Total Synthesis of Eleganine A Core

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Supporting Information

General Experimental Details. All reactions were performed under an atmosphere of argon unless otherwise indicated. Reagents and starting materials were obtained from commercial sources and used as received. The solvents were purified and dried by standard procedures prior to use; petroleum ether of boiling range 60−80 °C was used. Flash chromatography was carried out using Merck Kieselgel (230−400 mesh). NMR spectra were recorded on Varian Mercury (600 MHz and 400 MHz) and Bruker (300 MHz) spectrometers. Chemical shift values are referenced against residual protons in the deuterated solvents, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad). J values are reported in hertz. Infrared spectra were recorded in the range 4000−500 cm−1 as a film. HRMS were obtained on a Micromass AutoSpec Ultima Magnetic sector mass spectrometer (TOF). Optical rotations were measured using a PerkinElmer 141 polarimeter.

(*S*)-6-(benzyloxy)-2-((*tert*-butyldiphenylsilyl)oxy)hexan-3-one (16)

Preparation of the Grignard reagent **15**. A two necked flask equipped with a reflux condenser was charged with magnesium turnings (2.35 g, 89.356 mmol, 2 eq) and dry THF (100 mL) under Ar atmosphere. After that ¼ of the total amount of ((3-bromopropoxy)methyl)benzene was added and the mixture was heated to reflux with a heat gun. After ~2 min of refluxing, an

exothermic reaction started. Afterward the bromide (total amount 20.47 g, 89.356 mmol, 2 eq) was added at a rate to maintain gentle reflux. After the addition, the mixture was heated for another 5 min with a heat gun.

The above prepared Grignard reagent **15** was added to a solution of **14** (16.60 g, 44.678 mmol, 1 eq) in dry THF (100 mL) at 0 ^{o}C and stirred for the same temperature for 1 h. The reaction mixture was carefully quenched by addition of sat. NH_4Cl, and then extracted with Et_2O (100 mL, 3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc, 10:1) to give **16** (17.91 g, 87%) as pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ, ppm: 7.68 – 7.56 (4H, m), 7.48 – 7.27 (11H, m), 4.48 (2H, s), 4.20 (1H, q, *J*=6.8 Hz), 3.42 (2H, t, *J*=6.2 Hz), 2.67 (td, *J* = 7.2, 3.2 Hz, 1H) 1.81 (2H, p, *J*=6.6 Hz), 1.18 (3H, d, *J*=6.8 Hz), 1.11 (9H, s); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 213.14, 138.63, 135.89, 135.87, 133.77, 133.09, 130.06, 129.97, 128.47, 127.90, 127.79, 127.71, 127.63, 75.68, 72.92, 69.48, 33.96, 27.07, 23.34, 20.90, 19.35; α_D -16.1 (c=1, $CHCl_3$); **HRMS** (m/z): [M + H] calculated $C_{29}H_{37}O_3Si$ 461.2506; found 461.2519; **IR** ($\nu_{max,}$ neat): 2931, 1718, 1472, 1428, 1111 cm^{-1}.

(*S*,*Z*)-6-(benzyloxy)-2-((*tert*-butyldiphenylsilyl)oxy)hex-3-en-3-yl trifluoromethanesulfonate (SI-1)

A 2M solution of NaHMDS in THF (17.934 mL, 35.869 mmol, 1.65 eq) was diluted with dry THF (20 mL) under Ar atmosphere and the resulting solution cooled to -78 ^{o}C. After that, the solution of **16** (10 g, 21.707 mmol, 1 eq) in dry THF (30 mL) was added dropwise at the same temperature. After stirring for 1 h at -78 ^{o}C, dry Tf_2NPh (21.36 g, 59.781 mmol, 2.75 eq) was

added in one portion. The reaction mixture was warmed to 0 °C and stirred for 3 h at this temperature. After that brine was added and the resulting slurry extracted with Et_2O (100 mL, 3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Eluent: Pet/EtOAc, 20:1 to 5:1). The collected product **SI-1** contains a lot of triflating agent residues and this mixture was used in the next step without additional purification. An analytically pure sample was obtained by repeating the chromatographical purification 3 times. **SI-1** tends to undergo degradation and we were unable obtaining a reproducible $\boldsymbol{\alpha_D}$ value.

^{1}H NMR (300 MHz, $CDCl_3$), δ, ppm: 7.71 – 7.64 (4H, m), 7.50 – 7.29 (11H, m), 5.70 (1H, t, *J*=6.6 Hz), 4.50 (2H, s), 4.35 (1H, q, *J*=6.3 Hz), 3.50 (2H, t, *J*=6.6 Hz), 2.47 (2H, q, *J*=6.6 Hz), 1.17 (3H, d, *J* =6.3 Hz), 1.07 (9H, s); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.02, 138.31, 136.03, 135.99, 133.67, 132.90, 130.03, 127.81, 127.75, 118.07, 73.05, 68.97, 68.50, 26.97, 26.31, 21.86, 19.30; **HRMS** (m/z): [M + Na] calculated $C_{30}H_{35}O_5SiF_3Na$ 615.1819; found 615.1819.

Methyl (*S*,*Z*)-5-(benzyloxy)-2-(1-((*tert*-butyldiphenylsilyl)oxy)ethyl)pent-2-enoate (17)

To the freshly distilled MeOH (600 mL) was added $PdCl_2$*dppf* DCM (177 mg, 0.217 mmol, 10 mol%), followed by DIPEA (7.511 mL, 43.415 mmol, 2 eq). After stirring for 5 min a solution of the above-prepared triflate **SI-1** in MeOH (50 mL) was added. Then CO was bubbled through the mixture for 15 min and the mixture stirred under CO atmosphere (balloon) for an additional 4 h. After that Ar was bubbled through the reaction mixture for 20 min to remove CO and volatiles further evaporated *in vacuo*. The oily residue was taken up in the water and extracted with Et_2O (100 mL, 3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and

concentrated *in vacuo*. The residue was purified by flash column chromatography (Eluent: Pet/EtOAc 95:5 to 80:20) to give **17** (7.64 g, 70% in 2 steps) as pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ, ppm: 7.70 – 7.58 (4H, m), 7.44 – 7.27 (11H, m), 6.41 (1H, t, *J*=6.6 Hz), 4.64 (1H, q, *J*=6.2 Hz), 4.50 (3H, s), 3.62 (3H, s), 3.51 (2H, t, *J*=6.6 Hz), 2.72 (2H, p, *J* = 7.8 Hz), 1.19 (d, *J*=6.2 Hz), 1.04 (9H, s); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 167.40, 138.56, 137.66, 136.72, 135.98, 134.35, 133.88, 129.73, 129.69, 128.48, 127.77, 127.66, 127.64, 127.61, 73.05, 69.61, 69.31, 51.23, 30.04, 27.11, 24.82, 19.37; $\boldsymbol{\alpha_D}$ -39.5 (c=1, $CHCl_3$); **HRMS** (m/z): [M + H] calculated for $C_{31}H_{39}O_4Si$ 503.2612; found 503.2603;

IR ($\nu_{max,}$ neat): 2951, 1718, 1645, 1207, 1111 cm^{-1}.

(*S*,*E*)-5-(benzyloxy)-2-(1-((*tert*-butyldiphenylsilyl)oxy)ethyl)pent-2-en-1-ol (SI-2)

To a stirred solution of ester **17** (8.66 g, 17.226 mmol) in dry DCM (50 mL) was slowly added DIBAL-H (1.2 M in toluene, 43 mL, 7.35 g, 51.679 mmol, 3 eq) at –78 °C. After 4 h at the same temperature, the mixture was quenched by adding MeOH, and the resulting mixture was warmed to room temp. and diluted with a saturated Rochelle salt solution. The mixture was extracted with DCM (3 x). The combined organic layers were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc, 9:1 to 2:1) to give alcohol **SI-2** (7.11 g, 87%) as pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ, ppm: 7.80 – 7.54 (4H, m), 7.50 – 7.28 (11H, m), 5.37 (1H, t *J*=6.6 Hz), 4.49 (2H, s), 4.35 (1H, q, *J*=6.4 Hz), 4.16 (2H, s), 3.50 – 3.31 (2H, m), 2.86 (1H, broad s), 2.53 – 2.19 (2H, m), 1.21 (3H, d, *J*=6.4 Hz), 1.05 (9H, s); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 144.03, 137.99, 136.08, 136.01, 134.25, 133.84, 129.79, 129.75, 128.53, 127.87, 127.66, 127.59, 125.39, 74.52, 73.26, 69.04, 57.50, 28.25, 27.12, 23.70, 19.33.

α_D -22.3 (c=1, $CHCl_3$); **HRMS** (m/z): [M + Na] calculated $C_{30}H_{38}O_3SiNa$ 497.2482; found 497.2476; **IR** ($\nu_{max,}$ neat): 3453, 2961, 1667, 1111 cm^{-1}.

(*S*,*Z*)-((6-(benzyloxy)-3-(bromomethyl)hex-3-en-2-yl)oxy)(*tert*-butyl)diphenylsilane (18)

To a stirred solution of alcohol **SI-2** (5.93 g, 12.492 mmol, 1 eq) and PPh_3 (3.60 g, 13.741 mmol, 1.1 eq) in dry DCM under argon was added CBr_4 (4.56 g, 13.741 mmol, 1.1 eq) at 0 °C, and the resulting mixture was warmed to ambient temperature. The reaction mixture was stirred for 2 h and then concentrated *in vacuo*. The residue was purified by flash column chromatography (Eluent: Pet/EtOAc, 20:1 to 9:1) to give **18** (5.57 g, 83 %) as pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ, ppm: 7.67- 7.59 (4H, m), 7.42 – 7.28 (11H, m), 5.59 (1H, t, *J*=7.0 Hz), 4.49 (2H, s), 4.36 (1H, q, *J*=6.4 Hz), 4.01 (2H, AB m), 3.46 (2H, t, *J*=7.0 Hz), 2.39 (2H, q, *J*=7.0 Hz),1.26 (3H, d, *J*=6.4 Hz), 1.05 (9H, s); **^{13}C NMR** (100 MHz, $CDCl_3$) δ,ppm: 140.70, 138.50, 136.05, 135.99, 134.36, 133.88, 129.76, 129.73, 128.67, 128.51, 127.76, 127.71, 127.66, 127.59, 73.08, 72.72, 69.07, 28.51, 27.14, 26.17, 23.94, 19.39.

α_D -38.3 (c=1, $CHCl_3$); **IR** ($\nu_{max,}$ neat): 2960, 1661, 1427, 1111 cm^{-1}.

2-(trimethylsilyl)ethyl (4-methoxybenzyl)glycinate SI-3

A mixture containing 4-methoxybenzylamine (7.81 mL, 8.20 g, 59.787 mmol, 1.3 eq), 2-(trimethylsilyl)ethyl 2-bromoacetate[1] (11 g, 45.990 mmol, 1 eq), and DIPEA (11.93 mL, 8.91 g, 68.985 mmol, 1.5 eq) in dry THF (150 mL) was stirred in a sealed tube for 3 d under argon. The reaction mixture was concentrated *in vacuo*, and the residue was diluted with a saturated aqueous $NaHCO_3$ solution. The resulting mixture was extracted with Et_2O (3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was

purified by flash column chromatography (Pet/EtOAc, 90:10 to 40:60) to give **SI-3** (7.47 g, 55%) as pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 7.25 (2H, d, *J*=8.7 Hz), 6.86 (2H, d, *J*=8.7 Hz), 4.26 – 4.19 (2H, m), 3.80 (3H, s), 3.74 (2H, s), 3.38 (2H, s), 1.82 (1H, broad s), 1.04 – 0.95 (2H, m), 0.04 (9H, s); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 172.71, 158.93, 131.74, 129.63, 113.96, 63.15, 55.39, 52.81, 50.22, 17.52, -1.38; **HRMS-ESI** (m/z): [M + H] calculated $C_{15}H_{26}NO_3Si$ 296.1676; found 296.1678; **IR** ($\nu_{max,}$ neat): 3339, 2954, 1735, 1513, 1248, 1176 cm^{-1}.

2-(trimethylsilyl)ethyl (*S*,*E*)-*N*-(5-(benzyloxy)-2-(1-((*tert*-butyldiphenylsilyl)oxy)ethyl)pent-2-en-1-yl)-*N*-(4-methoxybenzyl)glycinate (19)

A mixture containing **SI-3** (9.00 g, 16.741 mmol, 1 eq), bromide **18** (5.44 g, 18.415 mmol, 1.1 eq), and DIPEA (5.79 mL, 4.33 g, 33.482 mmol, 2 eq) in dry THF (40 mL) was stirred in a sealed tube for 7 d under argon. The reaction mixture was concentrated *in vacuo*, and the residue diluted with a saturated aqueous $NaHCO_3$ solution. The resulting mixture was extracted with DCM (3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc, 90:10) to give **19** (11.02 g, 93%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 7.77 – 7.55 (4H, m), 7.49 – 7.24 (11H, m), 7.06 (2H, d, *J*=8.7 Hz), 6.73 (2H, d, *J*=8.7 Hz), 5.88 (1H, t, *J*=7.3 Hz), 4.51 (2H, s), 4.41 (1H, q, *J*=6.4 Hz), 4.18 – 4.03 (2H, m), 3.77 (2H, s), 3.61 (1H, d, *J*=13.0 Hz), 3.50 – 3.35 (2H, m), 3.23 (1H, d, *J*=13.0 Hz), 3.04 (2H, q, *J*=17.0 Hz), 2.52 – 2.35 (2H, m), 1.08 (1H, d, *J* = 6.2 Hz), 1.06 (9H, s), 0.99 – 0.84 (2H, m), 0.03 (9H, s); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 171.85, 158.69, 141.57, 138.71, 136.10, 136.03, 134.75, 134.38, 131.29, 130.20, 129.57, 129.51, 128.47, 127.71, 127.58,

127.54, 127.47, 124.29, 113.59, 73.04, 71.14, 70.28, 62.37, 57.38, 55.34, 53.27, 50.30, 28.26, 27.21, 24.00, 19.43, 17.55, -1.38; α_D -29.6 (c=1, $CHCl_3$); **HRMS** (m/z): [M + H] calculated $C_{45}H_{62}O_5Si_2N$ 752.4161; found 752.4147; **IR** ($\nu_{max,}$ neat): 2952, 1733, 1616, 1511, 1249, 1111 cm^{-1}.

(*S*,*E*)-6-(3-(benzyloxy)propylidene)-4-(4-methoxybenzyl)-7-methyl-1,4-oxazepan-2-one (20)

A mixture containing ester **19** (10.14 g, 14.322 mmol, 1 eq) and TBAF·$3H_2O$ (18.07 g, 57.287 mmol, 4 eq) in dry THF (40 mL) was stirred in a sealed tube for 20 h at 60 ^oC. The reaction mixture was cooled to rt and slowly added to a mixture containing HBTU (16.294 g, 42.965 mmol, 3 eq), DMAP (10.49 g, 85.931 mmol, 6 eq) and dry DCM (500 mL). The resulting mixture was stirred overnight and then diluted with brine. The mixture was extracted with DCM (3 x) and the combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc 2:1 to 0:1) to give **20** (4.47 g, 79%) as a pale yellow wax.

^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 7.37 – 7.28 (5H, m), 7.21 (2H, d, *J*=8.6 Hz), 6.85(2H, d, *J*=8.6 Hz), 5.87 (1H, t, *J*=7.1 Hz), 5.18 (1H, q, *J*=6.7 Hz), 4.48 (2H, s), 3.79 (3H, s), 3.70 (1H, d, *J* = 16.6 Hz), 3.60 – 3.39 (5H, m), 3.31 (d, *J* = 14.0 Hz, 1H), 2.31 (2H, q, *J*=7.1 Hz), 1.52 (3H, d, *J*=6.7 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 172.29, 159.10, 138.26, 134.93, 130.01, 129.72, 128.79, 128.51, 127.74, 113.96, 73.07, 69.11, 58.64, 58.03, 55.34, 54.94, 28.39, 18.86; α_D -72.8 (c=1, $CHCl_3$); **HRMS** (m/z): [M + H] calculated $C_{24}H_{30}O_4N$ 396.2169; found 396.2156.

Methyl (2*S*,3*S*,*E*)-3-(2-(benzyloxy)ethyl)-4-ethylidene-1-(4-methoxybenzyl)pyrrolidine-2-carboxylate (23)

To a stirred solution of **17** (2.590 g, 6.549 mmol, 1 eq) in 20 mL of dry DCM was added Et_3N (8.21 mL, 5.964 g, 58.939 mmol, 9 eq, freshly distilled from sodium). The mixture was then cooled to 0 °C and Bu_2BOTf (1M solution in DCM, 19.65 mL, 5.385 g, 19.646 mmol, 3 eq) was added dropwise. The mixture was allowed to warm to rt and stirred for 2 h. After that MeOH (2.65 mL, 2.098 g, 65.488 mmol, 10 eq) was added followed by HBTU (7.451 g, 19.646 mmol, 3 eq). The obtained mixture was stirred for 16 h and then diluted with brine (100 mL) and extracted twice with 50 mL of DCM. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc 10:1 -> 2:1). The title compound **23** was isolated as a yellow oil (1.850 g, 69%).

^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 7.30 – 7.18 (5H, m), 7.14 (2H, d, *J*=8.6 Hz), 6.76 (2H, d, *J*=8.6 Hz), 5.26 (1H, q, *J*=6.9 Hz), 4.41 (2H, AB m), 3.72 (3H,s), 3.69 (1H, d, *J*=13.1 Hz), 3.55 (2H, s), 3.53 – 3.44 (3H, m), 3.33 (1H, d, *J*=11.8 Hz), 3.24 (1H, d, *J*=4.2 Hz), 3.09 (1H, d, *J* = 13.7 Hz), 3.04 – 2.97 (1H, m), 1.96 – 1.85 (1H, m), 1.83 – 1.72 (1H, m), 1.53 (3H, d, *J*=6.9 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 174.08, 158.86, 140.36, 138.61, 130.21, 128.44, 127.66, 127.60, 116.76, 113.67, 73.06, 71.30, 68.32, 57.68, 57.36, 55.34, 51.71, 42.29, 34.12, 14.24; **α_D** -33.6 (c=1, $CHCl_3$); **HRMS** (m/z): [M + H] calculated $C_{25}H_{32}O_4N$ 410.2331; found 410.2347; **IR** ($\nu_{max,}$ neat): 2951, 1732, 1612, 1514, 1247, 1170 cm^{-1}.

Methyl (2*S*,3*S*,*E*)-3-(2-(benzyloxy)ethyl)-4-ethylidene-1-((4-nitrophenyl)sulfonyl)pyrrolidine-2-carboxylate (24)

To a stirred solution of **18** (3.160 g, 7.716 mmol, 1 eq) in dry DCM (20 mL) at 0 °C was added 1-chloroethyl chloroformate (2.523 mL, 3.310 g, 23.149 mmol, 3 eq). The mixture was warmed

to rt and stirred for 2 h. After that the volatiles vere removed *in vacuo*, the oily residue disolved in MeOH (20 mL) and refluxed for 1 h. Then the reaction mixture was again evaporated and the oily residue washed with hexane (10 mL, 3 x), the washings were carefully decanted and discarred. After that, the oily residue was dissolved in dry DCM (40 mL) and treated with pyridine (3.117 mL, 3.052 g, 38.582 mmol, 5 eq), followed by NsCl (3.420 g, 15.433 mmol, 2 eq) at rt. After 2 h of stirring, the reaction mixture was diluted with a saturated aqueous $NaHCO_3$ solution and extracted with DCM (3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc, 10:1 to 4:1) to give **24** (2.929 g, 80%) as a pale yellow wax.

