Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Functionalised Bicyclic Tetramates Derived from Cysteine as Antibacterial Agents

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General procedure: Esterification of L-serine and DL-cysteine[1]

To a suspension of the amino acid (1.0 eq) in MeOH (2 mL/mmol) at 0°C, $SOCl_2$ (1.2 eq) was added drop-wise under continuous stirring and warmed to rt, then heated at reflux for 1-3 h. The reaction mixture was concentrated *in vacuo* to obtain the respective amino ester.

General procedure: Synthesis of *N*-acylated thiazolidines **6,7a-g**[1]

Step 1: To L-cysteine methyl ester hydrochloride (1.0 eq) in petrol (25 mL/1 g), Et_3N (1.2 eq) and aldehyde (1.2 eq) were added. The mixture was heated at reflux, with continuous removal of water using a Dean-Stark apparatus, for 19 h. It was then filtered and washed with Et_2O. The combined filtrates were concentrated *in vacuo* and residue was purified by silica gel flash column chromatography (eluent: EtOAc/petrol) to give the required thiazolidines as an inseparable mixture of diastereomers.

Step 2: A solution of ethyl hydrogen malonate (1.2 eq) in CH_2Cl_2 (2.5 mL/mmol) was added to a stirred solution of thiazolidine from step 1(1.0 eq), DCC (1.2 eq) and DMAP (0.1 eq) in CH_2Cl_2 (5 mL/mmol) at 0°C. The mixture was stirred at 0°C for 15 min and then at rt for 15 h. The reaction mixture was filtered to remove dicyclohexylurea and the residue was washed with CH_2Cl_2. The combined filtrates were concentrated *in vacuo* and purified by silica gel flash column chromatography (eluent: EtOAc/petrol) to give *N*-acylated thiazolidines **6,7a-g**.

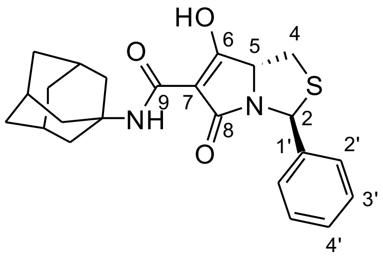
General procedure: Synthesis of bicyclic tetramates **8a-g**[1]

KO^{t}Bu (1.2 eq) was added to a solution of the *N*-acylated thiazolidine in THF and heated at reflux for 3 h. It was then cooled to rt, concentrated *in vacuo* and partitioned between Et_2O and water. The aqueous layer was extracted and acidified with 2M HCl (to pH 1) and extracted with EtOAc. The combined EtOAc extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (with 1% Et_3N) to give the desired product. The product was then dissolved in CH_2Cl_2 and washed with 5% citric acid. The organic fractions were dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield the desired bicyclic tetramates **9a-g**.

General procedure: Synthesis of carboxamide tetramates **9a-g'**

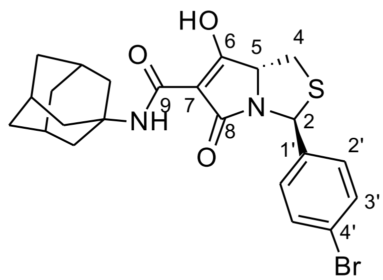
To tetramic acid (1.0 eq) dissolved in THF/toluene or DMSO/toluene (1:9, 10 mL/mmol), amine (1.5 eq) was added. The solution was heated at reflux for 16 h, cooled to rt and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (eluent: EtOAc/MeOH/1 % Et_3N). The product was dissolved in CH_2Cl_2 and washed with 5% citric acid. The organic fractions were dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield the bicyclic carboxamide tetramate. Where the major and minor tautomeric forms have distinct chemical shift values, they have been specified as either AB (major tautomeric form) or CD (minor tautomeric form) in compound characterisation.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-phenyl-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9a



Yield (0.19 g, 38 %); yellow solid, mp 94-96 °C; 2.7:1 AB:CD tautomers; R_f = 0.78 (EtOAc/MeOH 20:1); $[\alpha]_D^{25}$ = -132.0 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1623 (C=C), 1649 (C=O), 1691 (C=O), 3313 (N-H/O-H); δ_H (400 MHz, $CDCl_3$): 1.60 (6H, Adamantyl-C*H*$_2$), 1.95 (6H, Adamantyl-C*H*$_2$), 2.04 (3H, Adamantyl-C*H*), 2.84 - 2.98 (1H, m, $H4_A$), 3.10 - 3.20 (1H, m, $H4_B$), 4.35 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.58 (1H, app t, *J* = 7.7 Hz, H5 AB), 6.17 (1H, s, H2 AB), 6.26 (1H, s, H2 CD), 7.15 - 7.21 (1H, m, H4′), 7.22 - 7.29 (2H, m, H3′), 7.31 - 7.41 (2H, m, H2′), 7.85 (1H, br. s., NH/OH CD), 12.19 (1H, br. s., NH/OH AB); δ_C (100.6 MHz, $CDCl_3$): 29.2 (Adamantyl-*C*H), 32.4 (C4 AB), 32.6 (C4 CD), 35.7 (Adamantyl-*C*H_2 CD), 35.9 (Adamantyl-*C*H_2 AB), 41.4 (Adamantyl-*C*H_2), 52.9 (Adamantyl-C AB), 54.3 (Adamantyl-C CD), 61.9 (C2 AB), 62.4 (C2 CD), 67.2 (C5 AB), 70.5 (C5 CD), 85.3 (C7 CD), 94.9 (C7 AB), 126.1 (C2′ CD), 126.2 (C2′ AB), 127.8 (C4′ CD), 127.9 (C4′ AB), 128.4 (C3′ CD), 128.5 (C3′ AB), 140.2 (C1′ AB), 140.5 (C1′ CD), 165.8 (C9 AB), 166.4 (C9 CD), 172.2 (C8 AB), 178.0 (C8 CD), 187.8 (C6 AB), 191.1 (C6 CD); *m/z* (ESI^-) 409 ($[M-H]^-$, 100%); HRMS (ESI^-); $C_{23}H_{25}N_2O_3S$ $[M-H]^-$; found 409.1574, requires 409.1591.

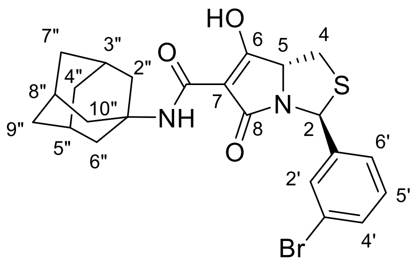
(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-bromophenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9b



Yield (2.80 g, 70 %); brown foam, 2.6:1 AB:CD tautomers, mp 108-110 °C; R_f = 0.72 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -159.5 (*c* = 0.25, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1625 (C=C), 1648 (C=O), 1688 (C=O), 3317 (O-H/N-H); δ_H (400 MHz, $CDCl_3$): 1.69 (6H, Adamantyl-C*H*$_2$), 2.05 (6H, Adamantyl-C*H*$_2$), 2.11 (3H, Adamantyl-C*H*), 2.96 - 3.06 (1H, m, $H4_A$), 3.20 - 3.27 (1H, m, $H4_B$), 4.39 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.63 (1H, app t, *J* = 7.7 Hz, H5 AB), 6.18 (1H, s, H2 AB), 6.27 (1H, s, H2 CD), 7.31- 7.36 (2H, m, Ar-C*H*), 7.40 (1H, br. s., NH AB), 7.46 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 7.94 (1H, br. s., NH CD), 10.78 (1H, br. s., OH); δ_C (100.6 MHz, $CDCl_3$): 29.2 (Adamantyl-*C*H), 32.5 (C4 AB), 32.8 (C4 CD), 35.8 (Adamantyl-*C*H_2 CD), 36.0 (Adamantyl-*C*H_2 AB), 41.5 (Adamantyl-*C*H_2 AB), 41.5 (Adamantyl-*C*H_2 CD), 53.1 (Adamantyl-C AB), 54.5 (Adamantyl-C CD), 61.5 (C2 AB),

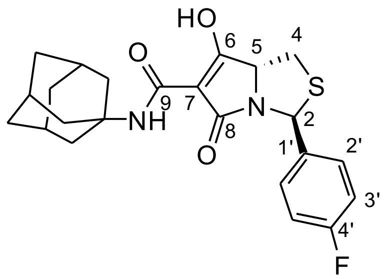
62.1 (C2 CD), 67.3 (C5 AB), 70.5 (C5 CD), 85.3 (C7 CD), 94.5 (C7 AB), 121.9 (C4' CD), 122.0 (C4' AB), 128.1 (C2' CD), 128.2 (C2' AB), 131.57 (C3' CD), 131.62 (C3' AB), 139.4 (C1' AB), 139.6 (C1' CD), 165.9 (C9 AB), 166.4 (C9 CD), 172.4 (C8 AB), 178.2 (C8 CD), 188.4 (C6 AB), 191.1 (C6 CD); *m/z* (ESI$^-$) 487, 489 ([M-H]$^-$, 100 %); HRMS (ESI$^-$); $C_{23}H_{24}N_2O_3BrS$ [M-H]$^-$; found 487.07009 and 489.06794, requires 487.06965 and 489.06760.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(3-bromophenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9c



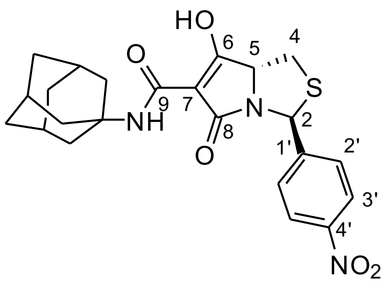
Yield (38%); R_f= 0.71 (EtOAc), $[\alpha]_D^{25}$ = -166.0 (*c* 0.15, MeOH), δ_H (400 MHz, CD_2Cl_2): 1.60 (s, 6H, 2xC2",6",10" major and minor), 1.96 (s, 6H, 2xC4",7",9" major and minor), 2.00 (s, 3H, C3",5",8" major and minor), 2.88 (dd, 1H J_1 12.0 Hz, J_2 8.0 Hz, H4 major and minor), 3.12 (dd, 1H 12.0 Hz, J_2 8.0 Hz, H4a major and minor), 4.56 (t, 1H, *J* 8.0 Hz, H5 minor), 4.56 (t, 1H, *J* 8.0 Hz, H5 major), 6.09 (s, 1H, H2 major), 6.18 (s, 1H, H2 minor), 7.12 (t, 1H, *J* 8.0 Hz, H5' major and minor), 7.28 (d, 1H, *J* 8.0 Hz, H4' major and minor), 7.32 (d, 1H, *J* 8.0 Hz, H6' major and minor), 7.52 (s, 1H, H2' major), 7.85 (s, 1H, H2' minor), 11.18 (s, 1H, N<u>H</u>), δ_C (100.6 MHz, CD_2Cl_2): 29.50 (C3",5",8" major and minor), 32.62 (C4 major), 32.93 (C4 minor), 35.84 (2xC2",6",10" minor), 36.07 (2xC2",6",10" major), 41.54 (2xC4",7",9" major and minor), 61.34 (C2 major), 62.16 (C2 minor), 67.34 (C5 major), 70.74 (C5 minor), 95.08 (C7 major and minor), 122.54 (C3' major and minor), 125.21 (C6' major and minor), 129.32 (C2' major and minor), 130.22 (C5' major and minor), 131.03 (C4' major and minor), 143.21 (C1' major), 143.45 (C1' minor), 165.98 (C9 major), 166.13 (C9 minor), 170.84 (C8 minor), 172.38 (C8 major), 188.08 (C6 major), 190.98 (C6 minor), *m/z* (ESI$^-$) 487 ([M-H]$^-$, 100%); HRMS (ESI$^-$); calculated for $C_{23}H_{24}BrN_2O_3S$; 487.0696; found; 487.0707.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-fluorophenyl)--6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9d



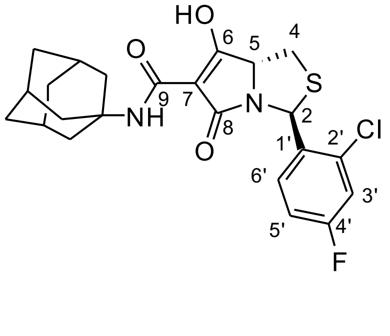
Yield (0.19 g, 56 %); brown oil; 2.7:1 AB:CD tautomers; R_f= 0.76 (EtOAc/MeOH 20:1); $[\alpha]_D^{25}$ = -177.5, (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1229 (C-F), 1625 (C=C), 1649 (C=O), 1690 (C=O), 3313 (N-H/O-H); δ_H (400 MHz, $CDCl_3$): 1.70 (6H, Adamantyl-C*H*$_2$), 2.05 (6H, Adamantyl-C*H*$_2$), 2.12 (3H, Adamantyl-C*H*), 2.96 - 3.05 (1H, m, $H4_A$), 3.26 (1H, dd, *J* = 11.3, 7.1 Hz, $H4_B$), 4.42 (1H, app t, *J* = 7.6 Hz, H5 CD), 4.66 (1H, app t, *J* = 7.8 Hz, H5 AB), 6.22 (1H, s, H2 AB), 6.31 (1H, s, H2 CD), 7.04 (2H, app t, *J* = 7.8 Hz, H3′), 7.38 - 7.51 (2H, m, H2′), 7.95 (1H, br. s., NH/OH CD), 11.34 (1H, br. s., NH/OH AB); δ_C (100.6 MHz, $CDCl_3$): 29.2 (Adamantyl-*C*H), 32.5 (C4 AB), 32.8 (C4 CD), 35.8 (Adamantyl-CH_2 CD), 36.0 (Adamantyl-CH_2 AB), 41.50 (Adamantyl-CH_2 AB), 41.54 (Adamantyl-CH_2 CD), 53.1 (Adamantyl-C AB), 54.5 (Adamantyl-C CD), 61.5 (C2 AB), 62.0 (C2 CD), 67.4 (C5 AB), 70.5 (C5 CD), 94.7 (C7), 115.38 (d, *J* = 21.5 Hz, C3′ CD), 115.43 (d, *J* = 21.5 Hz, C3′ AB), 128.1 (d, *J* = 8.0 Hz, C2′ CD), 128.2 (d, *J* = 8.0 Hz, C2′ AB), 136.1 (d, *J* = 3.2 Hz, C1′ AB), 136.3 (d, *J* = 3.2 Hz, C1′ CD), 162.3 (d, *J* = 246.4 Hz, C4′ CD), 162.4 (d, *J* = 247.2 Hz, C4′ AB), 166.0 (C9 AB), 166.5 (C9 CD), 172.4 (C8 AB), 178.1 (C8 CD), 188.3 (C6 AB), 191.1 (C6 CD); *m/z* (ESI^-) 427 ($[M-H]^-$, 100%); HRMS (ESI^-); $C_{23}H_{24}FN_2O_3S$ $[M-H]^-$; found 427.1502, requires 427.1497.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-nitrophenyl)--6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9e



Yield (0.53 g, 35 %); brown oil; 2.4:1 AB:CD tautomers; R_f = 0.76 (EtOAc/MeOH 20:1); $[\alpha]_D^{25}$ = -93.8, (*c* = 0.50, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1347 (sym $ArNO_2$), 1522 (asym $ArNO_2$), 1643 (C=O, br with shoulder towards lower wavenumber), 1682 (C=O), 3333 (N-H/O-H); δ_H (400 MHz, $CDCl_3$): 1.68 (6H, Adamantyl-CH_2), 2.00 - 2.08 (6H, m, Adamantyl-CH_2), 2.08 - 2.16 (3H, m, Adamantyl-C*H*), 2.99 - 3.09 (1H, m, $H4_A$), 3.21 - 3.30 (1H, m, $H4_B$), 4.40 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.64 (1H, app t, *J* = 7.3 Hz, H5 AB), 6.27 (1H, s, H2 AB), 6.36 (1H, s, H2 CD), 7.55 - 7.65 (2H, m, H2′), 8.15 - 8.21 (2H, m, H3′), 7.38 (1H, br. s., NH AB), 7.97 (1H, br. s., NH CD), 10.82 (1H, br. s., OH); δ_C (100.6 MHz, $CDCl_3$): 29.2 (Adamantyl-*C*H), 32.7 (C4 AB), 32.9 (C4 CD), 35.7 (Adamantyl-CH_2 CD), 35.9 (Adamantyl-CH_2 AB), 41.4 (Adamantyl-CH_2 AB), 41.5 (Adamantyl-CH_2 CD), 53.3 (Adamantyl-C AB), 54.6 (Adamantyl-C CD), 61.3 (C2 AB), 61.8 (C2 CD), 67.6 (C5 AB), 70.6 (C5 CD), 85.1 (C7 CD), 93.7 (C7 AB), 123.77 (C3' CD), 123.79 (C3′ AB), 127.2 (C2′ CD), 127.3 (C2′ AB), 147.4 (C1' CD), 147.5 (C1′ AB), 147.6 (C4′ AB), 147.8 (C4′ CD), 166.0 (C9 AB), 166.4 (C9 CD), 172.6 (C8 AB), 178.3 (C8 CD), 189.1 (C6 AB), 190.8 (C6 CD); *m/z* (ESI^-) 454 ($[M-H]^-$, 12%); HRMS (ESI^-); $C_{23}H_{24}N_3O_5S$ $[M-H]^-$; found 454.1438, requires 454.1442.

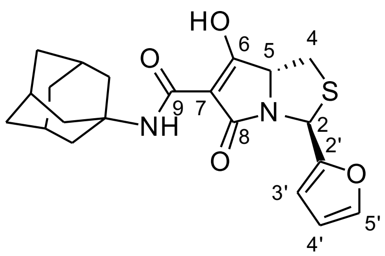
(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(2-chloro-4-fluorophenyl)--6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9f



Yield (0.15 g, 60 %); yellow solid, mp 120°C; 2.5:1 AB:CD tautomers; R_f = 0.78 (EtOAc/MeOH 20:1); $[\alpha]_D^{25}$ = -147.5, (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1234 (C-F), 1626 (C=C), 1649 (C=O), 1692 (s, C=O), 3318 (N-H/O-H); δ_H (400 MHz, $CDCl_3$):

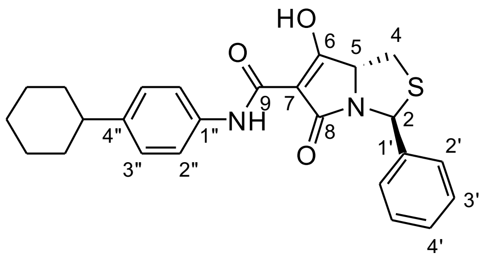
1.63 - 1.75 (6H, Adamantyl-CH_2), 2.00 - 2.09 (6H, Adamantyl-CH_2), 2.09 - 2.18 (3H, Adamantyl-C*H*), 2.96 - 3.04 (1H, m, $H4_A$), 3.20 - 3.28 (1H, m, $H4_B$), 4.57 (1H, dd, *J* = 8.6, 7.6 Hz, H5 CD), 4.79 (1H, dd, *J* = 8.8, 6.9 Hz, H5 AB), 6.42 (1H, s, H2 AB), 6.49 (1H, s, H2 CD), 6.98 (1H, app td, *J* = 8.3, 2.3 Hz, H5′), 7.13 (1H, dd, *J* = 8.3, 2.3 Hz, H3′), 7.36 - 7.44 (1H, m, H6′), 7.97 (1H, br. s., NH/OH CD), 11.69 (1H, br. s., NH/OH AB); δ_C (100.6 MHz, $CDCl_3$): 29.2 (Adamantyl-*C*H), 32.2 (C4 AB), 32.3 (C4 CD), 35.8 (Adamantyl-*C*H_2 CD), 36.0 (Adamantyl-*C*H_2 AB), 41.48 (Adamantyl-*C*H_2 AB), 41.54 (Adamantyl-*C*H_2 CD), 53.3 (Adamantyl-C AB), 54.6 (Adamantyl-C CD), 59.1 (C2 AB), 59.7 (C2 CD), 68.4 (C5 AB), 71.5 (C5 CD), 85.0 (C7 CD), 94.0 (C7 AB), 114.2 (d, *J* = 21.5 Hz, C5′ CD), 114.3 (d, *J* = 21.5 Hz, C5′ AB), 117.29 (d, *J* = 25.4 Hz, C3′ AB), 117.31 (d, *J* = 25.4 Hz, C3′ CD), 127.2 (d, *J* = 9.5 Hz, C6′ CD), 127.4 (d, *J* = 8.7 Hz, C6′ AB), 133.0 (d, *J* = 10.3 Hz, C2′ CD), 133.1 (d, *J* = 10.3 Hz, C2′ AB), 134.6 (d, *J* = 4.0 Hz, C1′ AB), 134.9 (d, *J* = 4.0 Hz, C1′ CD), 161.8 (d, *J* = 249.5 Hz, C4′ CD), 161.9 (d, *J* = 250.3 Hz, C4′ AB), 166.0 (C9 AB), 166.5 (C9 CD), 172.0 (C8 AB), 177.8 (C8 CD), 188.7 (C6 AB), 191.0 (C6 CD); *m/z* (ESI^-) 461 ($[M-H]^-$, 15%); HRMS (ESI^-); $C_{23}H_{23}ClFN_2O_3S$ $[M-H]^-$; found 461.1108, requires 461.1107.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(2-furanyl)--6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9g



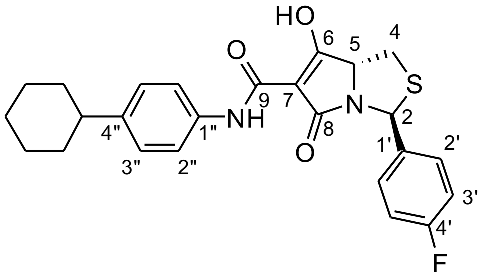
Yield (0.28 g, 92 %); brown soild, mp 88-90 °C; 3:1 AB:CD tautomers; R_f = 0.76 (EtOAc/MeOH 20:1); $[\alpha]_D^{25}$ = -141.7 (*c* = 0.06, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1627 (C=C), 1649 (C=O), 1692 (C=O), 3318 (N-H/O-H); δ_H (500 MHz, CD_2Cl_2): 1.70 (6H, Adamantyl-CH_2), 2.06 (6H, Adamantyl-CH_2), 2.10 (3H, Adamantyl-C*H*), 3.06 (1H, dd, *J* = 11.0, 7.1 Hz, $H4_A$), 3.41 (1H, dd, *J* = 11.0, 8.1 Hz, $H4_B$), 4.42 (1H, app t, *J* = 7.4 Hz, H5 CD), 4.69 (1H, app t, *J* = 7.5 Hz, H5 AB), 6.26 (1H, s, H2 AB), 6.32 - 6.35 (3H, m, H2 CD + H3' + H4'), 7.35 (1H, br. s., NH/OH AB), 7.39 - 7.44 (1H, m, H5′), 7.94 (1H, br. s., NH/OH CD); δ_C (125.8 MHz, CD_2Cl_2): 30.0 (Adamantyl-*C*H), 32.6 (C4 AB), 33.1 (C4 CD), 36.4 (Adamantyl-*C*H_2, CD), 36.6 (Adamantyl-*C*H_2, AB), 42.07 (Adamantyl-*C*H_2 AB), 42.13 (Adamantyl-*C*H_2 CD), 53.6 (Adamantyl-C, obscured by CD_2Cl_2 signal but HMBC corrleation seen with adamantyl-CH_2), 56.1 (C2 AB), 56.6 (C2 CD), 67.2 (C5 AB), 70.5 (C5 CD), 85.4 (C7 CD), 95.0 (C7 AB), 107.4 (C3′), 110.9 (C4′), 143.4 (C5'), 153.5 (C2′ AB), 153.7 (C2′ CD), 166.6 (C9 AB), 167.1 (C9 CD), 172.8 (C8 AB), 178.7 (C8 CD), 189.5 (C6 AB), 192.0 (C6 CD); *m/z* (ESI^-) 399 ($[M-H]^-$, 62 %); HRMS (ESI^-); $C_{21}H_{23}N_2O_4S$ $[M-H]^-$; found 399.13827, requires 399.13840.

(-)-(2*S*,5*R*)-2-Phenyl-*N*-(4-cyclohexylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9h



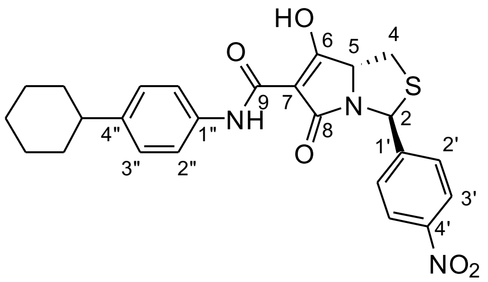
Yield (0.41 g, 54 %); yellow foam, mp 88 °C; 15:1 AB:CD tautomers; R_f= 0.73 (EtOAc/MeOH 20:1); $[\alpha]_D^{25}$ = -159.0 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1630 (C=C), 1651 (C=O), 1692 (C=O), 3281 (N-H/O-H); δ_H (400 MHz, CD_2Cl_2): 1.20 - 1.33 (1H, m, Cy-C*H*$_2$), 1.34 - 1.46 (4H, m, Cy-C*H*$_2$), 1.70 - 1.79 (1H, m, Cy-C*H*$_2$), 1.80 - 1.92 (4H, m, Cy-C*H*$_2$), 2.41 - 2.59 (1H, m, Cy-C*H*), 3.04 (1H, dd, *J* = 11.2, 8.7 Hz, $H4_A$), 3.32 (1H, dd, *J* = 11.2, 6.9 Hz, $H4_B$), 4.56 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.89 (1H, app t, *J* = 7.7 Hz, H5 CD), 6.26 (1H, s, H2 AB), 6.35 (1H, s, H2 CD), 7.20 (2H, d, *J* = 8.6 Hz, H3″), 7.29 - 7.35 (1H, m, H4′), 7.36 - 7.42 (2H, m, H3′), 7.46 - 7.53 (4H, m, H2′ and H2″), 7.98 (1H, br. s., OH), 9.28 (1H, br. s., NH); δ_C (125.8 MHz, CD_2Cl_2): 26.7 (Cy-*C*H$_2$), 27.4 (Cy-*C*H$_2$), 33.0 (C4), 35.0 (Cy-*C*H$_2$), 44.6 (Cy-*C*H), 62.2 (C2 AB), 63.1 (C2 CD), 67.2 (C5 AB), 71.8 (C5 CD), 99.3 (C7), 121.0 (C2″), 126.9 (C2′), 127.9 (C3″), 128.7 (C4′), 129.2 (C3′), 134.8 (C1″), 140.9 (C1′), 145.8 (C4″), 164.4 (C9 AB), 165.4 (C9 CD), 172.1 (C8 AB), 178.6 (C8 CD), 184.9 (C6 AB), 191.7 (C6 CD); *m/z* (ESI^-) 433 ($[M-H]^-$, 34%); HRMS (ESI^-); $C_{25}H_{25}N_2O_3S$ $[M-H]^-$; found 433.1598, requires 433.1591.

(-)-(2*S*,5*R*)-2--(4-Fluorophenyl)--*N*-(4-cyclohexylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9i



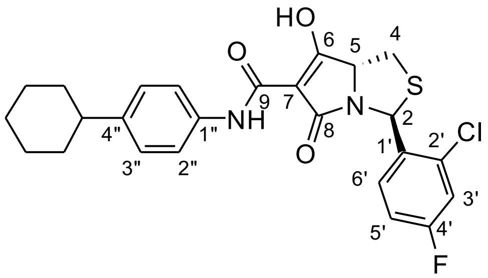
Yield (0.17 g, 45 %); brown oil; 13:1 AB:CD tautomers; R_f = 0.66 (EtOAc 100 %); $[\alpha]_D^{25}$ = -220.5 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1228 (C-F), 1636 (C=C), 1648 (C=O), 1689 (C=O), 3290, 3307 (N-H/O-H); δ_H (400 MHz, CD_2Cl_2): 1.21 - 1.32 (1H, m, Cy-C*H*$_2$), 1.33 - 1.48 (4H, m, Cy-C*H*$_2$), 1.70 - 1.79 (1H, m, Cy-C*H*$_2$), 1.80 - 1.91 (4H, m, Cy-C*H*$_2$), 2.45 - 2.56 (1H, m, Cy-C*H*), 3.04 (1H, dd, *J* = 11.2, 8.7 Hz, $H4_A$), 3.32 (1H, dd, *J* = 11.2, 6.9 Hz, $H4_B$), 4.53 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.87 (1H, app t, *J* = 7.7 Hz, H5 AB), 6.23 (1H, s, H2 AB), 6.33 (1H, s, H2 CD), 7.08 (2H, app t, *J* = 8.6 Hz, H3′), 7.20 (2H, d, *J* = 8.3 Hz, H3″), 7.43 - 7.52 (4H, m, H2′ and H2″), 9.26 (1H, s, NH), 9.45 (1H, br. s., OH); δ_C (100.6 MHz, CD_2Cl_2): 26.7 (Cy-*C*H$_2$), 27.4 (Cy-*C*H$_2$), 33.0 (C4), 35.0 (Cy-*C*H$_2$), 44.6 (Cy-*C*H), 61.7 (C2), 67.1 (C5), 99.3 (C7), 116.0 (d, *J* = 21.5 Hz, C3′), 121.0 (C2″), 127.9 (C3″), 128.9 (d, *J* = 8.0 Hz, C2′), 134.7 (C1″), 136.7 (d, *J* = 3.2 Hz, C1′), 145.8 (C4″), 163.1 (d, *J* = 246.4 Hz, C4′), 164.3 (C9), 172.2 (C8), 185.0 (C6); *m/z* (ESI^-) 451 ($[M-H]^-$, 5%); HRMS (ESI^-); $C_{25}H_{24}FN_2O_3S$ $[M-H]^-$; found 451.1501, requires 451.1497.

(-)-(2*S*,5*R*)-2--(4-Nitrophenyl)--*N*-(4-cyclohexylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9j



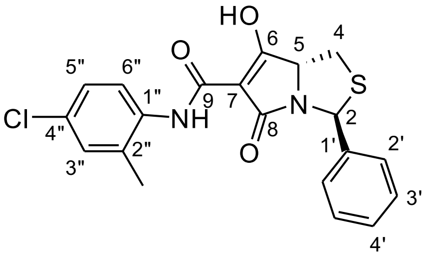
Yield (0.076 g, 59 %); brown solid, mp 108-110 °C; 12.5:1 AB:CD tautomers; R_f= 0.46 (EtOAc 100 %); $[\alpha]_D^{25}$ = -89.5 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1347 (sym $ArNO_2$), 1522 (asym $ArNO_2$), 1630 (C=C), 1651 (C=O), 1695 (C=O), 3323 (N-H/O-H); δ_H (400 MHz, CD_2Cl_2): 1.18 - 1.32 (1H, m, Cy-C*H*2), 1.33 - 1.48 (4H, m, Cy-C*H*2), 1.69 - 1.78 (1H, m, Cy-C*H*2), 1.78 - 1.90 (4H, m, Cy-C*H*2), 2.46- 2.54 (1H, m, Cy-C*H*), 3.10 (1H, dd, *J* = 11.3, 8.6 Hz, $H4_A$), 3.34 (1H, dd, *J* = 11.3, 7.1 Hz, $H4_B$), 4.53 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.87 (1H, dd, *J* = 8.3, 7.1 Hz, H5 AB), 6.32 (1H, s, H2 AB), 6.42 (1H, s, H2 CD), 7.21 (2H, d, *J* = 8.3, H3″), 7.47 (2H, d, *J* = 8.3 Hz, H2″), 7.66 (2H, d, *J* = 8.6 Hz, H2′), 7.89 (1H, br. s., OH), 8.22 (2H, d, *J* = 8.8 Hz, H3′), 9.20 (1H, br. s., NH); δ_C (125.8 MHz, CD_2Cl_2): 26.7 (Cy-*C*H2), 27.4 (Cy-*C*H2), 33.2 (C4 AB), 33.6 (C4 CD), 35.0 (Cy-*C*H2), 44.6 (Cy-*C*H), 61.6 (C2 AB), 62.5 (C2 CD), 67.2 (C5 AB), 71.6 (C5 CD), 86.3 (C7 CD), 99.0 (C7 AB), 121.0 (C2″), 124.4 (C3′), 127.9 (C2′), 127.9 (C3″), 134.6 (C1″), 146.0 (C4″), 148.0 (C1′), 148.3 (C4′), 164.3 (C9 AB), 165.3 (C9 CD), 172.4 (C8 AB), 178.7 (C8 CD), 185.4 (C6 AB), 191.5 (C6 CD); *m/z* (ESI^-) 478 ($[M-H]^-$, 12%); HRMS (ESI^-); $C_{25}H_{24}N_3O_5S$ $[M-H]^-$; found 478.1437, requires 478.1442.

(-)-(2*S*,5*R*)-2-(2-Chloro-4-fluorophenyl)-*N*-(4-cyclohexylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9k



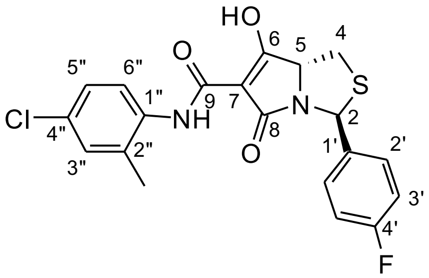
Yield (0.41 g, 73 %); yellow foam, mp 100-102 °C; 15:1 AB:CD tautomers; R_f= 0.57 (EtOAc 100 %); $[\alpha]_D^{25}$ = -184.8 (*c* = 0.40, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1234 (C-F), 1654 (C=O), 1694 (C=O); δ_H (400 MHz, CD_2Cl_2): 1.18 - 1.32 (1H, m, Cy-C*H*2), 1.33 - 1.48 (4H, m, Cy-C*H*2), 1.68 - 1.77 (1H, m, Cy-C*H*2), 1.78 - 1.91 (4H, m, Cy-C*H*2), 2.41 - 2.57 (1H, m, Cy-C*H*), 3.05 (1H, dd, *J* = 11.0, 9.1 Hz, $H4_A$), 3.32 (1H, dd, *J* = 11.0, 6.9 Hz, $H4_B$), 4.67 (1H, app t , *J* = 7.5 Hz, H5 CD), 5.00 (1H, dd, *J* = 9.1, 6.9 Hz, H5 AB), 6.43 (1H, s, H2 AB), 6.43 (1H, s, H2 CD), 7.05 (1H, app td, *J* = 8.3, 2.7 Hz, H5′), 7.16 - 7.23 (3H, m, H3′ and H3″), 7.44 - 7.51 (3H, m, H6′ and H2″), 9.22 (1H, br. s., NH), 10.04 (1H, br. s., OH); δ_C (125.8 MHz, CD_2Cl_2): 26.7 (Cy-*C*H2), 27.4 (Cy-*C*H2), 32.8 (C4), 35.0 (Cy-*C*H2), 44.6 (Cy-*C*H), 59.3 (C2 AB), 60.3 (C2 CD), 67.8 (C5 AB), 72.4 (C5 CD), 86.2 (C7 CD), 98.9 (C7 AB), 115.0 (d, *J* = 20.7 Hz, C5′), 117.8 (d, *J* = 25.4 Hz, C3′), 121.0 (C2″), 127.9 (C3″), 128.2 (d, *J* = 9.5 Hz, C6′), 133.5 (d, *J* = 10.3 Hz, C2′), 134.7 (C1″), 135.1 (d, J = 2.4 Hz, C1′), 145.9 (C4″), 162.6 (d, J = 249.9 Hz, C4′), 164.3 (C9 AB), 165.4 (C9 CD), 171.7 (C8 AB), 178.2 (C8 CD), 185.2 (C6 AB), 191.5 (C6 CD); *m/z* (ESI^-) 485 ($[M-H]^-$, 100%); HRMS (ESI^-); $C_{25}H_{23}ClFN_2O_3S$ $[M-H]^-$; found 485.1125, requires 485.1107.

(-)-(2*S*,5*R*)-2-(Phenyl)--*N*-(4-chloro-2-methylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9l



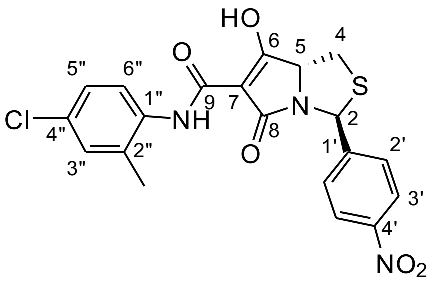
Yield (0.13 g, 40 %); yellow solid, mp 88 °C; R_f = 0.63 (EtOAc/MeOH 12:1); $[\alpha]_D^{25}$ = -145.0 (c = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1636 (C=C), 1691 (C=O), 3210, 3266 (N-H/O-H); δ_H (400 MHz, $CDCl_3$): 2.34 (3H, s, CH_3), 3.06 (1H, dd, J = 11.1, 8.4 Hz, $H4_A$), 3.34 (1H, dd, J = 11.1, 7.0 Hz, $H4_B$), 4.50 (1H, br. s., OH), 4.90 (1H, dd, J = 8.3, 7.0 Hz, H5), 6.31 (1H, s, H2), 7.17 - 7.23 (2H, m, H3″ + H5″), 7.29 - 7.35 (1H, m, H4′), 7.36 - 7.42 (2H, m, H3′), 7.47 - 7.52 (2H, m, H2′), 8.04 (1H, d, J = 9.4 Hz, H6”), 9.39 (1H, br. s., NH); δ_C (100.6 MHz, CD_2Cl_2): 17.9 (CH_3), 32.9 (C4), 62.1 (C2), 67.2 (C5), 99.8 (C7), 123.0 (C6″), 126.8 (C2′), 127.0 (C5″), 128.8 (C4′), 129.2 (C3′), 130.1 (C1″), 130.8 (C3" + C4″), 134.4 (C2″), 140.2 (C1′), 164.1 (C9), 172.1 (C8), 184.3 (C6); *m/z* (ESI^-) 399 ($[M-H]^-$, 100%); HRMS (ESI^-); $C_{20}H_{16}ClN_2O_3S$ $[M-H]^-$; found 399.0576, requires 399.0576.

(-)-(2*S*,5*R*)-2-(4-Fluorophenyl)-*N*-(4-chloro-2-methylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9m



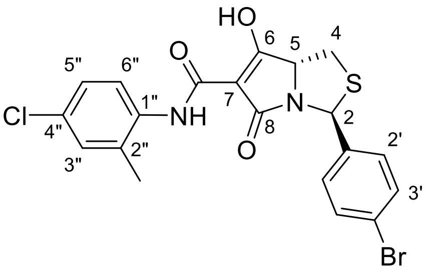
Yield (0.082 g, 40 %); brown solid, mp 126 °C; R_f = 0.57 (EtOAc/MeOH 12:1); $[\alpha]_D^{25}$ = -165.14 (c = 0.39, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1226 (C-F), 1631 (C=C), 1655 (C=O), 1690 (C=O); δ_H (400 MHz, CD_2Cl_2): 2.31 (3H, s, CH_3), 3.05 (1H, dd, J = 10.9, 8.9 Hz, $H4_A$), 3.33 (1H, dd, J = 11.0, 6.9 Hz, $H4_B$), 4.83 - 4.92 (1H, m, H5), 6.23 (1H, s, H2), 7.09 (2H, app t, J = 8.4 Hz, H3′), 7.16 - 7.24 (2H, m, H3″ + H5″), 7.49 (2H, dd, J = 8.3, 5.3 Hz, H2′), 8.04 (1H, d, J = 9.3 Hz, H6″), 9.39 (1H, br. s., NH), 11.00 (1H, br. s., OH); δ_C (125.8 MHz, $CDCl_3$): 17.6 (CH_3), 32.4 (C4), 61.1 (C2), 66.4 (C5), 99.2 (C7), 115.7 (d, J = 21.9 Hz, C3′), 122.7 (C6″), 126.7 (C5″), 128.3 (d, J = 8.6 Hz, C2′), 130.0 (C1″), 130.1 (C4″), 130.4 (C3″), 133.4 (C2″), 135.5 (d, J = 3.8 Hz, C1′), 162.6 (d, J = 248.0 Hz, C4′), 163.6 (C9), 171.7 (C8), 184.1 (C6); *m/z* (ESI^-) 417 ($[M-H]^-$, 76%); HRMS (ESI^-); $C_{20}H_{15}ClFN_2O_3S$ $[M-H]^-$; found 417.0484, requires 417.0481.

(-)-(2*S*,5*R*)-2-(4-Nitrophenyl)-*N*-(4-chloro-2-methylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9n



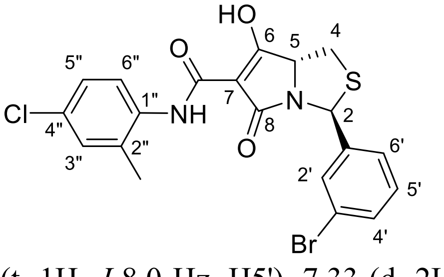
Yield (0.056 g, 37 %); brown solid, mp 190 °C; R_f = 0.62 (EtOAc/MeOH 12:1); $[\alpha]_D^{25}$ = -94.0 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1347 (sym $ArNO_2$), 1522 (asym $ArNO_2$), 1634 (C=C), 1693 (C=O); δ_H (400 MHz, CD_2Cl_2): 2.32 (3H, s, C*H*$_3$), 3.11 (1H, dd, *J* = 11.2, 8.6 Hz, $H4_A$), 3.36 (1H, dd, *J* = 11.2, 7.0 Hz, $H4_B$), 4.92 (1H, dd, *J* = 8.4, 7.0 Hz, H5), 5.02 (1H, br. s., OH), 6.32 (1H, s, H2), 7.18 - 7.24 (2H, m, H3″ + H5″), 7.67 (2H, d, *J* = 8.6 Hz, H2′), 8.03 (1H, d, *J* = 8.6 Hz, H6″), 8.23 (2H, d, *J* = 8.8 Hz, H3′), 9.32 (1H, br. s., NH); δ_C (125.8 MHz, CD_2Cl_2): 17.9 (*C*H$_3$), 33.2 (C4), 61.5 (C2), 67.2 (C5), 99.7 (C7), 123.3 (C6″), 124.5 (C3′), 127.1 (C5″), 127.9 (C2′), 130.5 (C1″), 130.9 (C3″), 131.0 (C4″), 134.2 (C2″), 147.9 (C1′), 148.3 (C4′), 164.2 (C9), 172.4 (C8), 184.9 (C6); *m/z* (ESI^-) 444 ($[M-H]^-$, 69%); HRMS (ESI^-); $C_{20}H_{15}ClN_3O_5S$ $[M-H]^-$; found 444.0426, requires 444.0426.

(-)-(2*S*,5*R*)-2-(4-Bromophenyl)-*N*-(4-chloro-2-methylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9o



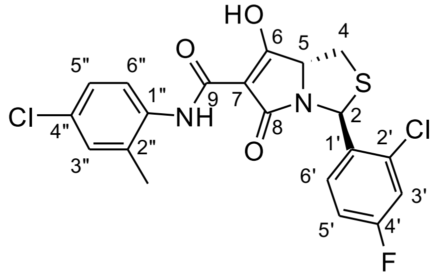
Yield (40%); brown solid; R_f = 0.71 (EtOAc), $[\alpha]_D^{25}$ = -148.0 (*c* = 0.15, MeOH); δ_H (400 MHz, CD_2Cl_2): 2.23 (s, 3H, C<u>H</u>$_3$), 2.94 (dd, 1H J_1 12.0 Hz, J_2 8.0 Hz, H4), 3.22 (dd, 1H .0 Hz, J_2 8.0 Hz, H4a), 4.79 (t, 1H, *J* 8.0 Hz, H5), 6.11 (s, 1H, H2), 7.10 (d, 2H, *J* 12.0 Hz, H3'',5''), 7.28 (d, 2H, *J* 12.0 Hz, H2',6'), 7.42 (d, 2H, *J* 12.0 Hz, H3',5'), 7.94 (d, 2H, *J* 8.0 Hz, H6''), 9.28 (s, 1H, N<u>H</u>), δ_C (100.6 MHz, CD_2Cl_2):17.37 (<u>C</u>H$_3$), 32.45 (C4), 61.17 (C2), 66.60 (C5), 99.28 (C7), 122.11 (C4'), 122.61 (C6''), 126.51 (C5''), 128.22 (C2',6'), 129.01 (C4''), 130.27 (C3''), 131.76 (C3',5'), 133.74 (C1''), 139.32 (C2''), 142.8 (C1'), 163.69 (C9), 171.70 (C8), 184.03 (C6), *m/z* (ESI^-) 477 ($[M-H]^-$); HRMS (ESI^-); calculated for $C_{20}H_{17}N_2SClBrO_3$; 476.9681; found; 476.9692.

(-)-(2*S*,5*R*)-2-(3-Bromophenyl)-*N*-(4-chloro-2-methylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9p



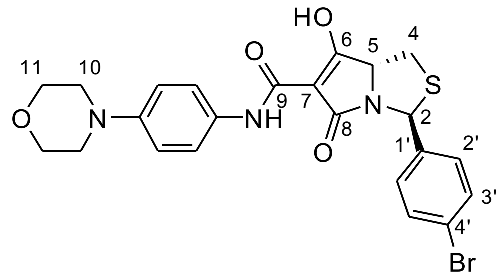
Yield (38% ,reactant used was impure); brown solid; R_f = 0.47 (EtOAc), $[\alpha]_D^{25}$ = -185.0 (*c* = 0.13, MeOH); δ_H (400 MHz, CD_2Cl_2): 2.23 (s, 3H, C<u>H</u>$_3$), 2.95 (dd, 1H J_1 12.0 Hz, J_2 8.0 Hz, H4), 3.23 (dd, 1H 12.0 Hz, J_2 8.0 Hz, H4a), 4.82 (t, 1H, *J* 8.0 Hz, H5), 6.12 (s, 1H, H2), 7.10 (d, 2H, *J* 12.0 Hz, H3'',5''), 7.19 (t, 1H, *J* 8.0 Hz, H5'), 7.33 (d, 2H, *J* 8.0 Hz, H4'), 7.37 (d, 2H, *J* 8.0 Hz, H6'), 7.56 (s, 1H, H2'), 7.94 (d, 2H, *J* 8.0 Hz, H6''), 9.29 (s, 1H, N<u>H</u>), δ_C (100.6 MHz, CD_2Cl_2): 17.38 (<u>C</u>H$_3$), 32.50 (C4), 60.93 (C2), 66.63 (C5), 99.28 (C7), 122.66 (C6''), 125.22 (C4'), 126.51 (C5''), 129.12 (C4''), 129.32 (C2'), 130.27 (C5'), 130.35 (C3''), 131.31 (C6'), 131.12 (C2''), 133.73 (C1''), 142.55 (C1'), 163.69 (C9), 172.70 (C8), 184.03 (C6), *m/z* (ESI^-) 477 ($[M-H]^-$); HRMS (ESI^-); calculated for $C_{20}H_{17}N_2SClBrO_3$; 476.9681; found; 476.9675.

(-)-(2*S*,5*R*)-2-(2-Chloro-4-fluorophenyl)-*N*-(4-chloro-2-methylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9q



Yield (0.06 g, 35 %); brown solid, mp 108-110 °C; R_f = 0.63 (EtOAc/MeOH 12:1); $[\alpha]_D^{25}$ = -218.0 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1235 (C-F), 1635 (C=C), 1697 (C=O); δ_H (400 MHz, CD_2Cl_2): 2.31 (3H, s, C*H*3), 3.06 (1H, dd, *J* = 11.0, 9.3 Hz, $H4_A$), 3.34 (1H, dd, *J* = 11.0, 6.6 Hz, $H4_B$), 5.04 (1H, dd, *J* = 9.3, 6.7 Hz, H5), 6.42 (1H, s, H2), 6.54 (1H, br. s., OH), 7.06 (1H, app td, *J* = 8.3, 2.7 Hz, H5′), 7.16 - 7.24 (3H, m, H3′ + H3″ + H5″), 7.48 (1H, dd, *J* = 8.8, 5.9 Hz, H6′), 8.04 (1H, d, *J* = 8.3 Hz, H6″), 9.35 (1H, br. s., NH); δ_C (125.8 MHz, CD_2Cl_2): 17.9 (*C*H3), 32.8 (C4), 59.2 (C2), 67.9 (C5), 99.6 (C7), 115.1 (d, *J* = 21.5 Hz, C5′), 117.8 (d, *J* = 24.6 Hz, C3′), 123.2 (C6″), 127.1 (C5″), 128.1 (d, *J* = 8.7 Hz, C6′), 130.3 (C1″), 130.8 (C3″), 130.9 (C4″), 133.5 (d, *J* = 10.3 Hz, C2′), 134.3 (C2″), 135.0 (d, *J* = 4.0 Hz, C1′), 162.6 (d, *J* = 249.9 Hz, C4′), 164.3 (C9), 171.7 (C8), 184.7 (C6); *m/z* (ESI^-) 451 ($[M-H]^-$, 100%); HRMS (ESI^-); $C_{20}H_{14}Cl_2FN_2O_3S$ $[M-H]^-$; found 451.0080, requires 451.0092.

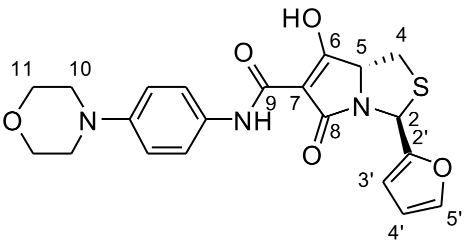
(-)-(2*S*,5*R*)-2--(4-Bromophenyl)-*N*-(4-morpholinophenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9r



Yield (0.15 g, 24 %); brown solid, mp 116 °C; R_f = 0.29 (EtOAc/MeOH 12:1); $[\alpha]_D^{25}$ = -154.5 (*c* = 0.22, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1627 (C=C), 1686 (C=O); δ_H (400 MHz, CD_2Cl_2): 3.04 (1H, dd, *J* = 11.2, 8.4 Hz, $H4_A$), 3.12 (4H, br. t, *J* = 4.7 Hz, H10), 3.30 (1H, dd, *J* = 11.2, 7.1 Hz, $H4_B$), 3.82 (4H, br. t, *J* = 4.7 Hz, H11), 4.80 (1H, br signal, H5), 6.22 (1H, s, H2), 6.90 (2H, d, *J* = 8.8 Hz, morpholinophenyl Ar-C*H*), 7.37 (2H, d, *J* = 8.3 Hz, H2′), 7.45 (2H, d, *J* = 8.8 Hz, morpholinophenyl Ar-C*H*), 7.51 (2H, d, *J* = 8.3 Hz, H3′), 8.08 (1H, br. s., NH/OH), 9.20 (1H, br. s., NH/OH); δ_C (125.8 MHz, CD_2Cl_2): 33.1 (C4), 49.9 (C10), 61.9 (C2), 67.3 (C5 + C11), 98.9 (C7), 116.4, 122.3 (morpholinophenyl Ar-*C*H), 122.5 (C4′), 128.8 (C2′), 129.3, 149.4 (morpholinophenyl Ar-C), 132.3 (C3'), 140.1 (C1′), 164.1 (C9), 172.4 (C8), 185.3 (C6); *m/z* (ESI^-) 514.0, 516.0 ([M-

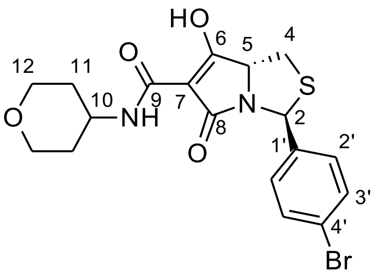
H]$^-$, 100%); HRMS (ESI$^-$); $C_{23}H_{21}O_4N_3BrS$ [M-H]$^-$; found 514.04451 and 516.04235, requires 514.04416, 516.04212.

(-)-(2*S*,5*R*)-2--(2-Furyl)-*N*-(4-morpholinophenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9s



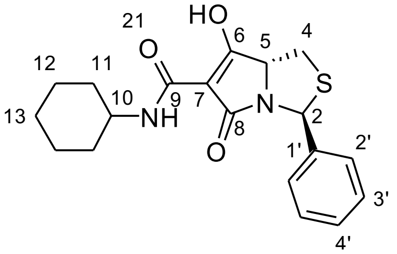
Yield (0.11 g, 85 %); brown solid, mp 110 °C; R_f = 0. 47 (EtOAc/MeOH 12:1); $[\alpha]_D^{25}$ = -153.3 (*c* = 0.06, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1630 (C=C), 1688 (C=O), 3274 (N-H/O-H); δ_H (400 MHz, CD_2Cl_2): 3.06 - 3.11 (1H, m, H4$_A$, obscured by H10), 3.12 (4H, br. t, *J* = 4.8 Hz, H10), 3.46 (1H, dd, *J* = 11.0, 8.1 Hz, H4$_B$), 3.82 (4H, br. t, *J* = 4.7 Hz, H11), 4.85 (1H, H5), 6.30 (1H, s, H2), 6.34 - 6.40 (2H, m, H3' + H4'), 6.90 (2H, d, *J* = 9.0 Hz, morpholinophenyl Ar-C*H*), 7.41 - 7.49 (3H, m, H5' + morpholinophenyl Ar-C*H*), 8.38 (1H, br. s., NH/OH), 9.18 (1H, br. s., NH/OH); δ_C (125.8 MHz, CD_2Cl_2): 32.5 (C4), 49.9 (C10), 55.7 (C2), 66.4 (C5), 67.3 (C11), 98.4 (C7), 107.7 (H3'), 111.0 (H4'), 116.4, 122.3 (morpholinophenyl Ar-*C*H), 129.3, 149.4 (morpholinophenyl Ar-C), 143.6 (C5'), 153.2 (C2′), 164.1 (C9), 172.2 (C8), 186.1 (C6); *m/z* (ESI$^-$) 426 ([M-H]$^-$, 100%); HRMS (ESI$^-$); $C_{21}H_{20}O_5N_3S$ [M-H]$^-$; found 426.11310, requires 426.11291.

(-)-(2*S*,5*R*)-2-(4-Bromophenyl)-*N*-(tetrahydro-2*H*-pyran-4-yl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9t



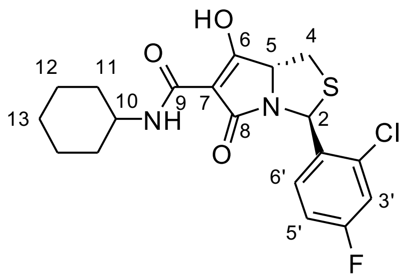
Yield (0.63 g, 55 %); yellow solid, mp 90-92 °C, 5.2:1 AB:CD tautomers; R_f = 0.37 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -171.9 (*c* = 0.39, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1623 (C=C), 1647 (C=O), 1688 (C=O), 3319 (O-H/N-H); δ_H (400 MHz, CD_2Cl_2): 1.50 - 1.71 (2H, m, H11), 1.83 - 1.98 (2H, m, H11), 3.01 (1H, dd, *J* = 11.3, 8.3 Hz, H4$_A$), 3.27 (1H, dd, *J* = 11.3, 7.1 Hz, H4$_B$), 3.41 - 3.52 (2H, m, H12), 3.88 - 3.99 (2H, m, H12), 4.00 - 4.11 (1H, m, H10), 4.42 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.75 (1H, app t, *J* = 7.7 Hz, H5 AB), 6.18 (1H, s, H2 AB), 6.27 (1H, s, H2 CD), 6.89 (2H, br. s., NH + OH), 7.35 (2H, d, *J* = 8.3 Hz, H2'), 7.50 (2H, d, *J* = 8.5 Hz, H3'); δ_C (125.8 MHz, CD_2Cl_2): 33.0 (C4), 33.3 (C11), 45.9 (C10 AB), 47.7 (C10 CD), 62.0 (C2 AB), 62.7 (C2 CD), 66.9 (C12), 67.4 (C5 AB), 71.4 (C5 CD), 85.5 (C7 CD), 97.2 (C7 AB), 122.4 (C4'), 128.8 (C2'), 132.2 (C3'), 140.3 (C4'), 165.9 (C9 AB), 166.5 (C9 CD), 172.5 (C8 AB), 178.8 (C8 CD), 186.6 (C6 AB), 191.6 (C6 CD); *m/z* (ESI$^-$) 437, 439 ([M-H]$^-$, 100 %); HRMS (ESI$^-$); $C_{18}H_{18}N_2O_4BrS$ [M-H]$^-$; found 437.01407 and 439.01190, requires 437.01761 and 439.01557.

(-)-(2*S*,5*R*)-2-Phenyl-*N*-(cyclohexyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9u



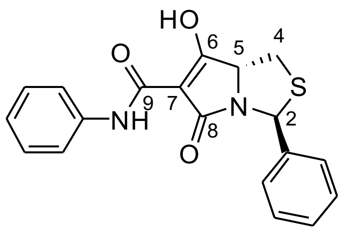
Yield (0.29 g, 49 %); brown solid, mp 54 °C; R_f = 0.77 (EtOAc/MeOH 96:4); $[\alpha]_D^{25}$ = -261.5 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1619 (C=C), 1645 (C=O), 1686 (C=O), 3324 (N-H/O-H); δ_H (500 MHz, Methanol-*d*$_4$) 1.23 - 1.47 (5H, m, 2 x H11, 2 x H12, H13), 1.57 - 1.67 (1H, m, H13), 1.70 - 1.82 (2H, m, H12), 1.86 - 1.96 (2H, m, H11), 3.01 (1H, dd, *J* = 11.0, 8.4 Hz, H4$_A$), 3.27 - 3.30 (1H, m, H4$_B$, obscured by solvent peak), 3.79 - 3.89 (1H, m, H10), 4.82 (1H, app t, *J* = 7.7 Hz, H5), 6.24 (1H, s, H2), 7.26 - 7.29 (1H, m, H4'), 7.32 - 7.37 (2H, m, H3'), 7.44 - 7.48 (2H, m, H2'); δ_C (125.8 MHz, Methanol-*d*$_4$): 25.8 (C12), 26.6 (C13), 33.4 (C4), 33.7 (C11), 49.8 (C10), 63.5 (C2), 69.4 (C5), 95.3 (C7), 127.6 (C2'), 129.1 (C4'), 129.7 (C3'), 142.3 (C1'), 166.1 (C9), 175.5 (C8), 188.6 (C6); *m/z* (ESI$^-$) 357 ([M-H]$^-$, 100 %); HRMS (ESI$^+$); $C_{19}H_{23}O_3N_2S$ [M+H]$^+$; found 359.14265, requires 359.14239.

(-)-(2*S*,5*R*)-2-(2-Chloro-4-fluorophenyl)-*N*-(cyclohexyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9v



Yield (0.16 g, 40 %); yellow foam; mp 80-82 °C; R_f = 0.70 (EtOAc/MeOH 96:4); $[\alpha]_D^{25}$ = -291.6 (*c* = 0.27, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1620 (C=C), 1646 (C=O), 1689 (C=O), 3326 (NH/OH); δ_H (400 MHz, Methanol-*d*$_4$) 1.23 - 1.47 (5H, m, 2 x H11, 2 x H12, H13), 1.57 - 1.67 (1H, m, H13), 1.70 - 1.82 (2H, m, H12), 1.86 - 1.96 (2H, m, H11), 3.03 (1H, dd, *J* = 10.8, 8.8 Hz, H4$_A$), 3.27 - 3.33 (1H, m, H4$_B$, obscured by solvent peak), 3.79 - 3.89 (1H, m, H10), 4.97 (1H, dd, *J* = 8.2, 7.2 Hz, H5), 6.40 (1H, s, H2), 7.11 (1H, app td, *J* = 8.4, 2.5 Hz, H5'), 7.26 (1H, dd, *J* = 8.6, 2.5 Hz, H3'), 7.58 (1H, dd, *J* = 8.6, 6.0 Hz, H6'); δ_C (125.8 MHz, Methanol-*d*$_4$): 25.8 (C12), 26.5 (C13), 33.0 (C4), 33.7 (C11), 49.6 (C10), 60.5 (C2), 70.2 (C5), 94.6 (C7), 115.6 (d, *J* = 21.9 Hz, C5′), 118.1 (d, *J* = 24.8 Hz, C3′), 129.3 (d, *J* = 9.5 Hz, C6′), 134.1 (d, *J* = 10.5 Hz, C2′), 136.8 (d, *J* = 3.8 Hz, C1′), 163.5 (d, *J* = 248.9 Hz, C4′), 166.1 (C9), 175.2 (C8), 189.2 (C6); *m/z* (ESI$^-$) 409 ([M-H]$^-$, 100 %); HRMS (ESI$^+$); $C_{19}H_{19}O_3N_2ClFS$ [M+H]$^+$; found 409.07999, requires 409.07835.

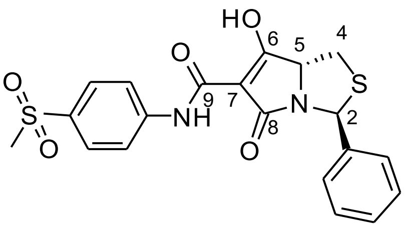
(-)-(2*S*,5*R*)-2-Phenyl-*N*-(phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9w



Yield (0.16 g, 55 %); brown solid, mp 156-160 °C; R_f = 0.51 (EtOAc/MeOH 98:2); $[\alpha]_D^{25}$ = -72.5 (*c* = 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1633 (C=C), 1651 (C=O), 1691 (C=O), 3289 (N-H/O-H); δ_H (400

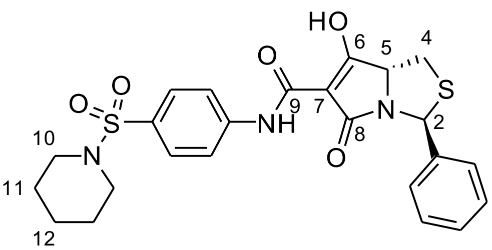
MHz, CD_2Cl_2): 3.05 (1H, dd, *J* = 11.1, 8.6 Hz, $H4_A$), 3.33 (1H, dd, *J* = 11.1, 6.9 Hz, $H4_B$), 4.90 (1H, app t, *J* = 7.7 Hz, H5), 6.28 (1H, s, H2), 7.13 - 7.19 (1H, m, Ar-C*H*), 7.30 - 7.42 (5H, m, Ar-C*H*), 7.46 - 7.52 (2H, m, Ar-C*H*), 7.57 - 7.63 (2H, m, Ar-C*H*), 9.42 (1H, br. s., OH/NH), 9.69 (1H, br. s., OH/NH); δ_C (125.8 MHz, CD_2Cl_2): 33.1 (C4), 62.4 (C2), 67.6 (C5), 98.4 (C7), 120.9, 125.3, 126.9, 128.7, 129.2, 129.6 (Ar-*C*H), 137.4, 141.0 (Ar-C), 164.6 (C9), 172.8 (C8), 185.7 (C6); *m/z* (ESI^-) 351 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{19}H_{15}O_3N_2S$ $[M-H]^-$; found 351.08051, requires 351.08089.

(-)-(2*S*,5*R*)-2-Phenyl)-*N*-(4-(methylsulfonyl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9x



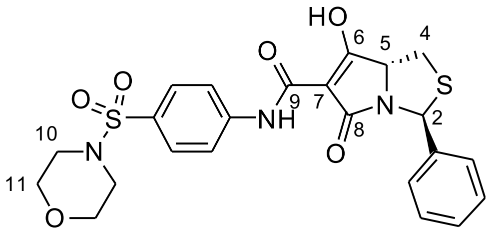
Yield (0.26 g, 40 %); yellow foam; mp 126-130 °C; R_f = 0.62 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -195.9 (*c* = 0.19, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1144, 1291 (S=O), 1621 (C=C), 1667 (C=O), 1687 (C=O); δ_H (500 MHz, $CDCl_3$): 3.03 - 3.09 (1H, m, $H4_A$, obscured by C*H*$_3$), 3.05 (3H, s, C*H*$_3$), 3.34 (1H, dd, *J* = 11.2, 7.2 Hz, $H4_B$), 4.91 (1H, dd, *J* = 8.3, 7.3 Hz, H5), 6.29 (1H, s, H2), 6.83 (1H, br. s, OH), 7.31 - 7.36 (1H, m, Ar-C*H*), 7.37 - 7.42 (2H, m, Ar-C*H*), 7.48 - 7.53 (2H, m, Ar-C*H*), 7.80 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.93 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 9.70 (1H, s, NH); δ_C (125.8 MHz, $CDCl_3$): 32.2 (C4), 44.6 (*C*H$_3$), 61.7 (C2), 66.2 (C5), 99.3 (C7), 120.1, 126.4, 128.4, 128.8, 128.9 (Ar-C*H*), 136.0, 139.4, 141.5 (Ar-*C*), 163.9 (C9), 171.2 (C8), 184.1 (C6); *m/z* (ESI^-) 429 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{20}H_{17}O_5N_2S_2$ $[M-H]^-$; found 429.05888, requires 429.05844.

(-)-(2*S*,5*R*)-2-Phenyl-*N*-(4-(piperidine-1-sulfonyl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9y



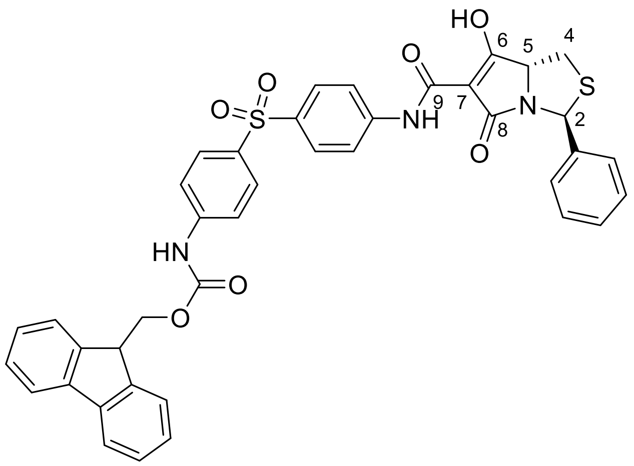
Yield (0.24 g, 25 %); light brown foam; mp 126-130 °C; R_f = 0.35 (EtOAc: MeOH; 98:2); $[\alpha]_D^{25}$ = -192.3 (*c* = 0.16, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1162, 1338 (S=O), 1631 (C=C), 1651 (C=O), 1689 (C=O); δ_H (400 MHz, $CDCl_3$): 1.36 - 1.48 (2H, m, H12), 1.65 (4H, br. quin, *J* = 5.6 Hz, H11), 2.99 (4H, br. t, *J* = 5.4 Hz, H10), 3.06 (1H, dd, *J* = 11.3, 8.6 Hz, $H4_A$), 3.34 (1H, dd, *J* = 11.3, 7.1 Hz, $H4_B$), 4.92 (1H, dd, *J* = 8.4, 7.1 Hz, H5), 6.29 (1H, s, H2), 7.30 - 7.36 (1H, m, Ar-C*H*), 7.37 - 7.42 (2H, m, Ar-C*H*), 7.48 - 7.64 (3H, m, Ar-C*H* + OH), 7.74, 7.75 (4H, ABq, J_{AB} = 9.8 Hz, Ar-C*H*), 9.63 (1H, s, NH); δ_C (125.8 MHz, $CDCl_3$): 23.5 (C12), 25.1 (C11), 32.2 (C4), 46.9 (C10), 61.8 (C2), 66.2 (C5), 99.3 (C7), 119.8, 126.4, 128.4, 128.8, 129.0 (Ar-C*H*), 131.9, 139.4, 140.5 (Ar-*C*), 163.9 (C9), 171.2 (C8), 184.1 (C6); *m/z* (ESI$^-$) 498 ([M-H]$^-$, 26 %); HRMS (ESI$^-$); $C_{24}H_{24}O_5N_3S_2$ [M-H]$^-$; found 498.11756, requires 498.11629.

(-)-(2*S*,5*R*)-2-Phenyl-*N*-(4-(morpholinosulfonyl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9z



Yield (0.14 g, 30 %); light brown solid; mp 118-120 °C; R_f = 0.47 (EtOAc/MeOH 96:4); $[\alpha]_D^{25}$ = -203.4 (*c* = 0.23, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1162, 1347 (S=O), 1629 (C=C), 1655 (C=O), 1688 (C=O); δ_H (400 MHz, $CDCl_3$): 3.00 (4H, br. t, *J* = 4.7 Hz, H10), 3.06 (1H, dd, *J* = 11.3, 8.6 Hz, $H4_A$), 3.34 (1H, dd, *J* = 11.3, 7.0 Hz, $H4_B$), 3.75 (4H, br. t, *J* = 4.7 Hz, H11), 4.92 (1H, dd, *J* = 8.3, 7.3 Hz, H5), 6.28 (1H, s, H2), 7.30 - 7.36 (1H, m, Ar-C*H*), 7.36 - 7.42 (2H, m, Ar-C*H*), 7.47 - 7.53 (2H, m, Ar-C*H*), 7.75, 7.78 (4H, ABq, J_{AB} = 9.0 Hz, Ar-C*H*), 8.55 (1H, br. s, OH), 9.68 (1H, s, NH); δ_C (100.6 MHz, $CDCl_3$): 32.2 (C4), 45.9 (C10), 61.7 (C2), 66.0 (C11), 66.2 (C5), 99.3 (C7), 119.9, 126.4, 128.4, 128.8, 129.2 (Ar-C*H*), 130.5, 139.4, 141.0 (Ar-*C*), 163.9 (C9), 171.2 (C8), 184.0 (C6); *m/z* (ESI$^-$) 500 ([M-H]$^-$, 100 %); HRMS (ESI$^-$); $C_{23}H_{22}O_6N_3S_2$ [M-H]$^-$; found 500.09556, requires 500.09555.

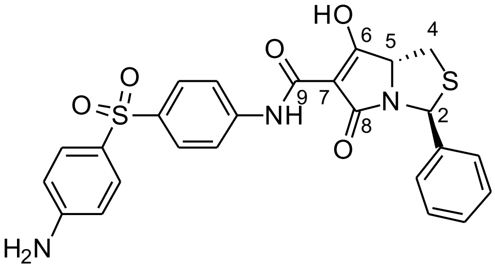
(-)-(9*H*-Fluoren-9-yl)methyl(4-((4-((2*S*,5*R*)-6-hydroxy-8-oxo-2-phenyl-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamido)phenyl)sulfonyl)phenyl)carbamate 9a'



Yield (0.32 g, 30 %); yellow solid, mp 170 °C; 1.3:1 tautomers; R_f = 0.59 (EtOAc/MeOH 98:2); $[\alpha]_D^{25}$ = -118.3 (*c* = 0.21, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1148, 1364 (S=O), 1629 (C=C), 1649 (C=O), 1690 (C=O), 1736 (C=O), 3302 (N-H/O-H); δ_H (500 MHz, Acetone-d_6) major tautomer: 3.13 - 3.25 (1H, m, $H4_A$), 3.45 (1H, dd, *J* = 10.9, 6.8 Hz, $H4_B$), 4.30 (1H, t, *J* = 6.5 Hz, OCH_2CH-), 4.54 (2H, d, *J* = 6.6 Hz, OCH_2CH-), 5.14 - 5.20 (1H, m, H5), 6.25 (1H, s, H2), 7.22 - 7.44 (8H, m, Ar-C*H*), 7.45 - 7.56 (3H, m, Ar-C*H*), 7.68 - 7.76 (4H, m, Ar-C*H*), 7.84 - 7.91 (4H, m, Ar-C*H*), 7.92 - 7.97 (2H, m, Ar-C*H*), 9.31 (1H, br. s, NH/OH), 9.91 (1H, br. s, NH/OH); minor tautomer: 2.99 - 3.05 (1H, m, $H4_A$), 3.40 (1H, dd, *J* = 11.0, 6.6 Hz, $H4_B$), 4.30 (1H, t, *J* = 6.5 Hz, OCH_2CH-), 4.55 (2H, d, *J* = 6.6 Hz, OCH_2CH-), 5.01 (1H, app t, *J* = 7.5 Hz, H5), 6.20 (1H, s, H2), 7.22 - 7.44 (8H, m, Ar-C*H*), 7.45 - 7.56 (3H, m, Ar-C*H*), 7.68 - 7.76 (4H, m, Ar-C*H*), 7.84 - 7.91 (4H, m, Ar-C*H*), 7.92 - 7.97 (2H, m, Ar-C*H*), 9.31

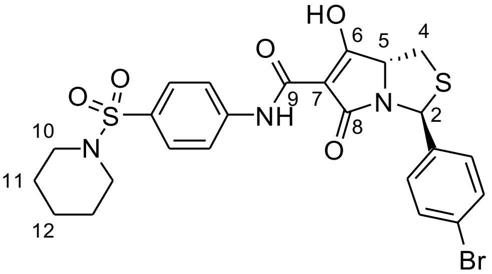
(1H, br. s, NH/OH), 9.91 (1H, br. s, NH/OH); δ_C (125.8 MHz, Acetone-d_6) major tautomer: 32.9 (C4), 47.9 (OCH_2CH-), 62.5 (C2), 67.4 (OCH_2CH-), 67.8 (C5), 94.4 (C7), 119.1, 119.2, 121.0, 126.0, 127.3, 127.4, 128.1, 128.7, 129.3, 129.5, 129.7, 129.8 (Ar-*C*H), 129.6, 130.2, 136.5, 138.6, 142.3, 144.9, 146.2 (Ar-C), 154.2 ($HNCO_2$), 164.4 (C9), 172.6 (C8), 185.0 (C6); minor tautomer: 35.4 (C4), 47.9 (OCH_2CH-), 62.9 (C2), 67.4 (OCH_2CH-), 69.6 (C5), 94.4 (C7), 119.1, 119.2, 121.0, 126.0, 127.3, 127.4, 128.1, 128.7, 129.3, 129.5, 129.7, 129.8 (Ar-*C*H), 129.6, 130.2, 136.5, 138.6, 142.3, 144.9, 146.2 (Ar-C), 154.2 ($HNCO_2$), 164.4 (C9), 176.6 (C8), 185.0 (C6); *m/z* (ESI/FI) molecular ion not detected.

(-)-(2*S*,5*R*)-*N*-(4-((4-Aminophenyl)sulfonyl)phenyl)-6-hydroxy-8-oxo-2-phenyl-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9b'



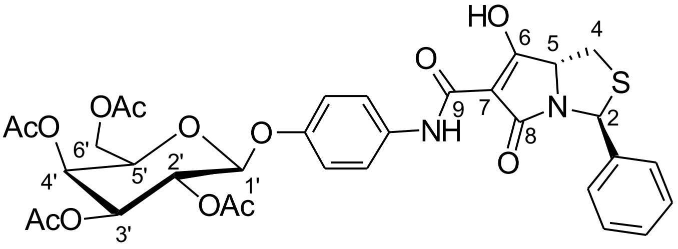
Tetramate **9a'** (0.22 g, 0.31 mmol, 1.0 eq) was dissolved in DMF (2 mL) and piperidine (0.03 mL, 0.31 mmol, 1.0 eq) was added. The reaction was stirred at rt for 1 h until complete deprotection was observed by TLC. The crude was purified by silica gel flash column chromatography to obtain **9b'** (eluent: 100 % EtOAc to EtOAc/MeOH 9:1). Yield (62 mg, 40 %); brown solid, mp 152-156 °C; R_f = 0.56 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -209.4 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1146, 1366 (S=O), 1627 (C=C), 1654 (C=O), 1687 (C=O); δ_H (500 MHz, Acetone-d_6): 3.18 (1H, dd, J = 11.0, 8.9 Hz, $H4_A$), 3.45 (1H, dd, J = 10.9, 6.8 Hz, $H4_B$), 5.16 (1H, app t, J = 7.7 Hz, H5), 6.25 (1H, s, H2), 6.74 (2H, d, J = 8.8 Hz, Ar-C*H*), 7.29 - 7.34 (1H, m, Ar-C*H*), 7.35 - 7.41 (2H, m, Ar-C*H*), 7.52 - 7.56 (2H, m, Ar-C*H*), 7.63 (2H, d, J = 8.8 Hz, Ar-C*H*), 7.84, 7.88 (4H, ABq, J_{AB} = 8.8 Hz, Ar-C*H*); δ_C (125.8 MHz, Acetone-d_6): 32.9 (C4), 62.5 (C2), 67.8 (C5), 99.7 (C7), 114.3, 120.6, 127.4, 128.9, 129.2, 129.5, 130.5 (Ar-*C*H), 129.0, 140.1, 141.9, 142.0, 154.1 (Ar-C), 164.3 (C9), 172.7 (C8), 184.8 (C6); *m/z* (ESI^-) 506 ($[M-H]^-$, 47 %); HRMS (ESI^+); $C_{25}H_{22}N_3O_5S_2$ $[M+H]^+$; found 508.09978, requires 508.09954.

(-)-(2*S*,5*R*)-2-(4-Bromophenyl)-6-hydroxy-8-oxo-*N*-(4-(piperidin-1-ylsulfonyl)phenyl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9c'



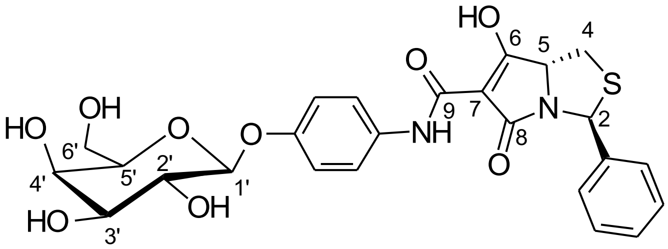
Yield (0.57 g, 40 %); brown foam; mp 148-150 °C; R_f = 0.70 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -263.4 (*c* = 0.15, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1162,1337 (S=O), 1631 (C=C), 1650 (C=O), 1690 (C=O); δ_H (500 MHz, Acetone-d_6): 1.35 - 1.47 (2H, m, H12), 1.61 (4H, br. quin, J = 5.7 Hz, H11), 2.96 (4H, br. t, J = 5.4 Hz, H10), 3.21 (1H, dd, J = 11.0, 8.8 Hz, $H4_A$), 3.49 (1H, dd, J = 11.0, 7.0 Hz, H4$_B$), 3.78 (2H, br. s, N-H + O-H), 5.21 (1H, app t, *J* = 7.7 Hz, H5), 6.25 (1H, s, H2), 7.53, 7.59 (4H, ABq, J_{AB} = 8.6 Hz, Ar-C*H*), 7.76 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.92 (2H, d, *J* = 8.8 Hz, Ar-C*H*); δ_C (125.8 MHz, Acetone-d_6): 24.2 (C12), 26.0 (C11), 32.9 (C4), 47.8 (C10), 61.9 (C2), 67.7 (C5), 99.9 (C7), 120.5, 129.6, 130.0, 132.5 (Ar-C*H*), 122.4, 132.7, 141.3, 142.1 (Ar-*C*), 164.3 (C9), 172.7 (C8), 184.8 (C6); *m/z* (ESI$^-$) 576, 578 ([M-H]$^-$, 100 %); HRMS (ESI$^+$); $C_{24}H_{25}O_5N_3BrS_2$ [M+H]$^+$; found 578.04135 and 580.03904 requires 578.04135 and 580.03930.

(-)-(2*R*,3*S*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(4-((2*S*,5*R*)-6-hydroxy-8-oxo-2-phenyl-6a,8-dihydro-1*H*,2*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamido)phenoxy)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate 9d'



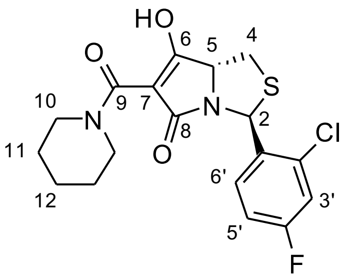
Yield (0.17 g, 60 %); yellow foam, mp 130-132 °C; R_f = 0.72 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -148.7 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1213 (C-O), 1647 (C=O, br with shoulder towards smaller wave number), 1689 (C=O), 1747 (C=O); δ_H (500 MHz, CD_2Cl_2): 1.99 (3H, s, C*H*$_3$-C(=O)-O-), 2.04 (3H, s, C*H*$_3$-C(=O)-O-), 2.06 (3H, s, C*H*$_3$-C(=O)-O-), 2.17 (3H, s, C*H*$_3$-C(=O)-O-), 3.03 (1H, dd, *J* = 11.1, 7.8 Hz, H4$_A$), 3.26 (1H, dd, *J* = 11.0, 7.4 Hz, H4$_B$), 4.04 - 4.09 (1H, m, H5'), 4.15 (1H, dd, *J* = 11.3, 6.0 Hz, H6'$_A$), 4.21 (1H, dd, *J* = 11.3, 7.2 Hz, H6'$_B$), 4.58 (1H, br signal, H5), 5.01 (1H, d, *J* = 7.9 Hz, H1'), 5.10 (1H, dd, *J* = 10.5, 3.6 Hz, H3'), 5.39 (1H, dd, *J* = 10.5, 8.0 Hz, H2'), 5.44 (1H, dd, *J* = 3.4, 0.9 Hz, H4'), 6.33 (1H, s, H2), 6.97 (2H, d, *J* = 9.0 Hz, Ar-C*H*), 7.26 - 7.32 (1H, m, Ar-C*H*), 7.33 - 7.40 (2H, m, Ar-C*H*), 7.45 - 7.49 (2H, m, Ar-C*H*), 7.51 (2H, d, *J* = 9.0 Hz, Ar-C*H*); δ_C (125.8 MHz, CD_2Cl_2): 20.9, 21.0, 21.0, 21.1 (4x*C*H$_3$-C(=O)-O-), 33.7 (C4), 62.0 (C6'), 63.4 (C2), 67.5 (C4'), 68.7 (C5), 69.1 (C2'), 71.4 (C3'), 71.7 (C5'), 100.7 (C1'), 118.1, 121.8, 126.8, 128.3, 129.0 (Ar-*C*H), 134.4, 142.0, 153.6 (Ar-C), 164.7 (C9), 169.9, 170.5, 170.7, 170.8 (CH$_3$-*C*(=O)-O-), 175.8 (C8), 189.0 (C6); *m/z* (ESI$^-$) 697 ([M-H]$^-$, 100 %); HRMS (ESI$^-$); $C_{33}H_{33}O_{13}N_2S$ [M-H]$^-$; found 697.16989, requires 697.16979.

(-)-(2*S*,5*R*)-6-Hydroxy-8-oxo-2-phenyl-*N*-(4-(((2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl)oxy)phenyl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9e'



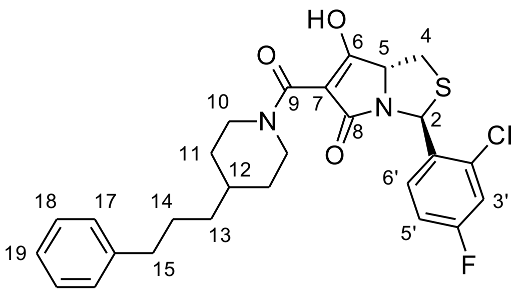
Tetramate **9d'** (20 mg, 0.03 mmol, 1.0 eq) was dissolved in MeOH (2 mL) and aq. K_2CO_3 (4.8 mg in 0.5 mL of H_2O, 0.034 mmol, 1.2 eq) was added. The reaction was stirred at rt for 10-15 min and upon completion, solvents were removed *in vacuo*. The residue was treated with MeOH, filtered and concentrated *in vacuo* to obtain **9e'**. Yield (15 mg, 89 %); yellow solid, mp >250 °C; R_f = 0.10 (EtOAc/MeOH 3:1); $[\alpha]_D^{25}$ = -221.7 (*c* = 0.12, H_2O); ν_{max}/cm^{-1} (neat) 1215 (C-O), 1630 (C=C, br with shoulder towards larger wave number), 1664 (C=O), 3233 (O-H); δ_H (500 MHz, D_2O): 2.98 (1H, dd, *J* = 10.4, 8.5 Hz, $H4_A$), 3.24 (1H, dd, *J* = 10.8, 7.6 Hz, $H4_B$), 3.68 - 3.82 (5H, m, H2', H3', H5', 2xH6'), 3.95 (1H, app d, *J* = 3.0 Hz, H4'), 4.48 (1H, app t, *J* = 7.6 Hz, H5), 4.97 (1H, d, *J* = 7.6 Hz, H1'), 6.29 (1H, s, H2), 7.08 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.30 - 7.50 (7H, m, Ar-C*H*); δ_C (125.8 MHz, D_2O): 32.6 (C4), 60.7 (C6'), 62.8 (C2), 68.5 (C4'), 69.4 (C5), 70.5, 72.5, 75.3 (C2', C3', C5'), 93.0 (C7), 101.0 (C1'), 117.0, 123.4, 125.9, 128.0, 128.9 (Ar-*C*H), 132.6, 141.4, 153.3 (Ar-C), 165.0 (C9), 179.0 (C8), 193.6 (C6); *m/z* (ESI^-) 529 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{25}H_{26}O_9N_2NaS$ $[M+Na]^+$; found 553.12523, requires 553.12512.

(-)-(2*S*,5*R*)-2-(2-Chloro-4-fluorophenyl)-6-hydroxy-8-oxo-*N*-(4-(piperidinyl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9f'



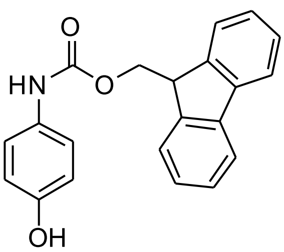
Yield (0.10 g, 30 %); light brown foam; mp 80-84 °C; R_f = 0.54 (EtOAc/MeOH 4:1); $[\alpha]_D^{25}$ = -320.5 (*c* = 0.15, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1649 (C=O), 1685 (C=O); δ_H (500 MHz, CD_2Cl_2): 1.60 - 1.74 (6H, m, H11, H12), 3.04 (1H, dd, *J* = 11.2, 8.4 Hz, $H4_A$), 3.27 (1H, dd, *J* = 11.2, 7.1 Hz, $H4_B$), 3.75 - 3.91 (4H, m, H10), 4.68 (1H, app t, *J* = 7.7 Hz, H5), 6.51 (1H, s, H2), 7.03 (1H, app td, *J* = 8.4, 2.5 Hz, H5'), 7.16 (1H, dd, *J* = 8.4, 2.5 Hz, H3'), 7.45 (1H, dd, *J* = 8.7, 6.0 Hz, H6'); δ_C (125.8 MHz, CD_2Cl_2): 24.6, 26.8 (C12, C11), 33.5 (C4), 47.9 (C10), 61.2 (C2), 69.8 (C5), 90.0 (C7), 114.8 (d, *J* = 21.9 Hz, C5′), 117.7 (d, *J* = 24.8 Hz, C3′), 128.2 (d, *J* = 9.5 Hz, C6′), 133.5 (d, *J* = 10.5 Hz, C2′), 135.8 (d, *J* = 3.8 Hz, C1′), 162.4 (d, *J* = 249.9 Hz, C4′), 166.1 (C9), 175.9 (C8), 192.7 (C6); *m/z* (ESI^-) 395 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{18}H_{19}O_3N_2ClFS$ $[M+H]^+$; found 397.07851, requires 397.07835.

(-)-(2*S*,5*R*)-2-(2-Chloro-4-fluorophenyl)-6-hydroxy-8-oxo-*N*-(4-(3-phenylpropyl)piperidinyl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 9g'



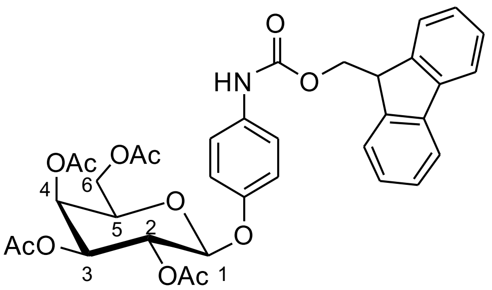
Yield (0.15 g, 36 %); yellow foam; mp 78-80 °C; R_f = 0.34 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -175.8 (*c* = 0.27, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1686 (C=O); δ_H (500 MHz, CD_2Cl_2): 1.13 - 1.35 (3H, m, H11, H15), 1.53 - 1.69 (3H, m, H12, H14), 1.75 - 1.87 (2H, m, H11), 2.56 - 2.63 (1H, m, H15), 2.65 - 2.80 (1H, m, H13), 2.88 - 2.98 (2H, m, H10), 3.03 (1H, dd, *J* = 11.3, 8.1 Hz, $H4_A$), 3.25 (1H, dd, *J* = 11.3, 7.3 Hz, $H4_B$), 3.32 - 3.38 (1H, m, H13), 4.55 - 4.68 (3H, m, H5, H10), 6.50 (1H, s, H2), 7.02 (1H, app td, *J* = 8.4, 2.6 Hz, H5'), 7.13 - 7.20 (4H, m, H3', H17, H19), 7.23 - 7.29 (2H, m, H18), 7.45 (1H, dd, *J* = 8.8, 6.1 Hz, H6'); δ_C (125.8 MHz, CD_2Cl_2): 29.1 (C14), 33.0 (C11), 33.5 (C4), 36.1 (C12), 36.5 (C15), 44.9 (C13), 47.0 (C10), 61.3 (C2), 69.9 (C5), 91.2 (C7), 114.8 (d, *J* = 21.0 Hz, C5′), 117.7 (d, *J* = 24.8 Hz, C3′), 126.2 (C19), 128.2 (d, *J* = 8.6 Hz, C6′), 128.8 (C18), 128.9 (C17), 133.5 (d, *J* = 10.5 Hz, C2′), 136.0 (d, *J* = 2.9 Hz, C1′), 143.2 (C16), 162.4 (d, *J* = 249.9 Hz, C4′), 166.2 (C9), 175.9 (C8), 191.9 (C6); *m/z* (ESI^-) 513 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{27}H_{29}O_3N_2ClFS$ $[M+H]^+$; found 515.15651, requires 515.15660.

9-Fluorenylmethyl (4-hydroxyphenyl)carbamate, 11b



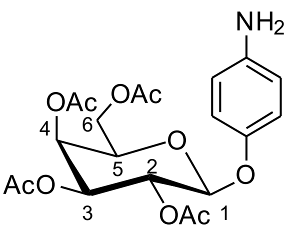
To 4-aminophenol **11a** (1.0 g, 9.13 mmol, 1.0 eq) in THF (20 mL), DIPEA (1.91 mL, 11.0 mmol, 1.2 eq) and Fmoc chloride (2.85 g, 11.0 mmol, 1.2 eq) were added and stirred at reflux for 1 h. The reaction was cooled to rt, and concentrated *in vacuo*. The residue was dissolved in 10 mL of CH_2Cl_2 and treated with 25 mL of sat. NH_4Cl. The precipitate formed was filtered and washed with NH_4Cl (2x15 mL) to obtain **11b**. Yield (2.12 g, 70 %); brown solid, mp 230-232 °C; R_f = 0.47 (EtOAc/petrol 1:2); ν_{max}/cm^{-1} (neat) 1697 (C=O), 3337 (O-H); δ_H (400 MHz, Dimethyl sulfoxide-d_6): 4.28 (1H, t, *J* = 6.6 Hz, OCH_2CH-), 4.43 (2H, br. d, *J* = 5.9 Hz, OCH_2CH-), 6.69 (2H, d, *J* = 7.3 Hz, Ar-C*H*), 7.26 (2H, Ar-C*H*), 7.34 (2H, app t, *J* = 7.1 Hz, Ar-C*H*), 7.42 (2H, app t, *J* = 7.1 Hz, Ar-C*H*), 7.74 (2H, br. d, *J* = 6.4 Hz, Ar-C*H*), 7.90 (2H, d, *J* = 7.6 Hz, Ar-C*H*), 9.15 (1H, br. s., NH/OH), 9.42 (1H, br. s., NH/OH); δ_C (100.6 MHz, Dimethyl sulfoxide-d_6): 46.7 (OCH_2CH-), 65.4 (OCH_2CH-), 115.1, 120.2, 120.2, 125.1, 127.1, 127.7 (Ar-*C*H), 130.5, 140.8, 143.9, 152.9 (Ar-C), 153.6 (HN*C*O_2); *m/z* (ESI^+) 354 ($[M+Na]^+$, 75 %); HRMS (ESI^+); $C_{21}H_{17}O_3NNa$ $[M+Na]^+$; found 354.10922, requires 354.11006.

(+)-9-Fluorenylmethyl (4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyloxy)phenyl)carbamate 12a



Aryl glycosylation of **11b** was according to a modified literature procedure.[2] β-D-Galactose pentaacetate (0.87 g, 2.23 mmol, 1.0 eq) and **11b** (0.89 g, 2.68 mmol, 1.2 eq) in CH_2Cl_2 (10 mL) was cooled to 0 °C. $BF_3.OEt_2$ (0.33 mL, 2.68 mmol, 1.2 eq) was added dropwise under N_2. The reaction flask was warmed to rt and stirred for 18 h. The reaction mixture was quenched with sat. $NaHCO_3$ (10 mL) and left to stir for 30 min. The product was extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography to obtain **12a** (eluent: EtOAc/petrol). Yield (0.57 g, 39 %); brown solid; R_f = 0.47 (EtOAc/petrol 1:2); $[\alpha]_D^{25}$ = +35.4 (*c* = 0.23, $CHCl_3$) ν_{max}/cm^{-1} (neat) 1216 (C-O), 1745 (C=O); δ_H (400 MHz, CD_2Cl_2): 1.99 (3H, s, C*H*₃-C(=O)-O-), 2.03 (3H, s, C*H*₃-C(=O)-O-), 2.06 (3H, s, C*H*₃-C(=O)-O-), 2.17 (3H, s, C*H*₃-C(=O)-O-), 4.02 - 4.24 (3H, m, $H6_A$, $H6_B$, H5), 4.28 (1H, t, *J* = 6.4 Hz, OCH_2CH-), 4.52 (2H, d, *J* = 6.6 Hz, OC*H*₂CH-), 5.00 (1H, d, *J* = 8.1 Hz, H1), 5.11 (1H, dd, *J* = 10.3, 3.4 Hz, H3), 5.39 (1H, dd, *J* = 10.5, 8.1 Hz, H2), 5.44 (1H, app d, *J* = 2.7 Hz, H4), 6.90 (1H, br. s., NH), 6.95 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.33 (4H, app t, *J* = 7.1 Hz, Ar-C*H*), 7.42 (2H, app t, *J* = 7.3 Hz, Ar-C*H*), 7.63 (2H, d, *J* = 7.3 Hz, Ar-C*H*), 7.80 (2H, d, *J* = 7.3 Hz, Ar-C*H*); δ_C (100.6 MHz, CD_2Cl_2): 20.9, 21.0, 21.0, 21.1 (*C*H₃-C(=O)-O-), 47.7 (OCH_2CH-), 62.0 (C6), 67.2 (OC*H*₂CH-), 67.6 (C4), 69.1 (C2), 71.4 (C3), 71.7 (C5), 100.7 (C1), 118.3, 120.5, 120.8, 125.5, 127.6, 128.3 (Ar-*C*H) 141.9, 144.4, 153.6, 154.1 (Ar-C), 169.9, 170.6, 170.7, 170.8 (CH₃-*C*(=O)-O-); *m/z* (ESI^+) 684 ($[M+Na]^+$, 44 %); HRMS (ESI^+); $C_{35}H_{35}O_{12}NNa$ $[M+Na]^+$; found 684.20315, requires 684.20515.

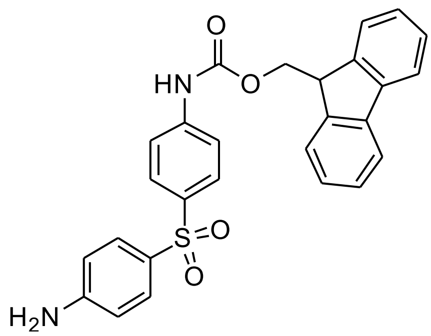
(+)-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyloxy)aniline, 12b



12a (0.46 g, 0.7 mmol, 1.0 eq) was dissolved in DMF (4 mL) and piperidine (0.07 mL, 0.7 mmol, 1.0 eq) was added. The reaction was stirred at rt for 1 h until complete deprotection was observed by TLC. The crude was purified by silica gel flash column chromatography to obtain **12b** (eluent: EtOAc/petrol). Yield (0.23 g, 75 %); yellow oil; R_f = 0.18 (EtOAc/petrol 1:1); $[\alpha]_D^{25}$ = +3.84 (*c* = 0.43, $CHCl_3$) {lit. $[\alpha]_D^{22}$ = +5.83 (*c* = 2.0, $CHCl_3$)}[3] ν_{max}/cm^{-1} (neat) 1216 (C-O), 1743 (C=O), 3368, 3452 (N-H); δ_H (500 MHz, CD_2Cl_2): 1.98 (3H, s, C*H*₃-C(=O)-O-), 2.03 (3H, s, C*H*₃-C(=O)-O-), 2.06 (3H, s, C*H*₃-C(=O)-O-), 2.17 (3H, s, C*H*₃-C(=O)-O-), 3.60 (2H, br. s., NH), 3.96 - 4.04 (1H, m, H5), 4.14 (1H, dd, *J* = 11.4, 6.0 Hz, $H6_A$), 4.20 (1H, dd, *J* = 11.4, 7.1 Hz, $H6_B$), 4.88 (1H, d, *J* = 8.0 Hz, H1), 5.07 (1H, dd, *J* = 10.4, 3.5 Hz, H3), 5.31 - 5.36 (1H, m, H2, obscured by solvent peak), 5.42 (1H, dd, *J* = 3.4, 0.9 Hz, H4), 6.60 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 6.82 (2H, d, *J* = 8.8 Hz, Ar-C*H*); δ_C (125.8 MHz, CD_2Cl_2): 20.9, 21.0, 21.0, 21.1 (*C*H₃-

C(=O)-O-), 62.0 (C6), 67.6 (C4), 69.2 (C2), 71.4 (C3), 71.6 (C5), 101.7 (C1), 116.1, 119.4 (Ar-*C*H) 143.5, 150.3 (Ar-C), 169.9, 170.6, 170.7, 170.7 (CH_3-*C*(=O)-O-); *m/z* (ESI^+) 462 ($[M+Na]^+$, 20 %); HRMS (ESI^+); $C_{20}H_{25}O_{10}NNa$ $[M+Na]^+$; found 462.13580, requires 462.13707.

9-Fluorenylmethyl (4-((4-aminophenyl)sulfonyl)phenyl)carbamate 10b

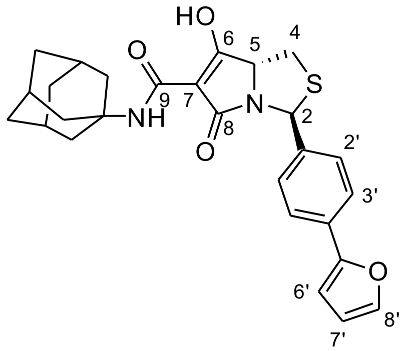


To 4-aminophenylsulfone **10a** (1.0 g, 4.0 mmol, 1.0 eq) in THF (20 mL), DIPEA (0.77 mL, 4.4 mmol, 1.1 eq) and Fmoc chloride (1.15 g, 4.4 mmol, 1.1 eq) were added and stirred at reflux for 3 h. The reaction mixture was cooled to rt, treated with sat. NH_4Cl (20 mL) and the product was extracted with EtOAc. The organic fractions were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography to obtain **10b** (eluent: EtOAc/petrol). Yield (1.18 g, 63 %); white foam, mp 144 °C; R_f = 0.61 (EtOAc/petrol 2:1); ν_{max}/cm^{-1} (neat) 1145, 1315 (S=O), 1722 (C=O), 3335, 3375, 3478 (N-H); δ_H (400 MHz, $CDCl_3$): 4.15 (2H, br. s., NH), 4.23 (1H, t, *J* = 6.4 Hz, OCH_2C*H*-), 4.54 (2H, d, *J* = 6.6 Hz, OC*H*$_2$CH-), 6.60 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.21 (1H, br. s, NH), 7.30 (2H, td, *J* = 7.5, 1.2 Hz, Ar-C*H*), 7.37 - 7.47 (4H, m, Ar-C*H*), 7.59 (2H, d, *J* = 7.6 Hz, Ar-C*H*), 7.65 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.74 - 7.80 (4H, m, Ar-C*H*); δ_C (100.6 MHz, $CDCl_3$): 46.9 (OCH_2C*H*-), 67.0 (OC*H*$_2$CH-), 114.1, 118.3, 120.0, 124.8, 127.1, 127.8, 128.4, 129.5 (Ar-*C*H), 129.6, 136.8, 141.3, 141.8, 143.4, 150.9 (Ar-C), 152.9 (HN*C*O$_2$); *m/z* (ESI^+) 471 ($[M+H]^+$, 100 %); HRMS (ESI^+); $C_{27}H_{23}O_4N_2S$ $[M+H]^+$; found 471.13716, requires 471.13730.

General procedure: Suzuki-Miyaura cross-coupling reactions

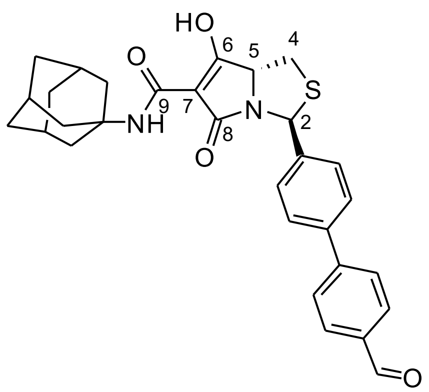
Suzuki-Miyaura cross-coupling reactions were carried out according to a modified literature procedure.[90] Tetramic acid (1.0 eq), the appropriate boronic acid (3 eq), $Pd(OAc)_2$ (0.05 eq) XPhos (0.15 eq), aq. Na_2CO_3 (2 M, 6.3 eq) and 1,2-dimethoxyethane (6.3 mL/mmol) were placed in a sealed flask and degassed with N_2. The suspension was refluxed for 15-48 h as required with the progress of the reaction monitored by TLC and LRMS. The crude mixture was filtered through a Celite plug and the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography (eluent: EtOAc/petrol to EtOAc/MeOH/1% Et_3N). The product isolated was dissolved in CH_2Cl_2 and washed with 5% citric acid. The organic fractions were dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield the desired bicyclic carboxamide tetramate. Where the major and minor tautomeric forms have distinct chemical shift values, they have been specified as either AB (major tautomeric form) or CD (minor tautomeric form) in compound characterisation.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-(furan-2-yl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14a



Yield (0.35 g, 72 %); brown foam, 2.7:1 AB:CD tautomers, mp 130-132 °C; R*f* = 0.63 (EtOAc/MeOH 98:2); $[\alpha]_D^{25}$ = -240.7 (*c* = 0.25, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1625 (C=C), 1648 (C=O), 1689 (C=O), 3315 (O-H/N-H); δ_H (400 MHz, $CDCl_3$): 1.70 (6H, Adamantyl-C*H*$_2$), 2.06 (6H, Adamantyl-C*H*$_2$), 2.12 (3H, Adamantyl-C*H*), 2.98 - 3.09 (1H, m, H4$_A$), 3.27 (1H, dd, *J* = 11.1, 7.2 Hz, H4$_B$), 4.45 (1H, app t, *J* = 7.7 Hz, H5 CD), 4.69 (1H, app t, *J* = 7.7 Hz, H5 AB), 6.27 (1H, s, H2 AB), 6.37 (1H, s, H2 CD), 6.47 (1H, dd, *J* = 3.4, 1.7 Hz, H7'), 6.65 (1H, app d, *J* = 3.4 Hz, H6'), 7.43 (1H, br. s, NH AB), 7.45 - 7.50 (3H, m, H2' and H8'), 7.65 (2H, d, *J* = 8.3 Hz, H3'), 7.94 (1H, br. s, NH CD), 11.75 (1H, br. s, OH); δ_C (100.6 MHz, $CDCl_3$): 29.3 (Adamantyl-*C*H), 32.4 (C4 AB), 32.7 (C4 CD), 35.8 (Adamantyl-*C*H$_2$ CD), 36.0 (Adamantyl-*C*H$_2$ AB), 41.5 (Adamantyl-*C*H$_2$ AB), 41.6 (Adamantyl-*C*H$_2$ CD), 53.1 (Adamantyl-C AB), 54.5 (Adamantyl-C CD), 61.9 (C2 AB), 62.5 (C2 CD), 67.3 (C5 AB), 70.6 (C5 CD), 85.3 (C7 CD), 94.9 (C7 AB), 105.3 (C6'), 111.6 (C7'), 123.9 (C3'), 126.7 (C2' CD), 126.8 (C2' AB), 130.5 (C4' CD), 130.6 (C4' AB), 139.2 (C1' AB), 139.5 (C1' CD), 142.2 (C8'), 153.4 (C5'), 166.0 (C9 AB), 166.5 (C9 CD), 172.4 (C8 AB), 178.3 (C8 CD), 188.2 (C6 AB), 191.2 (C6 CD); *m/z* (ESI$^-$) 475 ([M-H]$^-$, 100 %); HRMS (ESI$^-$); $C_{27}H_{27}N_2O_4S$ [M-H]$^-$; found 475.16905, requires 475.16860.

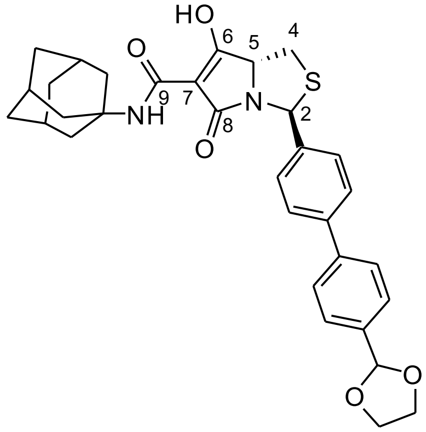
(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4'-formyl-[1,1'-biphenyl]-4-yl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14b



Yield (0.31 g, 74 %); brown foam, 2.6:1 AB:CD tautomers, mp 150-152 °C; R*f* = 0.49 (EtOAc: MeOH; 96:4); $[\alpha]_D^{25}$ = -216.1 (*c* = 0.19, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1623 (C=C), 1646 (C=O), 1687 (C=O), 3315 (O-H/N-H); δ_H (400 MHz, $CDCl_3$): 1.57 - 1.80 (6H, m, Adamantyl-C*H*$_2$), 2.02 - 2.09 (6H, m, Adamantyl-C*H*$_2$), 2.10 - 2.20 (3H, m, Adamantyl-C*H*), 2.99 - 3.10 (1H, m, H4$_A$), 3.29 (1H, dd, *J* = 11.3, 7.1 Hz, H4$_B$), 4.48 (1H, app t, *J* = 7.7 Hz, H5 CD), 4.72 (1H, app t, *J* = 7.8 Hz, H5 AB), 6.30 (1H, s, H2 AB), 6.40 (1H, s, H2 CD), 7.43 (1H, br. s, NH), 7.54 - 7.60 (2H, m, Ar-C*H*), 7.60 - 7.64 (2H, m, Ar-C*H*), 7.73 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 7.95 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 10.05 (1H, s, C*H*O), 11.00 (1H, br. s, OH); δ_C (100.6 MHz, $CDCl_3$): 29.3 (Adamantyl-*C*H), 32.6 (C4 AB), 32.9 (C4 CD), 35.8 (Adamantyl-*C*H$_2$ CD), 36.0 (Adamantyl-*C*H$_2$ AB), 41.5 (Adamantyl-*C*H$_2$ AB), 41.6 (Adamantyl-*C*H$_2$ CD), 53.1 (Adamantyl-C AB), 54.5 (Adamantyl-C CD), 61.7 (C2 AB), 62.3 (C2 CD), 67.5 (C5 AB), 70.7 (C5 CD), 85.3 (C7

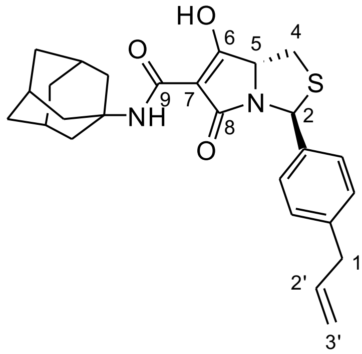
CD), 94.7 (C7 AB), 127.0, 127.1, 127.6, 130.2 (Ar-*C*H), 135.3, 139.5, 140.7, 146.4 (Ar-C), 166.0 (C9 AB), 166.5 (C9 CD), 172.4 (C8 AB), 178.2 (C8 CD), 188.4 (C6 AB), 191.1 (C6 CD), 191.8 (*C*HO); *m/z* (ESI^-) 513 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{30}H_{29}N_2O_4S$ $[M-H]^-$; found 513.19140, requires 513.18535.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4'-(1,3-dioxolan-2-yl)-[1,1'-biphenyl]-4-yl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14c



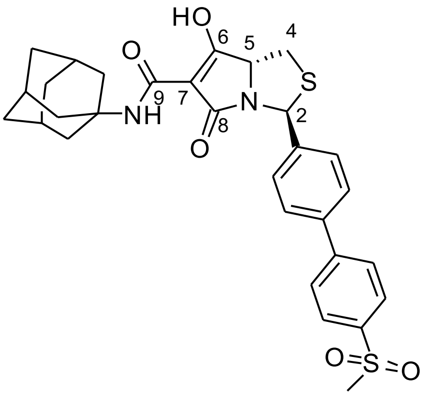
Yield (92 mg, 80 %); yellow oil; 3:1 AB:CD tautomers; R_f = 0.56 (EtOAc/MeOH 96:4); $[\alpha]_D^{25}$ = -182.5 (*c* = 0.47, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1622 (C=C), 1647 (C=O), 1687 (C=O), 3316 (O-H/N-H); δ_H (400 MHz, $CDCl_3$) 1.71 (6H, Adamantyl-C*H*$_2$), 2.01 - 2.16 (9H, m, Adamantyl-C*H*$_2$ + Adamantyl-C*H*), 3.02 (1H, dd, *J* = 11.1, 8.4 Hz, $H4_A$), 3.29 (1H, dd, *J* = 11.1, 7.0 Hz, $H4_B$), 4.00 - 4.07 (2H, m, dioxolane-C*H*$_2$), 4.08 - 4.15 (2H, m, dioxolane-C*H*$_2$), 4.49 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.75 (1H, dd, *J* = 8.1, 7.3 Hz, H5 AB), 5.82 (1H, s, dioxolane-C*H*), 6.27 (1H, s, H2 AB), 6.36 (1H, s, H2 CD), 7.38 (1H, br. s, NH AB), 7.50 - 7.55 (4H, m, Ar-C*H*), 7.58 - 7.64 (4H, m, Ar-C*H*), 7.94 (1H, br. s, NH CD), 9.75 (1H, br. s, OH); δ_C (100.6 MHz, $CDCl_3$): 30.1 (Adamantyl-*C*H), 33.1 (C4 AB), 33.5 (C4 CD), 36.4 (Adamantyl-*C*H$_2$ CD), 36.6 (Adamantyl-*C*H$_2$ AB), 42.1 (Adamantyl-*C*H$_2$ AB), 42.2 (Adamantyl-*C*H$_2$ CD), 53.5 (Adamantyl-C AB), 54.4 (Adamantyl-C CD), 62.4 (C2 AB), 62.9 (C2 CD), 65.9 (dioxolane-*C*H$_2$), 68.0 (C5 AB), 71.6 (C5 CD), 96.0 (C7), 104.0 (dioxolane-C*H*), 127.4, 127.5, 127.6, 127.9 (Ar-*C*H), 138.0, 140.6, 141.0, 141.8 (Ar-C), 166.6 (C9), 172.9 (C8), 188.4 (C6 AB), 191.1 (C6 CD); *m/z* (ESI^-) 557 ($[M-H]^-$, 50 %); HRMS (ESI^-); $C_{32}H_{33}N_2O_5S$ $[M-H]^-$; found 557.21398, requires 557.21157.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-allylphenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14d



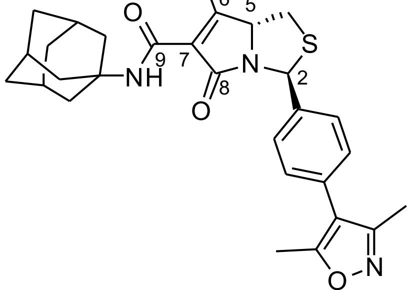
Yield (25 mg, 45 %); brown oil, 2.5:1 AB:CD tautomers; R_f = 0.58 (EtOAc/Petrol 1:1); $[\alpha]_D^{25}$ = -175.4 (*c* = 0.53, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1621 (C=C), 1646 (C=O), 1686 (C=O), 3315 (O-H/N-H); δ_H (200 MHz, $CDCl_3$); 1.70 (6H, Adamantyl-C*H*$_2$), 2.06 (6H, Adamantyl-C*H*$_2$), 2.12 (3H, Adamantyl-C*H*), 2.92 - 3.08 (1H, m, $H4_A$), 3.26 (1H, dd, *J* = 11.1, 7.2 Hz, $H4_B$), 3.38 (2H, app d, *J* = 5.9 Hz, H1'), 4.44 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.68 (1H, app t, *J* = 7.7 Hz, H5 AB), 5.01 - 5.15 (2H, m, H3'), 5.83 - 6.06 (1H, m, H2'), 6.24 (1H, s, H2 AB), 6.34 (1H, s, H2 CD), 7.18 (2H, d, J = 8.1 Hz, Ar-CH), 7.40 (2H, d, J = 8.1 Hz, Ar-CH), 7.93 (1H, br. s., NH/OH CD), 10.40 (3H, br. s., NH+OH AB and NH/OH CD); δ_C (100.6 MHz, $CDCl_3$): 29.3 (Adamantyl-CH), 32.5 (C4 AB), 32.7 (C4 CD), 35.8 (Adamantyl-CH_2 CD), 36.0 (Adamantyl-CH_2 AB), 39.8 (C1'), 41.5 (Adamantyl-CH_2 AB), 41.6 (Adamantyl-CH_2 CD), 53.1 (Adamantyl-C AB), 54.5 (Adamantyl-C CD), 61.9 (C2 AB), 62.4 (C2 CD), 67.3 (C5 AB), 70.6 (C5 CD), 85.4 (C7 CD), 95.0 (C7 AB), 116.0 (C3'), 126.4, 128.8 (Ar-CH CD), 126.5, 128.8 (Ar-CH AB), 137.1 (C2'), 138.1, 140.0 (Ar-C AB), 138.4, 139.9 (Ar-C CD), 166.0 (C9 AB), 166.5 (C9 CD), 172.3 (C8 AB), 178.2 (C8 CD), 188.0 (C6 AB), 191.3 (C6 CD); *m/z* (ESI^-) 449 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{26}H_{31}N_2O_3S$ $[M+H]^+$; found 451.20477, requires 451.20499.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14e



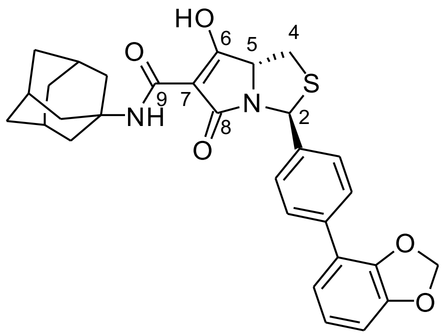
Yield (0.16 g, 53 %); brown foam; 3:1 AB:CD tautomers; mp 154-156 °C; R_f = 0.55 (EtOAc/MeOH 94:6); $[\alpha]_D^{25}$ = -218.6 (c = 0.15, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1149, 1305 (S=O), 1622 (C=C), 1646 (C=O), 1685 (C=O), 3314 (N-H/O-H); δ_H (400 MHz, CD_2Cl_2) 1.70 (6H, Adamantyl-CH_2), 2.01 - 2.16 (9H, m, Adamantyl-CH_2 + Adamantyl-CH), 3.03 (1H, dd, J = 11.3, 8.6 Hz, $H4_A$), 3.07 (3H, s, CH_3), 3.29 (1H, dd, J = 11.3, 7.1 Hz, $H4_B$), 4.47 (1H, app t, J = 7.8 Hz, H5 CD), 4.74 (1H, dd, J = 8.1, 7.3 Hz, H5 AB), 6.28 (1H, s, H2 AB), 6.37 (1H, s, H2 CD), 7.17 (1H, br. s, OH), 7.36 (1H, br. s, NH AB), 7.58, 7.64 (4H, ABq, J_{AB} = 8.3 Hz, Ar-CH), 7.79 (2H, d, J = 8.5 Hz, Ar-CH), 7.94 (1H, br. s, NH CD), 7.98 (2H, d, J = 8.5 Hz, Ar-CH); δ_C (125.8 MHz, CD_2Cl_2): 30.0 (Adamantyl-CH), 33.2 (C4), 36.6 (Adamantyl-CH_2), 42.1 (Adamantyl-CH_2), 45.0 (CH_3), 53.5 (Adamantyl-C), 62.3 (C2 AB), 62.9 (C2 CD), 68.1 (C5 AB), 71.6 (C5 CD), 85.7 (C7 CD), 95.8 (C7 AB), 127.5, 127.6, 128.2, 128.4 (Ar-CH), 139.3, 140.0, 142.2, 146.4 (Ar-C CD), 139.4, 140.0, 141.9, 146.4 (Ar-C AB), 166.6 (C9 AB), 167.2 (C9 CD), 172.9 (C8 AB), 179.0 (C8 CD), 188.5 (C6 AB), 191.5 (C6 CD); *m/z* (ESI^-) 563 ($[M-H]^-$, 21 %); HRMS (ESI^-); $C_{30}H_{31}O_5N_2S_2$ $[M-H]^-$; found 563.16921, requires 563.16799.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-(3,5-dimethylisoxazol-4-yl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14f



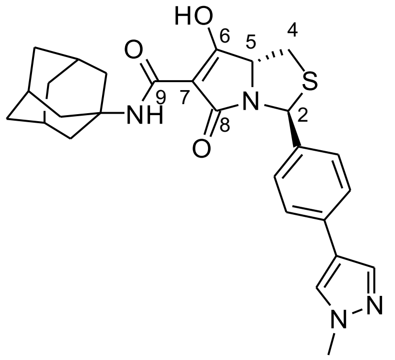
Yield (0.23 g, 72 %); yellow solid; 2.5:1 AB:CD tautomers; mp 130-134 °C; R_f = 0.60 (EtOAc/MeOH 96:4); $[\alpha]_D^{25}$ = -195.5 (c = 0.23, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1624 (C=C, br with shoulder towards higher wavenumber), 1686 (C=O), 3311 (N-H/O-H); δ_H (400 MHz, $CDCl_3$) 1.68 (6H, Adamantyl-C*H*$_2$), 2.00 - 2.07 (6H, m, Adamantyl-C*H*$_2$), 2.08 - 2.16 (3H, m, Adamantyl-C*H*), 2.24 (3H, s, C*H*$_3$), 2.38 (3H, s, C*H*$_3$), 2.95 - 3.07 (1H, m, H4$_A$), 3.24 - 3.32 (1H, m, H4$_B$), 4.47 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.72 (1H, dd, *J* = 8.6, 6.9 Hz, H5 AB), 6.25 (1H, s, H2 AB), 6.35 (1H, s, H2 CD), 7.23 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 7.41 (1H, s, NH AB), 7.48 - 7.55 (2H, m, Ar-C*H*), 7.93 (1H, s, NH CD), 11.16 (1H, br. s, OH); δ_C (100.6 MHz, $CDCl_3$): 10.7 (*C*H$_3$), 11.4 (*C*H$_3$), 29.2 (Adamantyl-*C*H), 32.6 (C4 AB), 32.8 (C4 CD), 35.7 (Adamantyl-*C*H$_2$ CD), 35.9 (Adamantyl-*C*H$_2$ AB), 41.4 (Adamantyl-*C*H$_2$ AB), 41.5 (Adamantyl-*C*H$_2$ CD), 53.0 (Adamantyl-C AB), 53.4 (Adamantyl-C CD), 61.6 (C2 AB), 62.1 (C2 CD), 67.5 (C5 AB), 70.7 (C5 CD), 85.2 (C7 CD), 94.7 (C7 AB), 116.0, 130.2, 139.6, 158.5, 165.2 (Ar-C, AB), 116.0, 130.1, 139.9, 158.5, 165.2 (Ar-C CD), 126.6, 129.1 (Ar-*C*H CD), 126.8, 129.2 (Ar-*C*H AB), 165.9 (C9 AB), 166.4 (C9 CD), 172.2 (C8 AB), 178.0 (C8 CD), 188.1 (C6 AB), 191.0 (C6 CD); *m/z* (ESI$^-$) 504 ([M-H]$^-$, 100 %); HRMS (ESI$^-$); $C_{28}H_{30}O_4N_3S$ [M-H]$^-$; found 504.19749, requires 504.19625.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-(benzo[*d*][1,3]dioxol-4-yl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14g



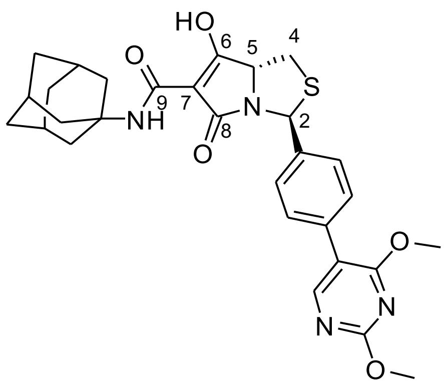
Yield (75 mg, 60 %); yellow solid, mp 130-132 °C; 3:1 AB:CD tautomers; R_f = 0.72 (EtOAc; 100 %); $[\alpha]_D^{25}$ = - 199.7 (*c* = 0.18, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1621 (C=C), 1646 (C=O), 1686 (C=O), 3310 (N-H/O-H); δ_H (400 MHz, $CDCl_3$) 1.65 - 1.74 (6H, m, Adamantyl-C*H*$_2$), 2.02 - 2.16 (9H, m, Adamantyl-C*H* + Adamantyl-C*H*$_2$), 2.98 - 3.05 (1H, m, H4$_A$), 3.24 - 3.32 (1H, m, H4$_B$), 4.47 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.74 (1H, dd, *J* = 8.1, 7.3 Hz, H5 AB), 6.00 (2H, s, C*H*$_2$), 6.25 (1H, s, H2 AB), 6.34 (1H, s, H2 CD), 6.87 - 6.90 (1H, m, Ar-C*H*), 7.05 - 7.09 (2H, m, Ar-C*H*), 7.37 (1H, br. s, NH, AB), 7.50, 7.51 (4H, ABq, J_{AB} = 8.6 Hz, Ar-C*H*), 7.93 (1H, br. s, NH CD), 9.01 (1H, br. s, OH); δ_C (125.8 MHz, $CDCl_3$): 30.0 (Adamantyl-*C*H), 33.1 (C4 AB), 33.4 (C4 CD), 36.4 (Adamantyl-*C*H$_2$ CD), 36.6 (Adamantyl-*C*H$_2$ AB), 42.1 (Adamantyl-*C*H$_2$ AB), 42.2 (Adamantyl-*C*H$_2$ CD), 55.0 (Adamantyl-C), 62.3 (C2 AB), 62.9 (C2 CD), 68.0 (C5 AB), 71.5 (C5 CD), 85.7 (C7 CD), 96.1 (C7 AB), 102.0 (*C*H$_2$), 107.9, 109.0, 121.1, 127.3, 127.5 (Ar-*C*H), 135.3, 140.0, 140.3, 141.0, 141.1, 147.8, 147.9, 148.8 (Ar-C), 166.6 (C9 AB), 167.2 (C9 CD), 172.8 (C8 AB), 179.0 (C8 CD), 188.3 (C6 AB), 191.6 (C6 CD); *m/z* (ESI$^-$) 529 ([M-H]$^-$, 100 %); HRMS (ESI$^+$); $C_{30}H_{31}O_5N_2S$ [M+H]$^+$; found 531.19469, requires 531.19482.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-(1-methyl-1*H*-pyrazol-4-yl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14h



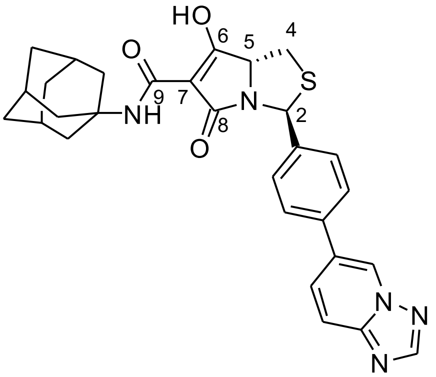
Yield (0.24 g, 78 %); light brown foam, mp 140-142 °C; 2.7:1 AB:CD tautomers; R_f = 0.72 (EtOAc/MeOH 4:1); $[\alpha]_D^{25}$ = -293.5 (*c* = 0.17, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1618 (C=C), 1645 (C=O), 1684 (C=O), 3310 (N-H/O-H); δ_H (400 MHz, $CDCl_3$) 1.69 (6H, Adamantyl-CH_2), 2.04 (6H, Adamantyl-CH_2), 2.11 (3H, Adamantyl-C*H*), 3.00 (1H, dd, *J* = 11.0, 8.6 Hz, $H4_A$), 3.26 (1H, dd, *J* = 11.0, 7.2 Hz, $H4_B$), 3.93 (3H, s, CH_3), 4.44 (1H, app t, *J* = 7.7 Hz, H5 CD), 4.69 (1H, app t, *J* = 7.8 Hz, H5 AB), 6.24 (1H, s, H2 AB), 6.34 (1H, s, H2 CD), 7.42 (1H, br. s, NH AB), 7.44, 7.44 (4H, ABq, J_{AB} = 10.8 Hz, Ar-C*H*), 7.59 (1H, s, Ar-C*H*), 7.74 (1H, s, Ar-C*H*), 7.92 (1H, s, NH CD), 10.70 (1H, br. s, OH); δ_C (125.8 MHz, $CDCl_3$): 29.2 (Adamantyl-*C*H), 32.4 (C4 AB), 32.7 (C4 CD), 35.8 (Adamantyl-*C*H_2 CD), 36.0 (Adamantyl-*C*H_2 AB), 39.0 (*C*H_3), 41.4 (Adamantyl-*C*H_2 AB), 41.5 (Adamantyl-*C*H_2 CD), 53.4 (Adamantyl-*C* AB), 54.4 (Adamantyl-*C* CD), 61.8 (C2 AB), 62.4 (C2 CD), 67.3 (C5 AB), 70.6 (C5 CD), 85.3 (C7 CD), 95.0 (C7 AB), 125.6, 126.8, 126.9, 136.7 (Ar-*C*H AB), 125.5, 126.7, 126.9, 136.7 (Ar-*C*H CD), 122.5, 132.3, 138.5 (Ar-C CD), 122.5, 132.4, 138.2 (Ar-C AB), 165.9 (C9 AB), 166.5 (C9 CD), 172.3 (C8 AB), 178.2 (C8 CD), 188.0 (C6 AB), 191.2 (C6 CD); *m/z* (ESI^-) 489 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{27}H_{31}O_3N_4S$ $[M+H]^+$; found 491.21116, requires 491.21114.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-(2,4-dimethoxypyrimidin-5-yl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14i



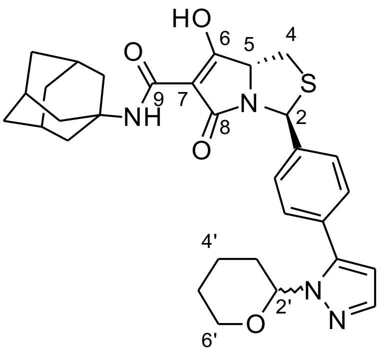
Yield (0.18 g, 56 %); light brown foam, mp 106-108 °C; 2.5:1 AB:CD tautomers; R_f = 0.66 (EtOAc/MeOH 96:4); $[\alpha]_D^{25}$ = -290.3 (*c* = 0.15, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1624 (C=C), 1647 (C=O), 1687 (C=O), 3313 (N-H/O-H); δ_H (400 MHz, $CDCl_3$) 1.68 - 1.74 (6H, m, Adamantyl-CH_2), 2.02 - 2.10 (6H, m, Adamantyl-CH_2), 2.11 - 2.20 (3H, m, Adamantyl-C*H*), 2.98 - 3.10 (1H, m, $H4_A$), 3.30 (1H, dd, *J* = 11.0, 7.1 Hz, $H4_B$), 4.02 (3H, s, OCH_3), 4.04 (3H, s, OCH_3), 4.47 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.71 (1H, dd, *J* = 8.3, 7.3 Hz, H5 AB), 6.28 (1H, s, H2 AB), 6.38 (1H, s, H2 CD), 6.40 (1H, br. s, OH), 7.43 (1H, br. s, NH AB), 7.47 - 7.56 (4H, m, Ar-C*H*), 7.94 (1H, s, NH CD), 8.24 - 8.27 (1H, m, Ar-C*H*, overlapping singlet peaks for AB and CD tautomers); δ_C (125.8 MHz, $CDCl_3$): 29.3 (Adamantyl-*C*H), 32.6 (C4 AB), 32.9 (C4 CD), 35.8 (Adamantyl-*C*H_2 CD), 36.0 (Adamantyl-*C*H_2 AB), 41.5 (Adamantyl-*C*H_2 AB), 41.6 (Adamantyl-*C*H_2 CD), 53.2 (Adamantyl-C AB), 54.1 (O*C*H_3), 54.5 (Adamantyl-C CD), 54.9 (OCH_3), 61.9 (C2 AB), 62.4 (C2 CD), 67.5 (C5 AB), 70.7 (C5 CD), 85.4 (C7 CD), 94.8 (C7 AB), 126.5, 129.0, 157.5 (Ar-*C*H CD), 126.6, 129.1, 157.5 (Ar-*C*H AB), 115.7, 133.1, 139.8, 164.6, 168.1 (Ar-C CD), 115.7, 133.0, 140.1, 164.6, 168.1 (Ar-C CD), 166.0 (C9 AB), 166.6 (C9 CD), 172.4 (C8 AB), 178.2 (C8 CD), 188.3 (C6 AB), 191.2 (C6 CD); *m/z* (ESI^-) 547 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{29}H_{33}O_5N_4S$ $[M+H]^+$; found 549.21610, requires 549.21662.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-([1,2,4])triazolo[1,5-*a*]pyridin-6-yl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14j



Yield (0.12 g, 70 %); light brown solid, mp 220 °C; 3:1 AB:CD tautomers; R_f = 0.68 (EtOAc/MeOH 4:1); $[\alpha]_D^{25}$ = -217.8 (*c* = 0.19, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1620 (C=C, br with shoulder towards higher wavenumber), 1684 (C=O), 3307 (N-H/O-H); δ_H (400 MHz, CD_2Cl_2) 1.70 (6H, Adamantyl-CH_2), 2.01 - 2.16 (9H, m, Adamantyl-CH_2 + Adamantyl-C*H*), 3.04 (1H, dd, *J* = 11.0, 8.6 Hz, $H4_A$), 3.30 (1H, dd, *J* = 11.0, 7.1 Hz, $H4_B$), 4.48 (1H, app t, *J* = 7.0 Hz, H5 CD), 4.75 (1H, app t, *J* = 7.7 Hz, H5 AB), 6.28 (1H, s, H2 AB), 6.37 (1H, s, H2 CD), 7.37 (1H, br. s, NH AB), 7.59, 7.62 (4H, ABq, J_{AB} = 8.6 Hz, Ar-C*H*), 7.80, 7.80 (2H, ABq, J_{AB} = 9.3 Hz, Ar-C*H*), 7.95 (1H, br. s, NH CD), 8.32 (1H, s, Ar-C*H*), 8.82 (1H, s, Ar-C*H*); δ_C (125.8 MHz, CD_2Cl_2): 30.1 (Adamantyl-*C*H), 33.2 (C4), 36.6 (Adamantyl-*C*H_2), 42.1 (Adamantyl-*C*H_2), 53.6 (Adamantyl-C, obscured by CD_2Cl_2 signals, but HMBC correlation seen with adamantyl-CH_2), 62.3 (C2 AB), 62.8 (C2 CD), 68.1 (C5 AB), 71.6 (C5 CD), 95.8 (C7), 117.1, 126.5, 127.9, 127.9, 130.4, 154.9 (Ar-*C*H), 128.4, 136.6, 141.7, 150.4 (Ar-C), 166.6 (C9 AB), 167.2 (C9 CD), 173.0 (C8), 188.5 (C6 AB), 191.5 (C6 CD); *m/z* (ESI^-) 526 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{29}H_{30}O_3N_5S$ $[M+H]^+$; found 528.20630, requires 528.20748.

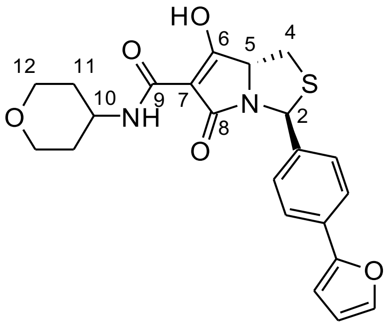
(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-(1-(tetrahydro-2*H*-pyran-2'-yl)-1*H*-pyrazol-5-yl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14k



Yield (0.14 g, 60 %); yellow foam; 1:1 dr, each diastereomer exists as 2.6:1 AB:CD tautomers; R_f = 0.63 (EtOAc/MeOH 9:1); ν_{max}/cm^{-1} (neat) 1622 (C=C), 1646 (C=O), 1686 (C=O), 3315 (N-H/O-H); since the diastereomers are overlapping, the ^{1}H resonances are reported together as multiplets, δ_H (500 MHz, CD_2Cl_2) 1.50 - 1.61 (2H, m, H4' + H5'), 1.68 - 1.74 (7H, Adamantyl-CH_2 + H5'), 1.76 - 1.82 (1H, m, H3'), 1.99 - 2.16 (10H, m, Adamantyl-CH_2 + Adamantyl-C*H* + H4'), 2.48 - 2.57 (1H, m, H3'), 3.00 - 3.06 (1H, m, $H4_A$), 3.26 - 3.33 (1H, m,

$H4_B$), 3.56 - 3.64 (1H, m, H6'), 4.05 - 4.11 (1H, m, H6'), 4.45 - 4.51 (1H, m, H5 CD), 4.73 - 4.78 (1H, m, H5 AB), 4.88 (1H, br. s, OH), 5.15 - 5.20 (1H, m, H2'), 6.27 (1H, s, H2 AB), 6.33 - 6.35 (1H, m, Ar-C*H*), 6.36 (1H, s, H2 CD), 7.36 (1H, br. s, NH AB), 7.50 - 7.58 (5H, m, Ar-C*H*), 7.94 (1H, br. s, NH CD); δ_C (125.8 MHz, CD_2Cl_2): 23.6 (C4'), 25.5 (C5'), 30.1 (Adamantyl-*C*H), 30.2 (C3'), 33.2, 33.3 (C4 AB), 33.5, 33.6 (C4 CD), 36.4 (Adamantyl-*C*H_2 CD), 36.6 (Adamantyl-*C*H_2 AB), 42.1 (Adamantyl-*C*H_2 AB), 42.2 (Adamantyl-*C*H_2 CD), 53.6 (Adamantyl-C, obscured by CD_2Cl_2 signals, but HMBC correlation seen with adamantyl-C*H_2*), 62.2, 62.3 (C2 AB), 62.8, 62.9 (C2 CD), 68.1 (C5 AB), 68.2 (C6'), 71.6 (C5 CD), 84.8 (C2'), 85.6 (C7 CD), 95.8 (C7 AB), 107.1, 127.2, 129.7, 139.6 (Ar-C*H* AB), 107.1, 127.1, 129.7, 139.6 (Ar-C*H* CD), 107.1, 127.2, 129.7, 139.6 (Ar-C*H* AB), 130.8, 141.8, 144.2 (Ar-C AB), 130.7, 142.1, 144.2 (Ar-C CD), 166.6 (C9 AB), 167.2 (C9 CD), 172.9 (C8 AB), 179.0 (C8 CD), 188.5 (C6 AB), 191.5 (C6 CD); *m/z* (ESI^-) 559 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{31}H_{37}O_4N_4S$ $[M+H]^+$; found 561.25289, requires 561.25300.

