Supporting Information

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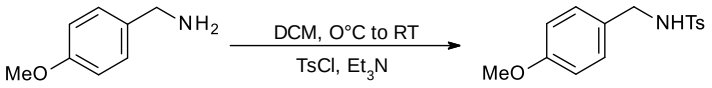
1. General Information

- All reagents and solvents were purchased from Acros or Sigma-Aldrich and used directly as received without any purification.
- Thin layer chromatography was performed on prepared thin layers precoated plates: Silica gel Merck 60 F_{254}. The visualisation of spots on TLC plates was effected by exposure to UV and/or by using basic $KMnO_4$ solution. Column chromatography was performed over Silica gel 60 (30 – 200µ mesh) using relevant eluent.
- NMR spectra were recorded on a JEOL ECA 500 spectrometer. using $CDCl_3$ and DMSO-d6 as deuterated solvents, with proton and carbon resonances at 500 MHz and 126 MHz, respectively. Coupling constants are reported and expressed in Hz, splitting patterns are designated as br (broad), s (singlet), d (doublet), dd (double doublet), q (quartet), dt (double triplet), ddd (doublet of doublet of doublet), m (multiplet). Structures of known compounds were confirmed by comparison with data reported in literature.
- NMR Fourier transform, integration and pick picking were done with MestReNova software or ACD NMR software.
- Infrared spectra were recorded on Shimadzu FTIR-8400S spectrometer and the absorption bands are reported in reciprocal centimetres (cm^{-1}).

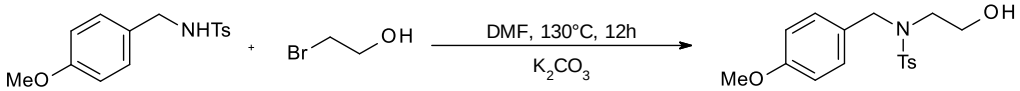
Elemental analysis was performed on a UNICUBE® trace ORGANIC ELEMENTAL ANALYZER

2. Synthesis of starting materials



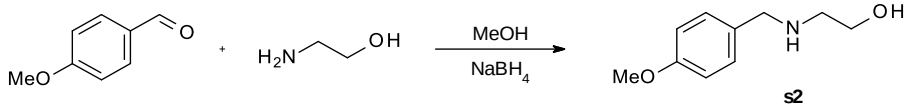
s1

N-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide (s1). A 250 mL round bottom flask wash charged with *p*-methoxybenzylamine (21 mmol, 1.05 equiv., 2.8 mL), Et_3N (24 mmol, 1.2 equiv., 3.3 mL), DCM (100mL) and chilled with an ice bath. Then TsCl (20 mmol, 3.81 g) was added and the mixture was stirred overnight. The reaction mixture was washed with 5% H_2SO_4, water and 50% brine, dried with $MgSO_4$, the solvent was evaporated and the residue dried in vacuum to afford the desired product as a white solid. Yield 5.77g (99%). **^{1}H ^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.76 (d, *J*=8.0 Hz, 2 H), 7.32 (d, *J*=8.0 Hz, 2 H), 7.11 (d, *J*=8.6 Hz, 2 H), 6.80 (d, *J*=8.6 Hz, 2 H), 4.55 (t, *J*=5.7 Hz, 1 H), 4.05 (d, *J*=6.3 Hz, 2 H), 3.77 (s, 3 H), 2.44 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 159.2, 143.4, 136.8, 129.7, 129.2, 128.2, 127.1, 114.0, 55.2, 46.7, 21.5 ppm. The analytical data matched those reported in the literature.[1]



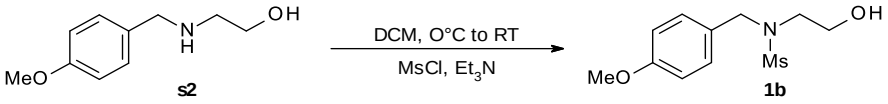
s1 **1a**

N-(2-hydroxyethyl)-N-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide (1a). A 25 mL round bottom flask was charged with *N*-tosyl- *p*-methoxymenzylamine (**s1**) (6 mmol, 1.749 g), grinded K_2CO_3 (12 mmol, 2 equiv., 1.66g), DMF (10 mL) and bromoethanol (12mmol, 2 equiv, 1.45 ml). The mixture was stirred at 130°C for 12 hours, then after cooling down water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated. The residue was subjected to column chromatography on silica gel, eluting with hexane/ethyl acetate 1:1 then 1:2. Yield 1.702 g (85%) white powder. **M.p.** 69.2-70.5°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.73 (d, *J*=8.6 Hz, 2 H), 7.33 (d, *J*=8.0 Hz, 2 H), 7.20 (d, *J*=8.6 Hz, 2 H), 6.84 (d, *J*=8.6 Hz, 2 H), 4.27 (s, 2 H), 3.79 (s, 3 H), 3.46 (q, *J*=5.4 Hz, 2 H), 3.19 (t, *J*=5.5 Hz, 2 H), 2.44 (s, 3 H), 1.98 ppm (t, *J*=5.7 Hz, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 159.3, 143.6, 135.9, 129.8, 129.7, 128.0, 127.2, 114.1, 61.0, 55.2, 53.0, 50.4, 21.5 ppm. **IR** (neat): ν = 3542, 2964, 1611, 1512, 1324, 1248, 1156 1032 cm^{-1}. **Elemental analysis** found: C, 61.2; H, 5.8; N, 4.5; S, 9.6. Calc. for $C_{17}H_{21}NO_4S$: C, 60.9; H, 6.3; N, 4.2; S, 9.6%.



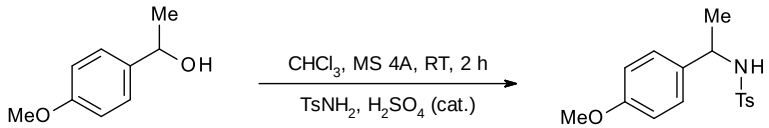
s2

2-[(4-methoxyphenyl)methylamino]ethanol (s2). The mixture of *p*-methoxybenzaldehyde (50 mmol, 6.8 g, 6.1 mL) and ethanolamine (75 mmol, 1.5 equiv, 4.58 g, 4.5 mL) in methanol (50 mL) was stirred at ambient temperature for 4 hours, then cooled with an ice bath and $NaBH_4$ (100 mmol, 2 equiv., 3.80 g) was added portionwise and the mixture was stirred overnight. Then most of the solvent was removed on a rotary evaporator, the reaction mixture was quenched with water, then diluted H_2SO_4 was added until pH 1. The aqueous phase was extracted with DCM (the organic phase was disposed), then neutralized with solid $NaHCO_3$ (careful) and the pH was adjusted to 12 with NaOH. The aqueous phase was extracted with diethyl ether, the combined ether extracts were washed with brine, dried with $MgSO_4$, evaporated and dried in vacuum. Yield 6.90 g (76%), colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.22 (d, *J*=8.6 Hz, 2 H), 6.86 (d, *J*=8.6 Hz, 2 H), 3.79 (s, 3 H), 3.72 (s, 2 H), 3.63 (t, *J*=5.2 Hz, 2 H), 2.76 (t, *J*=5.2 Hz, 2 H), 2.35 ppm (br. s, 2 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 158.7, 132.1, 129.3, 113.8, 60.8, 55.2, 52.9, 50.4 ppm. The analytical data matched those reported in the literature.[2]



s2 **1b**

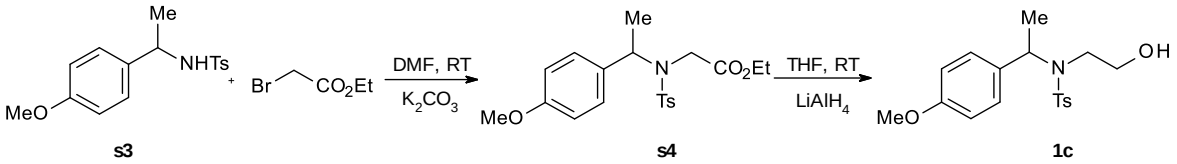
***N*-(2-hydroxyethyl)-N-[(4-methoxyphenyl)methyl]methanesulfonamide (1b)**. The mixture of 2-[(4-methoxyphenyl)methylamino]ethanol (**s2**) (3.76 mmol, 682 mg) and Et_3N (4 mmol, 405 mg, 0.55 mL) in DCM (20 mL) was chilled with an ice bath and MsCl (3.42 mmol, 392 mg, 0.26 ml) was added dropwise and the mixture was stirred overnight. The reaction mixture was diluted with DCM, washed with 5% H_2SO_4, water, 50% brine and dried with MgSO4. The solvent was removed under reduced pressure and the residue was subjected to column chromatography on silica gel, eluting with hexane/ethyl acetate 1:1 to 1:2 then pure EA. Yield 236 mg (27%), white solid. **M.p.** 65.0-66.7°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.28 (d, *J*=8.6 Hz, 2 H), 6.88 (d, *J*=8.6 Hz, 2 H), 4.38 (s, 2 H), 3.80 (s, 3 H), 3.62 (t, *J*=5.5 Hz, 2 H), 3.33 (t, *J*=5.2 Hz, 2 H), 2.90 (s, 3 H), 2.13 ppm (br. s, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 159.4, 129.8, 127.7, 114.2, 60.3, 55.3, 51.2, 49.2, 38.7 ppm. **IR** (neat): ν = 3485, 3358, 2931, 1610, 1512, 1315, 1246, 1137 cm^{-1}. **Elemental analysis** found: C, 51.2; H, 6.9; N, 5.5; S, 12.5. Calc. for $C_{11}H_{17}NO_4S$: C, 50.9; H, 6.6; N, 5.4; S, 12.4%.



s3

***N*-[1-(4-methoxyphenyl)ethyl]-4-methyl-benzenesulfonamide (s3)**. To the stirred mixture of 1-(4-methoxyphenyl)ethanol (21.4 mmol, 3.258 g), $TsNH_2$ (22 mmol, 3.767 g) and molecular

sieves 4Å in chloroform (100 mL) a 8 drops of sulfuric acid were added at room temperature. The mixture was stirred for 2 hours (control by TLC), then the solids were filtered off and washed with chloroform, the combined chloroform fractions were washed with $NaHCO_3$ solution, dried with $MgSO_4$, evaporated to afford the desired product of decent purity which was used in the next step. Yield 6.284g (96%), white solid. An analytically pure sample was obtained by column chromatography on silica gel, eluent: hexane/ethyl acetate 4:1 to 2:1. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.62 (d, *J*=8.0 Hz, 2 H), 7.20 (d, *J*=8.6 Hz, 2 H), 7.01 (d, *J*=8.6 Hz, 2 H), 6.72 (d, *J*=8.6 Hz, 2 H), 4.74 (d, *J*=6.3 Hz, 1 H), 4.41 (quin, *J*=6.8 Hz, 1 H), 3.76 (s, 3 H), 2.39 (s, 3 H), 1.40 ppm (d, *J*=6.9 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 158.9, 143.0, 137.6, 134.1, 129.4, 127.3, 127.1, 113.8, 55.2, 53.0, 23.4, 21.5 ppm. The analytical data matched those reported in the literature.[3]

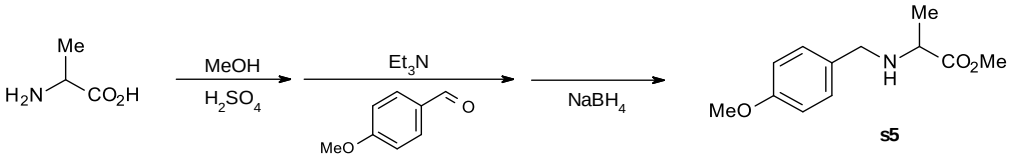


s3 **s4** **1c**

Ethyl 2-[1-(4-methoxyphenyl)ethyl-(p-tolylsulfonyl)amino]acetate (s4). A 25 mL round bottom flask was charged with **s3** (7.47 mmol, 2.28 g), grinded K_2CO_3 (15 mmol, 2 equiv., 2.06 g), DMF (10 mL) and ethyl bromoacetate (7.84 mmol, 1.05 equiv., 0.9 ml). The mixture was stirred at room temperature for 24 hours, then water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated. The residue was subjected to column chromatography on silica gel, eluting with hexane/ethyl acetate 4:1, then 2:1. Yield 2.064 g (71%), colourless oil, solidified on standing. **M.p.** 77.9-79.6°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.89 (d, *J*=8.0 Hz, 2 H), 7.32 (d, *J*=8.0 Hz, 2 H), 7.11 (d, *J*=8.6 Hz, 2 H), 6.78 (d, *J*=8.6 Hz, 2 H), 5.03 (q, *J*=6.9 Hz, 1 H), 3.94 - 4.10 (m, 2 H), 3.92 (d, *J*=18.4 Hz, 1 H), 3.76 (s, 3 H), 3.68 (d, *J*=18.4 Hz, 1 H), 2.44 (s, 3 H), 1.40 (d, *J*=6.9 Hz, 3 H), 1.15 ppm (t, *J*=7.2 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 169.9, 159.1, 143.4, 137.6, 130.7, 129.4, 128.9, 127.9, 113.6, 61.1, 55.2, 55.1, 44.2, 21.6, 17.1, 13.9 ppm. **IR** (neat): ν = 2982, 1755, 1515, 1325, 1150, 1095, 1024 cm^{-1}.

***N*-(2-hydroxyethyl)-N-[1-(4-methoxyphenyl)ethyl]-4-methyl-benzenesulfonamide (1c).** To a solution of **s4** (412 mg, 1.1 mmol) in THF (40 mL) $LiAlH_4$ (1.2 mmol, 1.1 equiv., 44 mg) was added in small portions, then the mixture was stirred for 10 minutes (control by TLC). The reaction was quenched with ethyl acetate, then carefully with water and diluted H_2SO_4 until clear solution was obtained. Then the mixture was extracted with ethyl acetate, the combined organic phases were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated, the residue was subjected to column chromatography on silica gel, eluting with

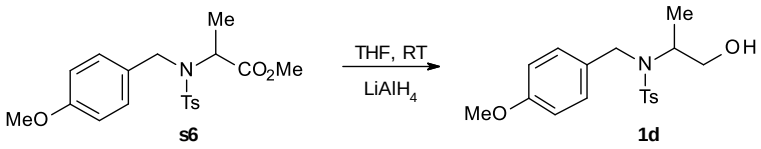
hexane/ethyl acetate 1:1. Yield 199 mg (54%), colourless oil, solidified on standing. **M.p.** 86.1-88.2°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.76 (d, *J*=8.0 Hz, 2 H), 7.32 (d, *J*=8.0 Hz, 2 H), 7.17 (d, *J*=8.6 Hz, 2 H), 6.81 (d, *J*=8.6 Hz, 2 H), 5.17 (q, *J*=6.9 Hz, 1 H), 3.77 (s, 3 H), 3.34 (s, 2 H), 3.18 - 3.26 (m, 1 H), 3.04 - 3.12 (m, 1 H), 2.44 (s, 3 H), 2.23 (br. s, 1 H), 1.30 ppm (d, *J*=6.9 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 159.1, 143.4, 137.4, 131.9, 129.8, 128.6, 127.2, 113.8, 62.2, 55.2, 55.0, 45.6, 21.5, 16.2 ppm. **IR** (neat): ν = 3530, 2963, 1612, 1511, 1305, 1250, 1160, 1029 cm^{-1}. **Elemental analysis** found: C, 61.6; H, 6.2; N, 2.7; S, 9.0. Calc. for $C_{18}H_{23}NO_4S$: C, 61.9; H, 6.6; N, 4.0; S, 9.2%.



Methyl 2-[(4-methoxyphenyl)methylamino]propanoate (s5). The 100 mL round bottom flask was charged with H_2SO_4 (22 mmol, 2.15 g), MeOH (50 mL) was added followed by alanine (20 mmol, 1.78 g). The mixture was refluxed for 8 hours, cooled to room temperature, Et_3N (45 mmol, 6.5mL) and *p*-anisaldehyde (21 mmol, 2.86 g, 2.6 mL) were added and the mixture was stirred overnight. The reaction mixture was cooled with an ice bath and NaBH4 (40 mmol, 1.51 g) was added portionwise and stirring was continued for 5 hours. Then MeOH was removed on a rotary evaporator, the residue was quenched with water, and acidified with 10% H_2SO_4 and extracted with Et_2O (organic phase disposed). The aqueous phase neutralized with solid $NaHCO_3$, then basified with NaOH, extracted with Et_2O. the combined organic phases were washed with 50% brine, brine, dried with $MgSO_4$, evaporated and the residue was dried in vacuum to afford pure desired product as a colourless oil. Yield 2.11 g (47%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.24 (d, *J*=8.6 Hz, 2 H), 6.85 (d, *J*=8.6 Hz, 2 H), 3.79 (s, 3 H), 3.73 (s, 3 H), 3.73 (d, *J*=12.6 Hz, 1 H), 3.61 (d, *J*=12.6 Hz, 1 H), 3.38 (q, *J*=6.9 Hz, 1 H), 1.90 (br. s, 1 H), 1.31 ppm (d, *J*=6.9 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 176.1, 158.6, 131.7, 129.4, 128.4, 113.7, 55.6, 55.1, 51.7, 51.3, 19.0 ppm. The analytical data matched those reported in the literature.[4]

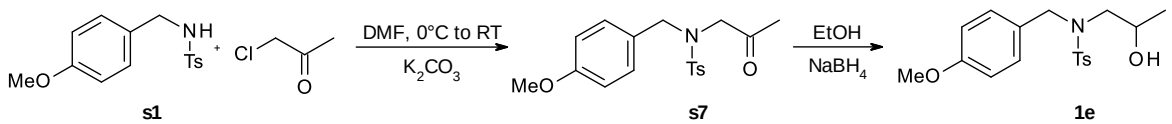
Methyl 2-[(4-methoxyphenyl)methyl-(p-tolylsulfonyl)amino]propanoate (s6). To the mixture of amine **s6** (8.29 mmol, 1.851g), Et_3N (12 mmol, 1.8 mL) and DMAP (0.8 mmol, 93

mg) in DCM (20 mL) TsCl (9.12 mmol, 1.74 g) was added and the mixture was stirred for 24 hours. Then the reaction mixture was washed with 5% H_2SO_4, $NaHCO_3$, dried with $MgSO_4$, evaporated and the residue was dried in vacuum. Yield 2.478 g (79%), orange oil, solidified on standing. **M.p.** 62.7-64.9°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.71 (d, *J*=8.0 Hz, 2 H), 7.29 (d, *J*=8.6 Hz, 2 H), 7.23 (d, *J*=8.6 Hz, 2 H), 6.81 (d, *J*=8.6 Hz, 2 H), 4.60 (q, *J*=7.3 Hz, 1 H), 4.45 (d, *J*=15.5 Hz, 1 H), 4.35 (d, *J*=15.5 Hz, 1 H), 3.78 (s, 3 H), 3.44 (s, 3 H), 2.43 (s, 3 H), 1.27 ppm (d, *J*=7.5 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.6, 159.0, 143.3, 137.1, 129.4, 129.4, 128.9, 127.4, 113.6, 55.2, 54.8, 52.0, 48.5, 21.5, 16.2 ppm. **IR** (neat): ν = 2945, 1737, 1610, 1511, 1369, 1287, cm^{-1}. **Elemental analysis** found: C, 60.0; H, 5.7; N, 2.4; S, 8.5. Calc. for $C_{19}H_{23}NO_5S$: C, 60.5; H, 6.1; N, 3.7; S, 8.5%.



s6 **1d**

***N*-(2-hydroxy-1-methyl-ethyl)-N-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide (1d).** To a solution of **s6** (2.1 mmol, 794 mg) in THF (20 mL) $LiAlH_4$ (2.2 mmol, 88 mg) was added in small portions, then the mixture was stirred for 30 minutes (control by TLC). The reaction was quenched with ethyl acetate, then carefully with water and diluted H_2SO_4 until clear solution was obtained. Then the mixture was extracted with ethyl acetate, the combined organic phases were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated, the residue was dried in vacuum to afford the pure desired product as a white solid. Yield 693 mg (94%), white solid. **M.p.** 114.9-117.4°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.71 (d, *J*=8.6 Hz, 2 H), 7.33 (d, *J*=8.6 Hz, 2 H), 7.30 (d, *J*=8.0 Hz, 2 H), 6.86 (d, *J*=8.6 Hz, 2 H), 4.61 (d, *J*=15.5 Hz, 1 H), 4.08 (d, *J*=15.5 Hz, 1 H), 4.00 (sxt, *J*=6.9 Hz, 1 H), 3.79 (s, 3 H), 3.25 (d, *J*=6.9 Hz, 2 H), 2.43 (s, 3 H), 1.74 (br. s., 1 H), 0.90 ppm (d, *J*=6.9 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 159.2, 143.4, 137.7, 129.8, 129.7, 129.2, 127.0, 114.1, 64.7, 55.8, 55.2, 46.8, 21.5, 14.0 ppm. **IR** (neat): ν = 3531, 2956, 1612, 1322, 1249, 1146, 1015 cm^{-1}. **Elemental analysis** found: C, 62.2; H, 6.2; N, 4,3; S, 9.4. Calc. for $C_{18}H_{23}NO_4S$: C, 61.9; H, 6.6; N, 4.0; S, 9.2%.

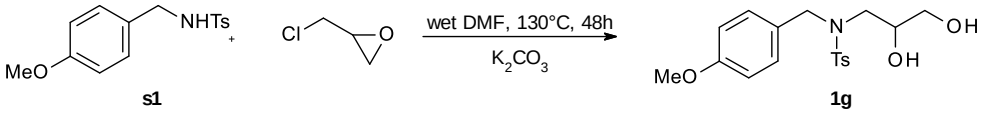


s1 **s7** **1e**

N-acetonyl-N-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide (s7). A 25 mL round bottom flask was charged with *N*-tosyl- *p*-methoxymenzylamine (**s1**) (2 mmol, 583 mg),

grinded K_2CO_3 (4 mmol, 2 equiv., 620 mg), DMF (5 mL), chilled on an ice bath and chloroacetone (2.2 mmol, 1.12 equiv, 0.18 ml) was added and the mixture was stirred overnight. Water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated to afford pure product as a white solid. Yield. 629 mg (91%), white solid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.74 (d, *J*=8.0 Hz, 2 H), 7.34 (d, *J*=8.0 Hz, 2 H), 7.14 (d, *J*=8.6 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 4.28 (s, 2 H), 3.79 (s, 2 H), 3.79 (s, 3 H), 2.45 (s, 3 H), 1.95 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 204.1, 159.6, 143.6, 136.1, 130.3, 129.7, 127.5, 126.7, 114.1, 55.5, 55.3, 51.8, 26.8, 21.6 ppm.

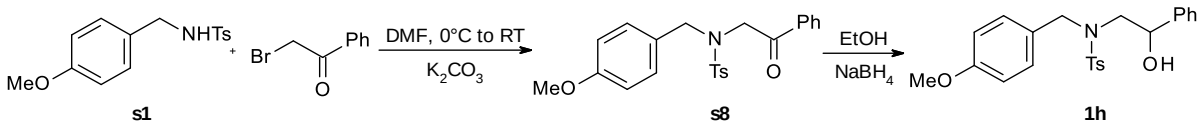
N-(2-hydroxypropyl)-N-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide (1e). To a solution of **s7** (1.75 mmol, 609 mg) in EtOH (20 mL) $NaBH_4$ (3.5 mmol, 152 mg) was added and the mixture was stirred for 2 hours (TLC control). Then EtOH was removed on a rotary evaporator, water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated to afford pure product as an amorphous solid. Yield 585 mg (95%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.73 (d, *J*=8.0 Hz, 2 H), 7.33 (d, *J*=8.0 Hz, 2 H), 7.19 (d, *J*=8.6 Hz, 2 H), 6.84 (d, *J*=8.6 Hz, 2 H), 4.40 (d, *J*=14.4 Hz, 1 H), 4.15 (d, *J*=14.4 Hz, 1 H), 3.79 (s, 4 H), 3.64 (dqd, *J*=9.2, 6.2, 3.2 Hz, 1 H), 3.08 (dd, *J*=14.9, 8.6 Hz, 1 H), 2.92 (dd, *J*=14.7, 3.2 Hz, 1 H), 2.44 (s, 3 H), 0.97 ppm (d, *J*=6.3 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 159.4, 143.6, 135.9, 129.8, 129.8, 128.0, 127.3, 114.1, 65.9, 56.1, 55.2, 53.5, 21.5, 20.3 ppm. **IR** (neat): ν = 3513, 2929, 1612, 1512, 1324, 1286, 1213, cm^{-1}. **Elemental analysis** found: C, 61.5; H, 6.3; N, 3.7; S, 9.0. Calc. for $C_{18}H_{23}NO_4S$: C, 61.9; H, 6.6; N, 4.0; S, 9.2%.



s1 **1g**

N-(2,3-dihydroxypropyl)-N-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide. The mixture of *N*-tosyl- *p*-methoxymenzylamine (**s1**) (5 mmol, 1.457 g), grinded K_2CO_3 (10 mmol, 2 equiv., 1.38 g), wet DMF (10 mL, from “old” bottle), and epichlorohydrin (30 mmol, 1.2 ml) was stirred and 130°C for 48 hours. After cooling water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated and the residue was subjected to column chromatograph on silica gel eluting with ethyl acetate. Yield 596 mg (16%), white solid. **M.p.** 76.3-79.2°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.72 (d, *J*=8.6 Hz, 2 H), 7.34 (d, *J*=8.6 Hz, 2 H), 7.19 (d, *J*=8.6 Hz, 2 H), 6.84 (d, *J*=8.6 Hz, 2 H), 4.33 (d, *J*=13.8 Hz, 1 H), 4.15 (d, *J*=13.8 Hz, 1 H), 3.79 (s, 3 H), 3.51 (dd, *J*=12.2, 3.4 Hz, 1 H), 3.44 (dd, *J*=12.2, 3.4 Hz, 1 H), 3.27 - 3.35 (m, *J*=6.3, 3.2, 3.2 Hz, 1 H), 3.17 (dd, *J*=15.0, 5.7 Hz, 1 H), 3.07 (dd, *J*=15.0, 7.2 Hz, 1

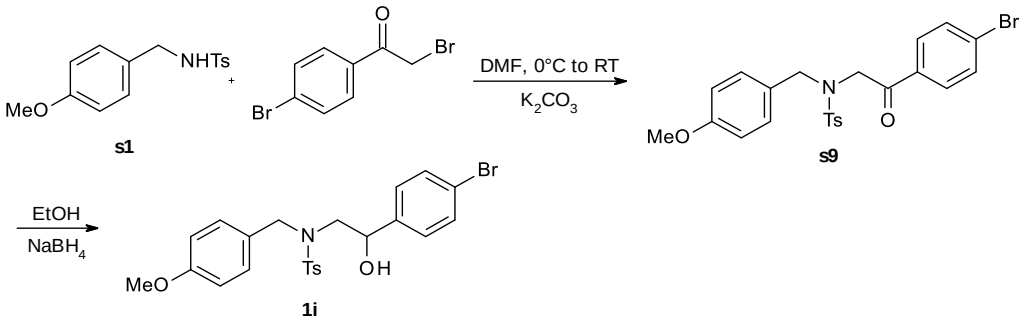
H), 2.65 (br. s, 1 H), 2.45 (s, 3 H), 2.30 ppm (br. s, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 159.5, 143.9, 135.4, 130.0, 129.9, 127.7, 127.2, 114.2, 69.7, 63.0, 55.2, 53.9, 51.0, 21.5 ppm. **IR** (neat): ν = 3536, 3405, 2917, 1794, 1611, 1513, 1329, 1250, 1157, 1032 cm^{-1}. **Elemental analysis** found: C, 59.3; H, 6.5; N, 3,5; S, 8.7. Calc. for $C_{17}H_{23}NO_5S$: C, 59.2; H, 6.3; N, 3.8; S, 8.8%.



s1 **s8** **1h**

N-[(4-methoxyphenyl)methyl]-4-methyl-N-phenacyl-benzenesulfonamide (s8). A 25 mL round bottom flask was charged with *N*-tosyl-*p*-methoxymenzylamine (**s1**) (2 mmol, 583 mg), grinded K_2CO_3 (4 mmol, 2 equiv., 620 mg), DMF (5 mL), chilled on an ice bath, 2-bromoacetophenone (2.05 mmol, 402 mg) was added and the mixture was stirred until full conversion (TLC control). Water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated and the residue was subjected to column chromatograph on silica gel eluting with hexane/ethyl acetate 4:1 mixture. Yield 378 mg (46%), white solid. **M.p.** 62.7-64.4°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.78 (d, *J*=8.6 Hz, 2 H), 7.75 (d, *J*=7.5 Hz, 2 H), 7.55 (t, *J*=7.5 Hz, 1 H), 7.40 (t, *J*=7.5 Hz, 2 H), 7.32 (d, *J*=8.0 Hz, 2 H), 7.13 (d, *J*=8.6 Hz, 2 H), 6.77 (d, *J*=8.6 Hz, 2 H), 4.60 (s, 2 H), 4.46 (s, 2 H), 3.76 (s, 3 H), 2.45 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 194.1, 159.4, 143.4, 137.0, 134.8, 133.6, 130.2, 129.5, 128.6, 127.8, 127.5, 126.9, 114.0, 55.2, 51.4, 50.7, 21.6 ppm.

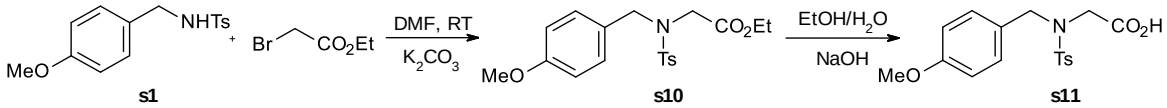
N-(2-hydroxy-2-phenyl-ethyl)-N-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide (1h). To a solution of **s8** (0.88 mmol, 362 mg) in MeOH (10 mL) $NaBH_4$ (1.3 mmol, 50 mg) was added and the mixture was stirred for 2 hours (TLC control). Then MeOH was removed on a rotary evaporator, water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated to afford pure product as a colorless oil which solidified on standing, yield 370 mg (quant.). **M.p.** 97.8-99.7°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.73 (d, *J*=8.6 Hz, 2 H), 7.31 (d, *J*=8.0 Hz, 2 H), 7.17 - 7.28 (m, 5 H), 7.12 (d, *J*=7.5 Hz, 2 H), 6.86 (d, *J*=8.6 Hz, 2 H), 4.55 (d, *J*=14.4 Hz, 1 H), 4.49 (dd, *J*=9.5, 2.6 Hz, 1 H), 4.06 (d, *J*=14.4 Hz, 1 H), 3.80 (s, 3 H), 3.33 (dd, *J*=14.9, 9.8 Hz, 1 H), 3.03 (dd, *J*=14.9, 2.9 Hz, 1 H), 2.43 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 159.5, 143.7, 141.2, 135.9, 130.1, 129.8, 128.4, 127.7, 127.7, 127.3, 125.8, 114.2, 72.5, 56.5, 55.3, 53.5, 21.5 ppm. **IR** (neat): ν = 3499, 2925, 1611, 1494, 1425, 1090 cm^{-1}.



N-[2-(4-bromophenyl)-2-oxo-ethyl]-N-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide (s9). A 25 mL round bottom flask was charged with *N*-tosyl- *p*-methoxymenzylamine (**s1**) (2 mmol, 583 mg), grinded K_2CO_3 (4 mmol, 2 equiv., 620 mg), DMF (5 mL), chilled on an ice bath, 2,4′-dibromoacetophenone (2.05 mmol, 570 mg) was added and the mixture was stirred until full conversion (TLC control, 2 hours). Water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated and the residue was subjected to column chromatograph on silica gel eluting with hexane/ethyl acetate 4:1 mixture. Yield 615 mg (63%), light brown solid. **M.p.** 81.4-82.6°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.76 (d, *J*=8.0 Hz, 2 H), 7.57 - 7.63 (m, 2 H), 7.50 - 7.55 (m, 2 H), 7.33 (d, *J*=8.6 Hz, 2 H), 7.08 (d, *J*=8.0 Hz, 2 H), 6.74 (d, *J*=8.6 Hz, 2 H), 4.50 (s, 2 H), 4.40 (s, 2 H), 3.75 (s, 3 H), 2.45 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 193.4, 159.4, 143.5, 136.6, 133.5, 131.9, 130.3, 129.6, 129.4, 128.7, 127.4, 126.6, 113.9, 55.2, 51.8, 51.0, 21.6 ppm. **IR** (neat): ν = 2919, 1693, 1586, 1508, 1318, 1173 cm^{-1}. **Elemental analysis** found: C, 56.1; H, 4.1; N, 2.5; S, 6.5. Calc. for $C_{23}H_{22}BrNO_4S$: C, 56.6; H, 4.5; N, 2.9; S, 6.6%.

N-[2-(4-bromophenyl)-2-hydroxy-ethyl]-N-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide (1i). To a solution of **s9** (1.15 mmol, 563 mg) in MeOH (10 mL) $NaBH_4$ (2.3 mmol, 88 mg) was added and the mixture was stirred for 2 hours (TLC control). Then MeOH was removed on a rotary evaporator, water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated to afford pure product as a colorless oil which solidified on standing. Yield 556 mg (99%). **M.p.** 112.4-113.1°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.72 (d, *J*=8.0 Hz, 2 H), 7.36 (d, *J*=8.6 Hz, 2 H), 7.33 (d, *J*=8.0 Hz, 2 H), 7.18 (d, *J*=8.6 Hz, 2 H), 6.97 (d, *J*=8.6 Hz, 2 H), 6.86 (d, *J*=8.6 Hz, 2 H), 4.54 (d, *J*=14.4 Hz, 1 H), 4.45 (dd, *J*=9.2, 2.3 Hz, 1 H), 4.00 (d, *J*=14.4 Hz, 1 H), 3.81 (s, 3 H), 3.26 (dd, *J*=14.9, 9.2 Hz, 1 H), 3.14 (br. s, 1 H), 2.98 (dd, *J*=14.9, 2.9 Hz, 1 H), 2.44 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 159.6, 143.9, 140.2, 135.5, 131.4, 130.1, 129.9, 127.5, 127.4, 127.3, 121.4, 114.2, 72.0, 56.3, 55.3, 53.7, 21.5 ppm. **IR** (neat): ν = 3520, 2929, 2836, 1612, 1358, 1153 cm^{-1}. **Elemental**

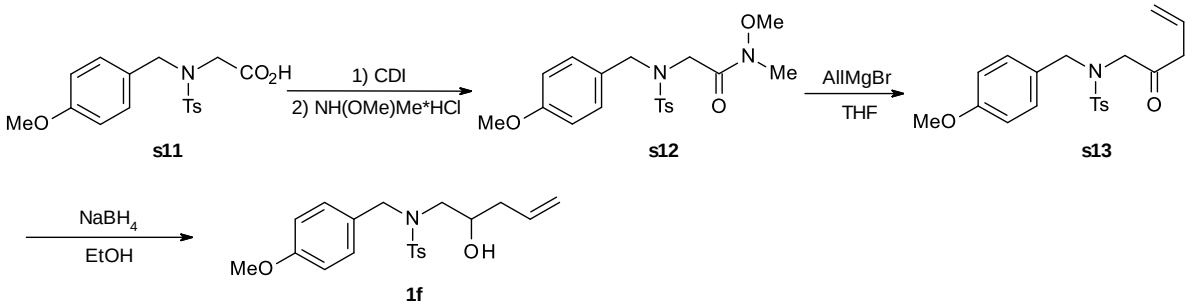
analysis found: C, 56.1; H, 5.3; N, 4,5; S, 6.7. Calc. for $C_{23}H_{24}BrNO_4S$: C, 56.3; H, 4.9; N, 2.9; S, 6.5%.



s1 **s10** **s11**

Ethyl 2-[(4-methoxyphenyl)methyl-(p-tolylsulfonyl)amino]acetate (s10). A 50 mL round bottom flask was charged with *N*-tosyl-*p*-methoxymenzylamine (**s1**) (5 mmol, 1.457 g), grinded K_2CO_3 (10 mmol, 2 equiv., 1.38 g), DMF (20 mL), chilled on an ice bath, ethyl bromoacetate (5.25 mmol, 877 mg, 0.6 mL) was added and the mixture was stirred until full conversion (TLC control). Water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated and the residue was dried in vacuum to afford pure desired product as a white solid. **M.p.** 72.8-75.0°C. Yield 1.846 g (98%).**^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.77 (d, *J*=8.0 Hz, 2 H), 7.31 (d, *J*=8.0 Hz, 2 H), 7.15 (d, *J*=8.6 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 4.41 (s, 2 H), 3.99 (q, *J*=7.5 Hz, 2 H), 3.88 (s, 2 H), 3.78 (s, 3 H), 2.43 (s, 3 H), 1.13 ppm (t, *J*=7.2 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 168.7, 159.4, 143.4, 136.9, 130.0, 129.5, 127.4, 126.7, 114.0, 61.0, 55.2, 50.6, 46.3, 21.5, 13.9 ppm. **IR** (neat): ν = 2985, 2833, 1753, 1613, 1513, 1332, 1147 cm^{-1}. **Elemental analysis** found: C, 61.1; H, 5.8; N, 3.4; S, 8.4. Calc. for $C_{19}H_{23}NO_5S$: C, 60.5; H, 6.1; N, 3.7; S, 8.5%.

2-[(4-Methoxyphenyl)methyl-(p-tolylsulfonyl)amino]acetic acid (s11). To a solution of **s10** (1.80 g, 4.77 mmol) in EtOH (20 mL) aqueous solution of NaOH (24 mmol, 1.00 g, in 20 mL H_2O) was added and the mixture was stirred overnight. Then EtOH was removed under reduced pressure, the mixture was diluted with water and acidified with 10% H_2SO_4. The formed precipitate was filtered off, washed with water and dried under air. Yield 1.601 g (96%), white powder. **M.p.** 147.6-149.8°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.73 (d, *J*=8.0 Hz, 2 H), 7.39 (d, *J*=8.6 Hz, 2 H), 7.12 (d, *J*=8.6 Hz, 2 H), 6.86 (d, *J*=8.6 Hz, 2 H), 4.31 (s, 2 H), 3.76 (s, 2 H), 3.72 (s, 3 H), 2.39 ppm (s, 3 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 169.8, 158.9, 143.2, 136.9, 129.9, 129.7, 127.3, 127.2, 113.9, 55.1, 50.6, 47.0, 21.1 ppm. **IR** (neat): ν = 2920, 2841, 1726, 1712, 1512, 1330, 1238, 1155 cm^{-1}. **Elemental analysis** found: C, 58.0; H, 5.8; N, 3,8; S, 9.3. Calc. for $C_{17}H_{19}NO_5S$: C, 58.4; H, 5.5; N, 4.0; S, 9.2%.

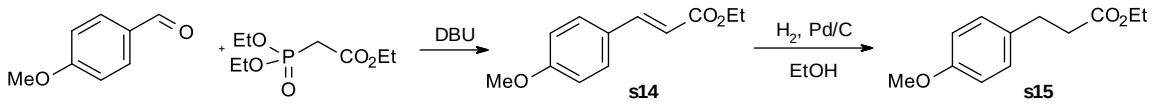


***N*-methoxy-2-[(4-methoxyphenyl)methyl-(p-tolylsulfonyl)amino]-*N*-methyl-acetamide (s12).** A 25 mL round bottom flask was charged with **s11** (5 mmol, 1.745 g) and THF (10 mL), 1,1'-carbonyldiimidazole (5.5 mmol, 892 mg) was added and the mixture was stirred for 1 hour. Then *N,O*-dimethylhydroxylamine hydrochloride (5.5 mmol, 538 mg) was added and the mixture was stirred overnight. After addition of diluted H_2SO_4 (50 mL, 5%) the organic layer was separated, the aqueous layer was extracted with ethyl acetate. The combined organic phases were washed with 5% H_2SO_4, 5% K_2CO_3, brine, dried with $MgSO_4$. The solvent was evaporated and the residue was dried in vacuum. Yield 1.408 g (72%), colourless oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.81 (d, *J*=8.0 Hz, 2 H), 7.30 (d, *J*=8.0 Hz, 2 H), 7.19 (d, *J*=8.6 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 4.46 (s, 2 H), 4.10 (s, 2 H), 3.79 (s, 3 H), 3.51 (s, 3 H), 3.06 (s, 3 H), 2.43 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 169.1, 159.3, 143.1, 137.3, 130.1, 129.4, 127.6, 127.2, 113.9, 61.2, 55.2, 50.3, 45.2, 32.2, 21.6, 14.2 ppm. The analytical data matched those reported in the literature.[5]

N-[(4-methoxyphenyl)methyl]-4-methyl-N-(2-oxopent-4-enyl)benzenesulfonamide (s13). To a solution of Weinreb amide **s12** (1.72 mmol, 677 mg) in THF (10 mL) allylmagnesium bromide (2 mmol, 2.0 mL of 1.0 M solution in Et_2O) was added dropwise and the mixture was stirred for additional 1 hour. Then the reaction mixture was quenched with water, extracted with ethyl acetate, the combined organic phases were dried with $MgSO_4$, evaporated and the residue was subjected to column chromatography on silica gel, eluting with hexane/ ethyl acetate 4:1. Yield 415 mg (65%).**^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.74 (d, *J*=8.0 Hz, 2 H), 7.33 (d, *J*=8.6 Hz, 2 H), 7.13 (d, *J*=8.6 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 5.69 (ddt, *J*=17.2, 10.3, 7.0 Hz, 1 H), 5.11 (d, *J*=10.3 Hz, 1 H), 5.01 (dd, *J*=16.9, 1.4 Hz, 1 H), 4.28 (s, 2 H), 3.85 (s, 2 H), 3.79 (s, 3 H), 3.01 (d, *J*=6.9 Hz, 2 H), 2.44 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 203.8, 159.6, 143.6, 136.1, 130.4, 129.7, 129.4, 127.5, 126.6, 119.4, 114.1, 55.3, 54.5, 51.6, 44.2, 21.6 ppm.

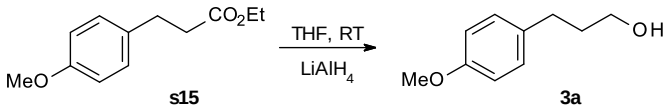
***N*-(2-hydroxypent-4-enyl)-*N*-[(4-methoxyphenyl)methyl]-4-methyl-benzenesulfonamide (1f)**. To a solution of ketone **s13** (0.878 mmol, 328 mg) in MeOH (10mL) $NaBH_4$ (1 mmol, 38 mg) was added and the reaction mixture was stirred for 20 minutes (TLC control). Then the mixture was diluted with 100mL of water and extracted with ethyl acetate. The combined

organic phases were washed with water, brine, dried with $MgSO_4$, the solvent was evaporated and the residue was dried in vacuum. Yield 311 mg (94%), white solid. **M.p.** 63.8-65.2°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.73 (d, *J*=8.0 Hz, 2 H), 7.33 (d, *J*=8.0 Hz, 2 H), 7.19 (d, *J*=8.6 Hz, 2 H), 6.84 (d, *J*=8.6 Hz, 2 H), 5.60 (ddt, *J*=17.1, 10.1, 7.1 Hz, 1 H), 4.95 - 5.05 (m, 2 H), 4.38 (d, *J*=14.4 Hz, 1 H), 4.18 (d, *J*=14.4 Hz, 1 H), 3.79 (s, 3 H), 3.49 - 3.57 (m, *J*=7.2, 3.7 Hz, 1 H), 3.00 - 3.11 (m, 2 H), 2.44 (s, 4 H), 2.38 (br. s., 1 H), 2.03 - 2.08 ppm (m, 2 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 210.8, 195.0, 187.3, 185.3, 181.3, 181.2, 179.3, 178.7, 169.3, 165.5, 120.5, 106.6, 105.5, 104.8, 90.4, 72.9 ppm. **IR** (neat): ν = 3546, 3495, 2957, 2917, 1611, 1511, 1326, 1245, 1152 cm^{-1}. **Elemental analysis** found: C, 64.0; H, 7.0; N, 3,6; S, 8.7. Calc. for $C_{20}H_{25}NO_4S$: C, 64.0; H, 6.7; N, 3.7; S, 8.5%.



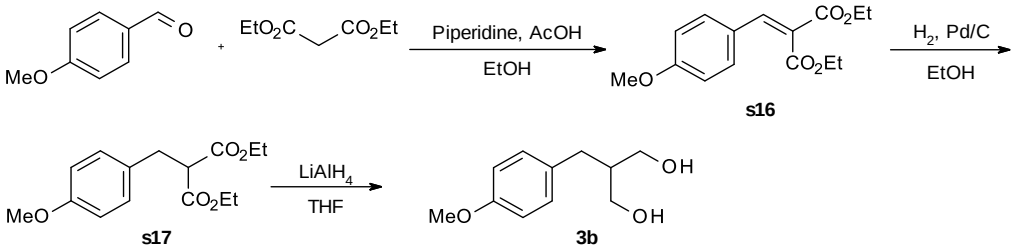
Ethyl (E)-3-(4-methoxyphenyl)prop-2-enoate (s14). The synthesis was performed according to the procedure, developed by Ando and Yamada.[6] The neat mixture of *p*-anisaldehyde (14.7 mmol, 2.00 g), triethyl phosphonoacetate (16.2 mmol, 3.63 g) and DBU (22.1 mmol, 3.36 g) was stirred overnight. Then the mixture was diluted with ethyl acetate, washed with 10% H_2SO_4, water and brine, dried with $MgSO_4$ and evaporated. The crude mixture was passed through a short pad of silica gel, eluting with hexane/ethyl acetate 2:1. Yield 2.69 g (92%), colorless liquid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.64 (d, *J*=16.1 Hz, 1 H), 7.47 (d, *J*=8.6 Hz, 2 H), 6.89 (d, *J*=8.6 Hz, 2 H), 6.30 (d, *J*=16.1 Hz, 1 H), 4.24 (q, *J*=6.9 Hz, 2 H), 3.82 (s, 3 H), 1.32 ppm (t, *J*=7.2 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.3, 161.2, 144.2, 129.6, 127.1, 115.7, 114.2, 60.3, 55.3, 14.3 ppm. The analytical data matched those reported in the literature.[7]

Ethyl 3-(4-methoxyphenyl)propanoate (s15). A 100 ml round bottom flask was charged with ethyl (E)-3-(4-methoxyphenyl)prop-2-enoate (**s14**) (1.87 mmol, 385 mg), palladium on carbon (0.33 mmol, 1.8 mol %, 35 mg of 10% Pd catalyst) and EtOH (50 mL). The flask was flushed with H_2 (balloon) 3 times and the mixture was vigorously stirred under H_2 atmosphere overnight. Then the mixture was filtered through celite, the solvent was evaporated and the residue was dried in vacuum to afford pure product as a colourless oil. Yield 380 mg (98%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.12 (d, *J*=8.6 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 4.12 (q, *J*=7.5 Hz, 2 H), 3.78 (s, 3 H), 2.89 (t, *J*=7.8 Hz, 2 H), 2.58 (t, *J*=7.8 Hz, 2 H), 1.23 ppm (t, *J*=7.2 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.9, 157.9, 132.6, 129.2, 113.8, 60.3, 55.1, 36.2, 30.0, 14.1 ppm. The analytical data matched those reported in the literature.[8]



s15 **3a**

3-(4-methoxyphenyl)propan-1-ol (3a). To a solution of ethyl 3-(4-methoxyphenyl)propanoate (**s15**) (1.78 mmol, 370 mg) in THF (20 mL) $LiAlH_4$ (2.1 mmol, 87 mg) was added in small portions, then the mixture was stirred for 30 minutes (control by TLC). The reaction was quenched with ethyl acetate, then carefully with water and diluted H_2SO_4 until clear solution was obtained. Then the mixture was extracted with ethyl acetate, the combined organic phases were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated, the residue was dried in vacuum to afford the pure desired product as a colorless liquid. Yield 280 mg (95%).**^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.12 (d, *J*=8.0 Hz, 2 H), 6.84 (d, *J*=8.6 Hz, 2 H), 3.79 (s, 3 H), 3.67 (t, *J*=6.6 Hz, 2 H), 2.65 (t, *J*=7.5 Hz, 2 H), 1.86 (quin, *J*=7.2 Hz, 2 H), 1.41 ppm (br. s, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 157.9, 134.0, 129.4, 113.9, 62.3, 55.4, 34.5, 31.2 ppm. The analytical data matched those reported in the literature.[9]



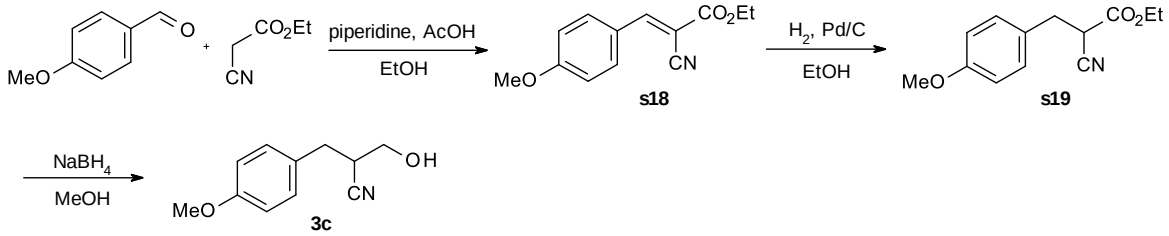
s16 **s17** **3b**

Diethyl 2-[(4-methoxyphenyl)methylene]propanedioate (s16). The mixture of *p*-anisaldehyde (5 mmol, 681 mg), diethyl malonate (7.5 mmol, 1.2 g), piperidine (2 mmol, 172 mg, 0.2 mL) and acetic acid (10 mmol, 600 mg, 0.6 mL) in ethanol (20 mL) was refluxed for 5 hours (TLC control). Then the volatiles were removed in vacuum, the residue was dissolved in ethyl acetate, washed with water 3 times, brine, dried with $MgSO_4$, evaporated. According to ^{1}H NMR, the residue consisted of the desired product **s16** and malonic ester and was used in the next step without further purification.

Diethyl 2-[(4-methoxyphenyl)methyl]propanedioate (s17). A 100 ml round bottom flask was charged with crude diethyl 2-[(4-methoxyphenyl)methylene]propanedioate (**s16**), obtained from the above described experiment (contains diethyl malonate as impurity), palladium on carbon (0.047 mmol Pd, 1 mol %, 50 mg of 10% Pd catalyst) and EtOH (50 mL). The flask was flushed with H_2 (balloon) 3 times and the mixture was vigorously stirred under H_2 atmosphere overnight. Then the mixture was filtered through celite, the solvent was

removed in vacuum, the residue was dried in vacuum and used in the next step without further purification.

2-[(4-Methoxyphenyl)methyl]propane-1,3-diol (3b). To a solution of crude diethyl 2-[(4-methoxyphenyl)methyl]propanedioate (**s17**), obtained from the above described experiment (contains diethyl malonate as impurity) in THF (50 mL) $LiAlH_4$ (12.7 mmol, 480 mg) was added in small portions, then the mixture was stirred for 30 minutes (control by TLC). The reaction was quenched with ethyl acetate, then carefully with water and diluted H_2SO_4 until clear solution was obtained. Then the mixture was extracted with ethyl acetate, the combined organic phases were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated, the residue was submitted to flush chromatography on a short pad of silica gel eluting with hexane/ethyl acetate 1:1. Yield 597 mg (61 % for 3 steps), white solid **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.09 (d, *J*=8.0 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 3.78 (s, 3 H), 3.75-3.81 (m, 2 H), 3.65 (dd, *J*=10.9, 6.9 Hz, 2 H), 2.70 (br. s., 2 H), 2.55 (d, *J*=7.5 Hz, 2 H), 1.94 - 2.06 ppm (m, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 157.9, 131.8, 129.9, 113.8, 65.5, 55.2, 43.9, 33.3 ppm. The analytical data matched those reported in the literature.[10]

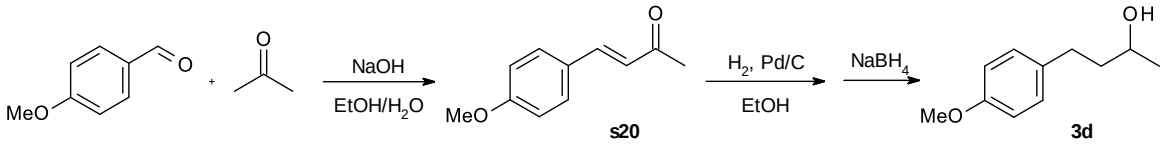


Ethyl (E)-2-cyano-3-(4-methoxyphenyl)prop-2-enoate (s18). The mixture of *p*-anisaldehyde (5 mmol, 681 mg), ethyl cyanoacetate (5 mmol, 566 mg), piperidine (2 mmol, 172 mg, 0.2 mL) and acetic acid (10 mmol, 600 mg, 0.6 mL) in ethanol (20 mL) was refluxed for 5 hours (TLC control). Then the volatiles were removed in vacuum, the residue was dissolved in ethyl acetate, washed with water 3 times, brine, dried with $MgSO_4$, evaporated. The residue was dried in vacuum to afford pure desired product as a yellow solid. Yield 1.125 g (97%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 7.98 (d, *J*=8.6 Hz, 2 H), 6.97 (d, *J*=9.2 Hz, 2 H), 4.35 (q, *J*=7.5 Hz, 2 H), 3.87 (s, 3 H), 1.37 ppm (t, *J*=7.2 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 163.7, 163.0, 154.3, 133.6, 124.3, 116.2, 114.7, 99.2, 62.4, 55.6, 14.1 ppm. The analytical data matched those reported in the literature.[11]

Ethyl 2-cyano-3-(4-methoxyphenyl)propanoate (s19). A 100 ml round bottom flask was charged with ethyl (E)-2-cyano-3-(4-methoxyphenyl)prop-2-enoate (**s18**) (4.7 mmol, 1.083 g), palladium on carbon (0.047 mmol Pd, 1 mol %, 50 mg of 10% Pd catalyst) and EtOH (50 mL).

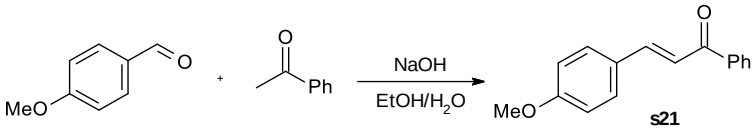
The flask was flushed with H_2 (balloon) 3 times and the mixture was vigorously stirred under H_2 atmosphere overnight. Then the mixture was filtered through celite, the solvent was removed in vacuum and the residue was subjected to column chromatography on silica gel eluting with hexane/ethyl acetate 9:1 to 4:1 mixture. Yield 737 mg (67%), colorless liquid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.19 (d, *J*=8.0 Hz, 2 H), 6.87 (d, *J*=8.6 Hz, 2 H), 4.23 (q, *J*=7.3 Hz, 2 H), 3.80 (s, 3 H), 3.68 (dd, *J*=8.0, 5.7 Hz, 1 H), 3.22 (dd, *J*=13.8, 5.7 Hz, 1 H), 3.15 (dd, *J*=13.8, 8.1 Hz, 1 H), 1.28 ppm (t, *J*=7.2 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 165.5, 159.1, 130.1, 127.2, 116.2, 114.2, 62.8, 55.2, 39.9, 35.0, 13.9 ppm. The analytical data matched those reported in the literature.[12]

2-(Hydroxymethyl)-3-(4-methoxyphenyl)propanenitrile (3c). To a solution of ethyl 2-cyano-3-(4-methoxyphenyl)propanoate (**s19**) (1.75 mmol, 409 mg) in MeOH (10 mL) $NaBH_4$ (3.5 mmol, 133 mg) was added portionwise (without cooling). Exothermic reaction was observed and the mixture was stirred for 20 minutes, then additional $NaBH_4$ (3.5 mmol, 133 mg) was added and the stirring was continued for additional 30 minutes (TLC control). After full consumption of the starting material the solvent was removed under reduced pressure, water was added and extracted with DCM. The combined organic phases were washed with 50% brine, dried with $MgSO_4$, evaporated and the residue was dried in vacuum to afford pure desired product as a white solid. Yield 329 mg (98%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.17 (d, *J*=8.6 Hz, 2 H), 6.87 (d, *J*=8.6 Hz, 2 H), 3.79 (s, 3 H), 3.68 - 3.83 (m, 2 H), 2.86 - 2.96 (m, 3 H), 2.50 ppm (br. s., 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 158.7, 130.0, 128.3, 120.6, 114.1, 61.6, 55.2, 37.0, 33.5 ppm. The analytical data matched those reported in the literature.[13]



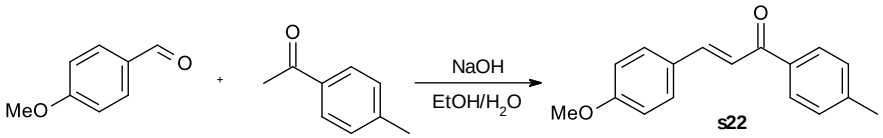
(*E*)-4-(4-methoxyphenyl)but-3-en-2-one (s20). The mixture of *p*-anisaldehyde (10 mmol, 1.36 g), NaOH (10 ml of 1% aqueous solution) and acetone (3 mL) was refluxed for 2 hours (TLC control). After cooling the mixture was diluted with water, the precipitate was filtered off, washed with water and dried in air. Yield 1.72 g (88%), yellow powder. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.43 - 7.53 (m, 3 H), 6.91 (d, *J*=8.6 Hz, 2 H), 6.60 (d, *J*=16.1 Hz, 1 H), 3.84 (s, 3 H), 2.36 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 198.4, 161.6, 143.2, 129.9, 127.0, 125.0, 114.4, 55.3, 27.4 ppm. The analytical data matched those reported in the literature.[14]

4-(4-Methoxyphenyl)butan-2-ol (3d). A 100 ml round bottom flask was charged with ethyl (E)-4-(4-methoxyphenyl)but-3-en-2-one (3.3 mmol, 585 mg), palladium on carbon (0.027 mmol Pd, 0.8 mol %, 29 mg of 10% Pd catalyst) and EtOH (50 mL). The flask was flushed with H_2 (balloon) 3 times and the mixture was vigorously stirred under H_2 atmosphere overnight. Then the mixture was filtered through celite and $NaBH_4$ (6.6 mmol, 252 mg) was added and the reaction mixture was stirred for 2 hours (TLC control). Then EtOH was removed on a rotary evaporator, water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated to afford pure product as a colorless liquid. Yield 580 mg (98% for 2 steps). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.12 (d, *J*=8.6 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 3.79 - 3.86 (m, 1 H), 3.79 (s, 3 H), 2.66 - 2.74 (m, 1 H), 2.58 - 2.65 (m, 1 H), 1.67 - 1.81 (m, 2 H), 1.48 (br. s, 1 H), 1.22 ppm (d, *J*=6.3 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 157.7, 134.0, 129.2, 113.7, 67.4, 55.2, 41.0, 31.1, 23.6 ppm. The analytical data matched those reported in the literature.[15]



s21

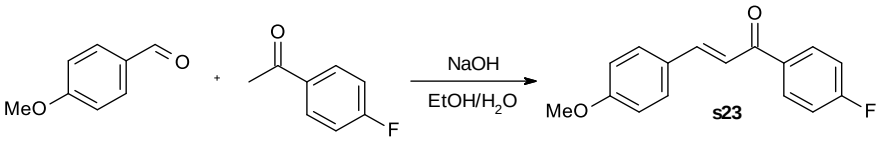
(*E*)-3-(4-methoxyphenyl)-1-phenyl-prop-2-en-1-one (s21). To a mixture of NaOH (13.6 mmol, 545 mg), water (5 mL) and EtOH (3 mL) acetophenone (10.9 mmol, 1.31 g, 1.2 mL) was added followed by *p*-anisaldehyde (10 mmol, 1.36 g, 1.2 mL); then the mixture was stirred overnight (no precipitate was observed at this time). Then, after keeping the at -20°C for 2 hours, the mixture solidified, the solids were crushed, filtered off, washed with water, hexane and dried under air. Yield 1.70 g (71%), yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.02 (d, *J*=7.5 Hz, 2 H), 7.79 (d, *J*=15.5 Hz, 1 H), 7.61 (d, *J*=8.6 Hz, 1 H), 7.58 (t, *J*=7.5 Hz, 2 H), 7.50 (t, *J*=7.5 Hz, 2 H), 7.42 (d, *J*=15.5 Hz, 1 H), 6.94 (d, *J*=8.6 Hz, 2 H), 3.86 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 190.6, 161.6, 144.7, 138.5, 132.6, 130.2, 128.5, 128.4, 127.6, 119.7, 114.4, 55.4 ppm. The analytical data matched those reported in the literature.[16]



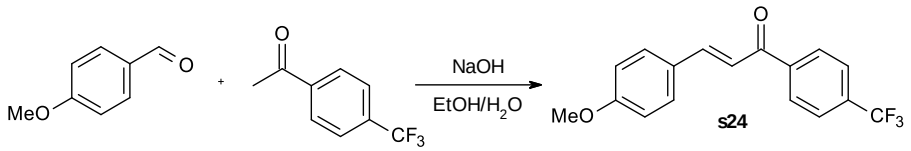
s22

(E)-3-(4-methoxyphenyl)-1-(p-tolyl)prop-2-en-1-one (s22). To a mixture of NaOH (6.8 mmol, 272 mg), water (1.5 mL) and EtOH (2.5 mL) 4'-methylacetophenone (5.45 mmol, 7311 g, 0.73 mL) followed by *p*-anisaldehyde (5 mmol, 681 mg, 0.6 mL) were added, then the mixture was stirred overnight. The precipitate was filtered off, washed with water and dried under air. Yield 1.28 g (quant.), yellow powder. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.93 (d, *J*=8.6

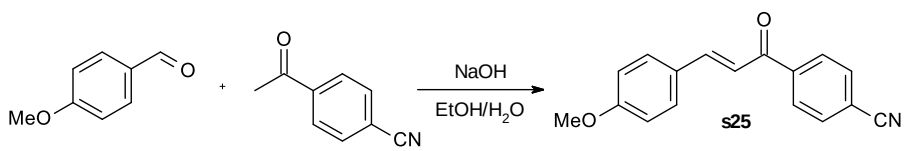
Hz, 2 H), 7.78 (d, *J*=15.5 Hz, 1 H), 7.60 (d, *J*=8.6 Hz, 2 H), 7.42 (d, *J*=15.5 Hz, 1 H), 7.29 (d, *J*=8.0 Hz, 2 H), 6.93 (d, *J*=9.2 Hz, 2 H), 3.84 (s, 3 H), 2.43 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 189.9, 161.5, 144.2, 143.3, 135.8, 130.1, 129.2, 128.5, 127.6, 119.6, 114.3, 55.3, 21.6 ppm. The analytical data matched those reported in the literature.[17]



(E)-1-(4-fluorophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (s23). The synthesis was carried out analogously to the above described procedure for (E)-3-(4-methoxyphenyl)-1-(p-tolyl)prop-2-en-1-one (**s22**). Yield 1.34 g (104%), yellow powder. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.05 (dd, *J*=8.6, 5.7 Hz, 2 H), 7.79 (d, *J*=15.5 Hz, 1 H), 7.60 (d, *J*=8.6 Hz, 2 H), 7.38 (d, *J*=15.5 Hz, 1 H), 7.16 (t, *J*=8.6 Hz, 2 H), 6.94 (d, *J*=9.2 Hz, 2 H), 3.85 ppm (s, 3 H).**^{13}C NMR** (126 MHz, $CDCl_3$): δ = 188.8, 165.4 (d, *J*=253 Hz), 144.9, 134.8 (d, *J*=4 Hz), 130.9 (d, *J*=10 Hz), 130.2, 127.4, 119.1, 115.5, 114.4, 55.4 ppm. **^{19}F NMR** (471 MHz, $CDCl_3$) δ = -105.9 ppm. The analytical data matched those reported in the literature.[18]

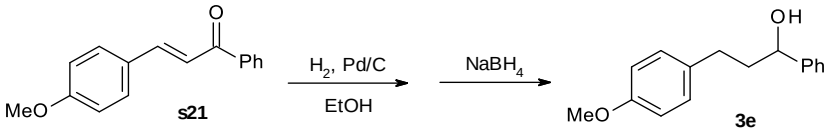


(E)-3-(4-methoxyphenyl)-1-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (s24). The synthesis was carried out analogously to the above described procedure for (E)-3-(4-methoxyphenyl)-1-(p-tolyl)prop-2-en-1-one (**s22**). Yield 1.44 g (94%), pale yellow powder. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.08 (d, *J*=8.0 Hz, 2 H), 7.80 (d, *J*=15.5 Hz, 1 H), 7.76 (d, *J*=8.0 Hz, 2 H), 7.61 (d, *J*=8.6 Hz, 2 H), 7.37 (d, *J*=15.5 Hz, 1 H), 6.95 (d, *J*=8.6 Hz, 2 H), 3.86 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 189.6, 162.0, 146.0, 141.4, 130.5, 128.7 (q, *J*=3.8 Hz), 127.2, 125.6, 124.8, 119.2, 114.5 ppm. **^{19}F NMR** (471 MHz, $CDCl_3$) δ = -62.8 ppm. The analytical data matched those reported in the literature.[19]

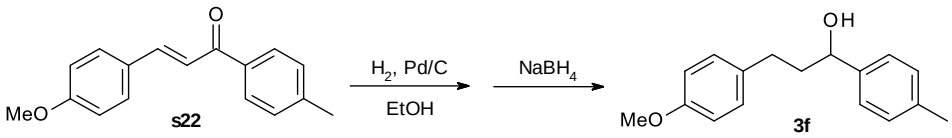


4-[(E)-3-(4-methoxyphenyl)prop-2-enoyl]benzonitrile (s25). The synthesis was carried out analogously to the above described procedure for (E)-3-(4-methoxyphenyl)-1-(p-tolyl)prop-2-en-1-one (**s22**). Yield 644 mg (94%), pale yellow powder. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.06 (d, *J*=8.6 Hz, 2 H), 7.80 (d, *J*=16.1 Hz, 1 H), 7.79 (d, *J*=8.0 Hz, 2 H), 7.61 (d, *J*=8.6 Hz, 2 H),

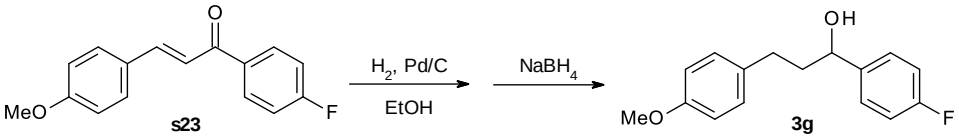
7.34 (d, *J*=15.5 Hz, 1 H), 6.94 (d, *J*=8.6 Hz, 2 H), 3.86 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 189.1, 162.1, 146.4, 141.8, 132.4, 130.5, 128.7, 127.0, 118.7, 118.1, 115.6, 114.5, 55.4 ppm. The analytical data matched those reported in the literature.[19]



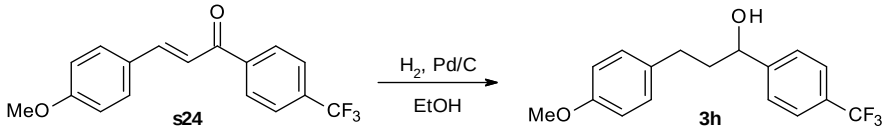
3-(4-methoxyphenyl)-1-phenyl-propan-1-ol (3e). A 100 ml round bottom flask was charged with (E)-3-(4-methoxyphenyl)-1-phenyl-prop-2-en-1-one (**s21**) (3 mmol, 717 mg), palladium on carbon (0.023 mmol Pd, 0.8 mol %, 24 mg of 10% Pd catalyst) and EtOH (50 mL). The flask was flushed with H_2 (balloon) 3 times and the mixture was vigorously stirred under H_2 atmosphere for 3 hours (TLC control). Then the mixture was filtered through celite and $NaBH_4$ (6 mmol, 228 mg) was added and the reaction mixture was stirred for 2-3 hours (TLC control). Then EtOH was removed on a rotary evaporator, water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated to afford pure product as a colourless oil, which solidified on standing. Yield 700 mg (96% for 2 steps). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.33 - 7.42 (m, 4 H), 7.27 - 7.33 (m, 1 H), 7.12 (d, *J*=8.6 Hz, 2 H), 6.84 (d, *J*=8.6 Hz, 2 H), 4.67 (dd, *J*=7.8, 5.5 Hz, 1 H), 3.79 (s, 3 H), 2.57 - 2.75 (m, 2 H), 2.06 - 2.18 (m, 1 H), 1.94 - 2.05 ppm (m, 2 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 157.7, 144.6, 133.7, 129.3, 128.4, 127.5, 125.9, 113.7, 73.8, 55.2, 40.6, 31.1 ppm. The analytical data matched those reported in the literature.[20]



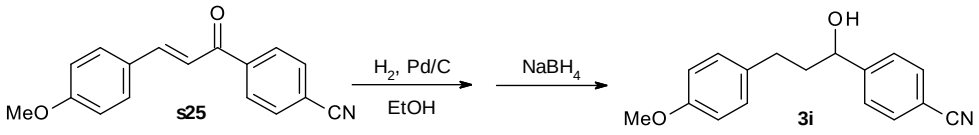
3-(4-Methoxyphenyl)-1-(p-tolyl)propan-1-ol (3f). The synthesis was carried out analogously to the above described procedure for 3-(4-methoxyphenyl)-1-phenyl-propan-1-ol (**3e**). Yield 582 mg (98% for 2 steps), colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.24 (d, *J*=8.0 Hz, 2 H), 7.17 (d, *J*=8.0 Hz, 2 H), 7.11 (d, *J*=8.6 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 4.64 (t, *J*=6.3 Hz, 1 H), 3.79 (s, 3 H), 2.55 - 2.74 (m, 2 H), 2.35 (s, 3 H), 2.04 - 2.18 (m, 1 H), 1.92 - 2.04 (m, 1 H), 1.81 ppm (br. s, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 157.7, 141.6, 137.3, 133.8, 129.3, 129.2, 125.9, 113.7, 73.7, 55.2, 40.6, 31.1, 21.1 ppm. The analytical data matched those reported in the literature.[19]



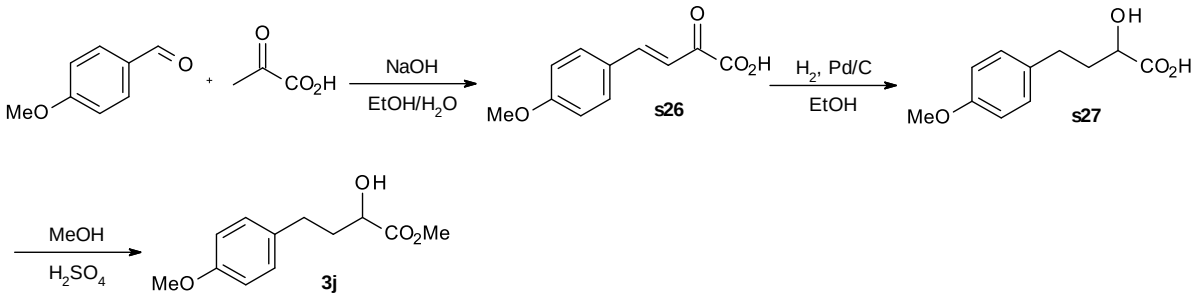
1-(4-Fluorophenyl)-3-(4-methoxyphenyl)propan-1-ol (3g). The synthesis was carried out analogously to the above described procedure for 3-(4-methoxyphenyl)-1-phenyl-propan-1-ol (**3e**). Yield 628 mg (97% for 2 steps), colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.31 (dd, *J*=8.6, 5.2 Hz, 2 H), 7.10 (d, *J*=8.6 Hz, 2 H), 7.03 (t, *J*=8.6 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 4.66 (t, *J*=7.8 Hz, 1 H), 3.79 (s, 3 H), 2.55 - 2.71 (m, 2 H), 2.02 - 2.15 (m, 1 H), 1.93 - 2.01 (m, 1 H), 1.92 ppm (br. d, *J*=3.4 Hz, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 163.1, 157.8, 140.3, 133.5, 129.3, 127.6, 127.5, 115.3, 115.2, 113.8, 73.1, 55.2, 40.8, 31.0 ppm. **^{19}F NMR** (471 MHz, $CDCl_3$) δ = -114.9 ppm. **IR** (neat): ν = 3390, 2935, 1604, 1508, 1243, 1219, 1033 cm^{-1}.



3-(4-Methoxyphenyl)-1-[4-(trifluoromethyl)phenyl]propan-1-ol (3h). The synthesis was carried out analogously to the above described procedure for 3-(4-methoxyphenyl)-1-phenyl-propan-1-ol (**3e**). After 2 hours of hydrogenation under 1 atm. of H_2 the ketone was completely reduced to alcohol. Yield 745 mg (96%), colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.61 (d, *J*=8.0 Hz, 2 H), 7.44 (d, *J*=8.6 Hz, 2 H), 7.09 (d, *J*=8.0 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 4.73 (dd, *J*=7.8, 4.9 Hz, 1 H), 3.78 (s, 3 H), 2.58 - 2.74 (m, 2 H), 2.26 (br. s., 1 H), 1.89 - 2.11 ppm (m, 2 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 157.8, 148.6, 133.3, 129.3, 129.6 (q, *J*=32 Hz), 126.1, 125.4 (q, *J*=4 Hz), 113.8, 73.1, 55.2, 40.7, 30.9. **^{19}F NMR** (471 MHz, $CDCl_3$) δ = -62.3 ppm. **IR** (neat): ν = 3386, 2938, 1612, 1512, 1323, 1245, 1112, 1066 cm^{-1}.



4-[1-hydroxy-3-(4-methoxyphenyl)propyl]benzonitrile (3i). The synthesis was carried out analogously to the above described procedure for 3-(4-methoxyphenyl)-1-phenyl-propan-1-ol (**3e**). Yield 504 mg (94% for 2 steps), colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.60 (d, *J*=8.6 Hz, 2 H), 7.43 (d, *J*=8.0 Hz, 2 H), 7.09 (d, *J*=8.6 Hz, 2 H), 6.82 (d, *J*=8.6 Hz, 1 H), 4.72 (dd, *J*=8.0, 4.6 Hz, 1 H), 3.77 (s, 3 H), 2.67 (s, 2 H), 2.47 (br. s, 1 H), 1.87 - 2.10 ppm (m, 2 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 157.8, 150.1, 133.1, 132.2, 129.2, 126.4, 118.8, 113.8, 110.9, 72.7, 55.2, 40.7, 30.8 ppm. **IR** (neat): ν = 3421, 2911, 2227, 1608, 1511, 1243, 1176, 1033 cm^{-1}.

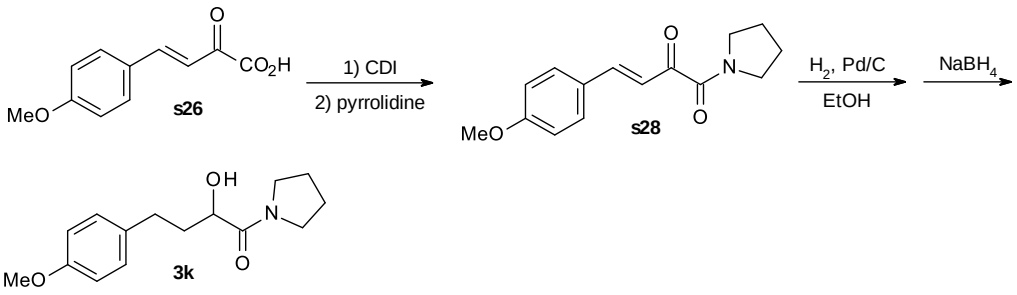


(E)-4-(4-methoxyphenyl)-2-oxo-but-3-enoic acid (s26). The mixture of *p*-anisaldehyde (20 mmol, 2.72 g), pyruvic acid (21.8 mmol, 1.85 g, 2.18 mL), NaOH (47.2 mmol, 1.89 g in 100 mL H_2O) and EtOH (60 mL) was stirred overnight. Then the orange precipitate was filtered off, washed with water, transferred into a beaker, 10% H_2SO_4 was added and the mixture was stirred for 30 minutes. The yellow precipitate was filtered off, washed with water and dried under air Yield 2.64 g. After standing overnight, additional amount of precipitate was formed, which was filtered off, washed with water and dried. Combined yield 3.16 g (77 %), orange-yellow powder. **M.p.** 127.7-130.4°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.78 (d, *J*=8.6 Hz, 2 H), 7.70 (d, *J*=16.1 Hz, 1 H), 7.14 (d, *J*=16.1 Hz, 1 H), 7.02 (d, *J*=8.6 Hz, 2 H), 3.82 ppm (s, 3 H).**^{13}C NMR** (126 MHz, DMSO-d_6): δ = 186.1, 164.9, 162.2, 147.8, 131.3, 126.5, 119.1, 114.7, 55.5 ppm. **IR** (neat): ν = 2844, 2504, 1736, 1713, 1671, 1585, 1564, 1511, 1244 cm^{-1}.

2-Hydroxy-4-(4-methoxyphenyl)butanoic acid (s27). A 100 ml round bottom flask was charged with (E)-4-(4-methoxyphenyl)-2-oxo-but-3-enoic acid (**s26**) (5 mmol, 1031 mg), palladium on carbon (0.1 mmol Pd, 2 mol %, 106 mg of 10% Pd catalyst) and EtOH (50 mL). The flask was flushed with H_2 (balloon) 3 times and the mixture was vigorously stirred under H_2 atmosphere overnight. Then the mixture was filtered through celite, the solvent was removed in vacuum and the residue was dried in vacuum. Yield 1053 mg (quant.), white solid. **M.p.** 114.9-116.1°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 12.38 (br. s, 1 H), 7.06 (d, *J*=8.0 Hz, 2 H), 6.80 (d, *J*=8.6 Hz, 2 H), 5.21 (br. s., 1 H), 3.84 (dd, *J*=8.3, 3.7 Hz, 1 H), 3.67 (s, 3 H), 2.54 (t, *J*=8.0 Hz, 2 H), 1.76 - 1.88 (m, 1 H), 1.64 - 1.75 ppm (m, 1 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 176.3, 157.9, 133.8, 129.7, 114.2, 69.3, 55.4, 36.5, 30.4 ppm. **IR** (neat): ν = 3444, 2911, 2583, 1712, 1612, 1510, 1238 1175 cm^{-1}.

Methyl 2-hydroxy-4-(4-methoxyphenyl)butanoate (3j). To a solution of 2-hydroxy-4-(4-methoxyphenyl)butanoic acid (**s27**) (1.94 mmol) in MeOH (20 mL) few drops of H_2SO_4 were added and the mixture was refluxed for 8 hours. Then the solvent was evaporated, the residue was dissolved in DCM, washed with $NaHCO_3$, 50% brine, dried with $MgSO_4$, the solvent was evaporated and the residue was dried in vacuum. Yield 416 mg (96%), colorless liquid. **^{1}H**

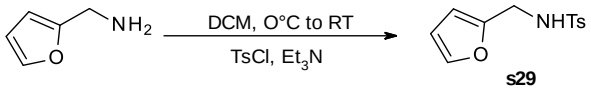
NMR (500 MHz, $CDCl_3$): δ = 7.13 (d, *J*=8.6 Hz, 2 H), 6.83 (d, *J*=8.6 Hz, 2 H), 4.18 (dd, *J*=7.8, 3.7 Hz, 1 H), 3.79 (s, 3 H), 3.75 (s, 3 H), 2.63 - 2.78 (m, 2 H), 2.03 - 2.15 (m, 1 H), 1.86 - 1.97 ppm (m, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 175.7, 157.9, 133.0, 129.5, 113.8, 69.5, 55.2, 52.6, 36.1, 30.0 ppm. **IR** (neat): ν = 3481, 2953, 1732, 1611, 1511, 1440, 1242, 1176, 1090, 1032 cm^{-1}.



(E)-4-(4-methoxyphenyl)-1-pyrrolidin-1-yl-but-3-ene-1,2-dione (s28). A 25 ml round bottom flask was charged with (E)-4-(4-methoxyphenyl)-2-oxo-but-3-enoic acid (**s26**) (2 mmol, 412 mg) and THF (10mL). After addition of 1,1'-carbonyldiimidazole (2.2 mmol, 357 mg) the mixture was stirred for 1 hour at room temperature followed by addition of pyrrolidine (2.2 mmol, 156 mg, 185 µL). Then the reaction mixture was stirred overnight, diluted with water, extracted with ethyl acetate, the combined organic phases were washed with 5% H_2SO_4, sat. $NaHCO_3$, brine, washed with $MgSO_4$ and evaporated to afford the product of decent purity which was used in the next step. Yield 337 mg (65%), orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.68 (d, *J*=16.1 Hz, 1 H), 7.55 (d, *J*=8.6 Hz, 2 H), 7.02 (d, *J*=16.1 Hz, 1 H), 6.91 (d, *J*=9.2 Hz, 2 H), 3.84 (s, 3 H), 3.59 (q, *J*=6.1 Hz, 4 H), 1.88 - 1.99 ppm (m, 4 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 189.9, 164.3, 162.2, 147.5, 130.7, 126.9, 120.3, 114.5, 55.4, 47.2, 45.9, 26.2, 23.8 ppm. The analytical data matched those reported in the literature.[21]

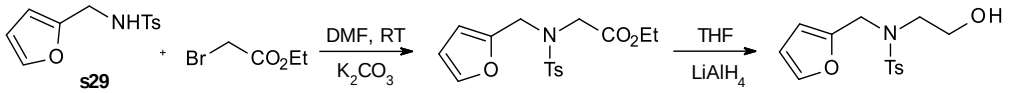
2-hydroxy-4-(4-methoxyphenyl)-1-pyrrolidin-1-yl-butan-1-one (3k). A 100 ml round bottom flask was charged with (E)-4-(4-methoxyphenyl)-1-pyrrolidin-1-yl-but-3-ene-1,2-dione (**s28**) (1.24 mmol, 323 mg), palladium on carbon (0.012 mmol Pd, 1 mol %, 13 mg of 10% Pd catalyst) and EtOH (50 mL). The flask was flushed with H_2 (balloon) 3 times and the mixture was vigorously stirred under H_2 atmosphere for 12 hours. The mixture was filtered through celite and $NaBH_4$ (2.5 mmol, 94 mg) was added and the reaction mixture was stirred for 12 hours. Then EtOH was removed on a rotary evaporator, water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated, the residue was dried in vacuum. Yield 265 mg (81% for 2 steps), yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.12 (d, *J*=8.6 Hz, 2 H), 6.82 (d, *J*=8.6 Hz, 2 H), 4.12 (d, *J*=8.0 Hz, 1 H), 3.77 (s, 3 H), 3.72 (br. s., 1 H), 3.52 (dt, *J*=11.8, 7.3 Hz, 1 H), 3.36 - 3.43 (m, 1 H), 3.21 - 3.30 (m, 1 H), 3.14 (dt, *J*=9.9, 6.8 Hz, 1 H),

2.65 - 2.83 (m, 2 H), 1.65 - 1.97 ppm (m, 6 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.7, 157.7, 133.3, 129.4, 113.7, 68.2, 55.2, 46.1, 45.6, 36.2, 30.2, 25.9, 23.7 ppm. **IR** (neat): ν = 3410, 2951, 2875, 1630, 1511, 1453, 1381, 1243, 1176, 1085, 1030 cm^{-1}.



s29

N-Tosylfurfurylamine (s29). A 50 mL round bottom flask wash charged with furfurylamine (11 mmol, 1.07 g), Et_3N (13 mmol, 1.34 g, 1.8 mL), DCM (25 mL) and chilled with an ice bath. Then TsCl (10 mmol, 2.00 g) was added and the mixture was stirred for 1 hour. The reaction mixture was washed with 5% H_2SO_4, water and 50% brine, dried with $MgSO_4$, the solvent was evaporated and the residue dried in vacuum to afford the desired product as a white solid. Yield 2.48g (94%). **M.p.** 114.1-116.3°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.70 (d, *J*=8.0 Hz, 2 H), 7.26 (d, *J*=9.2 Hz, 2 H), 7.23 (d, *J*=1.1 Hz, 1 H), 6.20 (dd, *J*=2.9, 1.7 Hz, 1 H), 6.08 (d, *J*=2.9 Hz, 1 H), 4.88 (t, *J*=5.7 Hz, 1 H), 4.15 (d, *J*=6.3 Hz, 2 H), 2.41 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 149.5, 143.4, 142.4, 136.7, 129.6, 127.1, 110.3, 108.2, 40.1, 21.5 ppm. **IR** (neat): ν = 3276, 1598, 1425, 1320, 1146 cm^{-1}. **Elemental analysis** found: C, 57.5; H, 5.5; N, 5.5; S, 13.1. Calc. for $C_{12}H_{13}NO_3S$: C, 57.4; H, 5.2; N, 5.6; S, 12.8%.



s29 **s30** **5a**

Ethyl 2-[2-furylmethyl(p-tolylsulfonyl)amino]acetate (s30). A 50 mL round bottom flask was charged with *N*-tosylfurfurylamine **(s29)** (5 mmol, 1.257 g), grinded K_2CO_3 (10 mmol, 2 equiv., 1.38 g) and DMF (50 mL). Then, ethyl bromoacetate (5.25 mmol, 877 mg, 0.6 mL) was added and the mixture was stirred until full conversion (TLC control). Water was added and the mixture was extracted with ethyl acetate. The combined organic fractions were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated and the residue was dried in vacuum to afford pure desired product as a colorless oil. Yield 1.58 g (94%).**^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.72 (d, *J*=8.6 Hz, 2 H), 7.26 - 7.31 (m, 3 H), 6.24 - 6.31 (m, 1 H), 6.18 (d, *J*=2.9 Hz, 1 H), 4.54 (s, 2 H), 4.06 (q, *J*=6.9 Hz, 2 H), 3.95 (s, 2 H), 2.42 (s, 3 H), 1.18 ppm (t, *J*=7.2 Hz, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 168.7, 148.8, 143.4, 142.9, 136.8, 129.5, 127.3, 110.4, 110.0, 61.2, 47.1, 43.9, 21.5, 14.0 ppm. **IR** (neat): ν = 2988, 2936, 1752, 1336, 1201, 1146, 1121 cm^{-1}. **Elemental analysis** found: C, 57.2; H, 5.2; N, 3.8; S, 9.4. Calc. for $C_{16}H_{19}NO_5S$: C, 57.0; H, 5.7; N, 4.2; S, 9.5%.

