Supporting information

Enantiopure Piperidines via Stereoselective Ireland-Claisen Rearrangement: Entry into Corynanthe Alkaloids

Niklāvs Ūdris, Rebeka Ločmele, Juris Pelšs, Anastasija Ture, Guna Sakaine, Artis Kinēns, and Gints Smits*

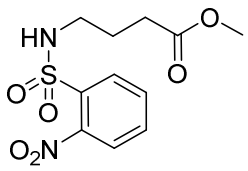
Contents

General Experimental Methods

Commercially available reagents and starting materials were used as received. All reactions in anhydrous solvents were performed under an atmosphere of argon. THF was dried over Na and benzophenone and distilled before use, and other solvents were purchased from commercial sources labeled as anhydrous over molecular sieves. For analytical thin-layer chromatography, Merck TLC Silica gel 60 F_{254} plates were used. Flash chromatography was carried out using Zeochem silica gel ZEOprep 60 (40-63µm) for the direct phase and Biotage KP-C18-HS for the reverse phase. NMR spectra were recorded on Varian Mercury (600 and 400 MHz) and Bruker (300 MHz) spectrometers. Chemical shift values were referenced against residual protons in the deuterated solvents. Cross peaks multiplicity marked as s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, h = sextet, hept = heptet, m = multiplet, br = broad). Infrared spectra were recorded in the range 4000-500 cm^{-1} as a film. HRMS spectra were obtained on Micromass AutoSpec Ultima Magnetic sector mass spectrometer (TOF). Optical rotations were measured on a Rudolph Research Analytical Autopol VI polarimeter. Melting points were determined on the Stanford Research System MPA100 apparatus and are uncorrected. Crystallographic data have been registered in the Cambridge Crystallographic Data Centre.

Synthesis of starting materials

Methyl 4-((2-nitrophenyl)sulfonamido)butanoate SI-1



To a stirred solution of ethyl 4-aminobutyrate hydrochloride (10.05 g, 65.428 mmol, 1 eq.) and TEA (27.36 mL, 196.284 mmol, 3 eq.) in 250 mL DCM 2-nitrobenzene sulfonyl chloride (14.50 g, 65.428 mmol, 1 eq.) was added in small portions over 1 h at 0ºC. After stirring the reaction at room temperature for 3 h, the mixture was diluted with 250 mL H_2O. Layers were separated and aqueous phase was extracted with DCM (2x250 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and evaporated. The oily residue was purified by CC (Pet:EtOAc 1:0 –> 1:2) to give the title compound **SI-1** 19.25 g (97%) as yellow oil.

R_f = 0.44 (PE 1: EA 1).

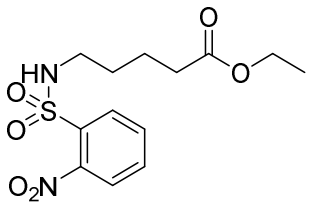
^{1}H NMR (400MHz; $CDCl_3$): δ 8.13 – 8.08 (m, 1H), 7.87 – 7.81 (m, 1H), 7.77 – 7.70 (m, 2H), 5.52 – 5.42 (m, 1H), 3.65 (s, 3H), 3.15 (q, *J* = 6.6 Hz, 2H), 2.39 (t, *J* = 7.1 Hz, 2H), 1.86 (p, *J* = 6.9 Hz, 2H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 173.4, 148.2, 133.7, 133.7, 132.9, 131.2, 125.5, 51.9, 43.1, 30.8, 24.9.

HRMS-ESI (m/z): [M+H] calculated for $C_{11}H_{14}N_2O_6SNa$, 325.0470; found 325.0474

IR (ν_{max}, film): 3325, 2952, 1732, 1538, 1365, 1342, 1164 cm^{-1}.

Ethyl 5-((2-nitrophenyl)sulfonamido)pentanoate SI-2



To a stirred solution of ethyl 5-aminopentanoate hydrochloride (9.10 g, 50.093 mmol, 1 eq.) and TEA (20.94 mL, 150.281 mmol, 3 eq.) in 150 mL DCM 2-nitrobenzene sulfonyl chloride (11.656 g, 52.598 mmol, 1.05 eq.) was added in small portions over 1 h at 0ºC. After stirring the reaction at room temperature for 3 h, the mixture was diluted with 200 mL H_2O. Layers were separated and aqueous phase was extracted with DCM (2x200 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and evaporated. The oily residue was purified by CC (Pet:EtOAc 2:1) to give the title compound **SI-2** 15.88 g (96%) as yellow oil.

$\mathbf{R}_f$ = 0.45 (PE 1: EA 1).

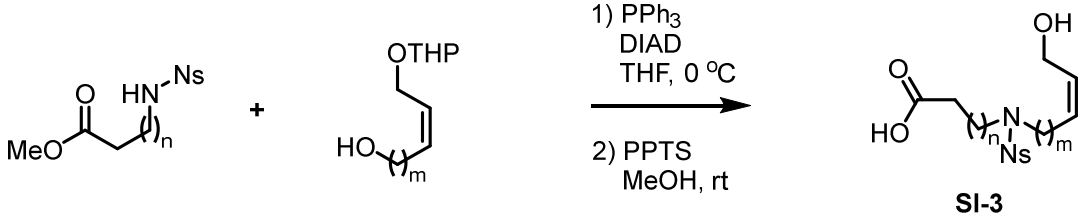
^{1}H NMR (400MHz; $CDCl_3$): δ 8.15 – 8.08 (m, 1H), 7.89 – 7.81 (m, 1H), 7.79 – 7.68 (m, 2H), 5.35 (t, *J* = 6.1 Hz, 1H), 4.10 (q, *J* = 7.2 Hz, 2H), 3.10 (q, *J* = 6.8 Hz, 2H), 2.27 (t, *J* = 7.1 Hz, 2H), 1.70 – 1.51 (m, 4H), 1.23 (t, *J* = 7.2 Hz, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 172.9, 147.9, 133.4, 133.4, 132.6, 130.9, 125.2, 60.2, 43.2, 33.3, 28.9, 21.6, 14.0.

HRMS-ESI (m/z): [M+Na] calculated for $C_{13}H_{18}N_2O_6SNa$, 353.0783; found 353.0794.

IR (ν_{max}, film): 3328, 2979, 2941, 1733, 1542, 1367, 1340, 1164 cm^{-1}.

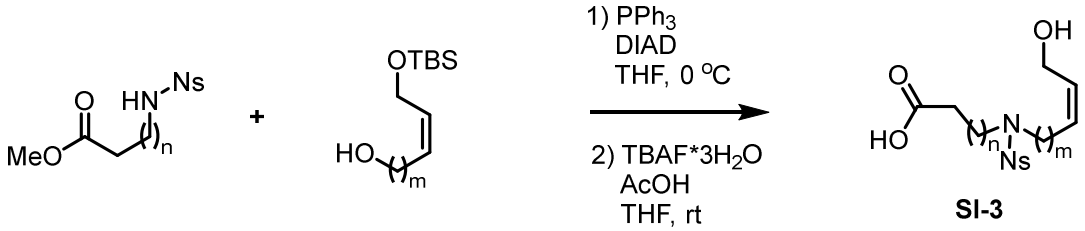
General procedure 1. Mitsunobu reaction followed by THP group cleavage



Mitsunobu reaction. To a stirred solution of the corresponding *N*-nosyl-protected amino acid ester (63.284 mmol, 1 eq), vinyl alcohol (82.264 mmol, 1.3 eq) and PPh_3 (24.90 g, 94.926 mmol, 1.5 eq) in dry THF (350 mL) was added DIAD (18.69 ml, 19.19 g, 94.926 mmol, 1.5 eq) at 0 °C dropwise. The mixture was allowed to warm to rt and stirred for 2h. After that, the reaction mixture was evaporated and the oily residue was purified by flash column chromatography. The collected fractions always contained some impurities from DIAD and unreacted vinyl alcohol. The obtained product was used in the next step like it is since the impurities do not interfere with the protecting group cleavage step and can be easily separated afterward.

THP cleavage. To a stirred solution of the substrate from the previous step (63.284 mmol, 1 eq, *theoretical yield of the 1st step*) in MeOH (300 mL) was added PPTS (1.12 g, 4.447 mmol, 0.07 eq) and the mixture stirred for 16 h at rt. After that $NaHCO_3$ (373 mg, 4.447 mmol, 0.07 eq) was added to quench the acid and the volatiles were removed in *vacuo,* and water was added to the oily residue. The slurry was extracted with EtOAc (2*200mL). The combined organic extracts were dried over anh. Na_2SO_4, filtered and evaporated. The oily residue was purified by flash column chromatography.

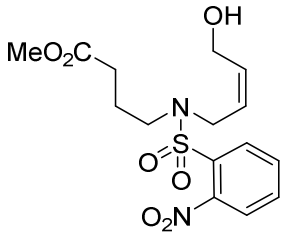
General procedure 2. Mitsunobu reaction followed by TBS group cleavage



Mitsunobu reaction was performed exactly as in **General procedure 1**.

TBS cleavage. To a stirred solution of the substrate from the previous step (3.475 mmol, 1 eq, *theoretical yield of the 1st step*) in THF (130 mL) was added TBAF*3H_2O (1.096 g, 3.475 mmol, 1 eq) and AcOH (0.2 mL, 209 mg, 3.475 mmol, 1 eq) and the resulting mixture stirred for 16h at rt. After that, the reaction mixture was evaporated and the oily residue was purified by flash column chromatography.

Methyl (Z)-4-((N-(4-hydroxybut-2-en-1-yl)-2-nitrophenyl)sulfonamido)butanoate SI-3a



The title compound prepared according to the General procedure 1 starting from **20** (19.13 g, 63.284 mmol, 1eq) and (*Z*)-4-((tetrahydro-2H-pyran-2-yl)oxy)but-2-en-1-ol[1] (14.17 g, 82.264 mmol, 1.3 eq) furnishing 19.87 g (84% over 2 steps) of **SI-3a** as a pale yellow wax.

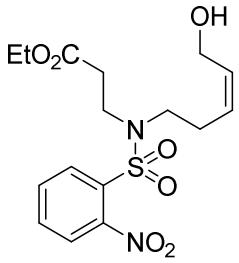
^{1}H NMR (400MHz; $CDCl_3$): δ 8.01 – 7.92 (m, 1H), 7.69 – 7.52 (m, 3H), 5.82 – 5.71 (m, 1H), 5.41 – 5.30 (m, 1H), 4.15 (t, *J* = 5.8 Hz, 2H), 3.98 (dd, *J* = 7.2, 1.6 Hz, 2H), 3.60 (s, 3H), 3.29 – 3.21 (m, 2H), 2.39 (t, *J* = 6.0 Hz, 1H), 2.29 (t, *J* = 6.7 Hz, 2H), 1.89 – 1.77 (m, 2H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 174.0, 148.1, 133.9, 133.7, 133.6, 131.9, 131.0, 126.1, 124.4, 58.1, 52.1, 46.6, 44.1, 30.4, 23.2.

HRMS-ESI (m/z): [M+Na] calculated for $C_{15}H_{20}N_2O_7SNa$, 395.0889; found 395.0899.

IR (ν_{max}, film): 2955, 1730, 1545, 1437, 1372, 1348, 1162, 1126 cm^{-1}.

Ethyl (*Z*)-3-((N-(5-hydroxypent-3-en-1-yl)-2-nitrophenyl)sulfonamido)propanoate SI-3b



The title compound prepared according to the General procedure 2 starting from ethyl 3-((2-nitrophenyl)sulfonamido)propanoate[2] (1.370g, 4.529 mmol, 1 eq) and (Z)-5-((tert-butyldimethylsilyl)oxy)pent-3-en-1-ol[3] (980 mg, 4.529 mmol, 1 eq) furnishing 928 mg (69% over 2 steps) of **SI-3b** as a colorless wax.

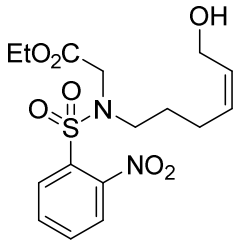
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.99 (m, 1H), 7.81 – 7.56 (m, 3H), 5.76 – 5.65 (m, 1H), 5.50 – 5.38 (m, 1H), 4.19 – 3.58 (m, 4H), 3.62 (t, *J* = 7.3 Hz, 2H), 3.36 (dd, *J* = 8.2, 6.7 Hz, 2H), 2.58 (t, *J* = 7.3 Hz, 2H), 2.38 (q, *J* = 6.7 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 171.4, 148.2, 133.9, 133.3, 131.9, 131.7, 131.1, 127.8, 124.4, 61.1, 58.4, 47.9, 43.3, 33.9, 26.9, 14.2.

HRMS-ESI (m/z): [M+Na] calculated for $C_{16}H_{22}N_2O_7SNa$, 409.1045; found 409.1044.

IR (ν_{max}, film): 3416, 2935, 1732, 1377, 1345, 1196, 1162, 1029, 779 m^{-1}.

Ethyl (Z)-N-(6-hydroxyhex-4-en-1-yl)-N-((2-nitrophenyl)sulfonyl)glycinate SI-3c



The title compound prepared according to the General procedure 2 starting from ethyl ((2-nitrophenyl)sulfonyl)glycinate[2] (9.633 g, 33.417 mmol, 1 eq) and (Z)-6-((tert-butyldimethylsilyl)oxy)hex-4-en-1-ol (7.70 g, 33.417 mmol, 1 eq)[4] furnishing 9.28 g (72% over 2 steps) of **SI-3c** as a white wax.

R_f = 0.42 (PE 1: EA 2).

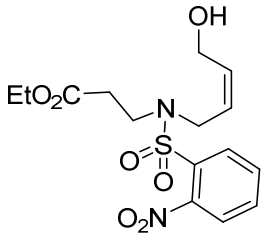
^{1}H NMR (400MHz; $CDCl_3$): δ 8.10 – 8.03 (m, 1H), 7.73 – 7.56 (m, 3H), 5.72 – 5.57 (m, 1H), 5.51 – 5.39 (m, 1H), 4.19 – 4.13 (m, 4H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.47 – 3.35 (m, 2H), 2.10 (d, *J* = 8.0 Hz, 2H), 1.74 – 1.58 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 168.8, 148.1, 133.7, 133.7, 133.4, 131.8, 131.0, 130.0, 124.3, 61.6, 58.6, 47.9, 47.8, 27.5, 24.4, 14.2.

HRMS-ESI (m/z): [M+Na] calculated for $C_{16}H_{22}N_2O_7SNa$, 409.1045; found 409.1040.

IR (ν_{max}, film): 2937, 1749, 1541, 1374, 1350, 1163, 1027, 779 cm^{-1}.

Ethyl (Z)-3-((N-(4-hydroxybut-2-en-1-yl)-2-nitrophenyl)sulfonamido)propanoate SI-3d



The title compound prepared according to the General procedure 1 starting from ethyl 3-((2-nitrophenyl)sulfonamido)propanoate[2] (16.71 g, 55.275 mmol, 1 eq) and (*Z*)-4-((tetrahydro-2H-pyran-2-yl)oxy)but-2-en-1-ol[1] (12.375 g, 71.858 mmol, 1.3 eq) furnishing 12.90 g (63% over 2 steps) of **SI-3d** as a colorless oil.

R_f = 0.14 (PE 1: EA 1).

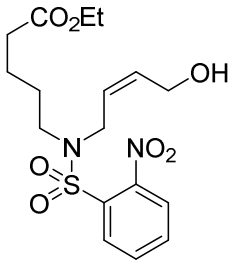
^{1}H NMR (400MHz; $CDCl_3$): δ 8.07 – 8.00 (m, 1H), 7.76 – 7.60 (m, 3H), 5.88 – 5,75 (m, 1H), 5.53 – 5,38 (m, 1H), 4.19 (d, *J* = 6.8 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 4.06 (d, *J* = 7.1 Hz, 2H), 3.59 (t, *J* = 7.0 Hz, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 1.25 (t, *J* = 7.2 Hz, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 171.9, 148.1, 133.9, 133.7, 133.3, 132.0, 131.1, 126.4, 124.4, 61.2, 58.0, 45.1, 43.2, 34.4, 14.2.

HRMS-ESI (m/z): [M+Na] calculated for $C_{15}H_{20}N_2O_7SNa$, 395.0889; found 395.0895.

IR (ν_{max}, film): 2982; 2936; 1735; 1728; 1538; 1437; 1370; 1350; 1196; 1162; 1028; 852; 776 cm^{-1}.

Ethyl (Z)-5-((N-(4-hydroxybut-2-en-1-yl)-2-nitrophenyl)sulfonamido)pentanoate SI-3e



The title compound prepared according to **General procedure 1** starting from **SI-2** (15.88 g, 48.069 mmol, 1 eq) and (*Z*)-4-((tetrahydro-2H-pyran-2-yl)oxy)but-2-en-1-ol[1] (10.762 g, 62.490 mmol, 1.3 eq) furnishing 13.70 g (68% over 2 steps) of **SI-3e** as a colorless oil.

R_f = 0.18 (PE 1: EA 1).

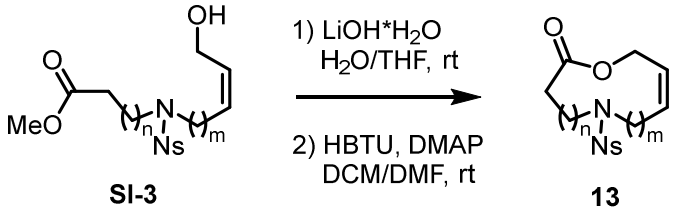
^{1}H NMR (400MHz; $CDCl_3$): δ 8.07 – 7.97 (m, 1H), 7.75 – 7.57 (m, 3H), 5.84 – 5.73 (m, 1H), 5.50 – 5,38 (m, 1H), 4.28 – 4.16 (m, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 4.01 (d, *J* = 7.1 Hz, 2H), 3.33 – 3.25 (m, 2H), 2.34 – 2.26 (m, 2H), 2.18 (t, *J* = 5.7 Hz, 1H), 1.61 – 1.51 (m, 4H), 1.24 (t, *J* = 7.2 Hz, 3H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 173.7, 148.1, 2 C 133.7, 133.3, 131.8, 131.0, 126.4, 124.4, 60.7, 58.2, 47.2, 44.1, 33.5, 27.5, 21.9, 14.3.

HRMS-ESI (m/z): [M+Na] calculated for $C_{17}H_{24}N_2O_7SNa$, 423.1202; found 423.1208.

IR (ν_{max}, film): 3448, 2982, 2940, 2874, 1729, 1544, 1373, 1350, 1162, 1030 cm^{-1}.

General procedure 3. Ester hydrolysis and macrolactonisation.

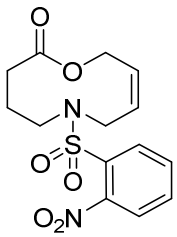


Ester hydrolysis. To a stirred solution of **SI-3** (61.763 mmol, 1 eq) in THF (40 mL) was added a solution of LiOH*H_2O (6.41 g, 247.049 mmol, 4 eq) in water (170 mL). The mixture slowly becomes homogeneous and the reaction is complete in ~2 h. After that, the pH was adjusted to

~1-2 by adding concentrated HCl and the mixture extracted with DCM (3*200 mL). The combined organic extracts were dried over anh. Na_2SO_4, filtered and evaporated. The obtained oily material used in the next step like it is.

Macrolactonisation. To a stirred slurry of HBTU (93.69 g, 247.052 mmol, 4 eq) and DMAP (30.18 g, 247.052 mmol, 4 eq) in dry DCM (3.5 L) was added a solution of the substrate from the previous step in dry DMF (200 mL) over a period of 6 h. The obtained mixture was stirred for an additional 16 h at rt. After that water was added and the mixture stirred vigorously for 15 min. Then the organic phase was separated and the aqueous phase was extracted with DCM (500 mL). The combined organic extracts were dried over anh. Na_2SO_4, filtered and evaporated. The residue was purified by flash column-chromatography (eluent: DCM/EtOAc).

(Z)-6-((2-nitrophenyl)sulfonyl)-3,4,5,6,7,10-hexahydro-2H-1,6-oxazecin-2-one 13a



The title compound was prepared according to **General procedure 3**. Starting from (23.00 g, 61.763 mmol, 1 eq) of **SI-3a** lactone **13a** (15.00 g, 71% yield in 2 steps) was obtained as a white solid.

R_f = 0.28 (PE 1: EA 1).

^{1}H NMR (400MHz; $CDCl_3$): δ 8.06 – 7.99 (m, 1H), 7.75 – 7.58 (m, 3H), 5.96 – 5.86 (m, 1H), 5.63 – 5.51 (m, 1H), 4.79 (d, *J* = 5.7 Hz, 2H), 4.11 (d, *J* = 8.4 Hz, 2H), 3.26 (t, *J* = 6.1 Hz, 2H), 2.44 – 2.35 (m, 2H), 2.08 – 1.96 (m, 2H).

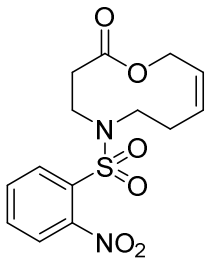
^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 171.8, 148.1, 133.8, 132.9, 131.8, 131.5, 131.1, 127.3, 124.2, 60.3, 44.6, 44.2, 32.8, 23.3.

HRMS-ESI (m/z): [M+H] calculated for $C_{14}H_{17}N_2O_6S$, 341.0807; found 341.0809.

IR (ν_{max}, film): 2926, 1738, 1545, 1374, 1162 cm^{-1}.

MP = 140-142 °C.

(Z)-5-((2-nitrophenyl)sulfonyl)-3,4,5,6,7,10-hexahydro-2H-1,5-oxazecin-2-one 13b



The title compound was prepared according to **General procedure 3**. Starting from (2.10 g, 5.434 mmol, 1 eq) of **SI-3b** lactone **13b** (900 mg, 49% yield in 2 steps) was obtained as a white solid.

R_f = 0.21 (PE 1: EA 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.95 (m, 1H), 7.77 – 7.63 (m, 2H), 7.61 – 7.51 (m, 1H), 5.81 – 5.70 (m, 1H), 5.49 – 5.37 (m, 1H), 4.74 (d, *J* = 4.6 Hz, 2H), 3.62 – 3.54 (m, 2H), 3.34 – 3.27 (m, 2H), 2.83 – 2.75 (m, 2H), 2.55 – 2.44 (m, 2H).

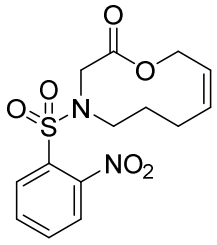
^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 170.7, 149.0, 2 C 134.0, 2 C 131.5, 131.2, 127.9, 123.8, 60.6, 50.1, 45.7, 36.1, 28.3.

HRMS-ESI (m/z): [M+Na] calculated for $C_{14}H_{16}N_2O_6SNa$, 363.0627; found 363.0628.

IR (ν_{max}, film): 1740, 1539, 1374, 1355, 1167, 746 cm^{-1}.

MP = 170-173 °C.

(Z)-4-((2-nitrophenyl)sulfonyl)-3,4,5,6,7,10-hexahydro-2H-1,4-oxazecin-2-one 13c



The title compound was prepared according to **General procedure 3**. Starting from (9.28 g, 24.015 mmol, 1 eq) of **SI-3c** lactone **13c** (3.20 g, 39% yield in 2 steps) was obtained as a white solid.

R_f = 0.36 (PE 1: EA 1).

^{1}H NMR (400MHz; $CDCl_3$): 8.07 – 7.97 (m, 1H), 7.76 – 7.59 (m, 3H), 5.72 – 5.60 (m, 1H), 5.53 (dt, *J* = 11.2, 3.8 Hz, 1H), 4.91 – 4.85 (m, 2H), 4.09 (s, 2H), 3.23 – 3.15 (m, 2H), 2.40 (q, *J* = 6.9 Hz, 2H), 1.74 – 1.63 (m, 2H).

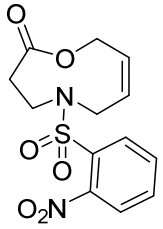
^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 168.7, 148.4, 134.0, 133.6, 132.3, 131.8, 131.3, 124.6, 124.5, 63.1, 52.3, 48.8, 28.4, 24.4.

HRMS-ESI (m/z): [M+Na] calculated for $C_{14}H_{16}N_2O_6SNa$, 363.0627; found 363.0628.

IR (ν_{max}, film): 2947, 1739, 1542, 1374, 1359, 1244, 1165 cm^{-1}.

MP = 130-131 °C.

(Z)-5-((2-nitrophenyl)sulfonyl)-4,5,6,9-tetrahydro-1,5-oxazonin-2(3H)-one 13d



The title compound was prepared according to **General procedure 3**. Starting from (12.80 g, 34.372 mmol, 1 eq) of **SI-3d** lactone **13d** (5.85 g, 66% yield in 2 steps) was obtained as a white solid.

R_f = 0.15 (Pet:EtOAc 1:1).

^{1}H NMR (400MHz; $CDCl_3$): δ 7.98 – 7.89 (m, 1H), 7.76 – 7.64 (m, 2H), 7.66 – 7.56 (m, 1H), 5.93 – 5.79 (m, 2H), 4.89 (d, *J* = 2.1 Hz, 2H), 4.01 – 3.90 (m, 2H), 3.77 (dd, *J* = 6.5, 5.5 Hz, 2H), 2.71 (dd, *J* = 6.5, 5.5 Hz, 2H).

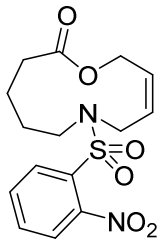
^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 171.0, 148.6, 133.9, 132.2, 131.8, 131.6, 130.7, 129.4, 124.2, 62.1, 2 C 50.6, 37.3.

HRMS-ESI (m/z): [M+H] calculated for $C_{13}H_{15}N_2O_6S$, 327.0651; found 327.0657.

IR (ν_{max}, film): 1746; 1541; 1364; 1346; 1007; 771 cm^{-1}.

MP = 150-152 °C.

(Z)-6-((2-nitrophenyl)sulfonyl)-1-oxa-6-azacycloundec-3-en-11-one 13e



The title compound was prepared according to **General procedure 3**. Starting from (13.17 g, 32.888 mmol, 1 eq) of **SI-3e** lactone **13e** (9.06 g, 78% yield in 2 steps) was obtained as a white solid.

R_f = 0.17 (Pet:EtOAc 1:1).

^{1}H NMR (400MHz; $CDCl_3$): δ 8.07 – 7.98 (m, 1H), 7.76 – 7.53 (m, 3H), 5.97 (dt, *J* = 10.8, 5.4 Hz, 1H), 5.50 (dt, *J* = 10.8, 8.3 Hz, 1H), 4.64 (d, *J* = 5.4 Hz, 2H), 4.15 (d, *J* = 8.3 Hz, 2H), 3.22 (t, *J* = 7.4 Hz, 2H), 2.42 – 2.34 (m, 2H), 1.83 – 1.64 (m, 4H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 148.0, 134.1, 133.6, 131.9, 130.8, 130.2, 129.3, 124.4, 59.4, 45.8, 45.2, 34.7 27.2, 21.9.

HRMS-ESI (m/z): [M+H] calculated for $C_{15}H_{19}N_2O_6S$, 355.0964; found 355.0974.

IR (ν_{max}, film): 1735, 1541, 1352, 1161 cm^{-1}.

MP = 109 – 110 °C.

Ireland-Claisen rearrangement studies

General procedure 4. The Ireland-Claisen rearrangement

To a stirred solution of the lactone **13** (0.235 mmol, 1 eq) in dry DCM (2 mL) at -78 ºC was added a solution of diazaborolidine **15** (0.259 mmol, 1.10 eq) in dry DCM (4 mL) followed by the amine base (0.353 mmol, 1.5 eq). The mixture was warmed to -25 ºC and stirred for 3 days at this temperature. After that, 0.06 mL of MeOH were added and the mixture was warmed to rt. Then aq. 1M HCl (2 mL) was added and the mixture stirred vigorously for 15 min and diluted with 10 mL H_2O and 10 mL DCM. After that the organic phase was separated and the aqueous phase was extracted with DCM (15 mL). The combined organic extracts were dried over anh. Na_2SO_4, filtered and evaporated. The residue was purified by flash column-chromatography (eluent: DCM/EtOAc).

General procedure 5. Derivatization of Ireland-Claisen products for chiral HPLC analyses

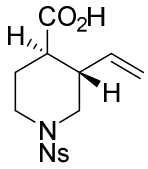
To a stirred solution of the acid **12** (~10 mg) in 1 mL of EtOAc was added excess of freshly prepared solution on diazomethane in Et_2O (~0.5 mL, CAUTION: very toxic) at 0 ºC. After 10 min the bright yellow solution was warmed up to room temperature and evaporated under the stream of argon in a well-ventilated fume hood and the residue was filtered through a silica gel pad using Pet:EtOAc 1:1 as an eluent. Solvents were removed to give methyl ester of **12** in a nearly quantitative yield.

Table S1. Screening of amine bases[a]

Entry	base	Isolated Yield %	*ee*	*dr (trans/cis)*	Temp.	Reaction time
1	2,4,6 - Collidine	71	53	5:1	-25 ºC	3 days
2	Pyridine	nr	-	-	-25 ºC	3 days
3	$EtMe_2N$	84	87	4:1	-25 ºC	3 days
4	NMM	89	93	5:1	-25 ºC	3 days
5	TEA	95	96	4:1	-25 ºC	3 days
6	DTBPy	nr	-	-	-25 ºC	3 days
7	N-Ethylmorpholine	89	93	3:2	-25 ºC	3 days
8	DIPEA	34	88	>1:20	-25 ºC	3 days
9	DIPEA	62	82	1:9	-78 ºC to rt	3 days at rt
10	DIPEA	80	82	1:16	-78 ºC to rt	7 days at rt

[a] 0.235 mmol **13a**, 0.259 mmol borolidine **(4*S*,5*S*)-15**, 0.353 mmol base, DCM (6 mL)

(3*S*,4*R*)-1-((4-nitrophenyl)sulfonyl)-3-vinylpiperidine-4-carboxylic acid (3*S*,4*R*)-12a



The title compound was prepared according to **General procedure 4**.

For the crystallization experiment, the title compound was prepared as follows: starting from lactone **13a** (4.00 g, 11.752 mmol, 1 eq), Me_2NEt and diazaborolidine **(4*R*,5*R*)-15** the title compound **(3*S*,4*R*)-12a** (3.63 g, 91% yield, *dr* 6:1 *trans/cis*, 92 *ee*) was obtained as pale yellow solid. This material was further crystallized from DCM/Hexane (2.39 g, 60% overall yield, *dr* >95:5 *trans/cis*, 95 *ee*).

^{1}H NMR (400MHz; MeOD-*d4*): δ 8.05 – 7.98 (m, 1H), 7.86 – 7.73 (m, 3H), 5.74 – 5.62 (m, 1H), 5.22 – 5.09 (m, 2H), 3.90 – 3.83 (m, 1H), 3.81 – 3.74 (m, 1H), 2.83 (td, *J* = 12.5, 2.8 Hz, 1H), 2.70 – 2.61 (m, 1H), 2.54 – 2.43 (m, 1H), 2.36 – 2.27 (m, 1H), 2.03 – 1.95 (m, 1H), 1.81 – 1.68 (m, 1H).

^{13}C{1H} NMR (100MHz; MeOD-*d4*) δ: 177.2, 149.8, 138.0, 135.4, 133.0, 132.3, 131.8, 125.4, 117.9, 50.4, 47.7, 46.2, 43.7, 29.4.

HRMS-ESI (m/z): [M+H] calculated for $C_{14}H_{17}N_2O_6S$, 341.0807; found 341.0811.

IR (ν_{max}, film): 3093, 2930, 1708, 1554, 1372, 1163, 760 cm^{-1}.

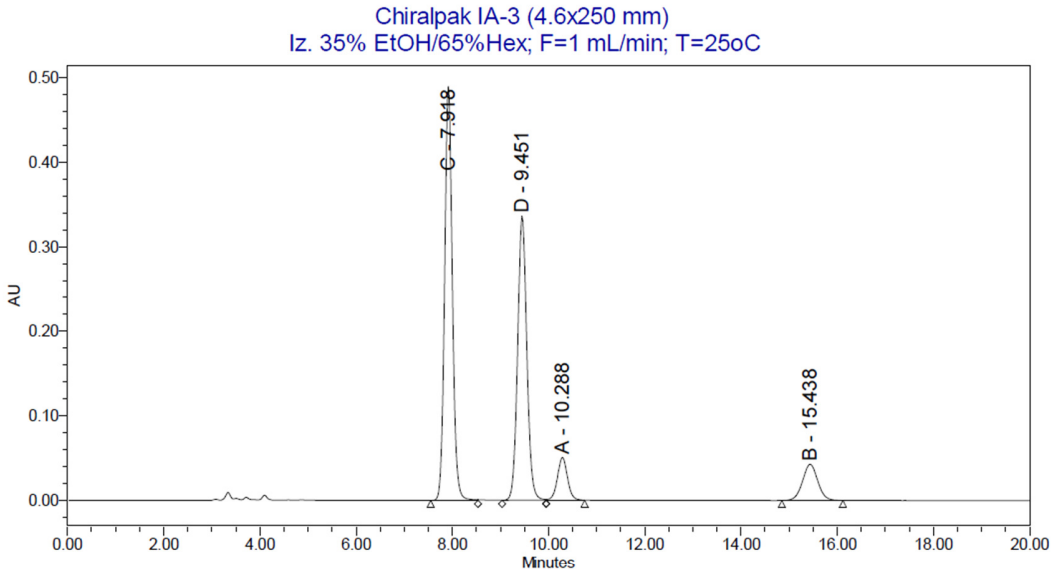
$[\alpha]_D^{20}$ = -43.4° (*c* = 0.1, $CHCl_3$).

MP = 165-169 °C.

Chiral HPLC analysis of (3*S*,4*R*)-12a

Chromatographic analyses for determination of stereoisomers were performed on Chiralpak IA-3 (4.6×250 mm, isocratic 35% EtOH/65% hexane, flow rate 1 mL/min at 25 °C) column.

Pseudoracemate was acquired by mixing equimolar amounts of **(3*S*,4*R*)-12a** and **(3*R*,4*S*)-12a** followed by derivatization according to **General procedure 5**.

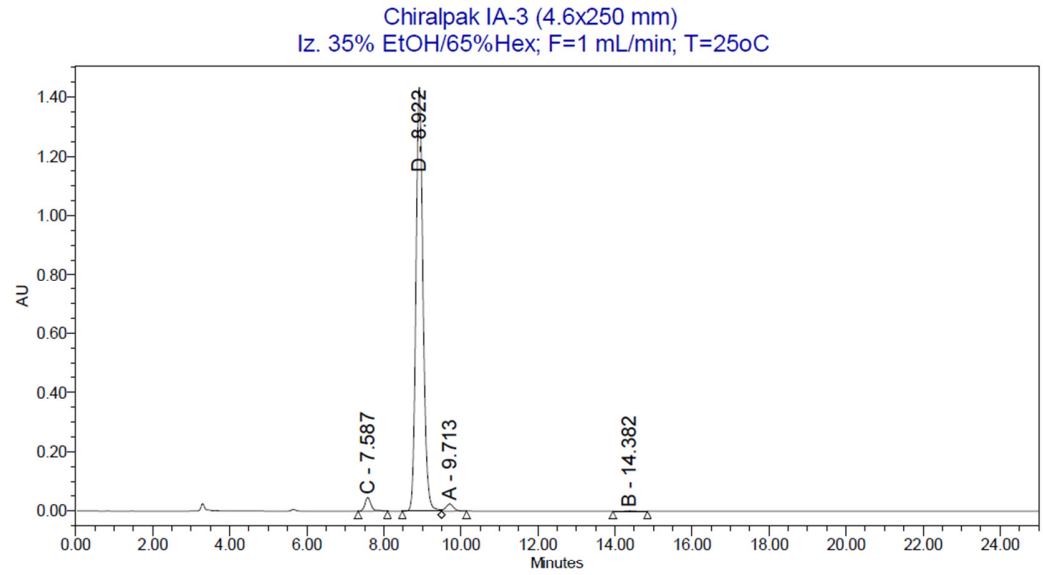


1 c =1mg/ml KF (35%EtOH_65%Hexane)

	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	C	7.918	5447886	47.11	488987	12242			0.168	1.596
2	D	9.451	4459059	38.56	335721	12185	4.889	1.315	0.202	2.099
3	A	10.288	724486	6.26	50273	12248	2.350	1.131	0.219	2.373
4	B	15.438	933140	8.07	42638	11770	10.975	1.712	0.335	4.062

Fig. S1. Chiral HPLC plot of pseudoracemate of **12a** after derivatisation

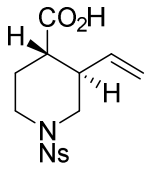
(3*S*,4*R*)-12a was derivatized according to **General procedure 5**.



	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	C	7.587	506320	2.65	45855	12431			0.160	1.520
2	D	8.922	18227147	95.50	1435204	11906	4.469	1.292	0.192	1.964
3	A	9.713	332302	1.74	23776	11862	2.320	1.134	0.210	2.227
4	B	14.382	21028	0.11	1076	12547	10.759	1.697	0.302	3.778

Fig. S2. HPLC plot of **(3*S*,4*R*)-12a** after crystallization and derivatisation

(3*R*,4*S*)-1-((4-nitrophenyl)sulfonyl)-3-vinylpiperidine-4-carboxylic acid (3*R*,4*S*)-12a



The title compound was prepared according to **General procedure 4** using diazaborolidine **(4*S*,5*S*)-15** and Me_2NEt. The title compound **(3*R*,4*S*)-12a** (67.3 mg, 84% yield, *dr* 4:1 *trans/cis*, 87 *ee*) was obtained as a pale yellow solid.

^{1}H NMR (400MHz; MeOD-*d4*): δ 8.05 – 7.98 (m, 1H), 7.86 – 7.73 (m, 3H), 5.74 – 5.62 (m, 1H), 5.22 – 5.09 (m, 2H), 3.90 – 3.83 (m, 1H), 3.81 – 3.74 (m, 1H), 2.83 (td, *J* = 12.5, 2.8 Hz, 1H), 2.70 – 2.61 (m, 1H), 2.54 – 2.43 (m, 1H), 2.36 – 2.27 (m, 1H), 2.03 – 1.95 (m, 1H), 1.81 – 1.68 (m, 1H).

^{13}C{1H} NMR (100MHz; MeOD-*d4*) δ: 175.8, 148.4, 136.6, 134.1, 131.6, 130.9, 130.4, 124.0, 116.5, 49.0, 46.3, 44.8, 42.3, 28.0.

HRMS-ESI (m/z): [M+H] calculated for $C_{14}H_{17}N_2O_6S$, 341.0807; found 341.0810.

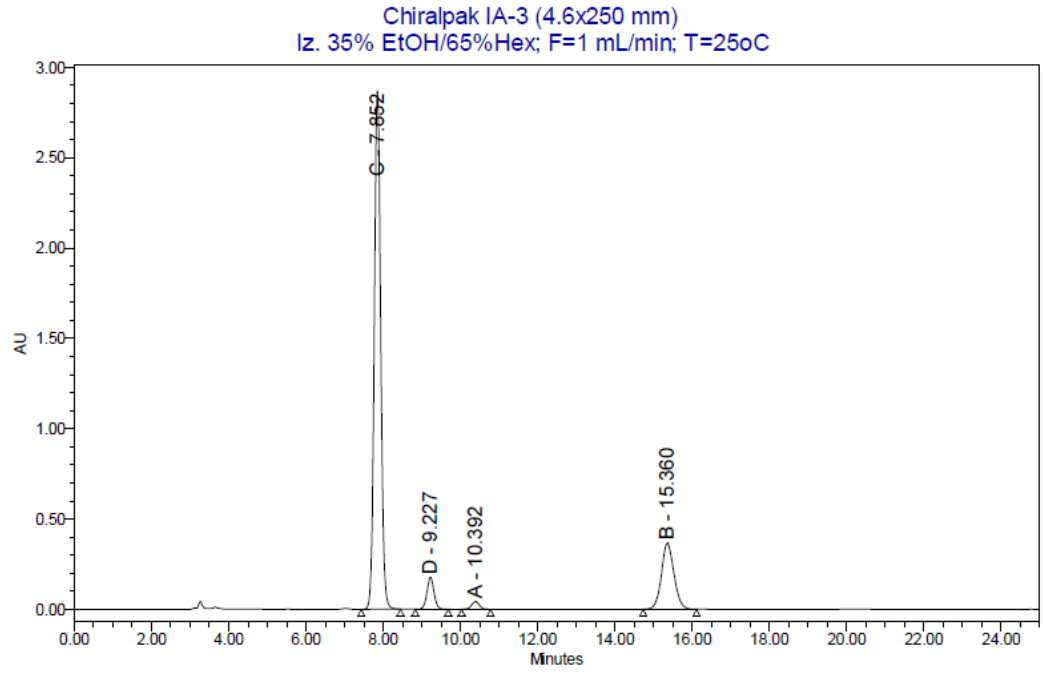
IR (ν_{max}, film): 3093, 2930, 1708, 1554, 1372, 1163, 760 cm^{-1}.

$[\alpha]_D^{20}$ = 43.6° (*c* = 0.1, $CHCl_3$).

MP = 166-169 °C.

Chiral HPLC analysis of (3*R*,4*S*)-12a

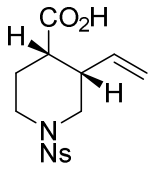
(3*R*,4*S*)-12a was derivatized according to **General procedure 5**.



	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	C	7.852	33060650	74.82	2868784	10958			0.177	1.575
2	D	9.227	2260298	5.12	175949	12315	4.356	1.286	0.196	2.025
3	A	10.392	602387	1.36	42180	12492	3.317	1.189	0.219	2.407
4	B	15.360	8265545	18.71	364158	10944	10.386	1.677	0.346	4.036

Fig. S3. HPLC plot of **(3*R*,4*S*)-12a** after flash column-chromatography and derivatisation

(3*S*,4*S*)-1-((4-nitrophenyl)sulfonyl)-3-vinylpiperidine-4-carboxylic acid (3*S*,4*S*)-12a



The title compound was prepared according to **General procedure 4**. The reaction time was extended to 1 week at -25 °C.

Using diazaborolidine **(4*R*,5*R*)-15** and DIPEA the title compound **(3*S*,4*S*)-12a** (47.1 mg, 59% yield, *dr* 1:9 *trans/cis*, 82 *ee*) was obtained as a pale yellow solid.

^{1}H NMR (400MHz; $CDCl_3$): δ 8.00 – 7.93 (m, 1H), 7.74 – 7.59 (m, 3H), 5.86 (ddd, *J* = 17.2, 10.5, 8.2 Hz, 1H), 5.23 – 5.09 (m, 2H), 3.79 – 3.67 (m, 2H), 3.21 (dd, *J* = 12.7, 3.5 Hz, 1H), 3.05 (ddd, *J* = 12.9, 9.5, 3.5 Hz, 1H), 2.86 – 2.78 (m, 1H), 2.69 (dt, *J* = 9.5, 4.3 Hz, 1H), 2.10 – 1.99 (m, 1H), 1.93 – 1.84 (m, 1H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 178.1, 148.5, 134.2, 133.8, 131.8, 131.7, 131.2, 124.3, 118.7, 49.2, 44.5, 43.7, 40.5, 24.1.

HRMS-ESI (m/z): [M+H] calculated for $C_{14}H_{17}N_2O_6S$, 341.0807; found 341.0800.

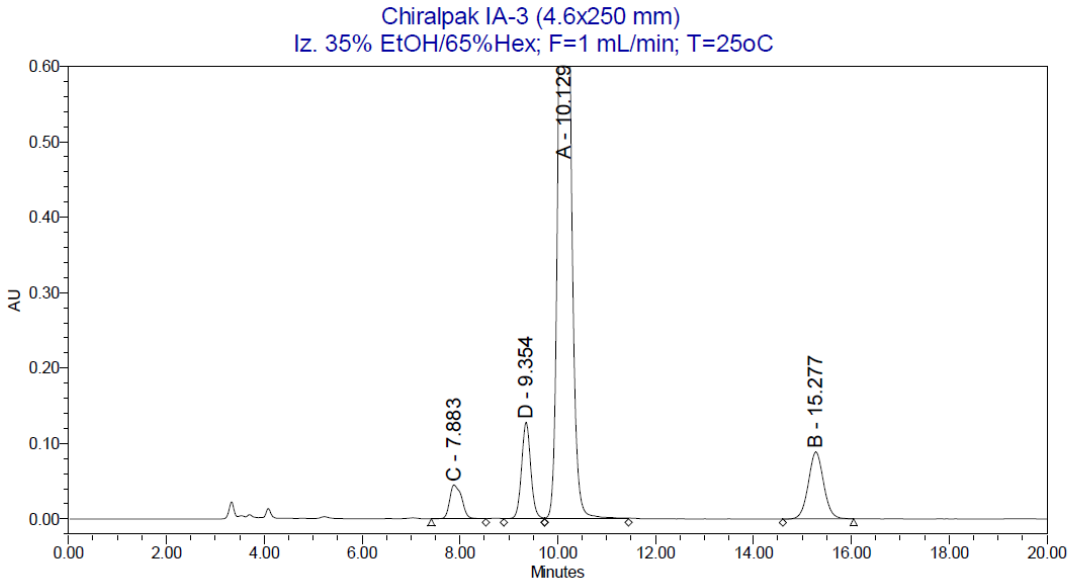
IR (ν_{max}, film): cm^{-1} 3096, 1708, 1544, 1373, 1165, 945 cm^{-1}.

$[\alpha]_D^{20}$ = 17.0° (*c* = 0.1, $CHCl_3$).

MP = 162-164 °C.

HPLC analysis of (3*S*,4*S*)-12a

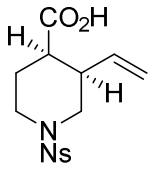
(3*S*,4*S*)-12a was derivatized according to **General procedure 5**.



	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	C	7.883	764700	3.21	44869	4476			0.277	1.585
2	D	9.354	1673818	7.03	128015	12311	3.648	1.304	0.198	2.067
3	A	10.129	19434865	81.68	1317485	11441	2.170	1.123	0.223	2.321
4	B	15.277	1921294	8.07	88456	11784	10.963	1.727	0.331	4.009

Fig. S4. HPLC plot of **(3*S*,4*S*)-12a** after flash column-chromatography and derivatisation

(3*R*,4*R*)-1-((4-nitrophenyl)sulfonyl)-3-vinylpiperidine-4-carboxylic acid (3*R*,4*R*)-12a



The title compound was prepared according to **General procedure 4**. The reaction time was extended to 1 week at -25 °C.

For the crystallization experiment the title compound was prepared as follows: starting from lactone **13a** (4.00 g, 11.752 mmol, 1 eq), DIPEA and diazaborolidine **(4*S*,5*S*)-15** the title compound **(3*R*,4*R*)-12a** (3.13 g, 78% yield, *dr* 1:16 *trans/cis*, 83 *ee*) was obtained as pale yellow solid. This material was further crystallized from DCM/Hexane (2.35 g, 59% overall yield, *dr* >95:5 *trans/cis*, 95 *ee*).

^{1}H NMR (400MHz; $CDCl_3$): δ 8.00 – 7.93 (m, 1H), 7.74 – 7.59 (m, 3H), 5.86 (ddd, *J* = 17.2, 10.5, 8.2 Hz, 1H), 5.23 – 5.09 (m, 2H), 3.79 – 3.67 (m, 2H), 3.21 (dd, *J* = 12.7, 3.5 Hz, 1H), 3.05 (ddd, *J* = 12.9, 9.5, 3.5 Hz, 1H), 2.86 – 2.78 (m, 1H), 2.69 (dt, *J* = 9.5, 4.3 Hz, 1H), 2.10 – 1.99 (m, 1H), 1.93 – 1.84 (m, 1H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 178.1, 148.5, 134.2, 133.8, 131.8, 131.7, 131.2, 124.3, 118.7, 49.2, 44.5, 43.7, 40.5, 24.1.

HRMS-ESI (m/z): [M+H] calculated for $C_{14}H_{17}N_2O_6S$, 341.0807; found 341.0809.

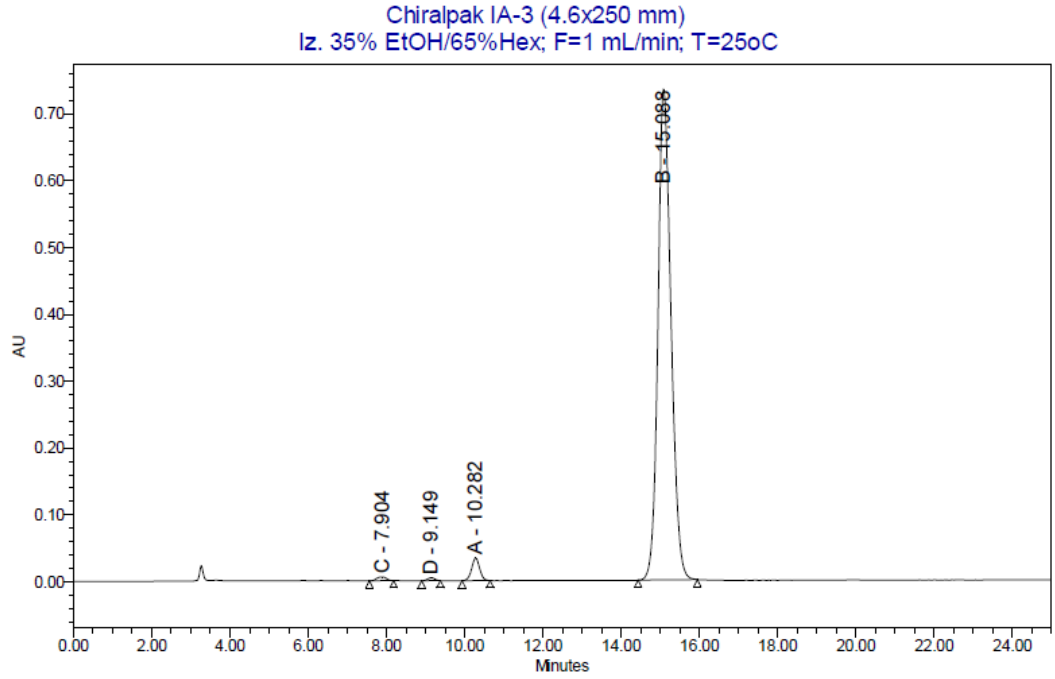
IR (ν_{max}, film): 3096, 1708, 1544, 1373, 1165, 945 cm^{-1}.

