 (s, 3H), 1.30 (s, 9H). ^{13}C NMR (75 MHz, DMSO- d_6) δ = 171.4, 155.6, 154.2, 135.0, 133.8, 132.3, 131.6, 130.6, 130.2, 128.2, 125.6, 123.4, 121.2, 118.7, 117.0, 114.6, 89.4, 73.7, 62.6, 51.3, 28.3. HRMS (ESI) calculated for $\text{C}_{24}\text{H}_{26}\text{BrN}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 469.1126, found 469.1123.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)-4-(4-nitrophenyl)but-3-enamide
(1s)



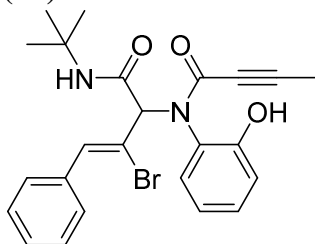
Pale yellow solid, Yield 41% (Mixture of rotamers \approx 2: 1), Melting point: 108-110 °C. ^1H NMR (400 MHz, DMSO- d_6) δ = 11.32 (s, 1H), 8.57 (s, 1H), 8.26 – 8.06 (m, 2H), 7.61 – 7.09 (m, 4H), 6.99 – 6.60 (m, 3H), 6.50 – 6.35 (m, 0.43H), 6.01 (dd, J = 15.9, 8.4 Hz, 0.60H), 5.44 (d, J = 8.4 Hz, 0.63H), 4.98 (d, J = 8.4 Hz, 0.30H), 1.70 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, DMSO- d_6) δ = 171.6, 155.9, 154.7, 147.3, 142.5, 133.6, 132.8, 131.0, 130.2, 130.1, 129.0, 128.3, 128.2, 127.8, 127.8, 127.5, 125.8, 124.5, 124.4, 124.0, 123.9, 119.3, 117.6, 90.2, 74.0, 62.9, 51.8, 51.6, 51.6, 51.1, 28.9, 28.7, 28.7, 28.5, 28.5, 14.6, 13.9, 4.0, 3.7, 3.6. HRMS (ESI) calculated for $\text{C}_{24}\text{H}_{26}\text{N}_3\text{O}_5^+$ ($[\text{M}+\text{H}]^+$): 436.1872, found 436.1873.

(*E*)-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)-3-methyl-4-phenylbut-3-enamide
(1t)



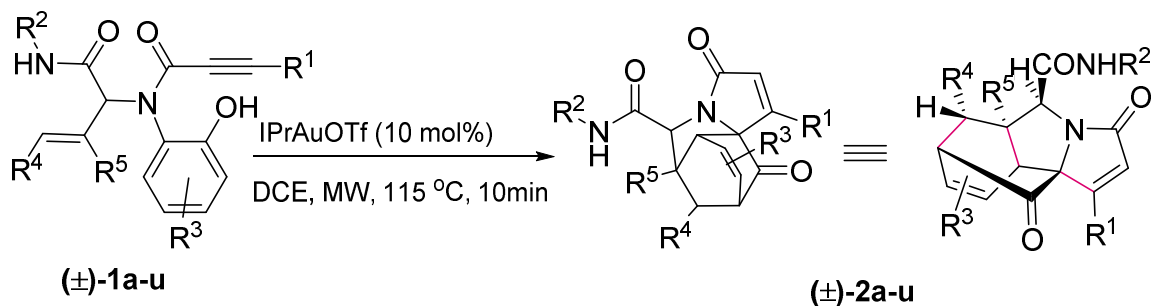
Pale yellow solid, Yield 44%, Melting point: 144-147 °C. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ = 11.50 (s, 1H), 8.50 (s, 1H), 7.27 (t, J = 7.4 Hz, 2H), 7.19 (dd, J = 7.5, 4.4 Hz, 2H), 7.12 (dd, J = 7.8, 1.6 Hz, 1H), 6.88 (d, J = 7.5 Hz, 2H), 6.81 (d, J = 8.1 Hz, 1H), 6.74 (s, 1H), 6.46 (s, 1H), 5.35 (s, 1H), 1.69 (s, 3H), 1.50 (s, 3H), 1.32 (s, 9H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ = 172.2, 156.3, 155.1, 136.8, 133.0, 133.0, 131.4, 130.8, 128.8, 128.8, 128.8, 128.7, 128.6, 127.5, 125.9, 118.7, 117.2, 90.0, 74.3, 68.0, 51.7, 28.6, 28.5, 17.9, 3.6. **HRMS** (ESI) calculated for $\text{C}_{25}\text{H}_{29}\text{N}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 405.2178, found 405.2175.

(*Z*)-3-bromo-*N*-(*tert*-butyl)-2-(*N*-(2-hydroxyphenyl)but-2-ynamido)-4-phenylbut-3-enamide (**1u**)



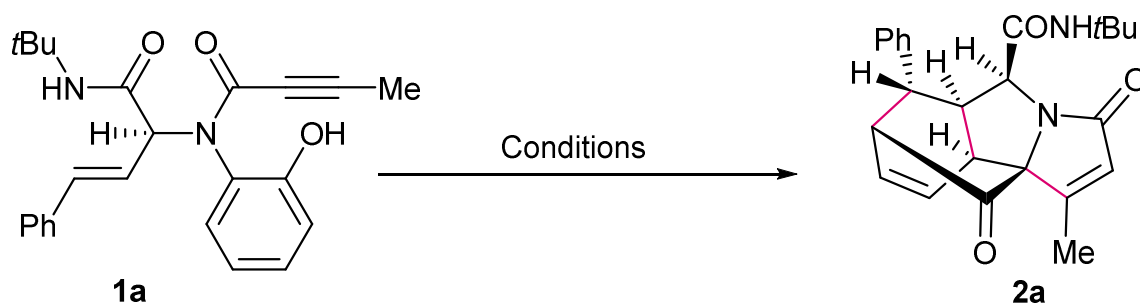
Pale yellow solid, Yield 37%, Melting point: 96-98 °C. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ = 11.25 (s, 1H), 8.74 (s, 1H), 7.34 – 7.28 (m, 3H), 7.26 – 7.21 (m, 3H), 7.17 – 7.10 (m, 2H), 6.82 (d, J = 7.8 Hz, 1H), 6.76 (td, J = 7.6, 1.4 Hz, 1H), 5.80 (s, 1H), 1.70 (s, 3H), 1.33 (s, 9H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ = 169.7, 156.5, 155.1, 136.2, 135.1, 133.6, 131.1, 129.1, 128.9, 128.7, 128.6, 125.1, 118.8, 117.8, 117.2, 90.6, 74.0, 69.5, 52.0, 28.5, 3.7. **HRMS** (ESI) calculated for $\text{C}_{24}\text{H}_{26}\text{BrN}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 469.1126, found 469.1114.

General procedure for the Microwave-assisted Intramolecular Diels-Alder Reaction



The cationic gold catalyst IPrAuOTf was first generated *in situ* by mixing of (IPr)AuCl (10 mol%) and AgOTf (10 mol%) along with dichloroethane (2 mL) in a 10 mL microwave vial loaded with a stirring bar and kept stirring for 5 min and used without filtration. To this vial Ugi products **1a-u** (0.20 mmol) was subsequently loaded and the reaction vessel was sealed and irradiated in the cavity of a CEM-Discover microwave reactor for 10 min at the set temperature of 115 °C. After completion, the reaction mixture was diluted with dichloromethane and evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography (EtOAc/Heptane = 1: 1) to afford the bridged compounds **2a-u**.

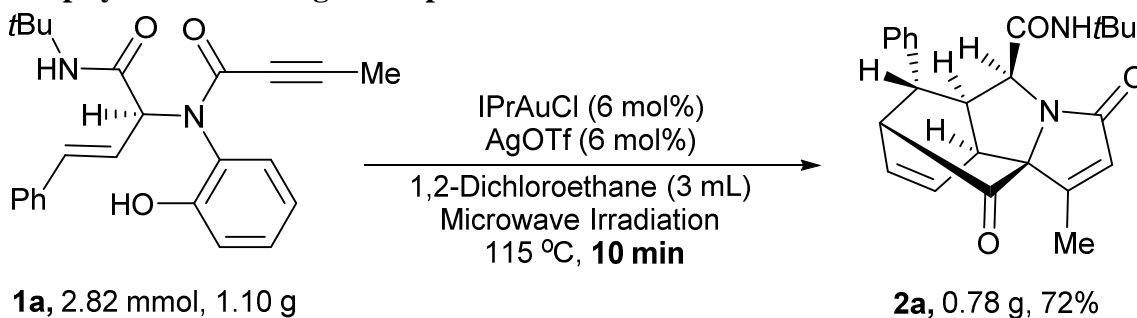
Table S2: Extended optimizations for the cascade dearomative spirocarbocyclization/Diels–Alder reaction process^a



Entry	Catalysts (10%)	Solvent	T/☐	Time	Conversion ^b	Yield ^b of 2a %	d.r
1	(IMes)AuCl/AgOTf	CDCl ₃	r.t.	16 h	75	52/43 ^c	3.3: 1
2	(IMes)AuCl/AgOTf	MeNO ₂	r.t.	16 h	43	Trace	0
3	(IMes)AuCl/AgOTf	Toluene	r.t.	16 h	54	30	15: 1
4	(IMes)AuCl/AgOTf	DCM	r.t.	16 h	65	38	7.6:1
5	(IMes)AuCl/AgOTf	DCE	r.t.	16 h	70	45	16: 1
6	HOTf (3 equiv.)	DCE	60	3h	100 ^d	0	0
7	H ₂ SO ₄ (3 equiv.)	DCE	60	3h	100 ^d	0	0

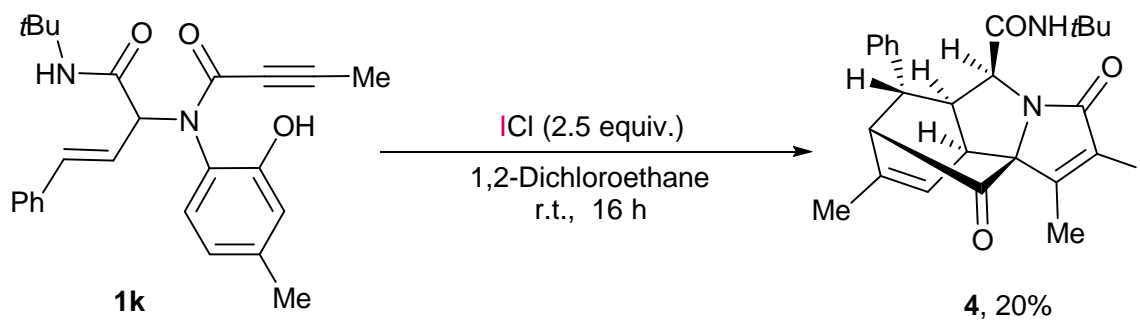
^a The reactions were run with **1a** (0.05 mmol) and a catalyst loading of 10 mol% in a screw-cap vial with solvent (1 mL). The catalyst was prepared by mixing the corresponding gold catalyst (10 mol%) and silver catalyst (10 mol%) *in situ*. ^b Conversion and yields based on ¹H NMR analysis using 2,4,6-trimethoxybenzaldehyde as internal standard. ^c Isolated yields. IMes = 1,3-bis(2,4,6-trimethylphenyl) imidazol-2-ylidene. ^d The decomposed of the starting material was observed.

Scale-up synthesis of bridged compound **2a**



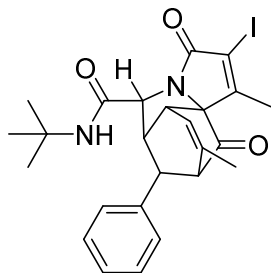
The cationic gold catalyst IPrAuOTf was first generated *in situ* by mixing of IPrAuCl (6 mol%) and AgOTf (6 mol%) along with dichloroethane (3 mL) in a 10 mL microwave vial loaded with a stirring bar and kept stirring for 5 min and used without filtration. To this vial the Ugi product **1a** (1.10 g, 2.82 mmol) was subsequently loaded and the reaction vessel was sealed and irradiated in the cavity of a CEM-Discover microwave reactor for 10 min at the set temperature of 115 °C. After completion, the reaction mixture was diluted with dichloromethane and evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography (EtOAc/Heptane = 1: 1) to afford the bridged *N*-heterocycle **2a** in 72% yield (0.78 g, 2.0 mmol).

Preliminary investigation on the cascade dearomative spirocarbocyclization/iodination process



To a screw capped vial equipped with a magnetic stir bar contained Ugi adducts **1k** (0.1 mmol) in DCE (2 mL) solvent, added iodine monochloride (2.5 equiv) dissolved in DCE (1 mL) slowly dropwise at 0 °C. The resulting reaction mixture allows reaching at rt. The reaction was stirred for 16 h. After completion, dilute the reaction mixture with DCM (25 mL) and washed with aqueous Na₂S₂O₃ solution (30 mL), and the aqueous solution was extracted with DCM. The combined organic layers dried over sodium sulfate and evaporated under reduced pressure. The subsequent residue obtained was purified by silica gel chromatography (15–30% EtOAc in hexane) to afford pure compounds **4** in yield of 20%.

N-(*tert*-butyl)-2-iodo-1,8-dimethyl-3,10-dioxo-6-phenyl-5a,6,7,9a-tetrahydro-3*H*,5*H*-7,9*b*-methanopyrrolo[2,1-*a*]isoindole-5-carboxamide (**4**)



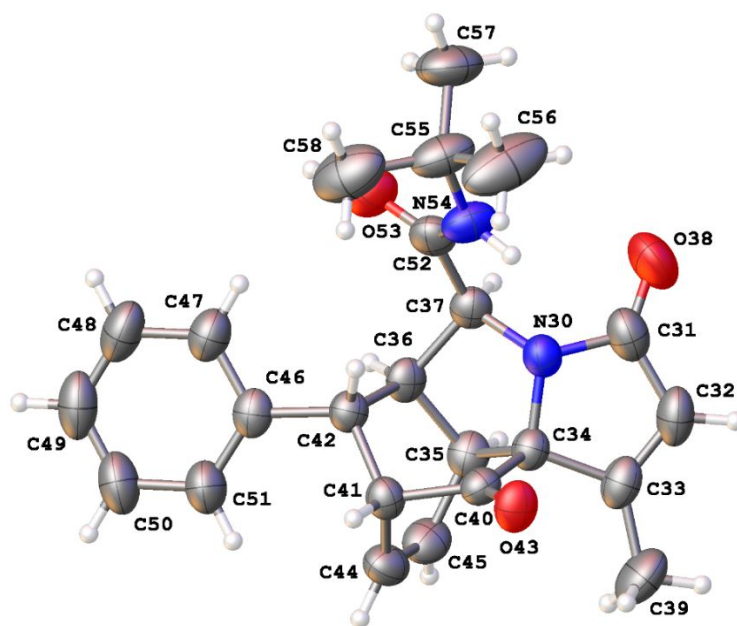
Brown solid, Yield 20% (d.r. \approx 10: 1), Melting point: 162-163 °C. NMR data of the major diastereoisomer: ^1H NMR (400 MHz, CDCl_3) δ = 7.26 – 7.18 (m, 3H), 7.10 – 7.03 (m, 2H), 6.66 (s, 1H), 6.12 (dt, J = 6.6, 1.7 Hz, 1H), 4.29 (d, J = 5.2 Hz, 1H), 3.50 – 3.40 (m, 1H), 3.37 (t, J = 2.7 Hz, 1H), 3.27 (dd, J = 3.2, 1.7 Hz, 1H), 3.01 (dd, J = 6.6, 4.1 Hz, 1H), 1.89 (s, 3H), 1.55 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ = 201.7, 174.6, 167.5, 164.4, 140.9, 139.1, 129.4, 128.3, 126.8, 126.7, 126.4, 120.6, 94.4, 66.7, 66.7, 61.4, 59.9, 51.7, 49.7, 45.2, 31.9, 30.6, 29.3, 28.0, 22.3 15.9. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{28}\text{IN}_2\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 531.1141, found 531.1146.

Crystallographic data for compound 2a and 2k

Single crystals suitable for X-ray diffraction were obtained by slow evaporation at room temperature from a *d*1-chloroform-heptane mixture (1:2 v/v) for **2a** and **2k**. X-ray intensity data were collected at room temperature for **2a** and **2k** on a Rigaku Ultra 18S generator (Xenocs mirrors, Mo $\text{K}\alpha$ radiation, λ = 0.71073 Å) using a MAR345 image plate. The images were interpreted and integrated with CrysAlisPRO^[9] and the implemented absorption correction was applied. The structures were solved using Olex2^[10] with the ShelXS^[11] structure solution program by Direct Methods and refined with the ShelXL^[12] refinement package using full-matrix least-squares minimization on F^2 . Non-hydrogen atoms were refined anisotropically and hydrogen atoms in the riding mode with isotropic temperature factors fixed at 1.2 times U_{eq} of the parent atoms (1.5 for methyl groups). CCDC 1900532 (compound **2a**), CCDC 1900531 (compound **2k**) contain the supplementary crystallographic data for this paper and can be obtained free of charge via <http://www.ccdc.cam.ac.uk/getstructures> or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; deposit@ccdc.cam.ac.uk).

Table S3: Crystal data and structure refinement details for compound 2a

Compound reference	2a
Empirical formula	C ₂₄ H ₂₆ N ₂ O ₃
Formula weight	390.47
Crystal system	triclinic
Space group	P-1
a/Å	11.7236(5)
b/Å	11.7540(5)
c/Å	17.2404(8)
α/°	73.252(4)
β/°	73.789(4)
γ/°	71.074(4)
Volume/Å ³	2106.23(18)
Temperature/K	294.15
Z	4
ρ _{calc} /cm ³	1.231
Crystal size/mm ³	0.3 × 0.15 × 0.05
Radiation	MoKα (λ = 0.71073 Å)
Absorption coefficient/mm ⁻¹	0.081
F(000)	832.0
Reflections collected	22533
Independent reflections	8322 [Rint = 0.0276, Rsigma = 0.0464]
Data/restraints/parameters	8322/54/544
Final R indexes [I ≥ 2σ (I)]	R1 = 0.0580, wR2 = 0.1230
Final R indexes [all data]	R1 = 0.0900, wR2 = 0.1407
Goodness-of-fit	1.044
Largest diff. peak/hole	0.24/-0.31 e.Å ⁻³
CCDC	1900532

**Figure S1.** Crystal structure of compound 2a. Thermal ellipsoids are drawn at the 50% probability level.**Table S4: Crystal data and structure refinement details for compound 2k**

Compound reference	2k
Empirical formula	C ₂₅ H ₂₈ N ₂ O ₃
Formula weight	404.49
Crystal system	monoclinic
Space group	<i>P</i> 2 ₁ / <i>n</i>
<i>a</i> /Å	13.4238(5)
<i>b</i> /Å	10.0908(3)
<i>c</i> /Å	16.9778(7)
α /°	90
β /°	96.486(4)
γ /°	90
Volume/Å ³	2285.05(15)
Temperature/K	294
<i>Z</i>	4
ρ_{calc} /cm ³	1.176
Crystal size/mm ³	0.25 × 0.2 × 0.15
Radiation	MoK α (λ = 0.71073 Å)
Absorption coefficient/mm ⁻¹	0.077
<i>F</i> (000)	864.0
Reflections collected	36041
Independent reflections	4653 [R _{int} = 0.0525, R _{sigma} = 0.0326]
Data/restraints/parameters	4653/0/277
Final R indexes [<i>I</i> ≥ 2 σ (<i>I</i>)]	R ₁ = 0.0677, wR ₂ = 0.1724
Final R indexes [all data]	R ₁ = 0.1043, wR ₂ = 0.1975
Goodness-of-fit	1.052
Largest diff. peak/hole	0.33/-0.21 e.Å ⁻³
CCDC	1900531

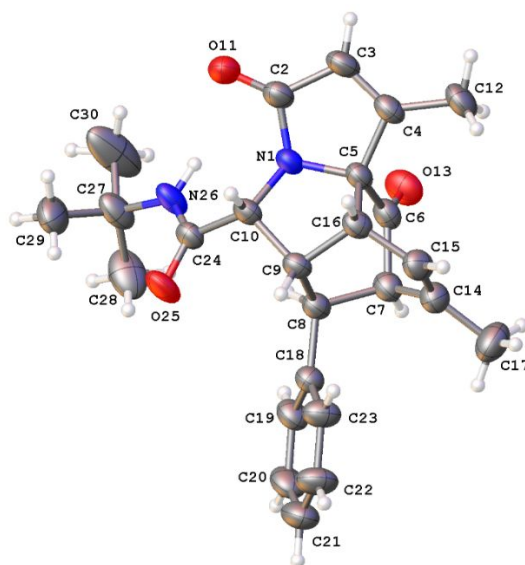


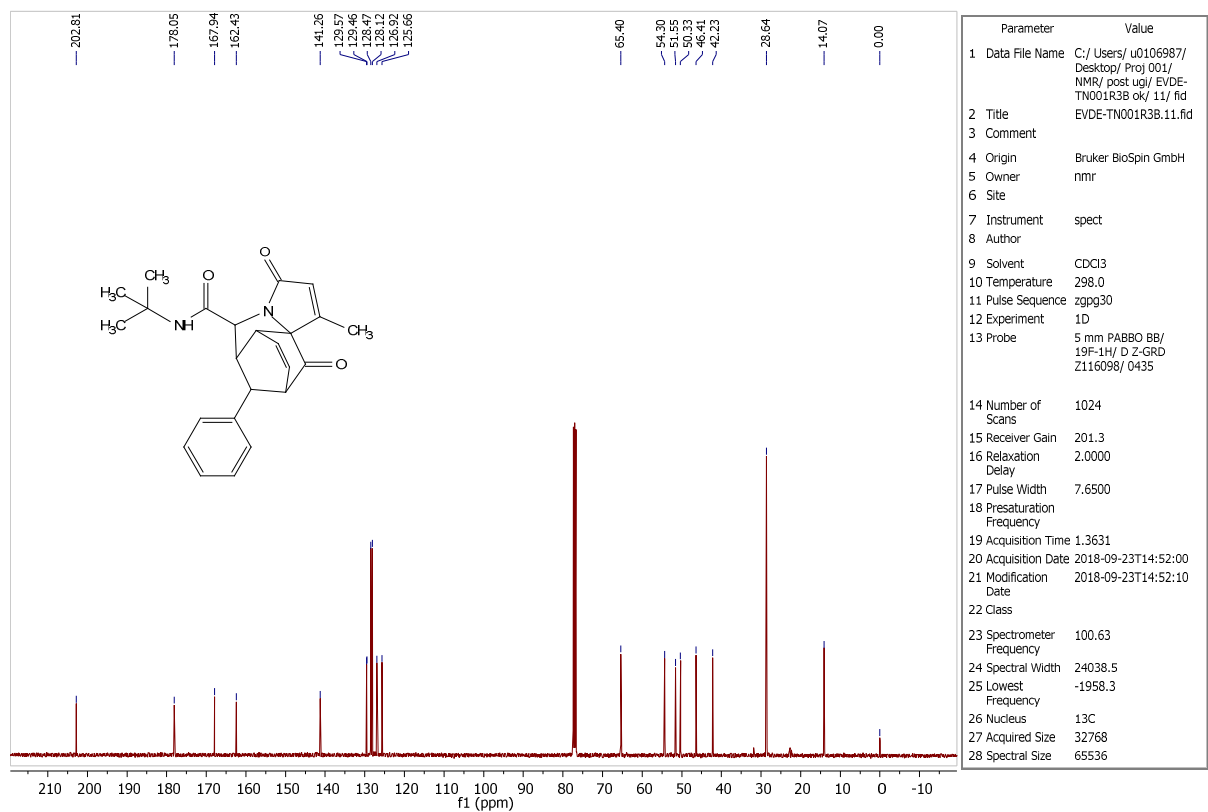
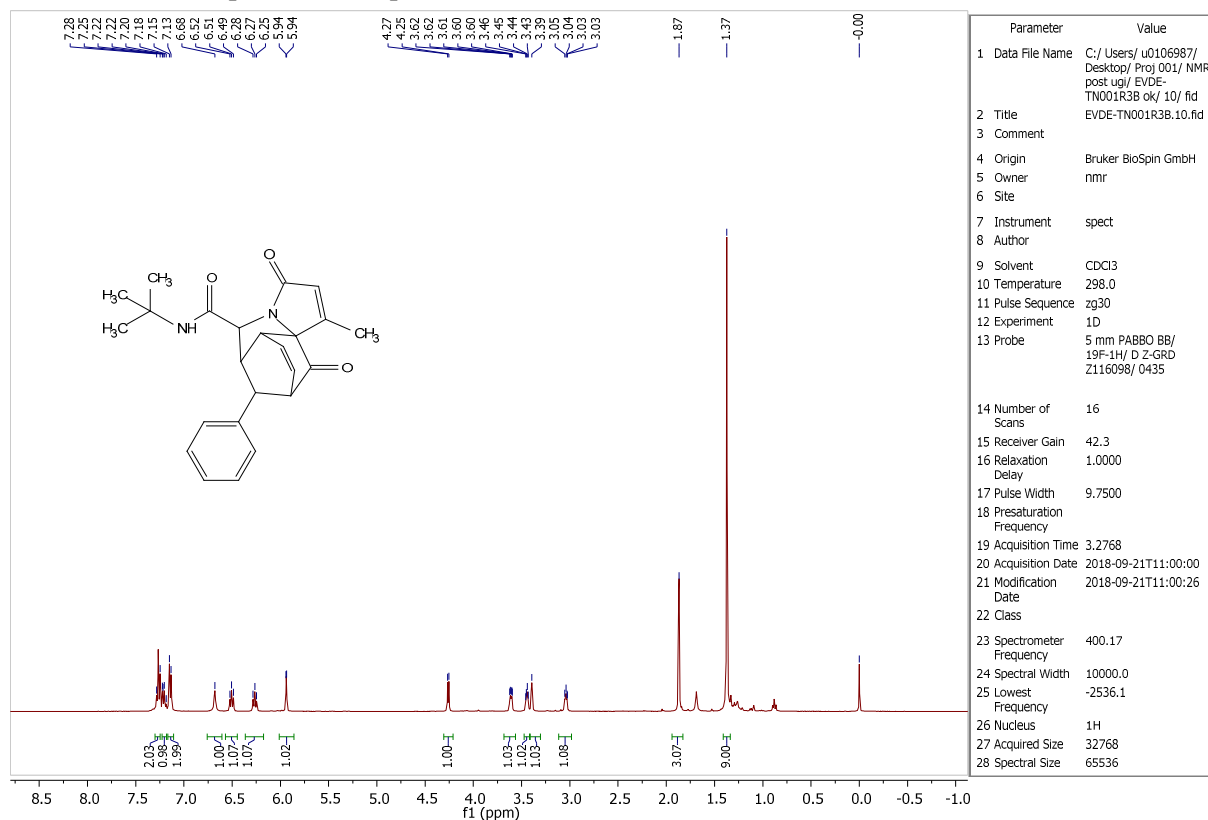
Figure S2. Crystal structure of compound **2k**. Thermal ellipsoids are drawn at the 50% probability level.

References

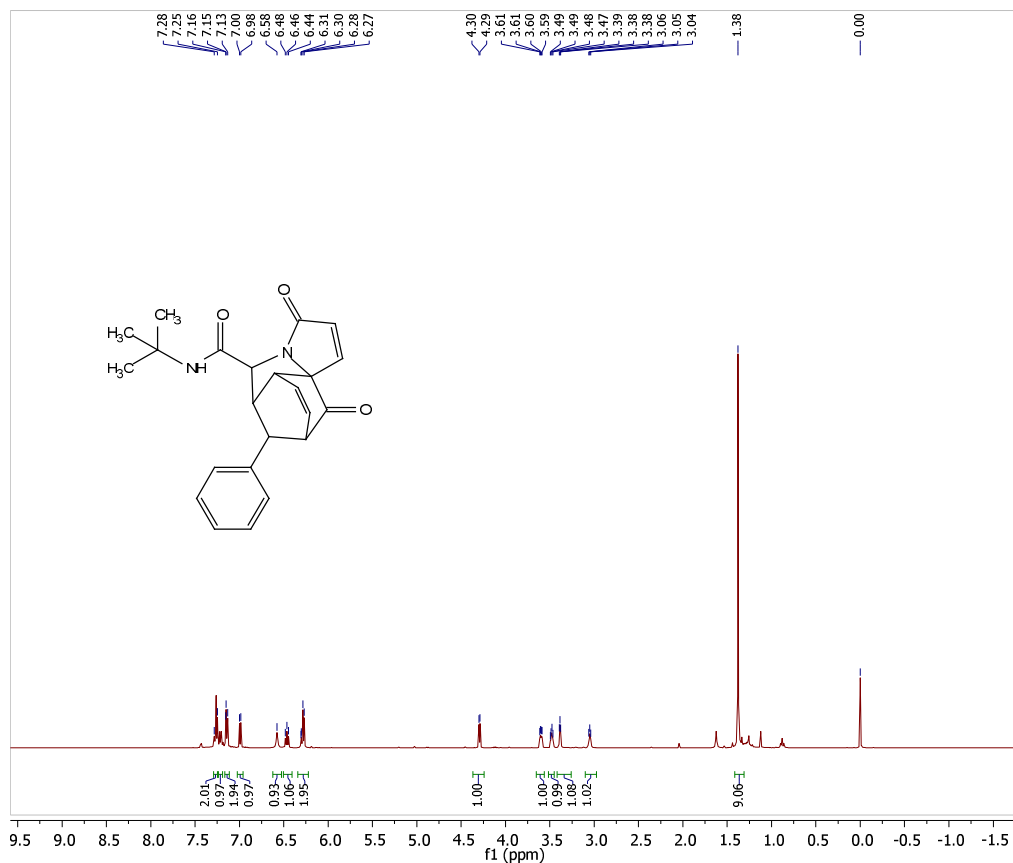
- [1] Ponder, J. W.; Richards, F. M., An efficient newton-like method for molecular mechanics energy minimization of large molecules. *J. Comput. Chem.* **1987**, *8* (7), 1016-1024.
- [2] Gaussian 09, Revision E.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, **2009**.
- [3] Riplinger, C.; Neese, F., An efficient and near linear scaling pair natural orbital based local coupled cluster method. *J. Chem. Phys.* **2013**, *138* (3), 034106/1-034106/18.
- [4] Riplinger, C.; Sandhoefer, B.; Hansen, A.; Neese, F., Natural triple excitations in local coupled cluster calculations with pair natural orbitals. *J. Chem. Phys.* **2013**, *139* (13), 134101.
- [5] Pinski, P.; Riplinger, C.; Valeev, E. F.; Neese, F., Sparse maps-A systematic infrastructure for reduced-scaling electronic structure methods. I. An efficient and simple linear scaling local MP2 method that uses an intermediate basis of pair natural orbitals. *J. Chem. Phys.* **2015**, *143* (3), 034108.
- [6] Riplinger, C.; Pinski, P.; Becker, U.; Valeev, E. F.; Neese, F., Sparse maps--A systematic infrastructure for reduced-scaling electronic structure methods. II. Linear scaling domain based pair natural orbital coupled cluster theory. *J. Chem. Phys.* **2016**, *144* (2), 024109.
- [7] Neese, F., The ORCA program system. *WIREs Comput. Mol. Sci.* **2012**, *2* (1), 73-78.
- [8] Truhlar, D. G., Basis-set extrapolation. *Chem. Phys. Lett.* **1998**, *294* (1-3), 45-48.
- [9] CrysAlis PRO. Agilent Technologies UK Ltd, Yarnton, Oxfordshire, England, **2012**.
- [10] Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339-341.
- [11] Sheldrick, G. M. *Acta Cryst.* **2015**, *A71*, 3-8.
- [12] Sheldrick, G. M. *Acta Cryst.* **2015**, *C71*, 3-8.

Copies of NMR spectra (Post-Ugi products)

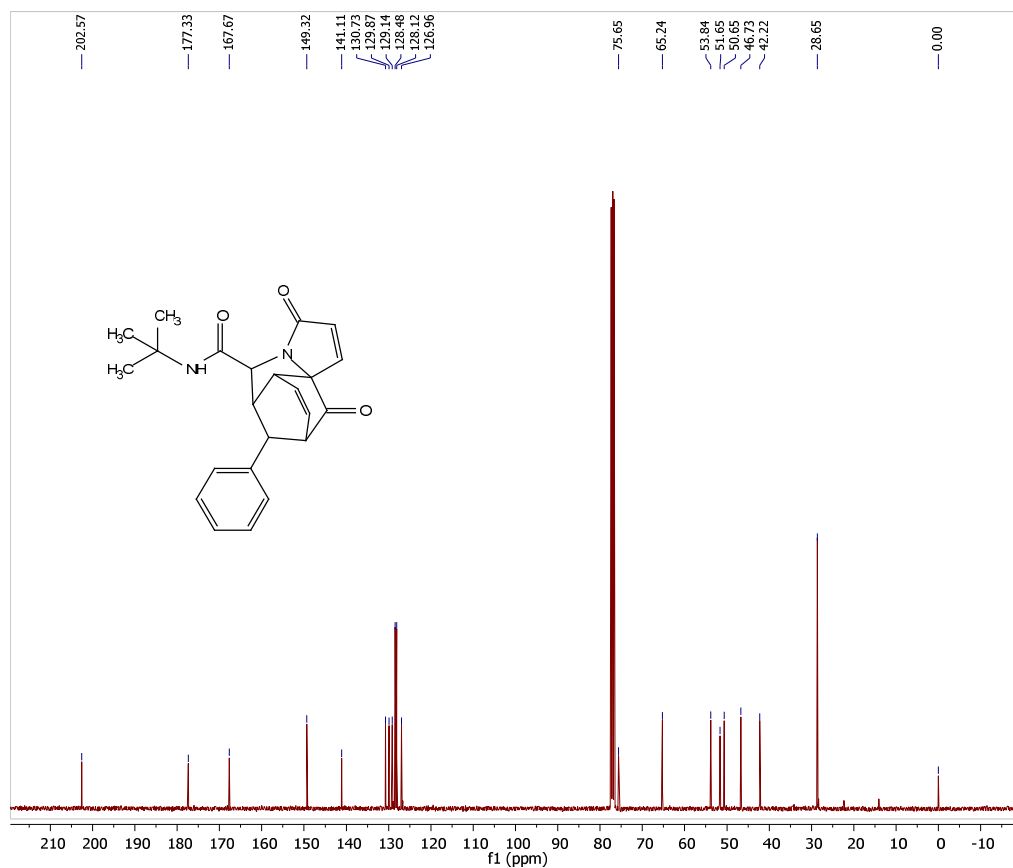
¹H and ¹³C NMR spectra of compound 2a



¹H and ¹³C NMR spectra of compound 2b

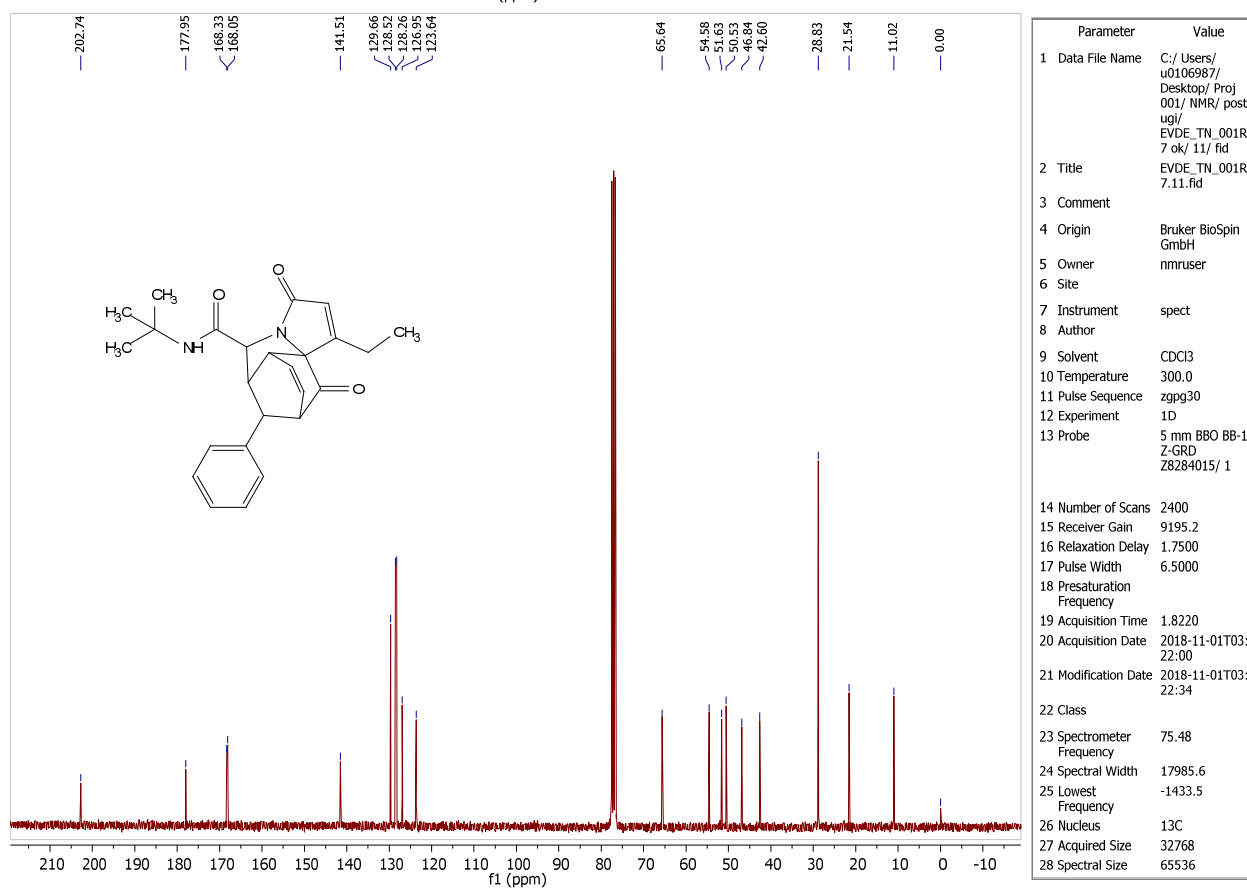
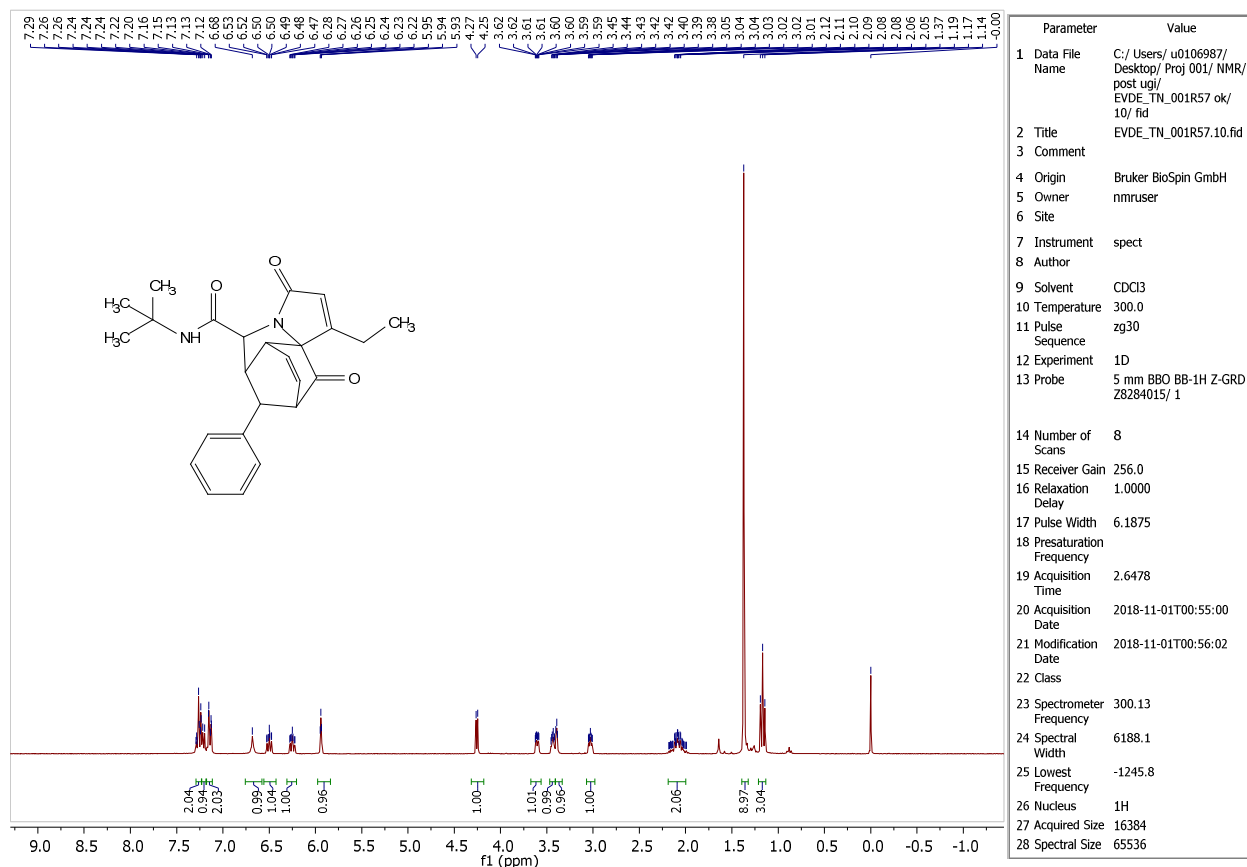