N-(2-furylmethyl)-N-(2-hydroxyethyl)-4-methyl-benzenesulfonamide (5a). To a solution of **s30** (2.1 mmol, 712 mg) in THF (40 mL) $LiAlH_4$ (2.3 mmol, 88 mg) was added in small portions, then the mixture was stirred for 30 minutes (control by TLC). The reaction was quenched with ethyl acetate, then carefully with water and diluted H_2SO_4 were added until clear solution was obtained. Then the mixture was extracted with ethyl acetate, the combined organic phases were washed with water, brine, dried with $MgSO_4$ and the solvent was evaporated, the residue was dried in vacuum to afford the pure desired product as a white solid. Yield 693 mg (94%), white solid. **^{1}H NMR** (500 MHz, $CDCl_3$): δ =7.66 (d, *J*=8.6 Hz, 2 H), 7.27 - 7.31 (m, 3 H), 6.27 - 6.30 (m, 1 H), 6.21 (d, *J*=3.4 Hz, 1 H), 4.45 (s, 2 H), 3.63 (t, *J*=5.2 Hz, 2 H), 3.27 (t, *J*=5.5 Hz, 2 H), 2.42 (s, 3 H), 2.33 ppm (br. s., 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 149.5, 143.5, 142.7, 136.0, 129.6, 127.3, 110.5, 109.7, 60.8, 50.0, 45.3, 21.5 ppm. **IR** (neat): $\nu =$ 3336, 2923, 1598, 1442, 1339, 1153 cm^{-1}. **Elemental analysis** found: C, 56.2; H, 5.3; N, 4.5; S, 10.8. Calc. for $C_{14}H_{17}NO_4S$: C, 56.9; H, 5.8; N, 4.7; S, 10.9%.

3. Electrochemical spirocyclisation

General procedure for the electrochemical spirocyclisation: A 20 mL undivided cell was charged with the appropriate spirocyclisation precursor (**1a-i** or **3a-l**, 0.5 mmol), KF (100 mg) and methanol (10 mL). The mixture was stirred to reach clear solution, graphite electrodes were adjusted (15mm x 10mm x 2mm, distance 10 mm), and constant current (10 mA) was passed through the solution for 12 h (TLC control of the conversion). After full consumption of the starting material, the solvent vas removed under reduced pressure and the residue was subjected to column chromatography on silica gel, neutralized with Et_3N, applying appropriate eluent.

Important tips: the spirocyclisation product is sensitive to acidic media, TLC analysis and column chromatography should be handled with neutralized silica gel, which can be achieved by addition of 5% Et_3N to the appropriate eluent. The product is not stable in acidic $CDCl_3$ (often contains HCl traces) and NMR analysis should be carried out using DMSO-d_6 as a solvent. It is noteworthy that the product is stable in wet DMSO-d_6 for at least 2 weeks.

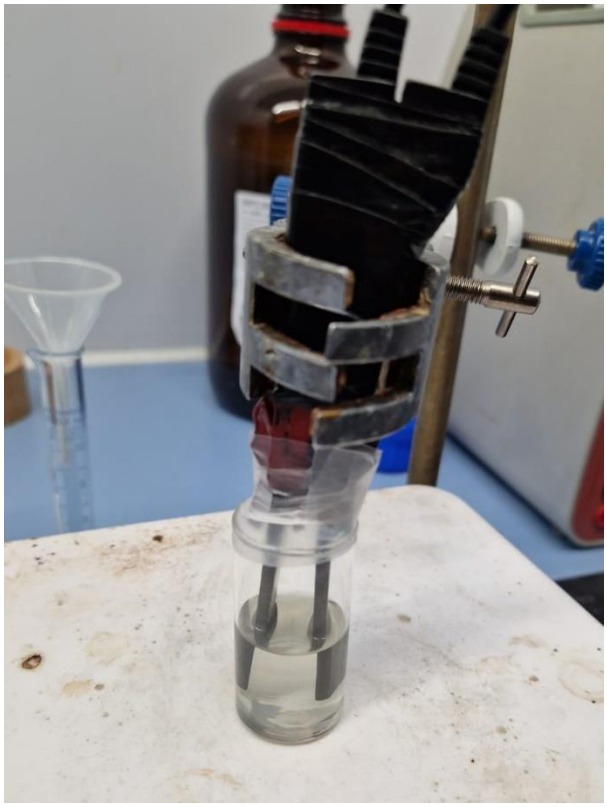


Figure S1. Undivided electrochemical cell with graphite electrodes

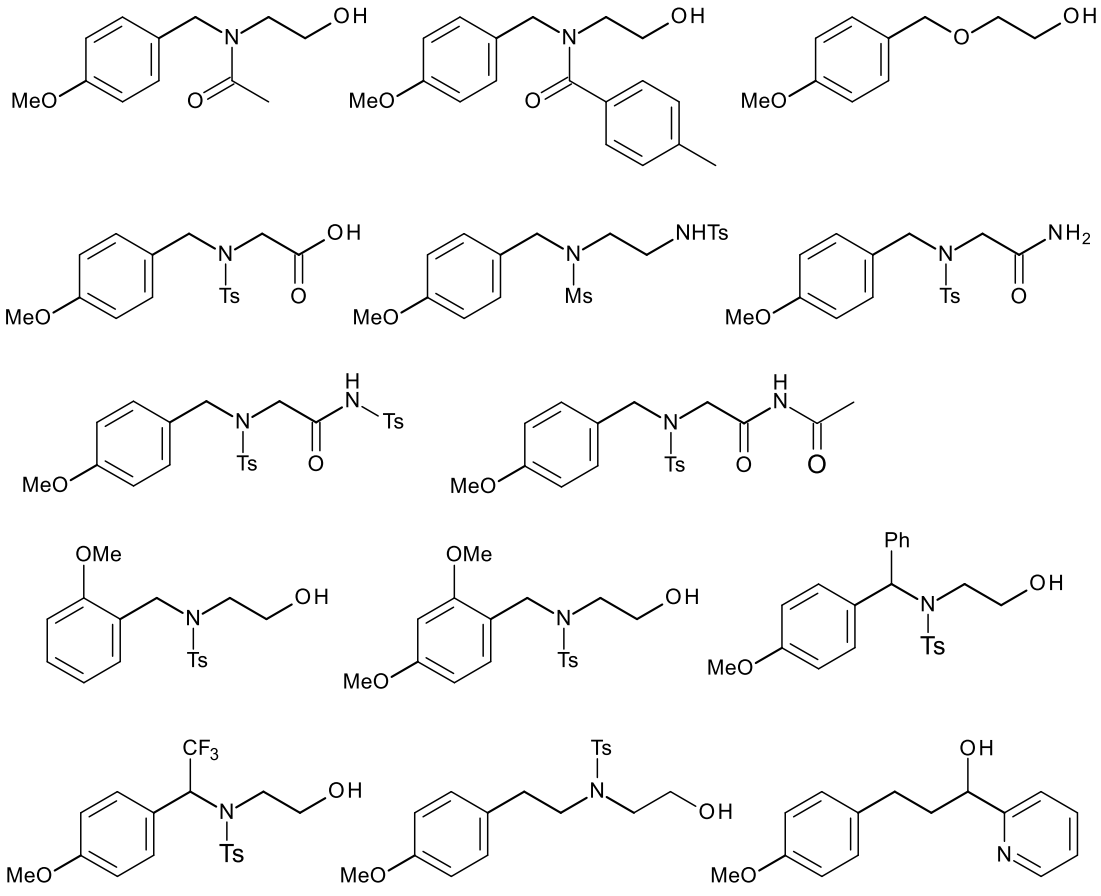
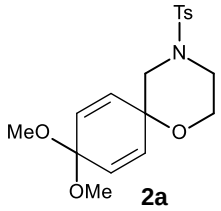


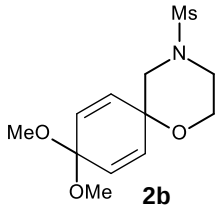
Figure S2. Unsuccessful cyclisation precursors.



2a

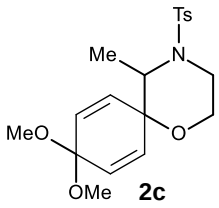
9,9-Dimethoxy-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undeca-7,10-diene (2a). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5%, yield 116 mg (64%), white solid. **M.p.** 111.5-115.9°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.62 (d, *J*=8.6 Hz, 2 H), 7.46 (d, *J*=8.0 Hz, 2 H), 6.27 (d, *J*=10.3 Hz, 2 H), 6.03 (d, *J*=10.3 Hz, 2 H), 3.84 (t, *J*=5.2 Hz, 2 H), 3.17 (s, 3 H), 3.15 (s, 3 H), 2.85 - 2.95 (m, 2 H), 2.70 (br. s, 2 H), 2.41 ppm (s, 3 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 144.0, 131.3, 130.8, 130.0, 128.4, 127.7, 93.0, 67.3, 59.9, 53.2, 49.3, 49.0, 45.5, 21.1 ppm. **IR** (neat): ν = 2923, 2953, 1597, 1347, 1337, 1165 1076 cm^{-1}. **Elemental analysis** found: C, 58.9; H, 6.2; N, 3.4; S, 8.3. Calc. for $C_{18}H_{23}NO_5S$: C, 59.2; H, 6.3; N, 3.8; S, 8.8%.

Scale up Synthesis of 2a. A 200 ml round bottom flask was charged with **1a** (1.133 g, 3.35 mmol), KF (700 mg) and MeOH (180 mL), then graphite electrodes were immersed into solution and constant current (10 mA) was passed until full conversion of the starting material (TLC control, eluent hexane/ethyl acetate/Et_3N 4/1/5%, 41 hours). The solvent was evaporated and the residue was subjected to column chromatography, eluent hexane/ethyl acetate/Et_3N 4/1/5% to hexane/ethyl acetate 2:1. Yield 1.110 g (91%), white solid.



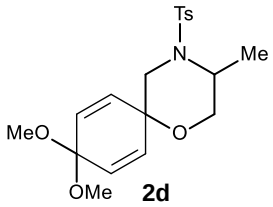
2b

9,9-Dimethoxy-4-methylsulfonyl-1-oxa-4-azaspiro[5.5]undeca-7,10-diene (2b). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 1/1/5%, yield 92 mg (64%), white solid. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 6.31 (d, *J*=10.3 Hz, 2 H), 6.04 (d, *J*=10.3 Hz, 2 H), 3.83 - 3.91 (m, 2 H), 3.14 - 3.20 (m, 8 H), 2.97 (s, 2 H), 2.89 ppm (s, 3 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 131.5, 128.8, 93.7, 67.9, 60.7, 53.4, 49.8, 49.5, 45.6, 34.2 ppm. **Elemental analysis** found: C, 49.5; H, 6.5; N, 5.6; S, 11.2. Calc. for $C_{12}H_{19}NO_5S$: C, 49.8; H, 6.6; N, 4.8; S, 11.1%.



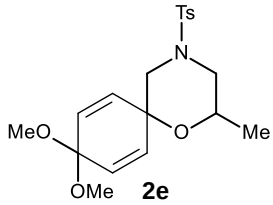
2c

9,9-Dimethoxy-5-methyl-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undeca-7,10-diene (2c). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5%, yield 148 mg (78 %), yellow oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.67 (d, *J*=8.6 Hz, 2 H), 7.42 (d, *J*=8.0 Hz, 2 H), 6.64 (dd, *J*=10.6, 2.6 Hz, 1 H), 5.98 (ddd, *J*=18.0, 10.5, 2.6 Hz, 2 H), 5.84 (dd, *J*=10.3, 2.3 Hz, 1 H), 3.89 (td, *J*=12.1, 3.4 Hz, 1 H), 3.66 - 3.71 (m, 1 H), 3.43 - 3.50 (m, 2 H), 3.15 (s, 3 H), 3.14 (s, 3 H), 3.09 - 3.18 (m, 1 H), 2.40 (s, 3 H), 0.95 ppm (d, *J*=6.9 Hz, 3 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 144.0, 137.2, 132.7, 130.5, 130.4, 128.8, 128.0, 127.4, 93.4, 70.4, 60.2, 56.0, 49.6, 39.2, 21.5, 12.4 ppm. **IR** (neat): ν = 2940, 2828, 2360, 1597, 1346, 1334, 1155, 1082 cm^{-1}. **Elemental analysis** found: C, 59.8; H, 6.8; N, 3.5; S, 8.5. Calc. for $C_{19}H_{25}NO_5S$: C, 60.1; H, 6.6; N, 3.7; S, 8.4%.



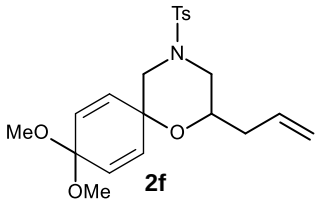
2d

9,9-Dimethoxy-3-methyl-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undeca-7,10-diene (2d). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5%, yield 121 mg (64 %), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.67 (d, *J*=8.0 Hz, 2 H), 7.42 (d, *J*=8.0 Hz, 2 H), 6.51 (dd, *J*=10.6, 2.0 Hz, 1 H), 5.97 - 6.05 (m, 2 H), 5.95 (dd, *J*=10.6, 2.0 Hz, 1 H), 3.97 (dd, *J*=11.8, 3.2 Hz, 1 H), 3.83 - 3.93 (m, 1 H), 3.42 (d, *J*=10.3 Hz, 1 H), 3.15 - 3.19 (m, 1 H), 3.14 (s, 3 H), 3.13 (s, 3 H), 3.05 (d, *J*=13.2 Hz, 1 H), 2.39 (s, 3 H), 0.96 ppm (d, *J*=6.9 Hz, 3 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 143.5, 136.4, 132.7, 130.0, 128.8, 128.7, 127.7, 127.0, 93.1, 67.3, 65.0, 49.3, 49.0, 47.9, 46.8, 21.0, 12.8 ppm. **IR** (neat): ν = 2939, 2829, 1597, 1340, 1183, 1106, 1038 cm^{-1}. **Elemental analysis** found: C, 60.2; H, 6.2; N, 3.4; S, 8.2. Calc. for $C_{19}H_{25}NO_5S$: C, 60.1; H, 6.6; N, 3.7; S, 8.4%.



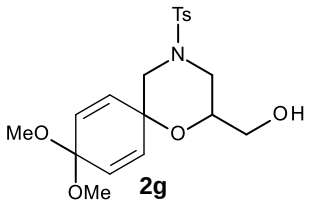
2e

9,9-Dimethoxy-2-methyl-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undeca-7,10-diene (2e). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5%, yield 89 mg (48 %), pale yellow solid. **M.p.** 105.4-108.6°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.62 (d, *J*=8.0 Hz, 2 H), 7.46 (d, *J*=8.0 Hz, 2 H), 6.73 (dd, *J*=10.6, 2.6 Hz, 1 H), 5.98 - 6.07 (m, 2 H), 5.77 (dd, *J*=10.3, 2.9 Hz, 1 H), 4.12 (ddd, *J*=10.3, 6.3, 2.9 Hz, 1 H), 3.62 (d, *J*=10.9 Hz, 1 H), 3.16 (s, 3 H), 3.16 (s, 3 H), 3.09 - 3.15 (m, 1 H), 2.41 (s, 3 H), 2.21 (d, *J*=11.5 Hz, 1 H), 1.85 (t, *J*=11.2 Hz, 1 H), 1.01 ppm (d, *J*=6.3 Hz, 3 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 144.0, 132.9, 131.4, 130.1, 129.2, 128.9, 127.7, 127.6, 93.0, 68.0, 65.1, 52.7, 51.0, 49.2, 49.0, 21.1, 18.7 ppm. **IR** (neat): ν = 2944, 2884, 2360, 1560, 1455, 1410, 1361 cm^{-1}. **Elemental analysis** found: C, 60.2; H, 6.1; N, 3.3; S, 8.0. Calc. for $C_{19}H_{25}NO_5S$: C, 60.1; H, 6.6; N, 3.7; S, 8.4%.



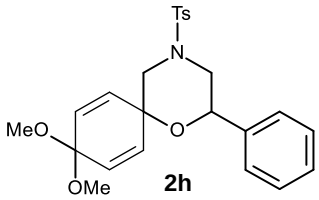
2f

2-Allyl-9,9-dimethoxy-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undeca-7,10-diene (2f). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5%, yield 170 mg (84 %), white solid. **M.p.** 103.3-106.4°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.62 (d, *J*=8.0 Hz, 2 H), 7.46 (d, *J*=8.0 Hz, 2 H), 6.73 (dd, *J*=10.6, 2.0 Hz, 1 H), 5.96 - 6.12 (m, 2 H), 5.78 (dd, *J*=10.3, 2.3 Hz, 1 H), 5.67 - 5.76 (m, 1 H), 4.94 - 5.15 (m, 2 H), 3.98 - 4.12 (m, 1 H), 3.60 (d, *J*=11.5 Hz, 1 H), 3.08 - 3.24 (m, 7 H), 2.41 (s, 3 H), 2.24 (d, *J*=11.5 Hz, 1 H), 2.13 (t, *J*=6.3 Hz, 2 H), 1.93 ppm (t, *J*=10.9 Hz, 1 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 144.0, 133.7, 132.8, 131.5, 130.1, 129.0, 128.9, 127.7, 117.8, 93.0, 68.3, 68.0, 52.8, 49.3, 49.2, 49.0, 37.2, 21.1 ppm. **IR** (neat): ν = 2962, 2881, 2836, 1644, 1597, 1458, 1344, 1160 cm^{-1}. **Elemental analysis** found: C, 62.3; H, 6.5; N, 3.0; S, 7.8. Calc. for $C_{21}H_{27}NO_5S$: C, 62.2; H, 6.7; N, 3.5; S, 7.9%.



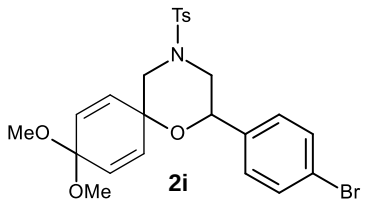
2g

[9,9-dimethoxy-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undeca-7,10-dien-2-yl]methanol (2g). The synthesis was carried out according to the general procedure, eluent for the column chromatography: ethyl acetate/Et_3N 95/5, yield 109 mg (55 %), yellow solid. **M.p.** 78.3-82.2°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.62 (d, *J*=8.0 Hz, 2 H), 7.47 (d, *J*=8.0 Hz, 2 H), 6.72 (dd, *J*=10.9, 2.3 Hz, 1 H), 5.99 - 6.10 (m, 2 H), 5.78 (dd, *J*=10.1, 2.0 Hz, 1 H), 4.80 (t, *J*=5.7 Hz, 1 H), 3.91 - 4.07 (m, 1 H), 3.66 (d, *J*=10.9 Hz, 1 H), 3.31 - 3.42 (m, 2 H), 3.26 (dt, *J*=11.5, 5.7 Hz, 1 H), 3.17 (d, *J*=1.7 Hz, 6 H), 2.42 (s, 3 H), 2.24 (d, *J*=11.5 Hz, 1 H), 1.99 ppm (t, *J*=10.9 Hz, 1 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 144.6, 133.3, 131.8, 130.6, 129.5, 129.5, 128.2, 128.2, 93.4, 70.3, 68.4, 62.6, 53.5, 49.7, 49.5, 48.1, 21.6 ppm. **IR** (neat): ν = 3486, 2925, 1674, 1506, 1342, 1163 1061 1033 cm^{-1}. **Elemental analysis** found: C, 57.4; H, 5.6; N, 3.1; S, 8.0. Calc. for $C_{19}H_{25}NO_6S$: C, 57.7; H, 6.4; N, 3.5; S, 8.1%.



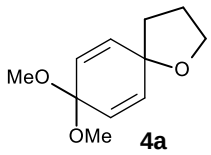
2h

9,9-Dimethoxy-2-phenyl-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undeca-7,10-diene (2h). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5%, yield 125 mg (59%), pale yellow solid. **M.p.** 140.6-143.5°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.63 (d, *J*=8.0 Hz, 2 H), 7.42 (d, *J*=8.0 Hz, 2 H), 7.26 - 7.39 (m, 5 H), 6.90 (dd, *J*=10.6, 2.6 Hz, 1 H), 6.11 (dd, *J*=10.6, 2.6 Hz, 1 H), 6.06 (dd, *J*=10.3, 2.3 Hz, 1 H), 5.94 (dd, *J*=10.3, 2.9 Hz, 1 H), 5.18 (dd, *J*=10.6, 2.6 Hz, 1 H), 3.70 (d, *J*=10.3 Hz, 1 H), 3.23 (dd, *J*=11.5, 1.7 Hz, 1 H), 3.19 (s, 3 H), 3.14 (s, 3 H), 2.42 (d, *J*=11.5 Hz, 1 H), 2.39 (s, 3 H), 2.08 ppm (t, *J*=11.2 Hz, 1 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 144.1, 138.9, 132.8, 131.3, 130.1, 129.2, 129.0, 128.4, 128.3, 127.9, 127.8, 126.5, 93.0, 70.8, 68.3, 52.7, 51.5, 49.3, 49.1, 21.1 ppm. **IR** (neat): ν = 2939, 2827, 1598, 1450, 1415, 1343, 1186 cm^{-1}. **Elemental analysis** found: C, 65.6; H, 6.5; N, 3.2; S, 7.2. Calc. for $C_{24}H_{27}NO_5S$: C 65.3; H, 6.2; N, 3.2; S, 7.3%.



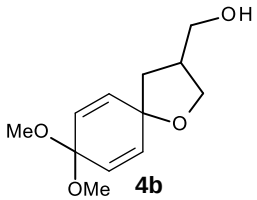
2i

2-(4-bromophenyl)-9,9-dimethoxy-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undeca-7,10-diene. The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5%, yield 98 mg (38%), white powder. **M.p.** 170.6-172.8°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.59 (d, *J*=8.0 Hz, 2 H), 7.49 (d, *J*=8.6 Hz, 2 H), 7.38 (d, *J*=8.0 Hz, 2 H), 7.30 (d, *J*=8.6 Hz, 2 H), 6.84 (dd, *J*=10.9, 2.3 Hz, 1 H), 6.07 (dd, *J*=10.6, 2.6 Hz, 1 H), 6.02 (dd, *J*=10.3, 2.3 Hz, 1 H), 5.90 (dd, *J*=10.3, 2.3 Hz, 1 H), 5.16 (dd, *J*=10.6, 2.6 Hz, 1 H), 3.67 (d, *J*=10.9 Hz, 1 H), 3.18 (d, *J*=12.1 Hz, 1 H), 3.15 (s, 3 H), 3.10 (s, 3 H), 2.38 (d, *J*=11.5 Hz, 1 H), 2.35 (s, 3 H), 2.02 ppm (t, *J*=11.2 Hz, 1 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 144.1, 138.2, 132.6, 131.3, 131.2, 130.1, 129.2, 128.8, 128.7, 127.9, 127.8, 121.3, 92.9, 70.1, 68.3, 52.6, 51.2, 49.2, 49.0, 21.0 ppm. **IR** (neat): ν = 2977, 2830, 2360, 1597, 1491, 1413, 1346, 1183 cm^{-1}. **Elemental analysis** found: C, 54.4; H, 4.4; N, 2.2; S, 6.3. Calc. for $C_{24}H_{26}BrNO_5S$: C, 55.4; H, 5.0; N, 2.7; S, 6.2%.



4a

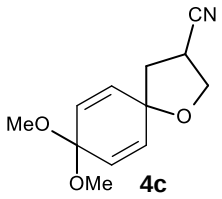
8,8-Dimethoxy-1-oxaspiro[4.5]deca-6,9-diene (4a). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 9/1/5%, yield 58 mg (59%), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 6.02 (d, *J*=10.3 Hz, 1 H), 5.79 (d, *J*=10.3 Hz, 2 H), 3.83 (t, *J*=6.9 Hz, 2 H), 3.14 (s, 3 H), 3.11 (s, 3 H), 2.00 (quin, *J*=7.0 Hz, 2 H), 1.78 ppm (t, *J*=7.2 Hz, 2 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 135.6, 125.0, 93.0, 76.0, 67.5, 49.2, 49.0, 37.2, 26.0 ppm. **Elemental analysis** found: C, 67.8; H, 8.5. Calc. for $C_{11}H_{16}O_3$: C, 67.3; H, 8.2%.



4b

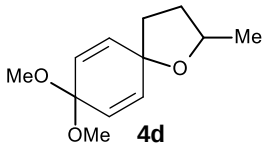
(8,8-Dimethoxy-1-oxaspiro[4.5]deca-6,9-dien-3-yl)methanol (4b). The synthesis was carried out according to the general procedure, eluent for the column chromatography:

hexane/Et_3N 95:5 yield 63 mg (56%), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 6.11 (dd, *J*=10.3, 2.3 Hz, 1 H), 5.99 (dd, *J*=10.1, 2.6 Hz, 1 H), 5.80 (dd, *J*=10.1, 2.6 Hz, 1 H), 5.75 (dd, *J*=10.3, 2.3 Hz, 1 H), 4.71 (t, *J*=5.2 Hz, 1 H), 3.93 (t, *J*=7.8 Hz, 1 H), 3.60 (t, *J*=7.8 Hz, 1 H), 3.35 - 3.46 (m, 2 H), 3.13 (s, 3 H), 3.10 (s, 3 H), 2.51 - 2.62 (m, 1 H), 1.84 (dd, *J*=12.6, 8.0 Hz, 1 H), 1.60 ppm (dd, *J*=12.9, 8.3 Hz, 1 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 136.2, 135.3, 125.4, 124.3, 92.9, 76.4, 70.0, 62.4, 49.2, 49.0, 42.4, 40.2 ppm. **IR** (neat): ν = 3448, 2939, 2870, 2829, 1411, 1103, 1033, 952 cm^{-1}. **Elemental analysis** found: C, 64.0; H, 7.6. Calc. for $C_{12}H_{18}O_4$: C, 63.7; H, 8.0%.



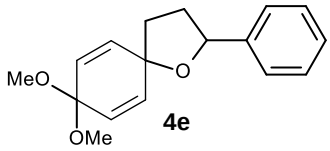
4c

8,8-Dimethoxy-1-oxaspiro[4.5]deca-6,9-diene-3-carbonitrile (4c). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5% to 2:1:5%, yield 46 mg (42%), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 6.12 (dd, *J*=10.3, 2.3 Hz, 1 H), 6.02 - 6.07 (m, *J*=2.3 Hz, 1 H), 5.90 - 5.95 (m, 1 H), 5.85 - 5.89 (m, 1 H), 4.07 - 4.12 (m, 1 H), 4.00 - 4.04 (m, 1 H), 3.60 - 3.69 (m, 1 H), 3.15 (s, 3 H), 3.12 (s, 3 H), 2.27 (dd, *J*=13.2, 8.0 Hz, 1 H), 2.14 ppm (dd, *J*=13.2, 6.3 Hz, 1 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 134.0, 133.7, 126.5, 126.0, 121.2, 92.5, 76.6, 69.3, 49.2, 49.0, 40.7, 28.9 ppm. **Elemental analysis** found: C, 65.4; H, 7.1; N, 6.0. Calc. for $C_{12}H_{15}NO_3$: C, 65.1; H, 6.8; N, 6.3%.



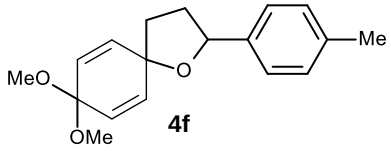
4d

8,8-dimethoxy-2-methyl-1-oxaspiro[4.5]deca-6,9-diene (4d). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 9/1/5%, yield 69 mg (66%), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 6.03 - 6.07 (m, 1 H), 5.97 - 6.00 (m, 1 H), 5.76 (dq, *J*=10.4, 2.1 Hz, 2 H), 4.08 - 4.18 (m, 1 H), 3.13 (s, 3 H), 3.11 (s, 3 H), 2.10 (dq, *J*=12.0, 6.0 Hz, 1 H), 1.82 - 1.86 (m, 2 H), 1.60 (dq, *J*=12.1, 8.2 Hz, 1 H), 1.17 ppm (d, *J*=5.7 Hz, 3 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 136.8, 136.0, 124.7, 124.6, 92.9, 76.2, 75.1, 49.2, 48.9, 37.5, 33.3, 21.6 ppm. **IR** (neat): ν = 2967, 2935, 1670, 1445, 1410, 1377, 1105 1066, cm^{-1}. **Elemental analysis** found: C, 68.9; H, 8.8. Calc. for $C_{12}H_{18}O_3$: C, 68.5; H, 8.6%.



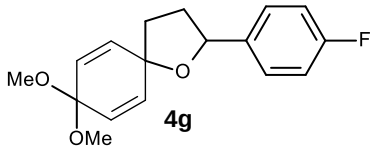
4e

8,8-Dimethoxy-2-phenyl-1-oxaspiro[4.5]deca-6,9-diene (4e). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 9/1/5%, yield 107 mg (79%), colourless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.31 - 7.40 (m, 4 H), 7.23 - 7.30 (m, 1 H), 6.18 (d, *J*=9.2 Hz, 2 H), 5.86 (d, *J*=10.3 Hz, 2 H), 5.06 (t, *J*=6.9 Hz, 1 H), 3.17 (s, 3 H), 3.14 (s, 3 H), 2.43 (s, 1 H), 1.97 - 2.06 (m, 1 H), 1.85 - 1.96 ppm (m, 2 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 142.7, 135.8, 135.8, 128.2, 127.3, 125.8, 125.2, 125.2, 92.9, 80.7, 76.8, 49.2, 49.0, 37.6, 34.9 ppm. **Elemental analysis** found: C, 75.2; H, 7.0. Calc. for $C_{17}H_{20}O_3$: C, 75.0; H, 7.4%.



4f

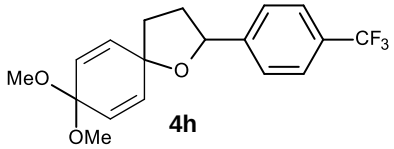
8,8-Dimethoxy-2-(p-tolyl)-1-oxaspiro[4.5]deca-6,9-diene (4f). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 9/1/5%, yield 85 mg (59%), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.24 (d, *J*=8.0 Hz, 2 H), 7.14 (d, *J*=8.0 Hz, 2 H), 6.17 (d, *J*=10.3 Hz, 2 H), 5.84 (d, *J*=9.8 Hz, 2 H), 4.99 - 5.04 (m, 1 H), 3.16 (s, 2 H), 3.13 (s, 3 H), 2.33 - 2.43 (m, 1 H), 2.28 (s, 3 H), 1.94 - 2.05 (m, 1 H), 1.83 - 1.95 ppm (m, 2 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 139.6, 136.3, 135.9, 135.8, 128.8, 125.8, 125.1, 125.1, 92.9, 80.6, 76.6, 49.2, 49.0, 37.6, 34.9, 20.7 ppm. **IR** (neat): ν = 2940, 2828, 1668, 1630, 1515, 1105, 1028, 1018 cm^{-1}. **Elemental analysis** found: C, 75.3; H, 7.4. Calc. for $C_{18}H_{22}O_3$: C, 75.5; H, 7.7%.



4g

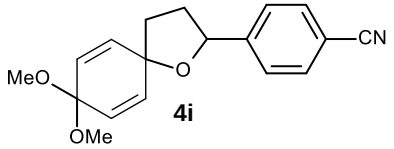
2-(4-Fluorophenyl)-8,8-dimethoxy-1-oxaspiro[4.5]deca-6,9-diene (4g). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 9/1/5%, yield 93 mg (64%), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.40 (dd, *J*=8.6, 5.7 Hz, 2 H), 7.17 (t, *J*=8.9 Hz, 2 H), 6.14 - 6.20 (m, 2 H), 5.82 - 5.88 (m, 2 H), 5.02 - 5.09 (m, 1 H), 3.16 (s, 3 H), 3.14 (s, 3 H), 2.41 (s, 1 H), 1.96 - 2.06 (m, 1 H), 1.84 - 1.96 ppm (m, 2 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ =162.4, 160.4, 138.8, 138.8,

135.7, 135.7, 127.9, 127.8, 125.3, 125.2, 115.1, 114.9, 92.9, 80.0, 76.8, 49.2, 49.0, 37.5, 34.9 ppm. **^{19}F NMR** (471 MHz, $CDCl_3$) δ = -115.4 ppm. **IR** (neat): ν = 2938, 2827, 1670, 1603, 1509, 1410, 1223, 1104, 1036 cm^{-1}.



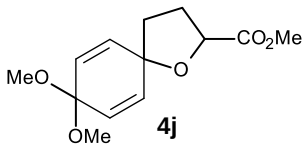
4h

8,8-Dimethoxy-2-[4-(trifluoromethyl)phenyl]-1-oxaspiro[4.5]deca-6,9-diene (4h). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 9/1/5%, yield 79 mg (46%), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 6.15 (d, *J*=9.2 Hz, 2 H), 5.84 (d, *J*=9.8 Hz, 2 H), 5.13 (t, *J*=6.9 Hz, 1 H), 3.14 (s, 3 H), 3.10 (s, 3 H), 2.43 - 2.52 (m, 1 H), 1.93 - 2.04 (m, 1 H), 1.82 - 1.93 ppm (m, 2 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 147.7, 135.4, 127.8 (q, *J*=31 Hz), 126.4, 125.5, 125.4, 125.2 (q, *J*=4 Hz), 123.2, 92.8, 79.9, 77.2, 49.2, 49.0, 37.4, 34.8 ppm. **^{19}F NMR** (471 MHz, $CDCl_3$) δ = -60.7 ppm. **IR** (neat): ν = 2940, 2829, 1670, 1619, 1323, 1161, 1107, 1065, 1038 cm^{-1}.



4i

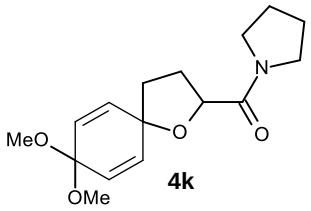
4-(8,8-Dimethoxy-1-oxaspiro[4.5]deca-6,9-dien-2-yl)benzonitrile (4i). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5%, yield 85 mg (57%), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.78 (d, *J*=8.6 Hz, 2 H), 7.52 (d, *J*=8.0 Hz, 2 H), 6.10 - 6.19 (m, 2 H), 5.81 - 5.86 (m, 2 H), 5.07 - 5.16 (m, 1 H), 3.13 (s, 3 H), 3.10 (s, 3 H), 2.41 - 2.51 (m, 1 H), 1.93 - 2.02 (m, 1 H), 1.77 - 1.92 ppm (m, 2 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ =148.7, 135.4, 135.4, 132.3, 126.6, 125.6, 125.5, 118.9, 109.9, 92.8, 79.8, 77.3, 49.3, 49.0, 37.4, 34.7 ppm. **IR** (neat): ν = 2938, 2827, 2226, 1669, 1608, 1459, 1410, 1190 cm^{-1}. **Elemental analysis** found: C, 73.1; H, 6.8; N, 4.3. Calc. for $C_{18}H_{19}NO_3$: C, 72.7; H, 6.4; N, 4.7%.



4j

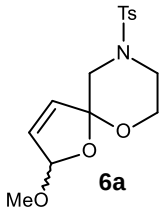
Methyl 8,8-dimethoxy-1-oxaspiro[4.5]deca-6,9-diene-2-carboxylate (4j). The synthesis was carried out according to the general procedure, eluent for the column chromatography:

hexane/ethyl acetate/Et_3N 4/1/5%, yield 68 mg (53%), colorless oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 6.10 (dd, J=10.3, 2.3 Hz, 1 H), 6.05 (dd, J=10.3, 2.3 Hz, 1 H), 5.84 (ddd, J=16.8, 10.2, 2.3 Hz, 2 H), 4.61 (dd, J=8.0, 5.2 Hz, 1 H), 3.66 (s, 3 H), 3.15 (s, 3 H), 3.12 (s, 3 H), 2.35 - 2.45 (m, J=12.6, 8.0 Hz, 1 H), 2.12 (dq, J=12.1, 6.1 Hz, 1 H), 1.85 ppm (t, J=6.9 Hz, 2 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 173.0, 135.4, 134.8, 125.8, 125.5, 92.7, 78.2, 76.9, 51.8, 49.2, 49.0, 36.2, 30.0 ppm. **IR** (neat): ν = 2948, 2828, 1735, 1670, 1632, 1436, 1411, 1280, 1207 cm^{-1}. **Elemental analysis** found: C, 60.9; H, 7.5. Calc. for $C_{13}H_{18}O_5$: C, 61.4; H, 7.1%.



4k

(8,8-dimethoxy-1-oxaspiro[4.5]deca-6,9-dien-2-yl)-pyrrolidin-1-yl-methanone (4k). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 1/1/5%, yield 73 mg (50%), yellow oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 6.12 (dd, *J*=10.3, 2.3 Hz, 1 H), 6.06 (dd, *J*=10.6, 2.6 Hz, 1 H), 5.79 - 5.84 (m, 2 H), 4.74 (t, *J*=6.6 Hz, 1 H), 3.51 (dt, *J*=9.9, 6.8 Hz, 1 H), 3.42 (s, 1 H), 3.29 (t, *J*=6.9 Hz, 2 H), 3.15 (s, 3 H), 3.11 (s, 3 H), 2.14 - 2.27 (m, 2 H), 1.80 - 1.94 (m, 4 H), 1.69 - 1.78 ppm (m, 2 H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 169.0, 135.9, 135.2, 125.3, 125.1, 92.8, 77.7, 77.0, 49.2, 49.0, 45.7, 45.7, 36.8, 28.5, 25.7, 23.6 ppm. **IR** (neat): ν = 2940, 2876, 2827, 2360, 2342, 1642, 1440, 1411, 1340, 1104, 1065, 1036 cm^{-1}. **Elemental analysis** found: C, 65.2; H, 7.8; N, 4.3; S, 9.6. Calc. for $C_{16}H_{23}NO_4$: C, 65.5; H, 7.9; N, 4.8%.

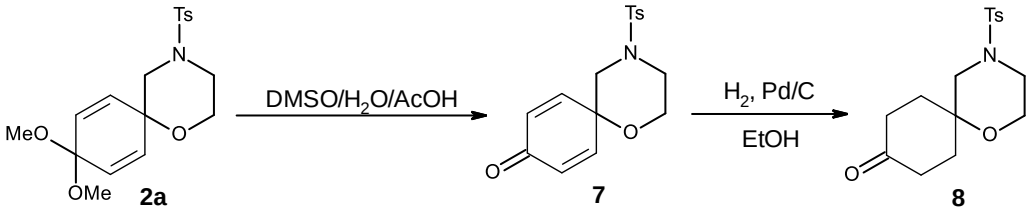


6a

2-Methoxy-7-(p-tolylsulfonyl)-1,10-dioxa-7-azaspiro[4.5]dec-3-ene (6a). The synthesis was carried out according to the general procedure, eluent for the column chromatography: hexane/ethyl acetate/Et_3N 4/1/5%, yield 81 mg (50%), white solid. **M.p.** 104.8-107.0°C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.58 - 7.67 (m, 2 H), 7.47 (d, *J*=8.0 Hz, 2 H), 6.11 - 6.20 (m, 2 H), 5.82 (s, 0.3 H), 5.71 (s, 0.7 H), 3.86 - 4.01 (m, 1 H), 3.71 - 3.78 (m, 1 H), 3.37 - 3.44 (m, 1 H), 3.28 (s, 1 H), 3.23 (s, 2 H), 3.18 (d, *J*=11.5 Hz, 1 H), 2.55 - 2.63 (m, 1 H), 2.38 - 2.46 (m, 1 H), 2.42 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ = 143.9, 132.8, 132.6, 132.3, 131.9,

131.6, 131.5, 130.0, 129.9, 127.7, 127.7, 108.4, 107.3, 106.5, 105.6, 60.9, 60.7, 53.6, 53.2, 51.6, 51.5, 44.5, 44.4, 21.0 ppm. **IR** (neat): ν = 3099, 2990, 2936, 1598, 1454, 1336, 1157 cm^{-1}. **Elemental analysis** found: C, 55.9; H, 5.6; N, 3.9; S, 9.7. Calc. for $C_{15}H_{19}NO_5S$: C, 55.4; H, 5.9; N, 4.3; S, 9.9%.

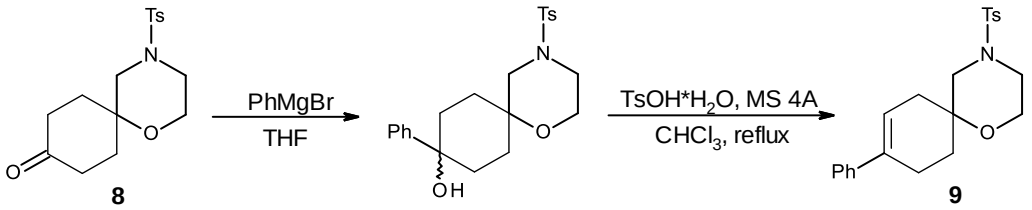
4. Modification of the spirocyclisation product



4-(*p*-Tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undeca-7,10-dien-9-one (7). Compound **2a** (849 mg, 2.32 mmol) was dissolved in DMSO (20 ml), then H2O (4 mL) and AcOH (1 mL) were added and the solution was stirred overnight to reach full conversion (TLC control, hexane/ethyl acetate/Et_3N 4/1/5%). The mixture was diluted with water and the white precipitate was filtered off, washed with water and dried on filter under air flow overnight. Yield 526 mg (71%), white powder. **M.p.** 138.2-139.8°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.61 (d, *J*=8.0 Hz, 2 H), 7.36 (d, *J*=8.0 Hz, 2 H), 7.07 (d, *J*=9.8 Hz, 2 H), 6.29 (d, *J*=9.8 Hz, 2 H), 4.00 (t, *J*=4.9 Hz, 2 H), 3.07 - 3.16 (m, 2 H), 2.97 (s, 2 H), 2.45 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 184.7, 144.5, 144.4, 131.8, 130.0, 130.0, 127.7, 68.5, 61.0, 52.5, 45.5, 21.6 ppm. **IR** (neat): ν = 3050, 2893, 1674, 1635, 1596, 1457, 1393, 1341, 1160 cm^{-1}. **Elemental analysis** found: C, 59.7; H, 5.1; N, 4.0; S, 10.0. Calc. for $C_{15}H_{17}NO_4S$: C, 60.2 H, 5.4; N, 4.4; S, 10.0 %.

4-(*p*-Tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undecan-9-one (8). A 100 ml round bottom flask was charged with unsaturated ketone 7 (526 mg, 1.65 mmol), Pd/C, 5% Pd load, 70 mg, 2% Pd) and EtOH, 50 mL. The flask was flushed with H2 several times and the mixture was stirred under H_2 atmosphere (balloon) for 2 hours. The solution was filtered through a celite pad, the solvent was evaporated and the residue was dried in vacuum. Yield 530 mg (99%). The compound was used for the following steps without further purification. For the analytically pure sample the compound was purified by column chromatography, eluent hexane/ethyl acetate 1:1. white solid. Yield 526 mg (71%), colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.60 (d, *J*=8.6 Hz, 2 H), 7.34 (d, *J*=8.0 Hz, 2 H), 3.81 (t, *J*=5.0 Hz, 2 H), 2.99 (t, *J*=4.6 Hz, 2 H), 2.80 (s, 2 H), 2.51 (td, *J*=14.2, 6.0 Hz, 2 H), 2.43 (s, 3 H), 2.18 - 2.35 (m, 4 H), 1.68 ppm (td, *J*=13.5, 4.6 Hz, 2 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 210.8, 144.0, 132.1, 129.8, 127.7,

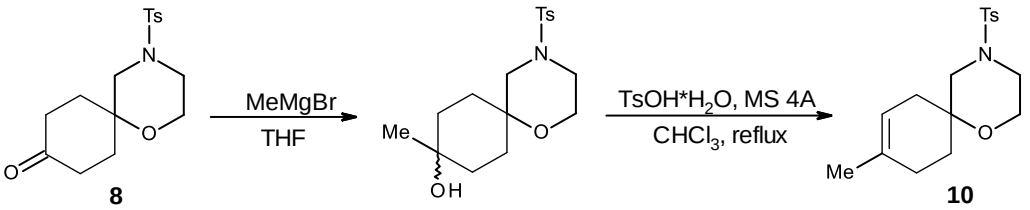
70.3, 60.0, 53.5, 45.7, 35.8, 31.6, 21.5 ppm. **IR** (neat): ν = 2959, 2874, 2848, 1711, 1597, 1454, 1338, 1184 cm^{-1}.



8 **9**

9-Phenyl-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undec-9-ene (9). To a solution of ketone **8** (91 mg, 0.28 mmol) in dry THF (5 mL) was added a solution of PhMgBr (1.0 M in THF, 0.35 mL, 1.25 eq.) and the mixture was stirred for 30 minutes. The reaction was quenched with water and diluted with saturated solution of NH_4Cl, water and extracted with ethyl acetate. The combined organic phases were washed with water, brine, dried with MgSO4 and evaporated. The crude mixture was subjected to column chromatography, eluent hexane/ethyl acetate 1:1, to afford the alcohol as a mixture of diastereomers. Yield 70 mg (62%). The mixture was directly used in the next step.

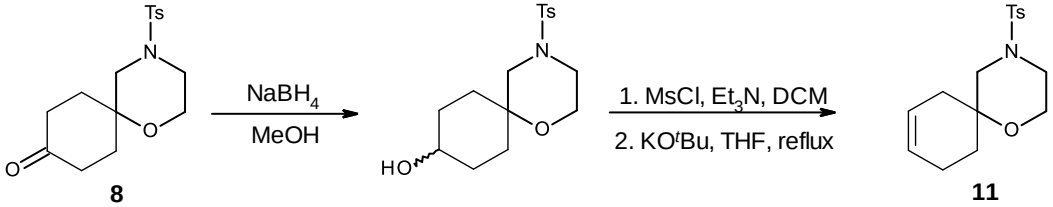
To a solution of above obtained alcohols (54 mg, 0.13 mmol) in $CHCl_3$ (5 mL) was added $TsOH*H_2O$ (20 mg) and molecular sieves 4Å, the mixture was refluxed for 2 hours. The solution was diluted with DCM, filtered, washed with saturated solution of $NaHCO_3$, water, dried with $MgSO_4$ and evaporated. The residue was subjected to column chromatography, eluent hexane/ethyl acetate 4:1 to obtain pure compound **9** as a white solid. An analytically pure sample can be obtained by trituration with Et_2O. Yield 33 mg (66%). **M.p.** 185.4-186.3°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.63 (d, *J*=8.0 Hz, 2 H), 7.39 (d, *J*=7.5 Hz, 2 H), 7.34 (d, *J*=8.0 Hz, 2 H), 7.31 (t, *J*=7.8 Hz, 2 H), 7.21 - 7.25 (m, 1 H), 5.97 (br. s., 1 H), 3.84 - 3.95 (m, 1 H), 3.80 (dt, *J*=11.9, 4.1 Hz, 1 H), 3.15 (d, *J*=10.9 Hz, 1 H), 3.01 (d, *J*=10.9 Hz, 1 H), 2.84 (t, *J*=8.0 Hz, 1 H), 2.69 (d, *J*=11.5 Hz, 1 H), 2.49 - 2.61 (m, 1 H), 2.44 (s, 3 H), 2.40 - 2.49 (m, 1 H), 2.34 (dd, *J*=50.0, 18.0 Hz, 2 H), 2.17 (dt, *J*=13.1, 6.4 Hz, 1 H), 1.89 ppm (dt, *J*=13.2, 6.6 Hz, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 143.8, 141.0, 136.0, 132.3, 129.7, 128.2, 127.8, 126.9, 125.0, 120.3, 70.9, 59.8, 52.5, 45.8, 34.8, 28.3, 24.2, 21.5 ppm. **IR** (neat): ν = 2926, 2883, 2845, 2359, 1596, 1448, 1344, 1164 cm^{-1}. **Elemental analysis** found: C, 68.4; H, 6.3; N, 3.3; S, 8.3. Calc. for $C_{22}H_{25}NO_3S$: C, 68.9; H, 6.6; N, 3.7; S, 8.4%.



8 **10**

9-Methyl-4-(p-tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undec-9-ene (10). To a solution of ketone **8** (176 mg, 0.54 mmol) in dry THF (5 mL) was added a solution of MeMgBr (3.0 M in Et_2O, 0.4 mL, 2.2 eq.) and the mixture was stirred for 30 minutes. The reaction was quenched with water and diluted with saturated solution of NH_4Cl, water and extracted with ethyl acetate. The combined organic phases were washed with water, brine, dried with $MgSO_4$ and evaporated to afford the alcohol as a mixture of diastereomers. Yield 182 mg (99%). The mixture was directly used in the next step.

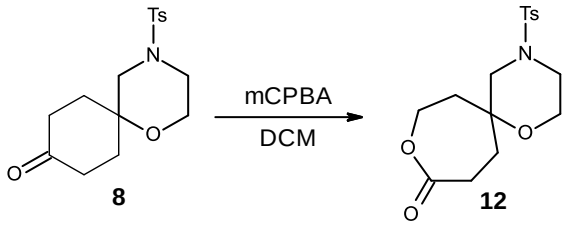
To a solution of above obtained alcohols (182 mg, 0.54 mmol) in $CHCl_3$ (10 mL) was added TsOH*H_2O (100 mg) and molecular sieves 4Å, the mixture was refluxed for 4 hours. The solution was diluted with DCM, filtered, washed with saturated solution of $NaHCO_3$, water, dried with $MgSO_4$ and evaporated. The residue was subjected to column chromatography, eluent hexane/ethyl acetate 4:1 to obtain pure compound **10** as a white solid. Yield 74 mg (43%). **M.p.** 147.2-148.6°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = .61 (d, *J*=8.0 Hz, 2 H), 7.33 (d, *J*=8.0 Hz, 2 H), 5.23 (br. s, 1 H), 3.83 (ddd, *J*=12.0, 8.0, 3.4 Hz, 1 H), 3.75 (ddd, *J*=12.0, 5.0, 3.4 Hz, 1 H), 3.07 - 3.16 (m, 1 H), 2.95 (d, *J*=10.9 Hz, 1 H), 2.77 (ddd, *J*=11.2, 8.0, 3.2 Hz, 1 H), 2.60 (d, *J*=10.9 Hz, 1 H), 2.43 (s, 3 H), 2.11 - 2.19 (m, 1 H), 1.97 - 2.09 (m, 3 H), 1.87 - 1.96 (m, 1 H), 1.67 - 1.75 (m, 1 H), 1.66 ppm (s, 3 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 143.8, 133.6, 132.2, 129.7, 127.7, 117.2, 71.0, 59.7, 52.5, 45.8, 34.4, 28.0, 26.9, 23.1, 21.5 ppm. **IR** (neat): ν = 2963, 2912, 2882. 2851, 1596, 1449, 1351, 1163 cm^{-1}. **Elemental analysis** found: C, 63.8; H, 7.4; N, 4.0; S, 9.9. Calc. for $C_{17}H_{23}NO_3S$: C, 63.5; H, 7.2; N, 4.4; S, 10.0%.



8 **11**

4-(p-Tolylsulfonyl)-1-oxa-4-azaspiro[5.5]undec-9-ene (11). To a solution of ketone **8** (71 mg, 0.21 mmol) in MeOH (3 mL) was added $NaBH_4$ (16 mg, 0.42 mmol) and the mixture was stirred for 2 hours. The mixture was diluted with water, extracted with DCM, the combined organic phases were washed with water, dried with $MgSO_4$ and evaporated to afford the corresponding alcohol as a mixture of diastereomers. Yield 68 mg (quant.).

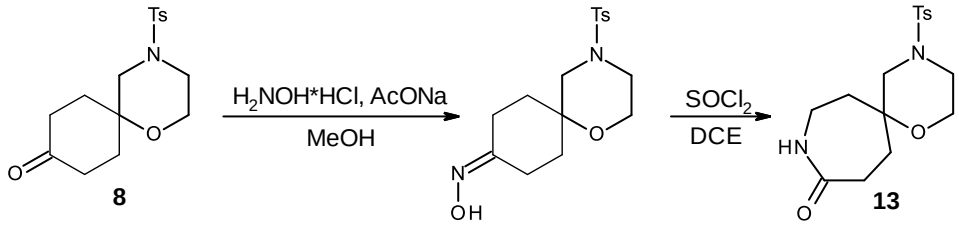
To a solution of above obtained alcohols (56 mg, 0.17 mmol) in DCM (5 mL) was added Et_3N (0.05 mL, 0.36 mmol) and MsCl (24mg, 0.20 mmol), the mixture was stirred overnight at room temperature. The reaction mixture was diluted with DCM, washed with 5% solution of H_2SO_4, saturated $NaHCO_3$, water, dried with $MgSO_4$ and evaporated. Yield of the O-Ms alcohols 65 mg (95%). The obtained crude mixture of the mesylated alcohols was dissolved in THF, KOtBu was added and the mixture was refluxed for 2 hours (TLC control). After reaching full conversion, the mixture was cooled down, diluted with water, extracted with ethyl acetate, the combined organic phases were washed with 50% brine, dried with MgSO4 and evaporated. The crude product was subjected to column chromatography, eluent hexane/ethyl acetate 4:1 to obtain pure compound **11** as a colourless oil. Yield 26 mg (53 % for 2 steps). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.61 (d, *J*=8.0 Hz, 1 H), 7.33 (d, *J*=7.5 Hz, 2 H), 5.69 (ddt, *J*=9.8, 3.4, 1.7 Hz, 1 H), 5.55 (ddt, *J*=9.7, 3.5, 1.7 Hz, 1 H), 3.81 - 3.88 (m, 1 H), 3.73 - 3.80 (m, 1 H), 3.03 - 3.17 (m, 1 H), 2.92 (d, *J*=11.5 Hz, 1 H), 2.82 (ddd, *J*=11.1, 7.6, 3.2 Hz, 1 H), 2.65 (d, *J*=11.5 Hz, 1 H), 2.43 (s, 3 H), 2.18 - 2.25 (m, 1 H), 2.09 - 2.18 (m, 1 H), 2.01 - 2.09 (m, 2 H), 1.92 - 2.01 (m, 1 H), 1.68 - 1.77 ppm (m, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 143.8, 132.4, 129.7, 127.7, 126.5, 123.2, 71.2, 59.7, 52.4, 45.8, 34.1, 28.0, 22.2, 21.5 ppm. **IR** (neat): ν = 3026, 2921, 2844, 1597, 1453, 1342, 1164 cm^{-1}.



8 **12**

4-(p-Tolylsulfonyl)-1,10-dioxa-4-azaspiro[5.6]dodecan-9-one (12). To a solution of ketone **8** (90 mg, 0.27 mmol) in DCM (2 mL) was added mCPBA (2 equiv., 137 mg of 70% wt. mCPBA) and the mixture was stirred at room temperature for 2 hours (TLC control). Then the mixture was diluted with DCM, washed with saturated solution of $NaHCO_3$, dried with $MgSO_4$ and evaporated. The residue was subjected to column chromatography, eluent hexane/ethyl acetate 1:1. Yield 67 mg (73%), white solid. **M.p.** 167.4-168.8°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.60 (d, *J*=8.0 Hz, 2 H), 7.34 (d, *J*=8.6 Hz, 2 H), 4.43 (dd, *J*=12.9, 10.6 Hz, 1 H), 3.97 - 4.14 (m, 1 H), 3.63 - 3.82 (m, 2 H), 2.96 - 3.06 (m, 1 H), 2.86 - 2.95 (m, 2 H), 2.80 (d, *J*=11.8 Hz, 1 H), 2.70 (d, *J*=11.8 Hz, 1 H), 2.44 (s, 2 H), 2.41 - 2.48 (m, 1 H), 2.15 - 2.36 (m, 2 H), 1.72 (ddd, *J*=16.0, 11.0, 1.2 Hz, 1 H), 1.57 ppm (t, *J*=13.8 Hz, 1 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 175.5, 144.1, 132.0, 129.8, 127.7, 71.1, 62.3, 59.6, 54.3, 45.6, 35.8, 28.8, 27.0,

21.5 ppm. **IR** (neat): ν = 2915, 1735, 1597, 1480, 1439, 1332, 1165 cm^{-1}. **Elemental analysis** found: C, 56.3; H, 5.8; N, 3.7; S, 9.3. Calc. for $C_{16}H_{21}NO_5S$: C, 56.6; H, 6.2; N, 4.1; S, 9.4%.



4-(p-Tolylsulfonyl)-1-oxa-4,10-diazaspiro[5.6]dodecan-9-one (13). To a solution of ketone **8** (188 mg, 0.58 mmol) in MeOH (10 mL) was added $H_2NOH*HCl$ (3 equiv., 121 mg), $AcONa*H_2O$ (3 equiv., 237 mg) and the mixture was refluxed for 3 hours (TLC control). Then the mixture was diluted with water, extracted with DCM, the combined organic phases were washed with water, dried with $MgSO_4$ and evaporated. The crude oxime was dissolved in DCE (2 mL) and $SOCl_2$ (0.2 mL) was added dropwise (exothermic reaction). The mixture was stirred for 10 minutes and quenched with saturated $NaHCO_3$, extracted with DCM, the combined organic phases were washed with water, dried with $MgSO_4$ and evaporated. The residue was subjected to column chromatography, eluent hexane/ethyl acetate 1:1 then ethyl acetate/MeOH 95:5. Yield 86 mg (42% for 2 steps), white solid. **M.p.** 186.9-188.0°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.59 (d, *J*=8.0 Hz, 2 H), 7.33 (d, *J*=8.0 Hz, 2 H), 6.56 (br. s., 1 H), 3.72 (t, *J*=4.9 Hz, 2 H), 3.50 (ddd, *J*=14.8, 11.1, 4.0 Hz, 1 H), 2.86 - 3.06 (m, 3 H), 2.63 - 2.81 (m, 3 H), 2.42 (s, 3 H), 2.14 - 2.22 (m, 2 H), 2.08 (dd, *J*=14.7, 5.5 Hz, 1 H), 1.39 - 1.57 ppm (m, 2 H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ =178.5, 144.0, 132.1, 129.8, 127.7, 72.2, 59.4, 54.7, 45.6, 36.0, 35.7, 29.1, 28.6, 21.5 ppm. **IR** (neat): ν = 3210, 2962, 2927, 2910, 2363, 1665, 1350, 1162, 1087 cm^{-1}. **Elemental analysis** found: C, 56.6; H, 6.3; N, 7.9; S, 9.1. Calc. for $C_{16}H_{22}N_2O_4S$: C, 56.8; H, 6.6; N, 8.3; S, 9.5%.

5. Electrochemical characterization

All cyclic voltammogram measurements were performed in a three electrode electrochemical cell using a Metrohm Autolab PGSTAT100N potentiostat and 10A booster (Netherlands). The cell consisted of a 3 mm diameter glassy carbon working electrode, a glassy carbon rod counter electrode, and a Ag/AgCl (sat. KCl) reference electrode (Instruments Inc., Austin, TX, USA).

The electrochemical activity was measured by scanning the working electrode potential between -0.0 and 1.30 V (V vs Ag/AgCl (sat. KCl)) at 0.100 V/s. At the end of each measurement, reference electrode potential was calibrated using a ferrocene oxidation process (0.10 mM in methanol). All working solutions were prepared using methanol as a

solvent. The concentration of **1a** and supporting electrolytes matched the conditions described in Scheme 1 in the main text. In summary, black and blue CVs appear similar in shape, and exhibit peaks are p1 = 0.31 V and p3 = 0.75 V (V vs Fc/Fc^+). No significant faradaic current is present when **1a** is absent from the working solutions.

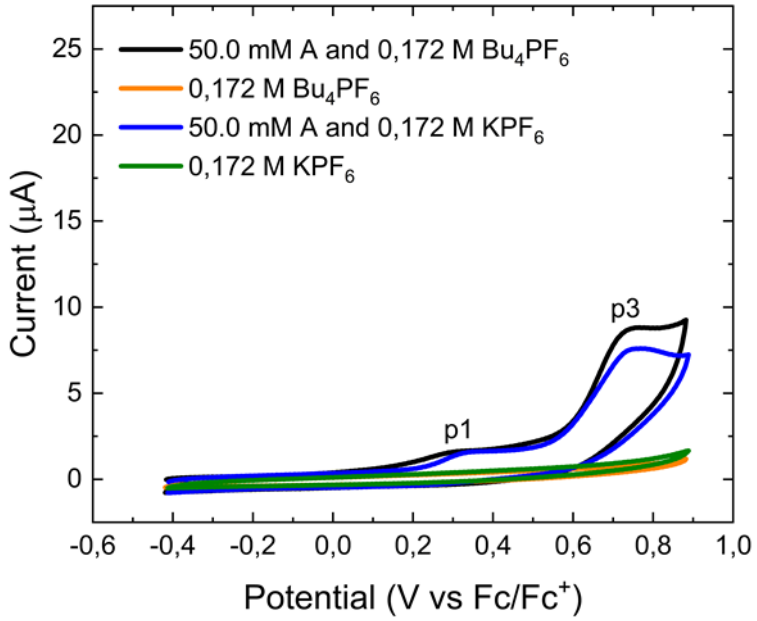


*Figure S3. . Cyclic voltammograms overlay of the electrochemical activity of the working solutions containing Bu_4PF_6 or KPF_6 supporting electrolyte with (black, blue) and without (orange, green) **1a**.*

6. References

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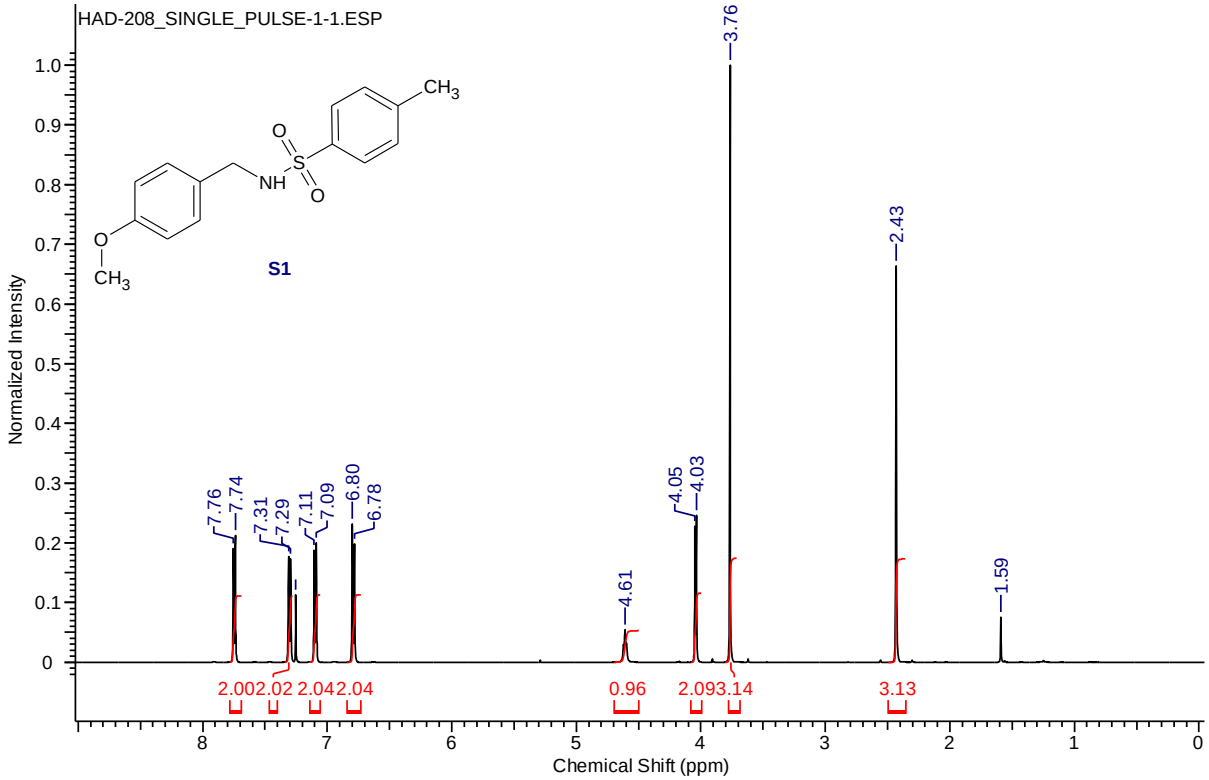
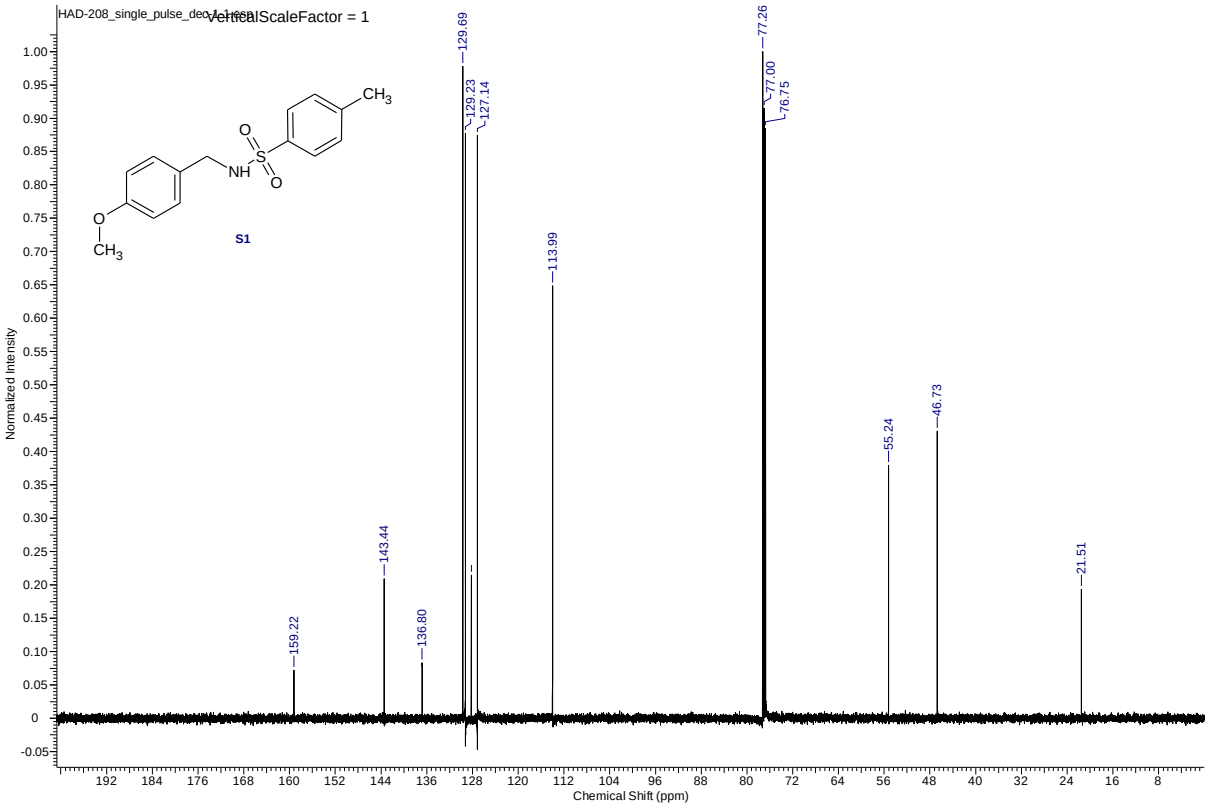
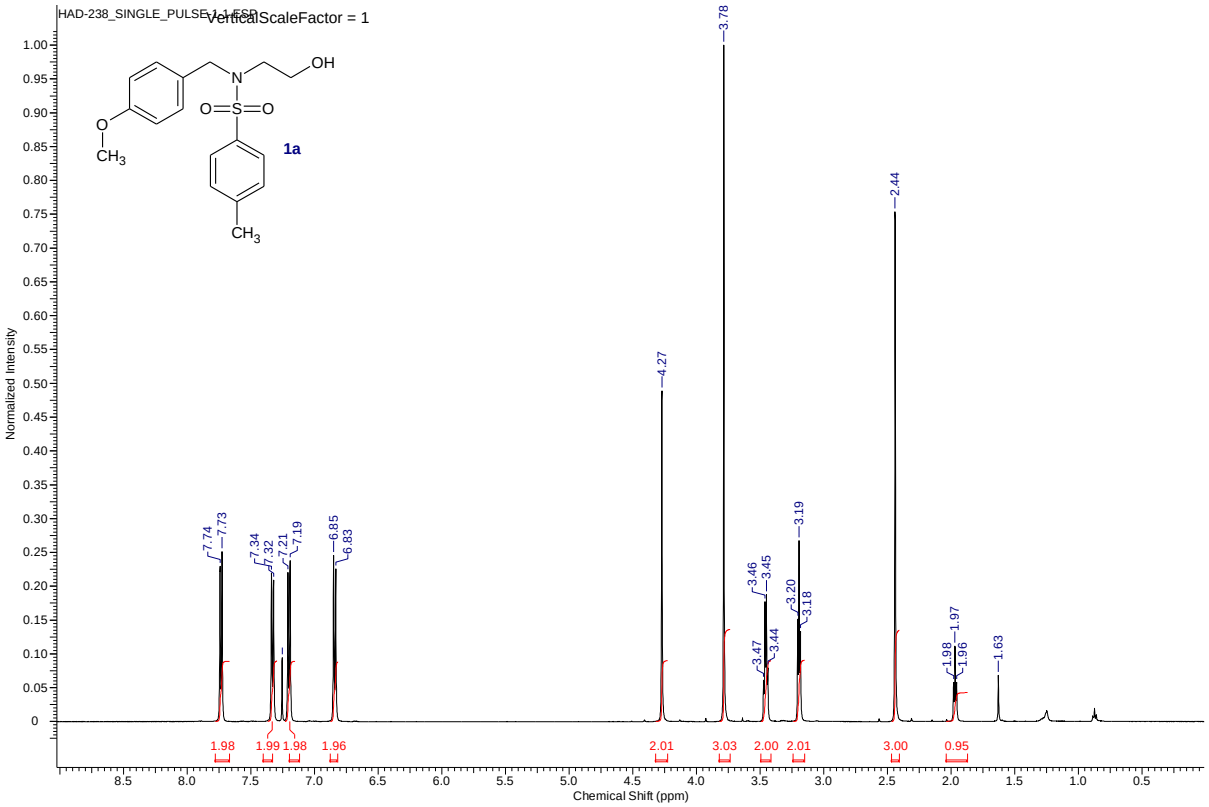
7. NMR spectra