$[\alpha]_D^{20}$ = -17.1° (*c* = 0.1, $CHCl_3$).

MP = 162-165 °C.

HPLC analysis of (3*R*,4*R*)-12a

(3*R*,4*R*)-12a was derivatized according to **General procedure 5**.

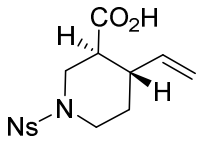


1 c=1mg/ml

	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	C	7.904	90259	0.51	5227	4527			0.276	1.592
2	D	9.149	52051	0.30	4329	12866	3.150	1.256	0.190	2.000
3	A	10.282	476834	2.71	33893	12648	3.302	1.186	0.215	2.371
4	B	15.088	16993765	96.48	734944	10176	9.997	1.664	0.352	3.947

Fig. S5. HPLC plot of **(3*R*,4*R*)-12a** after crystallization and derivatisation

(3*S*,4*S*)-1-((4-nitrophenyl)sulfonyl)-4-vinylpiperidine-3-carboxylic acid (3*S*,4*S*)-12b



The title compound was prepared according to **General procedure 4**.

Starting from lactone **12b** (80 mg, 0.235 mmol, 1 eq) and diazaborolidine **(4*R*,5*R*)-15** the title compound **(3*S*,4*S*)-12b** (58 mg, 73% yield *dr* 6:1 *trans/cis*, 96 *ee*) was obtained as pale yellow solid as a mixture of diastereomers.

^{1}H NMR (400MHz; MeOD – *d*4): δ (major diastereomer) 8.07 – 7.99 (m, 1H), 7.86 – 7.72 (m, 3H), 5,71 (ddd, *J* = 17.4, 10.4, 7.2 Hz, 1H), 5.11 – 4.98 (m, 2H), 4.02 – 3.94 (m, 1H), 3.96 – 3.82 (m, 1H), 2.92 – 2.79 (m, 2H), 2.43 – 2.28 (m, 2H), 1.86 – 1.77 (m, 1H), 1.55 – 1.42 (m, 1H), (minor diastereomer) 8.07 – 7.99 (m, 1H), 7.86 – 7.72 (m, 3H), 5.95 (ddd, *J* = 17.3, 10.5, 7.4 Hz, 1H), 5.18 – 5.07 (m, 2H), 3.60 – 3.54 (m, 1H), 3.45 – 3.33 (m, 2H), 2.80 – 2.71 (m, 2H), 1.85 – 1.77 (m, 1H), 1.49 – 1.41k (m, 1H).

^{13}C{1H} NMR (100 MHz, MeOD – *d*4): δ (major diastereomer) 175.4, 149.8, 140.6, 135.5, 133.0, 132.2, 131.9, 125.4, 116.1, 48.7, 46.7, 43.3, 31.5.

(minor diastereomer) 174.9, 149.8, 137.8, 135.4, 133.0, 132.2, 131.8, 125.4, 117.5, 45.9, 45.8, 44.2, 40.0.

HRMS-ESI (m/z): [M+H] [M+H] calculated for $C_{14}H_{17}N_2O_6S$, 341.0807; found 341.0803.

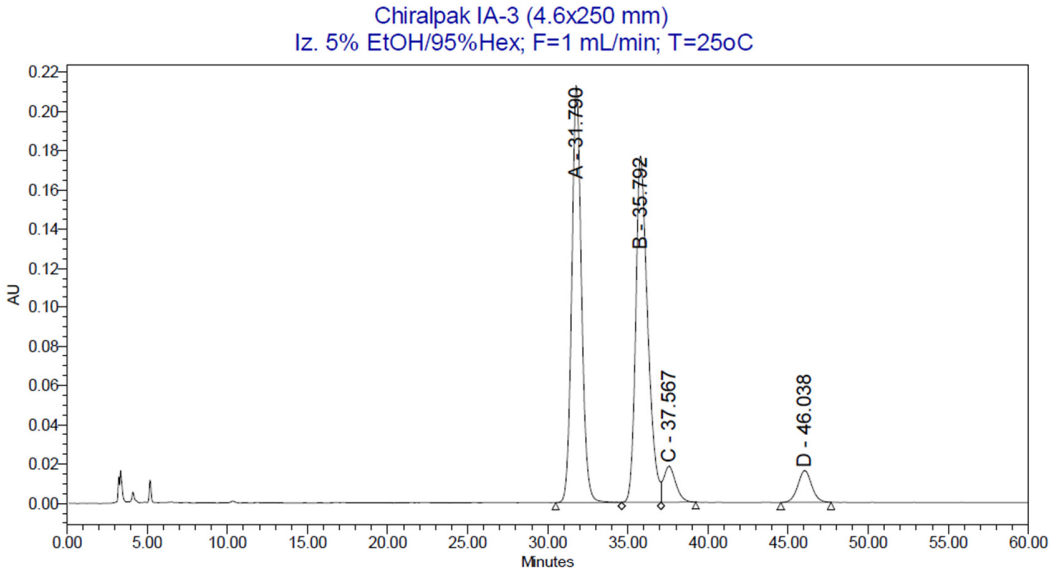
IR (ν_{max}, film): 3088, 2928, 2866, 1713, 1544, 1373, 1163, 945, 761 cm^{-1}.

$[\alpha]_D^{20}$ = -7° (*c* = 0.1, $CHCl_3$).

HPLC analysis of (3*S*,4*S*)-12b

Chromatographic analyses for determination of stereoisomers were performed on Chiralpak IA-3 (4.6×250 mm, isocratic 5% EtOH/95% hexane, flow rate 1 mL/min at 25 °C) column.

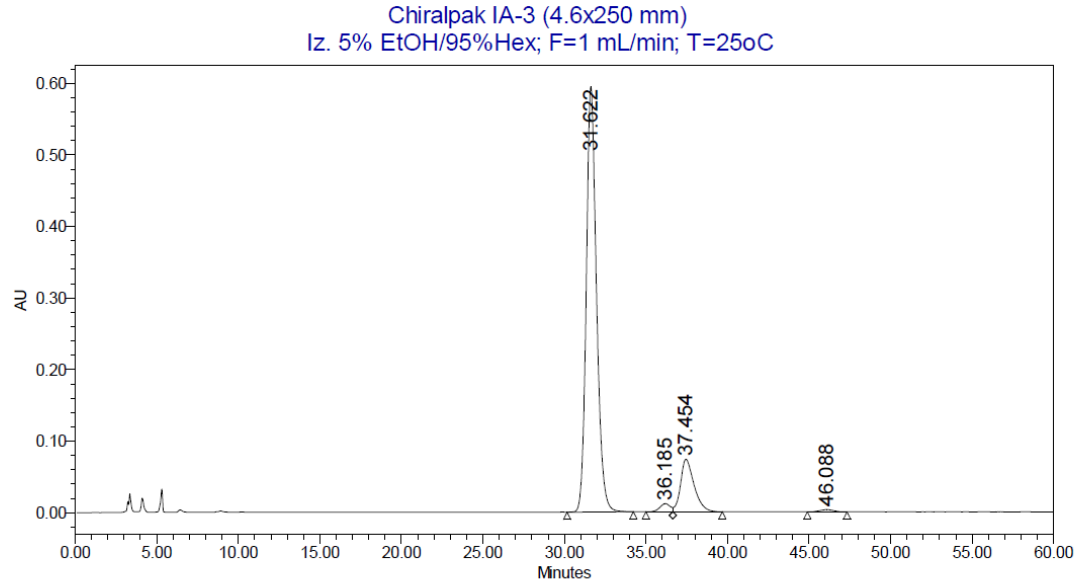
A racemic sample was acquired by mixing equimolar amounts of **(3*R*,4*R*)-12b** and **(3*S*,4*S*)-12b** followed by derivatization according to **General procedure 5**.



	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	A	31.790	8927138	44.52	212481	14045			0.631	9.423
2	B	35.792	9177021	45.76	176743	11703	3.349	1.139	0.779	10.735
3	C	37.567	976837	4.87	18284			1.054		11.317
4	D	46.038	972014	4.85	16218	14064		1.245	0.914	14.095

Fig. S6. Chiral HPLC plot of pseudoracemate of **12b** after derivatization

(3*S*,4*S*)-12b was derivatized according to **General procedure 5**.

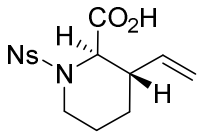


1 c =2mg/ml diluents - 35%EtOH_65%Hexane

	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	31.622	25792041	84.03	593986	13120			0.650	9.368
2	36.185	502774	1.64	11401			1.160		10.864
3	37.454	4214011	13.73	73392	10731		1.038	0.851	11.280
4	46.088	184477	0.60	3150	13926	5.755	1.251	0.919	14.111

Fig. S7. HPLC plot of **(3*S*,4*S*)-12b** after flash column-chromatography and derivatisation

(2*R*,3*S*)-1-((4-nitrophenyl)sulfonyl)-3-vinylpiperidine-2-carboxylic acid (2*R*,3*S*)-12c



The title compound was prepared according to **General procedure 4**. After combining all the reagents at -78 ºC the reaction mixture was warmed to room temperature and stirred for 3 days. Using diazaborolidine **(4*R*,5*R*)-15** and Me_2Net the title compound **(2*R*,3*S*)-12c** (25.7 mg, 32% yield, *dr* >20:1 *trans/cis*, 98 *ee*) was obtained as pale yellow solid.

^{1}H NMR (400MHz; $CDCl_3$): δ 8.11 – 8.01 (m, 1H), 7.75 – 7.62 (m, 3H), 5.99 – 5.78 (m, 1H), 5.19 – 5.01 (m, 2H), 4.62 (d, *J* = 5.5 Hz, 1H), 3.77 – 3.62 (m, 1H), 3.60 – 3.46 (m, 1H), 2.64 – 2.49 (m, 1H), 1.84 – 1.65 (m, 2H), 1.63 – 1.47 (m, 2H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 175.2, 147.8, 138.0, 134.0, 132.9, 132.1, 131.2, 124.6, 116.2, 43.0, 42.7, 29.8, 24.7.

HRMS-ESI (m/z): [M+H] calculated for $C_{14}H_{17}N_2O_6S$, 341.0807; found 341.0804.

IR (ν_{max}, film): 2929, 1716, 1544, 1369, 1346, 1161 cm^{-1}.

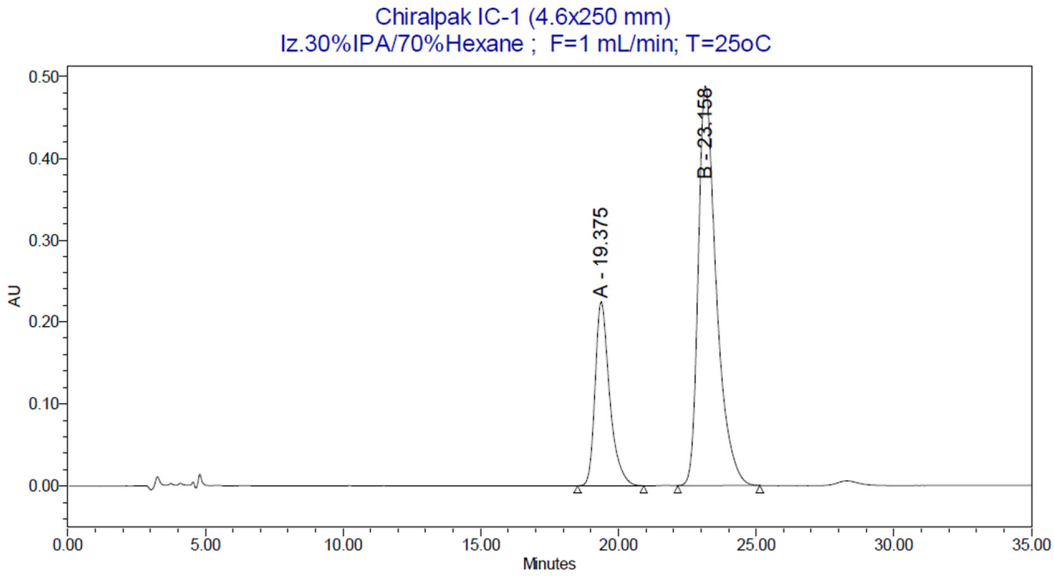
$[\alpha]_D^{20}$ = -42.0° (*c* = 0.1, MeOH).

MP = 143 °C dec.

HPLC analysis of (2*R*,3*S*)-12c

Chromatographic analyses for the determination of stereoisomers were performed on Chiralpak IC-1 (4.6×250 mm, isocratic 30% IPA/70% hexane, flow rate 1 mL/min at 25 °C) column.

A racemic sample was acquired by mixing equimolar amounts of **(2*S*,3*R*)-12c** and **(2*R*,3*S*)-12c** followed by derivatization according to **General procedure 5**.

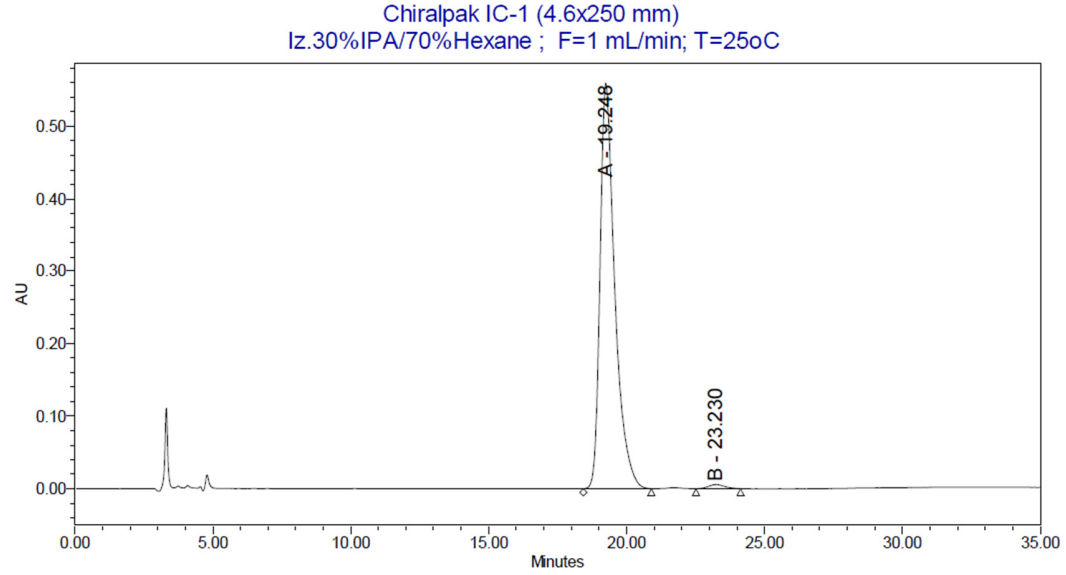


1 c=1 mg/ml 10% EtOH/ Hex

	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	A	19.375	8195870	26.93	223559	7180			0.538	5.151
2	B	23.158	22233095	73.07	487760	6610	3.694	1.233	0.670	6.352

Fig. S8. Chiral HPLC plot of pseudoracemate of **12c** after derivatization

(**2*R*,3*S*)-12c** was derivatized according to **General procedure 5**.

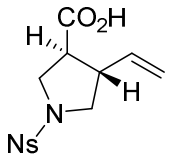


1 c=1 mg/ml 10% EtOH/ Hex

	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	A	19.248	20778655	98.90	558521	6939			0.544	5.111
2	B	23.230	231123	1.10	5753	7716	4.029	1.247	0.622	6.375

Fig. S9. HPLC plot of (**2*R*,3*S*)-12c** after flash column-chromatography and derivatisation

(3*S*,4*S*)-1-((4-nitrophenyl)sulfonyl)-4-vinylpyrrolidine-3-carboxylic acid (3*S*,4*S*)-12d



The title compound was prepared according to **General procedure 4** using diazaborolidine **(4*R*,5*R*)-15** and Me_2NEt. The title compound **(3*S*,4*S*)-12d** (57.0 mg, 74% yield, *dr* 11:1 *trans/cis*, 95 *ee*) was obtained as a pale yellow solid.

^{1}H NMR (400MHz; MeOD – *d*4): δ 8.09 – 8.02 (m, 1H), 7.85 – 7.74 (m, 3H), 5.77 (ddd, *J* = 17.2, 10.4, 7.5 Hz, 1H), 5.21 – 5.07 (m, 2H), 3.80 – 3.59 (m, 3H), 3.26 (dd, *J* = 9.9, 8.1 Hz, 1H), 3.11 – 3.01 (m, 1H), 2.96 – 2.88 (m, 1H)

^{13}C{1H} NMR (100 MHz, MeOD – *d*4): δ 174.7, 149.8, 137.2, 135.4, 133.0, 132.1, 131.7, 125.3, 117.7, 53.3, 51.0, 49.9, 47.7.

HRMS-ESI (m/z): [M+H] calculated for $C_{13}H_{15}N_2O_6S$, 327.0651; found 327.0658.

IR (ν_{max}, film): 2916, 1711, 1544, 1372, 1353, 1165 cm^{-1}.

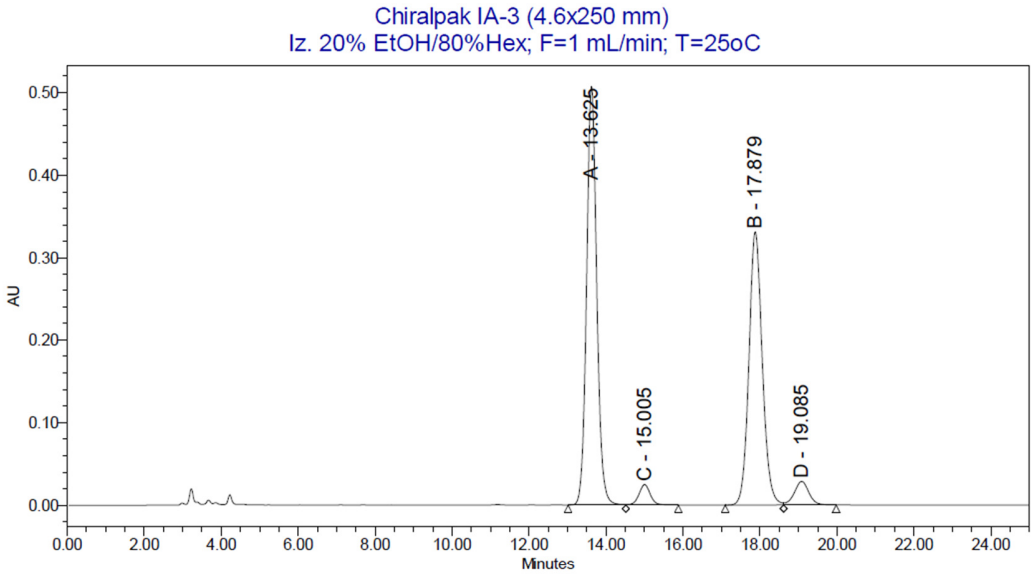
$[\alpha]_D^{20}$ = -18.4° (*c* = 0.1, MeOH).

MP = 142-145 °C.

HPLC analysis of (3*S*,4*S*)-12d

Chromatographic analyses for determination of stereoisomers were performed on Chiralpak IA-3 (4.6×250 mm, isocratic 20% EtOH/80% hexane, flow rate 1 mL/min at 25 °C) column.

A racemic sample was acquired by mixing equimolar amounts of **(3*R*,4*R*)-12d** and **(3*S*,4*S*)-12d** followed by derivatization according to **General procedure 5**.

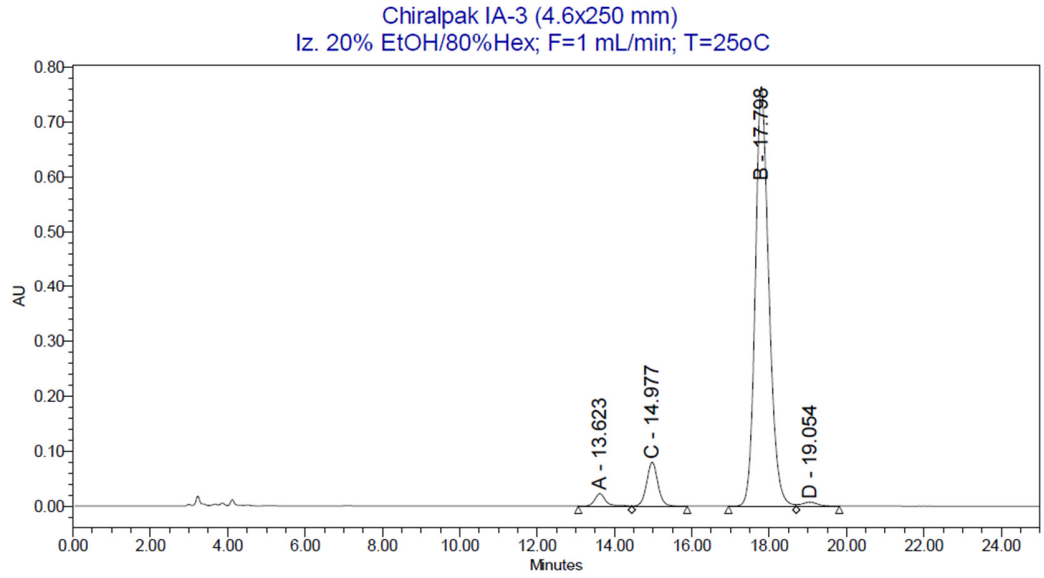


1 c =1mg/ml diluents - 35%EtOH_65%Hexane

	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	A	13.625	9260574	50.11	507642	13588			0.275	3.467
2	C	15.005	506404	2.74	24796	13447	2.809	1.131	0.305	3.920
3	B	17.879	7968647	43.12	331381	13437	5.080	1.240	0.363	4.862
4	D	19.085	746621	4.04	28621	13045	1.881	1.081	0.393	5.257

Fig. S10. Chiral HPLC plot of pseudoracemate of **12d** after derivatization

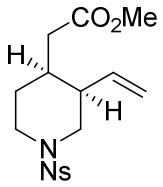
(3*S*,4*S*)-12d was derivatized according to **General procedure 5**.



	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	A	13.623	451893	2.16	22546	13367			0.277	3.466
2	C	14.977	1600631	7.64	79917	13563	2.756	1.128	0.303	3.911
3	B	17.798	18711538	89.26	764920	12968	4.963	1.236	0.368	4.835
4	D	19.054	198451	0.95	7238	10906	1.860	1.085	0.429	5.247

Fig. S11. HPLC plot of **(3*S*,4*S*)-12d** after flash column-chromatography and derivatisation

Methyl 2-((3*R*,4*S*)-1-((4-nitrophenyl)sulfonyl)-3-vinylpiperidin-4-yl)acetate (3*R*,4*S*)-11



To a slurry of **(3*R*,4*R*)-12a** (200 mg, 0.588 mmol, 1 eq) in 10 mL DCM was added DMF (0.5 µL, 0.006 mmol, 0.01 eq) and oxalyl chloride (0.15 mL, 1.763 mmol, 3 eq) at 0°C. The mixture was stirred at room temperature for 90 min. The solvent was removed (Rotovap filled with Ar), and the residue re-dissolved in 10 mL DCM and evaporated in the same manner. The resulting acid chloride was dissolved in 10 mL DCM and freshly made diazomethane solution in Et_2O (10 eq, CAUTION: very toxic) added at 0 °C. After stirring for 3 h at room temperature, the solvent was evaporated (Rotovap in a well-ventilated hood) to remove excess diazomethane. The residue was partitioned between DCM/H_2O. The organics layer was separated and the aqueous layer was washed with DCM (2 times). The combined organic extracts were dried over Na_2SO_4, filtered, and evaporated yielding a yellow oil, that solidified upon standing in the freezer. The obtained material was used in the next step like it is.

Diazoketone was partly dissolved in 15 mL MeOH and cooled to 0 °C. Silver (I) trifluoroacetate (12.7 mg, 0.057 mmol, 0.1 eq) was dissolved in TEA (0.40 mL, 2.868 mmol, 5 eq.) and added to the MeOH solution. The ice bath was removed after 30 min and the reaction was stirred overnight at room temperature wrapped with Al foil. Filtered through celite and washed with MeOH, evaporated. The residue was purified by CC (Pet:EtOAc 75:25 -> 60:40). Title compound was obtained as light yellow oil 208 mg (92% in 2 steps).

^{1}H NMR (400MHz; $CDCl_3$): δ 7.97 – 7.91 (m, 1H), 7.73 – 7.57 (m, 3H), 5.87 (ddd, *J* = 17.2, 10.5, 9.1 Hz, 1H), 5.17 – 5.05 (m, 2H), 3.86 – 3.78 (m, 1H), 3.70 – 3.63 (m, 4H), 3.05 (dd, *J* = 12.4, 3.0 Hz, 1H), 2.92 – 2.83 (m, 1H), 2.50 – 2.43 (m, 1H), 2.33 – 2.24 (m, 1H), 2.20 – 2.06 (m, 2H), 1.67 – 1.58 (m, 2H).

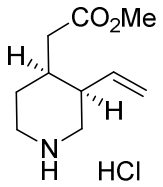
^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 172.9, 148.5, 134.4, 133.7, 131.6, 131.6, 131.2, 124.2, 118.6, 51.7, 50.6, 45.9, 42.1, 37.3, 34.9, 27.3.

HRMS-ESI (m/z): [M+H] calculated for $C_{16}H_{21}N_2O_6S$, 369.1120; found 369.1118.

IR (ν_{max}, film): 3093, 2927, 2865, 1732, 1541, 1376, 1167, 750, 579 cm^{-1}.

$[\alpha]_D^{20}$ = 25.0 ° (*c* = 0.1, $CHCl_3$).

Methyl 2-((3*R*,4*S*)-3-vinylpiperidin-4-yl)acetate hydrochloride 18; (+) meroquinene methyl ester hydrochloride



To a suspension of **(3*R*,4*S*)-11** (161 mg, 0.437 mmol, 1 eq.) and K_2CO_3 (163.1 mg, 1.180 mmol, 2.7 eq) in 4 mL MeCN thiophenol (0.067 mL, 0.656 mmol, 1.5 eq.) was added. The reaction was stirred overnight at room temperature. The mixture was diluted with 10 mL of Et_2O and 10 mL of H_2O. 10% HCl was carefully added to pH ~ 2. The aqueous layer was separated, washed with 15 mL of Et_2O, and evaporated. The residue was purified by reversed-phase CC (H_2O:MeOH 1%HCl 99:1 -> 0:1) to obtain the title compound as light yellow glass 46 mg (48%).

^{1}H NMR (400MHz; DMSO – *d*6): δ 9.36 (br.s, 1H), 8.97 (br.s, 1H), 6.02 (s, 1H), 5.24 – 4.96 (m, 2H), 3.57 (s, 3H), 3.12 – 2.86 (m, 4H), 2.63 (s, 1H), 2.32 – 2.12 (m, 3H), 1.79 – 1.65 (m, 1H), 1.64 – 1.47 (m, 1H).

^{13}C{1H} NMR (100 MHz, DMSO – *d*6): δ 172.2, 135.2, 118.1, 51.4, 45.0, 41.2, 34.7, 32.0, 24.4.

HRMS-ESI (m/z): [M+H] calculated for $C_{10}H_{18}NO_2$, 184.1338; found 184.1340.

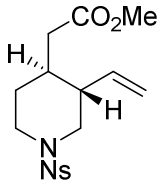
IR (ν_{max}, film): 3436, 2962, 2805, 1726, 1185 cm^{-1}.

$[\alpha]_D^{20}$ = 34.0 ° (*c* = 0.5, MeOH); Lit: 33.2 ° (*c* = 0.5, MeOH) *Enamine* database, Catalog ID EN300-27146874.

Table S2. ^{13}C Data comparison of meroquinene methyl ester hydrochloride (17)

Literature, $^{13}C\{1H\}$ NMR (125 MHz, DMSO – *d*6) Lit ref: *Enamine* database, Catalog ID EN300-27146874	**Synthetic**, $^{13}C\{1H\}$ NMR (100 MHz, DMSO – *d*6)
172.2	172.2
135.3	135.2
118.1	118.2
51.4	51.4
45.0	45.0
41.2	41.2
34.7	34.7
32.1	32.0
24.5	24.4

Methyl 2-((3*S*,4*S*)-1-((4-nitrophenyl)sulfonyl)-3-vinylpiperidin-4-yl)acetate (3*S*,4*S*)-11



The title compound was prepared similarly as **(3*R*,4*S*)-11**. Starting from **(3*S*,4*R*)-12a** (728 mg, 2.139 mmol, 1 eq) the title compound was obtained as a light yellow oil (741 mg, 94% in 2 steps).

^{1}H NMR (400MHz; $CDCl_3$): δ 8.02 – 7.93 (m, 1H), 7.76 – 7.56 (m, 3H), 5.54 – 5.40 (m, 1H), 5.23 – 5.07 (m, 2H), 3.86 (dp, *J* = 12.6, 2.4 Hz, 1H), 3.76 (ddd, *J* = 12.6, 4.4, 2.1 Hz, 1H), 3.64 (s, 3H), 2.77 (td, *J* = 12.8, 2.7 Hz, 1H), 2.65 – 2.50 (m, 2H), 2.13 – 1.96 (m, 2H), 1.89 (dd, *J* = 13.4, 3.8 Hz, 1H), 1.81 – 1.67 (m, 1H), 1.37 (qd, *J* = 12.6, 4.4 Hz, 1H).

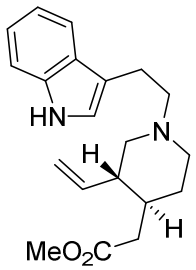
^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 173.1, 148.4, 137.0, 133.7, 131.9, 131.6, 131.0, 124.2, 119.2, 51.7, 50.5, 46.4, 46.14, 38.2, 36.6, 30.9.

HRMS-ESI (m/z): [M+H] calculated for $C_{16}H_{21}N_2O_6S$, 369.1120; found 369.1127.

IR (ν_{max}, film): 2974, 2875, 1736, 1544, 1373, 1347, 1162, 762 cm^{-1}.

$[\alpha]_D^{20}$ = -44.90 ° (*c* = 1, $CHCl_3$).

Methyl 2-((3S,4S)-1-(2-(1*H*-indol-3-yl)ethyl)-3-vinylpiperidin-4-yl)acetate 20a



To a suspension of **(3*S*,4*S*)-11** (814.0 mg, 2.210 mmol, 1 eq.) and K_2CO_3 (825.5 mg, 5.973 mmol, 2.7 eq) in 25 mL of MeCN thiophenol (0.34 mL, 3.318 mmol, 1.5 eq.) was added. The reaction was stirred overnight at room temperature. The mixture was diluted with 65 mL Et_2O and 65 mL H_2O. 10% HCl was carefully added to pH ~2. The aqueous layer was separated, washed with Et_2O (2x65 mL) and evaporated. Crude was purified by reversed-phase CC (H_2O:MeOH 1%HCl 99:1 - 0:1) to obtain intermediate unprotected piperidine as a light yellow solid 337.0 mg (83%). The collected material was used in the next step like it is.

Piperidine substrate (337 mg, 1.534 mmol, 1 eq) was dissolved in 4.5 mL of DMF. Then Na_2CO_3 (487.7 mg, 4.602 mmol, 3 eq) and 3-(2-bromoethyl)-1*H*-indole (515.6 mg, 1.5 eq) were charged. After stirring at 80ºC for 3h, the reaction mixture was diluted with 40 mL of EtOAc and 40 mL of H_2O. Layers were separated and the aqueous layer was extracted with EtOAc (3x40 mL). Organics were dried over Na_2SO_4, filtered, and evaporated. The residue was purified by CC (Pet:EtOAc:MeOH 2:1:0 -> 0:1:0.05) to give the title compound as colorless oil 351 mg (70%).

^{1}H NMR (600MHz; $CDCl_3$): δ 8.18 (br.s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.00 (s, 1H), 5.60 – 5.51 (m, 1H), 5.16 – 5.07 (m, 2H), 3.66 (s, 3H), 3.15 – 3.08 (m, 1H), 3.05 – 3.01 (m, 1H), 3.00 – 2.95 (m, 2H), 2.76 – 2.68 (m, 2H), 2.57 (dd, *J* = 15.4, 4.2 Hz, 1H), 2.15 – 2.07 (m, 2H), 2.04 (dd, *J* = 15.5, 9.4 Hz, 1H), 1.96 (t, *J* = 11.2 Hz, 1H), 1.88 – 1.81 (m, 1H), 1.73 – 1.65 (m, 1H), 1.44 (qd, *J* = 12.4, 4.0 Hz, 1H)

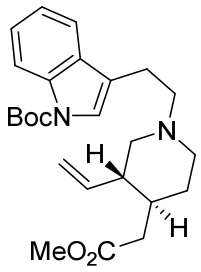
^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 173.7, 139.2, 136.4, 127.5, 122.1, 121.7, 119.3, 118.9, 117.4, 114.2, 111.3, 59.3, 59.2, 53.5, 51.6, 46.9, 38.8, 37.1, 31.1, 22.8.

HRMS-ESI (m/z): [M+H] calculated for $C_{20}H_{27}N_2O_2$, 327.2073; found 327.2080.

IR (ν_{max}, film): 3415, 2924, 1735, 1456, 1436, 1355, 1339, 1231, 1169, 997, 921, 742 cm^{-1}.

[α]$_D^{20}$ = -34.6° (*c* = 1, $CHCl_3$).

***tert*-butyl 3-(2-((3*S*,4*S*)-4-(2-methoxy-2-oxoethyl)-3-vinylpiperidin-1-yl)ethyl)-1*H*-indole-1-carboxylate 20b**



The title compound was prepared similarly as **20a** starting from **(3*S*,4*S*)-11** (626.0 mg, 1.700 mmol, 1 eq.) and tert-Butyl 3-(bromomethyl)-1*H*-indole-1-carboxylate (826.4 mg, 2.550 mmol 1.5 eq) the title compound was obtained as a colorless oil (530.0 mg, 73%).

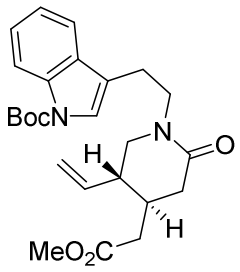
^{1}H NMR (400MHz; $CDCl_3$): δ 8.11 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.39 (s, 1H), 7.30 (t, *J* = 8.4 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 5.57 (ddd, *J* = 17.2, 10.2, 9.0 Hz, 1H), 5.17 – 5.02 (m, 2H), 3.66 (s, 3H), 3.10 – 3.00 (m, 1H), 3.01 – 2.92 (m, 1H), 2.93 – 2.84 (m, 2H), 2.73 – 2.62 (m, 2H), 2.57 (dd, *J* = 15.5, 4.2 Hz, 1H), 2.15 – 1.78 (m, 6H) 1.66 (s, 9H), 1.39 (qd, *J* = 12.4, 4.0 Hz, 1H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 173.7, 149.9, 139.4, 135.6, 130.8, 124.4, 122.8, 122.5, 119.1, 119.1, 117.2, 115.4, 83.5, 59.6, 58.5, 53.7, 51.6, 47.4, 38.9, 37.2, 31.5, 3 C 28.4, 22.9.

HRMS-ESI (m/z): [M+H] calculated for $C_{25}H_{35}N_2O_4$, 427.2597; found 427.2601.

[α]$_D^{20}$ = -36.1° (*c* = 0.1, $CHCl_3$).

***tert*-butyl 3-(2-((4*S*,5*S*)-4-(2-methoxy-2-oxoethyl)-2-oxo-5-vinylpiperidin-1-yl)ethyl)-1*H*-indole-1-carboxylate SI-4**



To a solution of **20b** (530 mg, 1.243 mmol, 1 eq) in 40 mL of THF and 16 mL of H_2O were added $NaHCO_3$ (1.044 g, 12.245 mmol, 10 eq) and iodine (2.365 g, 9.319 mmol, 7.5 eq) at ambient temperature and stirred for 90 min. After that, the reaction mixture was quenched by the addition of 15 mL of sat. aq. $Na_2S_2O_3$ and 15 mL of sat. aq. $NaHCO_3$ followed by extracted with DCM (3x100 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$, dried over Na_2SO_4, filtered, and evaporated. Purification by CC (Pet:EtOAc 2:1 -1:2) furnished the title compound as an orange oil 219 mg (40%).

^{1}H NMR (400 MHz; $CDCl_3$): δ 8.12 (d, *J* = 8.6 Hz, 1H), 7.60 (d, *J* = 9.9 Hz, 1H), 7.41 (s, 1H), 7.31 (t, *J* = 8.5 Hz, 1H), 7.29 – 7.20 (m, 1H), 5.56 – 5.42 (m, 1H), 5.16 – 5.05 (m, 2H), 3.72 – 3.66 (m, 1H), 3.62 – 3.51 (m, 1H), 3.66 (s, 3H), 3.12 (d, *J* = 6.9 Hz, 2H), 2.96 (t, *J* = 7.7 Hz, 2H), 2.67 (d, *J* = 12.3 Hz, 1H), 2.47 (dd, *J* = 15.4, 4.0 Hz, 1H), 2.25 – 2.01 (m, 4H), 1.66 (s, 9H).

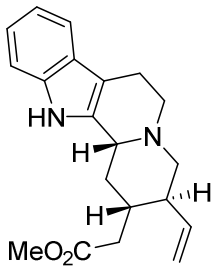
^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 172.4, 168.7, 149.8, 136.7, 135.6, 130.6, 124.6, 123.2, 122.6, 119.1, 119.0, 117.9, 115.4, 83.6, 52.8, 51.8, 47.7, 44.4, 38.4, 37.4, 34.0, 28.3, 22.9.

HRMS-ESI (m/z): [M+Na] calculated for $C_{25}H_{32}N_2O_5Na$, 463.2209; found 463.2225.

IR (ν_{max}, film): 2978, 2929, 1729, 1644, 1454, 1372, 1257, 1159, 1092, 750 cm^{-1}.

$[\alpha]_D^{20}$ = -43.2 ° (*c* = 0.1, $CHCl_3$).

Methyl 2-((2*S*,3*S*,12b*R*)-3-vinyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizin-2-yl)acetate 21



SI-4 (200 mg, 0.454 mmol, 1 eq) was dissolved in 6 mL of toluene and $POCl_3$ (0.64 mL, 6.810 mmol, 15 eq) was added. The resulting mixture was heated under reflux for 2 h, then cooled to room temperature and evaporated. The residue was dissolved in 6 mL of MeOH, and $NaBH_4$ (86 mg, 2.270 mmol, 5 eq) was added at 0 °C. The resulting mixture was stirred for 10 min at this temperature, then for 1 h at room temperature. After that 40 mL of H_2O and 40 mL of EtOAc were added. The organic phase was separated and the water phase was extracted with EtOAc (2x40 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and evaporated. The residue was purified by CC Pet:EtOAc (9:1 -> 7:3) to furnish 118 mg (80%) of the title compound as an off-white solid.

^{1}H NMR (400MHz; $CDCl_3$): δ 7.83 (br.s, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.17 – 7.05 (m, 2H), 5.59 (ddd, *J* = 17.2, 10.2, 8.9 Hz, 1H), 5.20 – 5.10 (m, 2H), 3.71 (s, 3H), 3.35 – 3.26 (m, 1H), 3.12 – 3.05 (m, 1H), 3.04 – 2.93 (m, 2H), 2.78 – 2.57 (m, 3H), 2.37 – 2.18 (m, 3H), 2.13 – 2.03 (m, 1H), 2.00 – 1.88 (m, 1H), 1.42 – 1.30 (m, 1H).

^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 173.7, 138.8, 136.2, 134.5, 127.5, 121.5, 119.5, 118.3, 117.8, 110.9, 108.4, 61.0, 59.5, 52.9, 51.7, 47.1, 38.5, 37.0, 35.5, 21.9.

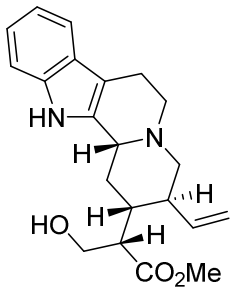
HRMS-ESI (m/z): [M+H] calculated for $C_{20}H_{25}N_2O_2$, 325.1916; found 325.1914.

IR (ν_{max}, film): 3398, 2911, 1735, 1719, 1435, 1324, 1154, 741 cm^{-1}.

$[\alpha]_D^{20}$ = -10.8° (*c* = 0.1, $CHCl_3$).

MP = 121-123 °C.

Methyl 3-hydroxy-2-((2S,3R,12bR)-3-vinyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizin-2-yl)propanoate 7; (+)-sitsirikine



To a solution of diisopropylamine (0.125 mL, 0.896 mmol, 3.3 eq.) in 1 mL of dry THF was added *n*-BuLi (0.36 mL, 0.896 mmol, 3.3 eq, 2.5M in hexane) at -78 ºC. After 5 min the mixture was warmed to 0 ºC and stirred for 30 min. The reaction was cooled down to -78 ºC and **21** (88 mg, 0.271 mmol, 1 eq.) in 2 mL of dry THF was slowly added. After 15 min methyl formate (0.168 mL, 2.713 mL, 10 eq) was added and the mixture was warmed up to 0 ºC and stirred for 1 h. After that, the reaction mixture was carefully quenched with 1 mL of H_2O and then diluted with 50 mL of DCM and 40 mL of H_2O. The organic layer was separated and the aqueous layer was extracted with DCM (2 x 50 mL). The combined organic extracts were dried over Na_2SO_4 and filtered. Removal of solvents under reduced pressure gave the intermediate aldehyde that was used in the next step like it is.

The intermediate aldehyde was dissolved in 5 mL of MeOH and AcOH (0.048 mL, 0.818 mmol, 3 eq) at 0 ºC and then $NaBH_4$ (61.8 mg, 1.634 mmol, 6 eq) was added in portions over 4 h at the same temperature. After complete addition, the reaction mixture was stirred at room temperature for 1 h. After that, the mixture was partitioned between 20 mL of DCM and 20 mL of sat. aq. $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with DCM (3x20 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and evaporated. Purification by CC (DCM:MeOH 1:0 -> 100:5) furnished 84 mg (87%) mixture of diastereomers in a 3:2 ratio in favor of the desired product. The mixture was further purified by CC (DCM:MeOH 1:0 -> 100:3) to obtain analytical samples of pure diastereomers.

(+)-sitsirikine (7): 33.1 mg (34% yield)

^{1}H NMR (400MHz; MeOD-*d4*): δ 7.38 (d, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 8.1, 1H), 7.08 – 6.93 (m, 2H), 5.71 – 5.58 (m, 1H), 5.31 – 5.18 (m, 2H), 4.01 (dd, *J* = 10.9, 8.3 Hz, 1H), 3.70 (dd, *J* =

10.9, 6.6 Hz, 1H), 3.66 (s, 3H), 3.29 – 3.23 (m, 1H), 3.10 – 3.03 (m, 1H), 3.02 – 2.88 (m, 3H), 2.76 – 2.67 (m, 1H), 2.60 (td, *J* = 11.3, 4.5 Hz, 1H), 2.55 – 2.48 (m, 1H), 2.42 – 2.27 (m, 2H), 1.88 – 1.78 (m, 1H), 1.46 – 1.33 (m, 1H).

^{13}C{1H} NMR (100 MHz, MeOD-*d4*): δ 174.8, 139.8, 138.1, 135.3, 128.3, 122.1, 119.8, 118.6, 112.0, 107.8, 62.4, 62.0, 61.3, 54.0, 51.8, 50.2, 45.4, 40.8, 31.3, 22.3.

HRMS-ESI (m/z): [M+H] calculated for $C_{21}H_{27}N_2O_3$, 355.2022; found 355.2030.

IR (ν_{max}, film): 3376, 2948, 2920, 2813, 1706, 1452, 1436, 1205, 1164, 1048, 917, 743 cm^{-1}.

$[\alpha]_D^{20}$ = 31.2 ° (*c* =1.0, MeOH). Lit[5] for (-)-sitsirikine **$[\alpha]_D^{25}$** = -58 ° (MeOH).

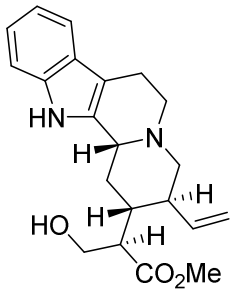
MP = 120 - 123 °C.

Table S3. ^{13}C Data comparison of (+)-sitsirikine (**8**)

Literature,[6] **^{13}C{1H} NMR** (100 MHz, MeOD-*d4*)	**Synthetic**, **^{13}C{1H} NMR** (100 MHz, MeOD-*d4*)
174.8	174.8
139.9	139.8
138.1	138.1
135.4	135.3
128.3	128.3
122.0	122.1
119.8	119.8
118.6	118.6
118.5	118.6
112.0	112.0
107.9	107.8
62.4	62.4
62.0	62.0
61.2	61.3
54.0	54.0

51.8	51.8
50.2	50.2
45.4	45.4
40.8	40.8
31.3	31.3
22.3	22.3

(+) 16-*epi*-sitsirikine (SI-5): 12.8 mg (13% yield)



^{1}H NMR (400MHz; MeOD-*d4*): δ 7.38 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.08 – 6.94 (m, 2H), 5.70 – 5.58 (m, 1H), 5.26 – 5.14 (m, 2H), 3.92 – 3.84 (m, 1H), 3.79 – 3.67 (m, 4H), 3.31 – 3.26 (m, 1H), 3.14 – 3.06 (m, 1H), 3.02 – 2.88 (m, 2 H), 2.84 – 2.78 (m, 1H), 2.77 – 2.69 (m, 1H), 2.67 – 2.58 (m, 1H), 2.51 – 2.41 (m, 1H), 2.40 – 2.31 (m, 2H), 2.04 – 1.94 (m, 1H), 1.47 – 1.35 (m, 1H).

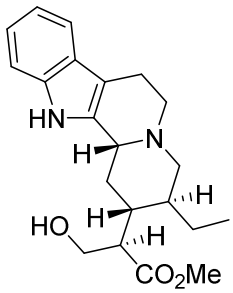
^{13}C{1H} NMR (100 MHz, MeOD-*d4*): δ 176.3, 139.9, 138.2, 135.2, 128.3, 122.1, 119.8, 118.6, 118.4, 112.0, 107.9, 62.1, 61.4, 60.2, 53.9, 52.2, 51.1, 46.1, 41.9, 32.0, 22.3.

HRMS-ESI (m/z): [M+H] calculated for $C_{21}H_{27}N_2O_3$, 355.2022; found 355.2033.

IR (ν_{max}, film): 3263, 2925, 1727, 1453, 1200, 1044, 743 cm^{-1}.

$[\alpha]_D^{20}$ = 22.0 ° (*c* = 0.1, MeOH).

Methyl (S)-2-((2S,3R,12bR)-3-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizin-2-yl)-3-hydroxypropanoate 8; (+)-dihydrositsirikine



(+)-sitsirikine (23 mg, 0.065 mmol, 1 eq) was dissolved in 2 mL of MeOH and then Pd/C (6.9 mg, 0.007 mmol, 0.1 eq, 10% w/w) was carefully added. After that, the reaction flask was purged with hydrogen (balloon) by three vacuum/hydrogen cycles and stirred overnight at room temperature under an H_2 atmosphere (balloon). Then the suspension was filtered and evaporated. Purification of the residue by CC (Pet:EtOAc 1:2 -> 1:9) furnished 17 mg (74%) title compound as a yellow wax.

^{1}H NMR (400MHz; MeOD-*d4*): δ 7.40 – 7.27 (m, 2H), 7.08 – 6.93 (m, 2H), 4.06 (dd, *J* = 10.8, 8.5 Hz, 1H), 3.72 (dd, *J* = 10.9, 6.1 Hz, 1H), 3.66 (s, 3H), 3.25 – 3.18 (m, 1H), 3.12 – 3.03 (m, 3H), 3.03 – 2.92 (m, 1H), 2.75 – 2.68 (m, 1H), 2.59 (td, *J* = 11.4, 4.5 Hz, 1H), 2.39 – 2.30 (m, 1H), 2.15 (t, *J* = 11.2 Hz, 1H), 1.88 – 1.63 (m, 2H), 1.43 (q, *J* = 11.9 Hz, 1H), 1.35 – 1.22 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H).

^{13}C{1H} NMR (100 MHz, MeOD-*d4*): δ 174.8, 138.1, 135.3, 128.3, 122.0, 119.8, 118.6, 112.0, 107.8, 62.6, 61.5, 61.1, 54.3, 51.9, 40.8, 40.3, 31.4, 24.1, 22.2, 10.9.

HRMS-ESI (m/z): [M+H] calculated for $C_{21}H_{29}N_2O_3$, 357.2178; found 357.2189.

IR (ν_{max}, film): 3464, 2956, 2917, 2874, 1668, 1491, 1368, 1127 cm^{-1}.

