Supporting Information

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Synthesis of novel 3,4-fused pyrazolidinone γ-lactam bicyclic moieties from 2,3-dioxo-4-carboxy-5-(substituted)pyrrolidines

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S1: Experimental Procedure

*General procedure for the synthesis of 2,3-dioxo-4-carboethoxy-5-(substituted)pyrrolidines (**1a-e**)[6,7]:*
An equimolar amount of sodium diethyl oxalacetate (47.62 mmol), 40% methylamine in water (47.62 mmol) and propianaldehyde (47.62 mmol) was heated under reflux in 100 mL EtOH for 1 hour. After cooling, the mixture was poured into ice cooled water and acidified with concentrated hydrochloric acid. The precipitate obtained was filtered out, washed with water and diethyl ether to afford the product 1a-e.

*Ethyl 4-hydroxy-5-oxo-2,5-dihydro-1H-pyrrole-3-carboxylate (**1a**):* Yield: 43%; m.p. 138-139°C; IR (KBr) 1692, 1654 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 4.85 (s, 2H, CH_2), 4.26 (q, J = 7.0 Hz, 2H, OCH_2), 1.29 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 169.01, 162.11, 147.88, 114.63, 66.86, 60.80, 13.02 ppm; CHN: Found C, 49.10; H, 5.26; N, 8.05 requires C, 49.12; H, 5.30; N, 8.18 %; LCMS (ESI): calculated for $C_7H_9NO_4$ 365.10 $[2M+Na]^+$, found 365.10.

*Ethyl 4-hydroxy-1-methyl-5-oxo-2,5-dihydro-1H-pyrrole-3-carboxylate (**1b**):* Yield: 45%; m.p. 136-137°C; IR (KBr) 1692, 1658 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 4.24 (q, J = 7.2 Hz, 2H, OCH_2), 4.00 (s, 2H, CH_2), 3.04 (s, 3H, NCH_3), 1.29 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 169.10, 165.65, 147.84, 114.64, 66.74, 60.22, 28.69, 13.18 ppm; CHN: Found C, 51.53; H, 5.97; N, 7.25 requires C, 51.89; H, 5.99; N, 7.56 %; LCMS (ESI): calculated for $C_8H_{11}NO_4$ 393.14 $[2M+Na]^+$, found 393.10.

*Ethyl 4-hydroxy-1,2-dimethyl-5-oxo-2,5-dihydro-1H-pyrrole-3-carboxylate (**1c**):* Yield: 68%; m.p. 104-105°C; IR (KBr) 1695, 1658 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 4.33-4.21 (m, 2H, OCH_2), 4.13 (q, J = 6.6 Hz, 1H, CH-5), 2.98 (s, 3H, NCH_3), 1.38 (d, J = 6.9 Hz, 3H, CH_3), 1.30 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 164.68, 163.79, 154.66, 112.98, 60.24, 54.86, 26.12, 16.09, 13.32 ppm; CHN: Found C, 54.16; H, 6.66; N, 7.10 requires C, 54.26; H, 6.58; N, 7.03 %; LCMS (ESI): calculated for $C_9H_{13}NO_4$ 421.16 $[2M+Na]^+$, found 421.10.

*Ethyl 2-ethyl-4-hydroxy-1-methyl-5-oxo-2,5-dihydro-1H-pyrrole-3-carboxylate (**1d**):* Yield: 62%; m.p. 106-107°C; IR (KBr) 1682, 1681 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 4.31-4.22 (m, 3H, OCH_2 & CH-5), 2.94 (s, 3H, NCH_3), 2.18-2.07 (m, 1H, CH_2), 2.00-1.89 (m, 1H, CH_2), 1.29 (t, J = 7.1 Hz, 3H, CH_3), 0.50 (t, J = 7.5 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 165.46, 163.73, 155.39, 110.01, 60.24, 58.56, 25.87, 20.71, 13.06, 4.29 ppm; CHN: Found C, 56.03; H, 7.16; N, 6.72 requires C, 56.33; H, 7.09; N, 6.57 %; LCMS (ESI): calculated for $C_{10}H_{15}NO_4$ 449.20 $[2M+Na]^+$, found 449.20.

*Ethyl 4-hydroxy-2-(4-methoxyphenyl)-1-methyl-5-oxo-2,5-dihydro-1H-pyrrole-3-carboxylate (**1e**):* Yield: 47%; m.p. 153-154°C; IR (KBr) 1675, 1612 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 8.7 Hz, 2H, CHAr), 6.89 (d, J = 8.7 Hz, 2H, CHAr), 5.07 (s, 1H, CH-5), 4.11-4.00 (m, 2H, OCH_2), 3.76 (s, 3H, OCH_3), 2.72 (s, 3H, NCH_3), 1.07 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 165.06, 163.29, 160.08, 150.45, 128.62, 126.89, 113.84, 112.68, 62.60, 59.99, 54.57, 26.62, 13.25 ppm; CHN: Found C, 60.10; H, 5.81; N, 4.72 requires C, 61.85; H, 5.88; N, 4.81 %; LCMS (ESI): calculated for $C_{15}H_{17}NO_5$ 605.22 $[2M+Na]^+$, found 605.20.

