

Supplementary Information for
**Sequential Reduction of Nitroalkanes Mediated by CS₂ and
Amidine/Guanidine Bases: A Controllable Nef Reaction**

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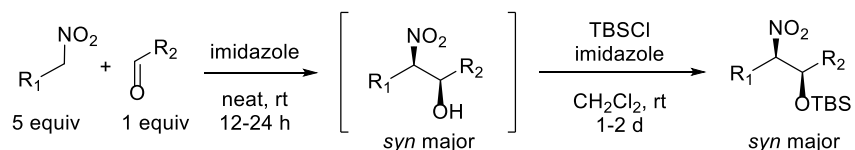
I. General Information

All glassware was either oven-dried overnight at 130 °C or flame-dried using a Bunsen burner. All glassware was then allowed to cool to room temperature in a desiccator filled with DrieriteTM as a desiccant or under a stream of dry nitrogen prior to use. Unless otherwise specified, reagents were directly used without further purification as obtained from Sigma-Aldrich, Oakwood Products, Alfa Aesar, Tokyo Chemical Industry, Combi-Blocks, Carbosynth, Acros Organics or Cayman Chemicals. Diethyl ether (Et₂O) was freshly distilled from Na/benzophenone ketyl. Tetrahydrofuran (THF) was either freshly distilled from Na/benzophenone ketyl or passed through an alumina column before use. Dichloromethane (CH₂Cl₂) was either dried over calcium hydride (CaH₂) and freshly distilled before use or passed through an alumina column before use. Acetonitrile (CH₃CN), toluene (PhMe) and benzene (C₆H₆) were all dried over CaH₂ and freshly distilled before use. All other solvents were purified using accepted procedures from the sixth edition of "Purification of Laboratory Chemicals".¹ Air- and moisture-sensitive reactions were performed using standard Schlenk techniques under a nitrogen atmosphere. Analytical thin layer chromatography (TLC) was performed utilizing pre-coated silica gel 60 F₂₄ plates containing a fluorescent indicator, while preparative chromatography was performed using SilicaFlash P60 silica gel (230-400 mesh) *via* Still's method.² Column chromatography was typically run using a gradient method employing mixtures of hexanes and ethyl acetate (EtOAc). Various stains were used to visualize reaction products, including *p*-anisaldehyde, KMnO₄, ceric ammonium molybdate (CAM stain) and iodine powder. ¹H NMR and ¹³C NMR spectra were obtained using Bruker Avance-400 (400 and 100 MHz) and Bruker Avance-500 (500 and 125 MHz) spectrometers. Chemical shifts were reported in accordance to residual protiated solvent peaks (note: CDCl₃ referenced at δ 7.26 and 77.16 ppm, respectively). High-performance liquid

chromatography (HPLC) was performed using Shimadzu LC-20AB system. A CHIRALPAK® AD-H (0.46 cm diameter x 25 cm) was employed, maintained at a temperature of 40 °C, using *i*-PrOH/hexane (HPLC) mobile phase. Accurate mass measurements were acquired at the University of Wisconsin-Madison using a Micromass LCT (electrospray ionization, time-of-flight analyzer or electron impact methods). The following instrumentation in the Paul Bender Chemistry Instrumentation Center was supported by: Thermo Q Exactive™ Plus by NIH 1S10 OD020022-1; Bruker Quazar APEX2 and Bruker Avance-500 by a generous gift from Paul J. and Margaret M. Bender; Bruker Avance-600 by NIH S10 OK012245; Bruker Avance-400 by NSF CHE-1048642 and the University of Wisconsin-Madison; Varian Mercury-300 by NSF CHE-0342998.

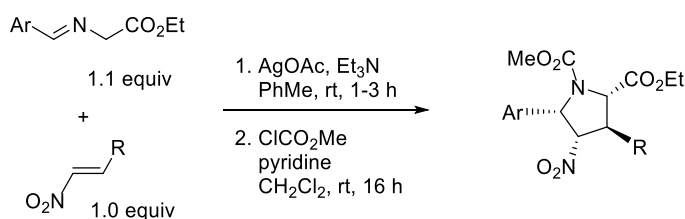
II. Synthesis of Starting Nitroalkanes

Commercially available (1-nitroethyl)benzene (**1j**) was purchased from Carbosynth and used as received.



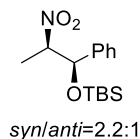
General procedure A for synthesis of Henry products 1a-g, 1i, 1x. To a mixture of nitroalkane (50 mmol, 5 equiv) and aldehyde (10 mmol, 1.0 equiv) was added imidazole (10 mmol, 1 equiv) at room temperature. The reaction was stirred until ¹H NMR analysis indicated complete consumption of the starting aldehyde (12-24 h). The crude reaction mixture was then diluted with anhydrous CH₂Cl₂ (50 mL) and transferred to a flame-dried round-bottom flask under N₂. TBSCl (20 mmol, 2 equiv) and additional imidazole (20 mmol, 2 equiv) were subsequently added to the

flask. The reaction mixture was stirred at room temperature until TLC analysis indicated complete consumption of the intermediate (1-2 d). The mixture was quenched by careful addition of H₂O and the aqueous layer was extracted with CH₂Cl₂ twice. The combined organic layers were washed with H₂O and brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude protected Henry product was purified by silica gel column chromatography (EtOAc/hexanes gradient).

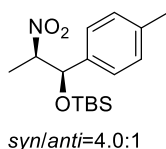


General procedure B for synthesis of nitropyrrolidines 1o-r, 1t-u. Following a literature procedure reported by Nyerges and Pak,³ ethyl (arylideneamino)acetate (3.3 mmol, 1.1 equiv) and nitroolefin (3 mmol, 1 equiv) were dissolved in anhydrous PhMe (15 mL, 0.2 M) then AgOAc (5.1 mmol, 1.7 equiv) and Et₃N (3.9 mmol, 1.3 equiv) were added to the well stirred reaction mixture. After reaction completion indicated by TLC analysis (1-3 h), sat. aq. NH₄Cl (7.5 mL) was added, the precipitate was filtered off and the residue was extracted with Et₂O. The combined organic phase was dried over Na₂SO₄ and concentrated under reduced pressure. The crude pyrrolidine product was purified by silica gel column chromatography (EtOAc/hexanes gradient). The purified pyrrolidine was then dissolved in anhydrous CH₂Cl₂ (0.33 M) and pyridine (0.1 mL/mmol) was added. The solution was cooled to 0 °C and then methyl chloroformate (1.5 equiv) was added dropwise. The orange mixture was stirred for further 16 h, allowing the temperature to rise to rt. The reaction mixture was quenched by adding 0.1 M HCl and extracted with CH₂Cl₂ twice. The combined organic layer was washed with sat. aq. NaHCO₃ and brine, dried over Na₂SO₄

and concentrated under reduced pressure. The crude protected nitropyrrolidine was purified by silica gel column chromatography (EtOAc/hexanes gradient).

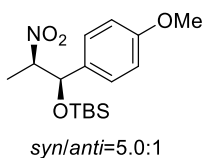


Compound 1a. Nitroalkane **1a** was prepared according to general procedure A using nitroethane and benzaldehyde on a 10 mmol scale. Silica gel column chromatography (0→5% EtOAc/hexanes) afforded the title compound as a colorless oil (2.0 g, 68% over 2 steps, 2.2:1 *dr*); $R_f = 0.44$ (5% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3) δ 7.39 – 7.28 (m, 10H, *syn* + *anti*), 5.39 (d, $J = 3.8$ Hz, 1H, *anti*), 4.92 (d, $J = 9.2$ Hz, 1H, *syn*), 4.70 (dq, $J = 9.2, 6.8$ Hz, 1H, *syn*), 4.56 (qd, $J = 6.7, 3.9$ Hz, 1H, *anti*), 1.43 (d, $J = 6.6$ Hz, 3H *anti*), 1.23 (d, $J = 6.8$ Hz, 3H, *syn*), 0.89 (s, 9H *anti*), 0.79 (s, 9H, *syn*), 0.01 (s, 3H *anti*), -0.01 (s, 3H, *syn*), -0.17 (s, 3H *anti*), -0.27 (s, 3H, *syn*); ^{13}C NMR (126 MHz, CDCl_3) δ 140.0 (*anti*), 139.2 (*syn*), 129.0 (*anti*), 128.8 (*syn*), 128.6 (*anti*), 128.4 (*anti*), 127.4 (*syn*), 126.4 (*syn*), 89.7 (*syn*), 88.5 (*anti*), 77.8 (*syn*), 76.0 (*anti*), 25.8 (*anti*), 25.6 (*syn*), 18.3 (*anti*), 18.1 (*syn*), 16.2 (*syn*), 11.5 (*anti*), -4.7 (*anti*), -4.7 (*syn*), -5.5 (*anti*), -5.6 (*syn*); HRMS (ESI) m/z calcd. for $\text{C}_{15}\text{H}_{25}\text{NO}_3\text{Si}$ $[\text{M}+\text{NH}_4]^+$: 313.1942, found: 313.1936.

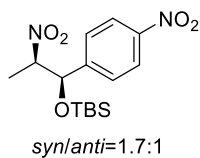


Compound 1b. Nitroalkane **1b** was prepared according to general procedure A using nitroethane and *p*-tolualdehyde on a 5 mmol scale. Silica gel column chromatography (0→5% EtOAc/hexanes) afforded the title compound as a colorless oil (0.89 g, 58% over 2 steps, 4.0:1 *dr*); ^1H NMR (400 MHz, CDCl_3) δ 7.25 – 7.13 (m, 8H, *syn* + *anti*), 5.35 (d, $J = 3.9$ Hz, 1H, *anti*), 4.89

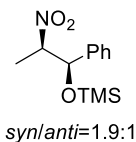
(d, $J = 9.2$ Hz, 1H, *syn*), 4.67 (dq, $J = 9.2, 6.8$ Hz, 1H, *syn*), 4.53 (qd, $J = 6.6, 3.9$ Hz, 1H, *anti*), 2.35 (s, 3H, *syn*), 2.34 (s, 3H, *anti*), 1.42 (d, $J = 6.6$ Hz, 3H, *anti*), 1.22 (d, $J = 6.8$ Hz, 3H, *syn*), 0.88 (s, 9H, *anti*), 0.79 (s, 9H, *syn*), 0.00 (s, 3H, *anti*), -0.02 (s, 3H, *syn*), -0.17 (s, 3H, *anti*), -0.26 (s, 3H, *syn*); ^{13}C NMR (101 MHz, CDCl_3) δ 138.7 (*syn*), 138.1 (*anti*), 137.0 (*anti*), 136.2 (*syn*), 129.5 (*syn*), 129.3 (*anti*), 127.3 (*syn*), 126.3 (*anti*), 89.8 (*syn*), 88.6 (*anti*), 77.6 (*syn*), 76.0 (*anti*), 25.8 (*anti*), 25.6 (*syn*), 21.4 (*syn*), 21.3 (*anti*), 18.3 (*anti*), 18.1 (*syn*), 16.2 (*syn*), 11.6 (*anti*), -4.6 (*syn*), -4.6 (*anti*), -5.5 (*anti*), -5.6 (*syn*); HRMS (ESI) m/z calcd. for $\text{C}_{16}\text{H}_{27}\text{NO}_3\text{Si}$ $[\text{M}+\text{Na}]^+$: 332.1652, found: 332.1649.



Compound 1c. Nitroalkane **1c** was prepared according to general procedure A using nitroethane and *p*-anisaldehyde on a 10 mmol scale. Silica gel column chromatography (0→5% EtOAc/hexanes) afforded the title compound as a yellow oil (1.75 g, 54% over 2 steps, 5.0:1 *dr*); ^1H NMR (400 MHz, CDCl_3) δ 7.27 – 7.21 (m, 4H, *syn* + *anti*), 6.91 – 6.86 (m, 4H, *syn* + *anti*), 5.30 (d, $J = 4.2$ Hz, 1H, *anti*), 4.87 (d, $J = 9.2$ Hz, 1H, *syn*), 4.66 (dq, $J = 9.2, 6.8$ Hz, 1H, *syn*), 4.52 (qd, $J = 6.7, 4.2$ Hz, 1H, *anti*), 3.82 (s, 3H, *syn*), 3.80 (s, 3H, *anti*), 1.44 (d, $J = 6.6$ Hz, 3H, *anti*), 1.22 (d, $J = 6.8$ Hz, 3H, *syn*), 0.88 (s, 9H, *anti*), 0.79 (s, 9H, *syn*), 0.00 (s, 3H, *anti*), -0.02 (s, 3H, *syn*), -0.17 (s, 3H, *anti*), -0.26 (s, 3H, *syn*); ^{13}C NMR (101 MHz, CDCl_3) δ 160.0 (*syn*), 159.6 (*anti*), 132.0 (*anti*), 131.3 (*syn*), 128.5 (*syn*), 127.6 (*anti*), 114.1 (*syn*), 113.9 (*anti*), 89.8 (*syn*), 88.6 (*anti*), 77.4 (*syn*), 75.8 (*anti*), 55.4 (*syn* + *anti*), 25.8 (*anti*), 25.6 (*syn*), 18.2 (*anti*), 18.1 (*syn*), 16.2 (*syn*), 11.9 (*anti*), -4.6 (*syn* + *anti*), -5.5 (*anti*), -5.6 (*syn*); HRMS (ESI) m/z calcd. for $\text{C}_{16}\text{H}_{27}\text{NO}_4\text{Si}$ $[\text{M}+\text{Na}]^+$: 348.1602, found: 348.1599.

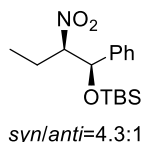


Compound 1d. Nitroalkane **1d** was prepared according to general procedure A using nitroethane and 4-nitrobenzaldehyde on a 5 mmol scale. Silica gel column chromatography (0→10% EtOAc/hexanes) afforded the title compound as a yellow solid (1.18 g, 69% over 2 steps, 1.7:1 *dr*); ^1H NMR (400 MHz, CDCl_3) δ 8.28 – 8.22 (m, 4H, *syn* + *anti*), 7.58 – 7.52 (m, 4H, *syn* + *anti*), 5.47 (d, J = 4.0 Hz, 1H, *anti*), 5.07 (d, J = 8.8 Hz, 1H, *syn*), 4.69 (dq, J = 8.9, 6.8 Hz, 1H, *syn*), 4.57 (qd, J = 6.7, 4.0 Hz, 1H, *anti*), 1.44 (d, J = 6.7 Hz, 3H, *anti*), 1.27 (d, J = 6.9 Hz, 3H, *syn*), 0.90 (s, 9H, *anti*), 0.81 (s, 9H, *syn*), 0.04 (s, 3H, *anti*), 0.02 (s, 3H, *syn*), -0.15 (s, 3H, *anti*), -0.23 (s, 3H, *syn*); ^{13}C NMR (101 MHz, CDCl_3) δ 148.4 (*syn*), 148.1 (*anti*), 147.2 (*anti*), 146.4 (*syn*), 128.2 (*syn*), 127.3 (*anti*), 124.1 (*syn*), 124.0 (*anti*), 89.0 (*syn*), 87.8 (*anti*), 76.7 (*syn*), 75.3 (*anti*), 25.7 (*anti*), 25.6 (*syn*), 18.2 (*anti*), 18.1 (*syn*), 15.9 (*syn*), 11.7 (*anti*), -4.6 (*syn*), -4.7 (*anti*), -5.5 (*anti*), -5.6 (*syn*); HRMS (ESI) m/z calcd. for $\text{C}_{15}\text{H}_{24}\text{N}_2\text{O}_5\text{Si}$ $[\text{M}+\text{H}]^+$: 341.1527, found: 341.1523.

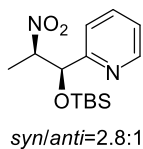


Compound 1e. Nitroalkane **1e** was prepared according to general procedure A using nitroethane and benzaldehyde on a 5 mmol scale. TMSCl was employed instead of TBSCl at the protection step. Silica gel column chromatography (0→5% EtOAc/hexanes) afforded the title compound as a colorless oil (0.89 g, 70% over 2 steps, 1.9:1 *dr*); ^1H NMR (500 MHz, CDCl_3) δ 7.39 – 7.28 (m, 10H, *syn* + *anti*), 5.39 (d, J = 4.1 Hz, 1H, *anti*), 4.93 (d, J = 9.3 Hz, 1H, *syn*), 4.69 (dq, J = 9.2, 6.8 Hz, 1H, *syn*), 4.58 (qd, J = 6.7, 4.1 Hz, 1H, *anti*), 1.40 (d, J = 6.6 Hz, 3H, *anti*), 1.24 (d, J = 6.8 Hz, 3H, *syn*), 0.03 (s, 9H, *anti*), -0.05 (s, 9H, *syn*); ^{13}C NMR (126 MHz, CDCl_3) δ 139.9 (*anti*),

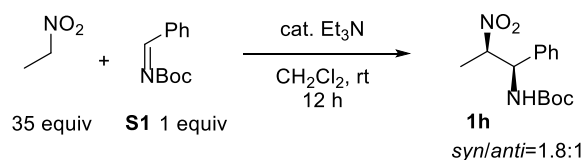
139.2 (*syn*), 128.9 (*anti*), 128.8 (*syn*), 128.6 (*anti*), 128.3 (*anti*), 127.3 (*syn*), 126.2 (*syn*), 89.7 (*syn*), 88.4 (*anti*), 77.5 (*syn*), 75.8 (*anti*), 16.3 (*syn*), 11.6 (*anti*), -0.2 (*anti*), -0.2 (*syn*); HRMS (ESI) m/z calcd. for $C_{12}H_{19}NO_3Si$ $[M+NH_4]^+$: 271.1473, found: 271.1466.



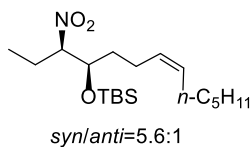
Compound 1f. Nitroalkane **1f** was prepared according to general procedure A using 1-nitropropane and benzaldehyde on a 10 mmol scale. Silica gel column chromatography (0→5% EtOAc/hexanes) afforded the title compound as a colorless oil (1.74 g, 56% over 2 steps, 4.3:1 *dr*); 1H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 10H, *syn* + *anti*), 5.08 (d, J = 5.9 Hz, 1H, *anti*), 4.92 (d, J = 9.3 Hz, 1H, *syn*), 4.53 (ddd, J = 11.3, 9.3, 3.2 Hz, 1H, *syn*), 4.45 (ddd, J = 10.9, 5.9, 2.8 Hz, 1H, *anti*), 2.14 (ddq, J = 14.5, 10.9, 7.2 Hz, 1H, *anti*), 1.89 (dq, J = 15.0, 7.6, 2.8 Hz, 1H, *anti*), 1.78 (ddq, J = 14.5, 11.2, 7.3 Hz, 1H, *syn*), 1.24 (dq, J = 14.9, 7.5, 3.2 Hz, 1H, *syn*), 0.91 (t, J = 7.4 Hz, 3H, *anti*), 0.88 (s, 9H, *anti*), 0.81 (t, J = 7.4 Hz, 3H, *syn*), 0.78 (s, 9H, *syn*), 0.02 (s, 3H, *anti*), -0.02 (s, 3H, *syn*), -0.21 (s, 3H, *anti*), -0.29 (s, 3H, *syn*); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.0 (*anti*), 139.6 (*syn*), 129.0 (*anti*), 128.8 (*syn*), 128.6 (*anti*), 128.6 (*anti*), 127.4 (*syn*), 126.7 (*syn*), 96.7 (*syn*), 96.1 (*anti*), 77.2 (*syn*), 76.3 (*anti*), 25.8 (*anti*), 25.6 (*syn*), 23.7 (*syn*), 21.5 (*anti*), 18.2 (*anti*), 18.1 (*syn*), 10.7 (*anti*), 10.4 (*syn*), -4.6 (*anti*), -4.7 (*syn*), -5.3 (*anti*), -5.6 (*syn*); HRMS (ESI) m/z calcd. for $C_{16}H_{27}NO_3Si$ $[M+Na]^+$: 332.1652, found: 332.1647.



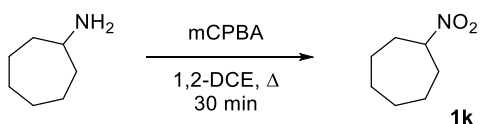
Compound 1g. Nitroalkane **1g** was prepared according to general procedure A using nitroethane and 2-pyridinecarboxaldehyde on a 5 mmol scale. Silica gel column chromatography (0→20% EtOAc/hexanes) afforded the title compound as a colorless oil (1.17 g, 79% over 2 steps, 2.8:1 *dr*); ¹H NMR (400 MHz, CDCl₃) δ 8.59 – 8.54 (m, 2H, *syn* + *anti*), 7.77 – 7.71 (m, 2H, *syn* + *anti*), 7.50 (dq, *J* = 7.9, 1.0 Hz, 1H, *anti*), 7.45 (dt, *J* = 7.9, 1.1 Hz, 1H, *syn*), 7.28 – 7.24 (m, 1H, *syn*), 7.22 (ddd, *J* = 7.7, 4.8, 1.1 Hz, 1H, *anti*), 5.59 (d, *J* = 2.9 Hz, 1H, *anti*), 5.11 (d, *J* = 8.3 Hz, 1H, *syn*), 4.97 (qd, *J* = 6.8, 2.9 Hz, 1H, *anti*), 4.83 (dq, *J* = 8.4, 6.8 Hz, 1H, *syn*), 1.33 (d, *J* = 6.8 Hz, 3H, *syn*), 1.30 (d, *J* = 6.7 Hz, 3H, *anti*), 0.92 (s, 9H, *anti*), 0.82 (s, 9H, *syn*), 0.04 (s, 3H, *anti*), 0.03 (s, 3H, *syn*), -0.08 (s, 3H, *anti*), -0.22 (s, 3H, *syn*); ¹³C NMR (101 MHz, CDCl₃) δ 159.7 (*anti*), 159.2 (*syn*), 149.3 (*anti*), 149.2 (*syn*), 137.1 (*syn*), 136.9 (*anti*), 123.6 (*syn*), 122.9 (*anti*), 121.9 (*syn*), 120.9 (*anti*), 88.7 (*syn*), 86.5 (*anti*), 78.3 (*syn*), 76.7 (*anti*), 25.9 (*anti*), 25.6 (*syn*), 18.2 (*anti*), 18.1 (*syn*), 15.9 (*syn*), 10.6 (*anti*), -4.7 (*anti*), -4.8 (*syn*), -5.5 (*syn*), -5.5 (*anti*); HRMS (ESI) *m/z* calcd. for C₁₄H₂₄N₂O₃Si [M+H]⁺: 297.1629, found: 297.1627.



Compound 1h. *N*-Boc imine **S1** was prepared following a literature procedure reported by Lam.⁴ The *N*-Boc imine **S1** (0.37 g, 1.8 mmol, 1 equiv), nitroethane (4.5 mL, 63 mmol, 35 equiv), and Et₃N (25 μ L, 0.18 mmol, 0.1 equiv) were dissolved in anhydrous CH₂Cl₂ (15 mL, 0.125 M) and stirred for 12 h at rt. The solvent was evaporated under reduced pressure and the crude *aza*-Henry product was purified by silica gel column chromatography (0 \rightarrow 25% EtOAc/hexanes) to afford the title compound as a white solid (0.33 g, 65%, 1.8:1 *dr*). The spectral data were in agreement with literature values.⁵⁻⁶

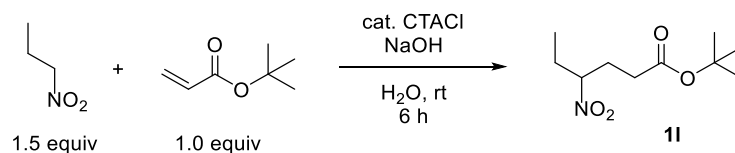


Compound 1i. Nitroalkane **1i** was prepared according to general procedure A using 1-nitropropane and *cis*-4-decenal on a 1.4 mmol scale. Silica gel column chromatography (0→5% EtOAc/hexanes) afforded the title compound as a colorless oil (0.46 g, 92% over 2 steps, 5.6:1 *dr*); R_f = 0.49 (5% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3) δ 5.44 – 5.37 (m, 2H, *syn* + *anti*), 5.33 – 5.26 (m, 2H, *syn* + *anti*), 4.45 (ddd, J = 11.2, 8.1, 3.4 Hz, 1H, *syn*), 4.38 (ddd, J = 10.9, 5.1, 3.0 Hz, 1H, *anti*), 4.14 (dt, J = 8.4, 4.4 Hz, 1H, *syn*), 4.09 (q, J = 5.5 Hz, 1H, *anti*), 2.21 – 2.13 (m, 2H, *syn* + *anti*), 2.08 – 1.98 (m, 6H, *syn* + *anti*), 1.90 (ddq, J = 14.5, 11.1, 7.2 Hz, 1H, *syn*), 1.81 (dtd, J = 14.9, 7.4, 2.9 Hz, 1H, *anti*), 1.76 – 1.67 (m, 2H, *syn* + *anti*), 1.65 – 1.52 (m, 4H, *syn* + *anti*), 1.38 – 1.24 (m, 12H, *syn* + *anti*), 0.99 – 0.94 (m, 6H, *syn* + *anti*), 0.91 – 0.87 (m, 15H, *syn* + *anti*), 0.86 (s, 9H, *syn*), 0.06 (s, 3H, *syn*), 0.05 (s, 3H, *anti*), 0.02 (s, 6H, *syn* + *anti*); ^{13}C NMR (126 MHz, CDCl_3) δ 131.3 (*anti*), 131.2 (*syn*), 128.4 (*syn*), 128.2 (*anti*), 94.2 (*syn*), 93.3 (*anti*), 73.3 (*anti*), 73.0 (*syn*), 34.2 (*anti*), 33.3 (*syn*), 31.7 (*syn*), 31.7 (*anti*), 29.5 (*syn* + *anti*), 27.4 (*syn*), 27.4 (*anti*), 25.9 (*anti*), 25.8 (*syn*), 23.1 (*syn*), 22.7 (*syn* + *anti*), 22.6 (*anti*), 21.8 (*anti*), 21.2 (*syn*), 18.1 (*anti*), 18.1 (*syn*), 14.2 (*syn* + *anti*), 10.9 (*anti*), 10.6 (*syn*), -4.3 (*anti*), -4.3 (*syn*), -4.7 (*anti*), -5.3 (*syn*); HRMS (ESI) m/z calcd. for $\text{C}_{19}\text{H}_{39}\text{NO}_3\text{Si}$ $[\text{M}+\text{H}]^+$: 358.2772, found: 358.2772.



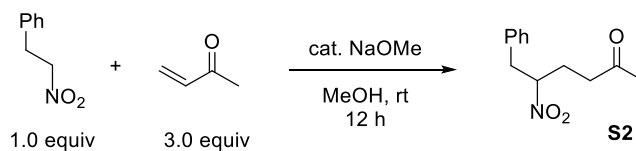
Compound 1k. Following a literature procedure reported by Borden,⁷ *m*-chloroperbenzoic acid (40 mmol, 4 equiv) was dissolved in 1,2-DCE (15 mL, 1.5 mL/mmol of amine) in a 3-neck round-bottom flask equipped with a condenser and a pressure-equalizing dropping funnel.

Cycloheptylamine (10 mmol, 1 equiv) in 1,2-DCE (10 mL, 1.0 mL/mmol of amine) was added dropwise to the refluxing peracid solution. Reflux was continued for 30 min after the addition and then the reaction mixture was cooled, filtered, washed with 1 M NaOH three times, dried over Na₂SO₄, and evaporated under reduced pressure. The crude nitrocycloheptane was purified by vacuum distillation to afford the title compound as a colorless oil (1.13 g, 79%); ¹H NMR (500 MHz, CDCl₃) δ 4.58 (tt, *J* = 9.3, 4.7 Hz, 1H), 2.27 – 2.19 (m, 2H), 2.14 – 2.06 (m, 2H), 1.85 – 1.77 (m, 2H), 1.75 – 1.64 (m, 1H), 1.63 – 1.57 (m, 3H), 1.55 – 1.46 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 87.8, 33.2, 28.2, 24.0; HRMS (ESI) *m/z* calcd. for C₇H₁₃NO₂ [M+H]⁺: 144.1019, found: 144.1018.

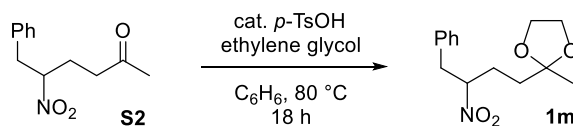


Compound 11. Following a literature procedure reported by Ballini,⁸ 1-nitropropane (4.0 mL, 45 mmol, 1.5 equiv) and *tert*-butyl acrylate (4.4 mL, 30 mmol, 1 equiv) were added to a solution of 0.025 M NaOH in H₂O (70 mL). Then, cetyltrimethylammonium chloride solution (25 wt % in H₂O, 4.0 mL, 3 mmol, 0.1 equiv) was added at rt and the resulting mixture was stirred until reaction completion confirmed by TLC analysis (6 h). The reaction mixture was then saturated with NaCl (28 g) and extracted with E₂O (4 x 50 mL). The combined organic layer was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The crude Michael addition product was purified by silica gel column chromatography (0→10% EtOAc/hexanes) to afford the title compound as a colorless oil (1.0 g, 15%); *R*_f = 0.40 (10% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 4.48 (tt, *J* = 9.1, 4.6 Hz, 1H), 2.35 – 2.13 (m, 3H), 2.10 – 1.95 (m, 2H), 1.81 (dq, *J* = 14.9, 7.5, 4.8 Hz, 1H), 1.45 (s, 9H), 0.97 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 171.4,

89.4, 81.2, 31.5, 28.6, 28.2, 27.4, 10.3; HRMS (ESI) m/z calcd. for $C_{10}H_{19}NO_4$ $[M+NH_4]^+$: 235.1652, found: 235.1648.

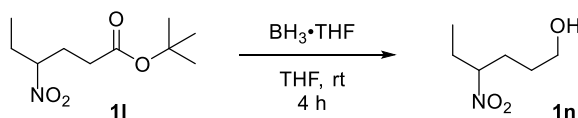


Compound S2. A solution of (2-nitroethyl)benzene (0.76 g, 5 mmol, 1 equiv), NaOMe (17.3 mg, 0.32 mmol, 6.3 mol %), and methyl vinyl ketone (1.25 mL, 15 mmol, 3 equiv) in MeOH (50 mL, 0.1 M) was stirred until TLC analysis indicated reaction completion (12 h). The solvent was evaporated under reduced pressure and the crude Michael addition product was purified by silica gel column chromatography (0→25% EtOAc/hexanes) to afford the title compound as a yellow oil (0.66 g, 60%); ^1H NMR (500 MHz, CDCl_3) δ 7.33 – 7.29 (m, 2H), 7.28 – 7.24 (m, 1H), 7.18 – 7.14 (m, 2H), 4.79 – 4.72 (m, 1H), 3.27 (dd, J = 14.2, 8.6 Hz, 1H), 3.05 (dd, J = 14.2, 5.8 Hz, 1H), 2.57 – 2.43 (m, 2H), 2.19 – 2.12 (m, 5H); ^{13}C NMR (126 MHz, CDCl_3) δ 206.4, 135.3, 129.0, 129.0, 127.6, 89.0, 40.3, 39.1, 30.2, 27.3; HRMS (ESI) m/z calcd. for $C_{12}H_{15}NO_3$ $[M+NH_4]^+$: 239.1390, found: 239.1387.

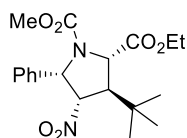


Compound 1m. Nitroketone **S2** (0.44 g, 2 mmol, 1 equiv) was dissolved in anhydrous C_6H_6 (4 mL, 2 mL/mmol) and ethylene glycol (0.17 mL, 3 mmol, 1.5 equiv) and *p*-toluenesulfonic acid monohydrate (7.6 mg, 0.044 mmol, 2.2 mol %) were added. The reaction mixture was stirred at 80 °C for 18 h, and then poured into H_2O . The aq. phase was extracted with Et_2O three times and the combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The

crude acetal product was purified by silica gel column chromatography (0→25% EtOAc/hexanes) to afford the title compound as a white solid (0.38 g, 71%); ^1H NMR (500 MHz, CDCl_3) δ 7.33 – 7.28 (m, 2H), 7.28 – 7.23 (m, 1H), 7.17 – 7.14 (m, 2H), 4.76 (dddd, $J = 9.8, 8.6, 5.8, 4.3$ Hz, 1H), 3.97 – 3.90 (m, 2H), 3.89 – 3.82 (m, 2H), 3.26 (dd, $J = 14.2, 8.6$ Hz, 1H), 3.03 (dd, $J = 14.2, 5.8$ Hz, 1H), 2.16 – 2.08 (m, 1H), 1.95 – 1.88 (m, 1H), 1.75 – 1.67 (m, 2H), 1.28 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 135.7, 129.0, 129.0, 127.5, 109.2, 90.0, 64.9, 64.8, 40.2, 35.0, 28.1, 24.1; HRMS (ESI) m/z calcd. for $\text{C}_{14}\text{H}_{19}\text{NO}_4$ $[\text{M}+\text{NH}_4]^+$: 283.1652, found: 283.1649.

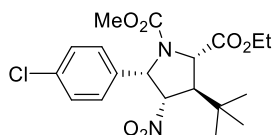


Compound 1n. To a solution of nitroester **1l** (0.44 g, 2 mmol, 1 equiv) in THF (3 mL, 1.5 mL/mmol of substrate) was added $\text{BH}_3\cdot\text{THF}$ (1 M in THF, 10 mL, 10 mmol, 5 equiv) at rt. The mixture was stirred for 4 h, then MeOH (14 mL, 35 mmol, 3.5 mmol/mmol of $\text{BH}_3\cdot\text{THF}$) was added dropwise. After 5 min the reaction mixture was poured into 0.5 M HCl. The aq. layer was extracted with Et_2O six times, the combined organic layer was washed with brine, dried over Na_2SO_4 , and carefully concentrated under reduced pressure. The crude nitroalcohol product was purified by silica gel column chromatography (0→70% Et_2O /pentane) to afford the title compound as a colorless oil (0.20 g, 68%); $R_f = 0.15$ (40% Et_2O /pentane); ^1H NMR (500 MHz, CDCl_3) δ 4.46 (tt, $J = 9.3, 4.5$ Hz, 1H), 3.73 – 3.63 (m, 2H), 2.09 – 1.94 (m, 2H), 1.92 – 1.76 (m, 2H), 1.62 – 1.54 (m, 2H), 1.32 (s, 1H, OH), 0.97 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 90.3, 61.9, 30.1, 28.9, 27.4, 10.4; HRMS (ESI) m/z calcd. for $\text{C}_6\text{H}_{13}\text{NO}_3$ $[\text{M}+\text{Na}]^+$: 170.0788, found: 170.0787.



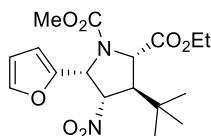
Compound 1o. Nitropyrrolidine **1o** was prepared according to general procedure B on a 5 mmol scale. Silica gel column chromatography (0→30% EtOAc/hexanes) afforded the title compound as a white solid (0.95 g, 50% over 2 steps); ^1H NMR (500 MHz, CDCl_3) δ 7.53 – 7.49 (m, 2H), 7.33 – 7.29 (m, 2H), 7.29 – 7.25 (m, 1H), 5.38 (d, J = 8.6 Hz, 1H, br), 5.26 (dd, J = 8.7, 2.5 Hz, 1H), 4.66 (s, 1H, br), 4.42 – 4.30 (m, 2H), 3.62 (s, 3H, br), 3.07 (t, J = 2.8 Hz, 1H), 1.37 (t, J = 7.1 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3) δ 171.4, 155.1 (br), 135.6 (br), 128.4, 128.3, 126.8, 91.6 (br), 66.5 (br), 62.2 (br), 61.9, 57.3 (br), 53.3, 33.0, 27.4, 14.2; HRMS (ESI) m/z calcd. for $\text{C}_{19}\text{H}_{26}\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 379.1864, found: 379.1857.

*Because of the carbamate bond rotation equilibrium, broadened signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



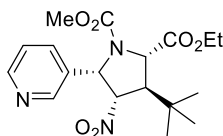
Compound 1p. Nitropyrrolidine **1p** was prepared according to general procedure B on a 5 mmol scale. Silica gel column chromatography (0→30% EtOAc/hexanes) afforded the title compound as a white solid (1.4 g, 68% over 2 steps); ^1H NMR (400 MHz, CDCl_3) δ 7.47 (d, J = 8.5 Hz, 2H), 7.28 (d, J = 8.5 Hz, 2H), 5.34 (d, J = 7.9 Hz, 1H, br), 5.25 (dd, J = 8.7, 2.5 Hz, 1H), 4.64 (s, 1H, br), 4.35 (q, J = 7.1 Hz, 2H), 3.64 (s, 3H, br), 3.05 (t, J = 2.7 Hz, 1H), 1.37 (t, J = 7.1 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.4, 155.3 (br), 143.5 (br), 134.5, 128.7, 128.5, 91.2 (br), 66.1 (br), 62.3 (br), 62.1, 56.9 (br), 53.5, 33.1, 27.5, 14.3; HRMS (ESI) m/z calcd. for $\text{C}_{19}\text{H}_{25}\text{ClN}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 413.1474, found: 413.1470.

*Because of the carbamate bond rotation equilibrium, broadened signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



Compound 1q. Nitropyrrolidine **1q** was prepared according to general procedure B on a 3 mmol scale. Silica gel column chromatography (0→40% EtOAc/hexanes) afforded the title compound as a white solid (0.80 g, 72% over 2 steps); ¹H NMR (500 MHz, CDCl₃) δ 7.31 (dd, *J* = 1.8, 0.9 Hz, 1H), 6.63 – 6.56 (m, 1H, br), 6.32 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.57 (d, *J* = 5.0 Hz, 1H, br), 5.21 (dd, *J* = 8.7, 5.0 Hz, 1H), 4.52 (s, 1H, br), 4.34 – 4.22 (m, 2H), 3.69 (s, 3H, br), 3.29 (t, *J* = 4.6 Hz, 1H, br), 1.31 (t, *J* = 7.1 Hz, 3H), 1.02 (s, 9H); ¹³C NMR (126 MHz, CDCl₃) δ 171.3, 154.5 (br), 148.9 (br), 142.8, 111.0, 109.7, 88.4 (br), 62.0, 61.1 (br), 59.6 (br), 55.4 (br), 53.5, 33.1, 27.4, 14.2; HRMS (ESI) *m/z* calcd. for C₁₇H₂₄N₂O₇ [M+H]⁺: 369.1656, found: 369.1646.

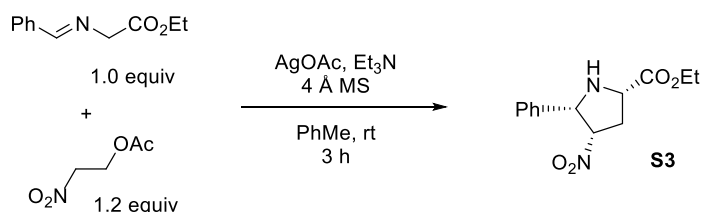
*Because of the carbamate bond rotation equilibrium, broadened signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



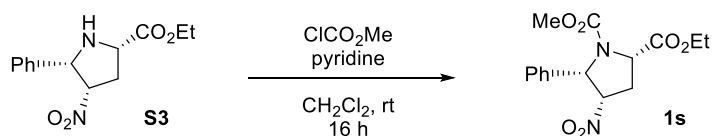
Compound 1r. Nitropyrrolidine **1r** was prepared according to general procedure B on a 4.4 mmol scale. Silica gel column chromatography (0→100% EtOAc/hexanes) afforded the title compound as a white solid (0.57 g, 34% over 2 steps); ¹H NMR (500 MHz, CDCl₃) δ 8.62 (s, 1H), 8.52 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.03 (s, 1H, br), 7.25 (dd, *J* = 7.9, 4.6 Hz, 1H), 5.38 (s, 1H, br), 5.28 (dd, *J* =

8.7, 2.4 Hz, 1H), 4.66 (s, 1H, br), 4.36 (q, $J = 7.1$ Hz, 2H), 3.68 (s, 3H, br), 3.08 (t, $J = 2.7$ Hz, 1H), 1.37 (t, $J = 7.1$ Hz, 3H), 1.07 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3) δ 171.4, 155.0 (br), 150.0, 148.8, 134.7, 131.7 (br), 123.6, 91.5 (br), 64.4 (br), 62.3 (br), 62.2, 57.6 (br), 53.6, 33.2, 27.5, 14.3; HRMS (ESI) m/z calcd. for $\text{C}_{18}\text{H}_{25}\text{N}_3\text{O}_6$ $[\text{M}+\text{H}]^+$: 380.1816, found: 380.1810.

*Because of the carbamate bond rotation equilibrium, broadened signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.

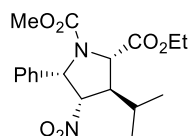


Compound S3. Following a literature procedure reported by Nyerges and Pak,¹¹ ethyl 2-(benzylideneamino)acetate (0.57 g, 3 mmol, 1 equiv) and 2-acetoxynitroethanol (0.48 g, 3.6 mmol, 1.2 equiv) were dissolved in anhydrous PhMe (15 mL, 0.2 M) then AgOAc (0.75 g, 4.5 mmol, 1.5 equiv) and 4 Å MS (3 g, 1 g/mmol of substrate) were added. The reaction mixture was cooled to 0 °C and Et₃N (0.84 mL, 6 mmol, 2 equiv) were added slowly to the well stirred reaction mixture. After 10 min, the reaction mixture was allowed to warm to rt. When reaction completion was indicated by TLC analysis (3 h), sat. aq. NH₄Cl (7.5 mL) was added, the precipitate was filtered off and the residue was extracted with Et₂O. The combined organic phase was dried over Na₂SO₄ and concentrated under reduced pressure. The crude pyrrolidine product was purified by silica gel column chromatography (0→50% EtOAc/hexanes) to afford the title compound as a yellow solid (0.15 g, 19%); $R_f = 0.23$ (50% EtOAc/hexanes). The spectral data were in agreement with literature values.¹¹



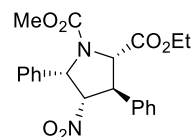
Compound 1s. Pyrrolidine **S3** (0.15 g, 0.56 mmol, 1 equiv) was dissolved in anhydrous CH_2Cl_2 (2 mL, 0.3 M) and pyridine (56 μL , 0.1 mL/mmol of substrate) was added. The solution was cooled to 0 $^\circ\text{C}$ and then methyl chloroformate (70 μL , 0.90 mmol, 1.6 equiv) was added dropwise. The orange mixture was stirred for further 16 h, allowing the temperature to rise to rt. The reaction mixture was quenched by adding 0.1 M HCl and extracted with CH_2Cl_2 twice. The combined organic layer was washed with sat. aq. NaHCO_3 and brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude protected nitropyrrolidine was purified by silica gel column chromatography (0 \rightarrow 50% EtOAc/hexanes) to afford the title compound as a yellow oil (0.16 g, 90%); R_f = 0.34 (50% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3) δ 7.53 (d, J = 7.1 Hz, 2H), 7.37 – 7.28 (m, 3H), 5.46 (s, 1H, br), 5.30 (dt, J = 8.3, 7.1 Hz, 1H), 4.61 (dd, J = 8.3, 7.1 Hz, 1H), 4.43 – 4.29 (m, 2H), 3.61 (s, 3H, br), 2.99 (s, 1H, br), 2.70 (dt, J = 14.3, 7.6 Hz, 1H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 170.7, 155.3 (br), 135.0 (br), 128.8, 128.6, 127.1, 86.4, 64.2 (br), 62.0, 58.6, 53.4, 31.0 (br), 14.3; HRMS (ESI) m/z calcd. for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 323.1238, found: 323.1227.

*Because of the carbamate bond rotation equilibrium, broadened signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



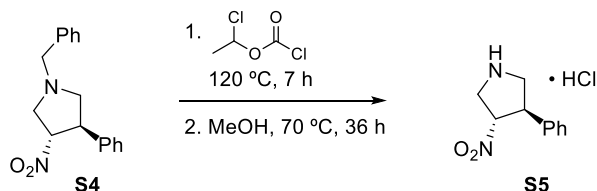
Compound 1t. Nitropyrrolidine **1t** was prepared according to general procedure G on a 2.7 mmol scale. Silica gel column chromatography (0→30% EtOAc/hexanes) afforded the title compound as a colorless oil (0.75 g, 76% over 2 steps); ^1H NMR (500 MHz, CDCl_3) δ 7.55 (d, $J = 7.0$ Hz, 2H), 7.36 – 7.27 (m, 3H), 5.41 (s, 1H, br), 5.17 (dd, $J = 8.9, 7.1$ Hz, 1H), 4.41 – 4.30 (m, 3H), 3.56 (s, 3H, br), 3.22 (td, $J = 7.0, 4.7$ Hz, 1H), 1.98 (pd, $J = 6.9, 4.8$ Hz, 1H), 1.38 (t, $J = 7.1$ Hz, 3H), 1.04 (d, $J = 6.9$ Hz, 3H), 1.02 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 171.6, 155.0 (br), 135.7 (br), 128.8, 128.5, 127.1, 89.8, 64.3 (br), 62.0, 61.8, 53.4, 49.9 (br), 28.8 (br), 19.7, 19.2 (br), 14.3; HRMS (ESI) m/z calcd. for $\text{C}_{18}\text{H}_{24}\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 365.1707, found: 365.1700.

*Because of the carbamate bond rotation equilibrium, broadened signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.

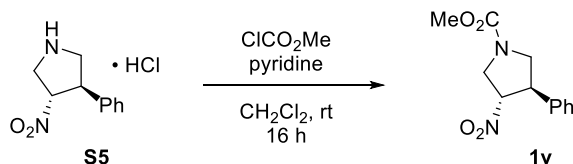


Compound 1u. Nitropyrrolidine **1u** was prepared according to general procedure G on a 9.4 mmol scale. Silica gel column chromatography (0→30% EtOAc/hexanes) afforded the title compound as a white solid (2.0 g, 53% over 2 steps); $R_f = 0.28$ (30% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3) δ 7.66 (d, $J = 7.2$ Hz, 2H), 7.41 – 7.31 (m, 6H), 7.29 – 7.26 (m, 2H), 5.72 – 5.54 (m, 1H, br), 5.47 (t, $J = 9.8$ Hz, 1H), 4.53 (d, $J = 9.9$ Hz, 1H), 4.42 – 4.15 (m, 3H), 3.78 – 3.56 (m, 3H, br), 1.16 (s, 3H, br); ^{13}C NMR (126 MHz, CDCl_3) δ 170.5, 155.2 (br), 135.3 (br), 133.8 (br), 129.4, 129.1, 129.0, 128.8, 127.8 (br), 127.2, 91.0 (br), 64.5, 63.9 (br, split), 63.0 (br, split), 61.9, 53.5, 50.0 (br, split), 48.7 (br, split), 14.2; HRMS (ESI) m/z calcd. for $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 399.1551, found: 399.1545.

*Because of the carbamate bond rotation equilibrium, broadened/split signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



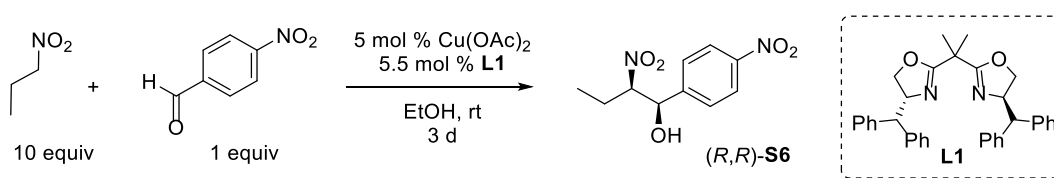
Compound S5. A solution of *N*-benzylated nitropyrrolidine **S4** (0.50 g, 1.77 mmol, 1 equiv) in 1-chloroethylchloroformate (4 mL, 8 mL/g of substrate) was heated to reflux. After 7 h, the reaction mixture was cooled to rt, and the volatile was removed under reduced pressure. The residue obtained was taken up in MeOH (10 mL, 20 mL/g of substrate) and the contents were heated to reflux. After 4 h, MeOH was removed under reduced pressure and the residue was triturated with Et₂O to afford the HCl salt of debenzylated pyrrolidine as a brown solid (0.37 g, 92% over 2 steps); ¹H NMR (500 MHz, CD₃OD, NH signal not visible) δ 7.47 – 7.37 (m, 5H), 5.49 (ddd, *J* = 8.2, 6.5, 3.7 Hz, 1H), 4.24 – 4.19 (m, 1H), 4.12 (ddd, *J* = 10.3, 7.8, 6.5 Hz, 1H), 3.99 (dd, *J* = 13.9, 8.3 Hz, 1H), 3.93 (dd, *J* = 11.9, 7.8 Hz, 1H), 3.54 (dd, *J* = 11.9, 10.3 Hz, 1H); ¹³C NMR (126 MHz, CD₃OD) δ 136.8, 130.5, 129.8, 128.5, 89.4, 52.1, 51.1, 49.7; HRMS (ESI) *m/z* calcd. for C₁₀H₁₂N₂O₂ [M+H]⁺: 193.0972, found: 193.0972.



Compound 1v. To a flame-dried flask containing pyrrolidine-HCl salt **S5** (0.36 g, 1.57 mmol, 1 equiv) were added anhydrous CH₂Cl₂ (5 mL, 0.33 M) and pyridine (0.31 mL, 0.2 mL/mmol). The

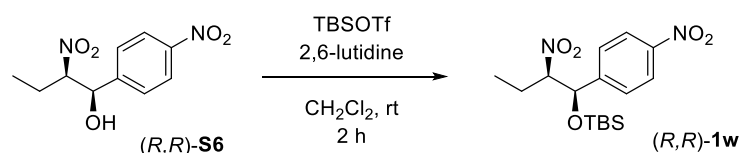
mixture was cooled to 0 °C and then methyl chloroformate (0.18 mL, 2.4 mmol, 1.5 equiv) was added dropwise. The orange mixture was stirred for further 16 h, allowing the temperature to rise to rt. The reaction mixture was quenched by adding 0.1 M HCl and extracted with CH₂Cl₂ twice. The combined organic layer was washed with sat. aq. NaHCO₃ and brine, dried over Na₂SO₄ and concentrated under reduced pressure. The crude protected nitropyrrolidine was purified by silica gel column chromatography (0→30% EtOAc/hexanes) to afford the title compound as a yellow oil (0.33 g, 84%); *R*_f = 0.55 (50% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 7.41 – 7.35 (m, 2H), 7.35 – 7.30 (m, 1H), 7.24 (d, *J* = 7.4 Hz, 2H, br), 4.98 (s, 1H, br), 4.19 – 3.91 (m, 4H), 3.82 – 3.70 (m, 4H); ¹³C NMR (126 MHz, CDCl₃) δ 155.1 (br, split), 154.9 (br, split), 137.7 (br, split), 137.6 (br, split), 129.5, 128.4, 127.1, 89.8 (br, split), 88.9 (br, split), 53.1, 50.5 (br, split), 50.4 (br, split), 49.4 (br, split), 49.2 (br, split), 48.9 (br, split), 48.2 (br, split); HRMS (ESI) *m/z* calcd. for C₁₂H₁₄N₂O₄ [M+H]⁺: 251.1026, found: 251.1027.

*Because of the carbamate bond rotation equilibrium, broadened/split signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰

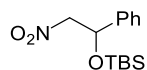


Compound (R,R)-S6. Following a literature procedure reported by Evans,¹² chiral box ligand **L1** (14.1 mg 0.0275 mmol, 5.5 mol %) and Cu(OAc)₂ (4.5 mg, 0.025 mmol, 5 mol %) were added to a screw cap vial containing a stir bar. EtOH (0.75 mL) was added and the mixture was stirred for 1 h. To the resulting solution 1-nitropropane (0.45 mL, 5 mmol, 10 equiv) and 4-nitrobenzaldehyde (76 mg, 0.5 mmol, 1 equiv) were added. The reaction was stirred at rt until ¹H NMR analysis indicated reaction completion (3 d). The reaction was concentrated under reduced pressure and the

crude material was purified by silica gel column chromatography (0→10% then 10→15% EtOAc/hexanes) to afford the major *syn* diastereomer **S6** as a yellow solid (54.2 mg, 45%, >20:1 *dr*). The spectral data were in agreement with literature values.¹³ The enantiomeric ratio (70:30) was determined by chiral HPLC analysis of compound (*R,R*)-**S6** in comparison with an authentic sample of racemic material (CHIRALPAK® AD-H, 5 to 50% *i*PrOH/hexane gradient over 22 min, 0.7 mL/min, 254 nm): *t*_R = 14.5min (major), 17.2 min (minor).



Compound (*R,R*)-1w. To a solution of nitroalcohol (*R,R*)-**S6** (48.0 mg, 0.2 mmol, 1 equiv) in anhydrous CH₂Cl₂ (1 mL, 0.2 M) were added TBSOTf (92 μL, 0.4 mmol, 2 equiv) and 2,6-lutidine (47 μL, 0.4 mmol, 2 equiv). The reaction mixture was stirred for 2 h at rt and then quenched by careful addition of H₂O. The aqueous layer was extracted with CH₂Cl₂ twice. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude protected Henry product was purified by silica gel column chromatography (0→5% EtOAc/hexanes) to afford the title compound as a yellow solid (48.2 mg, 68%); *R*_f = 0.23 (5% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 8.26 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 8.7 Hz, 2H), 5.05 (d, *J* = 9.1 Hz, 1H), 4.51 (ddd, *J* = 11.3, 9.1, 3.2 Hz, 1H), 1.82 (ddq, *J* = 14.4, 11.4, 7.2 Hz, 1H), 1.27 – 1.18 (m, 1H), 0.85 (t, *J* = 7.4 Hz, 3H), 0.80 (s, 9H), 0.01 (s, 3H), -0.25 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 148.4, 146.8, 128.3, 124.2, 96.1, 76.2, 25.6, 23.6, 18.1, 10.3, -4.6, -5.6; HRMS (ESI) *m/z* calcd. for C₁₆H₂₆N₂O₅Si [M+H]⁺: 355.1684, found: 355.1684.



Compound 1x. Nitroalkane **1x** was prepared according to general procedure A using nitromethane and benzaldehyde on a 10 mmol scale. Silica gel column chromatography (0→5% EtOAc/hexanes) afforded the title compound as a yellow oil (2.2 g, 78% over 2 steps); ¹H NMR (500 MHz, CDCl₃) δ 7.40 – 7.31 (m, 5H), 5.42 (dd, *J* = 9.9, 3.1 Hz, 1H), 4.54 (dd, *J* = 11.9, 9.9 Hz, 1H), 4.38 (dd, *J* = 11.9, 3.1 Hz, 1H), 0.84 (s, 9H), 0.03 (s, 3H), -0.15 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 139.4, 128.9, 128.8, 126.3, 83.0, 72.9, 25.7, 18.2, -4.7, -5.4; HRMS (ESI) *m/z* calcd. for C₁₄H₂₃NO₃Si [M+H]⁺: 282.1520, found: 282.1527.

III. Reaction Optimization

General procedure for reaction optimization. A pre-dried 1-dram vial equipped with a magnetic stir bar was charged with nitroalkane **1a** (29.5 mg, 0.1 mmol, 1 equiv) and anhydrous CH₃CN (1 mL, 0.1 M). CS₂ (36 μ L, 0.6 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to 0 °C using an ice/water bath. Subsequently, base (0.3 mmol, 3 equiv) was added in one portion and the vial was capped immediately. The yellow/orange reaction mixture was stirred for 5 min at 0 °C and then for 1 h at rt. The imine intermediate was hydrolyzed by adding H₂O (0.5 mL) and stirring for a minimum period of 2 h; lower yield was observed with insufficient hydrolysis period (< 2 h). The mixture was then diluted with CH₂Cl₂, washed with 1 M HCl, and extracted with CH₂Cl₂ three times. The combined organic phase was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The yield was obtained by ¹H NMR spectroscopic analysis of the crude reaction mixture (relative to mesitylene as an internal standard).

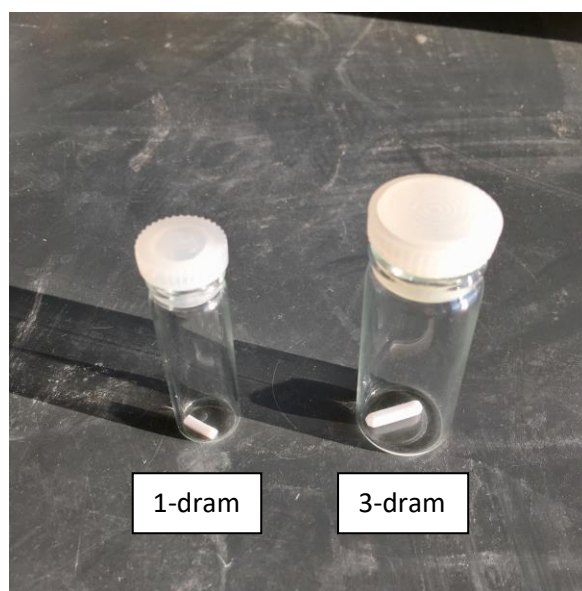
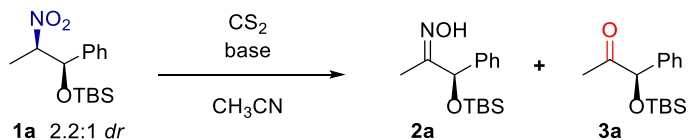


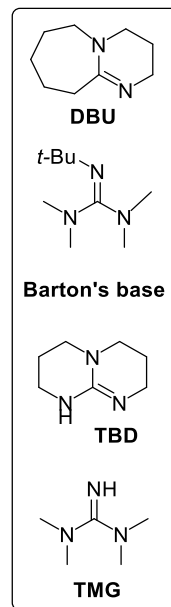
Figure S-1. Vials used for CS₂-mediated Nef reaction.