$[\alpha]_D^{20}$ = 53.0 ° (*c* = 0.1, MeOH). Lit for (-)-dihydrositsirikine.[7] **$[\alpha]_D^{25}$** = -55 ° (MeOH)

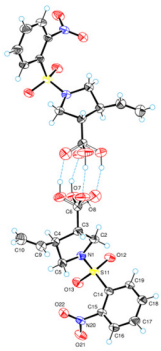
Table S4. ^{13}C Data comparison of (+)-dihydrositsirikine (**8**)

Literature,[6] **^{13}C{1H} NMR** (100 MHz, MeOD-*d4*)	**Synthetic**, **^{13}C{1H} NMR** (100 MHz, MeOD-*d4*)
174.9	174.8
138.1	138.1
135.5	135.3
128.3	128.3
122.0	122.0
119.7	119.8
118.6	118.6
112.0	112.0
107.8	107.8
62.6	62.6
61.5	61.5
61.2	61.1
54.8	54.3
51.8	51.9
41.0	40.8
40.4	40.3
31.5	31.4
24.1	24.1
22.3	22.2
10.9	10.9

X-ray crystallographic data

X-ray structure of **(3*S*,4*S*)-12d**

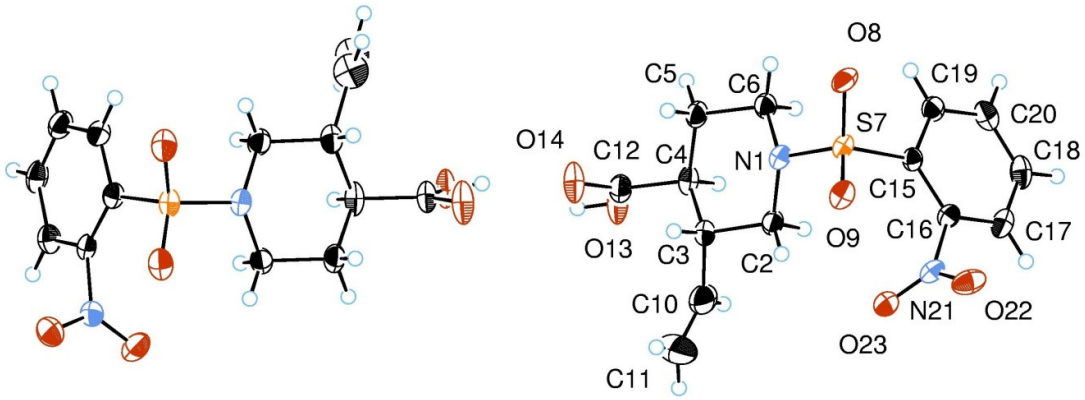
Deposition Number 2388652



Identification code	NU_868
Empirical formula	$C_{26}H_{28}N_4O_{12}S_2$
Formula weight	652.66
Temperature/K	150.0(1)
Crystal system	triclinic
Space group	*P*1
a/Å	5.1440(3)
b/Å	11.1424(3)
c/Å	14.0974(4)
α/°	111.856(3)
β/°	90.041(2)
γ/°	103.384(3)
Volume/Å^3	726.18(5)
Z	1
ρ_{calc}g/cm^3	1.4923
μ/mm^{-1}	2.291
F(000)	340
Crystal size/mm^3	0.22 × 0.03 × 0.01
Radiation	Cu Kα (λ = 1.54184 Å)
2Θ max. for data collection/°	160.0
Index ranges	$-6 \le h \le 6$, $-14 \le k \le 14$, $-17 \le l \le 17$
Reflections collected	22401
Independent reflections	5708 [R_{int} = 0.0541, R_{sigma} = 0.0475]
Data/restraints/parameters	5708/3/433
Goodness-of-fit on F^2	1.044
Final *R* indexes [$I \ge 2\sigma(I)$]	R_1 = 0.0459, wR_2 = 0.1177
Final *R* indexes [all data]	R_1 = 0.0473, wR_2 = 0.1188
Largest diff. peak/hole / e Å^{-3}	0.41/-0.39
Flack's *x* parameter	0.02(3)

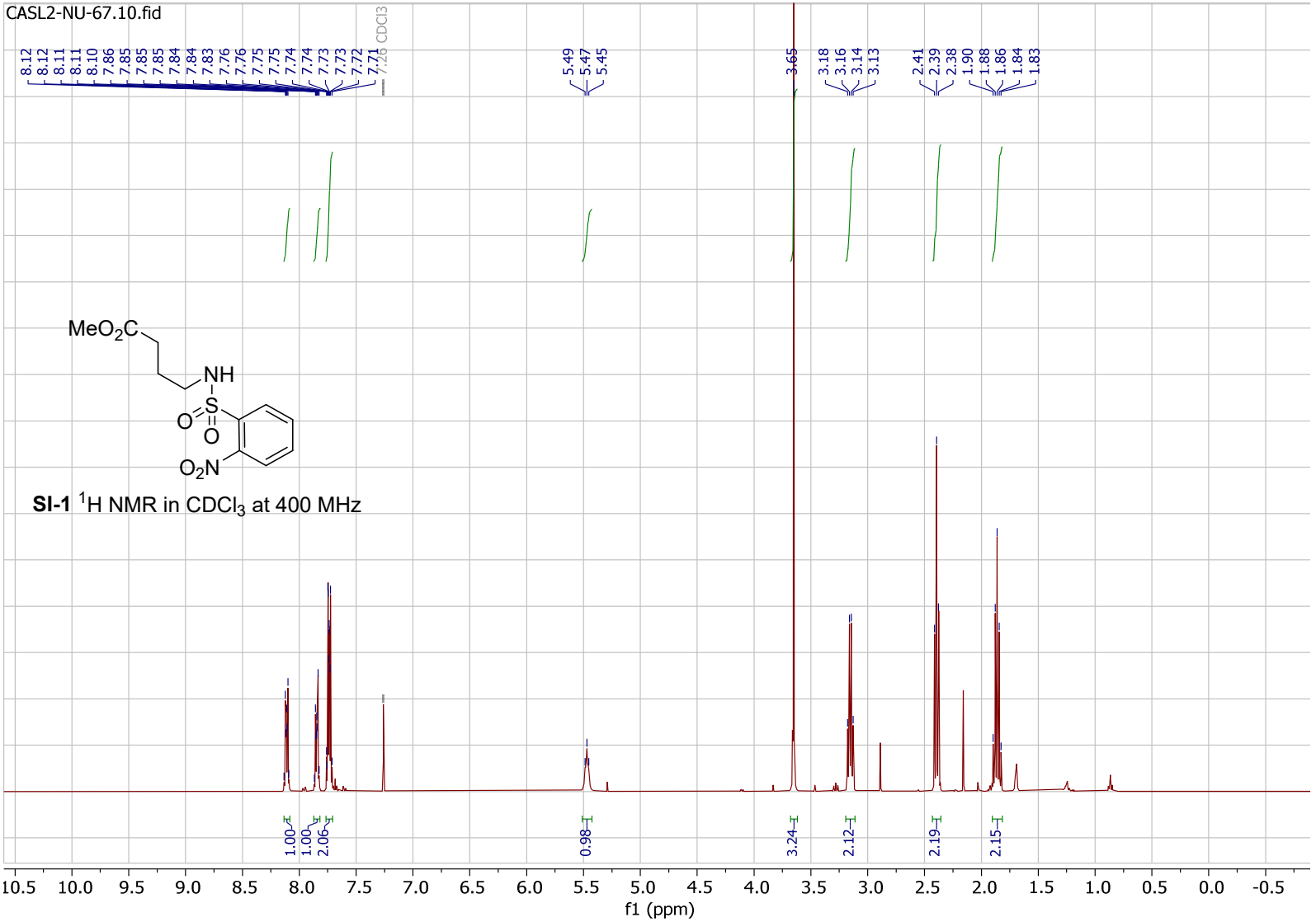
X-ray structure of **(3*R*,4*S*)-12a**

Deposition Number 2388419

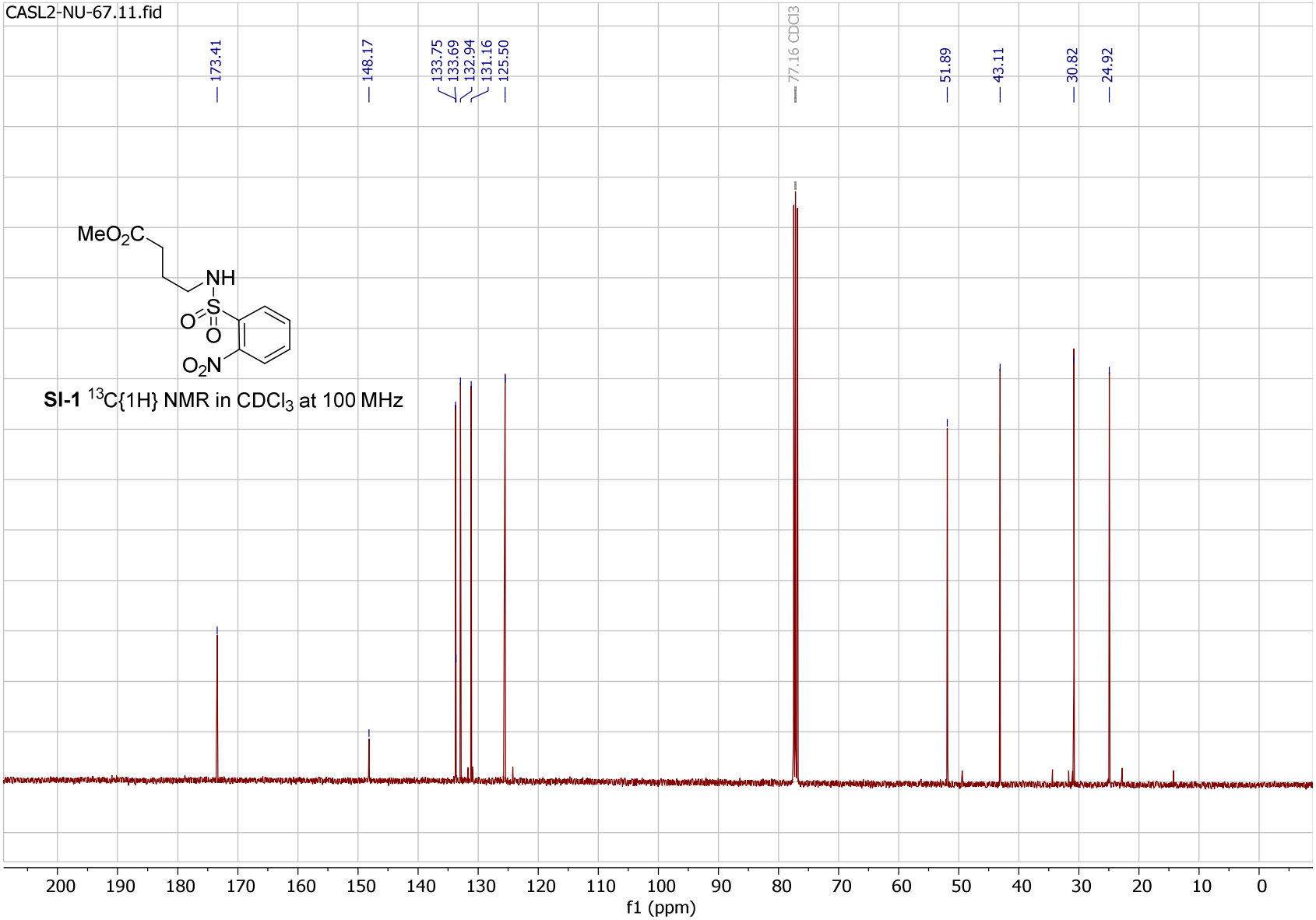


Identification code	NU-318
Empirical formula	$C_{14}H_{16}N_2O_6S$
Formula weight	340.35
Temperature/K	150.0(2)
Crystal system	triclinic
Space group	*P*1
a/Å	5.32882(9)
b/Å	7.28248(13)
c/Å	21.3012(4)
α/°	91.5829(14)
β/°	95.3795(14)
γ/°	106.9519(15)
Volume/Å^3	785.93(2)
Z	2
ρ_{calc}g/cm^3	1.438
μ/mm^{-1}	2.140
F(000)	356.0
Crystal size/mm^3	0.19 × 0.14 × 0.02
Radiation	CuKα (λ = 1.54184 Å)
2Θ max. for data collection/°	155°
Index ranges	$-6 \le h \le 4$, $-9 \le k \le 9$, $-26 \le l \le 26$
Reflections collected	12660
Independent reflections	4462 [R_{int} = 0.0402, R_{sigma} = 0.0355]
Data/restraints/parameters	4462/3/426
Goodness-of-fit on F^2	1.070
Final *R* indexes [$I > 2\sigma(I)$]	R_1 = 0.0406, wR_2 = 0.1093
Final *R* indexes [all data]	R_1 = 0.0410, wR_2 = 0.1097
Largest diff. peak/hole / e Å^{-3}	0.60/-0.31
Flack's *x* parameter	0.01(3)

Copies of NMR spectra



SI-1 ^{1}H NMR in $CDCl_3$ at 400 MHz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30.82
24.92
MeO2C
NH
S
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O
O2N
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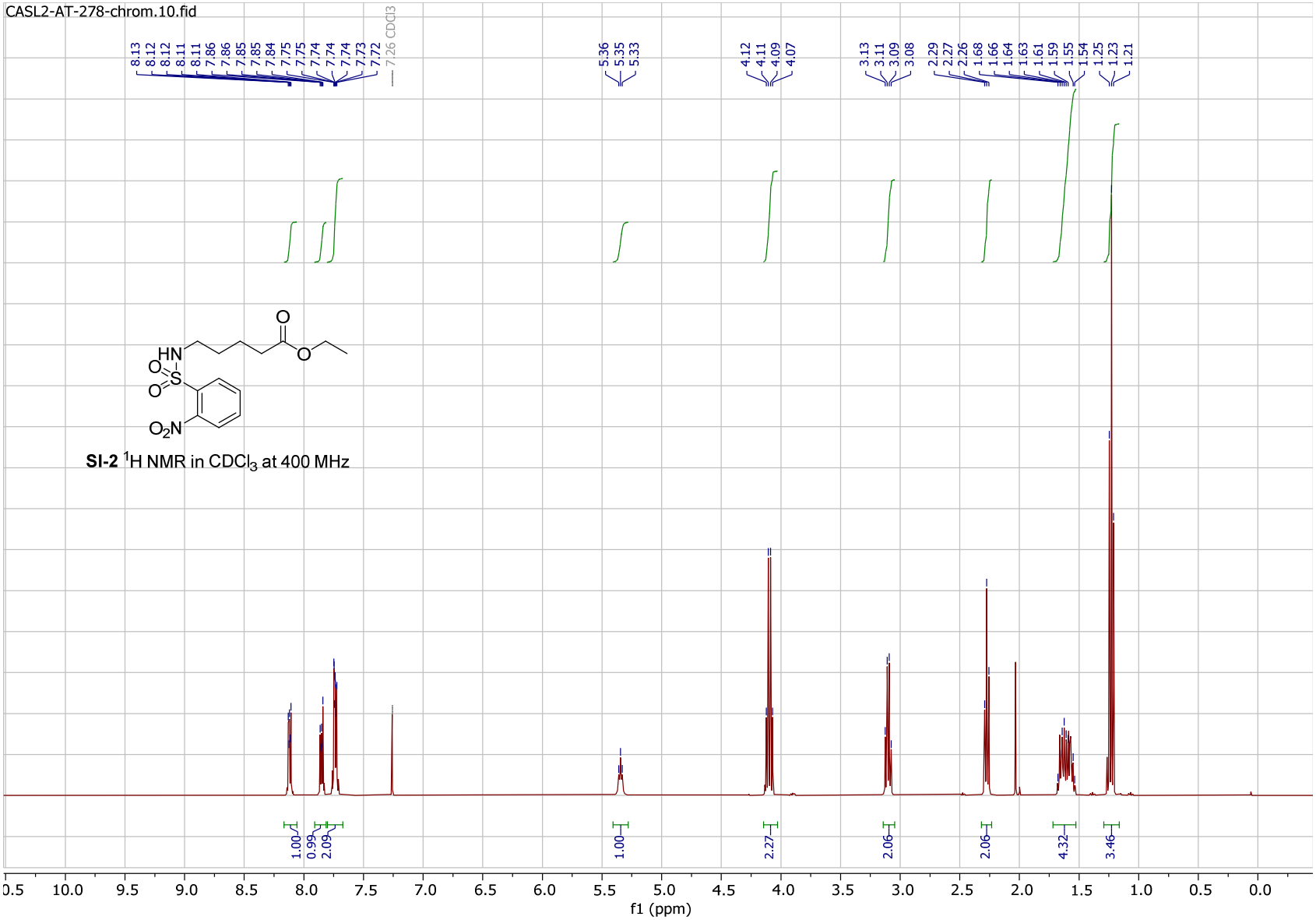
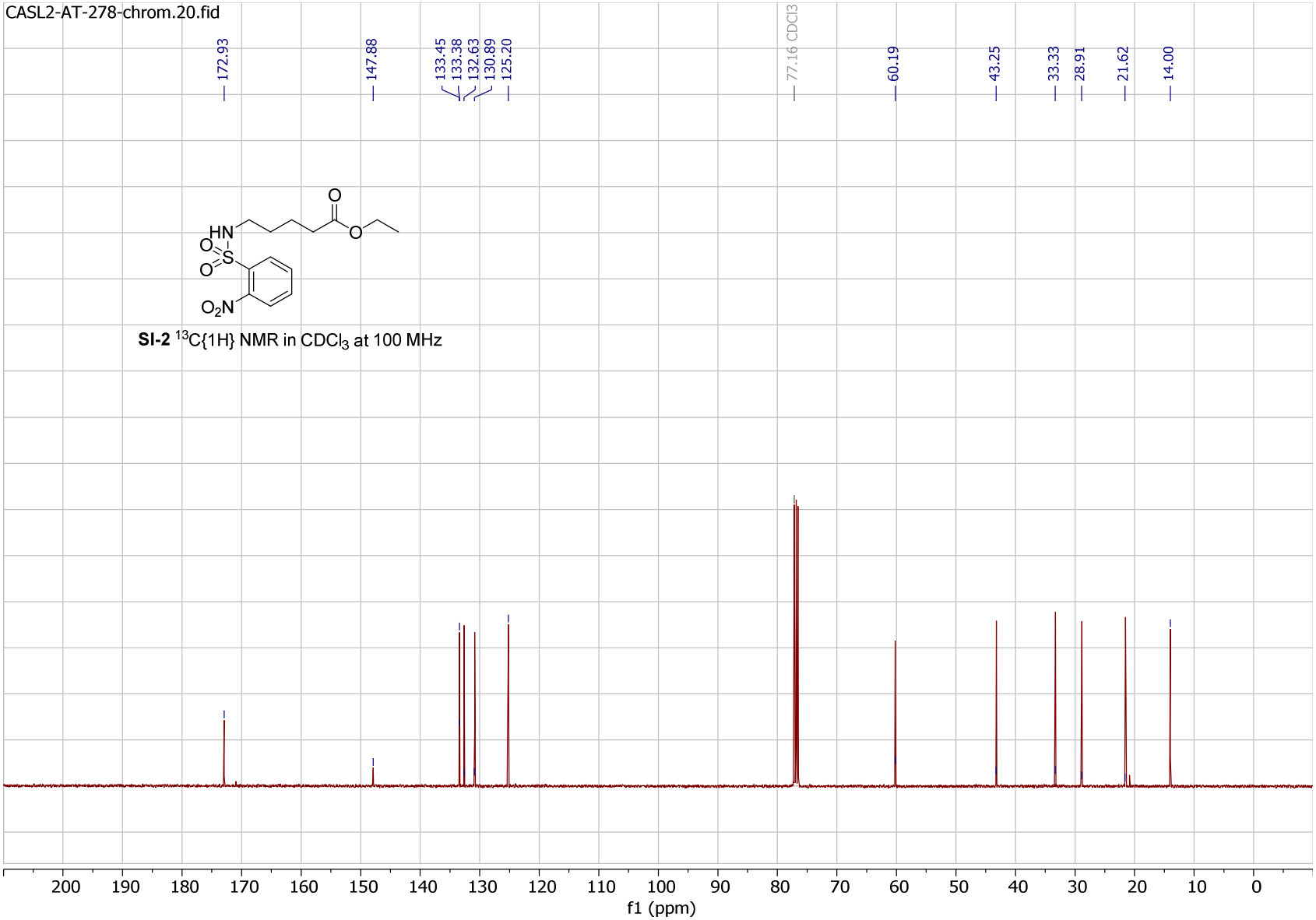
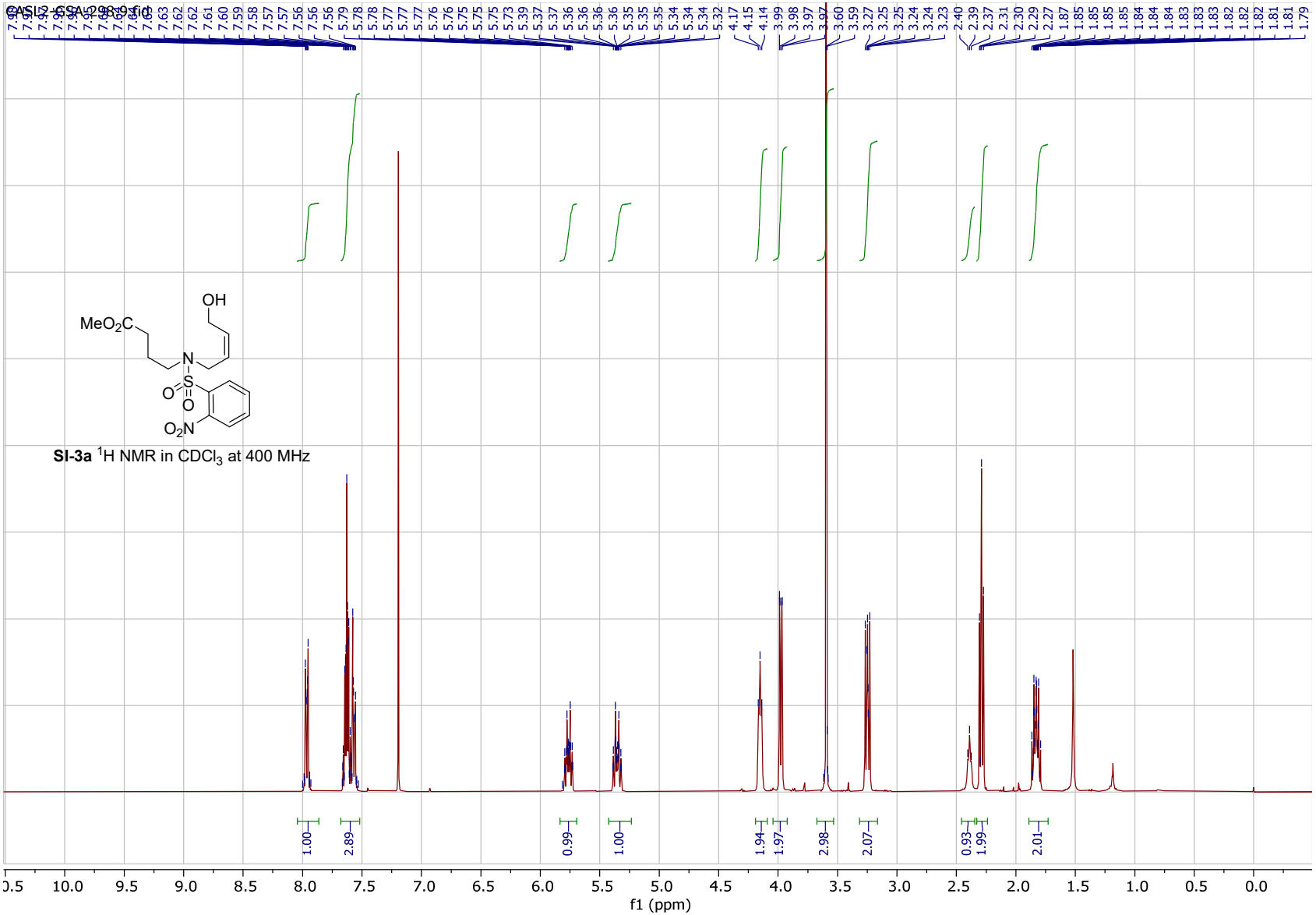
f1 (ppm)



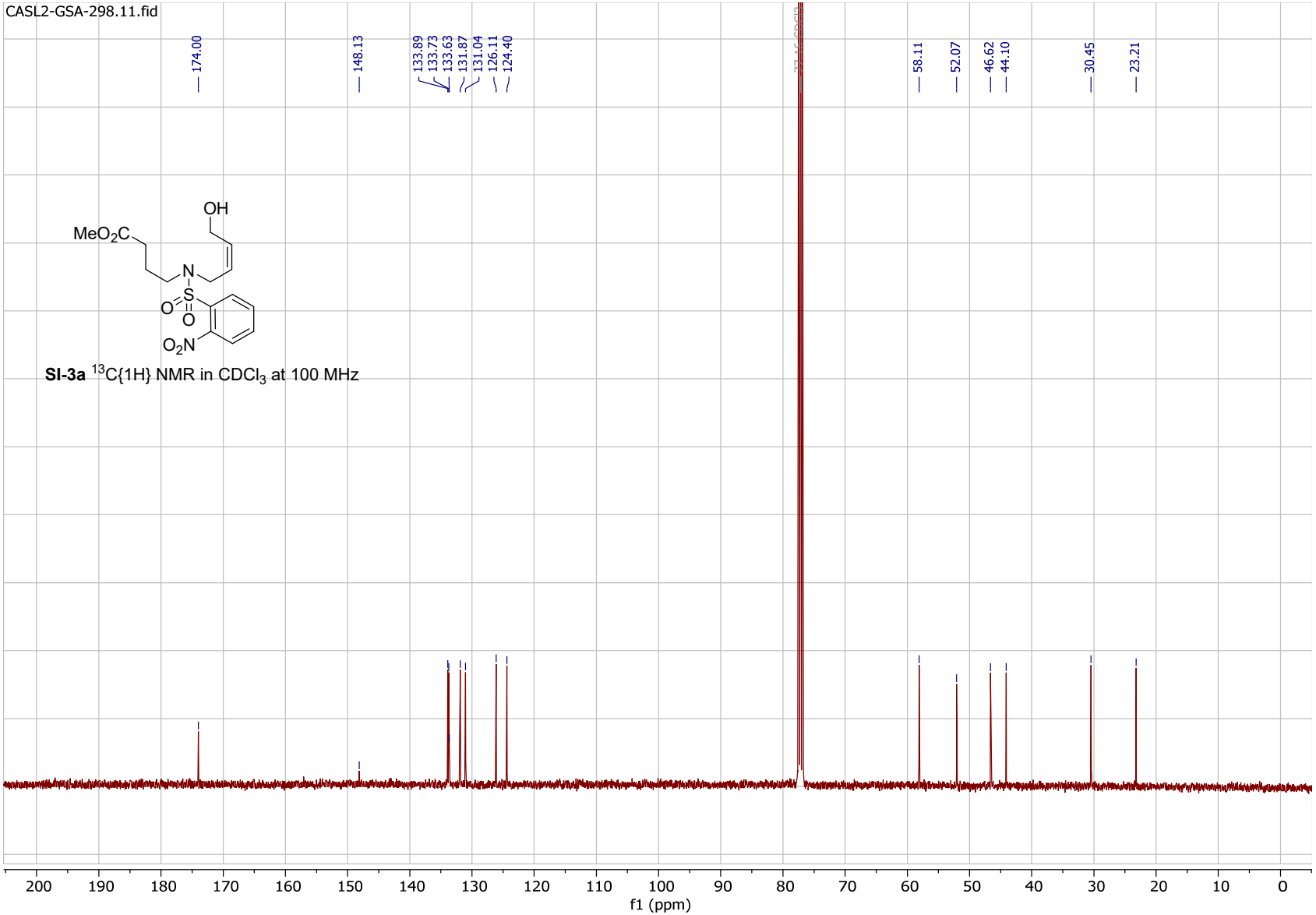
SI-2 ^{1}H NMR in $CDCl_3$ at 400 MHz



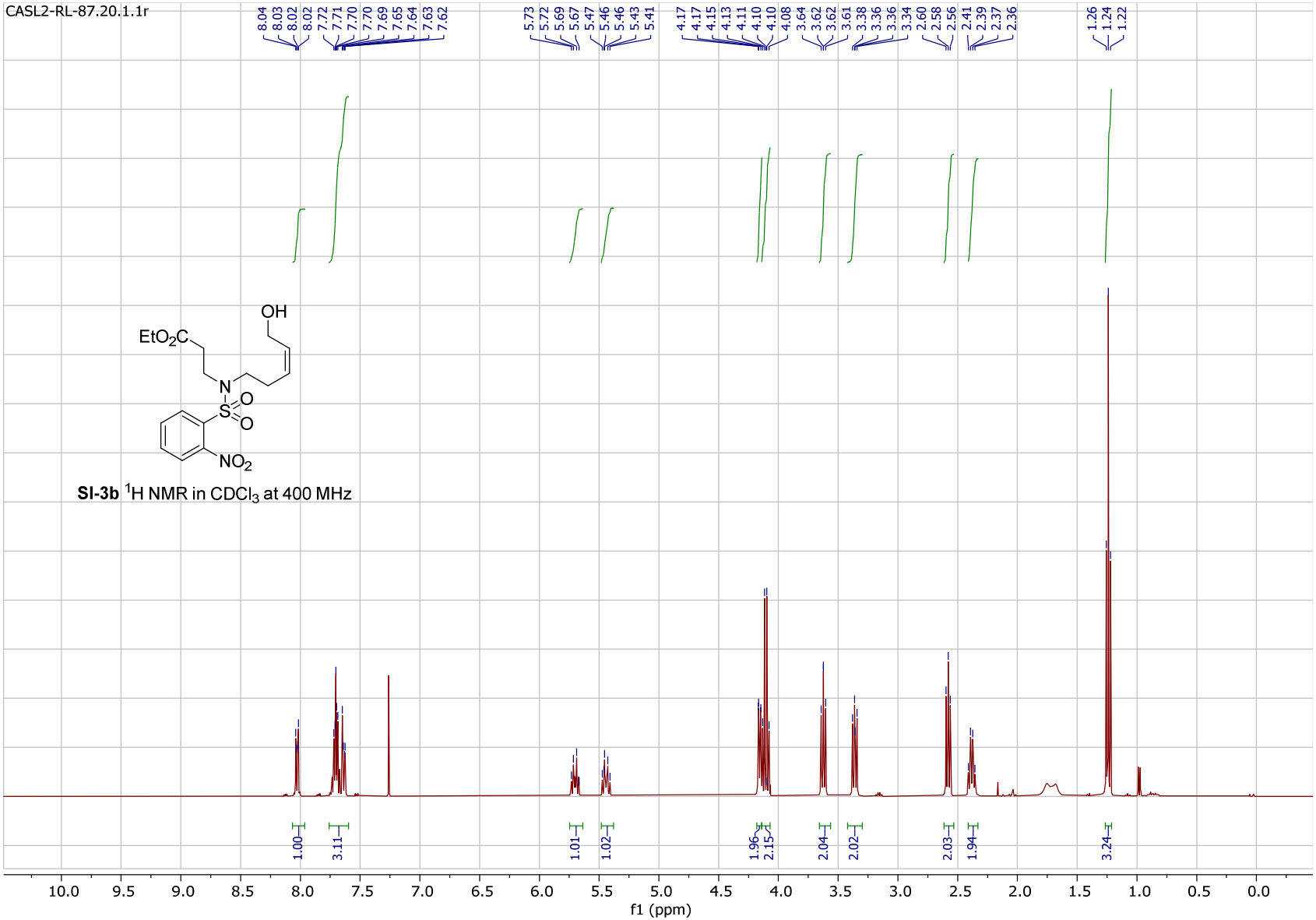
SI-2 $^{13}C\{1H\}$ NMR in $CDCl_3$ at 100 MHz



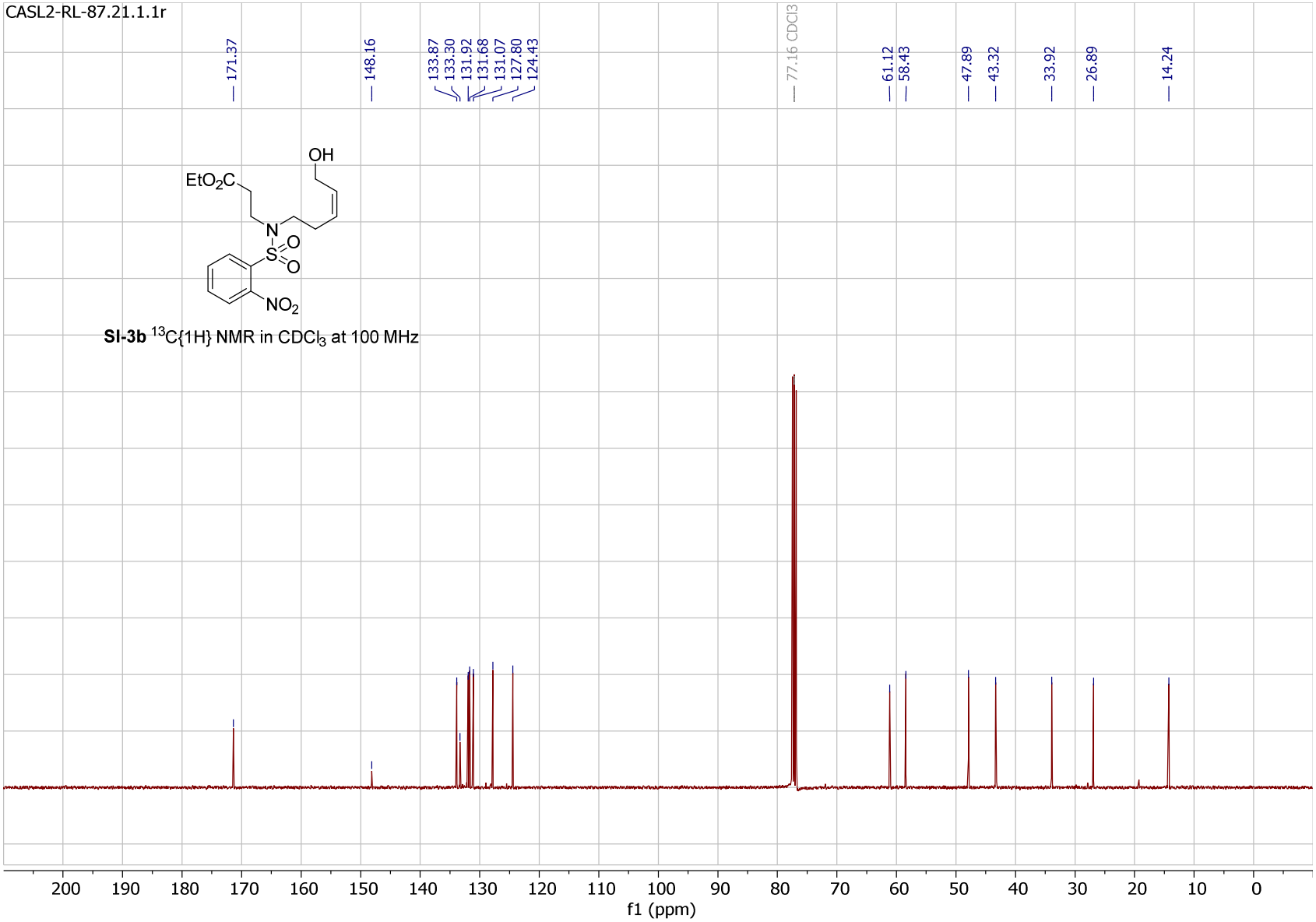
SI-3a ^{1}H NMR in $CDCl_3$ at 400 MHz



SI-3a $^{13}C\{1H\}$ NMR in $CDCl_3$ at 100 MHz



SI-3b ^{1}H NMR in $CDCl_3$ at 400 MHz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133.30
131.92
131.68
131.07
127.80
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77.16 CDCl3
61.12
58.43
47.89
43.32
33.92
26.89
14.24
OH
EtO2C
N
S
O
O
NO2
SI-3b 13C{1H} NMR in CDCl3 at 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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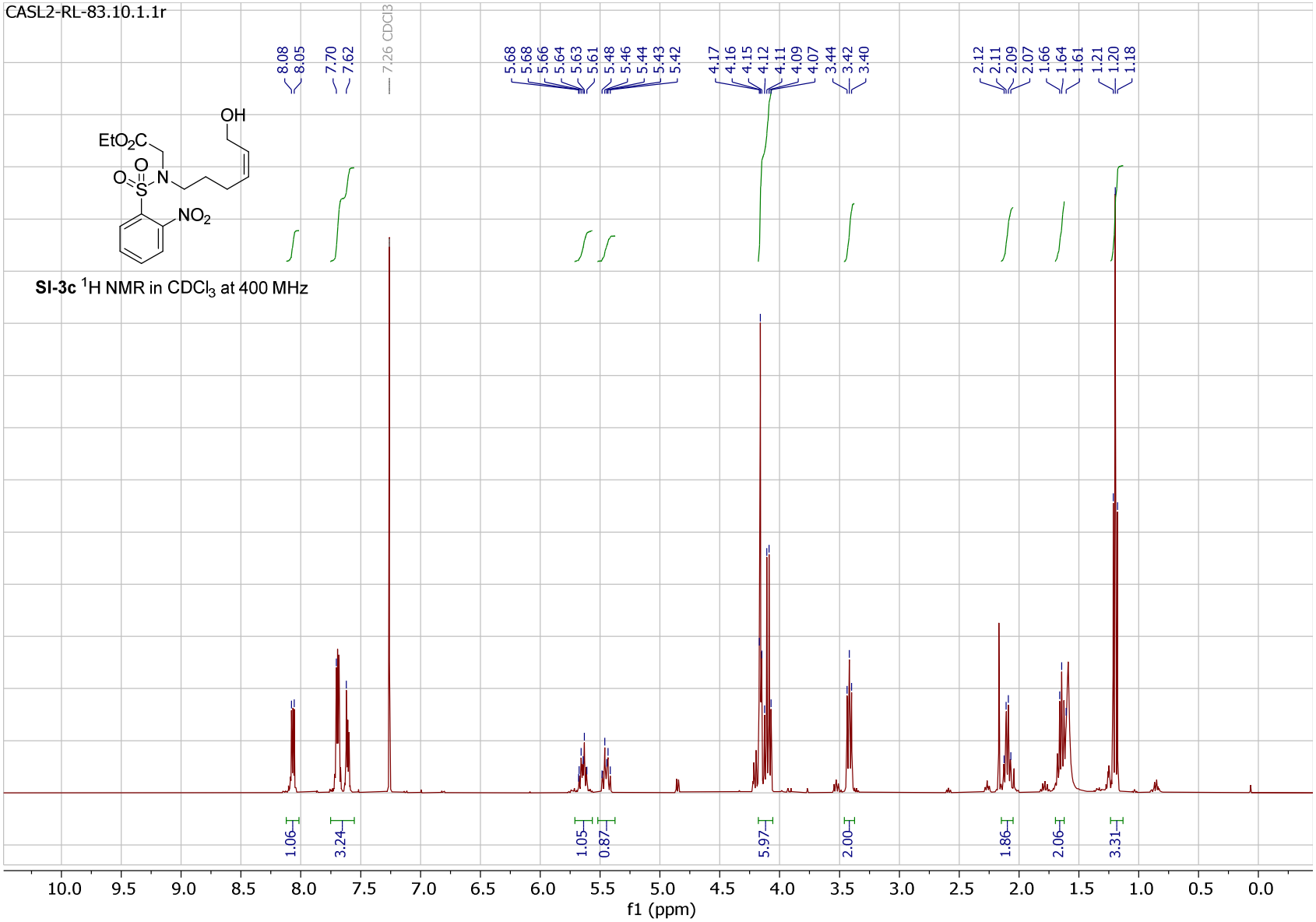
50
40
30
20
10
0
f1 (ppm)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4.12
4.11
4.09
4.07
3.44
3.42
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2.11
2.09
2.07
1.66
1.64
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1.20
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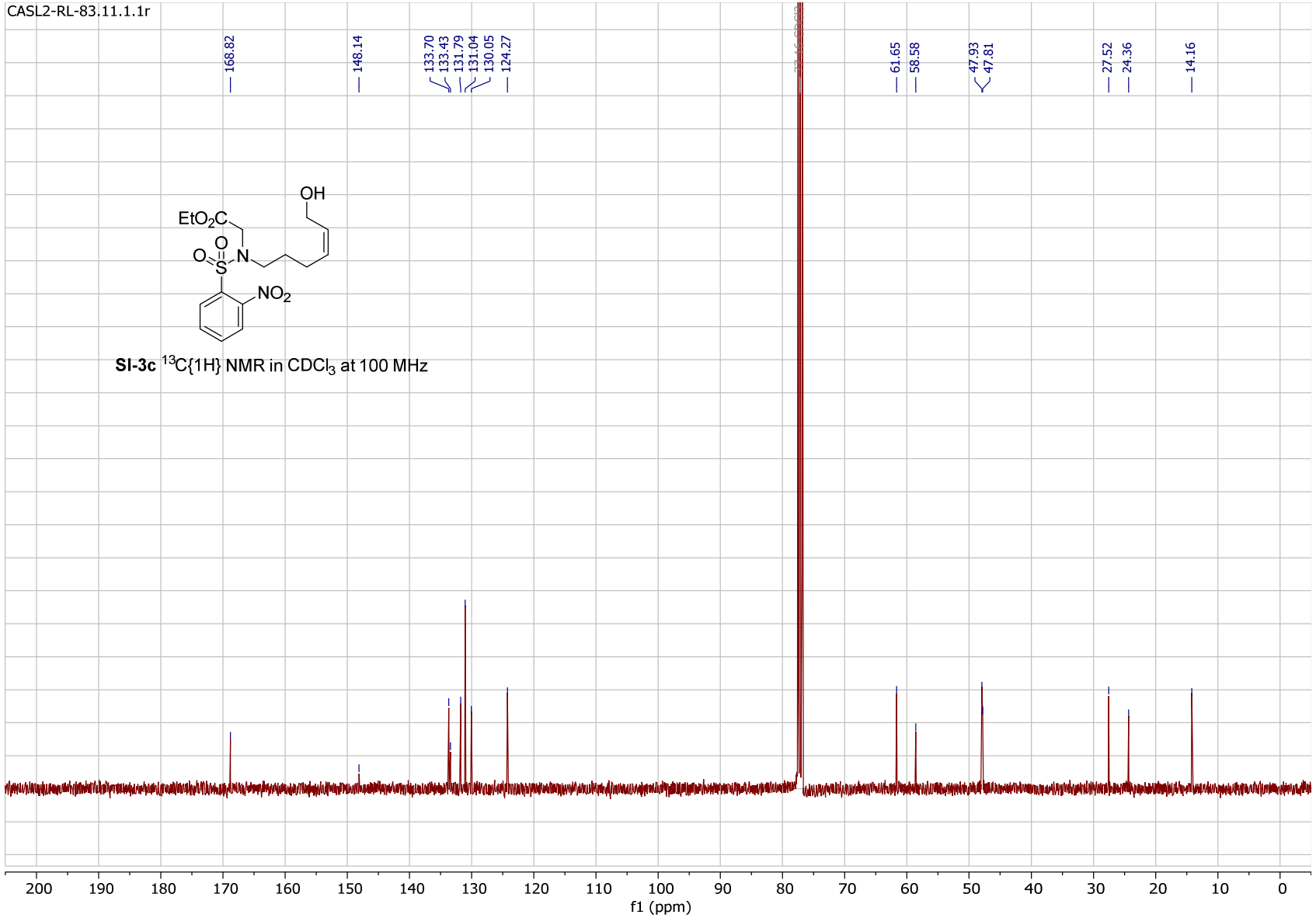
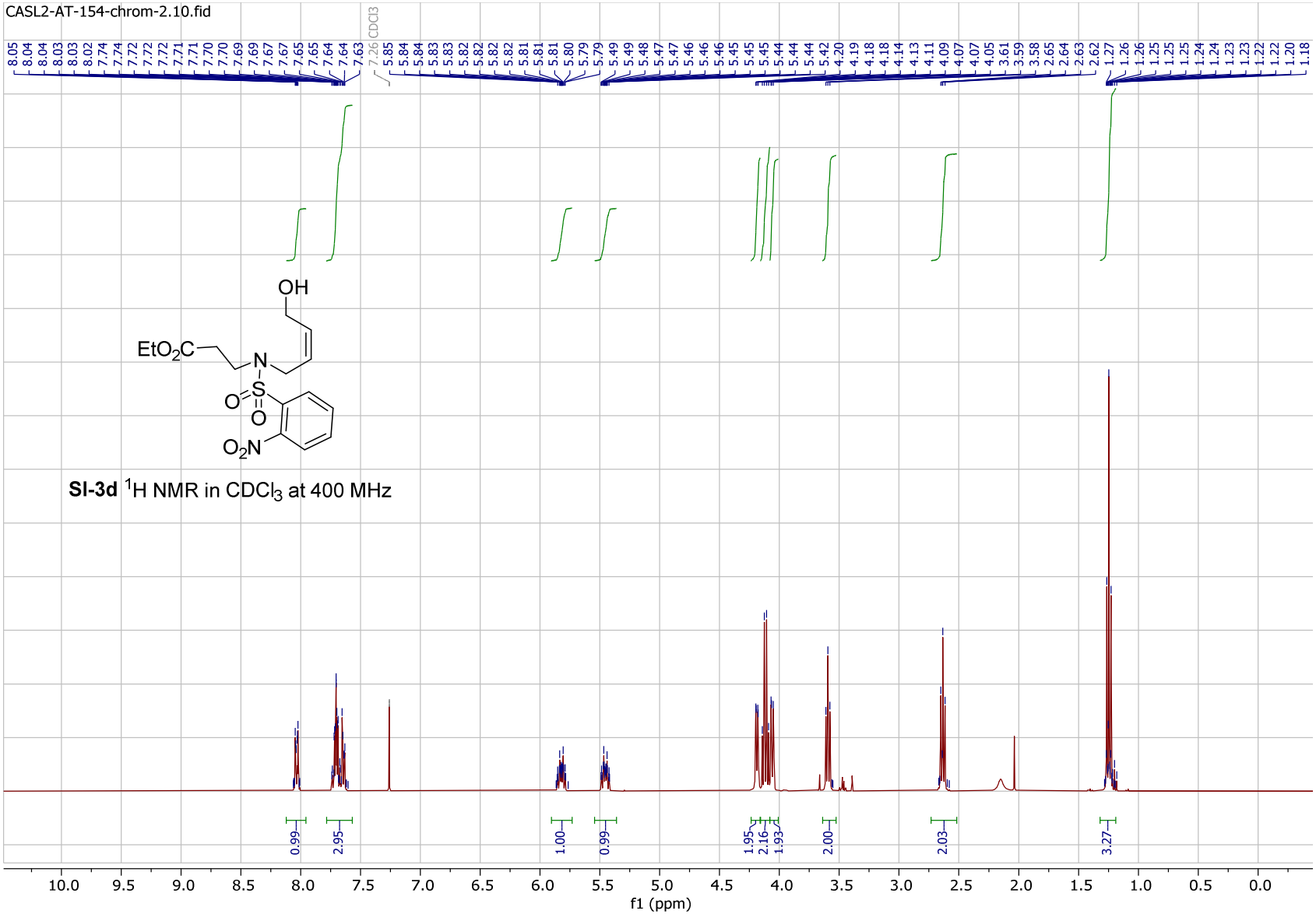
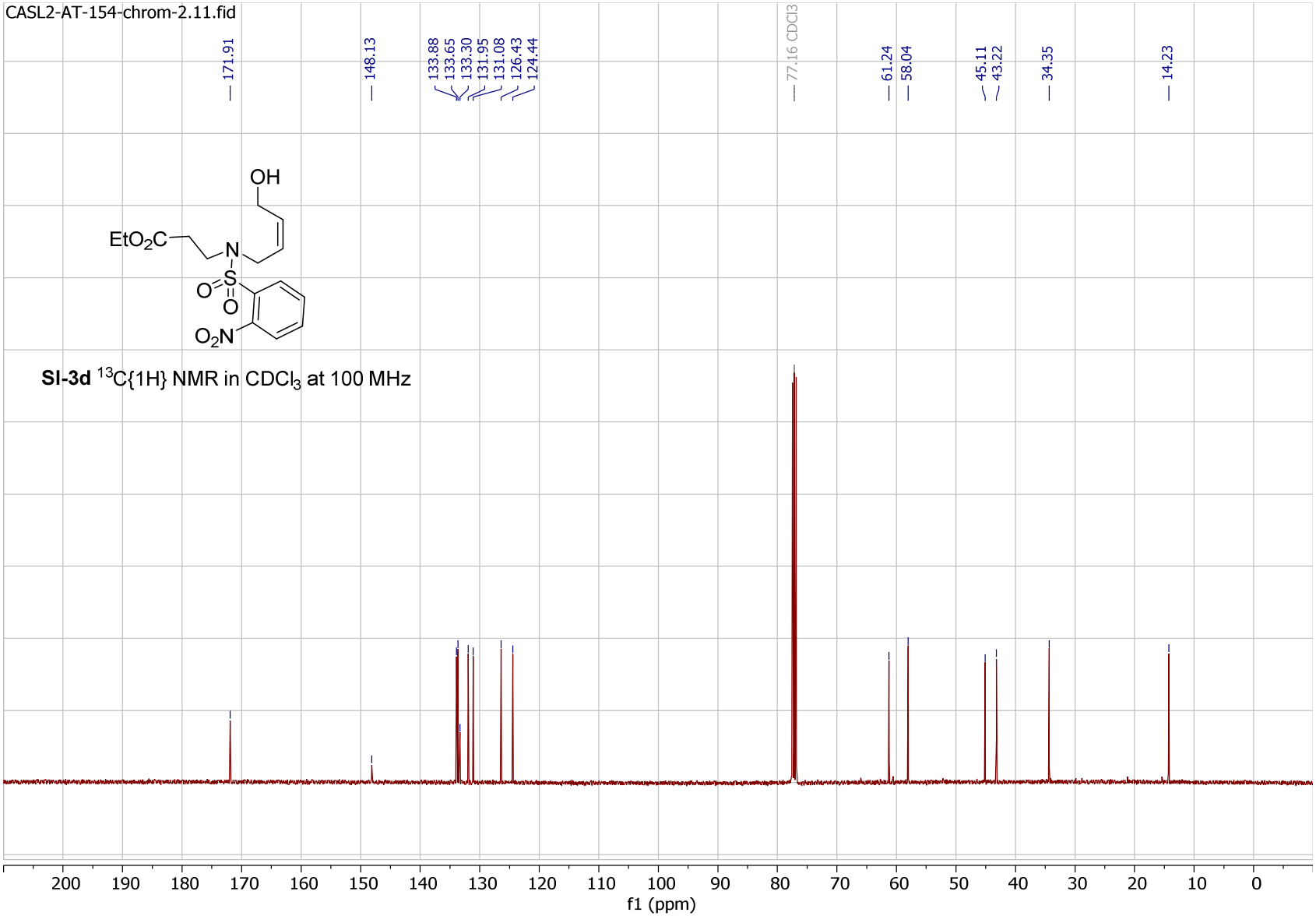
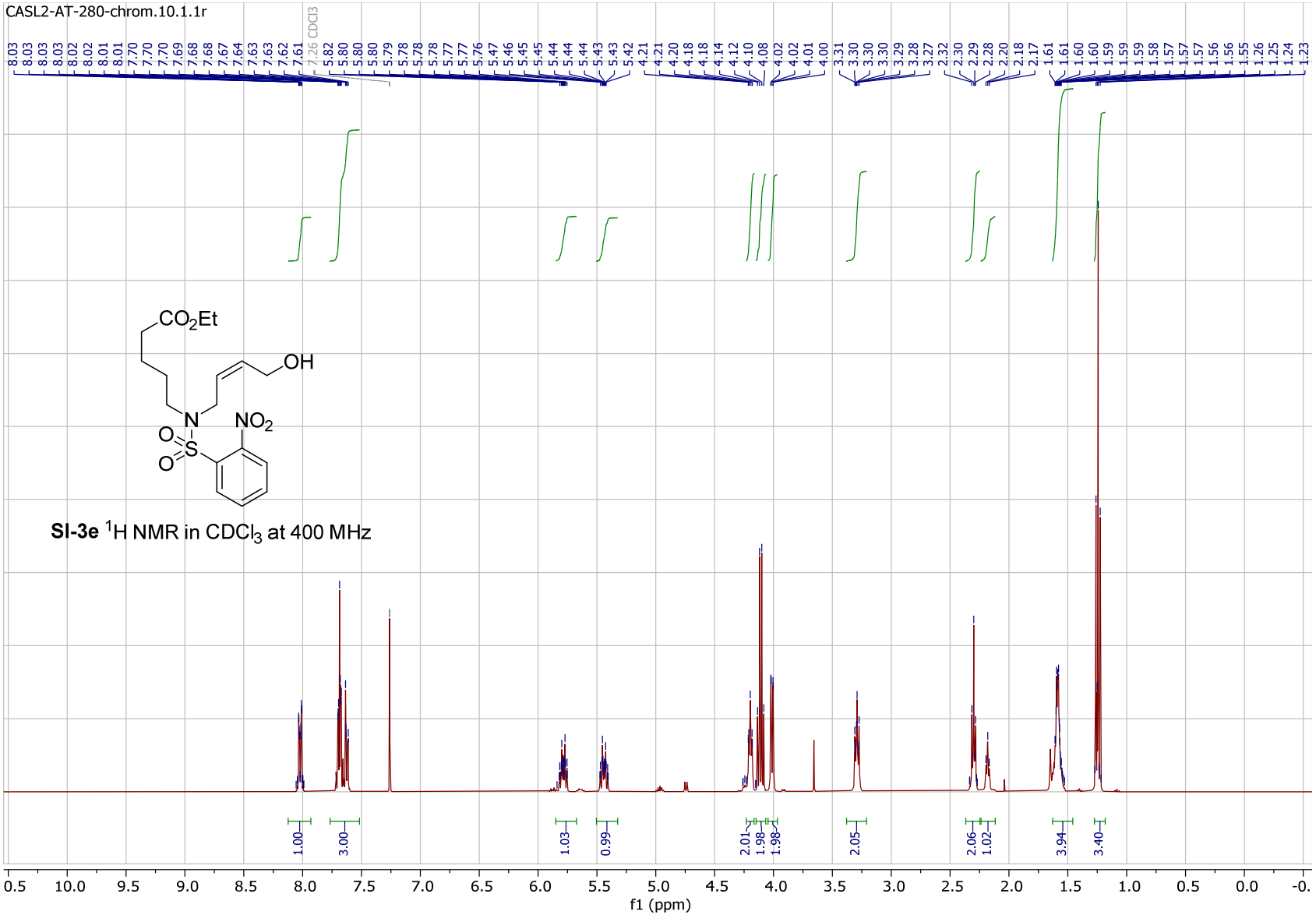
O
S
N
NO2
SI-3c 1H NMR in CDCl3 at 400 MHz
1.06
3.24
1.05
0.87
5.97
2.00
1.86
2.06
3.31
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