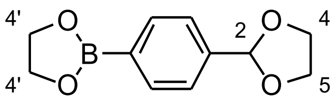
(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-2-(4-(1-(tetrahydro-2*H*-pyran-2'-yl)-*1H*-pyrazol-5-yl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 14l



Yield (70 mg, 30 %); yellow oil, 5.3:1 AB:CD tautomers; R_f = 0.45 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -181.7 (*c* = 0.12, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1624 (C=C with shoulder towards higher wavenumber), 1687 (C=O), 3317 (O-H/N-H); δ_H (400 MHz, CD_2Cl_2) major tautomer (AB): 1.51 - 1.73 (2H, m, H11), 1.83 - 1.99 (2H, m, H11), 2.98 - 3.07 (1H, m, $H4_A$), 3.29 (1H, dd, *J* = 11.1, 7.0 Hz, $H4_B$), 3.47 (2H, app t, *J* = 11.6, 2.2 Hz, H12), 3.88 - 3.99 (2H, m, H12), 4.01 - 4.12 (1H, m, H10), 4.48 (1H, app t, *J* = 7.8 Hz, H5 CD), 4.80 (1H, dd, *J* = 8.0, 7.2 Hz, H5 AB), 6.24 (1H, s, H2 AB), 6.33 (1H, s, H2 CD), 6.47 - 6.54 (1H, m, Ar-C*H*), 6.69 - 6.73 (1H, m, Ar-C*H*), 7.45 - 7.51 (3H, m, Ar-C*H*), 7.64 - 7.69 (2H, m, Ar-C*H*), 8.84 (1H, br. s, NH/OH); δ_C (100.6 MHz, CD_2Cl_2): 33.0 (C4), 33.3 (C11), 45.9 (C10 AB), 47.6 (C10 CD), 62.3 (C2 AB), 63.0 (C2 CD), 66.9 (C12), 67.5 (C5 AB), 71.6 (C5 CD), 97.5 (C7), 106.0, 112.3, 124.4, 127.3, 142.9 (Ar-*C*H), 131.2, 140.1, 154.0 (Ar-C), 165.9 (C9 AB), 166.6 (C9 CD), 172.4 (C8 AB), 178.5 (C8 CD), 186.5 (C6 AB), 191.3 (C6 CD); *m/z* (ESI^-) 425 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{22}H_{21}N_2O_5S$ $[M-H]^-$; found 425.11872, requires 425.11767.

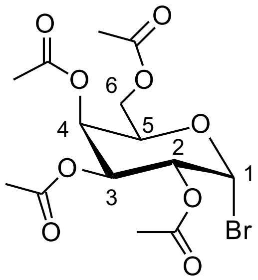
2-(4-(1,3-Dioxolan-2-yl)phenyl)-1,3,2-dioxaborolane [4]

To 4-formylphenyl boronic acid (0.5 g, 3.33 mmol, 1.0 eq) in toluene (30 mL), ethylene glycol (0.93 mL, 16.7 mmol, 5.0 eq) and *p*-toluenesulfonic acid (15.8 mg, 0.08 mmol, 0.025 eq) was added and refluxed with a Dean-Stark apparatus. The reaction was not complete in 5 h and was refluxed overnight. The reaction flask was cooled to rt and concentrated under reduced pressure.The residue



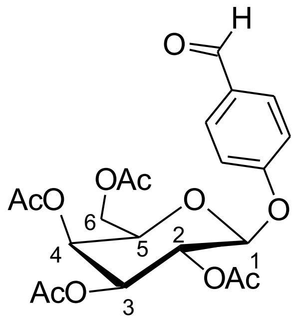
was dissolved in 5 mL of CH_2Cl_2 and treated with 1.0 g of $MgSO_4$. The mixture was stirred at rt for 1 h, filtered and washed with CH_2Cl_2. The filtrate was concentrated *in vacuo* to obtain the desired product. Yield (0.69 g, 94 %); white solid, mp 102-104 °C {lit. mp = 104-106 °C}{Iwai, 2008 #2872}; R_f = 0.44 (EtOAc/petrol 2:1); ν_{max}/cm^{-1} (neat) 1070, 1093 (C-O), 1334 (B-O), 2915, 2984 (C-H); δ_H (400 MHz, CD_2Cl_2): 3.98 - 4.05 (2H, m, H4/H5), 4.06 - 4.13 (2H, m, H4/H5), 4.36 (4H, s, H4'), 5.78 (1H, s, H2), 7.48 (2H, d, *J* = 8.2 Hz, Ar-C*H*), 7.81 (2H, d, *J* = 8.2 Hz, Ar-C*H*); δ_C (100.6 MHz, CD_2Cl_2): 65.9 (C4, C5), 66.7 (C4'), 104.0 (C2), 126.5, 135.3 (Ar-*C*H) 130.5, 141.9 (Ar-C); *m/z* HRMS (FI^+); $C_{11}H_{13}BO_4$ $[M]^+$; found 220.0910, requires 220.0909.

(+)-2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide, 15b [5]



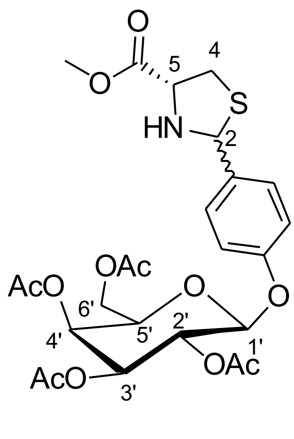
To a stirred solution of β-D-galactose pentaacetate (0.3 g, 0.77 mmol, 1.0 eq) and $BiBr_3$ (17 mg, 0.039 mmol, 0.05 eq) in 3 mL of CH_2Cl_2 was added under N_2, TMSBr (0.41 mL, 3.08 mmol, 4 eq). The reaction was stirred at rt and monitored by TLC. After 2 h, upon completion of reaction, the reaction mixture was poured into cold sat. $NaHCO_3$ and extracted twice with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to obtain **15b**. Yield (0.32 g, quant.); white solid, mp 82-84 °C {lit. mp = 84-85 °C}[5] R_f = 0.39 (EtOAc/Petrol 1:3); $[\alpha]_D^{25}$ = +200.7 (*c* = 0.5, $CHCl_3$) {lit. $[\alpha]_D$ = +217 (*c* = 1, $CHCl_3$)} [5] ν_{max}/cm^{-1} (neat) 1220 (C-O), 1749 (C=O); δ_H (400 MHz, $CDCl_3$): 2.02 (3H, s, C*H*$_3$-C(=O)-O-), 2.07 (3H, s, C*H*$_3$-C(=O)-O-), 2.12 (3H, s, C*H*$_3$-C(=O)-O-), 2.17 (3H, s, C*H*$_3$-C(=O)-O-), 4.12 (1H, dd, *J* = 11.4, 6.8, $H6_A$), 4.19 (1H, dd, *J* = 11.4, 6.4, $H6_B$), 4.49 (1H, app t, *J* = 6.6, H5), 5.06 (1H, dd, *J* = 10.6, 4.0 Hz, H2), 5.41 (1H, dd, *J* = 10.7, 3.3 Hz, H3), 5.53 (1H, dd, *J* = 3.2, 1.2 Hz, H4), 6.70 (1H, d, *J* = 4.1 Hz, H1); δ_C (125.8 MHz, $CDCl_3$): 20.5, 20.6, 20.6, 20.7 (*C*H$_3$-C(=O)-O-), 60.8 (C6), 66.9 (C4), 67.7 (C2), 68.0 (C3), 71.0 (C5), 88.1 (C1), 169.7, 169.9, 170.1, 170.3 (CH$_3$-*C*(=O)-O-); *m/z* (ESI^+ and FI^+) 331 ($[M-Br]^+$, 100 %); molecular ion not detected.

(-)-4-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)benzaldehyde, 15c [6]

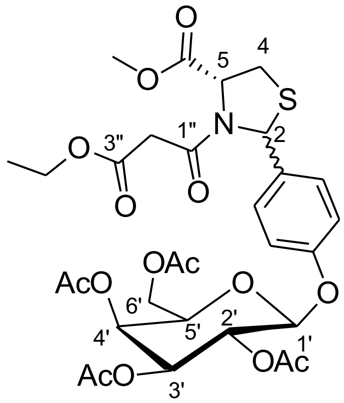


To **15b** (1.0 g, 2.44 mmol, 1.0 eq), 4-hydroxybenzaldehyde (0.36 g, 2.93 mmol, 1.2 eq) and benzyltributylammonium chloride (0.17 g, 0.49 mmol, 0.2 eq) in $CHCl_3$ (5 mL), was added powdered K_2CO_3 (1.69 g, 12.2 mmol, 5 eq) and stirred at rt for 24 h. The reaction mixture was neutralised with 10 % HCl and the organic layer was separated. The organic layer was washed with sat. $NaHCO_3$ and brine, then dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (eluent: EtOAc/petrol) to furnish **15c**. Yield (0.95 g, 86 %); white solid, mp 132 °C {lit. mp = 140-141 °C}[6] R_f = 0.18 (EtOAc/petrol 1:2); $[\alpha]_D^{25}$ = -1.87 (*c* = 1.0, $CHCl_3$) ν_{max}/cm^{-1} (neat) 1212 (C-O), 1694 (C=O), 1746 (C=O); δ_H (400 MHz, $CDCl_3$): 2.02 (3H, s, C*H*$_3$-C(=O)-O-), 2.06 (6H, s, 2xC*H*$_3$-C(=O)-O-), 2.18 (3H, s, C*H*$_3$-C(=O)-O-), 4.10 - 4.26 (3H, m, H6$_A$ + H6$_B$ + H5), 5.14 (1H, dd, *J* = 10.3, 3.4 Hz, H3), 5.18 (1H, d, *J* = 7.8 Hz, H1), 5.48 (1H, app d, *J* = 3.4 Hz, H4), 5.52 (1H, dd, *J* = 10.4, 8.0 Hz, H2), 7.11 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.85 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 9.92 (1H, s, C*H*O); δ_C (100.6 MHz, $CDCl_3$): 20.5, 20.6, 20.6, 20.7 (*C*H$_3$-C(=O)-O-), 61.3 (C6), 66.7 (C4), 68.3 (C2), 70.6 (C3), 71.3 (C5), 98.5 (C1), 116.7, 131.8 (Ar-*C*H), 161.2 (Ar-C), 169.3, 170.0, 170.1, 170.3 (CH$_3$-*C*(=O)-O-), 190.7 (*C*HO); *m/z* (ESI^+) 475 ($[M+Na]^+$, 100 %); HRMS (ESI^+); $C_{21}H_{24}O_{11}Na$ $[M+Na]^+$; found 475.11966, requires 475.12108.

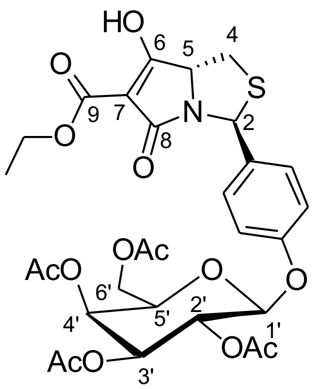
(-)-(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(Acetoxymethyl)-6-(4-((2*S*,5*R*)-7-(ethoxycarbonyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazol-2-yl)phenoxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate 16



Thiazolidine derived from the condensation of L-cysteine methyl ester hydrochloride and aldehyde **15c** followed the general procedure. Yield (0.14 g, 70 %); colourless oil; 1.6:1 *cis* and *trans* diastereomers; R_f = 0.4 (EtOAc/petrol 1:1); ν_{max}/cm^{-1} (neat) 1223 (C-O), 1745 (C=O), 3314 (N-H); δ_H (400 MHz, $CDCl_3$) major isomer (*cis*): 1.97 (3H, s, C*H*$_3$-C(=O)-O-), 2.01 (3H, s, C*H*$_3$-C(=O)-O-), 2.02 (3H, s, C*H*$_3$-C(=O)-O-), 2.14 (3H, s, C*H*$_3$-C(=O)-O-), 2.60 (1H, br. s., NH), 3.06 (1H, dd, *J* = 10.3, 8.8 Hz, H4$_A$), 3.41 (1H, dd, *J* = 10.3, 7.1 Hz, H4$_B$), 3.76 (3H, s, -CO$_2$C*H*$_3$), 3.93 (1H, dd, *J* = 8.6, 7.3 Hz, H5), 4.01 - 4.20 (3H, m, H6'$_A$ + H6'$_B$ + H5'), 5.03 (1H, d, *J* = 8.1 Hz, H1'), 5.05 - 5.11 (1H, m, H3', obscured by H3' of minor isomer), 5.39 - 5.46 (2H, m, H2' + H4'), 5.47 (1H, s, H2), 6.96 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.42 (2H, d, *J* = 8.6 Hz, Ar-C*H*); minor isomer (*trans*): 1.97 (3H, s, C*H*$_3$-C(=O)-O-), 2.01 (3H, s, C*H*$_3$-C(=O)-O-), 2.02 (3H, s, C*H*$_3$-C(=O)-O-), 2.13 (3H, s, C*H*$_3$-C(=O)-O-), 2.60 (1H, br. s., NH), 3.15 (1H, dd, *J* = 10.6, 5.8 Hz, H4$_A$), 3.34 (1H, dd, *J* = 10.5, 7.1 Hz, H4$_B$), 3.74 (3H, s, -CO$_2$C*H*$_3$), 4.01 - 4.20 (4H, m, H6'$_A$ + H6'$_B$ + H5' + H5), 5.00 (1H, d, J = 7.8 Hz, H1'), 5.05 - 5.11 (1H, m, H3', obscured by H3' of major isomer), 5.39 - 5.46 (2H, m, H2' + H4'), 5.73 (1H, s, H2), 6.92 (2H, d, J = 8.6 Hz, Ar-C*H*), 7.38 (2H, d, J = 8.6 Hz, Ar-C*H*); δ_C (100.6 MHz, $CDCl_3$): major isomer (*cis*): 20.4, 20.5, 20.5, 20.5 (*C*H_3-C(=O)-O-), 39.0 (C4), 52.4 (-CO_2*C*H_3), 61.2 (C6'), 65.3 (C5), 66.7 (C4'), 68.4 (C2'), 70.6 (C3'), 70.9 (C5'), 71.8 (C2), 99.3 (C1'), 116.8, 128.7 (Ar-*C*H), 132.9, 156.9 (Ar-C), 169.2, 169.9, 170.0, 170.1 (CH_3-*C*(=O)-O-), 171.4 (-*C*O_2CH_3); minor isomer (*trans*): 20.4, 20.5, 20.5, 20.5 (*C*H_3-C(=O)-O-), 37.9 (C4), 52.4 (-CO_2*C*H_3), 61.2 (C6'), 64.0 (C5), 66.7 (C4'), 68.4 (C2'), 70.0 (C2), 70.6 (C3'), 70.9 (C5'), 99.4 (C1'), 116.6, 128.1 (Ar-*C*H), 135.9, 156.4 (Ar-C), 169.2, 169.9, 170.0, 170.1 (CH_3-*C*(=O)-O-), 172.0 (-*C*O_2CH_3); *m/z* (ESI^+) 570 ($[M+H]^+$ 35 %); HRMS (ESI^+); $C_{25}H_{32}O_{12}NS$ $[M+H]^+$; found 570.16190, requires 570.16397.



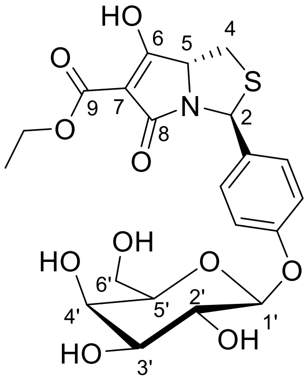
The *N*-acylthiazolidine was obtained *via* *N*-acylation of thiazolidine using the general procedure. Yield (68 mg, 52 %); colourless oil; 1.1:1 *cis* and *trans* diastereomers; R_f = 0.18 (EtOAc/petrol 1:1); ν_{max}/cm^{-1} (neat) 1223 (C-O), 1663 (C=O), 1745 (C=O); δ_H (500 MHz, $CDCl_3$) major isomer (*cis*, a mixture of two conformers): 1.20 - 1.31 (3H, m, OCH_2C*H_3*), 2.01 (3H, s, C*H_3*-C(=O)-O-), 2.05 - 2.11 (6H, m, 2xC*H_3*-C(=O)-O-), 2.18 (3H, s, C*H_3*-C(=O)-O-), 3.07 - 3.46 (4H, m, $H4_A$ + $H4_B$ + $H2''_A$ + $H2''_B$), 3.82 (3H, s, CO_2C*H_3* major conformer), 3.83 (3H, s, CO_2C*H_3* minor conformer), 4.03 - 4.24 (5H, m, OC*H_2*CH_3, $H6'_A$ + $H6'_B$ + H5'), 4.99 - 5.08 (2H, m, H5 + H1'), 5.11 (1H, dd, J = 10.6, 3.1 Hz, H3'), 5.43 - 5.52 (2H, m, H2' + H4'), 6.12 (1H, s, H2 major conformer), 6.28 (1H, s, H2 minor conformer), 6.91 - 6.96 (2H, m, Ar-C*H* minor conformer), 6.98 - 7.04 (2H, m, Ar-C*H* major conformer), 7.46 (2H, d, J = 8.5 Hz, Ar-C*H* minor conformer); 7.62 (2H, d, J = 8.7 Hz, Ar-C*H* major conformer); minor isomer (*trans*, a mixture of two conformers): 1.20 - 1.31 (3H, m, OCH_2C*H_3*), 2.01 (3H, s, C*H_3*-C(=O)-O-), 2.05 - 2.11 (6H, m, 2xC*H_3*-C(=O)-O-), 2.18 (3H, s, C*H_3*-C(=O)-O-), 3.07 - 3.46 (4H, m, $H4_A$ + $H4_B$ + $H2''_A$ + $H2''_B$), 3.79 (3H, s, CO_2C*H_3* major conformer), 3.85 (3H, s, CO_2C*H_3* minor conformer), 4.03 - 4.24 (5H, m, OC*H_2*CH_3 + $H6'_A$ + $H6'_B$ + H5'), 4.99 - 5.08 (1H, m, H1' obscured by H5 of major isomer), 5.11 (1H, dd, J = 10.6, 3.1 Hz, H3'), 5.18 (1H, app d, J = 5.4 Hz, H5 minor conformer), 5.28 - 5.31 (1H, m, H5 major conformer), 5.43 - 5.52 (2H, m, H2' + H4'), 6.16 (1H, s, H2 major conformer), 6.28 (1H, s, H2 minor conformer), 6.91 - 6.96 (2H, m, Ar-C*H* minor conformer), 6.98 - 7.04 (2H, m, Ar-C*H* major conformer), 7.16 (2H, d, J = 8.7 Hz, Ar-C*H* major conformer); 7.22 (2H, d, J = 8.6 Hz, Ar-C*H* minor conformer); δ_C (125.8 MHz, $CDCl_3$): major isomer (*cis*, a mixture of two conformers): 14.0, 14.2 (OCH_2*C*H_3), 20.6, 20.6, 20.6, 20.7 (*C*H_3-C(=O)-O-), 33.1, 33.8 (C4), 42.1, 43.1 (C2″), 52.7, 53.4 (CO_2*C*H_3), 61.2, 61.3 (C6'), 61.6, 61.7 (O*C*H_2CH_3), 63.8, 64.6 (C5), 65.8, 66.7 (C2), 66.8 (C4'), 68.5 (C2'), 70.7, 70.8 (C3'), 70.9, 71.1 (C5'), 99.3, 99.5 (C1'), 116.6, 117.2, 127.9, 128.6 (Ar-*C*H), 133.5, 134.5, 156.6, 157.0 (Ar-C), 165.0, 165.4 (C1''), 166.7, 167.1 (C3''), 169.3, 169.4, 170.06, 170.08, 170.15, 170.18, 170.20, 170.23, 170.3, 170.4 (CO_2CH_3 and CH_3-*C*(=O)-O-); minor isomer (*trans*, a mixture of two conformers): 14.0, 14.1 (OCH_2CH_3), 20.6, 20.6, 20.6, 20.7 (CH_3-C(=O)-O-), 31.0, 32.0 (C4), 42.4, 43.3 (C2″), 52.8, 53.4 (CO_2CH_3), 61.2, 61.3 (C6'), 61.5, 61.8 (OCH_2CH_3), 64.0, 64.2 (C5), 64.5, 65.2 (C2), 66.8 (C4'), 68.5 (C2'), 70.7, 70.8 (C3'), 70.9, 71.1 (C5'), 99.3, 99.6 (C1'), 116.9, 117.4, 126.1, 126.3 (Ar-*C*H), 136.6, 137.0, 156.3, 156.8 (Ar-C), 164.6, 165.3 (C1''), 166.3, 167.3 (C3''), 169.30, 169.33, 170.06, 170.08, 170.15, 170.18, 170.20, 170.23, 170.3, 170.4 (CO_2CH_3 and CH_3-*C*(=O)-O-); *m/z* (ESI^+) 706 ($[M+Na]^+$ 43 %); HRMS (ESI^+); $C_{30}H_{37}O_{15}NNaS$ $[M+Na]^+$; found 706.17535, requires 706.17761.



Tetramate **16** was obtained following the general procedure for Dieckmann cyclisation. The product isolated by flash column chromatography (eluent: 100 % EtOAc to EtOAc/MeOH/1 % Et_3N) was then dissolved in CH_2Cl_2 and washed with 5% citric acid. The organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield **16**. Yield (0.66 g, 52 %); yellow solid, mp 114 °C; R_f = 0.45 (EtOAc/ MeOH 9:1); $[\alpha]_D^{25}$ = -152.6 (*c* = 0.27, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1217 (C-O), 1613 (C=C), 1746 (C=O, br with shoulder towards smaller wave number); δ_H (400 MHz, $CDCl_3$): 1.39 (3H, t, *J* = 7.1 Hz, OCH_2CH_3), 2.02 (3H, s, CH_3-C(=O)-O-), 2.07 (3H, s, CH_3-C(=O)-O-), 2.07 (3H, s, CH_3-C(=O)-O-), 2.19 (3H, s, CH_3-C(=O)-O-), 2.99 (1H, dd, *J* = 11.0, 8.3 Hz, $H4_A$), 3.29 (1H, dd, *J* = 11.1, 7.0 Hz, $H4_B$), 4.03 - 4.09 (1H, m, H5'), 4.15 (1H, dd, *J* = 11.4, 5.8 Hz, $H6'_A$), 4.19 (1H, dd, *J* = 11.4, 7.1 Hz, $H6'_B$), 4.40 (2H, q, *J* = 7.1 Hz, OCH_2CH_3), 4.75 (1H, app t, *J* = 7.6 Hz, H5), 5.03 (1H, d, *J* = 8.1 Hz, H1'), 5.11 (1H, dd, *J* = 10.5, 3.4 Hz, H3'), 5.44 - 5.52 (2H, m, H2' + H4'), 6.27 (1H, s, H2), 6.97 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.43 (2H, d, *J* = 8.6 Hz, Ar-C*H*); δ_C (125.8 MHz, CD_2Cl_2): 14.5 (OCH_2CH_3), 20.9, 21.0, 21.1, 21.1 (CH_3-C(=O)-O-), 33.4 (C4), 62.0 (C6'), 62.2 (OCH_2CH_3), 62.5 (C2), 66.1 (C5), 67.5 (C4'), 69.0 (C2'), 71.3 (C3'), 71.8 (C5'), 100.2 (C1'), 117.5, 128.3 (Ar-*C*H), 136.0, 157.3 (Ar-C), 167.6 (C9), 169.2 (C8), 169.9, 170.5, 170.7, 170.8 (CH_3-*C*(=O)-O-), 186.7 (C6); *m/z* (ESI^+) 674 ($[M+Na]^+$, 15 %); HRMS (ESI^+); $C_{29}H_{33}O_{14}NNaS$ $[M+Na]^+$; found 674.15101, requires 674.15140.

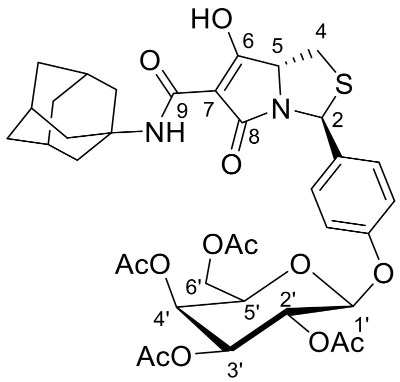
(-)- Ethyl (2*S*,5*R*)-6-hydroxy-8-oxo-2-(4-((2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2*H*-pyran-2-yl)oxy)phenyl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxylate 17

Tetramate /**16** (28 mg, 0.04 mmol, 1.0 eq) was dissolved in MeOH (2 mL) and aq. K_2CO_3 (6.6 mg in 0.5 mL of H_2O, 0.048 mmol, 1.2 eq) was added. The reaction was stirred at rt for 5 min and upon completion, solvents were removed *in vacuo* to afford **17**. (An acidic work-up was not possible due



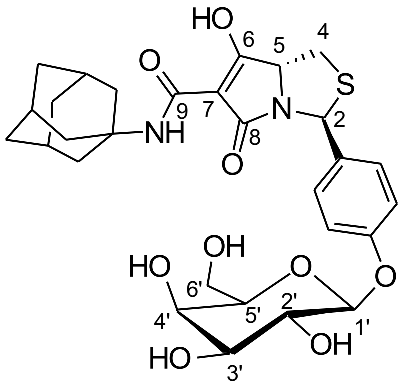
to the acid-labile glycosidic linkage). Yield (25 mg, quant.); yellow solid, mp >260 °C; R_f = 0.07 (EtOAc/MeOH 3:1); $[\alpha]_D^{25}$ = - 215.1 (*c* = 0.18, DMSO); ν_{max}/cm^{-1} (neat) 1227 (C-O), 1627 (C=C, br. with shoulder towards higher wavenumber), 1689 (C=O), 3246 (O-H); δ_H (400 MHz, D_2O): 1.32 (3H, t, *J* = 7.1 Hz, OCH_2CH_3), 3.04 (1H, dd, *J* = 11.1, 7.9 Hz, $H4_A$), 3.30 (1H, dd, *J* = 11.1, 7.5 Hz, $H4_B$), 3.77 - 3.87 (4H, m, $H6'_A$ + $H6'_B$ + H3'+ H2'), 3.88 - 3.94 (1H, m, H5'), 4.05 (1H, app d, *J* = 2.5 Hz, H4'), 4.23 (2H, q, *J* = 7.1 Hz, OCH_2CH_3), 4.49 (1H, app t, *J* = 7.6 Hz, H5), 5.11 (1H, d, *J* = 7.2 Hz, H1'), 6.36 (1H, s, H2), 7.14 (2H, d, *J* = 8.7 Hz, Ar-C*H*), 7.47 (2H, d, *J* = 8.7 Hz, Ar-C*H*); δ_C (100.6 MHz, D_2O): 13.9 (OCH_2CH_3), 32.9 (C4), 59.7 (OCH_2CH_3), 60.8 (C6'), 62.6 (C2), 68.5 (C4'), 69.2 (C5), 70.6, 72.6 (C2', C3'), 75.4 (C5'), 91.1 (C7), 100.8 (C1'), 116.7, 127.6 (Ar-*C*H), 136.1, 156.3 (Ar-C), 166.2 (C9), 178.7 (C8), 194.4 (C6); *m/z* (ESI^-) 482 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{21}H_{25}O_{10}NNaS$ $[M+Na]^+$; found 506.10689, requires 506.10914.

(-)-(2*R*,3*S*,4*S*,5*R*,6*S*)-2-(Acetoxymethyl)-6-(4-(3*S*,5*R*)-6-((adamantan-1-yl)carbamoyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazol-2-yl)phenoxy)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate 18



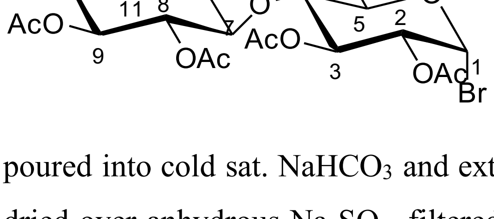
Carboxamide tetramate **18a** was obtained by aminolysis of **16** with 1-adamantylamine according to the general procedure for the synthesis of carboxamides with THF/toluene as solvent. Yield (22 mg, 30 %); yellow foaming solid, mp 142-146 °C; 2.9:1 AB:CD tautomers; R_f = 0.38 (EtOAc/petrol 4:1); $[\alpha]_D^{25}$ = -148.2 (*c* = 0.74, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1227 (C-O), 1626 (C=C), 1650 (C=O), 1690 (C=O), 1753 (C=O); δ_H (400 MHz, CD_2Cl_2): 1.69 (6H, Adamantyl-C*H*$_2$), 1.98 (3H, s, C*H*$_3$-C(=O)-O-), 2.04 (12H, Adamantyl-C*H*$_2$ + 2xC*H*$_3$-C(=O)-O-), 2.09 (3H, Adamantyl-C*H*), 2.16 (3H, s, C*H*$_3$-C(=O)-O-), 2.98 (1H, dd, *J* = 11.0, 8.6 Hz, $H4_A$), 3.25 (1H, dd, *J* = 11.0, 7.1 Hz, $H4_B$), 3.47 (1H, br. s., OH), 4.04 - 4.22 (3H, m, $H6'_A$ + $H6'_B$ + H5'), 4.41 (1H, app t, *J* = 6.9 Hz, H5 CD), 4.69 (1H, app t, *J* = 7.6 Hz, H5 AB), 5.05 (1H, d, *J* = 7.8 Hz, H1'), 5.10 (1H, dd, *J* = 10.4, 3.6 Hz, H3'), 5.40 (1H, dd, *J* = 10.5, 8.0 Hz, H2'), 5.44 (1H, app d, *J* = 3.4 Hz, H4'), 6.18 (1H, s, H2 AB), 6.27 (1H, s, H2 CD), 6.99 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.34 (1H, br. s., NH AB), 7.40 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.91 (1H, br. s., NH CD); δ_C (100.6 MHz, CD_2Cl_2): 20.8, 20.9, 21.0, 21.0 (*C*H$_3$-C(=O)-O-), 30.0 (Adamantyl-*C*H), 33.1 (C4), 36.5 (Adamantyl-*C*H$_2$), 42.0 (Adamantyl-*C*H$_2$), 53.3 (Adamantyl-C), 62.0 (C6'), 62.0 (C2), 67.5 (C4'), 67.8 (C5), 69.0 (C2'), 71.3 (C3'), 71.7 (C5'), 96.0 (C7), 100.1 (C1'), 117.4, 128.3 (Ar-*C*H), 136.1, 157.2 (Ar-C), 166.5 (C9), 169.8, 170.5, 170.7, 170.7 (CH$_3$-*C*(=O)-O-), 172.7 (C8), 188.1 (C6); *m/z* (ESI$^-$) 755 ([M-H]$^-$, 29 %); HRMS (ESI$^-$); $C_{37}H_{43}O_{13}N_2S$ [M-H]$^-$; found 755.24963, requires 755.24913.

(2*S*,5*R*)-*N*-((Adamantan-1-yl)-6-hydroxy-8-oxo-2-(4-(((2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl)oxy)phenyl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 19



Tetramate **18a** (31 mg, 0.04 mmol, 1.0 eq) was dissolved in MeOH (2 mL) and aq. K_2CO_3 (6.6 mg in 0.5 mL of H_2O, 0.048 mmol, 1.2 eq) was added. The reaction was stirred at rt for 10-15 min and upon completion, solvents were removed *in vacuo*. The residue was dissolved in MeOH, filtered and concentrated *in vacuo* to afford **19**. Yield (20 mg, 85 %); yellow solid, mp >260 °C; R_f = 0.08 (EtOAc/MeOH 3:1); $[\alpha]_D^{25}$ = -130.8 (*c* = 0.11, H_2O); ν_{max}/cm^{-1} (neat) 1228 (C-O), 1607 (br with shoulder towards higher wavenumber), 3339 (O-H); δ_H (500 MHz, Methanol-*d4*): 1.71 (6H, Adamantyl-CH_2), 2.05 (9H, Adamantyl-CH_2 + Adamantyl-C*H*), 2.93 (1H, dd, *J* = 11.0, 6.9 Hz, $H4_A$), 3.17 (1H, dd, *J* = 11.0, 7.8 Hz, $H4_B$), 3.60 - 3.66 (1H, m, H3'), 3.70 - 3.82 (4H, m, $H6'_A$ + $H6'_B$ + H5' + H2'), 3.94 (1H, app d, *J* = 3.0 Hz, H4'), 4.21 (1H, app t, *J* = 7.3 Hz, H5), 4.90 (1H, d, *J* = 7.9 Hz, H1'), 6.25 (1H, s, H2), 7.08 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.39 (2H, d, *J* = 8.5 Hz, Ar-C*H*); δ_C (125.8 MHz, Methanol-*d4*): 31.0 (Adamantyl-*C*H), 34.4 (C4), 37.7 (Adamantyl-*C*H_2), 43.3 (Adamantyl-*C*H_2), 51.9 (Adamantyl-C), 62.3 (C6'), 64.7 (C2), 70.1 (C4'), 70.4 (C5), 72.3 (C2'), 74.7 (C3'), 76.9 (C5'), 94.6 (C7), 102.9 (C1'), 117.7, 128.8 (Ar-*C*H), 137.6, 158.4 (Ar-C), 167.4 (C9), 181.0 (C8), 194.0 (C6); *m/z* (ESI$^-$) 587 ([M-H]$^-$, 38 %); HRMS (ESI$^-$); $C_{29}H_{35}O_9N_2S$ [M-H]$^-$; found 587.20687, requires 587.20687.

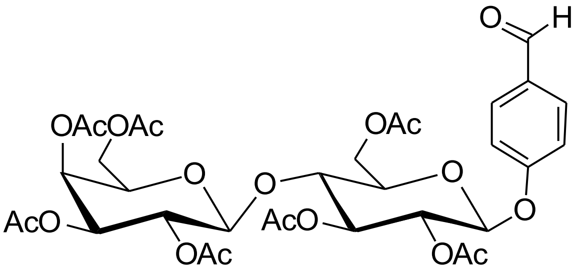
(+)-4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-D-glucopyranosyl bromide, 20b [5]



To a stirred solution of lactose octaacetate (2.0 g, 2.95 mmol, 1.0 eq) and $BiBr_3$ (66 mg, 0.15 mmol, 0.05 eq) in 20 mL of CH_2Cl_2 was added under N_2, TMSBr (1.56 mL, 11.8 mmol, 4 eq). The reaction was stirred at rt and after 15 h, upon completion of reaction, the reaction mixture was poured into cold sat. $NaHCO_3$ and extracted twice with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to obtain **20b**. Yield (1.95 g, 92 %); white solid, mp 98 °C; R_f = 0.33 (EtOAc/petrol 1:1); $[\alpha]_D^{25}$ = +94.1 (*c* = 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1211 (C-O), 1743 (C=O); δ_H (400 MHz, CD_2Cl_2): 1.94 (3H, s, CH_3-C(=O)-O-), 2.02 - 2.06

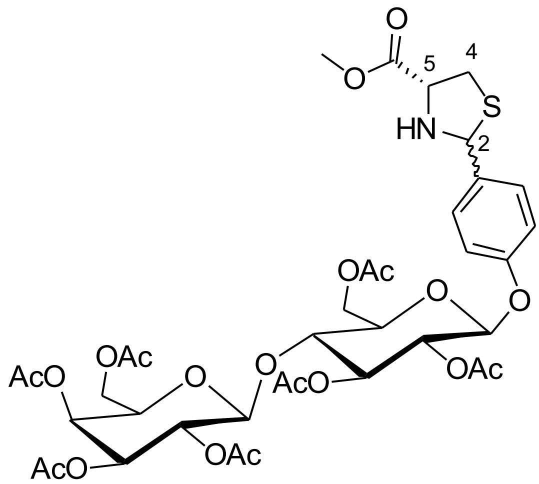
(9H, s, CH_3-C(=O)-O-), 2.07 (3H, s, CH_3-C(=O)-O-), 2.11 (3H, s, CH_3-C(=O)-O-), 2.14 (3H, s, CH_3-C(=O)-O-), 3.79 - 3.93 (2H, m, H5 + H11), 4.04 - 4.23 (4H, m, H6 + H12 + H4), 4.41 - 4.54 (1H, m, H6/H12), 4.50 (1H, d, *J* = 7.8 Hz, H7), 4.74 (1H, dd, *J* = 9.9, 4.1 Hz, H2), 4.87 - 4.99 (1H, m, H9), 5.04 - 5.17 (1H, m, H8), 5.33 (1H, app d, *J* = 3.2 Hz, H10), 5.53 (1H, app t, *J* = 9.6 Hz, H3), 6.51 (1H, d, *J* = 4.0 Hz, H1); δ_C (100.6 MHz, CD_2Cl_2): 20.4, 20.6, 20.7 (*C*H_3-C(=O)-O-), 60.8, 61.0 (C6, C12), 66.6 (C10), 69.0 (C8), 69.5 (C3), 70.7 (C5/C11), 70.8 (C2), 70.9 (C9), 72.9 (C4), 74.9 (C5/C11), 86.3 (C1), 110.7 (C7); *m/z* (ESI$^+$) 721,723 ([M+Na]$^+$, 78 %); HRMS (ESI$^+$); $C_{26}H_{35}O_{17}BrNa$ [M+Na]$^+$; found 721.09288 and 723.09099, requires 721.09498 and 723.09294.

(+)-4-(4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-D-glucopyranosyloxy)benzaldehyde, 20c [6]

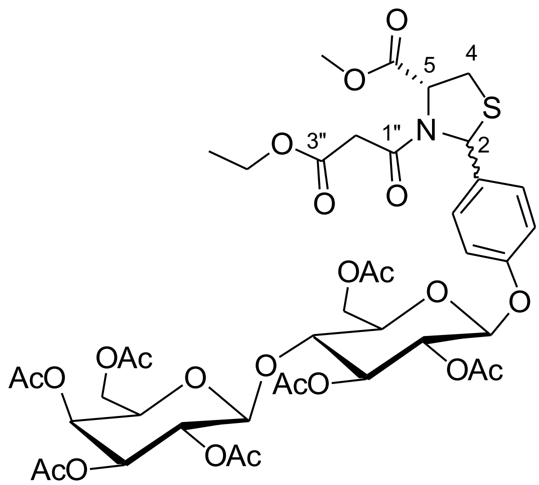


To **20b** (2.63 g, 3.76 mmol, 1.0 eq), 4-hydroxybenzaldehyde (0.55 g, 4.51 mmol, 1.2 eq) and benzyltributylammonium chloride (0.23 g, 0.75 mmol, 0.2 eq) in $CHCl_3$ (15 mL), was added powdered K_2CO_3 (1.69 g, 12.2 mmol, 5 eq) and stirred at rt for 24 h. The reaction mixture was neutralised with 10 % HCl and the organic layer was separated. The organic layer was washed with sat. $NaHCO_3$ and brine, then dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (eluent: EtOAc/petrol) to furnish **20c**. Yield (2.45 g, 88 %); white foam, mp 98-104 °C; R_f = 0.28 (EtOAc/petrol 1:1); $[\alpha]_D^{25}$ = +14.9 (*c* = 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1699 (C=O), 1744 (C=O); δ_H (400 MHz, $CDCl_3$): 1.95 (3H, s, CH_3-C(=O)-O-), 2.01 - 2.10 (15H, m, 5xCH_3-C(=O)-O-), 2.13 (3H, s, CH_3-C(=O)-O-), 3.78 - 3.93 (2H, m, lactose-C*H*), 4.01 - 4.25 (4H, m, lactose-CH_2 + lactose-C*H*), 4.36 - 4.54 (1H, m, lactose-CH_2), 4.51 (1H, d, *J* = 7.8 Hz, lactose-C*H*), 4.93 - 5.00 (1H, m, lactose-C*H*), 5.07 - 5.21 (4H, m, lactose-C*H*), 5.25 - 5.30 (1H, m, lactose-C*H*), 7.06 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.82 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 9.89 (1H, s, C*H*O); δ_H (100.6 MHz, $CDCl_3$) 20.4, 20.4, 20.5, 20.6, 20.7, 20.7, 20.9 (*C*H_3-C(=O)-O-), 60.7, 61.3 (lactose-*C*H_2), 68.2, 69.0, 70.6, 70.7, 71.2, 72.6, 72.9, 76.0, 97.6, 101.0 (lactose-*C*H), 116.6, 131.7 (Ar-C*H*), 127.4, 139.3 (Ar-C), 169.0, 169.1, 169.4, 169.6, 169.9, 170.0, 170.3 (CH_3-*C*(=O)-O-), 190.6 (1H, s, *C*HO); *m/z* (ESI$^+$) 763 ([M+Na]$^+$, 4 %); HRMS (ESI$^+$); $C_{33}H_{40}O_{19}Na$ [M+Na]$^+$; found 763.20569, requires 763.20560.

(2*R*,3*S*,4*S*,5*R*,6*S*)-2-(Acetoxymethyl)-6-(((2*R*,3*R*,4*S*,5*R*,6*S*)-4,5-diacetoxy-2-(acetoxymethyl)-6-(4-((2*S*,5*R*)-7-(ethoxycarbonyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazol-2-yl)phenoxy)tetrahydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate 21

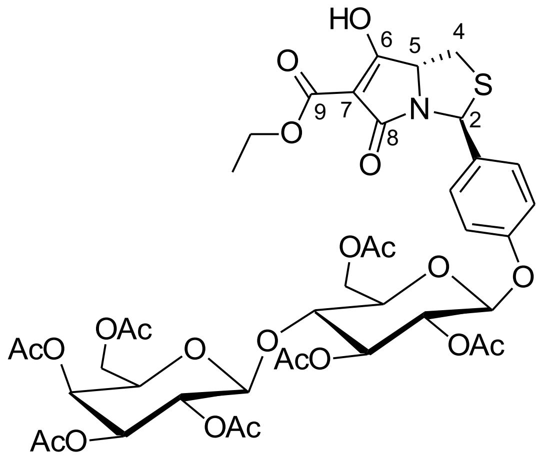


Thiazolidine derived from the condensation of L-cysteine methyl ester hydrochloride and aldehyde **20c** was prepared following the general procedure for thiazolidine synthesis . Yield (2.05 g, 30 %); white foam; 1.7:1 *cis* and *trans* diastereomers; R_f = 0.37 (EtOAc/petrol 2:1); ν_{max}/cm^{-1} (neat) 1738 (C=O); δ_H (400 MHz, $CDCl_3$) major isomer (*cis*): 1.95 (3H, s, CH_3-C(=O)-O-), 2.02 - 2.07 (12H, m, 4xCH_3-C(=O)-O-), 2.10 - 2.16 (6H, m, 2xCH_3-C(=O)-O-), 2.58 (1H, br. s., NH), 3.09 (1H, dd, *J* = 10.3, 8.8 Hz, $H4_A$), 3.44 (1H, dd, *J* = 10.3, 7.1 Hz, $H4_B$), 3.73 - 3.77 (1H, m, lactose-C*H*), 3.79 (3H, s, CO_2CH_3), 3.84 - 3.91 (1H, m, lactose-C*H*), 4.01 - 4.20 (3H, m, H5 + lactose-CH_2), 4.44 - 4.58 (3H, m, lactose-C*H* + lactose-CH_2), 4.66 - 4.83 (2H, m, lactose-C*H*), 4.90 - 5.40 (4H, m, lactose-C*H*), 5.46 - 5.55 (2H, H2 + lactose-C*H*), 6.95 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.43 (2H, d, *J* = 8.6 Hz, Ar-C*H*); minor isomer (*trans*): 1.95 (3H, s, CH_3-C(=O)-O-), 2.02 - 2.07 (12H, m, 4xCH_3-C(=O)-O-), 2.10 - 2.16 (6H, m, 2xCH_3-C(=O)-O-), 2.58 (1H, br. s., NH), 3.16 - 3.21 (1H, m, $H4_A$), 3.33 - 3.40 (1H, m, $H4_B$), 3.73 - 3.77 (1H, m, lactose-C*H*), 3.79 (3H, s, CO_2CH_3), 3.84 - 3.91 (1H, m, lactose-C*H*), 4.01 - 4.20 (3H, m, H5 + lactose-CH_2), 4.44 - 4.58 (3H, m, lactose-C*H* + lactose-CH_2), 4.66 - 4.83 (2H, m, lactose-C*H*), 4.90 - 5.40 (4H, m, lactose-C*H*), 5.46 - 5.55 (2H, H2 + lactose-C*H*), 6.91 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.39 (2H, d, *J* = 8.6 Hz, Ar-C*H*); δ_C (125.8 MHz, $CDCl_3$) major isomer (*cis*): 20.4, 20.6, 20.7, 20.7, 20.8, 20.8, 21.0 (*C*H_3-C(=O)-O-), 39.1 (C4), 52.6 (CO_2CH_3), 60.8, 61.8 (lactose-*C*H_2), 66.6 (lactose-*C*H), 68.1 (C5), 69.1 (lactose-*C*H), 69.5 (C2), 70.5, 70.9, 71.0, 71.3, 72.7, 76.3, 89.9, 100.9 (lactose-*C*H), 116.9, 128.8 (Ar-C*H*), 132.9, 156.9 (Ar-C), 169.0, 169.6, 170.1, 170.2, 170.3, 170.3, 170.5 (CH_3-*C*(=O)-O-), 171.5 (*C*O_2CH_3); minor isomer (*trans*): 20.4, 20.6, 20.7, 20.7, 20.8, 20.8, 21.0 (*C*H_3-C(=O)-O-), 38.0 (C4), 52.5 (CO_2CH_3), 60.4, 61.7 (lactose-*C*H_2), 66.5 (lactose-*C*H), 68.1 (C5), 69.0 (lactose-*C*H), 69.5 (C2), 70.6, 70.9, 71.0, 71.4, 72.8, 76.1, 89.9, 101.0 (lactose-*C*H), 116.7, 128.2 (Ar-C*H*), 135.9, 156.4 (Ar-C), 169.1, 169.6, 170.0, 170.1, 170.3, 170.3, 170.5 (CH_3-*C*(=O)-O-), 172.1 (*C*O_2CH_3); *m/z* (ESI^+) 858 ($[M+H]^+$, 89 %); HRMS (ESI^+); $C_{37}H_{48}NO_{20}S$ $[M+H]^+$; found 858.24967, requires 858.24959.



The *N*-acylthiazolidine was synthesised following the general procedure for *N*-acylation . Yield 27 % (0.60 g); white solid; 1.2:1 *cis* and *trans* diastereomers; R_f = 0.32 (EtOAc/petrol 3:2); ν_{max}/cm^{-1} (neat) 1661 (C=O), 1742 (C=O); δ_H (400 MHz, $CDCl_3$) major isomer (*cis*, a mixture of two conformers): 1.19 - 1.31 (3H, m,

OCH_2CH_3), 1.96 - 2.18 (21H, m, 7 x CH_3-C(=O)-O- major conformer + 21H, m, 7 x CH_3-C(=O)-O- minor conformer), 3.04 - 3.55 (4H, m, $H4_A$ + $H4_B$ + $H2''_A$ + $H2''_B$), 3.75 - 3.81 (1H, m, lactose-C*H*), 3.83 (3H, s, CO_2CH_3 major conformer), 3.85 (3H, s, CO_2CH_3 minor conformer), 3.86 - 3.93 (2H, m, lactose-C*H*), 4.05 - 4.19 (4H, m, OCH_2CH_3 + lactose-CH_2), 4.43 - 4.62 (3H, m, lactose-C*H* + lactose-CH_2), 4.92 - 5.42 (6H, m, H5 + 5 x lactose-C*H*), 6.11 (1H, s, H2 major conformer), 6.27 (1H, s, H2 minor conformer), 6.87 - 6.94 (2H, m, Ar-C*H* minor conformer), 6.95 - 7.02 (2H, m, Ar-C*H* major conformer), 7.45 (2H, d, *J* = 8.6 Hz, Ar-C*H* minor conformer), 7.61 (2H, d, *J* = 8.8 Hz, Ar-C*H* major conformer); minor isomer (*trans*, a mixture of two conformers): 1.19 - 1.31 (3H, m, OCH_2CH_3), 1.96 - 2.18 (21H, m, 7 x CH_3-C(=O)-O- major conformer + 21H, m, 7 x CH_3-C(=O)-O- minor conformer), 3.04 - 3.55 (4H, m, $H4_A$ + $H4_B$ + $H2''_A$ + $H2''_B$), 3.75 - 3.81 (4H, m, CO_2CH_3 + lactose-C*H*), 3.86 - 3.93 (2H, m, lactose-C*H*), 4.05 - 4.19 (4H, m, OCH_2CH_3 + lactose-CH_2), 4.43 - 4.62 (3H, m, lactose-C*H* + lactose-CH_2), 4.92 - 5.42 (6H, m, H5 + 5 x lactose-C*H*), 6.15 (1H, s, H2 major conformer), 6.27 (1H, s, H2 minor conformer), 6.87 - 6.94 (2H, m, Ar-C*H* minor conformer), 6.95 - 7.02 (2H, m, Ar-C*H* major conformer), 7.15 (2H, d, *J* = 8.6 Hz, Ar-C*H* major conformer), 7.22 (2H, d, *J* = 8.8 Hz, Ar-C*H* minor conformer); δ_C (125.8 MHz, $CDCl_3$) major isomer (*cis*, a mixture of two conformers): 14.0, 14.1 (OCH_2CH_3), 20.3, 20.4, 20.5, 20.6, 20.6, 20.8, 21.0 (CH_3-C(=O)-O-), 32.0, 33.0 (C4), 42.1, 43.0 (C2″), 52.7, 53.2 (CO_2CH_3), 60.4, 60.7, 60.8, 61.5, 61.6, 61.7, 61.8, 61.9, 61.9, 62.4 (OCH_2CH_3, lactose-CH_2, obscured by *trans* isomer), 63.8, 64.0 (C5), 65.7, 65.8 (C2), 66.6, 66.7, 68.6, 69.0, 70.7, 70.9, 71.3, 71.5, 72.6, 72.7, 72.7, 72.8, 72.8, 73.3, 76.1, 76.1, 98.4, 98.6, 101.1, 102.0 (lactose-*C*H), 116.5, 117.1, 127.9, 128.6 (Ar-*C*H), 134.2, 134.5, 156.9, 157.1 (Ar-C), 165.0, 165.4 (C1″), 166.7, 167.1 (C2″), 169.1, 170.0, 169.6, 169.7, 170.0, 170.1, 170.2, 170.3, 170.3 (CO_2CH_3 + CH_3-*C*(=O)-O-); minor isomer (*trans*, a mixture of two conformers): 14.0, 14.1 (OCH_2CH_3), 20.3, 20.4, 20.5, 20.6, 20.6, 20.8, 21.0 (CH_3-C(=O)-O-), 31.0, 33.0 (C4), 42.4, 43.3 (C2″), 52.8, 53.4 (CO_2CH_3), 60.4, 60.7, 60.8, 61.5, 61.6, 61.7, 61.8, 61.9, 61.9, 62.4 (OCH_2CH_3, lactose-CH_2, obscured by *cis* isomer), 64.2, 64.6 (C5), 64.6, 65.2 (C2), 66.6, 66.7, 68.6, 69.0, 70.9, 70.9, 71.3, 71.4, 72.6, 72.7, 72.7, 72.8, 72.8, 73.3, 76.0, 76.1, 98.4, 98.6, 101.01, 101.1 (lactose-*C*H), 116.9, 117.4, 126.1, 126.3 (Ar-*C*H), 136.6, 137.0, 156.7, 157.1 (Ar-C), 164.5, 165.3 (C1″), 166.2, 167.3 (C2″), 169.0, 169.3, 169.5, 170.0, 170.1, 170.2, 170.3, 170.3 (CO_2CH_3 + CH_3-*C*(=O)-O-); *m/z* (ESI/FI) molecular ion not detected.

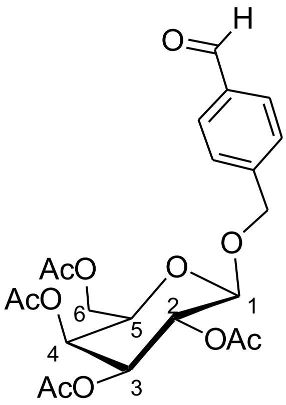


Tetramate **21** was obtained using the general procedure for Dieckmann cyclisation. The product isolated by flash column chromatography (eluent: 100 % EtOAc to EtOAc/MeOH/1% Et_3N) was then dissolved in CH_2Cl_2 and washed with 5% citric acid. The organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield **21**. Yield (0.15 g, 31 %); yellow solid, mp 144-146 °C; R_f = 0.38 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -96.8 (*c* = 0.16, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1215 (C-O), 1620 (C=O), 1659 (C=O), 1744 (C=O); δ_H (400 MHz, CD_2Cl_2): 1.36 (3H, t, *J* = 7.1 Hz, OCH_2CH_3), 1.95 (3H, s, CH_3-C(=O)-O-), 2.03 (3H, s, CH_3-C(=O)-O-), 2.05 (6H, s, CH_3-C(=O)-O-), 2.06 (3H, s, CH_3-C(=O)-O-), 2.08 (3H, s, CH_3-C(=O)-O-), 2.12 (3H, s, CH_3-C(=O)-O-), 3.00 (1H, dd, *J* = 11.3, 8.3 Hz, $H4_A$), 3.28 (1H, dd, *J* = 11.3, 7.1 Hz, $H4_B$), 3.73 - 3.82 (1H, m, lactose-C*H*), 3.87 - 3.95 (2H, m, lactose-C*H*), 4.04 - 4.20 (3H, m, lactos-CH_2), 4.37 (2H, q, *J* = 7.1 Hz, OCH_2CH_3), 4.46 - 4.55 (2H, m, lactose-C*H* + lactose-CH_2), 4.76 (1H, app t, *J* = 7.6 Hz, H5), 4.94 - 5.01 (1H, m, lactose-C*H*), 5.04 - 5.10 (2H, m, lactose-C*H*), 5.12 - 5.17 (1H, m, lactose-C*H*), 5.22 - 5.28 (1H, m, lactose-C*H*), 5.36 (1H, dd, *J* = 3.4, 1.0 Hz, lactose-C*H*), 6.23 (1H, s, H2), 6.96 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.39 (2H, d, *J* = 8.6 Hz, Ar-C*H*); δ_C (125.8 MHz, CD_2Cl_2): 14.5 (OCH_2CH_3), 20.8, 20.9, 21.0, 21.2 (CH_3-C(=O)-O-), 33.4 (C4), 61.5 (lactose-CH_2), 62.2 (OCH_2CH_3), 62.3 (lactose-CH_2), 62.4 (C2), 66.0 (C5), 67.3, 69.5, 71.5, 71.7, 72.9, 73.6, 76.5, 99.5, 101.6 (lactose-*C*H), 117.4, 128.3 (Ar-*C*H), 136.0, 157.1 (Ar-C), 167.6 (C9), 169.2 (C8), 169.7, 170.5, 170.3, 170.5, 170.6, 170.8 (CH_3-*C*(=O)-O-), 186.6 (C6); *m/z* (ESI^-) 938 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{41}H_{48}O_{22}NS$ $[M-H]^-$; found 938.2412, requires 938.23942.

4-(Hydroxymethyl)benzaldehyde [7]

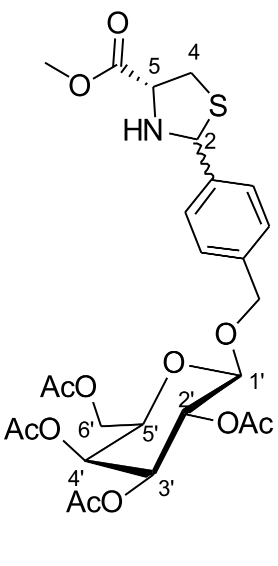
Terephthalaldehyde (2.0 g, 15 mmol, 1.0 eq) in EtOH:THF (5:7, 60 mL) was cooled to -5 °C. $NaBH_4$ (0.28 g, 7.5 mmol, 0.5 eq) was added with continuous stirring over 30 min, while maintaining the temperature at -5 °C. The mixture was stirred for 6 h at 0-2 °C and then neutralized with 2M HCl to pH 5. Solvents were removed *in vacuo* and H_2O was added to the residue. The product was extracted twice with EtOAc and the combined organic extracts were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography to furnish the product. Yield (0.81 g, 70 %); white crystalline solid, mp 40 °C; R_f = 0.28 (EtOAc/petrol 1:2); ν_{max}/cm^{-1} (neat) 1684 (C=O), 3369 (OH); δ_H (400 MHz, $CDCl_3$) 2.29 (1H, br. s, OH), 4.80 (2H, s, OCH_2), 7.53 (2H, d, *J* = 8.1 Hz, Ar-C*H*), 7.87 (2H, d, *J* = 8.1 Hz, Ar-C*H*), 9.99 (1H, s, C*H*O); δ_C (125.8 MHz, $CDCl_3$): 64.5 (O*C*H_2), 126.9, 130.0 (Ar-C*H*), 135.6, 147.8 (Ar-C), 192.1 (*C*HO); *m/z* (ESI) molecular ion not detected.

(-)-4-((2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)methyl)benzaldehyde, 22 [2]



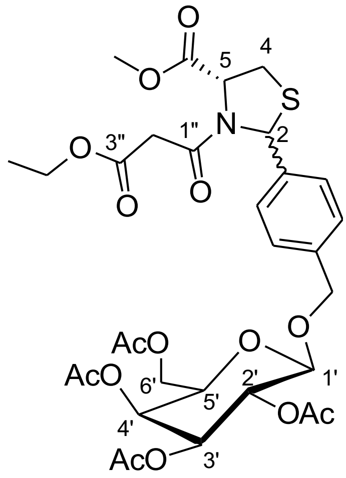
β-D-Galactose pentaacetate (5.5 g, 14.1 mmol, 1.5 eq) and 4-(hydroxymethyl)benzaldehyde (1.28 g, 9.39 mmol, 1.0 eq) in CH_2Cl_2 (50 mL) was cooled to 0 °C and $BF_3.OEt_2$ (1.73 mL, 14.1 mmol, 1.5 eq) was added dropwise under N_2. The reaction flask was warmed to rt and stirred for 18 h. The reaction mixture was quenched with sat. $NaHCO_3$ (20 mL) and left to stir for 30 min. The product was extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography to obtain **22** (eluent: EtOAc/petrol). Yield (3.09 g, 71 %); white crystalline solid, mp 88-90 °C; R_f = 0.12 (EtOAc/petrol 1:2); $[\alpha]_D^{25}$ = -30.3 (*c* = 1.25, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1217 (C-O), 1699 (C=O), 1747 (C=O); δ_H (400 MHz, $CDCl_3$): 1.99 (3H, s, CH_3-C(=O)-O-), 2.05 (3H, s, CH_3-C(=O)-O-), 2.06 (3H, s, CH_3-C(=O)-O-), 2.17 (3H, s, CH_3-C(=O)-O-), 3.93 (1H, app td, *J* = 6.6, 1.0 Hz, H5), 4.15, 4.21 (2H, ABq, J_{AB} = 11.3, 6.6 Hz, H6), 4.58 (1H, d, *J* = 7.9 Hz, H1), 4.71 (1H, d, *J* = 13.2 Hz, OCH_2), 4.98 - 5.05 (2H, m, OCH_2 + H3), 5.32 (1H, dd, *J* = 10.3, 7.9 Hz, H2), 5.41 (1H, dd, *J* = 3.4, 1.0 Hz, H4), 7.46 (2H, d, *J* = 8.1 Hz, Ar-C*H*), 7.87 (2H, d, *J* = 8.1 Hz, Ar-C*H*), 10.01 (1H, s, C*H*O); δ_H (100.6 MHz, $CDCl_3$): 20.5, 20.6, 20.7, 20.8 (*C*H_3-C(=O)-O-), 61.2 (C6), 66.9 (C4), 68.7 (C2), 70.0 (O*C*H_2), 70.7 (C3), 70.8 (C5), 100.4 (C1), 127.5, 129.9 (Ar-*C*H), 135.9, 143.8 (Ar-C), 169.4, 170.1, 170.2, 170.4 (CH_3-*C*(=O)-O-), 191.8 (*C*HO); *m/z* (ESI^+) 489 ($[M+Na]^+$, 100 %); HRMS (ESI^+); $C_{22}H_{26}O_{11}Na$ $[M+Na]^+$; found 489.13711, requires 489.13673.

(2*R*,3*S*,4*S*,5*R*,6*R*)-2-(Acetoxymethyl)-6-((4-((3*S*,7a*R*)-7-(ethoxycarbonyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazol-2-yl)benzyl)oxy)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate, 23



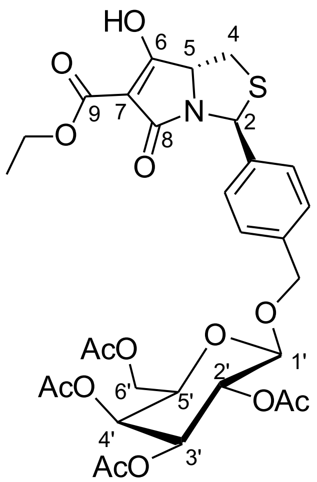
Condensation of L-cysteine methyl ester hydrochloride and aldehyde **22** following the general procedure gave the corresponding thiazolidine. Yield (2.08 g, 54 %); yellow foam; 1.7:1 *cis* and *trans* diastereomers; R_f = 0.53 (EtOAc/petrol 2:1); ν_{max}/cm^{-1} (neat) 1217 (C-O), 1742 (C=O); δ_H (500 MHz, $CDCl_3$) major isomer (*cis*) 1.98 (3H, s, CH_3-C(=O)-O-), 2.03 (3H, s, CH_3-C(=O)-O-), 2.07 (3H, s, CH_3-C(=O)-O-), 2.16 (3H, s, CH_3-C(=O)-O-), 2.61-2.71 (1H, m, NH), 3.12 (1H, dd, *J* = 10.3, 9.1 Hz, $H4_A$), 3.48 (1H, dd, *J* = 10.3, 7.2 Hz, $H4_B$), 3.82 (3H, s, -CO_2CH_3), 3.86 - 3.91 (1H, m, H5'), 3.95 -

4.03 (1H, m, H5), 4.12 - 4.24 (2H, m, H6'), 4.49 - 4.54 (1H, m, H1'), 4.60 - 4.66 (1H, m, OC*H*$_2$), 4.88 - 4.93 (1H, m, OC*H*$_2$), 4.96 - 5.02 (1H, m, H3'), 5.25 - 5.32 (1H, m, H2'), 5.37 - 5.40 (1H, m, H4'), 5.56 (1H, d, *J* = 9.3 Hz, H2), 7.30 (2H, d, *J* = 8.1 Hz, Ar-C*H*), 7.51 (2H, d, *J* = 8.1 Hz, Ar-C*H*); minor isomer (*trans*): 1.98 (3H, s, C*H*$_3$-C(=O)-O-), 2.02 (3H, s, C*H*$_3$-C(=O)-O-), 2.07 (3H, s, C*H*$_3$-C(=O)-O-), 2.16 (3H, s, C*H*$_3$-C(=O)-O-), 2.86 (1H, br. s., NH), 3.21 (1H, dd, *J* = 10.7, 6.0 Hz, H4$_A$), 3.40 (1H, dd, *J* = 10.7, 7.1 Hz, H4$_B$), 3.80 (3H, s, -CO$_2$C*H*$_3$), 3.86 - 3.91 (1H, m, H5'), 4.12 - 4.24 (3H, m, H5 + H6'), 4.49 - 4.54 (1H, m, H1'), 4.60 - 4.66 (1H, m, OC*H*$_2$), 4.88 - 4.93 (1H, m, OC*H*$_2$), 4.96 - 5.02 (1H, m, H3'), 5.25 - 5.32 (1H, m, H2'), 5.37 - 5.40 (1H, m, H4'), 5.82 (1H, s, H2), 7.25 (2H, d, *J* = 8.1 Hz, Ar-C*H*), 7.47 (2H, d, *J* = 8.2 Hz, Ar-C*H*); δ_H (125.8 MHz, CDCl$_3$): major isomer (*cis*): 20.5, 20.6, 20.7, 20.8 (*C*H$_3$-C(=O)-O-), 39.2 (C4), 52.6 (-CO$_2$*C*H$_3$), 61.3 (C6'), 65.5 (C5), 67.0 (C4'), 68.8 (C2'), 70.1 (O*C*H$_2$), 70.7 (C5'), 70.9 (C3'), 72.2 (C2), 99.8 (C1'), 127.6, 127.9 (Ar-*C*H), 137.3, 137.9 (Ar-C), 169.4, 170.1, 170.2, 170.4 (CH$_3$-*C*(=O)-O-), 171.6 (-*C*O$_2$CH$_3$); minor isomer (*trans*): 20.5, 20.6, 20.7, 20.8 (*C*H$_3$-C(=O)-O-), 38.1 (C4), 52.6 (-CO$_2$*C*H$_3$), 61.3 (C6'), 64.2 (C5), 66.7 (C4'), 68.48 (C2'), 70.2 (O*C*H$_2$), 70.4 (C2), 70.7 (C5'), 70.9 (C3'), 99.7 (C1'), 127.0, 127.8 (Ar-*C*H), 136.4, 141.1 (Ar-C), 169.4, 170.1, 170.2, 170.4 (CH$_3$-*C*(=O)-O-), 172.1 (-*C*O$_2$CH$_3$); *m/z* (ESI$^+$) 584 ([M+H]$^+$ 100 %); HRMS (ESI$^+$); C$_{26}$H$_{34}$O$_{12}$NS [M+H]$^+$; found 584.17932, requires 584.17962.



N-Acylthiazolidine was obtained following the general procedure for *N*-acylation. Yield (1.93 g, 80 %); white foam; 1.3:1 *cis* and *trans* diastereomers; R$_f$ = 0.42 (EtOAc/petrol 2:1); ν_{max}/cm^{-1} (neat) 1216 (C-O), 1662 (C=O), 1741 (C=O); δ_H (500 MHz, CDCl$_3$) major isomer (*cis*, a mixture of two conformers): 1.21 - 1.31 (3H, m, OCH$_2$C*H*$_3$), 1.99 (3H, s, C*H*$_3$-C(=O)-O-), 2.04 (3H, s, C*H*$_3$-C(=O)-O-), 2.07 (3H, s, C*H*$_3$-C(=O)-O-), 2.17 (3H, s, C*H*$_3$-C(=O)-O-), 3.07 - 3.57 (4H, m, H4$_A$ + H4$_B$ + H2″$_A$ + H2″$_B$), 3.83 (3H, s, CO$_2$C*H*$_3$ minor conformer), 3.85 (3H, s, CO$_2$C*H*$_3$ major conformer), 3.87 - 3.94 (1H, m, H5'), 4.09 - 4.27 (4H, m, OC*H*$_2$CH$_3$ + H6'), 4.50 - 4.66 (2H, m, H1' + OC*H*$_2$), 4.86 - 4.93 (1H, m, OC*H*$_2$), 4.97 - 5.05 (1H, m, H3'), 5.07 (1H, app t, *J* = 7.1 Hz, H5), 5.24 - 5.32 (1H, m, H2'), 5.37 - 5.42 (1H, m, H6'), 6.16 (1H, s, H2 major conformer), 6.35 (1H, s, H2 minor conformer), 7.22 - 7.27 (2H, m, Ar-C*H* minor conformer), 7.31 - 7.33 (2H, m, Ar-C*H* major conformer), 7.51 (2H, d, *J* = 7.9 Hz, Ar-C*H* minor conformer), 7.66 (2H, d, *J* = 8.1 Hz, Ar-C*H* major conformer); minor isomer (*trans*, a mixture of two conformers): 1.21 - 1.31 (3H, m, OCH$_2$C*H*$_3$), 1.99 (3H, s, C*H*$_3$-C(=O)-O-), 2.05 (3H, s, C*H*$_3$-C(=O)-O-), 2.08 (3H, s, C*H*$_3$-C(=O)-O-), 2.16 (3H, s, C*H*$_3$-C(=O)-O-), 3.07 - 3.57 (4H, m, H4$_A$ + H4$_B$ + H2″$_A$ + H2″$_B$), 3.80 (3H, s, CO$_2$C*H*$_3$ major conformer), 3.86 (3H, s, CO$_2$C*H*$_3$

minor conformer), 3.87 - 3.94 (1H, m, H5'), 4.09 - 4.27 (4H, m, OCH_2CH_3 + H6'), 4.50 - 4.66 (2H, m, H1' + OCH_2), 4.86 - 4.93 (1H, m, OCH_2), 4.97 - 5.05 (1H, m, H3'), 5.20 (1H, app d, J = 5.7 Hz, H5 minor conformer), 5.24 - 5.32 (2H, m, H5 major conformer + H2'), 5.37 - 5.42 (1H, m, H6'), 6.19 (1H, s, H2 major conformer), 6.32 (1H, s, H2 minor conformer), 7.21 (2H, d, J = 8.2 Hz, Ar-C*H* major conformer), 7.22 - 7.27 (4H, m, Ar-C*H* minor conformer), 7.31 - 7.33 (2H, m, Ar-C*H* major conformer); δ_C (125.8 MHz, $CDCl_3$): major isomer (*cis*, a mixture of two conformers): 14.0, 14.1 (OCH_2*C*H_3), 20.6, 20.7, 20.7, 20.8 (*C*H_3-C(=O)-O-), 32.1, 33.1 (C4), 42.2, 43.0 (C2″), 52.7, 53.4 (CO_2*C*H_3), 61.3 (C6'), 61.7, 62.0 (O*C*H_2CH_3), 63.8, 64.7 (C5), 66.1, 66.9 (C2), 67.1 (C4'), 68.8 (C2'), 70.2, 70.3 (O*C*H_2), 70.7, 70.8 (C3'), 70.9 (C5'), 99.8, 100.0 (C1'), 126.6, 127.3, 127.6, 128.2 (Ar-*C*H), 136.5, 137.4, 138.5, 139.6 (Ar-C), 165.0, 165.5 (C1"), 166.7, 167.1 (C3"), 169.3, 169.4, 169.4, 170.1, 170.1, 170.2, 170.2, 170.3, 170.4 (*C*O_2CH_3 + CH_3-*C*(=O)-O-); minor isomer (*trans*, a mixture of two conformers): 14.0, 14.1 (OCH_2*C*H_3), 20.6, 20.7, 20.7, 20.8 (*C*H_3-C(=O)-O-), 31.0, 33.9 (C4), 42.5, 43.3 (C2″), 52.8, 53.5 (CO_2*C*H_3), 61.2, 61.3 (C6'), 61.6, 61.8 (O*C*H_2CH_3), 64.0, 64.3 (C5), 64.8, 65.5 (C2), 67.1 (C4'), 68.8 (C2'), 70.0, 70.3 (O*C*H_2), 70.7, 70.9 (C3'), 70.8, 70.9 (C5'), 99.8, 100.2 (C1'), 124.9, 125.1, 127.9, 128.3 (Ar-*C*H), 136.1, 137.4, 141.5, 141.9 (Ar-C), 164.6, 165.3 (C1"), 166.3, 167.3 (C3"), 169.3, 169.4, 169.4, 170.1, 170.1, 170.2, 170.2, 170.3, 170.4 (*C*O_2CH_3 + CH_3-*C*(=O)-O-); *m/z* (ESI$^+$) 698 ([M+H]$^+$ 100 %); HRMS (ESI$^+$); $C_{31}H_{40}O_{15}NS$ [M+H]$^+$; found 698.21035, requires 698.21132.

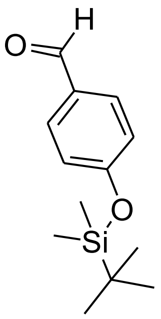


Tetramate **23** was obtained following the general procedure for Dieckmann cyclisation. Yield (0.44 g, 30 %); yellow foam, mp 110-114 °C; R_f = 0.20 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -143.0 (c = 0.17, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1217 (C-O), 1618 (C=O), 1660 (C=O), 1744 (C=O); δ_H (400 MHz, $CDCl_3$): 1.37 (3H, t, J = 7.1 Hz, OCH_2CH_3), 1.95 (3H, s, CH_3-C(=O)-O-), 2.01 (3H, s, CH_3-C(=O)-O-), 2.04 (3H, s, CH_3-C(=O)-O-), 2.14 (3H, s, CH_3-C(=O)-O-), 3.02 (1H, dd, J = 11.1, 8.3 Hz, $H4_A$), 3.30 (1H, dd, J = 11.1, 7.1 Hz, $H4_B$), 3.91 (1H, td, J = 6.5, 1.1 Hz, H5'), 4.13, 4.18 (2H, ABq, J_{AB} = 11.4, 6.8 Hz, H6'), 4.38 (2H, q, J = 7.1 Hz, OCH_2CH_3), 4.54 (1H, d, J = 8.0 Hz, H1'), 4.62 (1H, d, J= 12.3 Hz, OCH_2), 4.80 (1H, app t, J = 7.7 Hz, H5), 4.87 (1H, d, J= 12.3 Hz, OCH_2), 4.98 (1H, dd, J = 10.5, 3.5 Hz, H3'), 5.18 (1H, dd, J = 10.5, 8.0 Hz, H2'), 5.37 (1H, dd, J = 3.5, 1.1 Hz, H4'), 6.27 (1H, s, H2), 7.29 (2H, d, J = 8.1 Hz, Ar-C*H*), 7.44 (2H, d, J = 8.1 Hz, Ar-C*H*); δ_C (125.8 MHz, CD_2Cl_2): 14.5 (OCH_2*C*H_3), 20.9, 21.0, 21.1, 21.1 (*C*H_3-C(=O)-O-), 33.4 (C4), 62.0 (C6'), 62.3 (O*C*H_2CH_3), 62.6 (C2), 65.9 (C5), 67.7 (C4'), 69.3 (C2'), 70.8 (OCH_2), 71.4 (C3'), 71.5 (C5'), 99.7 (C7), 100.5 (C1'), 127.0, 128.5 (Ar-*C*H), 137.5, 140.9 (Ar-C), 167.6 (C9), 169.0 (C8), 169.9, 170.5, 170.7, 170.8 (CH_3-*C*(=O)-O-), 186.6

(C6); *m/z* (ESI^-) 664 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{30}H_{34}O_{14}NS$ $[M-H]^-$; found 664.17073, requires 664.17055.

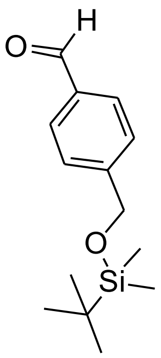
4-((*tert*-Butyldimethylsilyl)oxy)benzaldehyde, 24a

To 4-hydroxybenzaldehyde (2.0 g, 16.4 mmol, 1 eq) and Et_3N (3.42 mL, 24.6 mmol, 1.5 eq) in CH_2Cl_2 (40 mL) at 0 °C, a solution of TBDMSCl in CH_2Cl_2 (3.7 g, 24.6 mmol, 1.5 eq) was added portionwise. The reaction mixture was stirred at rt for 2 h and quenched with water. The organic layer was separated and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (eluent: EtOAc/petrol).



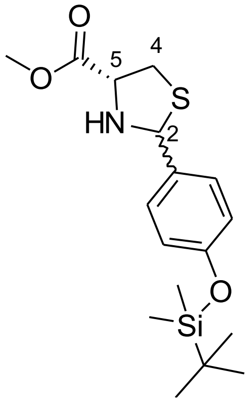
Yield (3.86 g, quant.); yellow oil, R_f = 0.74 (EtOAc/petrol 1:9); ν_{max}/cm^{-1} (neat) 1102 (Si-O), 1257 (Si-C), 1698 (C=O); δ_H (400 MHz, $CDCl_3$): 0.24 (6H, s, Si(CH_3)$_2$), 0.99 (9H, s, SiC(CH_3)$_3$), 6.94 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.78 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 9.87 (1H, s, C*H*O); δ_C (100.6 MHz, $CDCl_3$): -4.4 (Si(CH_3)$_2$), 18.2 (Si*C*(CH_3)$_3$), 25.5 (SiC(CH_3)$_3$), 120.4, 131.8 (Ar-*C*H), 130.3, 161.4 (Ar-C), 190.8 (*C*HO); *m/z* (ESI^+) 237 ($[M+H]^+$, 100 %); HRMS (ESI^+); $C_{13}H_{21}O_2Si$ $[M+H]^+$; found 237.13038, requires 237.13053.

4-((*tert*-Butyldimethylsilyl)oxy)methyl)benzaldehyde, 24b

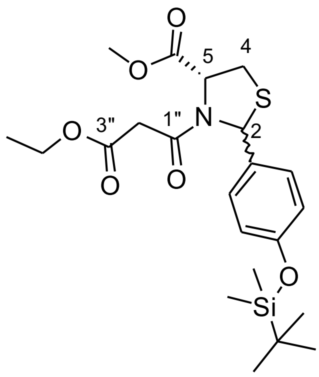


To the aldehyde (0.81 g, 5.96 mmol, 1.0 eq) in CH_2Cl_2 (20 mL), imidazole (0.61 g, 8.94 mmol, 1.5 eq) was added and stirred at rt for 30 min. TBDMSCl (1.35 g, 8.94 mmol, 1.5 eq) was then added portionwise and the reaction mixture was stirred at rt for 6 h. The reaction was quenched with water and the product extracted with CH_2Cl_2. The organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (eluent: EtOAc/petrol). Yield (1.47 g, 99 %); colourless oil; R_f = 0.56 (EtOAc/petrol 1:9); ν_{max}/cm^{-1} (neat) 1107 (Si-O), 1255 (Si-C), 1703 (C=O); δ_H (400 MHz, $CDCl_3$): 0.13 (6H, s, Si(CH_3)$_2$), 0.96 (9H, s, SiC(CH_3)$_3$), 4.83 (2H, s, OCH_2), 7.50 (2H, d, *J* = 8.1 Hz, Ar-C*H*), 7.86 (2H, d, *J* = 8.1 Hz, Ar-C*H*), 10.01 (1H, s, C*H*O); δ_C (100.6 MHz, $CDCl_3$): -5.4 (Si(CH_3)$_2$), 18.4 (Si*C*(CH_3)$_3$), 25.9 (SiC(CH_3)$_3$), 64.4 (OCH_2), 126.2, 129.8 (Ar-*C*H), 135.3, 148.7 (Ar-C), 192.1 (*C*HO); *m/z* (ESI) molecular ion not detected.

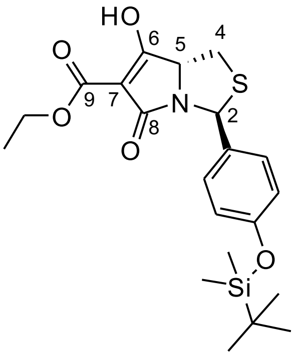
(-)-Ethyl (2*S*,5*R*)-2-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxylate 25a



Thiazolidine was obtained from the condensation of L-cysteine methyl ester hydrochloride and aldehyde **24a** following the general procedure. Yield (4.81 g, 85 %); yellow oil; 2:1 *cis* and *trans* diastereomers; R_f = 0.20 (EtOAc/petrol 1:9); ν_{max}/cm^{-1} (neat) 1254 (Si-C), 1742 (C=O), 3309 (N-H); δ_H (400 MHz, $CDCl_3$) major isomer (*cis*): 0.19 (6H, s, Si(CH_3)$_2$), 0.97 (9H, s, SiC(CH_3)$_3$), 2.60 (1H, app t, *J* = 12.4, NH), 3.08 (1H, dd, *J* = 10.3, 9.1 Hz, H4$_A$), 3.42 (1H, dd, *J* = 10.3, 7.1 Hz, H4$_B$), 3.77 (3H, s, CO_2CH_3), 3.89 - 3.99 (1H, m, H5), 5.49 (1H, d, *J* = 12.2 Hz, H2), 6.81 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.38 (2H, d, *J* = 8.6 Hz, Ar-C*H*); minor isomer (*trans*): 0.17 (6H, s, Si(CH_3)$_2$), 0.97 (9H, s, SiC(CH_3)$_3$), 2.76 (1H, br. s., NH), 3.20 (1H, dd, *J* = 10.6, 5.5 Hz, H4$_A$), 3.36 (1H, dd, *J* = 10.5, 7.1 Hz, H4$_B$), 3.75 (3H, s, CO_2CH_3), 4.21(1H, app t, *J* = 6.1 Hz, H5), 5.72 (1H, s, H2), 6.78 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.34 (2H, d, *J* = 8.3 Hz, Ar-C*H*); δ_C (100.6 MHz, $CDCl_3$): major isomer (*cis*): -4.6 (Si(*C*H_3)$_2$), 18.0 (Si*C*(CH_3)$_3$), 25.5 (SiC(*C*H_3)$_3$), 39.0 (C4), 52.4 (CO_2*C*H_3), 65.3 (C5), 72.2 (C2), 120.0, 128.5 (Ar-*C*H), 130.6, 155.8 (Ar-C), 171.5 (*C*O_2CH_3); minor isomer (*trans*): -4.6 (Si(*C*H_3)$_2$), 18.0 (Si*C*(CH_3)$_3$), 25.5 (SiC(*C*H_3)$_3$), 37.9 (C4), 52.3 (CO_2*C*H_3), 64.1 (C5), 70.5 (C2), 119.7, 128.1 (Ar-*C*H), 133.3, 155.2 (Ar-C), 172.1 (*C*O_2CH_3); *m/z* (ESI$^+$) 354 ([M+H]$^+$ 100 %); HRMS (ESI$^+$); $C_{17}H_{28}O_3NSSi$ [M+H]$^+$; found 354.15499, requires 354.15537.

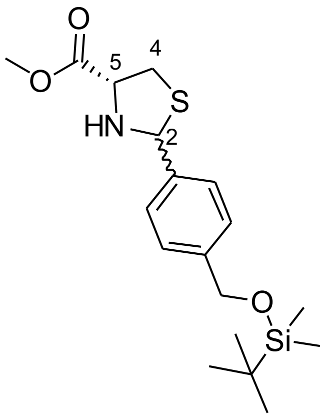


N-Acylthiazolidine was derived following the general procedure for *N*-acylation. Yield (5.2 g, 83 %); yellow oil; 2:1 *cis* and *trans* diastereomers; R_f = 0.15 (EtOAc/petrol 1:4); ν_{max}/cm^{-1} (neat) 1252 (Si-C), 1662 (C=O), 1742 (C=O); δ_H (400 MHz, $CDCl_3$) major isomer (*cis*, a mixture of two conformers): 0.16 and 0.19 (6H, s, Si(CH_3)$_2$), 0.95 and 0.97 (9H, s, SiC(CH_3)$_3$), 1.19 - 1.28 (3H, m, OCH_2CH_3), 3.05 - 3.47 (4H, m, H4$_A$ + H4$_B$ + H2″$_A$ + H2″$_B$), 3.82 (3H, s, CO_2CH_3), 4.06 - 4.17 (2H, m, O$CH_2$$CH_3$), 4.99 - 5.04 (1H, m, H5 minor conformer), 5.07 (1H, app t, *J* = 6.5 Hz, H5 major conformer), 6.08 (1H, s, H2 major conformer), 6.33 (1H, s, H2 minor conformer), 6.78 - 6.87 (2H, m, Ar-C*H*, major conformer), 6.93 (2H, d, *J* = 8.6 Hz, Ar-C*H*, minor conformer), 7.37 (2H, d, *J* = 8.3 Hz, Ar-C*H*, minor conformer), 7.51 (2H, d, *J* = 8.6 Hz, Ar-C*H*, major conformer); minor isomer (*trans*, a mixture of two conformers: 0.16 and 0.19 (6H, s, Si(CH_3)$_2$), 0.95 and 0.97 (9H, s, SiC(CH_3)$_3$), 1.19 - 1.28 (3H, m, OCH_2CH_3), 3.05 - 3.47 (4H, m, H4$_A$ + H4$_B$ + H2″$_A$ + H2″$_B$), 3.77 (3H, s, CO_2CH_3), 4.06 - 4.17 (2H, m, O$CH_2$$CH_3$), 5.16 (1H, app d, *J* = 5.9 Hz, H5 minor conformer), 5.25 - 5.29 (1H, m, H5 major conformer), 6.12 (1H, s, H2 major conformer), 6.30 (1H, s, H2 minor conformer), 6.74 (2H, d, *J* = 8.6 Hz, Ar-C*H*, minor conformer), 6.78 - 6.87 (2H, m, Ar-C*H*, major conformer), 7.07 (2H, d, *J* = 8.6 Hz, Ar-C*H*, major conformer), 7.13 (2H, d, *J* = 8.6 Hz, Ar-C*H*, minor conformer); δ_H (100.6 MHz, $CDCl_3$): major isomer (*cis*, a mixture of two conformers): -4.5 (Si(*C*H_3)$_2$), 13.9, 14.1 (OCH_2*C*H_3), 18.1 (Si*C*(CH_3)$_3$), 25.5 (SiC(*C*H_3)$_3$), 32.0, 33.1 (C4), 42.0, 43.4 (C2″), 52.6, 53.3 (CO_2*C*H_3), 61.5, 61.7 (O*C*H_2CH_3), 63.6, 64.5 (C5), 66.1, 66.5 (C2), 119.5, 120.4, 127.9, 128.5 (Ar-*C*H), 132.0, 155.9 (Ar-*C*), 165.5 (C1"), 166.8 (C3"), 170.2 (*C*O_2CH_3); minor isomer (*trans*, a mixture of two conformers): -4.5 (Si(*C*H_3)$_2$), 13.9, 14.1 (OCH_2*C*H_3), 18.1 (Si*C*(CH_3)$_3$), 25.5 (SiC(*C*H_3)$_3$), 31.0, 33.8 (C4), 42.3, 42.9 (C2″), 52.7, 53.4 (CO_2*C*H_3), 60.3, 61.4 (O*C*H_2CH_3), 63.9, 64.1 (C5), 64.8, 65.4 (C2), 119.7, 120.5, 126.0, 126.2 (Ar-*C*H), 134.2, 155.8 (Ar-*C*), 165.4 (C1"), 166.3 (C3"), 169.4 (*C*O_2CH_3); *m/z* (ESI$^+$) 468 ([M+H]$^+$ 100 %); HRMS (ESI$^+$); $C_{22}H_{34}O_6NSSi$ [M+H]$^+$; found 468.18630, requires 468.18706.



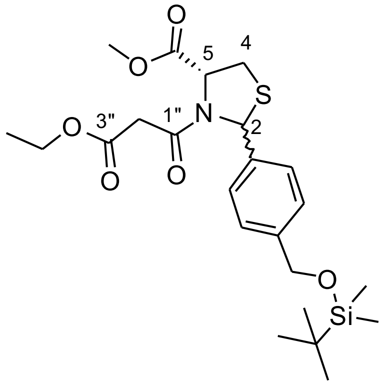
Tetramate **25a** was obtained following the general procedure for Dieckmann cyclisation. Yield (0.14 g, 30 %); yellow solid, mp 118-122 °C; R_f = 0.42 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -105.3 (*c* = 1.0, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1261 (Si-C), 1610 (C=C), 1651 (C=O), 1685 (C=O), 3311 (O-H); δ_H (400 MHz, CD_2Cl_2): 0.20 (6H, s, Si(C*H*$_3$)$_2$), 0.98 (9H, s, SiC(C*H*$_3$)$_3$), 1.36 (3H, t, *J* = 7.1 Hz, OCH_2C*H*$_3$), 2.99 (1H, dd, *J* = 11.0, 8.3 Hz, $H4_A$), 3.30 (1H, dd, *J* = 11.1, 7.0 Hz, $H4_B$), 4.36 (2H, q, *J* = 7.1 Hz, OC*H*$_2CH_3$), 4.77 (1H, app t, *J* = 7.7 Hz, H5), 6.22 (1H, s, H2), 6.82 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 7.32 (2H, d, *J* = 8.3 Hz, Ar-C*H*); δ_C (100.6 MHz, CD_2Cl_2): -4.2 (Si(*C*H_3)$_2$), 14.6 (OCH_2*C*H_3), 18.6 (Si*C*(CH_3)$_3$), 26.0 (SiC(*C*H_3)$_3$), 33.4 (C4), 62.1 (O*C*H_2CH_3), 62.5 (C2), 66.2 (C5), 120.6, 128.1 (Ar-*C*H), 133.8, 156.1 (Ar-C), 167.5 (C9), 186.8 (C6); *m/z* (ESI$^-$) 434 ([M-H]$^-$, 100 %); HRMS (ESI$^-$); $C_{21}H_{28}O_5NSSi$ [M-H]$^-$; found 434.14657, requires 434.14629.

(-)-Ethyl (2*S*,5*R*)-2-(4-(((*tert*-butyldimethylsilyl)oxy)methyl)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxylate 25b

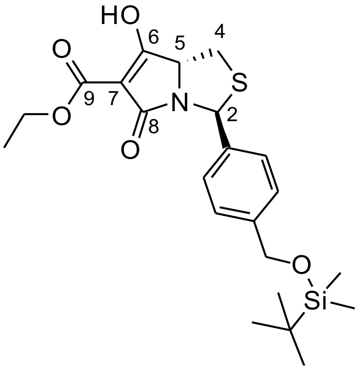


Thiazolidine was obtained from the condensation of L-cysteine methyl ester hydrochloride and aldehyde **24b** following the general procedure. Yield (1.89 g, 88 %); colourless oil; 1.6:1 *cis* and *trans* diastereomers; R_f = 0.54 (EtOAc/petrol 1:4); ν_{max}/cm^{-1} (neat) 1253 (Si-C), 1742 (C=O), 3311 (N-H); δ_H (400 MHz, $CDCl_3$) major isomer (*cis*): 0.11 (6H, s, Si(C*H*$_3$)$_2$), 0.95 (9H, s, SiC(C*H*$_3$)$_3$), 2.36 (1H, br. s, NH), 3.12 (1H, dd, *J* = 10.3, 9.1 Hz, $H4_A$), 3.47 (1H, dd, *J* = 10.3, 7.2 Hz, $H4_B$), 3.82 (3H, s, CO_2C*H*$_3$), 4.00 (1H, dd, *J* = 8.9, 7.2 Hz, H5), 4.75 (2H, s, OC*H*$_2$), 5.57 (1H, d, *J* = 12.2 Hz, H2), 7.34 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 7.49 (2H, d, *J* = 8.3 Hz, Ar-C*H*); minor isomer (*trans*): 0.10 (6H, s, Si(C*H*$_3$)$_2$), 0.94 (9H, s, SiC(C*H*$_3$)$_3$), 2.36 (1H, br. s., NH), 3.22 (1H, dd, *J* = 10.7, 5.8 Hz, $H4_A$), 3.40 (1H, dd, *J* = 10.7, 7.1 Hz, $H4_B$), 3.80 (3H, s, CO_2C*H*$_3$), 4.24 (1H, dd, *J*

= 7.1, 5.9 Hz, H5), 4.73 (2H, s, OCH_2), 5.82 (1H, s, H2), 7.29 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 7.45 (2H, d, *J* = 8.3 Hz, Ar-C*H*); δ_C (125.8 MHz, $CDCl_3$): major isomer (*cis*): -5.3 (Si(CH_3)$_2$), 18.4 (Si*C*(CH_3)$_3$), 25.9 (SiC(CH_3)$_3$), 39.3 (C4), 52.6 (CO_2CH_3), 64.6 (O*C*H_2), 65.6 (C5), 72.5 (C2), 126.3, 127.3 (Ar-*C*H), 136.7, 142.1 (Ar-C), 171.6 (*C*O_2CH_3); minor isomer (*trans*): -5.3 (Si(CH_3)$_2$), 15.3 (Si*C*(CH_3)$_3$), 25.9 (SiC(CH_3)$_3$), 38.1 (C4), 52.5 (CO_2CH_3), 64.3 (C5), 64.6 (O*C*H_2), 70.7 (C2), 126.1, 126.8 (Ar-*C*H), 139.6, 141.3 (Ar-C), 172.2 (*C*O_2CH_3); *m/z* (ESI^+) 368 ($[M+H]^+$ 43 %); HRMS (ESI^+); $C_{18}H_{30}O_3NSSi$ $[M+H]^+$; found 368.17144, requires 368.17102.



N-Acylthiazolidine was obtained following the general procedure for *N*-acylation. Yield (2.25 g, 91 %); colourless oil; inseparable 1.7:1 *cis* and *trans* diastereomers; R_f = 0.20 (EtOAc/petrol 1:3); ν_{max}/cm^{-1} (neat) 1250 (Si-C), 1662 (C=O), 1742 (C=O); δ_H (500 MHz, $CDCl_3$) major isomer (*cis*, a mixture of two conformers): 0.09 and 0.11 (6H, s, Si(CH_3)$_2$), 0.94 and 0.95 (9H, s, SiC(CH_3)$_3$), 1.20 - 1.30 (3H, m, OCH_2CH_3), 3.07 - 3.58 (4H, m, $H4_A + H4_B + H2''_A + H2''_B$), 3.81 and 3.85 (3H, s, CO_2CH_3), 4.06 - 4.25 (2H, m, OC$H_2$$CH_3$), 4.70 and 4.75 (OC$H_2$), 5.08 (1H, app t, *J* = 6.8 Hz, H5), 6.14 and 6.37 (1H, s, H2), 7.21 - 7.27 (2H, m, Ar-C*H* minor conformer), 7.32 - 7.38 (2H, m, Ar-C*H* major conformer), 7.48 (2H, d, *J* = 8.1 Hz, Ar-C*H* minor conformer), 7.62 (2H, d, *J* = 8.2 Hz, Ar-C*H* major conformer),; minor isomer (*trans*, a mixture of two conformers: 0.09 and 0.11 (6H, s, Si(CH_3)$_2$), 0.94 and 0.95 (9H, s, SiC(CH_3)$_3$), 1.20 - 1.30 (3H, m, OCH_2CH_3), 3.07 - 3.58 (4H, m, $H4_A + H4_B + H2''_A + H2''_B$), 3.80 and 3.86 (3H, s, CO_2CH_3), 4.06 - 4.25 (2H, m, OC$H_2$$CH_3$), 4.70 and 4.74 (OC$H_2$), 5.20 (1H, app d, *J* = 5.9 Hz, H5 minor conformer), 5.29 - 5.33 (1H, m, H5 major conformer), 6.18 and 6.33 (1H, s, H2), 7.19 (2H, d, *J* = 8.2 Hz, Ar-C*H* major conformer), 7.21 - 7.27 (4H, m, Ar-C*H* minor conformer), 7.32 - 7.38 (2H, m, Ar-C*H* major conformer); δ_C (125.8 MHz, $CDCl_3$): major isomer (*cis*, a mixture of two conformers): -5.3 (Si(CH_3)$_2$), 14.0 (OCH_2CH_3), 18.4 (Si*C*(CH_3)$_3$), 25.9 (SiC(CH_3)$_3$), 32.1, 33.8 (C4), 42.1, 43.4 (C2″), 52.7, 53.1 (CO_2CH_3), 61.6, 61.8 (O*C*H_2CH_3), 63.8, 64.7 (C5), 64.5, 64.6 (OCH_2), 66.2, 67.0 (C2), 125.8, 126.4, 126.6, 127.0 (Ar-*C*H), 137.2, 138.3, 141.2, 142.1 (Ar-*C*), 164.4, 165.6 (C1"), 166.8, 167.2 (C3"), 170.2, 170.3 (*C*O_2CH_3); minor isomer (*trans*, a mixture of two conformers): -5.3 (Si(CH_3)$_2$), 14.0, 14.2 (OCH_2CH_3), 18.4 (Si*C*(CH_3)$_3$), 25.9 (SiC(CH_3)$_3$), 31.0, 33.1 (C4), 42.4, 43.0 (C2″), 52.8, 53.4 (CO_2CH_3), 61.5, 61.8 (O*C*H_2CH_3), 64.0, 64.3 (C5), 64.4, 64.6 (OCH_2), 65.0, 65.6 (C2), 124.6, 124.9, 126.2, 126.8 (Ar-*C*H), 140.4, 140.6, 140.8, 142.0 (Ar-*C*), 164.9, 165.4 (C1"), 166.3, 167.2 (C3"), 169.5, 170.2 (*C*O_2CH_3); *m/z* (ESI^+) 482 ($[M+H]^+$ 100 %); HRMS (ESI^+); $C_{23}H_{36}O_6NSSi$ $[M+H]^+$; found 482.20171, requires 482.20271.

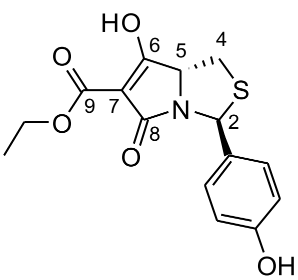


Tetramate **25b** was obtained following the general procedure for Dieckmann cyclisation. Yield (0.31 g, 15 %); yellow foam, mp 94 - 96 °C; R_f = 0.47 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -172.2 (*c* = 0.17, MeOH); ν_{max}/cm^{-1} (neat) 1610 (C=C), 1689 (C=O, br with shoulder towards smaller wavenumber); δ_H (400 MHz, Methanol-*d*$_4$): 0.07 (6H, s, Si(C*H*$_3$)$_2$), 0.91 (9H, s, SiC(C*H*$_3$)$_3$), 1.31 (3H, t, *J* = 7.0 Hz, OCH$_2$C*H*$_3$), 2.98 (1H, dd, *J* = 10.5, 8.8 Hz, H4$_A$), 3.23 - 3.33 (1H, m, H4$_B$), 4.29 (2H, q, *J* = 7.0 Hz, OC*H*$_2$CH$_3$), 4.59 (OC*H*$_2$), 4.87 (1H, app t, *J* = 7.3 Hz, H5), 6.22 (1H, s, H2), 7.35 (2H, d, *J* = 8.0 Hz, Ar-C*H*), 7.45 (2H, d, *J* = 8.0 Hz, Ar-C*H*); δ_C (100.6 MHz, Methanol-*d*$_4$): -5.6 (Si(*C*H$_3$)$_2$), 14.8 (OCH$_2$*C*H$_3$), 19.3 (Si*C*(CH$_3$)$_3$), 26.5 (SiC(*C*H$_3$)$_3$), 33.7 (C4), 61.7 (O*C*H$_2$CH$_3$), 63.4 (C2), 64.9 (O*C*H$_2$), 67.6 (C5), 99.5 (C7), 127.5, 128.2 (Ar-*C*H), 141.1, 142.7 (Ar-C), 164.9 (C9), 172.8 (C8), 184.9 (C6); *m/z* (ESI$^-$) 448 ([M-H]$^-$, 100 %); HRMS (ESI$^-$); $C_{22}H_{30}O_5NSSi$ [M-H]$^-$; found 448.16259, requires 448.16194.

General procedure for silyl ether deprotection

The deprotection of silyl ethers was according to a modified literature procedure. [8] To tetramate (1.0 eq) dissolved in THF (2 mL/mmol), tetraethylene glycol (5 eq) and KF (2 eq) were added. The reaction was stirred at rt for 0.5 - 2 h (for the deprotection of **25b**, the reaction mixture was heated at 80 °C for 5 h). Solvent was evapourated *in vacuo* and the residue was purified by silica gel flash column chromatography (eluent: EtOAc/MeOH/1% Et$_3$N). The product isolated was dissolved in CH_2Cl_2 (a few drops of MeOH was needed to aid solubility) and washed with 0.1 M HCl. The organic fraction was dried over Na_2SO_4, filtered and concentrated *in vacuo* to obtain the required product.

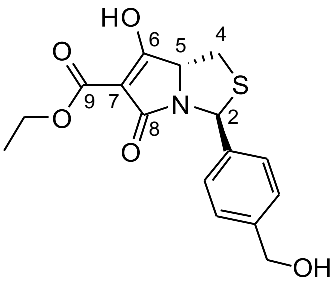
(-)-Ethyl (2*S*,5*R*)-6-hydroxy-2-(4-hydroxyphenyl)-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxylate 26a



Yield (88 mg, 30 %); yellow solid, mp 172 °C; R_f = 0.21 (EtOAc/ MeOH 9:1); $[\alpha]_D^{25}$ = - 188.9 (*c* = 0.13, MeOH); ν_{max}/cm^{-1} (neat) 1611 (C=C), 1642 (C=O), 1686 (C=O), 3369 (O-H); δ_H (200 MHz, Acetone-*d*$_6$): 1.29 (3H, t, *J* = 7.1 Hz, OCH$_2$C*H*$_3$), 3.08 (1H, dd, *J* = 11.0, 8.0 Hz, H4$_A$), 3.38 (1H, dd, *J* = 11.0, 7.0 Hz, H4$_A$), 4.30 (2H, q, *J* = 7.1 Hz, OC*H*$_2$CH$_3$), 4.96 (1H, app t, *J* = 7.6 Hz, H5), 6.18 (1H, s, H2), 6.80 (2H, d, *J* = 8.5 Hz, Ar-C*H*), 7.33 (2H, d, *J* = 8.5 Hz, Ar-C*H*); δ_C (125.8 MHz, Acetone-*d*$_6$): 14.6 (OCH$_2$*C*H$_3$), 33.4 (C4), 61.4 (O*C*H$_2$CH$_3$), 63.1 (C2), 66.6 (C5), 99.3 (C7), 116.0, 128.8 (Ar-*C*H), 133.0, 158.1 (Ar-C), 166.3 (C9), 169.9 (C8), 186.0 (C6);

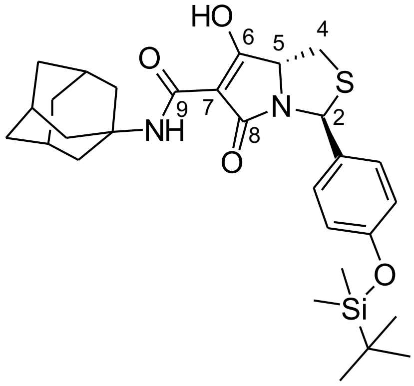
m/z (ESI^-) 320 ($[M-H]^-$, 73 %); HRMS (ESI^-); $C_{15}H_{14}O_5NS$ $[M-H]^-$; found 320.06016, requires 320.05982.

(-)-Ethyl (2*S*,5*R*)-6-hydroxy-2-(4-(hydroxymethyl)phenyl)-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxylate 26b



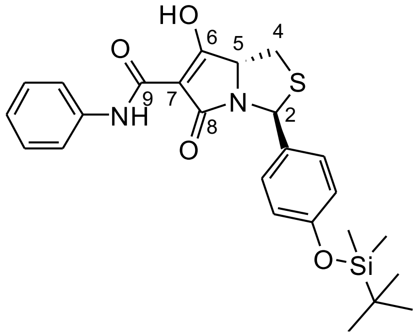
Yield (24 mg, 20 %); white foam, mp 78-80 °C; R_f = 0.18 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -273.7 (*c* = 0.11, MeOH); ν_{max}/cm^{-1} (neat) 1609 (C=C), 1690 (C=O, br with shoulder towards smaller wavenumber), 3350 (O-H); δ_H (200 MHz, Acetone-d_6): 1.29 (3H, t, *J* = 7.1 Hz, OCH_2CH_3), 3.12 (1H, dd, *J* = 11.1, 8.0 Hz, $H4_A$), 3.39 (1H, dd, *J* = 11.1, 7.0 Hz, $H4_A$), 4.30 (2H, q, *J* = 7.1 Hz, OCH_2CH_3), 4.62 (OCH_2), 5.00 (1H, app t, *J* = 7.6 Hz, H5), 6.25 (1H, s, H2), 7.34 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 7.45 (2H, d, *J* = 8.3 Hz, Ar-C*H*); δ_C (125.8 MHz, Acetone-d_6): 14.6 (OCH_2CH_3), 33.4 (C4), 61.5 (OCH_2CH_3), 63.2 (C2), 64.4 (OCH_2), 66.6 (C5), 99.4 (C7), 127.2, 127.5 (Ar-*C*H), 140.8, 143.2 (Ar-C), 166.3 (C9), 169.7 (C8), 186.0 (C6); *m/z* (ESI^-) 334 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{16}H_{16}O_5NS$ $[M-H]^-$; found 334.07552, requires 334.07547.

(-)-(2*S*,5*R*)-2-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-6-hydroxy-8-oxo-*N*-adamantyl-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 27a



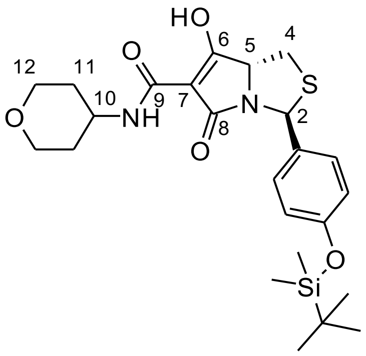
Carboxamide tetramate **27a** was obtained by aminolysis of **25a** with 1-adamantylamine according to the general procedure for the synthesis of carboxamides with THF/toluene as solvent. Yield (0.46 g, 54 %); brown foaming solid, mp 158-160 °C; R_f = 0.78 (EtOAc/petrol 1:1); $[\alpha]_D^{25}$ = -144.1 (*c* = 0.25, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1262 (Si-C), 1627 (C=C), 1648 (C=O), 1688 (C=O), 3309 (O-H); δ_H (400 MHz, CD_2Cl_2): 0.20 (6H, s, $Si(CH_3)_2$), 0.98 (9H, s, $SiC(CH_3)_3$), 1.70 (6H, Adamantyl-CH_2), 2.06 (6H, Adamantyl-CH_2), 2.10 (3H, br.signal, Adamantyl-C*H*), 2.97 (1H, dd, *J* = 11.0, 8.6 Hz, $H4_A$), 3.25 (1H, dd, *J* = 11.1, 7.1 Hz, $H4_B$), 4.70 (1H, H5), 6.18 (1H, s, H2), 6.81 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.31 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 9.74 (1H, br. s., NH/OH); δ_C (125.8 MHz, CD_2Cl_2): -4.2 ($Si(CH_3)_2$), 18.6 ($SiC(CH_3)_3$), 26.0 ($SiC(CH_3)_3$), 30.1 (Adamantyl-*C*H), 33.1 (C4), 36.6 (Adamantyl-CH_2), 42.1 (Adamantyl-CH_2), 53.4 (Adamantyl-C), 62.2 (C2), 67.8 (C5), 96.2 (C7), 120.6, 128.2 (Ar-*C*H), 133.9, 156.1 (Ar-C), 166.6 (C9), 172.7 (C8), 188.0 (C6); *m/z* (ESI^-) 539 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{29}H_{39}O_4N_2SSi$ $[M-H]^-$; found 539.24045, requires 539.23943.

(-)-(2*S*,5*R*)-2-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-6-hydroxy-8-oxo-*N*-phenyl-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 27b



Carboxamide tetramate **27b** was obtained by aminolysis of **25a** with aniline according to the general procedure with THF/toluene as solvent. Yield (0.35 g, 27 %); yellow foam, mp 80-84 °C; R_f = 0.68 (EtOAc/MeOH 98:2); $[\alpha]_D^{25}$ = -174.6 (*c* = 0.19, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1261 (Si-C), 1651 (C=O, br with shoulder towards smaller wave number), 1693 (C=O); δ_H (400 MHz, CD_2Cl_2): 0.21 (6H, s, Si(C*H*$_3$)$_2$), 0.99 (9H, s, SiC(C*H*$_3$)$_3$), 3.02 (1H, dd, *J* = 11.0, 8.8 Hz, $H4_A$), 3.31 (1H, dd, *J* = 11.1, 7.0 Hz, $H4_B$), 4.86 (1H, app t, *J* = 7.7 Hz, H5), 6.24 (1H, s, H2), 6.84 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.16 (1H, app t, *J* = 7.4 Hz, Ar-C*H*), 7.32 - 7.40 (4H, m, Ar-C*H*), 7.58 (2H, d, *J* = 7.8 Hz, Ar-C*H*), 9.20 (1H, br. s, NH/OH), 9.38 (1H, br. s, NH/OH); δ_C (100.6 MHz, CD_2Cl_2): -4.4 (Si(*C*H$_3$)$_2$), 18.2 (Si*C*(CH$_3$)$_3$), 25.6 (SiC(*C*H$_3$)$_3$), 32.3 (C4), 61.5 (C2), 66.3 (C5), 120.2, 120.3, 125.0, 127.8, 129.1 (Ar-*C*H), 132.3, 136.4, 155.7 (Ar-C), 163.8 (C9), 171.5 (C8), 184.2 (C6); *m/z* (ESI^-) 481 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{25}H_{29}O_4N_2SSi$ $[M-H]^-$; found 481.16199, requires 481.16228.

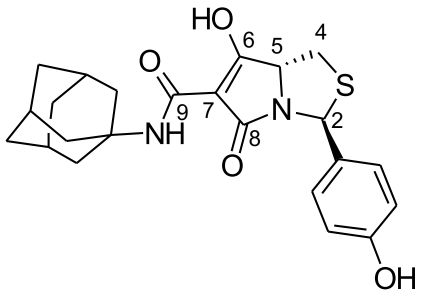
(-)-(2*S*,5*R*)-2-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-6-hydroxy-8-oxo-*N*-(tetrahydro-2H-pyran-4-yl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 27c



Carboxamide tetramate **27c** was obtained by aminolysis of **25a** with 4-aminotetrahydropyran according to the general procedure for the synthesis of carboxamides with THF/toluene as solvent. Yield (0.33 g, 30 %); yellow foam, 5.4:1 AB:CD tautomers, mp 76-80 °C; R_f = 0.49 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -161.3 (*c* = 0.25, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1263 (Si-C), 1650 (C=O, br with shoulder towards smaller wavenumber), 1692 (C=O), 3324 (O-H/N-H); δ_H (400 MHz, $CDCl_3$): 0.18 (6H, s, Si(C*H*$_3$)$_2$), 0.97 (9H, s, SiC(C*H*$_3$)$_3$), 1.49 - 1.70 (2H, m, H11), 1.82 - 1.99 (2H, m, H11), 2.97 (1H, dd, *J* = 11.0, 8.6 Hz, $H4_A$), 3.26 (1H, dd, *J* = 11.0, 7.1 Hz, $H4_B$), 3.44 - 3.52 (2H, m, H12), 3.87 - 4.10 (3H, m, H10 + H12), 4.45 (1H, app t, *J* = 7.7 Hz, H5 CD), 4.75 (1H, app t, *J* = 7.7 Hz, H5 AB), 6.19 (1H, s, H2 AB), 6.29 (1H, s, H2 CD), 6.80 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.33 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 10.87 (1H, br. s, NH/OH); δ_C (100.6 MHz, $CDCl_3$): -4.5 (Si(*C*H$_3$)$_2$), 18.1 (Si*C*(CH$_3$)$_3$), 25.6 (SiC(*C*H$_3$)$_3$), 32.3 (C4), 32.6 (C11), 45.1 (C10), 61.5 (C2 AB), 62.3 (C2 CD), 66.3 (C12), 66.6 (C5 AB), 70.6 (C5 CD), 97.0 (C7), 120.0, 127.7 (Ar-*C*H), 132.5, 155.6 (Ar-C), 165.1 (C9 AB), 165.9 (C9 CD), 171.7 (C8 AB), 179.3 (C8 CD), 185.4 (C6 AB), 191.4 (C6 CD);

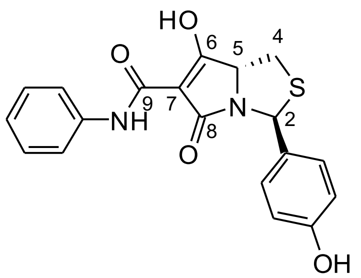
m/z (ESI^-) 489 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{24}H_{33}O_5N_2SSi$ $[M-H]^-$; found 489.18805, requires 489.18740.

(-)-(2*S*,5*R*)-2-(4-Hydroxyphenyl)-6-hydroxy-8-oxo-*N*-adamantyl-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 28a



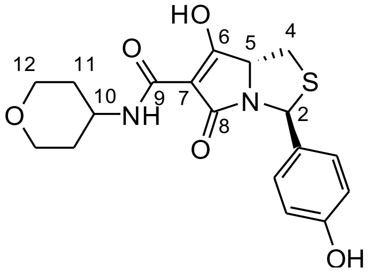
The synthesis of **28a** from **27a** was according to the procedure for silyl ether deprotection outlined in general procedure. Yield (0.16 g, 40 %); yellow solid, mp 220 °C; R_f = 0.49 (EtOAc/MeOH 96:4); $[\alpha]_D^{25}$ = -249.1 (*c* = 0.15, DMSO); ν_{max}/cm^{-1} (neat) 1612 (C=C), 1637 (C=O), 1676 (C=O), 3333 (O-H); δ_H (500 MHz, Dimethyl sulfoxide-*d₆*): 1.63 (6H, Adamantyl-C*H*$_2$), 1.97 (6H, Adamantyl-C*H*$_2$), 2.04 (3H, Adamantyl-C*H*), 2.96 (1H, dd, *J* = 10.9, 8.7 Hz, $H4_A$), 3.28 (1H, dd, *J* = 11.0, 6.9 Hz, $H4_B$), 4.90 (1H, app t, *J* = 7.7 Hz , H5), 6.03 (1H, s, H2), 6.72 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.24 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.66 (1H, br. s., NH/OH), 9.45 (1H, br. s., NH/OH); δ_H (125.8 MHz, Dimethyl sulfoxide-*d₆*): 28.8 (Adamantyl-*C*H), 33.9 (C4), 35.7 (Adamantyl-*C*H$_2$), 41.1 (Adamantyl-*C*H$_2$), 51.3 (Adamantyl-C), 61.2 (C2), 67.0 (C5), 96.4 (C7), 115.0, 127.7 (Ar-*C*H), 131.1, 157.0 (Ar-C), 163.3 (C9), 172.9 (C8), 183.5 (C6); *m/z* (ESI^-) 425 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{23}H_{25}O_4N_2S$ $[M-H]^-$; found 425.15378, requires 425.15295.

(-)-(2*S*,5*R*)-2-(4-hydroxyphenyl)-6-hydroxy-8-oxo-*N*-phenyl-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 28b



The synthesis of **28b** from **27b** was according to the procedure for silyl ether deprotection outlined in general procedure. Yield (75 mg, 45 %); yellow solid, mp 100-104 °C; R_f = 0.64 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -257.9 (*c* = 0.15, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1648 (C=O, br with shoulder towards smaller wave number), 1676 (C=O), 3303 (N-H/O-H); δ_H (500 MHz, Methanol-*d₄*): 3.02 (1H, dd, *J* = 11.0, 8.7 Hz, $H4_A$), 3.33 (1H, dd, *J* = 11.0, 6.9 Hz, $H4_B$), 4.97 (1H, dd, *J* = 8.4, 7.0 Hz, H5), 6.17 (1H, s, H2), 6.77 (2H, d, *J* = 8.5 Hz, Ar-C*H*), 7.12 (1H, app t, *J* = 7.4 Hz Ar-C*H*), 7.30 - 7.36 (4H, m, Ar-C*H*), 7.60 (2H, d, *J* = 7.7 Hz, Ar-C*H*); δ_C (125.8 MHz, Methanol-*d₄*): 33.3 (C4), 63.1 (C2), 68.4 (C5), 99.7 (C7), 116.4, 121.4, 125.8, 129.2, 130.2 (Ar-*C*H), 132.6, 138.7, 158.7 (Ar-C), 164.2 (C9), 174.4 (C8), 185.0 (C6); *m/z* (ESI^-) 367 ($[M-H]^-$, 74 %); HRMS (ESI^-); $C_{19}H_{15}O_4N_2S$ $[M-H]^-$; found 367.07512, requires 367.07580.

(-)-(2*S*,5*R*)-2-(Tetrahydro-2*H*-pyran-4-yl)-6-hydroxy-8-oxo-*N*-phenyl-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 28c

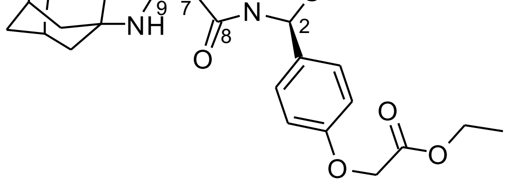


The synthesis of **28c** from **27c** was according to the procedure for silyl ether deprotection outlined in general procedure. Yield (0.11 g, 45 %); yellow solid, mp 200 °C; R_f= 0.47 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -237.9 (*c* = 0.14, DMSO); ν_{max}/cm^{-1} (neat) 1639 (C=O), 1691 (C=O), 3295 (O-H); δ_H (500 MHz, DMSO-*d*$_6$): 1.42 - 1.54 (2H, m, H11), 1.68 - 1.81 (2H, m, H11), 2.95 (1H, dd, *J* = 11.0, 8.4 Hz, H4$_A$), 3.27 (1H, dd, *J* = 11.0, 6.9 Hz, H4$_B$), 3.35 - 3.43 (2H, m, H12), 3.76 - 3.84 (2H, m, H12), 3.86 - 3.98 (1H, m, H10), 4.82 (1H, app t, *J* = 7.6 Hz, H5), 6.06 (1H, s, H2), 6.72 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.24 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 8.03 (1H, br. s, NH/OH), 9.45 (1H, br. s, NH/OH); δ_C (125.8 MHz, DMSO-*d*$_6$): 32.3 (C4), 32.4 (C11), 44.4 (C10), 61.6 (C2), 65.7 (C12), 67.2 (C5), 95.4 (C7), 115.0, 127.7 (Ar-*C*H), 131.4, 157.0 (Ar-C), 162.8 (C9), 173.4 (C8), 184.1 (C6); *m/z* (ESI$^-$) 375 ([M-H]$^-$, 100 %); HRMS (ESI$^-$); $C_{18}H_{19}N_2O_5S$ [M-H]$^-$; found 375.10159, requires 375.10202.

General procedure for the synthesis of *O*-aryl ether tetramic acids 29a and 30

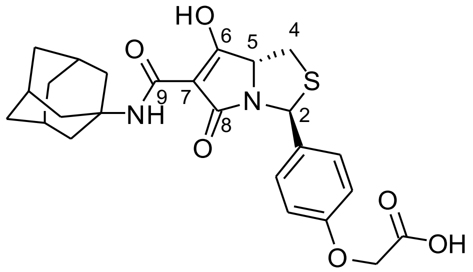
To tetramate (1.0 eq) dissolved in THF, K_2CO_3 (2.1 eq) and the relevant alkyl halide (1.5 eq) were added and the reaction stirred at rt for 18 h. Solvents were removed *in vacuo* and water and EtOAc were added to the residue. The aqueous layer was acidifeid with 10 % HCl and extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo* to give the crude, which was purified by silica gel flash column chromatography (eluent: EtOAc/petrol to EtOAc/MeOH/1% Et_3N). The product isolated was dissolved in CH_2Cl_2 and washed with 5% citric acid. The organic fraction was dried over Na_2SO_4, filtered and concentrated *in vacuo* to obtain the required ether.

(-)-Ethyl 2-(4-((2*S*,5*R*)-6-((Adamantan-1-yl)carbamoyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazol-2-yl)phenoxy)acetate 29a



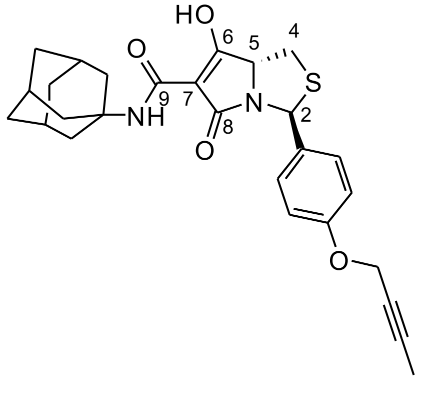
Yield (0.22 g, 70 %); yellow oil; 3.3:1 AB:CD tautomers; R_f= 0.75 (EtOAc/MeOH 98:2); $[\alpha]_D^{25}$ = -184.6 (*c* = 0.18, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1624 (C=C), 1648 (C=O), 1688 (C=O), 1737 (C=O), 3311 (N-H/O-H); δ_H (500 MHz, $CDCl_3$) 1.30 (3H, t, *J* = 7.1 Hz, OCH_2CH_3), 1.70 (6H, Adamantyl-C*H*$_2$), 2.05 (6H, Adamantyl-C*H*$_2$), 2.12 (3H, Adamantyl-C*H*), 2.93 - 3.06 (1H, m, H4$_A$), 3.25 (1H, dd, *J* = 11.1, 7.2 Hz, H4$_B$), 4.27 (2H, q, *J* = 7.1 Hz, OC*H*$_2$CH$_3$), 4.37 - 4.46 (1H, m, H5 CD), 4.61 (2H, s, OC*H*$_2$), 4.66 (1H, app t, *J* = 7.7 Hz, H5 AB), 6.20 (1H, s, H2 AB), 6.30 (1H, s, H2 CD), 6.88 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.40 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.98 (2H, br. s, N-H + O-H); δ_C (125.8 MHz, $CDCl_3$): 14.1 (OCH_2CH_3), 29.3 (Adamantyl-*C*H), 32.5 (C4), 36.0 (Adamantyl-CH_2), 41.5 (Adamantyl-CH_2), 53.1 (Adamantyl-C), 61.4 (OCH_2CH_3), 61.6 (C2 AB), 62.2 (C2 CD), 65.5 (OCH_2), 67.3 (C5 AB), 70.6 (C5 CD), 85.4 (C7 CD), 93.7 (C7 AB), 114.7, 127.9 (Ar-C*H*), 133.5, 157.6 (Ar-C), 166.0 (C9 AB), 166.5 (C9 CD), 168.7 ($CO_2CH_2CH_3$), 172.3 (C8 AB), 178.2 (C8 CD), 188.0 (C6 AB), 191.2 (C6 CD); *m/z* (ESI^-) 511 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{27}H_{33}O_6N_2S$ $[M+H]^+$; found 513.20572, requires 513.20538.

(-)-2-(4-((2*S*,5*R*)-6-(Adamantan-1-yl)carbamoyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazol-2-yl)phenoxy)acetic acid 29b



To tetramate **29a** (1.51 g, 2.95 mmol, 1.0 eq) dissolved in THF:H_2O (1:1) was added LiOH.H_2O (0.25 g, 5.9 mmol, 2 eq) and the reaction stirred at rt for 2 h. Upon completion, the aqueous layer was acidifeid with 10 % HCl and extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo* to give **29b**. Yield (0.14 g, 98 %); yellow solid, mp 128-130 °C; R_f = 0.06 (EtOAc/MeOH 3:1); $[\alpha]_D^{25}$ = -187.9 (*c* = 0.17, MeOH); ν_{max}/cm^{-1} (neat) 1608 (C=C), 1645 (C=O), 1682 (C=O), 1737 (C=O); δ_H (400 MHz, Methanol-d_4) 1.74 (6H, Adamantyl-CH_2), 2.09 (9H, Adamantyl-CH_2 + Adamantyl-C*H*), 2.98 (1H, dd, *J* = 11.1, 8.2 Hz, $H4_A$), 3.24 - 3.30 (1H, m, $H4_B$), 4.66 (2H, s, OCH_2), 4.79 (1H, app t, *J* = 7.6 Hz, H5), 6.18 (1H, s, H2), 6.92 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.40 (2H, d, *J* = 8.6 Hz, Ar-C*H*); δ_C (125.8 MHz, Methanol-d_4): 31.0 (Adamantyl-*C*H), 33.3 (C4), 37.3 (Adamantyl-CH_2), 42.8 (Adamantyl-CH_2), 54.1 (Adamantyl-C), 63.1 (C2), 66.0 (OCH_2), 69.3 (C5), 95.5 (C7), 115.8, 129.0 (Ar-C*H*), 135.1, 159.4 (Ar-*C*), 166.8 (C9), 172.7 ($CO_2CH_2CH_3$), 175.6 (C8), 189.0 (C6); *m/z* (ESI^-) 483 ($[M-H]^-$, 100 %); HRMS (ESI^+); $C_{25}H_{29}O_6N_2S$ $[M+H]^+$; found 485.17412, requires 485.17408.

(-)-(2*S*,5*R*)-*N*-((Adamantan-1-yl)-2-(4-(but-2-yn-1-yloxy)phenyl)-6-hydroxy-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 30



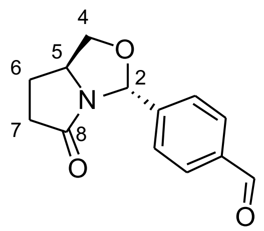
Yield (62 mg, 30 %); brown oil; 2.8:1 AB:CD tautomers; R_f = 0.66 (EtOAc/MeOH 98:2); $[\alpha]_D^{25}$ = -209.4 (*c* = 0.14, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1622 (C=C), 1648 (C=O), 1684 (C=O), 3306 (O-H/N-H); δ_H (400 MHz, $CDCl_3$): 1.64 - 1.74 (6H, m, Adamantyl-CH_2), 1.86 (3H, t, *J* = 2.3 Hz, -C≡C-CH_3), 2.02 - 2.08 (6H, m, Adamantyl-CH_2), 2.09 - 2.18 (3H, m, Adamantyl-C*H*), 2.94 -

3.04 (1H, m, $H4_A$), 3.26 (1H, dd, *J* = 11.0, 7.1 Hz, $H4_B$), 4.43 (1H, app t, *J* = 7.7 Hz, H5 CD), 4.64 (2H, q , *J* = 2.3 Hz, O*C*H_2-C≡C-), 4.68 (1H, dd, *J* = 8.3, 7.2 Hz, H5 AB), 6.21 (1H, s, H2 AB), 6.30 (1H, s, H2 CD), 6.94 (2H, d, *J* = 8.8 Hz, Ar-C*H*), 7.40 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 9.79 (2H, br. s., NH + OH); δ_C (125.8 MHz, $CDCl_3$): 3.7 (-C≡C-*C*H_3), 29.3 (Adamantyl-*C*H), 32.5 (C4 AB), 32.8 (C4 CD), 35.8 (Adamantyl-*C*H_2 CD), 36.0 (Adamantyl-*C*H_2 AB), 40.9 (Adamantyl-*C*H_2 CD), 41.5 (Adamantyl-*C*H_2 AB), 53.1 (Adamantyl-C), 56.4 (O*C*H_2-C≡C-), 61.6 (C2 AB), 62.2 (C2 CD), 67.3 (C5 AB), 70.6 (C5 CD), 73.8 (-C≡C-), 83.8 (-C≡C-), 85.4 (C7 CD), 95.1 (C7 AB), 114.8, 127.7 (Ar-*C*H), 132.8, 157.6 (Ar-C), 166.0 (C9 AB), 166.5 (C9 CD), 172.2 (C8 AB), 178.1 (C8 CD), 187.9 (C6 AB), 191.2 (C6 CD); *m/z* (ESI^-) 477 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{27}H_{29}N_2O_4S$ $[M-H]^-$; found 477.18466, requires 477.18535.

(*S*)-5-(Hydroxymethyl)-2-pyrrolidinone, 31

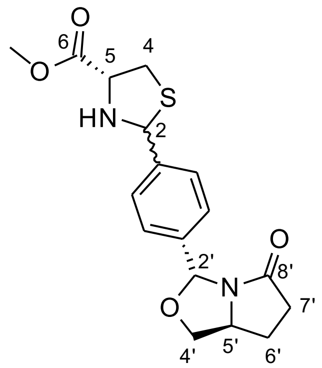
Compound **31** was synthesised according to the literature.[9] δ_H (400 MHz, $CDCl_3$): 1.74 - 1.86 (1H, m, H6), 2.11 - 2.24 (1H, m, H6), 2.28 - 2.45 (2H, m, H7), 3.47 (1H, dd, *J* = 11.4, 7.0 Hz, H4), 3.69 (1H, dd, *J* = 11.4, 3.2 Hz, H4), 3.77 - 3.85 (1H, m, H5), 4.92 (1H, br.s., OH), 7.56 (1H, br.s., NH); δ_C (100.6 MHz, $CDCl_3$): 22.4 (C6), 30.1 (C7), 56.3 (C5), 65.3 (C4), 179.4 (C8); *m/z* (ESI^+) 138 ($[M+Na]^+$, 4 %); HRMS (ESI^+); $C_5H_9O_2NNa$ $[M+Na]^+$; found 138.05243, requires 138.05255.

(+)-(2*R*, 5*S*)-1-Aza-2-(4-formylphenyl)-3-oxa-8-oxo-bicyclo[3.3.0]octane, 33

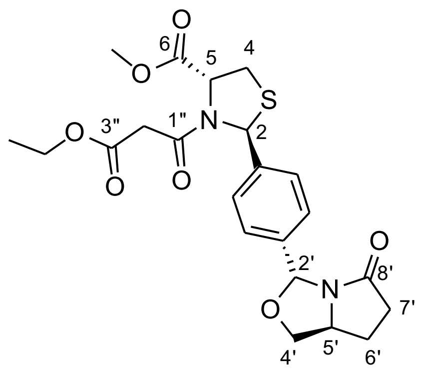


A mixture of **33** (0.46 g, 4.0 mmol, 1.0 eq), terephthalaldehyde (1.07 g, 8.0 mmol, 2.0 eq) and *p*-toluenesulphonic acid (8 mg, 0.04 mmol, 0.01 eq) in toluene (25 mL) was refluxed with a Dean-Stark apparatus for 22 h. After cooling to rt, EtOAc (10 mL) and water (10 mL) were added. The aqueous layer was separated and extracted with EtOAc. The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified by silica gel flash column chromatography (eluent: EtOAc/petrol). Yield (0.37 g, 40 %); colourless oil; R_f = 0.28 (EtOAc/petrol 2:1); $[\alpha]_D^{25}$ = +245.7 (*c* = 1.52, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1699 (C=O); δ_H (400 MHz, $CDCl_3$): 1.91 - 2.05 (1H, m, H6), 2.35 - 2.45 (1H, m, H6), 2.52 - 2.62 (1H, m, H7), 2.83 (1H, ddd, *J* = 17.5, 10.0, 9.2 Hz, H7), 3.51 (1H, t, *J* = 8.3 Hz, H4), 4.07 - 4.16 (1H, m, H5), 4.25 (1H, dd, *J* = 8.1, 6.4 Hz, H4), 6.35 (1H, s, H2), 7.62 (2H, d, *J* = 8.5 Hz, Ar-C*H*), 7.87 (2H, d, *J* = 8.5, Ar-C*H*), 10.01 (1H, s, C*H*O); δ_C (100.6 MHz, $CDCl_3$): 22.9 (C6), 33.2 (C7), 58.6 (C5), 71.8 (C4), 86.4 (C2), 126.6, 129.8 (Ar-*C*H), 136.4, 145.3 (Ar-C), 178.3 (C8), 191.8 (*C*HO); *m/z* (ESI^+) 254 ($[M+Na]^+$, 50 %); HRMS (ESI^+); $C_{13}H_{13}NO_3NNa$ $[M+Na]^+$; found 254.07888, requires 254.07876.

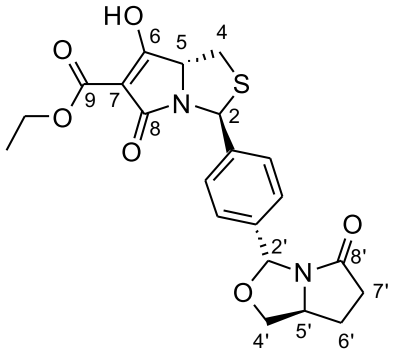
(-)-Ethyl (2*S*,5*R*)-6-hydroxy-8-oxo-2-(4-((2’*R*,5’*S*)-5-oxotetrahydro-1*H*,3*H*-pyrrolo[1,2-*c*]oxazol-2-yl)phenyl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxylate 34a



Thiazolidine obtained from the condensation of L-cysteine methyl ester hydrochloride and aldehyde **33** following the general procedure . Yield (1.54 g, 30 %); colourless oil; 1:1 *cis* and *trans* diastereomers; R_f = 0.24 (EtOA/petrol 3:1); ν_{max}/cm^{-1} (neat) 1704 (C=O), 1734 (C=O), 3305 (N-H); δ_H (400 MHz, $CDCl_3$) *cis* diastereomer: 1.63 - 1.99 (1H, m, H6), 2.28 - 2.41 (1H, m, H6), 2.44 - 2.59 (1H, m, H7), 2.71 - 2.92 (1H, m, H7), 3.02 - 3.18 (1H, m, $H4_A$), 3.29 - 3.51 (2H, m, $H4_B$ + H4'), 3.72 (3H, s, CO_2CH_3), 3.95 (1H, app t, *J* = 7.8 Hz, H5), 4.03 - 4.23 (2H, m, H5' + H4'), 5.51 (1H, s, H2), 6.26 (1H, s, H2'), 7.34 - 7.51 (4H, m, Ar-C*H*); *trans* diastereomer: 1.63 - 1.99 (1H, m, H6), 2.28 - 2.41 (1H, m, H6), 2.44 - 2.59 (1H, m, H7), 2.71 - 2.92 (1H, m, H7), 3.02 - 3.18 (1H, m, $H4_A$), 3.29 - 3.51 (2H, m, $H4_B$ + H4'), 3.72 (3H, s, CO_2CH_3), 4.03 - 4.23 (3H, m, H5 + H5' + H4'), 5.78 (1H, s, H2), 6.28 (1H, s, H2'), 7.34 - 7.51 (4H, m, Ar-C*H*); δ_C (100.6 MHz, $CDCl_3$) *cis* diastereomer: 23.0 (C6'), 33.2 (C7'), 39.1 (C4), 53.3 (CO_2CH_3), 58.6 (C5'), 65.4 (C5), 71.5 (C4'), 72.1 (C2), 86.6 (C2'), 126.2, 127.4 (Ar-*C*H), 138.4, 139.3 (Ar-C), 171.4 (*C*O_2CH_3), 178.0 (C8); *trans* diastereomer: 23.0 (C6'), 33.2 (C7'), 38.0 (C4), 52.2 (CO_2CH_3), 58.6 (C5'), 64.1 (C5), 70.3 (C4'), 71.5 (C2), 86.6 (C2'), 125.9, 126.9 (Ar-*C*H), 138.4, 141.6 (Ar-*C*), 172.1 (*C*O_2CH_3), 178.0 (C8); *m/z* (ESI^+) 349 ($[M+H]^+$, 100 %); HRMS (ESI^+); $C_{17}H_{21}O_4N_2S$ $[M+H]^+$; found 349.12180, requires 349.12165.