Table S-1. Reaction optimization with nitroalkane **1a**.

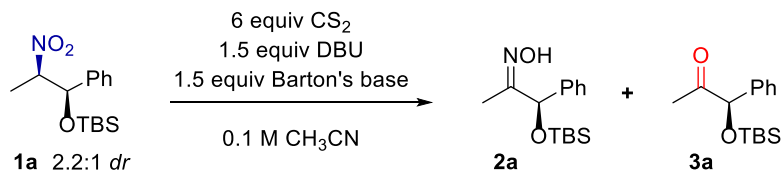


entry	CS ₂ equiv	base (equiv)	conc	time	temp	2a	3a	1a
1	6	Et ₃ N (3)	0.1 M	1 h	rt	8%	nd	90%
2	6	DIPA (3)	0.1 M	1 h	rt	nd	nd	95%
3	6	DBU (3)	0.1 M	1 h	rt	4%	53%	nd
4 ^a	6	DBU (3)	0.1 M	1 h	rt	trace	8%	nd
5	6	DBU (3)	0.5 M	1 h	rt	2%	43%	nd
6	6	DBU (3)	0.1 M	2 h	rt	trace	53%	nd
7	6	DBU (3)	0.1 M	30 min	rt	16%	52%	nd
8	6	DBU (3)	0.1 M	4 h	rt	trace	37%	nd
9	3	DBU (1.5)	0.1 M	2 h	rt	19%	40%	nd
10 ^b	6	DBU (3)	0.1 M	12 h	rt	73%	11%	12%
11 ^c	6	DBU (3)	0.1 M	12 h	rt	67%	13%	18%
12 ^d	6	DBU (3)	0.1 M	12 h	rt	71%	15%	14%
13	6	DBU (3)	0.01 M	1 h	rt	13%	67%	nd
14	6	DBU (3)	0.01 M	2 h	rt	13%	63%	nd
15	6	Barton's base (3)	0.1 M	1 h	rt	trace	38%	46%
16	6	Barton's base (3)	0.1 M	3 h	rt	3%	49%	40%
17	6	Barton's base (3)	0.01 M	1 h	rt	trace	29%	69%
18	6	Barton's base (3)	0.01 M	10 h	rt	trace	33%	63%
19	3	DBU (3)	0.01 M	1 h	rt	7%	36%	nd
20	12	DBU (3)	0.01 M	1 h	rt	6%	63%	nd
21	6	Et ₃ N (1.5) + DBU (3)	0.1 M	1 h	rt	trace	61%	nd
22	6	DBU (1.5) + Barton's base (1.5)	0.1 M	1 h	rt	7%	63%	nd
23	6	DBU (1.5) + Barton's base (1.5)	0.1 M	1 h	0 °C	42%	52%	nd
24	6	DBU (1.5) + Barton's base (1.5)	0.01 M	1 h	rt	8%	76%	nd
25	6	DBU (1.5) + Barton's base (1.5)	0.5 M	1 h	0 °C	55%	22%	nd
26 ^e	6	DBU (1.5) + Barton's base (1.5)	0.2 M	3 h	0-15 °C	11%	75%	nd
27	6	DBU (0.3) + Barton's base (0.3)	0.1 M	1 h	rt	42%	18%	38%
28	6	DBU (3)	0.1 M	5 min	0 °C	60%	32%	nd
29	3	DBU (1.5)	0.1 M	5 min	0 °C	62%	32%	nd
30	1.5	DBU (1.5)	0.1 M	5 min	0 °C	46%	11%	43%
31	3	DBU (0.5)	0.1 M	5 min	0 °C	34%	7%	58%
32	3	DBU (1)	0.05 M	5 min	0 °C	33%	6%	60%
33	3	DBU (1)	0.05 M	30 min	0 °C	45%	10%	42%
34	3	DBU (1)	0.05 M	3 h	rt	43%	13%	31%
36	3	DBU (1.5)	0.05 M	5 min	0 °C	37%	9%	53%
37	6	TBD (3)	0.1 M	1 h	rt	18%	47%	nd
38	3	TBD (1.5)	0.1 M	5 min	0 °C	52%	2%	44%
39	6	TBD (3)	0.2 M	30 min	0 °C	75%	5%	20%
40 ^e	6	TBD (3)	0.2 M	1 h	0-8 °C	81%	14%	5%
41	6	TMG (3)	0.1 M	1 h	rt	42%	5%	53%

Reactions were performed on a 0.1 mmol scale. Yields were determined by NMR using mesitylene internal standard. ^aHydrolysis period was 5 min. ^bReaction was run in 4:1 CH₃CN/H₂O. ^cReaction was run in 9:1 CH₃CN/H₂O. ^dReaction was run in 19:1 CH₃CN/H₂O. ^eReaction was slowly warmed up in an ice/water bath.



IV. Temperature Control Studies



General procedure for temperature control studies. A pre-dried 1-dram vial equipped with a magnetic stir bar was charged with nitroalkane **1a** (29.5 mg, 0.1 mmol, 1 equiv) and anhydrous CH₃CN (1 mL, 0.1 M). CS₂ (36 μ L, 0.6 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to 0 °C using an ice/water bath. Subsequently, DBU (23 μ L, 0.15 mmol, 1.5 equiv) was added in one portion and the vial was capped immediately. The yellow/orange reaction mixture was stirred for 5 min at 0 °C, and then Barton's base (30 μ L, 0.15 mmol, 1.5 equiv) was added in one portion. The reaction mixture was stirred for indicated period time while gradually warming up in the bath. The imine intermediate was hydrolyzed by adding H₂O (0.5 mL) and stirring for a minimum period of 2 h; lower yield was observed with insufficient hydrolysis period (< 2 h). The mixture was then diluted with CH₂Cl₂, washed with 1 M HCl, and extracted with CH₂Cl₂ three times. The combined organic phase was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The yield was obtained by ¹H NMR spectroscopic analysis of the crude reaction mixture (relative to mesitylene as an internal standard).

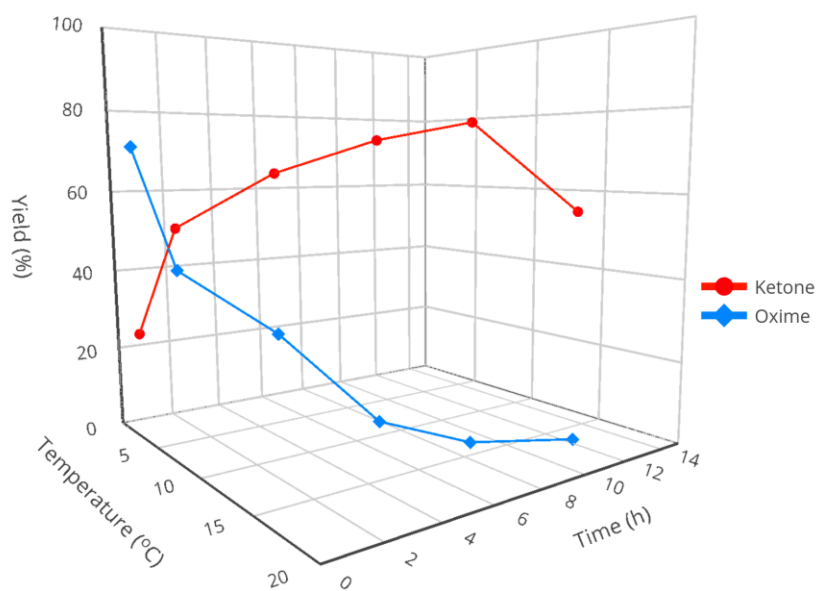
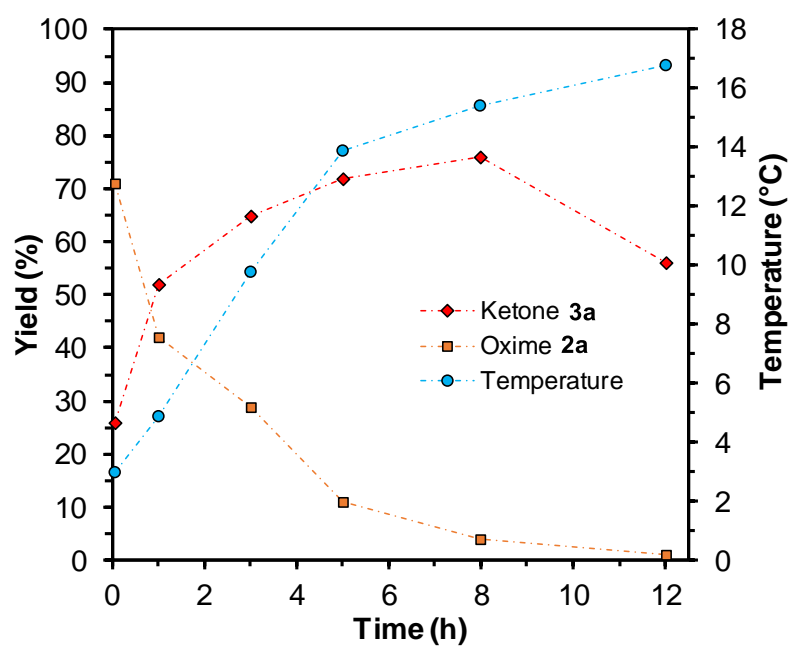


Figure S-2. Temperature control studies with nitroalkane **1a**. Scatter plots expressed in 2-D (top) and 3-D (bottom).

V. CS₂-Mediated Nef Reaction

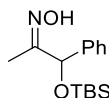
General procedure for CS₂-mediated Nef reaction. A pre-dried 3-dram vial equipped with a magnetic stir bar was charged with nitroalkane (0.2 mmol, 1 equiv) and anhydrous CH₃CN (4 mL, 0.05 M). CS₂ (72 μ L, 1.2 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to 0 °C using an ice/water bath. Subsequently, DBU (45 μ L, 0.3 mmol, 1.5 equiv) was added in one portion and the vial was capped immediately. The yellow/orange reaction mixture was stirred for 5 min at 0 °C, and then Barton's base (60 μ L, 0.3 mmol, 1.5 equiv) was added in one portion. The reaction mixture was stirred for another 5 min at 0 °C and then for 1 h at rt. The resulting imine intermediate was hydrolyzed by following below hydrolysis procedure 1/2/3.

Hydrolysis procedure 1. To the reaction mixture containing imine intermediate, H₂O (1 mL) was added and the mixture was stirred at rt for a minimum period of 2 h; lower yield was observed with insufficient hydrolysis period (< 2 h). The mixture was then diluted with CH₂Cl₂, washed with 1 M HCl, and extracted with CH₂Cl₂ three times. The combined organic phase was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford pure ketone product.

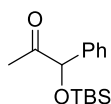
Hydrolysis procedure 2. The reaction mixture was diluted with 2-MTHF (20 mL) and 24% aq. NaCl (4 mL) was added. The mixture was cooled to 0 °C using an ice/water bath, and 1 M HCl (16 mL) was added slowly to the vigorously stirring mixture. Upon addition completion, the biphasic mixture was stirred at 0 °C for 30 min. Layers were separated, and the aq. layer was extracted with EtOAc three times. The combined organic phase was washed with sat. aq. NaHCO₃

and brine, dried over Na₂SO₄, and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford pure ketone product.

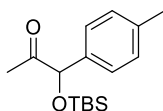
Hydrolysis procedure 3. The reaction mixture was diluted with 2-MTHF (20 mL) and 24% aq. NaCl (4 mL) was added. The mixture was cooled to 0 °C using an ice/water bath, and 2.5 M HCl (16 mL) was added slowly to the vigorously stirring mixture. Upon addition completion, the biphasic mixture was stirred at rt for a minimum period of 3 h. Layers were separated, and the aq. layer was extracted with EtOAc three times. The combined organic phase was washed with sat. aq. NaHCO₃ and brine, dried over Na₂SO₄, and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford pure ketone product.



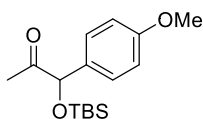
Compound 2a. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction (3 equiv of TBD was employed instead of the combination of DBU and Barton's base; the reaction was run at 0 °C for 30 min) and hydrolysis procedure 1 from nitroalkane **1a** (29.5 mg, 0.1 mmol). Silica gel column chromatography (0→10% EtOAc/hexanes) afforded oxime **2a** as a colorless oil (20.0 mg, 72%, 12.5:1 *dr*); R_f = 0.25 (10% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃, major diastereomer depicted) δ 7.40 (d, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 7.17 (s, 1H, br), 5.33 (s, 1H), 1.68 (d, *J* = 0.8 Hz, 3H), 0.95 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ¹³C NMR (126 MHz, CDCl₃, major diastereomer depicted) δ 160.7, 141.1, 128.3, 127.5, 125.7, 75.4, 25.9, 18.4, 8.6, -4.8, -5.0; HRMS (ESI) *m/z* calcd. for C₁₅H₂₅NO₂Si [M+H]⁺: 280.1727, found: 280.1728.



Compound 3a. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 1 from nitroalkane **1a** (59.0 mg, 0.2 mmol). Silica gel column chromatography (0→5% EtOAc/hexanes) afforded ketone **3a** as a colorless oil (36.9 mg, 70%); $R_f = 0.34$ (5% EtOAc/hexanes). The spectral data were in agreement with literature values.¹⁴

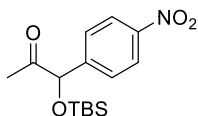


Compound 3b. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 3 from nitroalkane **1b** (61.9 mg, 0.2 mmol). Silica gel column chromatography (0→5% EtOAc/hexanes) afforded ketone **3b** as a yellow oil (39.6 mg, 71%); $R_f = 0.35$ (5% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 7.31 (d, $J = 8.0$ Hz, 2H), 7.15 (d, $J = 7.8$ Hz, 2H), 5.00 (s, 1H), 2.34 (s, 3H), 2.10 (s, 3H), 0.94 (s, 9H), 0.08 (s, 3H), -0.01 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 209.4, 137.9, 135.8, 129.3, 125.9, 81.3, 25.9, 24.0, 21.3, 18.4, -4.8, -5.0; HRMS (ESI) m/z calcd. for C₁₆H₂₆O₂Si [M+Na]⁺: 301.1594, found: 301.1593.

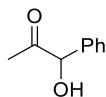


Compound 3c. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 2 from nitroalkane **1c** (65.1 mg, 0.2 mmol). Silica gel column chromatography (0→6% EtOAc/hexanes) afforded ketone **3c** as a yellow oil (39.4 mg, 67%); $R_f = 0.25$ (5% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 7.33 (d, $J = 8.4$ Hz, 2H),

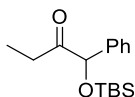
6.88 (d, $J = 8.8$ Hz, 2H), 4.99 (s, 1H), 3.80 (s, 3H), 2.10 (s, 3H), 0.94 (s, 9H), 0.08 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 209.4, 159.6, 130.9, 127.2, 114.1, 81.0, 55.4, 25.9, 24.0, 18.4, -4.8, -5.0; HRMS (ESI) m/z calcd. for $\text{C}_{16}\text{H}_{26}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$: 295.1724, found: 295.1727.



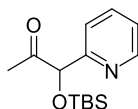
Compound 3d. The title compound was prepared following the general procedure for CS_2 -mediated Nef reaction and hydrolysis procedure 3 from nitroalkane **1d** (68.1 mg, 0.2 mmol). Silica gel column chromatography (0→8% EtOAc/hexanes) afforded ketone **3d** as a yellow oil (37.9 mg, 61%); $R_f = 0.16$ (5% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3) δ 8.22 (d, $J = 8.9$ Hz, 2H), 7.63 (d, $J = 8.4$ Hz, 2H), 5.12 (s, 1H), 2.14 (s, 3H), 0.97 (s, 9H), 0.12 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 208.1, 148.0, 145.9, 126.8, 123.9, 80.8, 25.8, 24.4, 18.3, -4.8, -5.0; HRMS (ESI) m/z calcd. for $\text{C}_{15}\text{H}_{23}\text{NO}_4\text{Si}$ $[\text{M}+\text{H}]^+$: 310.1469, found: 310.1469.



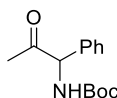
Compound 3e. The title compound was prepared following the general procedure for CS_2 -mediated Nef reaction and hydrolysis procedure 3 from nitroalkane **1e** (50.7 mg, 0.2 mmol). Silica gel column chromatography (0→25% EtOAc/hexanes) afforded α -hydroxy ketone **3e** as a white solid (22.9 mg, 76%); $R_f = 0.24$ (20% EtOAc/hexanes). The spectral data were in agreement with literature values.¹⁵



Compound 3f. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 2 from nitroalkane **1f** (61.9 mg, 0.2 mmol). Silica gel column chromatography (0→5% EtOAc/hexanes) afforded ketone **3f** as a colorless oil (24.0 mg, 43%); *R*_f = 0.37 (5% EtOAc/hexanes). The spectral data were in agreement with literature values.¹⁶

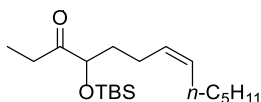


Compound 3g. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 1 (the organic phase was washed with H₂O instead of 1 M HCl) from nitroalkane **1g** (59.3 mg, 0.2 mmol). Silica gel column chromatography (0→20% EtOAc/hexanes) afforded ketone **3g** as a yellow oil (21.2 mg, 40%); *R*_f = 0.26 (20% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 8.56 (dt, *J* = 4.8, 1.3 Hz, 1H), 7.72 (td, *J* = 7.7, 1.8 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.22 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 5.21 (s, 1H), 2.17 (s, 3H), 0.94 (s, 9H), 0.12 (s, 3H), 0.02 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 207.1, 158.8, 149.3, 137.1, 123.0, 120.7, 82.5, 25.9, 25.3, 18.4, -4.9, -4.9; HRMS (ESI) *m/z* calcd. for C₁₄H₂₃NO₂Si [M+H]⁺: 266.1571, found: 266.1563.

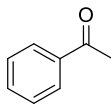


Compound 3h. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 1 (the organic phase was washed with H₂O instead of 1 M HCl) from nitroalkane **1h** (56.1 mg, 0.2 mmol). Silica gel column chromatography (0→20%

EtOAc/hexanes) afforded ketone **3h** as a yellow solid (24.2 mg, 49%); $R_f = 0.33$ (20% EtOAc/hexanes). The spectral data were in agreement with literature values.¹⁷



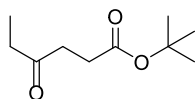
Compound 3i. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 1 from nitroalkane **1i** (71.5 mg, 0.2 mmol). Silica gel column chromatography (0→4% EtOAc/hexanes) afforded ketone **3i** as a yellow oil (35.2 mg, 54%); $R_f = 0.34$ (5% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 5.41 – 5.35 (m, 1H), 5.34 – 5.28 (m, 1H), 4.05 (dd, $J = 6.8, 5.0$ Hz, 1H), 2.56 (q, $J = 7.3$ Hz, 2H), 2.10 – 2.03 (m, 2H), 2.00 (qd, $J = 7.4, 1.4$ Hz, 2H), 1.73 – 1.57 (m, 2H), 1.36 – 1.24 (m, 6H), 1.03 (t, $J = 7.3$ Hz, 3H), 0.93 (s, 9H), 0.88 (t, $J = 7.1$ Hz, 3H), 0.06 (s, 3H), 0.05 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 214.9, 131.1, 128.5, 78.5, 35.3, 31.7, 30.9, 29.5, 27.3, 25.9, 22.8, 22.7, 18.2, 14.2, 7.5, -4.8, -4.8; HRMS (ESI) m/z calcd. for C₁₉H₃₈O₂Si [M+Na]⁺: 349.2533, found: 349.2529.



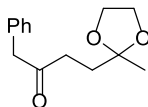
Compound 3j. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 1 (the solvent was evaporated at low temperature after work-up) from nitroalkane **1j** (30.2 mg, 0.2 mmol). Yield (43%) was determined by ¹H NMR using mesitylene internal standard, due to the volatility of the product. The spectral data were in agreement with literature values.¹⁸



Compound 3k. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 1 (the solvent was evaporated at low temperature after work-up) from nitroalkane **1k** (28.6 mg, 0.2 mmol). Yield (59%) was determined by ¹H NMR using mesitylene internal standard, due to the volatility of the product. The spectral data were in agreement with literature values.¹⁹

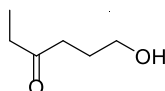


Compound 3l. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 1 (the organic phase was washed with H₂O instead of 1 M HCl) from nitroalkane **1l** (43.5 mg, 0.2 mmol). Silica gel column chromatography (0→15% EtOAc/hexanes) afforded ketone **3l** as a yellow oil (25.6 mg, 69%); R_f = 0.33 (15% EtOAc/hexanes). The spectral data were in agreement with literature values.²⁰

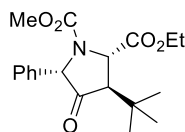


Compound 3m. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 1 (the organic phase was washed with H₂O instead of 1 M HCl) from nitroalkane **1m** (53.1 mg, 0.2 mmol). Silica gel column chromatography (0→30% EtOAc/hexanes) afforded ketone **3m** as a yellow oil (31.8 mg, 68%); R_f = 0.37 (30% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 7.32 (t, *J* = 7.3 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 7.20 (d, *J* = 6.8 Hz, 2H), 3.94 – 3.87 (m, 2H), 3.87 – 3.80 (m, 2H), 3.71 (s, 2H), 2.54 (t, *J* = 7.4 Hz, 2H), 1.97 (t, *J* = 7.5 Hz, 2H), 1.28 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 207.9, 134.5, 129.6,

128.8, 127.1, 109.4, 64.8, 50.2, 36.8, 32.9, 24.1; HRMS (ESI) m/z calcd. for $C_{14}H_{18}O_3$ $[M+H]^+$: 235.1329, found: 235.1328.

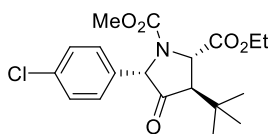


Compound 3n. The title compound was prepared following the general procedure for CS_2 -mediated Nef reaction and hydrolysis procedure 1 from nitroalkane **1n** (29.4 mg, 0.2 mmol). Silica gel column chromatography (0→50% Et_2O /pentane) afforded ketone **3n** as a yellow oil (9.8 mg, 42%); R_f = 0.25 (40% Et_2O /pentane). The spectral data were in agreement with literature values.²¹



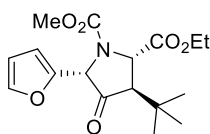
Compound 3o. The title compound was prepared following the general procedure for CS_2 -mediated Nef reaction and hydrolysis procedure 3 from nitropyrrolidine **1o** (71.5 mg, 0.2 mmol). Silica gel column chromatography (0→20% $EtOAc$ /hexanes) afforded pyrrolidinone **3o** as a white solid (66.9 mg, 96%); R_f = 0.47 (30% $EtOAc$ /hexanes); 1H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 7.6 Hz, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.29 (t, J = 7.3 Hz, 1H), 4.86 (s, 1H, br), 4.74 (s, 1H, br), 4.27 (qd, J = 7.2, 1.3 Hz, 2H), 3.84 – 3.51 (m, 3H, br), 2.54 (d, J = 4.4 Hz, 1H), 1.31 (t, J = 7.1 Hz, 3H), 1.10 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.6, 172.2, 156.2 (br), 136.6 (br), 128.5, 128.0, 126.9 (br), 67.8 (br), 61.9, 60.5 (br, split), 60.1 (br, split), 59.5, 53.4, 34.7, 27.6, 14.2; HRMS (ESI) m/z calcd. for $C_{19}H_{25}NO_5$ $[M+H]^+$: 348.1806, found: 348.1805.

*Because of the carbamate bond rotation equilibrium, broadened/split signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



Compound 3p. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 3 from nitropyrrolidine **1p** (82.6 mg, 0.2 mmol). Silica gel column chromatography (0→20% EtOAc/hexanes) afforded pyrrolidinone **3p** as a white solid (71.0 mg, 93%); *R*_f = 0.28 (20% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 7.52 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 4.97 – 4.61 (m, 2H, br), 4.26 (qd, *J* = 7.2, 1.4 Hz, 2H), 3.87 – 3.54 (m, 3H, br), 2.49 (dd, *J* = 4.3, 1.1 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.10 (s, 9H); ¹³C NMR (126 MHz, CDCl₃) δ 208.1, 172.2, 155.9 (br), 135.1 (br), 133.9, 128.7, 128.4 (br), 67.2 (br), 62.0, 60.9 (br, split), 60.2 (br, split), 59.4, 53.5, 34.9, 27.6, 14.2; HRMS (ESI) *m/z* calcd. for C₁₉H₂₄ClNO₅ [M+H]⁺: 382.1416, found: 382.1419.

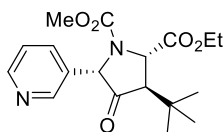
*Because of the carbamate bond rotation equilibrium, broadened/split signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



Compound 3q. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 3 from nitropyrrolidine **1q** (73.7 mg, 0.2 mmol). Silica gel column chromatography (0→20% EtOAc/hexanes) afforded pyrrolidinone **3q** as a yellow oil (54.3 mg, 80%); *R*_f = 0.45 (30% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃, major conformer depicted) δ 7.36 (s, 1H, br), 6.50 (d, *J* = 3.3 Hz, 1H), 6.34 (dd, *J* = 3.3, 1.9 Hz, 1H), 5.00 (s, 1H, br), 4.85 – 4.62 (m, 1H, br), 4.21 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H, br), 2.63 (dd, *J* =

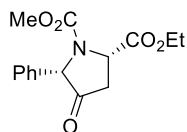
3.3, 1.2 Hz, 1H), 1.25 (t, $J = 7.1$ Hz, 3H), 1.09 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3 , major conformer depicted) δ 207.5 (br), 171.5, 156.7 (br), 149.4 (br), 142.8, 110.7, 109.5 (br, split), 108.9 (br, split), 61.9, 61.6, 60.6 (br, split), 60.2 (br, split), 59.4, 53.4, 35.0, 27.6, 14.2; HRMS (ESI) m/z calcd. for $\text{C}_{17}\text{H}_{23}\text{NO}_6$ $[\text{M}+\text{H}]^+$: 338.1598, found: 338.1594.

*Because of the carbamate bond rotation equilibrium, broadened/split signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



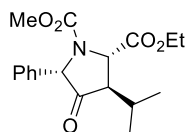
Compound 3r. The title compound was prepared following the general procedure for CS_2 -mediated Nef reaction and hydrolysis procedure 3 (aq. phase was neutralized with 3 M NaOH prior to extraction) from nitropyrrolidine **1r** (69.7 mg, 0.2 mmol). Silica gel column chromatography (0→80% EtOAc/hexanes) afforded pyrrolidinone **3r** as a colorless oil (40.5 mg, 58%); $R_f = 0.30$ (60% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3 , major conformer depicted) δ 8.54 (s, 2H, br), 7.99 (s, 1H, br), 7.29 (dd, $J = 8.1, 4.8$ Hz, 1H), 4.99 – 4.68 (m, 2H, br), 4.26 (q, $J = 7.1$ Hz, 2H), 3.81 – 3.57 (m, 3H, br), 2.49 (d, $J = 3.7$ Hz, 1H), 1.30 (t, $J = 7.1$ Hz, 3H), 1.11 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3 , major conformer depicted) δ 208.0 (br, split), 207.6 (br, split), 172.0, 155.7 (br), 149.2, 134.6 (br, split), 133.7 (br, split), 132.4 (br, split), 131.2 (br, split), 123.5 (br, split), 123.3 (br, split), 65.6 (br, split), 65.4 (br, split), 62.1, 60.8 (br, split), 60.5 (br, split), 59.4, 53.6, 35.0, 27.5, 14.2; HRMS (ESI) m/z calcd. for $\text{C}_{18}\text{H}_{24}\text{N}_2\text{O}_5$ $[\text{M}+\text{H}]^+$: 349.1758, found: 349.1753.

*Because of the carbamate bond rotation equilibrium, broadened/split signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



Compound 3s. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 3 from nitropyrrolidine **1s** (64.5 mg, 0.2 mmol). Silica gel column chromatography (0→40% EtOAc/hexanes) afforded pyrrolidinone **3s** as a yellow oil (30.3 mg, 52%); *R*_f = 0.28 (40% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 7.60 (d, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 1H), 4.99 (s, 1H, br), 4.82 (dd, *J* = 9.9, 6.7 Hz, 1H), 4.36 – 4.23 (m, 2H), 3.69 (s, 3H, br), 3.04 (dd, *J* = 19.0, 9.8 Hz, 1H), 2.79 (dd, *J* = 18.9, 6.7 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 206.2 (br), 171.5, 156.2 (br), 136.2 (br), 128.8, 128.2, 126.5, 66.7 (br), 62.1, 55.6, 53.4, 38.9 (br), 14.3; HRMS (ESI) *m/z* calcd. for C₁₅H₁₇NO₅ [M+H]⁺: 292.1180, found: 292.1174.

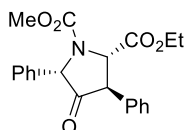
*Because of the carbamate bond rotation equilibrium, broadened/split signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



Compound 3t. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 3 from nitropyrrolidine **1t** (72.9 mg, 0.2 mmol). Silica gel column chromatography (0→20% EtOAc/hexanes) afforded pyrrolidinone **3t** as a

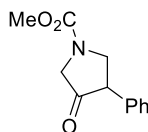
colorless oil (44.4 mg, 67%); $R_f = 0.57$ (30% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3) δ 7.61 (t, $J = 7.3$ Hz, 2H), 7.36 (t, $J = 7.4$ Hz, 2H), 7.30 (t, $J = 7.4$ Hz, 1H), 4.88 (s, 1H, br), 4.58 (s, 1H, br), 4.37 – 4.22 (m, 2H), 3.82 – 3.53 (m, 3H, br), 2.74 (ddd, $J = 6.5, 4.1, 0.9$ Hz, 1H), 2.36 (heptd, $J = 7.1, 4.2$ Hz, 1H), 1.33 (t, $J = 7.1$ Hz, 3H), 1.08 (d, $J = 7.0$ Hz, 3H), 1.00 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 208.6, 172.3, 156.7 (br), 136.6 (br), 128.7, 128.1, 126.5 (br), 67.5 (br), 61.9, 58.6, 56.0 (br), 53.4, 28.9 (br), 20.1, 18.4, 14.2; HRMS (ESI) m/z calcd. for $\text{C}_{18}\text{H}_{23}\text{NO}_5$ $[\text{M}+\text{H}]^+$: 334.1649, found: 334.1648.

*Because of the carbamate bond rotation equilibrium, broadened signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



Compound 3u. The title compound was prepared following the general procedure for CS_2 -mediated Nef reaction and hydrolysis procedure 3 from nitropyrrolidine **1u** (79.7 mg, 0.2 mmol). Silica gel column chromatography (0→20% EtOAc/hexanes) afforded pyrrolidinone **3u** as a colorless oil (47.0 mg, 64%); $R_f = 0.37$ (30% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3 , major conformer depicted) δ 7.69 (d, $J = 7.6$ Hz, 2H), 7.45 – 7.31 (m, 6H), 7.18 (d, $J = 6.8$ Hz, 2H), 5.15 (s, 1H, br), 4.81 (d, $J = 8.2$ Hz, 1H), 4.28 (q, $J = 7.1$ Hz, 2H), 4.01 (d, $J = 8.2$ Hz, 1H), 3.71 (s, 3H, br), 1.26 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3 , major conformer depicted) δ 204.9, 171.3, 158.0 (br, split), 156.2 (br, split), 154.6 (br, split), 130.2, 129.3, 128.9, 128.7 (br, split), 128.6 (br, split), 128.5, 128.4 (br), 128.3, 126.3 (br), 66.9 (br), 63.2 (br), 62.1, 56.1 (br), 53.6, 14.3 (br); HRMS (ESI) m/z calcd. for $\text{C}_{21}\text{H}_{21}\text{NO}_5$ $[\text{M}+\text{H}]^+$: 368.1493, found: 368.1489.

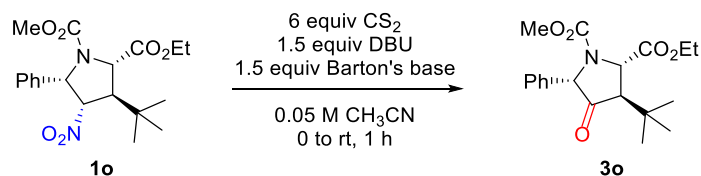
*Because of the carbamate bond rotation equilibrium, broadened/split signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.



Compound 3v. The title compound was prepared following the general procedure for CS₂-mediated Nef reaction and hydrolysis procedure 3 from nitropyrrolidine **1v** (50.1 mg, 0.2 mmol). Silica gel column chromatography (0→40% EtOAc/hexanes) afforded pyrrolidinone **3v** as a yellow oil (16.7 mg, 38%); *R*_f = 0.35 (40% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃, major conformer depicted) δ 7.37 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 7.4 Hz, 2H), 4.36 (s, 1H, br), 4.14 – 3.97 (m, 1H, br), 3.97 – 3.85 (m, 2H, br), 3.84 – 3.77 (m, 4H); ¹³C NMR (126 MHz, CDCl₃, major conformer depicted) δ 209.6 (br, split), 209.2 (br, split), 155.6 (br), 135.4 (br), 129.2, 128.0, 128.0, 54.0 (br, split), 53.4 (br, split), 53.1, 52.7 (br, split), 52.7 (br, split), 52.5 (br, split), 50.0 (br); HRMS (ESI) *m/z* calcd. for C₁₂H₁₃NO₃ [M+H]⁺: 220.0968, found: 220.0965.

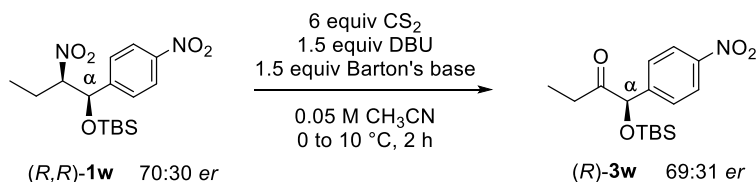
*Because of the carbamate bond rotation equilibrium, broadened/split signals were observed on the NMR. This phenomenon is seen with many tertiary carbamates.⁹⁻¹⁰ To further verify the NMR assignment, 2D NMR (HSQC and HMBC) spectra are provided.

VI. 1-mmol Scale Synthesis of Pyrrolidinone **3o**



Compound 3o. A pre-dried 50-mL round-bottom flask equipped with a magnetic stir bar was charged with nitropyrrolidine **1o** (0.38 g, 1 mmol, 1 equiv) and anhydrous CH₃CN (20 mL, 0.05 M). CS₂ (0.36 mL, 6 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to 0 °C using an ice/water bath. Subsequently, DBU (0.22 mL, 1.5 mmol, 1.5 equiv) was added in one portion and the flask was capped with glass stopper immediately. The yellow reaction mixture was stirred for 5 min at 0 °C, and then Barton's base (0.30 mL, 1.5 mmol, 1.5 equiv) was added in one portion. The reaction mixture was stirred for another 5 min at 0 °C and then for 1 h at rt. After dilution with 2-MTHF (100 mL), the mixture was cooled to 0 °C and 24% aq. NaCl (20 mL) was added. 2.5 M HCl (80 mL) was added slowly to the vigorously stirring biphasic mixture and stirring was continued for 8 h at rt. Layers were separated, and the aq. layer was extracted with EtOAc three times. The combined organic phase was washed with sat. aq. NaHCO₃ and brine, and the combined aq. phase was extracted with EtOAc three times. The combined organic phase was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography (0→20% EtOAc/hexanes) to afford pyrrolidinone **3o** as a white solid (0.34 g, 98%). Characterization data is given in Section V.

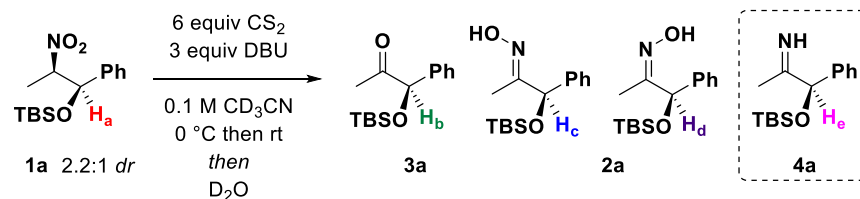
VII. Stereoretention Experiment



Compound (R)-1w. A pre-dried 1-dram vial equipped with a magnetic stir bar was charged with nitroalkane (*R,R*)-1w (47.9 mg, 0.135 mmol, 1 equiv) and anhydrous CH₃CN (2.7 mL, 0.05 M). CS₂ (49 μ L, 0.81 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to 0 $^\circ$ C using an ice/water bath. Subsequently, DBU (30 μ L, 0.20 mmol, 1.5 equiv) was added in one portion and the vial was capped immediately. The yellow/orange reaction mixture was stirred for 5 min at 0 $^\circ$ C, and then Barton's base (41 μ L, 0.20 mmol, 1.5 equiv) was added in one portion. The reaction mixture was stirred for 2 h while gradually warming up in the bath (0–10 $^\circ$ C). The imine intermediate was hydrolyzed by adding H₂O (0.7 mL) and stirring for 2 h. The mixture filtered through a pad of silica gel eluting with CH₂Cl₂, and the filtrate concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (0 \rightarrow 5% EtOAc/hexanes) to afford ketone (*R*)-3w as a yellow oil (23.1 mg, 53%); *R*_f = 0.22 (5% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 8.21 (d, *J* = 8.6 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 5.16 (s, 1H), 2.68 (dq, *J* = 18.8, 7.3 Hz, 1H), 2.48 (dq, *J* = 18.8, 7.2 Hz, 1H), 0.98 – 0.94 (m, 12H), 0.11 (s, 3H), 0.01 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 210.7, 147.9, 146.3, 126.8, 123.9, 80.6, 29.9, 25.8, 18.3, 7.4, -4.8, -5.0; HRMS (ESI) *m/z* calcd. for C₁₆H₂₅NO₄Si [M+H]⁺: 324.1626, found: 324.1621. The enantiomeric ratio (69:31) was determined by chiral HPLC analysis of compound (*R*)-3w in comparison with an authentic sample of racemic material (CHIRALPAK[®] AD-H, 1 to 5% *i*PrOH/hexane gradient over 22 min, 0.7 mL/min, 254 nm): *t*_R = 8.05 min (major), 8.55 min (minor).

VIII. Mechanistic Experiments

a. NMR monitoring studies



General procedure for NMR monitoring studies. A pre-dried 1-dram vial equipped with a magnetic stir bar was charged with nitroalkane **1a** (29.5 mg, 0.1 mmol, 1 equiv) and CD_3CN (1 mL, 0.1 M). CS_2 (36 μ L, 0.6 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to 0 °C using an ice/water bath. Subsequently, DBU (23 μ L, 0.3 mmol, 3 equiv) was added in one portion and the vial was capped immediately. The yellow/orange reaction mixture was stirred for 5 min at 0 °C, and then warmed to rt. A 50 μ L aliquot was removed from the reaction mixture at each time point and diluted with CD_3CN (0.5 mL) for 1H NMR analysis. After 3 h, the imine intermediate was hydrolyzed by adding D_2O (0.5 mL) and stirring for 2 h.

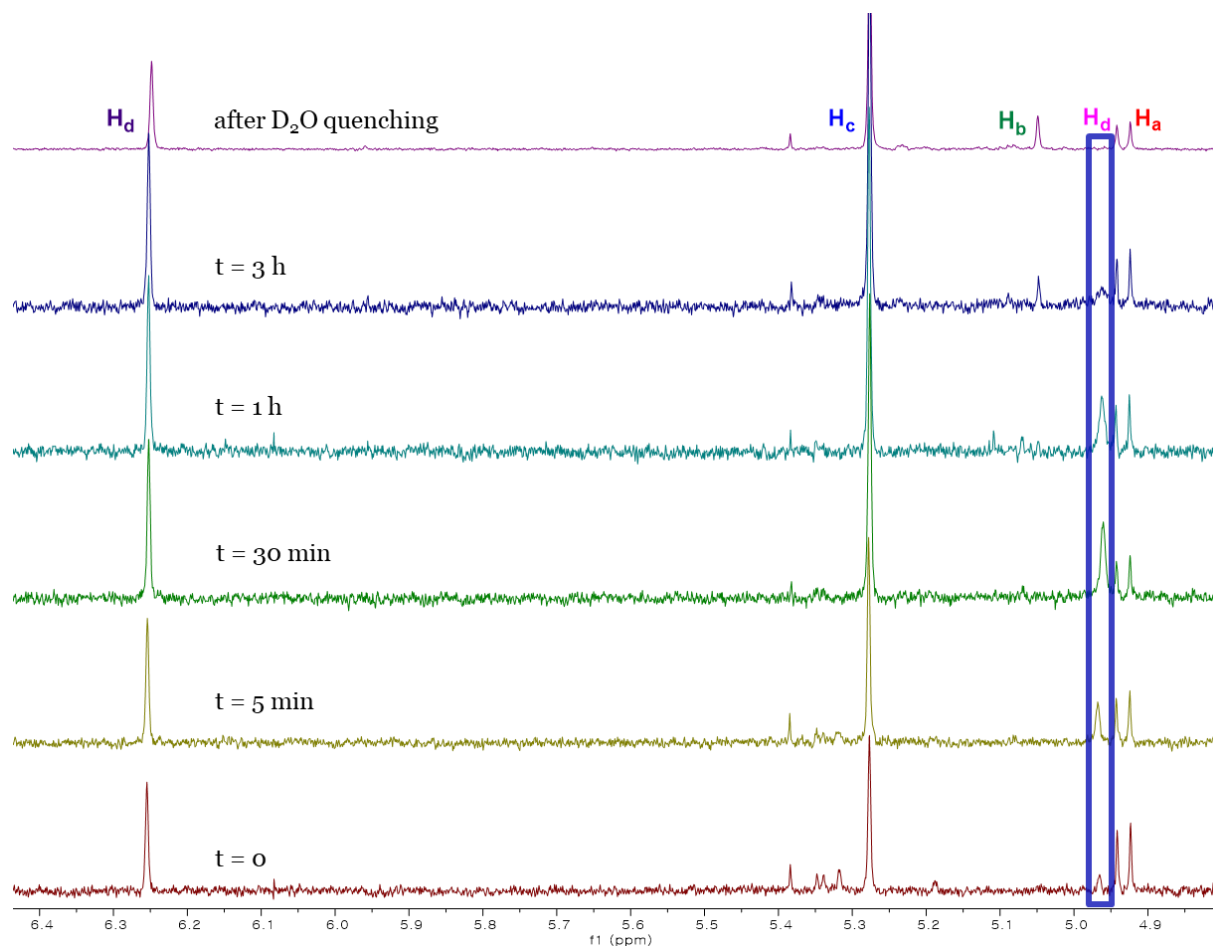
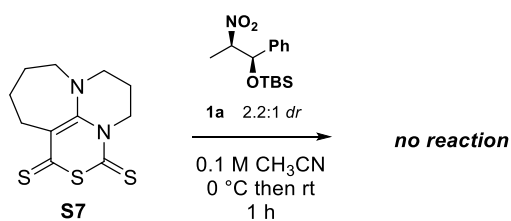


Figure S-3. NMR monitoring of CS₂-mediated Nef reaction indicating formation of imine intermediate **4w**.

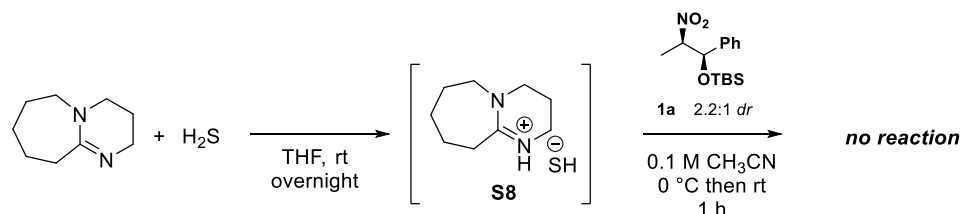
b. Reactivity of DBU-CS₂ adducts



Compound **S7** was prepared following a literature procedure reported by Jessop.²² To a suspension of CS₂-DBU adduct **S7** (81.1 mg, 0.3 mmol, 3 equiv) in anhydrous CH₃CN (1 mL) was added nitroalkane **1a** (29.5 mg, 0.1 mmol, 1 equiv) at 0 °C. The reaction was warmed to rt and stirred for

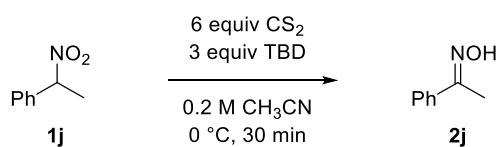
1 h. ^1H NMR analysis of crude reaction mixture indicated no consumption of starting nitroalkane

1a.



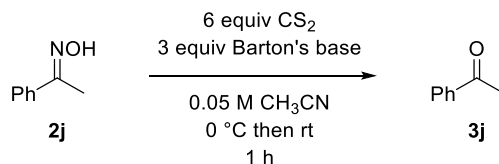
Compound **S8** was prepared by adding H_2S (0.8 M in THF, 0.75 mL, 0.6 mmol, 6 equiv) to DBU (90 μL , 0.6 mmol, 6 equiv) dropwise under N_2 atmosphere. A yellow-green solid formed immediately and solvent was evaporated under a flow of N_2 overnight. To the residue was added anhydrous CH_3CN (1 mL) and nitroalkane **1a** (29.5 mg, 0.1 mmol, 1 equiv) at $0\text{ }^\circ\text{C}$. The reaction was warmed to rt and stirred for 1 h. ^1H NMR analysis of crude reaction mixture indicated no consumption of starting nitroalkane **1a**.

c. Intermediacy of oxime/imine

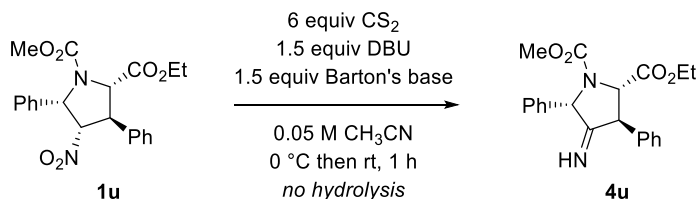


A pre-dried 1-dram vial equipped with a magnetic stir bar was charged with nitroalkane **1j** (30.2 mg, 0.2 mmol, 1 equiv) and anhydrous CH_3CN (1 mL, 0.2 M). CS_2 (72 μL , 1.2 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to $0\text{ }^\circ\text{C}$ using an ice/water bath. Subsequently, TBD (83.5 mg, 0.6 mmol, 3 equiv) was added in one portion and the vial was capped immediately. The yellow/orange reaction mixture was stirred for 30 min at $0\text{ }^\circ\text{C}$, and then quenched with 1 M HCl. Layers were separated, and the aq. phase was extracted with CH_2Cl_2 three

times. The combined organic phase was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography (0→15% Et₂O/pentane) to afford ketone **2j** as a white solid (23.0 mg, 85%, 3.8:1 *dr*); R_f = 0.44 (20% Et₂O/pentane). The spectral data were in agreement with literature values.²³



A pre-dried 1-dram vial equipped with a magnetic stir bar was charged with oxime **2j** (29.5 mg, 0.1 mmol, 1 equiv) and anhydrous CH₃CN (1 mL, 0.1 M). CS₂ (36 μL, 0.6 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to 0 °C using an ice/water bath. Subsequently, Barton's base (60 μL, 0.3 mmol, 3 equiv) was added in one portion and the vial was capped immediately. The yellow/orange reaction mixture was stirred for 5 min at 0 °C and then for 1 h at rt. The imine intermediate was hydrolyzed by adding H₂O (0.5 mL) and stirring overnight (12 h). The mixture was then diluted with CH₂Cl₂, washed with 1 M HCl, and extracted with CH₂Cl₂ three times. The combined organic phase was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The yield (14%; 70% BRSM yield) was obtained by ¹H NMR spectroscopic analysis of the crude reaction mixture (relative to mesitylene as an internal standard).



Compound 4u. A pre-dried 1-dram vial equipped with a magnetic stir bar was charged with nitropyrrolidine **1u** (39.8 mg, 0.1 mmol, 1 equiv) and anhydrous CH₃CN (2 mL, 0.05 M). CS₂ (36 μ L, 0.6 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to 0 °C using an ice/water bath. Subsequently, DBU (23 μ L, 0.15 mmol, 1.5 equiv) was added in one portion and the vial was capped immediately. The yellow/orange reaction mixture was stirred for 5 min at 0 °C, and then Barton's base (30 μ L, 0.15 mmol, 1.5 equiv) was added in one portion. The reaction mixture was stirred for another 5 min 0 °C and then for 1 h at rt. The resulting imine intermediate was directly diluted with CH₂Cl₂, washed with 1 M HCl, and extracted with CH₂Cl₂ three times. The combined organic phase was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. ¹H NMR spectroscopy showed a clean formation of imine intermediate **4u** which slowly decomposed at rt; 65% NMR yield relative to mesitylene internal standard. R_f = 0.28 (30% EtOAc/hexanes); HRMS (ESI) *m/z* calcd. for C₂₁H₂₂N₂O₄ [M+H]⁺: 367.1658, found: 367.1651.

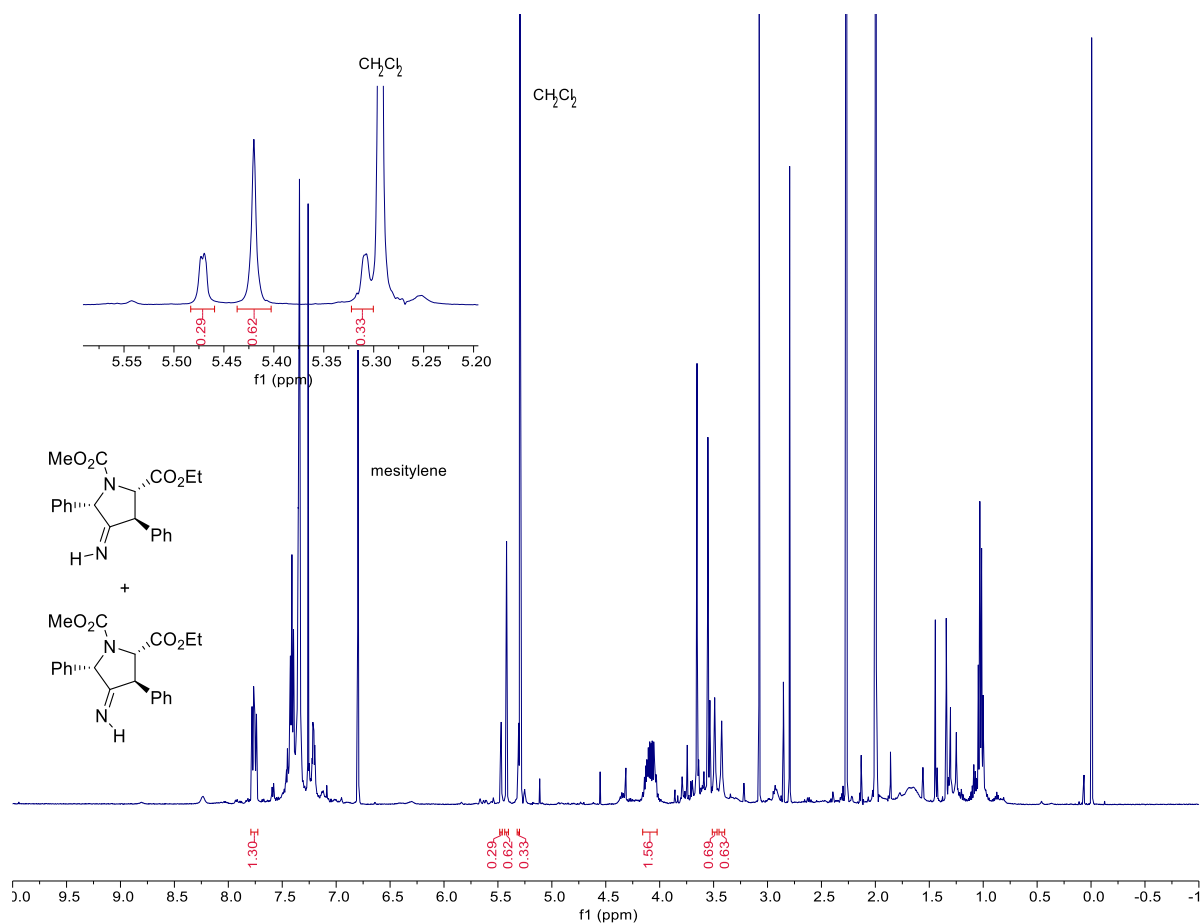
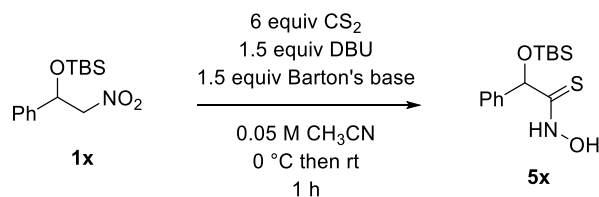


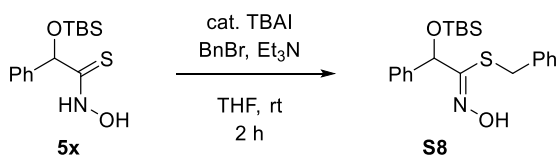
Figure 4. ^1H NMR (CDCl_3 , 500 MHz) spectrum of crude imine intermediate **4u**.

d. Formation and derivatization of thiohydroxamic acid **5x**



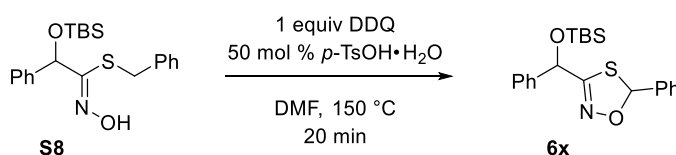
Compound 5x. A pre-dried 20-mL scintillation vial equipped with a magnetic stir bar was charged with nitroalkane **1x** (113 mg, 0.4 mmol, 1 equiv) and anhydrous CH_3CN (8 mL, 0.05 M). CS_2 (144 μL , 0.6 mmol, 6 equiv) was added to the well-stirring reaction mixture which was then cooled to

0 °C using an ice/water bath. Subsequently, DBU (90 μ L, 0.6 mmol, 1.5 equiv) was added in one portion and the vial was capped immediately. The yellow/orange reaction mixture was stirred for 5 min at 0 °C, and then Barton's base (120 μ L, 0.6 mmol, 1.5 equiv) was added in one portion. The reaction mixture was stirred for another 5 min 0 °C and then for 1 h at rt. The resulting mixture was directly diluted with CH₂Cl₂, washed with 1 M HCl, and extracted with CH₂Cl₂ three times. The combined organic phase was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography (0→10% EtOAc/hexanes) to afford thiohydroxamic acid **5x** as a yellow oil (55.9 mg, 47%); R_f = 0.54 (20% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃, one exchangeable proton not visible²⁴) δ 11.17 – 8.45 (m, 1H, br), 7.42 – 7.38 (m, 2H), 7.37 – 7.30 (m, 3H), 5.56 (s, 1H), 0.91 (s, 9H), 0.09 (s, 3H), -0.07 (s, 3H); ¹³C NMR (126 MHz, CDCl₃, C=S not visible²⁴) δ 139.8, 128.8, 128.7, 126.8, 25.9, 18.3, -4.7, -5.0; HRMS (ESI) m/z calcd. for C₁₄H₂₃NO₂SSi [M–H][–]: 296.1146, found: 296.1144.



Compound S8. Following a literature procedure reported by Pierce,²⁵ BnBn (18.2 μ L, 0.153 mmol, 1 equiv), TBAI (5.7 mg, 0.0153 mmol, 0.1 equiv), and Et₃N (21.3 μ L, 0.153 mmol, 1 equiv) were added to a stirred solution of thiohydroxamic acid **5x** (45.6 mg, 0.153 mmol, 1 equiv) in anhydrous THF (3 mL, 0.05 M). The reaction mixture was stirred at rt for 2 h, diluted with EtOAc, washed with sat. aq. Na₂SO₃ and extracted with EtOAc twice. The combined organic phase was washed with H₂O, 1 M HCl, and brine, dried over Na₂SO₄, and concentrated under reduced pressure. The crude benzylated product was purified by silica gel column chromatography (0→10% EtOAc/hexanes) to afford *N*-hydroxyimidothioate **S8** as a yellow oil (51.7 mg, 87%); R_f = 0.50

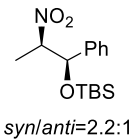
(20% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3) δ 7.78 – 7.71 (m, 1H), 7.47 (d, J = 8.1 Hz, 2H), 7.37 (t, J = 7.3 Hz, 2H), 7.31 (t, J = 7.2 Hz, 1H), 7.22 – 7.15 (m, 3H), 7.03 – 6.99 (m, 2H), 5.70 (s, 1H), 4.28 (d, J = 11.9 Hz, 1H), 3.62 (d, J = 11.9 Hz, 1H), 1.02 (s, 9H), 0.21 (s, 3H), 0.17 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 157.4, 140.5, 136.6, 129.2, 128.6, 128.5, 127.7, 127.5, 125.6, 76.8, 34.3, 26.0, 18.5, -4.6, -5.1; HRMS (ESI) m/z calcd. for $\text{C}_{21}\text{H}_{29}\text{NO}_2\text{SSi}$ $[\text{M}+\text{H}]^+$: 388.1761, found: 388.1760.