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/ EVDE-TN-001R78 ok/ 10/ fid
2 Title	EVDE-TN-001R78.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/ 19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	16
15 Receiver Gain	54.5
16 Relaxation Delay	1.0000
17 Pulse Width	9.7500
18 Presaturation Frequency	
19 Acquisition Time	3.2768
20 Acquisition Date	2018-11-27T13:30:00
21 Modification Date	2018-11-27T13:30:16
22 Class	
23 Spectrometer Frequency	400.17
24 Spectral Width	10000.0
25 Lowest Frequency	-2537.5
26 Nucleus	1H
27 Acquired Size	32768
28 Spectral Size	65536

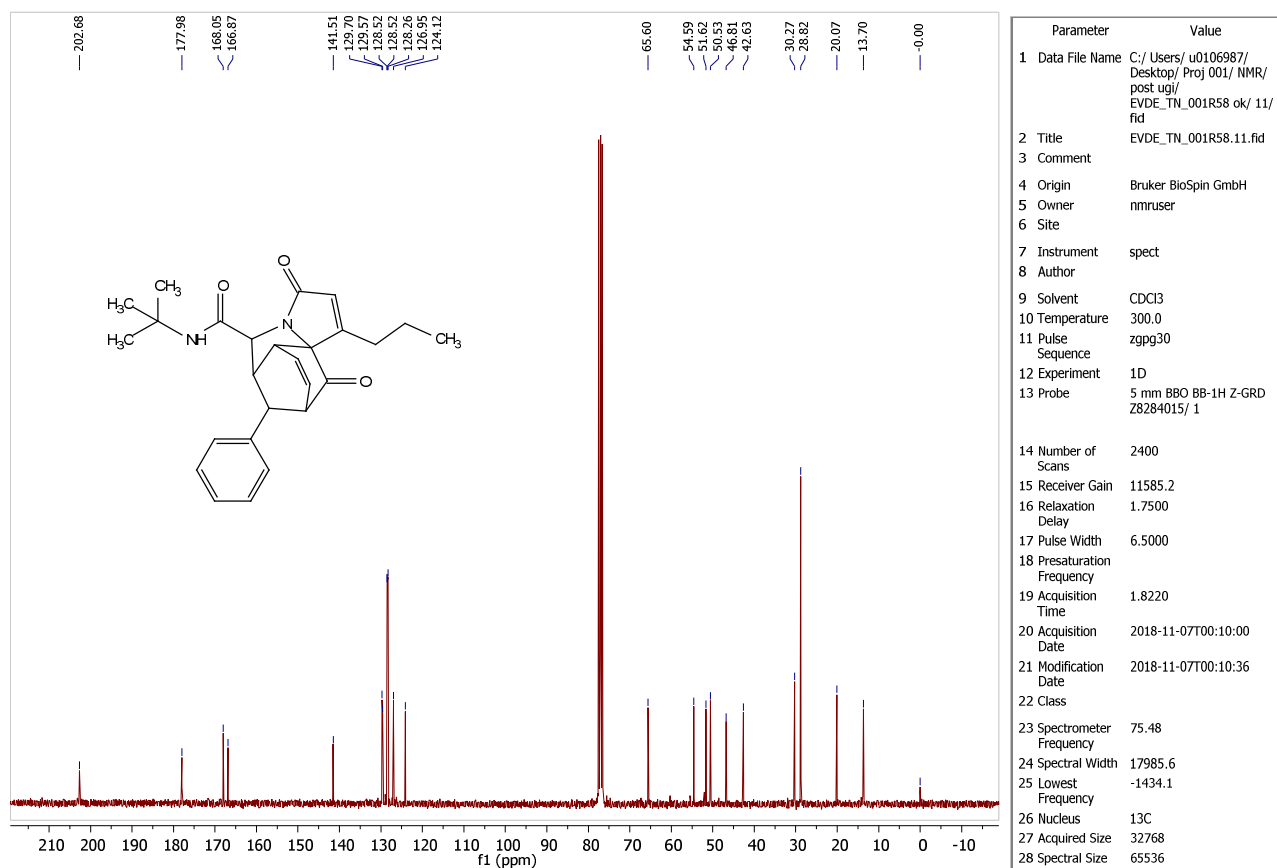
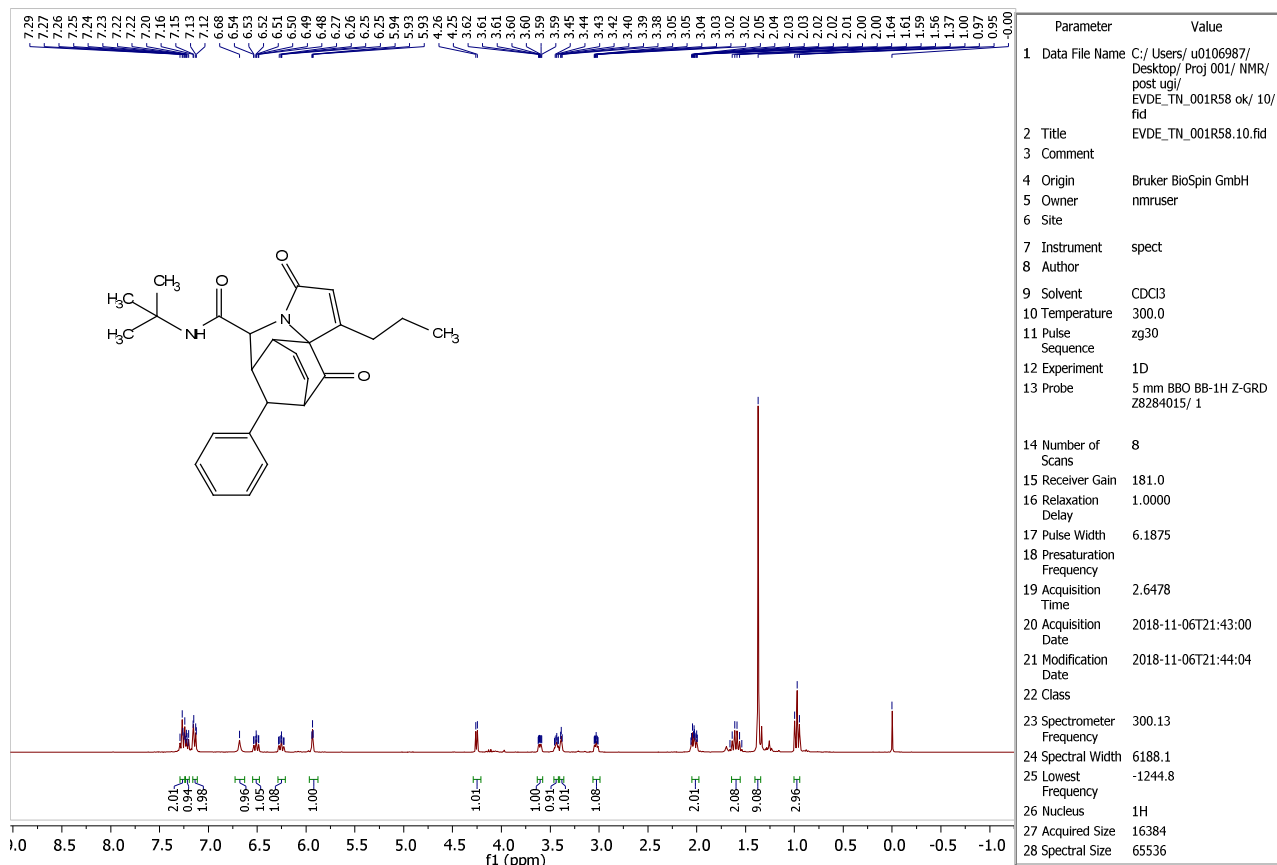


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/ EVDE-TN-001R78 ok/ 11/ fid
2 Title	EVDE-TN-001R78.11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zpg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/ 19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	2048
15 Receiver Gain	201.3
16 Relaxation Delay	2.0000
17 Pulse Width	7.6500
18 Presaturation Frequency	
19 Acquisition Time	1.3631
20 Acquisition Date	2018-11-27T20:00:00
21 Modification Date	2018-11-27T20:00:14
22 Class	
23 Spectrometer Frequency	100.63
24 Spectral Width	24038.5
25 Lowest Frequency	-1958.3
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

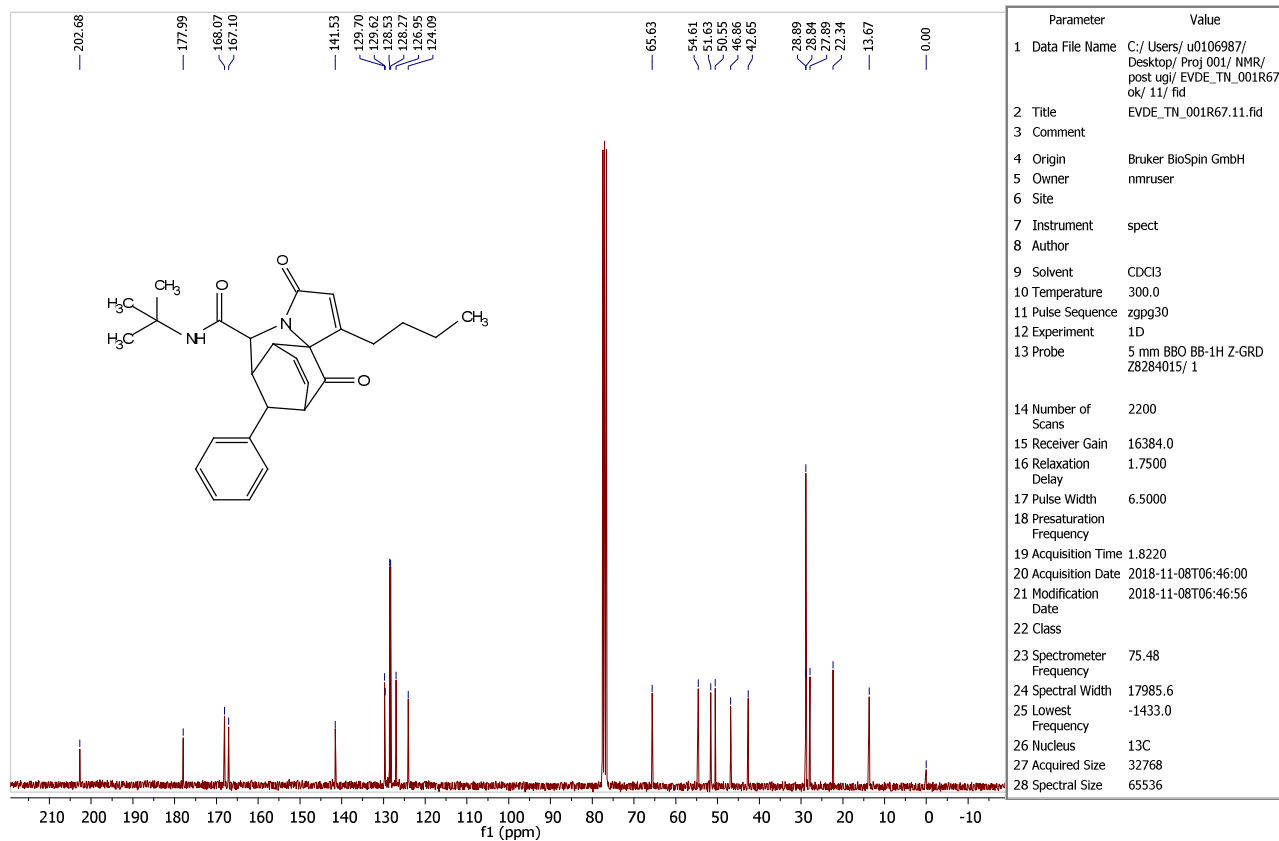
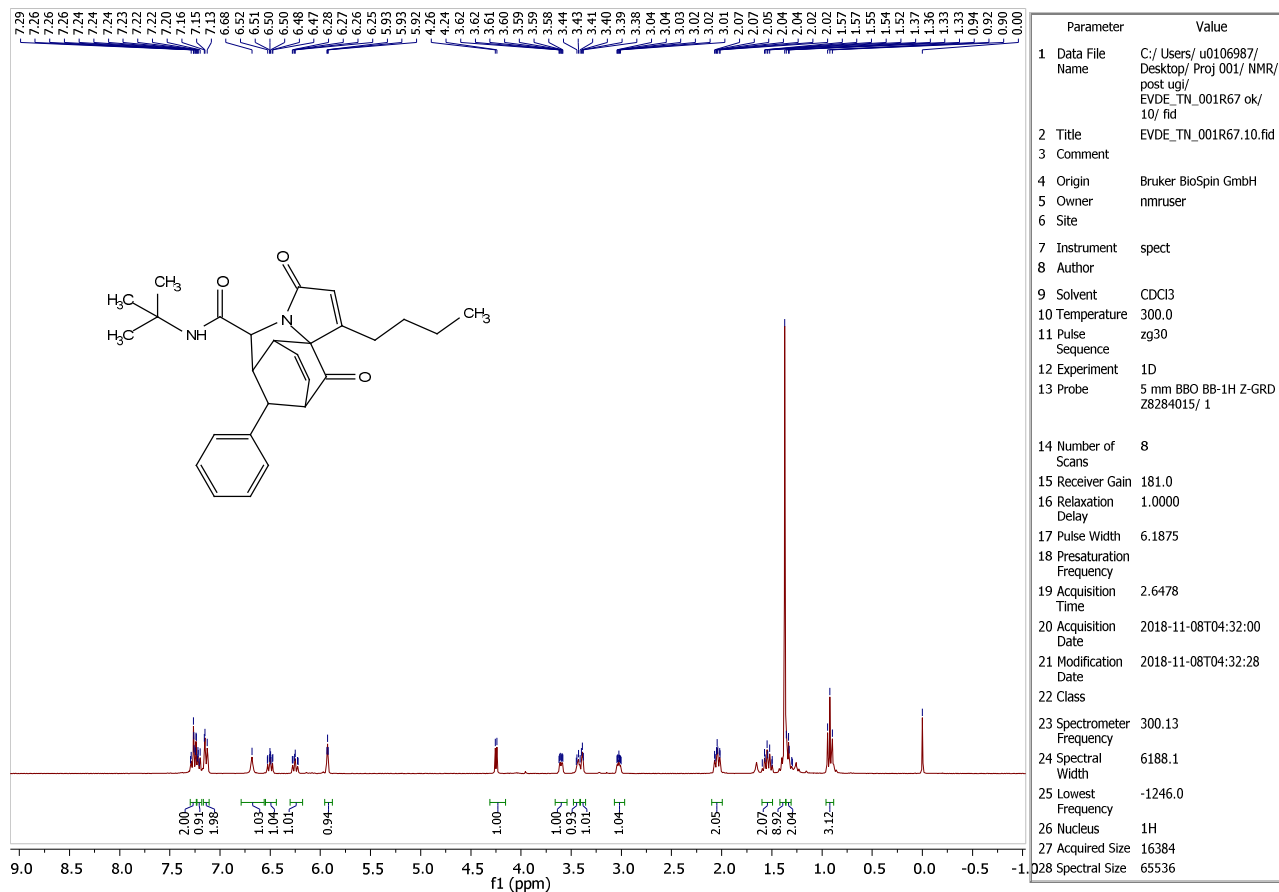
¹H and ¹³C NMR spectra of compound 2c



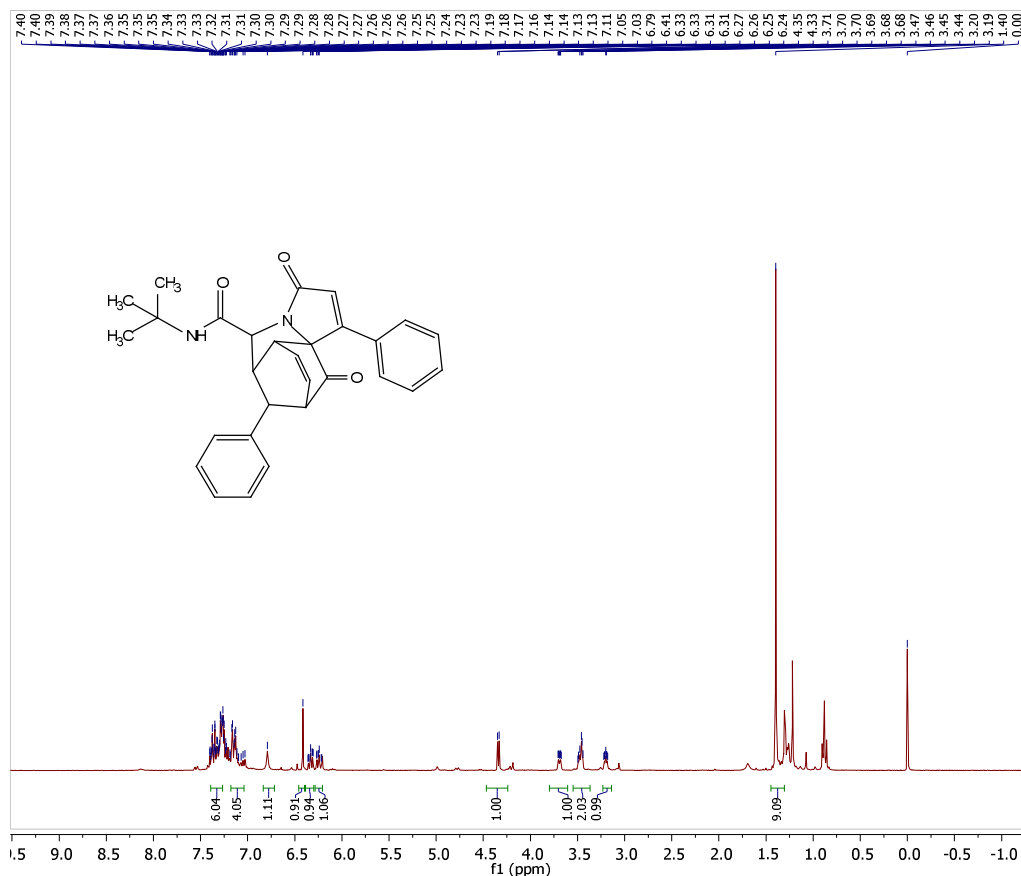
¹H and ¹³C NMR spectra of compound 2d



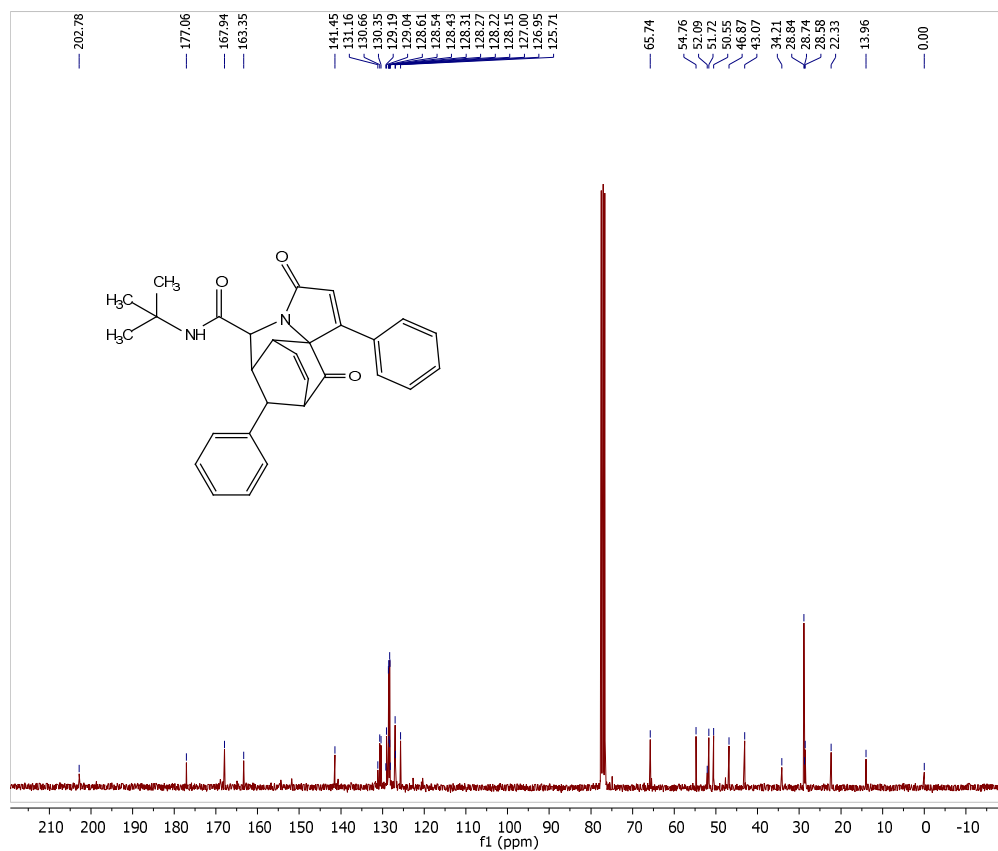
¹H and ¹³C NMR spectra of compound 2e



¹H and ¹³C NMR spectra of compound 2f

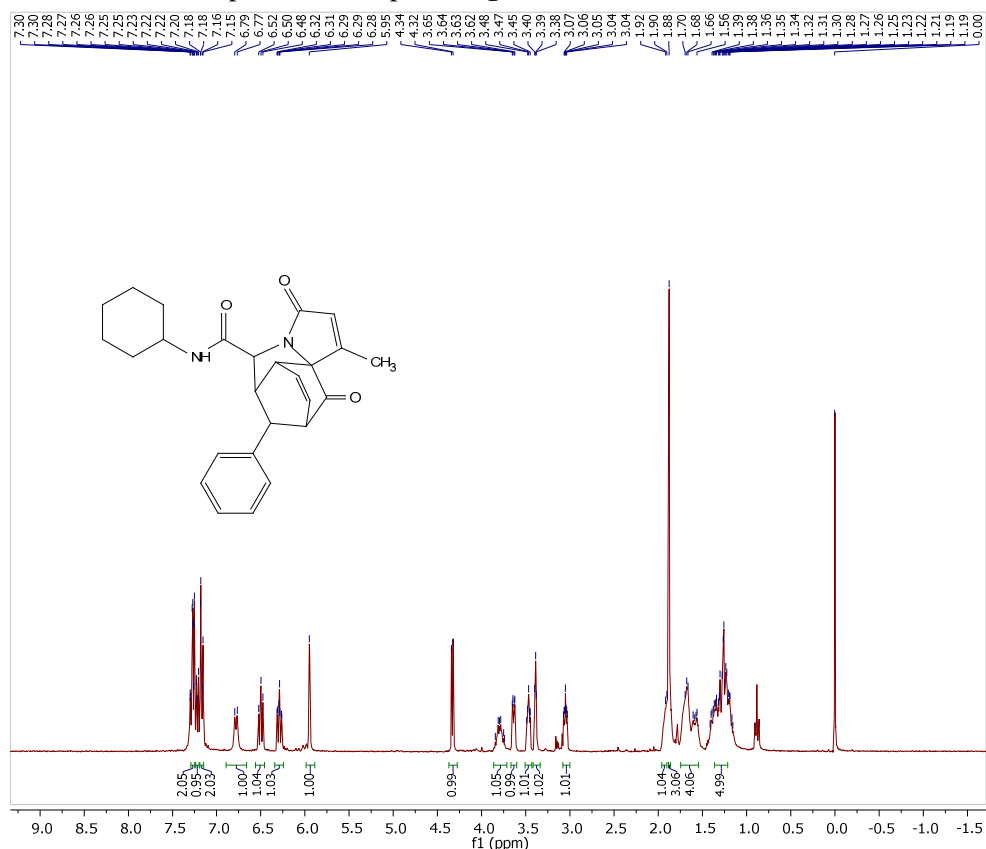


Parameter	Value
1 Data File Name	C:/ Users/ u0106987/ Desktop/ Proj 001/ NMR/ post ugi/ EVDE_TN001_R59B ok/ 10/ fid
2 Title	EVDE_TN001_R59B. 10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD Z8284015/ 1
14 Number of Scans	8
15 Receiver Gain	256.0
16 Relaxation Delay	1.0000
17 Pulse Width	6.1875
18 Presaturation Frequency	
19 Acquisition Time	2.6478
20 Acquisition Date	2018-11-08T12:42:00
21 Modification Date	2018-11-08T12:42:56
22 Class	
23 Spectrometer Frequency	300.13
24 Spectral Width	6188.1
25 Lowest Frequency	-1246.8
26 Nucleus	1H
27 Acquired Size	16384
28 Spectral Size	65536

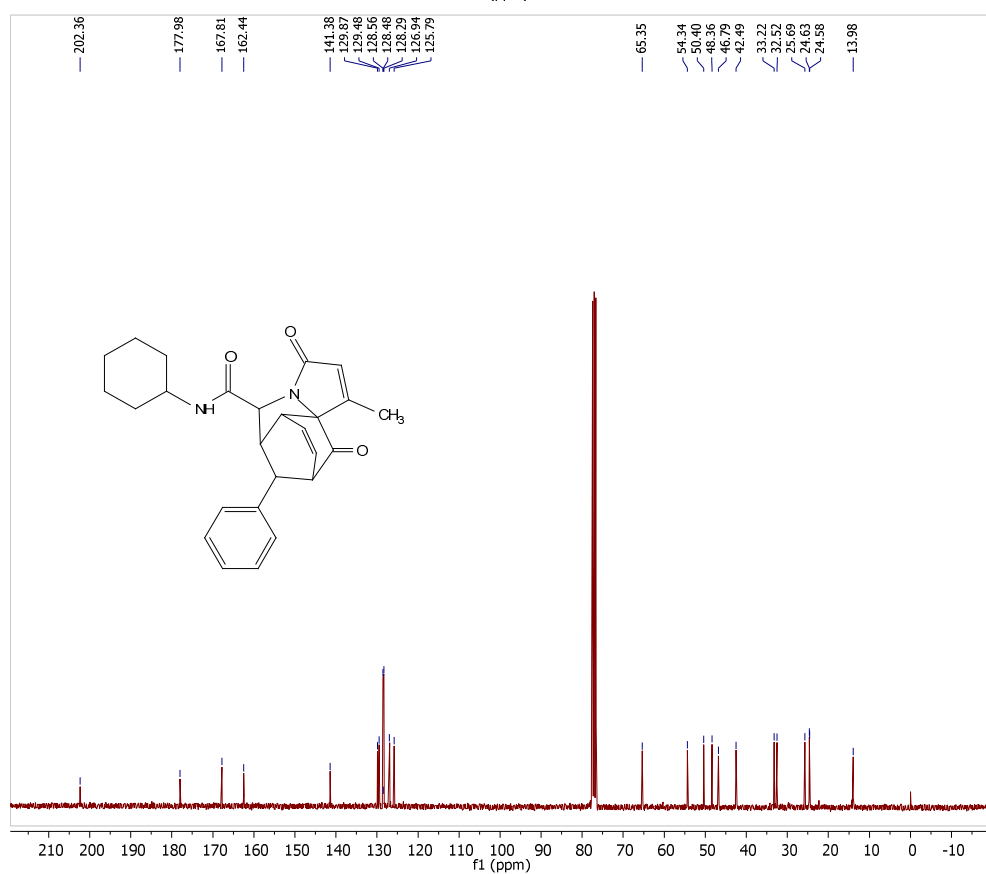


Parameter	Value
1 Data File Name	C:/ Users/ u0106987/ Desktop/ Proj 001/ NMR/ post ugi/ EVDE_TN001_R59B ok/ 11/ fid
2 Title	EVDE_TN001_R59B. 11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zgpg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD Z8284015/ 1
14 Number of Scans	2200
15 Receiver Gain	16384.0
16 Relaxation Delay	1.7500
17 Pulse Width	6.5000
18 Presaturation Frequency	
19 Acquisition Time	1.8220
20 Acquisition Date	2018-11-09T21:29:00
21 Modification Date	2018-11-09T21:29:22
22 Class	
23 Spectrometer Frequency	75.48
24 Spectral Width	17985.6
25 Lowest Frequency	-1433.9
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

¹H and ¹³C NMR spectra of compound 2g

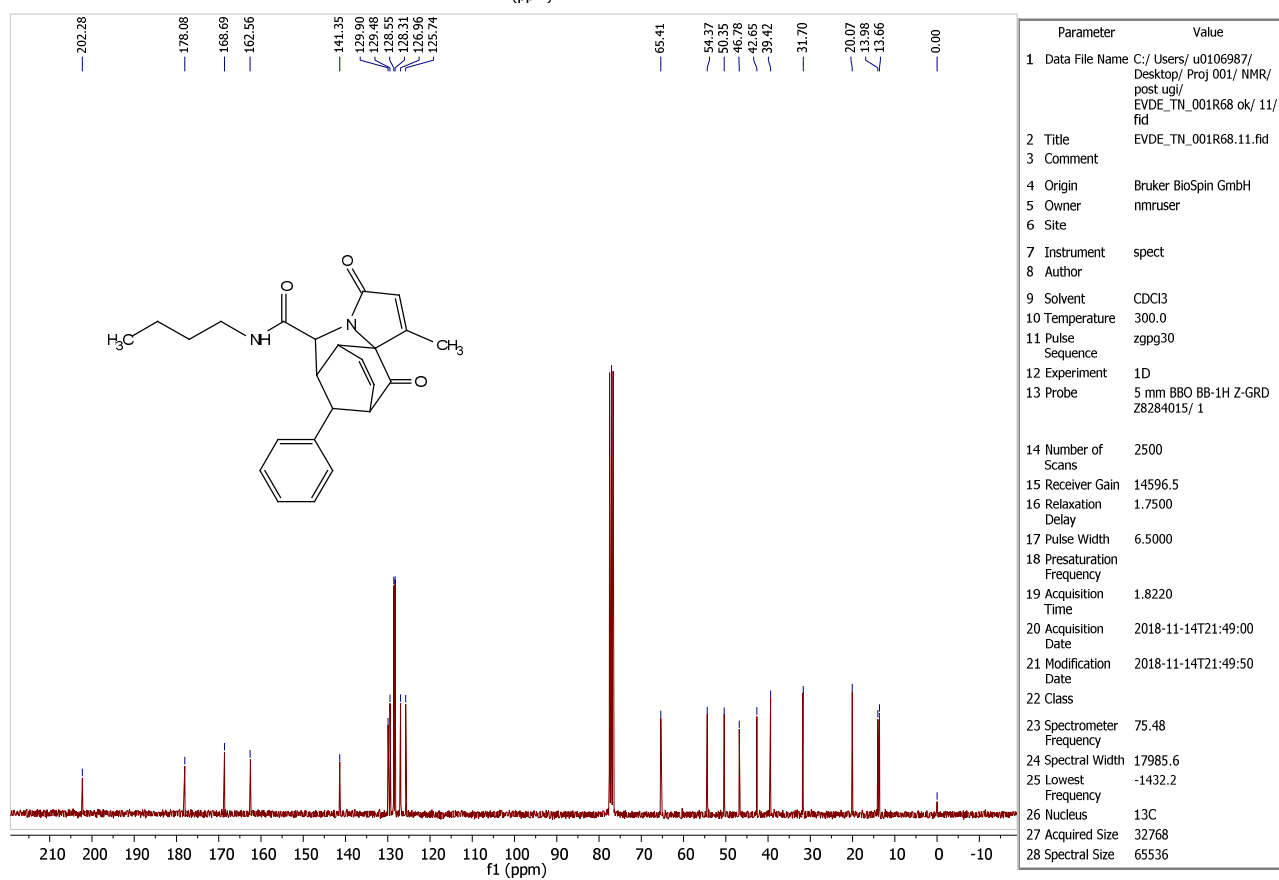
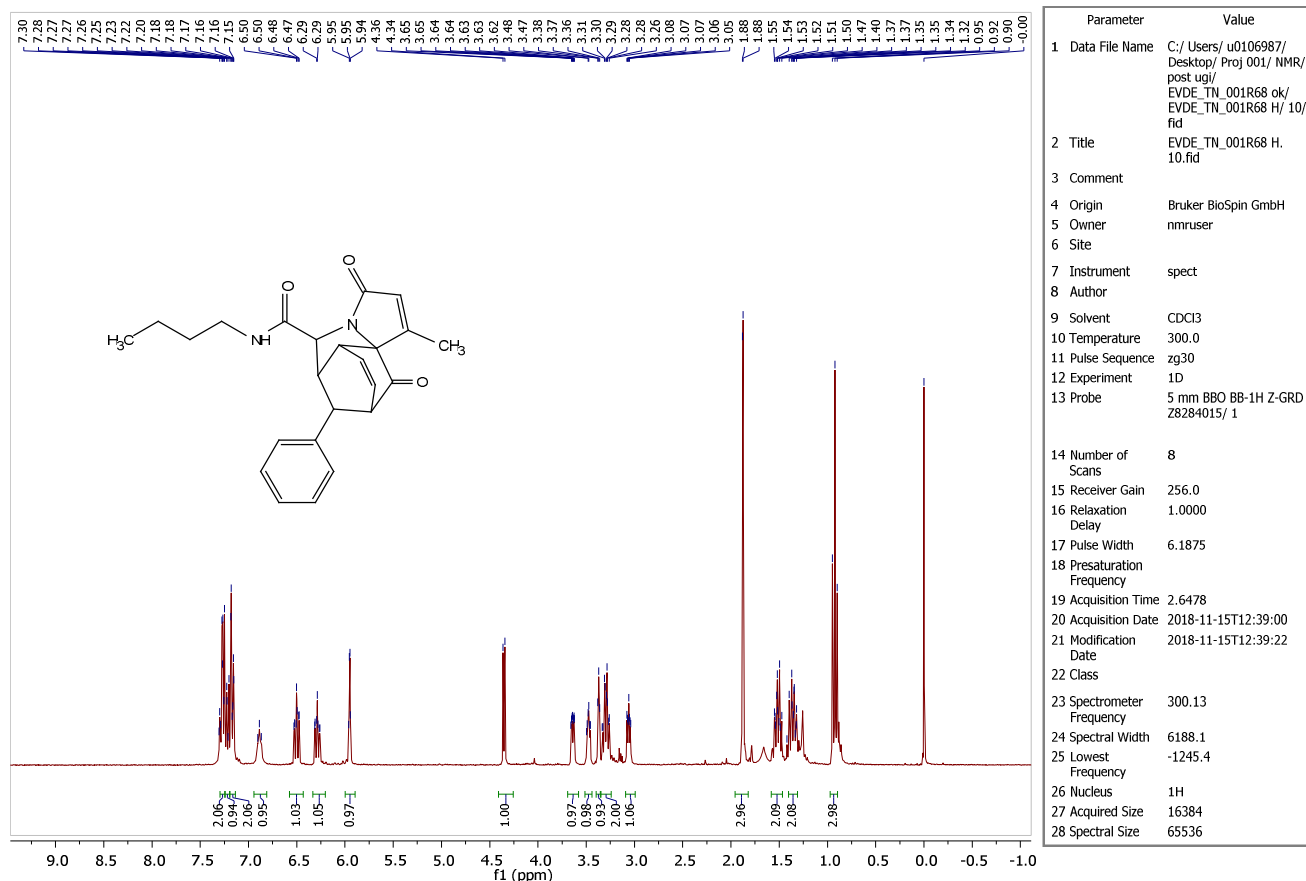


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/EVDE_TN_001R69 ok/EVDE_TN_001R69 H/10/fid
2 Title	EVDE_TN_001R69 H.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCI3
10 Temperature	300.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD 28284015/ 1
14 Number of Scans	8
15 Receiver Gain	256.0
16 Relaxation Delay	1.0000
17 Pulse Width	6.1875
18 Presaturation Frequency	
19 Acquisition Time	2.6478
20 Acquisition Date	2018-11-15T12:45:00
21 Modification Date	2018-11-15T12:45:32
22 Class	
23 Spectrometer Frequency	300.13
24 Spectral Width	6188.1
25 Lowest Frequency	-1245.1
26 Nucleus	1H
27 Acquired Size	16384
28 Spectral Size	65536

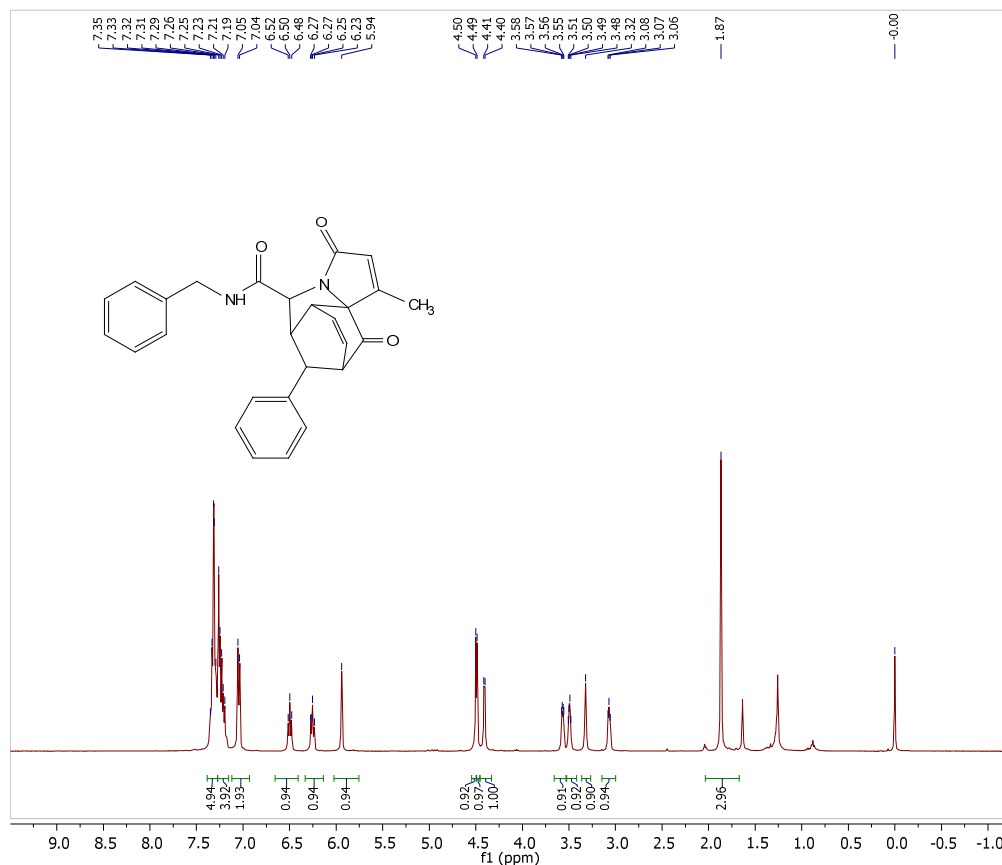


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/EVDE_TN_001R69 ok/11/fid
2 Title	EVDE_TN_001R69.11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCI3
10 Temperature	300.0
11 Pulse Sequence	zgpg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD 28284015/ 1
14 Number of Scans	2500
15 Receiver Gain	13004.0
16 Relaxation Delay	1.7500
17 Pulse Width	6.5000
18 Presaturation Frequency	
19 Acquisition Time	1.8220
20 Acquisition Date	2018-11-15T00:27:00
21 Modification Date	2018-11-15T00:27:36
22 Class	
23 Spectrometer Frequency	75.48
24 Spectral Width	17985.6
25 Lowest Frequency	-1433.2
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