^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 8.11 – 8.05 (m, 1H), 7.71 – 7.59 (m, 3H), 7.39 – 7.27 (m, 5H), 5.54 – 5.36 (m, 1H), 4.60 (s, 1H), 4.50 – 4.41 (AB m, 2H), 4.28 – 4.10 (AB m, 1H), 3.62 (s, 3H), 3.61 – 3.47 (m, 2H), 3.26 (t, *J* = 7.4 Hz, 1H), 1.89 – 1.76 (m, 1H), 1.74 – 1.65 (m, 1H), 1.63 (d, *J* = 7.0, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 171.65, 148.08, 138.39, 136.36, 133.59, 133.07, 131.78, 130.89, 128.52, 127.79, 127.75, 124.22, 119.95, 73.29, 67.80, 65.82, 52.50, 51.25, 42.83, 33.38, 14.46; **α_D** +0.16 (c=1.225, $CHCl_3$); **HRMS** (m/z): [M + H] calculated $C_{23}H_{27}O_7N_2S$ 475.1539; found 475.1549; **IR** ($\nu_{max,}$ neat): 2861, 1746, 1548, 1438, 1362, 1208, 1100 cm^{-1}.

Methyl (2*S*,3*S*,*E*)-4-ethylidene-3-(2-hydroxyethyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidine-2-carboxylate (SI-4)

To a stirred solution of **24** (3.160 g, 7.716 mmol, 1 eq) in dry DCM (20 mL) at -78 ^{o}C was added BCl_3 (1M in DCM, 2.523 mL, 3.310 g, 23.149 mmol, 3 eq). The mixture was warmed to rt and stirred for 2 h. After that, the reaction mixture was quenched by careful addition of sat. aq.

$NaHCO_3$ and extracted with DCM (3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc, 10:1 to 4:1) to give **SI-4** (2.370 g, 80%) as a pale yellow wax.

^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 8.12 – 8.07 (m, 1H), 7.72 – 7.66 (m, 2H), 7.66 – 4.61 (m, 1H), 5.47 (q, *J*=6.9 Hz, 1H), 4.62 (s, 1H), 4.27 – 4.11 (AB m, 2H), 3.82 – 3.68 (m, 2H), 3.63 (s, 3H), 3.23 (t, *J*=7.7 Hz, 1H), 1.81 – 1.67 (m, 2H), 1.65 (d, *J*=6.9 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 171.69, 148.06, 136.46, 133.67, 133.06, 131.85, 130.91, 124.28, 119.88, 65.77, 60.45, 52.61, 51.26, 42.52, 35.90, 14.51; **α_D** -16.3 (c=1, $CHCl_3$); **HRMS** (m/z): [M + H] calculated $C_{16}H_{21}O_7N_2S$ 385.1069; found 385.1079; **IR** ($\nu_{max,}$ neat): 2954, 2880, 1749, 1544, 1438, 1372, 1214, 1167 cm^{-1}.

2-((2*S*,3*S*,*E*)-4-ethylidene-2-(methoxycarbonyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidin-3-yl)acetic acid (25)

To a stirred solution of **SI-4** (300 mg, 0.780 mmol, 1 eq) in MeCN (4 mL) was added *N*-methyl morpholine *N*-oxide (NMO) monohydrate (1.055 g, 7.804 mmol, 10 eq). After a complete dissolution, tetra-*N*-propylammonium perruthenate (27 mg, 0.078 mmol, 10 mol%) was added and the reaction mixture stirred for 3 h at rt. The reaction mixture was quenched by addition of *iso*-propanol (5 mL), the volatiles were evaporated *in vacuo* and the residue purified by RP flash column chromatography (Eluent: Water + 1 %AcOH / MeOH +1 %AcOH, 90:10 to 10:90) to give **25** (300 mg, 96%) as a pale yellow wax.

^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm:8.12 – 8.07 (m, 1H), 7.74 – 7.63 (3H, m), 5.51 (q, *J*=6.9 Hz, 1H), 4.67 (s, 1H), 4.30 – 4.15 (AB m, 2H), 3.65 (s, 3H), 3.51 – 3.44 (m, 1H), 2.54 (dd, *J* = 16.6, 9.9 Hz, 1H), 2.43 (dd, *J* = 16.6, 4.9 Hz, 1H), 1.65 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (100

MHz, $CDCl_3$) δ, ppm: 176.69, 171.05, 147.98, 135.15, 133.90, 132.75, 131.94, 130.98, 124.37, 120.78, 65.76, 52.77, 50.97, 41.58, 36.68, 14.50; $\boldsymbol{\alpha_D}$ -22.7 (c=1, $CHCl_3$); **HRMS** (m/z): [M + H] calculated $C_{16}H_{19}O_8N_2S$ 399.0862; found 399.0870; **IR** ($\nu_{max,}$ neat): 3101, 3027, 2954, 1747,1712, 1544, 1435, 1372, 1215, 1166 cm^{-1}.

2-(Trimethylsilyl)ethyl 2-(1-methyl-1H-indol-3-yl)acetate (26)

A round bottom flask was charged with 1-methyl-3-indoleacetic acid (1.000 g, 5.285 mmol, 1 eq), EDC (2.026 g, 10.570 mmol, 2 eq), DMAP, (64 mg, 0.528 mmol, 10 mol%), 2-(trimethylsilyl)ethanol (1.136 mL, 937 mg, 7.928 mmol, 1.5 eq) and dry DCM (20 mL) and after stirring for 5 min DIPEA (3.657 mL, 2.732 g, 21.140 mmol, 4 eq) was added. After 16 h of stirring, the reaction mixture was diluted with a saturated aqueous $NaHCO_3$ solution and extracted with DCM (3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc, 90:10 to 50:50) to give **26** (1.070 g, 70%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm: 7.62 (1H, dt, *J* = 7.9, 1.0 Hz), 7.30 (1H, dt, *J* = 8.2, 1.0 Hz), 7.23 (1H, td, *J* = 7.6, 1.2 Hz), 7.16 – 7.11 (1H, m), 7.05 (1H, s), 4.24 – 4.16 (2H, m), 3.76 (3H, s), 3.75 (2H, s), 1.05 – 0.96 (2H, m), 0.07 – -0.01 (9H, m).

^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 172.42, 137.01, 127.86, 127.82, 121.82, 119.21, 119.15, 109.34, 107.11, 63.12, 32.80, 31.57, 17.45, -1.40.

HRMS (m/z): [M + H] calculated $C_{16}H_{24}O_2NSi$ 290.1576; found 290.1576.

IR ($\nu_{max,}$ neat): 2954, 2897, 1729, 1615, 1471, 1374, 1331, 1250, 1151 cm^{-1}.

Methyl (2*S*,3*S*,*E*)-4-ethylidene-3-(2-(1-methyl-3-(2-oxo-2-(2-(trimethylsilyl)ethoxy)ethyl)-1H-indol-2-yl)-2-oxoethyl)pyrrolidine-2-carboxylate (SI-5)

To a stirred solution of the acid **25** (100 mg, 0.251 mmol, 1 eq) in dry DCM (1 mL) under Ar atmosphere was added one drop of dry DMF followed by oxalyl chloride (109 μL, 159 mg, 1.255 mmol, 5 eq) at 0 °C. The mixture was warmed to rt and stirred for 2 h. After that the volatiles were evaporated (Ar filled rotovap) and then coevaporated with dry DCM (2 times). The oily residue was dissolved in dry Et_2O (1 mL) under Ar atmosphere and methyl indole **26** (87 mg, 0.301 mmol, 1.2 eq) was added. The resulting solution was cooled to 0 °C and treated with freshly distilled $SnCl_4$ (59 μL, 131 mg, 0.502 mmol, 2 eq). After stirring for 30 min at 0 °C the reaction mixture was poured into sat. aq. $NaHCO_3$ and extracted with DCM (3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc, 90:10 to 50:50). The product containing fractions were evaporated dissolved in dry MeCN (1 mL) and treated with K_2CO_3 (35 mg, 0.251 mmol, 1 eq) and thiophenol (26 μL, 28 mg, 0.251 mmol, 1 eq). The resulting slurry was vigorously stirred overnight at rt. After that the mixture was evaporated under flow of Ar to ~ ½ of the initial volume and directly purified by flash column chromatography (Pet/EtOAc, 50:50 to 0:100) to give **SI-5** (27 mg, 22%) as a yellow wax.

^{1}H NMR (300 MHz, $CDCl_3$), δ, ppm: 7.69 (1H, d, *J* = 7.7 Hz), 7.41 – 7.32 (2H, m), 7.21 – 7.14 (1H, m), 5.45 – 5.35 (1H, m), 4.22 – 4.02 (4H, m), 3.96 (3H, s), 3.84 – 3.70 (1H, m), 3.76 (3H, s), 3.70 – 3.56 (3H, m), 3.35 (1H, dd, *J* = 17.1, 9.9 Hz), 3.18 (1H, dd, *J* = 17.0, 3.6 Hz), 1.65 (3H, d, *J* = 7.7 Hz), 1.00 – 0.93 (2H, m), 0.03 – -0.04 (9H, m); **^{13}C NMR** (100 MHz, $CDCl_3$) δ, ppm: 194.12, 174.89, 171.14, 141.38, 138.80, 134.73, 127.00, 126.05, 120.88, 120.74, 116.52, 114.33, 110.48, 65.92, 63.69, 52.41, 50.81, 45.88, 40.50, 32.84, 32.12, 17.46, 14.83, -1.45; **α_D** -

16.8 (c=0.1, $CHCl_3$); **HRMS** (m/z): [M + H] calculated $C_{26}H_{37}O_5N_2Si$ 485.2472; found 485.2472; **IR** ($\nu_{max,}$ neat): 2924, 2854, 1732, 1660, 1476, 1249, 1168,87 cm^{-1}.

Methyl (1*Z*,3*S*,5*E*,8*Z*,14*S*)-5-ethylidene-8-hydroxy-9-methyl-2-oxo-2,4,5,6,7,9-hexahydro-3,6-methanoazecino[5,4-b]indole-14-carboxylate (28)

To a stirred solution of **SI-5** (10 mg, 0.021 mmol, 1 eq) in dry DCM (0.5 mL) was added TFA (0.5 mL) and the resulting solution stirred for 4 h at rt. The reaction mixture was evaporated *in vacuo* and dissolved in dry DCM (0.2 mL) and slowly added to a mixture containing DMAP (15 mg, 0.124 mmol, 6 eq), HBTU (23 mg, 0.062 mmol, 3 eq) and dry DCM (1 mL). After 16 h of stirring at rt, the reaction mixture was diluted with a saturated aqueous $NaHCO_3$ solution and extracted with DCM (3 x). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (Pet/EtOAc, 90:10 to 10:90) to give **28** (3 mg, 40%) as a yellow wax. The title compound tends to undergo rapid degradation and we were unable obtaining a reproducible $\boldsymbol{\alpha_D}$ value.

^{1}H NMR (600 MHz, CD_3OD), δ, ppm: 7.96 (1H, d, *J* = 7.8 Hz), 7.62 (1H, t, *J* = 8.4 Hz), 7.29 (1H, d, *J* = 8.4 Hz), 7.10 (1H, t, *J* = 8.2 Hz), 6.69 (1H, s), 5.45 (1H, q, *J* = 6.8 Hz), 3.82 (1H, broad s), 3.73 (3H, s), 3.67 (3H, s), 3.64 – 3.54 (2H, m), 3.57 – 3.54 (1H, m), 3.36 – 3,31 (2H, m), 1.36 (3H, d, *J*=6.8 Hz); **^{13}C NMR** (125 MHz, CD_3OD) δ, ppm: 174.8, 165.8, 151.1, 149.3, 146.8, 140.7, 134.8, 129.5, 125.0, 121.0, 120.4, 119.7, 110.4, 98.2, 66.4, 52.8, 51.4, 45.0, 35.9, 32.6, 14.8; **HRMS** (m/z): [M + H] calculated $C_{21}H_{23}O_4N_2$ 367.1658; found 367.1658.

1. K. C. Nicolaou, S. M. Dalby and U. Majumder, *Journal of the American Chemical Society*, 2008, **130**, 14942-14943.

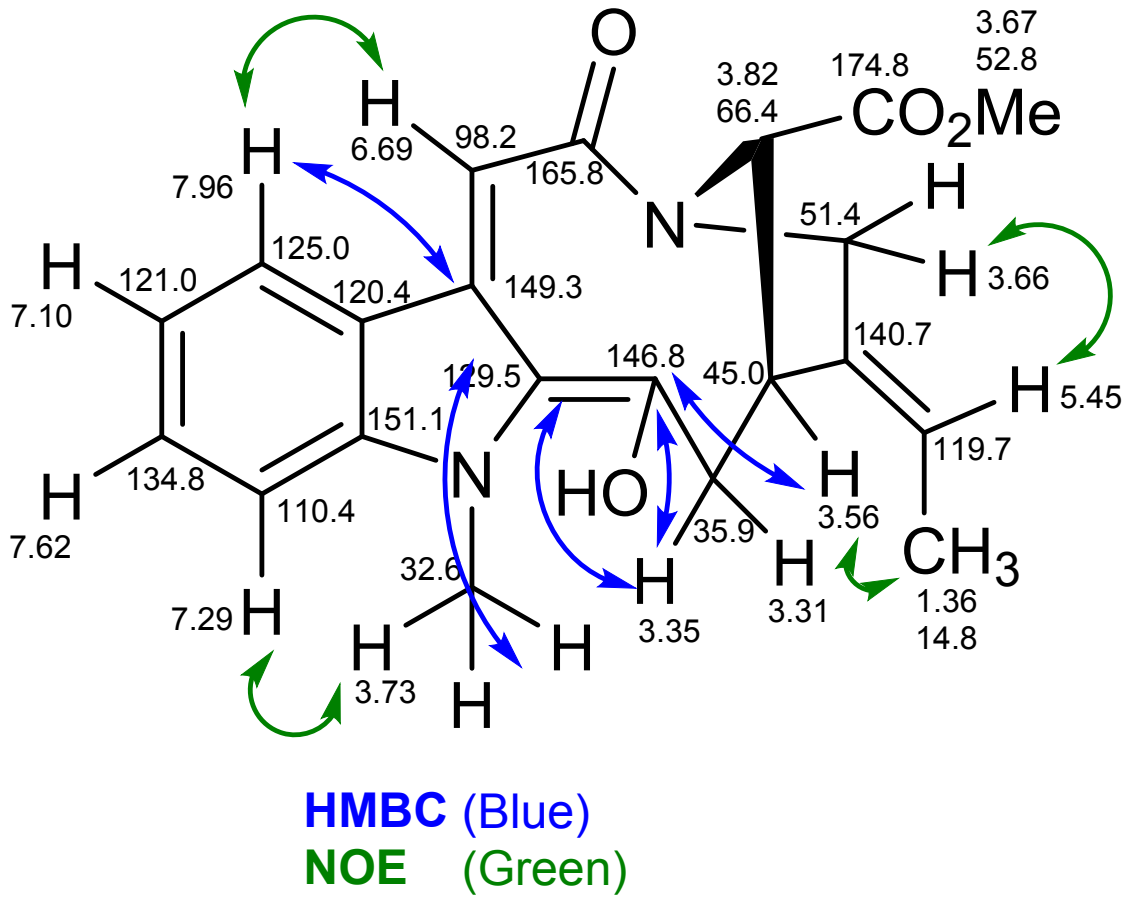
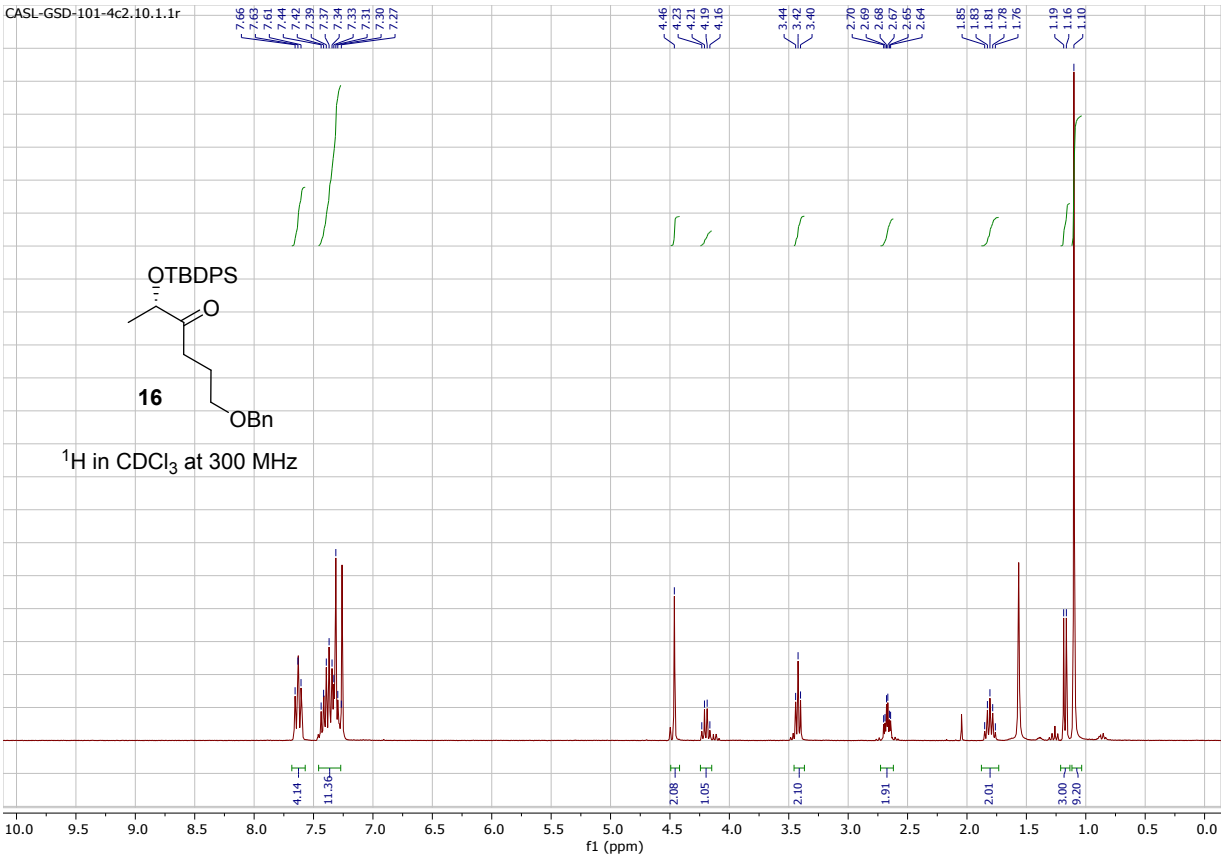