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7.32
7.21
7.19
6.85
6.83
4.27
3.78
3.46
3.45
3.20
3.19
3.18
3.47
3.44
2.44
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1.97
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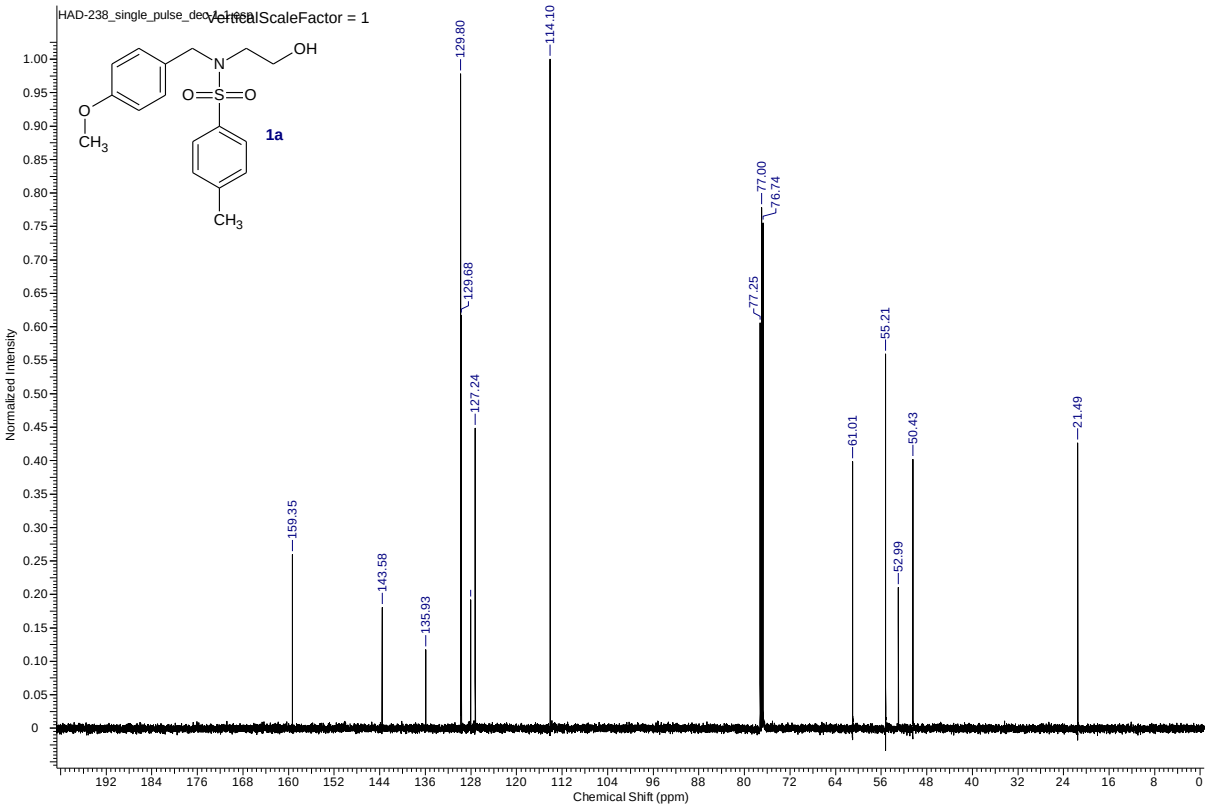
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52.99
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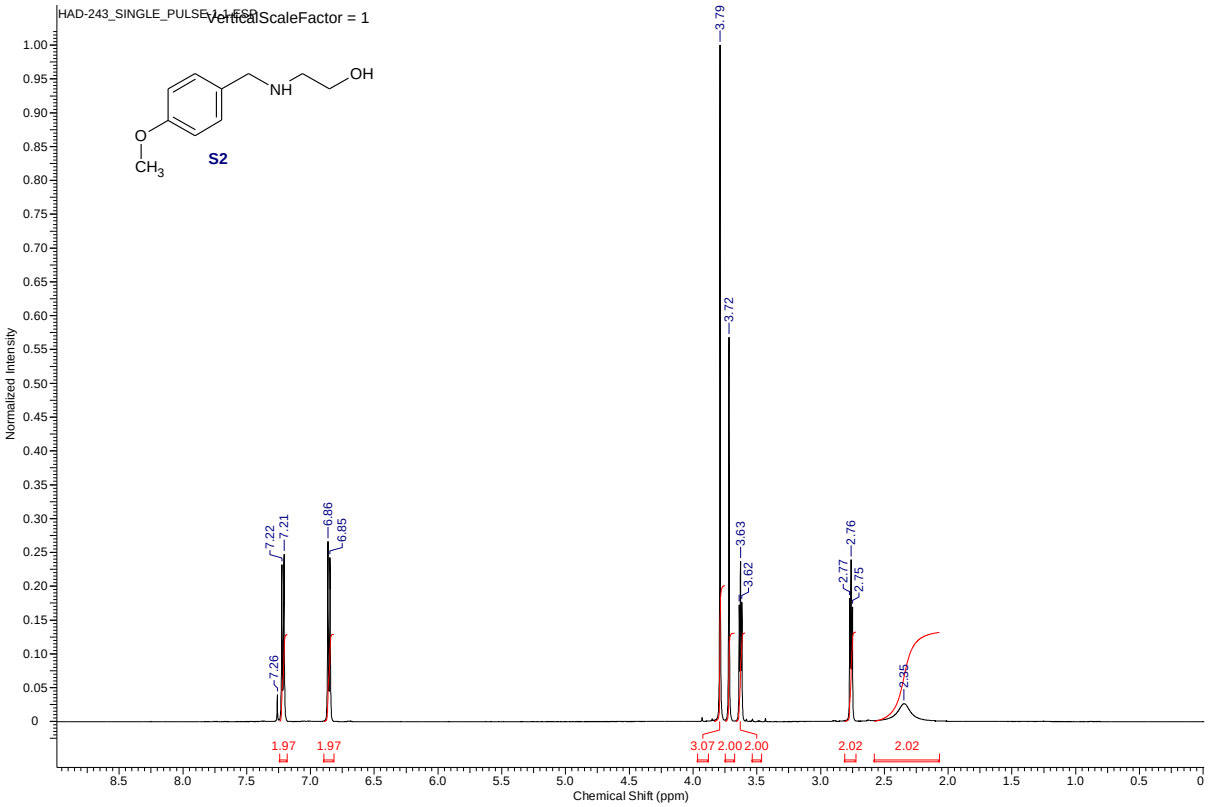
21.49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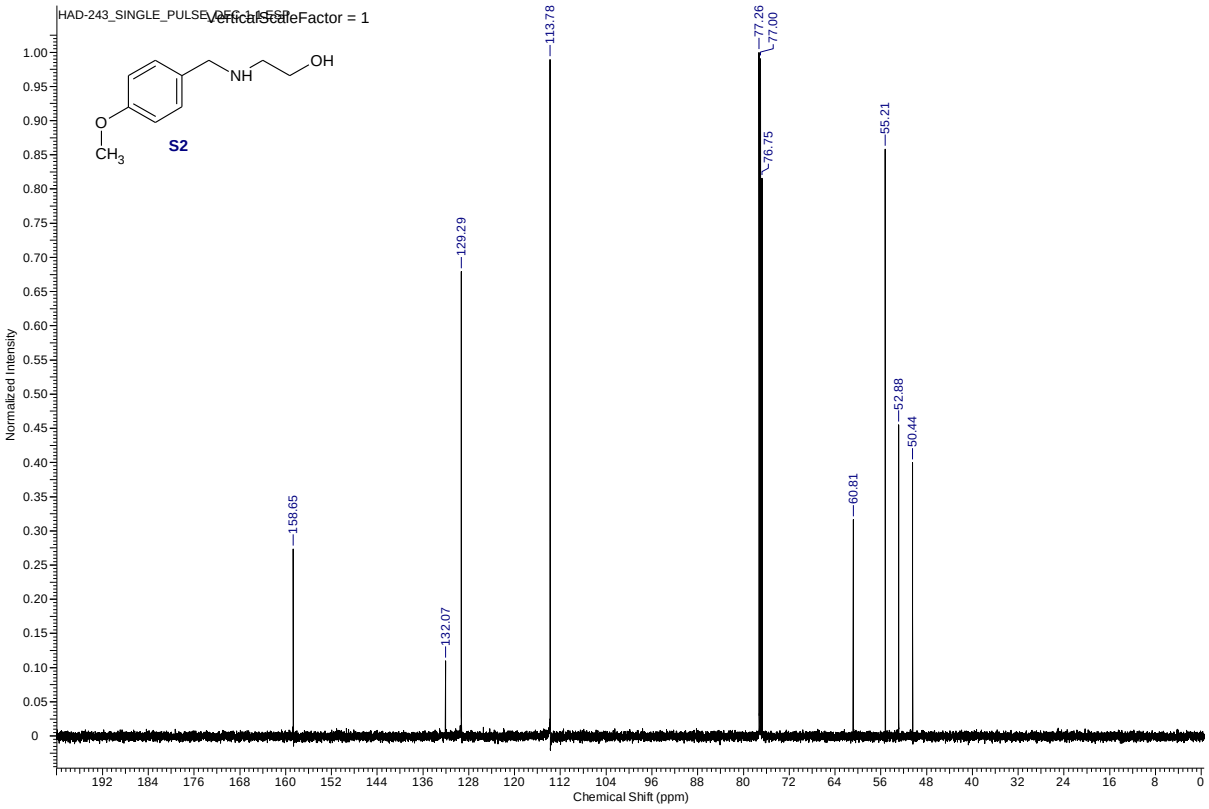
2.02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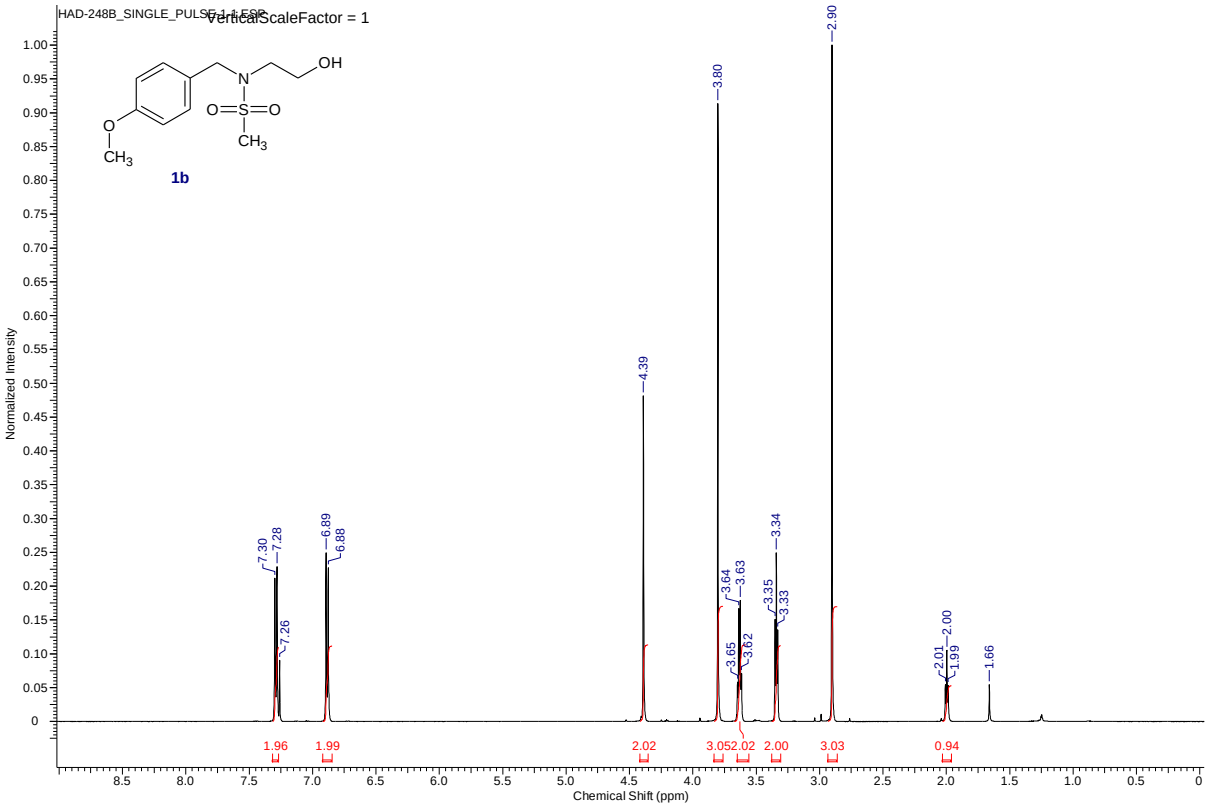
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3.62
3.35
3.34
3.33
2.90
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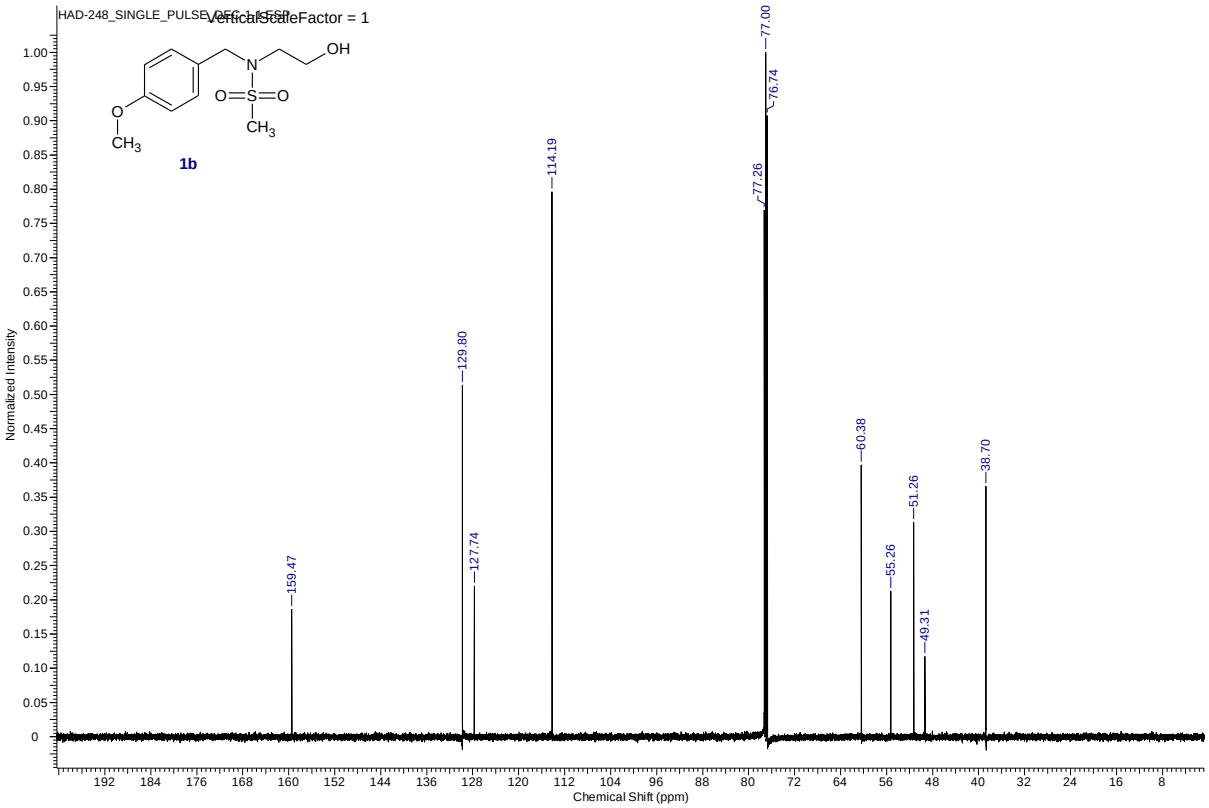
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49.31
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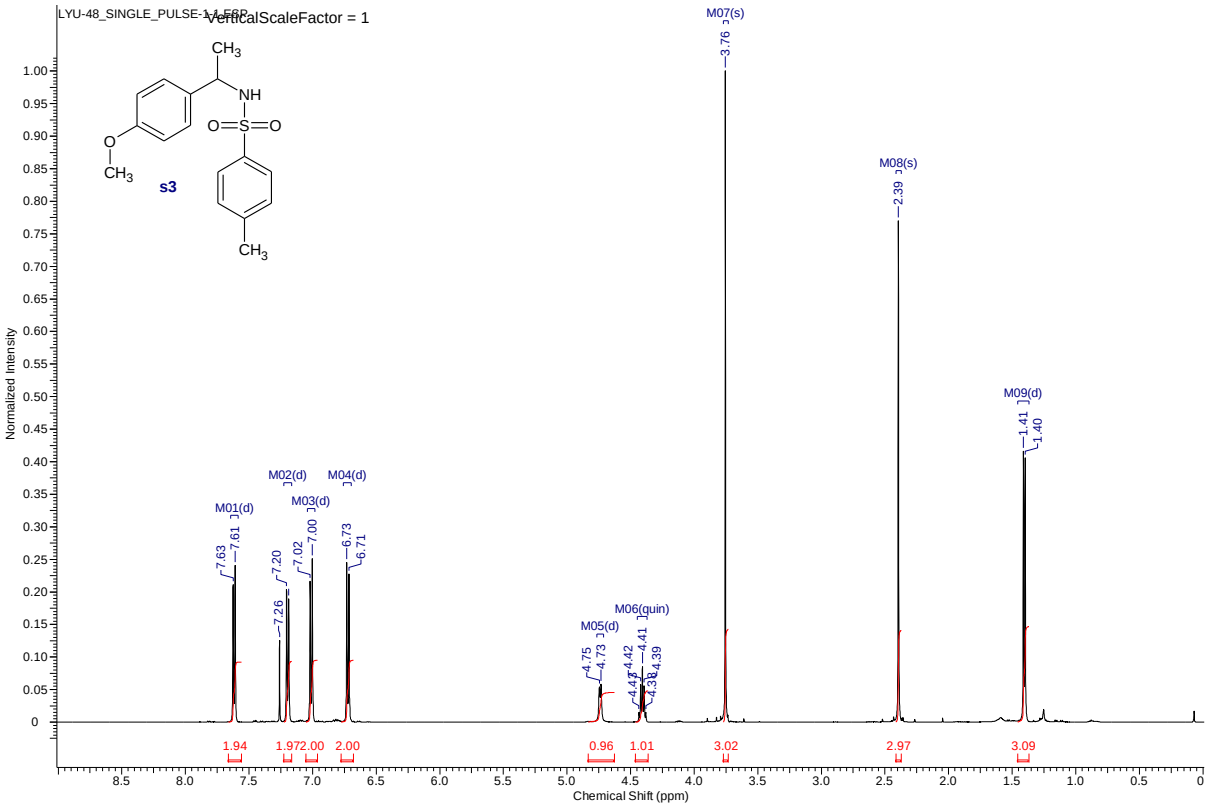
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7.61
M02(d)
7.20
7.26
M03(d)
7.02
7.00
M04(d)
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6.71
M05(d)
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4.73
M06(quin)
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4.41
4.39
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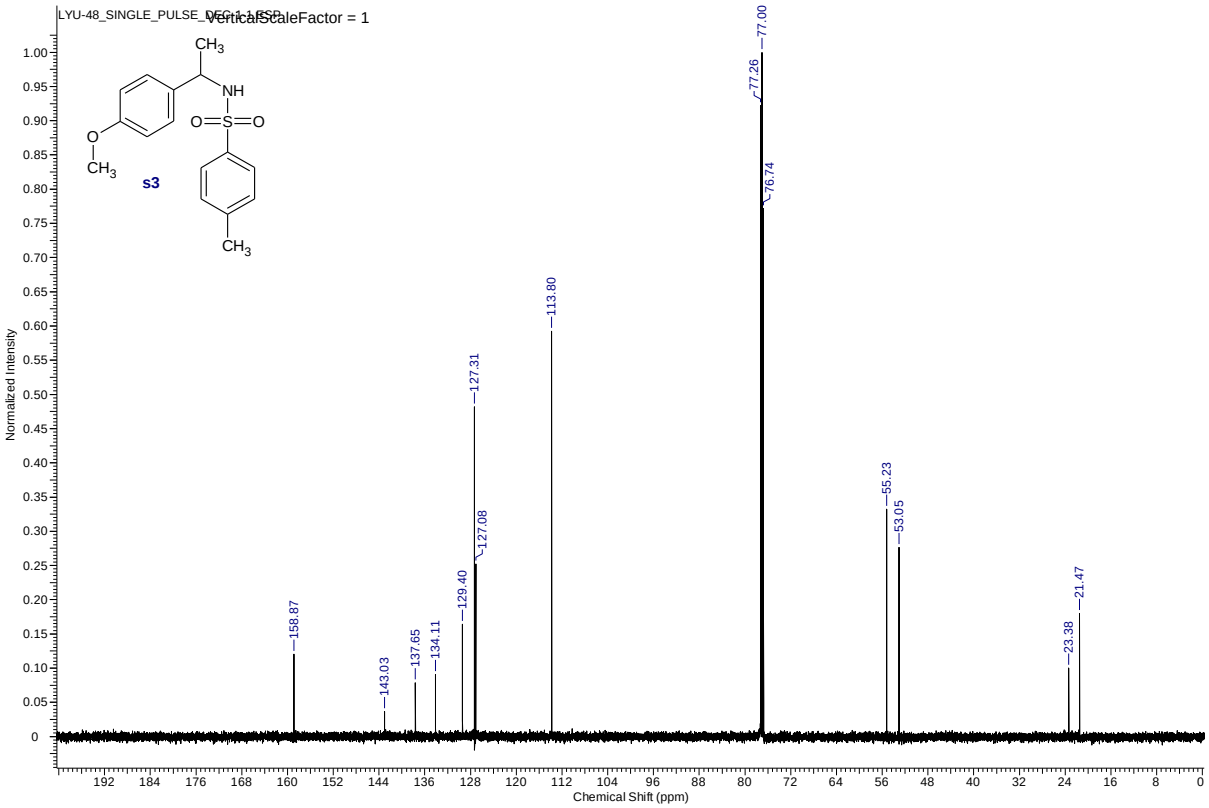
2.00
2.00
0.96
1.01
3.02
2.97
3.09
Normalized Intensity
Chemical Shift (ppm)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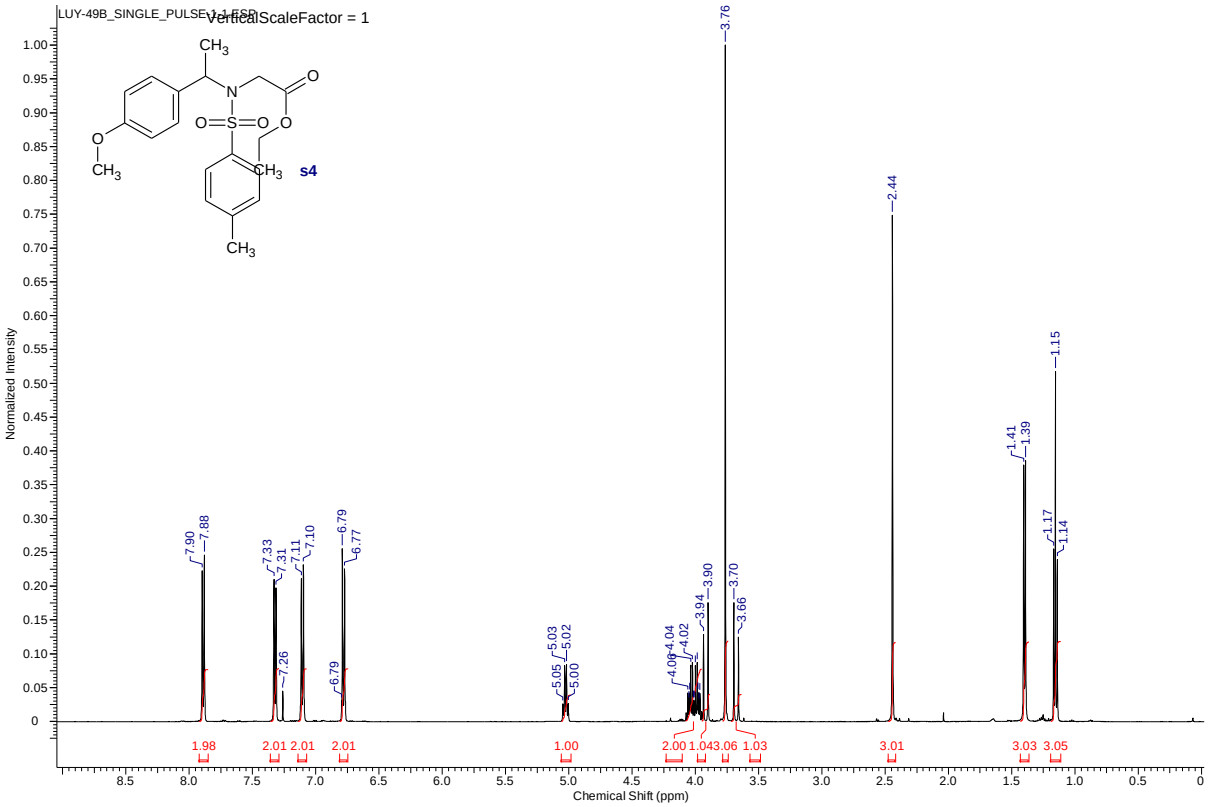
Chemical Shift (ppm)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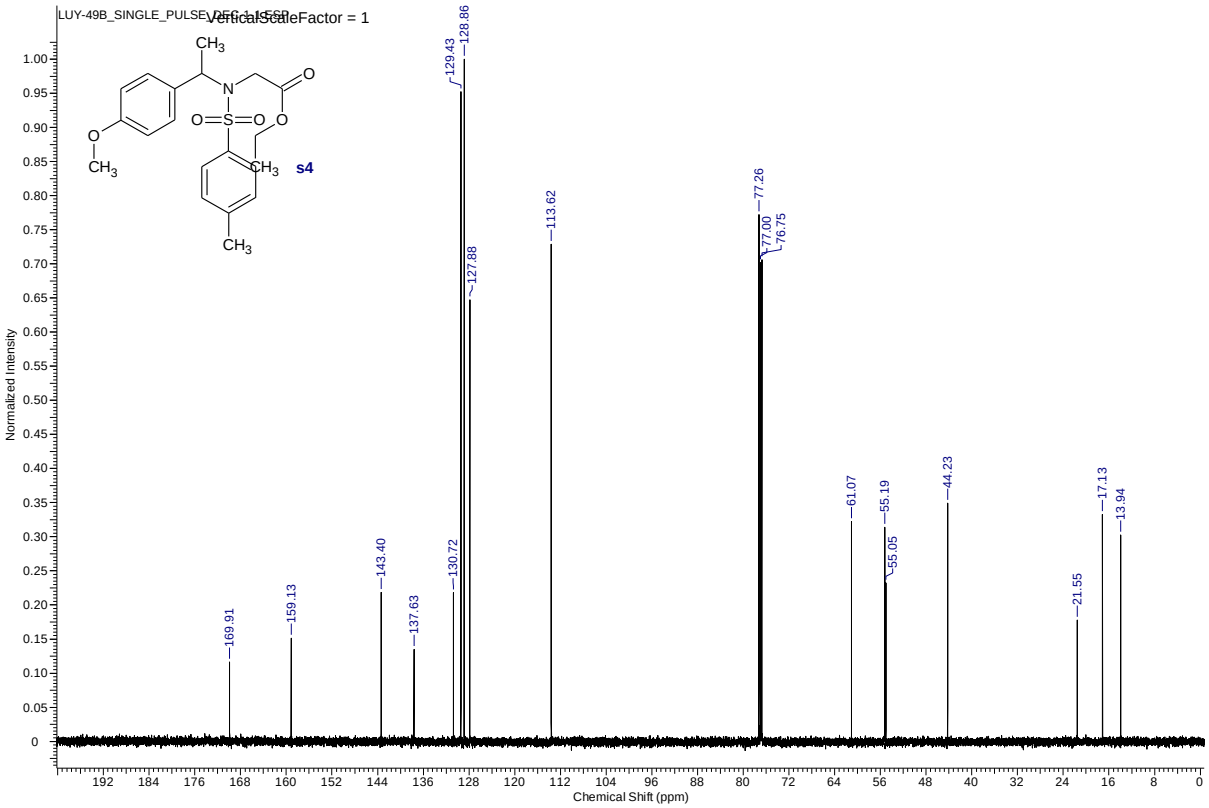
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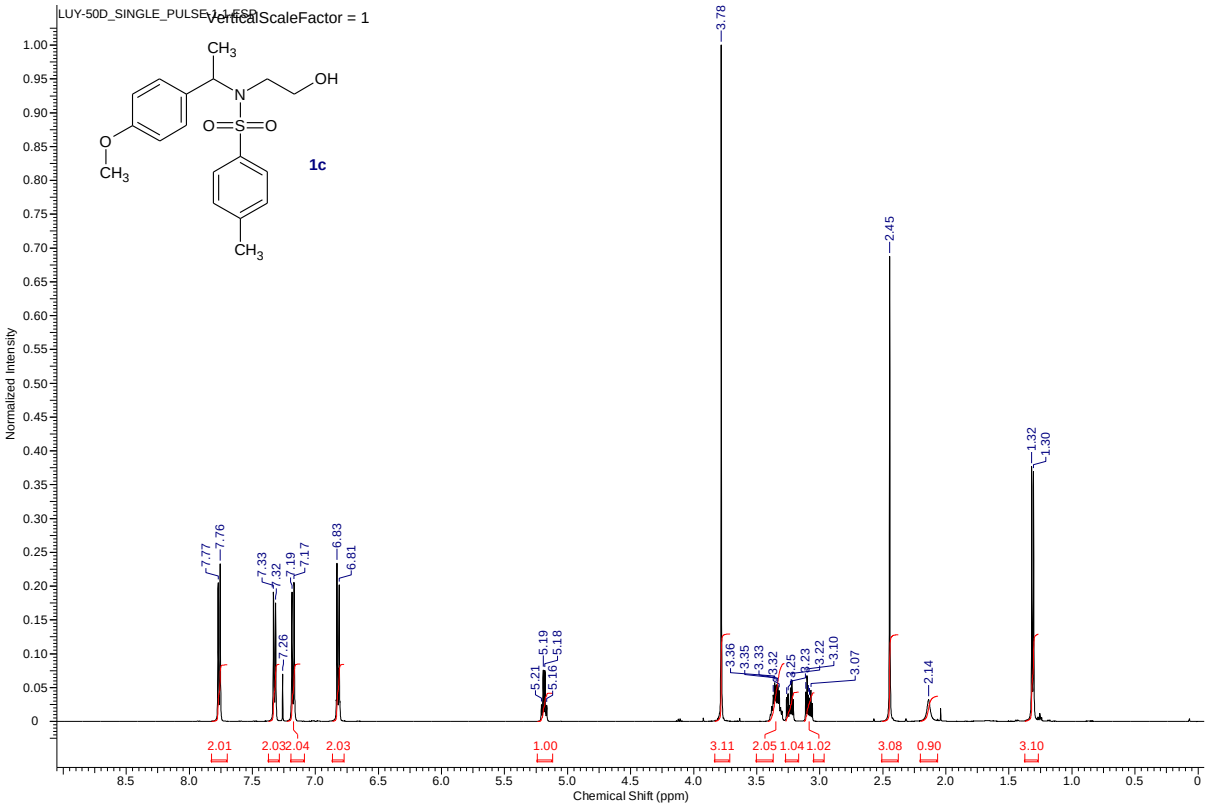
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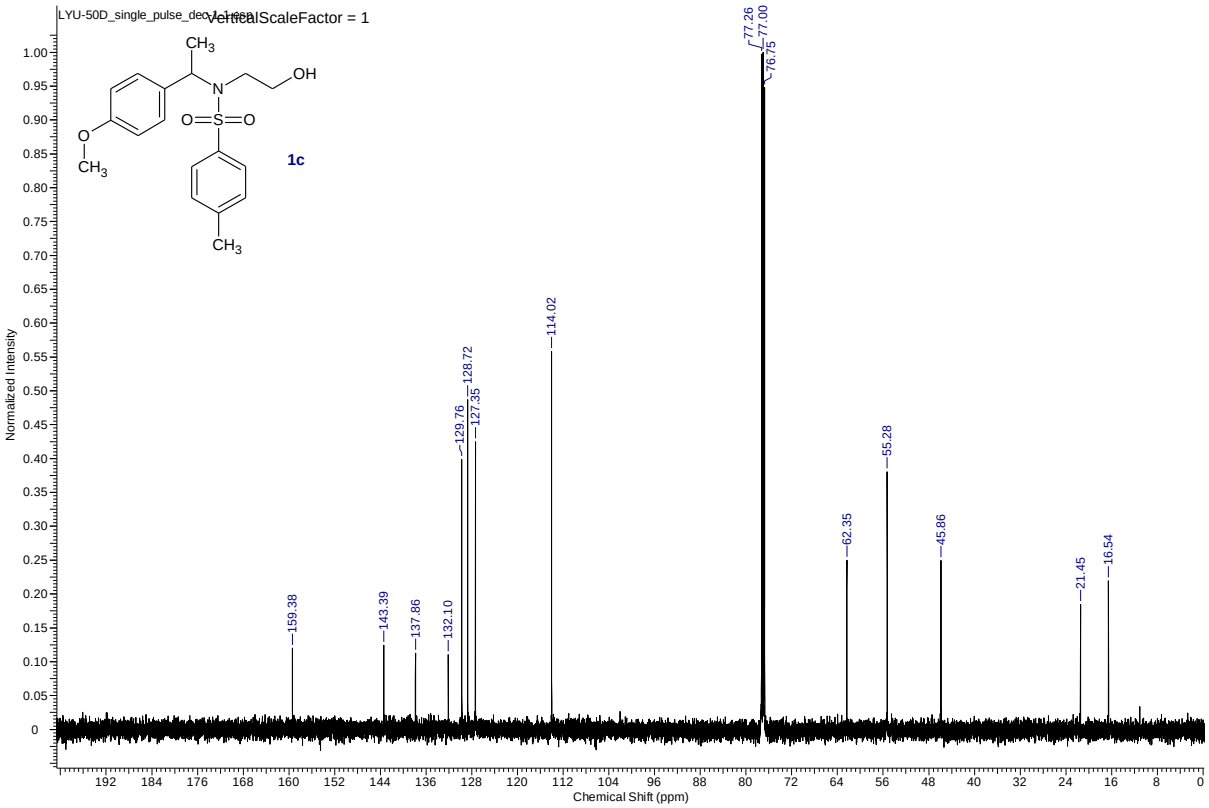
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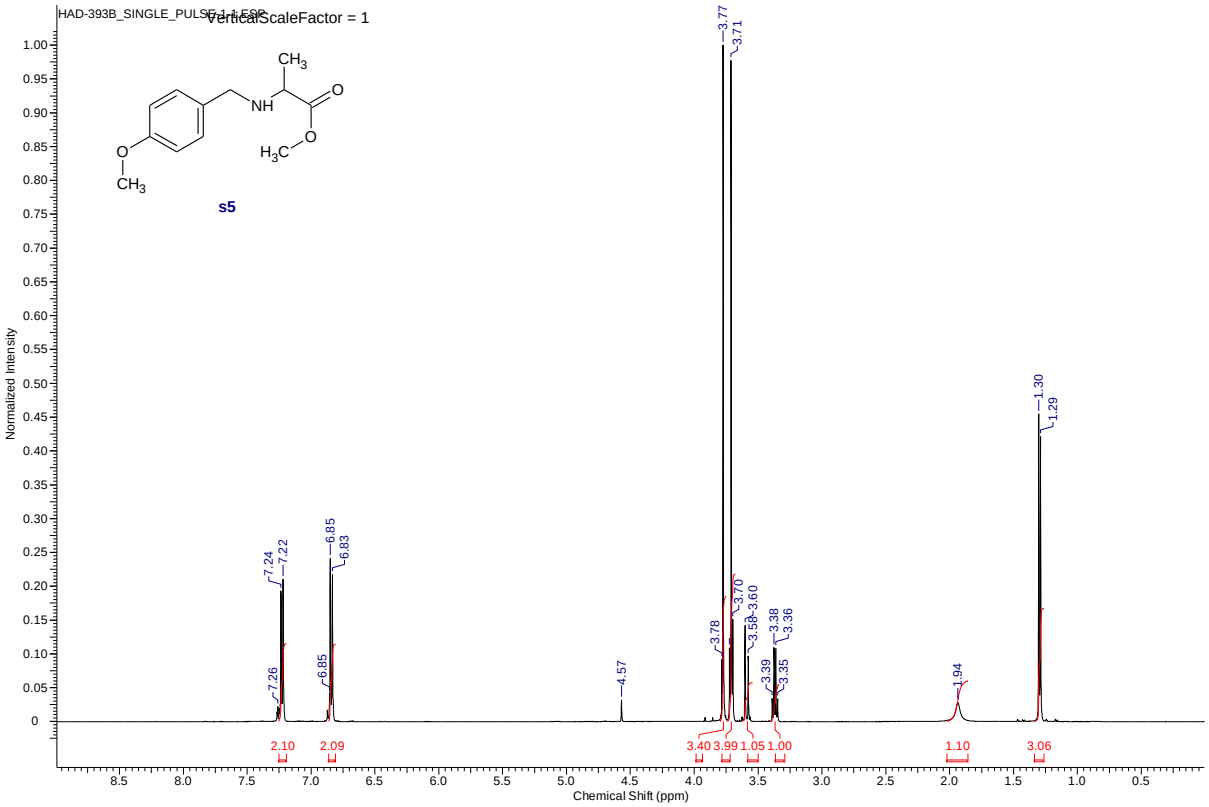
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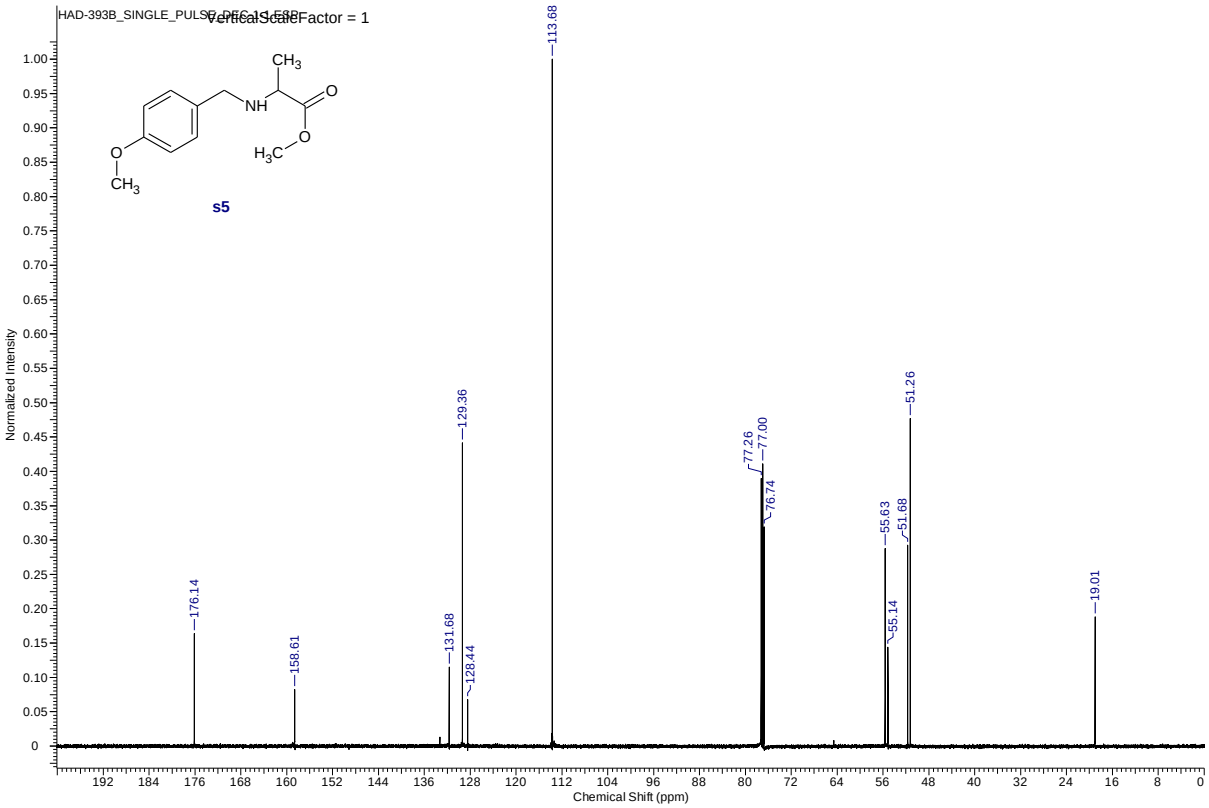
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51.68
51.26
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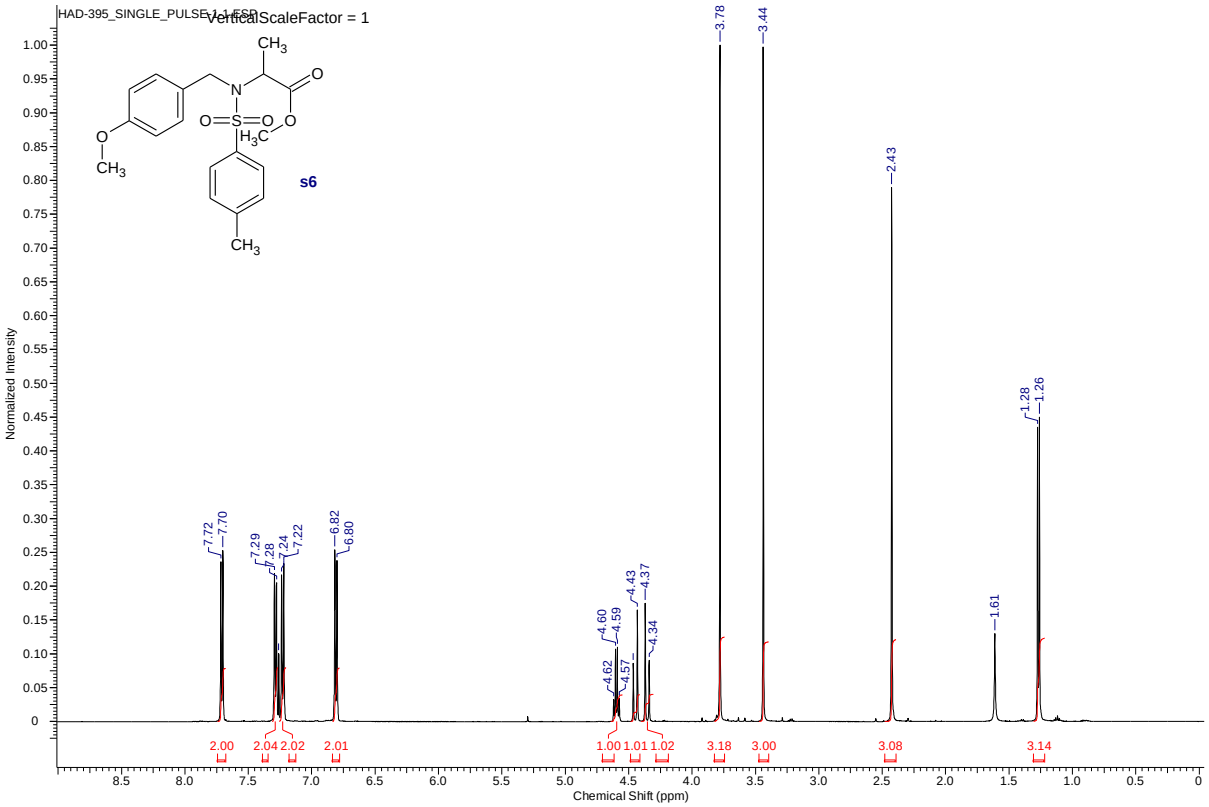
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7.22
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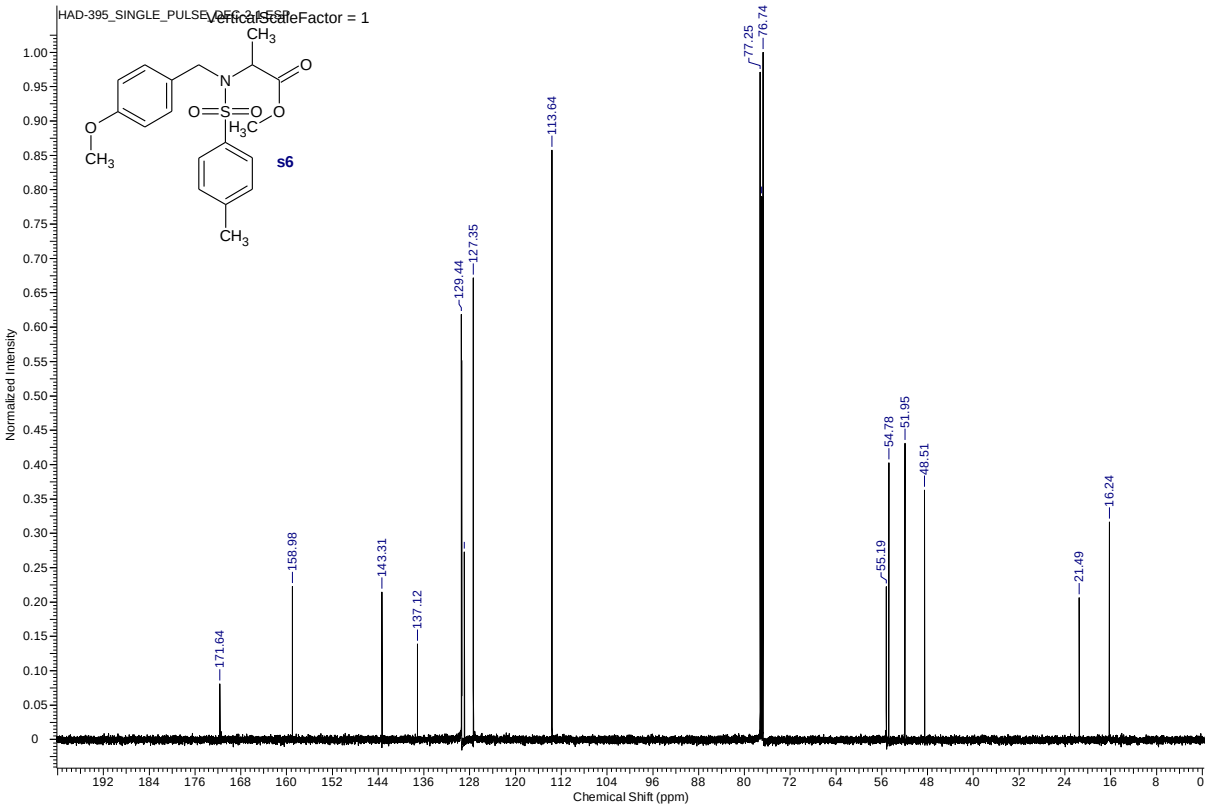
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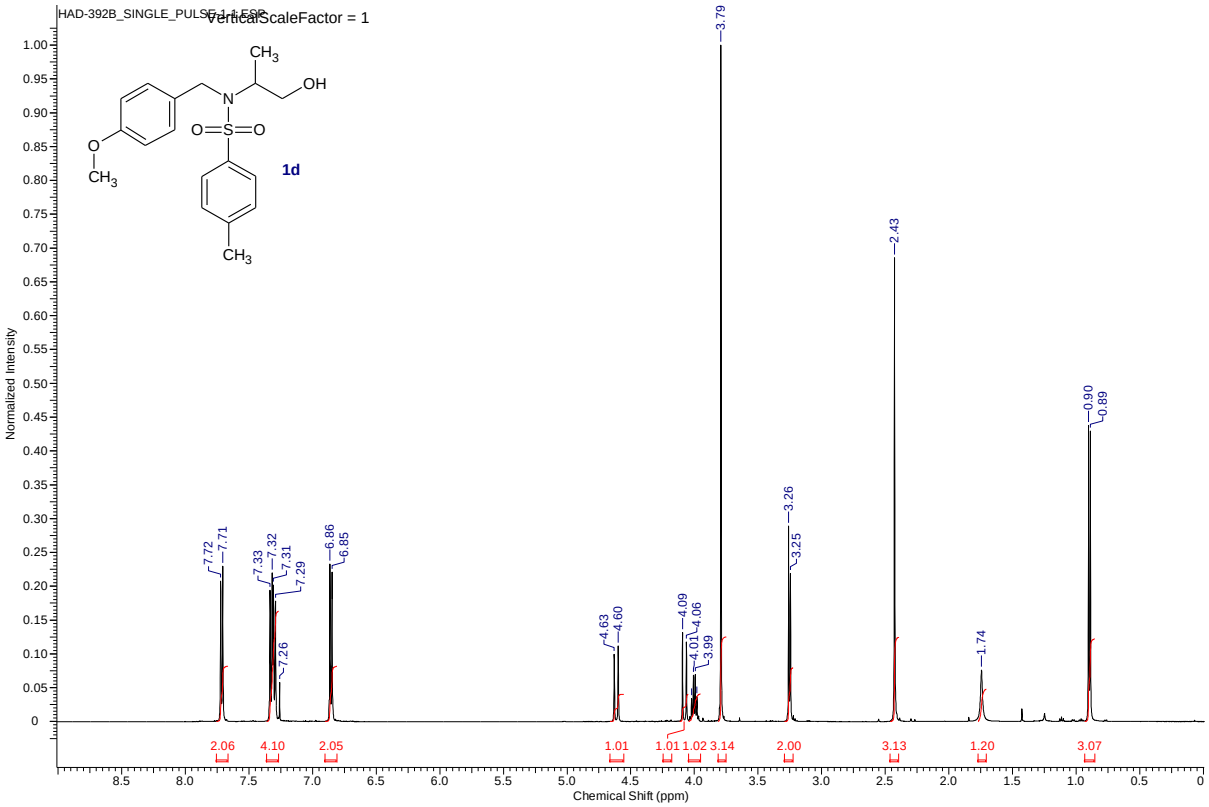
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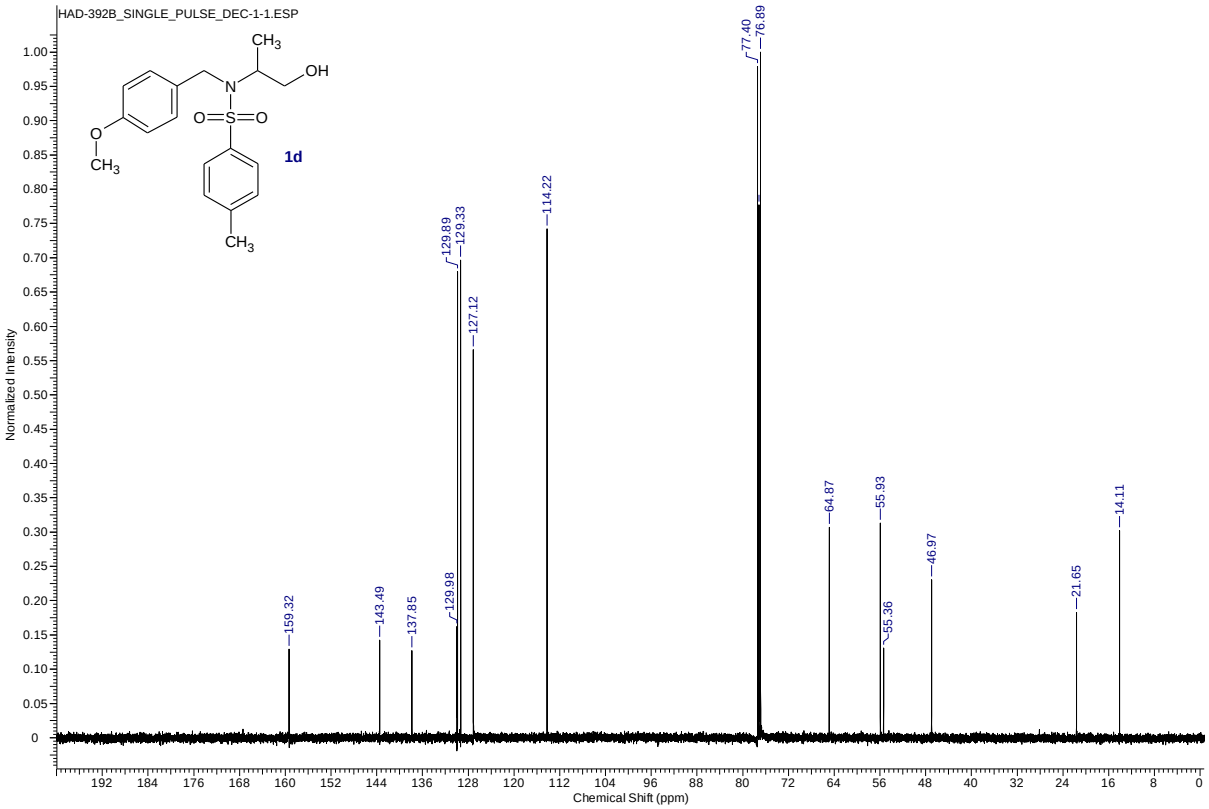
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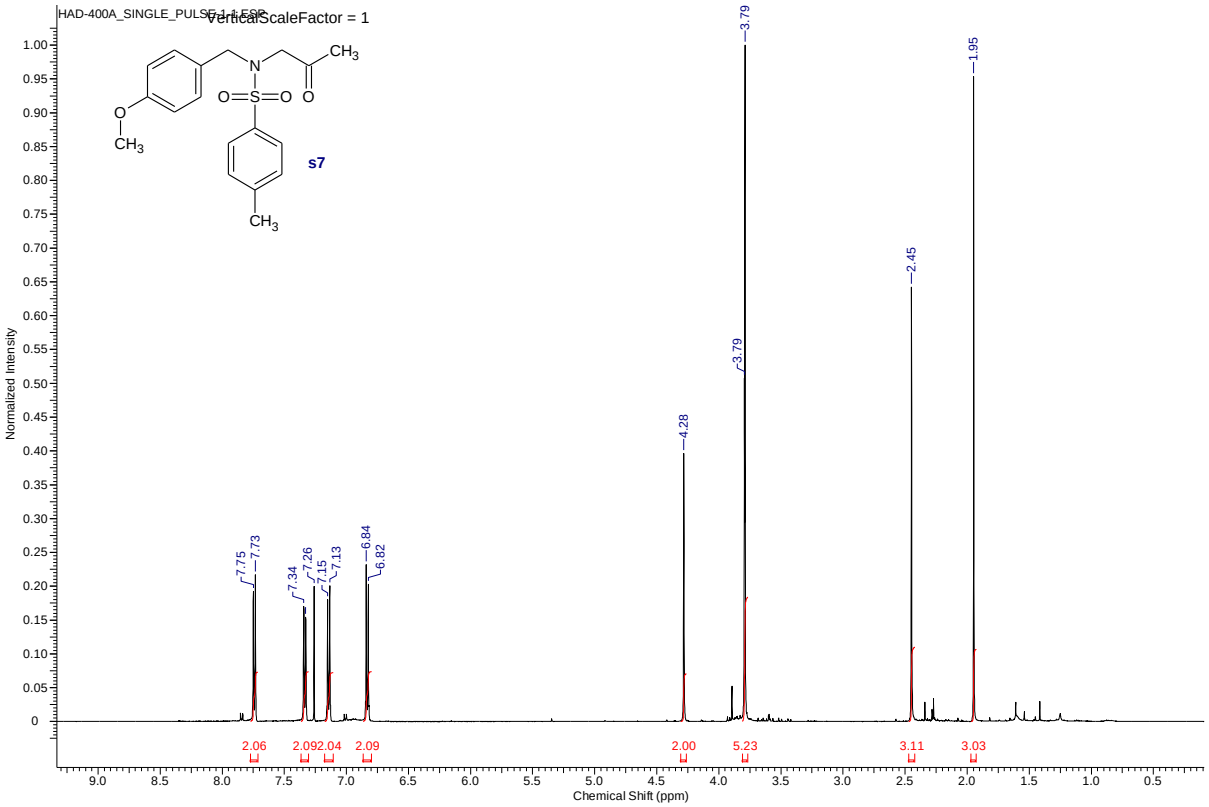
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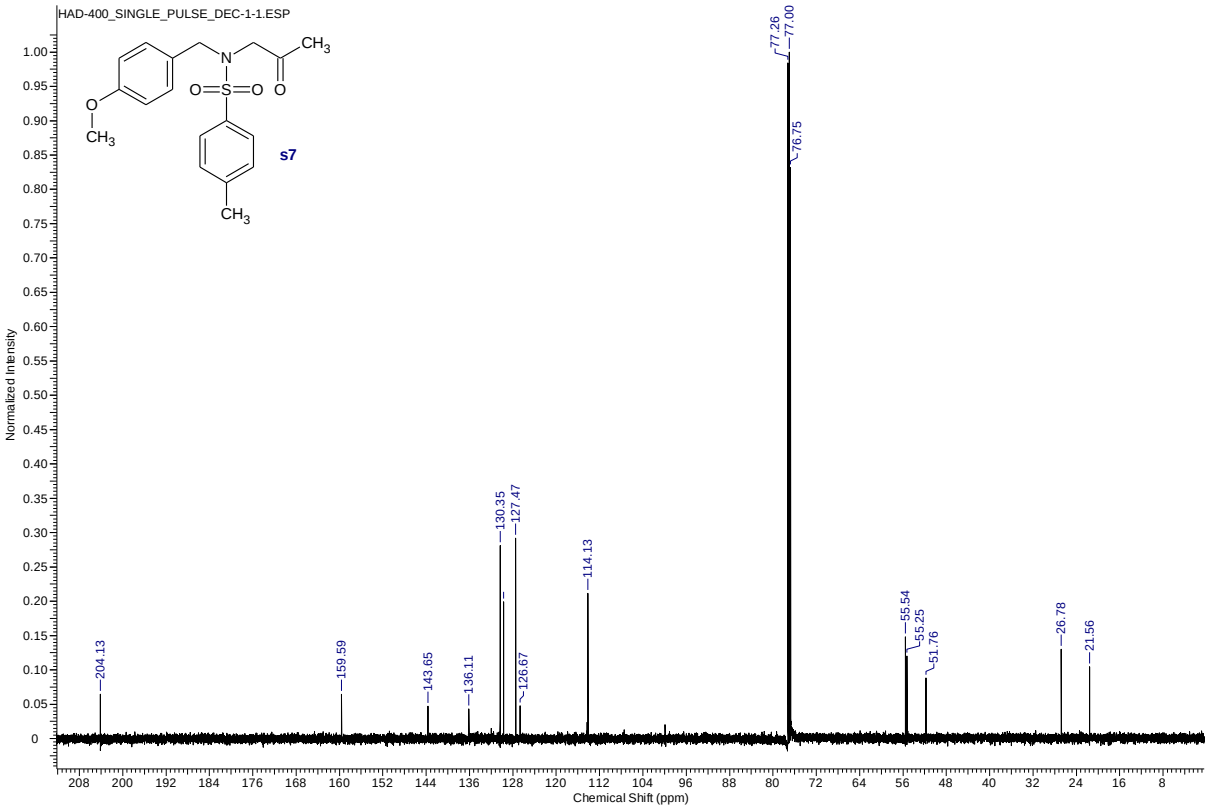
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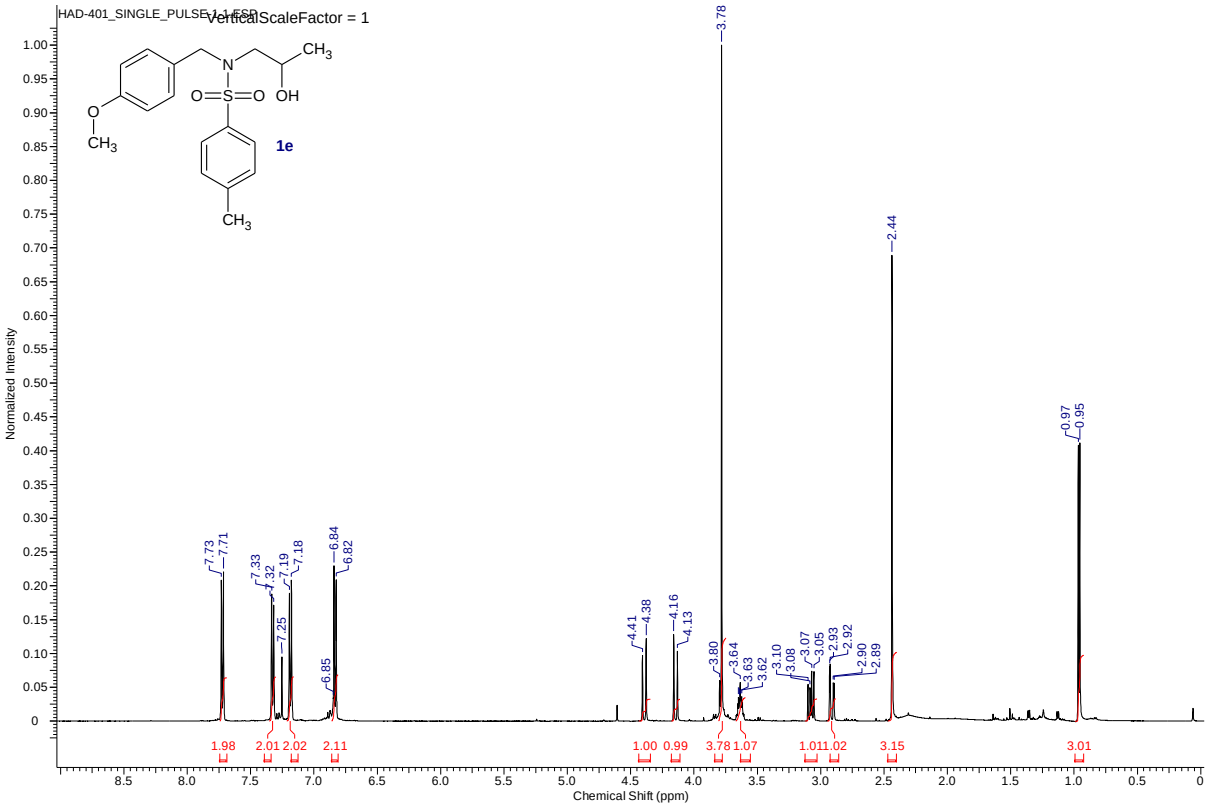
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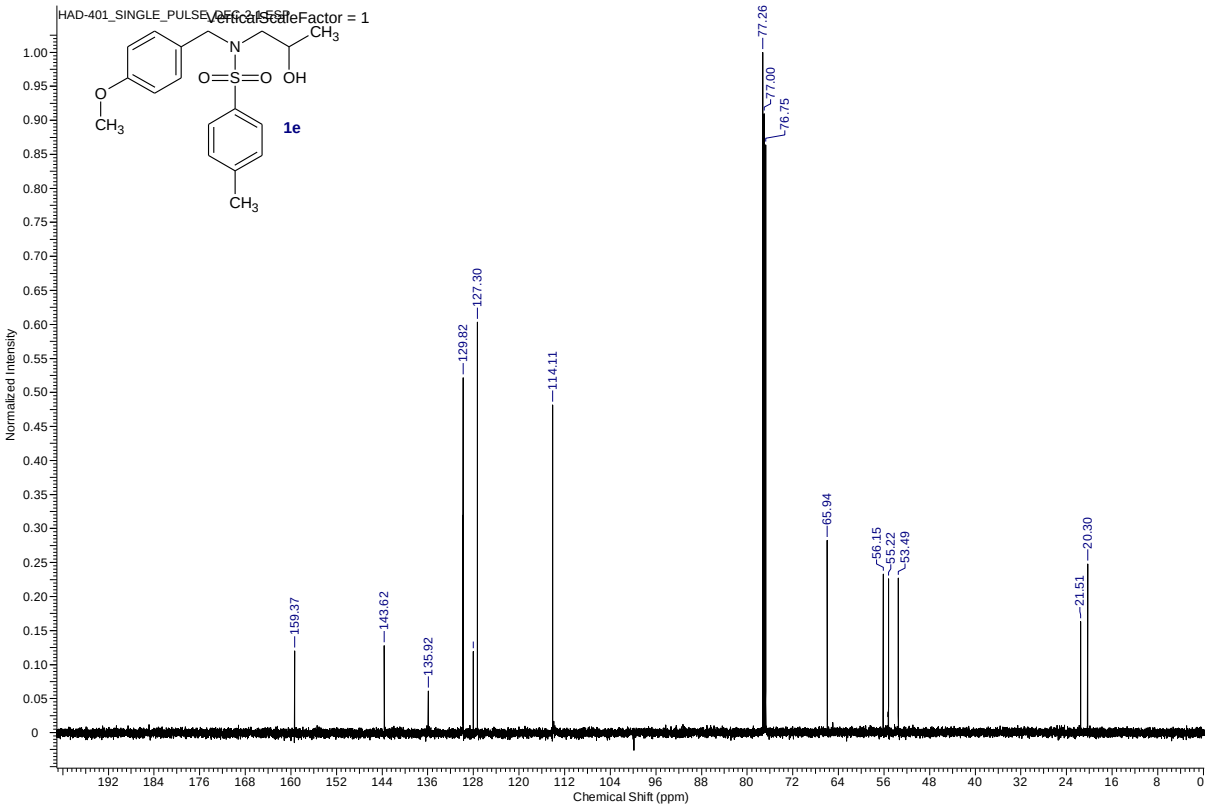
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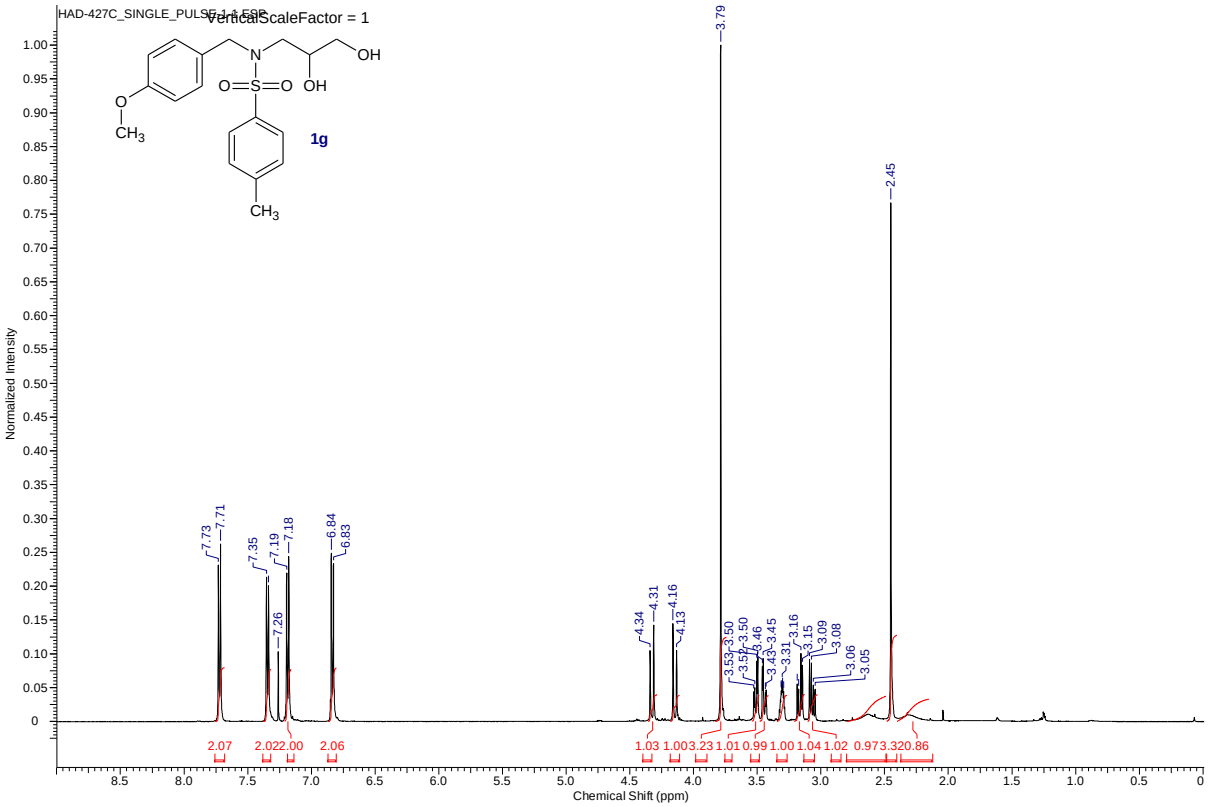
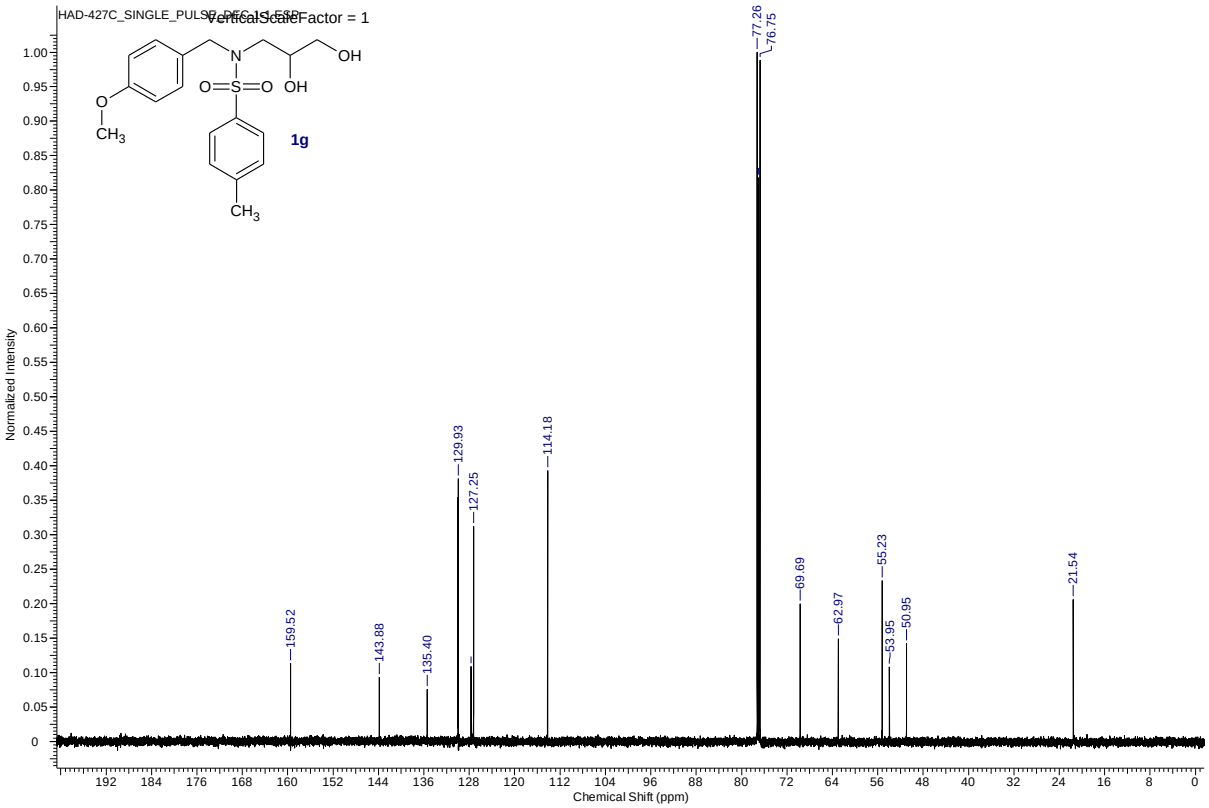
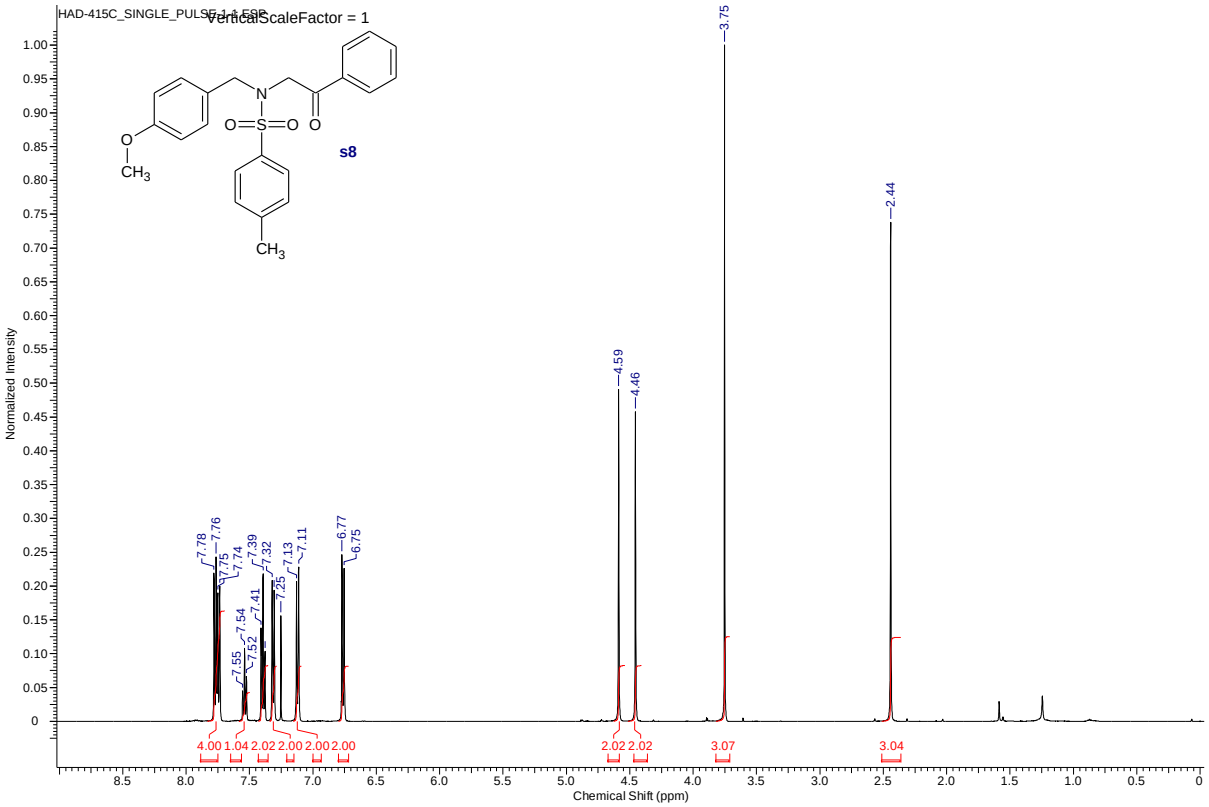
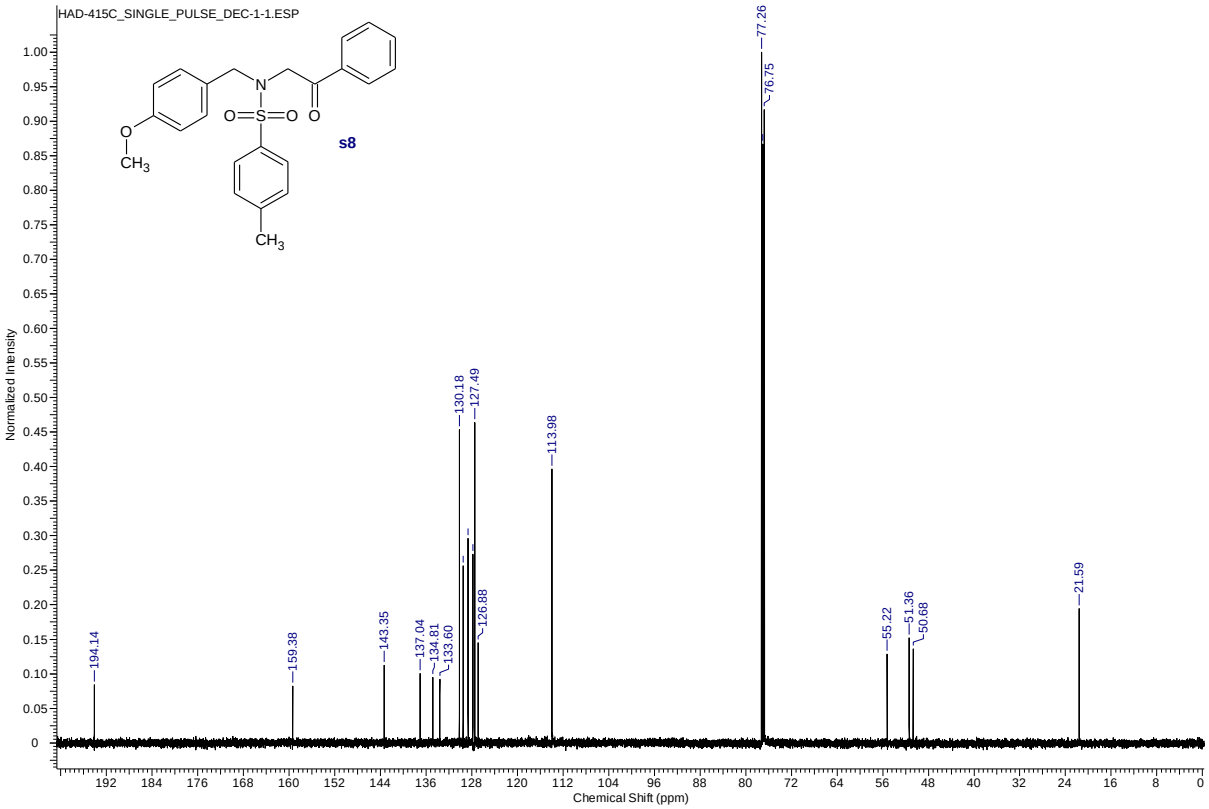
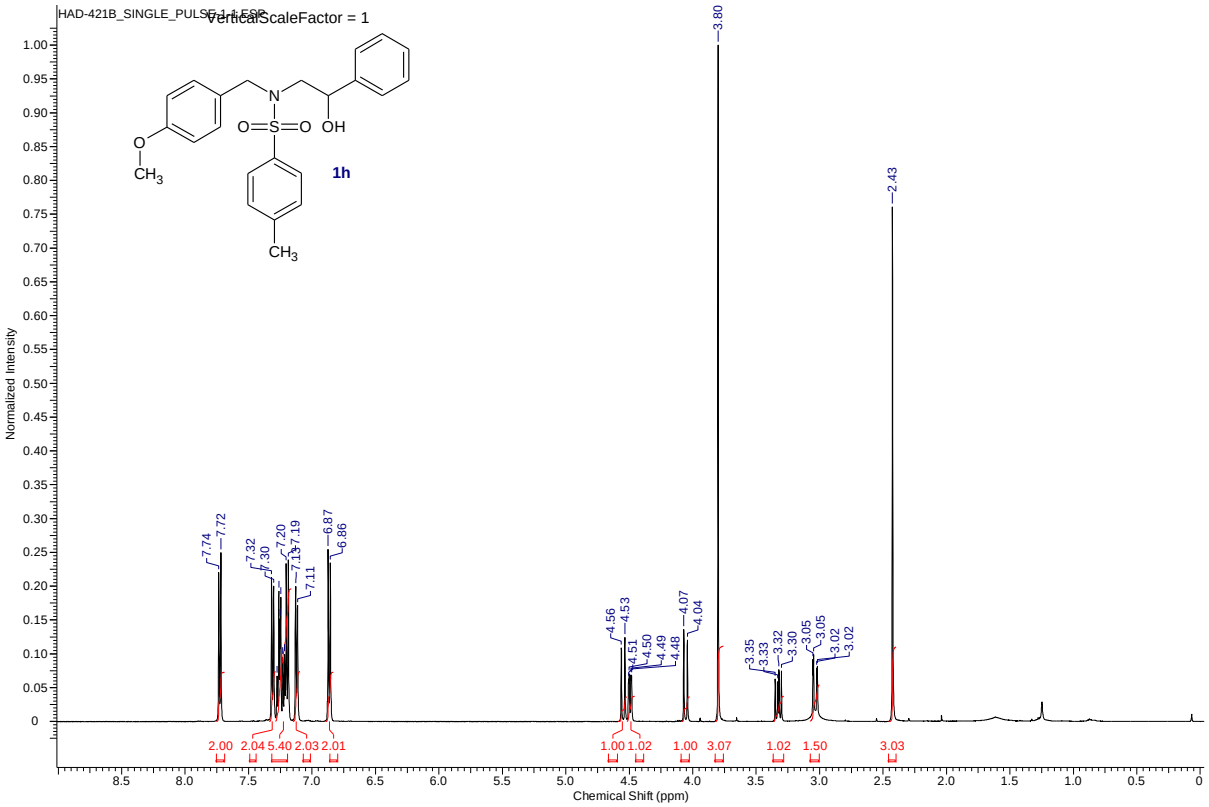
21.51
20.30

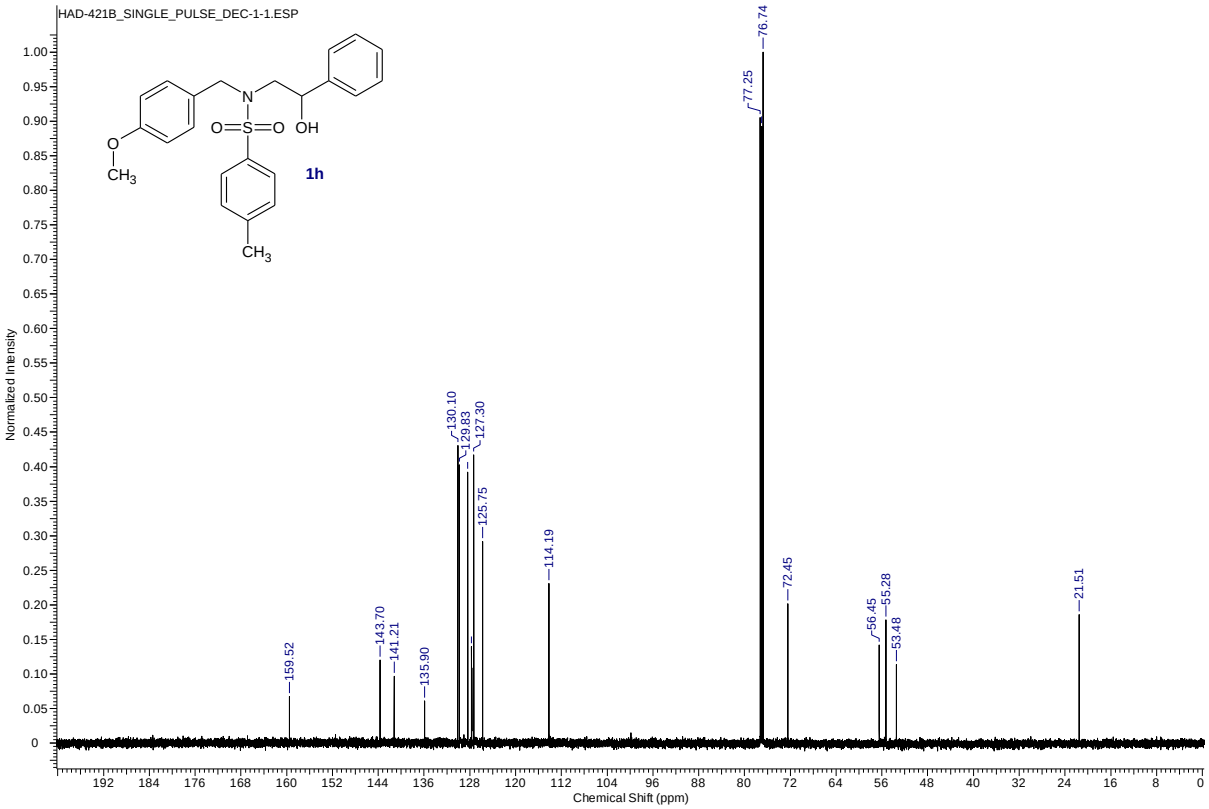

HAD-427C_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
1g
Normalized Intensity
Chemical Shift (ppm)
3.79
2.45
7.73
7.71
7.35
7.19
7.18
7.26
6.84
6.83
4.34
4.31
4.16
4.13
2.07
2.02
2.00
2.06
1.03
1.00
3.23
1.01
0.99
1.00
1.04
1.02
0.97
3.32
0.86

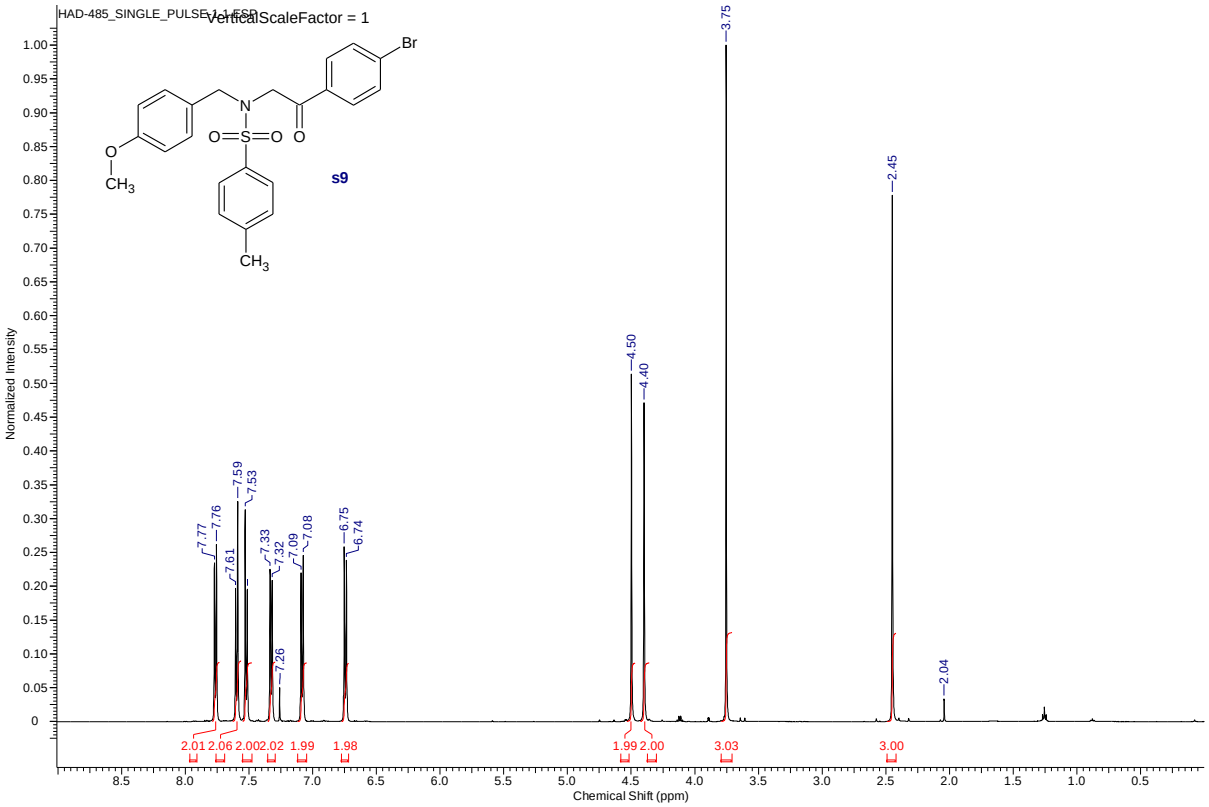

HAD-427C_SINGLE_PULSE_DEC_1.1.ESP
VerticalScaleFactor = 1
1g
Normalized Intensity
Chemical Shift (ppm)
77.26
76.75
129.93
127.25
114.18
159.52
143.88
135.40
69.69
62.97
55.23
53.95
50.95
21.54

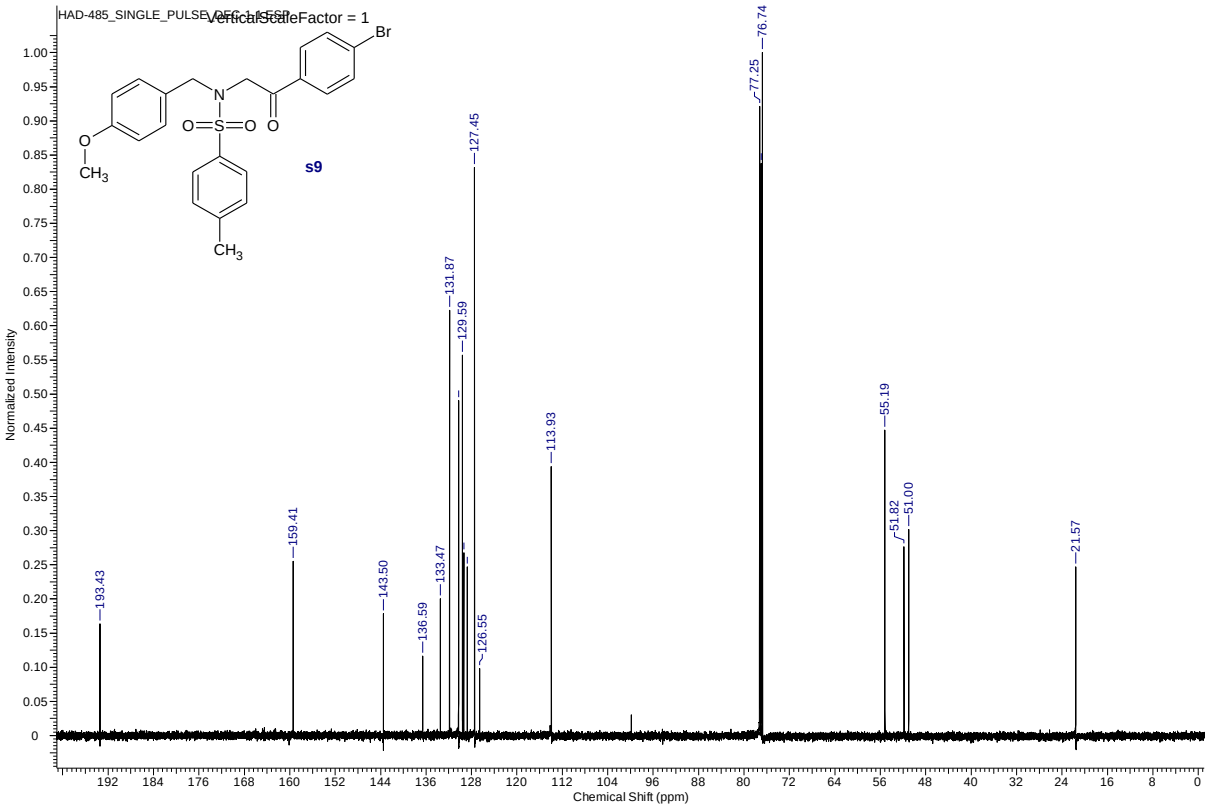

HAD-415C_SINGLE_PULSE_1-1.ESP
VerticalScaleFactor = 1
s8
Normalized Intensity
Chemical Shift (ppm)
3.75
2.44
4.59
4.46
7.78
7.76
7.75
7.74
7.39
7.32
7.13
7.11
6.77
6.75
7.55
7.54
7.52
7.41
7.25
4.00 1.04 2.02 2.00 2.00 2.00
2.02 2.02
3.07
3.04

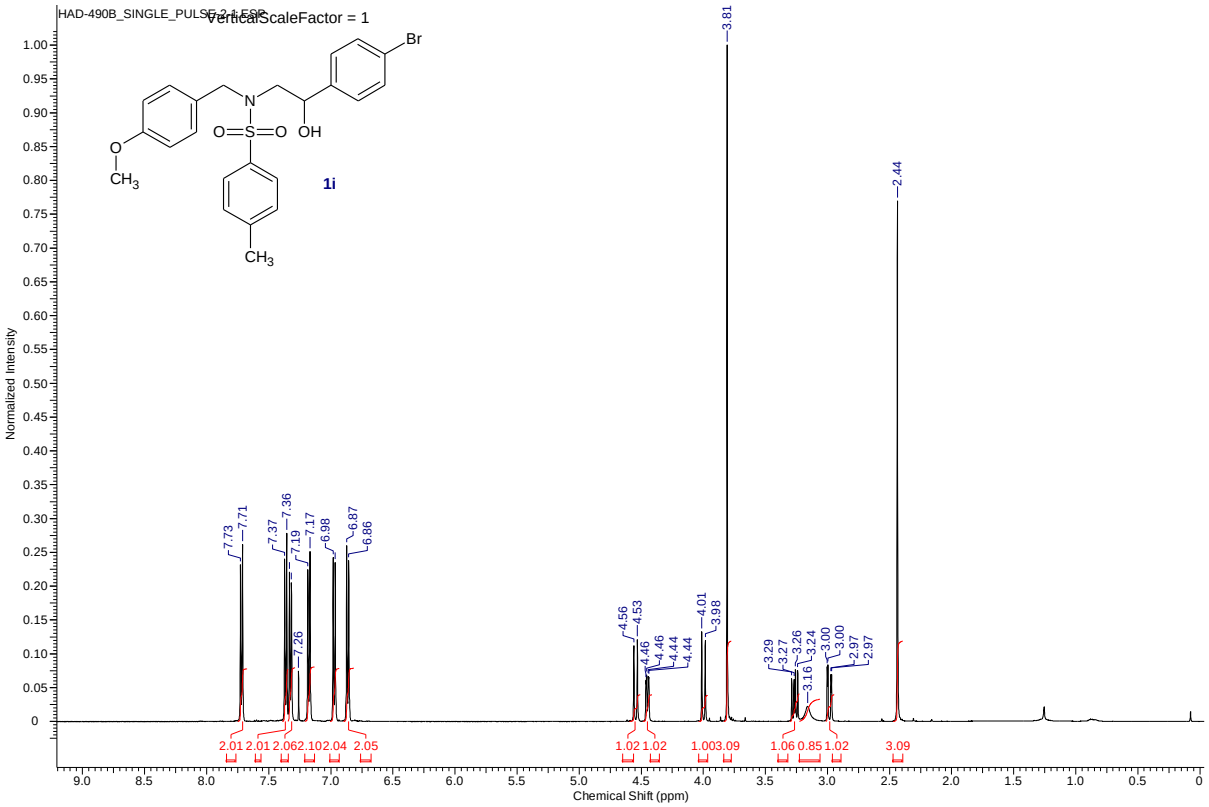

HAD-415C_SINGLE_PULSE_DEC-1-1.ESP
s8
Normalized Intensity
Chemical Shift (ppm)
77.26
76.75
130.18
127.49
113.98
126.88
194.14
159.38
143.35
137.04
134.81
133.60
55.22
51.36
50.68
21.59

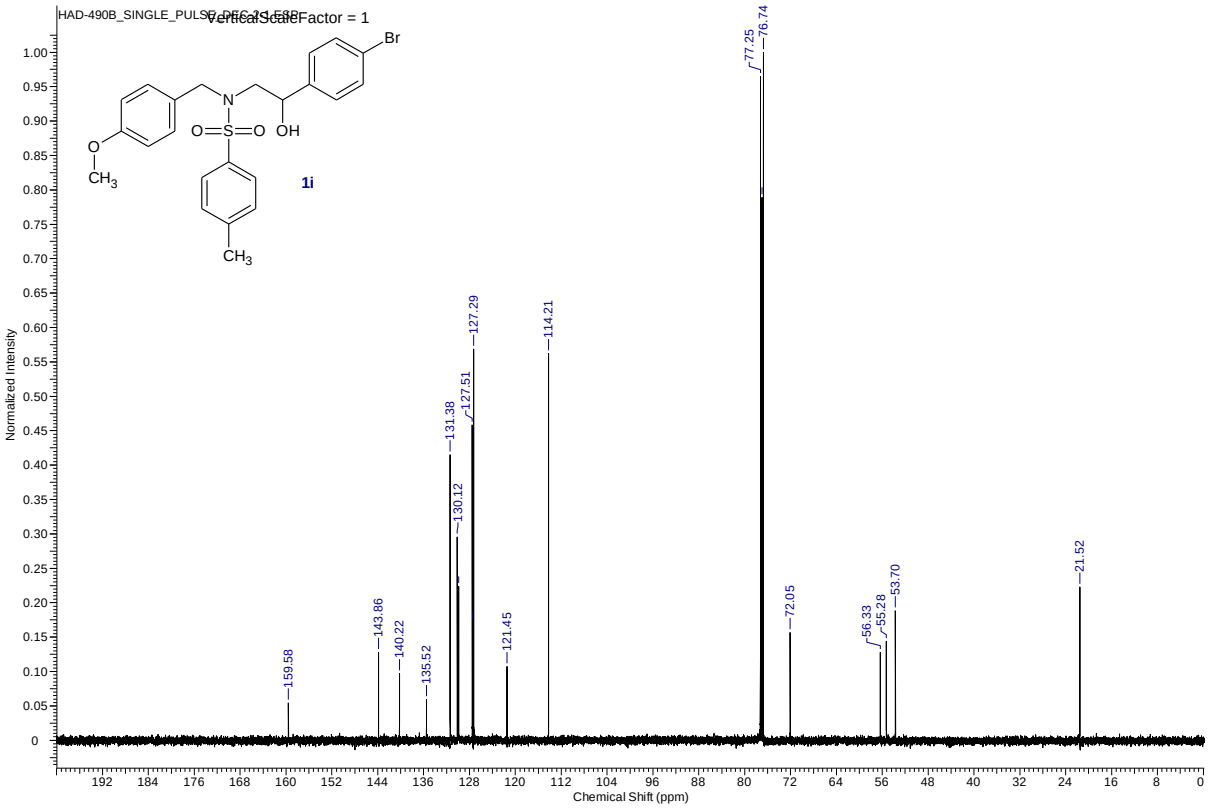

HAD-421B_SINGLE_PULSE-1-1.ESP
VerticalScaleFactor = 1
1h
Normalized Intensity
Chemical Shift (ppm)
7.74
7.72
7.32
7.30
7.20
7.19
7.13
7.11
6.87
6.86
4.56
4.53
4.51
4.50
4.49
4.48
4.07
4.04
3.80
3.35
3.33
3.32
3.30
3.05
3.02
3.02
2.43
2.00
2.04
5.40
2.03
2.01
1.00
1.02
1.00
3.07
1.02
1.50
3.03

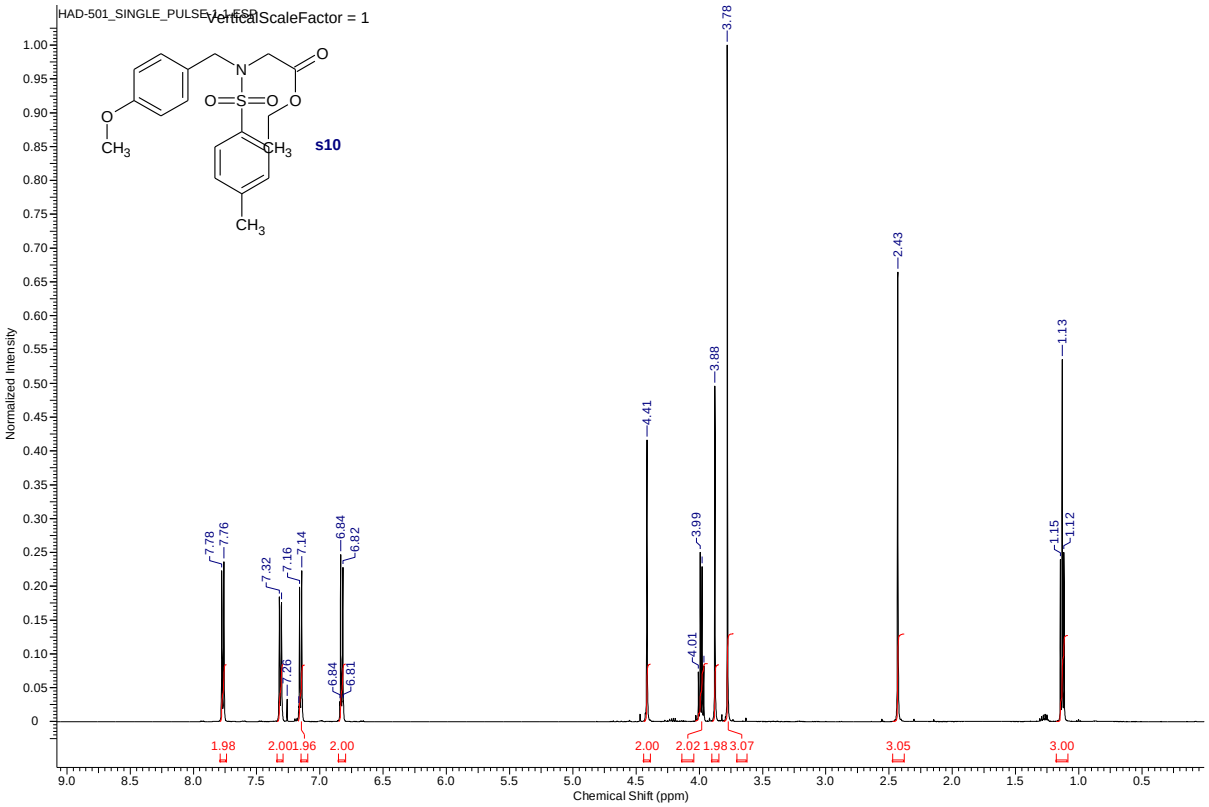

HAD-421B_SINGLE_PULSE_DEC-1-1.ESP
1h
Normalized Intensity
Chemical Shift (ppm)
159.52
143.70
141.21
135.90
130.10
129.83
127.30
125.75
114.19
77.25
76.74
72.45
56.45
55.28
53.48
21.51