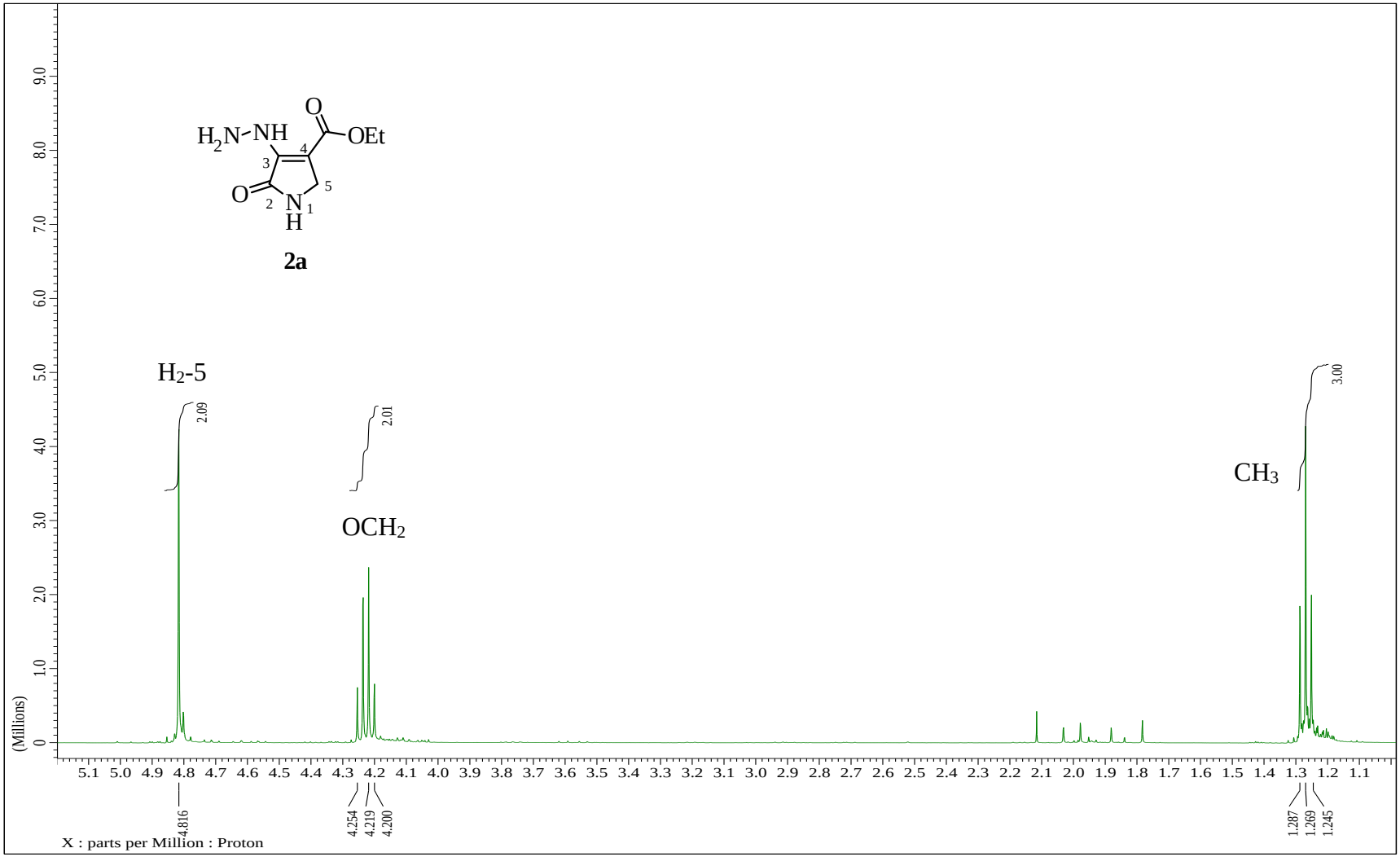


Figure S1: ^{1}H-NMR spectrum of compound 2a

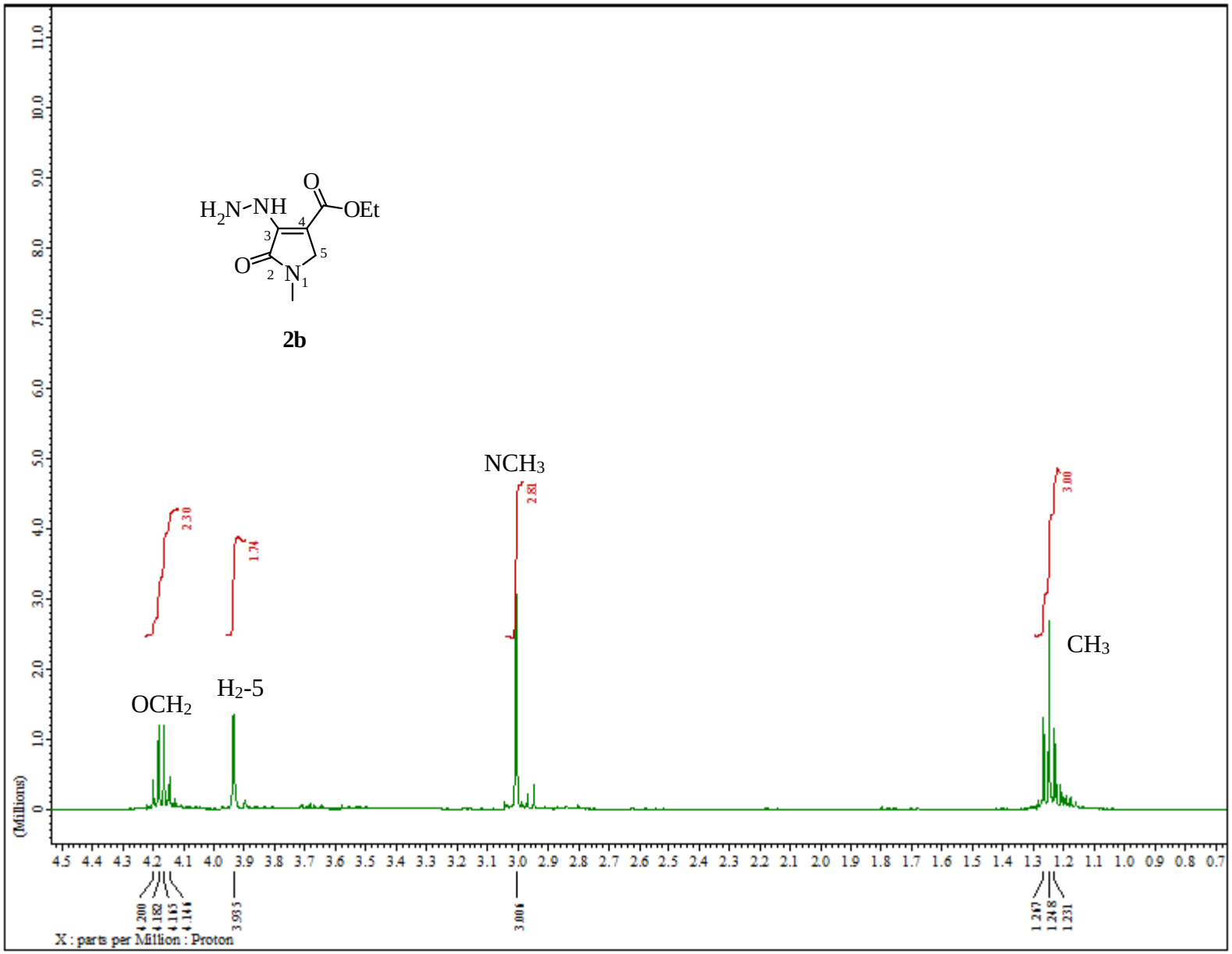


Figure S2: ^{1}H-NMR spectrum of compound 2b

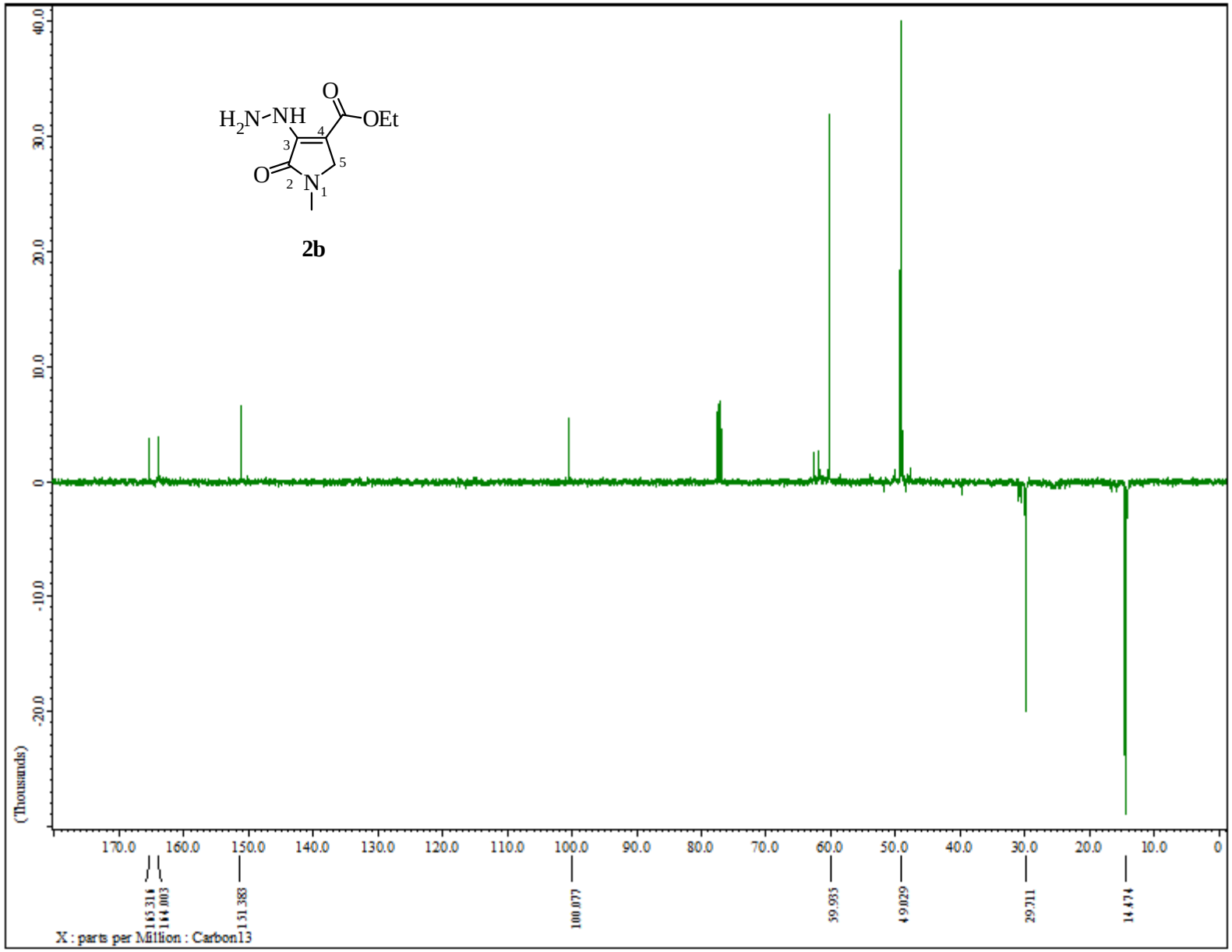


Figure S3: ^{13}C-NMR spectrum of compound 2b

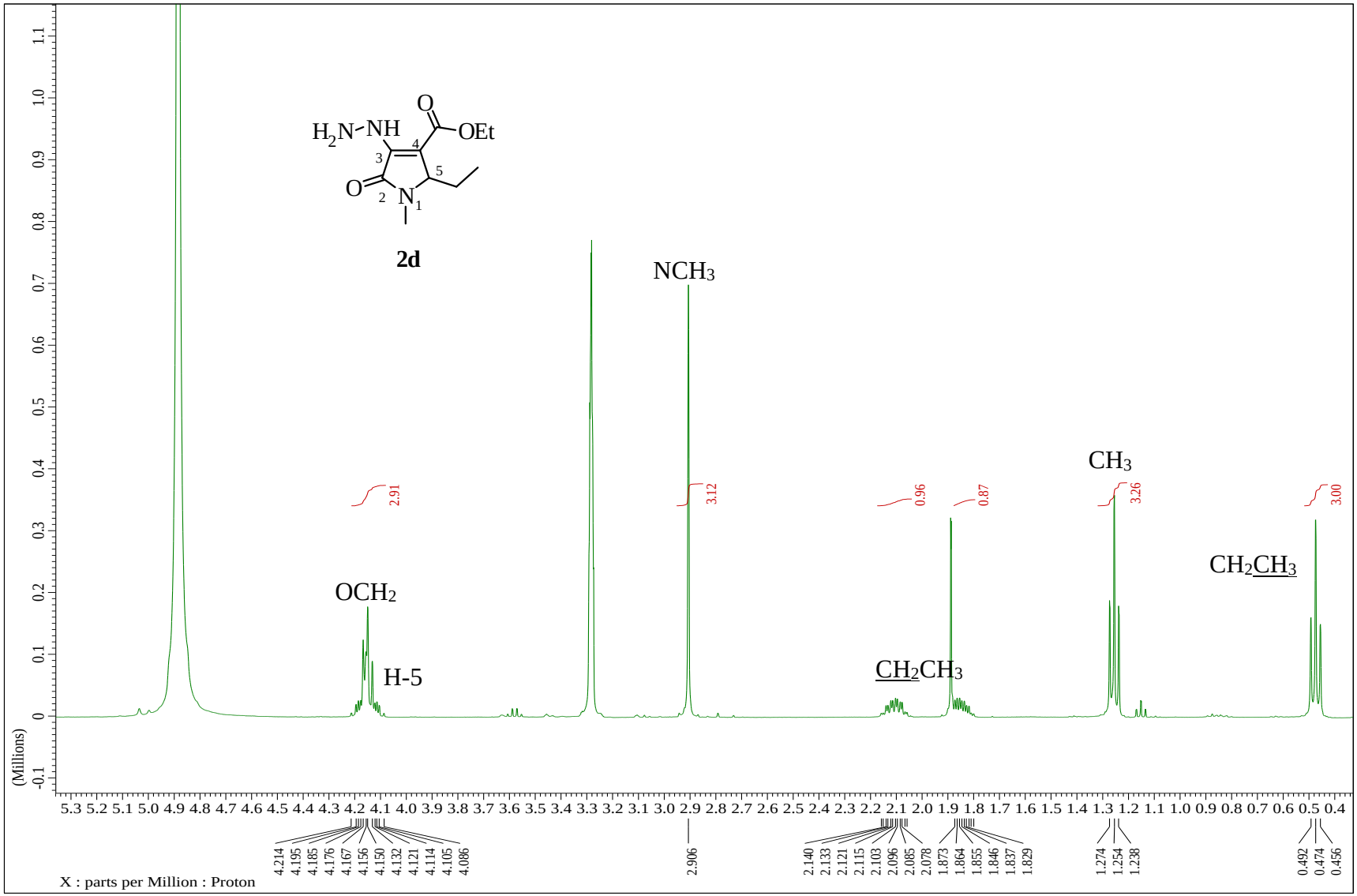


Figure S4: ^{1}H-NMR spectrum of compound 2d

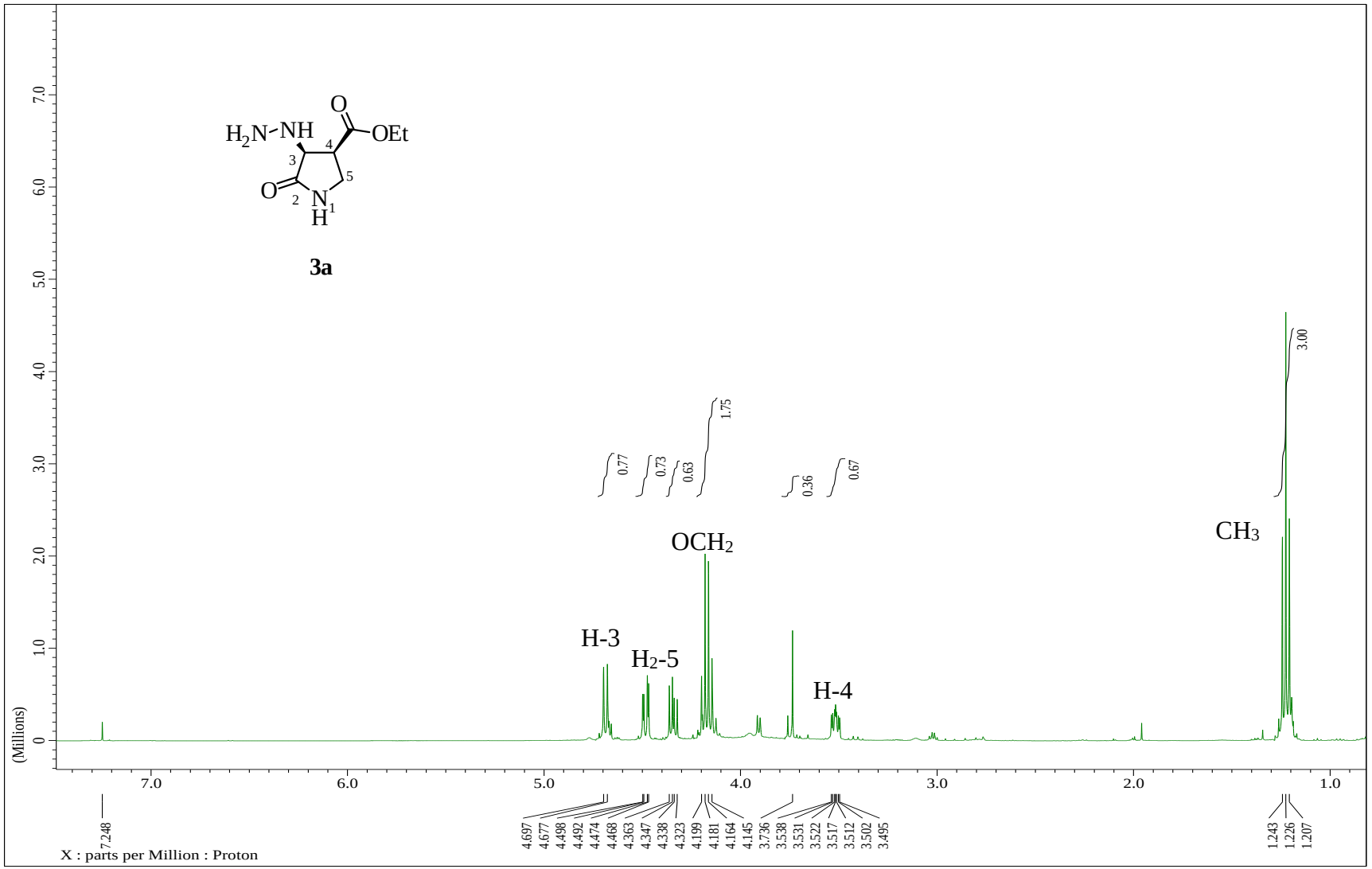


Figure S5: ^{1}H-NMR spectrum of compound 3a

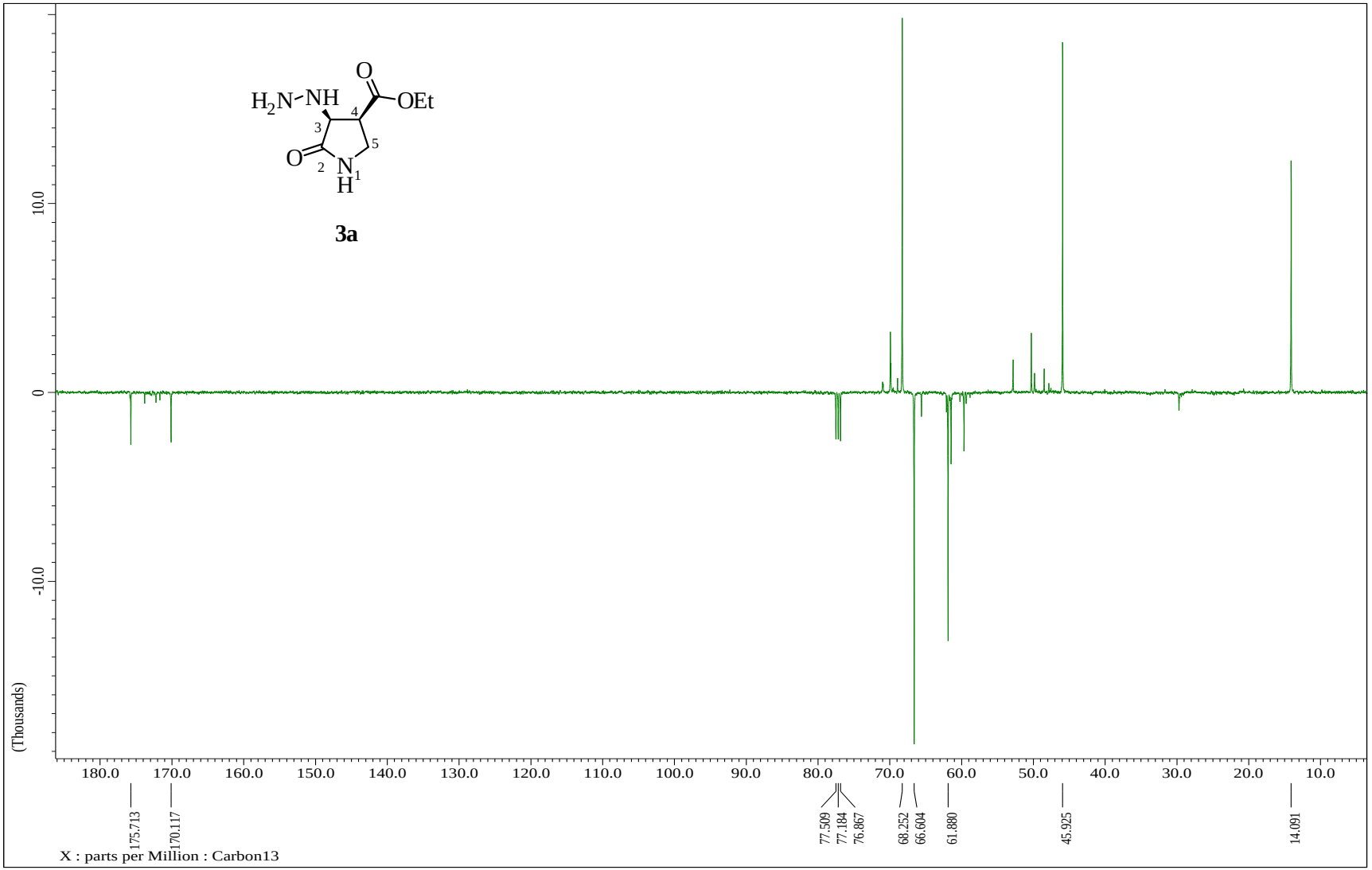