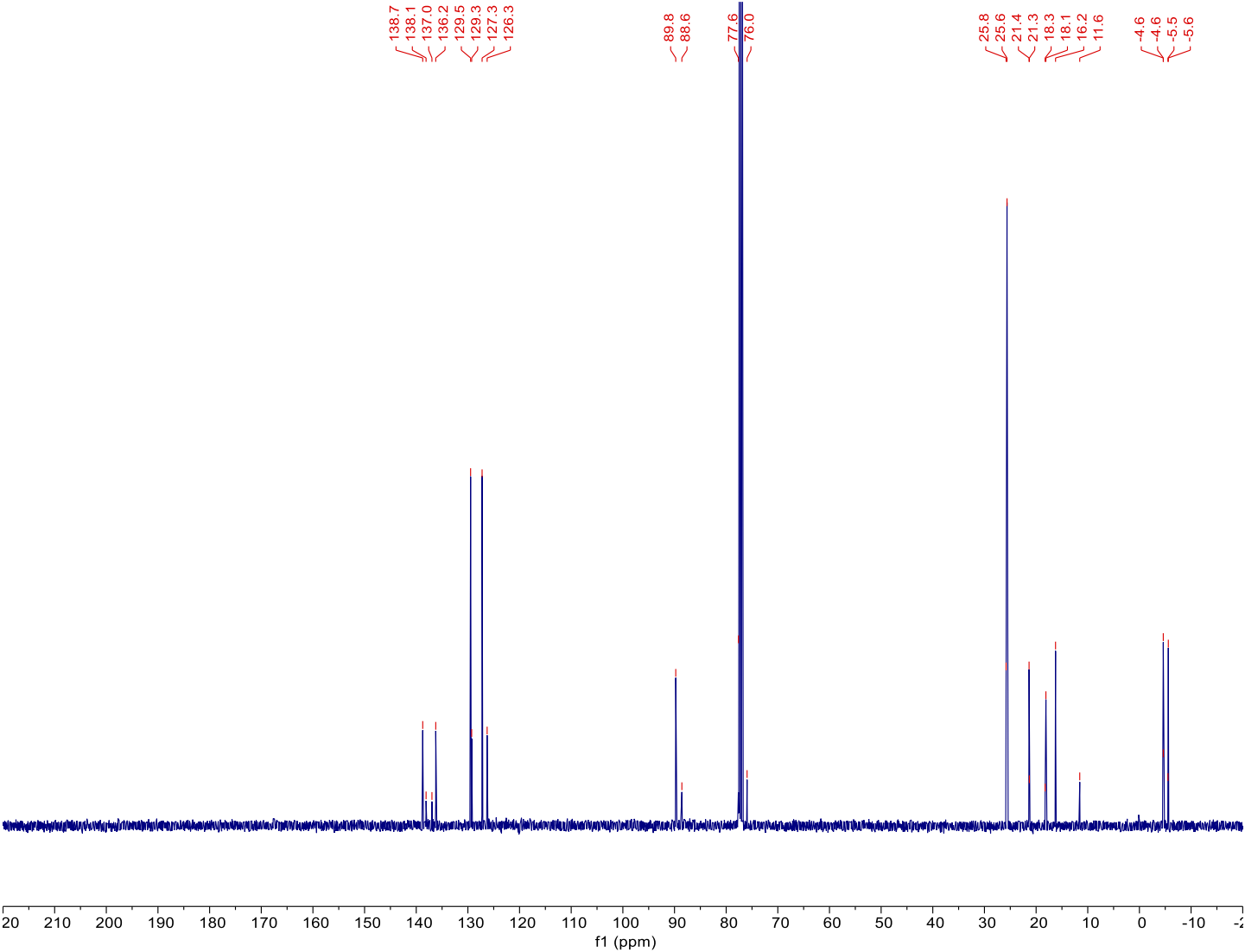
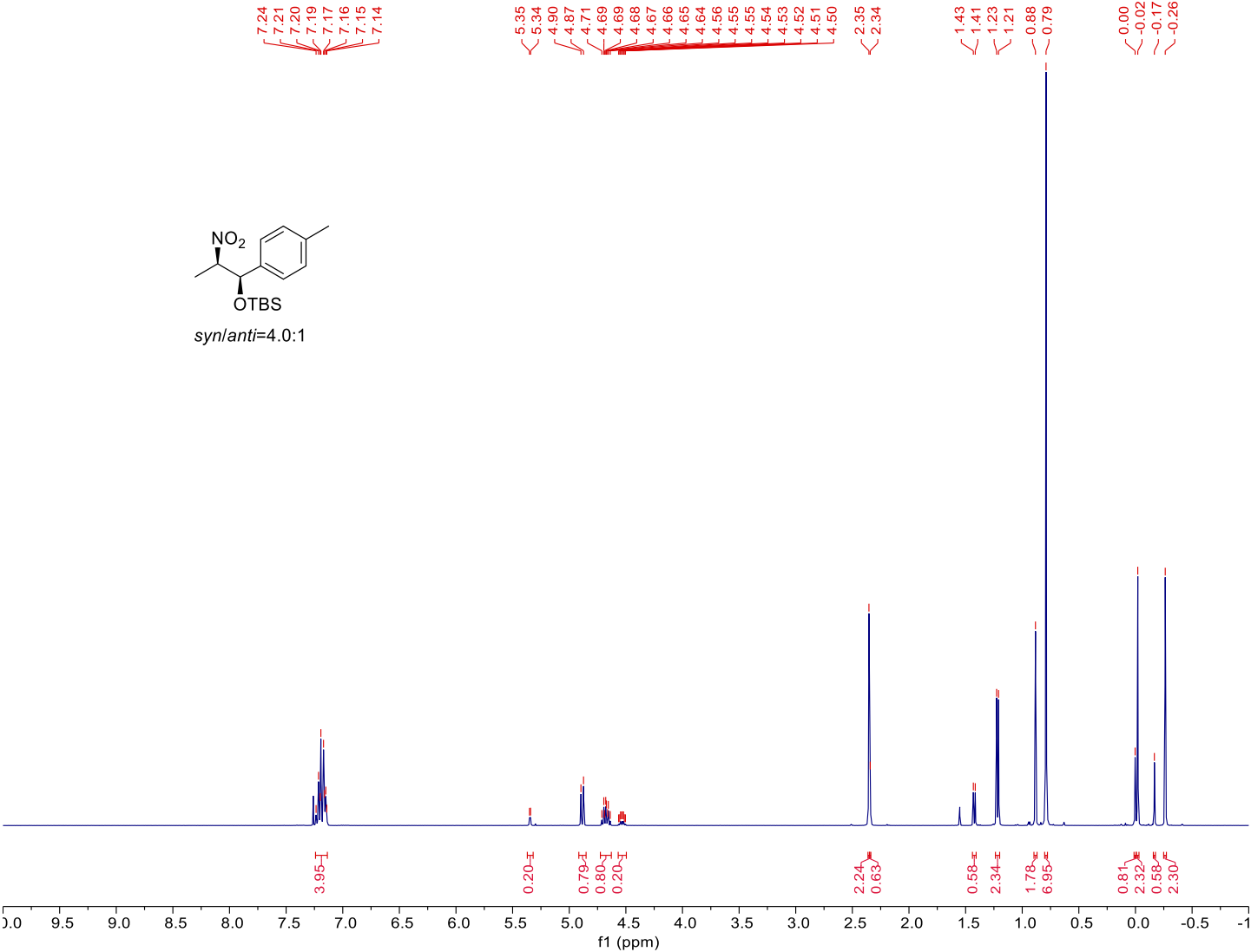
Compound 6x. Following a literature procedure reported by Pierce,²⁵ DDQ (28.7 mg, 0.126 mmol, 1 equiv) and *p*-TsOH·H₂O (12.0 mg, 0.063 mmol, 0.5 equiv) were added to a stirred solution of *N*-hydroxyimidothioate **S8** (49.0 mg, 0.126 mmol, 1 equiv) in anhydrous DMF (2.5 mL, 0.05 M). The reaction mixture was degassed with N₂ for 5 min and then heated to 150 °C for 20 min. Upon cooling down, the mixture was diluted with EtOAc and H₂O. Layers were separated, and the aq. phase was extracted with EtOAc three times. The combined organic phase was washed with sat. aq. NaHCO₃ and brine, dried over Na₂SO₄, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (0→5% EtOAc/hexanes) to afford oxathiazole **6x** as a yellow oil (23.7 mg, 49%, 1.8:1 *dr*); R_f = 0.23 (5% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3) δ 7.52 – 7.26 (m, 20H, major+minor), 6.95 (s, 1H, minor), 6.89 (s, 1H, major), 5.84 (s, 1H, minor), 5.82 (s, 1H, major), 0.97 (s, 9H, minor), 0.91 (s, 9H, major), 0.20 (s, 3H, minor), 0.11 (s, 3H, major), 0.10 (s, 3H, minor), 0.06 (s, 3H, major); ^{13}C NMR (126 MHz, CDCl_3) δ 163.0 (major), 162.6 (minor), 140.2 (major), 140.1 (minor), 137.9 (minor), 137.5 (major), 129.6 (major), 129.5 (minor), 128.8 (major), 128.7 (minor), 128.7 (major), 128.6 (minor), 128.4 (major),

128.3 (minor), 126.9 (major), 126.6 (minor), 125.8 (major), 125.8 (minor), 93.5 (major), 93.1 (minor), 70.7 (minor), 70.6 (major), 25.8 (minor), 25.8 (major), 18.4 (minor), 18.4 (major), -4.8 (minor), -4.9 (minor), -4.9 (major), -5.0 (major); HRMS (ESI) m/z calcd. for $C_{21}H_{27}NO_2SSi$ $[M+H]^+$: 386.1605, found: 386.1601.

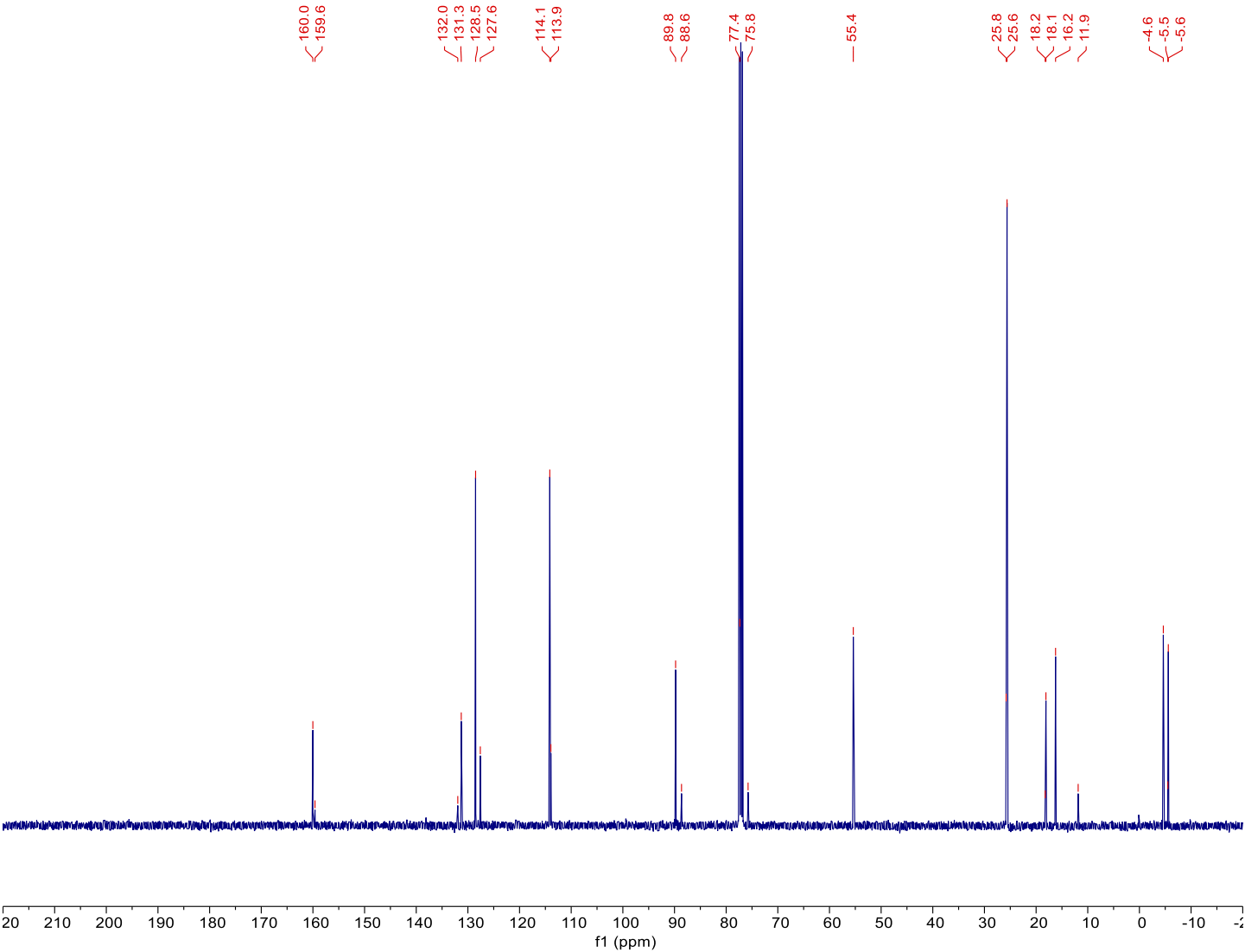
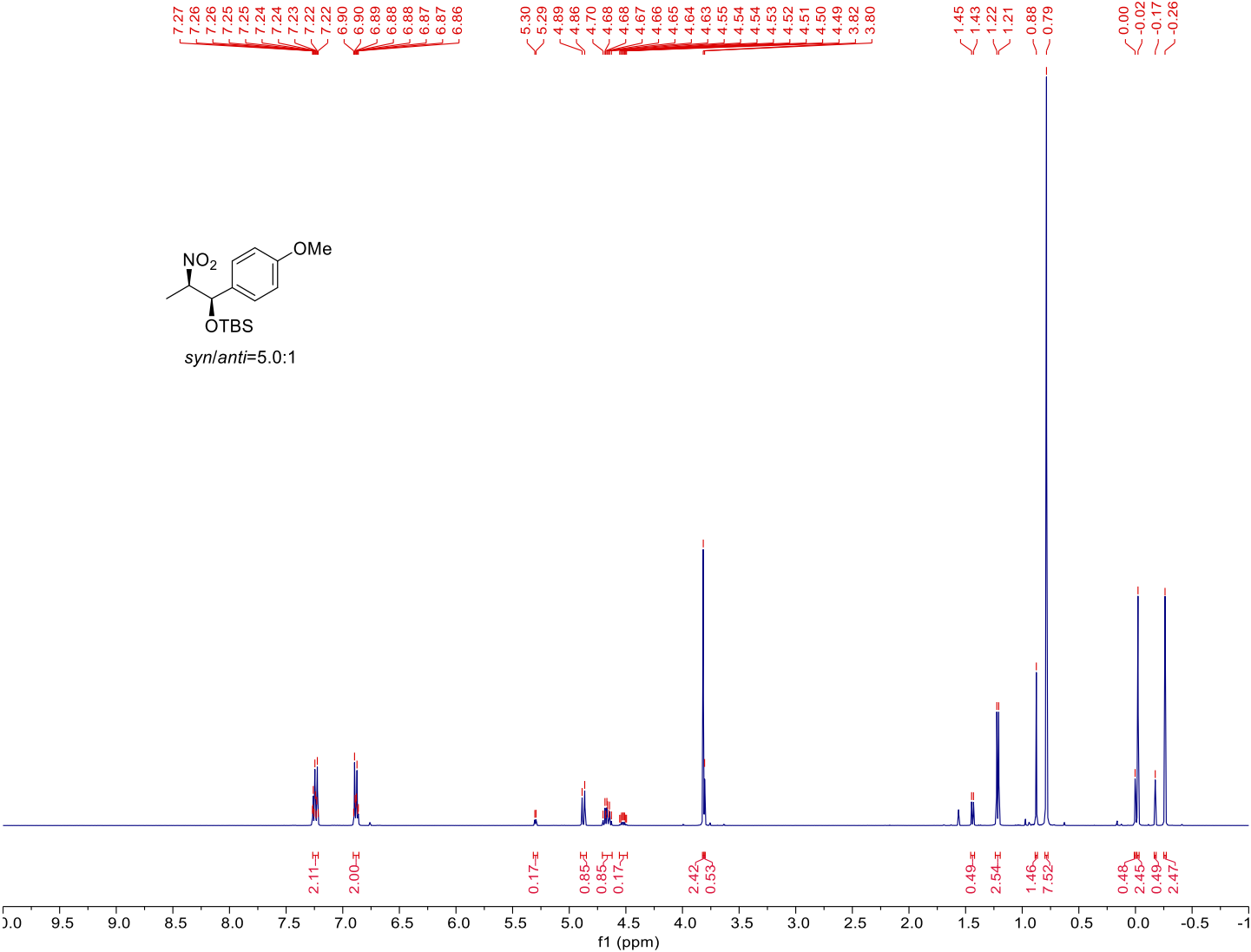
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1a**.



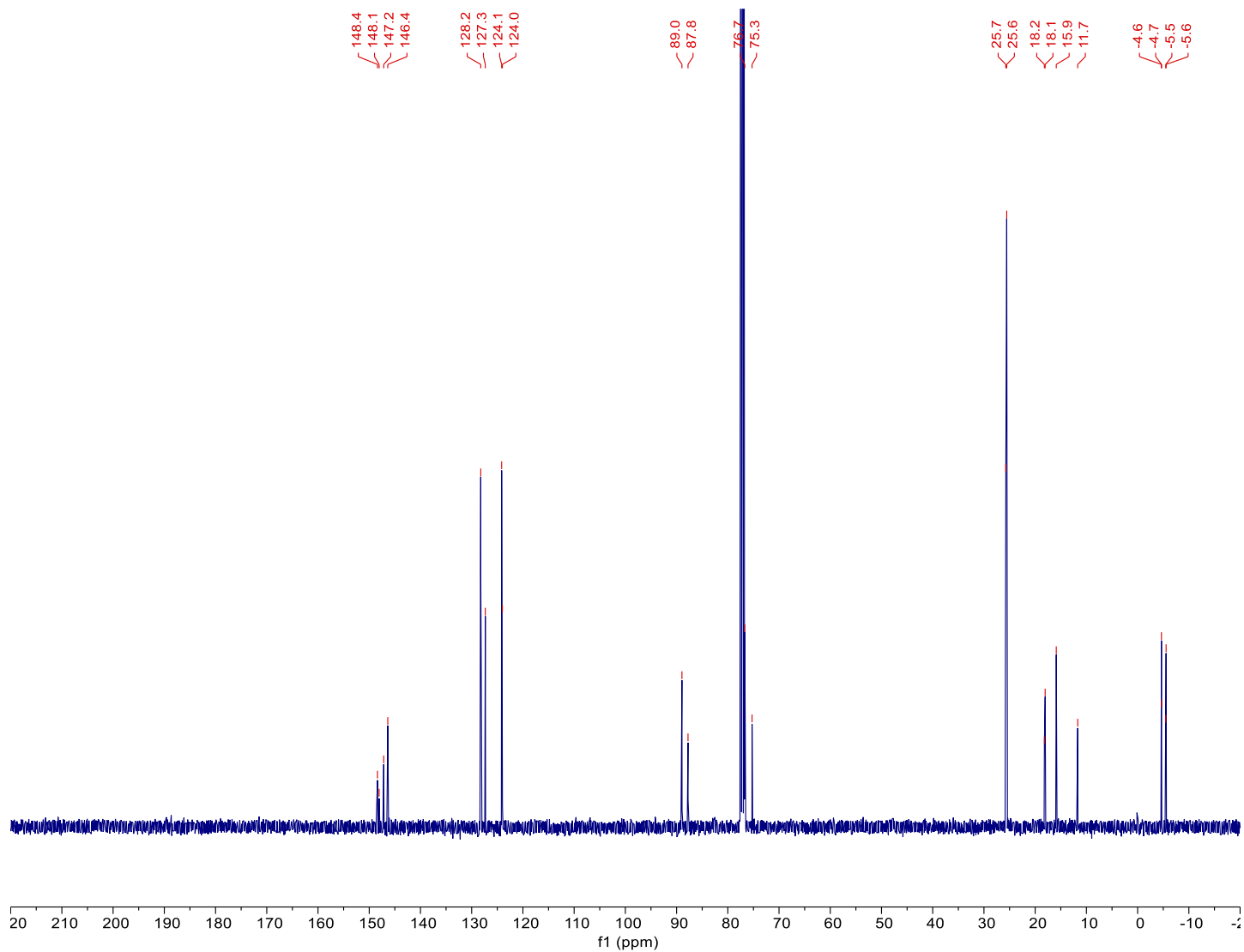
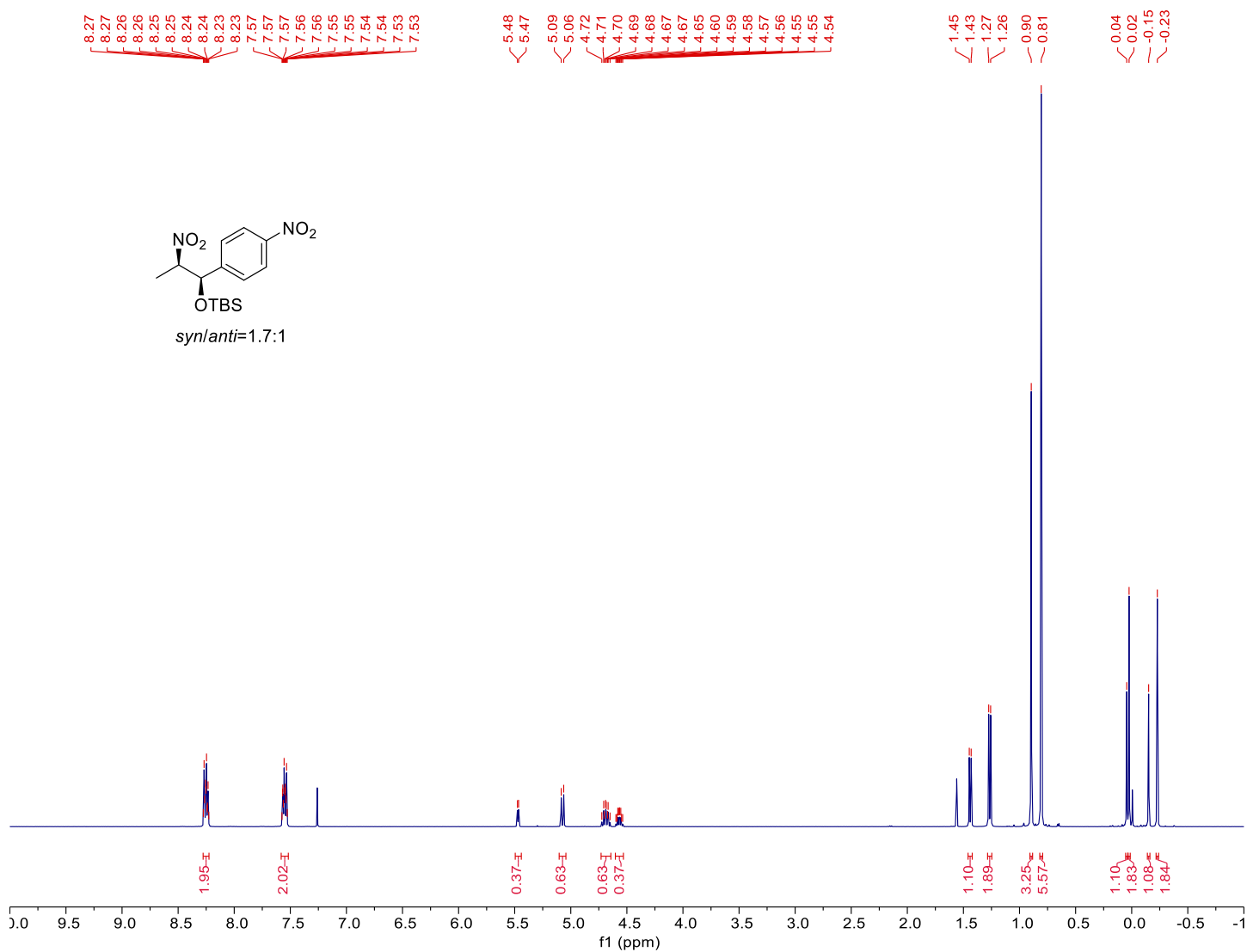
¹H NMR (400 MHz, CDCl₃) and ¹³C NMR (101 MHz, CDCl₃) spectra for compound **1b**.



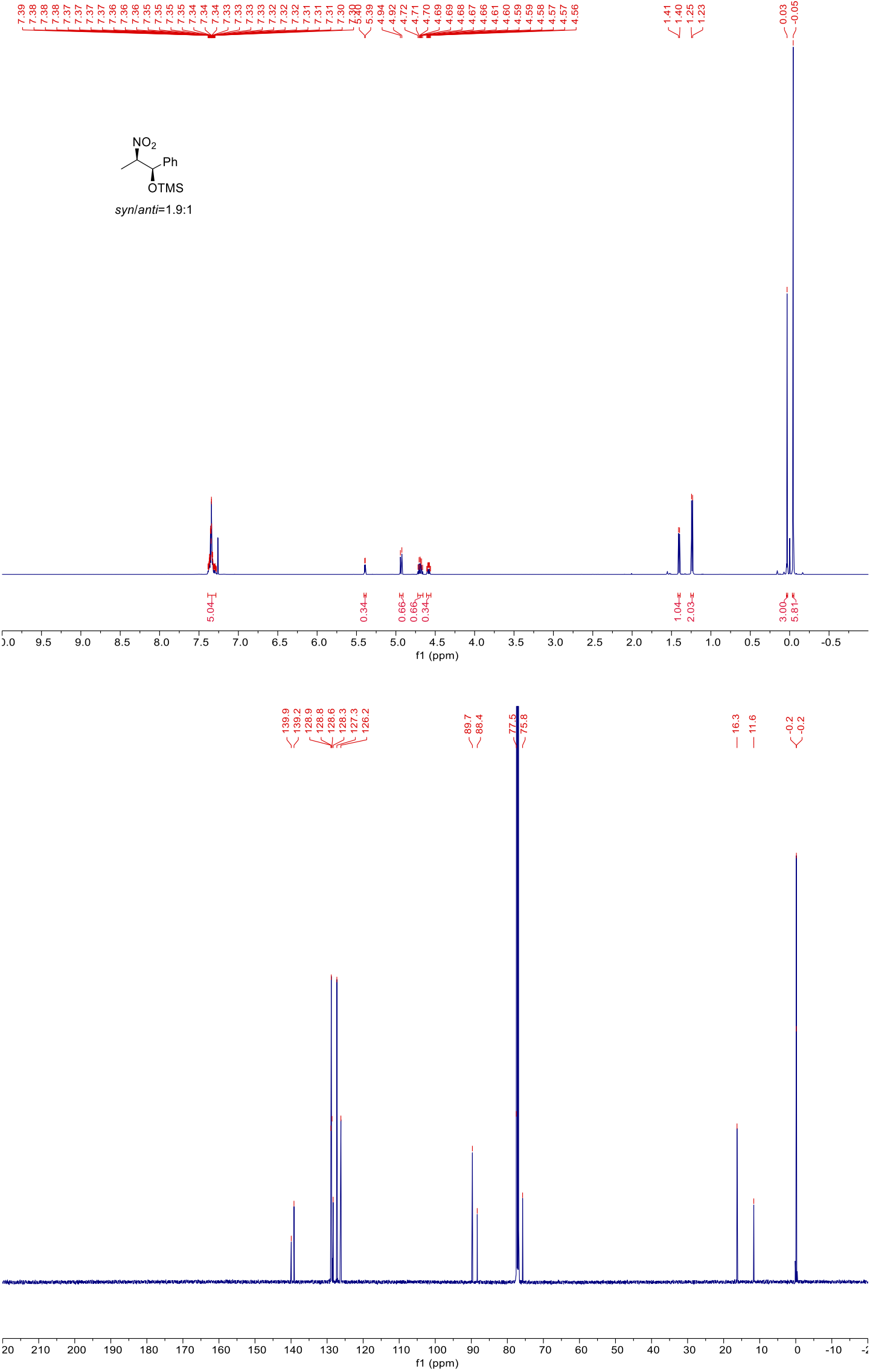
¹H NMR (400 MHz, CDCl₃) and ¹³C NMR (101 MHz, CDCl₃) spectra for compound **1c**.



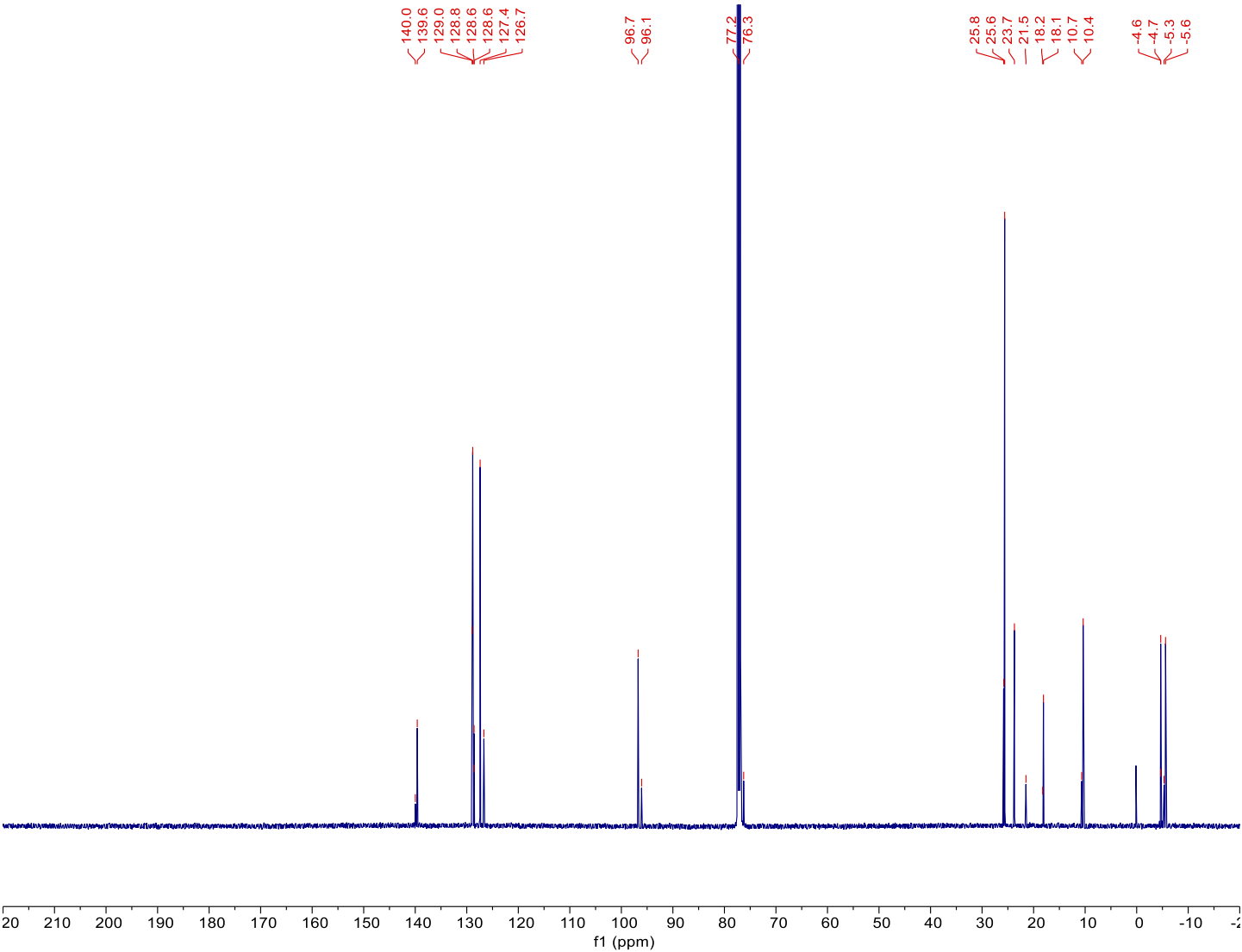
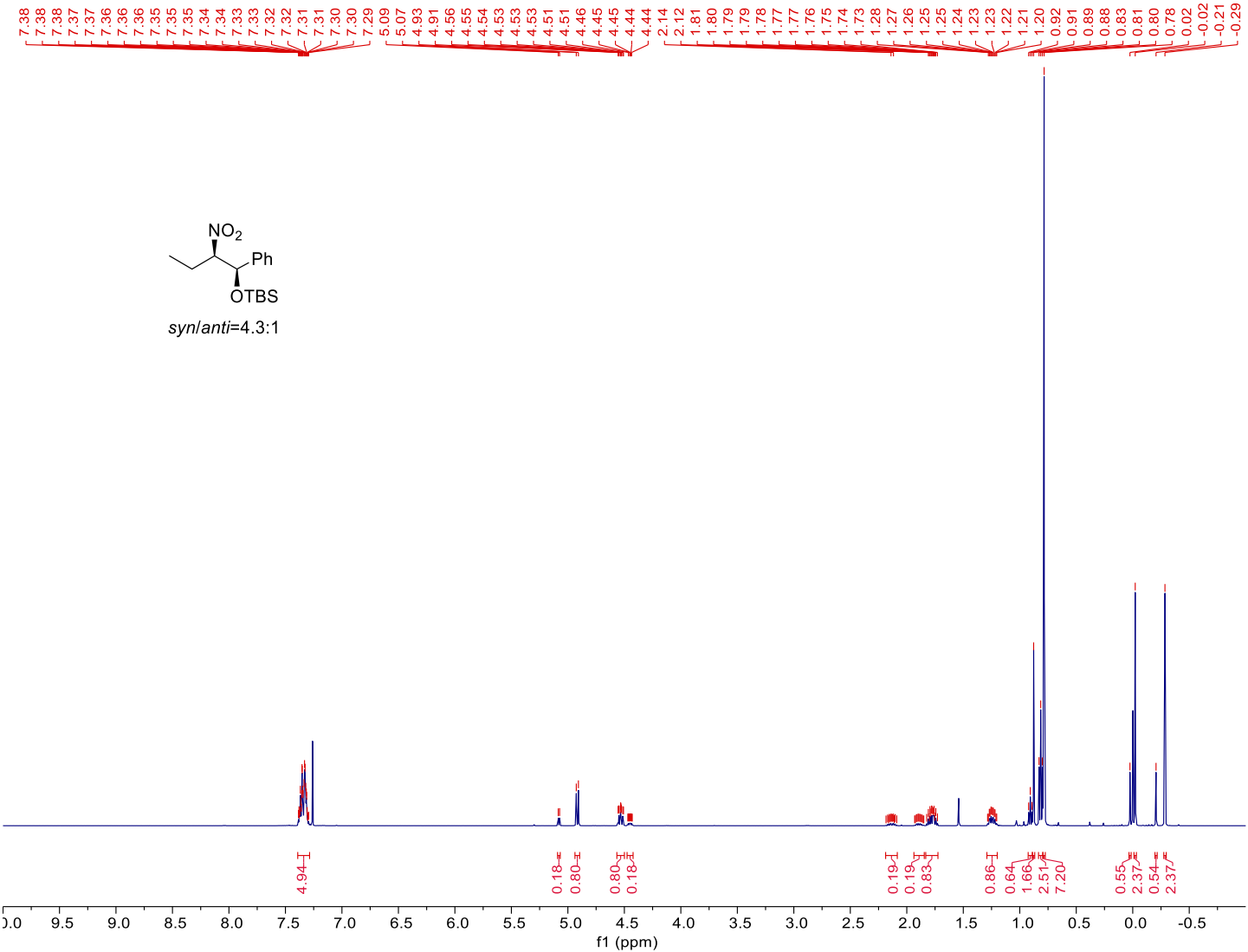
¹H NMR (400 MHz, CDCl₃) and ¹³C NMR (101 MHz, CDCl₃) spectra for compound **1d**.



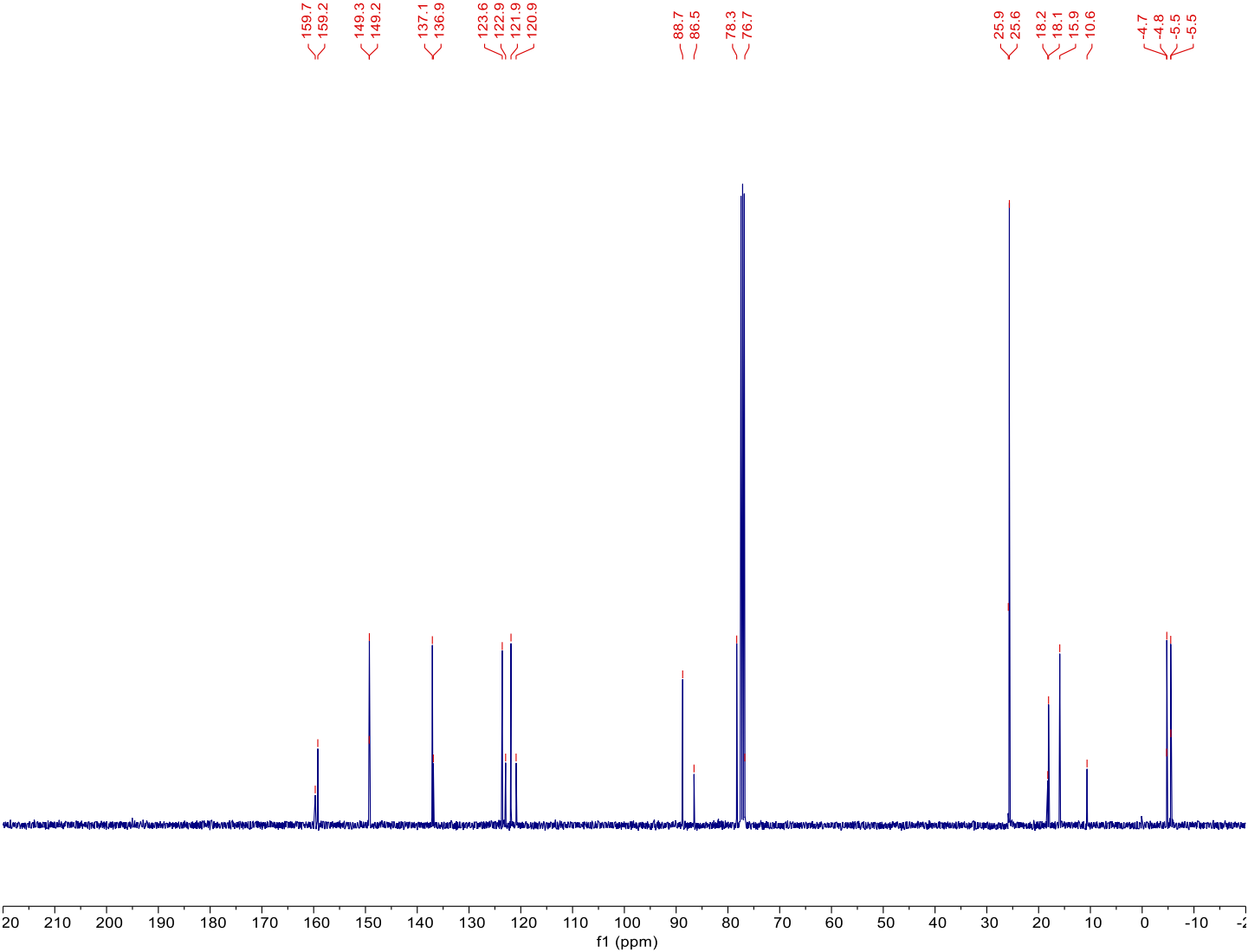
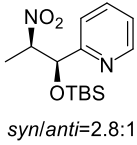
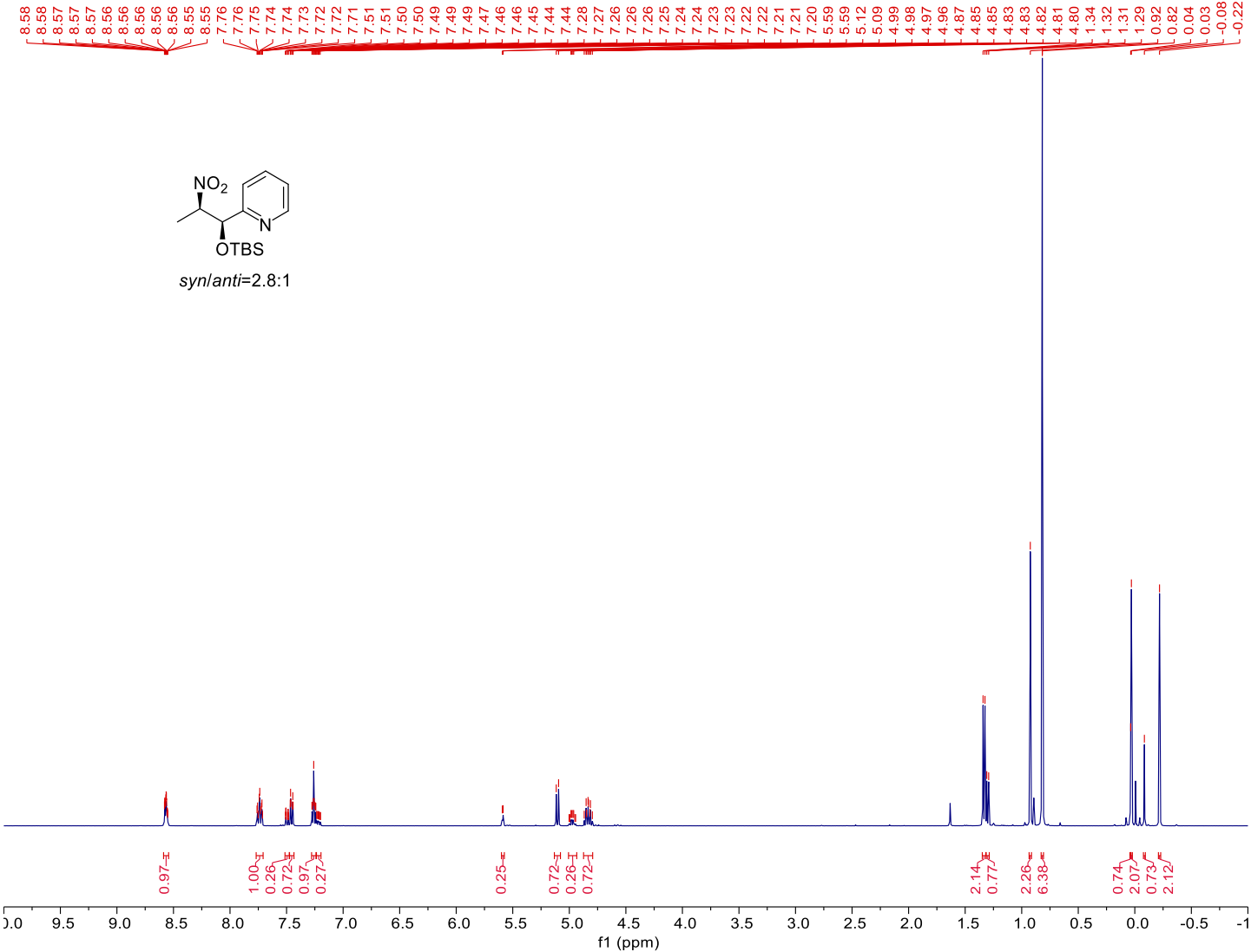
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1e**.



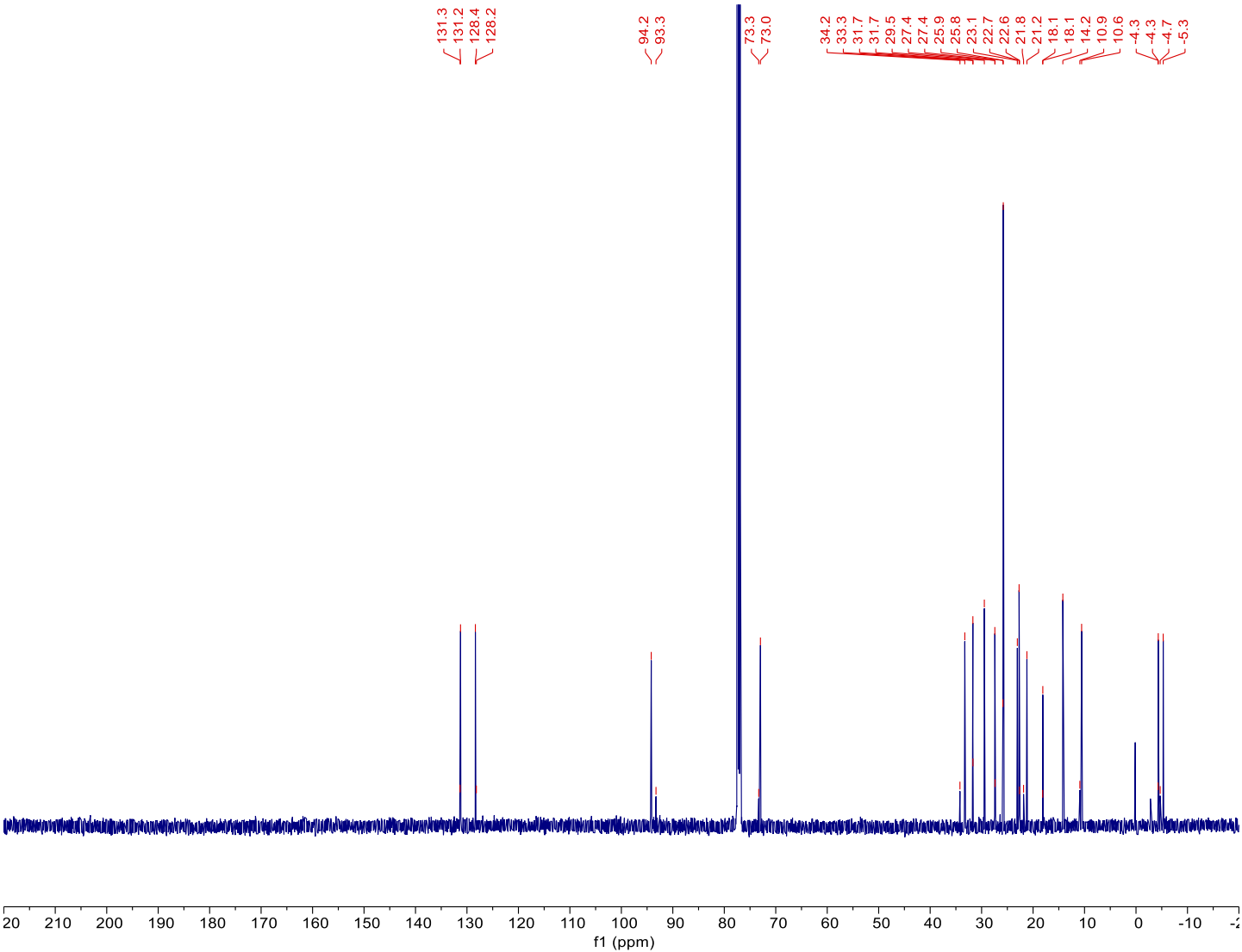
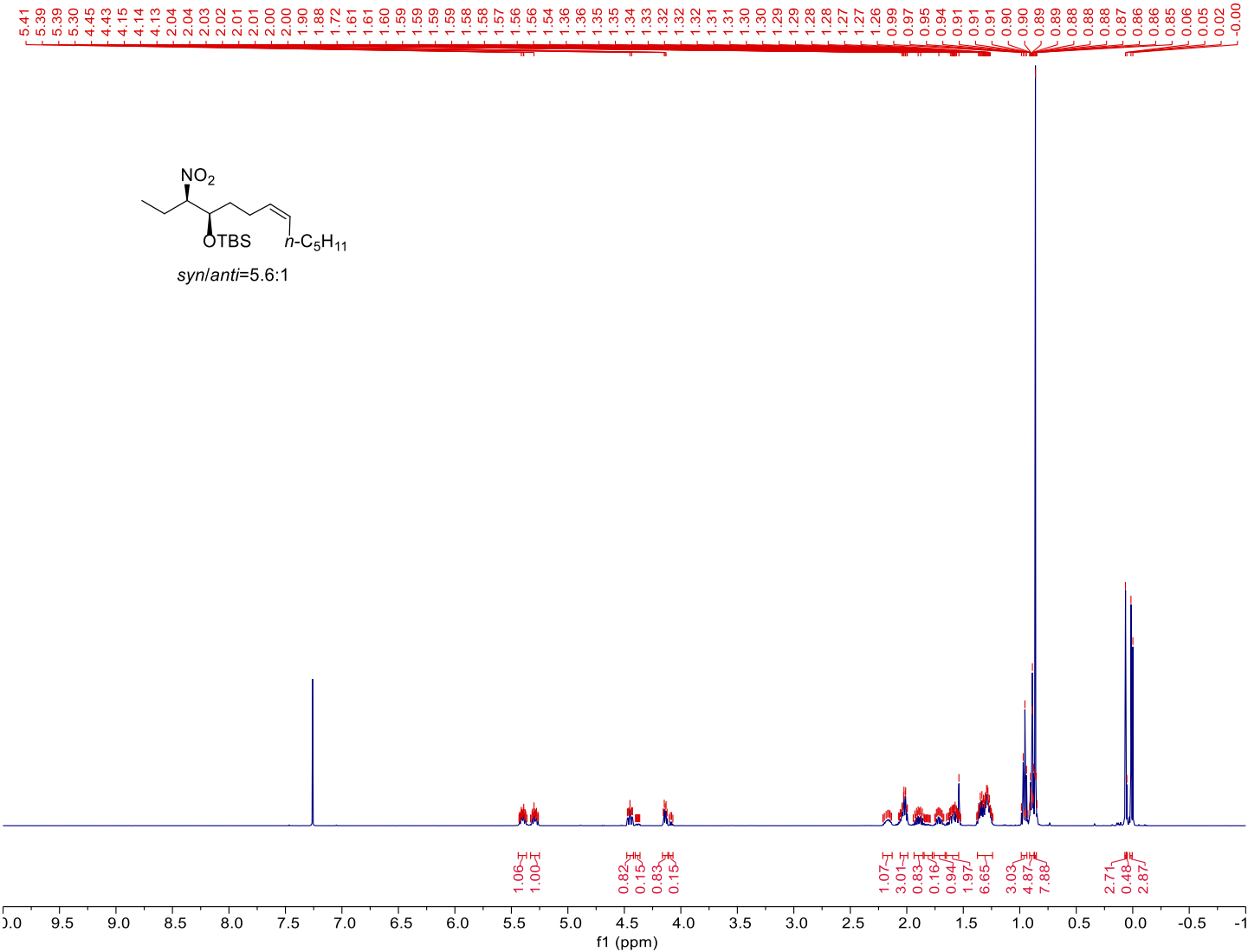
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1f**.



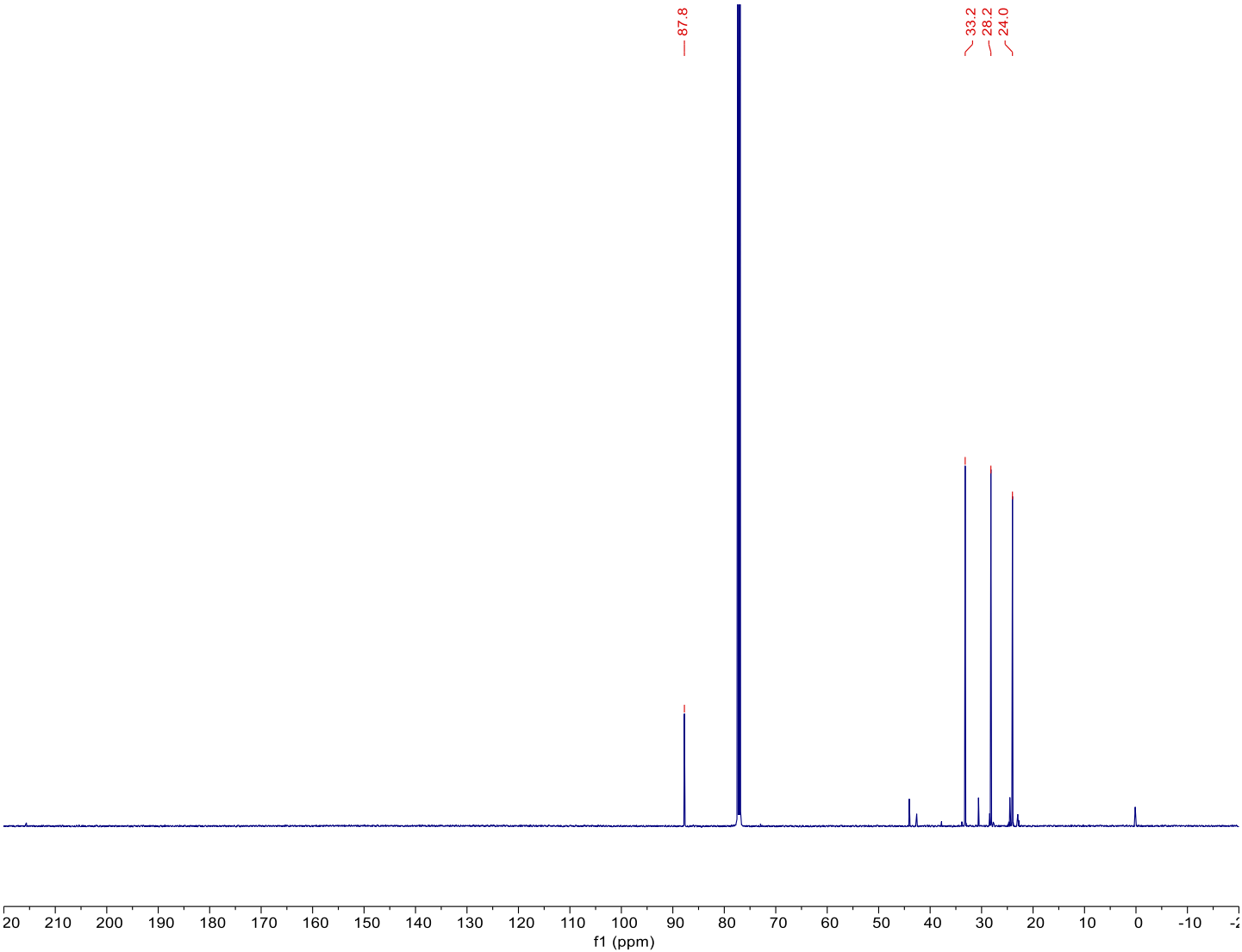
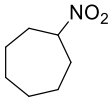
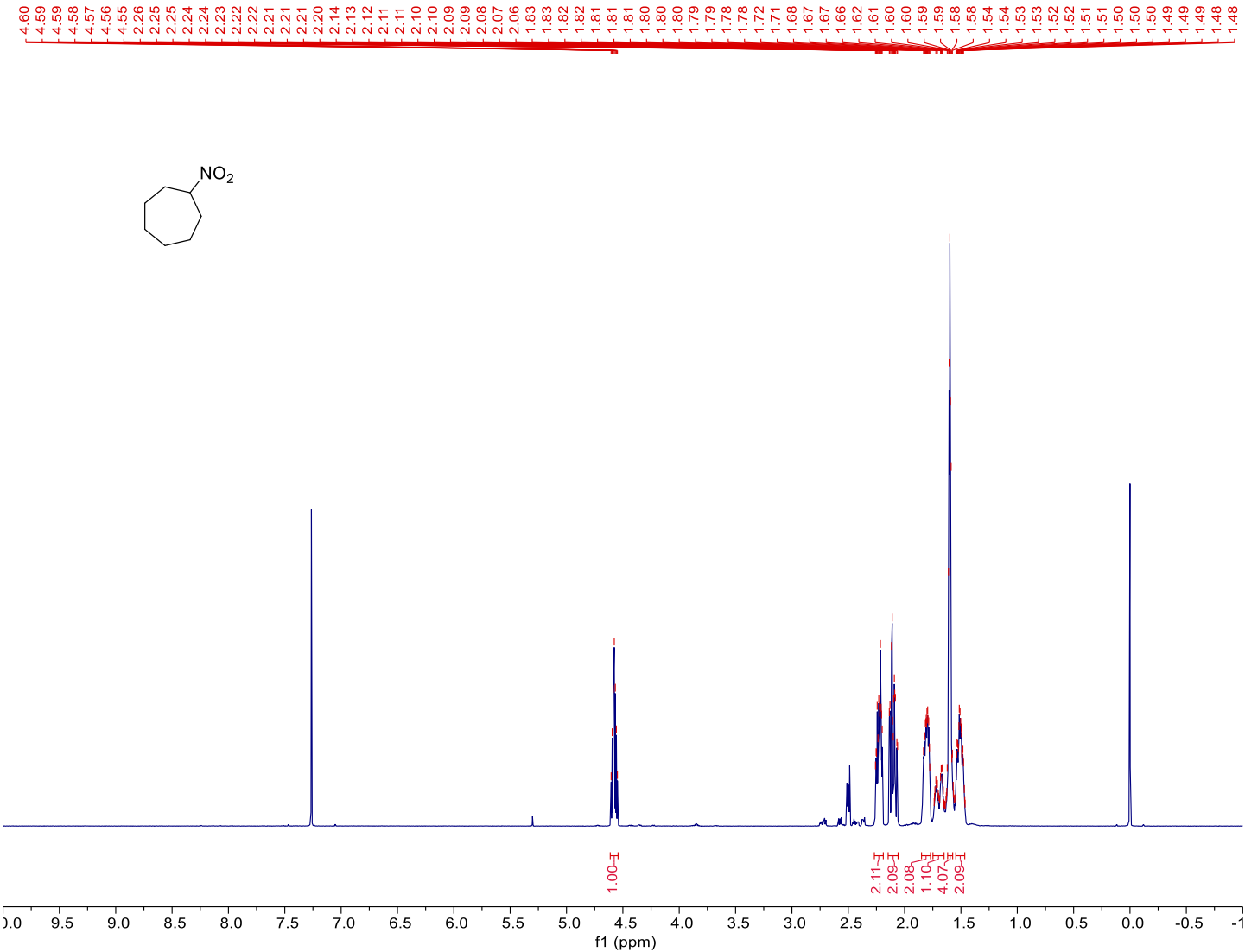
¹H NMR (400 MHz, CDCl₃) and ¹³C NMR (101 MHz, CDCl₃) spectra for compound **1g**.