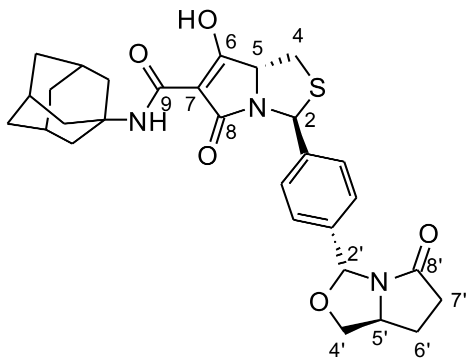


N-Acylthiazolidine obtained following the general procedure for *N*-acylation. Yield (0.67 g, 60 %); white foam; R_f = 0.16 (EtOAc/petrol 3:1); $[\alpha]_D^{25}$ = -258.0 (*c* = 1.02, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1660 (C=O), 1698 (C=O), 1738 (C=O); δ_H (400 MHz, $CDCl_3$) a mixture of two conformers: 1.21 (3H, t, *J* = 7.2 Hz, OCH_2CH_3 major conformer), 1.28 (3H, t, *J* = 7.2 Hz, OCH_2CH_3 minor conformer), 1.88 - 2.01 (1H, m, H6'), 2.33 - 2.44 (1H, m, H6'), 2.47 - 2.61 (1H, m, H7'), 2.73 - 2.87 (1H, m, H7'), 3.03 - 3.53 (5H, m, $H4_A$ + $H4_B$ + $H2''_A$ + $H2''_B$ + H4'), 3.78 (3H, s, CO_2CH_3 major conformer), 3.83 (3H, s, CO_2CH_3 minor conformer), 4.05 - 4.27 (4H, m, OCH_2CH_3 + H5' + H4'), 5.19 (1H, app d, *J* = 5.4 Hz, H5 minor conformer), 5.27 (1H, app d, *J* = 6.4 Hz, H5 major conformer), 6.18 (1H, s, H2 major conformer), 6.30 (1H, s, H2 minor conformer), 6.26 (1H, s, H2' major conformer), 6.28 (1H, s, H2' minor conformer), 7.20 (2H, d, *J* = 8.3 Hz, Ar-C*H* major conformer), 7.25 (2H, d, *J* = 8.3 Hz, Ar-C*H* minor conformer), 7.38 (2H, d, *J* = 8.3 Hz, Ar-C*H* minor conformer), 7.46 (2H, d, *J* = 8.3 Hz, Ar-C*H* major conformer); δ_C (100.6 MHz, $CDCl_3$) a mixture of two conformers: 13.9, 14.0 (OCH_2CH_3), 22.8, 23.0 (C6'), 30.9, 31.9 (C4), 33.3 (C7'), 42.4, 43.3 (C2″), 52.7, 53.4 (CO_2CH_3), 58.5, 58.8 (C5'), 61.4, 61.7 (OCH_2CH_3), 63.9, 64.2 (C5), 64.7, 65.4 (C2), 71.5, 71.8 (C4'), 86.6, 86.7 (C2'), 124.8, 125.0, 126.5, 126.9 (Ar-C*H*), 139.3, 139.4, 142.1, 142.3 (Ar-C), 164.5, 165.2 (C1″), 166.2, 167.1 (C3″), 169.3, 170.2 (*C*O_2CH_3), 177.9, 178.0 (C8); *m/z* (ESI^+) 485 ($[M+Na]^+$ 100 %); HRMS (ESI^+); $C_{22}H_{26}O_7N_2NaS$ $[M+Na]^+$; found 485.13478, requires 485.13529.



Tetramate **34a** was obtained following the general procedure for Dieckmann cyclisation. Yield (0.39 g, 70 %); white solid, mp >250 °C; R_f = 0.30 (EtOAc/MeOH 4:1); $[\alpha]_D^{25}$ = -104.8 (*c* = 0.15, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1681 (C=O), 1691 (C=O), 1712 (C=O); δ_H (400 MHz, CD_2Cl_2): 1.36 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.87 - 1.98 (1H, m, H6'), 2.36 (1H, dddd, *J* = 13.5, 10.0, 7.6, 3.7 Hz, H6'), 2.49 (1H, ddd, *J* = 17.3, 10.0, 3.7 Hz, H7'), 2.71 - 2.83 (1H, m, H7'), 3.01 (1H, dd, *J* = 11.1, 8.2 Hz, $H4_A$), 3.28 (1H, dd, *J* = 11.1, 7.2 Hz, $H4_B$), 3.46 (1H, app t, *J* = 8.1 Hz, H4'), 4.08 - 4.16 (1H, m, H5'), 4.21 (1H, dd, *J* = 8.1, 6.2 Hz, H4'), 4.37 (2H, q, *J* = 7.1 Hz, OCH_2CH_3), 4.78 (1H, app t, *J* = 7.6 Hz, H5), 6.23 (1H, s, H2'), 6.27 (1H, s, H2), 7.43, 7.44 (4H, ABq, J_{AB} = 8.8 Hz, Ar-C*H*); δ_C (100.6 MHz, CD_2Cl_2): 14.5 (OCH_2CH_3), 23.5 (C6'), 33.3 (C4), 33.9 (C7'), 59.4 (C5'), 62.2 (OCH_2CH_3), 62.6 (C2), 66.0 (C5), 72.3 (C4'), 87.3 (C2'), 126.8, 126.9 16.0 (Ar-C*H*), 139.7, 141.4 (Ar-C), 167.4 (C8), 178.6 (C8'), 186.5 (C6); *m/z* (ESI^-) 429 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{21}H_{21}O_6N_2S$ $[M-H]^-$; found 429.11295, requires 429.11258.

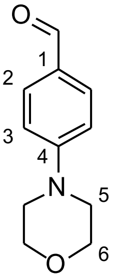
(-)-(2*S*,5*R*)-7-(Adamantylaminocarbonyl)-1-aza-2-(4-((2'*R*, 5'*S*)-1'-aza-3'-oxa-8'-oxo-bicyclo[3.3.0]octan-2'-yl)phenyl)-6-hydroxy-8-oxo-3-thiabicyclo[3.3.0]oct-6-ene, 34b



Carboxamide tetramate **34b** was obtained by aminolysis of **34a** with 1-adamantylamine according to the general procedure for the synthesis of carboxamides with THF/toluene as solvent. Yield (44 mg, 50 %); white foam, mp 152 °C; R_f= 0.47 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -121.8 (*c* = 0.13, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1625 (C=C), 1648 (C=O), 1691 (C=O), 3306 (N-H); δ_H (400 MHz, DMSO-d_6): 1.63 (6H, Adamantyl-CH_2), 1.87 - 1.98 (7H, m, Adamantyl-CH_2 + H6'), 2.04 (3H, Adamantyl-C*H*), 2.23 - 2.32 (1H, m, H6'), 2.42 (1H, ddd, *J* = 17.2, 10.1, 4.0 Hz, H7'), 2.72 (1H, ddd, *J* = 17.2, 10.0, 8.8 Hz, H7'), 3.01 (1H, dd, *J* = 10.9, 8.4 Hz, $H4_A$), 3.28 (1H, dd, *J* = 11.0, 7.1 Hz, $H4_B$), 3.44 (1H, app t, *J* = 7.6 Hz, H4'), 4.08 - 4.21 (2H, m, H4' + H5'), 4.90 (1H, app br. t, *J* = 7.2 Hz, H5), 6.07 (1H, s, H2'), 6.14 (1H, s, H2), 7.36 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 7.45 (2H, d, *J* = 8.3 Hz, Ar-C*H*), 7.69 (1H, br. s., NH/OH); δ_C (100.6 MHz, DMSO-d_6): 22.0 (C6'), 28.8

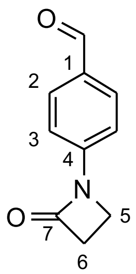
(Adamantyl-*C*H), 32.0 (C4), 32.8 (C7'), 35.8 (Adamantyl-*C*H$_2$), 41.2 (Adamantyl-*C*H$_2$), 51.2 (Adamantyl-C), 58.6 (C5'), 61.3 (C2), 67.1 (C5), 71.0 (C4'), 86.3 (C2'), 126.2, 126.3 (Ar-C*H*), 138.9, 141.5 (Ar-C), 163.3 (C9), 173.4 (C8), 178.0 (C8'); *m/z* (ESI$^-$) 534 ([M-H]$^-$, 20 %); HRMS (ESI$^-$); $C_{29}H_{32}N_3O_5S$ [M-H]$^-$; found 534.2078, requires 534.20682.

4-Morpholinobenzaldehyde, 35b



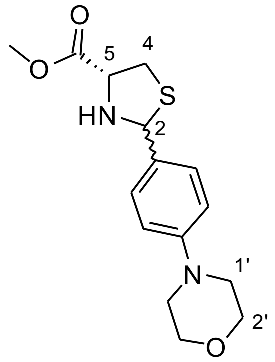
4-Bromobenzaldehyde (1.8 g, 9.72 mmol, 1.0 eq), $Pd_2(dba)_3$ (0.13 g, 0.15 mmol, 1.5 mol %), RuPhos (0.14 g, 0.29 mmol, 3 mol %), Cs_2CO_3 (4.43 g, 13.6 mmol, 1.4 eq) and *tert*-butanol (40 mL) were placed in a sealed round-bottomed flask and degassed with N_2. Morpholine (2 eq) was added via syringe and heated to reflux for 2 h. The reaction mixture was cooled to rt, diluted with EtOAc and filtered through a Celite plug. The filtrate was concentrated *in vacuo* and the residue was purified by silica gel flash column chromatography (eluent: EtOAc/petrol) to obtain **35a**. Yield (1.17 g, 63 %); yellow crystalline solid, mp 70 °C; R_f = 0.26 (EtOAc/petrol 1:3); ν_{max}/cm^{-1} (neat) 1682 (C=O); δ_H (400 MHz, $CDCl_3$) 3.33 - 3.39 (4H, m, H5), 3.84 - 3.90 (4H, m, H6), 6.93 (2H, d, *J* = 8.8 Hz, H3), 7.79 (2H, d, *J* = 8.8 Hz, H2), 9.81 (1H, s, C*H*O); δ_C (100.6 MHz, $CDCl_3$): 47.1 (C5), 66.4 (C6), 113.3 (C3), 127.5 (C1), 131.7 (C2), 155.0 (C4), 190.4 (*C*HO); *m/z* (ESI$^+$) 192 ([M+H]$^+$, 50 %); HRMS (ESI$^+$); $C_{11}H_{14}O_2N$ [M+H]$^+$; found 192.10154, requires 192.10191.

4-(2-oxoazetidin-1-yl)benzaldehyde, 35c

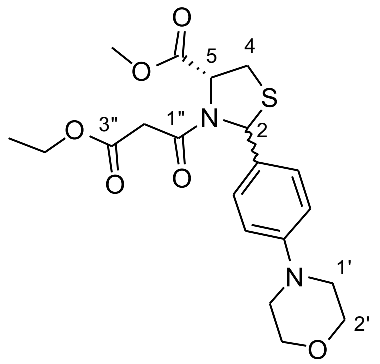


The synthesis of **35c** is according to a modified literature procedure. [10] 4-Bromobenzaldehyde (1.6 g, 8.76 mmol, 1.0 eq), 2-azetidinone (0.75 g, 10.5 mmol, 1.2 eq), $Pd_2(dba)_3$ (0.16 g, 0.18 mmol, 2 mol %), XantPhos (0.30 g, 0.53 mmol, 6 mol %), Cs_2CO_3 (4.0 g, 12.3 mmol, 1.4 eq) and 1,4-dioxane (40 mL) were placed in a sealed round-bottomed flask and degassed with N_2. The reaction mixture was heated to reflux for 20 h. The reaction mixture was cooled to rt, diluted with EtOAc and filtered through a Celite plug. The filtrate was concentrated *in vacuo* and the residue was purified by silica gel flash column chromatography (eluent: EtOAc/petrol) to obtain **35c**. Yield (0.92 g, 60 %); yellow solid; mp 108 °C; R_f = 0.28 (EtOAc/petrol 1:2); ν_{max}/cm^{-1} (neat) 1690 (C=O), 1747 (C=O); δ_H (400 MHz, $CDCl_3$) 3.20 (2H, t, *J* = 4.7 Hz, H5), 3.72 (2H, t, *J* = 4.7 Hz, H6), 7.48 (2H, d, *J* = 8.6 Hz, H3), 7.87 (2H, d, *J* = 8.6 Hz, H2), 9.92 (1H, s, C*H*O); δ_C (125.8 MHz, $CDCl_3$): 36.6 (C5), 38.4 (C6), 116.2 (C3), 131.3 (C2), 132.0 (C1), 143.2 (C4), 164.9 (C7), 190.8 (*C*HO); *m/z* (ESI$^+$) 176 ([M+H]$^+$, 38 %); HRMS (ESI$^+$); $C_{10}H_{10}O_2N$ [M+H]$^+$; found 176.07069, requires 176.07061.

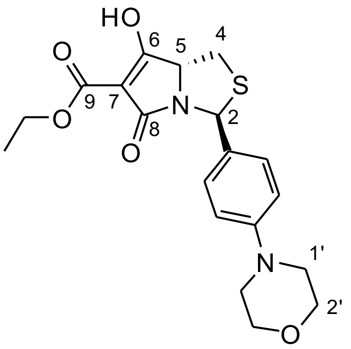
(-)-Ethyl (2*S*,5*R*)-6-Hydroxy-2-(4-morpholinophenyl)-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxylate 36a



Thiazolidine was obtained from the condensation of L-cysteine methyl ester hydrochloride and aldehyde **232/35b** following the general procedure. Yield (1.46 g, 78 %); yellow oil; 2.2:1 *cis* and *trans* diastereomers; R_f = 0.29 (EtOAc/petrol 1:1); ν_{max}/cm^{-1} (neat) 1737 (C=O), 3303 (N-H); δ_H (400 MHz, $CDCl_3$) major isomer (*cis*): 2.61 (1H, app t, *J* = 12.2 Hz, NH), 3.11 (1H, dd, *J* = 10.3, 8.8 Hz, $H4_A$), 3.14 - 3.20 (4H, m, H1'), 3.46 (1H, dd, *J* = 10.3, 7.1 Hz, $H4_B$), 3.81 (3H, s, CO_2CH_3), 3.83 - 3.89 (4H, m, H2'), 3.93 - 4.02 (1H, m, H5), 5.52 (1H, d, *J* = 12.3 Hz, H2), 6.85 - 6.93 (2H, m, Ar-C*H*), 7.37 - 7.47 (2H, m, Ar-C*H*); minor isomer (*trans*): 2.75 (1H, br. s., NH), 3.14 - 3.20 (4H, m, H1'), 3.24 (1H, dd, *J* = 10.6, 5.5 Hz, $H4_A$), 3.40 (1H, dd, *J* = 10.6, 7.2 Hz, $H4_B$), 3.80 (3H, s, CO_2CH_3), 3.83 - 3.89 (4H, m, H2'), 4.25 (1H, app t, *J* = 6.0 Hz, H5), 5.76 (1H, s, H2), 6.85 - 6.93 (2H, m, Ar-C*H*), 7.37 - 7.47 (2H, m, Ar-C*H*); δ_C (100.6 MHz, $CDCl_3$): major isomer (*cis*): 39.3 (C4), 49.0 (C1'), 52.6 (CO_2CH_3), 65.5 (C5), 66.8 (C2'), 72.4 (C2), 115.4, 128.4 (Ar-C*H*), 129.0, 151.5 (Ar-C), 171.7 (CO_2CH_3); minor isomer (*trans*): 38.0 (C4), 49.0 (C1'), 52.5 (CO_2CH_3), 64.2 (C5), 66.8 (C2'), 70.7 (C2), 115.3, 127.9 (Ar-C*H*), 131.9, 151.0 (Ar-C), 172.3 (CO_2CH_3); *m/z* (ESI^+) 309 ($[M+H]^+$, 100%); HRMS (ESI^+); $C_{15}H_{21}N_2O_3S$ $[M+H]^+$; found 309.12665, requires 309.12674.

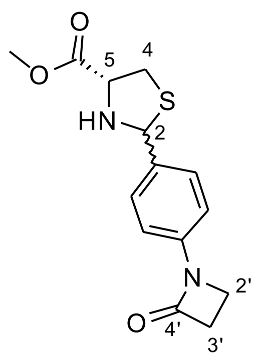


N-Acylthiazolidine was obtained following the general procedure. Yield (1.54 g, 78 %); yellow oil; 2.6:1 *cis* and *trans* diastereomers; R_f = 0.42 (*trans*), 0.51 (cis) (EtOAc/petrol 2:1); ν_{max}/cm^{-1} (neat) 1659 (C=O), 1738 (C=O); δ_H (400 MHz, $CDCl_3$): major isomer (*cis*, mixture of two conformers); 1.20 - 1.32 (3H, m, OCH_2CH_3), 3.06 - 3.57 (8H, m, $H4_A + H4_B + H2''_A + H2''_B$ + H1'), 3.81 - 3.88 (7H, m, CO_2CH_3 + H1'), 4.07 - 4.26 (2H, m, OCH_2CH_3), 5.07 (1H, app t, *J* = 6.5 Hz, H5), 6.08 (1H, s, H2 major conformer) and 6.30 (1H, s, H2 minor conformer), 6.81 - 6.93 (2H, m, Ar-C*H*), 7.40 - 7.45 (2H, m, Ar-C*H*, minor conformer), 7.55 (2H, d, *J* = 8.6 Hz, Ar-C*H*, major conformer); minor isomer (*trans*, mixture of two conformers); 1.20 - 1.32 (3H, m, OCH_2CH_3), 3.06 - 3.57 (4H, m, $H4_A + H4_B + H2''_A + H2''_B$), 3.81 - 3.88 (7H, m, CO_2CH_3 + H2'), 4.07 - 4.26 (2H, m, OCH_2CH_3), 5.18 (1H, app d, *J* = 5.6 Hz, H5 minor conformer), 5.26 - 5.31 (1H, m, H5 major conformer), 6.13 (1H, s, H2 major conformer), 6.29 (1H, s, H2 minor conformer), 6.81 - 6.93 (2H, m, Ar-C*H*), 7.11 (2H, d, *J* = 8.8 Hz, Ar-C*H* major conformer), 7.19 (2H, d, *J* = 8.8 Hz, Ar-C*H* minor conformer); δ_C (100.6 MHz, $CDCl_3$) major isomer (*cis*, mixture of two conformers): 13.9 (OCH_2CH_3), 31.9, 33.5 (C4), 41.9, 43.2 (C2″), 48.5, 49.0 (C1'), 52.5, 53.3 (CO_2CH_3), 61.3, 61.5 (OCH_2CH_3), 63.8, 64.0 (C5), 66.0, 66.6 (C2), 66.6 (C2'), 115.3, 115.4, 127.4, 128.2 (Ar-*C*H), 130.0, 151.1 (Ar-C), 165.4 (C1″), 166.7 (C3″), 170.1 (*C*O_2CH_3); minor isomer (*trans*, mixture of two conformers): 13.9 (OCH_2*C*H_3), 30.8, 33.6 (C4), 42.2, 42.8 (C2″), 48.5, 48.8 (C1'), 52.6, 52.9 (CO_2*C*H_3), 61.2, 61.3 (O*C*H_2CH_3), 63.5, 64.3 (C5), 64.7, 65.3 (C2), 66.6 (C2'), 114.9, 115.5, 125.6, 125.8 (Ar-*C*H), 132.2, 151.0 (Ar-C), 165.3 (C1″), 166.3 (C3″), 169.4 (*C*O_2CH_3); *m/z* (ESI^+) 423 ($[M+H]^+$, 100%); HRMS (ESI^+); $C_{20}H_{27}N_2O_6S$ $[M+H]^+$; found 423.15772, requires 423.15843.

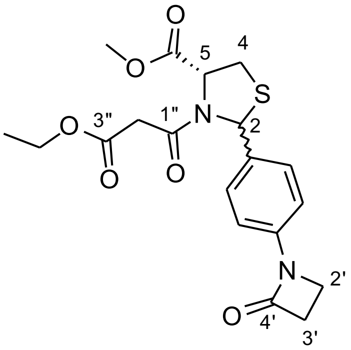


Tetramate **36a** was obtained following the general procedure for Dieckmann cyclisation. Yield (0.24 g, 22 %); brown oil; R_f = 0.42 (EtOAc/MeOH 84:16); $[\alpha]_D^{25}$ = -88.2 (*c* = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1611 (C=C), 1652 (C=O), 1688 (C=O); δ_H (500 MHz, CD_2Cl_2): 1.37 (3H, t, *J* = 7.1 Hz, OCH_2CH_3), 2.99 (1H, dd, *J* = 11.1, 8.3 Hz, $H4_A$), 3.14 (4H, br. t, *J* = 4.7 Hz, H1'), 3.28 (1H, dd, *J* = 11.1, 7.0 Hz, $H4_B$), 3.82 (4H, br. t, *J* = 4.7 Hz, H2'), 4.37 (2H, q, *J* = 7.1 Hz, OCH_2CH_3), 4.79 (1H, app t, *J* = 7.7 Hz, H5), 6.21 (1H, s, H2), 6.89 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.35 (2H, d, *J* = 8.6 Hz, Ar-C*H*); δ_C (125.8 MHz, CD_2Cl_2): 14.5 (OCH_2*C*H_3), 33.3 (C4), 49.7 (C1'), 62.2 (O*C*H_2CH_3), 62.6 (C2), 65.9 (C5), 67.3 (C2'), 99.8 (C7), 115.9, 127.8 (Ar-*C*H), 131.9, 151.8 (Ar-C), 167.6 (C9), 168.9 (C8), 186.5 (C6); *m/z* (ESI^-) 389 ($[M-H]^-$, 87 %); HRMS (ESI^+); $C_{19}H_{23}N_2O_5S$ $[M+H]^+$; found 391.13205, requires 391.13222.

(-)-Ethyl (2*S*,5*R*)-6-hydroxy-2-(4-(2-oxoazetidin-1-yl)phenyl)-8-oxo-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxylate 36b

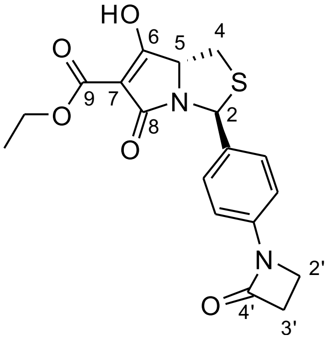


Thiazolidine was obtained from condensation of L-cysteine methyl ester hydrochloride and aldehyde **35c** following the general procedure. Yield (0.87 g, 58 %); white solid; 1.7:1 *cis* and *trans* diastereomers; R_f = 0.23 (EtOAc/petrol 1:1); ν_{max}/cm^{-1} (neat) 1738 (C=O), 3300 (N-H); δ_H (500 MHz, $CDCl_3$) major isomer (*cis*): 2.61 (1H, br. s, NH), 3.06 - 3.17 (3H, m, $H4_A$, H2'), 3.47 (1H, dd, *J* = 10.4, 7.1 Hz, $H4_B$), 3.61 - 3.66 (2H, m, H3'), 3.82 (3H, s, CO_2CH_3), 3.99 (1H, app t, *J* = 7.9 Hz, H5), 5.53 (1H, s, H2), 7.36 (2H, d, *J* = 8.6 Hz, Ar-C*H*), 7.50 (2H, d, *J* = 8.6 Hz, Ar-C*H*); minor isomer (*trans*): 2.81 (1H, br. s., NH), 3.06 - 3.17 (2H, m, H2'), 3.22 (1H, dd, *J* = 10.6, 5.7 Hz, $H4_A$), 3.40 (1H, dd, *J* = 10.6, 7.2 Hz, $H4_B$), 3.61 - 3.66 (2H, m, H3'), 3.81 (3H, s, CO_2CH_3), 4.21 (1H, app t, *J* = 6.5 Hz, H5), 5.79 (1H, s, H2), 7.33 (2H, d, *J* = 8.5 Hz, Ar-C*H*), 7.47 (2H, d, *J* = 8.5 Hz, Ar-C*H*); δ_C (125.8 MHz, $CDCl_3$): major isomer (*cis*): 36.2 (C2'), 38.1 (C1'), 39.3 (C4), 52.6 (CO_2*C*H_3), 65.5 (C5), 72.2 (C2), 116.3, 128.4 (Ar-*C*H), 133.4, 138.7 (Ar-C), 164.5 (C4'), 171.6 (*C*O_2CH_3); minor isomer (*trans*): 36.2 (C2'), 38.1 (C1'), 38.1 (C4), 52.6 (CO_2*C*H_3), 64.2 (C5), 70.4 (C2), 116.1, 127.9 (Ar-*C*H), 136.4, 138.1 (Ar-C), 164.4 (C4'), 172.2 (CO_2CH_3); *m/z* (ESI$^+$) 293 ([M+H]$^+$, 100%); HRMS (ESI$^+$); $C_{14}H_{17}N_2O_3S$ [M+H]$^+$; found 293.09541, requires 293.09544.



N-Acylthiazolidine was obtained following the general procedure for *N*-acylation. Yield (0.97 g, 81 %); colourless oil; 1.1:1 *cis* and *trans* diastereomers; R_f = 0.23 (*trans*), 0.31 (*cis*) (EtOAc/petrol 2:1); ν_{max}/cm^{-1} (neat) 1659 (C=O), 1734 (C=O); δ_H (400 MHz, $CDCl_3$): major isomer (*cis*, mixture of two conformers); 1.20 - 1.31 (3H, m, OCH_2CH_3), 3.06 - 3.67 (8H, m, H4$_A$ + H4$_B$ + H2″$_A$ + H2″$_B$ + H2' + H3'), 3.81 (3H, m, CO_2CH_3 minor conformer), 3.84 (3H, m, CO_2CH_3 major conformer), 4.07 - 4.24 (2H, m, OCH_2CH_3), 5.07 (1H, app t, *J* = 6.7 Hz, H5), 6.11 (1H, s, H2 major conformer), 6.30 (1H, s, H2 minor conformer), 7.28 - 7.33 (2H, m, Ar-C*H* minor conformer), 7.34 - 7.41 (2H, m, Ar-C*H* major conformer), 7.50 (2H, d, *J* = 8.6 Hz, Ar-C*H* minor conformer), 7.65 (2H, d, *J* = 8.6 Hz, Ar-C*H* major conformer); minor isomer (*trans*, mixture of two conformers); 1.20 - 1.31 (3H, m, OCH_2CH_3), 3.06 - 3.67 (8H, m, H4$_A$ + H4$_B$ + H2″$_A$ + H2″$_B$ + H2' + H3'), 3.79 (3H, m, CO_2CH_3 major conformer), 3.85 (3H, m, CO_2CH_3 minor conformer), 4.07 - 4.24 (2H, m, OCH_2CH_3), 5.20 (1H, app d, *J* = 5.4 Hz, H5 minor conformer), 5.27 - 5.32 (1H, m, H5 major conformer), 6.15 (1H, s, H2 major conformer), 6.28 (1H, s, H2 minor conformer), 7.20 (2H, *J* = 8.3 Hz, Ar-C*H* major conformer, 7.24 - 7.28 (2H, m, Ar-C*H* minor conformer), 7.28 - 7.33 (2H, m, Ar-C*H* minor conformer), 7.34 - 7.41 (2H, m, Ar-C*H* major conformer); δ_C (125.8 MHz, $CDCl_3$) major isomer (*cis*, mixture of two conformers): 14.0, 14.1 (OCH_2CH_3), 32.1, 33.8 (C4), 36.2, 36.3 (C2'), 38.0, 38.1 (C3'), 42.1, 43.0 (C2″), 52.8, 53.2 (CO_2CH_3), 61.6, 61.7 (OCH_2CH_3), 63.7, 64.6 (C5), 66.0, 66.8 (C2), 115.9, 116.6, 127.5, 128.4 (Ar-*C*H), 134.0, 134.8, 138.7, 138.7 (Ar-C), 164.3, 164.5 (C4'), 165.2, 165.5 (C1″), 166.7, 167.1 (C3″), 170.2, 171.6 (CO_2CH_3); minor isomer (*trans*, mixture of two conformers): 14.0, 14.1 (OCH_2CH_3), 31.0, 33.1 (C4), 36.1, 36.3 (C2'), 38.0, 38.1 (C3'), 42.4, 43.3 (C2″), 52.8, 53.4 (CO_2CH_3), 61.5, 61.8 (OCH_2CH_3), 64.0, 64.2 (C5), 64.7, 65.4 (C2), 116.3, 116.8, 125.7, 125.9 (Ar-*C*H), 137.0, 137.6, 138.6, 138.7 (Ar-C), 164.3, 164.5 (C4'), 164.9, 165.3 (C1″), 166.3, 167.2 (C3″), 169.4, 170.2 (CO_2CH_3); *m/z* (ESI$^+$) 407 ([M+H]$^+$, 85 %); HRMS (ESI$^+$); $C_{19}H_{23}N_2O_6S$ [M+H]$^+$; found 407.12658, requires 407.12713.

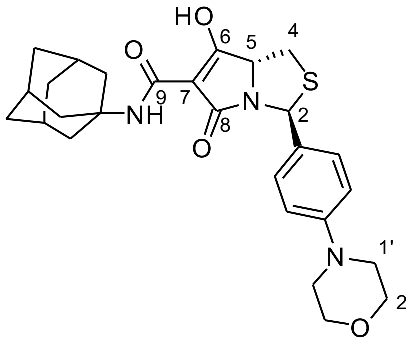
Tetramate **36b** was obtained following the general procedure for Dieckmann cyclisation. Yield



(0.23 g, 30 %); yellow solid, mp 124-126 °C; R_f = 0.32 (EtOAc/MeOH 84:16); $[\alpha]_D^{25}$ = -182.5 (*c* = 0.15, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1610 (C=C), 1658 (C=O), 1739 (C=O, br with shoulder towards lower wavenumber); δ_H (500 MHz, CD_2Cl_2): 1.37 (3H, t, *J* = 7.1 Hz, OCH_2CH_3), 3.01 (1H, dd, *J* = 11.2, 8.2 Hz, H4$_A$), 3.08 (2H, t, *J* = 4.6 Hz, H2'), 3.29 (1H, dd, *J* = 11.2, 7.1 Hz, H4$_B$), 3.61 (4H, t, *J* = 4.6 Hz, H3'), 4.38 (2H, q, *J* = 7.1

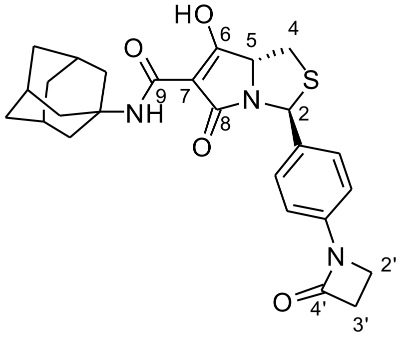
Hz, OCH_2CH_3), 4.79 (1H, app t, J = 7.5 Hz, H5), 6.24 (1H, s, H2), 7.33 (2H, d, J = 8.5 Hz, Ar-C*H*), 7.43 (2H, d, J = 8.5 Hz, Ar-C*H*); δ_C (125.8 MHz, CD_2Cl_2): 14.5 (OCH_2CH_3), 33.3 (C4), 36.8 (C2'), 38.7 (C3'), 62.3 (OCH_2CH_3), 62.6 (C2), 65.9 (C5), 99.7 (C7), 116.6, 127.8 (Ar-*C*H), 136.1, 139.1 (Ar-C), 165.0 (C4'), 167.6 (C9), 169.0 (C8), 186.6 (C6); *m/z* (ESI^-) 373 ($[M-H]^-$, 100 %); HRMS (ESI^-); $C_{19}H_{23}N_2O_5S$ $[M-H]^-$; found 373.08701, requires 373.08637.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-6-hydroxy-8-oxo-2-(4-morpholinophenyl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 37a



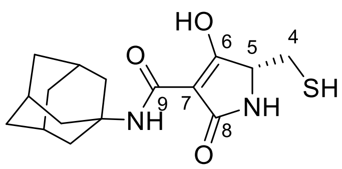
Carboxamide tetramate **37a** was obtained by aminolysis of **36a** with 1-adamantylamine according to the general procedure for the synthesis of carboxamides with THF/toluene as solvent. Yield (0.23 g, 25 %); brown solid, mp 120-124 °C; 3:1 AB:CD tautomers; R_f = 0.70 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = - 144.1 (c = 0.20, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1613 (C=C), 1647 (C=O), 1685 (C=O), 3310 (N-H/O-H); δ_H (500 MHz, CD_2Cl_2) 1.69 - 1.81 (6H, m, Adamantyl-CH_2), 2.06 - 2.20 (9H, m, Adamantyl-CH_2, Adamantyl-C*H*), 2.96 - 3.06 (1H, m, $H4_A$), 3.18 (4H, br. t, J = 4.7 Hz, H1'), 3.25 - 3.32 (1H, m, $H4_B$), 3.87 (4H, br. t, J = 4.5 Hz, H2'), 4.01 (2H, br. s, NH + OH AB), 4.47 (1H, app t, J = 7.9 Hz, H5 CD), 4.75 (1H, dd, J = 8.3, 7.2 Hz, H5 AB), 6.20 (1H, s, H2 AB), 6.28 (1H, s, H2 CD), 6.90 - 6.98 (2H, m, Ar-C*H*), 7.39 (2H, d, J = 8.7 Hz, Ar-C*H*), 7.93 (1H, br. s, NH/OH, CD); δ_C (125.8 MHz, CD_2Cl_2): 30.1 (Adamantyl-*C*H), 33.1 (C4 AB), 33.4 (C4 CD), 36.4 (Adamantyl-CH_2 CD), 36.6 (Adamantyl-CH_2 AB), 42.1 (Adamantyl-CH_2 AB), 42.2 (Adamantyl-CH_2 CD), 49.8 (C1'), 53.4 (Adamantyl-C AB), 54.9 (Adamantyl-C CD), 62.3 (C2 AB), 62.9 (C2 CD), 67.2 (C2'), 67.8 (C5 AB), 71.5 (C5 CD), 85.7 (C7 CD), 96.4 (C7 AB), 116.0, 127.9 (Ar-*C*H), 127.8, 151.6 (Ar-C), 166.6 (C9 AB), 167.2 (C9 CD), 172.7 (C8 AB), 178.9 (C8 CD), 187.9 (C6 AB), 191.6 (C6 CD); *m/z* (ESI^+) 496 ($[M+H]^+$, 75 %); HRMS (ESI^+); $C_{27}H_{34}O_4N_3S$ $[M+H]^+$; found 496.22607, requires 496.22645.

(-)-(2*S*,5*R*)-*N*-(Adamantan-1-yl)-6-hydroxy-8-oxo-2-(4-(2-oxoazetidin-1-yl)phenyl)-5,8-dihydro-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxamide 37b



Carboxamide tetramate **37b** was obtained by aminolysis of **36b** with 1-adamantylamine according to the general procedure 6for the synthesis of carboxamides with THF/toluene as solvent. Yield (47 mg, 30 %); brown solid, mp 148-150 °C; 3:1 AB:CD tautomers; R_f = 0.62 (EtOAc/MeOH 9:1); $[\alpha]_D^{25}$ = -240.0 (c = 0.19, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1622 (C=C), 1647 (C=O), 1687 (C=O), 1745 (C=O), 3315 (N-H/O-H); δ_H (500 MHz, CD_2Cl_2) 1.65 - 1.76 (6H, m, Adamantyl-C*H*$_2$), 2.02 - 2.16 (9H, m, Adamantyl-C*H*$_2$ + Adamantyl-C*H*), 2.96 - 3.03 (1H, m, H4$_A$), 3.08 (2H, t, *J* = 4.5 Hz, H2'), 3.20 - 3.28 (1H, m, H4$_B$), 3.60 (2H, t, *J* = 4.5 Hz, H3'), 4.42 (1H, app t, *J* = 7.7 Hz, H5 CD), 4.69 (1H, app t, *J* = 7.7 Hz, H5 AB), 4.98 (2H, br. s, NH + OH), 6.19 (1H, s, H2 AB), 6.28 (1H, s, H2 CD), 7.30 - 7.34 (2H, m, Ar-C*H*), 7.40 - 7.44 (2H, m, Ar-C*H*); δ_C (125.8 MHz, CD_2Cl_2): 30.1 (Adamantyl-*C*H), 33.1 (C4 AB), 33.4 (C4 CD), 36.4 (Adamantyl-*C*H$_2$ CD), 36.6 (Adamantyl-*C*H$_2$ AB), 36.8 (C2'), 38.7 (C3'), 42.1 (Adamantyl-*C*H$_2$ AB), 42.2 (Adamantyl-*C*H$_2$ CD), 53.5 (Adamantyl-C AB), 55.0 (Adamantyl-C CD), 62.3 (C2 AB), 62.9 (C2 CD), 67.9 (C5 AB), 71.4 (C5 CD), 85.7 (C7 CD), 96.0 (C7 AB), 116.0, 127.8 (Ar-*C*H, AB), 116.0, 127.7 (Ar-*C*H CD), 136.3, 139.0 (Ar-C AB), 136.6, 138.9 (Ar-C CD), 165.0 (C4'), 166.6 (C9 AB), 167.2 (C9 CD), 172.9 (C8 AB), 179.0 (C8 CD), 188.3 (C6 AB), 191.6 (C6 CD); *m/z* (ESI$^-$) 478 ([M-H]$^-$, 25 %); HRMS (ESI$^-$); $C_{26}H_{28}O_4N_3S$ [M-H]$^-$; found 478.18107, requires 478.18060.

(-)-(*R*)-*N*-(Adamantan-1-yl)-6-hydroxy-5-(mercaptomethyl)-2-oxo-2,5-dihydro-1*H*-pyrrole-3-carboxamide, 38[11]



9a (84 mg, 0.20 mmol, 1 eq) was added to a solution of 2 % HCl in trifluoroethanol (3.3 mL). 1,3-Propanedithiol (0.082 mL, 0.82 mmol, 4 eq) was added to this solution and heated at 50 °C for 7 h. The reaction flask was cooled and solvents removed *in vacuo*. The crude residue was purified by silica gel flash column chromatography (eluent: EtOAc/ Methanol/1 % citric acid). The product isolated was dissolved in CH_2Cl_2 and washed with 5 % citric acid. The organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* to obtain **38**. Yield (46 mg, 70 %); yellow solid, mp 84 °C; 2.1:1 AB:CD tautomers; R_f = 0.068 (EtOAc/MeOH 4:1); $[\alpha]_D^{25}$ = -39.0 (*c* = 0.4, $CHCl_3$); ν_{max}/cm^{-1} (neat) 1620 (C=C), 1650 (C=O), 1682 (C=O), 3294 (N-H/O-H); δ_H (400 MHz, $CDCl_3$): 1.66 - 1.76 (6H, m, Adamantyl-C*H*$_2$), 2.04 - 2.09 (6H, m, Adamantyl-C*H*$_2$), 2.12 (3H, Adamantyl-C*H*), 2.59 - 2.74 (1H, m, H4$_A$), 2.99 - 3.12 (1H, m, Hz, H4$_B$), 3.92 (1H, dd, *J* = 8.0, 3.6 Hz, H5 CD), 4.19 (1H, dd, *J* = 7.5, 3.6 Hz, H5 AB), 5.78 (1H, br. s., NH/OH/SH), 6.78 (2H, br. s., NH/OH/SH), 7.44 (1H, br. s., NH/OH/SH AB), 7.80 (1H, br. s., NH/OH/SH CD); δ_C (125.8 MHz, $CDCl_3$): 26.2 (C4 AB), 26.5 (C4 CD), 29.3 (Adamantyl-*C*H), 35.9 (Adamantyl-*C*H$_2$ CD), 36.1 (Adamantyl-*C*H$_2$ AB), 41.6 (Adamantyl-*C*H$_2$ AB), 41.7 (Adamantyl-*C*H$_2$ CD), 52.8 (Adamantyl-C AB), 54.2 (Adamantyl-C CD), 59.0 (C5 AB), 63.1 (C5 CD), 85.2 (C7 CD), 96.4 (C7 AB), 166.0 (C9 AB), 166.9 (C9 CD), 171.4 (C8 AB), 177.4 (C8 CD), 186.6 (C6 AB), 191.1 (C6 CD); *m/z* (ESI$^-$) 321 ([M-H]$^-$, 100%); HRMS (ESI$^+$); $C_{16}H_{23}N_2O_3S$ [M+H]$^+$; found 323.14259, requires 323.14239.

Table 1 (SI). Minimum energies for tautomers A-D of tetramates **9a-9u (**calculated using MM2 method of Chem3D version 15.**)**.

Tetramate	Energy (kcal/mol)			
	A	B	C	D
9a	16.0804	35.7000	22.6440	34.9795
9b	16.7081	36.3741	24.2766	35.7101
9d	16.0565	35.7281	22.4102	35.0636
9e	15.4563	34.8543	32.5050	34.1261
9f	18.9332	39.8570	26.8331	39.3211
9g	24.2832	43.2331	31.7748	42.6276
9h	2.4254	27.1156	8.8662	26.4327
9i	2.3728	27.1569	8.6121	26.5199
9j	4.0037	26.4523	17.2149	25.8123
9k	6.9345	31.2785	13.0366	30.7538
9l	1.8602	22.5116	8.4903	21.9308
9m	1.8348	22.5793	8.2859	22.0365
9n	0.2847	20.3548	10.2257	19.7059
9q	0.7964	25.5440	7.0510	26.2300
9r	17.6489	42.2161	23.9121	41.5968
9s	25.2820	49.0382	32.6301	48.4710
9t	7.6126	28.1248	13.8858	27.4426
9u	3.0170	23.7384	9.6134	23.0097
9v	7.5538	27.9121	13.7305	27.3651

Table 2 (SI): INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY for 9a

Compound 9a	Metal (ng/g)									
	Li7 (LR)	B11 (LR)	Na23 (LR)	Mg24 (LR)	Rb85 (LR)	Sr88 (LR)	Y89 (LR)	Zr90 (LR)	Nb93 (LR)	Mo97 (LR)
Acid washed (Avg)	Below DL	Below DL	18,754.99	15,863.64	Below DL	296.03	Below DL	2959.60	Below DL	651.56
Metal-chelated (Avg)	Below DL	Below DL	3,385,564.10	7,039,607.83	Below DL	9988.28	624.16	1957.61	Below DL	96.28
	Ru101 (LR)	Rh103 (LR)	Pd105 (LR)	Ag107 (LR)	Cd111 (LR)	In115 (LR)	Sn118 (LR)	Sb121 (LR)	Te128 (LR)	Cs133 (LR)
Acid washed (Avg)	Below DL	Below DL	880.38	44.72	Below DL	Below DL	3968.59	43.22	Below DL	Below DL
Metal-chelated (Avg)	Below DL	Below DL	1597.71	Below DL	Below DL	Below DL	86.46	Below DL	Below DL	808.77
	Ba138 (LR)	La139 (LR)	Ce140 (LR)	Pr141 (LR)	Nd143 (LR)	Sm147 (LR)	Eu151 (LR)	Gd157 (LR)	Tb159 (LR)	Dy161 (LR)
Acid washed (Avg)	35.92	Below DL	5.64	Below DL	6.04	Below DL	Below DL	Below DL	Below DL	Below DL
Metal-chelated (Avg)	1303.43	1092.41	449.46	249.85	962.36	186.46	29.76	151.34	24.32	138.35

Compound 9a	Metal (ng/g)									
	Ho165 (LR)	Er166 (LR)	Tm169 (LR)	Yb172 (LR)	Lu175 (LR)	Hf178 (LR)	Ta181 (LR)	W184 (LR)	Re187 (LR)	Os190 (LR)
Acid washed (Avg)	Below DL	Below DL	Below DL	Below DL	Below DL	29.32	Below DL	52.44	Below DL	Below DL
Metal-chelated (Avg)	24.57	68.19	6.66	62.81	10.93	15.05	Below DL	Below DL	Below DL	Below DL
	Ir193 (LR)	Pt195 (LR)	Au197 (LR)	Hg200 (LR)	Tl205 (LR)	Pb208 (LR)	Bi209 (LR)	Th232 (LR)	U238 (LR)	Al27 (MR)
Acid washed (Avg)	2067.40	Below DL	Below DL	10547.90	Below DL	133.01	Below DL	259.39	154.64	11,435.19
Metal-chelated (Avg)	Below DL	Below DL	Below DL	7829.05	Below DL	207.83	24.95	265.58	210.46	17,885.66
	Si28 (MR)	P31 (MR)	S32 (MR)	Ca44 (MR)	Sc45 (MR)	Ti47 (MR)	V51 (MR)	Cr52 (MR)	Mn55 (MR)	Fe56 (MR)
Acid washed (Avg)	Below DL	11,675.02	77,109,829.82	24,763.37	Below DL	608.87	1062.15	1945.30	Below DL	34,756.06
Metal-chelated (Avg)	Below DL	12,375.36	84,926,735.11	20,483,701.53	Below DL	1101.77	1006.78	1282.95	3088.25	38,189.35

Compound 9a	Metal (ng/g)									
	Co59 (MR)	Ni60 (MR)	Cu63 (MR)	Zn66 (MR)	Ga69 (MR)	Ge72 (MR)	K39 (HR)	Ge72 (HR)	As75 (HR)	Se78 (HR)
Acid washed (Avg)	291.10	2627.81	2586.13	9955.93	Below DL	24.65	Below DL	45.65	Below DL	12,234.66
Metal-chelated (Avg)	220.79	2784.16	2916.85	71,155.08	Below DL	Below DL	26,703.53	Below DL	38.46	21,974.08

DL = Detection Limit

MODE OF ACTION STUDIES[12, 13]

E. COLI GYRASE SUPERCOILING AND *M .TUBERCULOSIS* GYRASE SUPERCOILING INHIBITION ASSAYS

Assay Set Up

In all assays, the activity of the enzyme was determined prior to the testing of the compounds and 1 U defined as the amount of enzyme required to just fully supercoil or decatenate the substrate. Compounds were tested at 100 µM. Final DMSO concentration in the assays was 1% (v/v). Assays were carried out based on methods described previously.[12, 13]

E. coli gyrase supercoiling

1 U of DNA gyrase was incubated with 0.5 µg of relaxed pBR322 DNA in a 30 µl reaction at 37°C for 30 minutes under the following conditions: 35 mM Tris.HCl (pH 7.5), 24 mM KCl, 4 mM $MgCl_2$, 2 mM DTT, 1.8 mM Spermidine, 1 mM ATP, 6.5% (w/v) glycerol and 0.1 mg/ml BSA. Each reaction was stopped by the addition of 30 µl chloroform/iso-amyl alcohol (26:1) and 20 µl Stop Dye (40% sucrose, 100 mM Tris.HCl (pH 7.5), 10 mM EDTA, 0.5 µg/ml bromophenol blue), before being loaded on a 1.0% TAE (Tris.acetate 0.04 mM, EDTA 0.002 mM) gel run at 80V for 2 h.

M. tuberculosis gyrase supercoiling

1 U of *M. tuberculosis* gyrase (final concentration in assay 13nM) was incubated with 0.5 µg of relaxed pBR322 DNA in a 30 µl reaction at 37 °C for 30 minutes under the following conditions: 50 mM HEPES. KOH (pH 7.9), 6 mM magnesium acetate, 4 mM DTT, 1 mM ATP, 100 mM potassium glutamate, 2 mM spermidine and 0.05 mg/ml albumin. Each reaction was stopped by the addition of 30 µl chloroform/iso-amyl alcohol (26:1) and 20 µl Stop Dye and analysed as described above.

S.aureus topo IV decatenation

1 U of *S. aureus* topo IV was incubated with 200 ng kDNA DNA in a 30 µl reaction at 37 °C for 30 minutes under the following conditions: 50 mM Tris.HCl (7.5), 5 mM $MgCl_2$, 5 mM DTT, 1.5 mM ATP*,* 350 mM potassium glutamate and 0.05 mg/ml BSA.

Each reaction was stopped by the addition of 30 µl chloroform/iso-amyl alcohol (26:1) and 20 µl Stop Dye and analysed as described above.

Data acquisition and analysis

Bands were visualised by ethidium staining for 10 minutes, destained for 10 minutes in water and analysed by gel documentation equipment (Syngene, Cambridge, UK) and quantitated using

Syngene Gene Tools software. Raw gel data (fluorescent band volumes) collected from Syngene, GeneTools gel analysis software were converted to a % of the 100% control (the fully supercoiled or decatenated DNA band). These were analyzed using SigmaPlot Version 12.5 (2014).

Table 3 (SI). Results for enzyme inhibition of *E. coli* gyrase, *M. tuberculosis* gyrase and *S. aureus* topo IV supercoiling activity. CFX (ciprofloxacin) was used as a standard. No inhibition of *E. coli* gyrase supercoiling was observed. Average of two determinations.

Compound	*M. tuberculosis* gyrase supercoiling activity (%)	*S. aureus* topo IV decatenation activity (%)
Enzyme alone	100	100
DMSO	93.95	99.32
CFX	2.96	0.00
8a	107.85	102.53
8b	100.86	6.61
8d	104.64	92.36
8e	67.22	28.04
8f	94.94	65.86
8g	77.44	14.14
9a	26.70	16.39
9b	19.42	7.47
9d	12.87	12.40
9e	21.42	12.12
9f	26.66	10.36
9g	15.85	3.04
9h	20.74	12.88
9i	15.80	13.31
9j	18.06	10.38
9k	20.08	20.88
9l	14.29	7.72
9m	31.29	21.82
9n	13.26	5.47
9q	11.75	8.67
9r	7.77	9.34
9s	10.04	5.14
9w	52.07	19.00
9d’	7.19	51.23
9e’	81.84	105.70
14a	29.98	21.90
16	63.73	69.35
17	83.33	102.85
18	17.71	29.44
19	0	4.15

Table 4 (SI). IC_{50} values for *M. tuberculosis* gyrase and *S. aureus* topo IV inhibition (nd = not determined).

Compound Number	**IC_{50} (μM)**	
	***M. tuberculosis* gyrase supercoiling**	***S. aureus* topo IV decatenation**
CFX	29.6	4.11
9a	nd	3.8
9d	48.9	3.0
9i	54.1	1.22
9m	nd	61.0
9q	65.4	4.9
9r	60.3	10.3
9d'	78.0	nd
19	52.4	25.3

***E. coli* RNAP and *S. aureus* RNAP inhibition assays.**

Fluorescence-detected RNAP-inhibition assays were performed as in Zhang et al., 2014. Reaction mixtures contained (20 μl): 0-100 μM test compound, bacterial RNAP holoenzyme (75 nM E. coli RNAP holoenzyme or E. coli RNAP holoenzyme derivative or 75 nM Staphylococcus aureus RNAP core enzyme and 300 nM S. aureus σA; prepared as in Maffioli et al., 2017), 20 nM DNA fragment containing the bacteriophage T4 N25 promoter [positions -72 to +367; prepared by PCR from plasmid pARTaqN25-340-tR2 (Liu, 2007)], 100 μM ATP, 100 μM GTP, 100 μM UTP, and 100 μM CTP, in TB (50 mM Tris-HCl, pH 8.0, 100 mM KCl, 10 mM MgCl2, 1 mM DTT, 10 μg/ml bovine serum albumin, 5% methanol, and 5.5% glycerol). Reaction components other than DNA and NTPs were preincubated 10 min at 37°C. Reactions were carried out by addition of DNA and incubation 15 min at 37°C, followed by addition of NTPs and incubation 60 min at 37°C. DNA was removed by addition of 1 μl 5 mM CaCl2 and 2 U DNase I (Ambion, Grand Island, NY), followed by incubation 90 min at 37°C. RNA was quantified by addition of 100 μl Quant-iT RiboGreen RNA Reagent (Life Technologies, Grand Island, NY; 1:500 dilution in 10 mM Tris-HCl, pH 8.0, 1 mM EDTA), followed by incubation 10 min at 22°C, followed by measurement of fluorescence intensity (excitation wavelength = 485 nm and emission wavelength = 535 nm; GENios Pro microplate reader [Tecan, Männedorf, Switzerland]).

Table 5 (SI). IC_{50} (**µM**) values for *E. coli* RNAP and *S. aureus* RNAP inhibition.

Compound number	*E. coli* RNAP	*S. aureus* RNAP
9a	43	8.8
9h	61	5.9
9m	63	13.0

EVALUATION OF ANTIBACTERIAL ACTIVITY

Hole-plate antibacterial assay

The assessment of the antibiotic activiy of tetramic acids against *Staphylococcus aureus* DS267, a Gram-positive bacterium and *Escherichia coli* X580, a Gram-negative bacterium, was made using the hole plate method (diameter of well; 10 mm) with Cephalosporin C as a positive control.

Bioassay for drug candidates in the absence of serum albumin

The samples were prepared as 4 mg/mL solutions of 70 % DMSO in MeOH, with serial dilution to the desired concentrations where necessary. A 100 µL aliquot of each sample solution to be tested was loaded into 10 mm wells in agar plates and incubated overnight (18 h) at 37 °C. The assays were repeated in triplicates and the diameters of the resultant inhibition zones were measured (±1 mm) along two perpendicular axes and then averaged to obtain the zone of inhibition. A 'blank' was run with solvent alone, to ensure the solvent made no contribution to the zone of inhibition. The relative potency was estimated by reference to standards prepared with cephalosporin C.

Bioassay for drug candidates in the presence of serum albumin

The albumin binding assay for drug candidates were carried out, in the presence of human serum albumin (HSA) at 10 % the albumin concentration in human serum. A stock solution of 8 mg/mL of HSA was prepared by dissolving in H_2O. Solutions of the required concentration of compounds to be tested were prepared in 70 % DMSO in MeOH. A 50 µL aliquot of each sample solution was loaded into 10 mm wells in agar plates along with a 50 µL aliquot of an aqueous stock solution of HSA (8 mg/mL) and incubated overnight at 37 °C. The final concentration of HSA in the well was 4 mg/mL, which is 10 % of the physiological serum albumin concentration. The assays were repeated in triplicates and the diameters of the resultant inhibition zones were measured (±1 mm) along two perpendicular axes and then averaged to obtain the zone of inhibition. These data were compared with the bioactivity of each sample in the absence of HSA. The bactericidal effect of a given sample was compared with that of the Ceph C standard by determining the concentration of Ceph C required to confer the same zone of inhibition as the test compound. This is expressed as the 'relative potency' (rel. potency), where rel. potency = equivalent no. of moles of Ceph C/no. of moles of sample. The equivalent no. of moles of Ceph C for a given zone size was calculated from the calibration curves in Figures G.1-2.

Table 6 (SI). Antibacterial activity of tetramates against *S. aureus* determined by hole-plate method (na = not active).

Compound	Concentration (µg/mL)	Inhibition zone diameter (mm)	Relative potency
8a	4000	na	-
8b	4000	na	-
8d	4000	na	-
8e	4000	na	-
8f	4000	12	0.1
8g	4000	na	-
9a	1	19.3	980
9b	1	18	76
9c	1	19	91
9d	1	19.7	1100
9e	1	19.3	1100
9f	1	19.7	1200
9g	50	24.7	43
9h	2	18.3	450
9i	10	20	121
9j	50	12.7	8.6
9k	10	17	83
9l	25	20.7	48

9m	50	21	26
9n	100	14	4.9
9o	1	23	188
9q	25	19.7	46
9r	4000	23.3	0.6
9s	4000	18	0.2
9w	500	26	4.6
38	1000	19	0.7

Table 7 (SI). Antibacterial activity of tetramates against *E. coli* determined by hole-plate method (other tetramates were not active).

Compound	Concentration (μg/mL)	Inhibition zone diameter (mm)	Relative potency
38	4000	19.3	4.70×10^{-4}

Table 8 (SI). Antibacterial activity of tetramates against *S. aureus* compared in the presence/absence of HSA by hole-plate method.

Compound	Concentration (μg/mL)	HSA		Inhibition zone diameter (mm)
		with	without	
9a	1		√	19.3
	5	√		18.7
9b	10		√	22
	10	√		20
9c	5		√	21
	5	√		17
9d	1		√	19.7
	5	√		19.7
9e	1		√	19.3
	5	√		14
9f	1		√	19.7
	5	√		15.7
9g	50		√	24.7
	50	√		20.7
9h	2		√	18.3
	50	√		21
9i	10		√	20
	50	√		20
9j	50		√	12.7
	100	√		20 (H)
9k	10		√	17

	50	√		18
9l	25		√	20.7
	100	√		18
9m	50		√	21
	250	√		17.3
9n	100		√	14
	500	√		14.7
9o	100		√	30
	500	√		28
9r	25		√	19.7
	250	√		22
9r	4000		√	23.3
	4000	√		21.7
9s	4000		√	18
	4000	√		16.7
9w	500		√	26
	500	√		24.7
38	1000		√	19
	1000	√		18.7

Table 9 (SI). Antibacterial activity of tetramate **38** against *E.coli* compared in the presence/absence of HSA by hole-plate method.

Compound	**Concentration (µg/mL)**	**HSA**		**Inhibition zone diameter (mm)**
		with	**without**	
38	4000		√	19.3
	4000	√		18.7

Data from broth dilution assay to determine MICs

The extracts were tested in a primary 96 well plate-screening assay, according to SOP 0906. The substances were diluted in "MHB" for bacterial screening to a stock solution of 1000 µg/mL, serial diluted and overlaid with a microbe solution in a concentration of 10^4 CFU/ml. The plates were incubated for 24 h at 35°C. Assays were conducted with Gram-positive (Multi-drug resistant *Staphylococcus aureus (MRSA), Enterococcus faecalis, Streptococcus pneumoniae*) and Gram-negative (*Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae*) strains. Compounds tested were either only weakly active or not active against Gram-negative strains. Toxicity studies on some candidates were done on HaCat mammalian cell line. Data is given in Table 7, SI.

Table 10, SI. MICs of tetramates determined by broth dilution method (na = not active)

Compound	MIC (µg/mL)						Toxicity (µg/mL)
	Escherichia coli	*Pseudomonas aeruginosa*	*Klebsiella pneumoniae*	MRSA	*Enterococcus feacalis*	*Streptococcus pneumoniae*	
9a	na	na	na	0.98	0.98	0.98	1
9b	na	na	na	1.95	0.49	0.49	3
9d	na	na	na	1.95	0.49	0.49	5
9e	na	na	na	1.95	0.49	0.49	20
9f	na	na	na	1.95	0.49	0.98	15.6
9g	na	na	na	1.95	1.95	1.95	65
9h	na	na	na	7.81	0.49	0.98	16
9i	na	na	na	na	na	na	35
9j	na	na	na	na	na	na	6
9k	na	na	na	na	na	na	31
9l	na	na	na	1.95	0.49	1.95	16
9m	na	na	na	0.49	0.49	0.49	10
9n	na	na	na	31.25	0.98	31.25	31
9p	na	na	na	1.95	0.49	3.9	16
9q	na	na	na	na	na	na	250
9r	na	na	na	na	na	na	

Compound	MIC (µg/mL)						Toxicity (µg/mL)
	Escherichia coli	*Pseudomonas aeruginosa*	*Klebsiella pneumoniae*	MRSA	*Enterococcus feacalis*	*Streptococcus pneumoniae*	
9s	na	na	na	125	62.5	125	50
9t	na	na	-	0.49	0.49	-	-
9u	na	na	-	0.49	0.98	-	-
9v	250	250	250	na	125	125	16
9w	250	250	-	250	250	-	-
9x	na	na	-	na	-	-	-
9y	na	na	-	250	-	-	-
9z	250	250	-	0.49	0.49	-	-
9a’	na	-	-	na	-	-	-
9b’	na	-	-	na	-	-	-
9c’	na	-	-	na	-	na	-
9d’	na	na	na	na	na	na	200
9e’	na	na	na	na	na	na	125
9f’	250	-	-	125	-	250	-
9g’	na	-	-	3.91	-	0.98	-
14a	na	na	na	15.63	0.49	7.81	30
14b	na	na	na	3.91	3.91	3.91	1
14c	na	na	na	62.5	15.63	15.63	3.9
14d	na	na	-	0.49	0.49	-	-
14e	na	na	-	31.25	-	-	-

Compound	MIC (µg/mL)						Toxicity (µg/mL)
	Escherichia coli	***Pseudomonas aeruginosa***	***Klebsiella pneumoniae***	**MRSA**	***Enterococcus feacalis***	***Streptococcus pneumoniae***	
14f	na	na	-	1.95	-	-	-
14g	na	na	-	na	na	-	-
14h	na	na	-	0.49	0.49	-	-
14i	na	na	-	na	na	-	-
14j	na	-	-	na	na	-	-
14k	na	na	-	0.49	0.98	-	-
14l	na	na	na	na	na	na	150
16	na	na	na	15.63	1.95	7.81	125
17	na	na	na	na	na	na	250
18a	na	na	na	na	na	na	50
18b	250	250	-	na	na	-	-
19	na	na	na	na	na	na	31
21	na	na	na	na	na	na	31
23	250	250	-	0.49	0.49	-	-
26b	250	250	-	0.49	0.49	-	-
28a	na	250	-	0.49	0.49	-	-
28b	na	250	-	31.25	31.25	-	-
28c	250	250	-	na	na	-	-
29a	na	na	-	31.25	-	-	-
220/30	na	na	-	1.95	1.95	-	-

Compound	MIC (µg/mL)						Toxicity (µg/mL)
	Escherichia coli	*Pseudomonas aeruginosa*	*Klebsiella pneumoniae*	MRSA	*Enterococcus feacalis*	*Streptococcus pneumoniae*	
29b	na	na	-	250	-	-	-
34b	na	na	-	3.91	-	-	-
36a	na	-	-	250	-	-	-
36b	na	-	-	na	-	-	-
37a	na	-	-	0.98	1.95	-	-
37b	na	-	-	1.95	3.91	-	-

Table 11: Physicochemical and structure properties of some tetramate natural products.

Tetramate	MW	clogP	$clogD_{7.4}$	PSA	MSA	%PSA	H-bond donor	H-bond acceptor
Reutericyclin	349	5.21	1.68	74.7	578.3	12.9	1	4
Epicoccarine A	386	4.69	2.36	86.6	604.5	14.4	3	4
Vancoresmycin	1344	2.55	0.31	422.6	2174.4	19.4	17	22
Virgineone	750	4.82	1.57	223.3	1191.7	18.7	8	12
Virgineone aglycone	588	6.59	3.34	144.2	983.4	14.7	5	7
Equisetin	376	3.03	0.44	77.8	589.0	13.2	2	4
Altersetin	428	4.14	0.82	86.6	657.7	13.2	3	4
Zopfiellamide A	446	3.15	-1.84	115.1	658.2	17.5	3	6
Zopfiellamide B	460	3.60	-1.35	115.1	688.2	16.7	3	6
Signermycin	390	3.22	0.81	86.6	614.1	14.1	3	4
Kibdelomycin	940	3.67	0.73	258.5	1282.5	20.2	6	12
Amycolamycin	940	3.67	0.73	258.5	1280.0	20.2	6	12
Streptolydigin	601	2.09	-0.01	147.2	867.1	17.0	3	9
Tirandamycin A	417	1.61	-0.47	114.5	578.65	19.8	2	7
Tirandamycin B	433	0.56	-1.52	134.7	588.6	22.9	3	8

Table 12. Physicochemical and structure properties of the tetramate library.

Compound	MW	clogP	clogD7.4	PSA	MSA	%PSA	H-bond donor count	H-bond acceptor count
9a	410.5	2.57	0.28	69.64	542.39	12.83947	2	3
b	489.4	3.33	0.7	69.64	562.99	12.36967	2	3
9c	489.4	1.64	0.7	69.64	563.54	12.36	2	3
9d	428.5	2.71	0.12	69.64	549.61	12.6708	2	4
9e	455.5	2.51	-0.15	112.78	580.84	19.41671	2	5
9f	463	3.31	0.47	69.64	565.09	12.3237	2	4
9g	400.5	1.63	-0.98	82.78	515.13	16.06973	2	3
9h	434.6	4.61	3.96	69.64	587.77	11.84817	2	3
9i	452.5	4.75	3.82	69.64	594.51	11.71385	2	4
9j	479.6	4.55	3.57	112.78	626.99	17.98753	2	5
9k	487	5.35	4.16	69.64	611.07	11.3964	2	4
9l	400.9	3.61	2.77	69.64	482.25	14.44064	2	3
9m	418.9	3.75	2.64	69.64	489.6	14.22386	2	4
9n	445.9	3.35	2.39	112.78	520.6	21.66347	2	5

Compound	MW	clogP	clogD7.4	PSA	MSA	%PSA	H-bond donor count	H-bond acceptor count
9o	476.9	4.38	2.99	69.64	563.54	12.36	2	4
9p	476.9	4.36	2.99	69.64	503.69	13.82	2	4
9q	516.4	3.15	2.17	69.64	503.62	13.82	2	5
9r	427.5	1.44	0.46	95.25	541.85	17.57867	2	5
9s	439.3	1.2	-1.55	78.87	488.94	16.13081	2	4
9t	358.46	2.27	-0.01	69.64	482.97	14.41912	2	3
9u	410.9	3.02	0.12	69.64	505.13	13.78655	2	4
9v	352.4	2.49	1.9	69.64	434	16.04608	2	3
9x	430.5	1.33	0.29	103.78	528.49	19.63708	2	5
9y	499.6	2.4	1.36	107.02	645.64	16.5758	2	5
9z	501.6	1.33	0.29	116.25	631.18	18.41788	2	6
9d’	698.7	1.68	0.91	193.3	909.07	21.26349	2	9
9e’	530.6	-0.08	-0.85	169.02	651.78	25.93206	6	9
9w	410.1	2.13	-1.66	106.94	503.73	21.22963	3	5
9a’	729.8	6.49	5.43	142.11	916.35	15.50827	3	7
9b’	507.6	2.62	1.58	129.8	619.13	20.9649	3	6
9c’	578.5	3.16	1.87	107.02	665.71	16.07607	2	5
9f’	396.9	2.29	-0.67	60.85	478.85	12.70753	1	4
9g’	515	5.05	2.14	60.85	678.38	8.969899	1	4
14a	476.6	3.27	0.86	82.78	623.28	13.28135	2	3
14b	514.6	3.92	1.63	86.71	679.05	12.76931	2	4
14c	558.7	4.2	1.91	88.1	747.73	11.78233	2	4

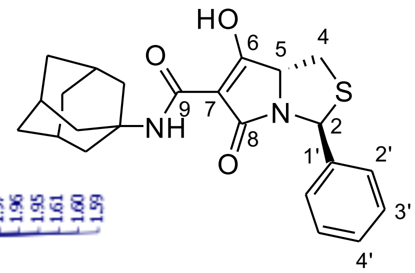
Compound	MW	clogP	clogD7.4	PSA	MSA	%PSA	H-bond donor count	H-bond acceptor count
14d	450.6	3.66	1.35	69.64	606.88	11.47509	2	3
14e	564.7	3.05	0.74	103.78	744.08	13.94743	2	5
14f	505.6	2.91	0.46	95.67	679.37	14.08216	2	4
14g	530.6	3.84	1.5	88.1	687.28	12.81865	2	5
14h	490.6	2.64	0.31	87.46	655.48	13.34289	2	4
14i	548.66	3.25	0.82	113.88	730.56	15.58804	2	7
14j	527.6	3.4	1.08	99.83	675.42	14.78043	2	5
14k	560.7	3.46	1.1	96.69	759.82	12.72538	2	5
14l	426.5	1.14	-1.37	92.01	547.43	16.80763	2	4
16	651.6	0.99	-2.52	190.5	865.53	22.00964	1	9
17	483.5	-0.78	-4.28	166.22	608.11	27.33387	5	9
26a	321.4	1.49	-2.01	87.07	400.5	21.74032	2	4
18a	756.8	1.76	-0.73	193.3	1018.15	18.98541	2	9
18b	756.7	1.32	-3.08	230.6	977.83	23.58283	2	11
19	588.7	-0.01	-2.49	169.02	759.97	22.24035	6	9
21	939.9	0.54	-2.96	287.86	1264.01	22.77355	1	14
23	665.7	1.02	-2.47	190.5	899.02	21.18974	1	9
26b	335.4	1.03	-2.47	87.07	432.12	20.1495	2	4
28a	426.5	2.26	-0.17	89.87	554.98	16.19338	3	4
28b	368.4	2.19	1.47	89.87	446.54	20.12586	3	4
28c	376.4	0.13	-2.41	99.1	480.67	20.61706	3	5
29a	512.6	2.39	-0.09	105.17	696.78	15.09372	2	5
30	478.6	3.47	0.99	78.87	642.1	12.28313	2	4

Compound	MW	clogP	clogD7.4	PSA	MSA	%PSA	H-bond donor count	H-bond acceptor count
29b	484.6	1.89	-4	116.17	628.51	18.4834	3	6
34b	535.7	2.13	-0.31	99.18	709.13	13.98615	2	5
36a	390.5	1.54	-1.81	79.31	525.28	15.09861	1	5
36b	374.4	0.83	-2.66	87.15	479	18.19415	1	4
37a	495.6	2.45	0.07	82.11	676.54	12.13675	2	5
37b	479.6	1.61	-0.83	89.95	630.41	14.26849	2	4

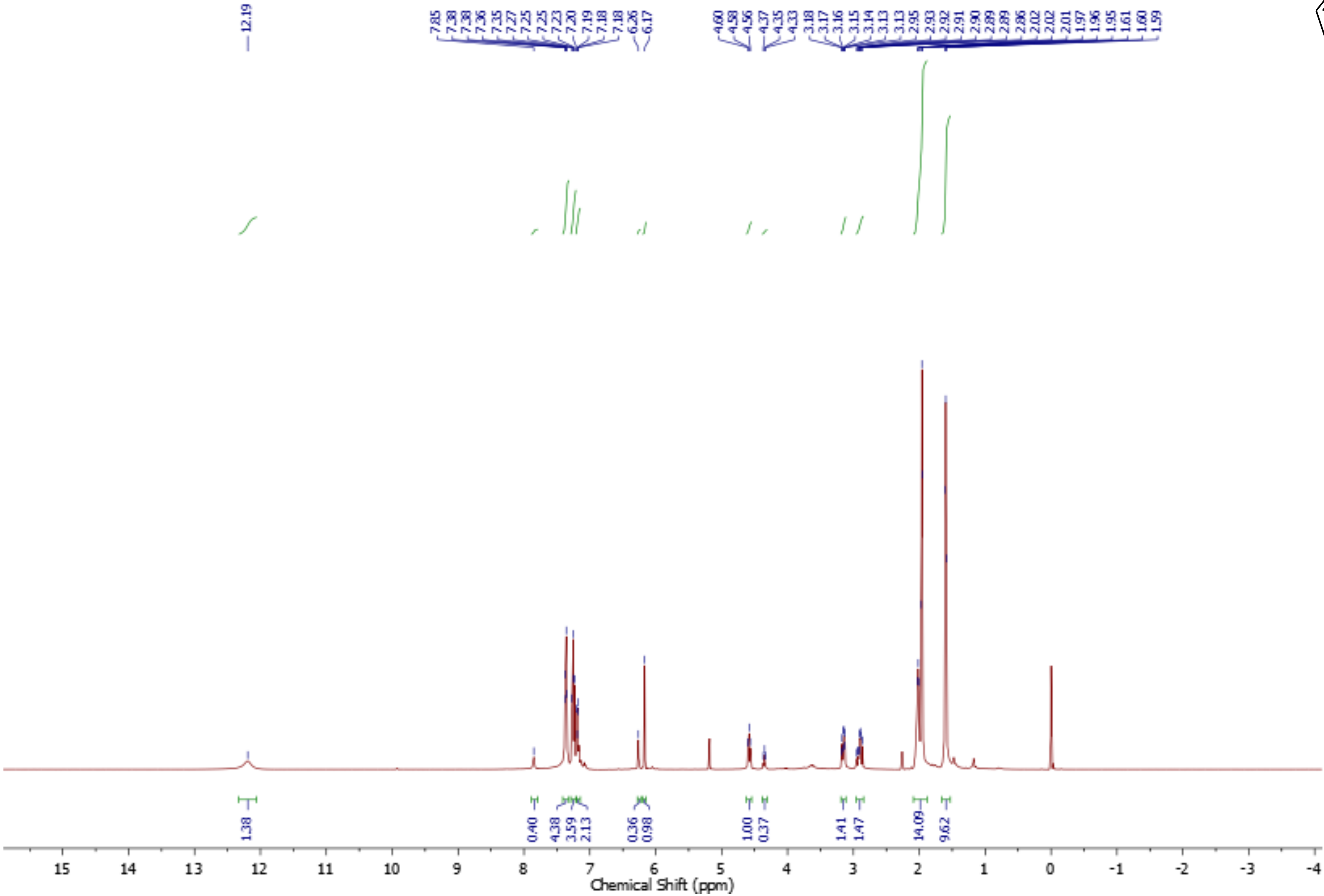
Physicochemical and structure properties calculated for the tetramate library are listed in Table J.1. Calculator Plugins were used for physicochemical and structure property prediction and calculation, Marvin (16.4.18.0), 2016 ChemAxon (http://www.chemaxon.com).

^{1}H and ^{13}C NMR Spectra

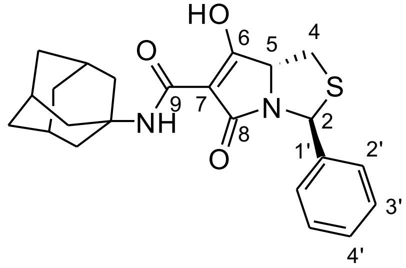
9a



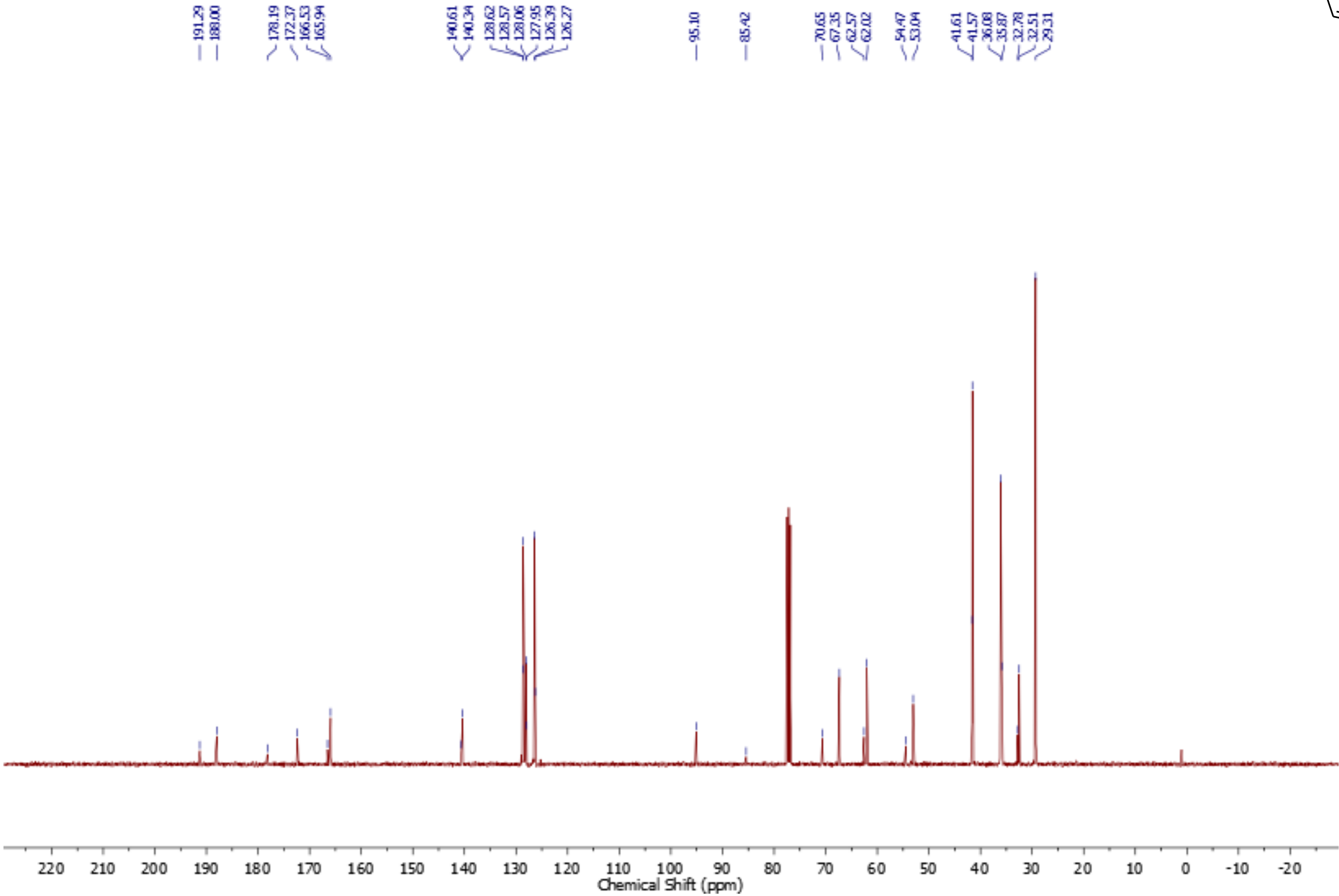
1H NMR (400 MHz, CDCl3)



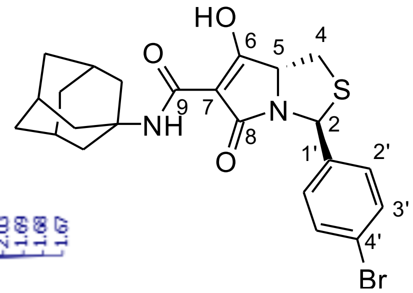
9a



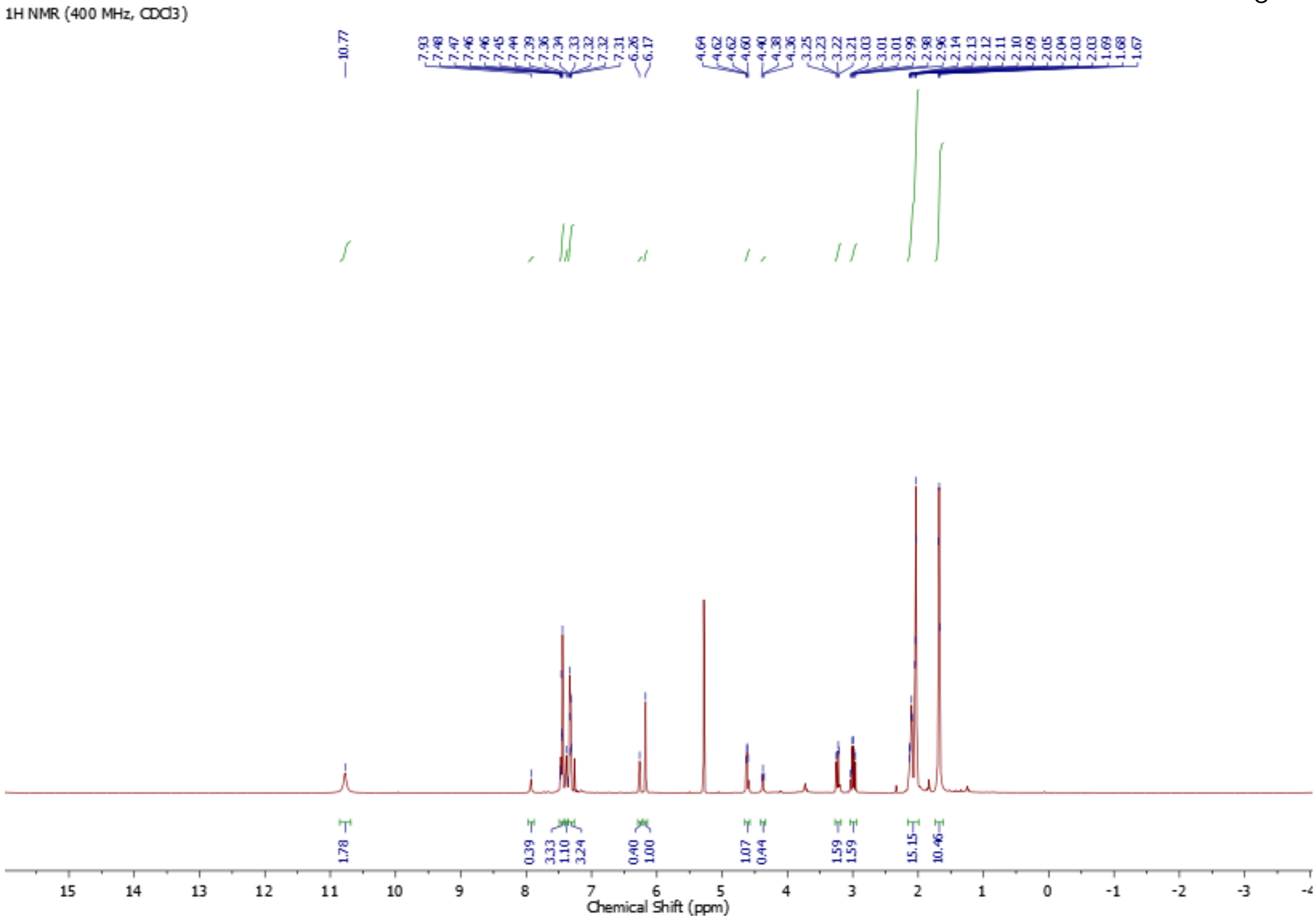
13C NMR (100.6 MHz, CDCl3)



9b

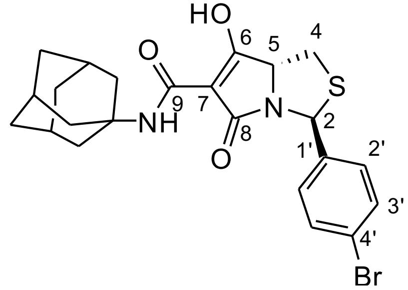


HO
O
6
5
4
S
9
7
NH
N
2
8
O
1'
2'
3'
4'
Br

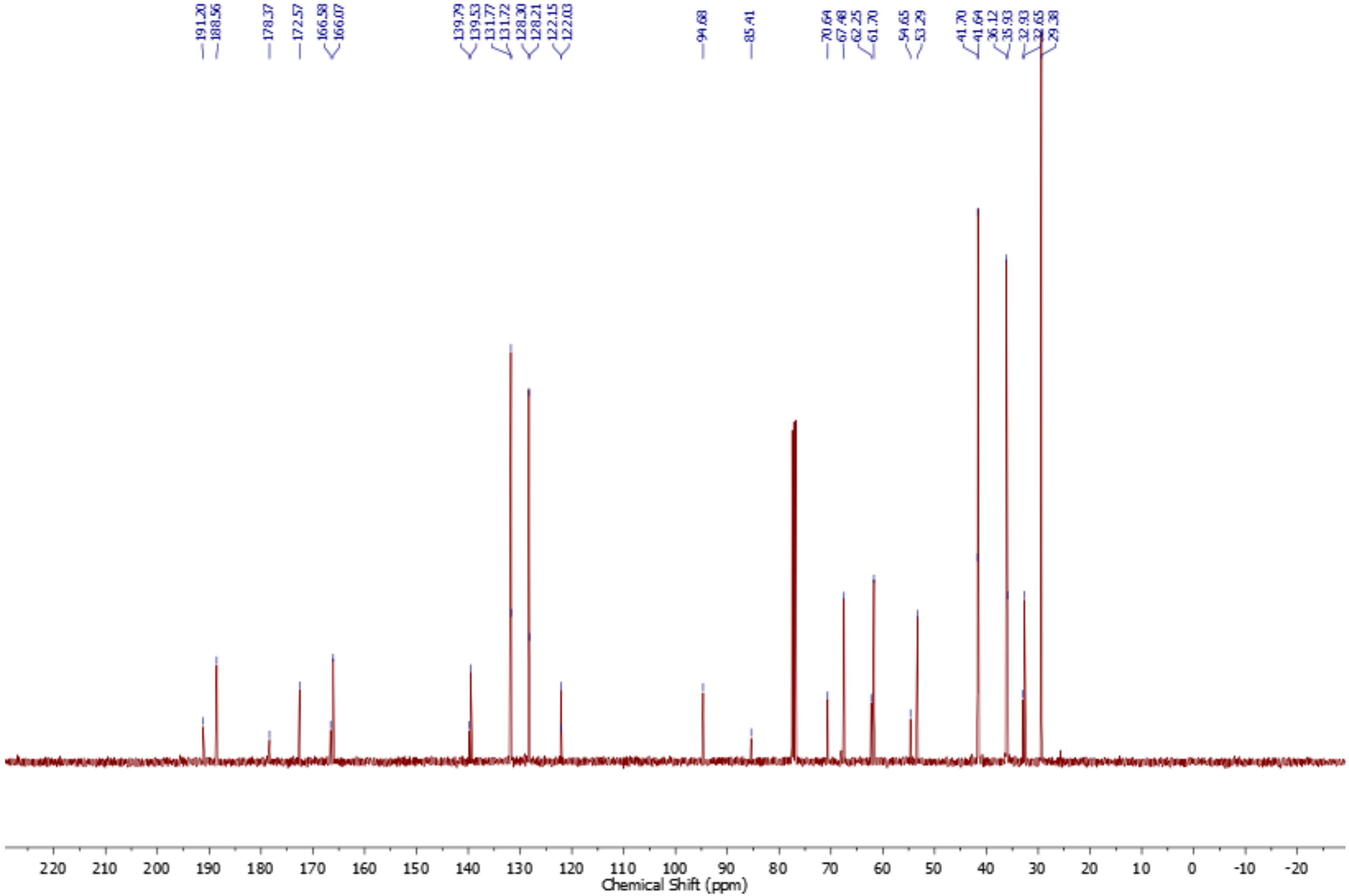


1H NMR (400 MHz, CDCl3)
10.77
7.93
7.48
7.47
7.46
7.46
7.45
7.44
7.39
7.36
7.34
7.33
7.32
7.32
7.31
6.26
6.17
4.64
4.62
4.62
4.60
4.40
4.38
4.36
3.25
3.23
3.22
3.21
3.03
3.01
3.01
2.99
2.98
2.96
2.14
2.13
2.12
2.11
2.10
2.09
2.05
2.04
2.03
2.03
1.69
1.68
1.67
1.78
0.39
3.33
1.10
3.24
0.40
1.00
1.07
0.44
1.59
1.59
15.15
10.46
Chemical Shift (ppm)

9b



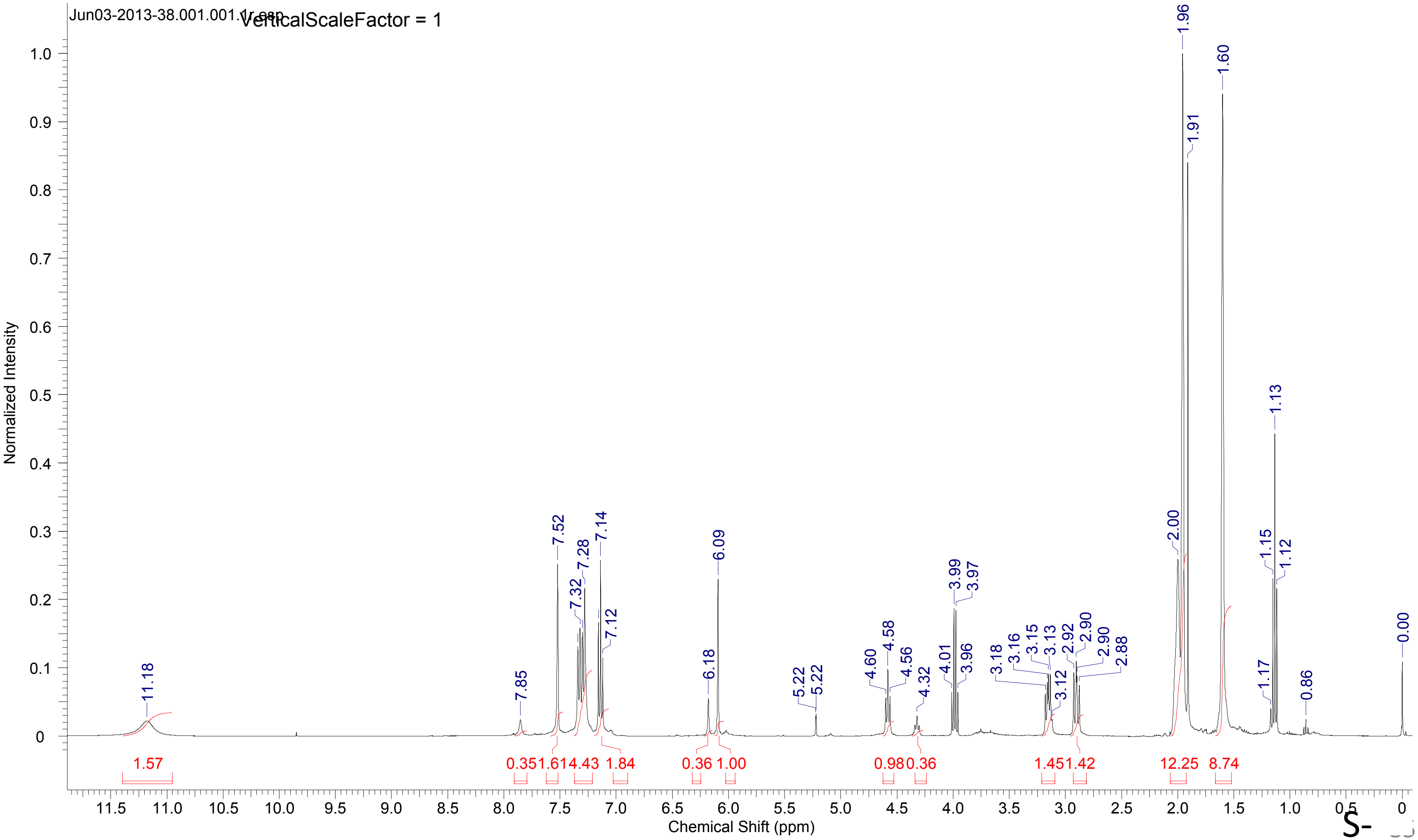
13C NMR (100.6 MHz, CDCl3)



9c

7/15/2013 5:42:41 PM

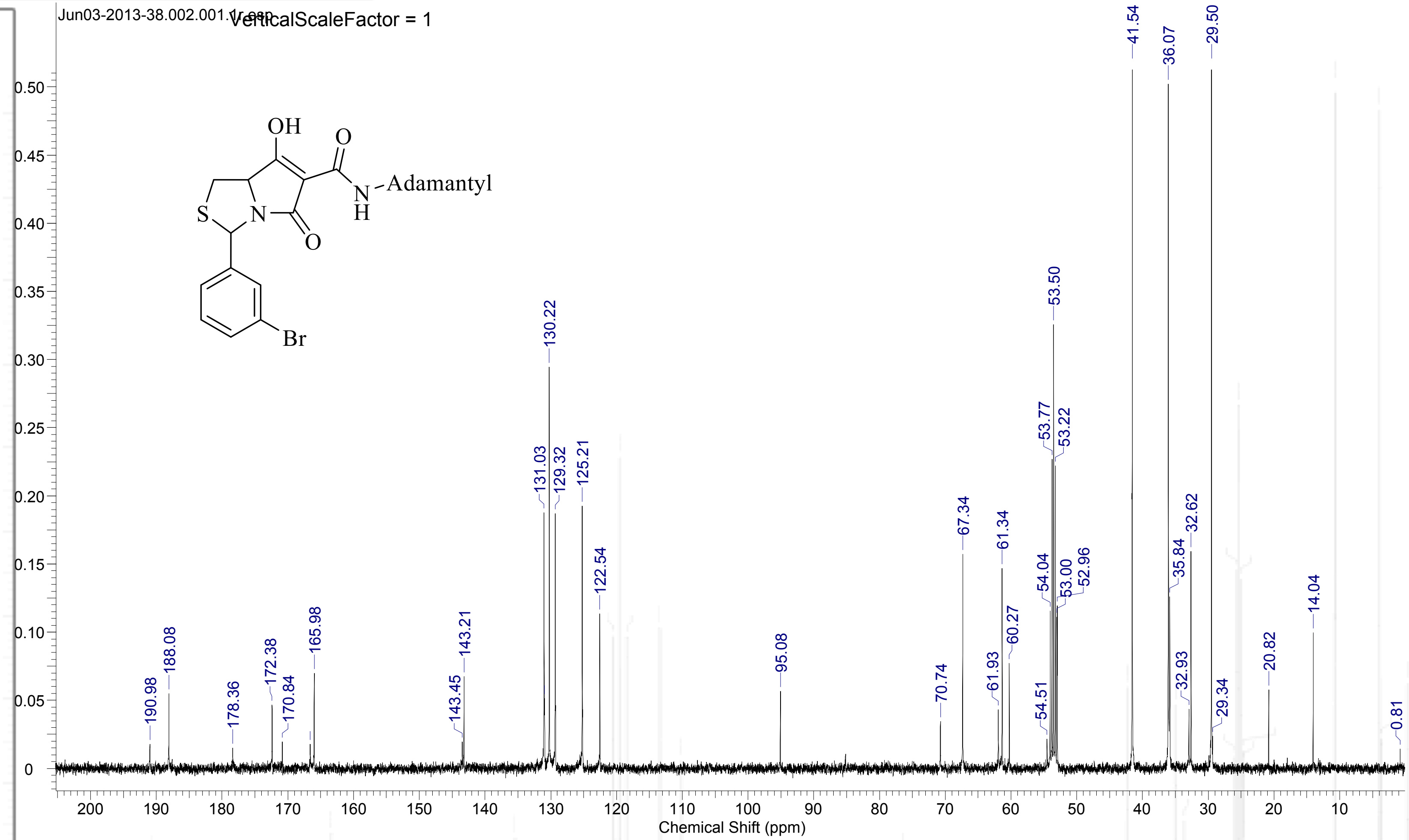
Acquisition Time (sec)	4.0894	***Comment***	Instrument AVN400 Chemist sarosh Group MGM SI-19 (R-1) AGAIN h1acq.crl CD2Cl2 {C:\NMR} mgmgrp 38		
Date	03 Jun 2013 17:40:32	***Date Stamp***	03 Jun 2013 17:40:32		
File Name	F:\mass+nmr record of lab work at oxf\SI-019\CORRECT SPECTRA\Jun03-2013-38\1\PDATA\1\1r				
Frequency (MHz)	400.25	***Nucleus***	1H	***Number of Transients***	16
Origin	avn400	***Original Points Count***	32768	***Owner***	dp-nmrgroup
Points Count	32768	***Pulse Sequence***	zg60	***Receiver Gain***	16.56
SW(cyclical) (Hz)	8012.82	***Solvent***	DICHLOROMETHANE-d2		
Spectrum Offset (Hz)	2345.3064	***Spectrum Type***	STANDARD	***Sweep Width (Hz)***	8012.58
Temperature (degree C)	21.735				



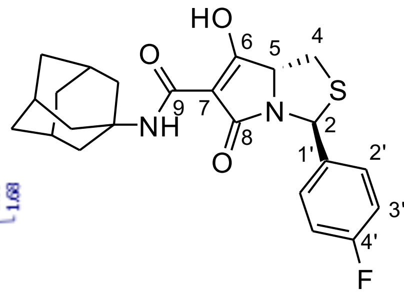
9c

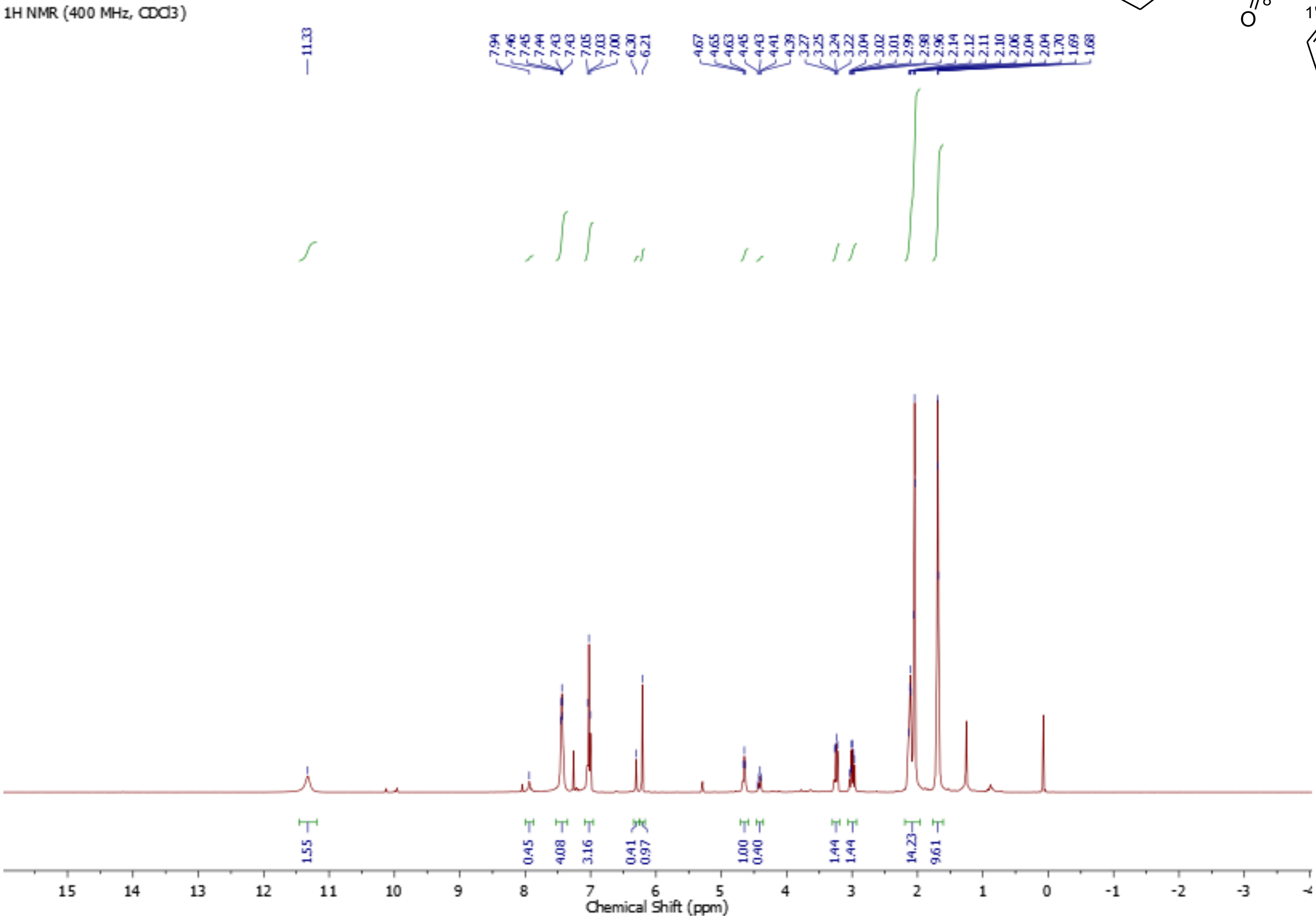
7/15/2013 5:44:14 PM

Acquisition Time (sec)	0.6291	***Comment***	Instrument AVN400 Chemist sarosh Group MGM SI-19 (R-1) AGAIN c13acq.crl CD2Cl2 {C:\NMR} mgmgrp 38		
Date	03 Jun 2013 18:12:32	***Date Stamp***	03 Jun 2013 18:12:32		
File Name	F:\mass+nmr record of lab work at oxf\SI-019\CORRECT SPECTRA\Jun03-2013-38\2\PDATA\1\1r				
Frequency (MHz)	100.64	***Nucleus***	13C	***Number of Transients***	256
Origin	avn400	***Original Points Count***	16384	***Owner***	dp-nmrgroup
Points Count	32768	***Pulse Sequence***	zgpg30	***Receiver Gain***	205.43
SW(cyclical) (Hz)	26041.67	***Solvent***	DICHLOROMETHANE-d2		
Spectrum Offset (Hz)	10064.2930	***Spectrum Type***	STANDARD	***Sweep Width (Hz)***	26040.87
Temperature (degree C)	22.795				

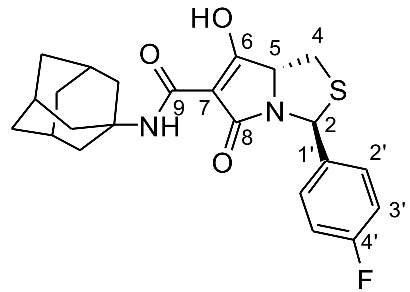


9d

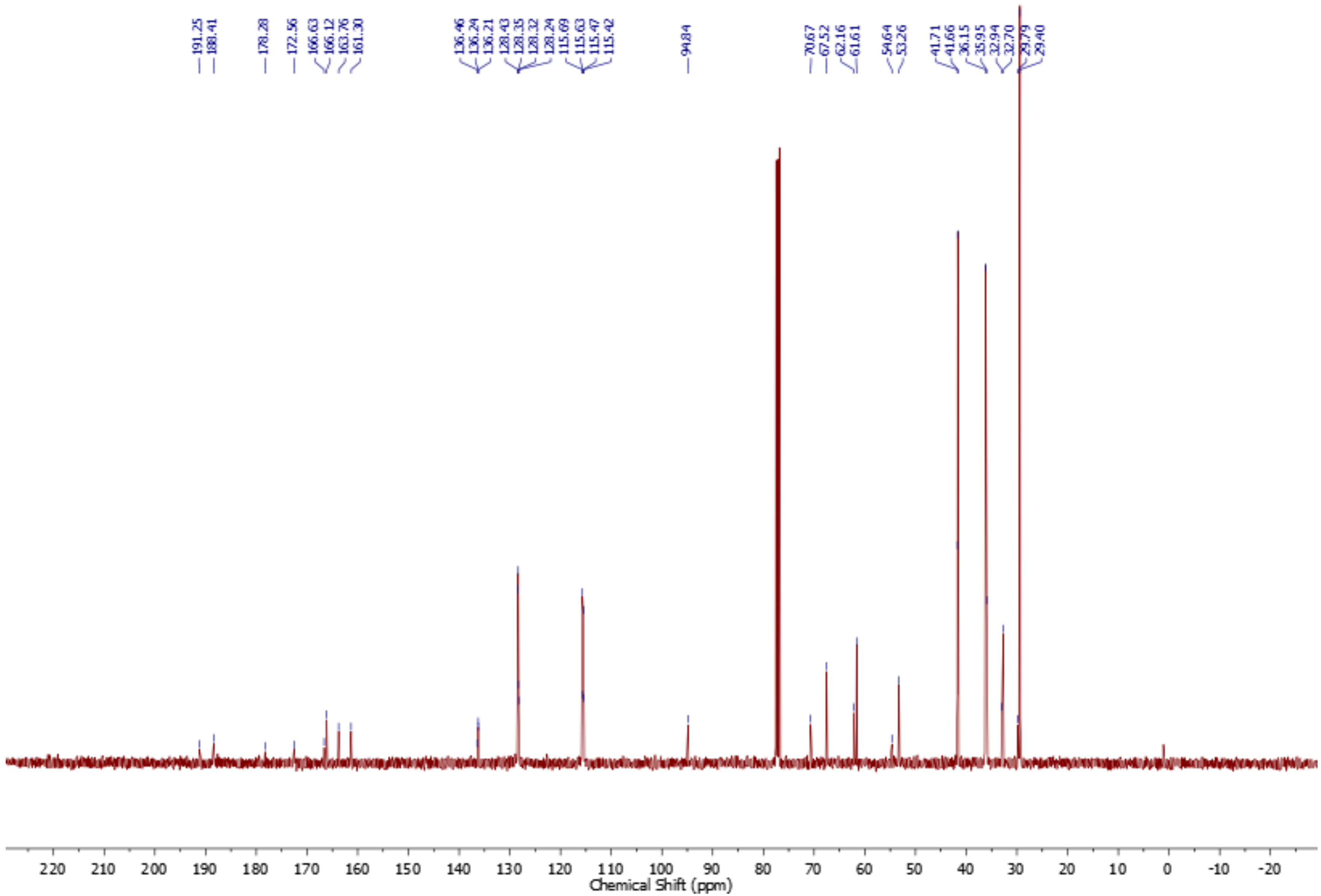

HO
O
O
NH
N
S
F
6
5
4
7
9
8
2
1'
2'
3'
4'


1H NMR (400 MHz, CDCl3)
11.33
7.94
7.46
7.45
7.44
7.43
7.43
7.05
7.03
7.00
6.30
6.21
4.67
4.65
4.63
4.45
4.43
4.41
4.39
3.27
3.25
3.24
3.22
3.04
3.02
3.01
2.99
2.98
2.96
2.14
2.12
2.11
2.10
2.06
2.04
2.04
1.70
1.69
1.68
1.55
0.45
4.08
3.16
0.41
0.97
1.00
0.40
1.44
1.44
14.23
9.61
Chemical Shift (ppm)

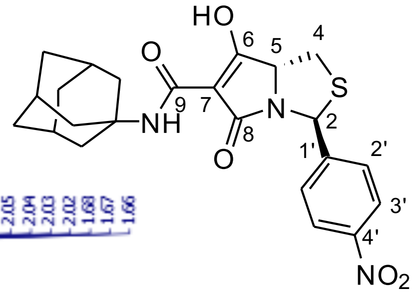
9d

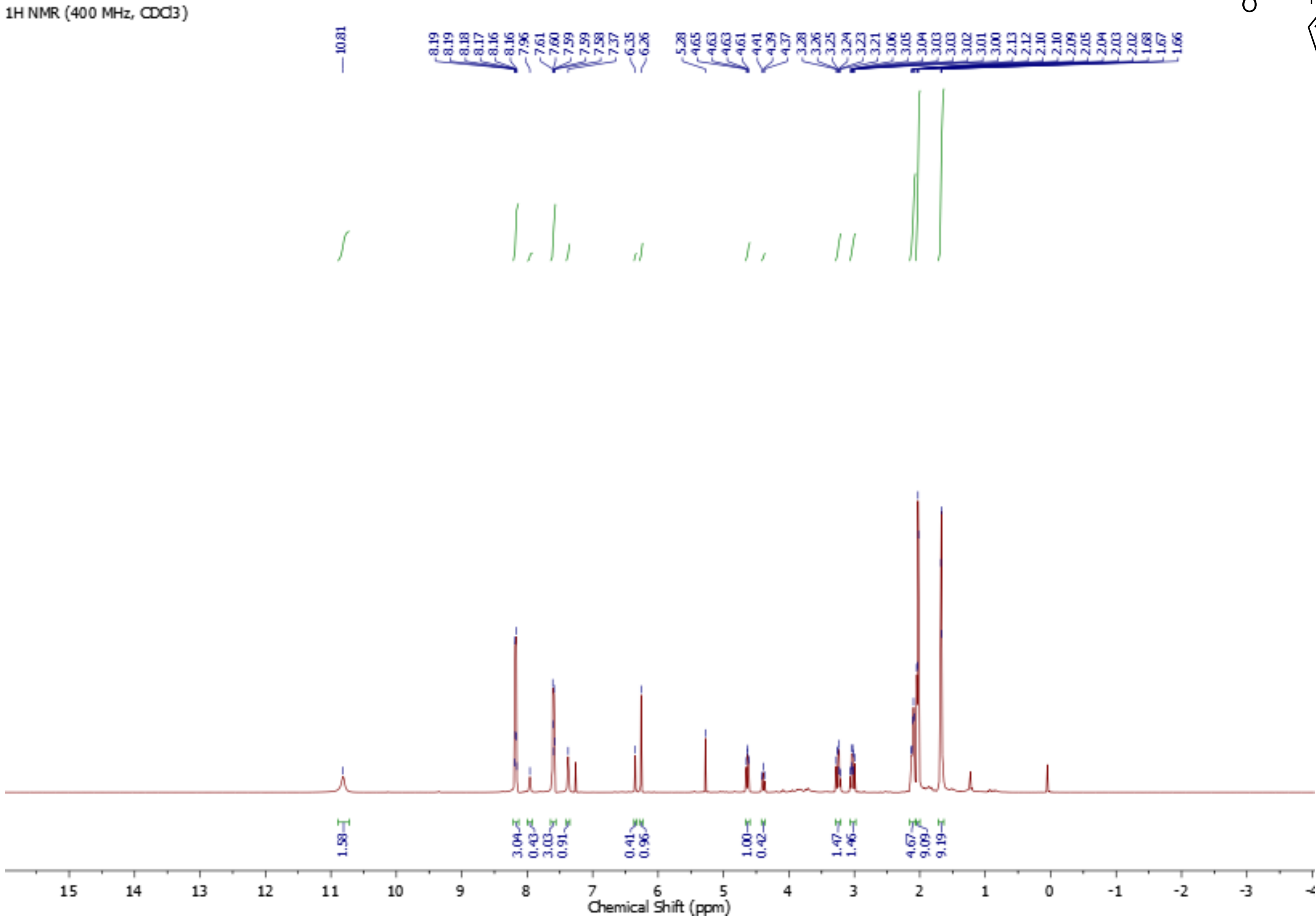


13C NMR (100.6 MHz, CDCl3)

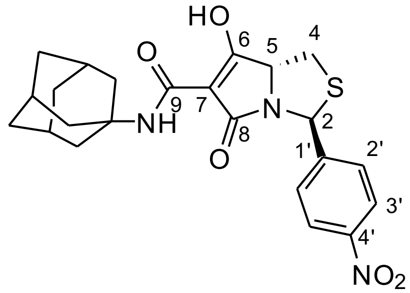


9e

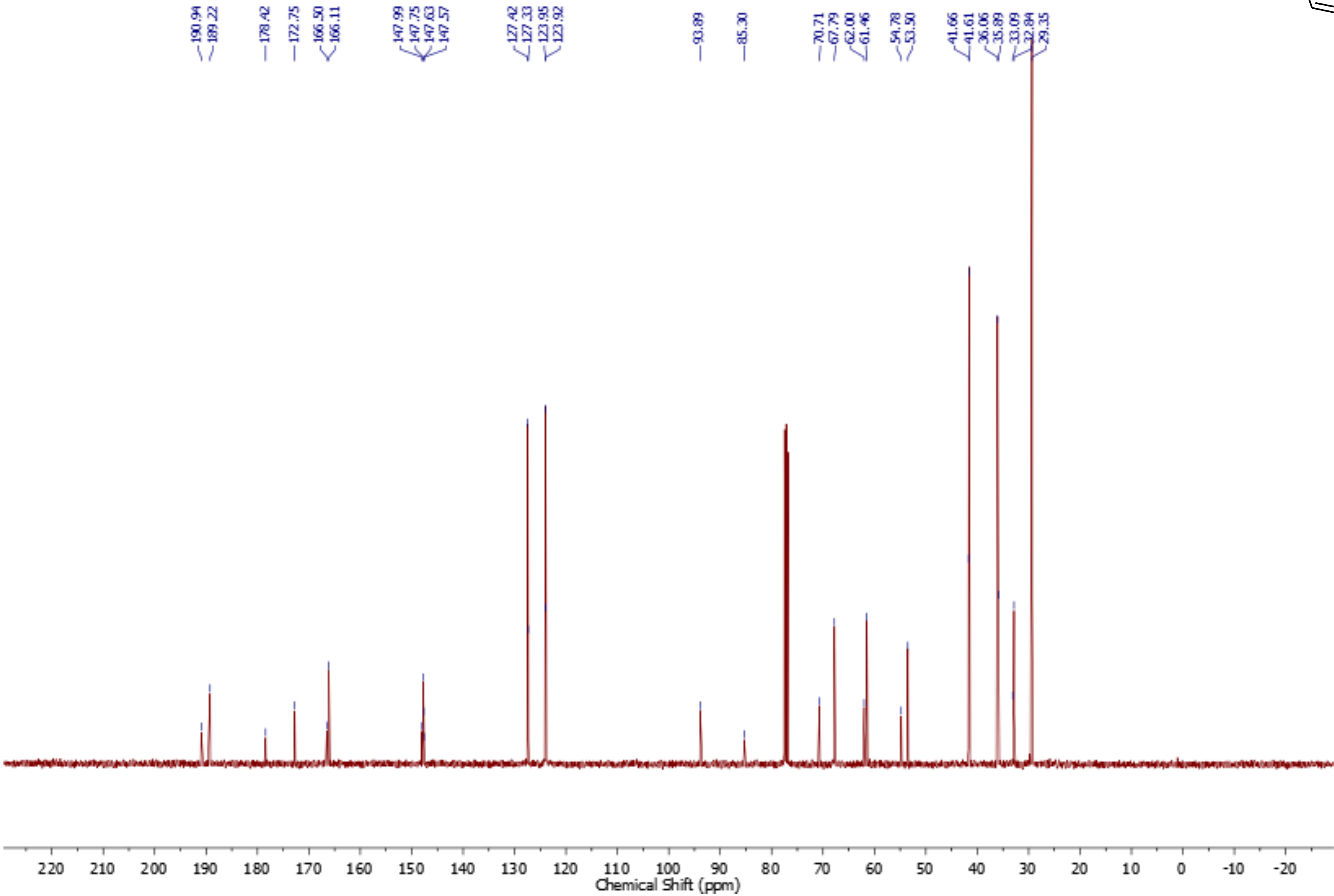




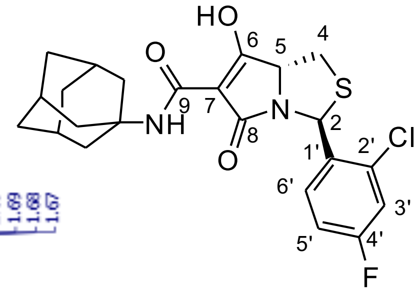
9e



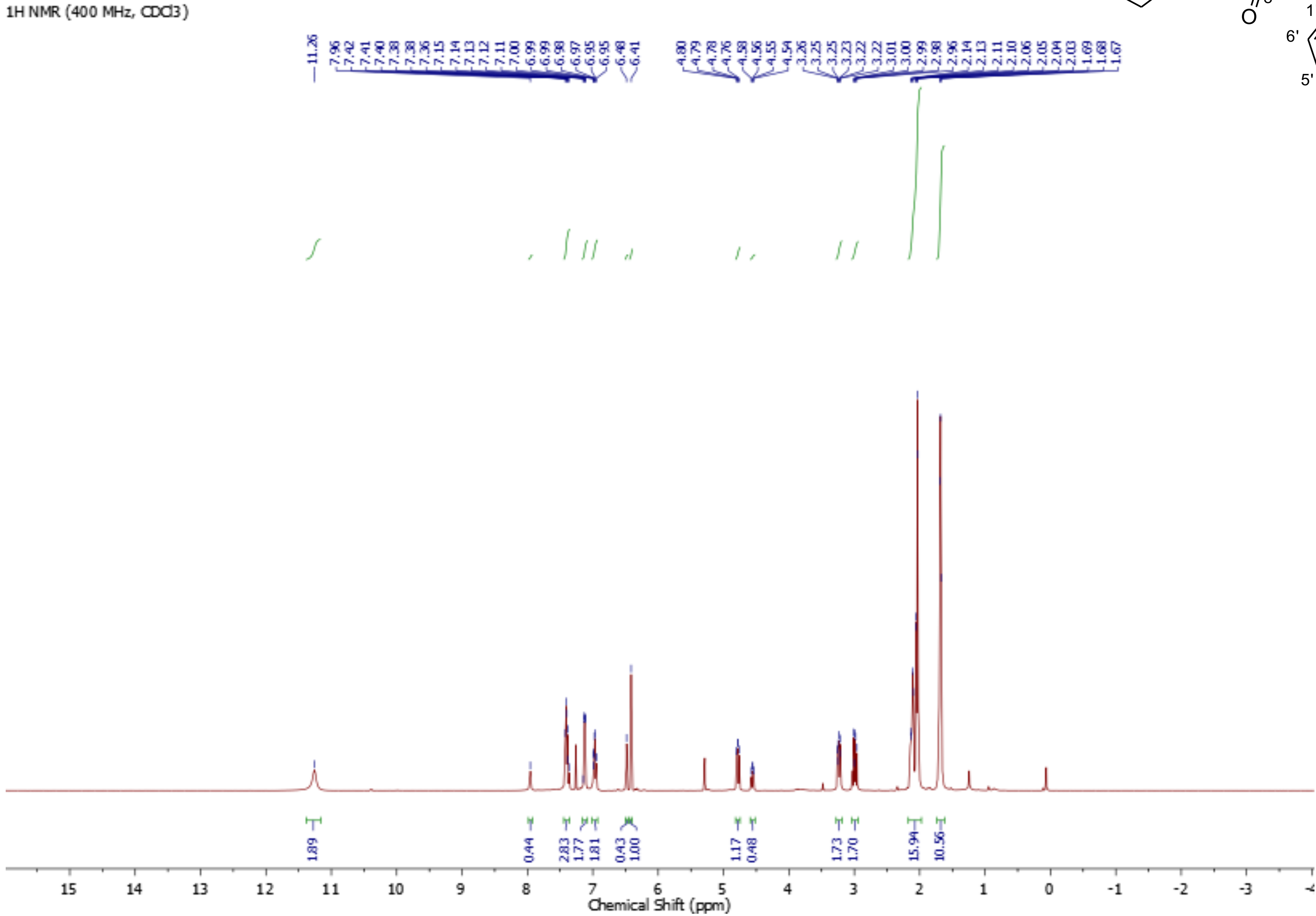
13C NMR (100.6 MHz, CDCl3)



9f

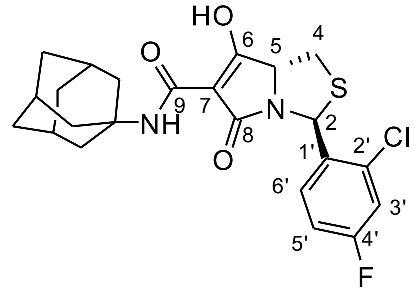


HO
O
6
5
4
S
9
7
NH
N
2
8
O
Cl
2'
1'
6'
3'
4'
5'
F

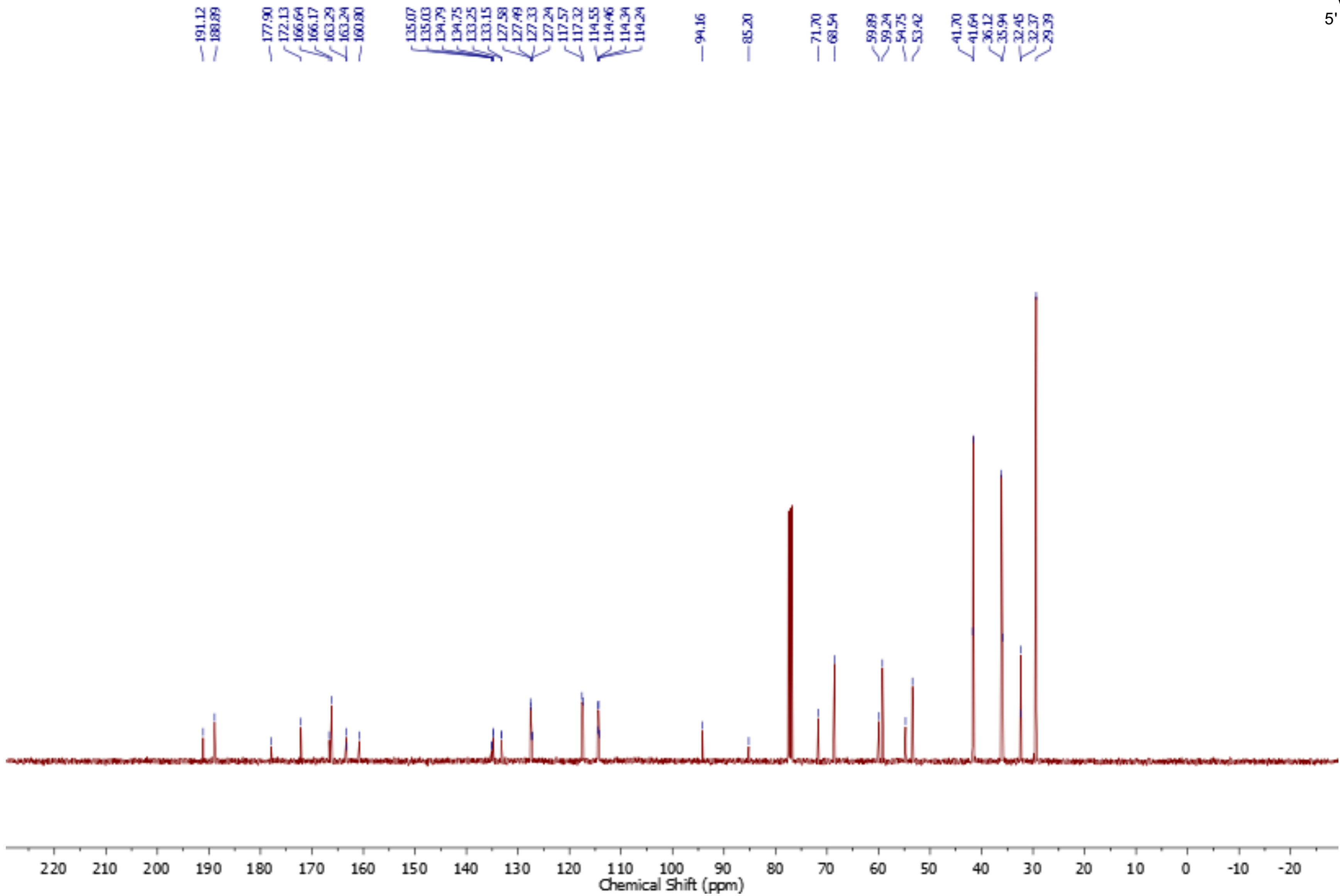


1H NMR (400 MHz, CDCl3)
11.26
7.96
7.42
7.41
7.40
7.38
7.38
7.36
7.15
7.14
7.13
7.12
7.11
7.00
6.99
6.99
6.98
6.97
6.95
6.95
6.48
6.41
4.80
4.79
4.78
4.76
4.58
4.56
4.55
4.54
3.26
3.25
3.25
3.23
3.22
3.22
3.01
3.00
2.99
2.98
2.96
2.14
2.13
2.11
2.10
2.06
2.05
2.04
2.03
1.69
1.68
1.67
1.89
0.44
2.83
1.77
1.81
0.43
1.00
1.17
0.48
1.73
1.70
15.94
10.56
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
Chemical Shift (ppm)

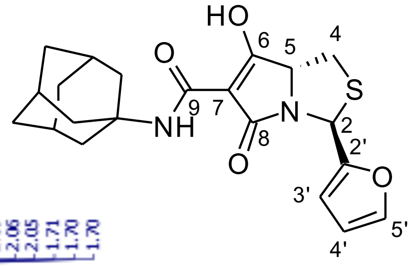
9f

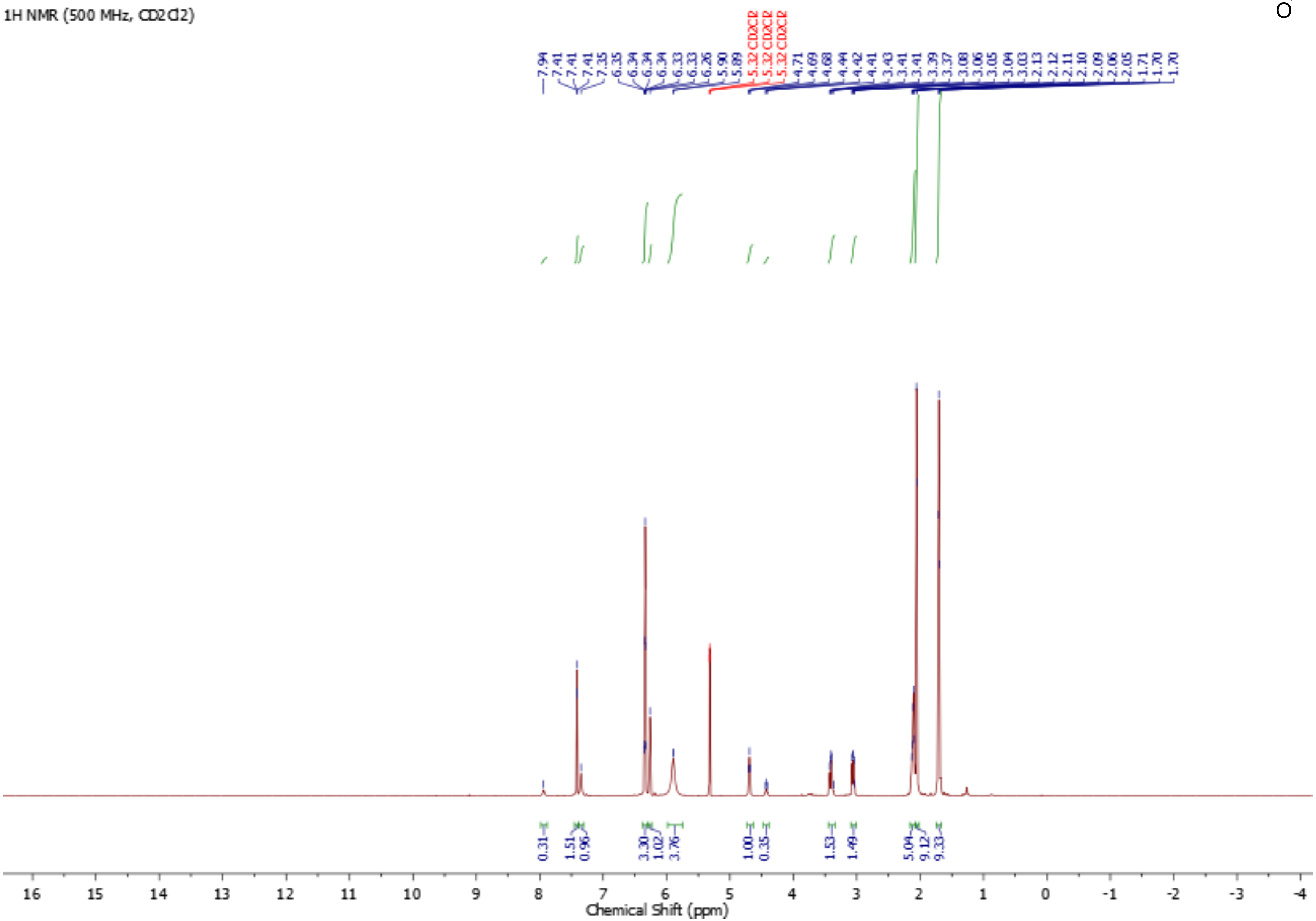


13C NMR (100.6 MHz, CDCl3)

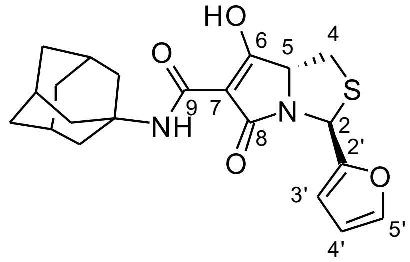


9g

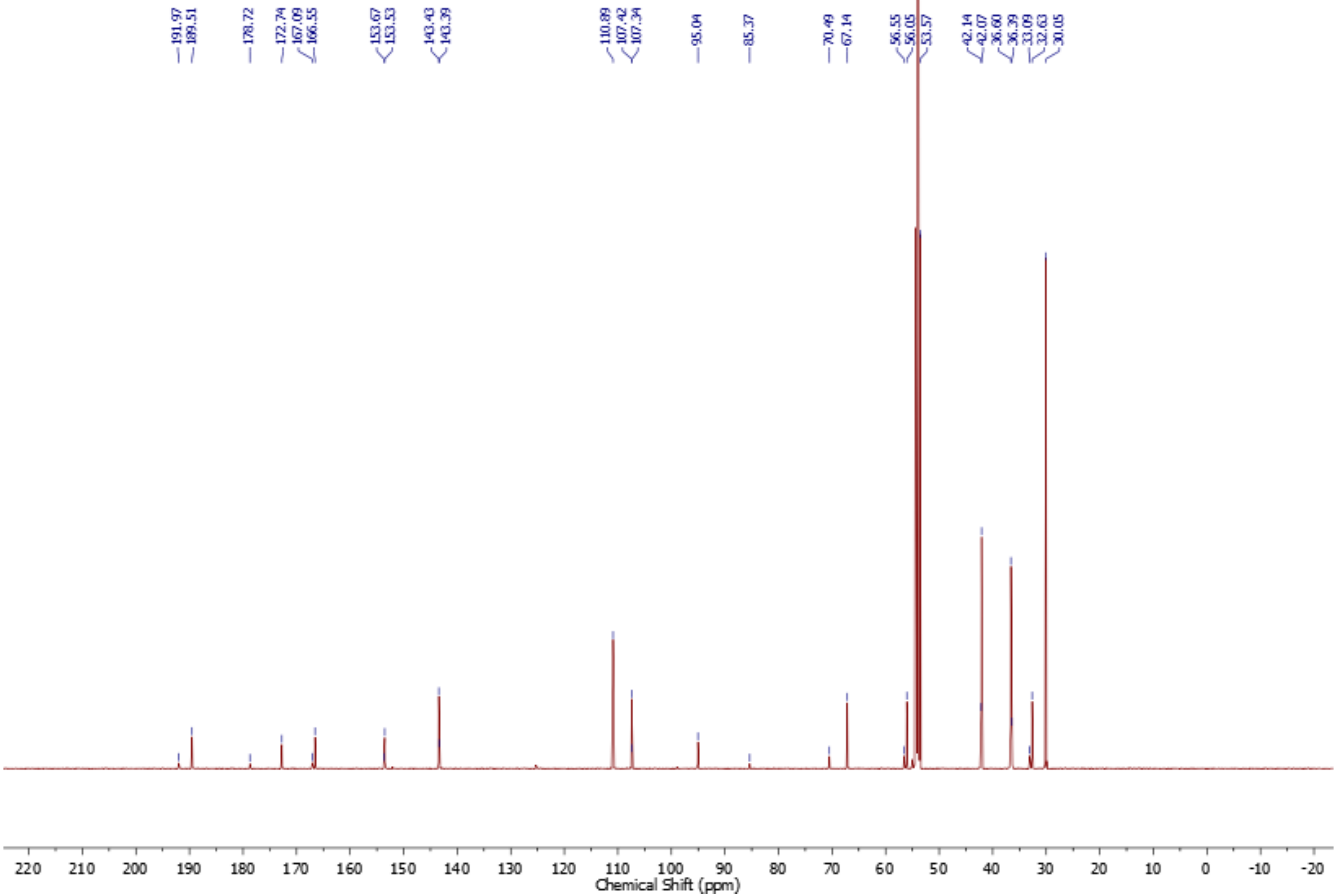

HO
6
5
4
O
9
7
S
N
NH
2
8
2'
O
O
3'
5'
4'


1H NMR (500 MHz, CD2Cl2)
7.94
7.41
7.41
7.41
7.35
6.35
6.34
6.34
6.34
6.33
6.33
6.26
5.90
5.89
5.32 CD2Cl2
5.32 CD2Cl2
5.32 CD2Cl2
4.71
4.69
4.68
4.44
4.42
4.41
3.43
3.41
3.41
3.39
3.37
3.08
3.06
3.05
3.04
3.03
2.13
2.12
2.11
2.10
2.09
2.06
2.05
1.71
1.70
1.70
0.31
1.51
0.96
3.30
1.02
3.76
1.00
0.35
1.53
1.49
5.04
9.12
9.33
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
Chemical Shift (ppm)

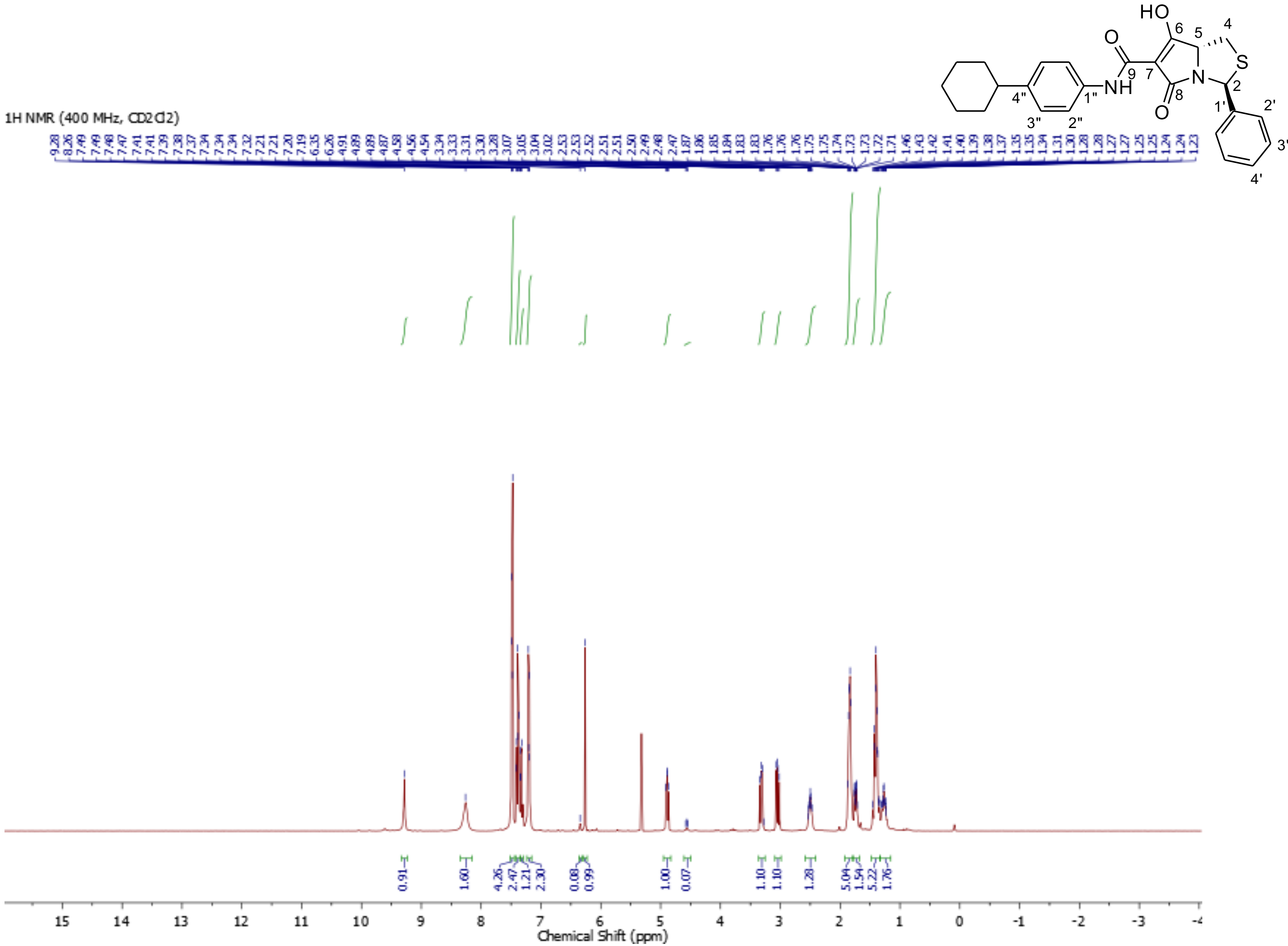
9g



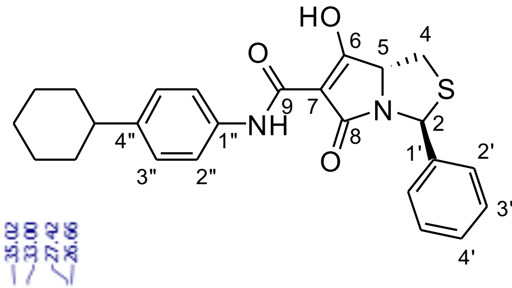
13C NMR (125.8 MHz, CD2Cl2)