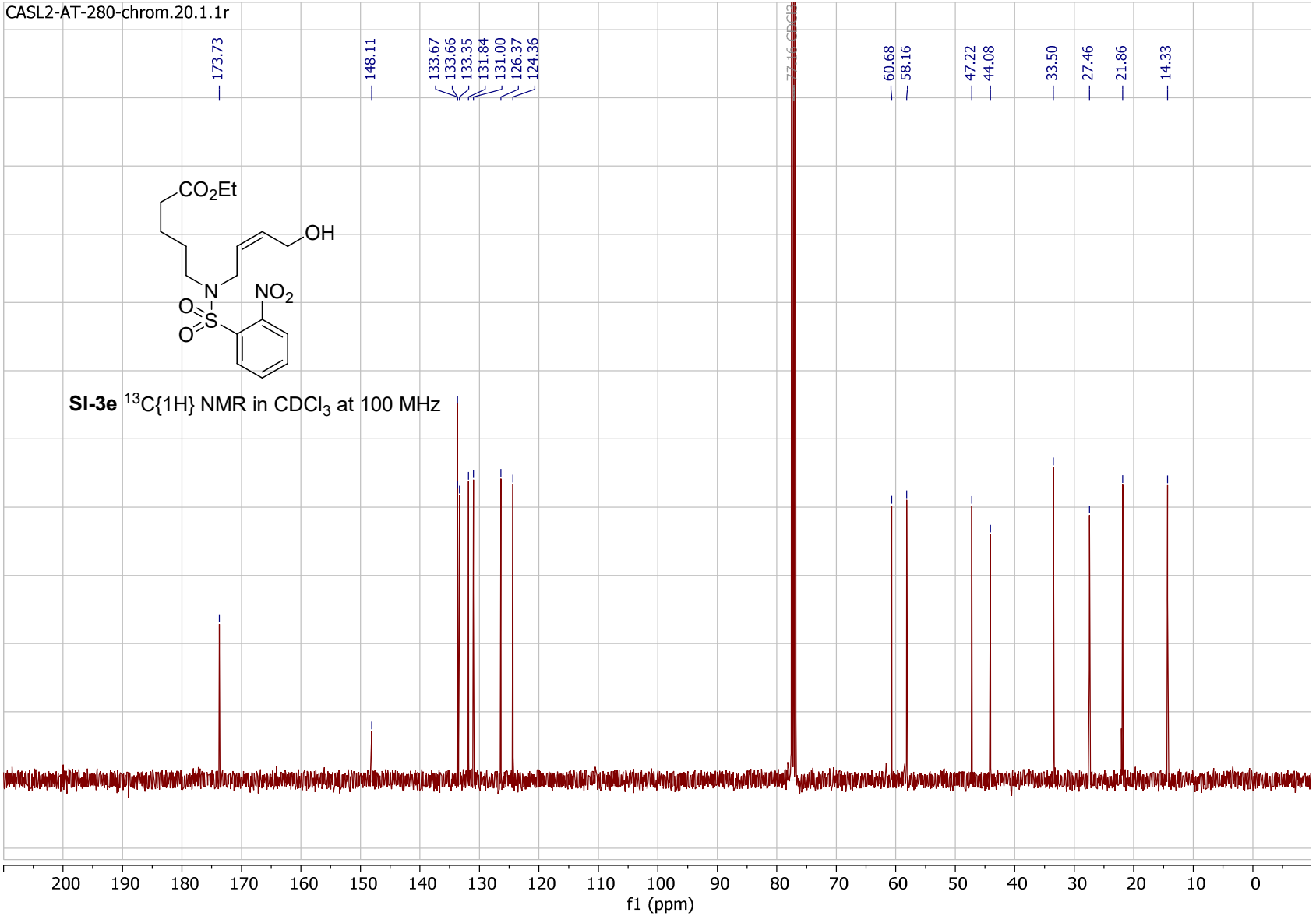


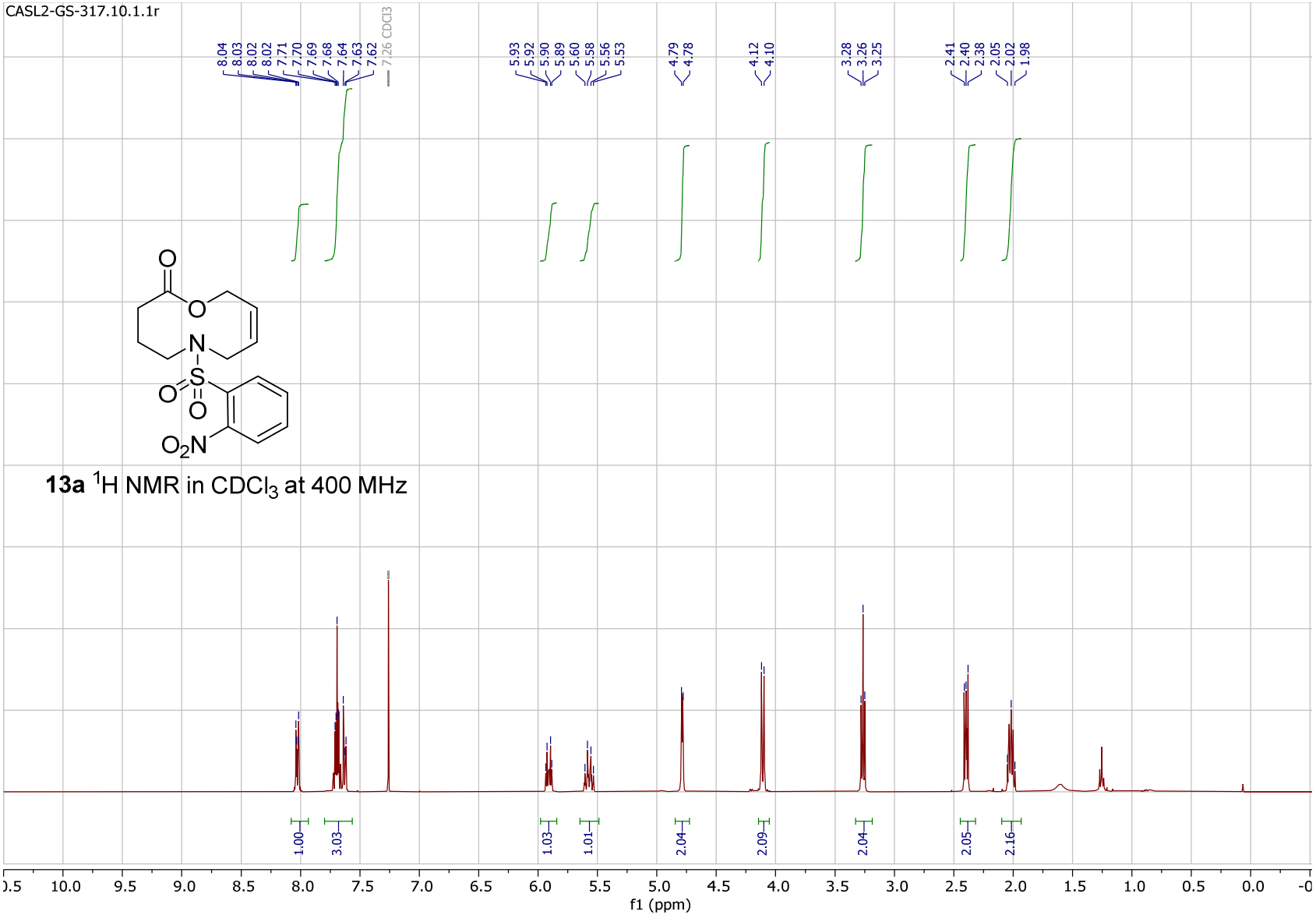
SI-3c $^{13}C\{1H\}$ NMR in $CDCl_3$ at 100 MHz

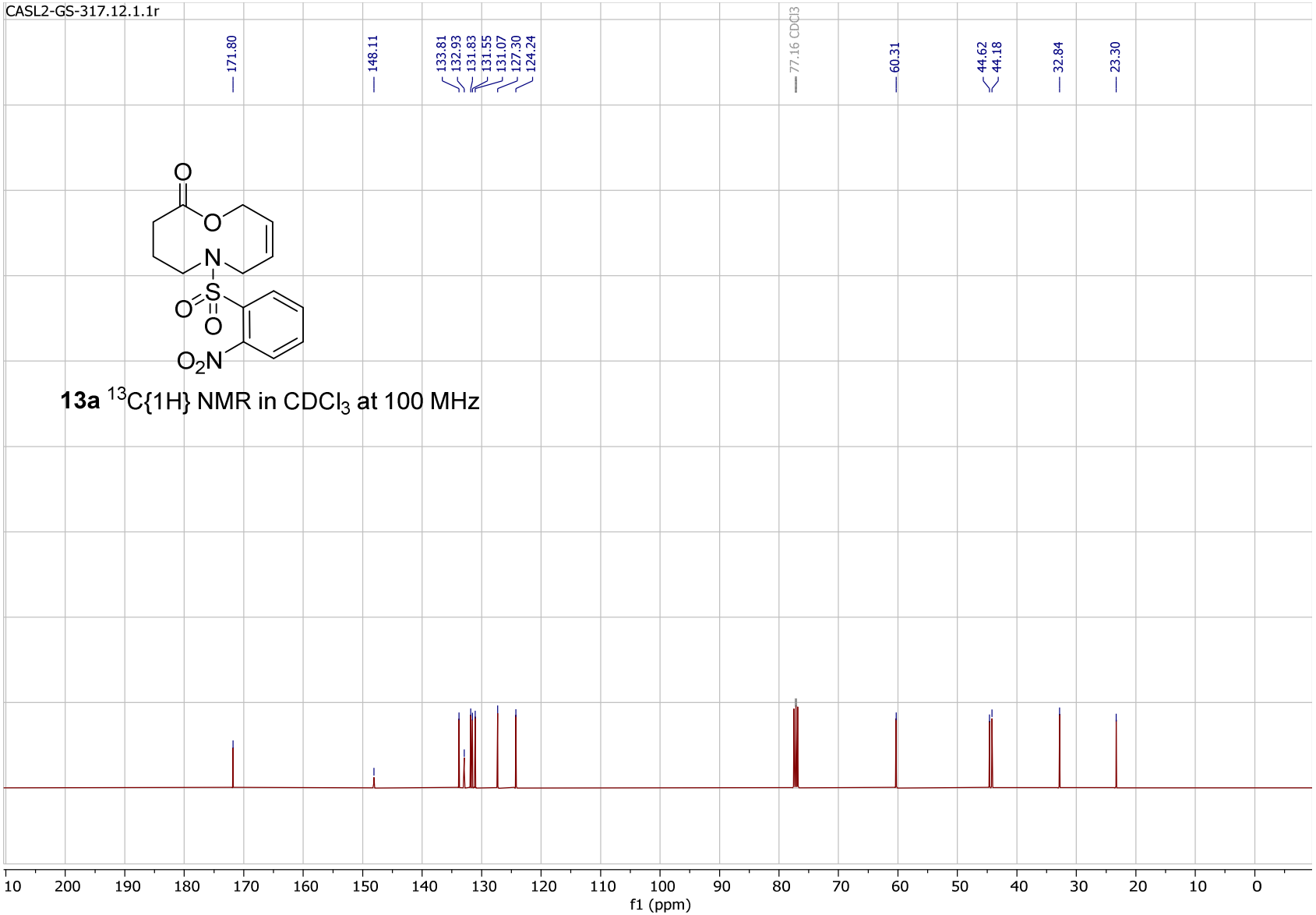

CASL2-AT-154-chrom-2.10.fid
CDCl3
OH
EtO2C
N
S
O
O
O2N
SI-3d 1H NMR in CDCl3 at 400 MHz
0.99
2.95
1.00
0.99
1.95
2.16
1.93
2.00
2.03
3.27
f1 (ppm)

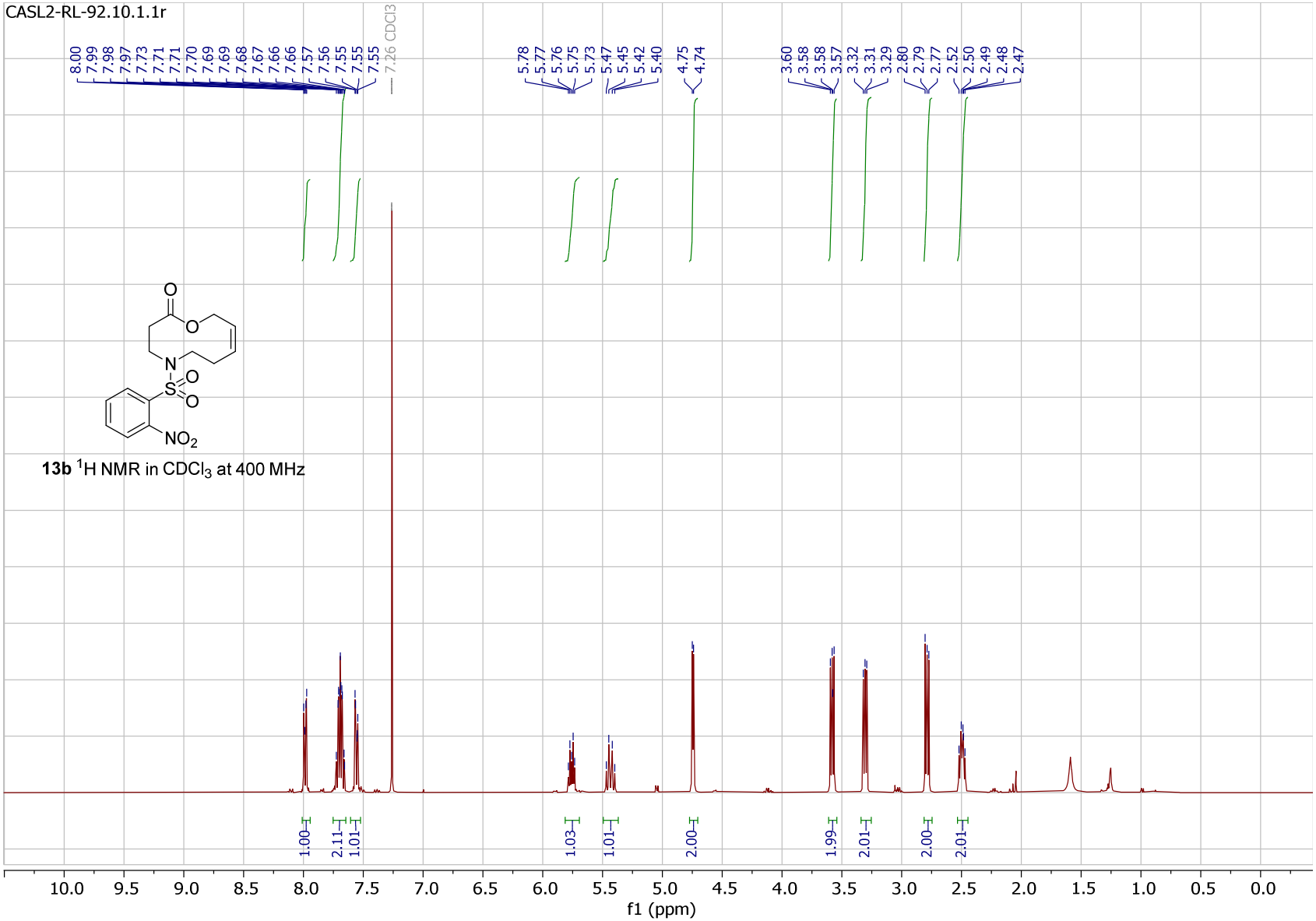

CASL2-AT-154-chrom-2.11.fid
171.91
148.13
133.88
133.65
133.30
131.95
131.08
126.43
124.44
77.16 CDCl3
61.24
58.04
45.11
43.22
34.35
14.23
OH
EtO2C
N
S
O
O
O2N
SI-3d 13C{1H} NMR in CDCl3 at 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


CASL2-AT-280-chrom.10.1.1r
CO2Et
OH
N
NO2
O
S
O
SI-3e 1H NMR in CDCl3 at 400 MHz
f1 (ppm)

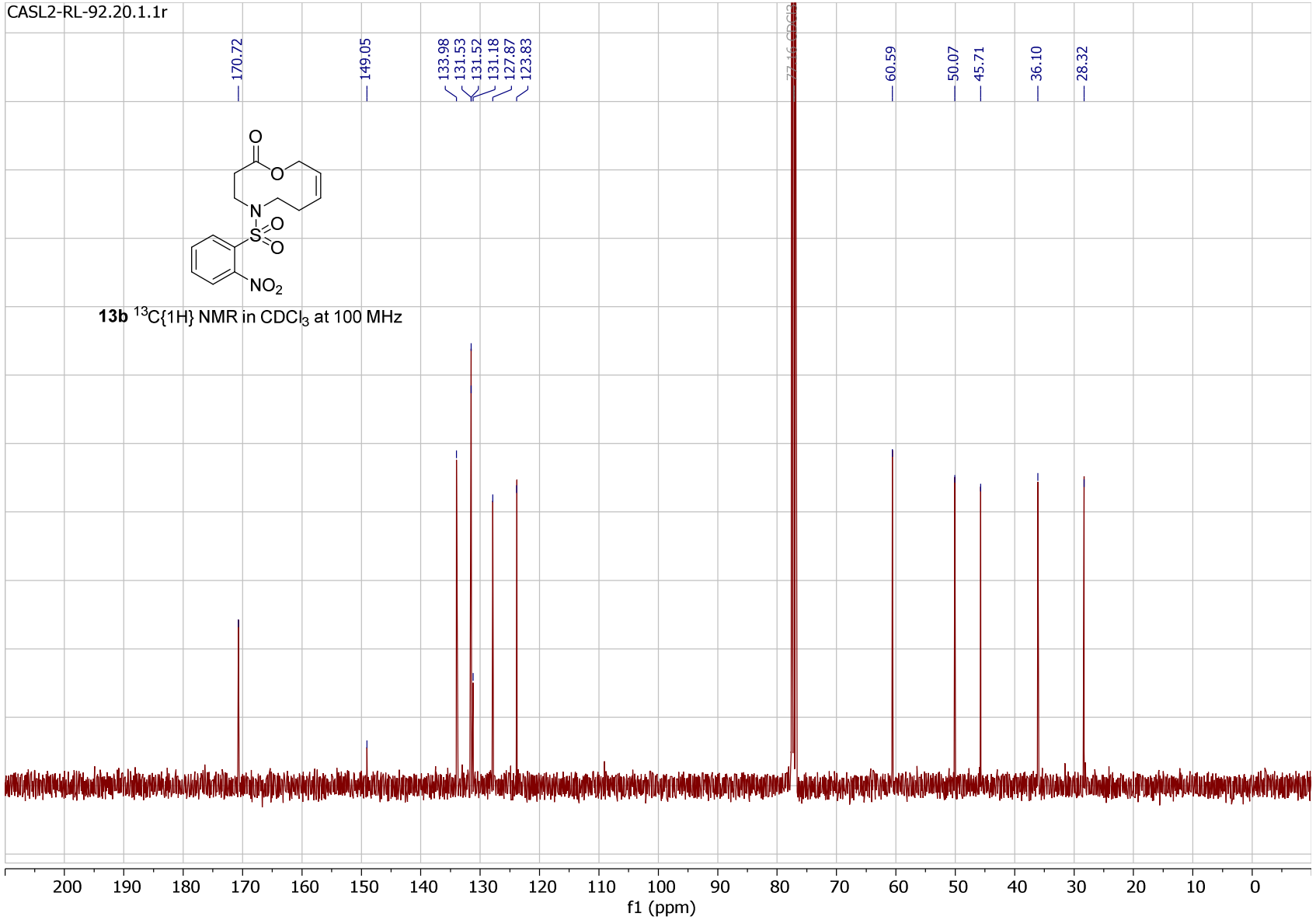

CASL2-AT-280-chrom.20.1.1r
173.73
148.11
133.67
133.66
133.35
131.84
131.00
126.37
124.36
77.16 CDCl3
60.68
58.16
47.22
44.08
33.50
27.46
21.86
14.33
CO2Et
OH
N
NO2
O
S
O
SI-3e 13C{1H} NMR in CDCl3 at 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

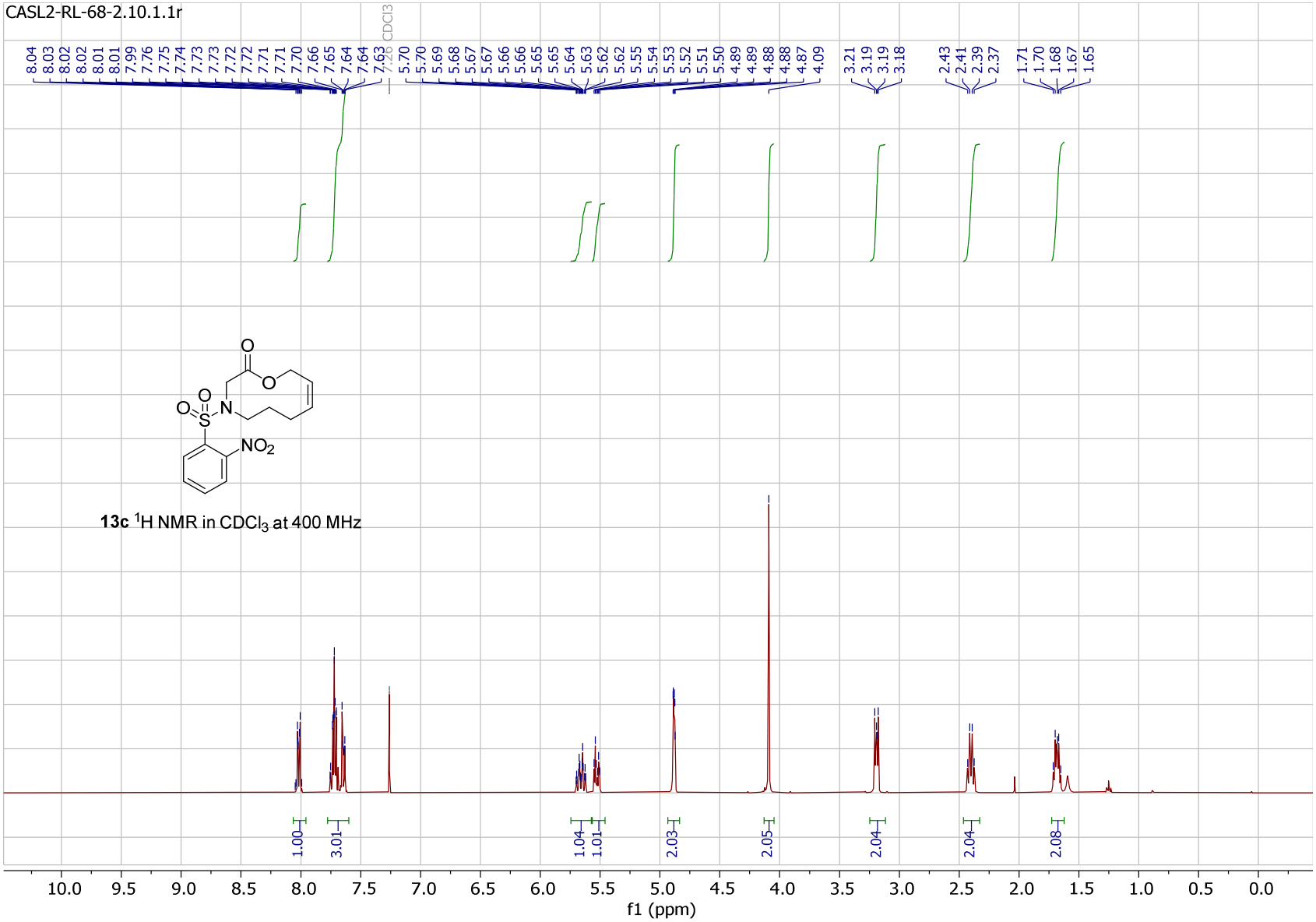

CASL2-GS-317.10.1.1r
8.04
8.03
8.02
8.02
7.71
7.70
7.69
7.68
7.64
7.63
7.62
7.26 CDCl3
5.93
5.92
5.90
5.89
5.60
5.58
5.56
5.53
4.79
4.78
4.12
4.10
3.28
3.26
3.25
2.41
2.40
2.38
2.05
2.02
1.98
O
O
N
S
O
O
O2N
13a 1H NMR in CDCl3 at 400 MHz
1.00
3.03
1.03
1.01
2.04
2.09
2.04
2.05
2.16
f1 (ppm)

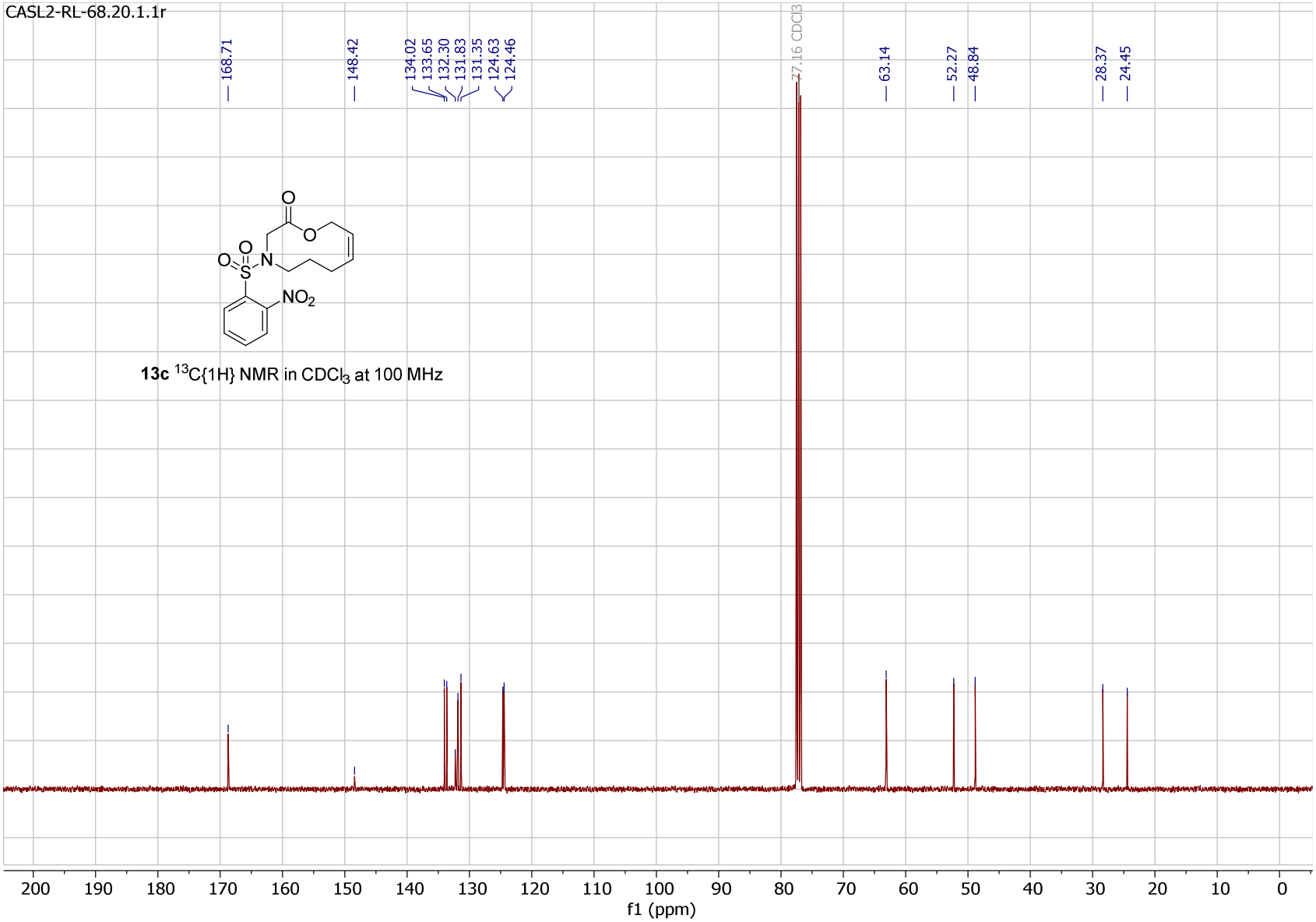

CASL2-GS-317.12.1.1r
171.80
148.11
133.81
132.93
131.83
131.55
131.07
127.30
124.24
77.16 CDCl3
60.31
44.62
44.18
32.84
23.30
O
O
N
S
O
O
O2N
13a 13C{1H} NMR in CDCl3 at 100 MHz
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



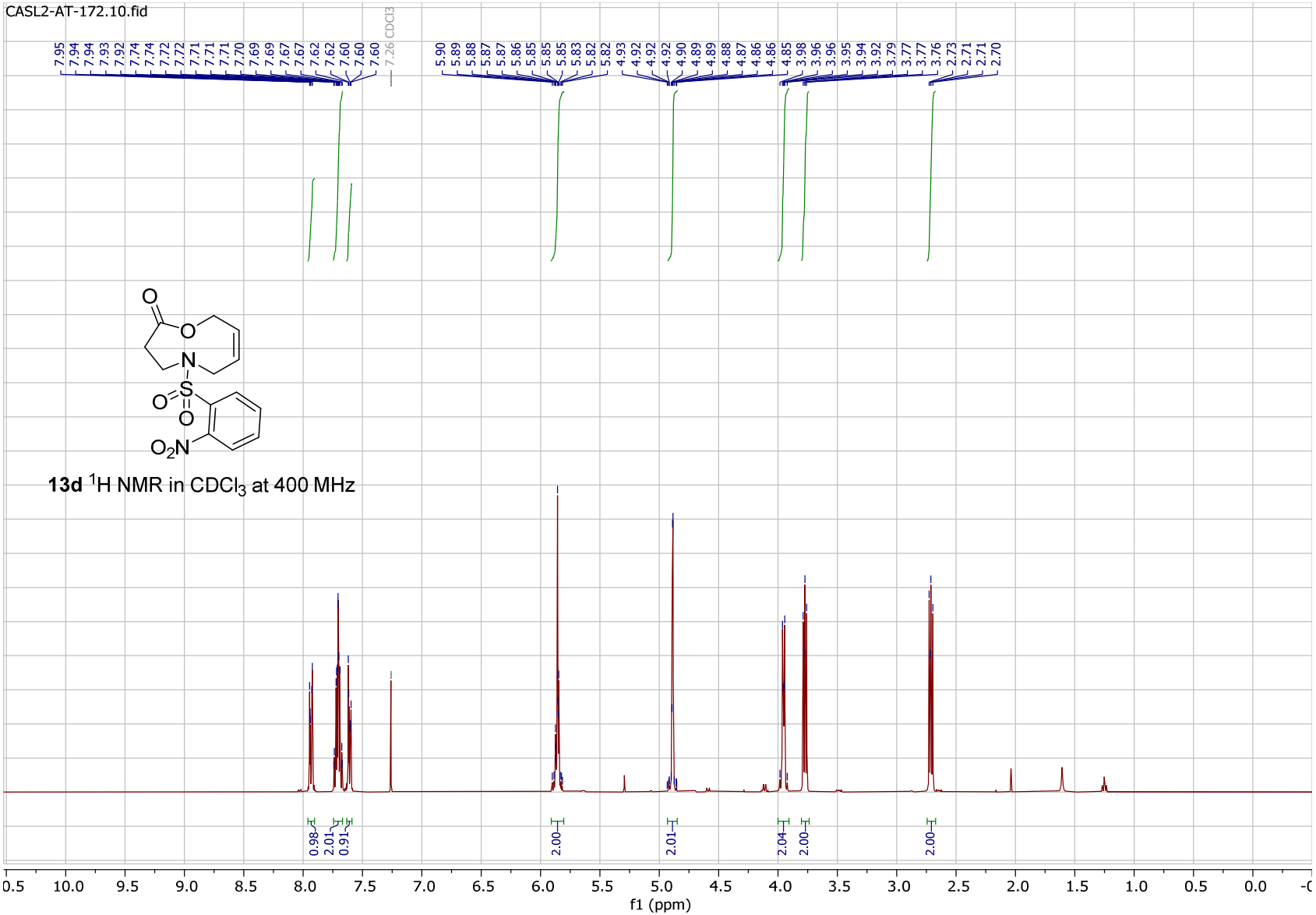
13b ^{1}H NMR in $CDCl_3$ at 400 MHz

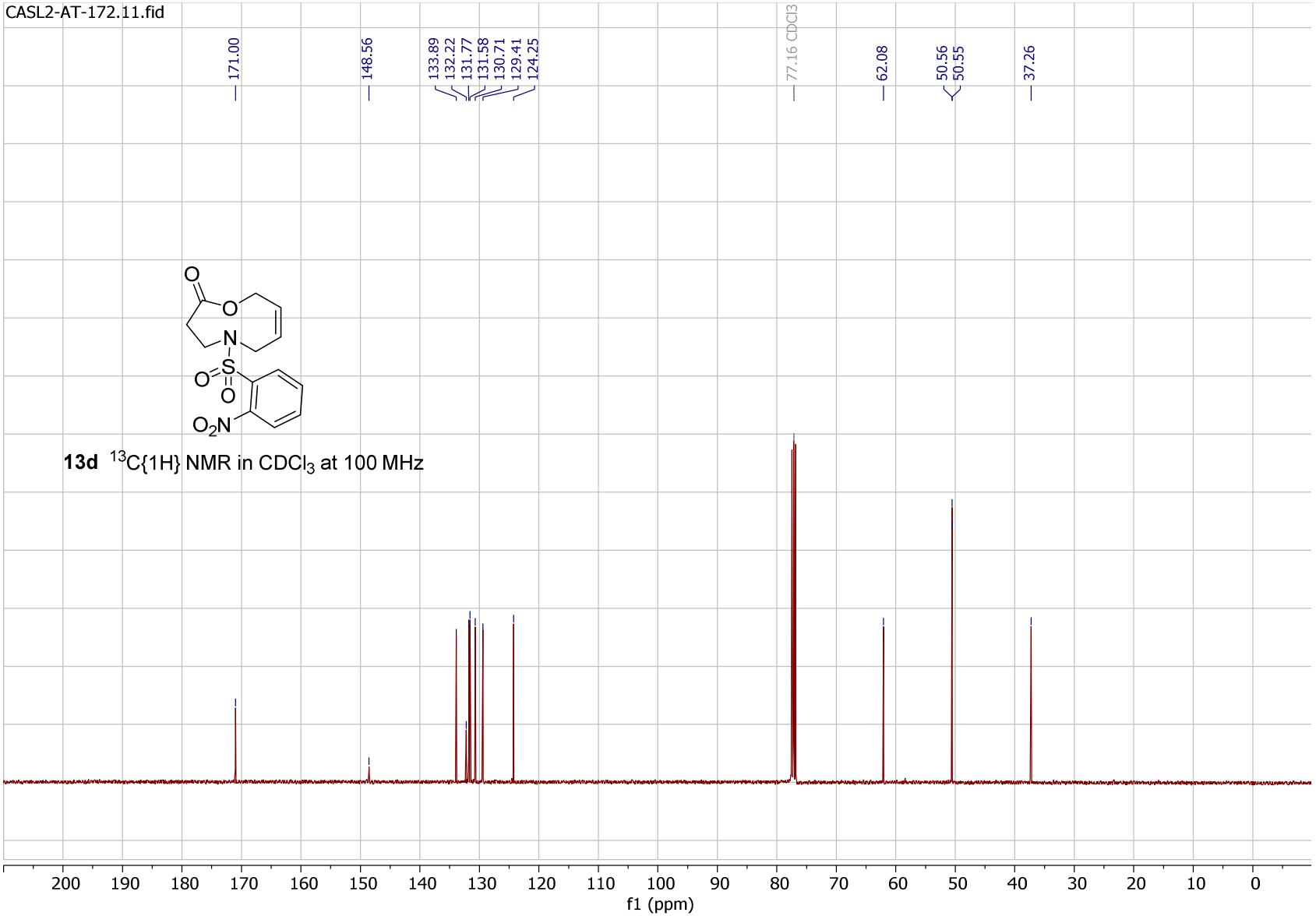

CASL2-RL-92.20.1.1r
170.72
149.05
133.98
131.53
131.52
131.18
127.87
123.83
77.16 CDCl3
60.59
50.07
45.71
36.10
28.32
O
O
N
O
S
O
O
NO2
13b 13C{1H} NMR in CDCl3 at 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

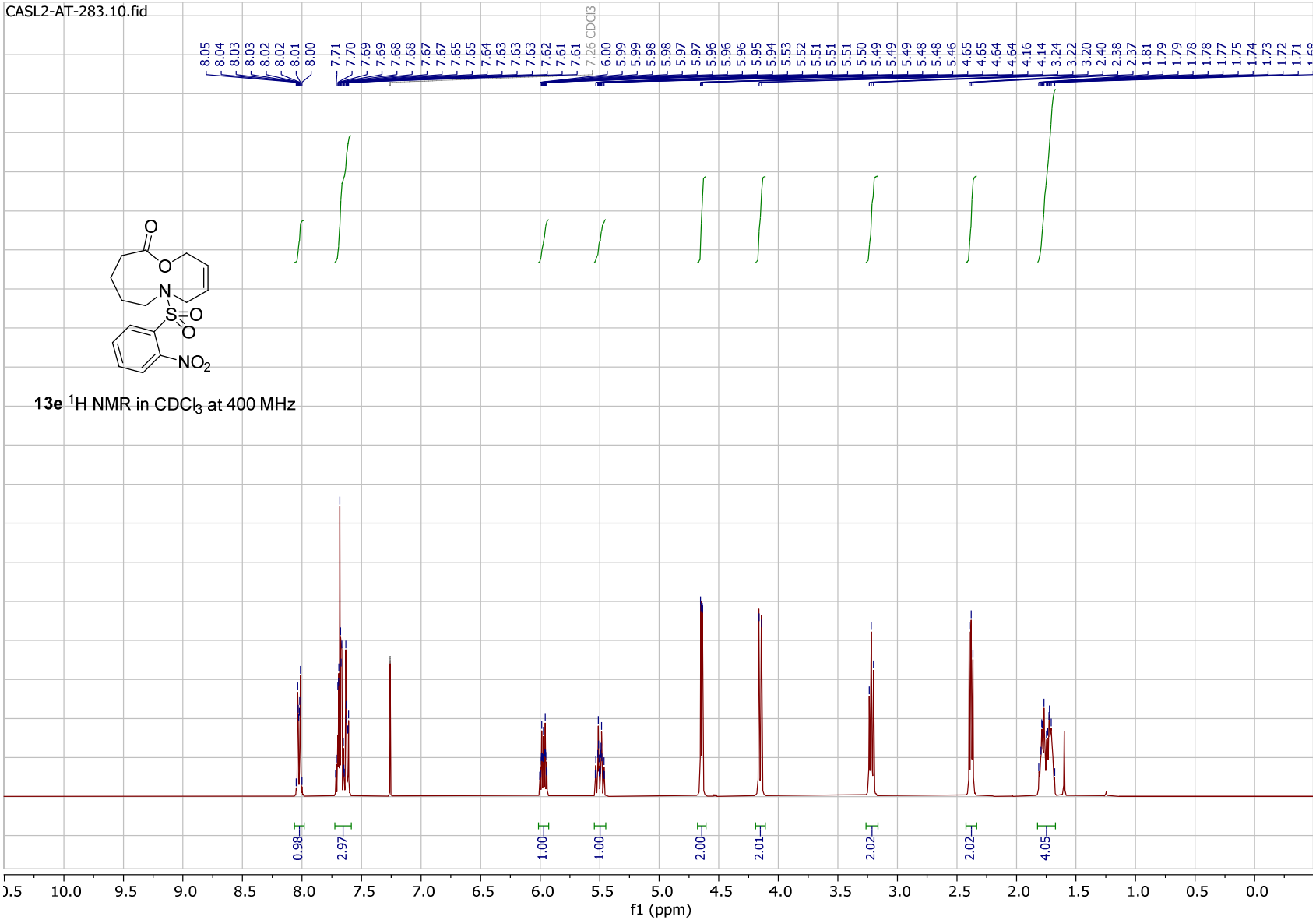

CASL2-RL-68-2.10.1.1r
7.26 CDCl3
O
O
O
O
N
S
NO2
13c 1H NMR in CDCl3 at 400 MHz
1.00
3.01
1.04
1.01
2.03
2.05
2.04
2.04
2.08
f1 (ppm)

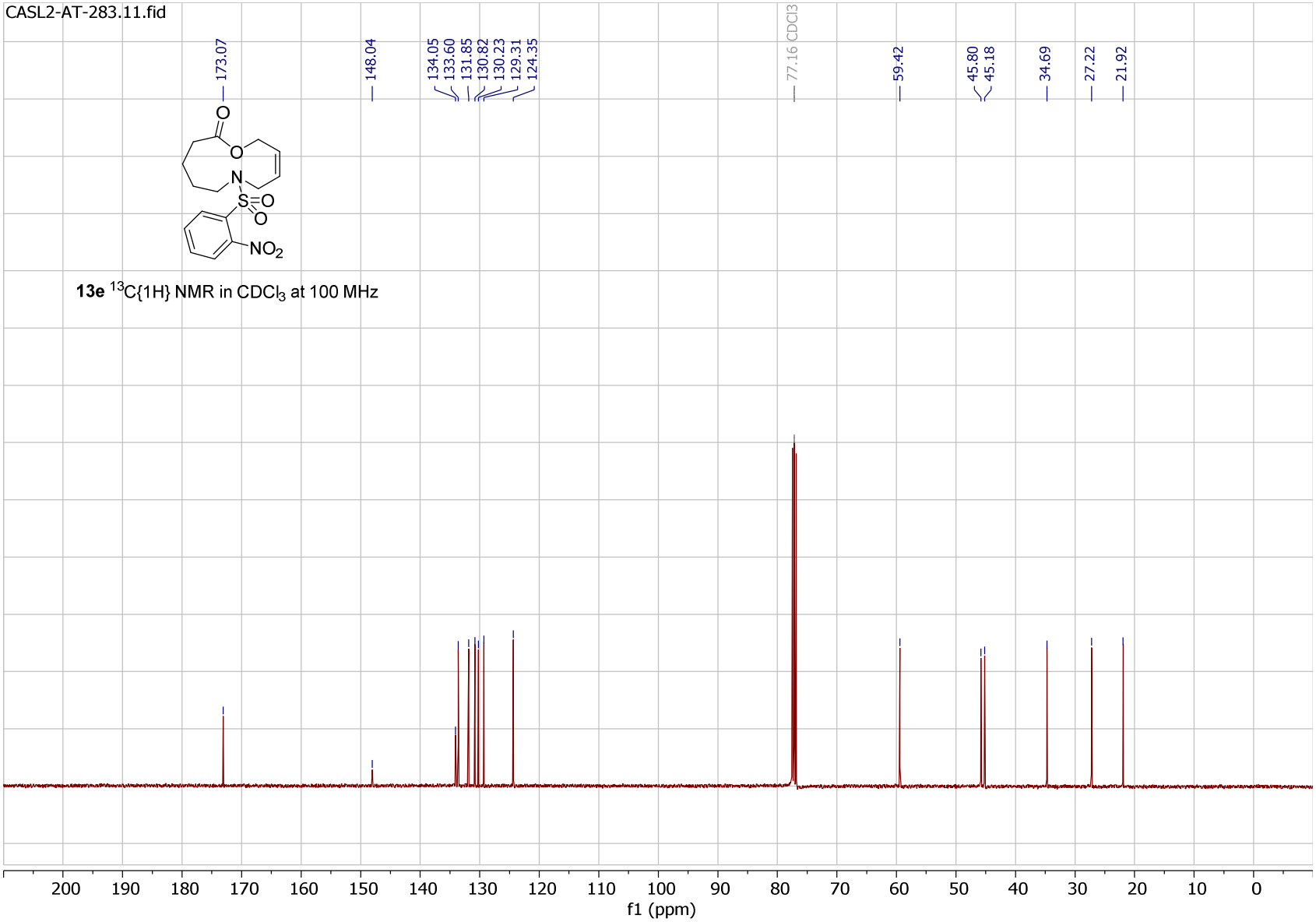


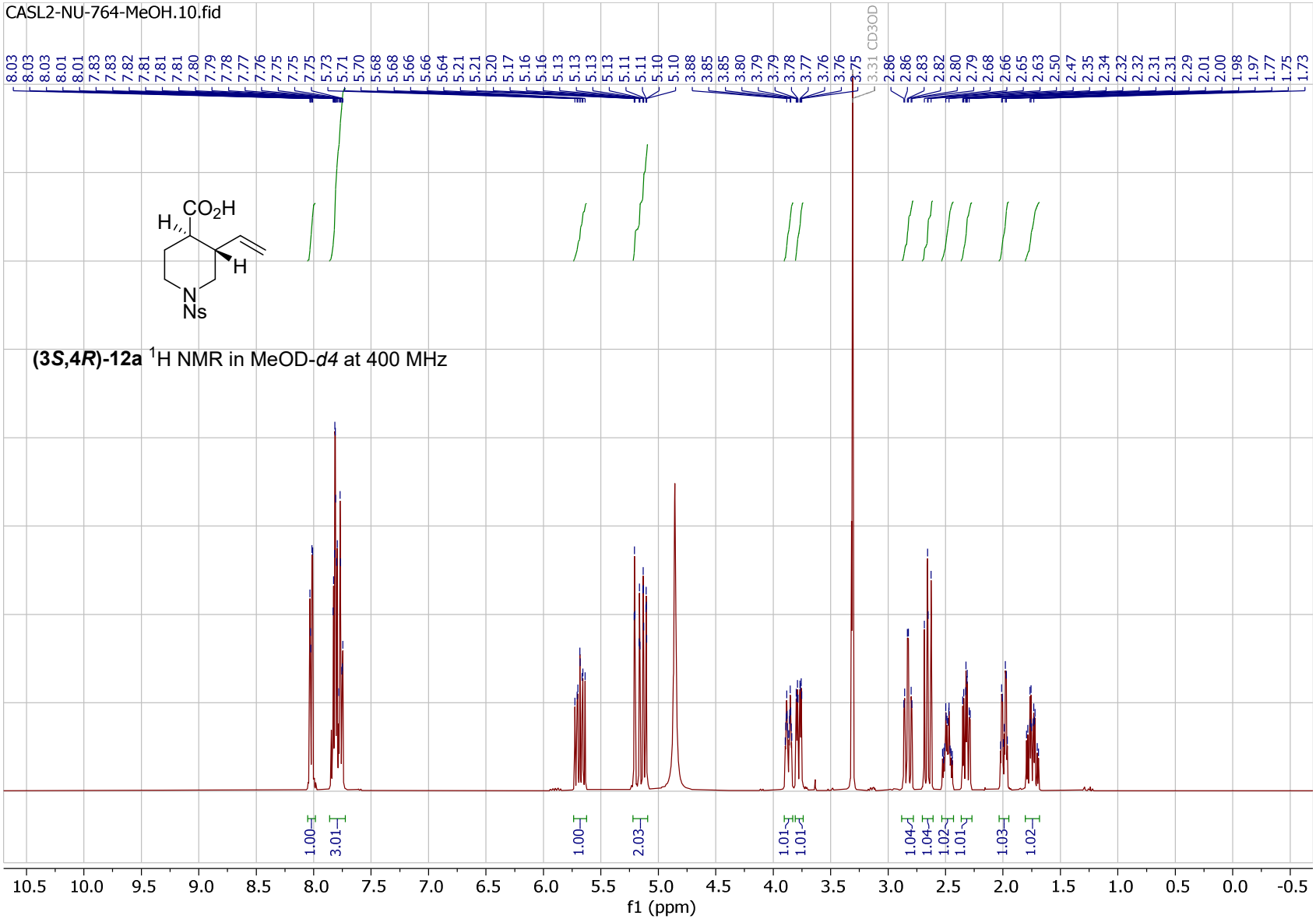
13c $^{13}C\{1H\}$ NMR in $CDCl_3$ at 100 MHz