Fig 1. Selected HMBC (blue) and NOE (Green) corelations for compound **28**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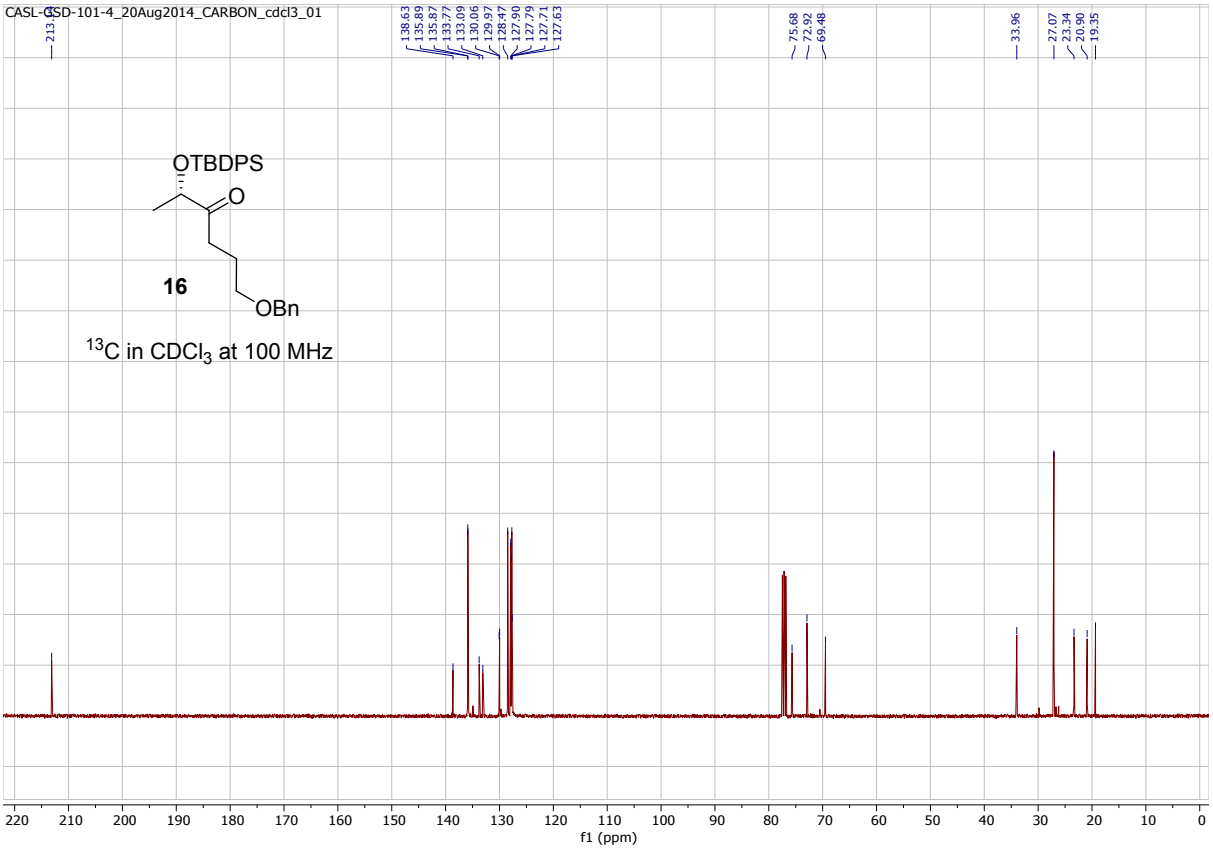
O
16
OBn
^{1}H in CDCl$_3$ at 300 MHz
f1 (ppm)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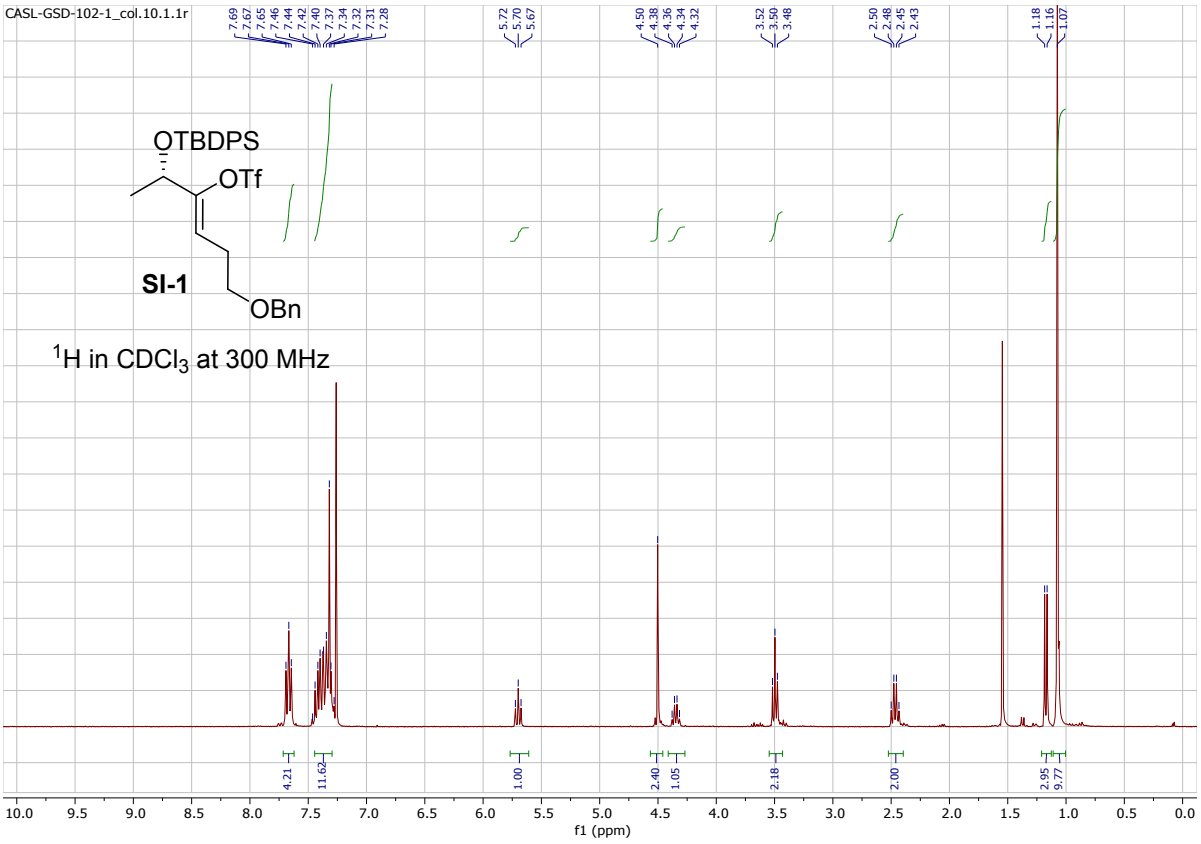
O
16
OBn
^{13}C in CDCl$_3$ at 100 MHz
f1 (ppm)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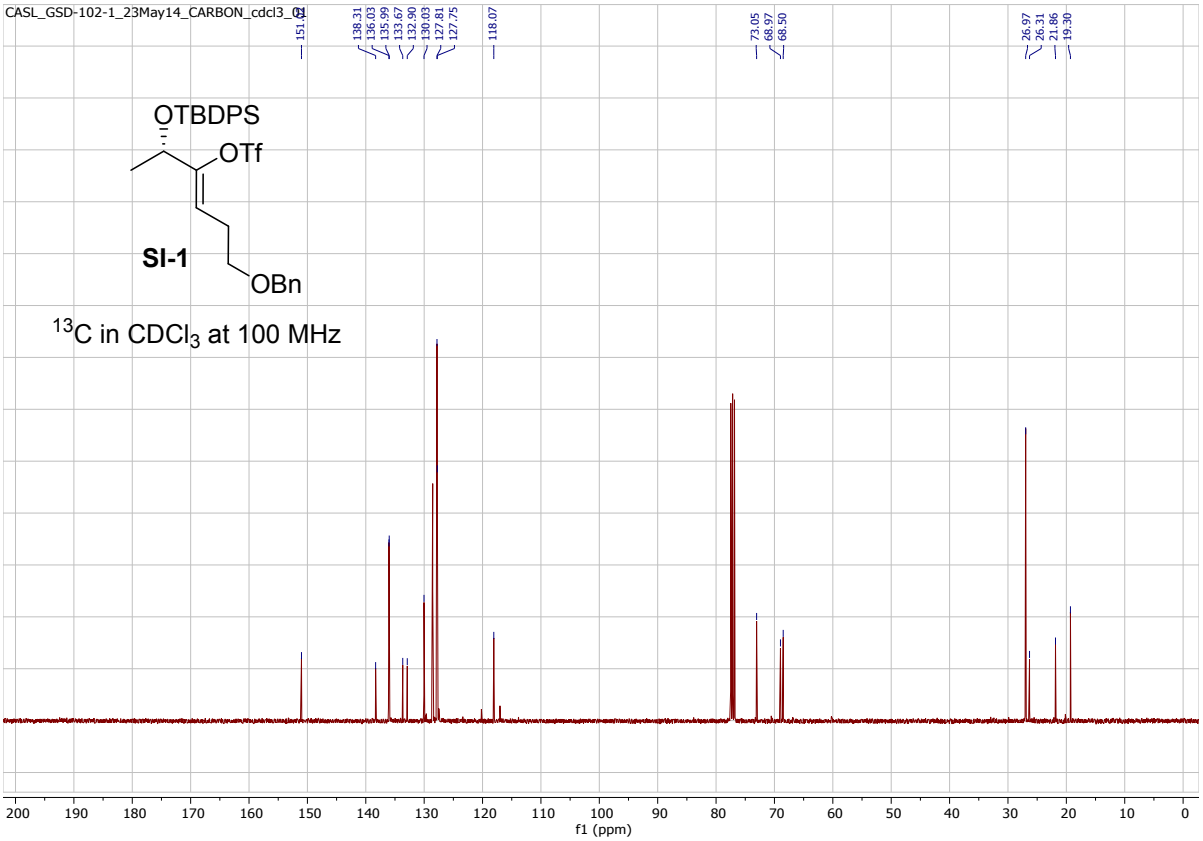
OTf
SI-1
OBn
^{1}H in $CDCl_3$ at 300 MHz
f1 (ppm)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OTf
SI-1
OBn
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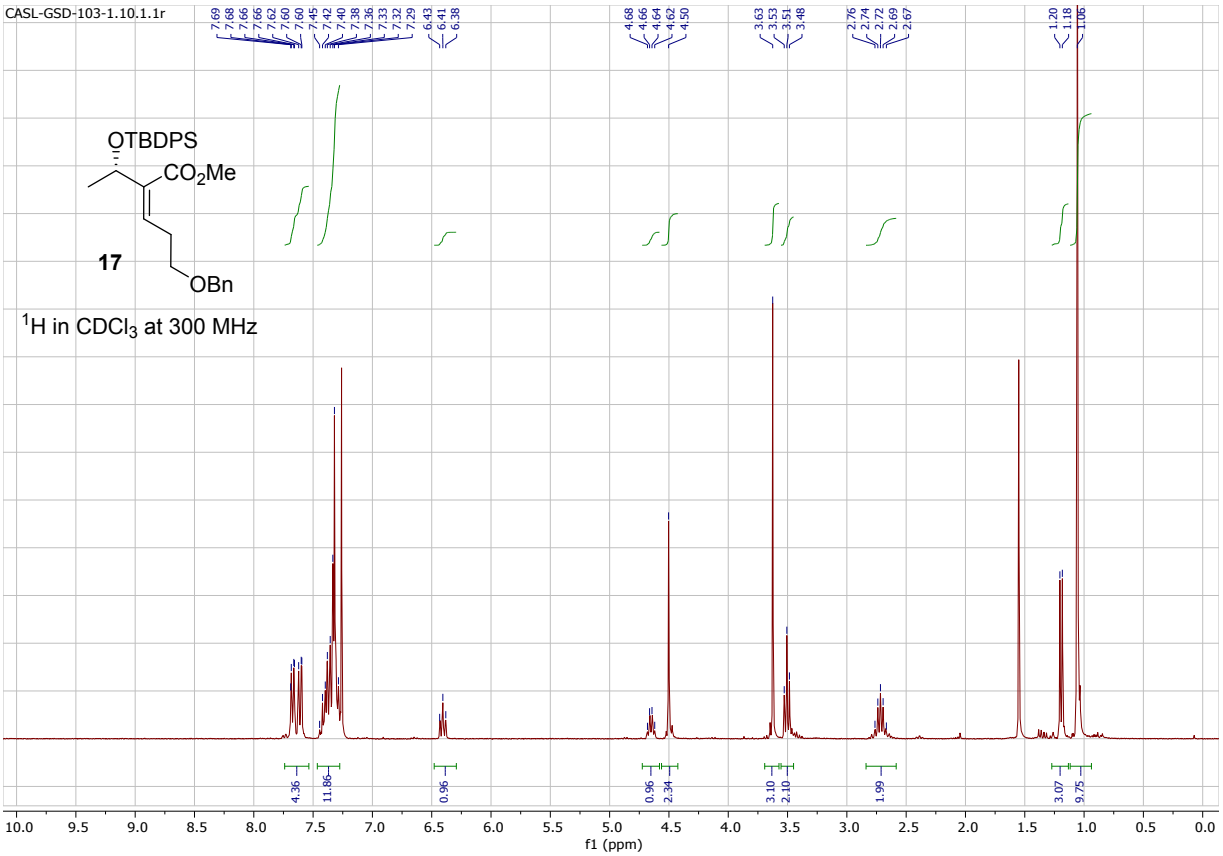
f1 (ppm)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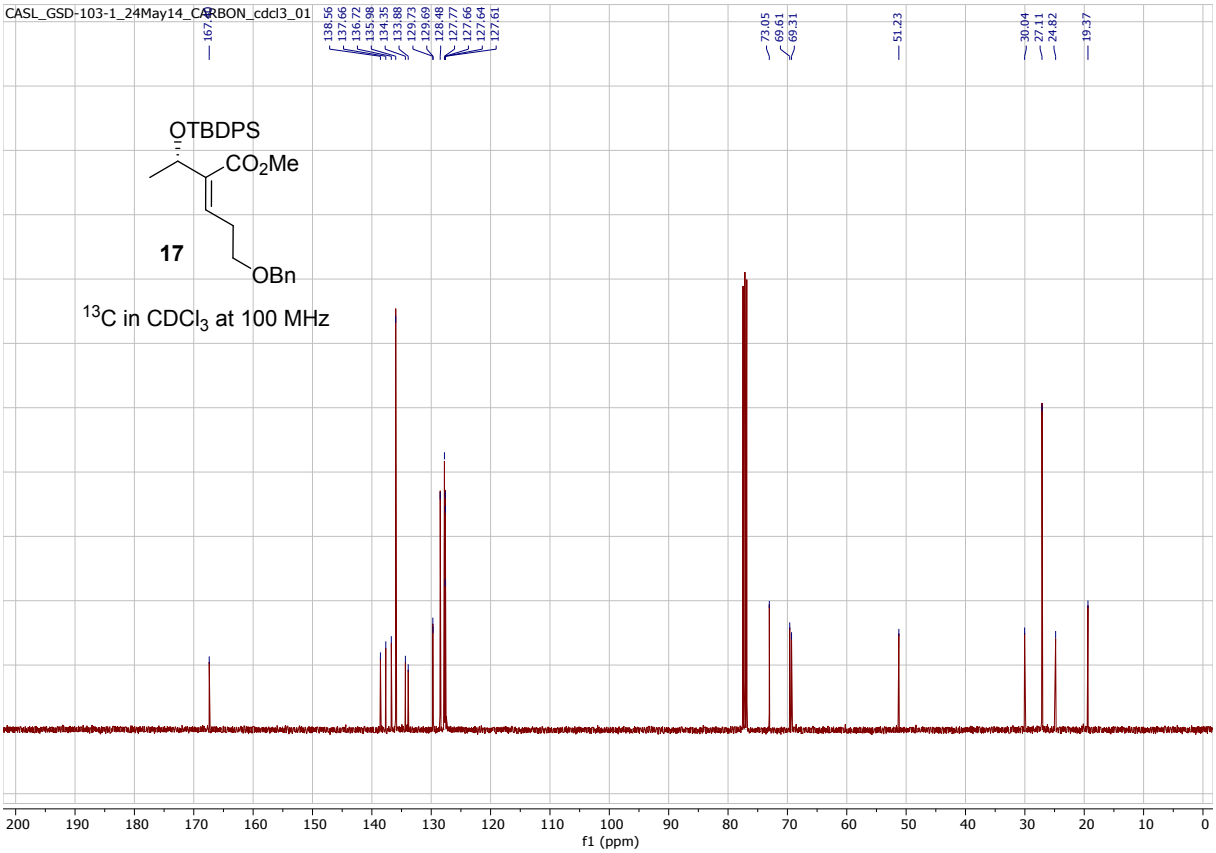
OTBDPS
CO2Me
17
OBn
1H in CDCl3 at 300 MHz
f1 (ppm)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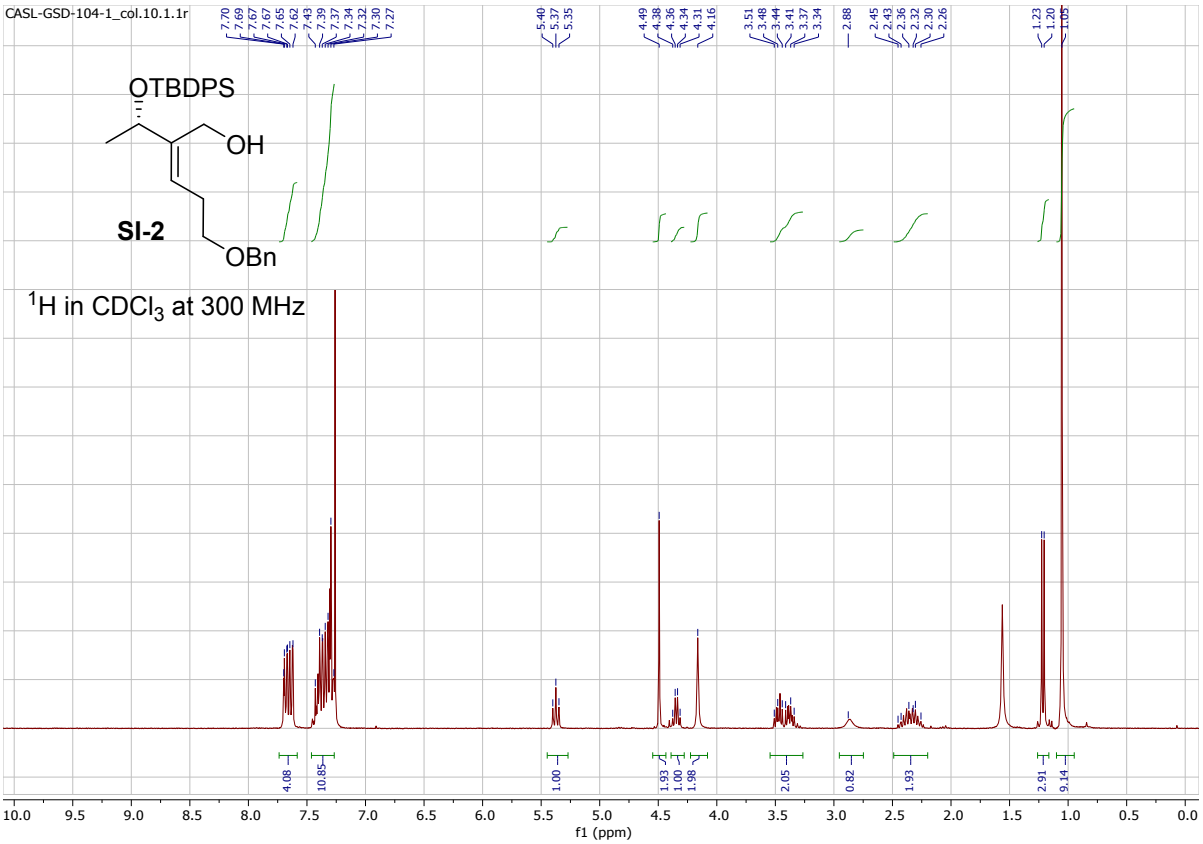
CO2Me
17
OBn
13C in CDCl3 at 100 MHz