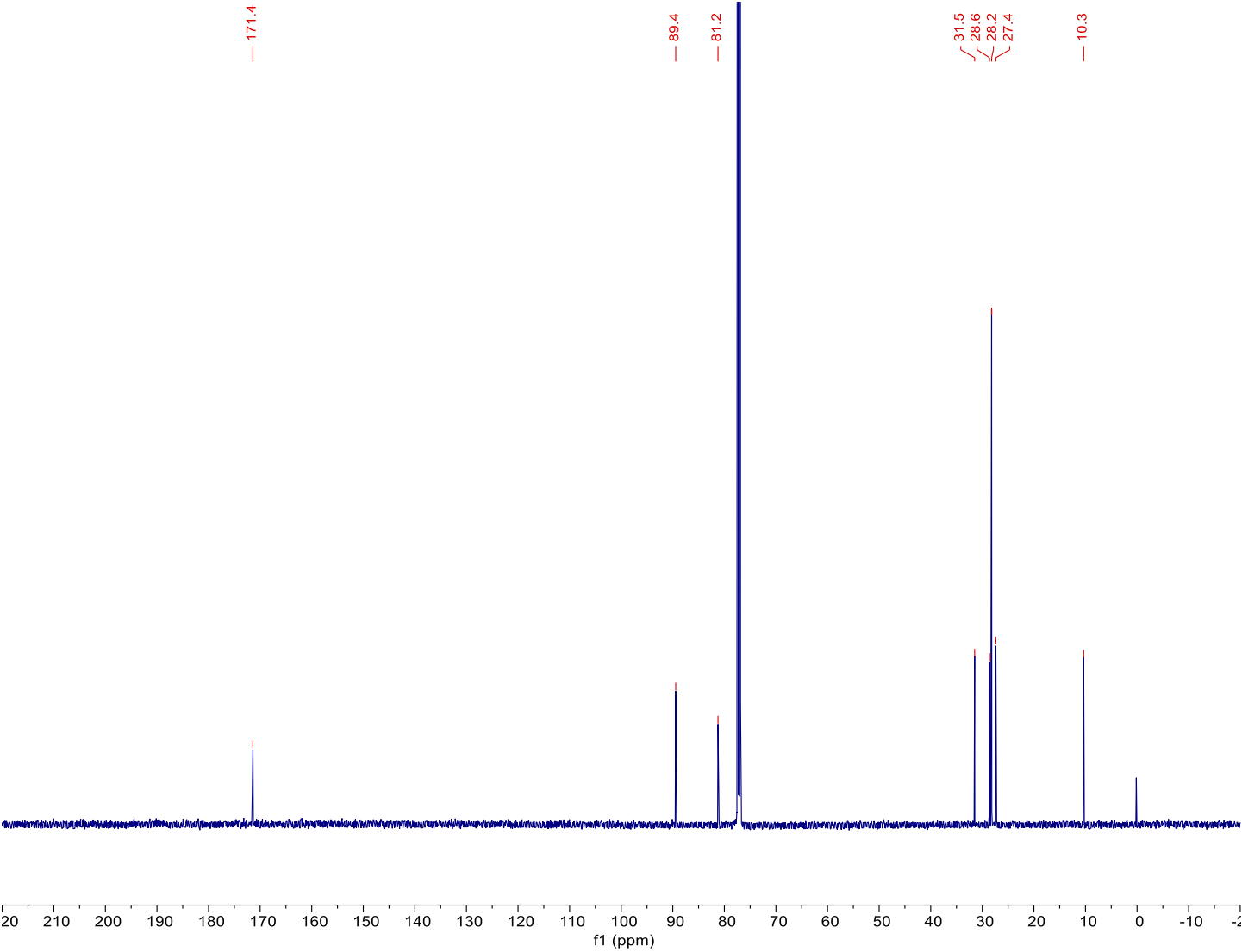
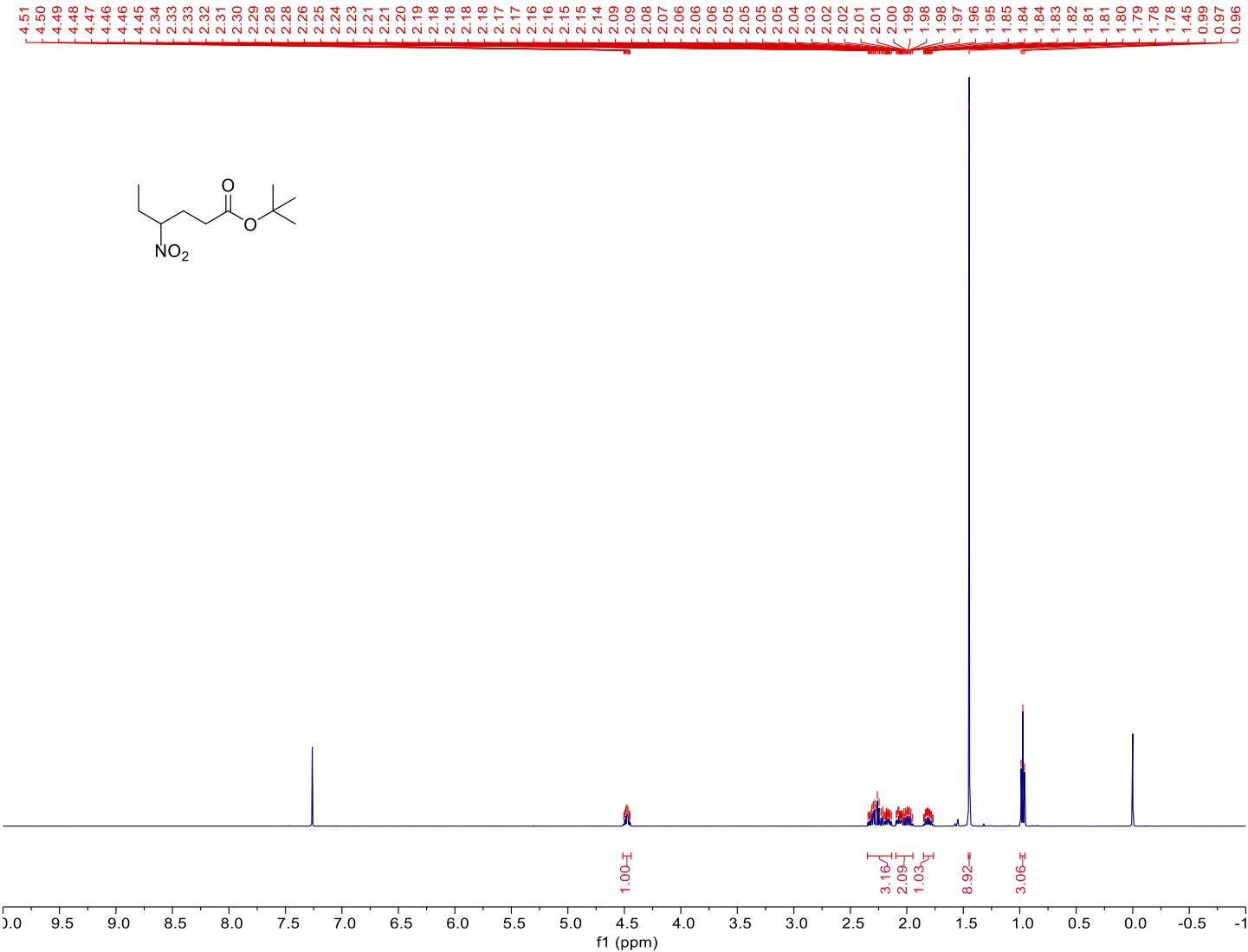
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1i**.



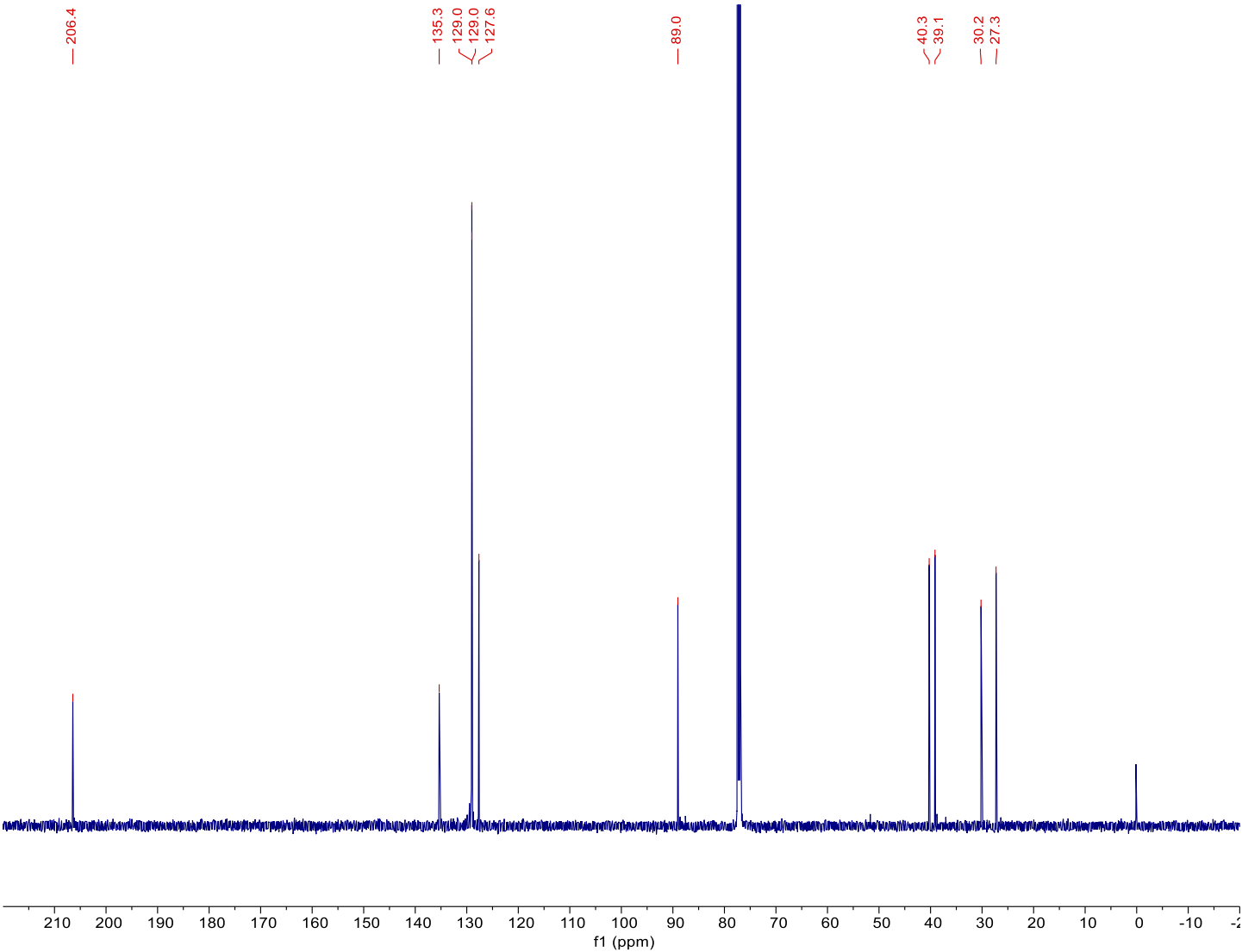
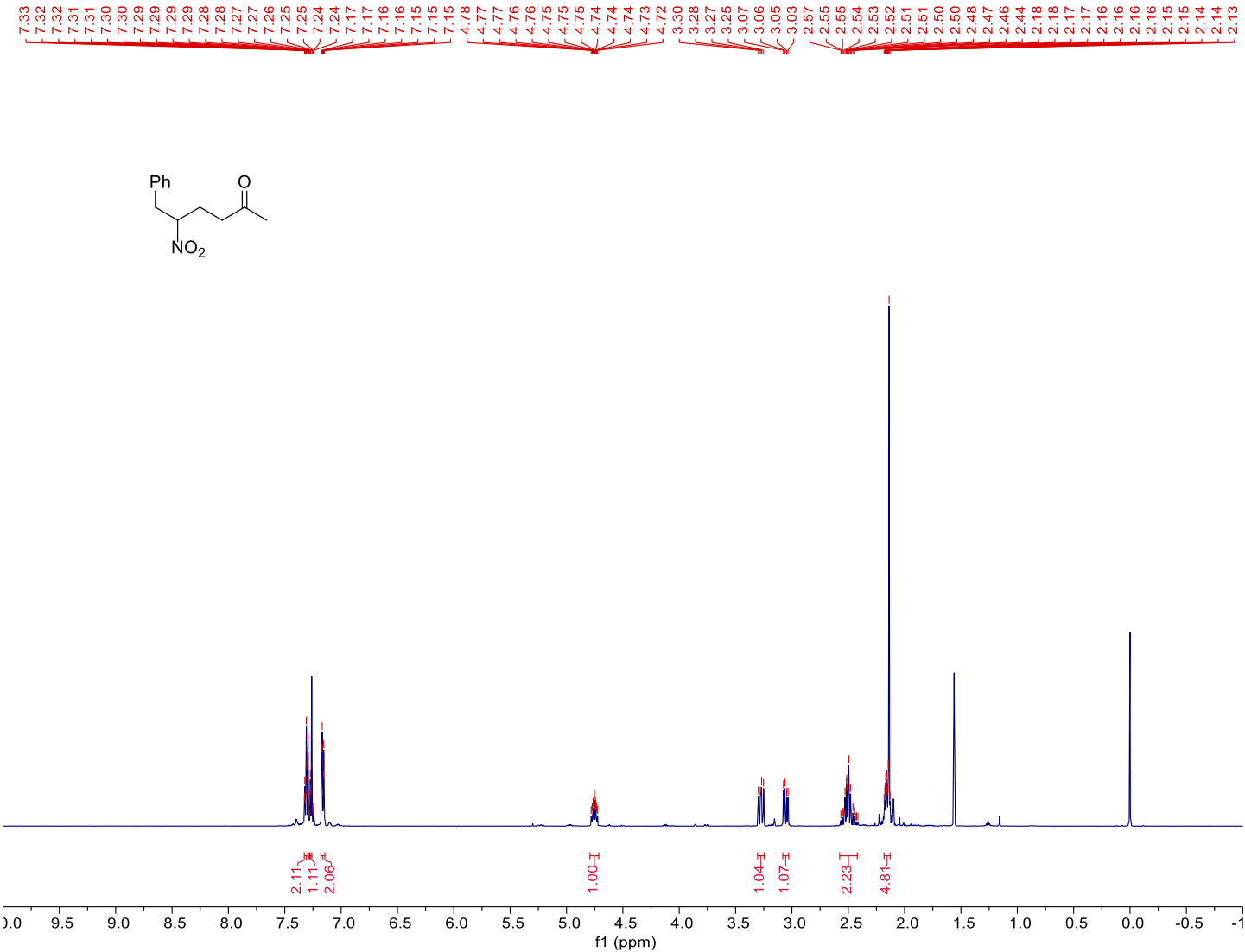
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1k**.



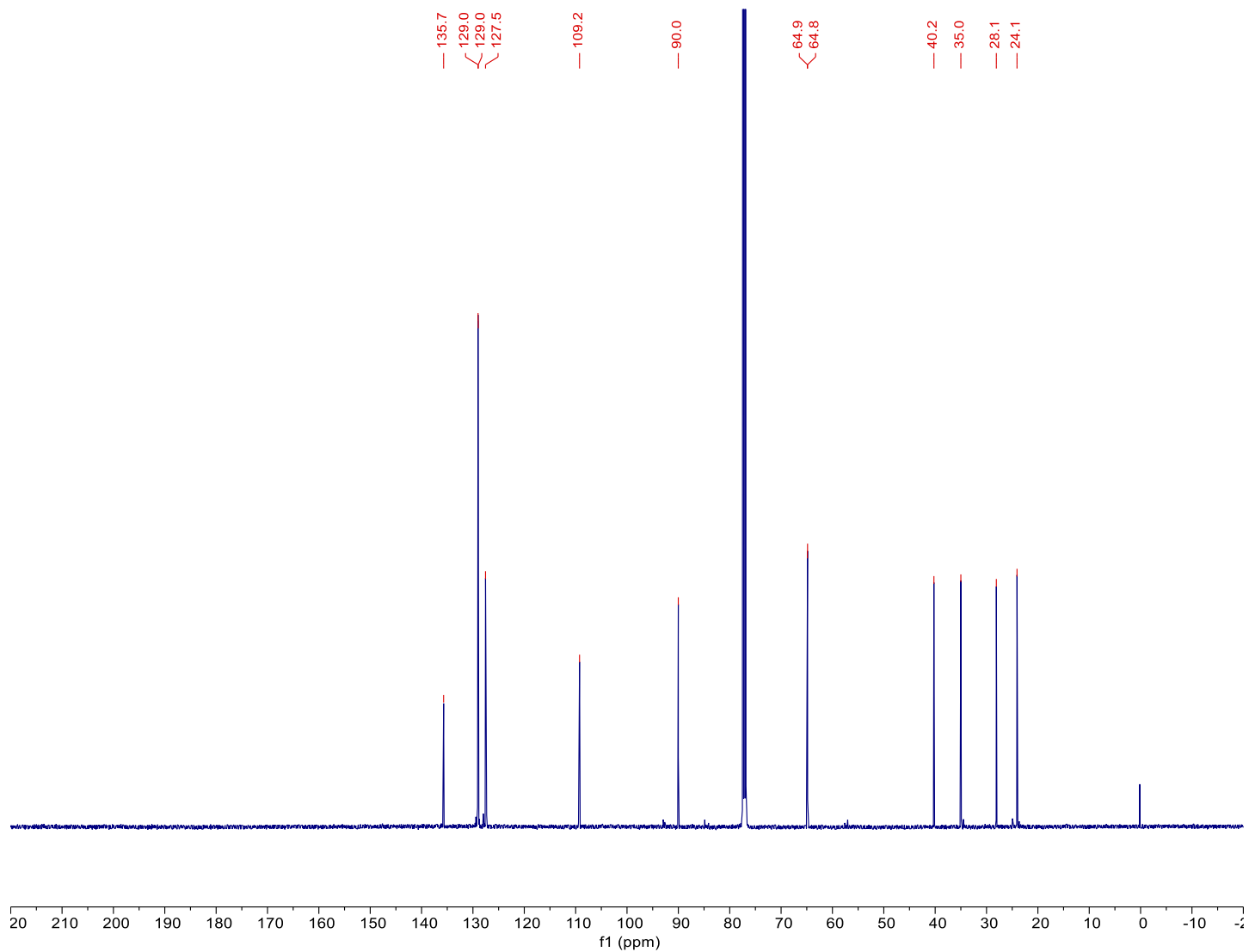
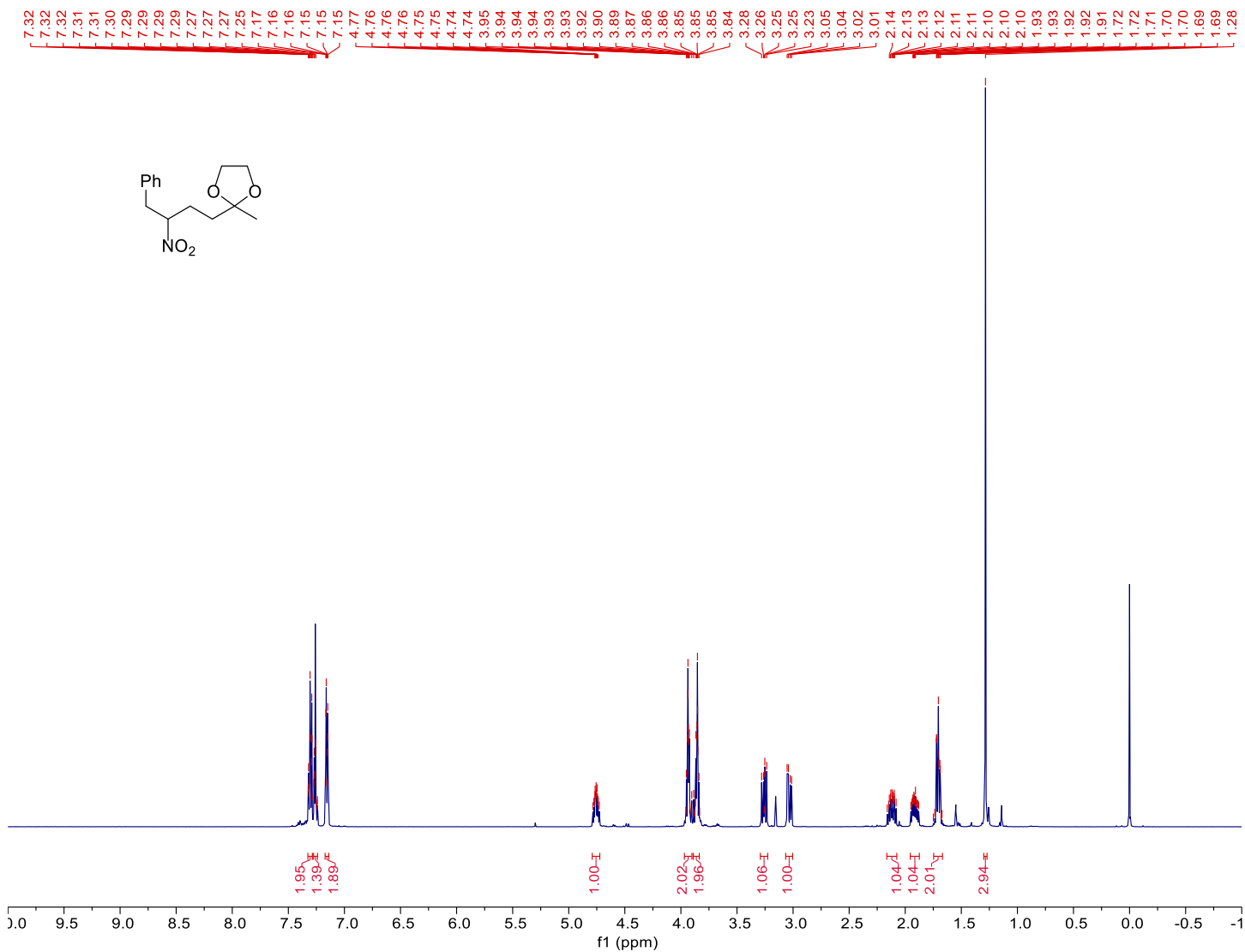
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **11**.



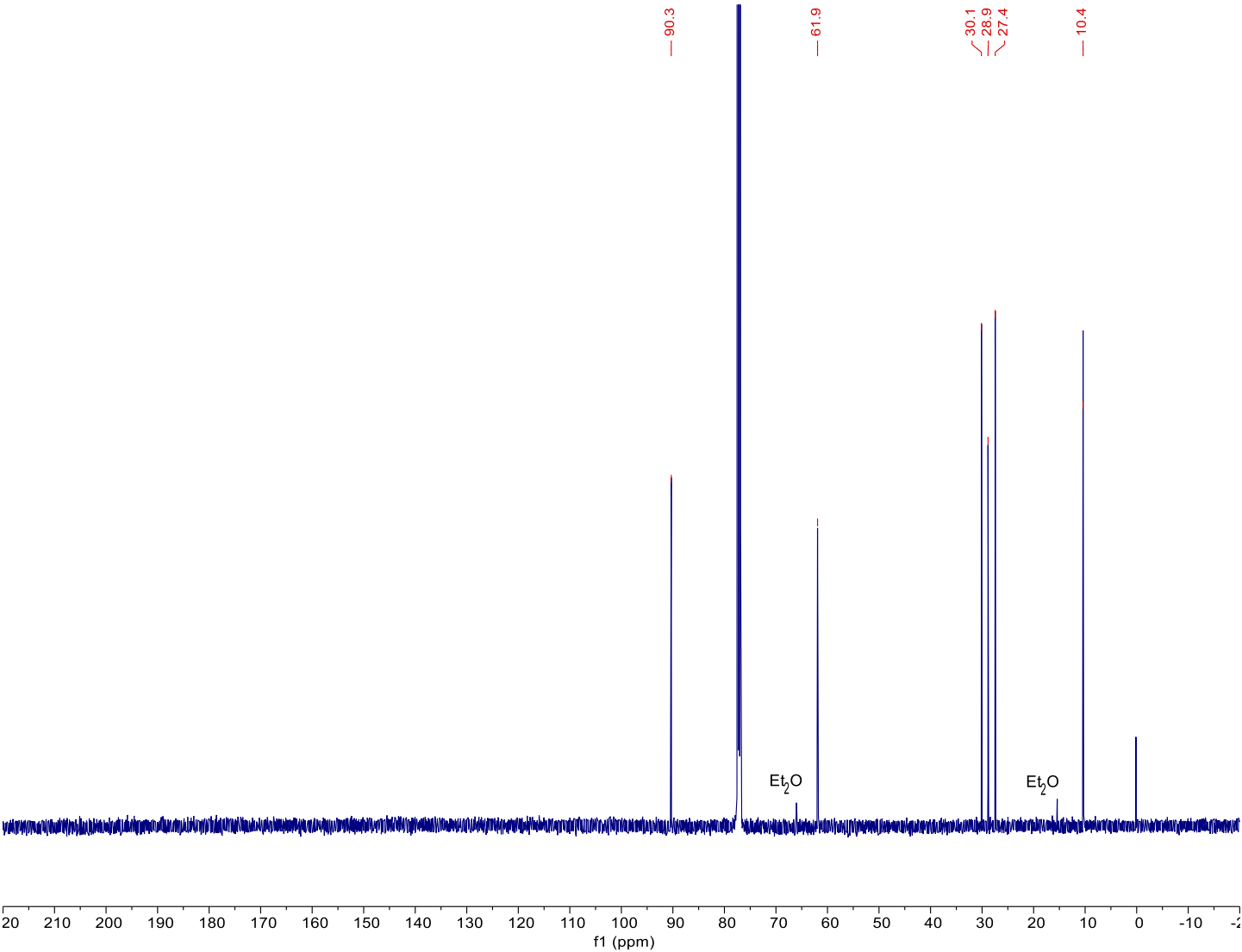
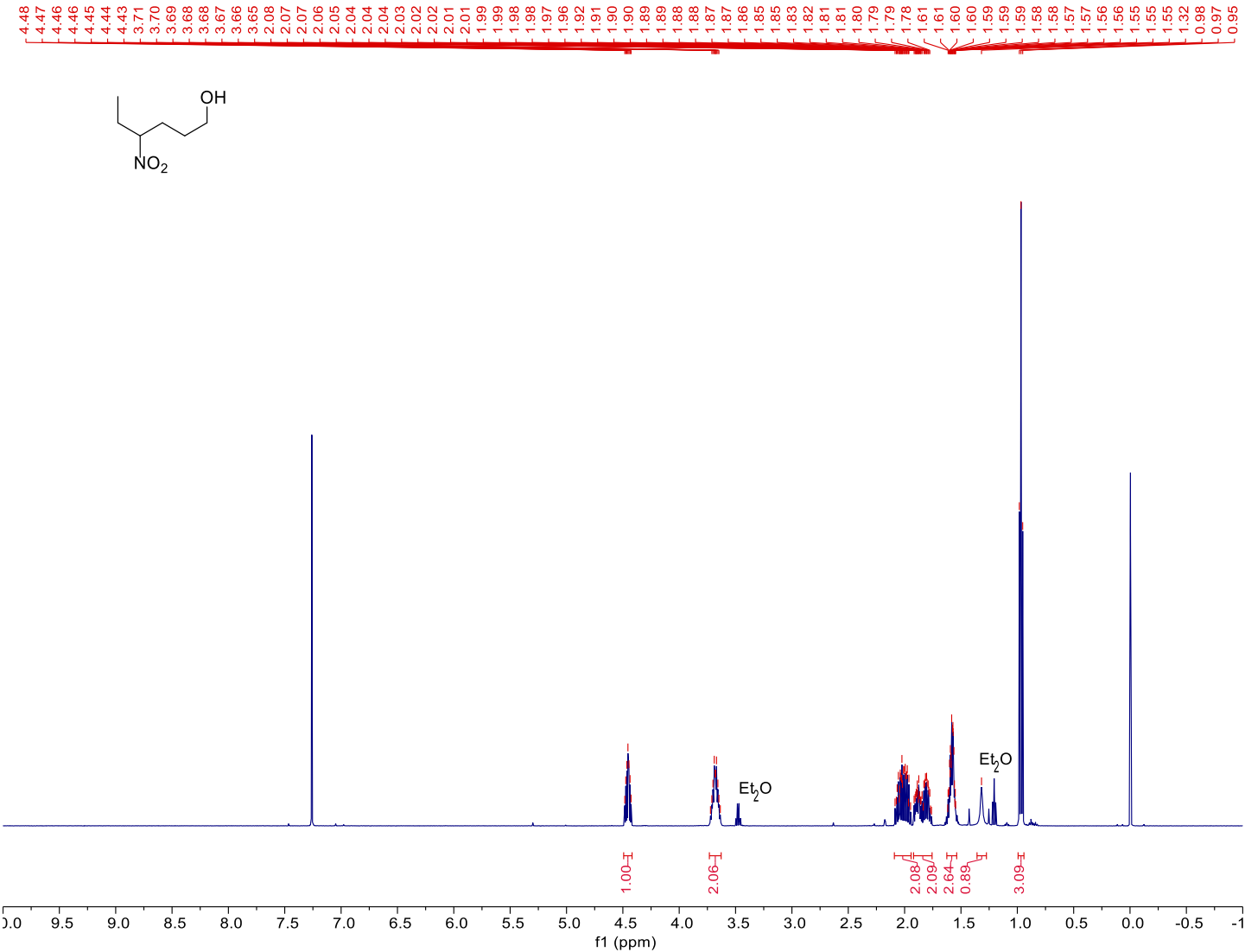
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **S2**.



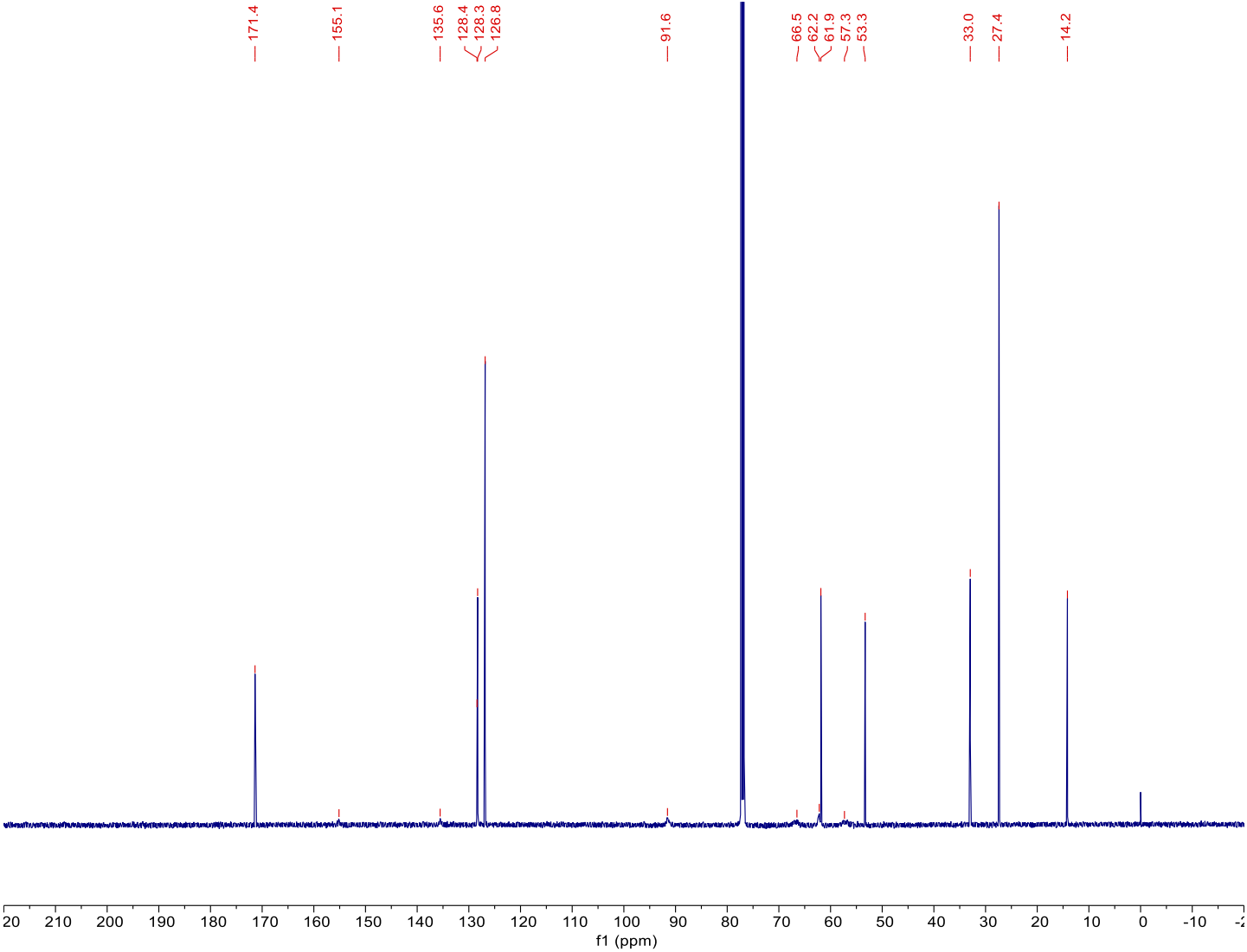
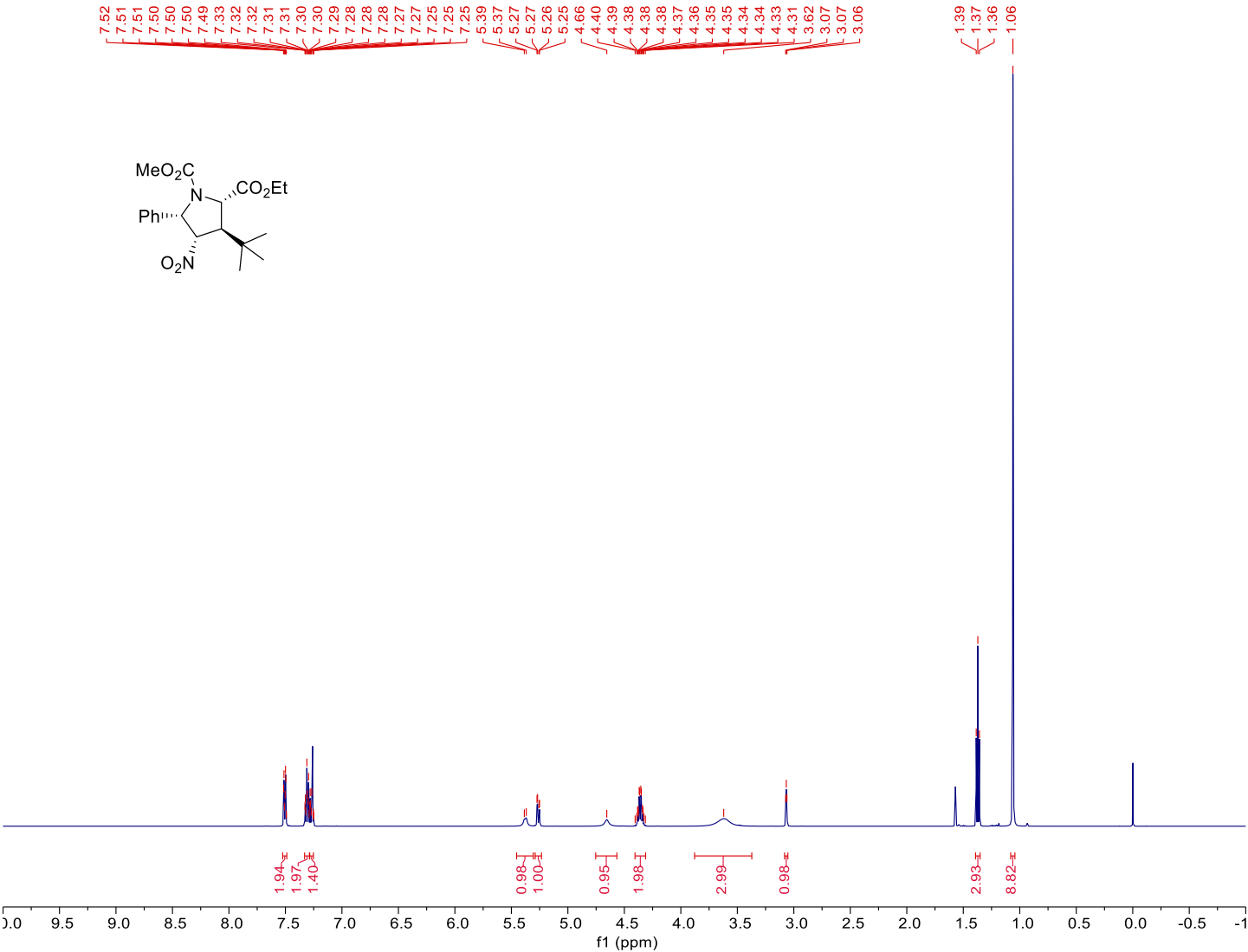
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1m**.



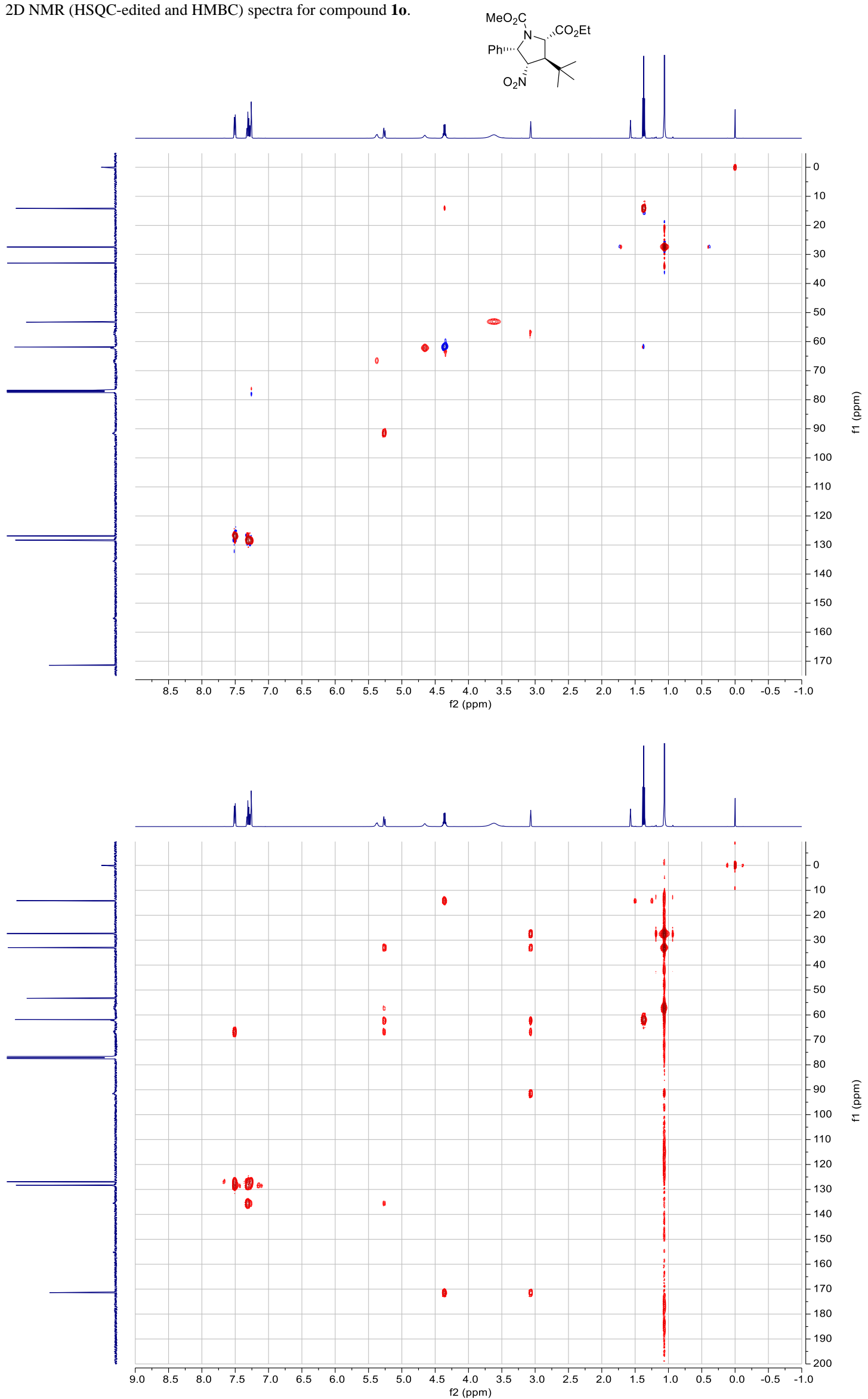
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1n**.



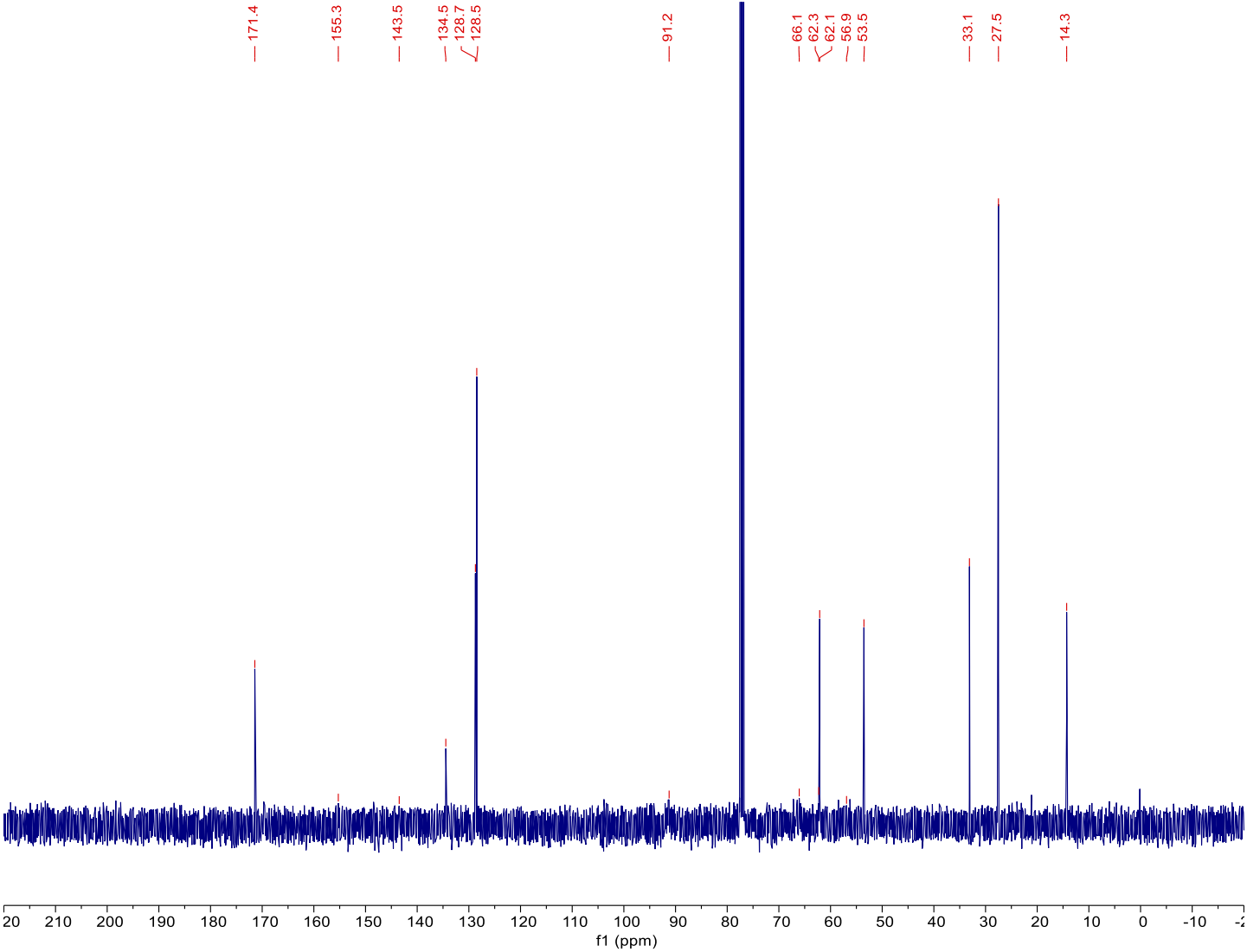
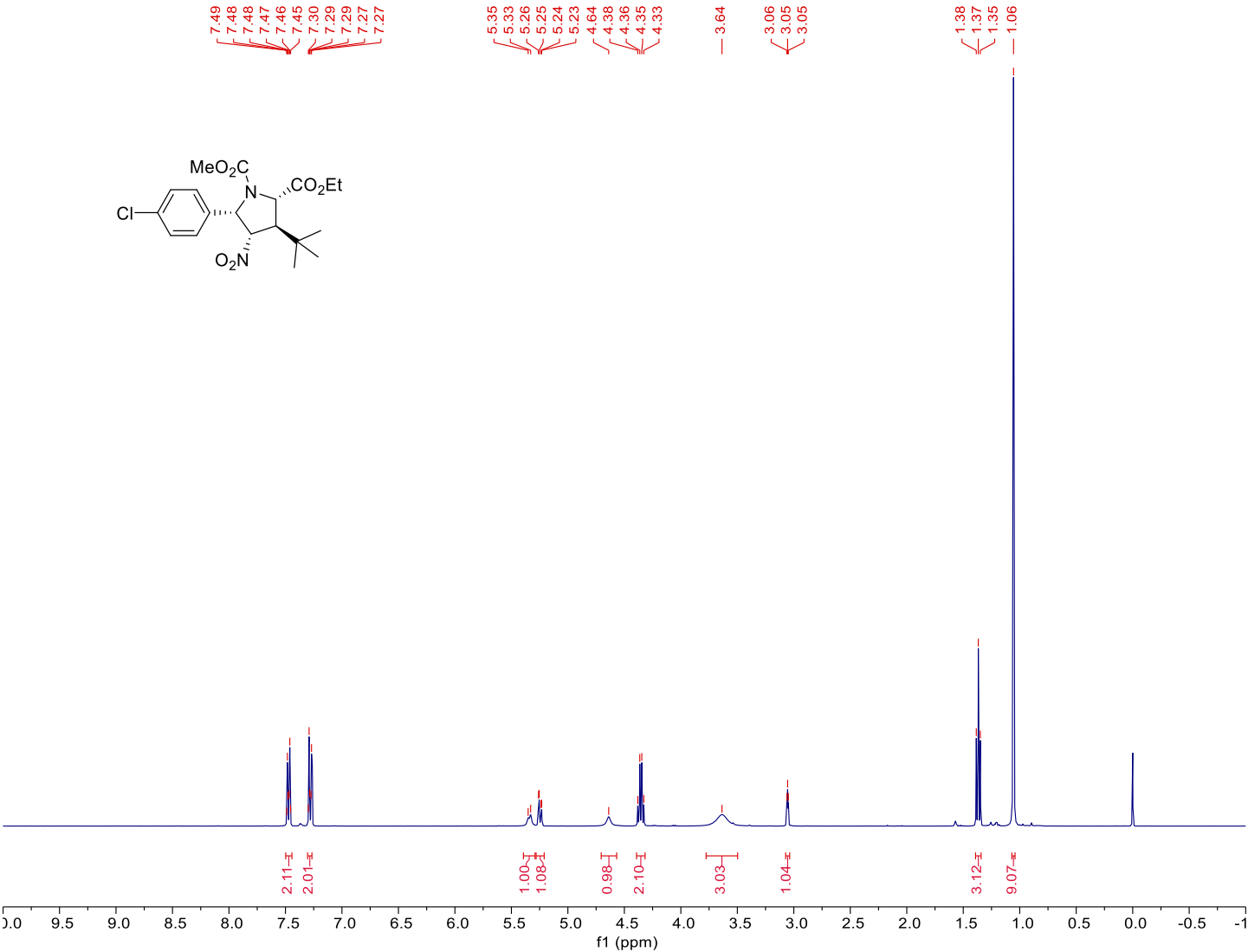
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1o**.



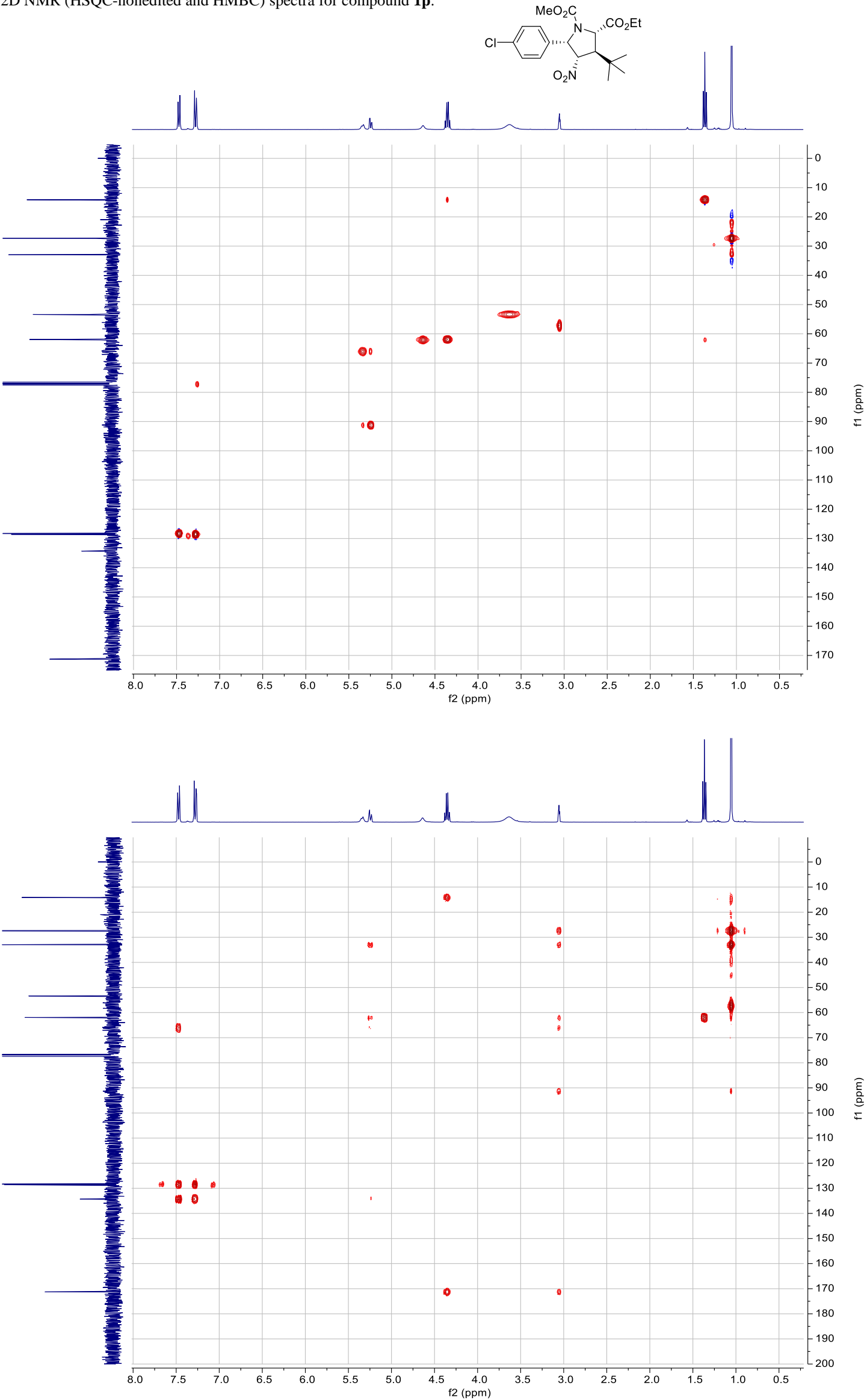
2D NMR (HSQC-edited and HMBC) spectra for compound **1o**.