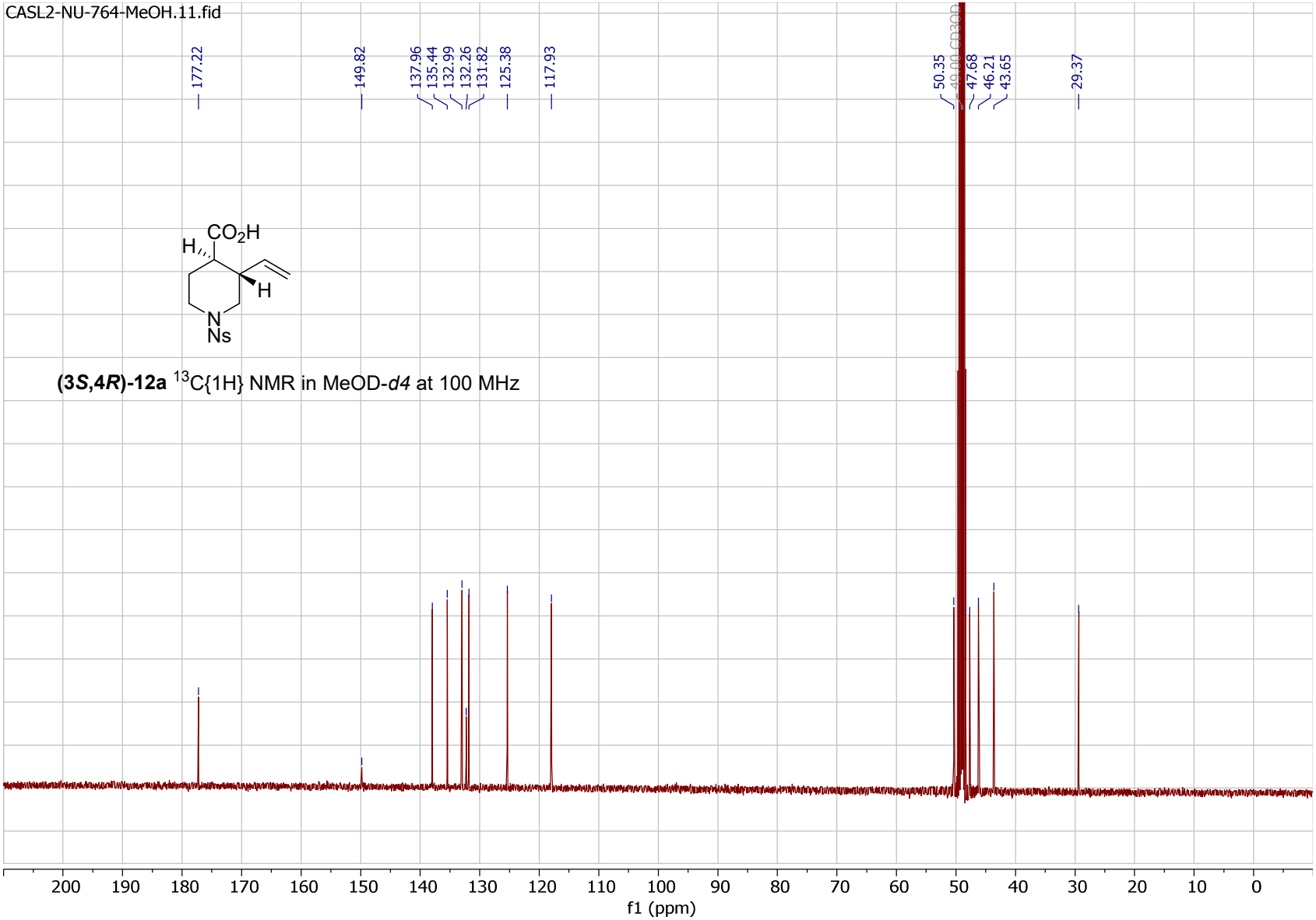

CASL2-AT-172.10.fid
7.26 CDCl3
13d ^{1}H NMR in $CDCl_3$ at 400 MHz
f1 (ppm)

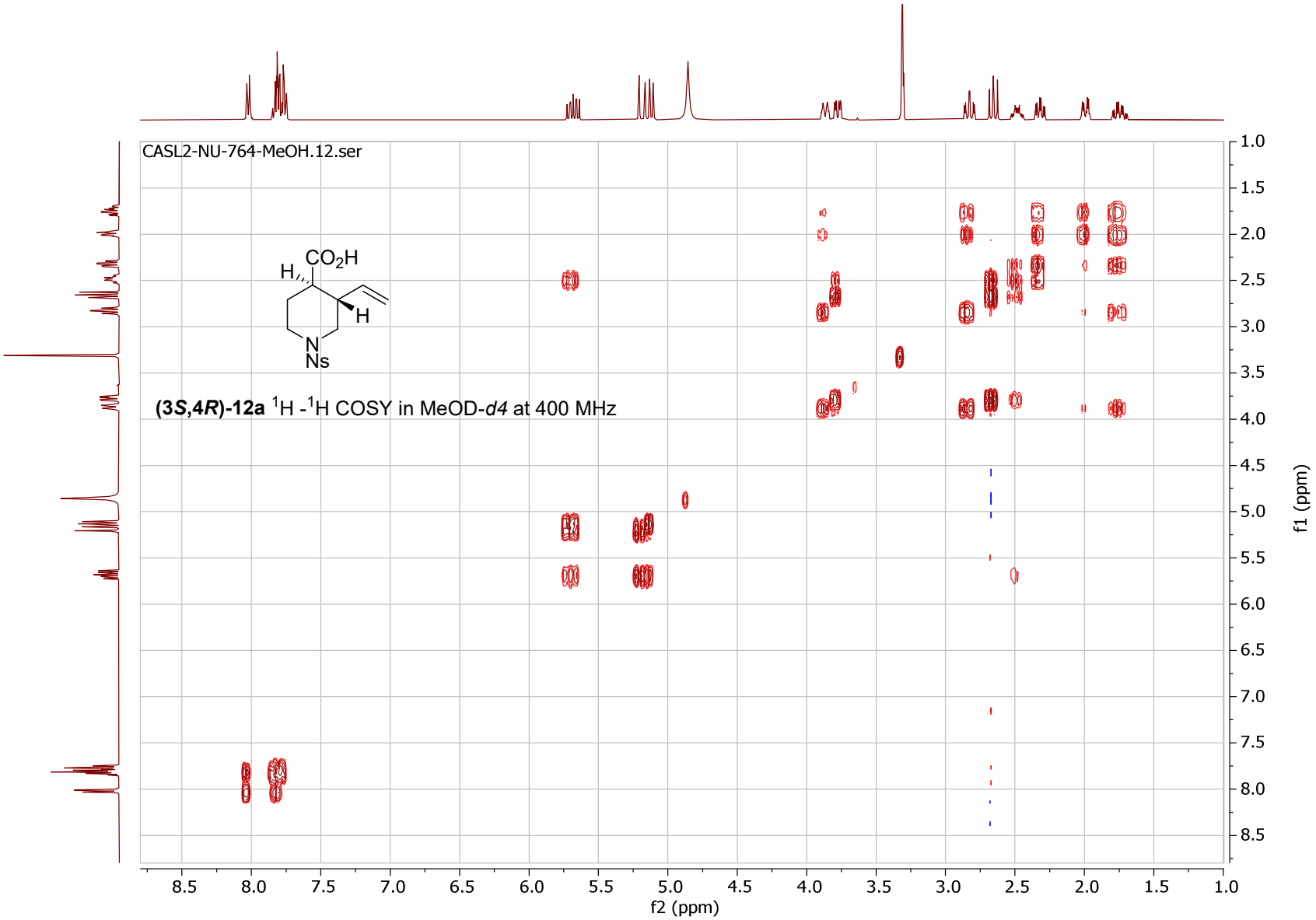

CASL2-AT-172.11.fid
171.00
148.56
133.89
132.22
131.77
131.58
130.71
129.41
124.25
77.16 CDCl3
62.08
50.56
50.55
37.26
O
O
N
S
O
O
O2N
13d 13C{1H} NMR in CDCl3 at 100 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

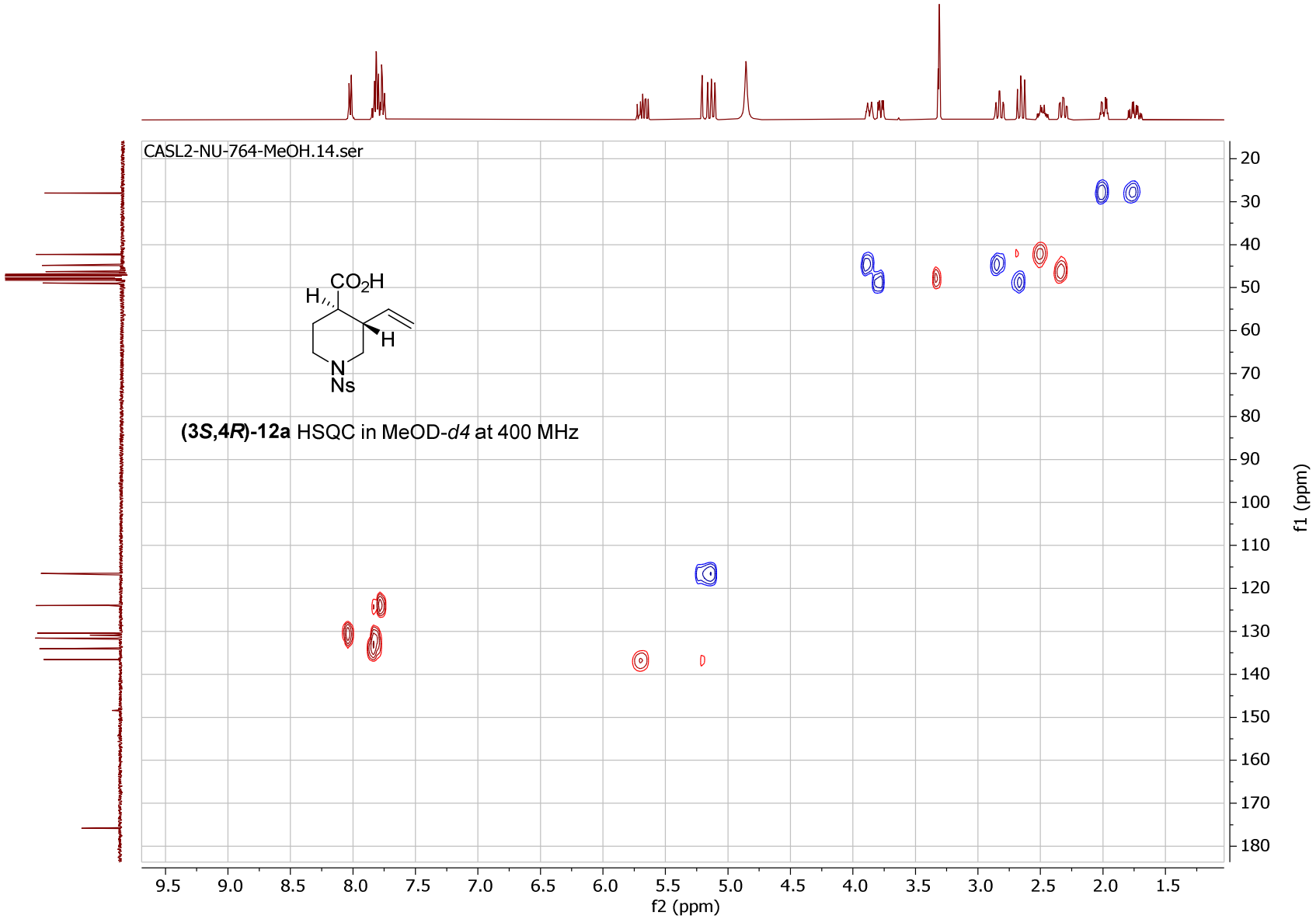

CASL2-AT-283.10.fid
7.26 CDCl3
O
O
N
S
O
O
NO2
13e 1H NMR in CDCl3 at 400 MHz
0.98
2.97
1.00
1.00
2.00
2.01
2.02
2.02
4.05
f1 (ppm)

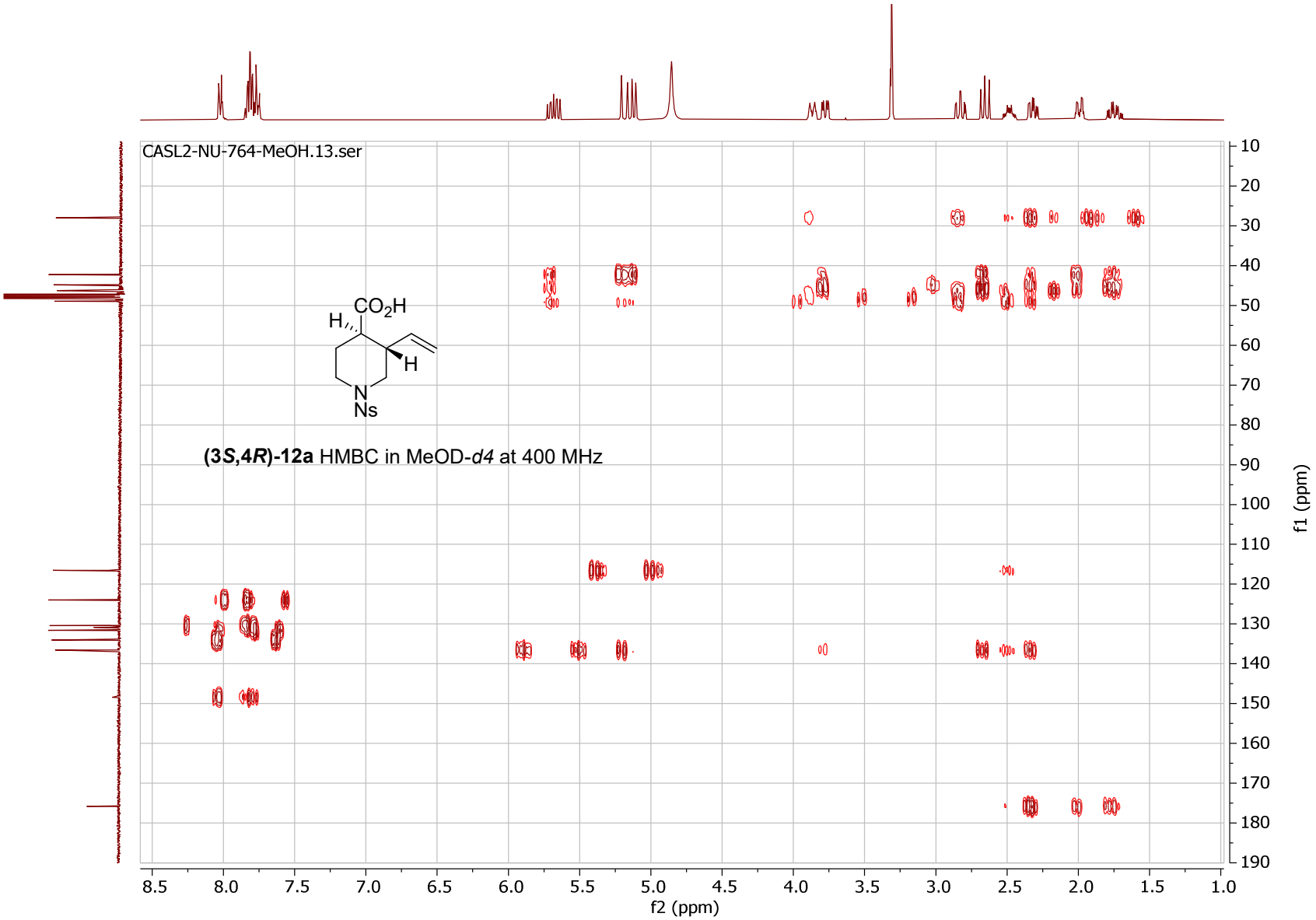

CASL2-AT-283.11.fid
173.07
148.04
134.05
133.60
131.85
130.82
130.23
129.31
124.35
77.16 CDCl3
59.42
45.80
45.18
34.69
27.22
21.92
O
O
N
S
O
O
NO2
13e 13C{1H} NMR in CDCl3 at 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

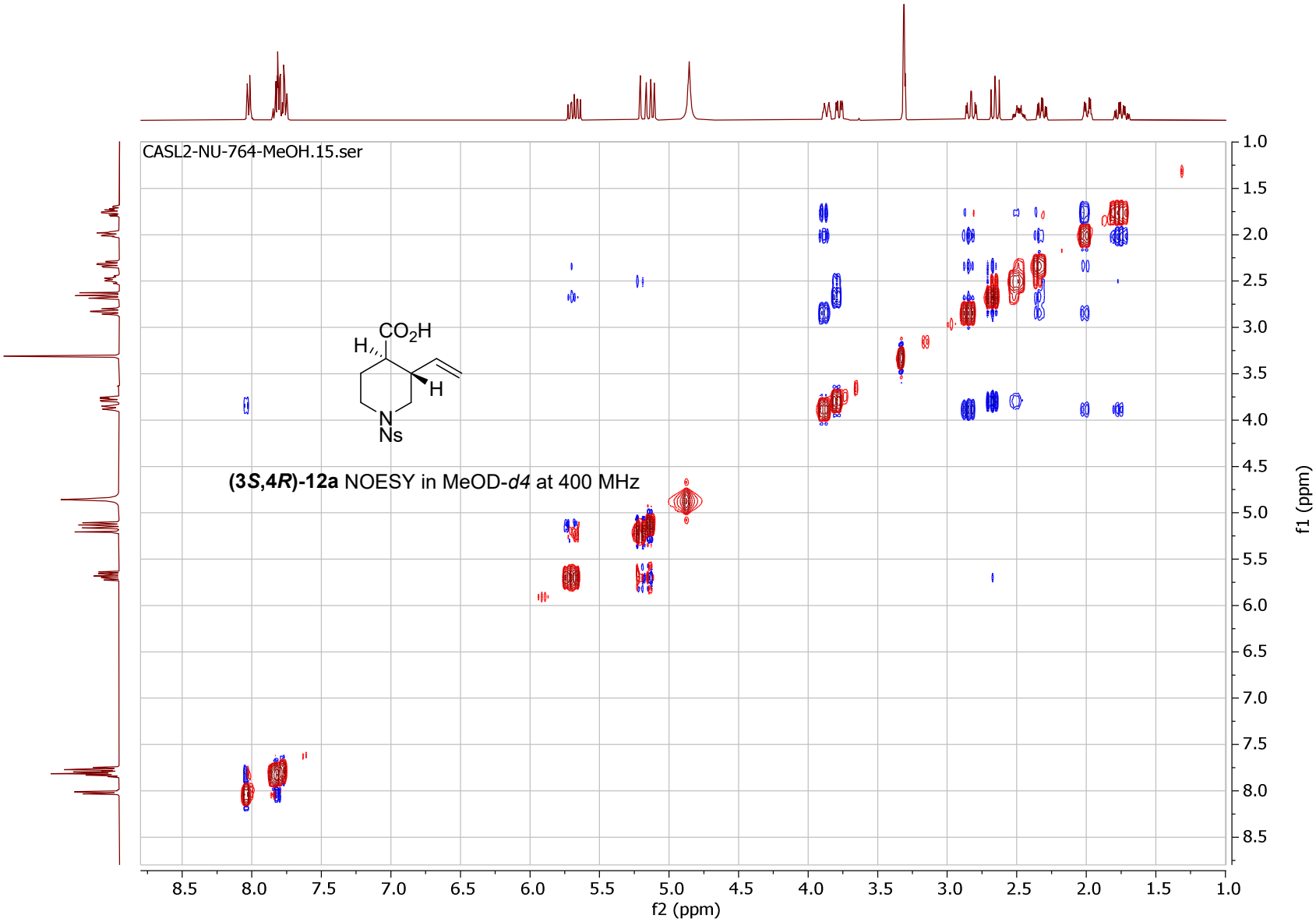

CASL2-NU-764-MeOH.10.fid
CD3OD
CO2H
H
H
N
Ns
(3S,4R)-12a 1H NMR in MeOD-d4 at 400 MHz
f1 (ppm)

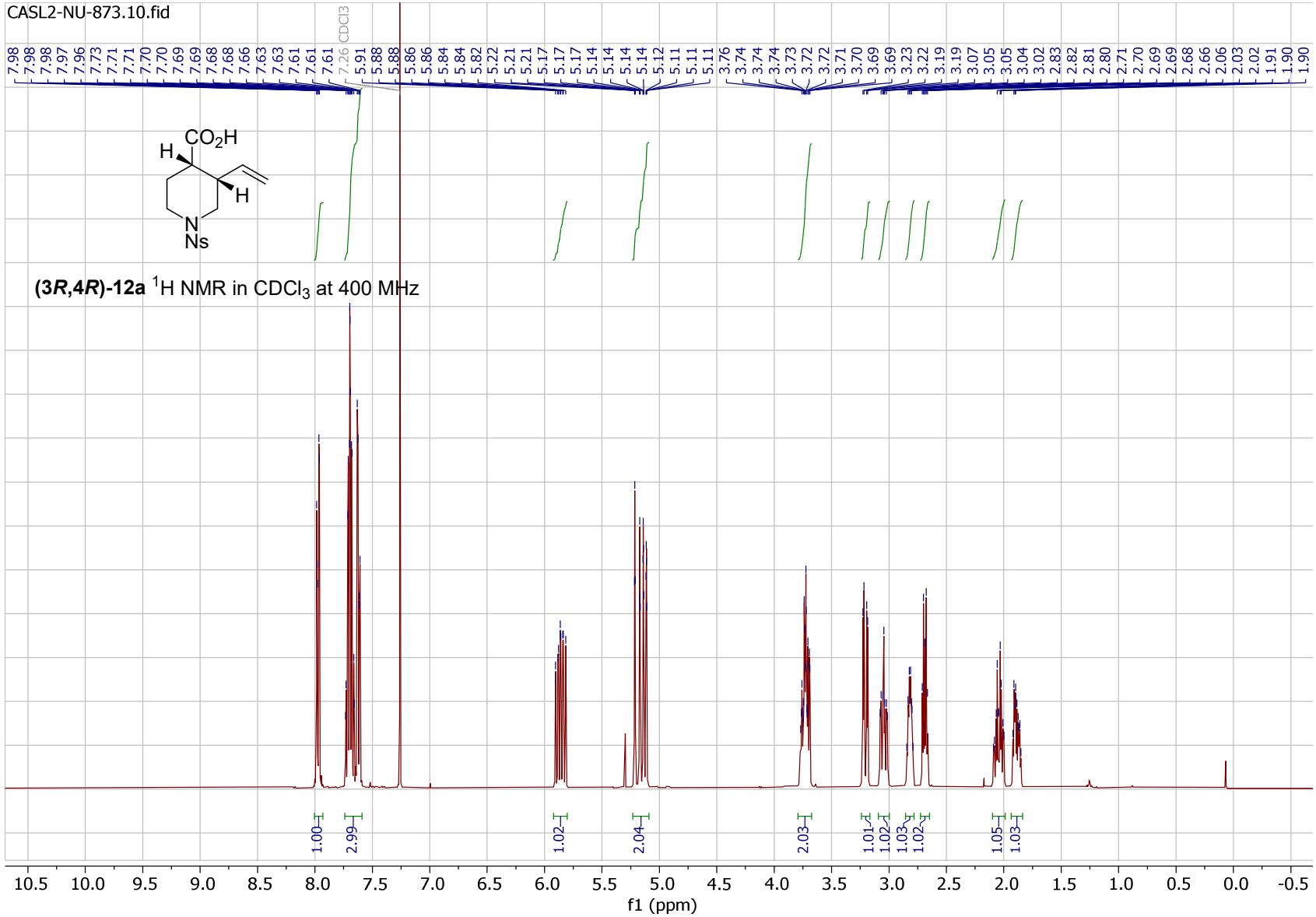

CASL2-NU-764-MeOH.11.fid
177.22
149.82
137.96
135.44
132.99
132.26
131.82
125.38
117.93
50.35
49.00 CD3OD
47.68
46.21
43.65
29.37
CO2H
H
H
N
Ns
(3S,4R)-12a 13C{1H} NMR in MeOD-d4 at 100 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

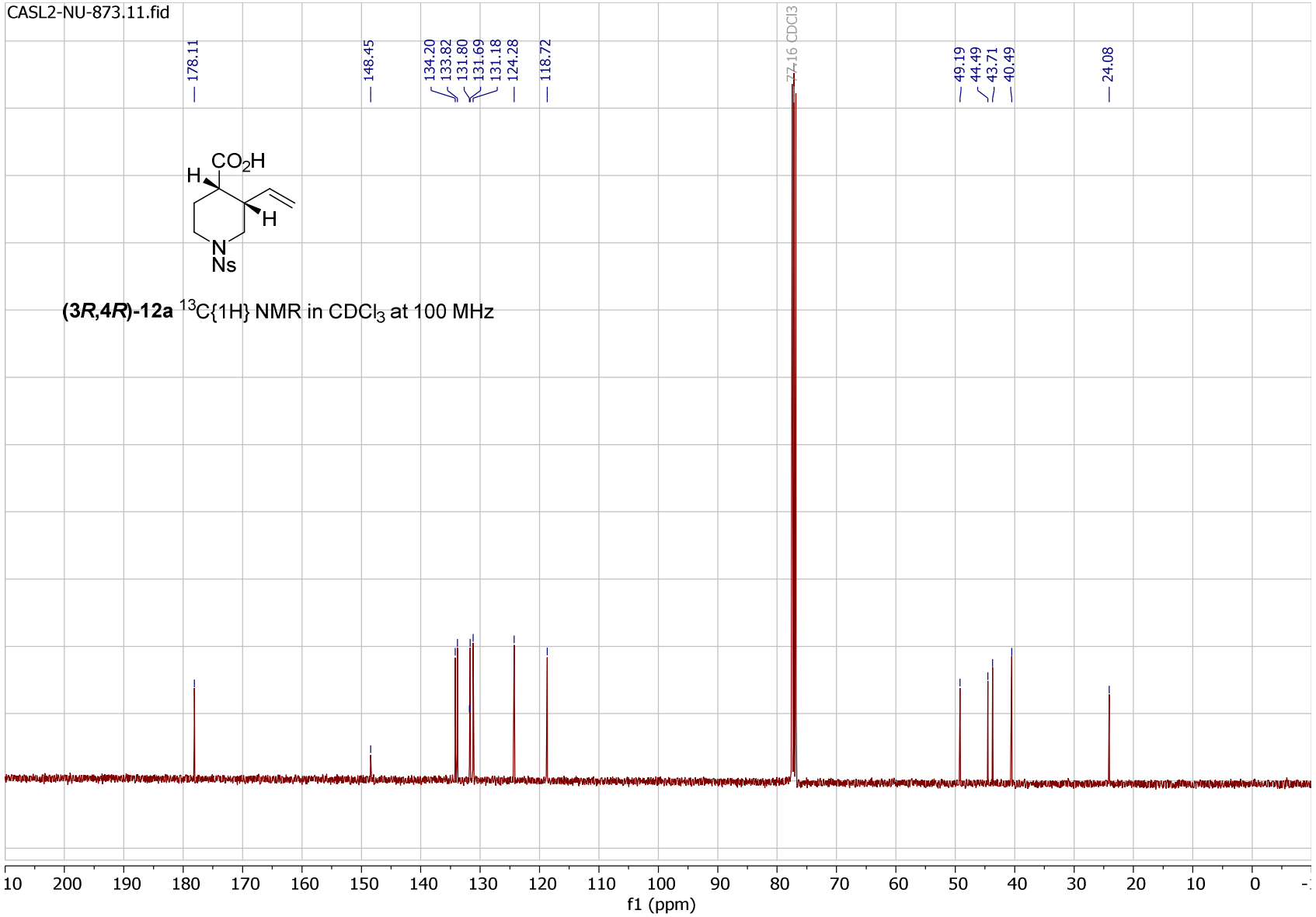

CASL2-NU-764-MeOH.12.ser
CO2H
H
H
N
Ns
(3S,4R)-12a 1H -1H COSY in MeOD-d4 at 400 MHz
f2 (ppm)
f1 (ppm)

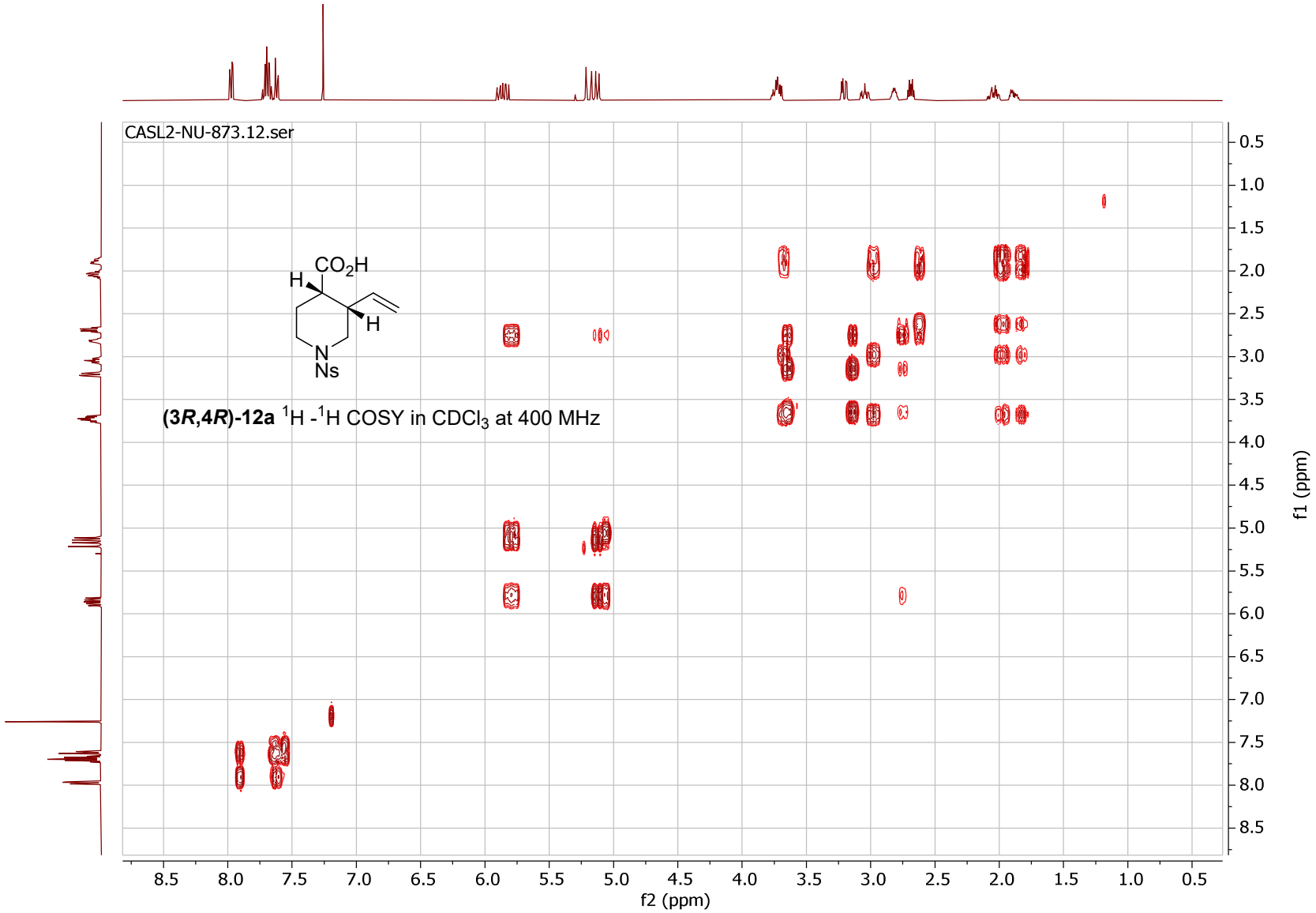

CASL2-NU-764-MeOH.14.ser
CO2H
H
H
N
Ns
(3S,4R)-12a HSQC in MeOD-d4 at 400 MHz
f2 (ppm)
f1 (ppm)

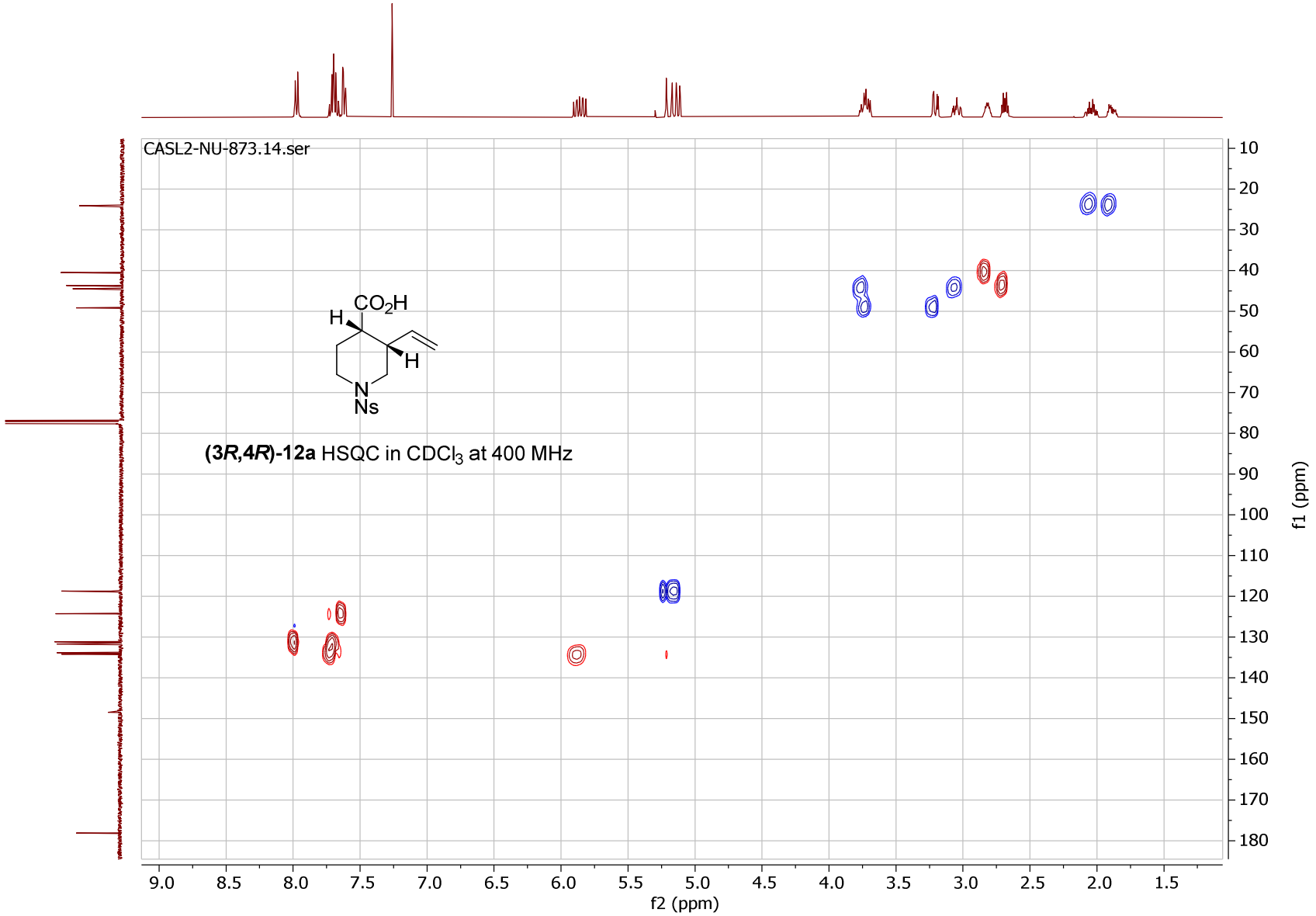

CASL2-NU-764-MeOH.13.ser
CO2H
H
H
N
Ns
(3S,4R)-12a HMBC in MeOD-d4 at 400 MHz
f2 (ppm)
f1 (ppm)

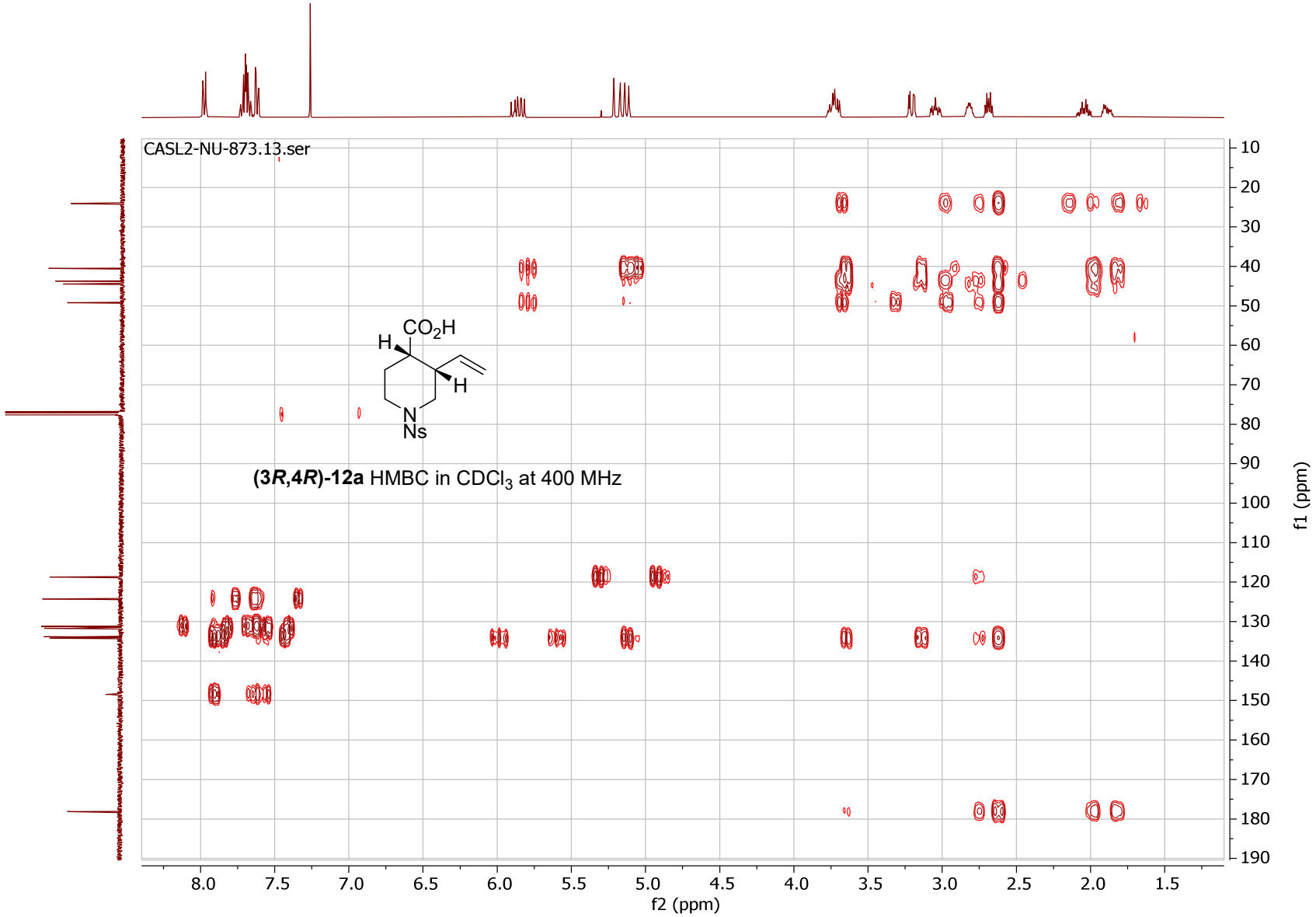

CASL2-NU-764-MeOH.15.ser
CO2H
H
H
N
Ns
(3S,4R)-12a NOESY in MeOD-d4 at 400 MHz
f2 (ppm)
f1 (ppm)

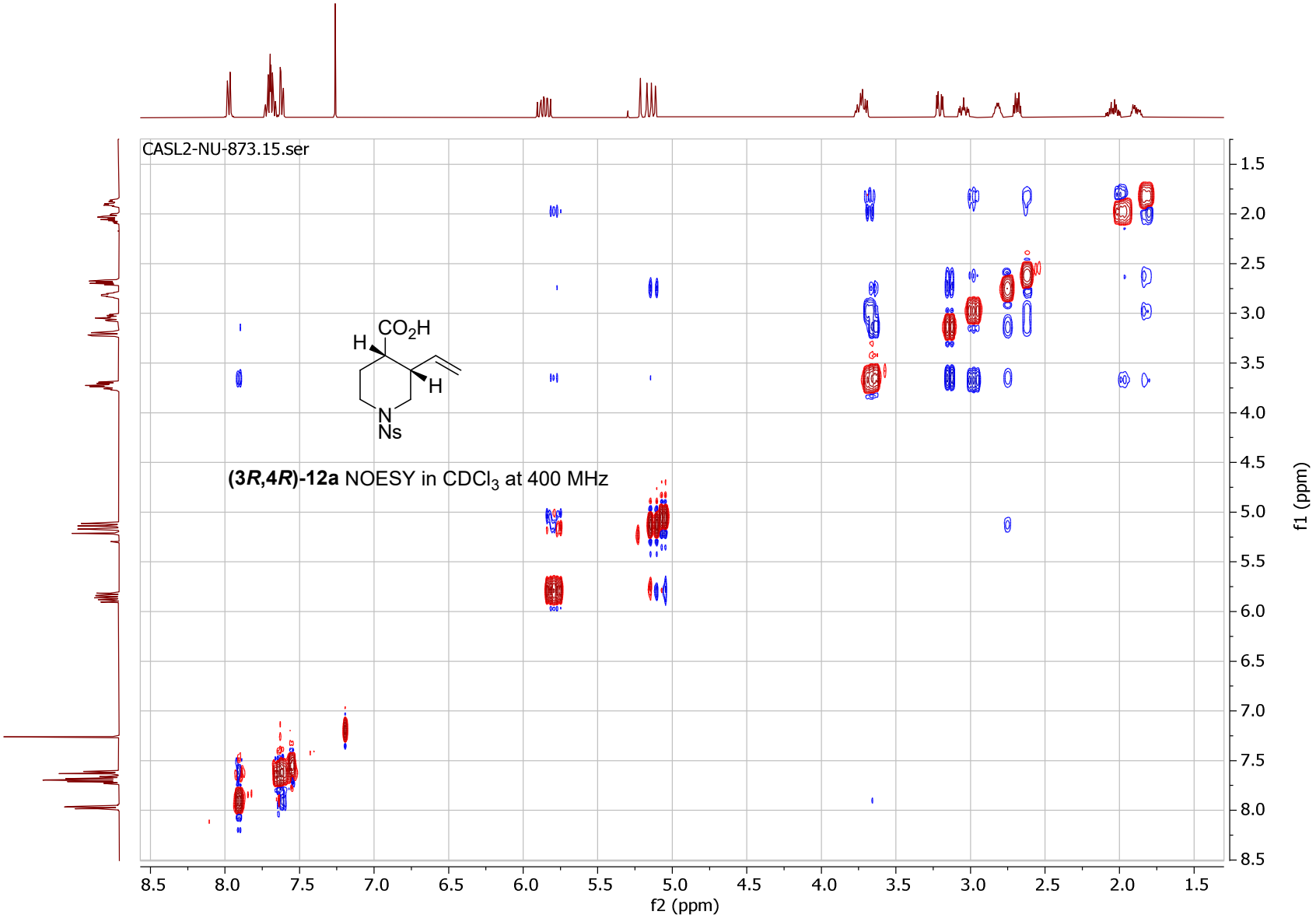

CASL2-NU-873.10.fid
CO2H
H
H
N
Ns
(3R,4R)-12a 1H NMR in CDCl3 at 400 MHz
f1 (ppm)

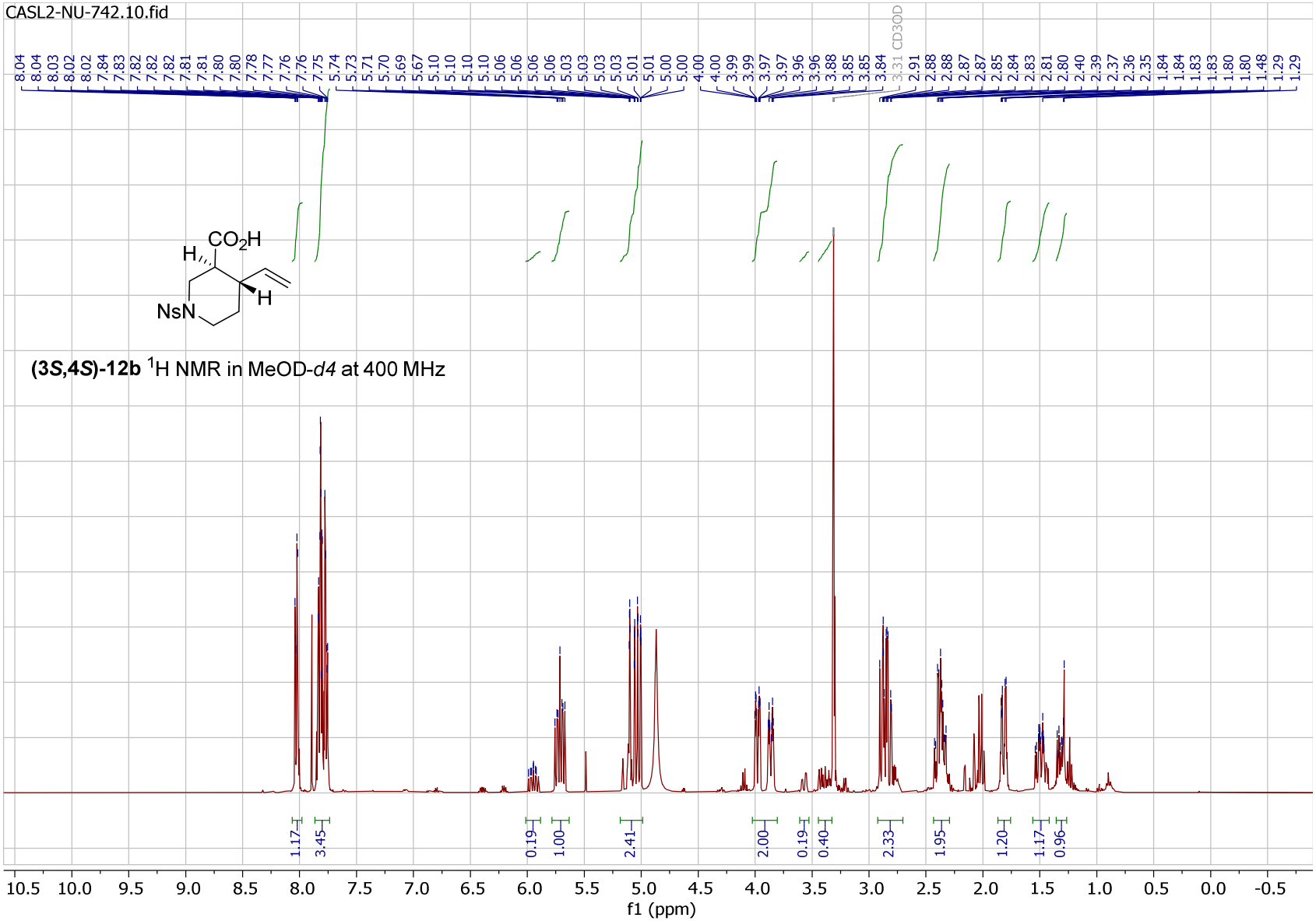

CASL2-NU-873.11.fid
178.11
148.45
134.20
133.82
131.80
131.69
131.18
124.28
118.72
77.16 CDCl3
49.19
44.49
43.71
40.49
24.08
CO2H
H
H
N
Ns
(3R,4R)-12a 13C{1H} NMR in CDCl3 at 100 MHz
f1 (ppm)