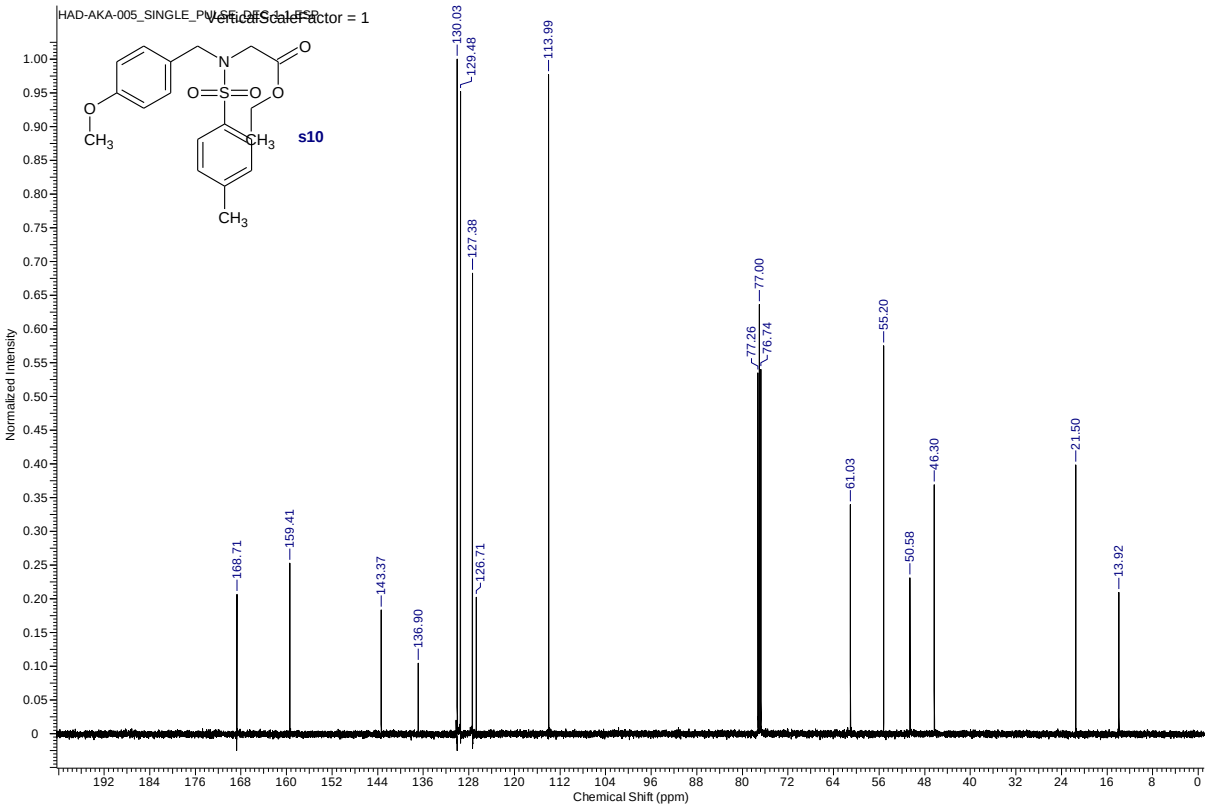

HAD-485_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
Br
N
O=S=O
O
O
CH3
CH3
s9
Normalized Intensity
Chemical Shift (ppm)
3.75
2.45
4.50
4.40
7.77
7.76
7.59
7.53
7.61
7.33
7.32
7.09
7.08
6.75
6.74
7.26
2.04
2.01
2.06
2.00
2.02
1.99
1.98
1.99
2.00
3.03
3.00

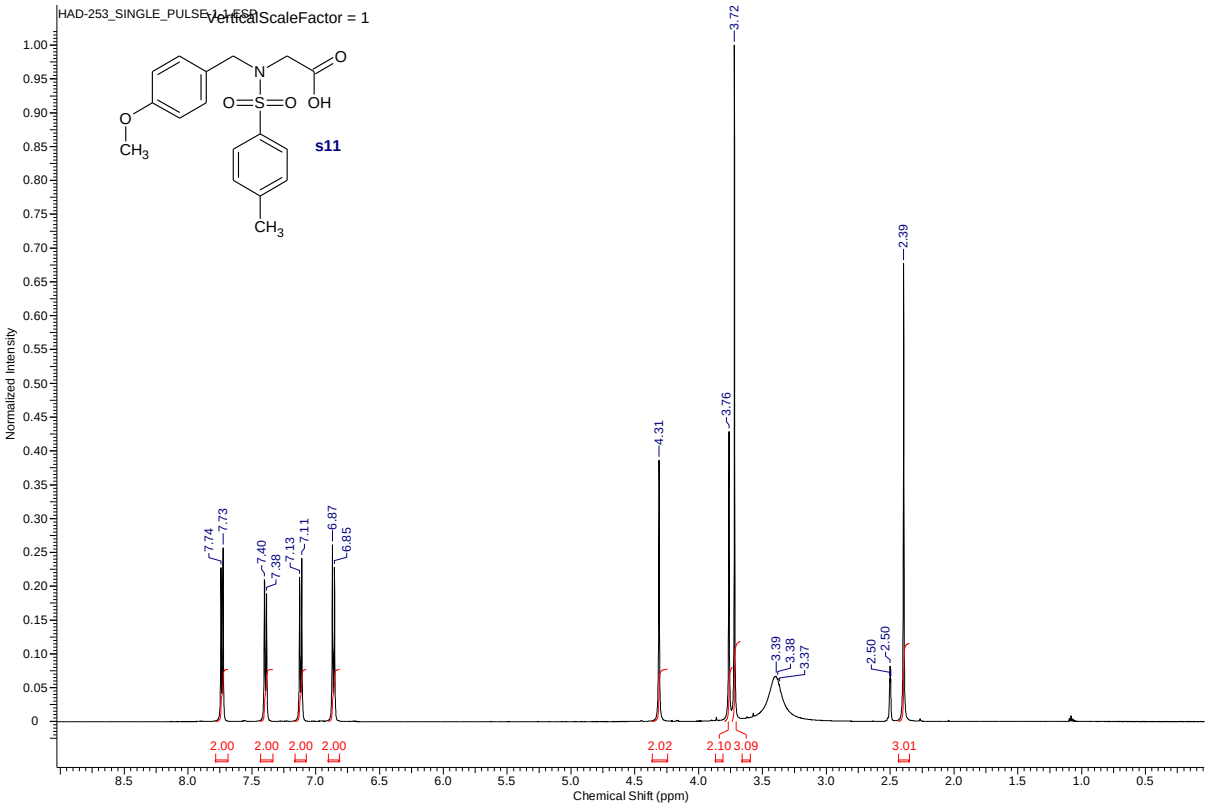

HAD-485_SINGLE_PULSE_QEC_1.ESP
VerticalScaleFactor = 1
Br
N
O=S=O
O
O
CH3
CH3
s9
Normalized Intensity
Chemical Shift (ppm)
76.74
77.25
127.45
131.87
129.59
113.93
55.19
51.82
51.00
159.41
193.43
143.50
133.47
136.59
126.55
21.57

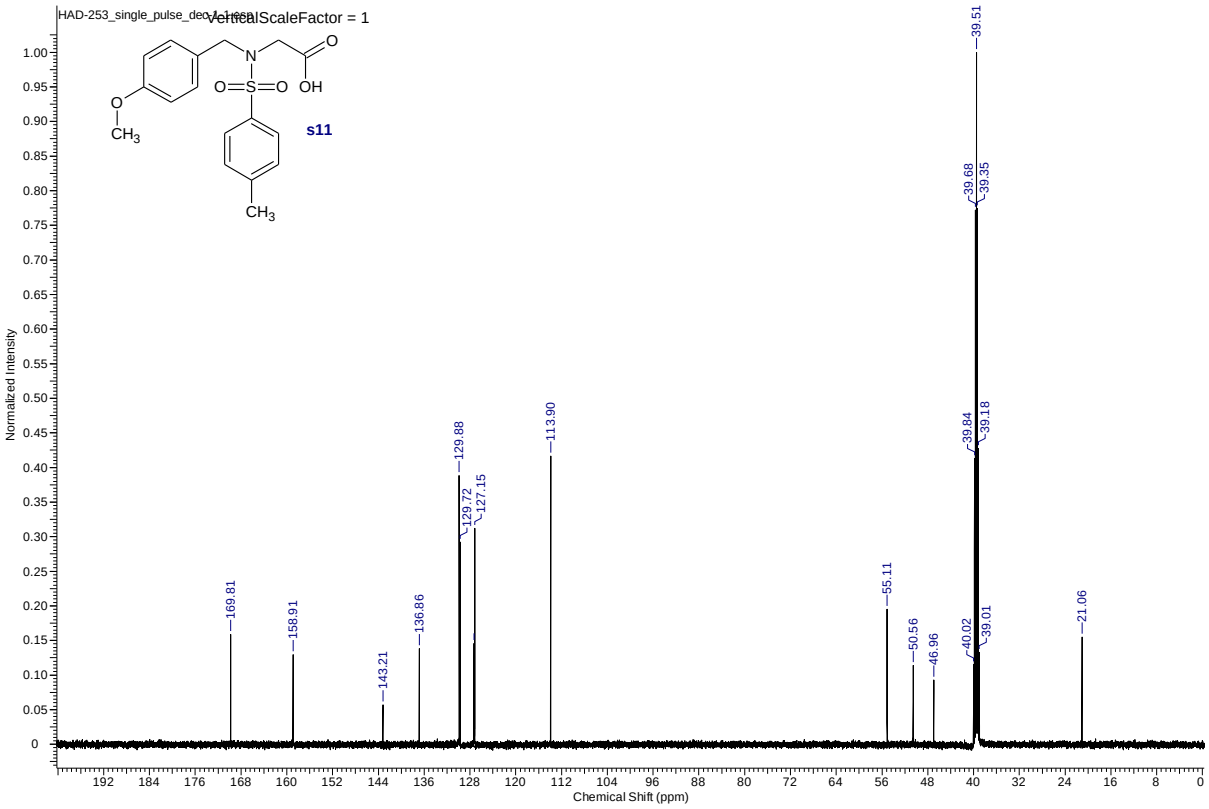

HAD-490B_SINGLE_PULSE.2.1.ESP
VerticalScaleFactor = 1
Br
N
O=S=O
OH
O
CH3
CH3
1i
Normalized Intensity
Chemical Shift (ppm)
7.73
7.71
7.37
7.36
7.19
7.17
7.26
6.98
6.87
6.86
4.56
4.53
4.46
4.44
4.44
4.01
3.98
3.81
3.29
3.27
3.26
3.24
3.16
3.00
3.00
2.97
2.97
2.44
2.01 2.01 2.06 2.10 2.04 2.05
1.02 1.02
1.00 3.09
1.06 0.85 1.02
3.09

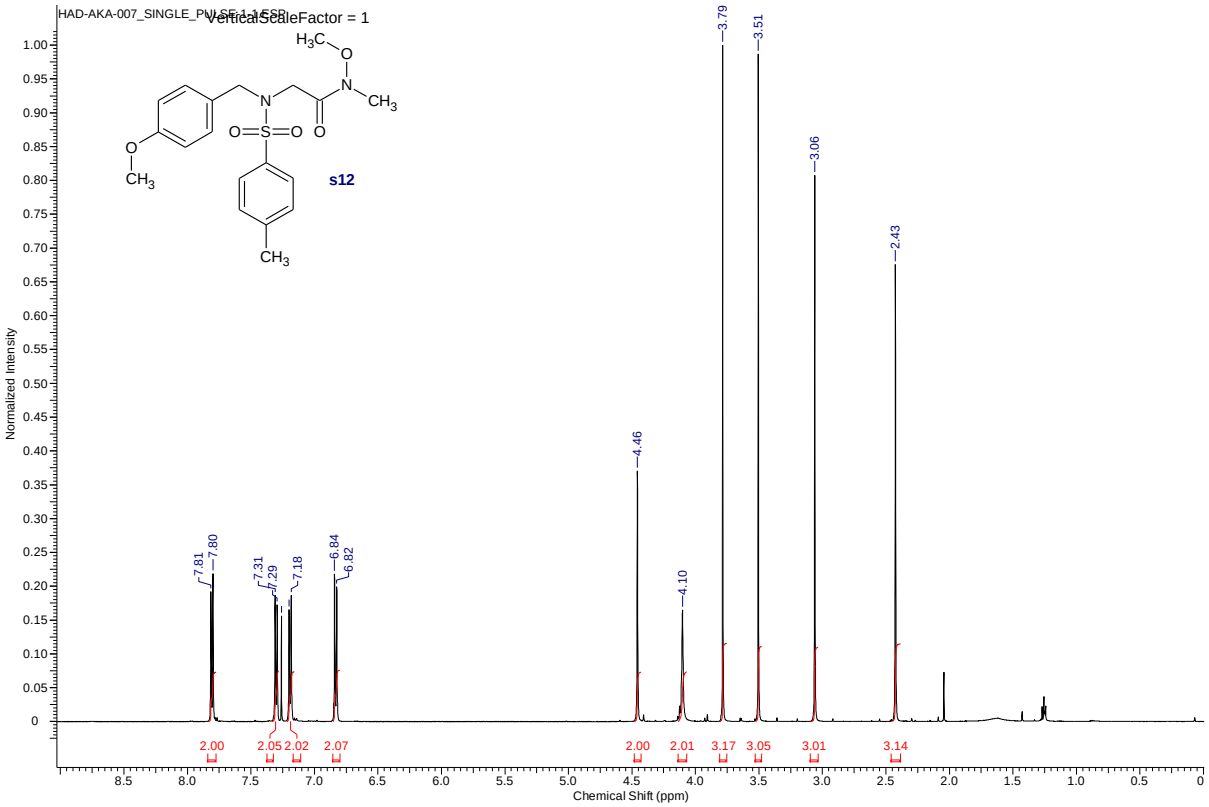

HAD-490B_SINGLE_PULSE.DEC.11.ESP
VerticalScaleFactor = 1
Br
N
O=S=O
OH
O
CH3
CH3
1i
Normalized Intensity
Chemical Shift (ppm)
159.58
143.86
140.22
135.52
131.38
130.12
127.51
127.29
121.45
114.21
77.25
76.74
72.05
56.33
55.28
53.70
21.52

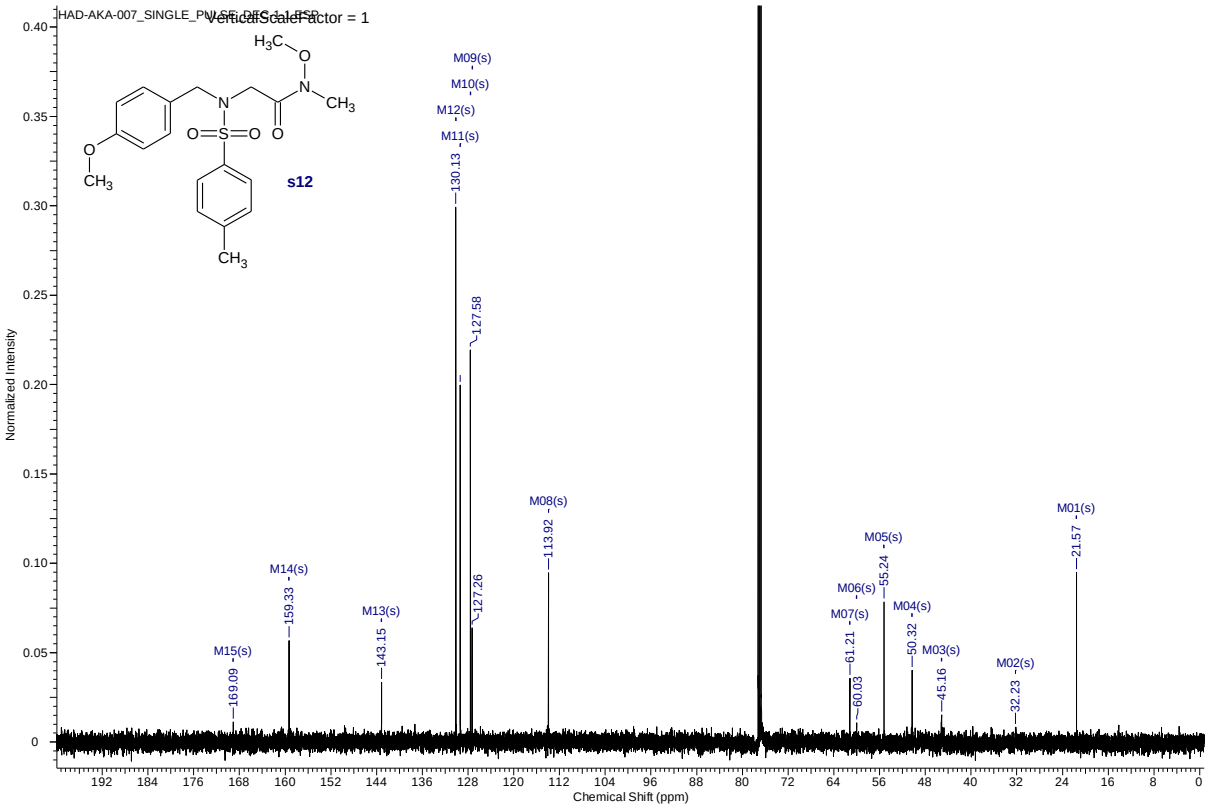

HAD-501_SINGLE_PULSE_1.1ESP
VerticalScaleFactor = 1
s10
Normalized Intensity
Chemical Shift (ppm)
7.78
7.76
7.32
7.26
7.16
7.14
6.84
6.82
6.84
6.81
4.41
3.99
4.01
3.88
3.78
2.43
1.15
1.13
1.12
1.98
2.00
1.96
2.00
2.00
2.02
1.98
3.07
3.05
3.00

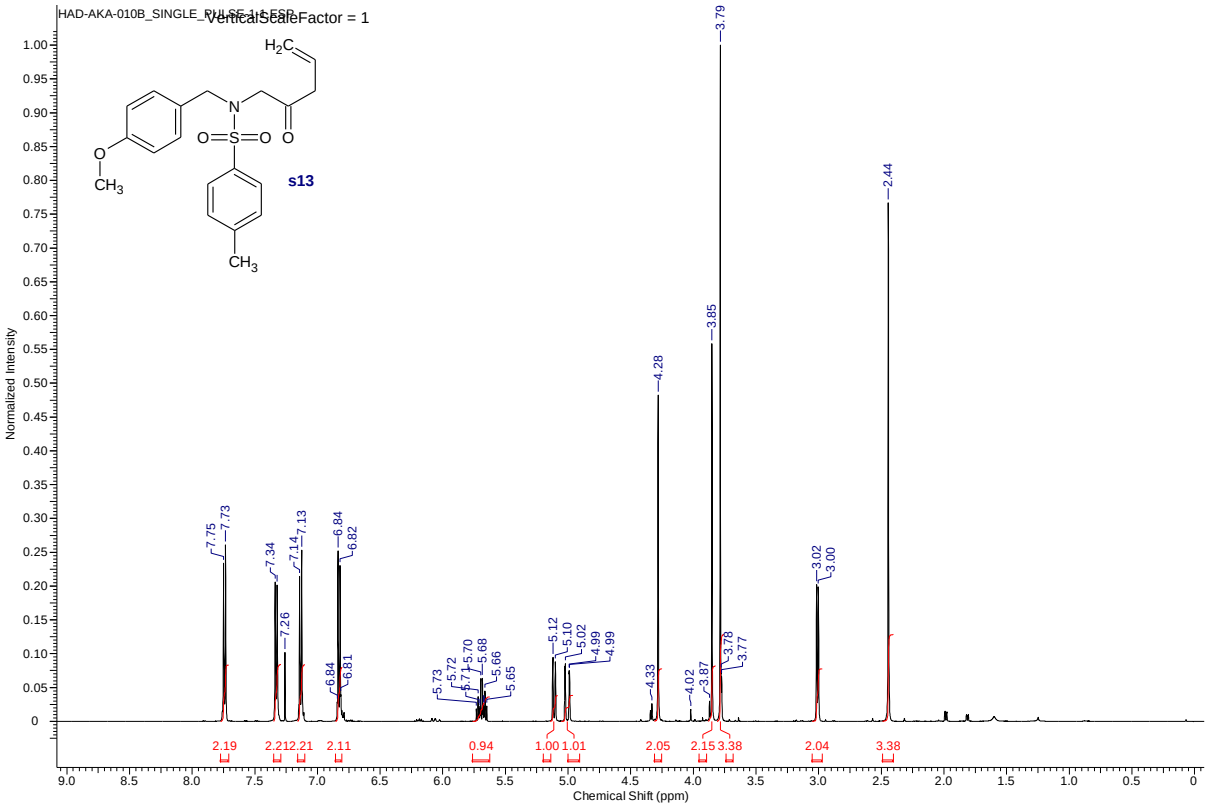

HAD-AKA-005_SINGLE_PULSE_DEC_1.1ESP
VerticalScaleFactor = 1
s10
Normalized Intensity
Chemical Shift (ppm)
130.03
129.48
127.38
126.71
143.37
136.90
168.71
159.41
113.99
77.26
77.00
76.74
61.03
55.20
50.58
46.30
21.50
13.92

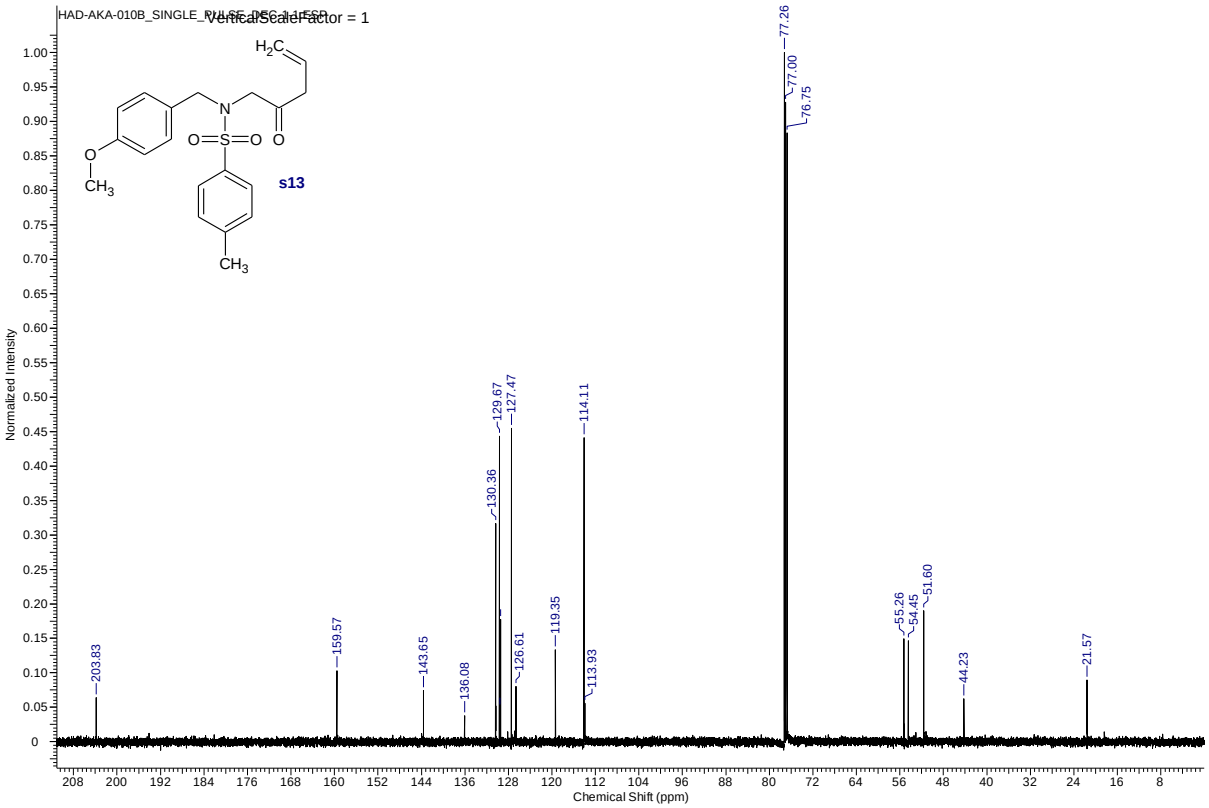

HAD-253_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
s11
Normalized Intensity
Chemical Shift (ppm)
7.74
7.73
7.40
7.38
7.13
7.11
6.87
6.85
4.31
3.76
3.72
3.39
3.38
3.37
2.50
2.50
2.39
2.00
2.00
2.00
2.00
2.02
2.10
3.09
3.01

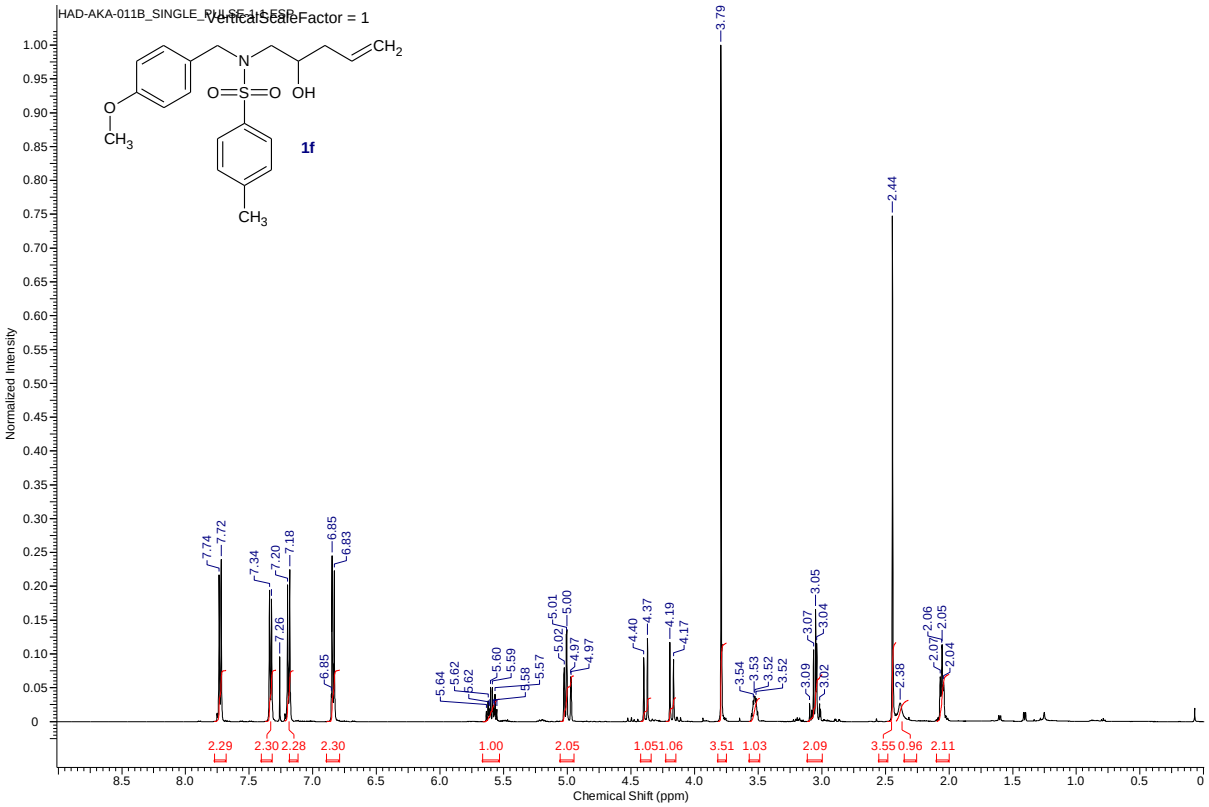

HAD-253_single_pulse_dec_1_1.esp
VerticalScaleFactor = 1
s11
Normalized Intensity
Chemical Shift (ppm)
169.81
158.91
143.21
136.86
129.88
129.72
127.15
113.90
55.11
50.56
46.96
40.02
39.84
39.68
39.51
39.35
39.18
39.01
21.06

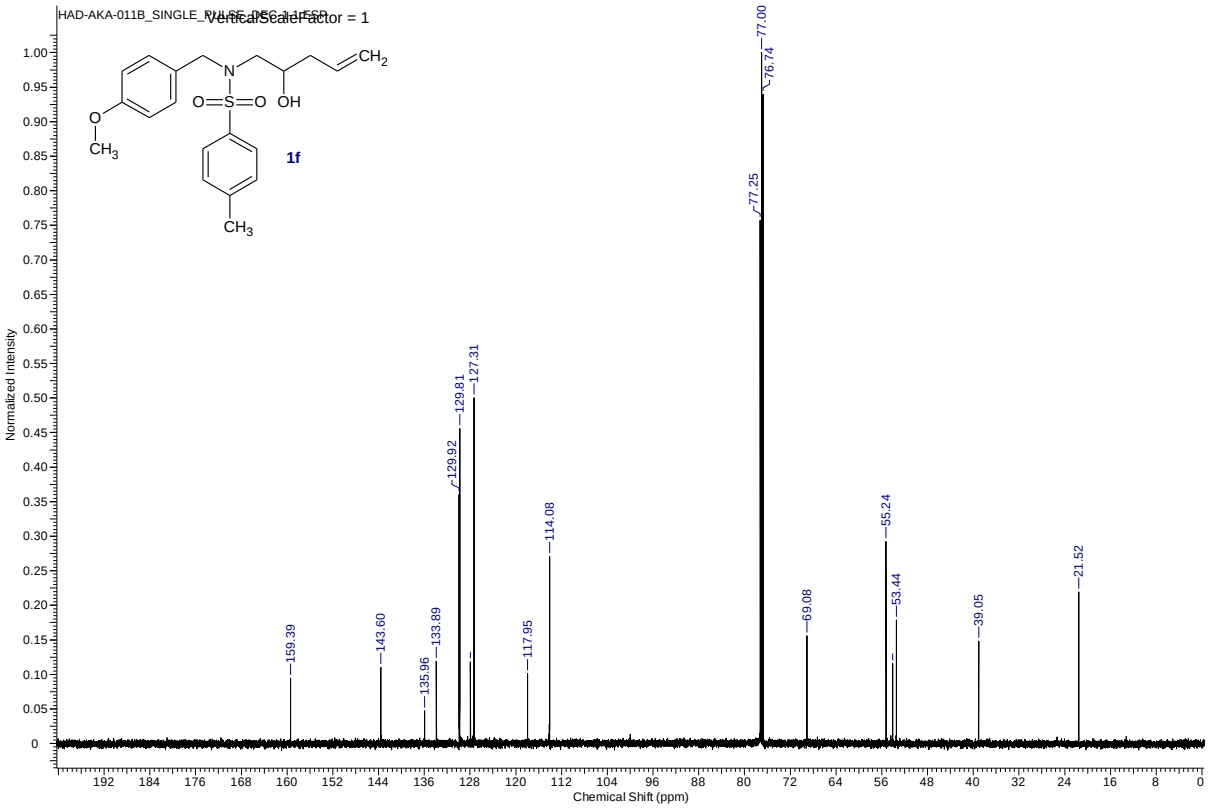

HAD-AKA-007_SINGLE_PULSE.1.1ESP
VerticalScaleFactor = 1
s12
Normalized Intensity
Chemical Shift (ppm)
7.81
7.80
7.31
7.29
7.18
6.84
6.82
4.46
4.10
3.79
3.51
3.06
2.43
2.00
2.05
2.02
2.07
2.00
2.01
3.17
3.05
3.01
3.14

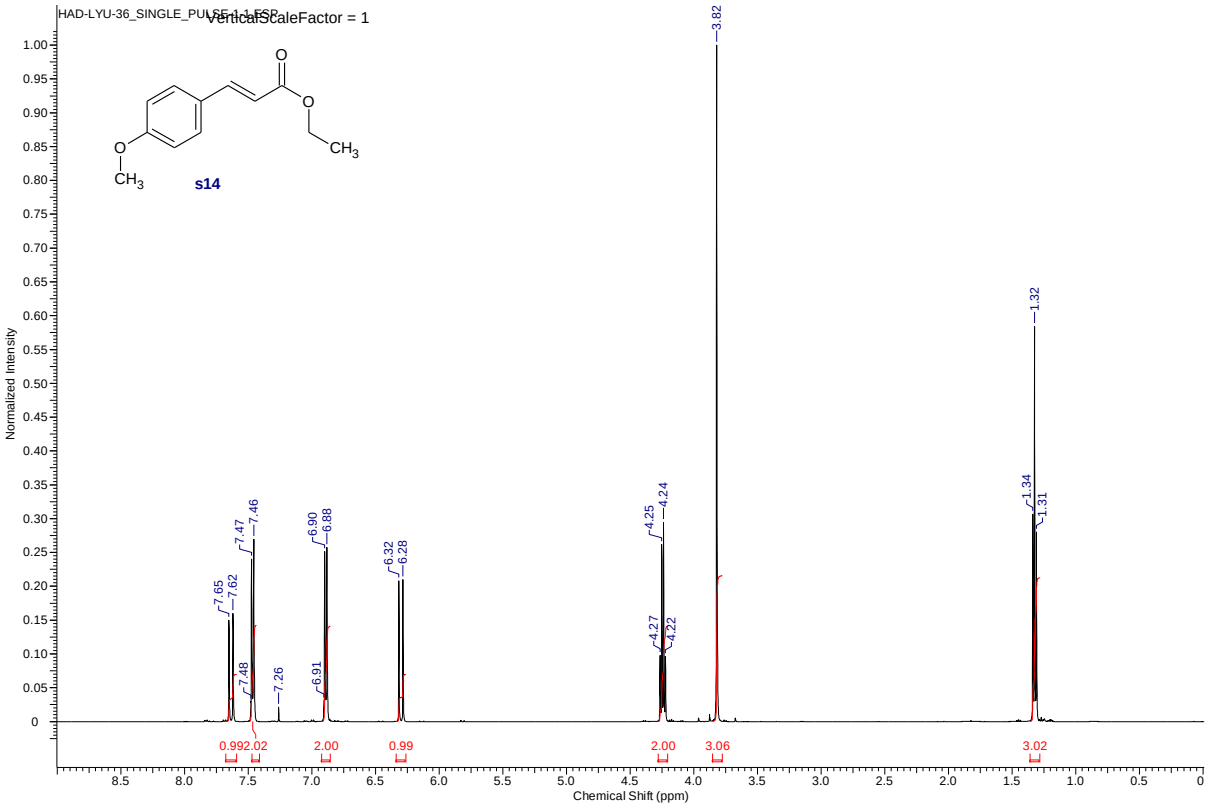

HAD-AKA-007_SINGLE_PULSE_DEC.1.1ESP
VerticalScaleFactor = 1
s12
Normalized Intensity
Chemical Shift (ppm)
M09(s)
M10(s)
M12(s)
M11(s)
130.13
127.58
127.26
M08(s)
113.92
M14(s)
159.33
M13(s)
143.15
M15(s)
169.09
M01(s)
21.57
M05(s)
55.24
M06(s)
M07(s)
61.21
60.03
M04(s)
50.32
M03(s)
45.16
M02(s)
32.23

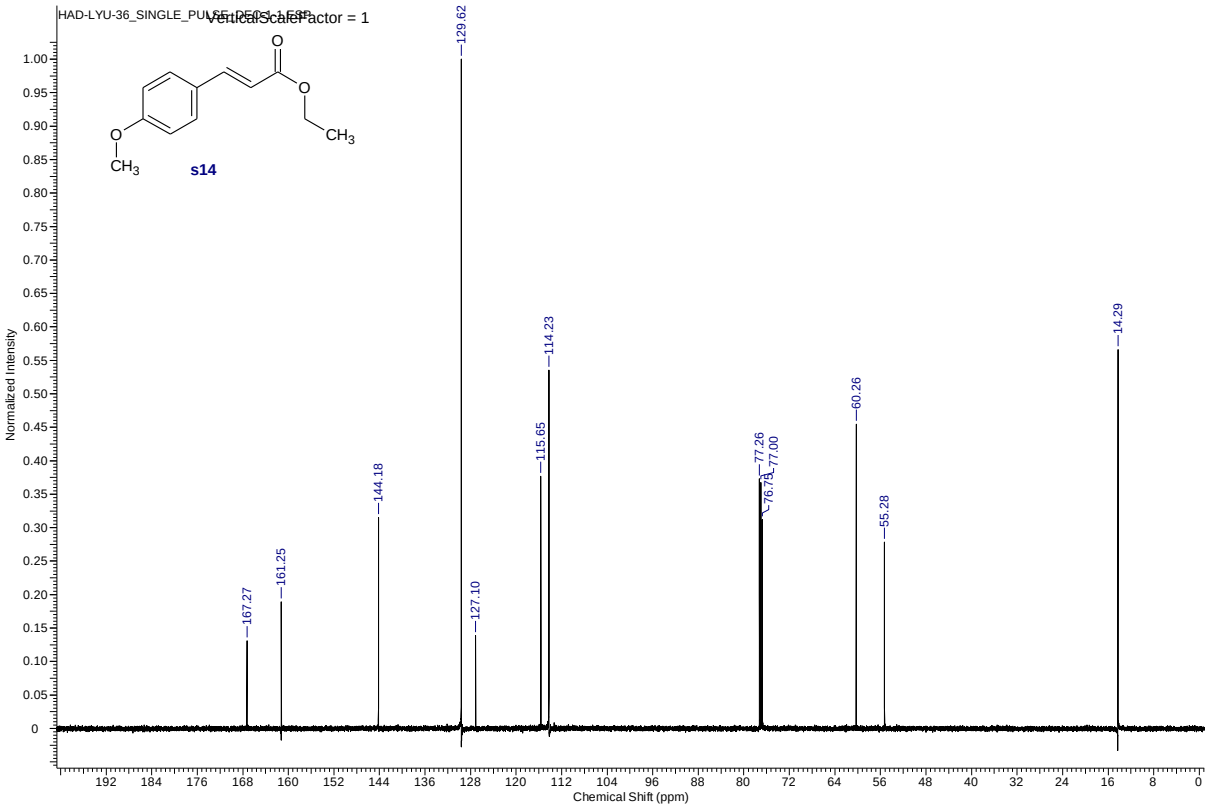

HAD-AKA-010B_SINGLE_PULSE_1H.ESP
VerticalScaleFactor = 1
s13
Normalized Intensity
Chemical Shift (ppm)
7.75
7.73
7.34
7.26
7.14
7.13
6.84
6.82
6.84
6.81
5.73
5.72
5.71
5.70
5.68
5.66
5.65
5.12
5.10
5.02
4.99
4.99
4.33
4.28
4.02
3.87
3.85
3.79
3.78
3.77
3.02
3.00
2.44
2.19
2.21
2.21
2.11
0.94
1.00
1.01
2.05
2.15
3.38
2.04
3.38

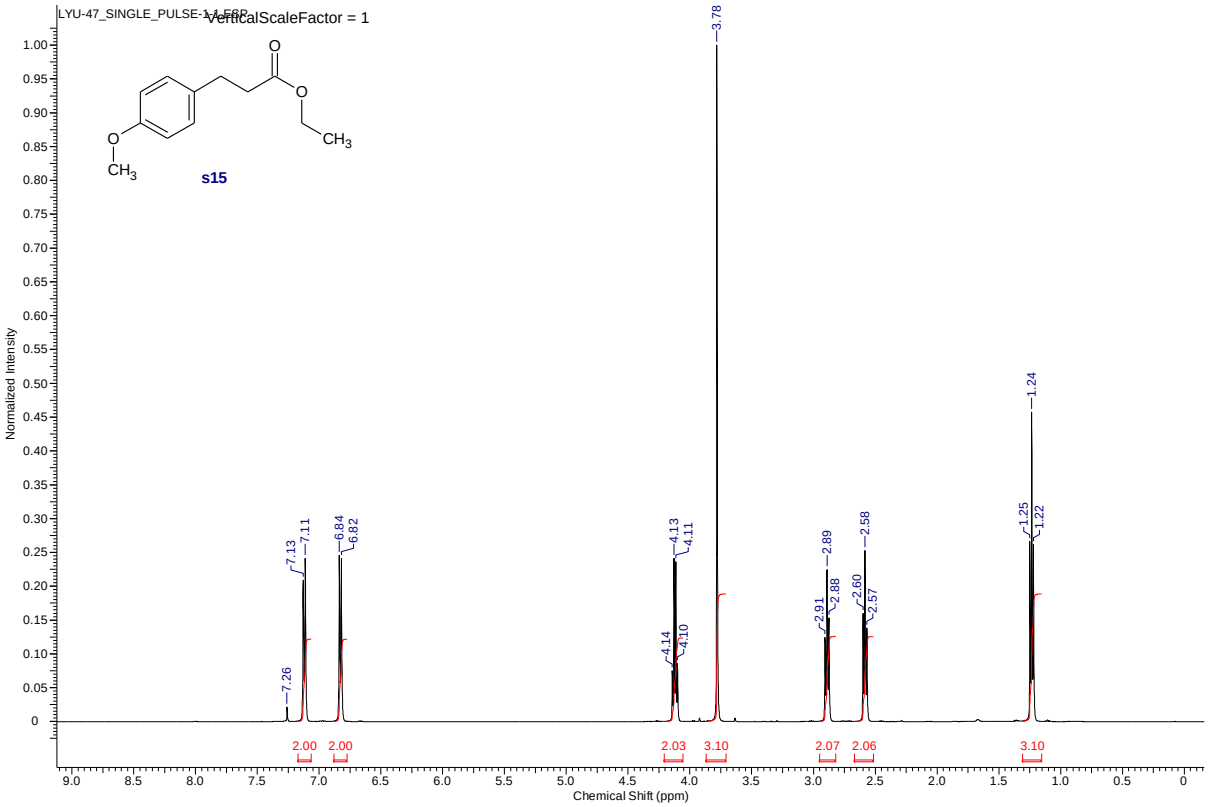

HAD-AKA-010B_SINGLE_PULSE_DEC_1H.ESP
VerticalScaleFactor = 1
s13
Normalized Intensity
Chemical Shift (ppm)
77.26
77.00
76.75
203.83
159.57
143.65
136.08
130.36
129.67
127.47
126.61
119.35
114.11
113.93
55.26
54.45
51.60
44.23
21.57

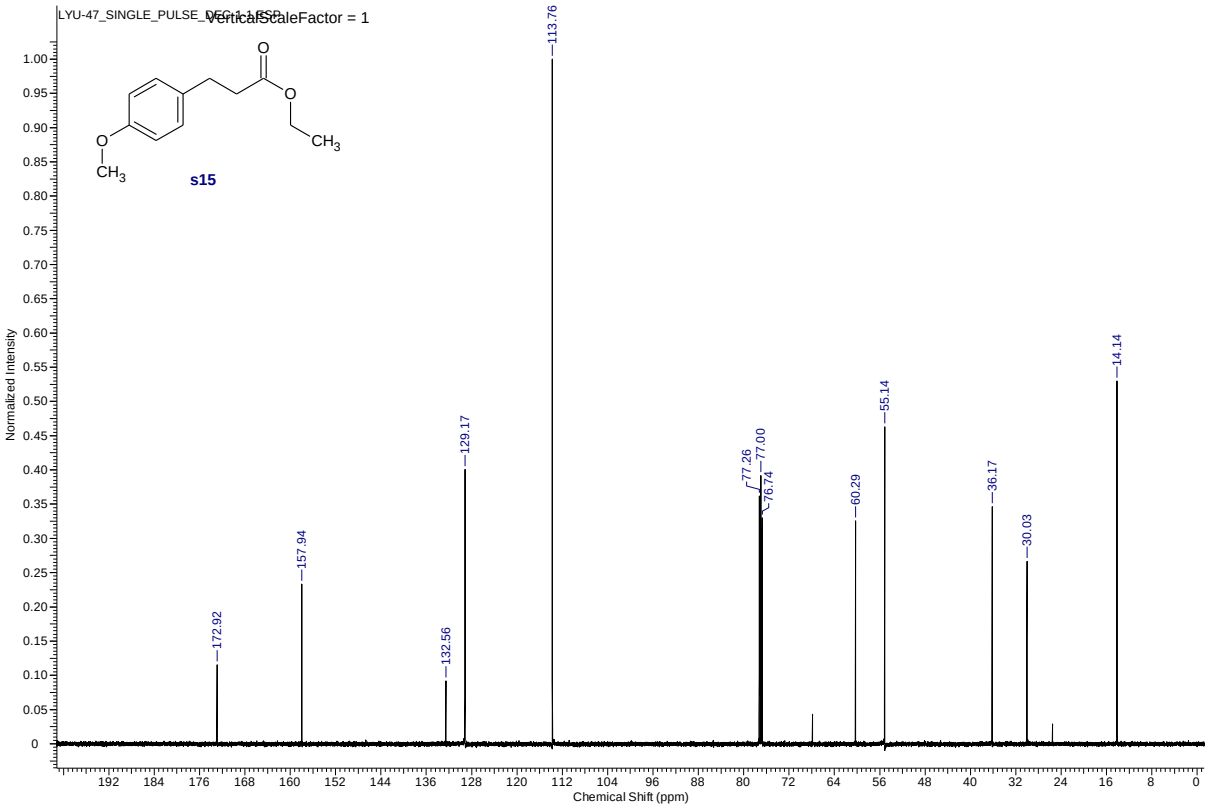

HAD-AKA-011B_SINGLE_PULSE_1H.ESP
VerticalScaleFactor = 1
1f
Normalized Intensity
Chemical Shift (ppm)

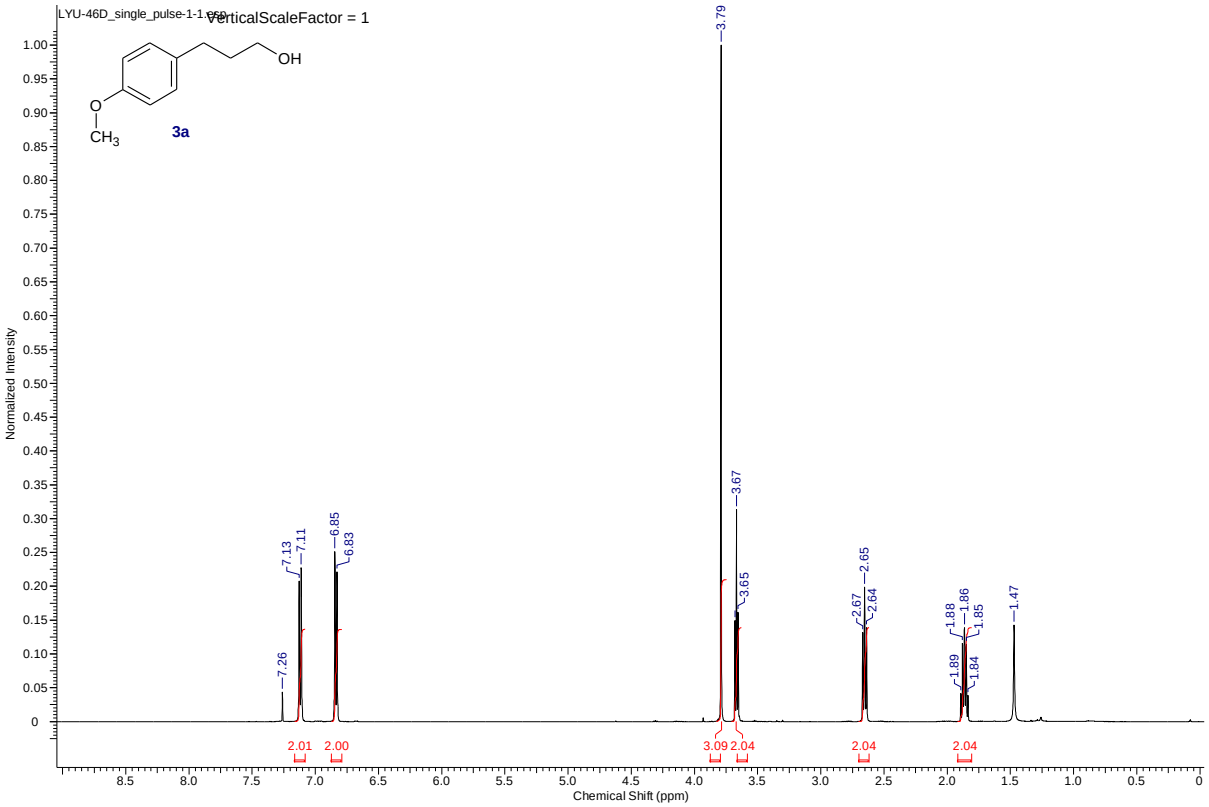

HAD-AKA-011B_SINGLE_PULSE_DEC_1H.ESP
VerticalScaleFactor = 1
1f
Normalized Intensity
Chemical Shift (ppm)

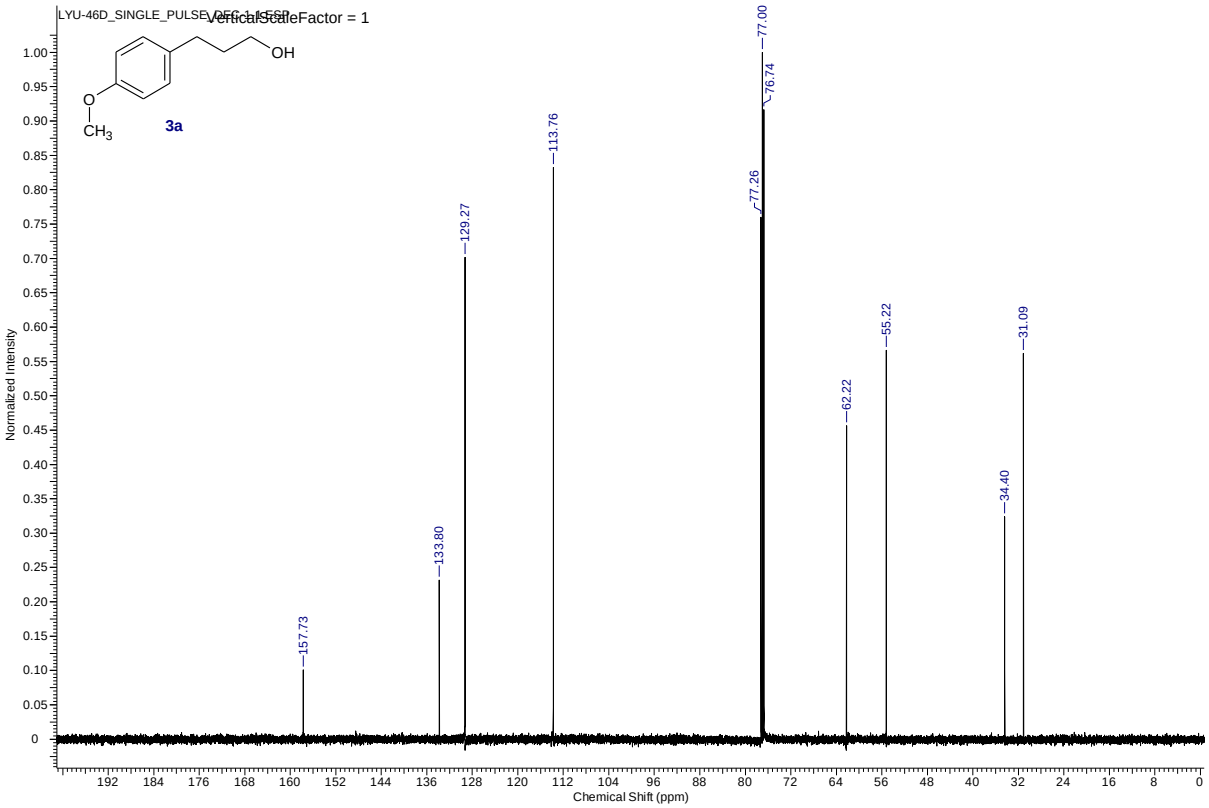

HAD-LYU-36_SINGLE_PULSE.1.ESP
VerticalScaleFactor = 1
s14
Normalized Intensity
Chemical Shift (ppm)
7.65
7.62
7.48
7.47
7.46
7.26
6.91
6.90
6.88
6.32
6.28
4.27
4.25
4.24
4.22
3.82
1.34
1.32
1.31
0.99
2.02
2.00
0.99
2.00
3.06
3.02

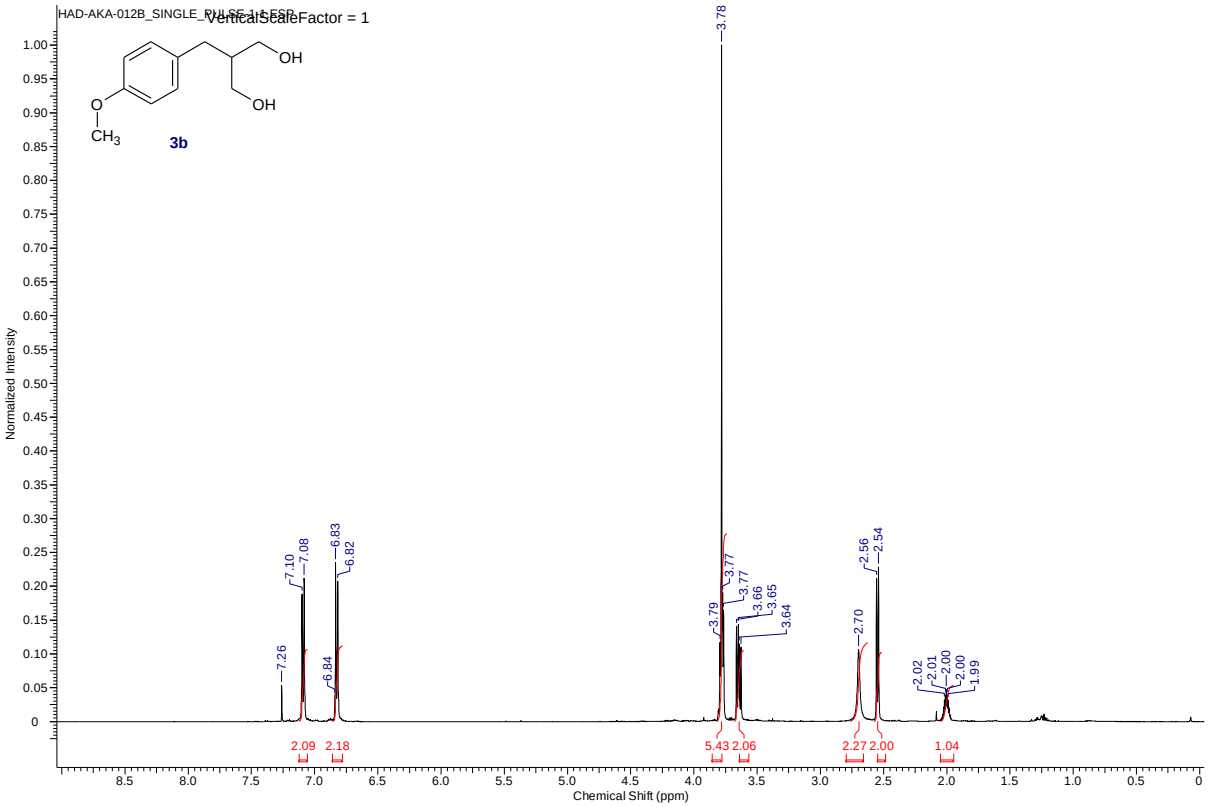

HAD-LYU-36_SINGLE_PULSE_DEC.1.ESP
VerticalScaleFactor = 1
s14
Normalized Intensity
Chemical Shift (ppm)
167.27
161.25
144.18
129.62
127.10
115.65
114.23
77.26
77.00
76.73
60.26
55.28
14.29

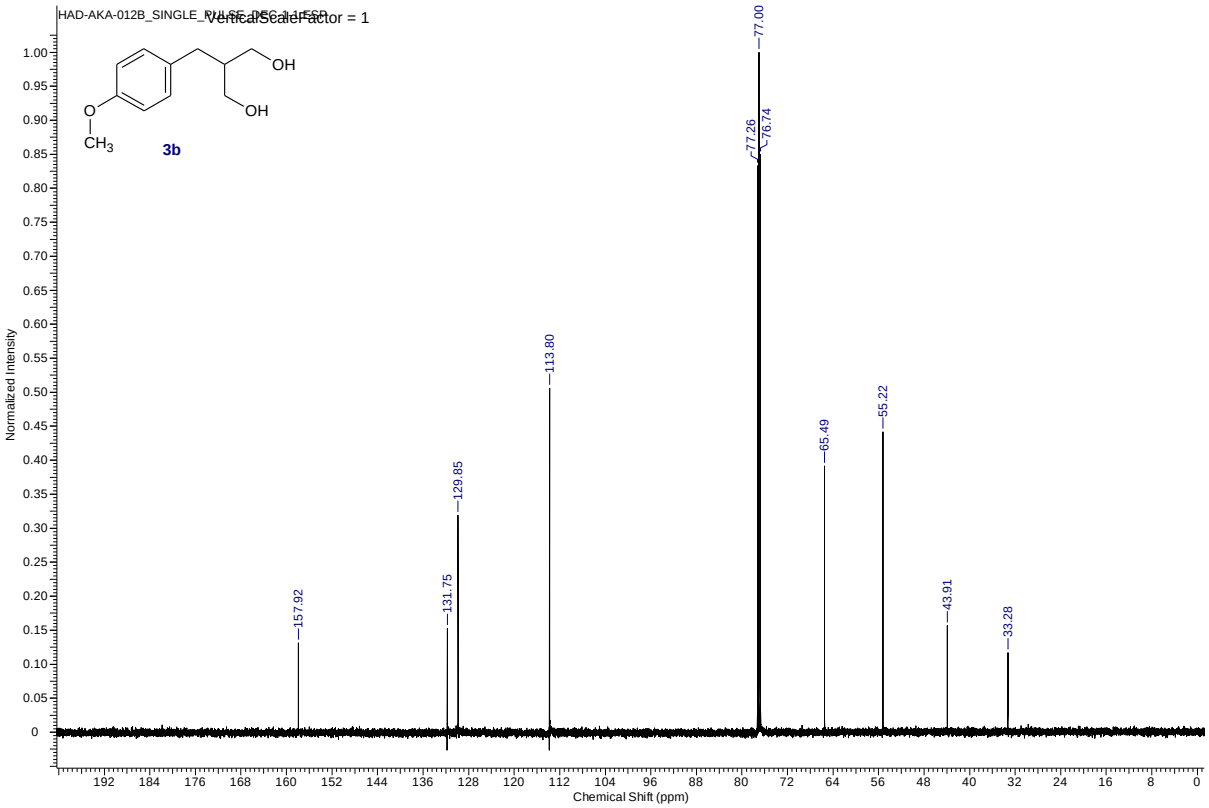

LYU-47_SINGLE_PULSE-1.1.ESP
VerticalScaleFactor = 1
s15
Normalized Intensity
Chemical Shift (ppm)
7.26
7.13
7.11
6.84
6.82
4.14
4.13
4.11
4.10
3.78
2.91
2.89
2.88
2.60
2.58
2.57
1.25
1.24
1.22
2.00
2.00
2.03
3.10
2.07
2.06
3.10

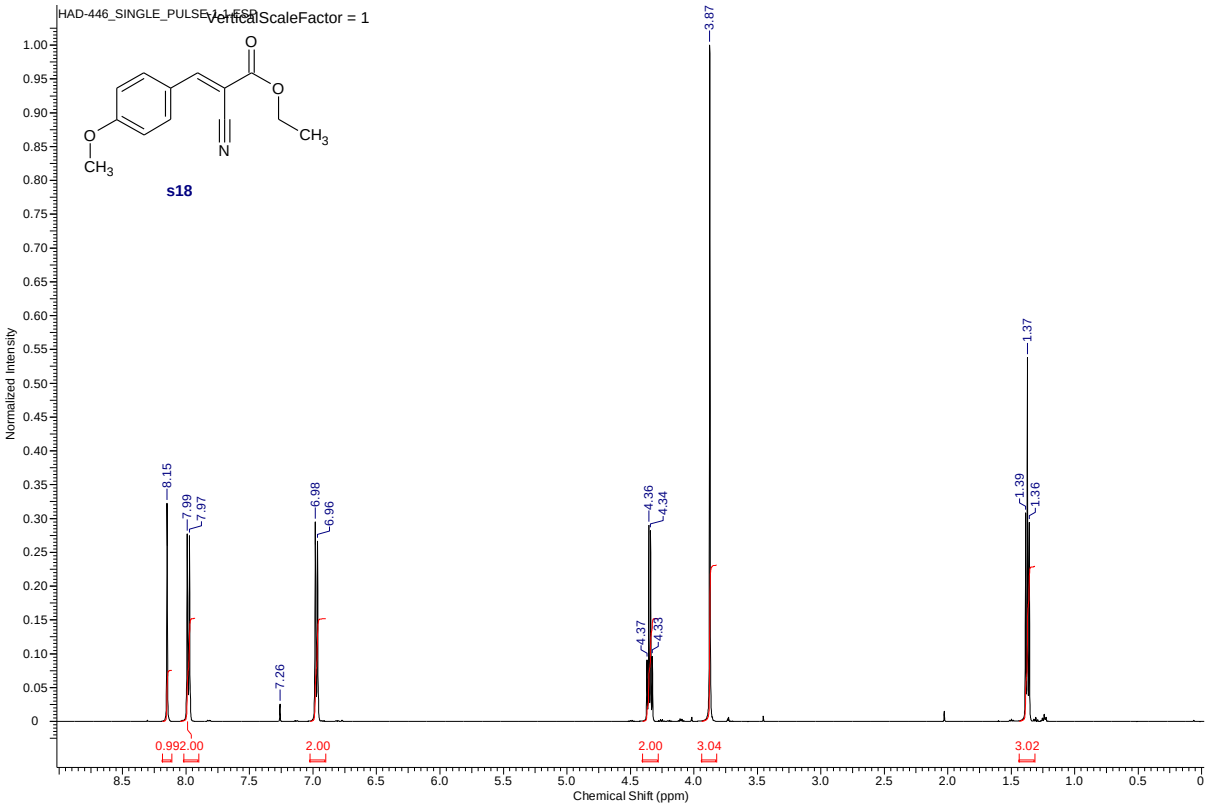

LYU-47_SINGLE_PULSE_DEC-1.1.ESP
VerticalScaleFactor = 1
s15
Normalized Intensity
Chemical Shift (ppm)
172.92
157.94
132.56
129.17
113.76
77.26
77.00
76.74
60.29
55.14
36.17
30.03
14.14

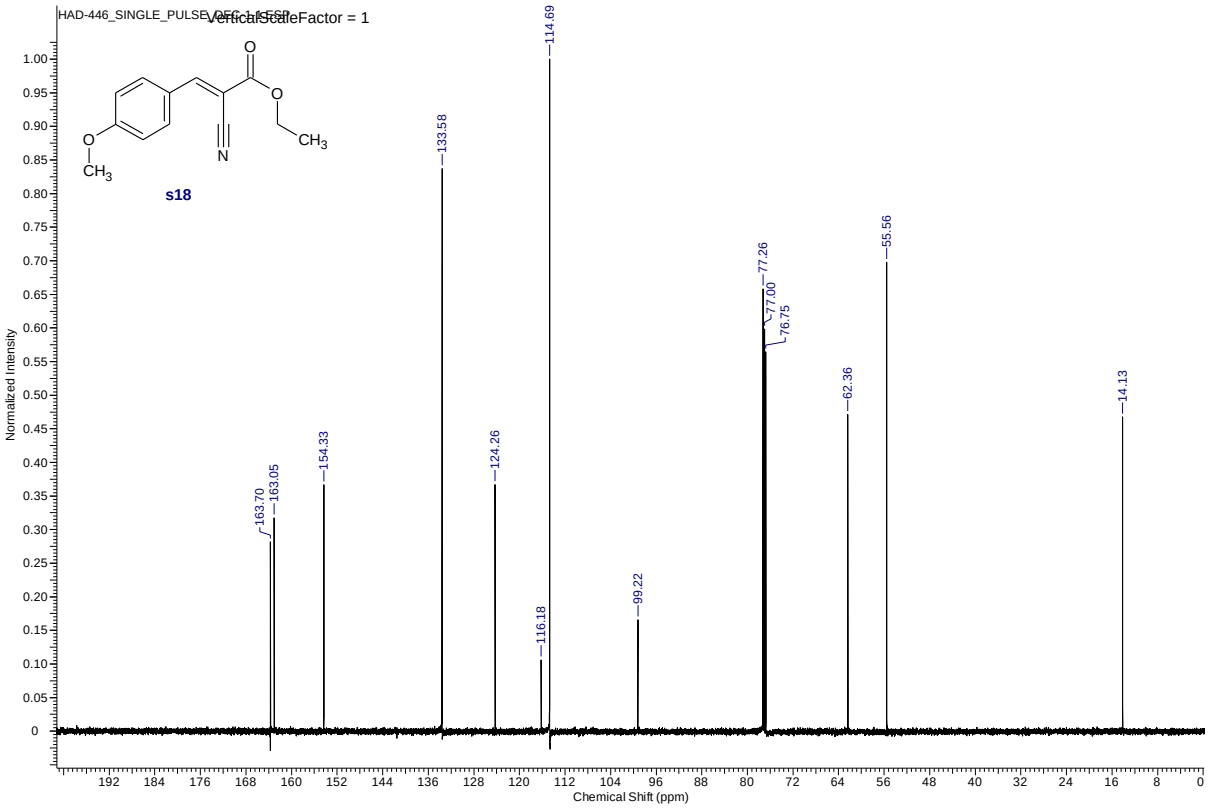

LYU-46D_single_pulse-1-1.esp
VerticalScaleFactor = 1
OH
O
CH3
3a
Normalized Intensity
Chemical Shift (ppm)
7.26
7.13
7.11
6.85
6.83
3.79
3.67
3.65
2.67
2.65
2.64
1.89
1.88
1.86
1.85
1.84
1.47
2.01
2.00
3.09
2.04
2.04
2.04

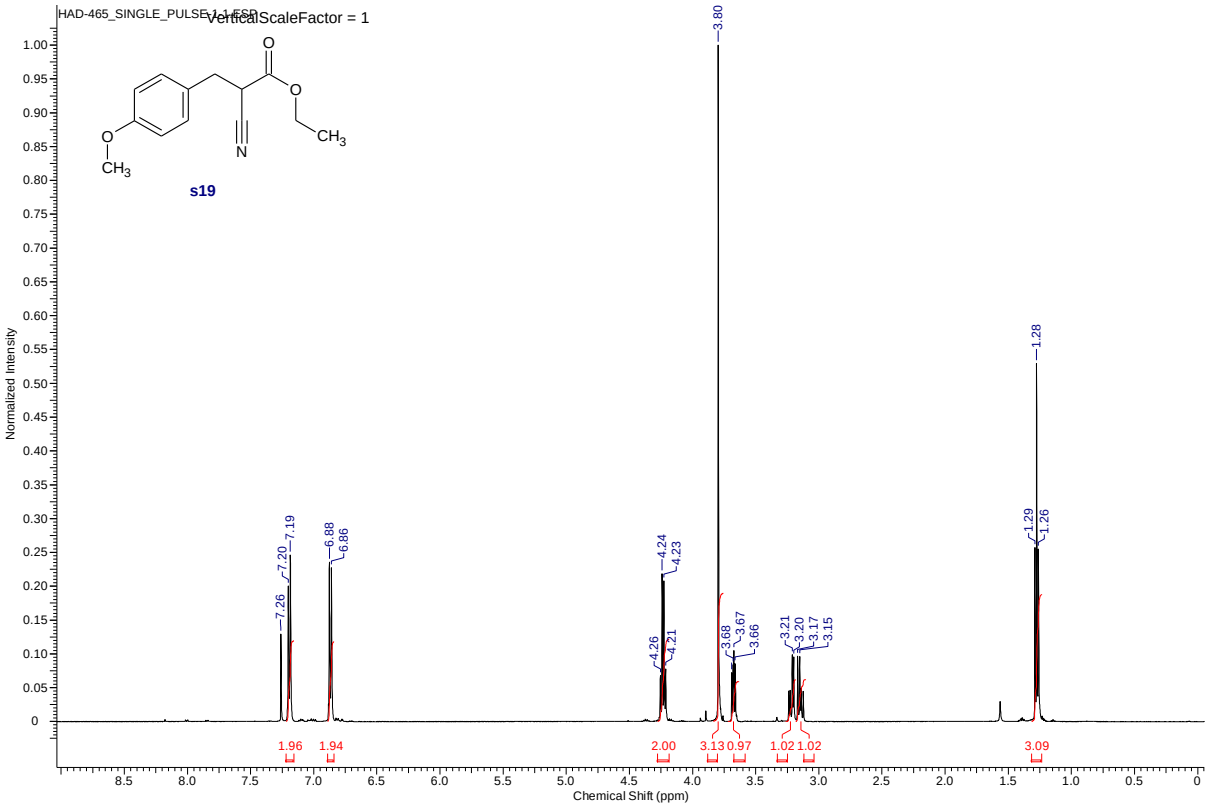

LYU-46D_SINGLE_PULSE_QFC-1.ESP
VerticalScaleFactor = 1
OH
O
CH3
3a
Normalized Intensity
Chemical Shift (ppm)
157.73
133.80
129.27
113.76
77.26
77.00
76.74
62.22
55.22
34.40
31.09

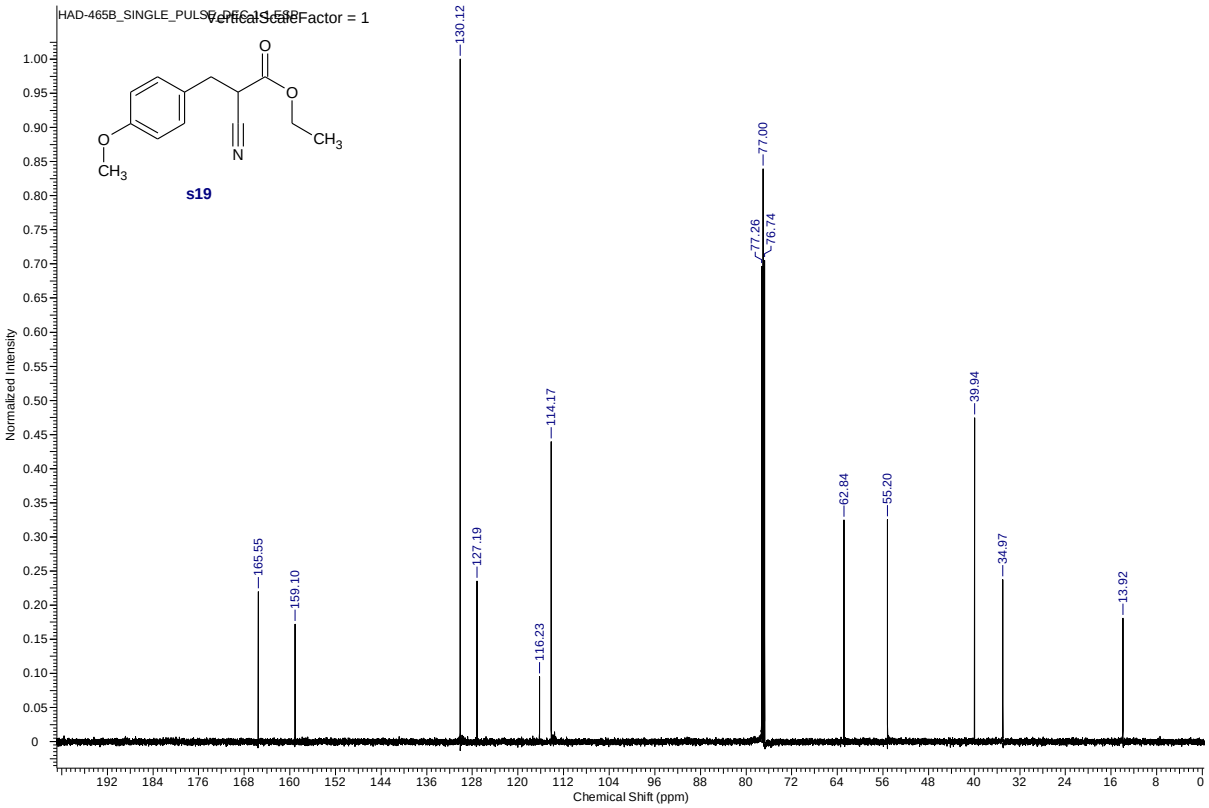

HAD-AKA-012B_SINGLE_PULSE_1H.ESP
VerticalScaleFactor = 1
OH
OH
O
CH3
3b
Normalized Intensity
Chemical Shift (ppm)
7.26
7.10
7.08
6.84
6.83
6.82
3.79
3.78
3.77
3.77
3.66
3.65
3.64
2.70
2.56
2.54
2.02
2.01
2.00
2.00
1.99
2.09
2.18
5.43
2.06
2.27
2.00
1.04

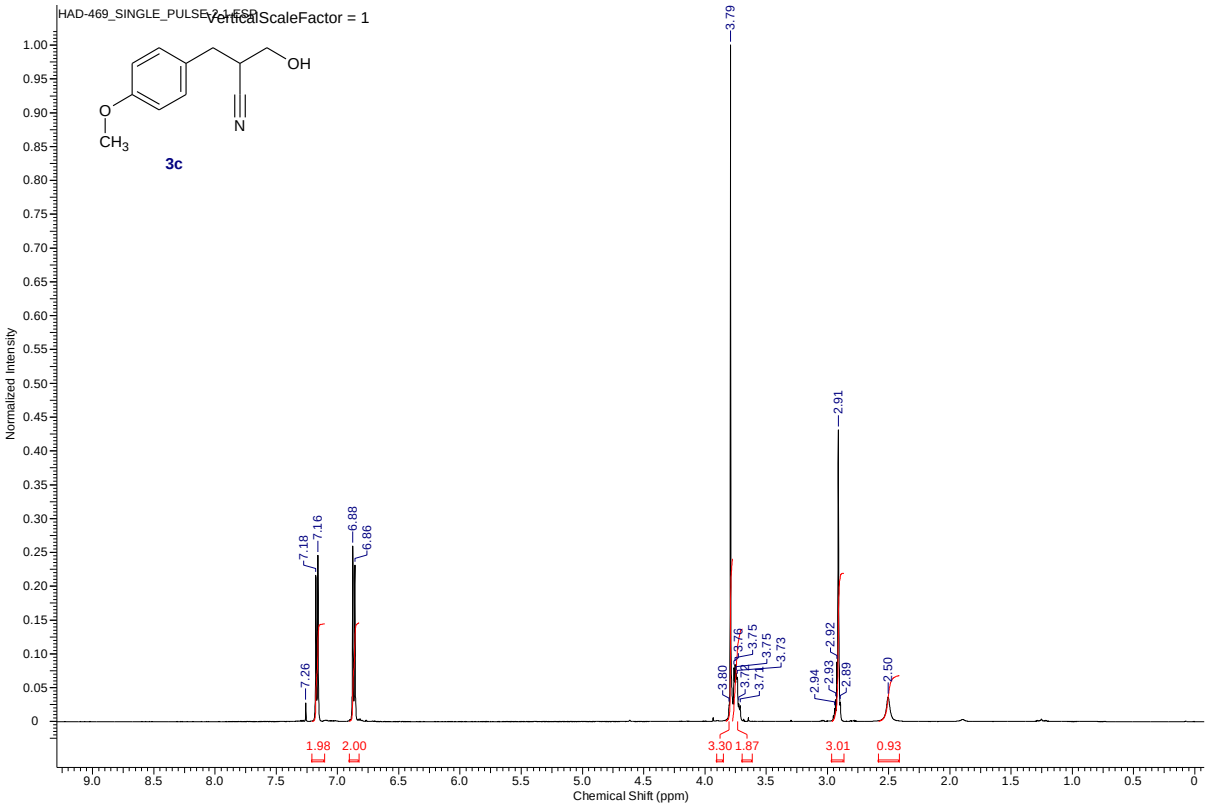

HAD-AKA-012B_SINGLE_PULSE_DEC_1H.ESP
VerticalScaleFactor = 1
OH
OH
O
CH3
3b
Normalized Intensity
Chemical Shift (ppm)
77.00
77.26
76.74
113.80
65.49
55.22
129.85
157.92
131.75
43.91
33.28

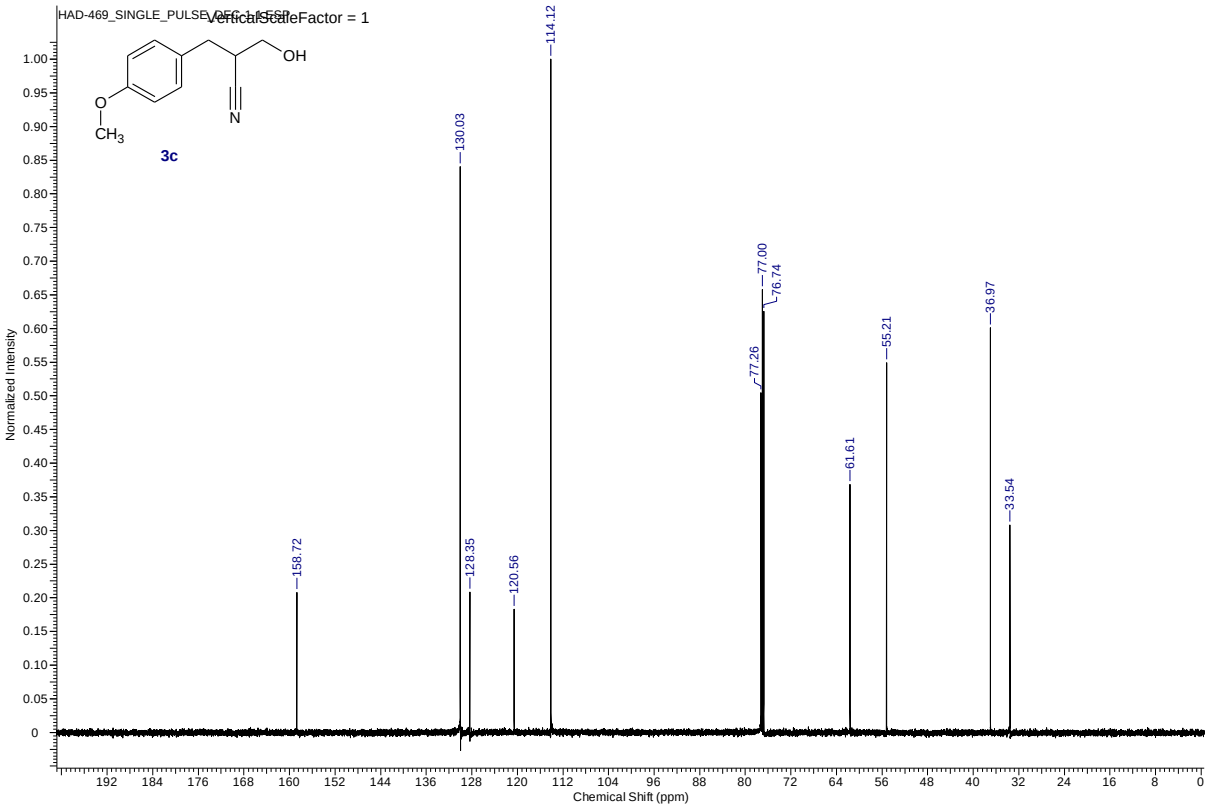

HAD-446_SINGLE_PULSE_1.ESP
VerticalScaleFactor = 1
s18
Normalized Intensity
Chemical Shift (ppm)
8.15
7.99
7.97
7.26
6.98
6.96
4.37
4.36
4.34
4.33
3.87
1.39
1.37
1.36
0.99
2.00
2.00
3.04
3.02

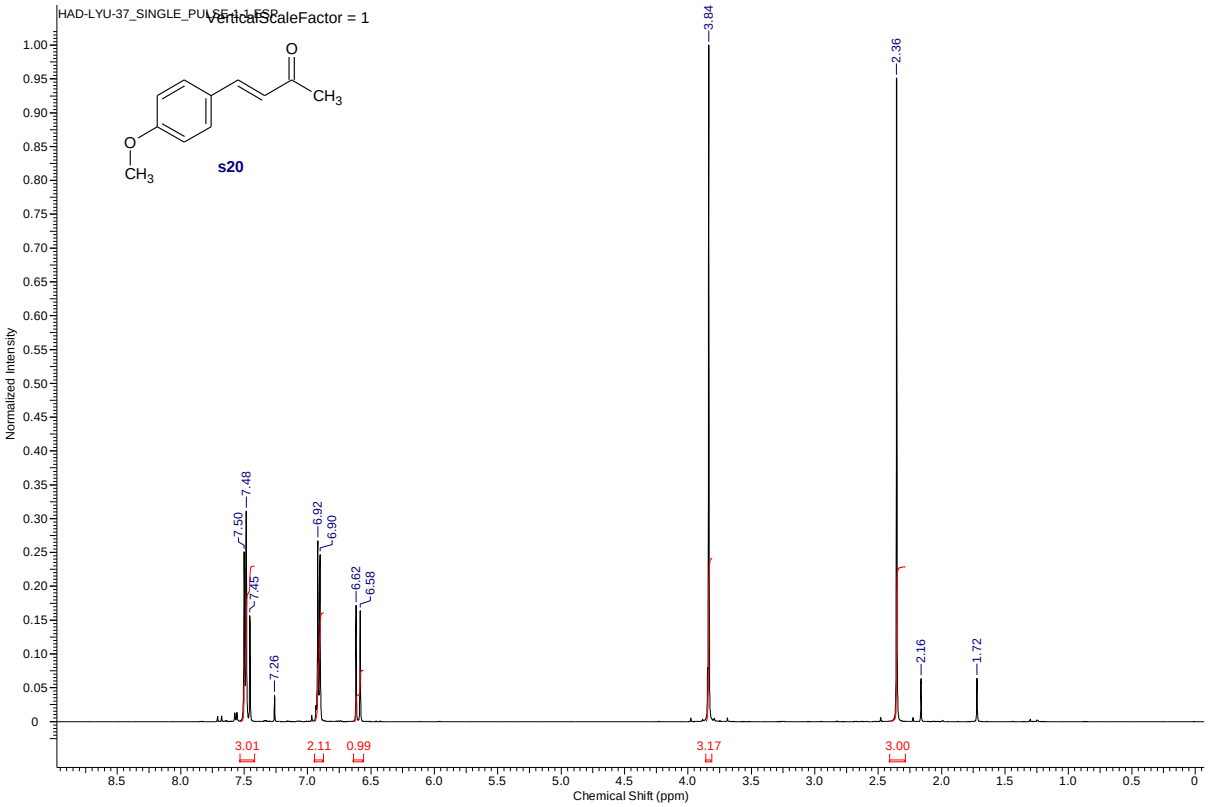

HAD-446_SINGLE_PULSE_QEC_1.ESP
VerticalScaleFactor = 1
s18
Normalized Intensity
Chemical Shift (ppm)
163.70
163.05
154.33
133.58
124.26
116.18
114.69
99.22
77.26
77.00
76.75
62.36
55.56
14.13