Figure S6: ^{13}C-NMR spectrum of compound 3a

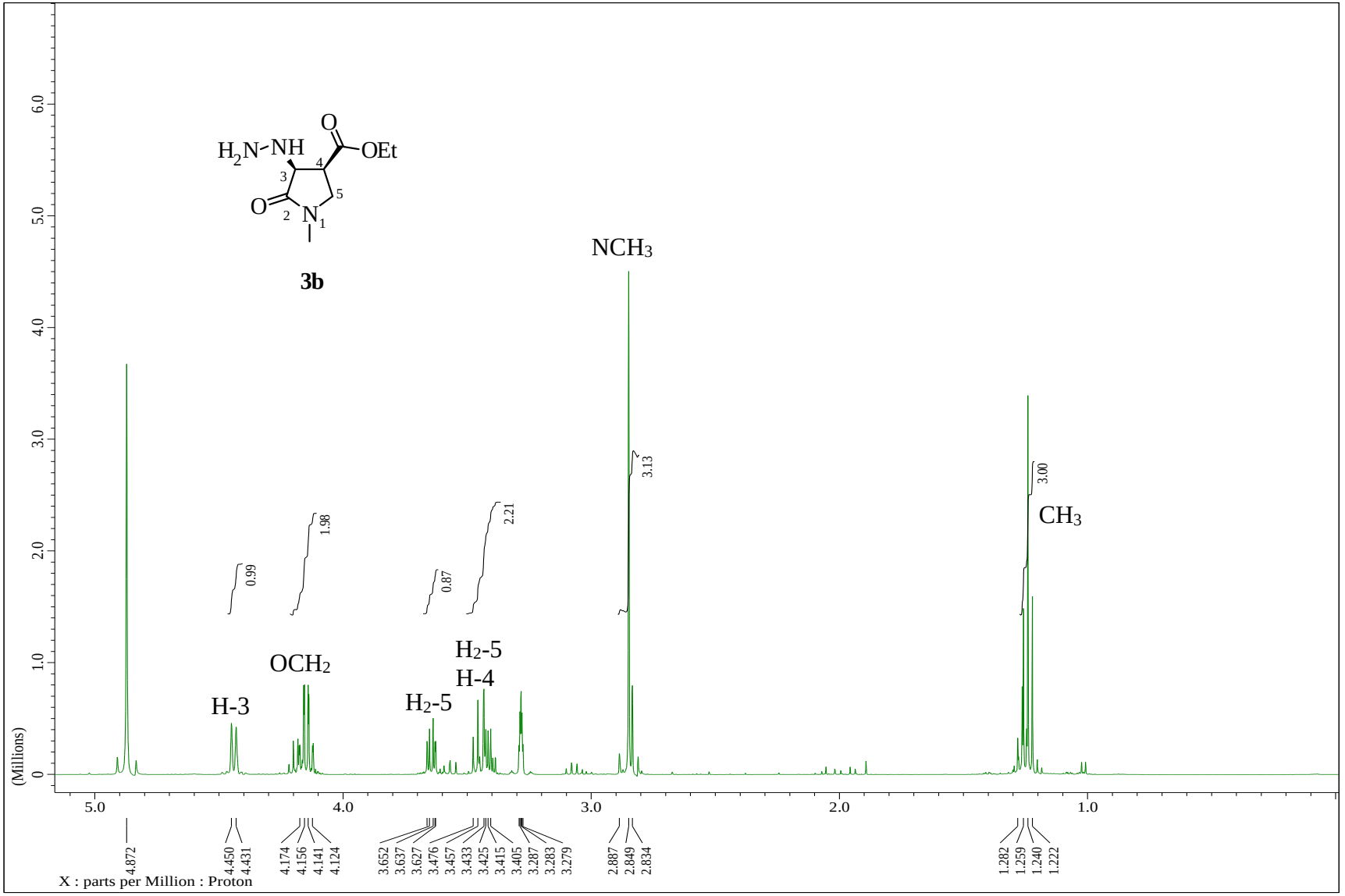
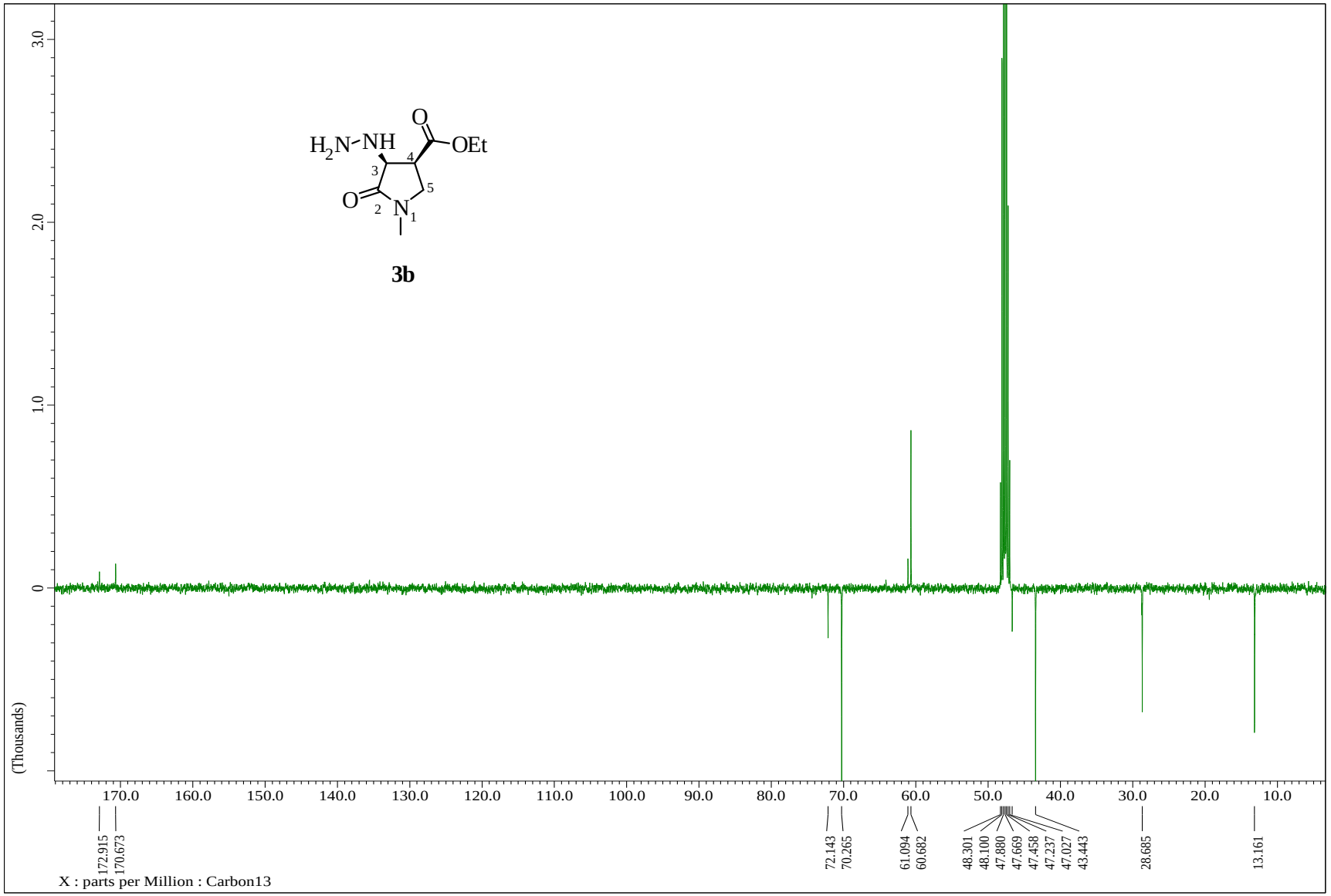


Figure S7: ^{1}H-NMR spectrum of compound 3b



3b

Figure S8: ^{13}C-NMR spectrum of compound 3b

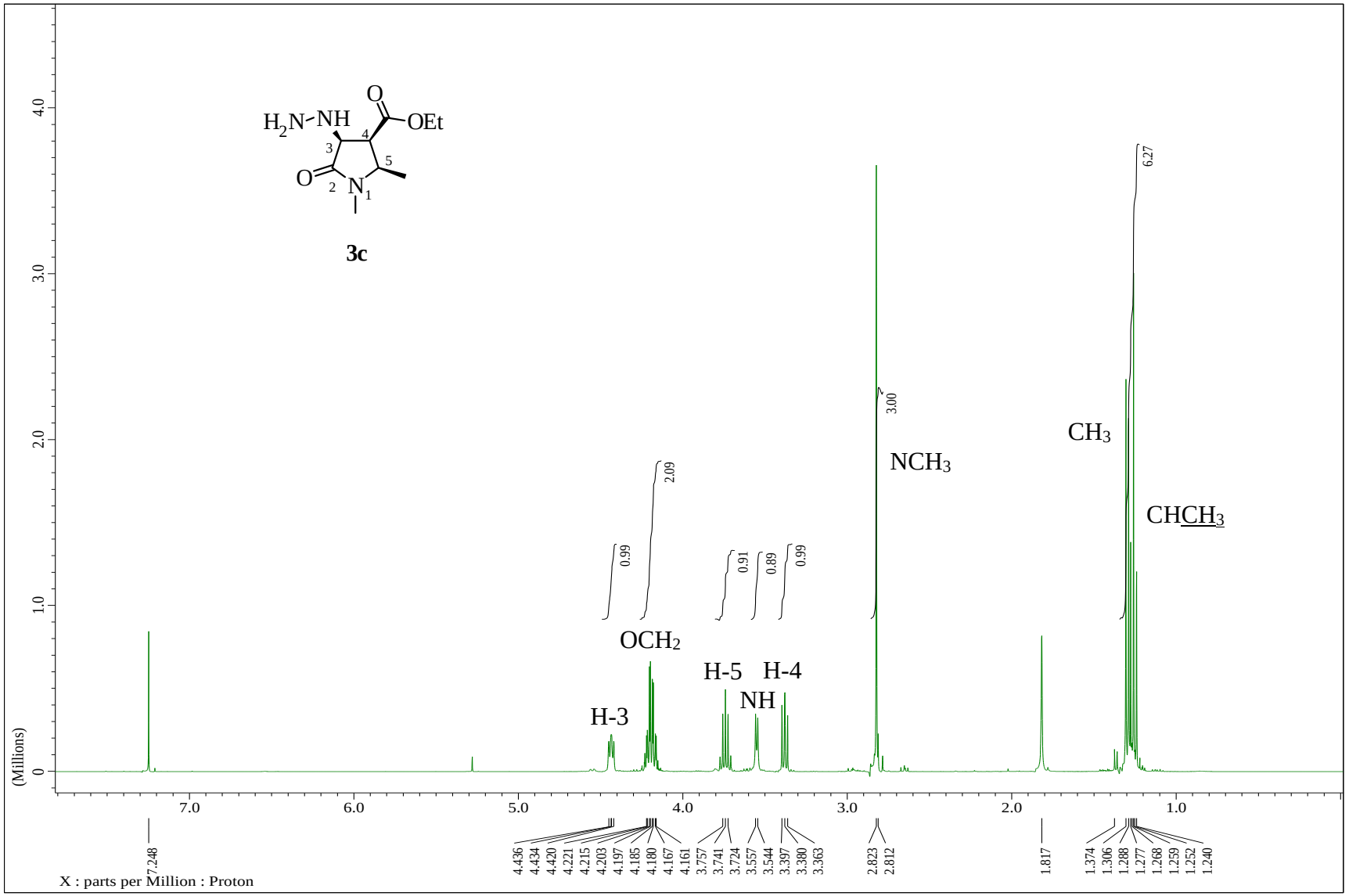


Figure S9: ^{1}H-NMR spectrum of compound 3c

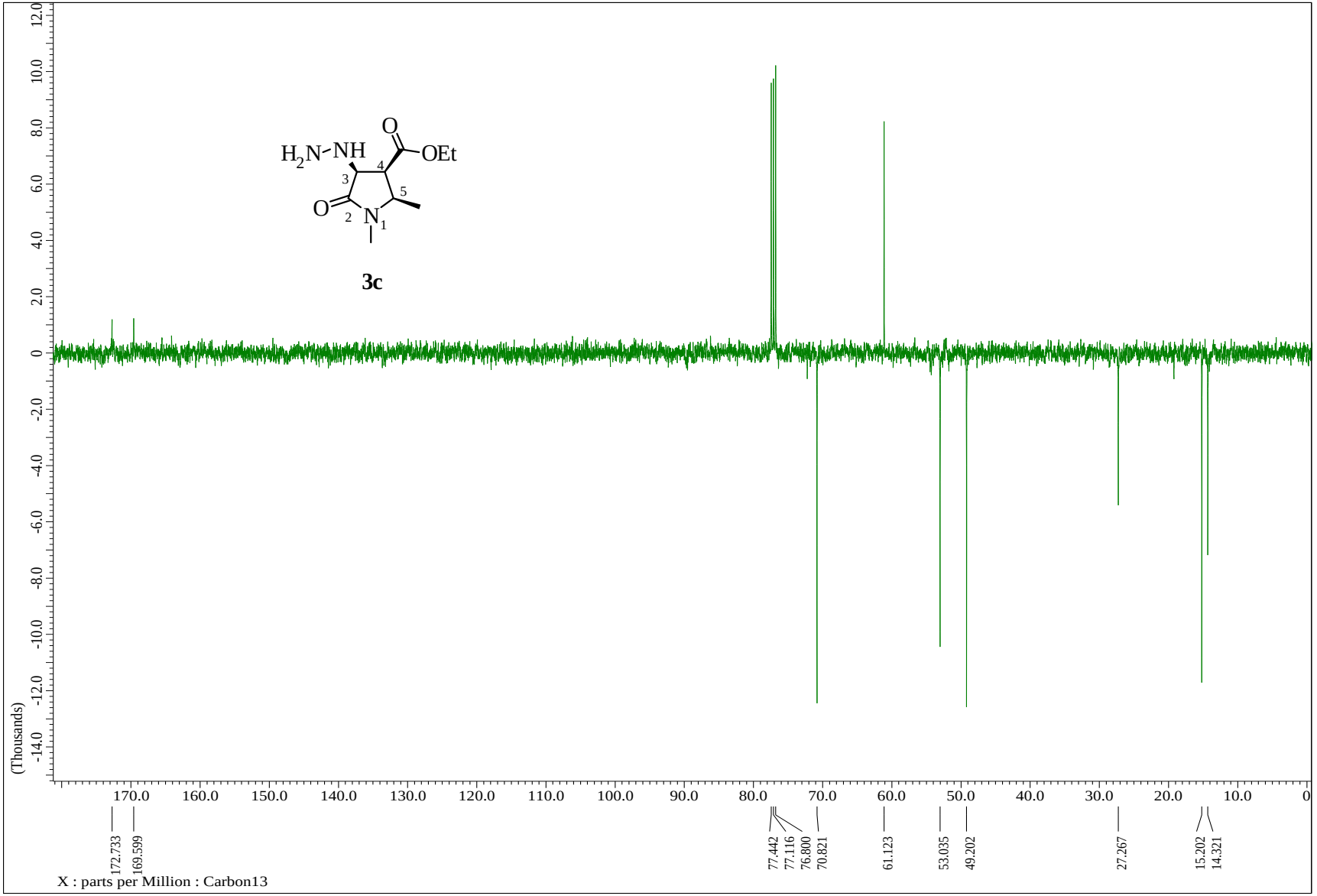


Figure S10: ^{13}C-NMR spectrum of compound 3c

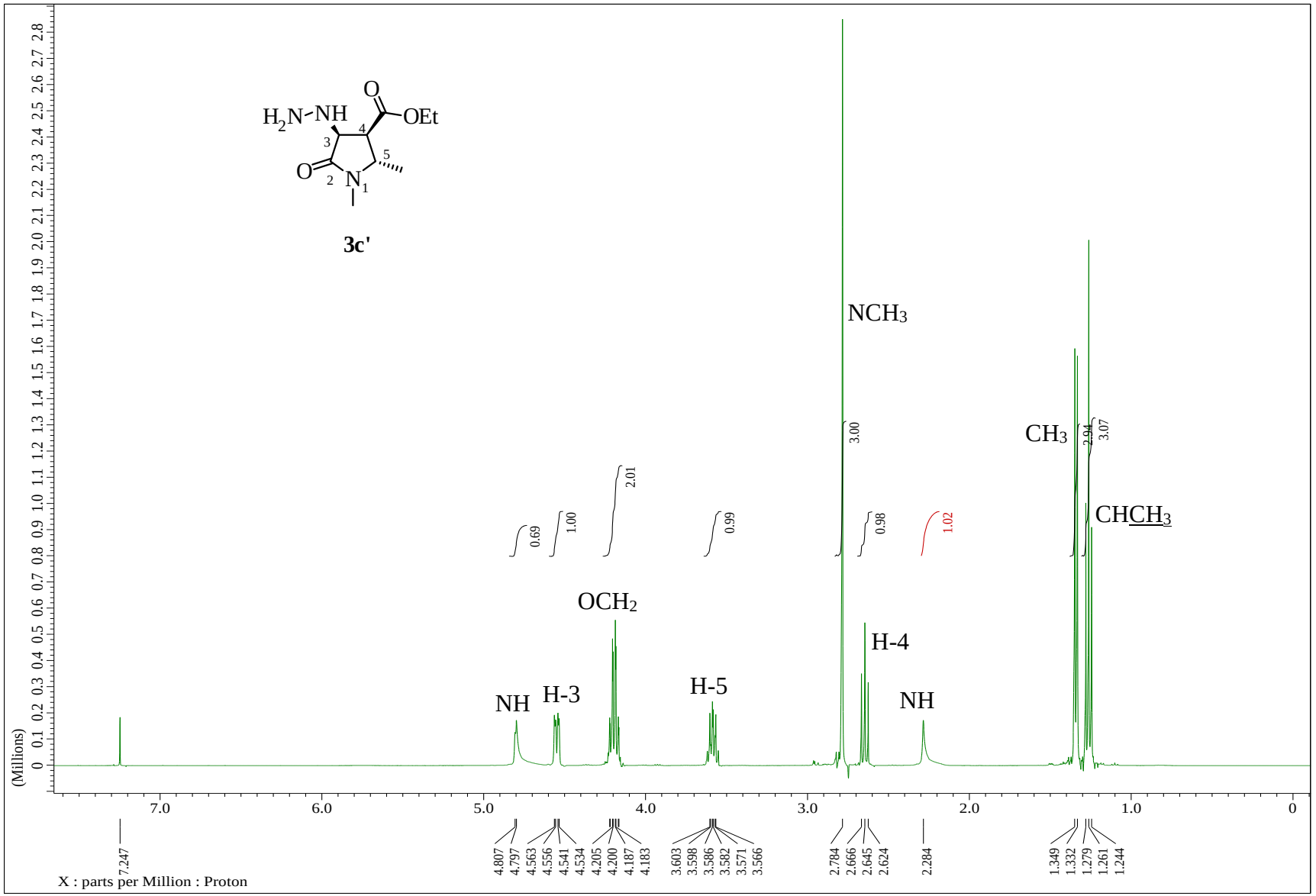


Figure S11: ^{1}H-NMR spectrum of compound 3c'