f1 (ppm)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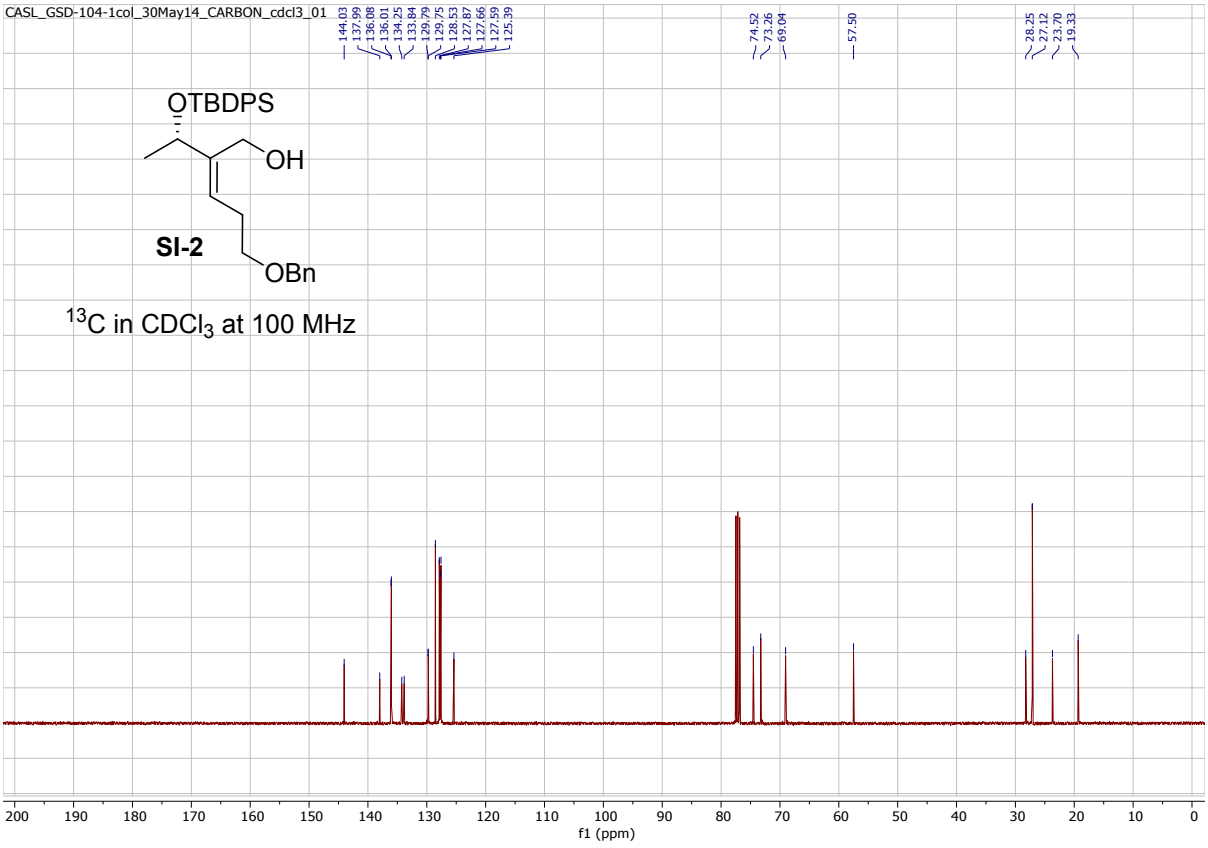
OH
SI-2
OBn
^{1}H in CDCl$_3$ at 300 MHz
f1 (ppm)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SI-2
OBn
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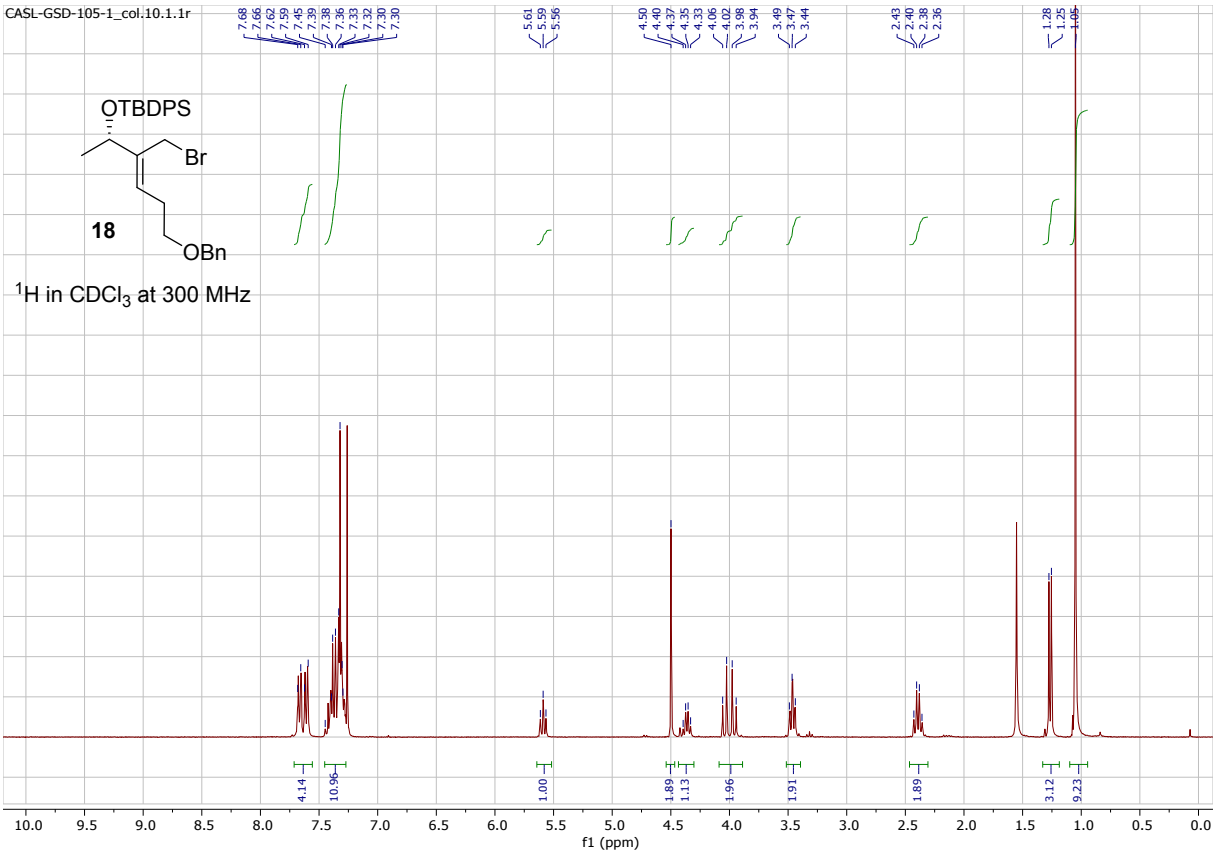
f1 (ppm)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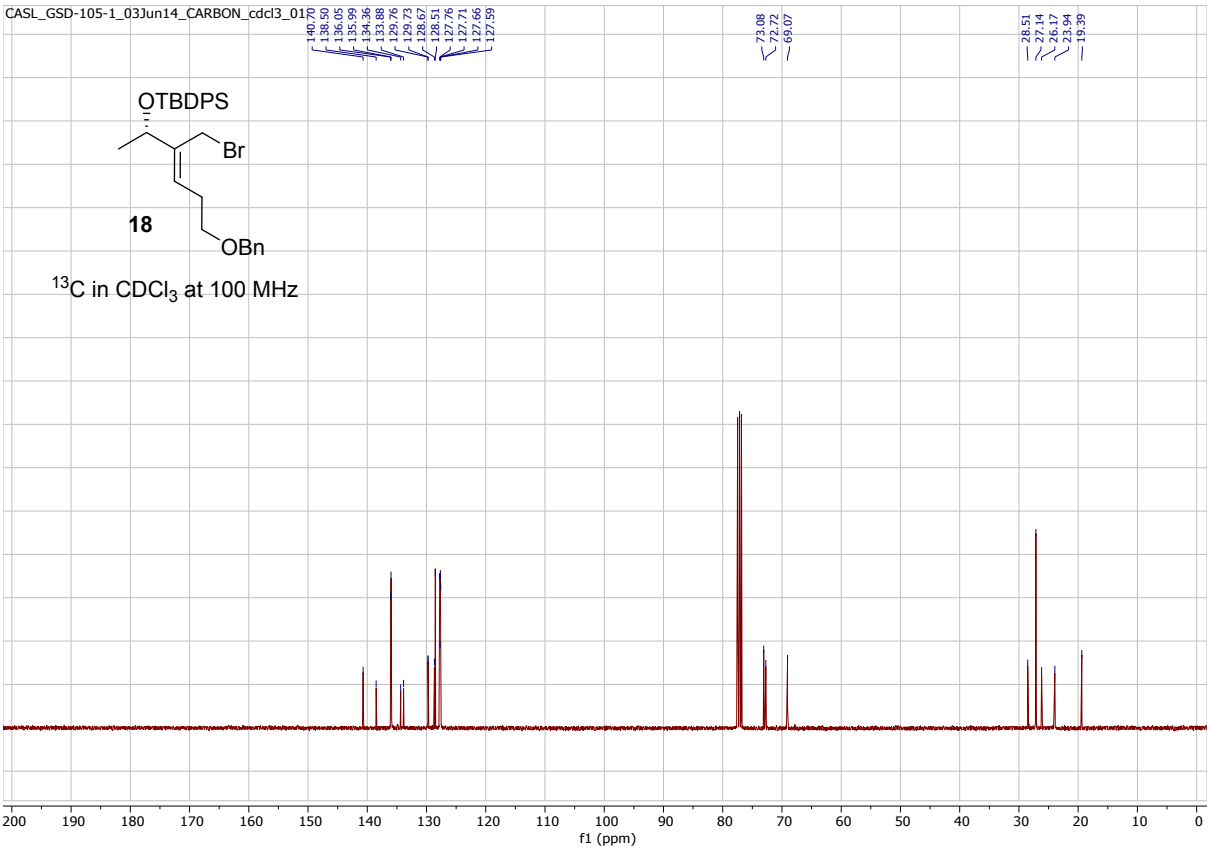
Br
18
OBn
1H in CDCl3 at 300 MHz
f1 (ppm)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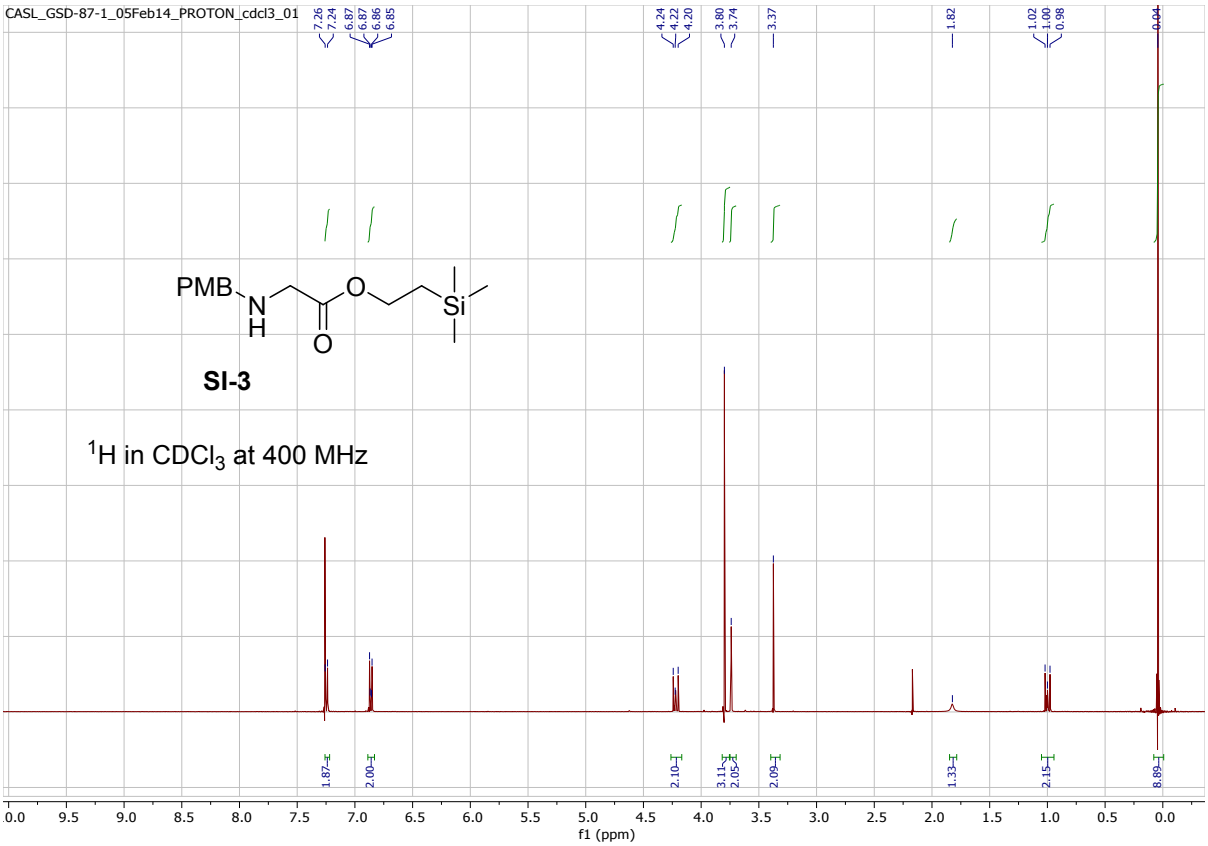
Br
18
OBn
13C in CDCl3 at 100 MHz
f1 (ppm)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O
O
Si
SI-3
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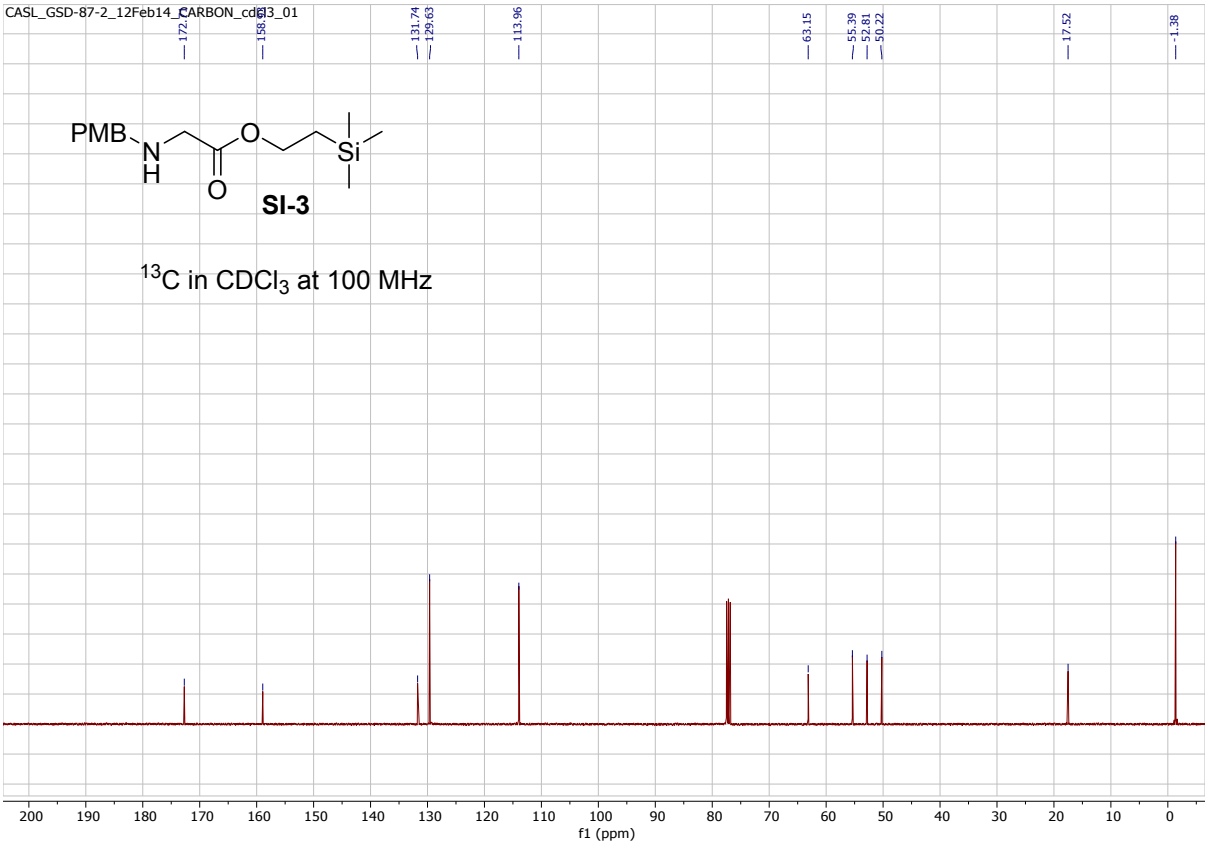
f1 (ppm)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H
O
O
Si
SI-3
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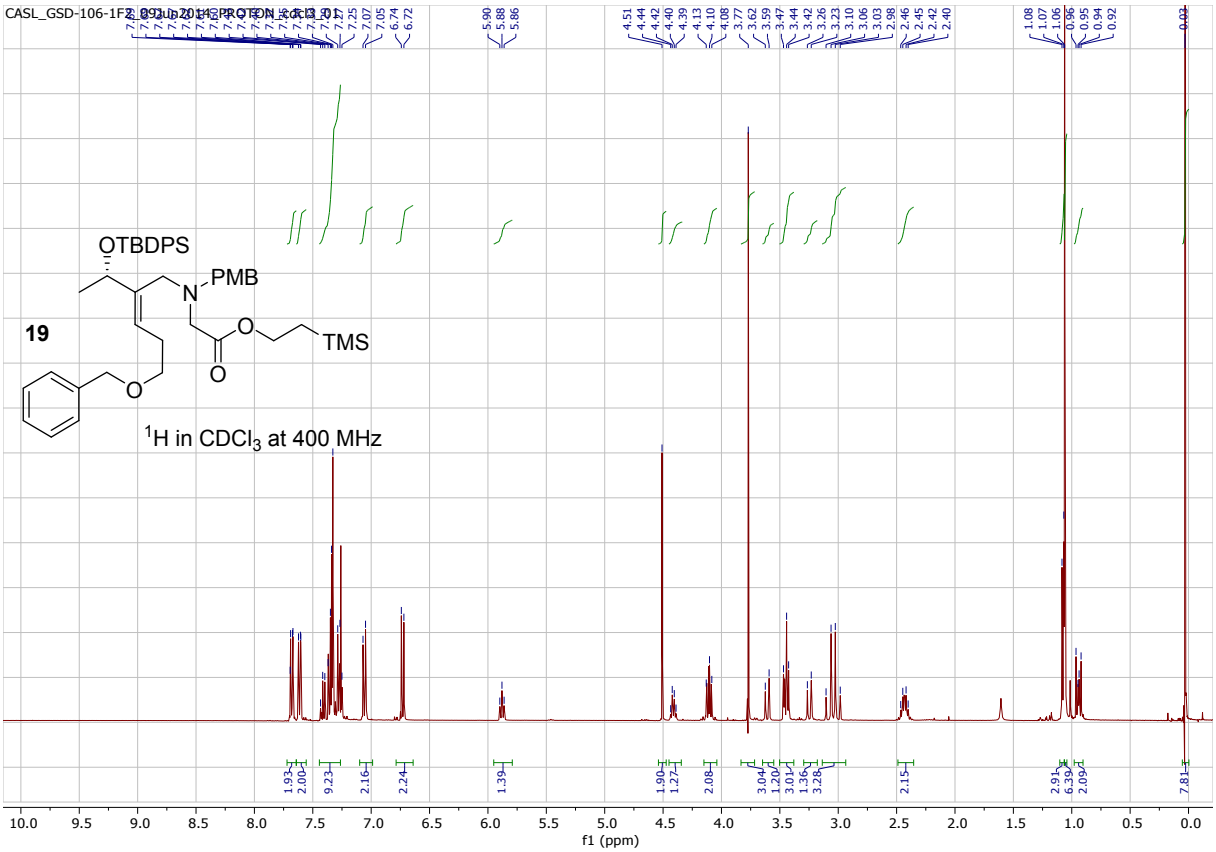
f1 (ppm)