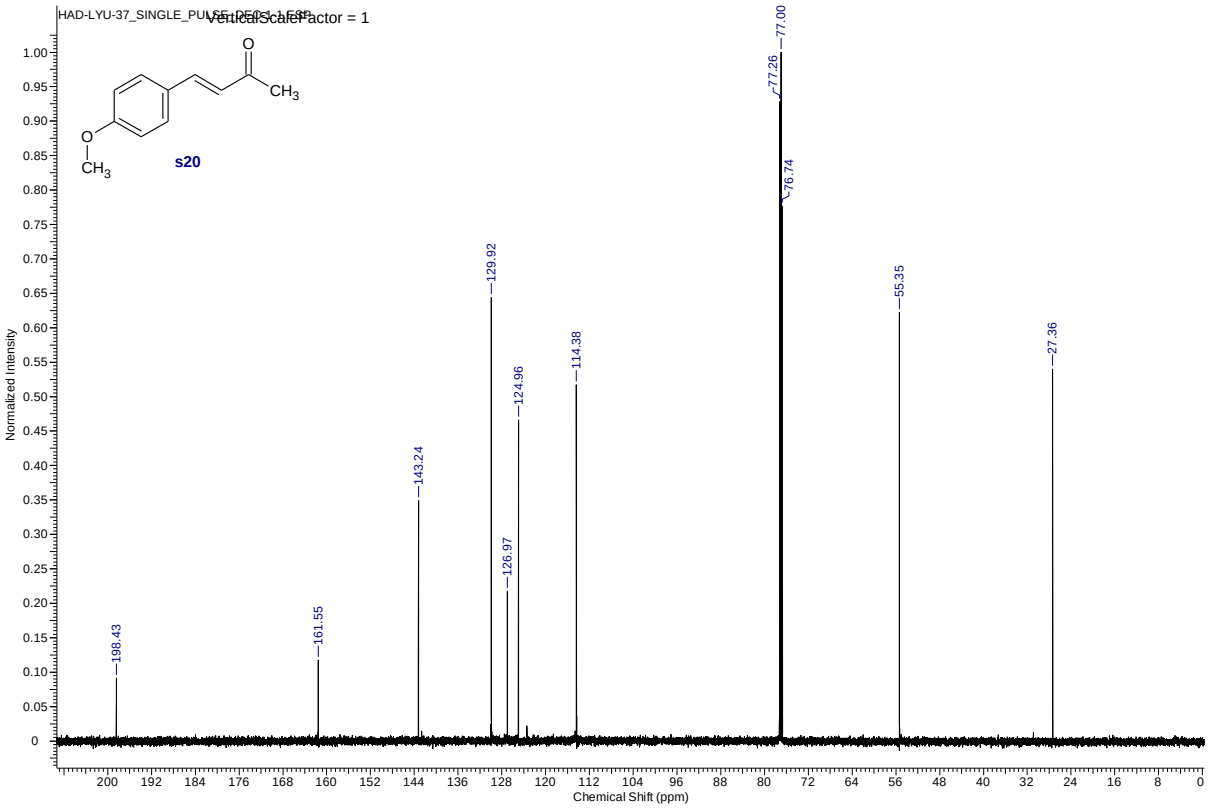

HAD-465_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
s19
Normalized Intensity
Chemical Shift (ppm)
7.26
7.20
7.19
6.88
6.86
4.24
4.23
4.26
4.21
3.80
3.68
3.67
3.66
3.21
3.20
3.17
3.15
1.28
1.29
1.26
1.96
1.94
2.00
3.13
0.97
1.02
1.02
3.09

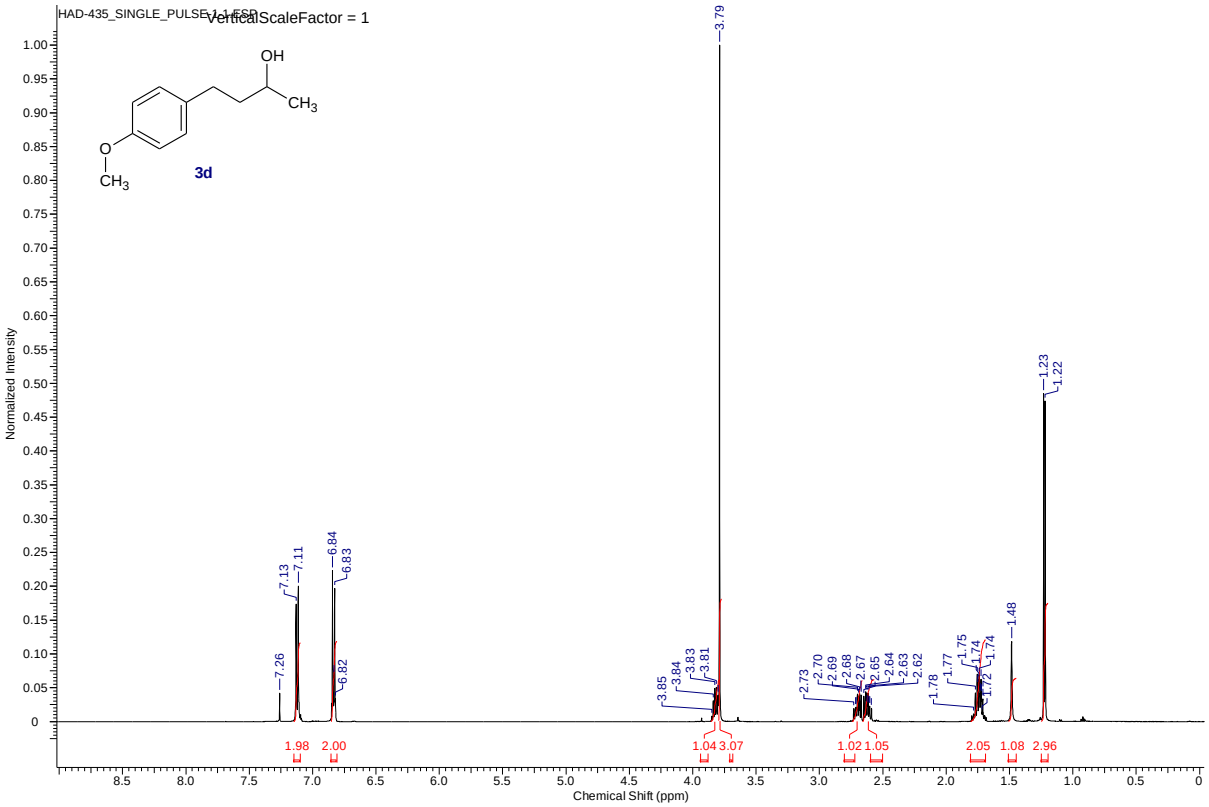

HAD-465B_SINGLE_PULSE_DEC_1_1.ESP
VerticalScaleFactor = 1
s19
Normalized Intensity
Chemical Shift (ppm)
130.12
77.00
77.26
76.74
165.55
159.10
127.19
116.23
114.17
62.84
55.20
39.94
34.97
13.92

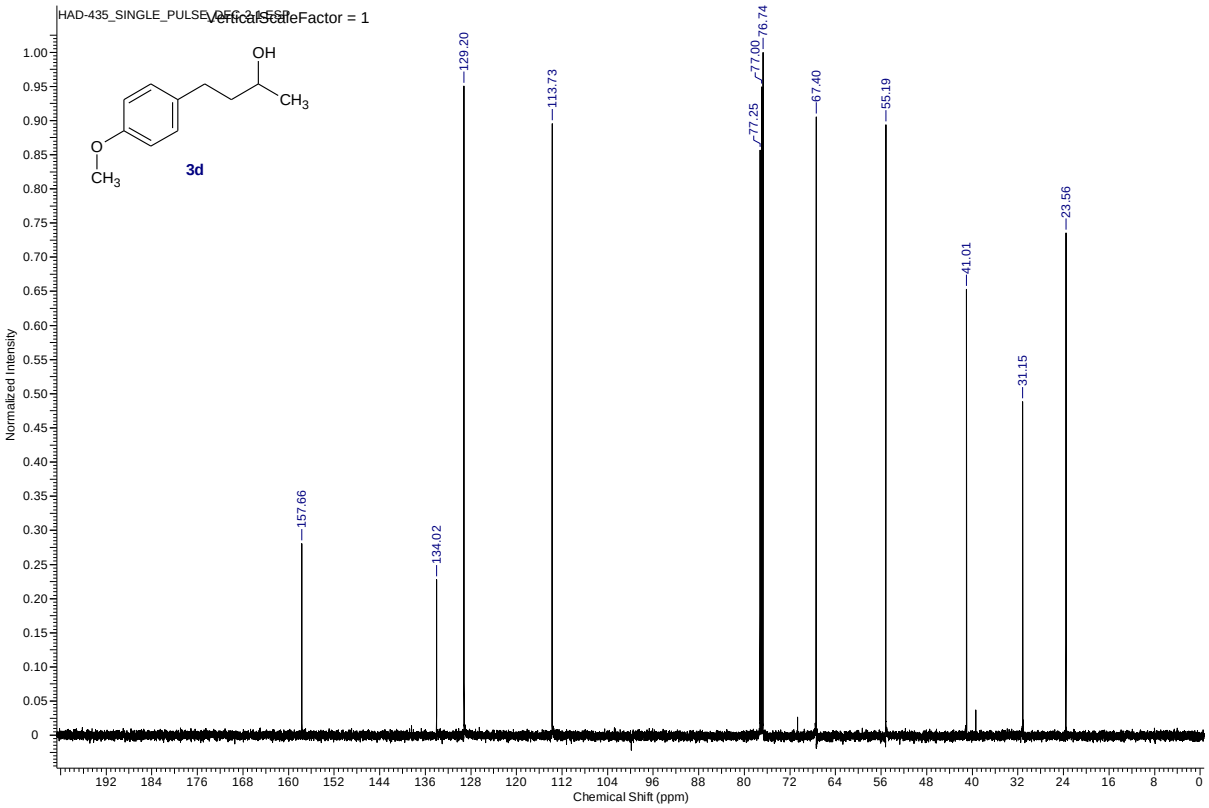

HAD-469_SINGLE_PULSE_2_1.ESP
VerticalScaleFactor = 1
OH
O
CH3
N
3c
Normalized Intensity
Chemical Shift (ppm)
3.79
2.91
7.18
7.16
6.88
6.86
7.26
3.80
3.76
3.75
3.71
3.73
2.94
2.93
2.92
2.89
2.50
1.98
2.00
3.30
1.87
3.01
0.93

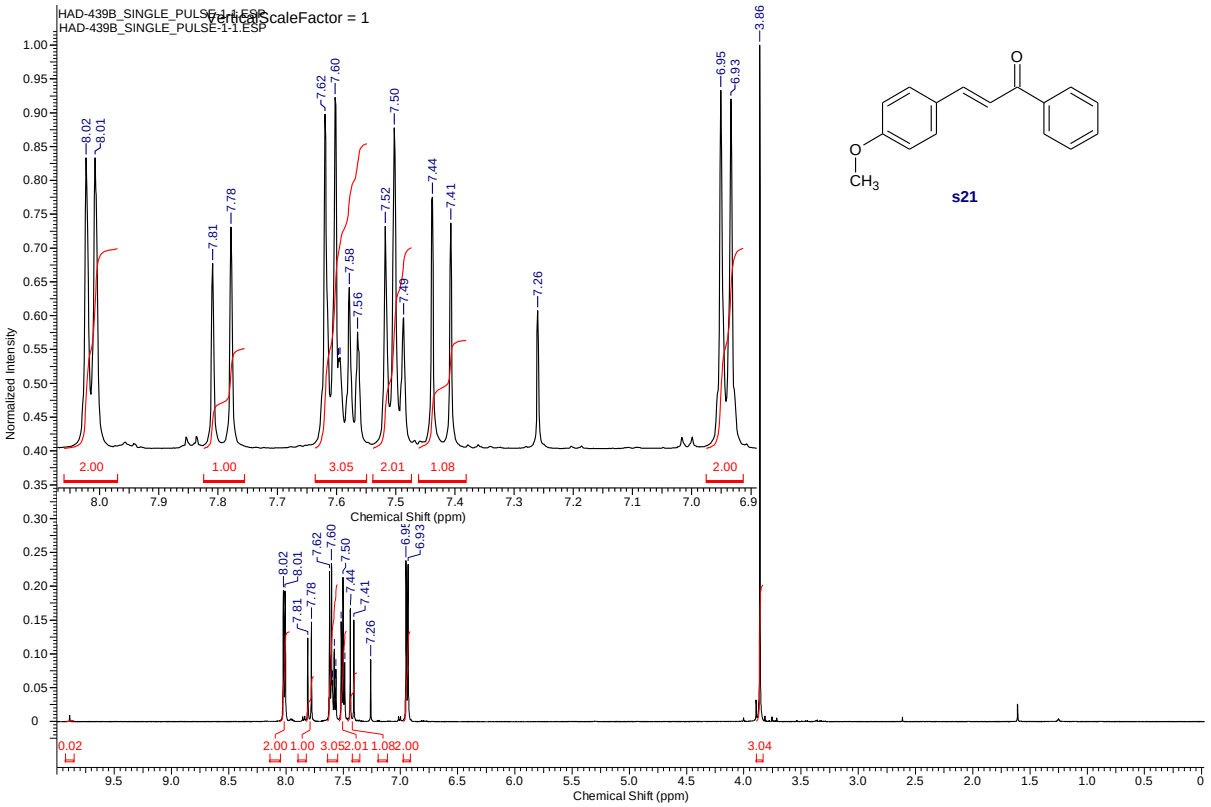

HAD-469_SINGLE_PULSE_QEC_1.ESP
VerticalScaleFactor = 1
OH
O
CH3
N
3c
Normalized Intensity
Chemical Shift (ppm)
114.12
130.03
77.00
76.74
77.26
36.97
55.21
61.61
33.54
158.72
128.35
120.56

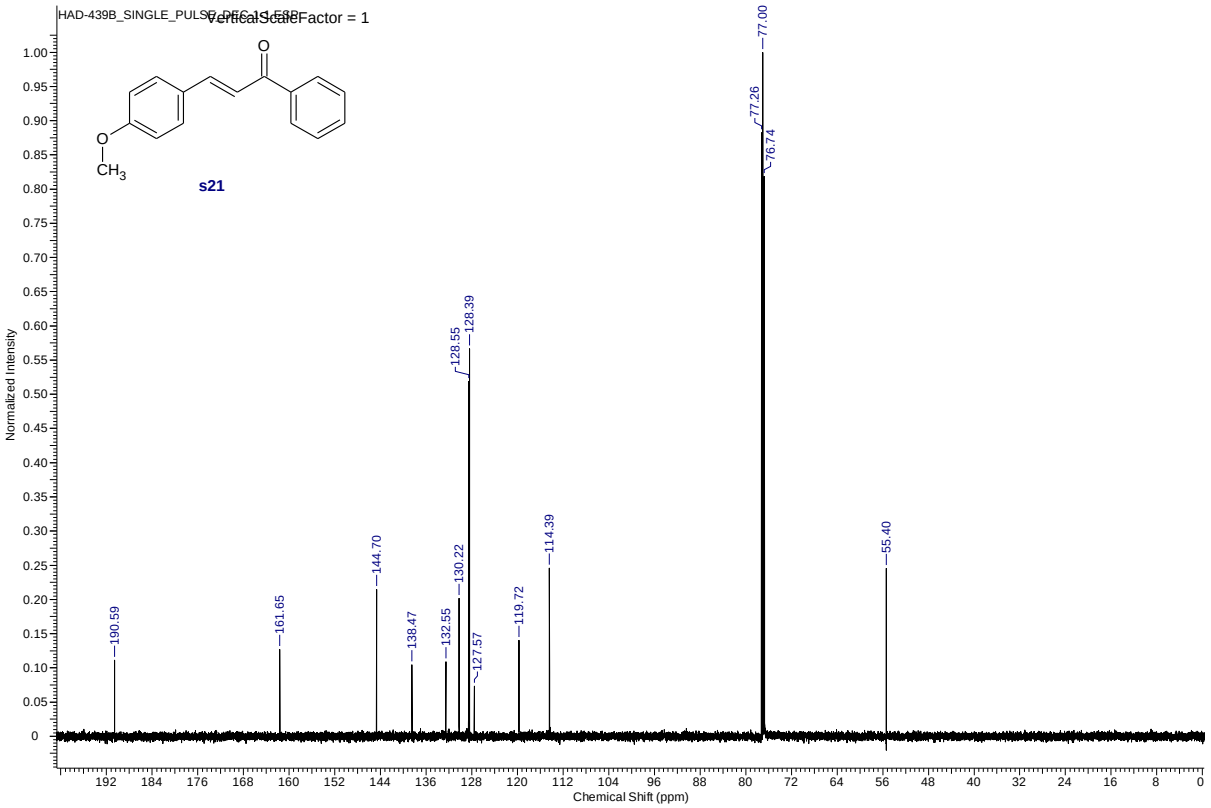

HAD-LYU-37_SINGLE_PULSE-1.ESP
VerticalScaleFactor = 1
s20
Normalized Intensity
Chemical Shift (ppm)
7.50
7.48
7.45
7.26
6.92
6.90
6.62
6.58
3.84
2.36
2.16
1.72
3.01
2.11
0.99
3.17
3.00

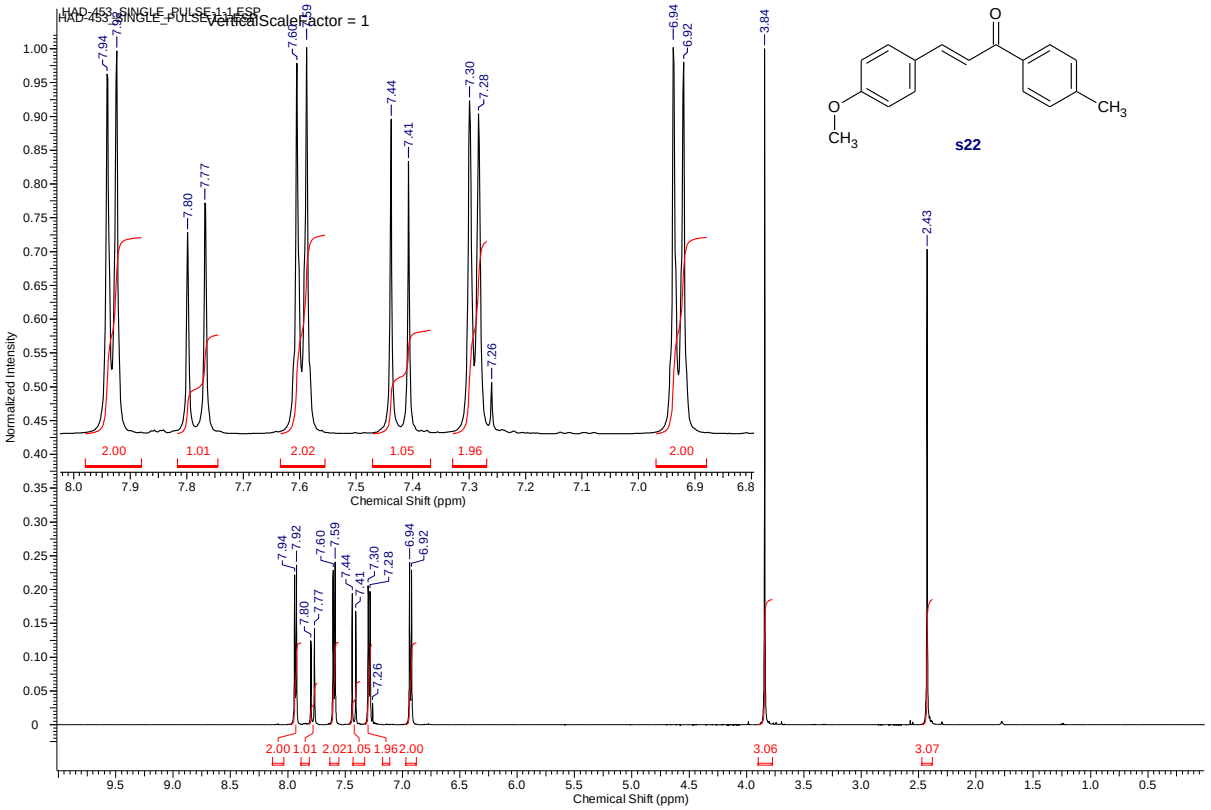

HAD-LYU-37_SINGLE_PULSE-DEPT-1.ESP
VerticalScaleFactor = 1
s20
Normalized Intensity
Chemical Shift (ppm)
198.43
161.55
143.24
129.92
126.97
124.96
114.38
77.26
77.00
76.74
55.35
27.36

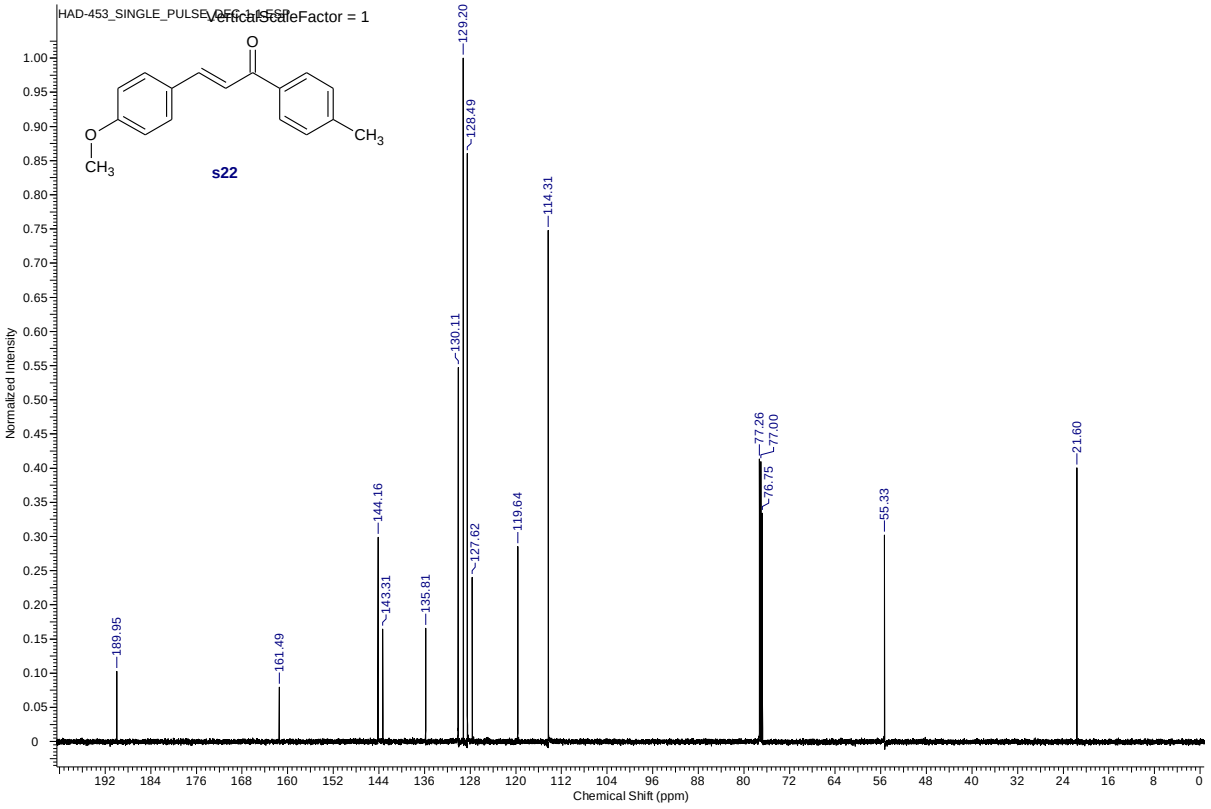

HAD-435_SINGLE_PULSE_1.1ESP
VerticalScaleFactor = 1
OH
CH3
O
CH3
3d
Normalized Intensity
Chemical Shift (ppm)
7.26
7.13
7.11
6.84
6.83
6.82
3.85
3.84
3.83
3.81
3.79
2.73
2.70
2.69
2.68
2.67
2.65
2.64
2.63
2.62
1.78
1.77
1.75
1.74
1.72
1.48
1.23
1.22
1.98
2.00
1.04
3.07
1.02
1.05
2.05
1.08
2.96

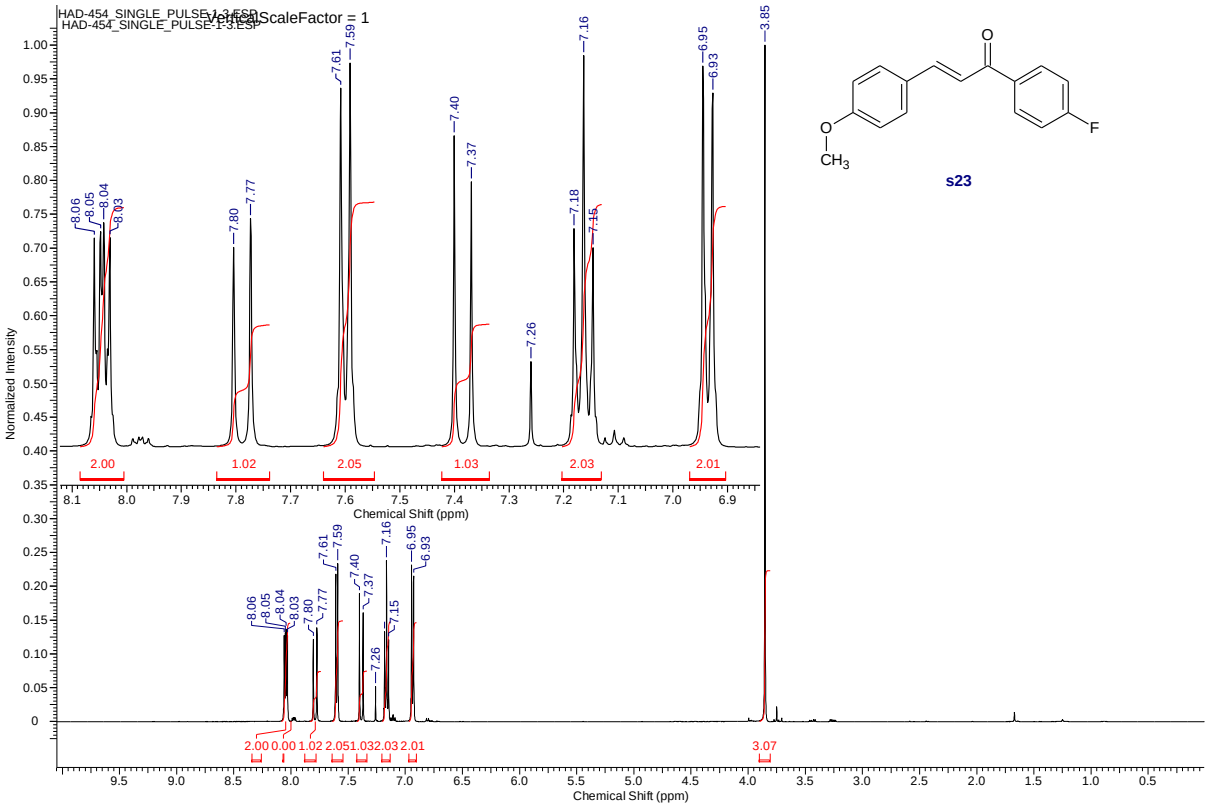

HAD-435_SINGLE_PULSE_QEC.2.1ESP
VerticalScaleFactor = 1
OH
CH3
O
CH3
3d
Normalized Intensity
Chemical Shift (ppm)
157.66
134.02
129.20
113.73
77.25
77.00
76.74
67.40
55.19
41.01
31.15
23.56

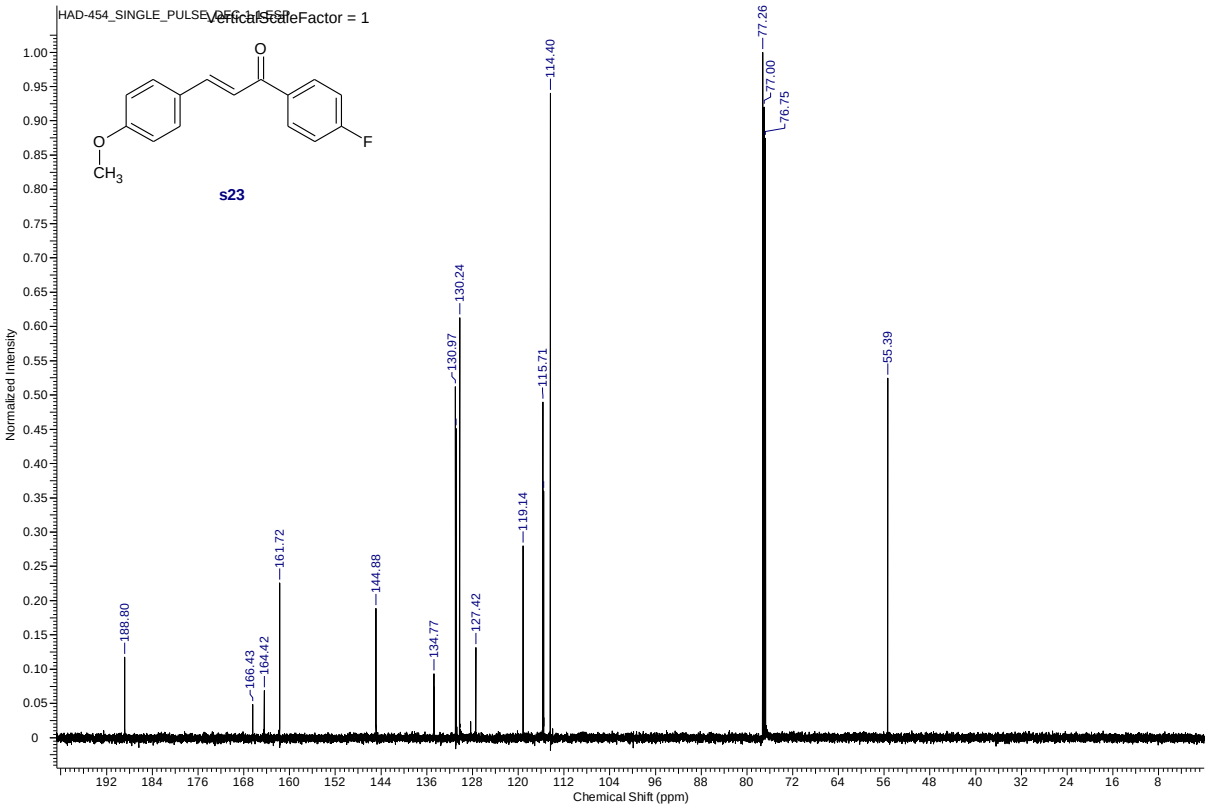

HAD-439B_SINGLE_PULSE-1-1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
8.02
8.01
7.81
7.78
7.62
7.60
7.58
7.56
7.52
7.50
7.49
7.44
7.41
7.26
6.95
6.93
3.86
2.00
1.00
3.05
2.01
1.08
2.00
0.02
2.00
1.00
3.05
2.01
1.08
2.00
3.04
O
O
CH3
s21

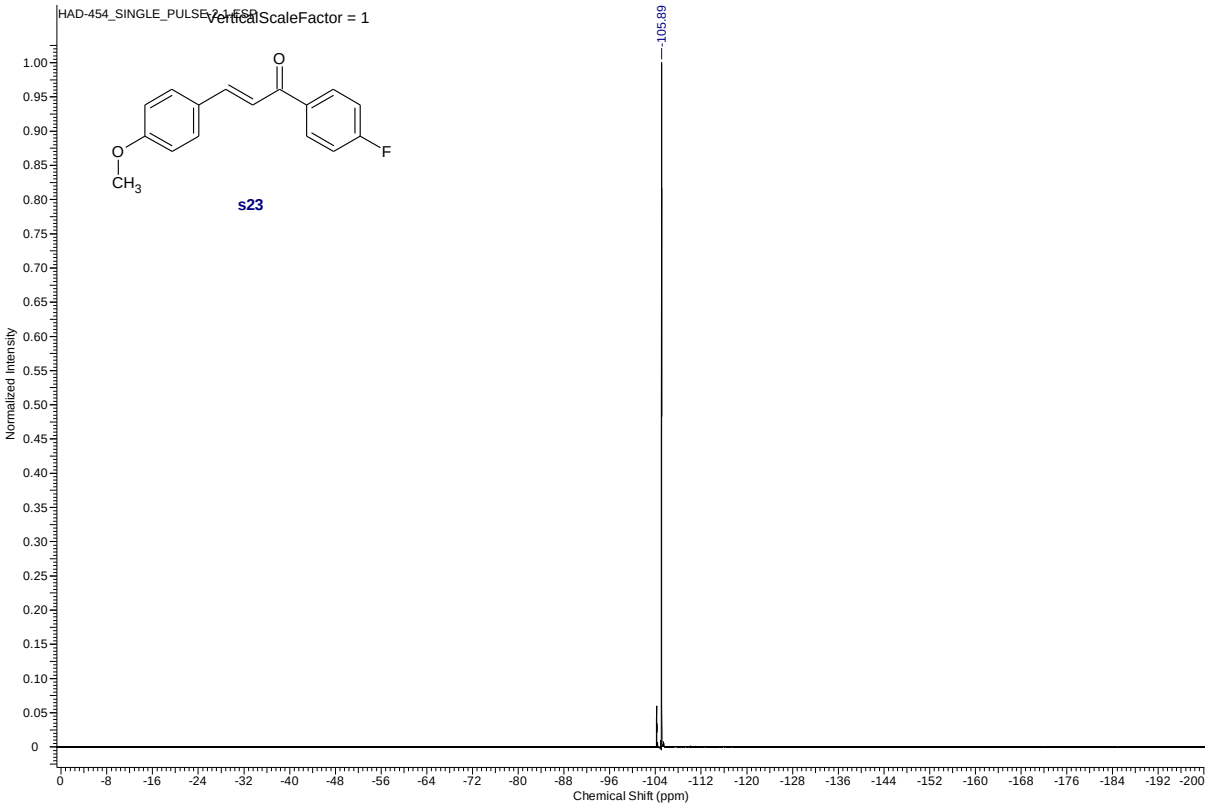

HAD-439B_SINGLE_PULSE_DEC-1-1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
77.00
77.26
76.74
128.55
128.39
144.70
130.22
114.39
55.40
190.59
161.65
138.47
132.55
127.57
119.72
O
O
CH3
s21

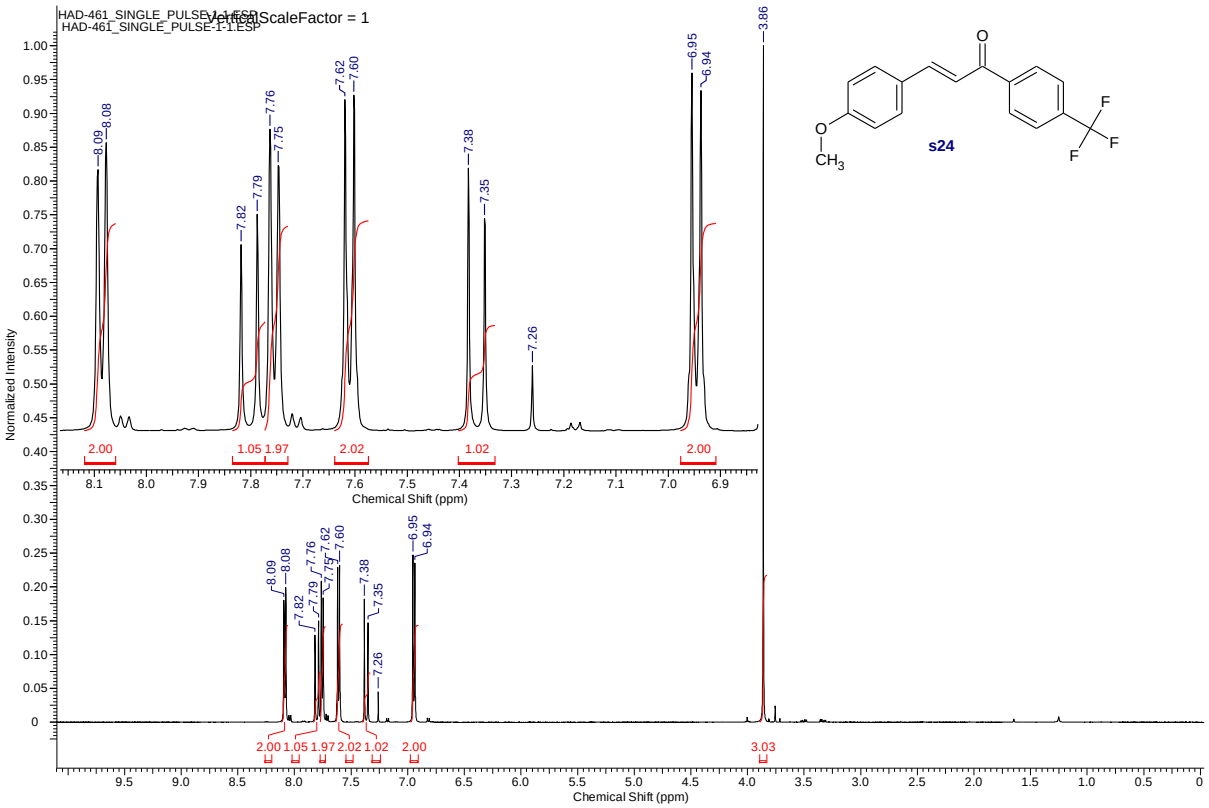

HAD-453_SINGLE_PULSE.1.1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
s22

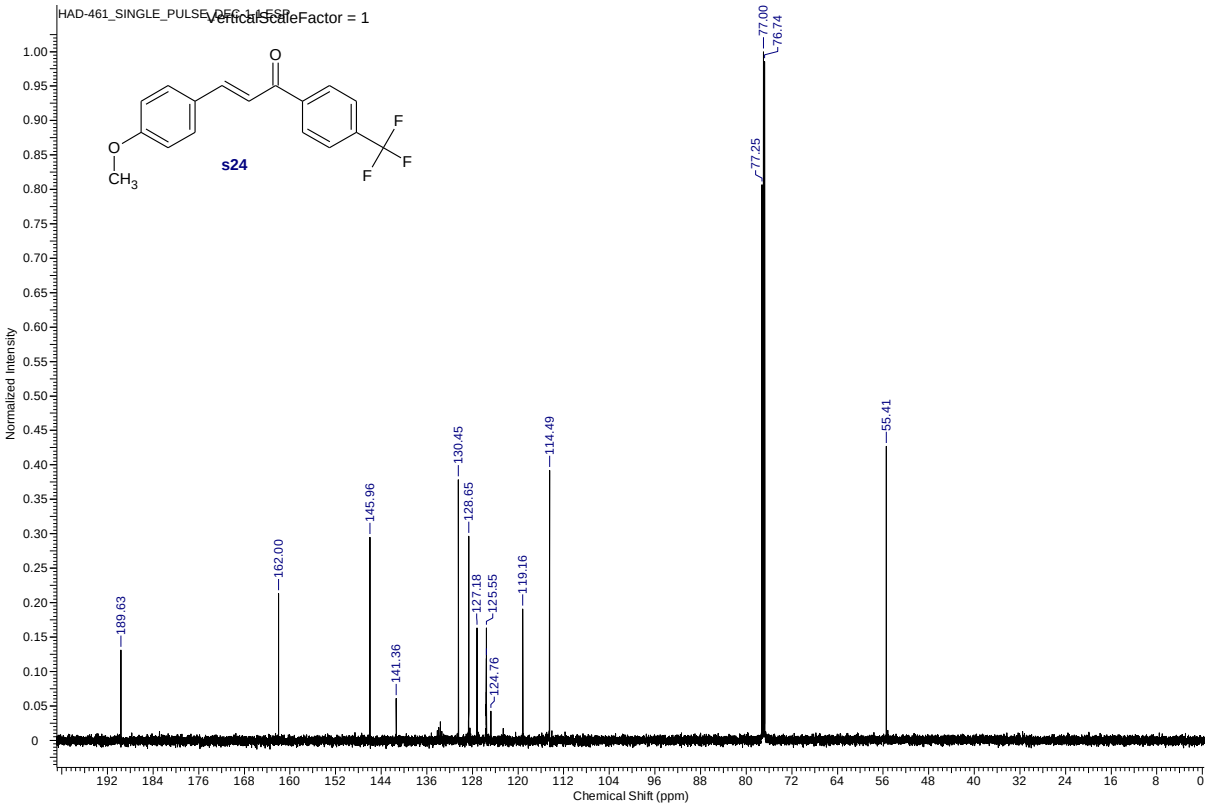

HAD-453_SINGLE_PULSE_QEC.1.1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
s22

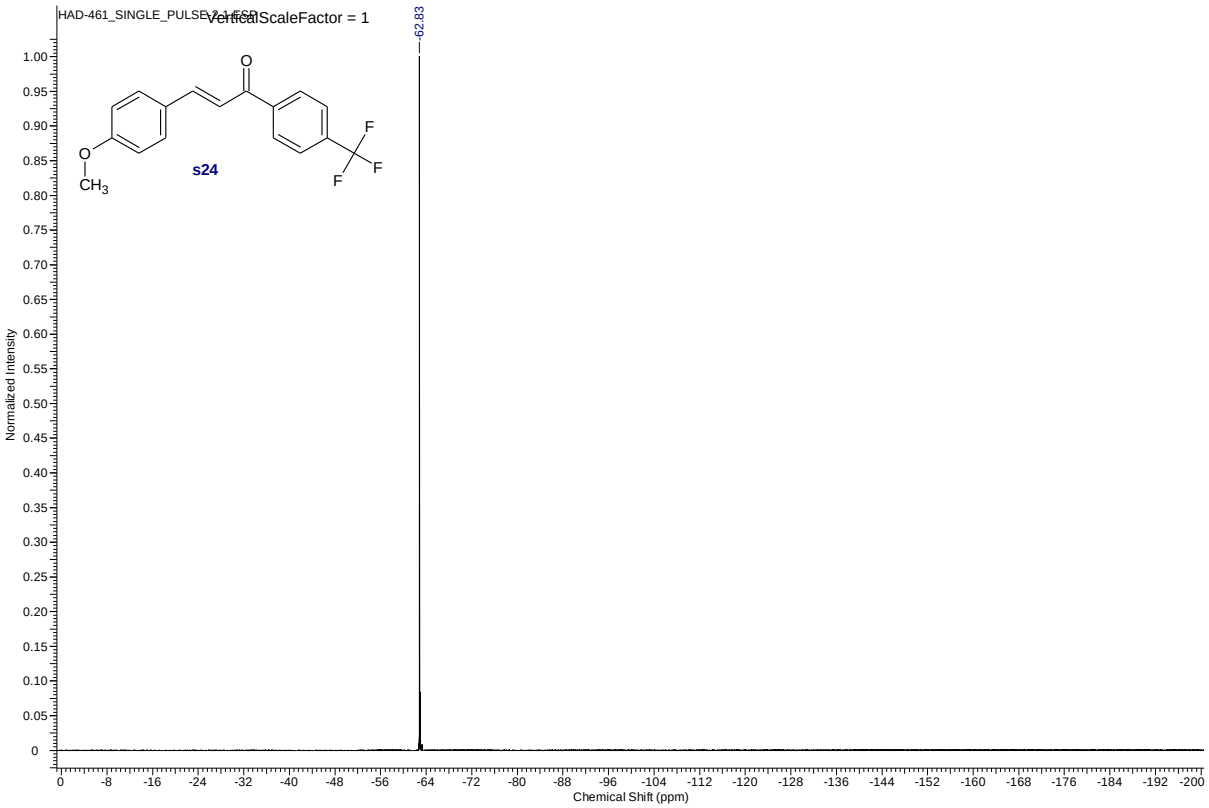

HAD-454_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
s23

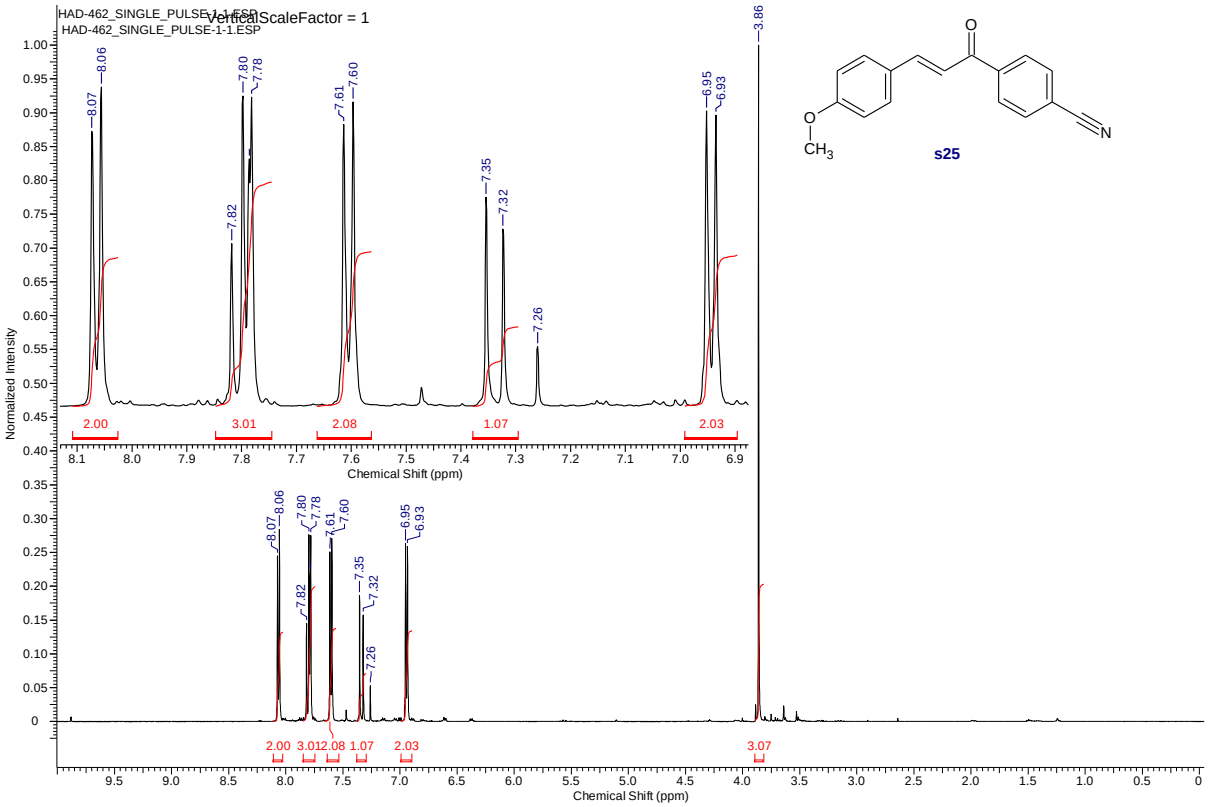

HAD-454_SINGLE_PULSE_OFC_1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
s23

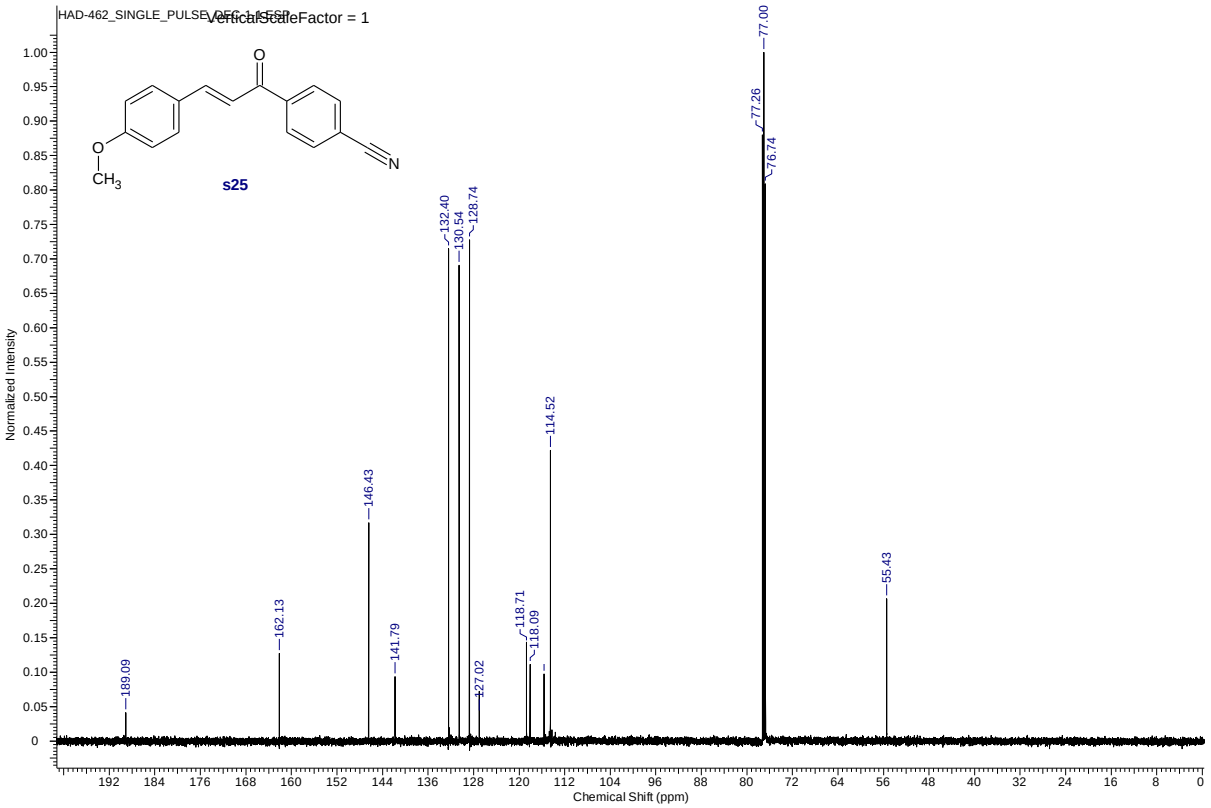

HAD-454_SINGLE_PULSE-2-1.ESP
VerticalScaleFactor = 1
-105.89
O
O
CH3
F
s23
Normalized Intensity
Chemical Shift (ppm)

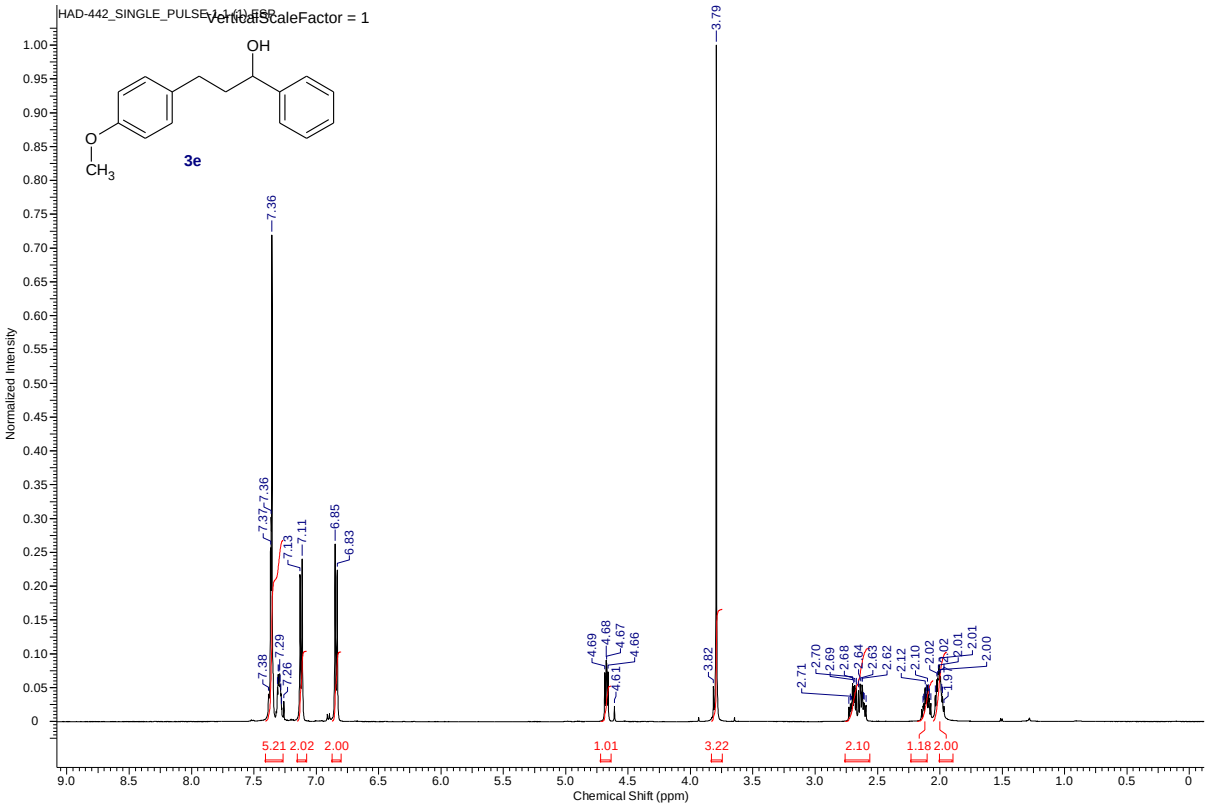

HAD-461_SINGLE_PULSE-1-1.ESP
HAD-461_SINGLE_PULSE-1-1.ESP
VerticalScaleFactor = 1
8.09
8.08
7.82
7.79
7.76
7.75
7.62
7.60
7.38
7.35
7.26
6.95
6.94
3.86
2.00
1.05
1.97
2.02
1.02
2.00
3.03
O
O
CH3
F
F
F
s24
Normalized Intensity
Chemical Shift (ppm)

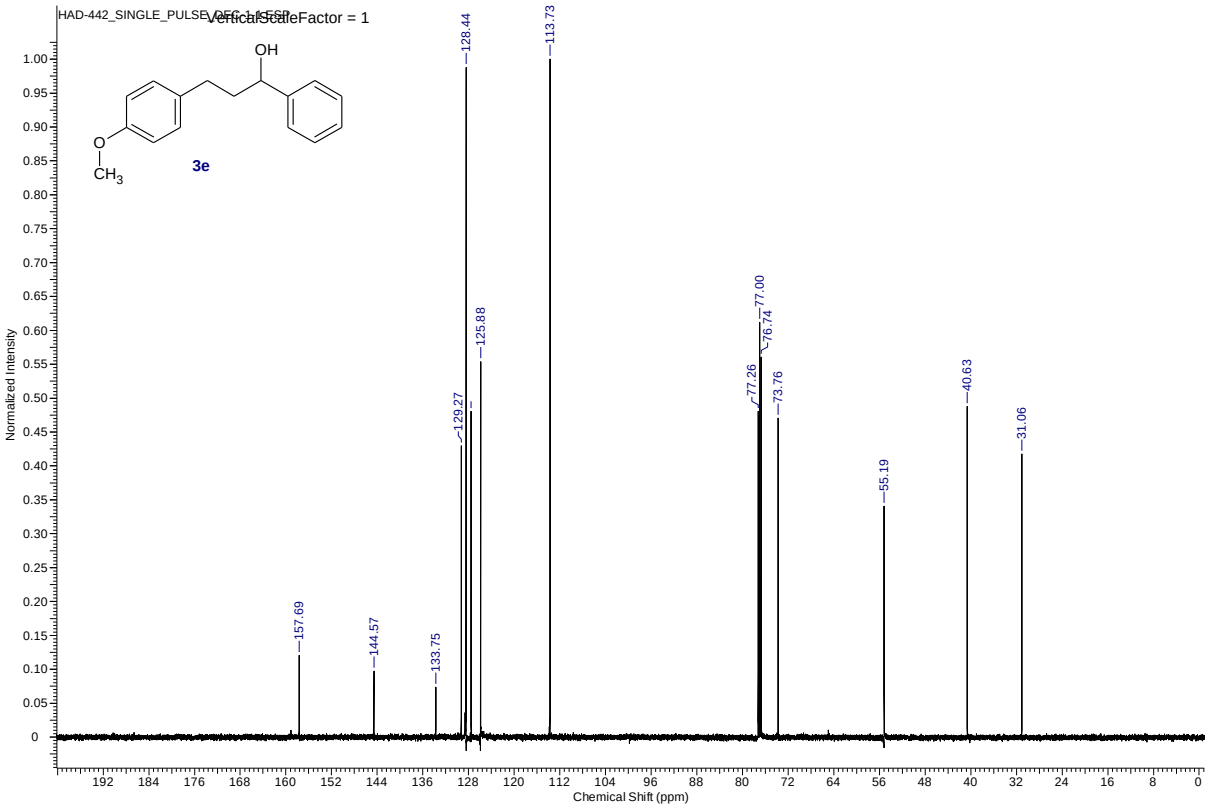

HAD-461_SINGLE_PULSE_DEC-1-1.ESP
VerticalScaleFactor = 1
s24
O
O
CH3
F
F
F
77.00
76.74
77.25
189.63
162.00
145.96
141.36
130.45
128.65
127.18
125.55
124.76
119.16
114.49
55.41
Normalized Intensity
Chemical Shift (ppm)

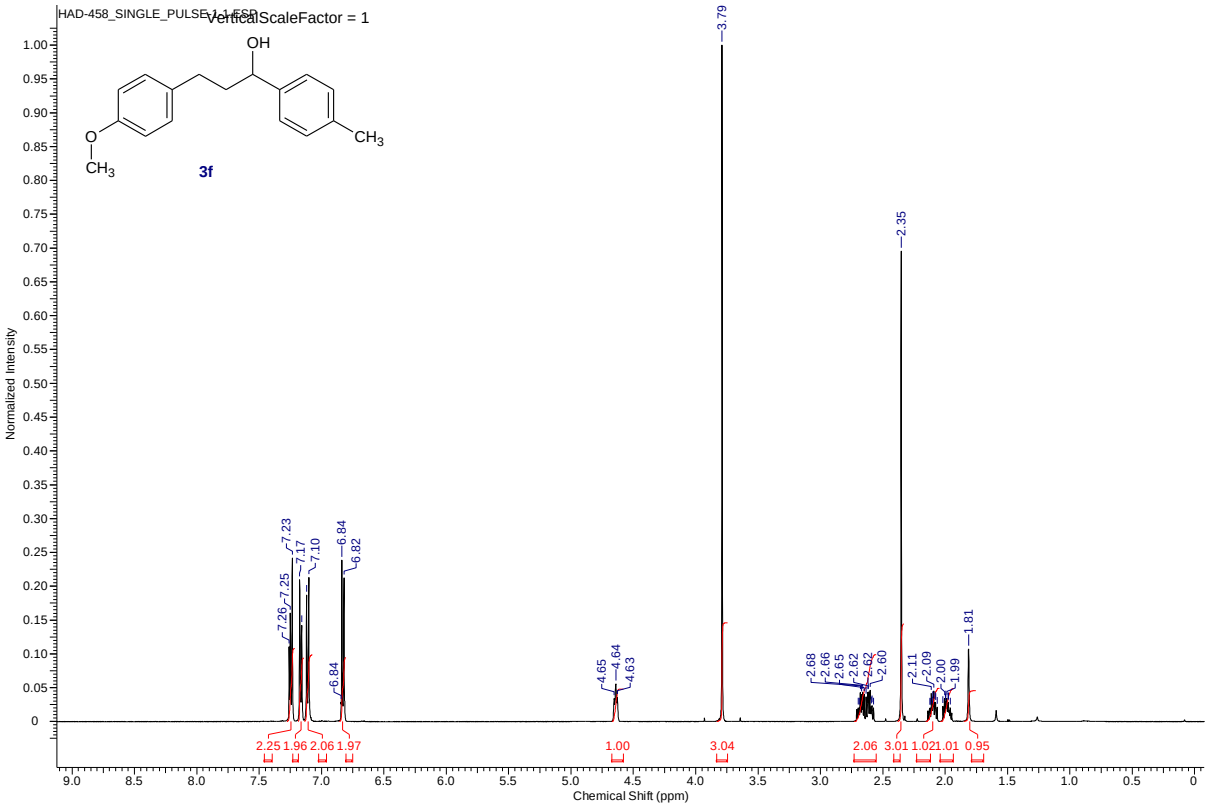

HAD-461_SINGLE_PULSE_2-1.ESP
VerticalScaleFactor = 1
s24
O
O
CH3
F
F
F
62.83
Normalized Intensity
Chemical Shift (ppm)

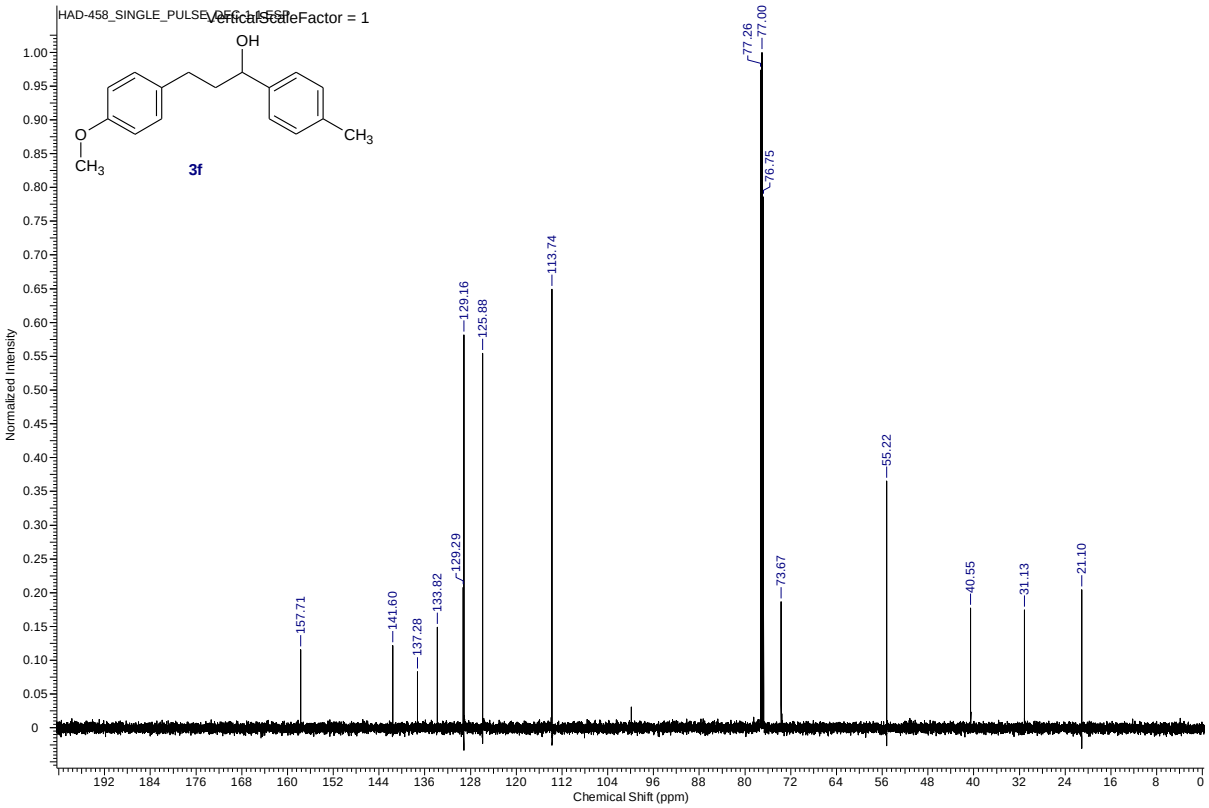

HAD-462_SINGLE_PULSE-1-1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
8.07
8.06
7.82
7.80
7.78
7.61
7.60
7.35
7.32
7.26
6.95
6.93
3.86
2.00
3.01
2.08
1.07
2.03
3.07
O
O
CH3
N
s25

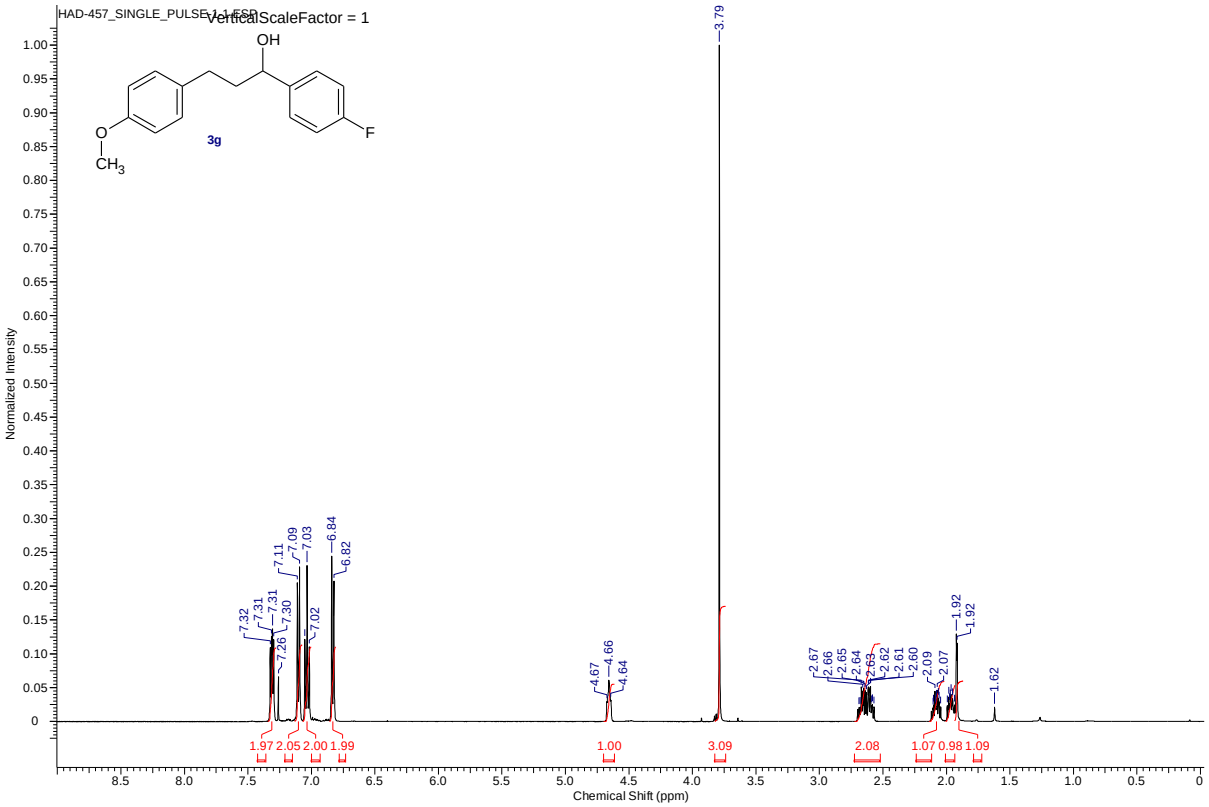

HAD-462_SINGLE_PULSE_QEC-1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
O
O
CH3
N
s25
77.00
77.26
76.74
132.40
130.54
128.74
114.52
146.43
162.13
141.79
118.71
118.09
127.02
189.09
55.43

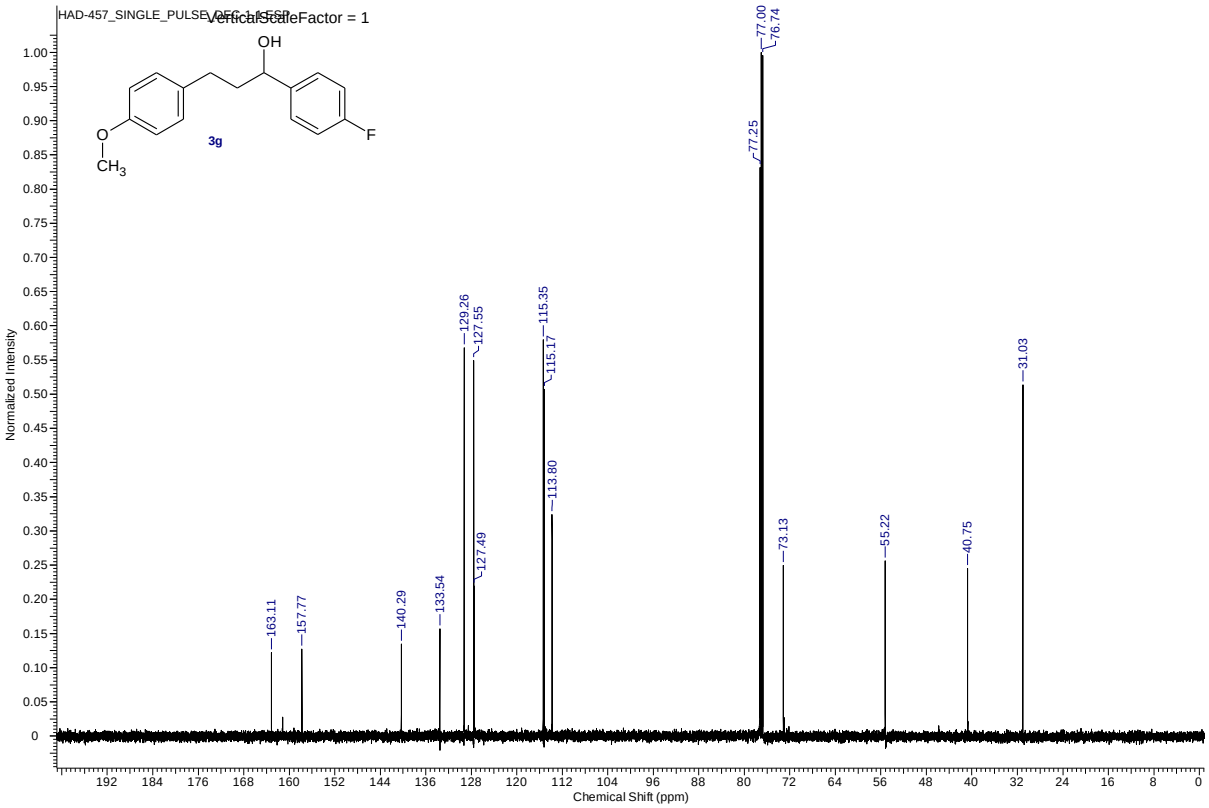

HAD-442_SINGLE_PULSE_1_1 (1).ESP
VerticalScaleFactor = 1
OH
O
CH3
3e
Normalized Intensity
Chemical Shift (ppm)
7.36
7.37
7.13
7.11
6.85
6.83
7.38
7.29
7.26
4.69
4.68
4.67
4.66
4.61
3.79
3.82
2.71
2.70
2.69
2.68
2.64
2.63
2.62
2.12
2.10
2.02
2.01
2.00
5.21
2.02
2.00
1.01
3.22
2.10
1.18
2.00

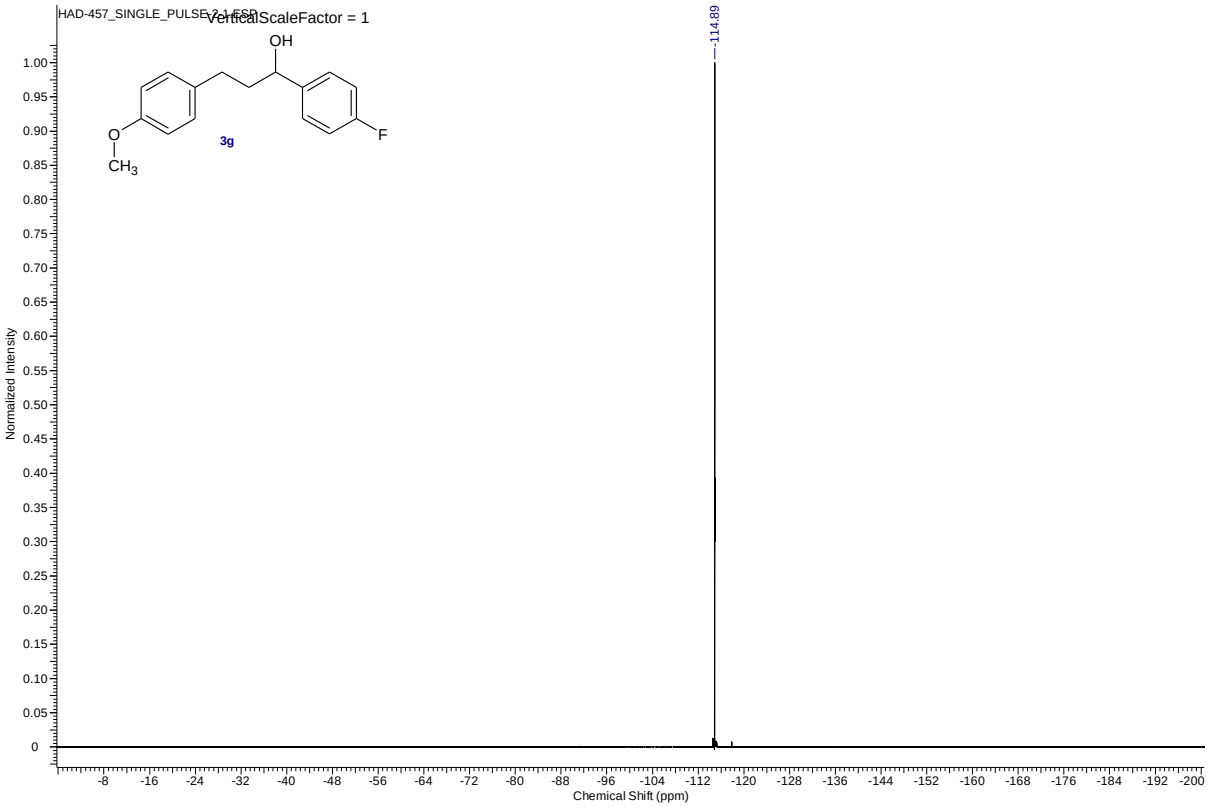

HAD-442_SINGLE_PULSE_QEC_1.ESP
VerticalScaleFactor = 1
OH
O
CH3
3e
Normalized Intensity
Chemical Shift (ppm)
128.44
113.73
125.88
129.27
77.00
76.74
77.26
73.76
40.63
31.06
55.19
157.69
144.57
133.75

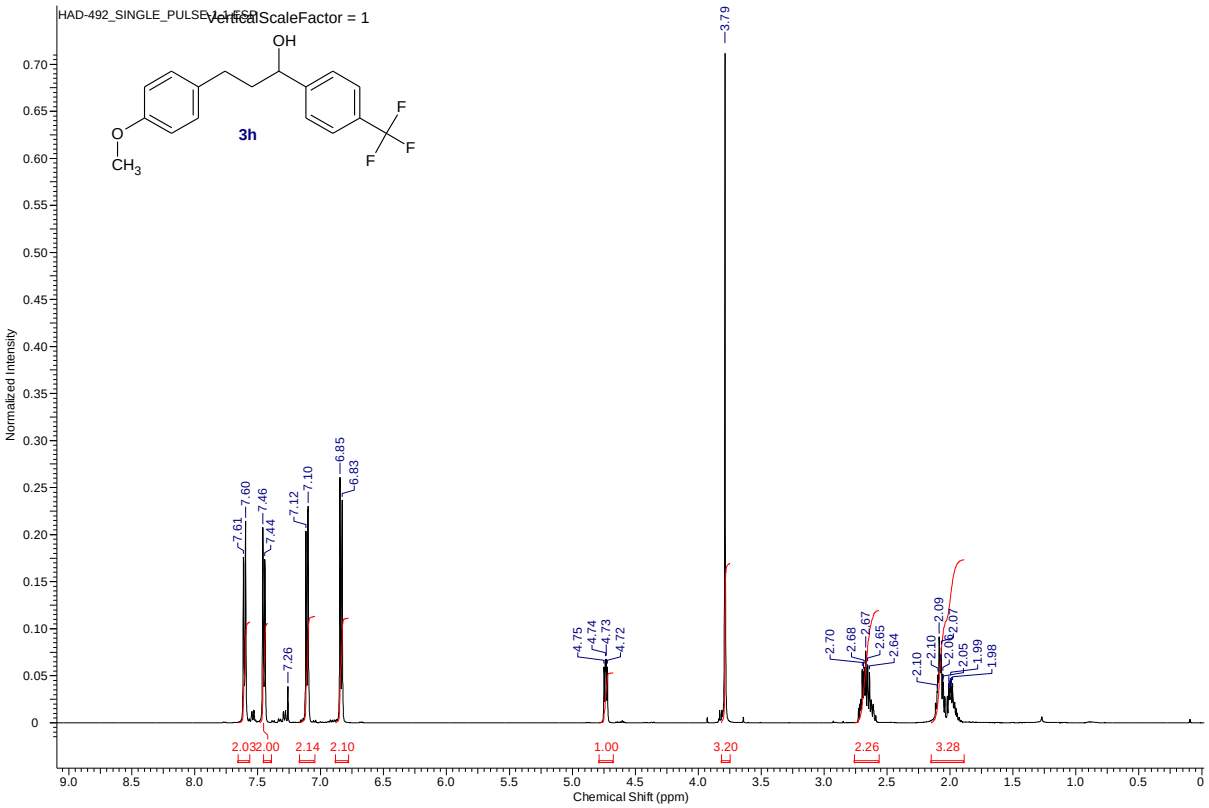

HAD-458_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
OH
O
CH3
CH3
3f
Normalized Intensity
Chemical Shift (ppm)
3.79
2.35
1.81
7.26
7.25
7.23
7.17
7.10
6.84
6.82
4.65
4.64
4.63
2.68
2.66
2.65
2.62
2.60
2.11
2.09
2.00
1.99
2.25
1.96
2.06
1.97
1.00
3.04
2.06
3.01
1.02
1.01
0.95

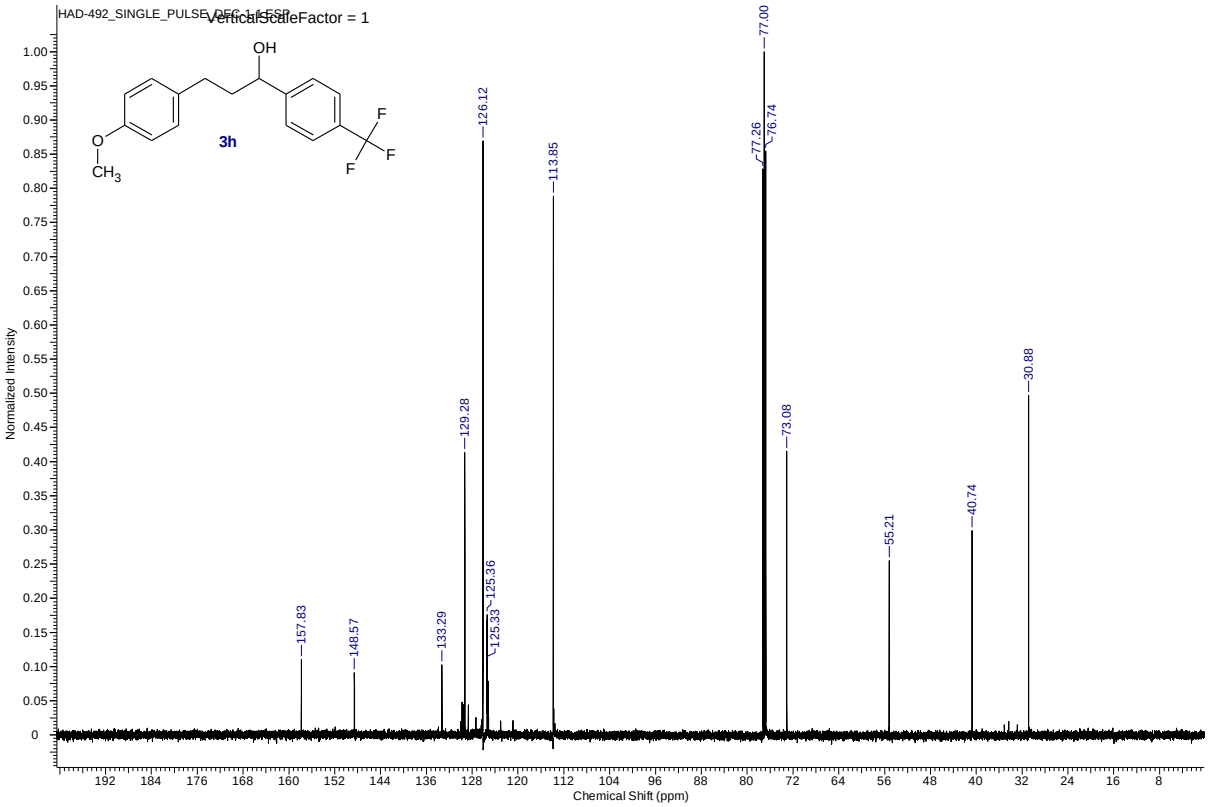

HAD-458_SINGLE_PULSE_QEC.1.ESP
VerticalScaleFactor = 1
OH
O
CH3
CH3
3f
Normalized Intensity
Chemical Shift (ppm)
77.26
77.00
76.75
129.16
125.88
113.74
129.29
133.82
141.60
137.28
157.71
73.67
55.22
40.55
31.13
21.10

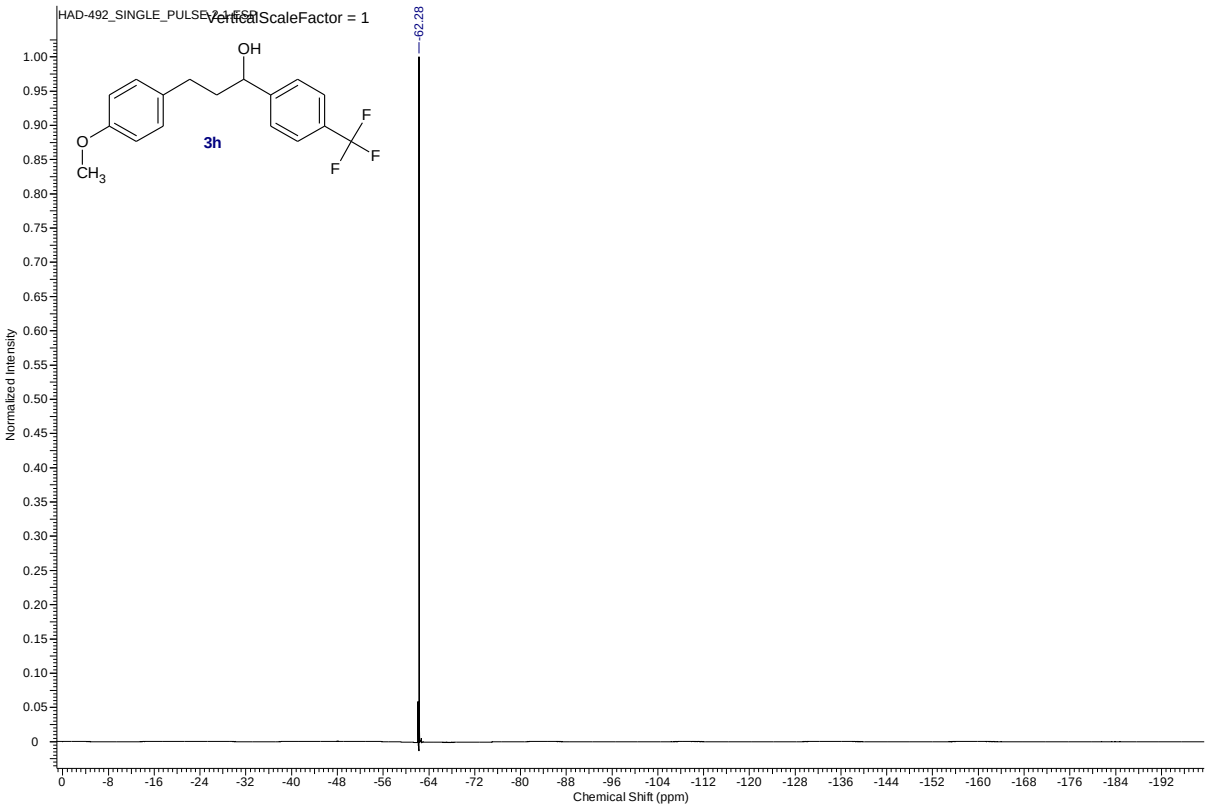

HAD-457_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
OH
O
CH3
F
3g
Normalized Intensity
Chemical Shift (ppm)
3.79
7.32
7.31
7.31
7.30
7.26
7.11
7.09
7.03
7.02
6.84
6.82
4.67
4.66
4.64
2.67
2.66
2.65
2.64
2.63
2.62
2.61
2.60
2.09
2.07
1.92
1.92
1.62
1.97
2.05
2.00
1.99
1.00
3.09
2.08
1.07
0.98
1.09

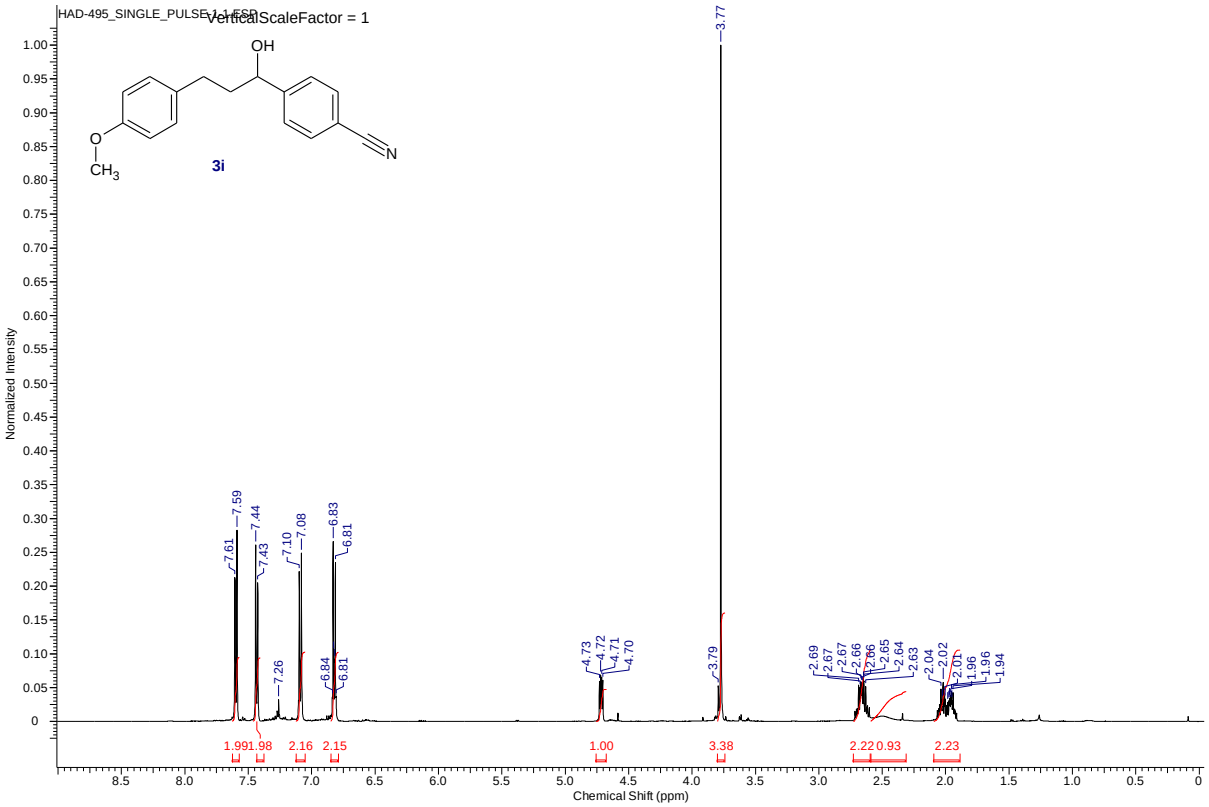

HAD-457_SINGLE_PULSE_OFF_1.ESP
VerticalScaleFactor = 1
OH
O
CH3
F
3g
Normalized Intensity
Chemical Shift (ppm)
77.00
76.74
77.25
163.11
157.77
140.29
133.54
129.26
127.55
127.49
115.35
115.17
113.80
73.13
55.22
40.75
31.03