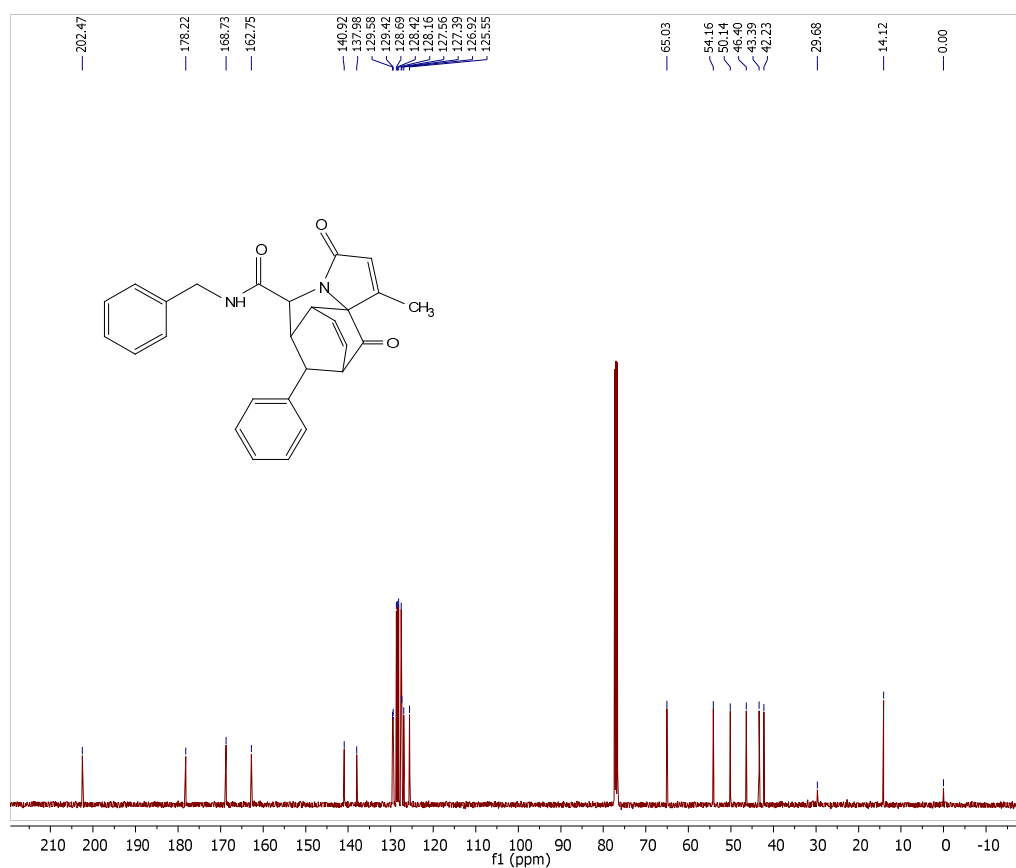
¹H and ¹³C NMR spectra of compound 2h



¹H and ¹³C NMR spectra of compound 2i

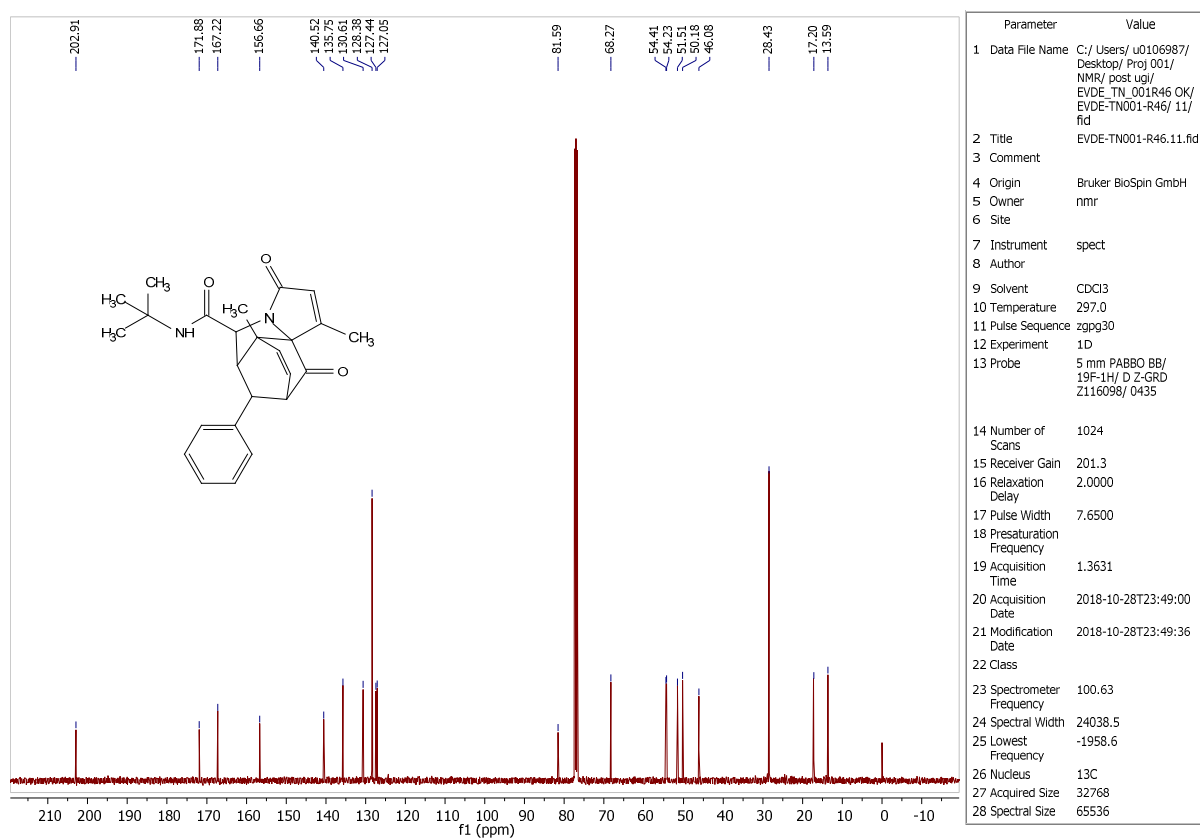
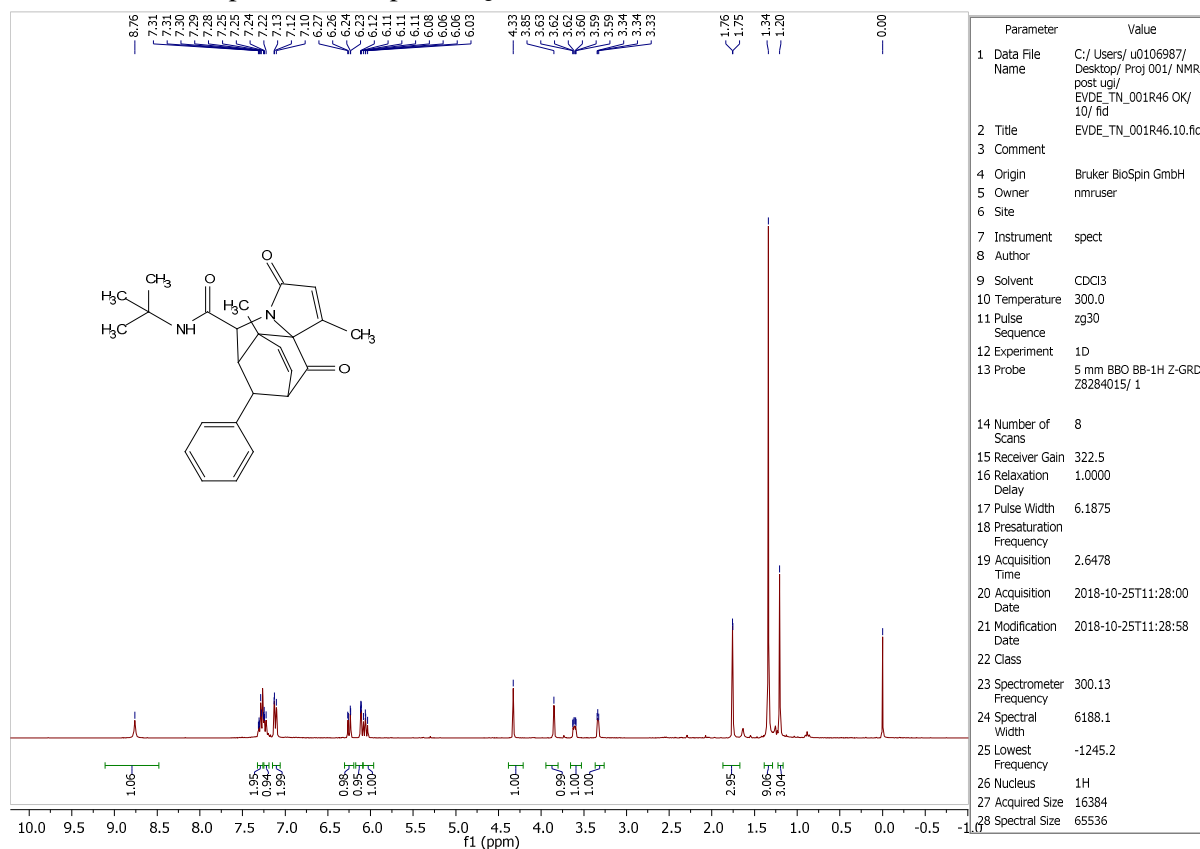


Parameter	Value
1 Data File Name	C:/ Users/ u0106987/ Desktop/ Proj 001/ NMR/ post ug/ EVDE- TN-001R84/ 10/ fid
2 Title	EVDE- TN-001R84.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/ 19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	16
15 Receiver Gain	48.4
16 Relaxation Delay	1.0000
17 Pulse Width	9.7500
18 Presaturation Frequency	
19 Acquisition Time	3.2768
20 Acquisition Date	2019-01-09T13:06:00
21 Modification Date	2019-01-09T13:06:23
22 Class	
23 Spectrometer Frequency	400.17
24 Spectral Width	10000.0
25 Lowest Frequency	-2538.9
26 Nucleus	1H
27 Acquired Size	32768
28 Spectral Size	65536

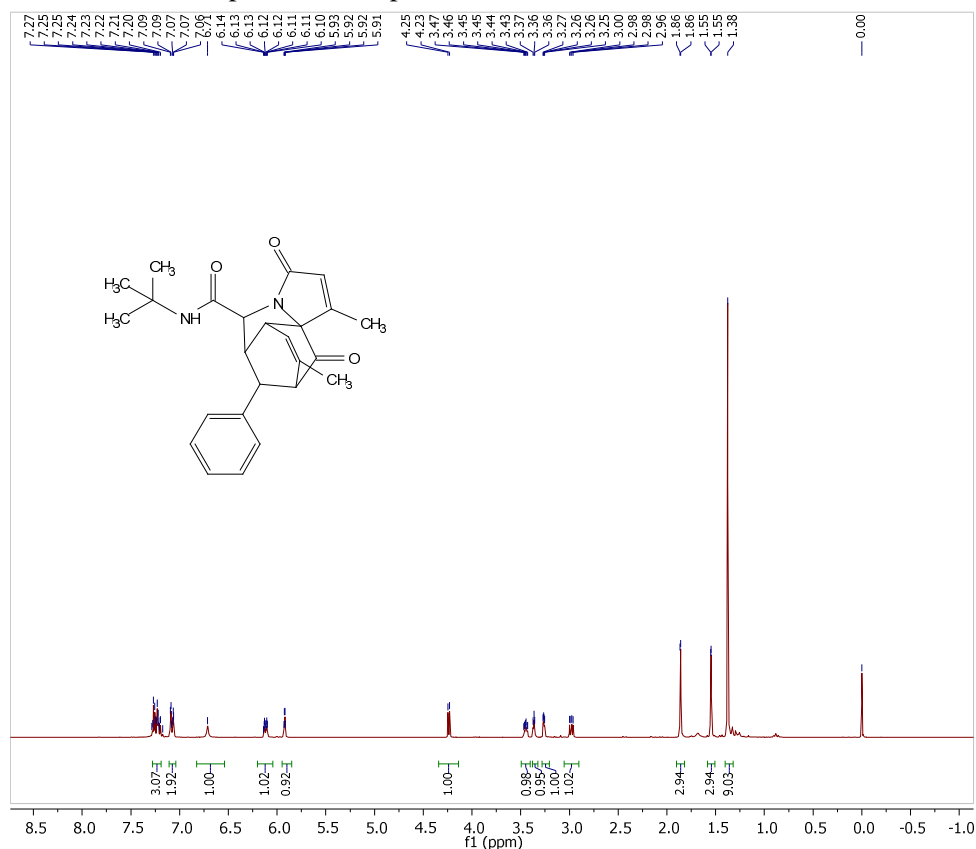


Parameter	Value
1 Data File Name	C:/ Users/ u0106987/ Desktop/ Proj 001/ NMR/ post ug/ EVDE- TN-001R84/ 11/ fid
2 Title	EVDE- TN-001R84.11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zgpg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/ 19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	1024
15 Receiver Gain	201.3
16 Relaxation Delay	2.0000
17 Pulse Width	7.6500
18 Presaturation Frequency	
19 Acquisition Time	1.3631
20 Acquisition Date	2019-01-11T04:55:00
21 Modification Date	2019-01-11T04:55:59
22 Class	
23 Spectrometer Frequency	100.63
24 Spectral Width	24038.5
25 Lowest Frequency	-1959.2
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

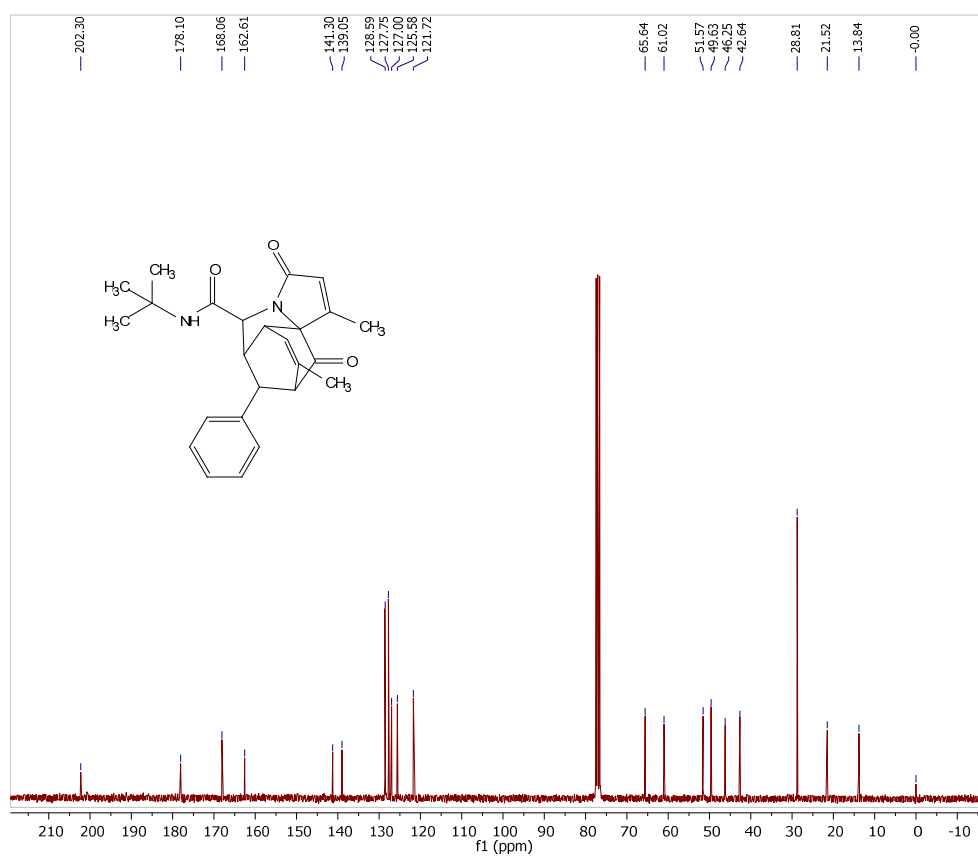
¹H and ¹³C NMR spectra of compound 2j



¹H and ¹³C NMR spectra of compound 2k

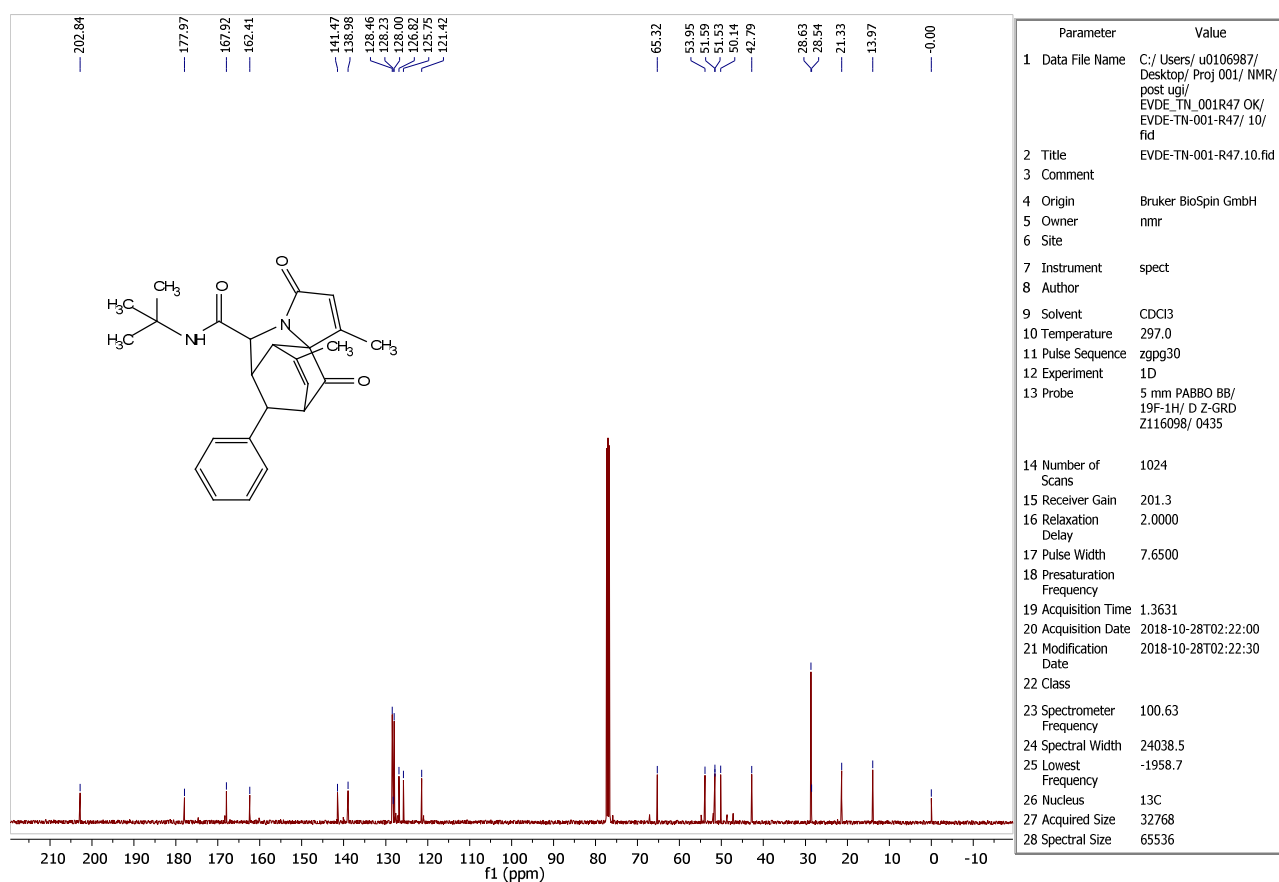
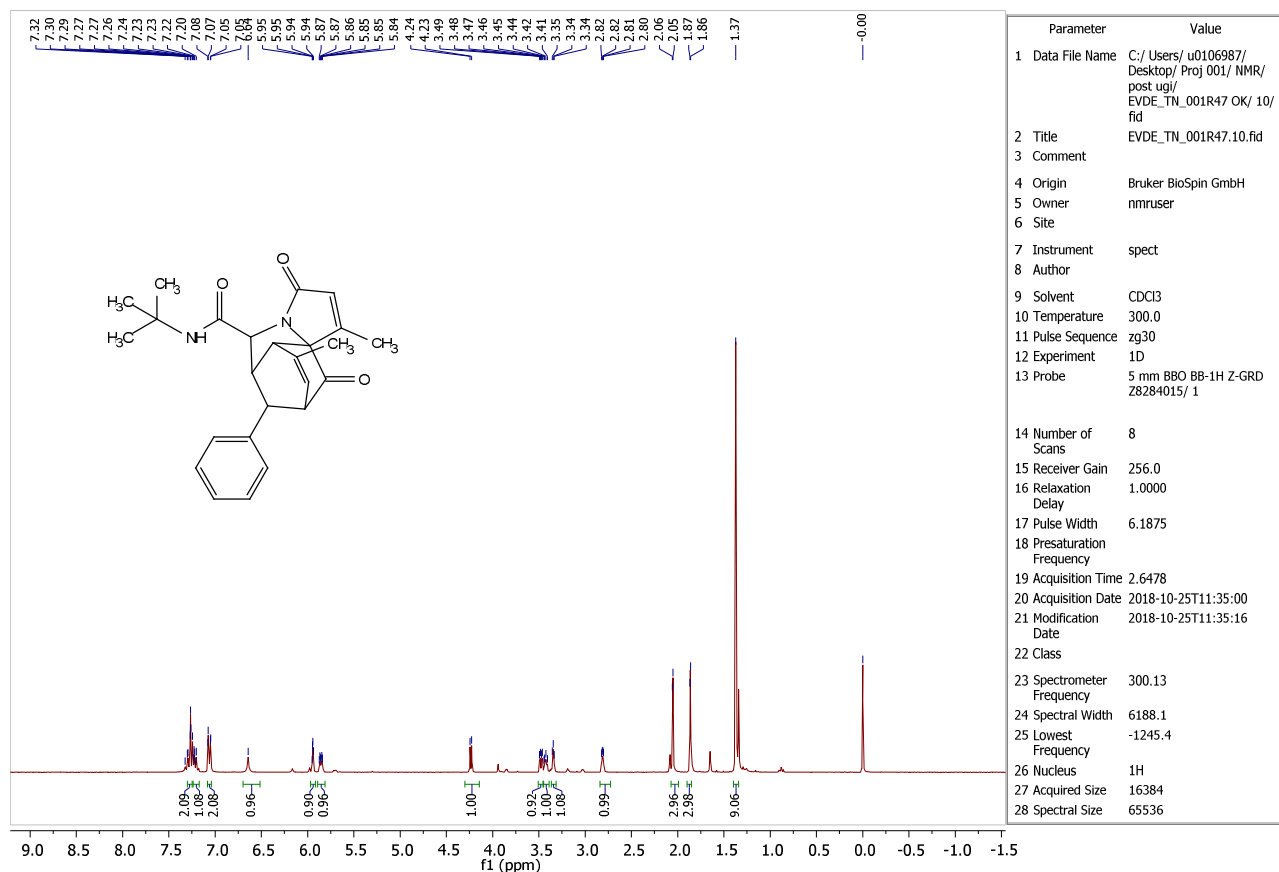


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/EVDE_TN_001R48B OK/10/fid
2 Title	EVDE_TN_001R48B.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD 28284015/ 1
14 Number of Scans	8
15 Receiver Gain	181.0
16 Relaxation Delay	1.0000
17 Pulse Width	6.1875
18 Presaturation Frequency	
19 Acquisition Time	2.6478
20 Acquisition Date	2018-10-28T20:33:00
21 Modification Date	2018-10-28T20:33:24
22 Class	
23 Spectrometer Frequency	300.13
24 Spectral Width	6188.1
25 Lowest Frequency	-1244.7
26 Nucleus	1H
27 Acquired Size	16384
28 Spectral Size	65536

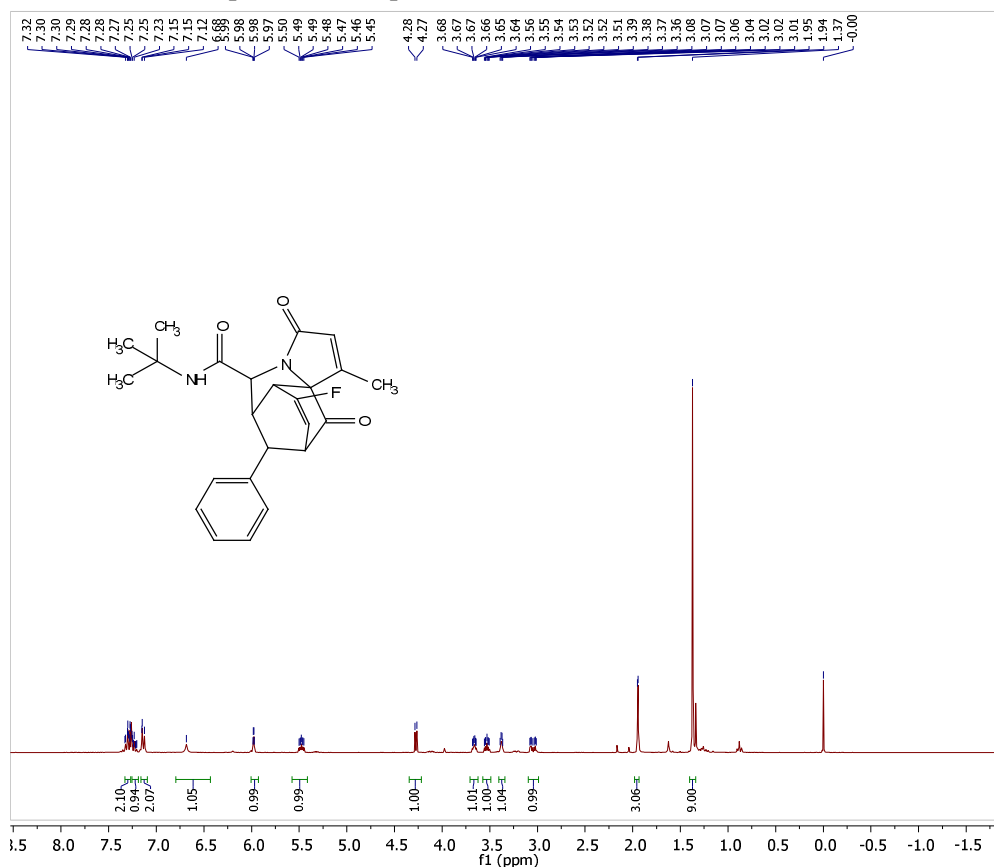


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/EVDE_TN_001R48B OK/11/fid
2 Title	EVDE_TN_001R48B.11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zpgp30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD 28284015/ 1
14 Number of Scans	2000
15 Receiver Gain	11585.2
16 Relaxation Delay	1.7500
17 Pulse Width	6.5000
18 Presaturation Frequency	
19 Acquisition Time	1.8220
20 Acquisition Date	2018-10-28T22:35:00
21 Modification Date	2018-10-28T22:35:52
22 Class	
23 Spectrometer Frequency	75.48
24 Spectral Width	17985.6
25 Lowest Frequency	-1434.0
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

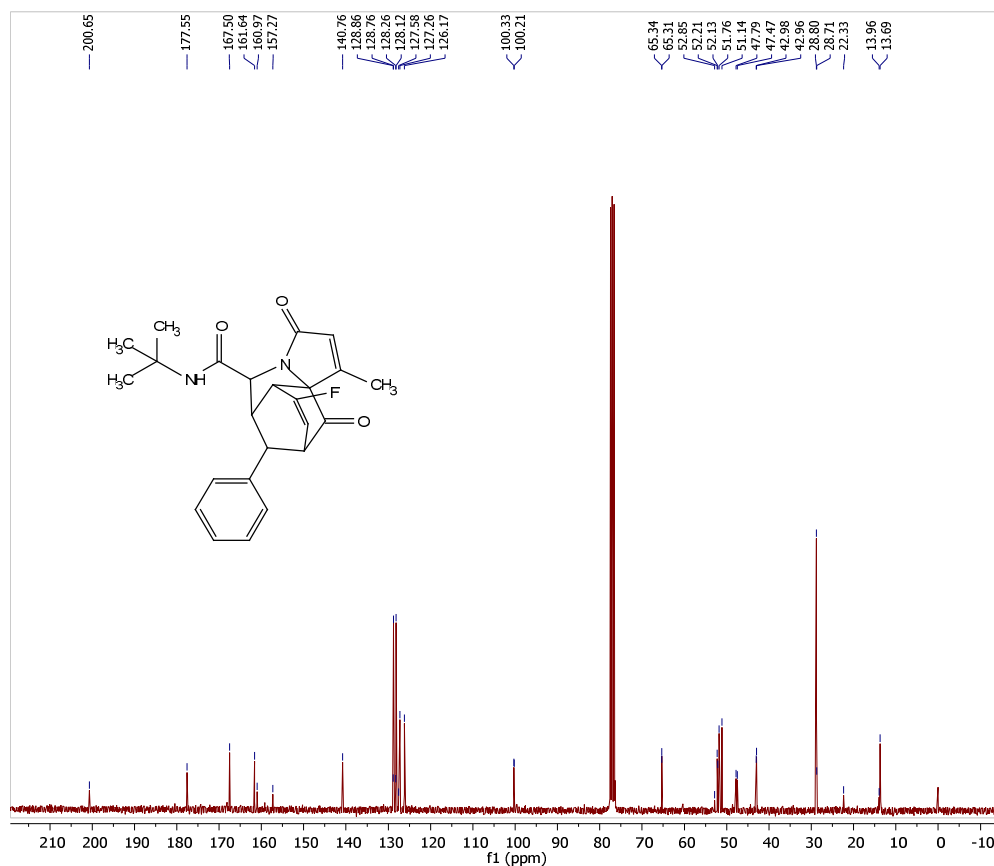
¹H and ¹³C NMR spectra of compound 21



¹H and ¹³C NMR spectra of compound 2m

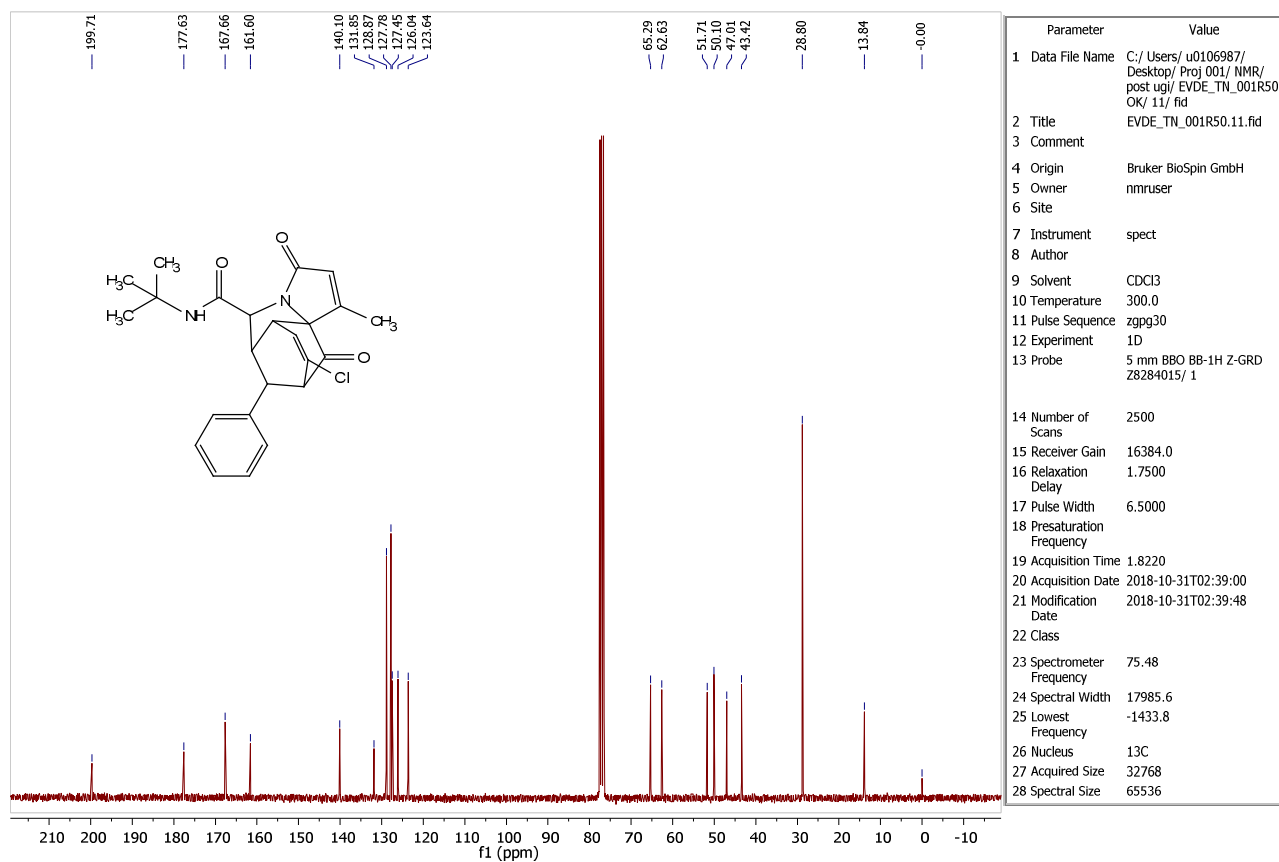
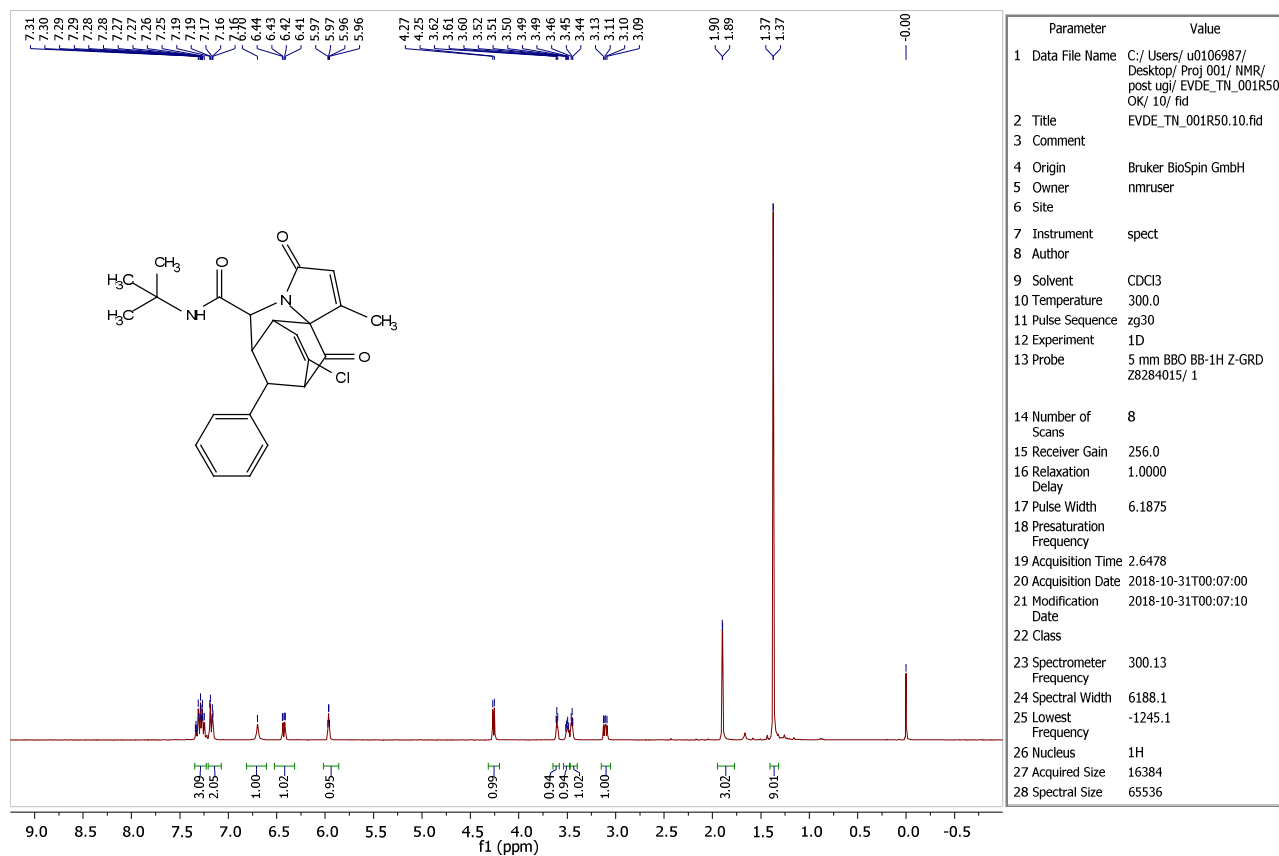


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/EVDE_TN_001R51 OK/ 10/ fid
2 Title	EVDE_TN_001R51.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD Z8284015/ 1
14 Number of Scans	8
15 Receiver Gain	322.5
16 Relaxation Delay	1.0000
17 Pulse Width	6.1875
18 Presaturation Frequency	
19 Acquisition Time	2.6478
20 Acquisition Date	2018-10-31T02:45:00
21 Modification Date	2018-10-31T02:46:04
22 Class	
23 Spectrometer Frequency	300.13
24 Spectral Width	6188.1
25 Lowest Frequency	-1246.3
26 Nucleus	1H
27 Acquired Size	16384
28 Spectral Size	65536