OTBDPS
PMB
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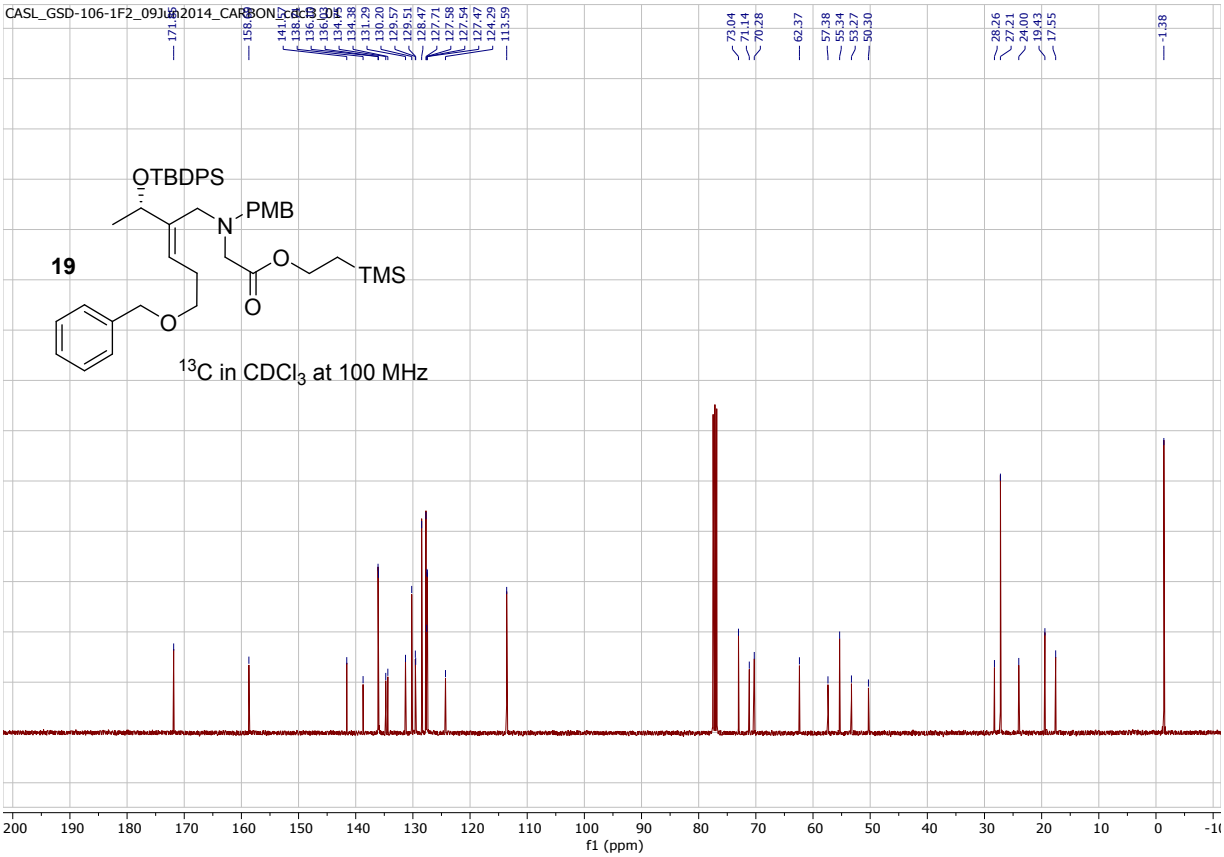
O
TMS
O
O
19
^{1}H in CDCl$_3$ at 400 MHz
f1 (ppm)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TMS
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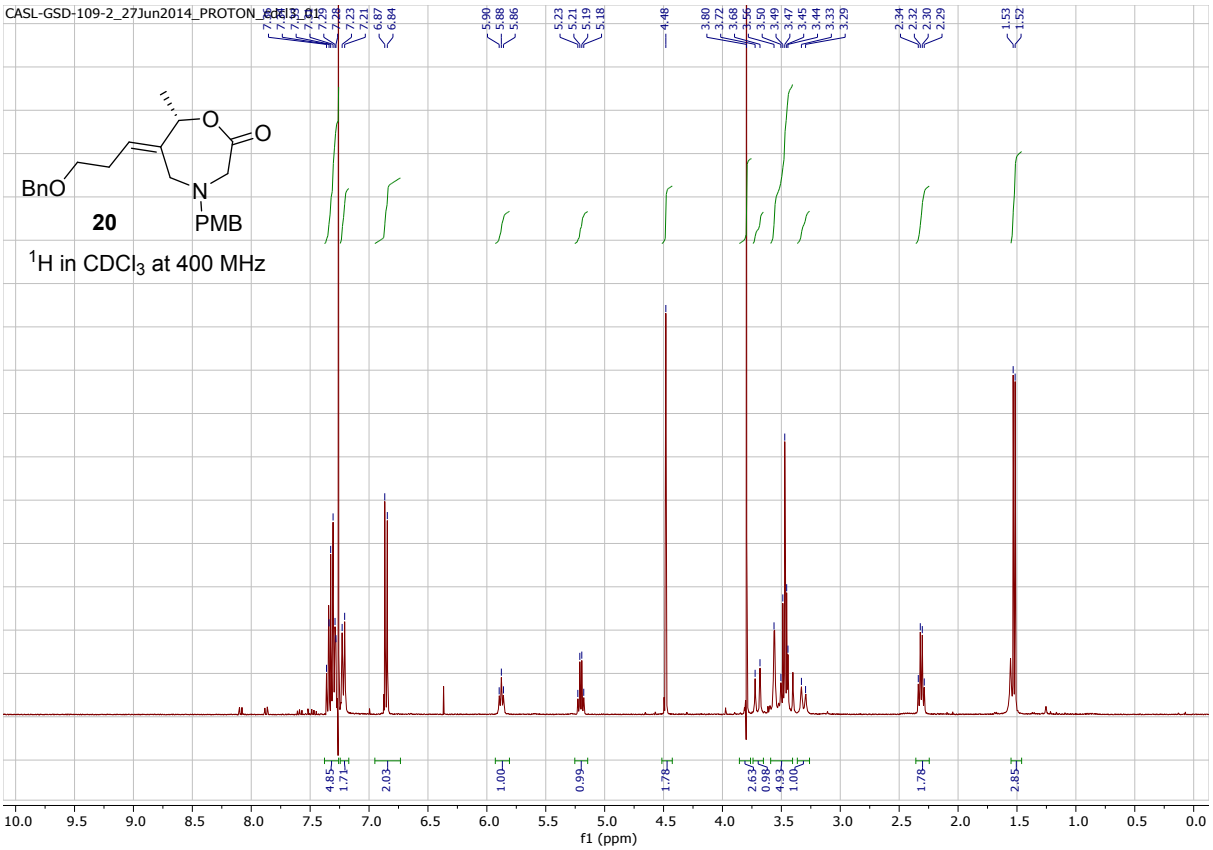
f1 (ppm)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O
O
N
PMB
20
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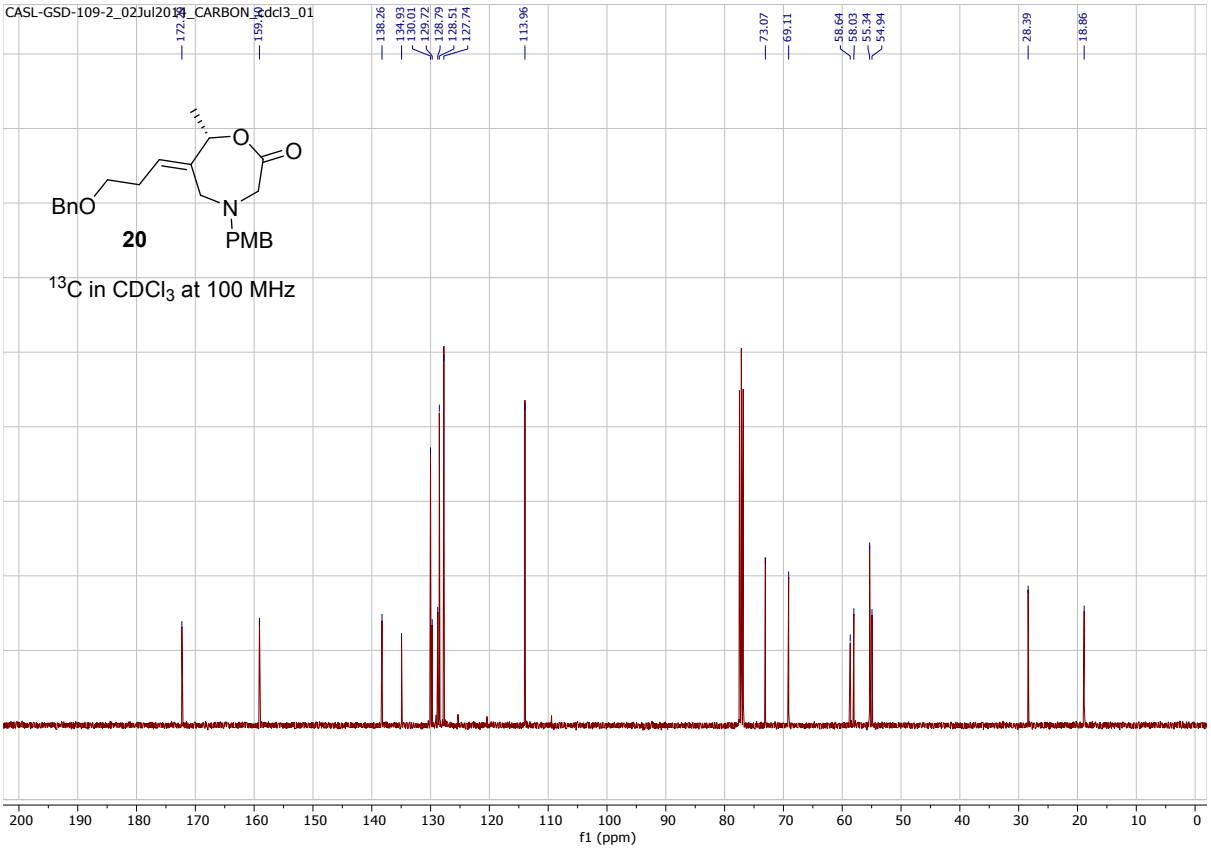
f1 (ppm)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O
O
N
PMB
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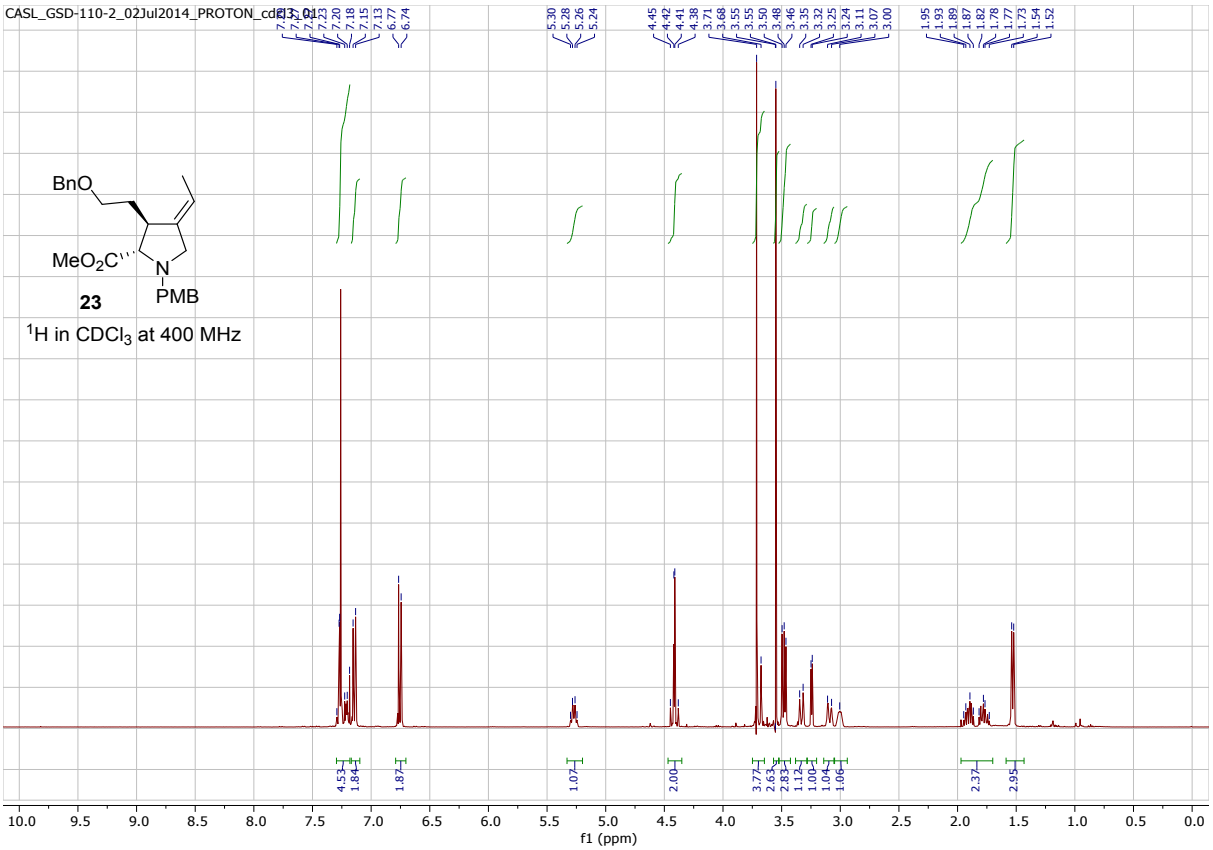
f1 (ppm)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MeO2C
N
PMB
23
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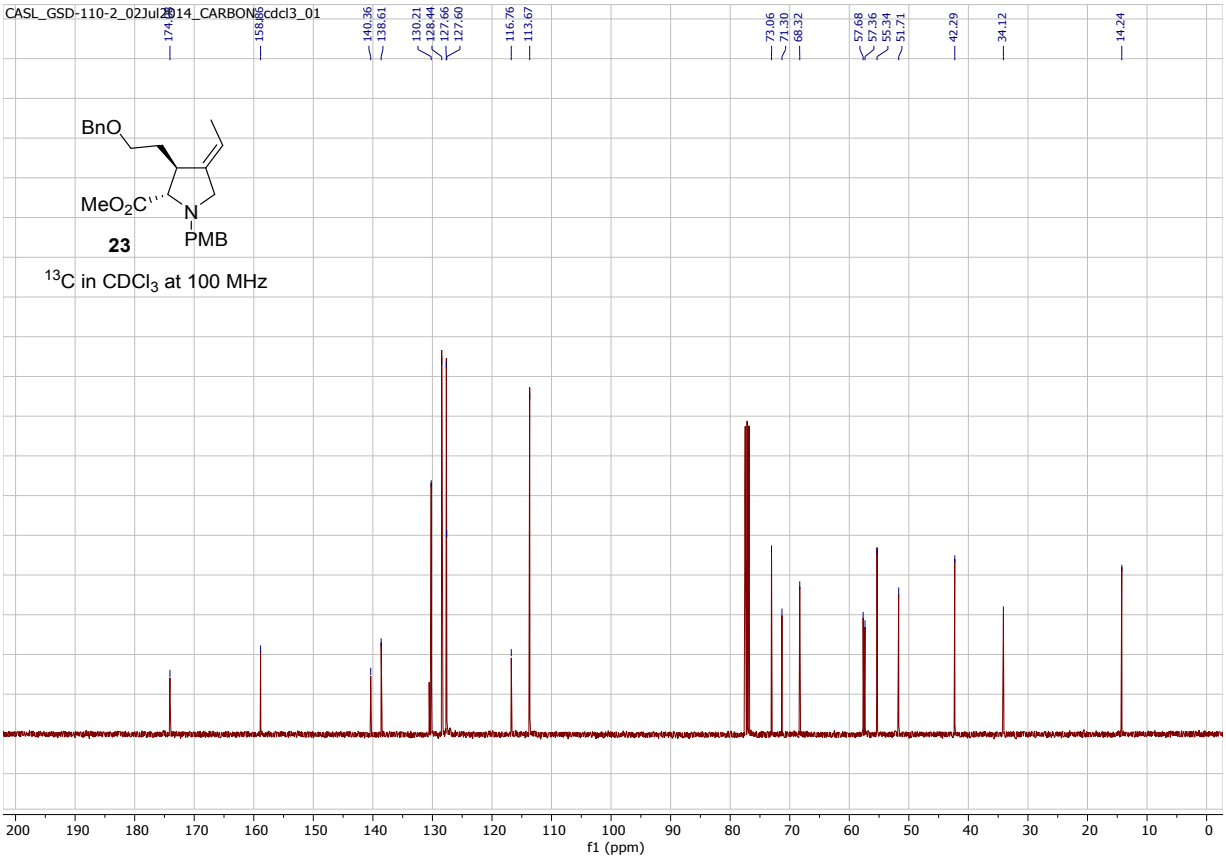
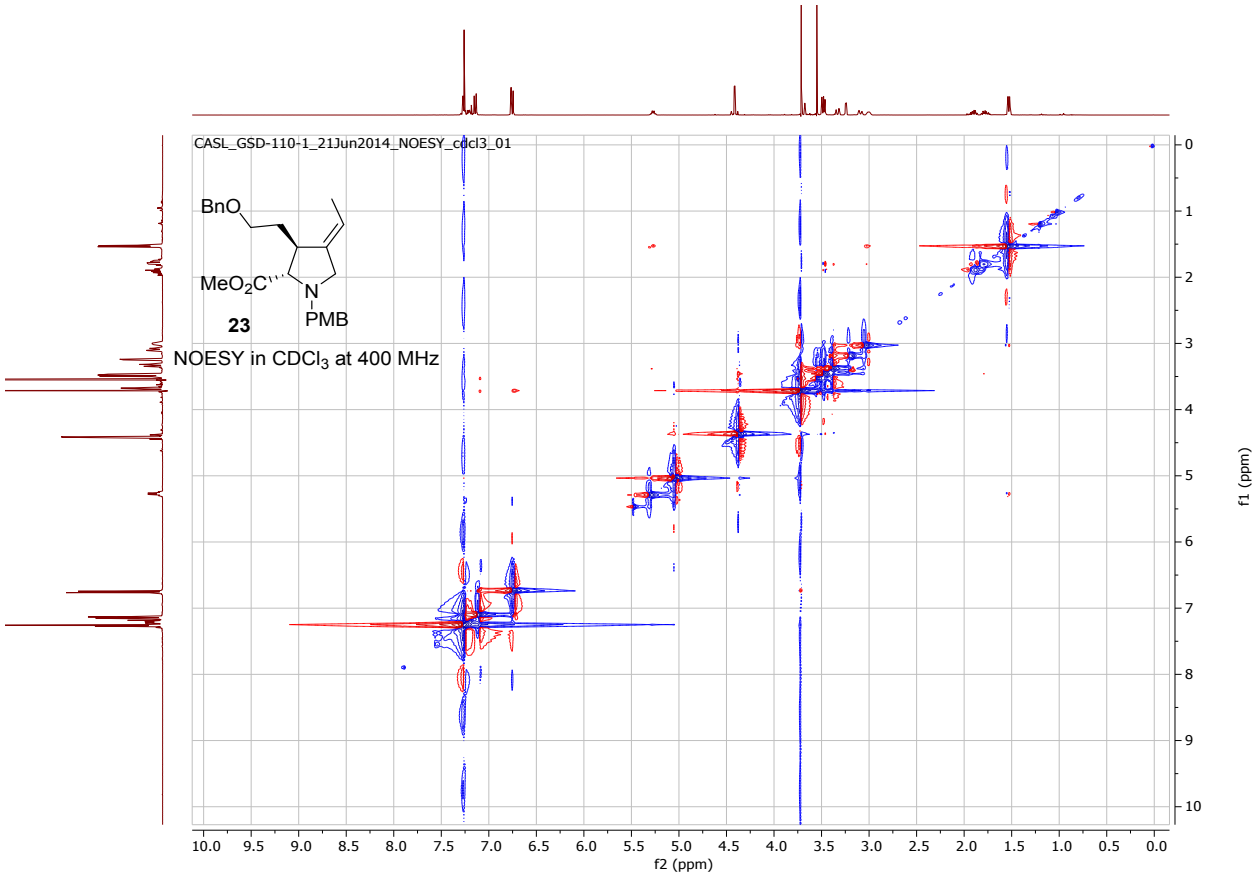
f1 (ppm)