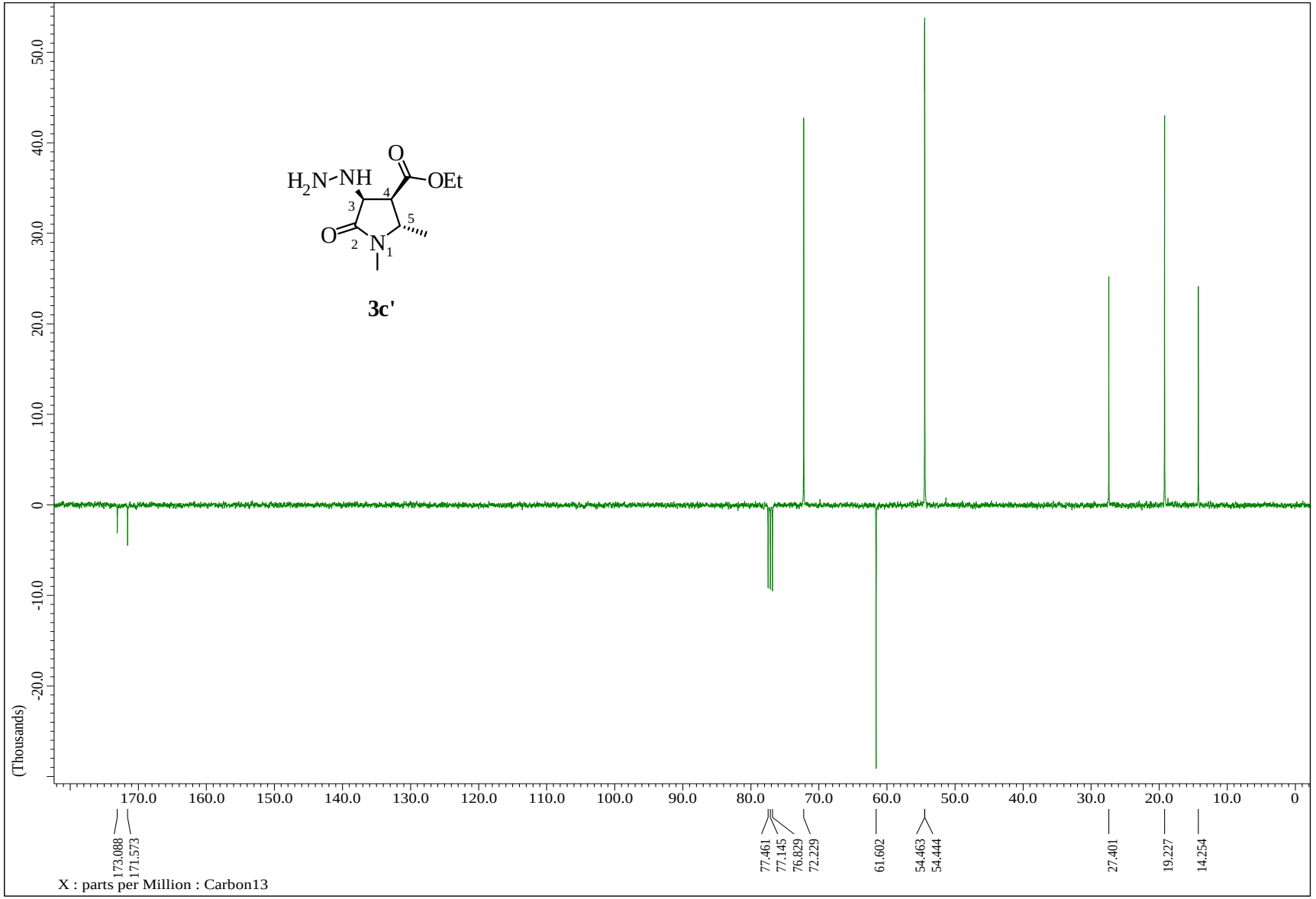


Figure S12: ^{13}C-NMR spectrum of compound 3c'