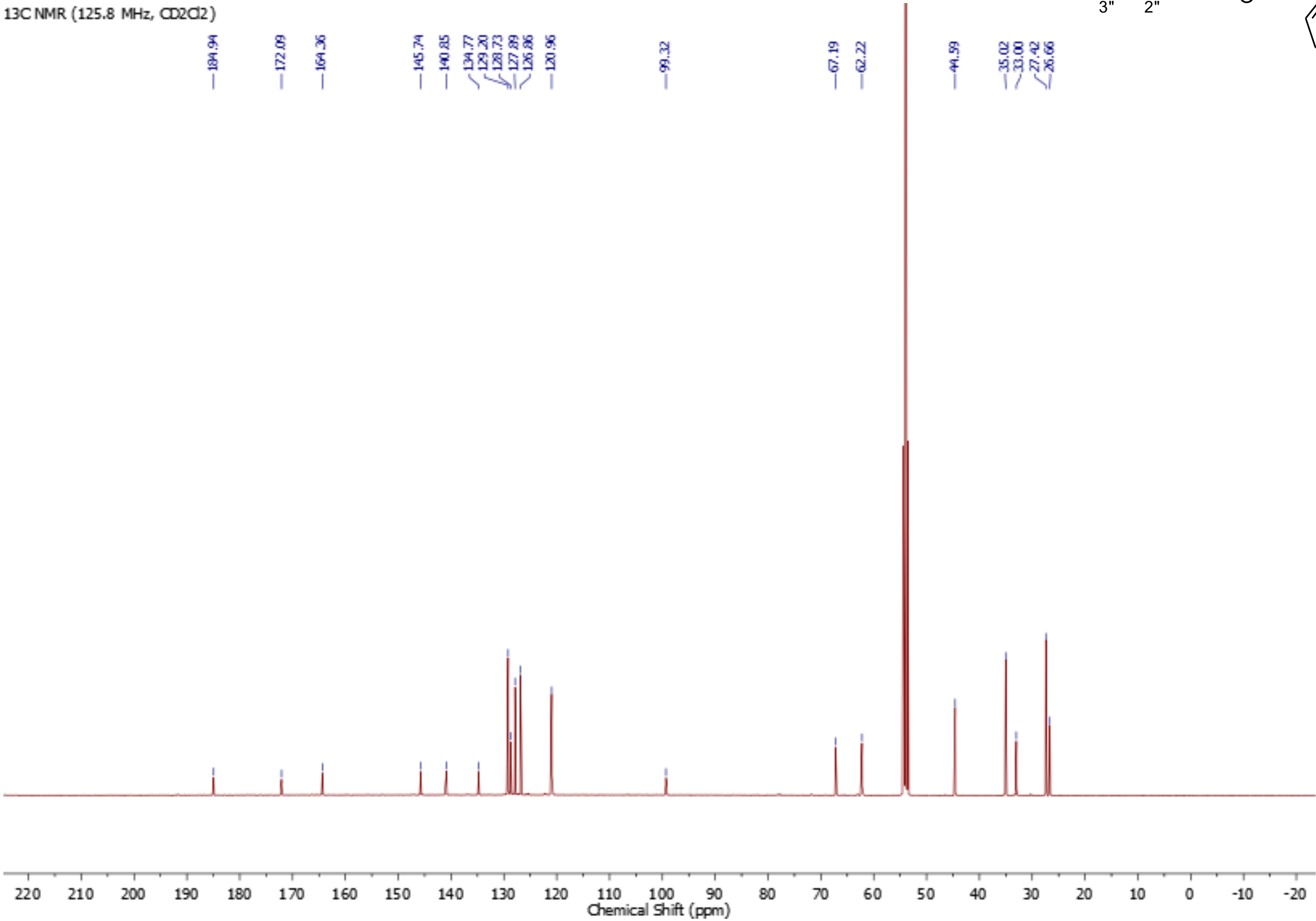


9h

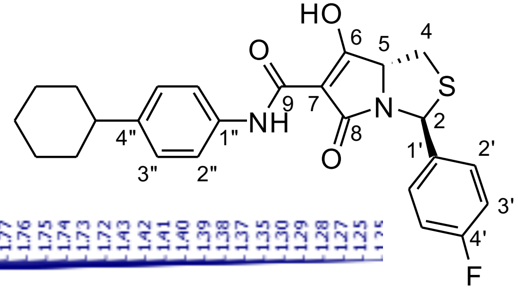


9h

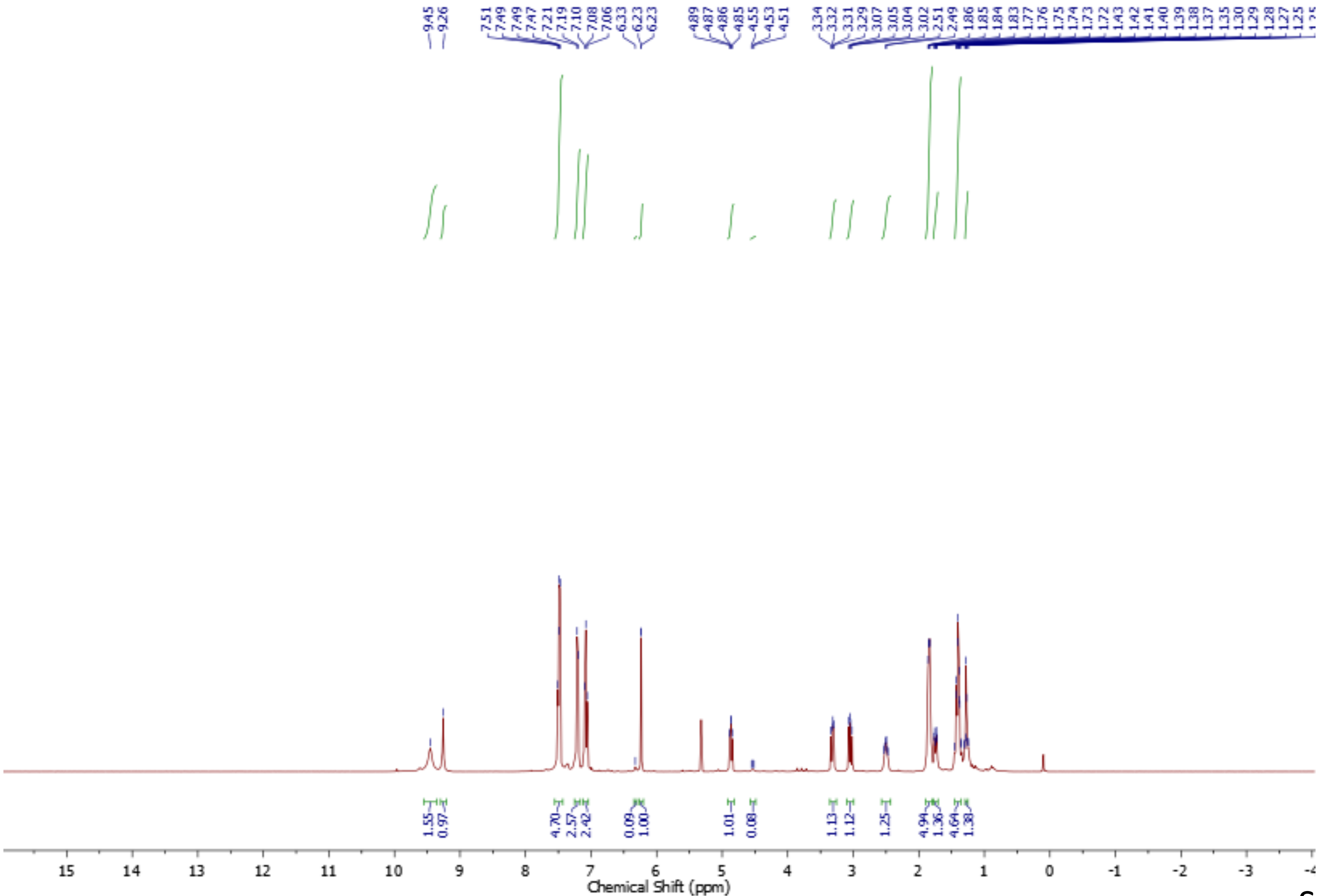

HO
O
O
NH
N
S
6
5
4
9
7
8
2
1'
2'
3'
4'
4"
3"
2"
1"


13C NMR (125.8 MHz, CD2Cl2)
184.94
172.09
164.36
145.74
140.85
134.77
129.20
128.73
127.89
126.86
120.96
99.32
67.19
62.22
44.59
35.02
33.00
27.42
26.66
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Chemical Shift (ppm)

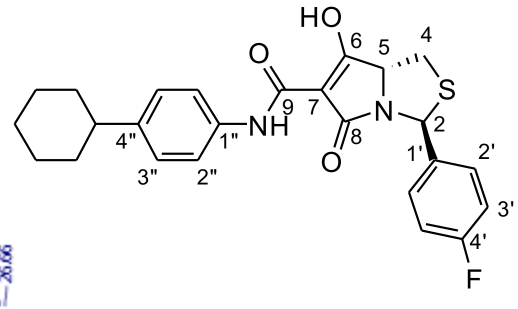
9i



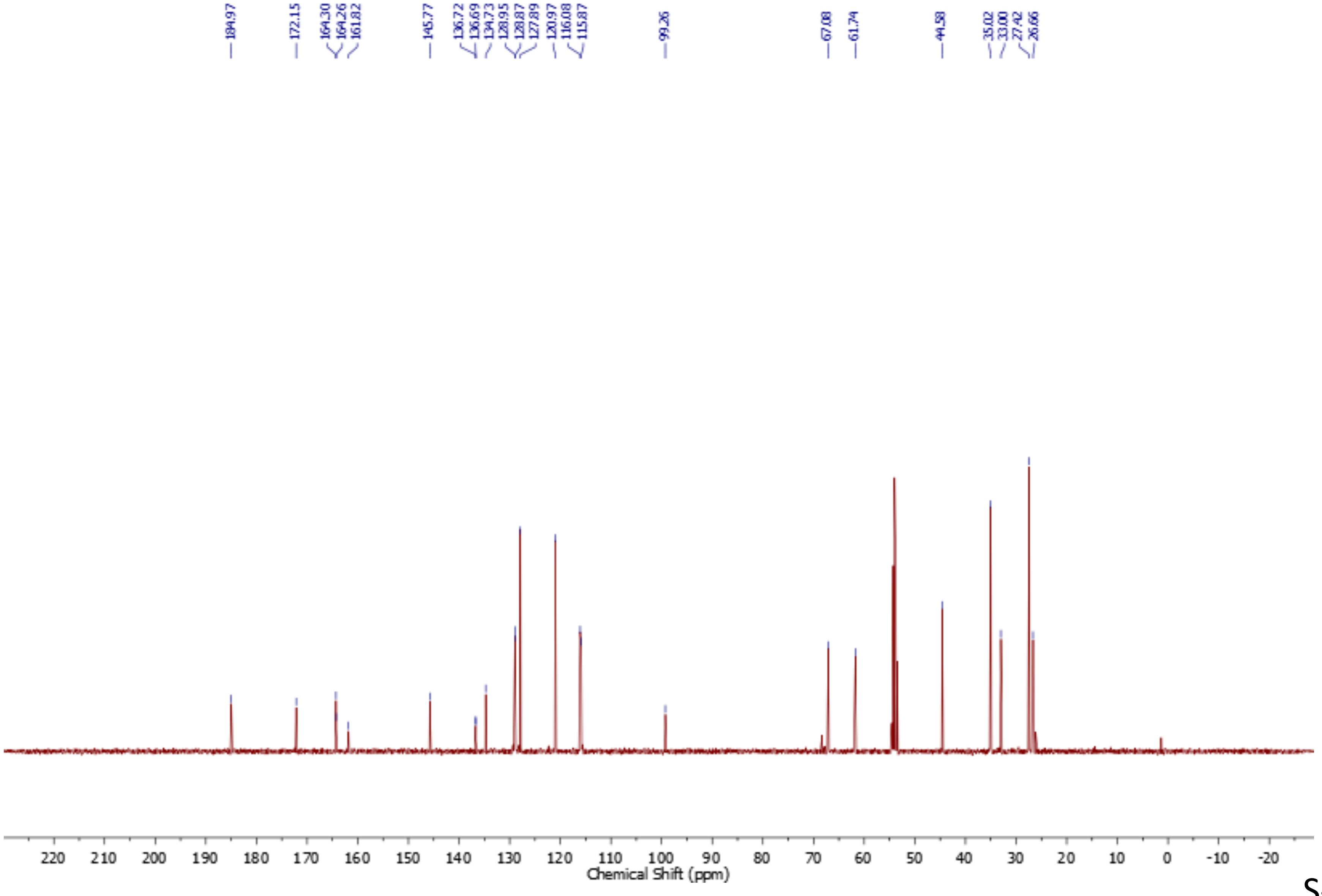
1H NMR (400 MHz, CD2Cl2)



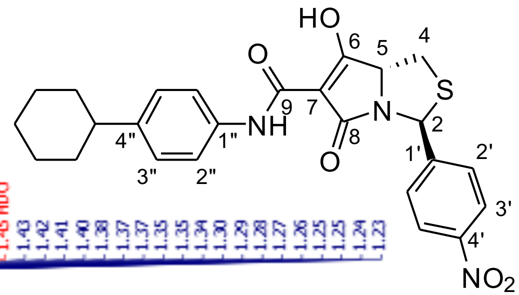
9i

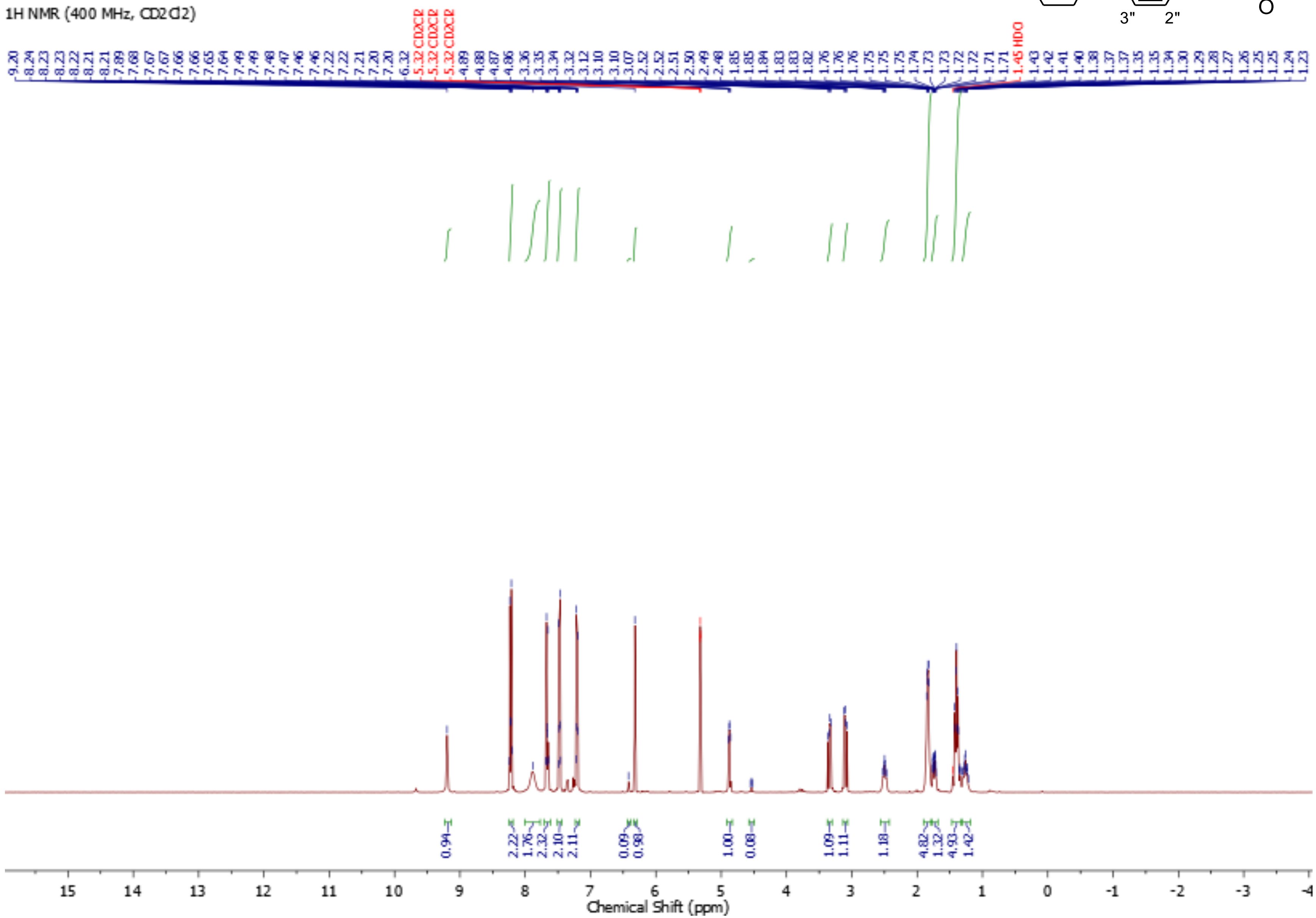


13C NMR (100.6 MHz, CD2Cl2)

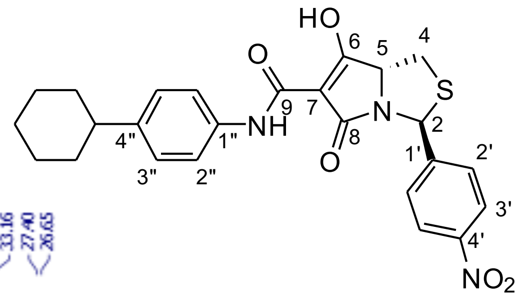


9j

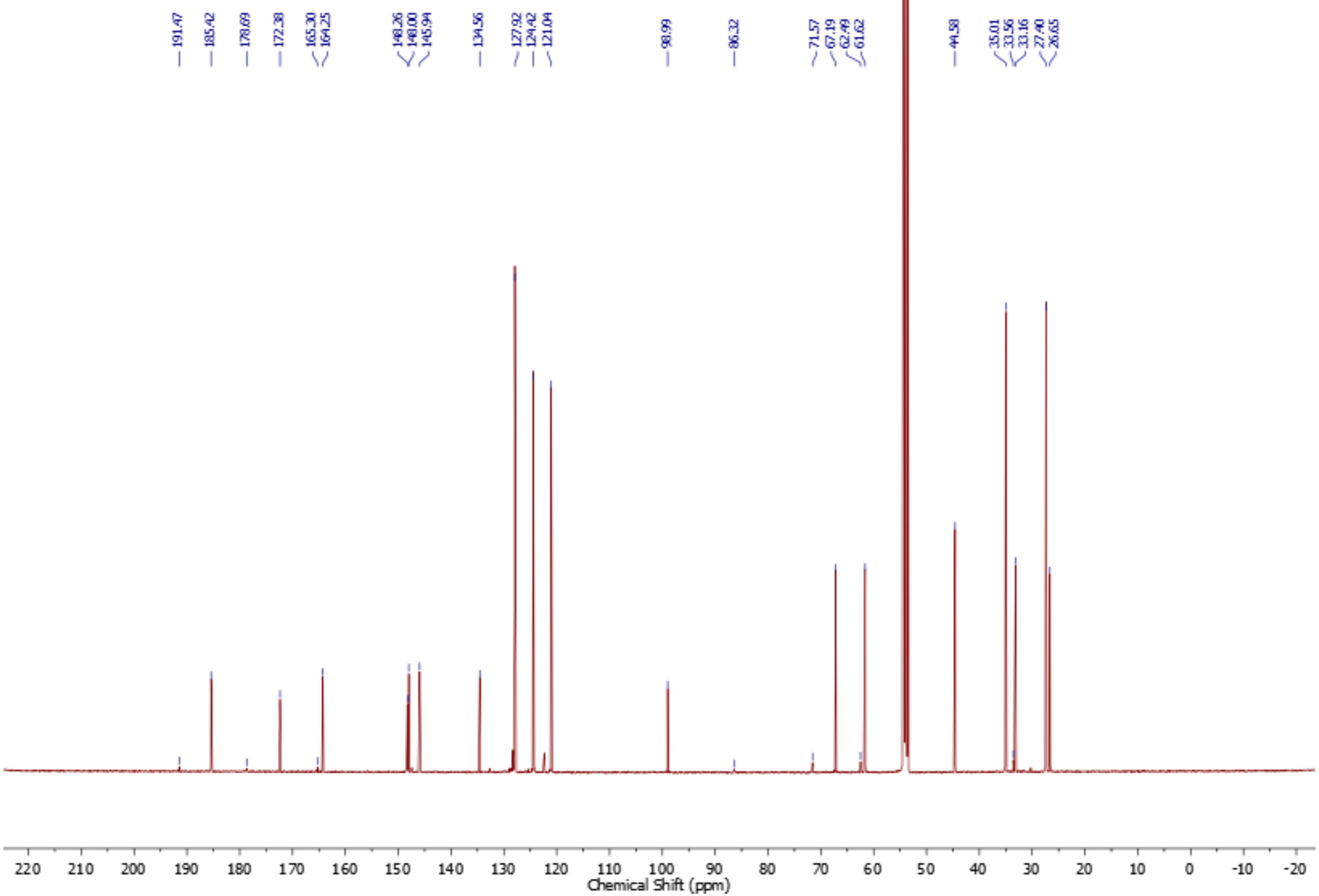

HO
O
NH
O
N
S
NO2
6
5
4
7
9
8
2
1''
4''
3''
2''
1'
2'
3'
4'


1H NMR (400 MHz, CD2Cl2)
9.20 8.24 8.23 8.23 8.22 8.21 8.21 7.89 7.68 7.67 7.67 7.66 7.66 7.65 7.64 7.49 7.49 7.48 7.47 7.46 7.46 7.22 7.22 7.21 7.20 7.20 6.32
5.32 CD2Cl2 5.32 CD2Cl2 5.32 CD2Cl2
4.89 4.88 4.87 4.86 3.36 3.35 3.34 3.32 3.12 3.10 3.10 3.07 2.52 2.52 2.51 2.50 2.49 2.48 1.85 1.85 1.84 1.83 1.83 1.82 1.76 1.76 1.76 1.75 1.75 1.75 1.74 1.73 1.73 1.72 1.72 1.71 1.71
1.45 HDO
1.43 1.42 1.41 1.40 1.38 1.37 1.37 1.35 1.35 1.34 1.30 1.29 1.28 1.27 1.26 1.25 1.25 1.24 1.23
0.94 2.22 1.76 2.32 2.10 2.11 0.09 0.98 1.00 0.08 1.09 1.11 1.18 4.82 1.32 4.93 1.42
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
Chemical Shift (ppm)

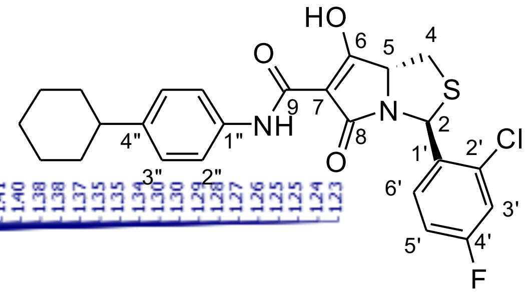
9j

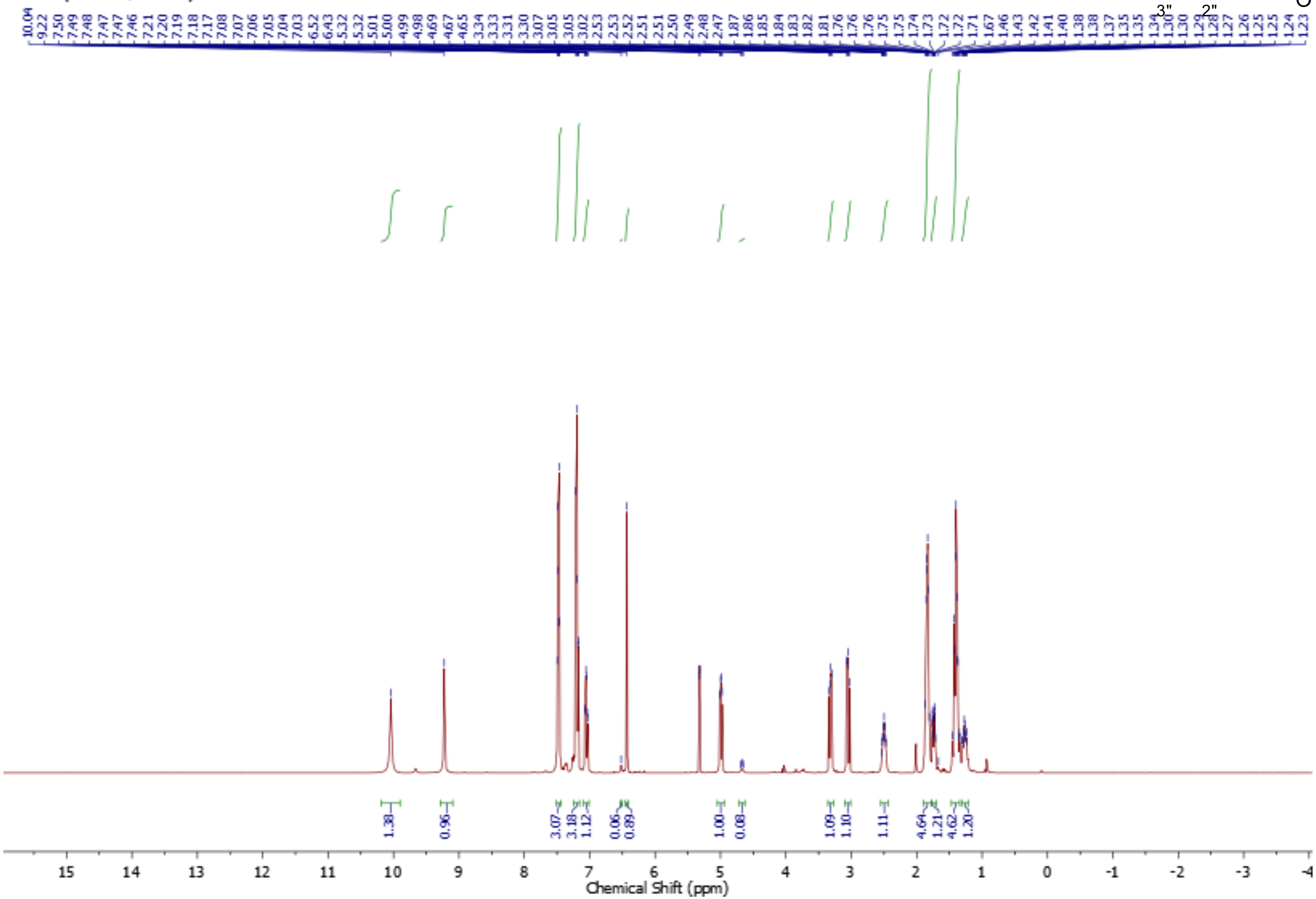


13C NMR (125.8 MHz, CD2Cl2)

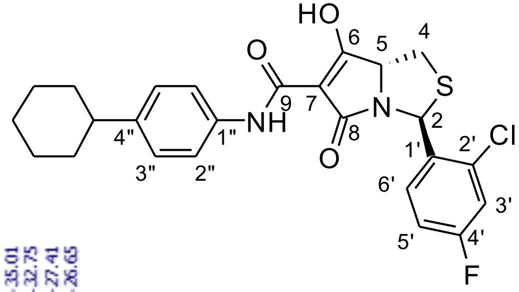


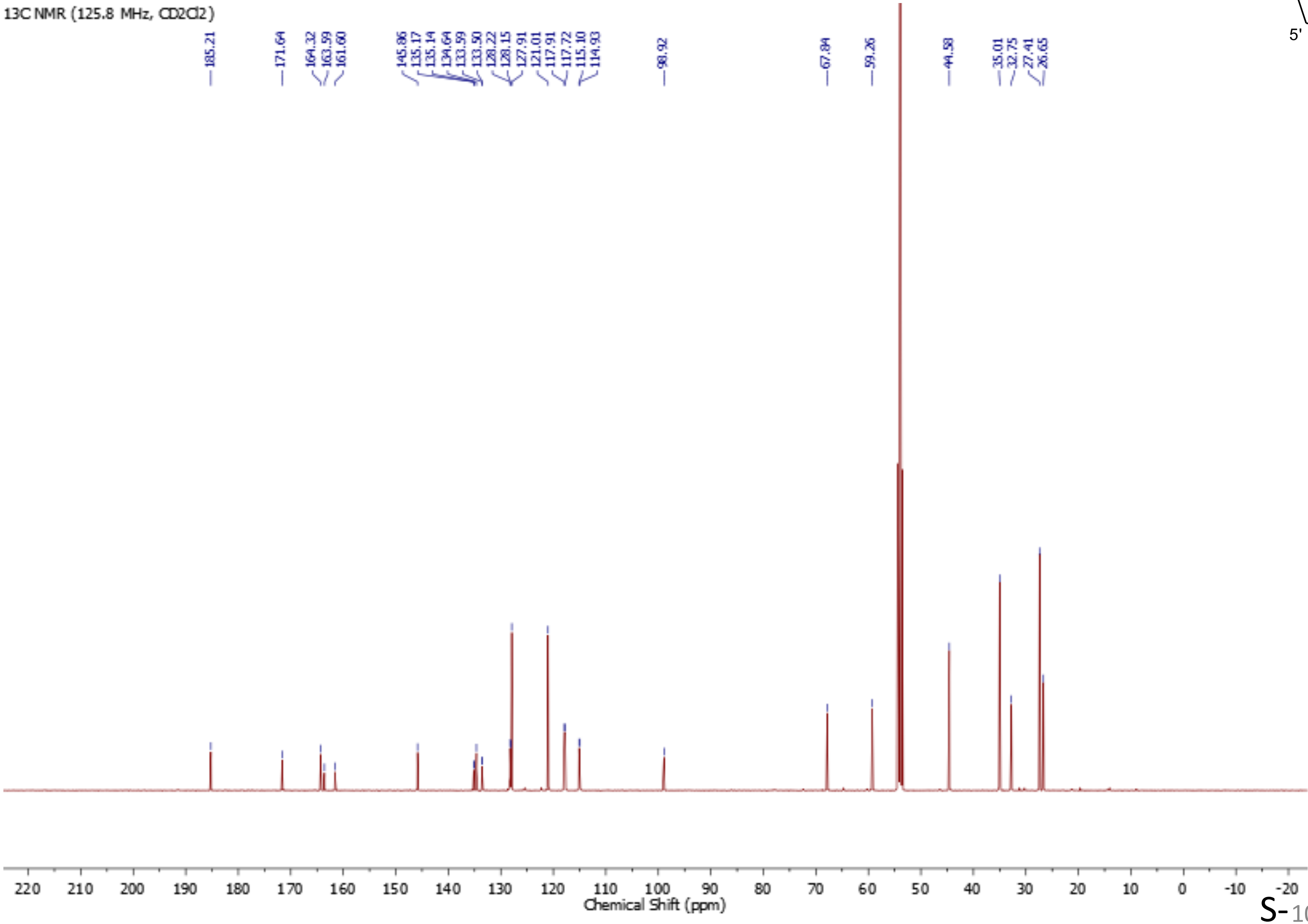
9k



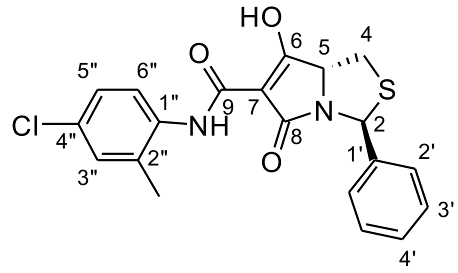


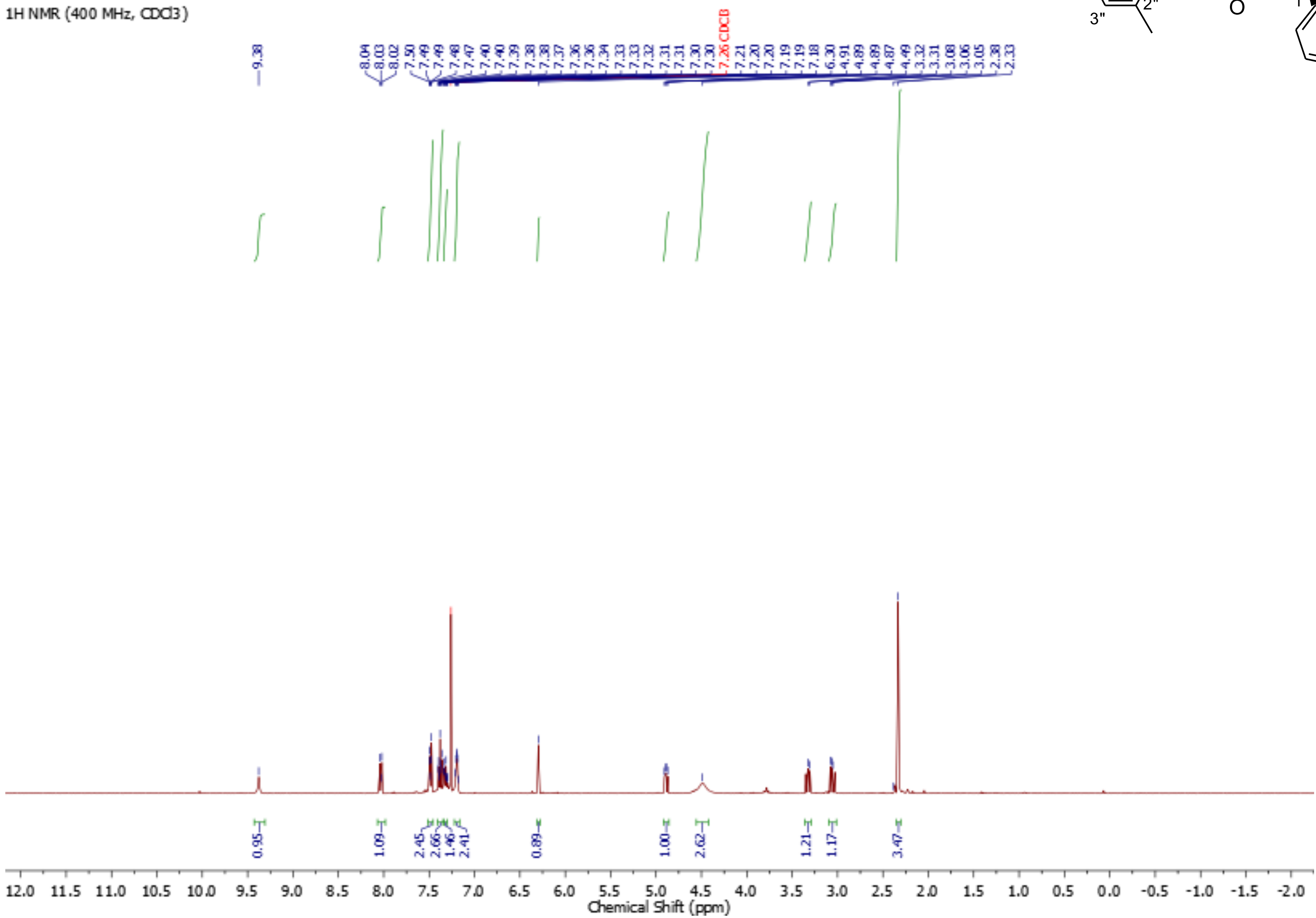
9k


HO
O
NH
N
S
Cl
F
O
4
5
6
7
8
9
2
1'
2'
3'
4'
5'
6'
1"
2"
3"
4"

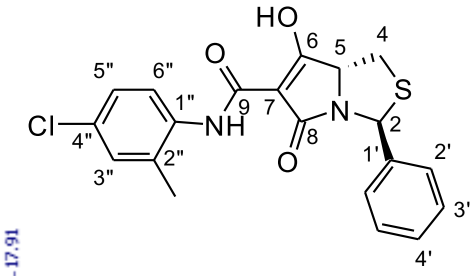

13C NMR (125.8 MHz, CD2Cl2)
185.21
171.64
164.32
163.59
161.60
145.86
135.17
135.14
134.64
133.59
133.50
128.22
128.15
127.91
121.01
117.91
117.72
115.10
114.93
98.92
67.84
59.26
44.58
35.01
32.75
27.41
26.65
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

9l

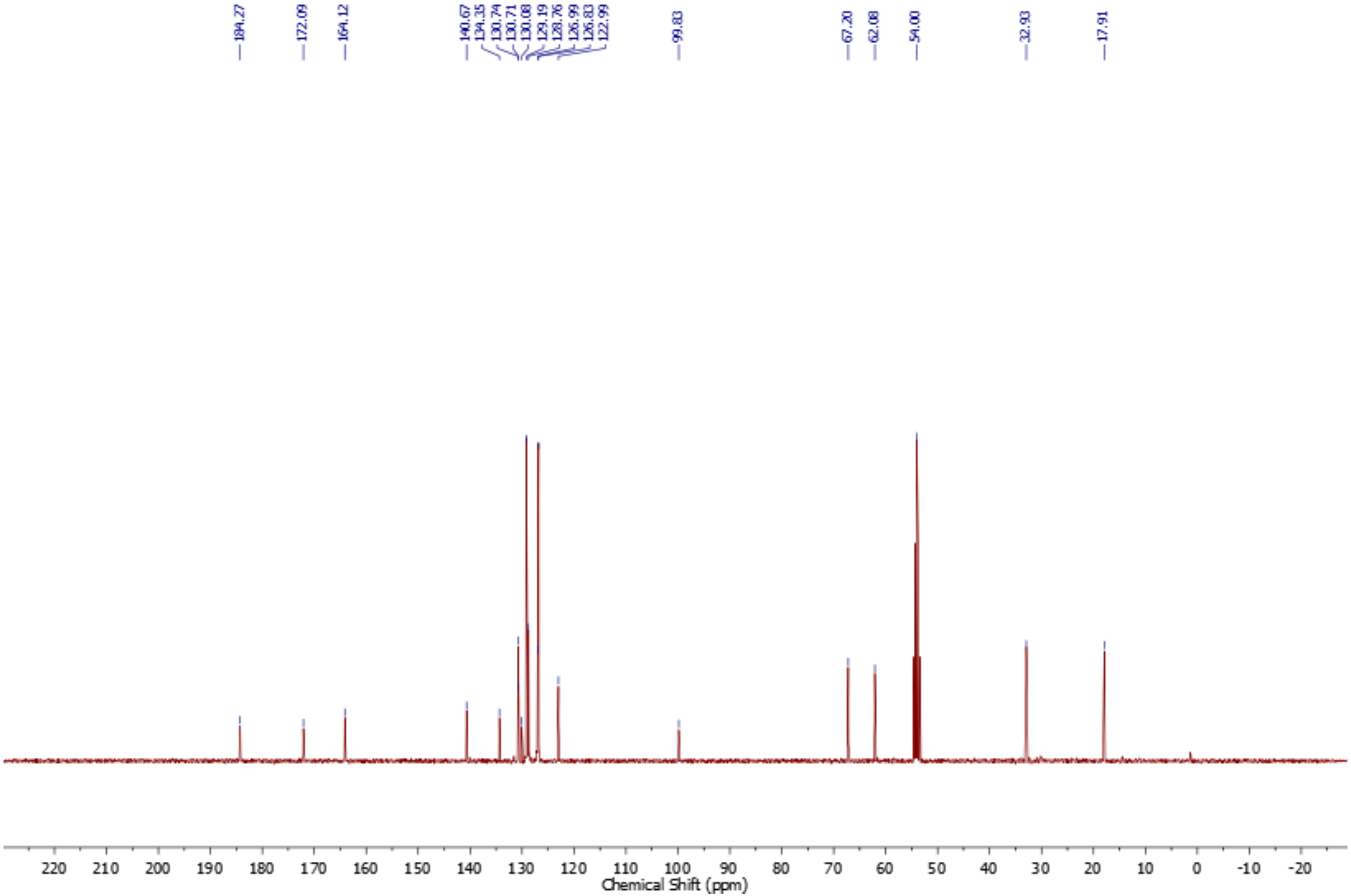

HO
O
NH
N
S
O
Cl
6
5
4
7
9
8
2
1'
2'
3'
4'
1"
2"
3"
4"
5"
6"


1H NMR (400 MHz, CDCl3)
9.38
8.04 8.03 8.02 7.50 7.49 7.49 7.48 7.47 7.40 7.40 7.39 7.38 7.38 7.37 7.36 7.36 7.34 7.33 7.33 7.32 7.31 7.31 7.30 7.30
7.26 CDCl3
7.21 7.20 7.20 7.19 7.19 7.18 6.30 4.91 4.89 4.89 4.87 4.49 3.32 3.31 3.08 3.06 3.05 2.38 2.33
0.95 1.09 2.45 2.66 1.46 2.41 0.89 1.00 2.62 1.21 1.17 3.47
12.0 11.5 11.0 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 -1.0 -1.5 -2.0
Chemical Shift (ppm)

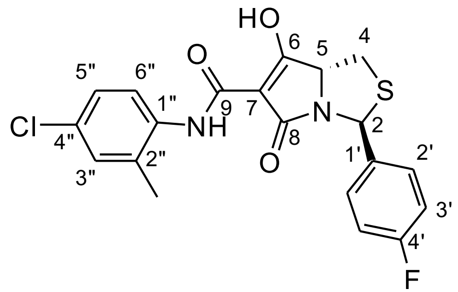
9l

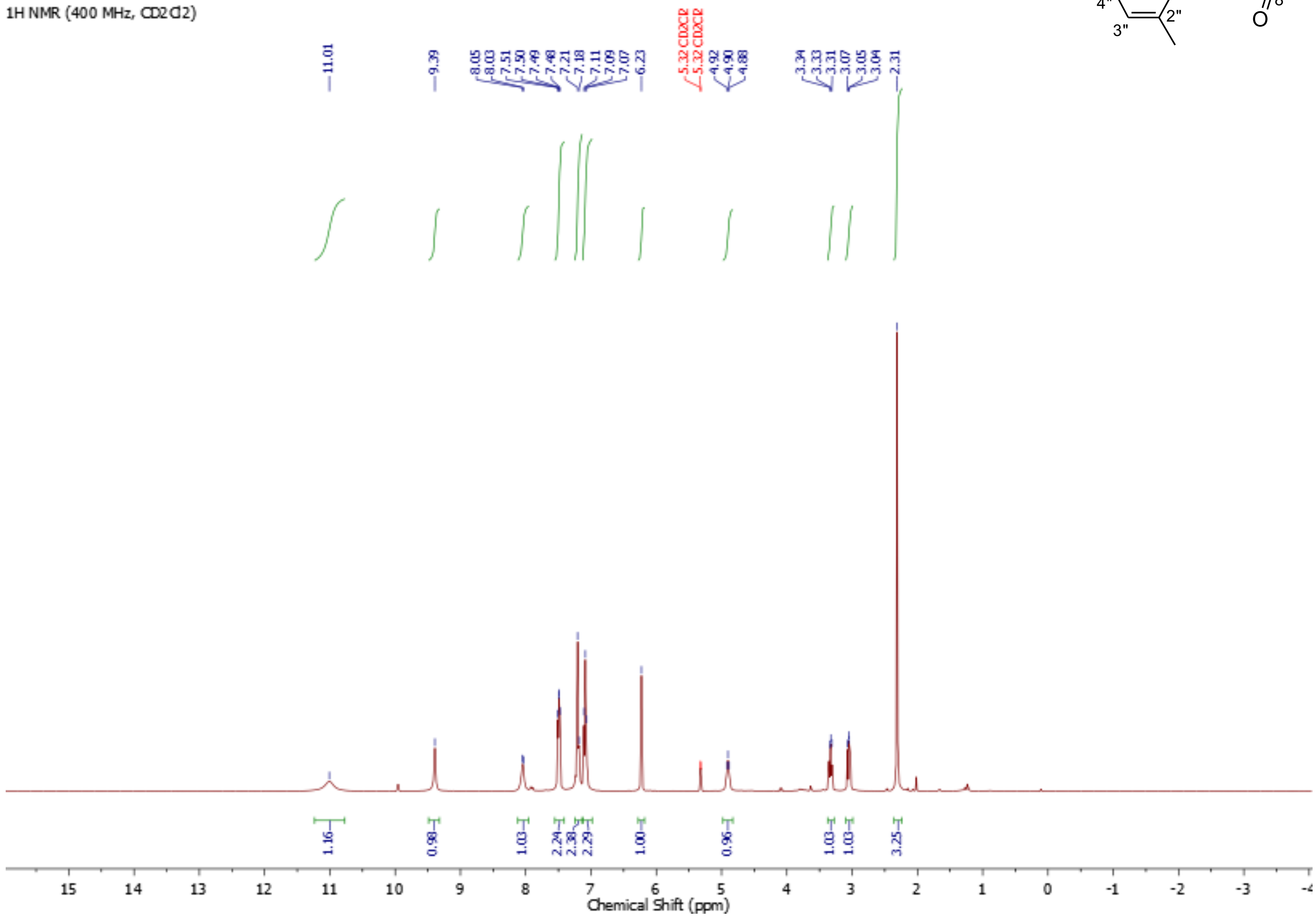


13C NMR (100.6 MHz, CD2Cl2)

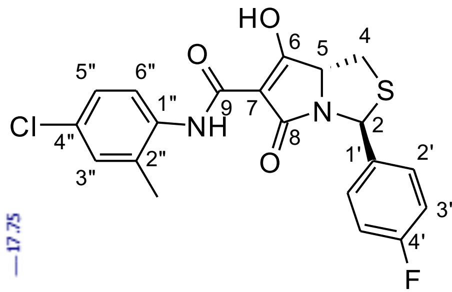


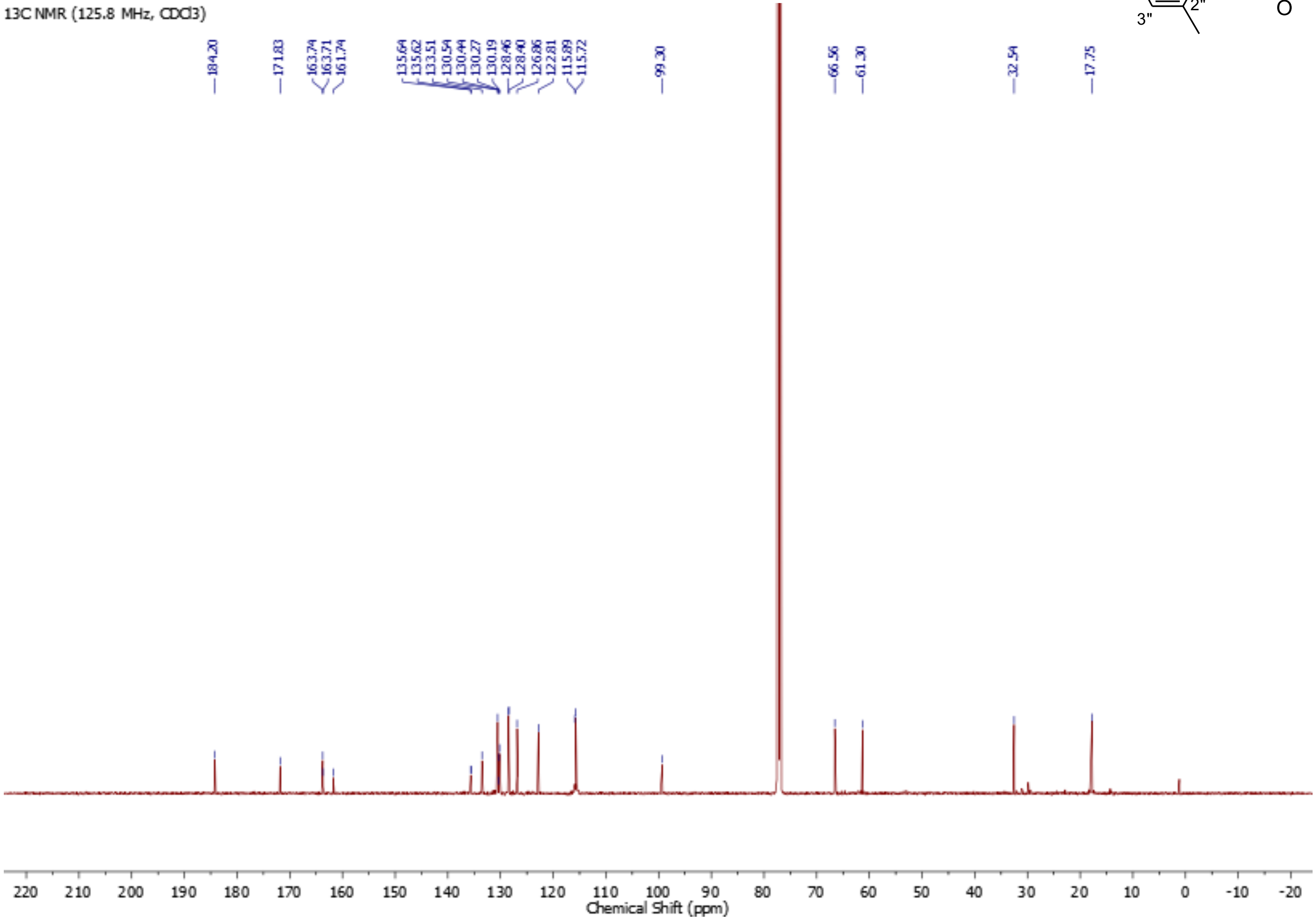
9m


HO
6
5
4
O
5"
6"
S
1"
9
7
Cl
4"
NH
N
2
8
O
2"
1'
2'
3"
3'
4'
F

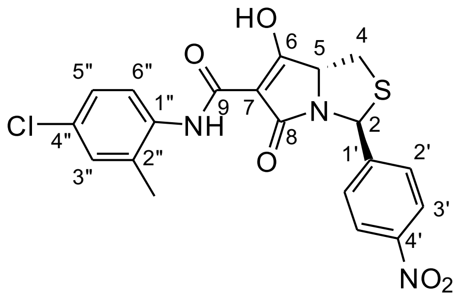

1H NMR (400 MHz, CD2Cl2)
11.01
9.39
8.05
8.03
7.51
7.50
7.49
7.48
7.21
7.18
7.11
7.09
7.07
6.23
5.32 CD2Cl2
5.32 CD2Cl2
4.92
4.90
4.88
3.34
3.33
3.31
3.07
3.05
3.04
2.31
1.16
0.98
1.03
2.24
2.38
2.29
1.00
0.96
1.03
1.03
3.25
Chemical Shift (ppm)

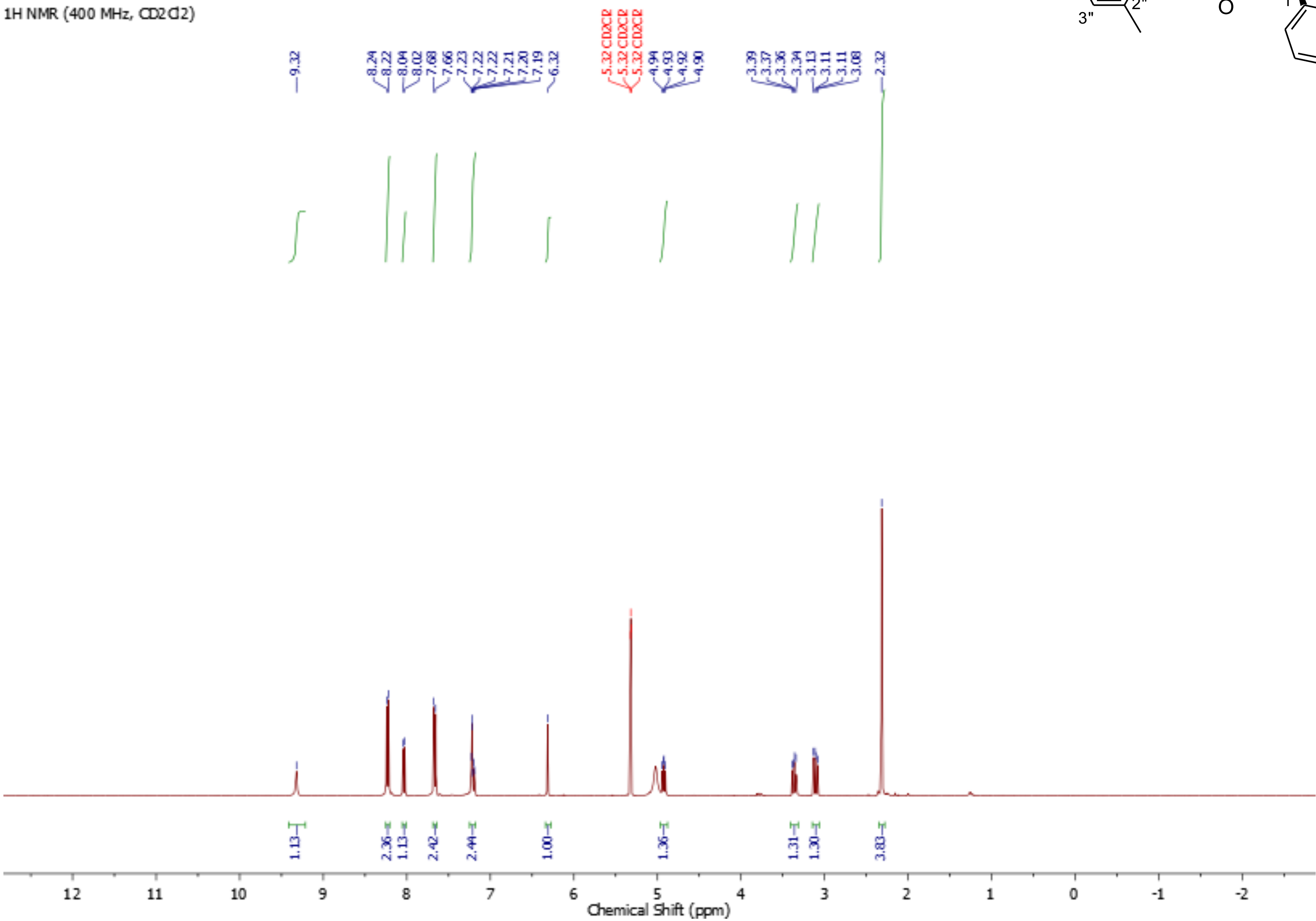
9m


HO
O
Cl
NH
N
S
O
F
1"
2"
3"
4"
5"
6"
2
4
5
6
7
8
9
1'
2'
3'
4'

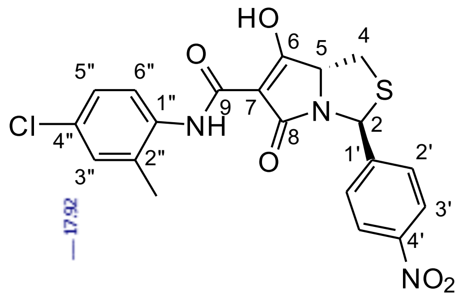

13C NMR (125.8 MHz, CDCl3)
184.20
171.83
163.74
163.71
161.74
135.64
135.62
133.51
130.54
130.44
130.27
130.19
128.46
128.40
126.86
122.81
115.89
115.72
99.30
66.56
61.30
32.54
17.75
Chemical Shift (ppm)

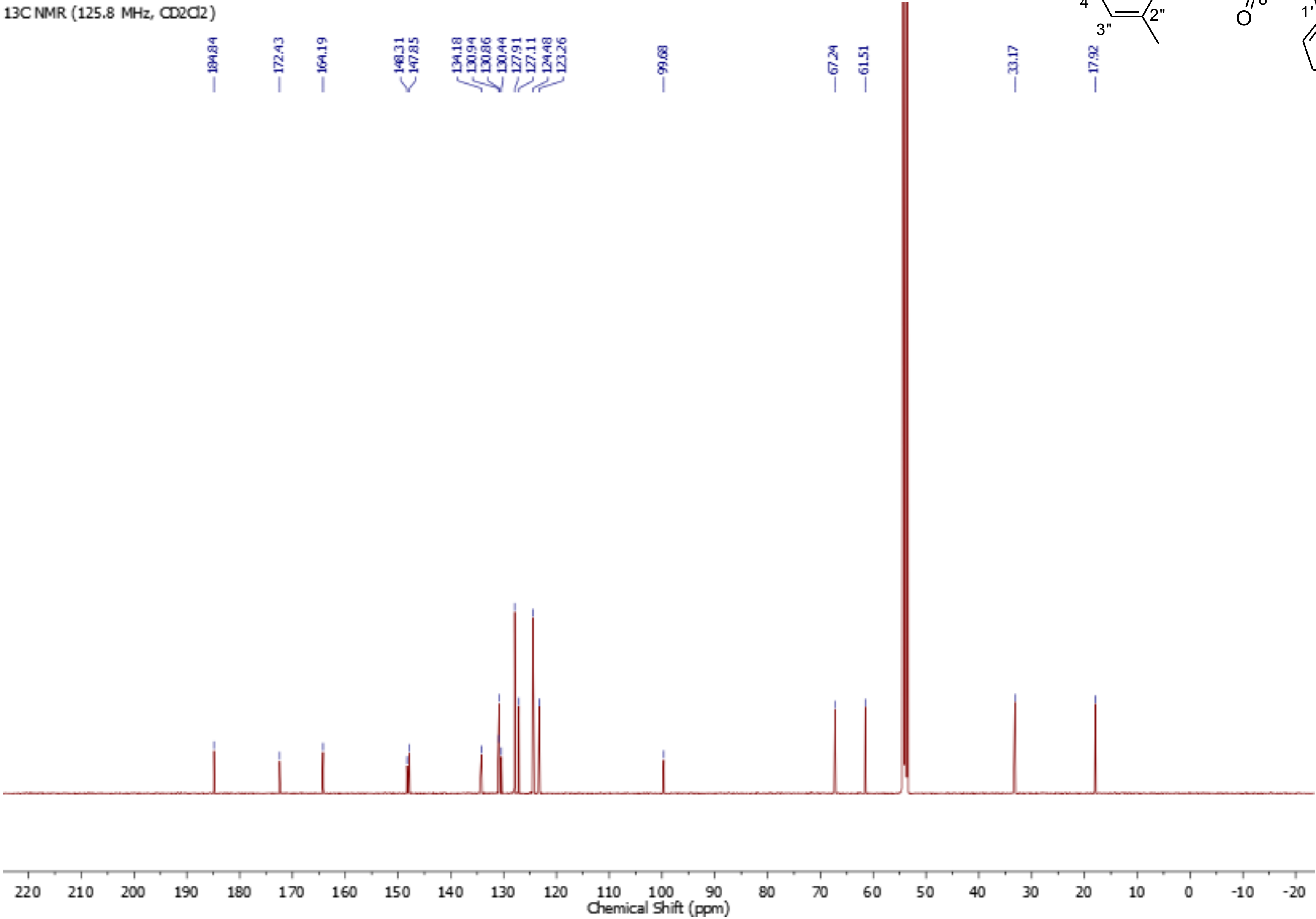
9n


HO
O
Cl
NH
N
S
O
NO2
6
5
4
5"
6"
1"
9
7
8
2
4"
2"
3"
1'
2'
3'
4'


1H NMR (400 MHz, CD2Cl2)
9.32
8.24
8.22
8.04
8.02
7.68
7.66
7.23
7.22
7.22
7.21
7.20
7.19
6.32
5.32 CD2Cl2
5.32 CD2Cl2
5.32 CD2Cl2
4.94
4.93
4.92
4.90
3.39
3.37
3.36
3.34
3.13
3.11
3.11
3.08
2.32
1.13
2.36
1.13
2.42
2.44
1.00
1.36
1.31
1.30
3.83
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
Chemical Shift (ppm)

9n

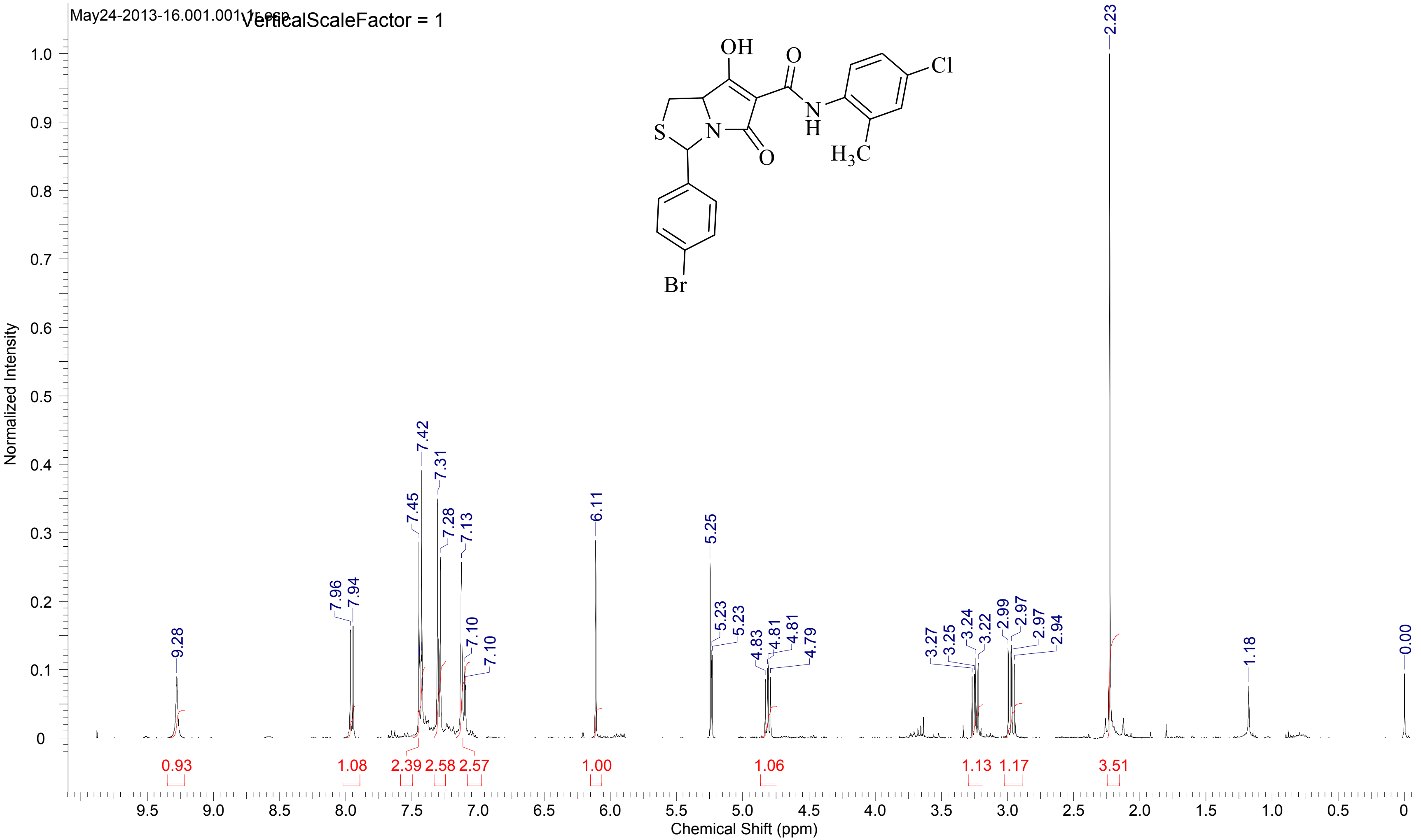

HO
6
5
4
S
2
N
7
8
O
9
O
NH
1"
2"
3"
4"
5"
6"
Cl
1'
2'
3'
4'
NO_2


13C NMR (125.8 MHz, CD2Cl2)
184.84
172.43
164.19
148.31
147.85
134.18
130.94
130.86
130.44
127.91
127.11
124.48
123.26
99.68
67.24
61.51
33.17
17.92
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

9o

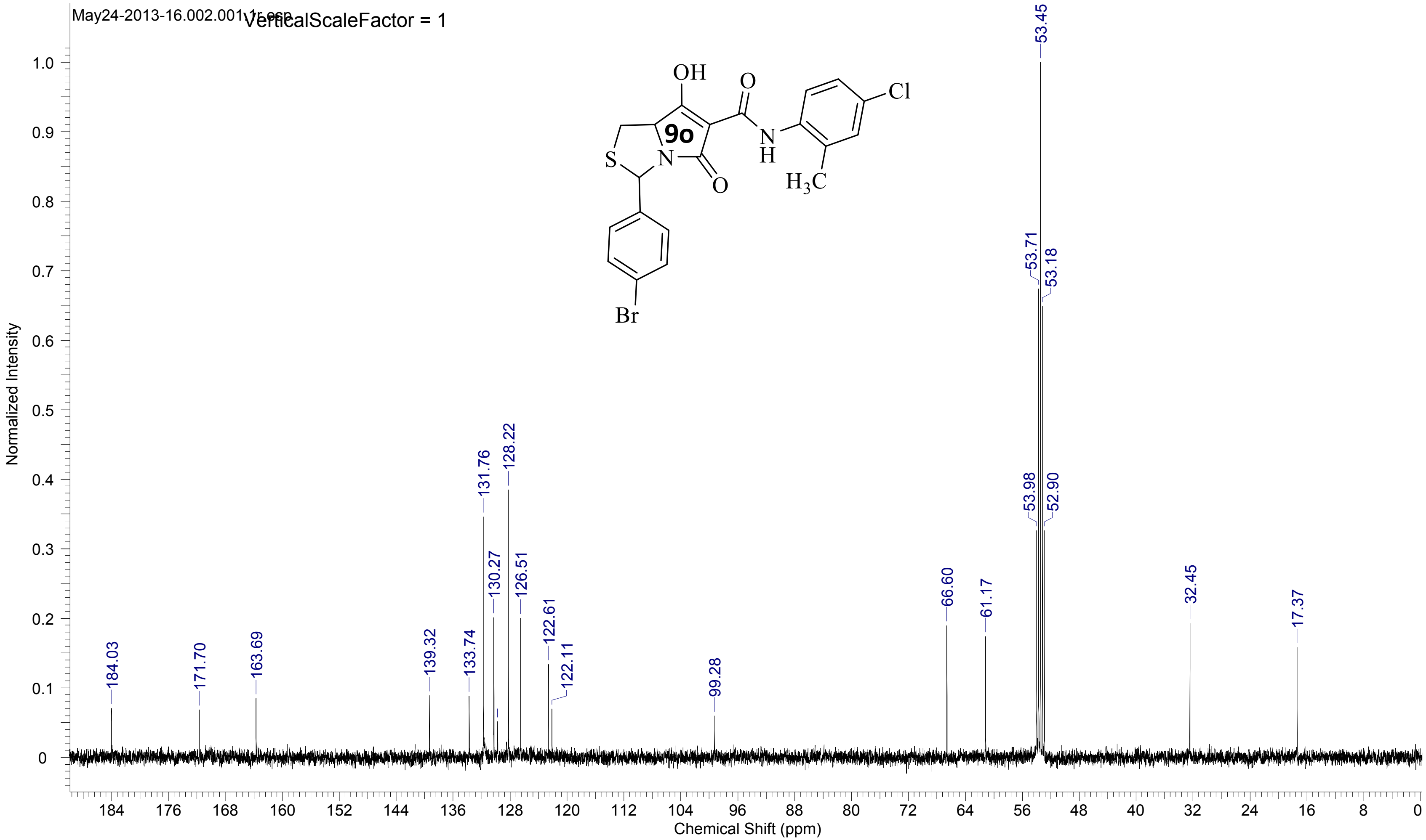
6/11/2013 9:19:56 PM

Acquisition Time (sec)	4.0894	***Comment***	Instrument AVN400 Chemist sarosh Group MGM SI-22 (1 M ACID WASH) h1acq.crl CD2Cl2 {C:\NMR} mgmgrp 16		
Date	25 May 2013 14:58:24	***Date Stamp***	25 May 2013 14:58:24		
File Name	F:\mass+nmr record of lab work at oxf\si-22\correct spectra\May24-2013-16\1\PDATA\1\1r				
Frequency (MHz)	400.25	***Nucleus***	1H	***Number of Transients***	16
Origin	avn400	***Original Points Count***	32768	***Owner***	dp-nmrgroup
Points Count	32768	***Pulse Sequence***	zg60	***Receiver Gain***	93.00
SW(cyclical) (Hz)	8012.82	***Solvent***	DICHLOROMETHANE-d2		
Spectrum Offset (Hz)	2349.8572	***Spectrum Type***	STANDARD	***Sweep Width (Hz)***	8012.58
Temperature (degree C)	21.868				



6/11/2013 9:21:26 PM

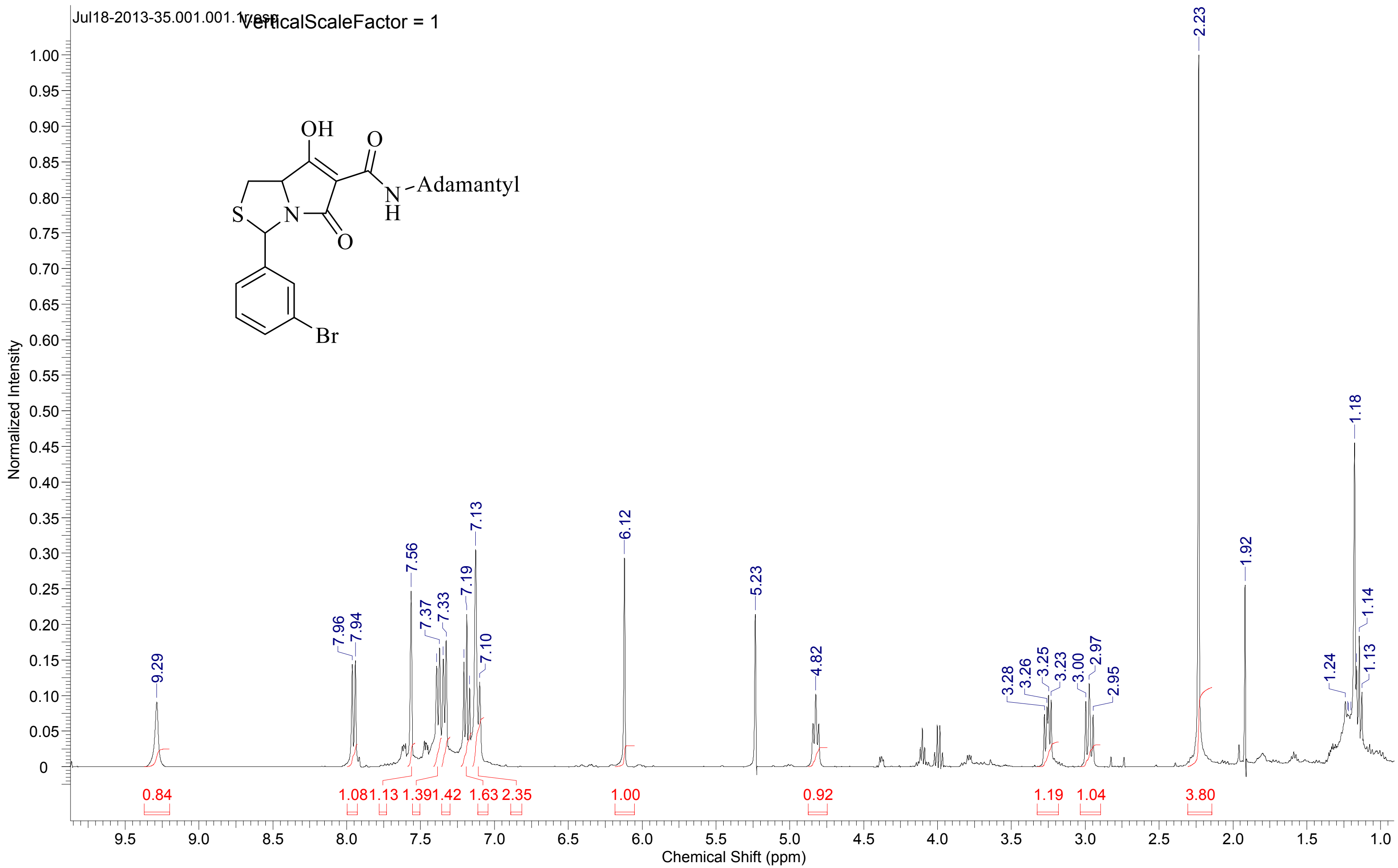
Acquisition Time (sec)	0.6291	***Comment***	Instrument AVN400 Chemist sarosh Group MGM SI-22 (1 M ACID WASH) c13acq.crl CD2Cl2 {C:\NMR} mgmgrp 16		
Date	25 May 2013 15:06:56	***Date Stamp***	25 May 2013 15:06:56		
File Name	F:\mass+nmr record of lab work at oxf\si-22\correct spectra\May24-2013-16\2\PDATA\1\1r				
Frequency (MHz)	100.64	***Nucleus***	13C	***Number of Transients***	256
Origin	avn400	***Original Points Count***	16384	***Owner***	dp-nmrgroup
Points Count	32768	***Pulse Sequence***	zgpg30	***Receiver Gain***	205.43
SW(cyclical) (Hz)	26041.67	***Solvent***	DICHLOROMETHANE-d2		
Spectrum Offset (Hz)	10064.2930	***Spectrum Type***	STANDARD	***Sweep Width (Hz)***	26040.87
Temperature (degree C)	23.050				



9o

7/22/2013 3:37:43 PM

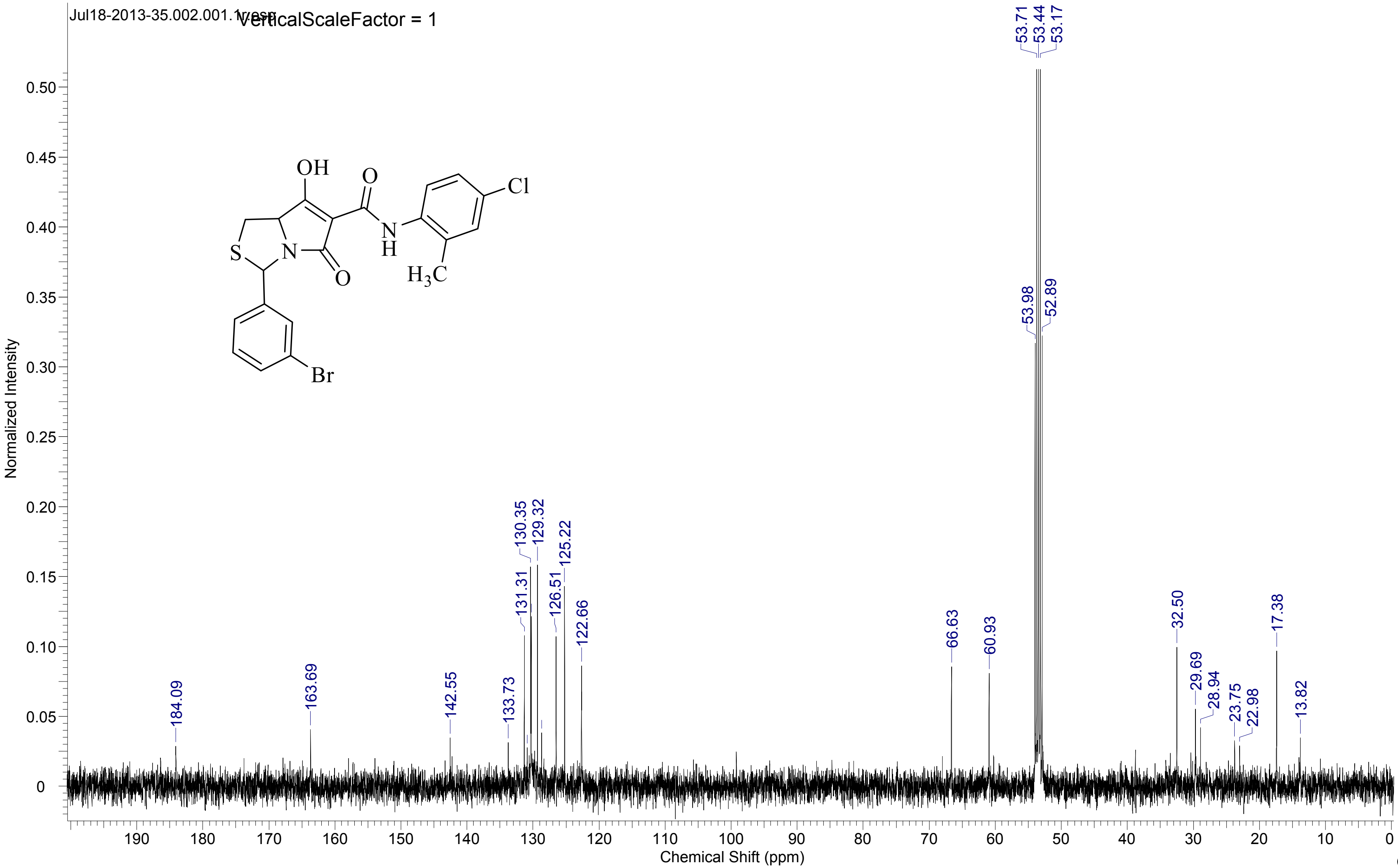
Acquisition Time (sec)	4.0894	***Comment***	Instrument AVN400 Chemist sarosh Group MGM si-21 h1acq.crl CD2Cl2 {C:\NMR} mgmgrp 35				
Date	19 Jul 2013 13:39:28	***Date Stamp***	19 Jul 2013 13:39:28				
File Name	F:\mass+nmr record of lab work at oxf\si-21\correct spectra\Jul18-2013-35\1\PDATA\1\1r					***Frequency (MHz)***	400.25
Nucleus	1H	***Number of Transients***	16	***Origin***	avn400	***Original Points Count***	32768
Owner	dp-nmrgroup	***Points Count***	32768	***Pulse Sequence***	zg60	***Receiver Gain***	93.00
SW(cyclical) (Hz)	8012.82	***Solvent***	DICHLOROMETHANE-d2			***Spectrum Offset (Hz)***	2349.9849
Spectrum Type	STANDARD	***Sweep Width (Hz)***	8012.58	***Temperature (degree C)***	22.210		



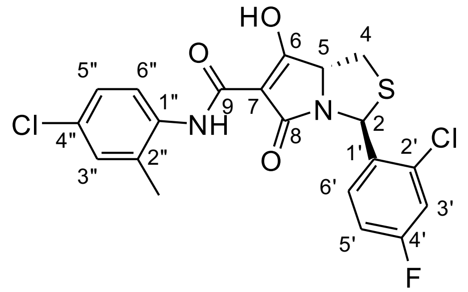
9o

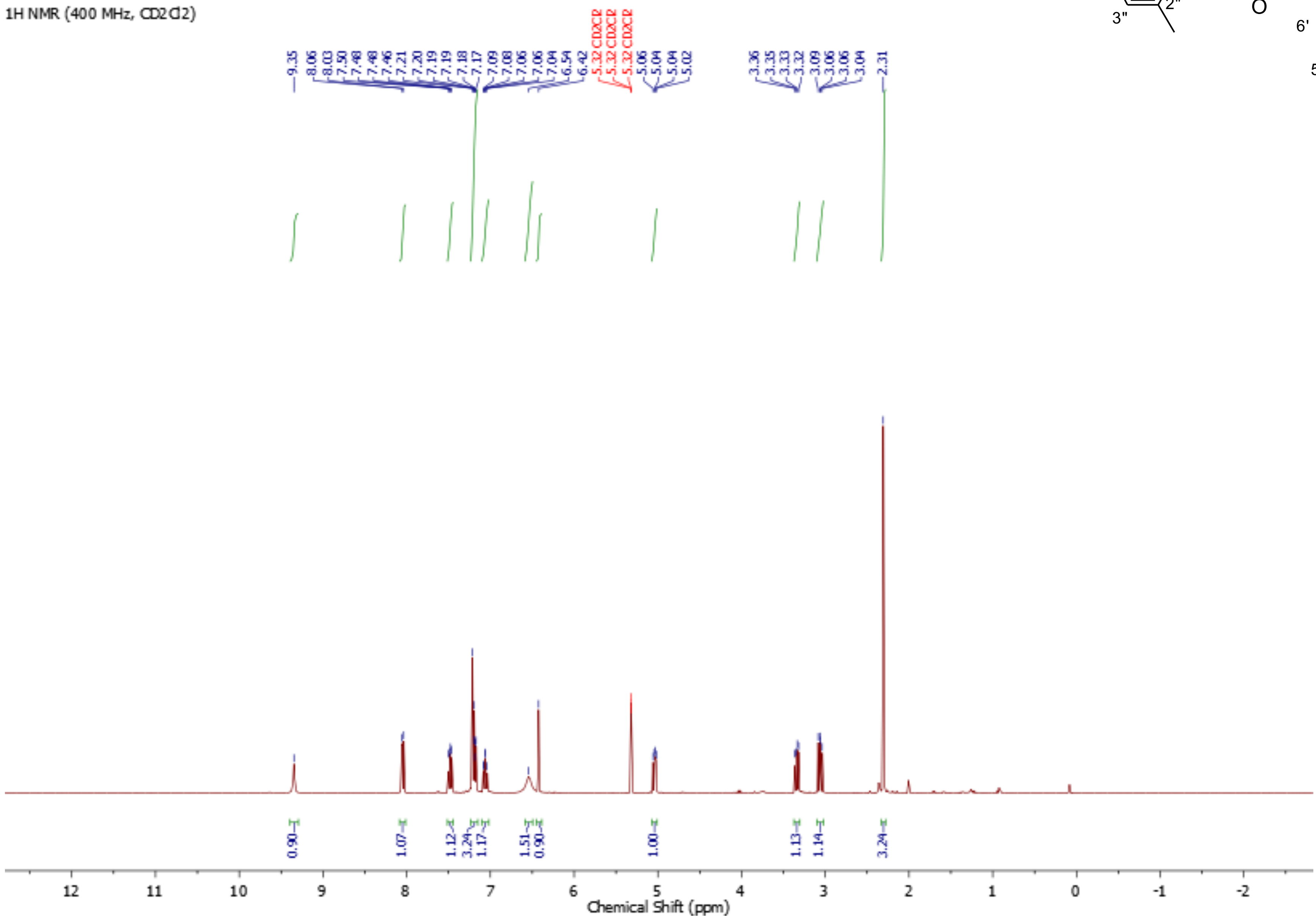
7/22/2013 3:46:22 PM

Acquisition Time (sec)	0.6291	***Comment***	Instrument AVN400 Chemist sarosh Group MGM si-21 c13acq.crl CD2Cl2 {C:\NMR} mgmgrp 35				
Date	19 Jul 2013 19:35:44	***Date Stamp***	19 Jul 2013 19:35:44				
File Name	F:\mass+nmr record of lab work at oxf\si-21\correct spectra\Jul18-2013-35\2\PDATA\1\1r					***Frequency (MHz)***	100.64
Nucleus	13C	***Number of Transients***	256	***Origin***	avn400	***Original Points Count***	16384
Owner	dp-nmrgroup	***Points Count***	32768	***Pulse Sequence***	zgpg30	***Receiver Gain***	205.43
SW(cyclical) (Hz)	26041.67	***Solvent***	DICHLOROMETHANE-d2			***Spectrum Offset (Hz)***	10064.2930
Spectrum Type	STANDARD	***Sweep Width (Hz)***	26040.87	***Temperature (degree C)***	23.813		



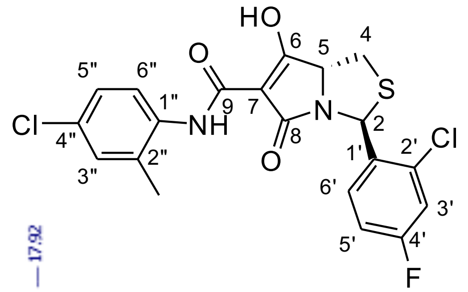
9q

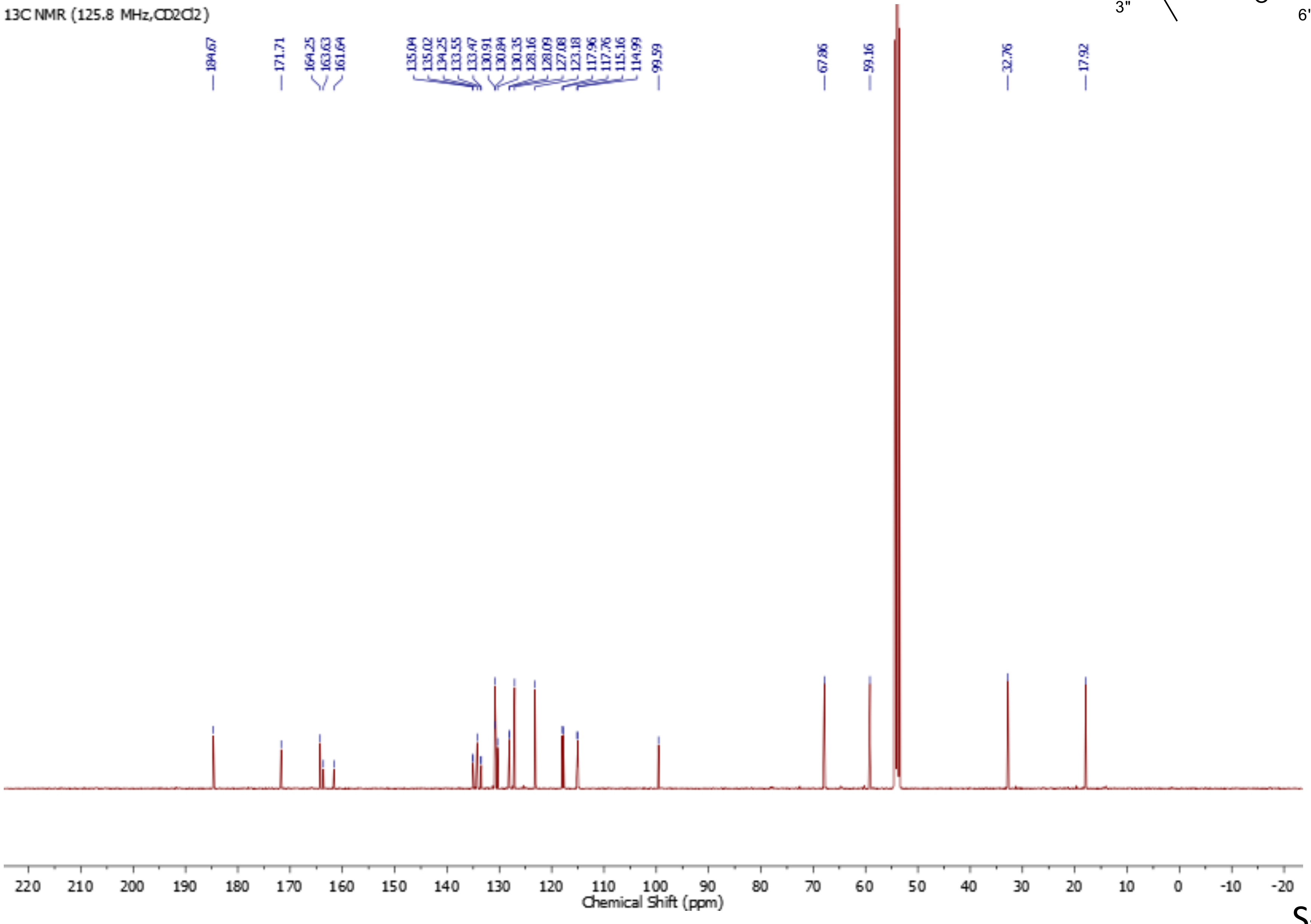

HO
6
5
4
O
5"
6"
S
1"
9
7
Cl
NH
N
2
4"
2"
8
2'
Cl
O
1'
3"
6'
3'
5'
4'
F


1H NMR (400 MHz, CD2Cl2)
9.35
8.06
8.03
7.50
7.48
7.48
7.46
7.21
7.20
7.19
7.19
7.18
7.17
7.09
7.08
7.06
7.06
7.04
6.54
6.42
5.32 CD2Cl2
5.32 CD2Cl2
5.32 CD2Cl2
5.06
5.04
5.04
5.02
3.36
3.35
3.33
3.32
3.09
3.06
3.06
3.04
2.31
0.90
1.07
1.12
3.24
1.17
1.51
0.90
1.00
1.13
1.14
3.24
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
Chemical Shift (ppm)

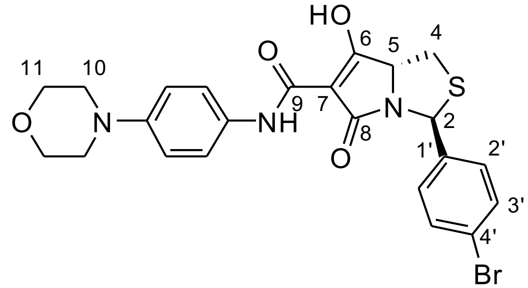
S-

9q

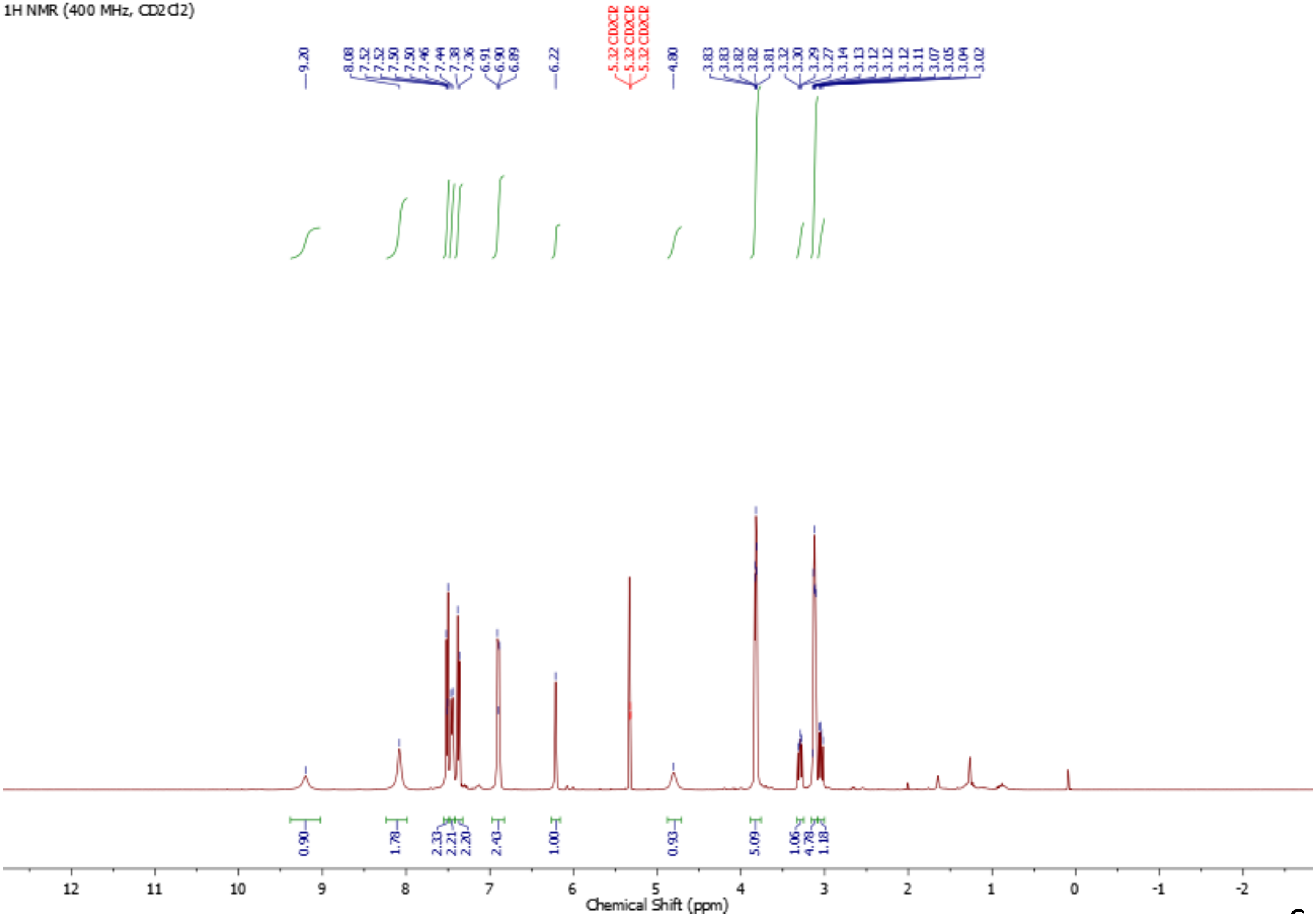

HO
6
5
4
S
2
N
8
O
7
9
O
NH
1"
2"
3"
4"
5"
6"
Cl
1'
2'
Cl
3'
4'
F
5'
6'


13C NMR (125.8 MHz,CD2Cl2)
184.67
171.71
164.25
163.63
161.64
135.04
135.02
134.25
133.55
133.47
130.91
130.84
130.35
128.16
128.09
127.08
123.18
117.96
117.76
115.16
114.99
99.59
67.86
59.16
32.76
17.92
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

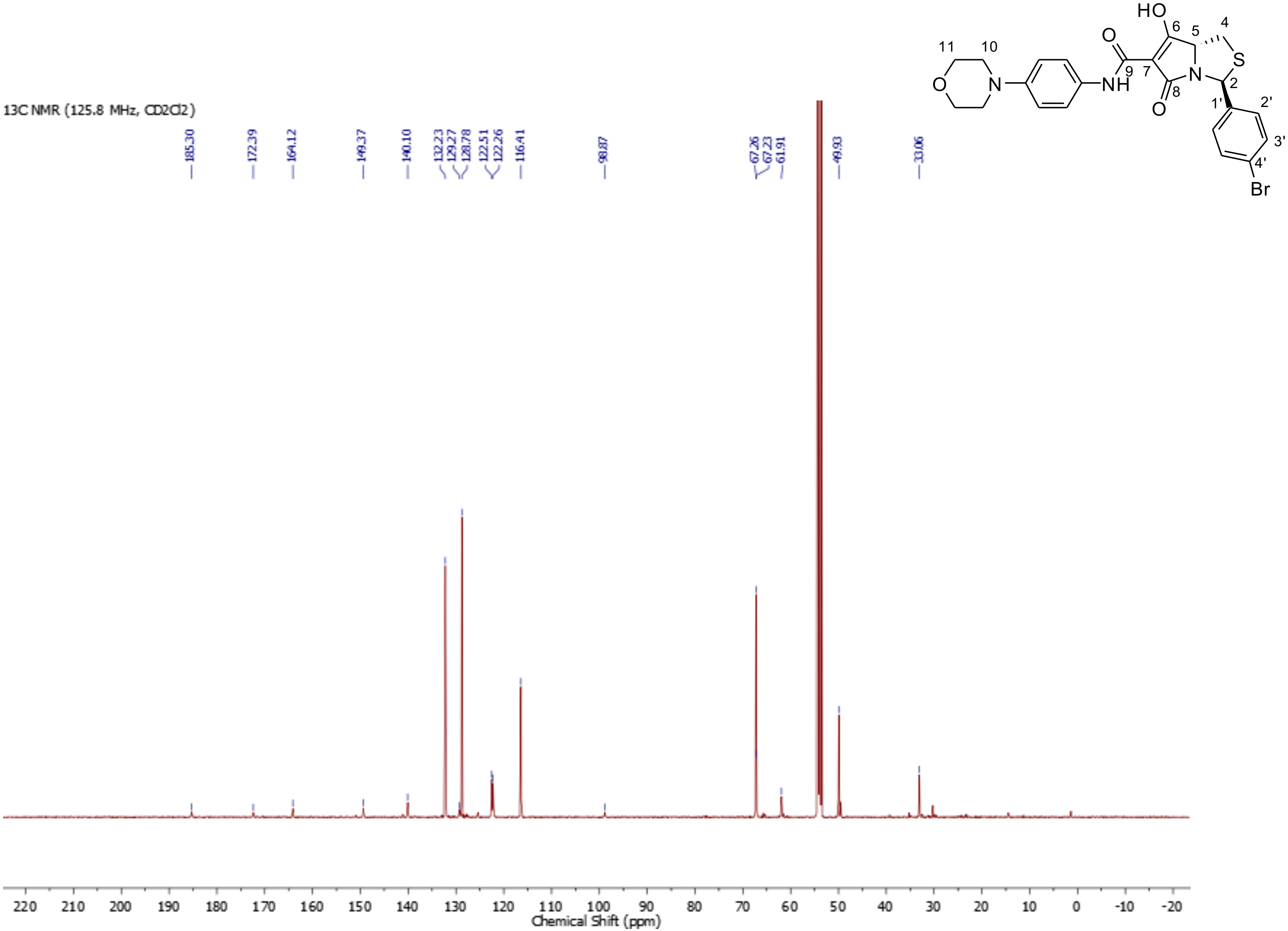
9r



1H NMR (400 MHz, CD2Cl2)

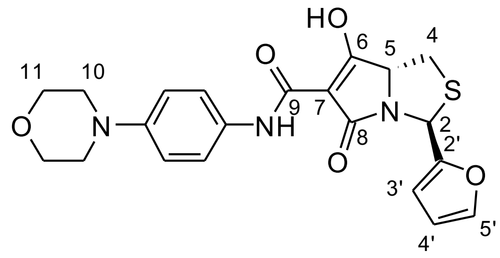


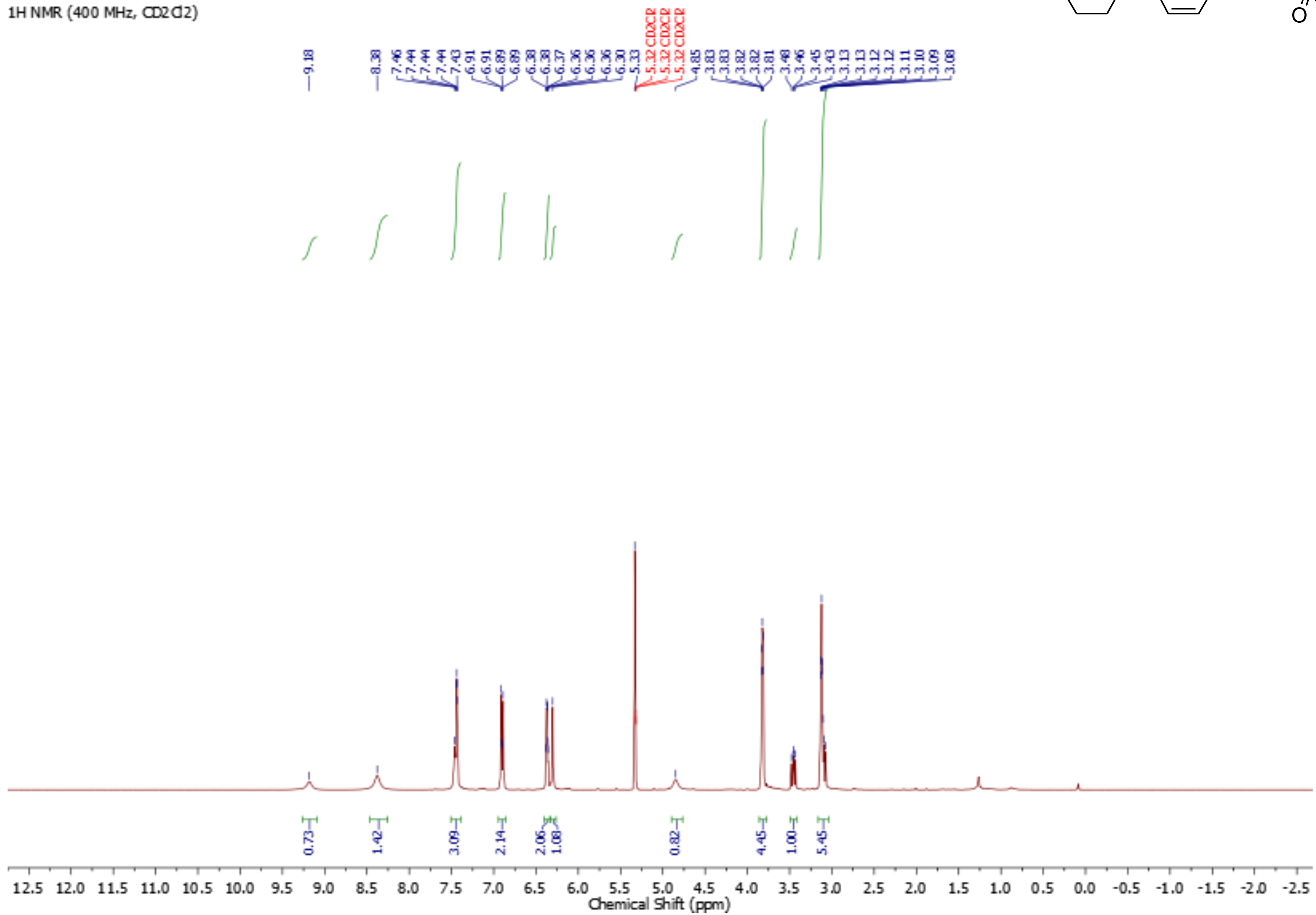
9r



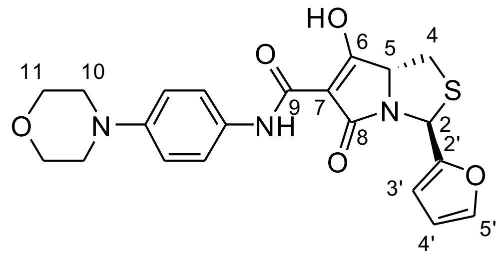
13C NMR (125.8 MHz, CD2Cl2)
185.30
172.39
164.12
149.37
140.10
132.23
129.27
128.78
122.51
122.26
116.41
98.87
67.26
67.23
61.91
49.93
33.06
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)
HO
O
N
NH
S
Br
O
O
11
10
9
8
7
6
5
4
2
1'
2'
3'
4'

9s

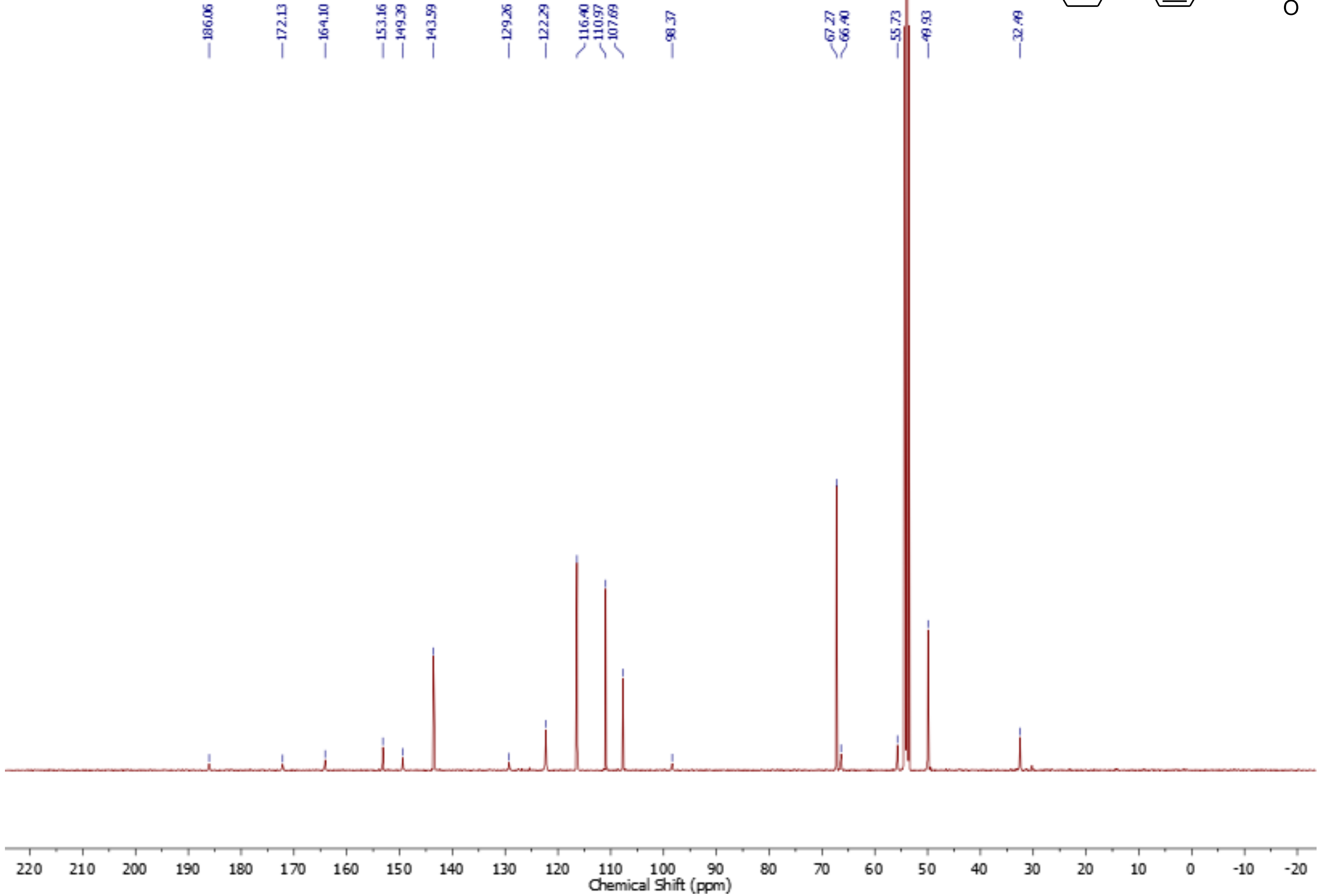

HO
6
5
4
O
11
10
S
9
7
N
2
O
N
NH
8
2'
O
O
3'
O
5'
4'


1H NMR (400 MHz, CD2Cl2)
9.18
8.38
7.46
7.44
7.44
7.44
7.43
6.91
6.91
6.89
6.89
6.38
6.38
6.37
6.36
6.36
6.36
6.30
5.33
5.32 CD2Cl2
5.32 CD2Cl2
5.32 CD2Cl2
4.85
3.83
3.83
3.82
3.82
3.81
3.48
3.46
3.45
3.43
3.13
3.13
3.12
3.12
3.11
3.10
3.09
3.08
0.73
1.42
3.09
2.14
2.06
1.08
0.82
4.45
1.00
5.45
Chemical Shift (ppm)

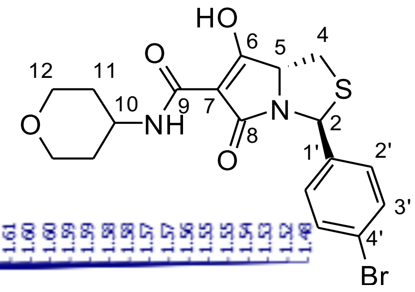
9s

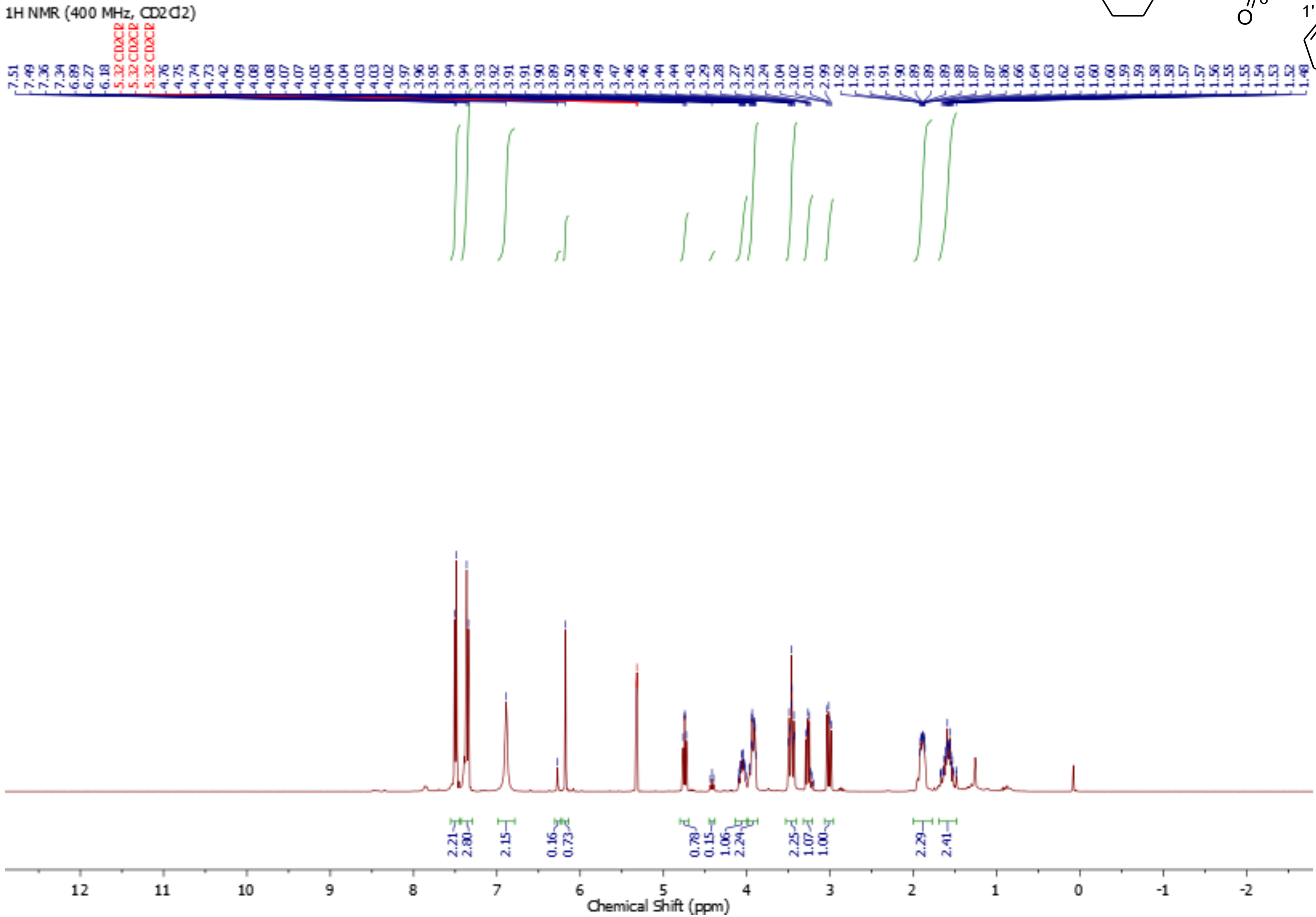


13C NMR (125.8 MHz, CD2Cl2)

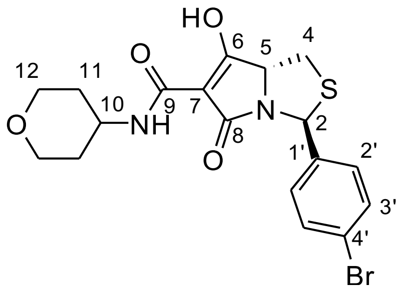


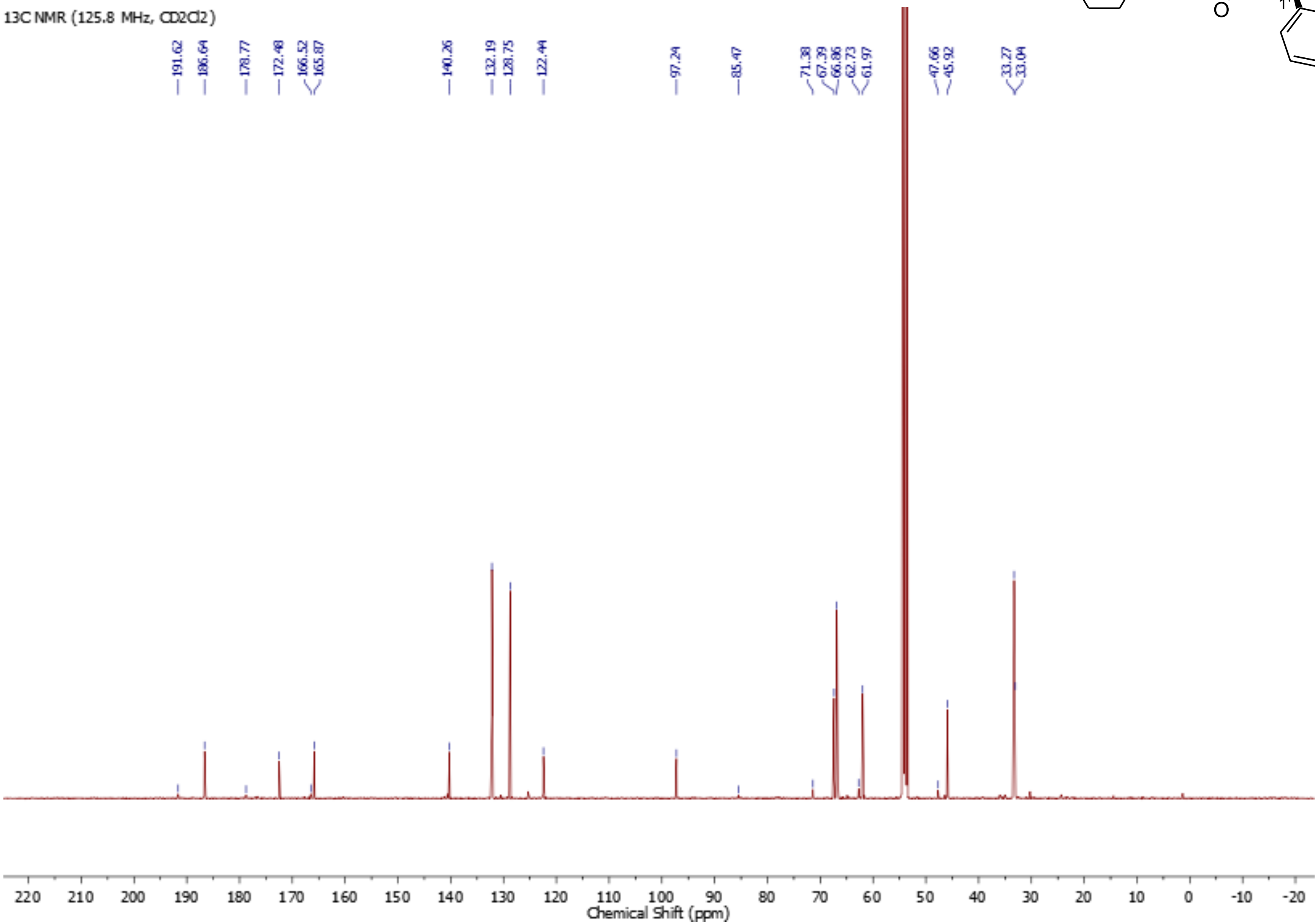
9t


HO
O
NH
N
S
O
O
Br
12
11
10
9
7
6
5
4
2
8
1'
2'
3'
4'

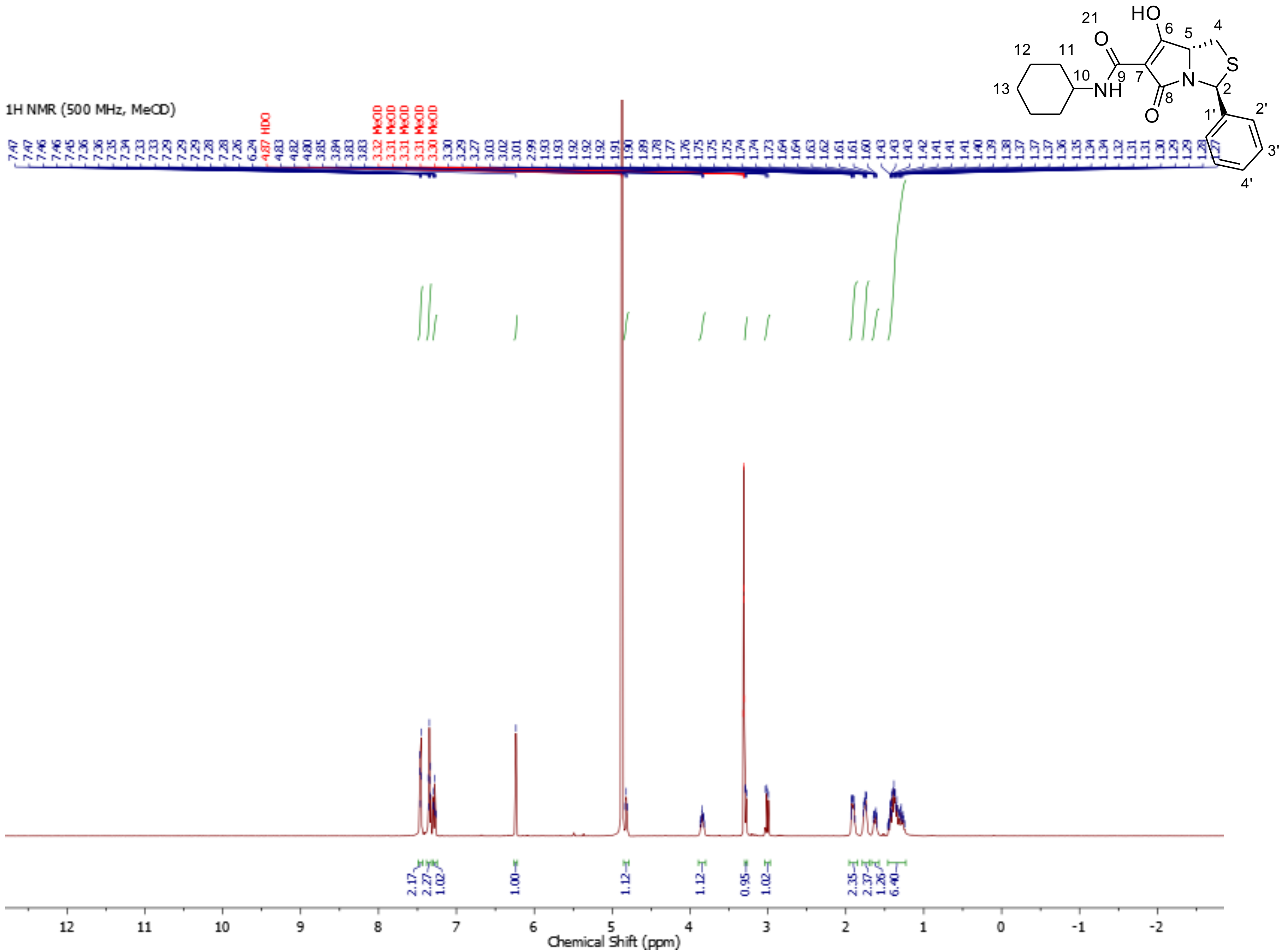

1H NMR (400 MHz, CD2Cl2)
Chemical Shift (ppm)

9t

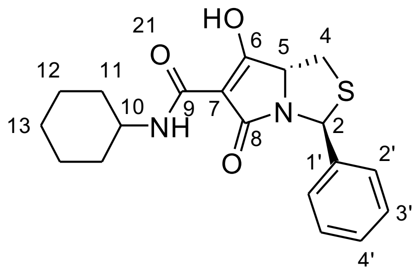

HO
O
N
S
NH
O
O
Br
6
5
4
12
11
10
9
7
2
8
1'
2'
3'
4'


13C NMR (125.8 MHz, CD2Cl2)
191.62
186.64
178.77
172.48
166.52
165.87
140.26
132.19
128.75
122.44
97.24
85.47
71.38
67.39
66.86
62.73
61.97
47.66
45.92
33.27
33.04
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

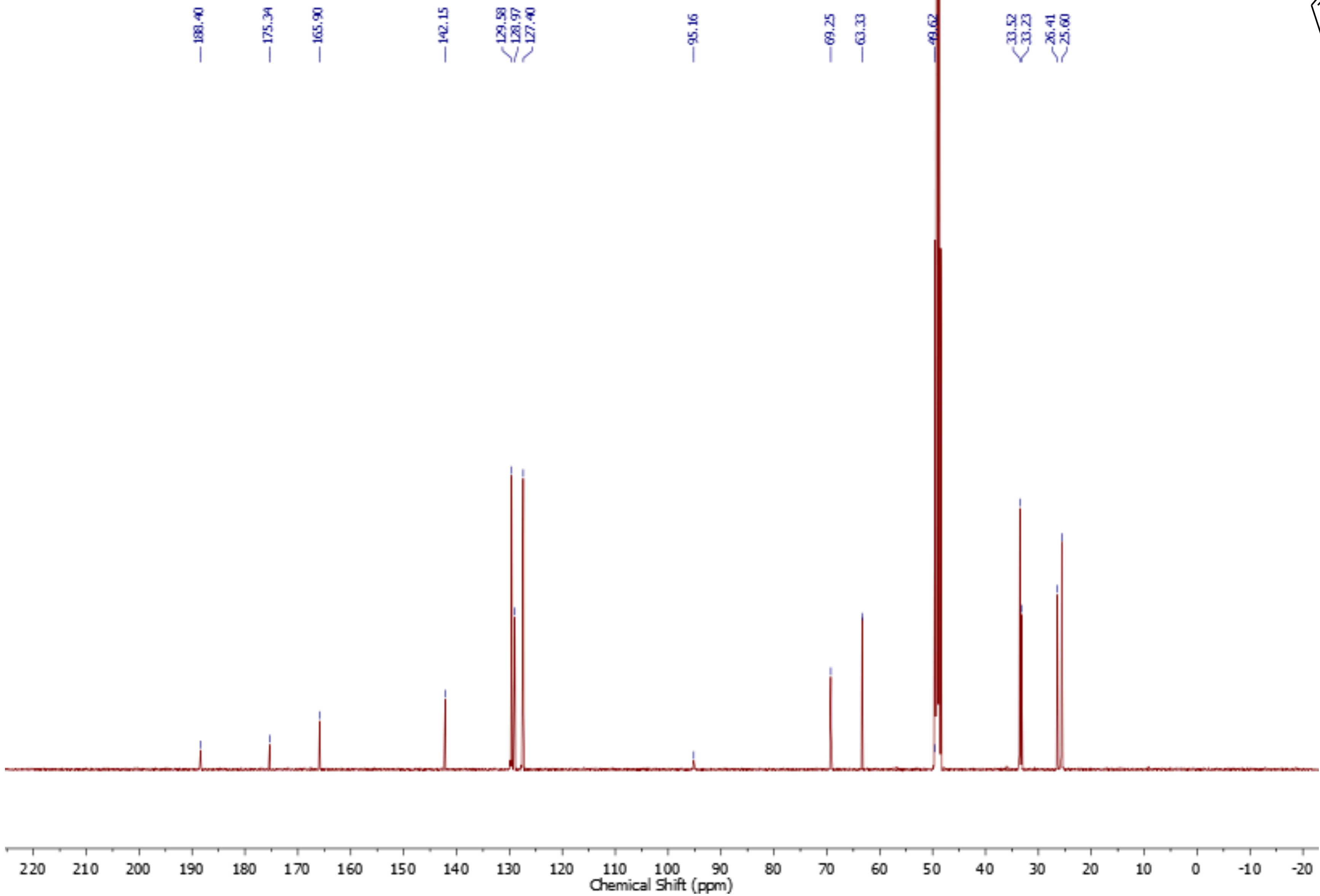
9u


1H NMR (500 MHz, MeOD)
Chemical Shift (ppm)
HDO
MeOD
2.17
2.27
1.02
1.00
1.12
1.12
0.95
1.02
2.35
2.37
1.26
6.40
HO
O
NH
N
S
O

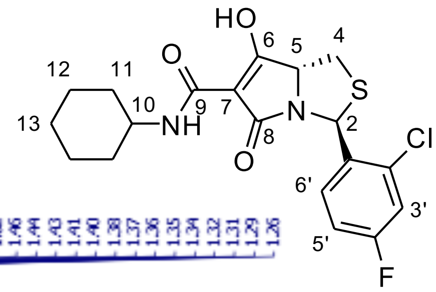
9u

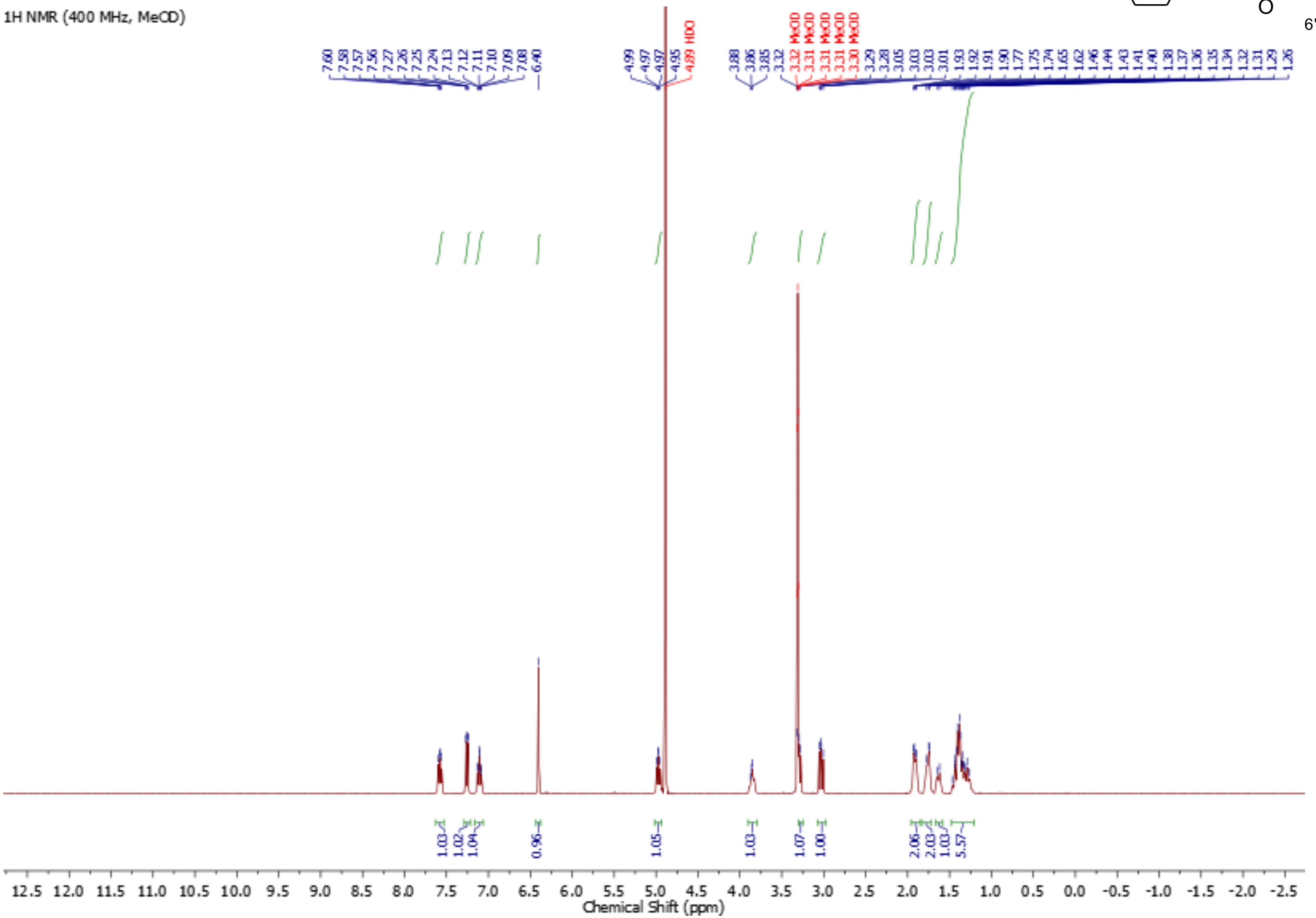


13C NMR (125.8 MHz, MeOD)

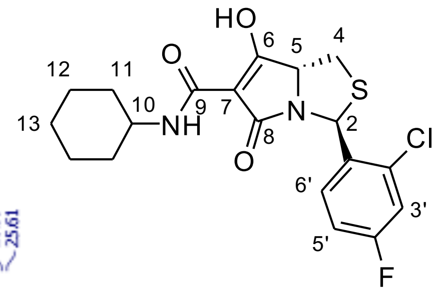


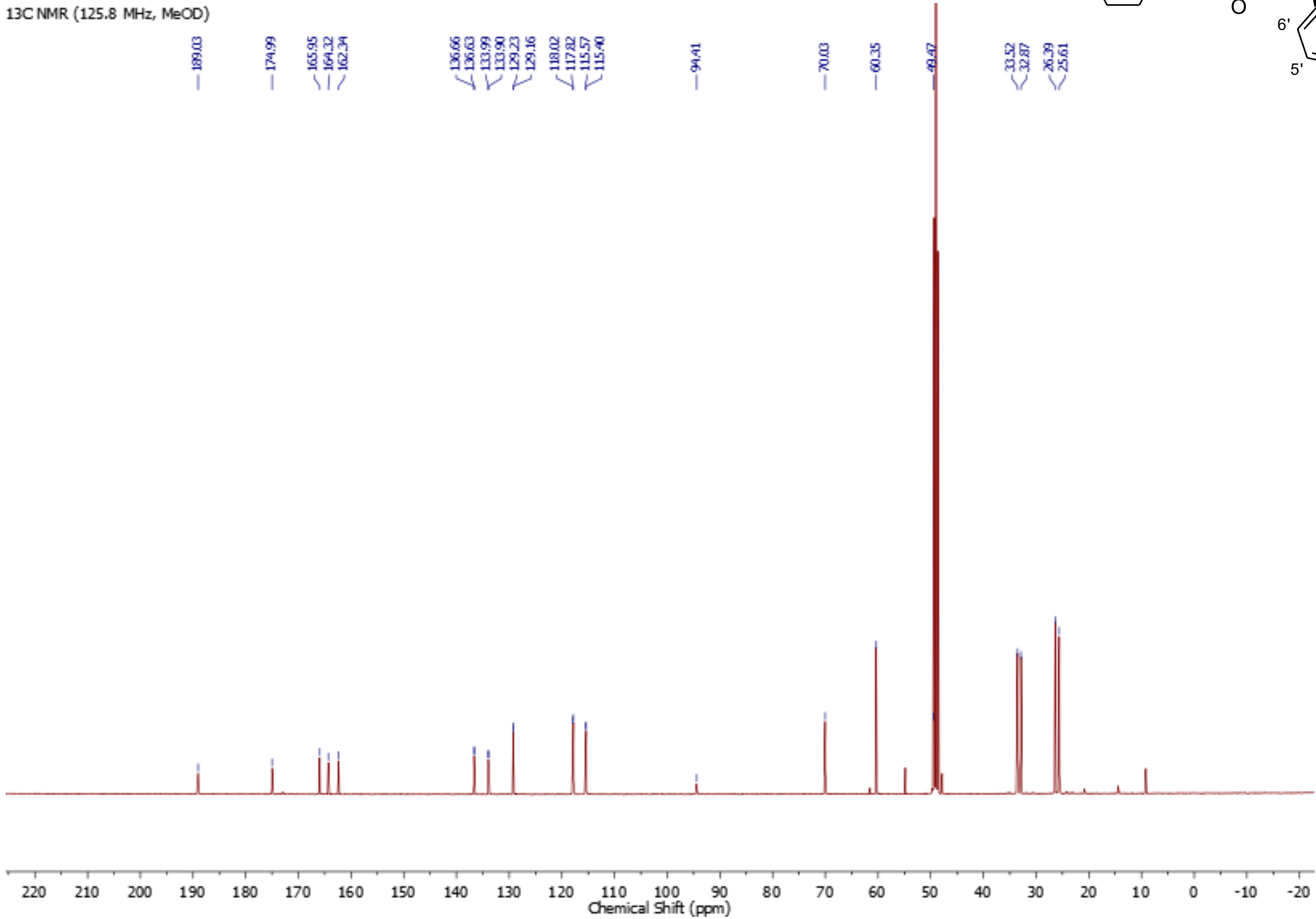
9v


HO
O
NH
N
S
Cl
F
O
2
3'
4
5
5'
6
6'
7
8
9
10
11
12
13

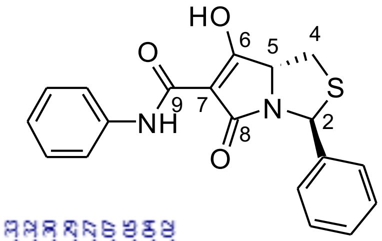

1H NMR (400 MHz, MeOD)
7.60 7.58 7.57 7.56 7.27 7.26 7.25 7.24 7.13 7.12 7.11 7.10 7.09 7.08 6.40
4.99 4.97 4.97 4.95 4.89 HDO
3.88 3.86 3.85 3.32 3.32 MeOD 3.31 MeOD 3.31 MeOD 3.31 MeOD 3.30 MeOD 3.29 3.28 3.05 3.03 3.03 3.01
1.93 1.92 1.91 1.90 1.77 1.75 1.74 1.63 1.62 1.46 1.44 1.43 1.41 1.40 1.38 1.37 1.36 1.35 1.34 1.32 1.31 1.29 1.26
1.03 1.02 1.04 0.96 1.05 1.03 1.07 1.00 2.06 2.03 1.03 5.57
12.5 12.0 11.5 11.0 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 -1.0 -1.5 -2.0 -2.5
Chemical Shift (ppm)