BnO
MeO2C
N
PMB
23
13C in CDCl3 at 100 MHz
f1 (ppm)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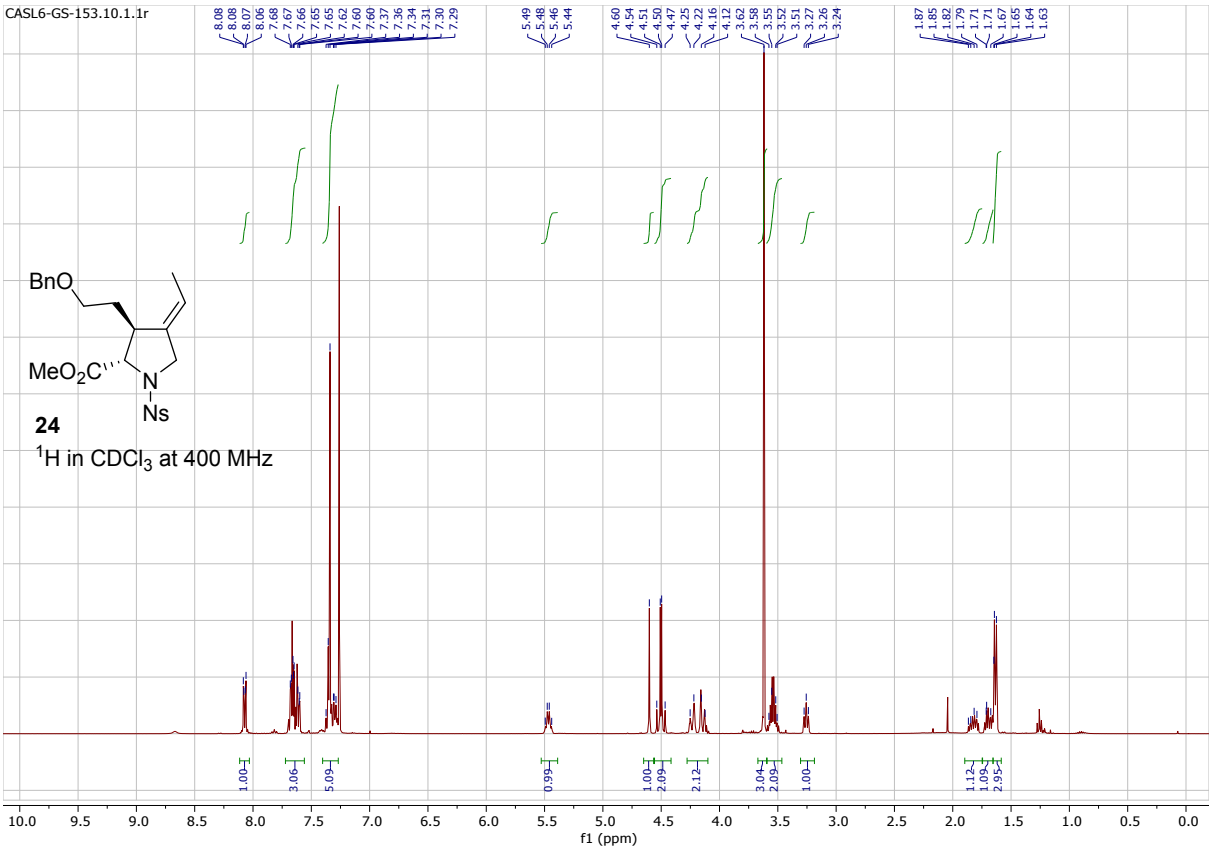
BnO
MeO2C
N
PMB
23
NOESY in CDCl3 at 400 MHz
f2 (ppm)
f1 (ppm)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Ns
24
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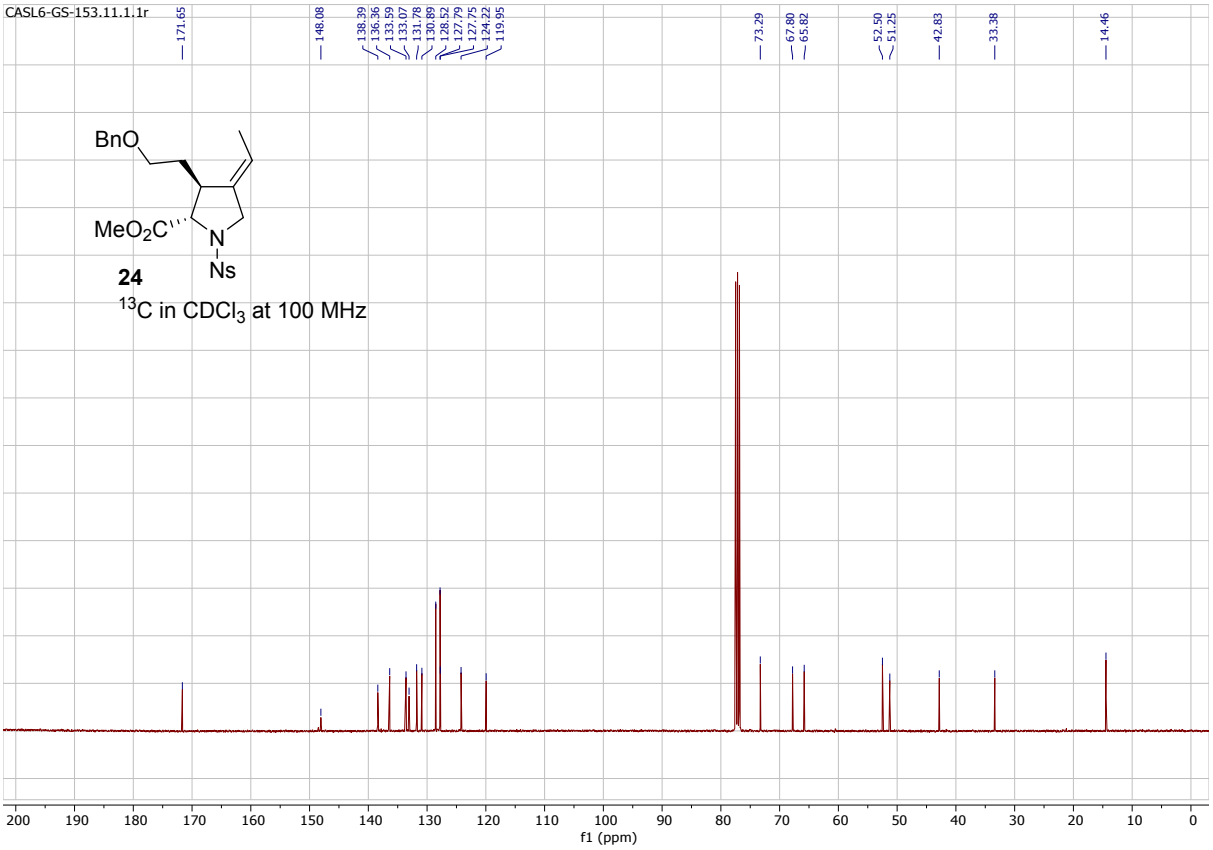
f1 (ppm)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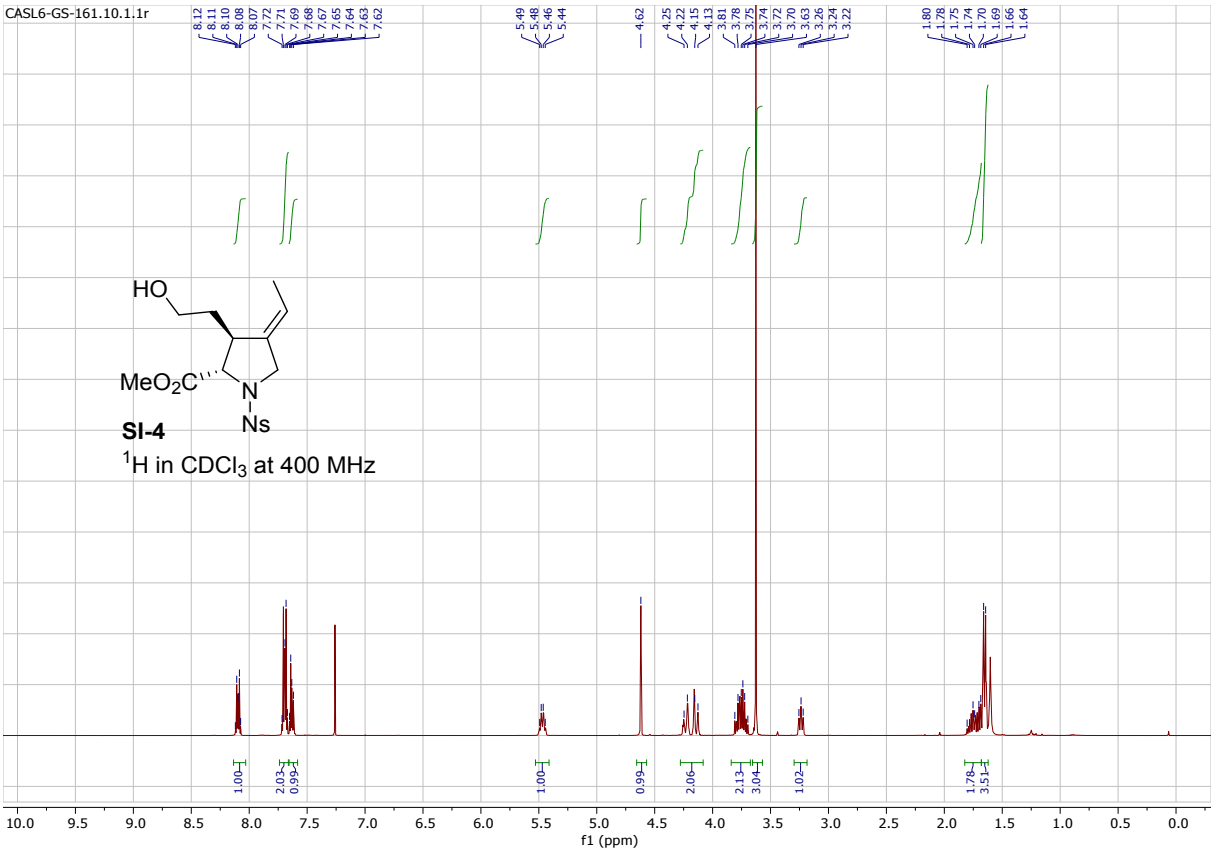
f1 (ppm)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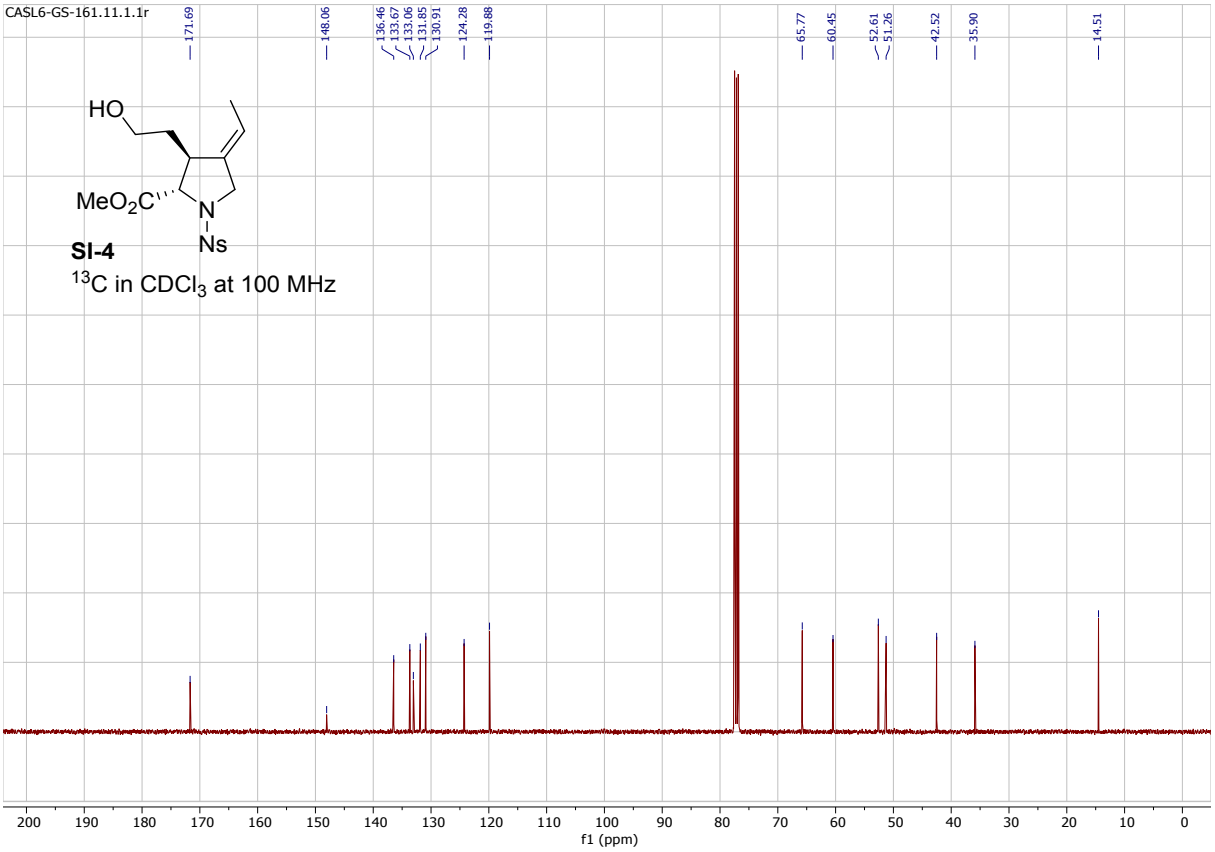
MeO2C
N
Ns
SI-4
1H in CDCl3 at 400 MHz
f1 (ppm)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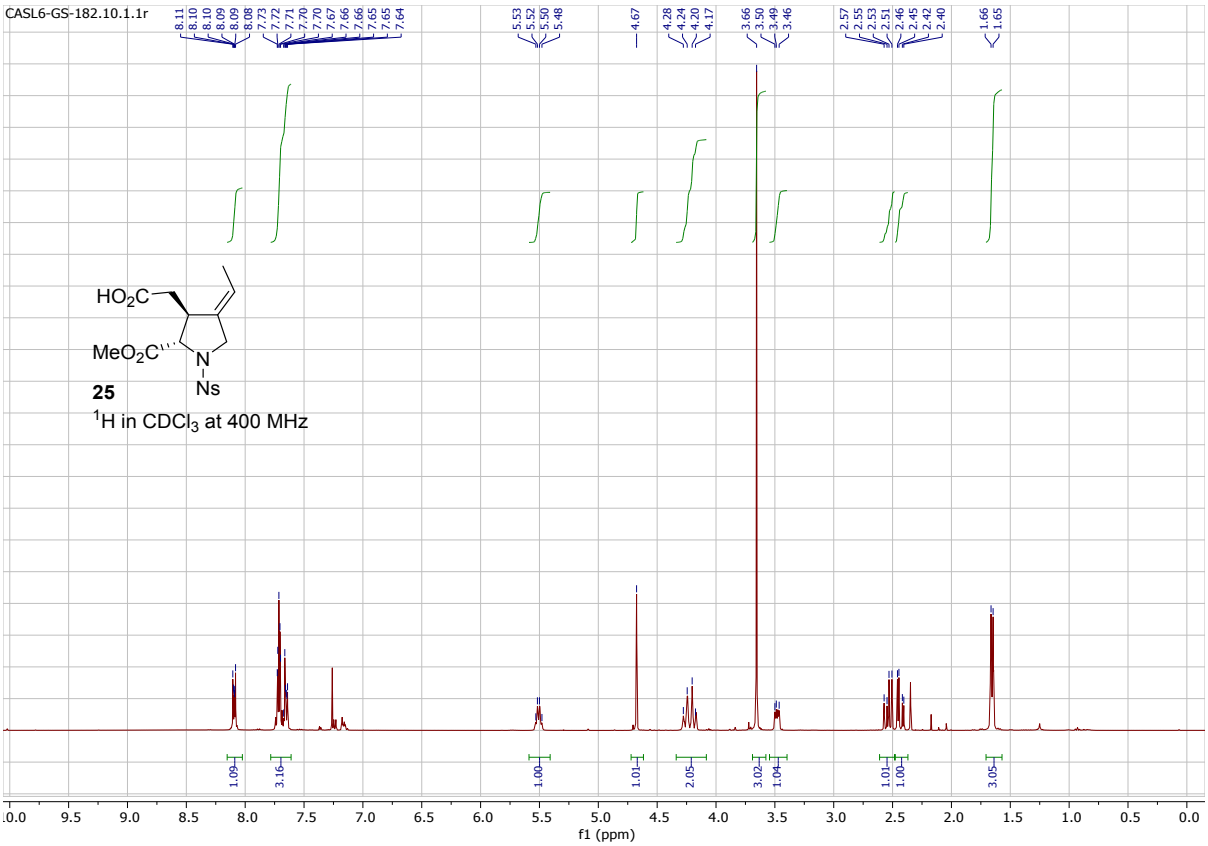
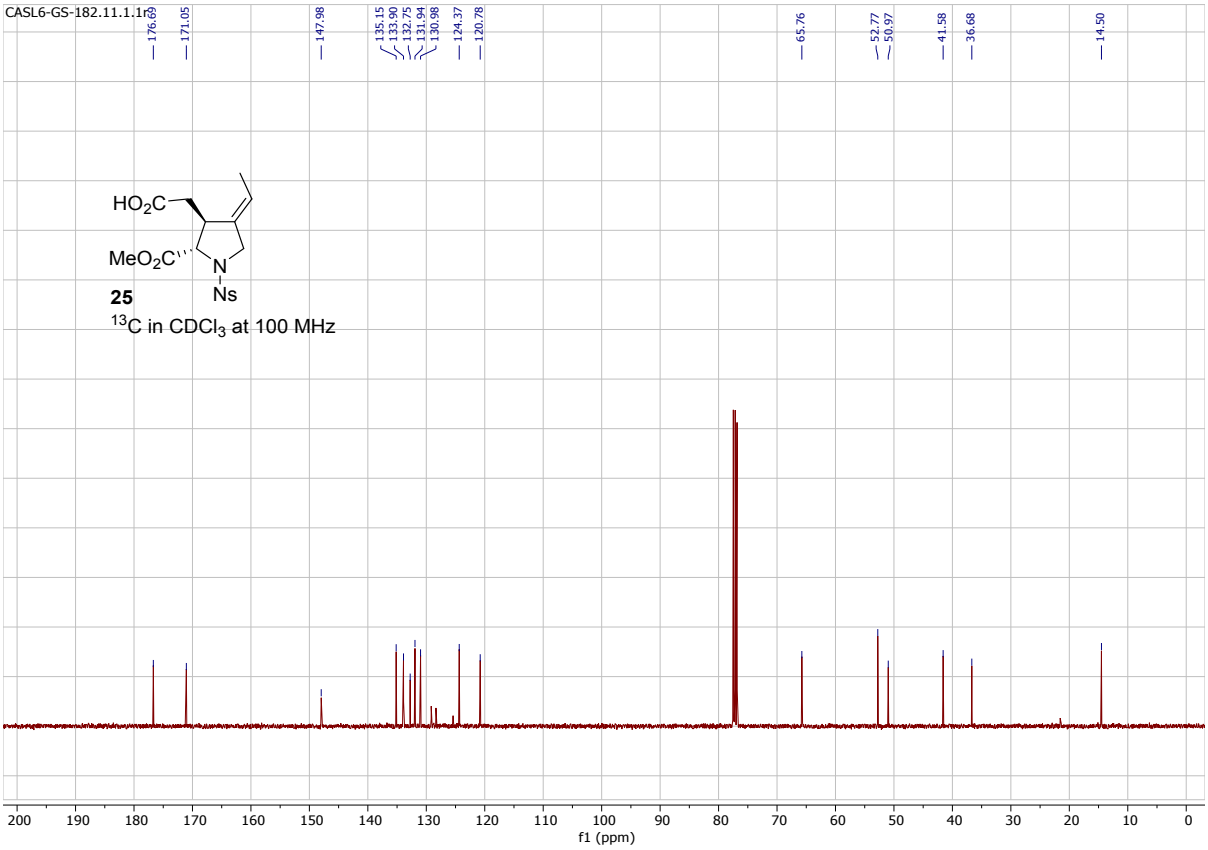
MeO2C
N
Ns
SI-4
13C in CDCl3 at 100 MHz
f1 (ppm)