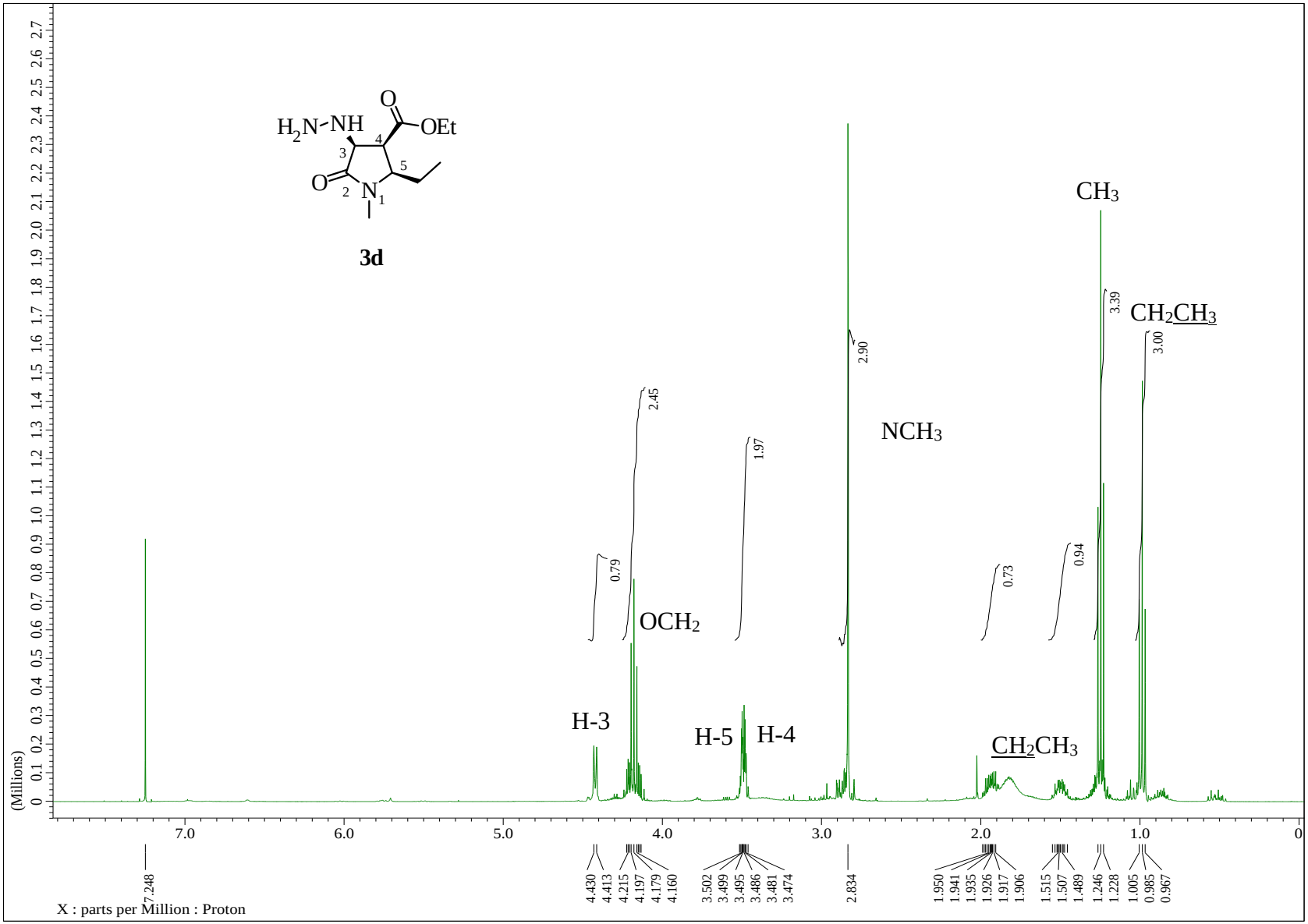


Figure S13: ^{1}H-NMR spectrum of compound 3d

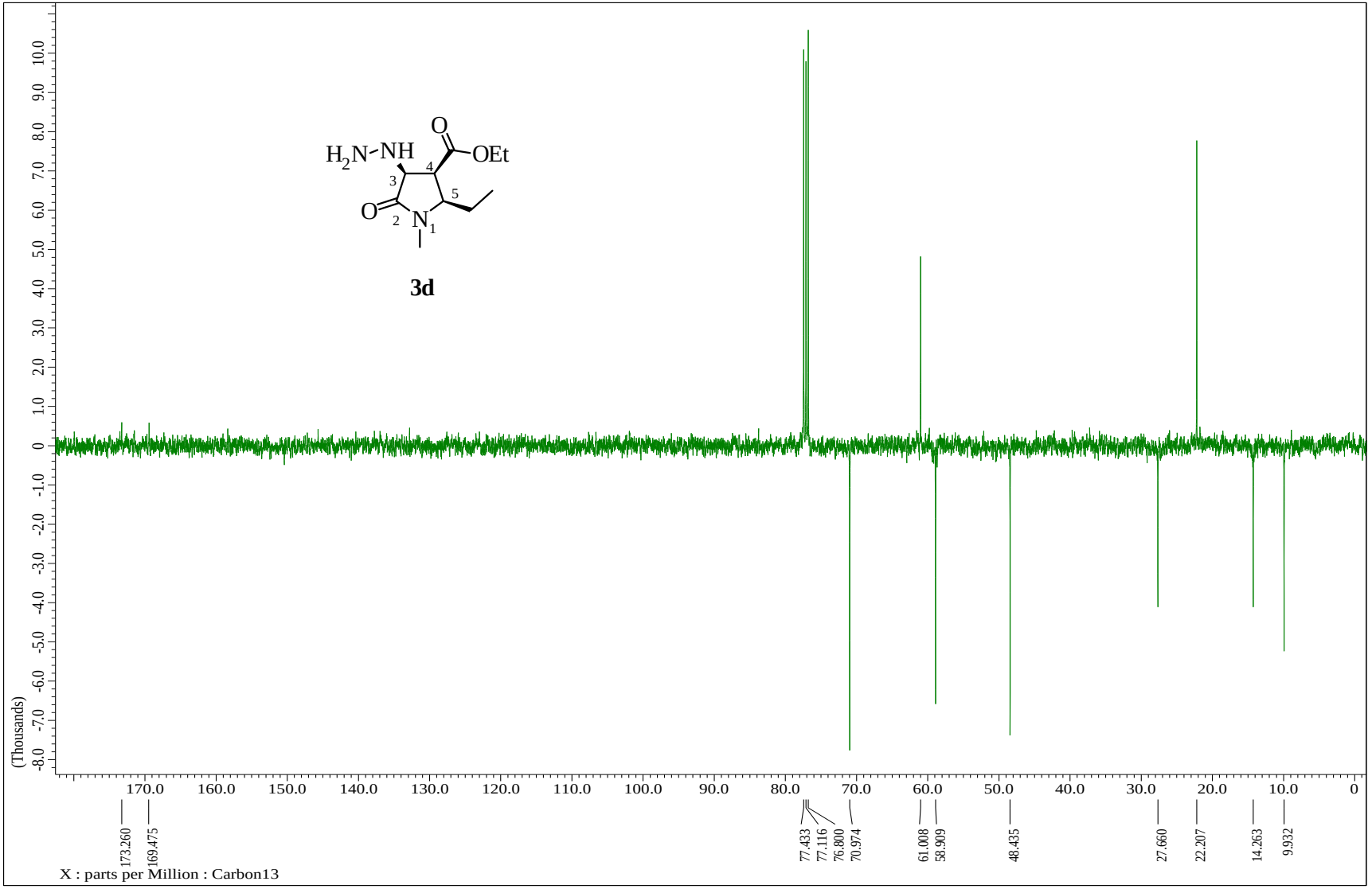


Figure S14: ^{13}C-NMR spectrum of compound 3d

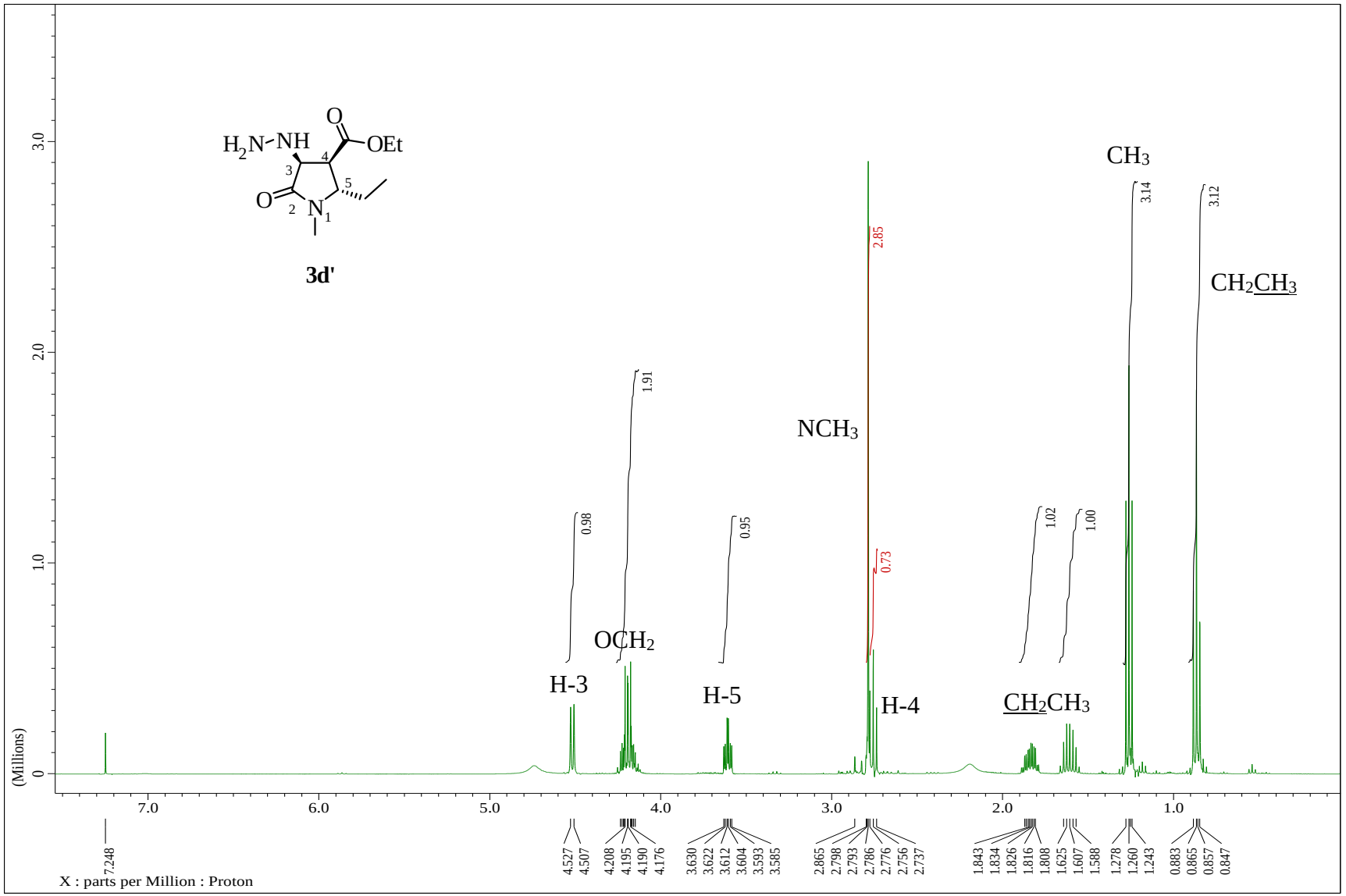


Figure S 15: ^{1}H-NMR spectrum of compound 3d'

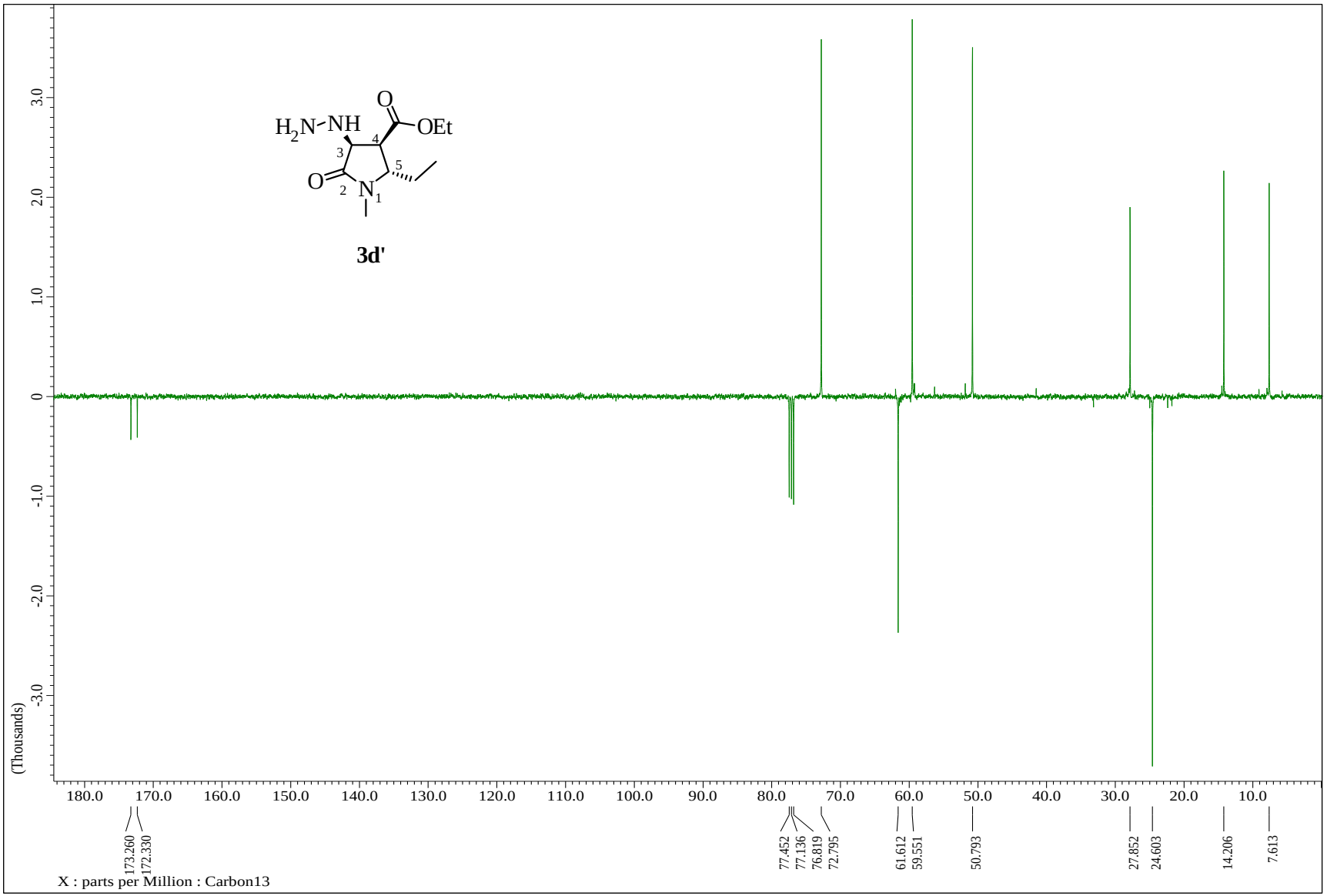


Figure S 16: ^{13}C-NMR spectrum of compound 3d'