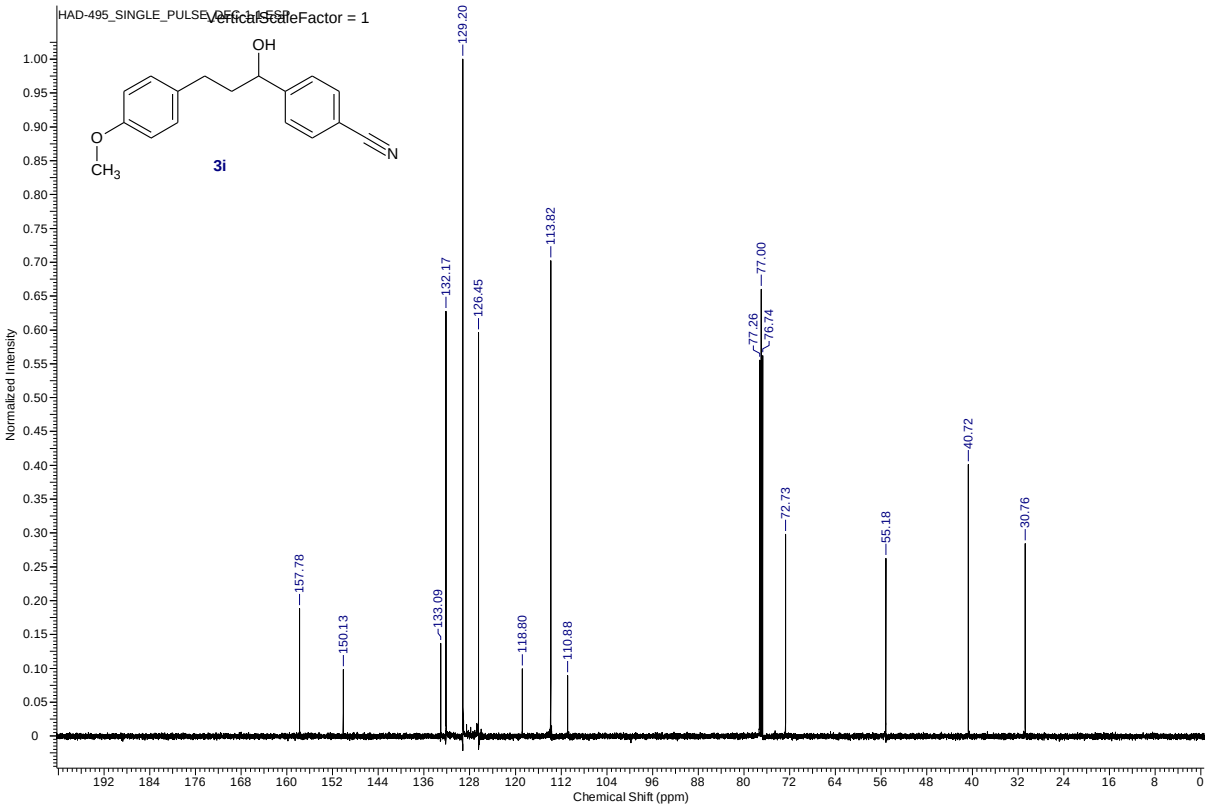

HAD-457_SINGLE_PULSE_2_1.ESP
VerticalScaleFactor = 1
OH
O
CH3
F
3g
-114.89
Normalized Intensity
Chemical Shift (ppm)

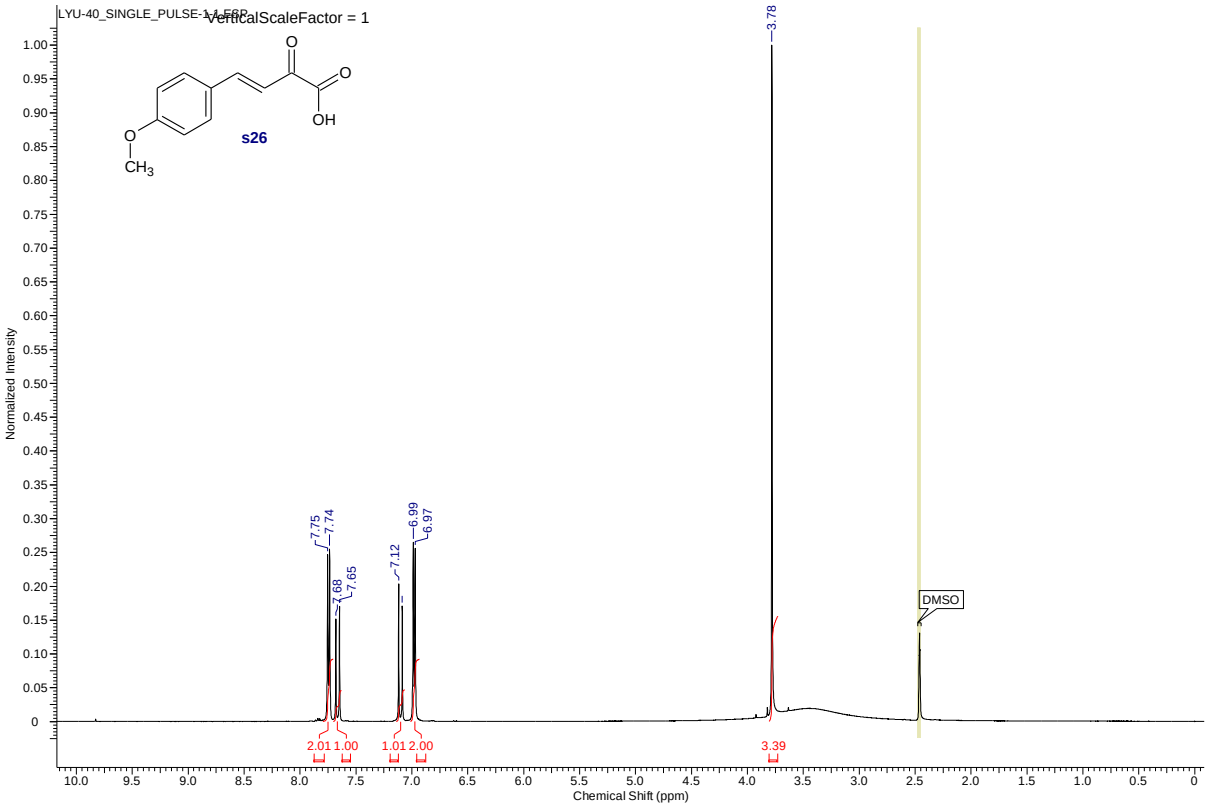

HAD-492_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
OH
O
CH3
F
F
F
3h
-3.79
7.61
7.60
7.46
7.44
7.26
7.12
7.10
6.85
6.83
4.75
4.74
4.73
4.72
2.70
2.68
2.67
2.65
2.64
2.10
2.09
2.07
2.06
2.05
1.99
1.98
2.03
2.00
2.14
2.10
1.00
3.20
2.26
3.28
Normalized Intensity
Chemical Shift (ppm)

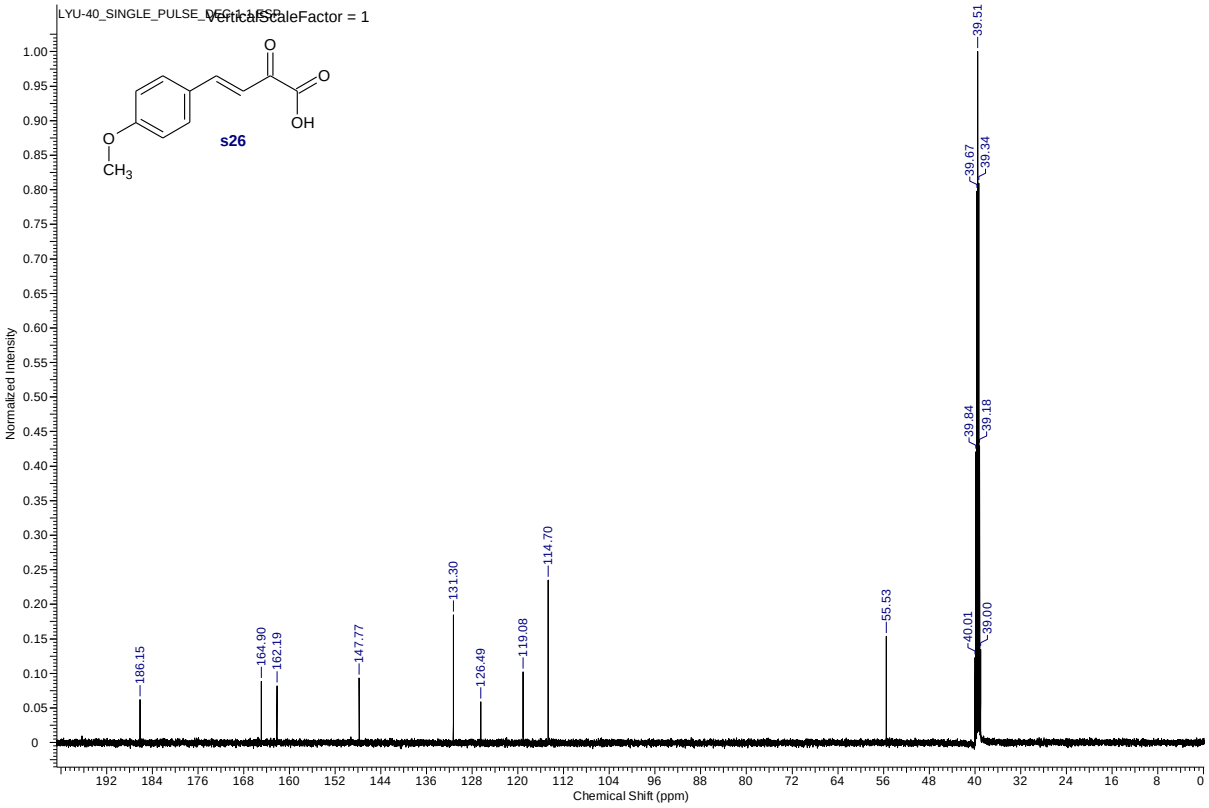

HAD-492_SINGLE_PULSE_DEC-1.4.ESP
VerticalScaleFactor = 1
OH
O
CH3
3h
F
F
F
Normalized Intensity
Chemical Shift (ppm)
157.83
148.57
133.29
129.28
126.12
125.36
125.33
113.85
77.26
77.00
76.74
73.08
55.21
40.74
30.88

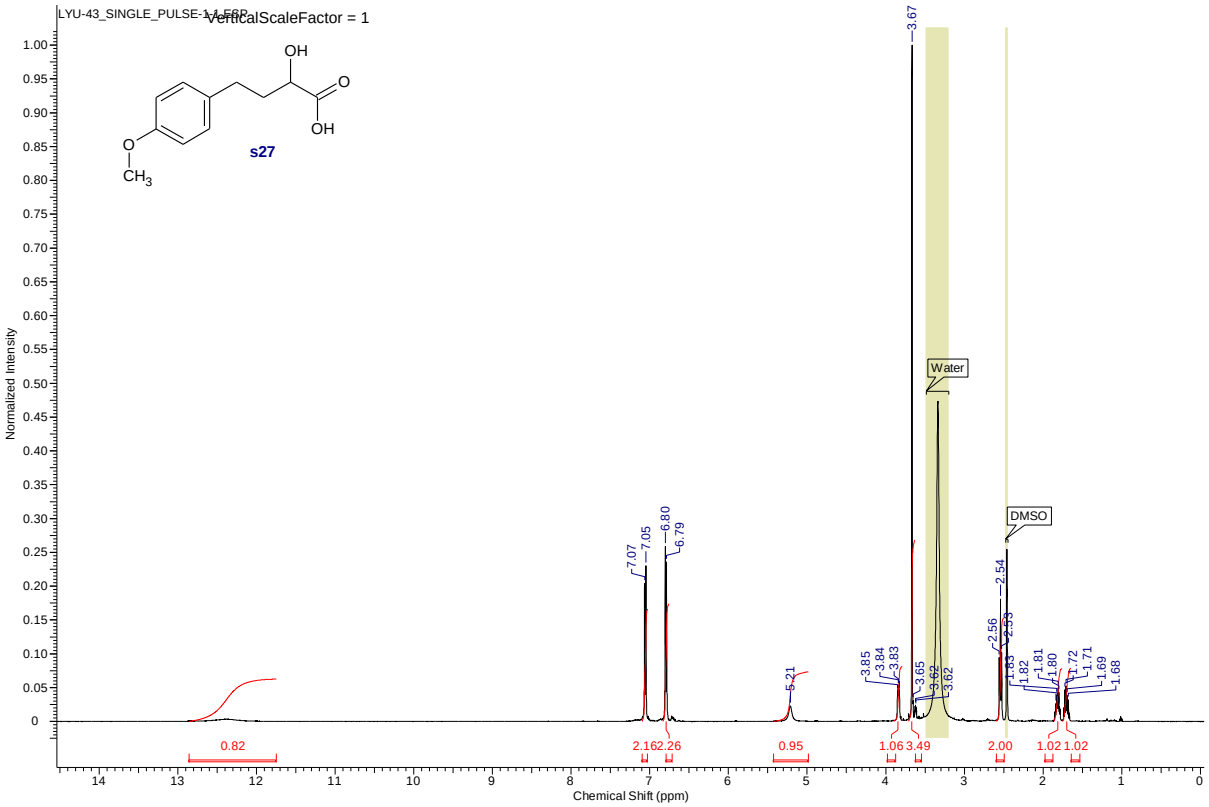

HAD-492_SINGLE_PULSE_2.1.ESP
VerticalScaleFactor = 1
OH
O
CH3
3h
F
F
F
Normalized Intensity
Chemical Shift (ppm)
62.28

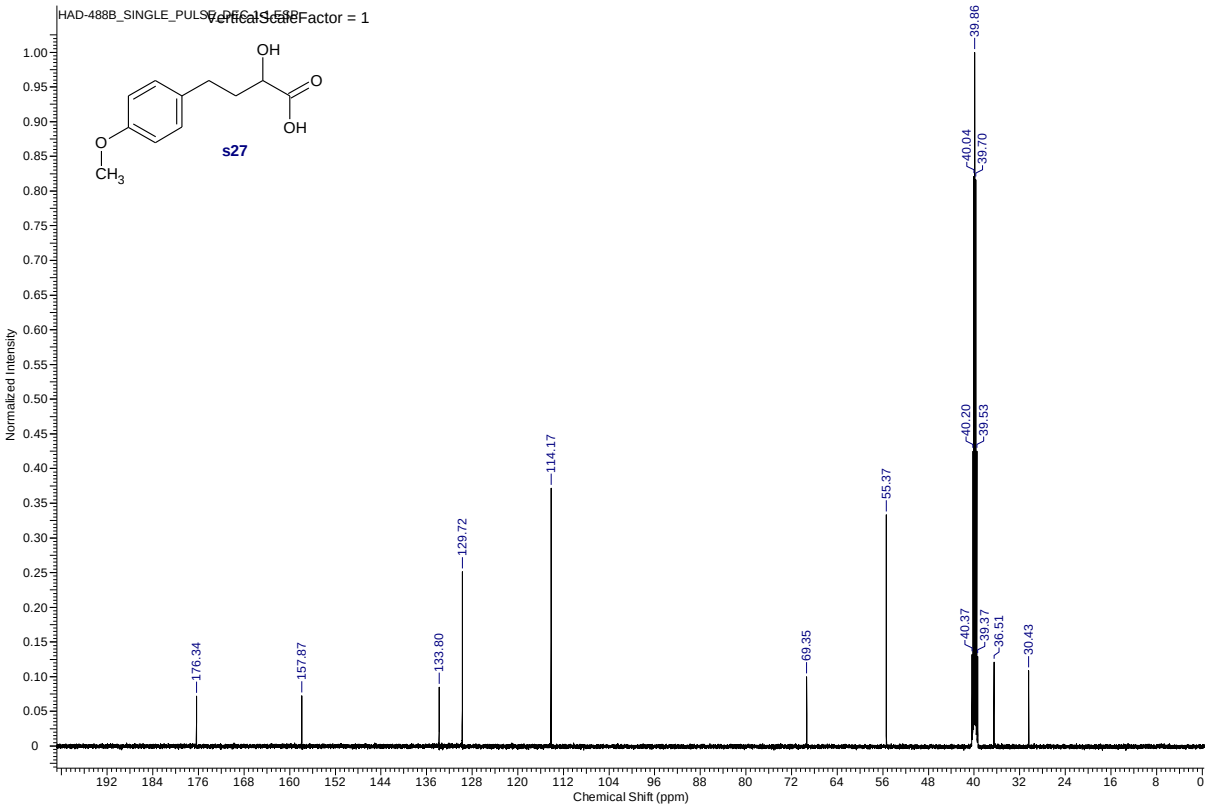

HAD-495_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
OH
O
CH3
N
3i
Normalized Intensity
Chemical Shift (ppm)
7.61
7.59
7.44
7.43
7.26
7.10
7.08
6.84
6.83
6.81
4.73
4.72
4.71
4.70
3.79
3.77
2.69
2.67
2.66
2.65
2.64
2.63
2.04
2.02
2.01
1.96
1.94
1.99
1.98
2.16
2.15
1.00
3.38
2.22
0.93
2.23

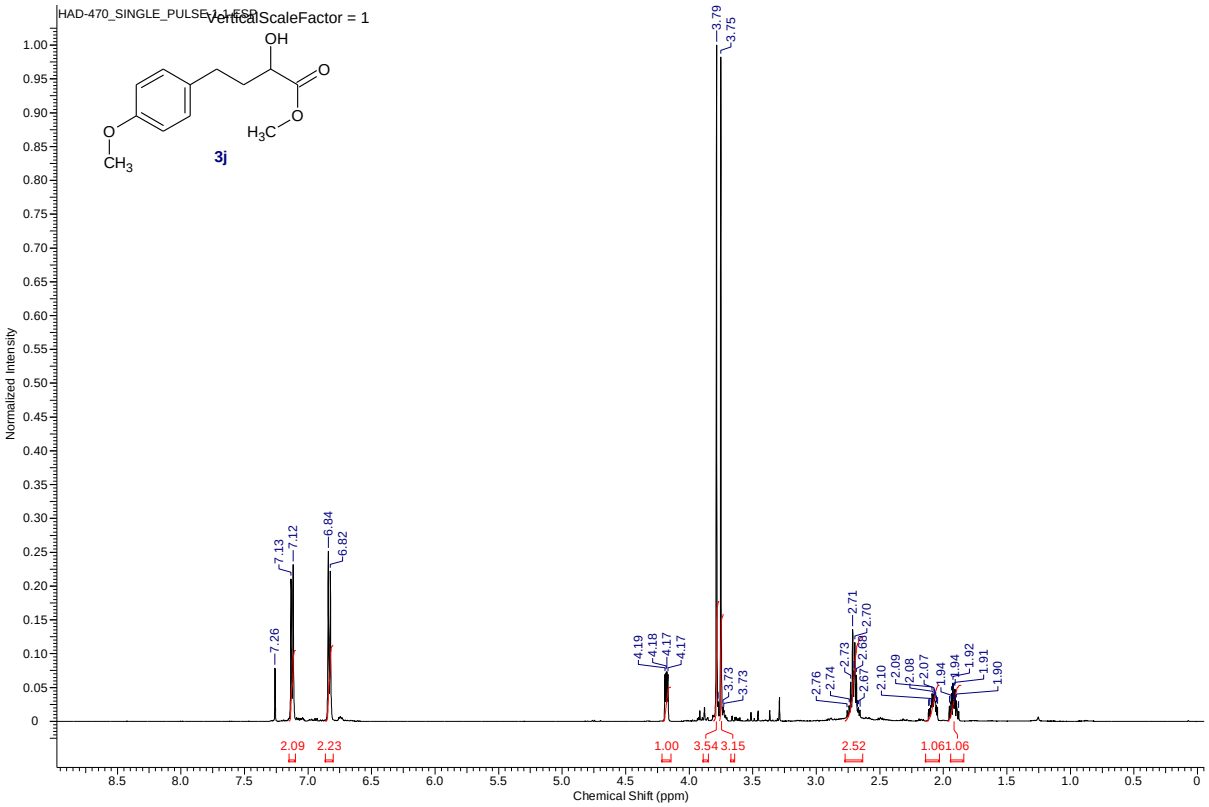

HAD-495_SINGLE_PULSE_QEC_1.ESP
VerticalScaleFactor = 1
OH
O
CH3
N
3i
Normalized Intensity
Chemical Shift (ppm)
157.78
150.13
133.09
132.17
129.20
126.45
118.80
113.82
110.88
77.26
77.00
76.74
72.73
55.18
40.72
30.76

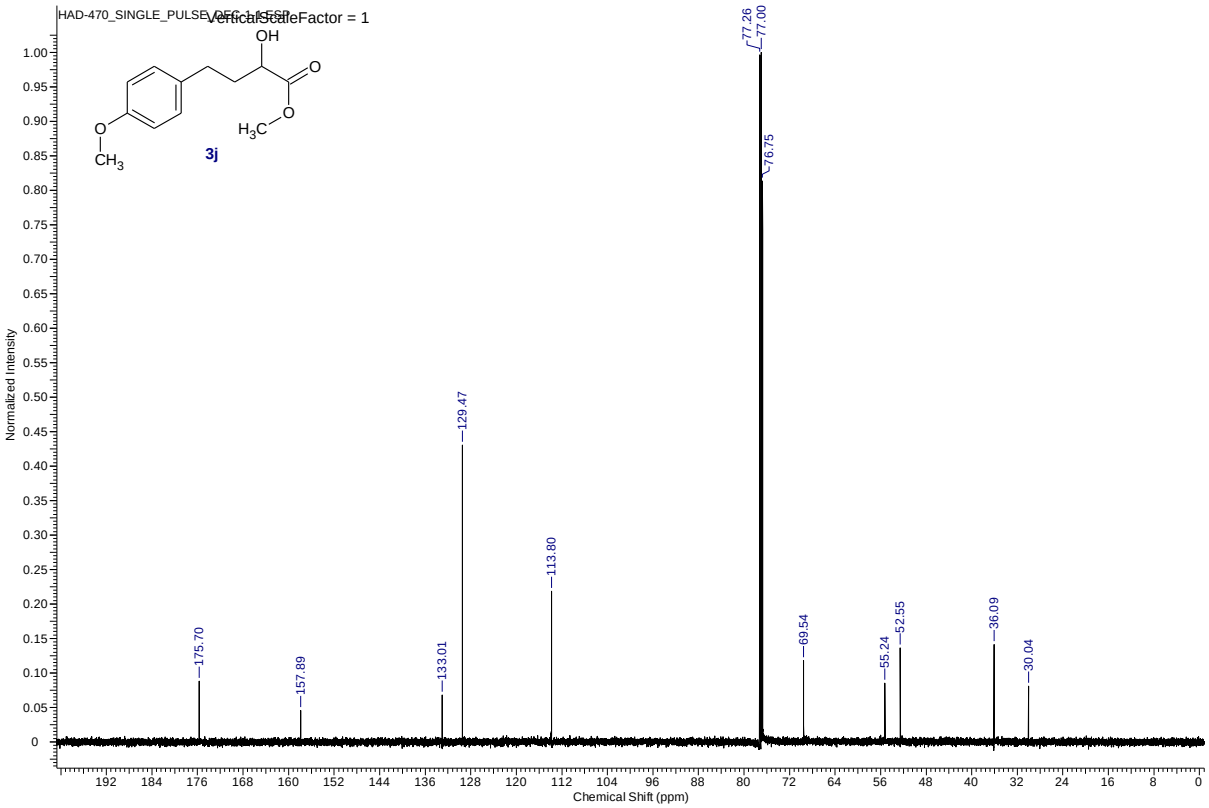

LYU-40_SINGLE_PULSE-1.1.ESP
VerticalScaleFactor = 1
s26
Normalized Intensity
Chemical Shift (ppm)
7.75
7.74
7.68
7.65
7.12
6.99
6.97
3.78
DMSO
2.01
1.00
1.01
2.00
3.39

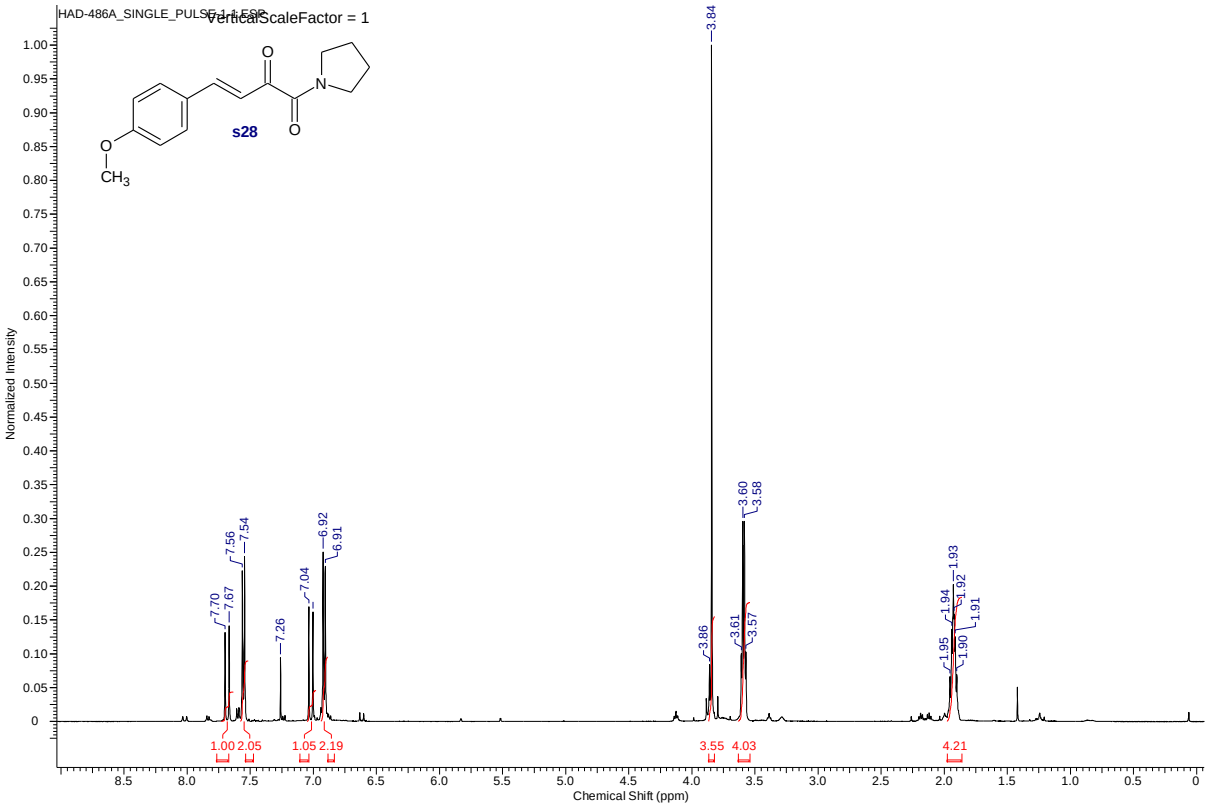

LYU-40_SINGLE_PULSE_DEC-1.1.ESP
VerticalScaleFactor = 1
s26
Normalized Intensity
Chemical Shift (ppm)
186.15
164.90
162.19
147.77
131.30
126.49
119.08
114.70
55.53
40.01
39.67
39.51
39.34
39.18
39.00

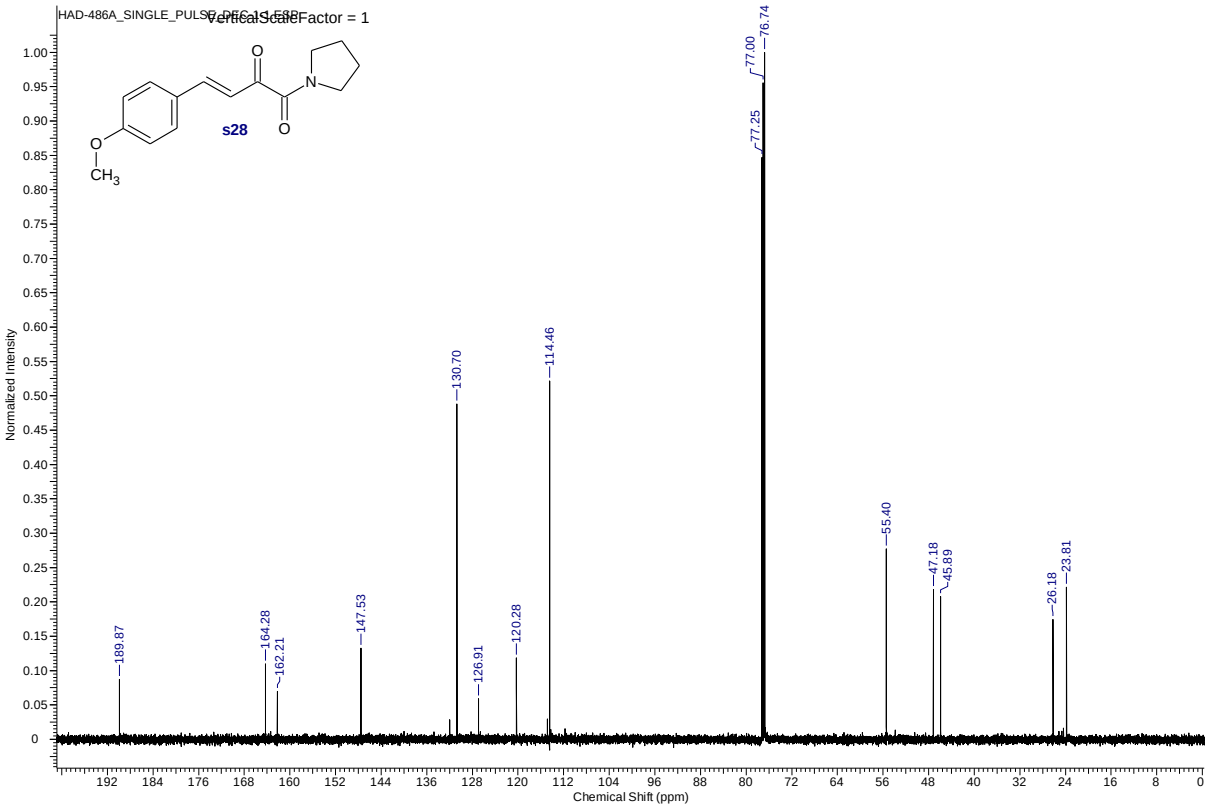

VerticalScaleFactor = 1
OH
O
OH
O
CH3
s27
Normalized Intensity
Chemical Shift (ppm)
Water
DMSO
3.67
7.07
7.05
6.80
6.79
5.21
3.85
3.84
3.83
3.65
3.62
2.56
2.54
2.53
1.83
1.82
1.81
1.80
1.72
1.71
1.69
1.68
0.82
2.16
2.26
0.95
1.06
3.49
2.00
1.02
1.02

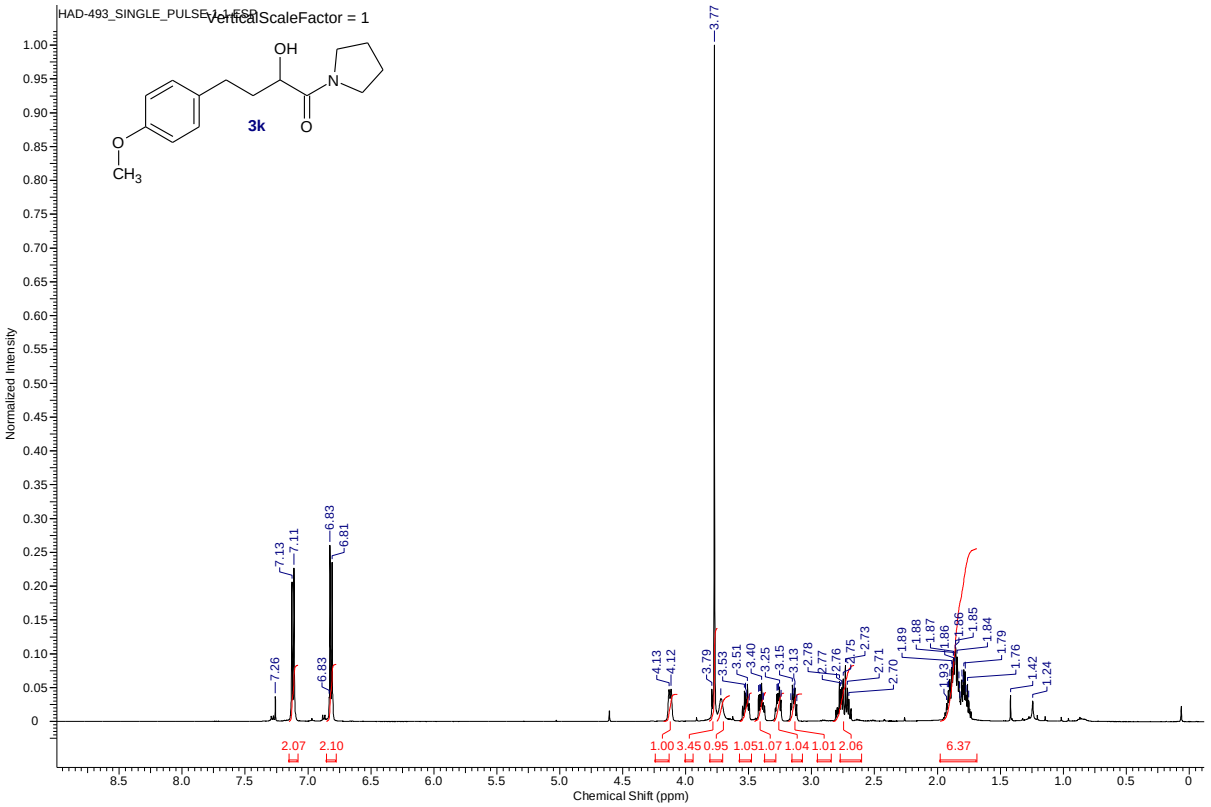

VerticalScaleFactor = 1
OH
O
OH
O
CH3
s27
Normalized Intensity
Chemical Shift (ppm)
39.86
40.04
39.70
40.20
39.53
114.17
55.37
129.72
176.34
157.87
133.80
69.35
40.37
39.37
36.51
30.43

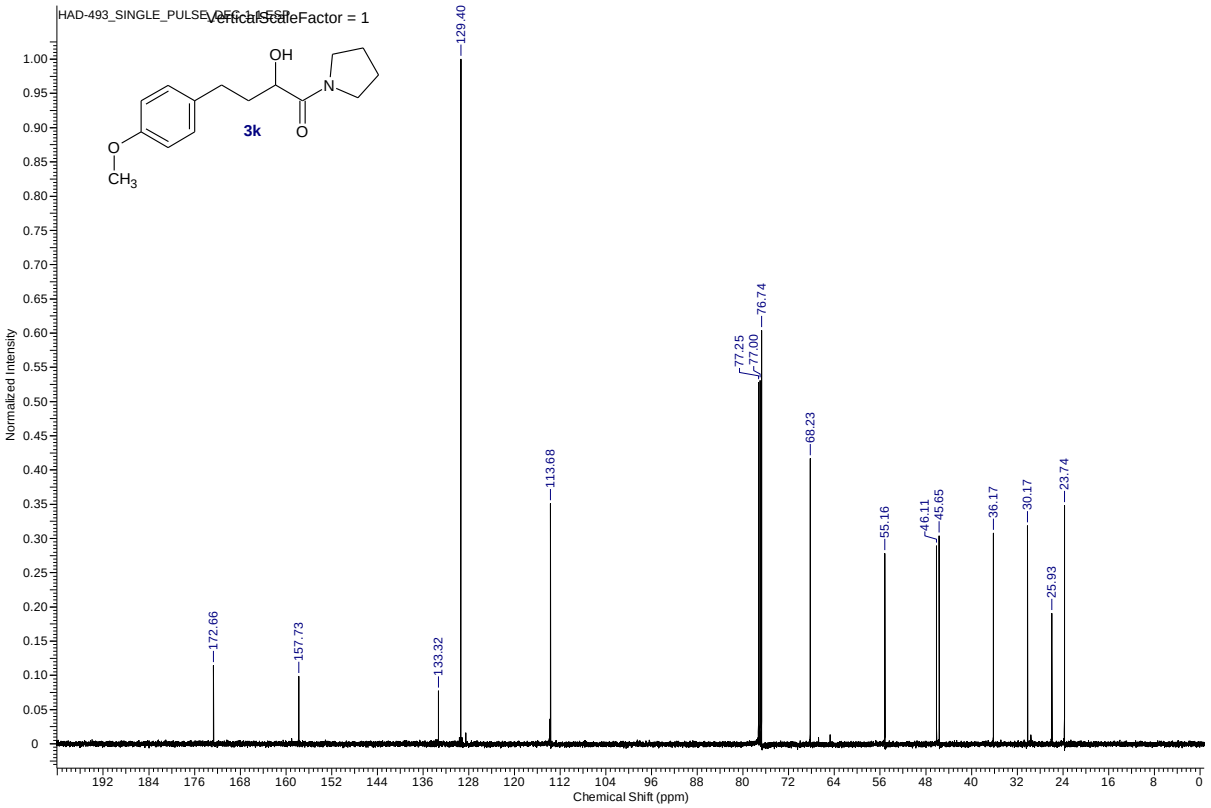

HAD-470_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
OH
O
O
O
H3C
O
CH3
3j
Normalized Intensity
Chemical Shift (ppm)
7.26
7.13
7.12
6.84
6.82
4.19
4.18
4.17
4.17
3.79
3.75
3.73
3.73
2.76
2.74
2.73
2.71
2.70
2.68
2.67
2.10
2.09
2.08
2.07
1.94
1.94
1.92
1.91
1.90
2.09
2.23
1.00
3.54
3.15
2.52
1.06
1.06

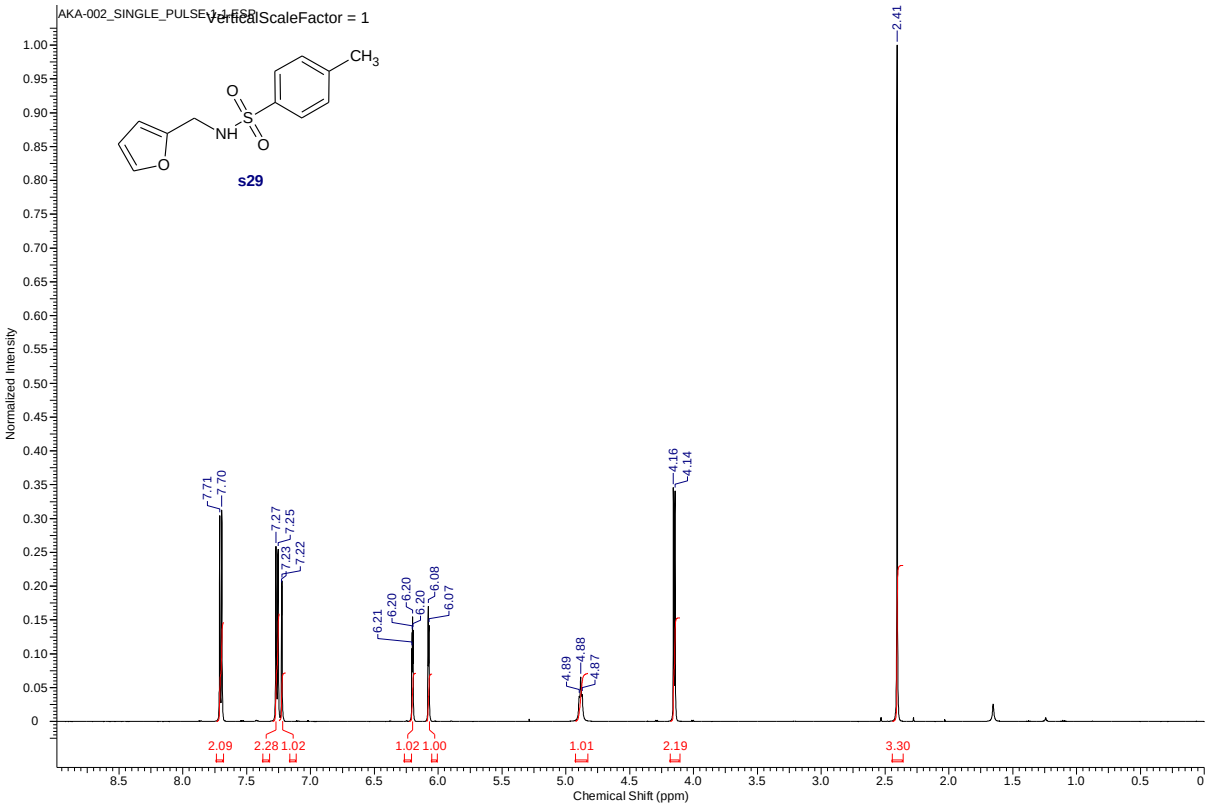

HAD-470_SINGLE_PULSE_QEC.1.ESP
VerticalScaleFactor = 1
OH
O
O
O
H3C
O
CH3
3j
Normalized Intensity
Chemical Shift (ppm)
77.26
77.00
76.75
175.70
157.89
133.01
129.47
113.80
69.54
55.24
52.55
36.09
30.04

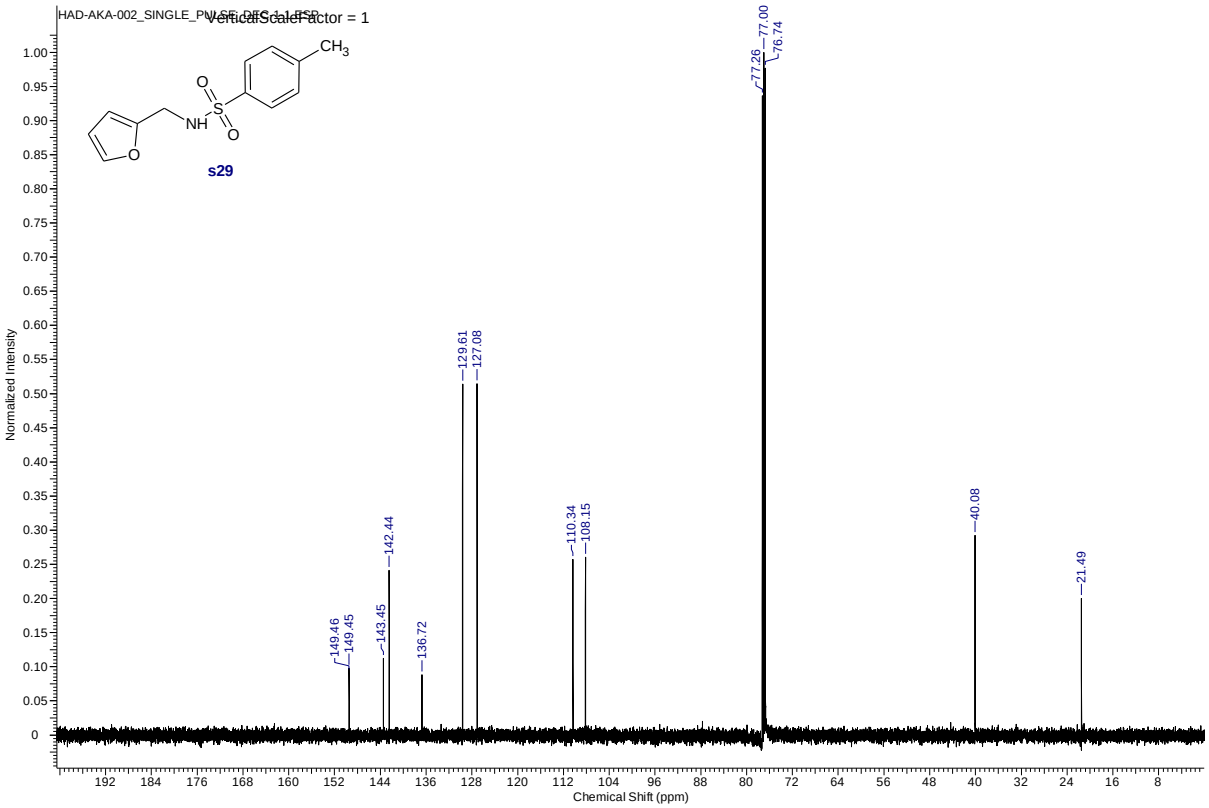

HAD-486A_SINGLE_PULSE_1-1.ESP
VerticalScaleFactor = 1
s28
Normalized Intensity
Chemical Shift (ppm)
3.84
7.70
7.67
7.56
7.54
7.26
7.04
6.92
6.91
3.86
3.61
3.60
3.58
3.57
1.95
1.94
1.93
1.92
1.91
1.90
1.00 2.05 1.05 2.19 3.55 4.03 4.21

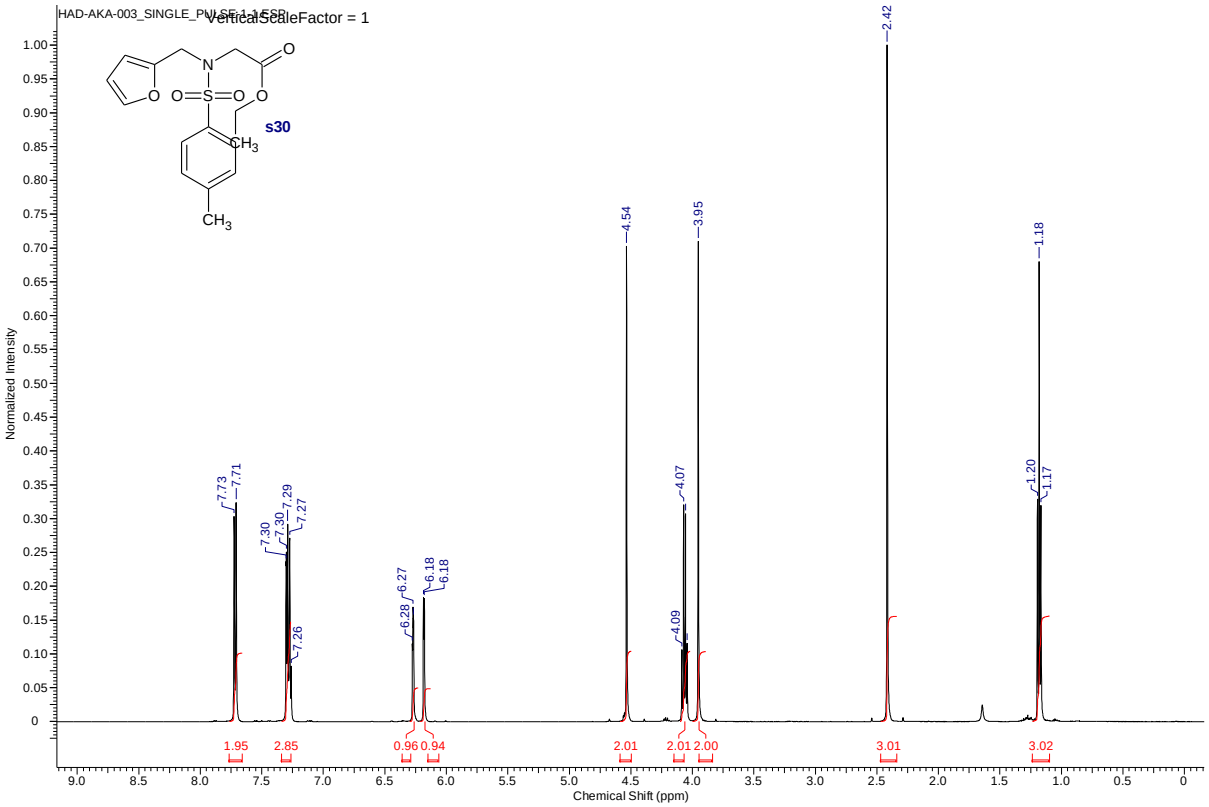

HAD-486A_SINGLE_PULSE_DEC_1-1.ESP
VerticalScaleFactor = 1
s28
Normalized Intensity
Chemical Shift (ppm)
77.00
76.74
77.25
130.70
114.46
55.40
47.18
45.89
26.18
23.81
189.87
164.28
162.21
147.53
126.91
120.28

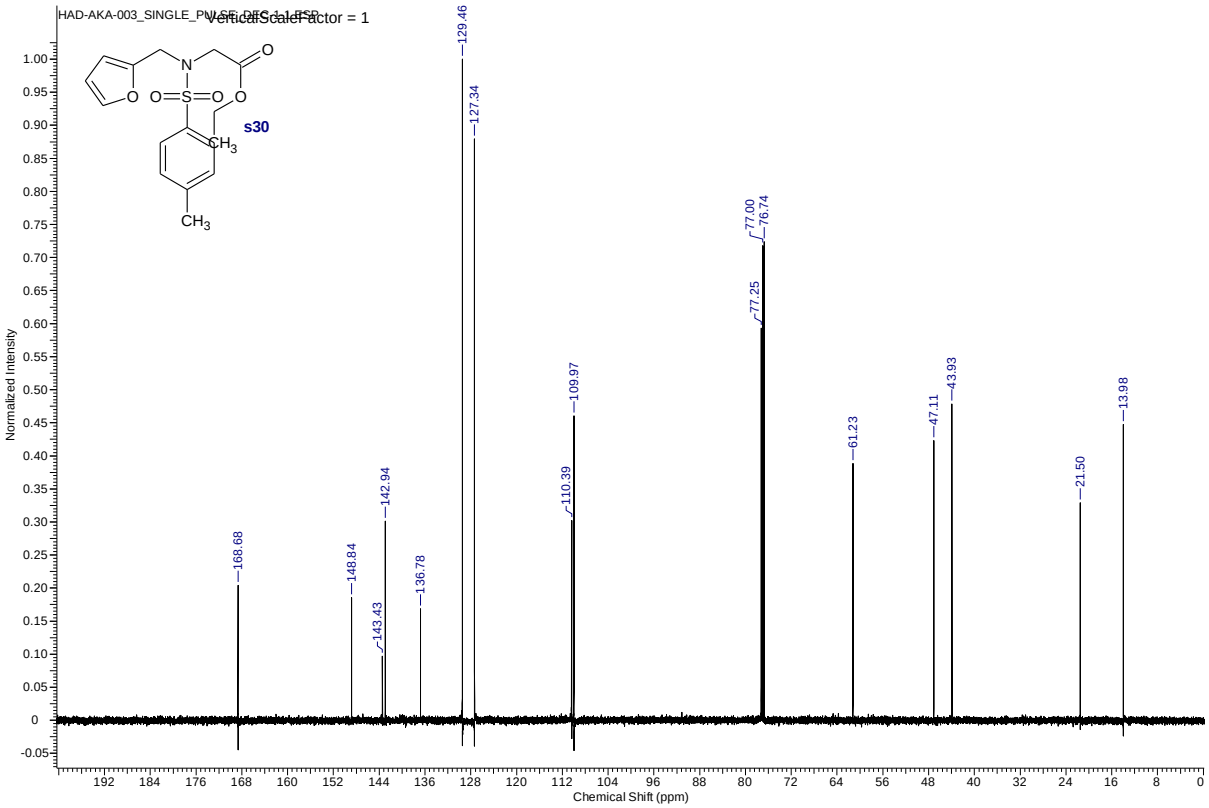

HAD-493_SINGLE_PULSE_1.1ESP
VerticalScaleFactor = 1
OH
N
O
O
CH3
3k
Normalized Intensity
Chemical Shift (ppm)
3.77
7.26
7.13
7.11
6.83
6.81
4.13
4.12
3.79
3.53
3.51
3.40
3.25
3.15
3.13
2.78
2.77
2.76
2.75
2.73
2.71
2.70
1.89
1.88
1.87
1.86
1.85
1.84
1.79
1.76
1.42
1.24
2.07
2.10
1.00
3.45
0.95
1.05
1.07
1.04
1.01
2.06
6.37

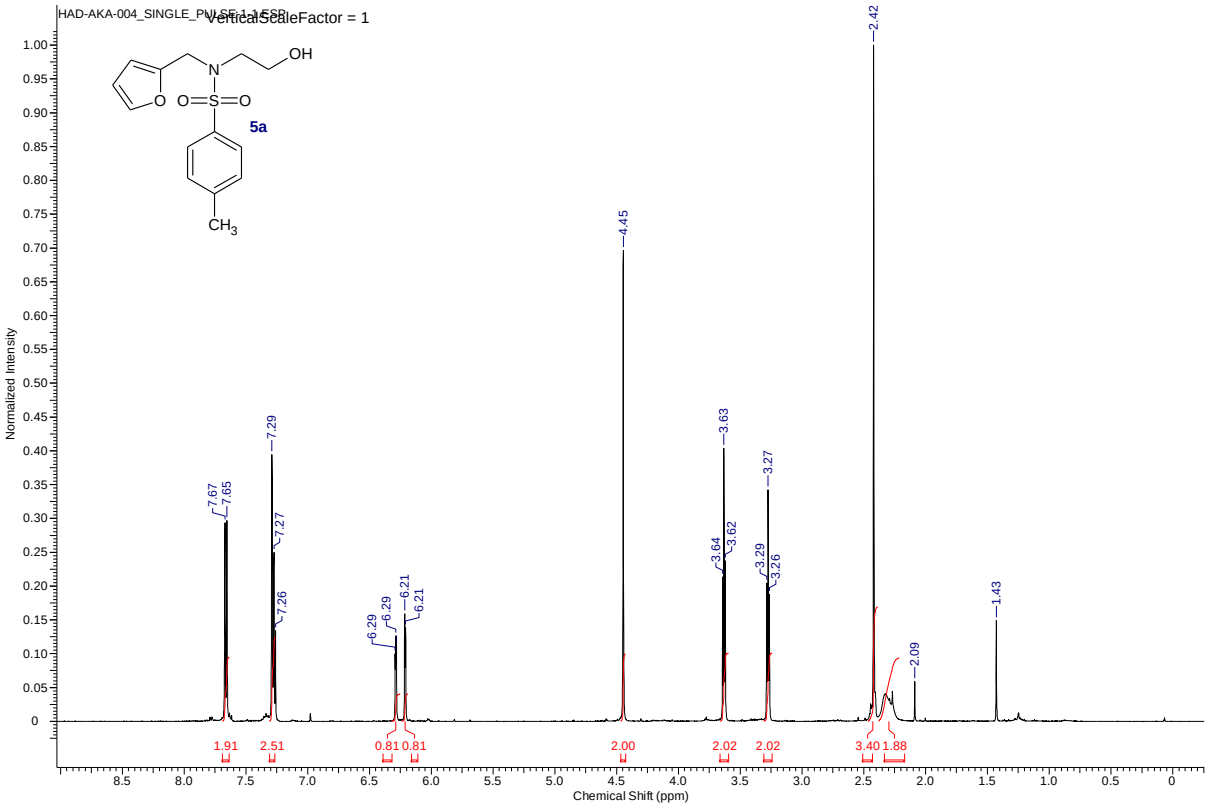

HAD-493_SINGLE_PULSE_QEC_1.1ESP
VerticalScaleFactor = 1
OH
N
O
O
CH3
3k
Normalized Intensity
Chemical Shift (ppm)
129.40
77.25
77.00
76.74
68.23
113.68
55.16
46.11
45.65
36.17
30.17
23.74
25.93
172.66
157.73
133.32

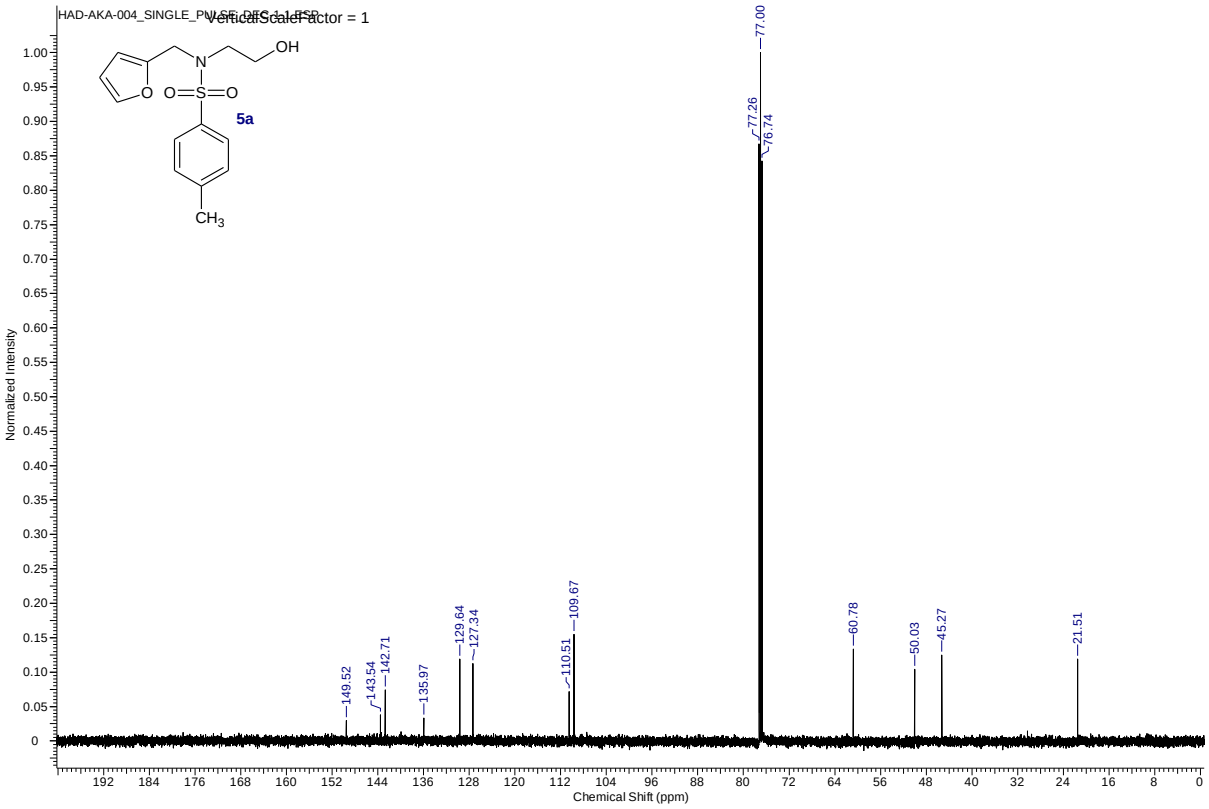

AKA-002_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
CH3
O
S
NH
O
O
s29
Normalized Intensity
Chemical Shift (ppm)
2.41
7.71
7.70
7.27
7.25
7.25
7.22
6.21
6.20
6.20
6.20
6.08
6.07
4.89
4.88
4.87
4.16
4.14
2.09
2.28
1.02
1.02
1.00
1.01
2.19
3.30

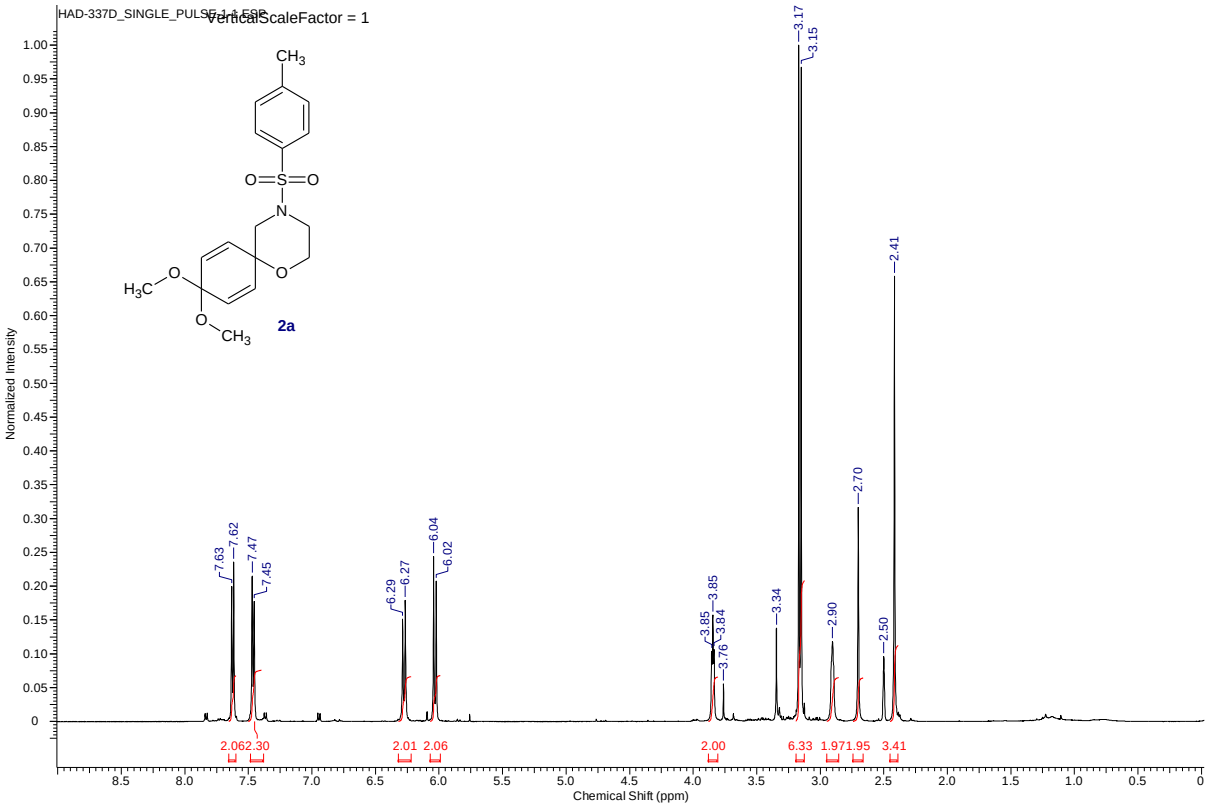

HAD-AKA-002_SINGLE_PULSE_DEC_1.1.ESP
VerticalScaleFactor = 1
CH3
O
S
NH
O
O
s29
Normalized Intensity
Chemical Shift (ppm)
77.26
77.00
76.74
129.61
127.08
142.44
149.46
149.45
143.45
136.72
110.34
108.15
40.08
21.49

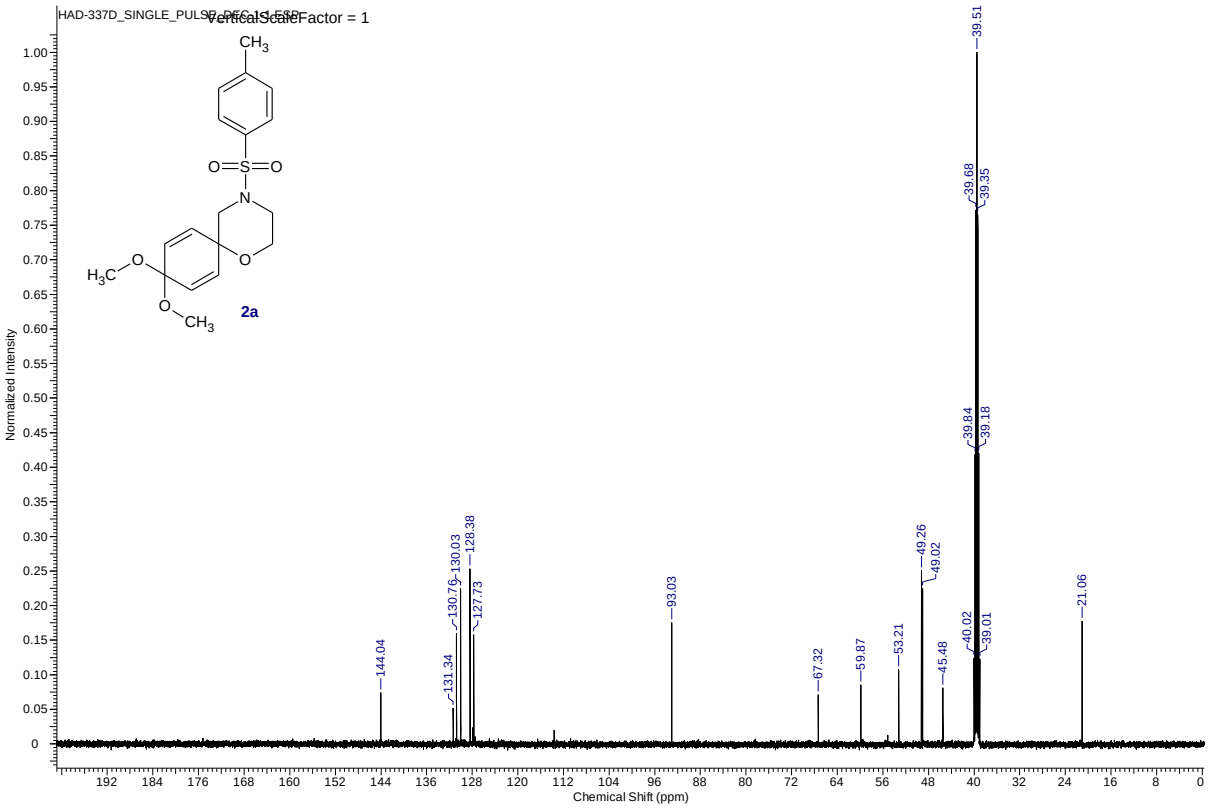

HAD-AKA-003_SINGLE_PULSE.1.1552
VerticalScaleFactor = 1
s30
Normalized Intensity
Chemical Shift (ppm)
7.73
7.71
7.30
7.30
7.29
7.27
7.26
6.28
6.27
6.18
6.18
4.54
4.09
4.07
3.95
2.42
1.20
1.17
1.18
1.95
2.85
0.96
0.94
2.01
2.01
2.00
3.01
3.02

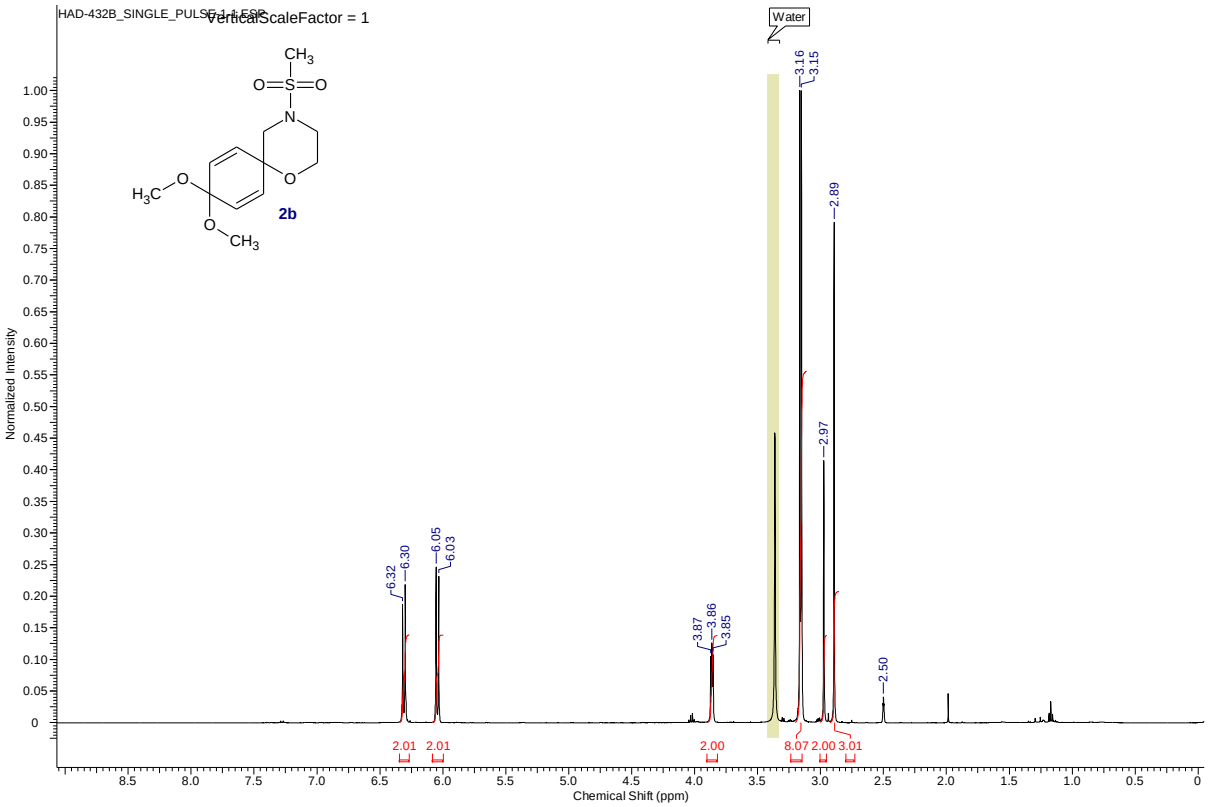

HAD-AKA-003_SINGLE_PULSE_DEC.1.1552
VerticalScaleFactor = 1
s30
Normalized Intensity
Chemical Shift (ppm)
168.68
148.84
143.43
142.94
136.78
129.46
127.34
110.39
109.97
77.00
76.74
77.25
61.23
47.11
43.93
21.50
13.98

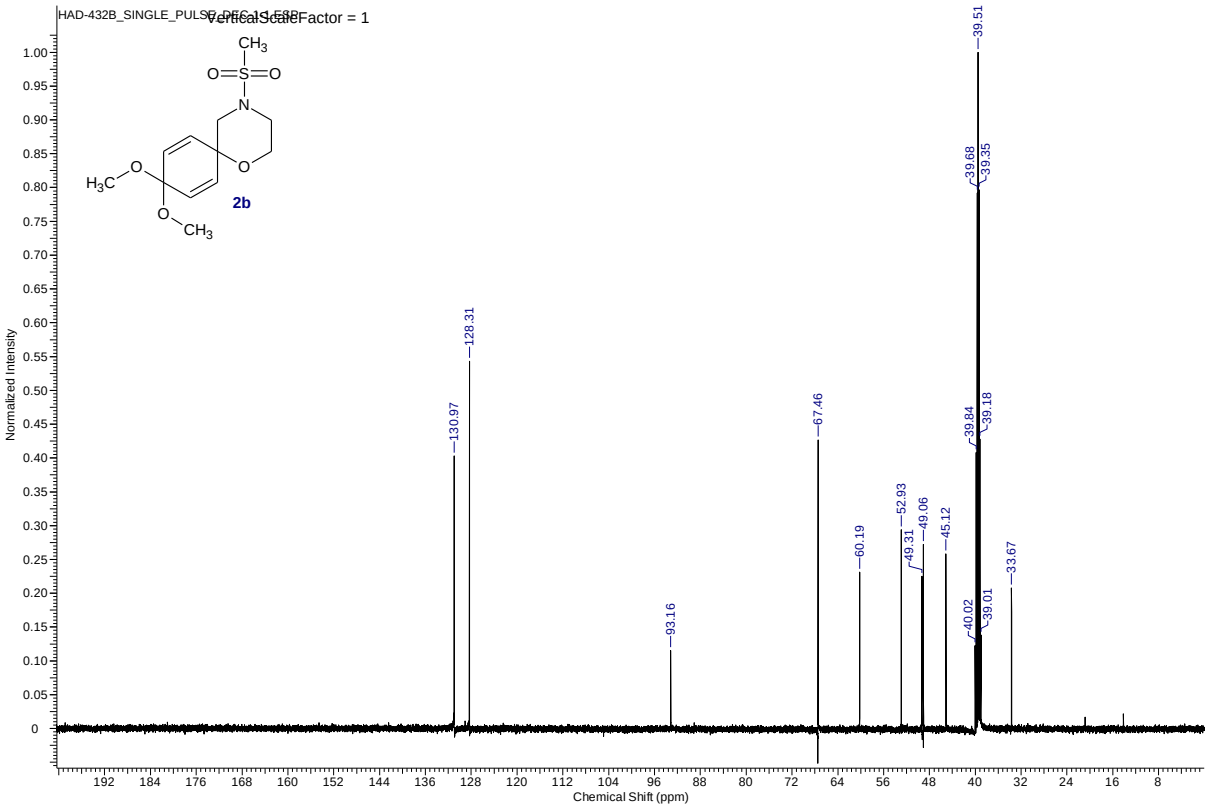

HAD-AKA-004_SINGLE_PULSE.1.1552
VerticalScaleFactor = 1
OH
N
O
O=S=O
5a
CH3
Normalized Intensity
Chemical Shift (ppm)
7.67
7.65
7.29
7.27
7.26
6.29
6.29
6.21
6.21
4.45
3.63
3.64
3.62
3.27
3.29
3.26
2.42
2.09
1.43
1.91
2.51
0.81
0.81
2.00
2.02
2.02
3.40
1.88

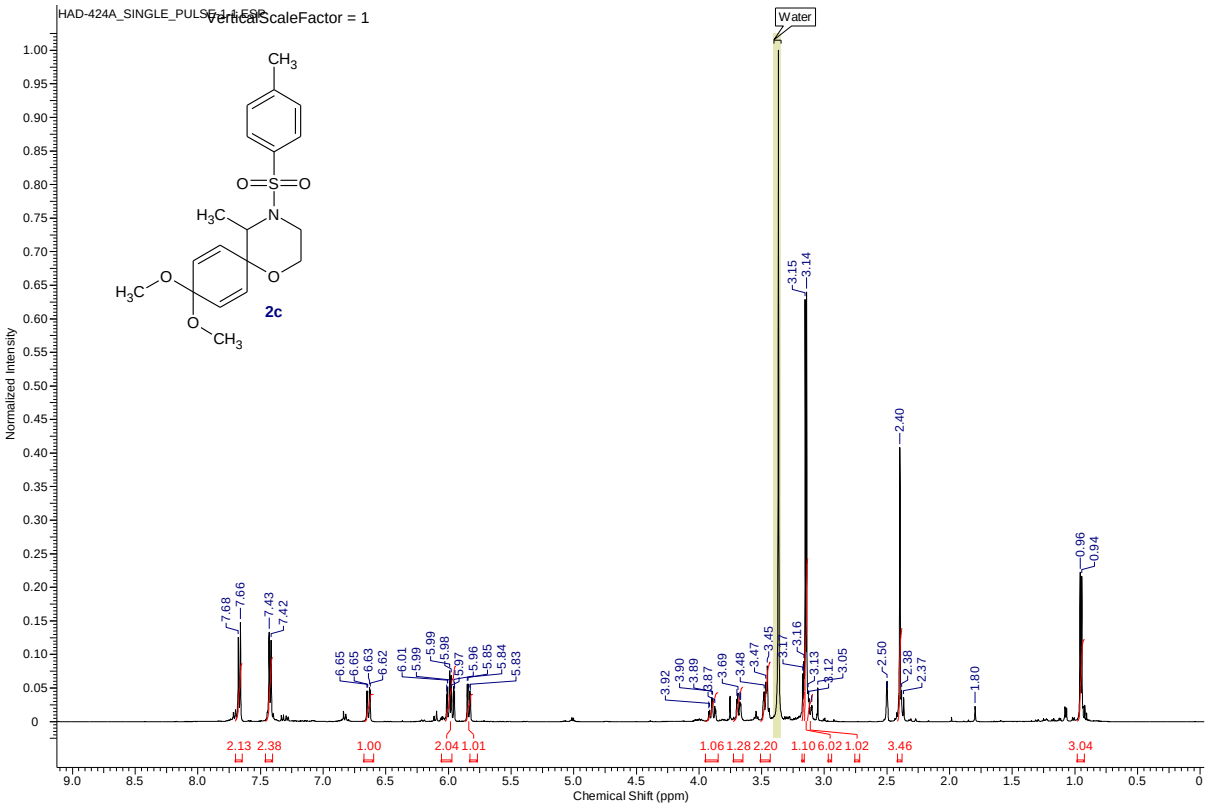

HAD-AKA-004_SINGLE_PULSE_DEC.1.1552
VerticalScaleFactor = 1
OH
N
O
O=S=O
5a
CH3
Normalized Intensity
Chemical Shift (ppm)
77.00
77.26
76.74
149.52
143.54
142.71
135.97
129.64
127.34
110.51
109.67
60.78
50.03
45.27
21.51

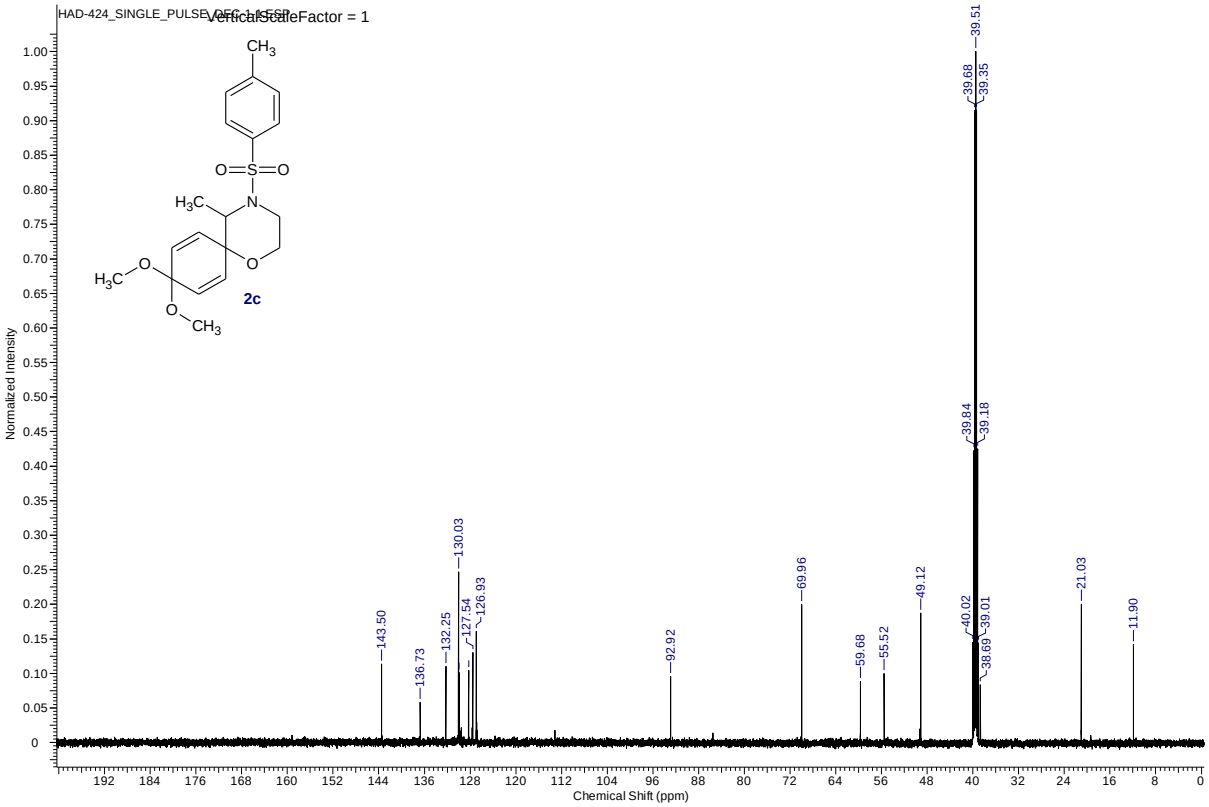

HAD-337D_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
2a
7.63
7.62
7.47
7.45
6.29
6.27
6.04
6.02
3.85
3.84
3.76
3.34
3.17
3.15
2.90
2.70
2.50
2.41
2.06
2.30
2.01
2.06
2.00
6.33
1.97
1.95
3.41

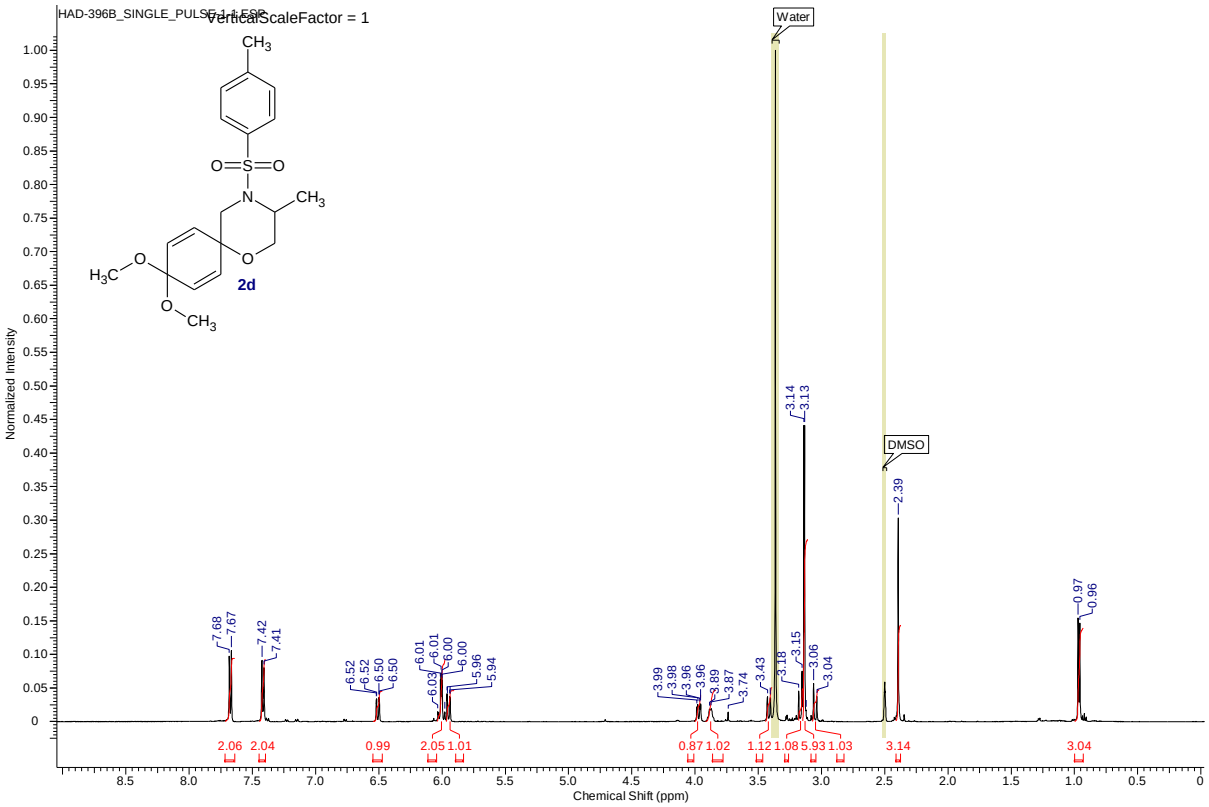

HAD-337D_SINGLE_PULSE_DEC_1.1.ESP
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
2a
144.04
131.34
130.76
130.03
128.38
127.73
93.03
67.32
59.87
53.21
49.26
49.02
45.48
40.02
39.84
39.68
39.51
39.35
39.18
39.01
21.06

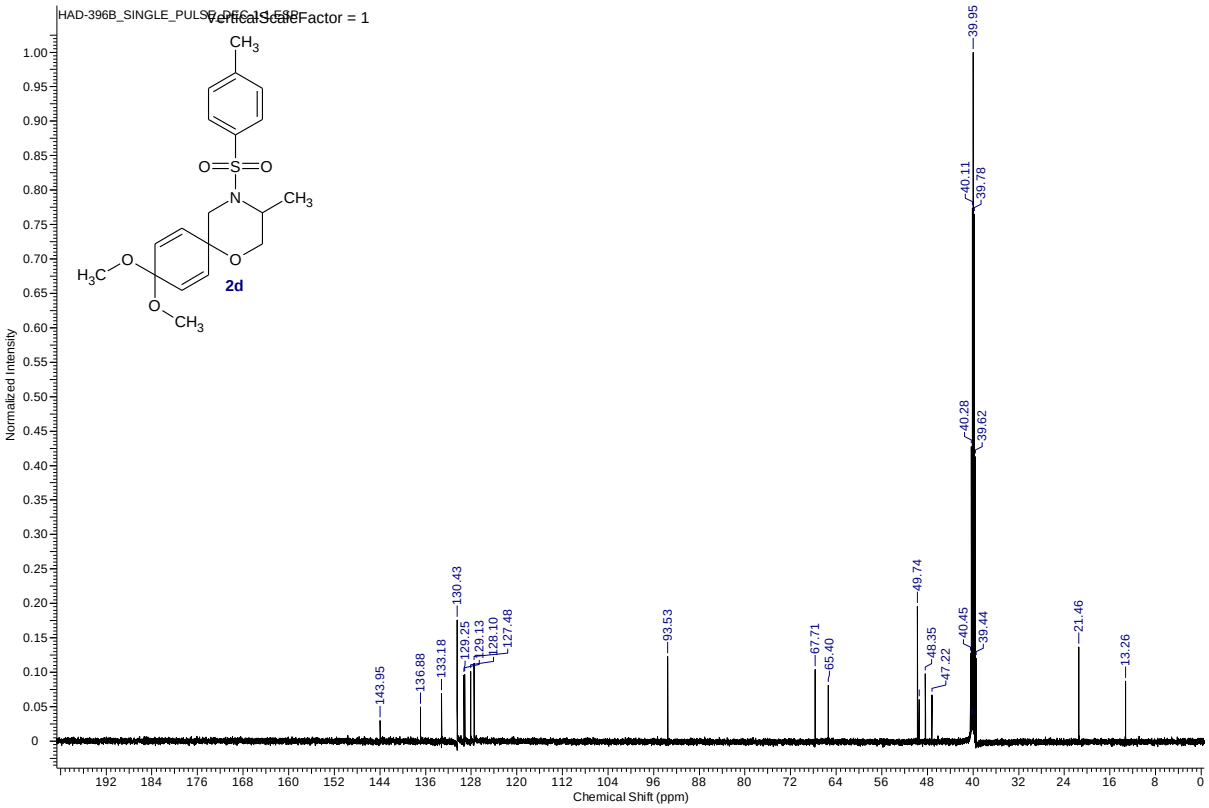

HAD-432B_SINGLE_PULSE.1.1.ESP
VerticalScaleFactor = 1
Water
2b
Normalized Intensity
Chemical Shift (ppm)
6.32
6.30
6.05
6.03
3.87
3.86
3.85
3.16
3.15
2.89
2.97
2.50
2.01
2.01
2.00
8.07
2.00
3.01