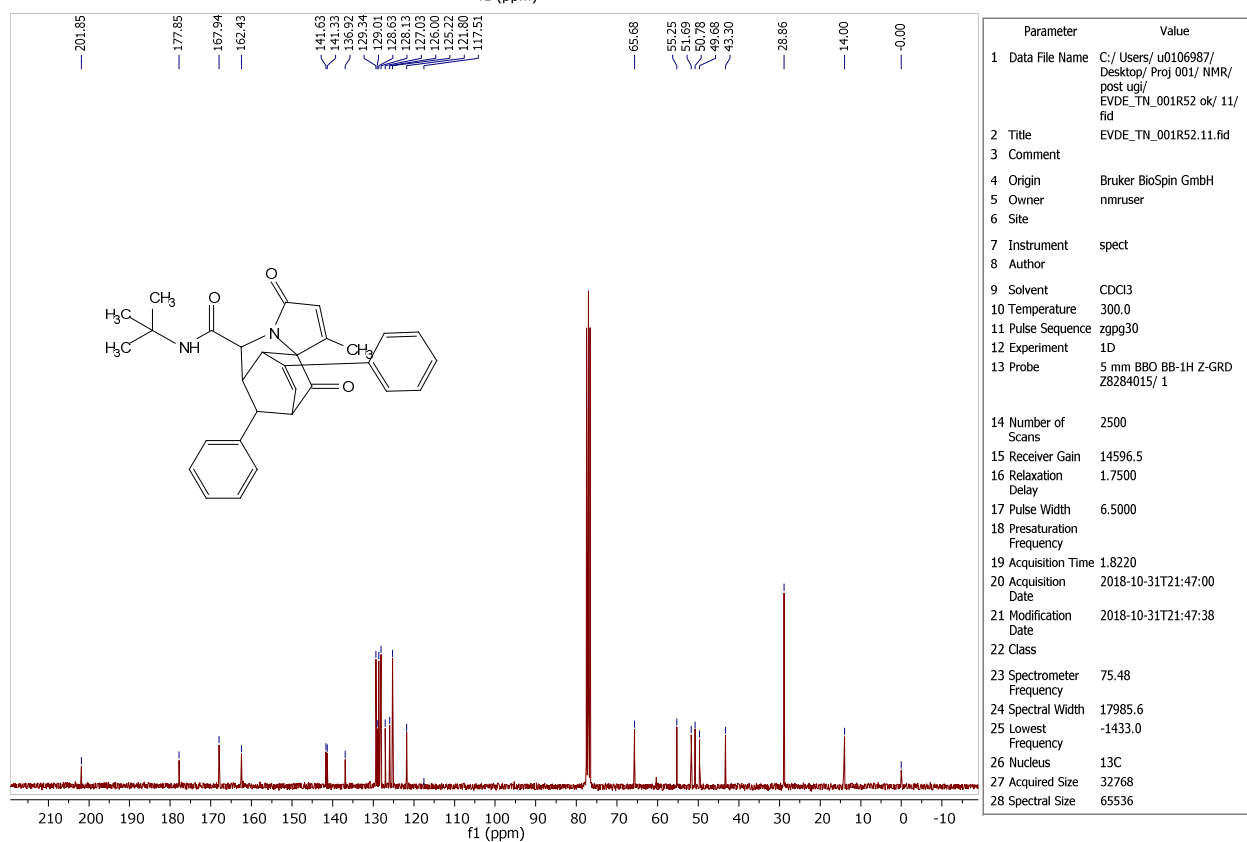
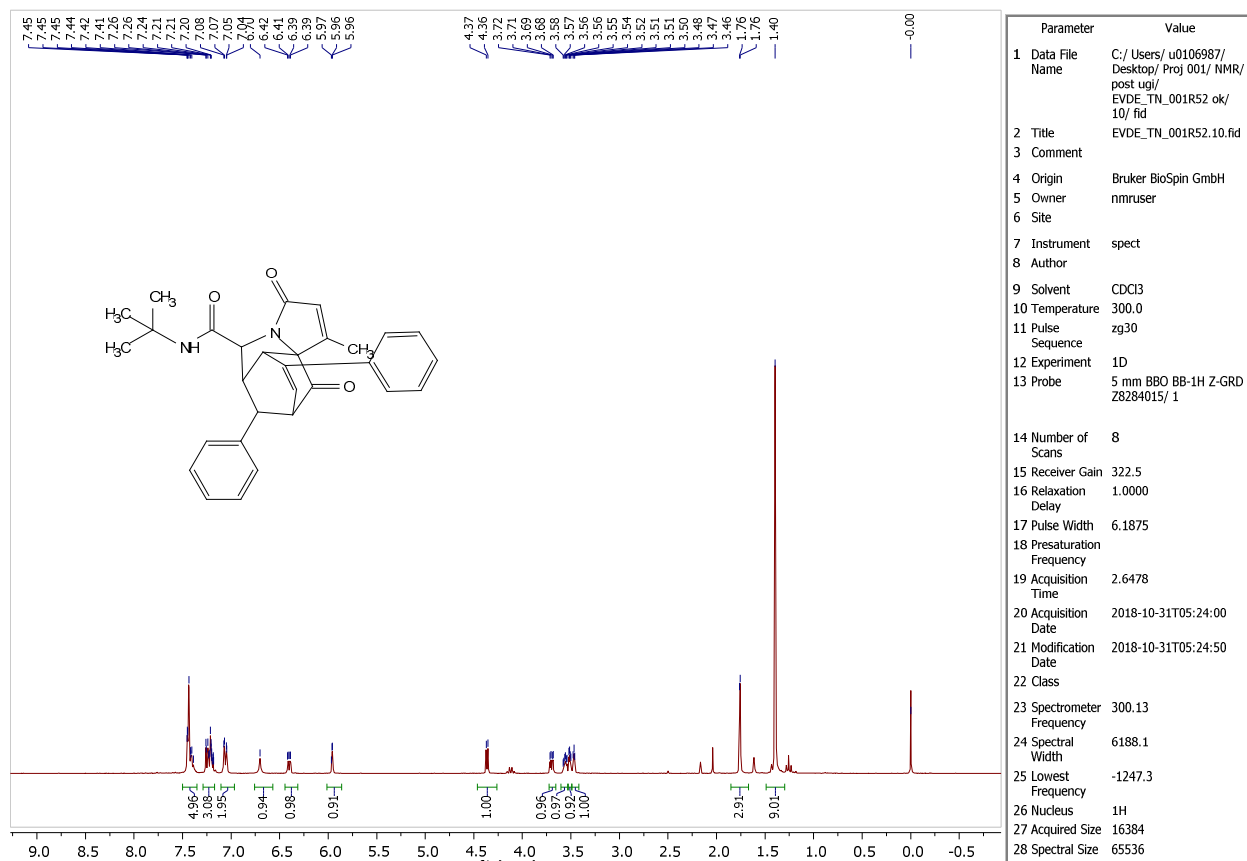


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/EVDE_TN_001R51 OK/ 11/ fid
2 Title	EVDE_TN_001R51.11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zgpg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD Z8284015/ 1
14 Number of Scans	2500
15 Receiver Gain	16384.0
16 Relaxation Delay	1.7500
17 Pulse Width	6.5000
18 Presaturation Frequency	
19 Acquisition Time	1.8220
20 Acquisition Date	2018-10-31T05:18:00
21 Modification Date	2018-10-31T05:18:42
22 Class	
23 Spectrometer Frequency	75.48
24 Spectral Width	17985.6
25 Lowest Frequency	-1432.9
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

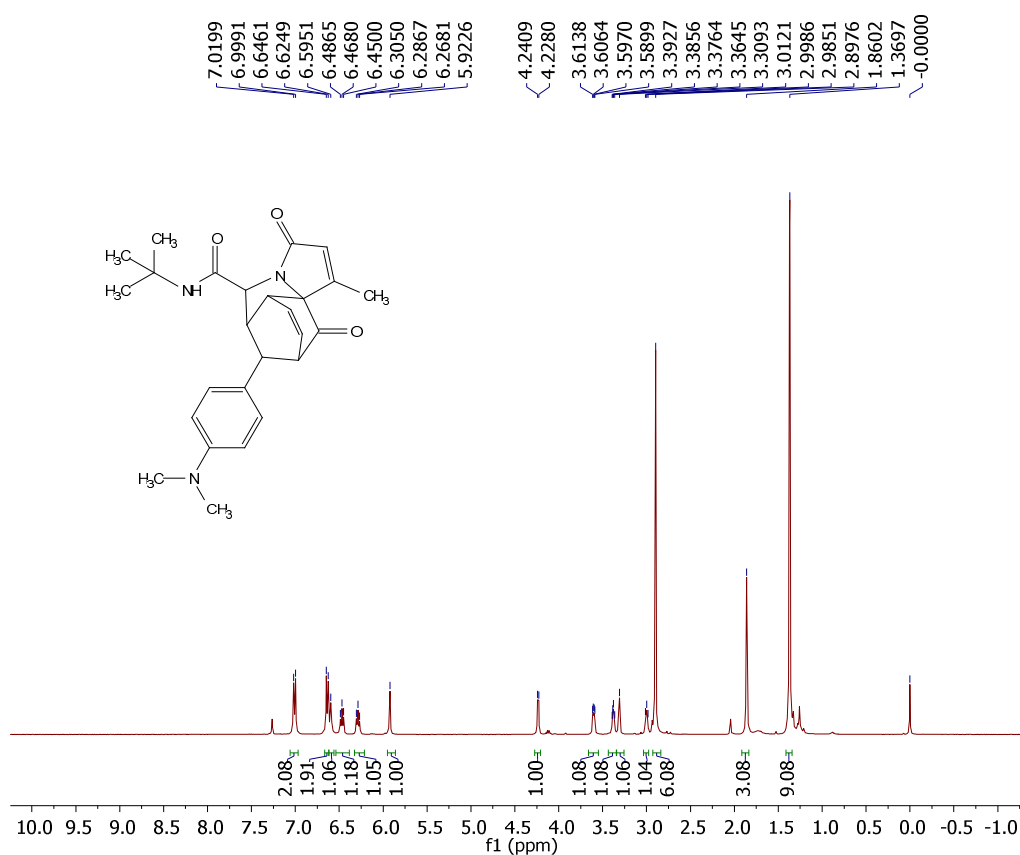
¹H and ¹³C NMR spectra of compound 2n



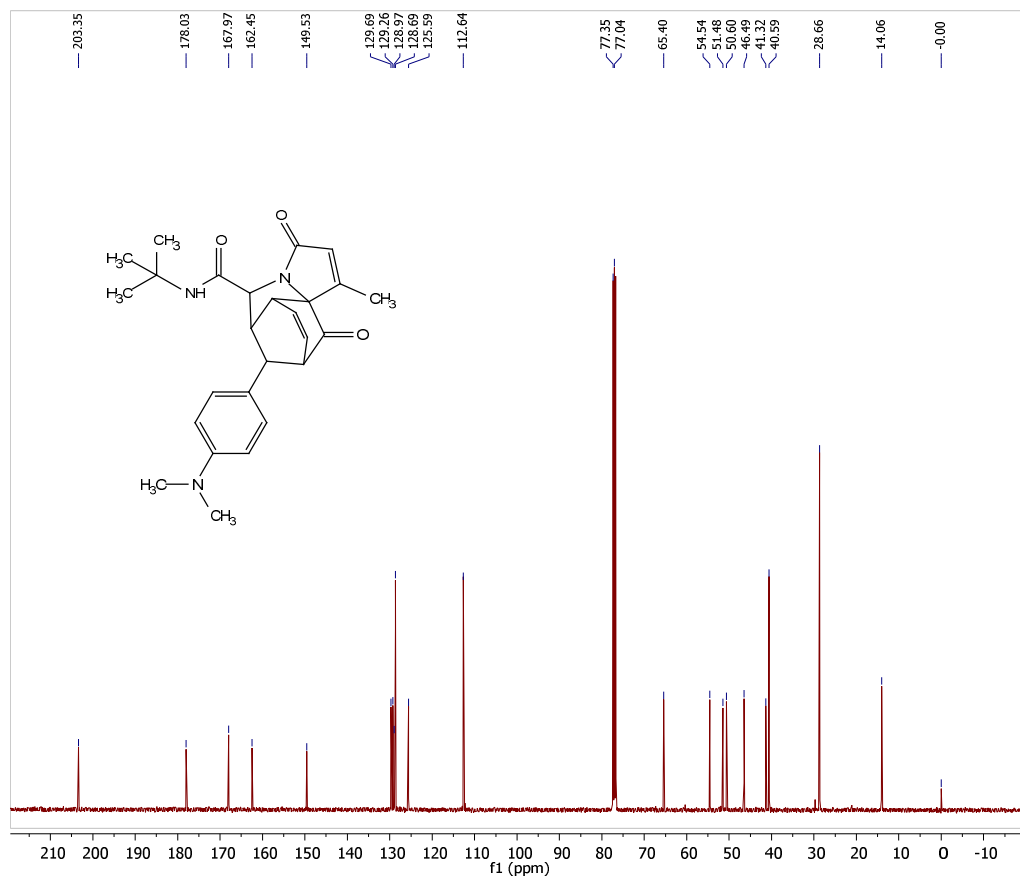
¹H and ¹³C NMR spectra of compound 2o



¹H and ¹³C NMR spectra of compound 2p

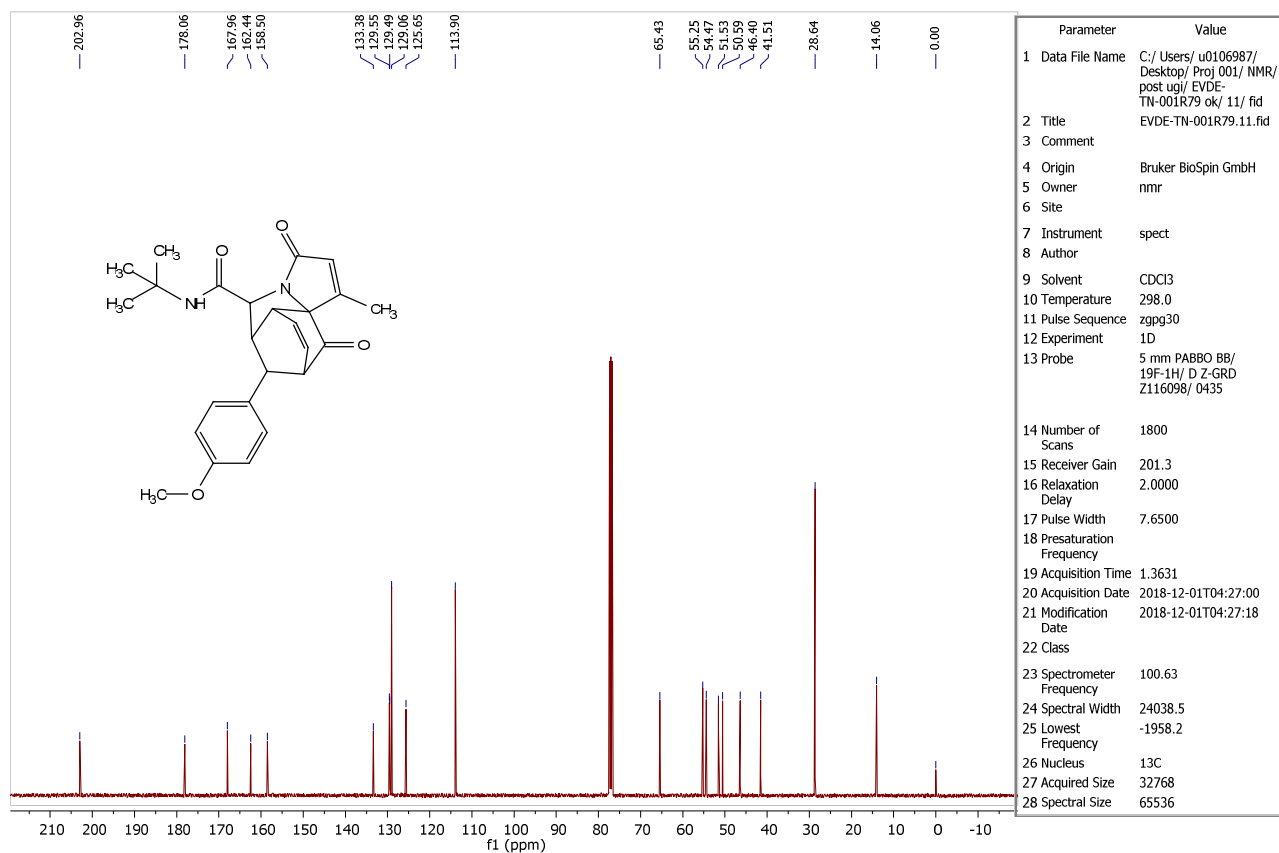
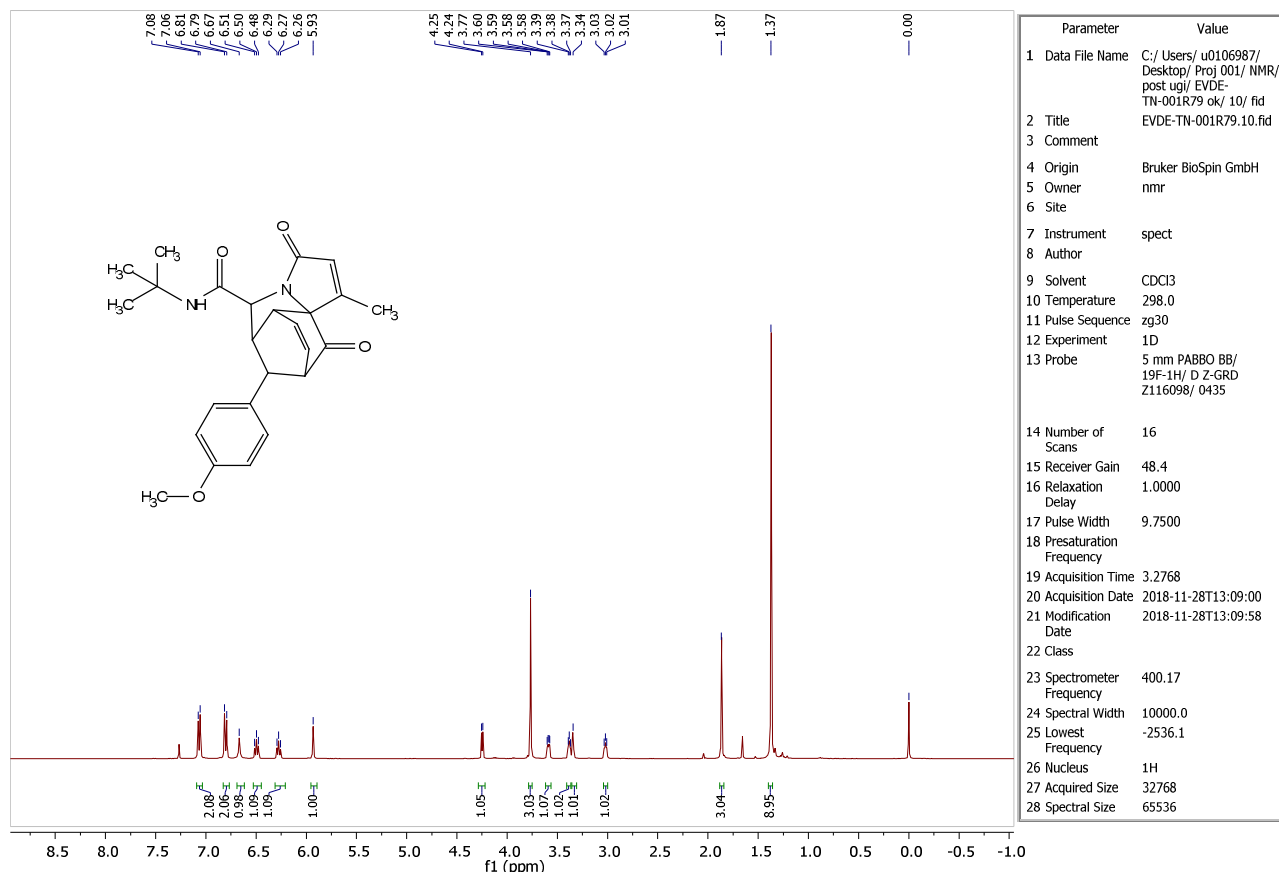


Parameter	Value
1 Data File Name	C:/Users/moke/Desktop/EVDE-TN001-R80B/10/fid
2 Title	EVDE-TN001-R80B.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/19F-1H/ D Z-GRD Z116098/0435
14 Number of Scans	16
15 Receiver Gain	42.3
16 Relaxation Delay	1.0000
17 Pulse Width	9.7500
18 Presaturation Frequency	
19 Acquisition Time	3.2768
20 Acquisition Date	2018-12-05T10:45:00
21 Modification Date	2018-12-05T10:45:50
22 Class	
23 Spectrometer Frequency	400.17
24 Spectral Width	10000.0
25 Lowest Frequency	-2536.8
26 Nucleus	1H
27 Acquired Size	32768
28 Spectral Size	65536

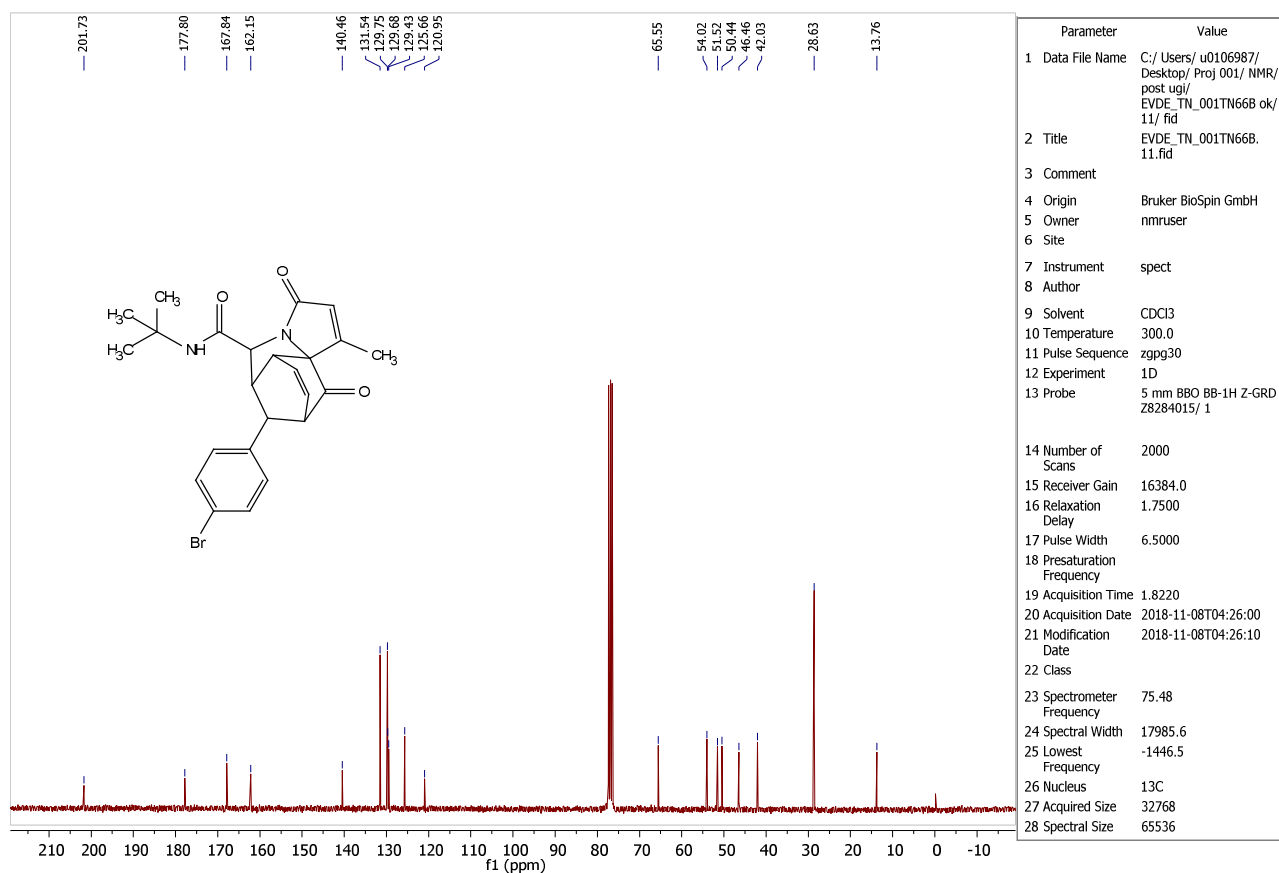
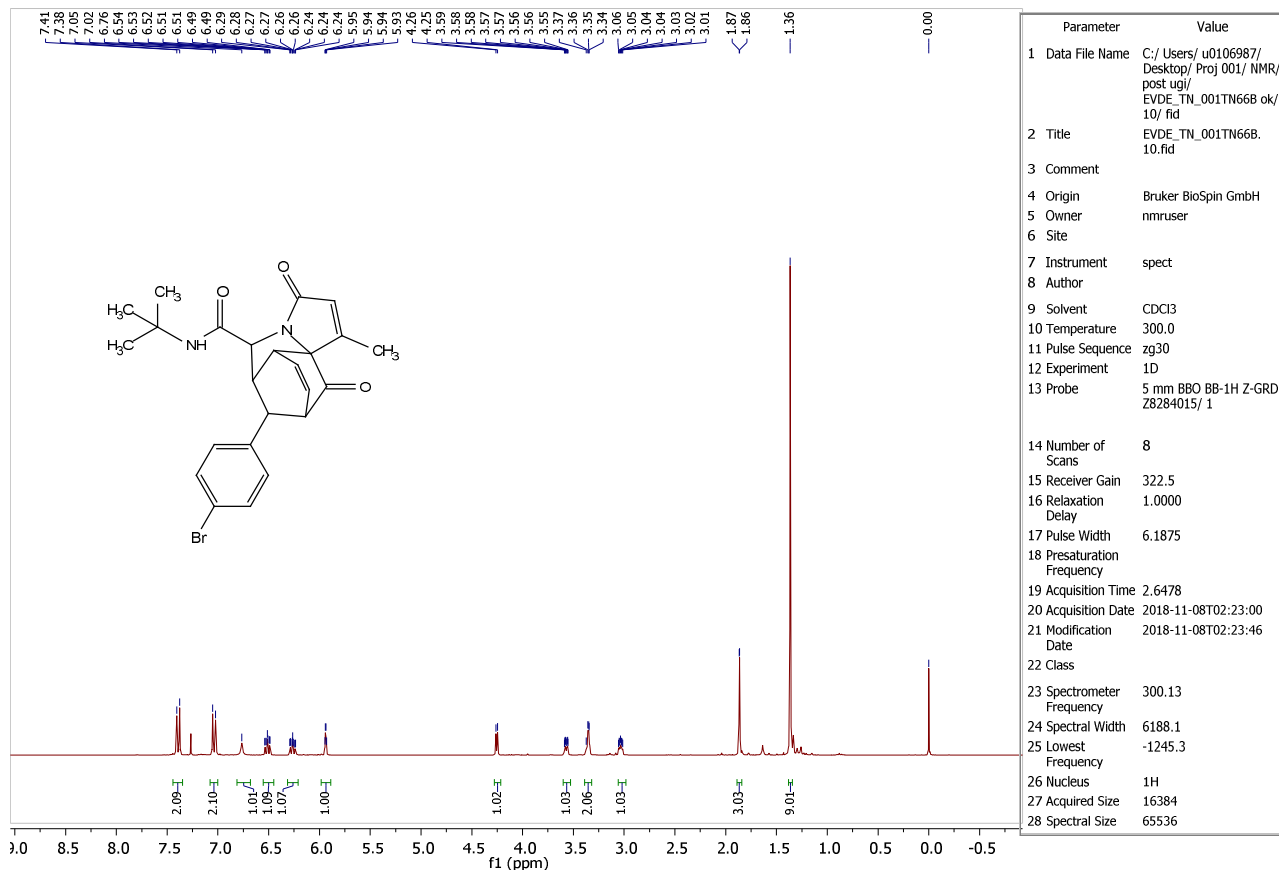


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/EVDE-TN001-R80B ok/11/fid
2 Title	EVDE-TN001-R80B.11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zpgg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/19F-1H/ D Z-GRD Z116098/0435
14 Number of Scans	2048
15 Receiver Gain	201.3
16 Relaxation Delay	2.0000
17 Pulse Width	7.6500
18 Presaturation Frequency	
19 Acquisition Time	1.3631
20 Acquisition Date	2018-12-07T00:03:00
21 Modification Date	2018-12-07T00:03:06
22 Class	
23 Spectrometer Frequency	100.63
24 Spectral Width	24038.5
25 Lowest Frequency	-1958.7
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

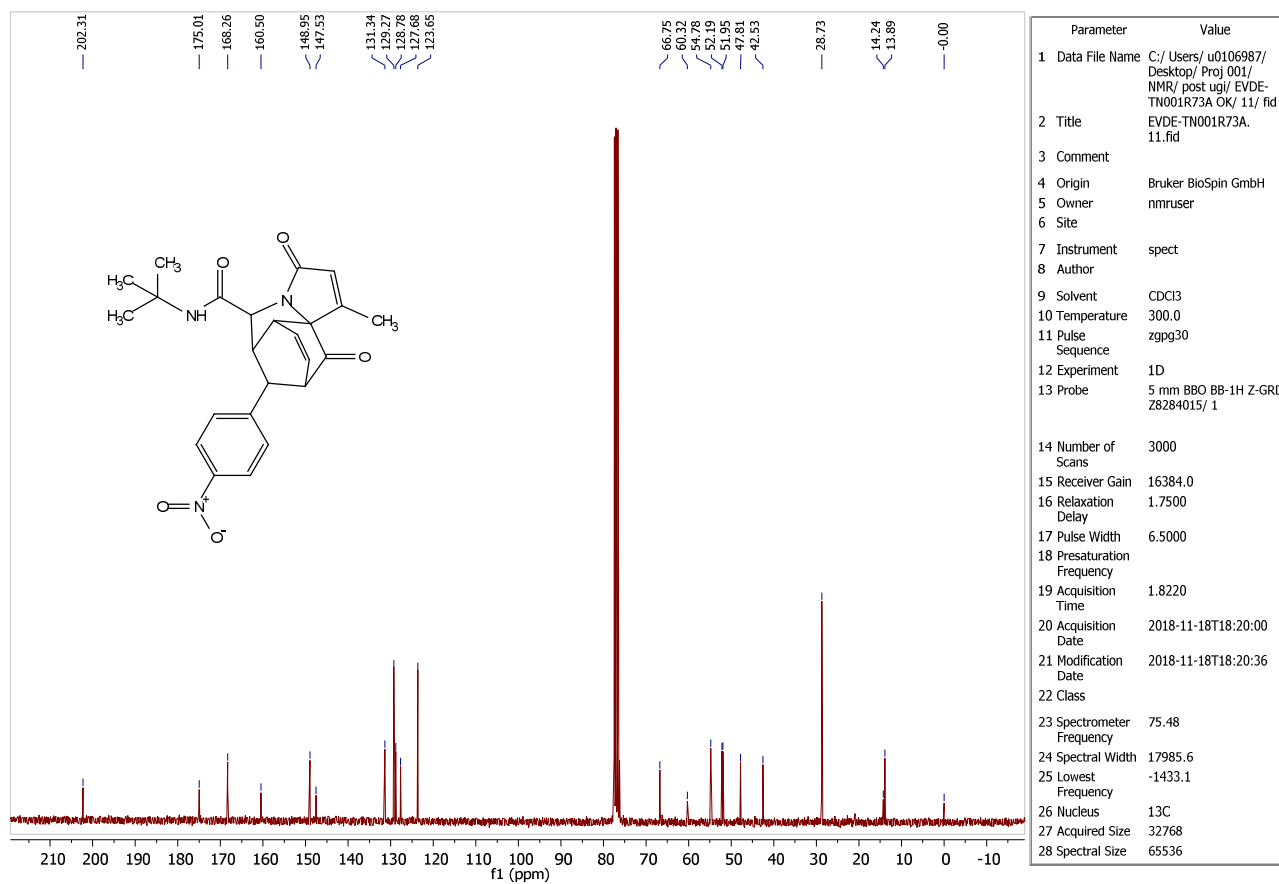
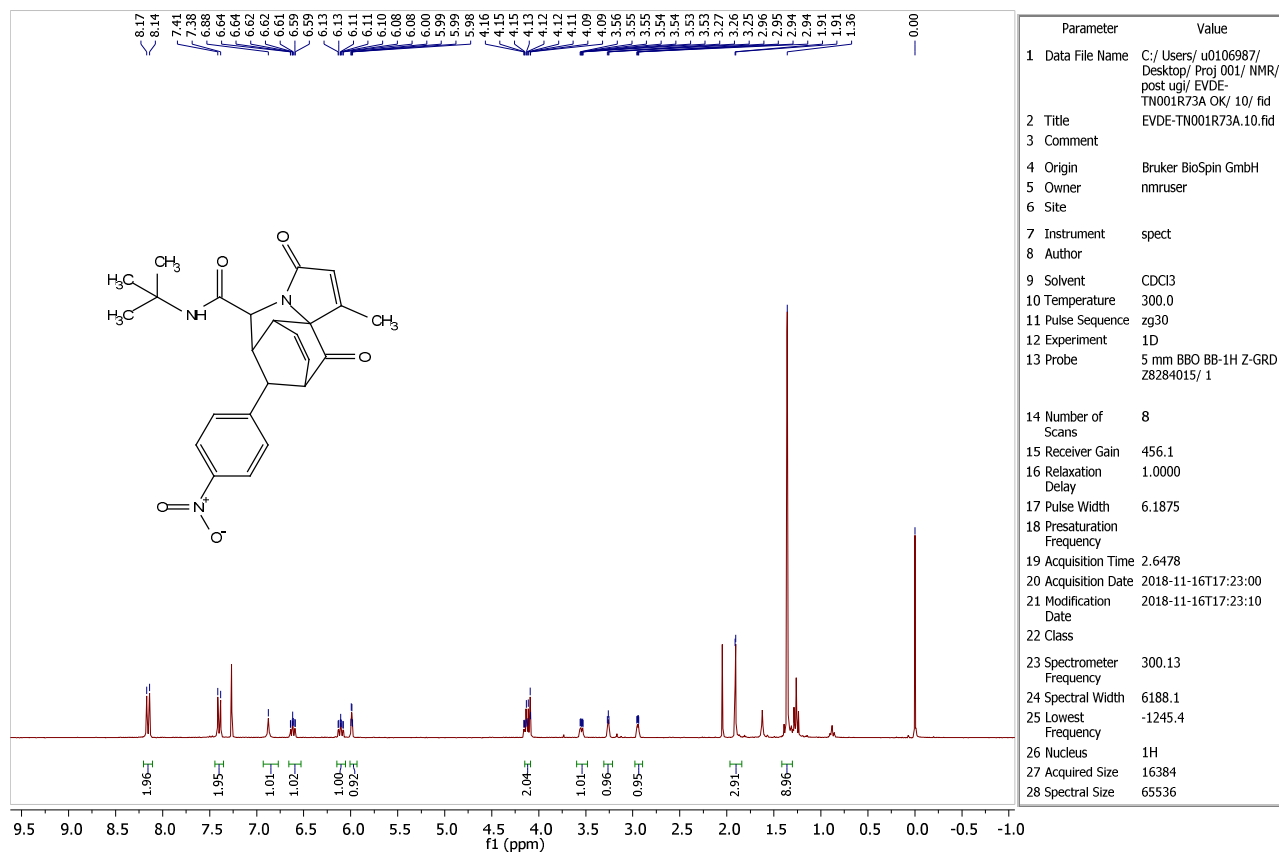
¹H and ¹³C NMR spectra of compound 2q



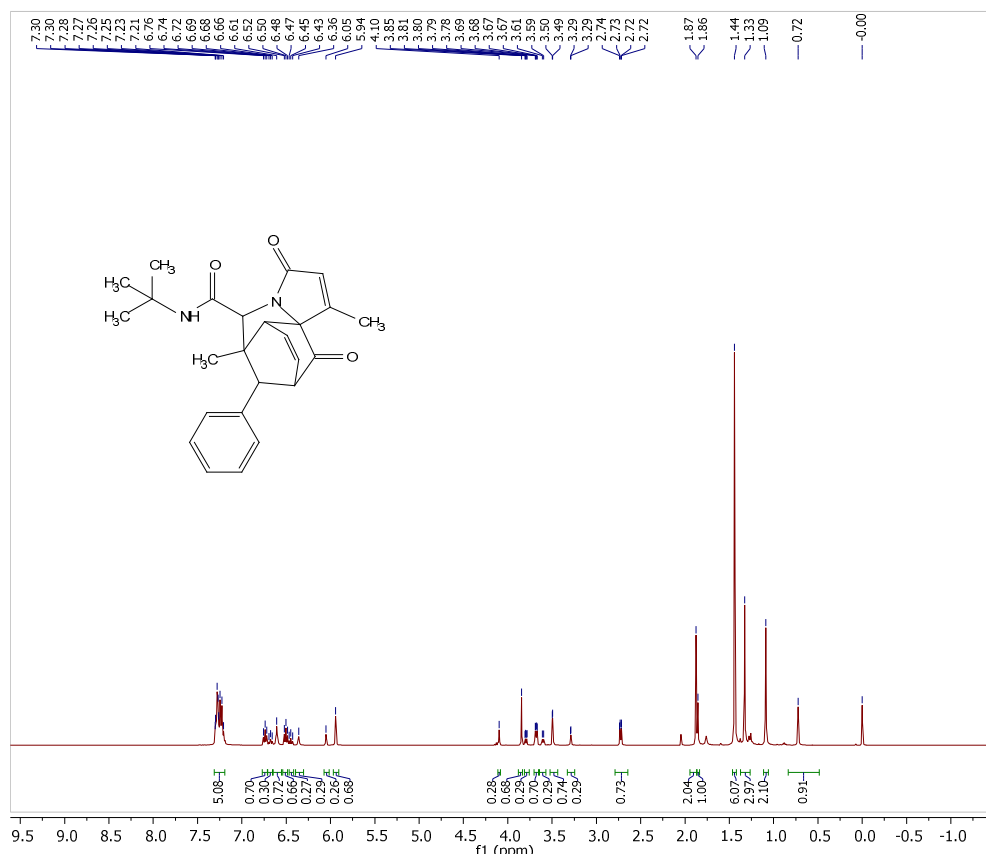
¹H and ¹³C NMR spectra of compound 2r



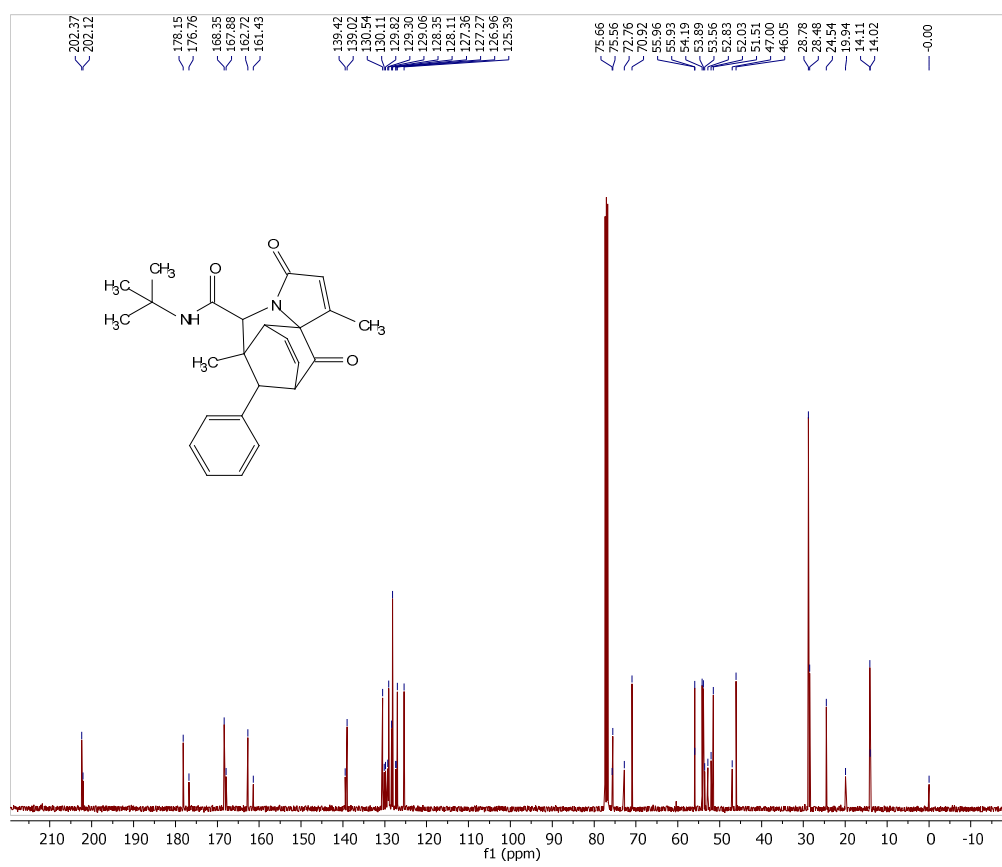
¹H and ¹³C NMR spectra of compound 2s



¹H and ¹³C NMR spectra of compound 2t

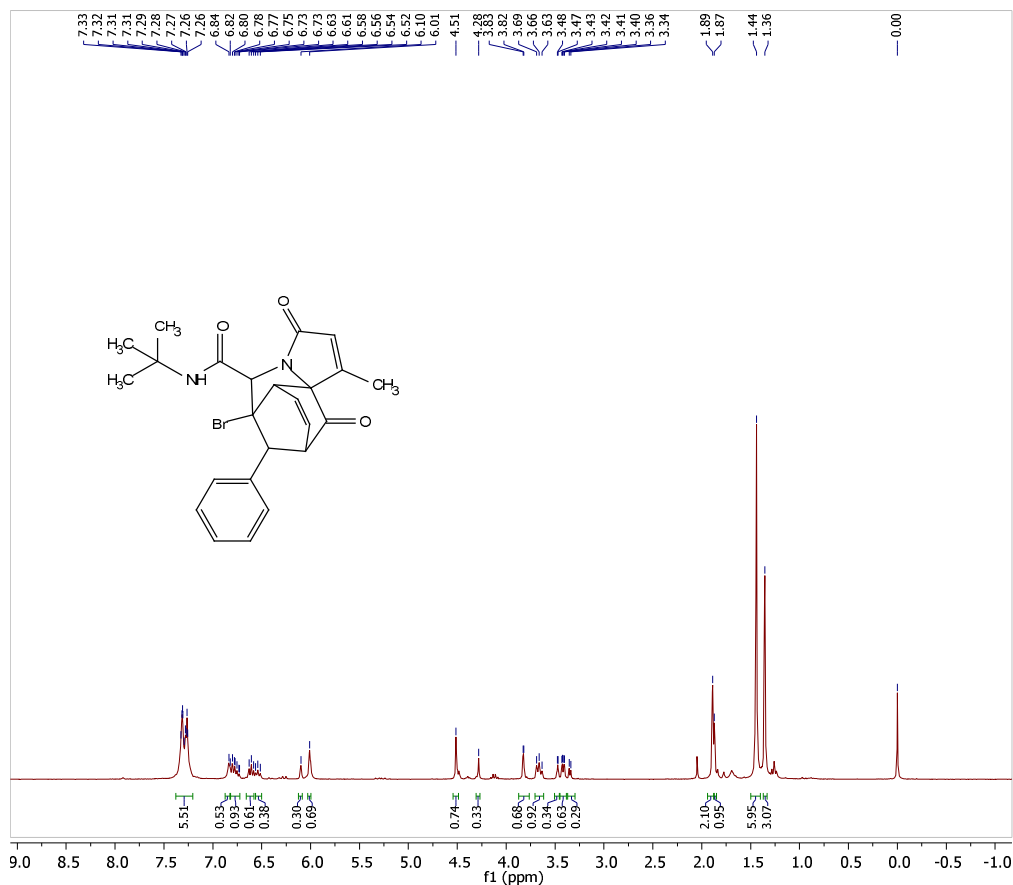


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/ EVDE-TN001R44 ok dr/ 10/ fid
2 Title	EVDE-TN001R44.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	295.2
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/ 19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	16
15 Receiver Gain	38.6
16 Relaxation Delay	1.0000
17 Pulse Width	9.7500
18 Presaturation Frequency	
19 Acquisition Time	3.2768
20 Acquisition Date	2018-10-24T13:22:00
21 Modification Date	2018-10-24T13:22:32
22 Class	
23 Spectrometer Frequency	400.17
24 Spectral Width	10000.0
25 Lowest Frequency	-2534.5
26 Nucleus	1H
27 Acquired Size	32768
28 Spectral Size	65536