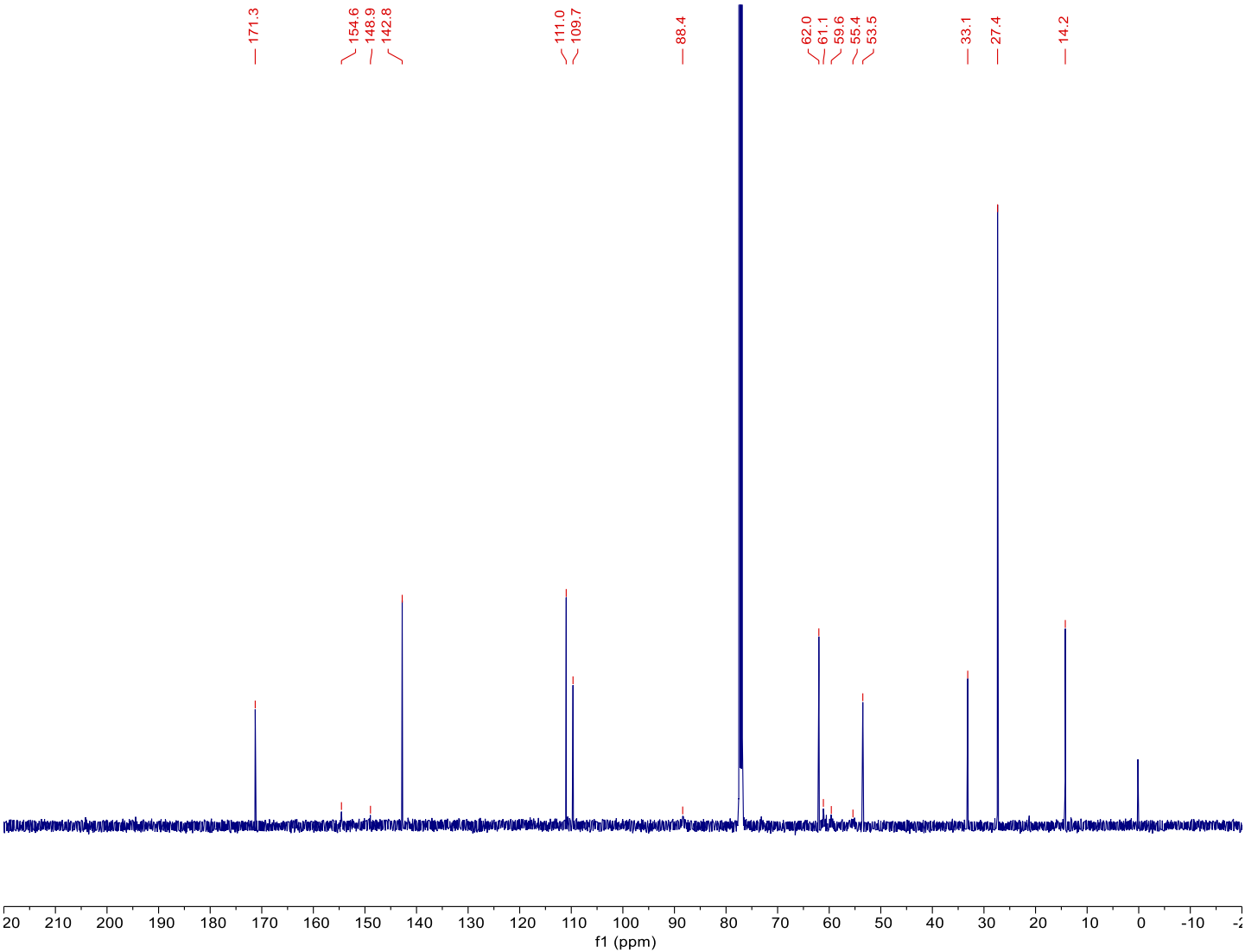
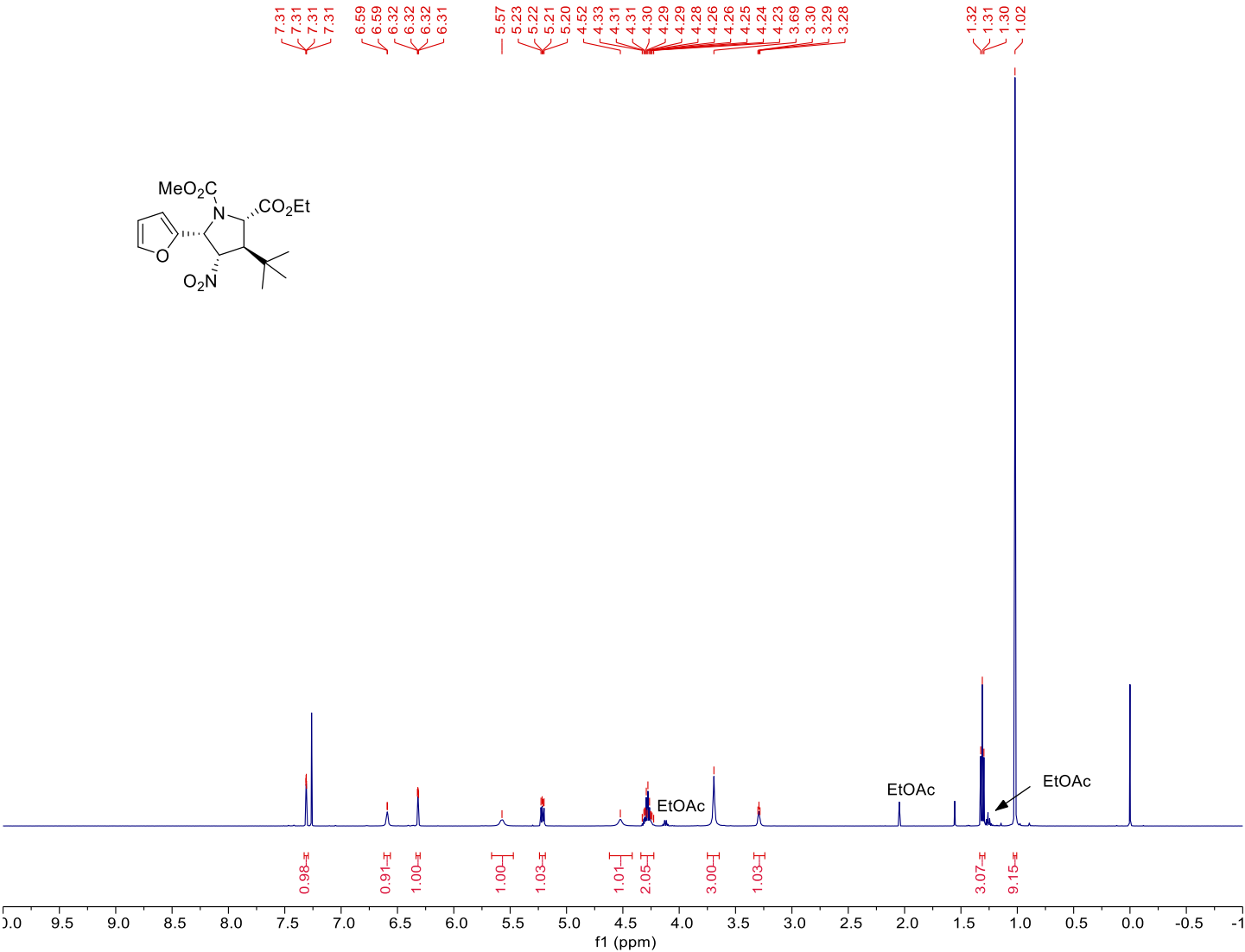
¹H NMR (400 MHz, CDCl₃) and ¹³C NMR (101 MHz, CDCl₃) spectra for compound **1p**.



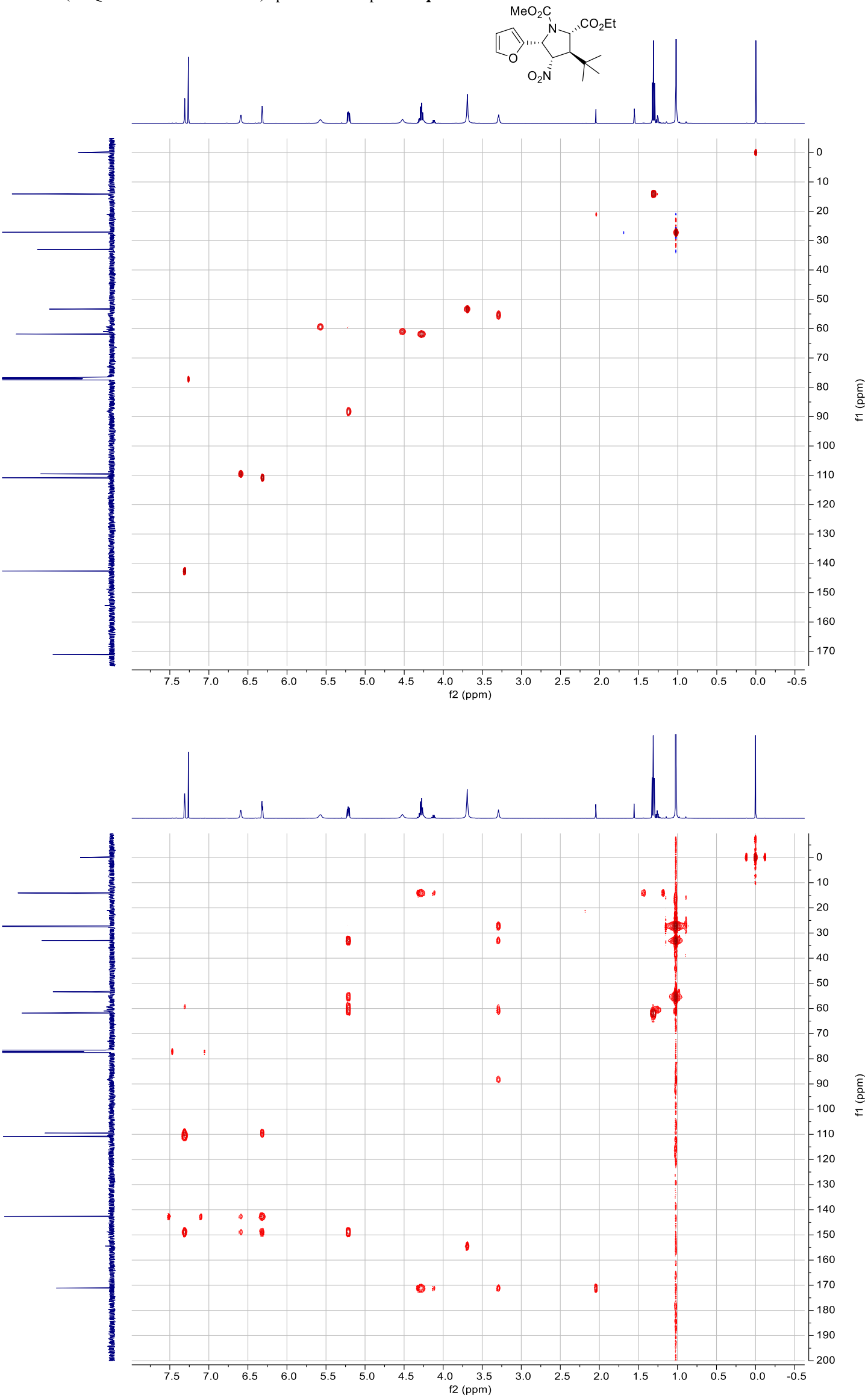
2D NMR (HSQC-nonedited and HMBC) spectra for compound **1p**.



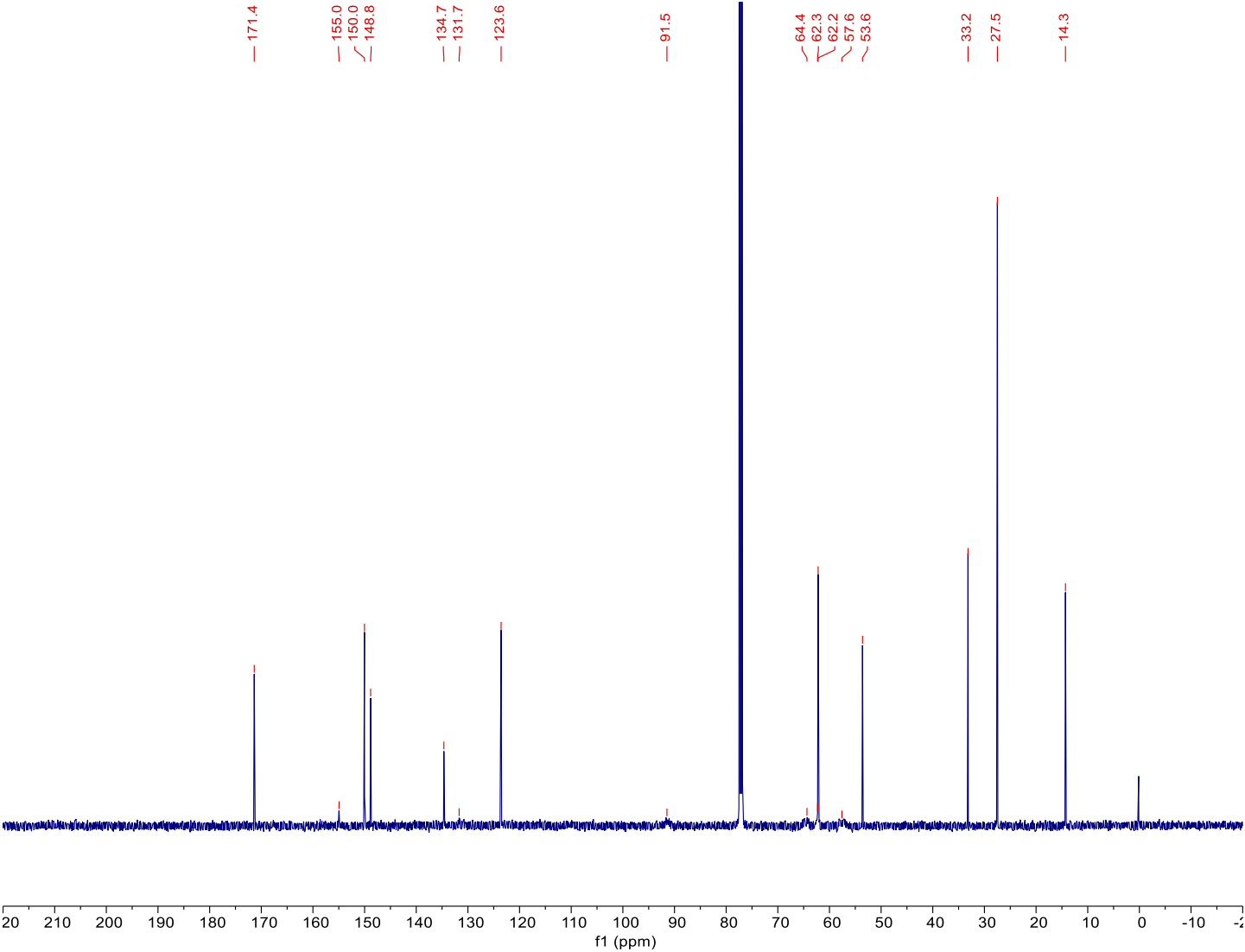
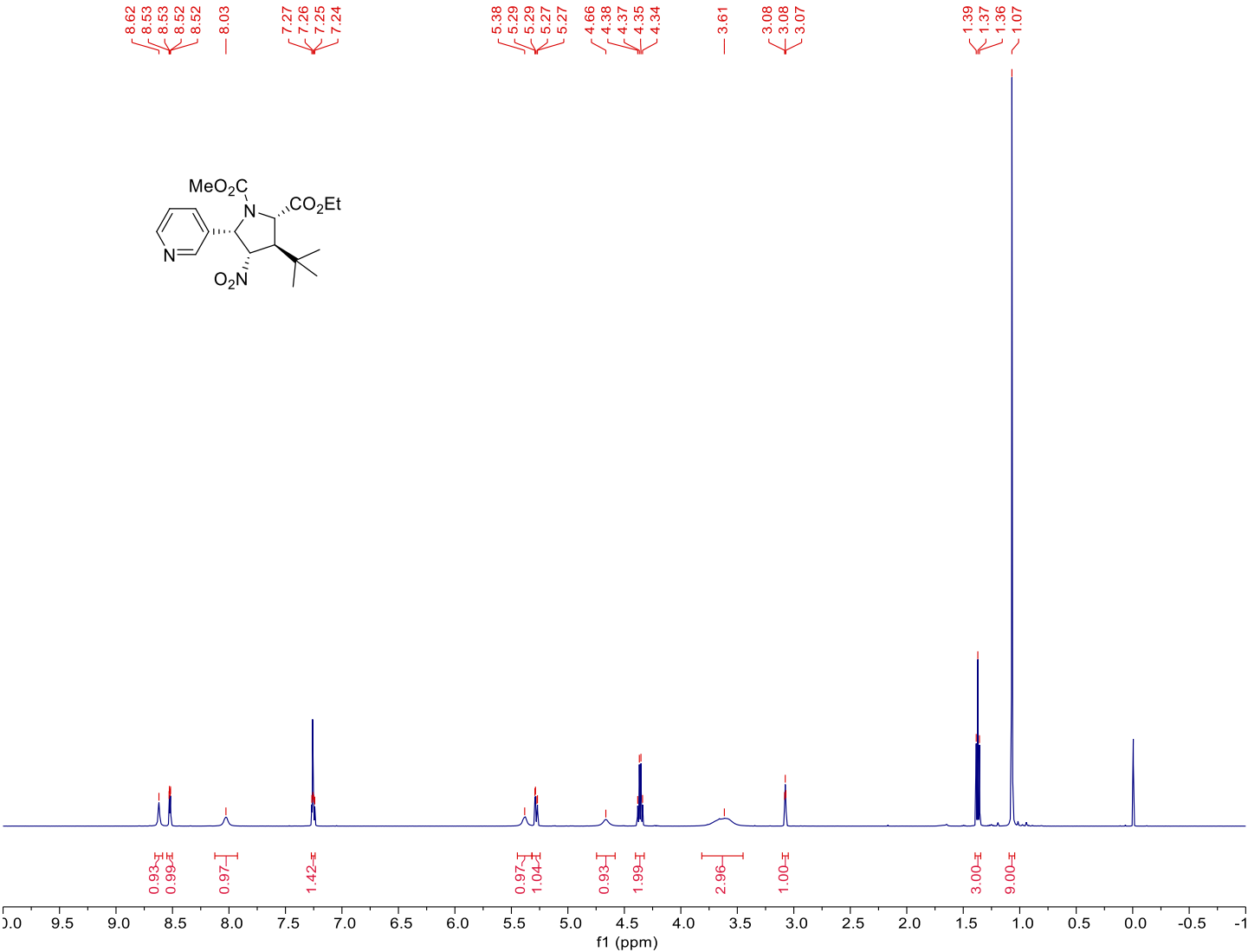
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1q**.



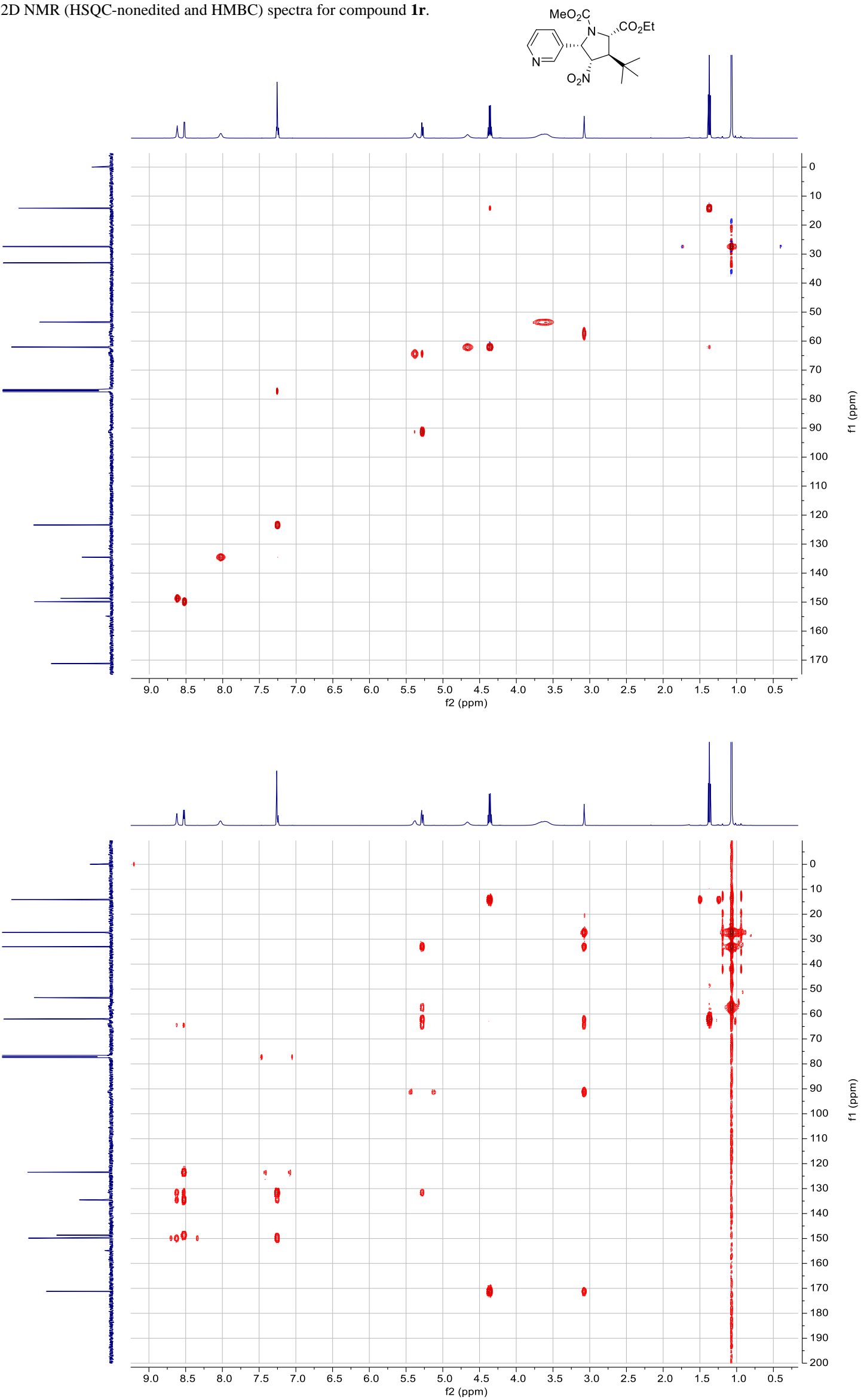
2D NMR (HSQC-nonedited and HMBC) spectra for compound **1q**.



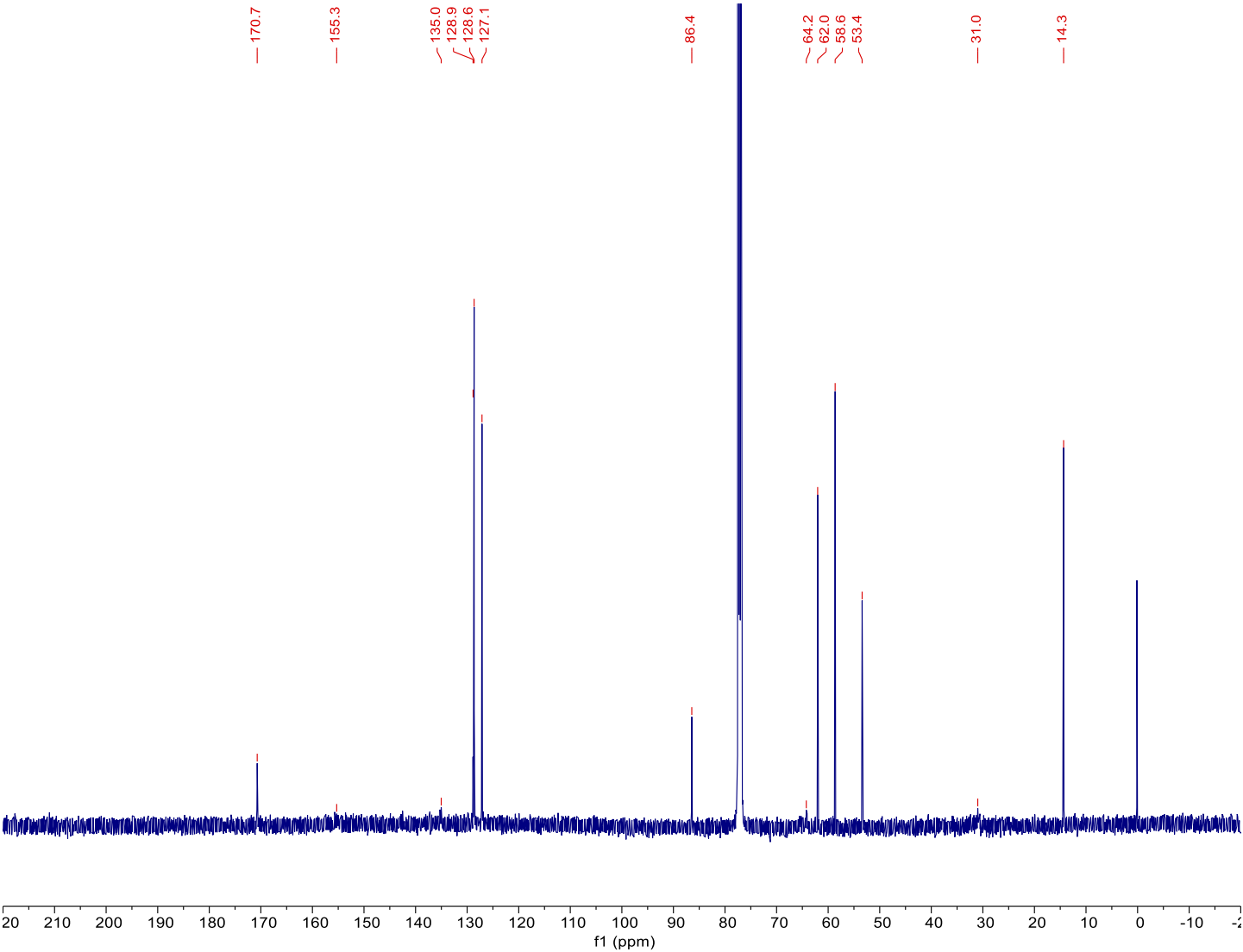
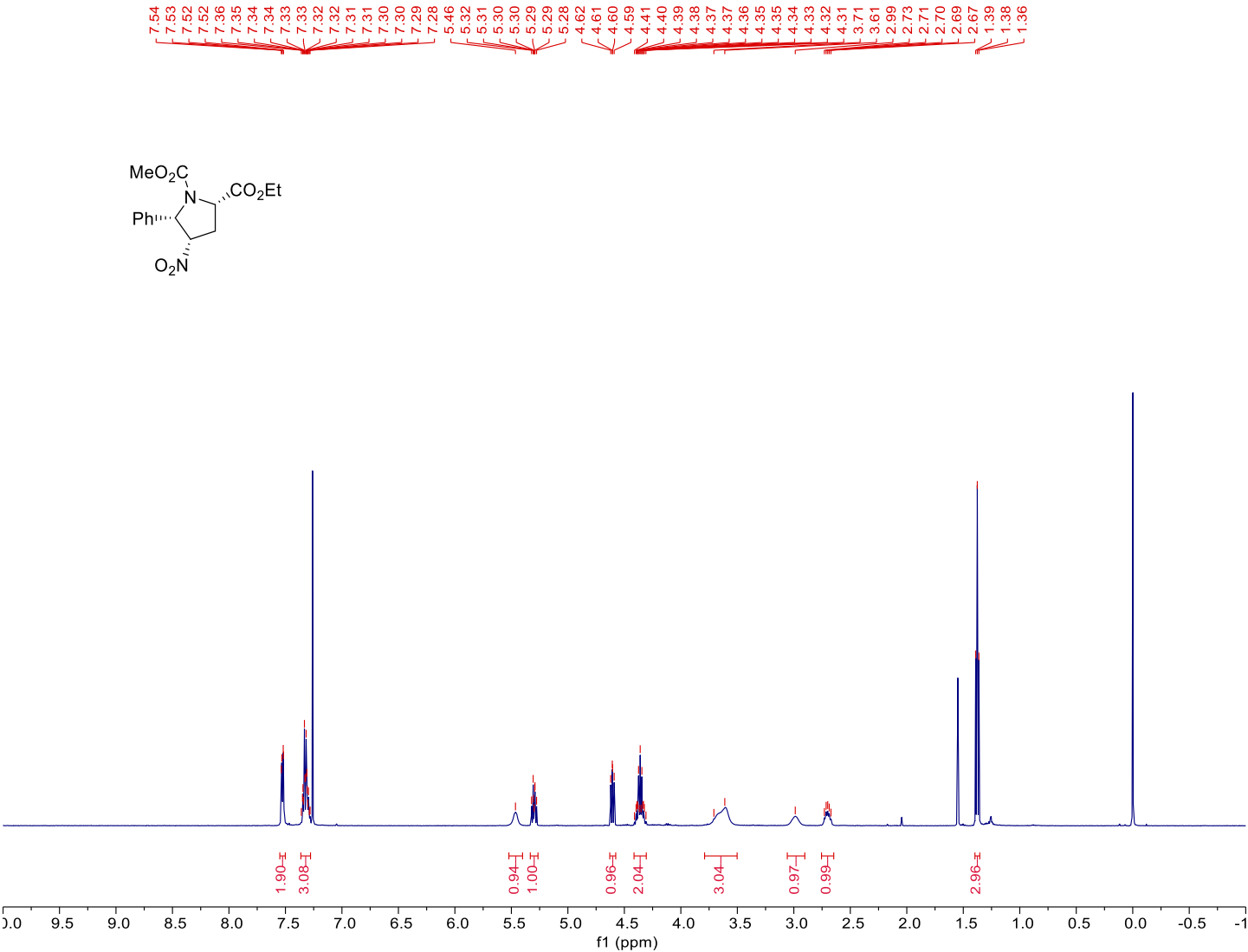
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1r**.



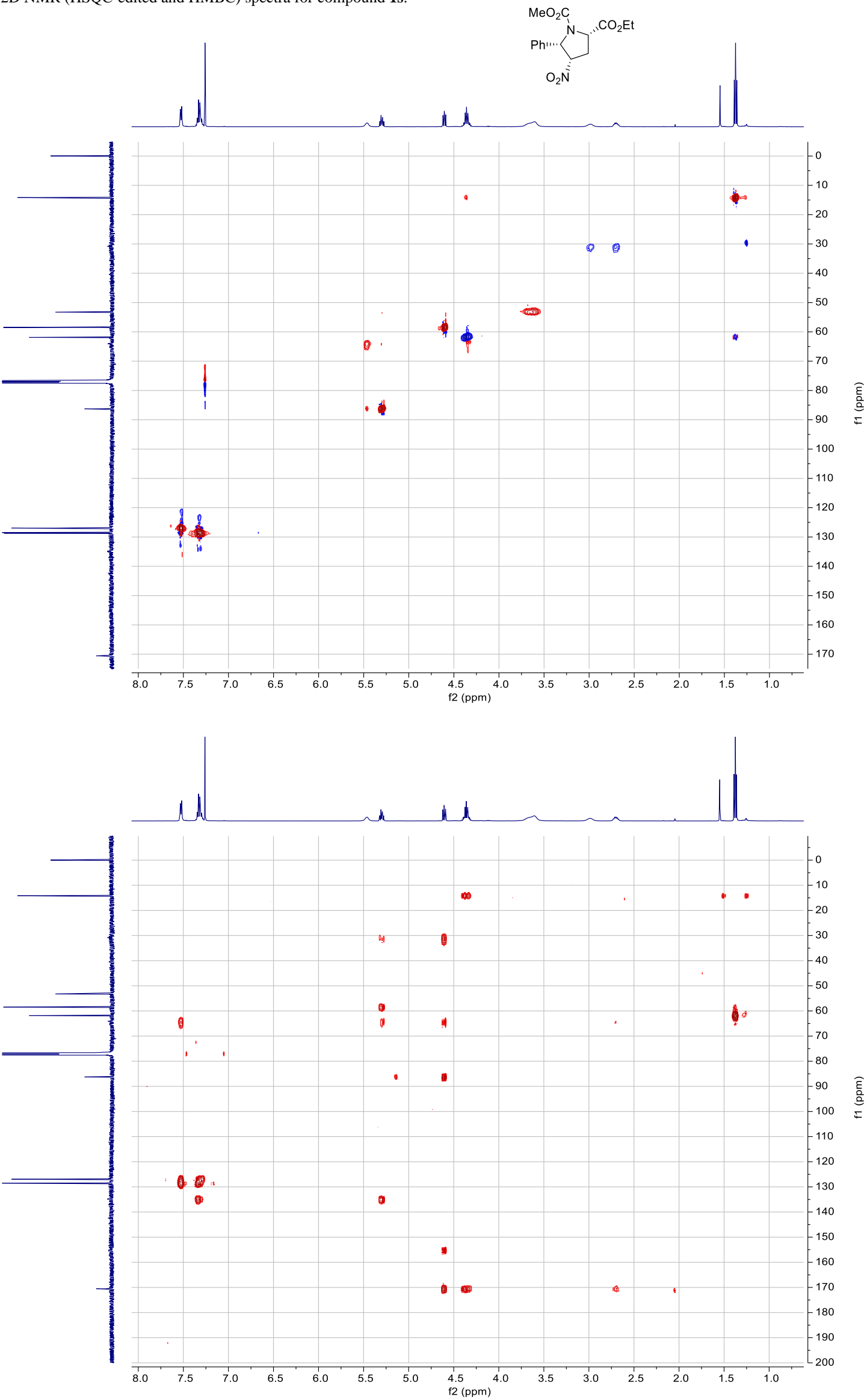
2D NMR (HSQC-nonedited and HMBC) spectra for compound **1r**.



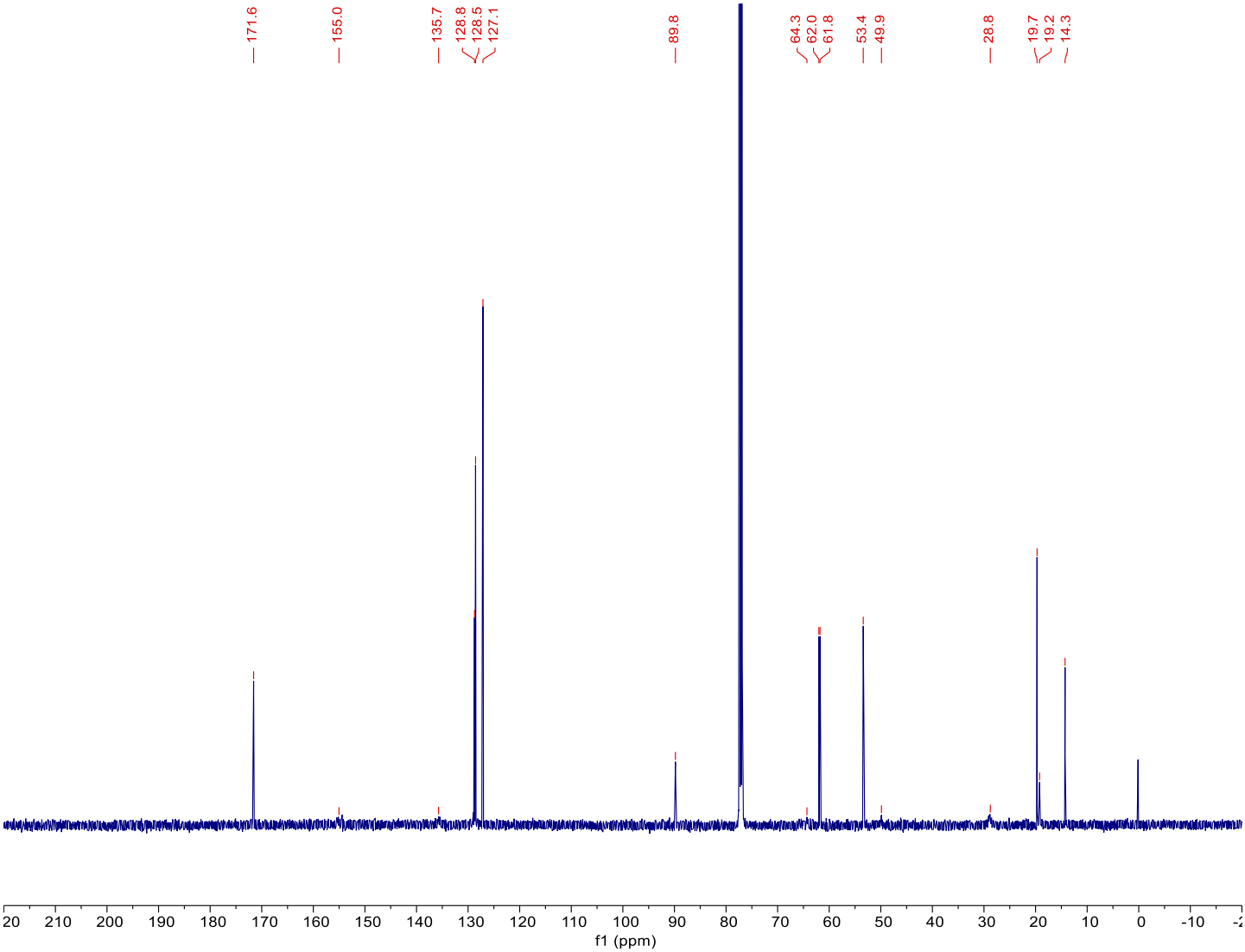
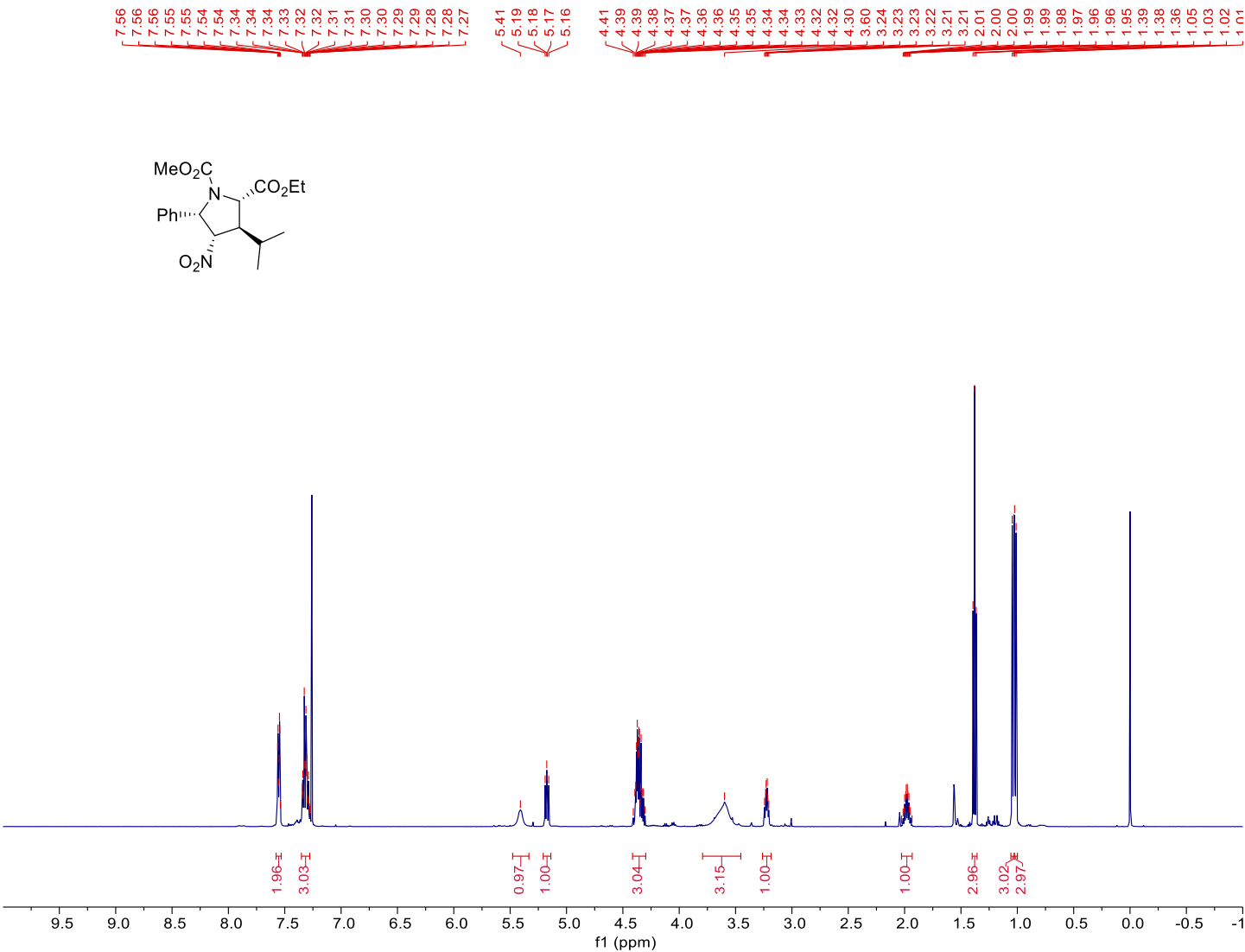
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1s**.



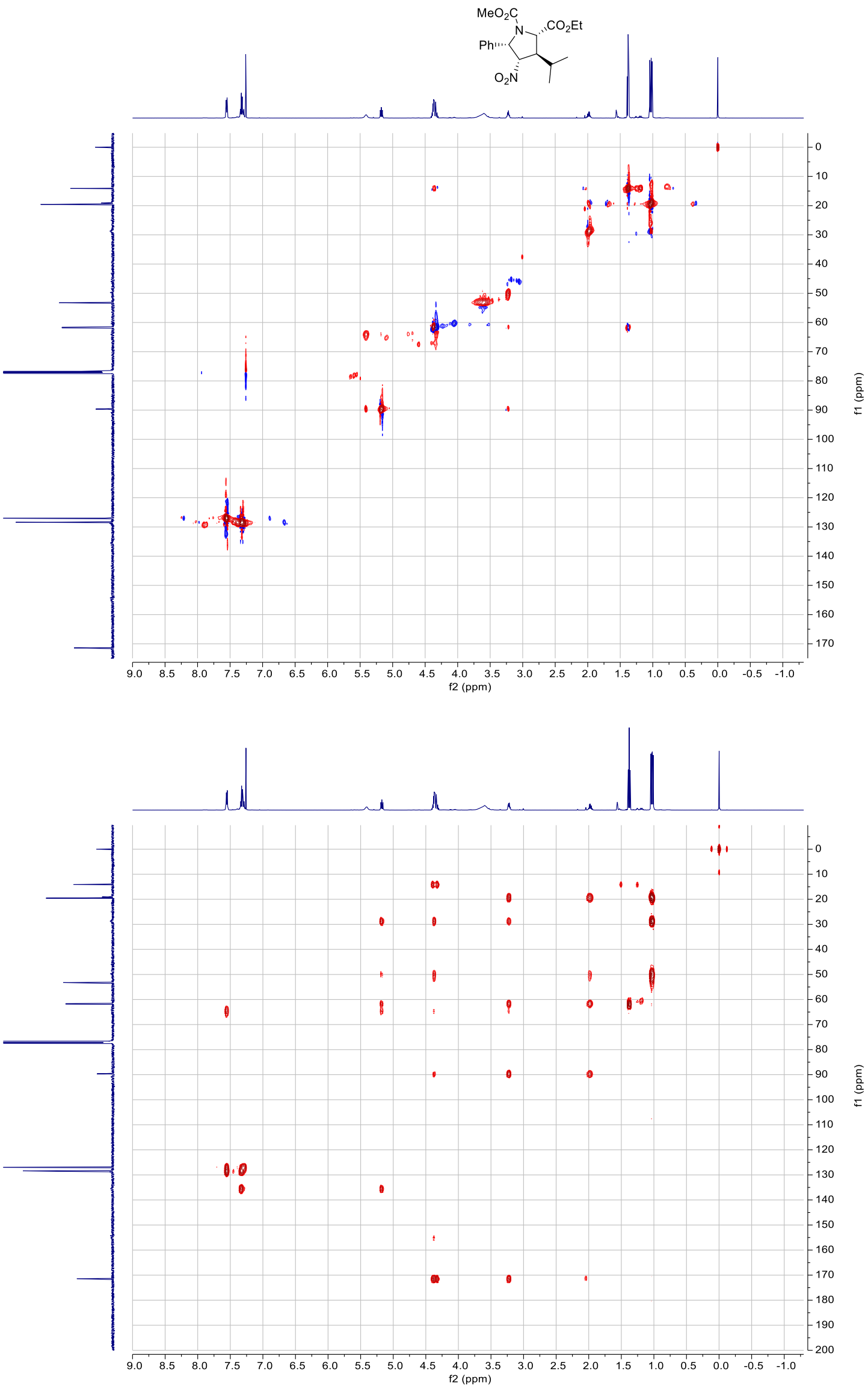
2D NMR (HSQC-edited and HMBC) spectra for compound **1s**.



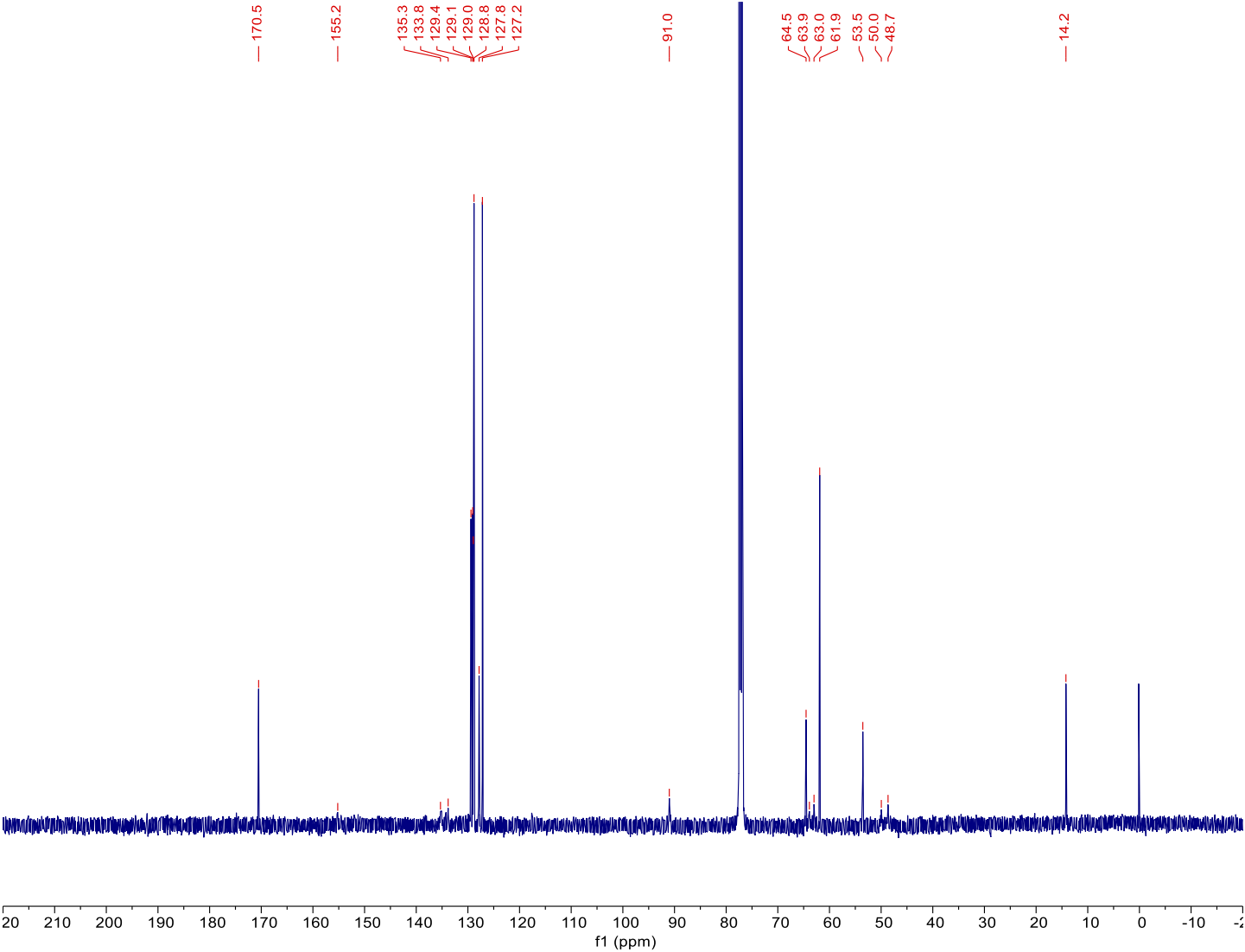
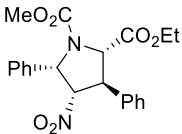
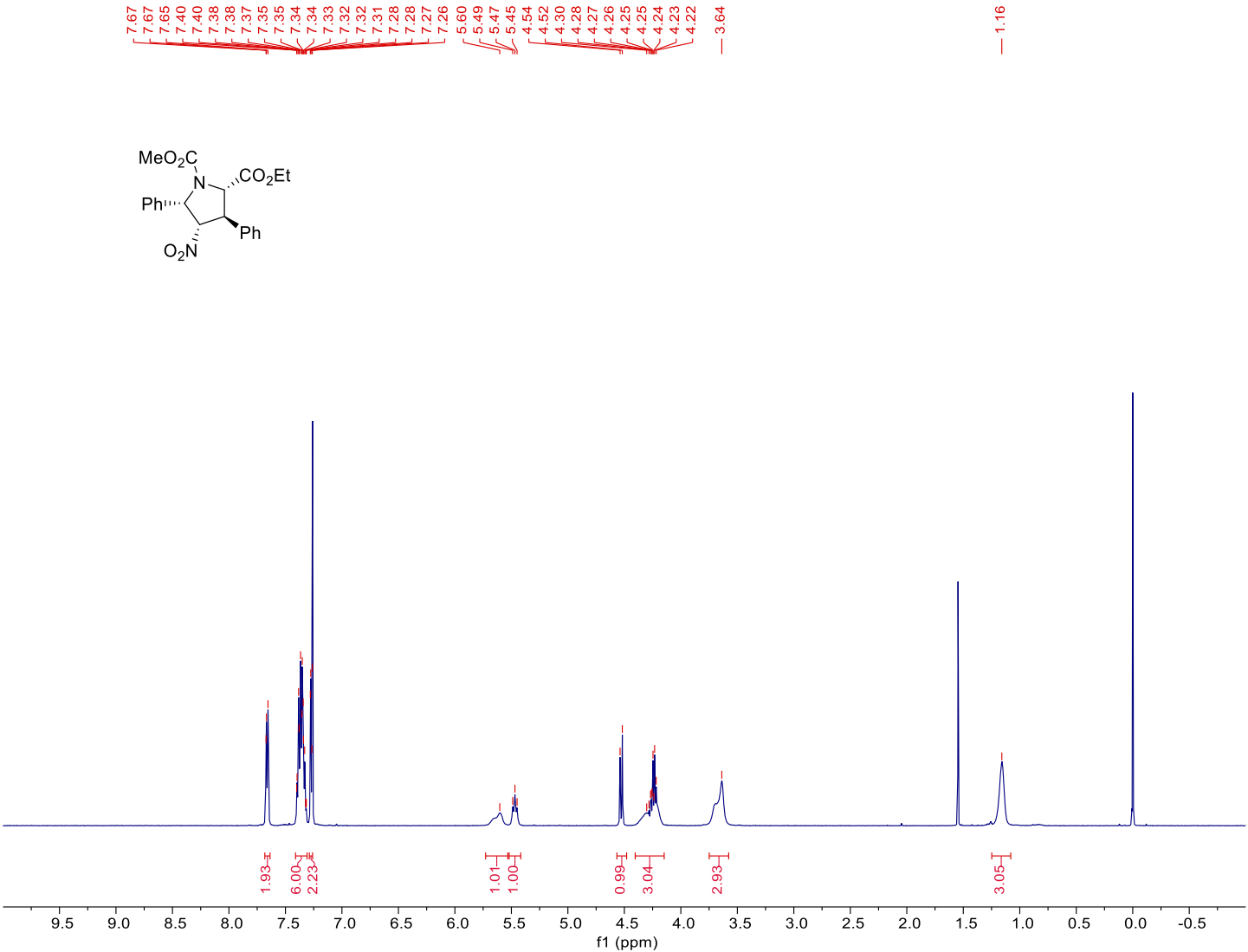
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1t**.



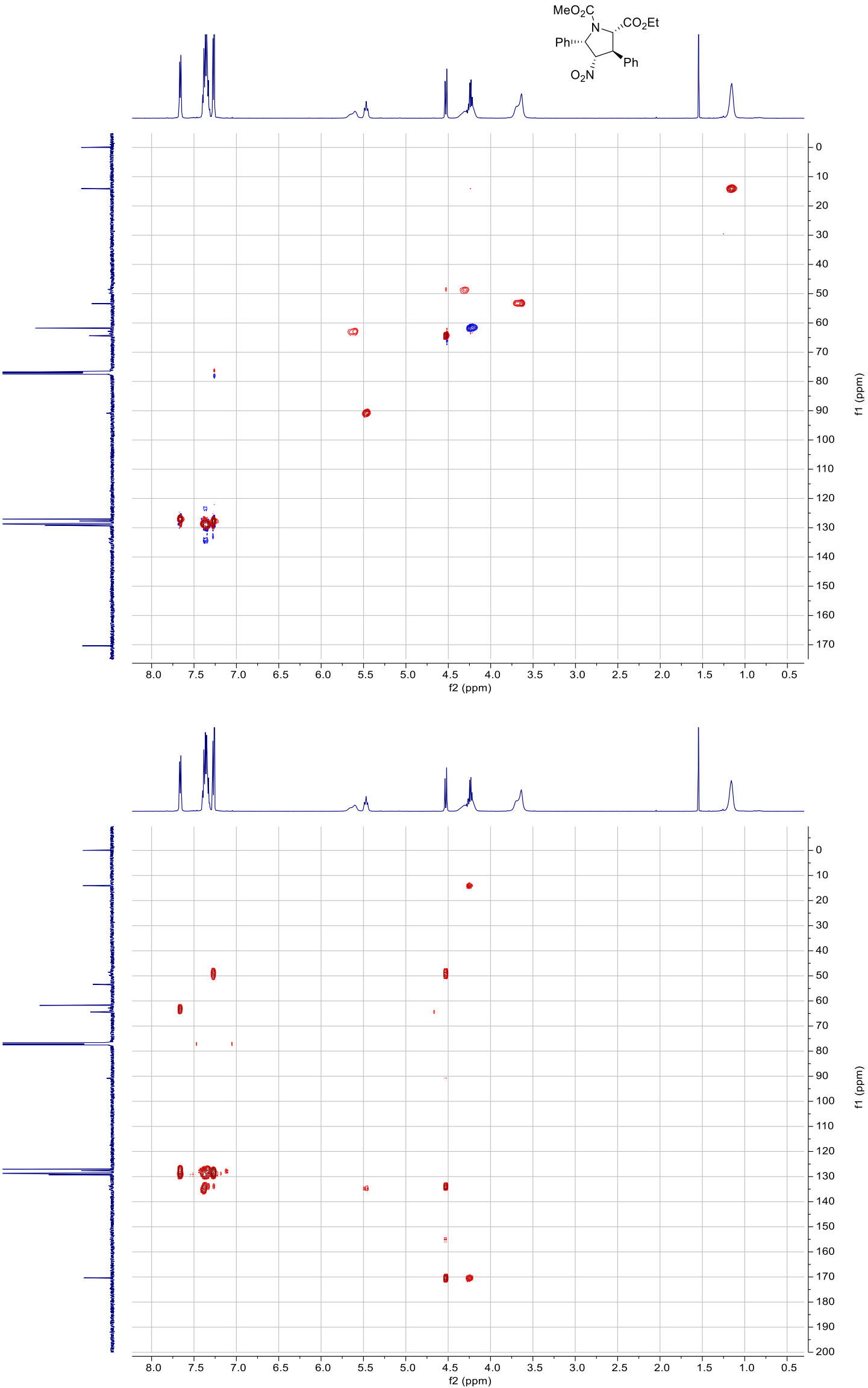
2D NMR (HSQC-edited and HMBC) spectra for compound **1t**.



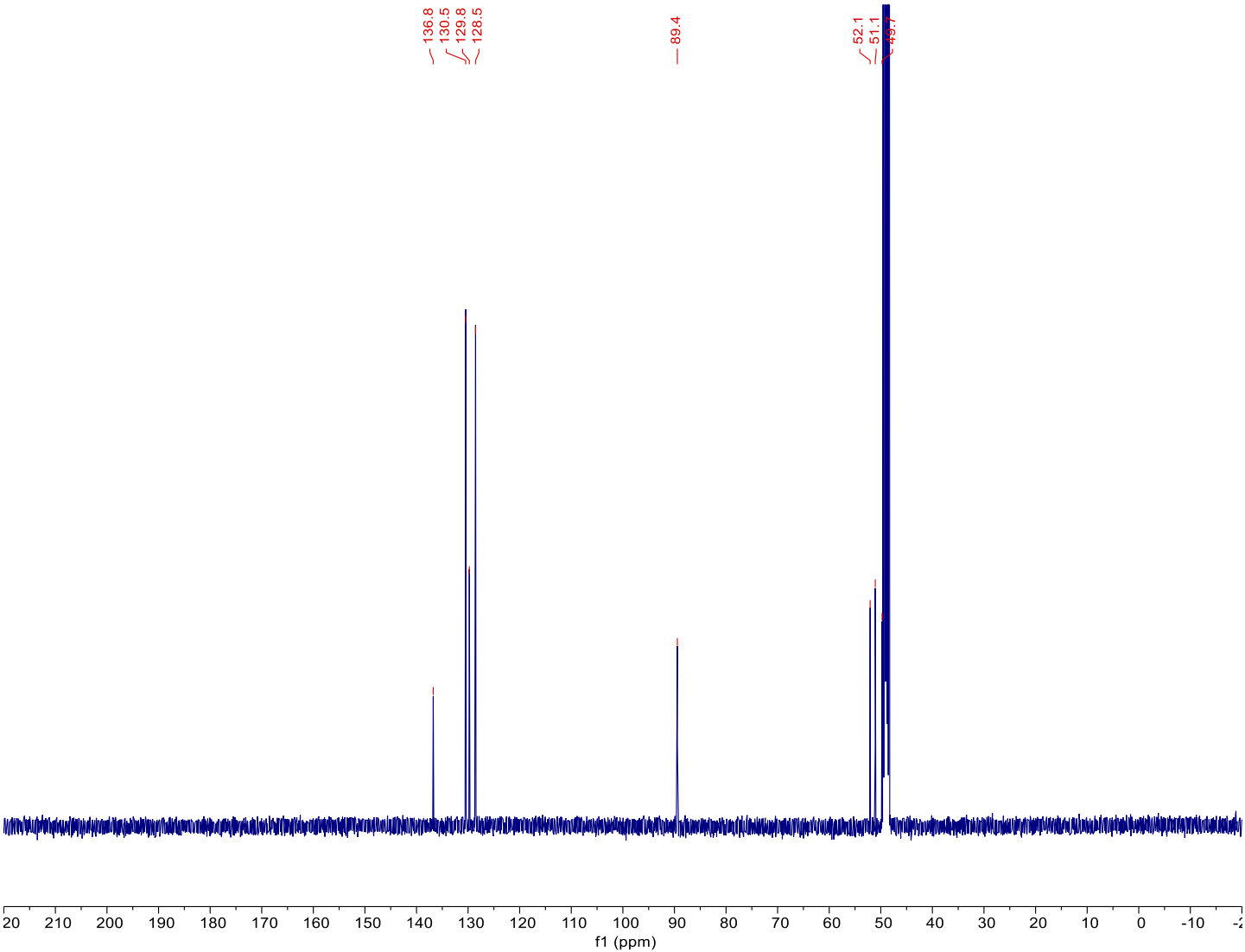
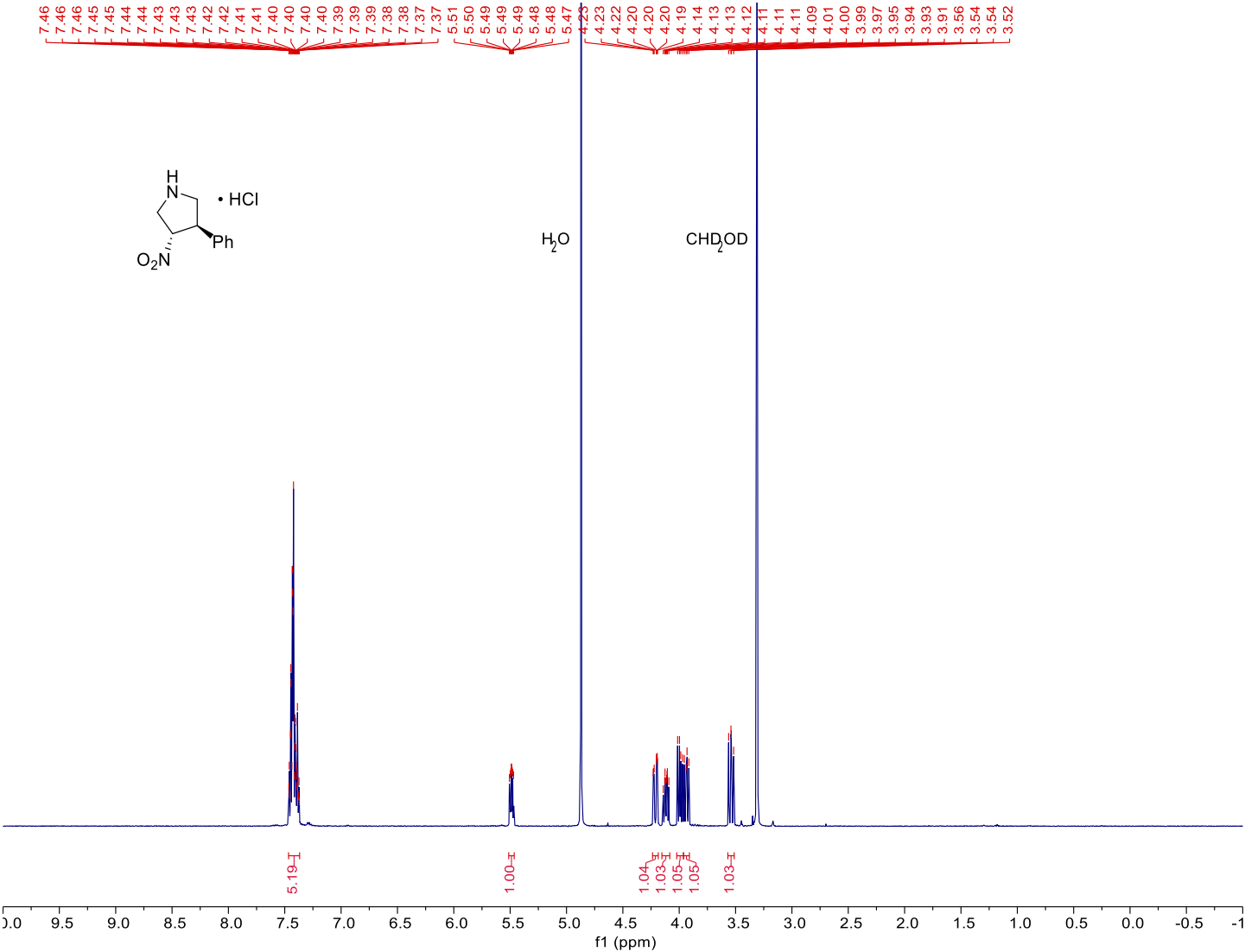
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1u**.