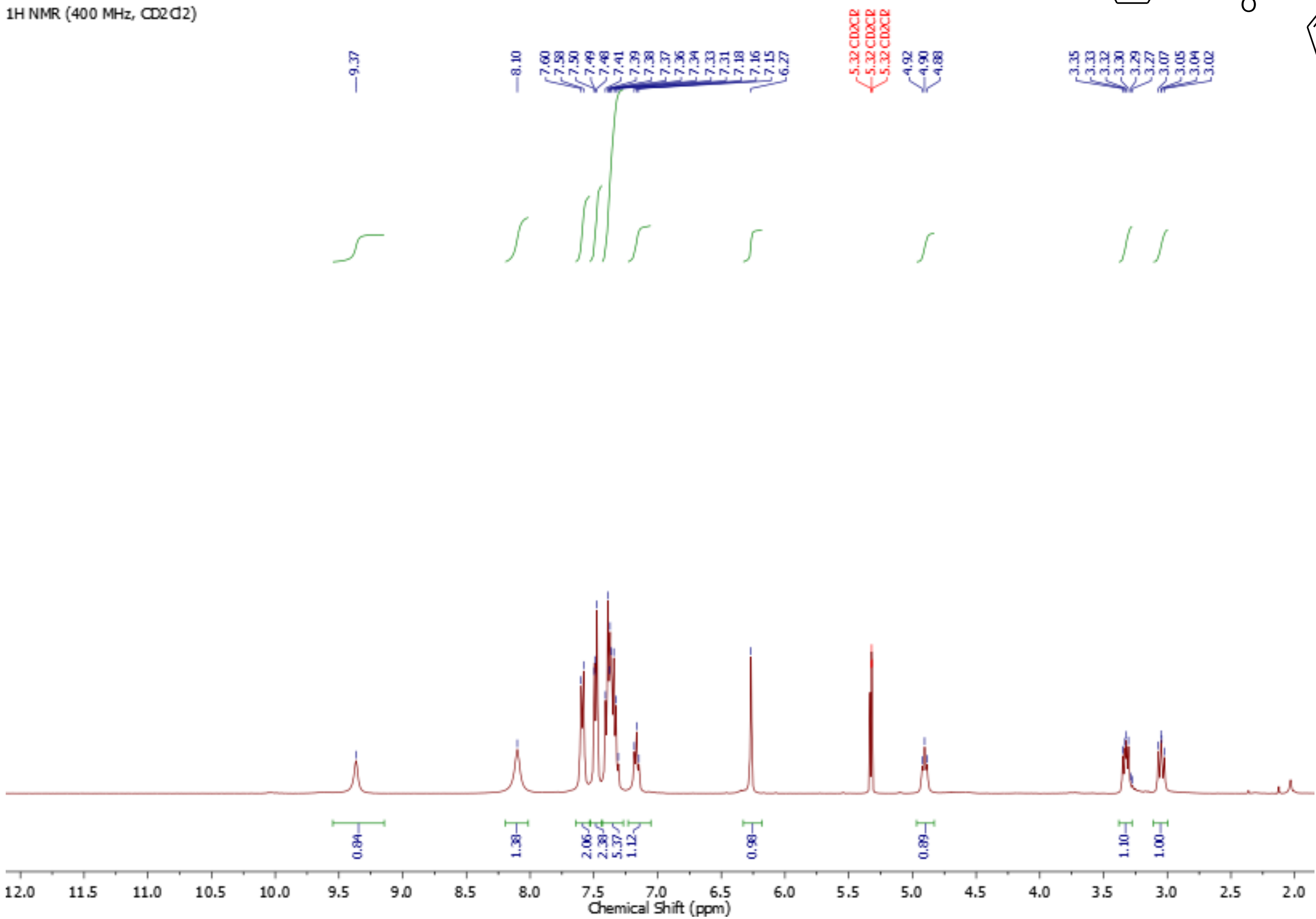
9v


HO
O
O
NH
N
S
Cl
F
2
3'
4
5
5'
6
6'
7
8
9
10
11
12
13

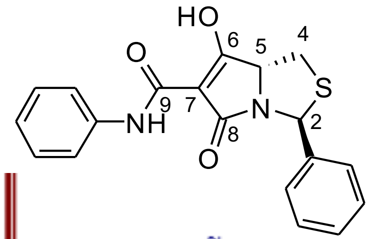

13C NMR (125.8 MHz, MeOD)
189.03
174.99
165.95
164.32
162.34
136.66
136.63
133.99
133.90
129.23
129.16
118.02
117.82
115.57
115.40
94.41
70.03
60.35
49.47
33.52
32.87
26.39
25.61
Chemical Shift (ppm)

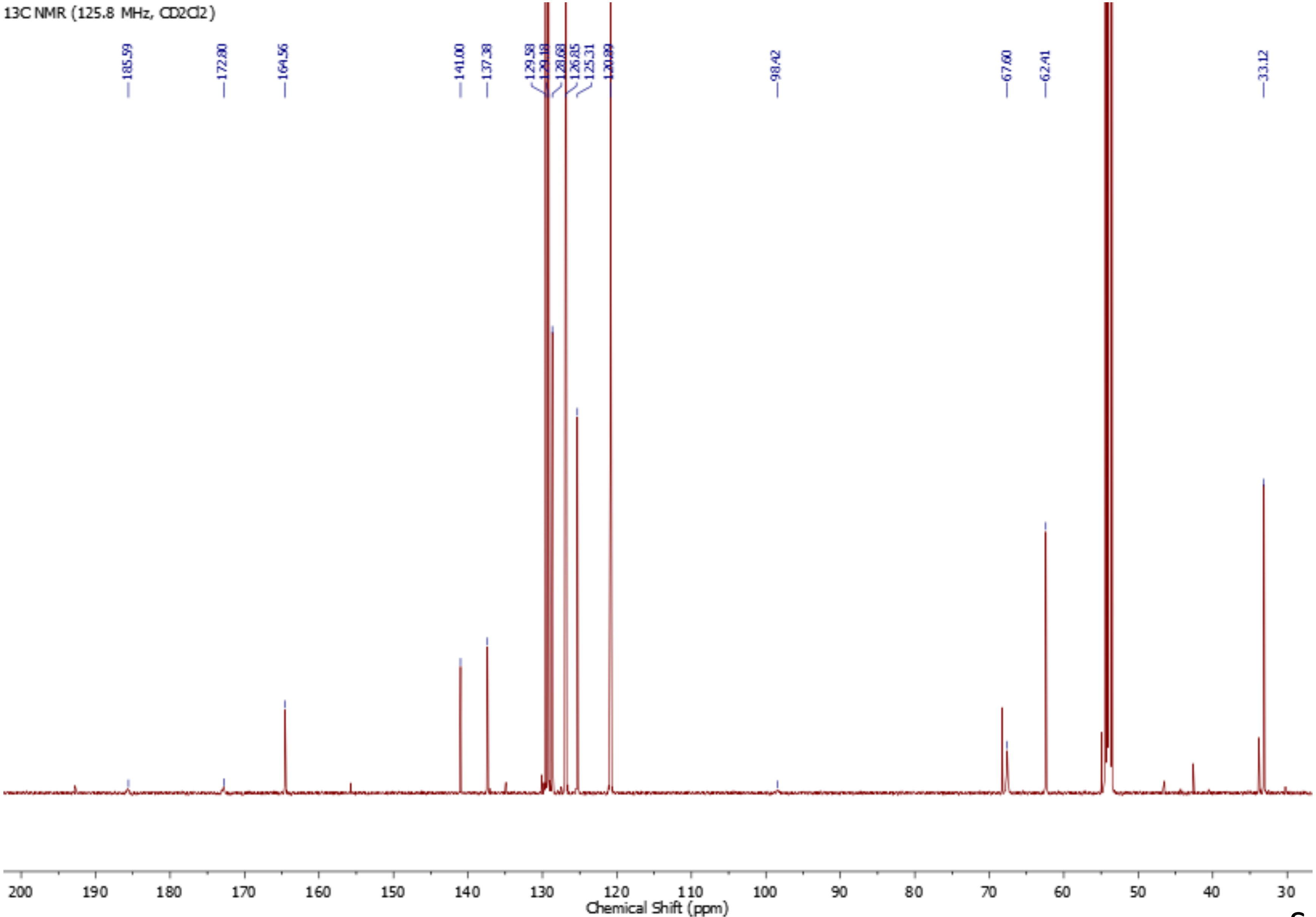
9w


HO
6
5
4
O
S
9
7
N
2
NH
8
O

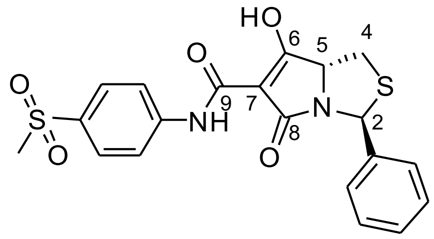

1H NMR (400 MHz, CD2Cl2)
9.37
8.10
7.60
7.58
7.50
7.49
7.48
7.41
7.39
7.38
7.37
7.36
7.34
7.33
7.31
7.18
7.16
7.15
6.27
5.32 CD2Cl2
5.32 CD2Cl2
5.32 CD2Cl2
4.92
4.90
4.88
3.35
3.33
3.32
3.30
3.29
3.27
3.07
3.05
3.04
3.02
0.84
1.38
2.06
2.38
5.37
1.12
0.98
0.89
1.10
1.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
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
Chemical Shift (ppm)

9w

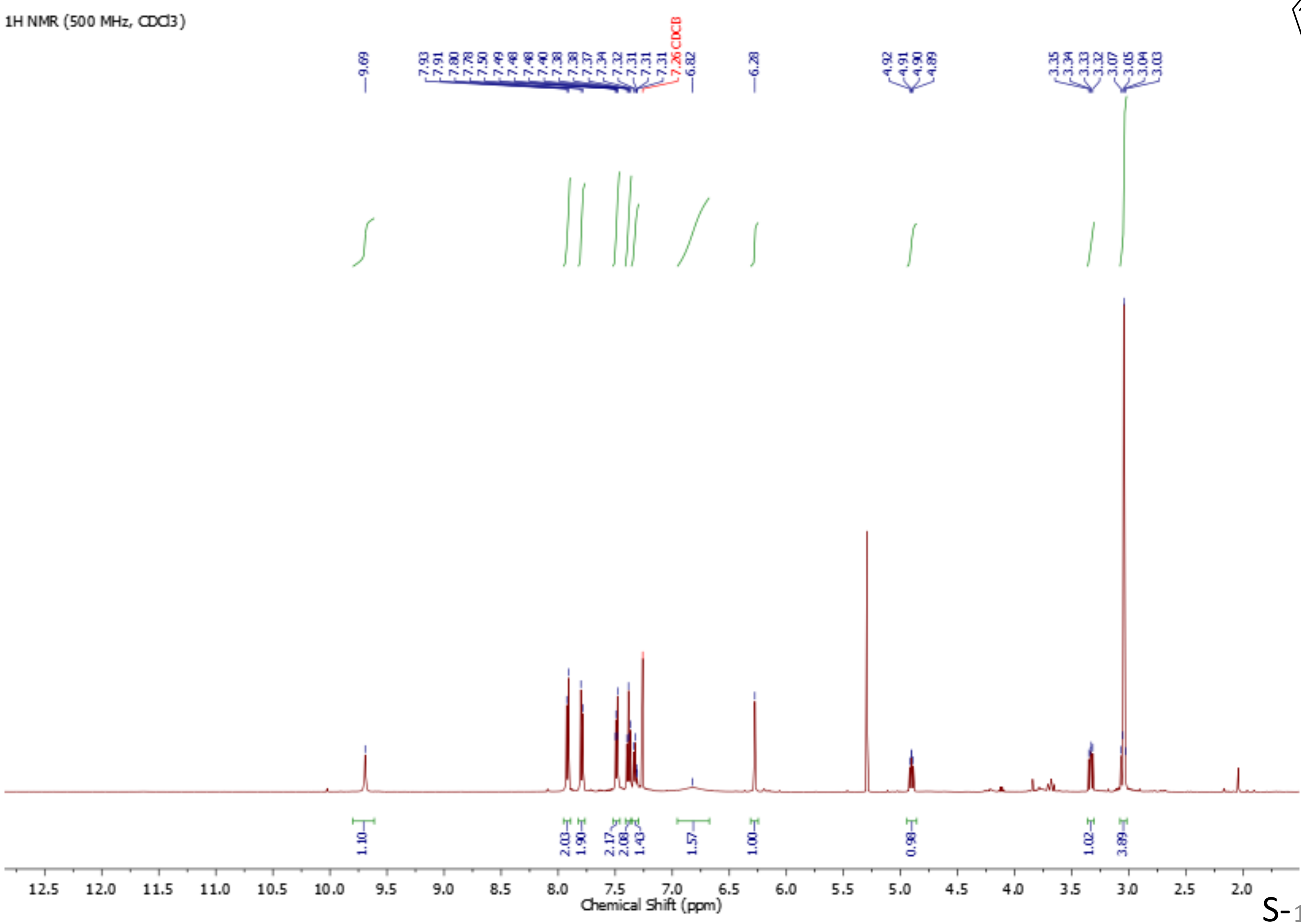

HO
6
5
4
O
S
9
7
NH
N
2
8
O


13C NMR (125.8 MHz, CD2Cl2)
185.59
172.80
164.56
141.00
137.38
129.58
129.18
128.68
126.85
125.31
120.89
98.42
67.60
62.41
33.12
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
Chemical Shift (ppm)

9x

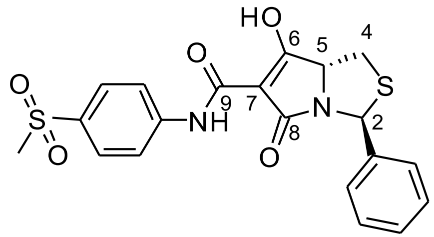


HO
6
5
4
O
S
O
S
O
NH
9
7
N
2
8
O

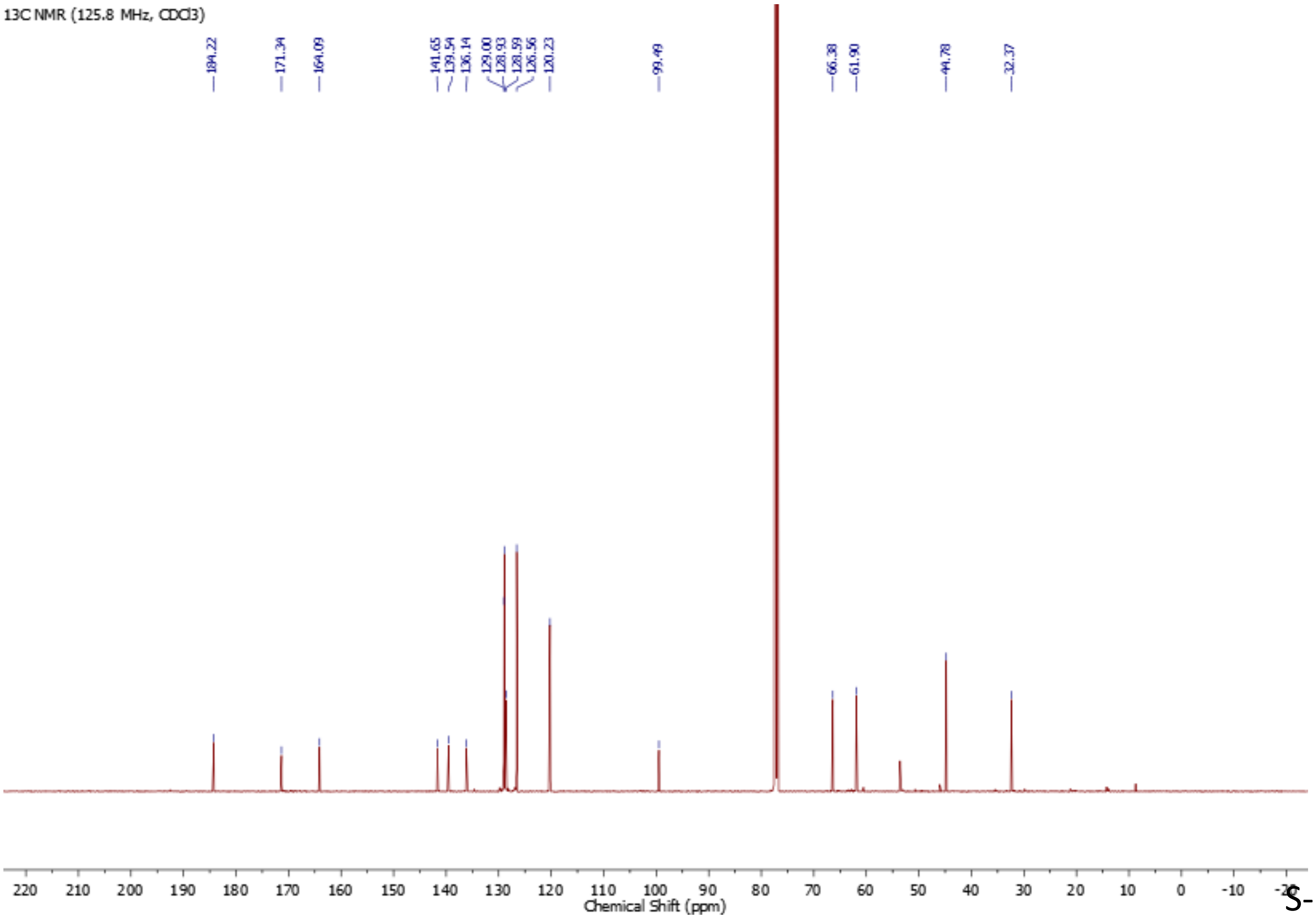


1H NMR (500 MHz, CDCl3)
9.69
7.93
7.91
7.80
7.78
7.50
7.49
7.48
7.48
7.40
7.38
7.38
7.37
7.34
7.32
7.31
7.31
7.31
7.26 CDCl3
6.82
6.28
4.92
4.91
4.90
4.89
3.35
3.34
3.33
3.32
3.07
3.05
3.04
3.03
1.10
2.03
1.90
2.17
2.08
1.43
1.57
1.00
0.98
1.02
3.89
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
Chemical Shift (ppm)

9x

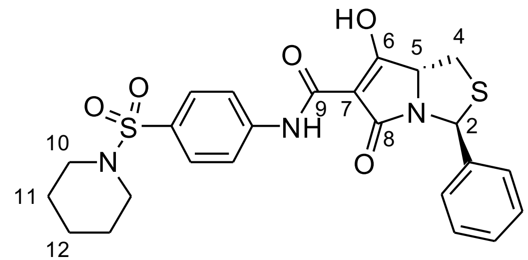


HO
6
5
4
O
S
O
9
7
N
2
NH
O
8
O
O

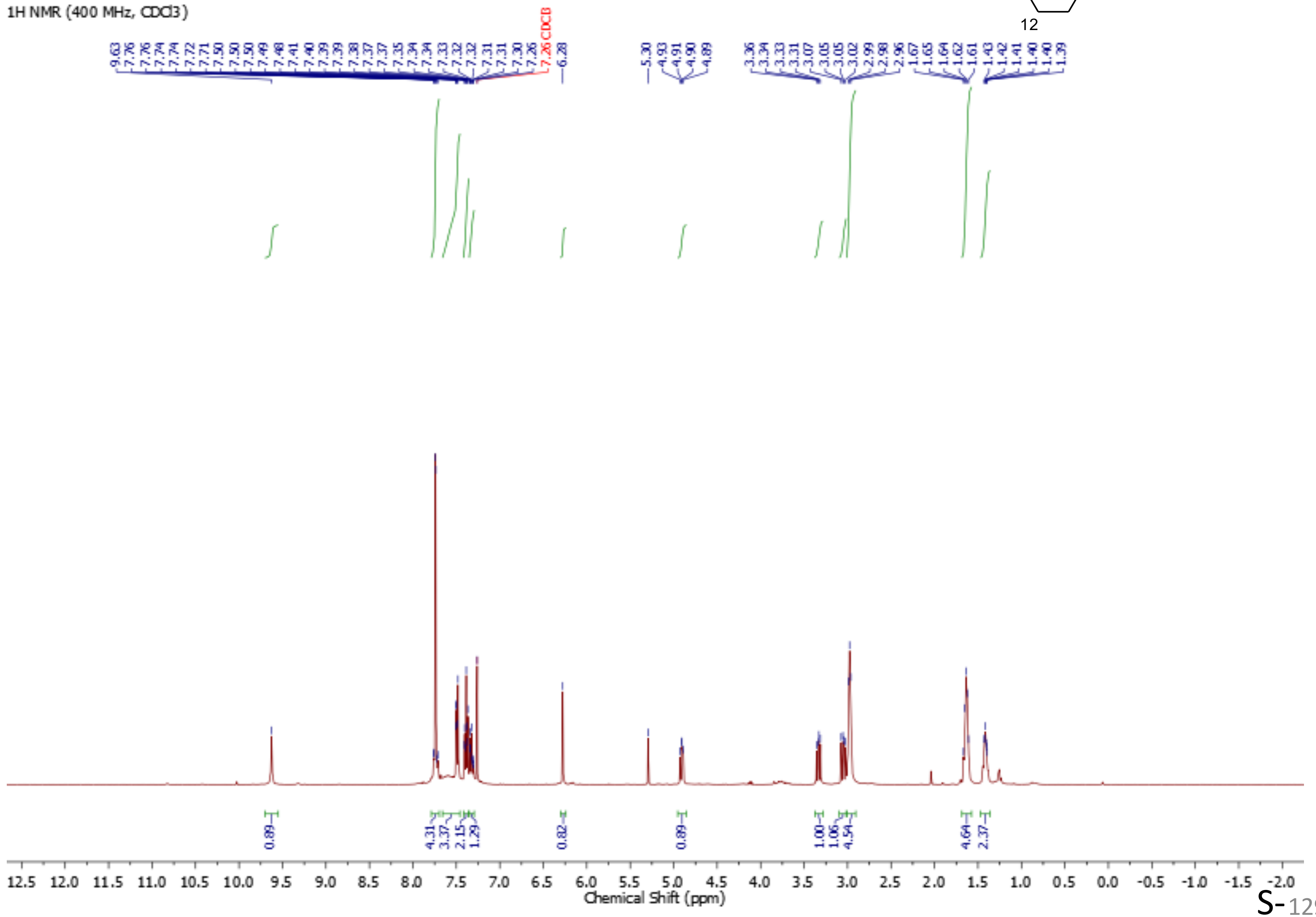


13C NMR (125.8 MHz, CDCl3)
184.22
171.34
164.09
141.65
139.54
136.14
129.00
128.93
128.59
126.56
120.23
99.49
66.38
61.90
44.78
32.37
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Chemical Shift (ppm)

9y

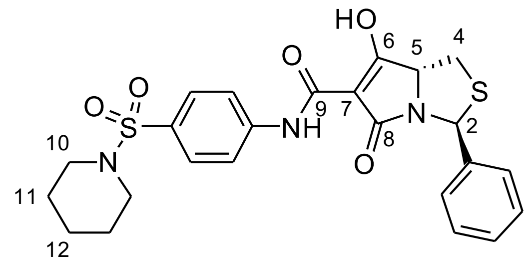


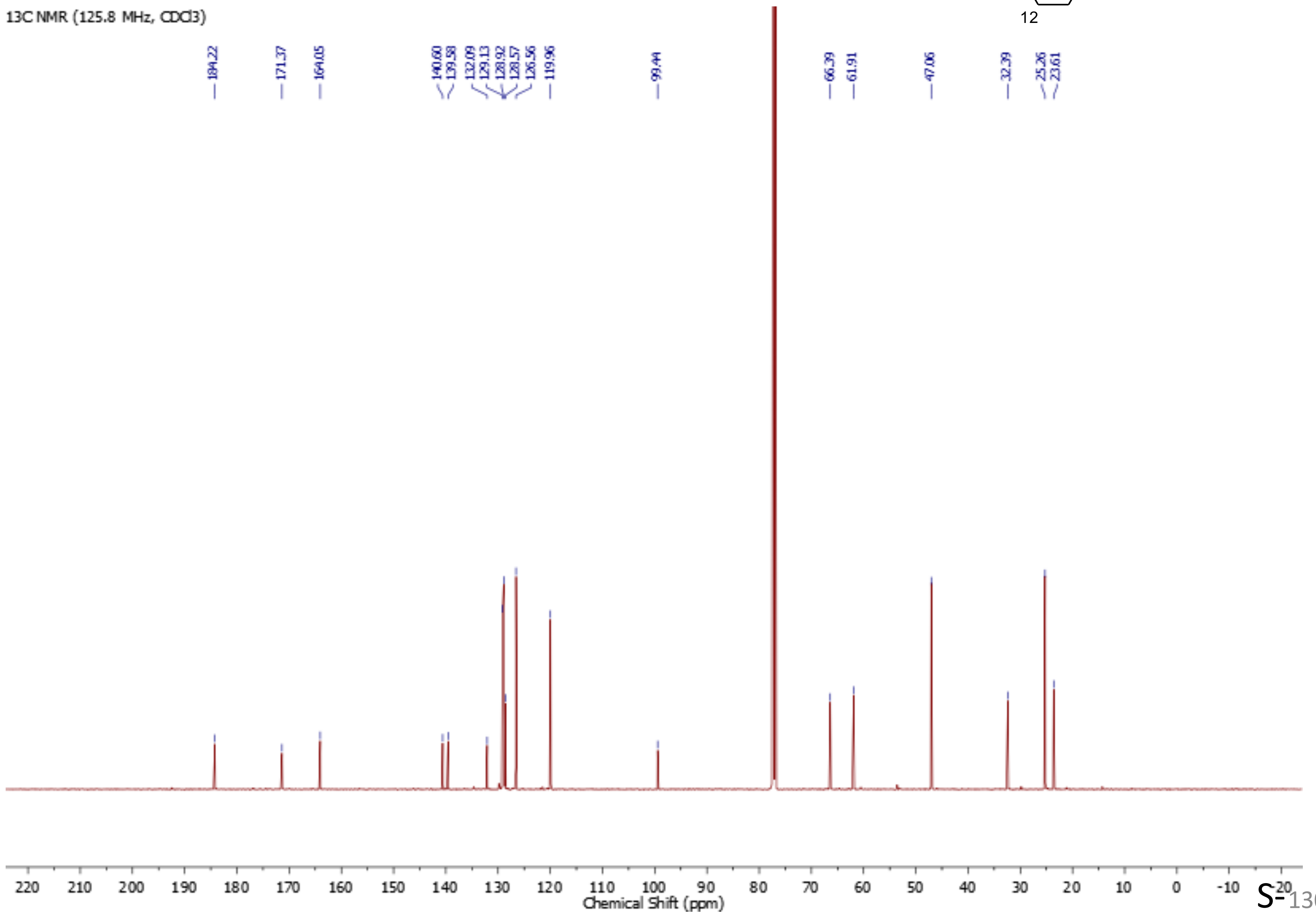
HO
O
O
O
S
N
NH
N
S
O
2
4
5
6
7
8
9
10
11
12



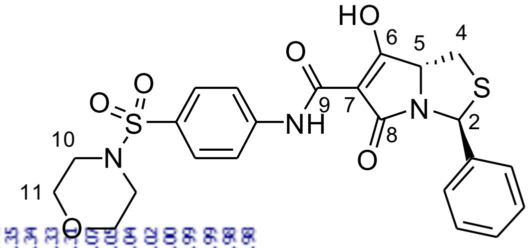
1H NMR (400 MHz, CDCl3)
7.26 CDCl3
Chemical Shift (ppm)

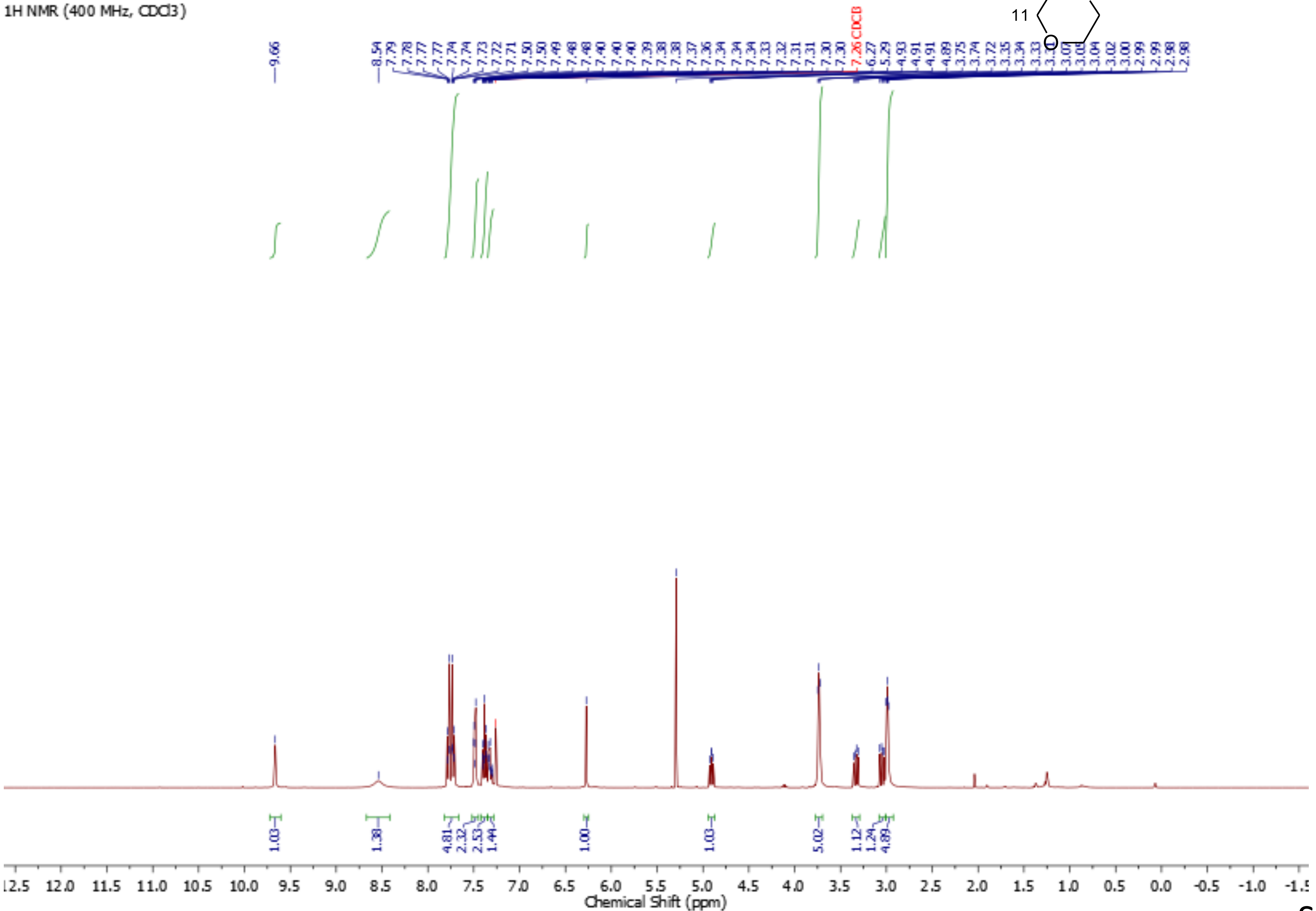
9y


HO
O
O
O
S
NH
N
N
S
O
2
4
5
6
7
8
9
10
11
12

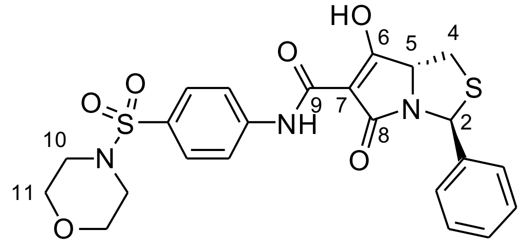

13C NMR (125.8 MHz, CDCl3)
184.22
171.37
164.05
140.60
139.58
132.09
129.13
128.92
128.57
126.56
119.96
99.44
66.39
61.91
47.06
32.39
25.26
23.61
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

9z

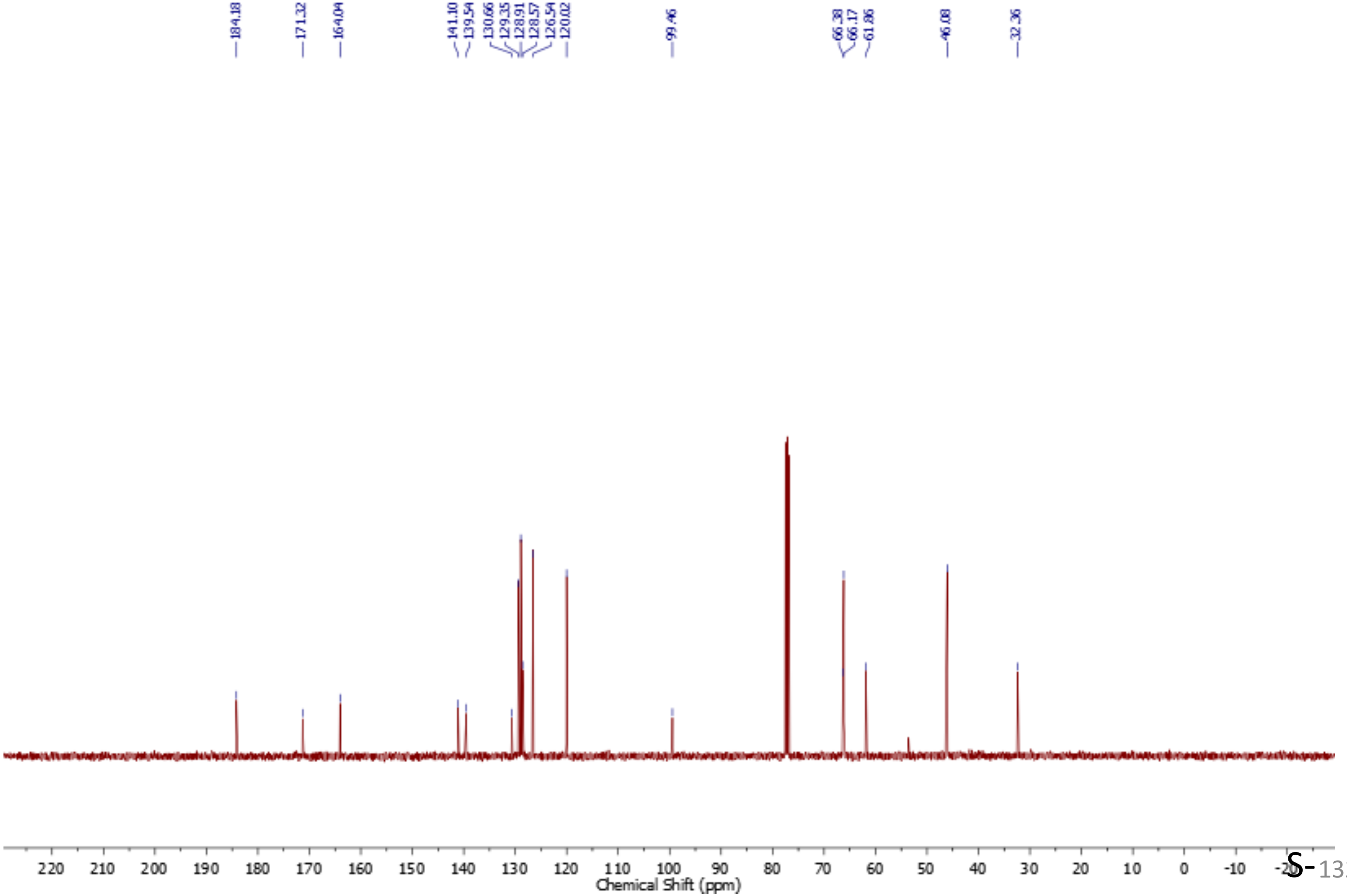

HO
O
O
O
S
N
NH
N
S
O
O
2
4
5
6
7
8
9
10
11


1H NMR (400 MHz, CDCl3)
Chemical Shift (ppm)

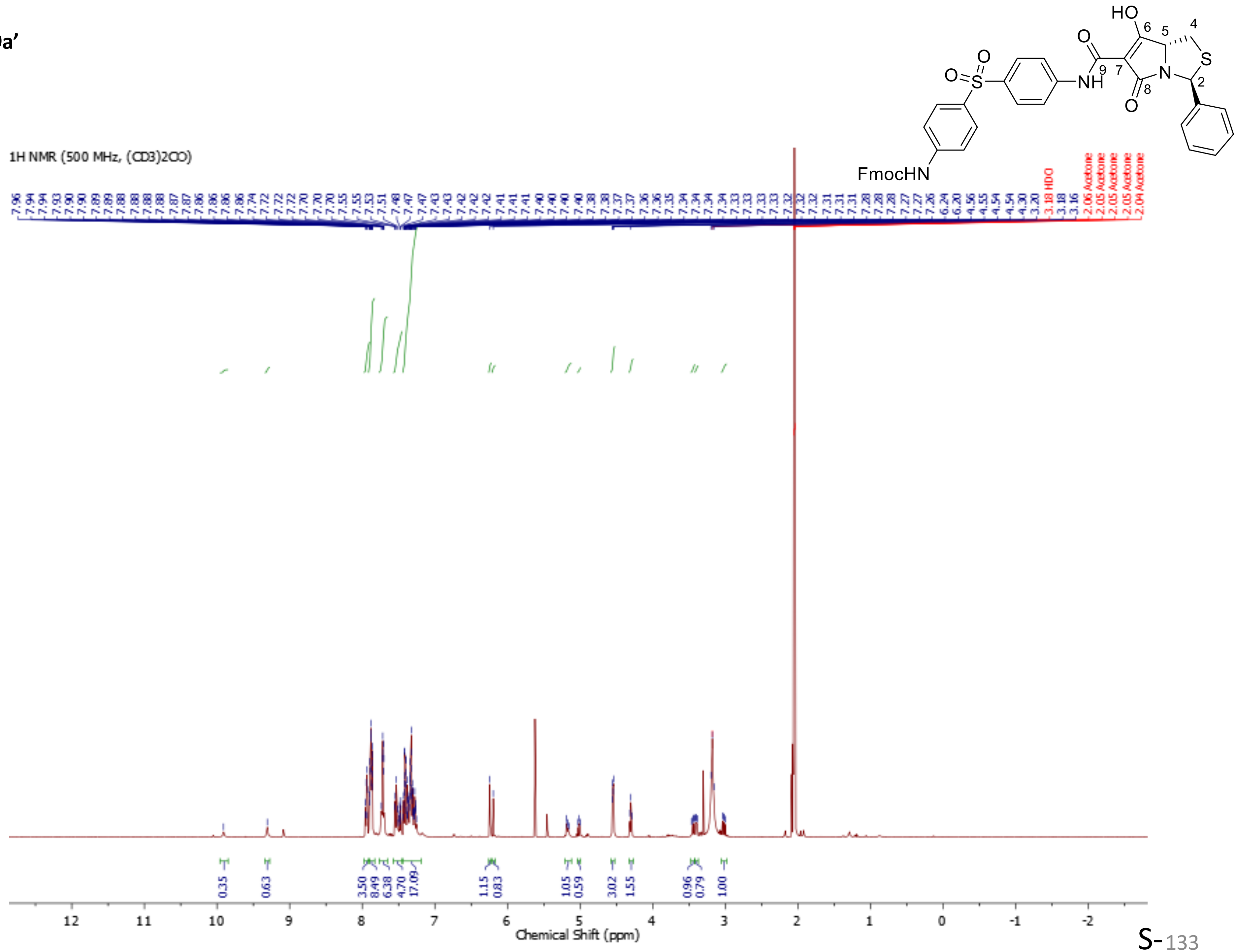
9z



13C NMR (100.6 MHz, CDCl3)

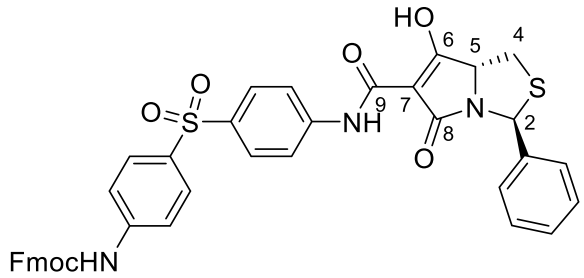


9a’

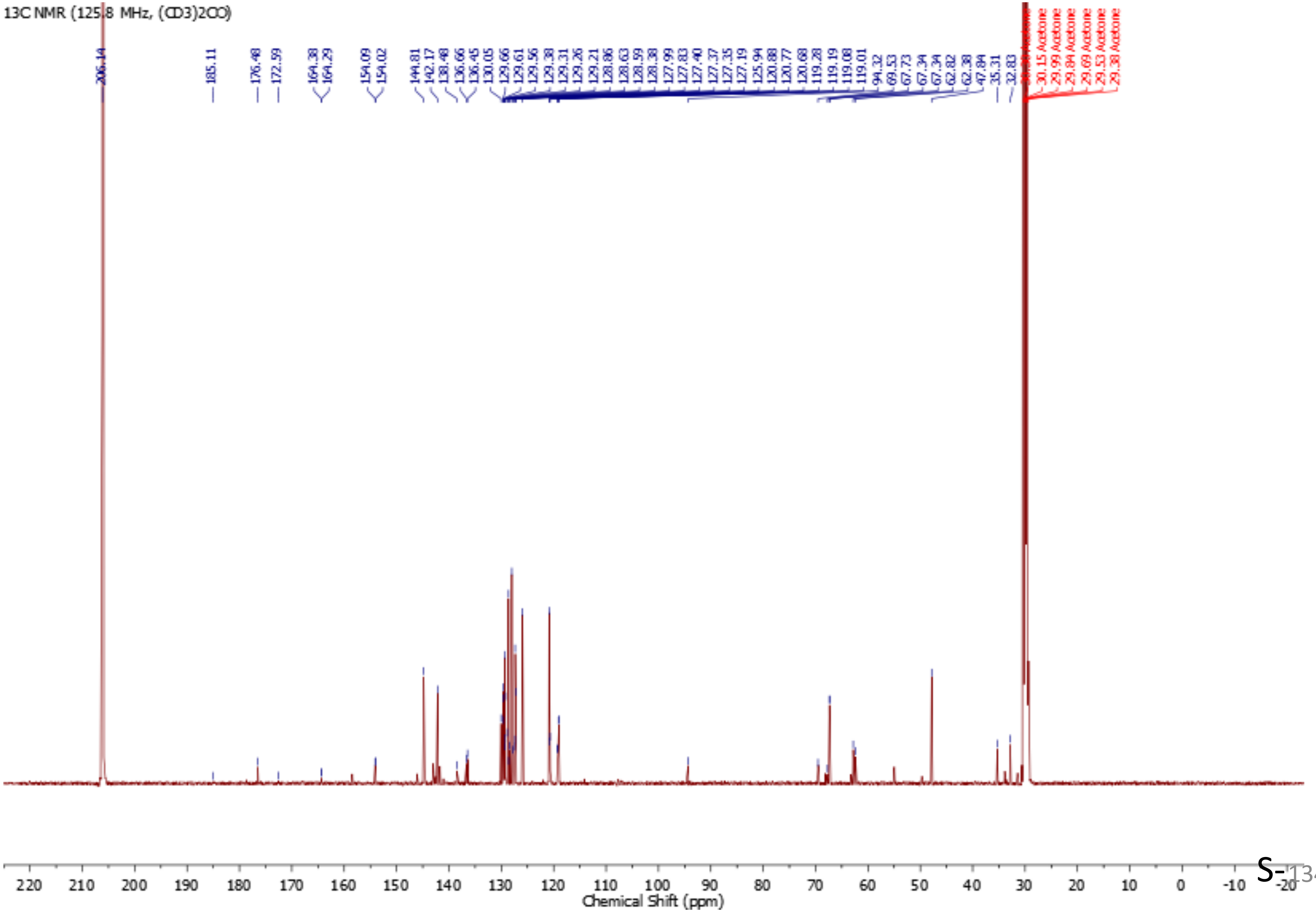


HO
O
O
O
S
NH
N
S
O
FmocHN
1H NMR (500 MHz, (CD3)2CO)
3.18 HDO
2.06 Acetone
2.05 Acetone
2.04 Acetone
Chemical Shift (ppm)

9a’

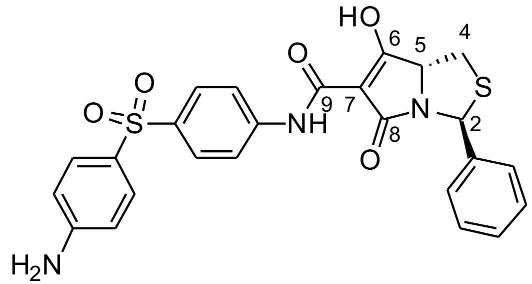


HO
6
5
4
O
S
O
O=S
NH
9
7
N
2
8
O
FmocHN

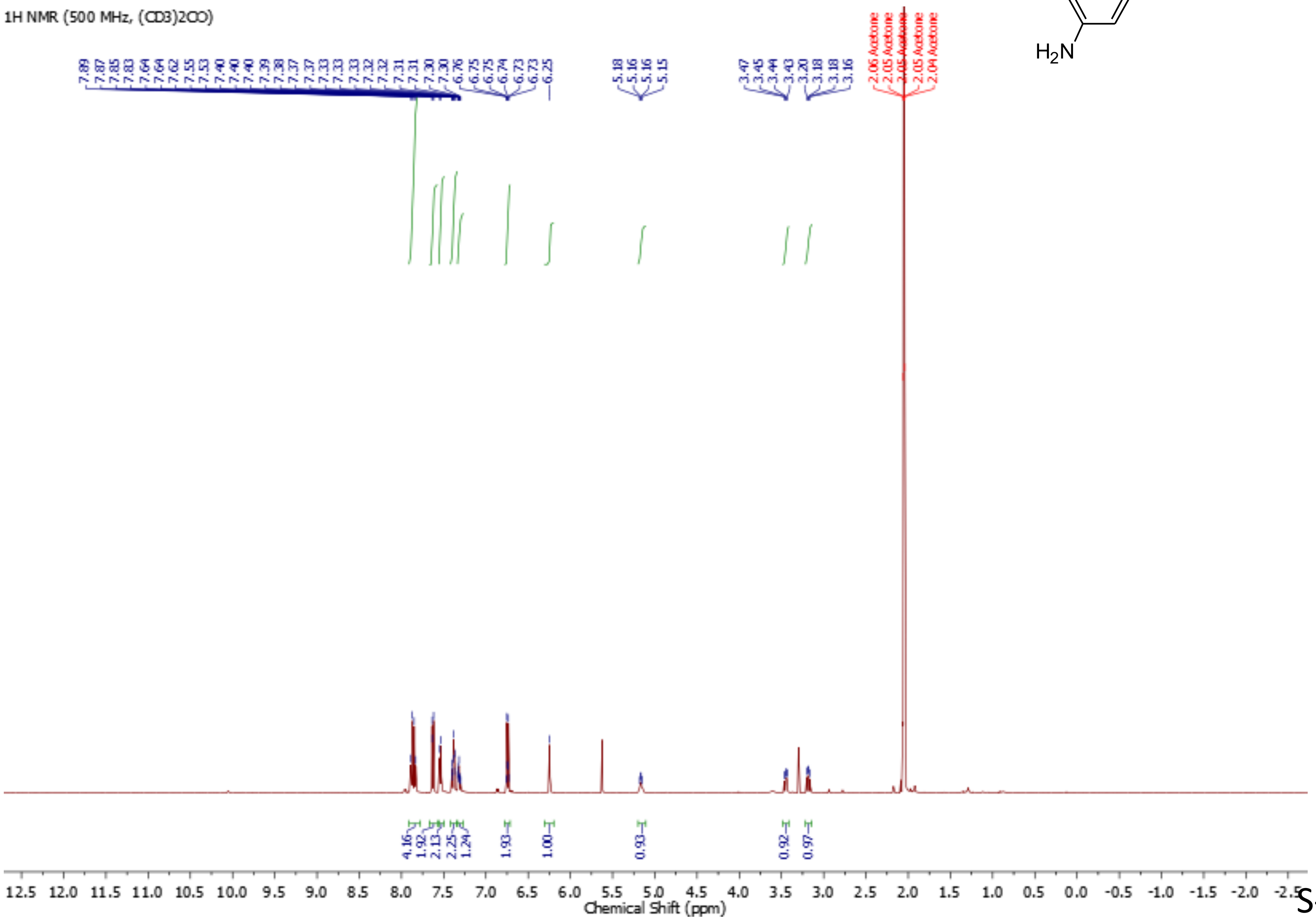


13C NMR (125.8 MHz, (CD3)2CO)
206.14
185.11
176.48
172.99
164.38
164.29
154.09
154.02
144.81
142.17
138.48
136.66
136.45
130.05
129.66
129.61
129.56
129.38
129.31
129.26
129.21
128.86
128.63
128.59
128.38
127.99
127.83
127.40
127.37
127.35
127.19
125.94
120.88
120.77
120.68
119.28
119.19
119.08
119.01
94.32
69.53
67.73
67.34
67.34
62.82
62.38
47.84
35.31
32.83
30.15 Acetone
29.99 Acetone
29.84 Acetone
29.69 Acetone
29.53 Acetone
29.38 Acetone
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

9b’

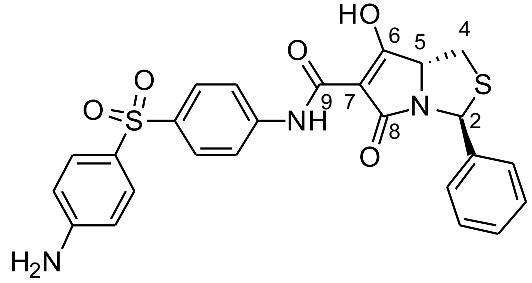


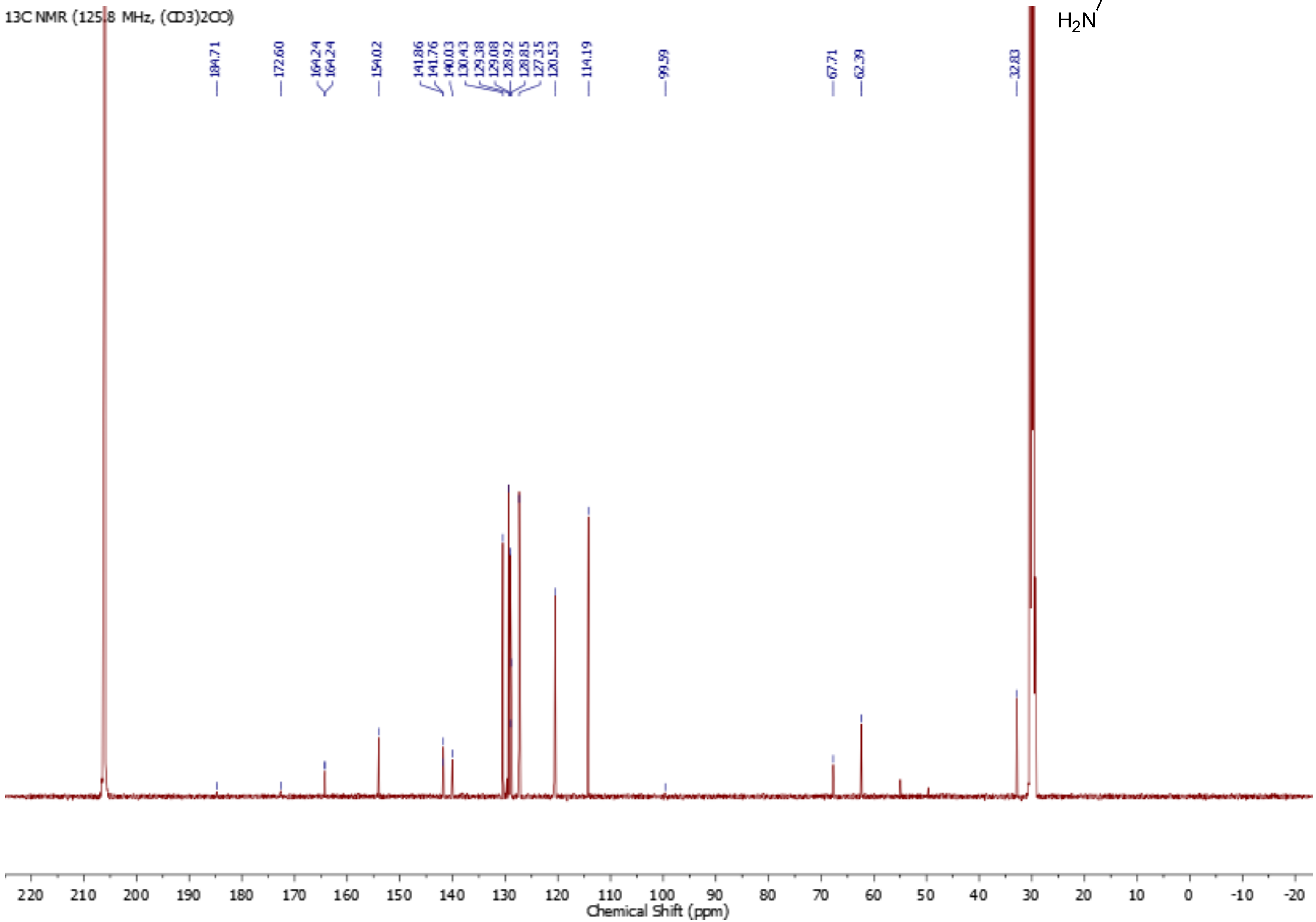
HO
6
5
4
O
O
O
S
9
7
N
S
NH
2
8
O
H2N



1H NMR (500 MHz, (CD3)2CO)
7.89 7.87 7.85 7.83 7.64 7.64 7.62 7.55 7.53 7.40 7.40 7.40 7.39 7.38 7.37 7.37 7.33 7.33 7.33 7.32 7.32 7.31 7.31 7.30 7.30 6.76 6.75 6.75 6.74 6.73 6.73 6.25
5.18 5.16 5.16 5.15
3.47 3.45 3.44 3.43 3.20 3.18 3.18 3.16
2.06 Acetone 2.05 Acetone 2.05 Acetone 2.05 Acetone 2.04 Acetone
4.16 1.92 2.13 2.25 1.24 1.93 1.00 0.93 0.92 0.97
12.5 12.0 11.5 11.0 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 -1.0 -1.5 -2.0 -2.5
Chemical Shift (ppm)

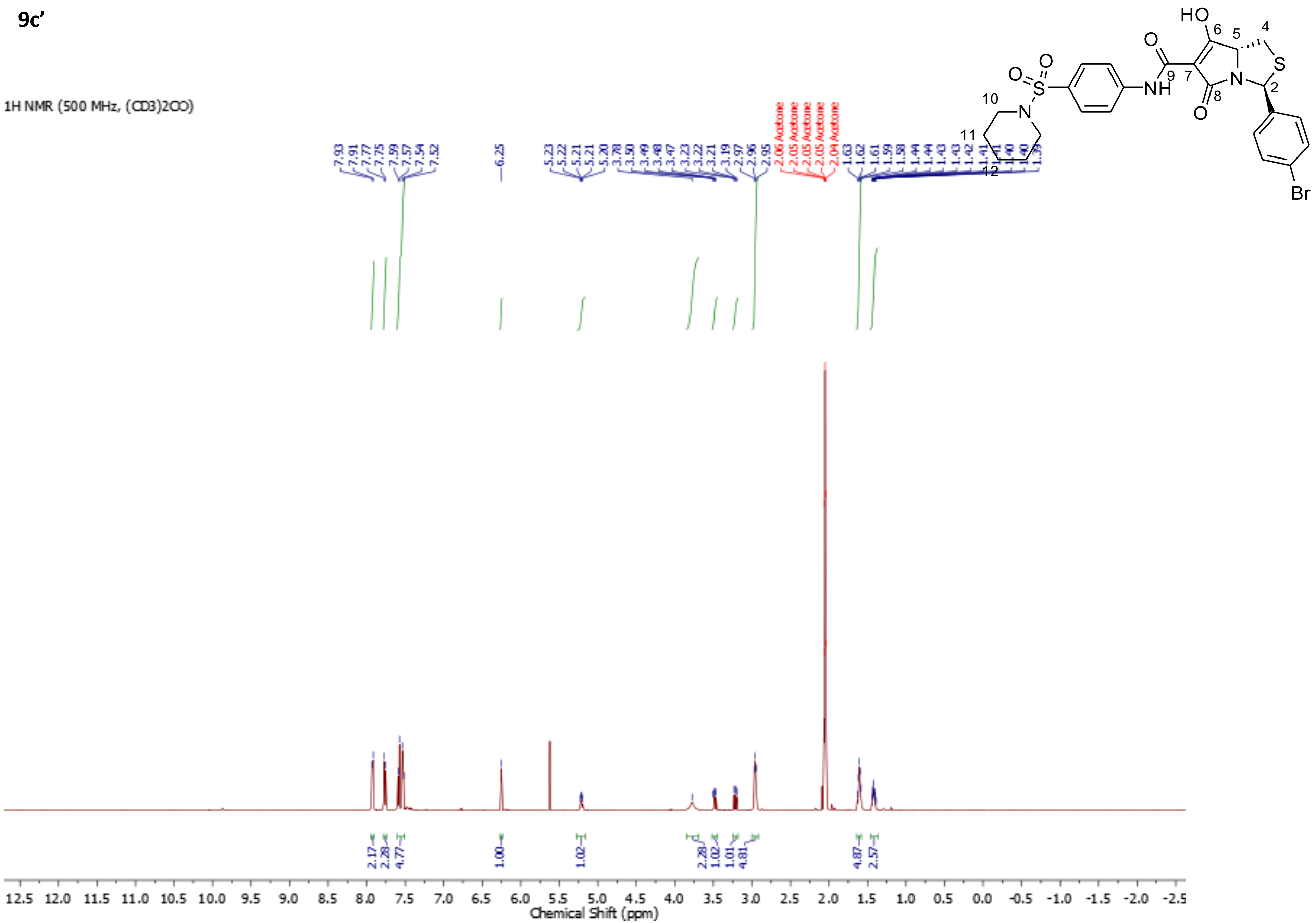
9b’



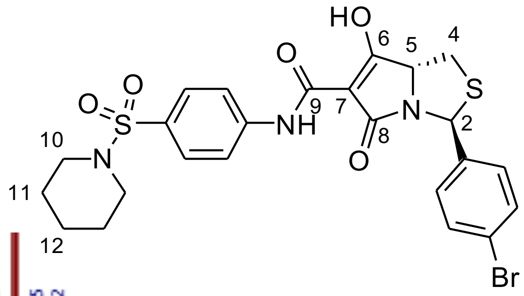

13C NMR (125.8 MHz, (CD3)2CO)
184.71
172.60
164.24
164.24
154.02
141.86
141.76
140.03
130.43
129.38
129.08
128.92
128.85
127.35
120.53
114.19
99.59
67.71
62.39
32.83
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

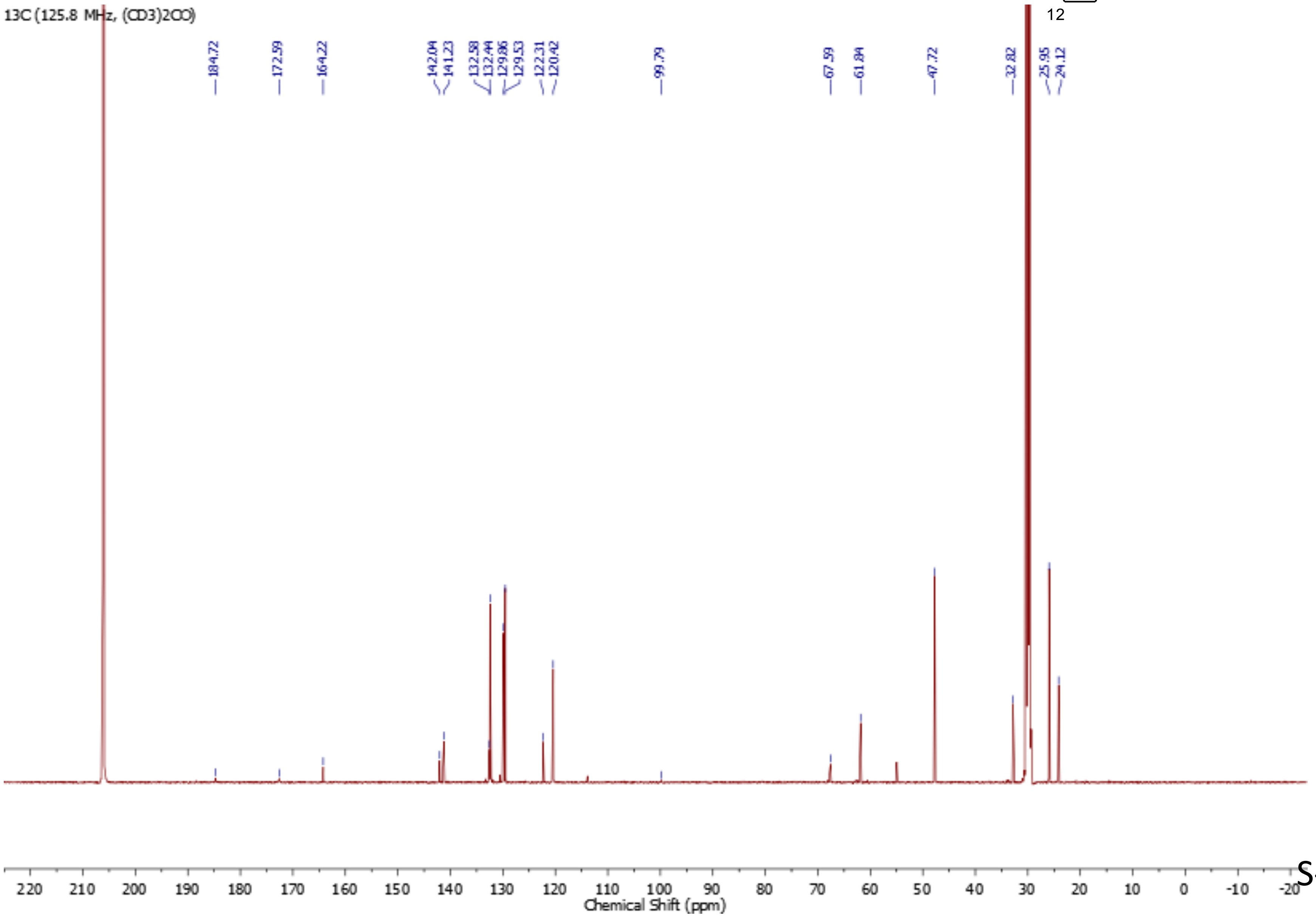
9c'

1H NMR (500 MHz, (CD3)2CO)

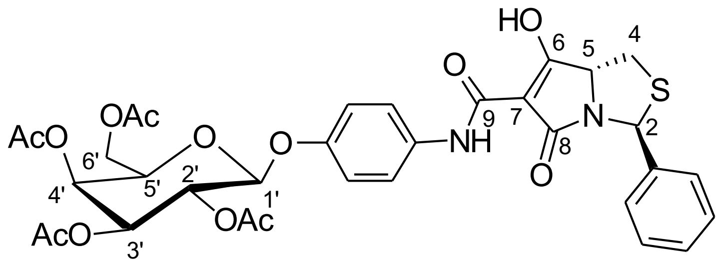


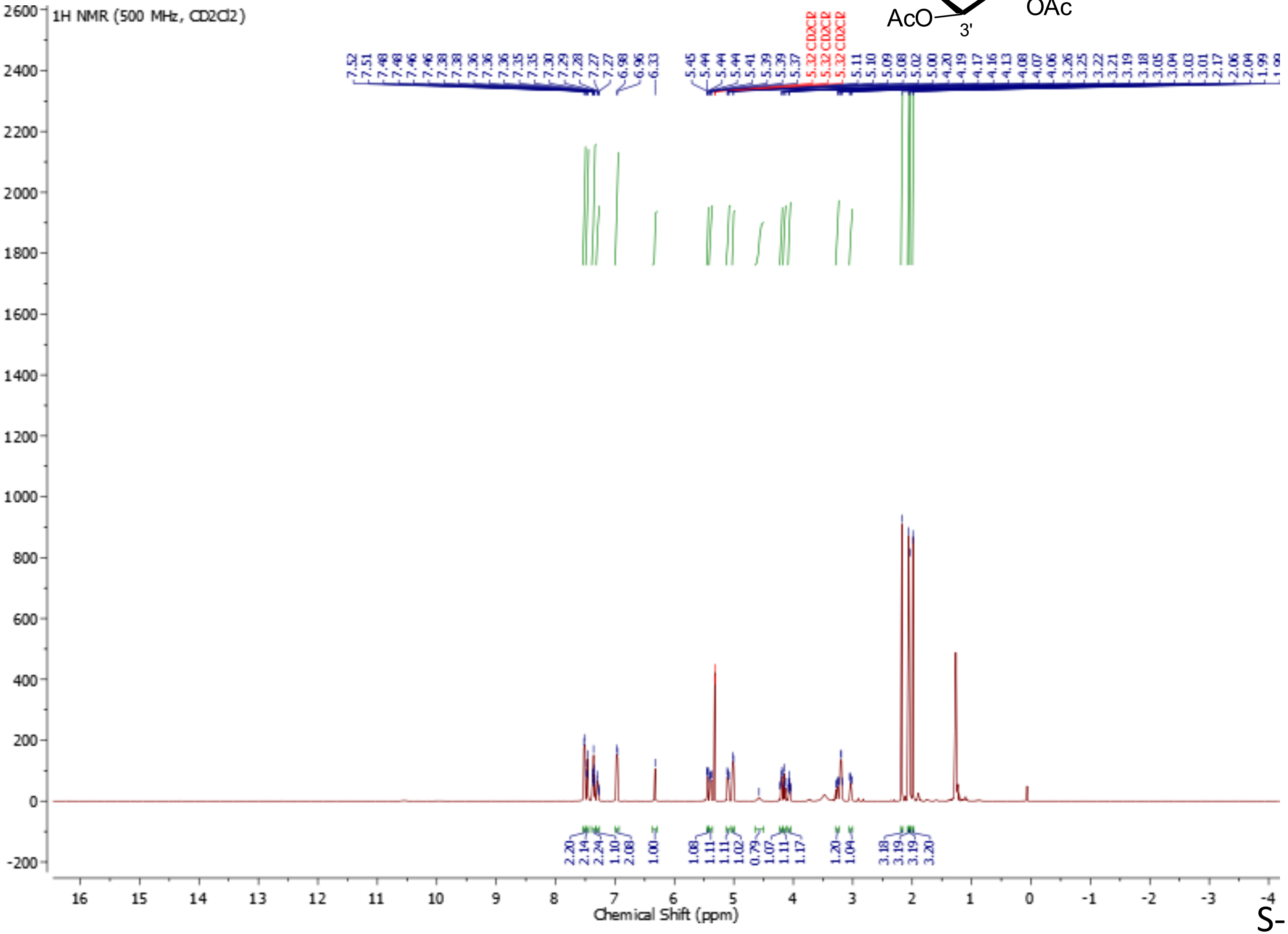
9c’


HO
6
5
4
O
S
O
O
9
7
N
2
S
NH
8
10
N
O
11
12
Br

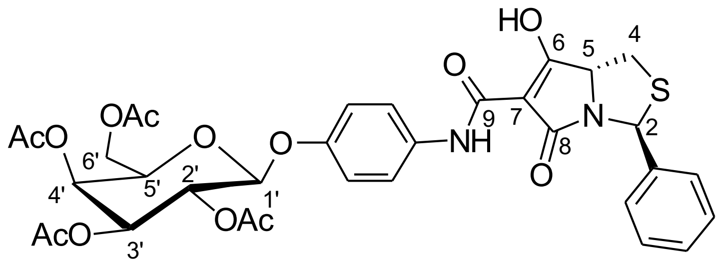

13C (125.8 MHz, (CD3)2CO)
184.72
172.59
164.22
142.04
141.23
132.58
132.44
129.86
129.53
122.31
120.42
99.79
67.59
61.84
47.72
32.82
25.95
24.12
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

(-)-(2*S*,5*R*)-1-Aza-6-hydroxy-8-oxo-2-phenyl-7-(4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyloxy)phenylaminocarbonyl)-3-thiabicyclo[3.3.0]oct-6-ene, 133/9d’

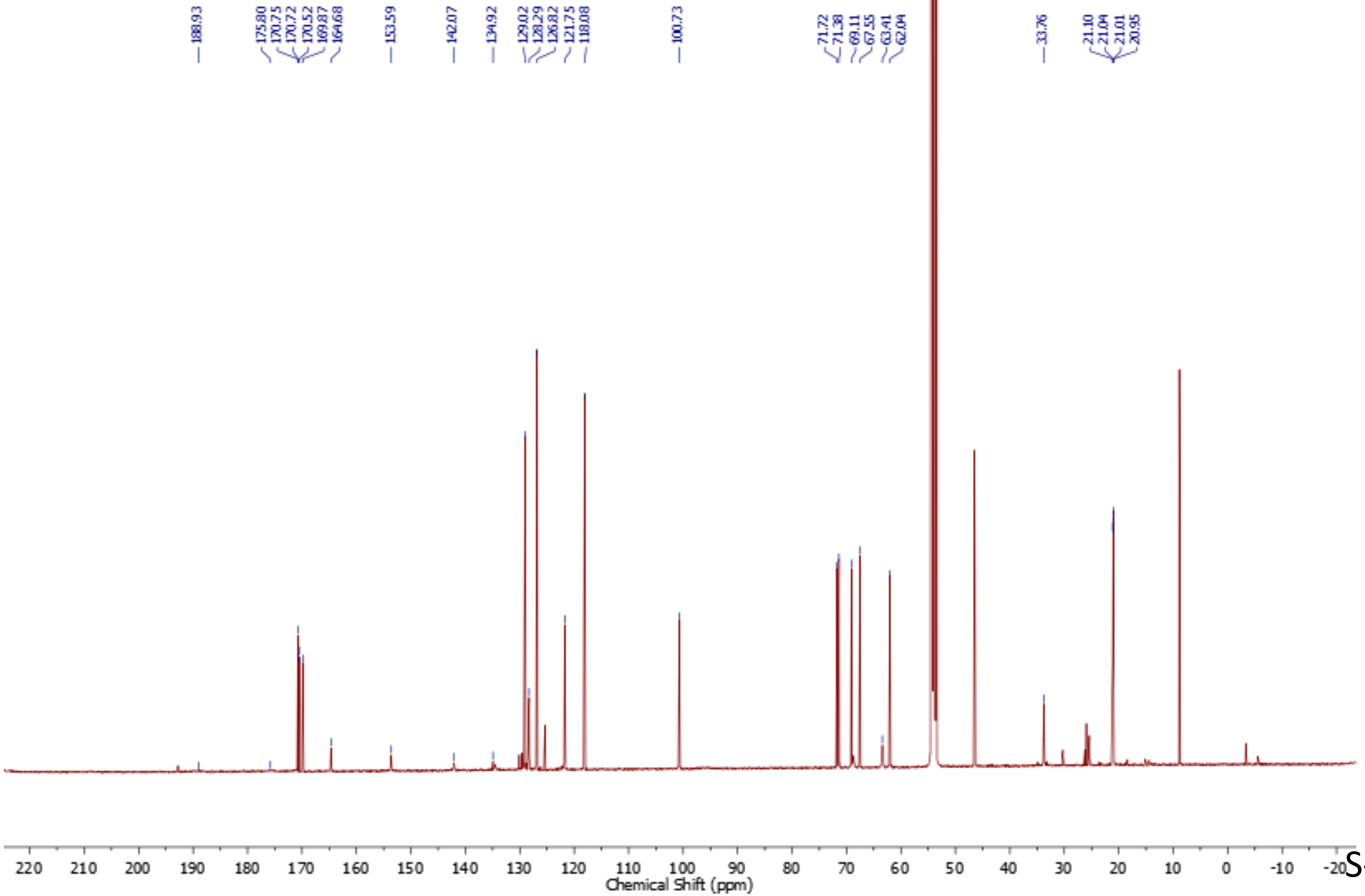




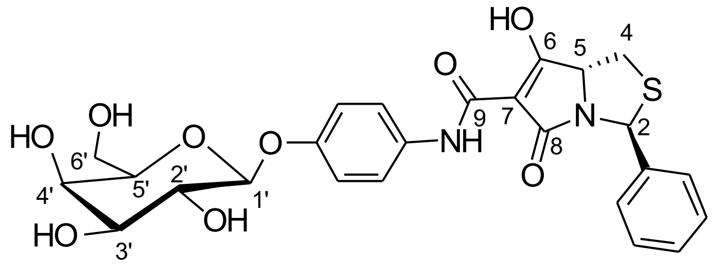
9d'



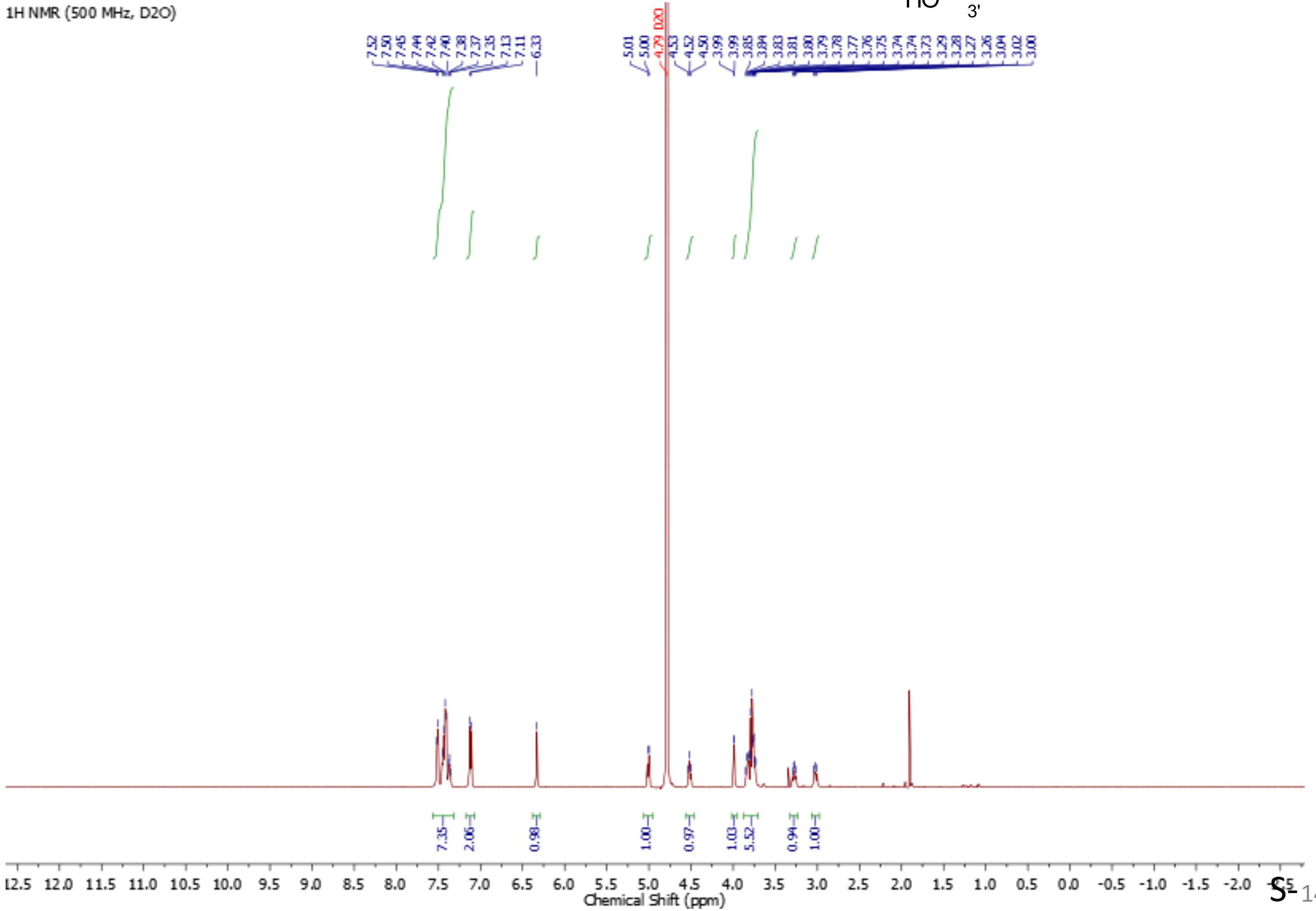
13C NMR (125.8 MHz, CD2Cl2)



9d'

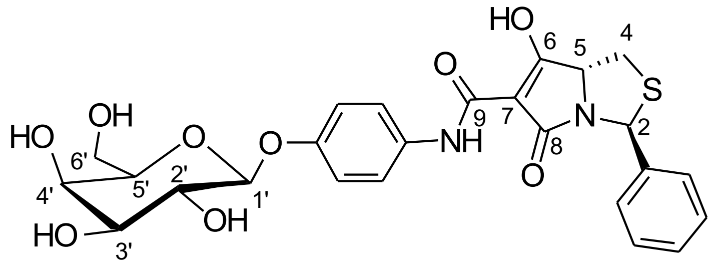


HO
6
5
4
O
S
OH
9
7
N
2
HO
O
O
NH
8
6'
2'
O
4'
5'
1'
OH
HO
3'

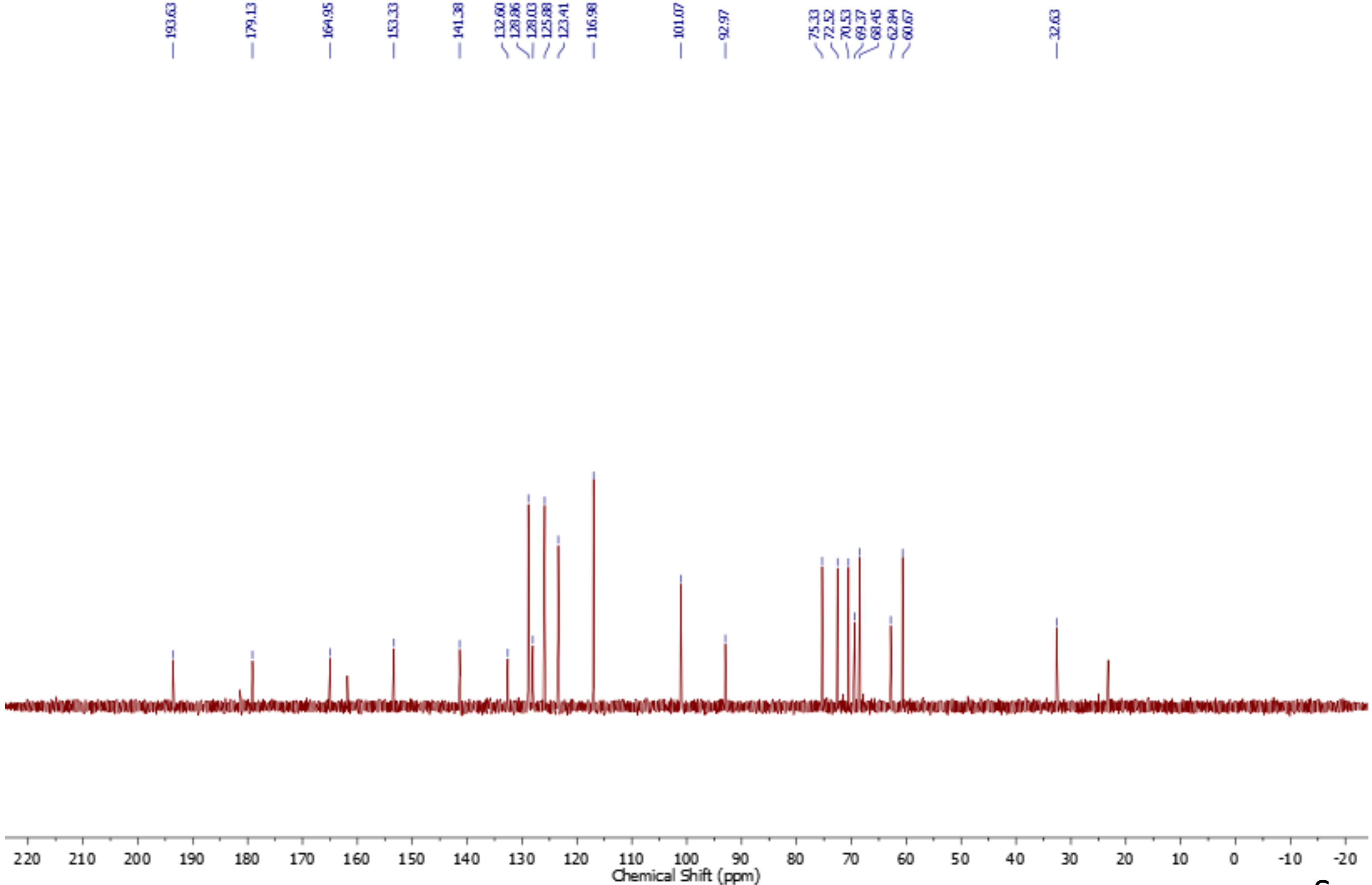


1H NMR (500 MHz, D2O)
7.52 7.50 7.45 7.44 7.42 7.40 7.38 7.37 7.35 7.13 7.11 6.33
5.01 5.00 4.79 D2O 4.53 4.52 4.50 3.99 3.99 3.85 3.84 3.83 3.81 3.80 3.79 3.78 3.77 3.76 3.75 3.74 3.74 3.73 3.29 3.28 3.27 3.26 3.04 3.02 3.00
7.35 2.06 0.98 1.00 0.97 1.03 5.52 0.94 1.00
12.5 12.0 11.5 11.0 10.5 10.0 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 -1.0 -1.5 -2.0 -2.5
Chemical Shift (ppm)

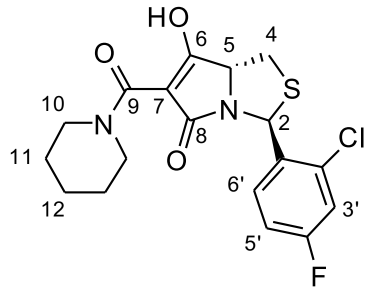
9e'

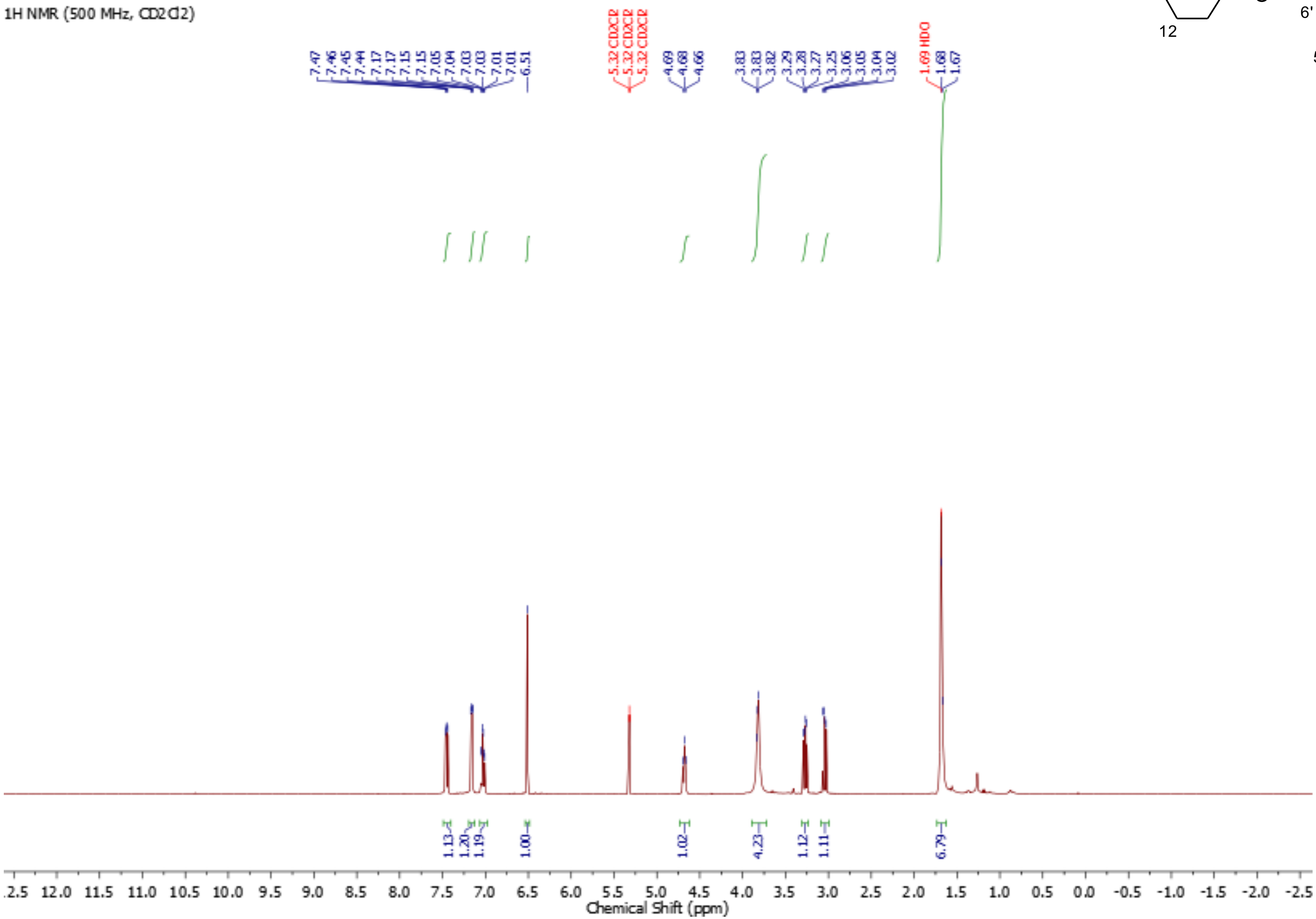


^{13}C NMR (125.8 MHz, D2O)

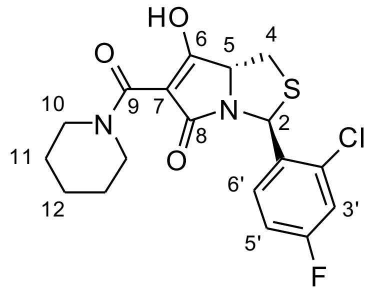


9f’

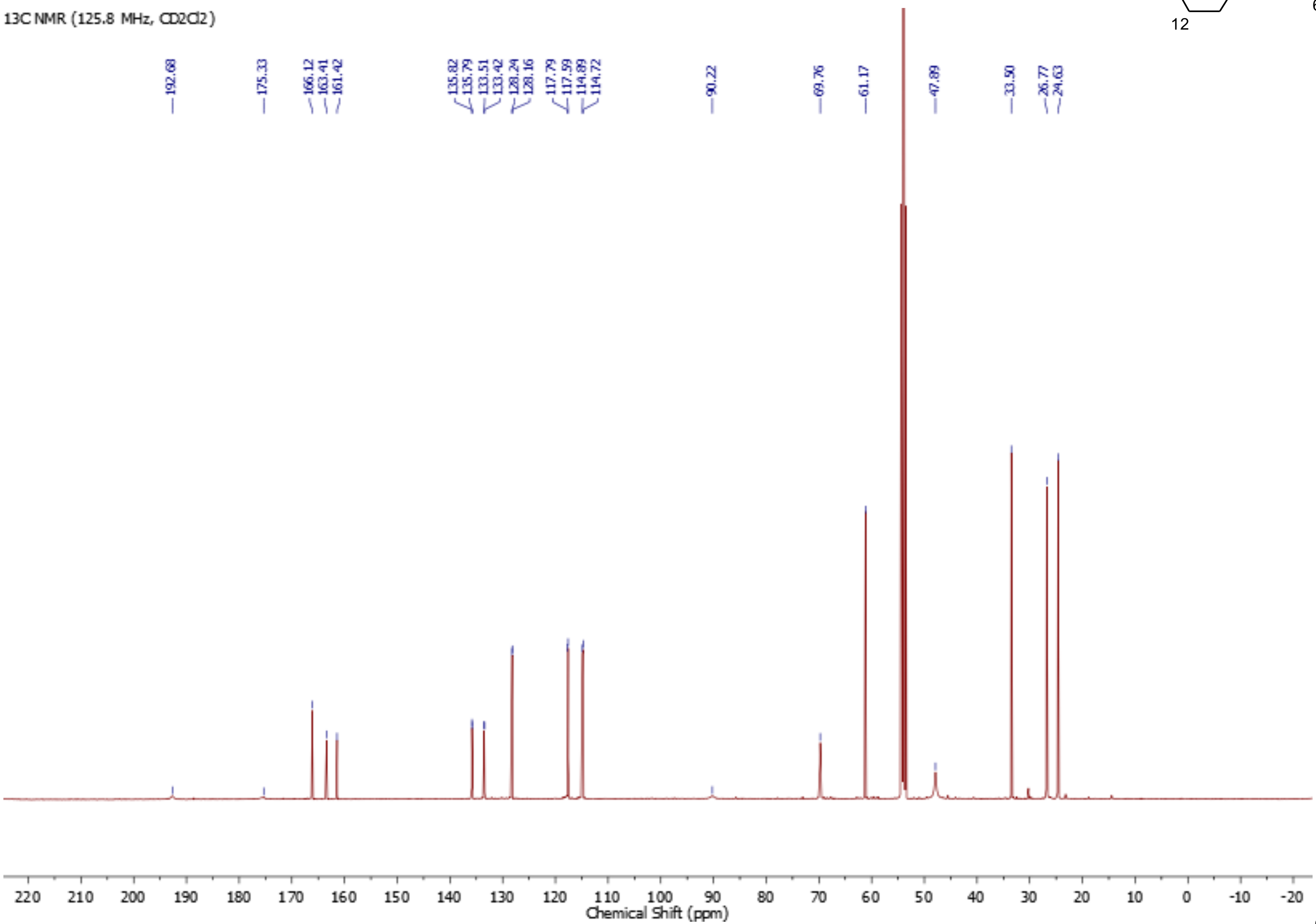

HO
6
5
4
O
S
10
9
7
N
2
Cl
N
8
11
O
6'
12
3'
5'
F


1H NMR (500 MHz, CD2Cl2)
7.47
7.46
7.45
7.44
7.17
7.17
7.15
7.15
7.05
7.04
7.03
7.03
7.01
7.01
6.51
5.32 CD2Cl2
5.32 CD2Cl2
5.32 CD2Cl2
4.69
4.68
4.66
3.83
3.83
3.82
3.29
3.28
3.27
3.25
3.06
3.05
3.04
3.02
1.69 HDO
1.68
1.67
1.13
1.20
1.19
1.00
1.02
4.23
1.12
1.11
6.79
Chemical Shift (ppm)

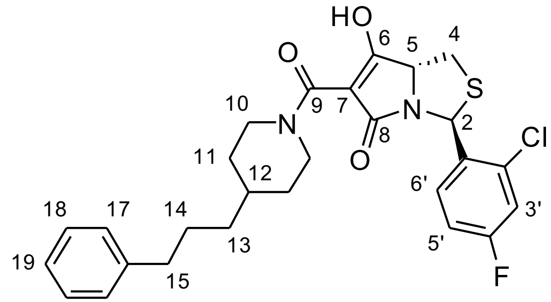
9f'

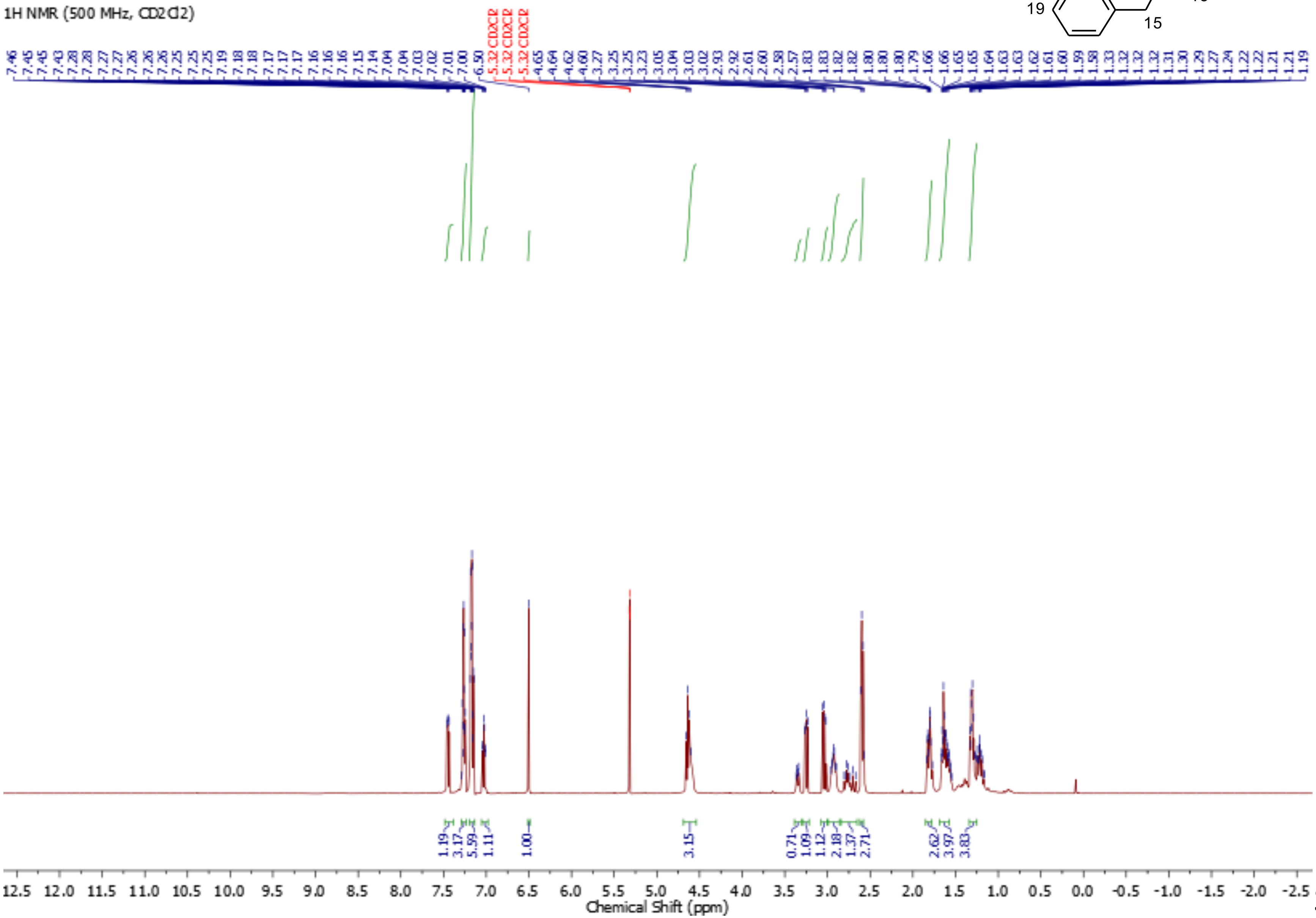


13C NMR (125.8 MHz, CD2Cl2)

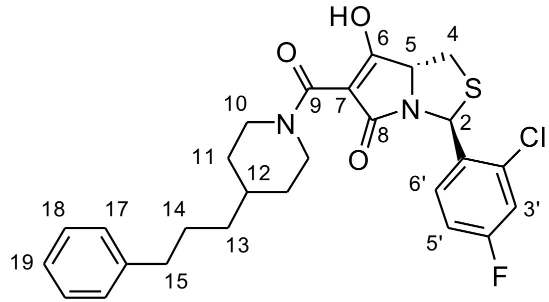


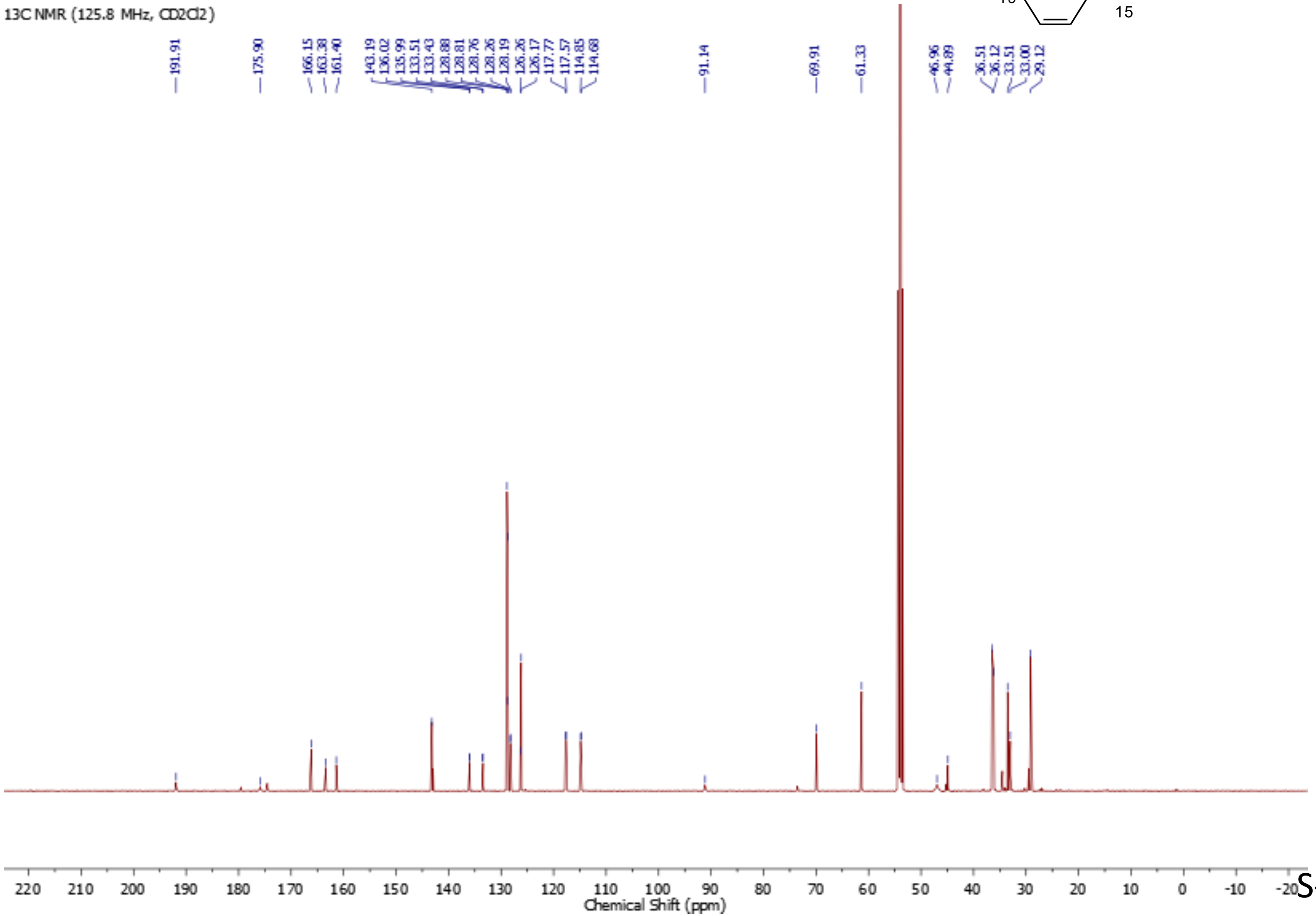
9g’



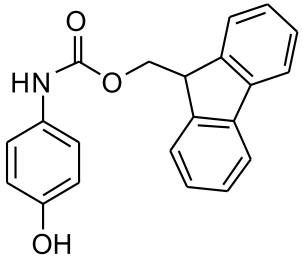


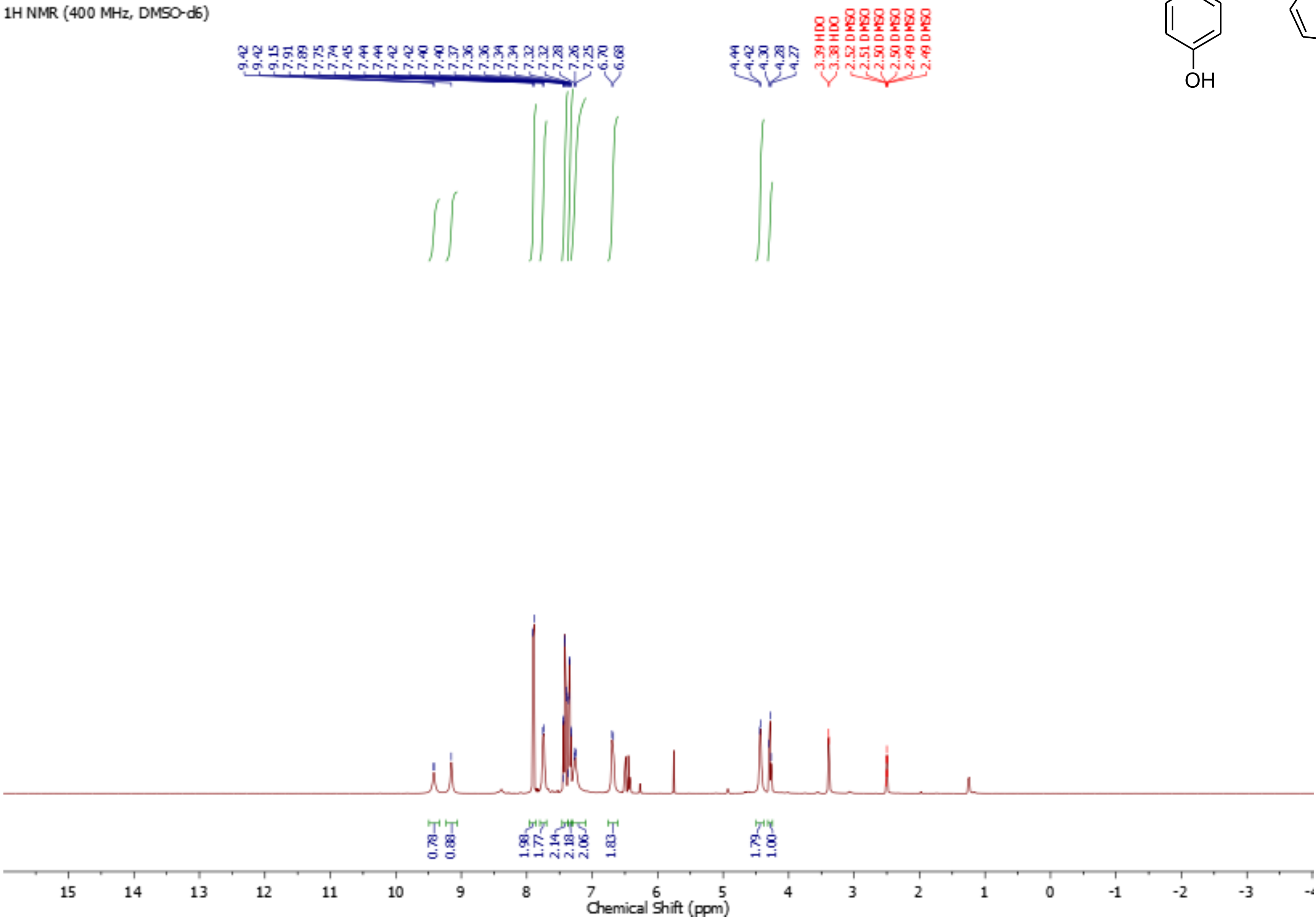
9g’



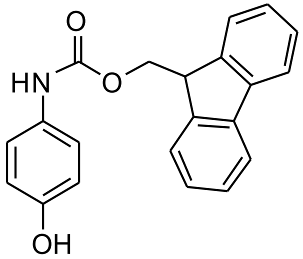

13C NMR (125.8 MHz, CD2Cl2)
191.91
175.90
166.15
163.38
161.40
143.19
136.02
135.99
133.51
133.43
128.88
128.81
128.76
128.26
128.19
126.26
126.17
117.77
117.57
114.85
114.68
91.14
69.91
61.33
46.96
44.89
36.51
36.12
33.51
33.00
29.12
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

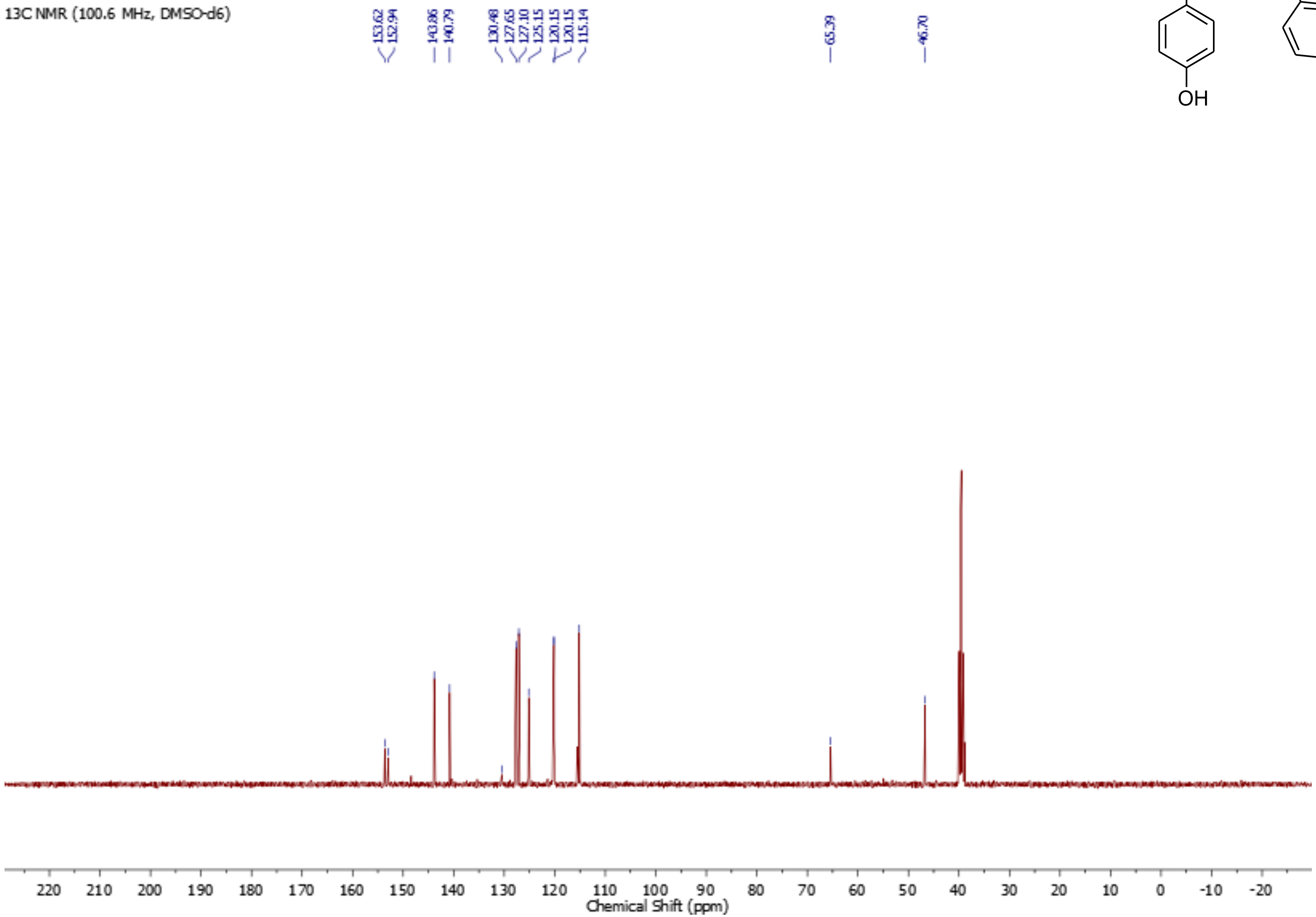
9-Fluorenylmethyl (4-hydroxyphenyl)carbamate



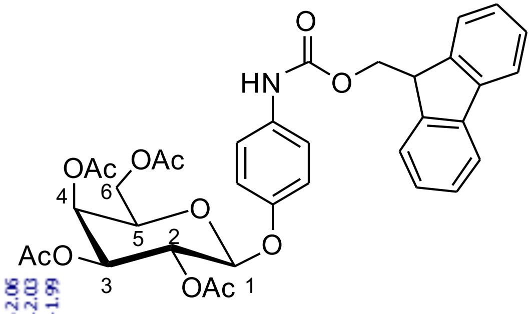


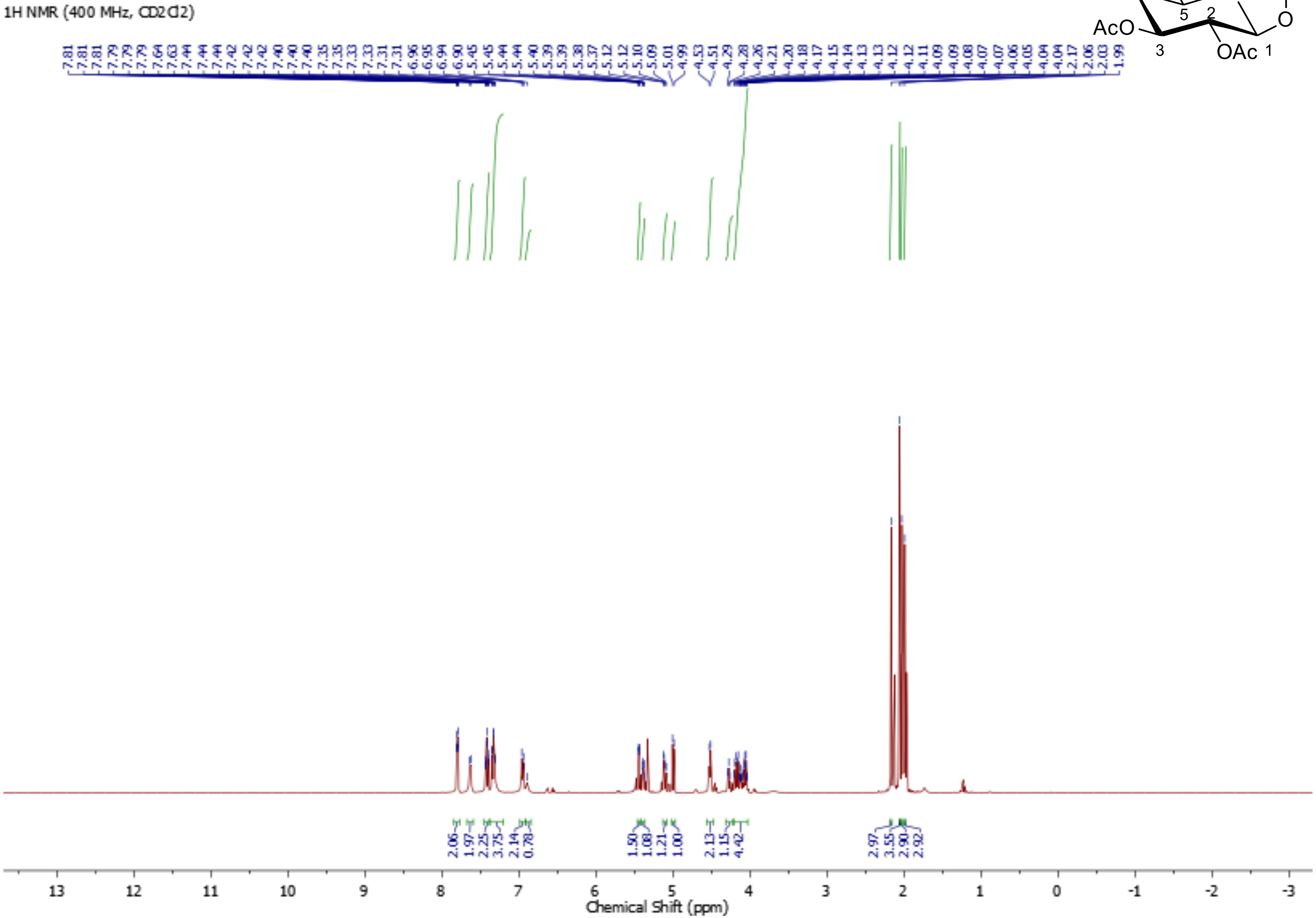
9-Fluorenylmethyl (4-hydroxyphenyl)carbamate



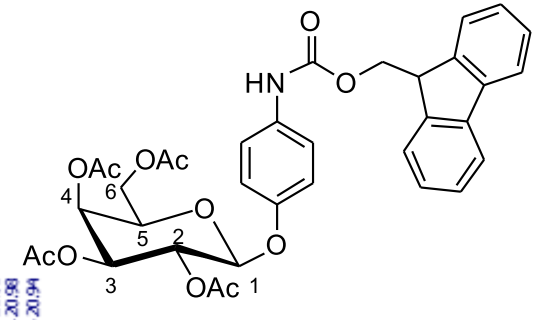


(+)-9-Fluorenylmethyl (4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyloxy)phenyl)carbamate

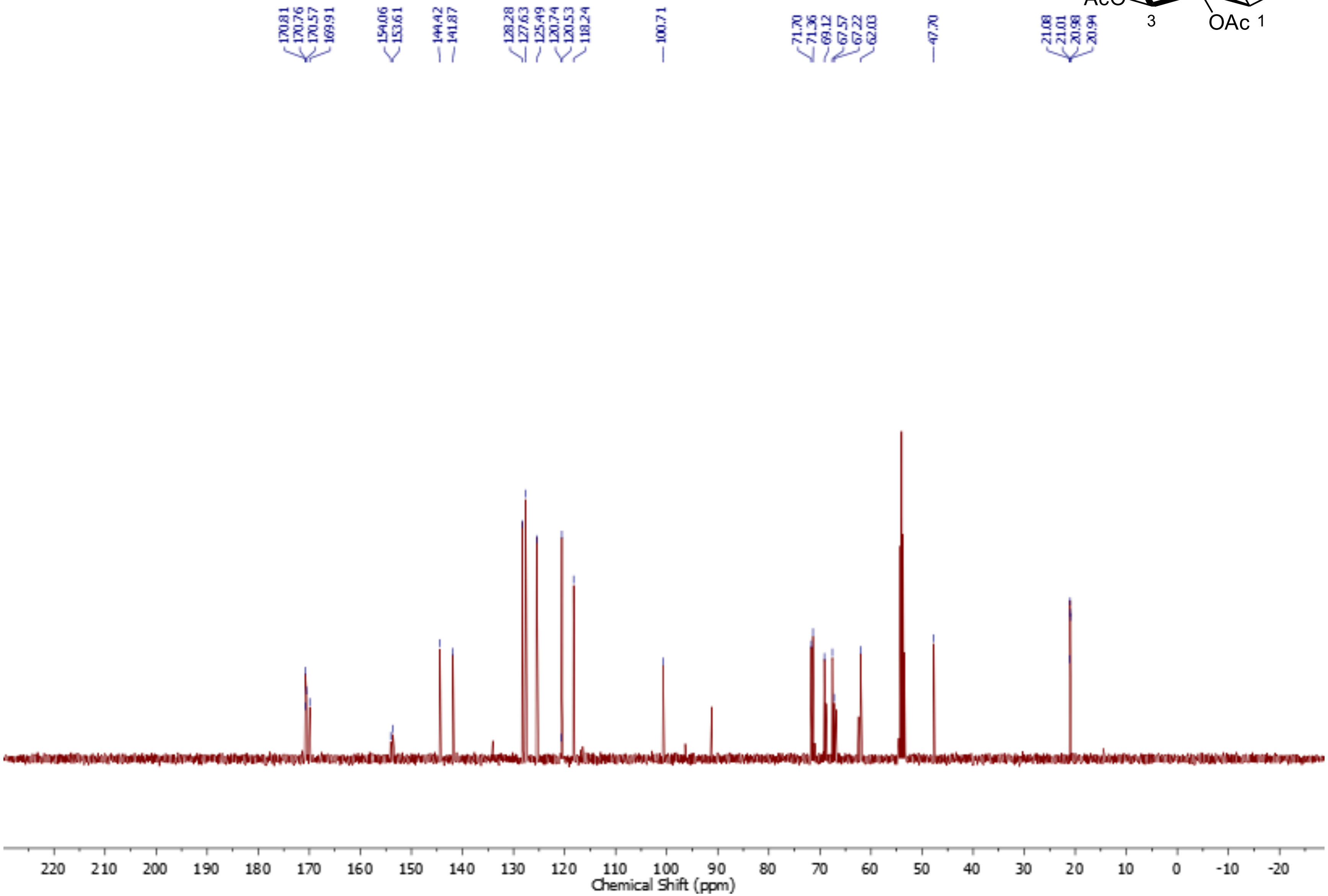




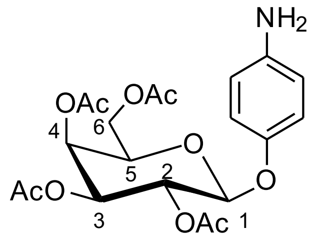
(+)-9-Fluorenylmethyl (4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyloxy)phenyl)carbamate



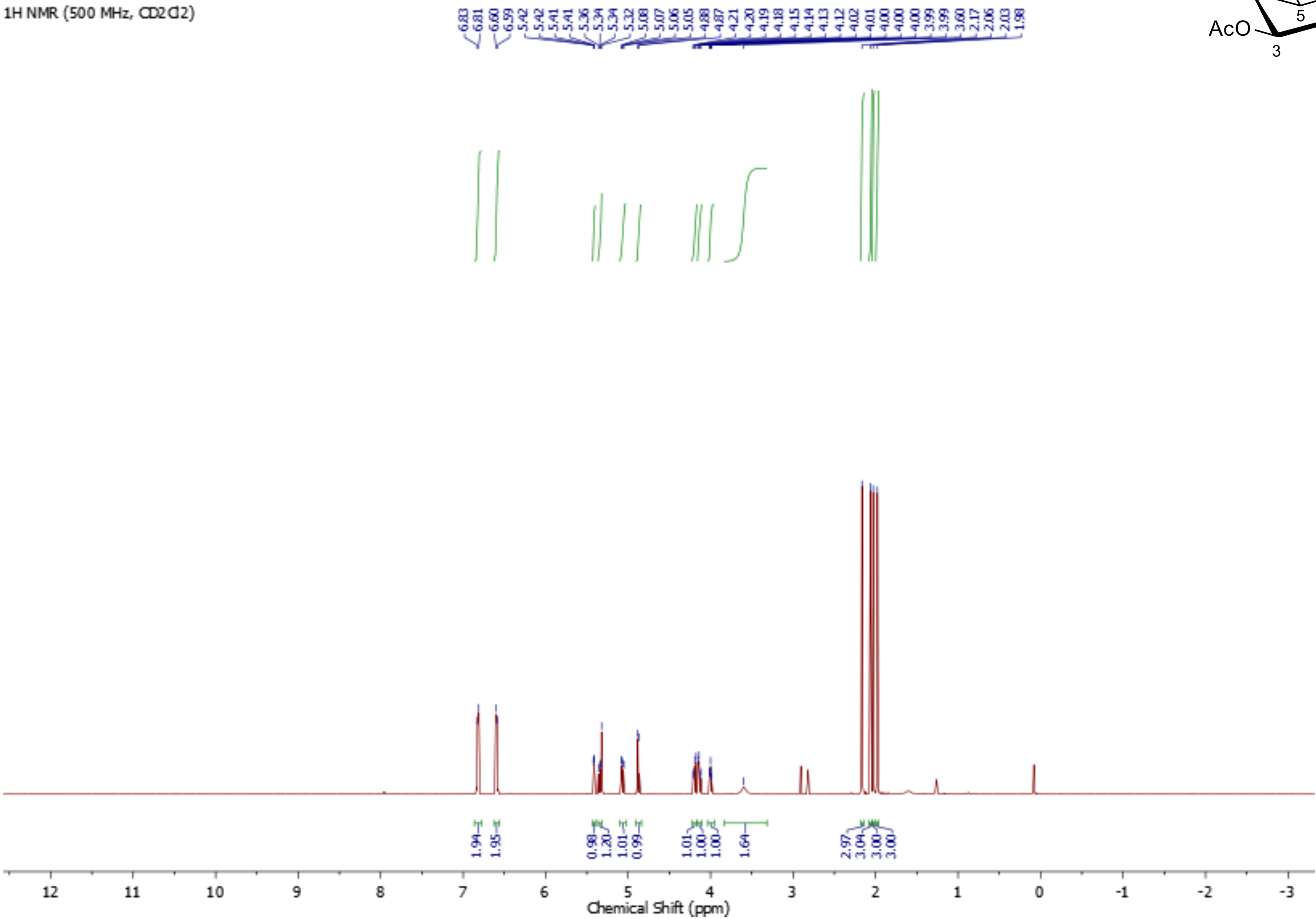
13C NMR (100.6 MHz, CD2Cl2)



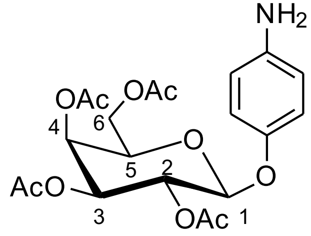
(+)-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyloxy)aniline

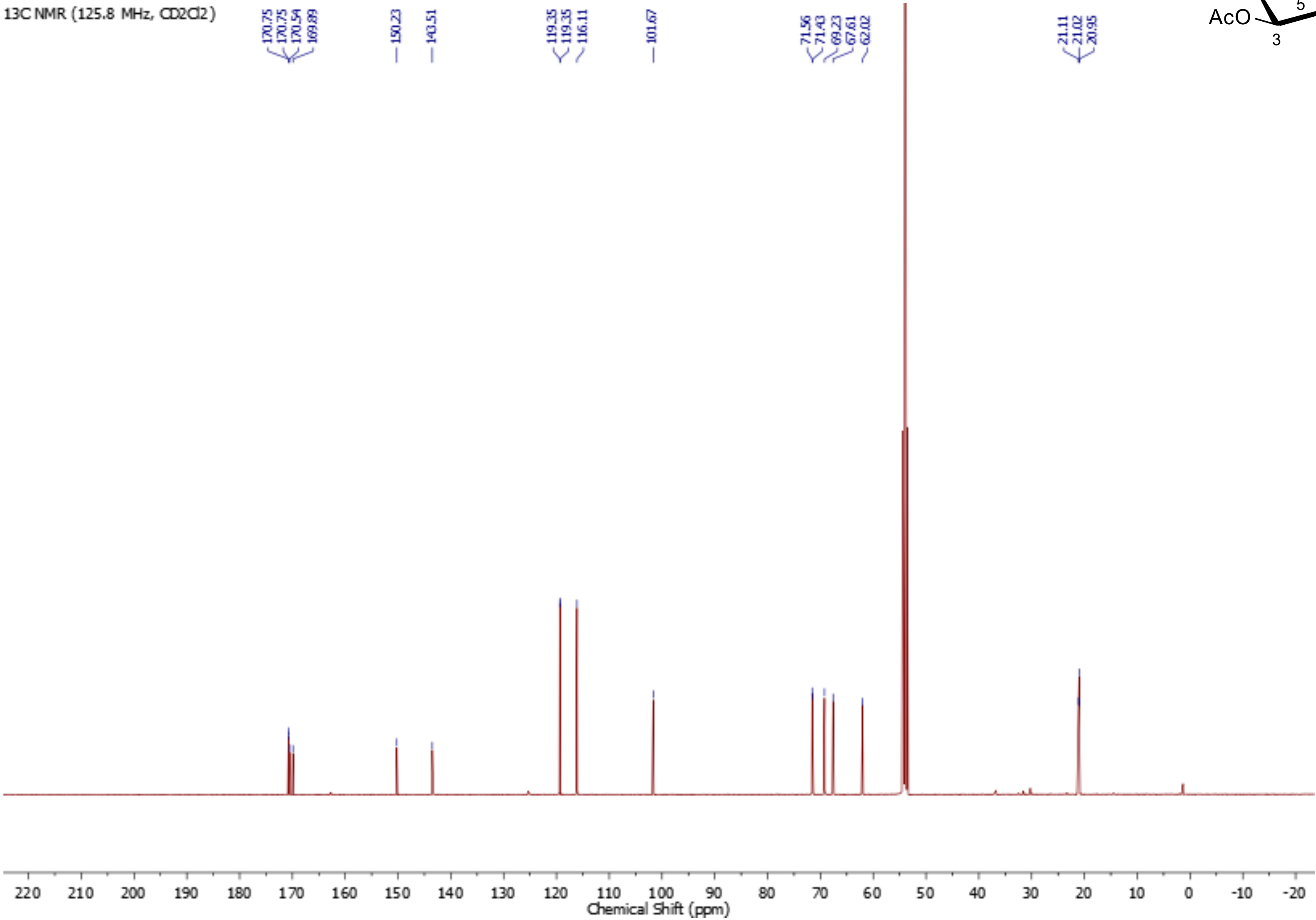


1H NMR (500 MHz, CD2Cl2)

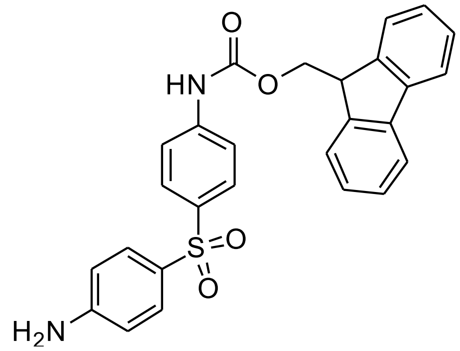


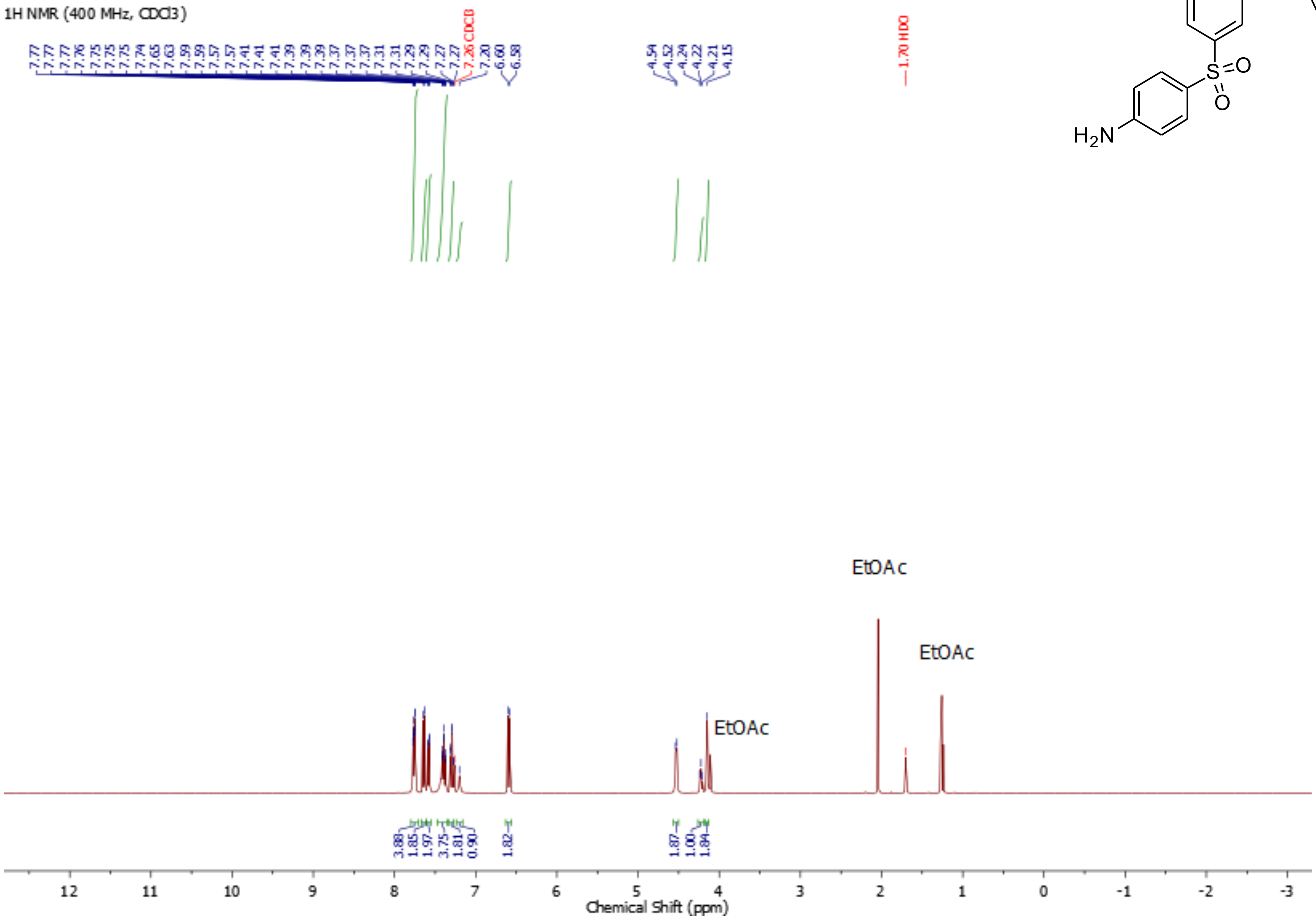
(+)-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyloxy)aniline



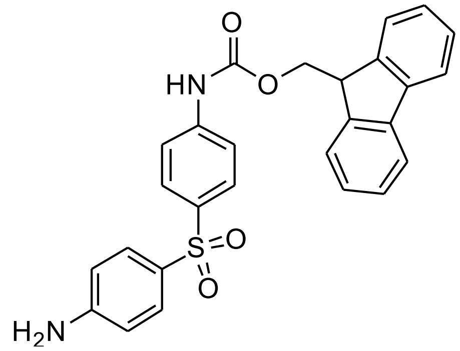


9-Fluorenylmethyl (4-((4-aminophenyl)sulfonyl)phenyl)carbamate

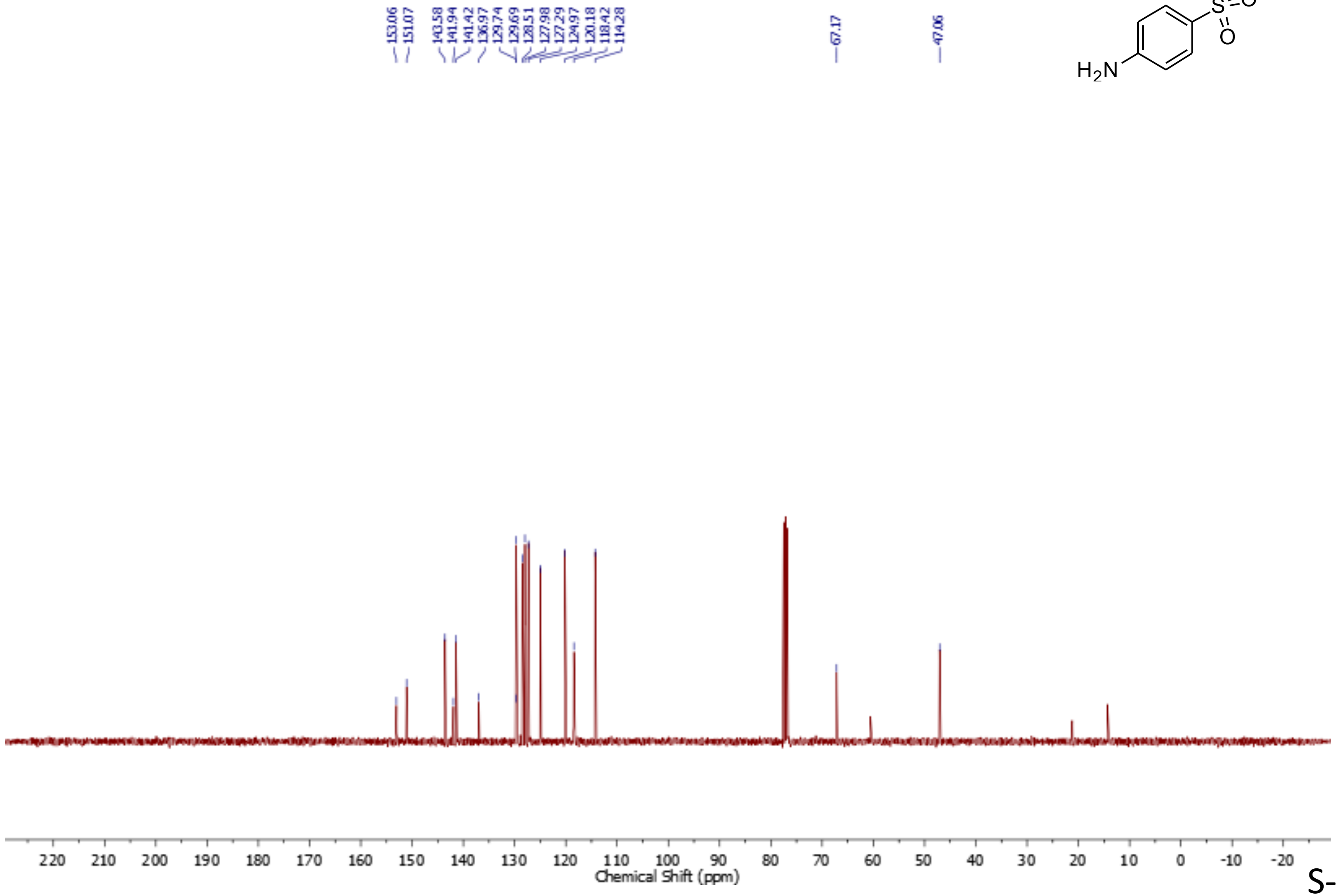




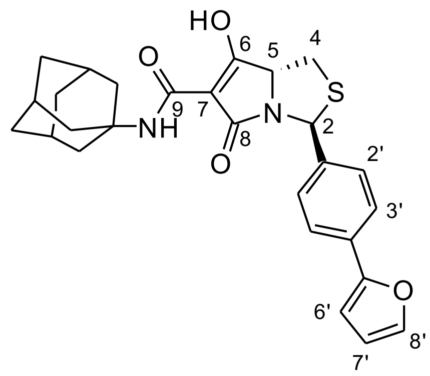
9-Fluorenylmethyl (4-((4-aminophenyl)sulfonyl)phenyl)carbamate