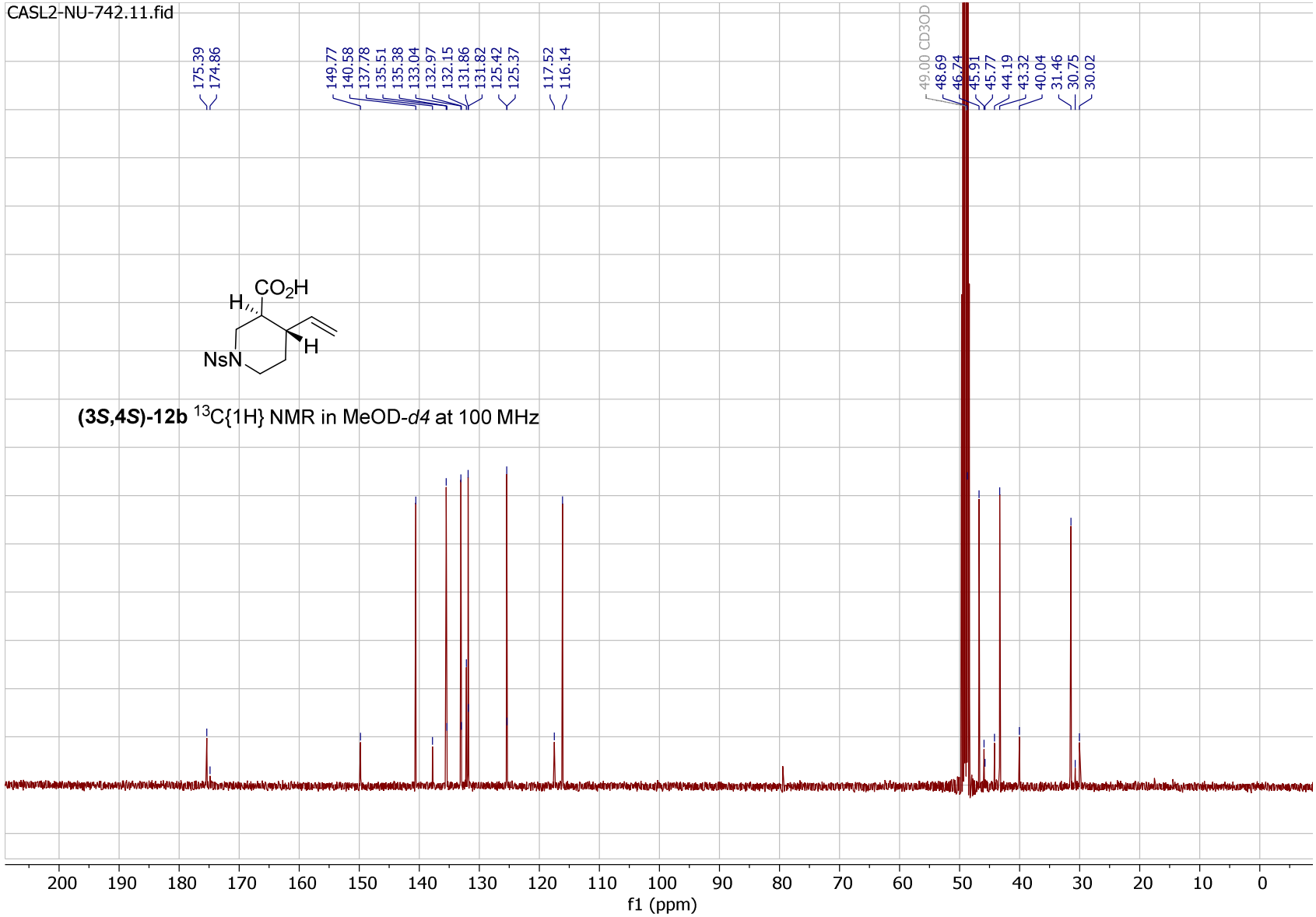

CASL2-NU-873.12.ser
CO2H
H
H
N
Ns
(3R,4R)-12a 1H -1H COSY in CDCl3 at 400 MHz
f2 (ppm)
f1 (ppm)

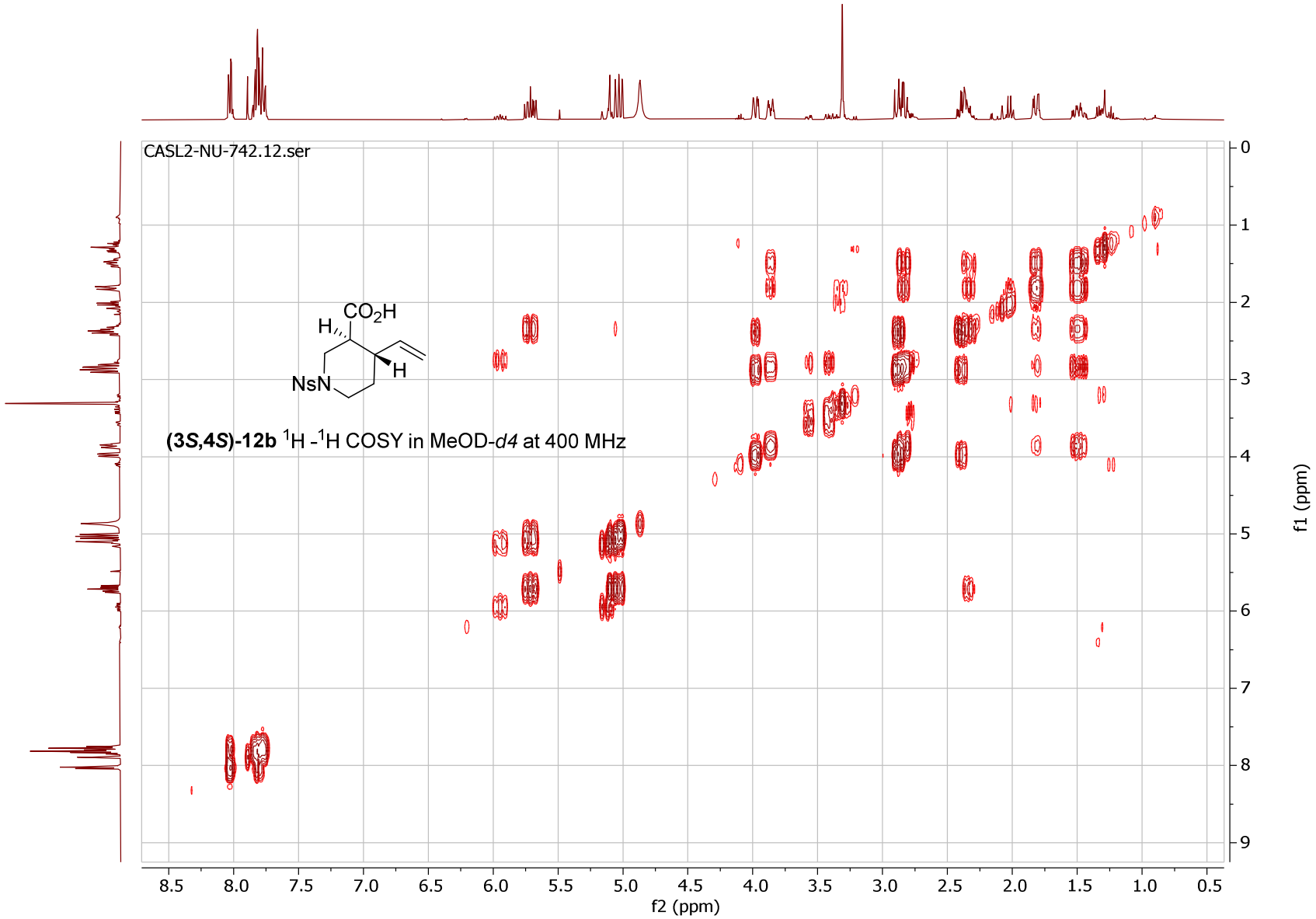

CASL2-NU-873.14.ser
CO2H
H
H
N
Ns
(3R,4R)-12a HSQC in CDCl3 at 400 MHz
f2 (ppm)
f1 (ppm)

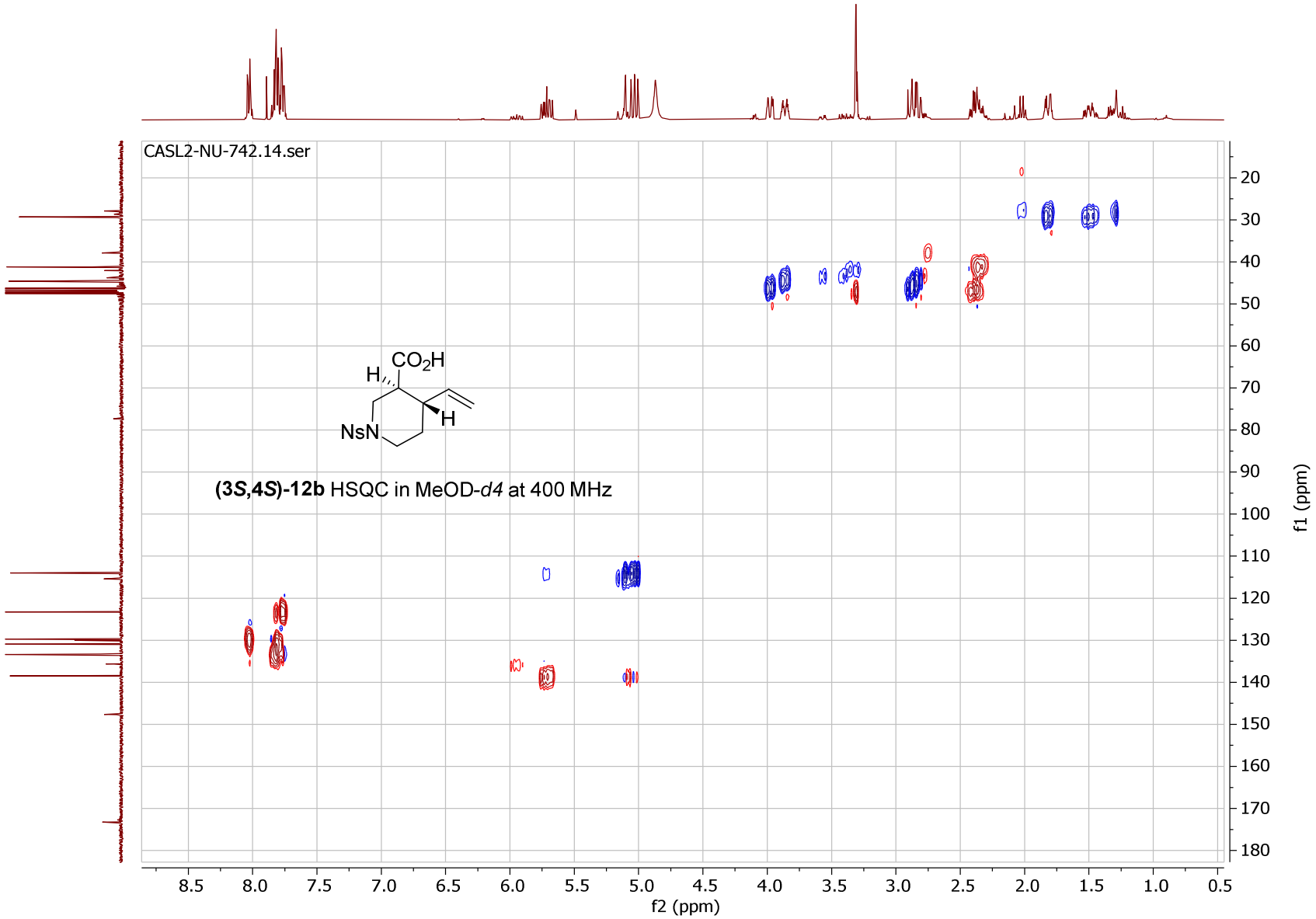

CASL2-NU-873.13.ser
CO2H
H
H
N
Ns
(3R,4R)-12a HMBC in CDCl3 at 400 MHz
f2 (ppm)
f1 (ppm)

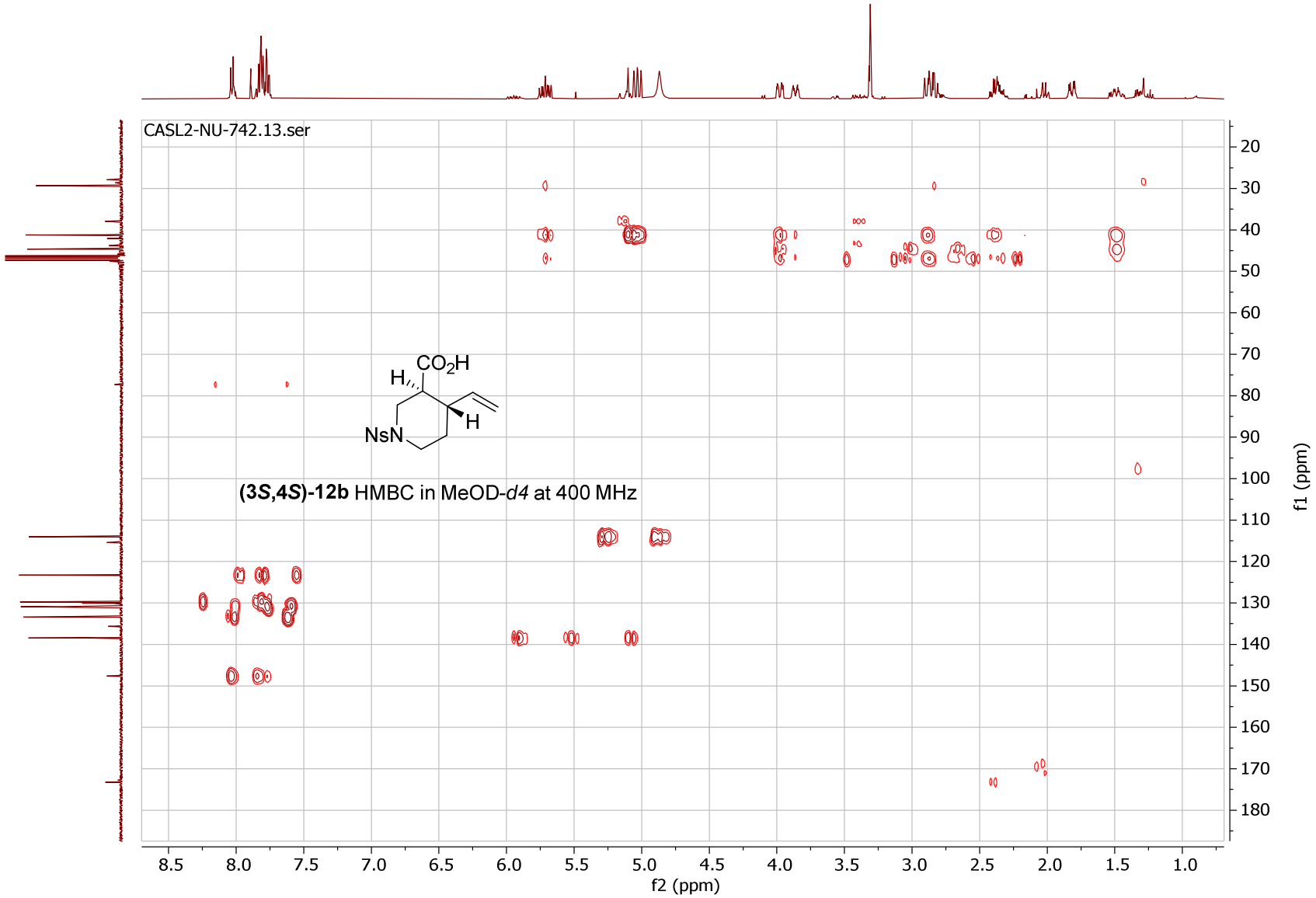

CASL2-NU-873.15.ser
CO2H
H
H
N
Ns
(3R,4R)-12a NOESY in CDCl3 at 400 MHz
f2 (ppm)
f1 (ppm)

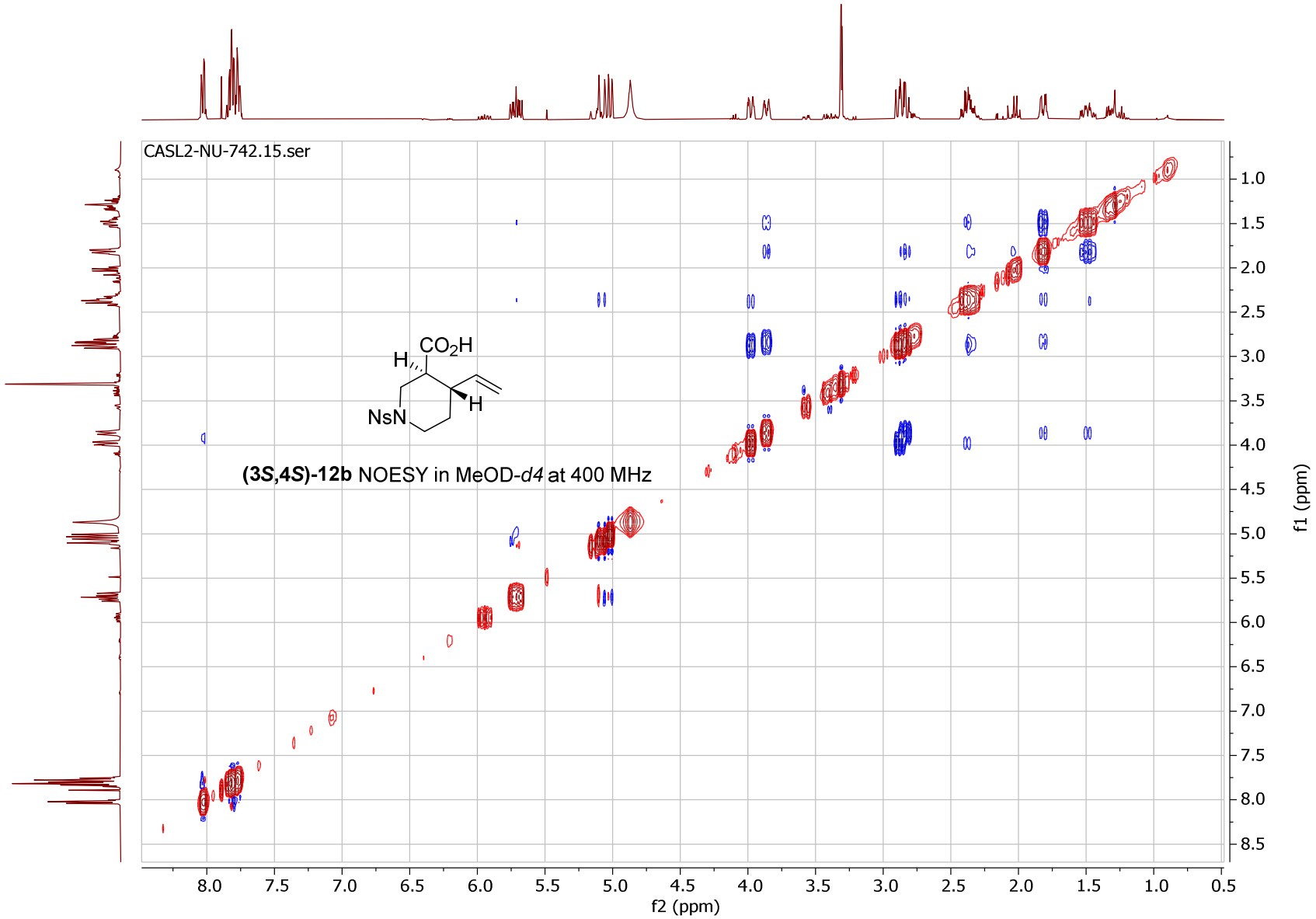

CASL2-NU-742.10.fid
CD3OD
CO2H
H
H
NsN
(3S,4S)-12b 1H NMR in MeOD-d4 at 400 MHz
1.17
3.45
0.19
1.00
2.41
2.00
0.19
0.40
2.33
1.95
1.20
1.17
0.96
f1 (ppm)

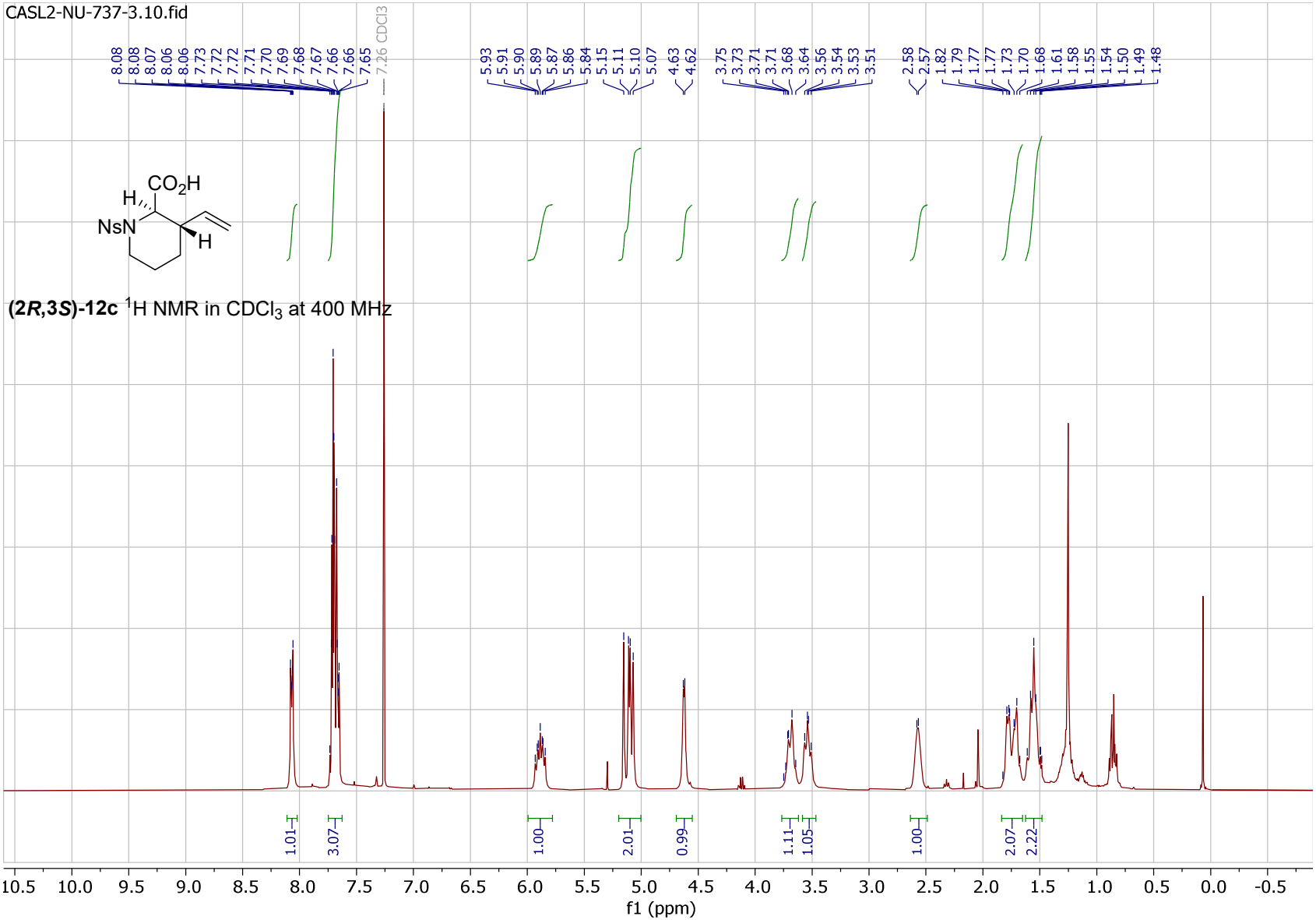

CASL2-NU-742.11.fid
175.39
174.86
149.77
140.58
137.78
135.51
135.38
133.04
132.97
132.15
131.86
131.82
125.42
125.37
117.52
116.14
49.00 CD3OD
48.69
46.74
45.91
45.77
44.19
43.32
40.04
31.46
30.75
30.02
CO2H
H
NsN
H
(3S,4S)-12b 13C{1H} NMR in MeOD-d4 at 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


CASL2-NU-742.12.ser
CO2H
H
H
NsN
(3S,4S)-12b 1H -1H COSY in MeOD-d4 at 400 MHz
f2 (ppm)
f1 (ppm)


CASL2-NU-742.14.ser
CO2H
H
NsN
H
(3S,4S)-12b HSQC in MeOD-d4 at 400 MHz
f2 (ppm)
f1 (ppm)


CASL2-NU-742.13.ser
CO2H
H
H
NsN
(3S,4S)-12b HMBC in MeOD-d4 at 400 MHz
f2 (ppm)
f1 (ppm)


CASL2-NU-742.15.ser
CO2H
H
NsN
H
(3S,4S)-12b NOESY in MeOD-d4 at 400 MHz
f2 (ppm)
f1 (ppm)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7.26 CDCl3
CO2H
H
NsN
H
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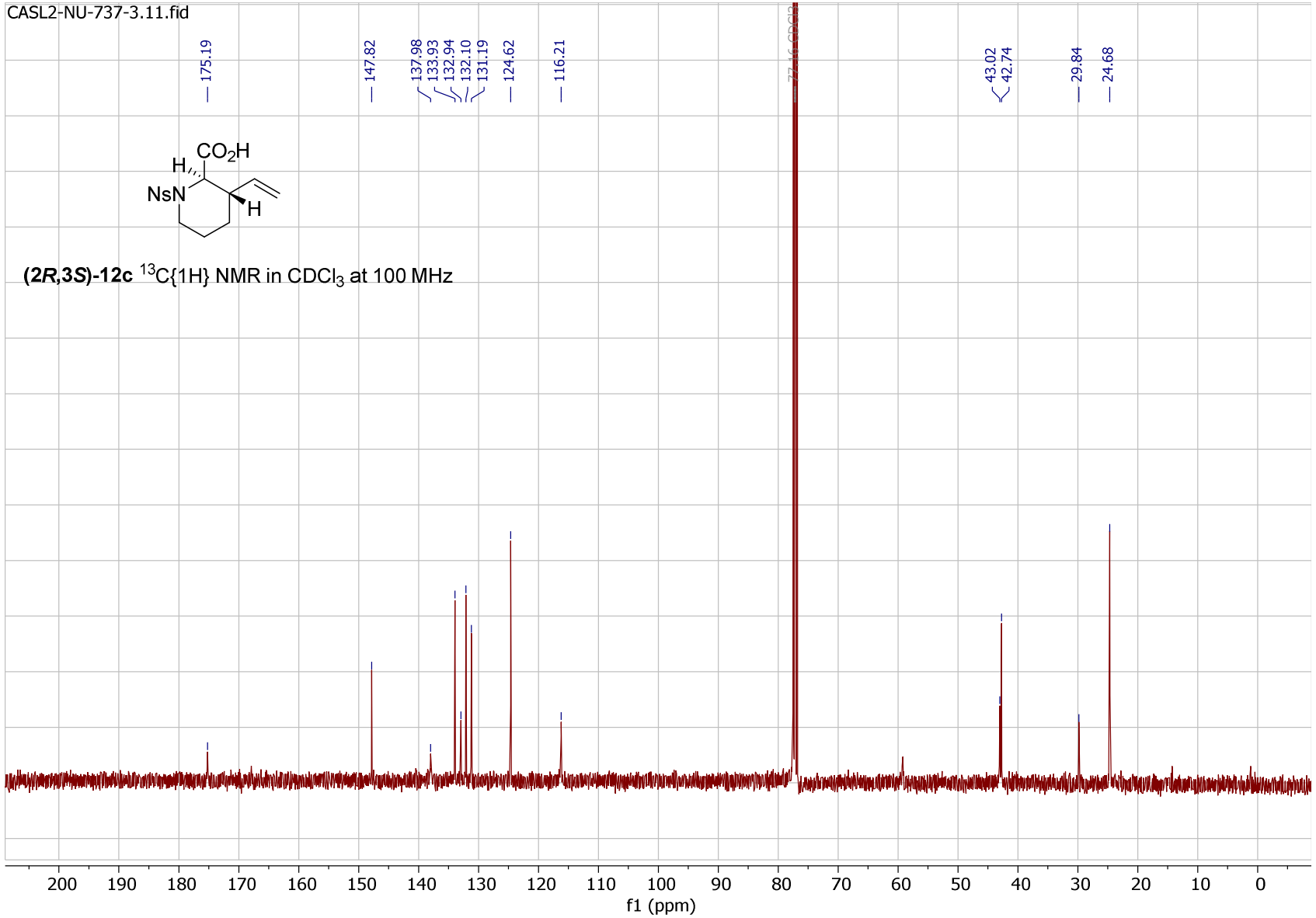
f1 (ppm)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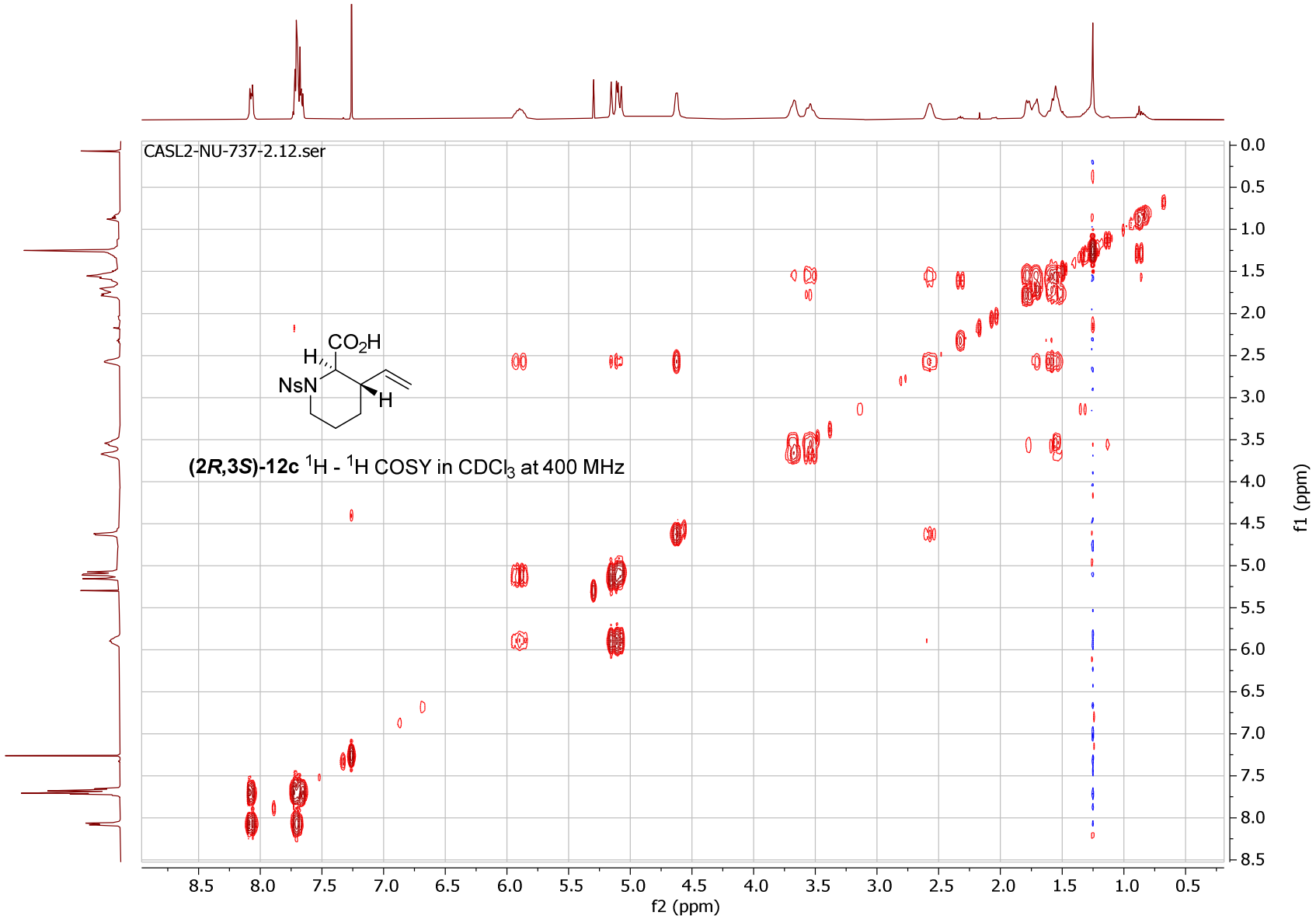
175.19
147.82
137.98
133.93
132.94
132.10
131.19
124.62
116.21
77.16 CDCl3
43.02
42.74
29.84
24.68
CO2H
H
NsN
H
(2R,3S)-12c 13C{1H} NMR in CDCl3 at 100 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CASL2-NU-737-2.12.ser
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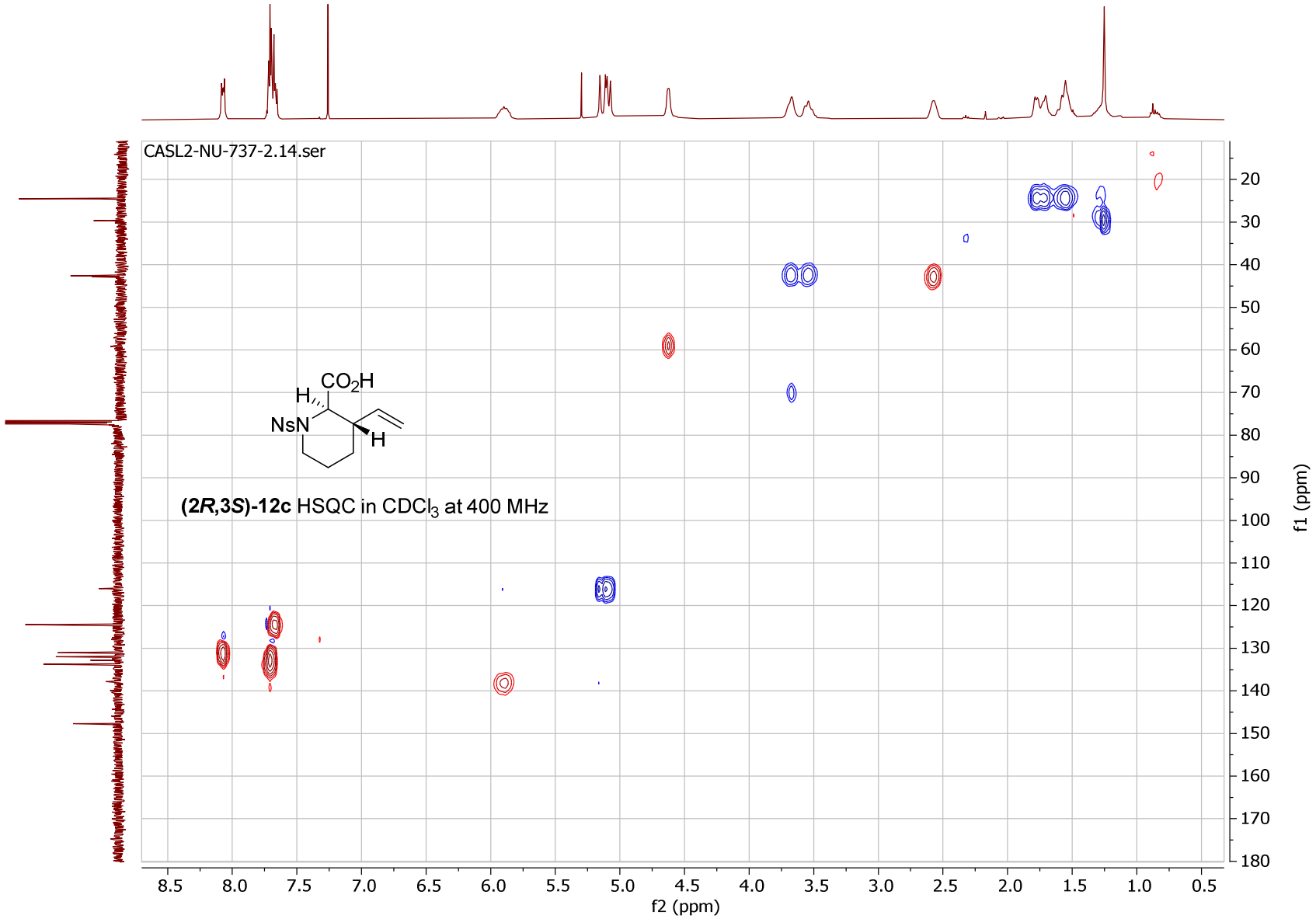
f2 (ppm)
f1 (ppm)


CASL2-NU-737-2.14.ser
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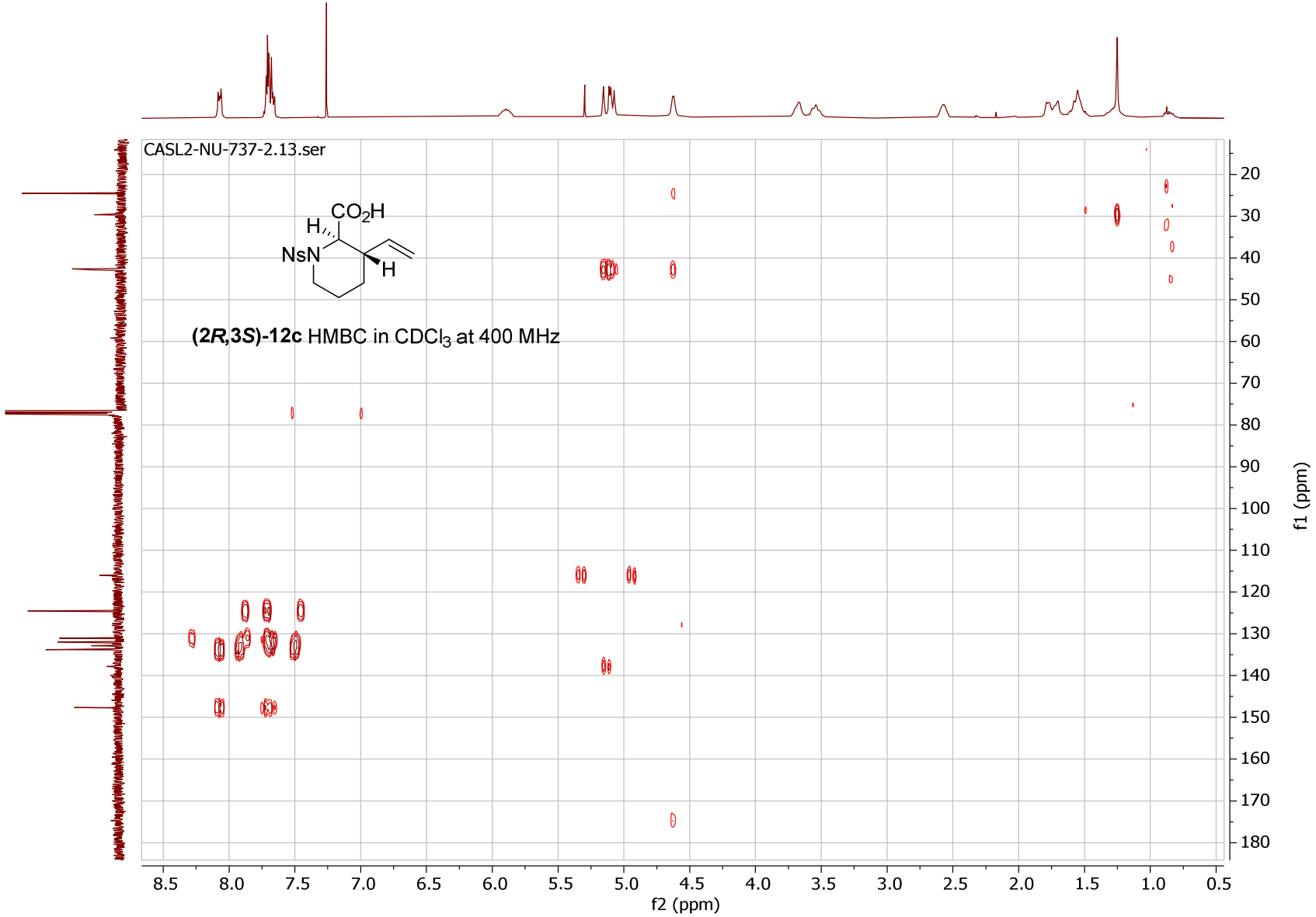
f2 (ppm)
f1 (ppm)


CASL2-NU-737-2.13.ser
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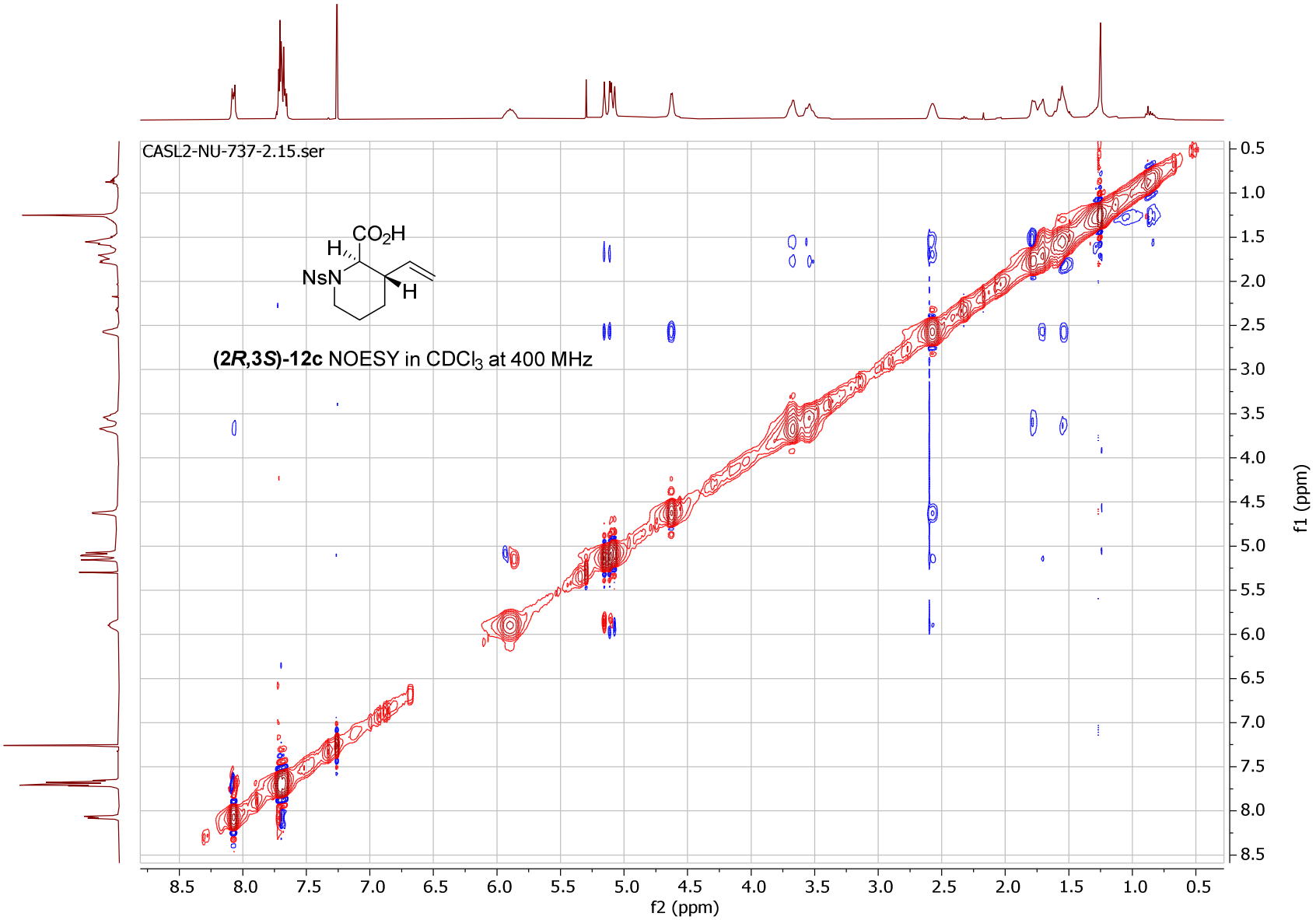
H
NsN
H
(2R,3S)-12c HMBC in CDCl3 at 400 MHz
f2 (ppm)
f1 (ppm)