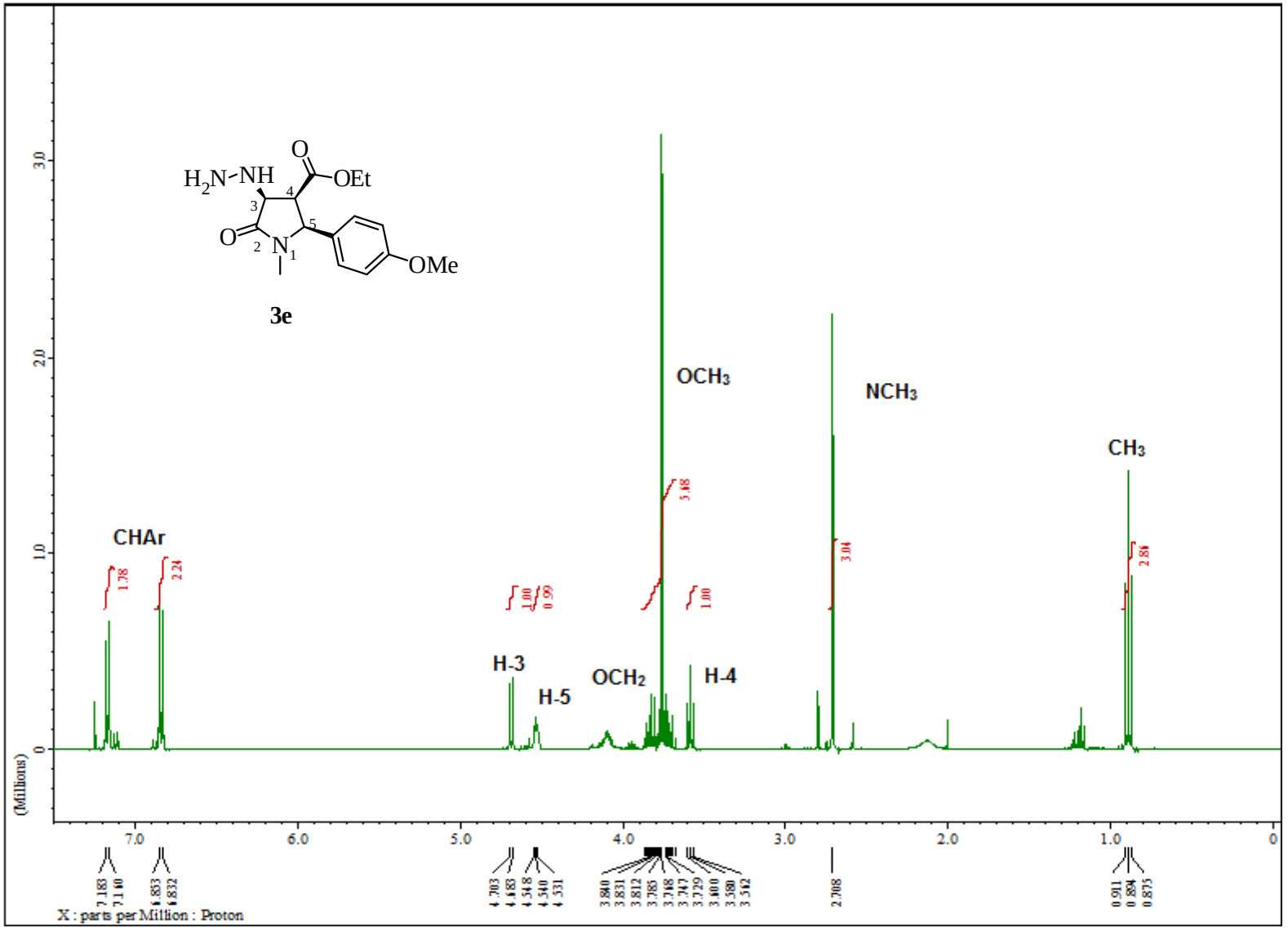


Figure S 17: ^{1}H-NMR spectrum of compound 3e

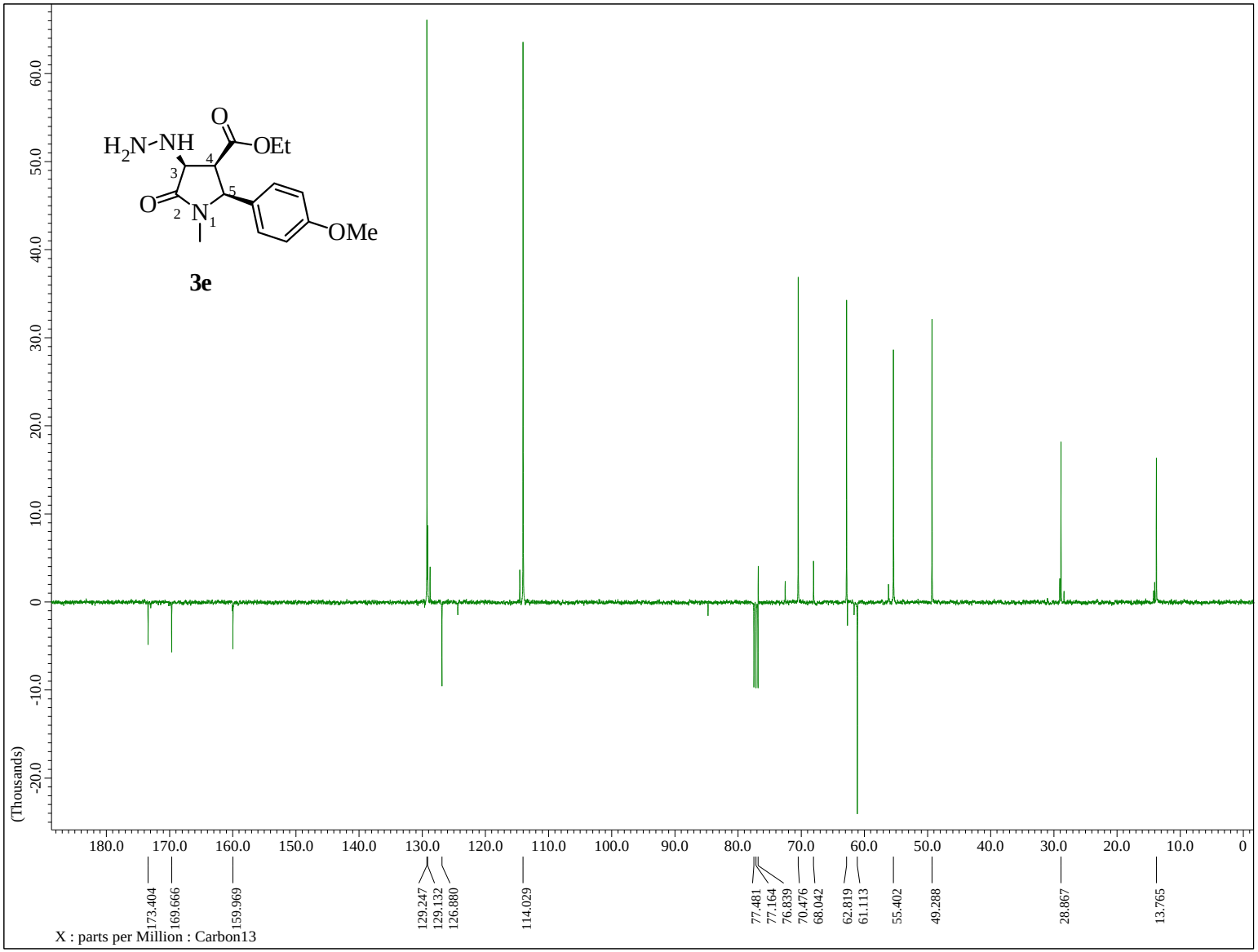


Figure S18: ^{13}C-NMR spectrum of compound 3e

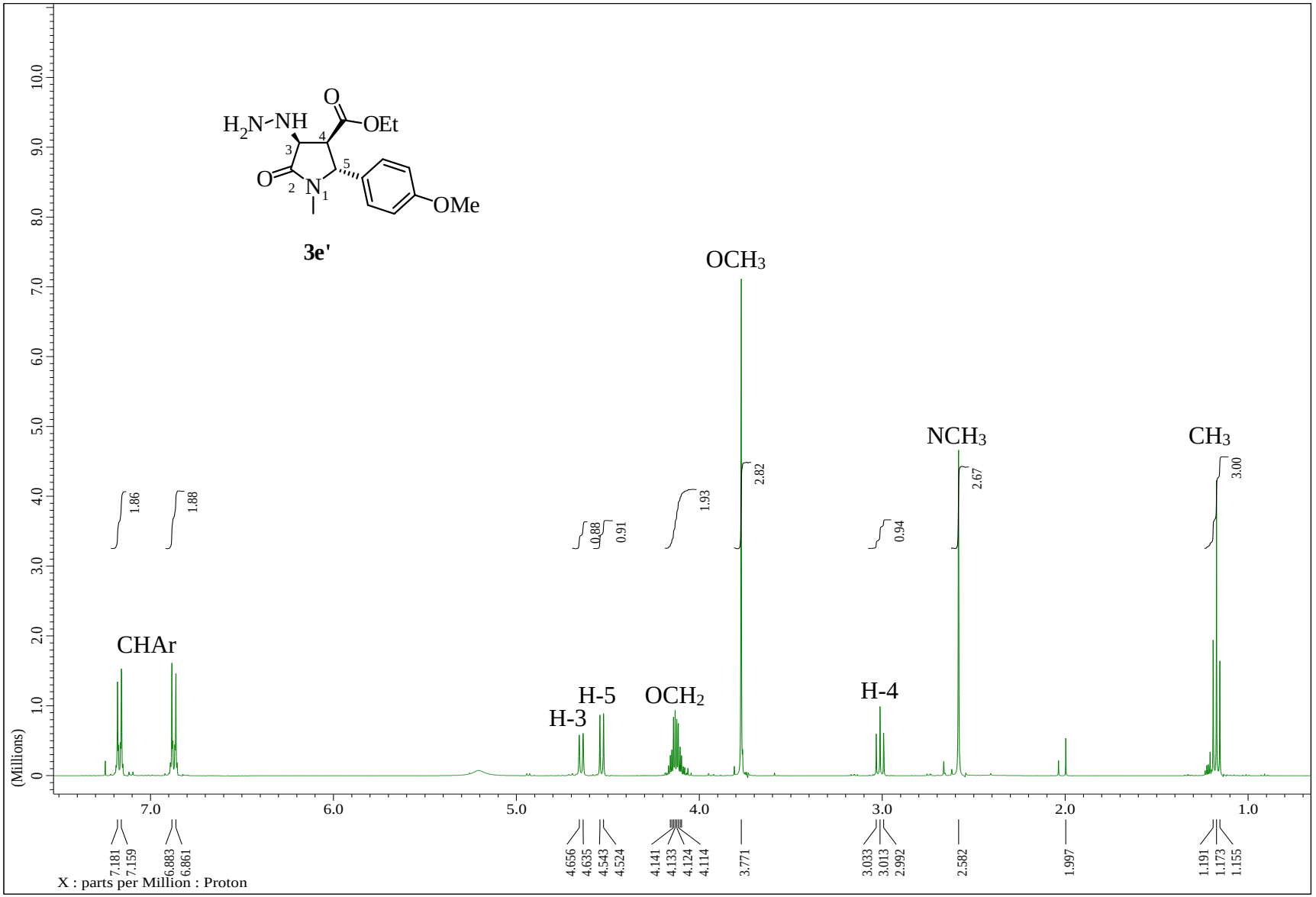


Figure S19: ^{1}H-NMR spectrum of compound 3e'

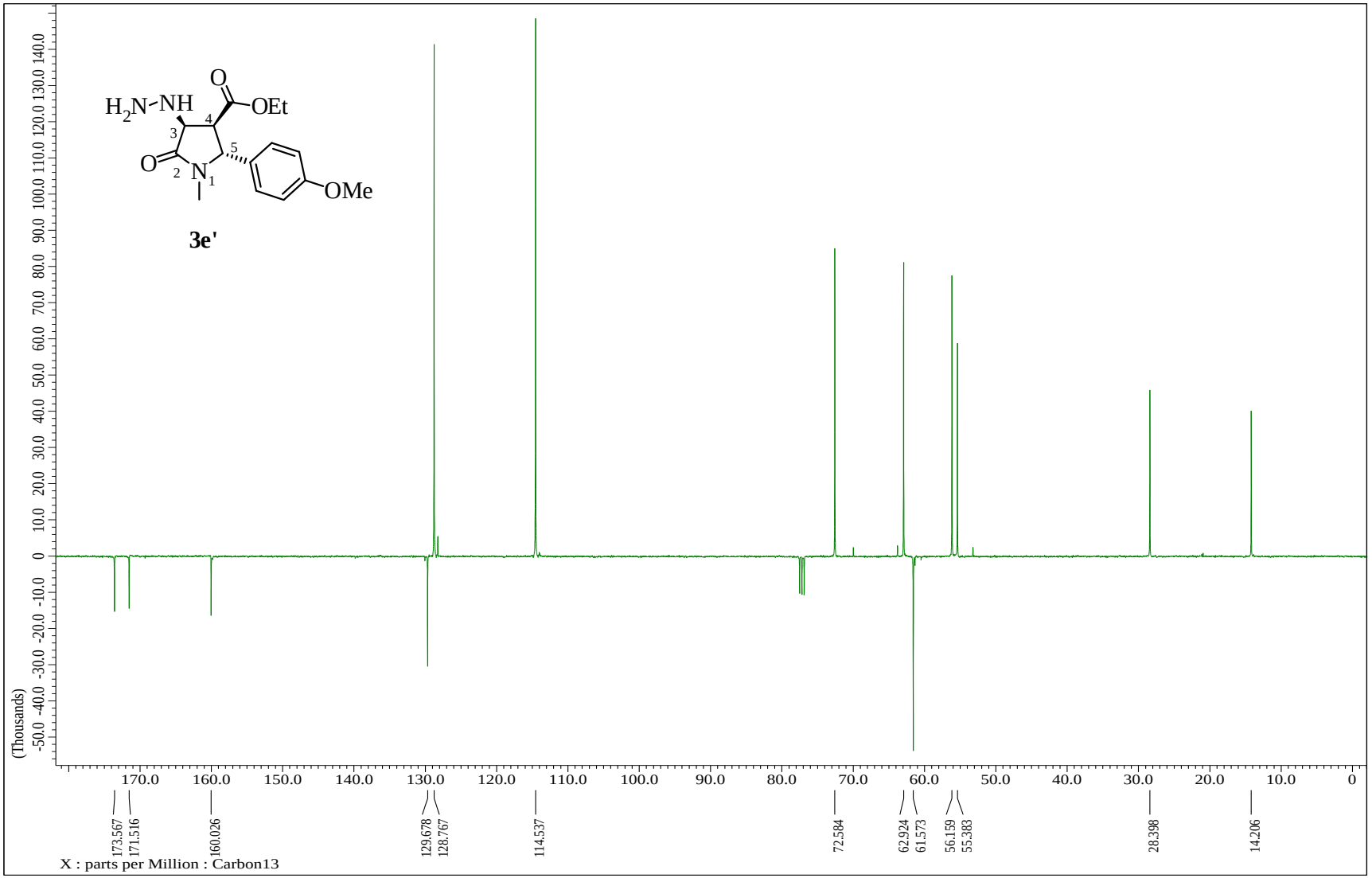


Figure S20: ^{13}C-NMR spectrum of compound 3e'