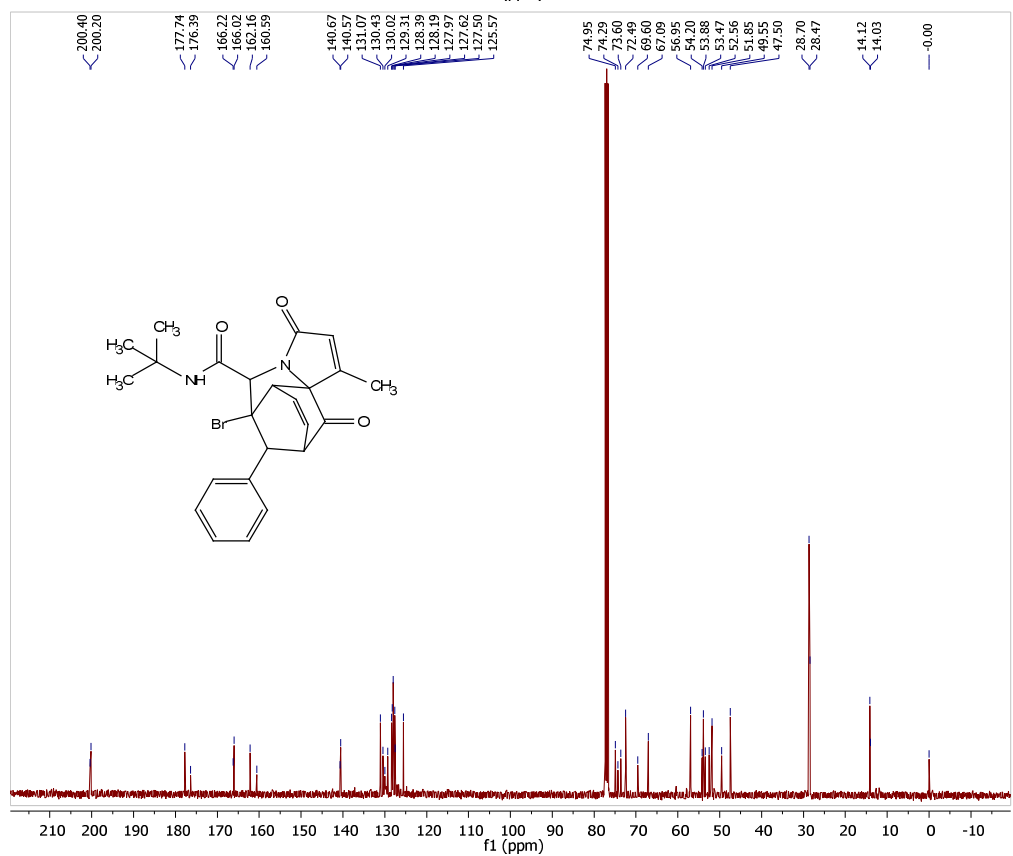


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/ EVDE-TN001R44 ok dr/ 11/ fid
2 Title	EVDE-TN001R44.11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	295.7
11 Pulse Sequence	zgpg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/ 19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	1024
15 Receiver Gain	201.3
16 Relaxation Delay	2.0000
17 Pulse Width	7.6500
18 Presaturation Frequency	
19 Acquisition Time	1.3631
20 Acquisition Date	2018-10-25T05:17:00
21 Modification Date	2018-10-25T05:17:24
22 Class	
23 Spectrometer Frequency	100.63
24 Spectral Width	24038.5
25 Lowest Frequency	-1959.3
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

¹H and ¹³C NMR spectra of compound 2u



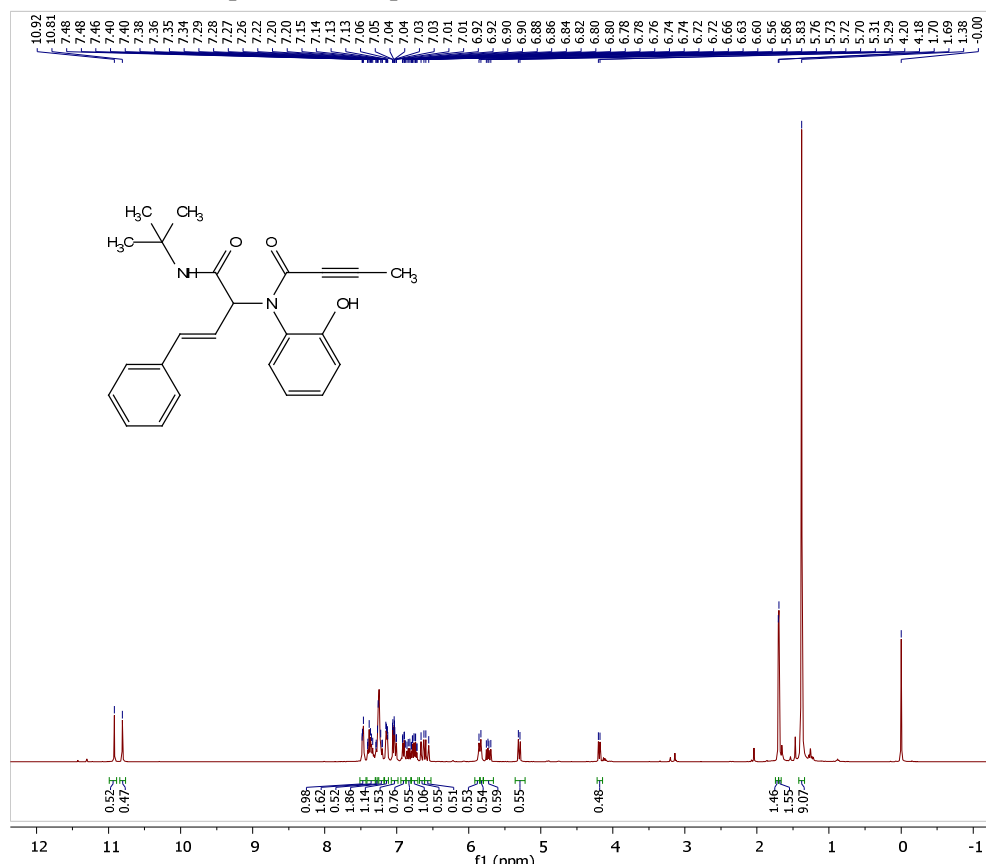
Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/EVDE_YN_001R45 ok,dr value/10/ fid
2 Title	EVDE_YN_001R45.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD 28284015/ 1
14 Number of Scans	8
15 Receiver Gain	228.1
16 Relaxation Delay	1.0000
17 Pulse Width	6.1875
18 Presaturation Frequency	
19 Acquisition Time	2.6478
20 Acquisition Date	2018-10-25T11:22:00
21 Modification Date	2018-10-25T11:22:18
22 Class	
23 Spectrometer Frequency	300.13
24 Spectral Width	6188.1
25 Lowest Frequency	-1245.2
26 Nucleus	1H
27 Acquired Size	16384
28 Spectral Size	65536



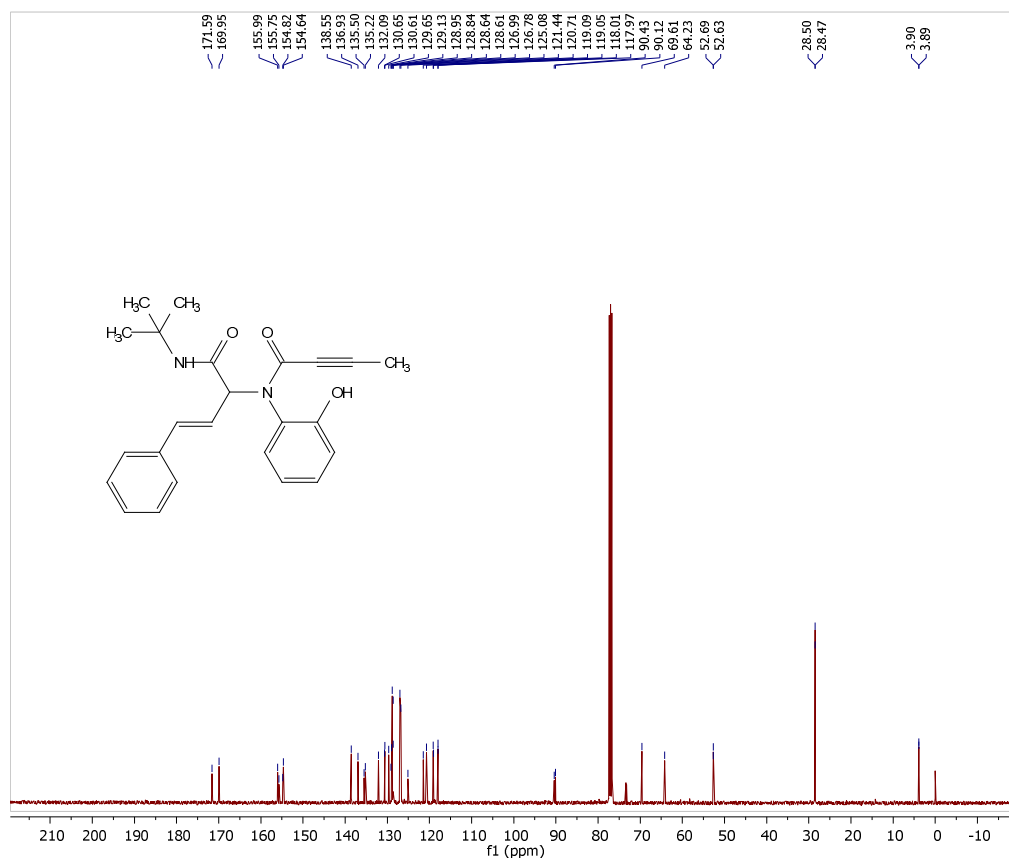
Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/post ugi/EVDE_YN_001R45 ok,dr value/EVDE-TN001-R45/11/ fid
2 Title	EVDE-TN001-R45.11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	296.9
11 Pulse Sequence	zpgg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/ 19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	1024
15 Receiver Gain	201.3
16 Relaxation Delay	2.0000
17 Pulse Width	7.6500
18 Presaturation Frequency	
19 Acquisition Time	1.3631
20 Acquisition Date	2018-10-28T22:45:00
21 Modification Date	2018-10-28T22:45:50
22 Class	
23 Spectrometer Frequency	100.63
24 Spectral Width	24038.5
25 Lowest Frequency	-1959.1
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

Copies of NMR spectra (Ugi products)

¹H and ¹³C NMR spectra of compound 1a

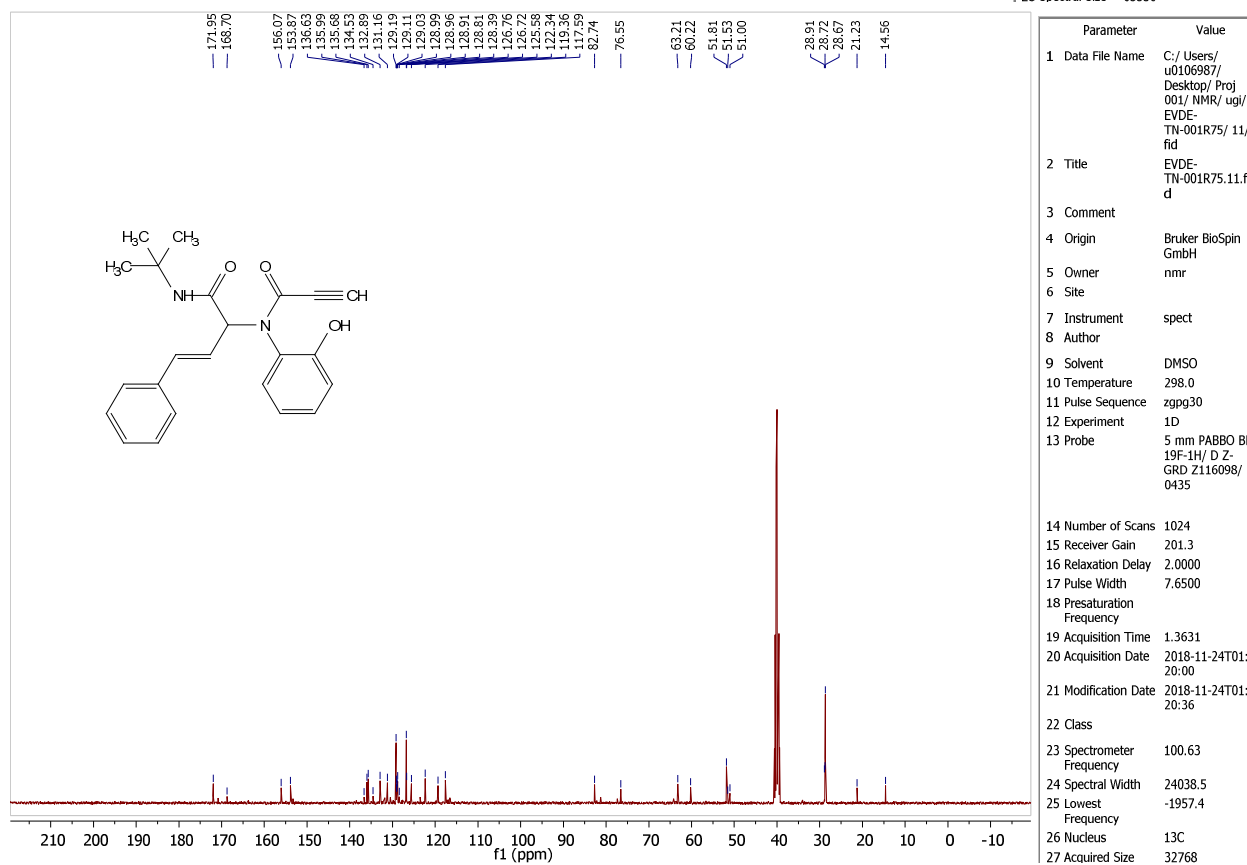
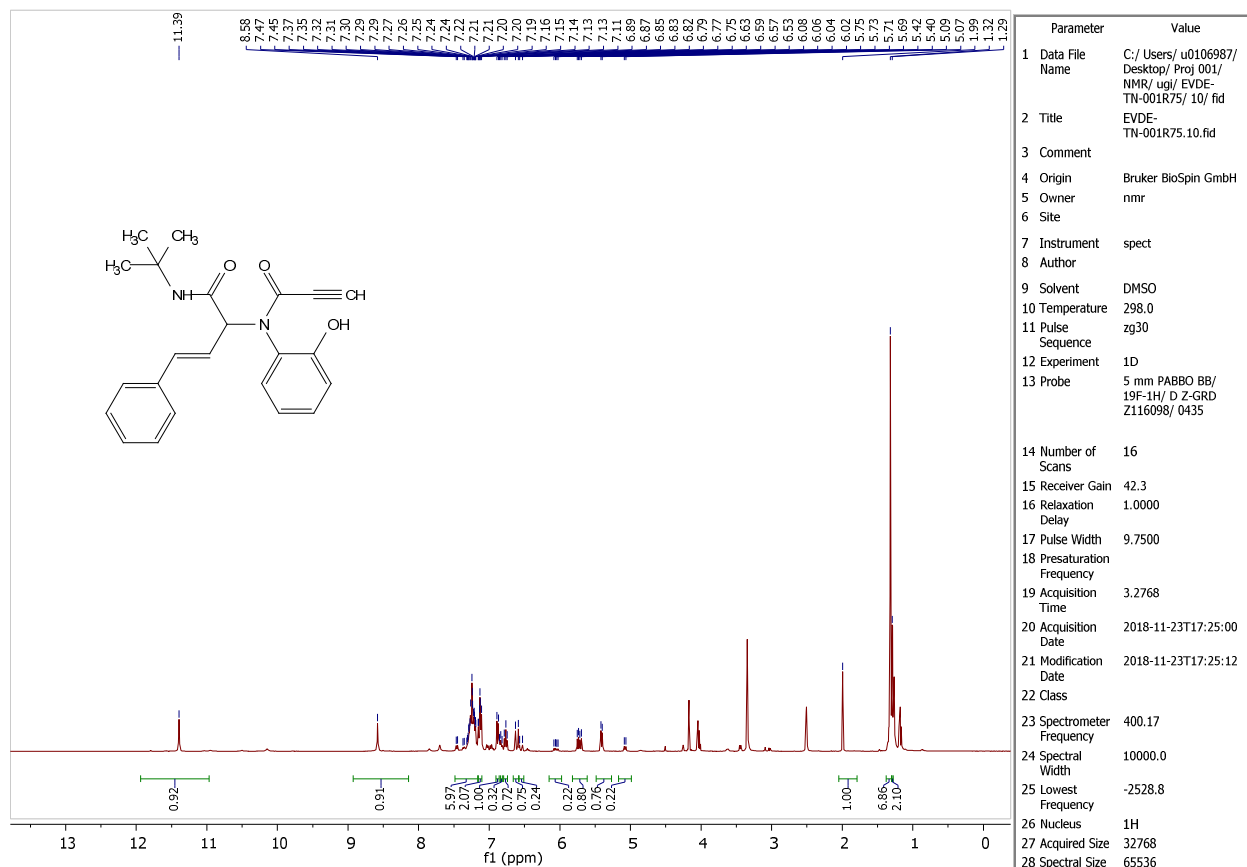


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/ugl/EVDE-TN001R2(P)/10/fid
2 Title	EVDE-TN001R2(P).10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	16
15 Receiver Gain	48.4
16 Relaxation Delay	1.0000
17 Pulse Width	9.7500
18 Presaturation Frequency	
19 Acquisition Time	3.2768
20 Acquisition Date	2018-09-25T11:23:00
21 Modification Date	2018-09-25T11:23:34
22 Class	
23 Spectrometer Frequency	400.17
24 Spectral Width	10000.0
25 Lowest Frequency	-2538.5
26 Nucleus	1H
27 Acquired Size	32768
28 Spectral Size	65536

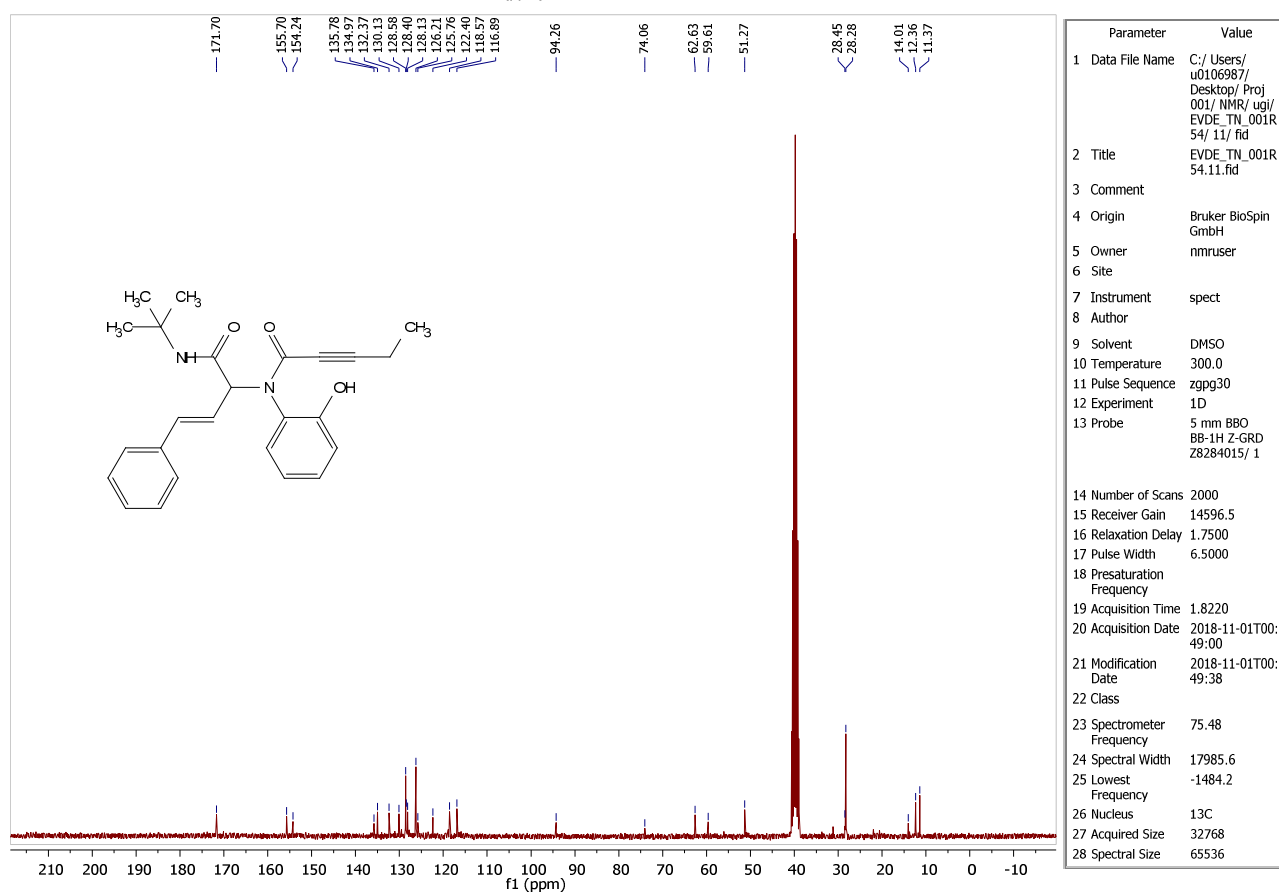
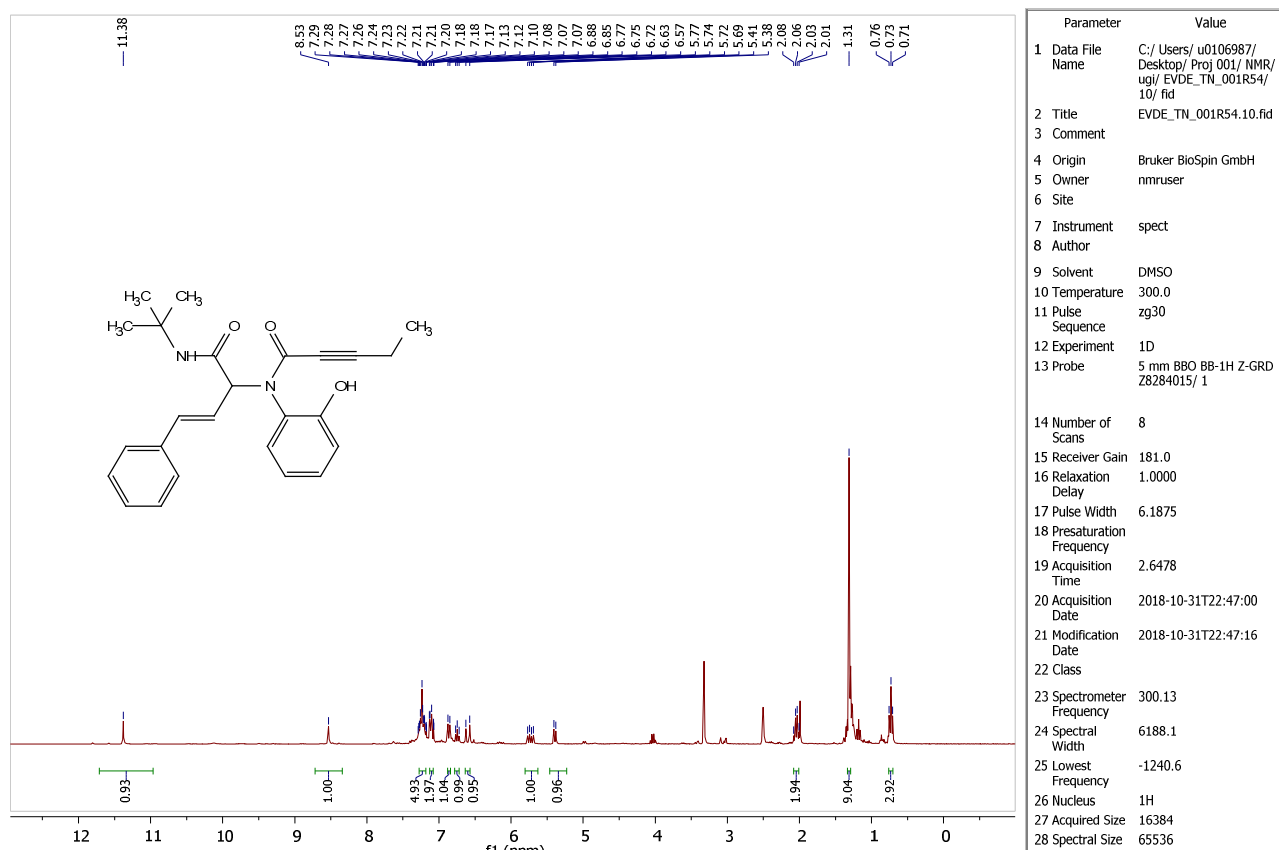


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/ugl/EVDE-TN001R2(P)/11/fid
2 Title	EVDE-TN001R2(P).11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zgpg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	2048
15 Receiver Gain	201.3
16 Relaxation Delay	2.0000
17 Pulse Width	7.6500
18 Presaturation Frequency	
19 Acquisition Time	1.3631
20 Acquisition Date	2018-09-27T02:22:00
21 Modification Date	2018-09-27T02:23:00
22 Class	
23 Spectrometer Frequency	100.63
24 Spectral Width	24038.5
25 Lowest Frequency	-1958.7
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

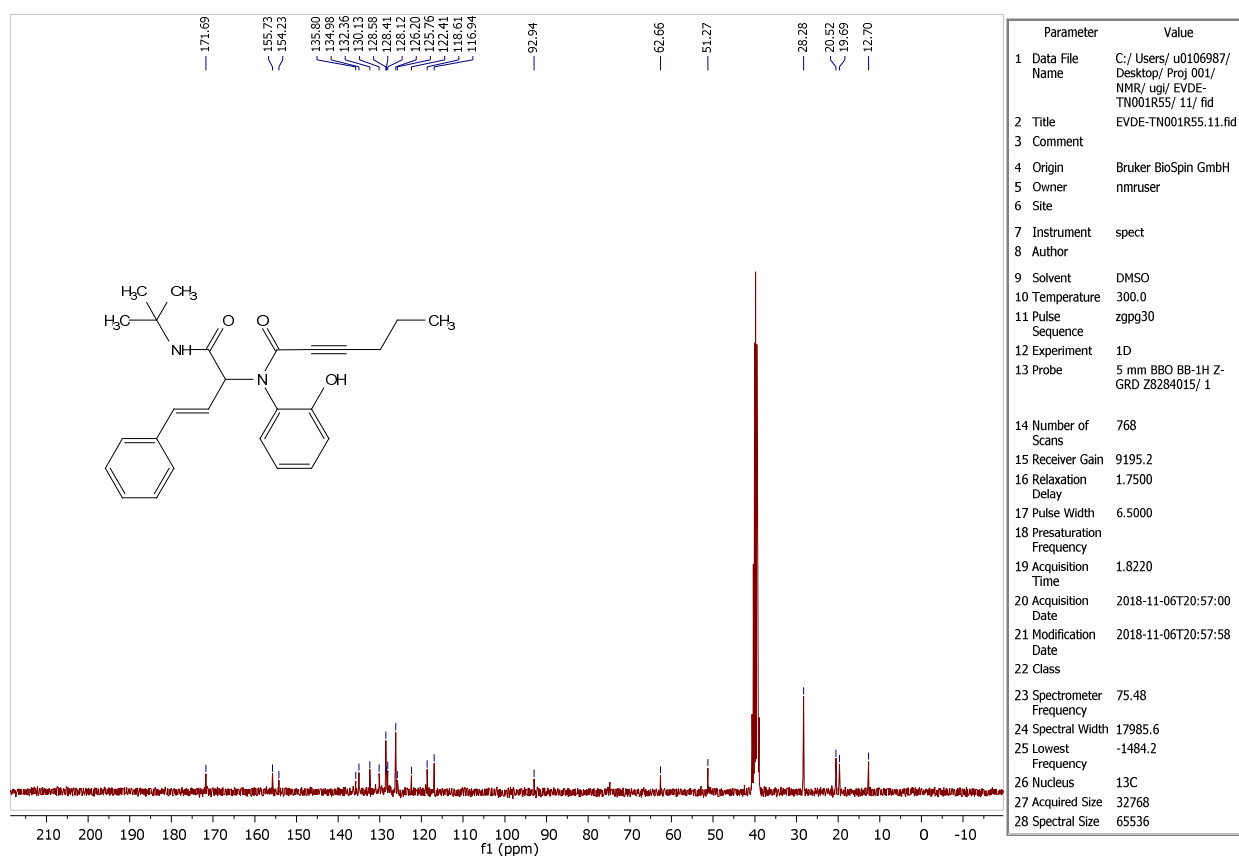
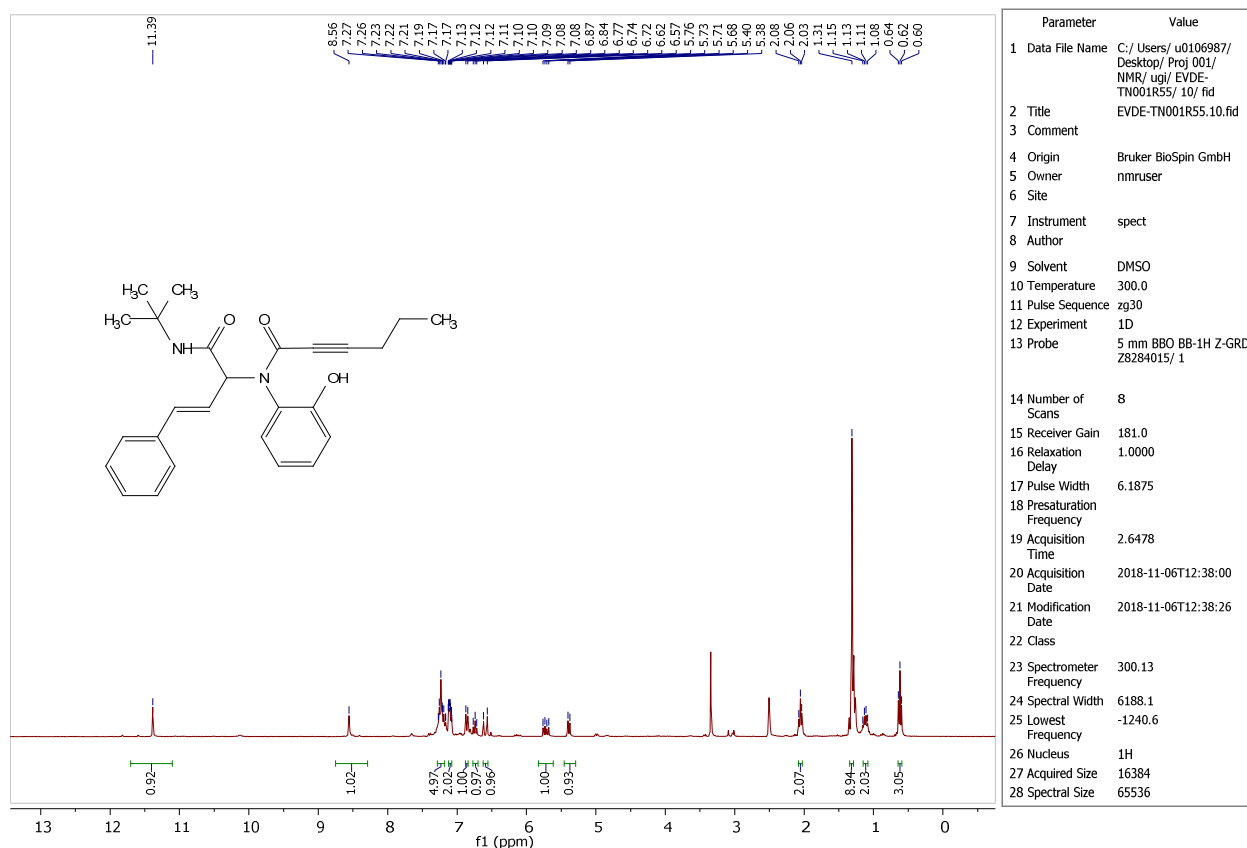
¹H and ¹³C NMR spectra of compound 1b



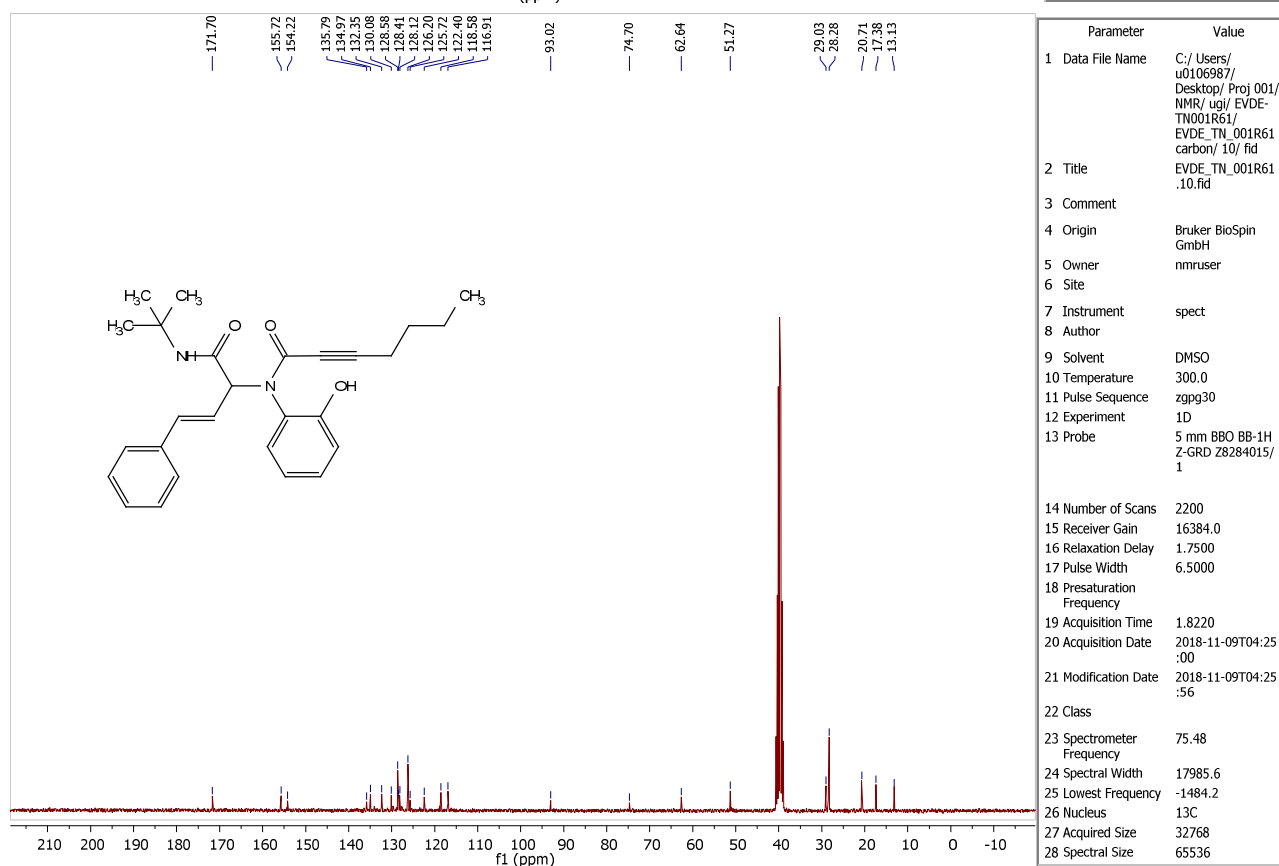
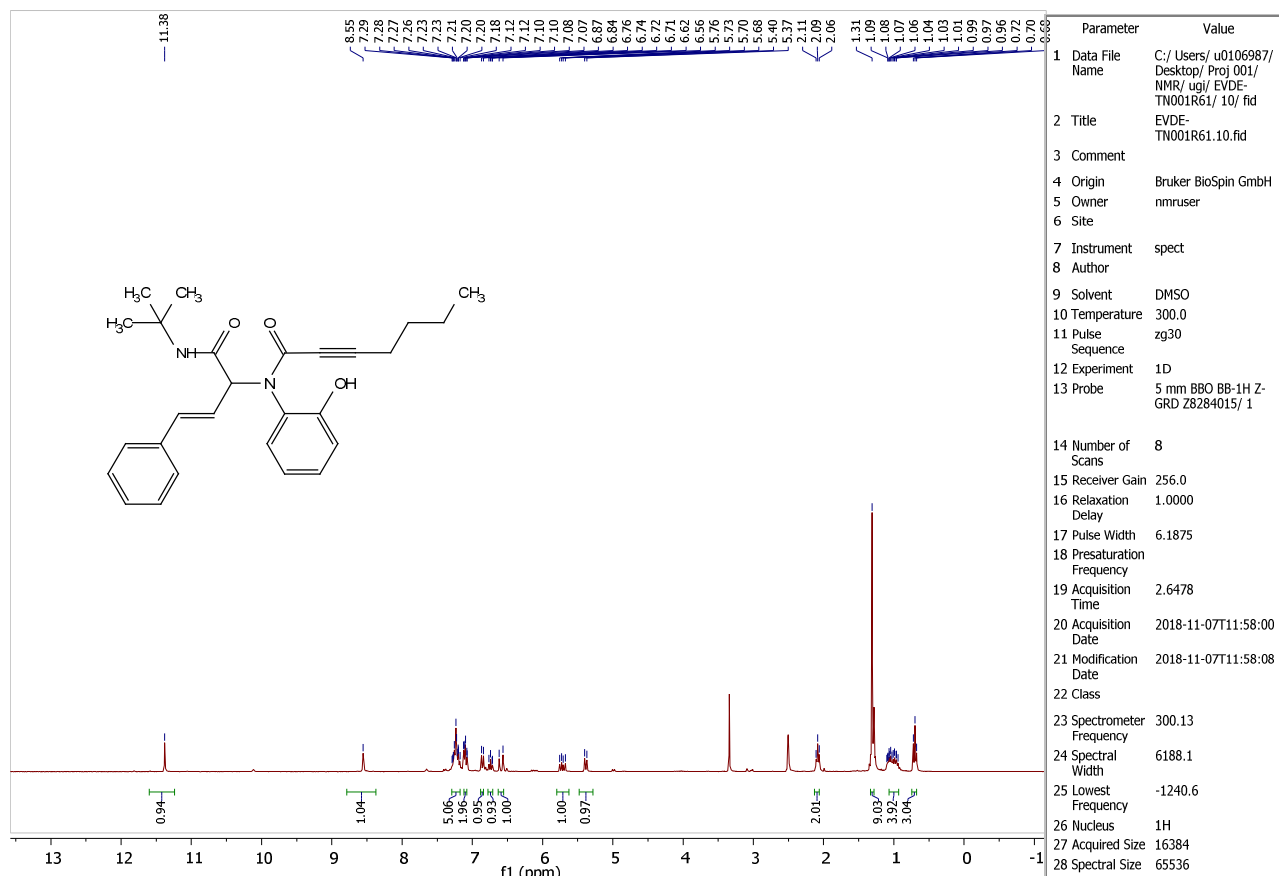
¹H and ¹³C NMR spectra of compound 1c