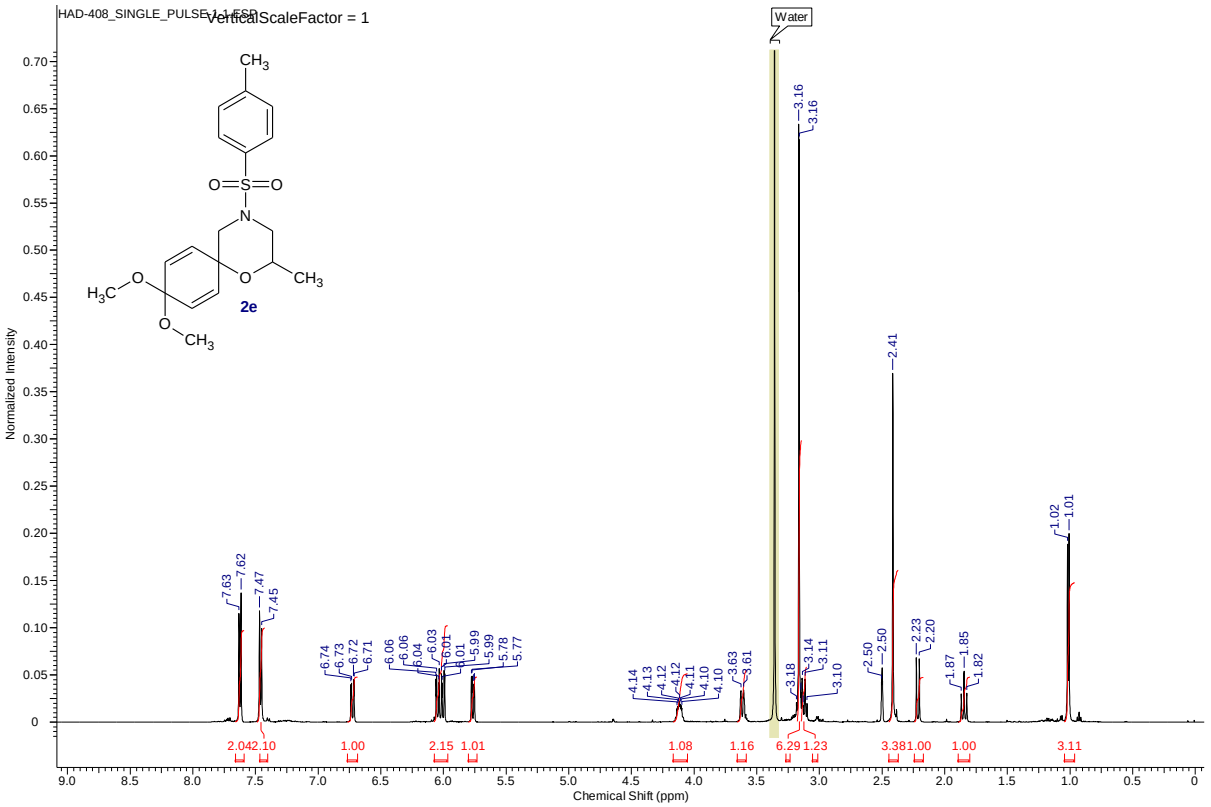

HAD-432B_SINGLE_PULSE_DEC.1.1.ESP
VerticalScaleFactor = 1
2b
Normalized Intensity
Chemical Shift (ppm)
130.97
128.31
93.16
67.46
60.19
52.93
49.31
49.06
45.12
40.02
39.84
39.68
39.51
39.35
39.18
39.01
33.67

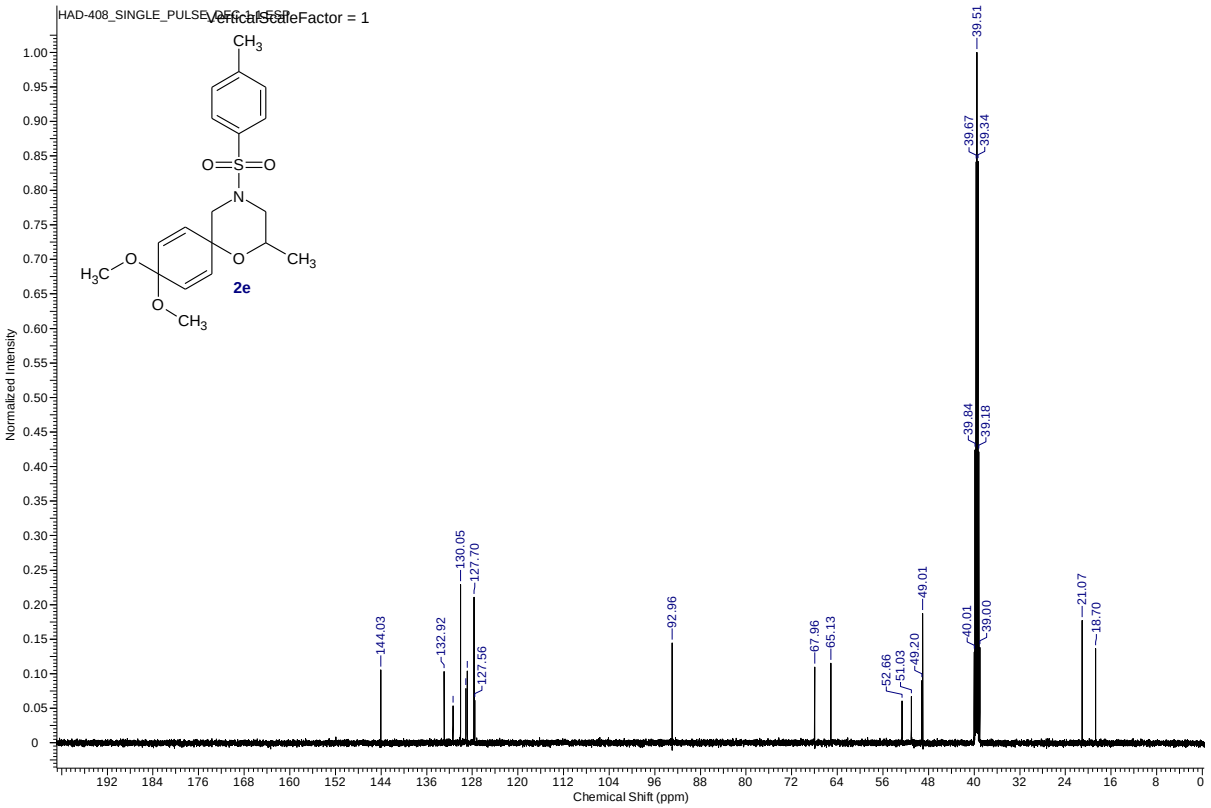

HAD-424A_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
Water
2c
Normalized Intensity
Chemical Shift (ppm)

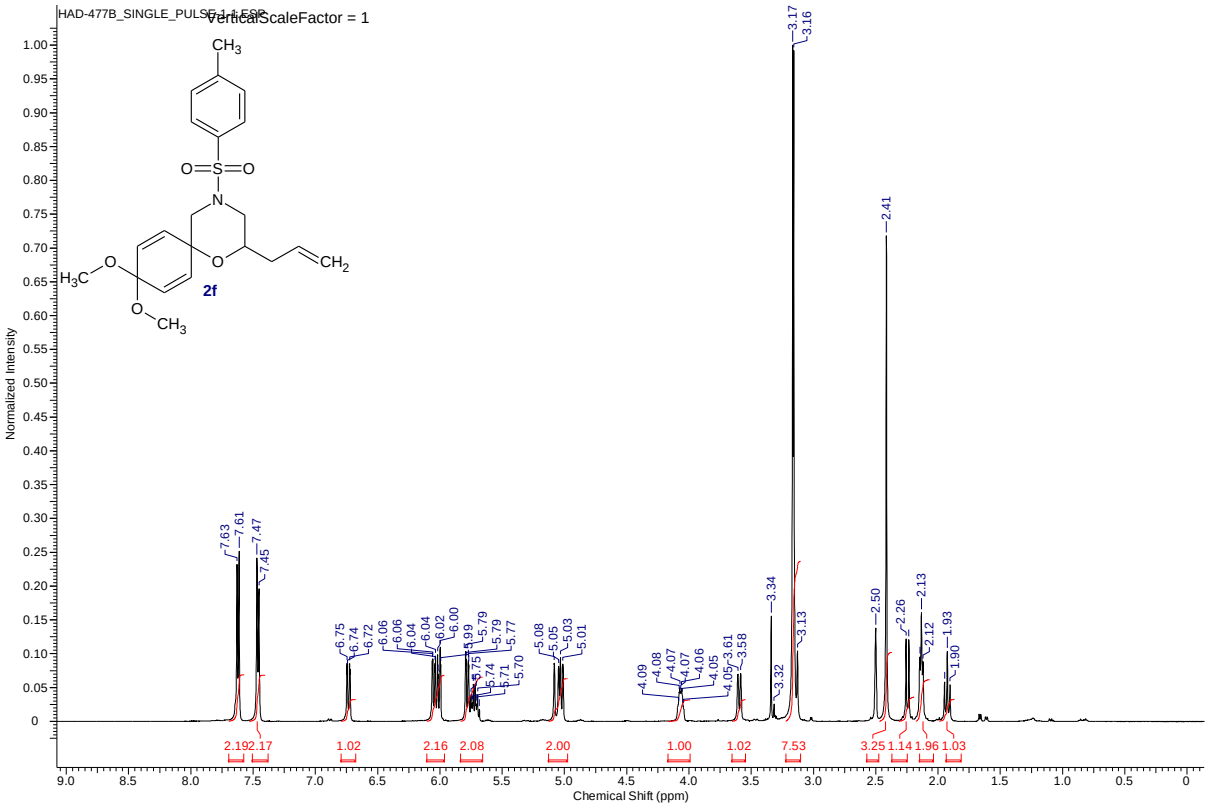

HAD-424_SINGLE_PULSE_QFC_1.ESP
VerticalScaleFactor = 1
2c
Normalized Intensity
Chemical Shift (ppm)

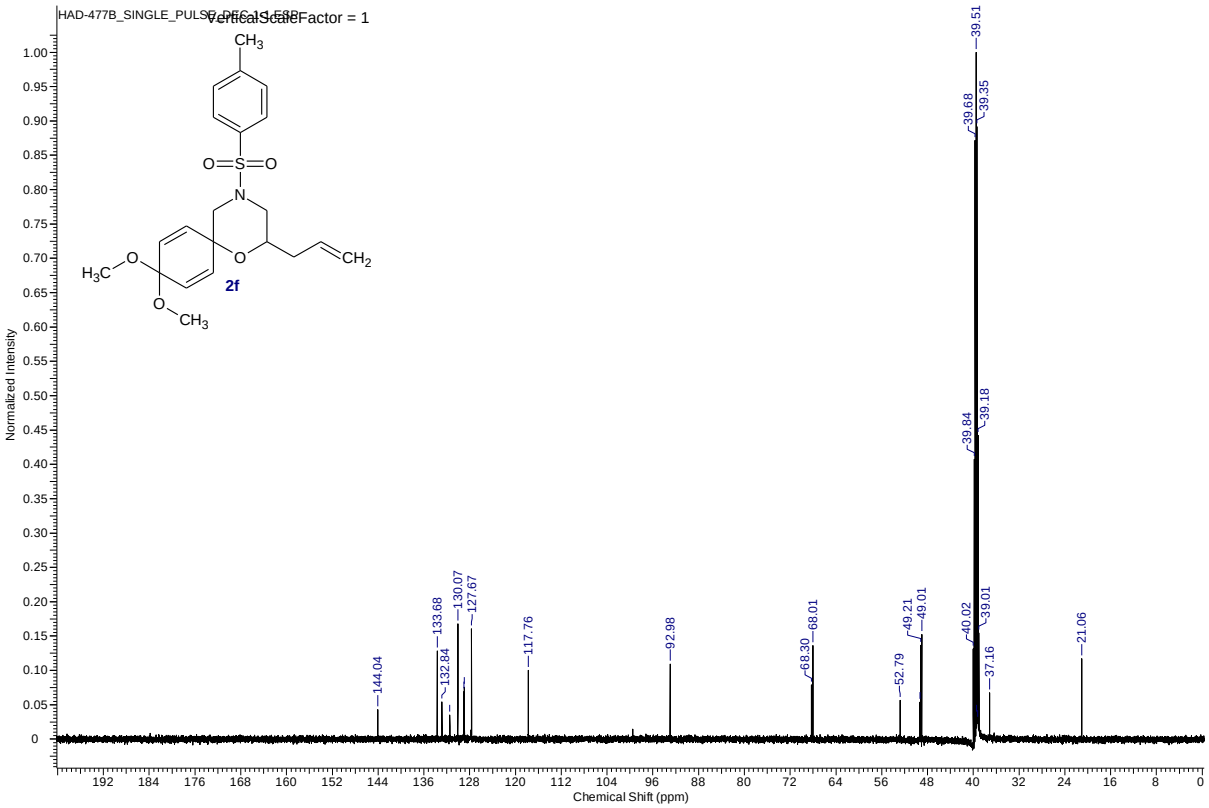

HAD-396B_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
Water
DMSO
2d
Normalized Intensity
Chemical Shift (ppm)

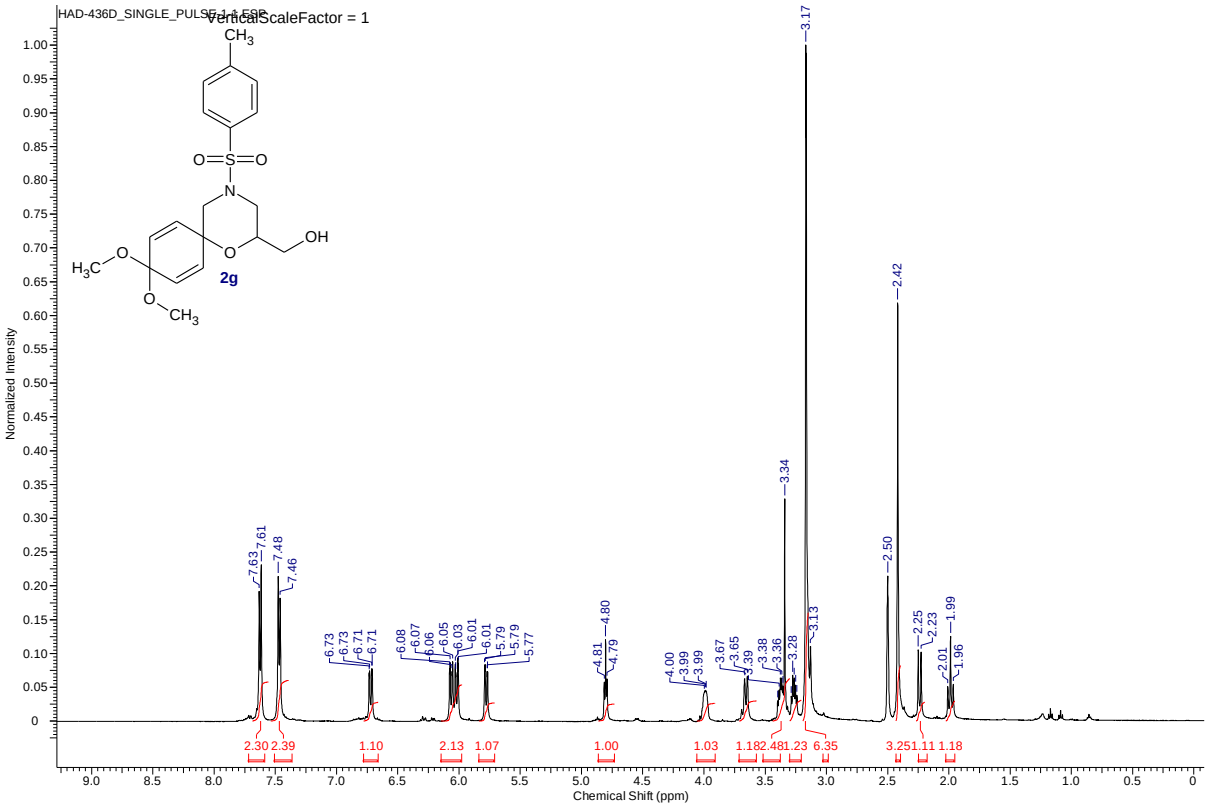

HAD-396B_SINGLE_PULSE_DEC_1.1.ESP
VerticalScaleFactor = 1
2d
Normalized Intensity
Chemical Shift (ppm)

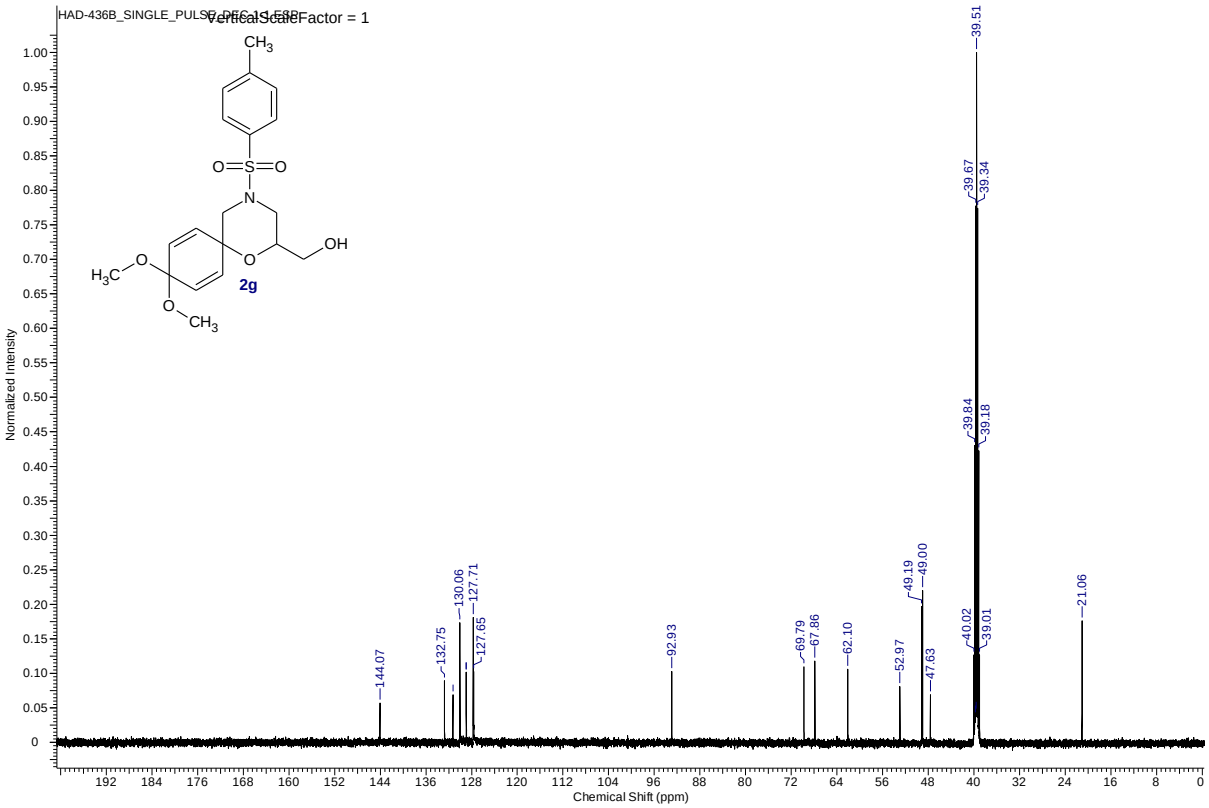

HAD-408_SINGLE_PULSE_1.1ESP
VerticalScaleFactor = 1
Water
2e
Normalized Intensity
Chemical Shift (ppm)

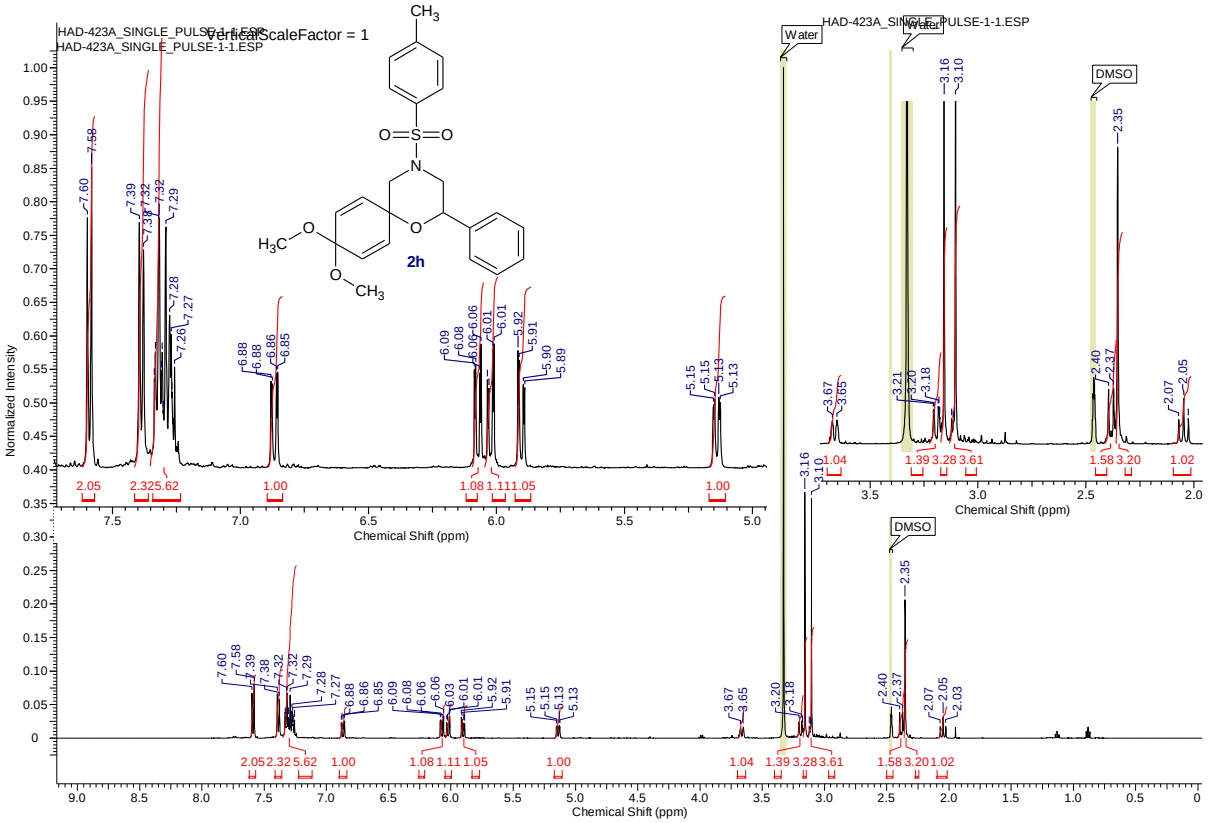

HAD-408_SINGLE_PULSE_QEC_1.1ESP
VerticalScaleFactor = 1
2e
Normalized Intensity
Chemical Shift (ppm)

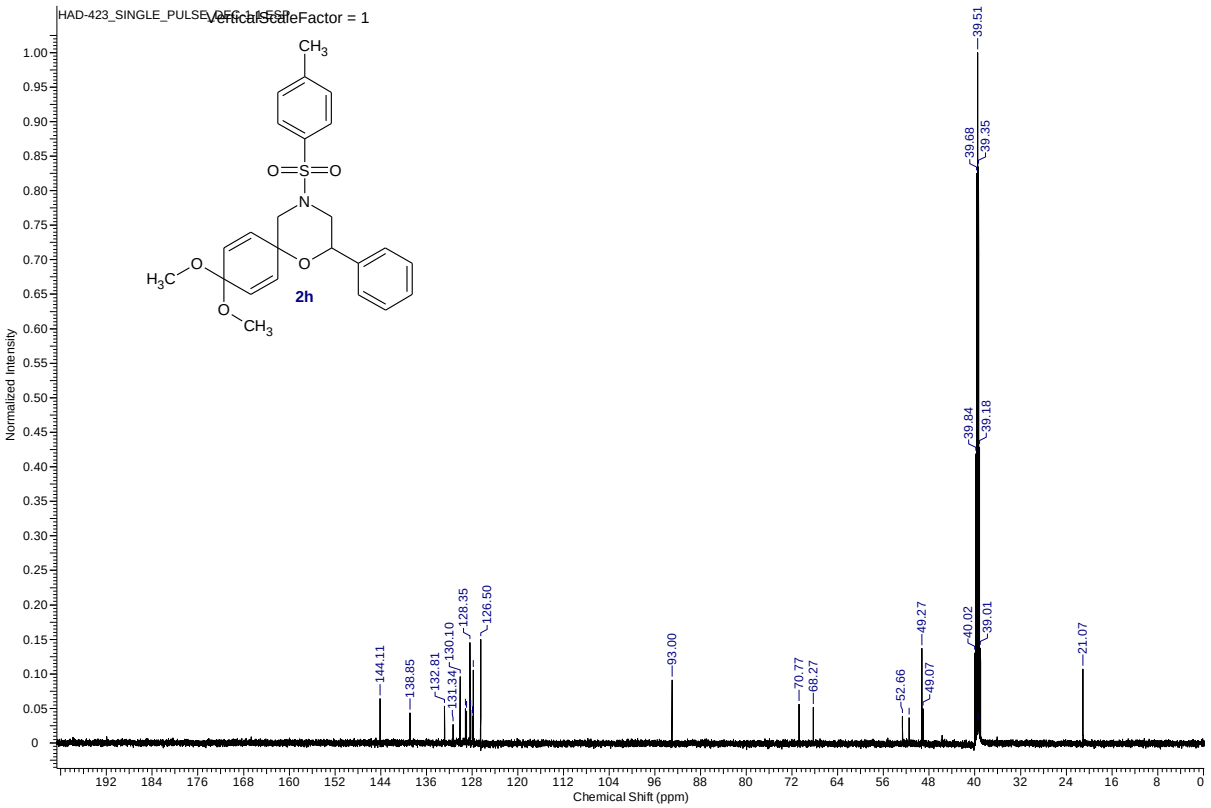

HAD-477B_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
2f
Normalized Intensity
Chemical Shift (ppm)

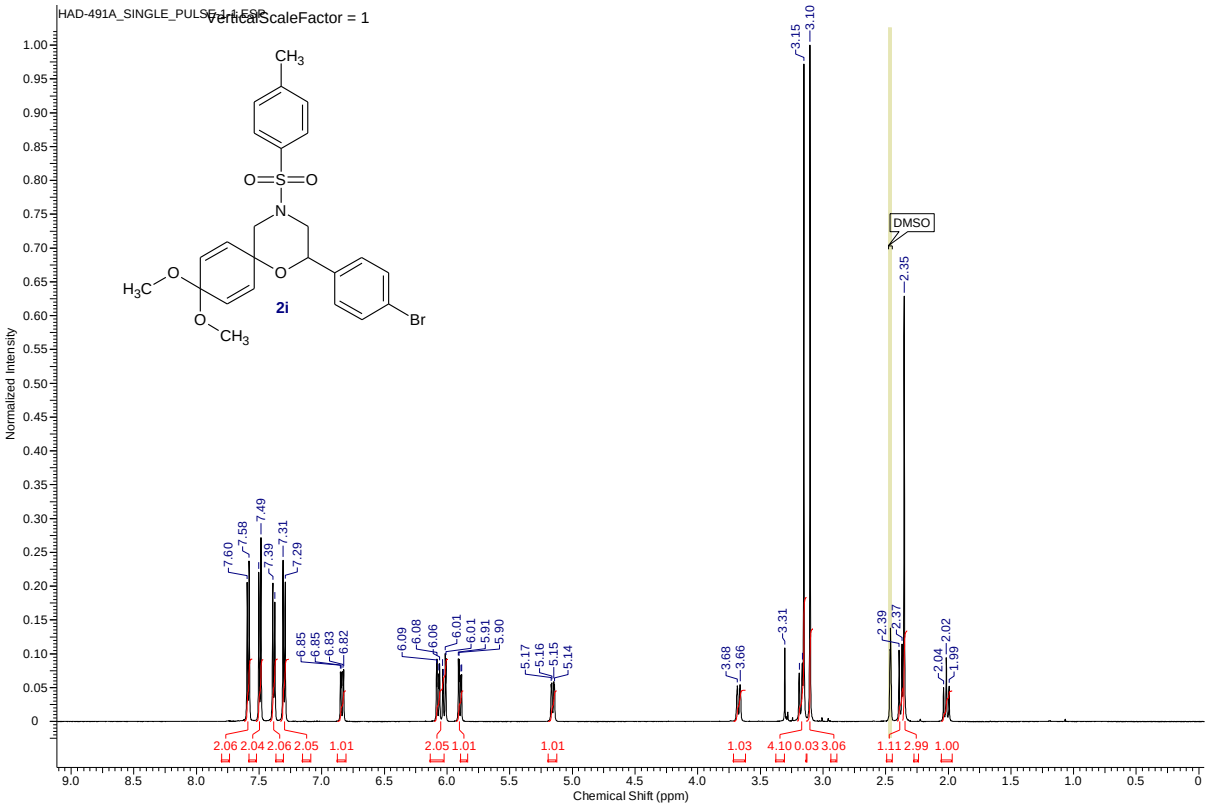

HAD-477B_SINGLE_PULSE_DEC_1_1.ESP
VerticalScaleFactor = 1
2f
Normalized Intensity
Chemical Shift (ppm)

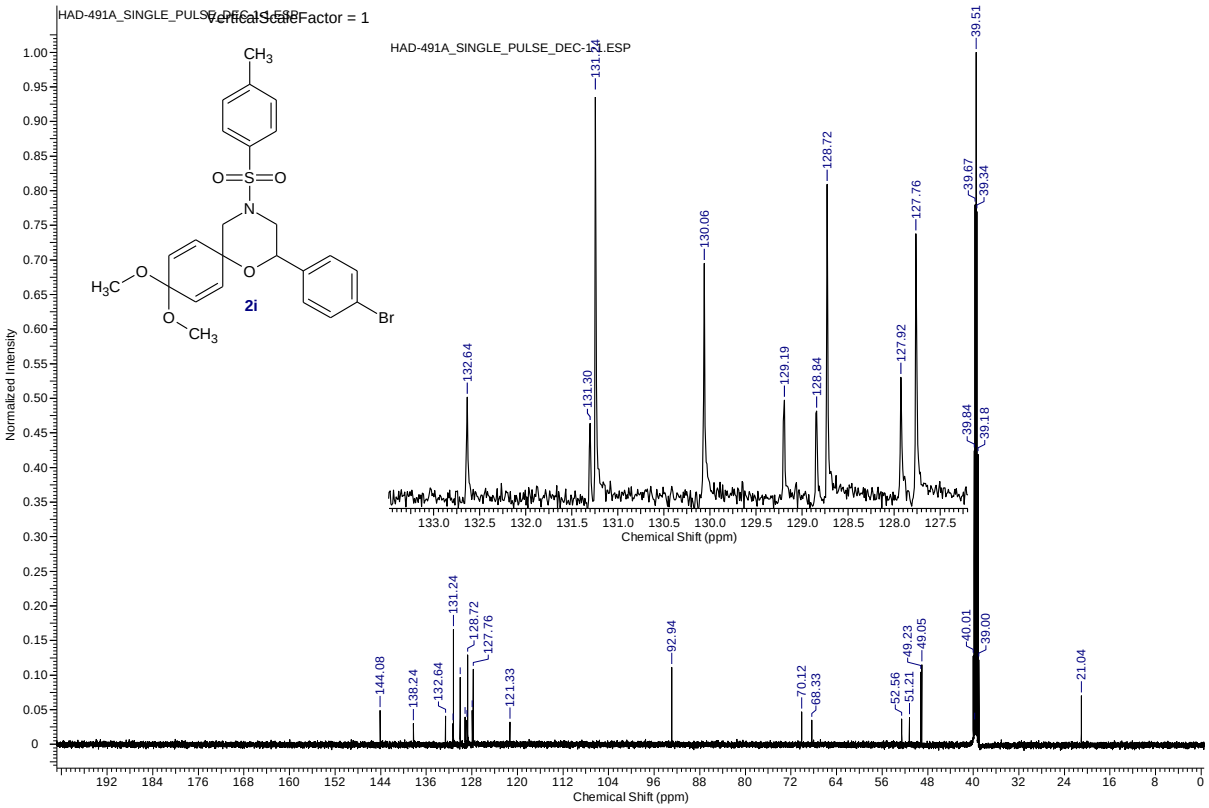

HAD-436D_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
2g
Normalized Intensity
Chemical Shift (ppm)

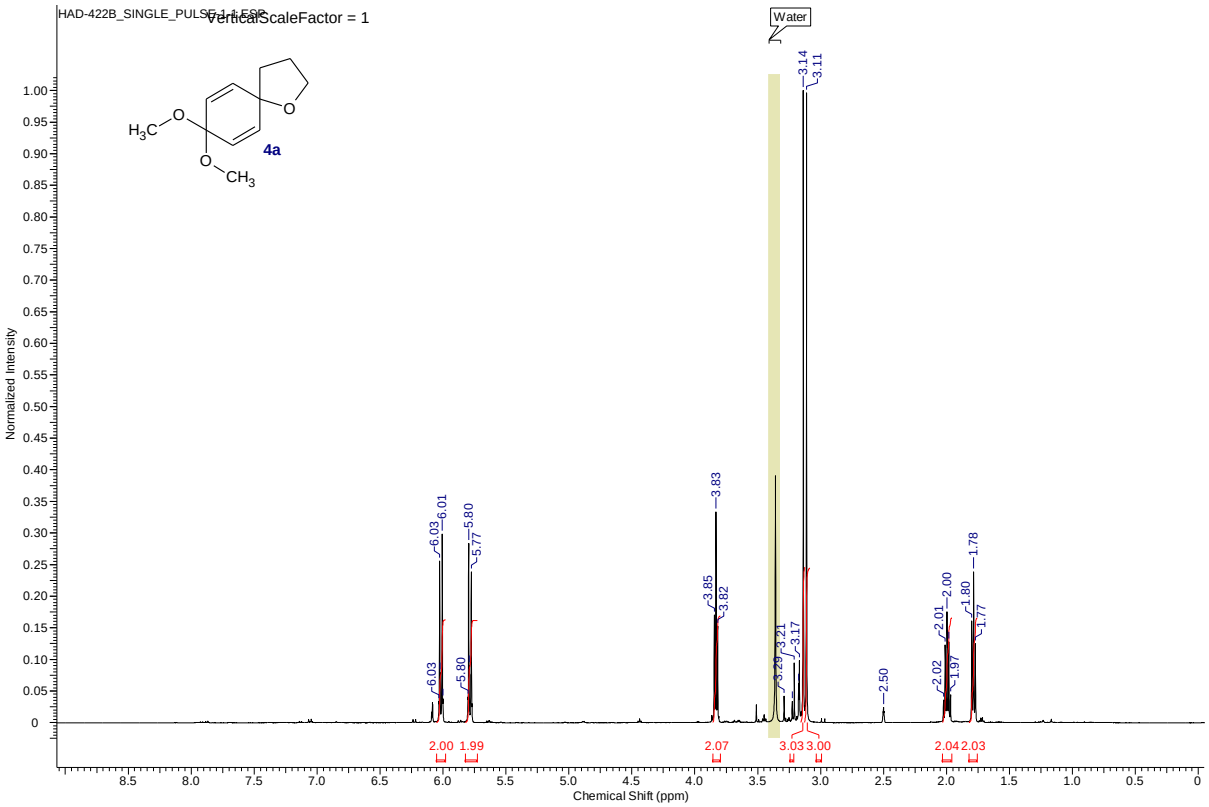

HAD-436B_SINGLE_PULSE_DEC_1.1.ESP
VerticalScaleFactor = 1
2g
Normalized Intensity
Chemical Shift (ppm)

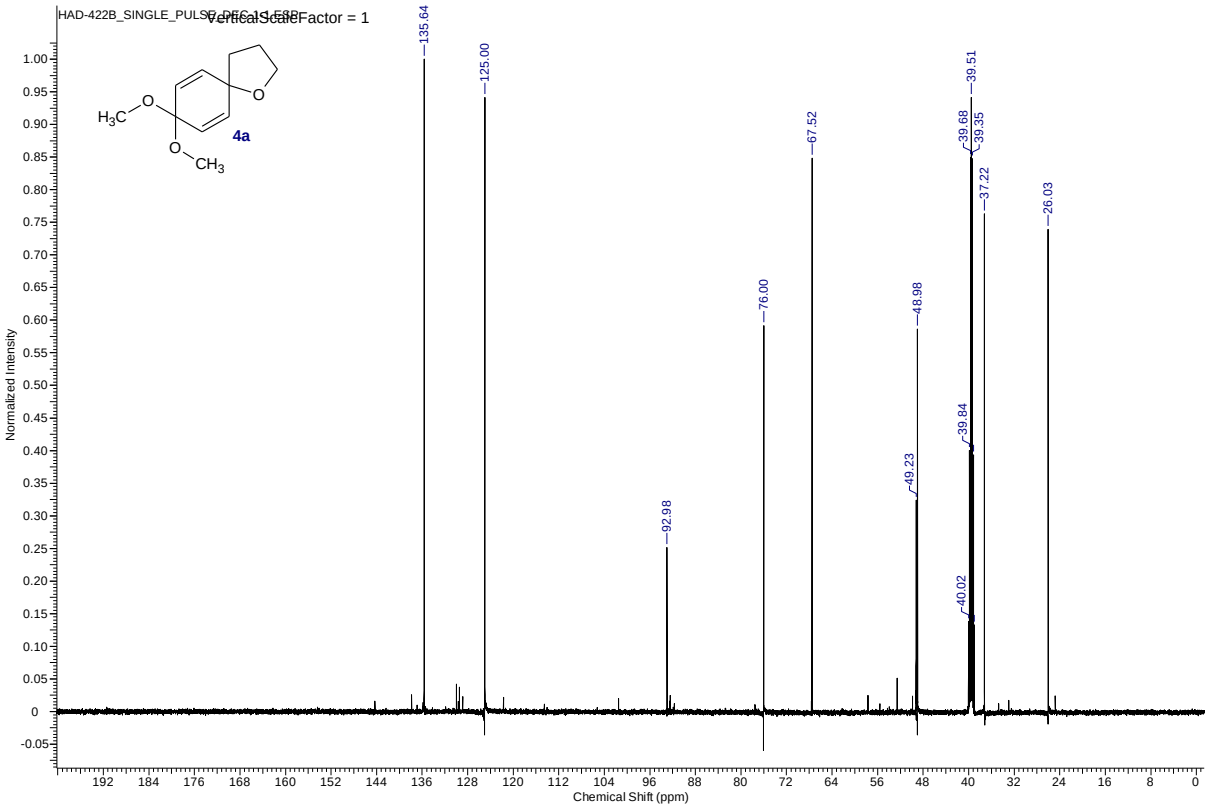

HAD-423A_SINGLE_PULSE-1-1.ESP
VerticalScaleFactor = 1
2h
Water
DMSO
Normalized Intensity
Chemical Shift (ppm)

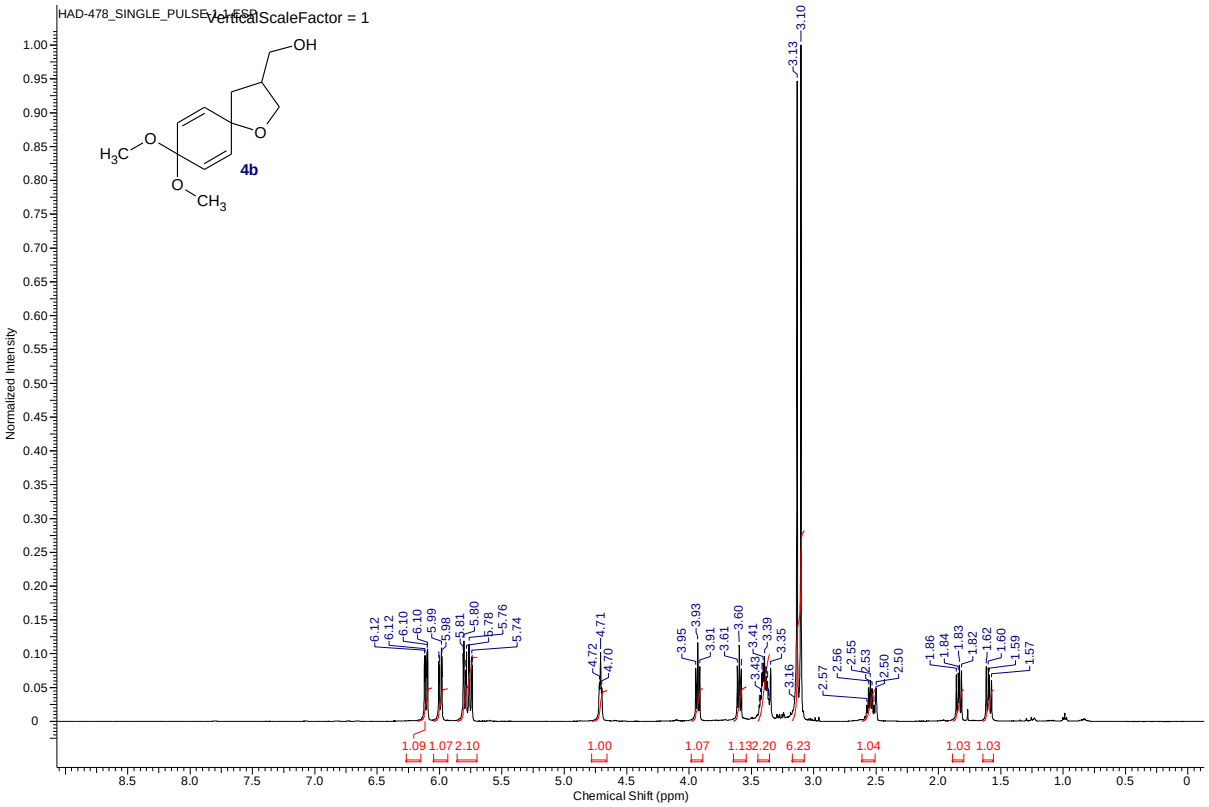

HAD-423_SINGLE_PULSE_DEC-1-1.ESP
VerticalScaleFactor = 1
2h
Normalized Intensity
Chemical Shift (ppm)

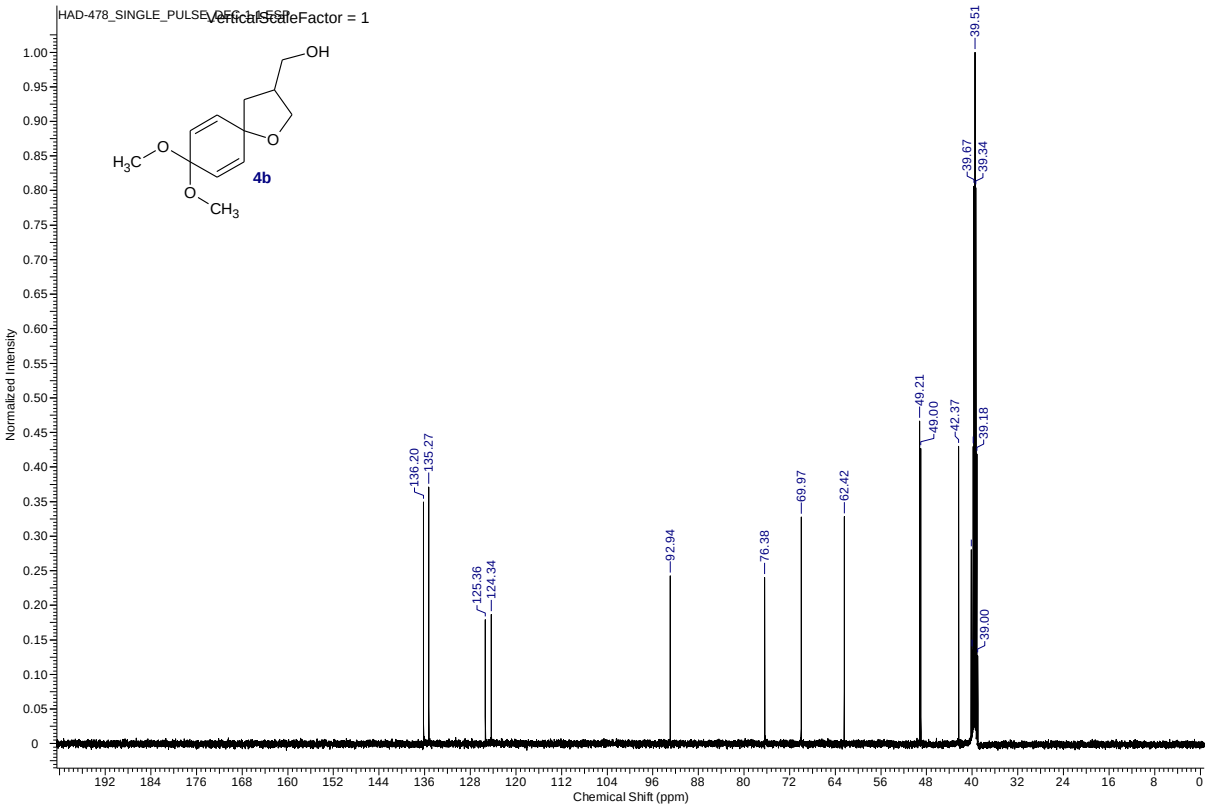

HAD-491A_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
2i
DMSO
Normalized Intensity
Chemical Shift (ppm)

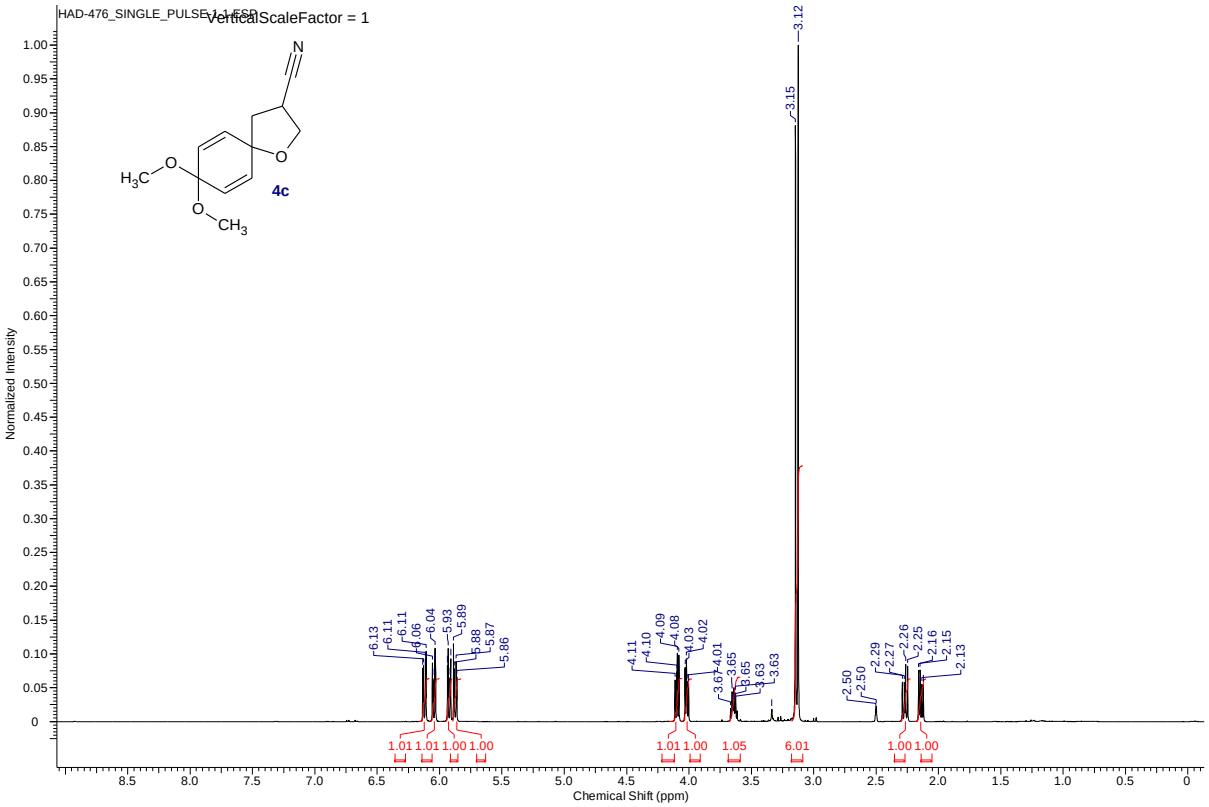

HAD-491A_SINGLE_PULSE_DEC_1_1.ESP
VerticalScaleFactor = 1
2i
Normalized Intensity
Chemical Shift (ppm)

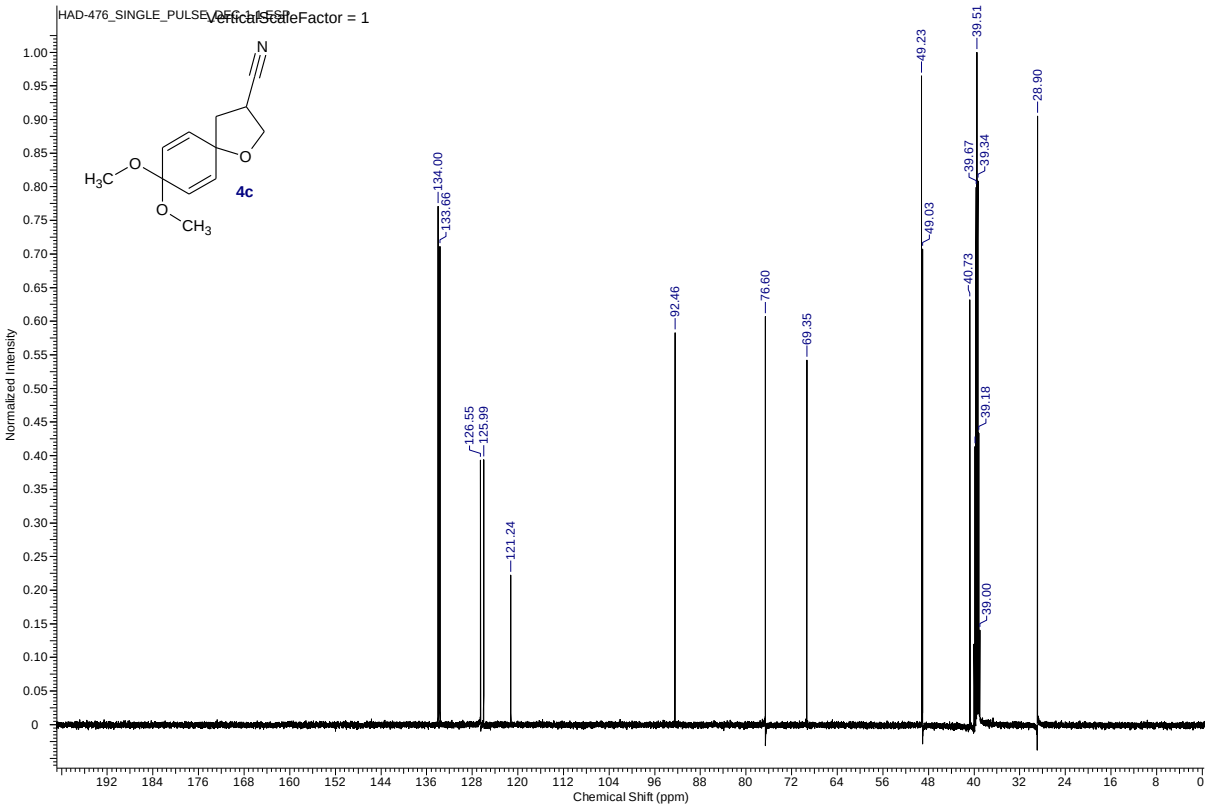

HAD-422B_SINGLE_PULSE.1.1.ESP
VerticalScaleFactor = 1
Water
4a
Normalized Intensity
Chemical Shift (ppm)

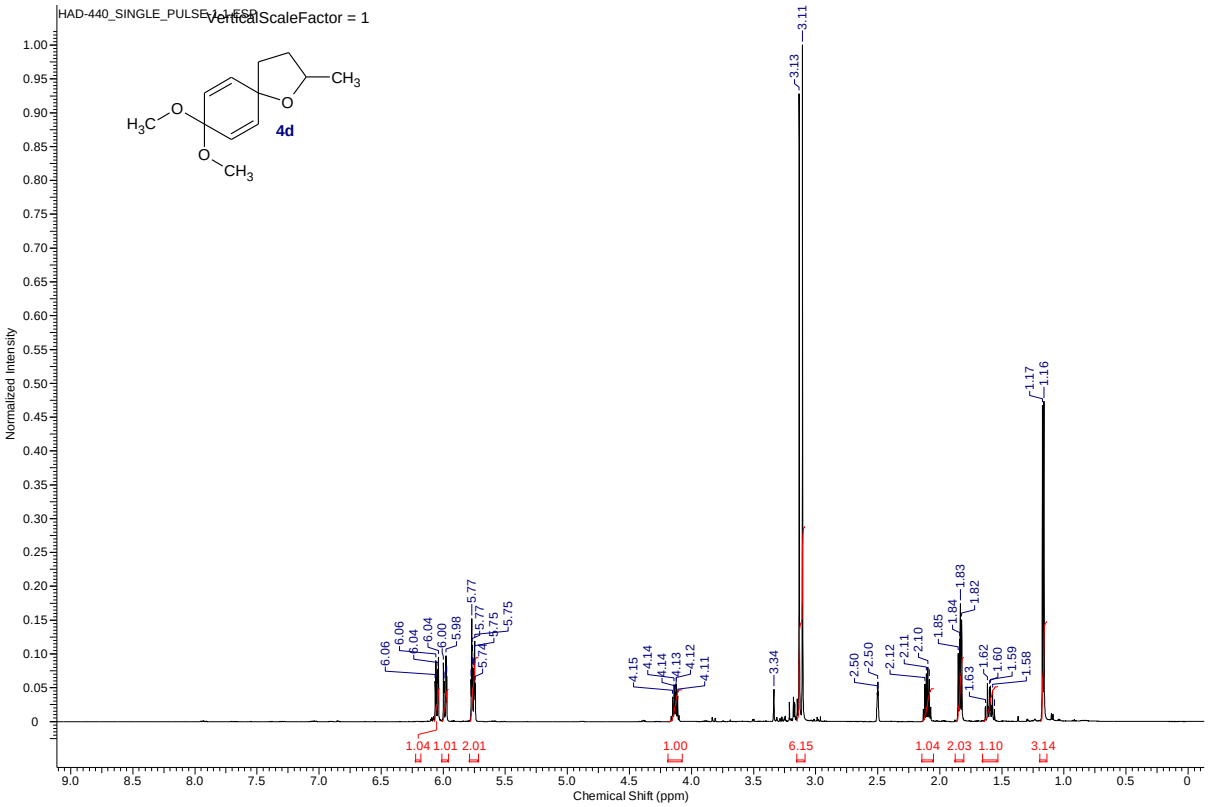

HAD-422B_SINGLE_PULSE_DEC.1.1.ESP
VerticalScaleFactor = 1
4a
Normalized Intensity
Chemical Shift (ppm)

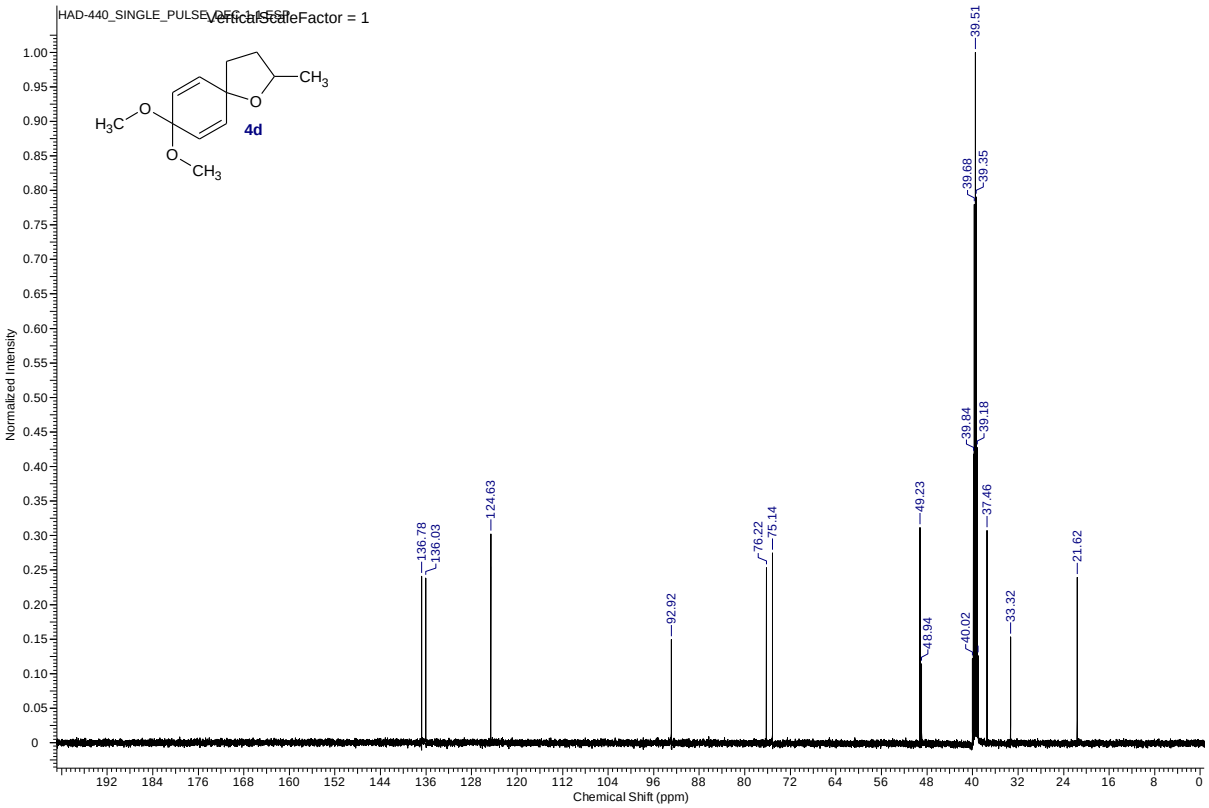

HAD-478_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
OH
O
H3C
O
O
CH3
4b
Normalized Intensity
Chemical Shift (ppm)
3.10
3.13
6.12
6.12
6.10
6.10
5.99
5.98
5.81
5.80
5.78
5.76
5.74
4.72
4.71
4.70
3.95
3.93
3.91
3.61
3.60
3.43
3.41
3.39
3.35
3.16
2.57
2.56
2.55
2.53
2.50
2.50
1.86
1.84
1.83
1.82
1.62
1.60
1.59
1.57
1.09
1.07
2.10
1.00
1.07
1.13
2.20
6.23
1.04
1.03
1.03

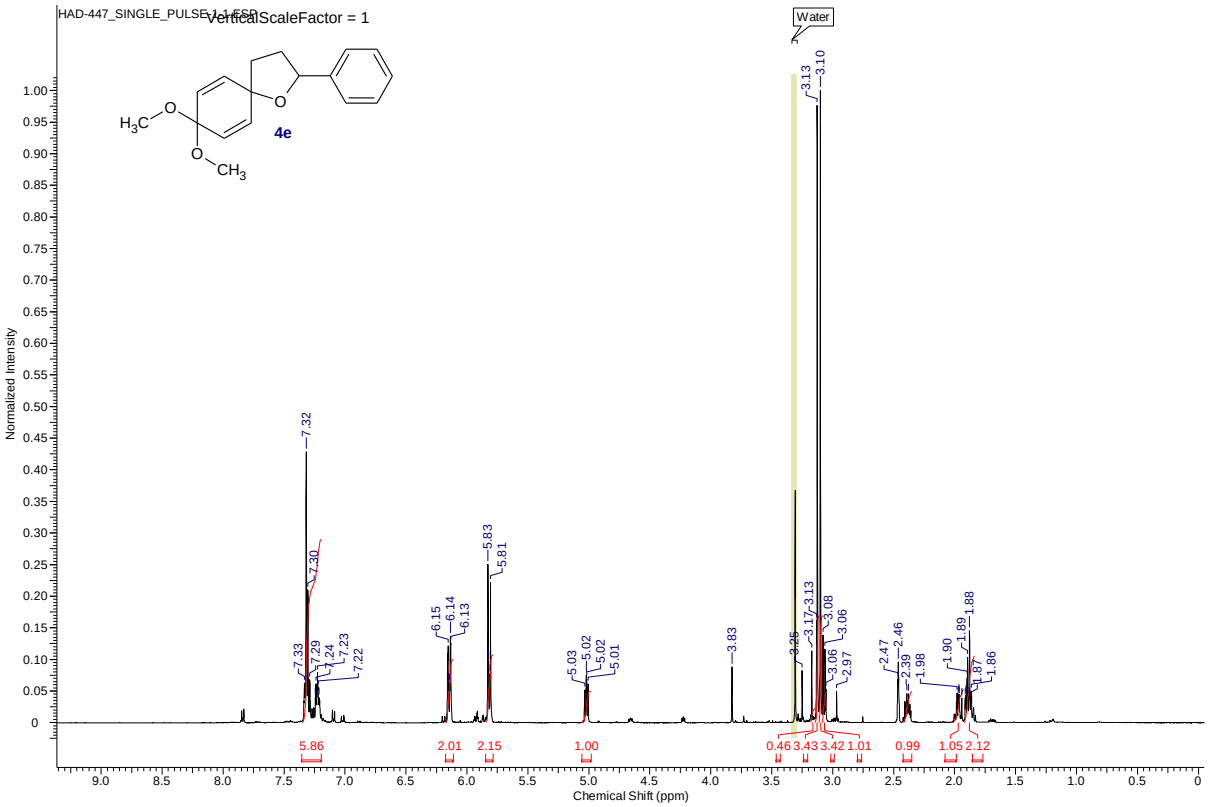

HAD-478_SINGLE_PULSE_QEC_1.ESP
VerticalScaleFactor = 1
OH
O
H3C
O
O
CH3
4b
Normalized Intensity
Chemical Shift (ppm)
39.51
39.67
39.34
49.21
49.00
42.37
39.18
39.00
136.20
135.27
125.36
124.34
92.94
76.38
69.97
62.42

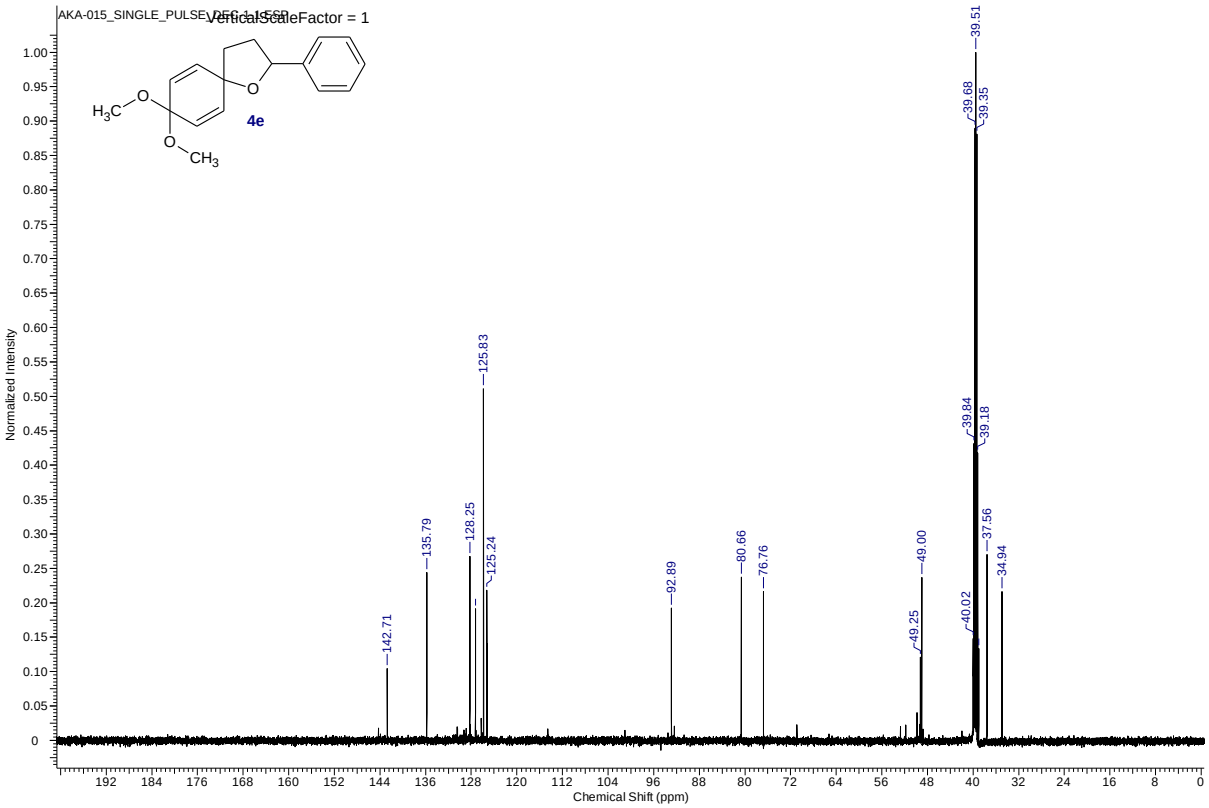

HAD-476_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
4c
Normalized Intensity
Chemical Shift (ppm)
3.12
3.15
6.13
6.11
6.11
6.06
6.04
5.93
5.89
5.88
5.87
5.86
4.11
4.10
4.09
4.08
4.03
4.02
4.01
3.67
3.65
3.63
3.63
2.50
2.50
2.29
2.27
2.26
2.25
2.16
2.15
2.13
1.01 1.01 1.00 1.00
1.01 1.00
1.05
6.01
1.00 1.00

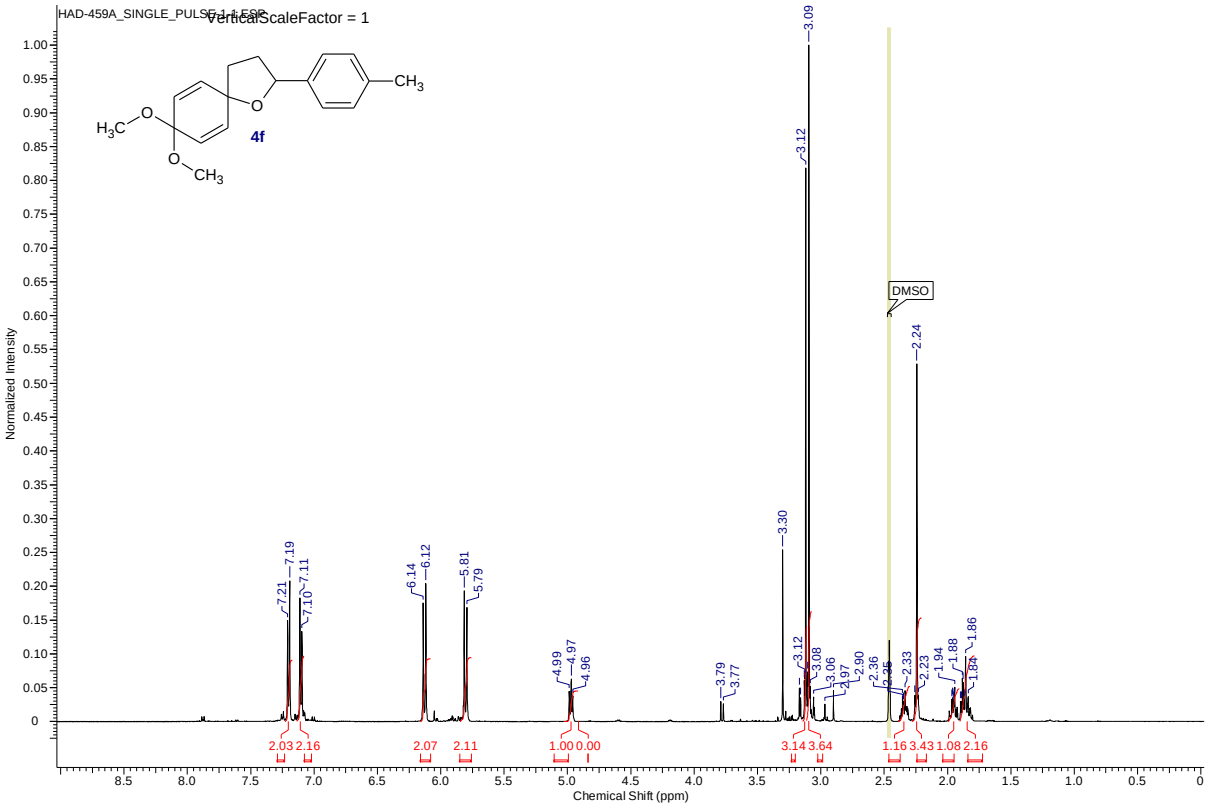

HAD-476_SINGLE_PULSE_QEC_1.1.ESP
VerticalScaleFactor = 1
4c
Normalized Intensity
Chemical Shift (ppm)
134.00
133.66
126.55
125.99
121.24
92.46
76.60
69.35
49.23
49.03
40.73
39.67
39.51
39.34
39.18
39.00
28.90

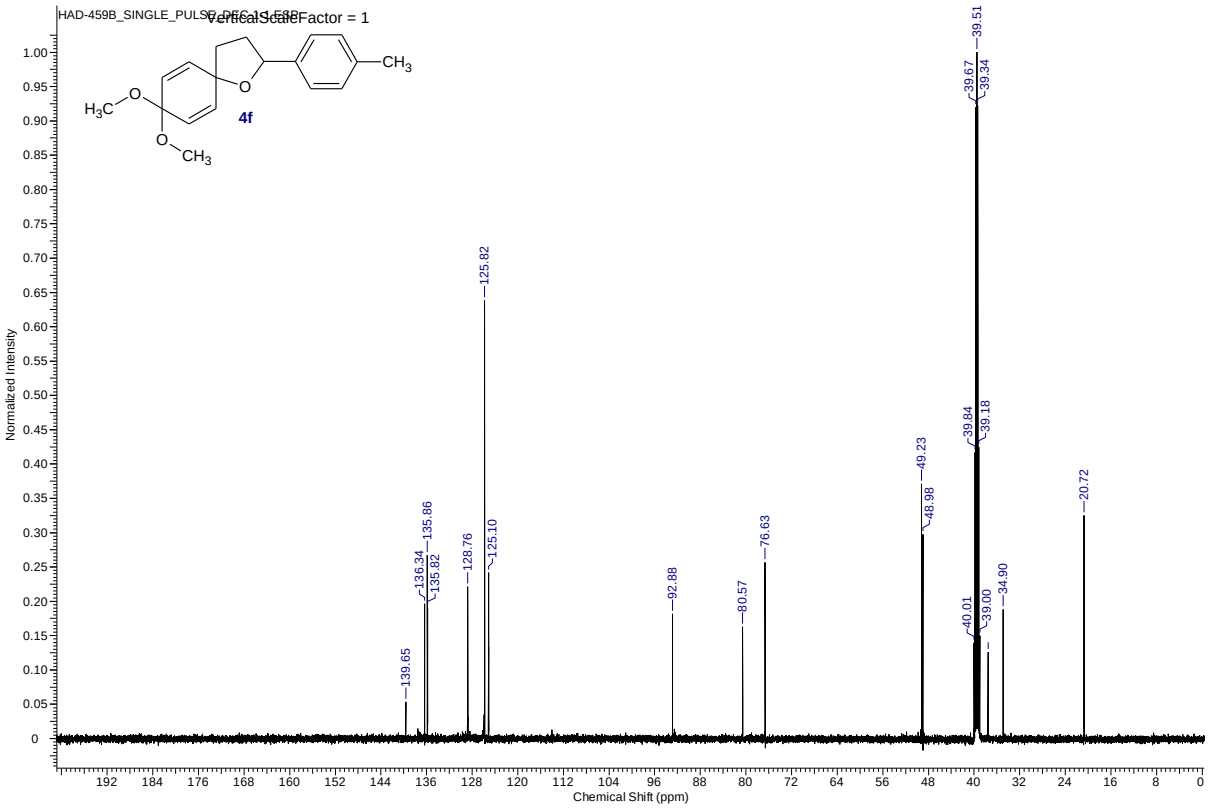

HAD-440_SINGLE_PULSE_1.1ESP
VerticalScaleFactor = 1
4d
Normalized Intensity
Chemical Shift (ppm)
6.06
6.04
6.04
6.00
5.98
5.77
5.77
5.75
5.74
4.15
4.14
4.14
4.13
4.12
4.11
3.34
3.13
3.11
2.50
2.50
2.12
2.11
2.10
1.85
1.84
1.83
1.82
1.63
1.62
1.60
1.59
1.58
1.17
1.16
1.04 1.01 2.01
1.00
6.15
1.04 2.03 1.10
3.14

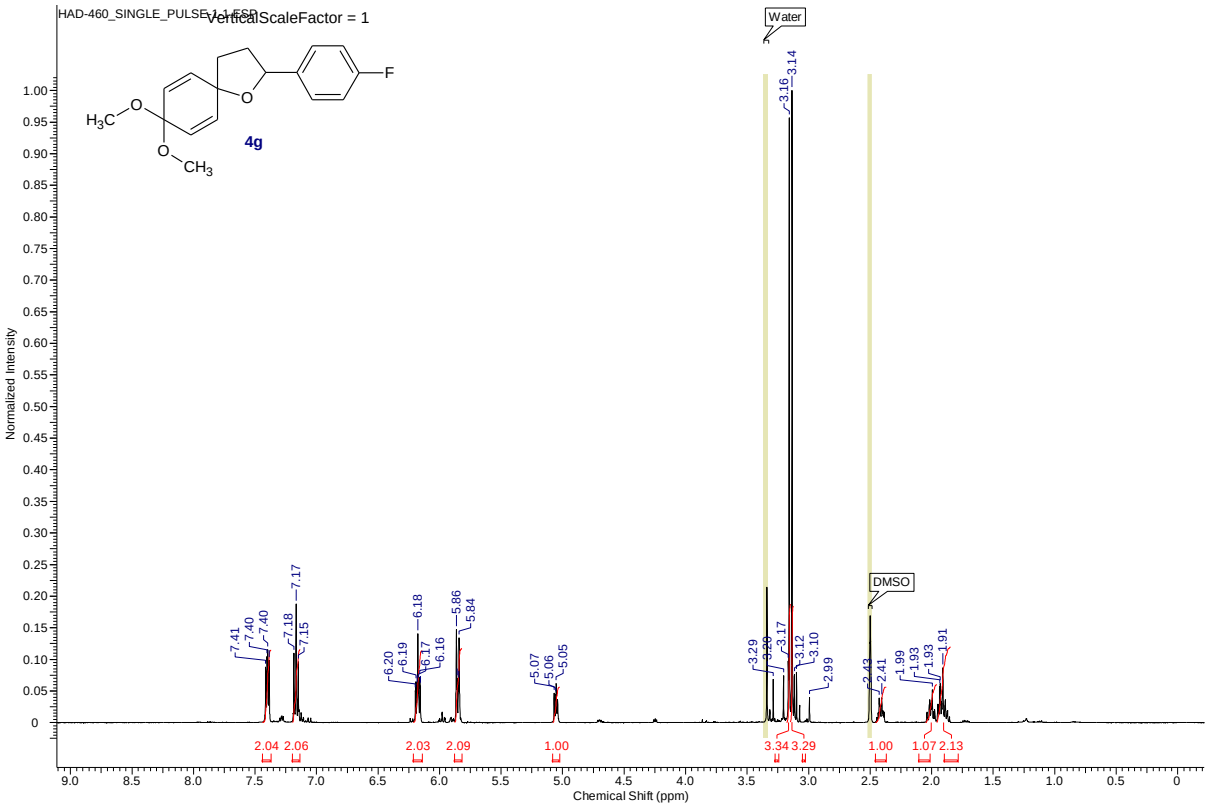

HAD-440_SINGLE_PULSE_QEC_1.1ESP
VerticalScaleFactor = 1
4d
Normalized Intensity
Chemical Shift (ppm)
136.78
136.03
124.63
92.92
76.22
75.14
49.23
48.94
40.02
39.84
39.68
39.51
39.35
39.18
37.46
33.32
21.62

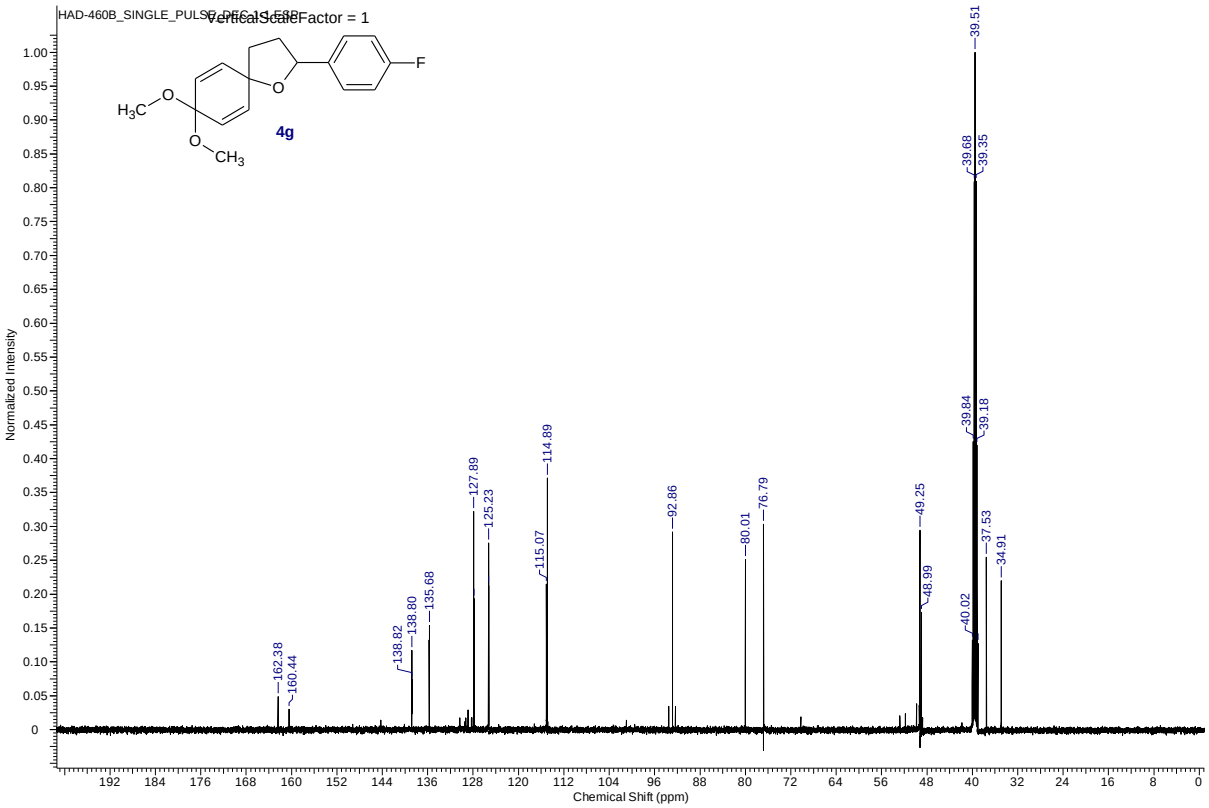

HAD-447_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
Water
4e
Normalized Intensity
Chemical Shift (ppm)

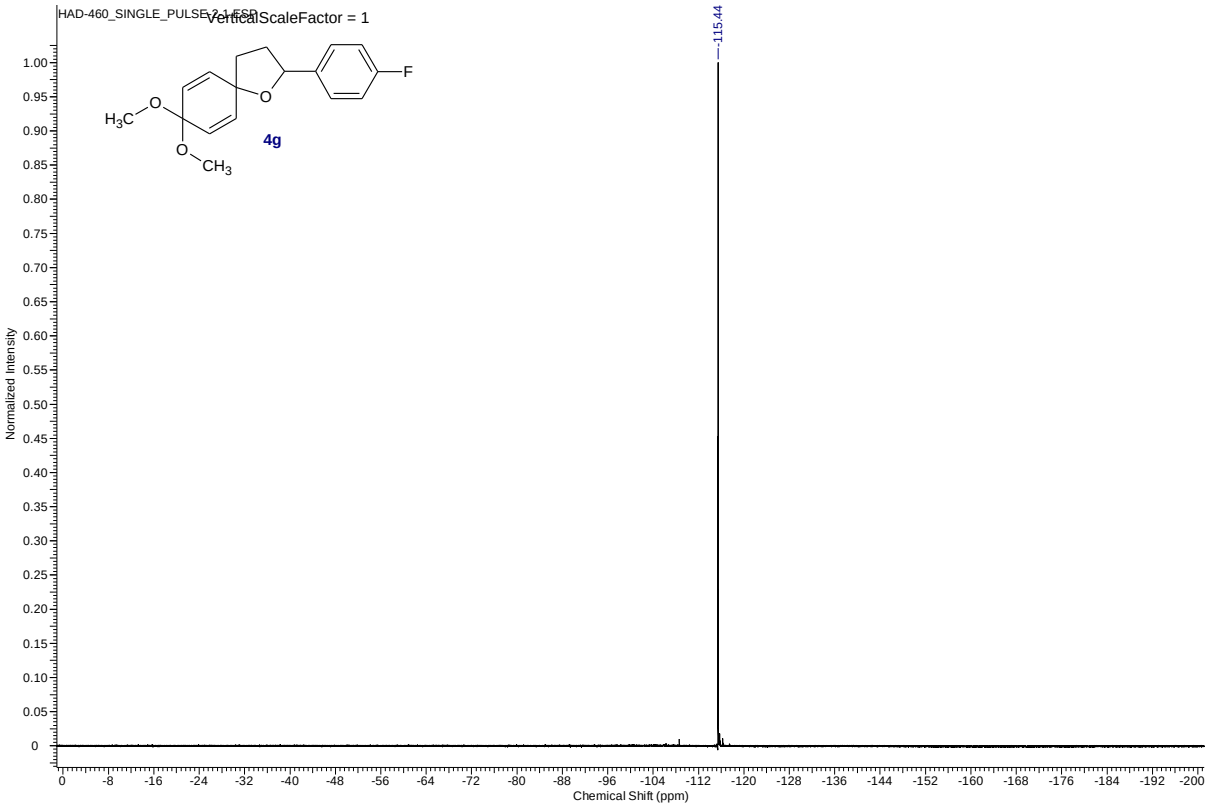

AKA-015_SINGLE_PULSE_DEC_1_1.ESP
VerticalScaleFactor = 1
4e
Normalized Intensity
Chemical Shift (ppm)