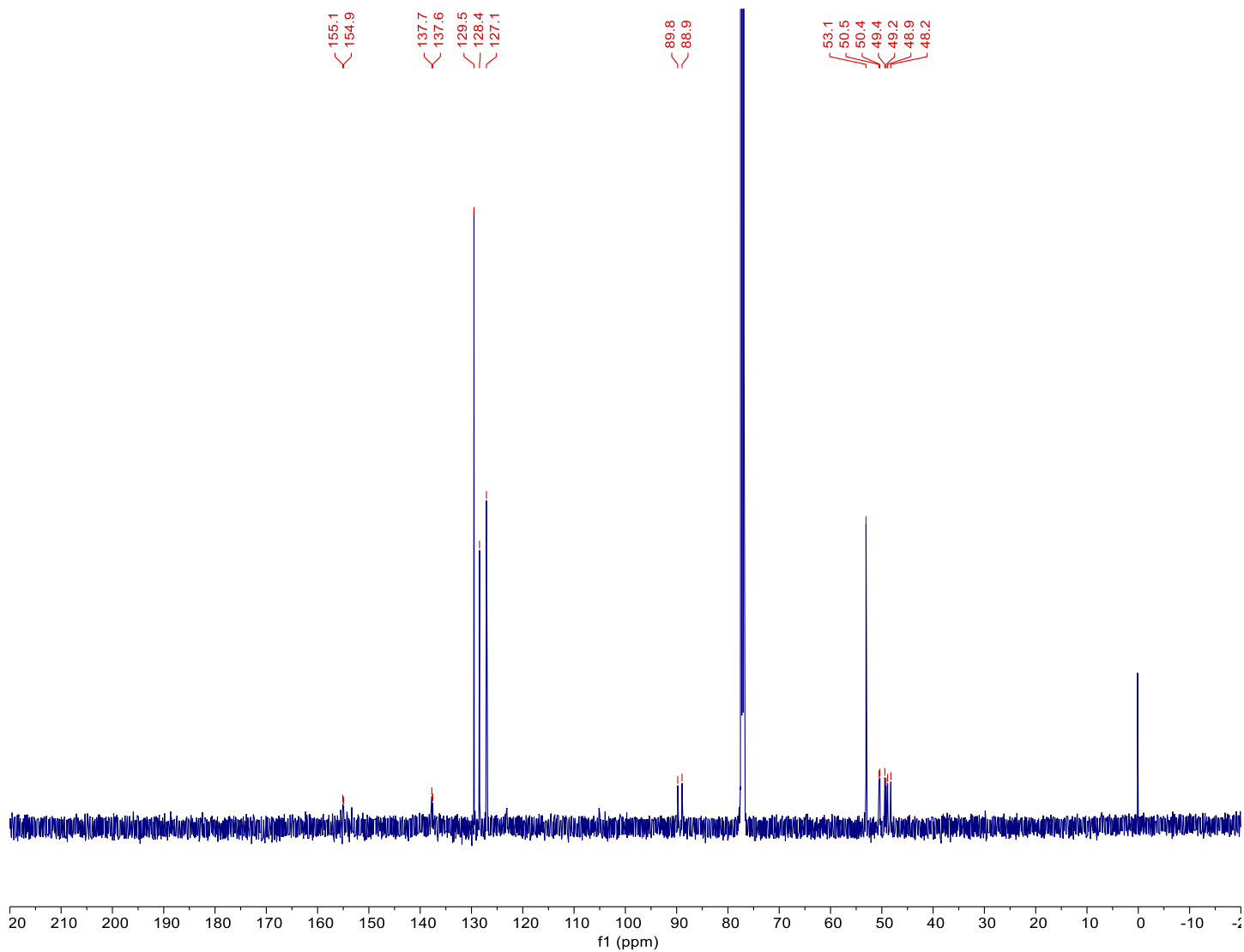
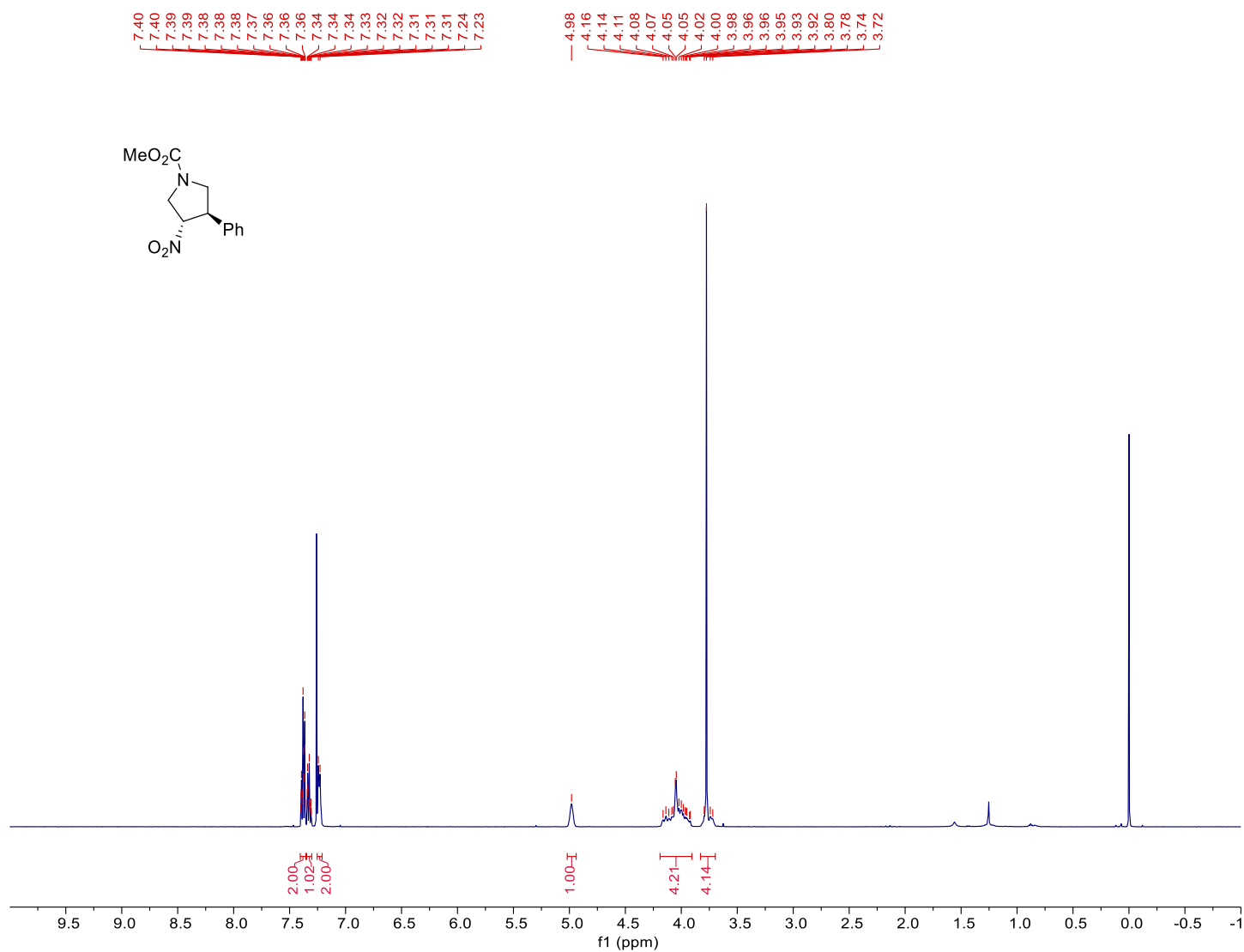
2D NMR (HSQC-edited and HMBC) spectra for compound **1u**.



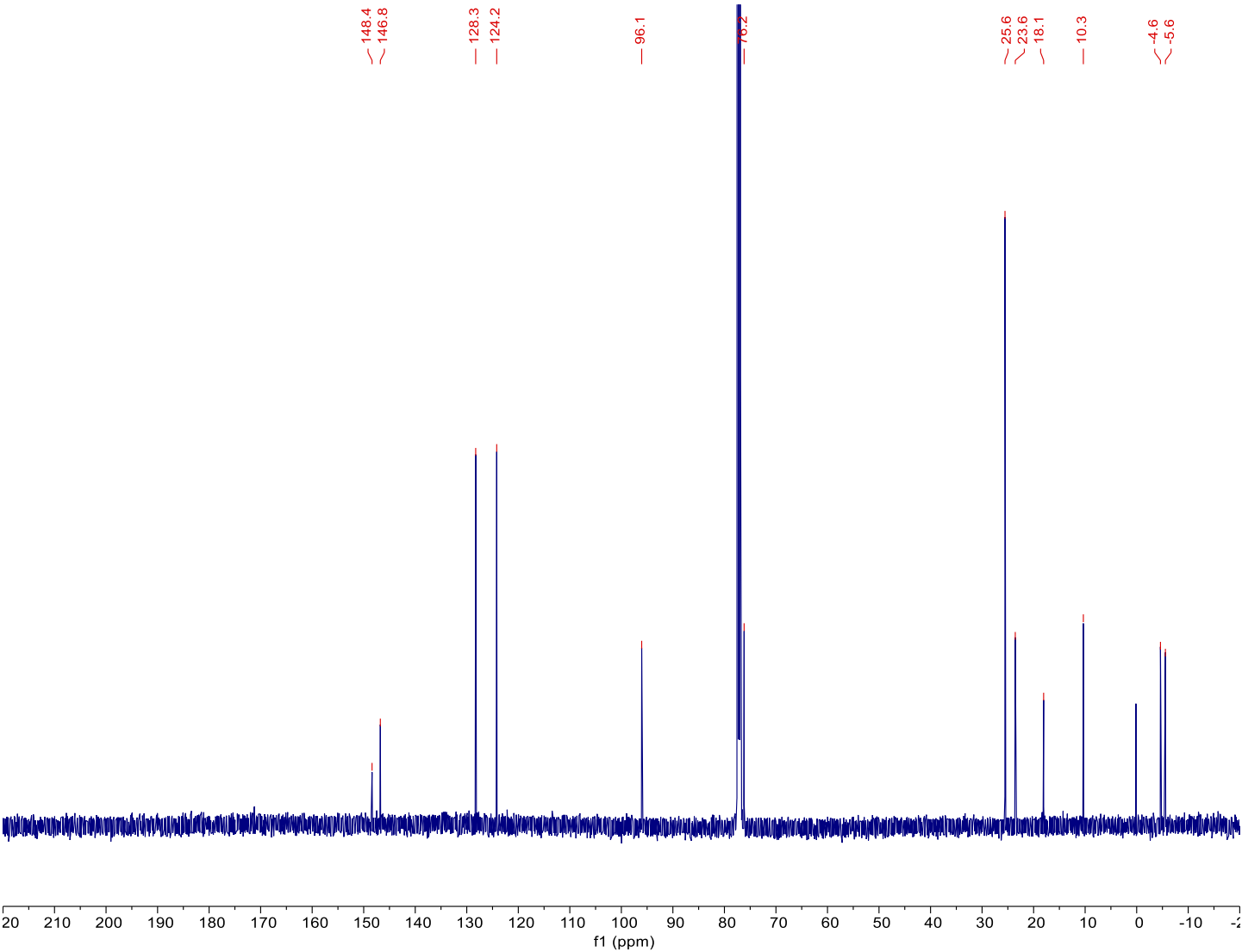
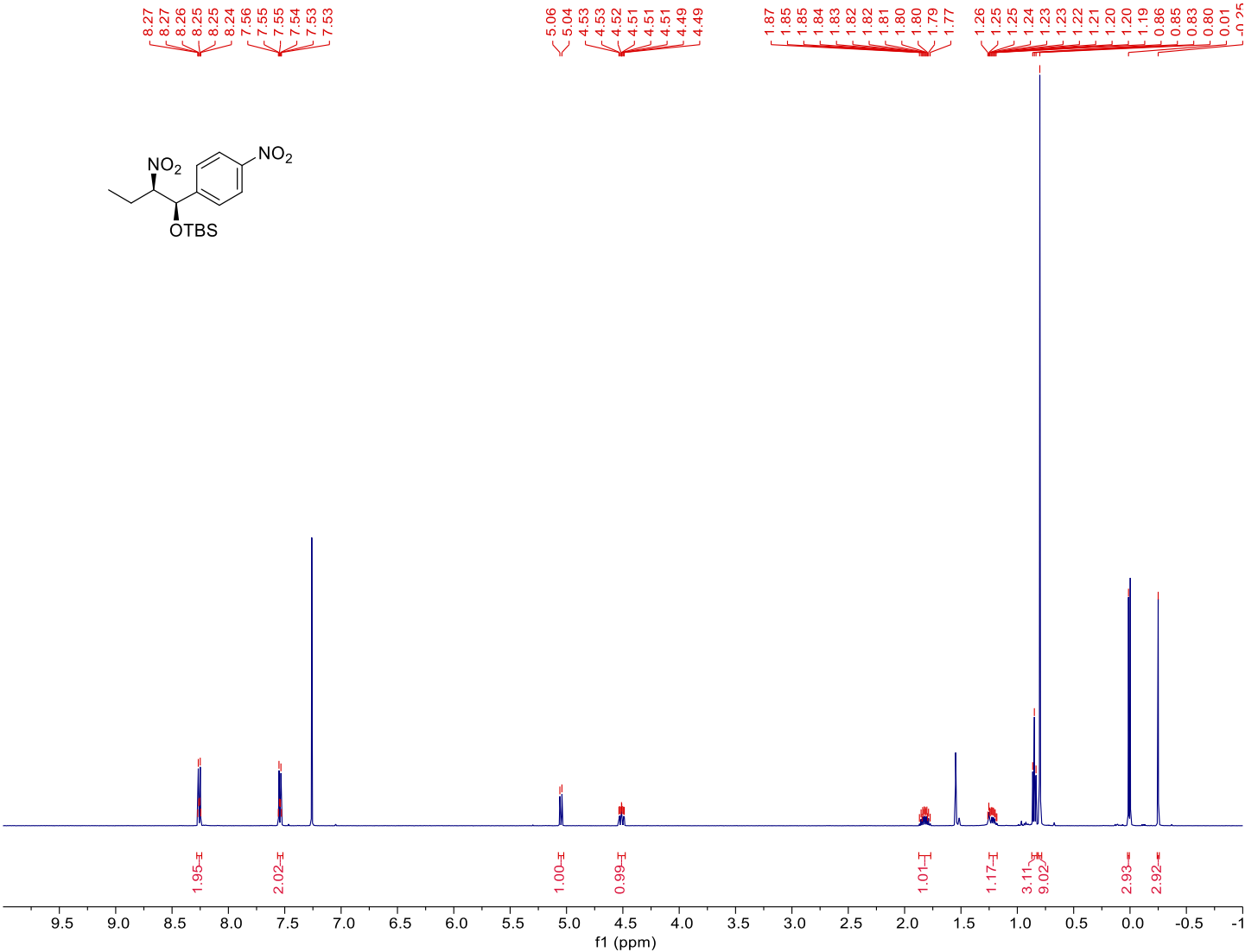
¹H NMR (500 MHz, CD₃OD) and ¹³C NMR (126 MHz, CD₃OD) spectra for compound **S4**.



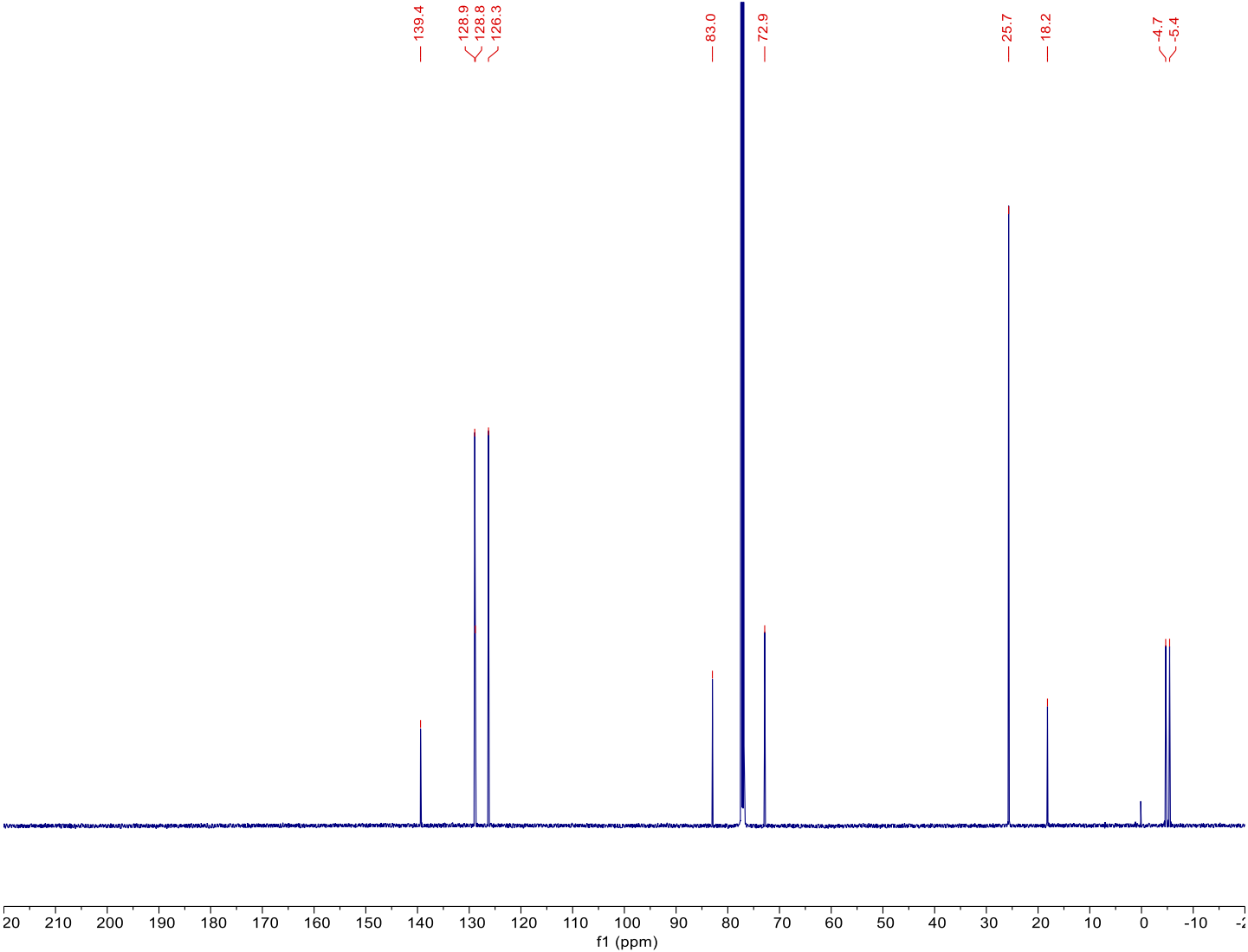
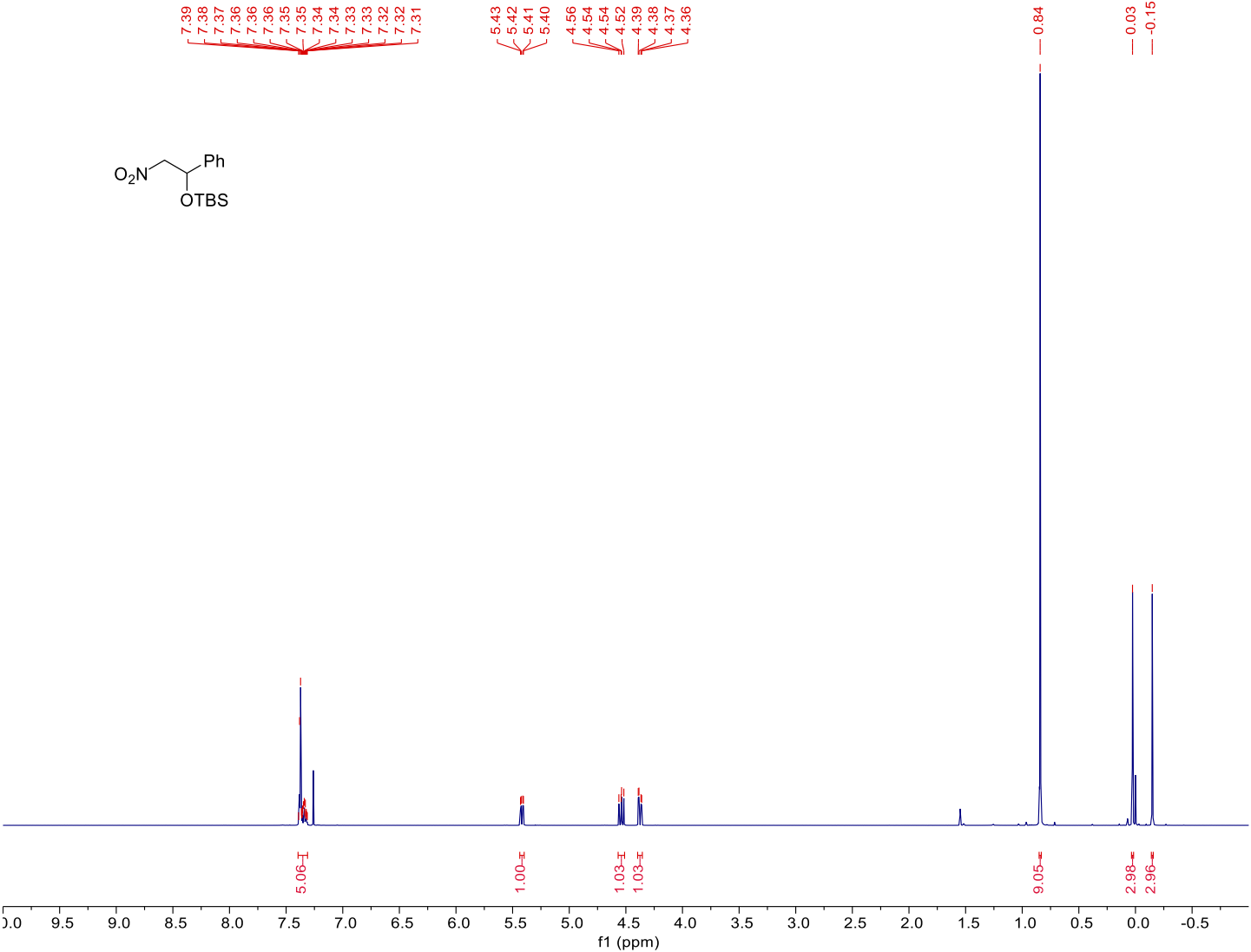
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1v**.



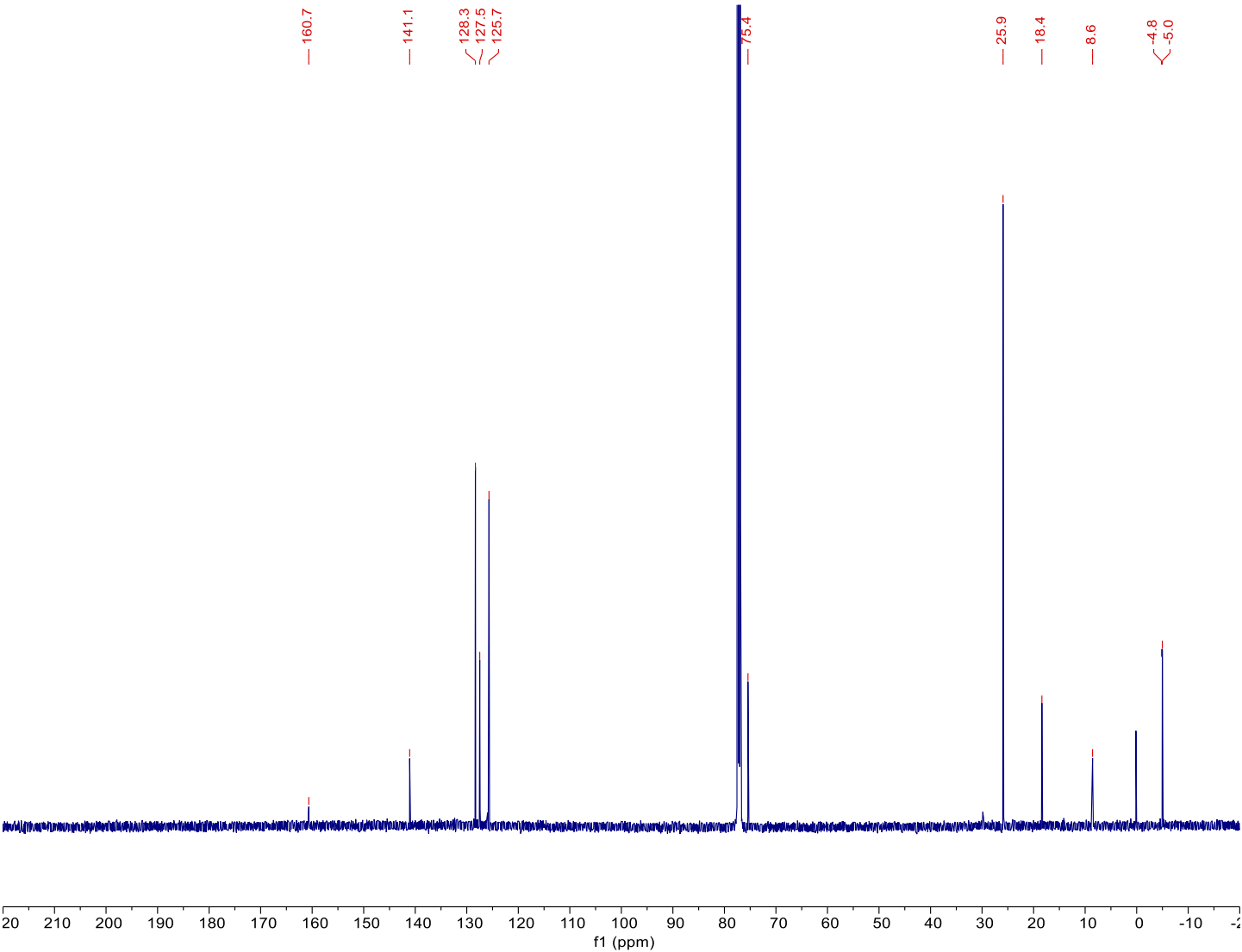
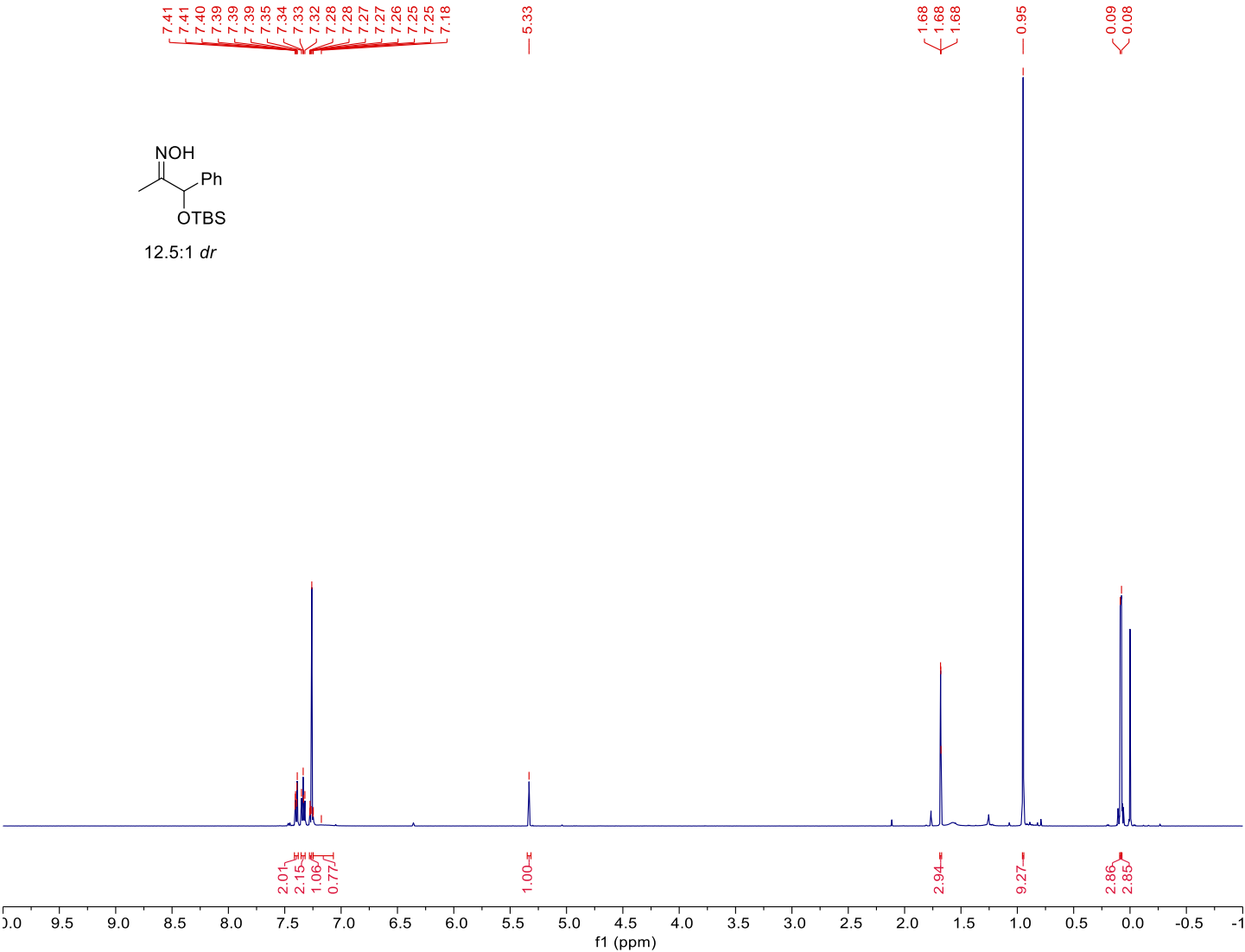
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1w**.



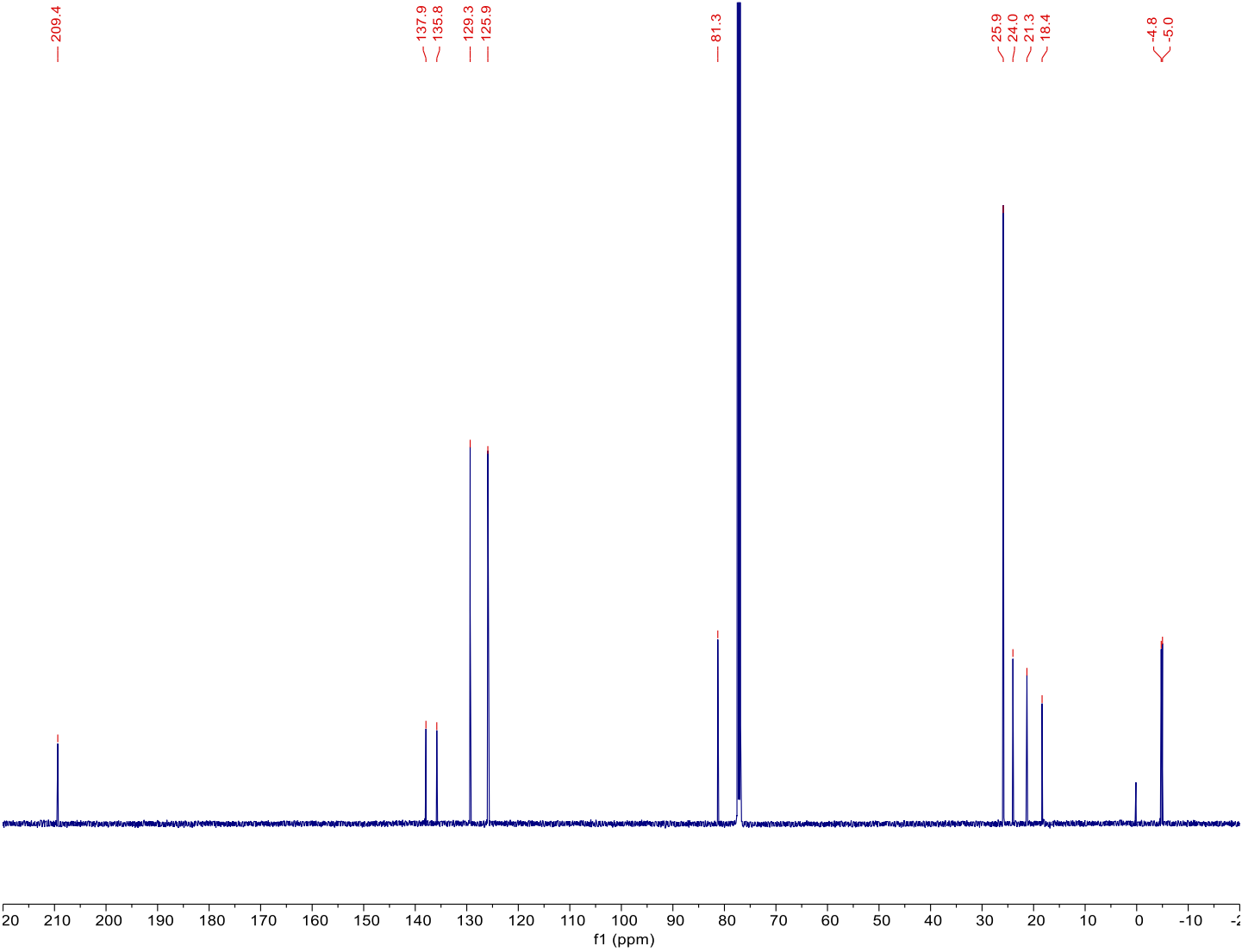
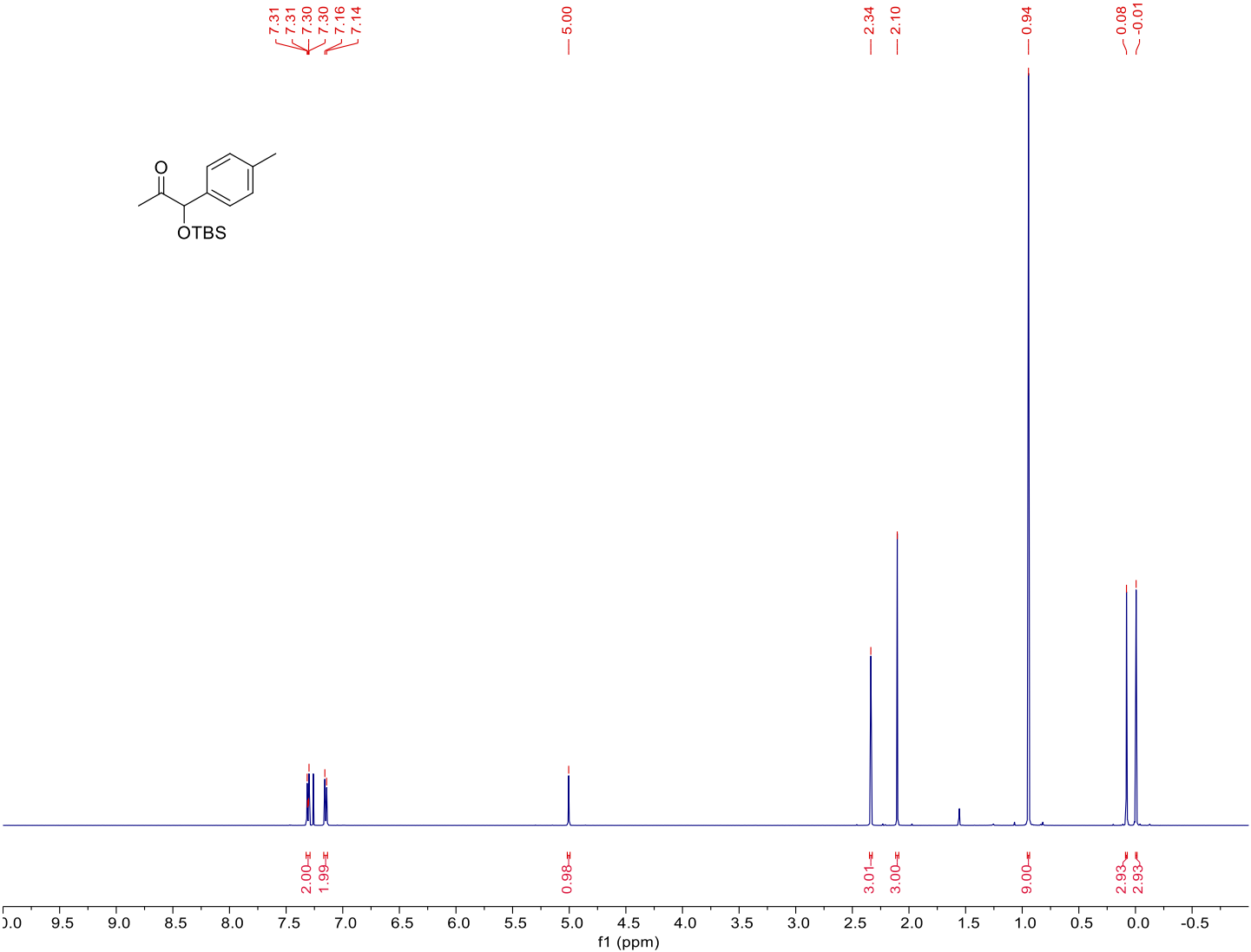
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **1x**.



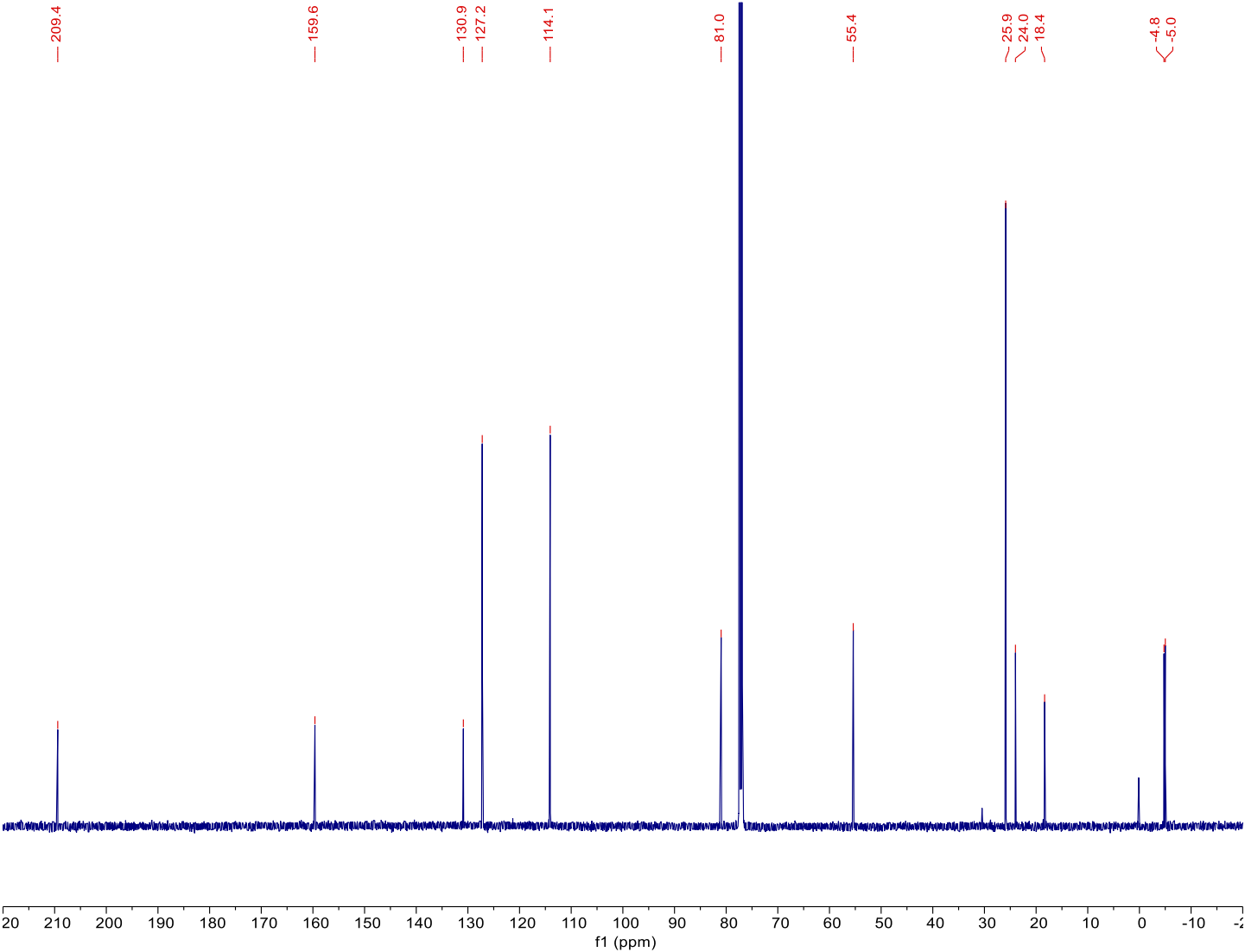
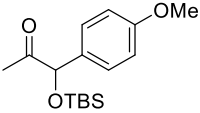
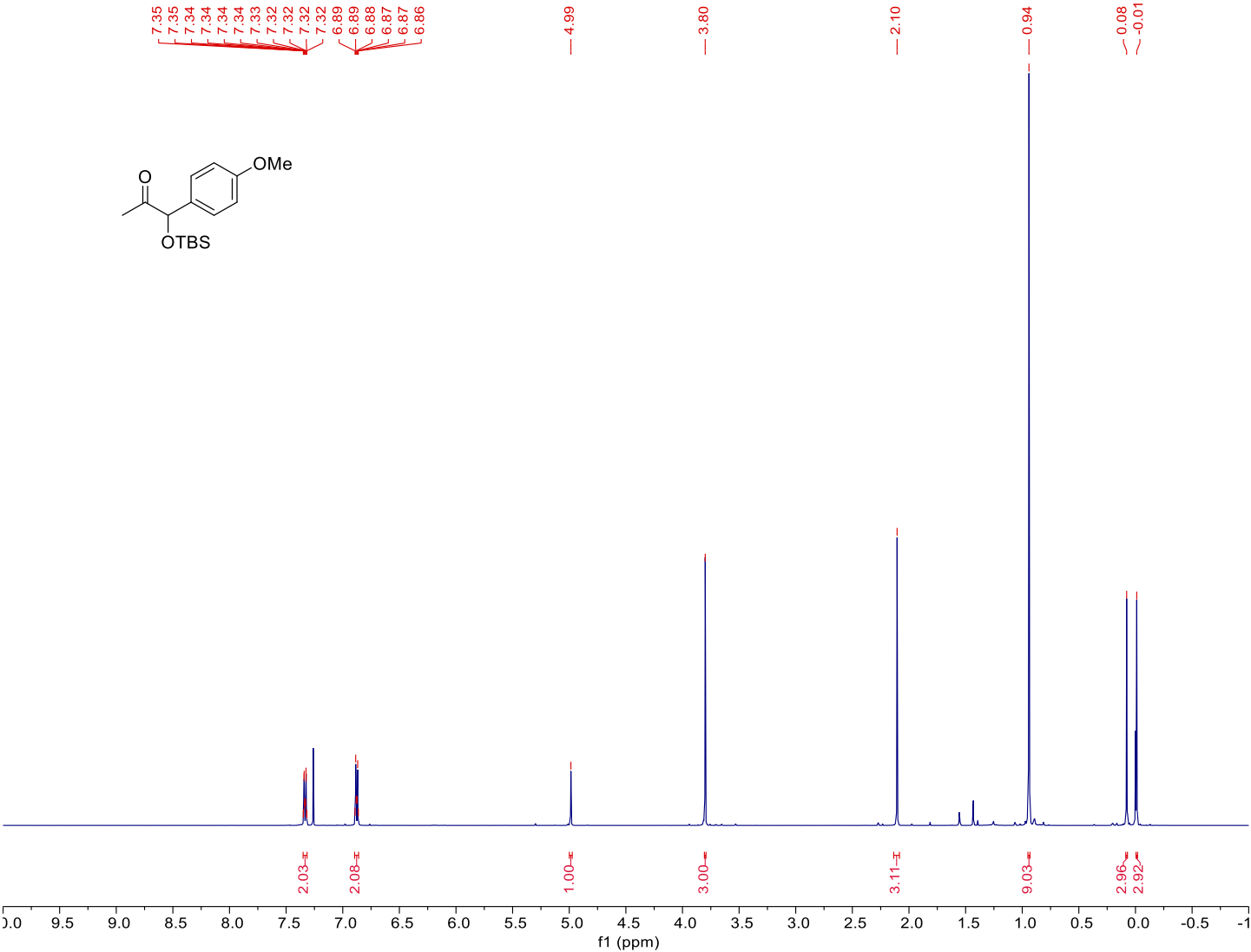
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **2a**.



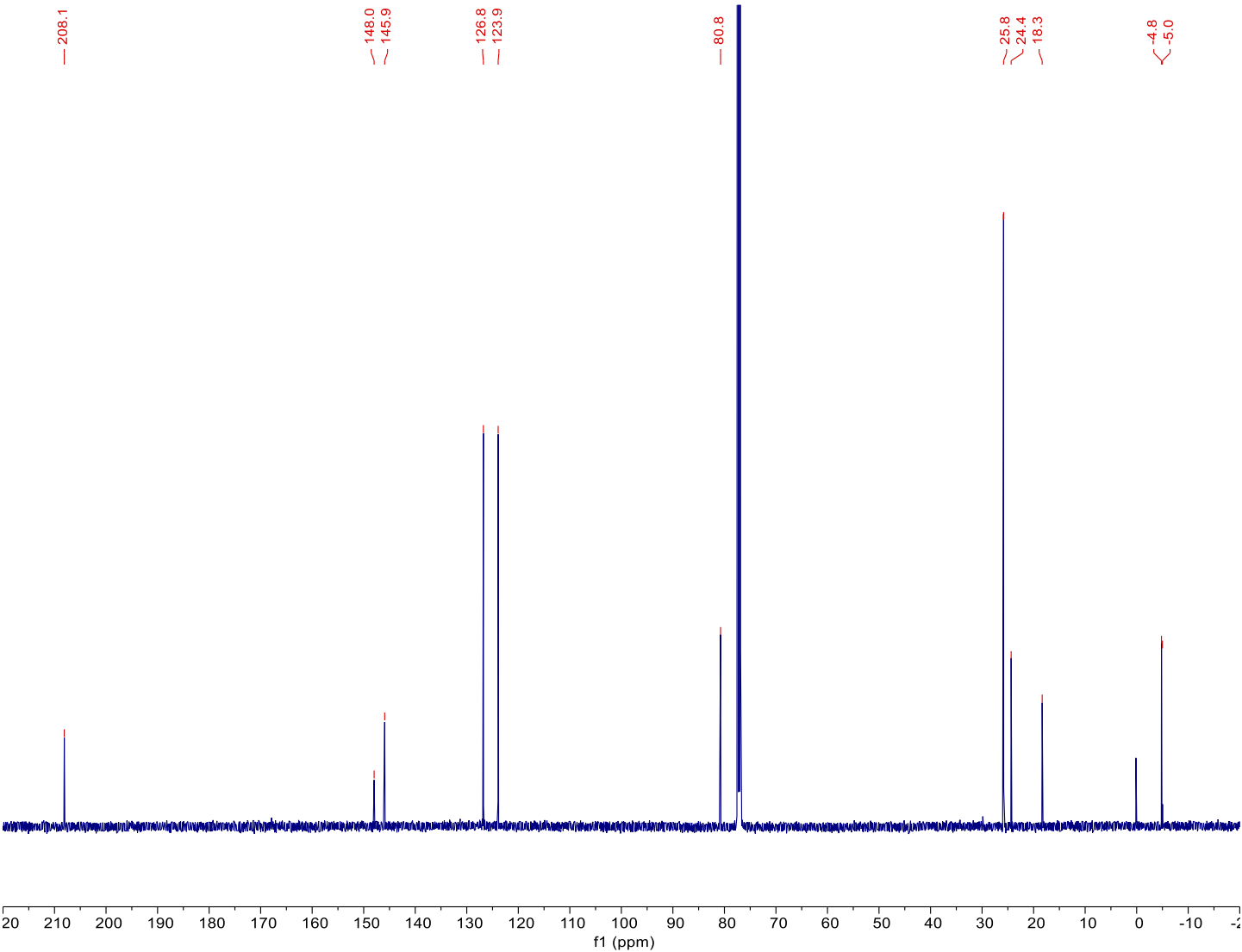
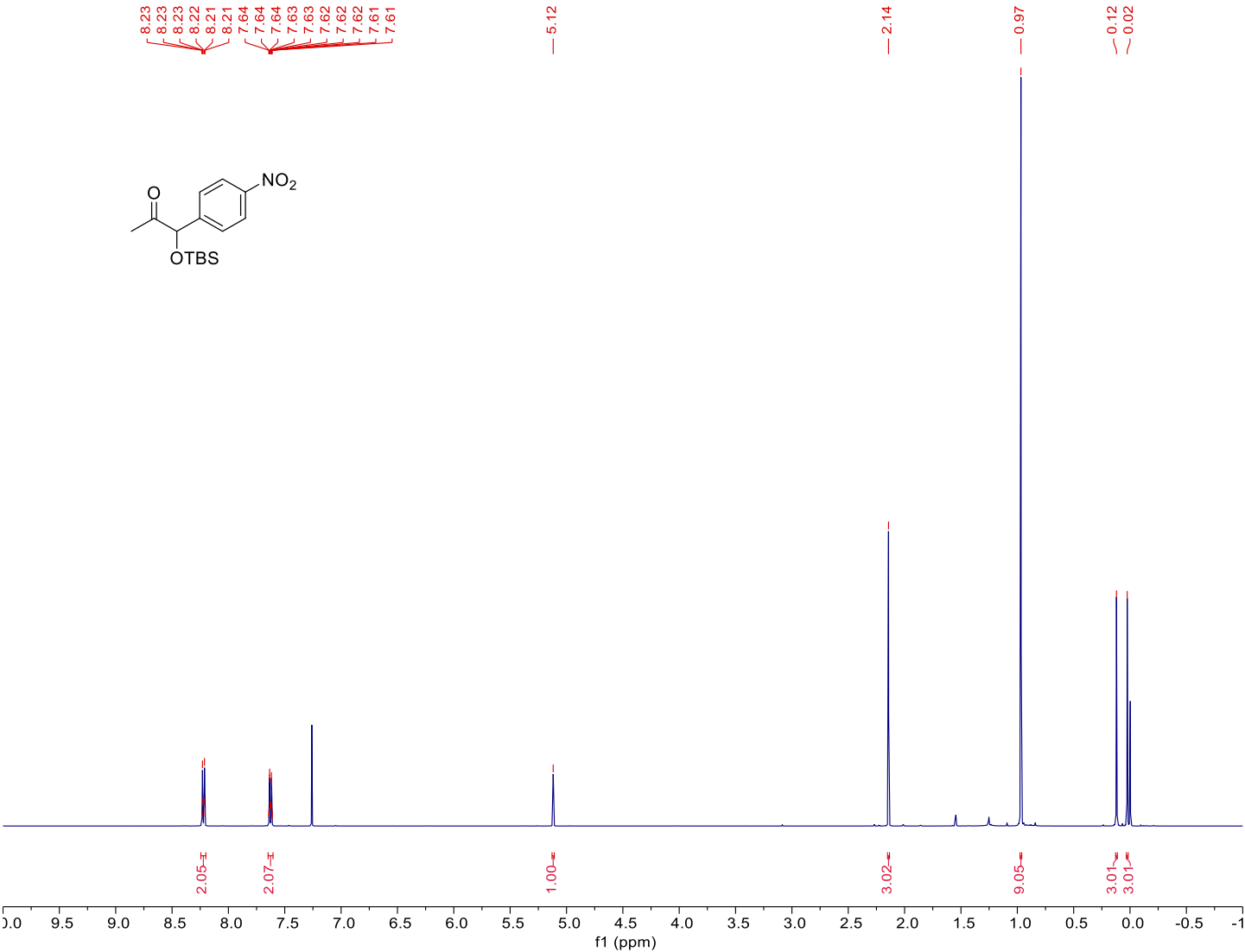
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3b**.