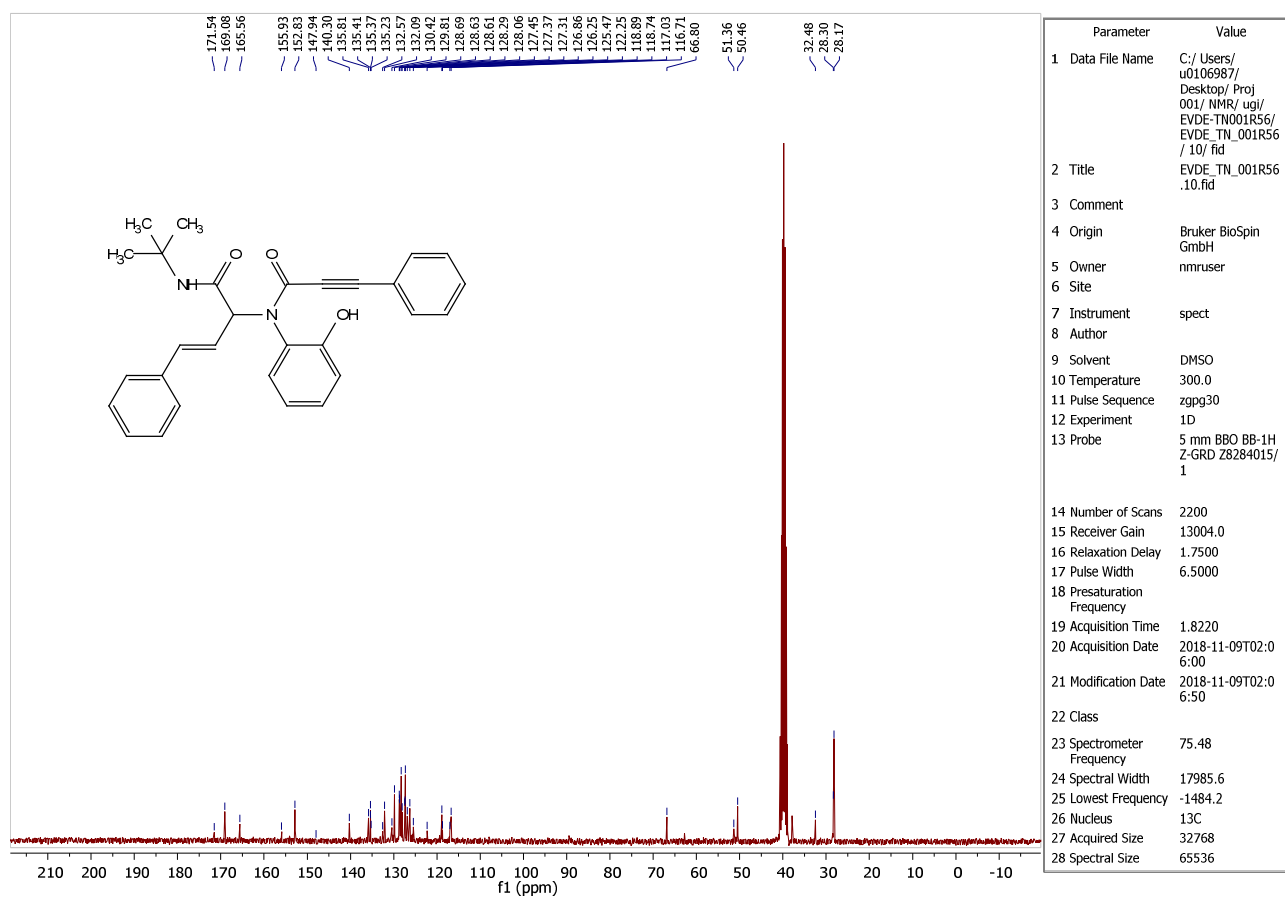
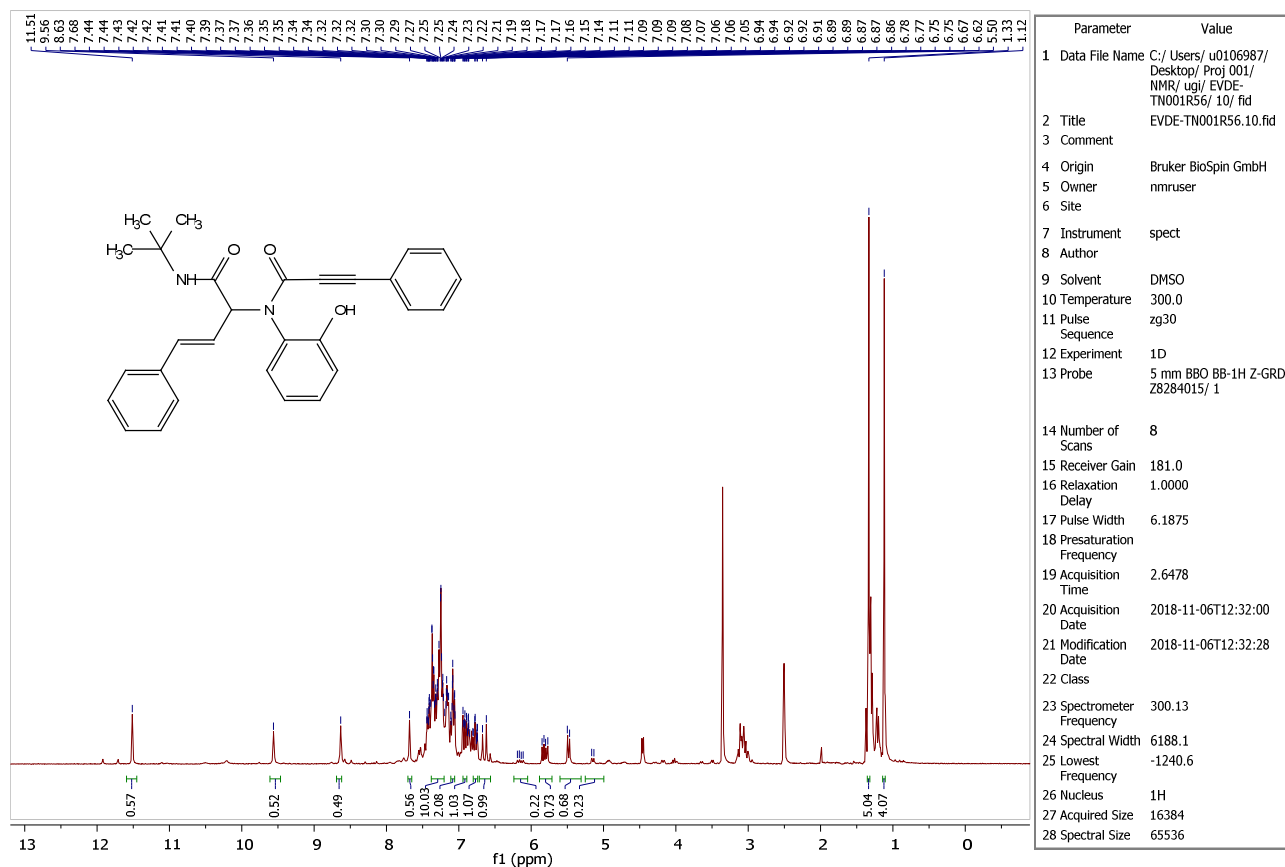
¹H and ¹³C NMR spectra of compound **1d**



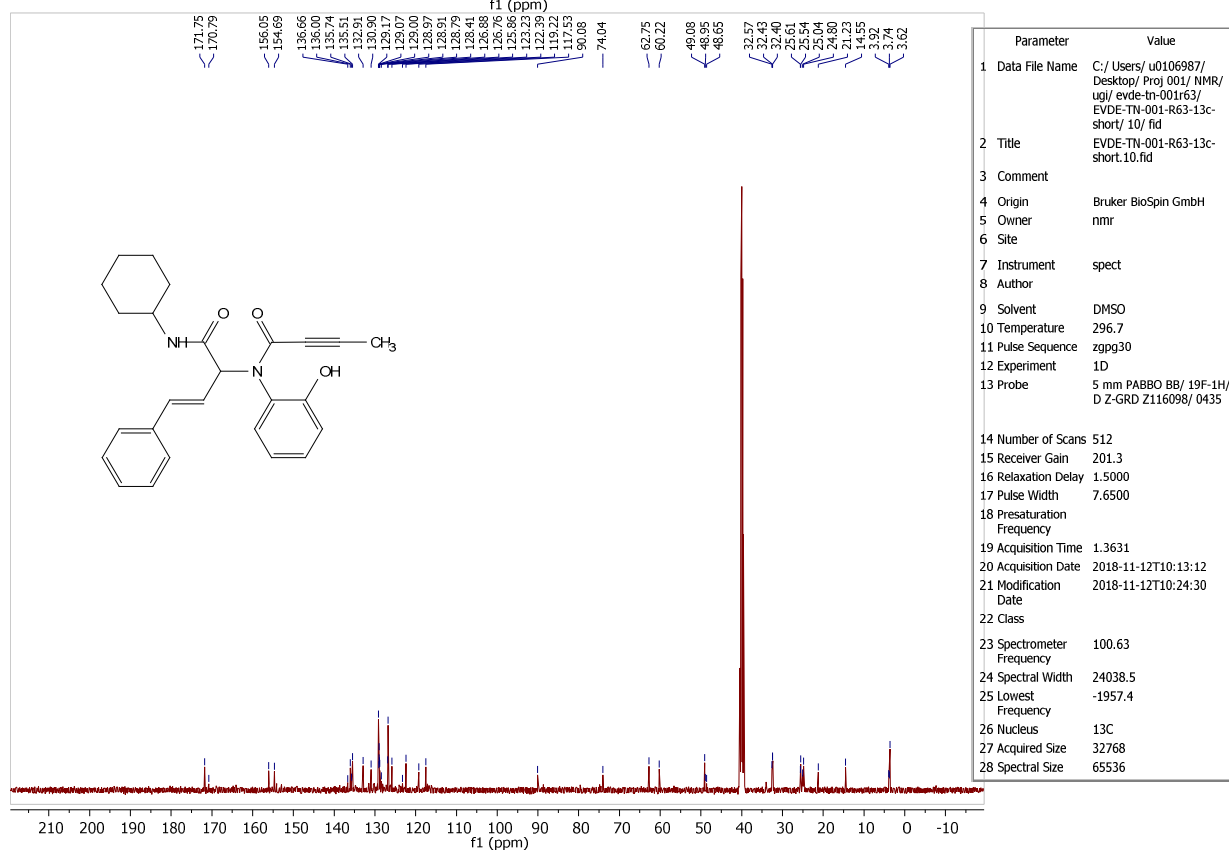
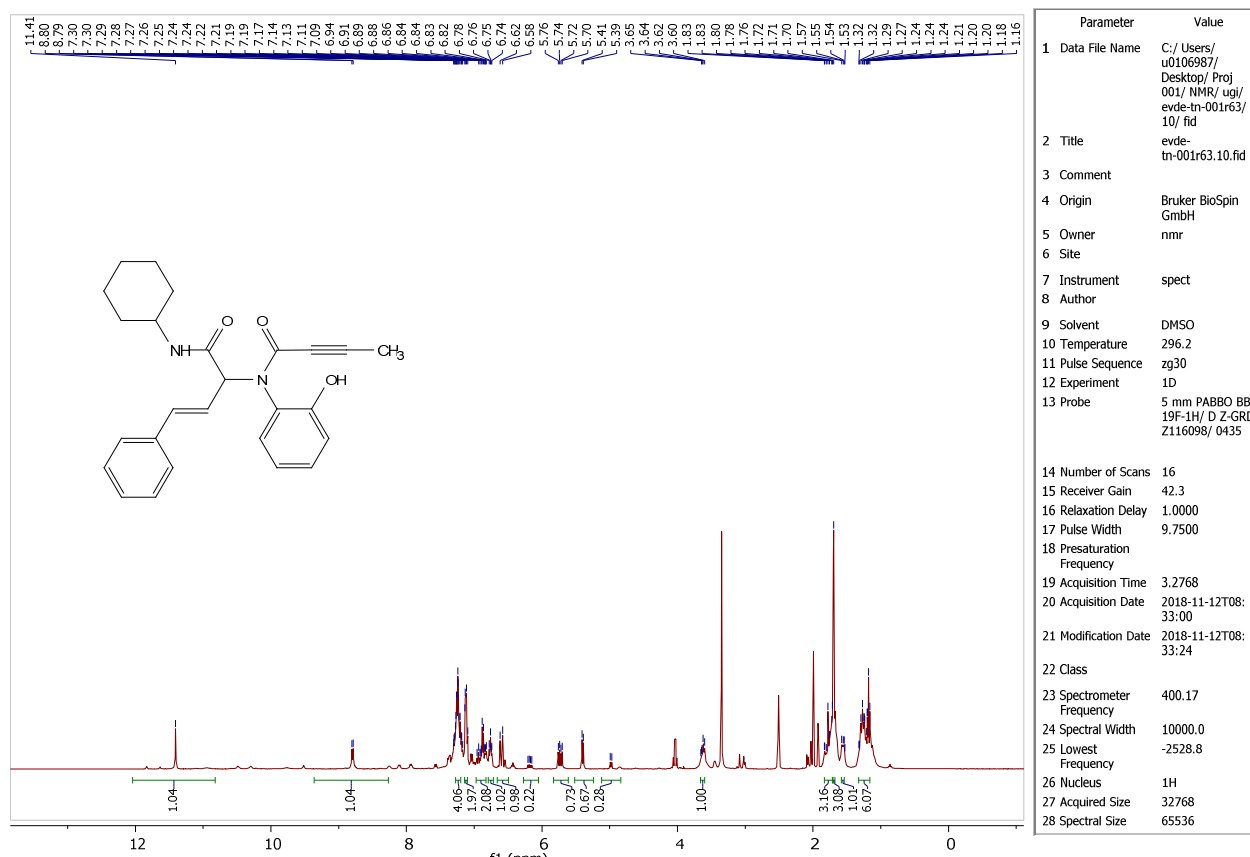
¹H and ¹³C NMR spectra of compound **1e**



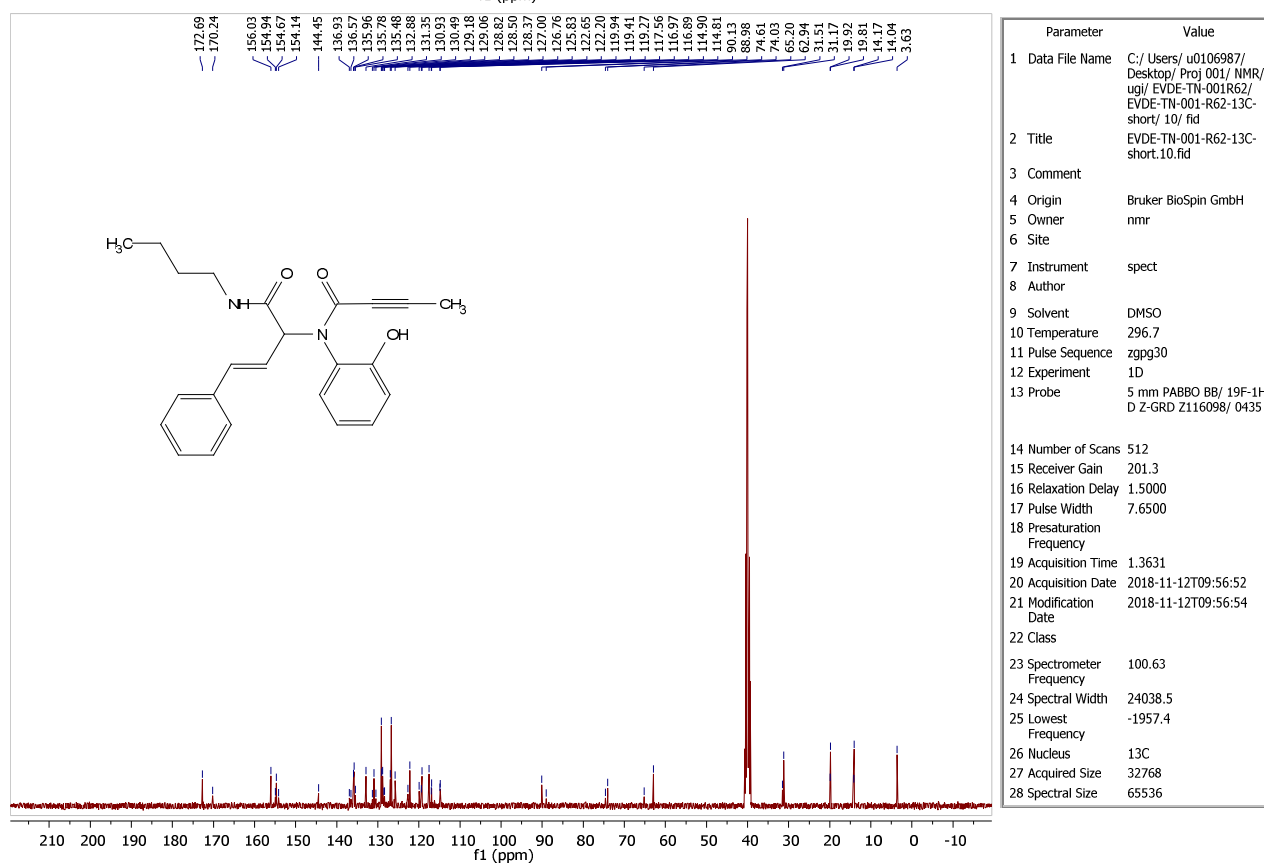
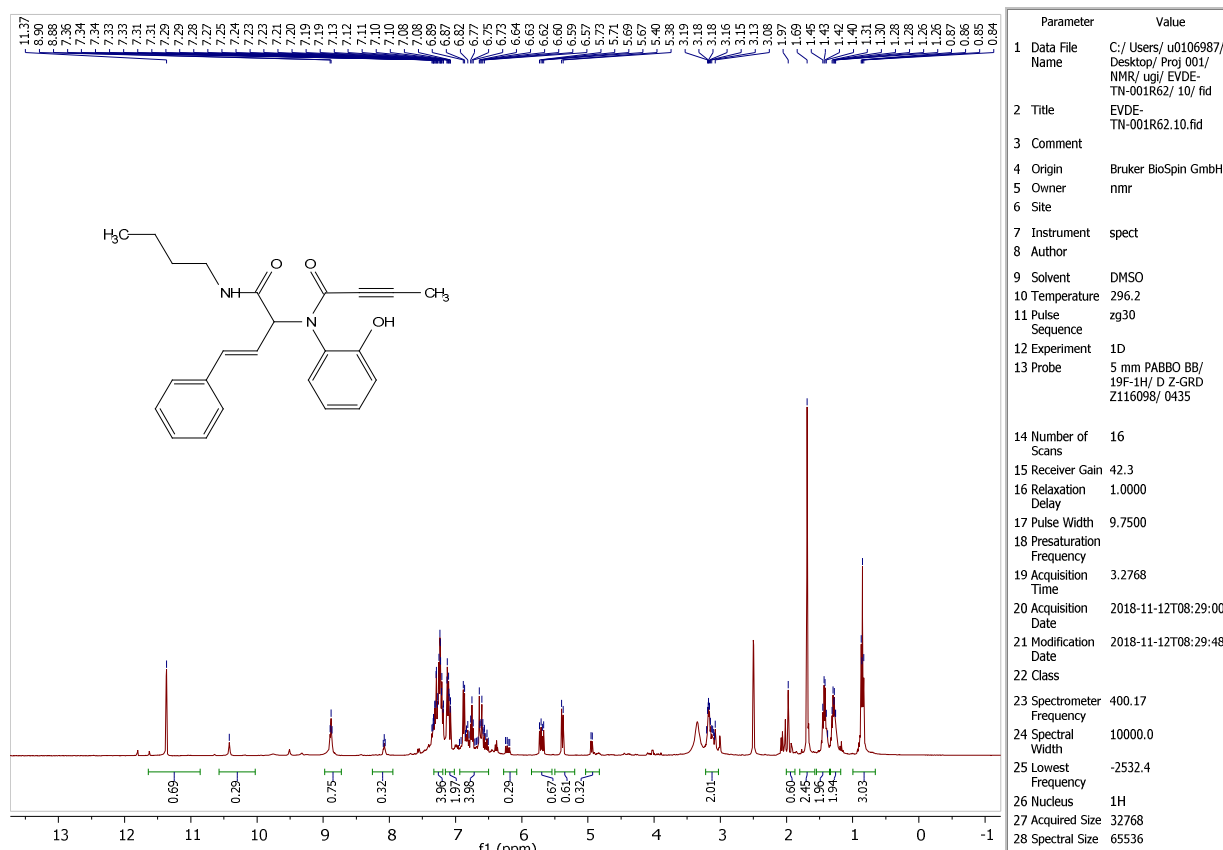
¹H and ¹³C NMR spectra of compound 1f



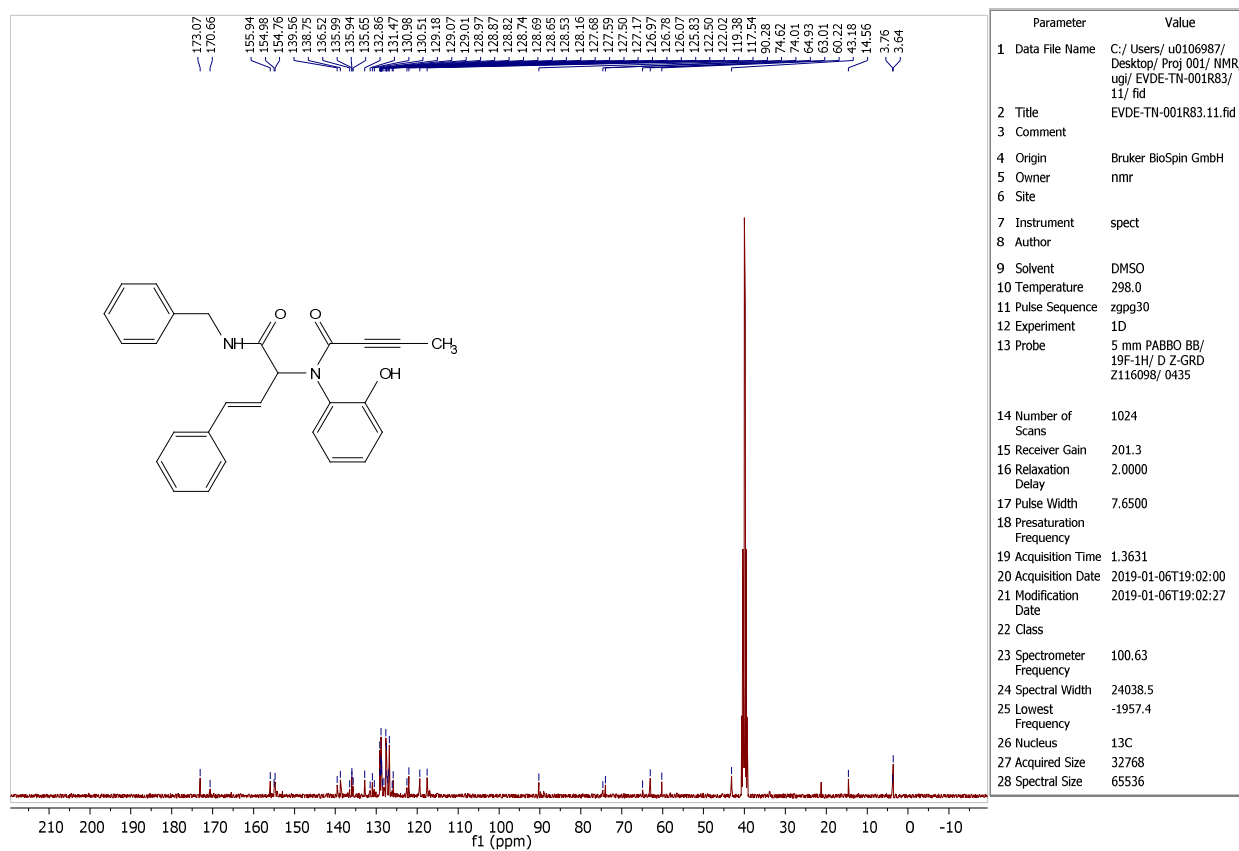
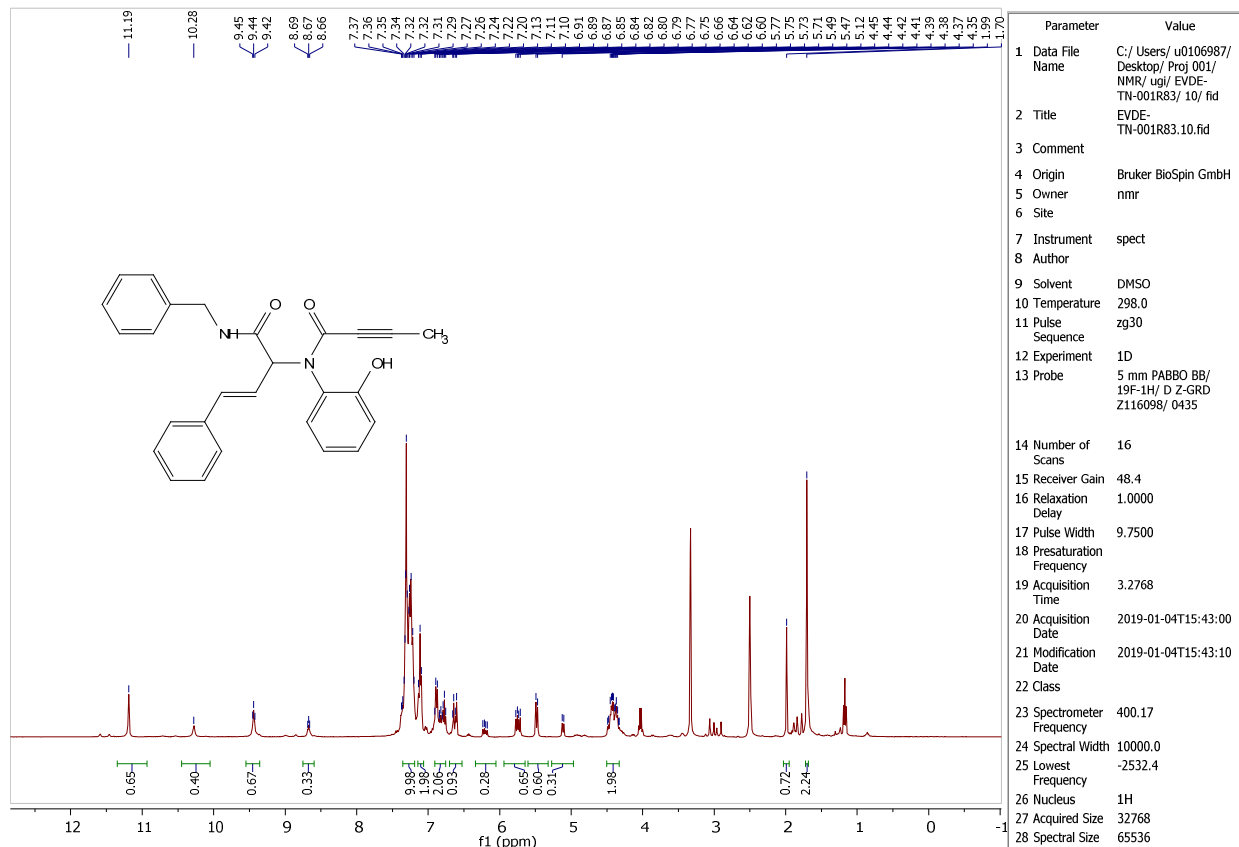
¹H and ¹³C NMR spectra of compound **1g**



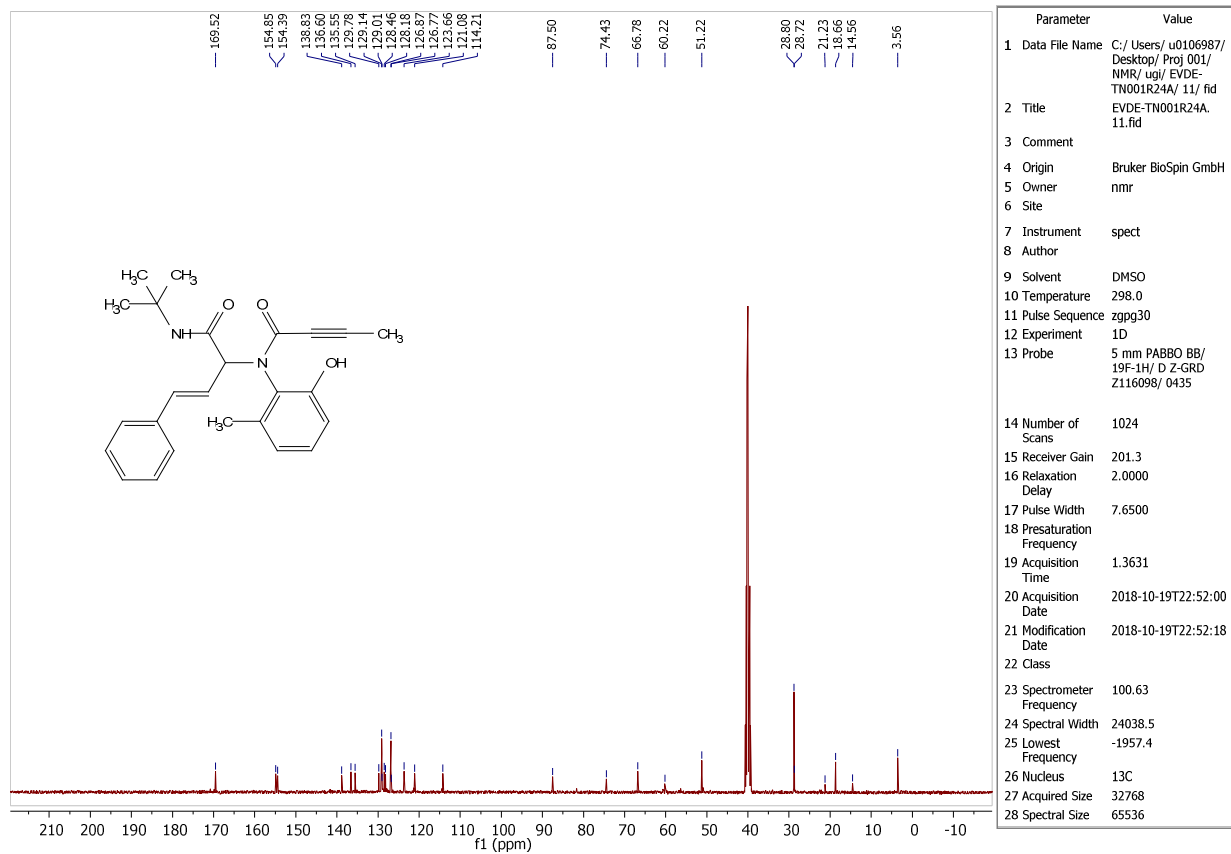
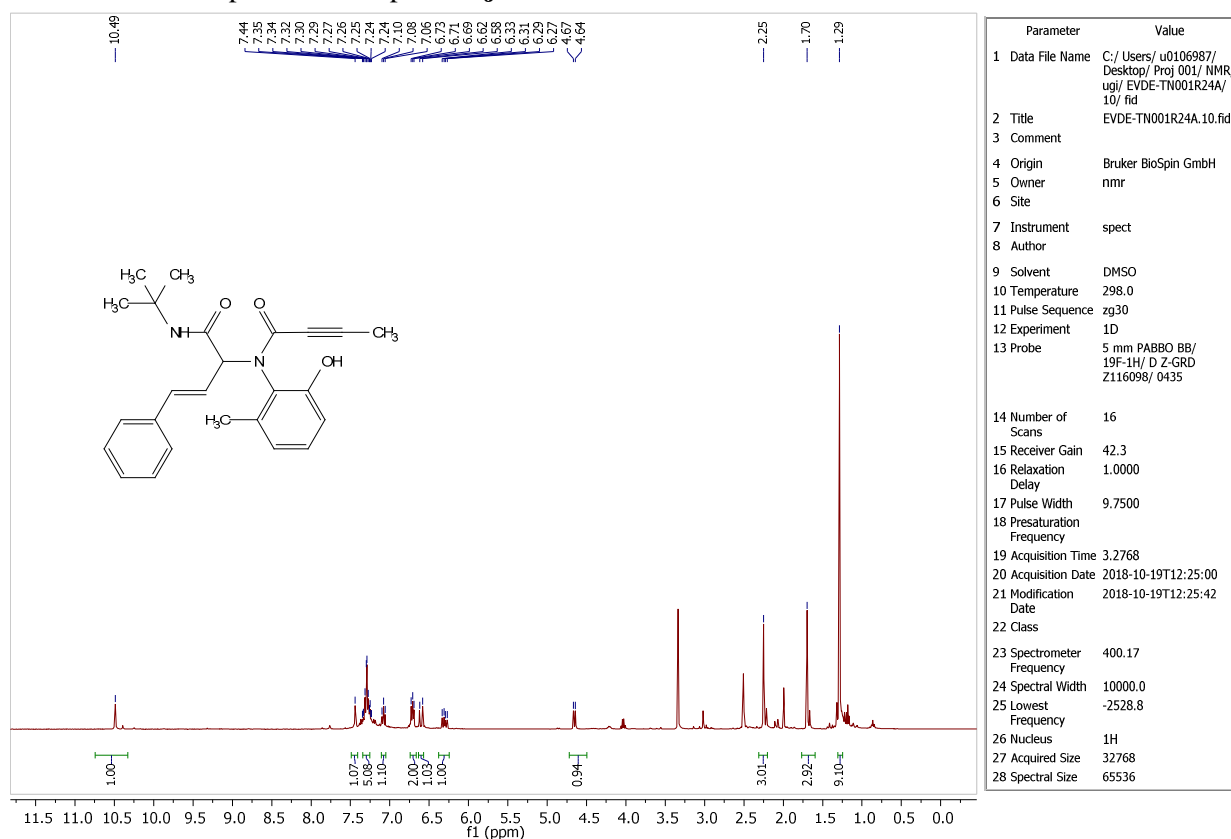
¹H and ¹³C NMR spectra of compound 1h



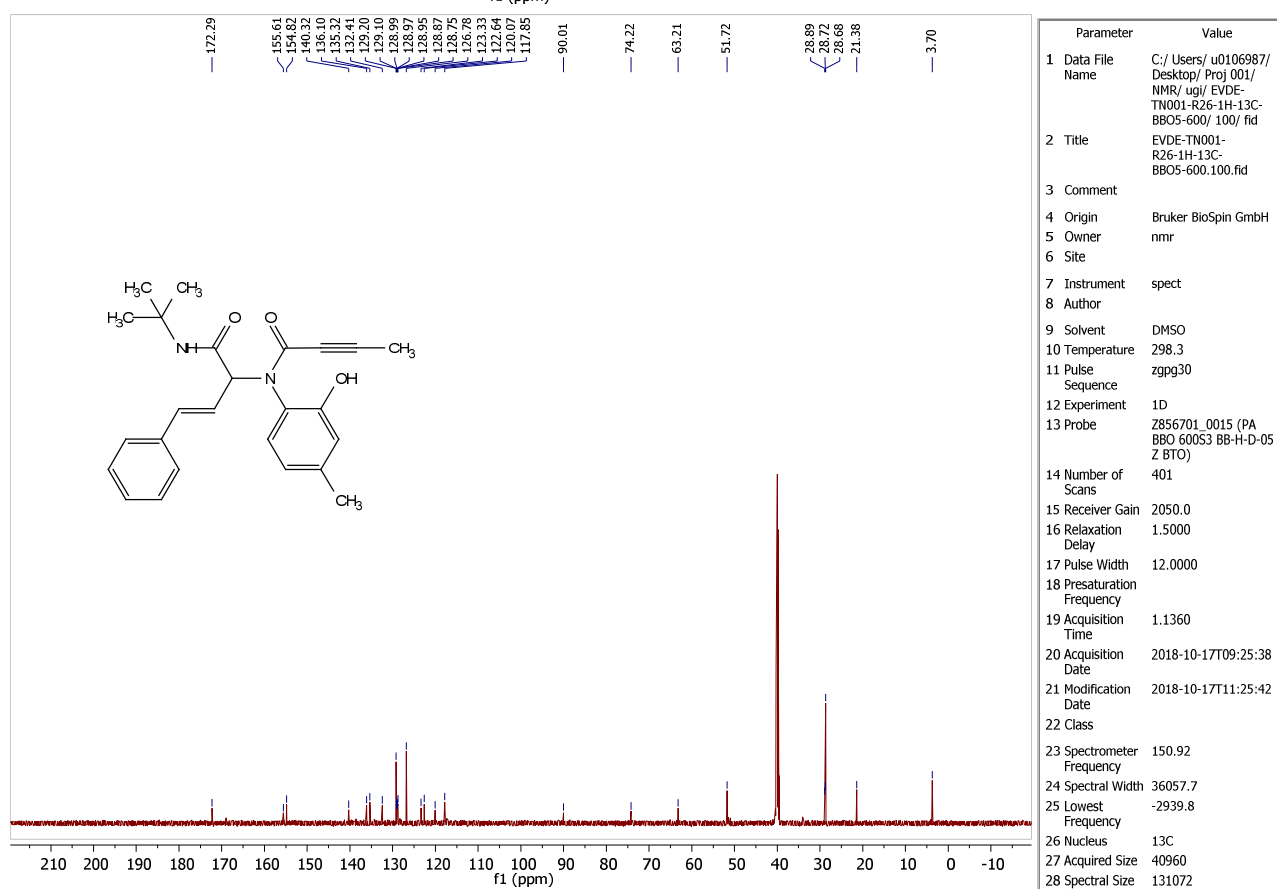
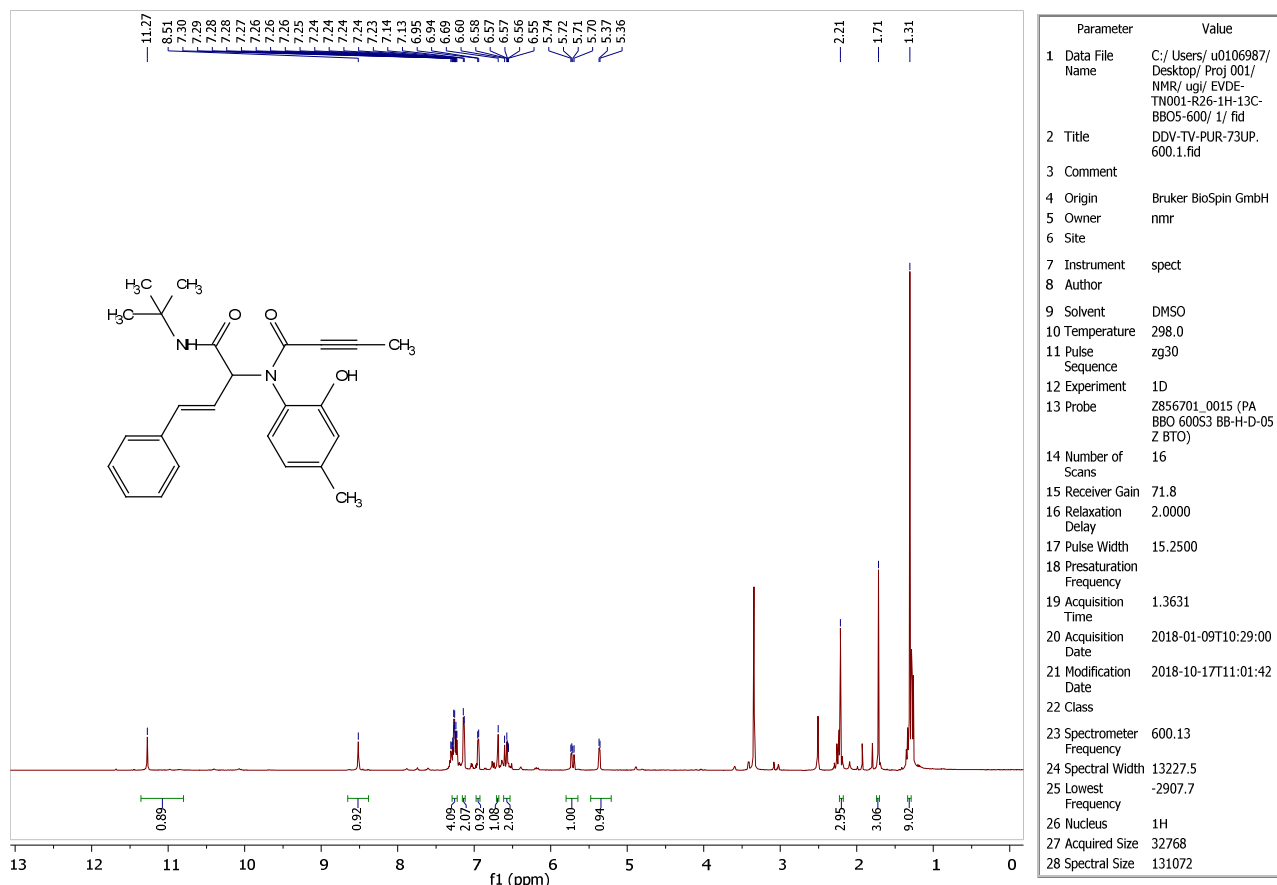
¹H and ¹³C NMR spectra of compound **1i**