CASL2-NU-737-2.15.ser
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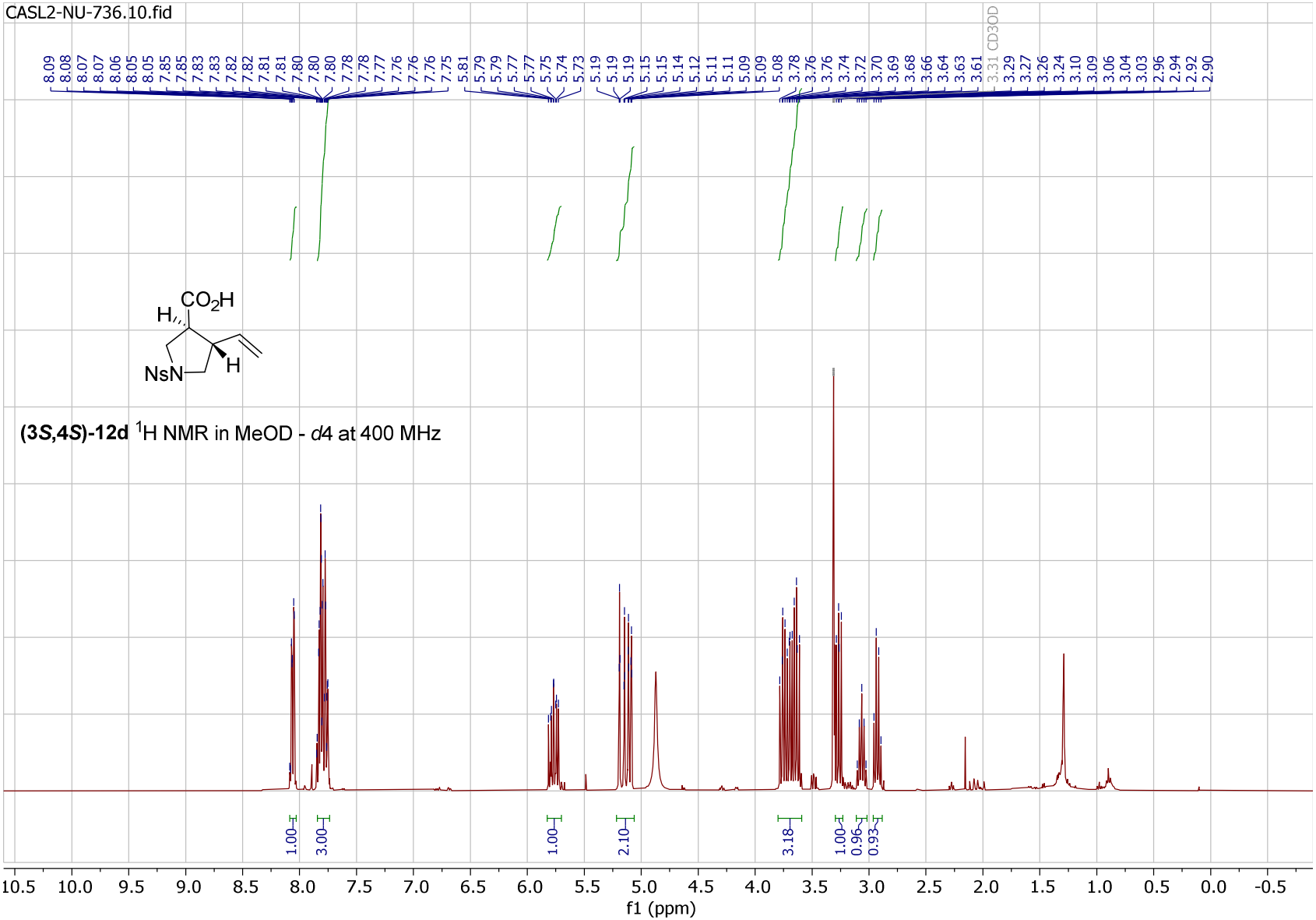
H
NsN
H
(2R,3S)-12c NOESY in CDCl3 at 400 MHz
f2 (ppm)
f1 (ppm)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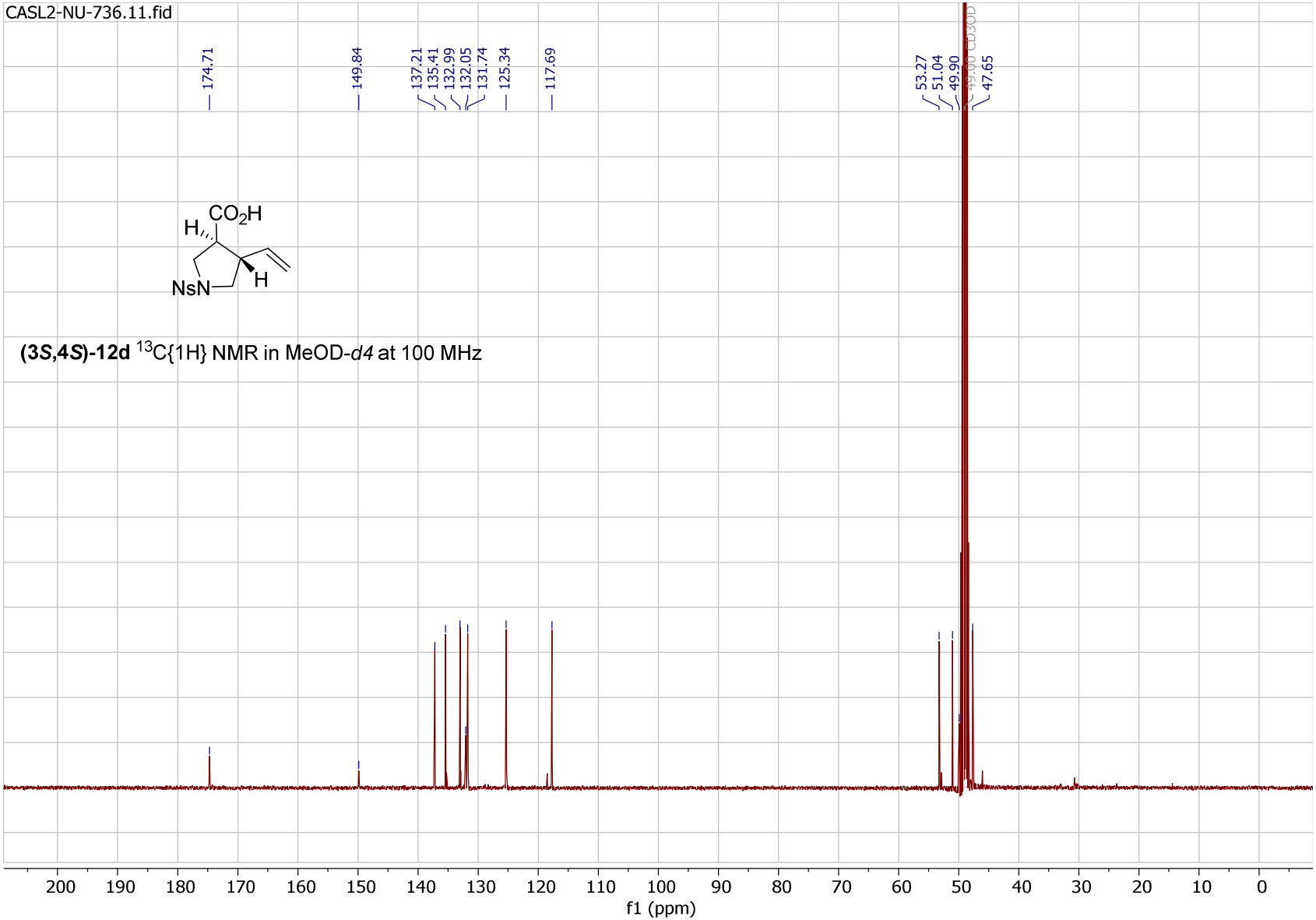
CO2H
H
NsN
H
(3S,4S)-12d 1H NMR in MeOD - d4 at 400 MHz
1.00 3.00 1.00 2.10 3.18 1.00 0.96 0.93
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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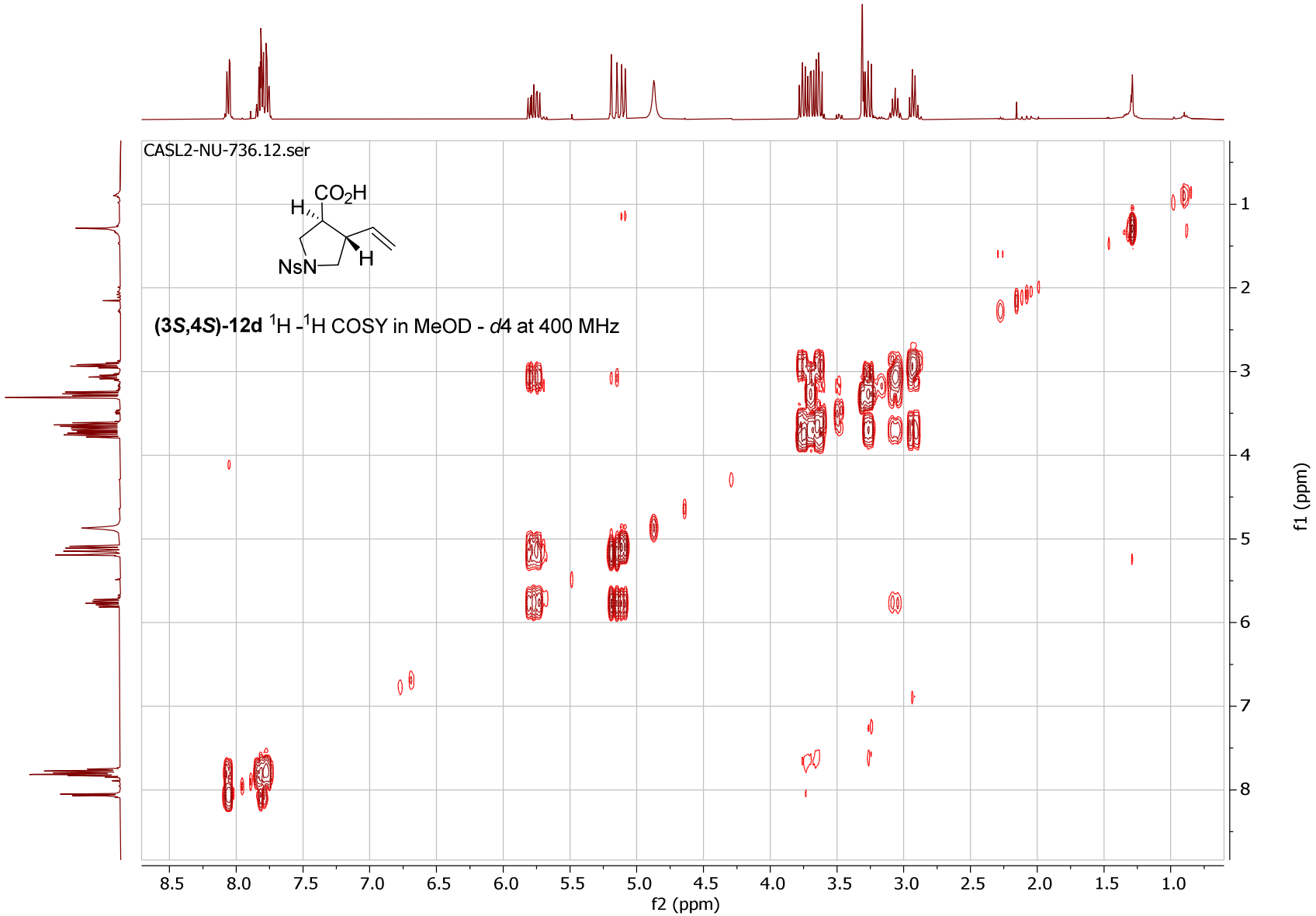
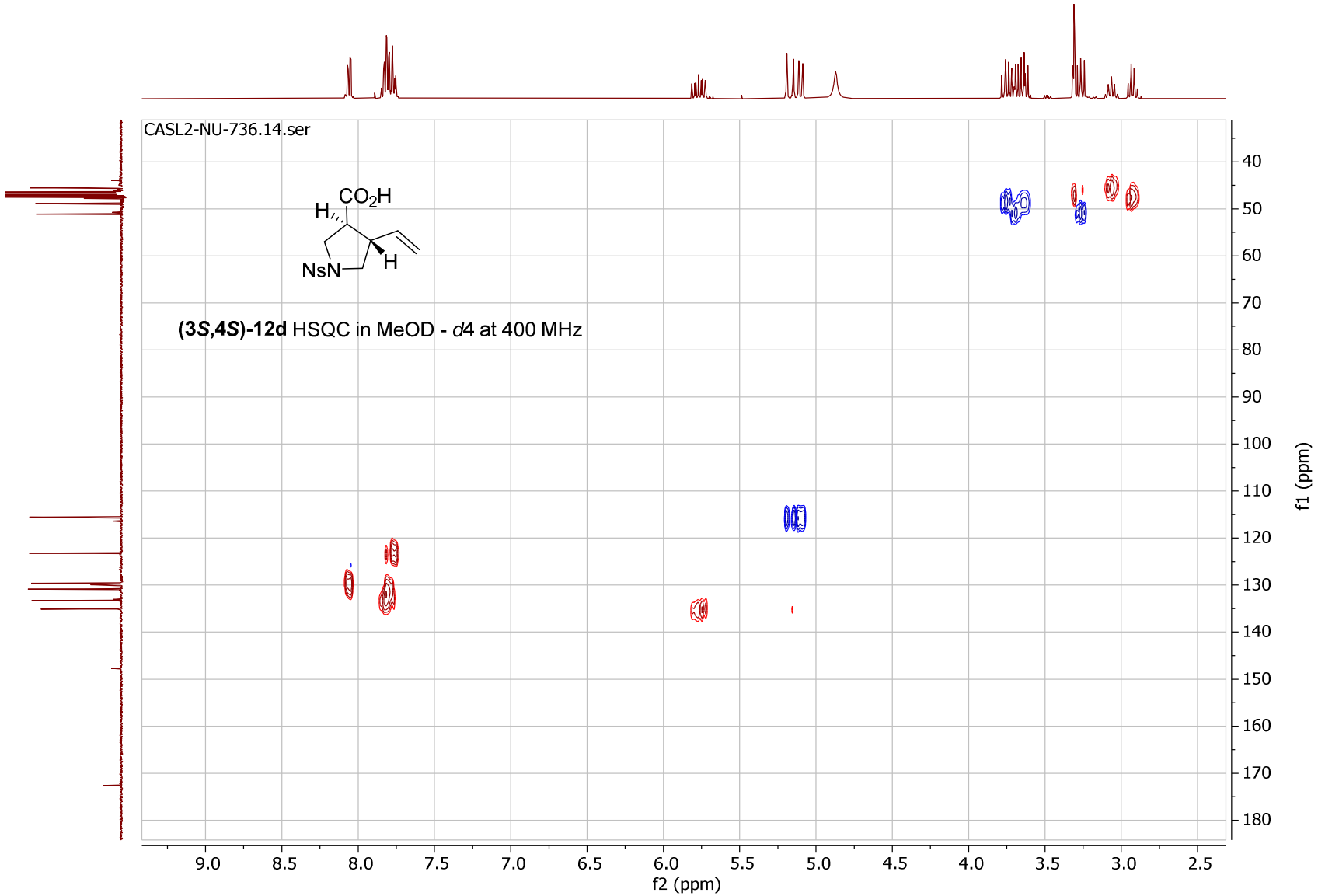
137.21
135.41
132.99
132.05
131.74
125.34
117.69
53.27
51.04
49.90
49.00 CD3OD
47.65
CO2H
H
NsN
H
(3S,4S)-12d 13C{1H} NMR in MeOD-d4 at 100 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CASL2-NU-736.12.ser
CO2H
H
NsN
H
(3S,4S)-12d 1H -1H COSY in MeOD - d4 at 400 MHz
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
f2 (ppm)
1
2
3
4
5
6
7
8
f1 (ppm)


CASL2-NU-736.14.ser
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H
NsN
H
(3S,4S)-12d HSQC in MeOD - d4 at 400 MHz
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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
f2 (ppm)
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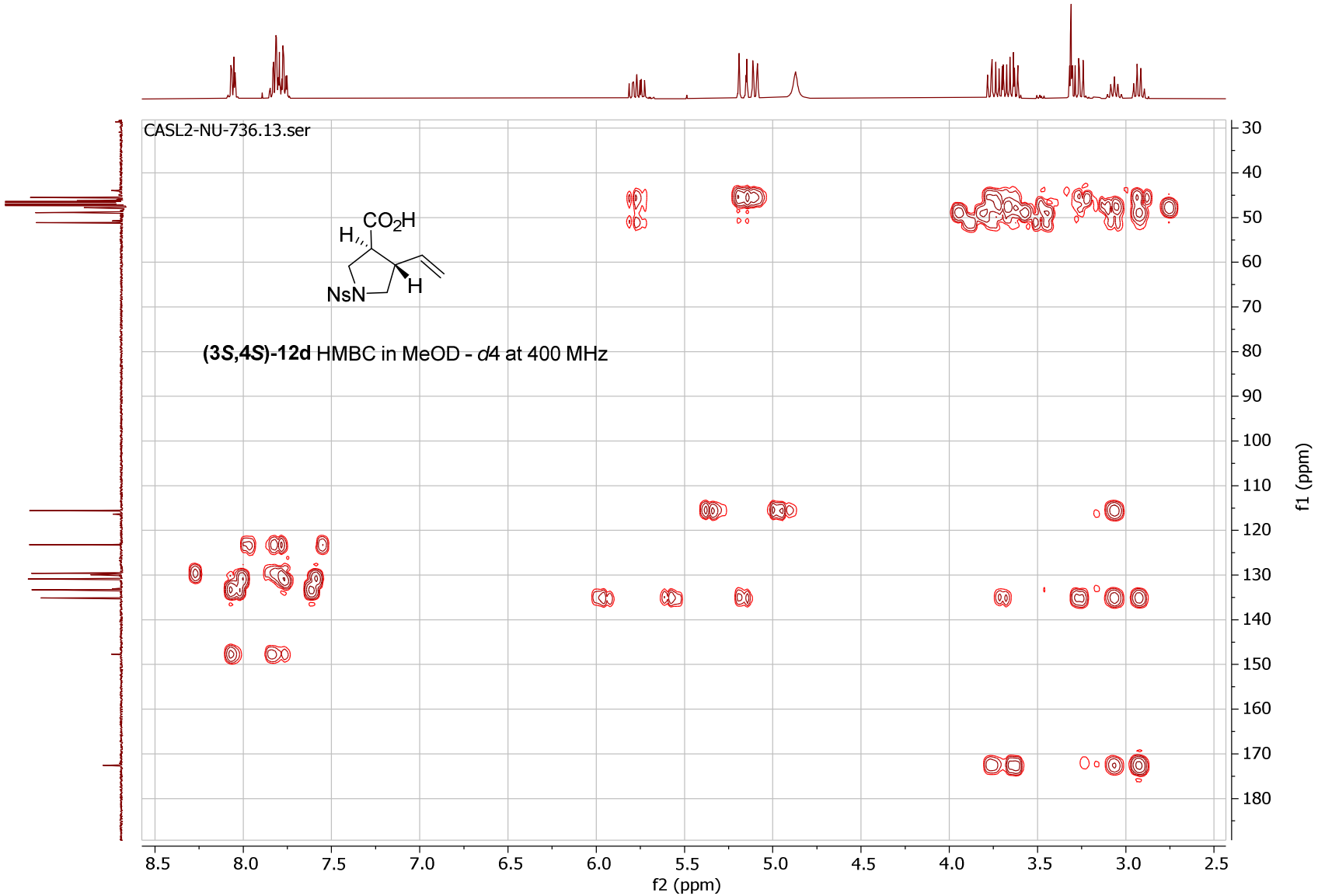
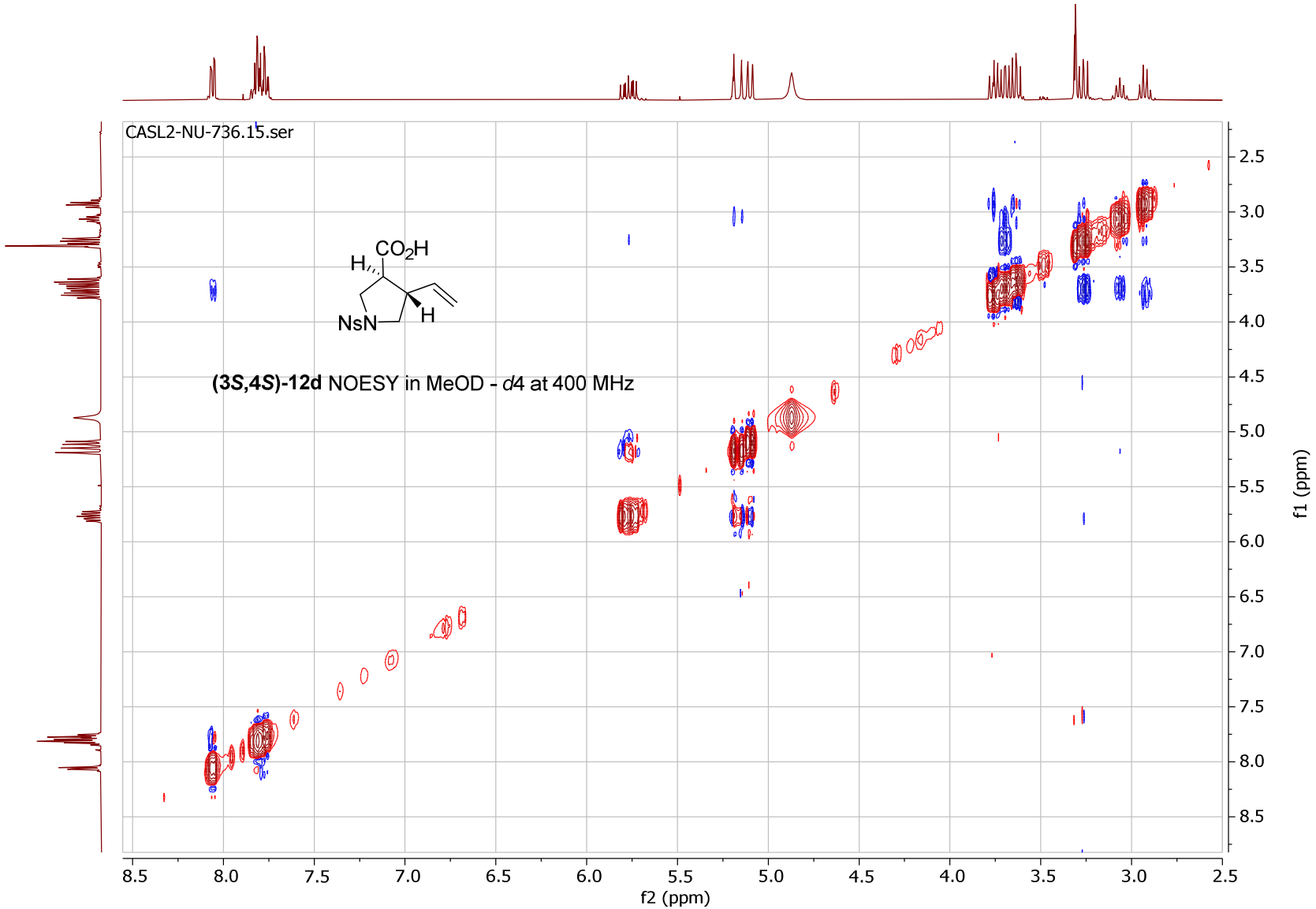
60
70
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)


CASL2-NU-736.13.ser
CO2H
H
NsN
H
(3S,4S)-12d HMBC in MeOD - d4 at 400 MHz
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
f2 (ppm)
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)


CASL2-NU-736.15.ser
CO2H
H
NsN
H
(3S,4S)-12d NOESY in MeOD - d4 at 400 MHz
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8.0
7.5
7.0
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5.0
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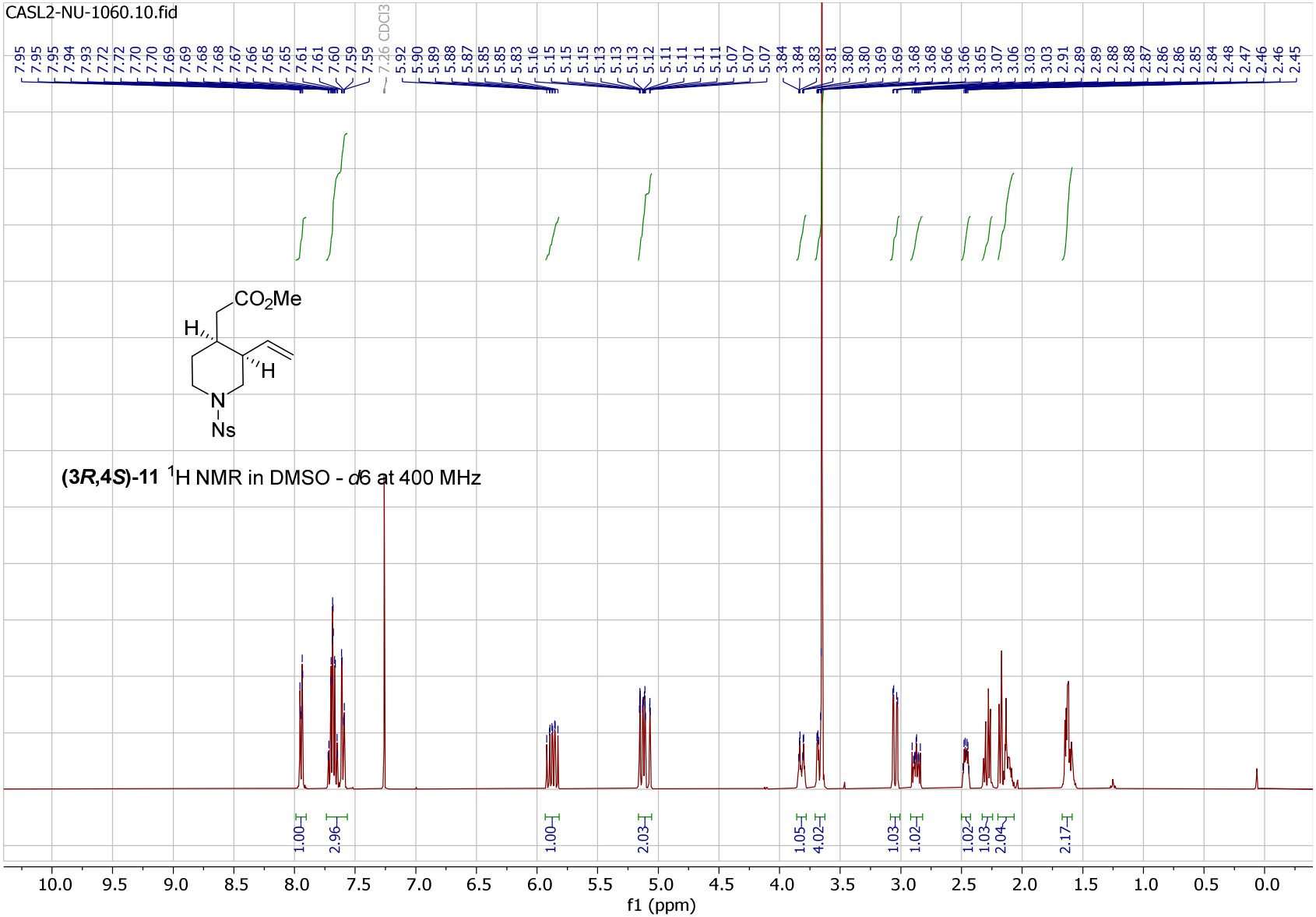
3.5
3.0
2.5
f2 (ppm)
f1 (ppm)


CASL2-NU-1060.10.fid
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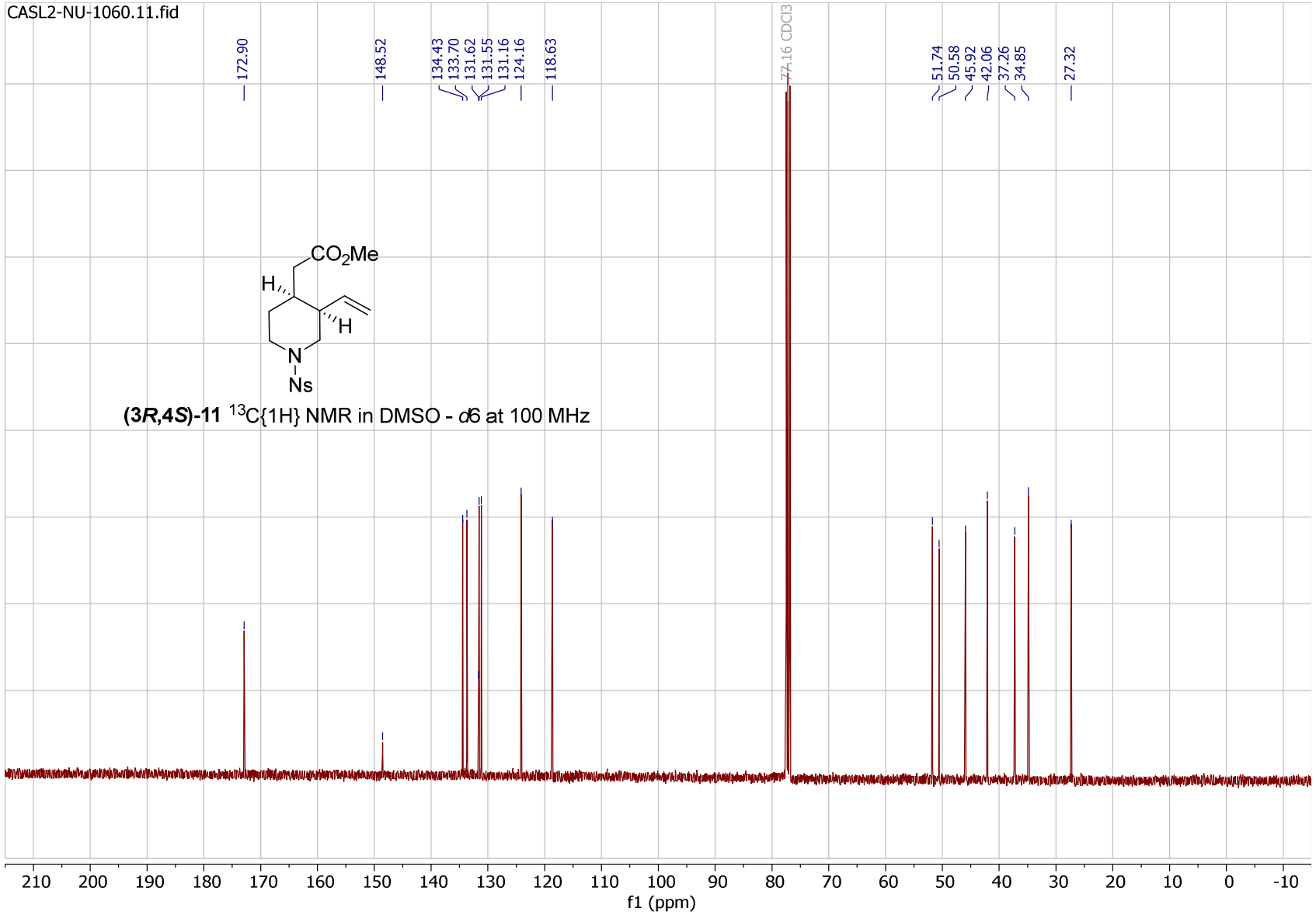
H
N
Ns
(3R,4S)-11 1H NMR in DMSO - d6 at 400 MHz
f1 (ppm)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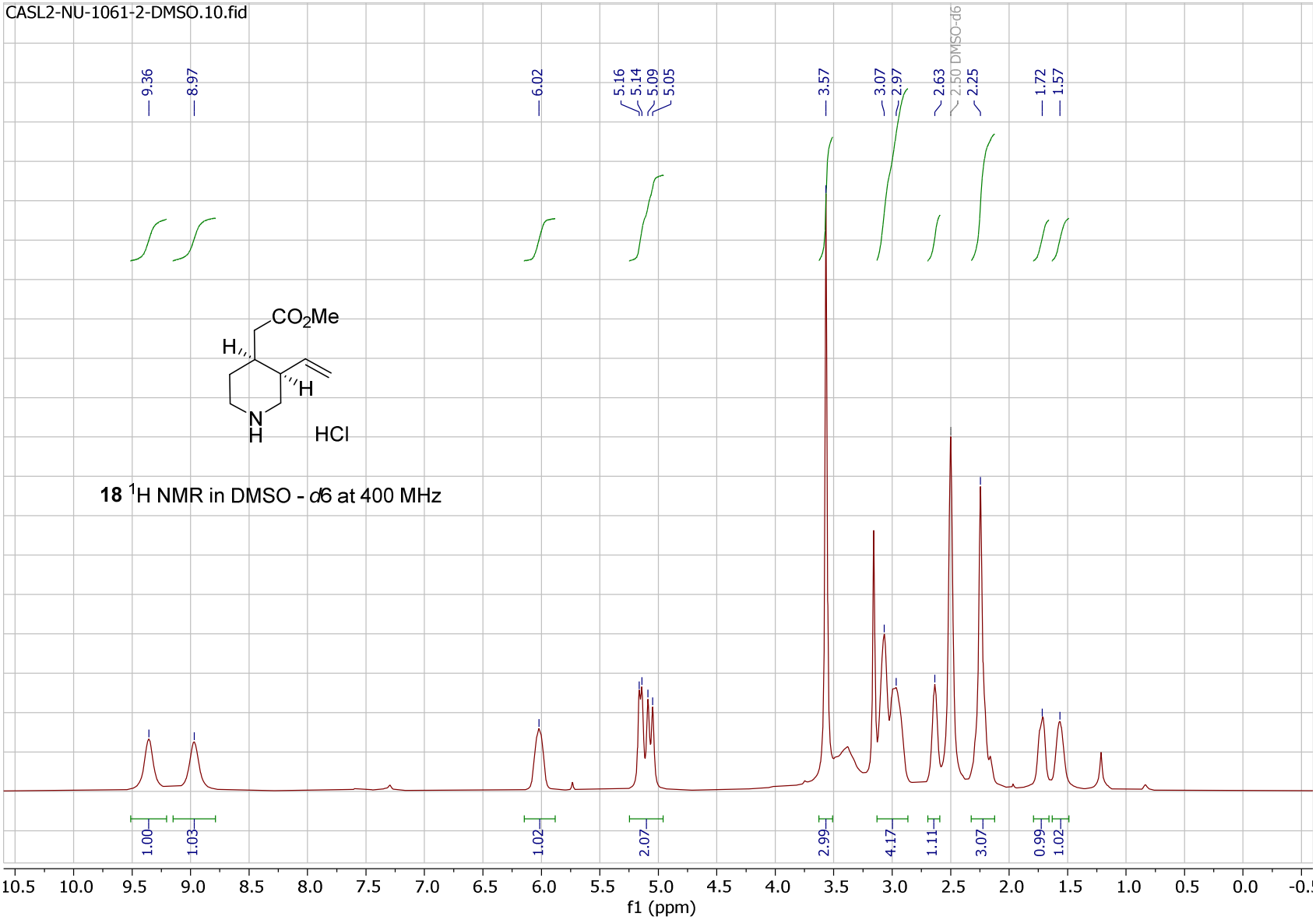
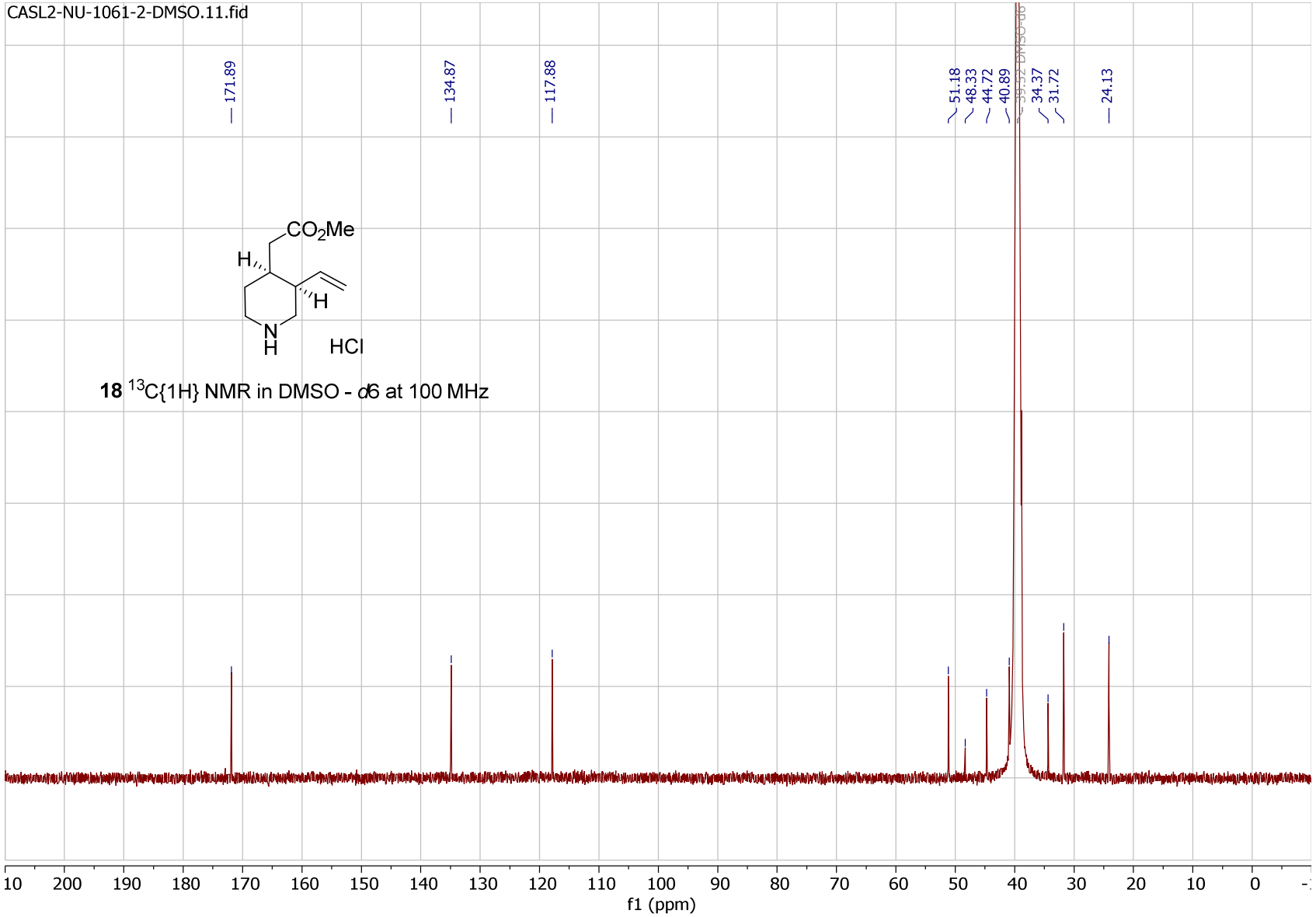
172.90
148.52
134.43
133.70
131.62
131.55
131.16
124.16
118.63
77.16 CDCl3
51.74
50.58
45.92
42.06
37.26
34.85
27.32
CO2Me
H
H
N
Ns
(3R,4S)-11 13C{1H} NMR in DMSO - d6 at 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


CASL2-NU-1061-2-DMSO.10.fid
9.36
8.97
6.02
5.16
5.14
5.09
5.05
3.57
3.07
2.97
2.63
2.50 DMSO-d6
2.25
1.72
1.57
CO2Me
H
H
N
H
HCl
18 1H NMR in DMSO - d6 at 400 MHz
1.00
1.03
1.02
2.07
2.99
4.17
1.11
3.07
0.99
1.02
10.5 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)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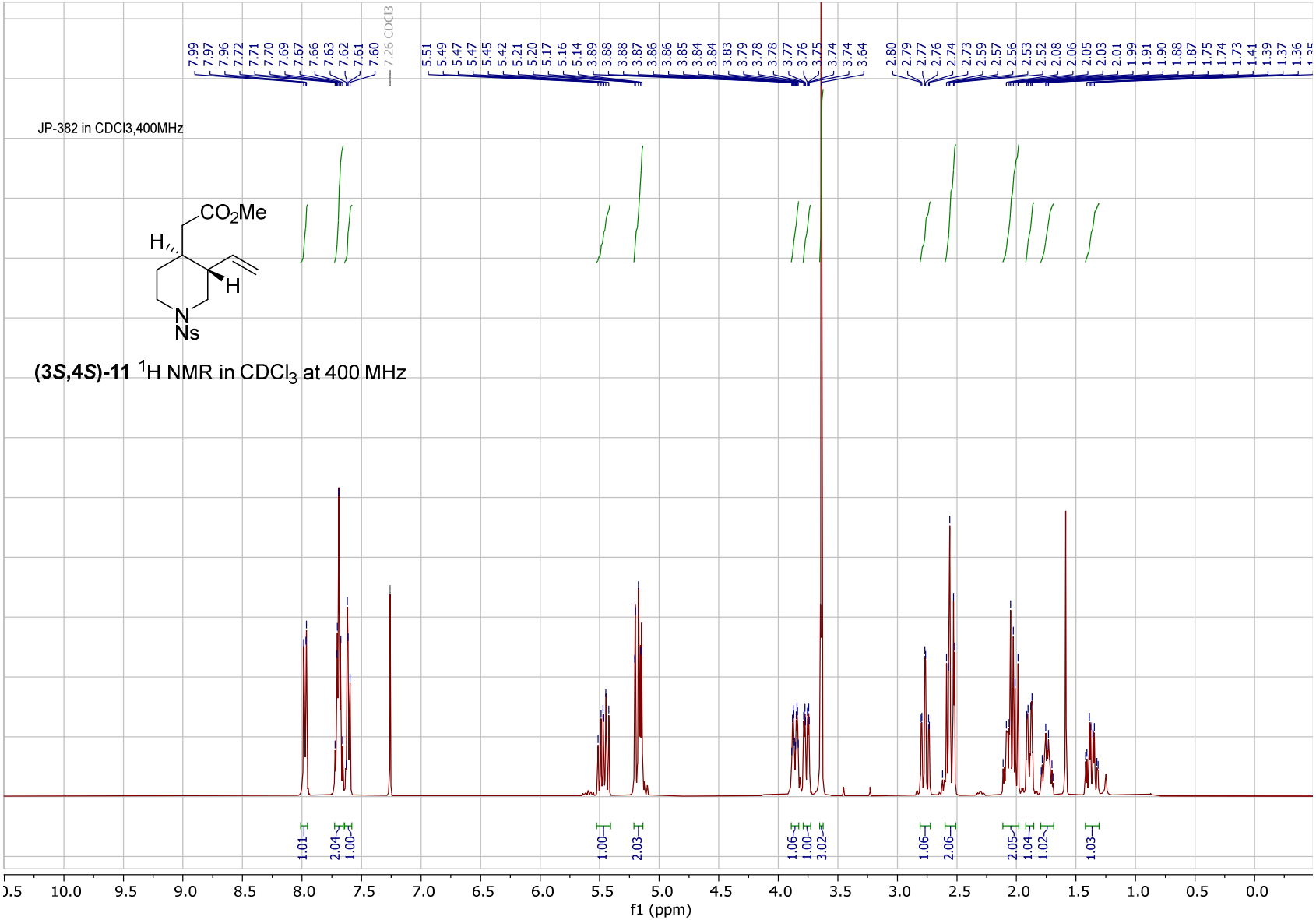
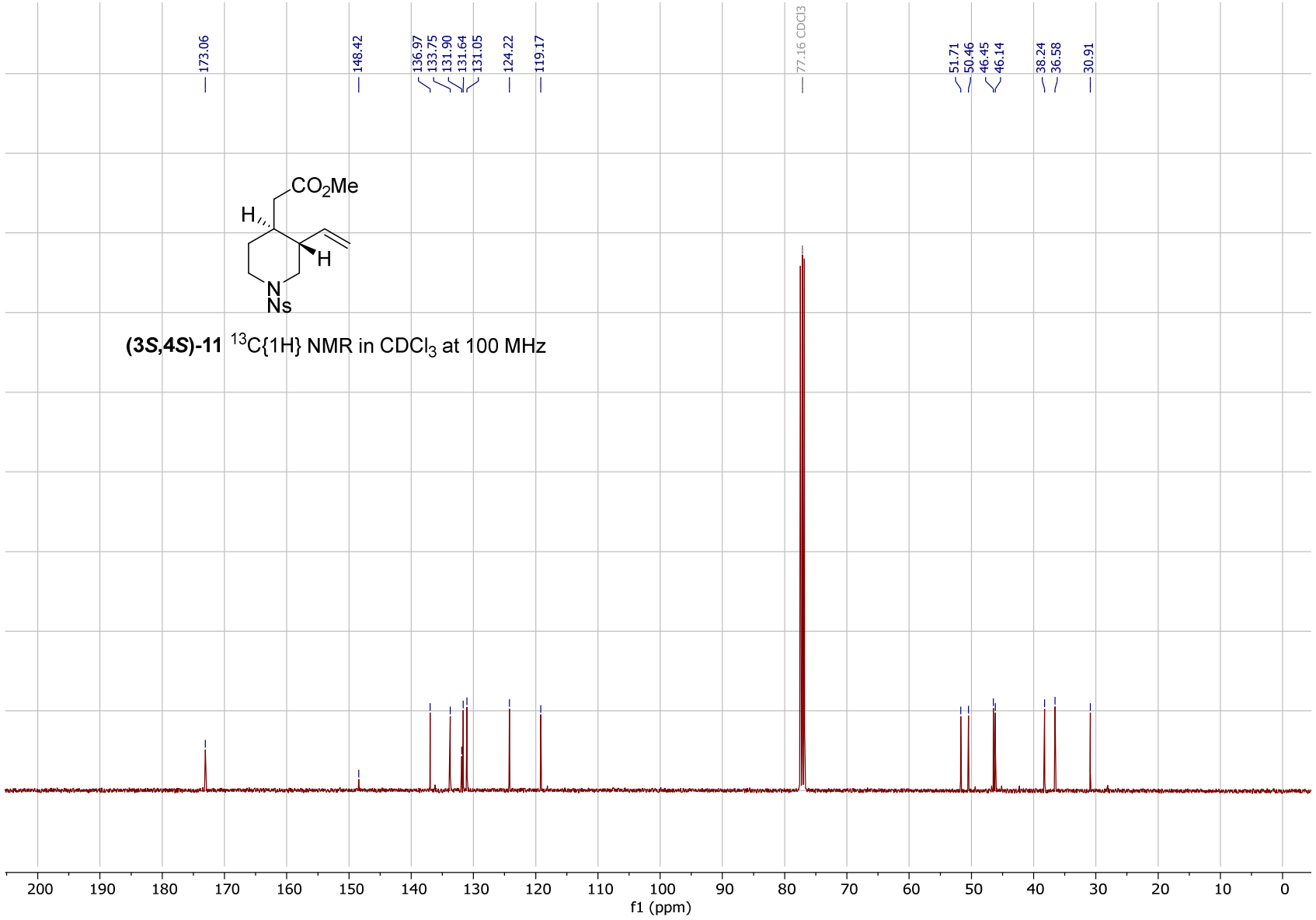
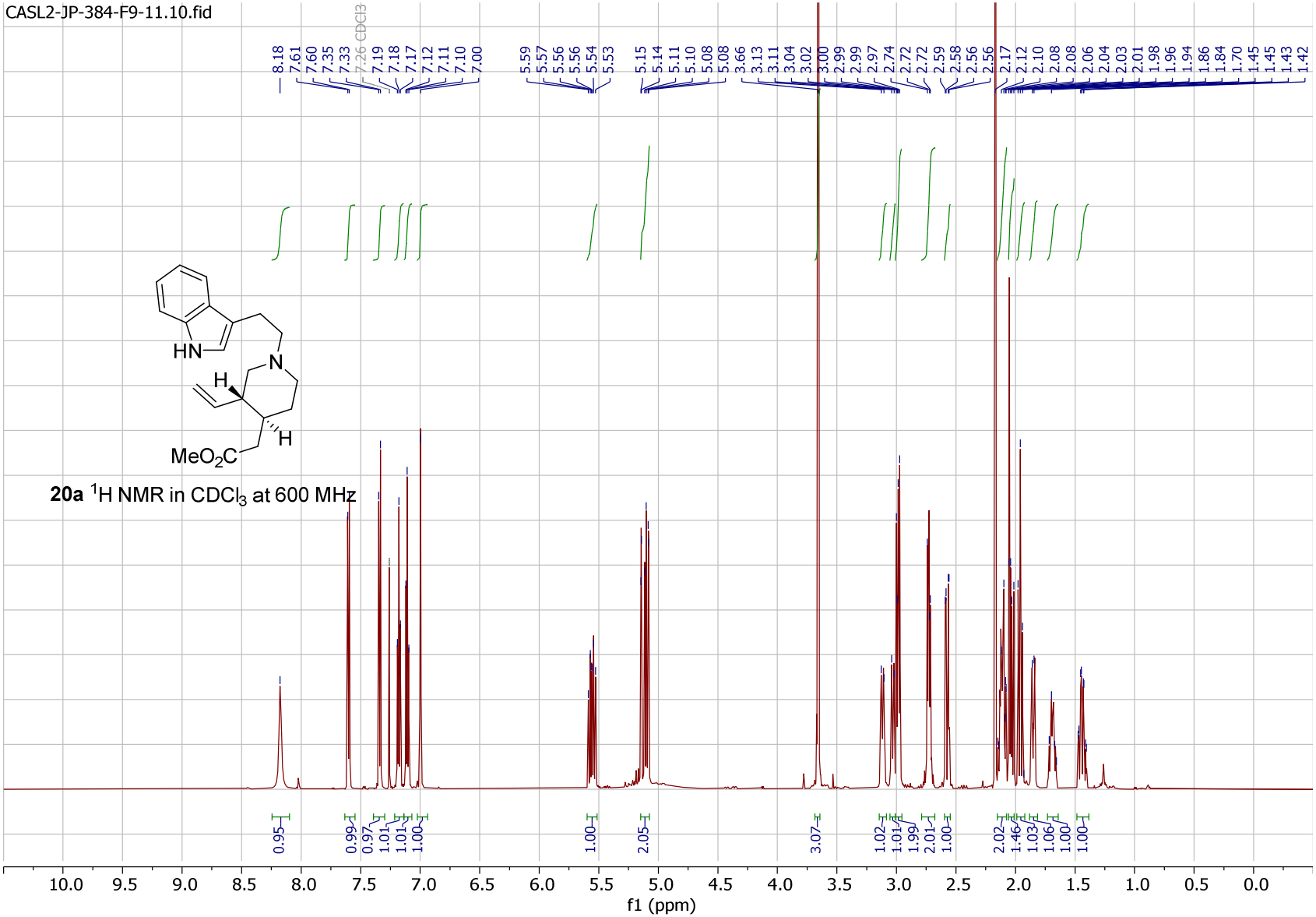
171.89
134.87
117.88
51.18
48.33
44.72
40.89
39.52 DMSO-d6
34.37
31.72
24.13
CO2Me
H
H
N
H
HCl
18 13C{1H} NMR in DMSO - d6 at 100 MHz
f1 (ppm)


JP-382 in CDCl3,400MHz
CO2Me
H
H
N
Ns
(3S,4S)-11 1H NMR in CDCl3 at 400 MHz
f1 (ppm)