CASL6-GS-182.10.1.1r
HO2C
MeO2C
N
Ns
25
1H in CDCl3 at 400 MHz
f1 (ppm)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MeO2C
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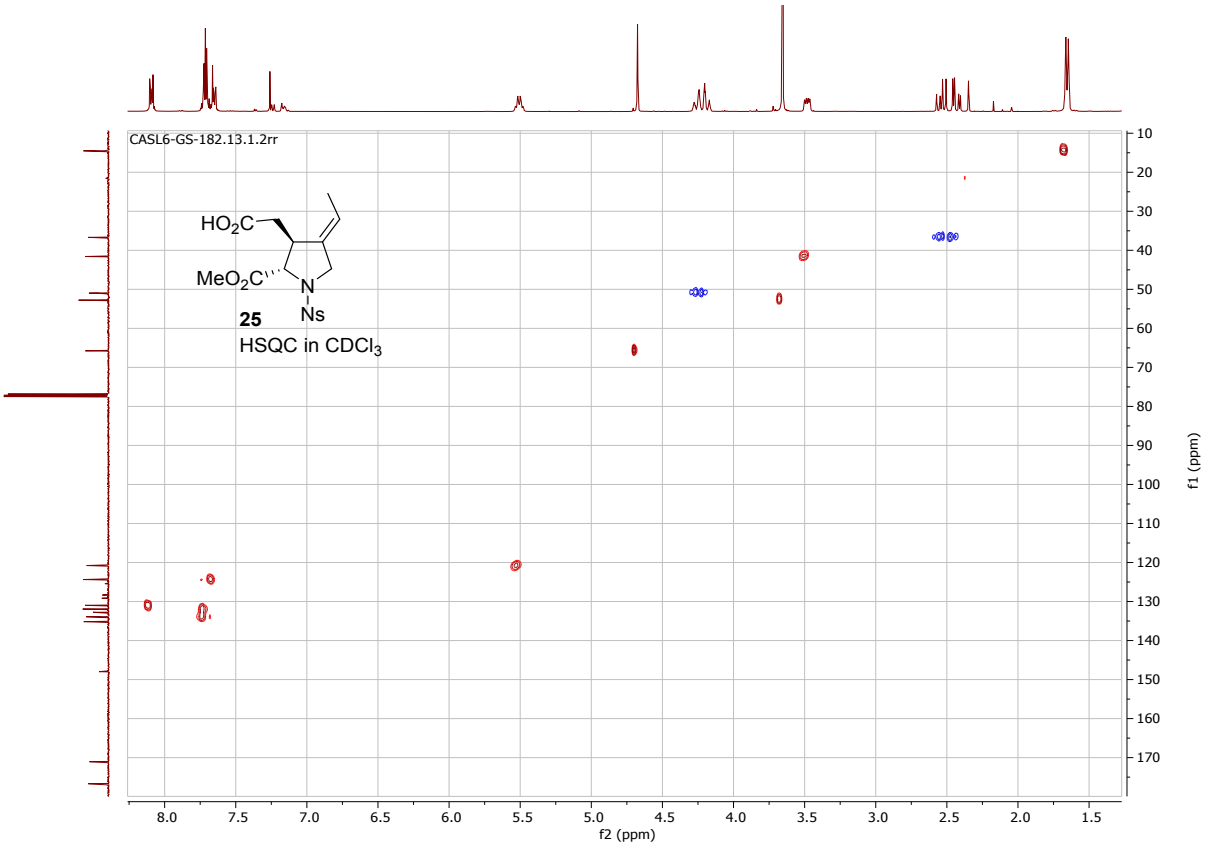
13C in CDCl3 at 100 MHz
f1 (ppm)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MeO2C
N
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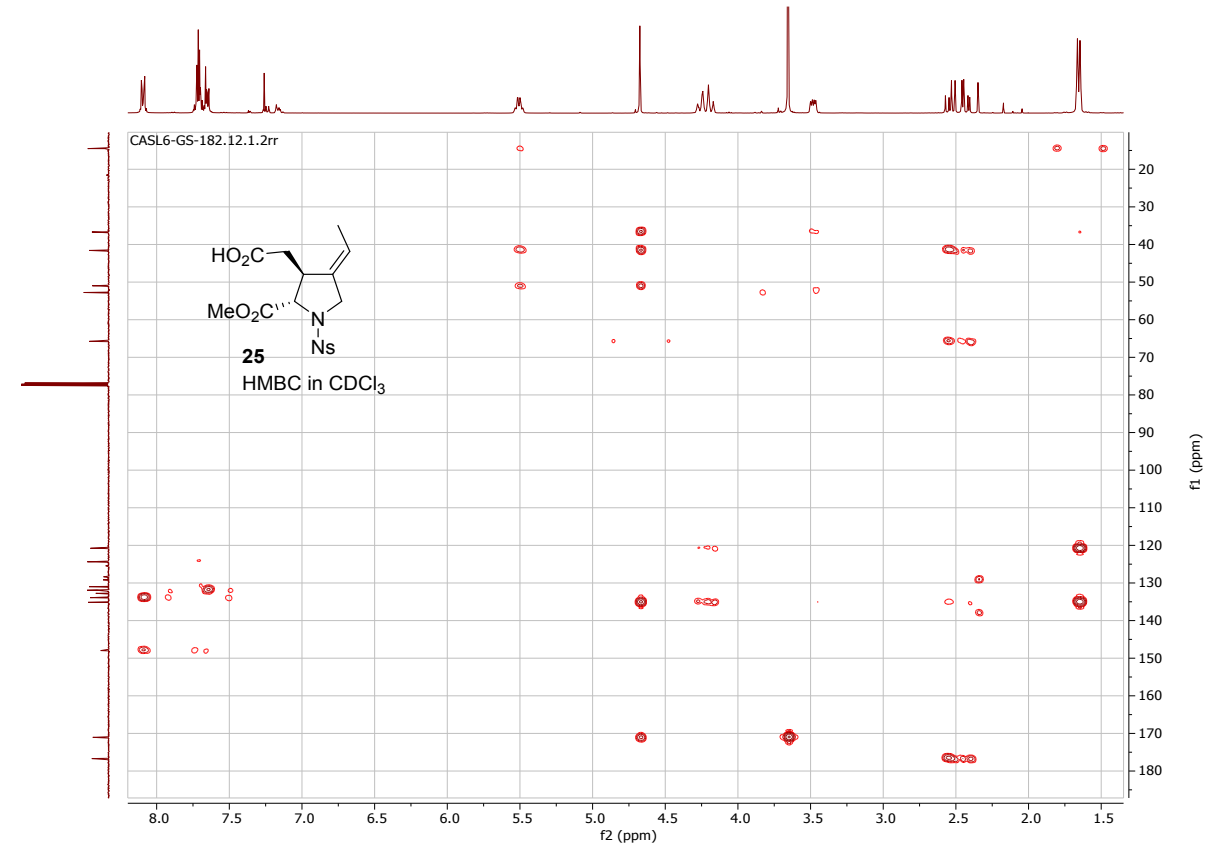
25
HSQC in CDCl3
f2 (ppm)
f1 (ppm)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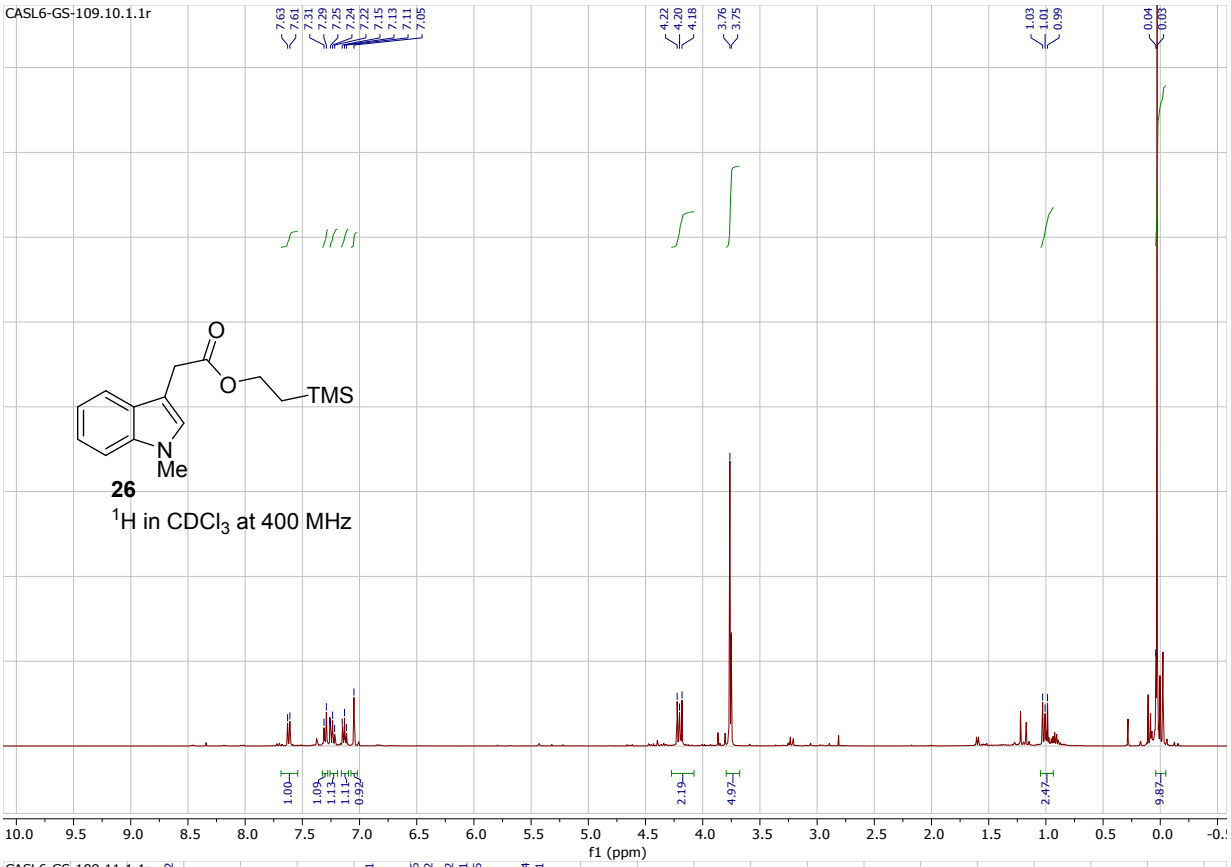
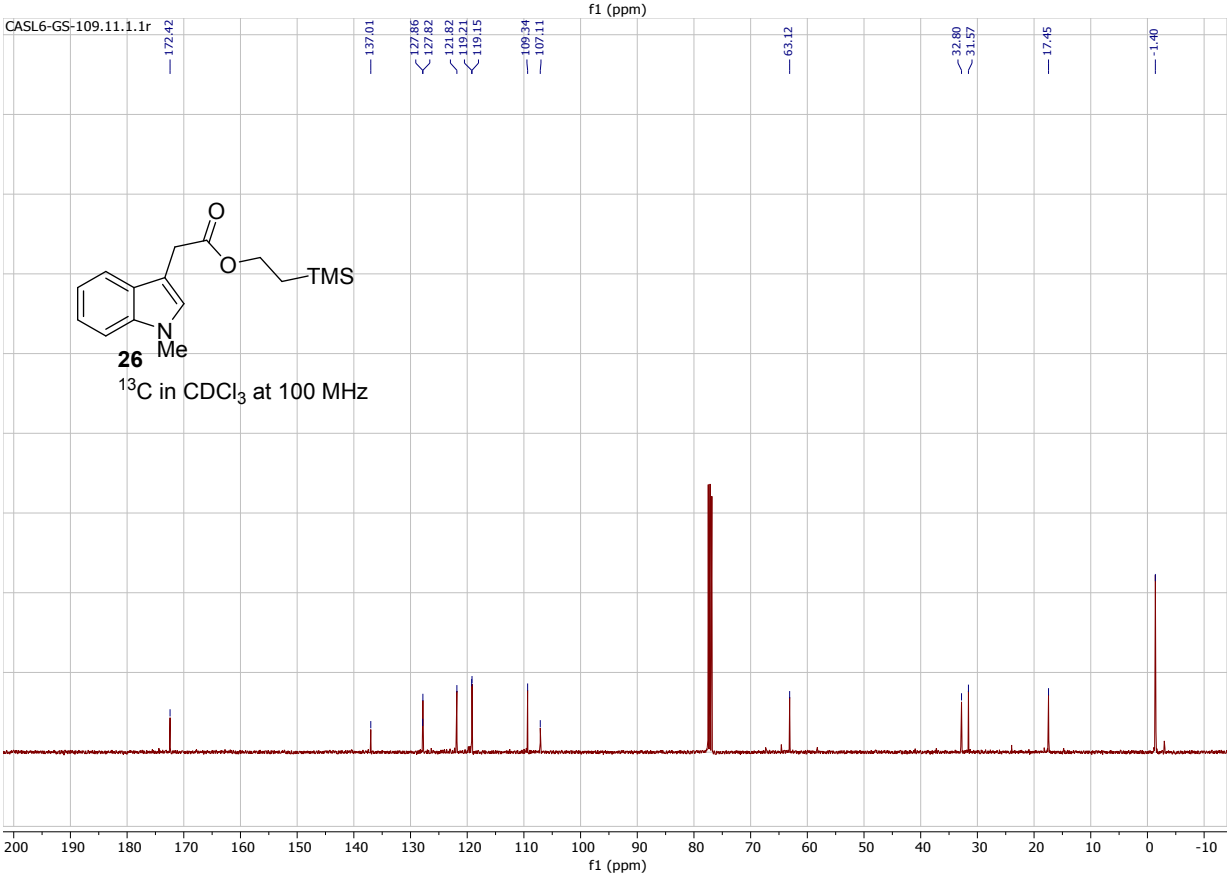
HMBC in CDCl3
f2 (ppm)
f1 (ppm)