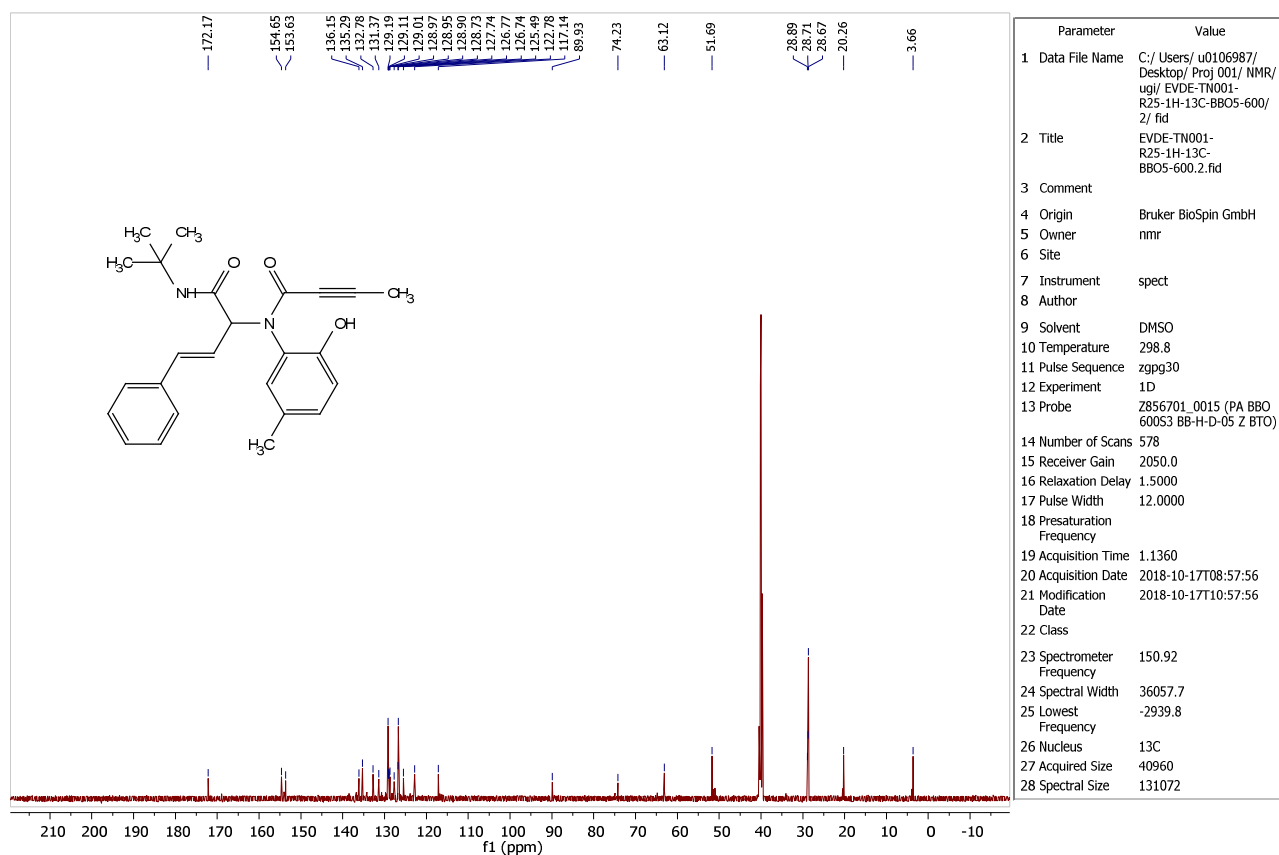
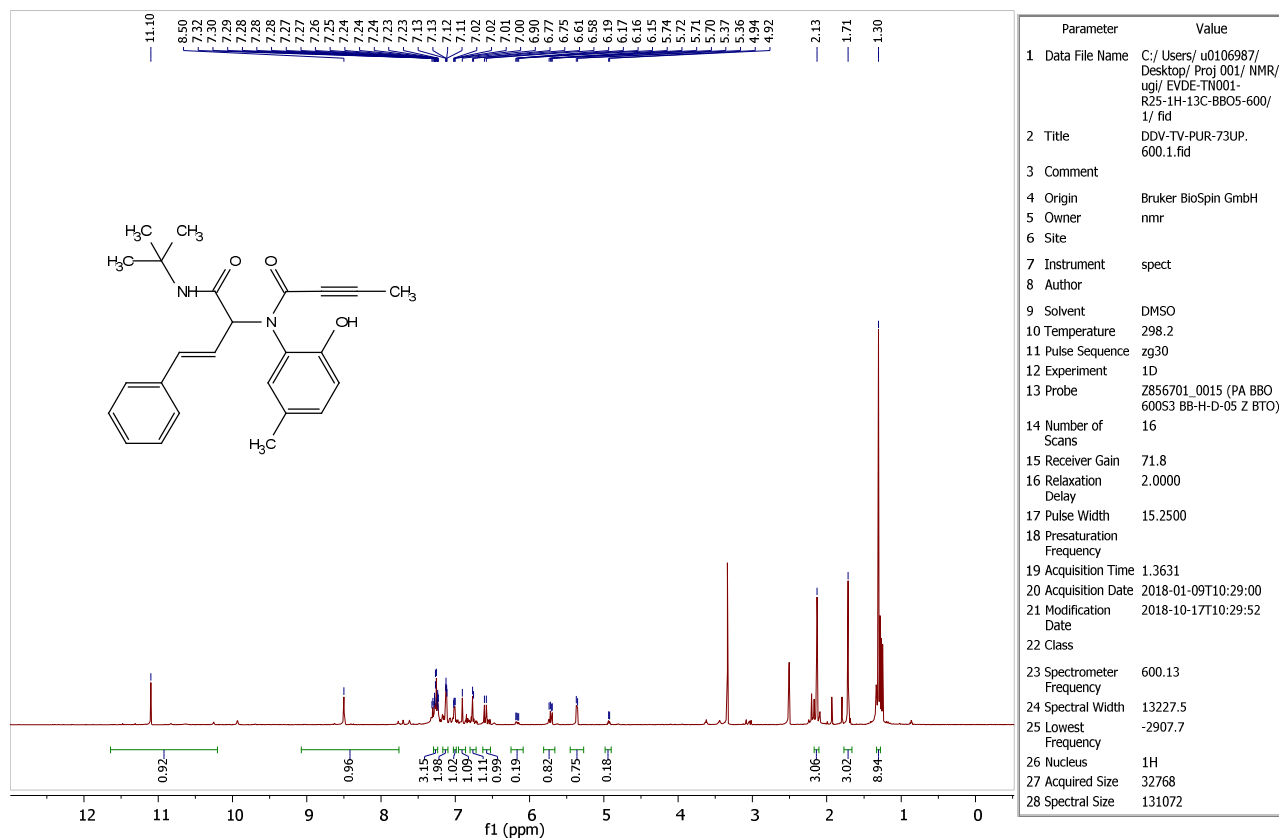
¹H and ¹³C NMR spectra of compound **1j**



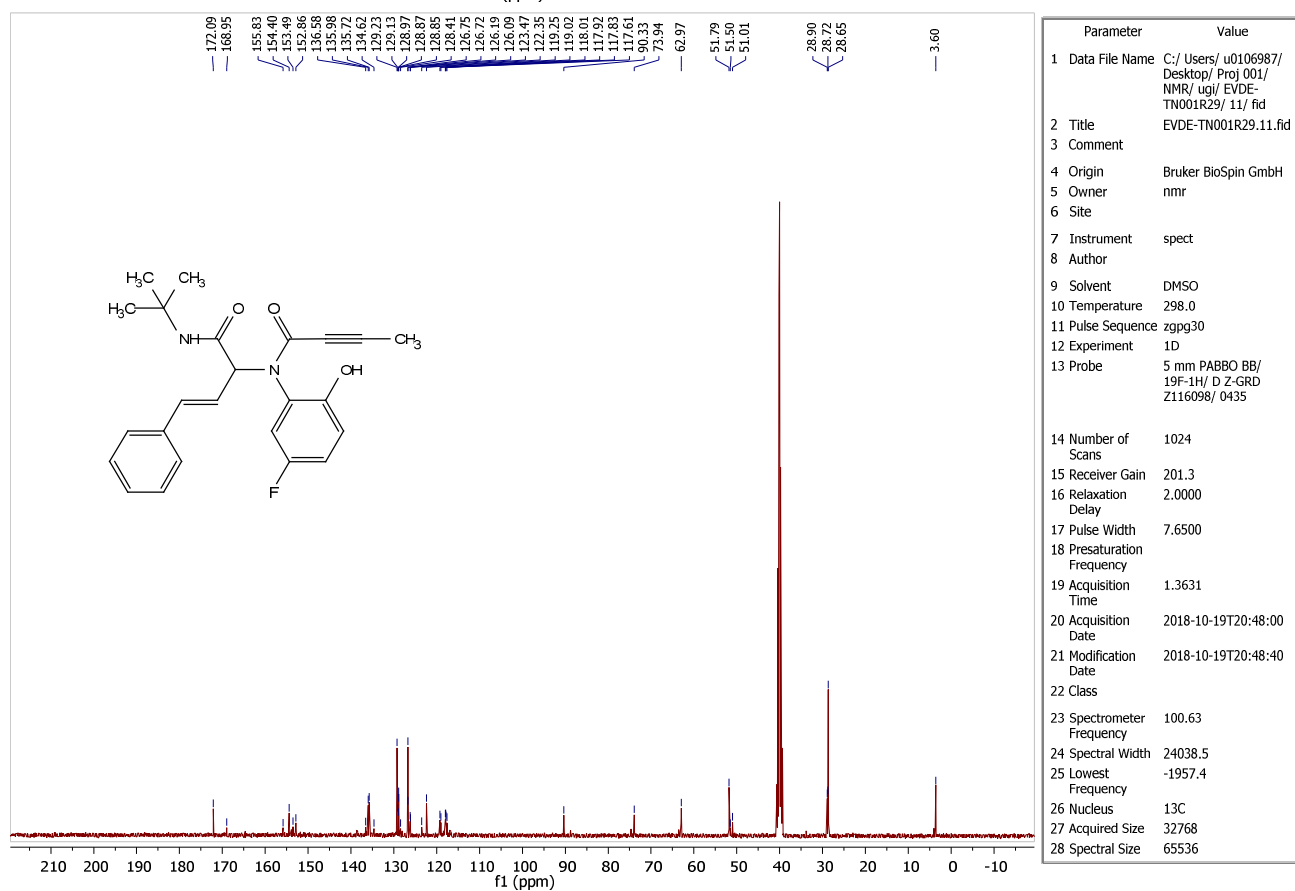
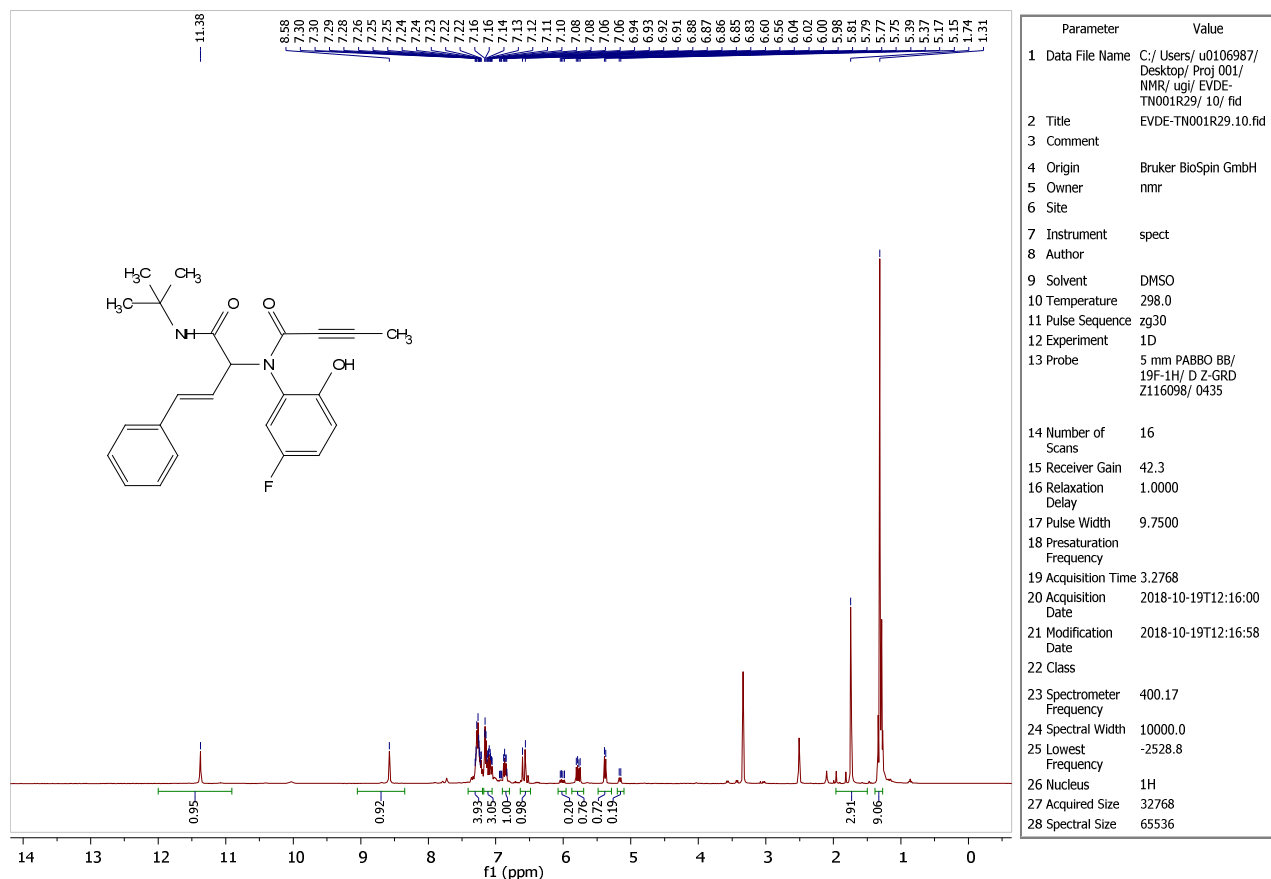
¹H and ¹³C NMR spectra of compound **1k**



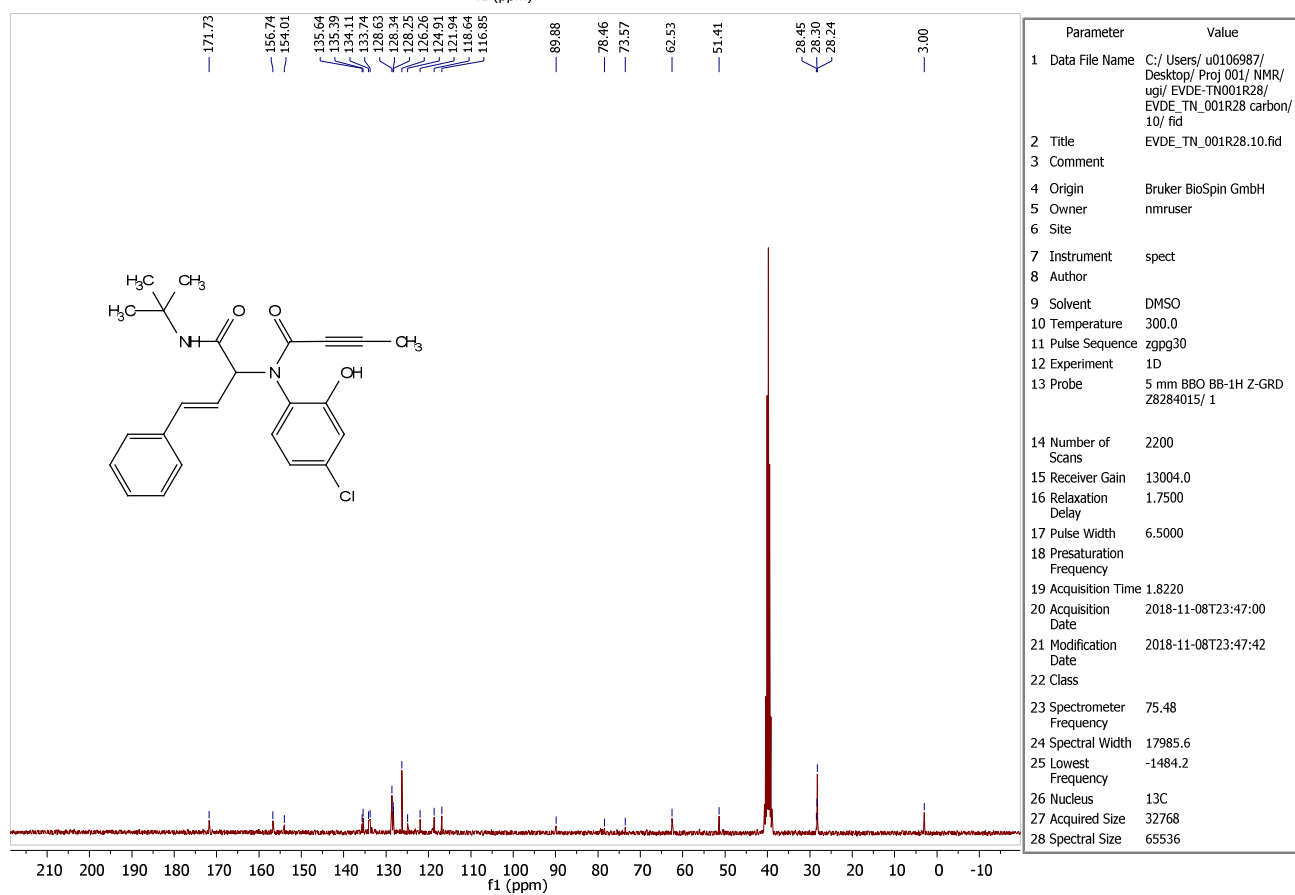
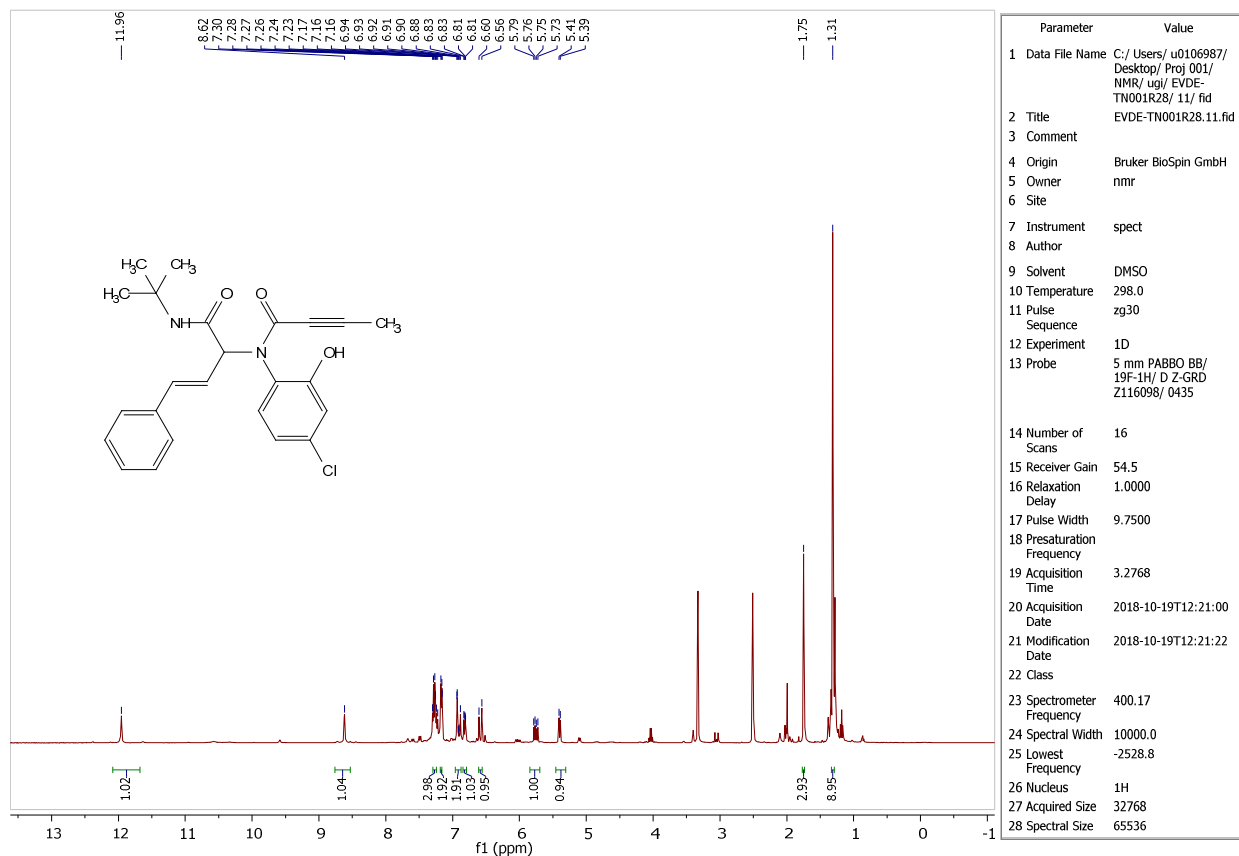
¹H and ¹³C NMR spectra of compound 11



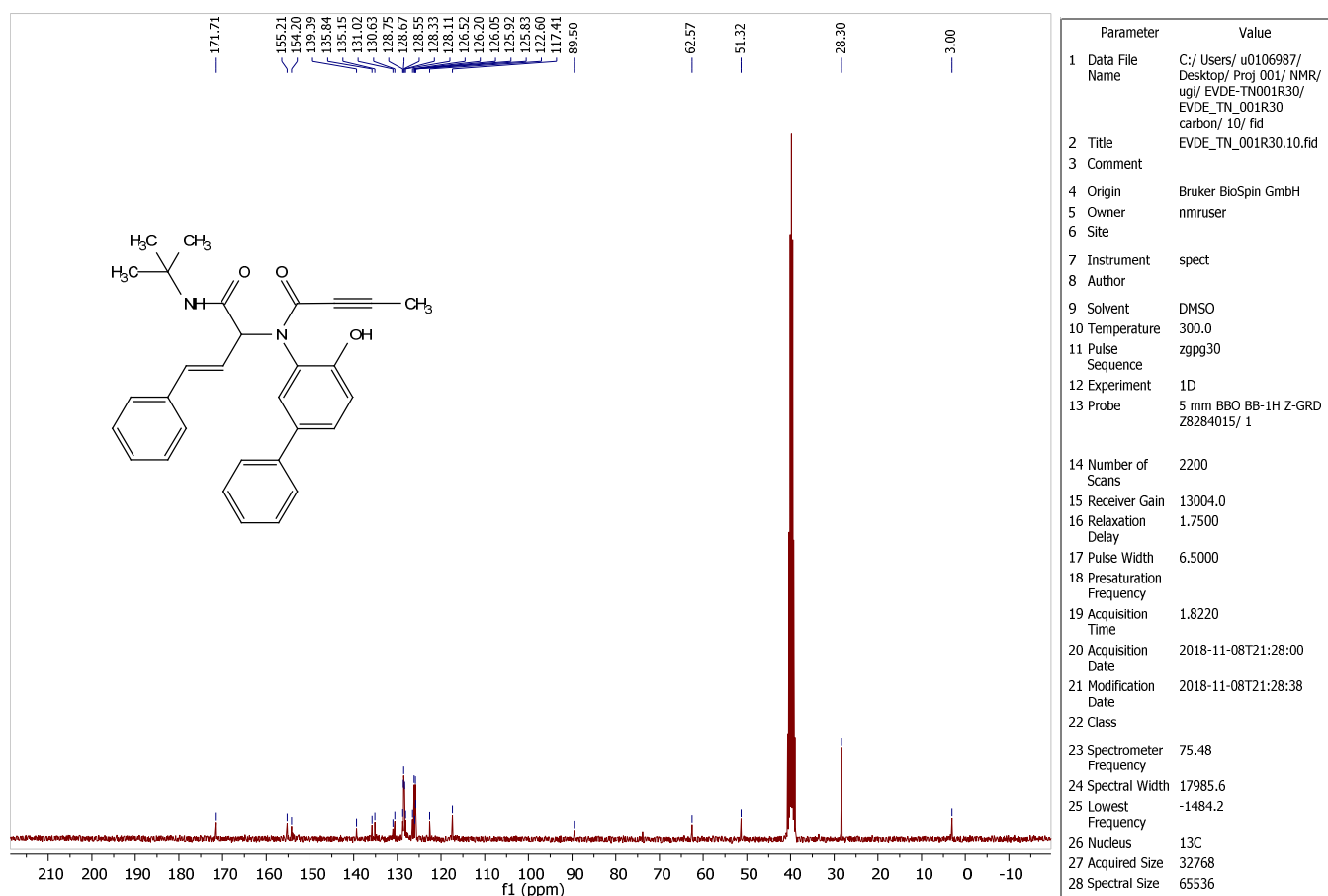
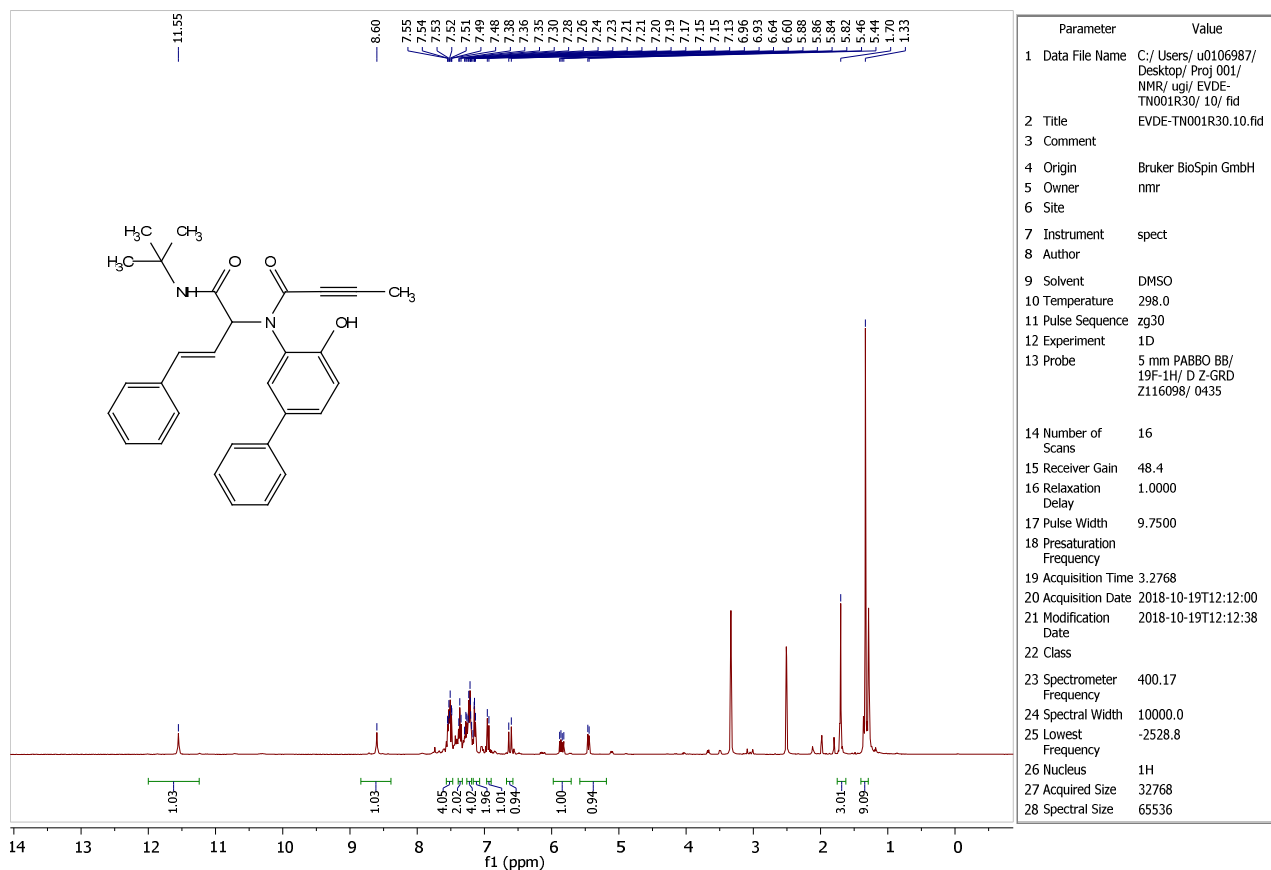
¹H and ¹³C NMR spectra of compound **1m**



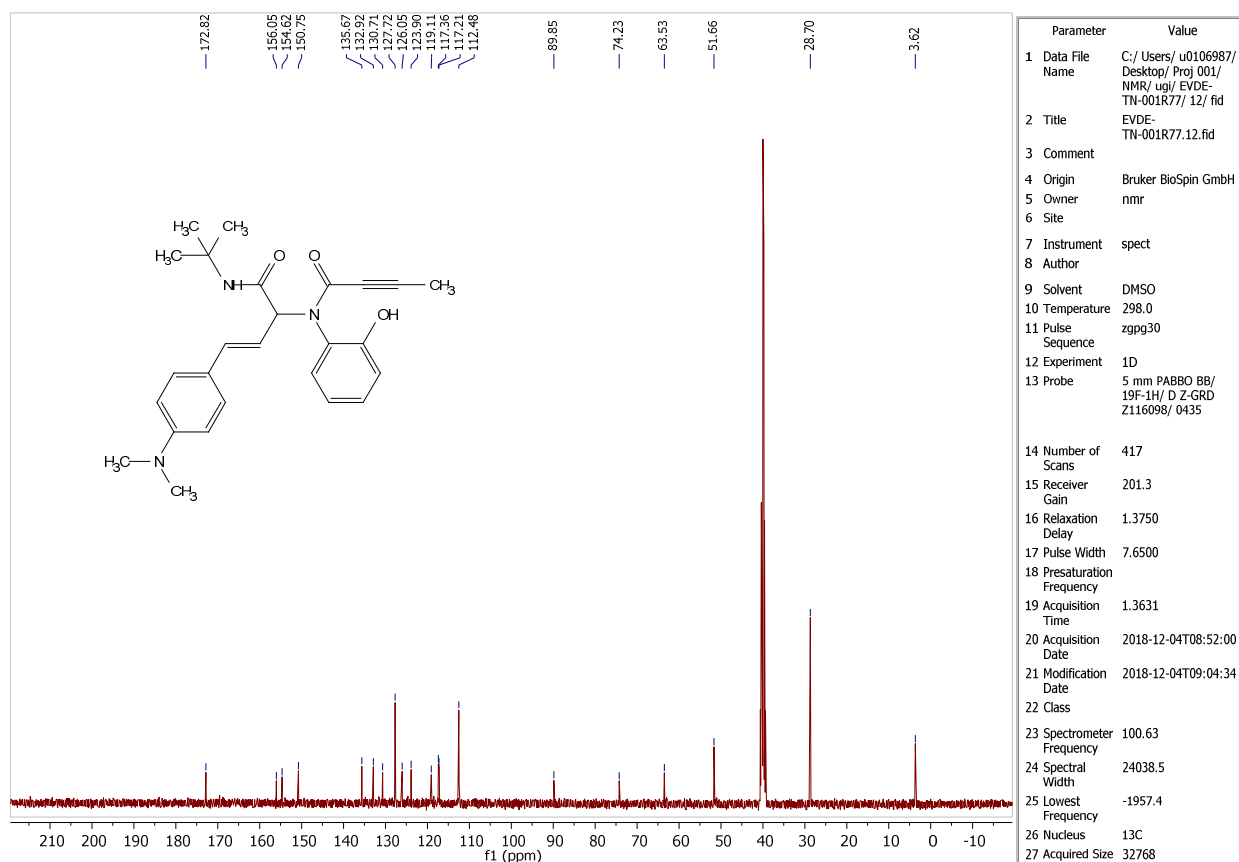
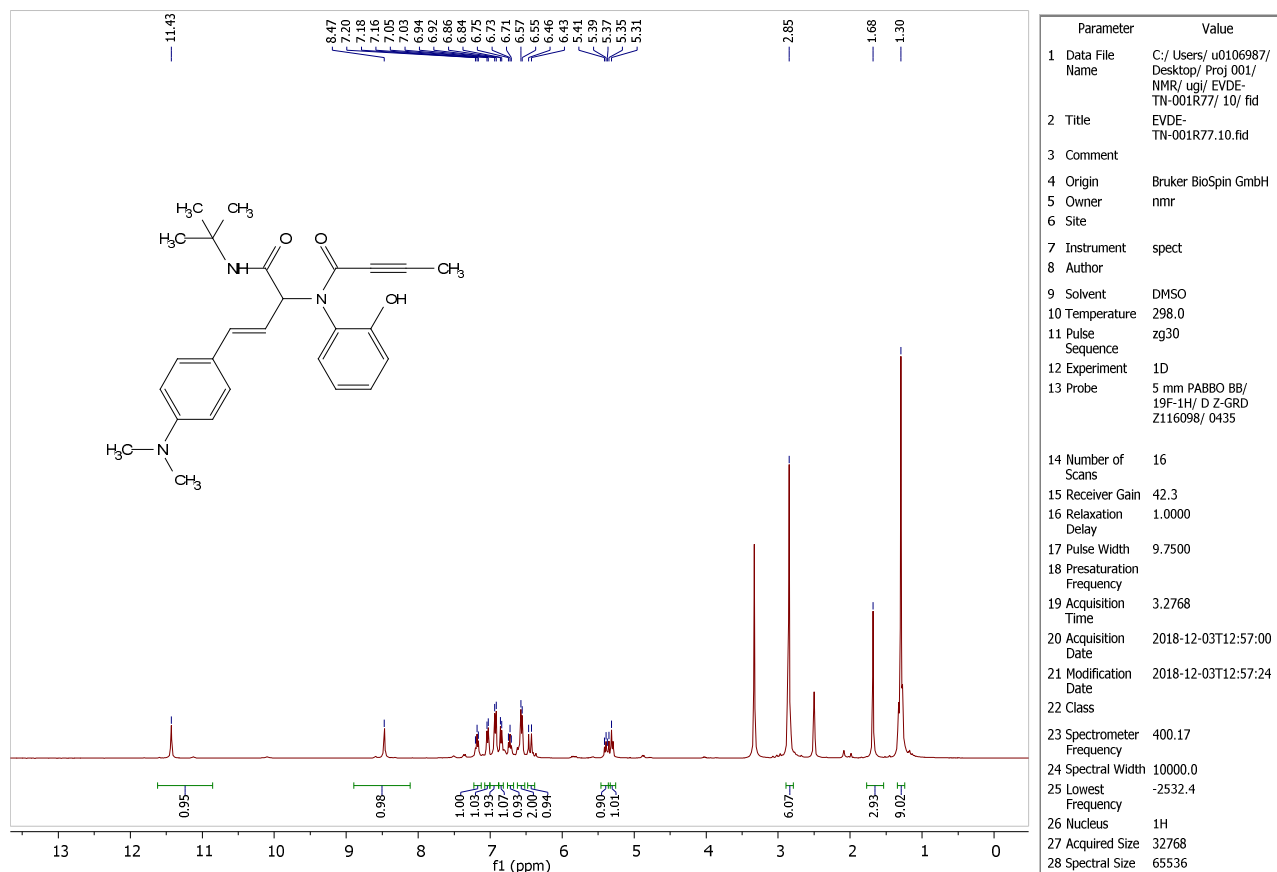
¹H and ¹³C NMR spectra of compound **1n**



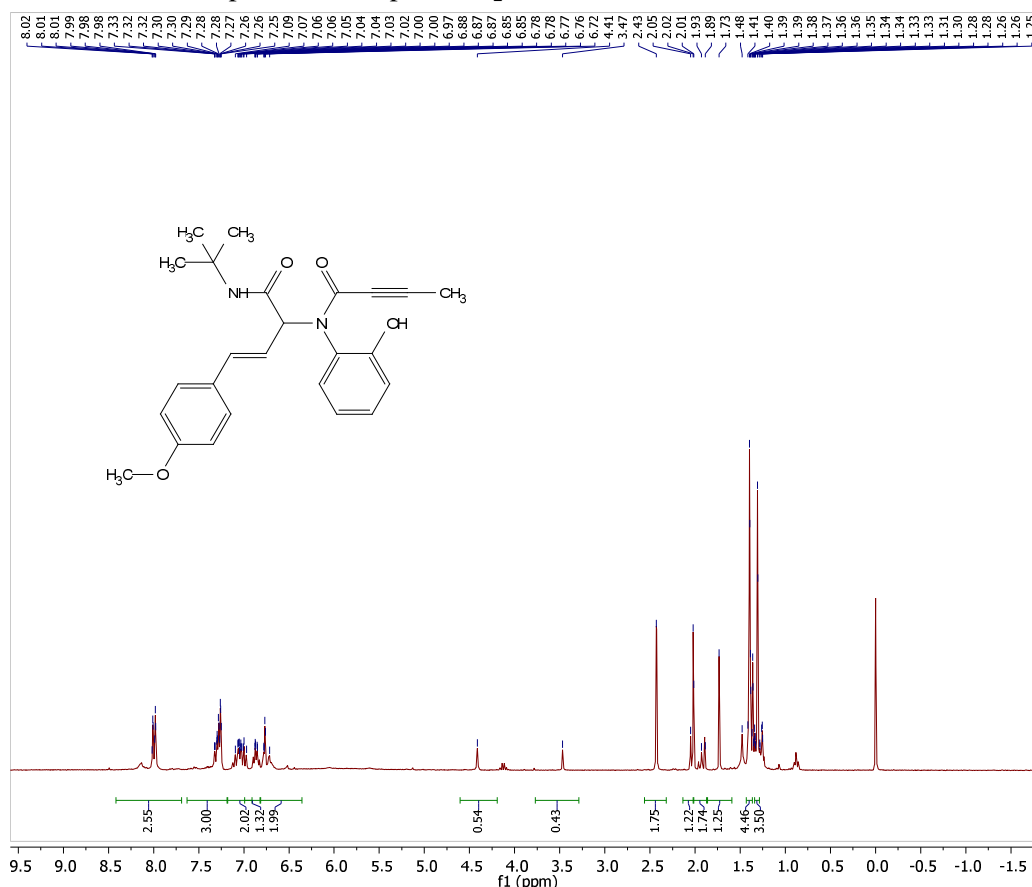
¹H and ¹³C NMR spectra of compound **10**