173.06
148.42
136.97
133.75
131.90
131.64
131.05
124.22
119.17
77.16 CDCl3
51.71
50.46
46.45
46.14
38.24
36.58
30.91
CO2Me
H
H
N
Ns
(3S,4S)-11 13C{1H} NMR in CDCl3 at 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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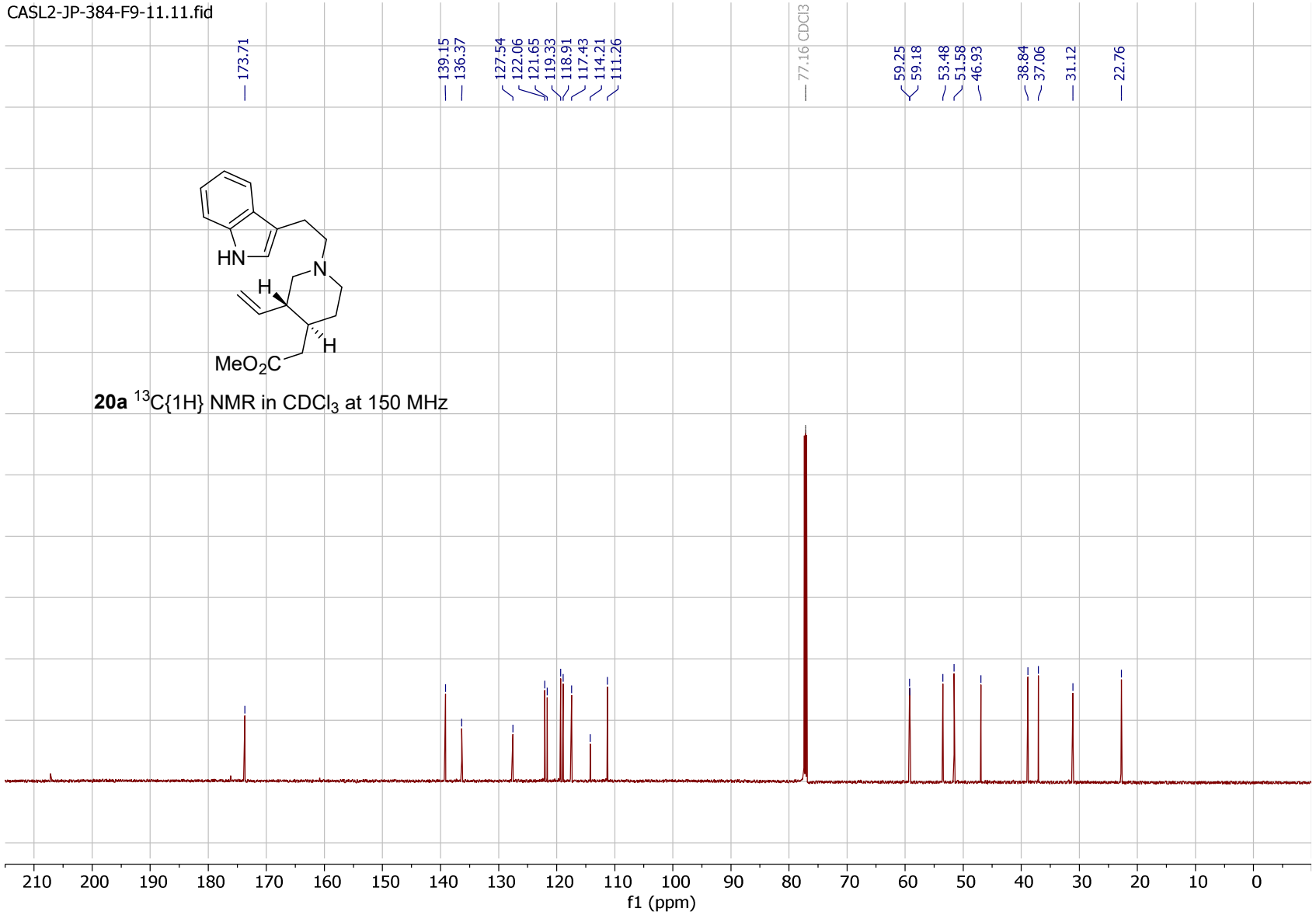
N
H
H
MeO2C
20a 1H NMR in CDCl3 at 600 MHz
f1 (ppm)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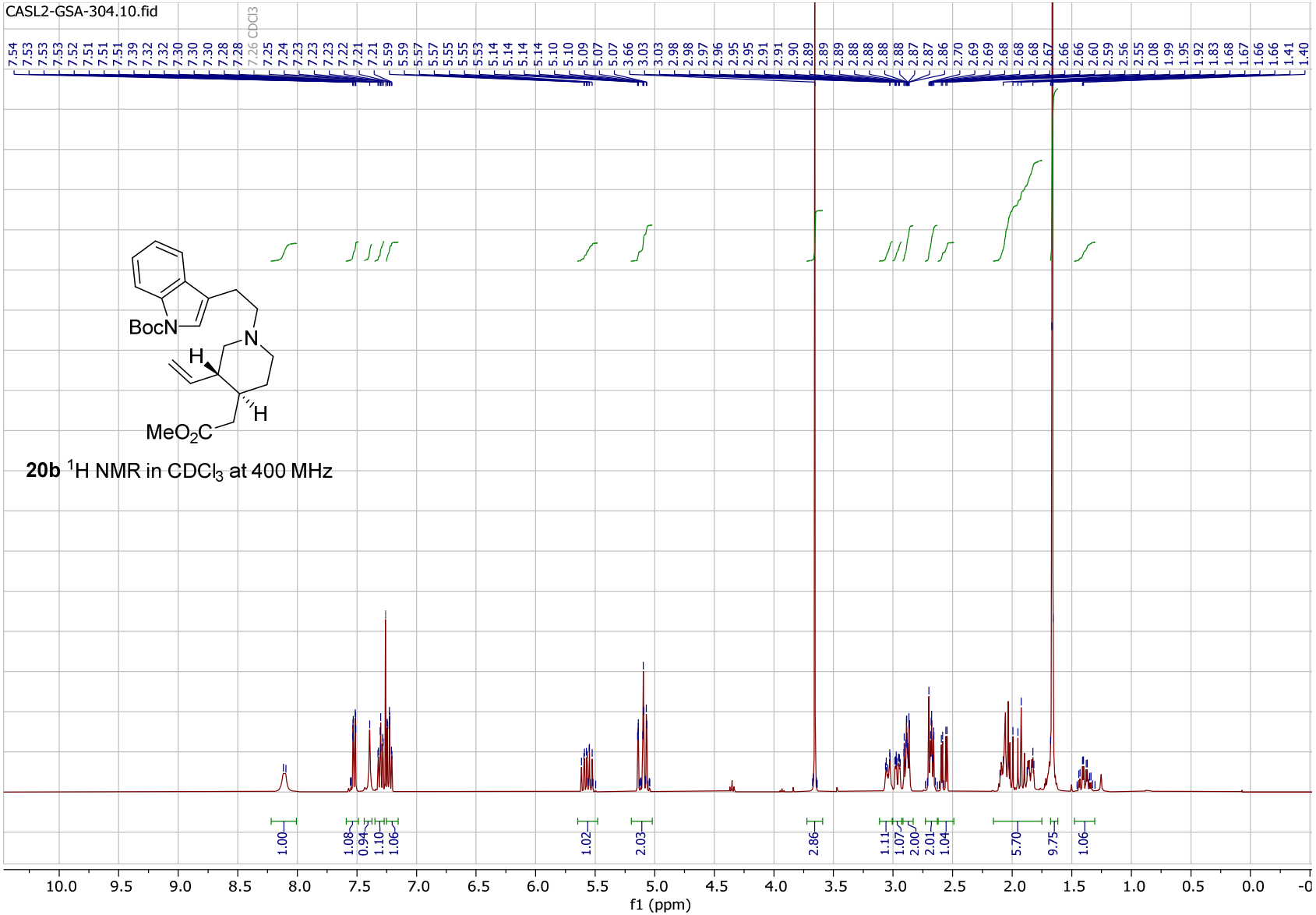
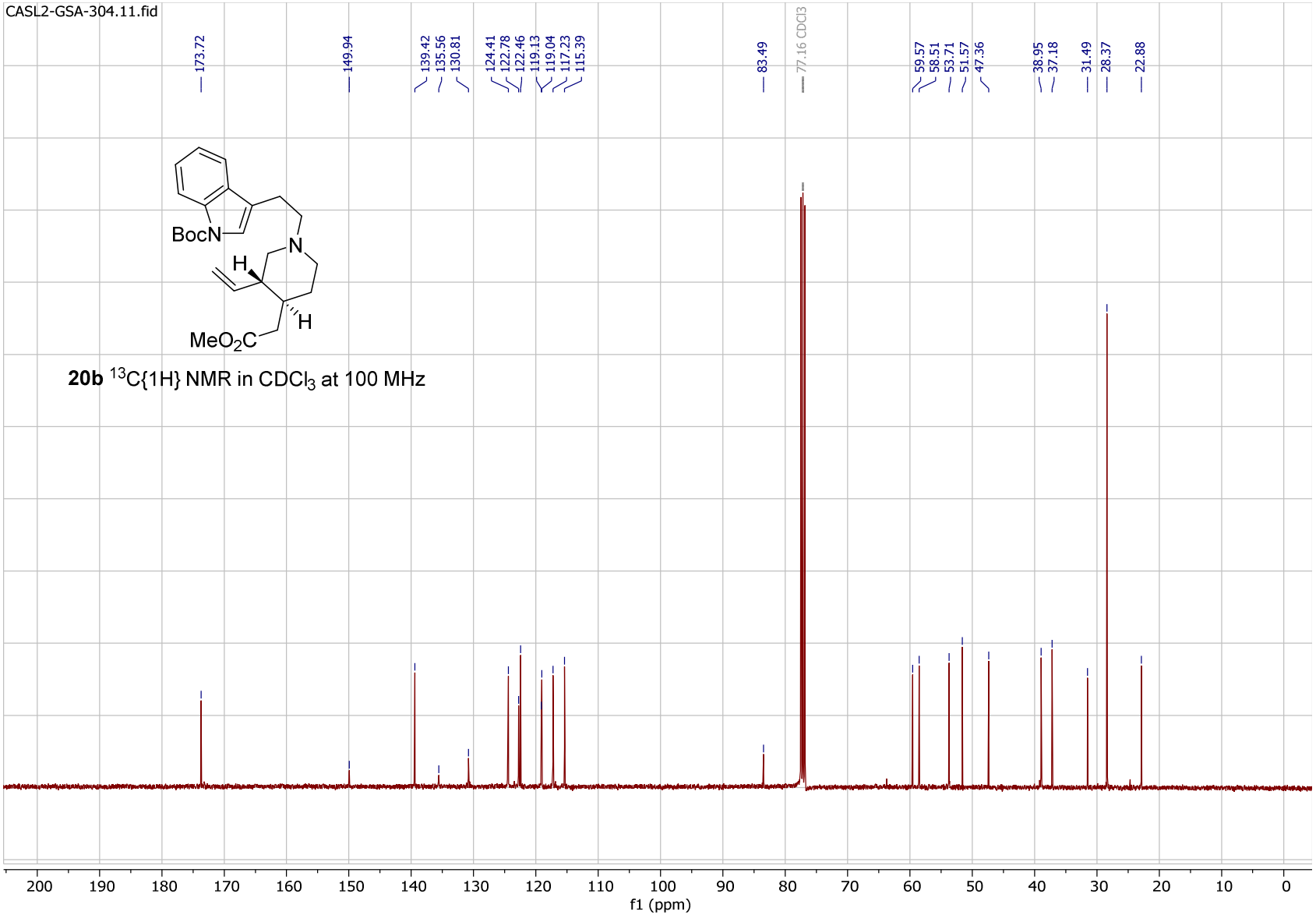
173.71
139.15
136.37
127.54
122.06
121.65
119.33
118.91
117.43
114.21
111.26
77.16 CDCl3
59.25
59.18
53.48
51.58
46.93
38.84
37.06
31.12
22.76
HN
N
H
H
MeO2C
20a 13C{1H} NMR in CDCl3 at 150 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



20b ^{1}H NMR in $CDCl_3$ at 400 MHz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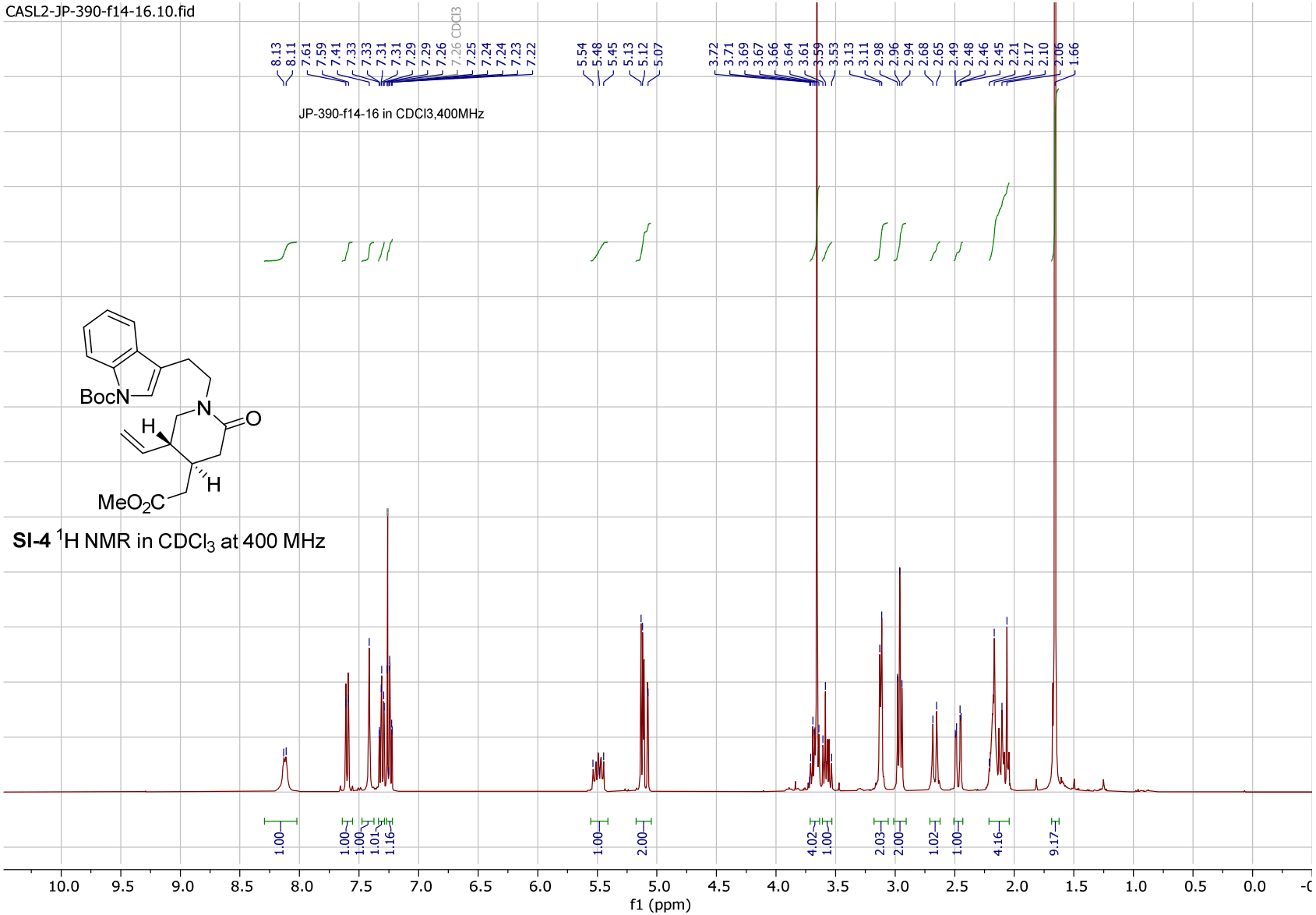
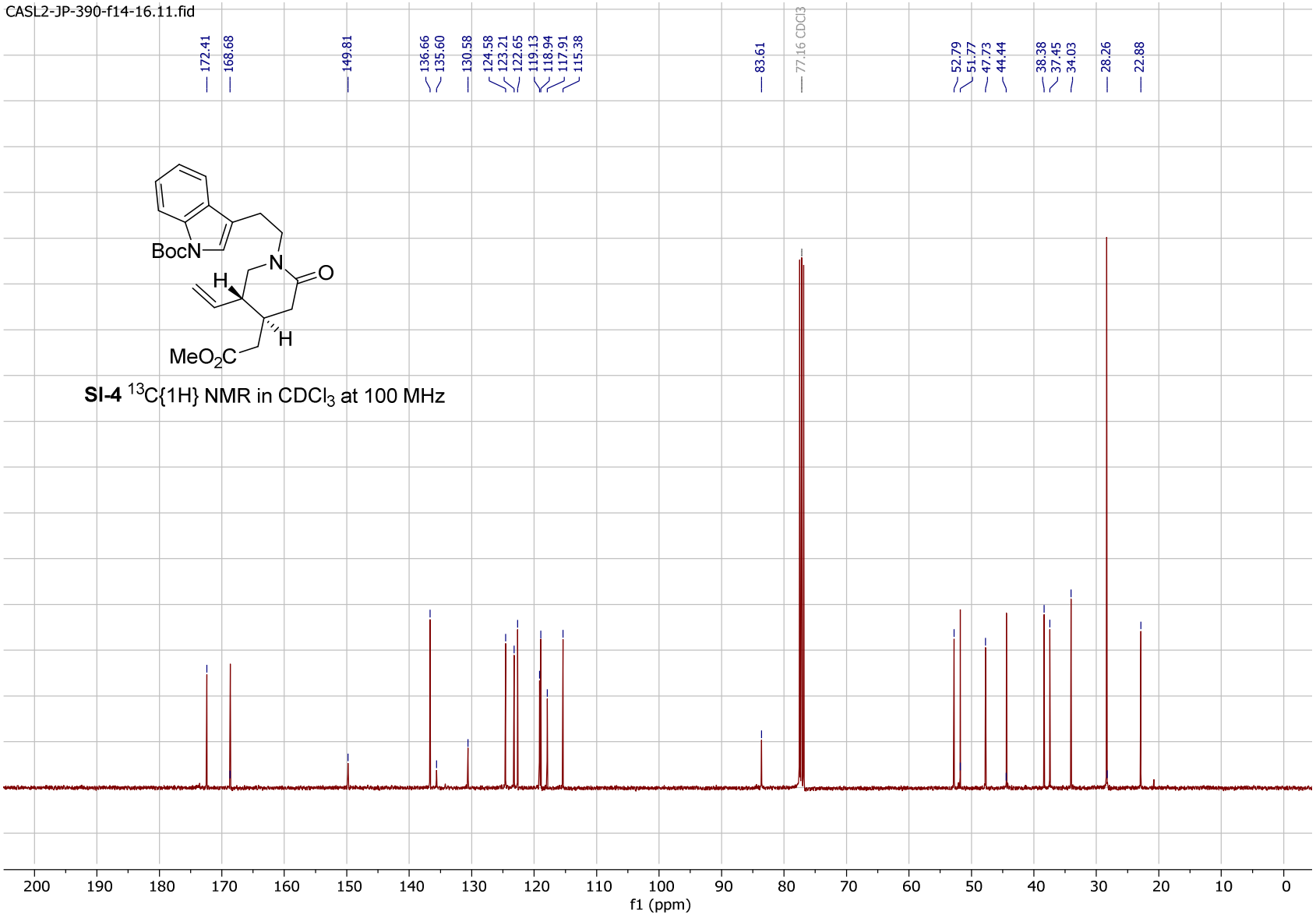
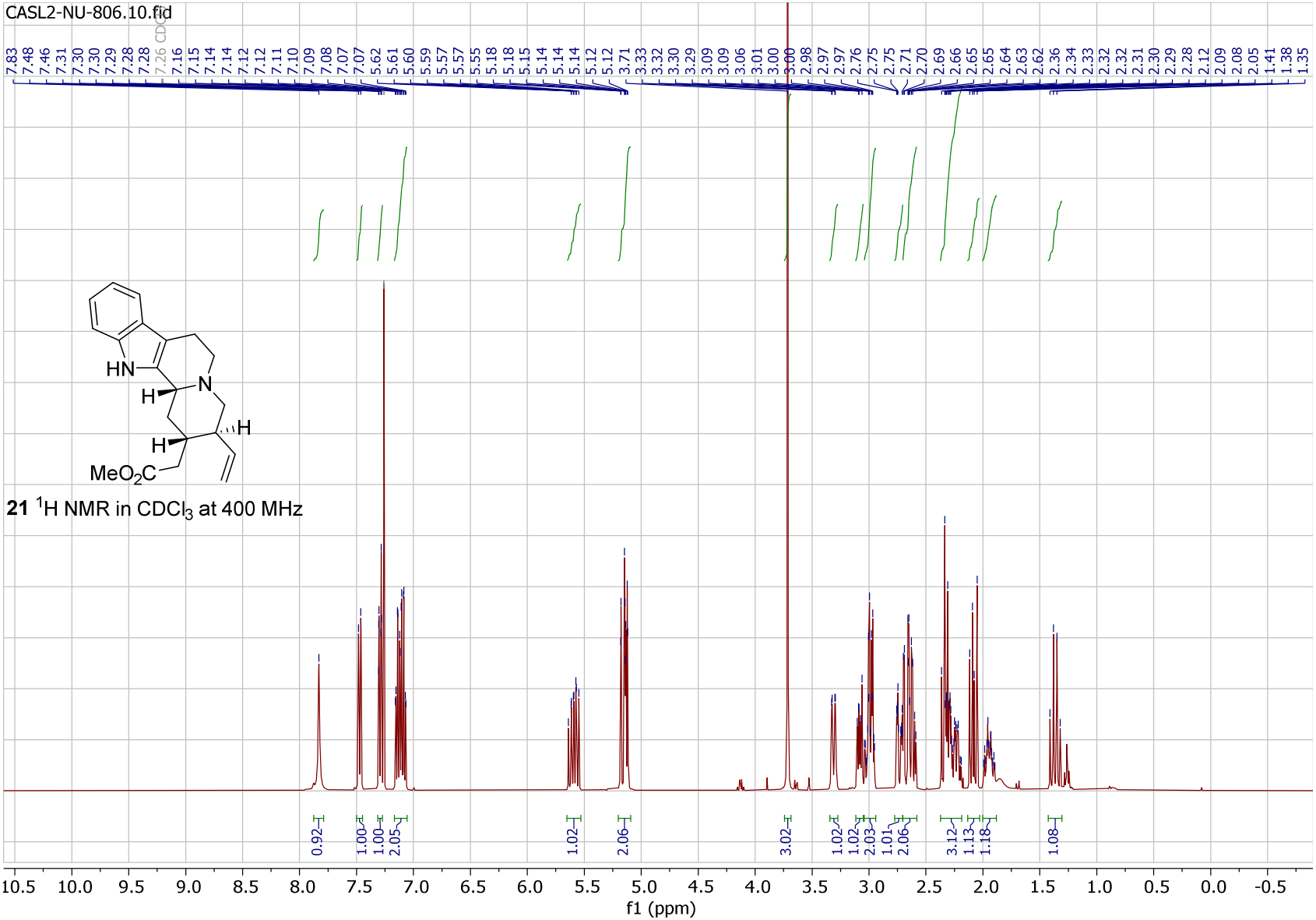
139.42
135.56
130.81
124.41
122.78
122.46
119.13
119.04
117.23
115.39
83.49
77.16 CDCl3
59.57
58.51
53.71
51.57
47.36
38.95
37.18
31.49
28.37
22.88
BocN
N
H
H
MeO2C
20b 13C{1H} NMR in CDCl3 at 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



SI-4 ^{1}H NMR in $CDCl_3$ at 400 MHz



SI-4 $^{13}C\{1H\}$ NMR in $CDCl_3$ at 100 MHz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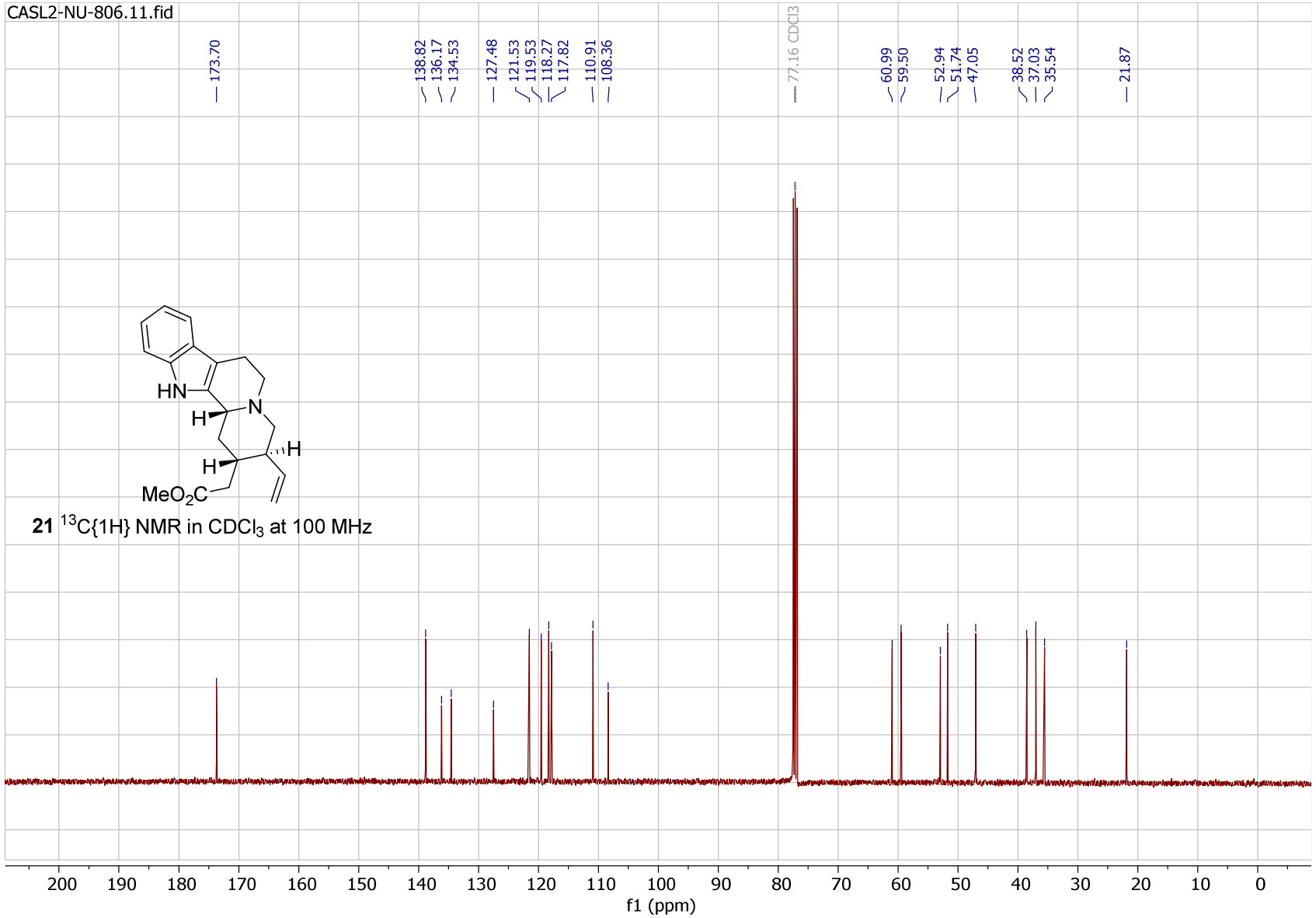
HN
N
H
H
H
MeO2C
21 1H NMR in CDCl3 at 400 MHz
f1 (ppm)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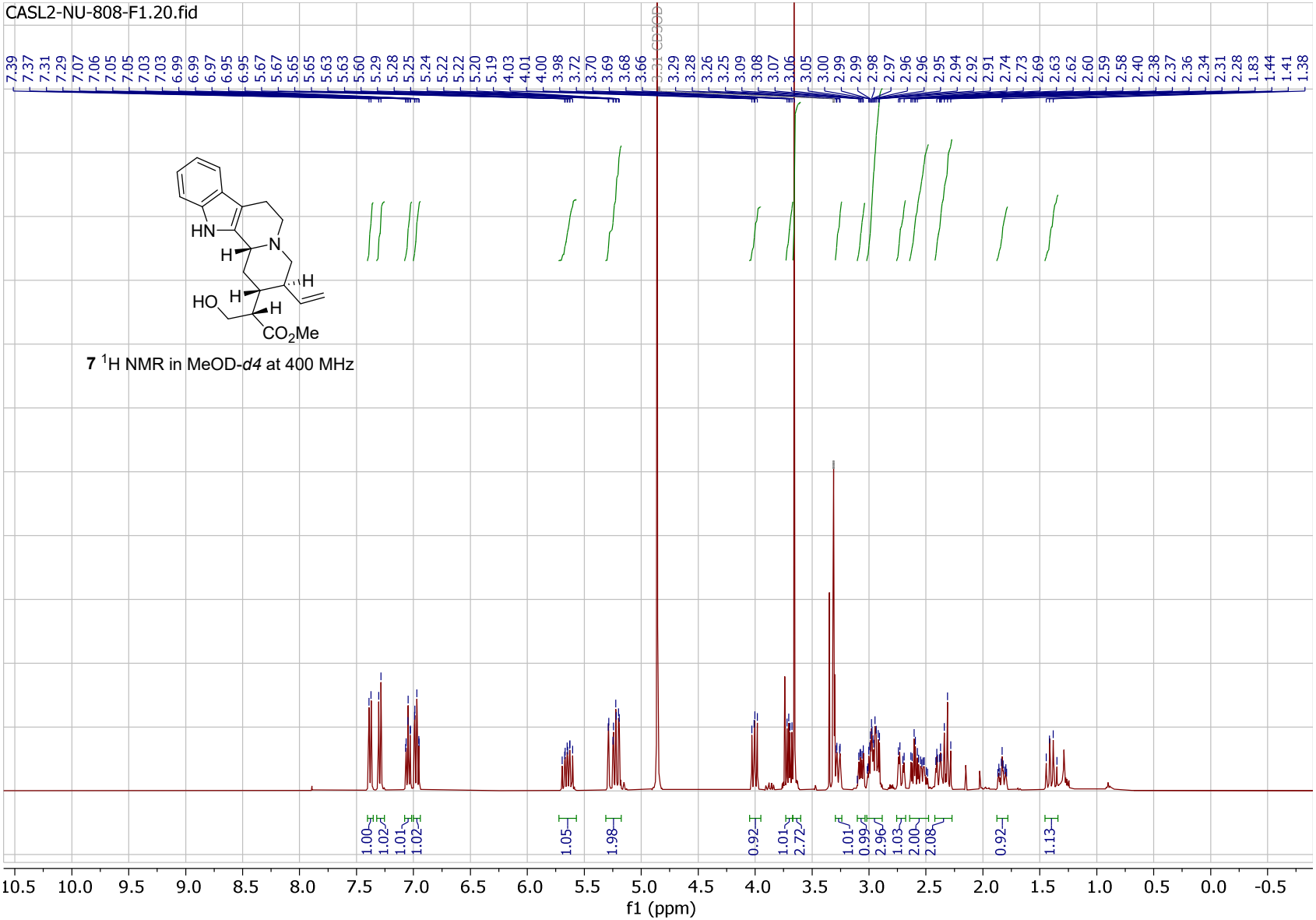
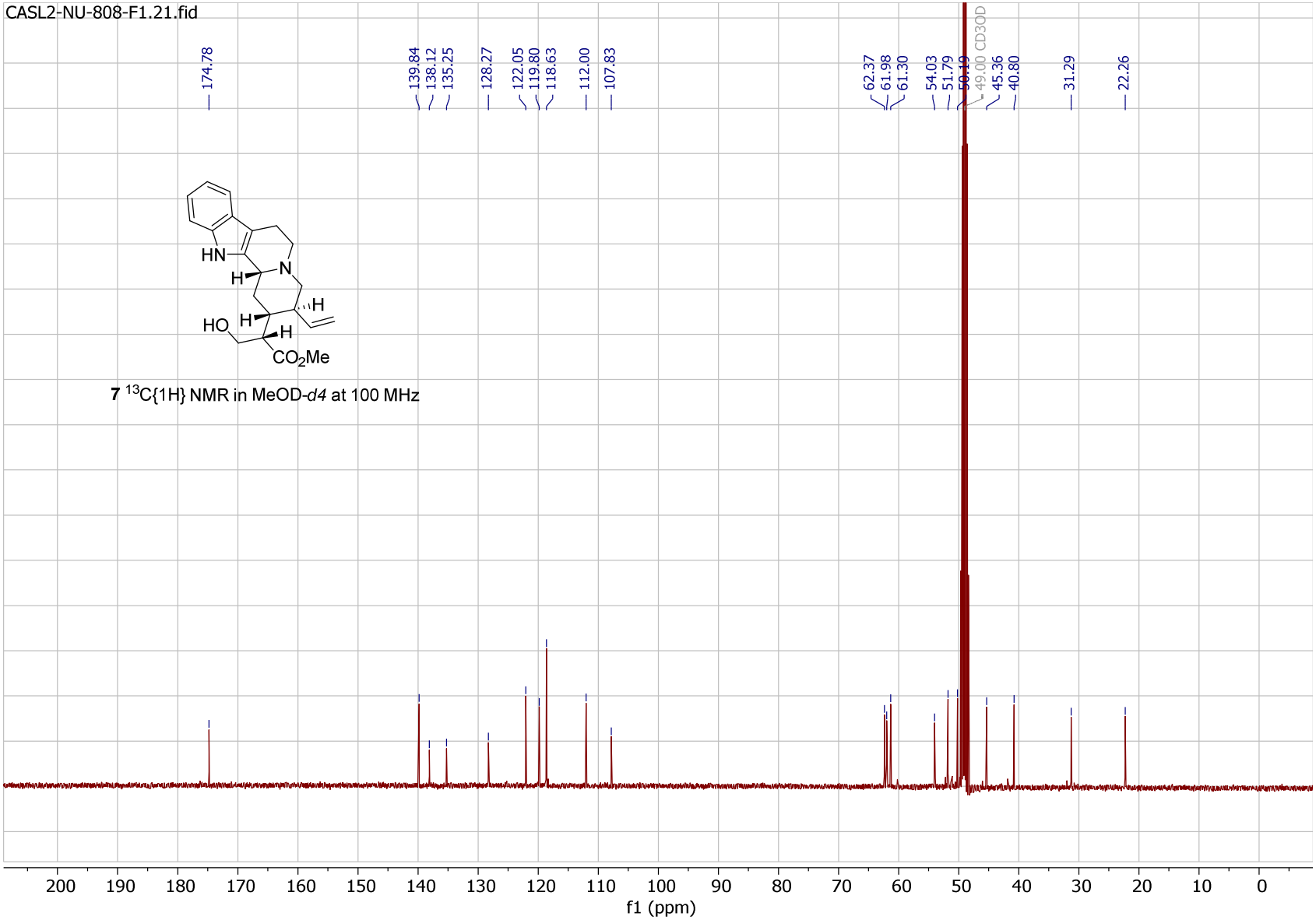
173.70
138.82
136.17
134.53
127.48
121.53
119.53
118.27
117.82
110.91
108.36
77.16 CDCl3
60.99
59.50
52.94
51.74
47.05
38.52
37.03
35.54
21.87
HN
H
N
H
H
MeO2C
21 13C{1H} NMR in CDCl3 at 100 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



7 ^{1}H NMR in MeOD-*d4* at 400 MHz


CASL2-NU-808-F1.21.fid
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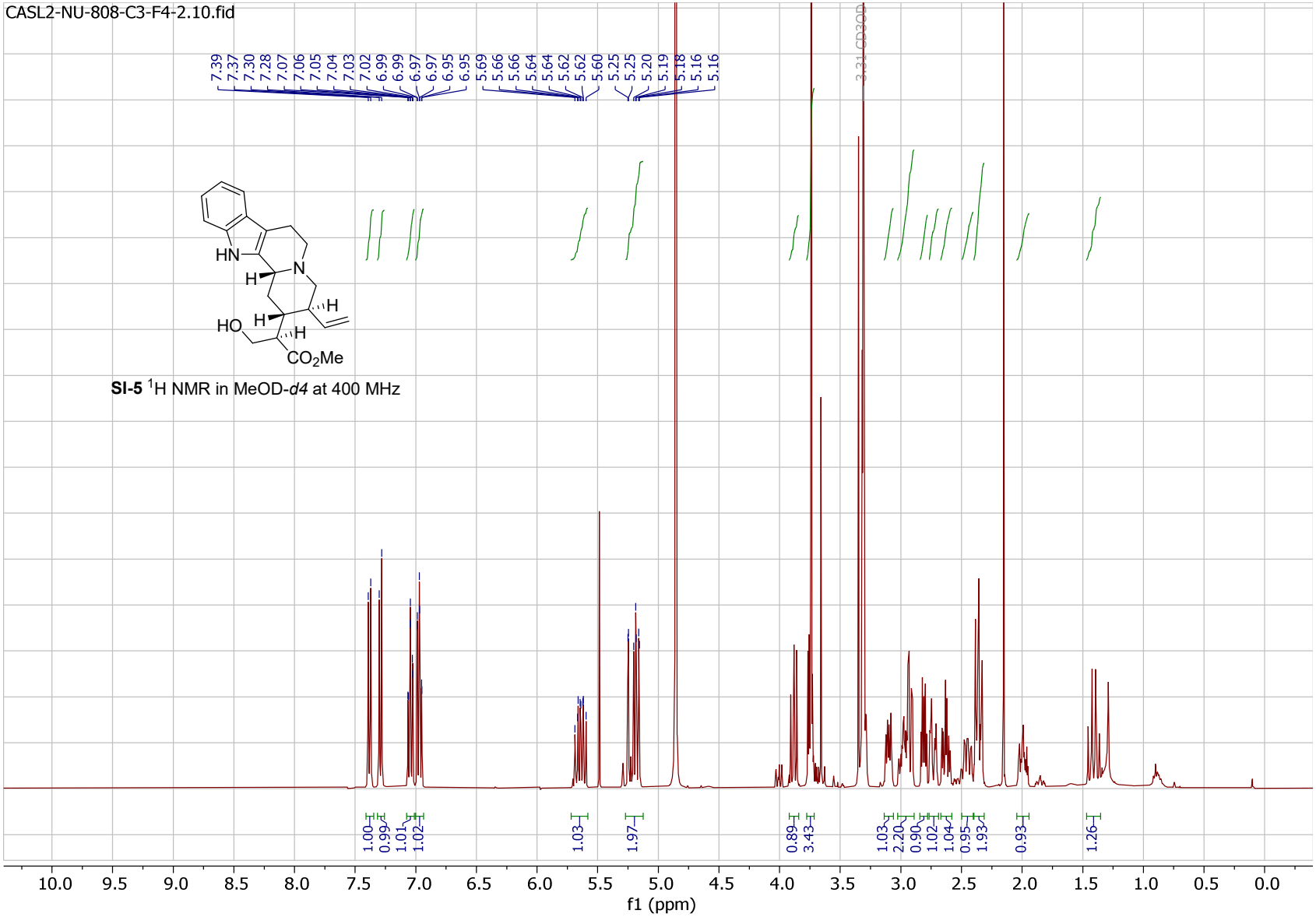
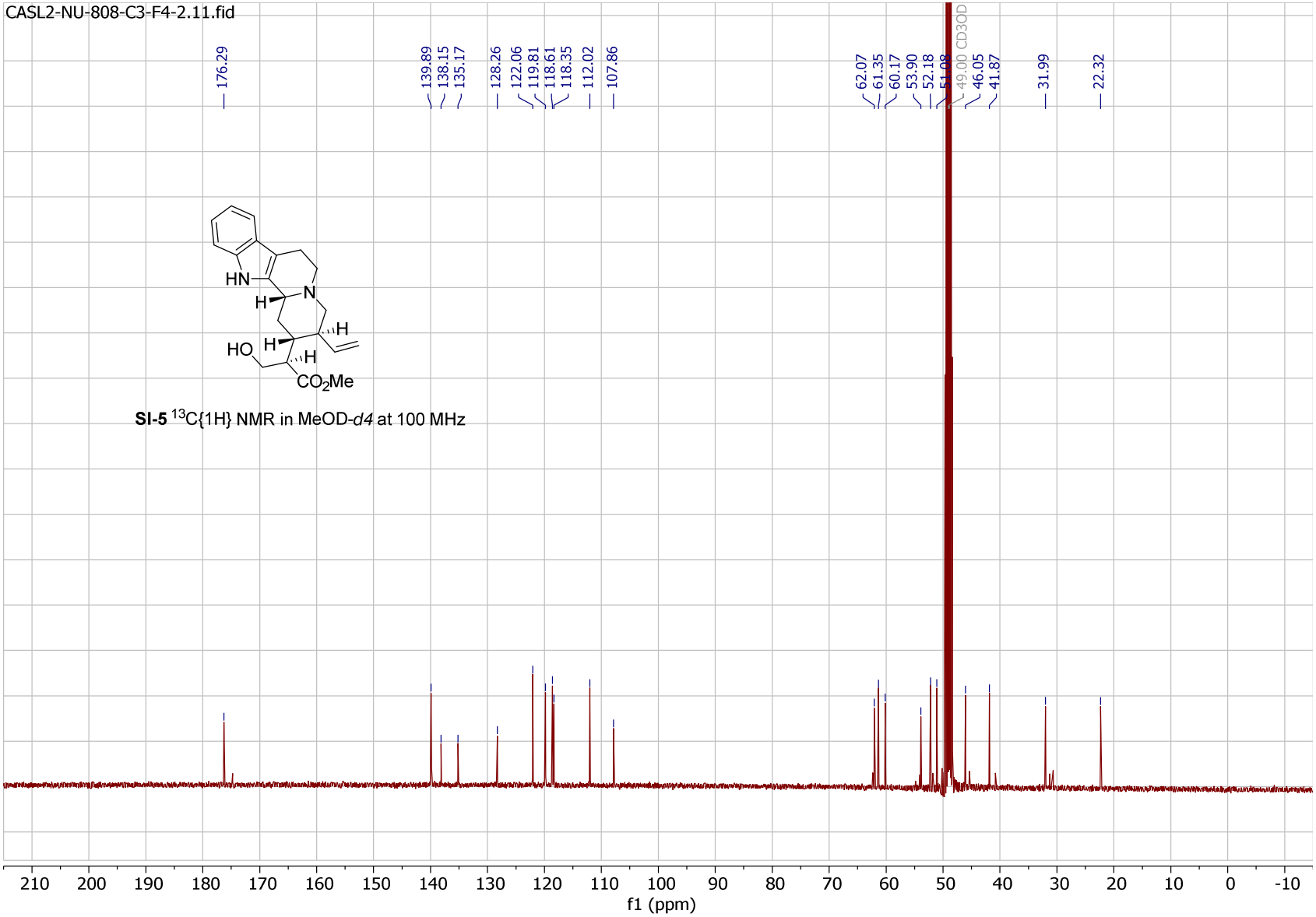
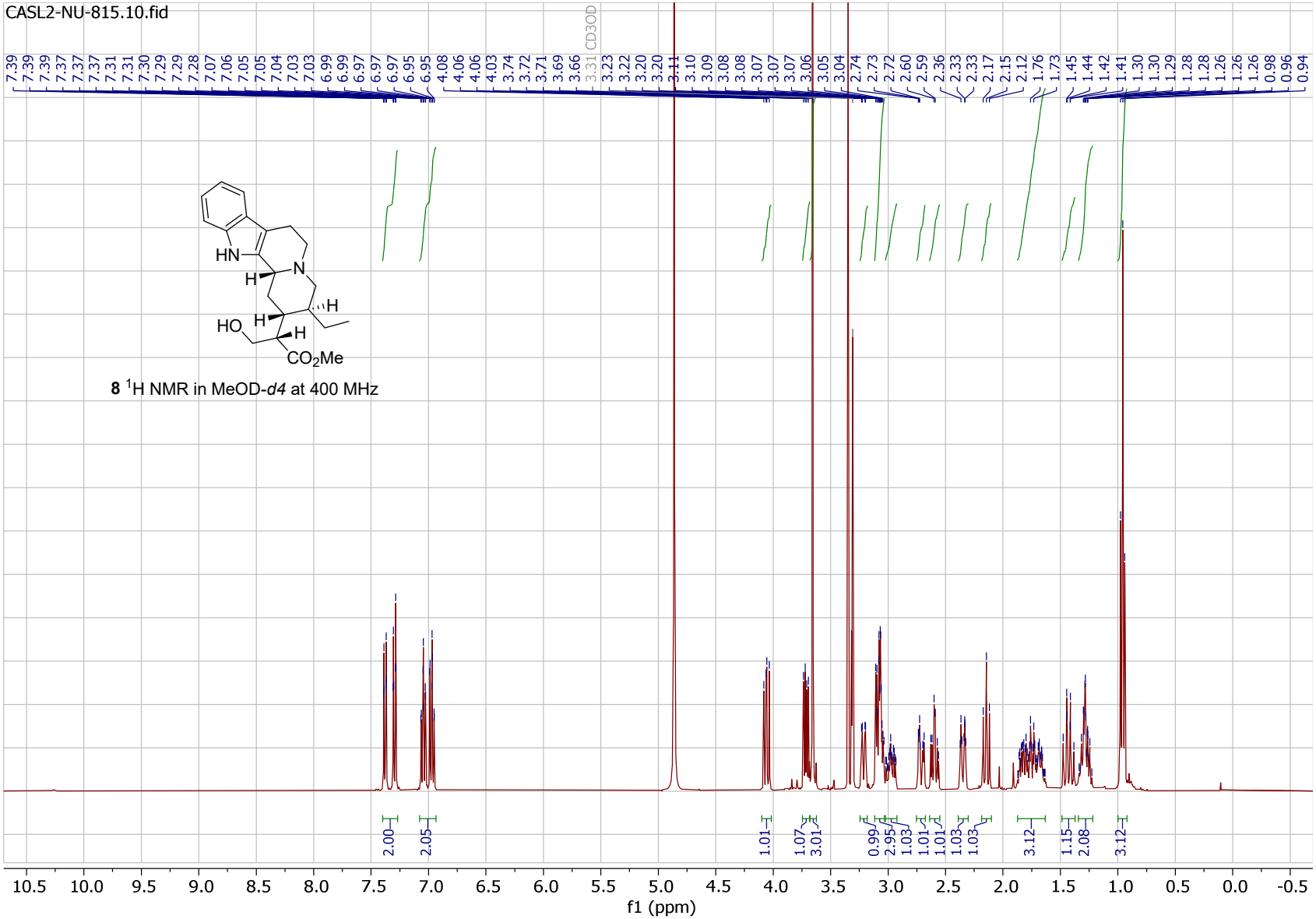
135.25
128.27
122.05
119.80
118.63
112.00
107.83
62.37
61.98
61.30
54.03
51.79
50.19
49.00 CD3OD
45.36
40.80
31.29
22.26
HN
H
N
H
HO
H
H
CO2Me
7 13C{1H} NMR in MeOD-d4 at 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



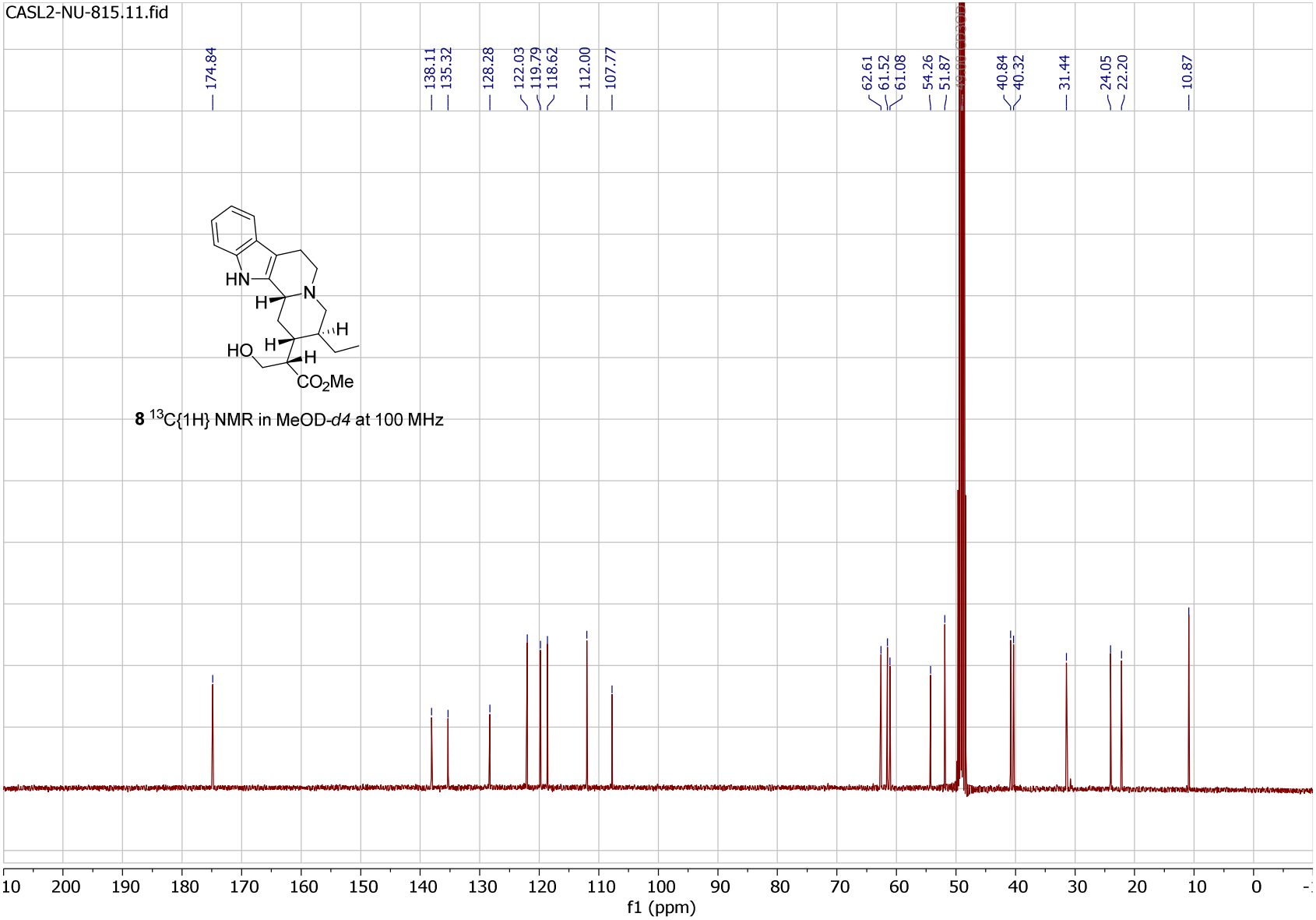
SI-5 ^{1}H NMR in MeOD-*d4* at 400 MHz



SI-5 $^{13}C\{1H\}$ NMR in MeOD-*d4* at 100 MHz



8 ^{1}H NMR in MeOD-*d4* at 400 MHz


CASL2-NU-815.11.fid
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138.11
135.32
128.28
122.03
119.79
118.62
112.00
107.77
62.61
61.52
61.08
54.26
51.87
40.84
40.32
31.44
24.05
22.20
10.87
HN
H
N
H
HO
H
H
CO2Me
8 13C{1H} NMR in MeOD-d4 at 100 MHz
f1 (ppm)

References

1. Afewerki, S.; Ma, G.; Ibrahem, I.; Liu, L.; Sun, J.; Córdova, A., Highly Enantioselective Control of Dynamic Cascade Transformations by Dual Catalysis: Asymmetric Synthesis of Polysubstituted Spirocyclic Oxindoles. *ACS Catalysis* **2015,** *5* (2), 1266-1272.
2. Burns, M. R.; Jenkins, S. A.; Wood, S. J.; Miller, K.; David, S. A., Structure−Activity Relationships in Lipopolysaccharide Neutralizers: Design, Synthesis, and Biological Evaluation of a 540-Membered Amphipathic Bisamide Library. *Journal of Combinatorial Chemistry* **2006,** *8* (1), 32-43.
3. Kutsumura, N.; Matsuo, K.; Saito, T., Total synthesis of aplysinoplide B. *Tetrahedron Letters* **2015,** *56* (20), 2602-2604.
4. Kim, N.-J.; Moon, H.; Park, T.; Yun, H.; Jung, J.-W.; Chang, D.-J.; Kim, D.-D.; Suh, Y.-G., Concise and Enantioselective Total Synthesis of 15-Deoxy-Δ12,14-Prostaglandin J2. *The Journal of Organic Chemistry* **2010,** *75* (21), 7458-7460.
5. Brown, R. T.; Leonard, J., On the C-16 configuration of sitsirikine. *Tetrahedron Letters* **1979,** *20* (20), 1805-1808.
6. Ahmed, A.; Li, W.; Chen, F.-F.; Zhang, J.-S.; Tang, Y.-Q.; Chen, L.; Tang, G.-H.; Yin, S., Monoterpene indole alkaloids from Rhazya stricta. *Fitoterapia* **2018,** *128*, 1-6.
7. Kutney, J. P.; Brown, R. T., The structural elucidation of sitsirikine, dihydrositsirikine and isositsirikine: Three new alkaloids from vinca rosea linn. *Tetrahedron* **1966,** *22* (1), 321-336.