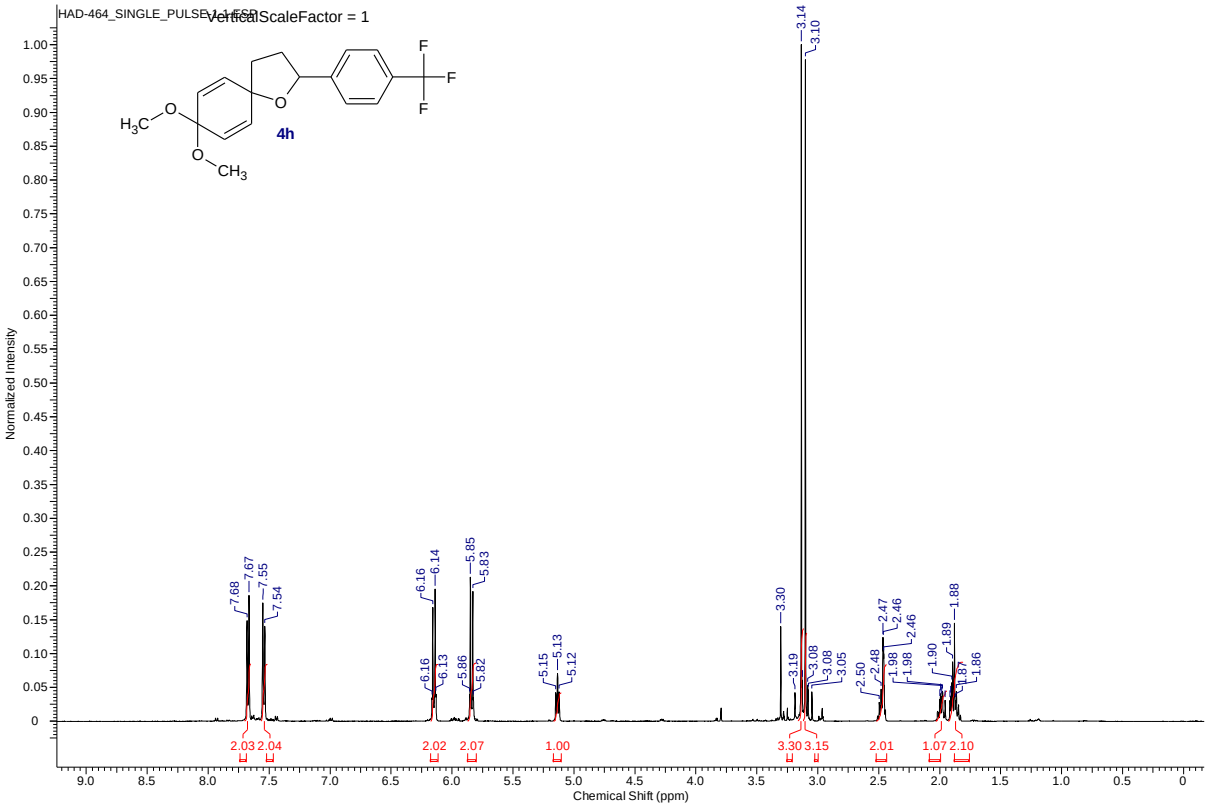

HAD-459A_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
4f
DMSO
Normalized Intensity
Chemical Shift (ppm)

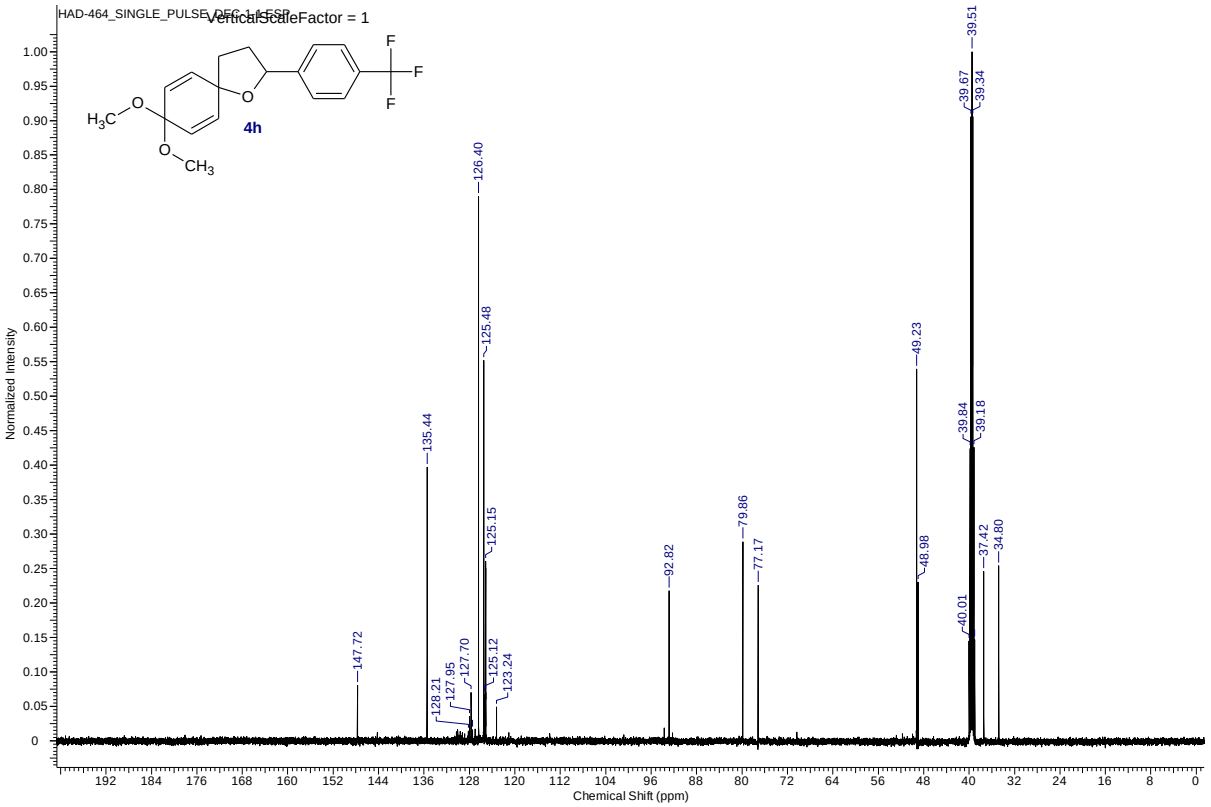

HAD-459B_SINGLE_PULSE_DEC_1_1.ESP
VerticalScaleFactor = 1
4f
Normalized Intensity
Chemical Shift (ppm)

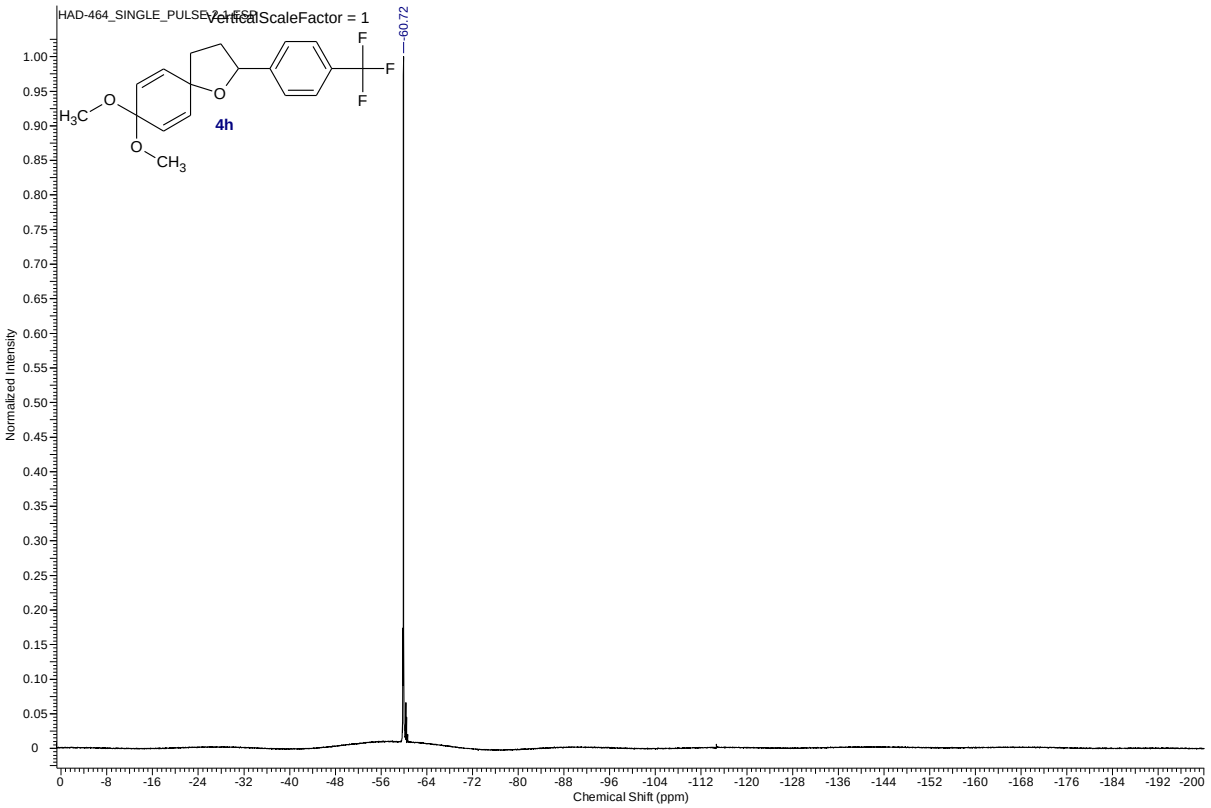

HAD-460_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
4g
Water
DMSO
Normalized Intensity
Chemical Shift (ppm)

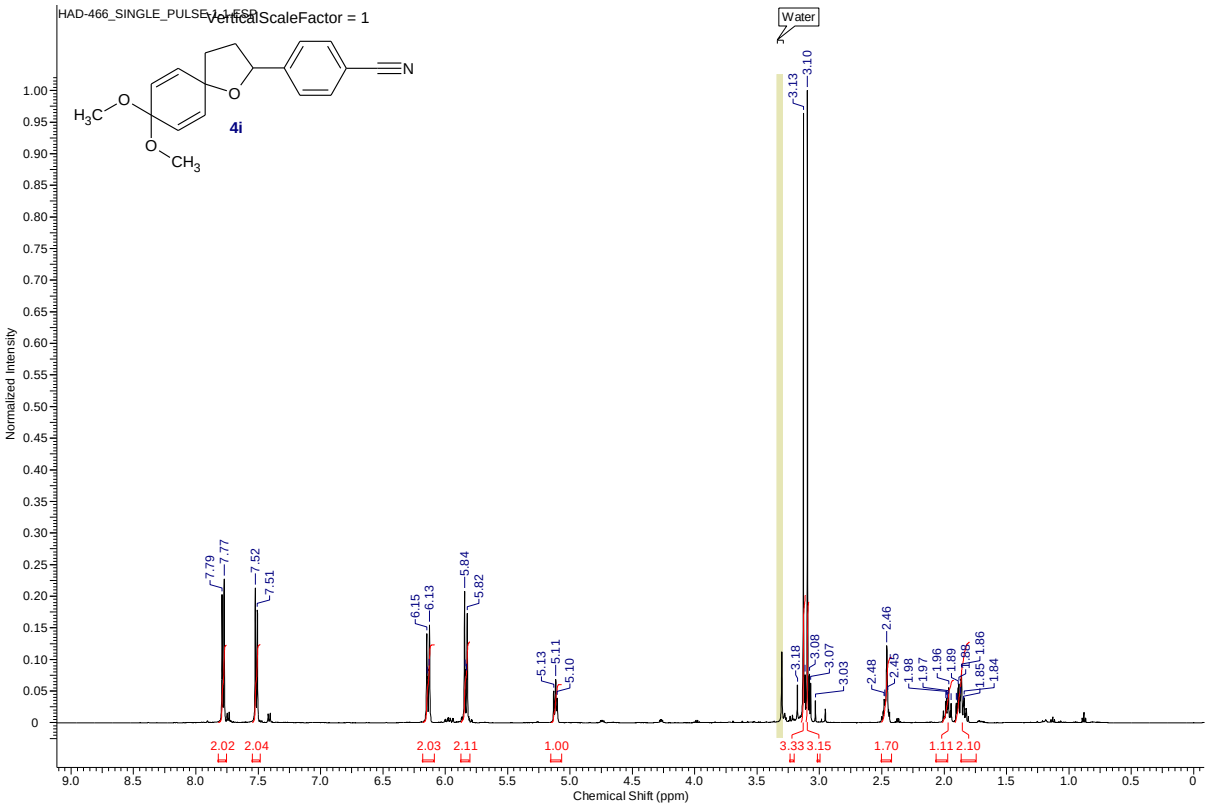

HAD-460B_SINGLE_PULSE_DEC_1_1.ESP
VerticalScaleFactor = 1
4g
Normalized Intensity
Chemical Shift (ppm)

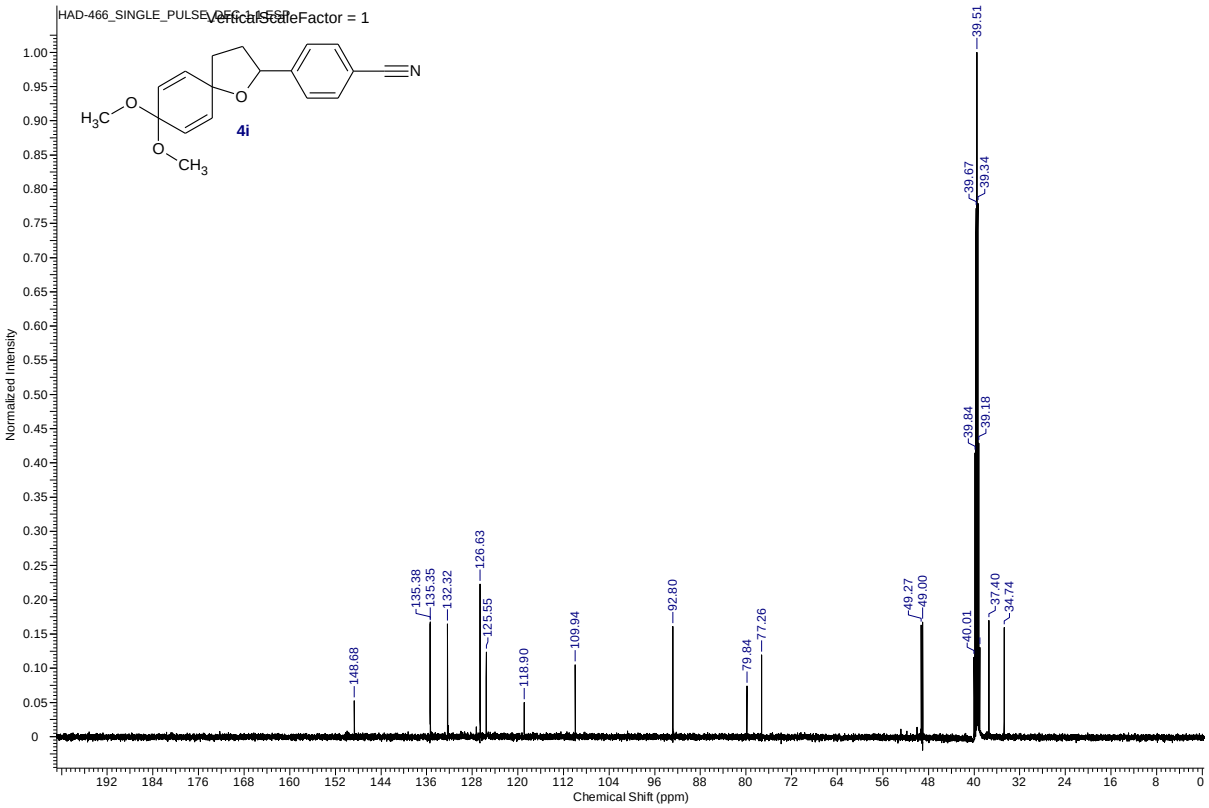

HAD-460_SINGLE_PULSE_2_1.ESP
VerticalScaleFactor = 1
4g
-115.44
Normalized Intensity
Chemical Shift (ppm)

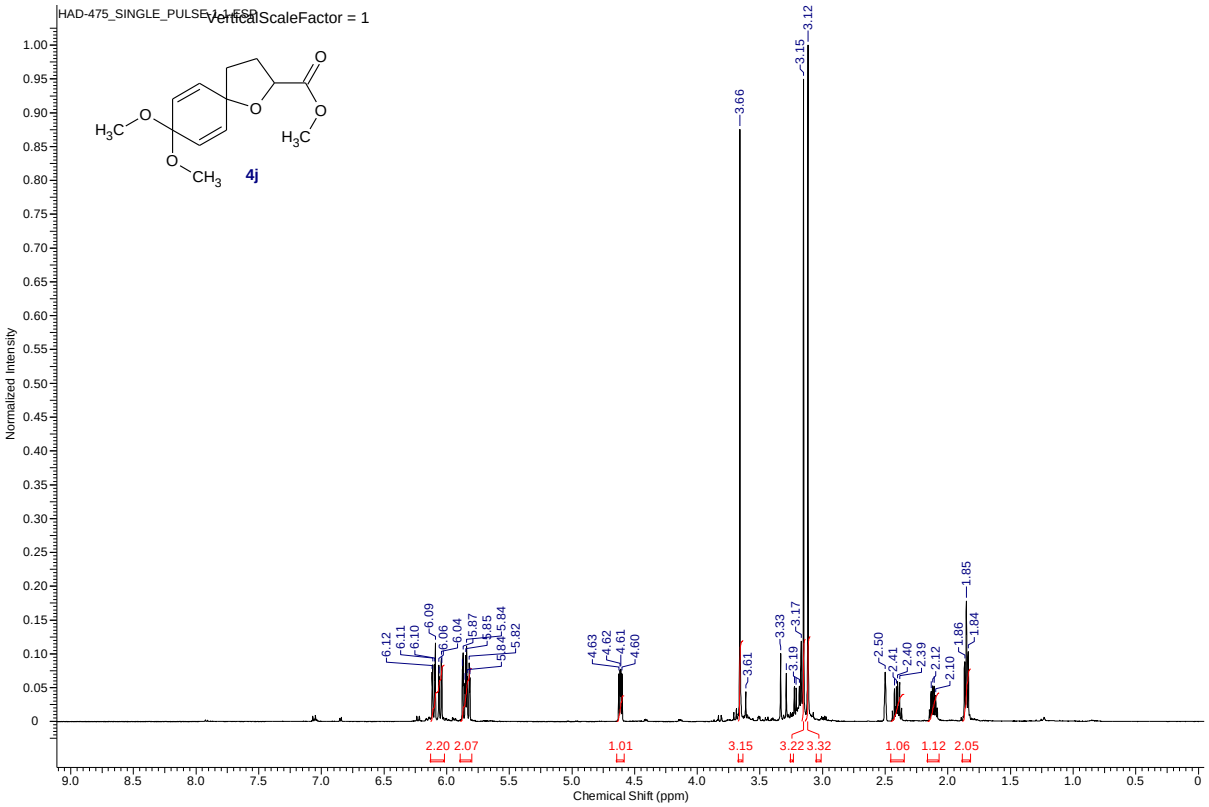

HAD-464_SINGLE_PULSE_1_1.ESP
VerticalScaleFactor = 1
4h
3.14
3.10
7.68
7.67
7.55
7.54
6.16
6.14
5.85
5.83
6.13
5.86
5.82
5.15
5.13
5.12
3.30
3.19
3.08
3.05
2.50
2.48
2.47
2.46
2.46
1.98
1.98
1.90
1.89
1.88
1.87
1.86
2.03
2.04
2.02
2.07
1.00
3.30
3.15
2.01
1.07
2.10
Normalized Intensity
Chemical Shift (ppm)

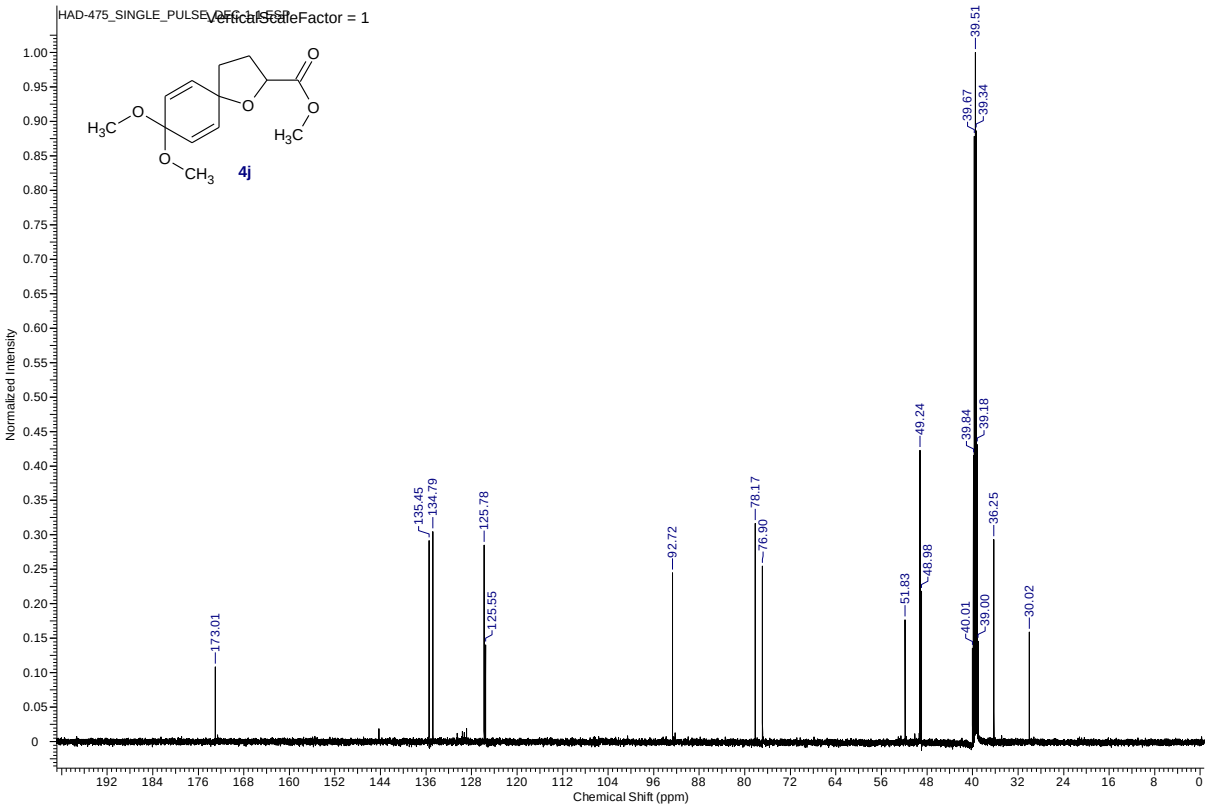

HAD-464_SINGLE_PULSE_DEC-1-1.ESP
VerticalScaleFactor = 1
4h
Normalized Intensity
Chemical Shift (ppm)
147.72
135.44
128.21
127.95
127.70
126.40
125.48
125.15
125.12
123.24
92.82
79.86
77.17
49.23
48.98
40.01
39.84
39.67
39.51
39.34
39.18
37.42
34.80

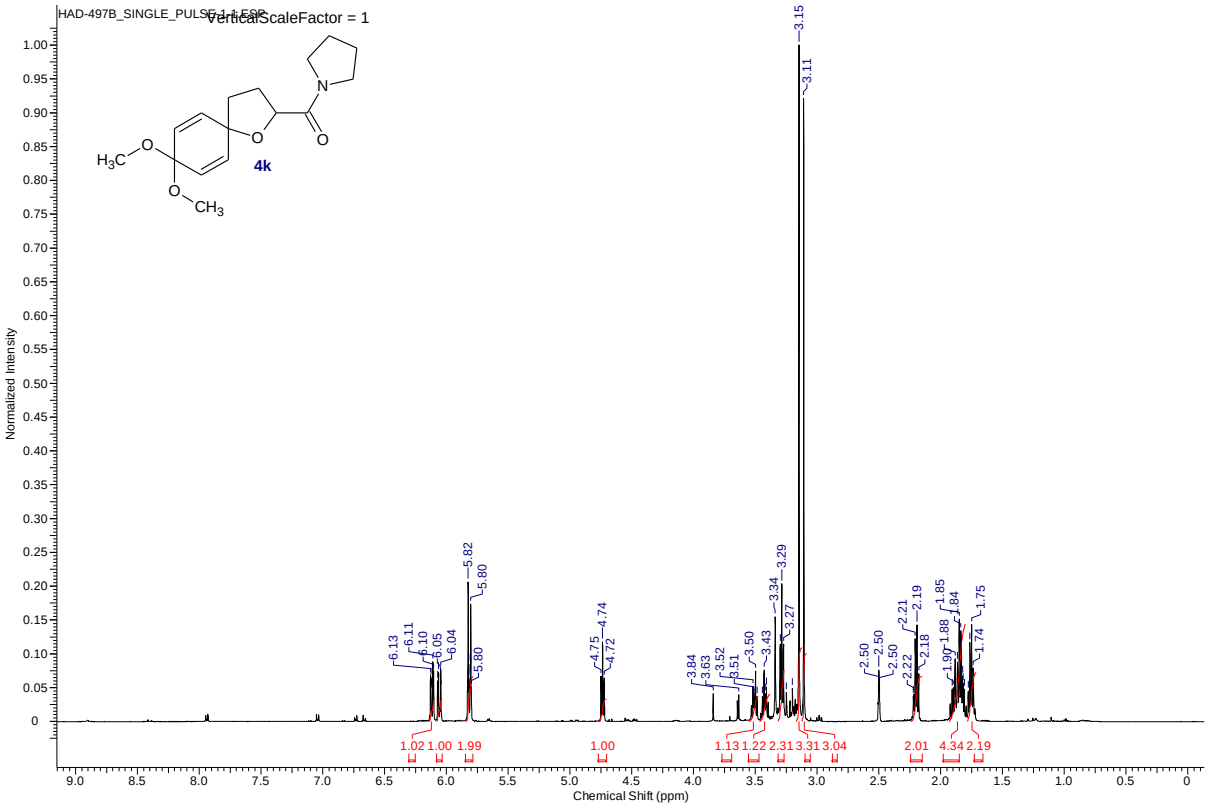

HAD-464_SINGLE_PULSE_2-1.ESP
VerticalScaleFactor = 1
4h
Normalized Intensity
Chemical Shift (ppm)
60.72

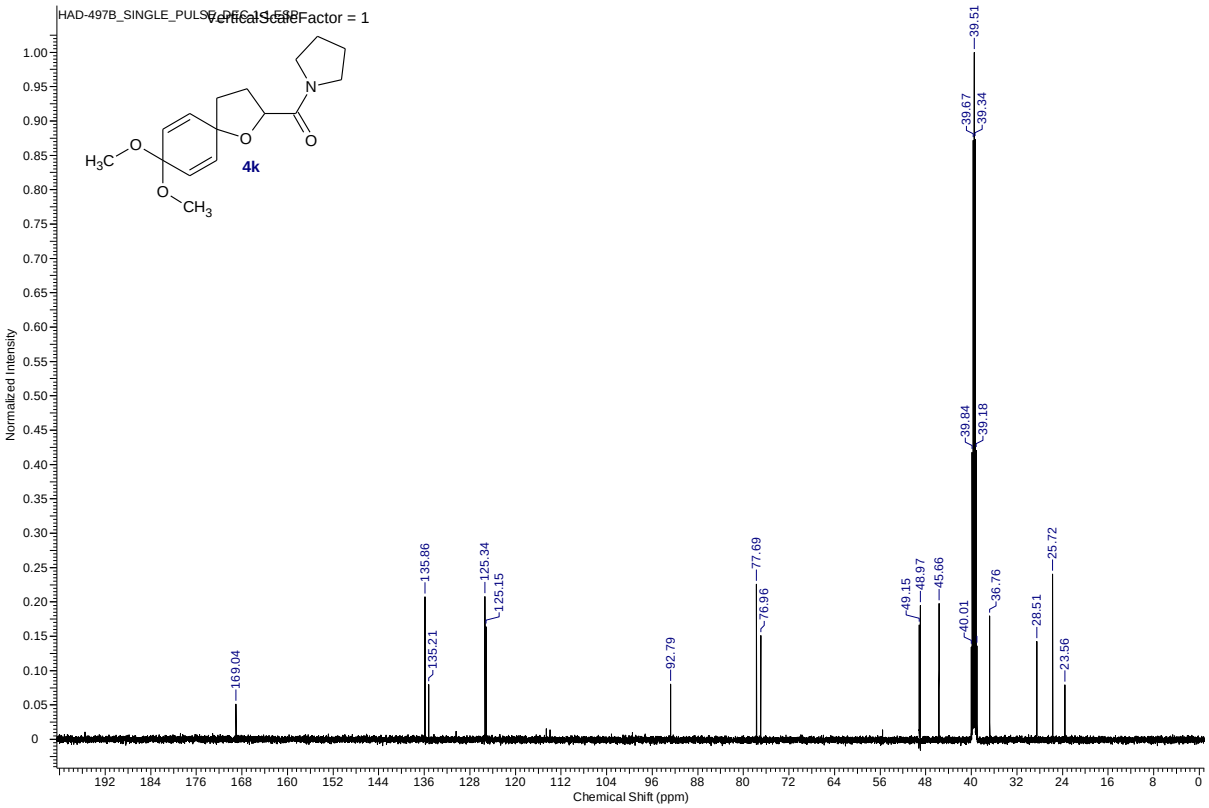

HAD-466_SINGLE_PULSE_1.1ESP
VerticalScaleFactor = 1
Water
4i
Normalized Intensity
Chemical Shift (ppm)

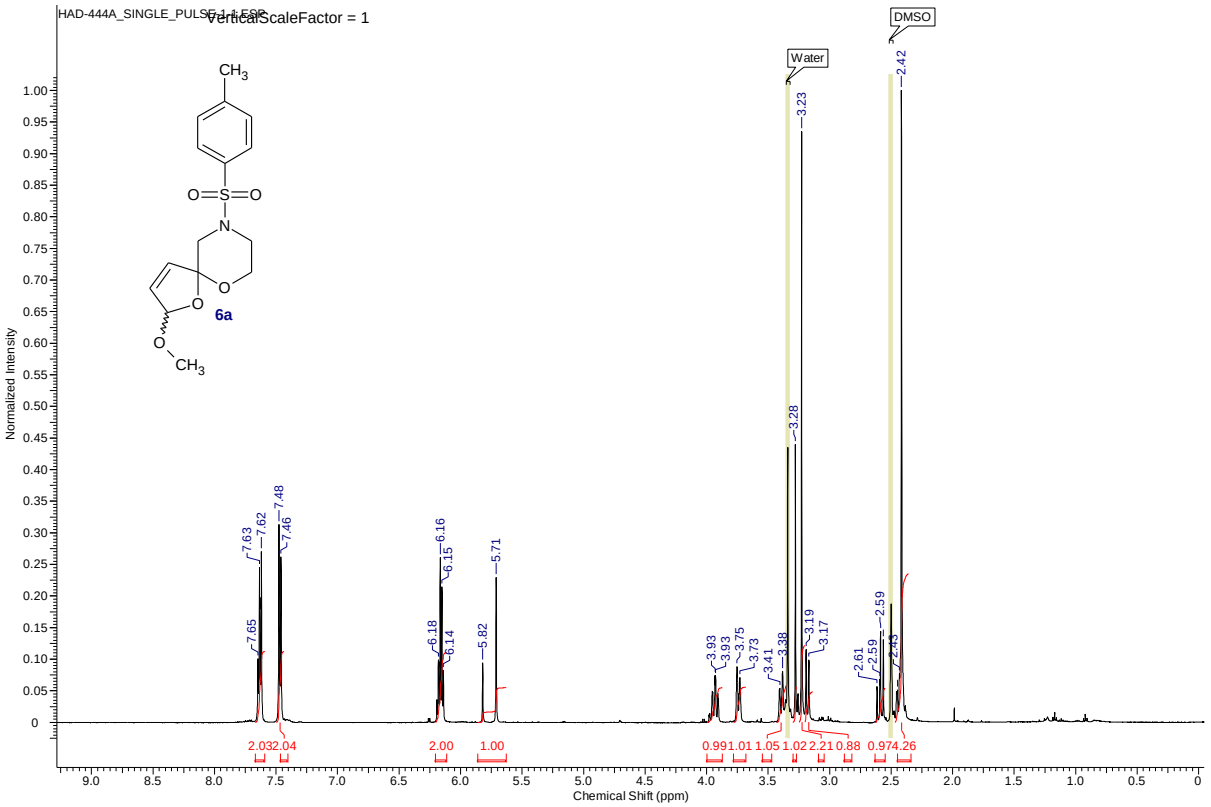

HAD-466_SINGLE_PULSE_QEC_1.1ESP
VerticalScaleFactor = 1
4i
Normalized Intensity
Chemical Shift (ppm)

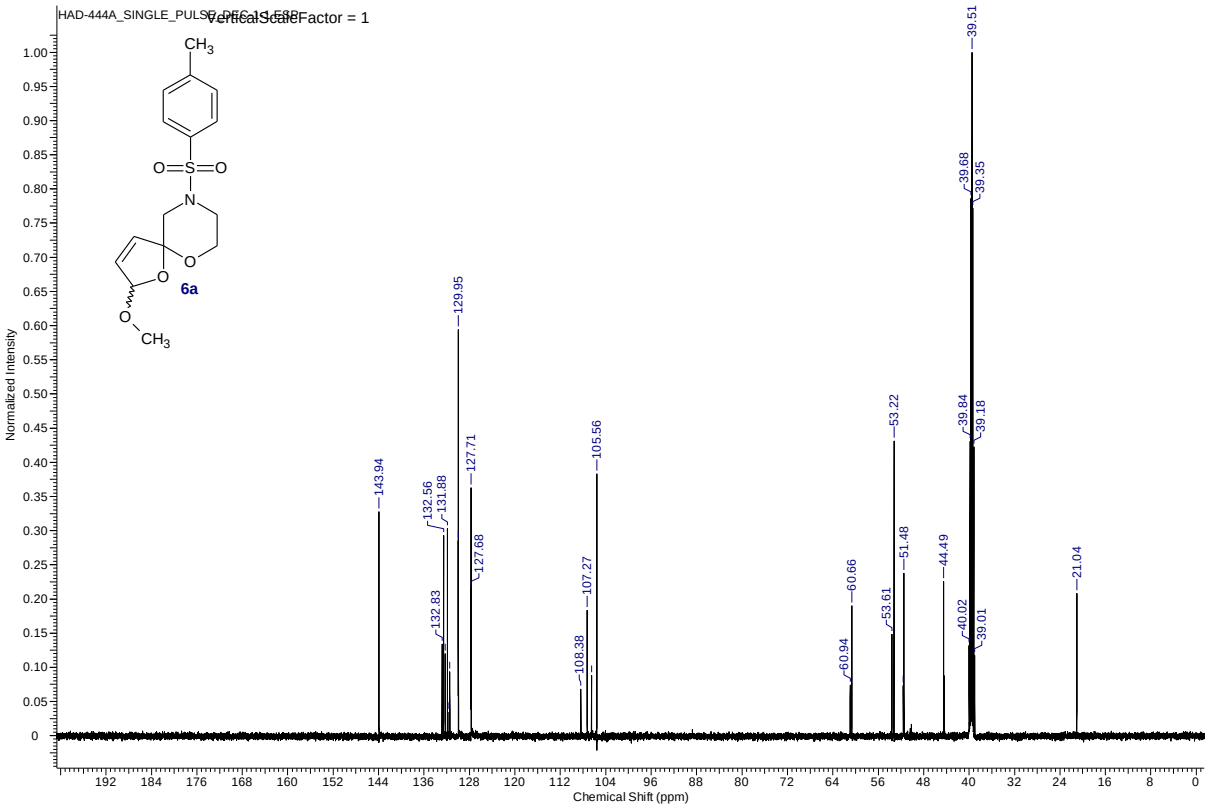

HAD-475_SINGLE_PULSE_1.1ESP
VerticalScaleFactor = 1
4j
Normalized Intensity
Chemical Shift (ppm)
6.12
6.11
6.10
6.09
6.06
6.04
5.87
5.85
5.84
5.82
4.63
4.62
4.61
4.60
3.66
3.61
3.33
3.17
3.15
3.12
3.19
2.50
2.41
2.40
2.39
2.12
2.10
1.86
1.85
1.84
2.20
2.07
1.01
3.15
3.22
3.32
1.06
1.12
2.05

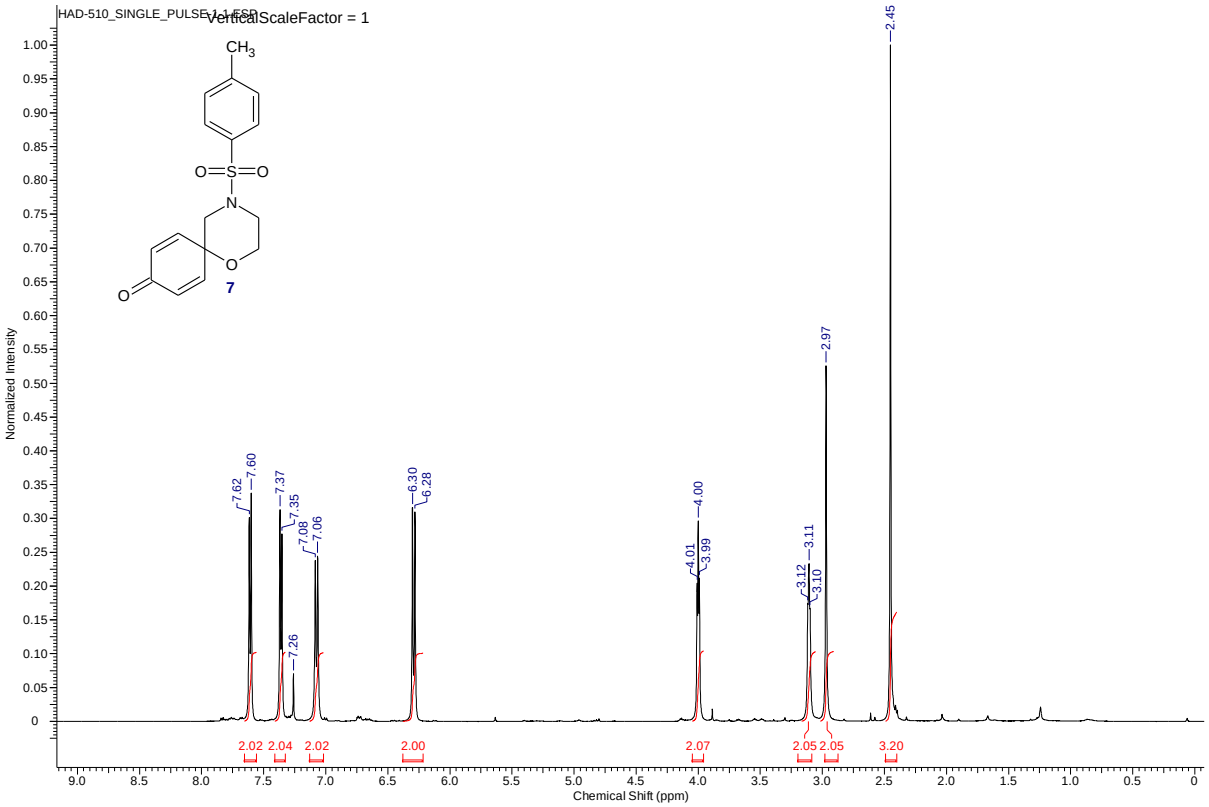

HAD-475_SINGLE_PULSE_QEC_1.1ESP
VerticalScaleFactor = 1
4j
Normalized Intensity
Chemical Shift (ppm)
173.01
135.45
134.79
125.78
125.55
92.72
78.17
76.90
51.83
49.24
48.98
40.01
39.84
39.67
39.51
39.34
39.18
39.00
36.25
30.02

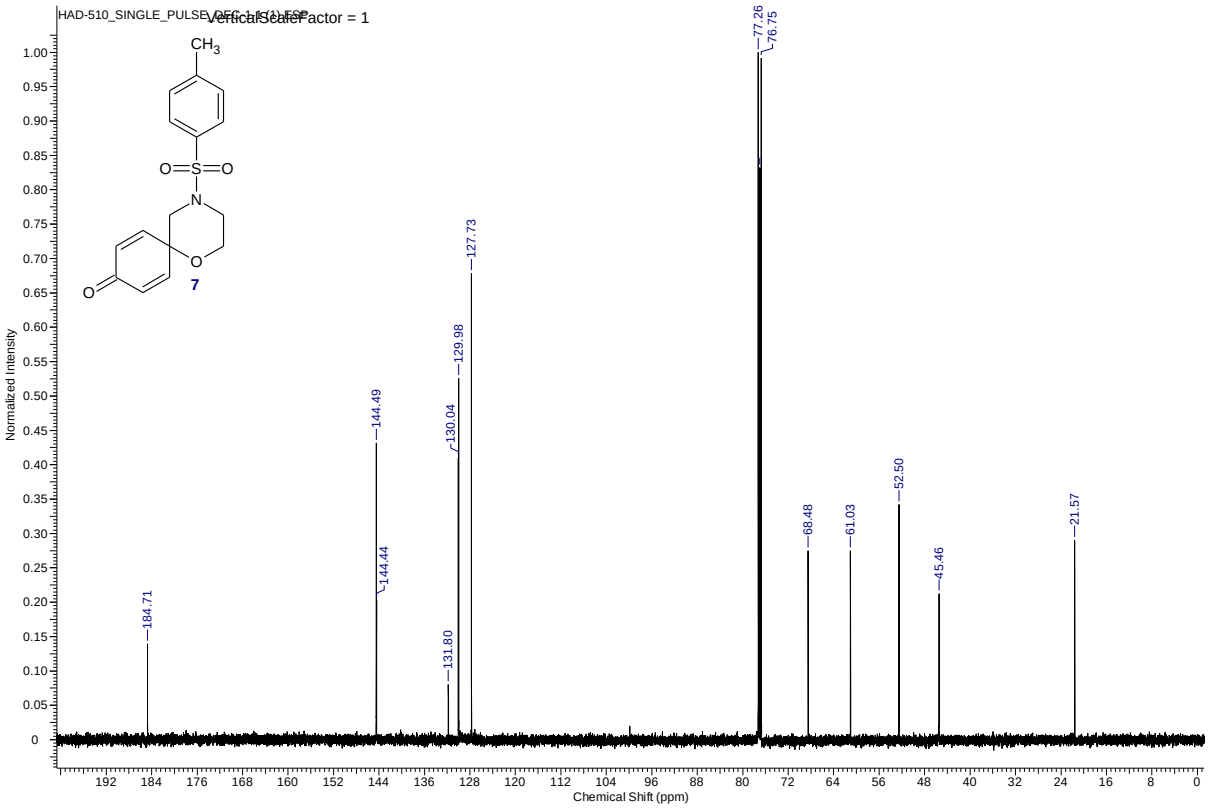

HAD-497B_SINGLE_PULSE.1.1.ESP
VerticalScaleFactor = 1
4k
Normalized Intensity
Chemical Shift (ppm)

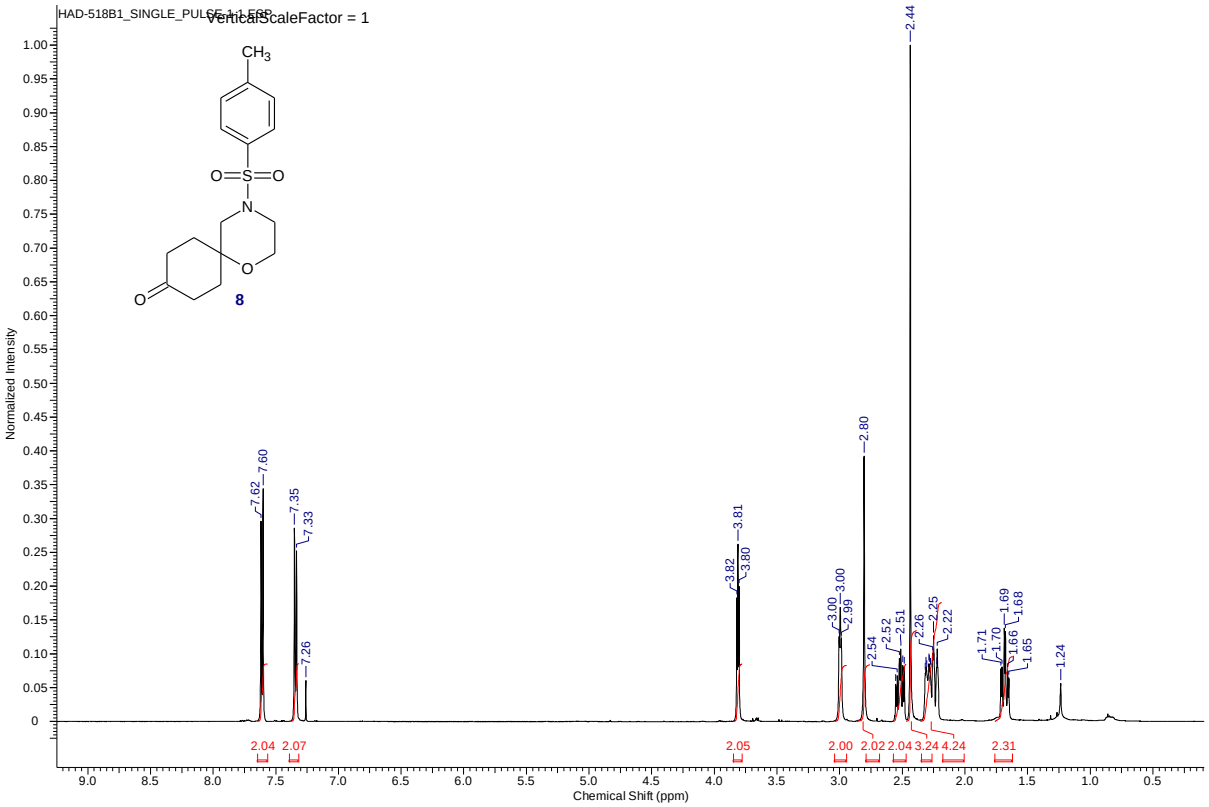

HAD-497B_SINGLE_PULSE_DEC.1.1.ESP
VerticalScaleFactor = 1
4k
Normalized Intensity
Chemical Shift (ppm)

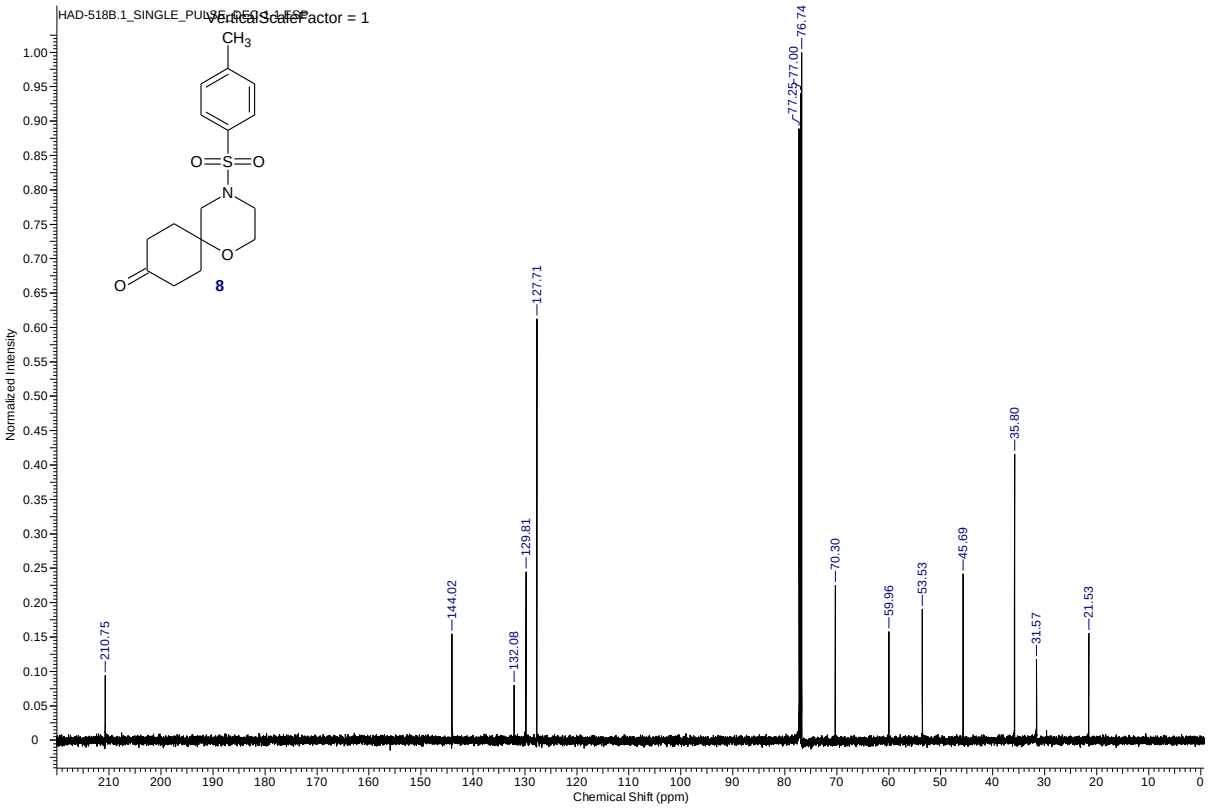

HAD-444A_SINGLE_PULSE_1-1.ESP
VerticalScaleFactor = 1
Water
DMSO
6a
Normalized Intensity
Chemical Shift (ppm)

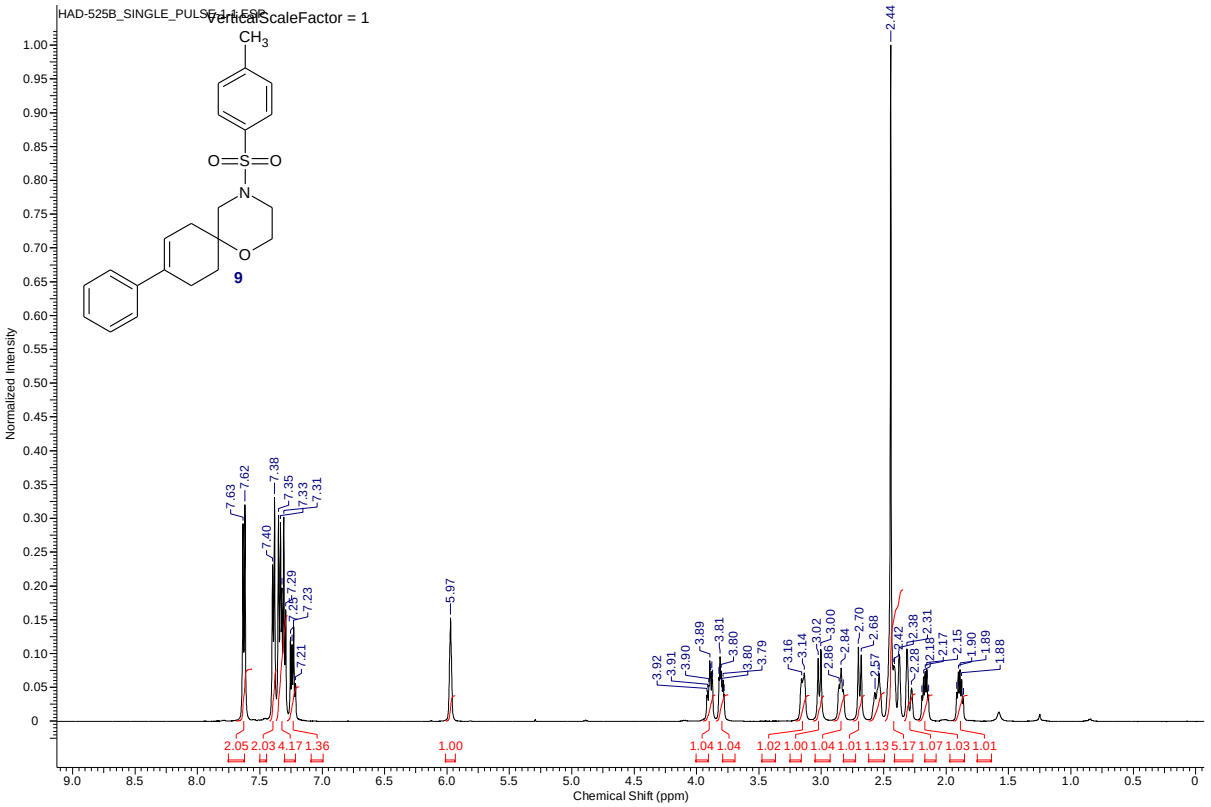

HAD-444A_SINGLE_PULSE_DEC_1-1.ESP
VerticalScaleFactor = 1
6a
Normalized Intensity
Chemical Shift (ppm)

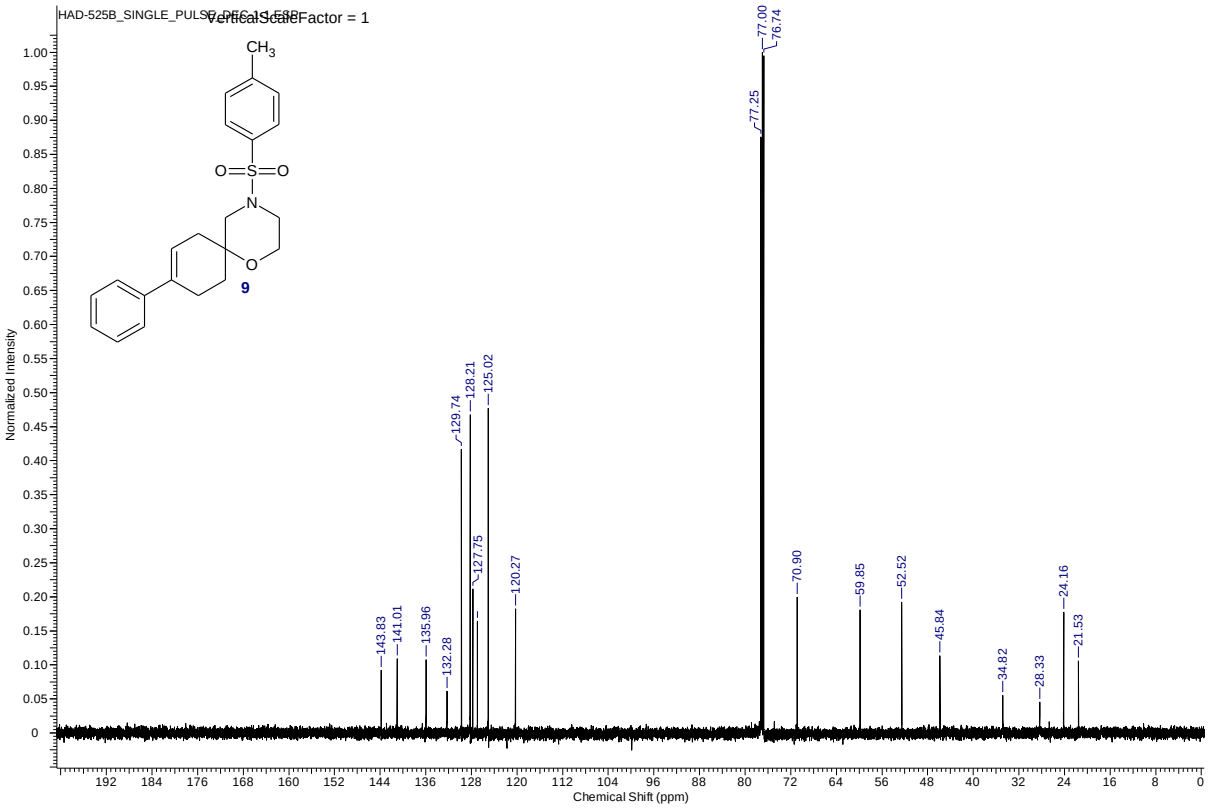

HAD-510_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
O
7
Normalized Intensity
Chemical Shift (ppm)
2.45
2.97
7.62
7.60
7.37
7.35
7.08
7.06
7.26
6.30
6.28
4.00
4.01
3.99
3.12
3.11
3.10
2.02
2.04
2.02
2.00
2.07
2.05
2.05
3.20

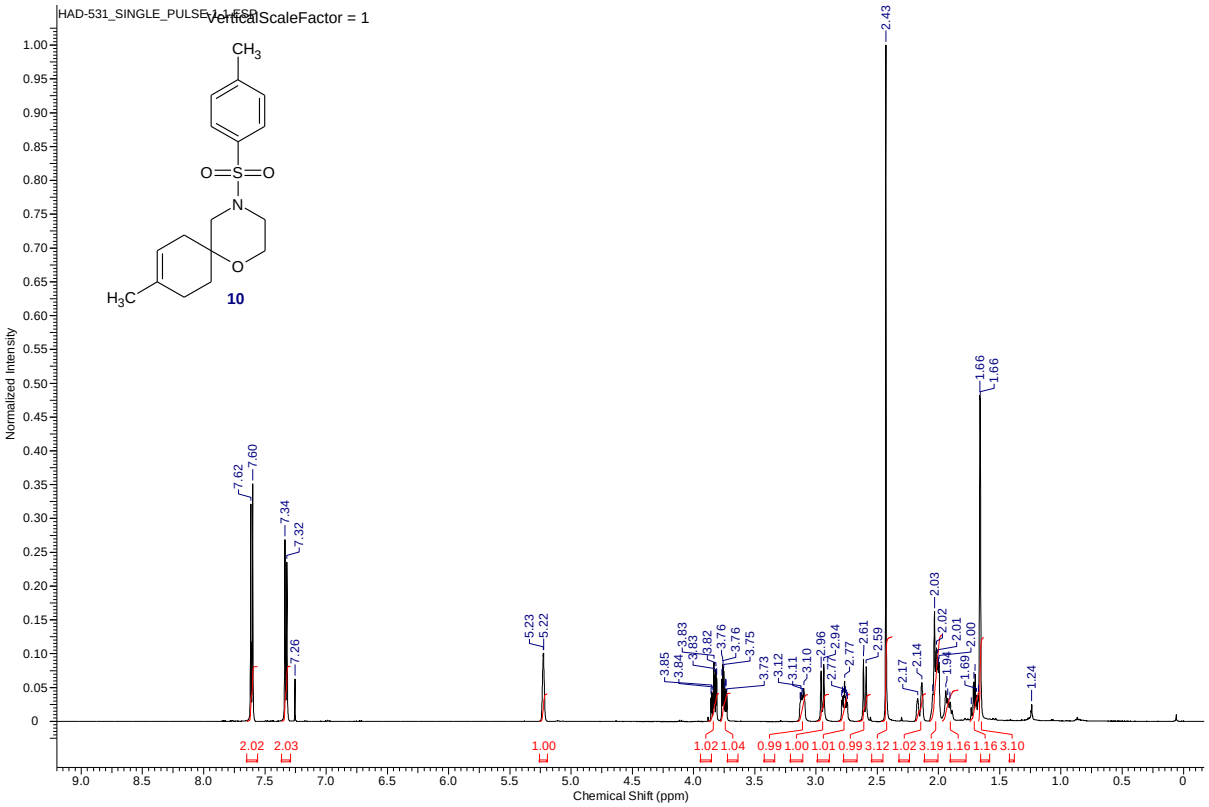

HAD-510_SINGLE_PULSE_QFG_1.1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
O
7
Normalized Intensity
Chemical Shift (ppm)
77.26
76.75
127.73
129.98
144.49
130.04
144.44
131.80
184.71
68.48
61.03
52.50
45.46
21.57

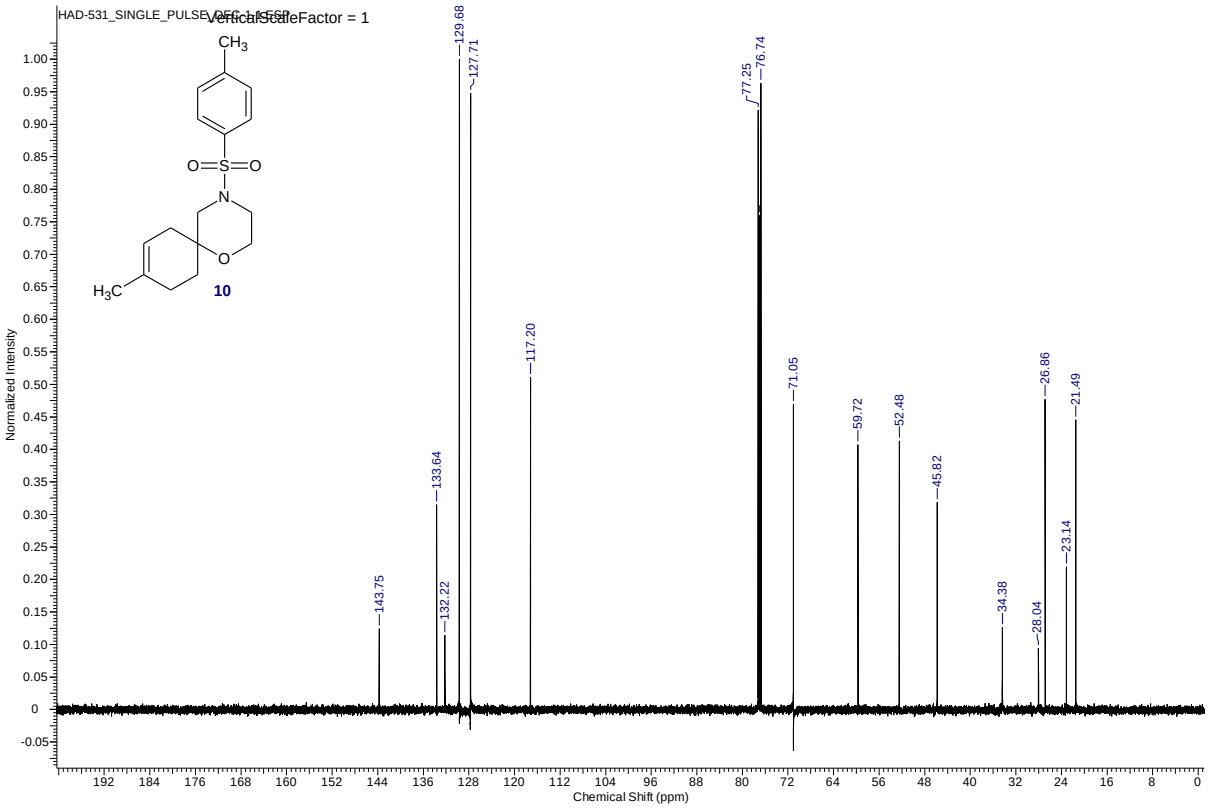

HAD-518B1_SINGLE_PULSE.1.1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
O
8
Normalized Intensity
Chemical Shift (ppm)
2.44
2.80
7.62
7.60
7.35
7.33
7.26
3.81
3.82
3.80
3.00
3.00
2.99
2.54
2.52
2.51
2.26
2.25
2.22
1.71
1.70
1.69
1.68
1.66
1.65
1.24
2.04
2.07
2.05
2.00
2.02
2.04
3.24
4.24
2.31

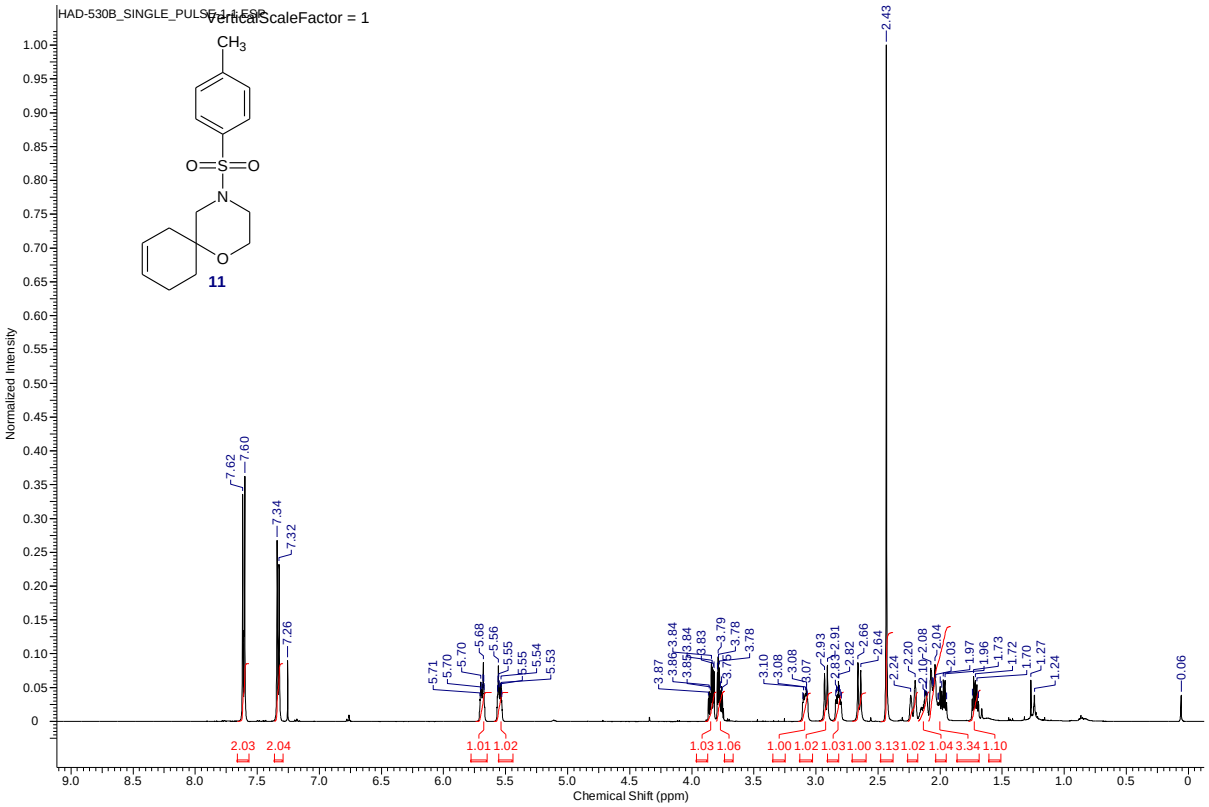

HAD-518B.1_SINGLE_PULSE_DEC.1.1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
O
8
Normalized Intensity
Chemical Shift (ppm)
77.25
77.00
76.74
127.71
144.02
129.81
132.08
210.75
70.30
59.96
53.53
45.69
35.80
31.57
21.53

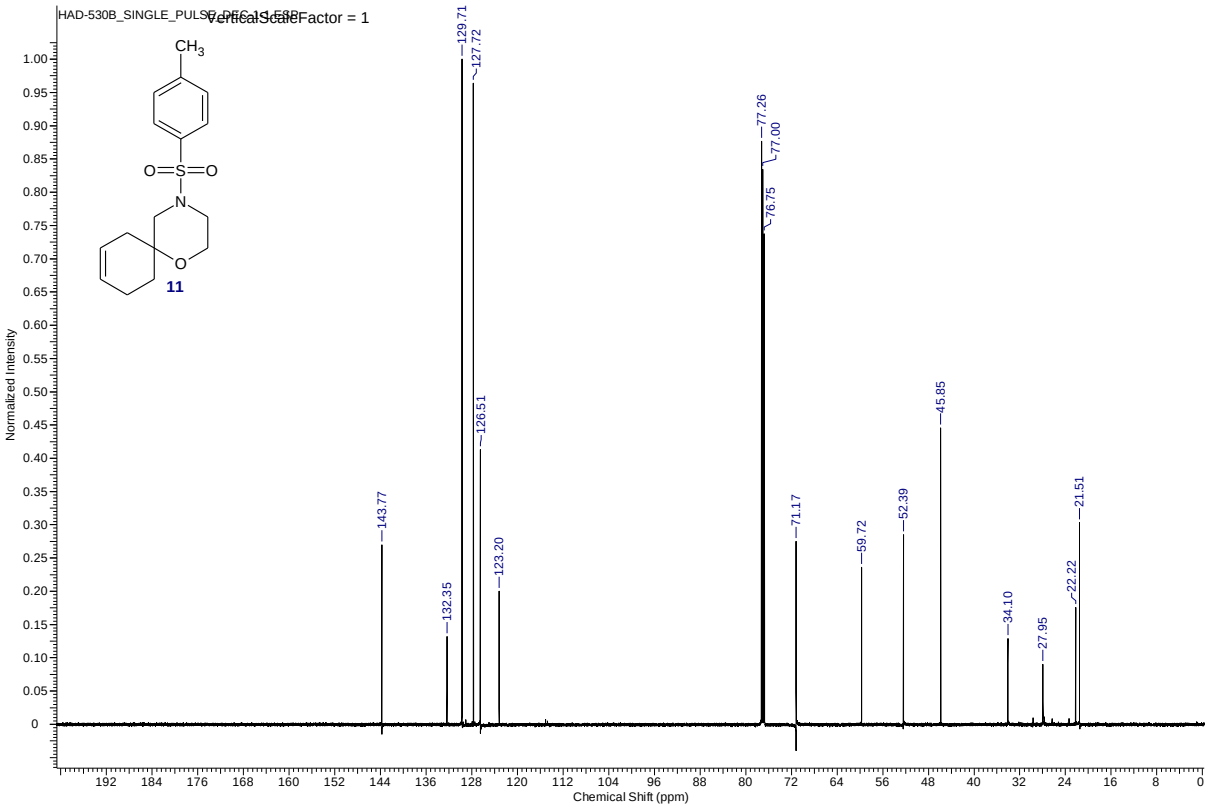

HAD-525B_SINGLE_PULSE.1.1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
9
Normalized Intensity
Chemical Shift (ppm)
7.63
7.62
7.40
7.38
7.35
7.33
7.31
7.29
7.25
7.23
7.21
5.97
3.92
3.91
3.90
3.89
3.81
3.80
3.80
3.79
3.16
3.14
3.02
3.00
2.86
2.84
2.70
2.68
2.57
2.44
2.42
2.38
2.31
2.17
2.15
1.90
1.89
1.88
2.05
2.03
4.17
1.36
1.00
1.04
1.04
1.02
1.00
1.04
1.01
1.13
5.17
1.07
1.03
1.01

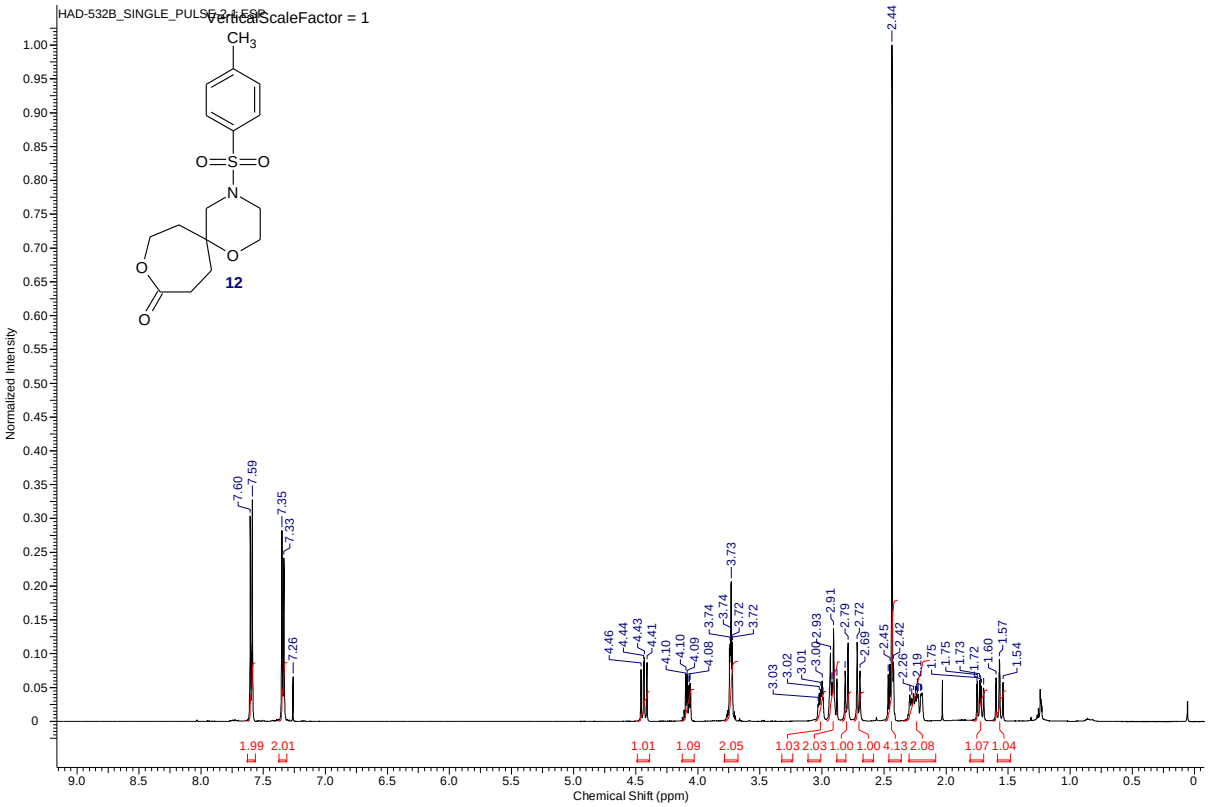

HAD-525B_SINGLE_PULSE_DEC.14.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
9
Normalized Intensity
Chemical Shift (ppm)
77.00
76.74
77.25
143.83
141.01
135.96
132.28
129.74
128.21
127.75
125.02
120.27
70.90
59.85
52.52
45.84
34.82
28.33
24.16
21.53

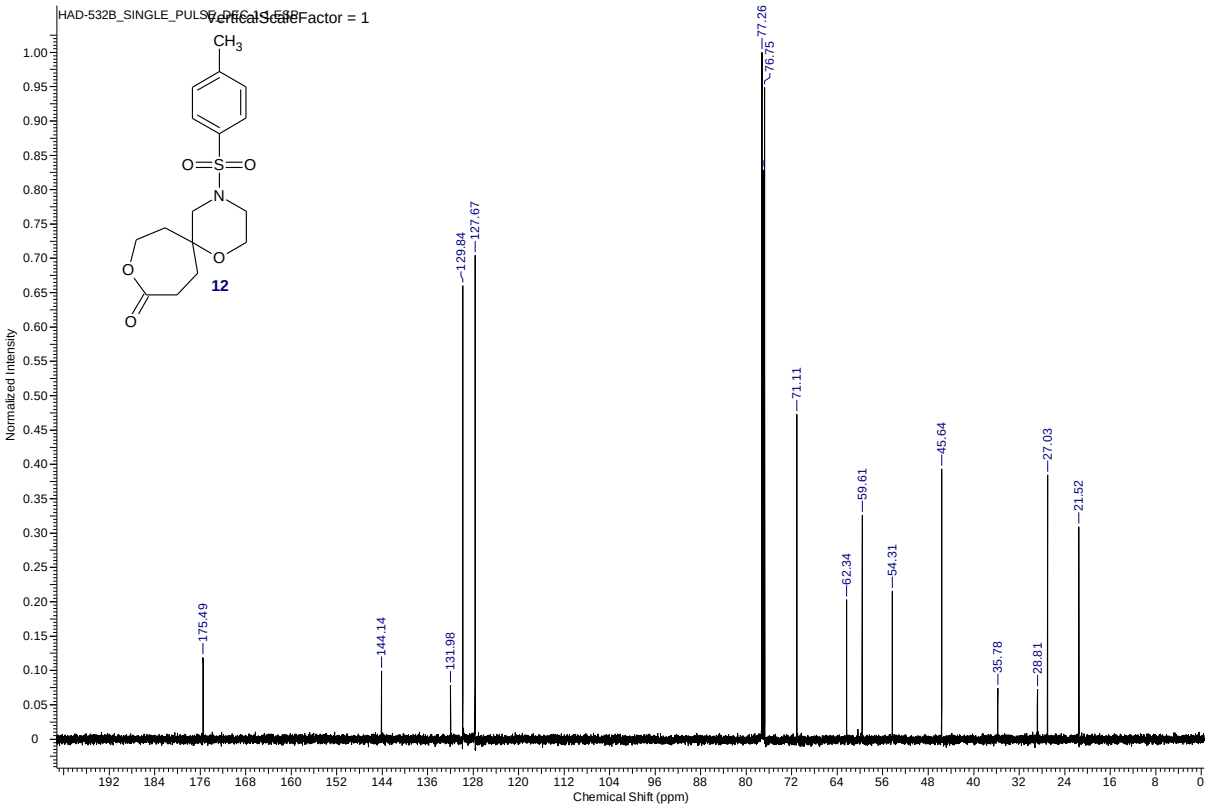

HAD-531_SINGLE_PULSE_1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
H3C
10
Normalized Intensity
Chemical Shift (ppm)
2.43
1.66
1.66
7.62
7.60
7.34
7.32
7.26
5.23
5.22
3.85
3.84
3.83
3.83
3.82
3.76
3.76
3.75
3.73
3.12
3.11
3.10
2.96
2.94
2.77
2.77
2.61
2.59
2.17
2.14
2.03
2.02
2.01
2.00
1.94
1.69
1.24
2.02 2.03
1.00
1.02 1.04
0.99 1.00 1.01 0.99 3.12 1.02 3.19 1.16 1.16 3.10

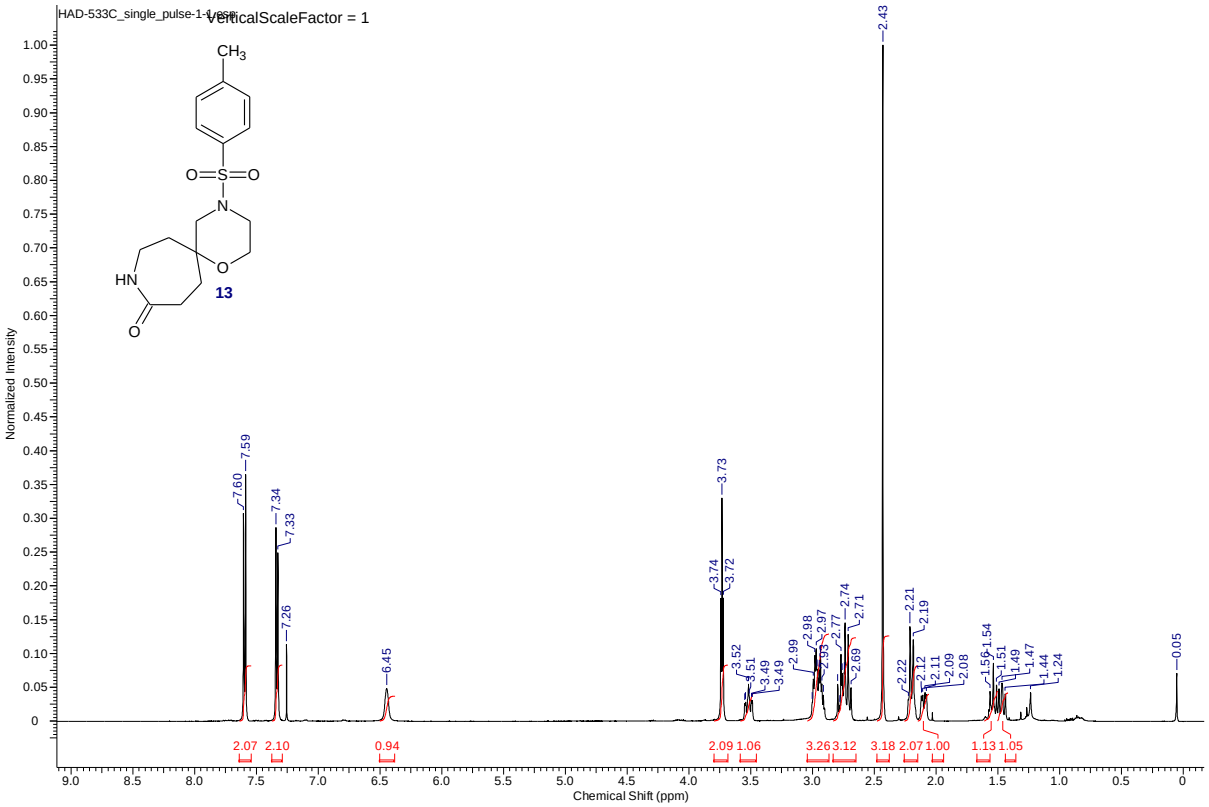

HAD-531_SINGLE_PULSE_QFC.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
H3C
10
Normalized Intensity
Chemical Shift (ppm)
129.68
127.71
77.25
76.74
143.75
133.64
132.22
117.20
71.05
59.72
52.48
45.82
34.38
28.04
26.86
23.14
21.49

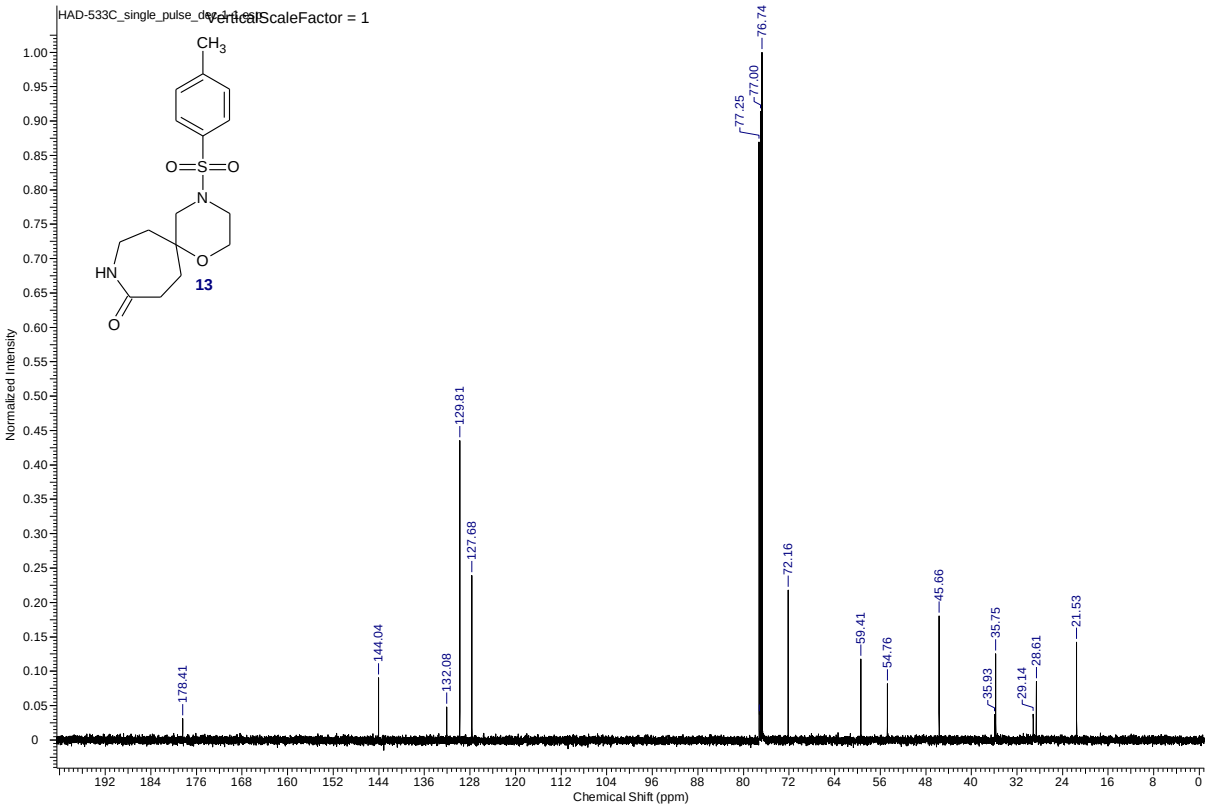

HAD-530B_SINGLE_PULSE_1.1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
11
Normalized Intensity
Chemical Shift (ppm)
2.43
7.62
7.60
7.34
7.32
7.26
5.71
5.70
5.70
5.68
5.56
5.55
5.55
5.54
5.53
3.87
3.86
3.85
3.84
3.84
3.83
3.79
3.78
3.76
3.10
3.08
3.08
3.07
2.93
2.83
2.91
2.82
2.66
2.64
2.24
2.20
2.10
2.08
2.04
2.03
1.97
1.96
1.73
1.72
1.70
1.27
1.24
0.06
2.03
2.04
1.01
1.02
1.03
1.06
1.00
1.02
1.03
1.00
3.13
1.02
1.04
3.34
1.10


HAD-530B_SINGLE_PULSE_DEC_1.1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
11
Normalized Intensity
Chemical Shift (ppm)
129.71
127.72
126.51
77.26
77.00
76.75
143.77
132.35
123.20
71.17
59.72
52.39
45.85
34.10
27.95
22.22
21.51


HAD-532B_SINGLE_PULSE_2.1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
O
O
12
Normalized Intensity
Chemical Shift (ppm)
7.60
7.59
7.35
7.33
7.26
4.46
4.44
4.43
4.41
4.10
4.09
4.08
3.74
3.73
3.72
3.03
3.02
3.01
3.00
2.93
2.91
2.79
2.72
2.69
2.45
2.42
2.26
2.19
1.75
1.73
1.72
1.60
1.57
1.54
2.44
1.99
2.01
1.01
1.09
2.05
1.03
2.03
1.00
1.00
4.13
2.08
1.07
1.04


HAD-532B_SINGLE_PULSE_DEC_13.1.ESP
VerticalScaleFactor = 1
CH3
O=S=O
N
O
O
O
12
Normalized Intensity
Chemical Shift (ppm)
77.26
76.75
129.84
127.67
71.11
59.61
45.64
27.03
21.52
62.34
54.31
175.49
144.14
131.98
35.78
28.81


HAD-533C_single_pulse-1-1.esp
VerticalScaleFactor = 1
CH3
O=S=O
N
O
HN
O
13
Normalized Intensity
Chemical Shift (ppm)
2.43
7.60
7.59
7.34
7.33
7.26
6.45
3.74
3.73
3.72
3.52
3.51
3.49
3.49
2.99
2.98
2.97
2.93
2.77
2.74
2.71
2.69
2.22
2.21
2.19
2.12
2.11
2.09
2.08
1.56
1.54
1.51
1.49
1.47
1.44
1.24
0.05
2.07
2.10
0.94
2.09
1.06
3.26
3.12
3.18
2.07
1.00
1.13
1.05


HAD-533C_single_pulse_dec-1-1.esp
VerticalScaleFactor = 1
CH3
O=S=O
N
O
HN
O
13
Normalized Intensity
Chemical Shift (ppm)
178.41
144.04
132.08
129.81
127.68
77.25
77.00
76.74
72.16
59.41
54.76
45.66
35.93
35.75
29.14
28.61
21.53