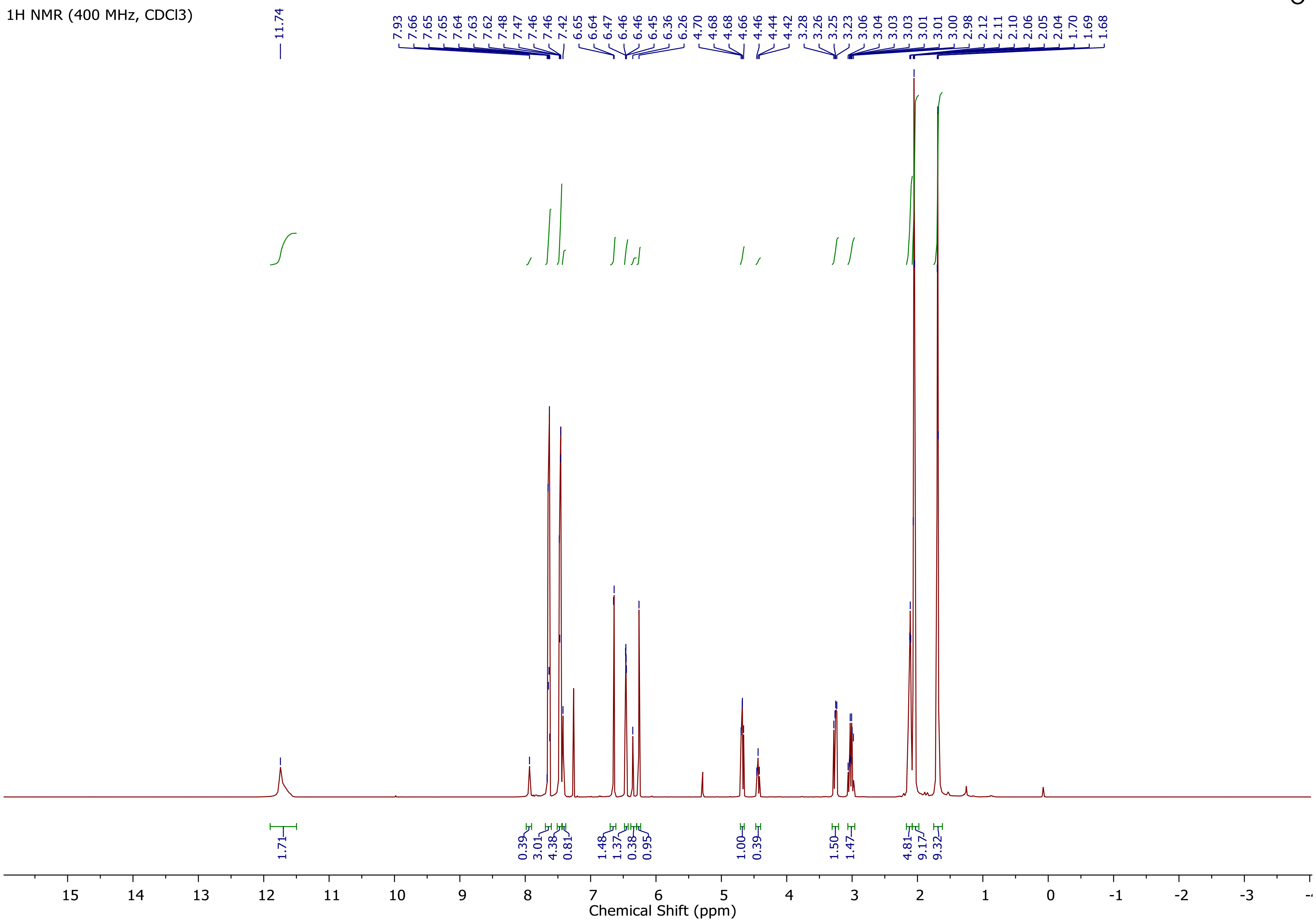


13C NMR (100.6 MHz, CDCl3)

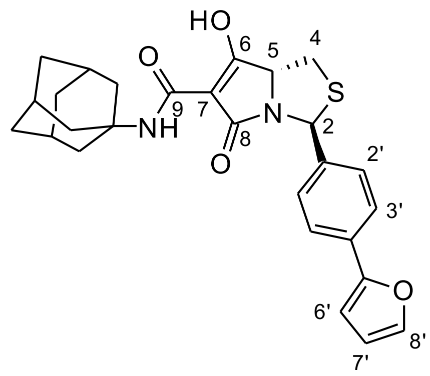


14a

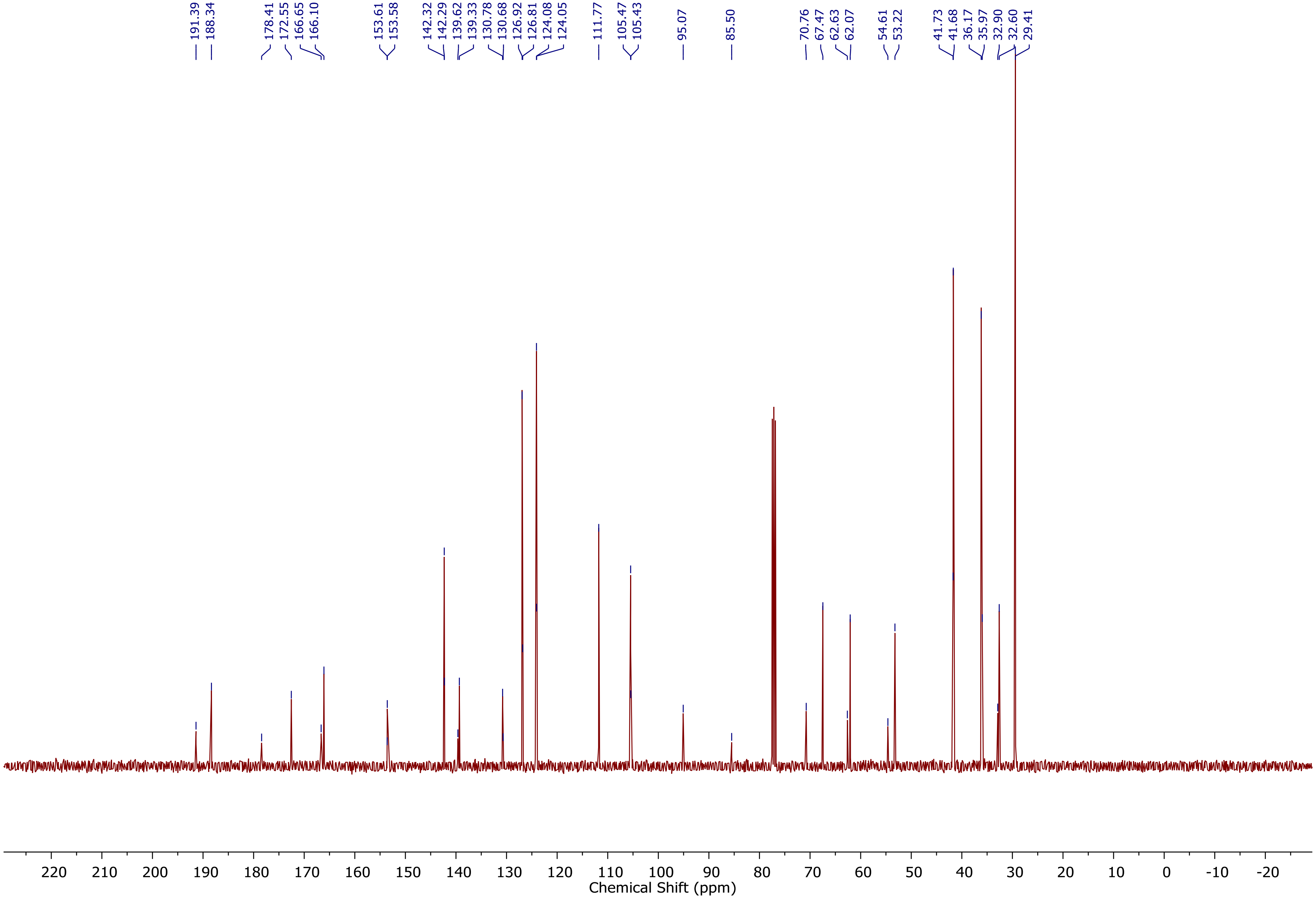

HO
O
O
NH
N
S
6
5
4
7
9
8
2
2'
3'
6'
7'
8'
O


1H NMR (400 MHz, CDCl3)
11.74
7.93
7.66
7.65
7.65
7.64
7.63
7.62
7.48
7.47
7.46
7.46
7.42
6.65
6.64
6.47
6.46
6.46
6.45
6.36
6.26
4.70
4.68
4.68
4.66
4.46
4.44
4.42
3.28
3.26
3.25
3.23
3.06
3.04
3.03
3.03
3.01
3.01
3.00
2.98
2.12
2.11
2.10
2.06
2.05
2.04
1.70
1.69
1.68
1.71
0.39
3.01
4.38
0.81
1.48
1.37
0.38
0.95
1.00
0.39
1.50
1.47
4.81
9.17
9.32
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
Chemical Shift (ppm)

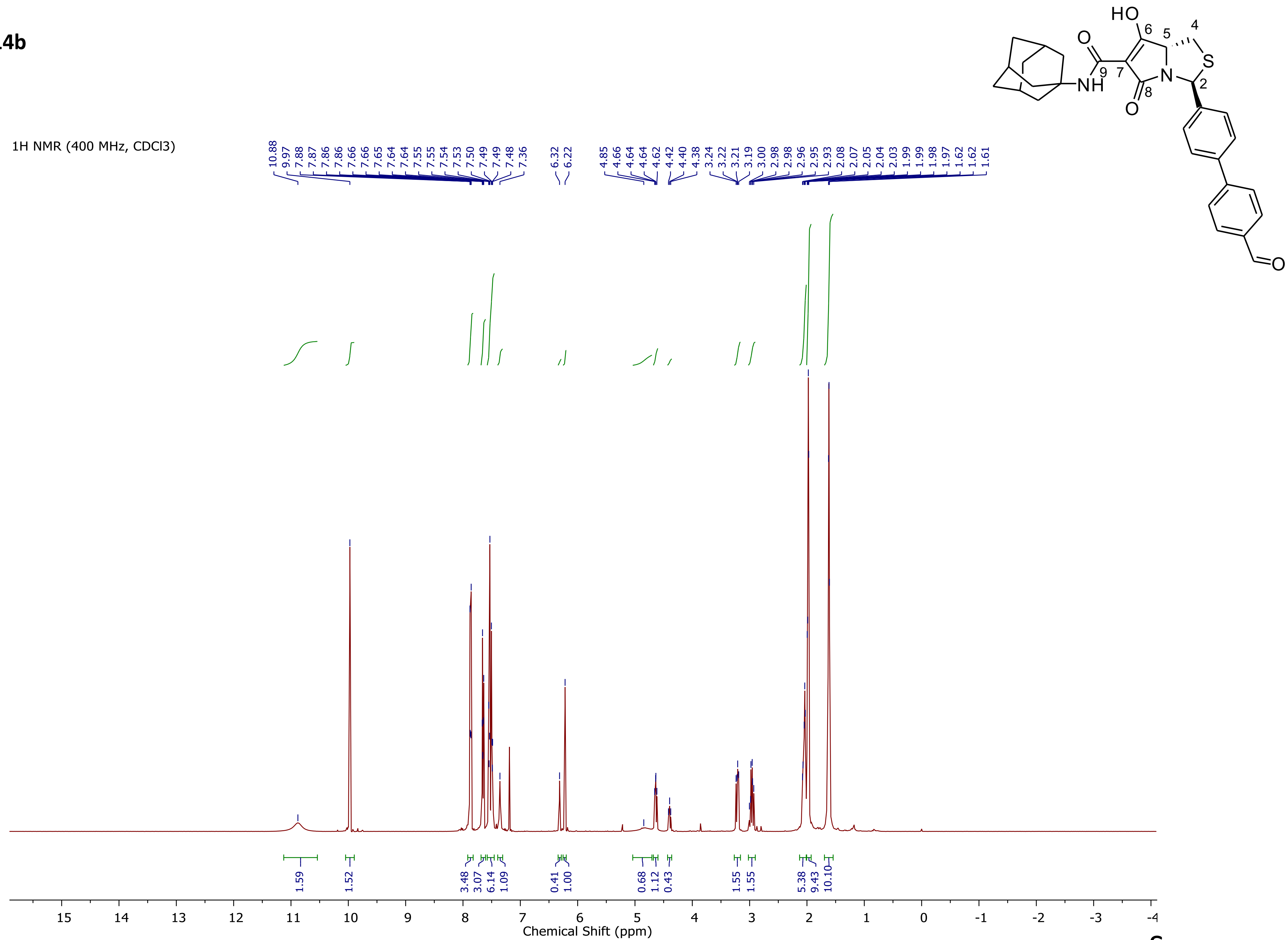
14a



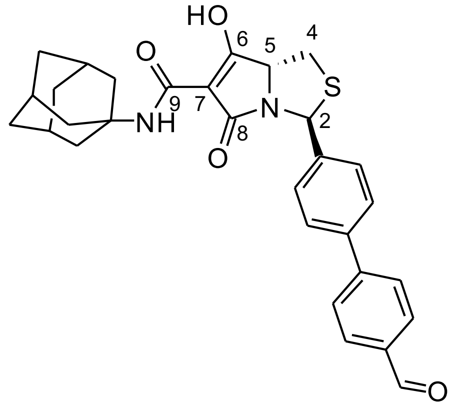
13C NMR (100.6 MHz, CDCl3)



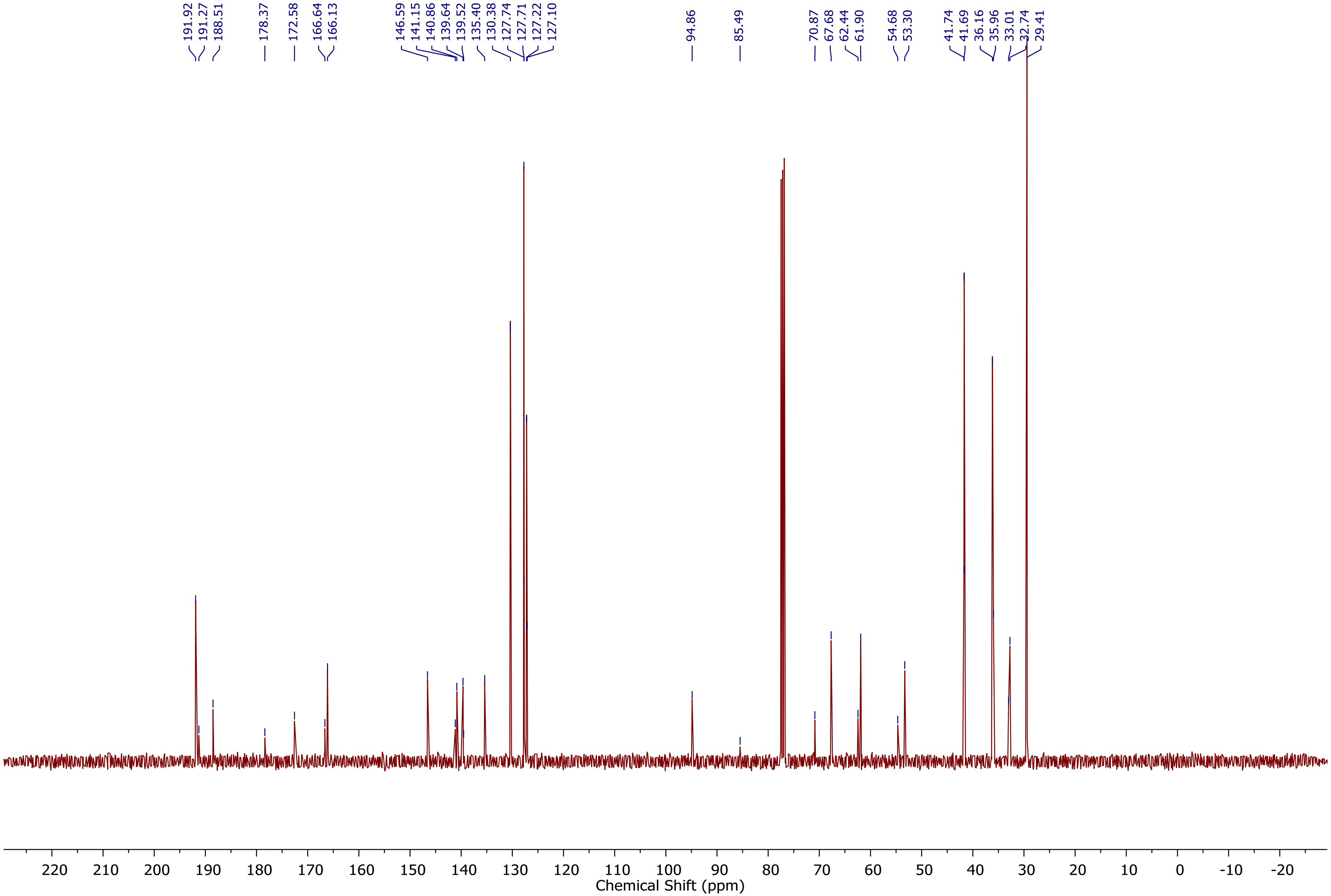
14b



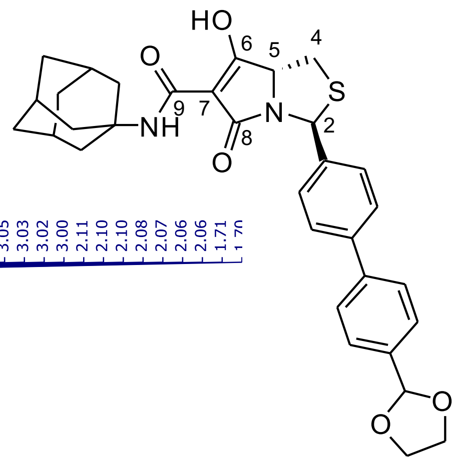
14b



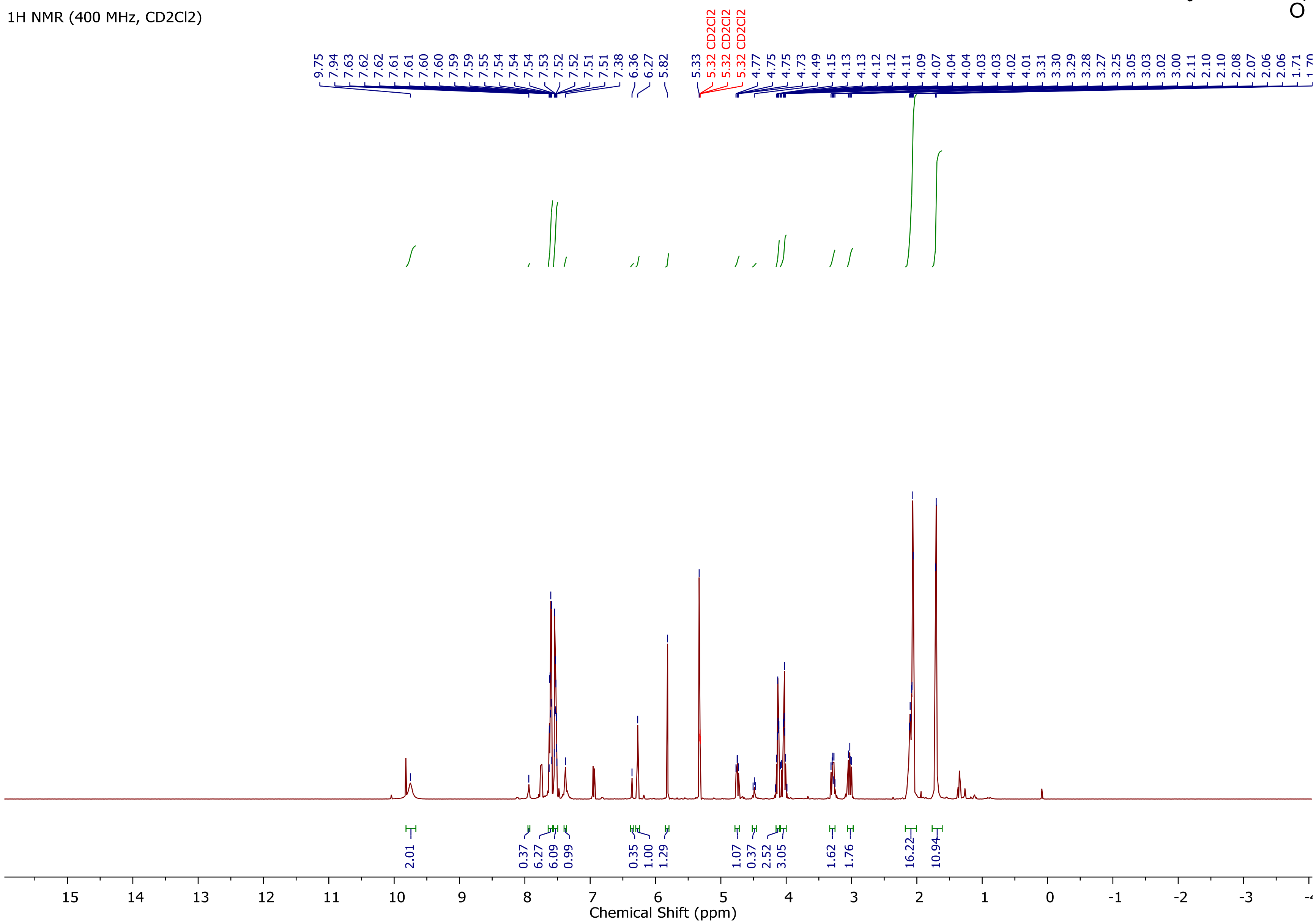
13C NMR (100.6 MHz,CDCl3)



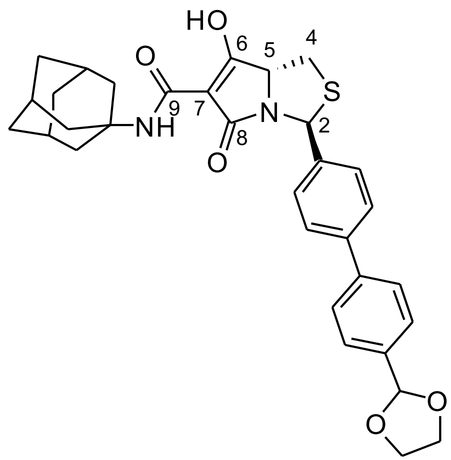
14c



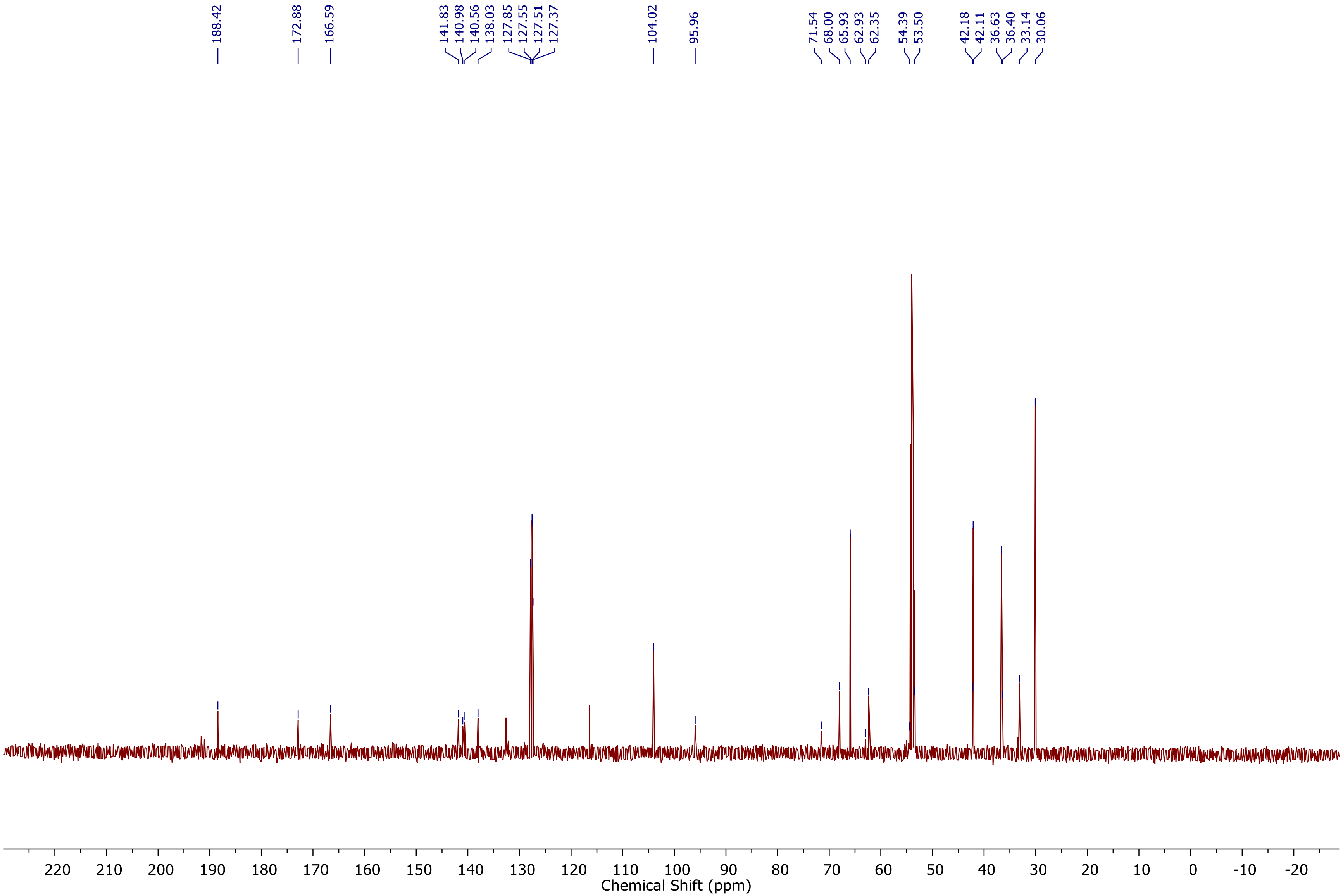
1H NMR (400 MHz, CD2Cl2)



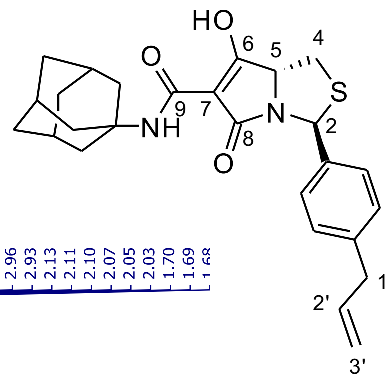
14c



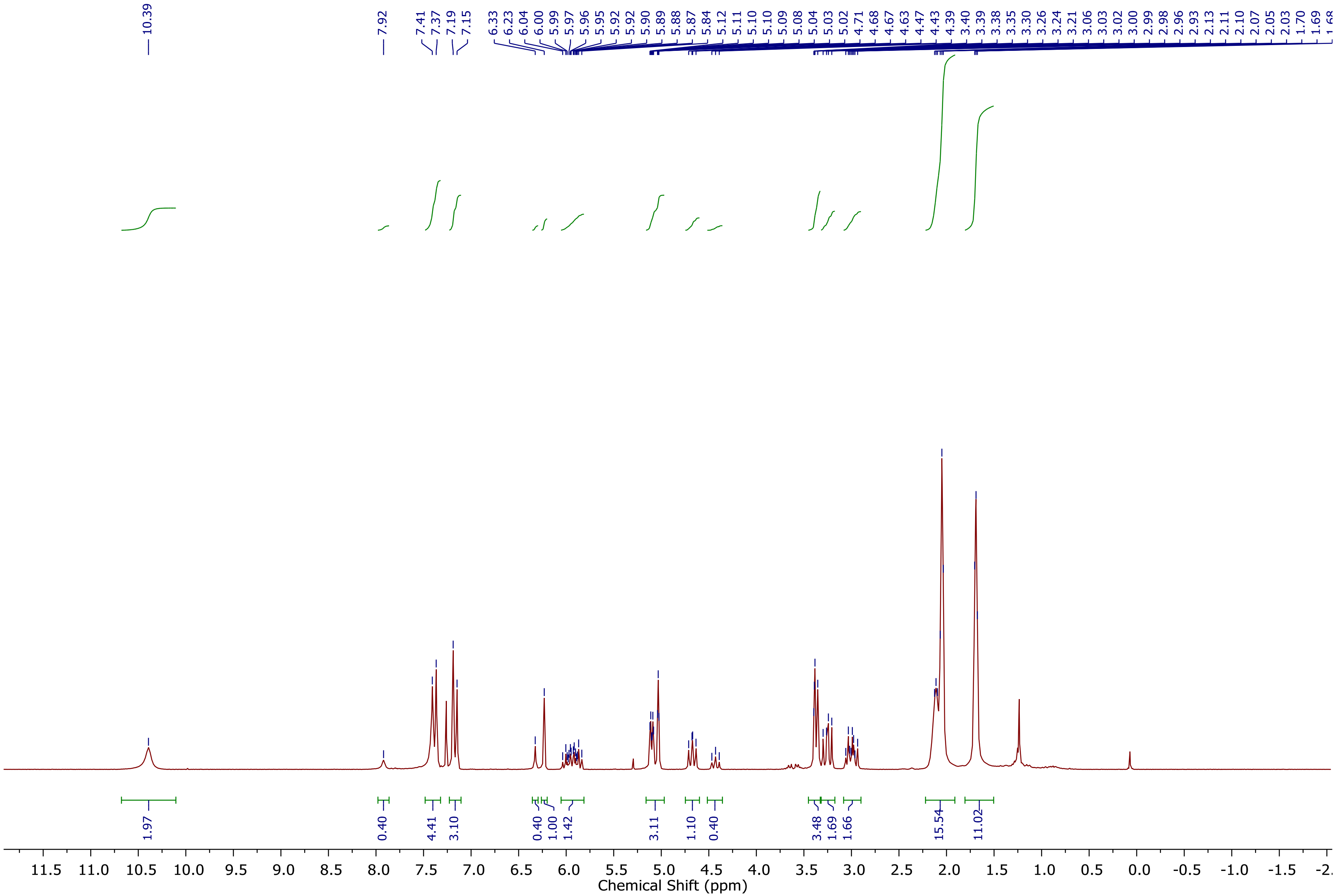
13C NMR (100.6 MHz, CD2Cl2)



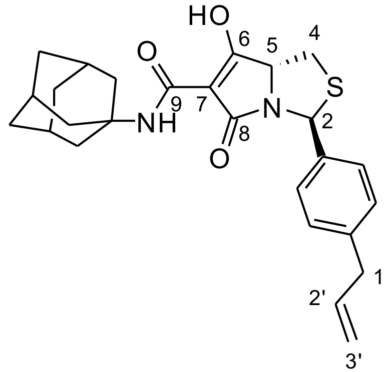
14d



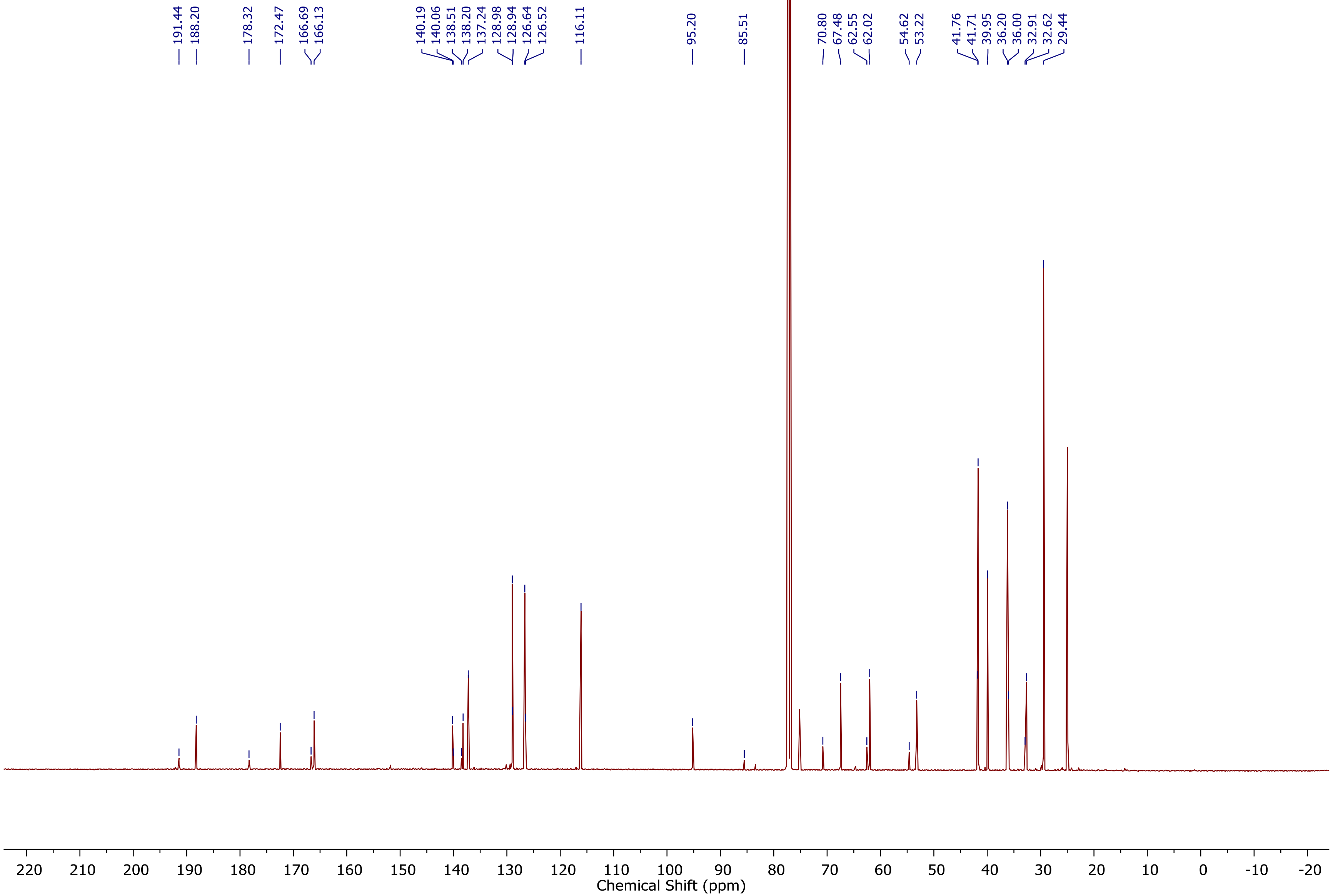
1H NMR (200 MHz, CDCl3)



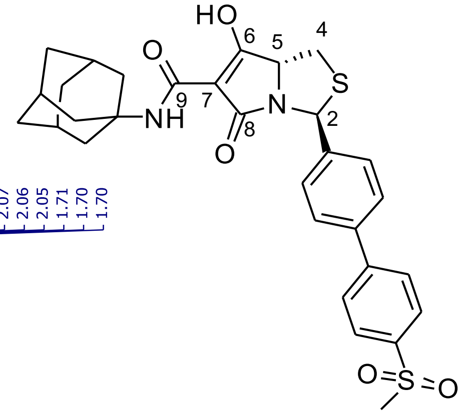
14d



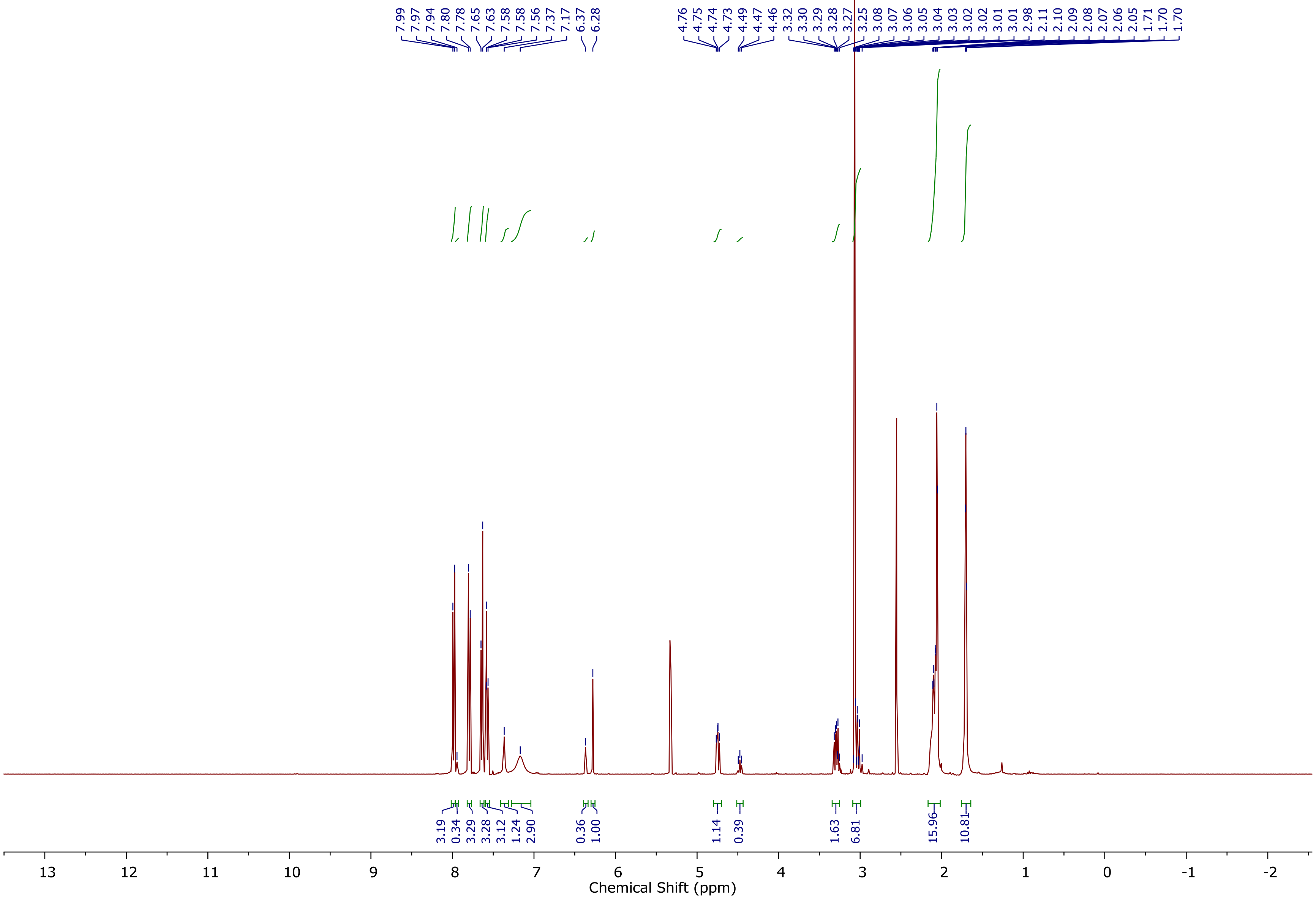
13C NMR (125.8 MHz, CDCl3)



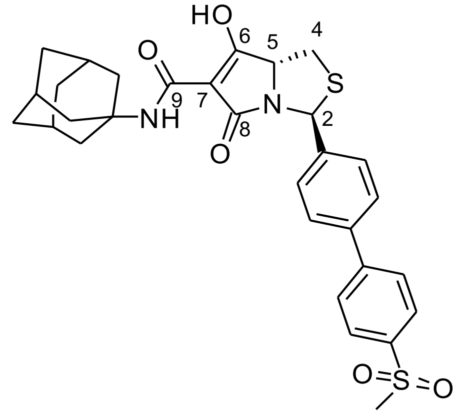
14e



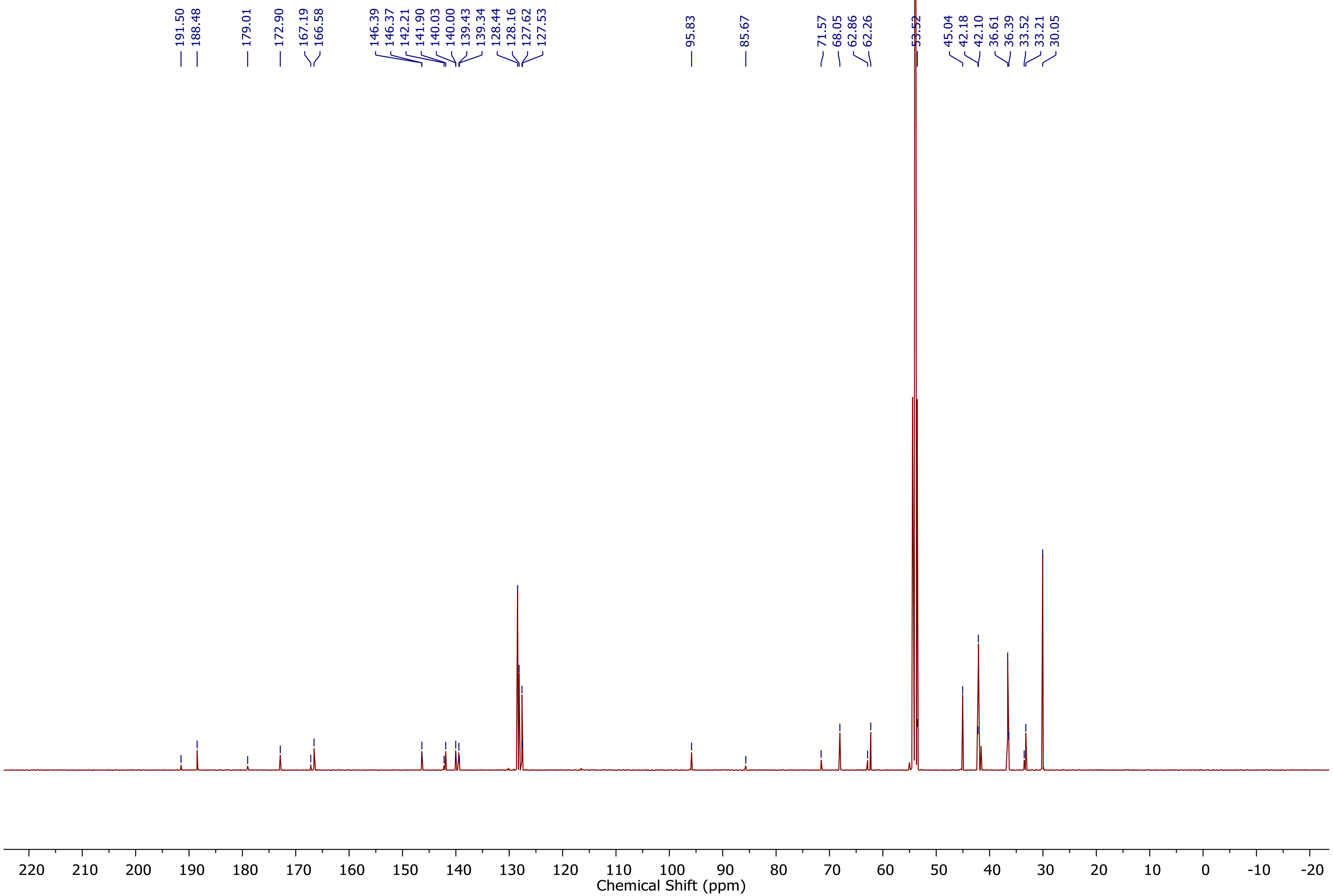
1H NMR (400 MHz, CD2Cl2)



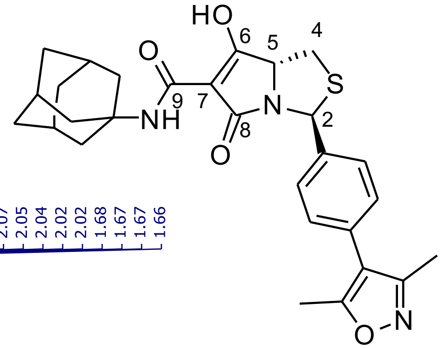
14e



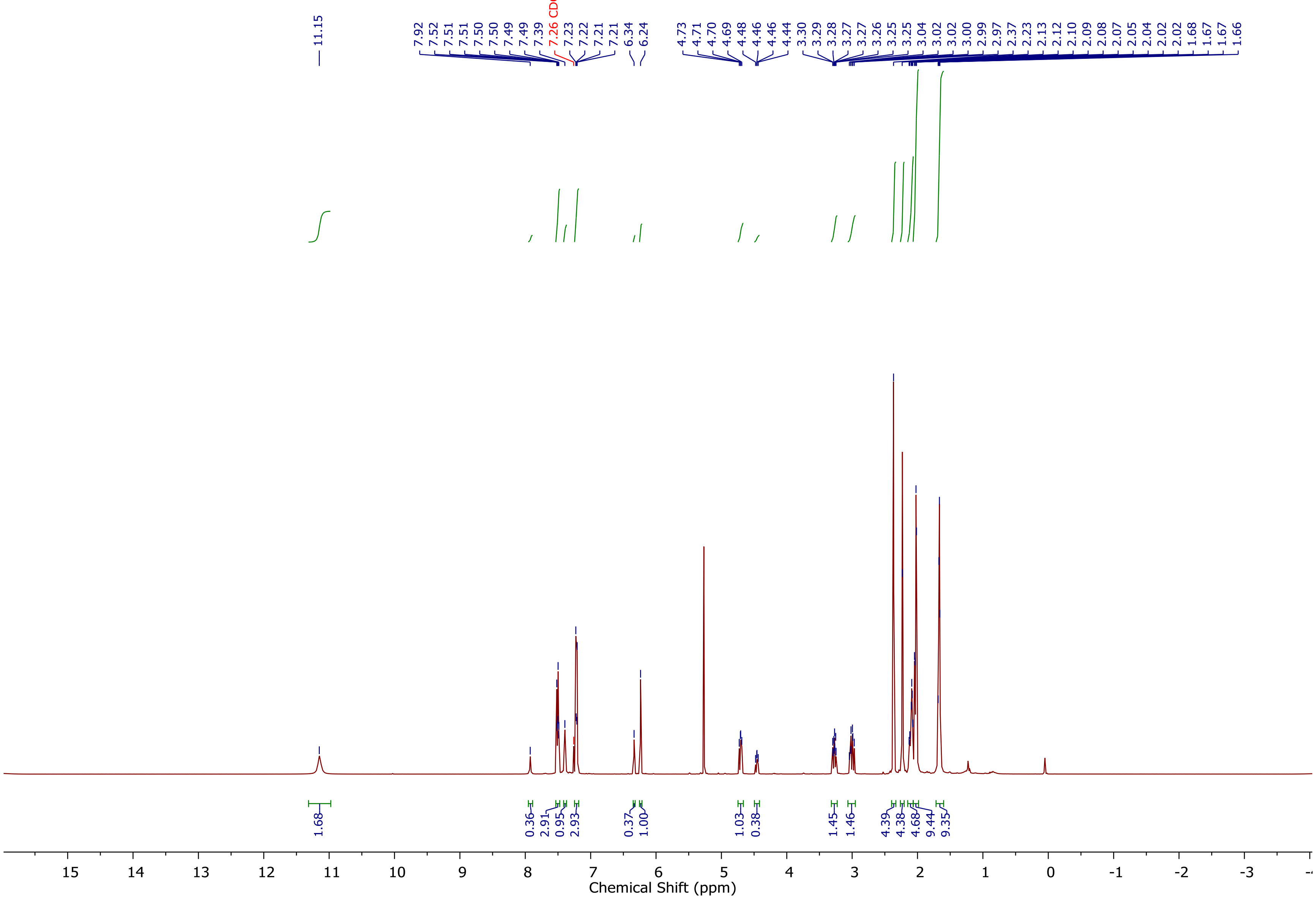
13C NMR (125.8 MHz, CD2Cl2)



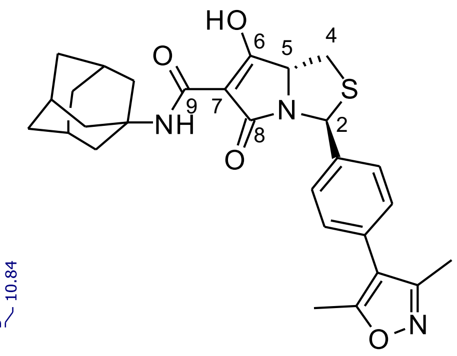
14f



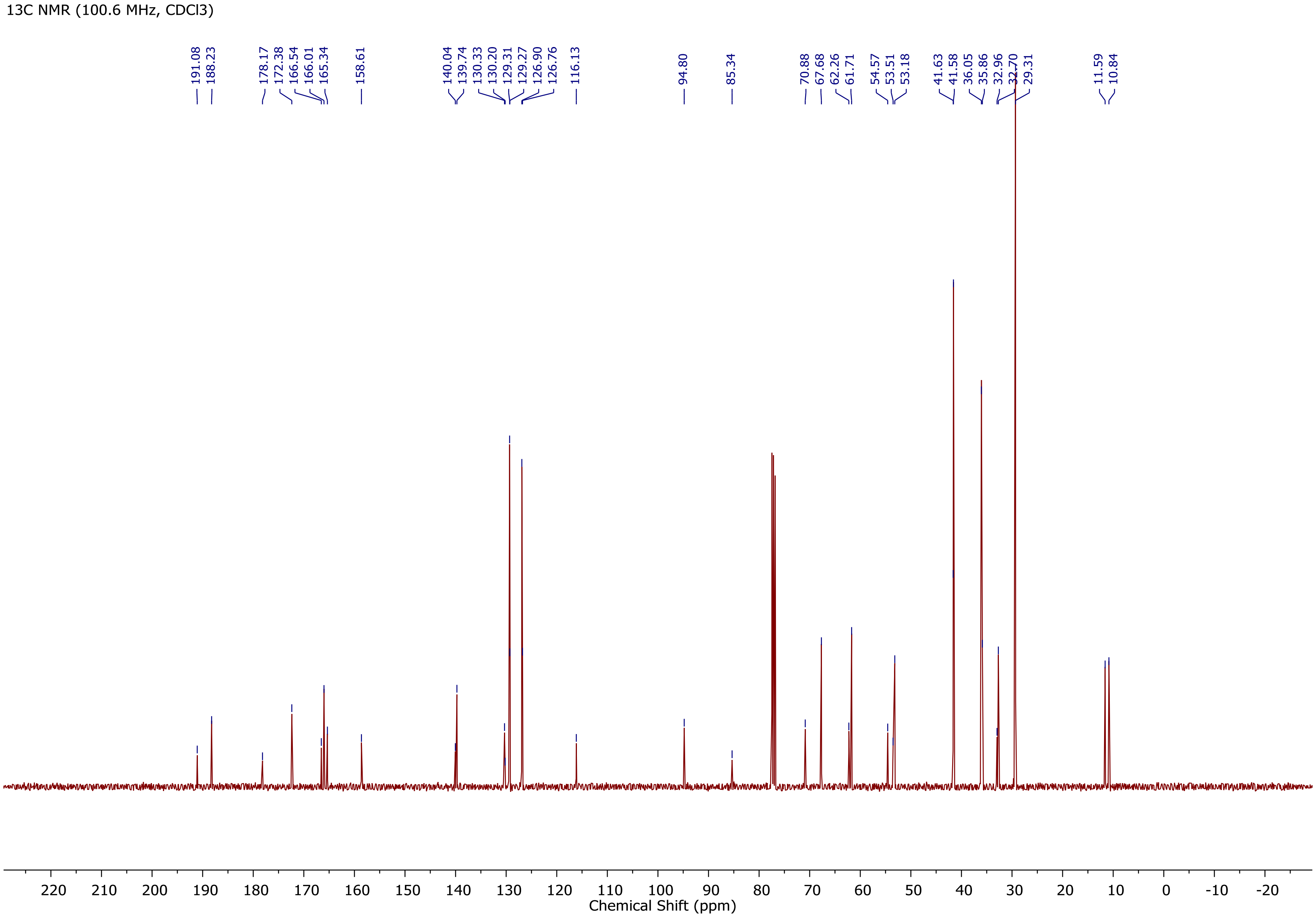
1H NMR (400 MHz, CDCl3)



14f

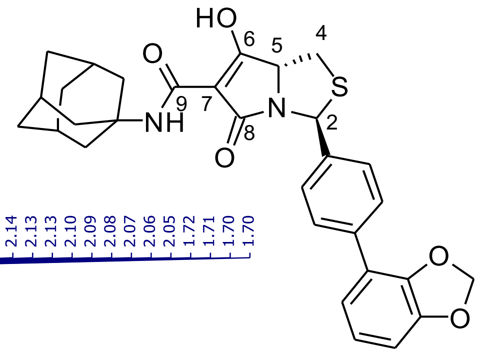


HO
6
5
4
O
S
9
7
NH
N
2
8
O
N
O

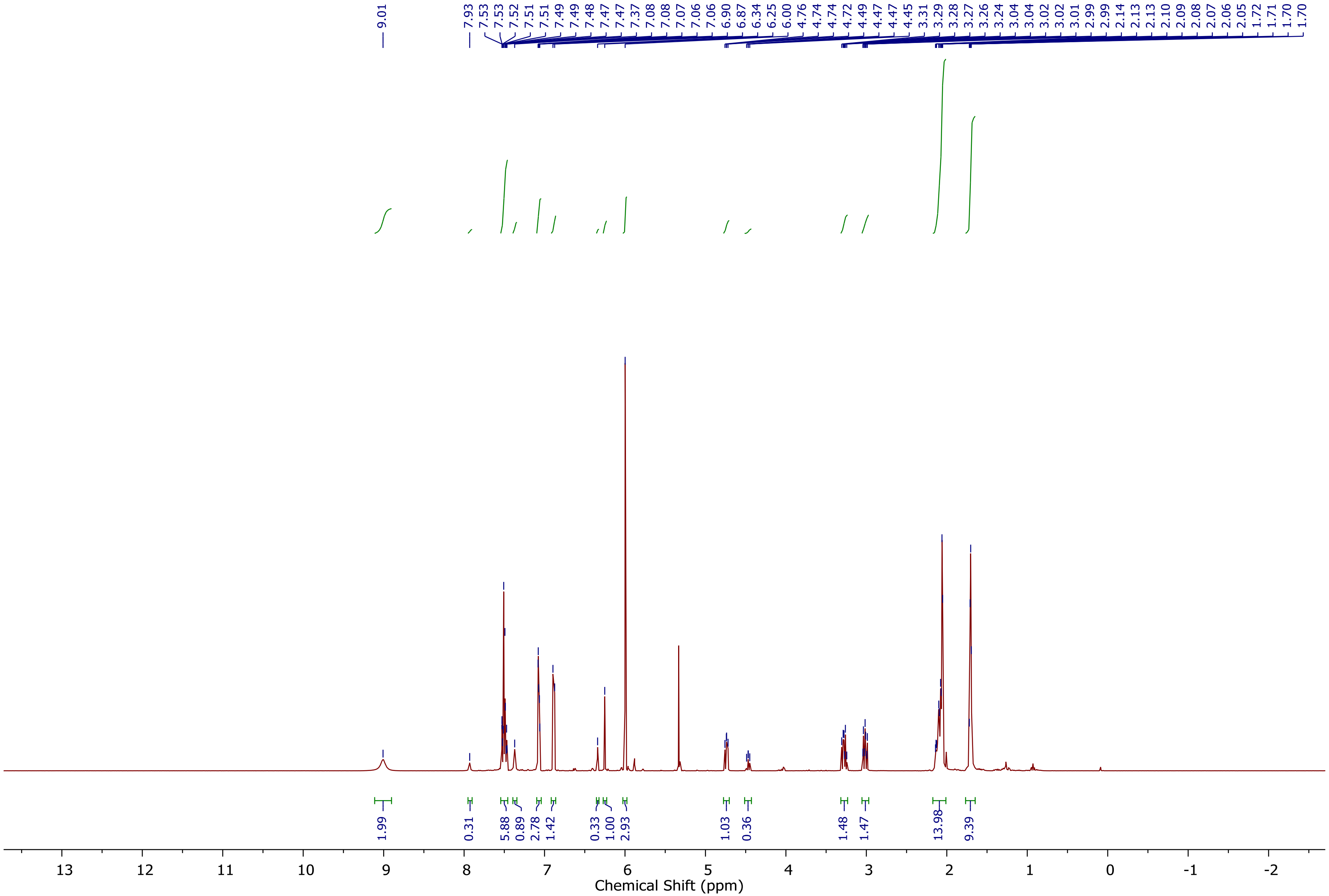


13C NMR (100.6 MHz, CDCl3)
191.08
188.23
178.17
172.38
166.54
166.01
165.34
158.61
140.04
139.74
130.33
130.20
129.31
129.27
126.90
126.76
116.13
94.80
85.34
70.88
67.68
62.26
61.71
54.57
53.51
53.18
41.63
41.58
36.05
35.86
32.96
32.70
29.31
11.59
10.84
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

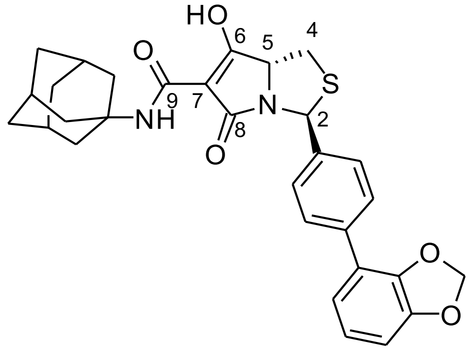
14g



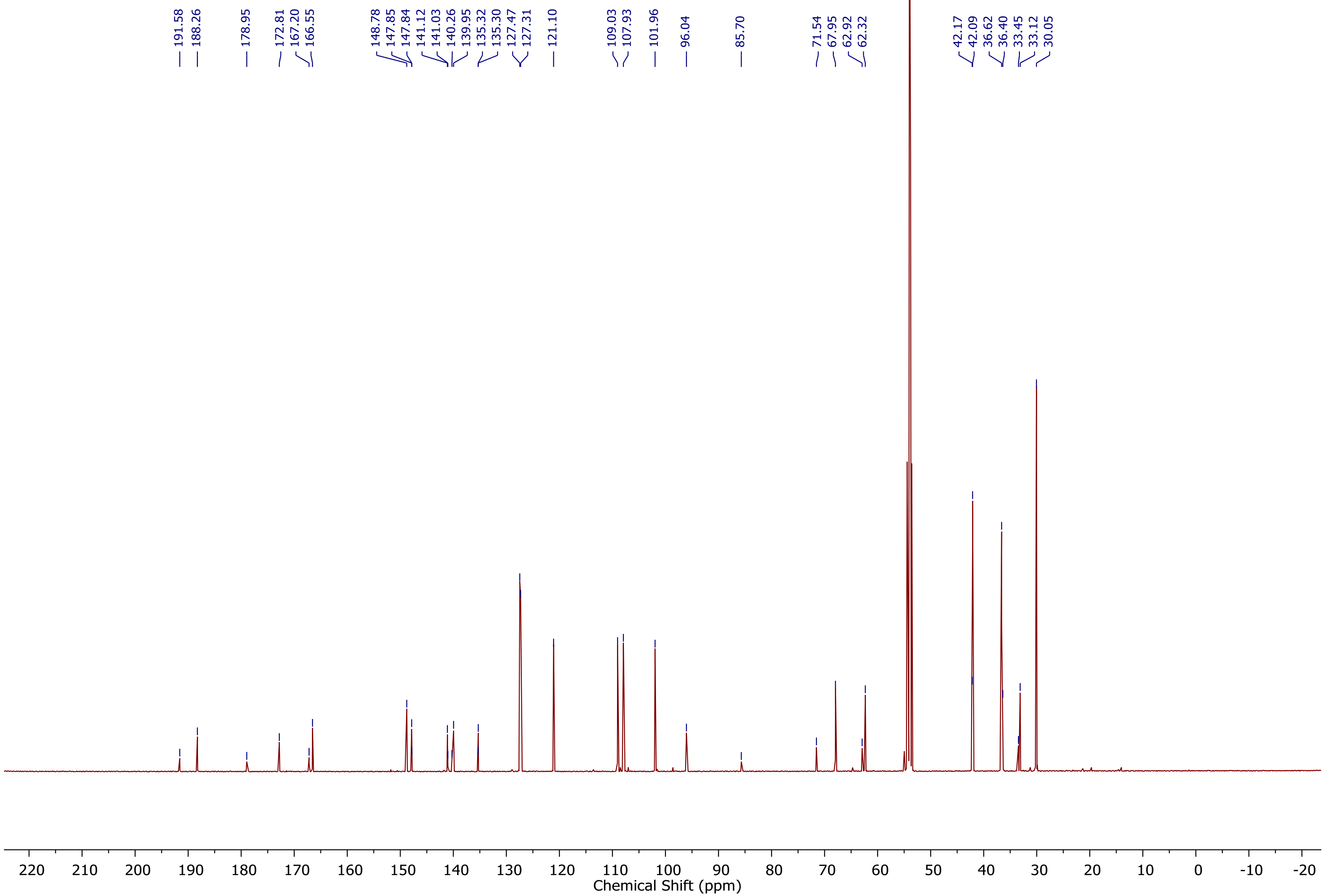
1H NMR (400 MHz, CD2Cl2)



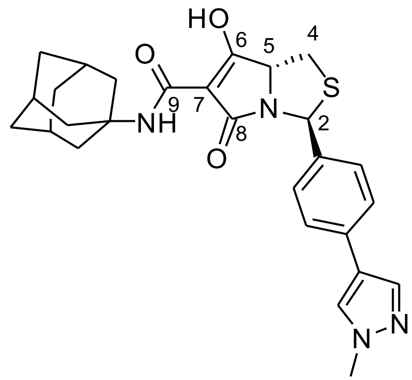
14g



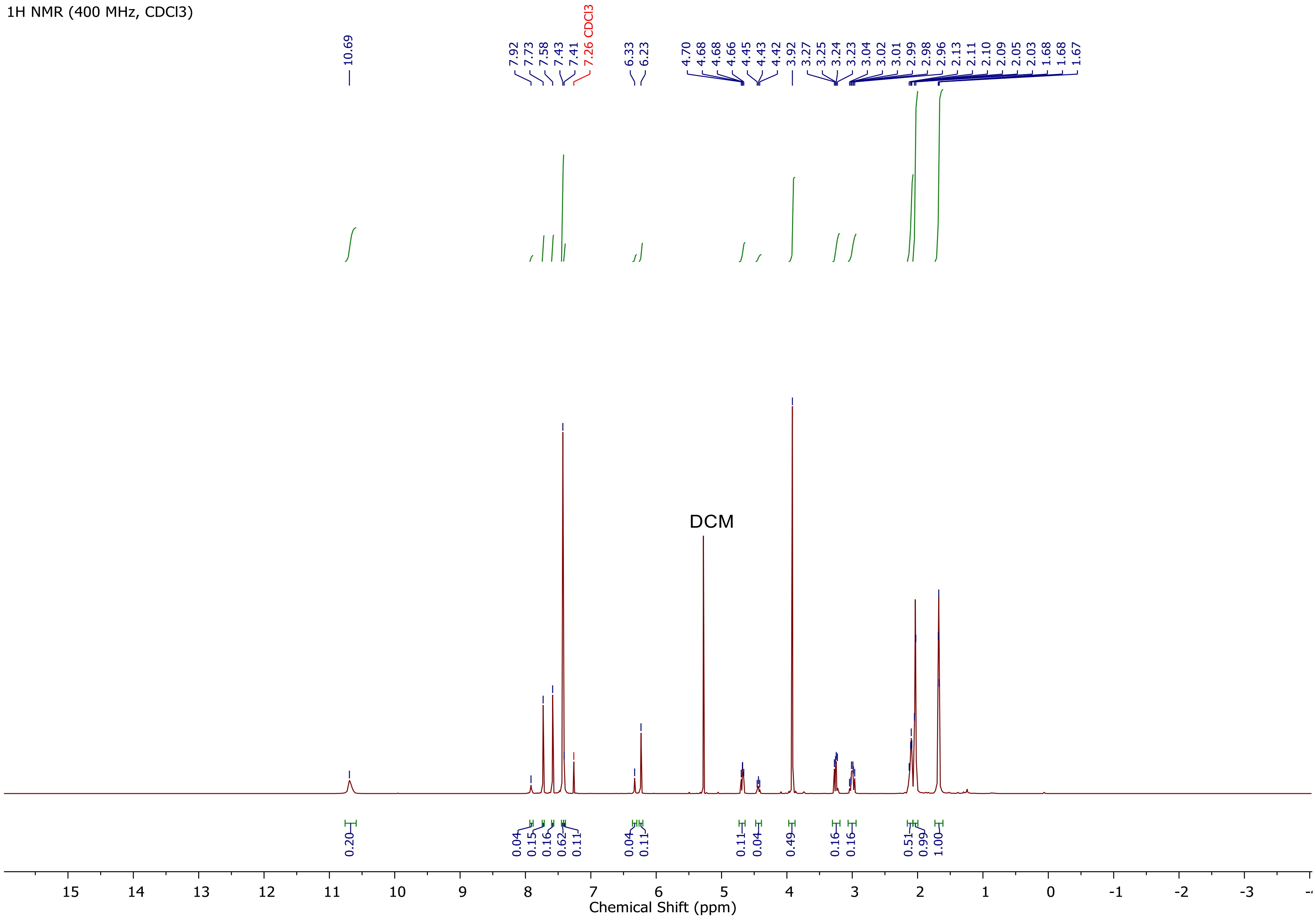
13C NMR (125.8 MHz, CD2Cl2)



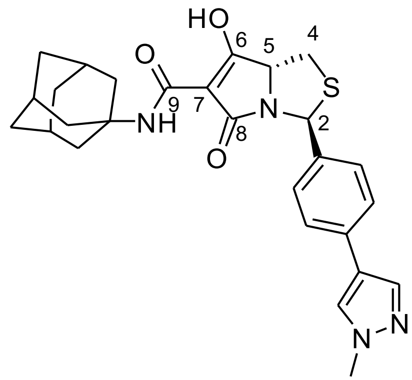
14h



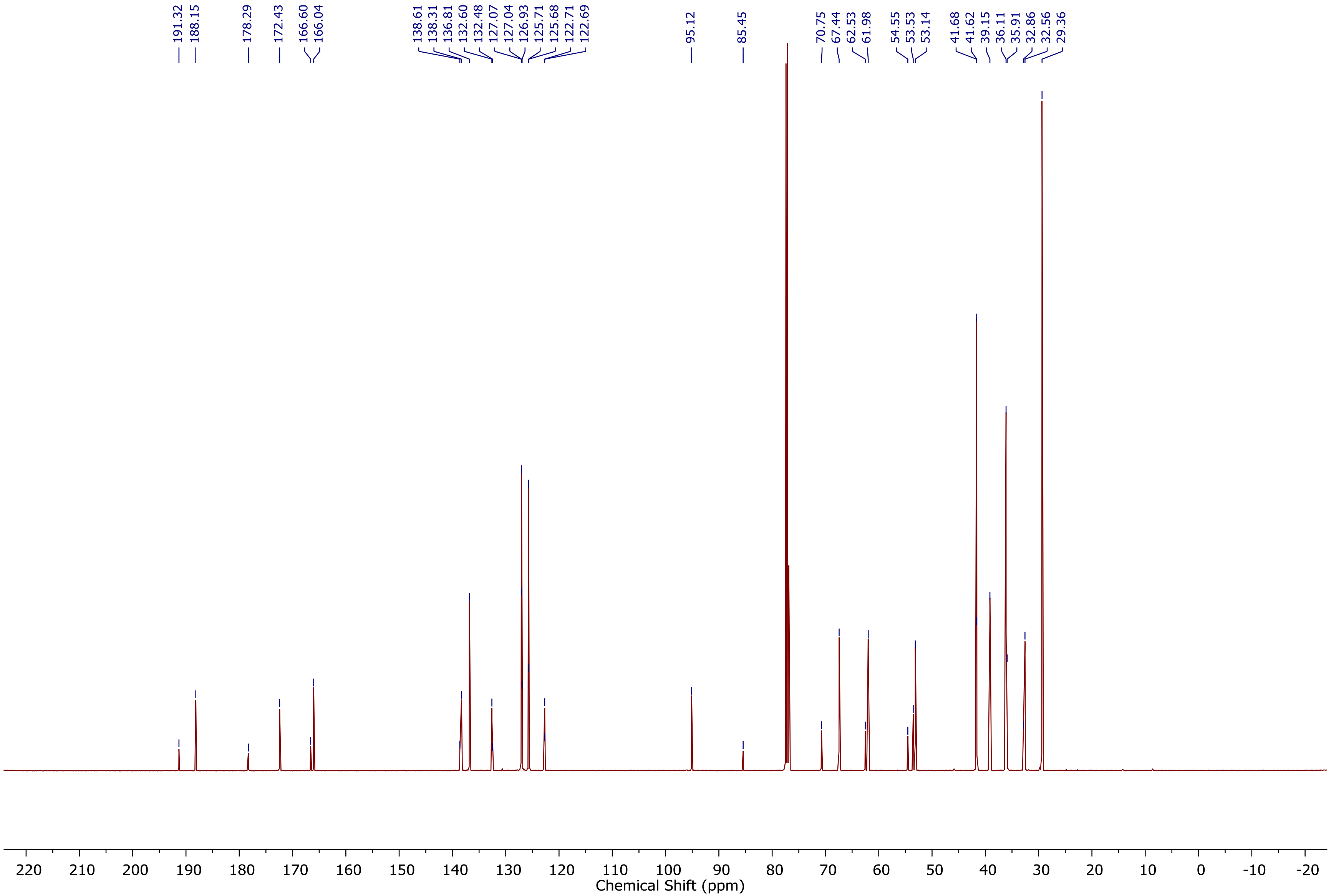
1H NMR (400 MHz, CDCl3)



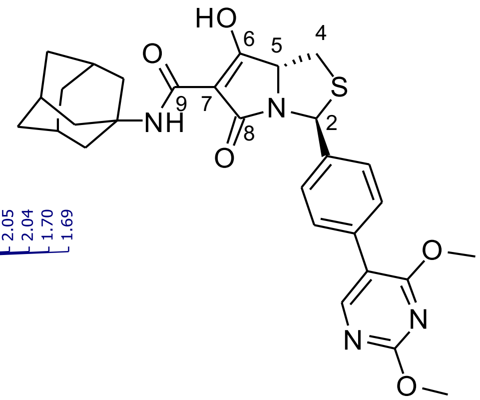
14h



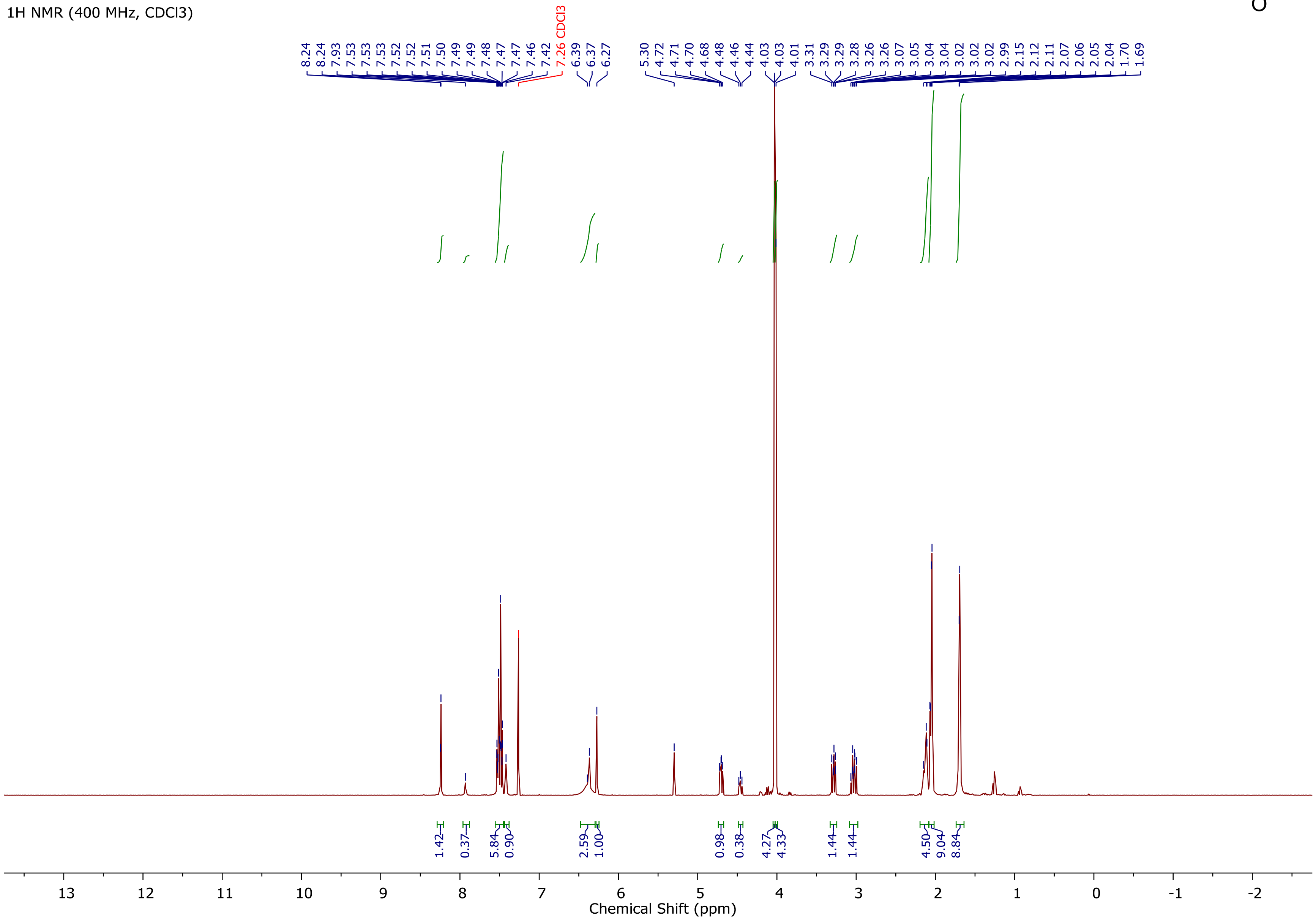
13C NMR (125.8 MHz, CDCl3)



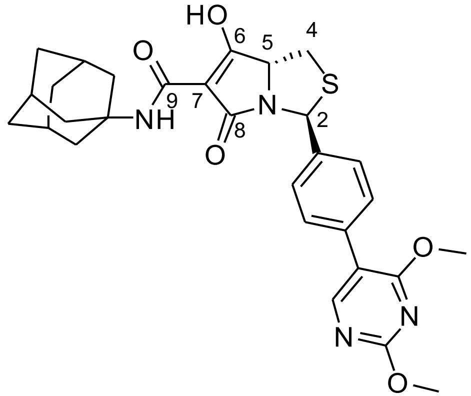
14i



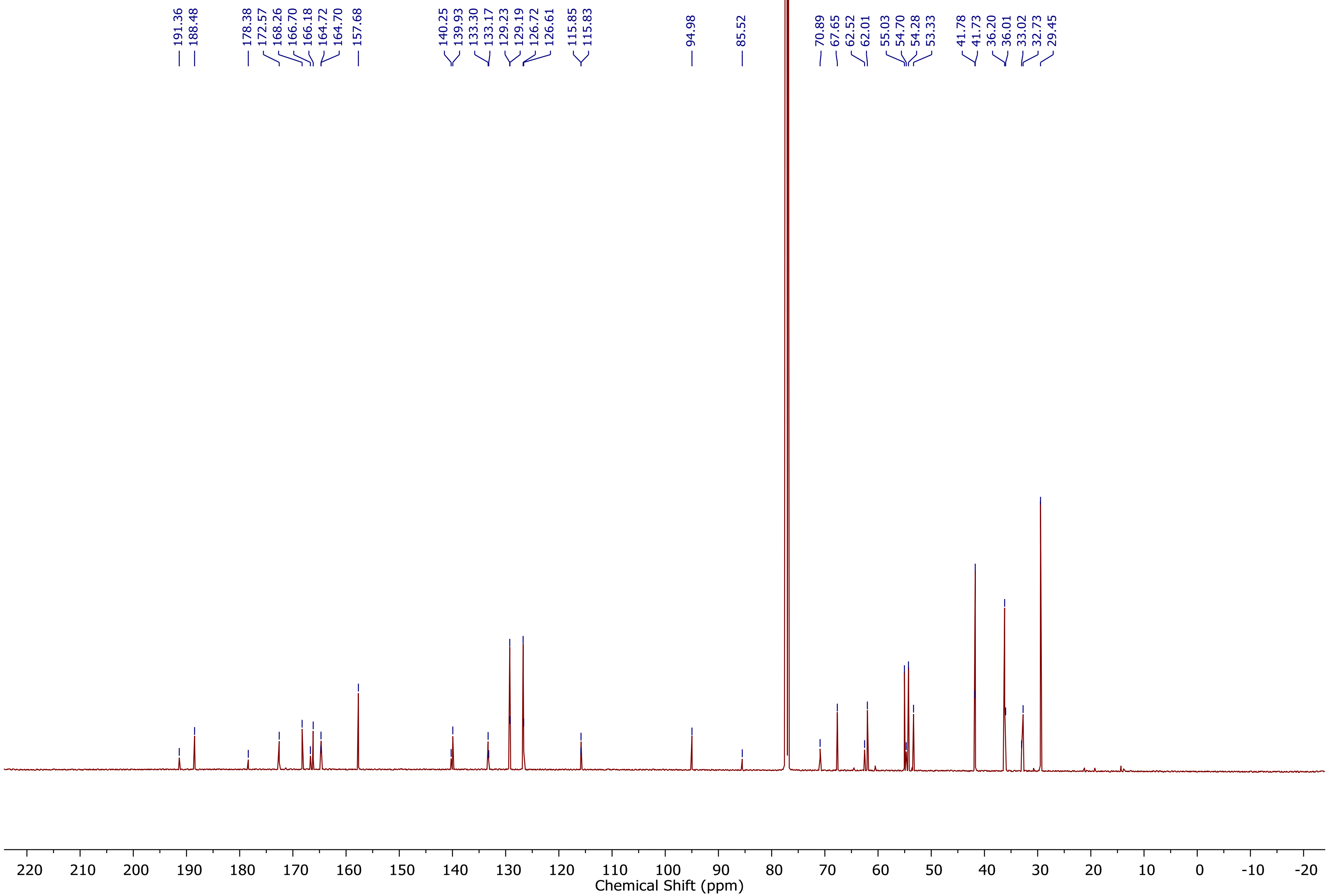
1H NMR (400 MHz, CDCl3)



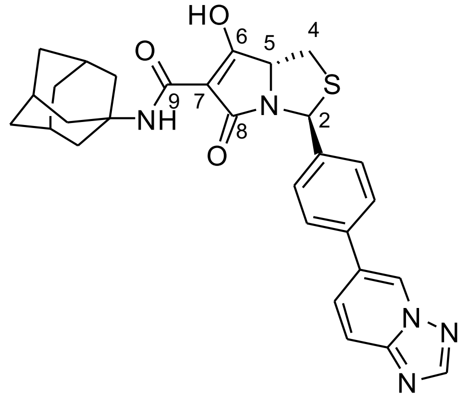
14i



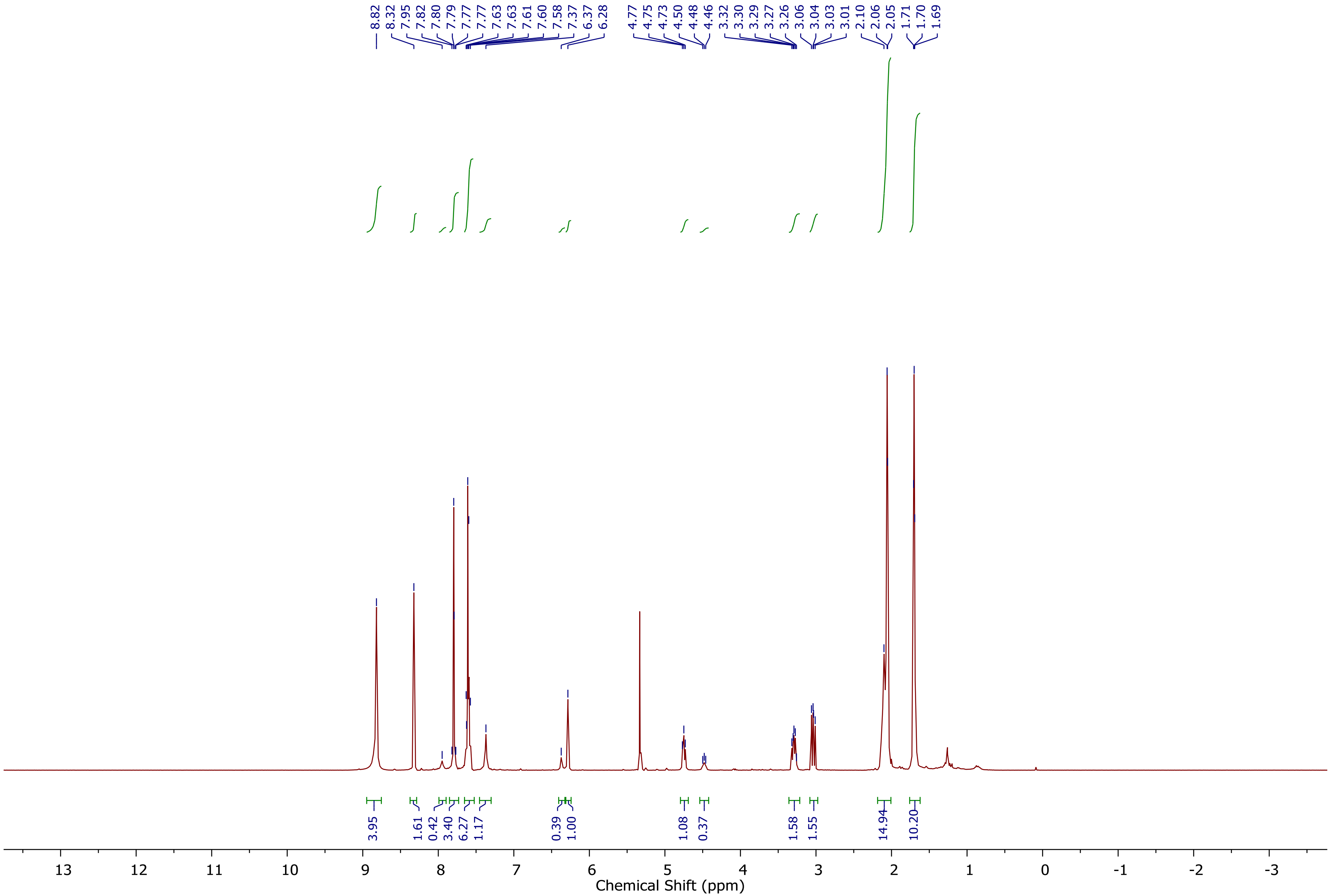
13C NMR (125.6 MHz, CDCl3)



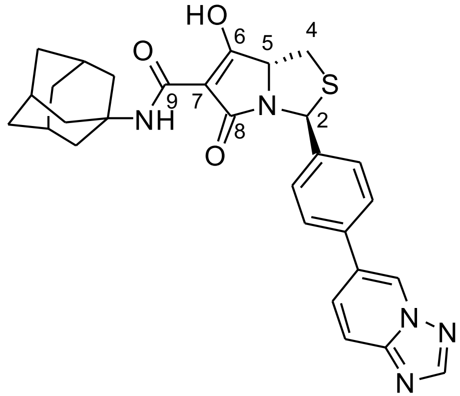
14j



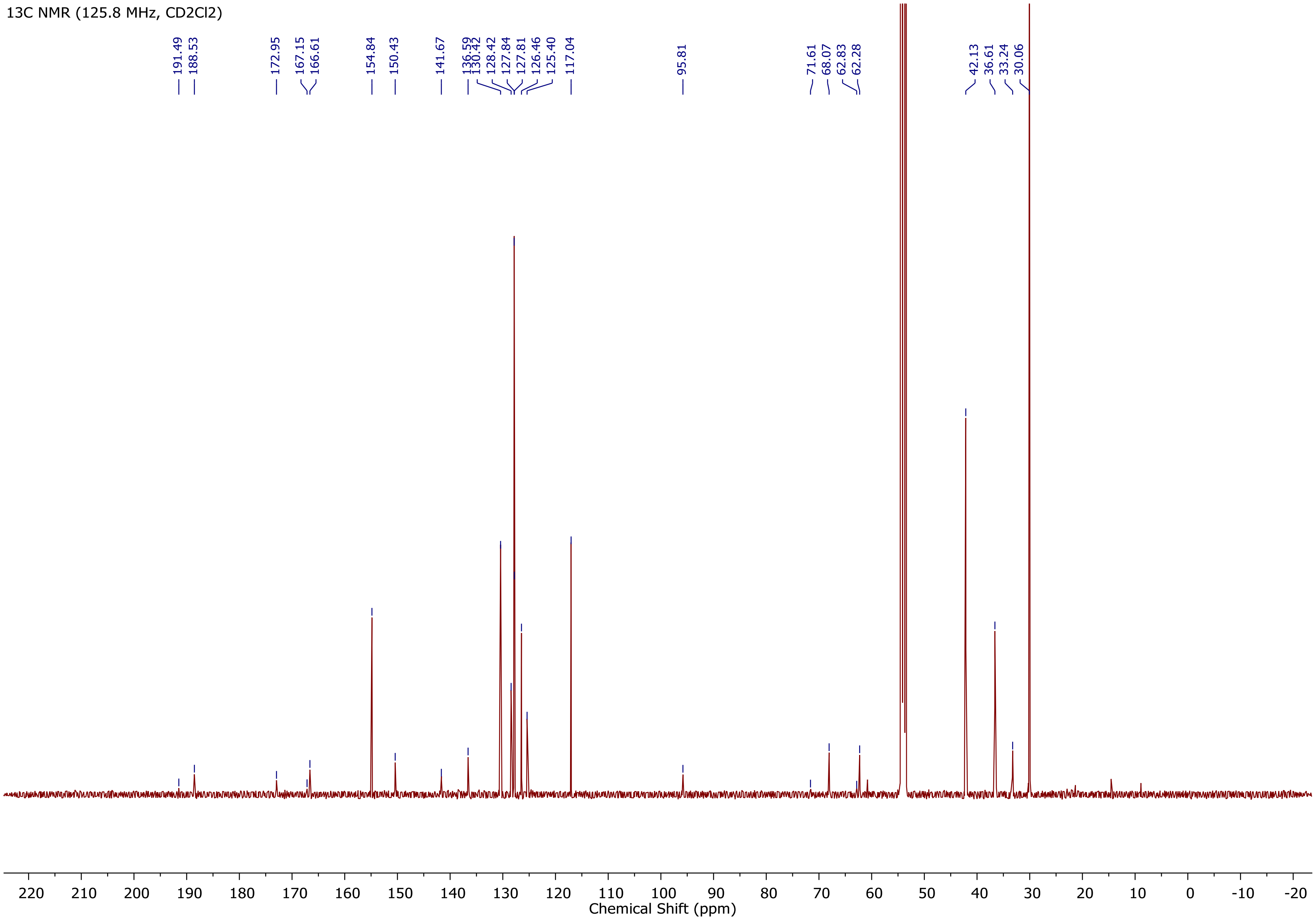
1H NMR (400 MHz, CD2Cl2)



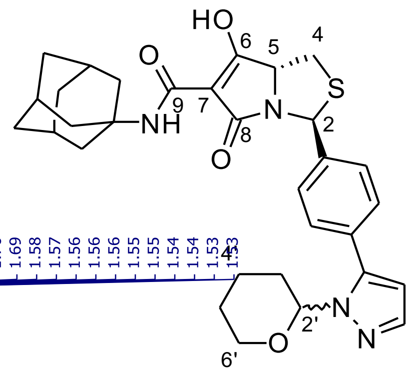
14j



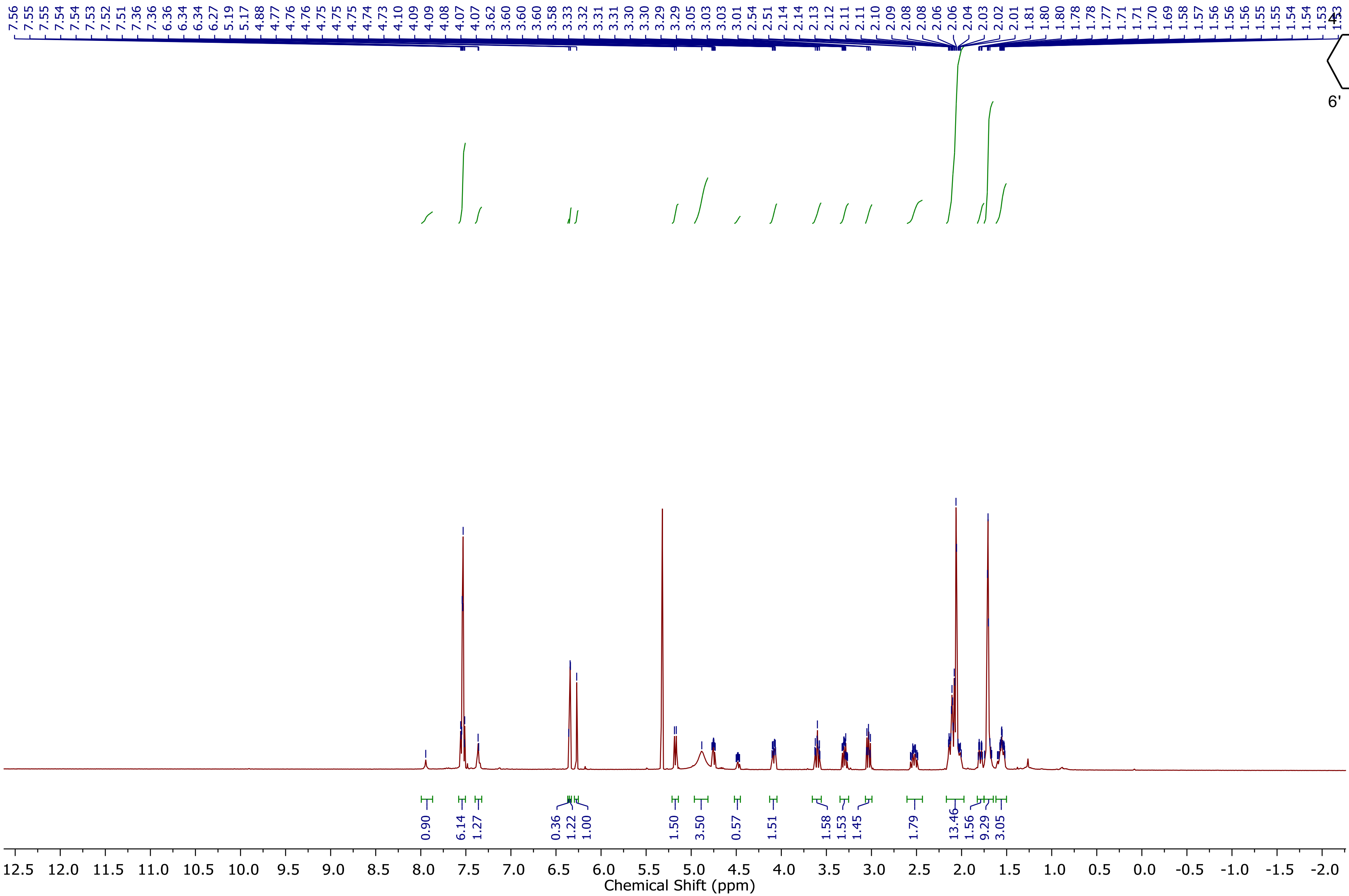
13C NMR (125.8 MHz, CD2Cl2)



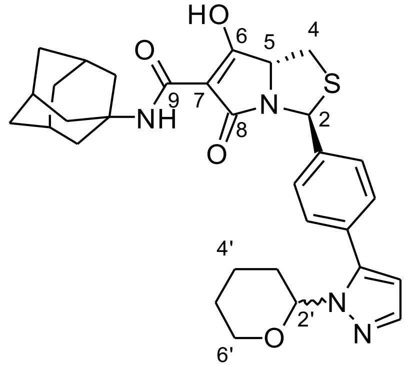
14k



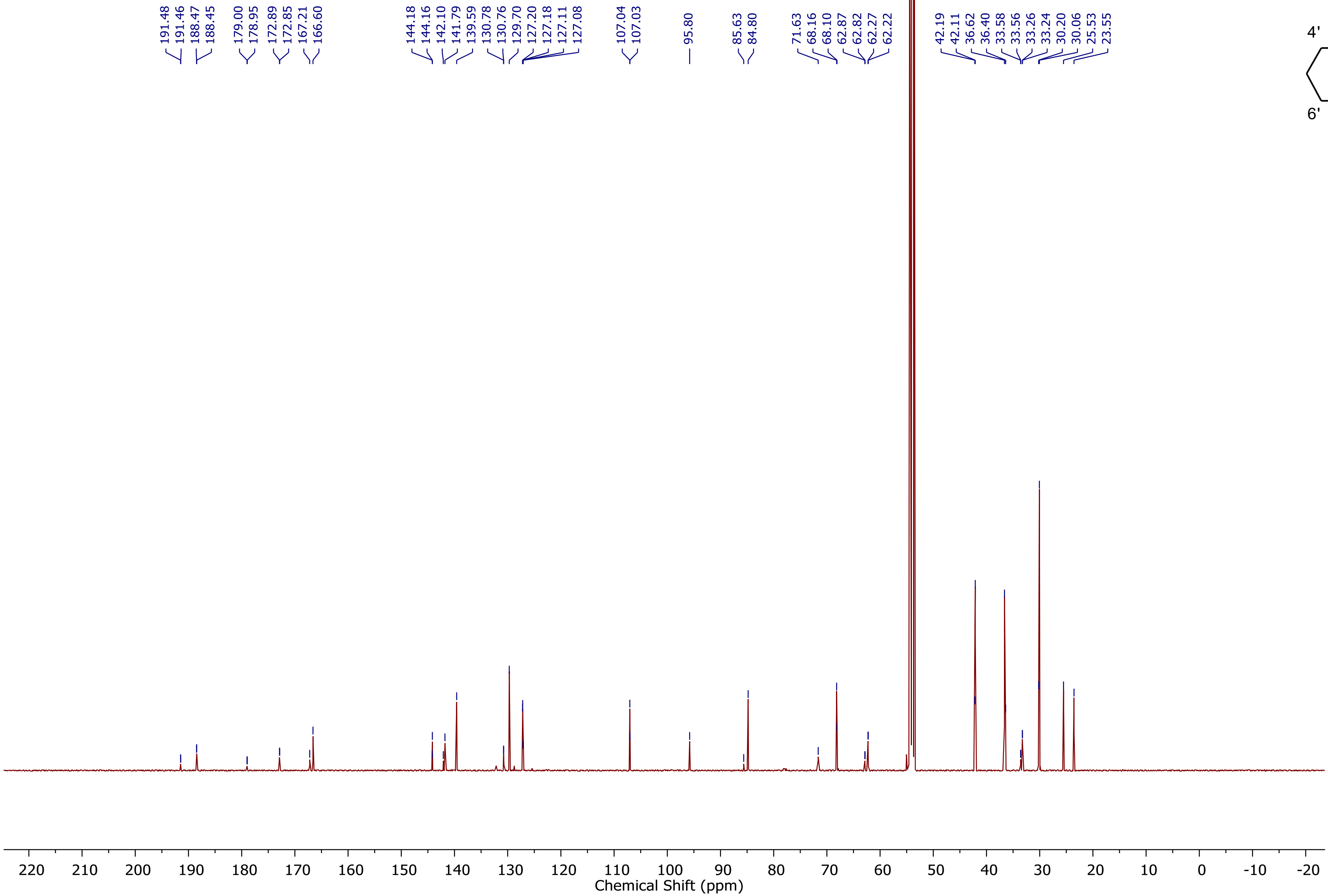
1H NMR (400 MHz, CD2Cl2)



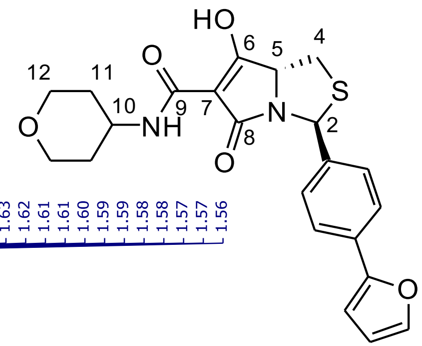
14k



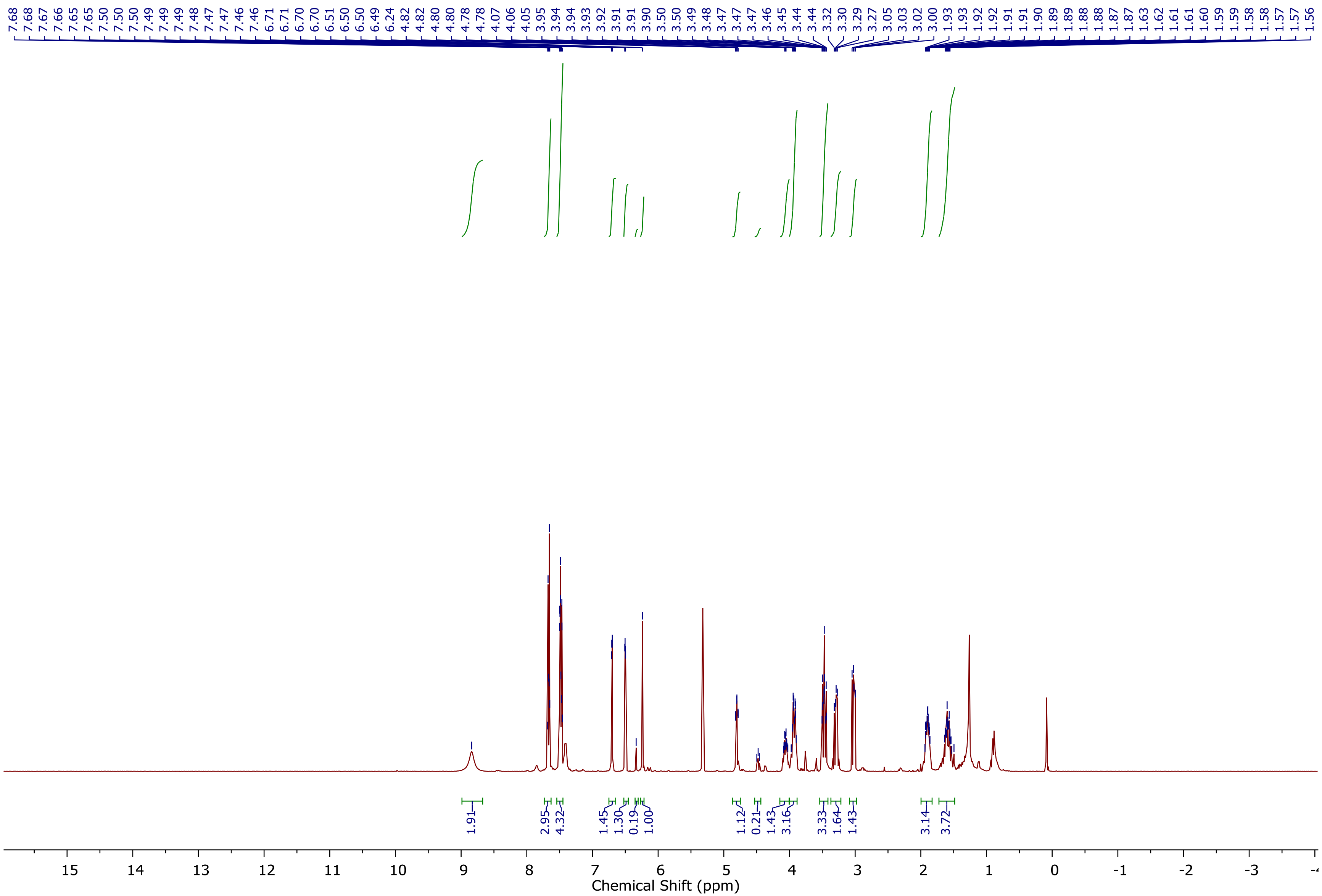
13C NMR (125.8 MHz, CD2Cl2)



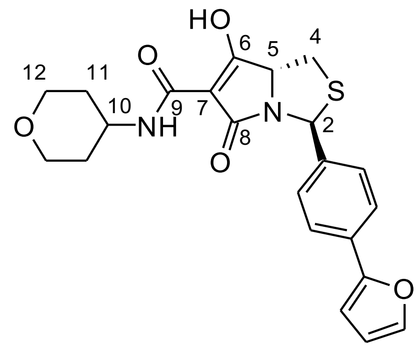
14l



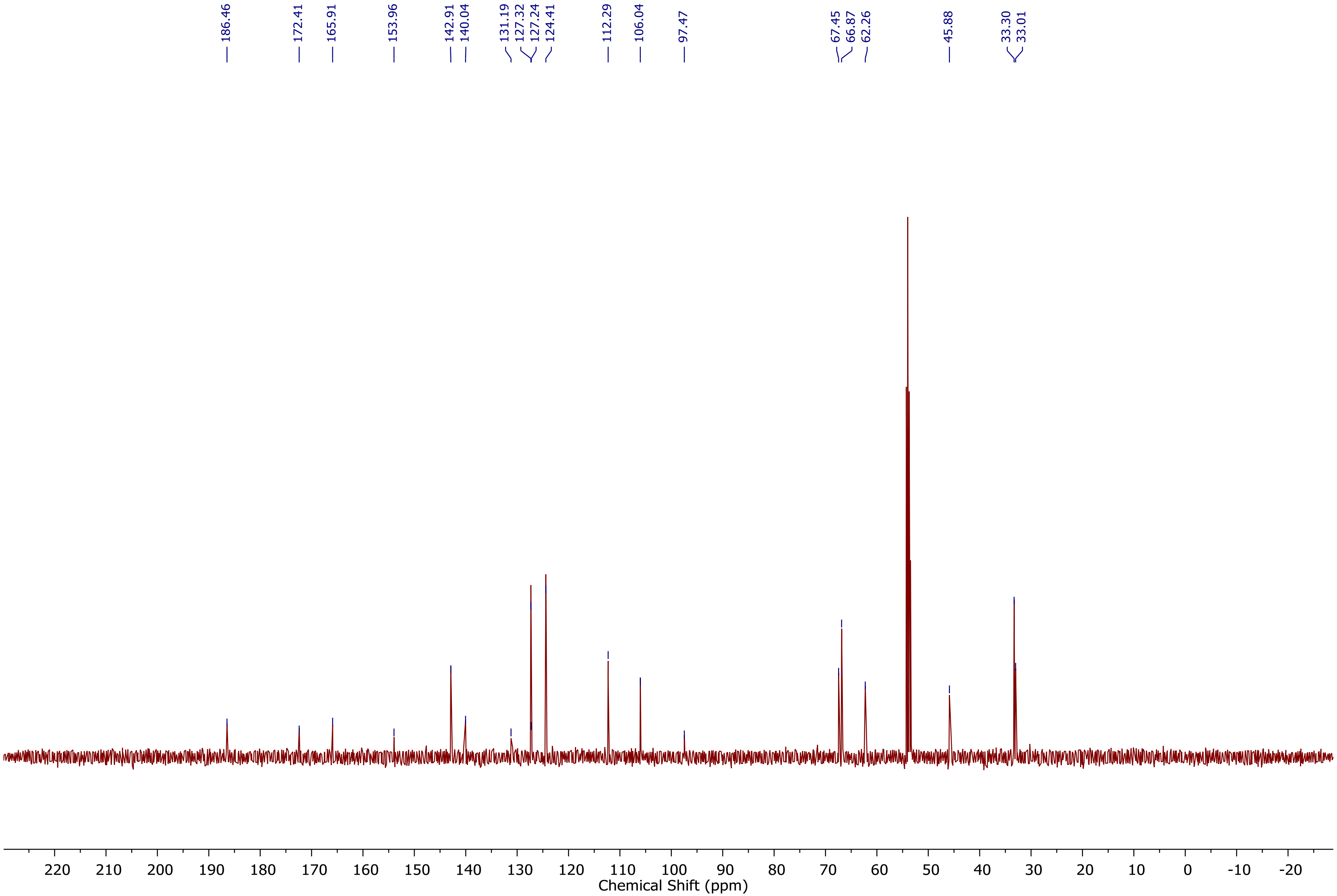
1H NMR (400 MHz, CD2Cl2)



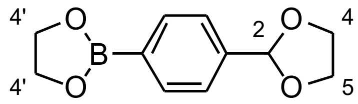
14l



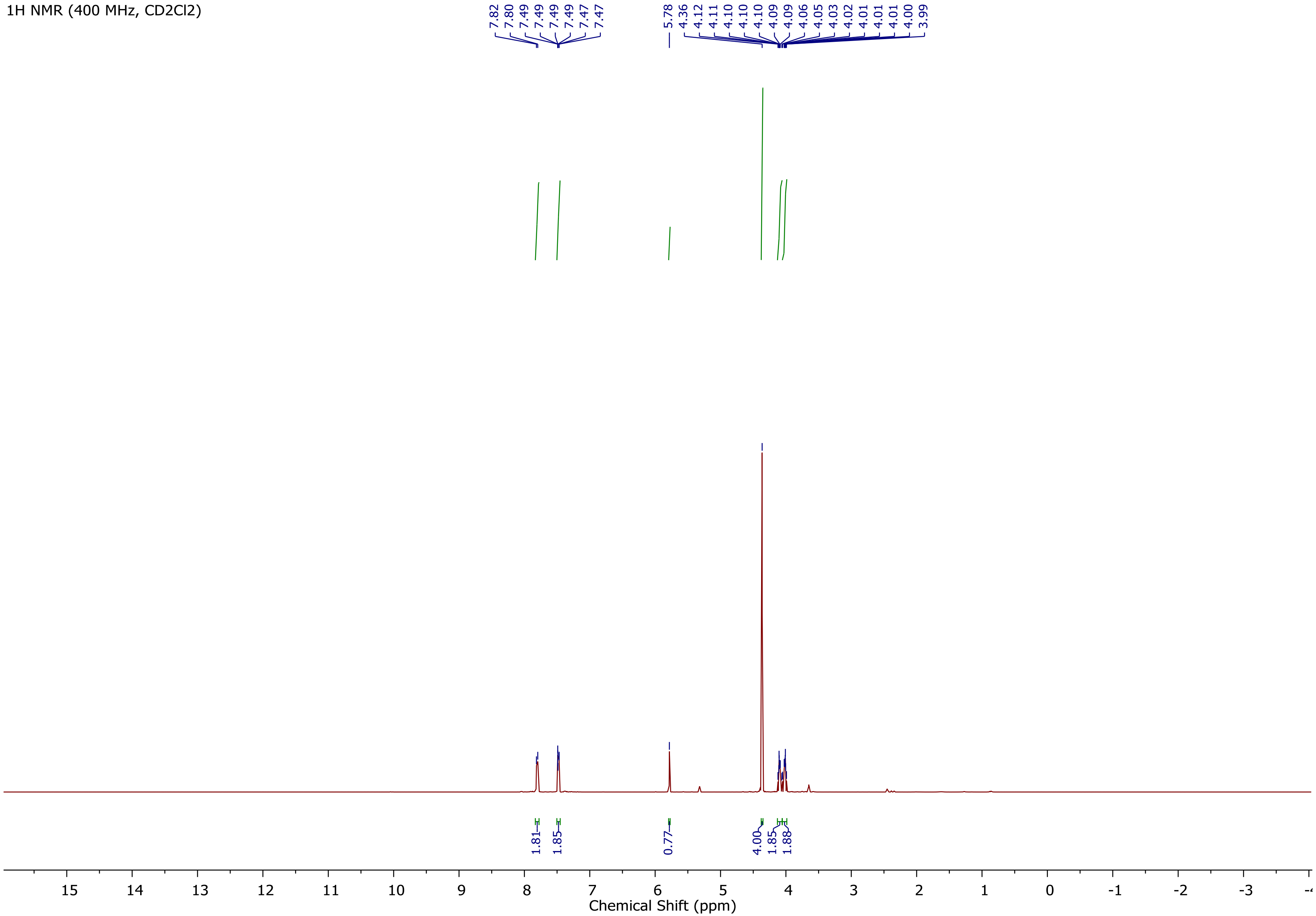
13C NMR (100.6 MHz, CD2Cl2)



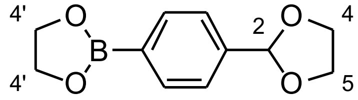
2-(4-(1,3-dioxolan-2-yl)phenyl)-1,3,2-dioxaborolane

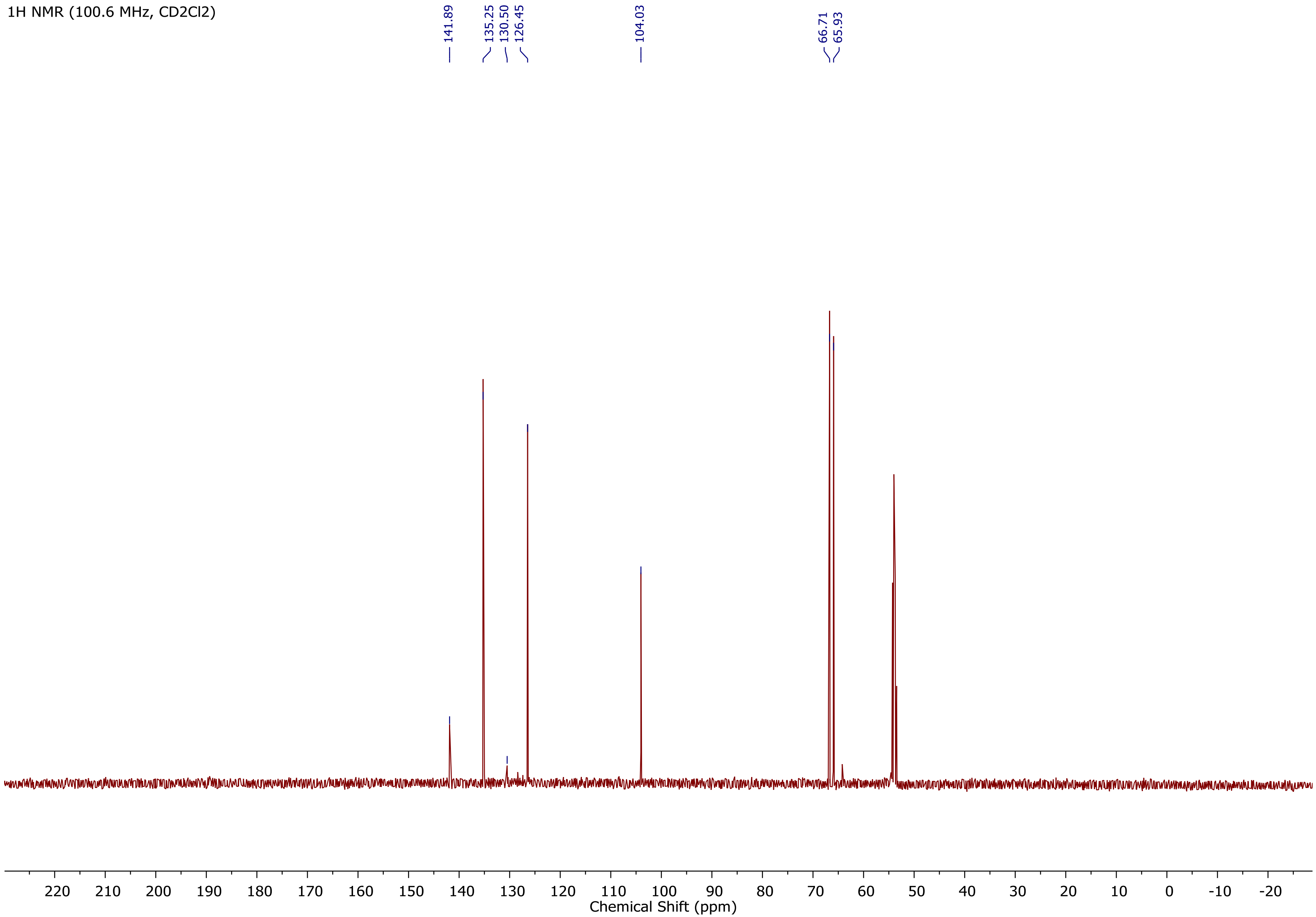


1H NMR (400 MHz, CD2Cl2)

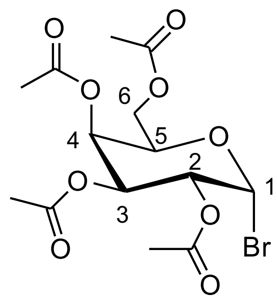


2-(4-(1,3-dioxolan-2-yl)phenyl)-1,3,2-dioxaborolane

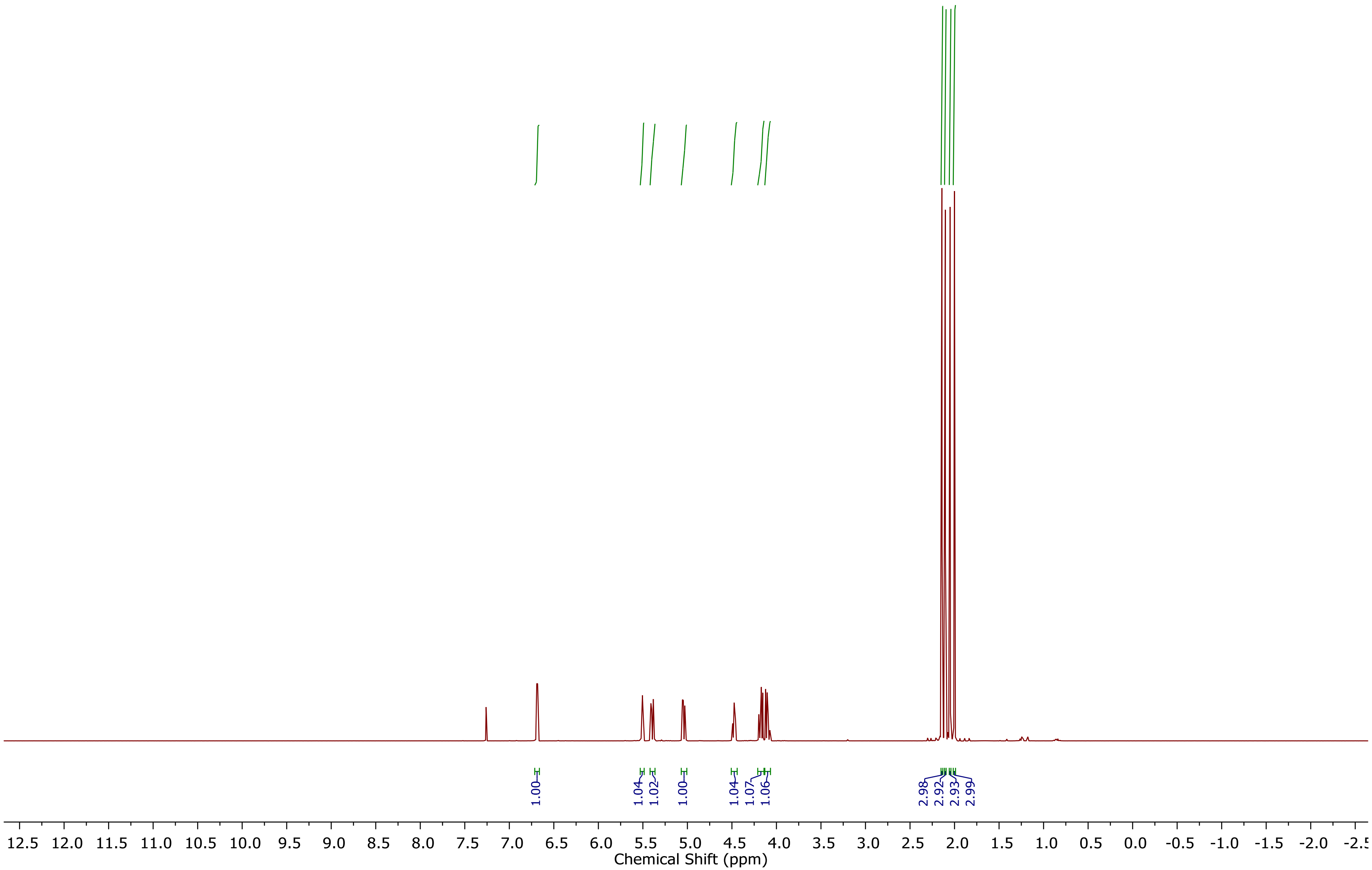




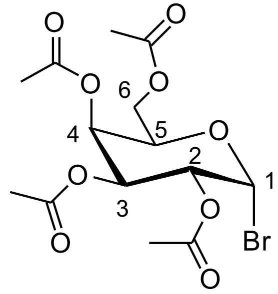
(+)-2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide 15b



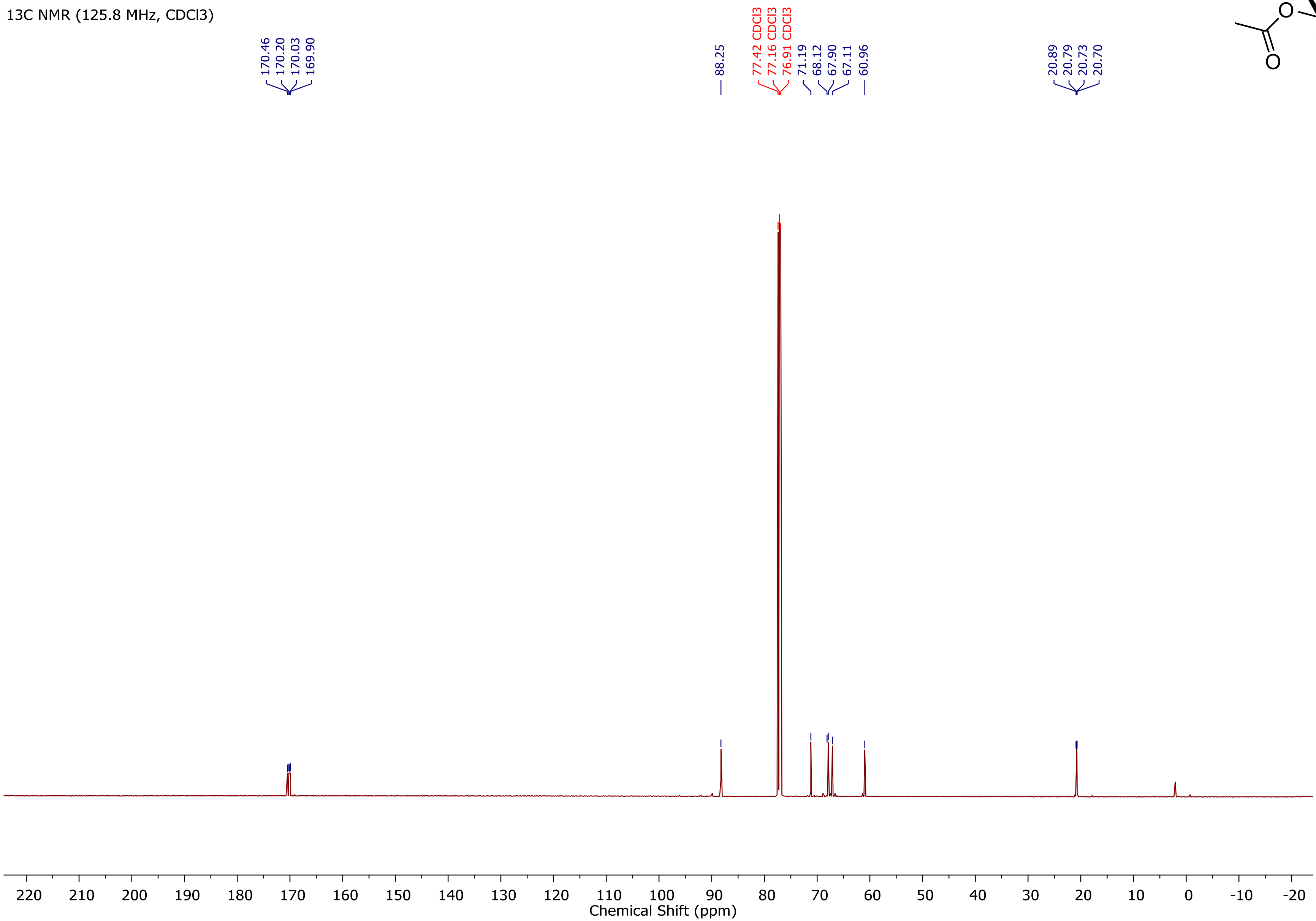
1H NMR (400 MHz, CDCl3)



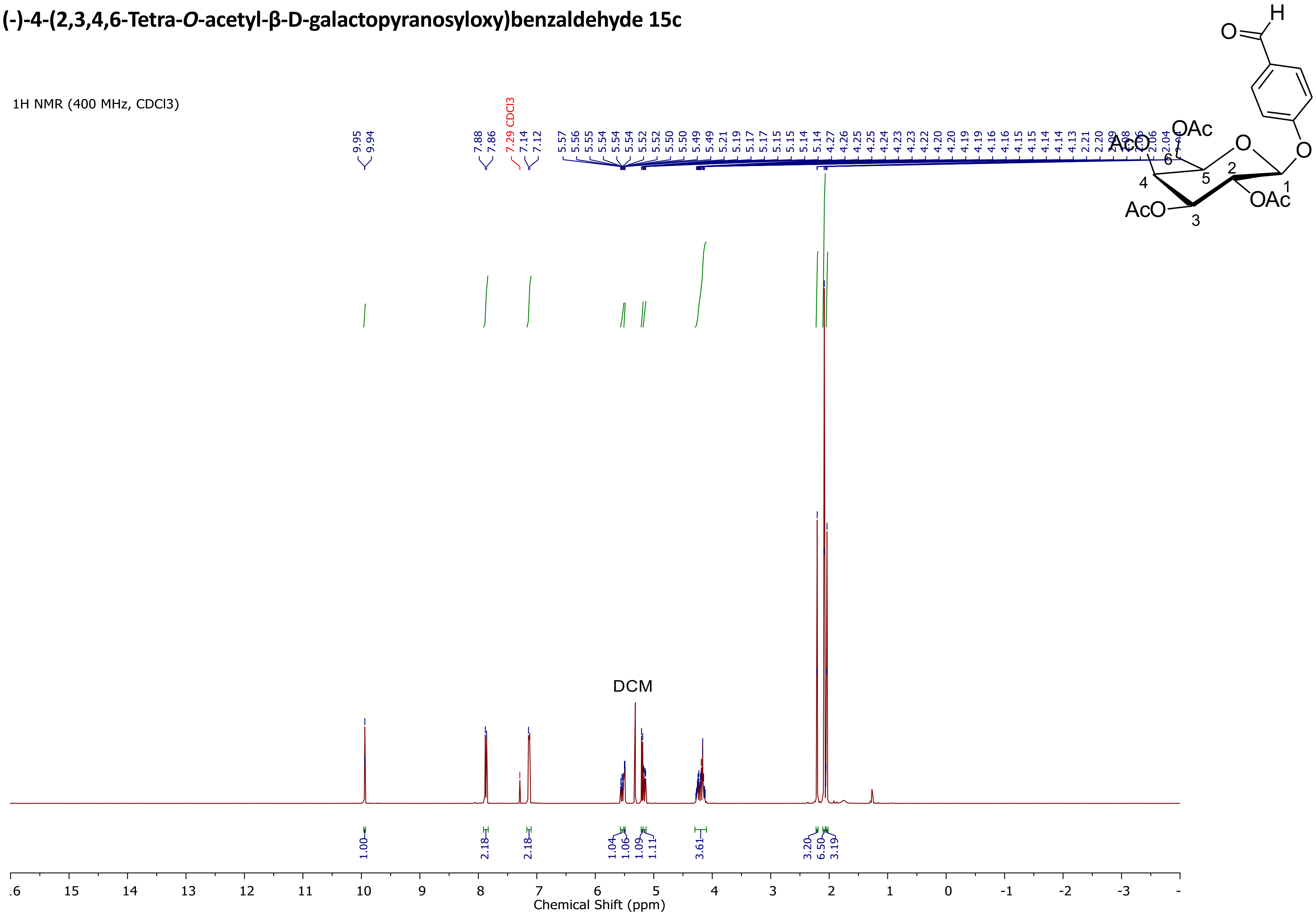
(+)-2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide 15b



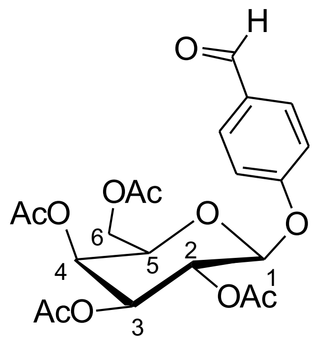
13C NMR (125.8 MHz, CDCl3)

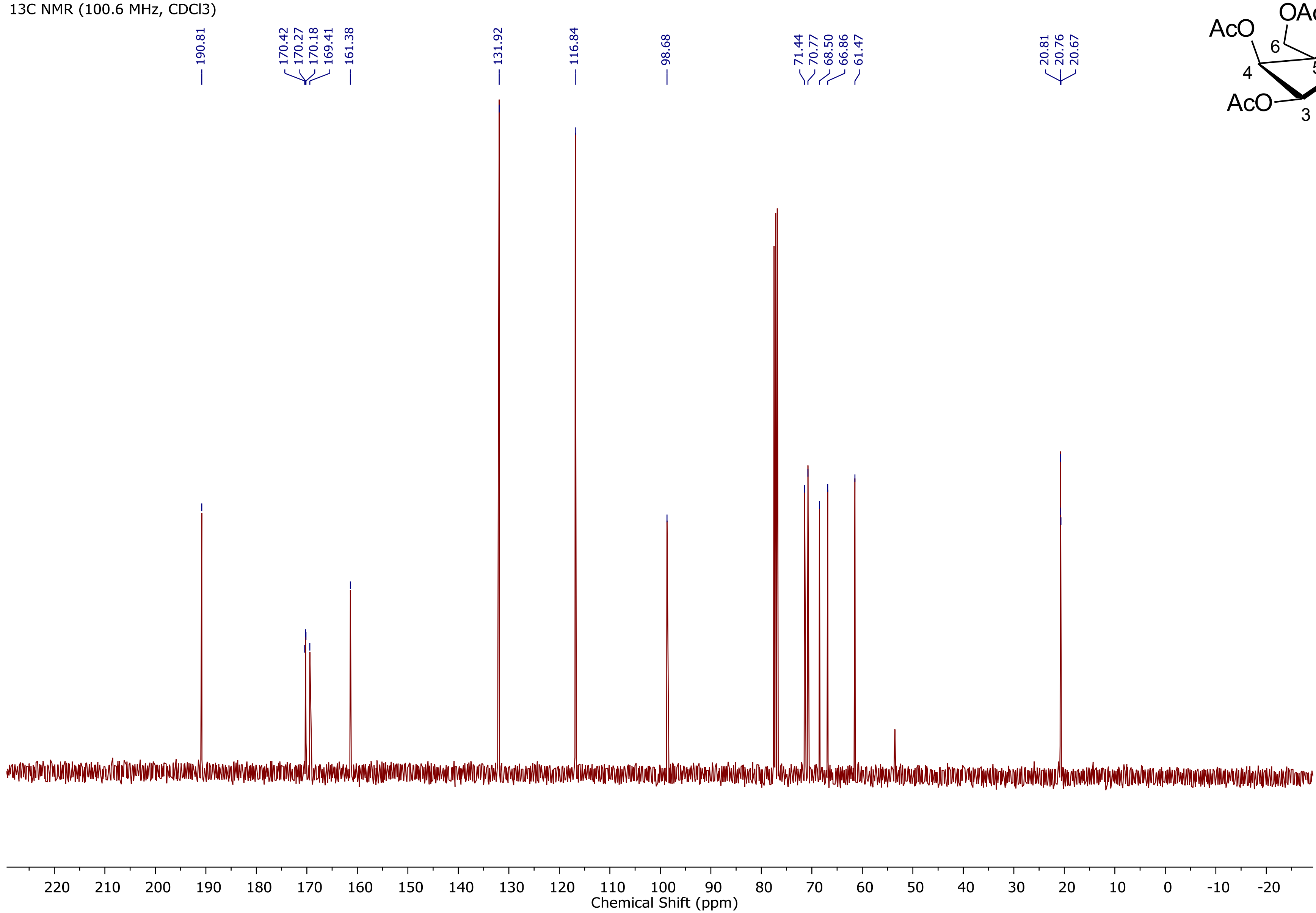


(-)-4-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)benzaldehyde 15c



(-)-4-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)benzaldehyde 15c





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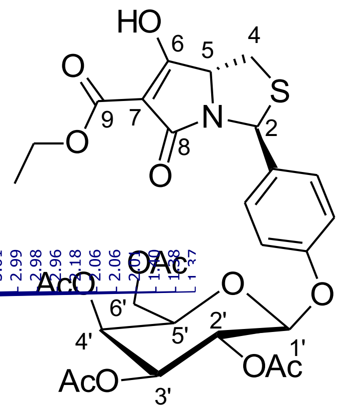
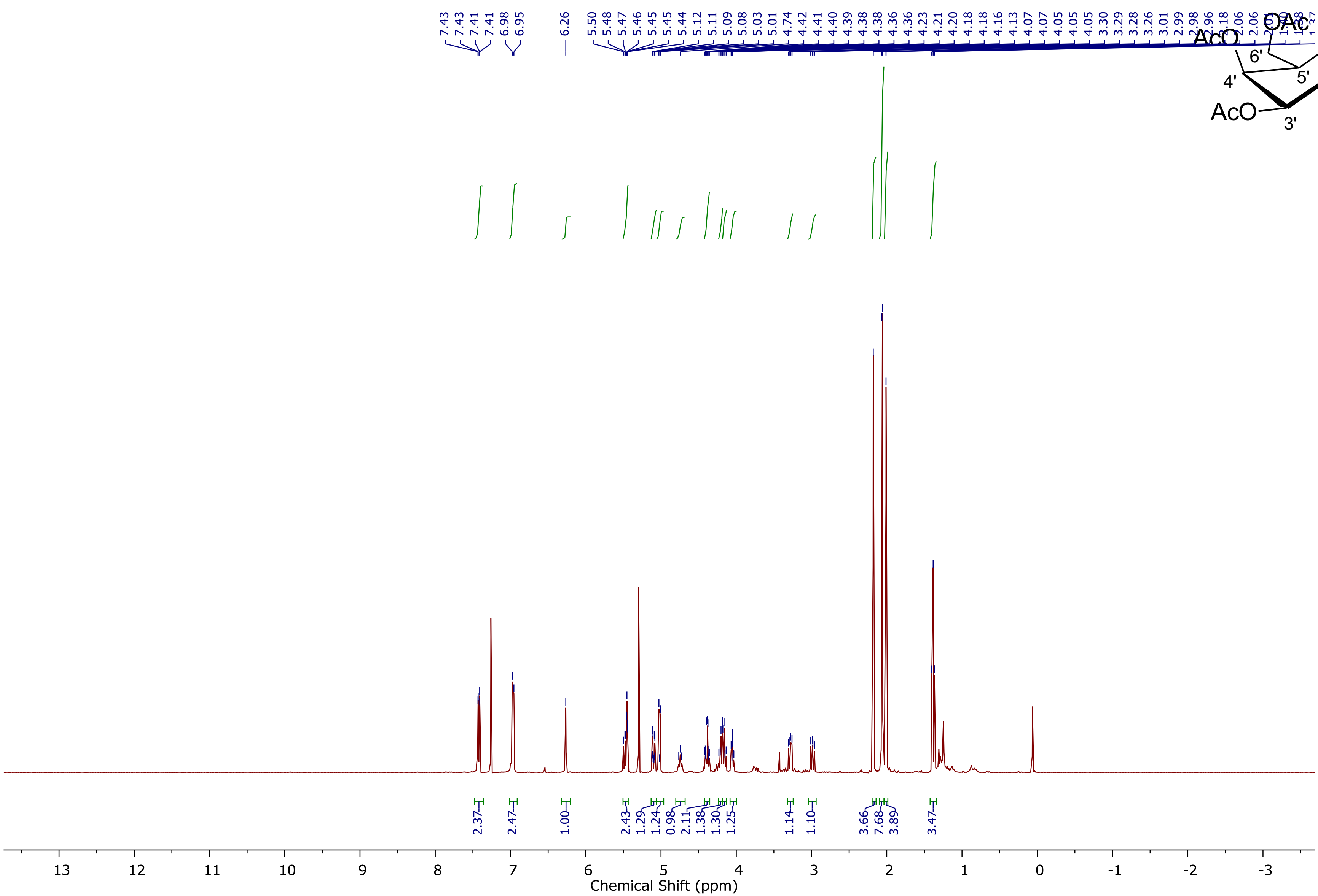


1H NMR (400 MHz, CDCl3)



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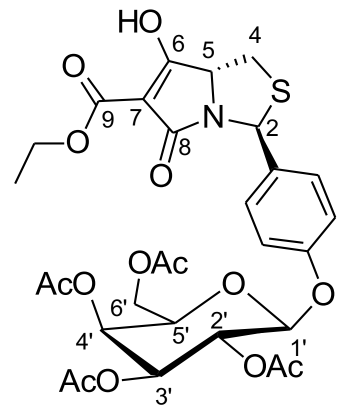
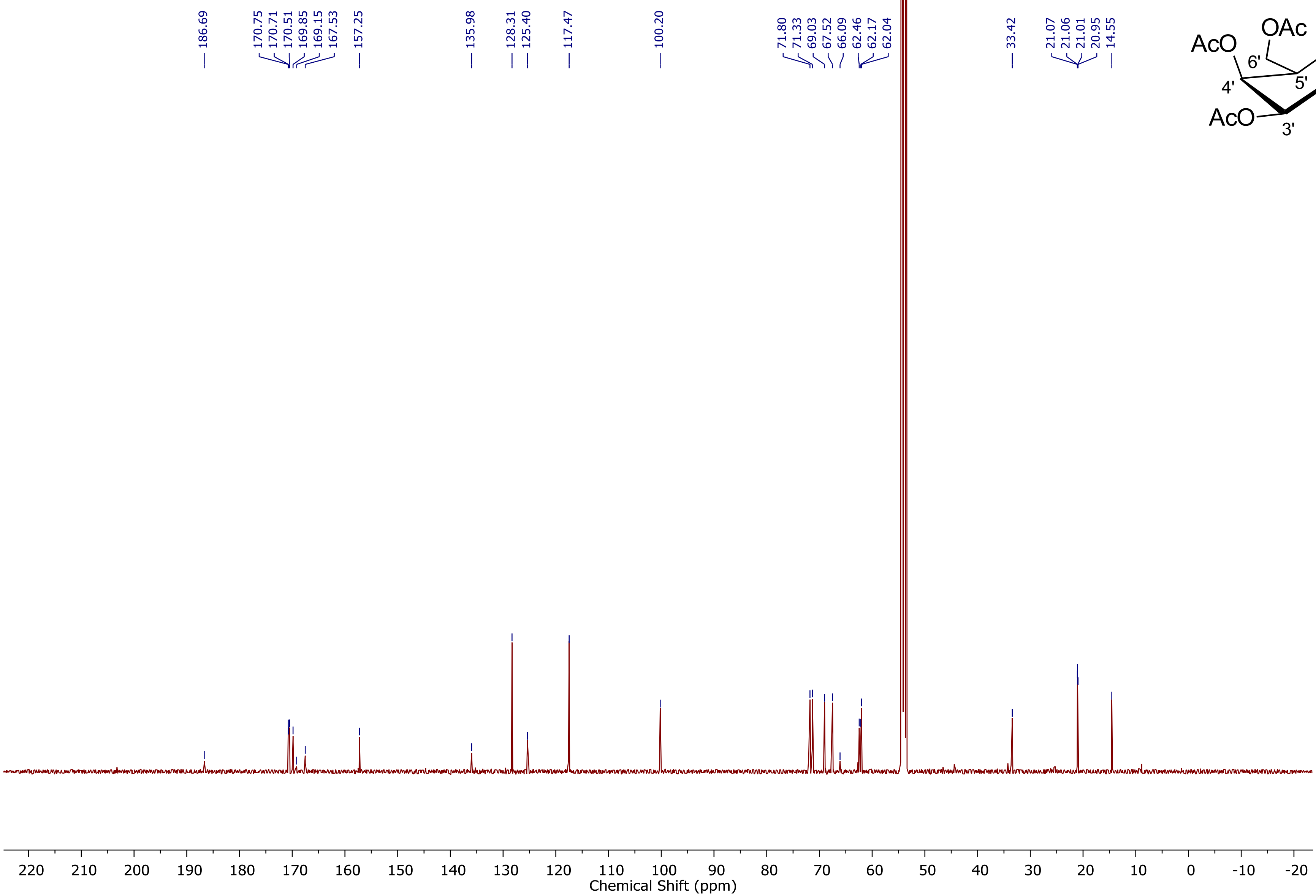