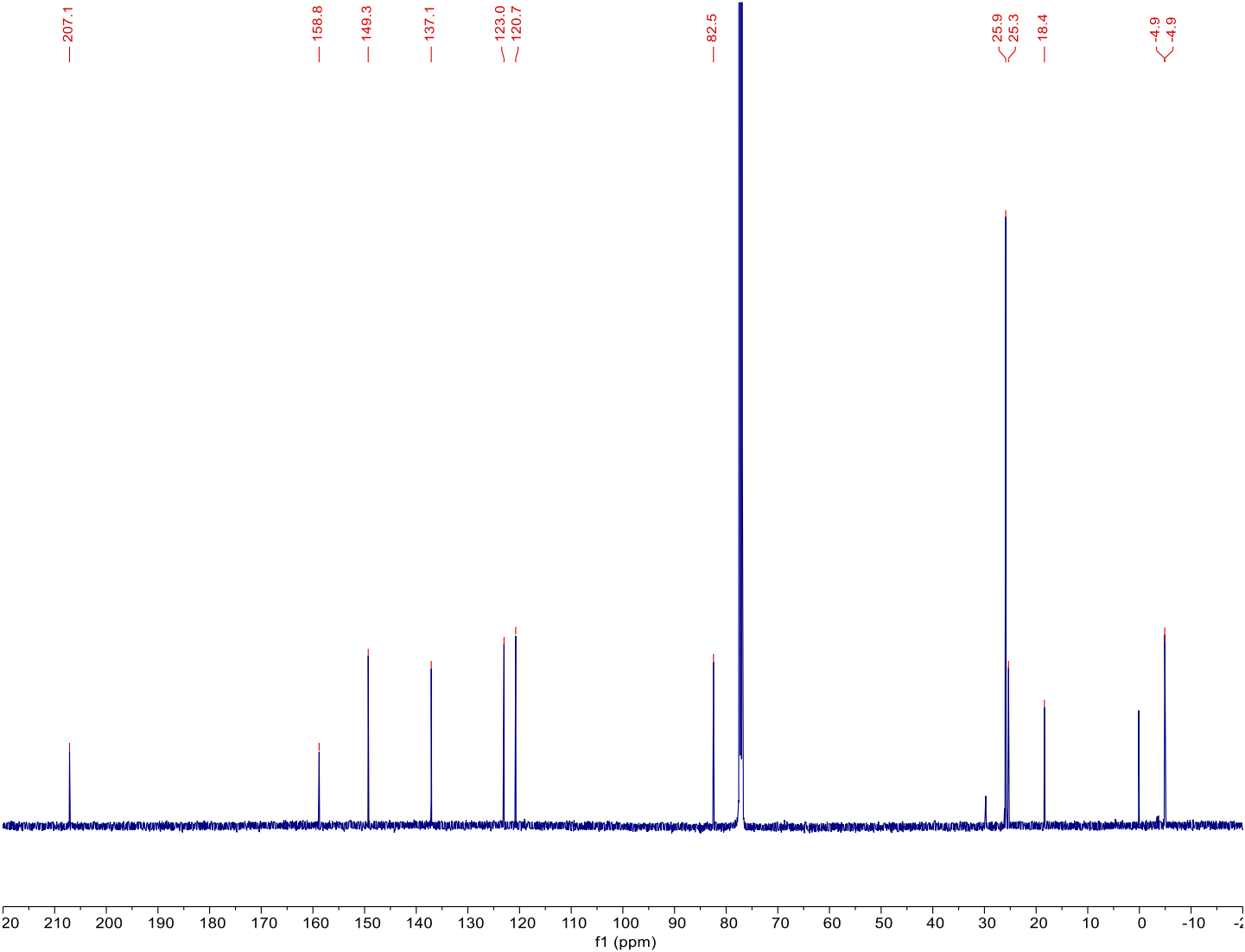
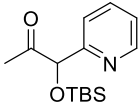
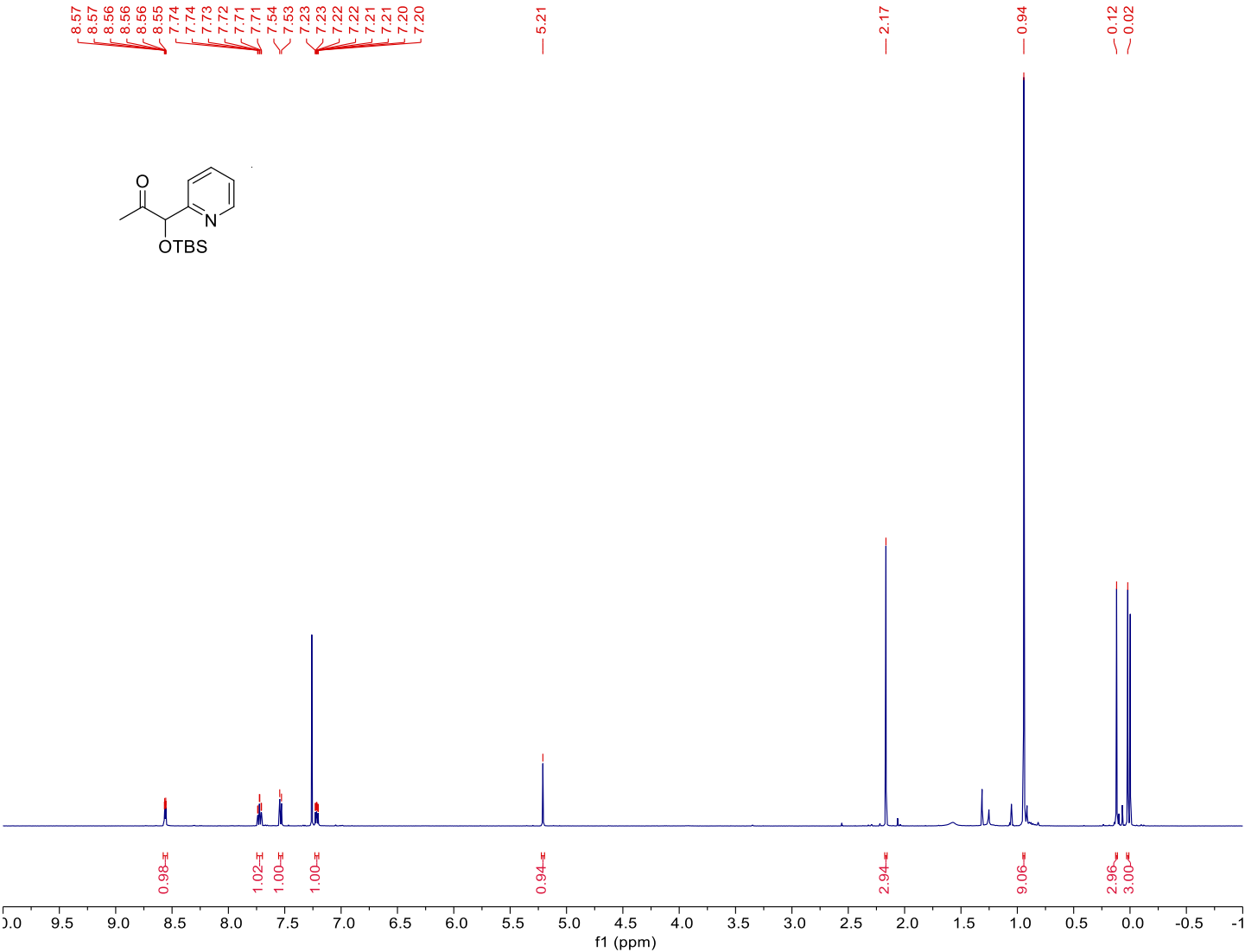
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3c**.



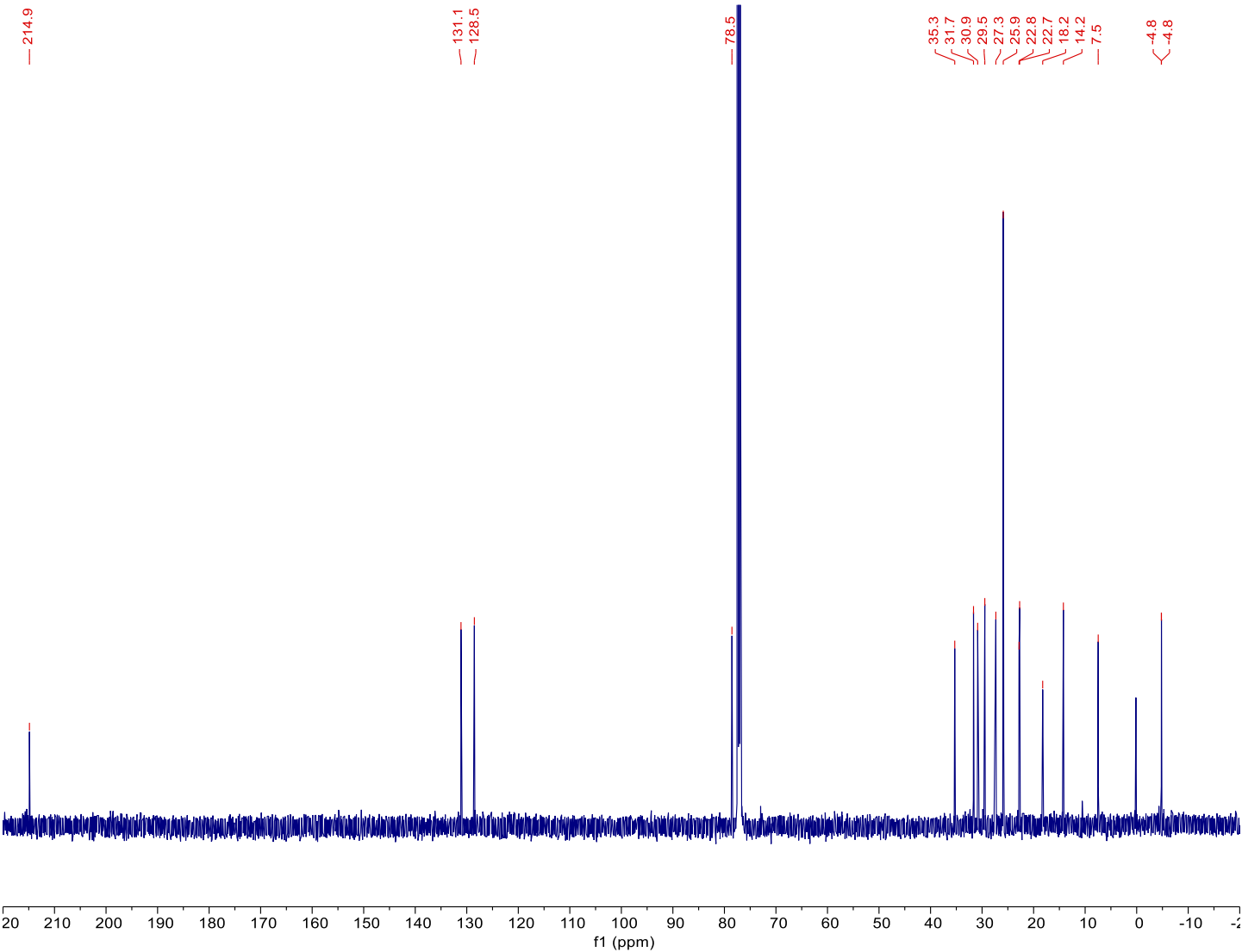
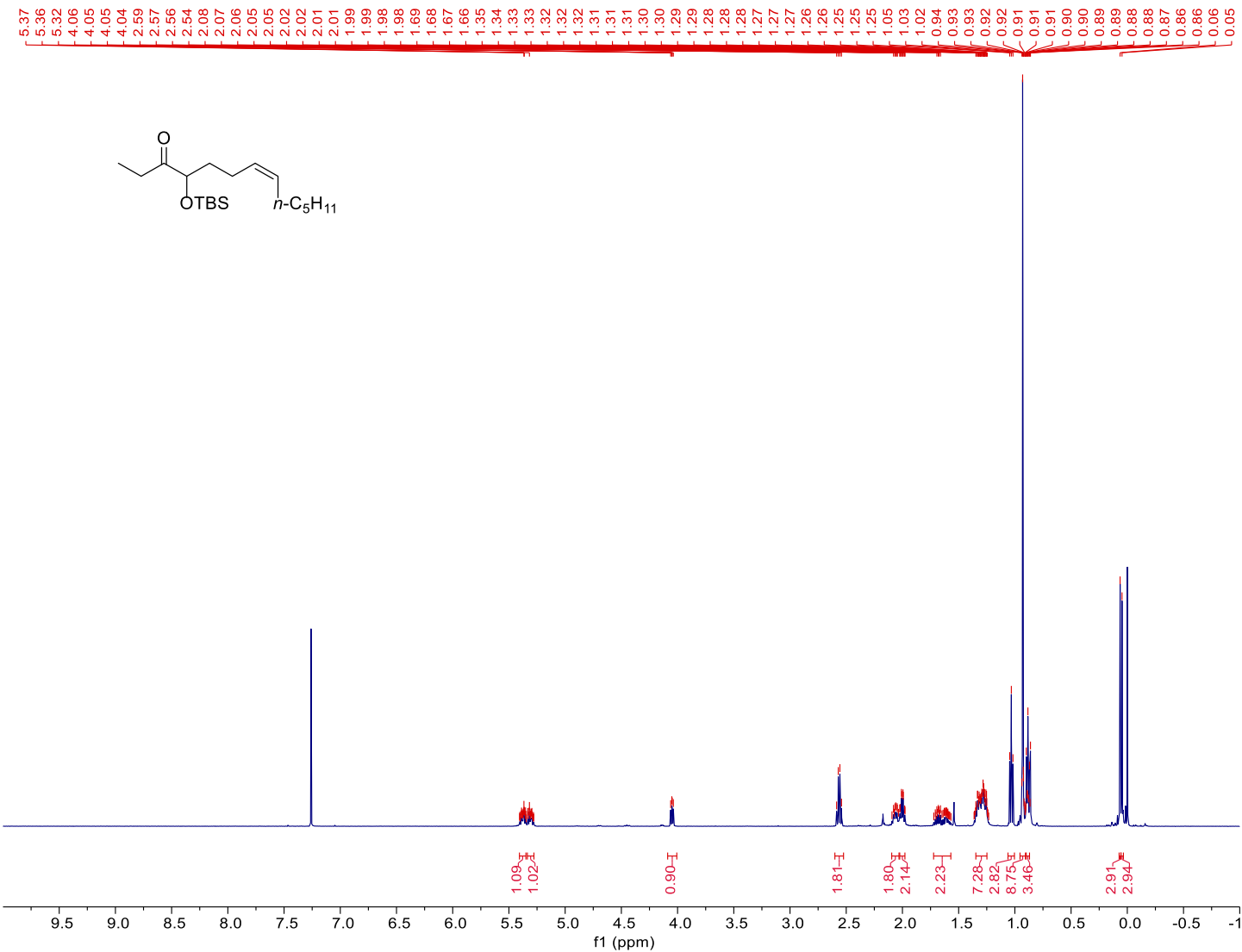
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3d**.



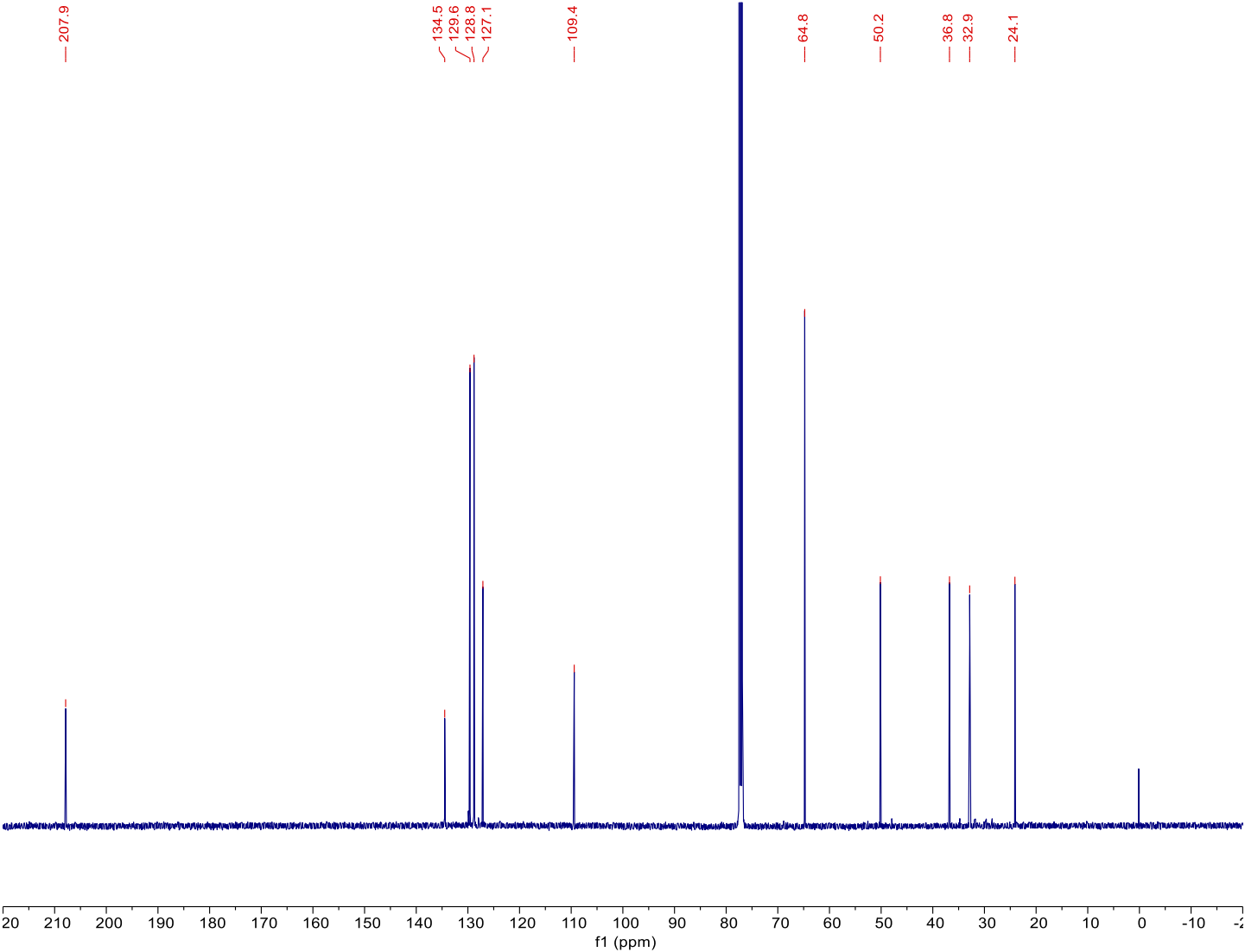
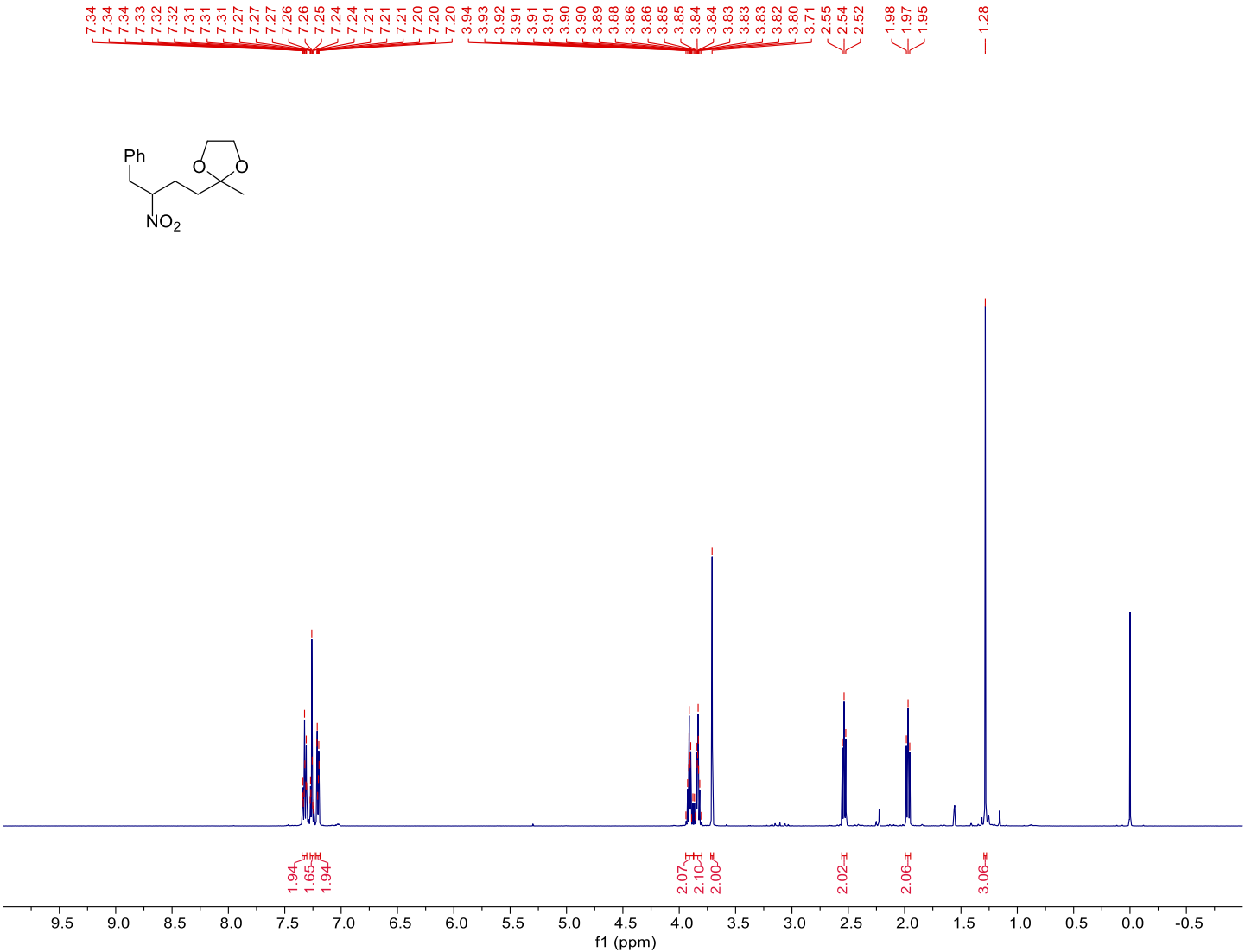
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3g**.



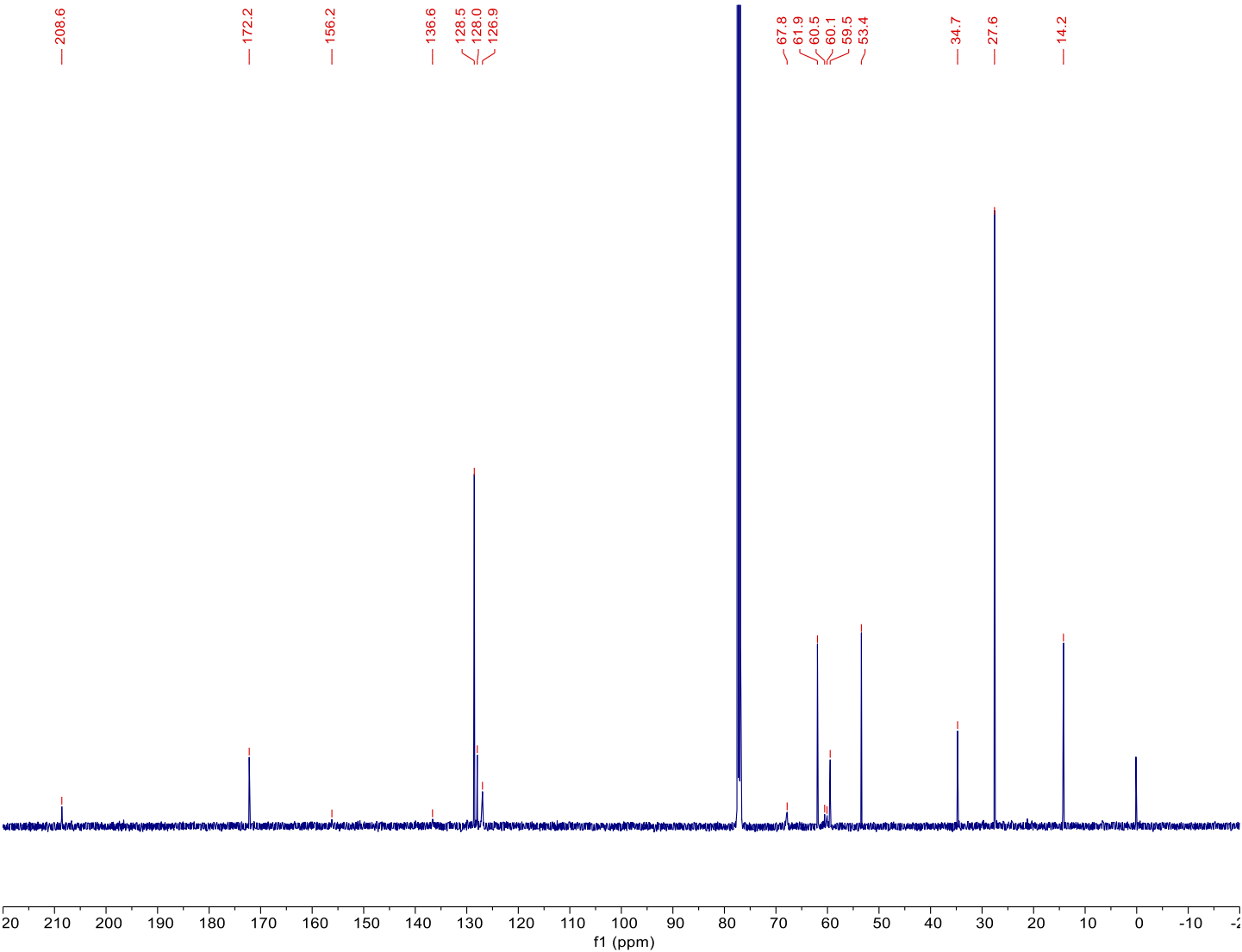
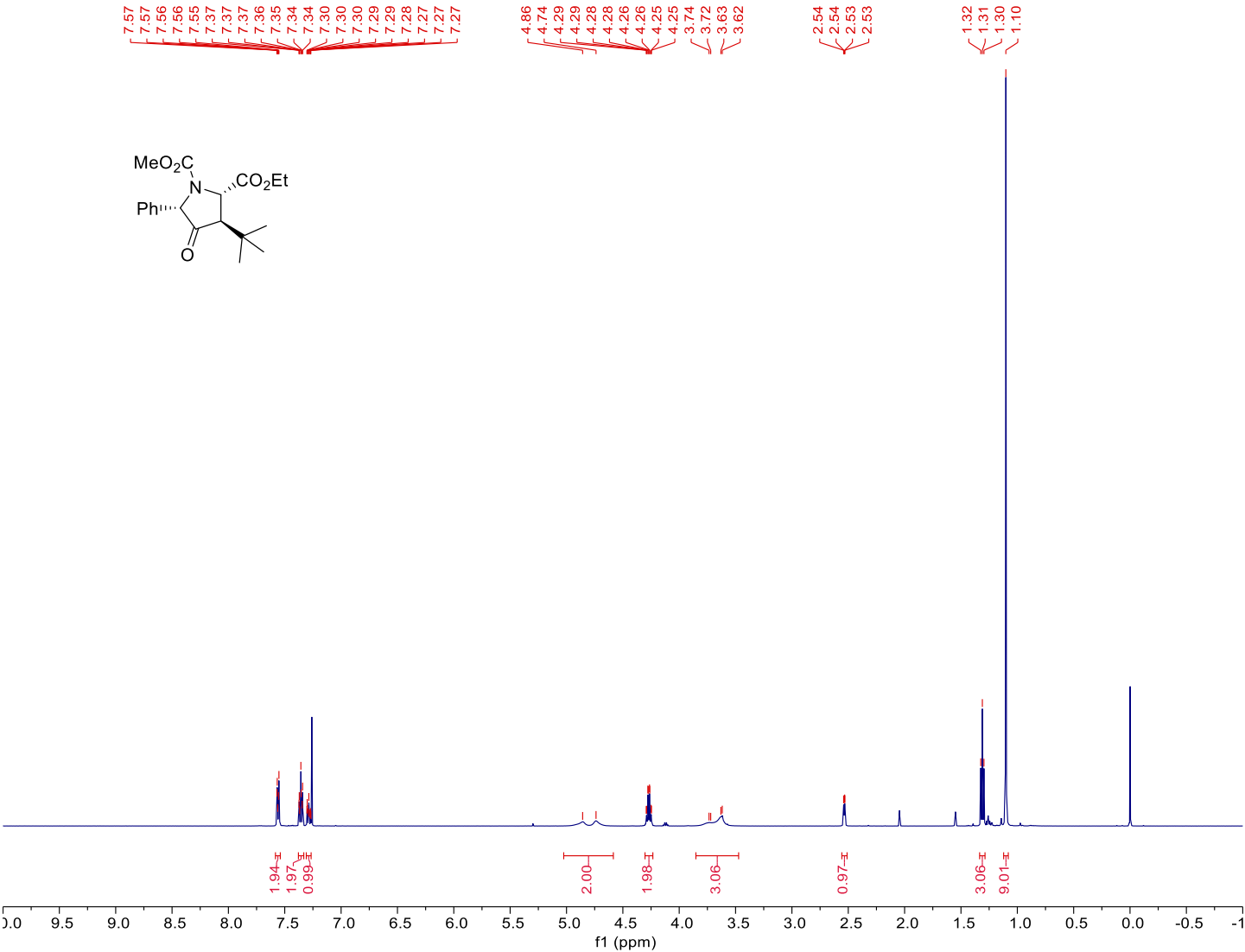
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3i**.



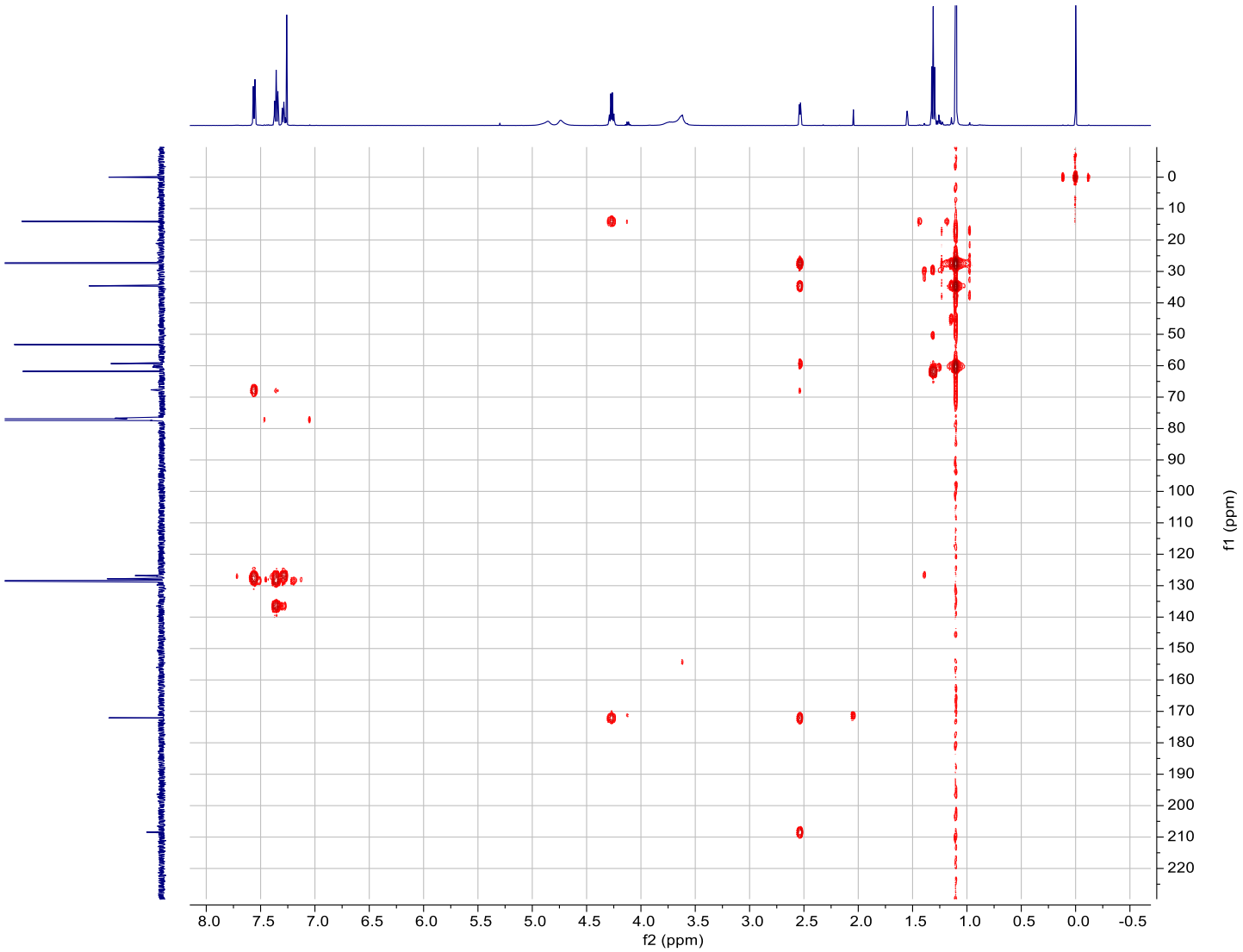
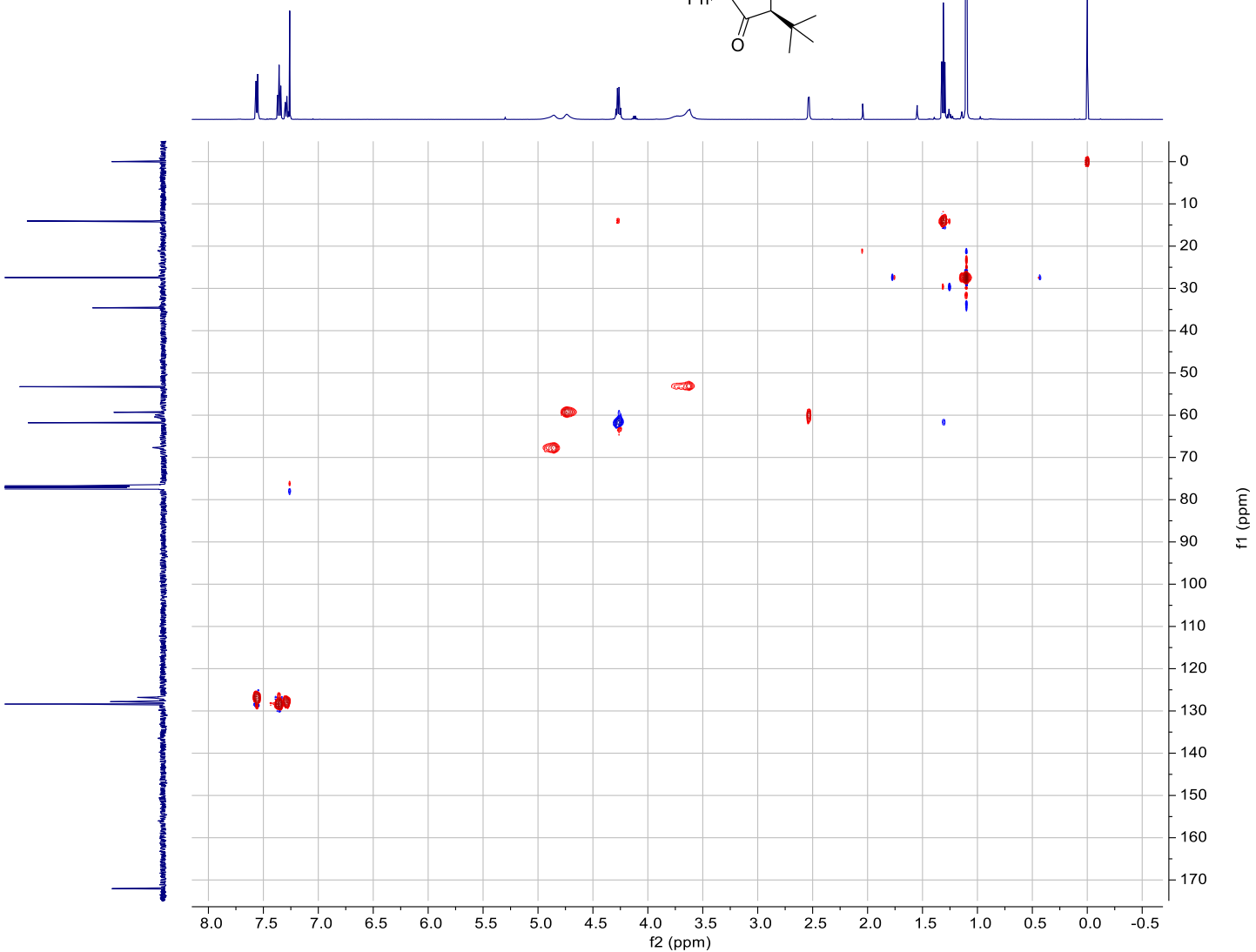
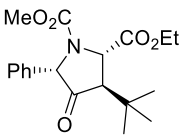
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3m**.



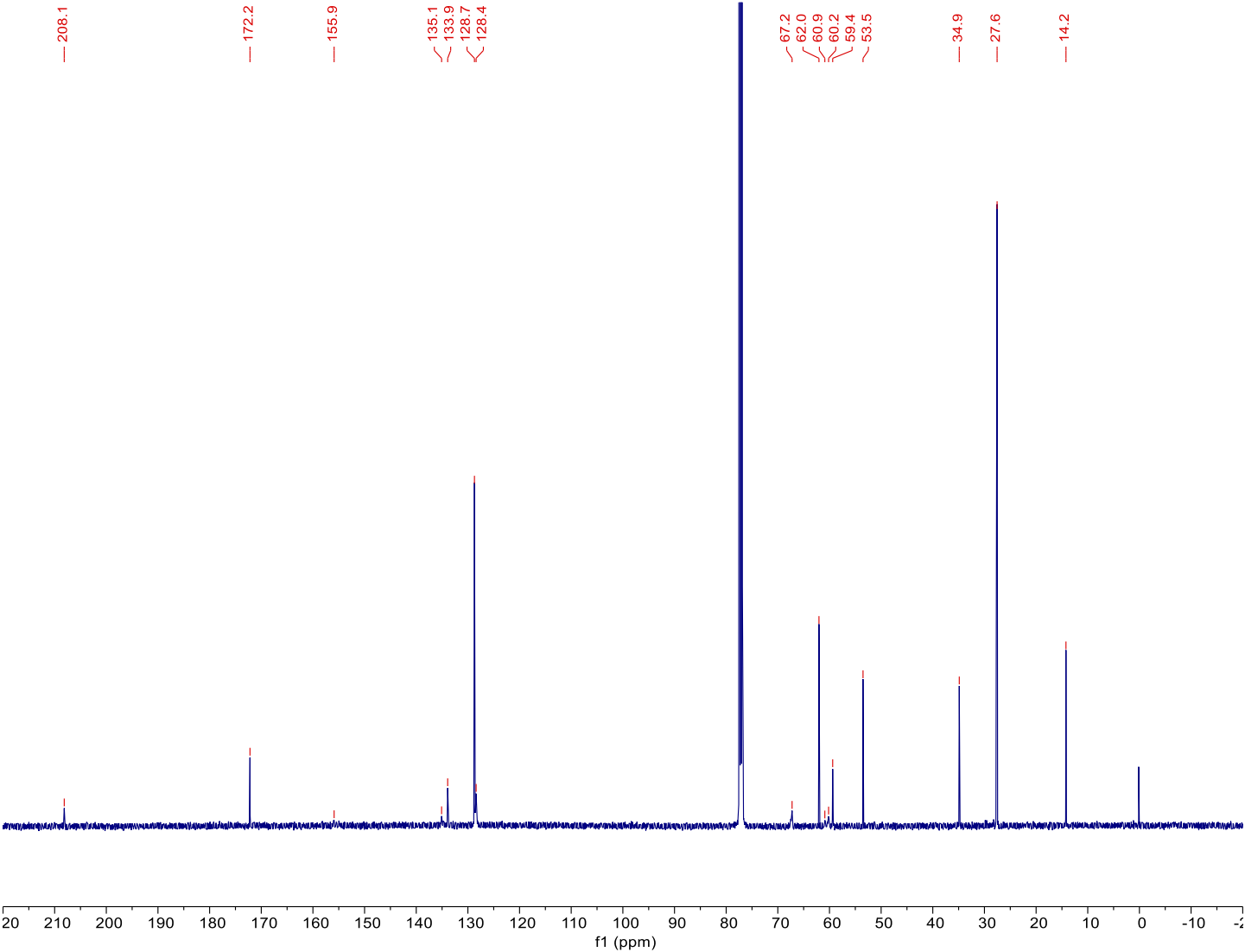
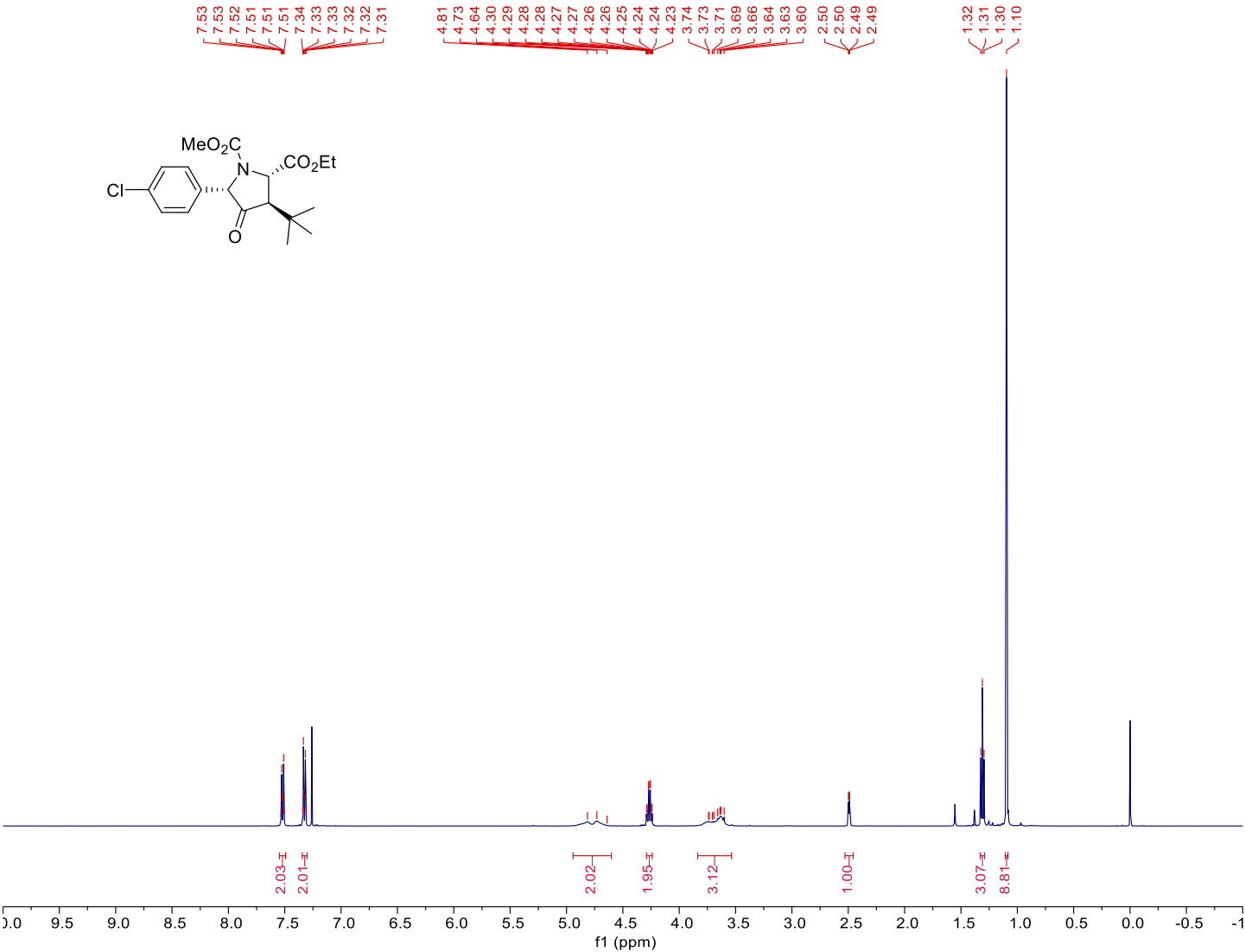
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3o**.



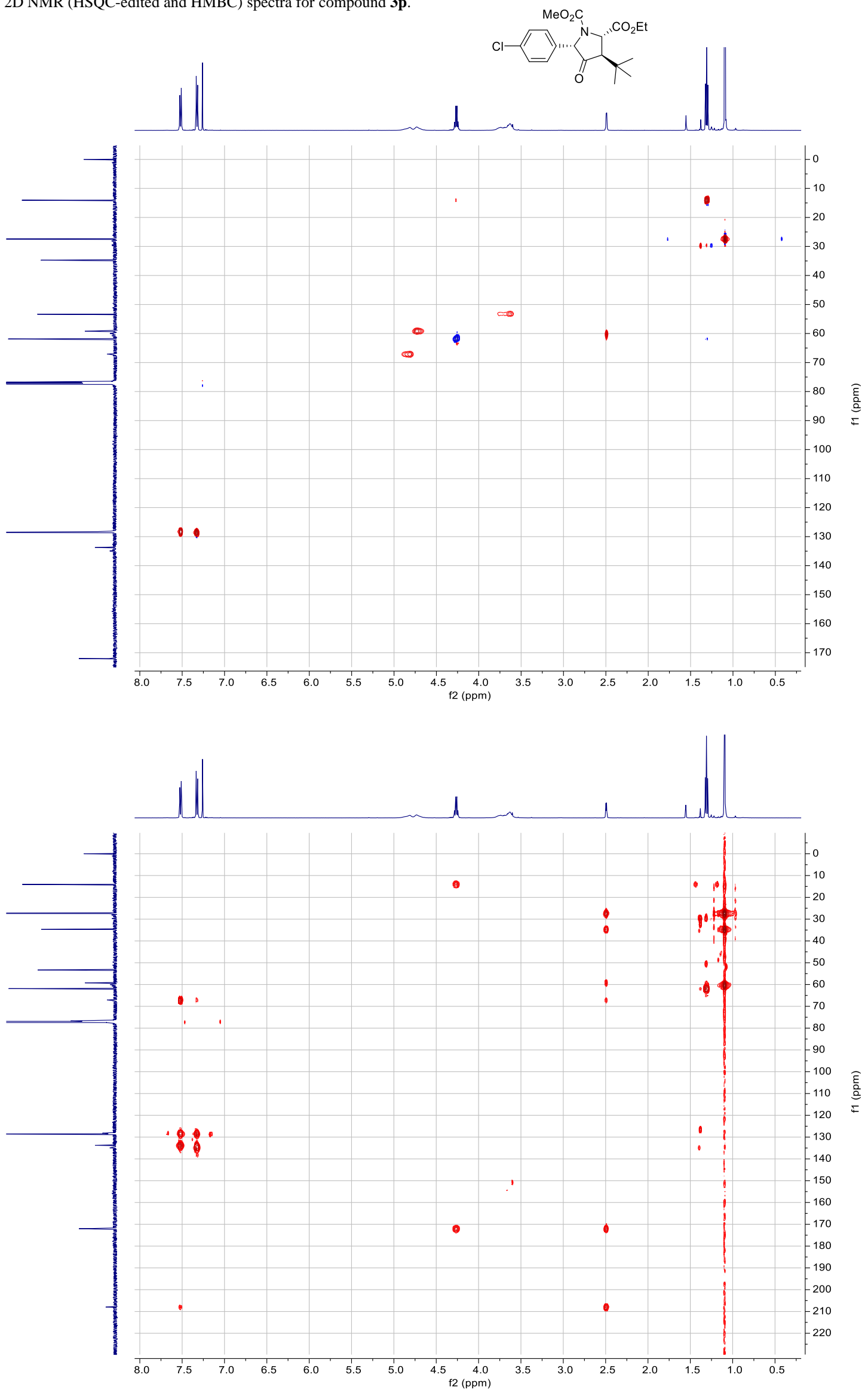
2D NMR (HSQC-edited and HMBC) spectra for compound **3o**.



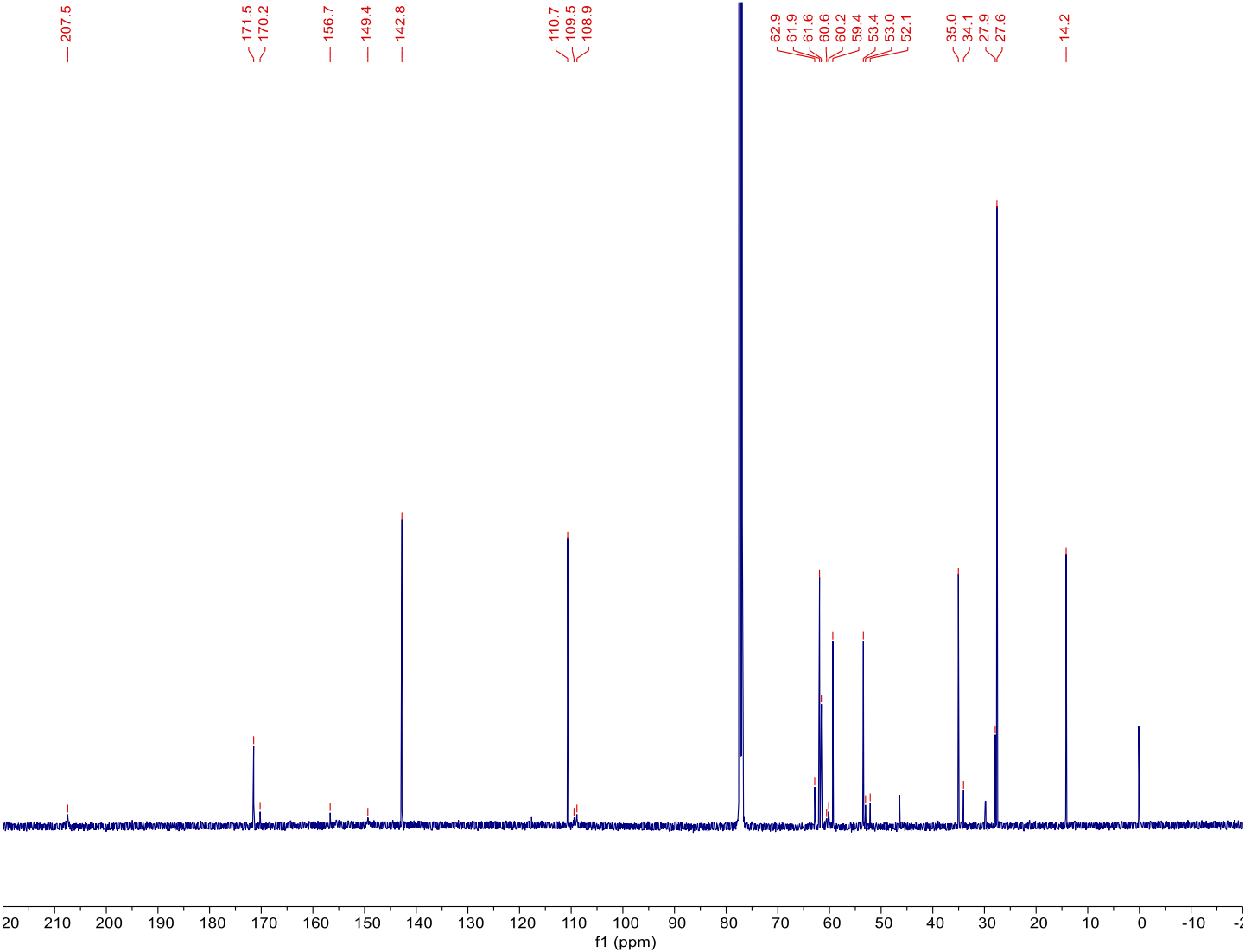
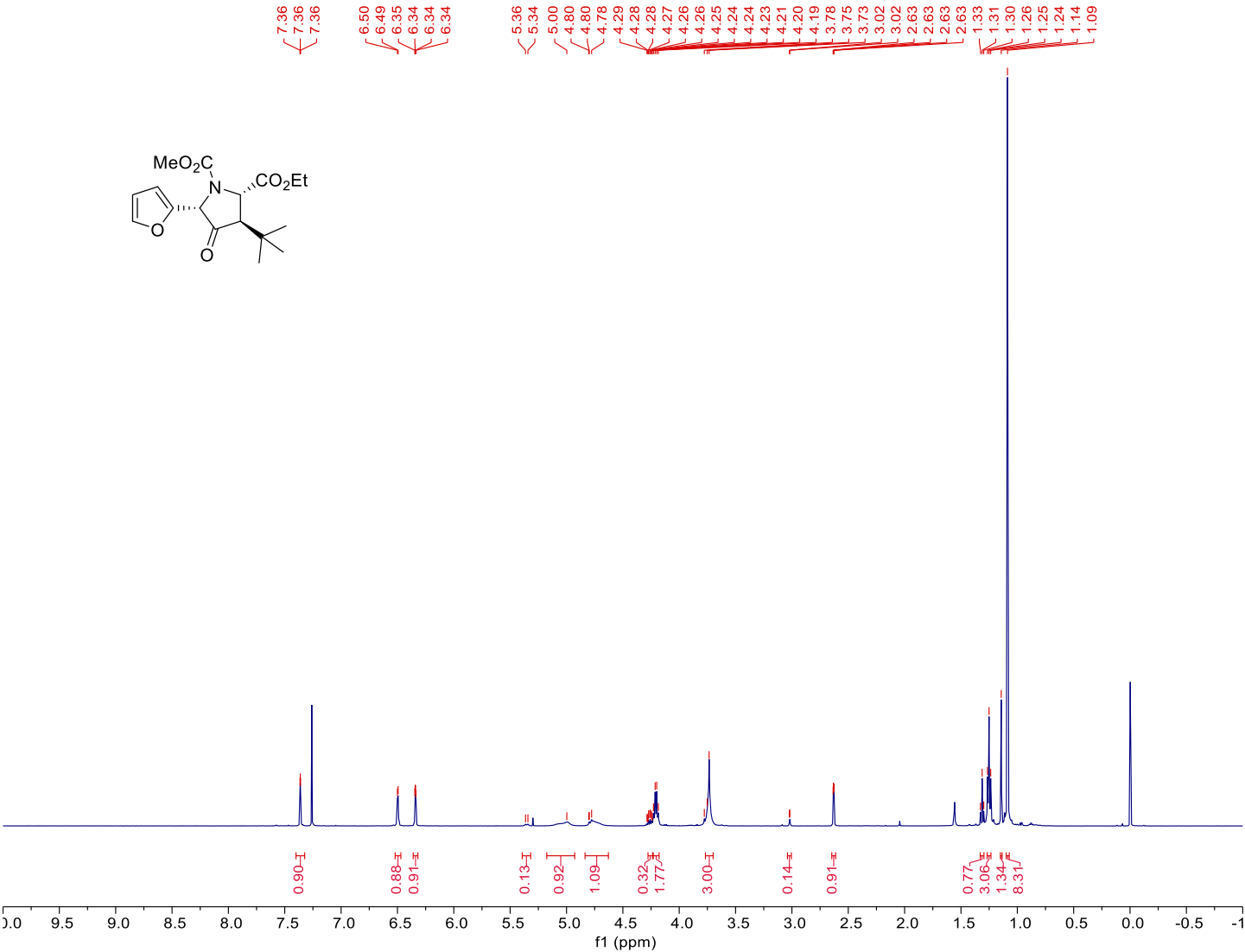
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3p**.



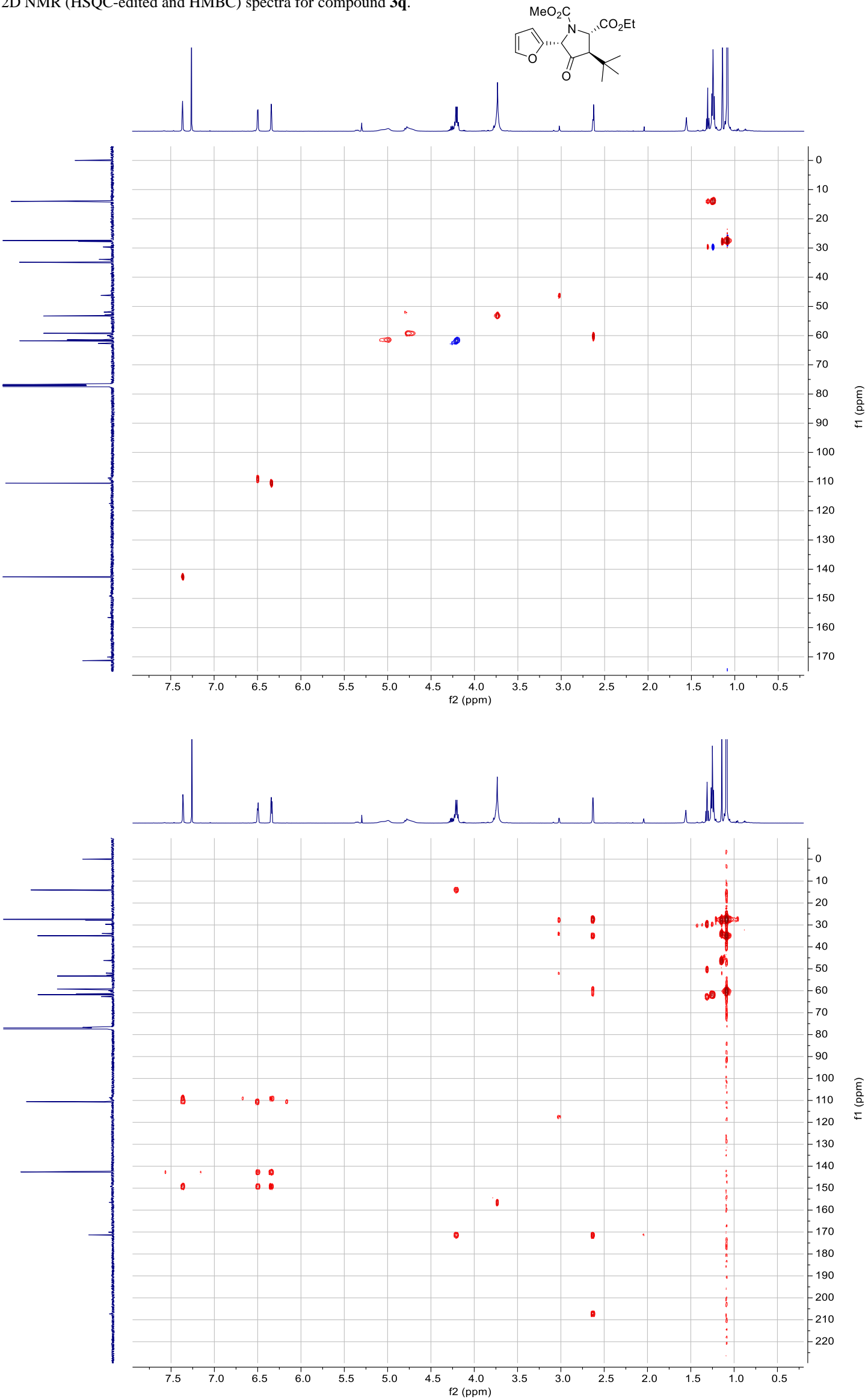
2D NMR (HSQC-edited and HMBC) spectra for compound **3p**.