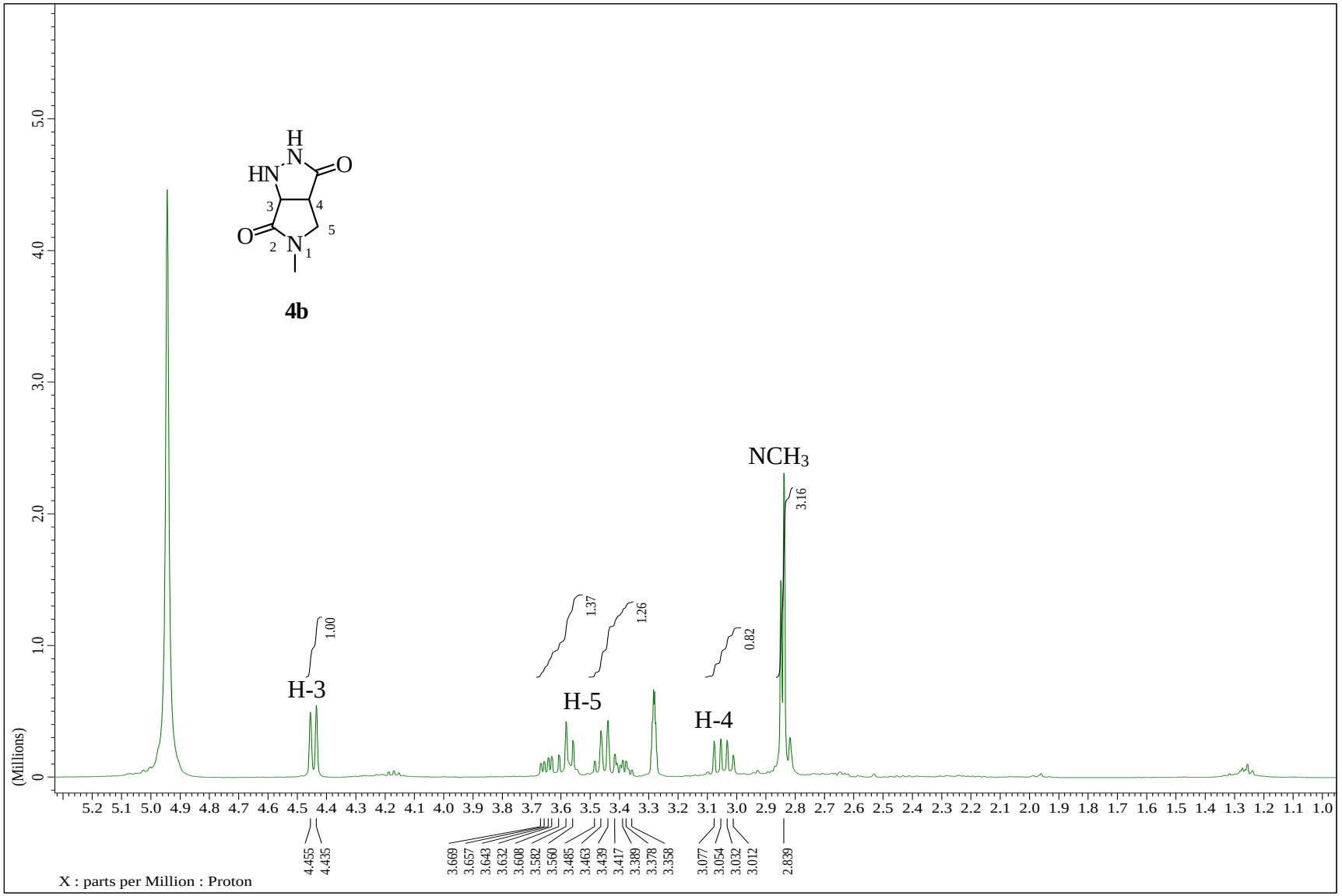


Figure S21: ^{1}H-NMR spectrum of compound 4b

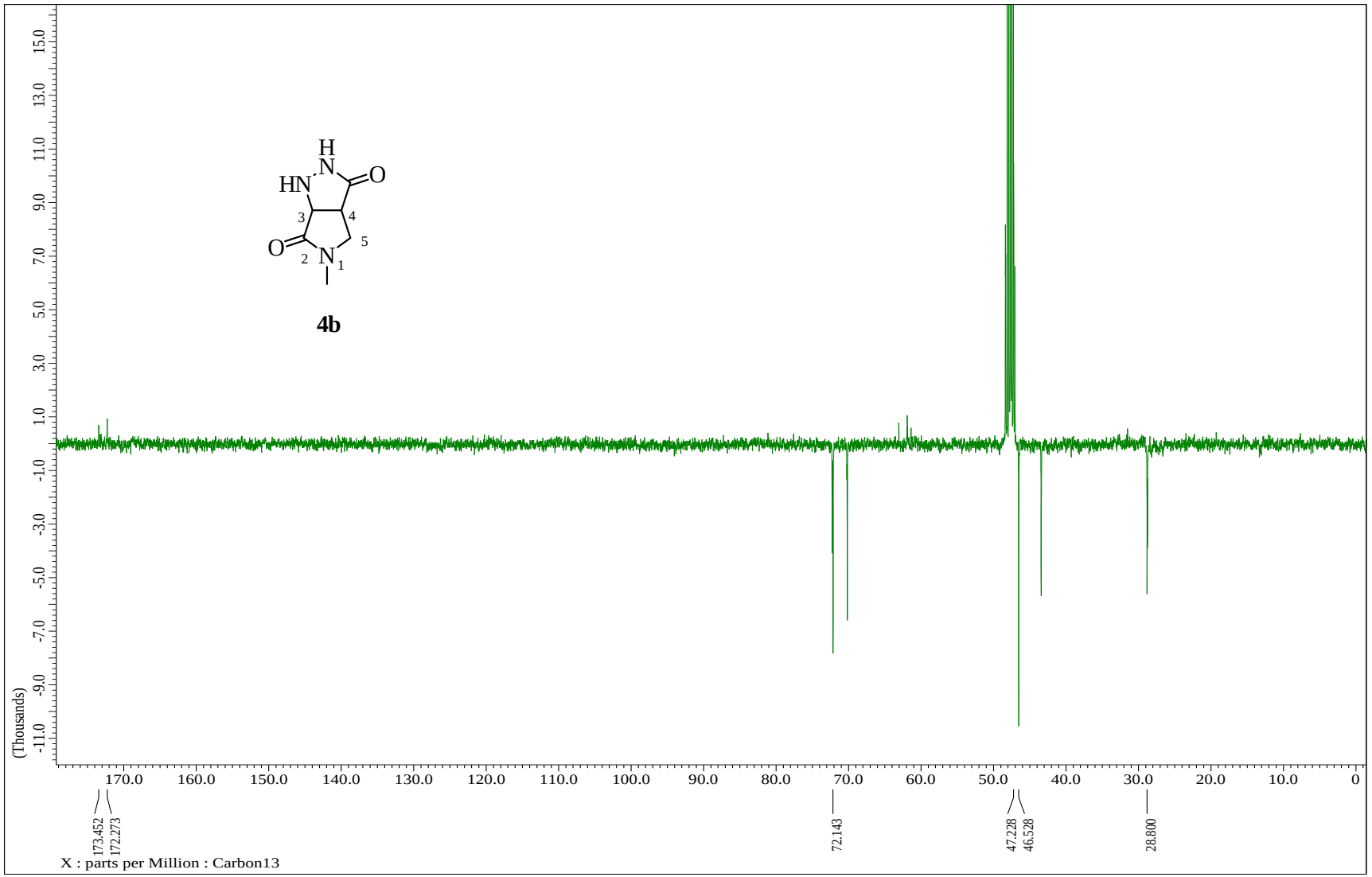


Figure S22: ^{13}C-NMR spectrum of compound 4b

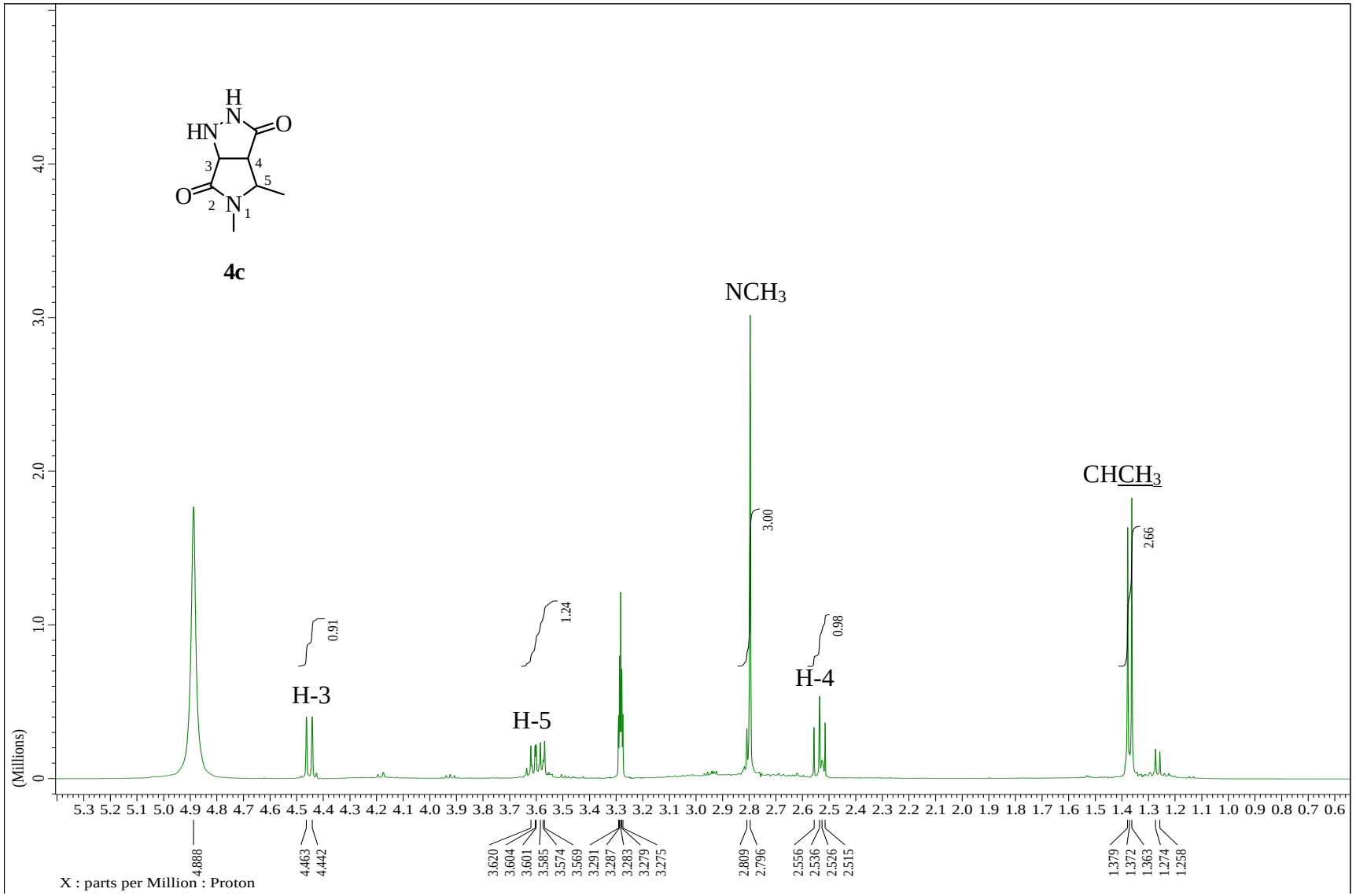


Figure S23: ^{1}H-NMR spectrum of compound 4c

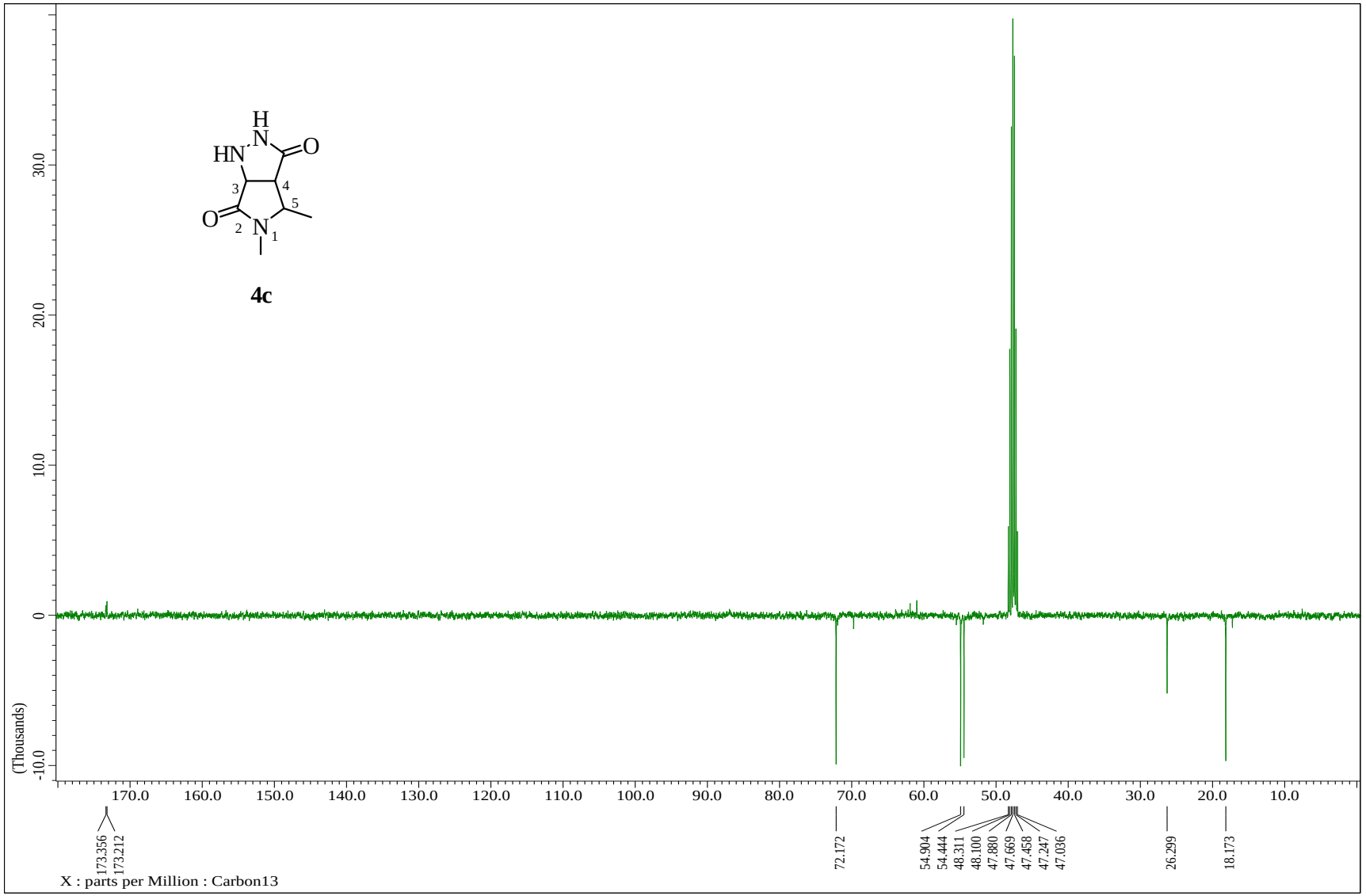


Figure S24: ^{13}C-NMR spectrum of compound 4c

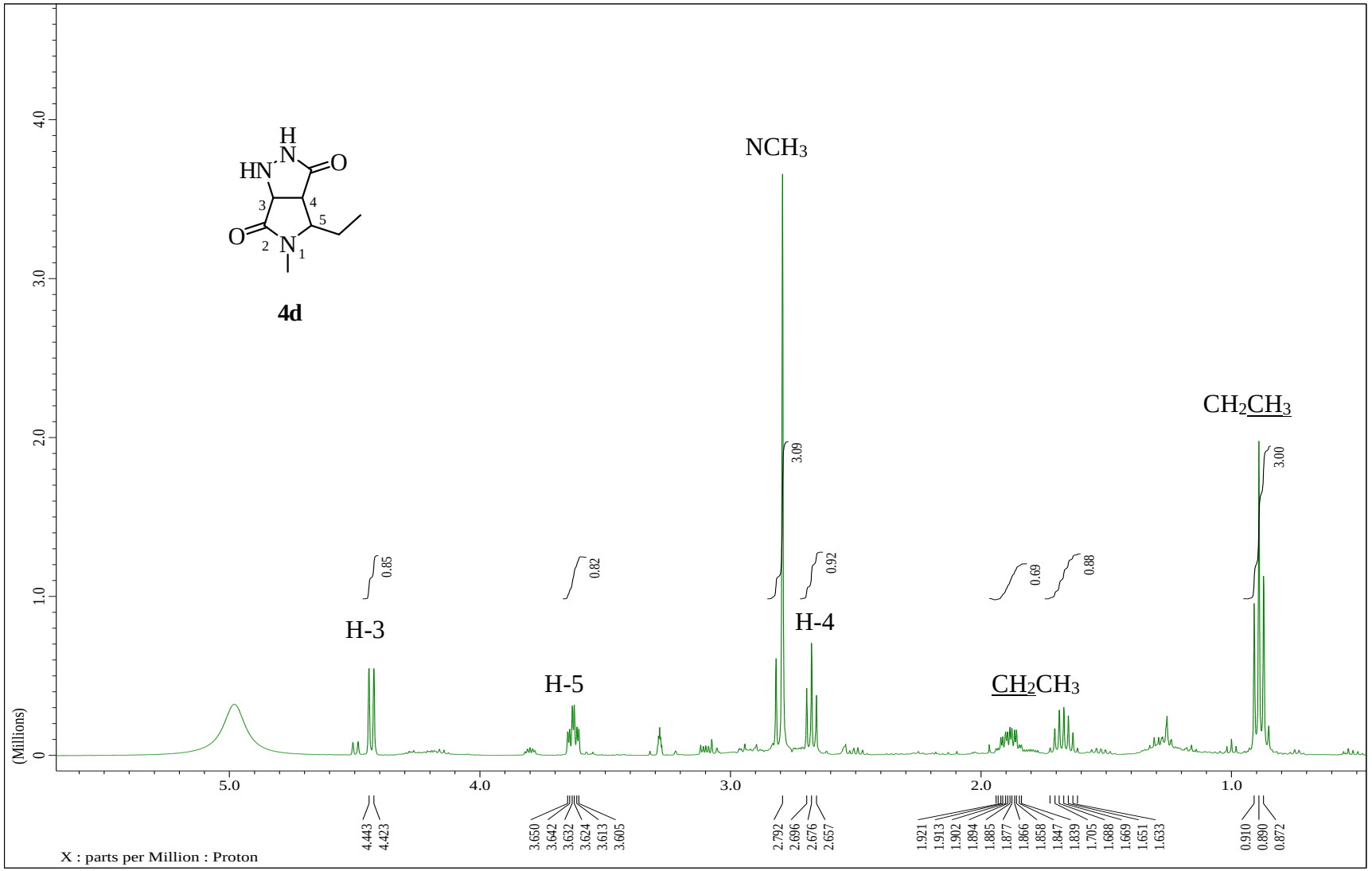


Figure S25: ^{1}H-NMR spectrum of compound 4d