13C NMR (100.6 MHz, CD2Cl2)



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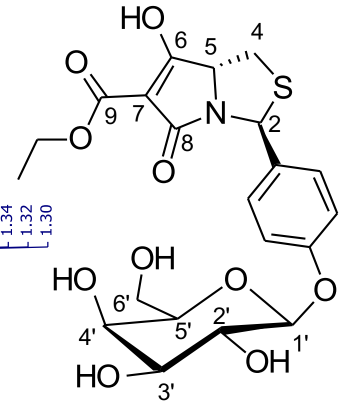
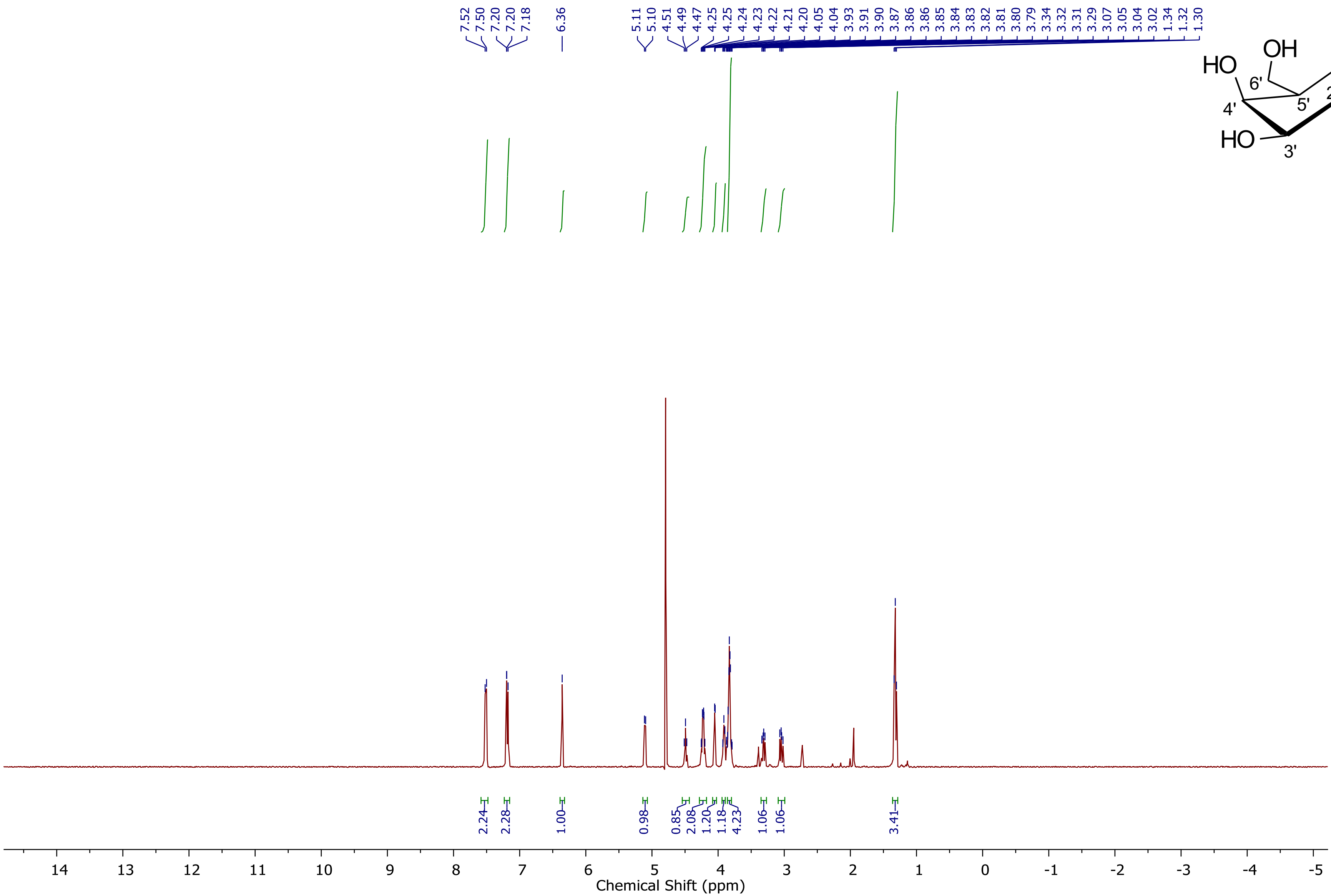


1H NMR (400 MHz, D2O with a few drops of DMSO)



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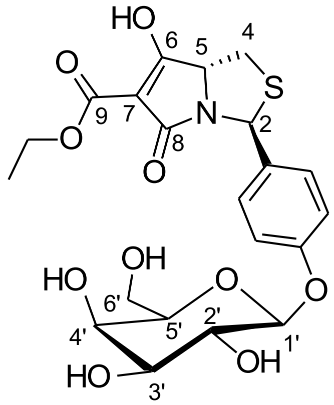
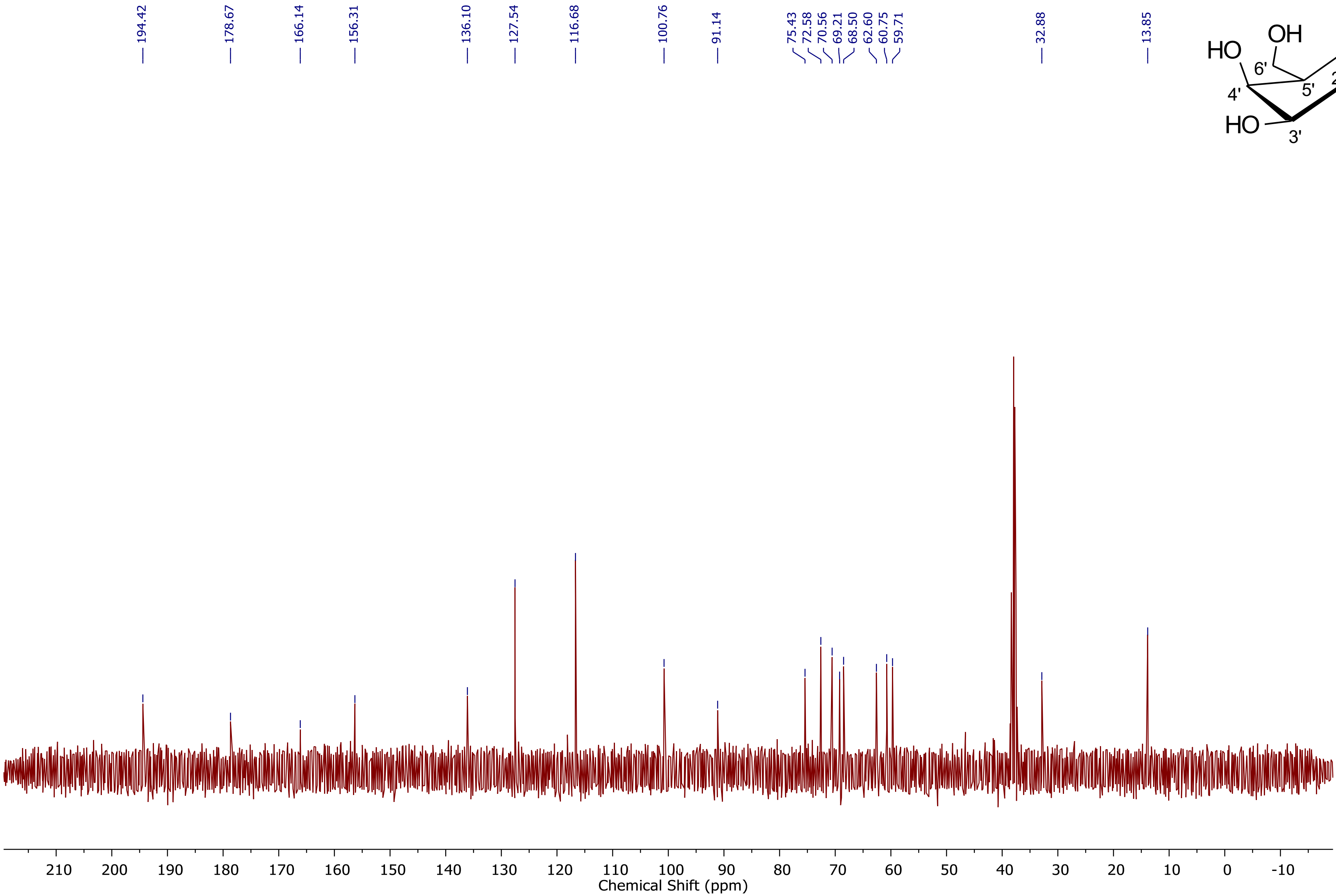
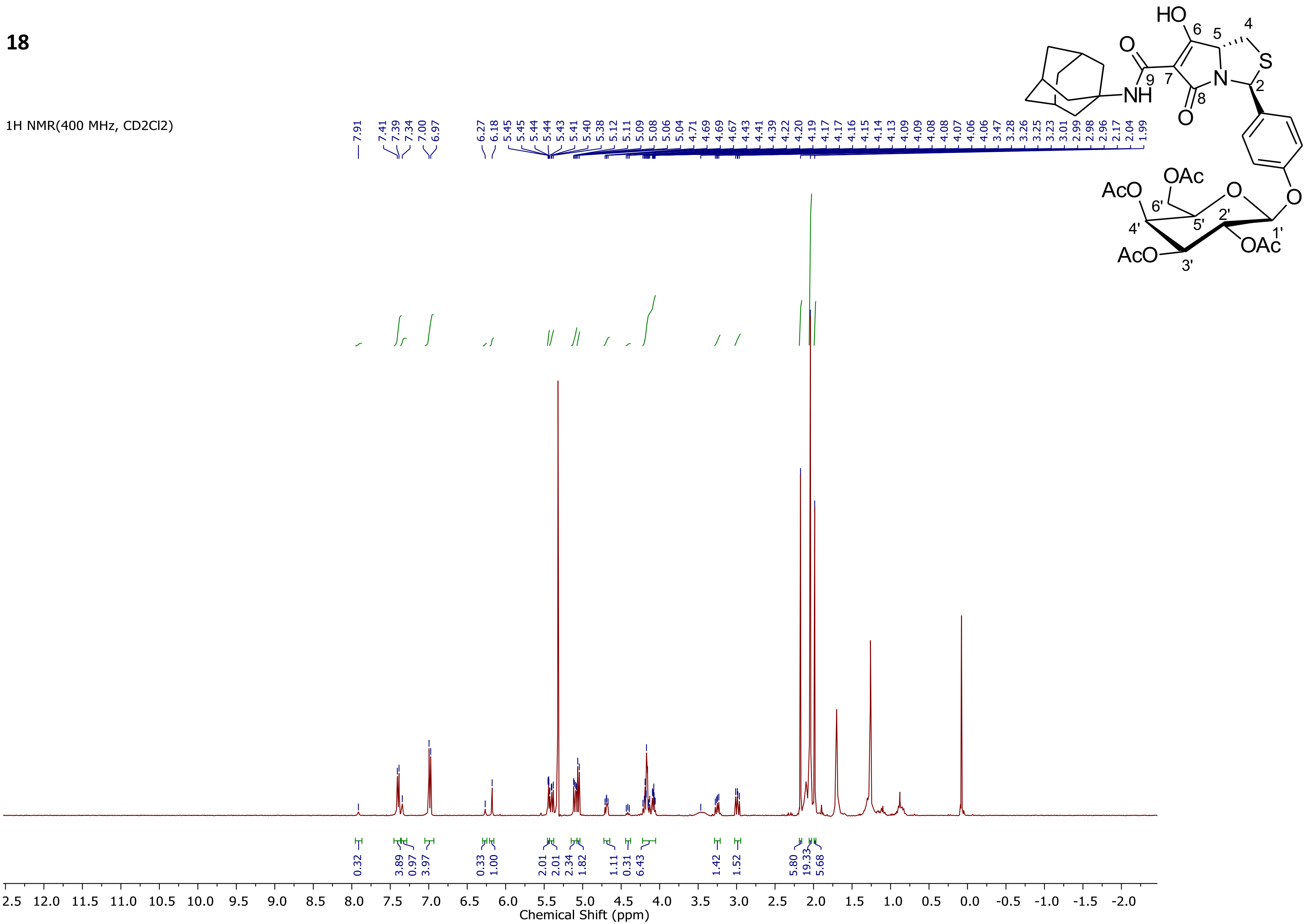


13C NMR (100.6 MHz, D2O with a few drops of DMSO-d6)



18

1H NMR(400 MHz, CD2Cl2)



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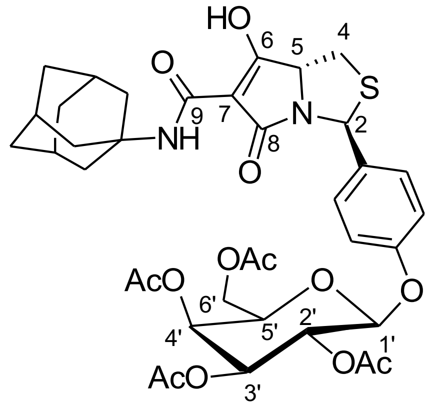
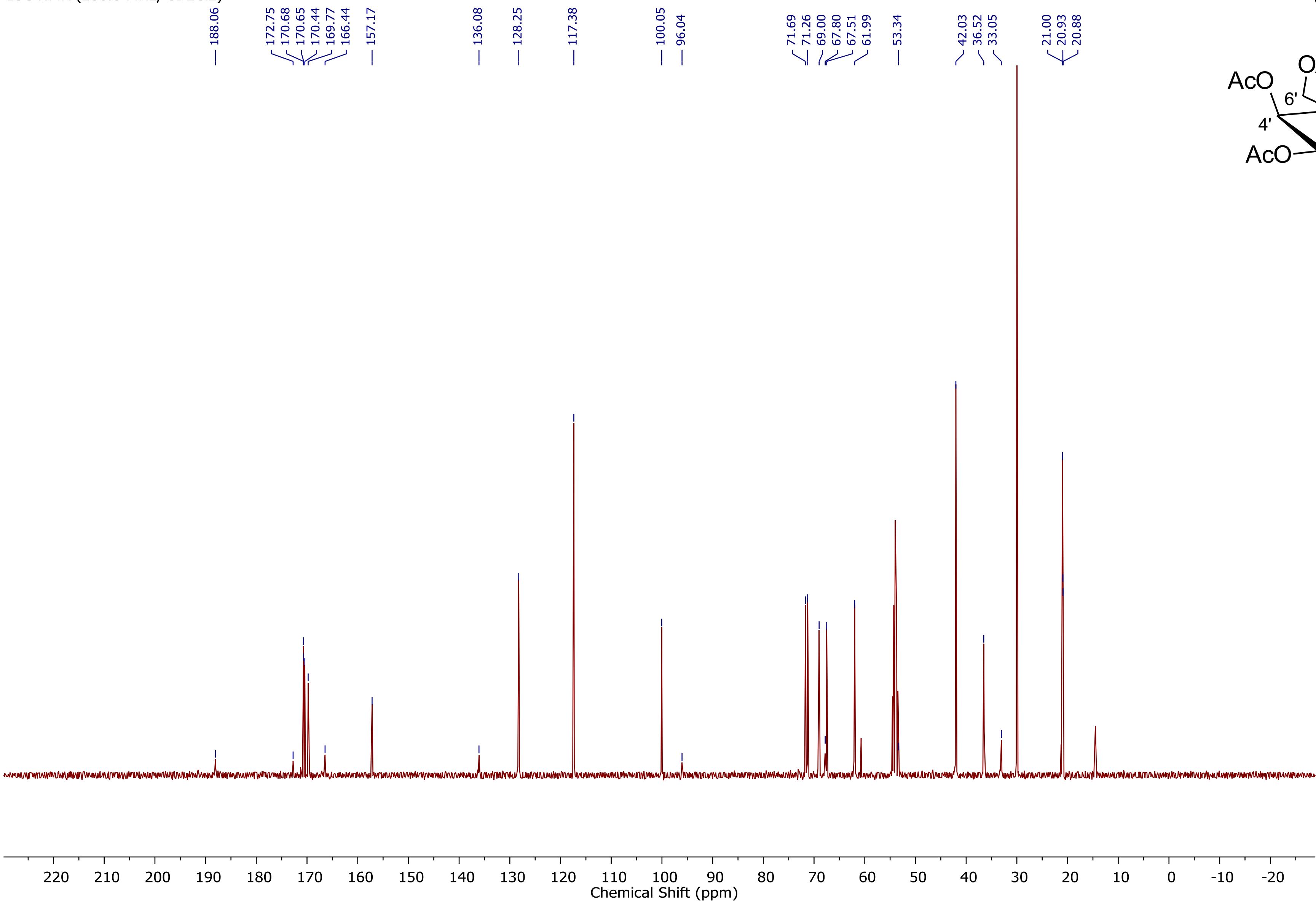
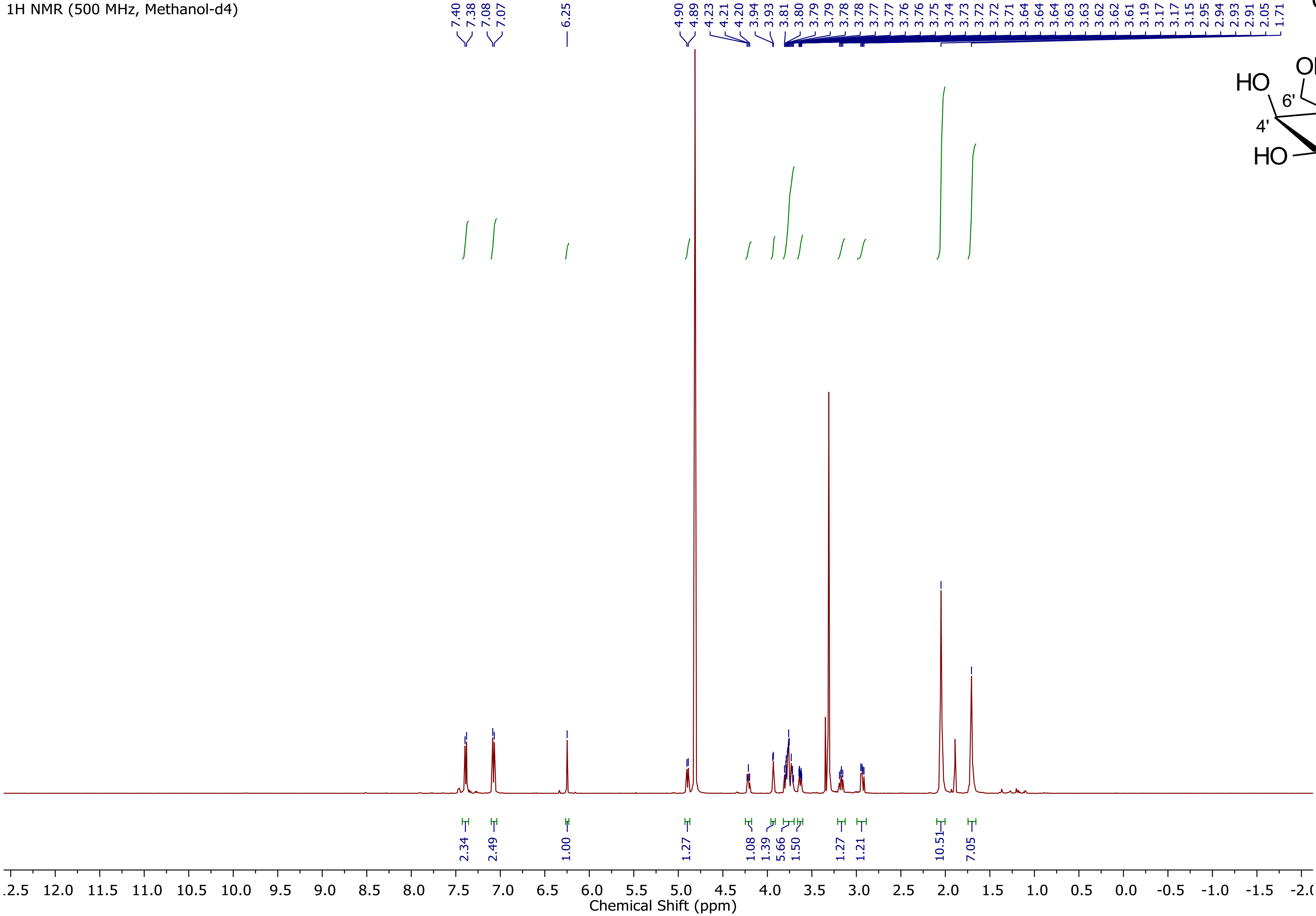


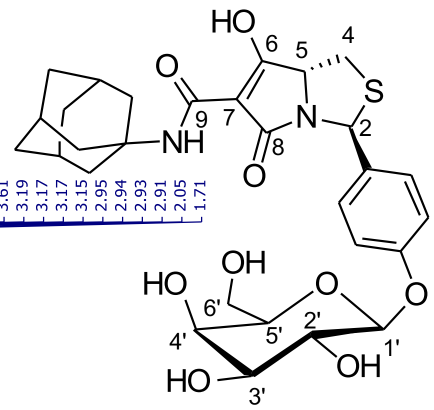
13C NMR (100.6 MHz, CD2Cl2)



19

1H NMR (500 MHz, Methanol-d4)





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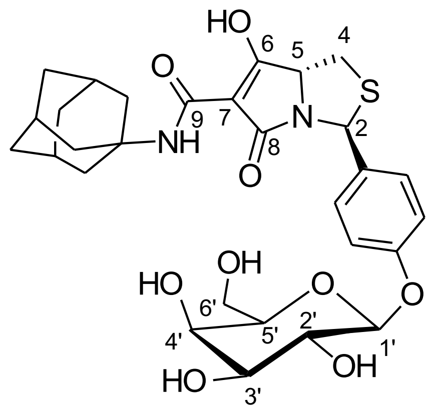
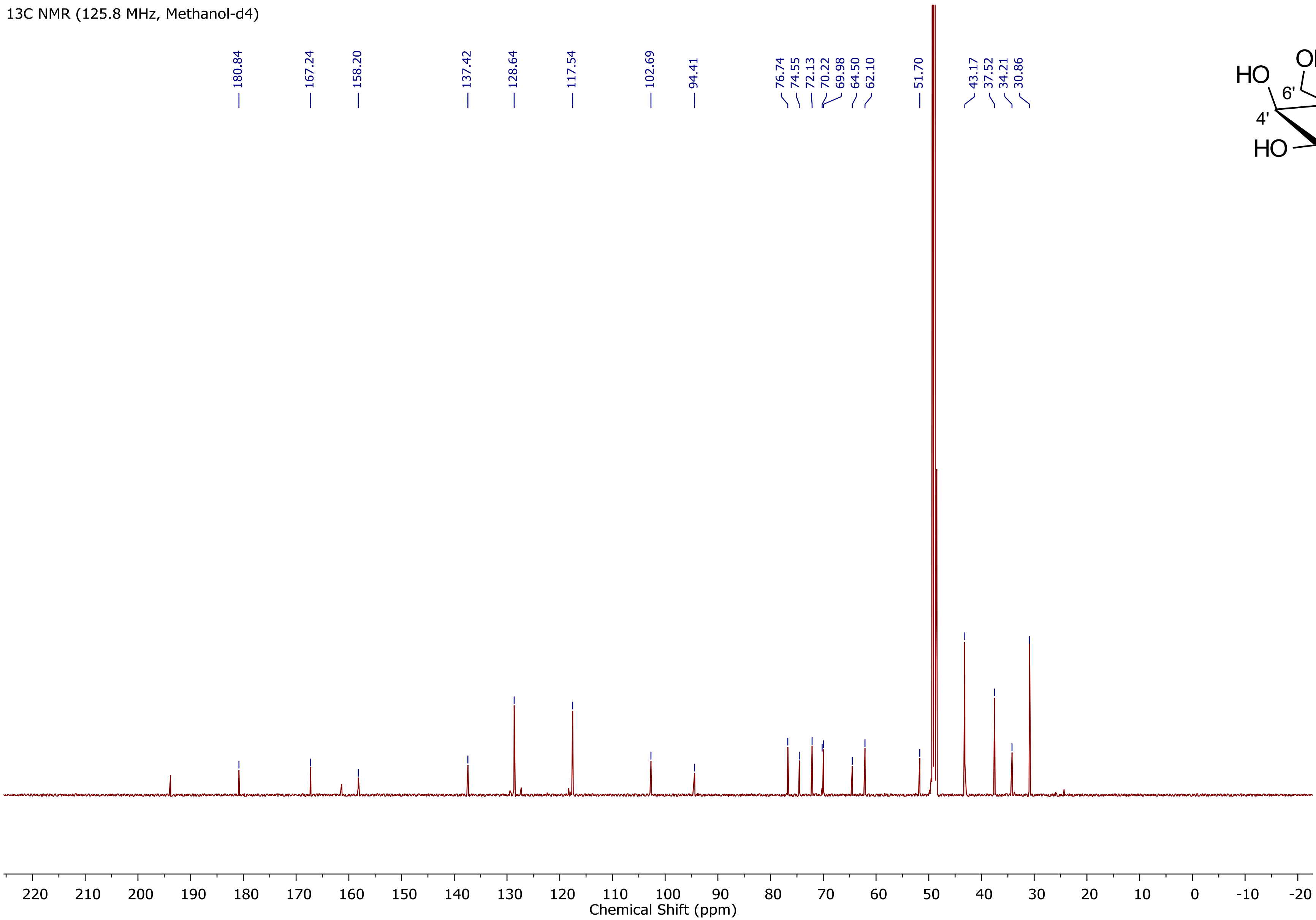
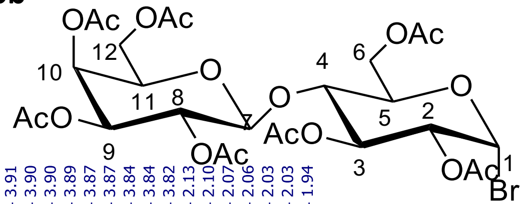


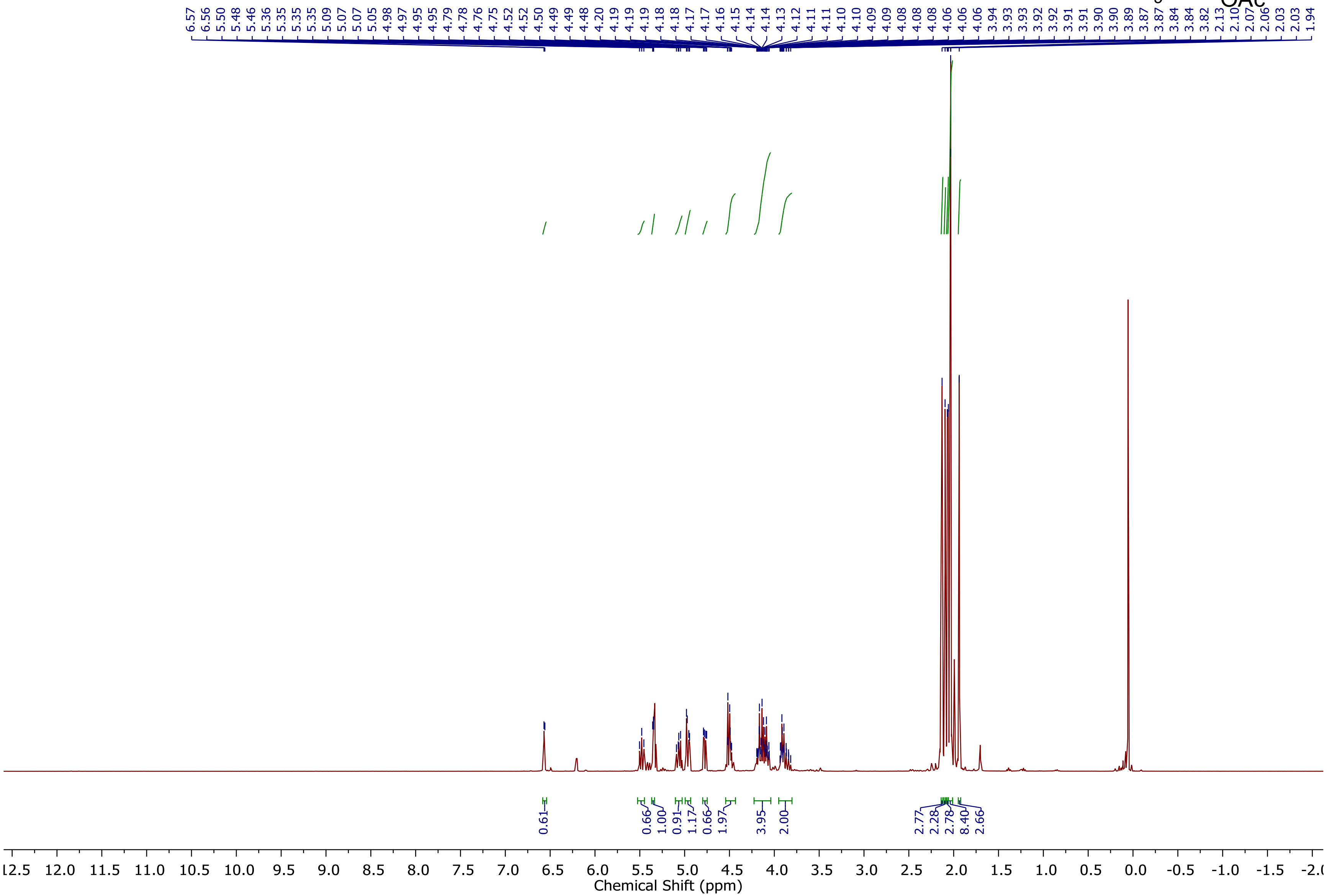
13C NMR (125.8 MHz, Methanol-d4)



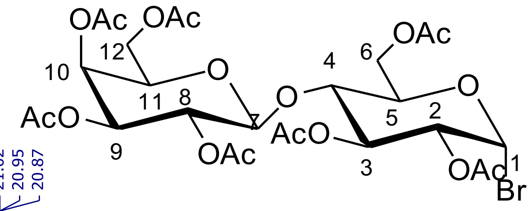
(+)-4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-D-glucopyranosyl bromide, 20b



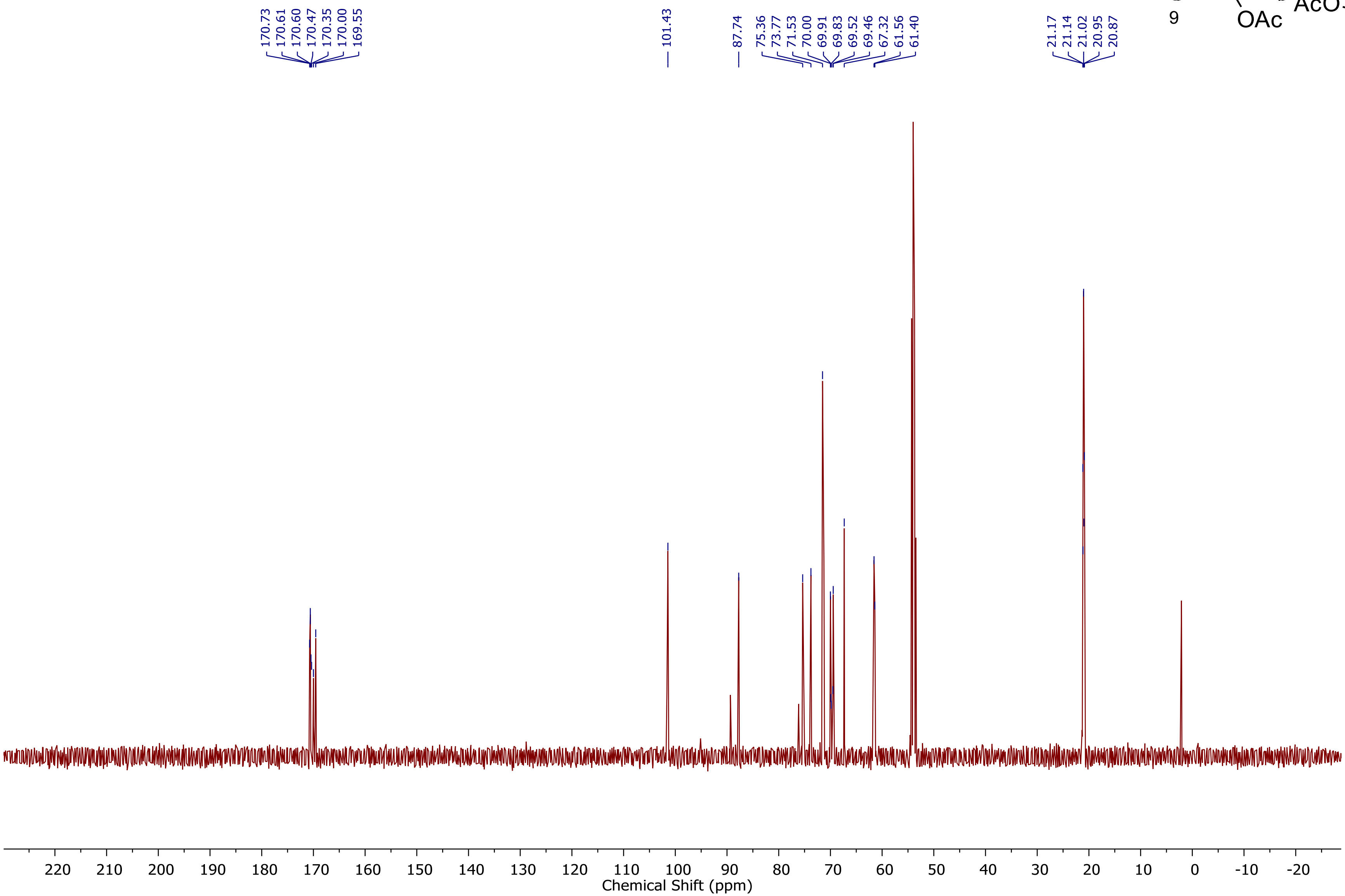
1H NMR (400 MHz, CD2Cl2)



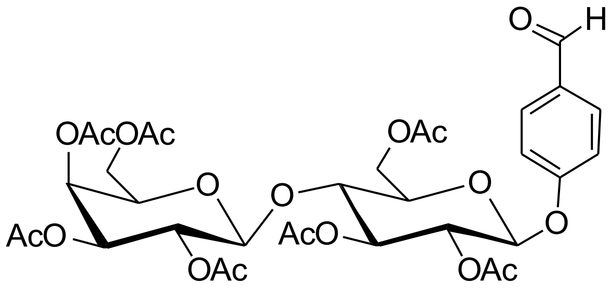
(+)-4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-D-glucopyranosyl bromide, 20b



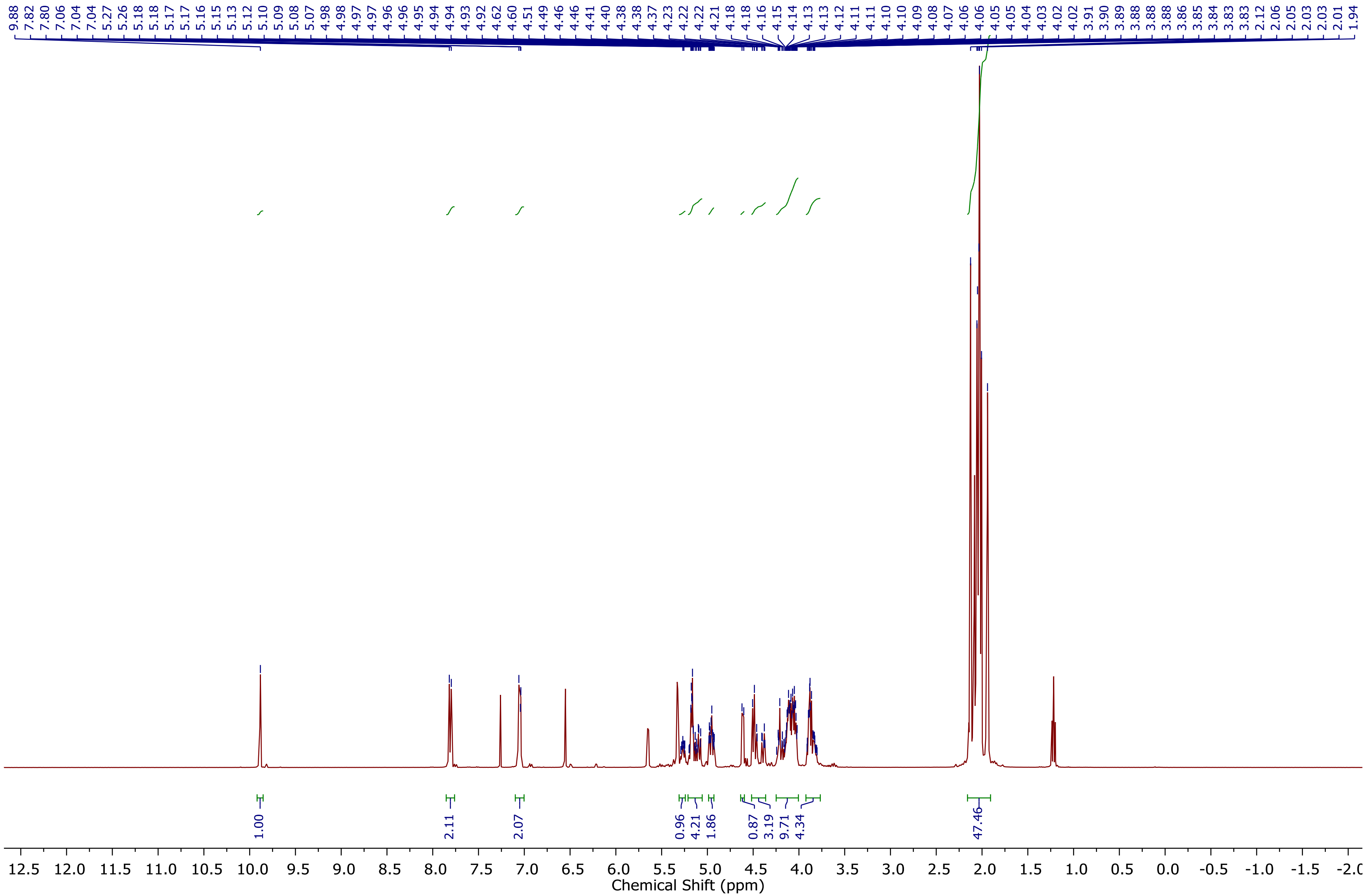
13C NMR (100.6 MHz, CD2Cl2)



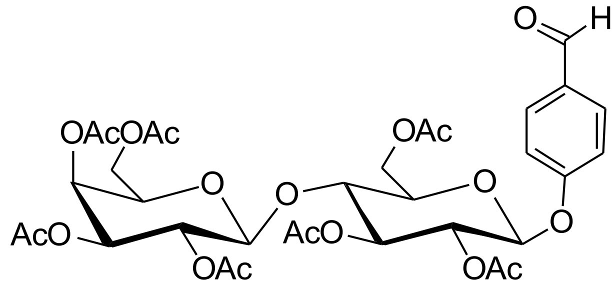
(+)-4-(4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-D-glucopyranosyloxy)benzaldehyde, 20c



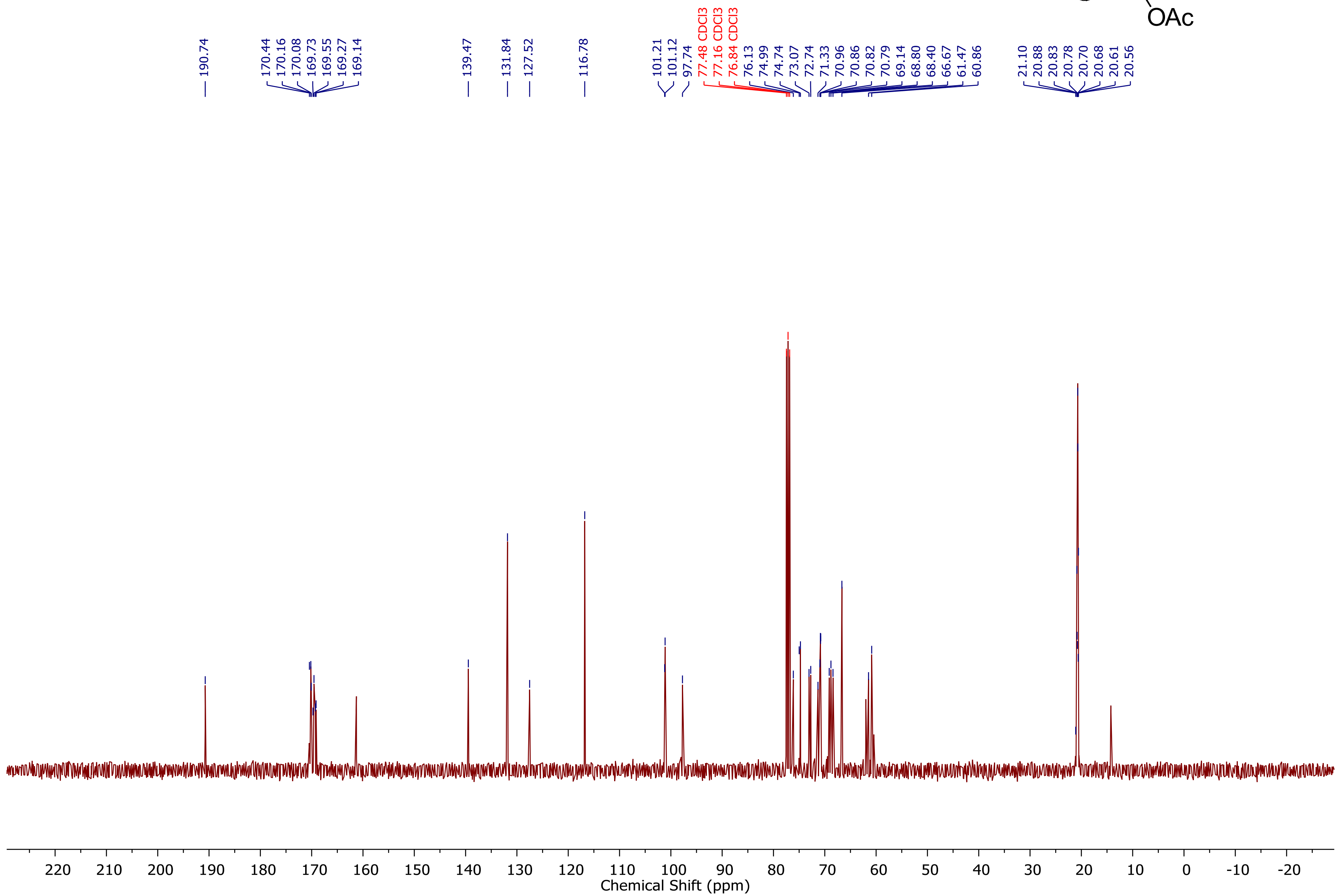
1H NMR (400 MHz, CDCl3)



(+)-4-(4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-D-glucopyranosyloxy)benzaldehyde, 20c



13C NMR (100.6 MHz, CDCl3)



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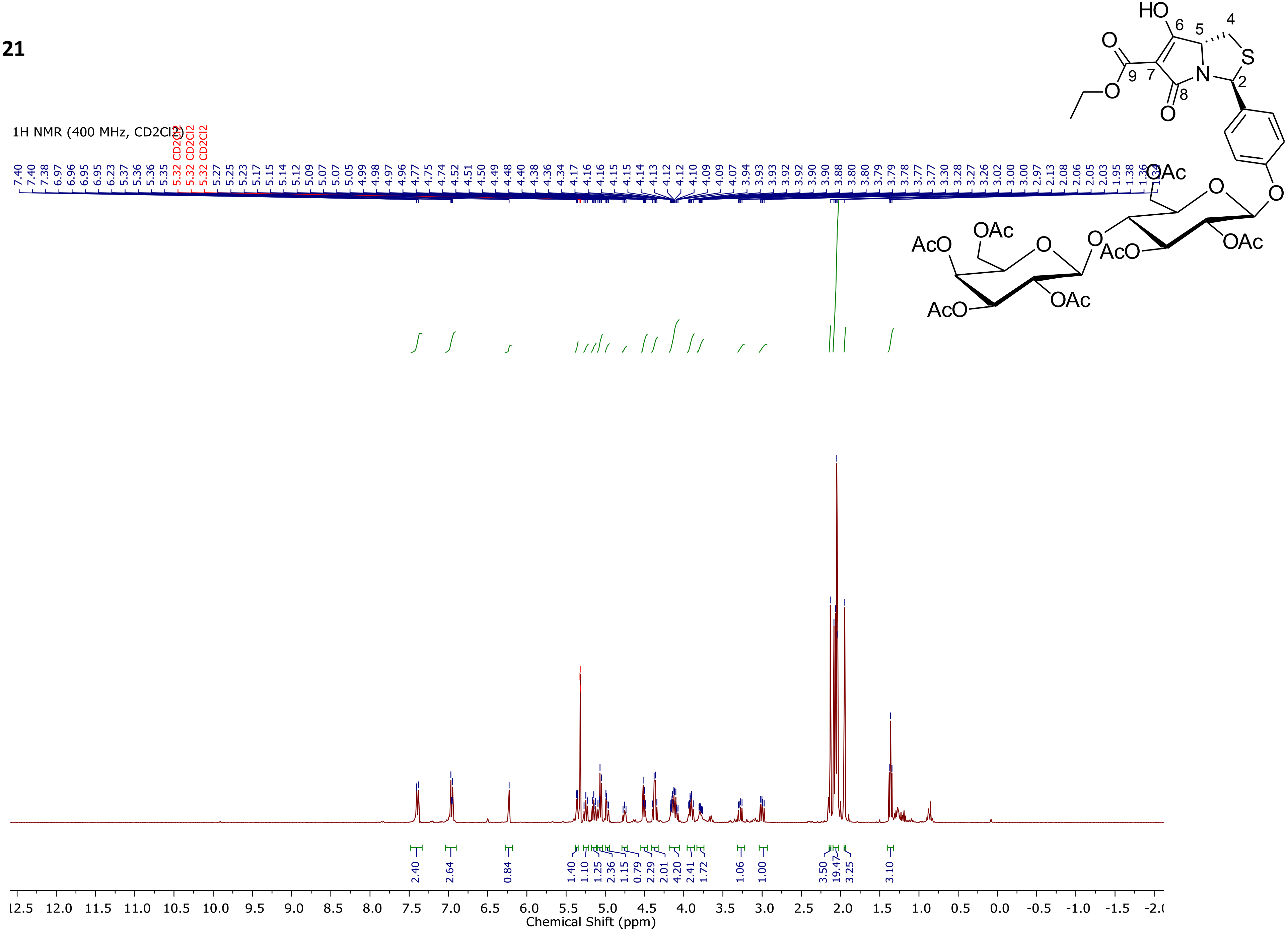

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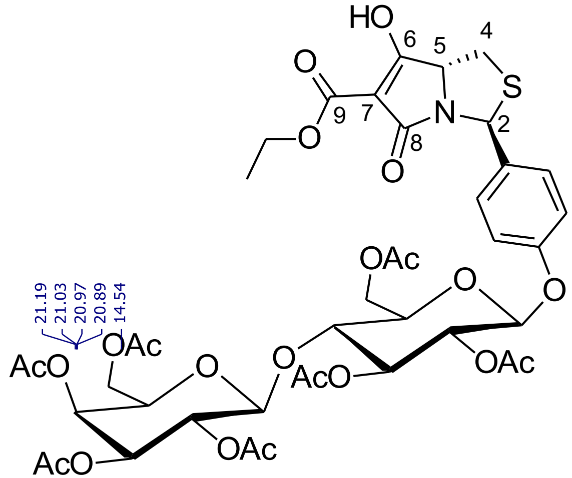
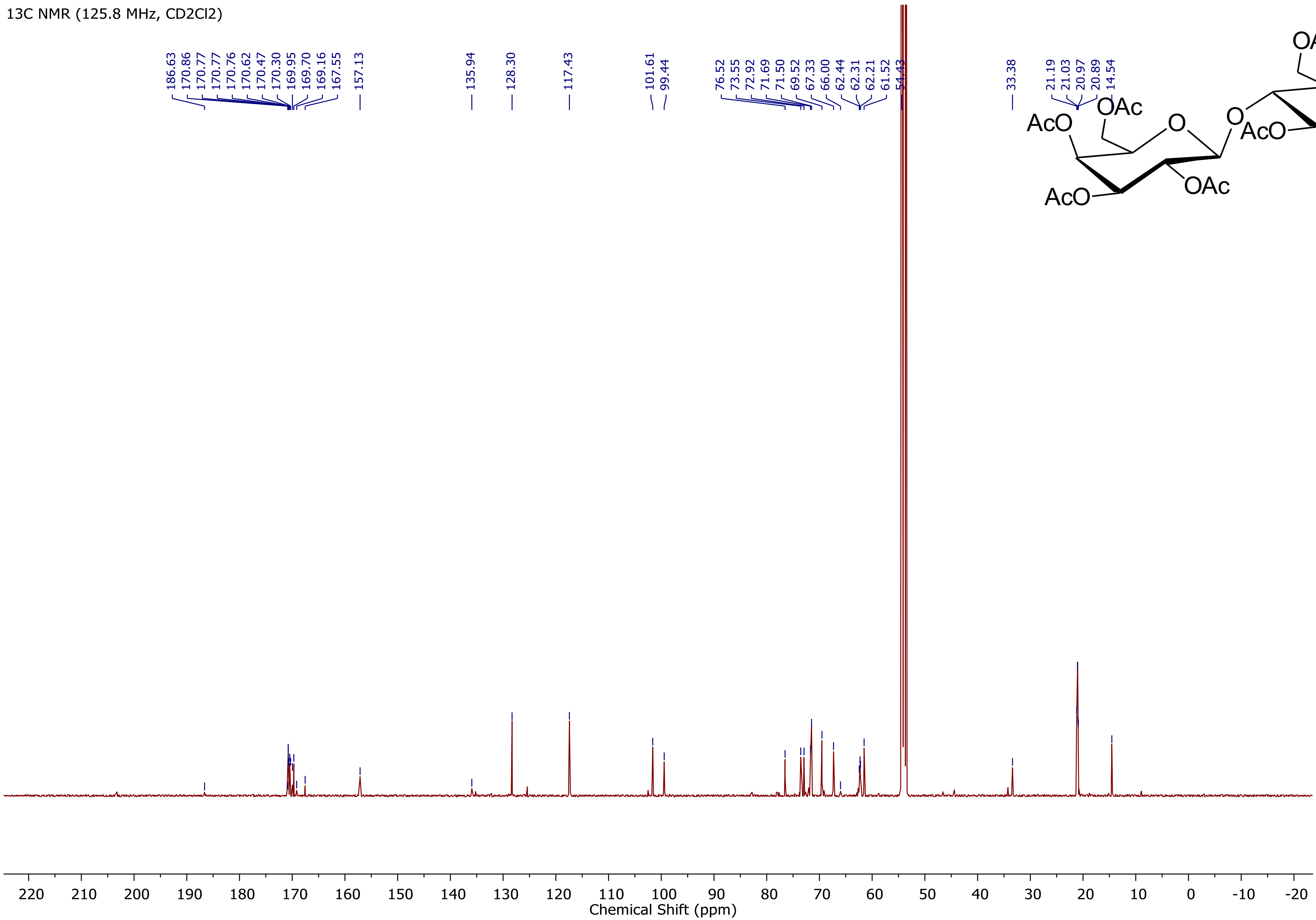
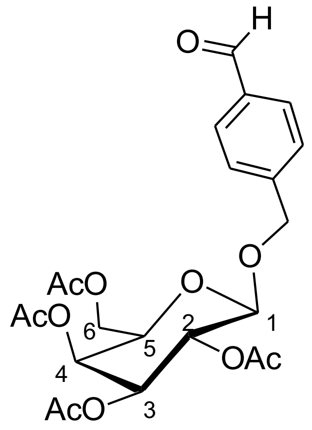
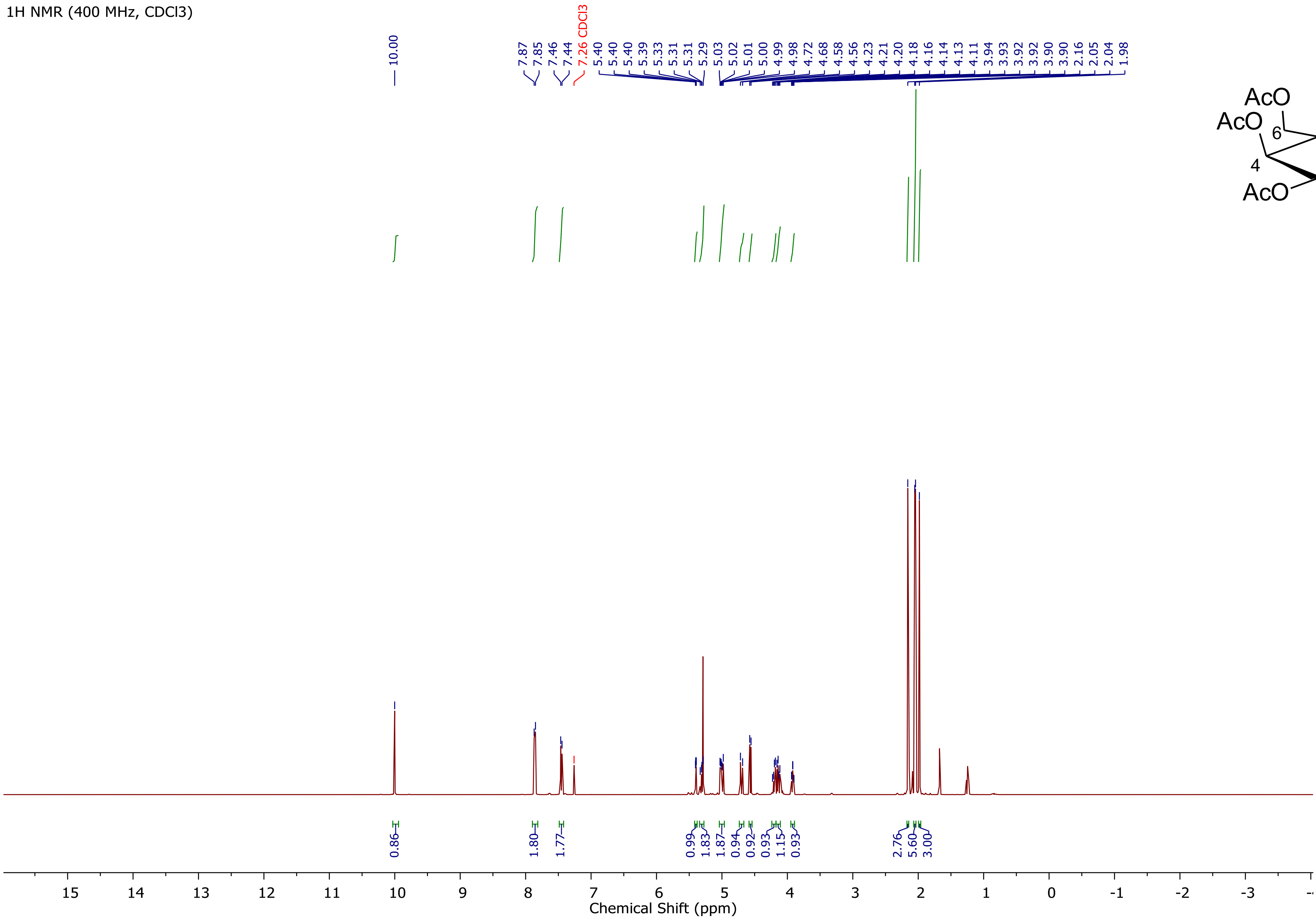


13C NMR (125.8 MHz, CD2Cl2)

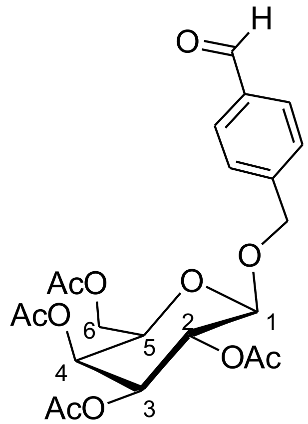


(-)-4-((2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)methyl)benzaldehyde, 22

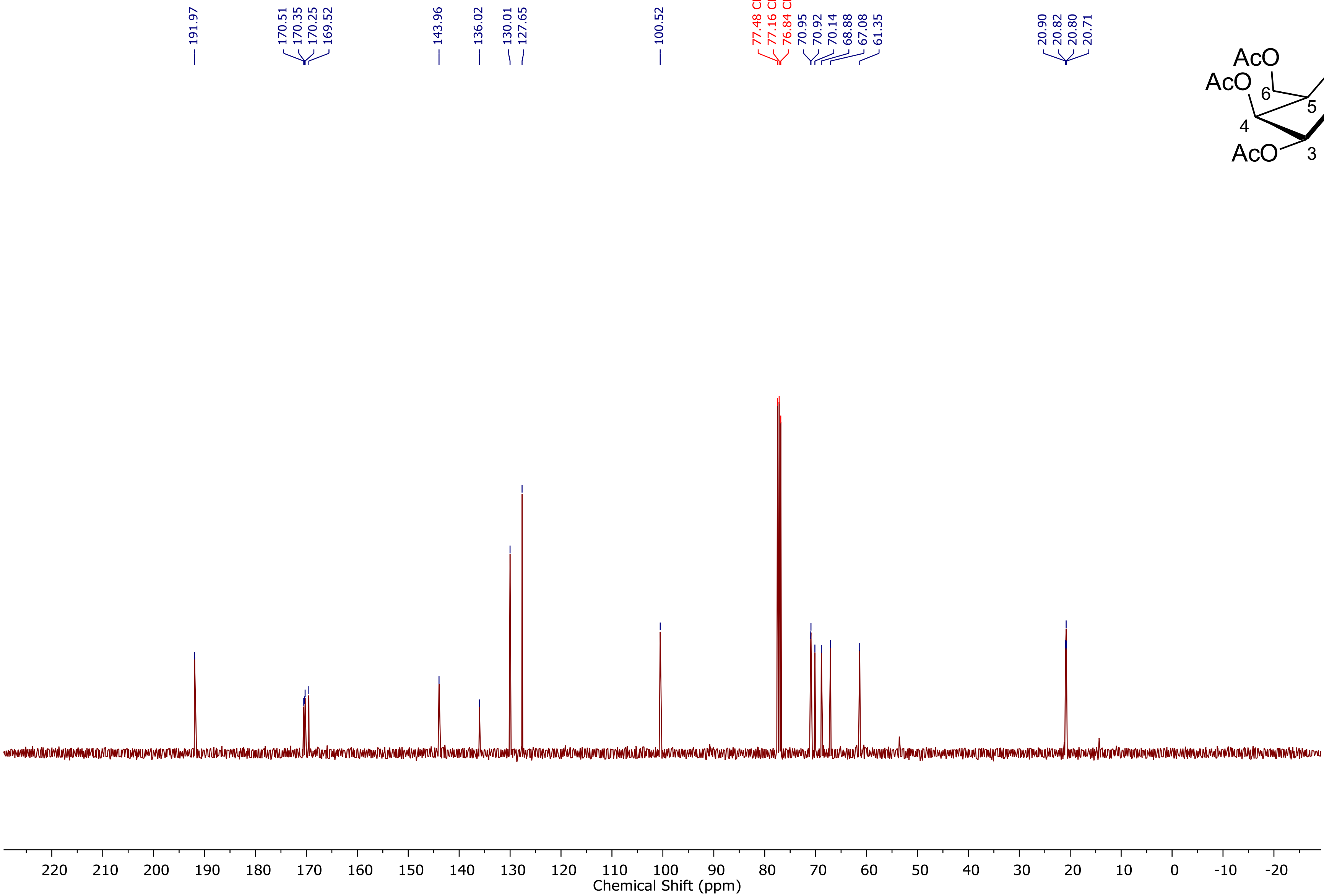




(-)-4-((2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)methyl)benzaldehyde, 22

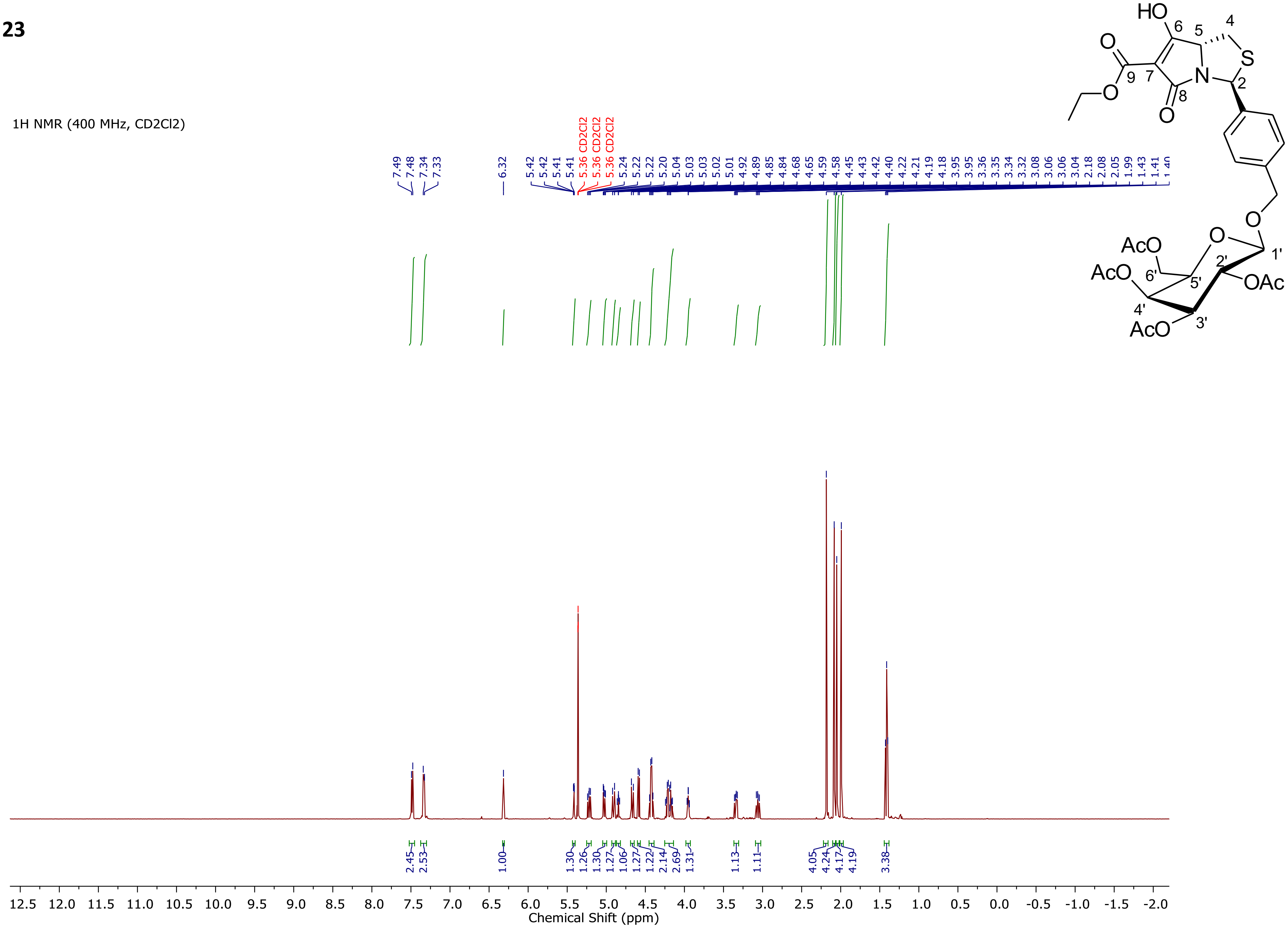


13C NMR (100.6 MHz, CDCl3)

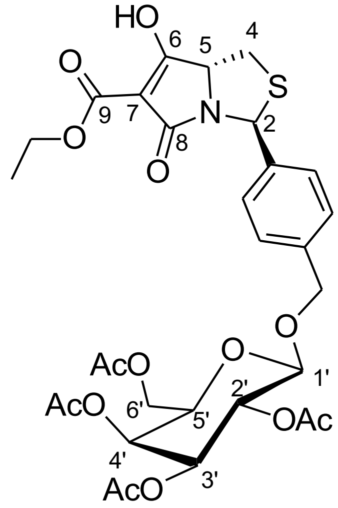


23

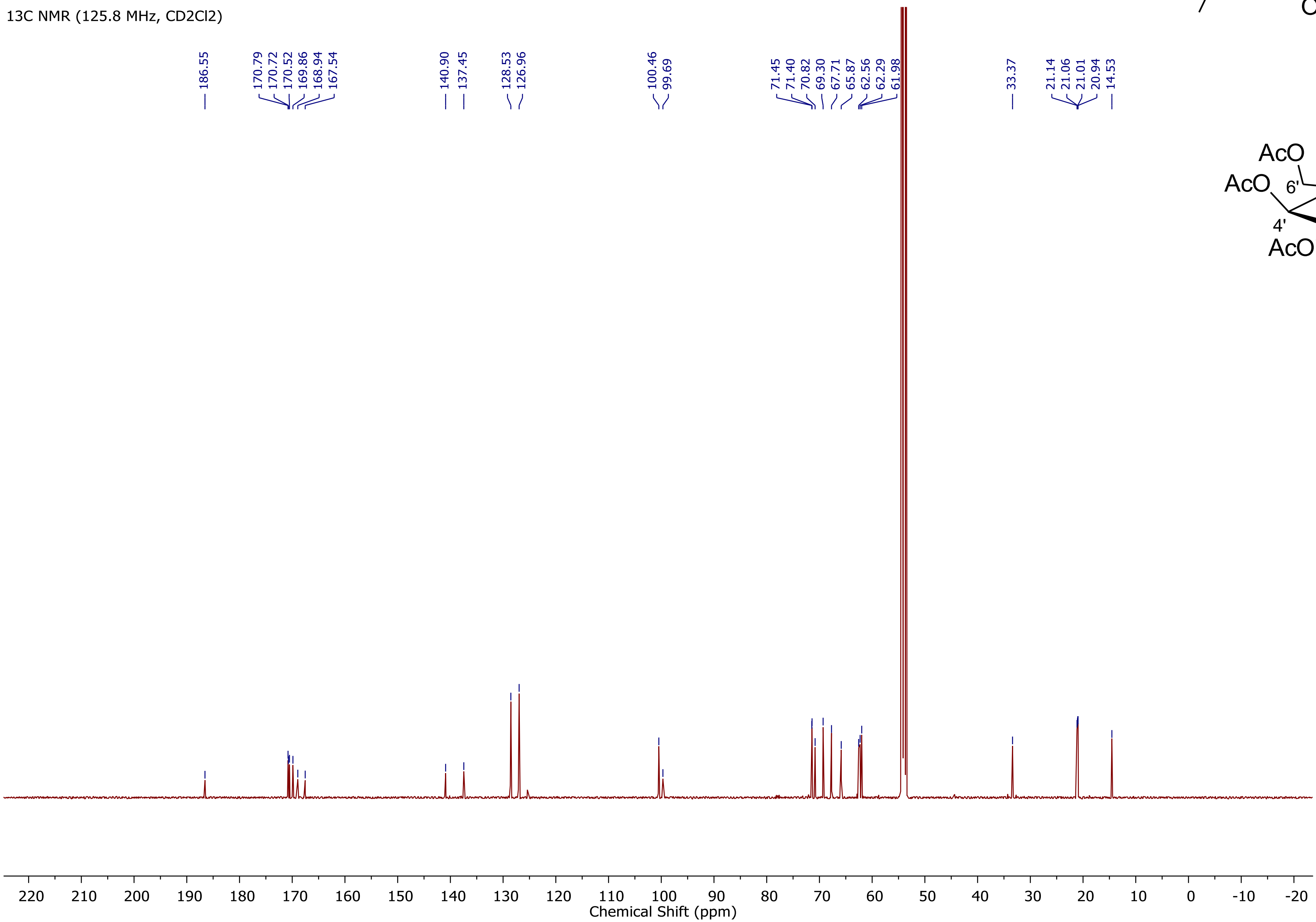
1H NMR (400 MHz, CD2Cl2)



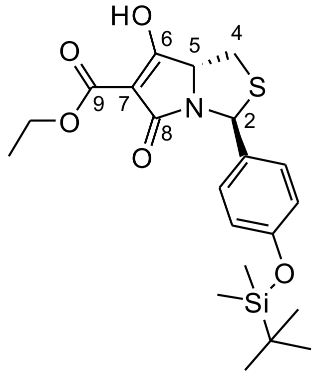
23



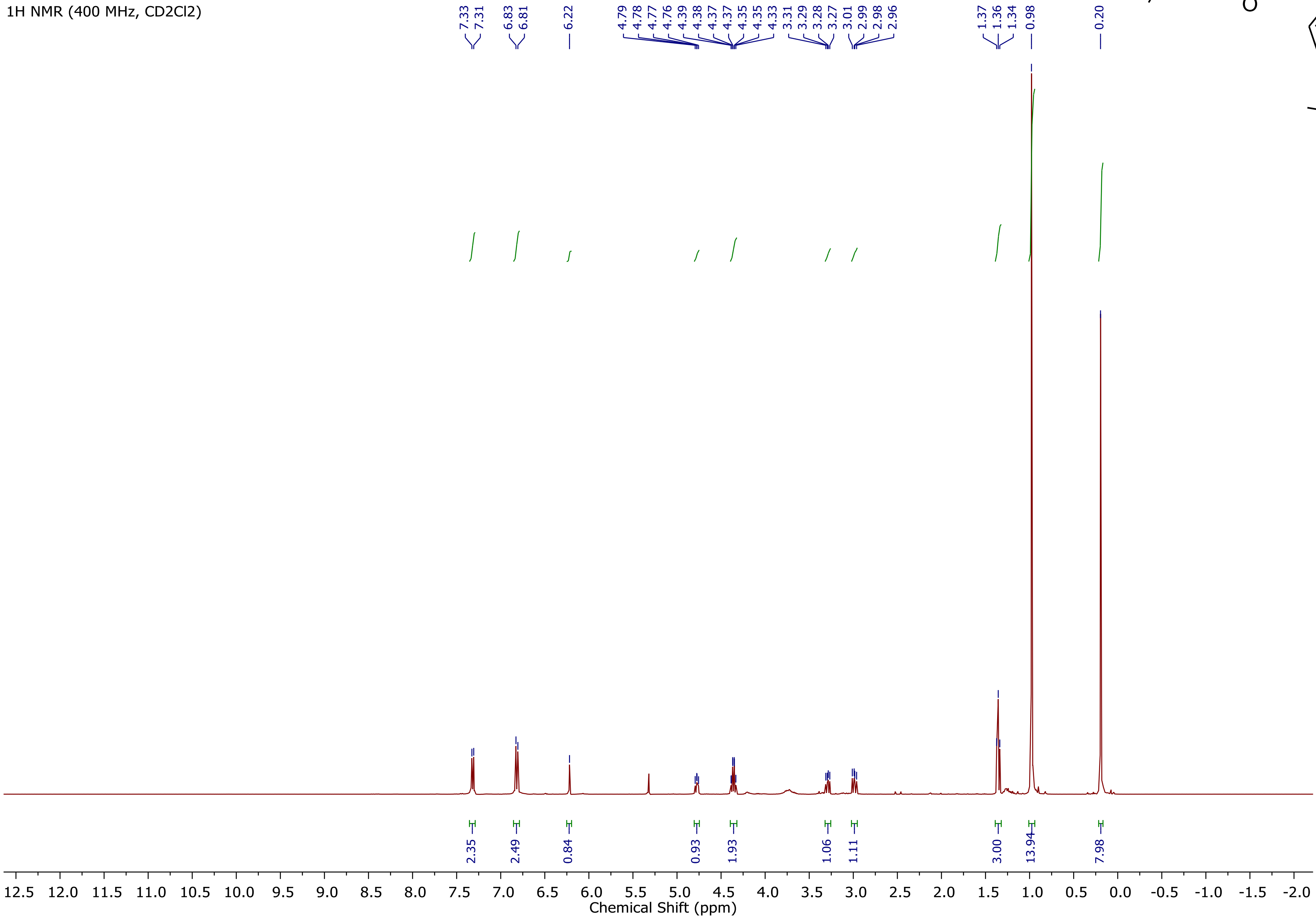
13C NMR (125.8 MHz, CD2Cl2)



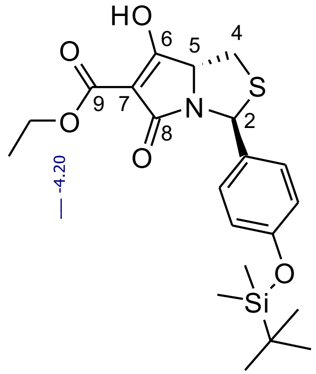
25a



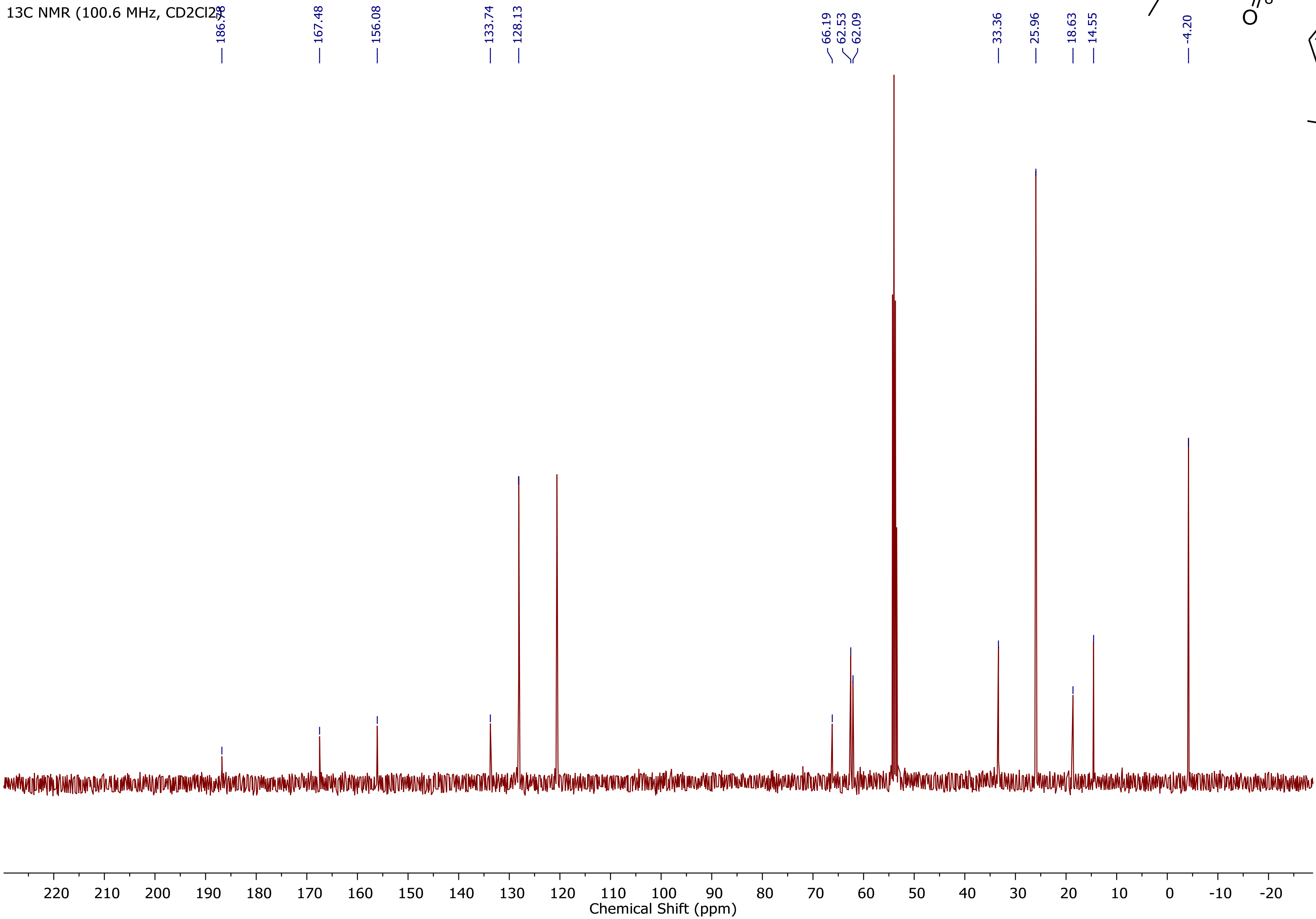
1H NMR (400 MHz, CD2Cl2)



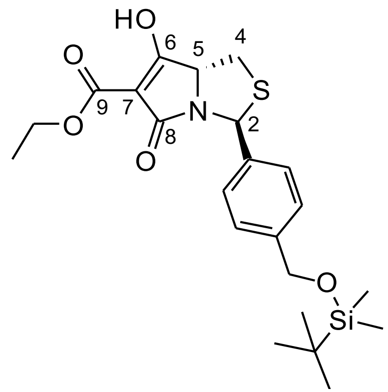
25a

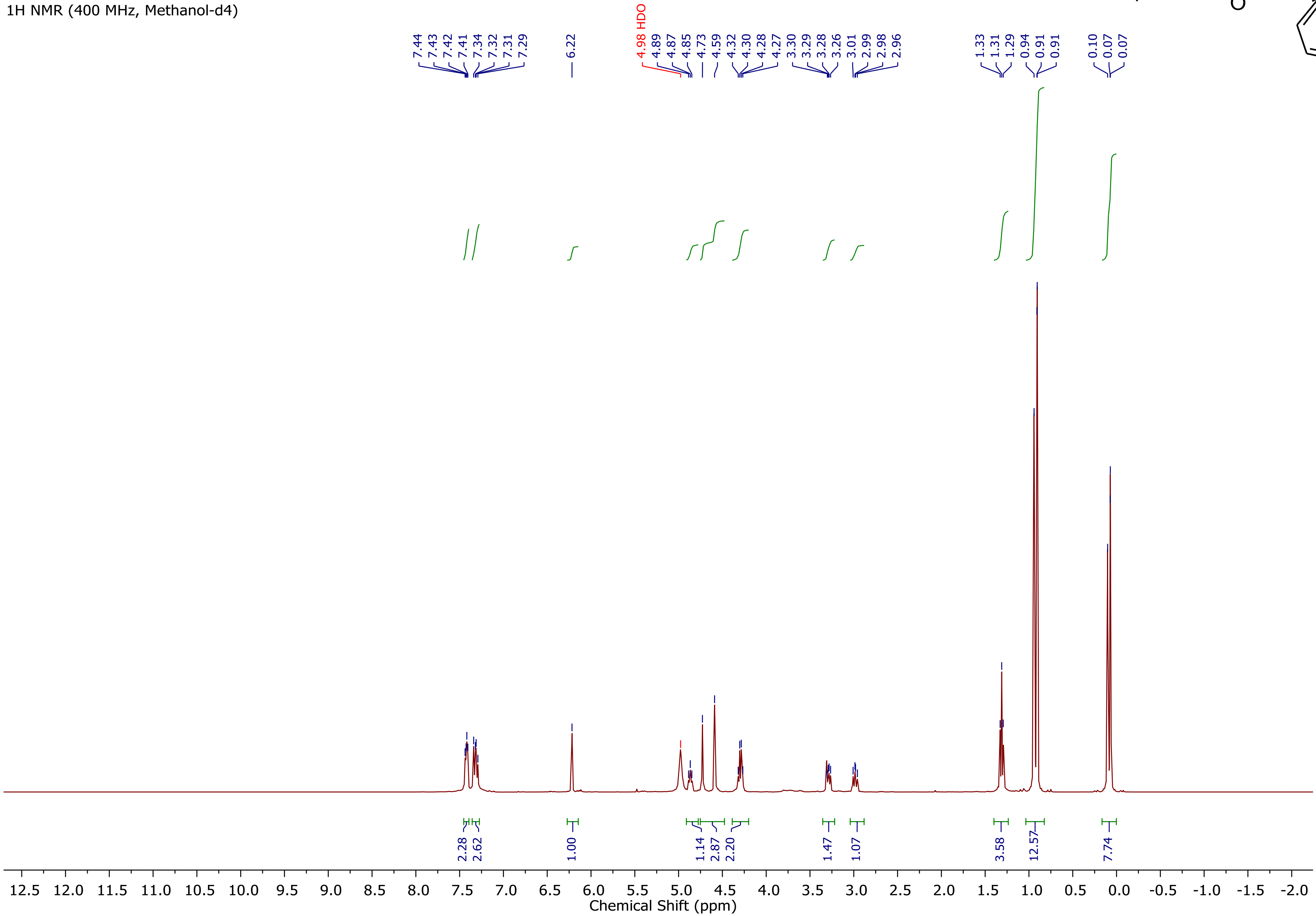


13C NMR (100.6 MHz, CD2Cl2)



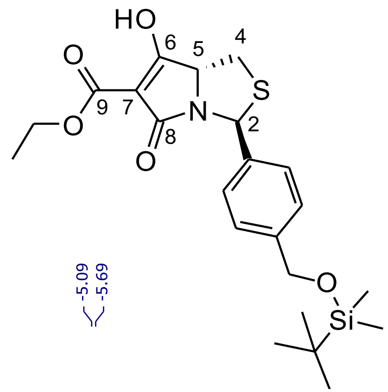
25b



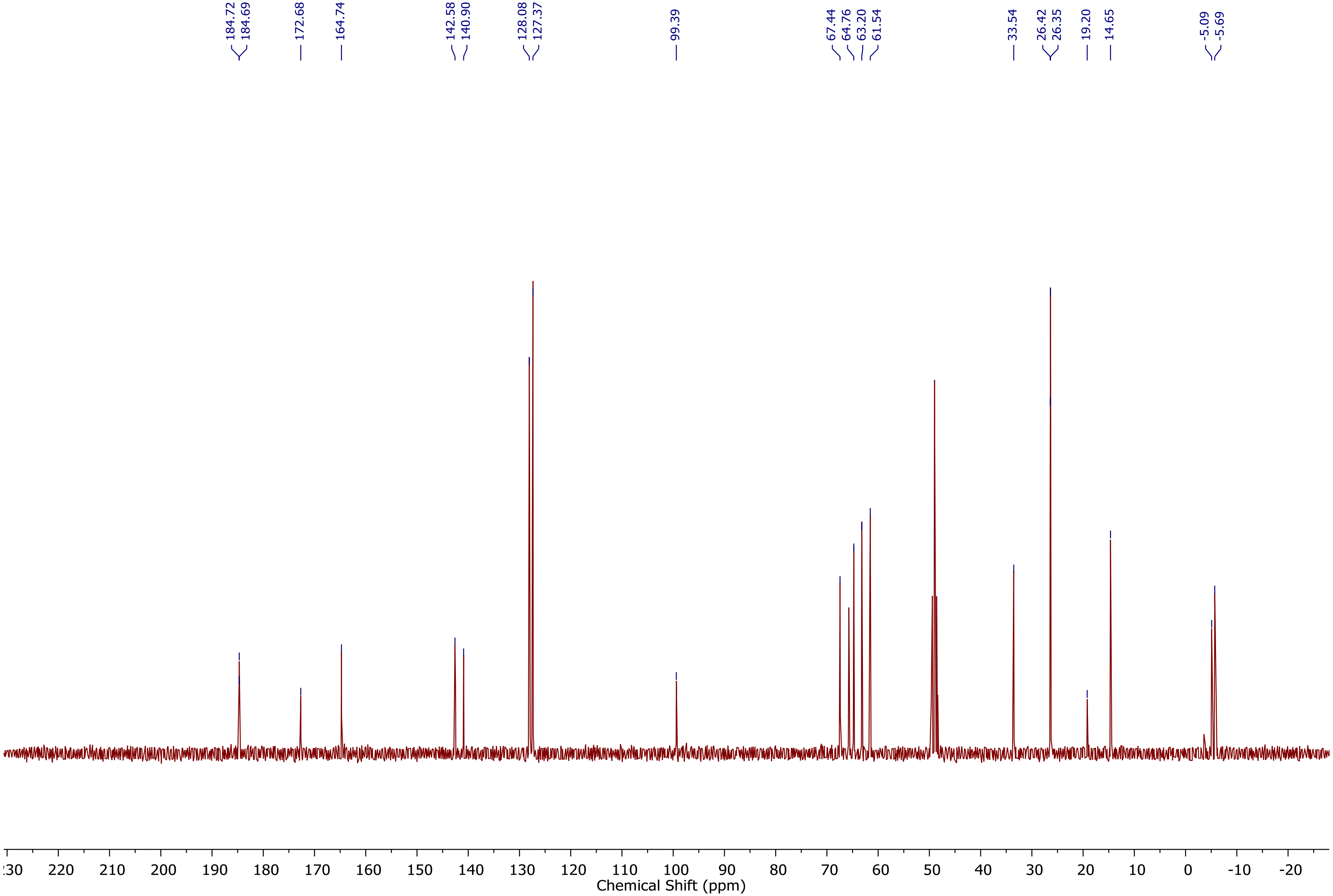


1H NMR (400 MHz, Methanol-d4)
7.44 7.43 7.42 7.41 7.34 7.32 7.31 7.29
6.22
4.98 HDO
4.89 4.87 4.85 4.73 4.59 4.32 4.30 4.28 4.27 3.30 3.29 3.28 3.26 3.01 2.99 2.98 2.96
1.33 1.31 1.29 0.94 0.91 0.91
0.10 0.07 0.07
2.28 2.62 1.00 1.14 2.87 2.20 1.47 1.07 3.58 12.57 7.74
12.5 12.0 11.5 11.0 10.5 10.0 9.5 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 -1.0 -1.5 -2.0
Chemical Shift (ppm)

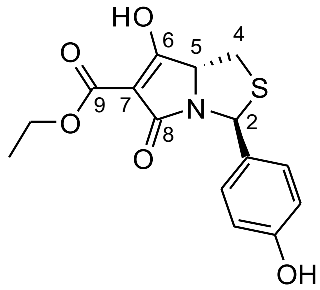
25b



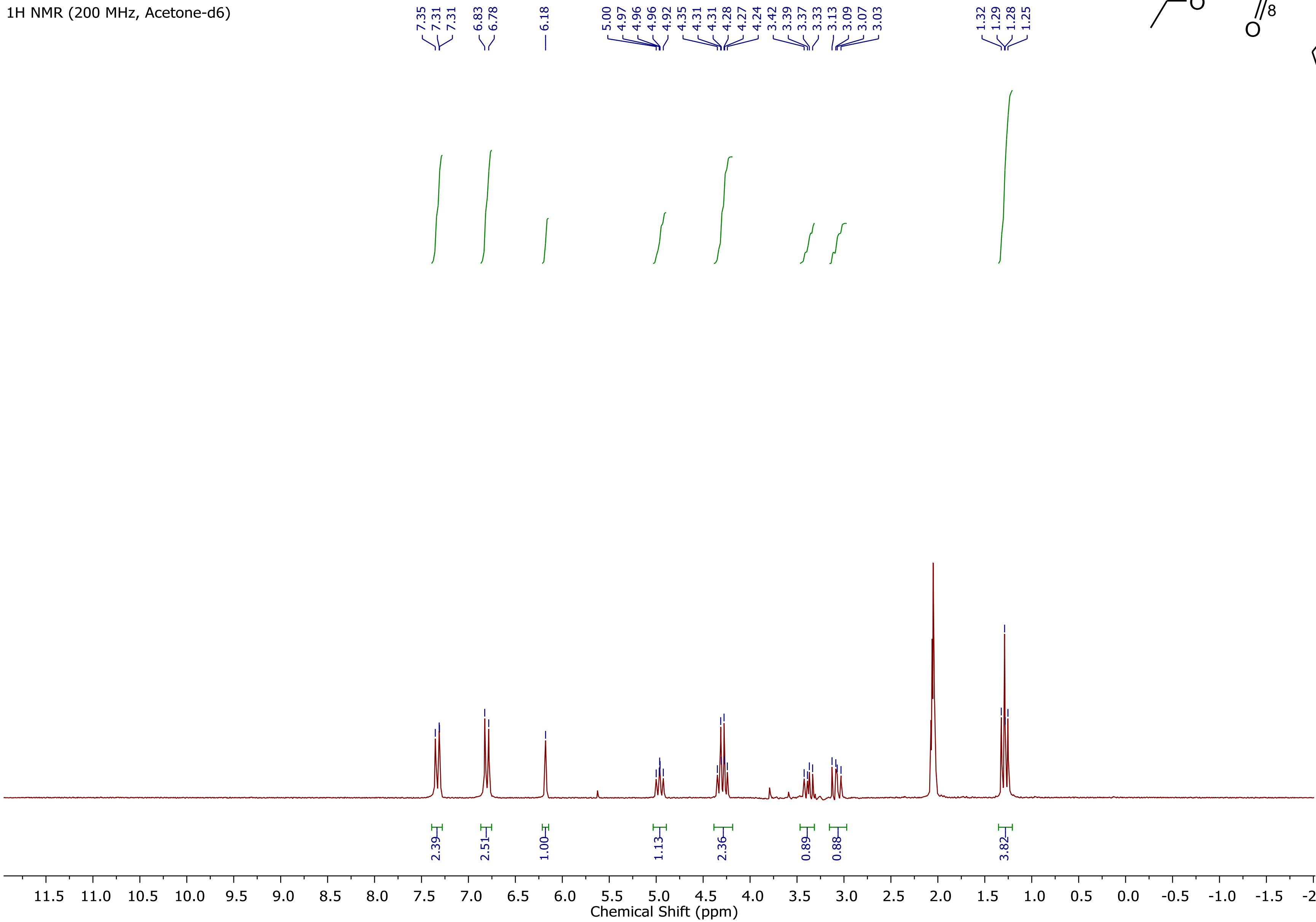
13C NMR (100.6 MHz, Methanol-d4)



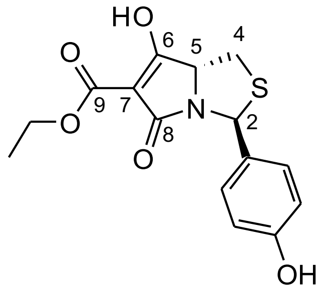
26a

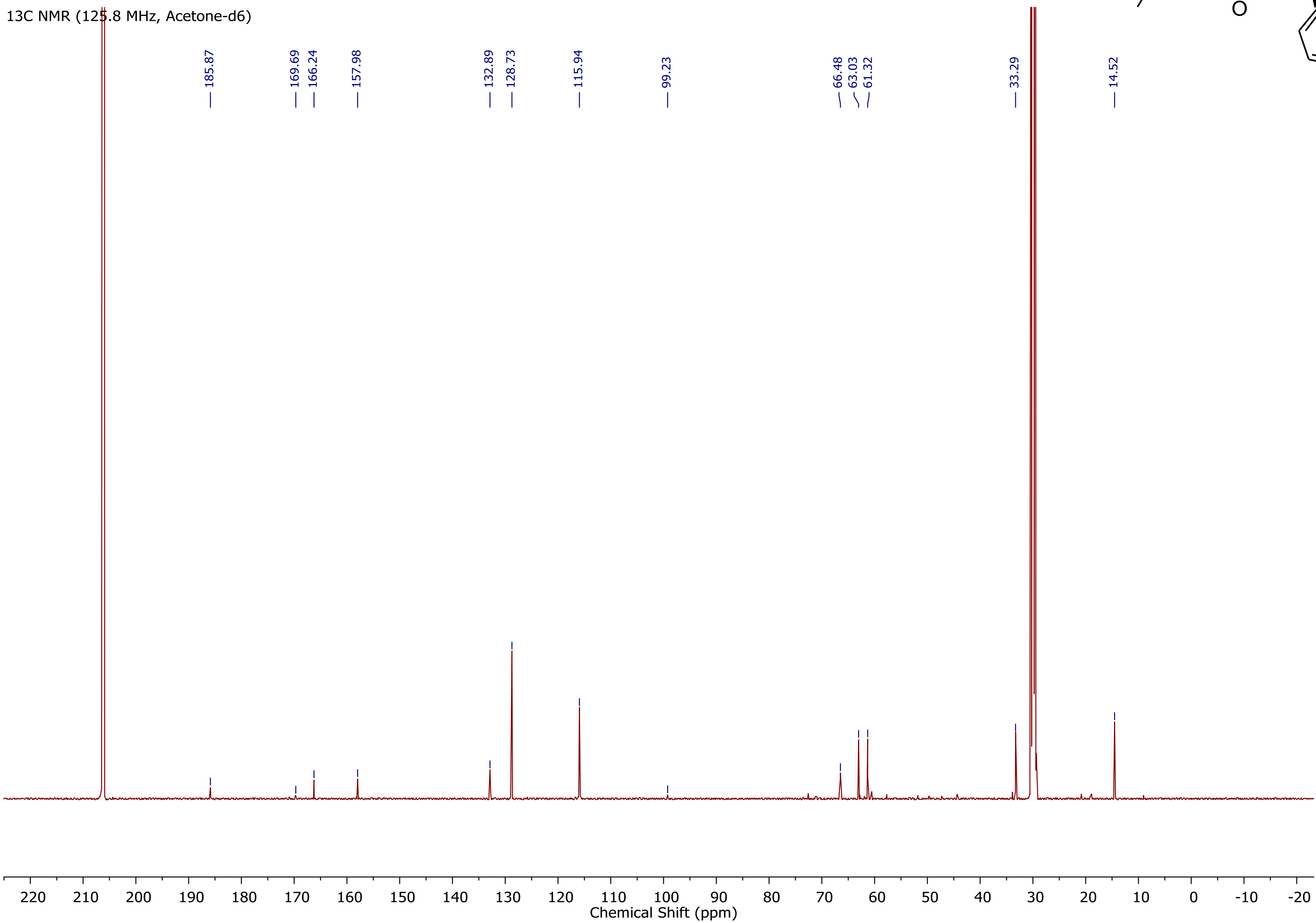


1H NMR (200 MHz, Acetone-d6)



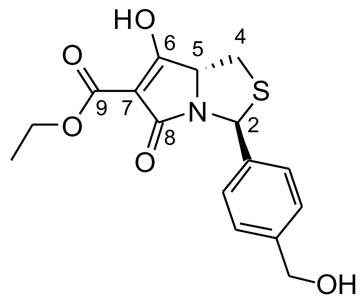
26a



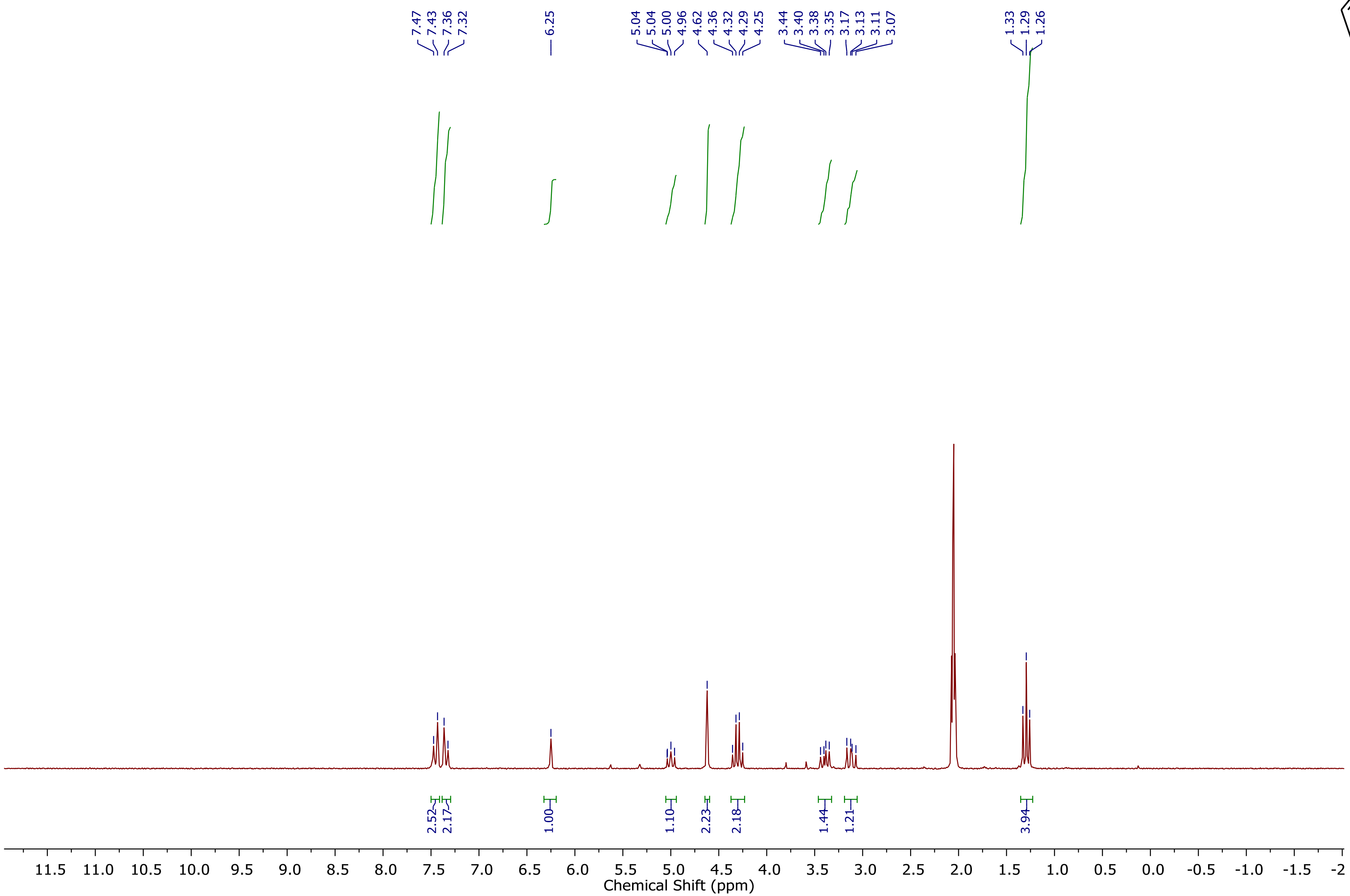


13C NMR (125.8 MHz, Acetone-d6)
185.87
169.69
166.24
157.98
132.89
128.73
115.94
99.23
66.48
63.03
61.32
33.29
14.52
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Chemical Shift (ppm)

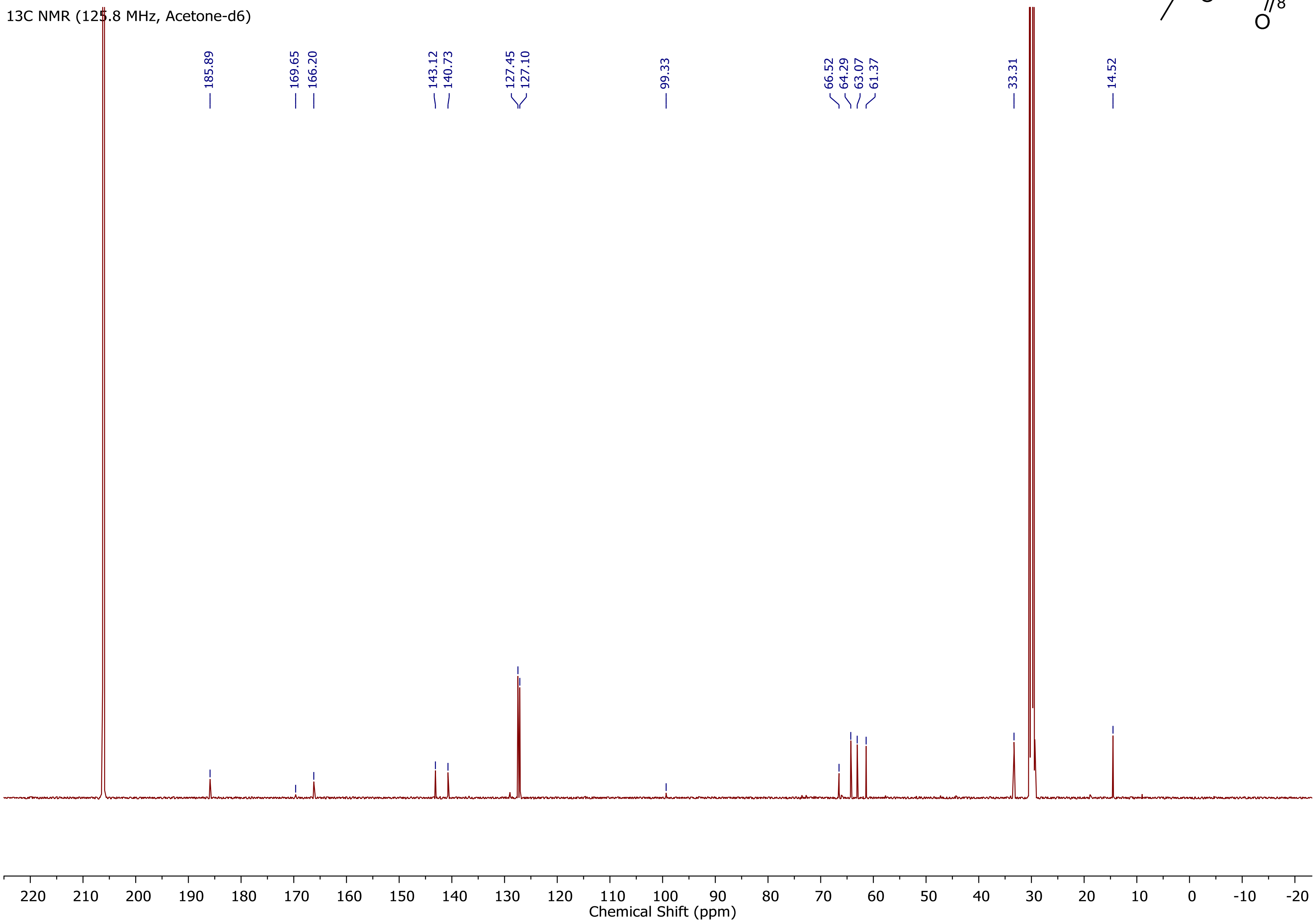
26b

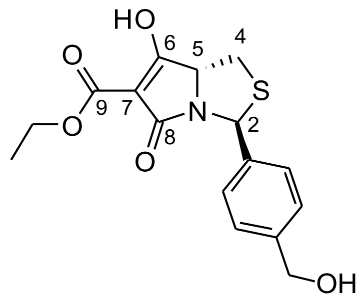


1H NMR (200 MHz, Acetone-d6)

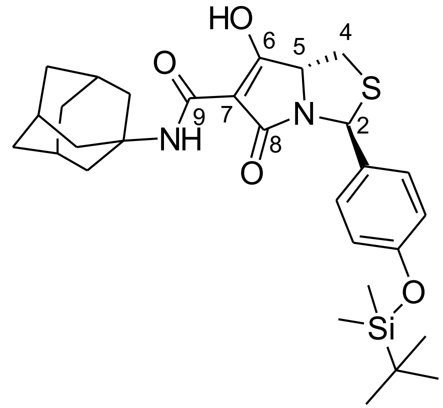


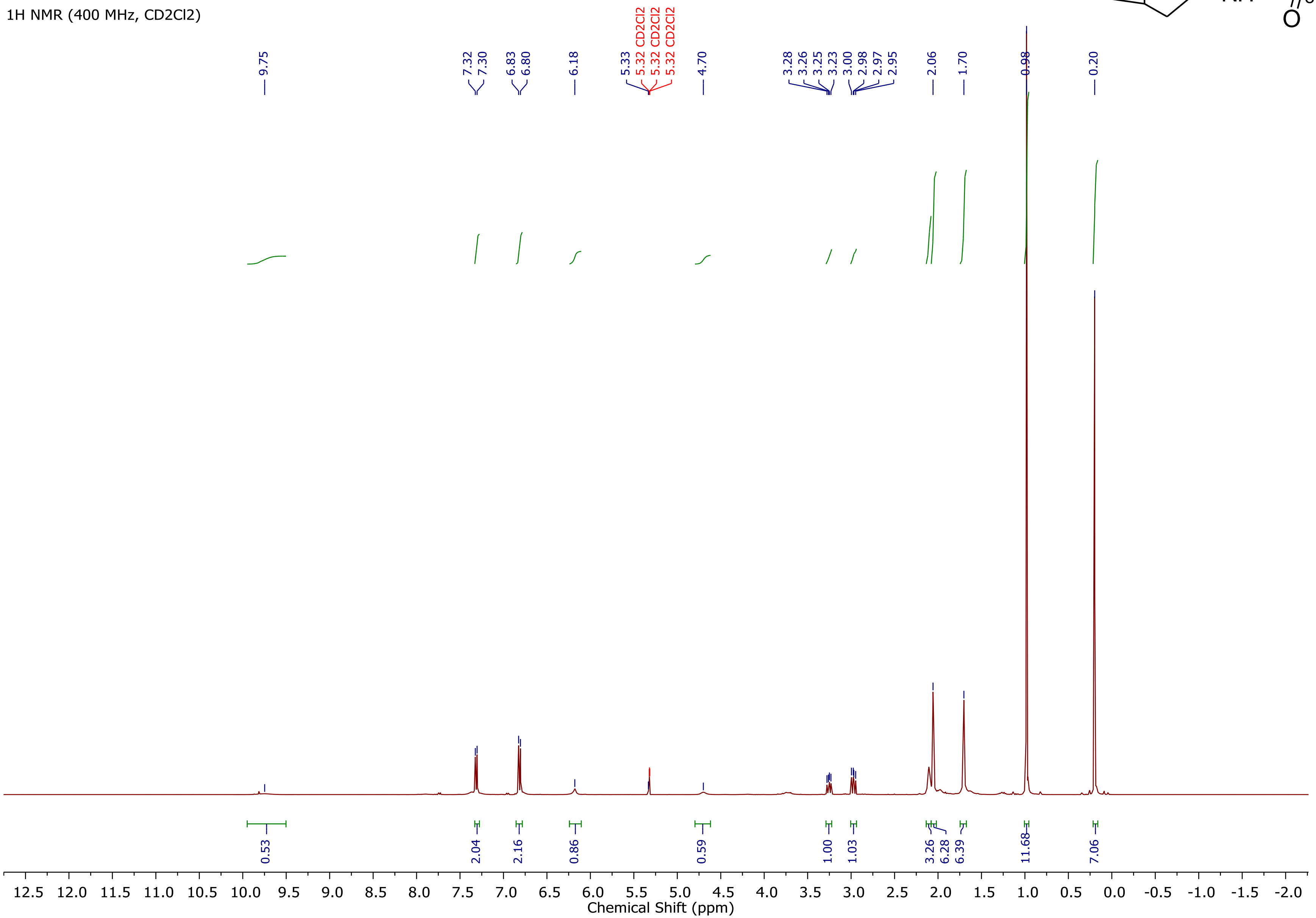
26b


13C NMR (125.8 MHz, Acetone-d6)
185.89
169.65
166.20
143.12
140.73
127.45
127.10
99.33
66.52
64.29
63.07
61.37
33.31
14.52
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

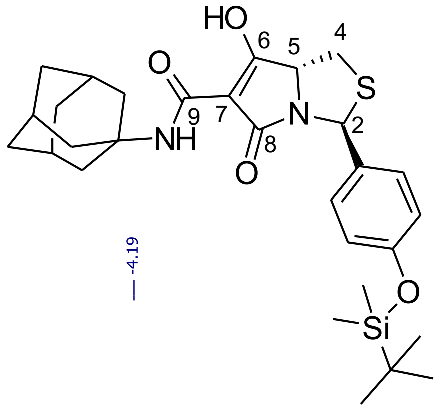

HO
O
O
N
S
O
OH
2
4
5
6
7
8
9

27a

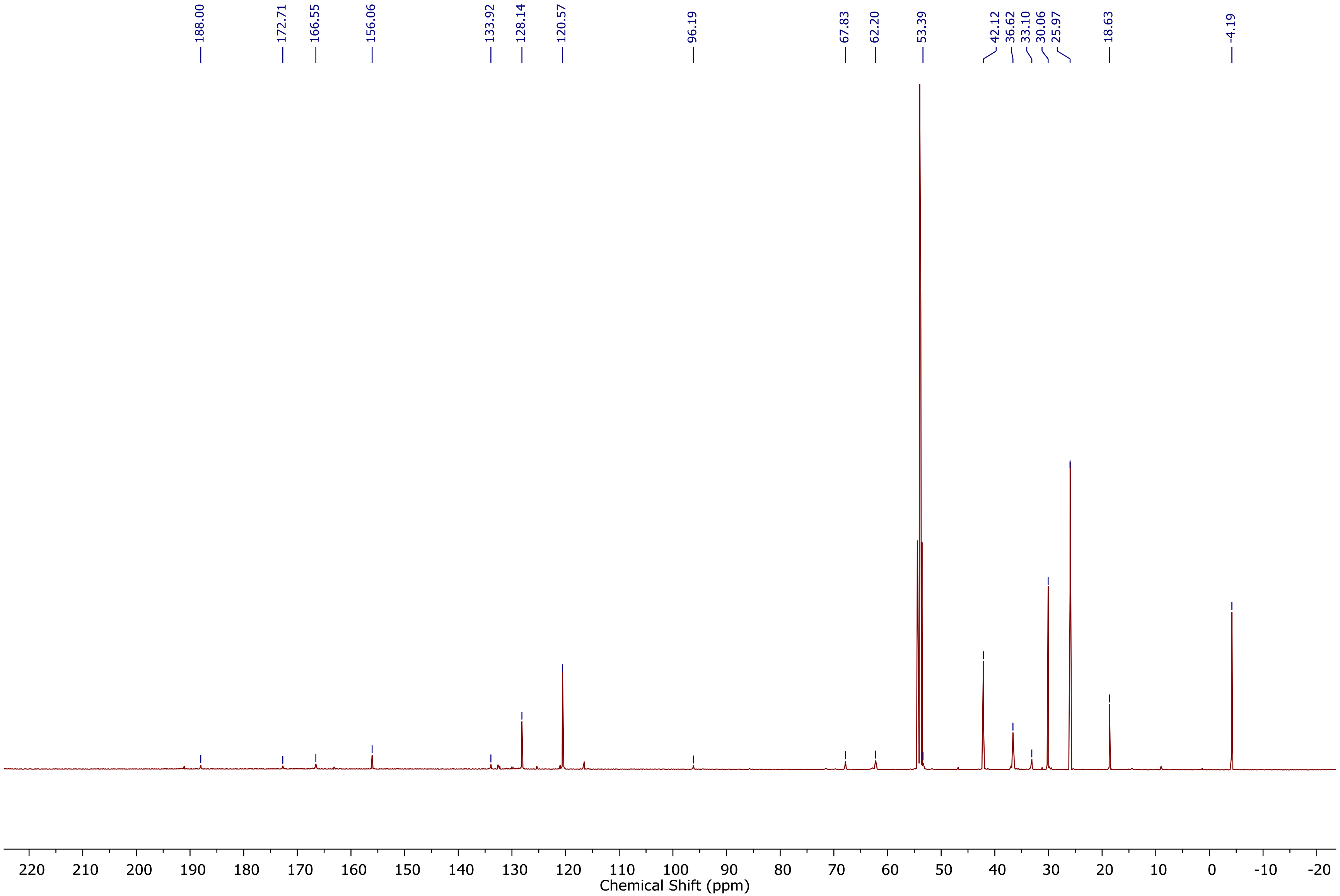

HO
6
5
4
O
S
9
7
N
2
NH
8
O
O
Si


1H NMR (400 MHz, CD2Cl2)
9.75
7.32
7.30
6.83
6.80
6.18
5.33
5.32 CD2Cl2
5.32 CD2Cl2
5.32 CD2Cl2
4.70
3.28
3.26
3.25
3.23
3.00
2.98
2.97
2.95
2.06
1.70
0.98
0.20
0.53
2.04
2.16
0.86
0.59
1.00
1.03
3.26
6.28
6.39
11.68
7.06
12.5 12.0 11.5 11.0 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 -1.0 -1.5 -2.0
Chemical Shift (ppm)

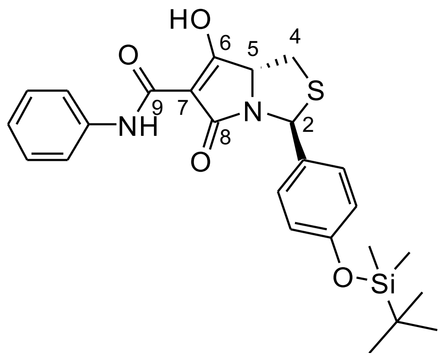
27a



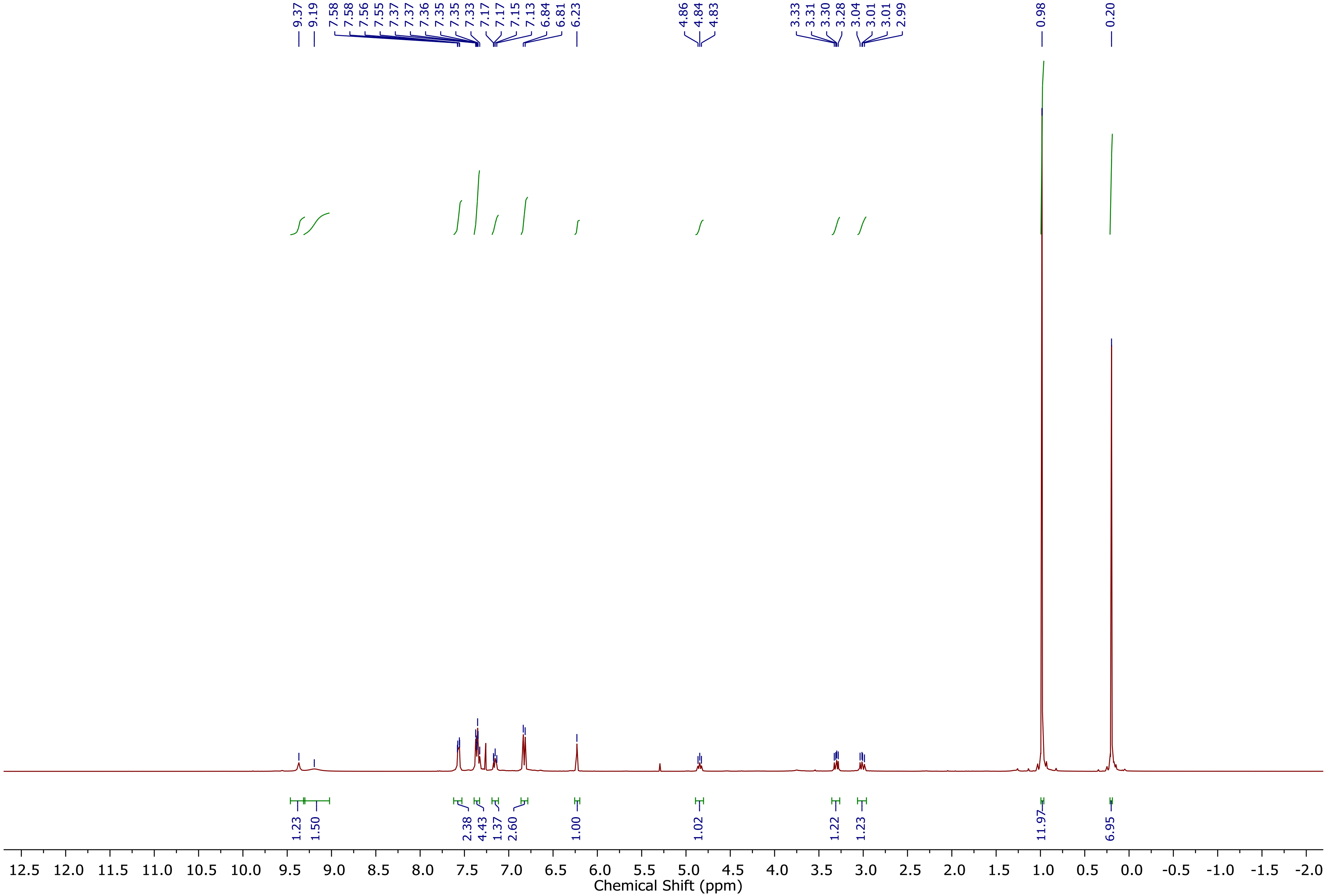
13C NMR (125.8 MHz, CD2Cl2)



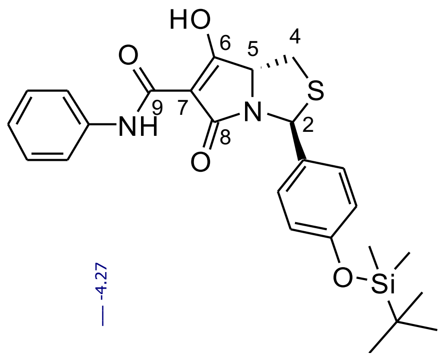
27b



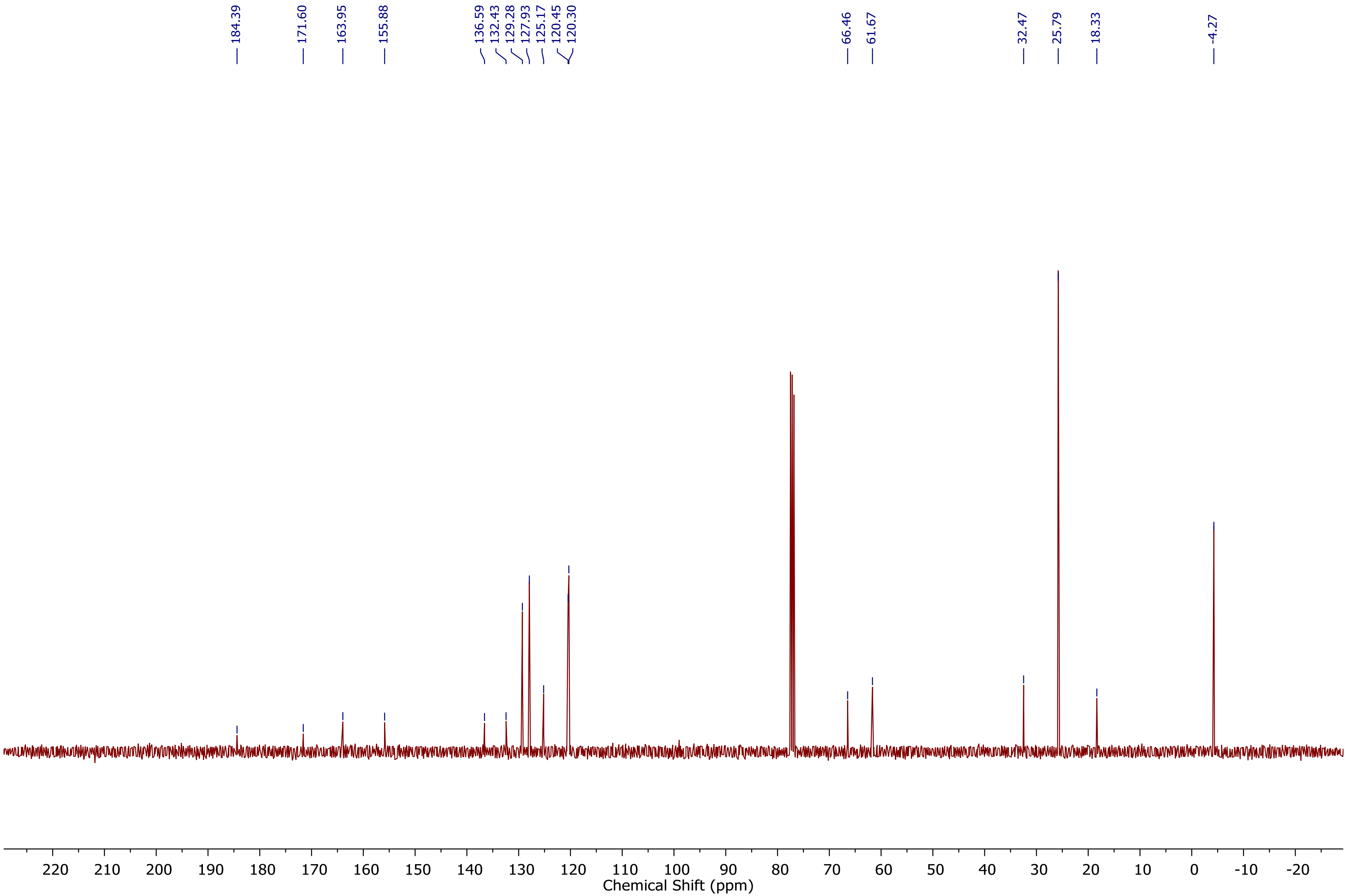
1H NMR (400 MHz, CDCl3)



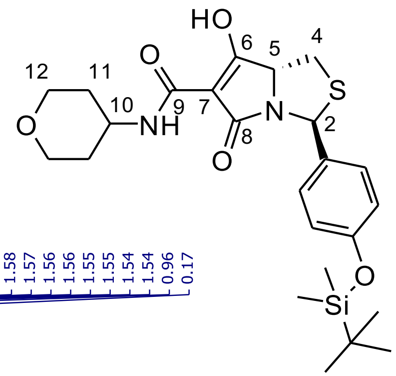
27b



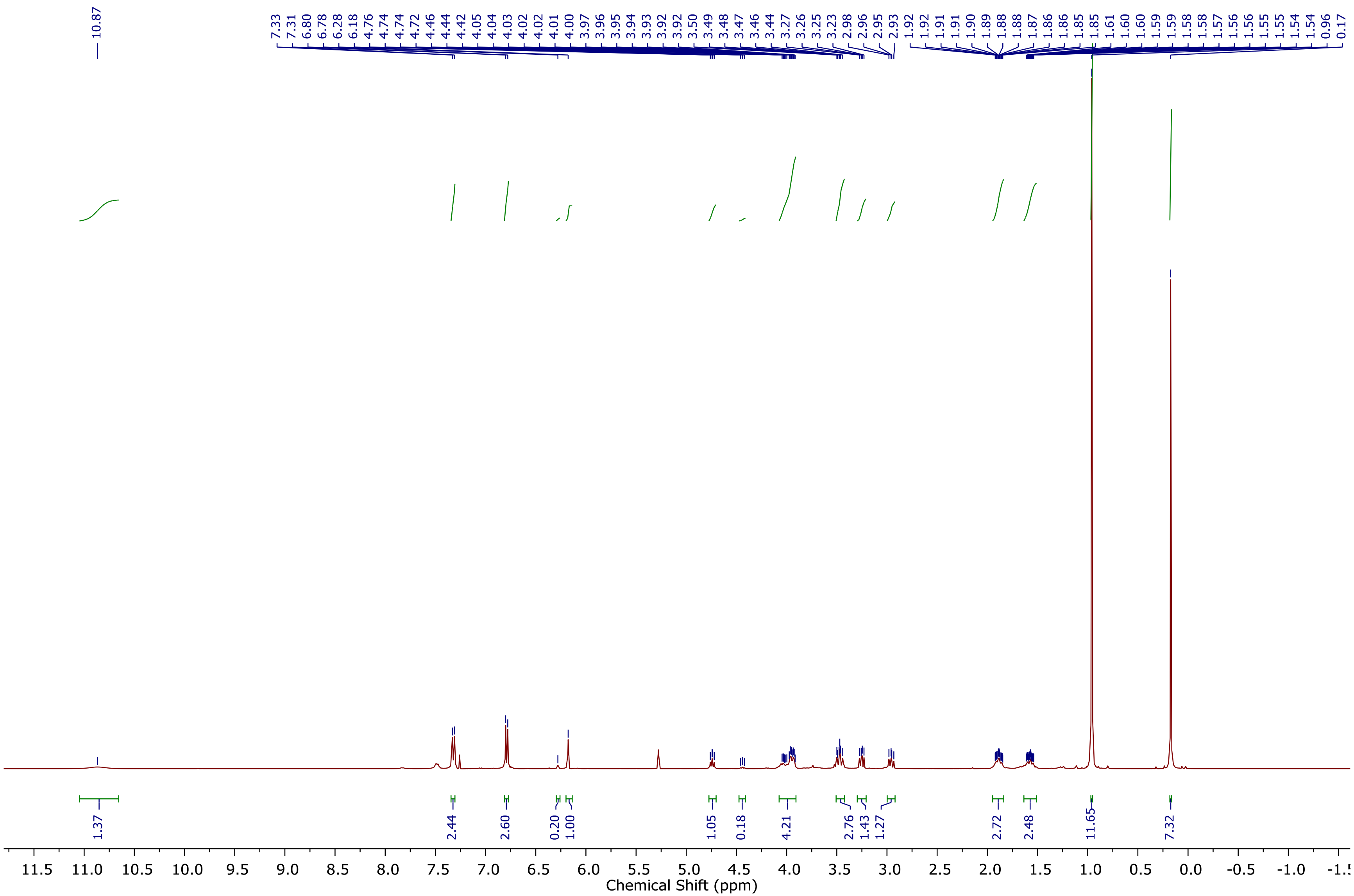
13C NMR (100.6 MHz, CDCl3)



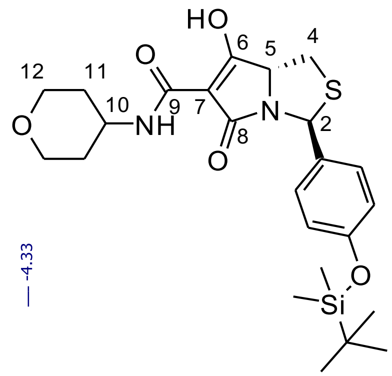
27c



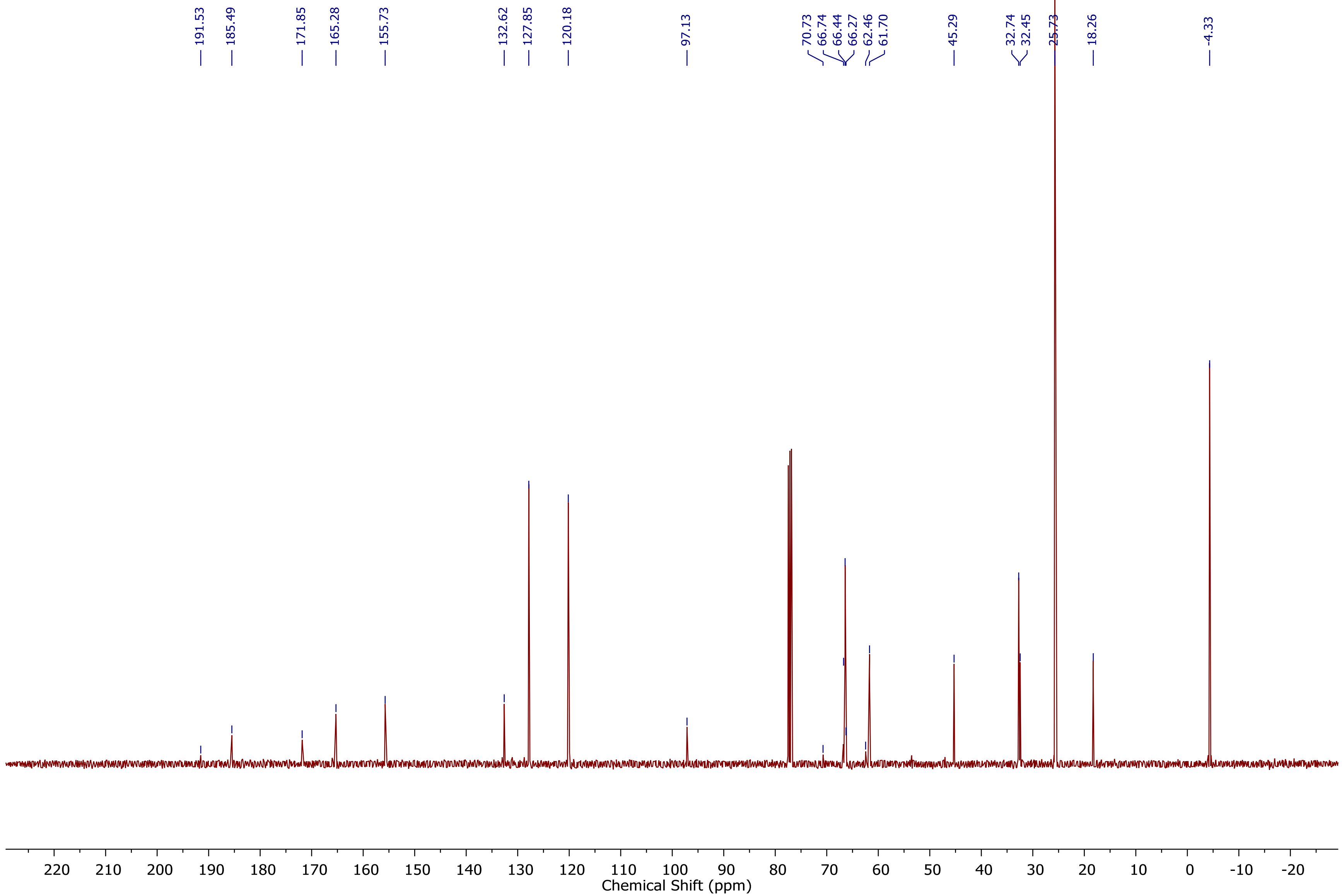
1H NMR (400 MHz, CDCl3)



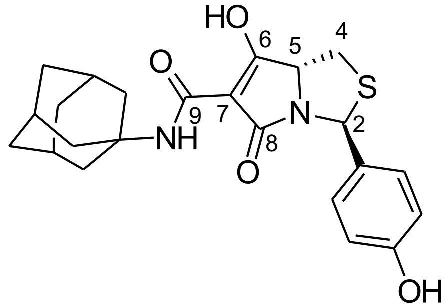
27c



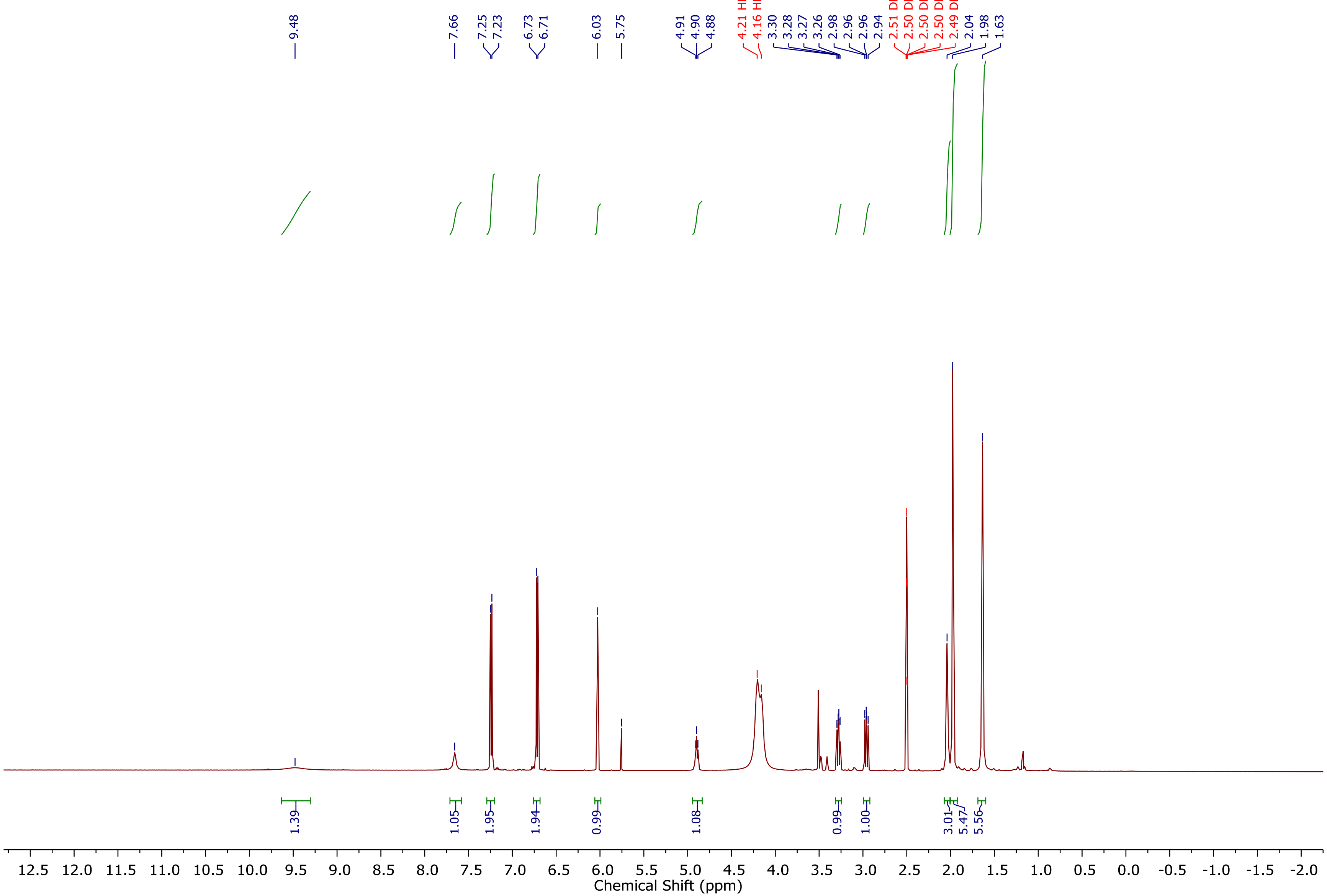
13C NMR (100.6 MHz, CDCl3)