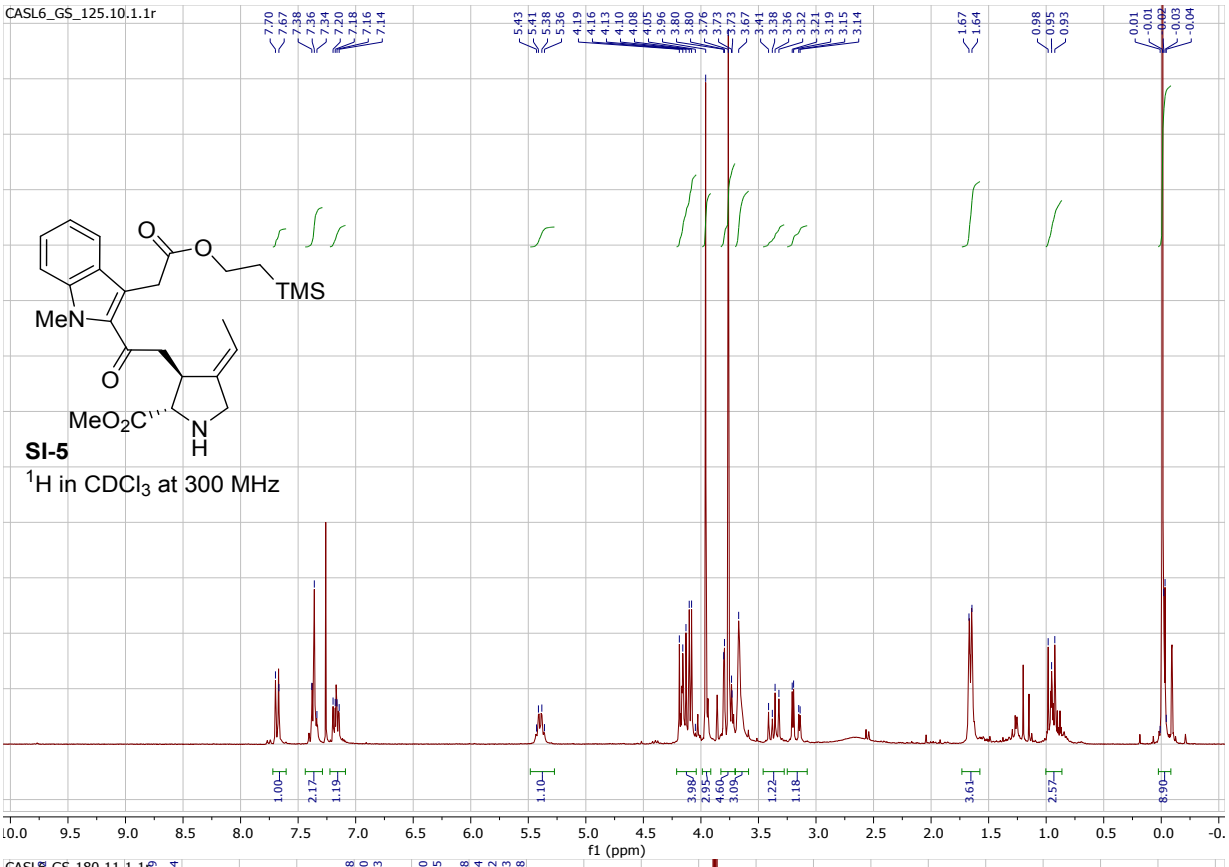
26

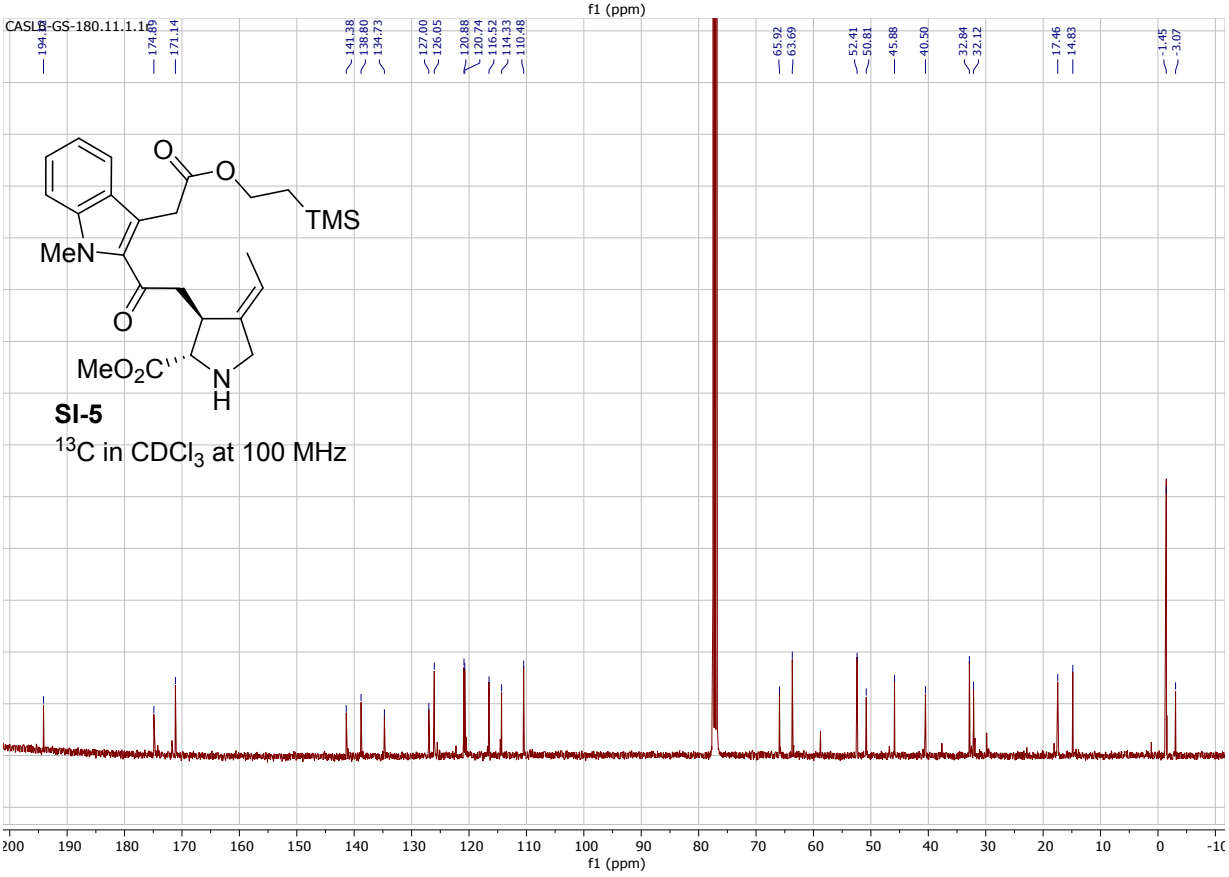
^{1}H in $CDCl_3$ at 400 MHz

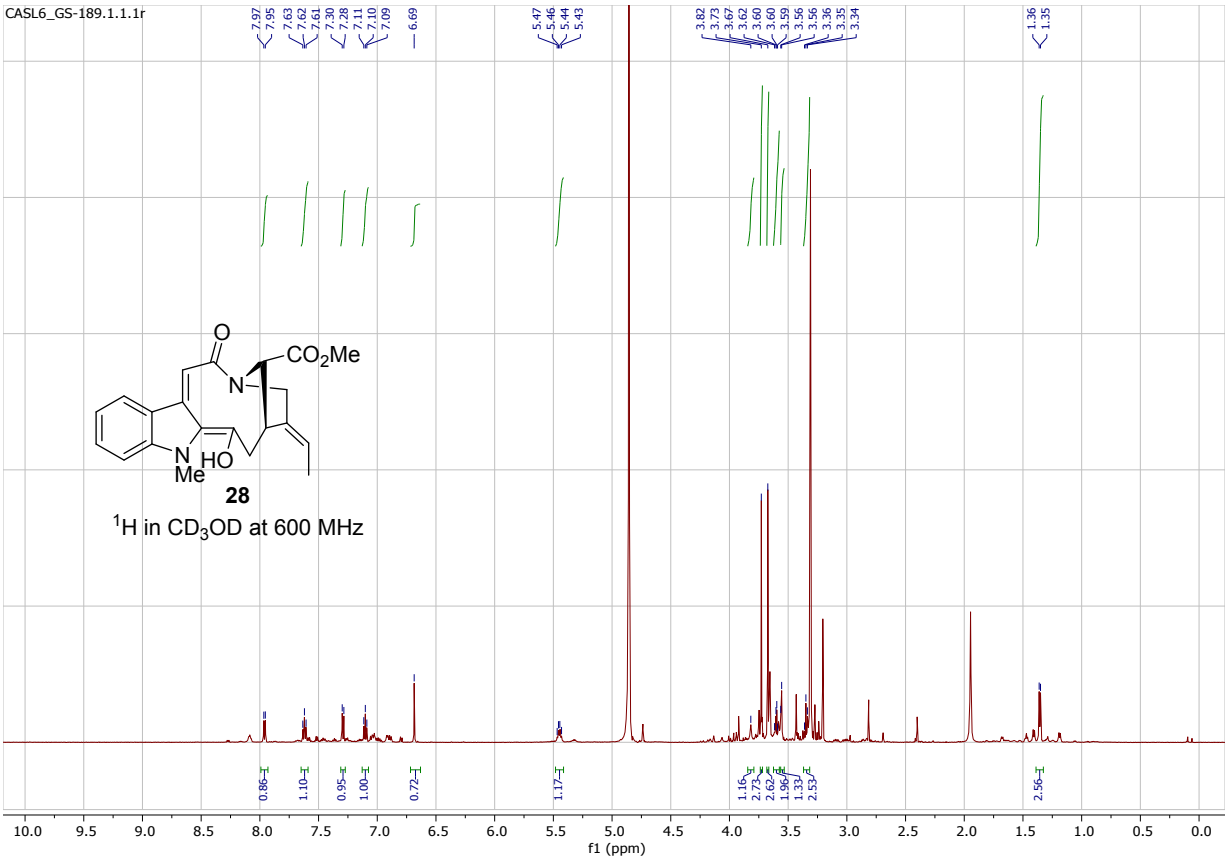


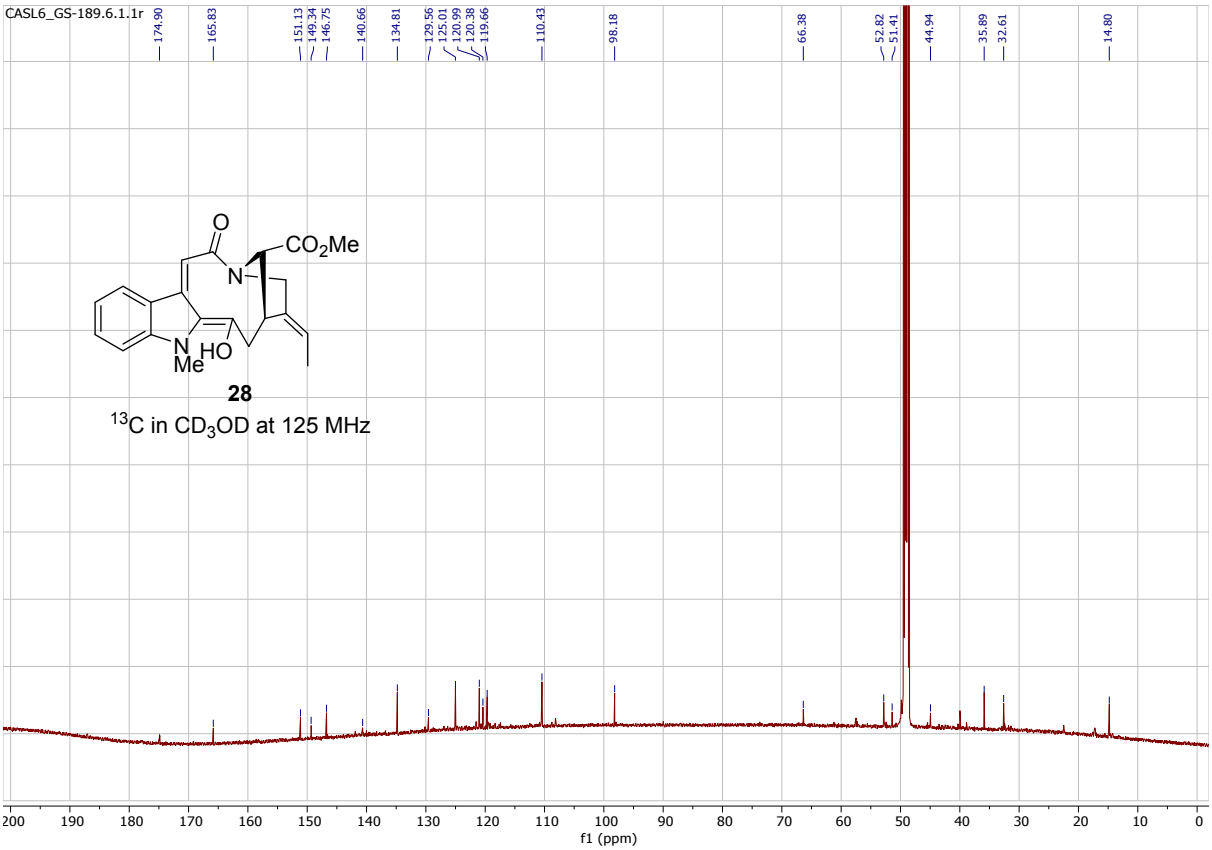
26

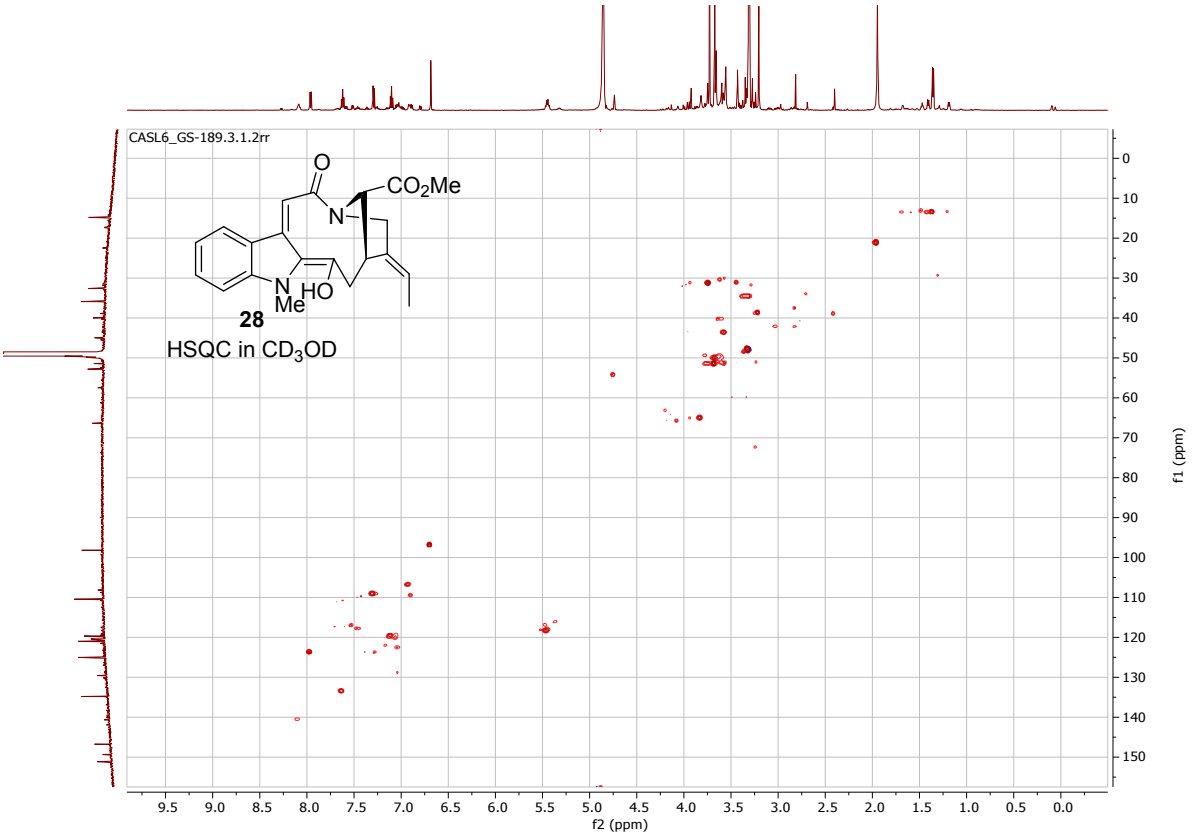
^{13}C in $CDCl_3$ at 100 MHz

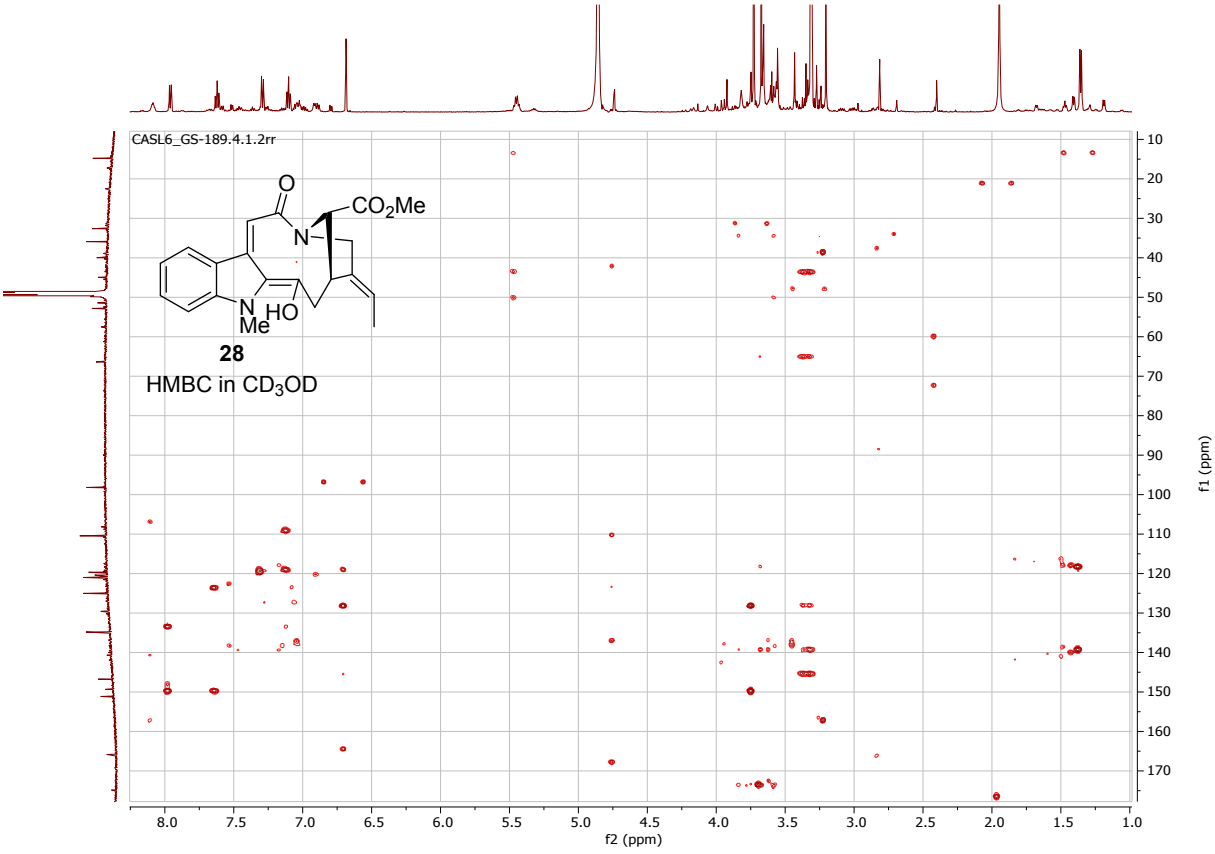

CASL6_GS_125.10.1.1r
TMS
MeN
MeO2C
N
H
SI-5
1H in CDCl3 at 300 MHz
f1 (ppm)

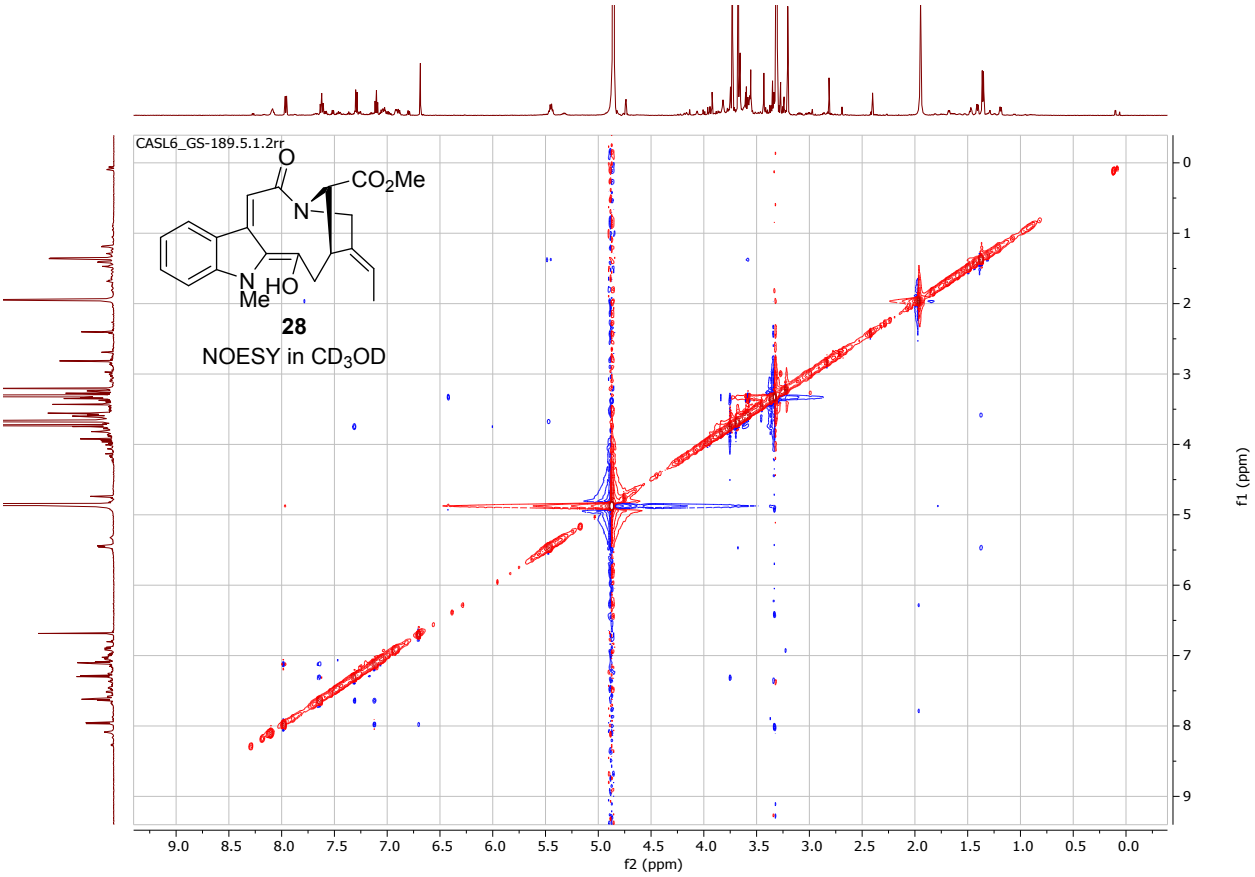

TMS
MeN
MeO2C
N
H
SI-5
13C in CDCl3 at 100 MHz
f1 (ppm)


CASL6_GS-189.1.1.1r
7.97
7.95
7.63
7.62
7.61
7.30
7.28
7.11
7.10
7.09
6.69
5.47
5.46
5.44
5.43
3.82
3.73
3.67
3.62
3.60
3.60
3.59
3.56
3.56
3.36
3.35
3.34
1.36
1.35
O
CO2Me
N
N
Me
HO
28
1H in CD3OD at 600 MHz
0.86
1.10
0.95
1.00
0.72
1.17
1.16
2.73
2.62
1.96
1.33
2.53
2.56
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


CASL6_GS-189.6.1.1r
174.90
165.83
151.13
149.34
146.75
140.66
134.81
129.56
125.01
120.99
120.38
119.66
110.43
98.18
66.38
52.82
51.41
44.94
35.89
32.61
14.80
O
CO2Me
N
N
Me
HO
28
13C in CD3OD at 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


CASL6_GS-189.3.1.2rr
O
CO2Me
N
N
Me
HO
28
HSQC in CD3OD
f2 (ppm)
f1 (ppm)


CASL6_GS-189.4.1.2rr
O
CO2Me
N
N
Me
HO
28
HMBC in CD3OD
f2 (ppm)
f1 (ppm)


CASL6_GS-189.5.1.2rr
O
CO2Me
N
N
Me
HO
28
NOESY in CD3OD
f2 (ppm)
f1 (ppm)