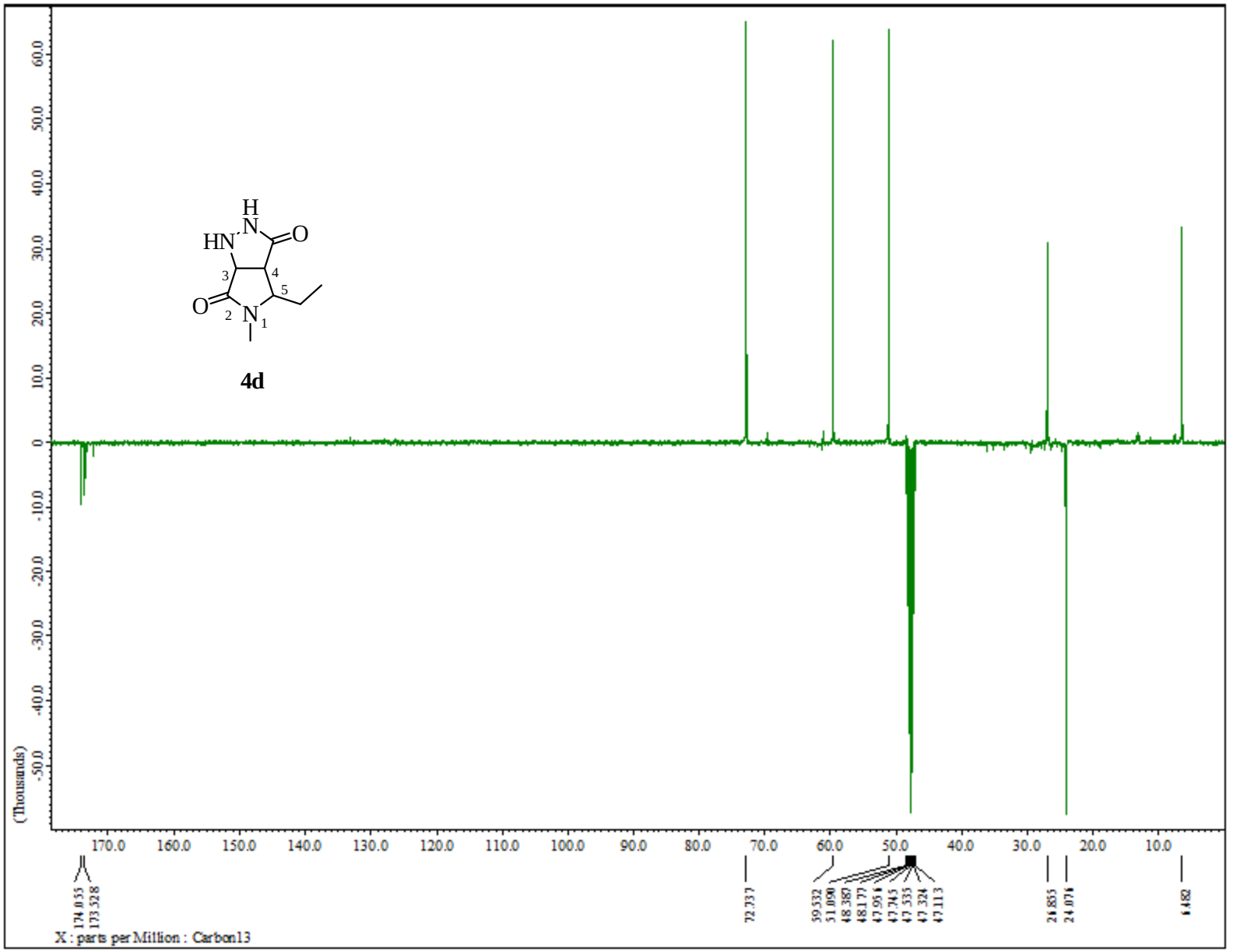


Figure S26: ^{13}C-NMR spectrum of compound 4d

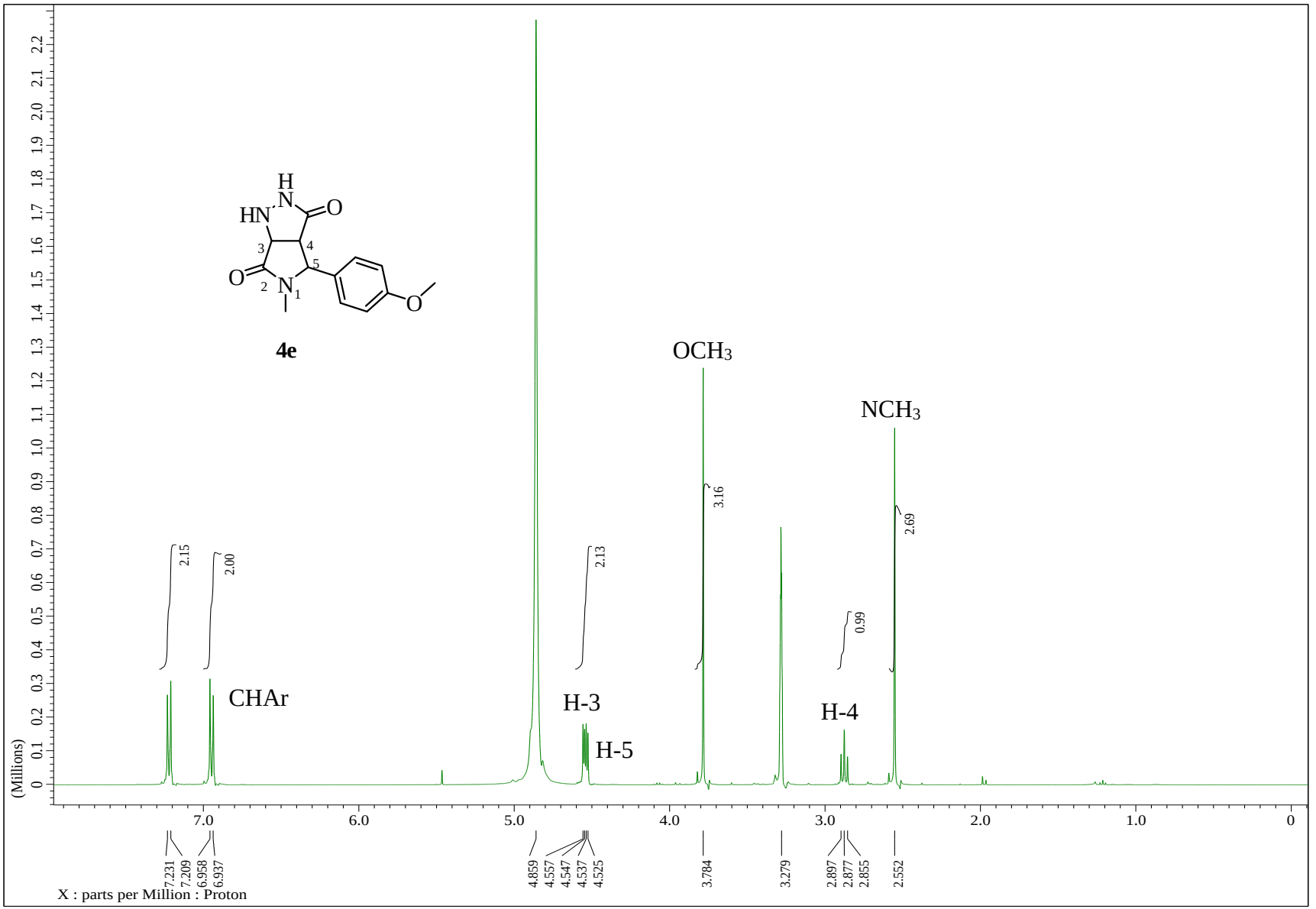


Figure S27: ^{1}H-NMR spectrum of compound 4e

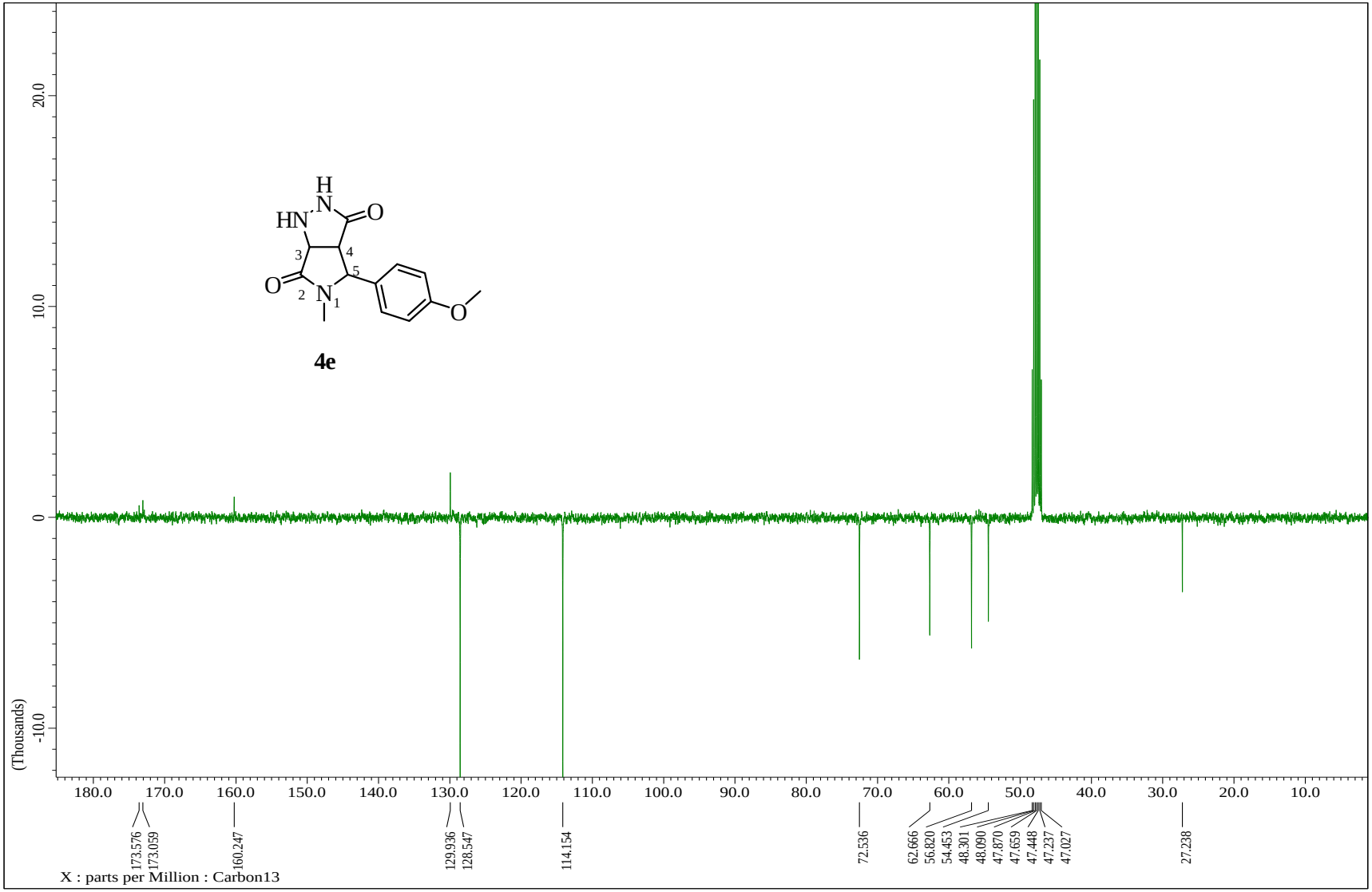


Figure S28: ^{13}C-NMR spectrum of compound 4e

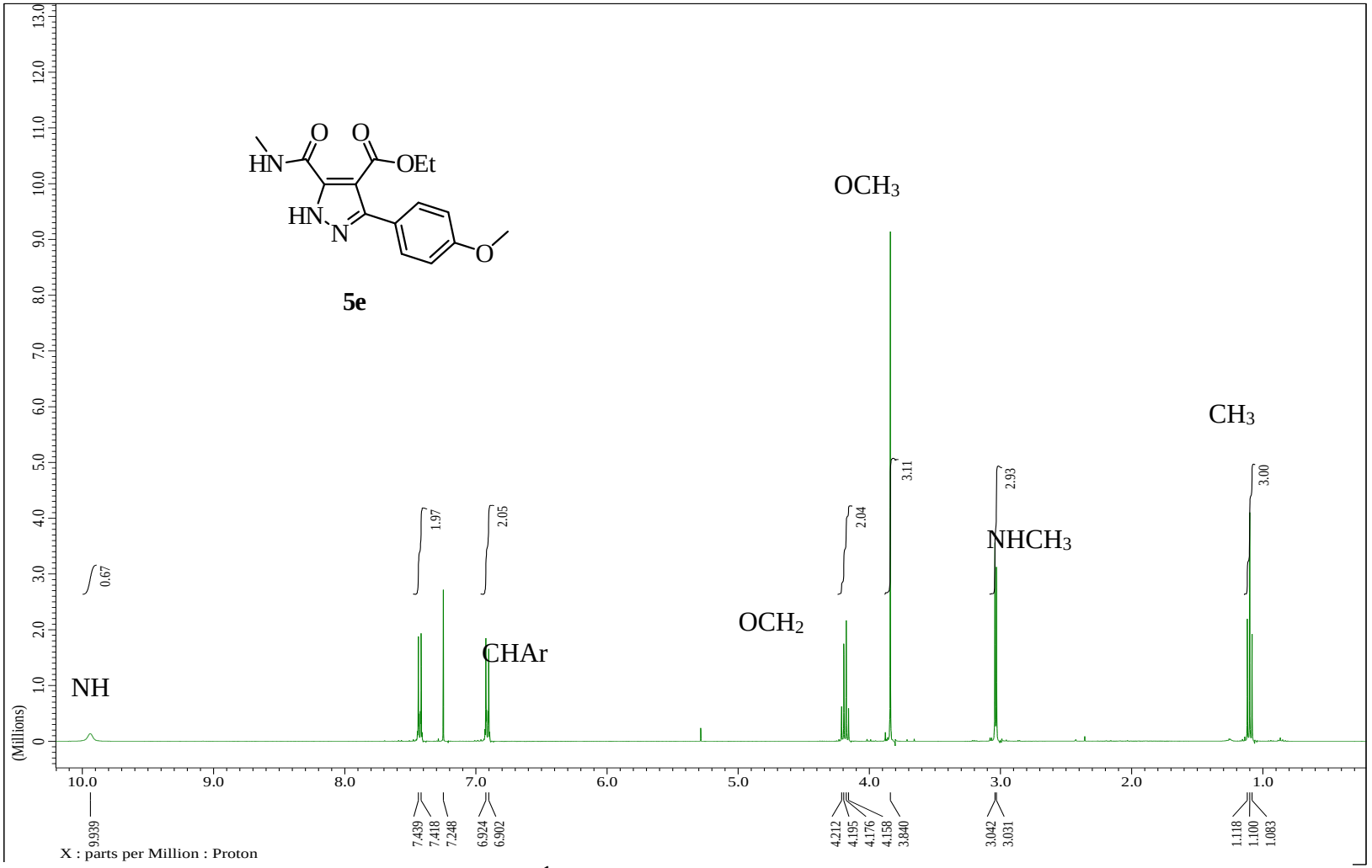


Figure S29: ^{1}H-NMR spectrum of compound 5e

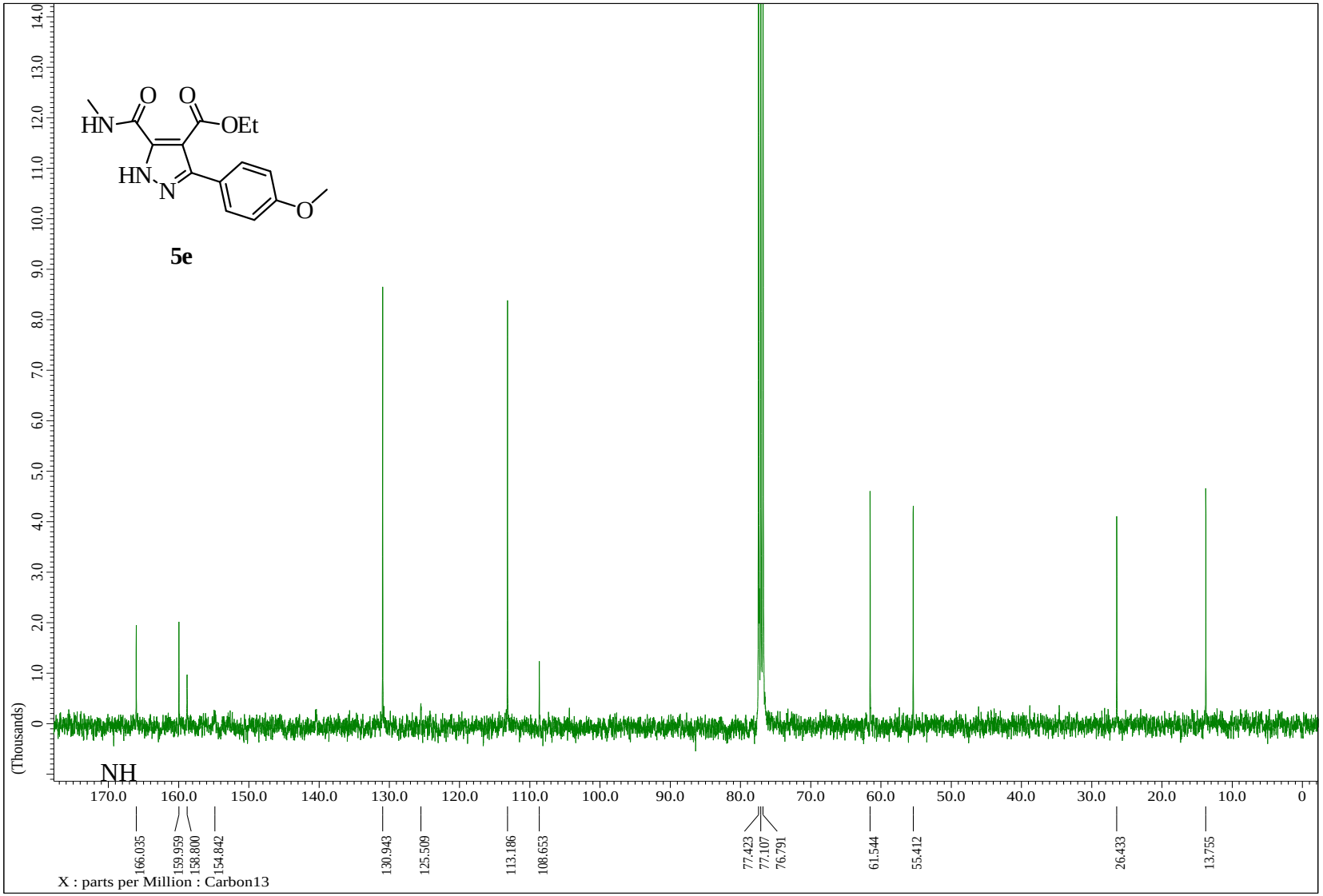


Figure S30: ^{13}C-NMR spectrum of compound 5e