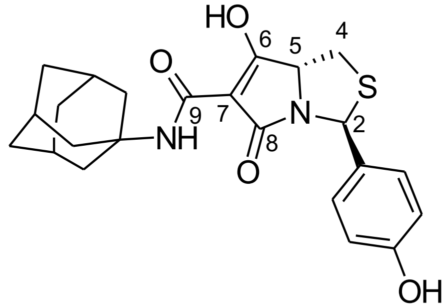
28a



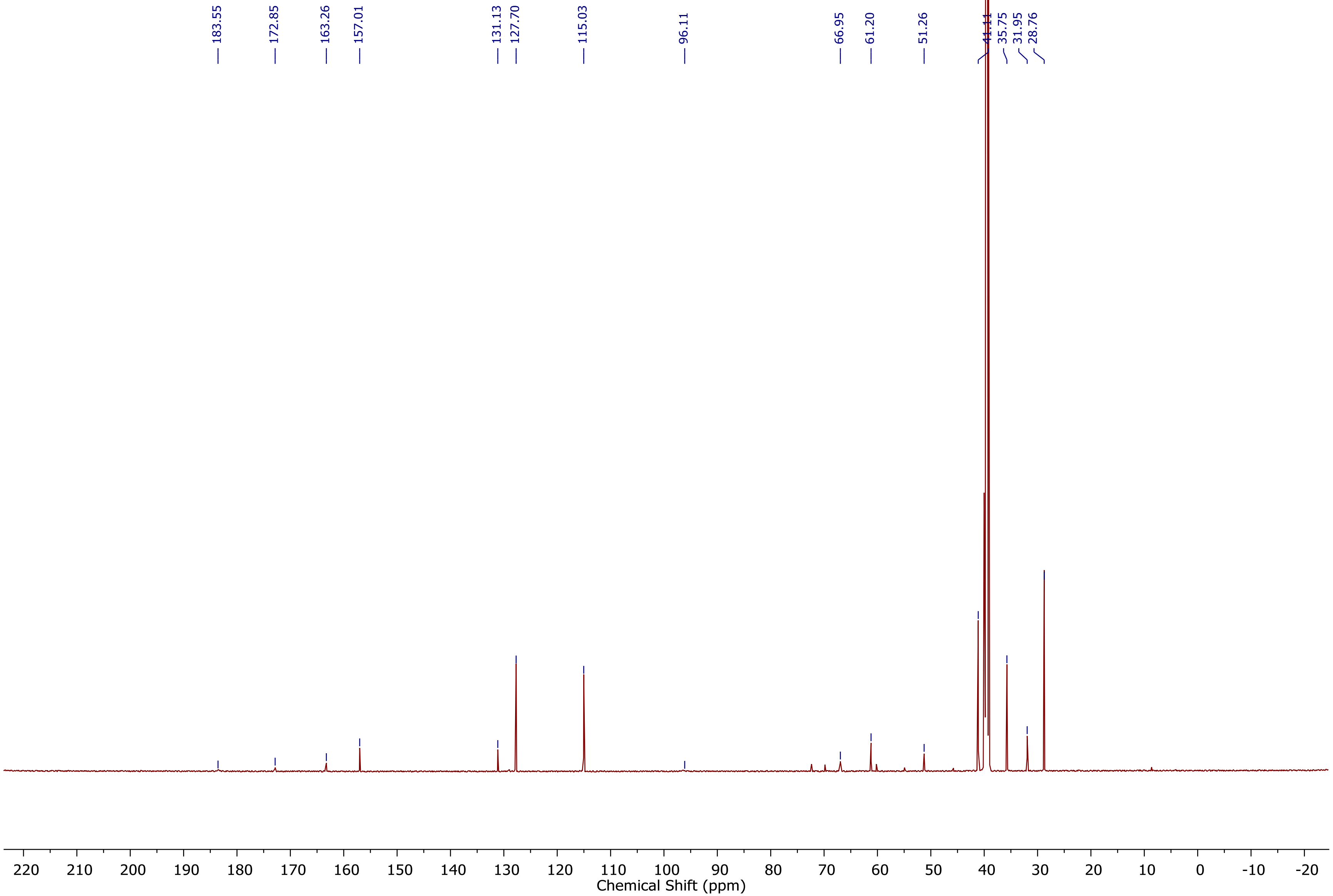
1H NMR (500 MHz, DMSO-d6)



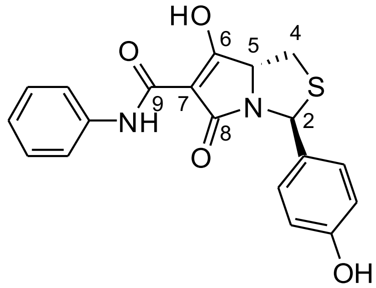
28a



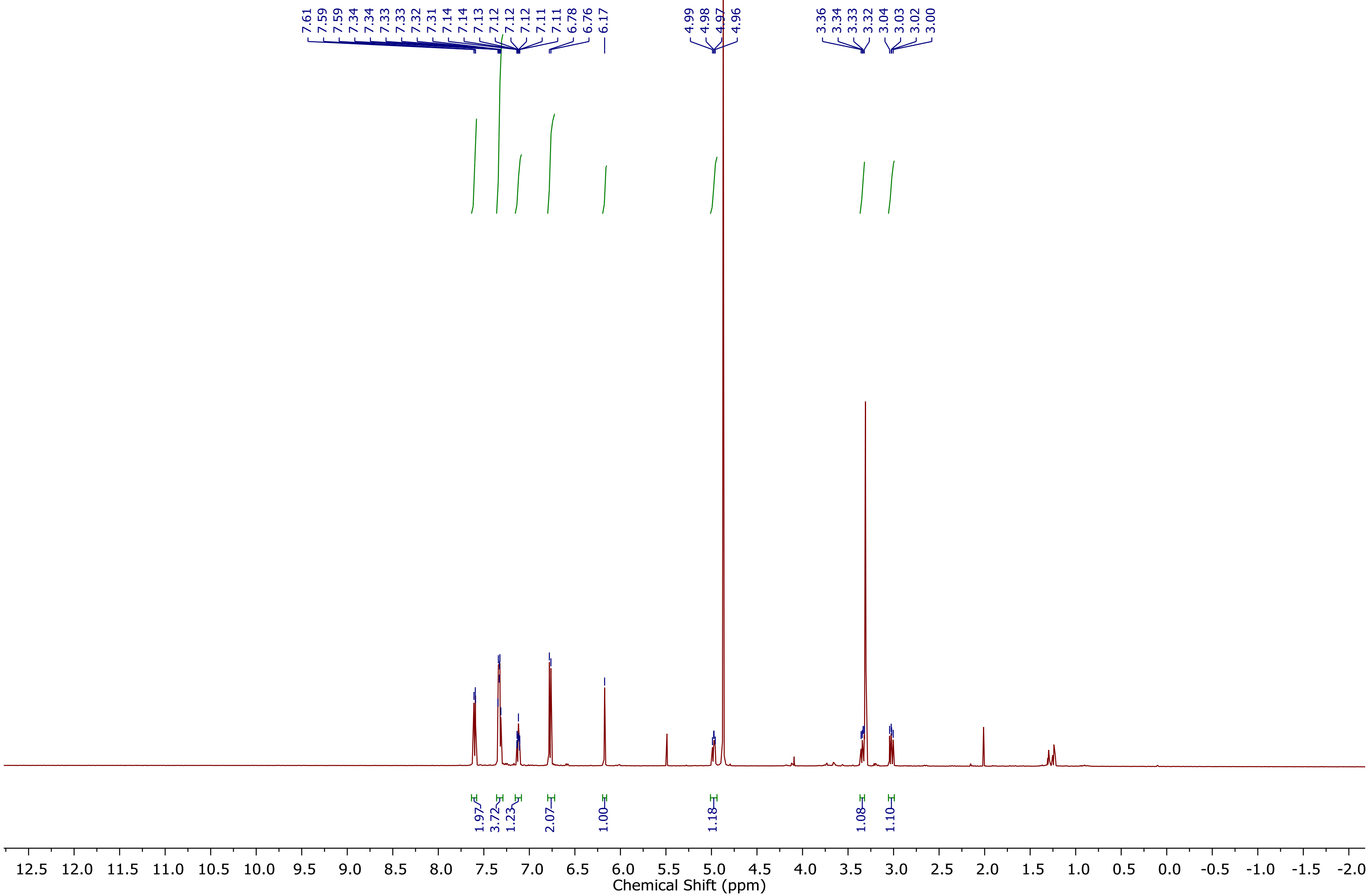
13C NMR (125.8 MHz, DMSO-d6)



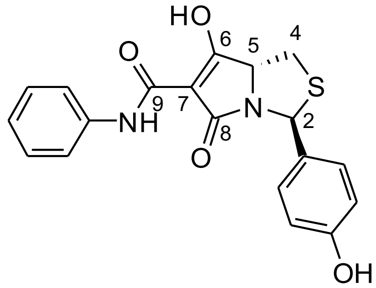
28b



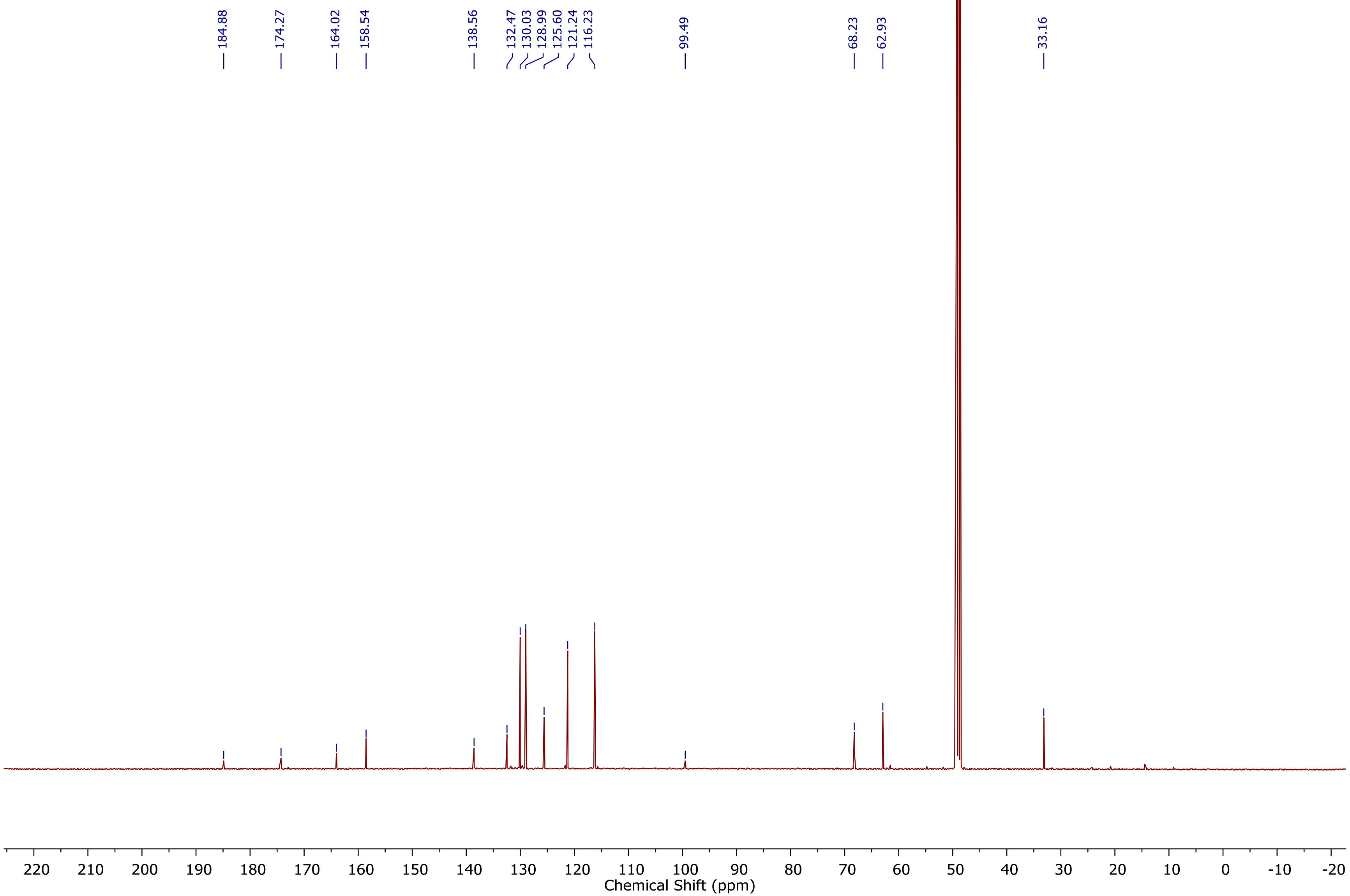
1H NMR (500 MHz, Methanol-d4)



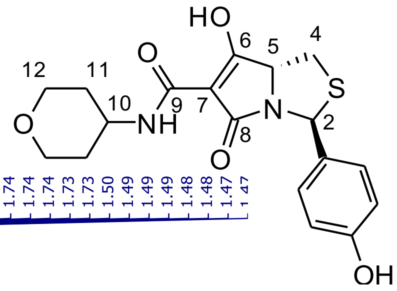
28b



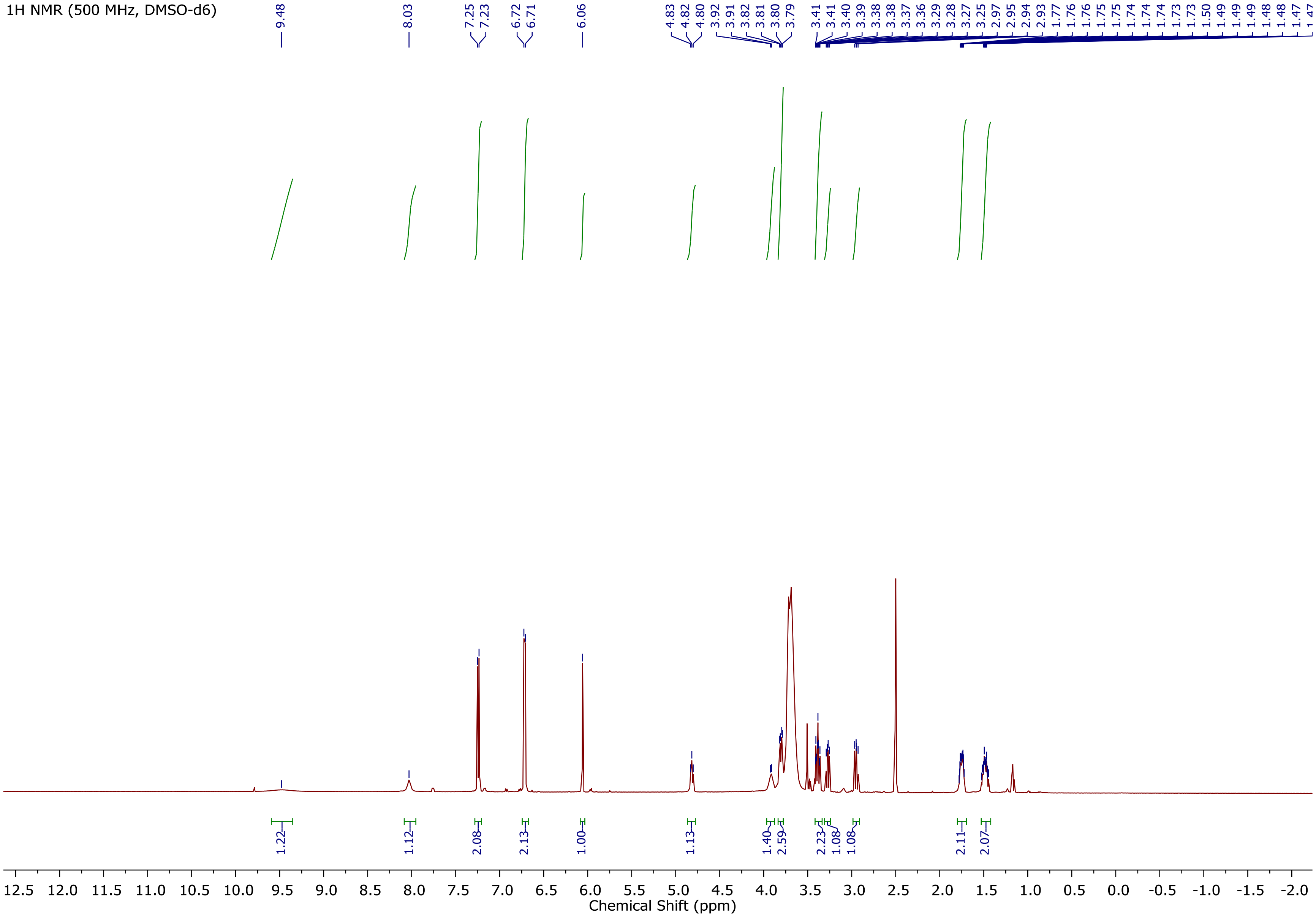
13C NMR (125.8 MHz, Methanol-d4)



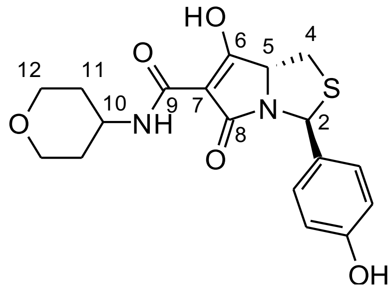
28c



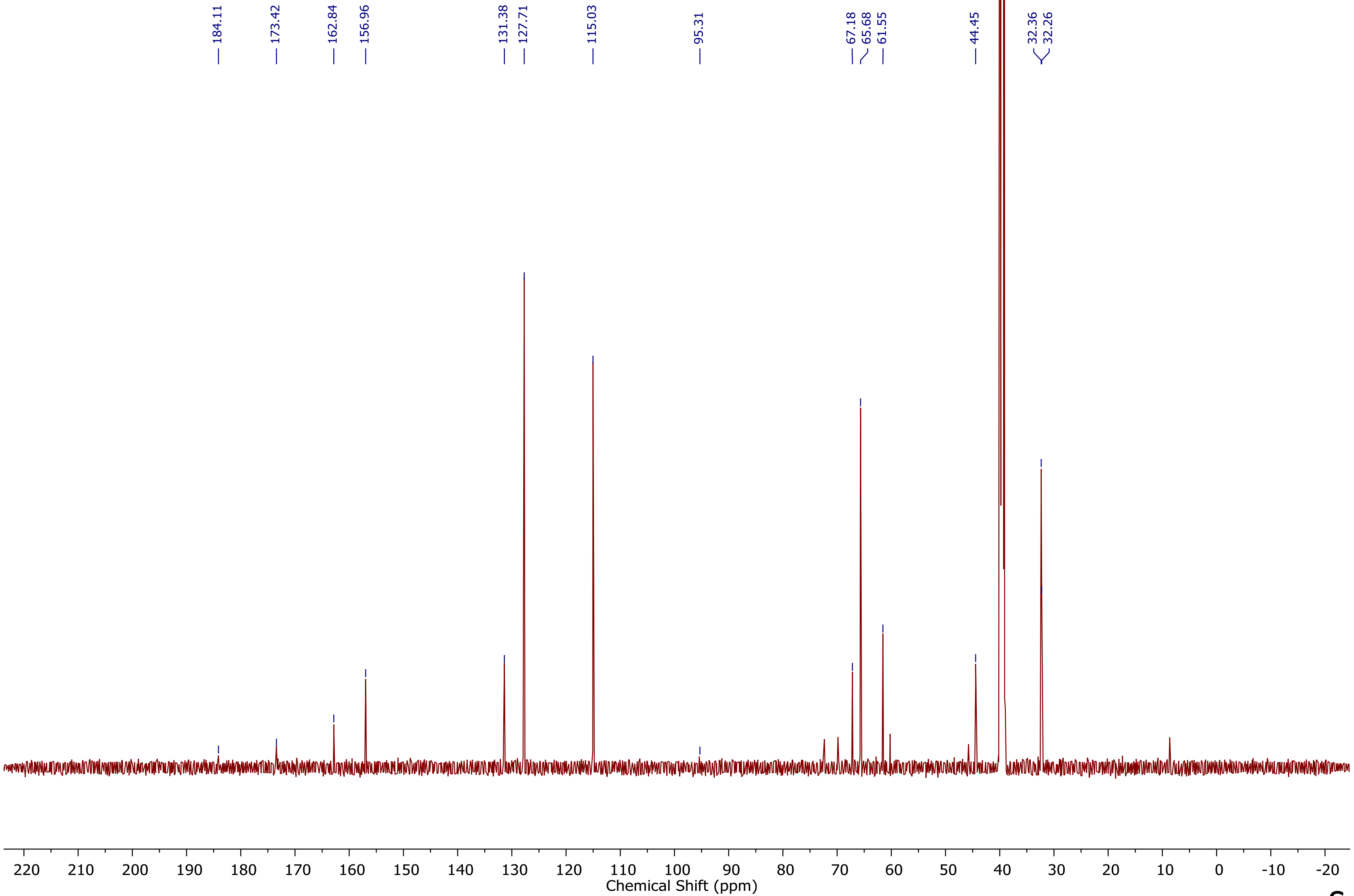
1H NMR (500 MHz, DMSO-d6)



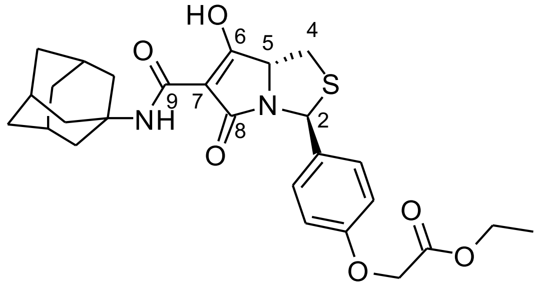
28c



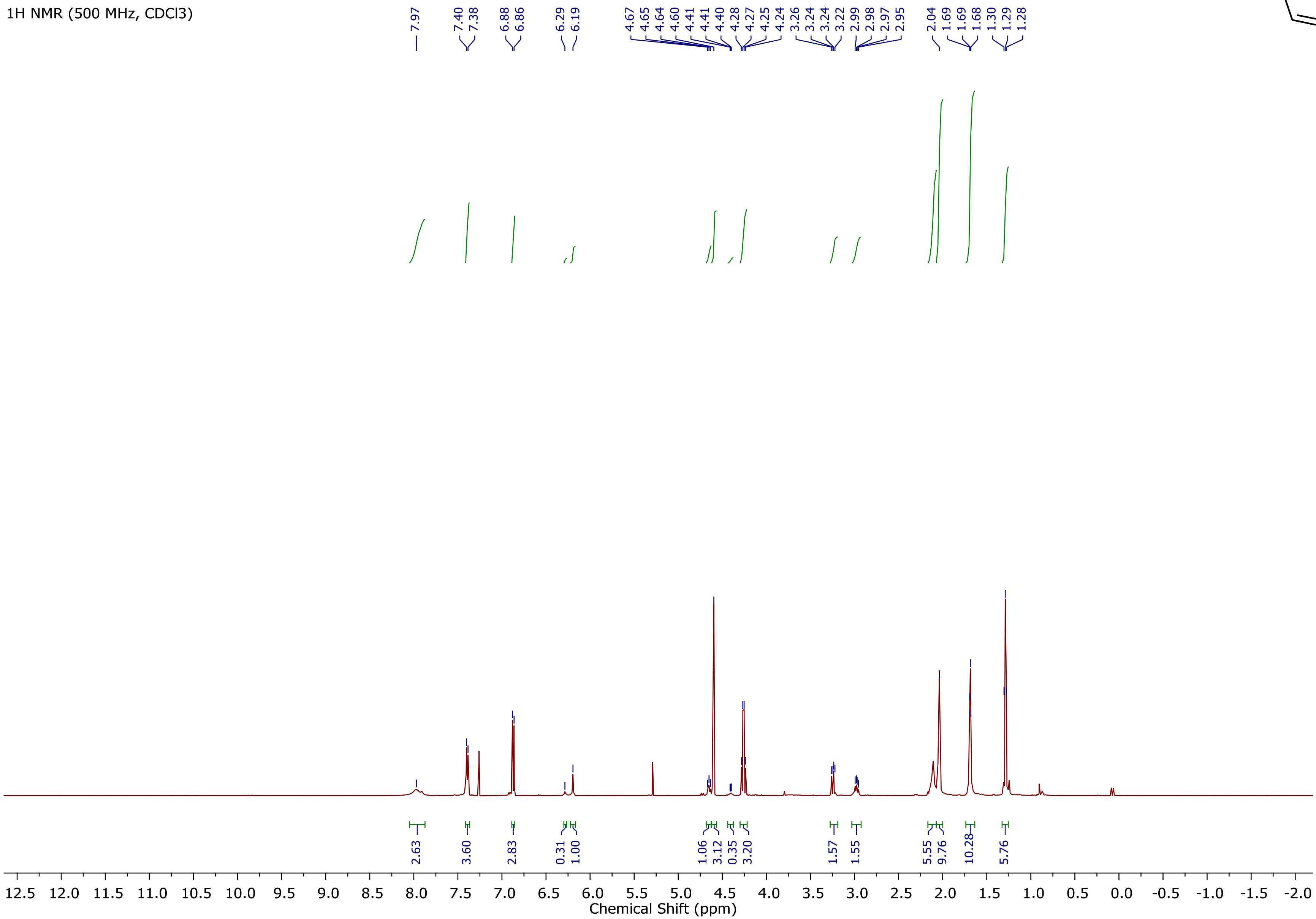
13C NMR (125.8 MHz, DMSO-d6)



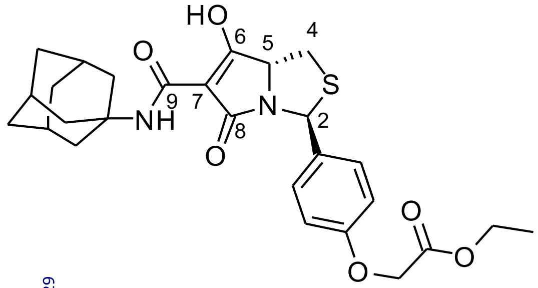
29a



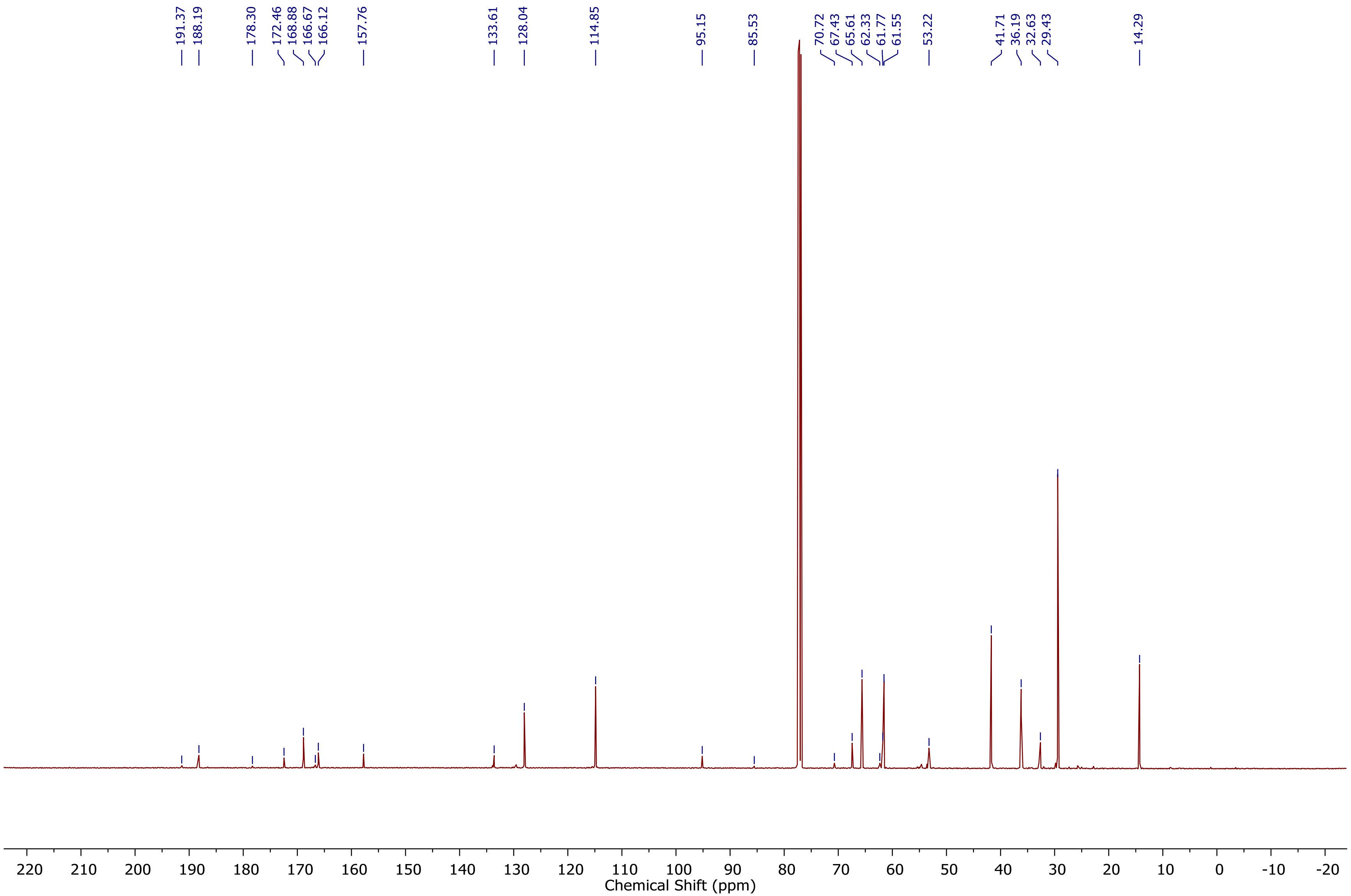
1H NMR (500 MHz, CDCl3)



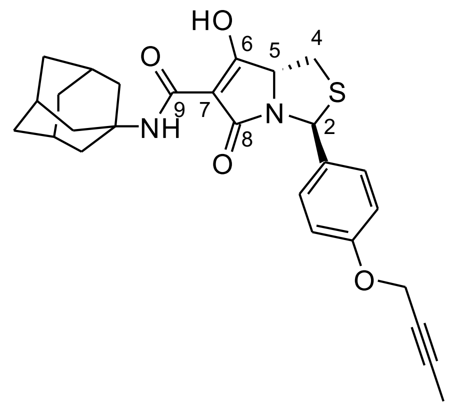
29a



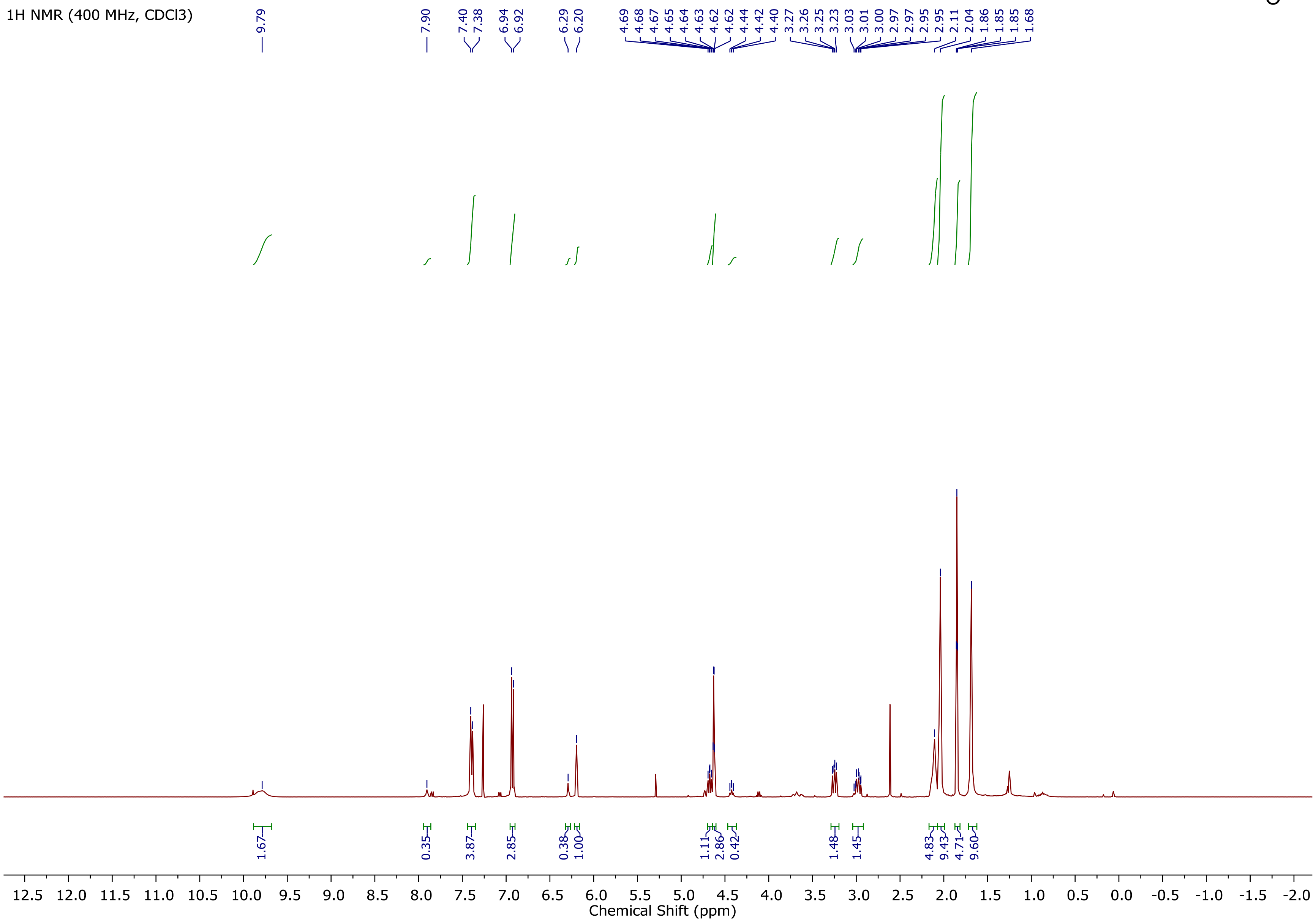
13C NMR (125.8 MHz, CDCl3)



30

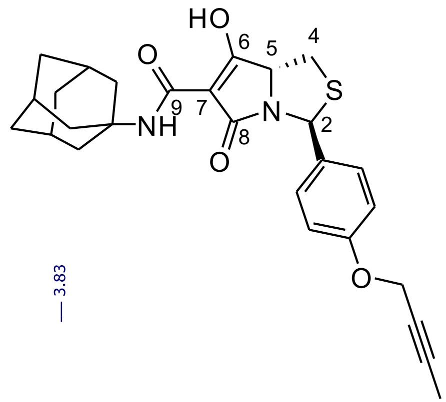


HO
O
O
NH
N
S
6
5
4
7
9
8
2
O

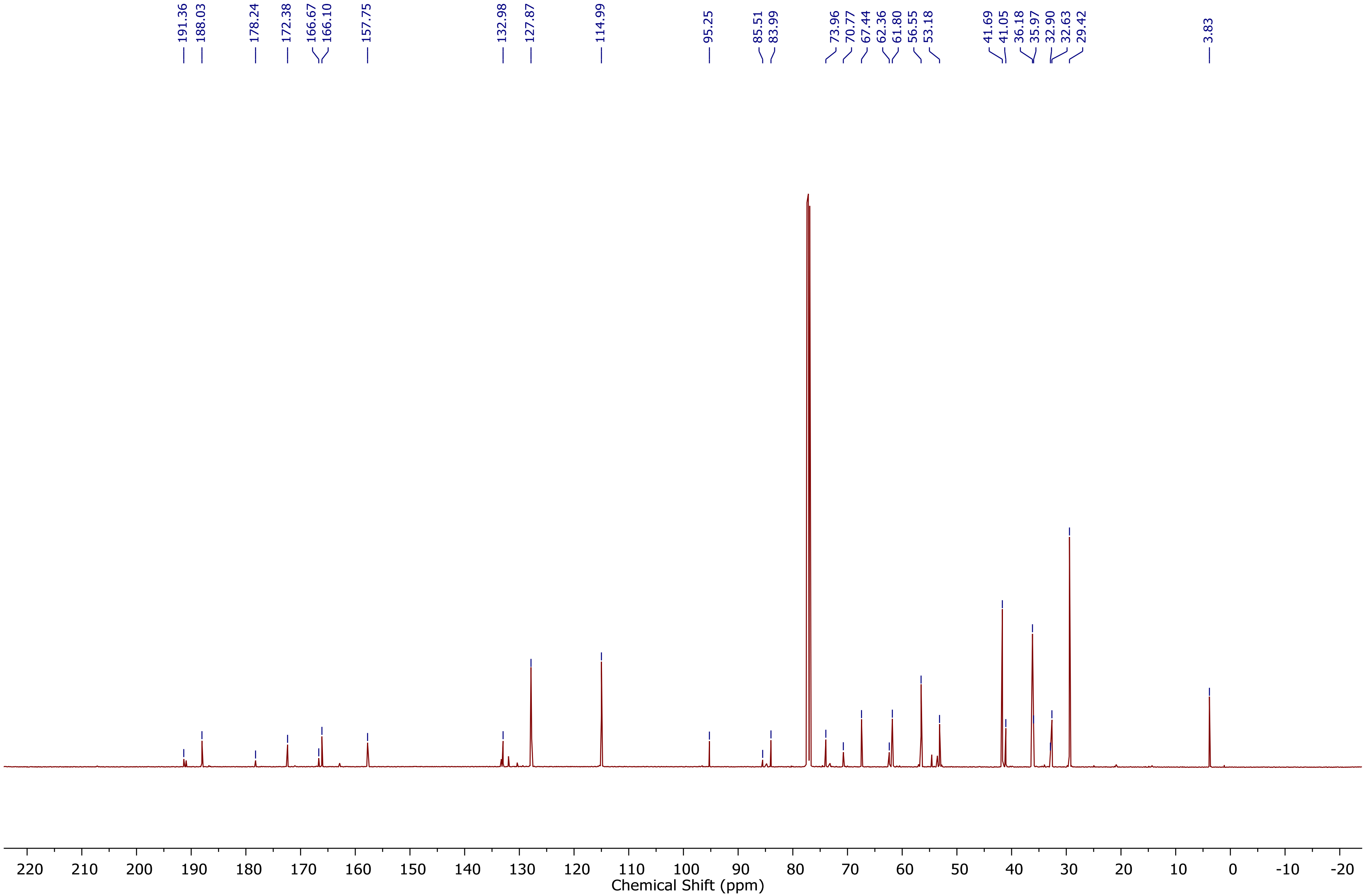


1H NMR (400 MHz, CDCl3)
9.79
7.90
7.40
7.38
6.94
6.92
6.29
6.20
4.69
4.68
4.67
4.65
4.64
4.63
4.62
4.62
4.44
4.42
4.40
3.27
3.26
3.25
3.23
3.03
3.01
3.00
2.97
2.97
2.95
2.95
2.11
2.04
1.86
1.85
1.85
1.68
1.67
0.35
3.87
2.85
0.38
1.00
1.11
2.86
0.42
1.48
1.45
4.83
9.43
4.71
9.60
12.5 12.0 11.5 11.0 10.5 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 -1.0 -1.5 -2.0
Chemical Shift (ppm)

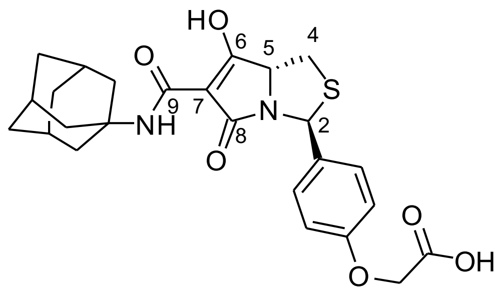
30



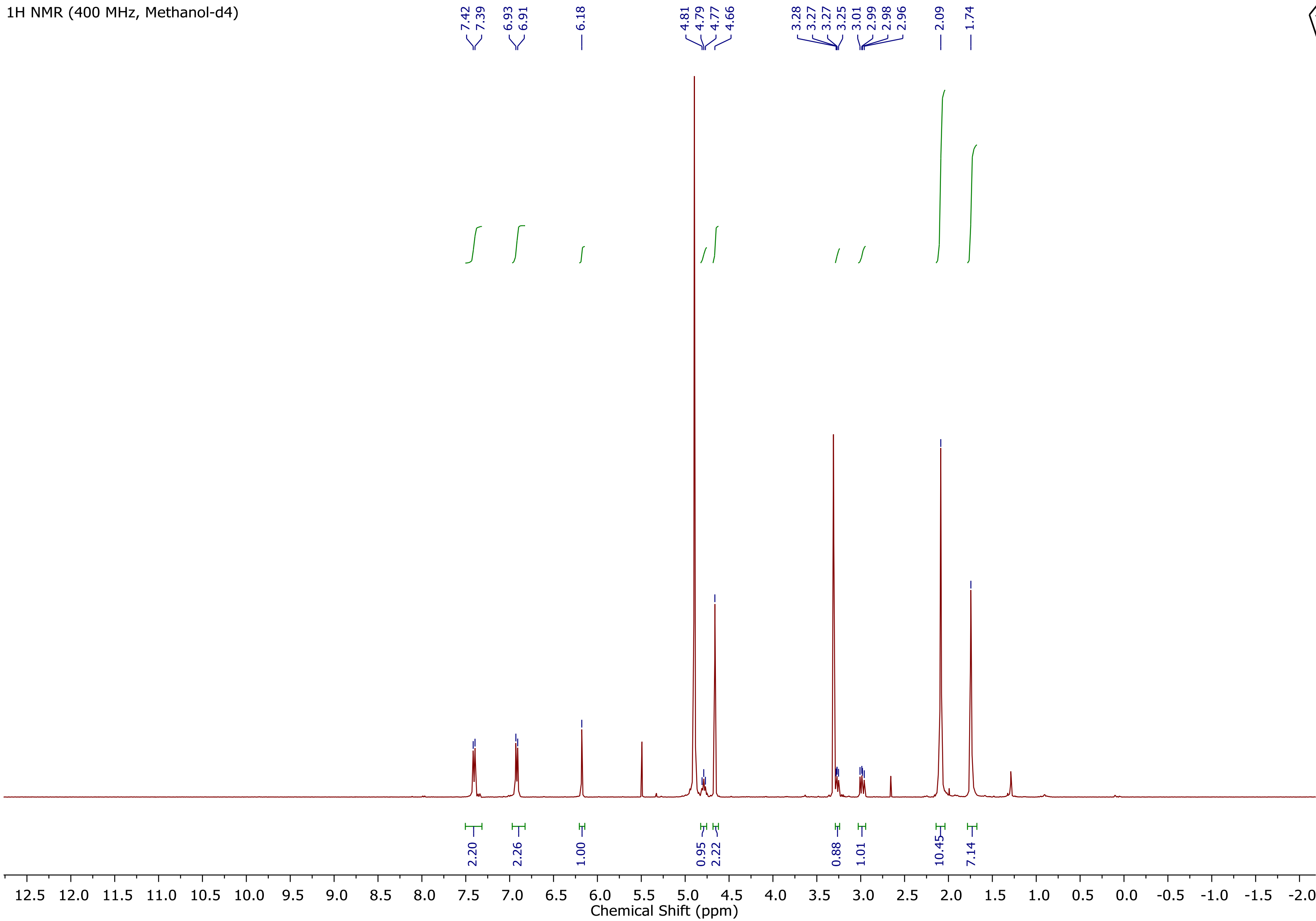
13C NMR (125.8 MHz, CDCl3)



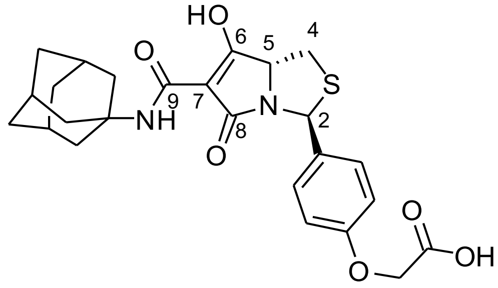
29b



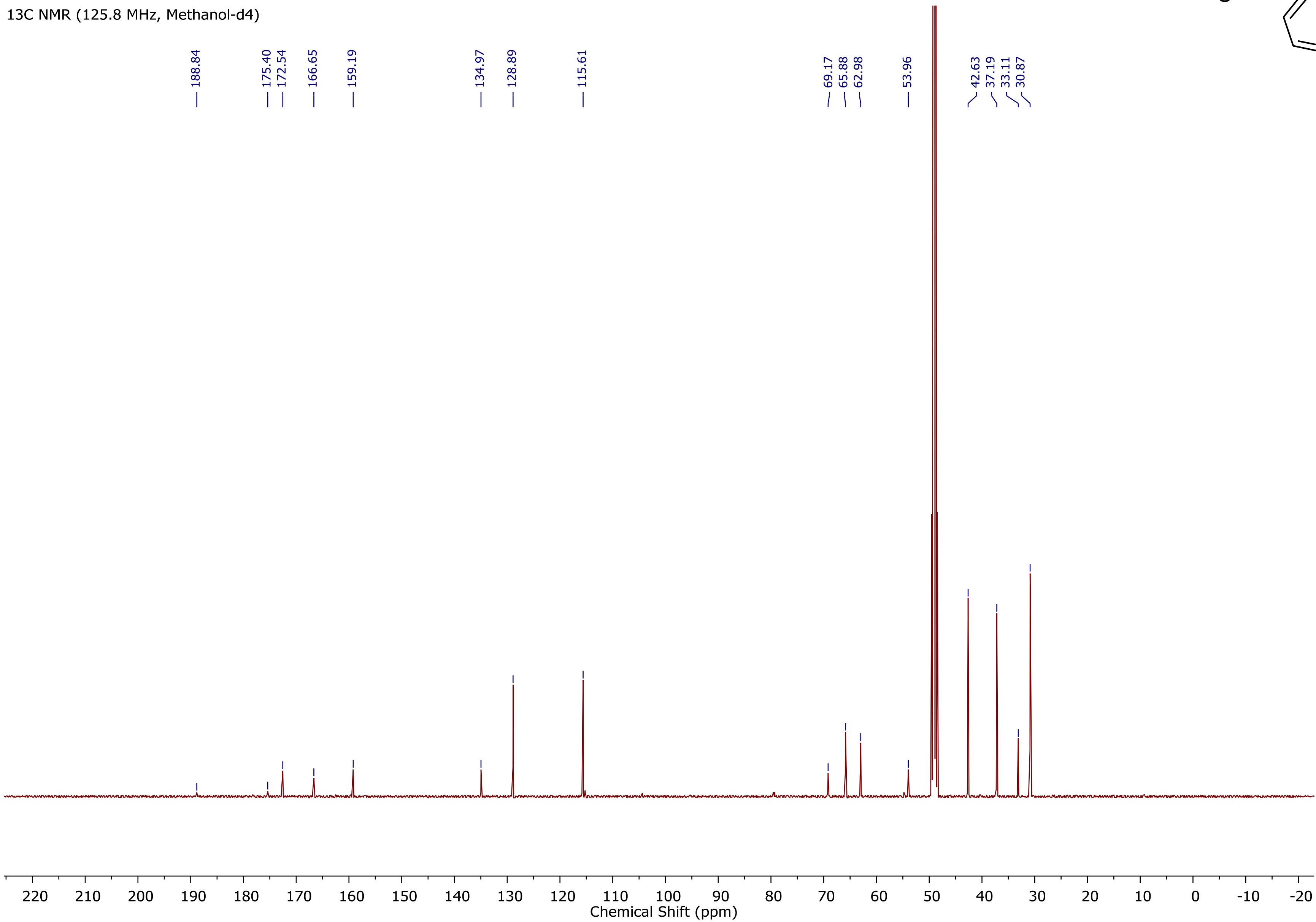
1H NMR (400 MHz, Methanol-d4)



29b



13C NMR (125.8 MHz, Methanol-d4)



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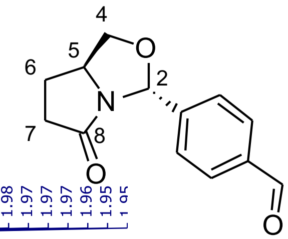
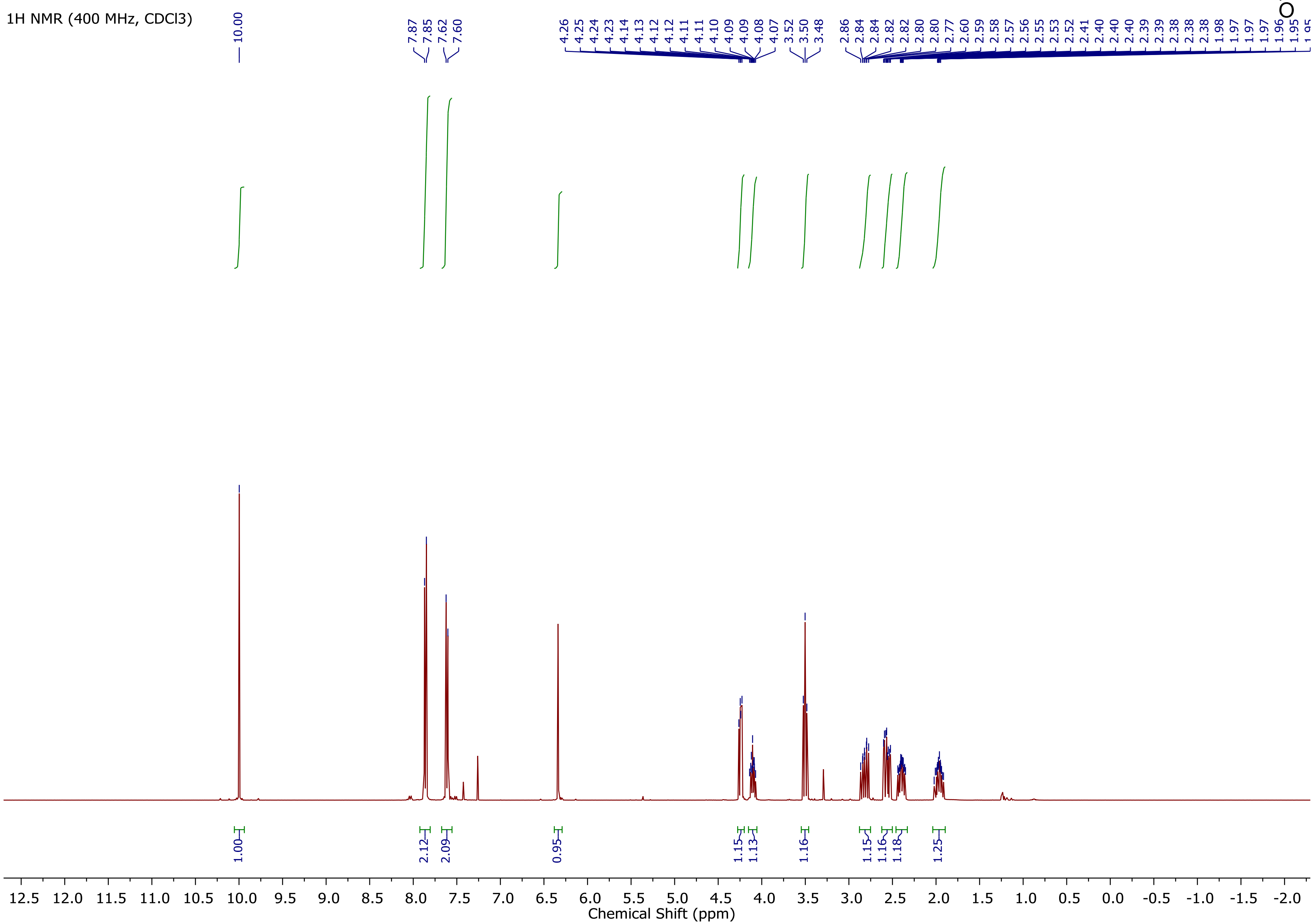
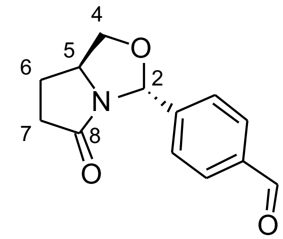


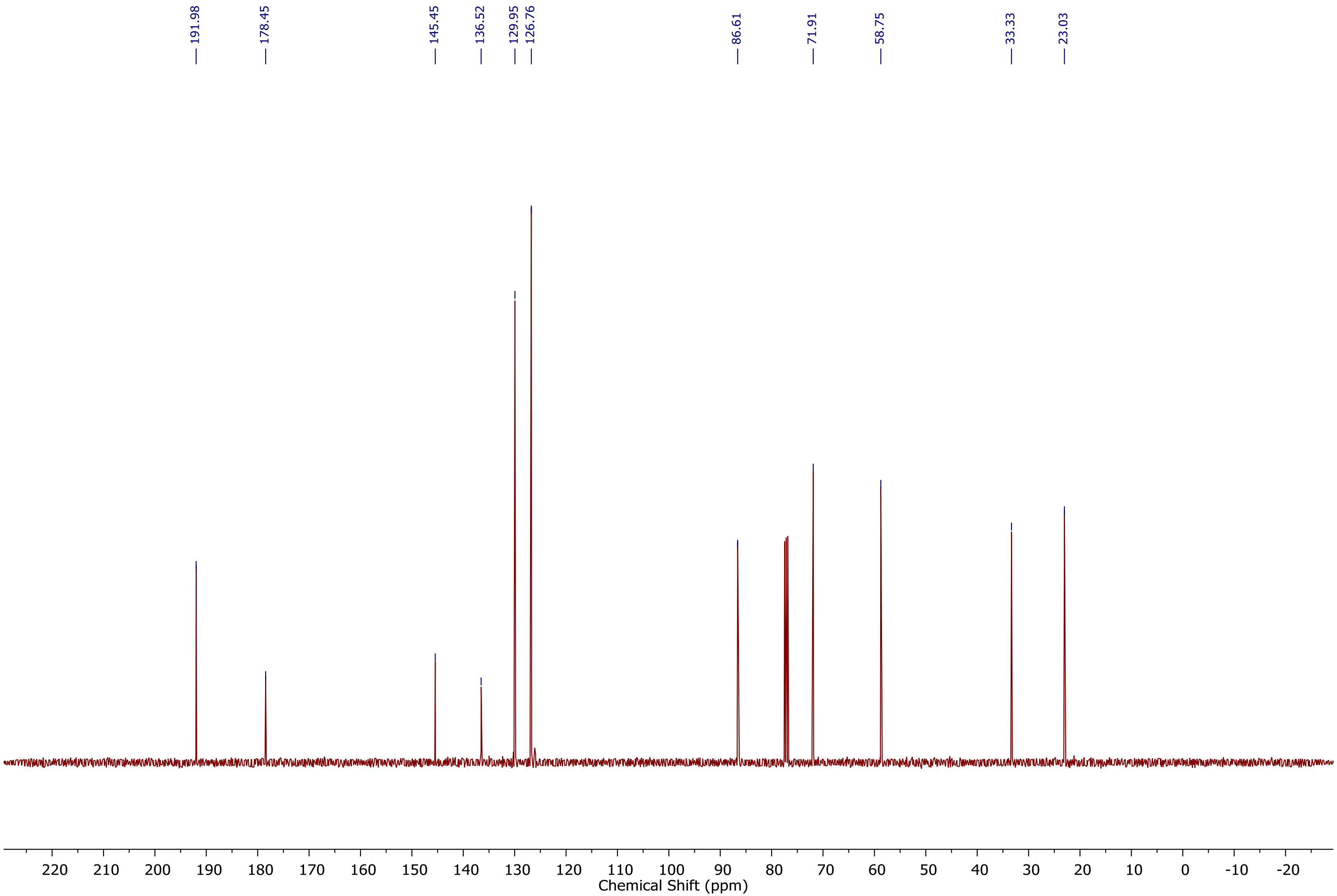
1H NMR (400 MHz, CDCl3)



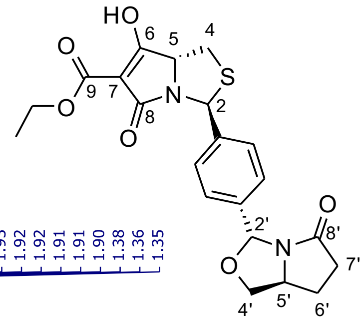
33



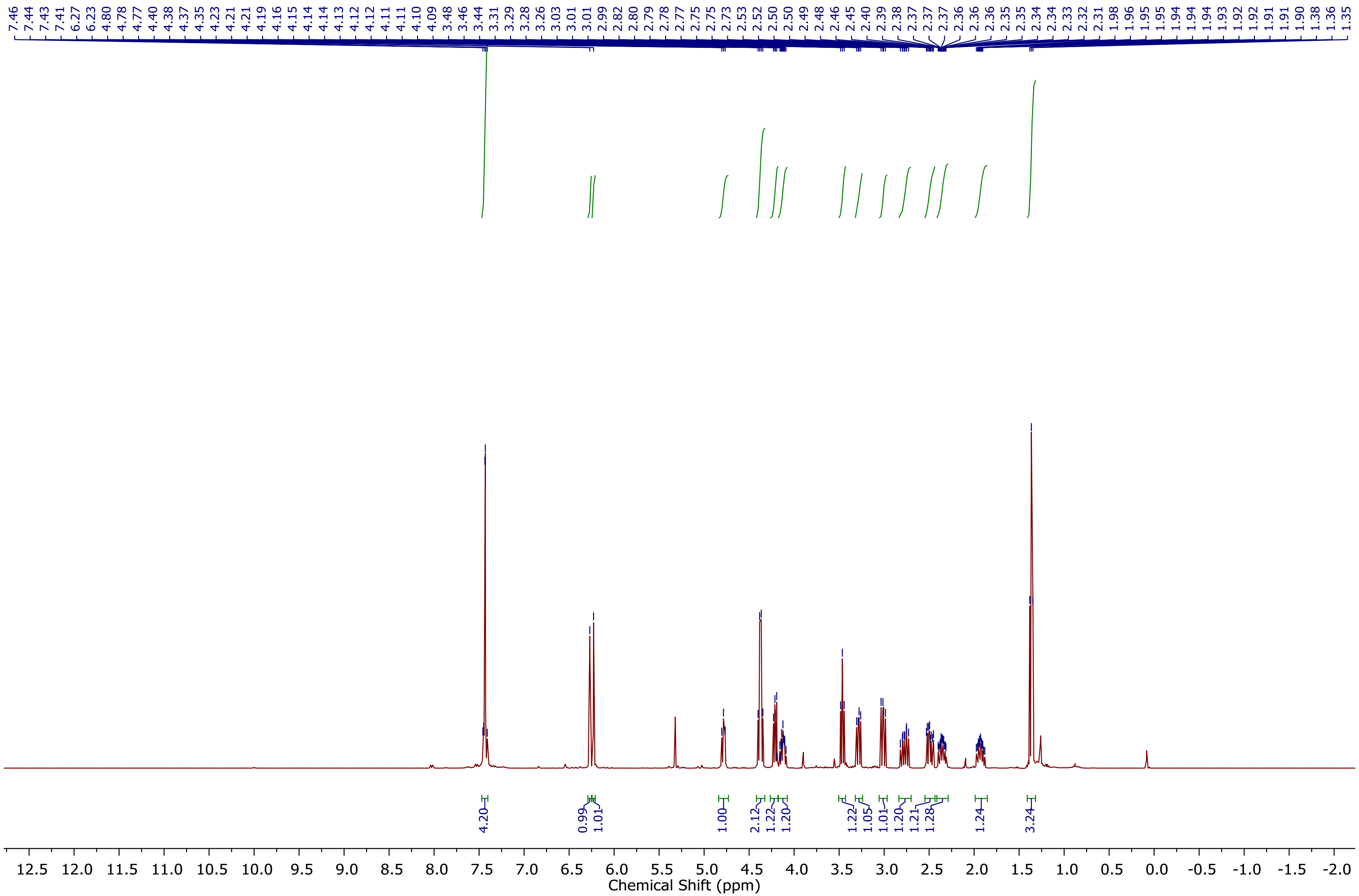
13C NMR (100.6 MHz, CDCl3)



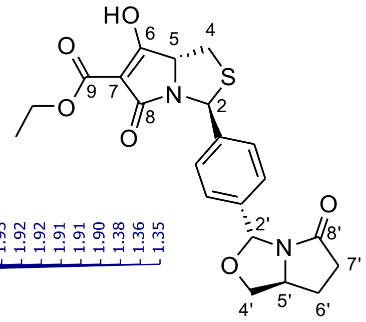
34a



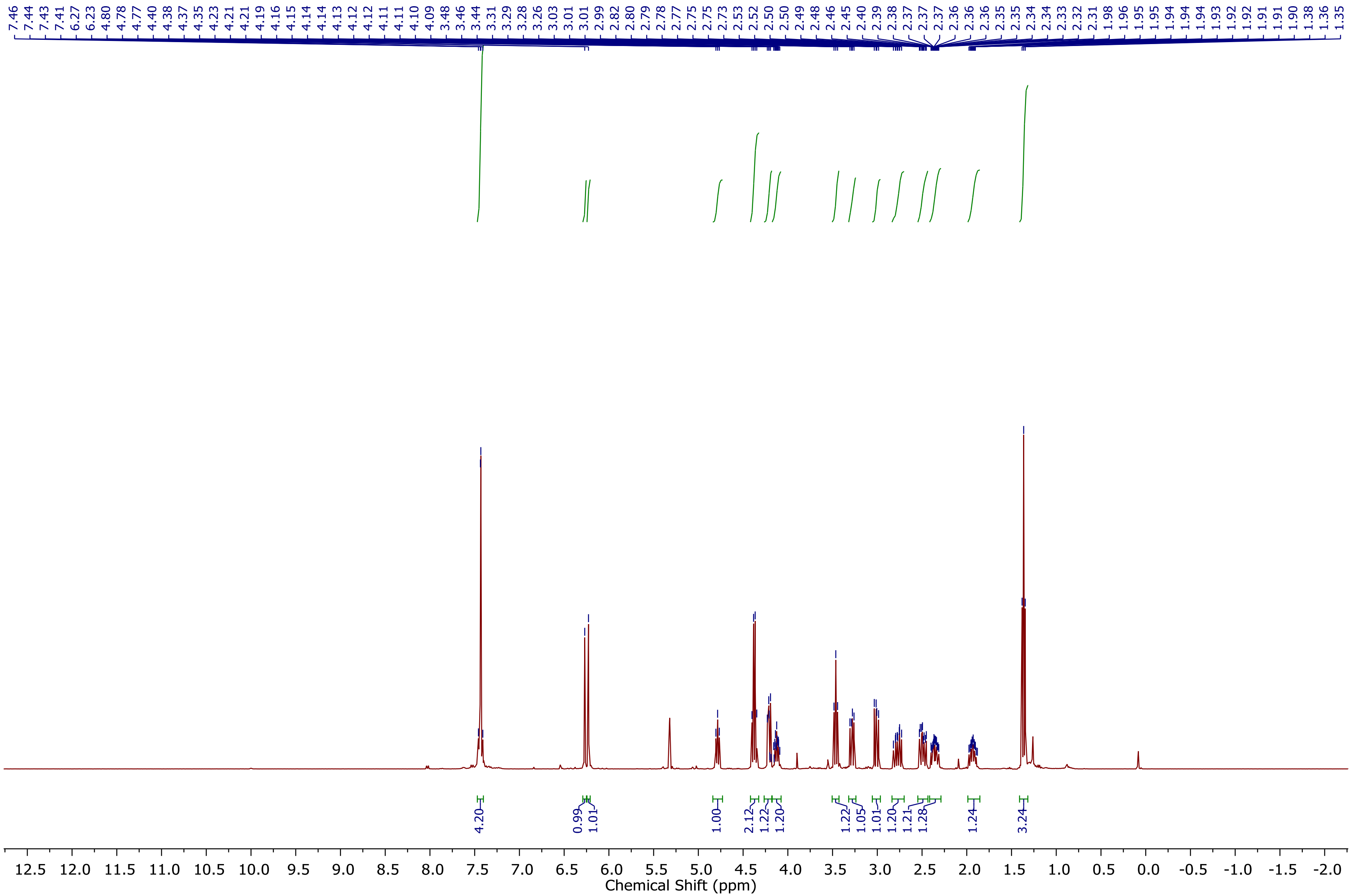
1H NMR (400 MHz, CDCl3)



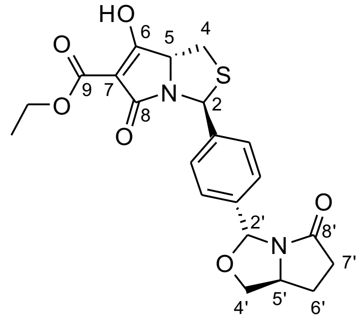
34a



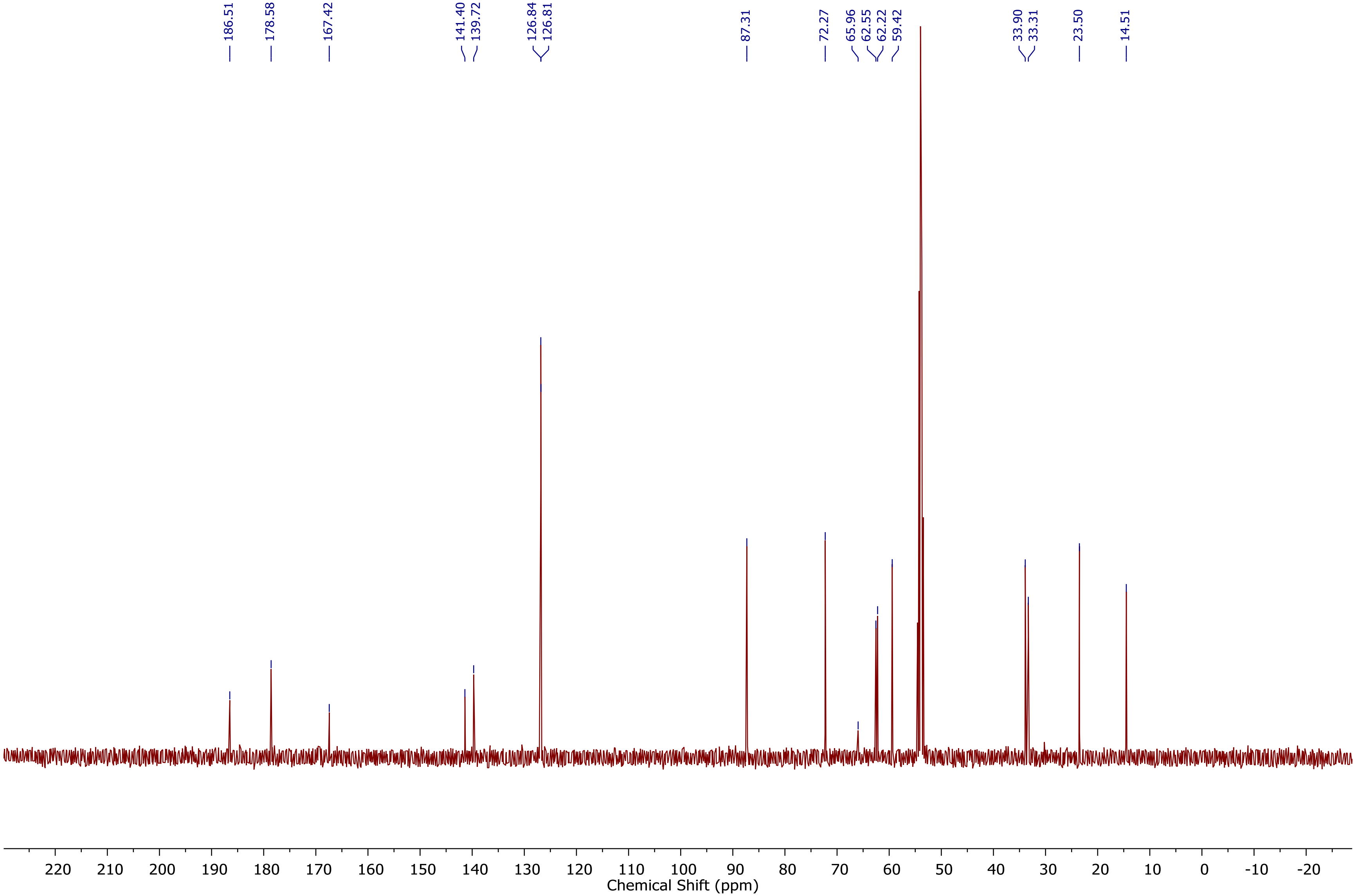
1H NMR (400 MHz, CD2Cl2)



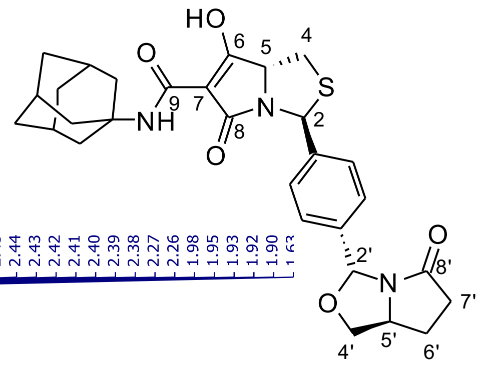
34a



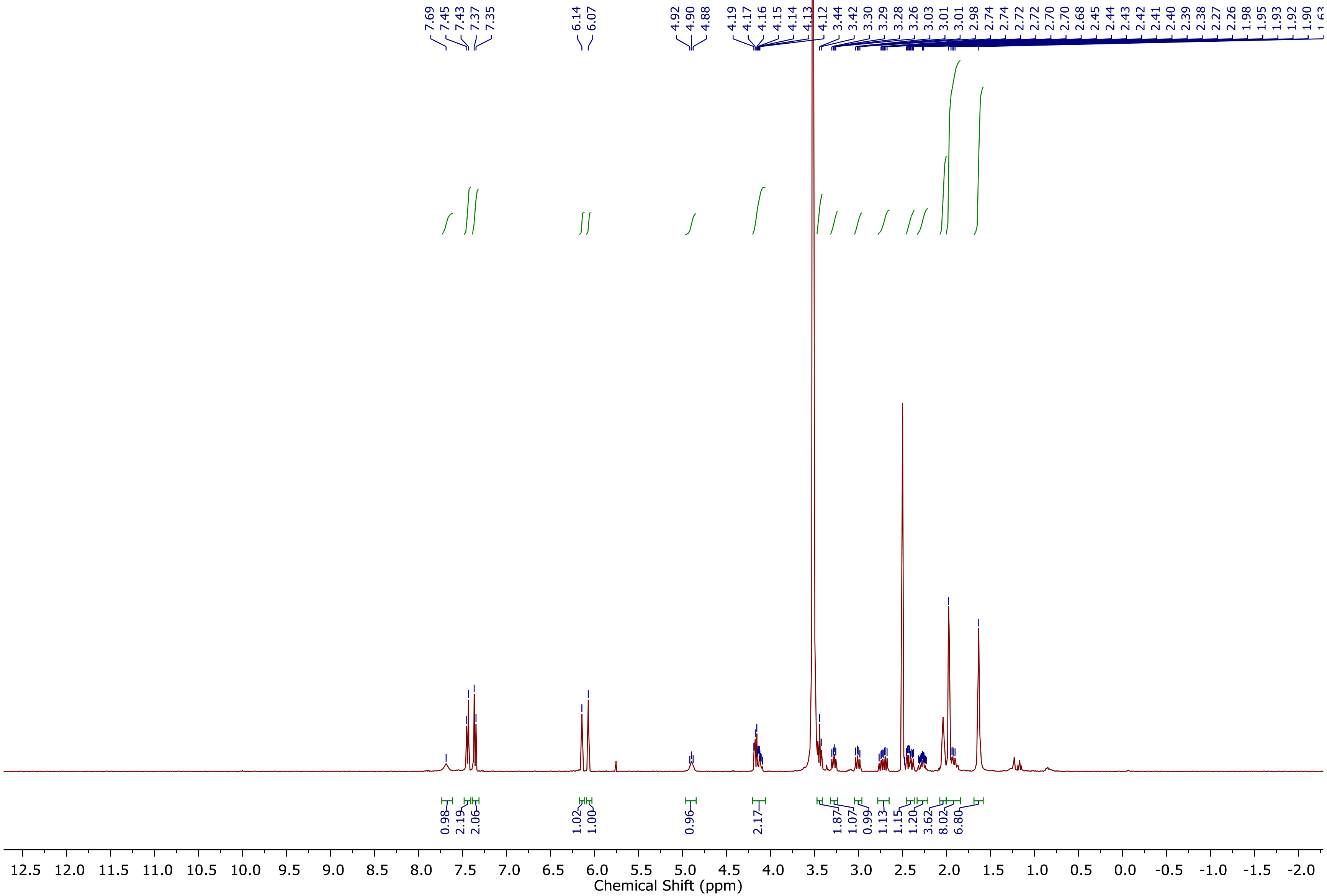
13C NMR (100.6 MHz, CD2Cl2)



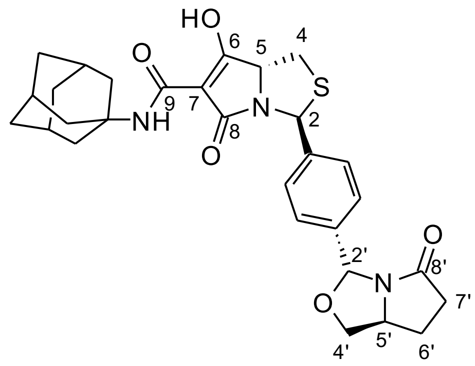
34b



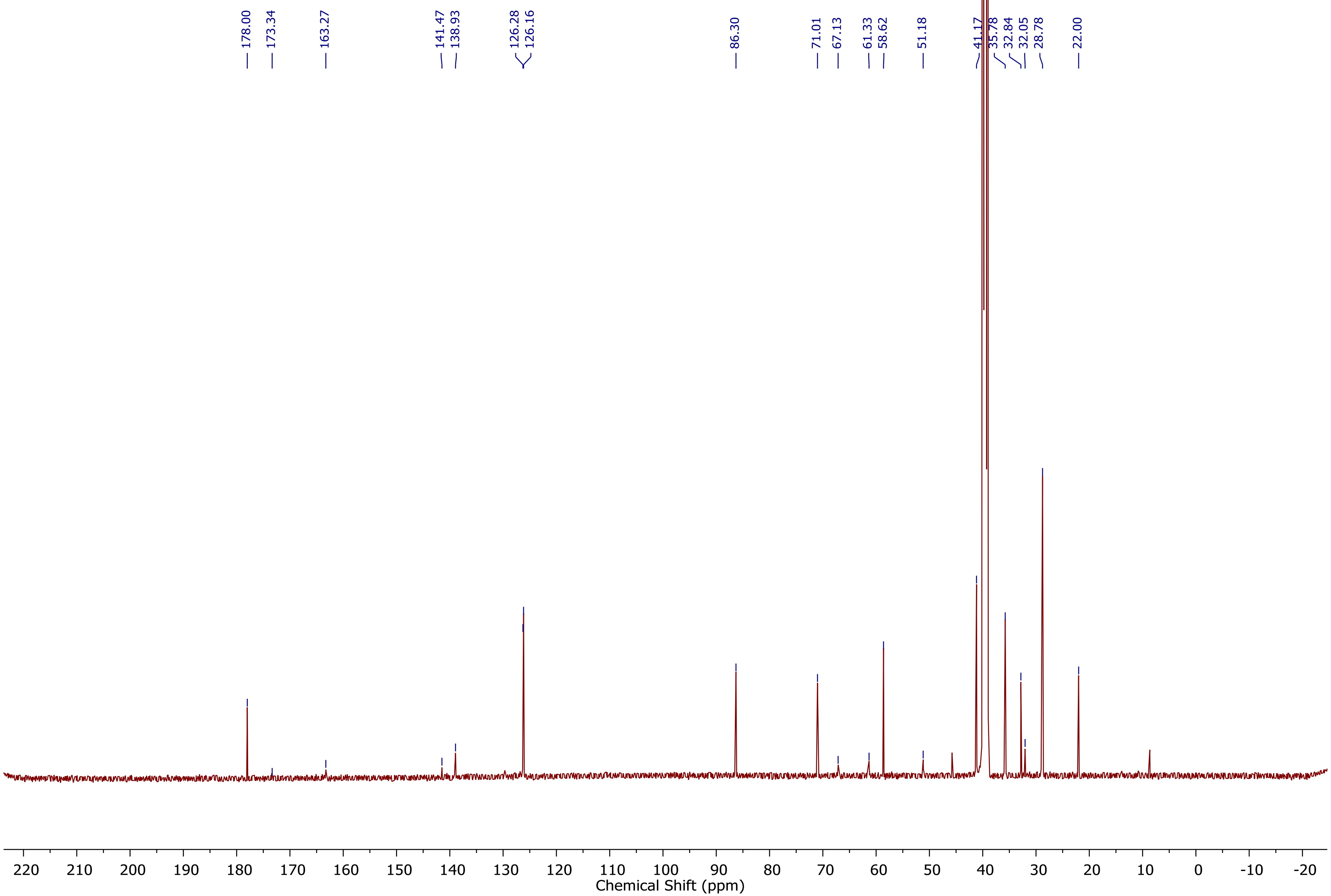
1H NMR (400 MHz, DMSO-d6)



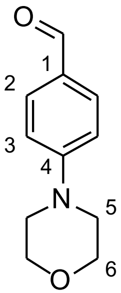
34b



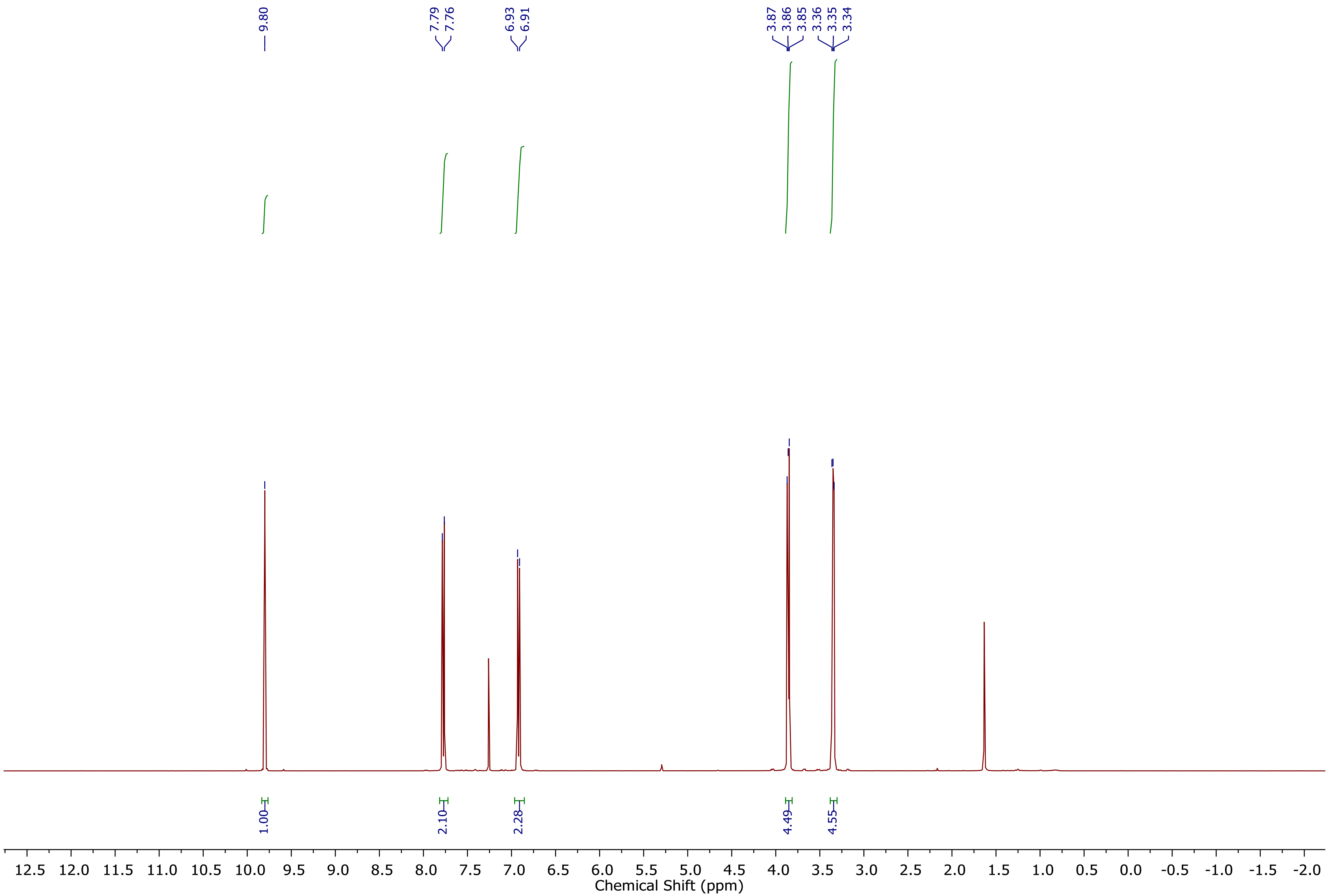
13C NMR (125.8 MHz, DMSO-d6)



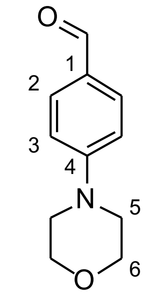
4-Morpholinobenzaldehyde, 35b



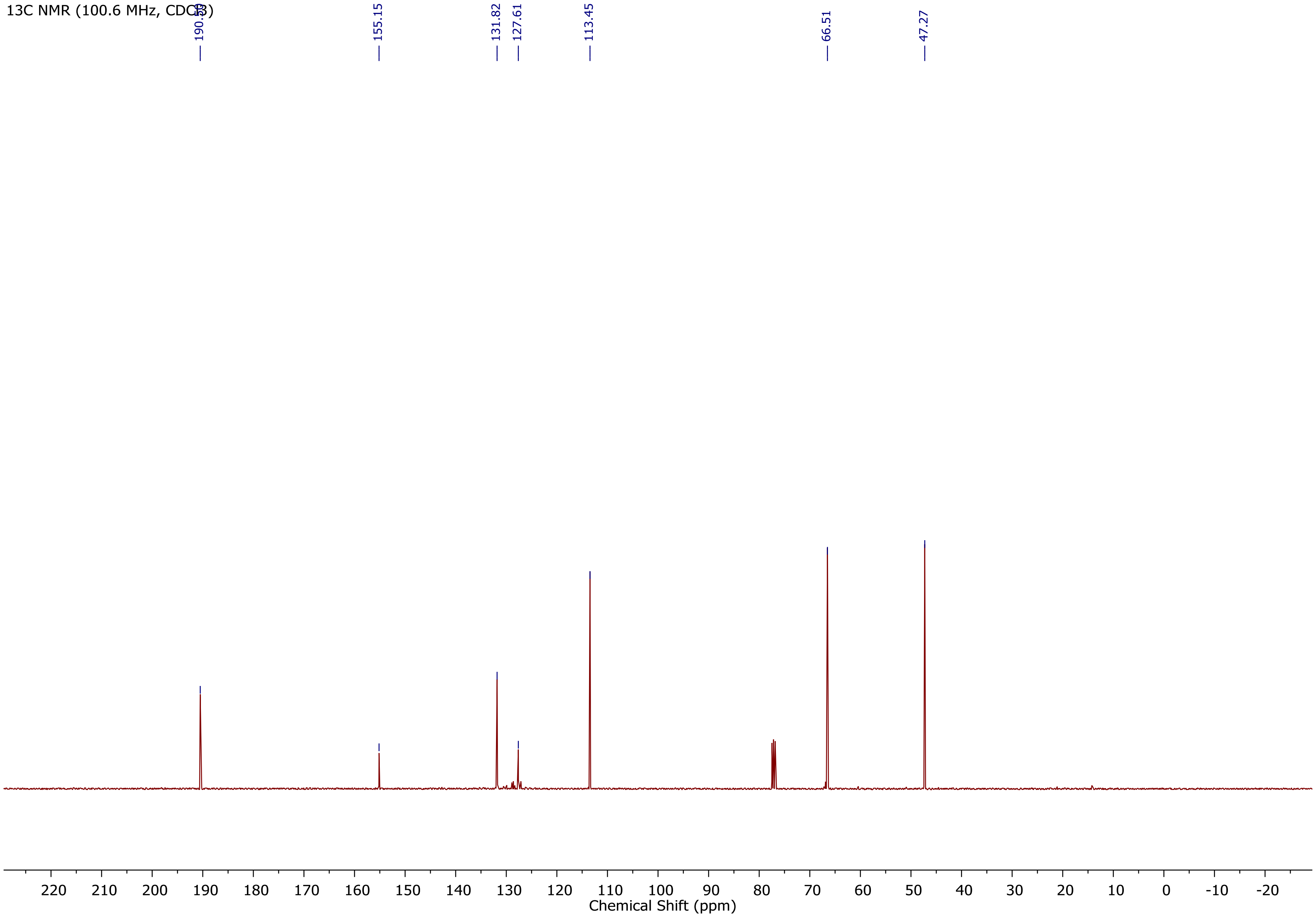
1H NMR (400 MHz, CDCl3)



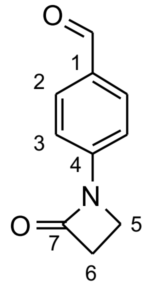
4-Morpholinobenzaldehyde, 35b



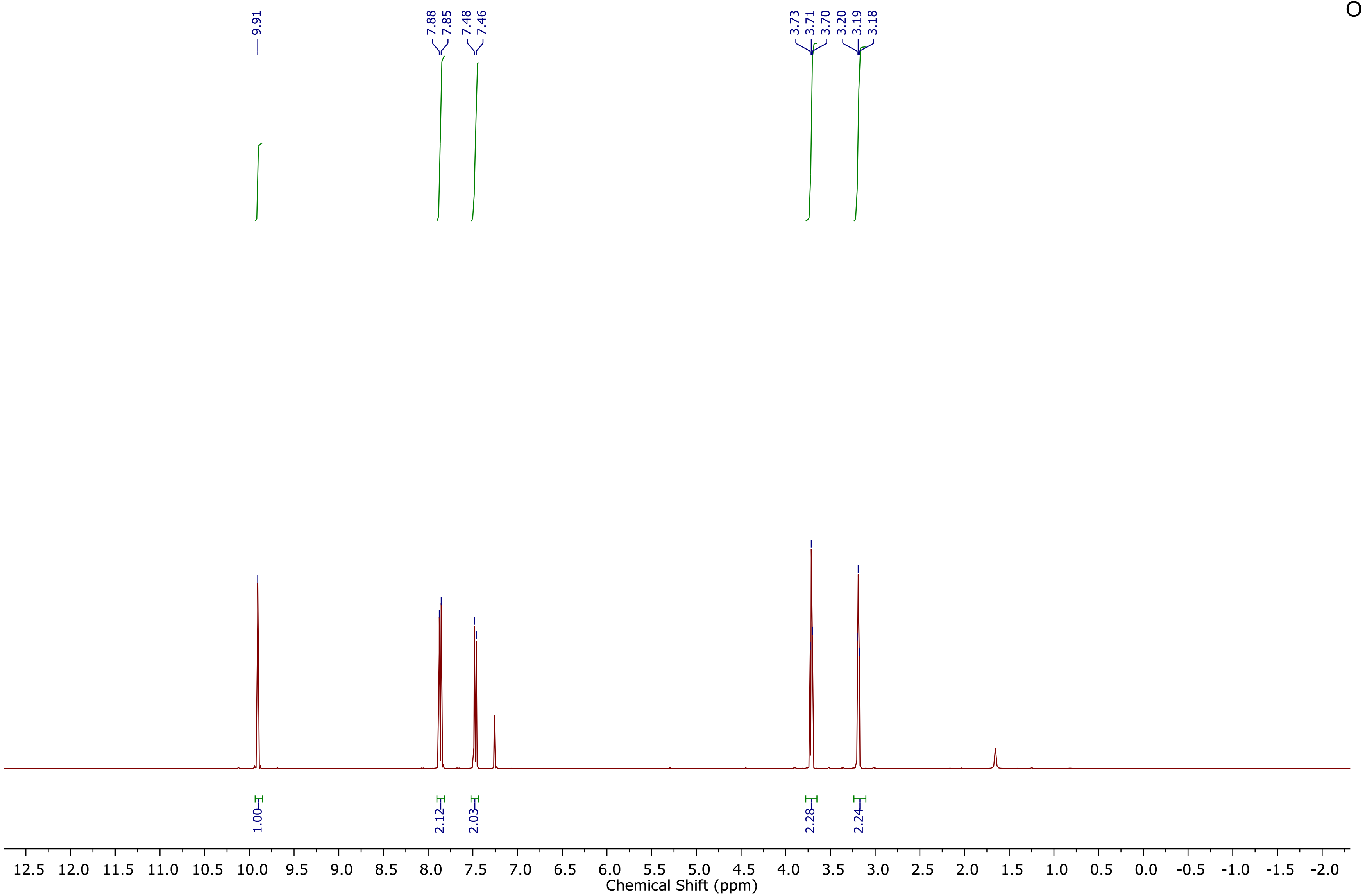
13C NMR (100.6 MHz, CDCl3)



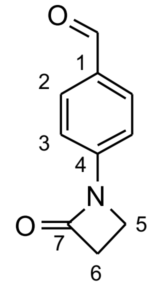
4-(2-oxoazetidin-1-yl)benzaldehyde, 35c



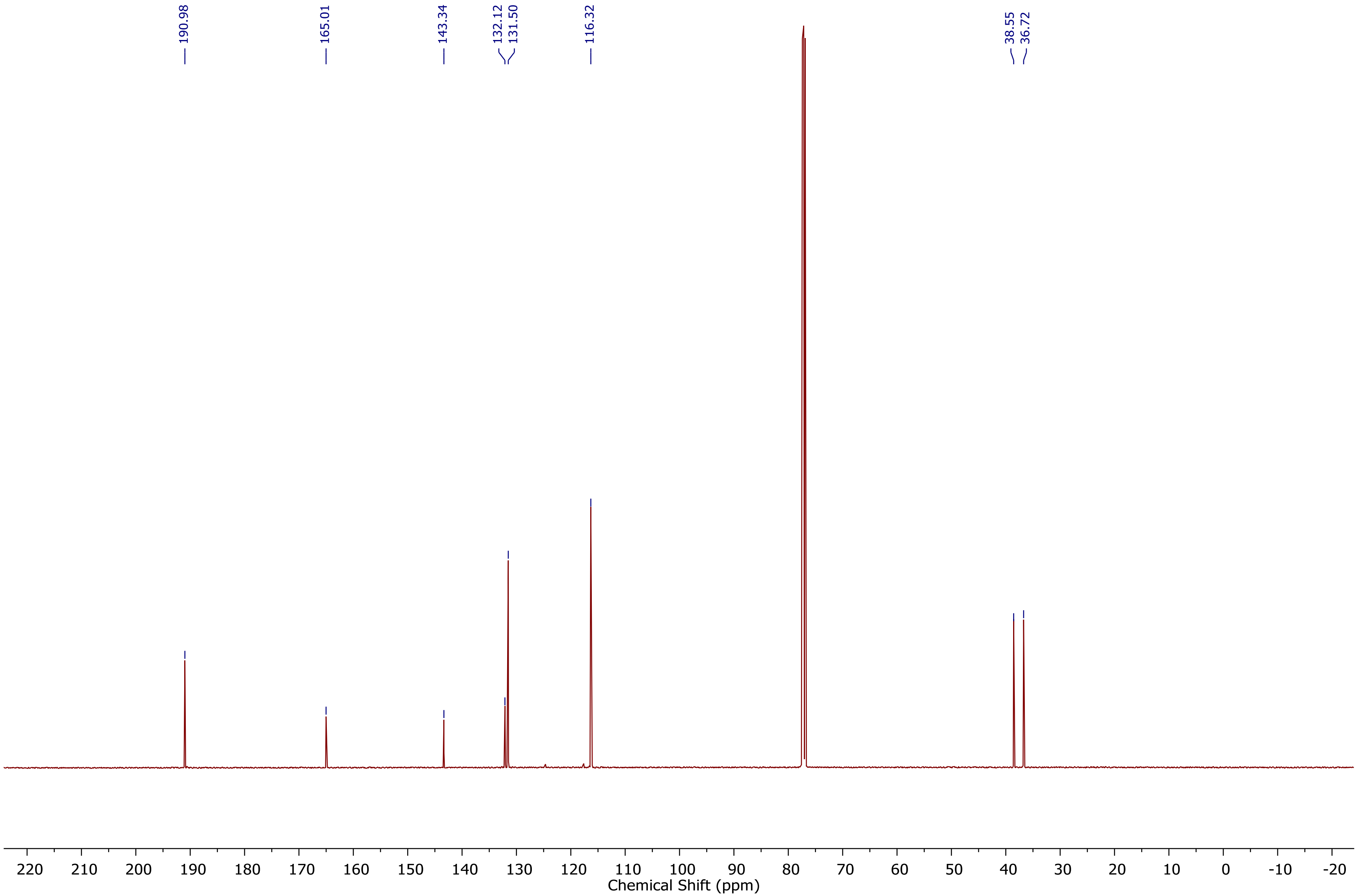
1H NMR (400 MHz, CDCl3)



4-(2-oxoazetidin-1-yl)benzaldehyde, 35c

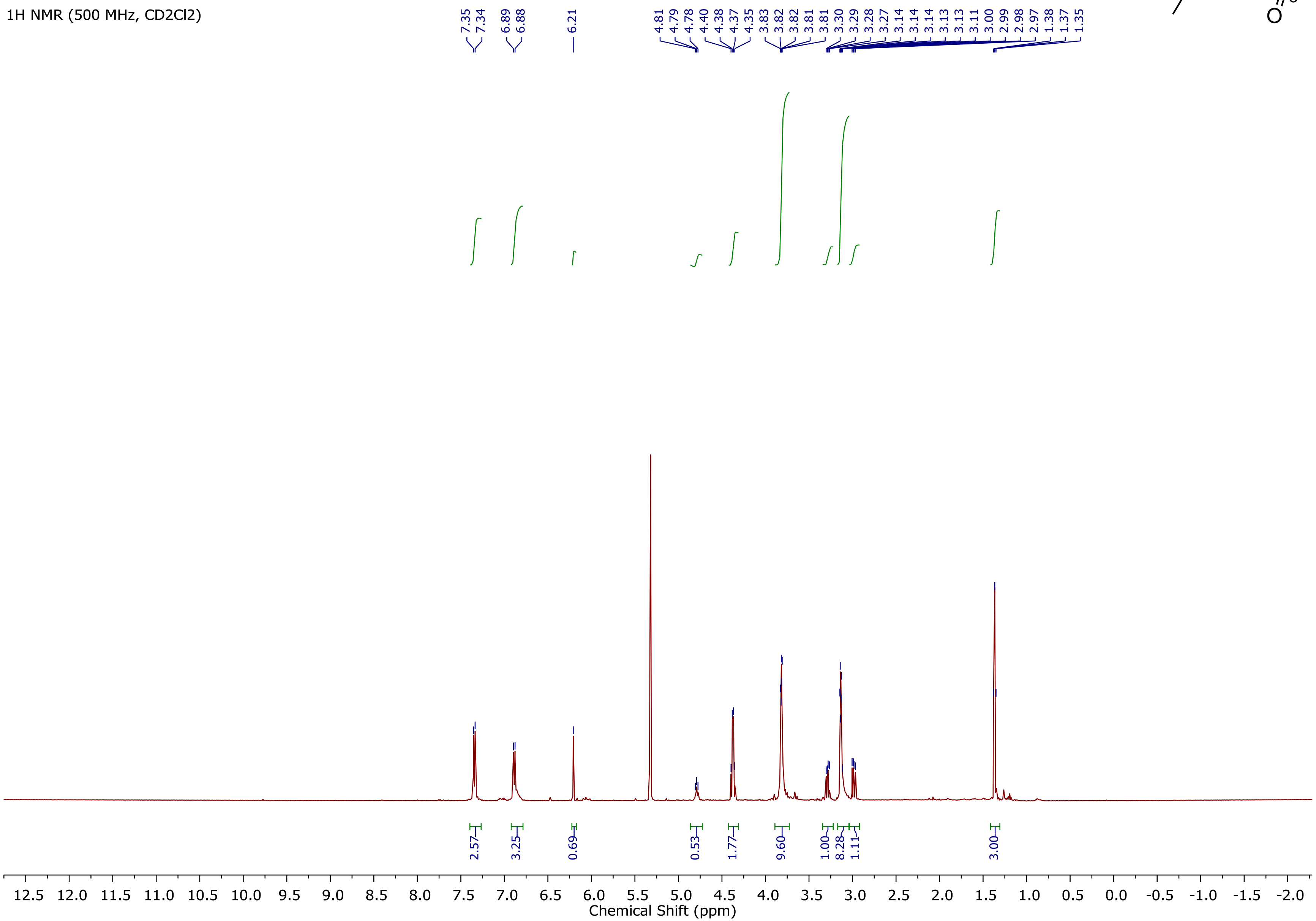


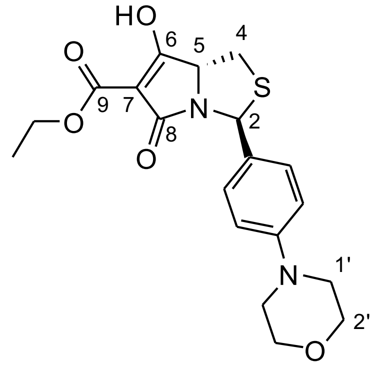
13C NMR (125.8 MHz, CDCl3)



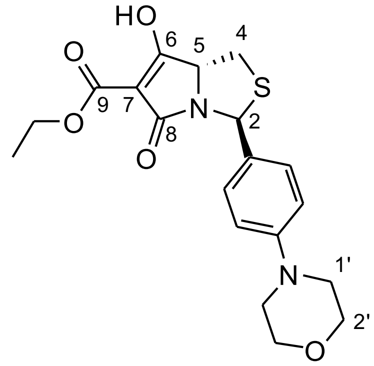
36a

1H NMR (500 MHz, CD2Cl2)

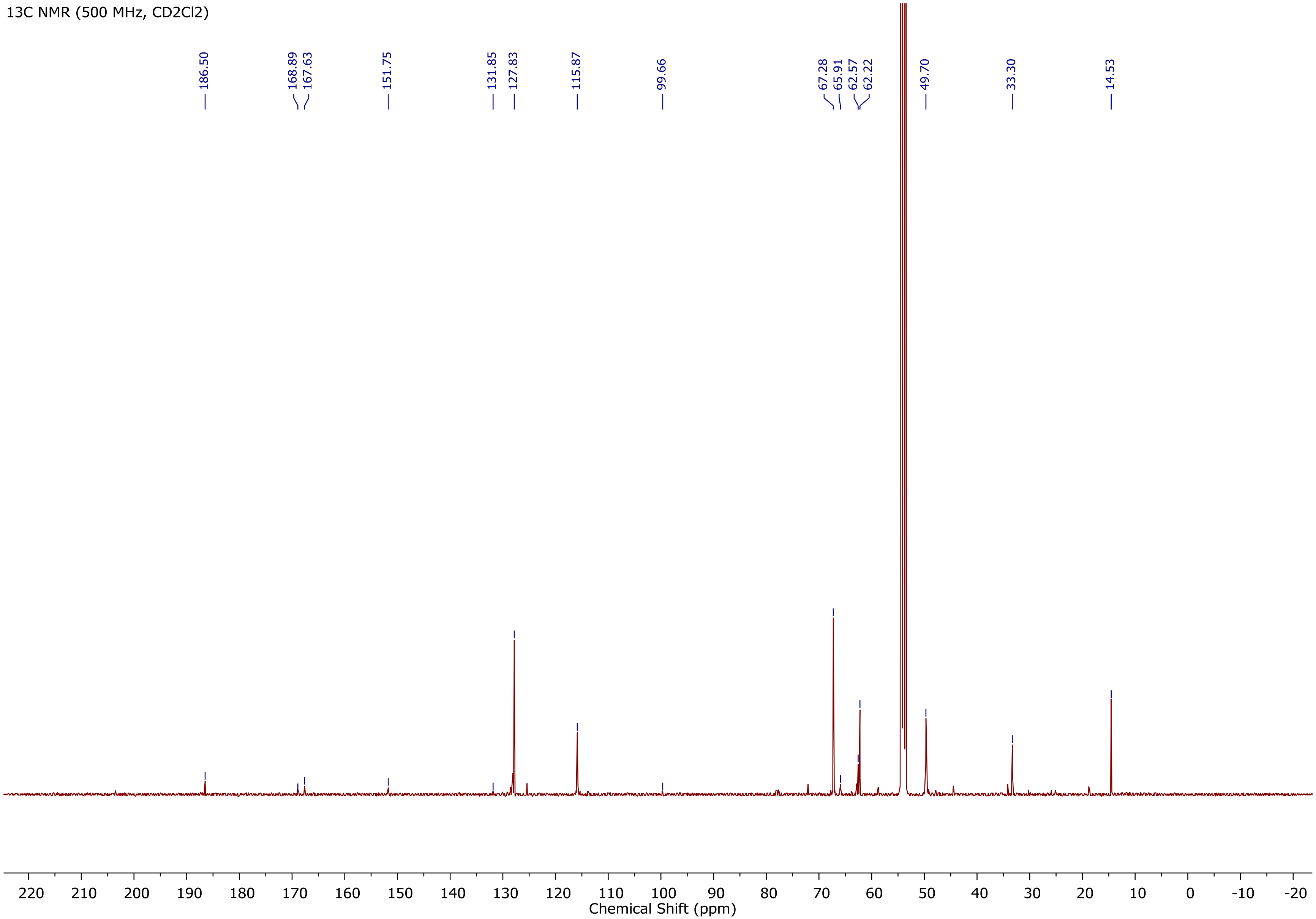




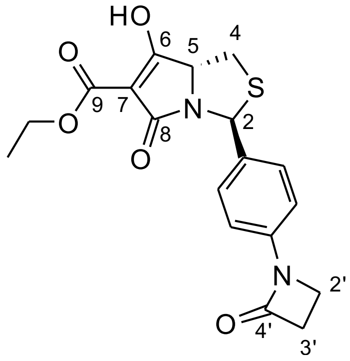
36a



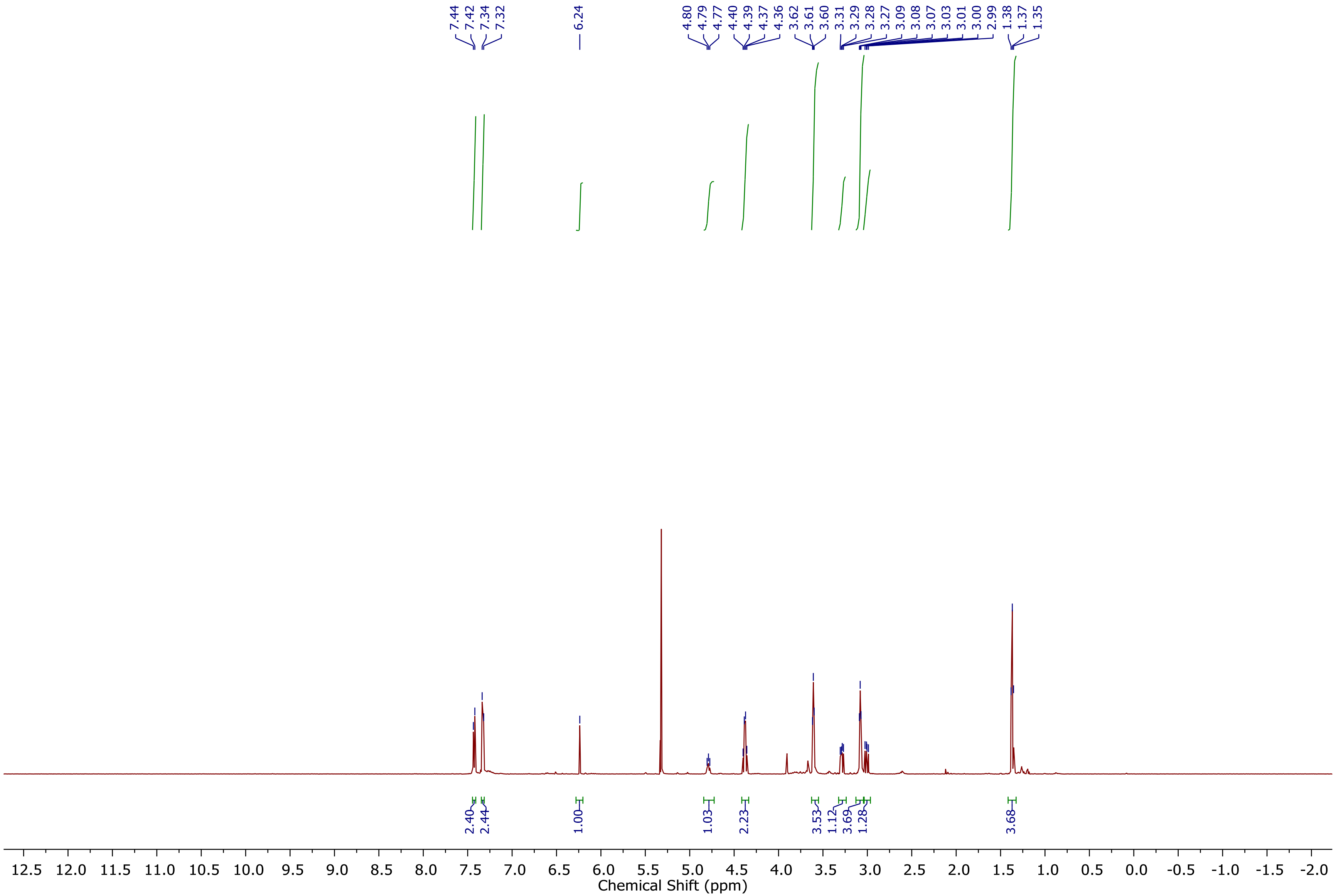
13C NMR (500 MHz, CD2Cl2)



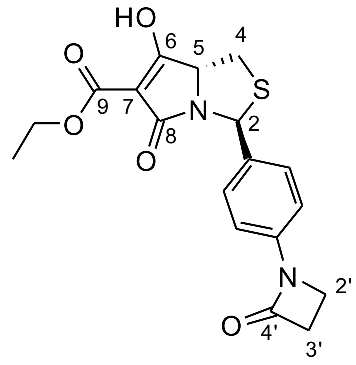
(-)-(2*S*,5*R*)-1-Aza-7-ethoxycarbonyl-6-hydroxy-2-(4-(2-oxoazetidin-1-yl)phenyl)-8-oxo-3-thiabicyclo[3.3.0]oct-6-ene, 239/36b



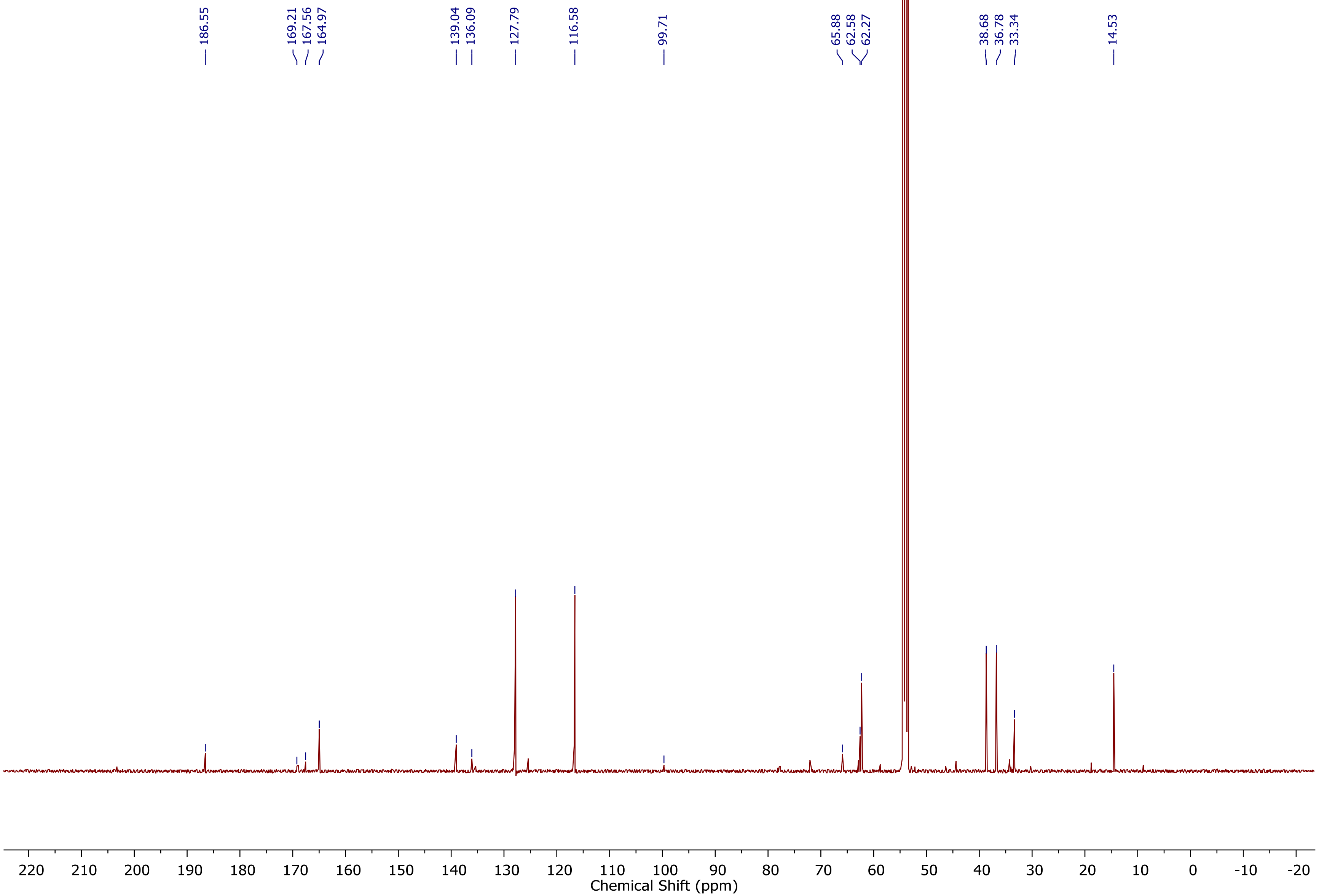
1H NMR (500 MHz, CD2Cl2)



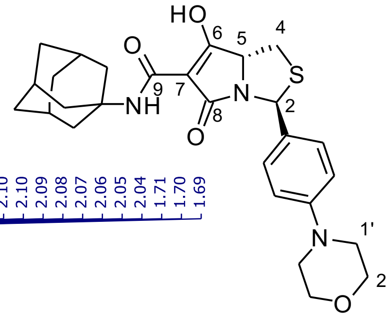
36b



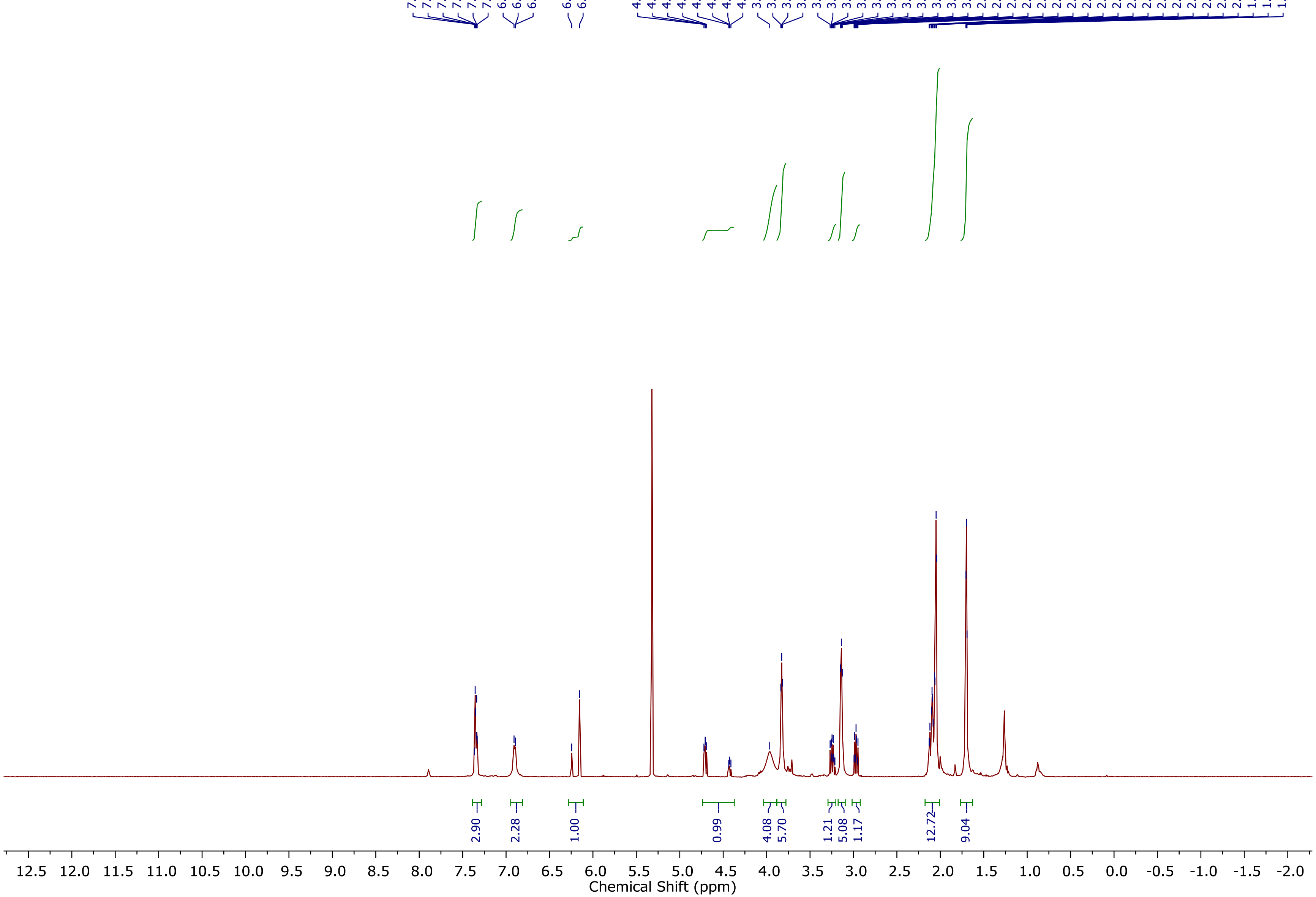
13C NMR (125.8 MHz, CD2Cl2)



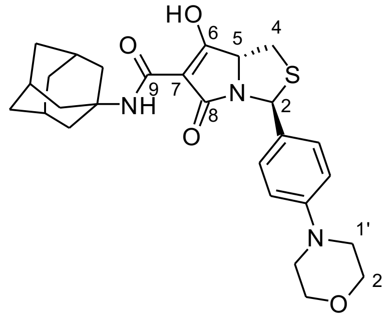
37a

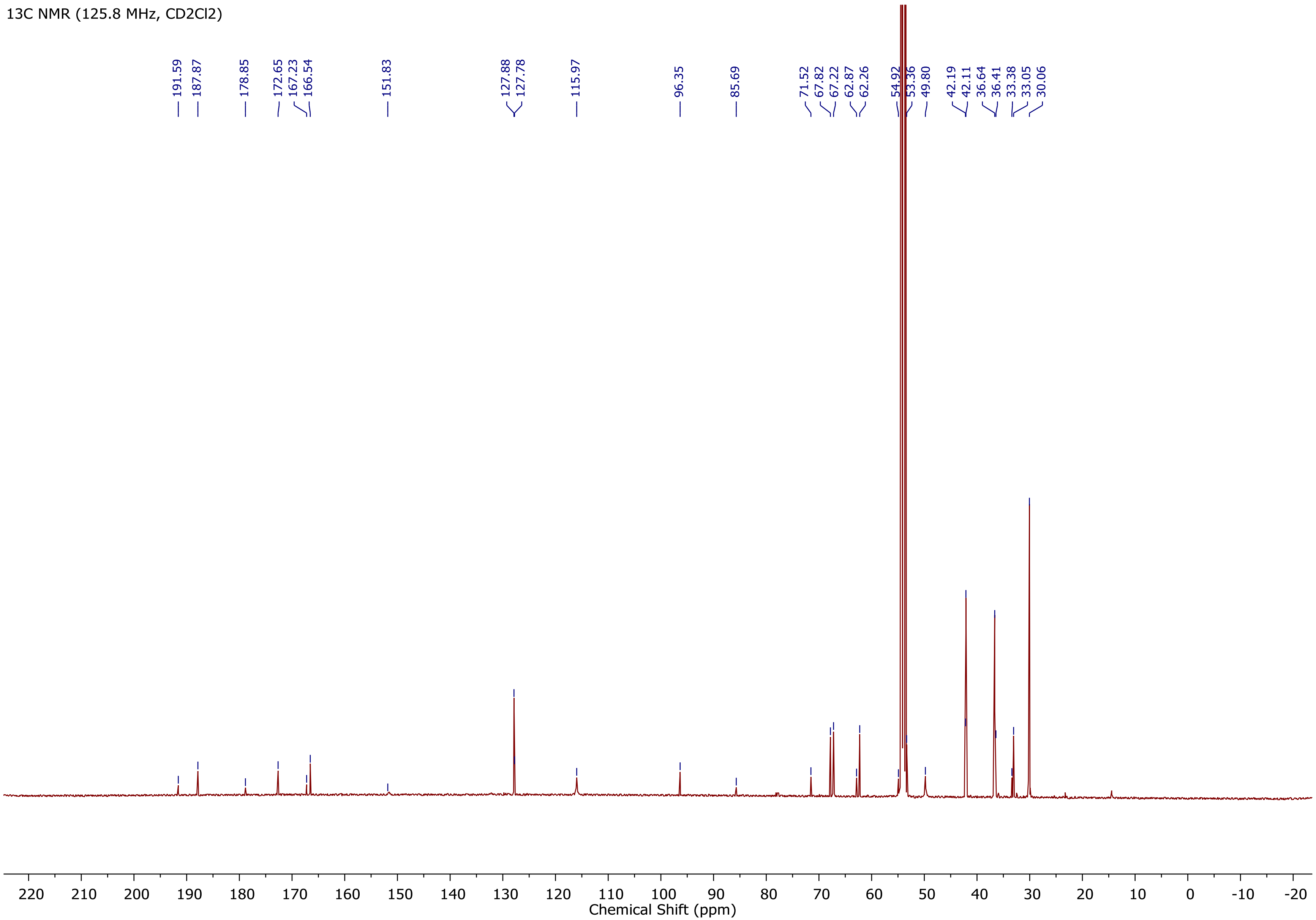


1H NMR (500 MHZ, CD2Cl2)



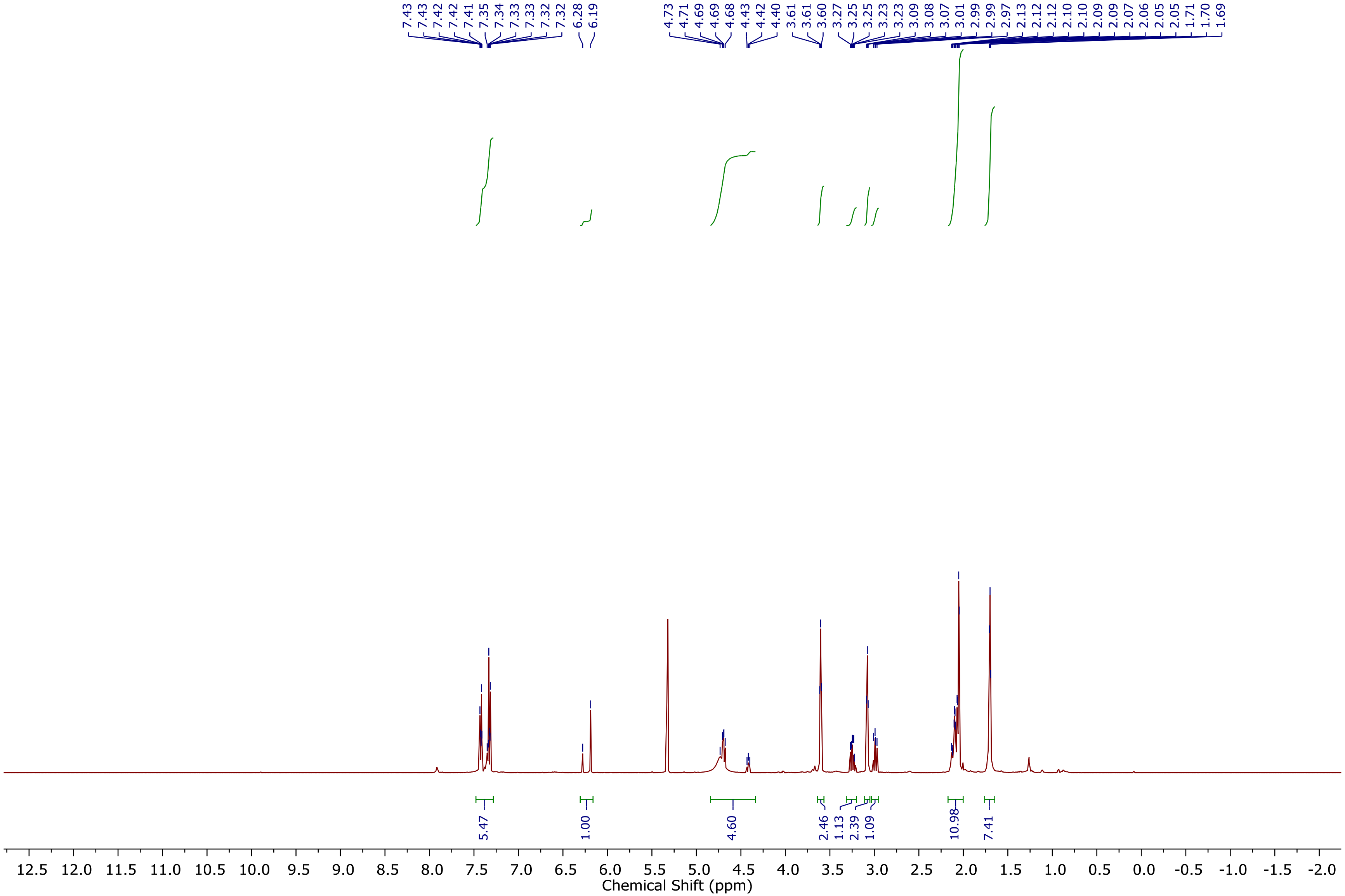
37a

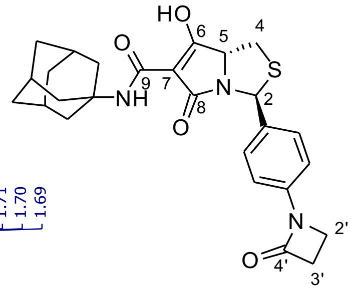

HO
O
S
N
NH
O
N
O
1'
2
4
5
6
7
8
9
2


13C NMR (125.8 MHz, CD2Cl2)
191.59
187.87
178.85
172.65
167.23
166.54
151.83
127.88
127.78
115.97
96.35
85.69
71.52
67.82
67.22
62.87
62.26
54.92
53.36
49.80
42.19
42.11
36.64
36.41
33.38
33.05
30.06
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Chemical Shift (ppm)

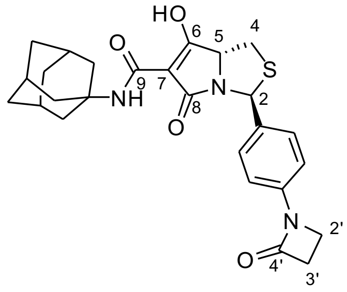
37b

1H NMR (500 MHz, CD2Cl2)

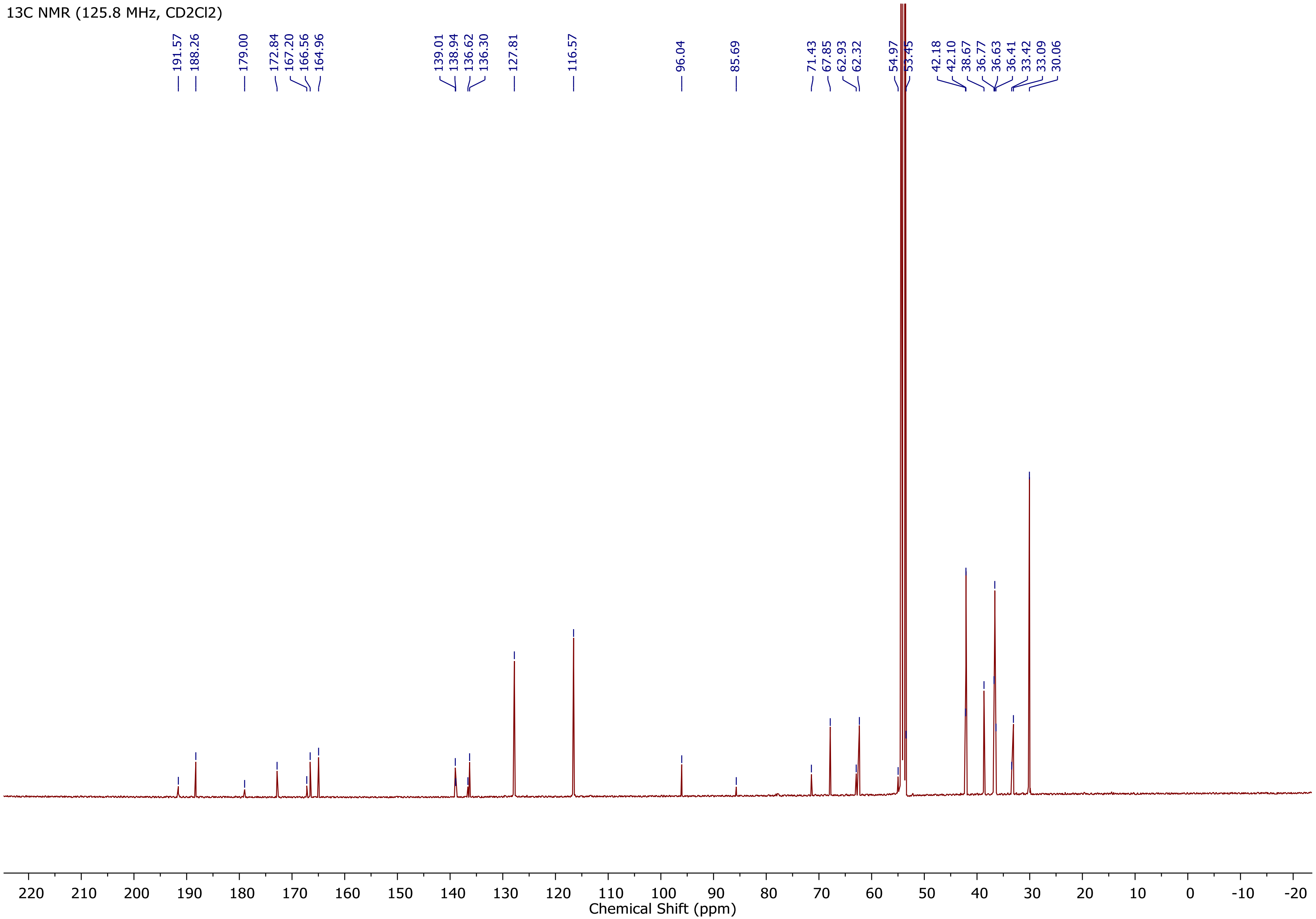




37b

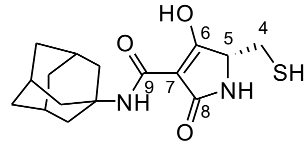


HO
O
6
5
4
S
9
7
NH
N
2
8
O
N
2'
O
4'
3'

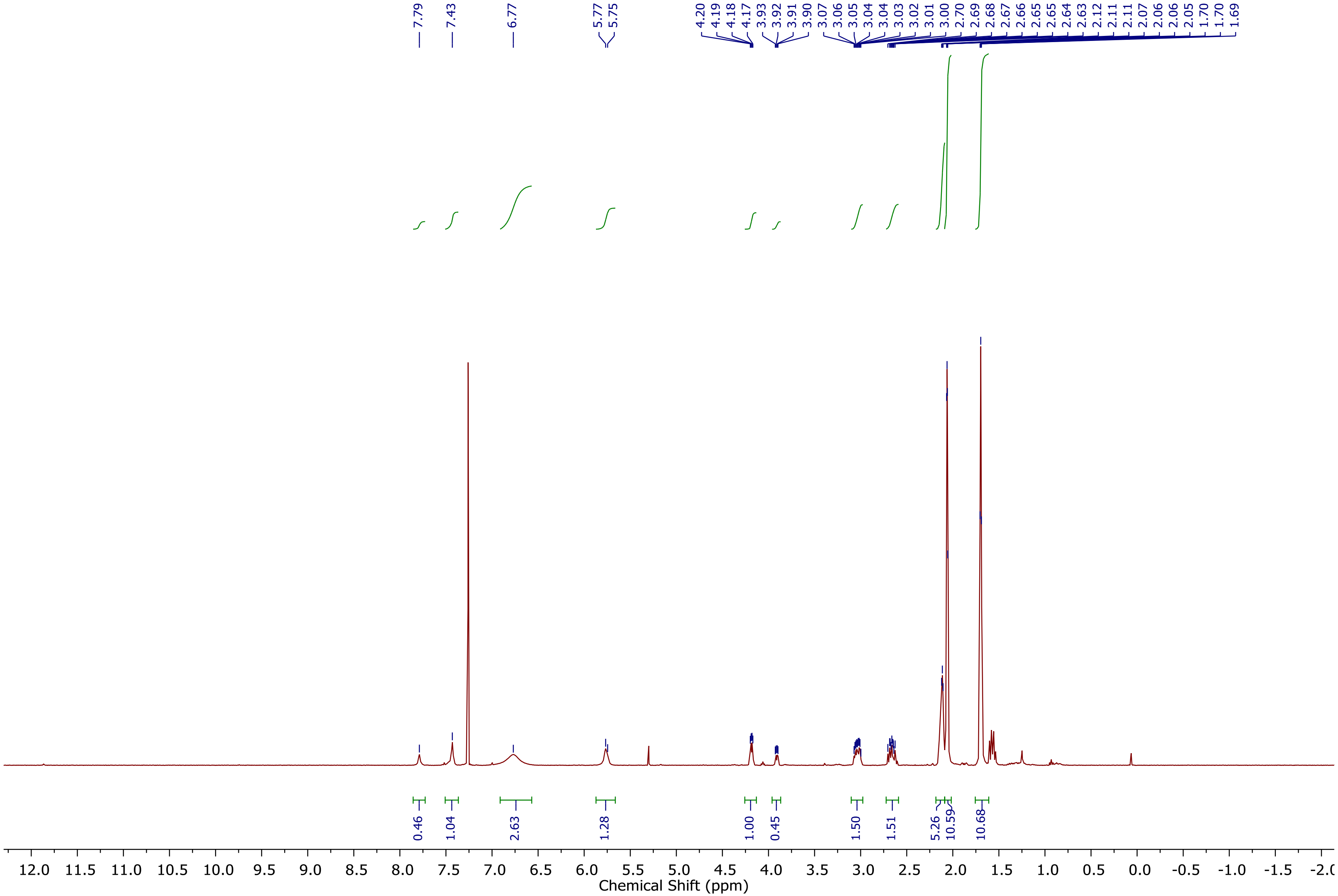


13C NMR (125.8 MHz, CD2Cl2)
191.57
188.26
179.00
172.84
167.20
166.56
164.96
139.01
138.94
136.62
136.30
127.81
116.57
96.04
85.69
71.43
67.85
62.93
62.32
54.97
53.45
42.18
42.10
38.67
36.77
36.63
36.41
33.42
33.09
30.06
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

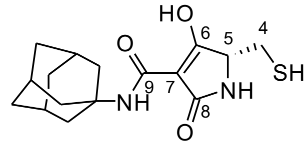
38



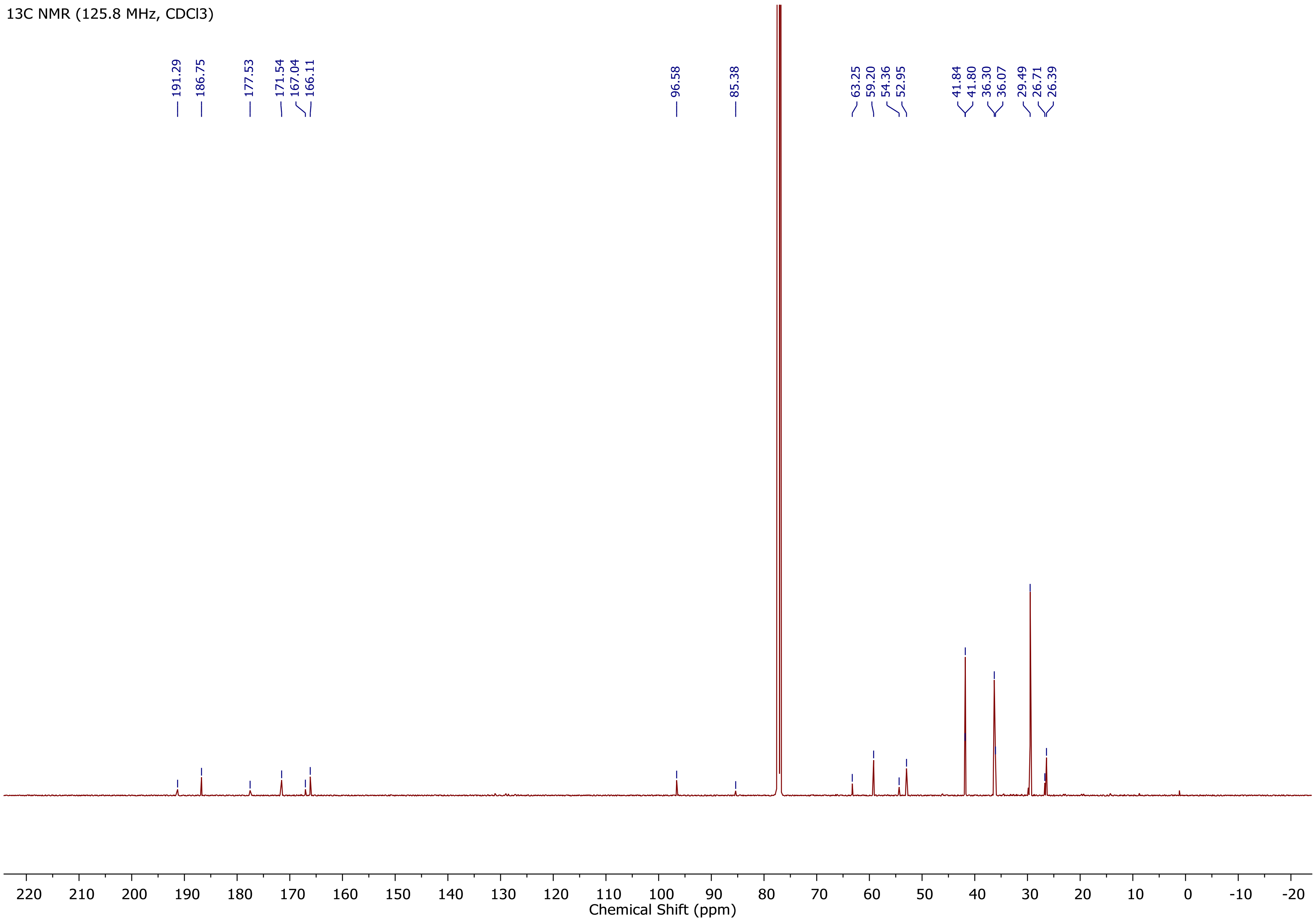
1H NMR (400 MHz, CDCl3)



38



13C NMR (125.8 MHz, CDCl3)



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