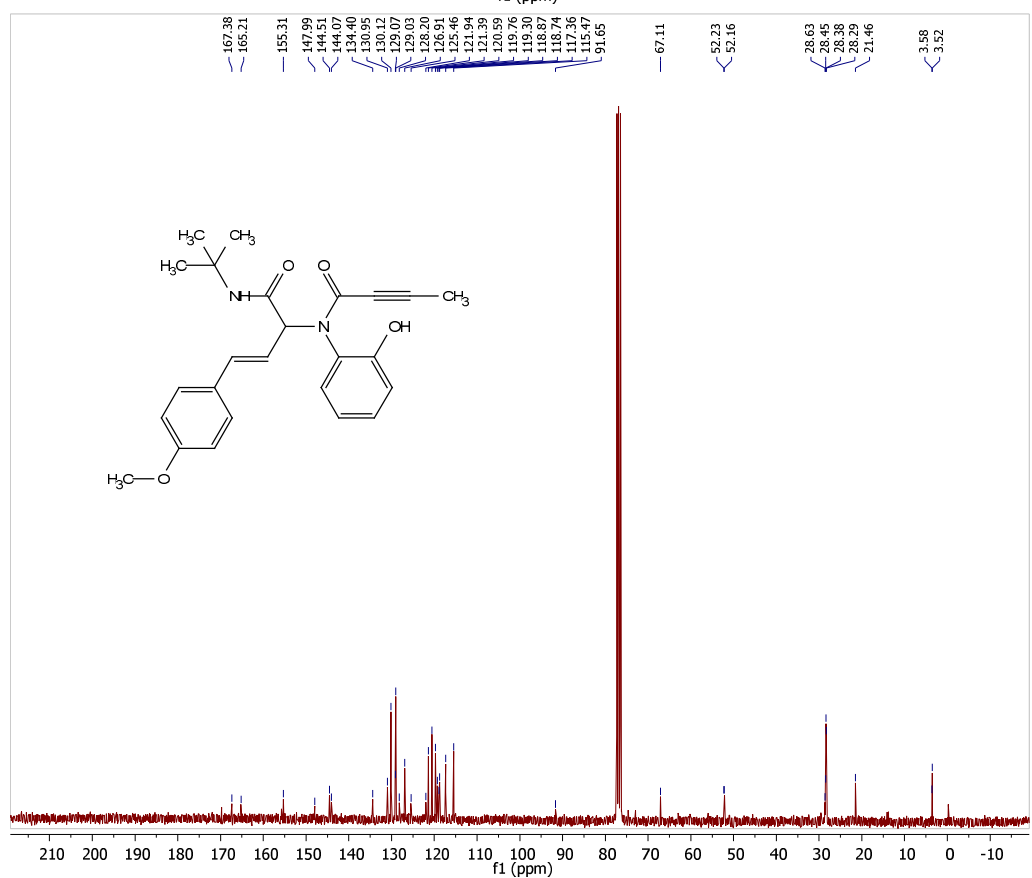
¹H and ¹³C NMR spectra of compound 1p



¹H and ¹³C NMR spectra of compound 1q

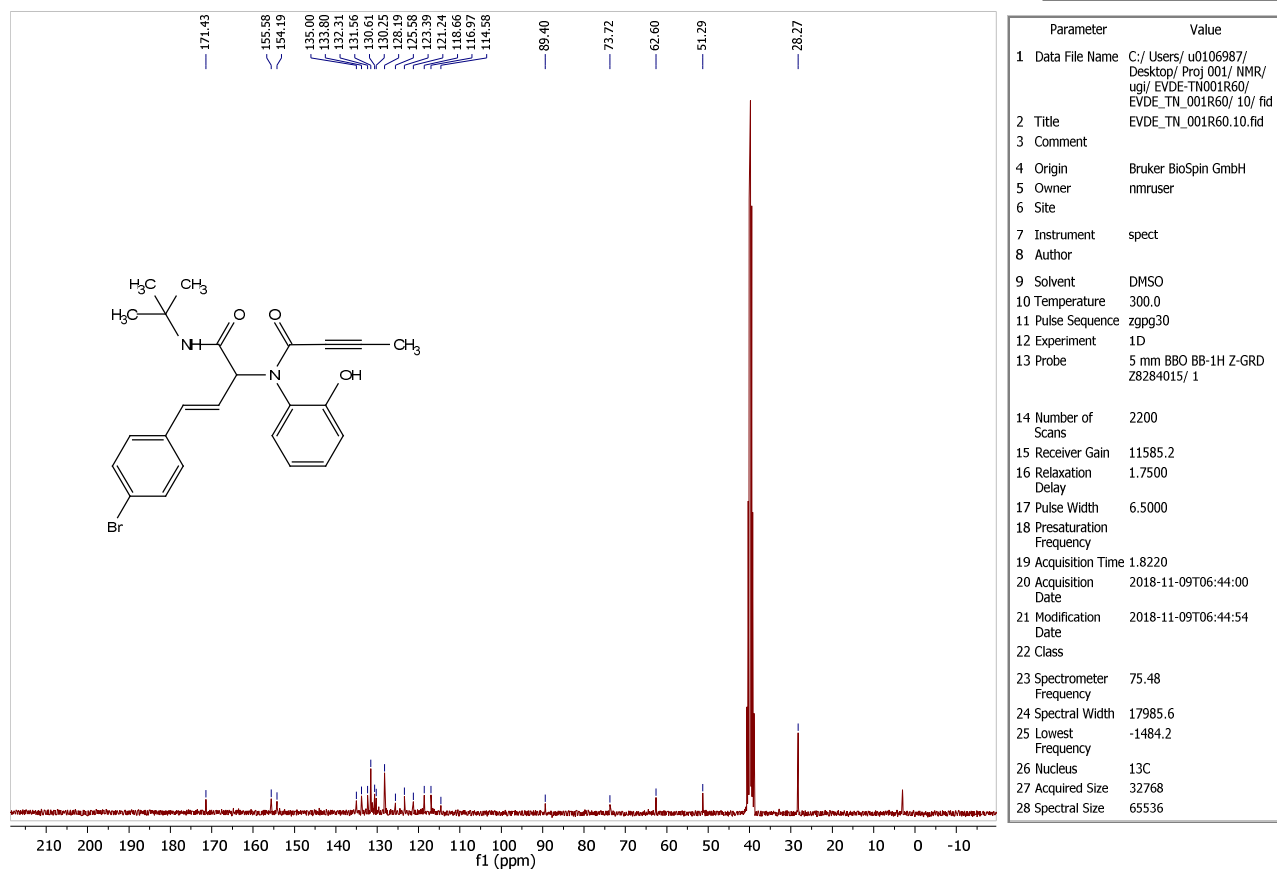
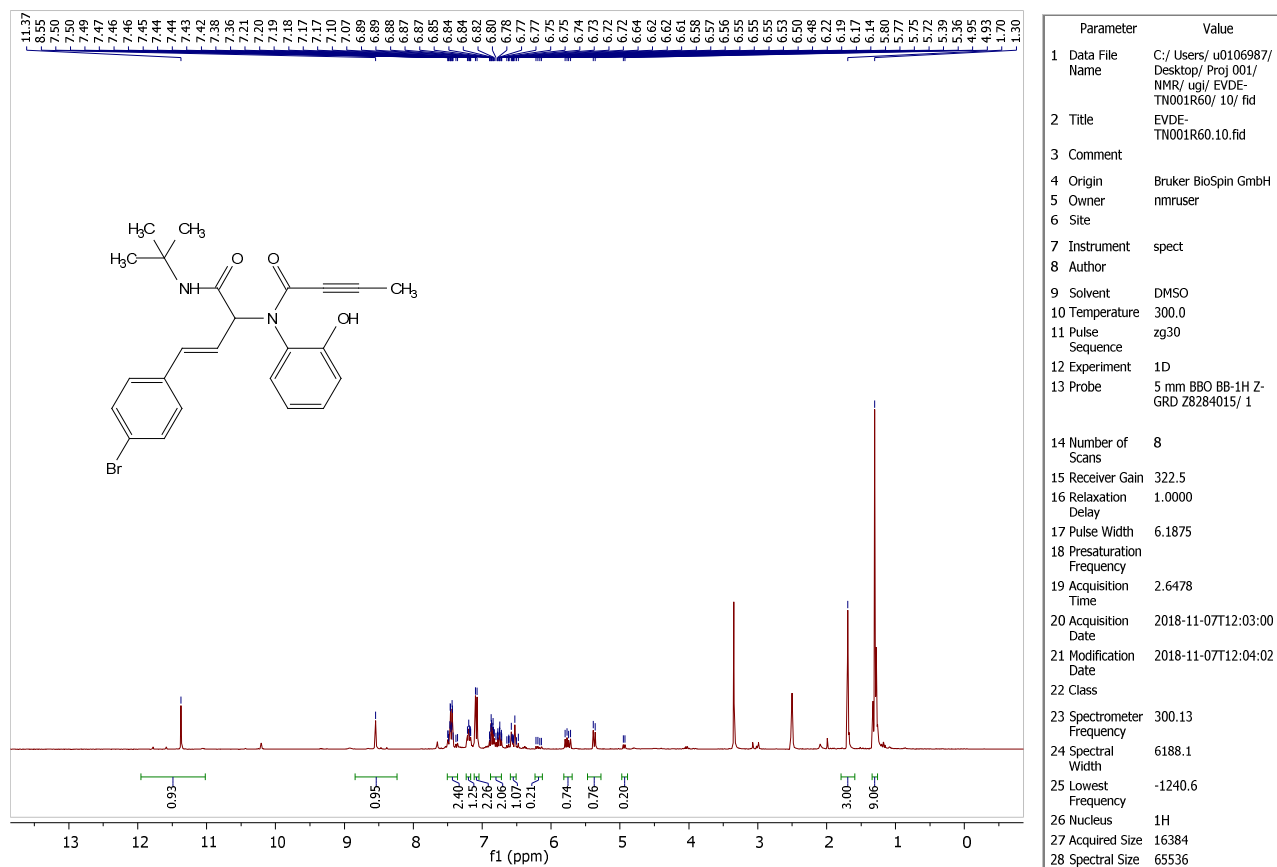


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/ugj/EVDE-TN001R71B/ 10.fid
2 Title	EVDE-TN001R71B. 10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD 28284015/ 1
14 Number of Scans	8
15 Receiver Gain	362.0
16 Relaxation Delay	1.0000
17 Pulse Width	6.1875
18 Presaturation Frequency	
19 Acquisition Time	2.6478
20 Acquisition Date	2018-11-16T17:07:00
21 Modification Date	2018-11-16T17:07:28
22 Class	
23 Spectrometer Frequency	300.13
24 Spectral Width	6188.1
25 Lowest Frequency	-1246.7
26 Nucleus	1H
27 Acquired Size	16384
28 Spectral Size	65536

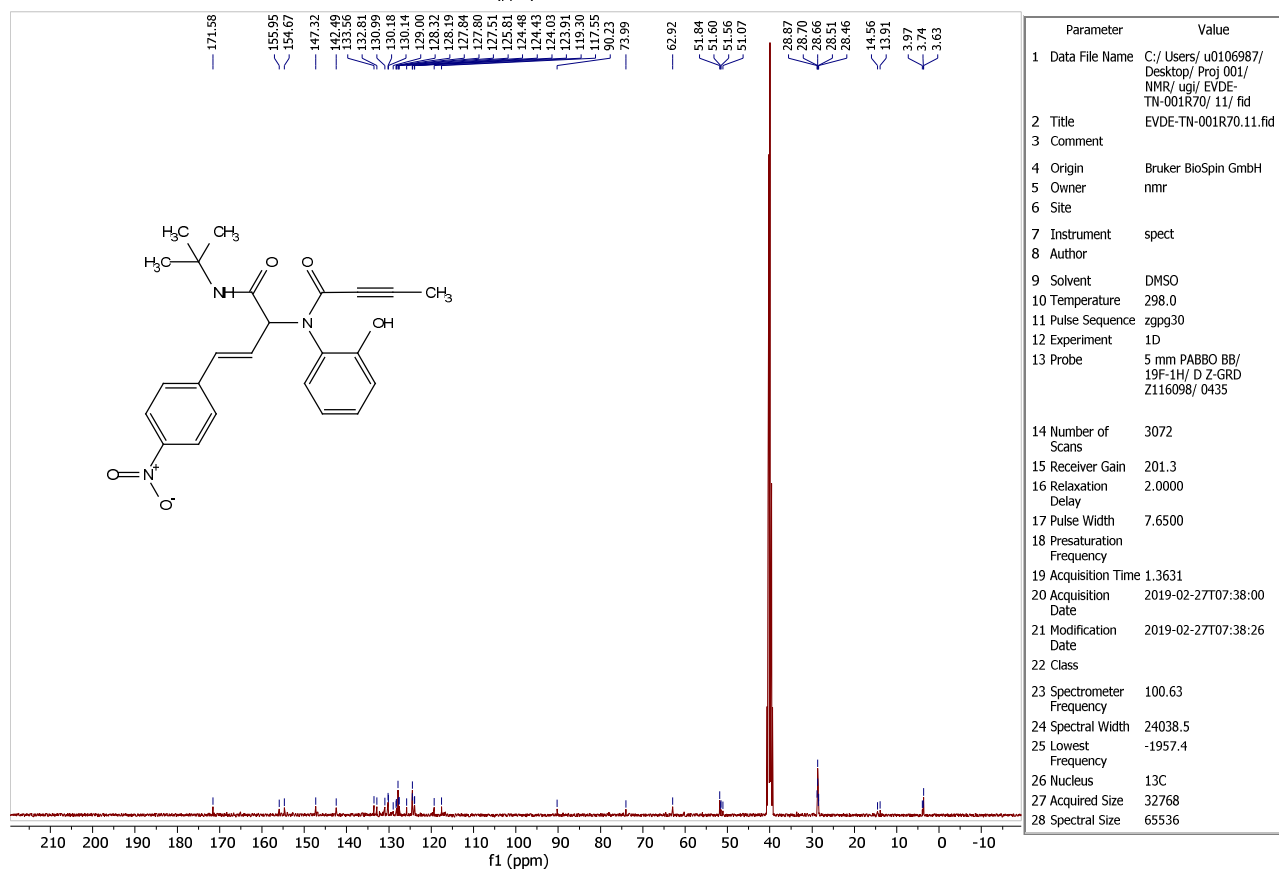
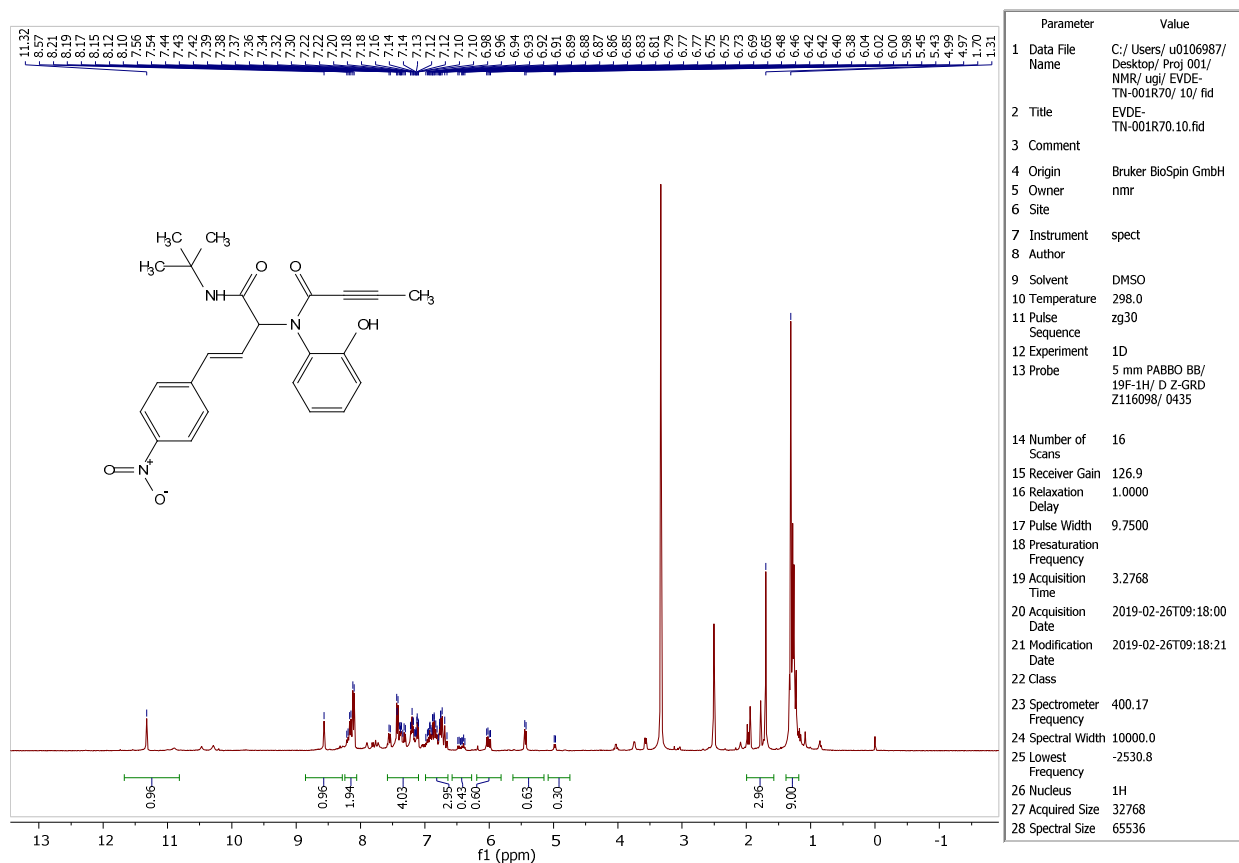


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/ugj/EVDE-TN001R71B/ 11.fid
2 Title	EVDE-TN001R71B. 11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmruser
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	300.0
11 Pulse Sequence	zgpg30
12 Experiment	1D
13 Probe	5 mm BBO BB-1H Z-GRD 28284015/ 1
14 Number of Scans	3000
15 Receiver Gain	9195.2
16 Relaxation Delay	1.7500
17 Pulse Width	6.5000
18 Presaturation Frequency	
19 Acquisition Time	1.8220
20 Acquisition Date	2018-11-18T11:54:00
21 Modification Date	2018-11-18T11:54:18
22 Class	
23 Spectrometer Frequency	75.48
24 Spectral Width	17985.6
25 Lowest Frequency	-1446.5
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

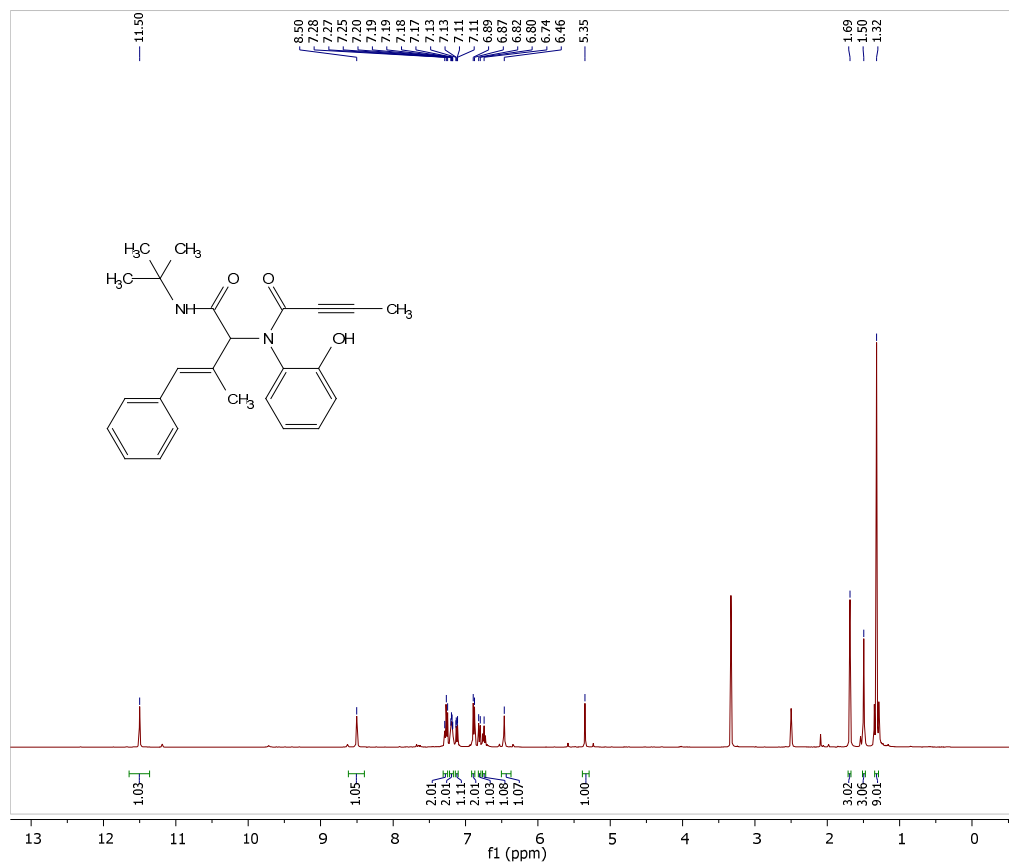
¹H and ¹³C NMR spectra of compound 1r



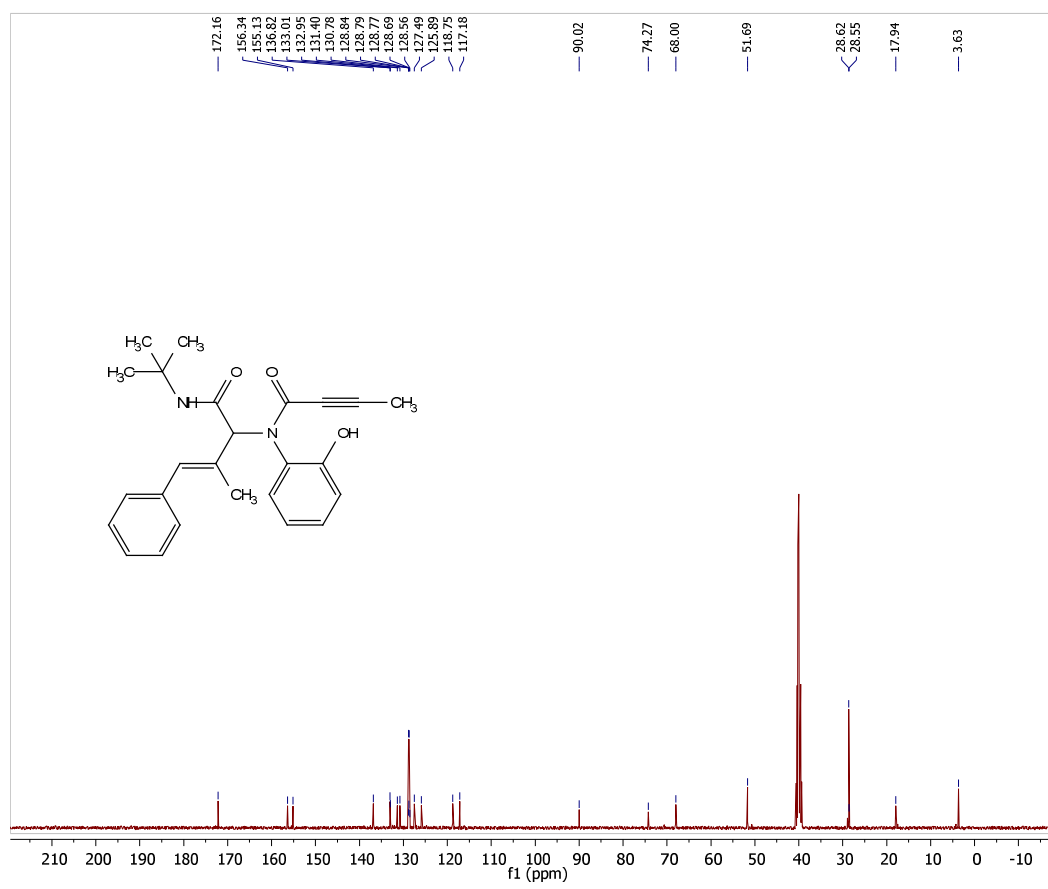
¹H and ¹³C NMR spectra of compound 1s



¹H and ¹³C NMR spectra of compound **1t**

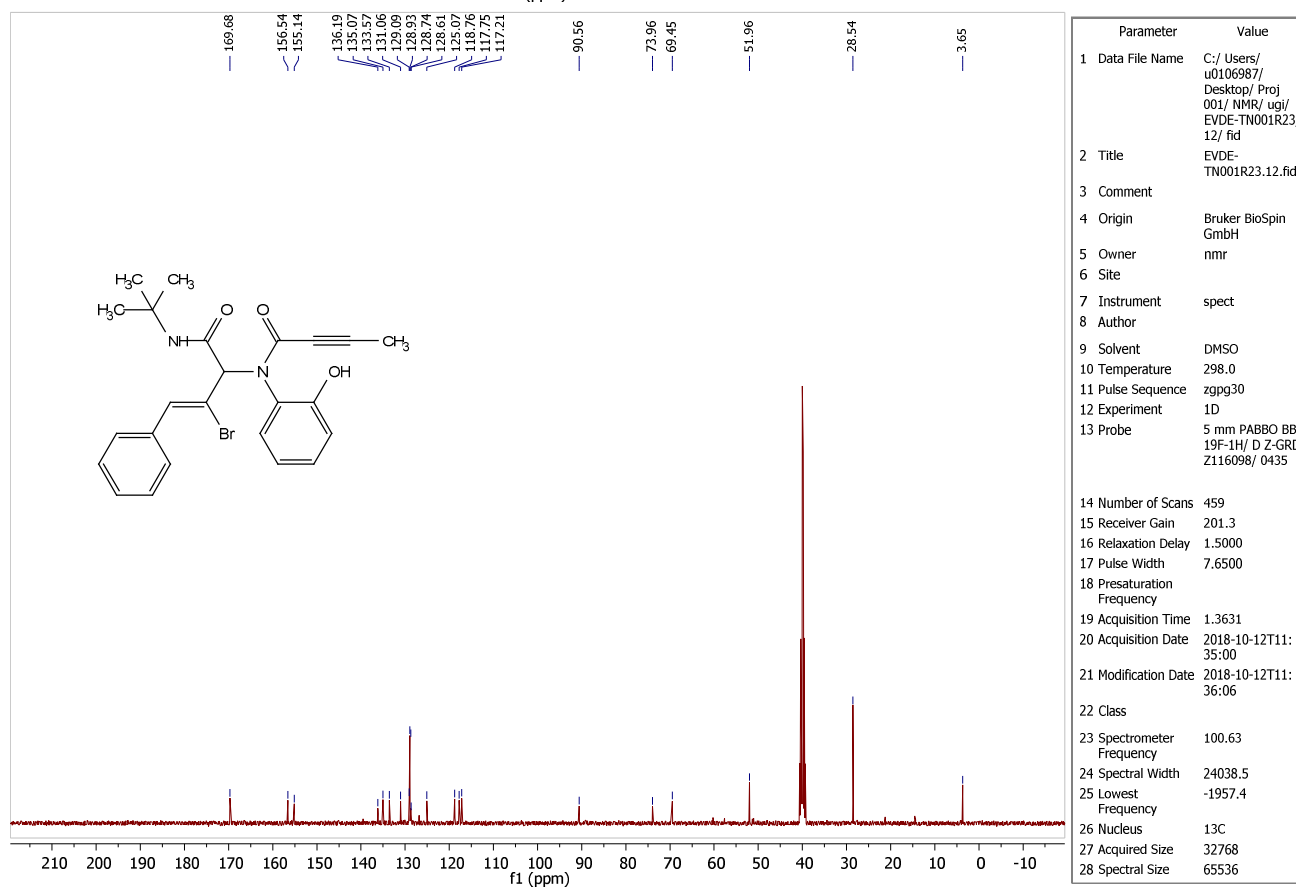
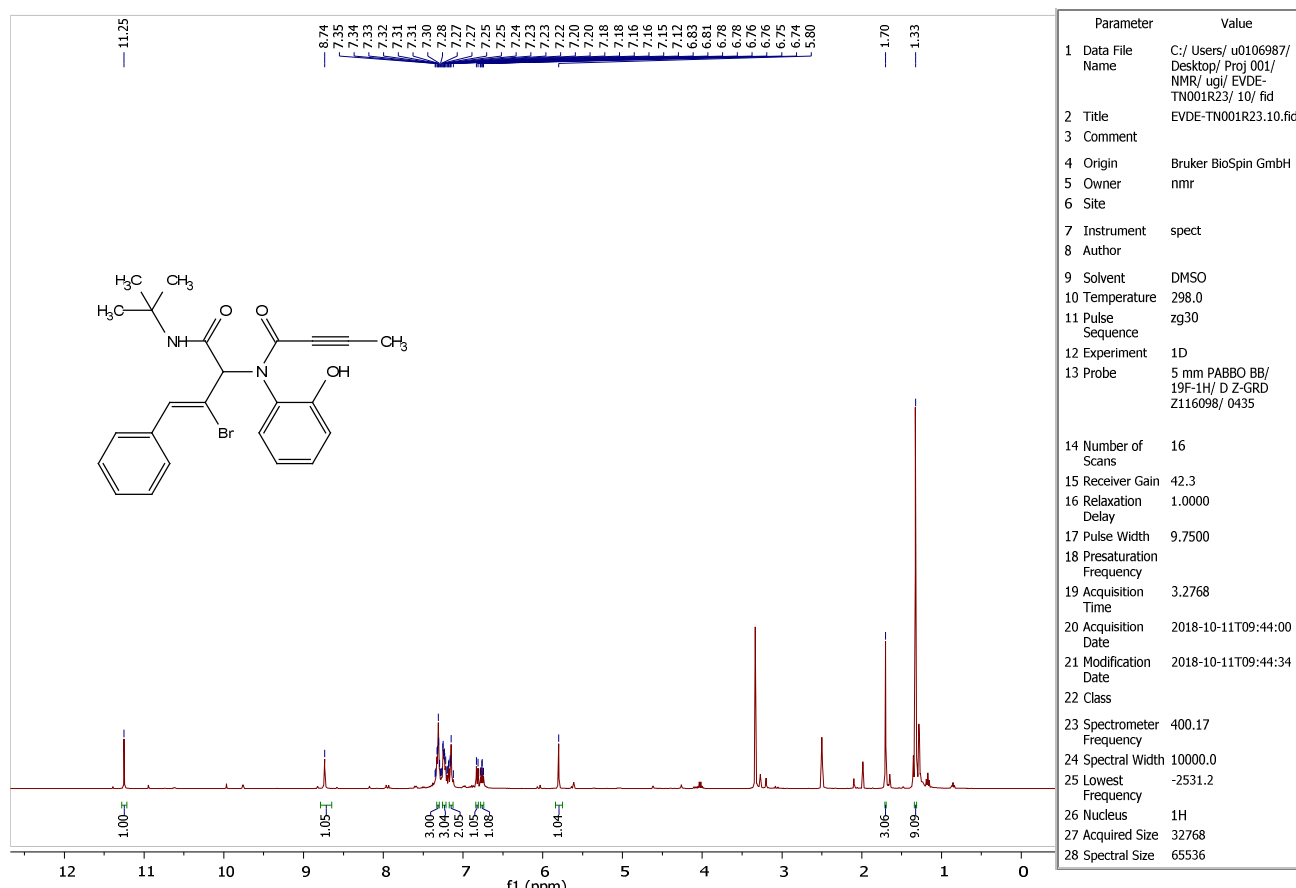


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/ugi/EVDE-TN001R22/10/ fid
2 Title	EVDE-TN001R22.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	DMSO
10 Temperature	298.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	5 mm PABBO BB/19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	16
15 Receiver Gain	42.3
16 Relaxation Delay	1.0000
17 Pulse Width	9.7500
18 Presaturation Frequency	
19 Acquisition Time	3.2768
20 Acquisition Date	2018-10-11T09:40:00
21 Modification Date	2018-10-11T09:40:52
22 Class	
23 Spectrometer Frequency	400.17
24 Spectral Width	10000.0
25 Lowest Frequency	-2531.2
26 Nucleus	1H
27 Acquired Size	32768
28 Spectral Size	65536

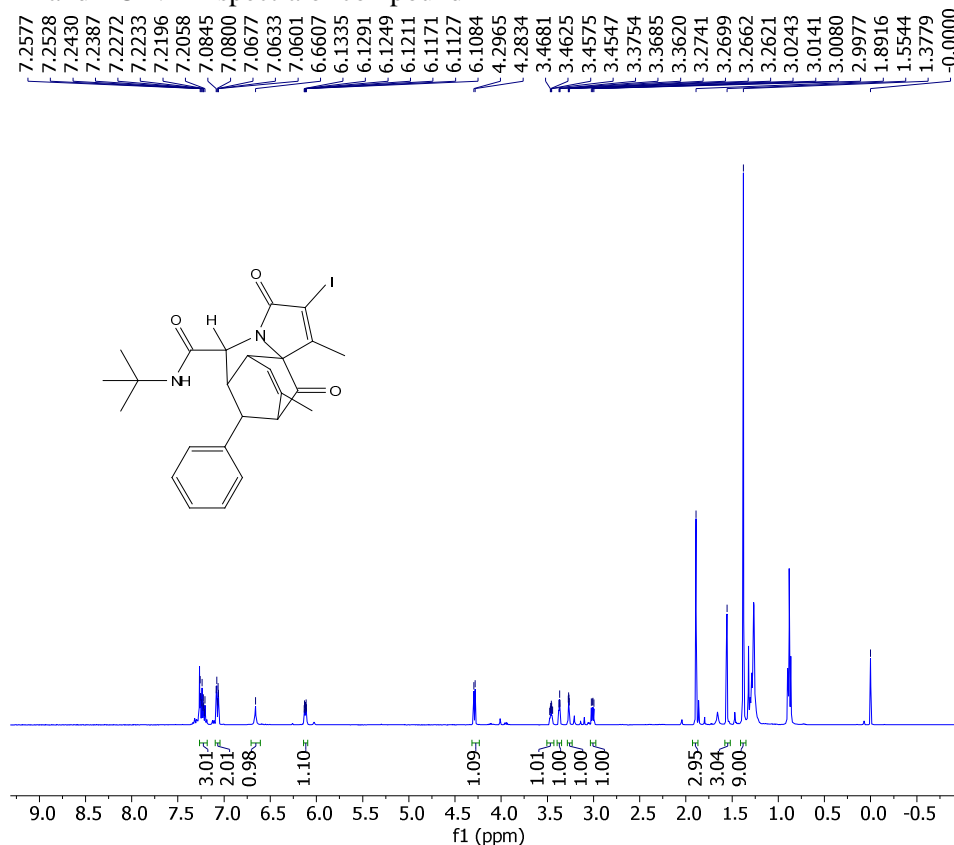


Parameter	Value
1 Data File Name	C:/Users/u0106987/Desktop/Proj 001/NMR/ugi/EVDE-TN001R22/12/ fid
2 Title	EVDE-TN001R22.12.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmr
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	DMSO
10 Temperature	298.0
11 Pulse Sequence	zpgq30
12 Experiment	1D
13 Probe	5 mm PABBO BB/19F-1H/ D Z-GRD Z116098/ 0435
14 Number of Scans	512
15 Receiver Gain	201.3
16 Relaxation Delay	1.5000
17 Pulse Width	7.6500
18 Presaturation Frequency	
19 Acquisition Time	1.3631
20 Acquisition Date	2018-10-12T09:39:00
21 Modification Date	2018-10-12T10:01:14
22 Class	
23 Spectrometer Frequency	100.63
24 Spectral Width	24038.5
25 Lowest Frequency	-1957.4
26 Nucleus	13C
27 Acquired Size	32768
28 Spectral Size	65536

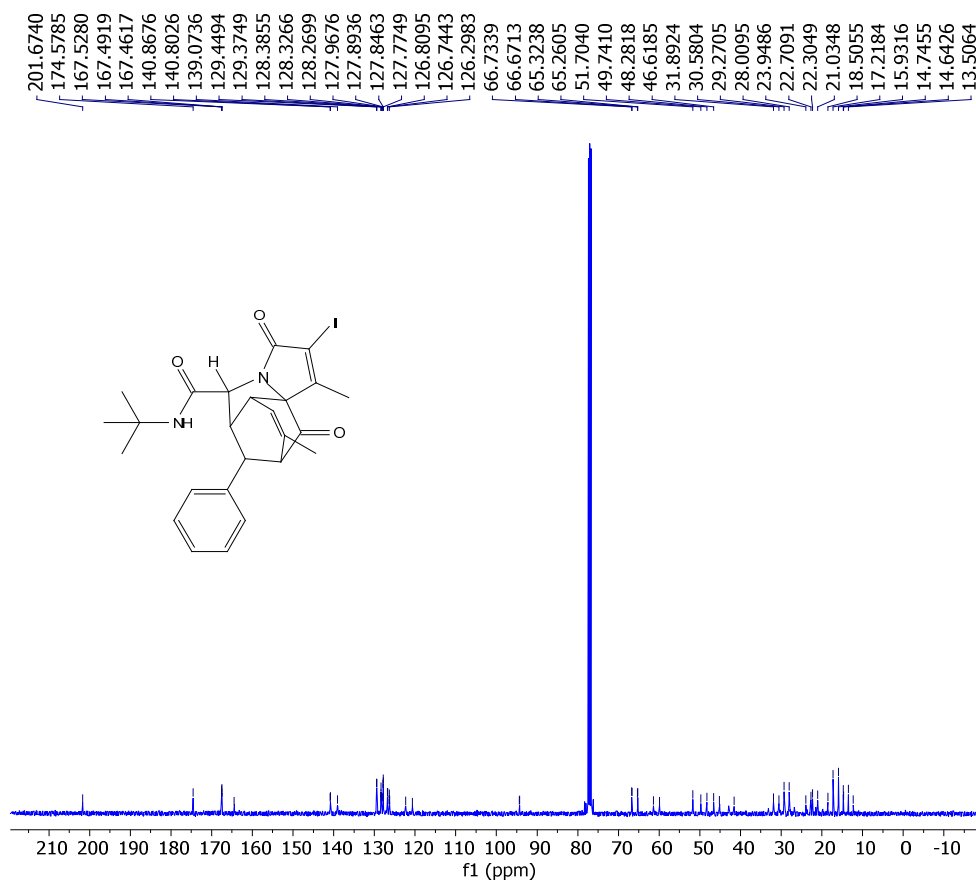
¹H and ¹³C NMR spectra of compound **1u**



¹H and ¹³C NMR spectra of compound 4



Parameter	Value
1 Data File Name	C:/Users/moke/Desktop/Project Management/ proj 001/ Manuscript and SI 0527/ OBC STYLE/ Reply to/ EVDE-YH-001AD-R7/ 10/ fid
2 Title	EVDE-YH-001AD-R7.10.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmsu
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zg30
12 Experiment	1D
13 Probe	Z116098_0435 (PA BBO 400S1 BBF-H-D-05 Z SP)
14 Number of Scans	16
15 Receiver Gain	42.3
16 Relaxation Delay	1.0000
17 Pulse Width	10.0500
18 Presaturation Frequency	
19 Acquisition Time	3.2768
20 Acquisition Date	2019-09-27T19:09:36
21 Modification Date	2019-09-27T19:09:36
22 Class	
23 Spectrometer Frequency	400.17
24 Spectral Width	10000.0
25 Lowest Frequency	-2536.2
26 Nucleus	¹ H
27 Acquired Size	32768
28 Spectral Size	65536



Parameter	Value
1 Data File Name	C:/Users/moke/Desktop/Project Management/ proj 001/ Manuscript and SI 0527/ OBC STYLE/ Reply to/ EVDE-YH-001AD-R7/ 11/ fid
2 Title	EVDE-YH-001AD-R7.11.fid
3 Comment	
4 Origin	Bruker BioSpin GmbH
5 Owner	nmsu
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	CDCl3
10 Temperature	298.0
11 Pulse Sequence	zggd30
12 Experiment	1D
13 Probe	Z116098_0435 (PA BBO 400S1 BBF-H-D-05 Z SP)
14 Number of Scans	1024
15 Receiver Gain	201.3
16 Relaxation Delay	5.0000
17 Pulse Width	7.9000
18 Presaturation Frequency	
19 Acquisition Time	1.3631
20 Acquisition Date	2019-09-29T22:01:32
21 Modification Date	2019-09-29T22:01:32
22 Class	
23 Spectrometer Frequency	100.63
24 Spectral Width	24038.5
25 Lowest Frequency	-1956.9
26 Nucleus	¹³ C
27 Acquired Size	32768
28 Spectral Size	65536