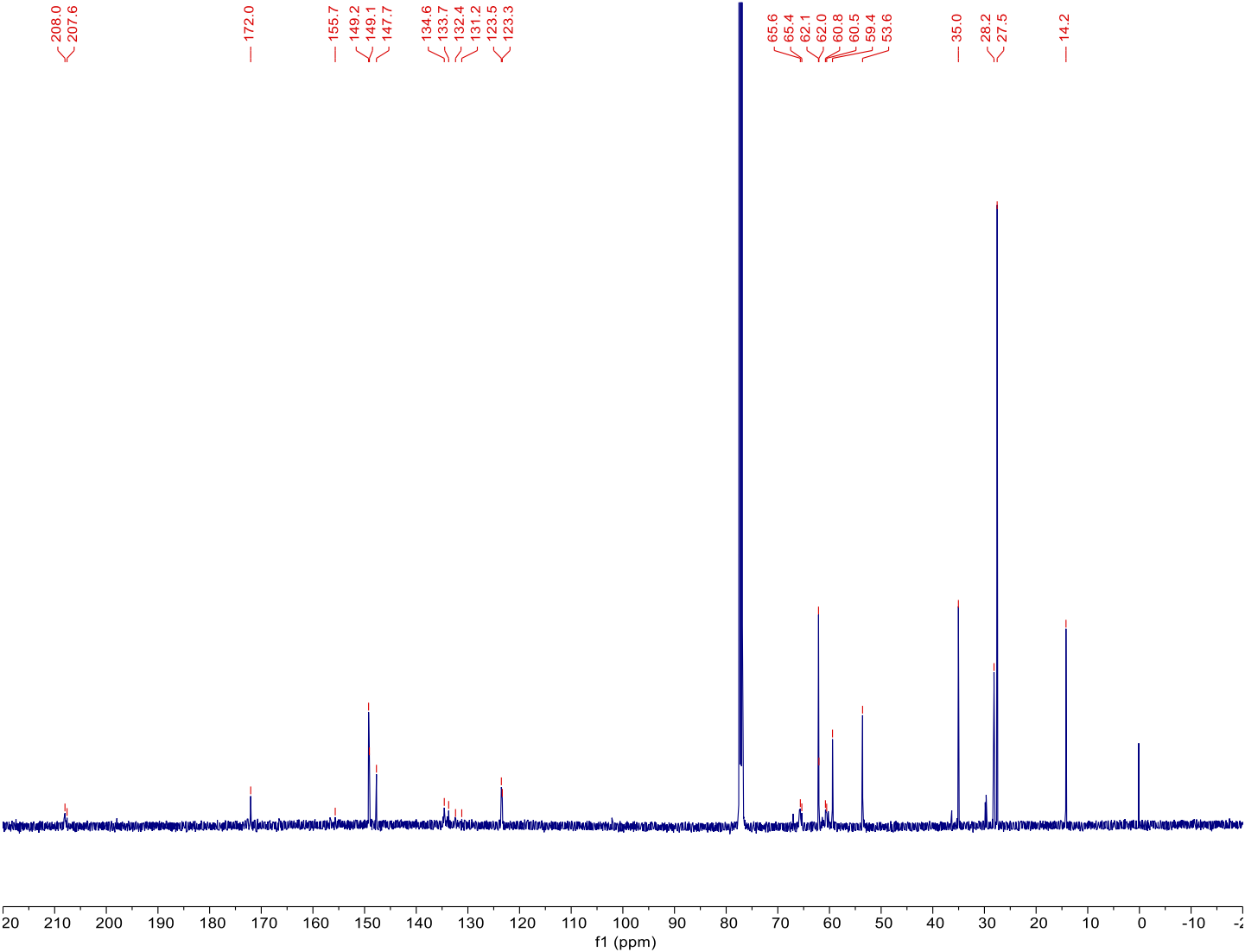
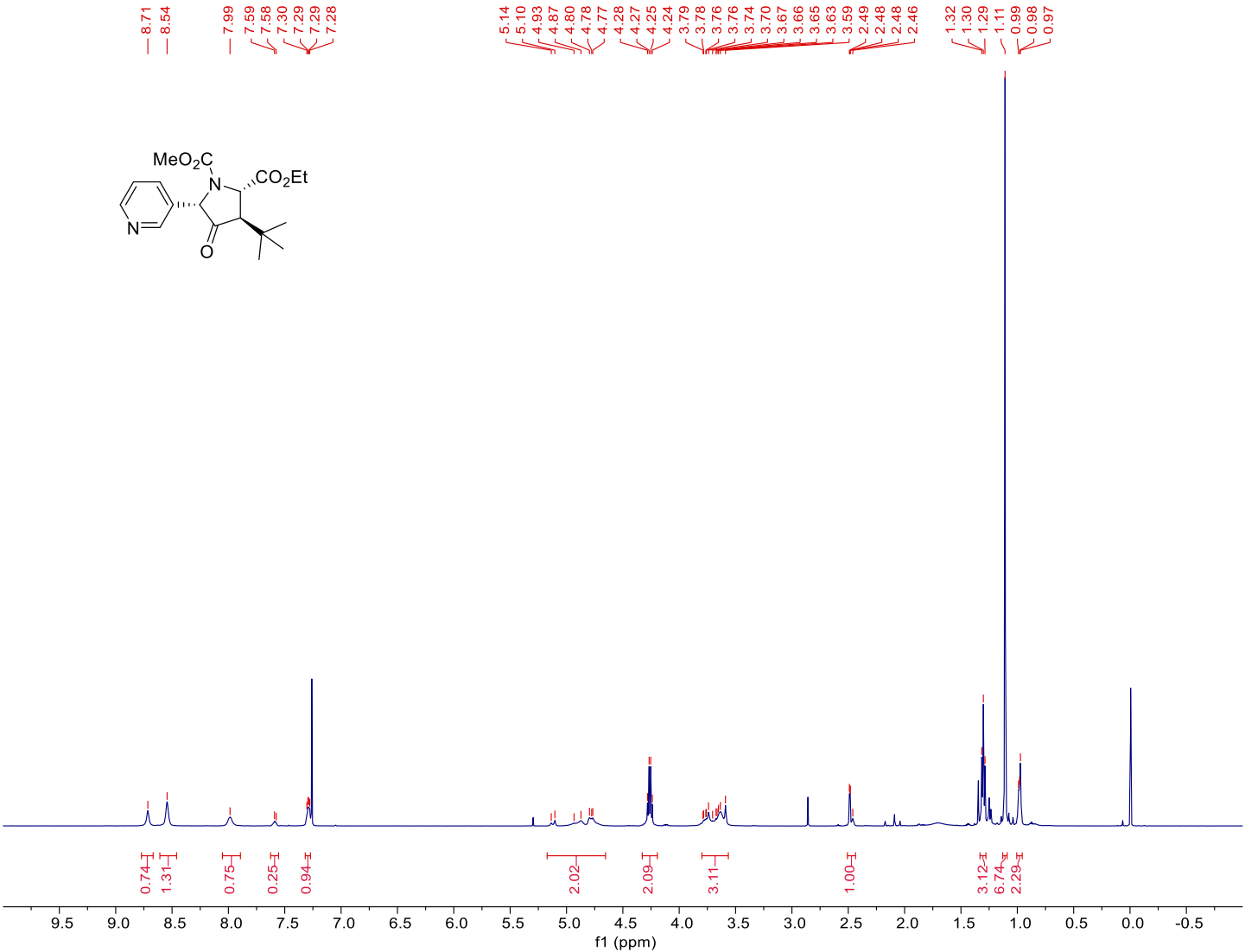
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3q**.



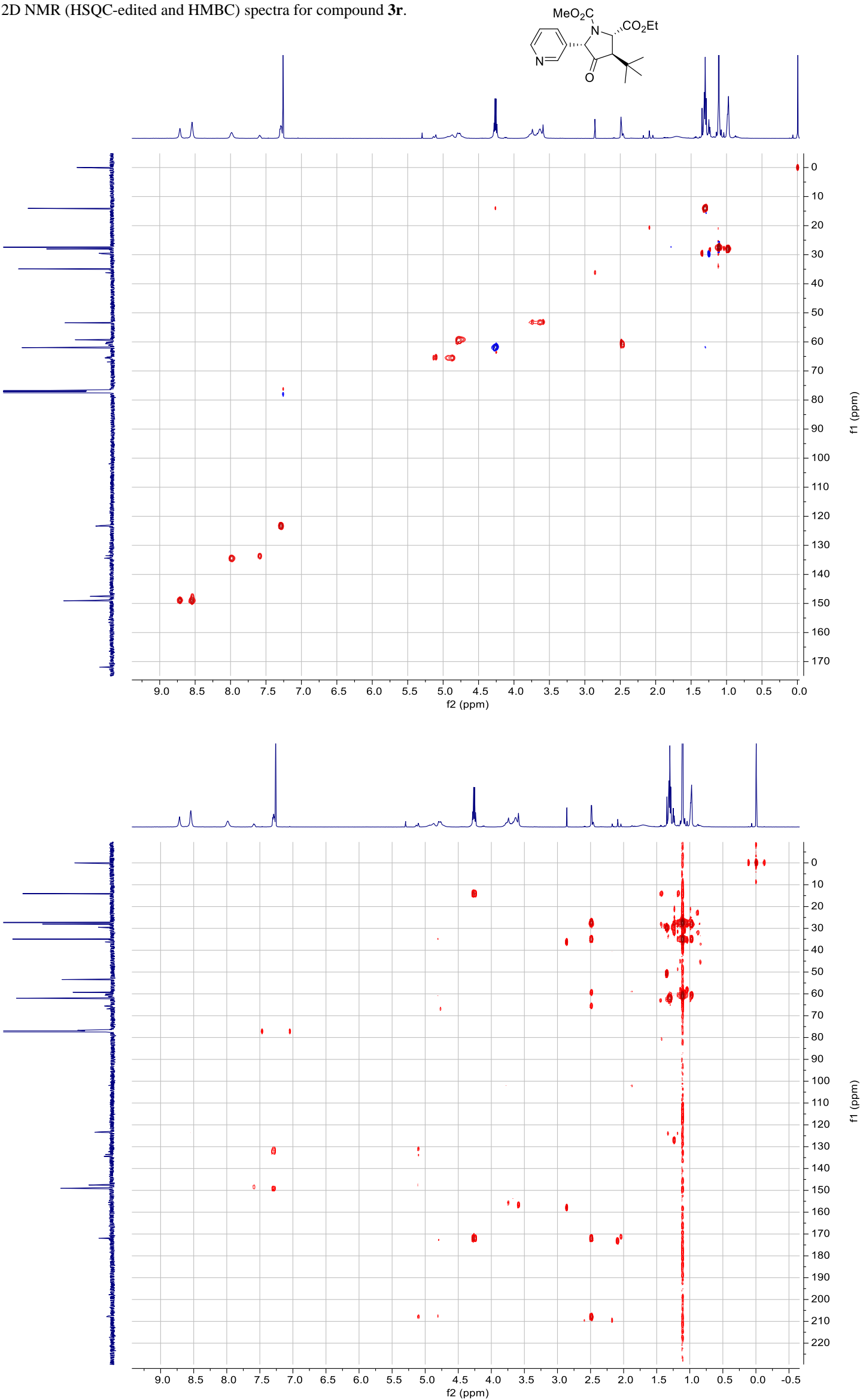
2D NMR (HSQC-edited and HMBC) spectra for compound **3q**.



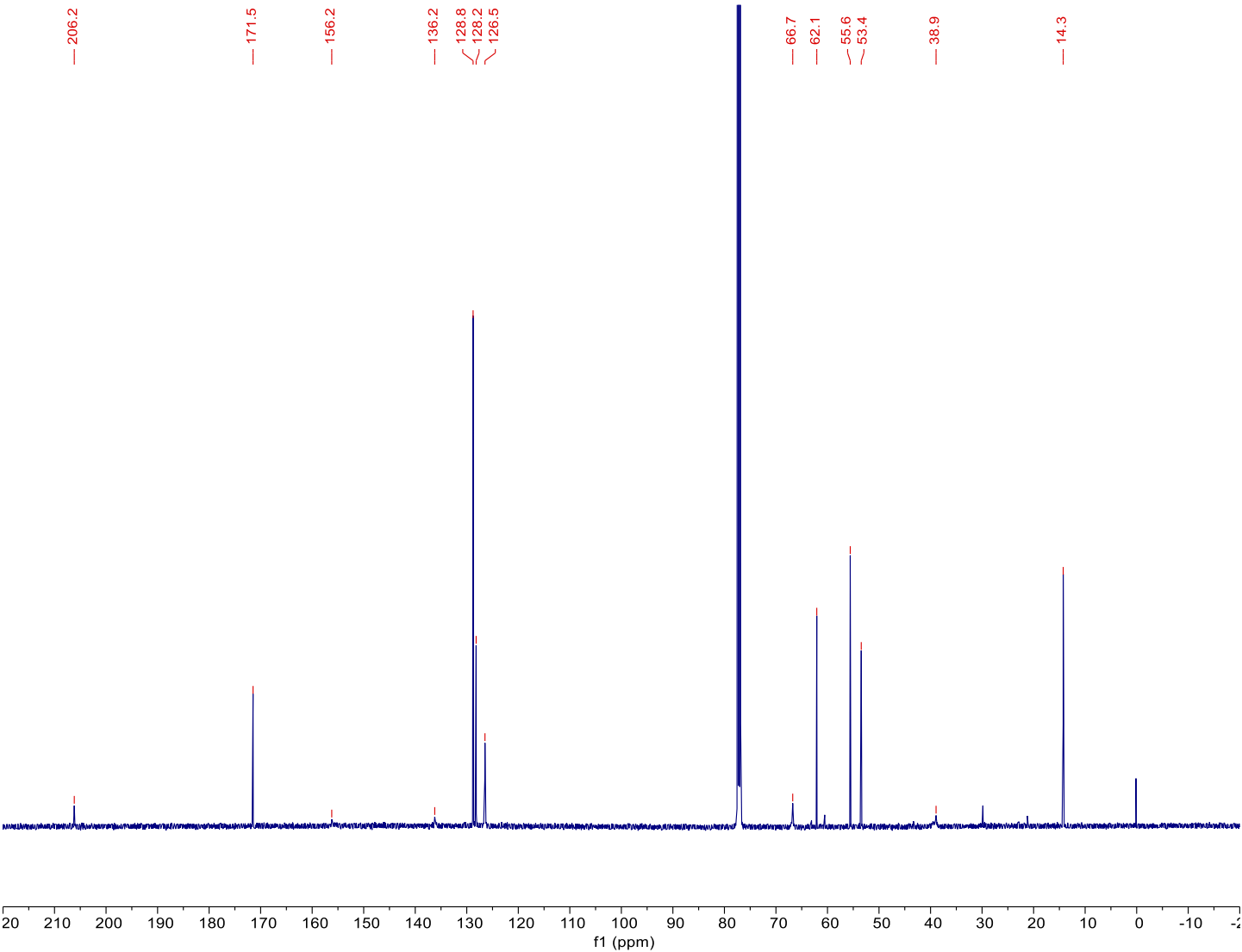
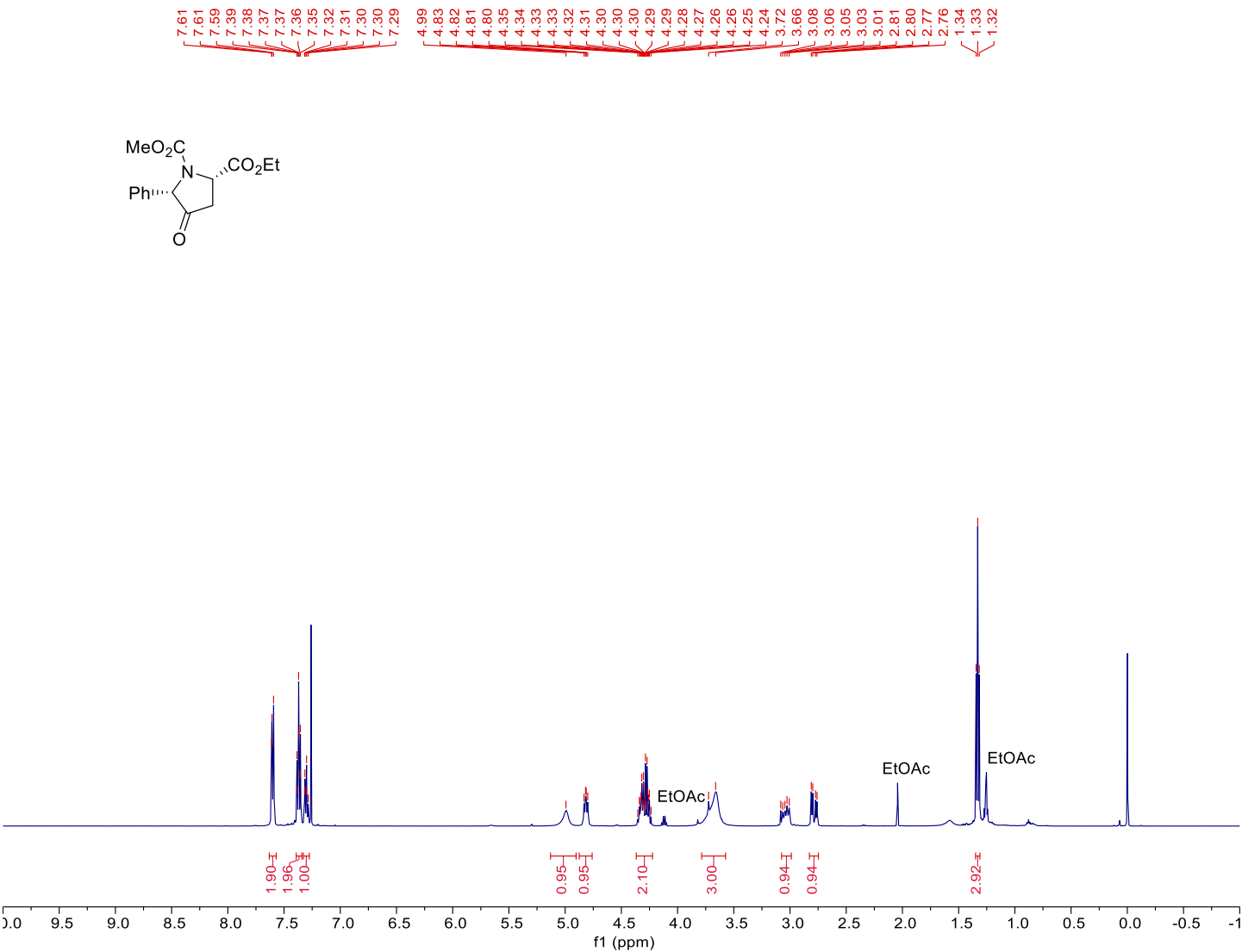
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3r**.



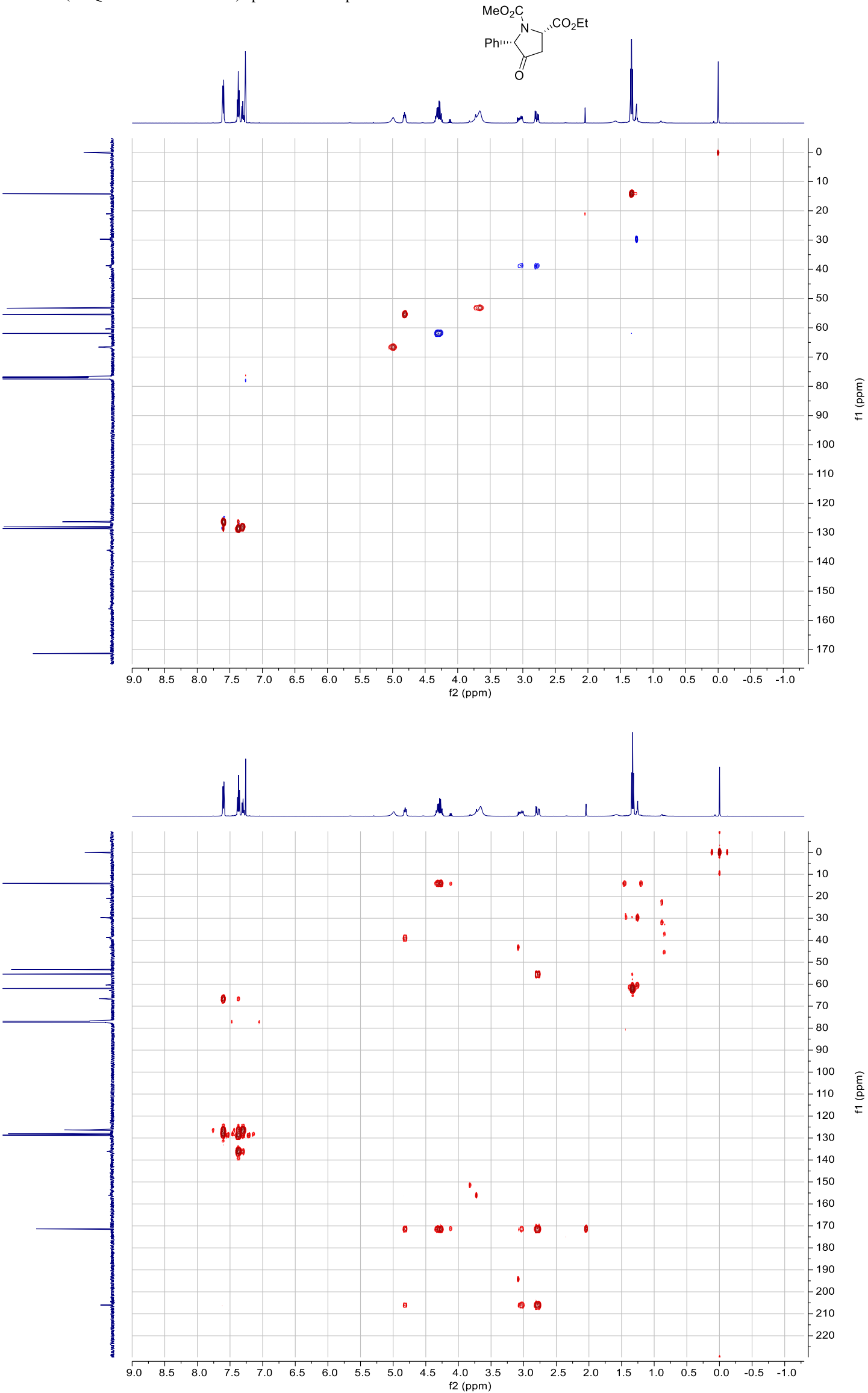
2D NMR (HSQC-edited and HMBC) spectra for compound **3r**.



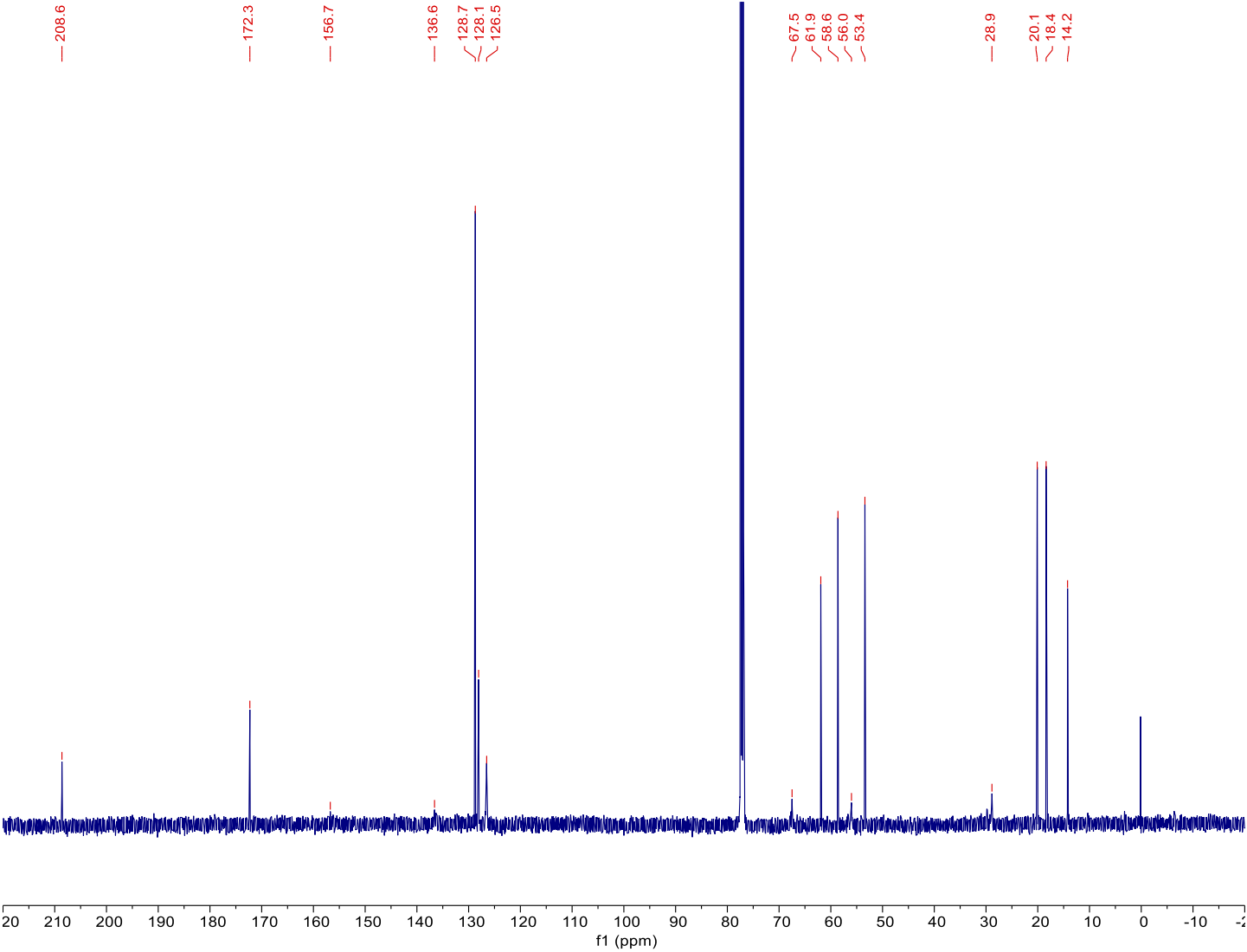
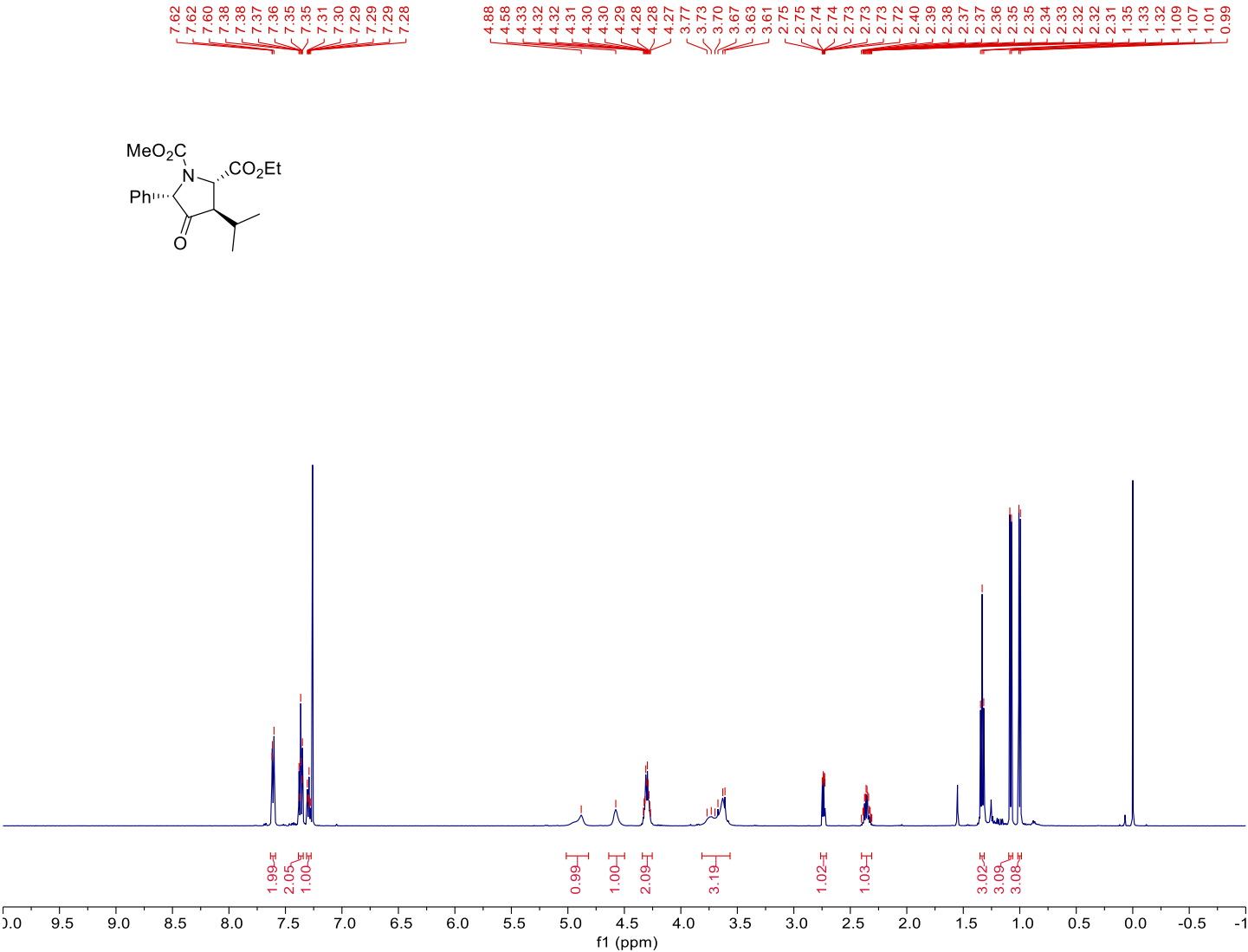
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3s**.



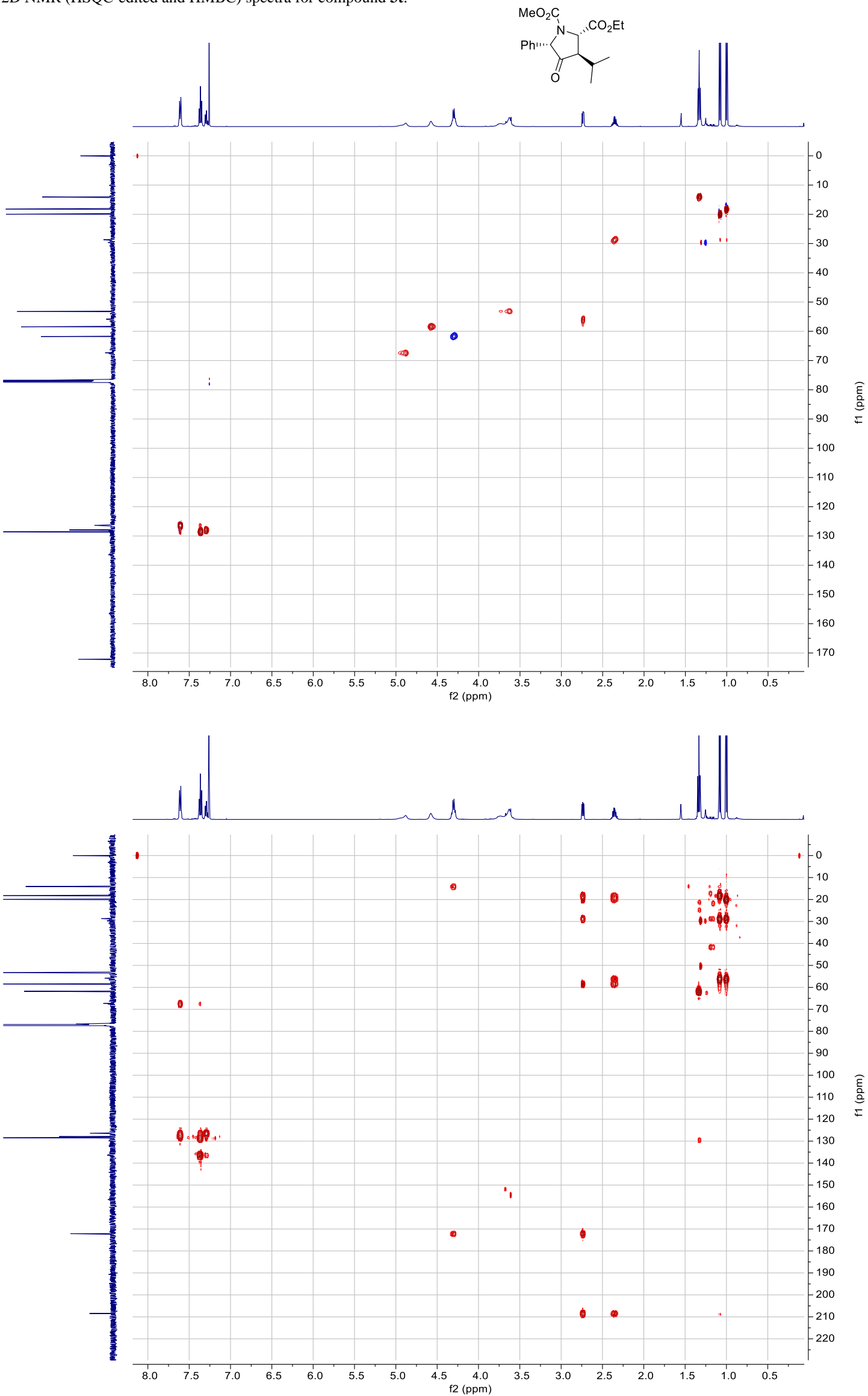
2D NMR (HSQC-edited and HMBC) spectra for compound **3s**.



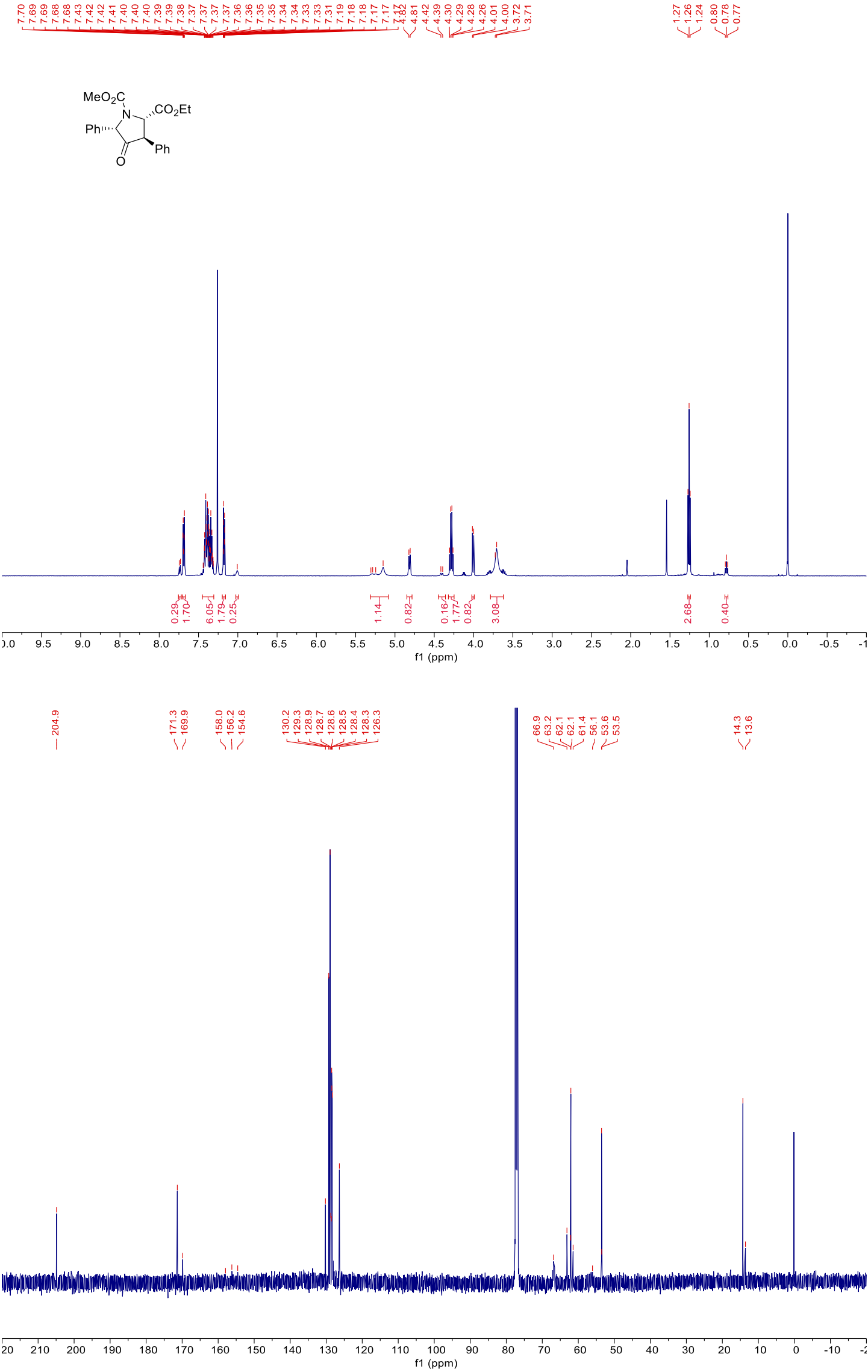
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3t**.



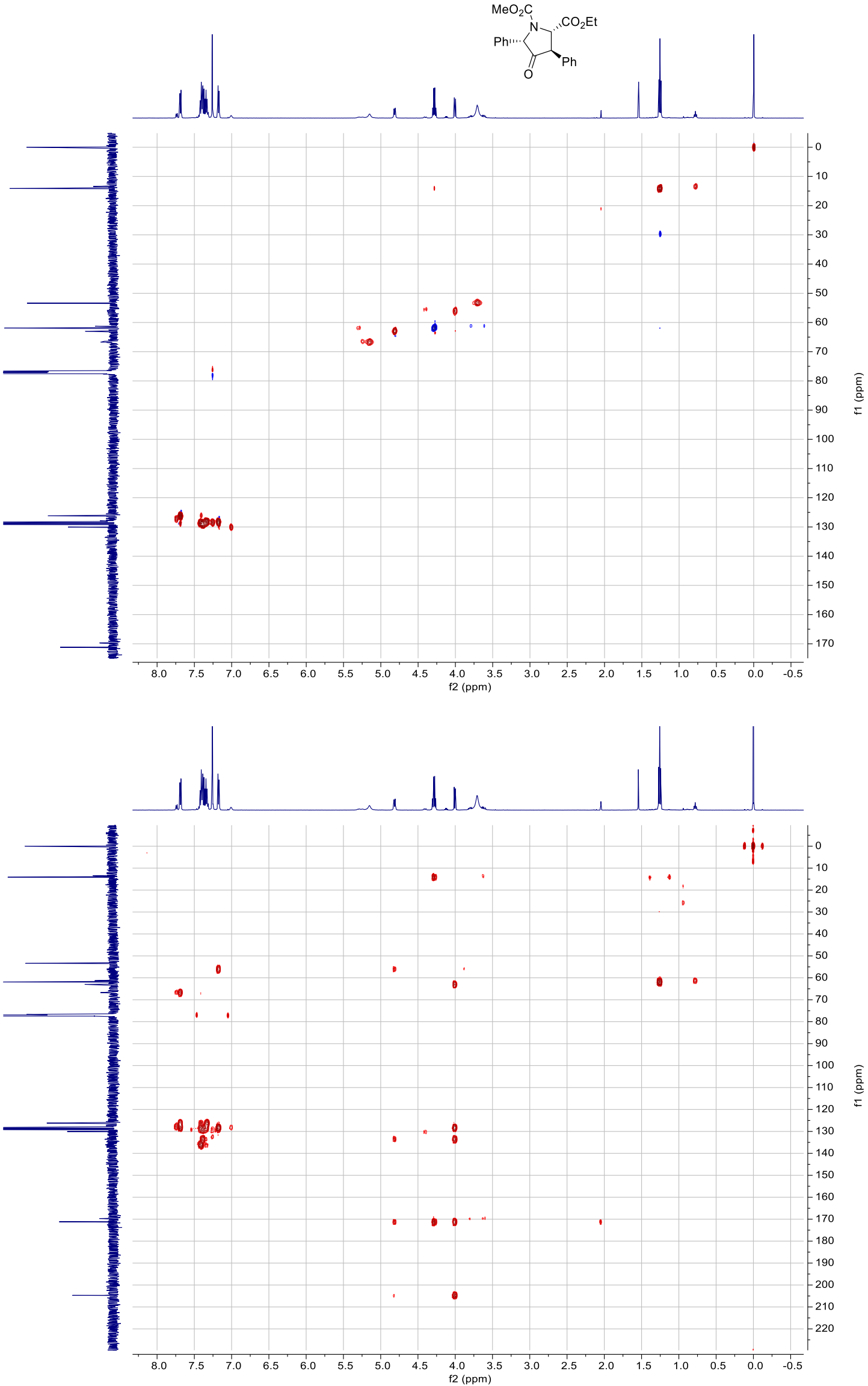
2D NMR (HSQC-edited and HMBC) spectra for compound **3t**.



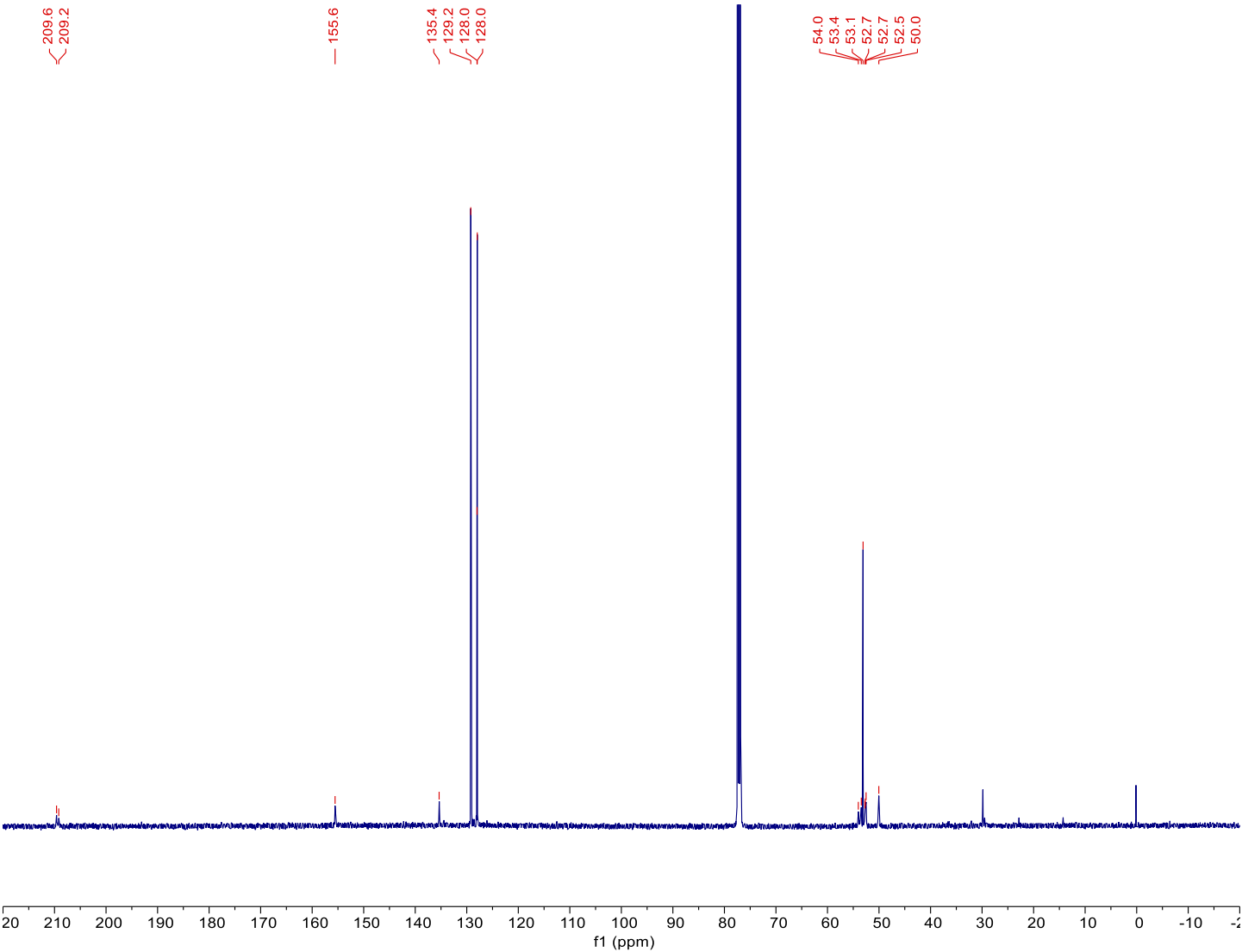
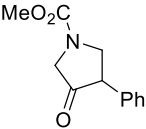
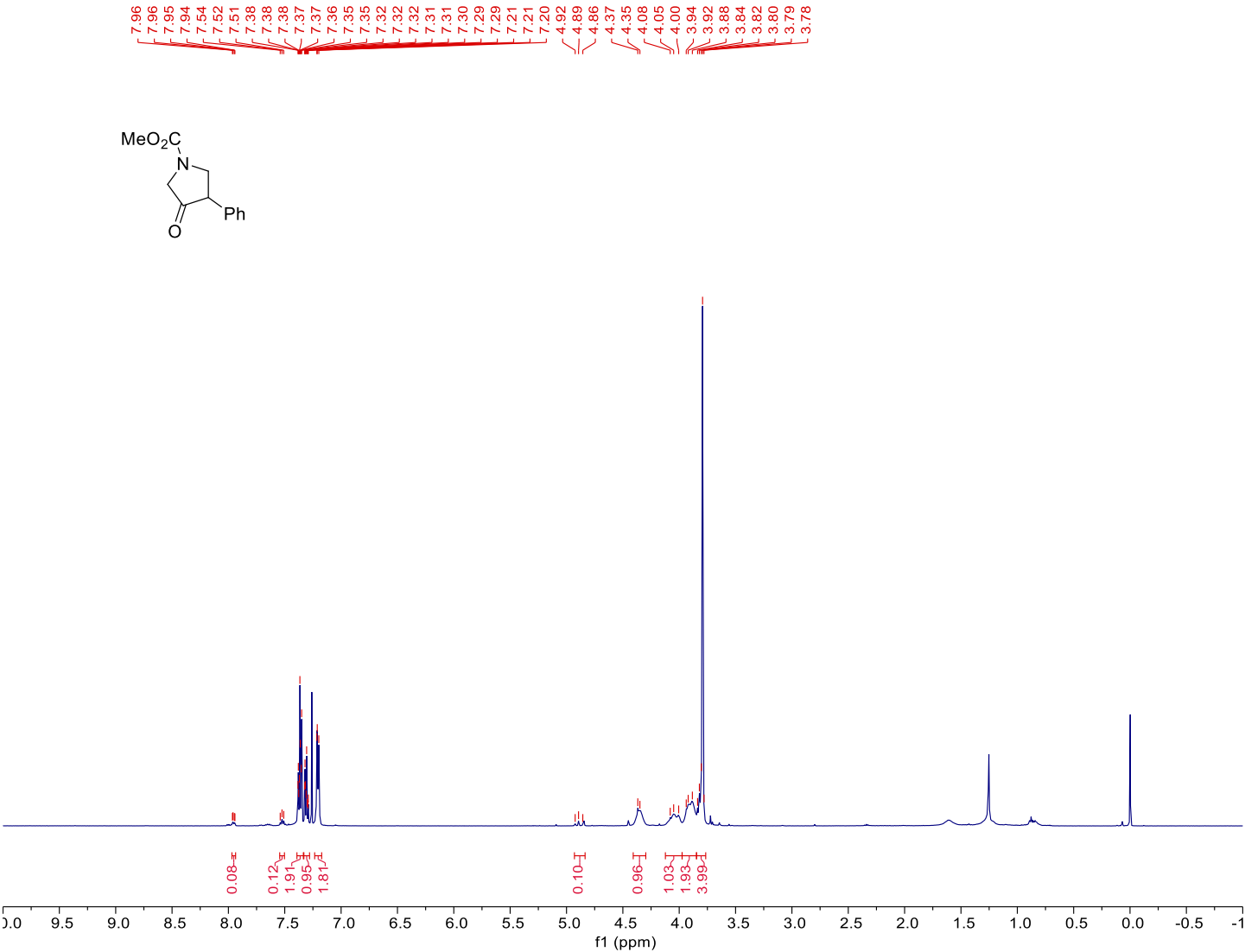
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3u**.



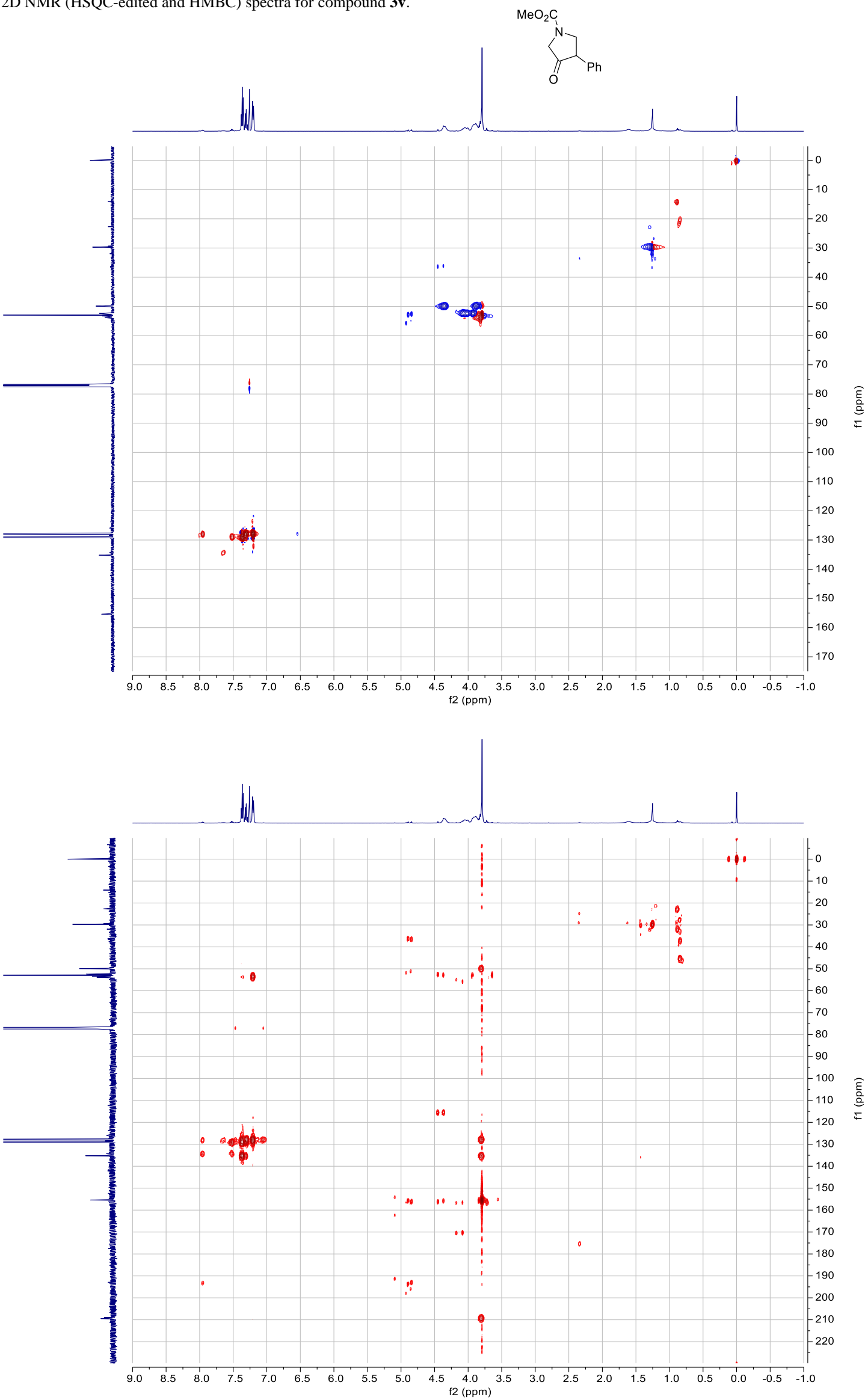
2D NMR (HSQC-edited and HMBC) spectra for compound **3u**.



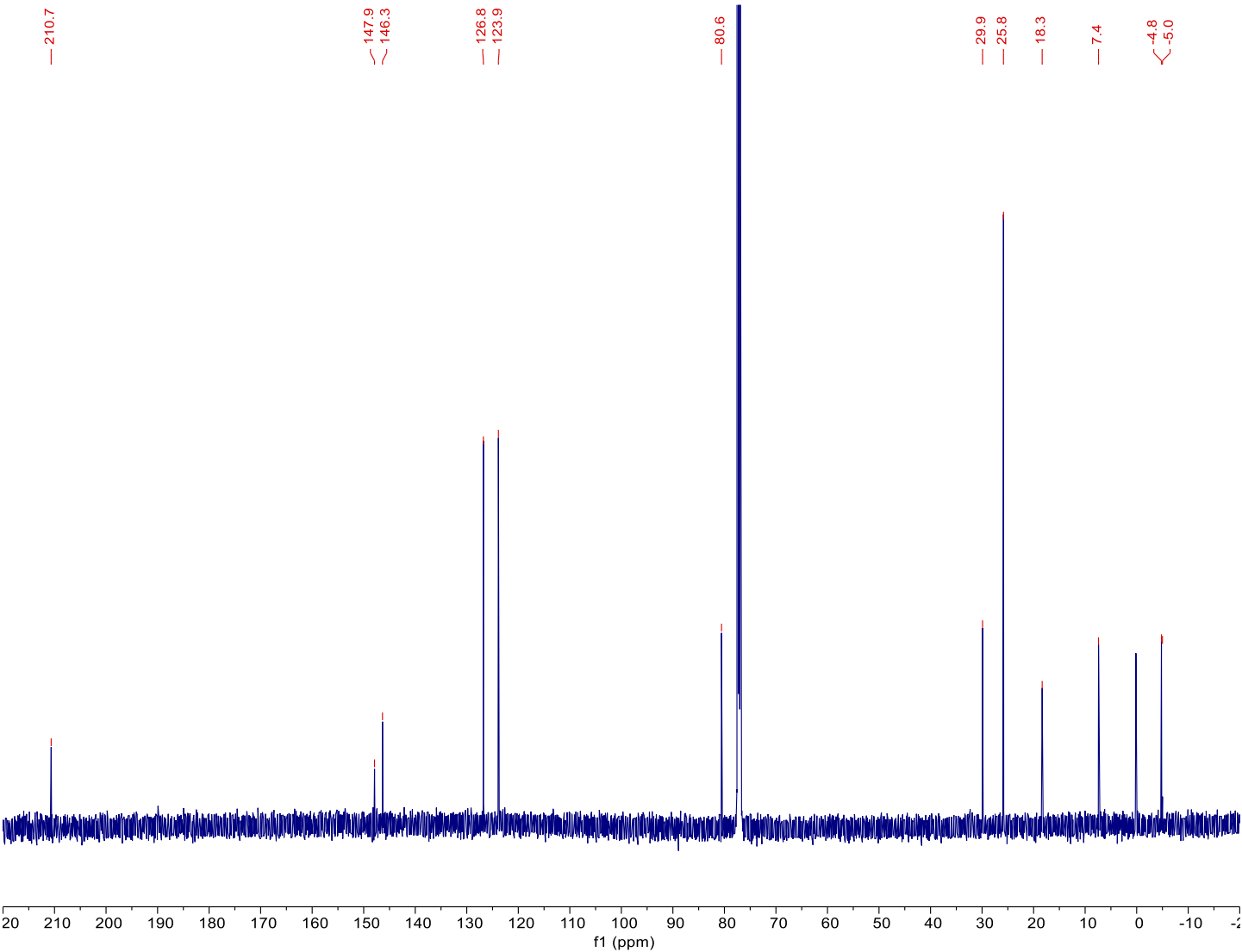
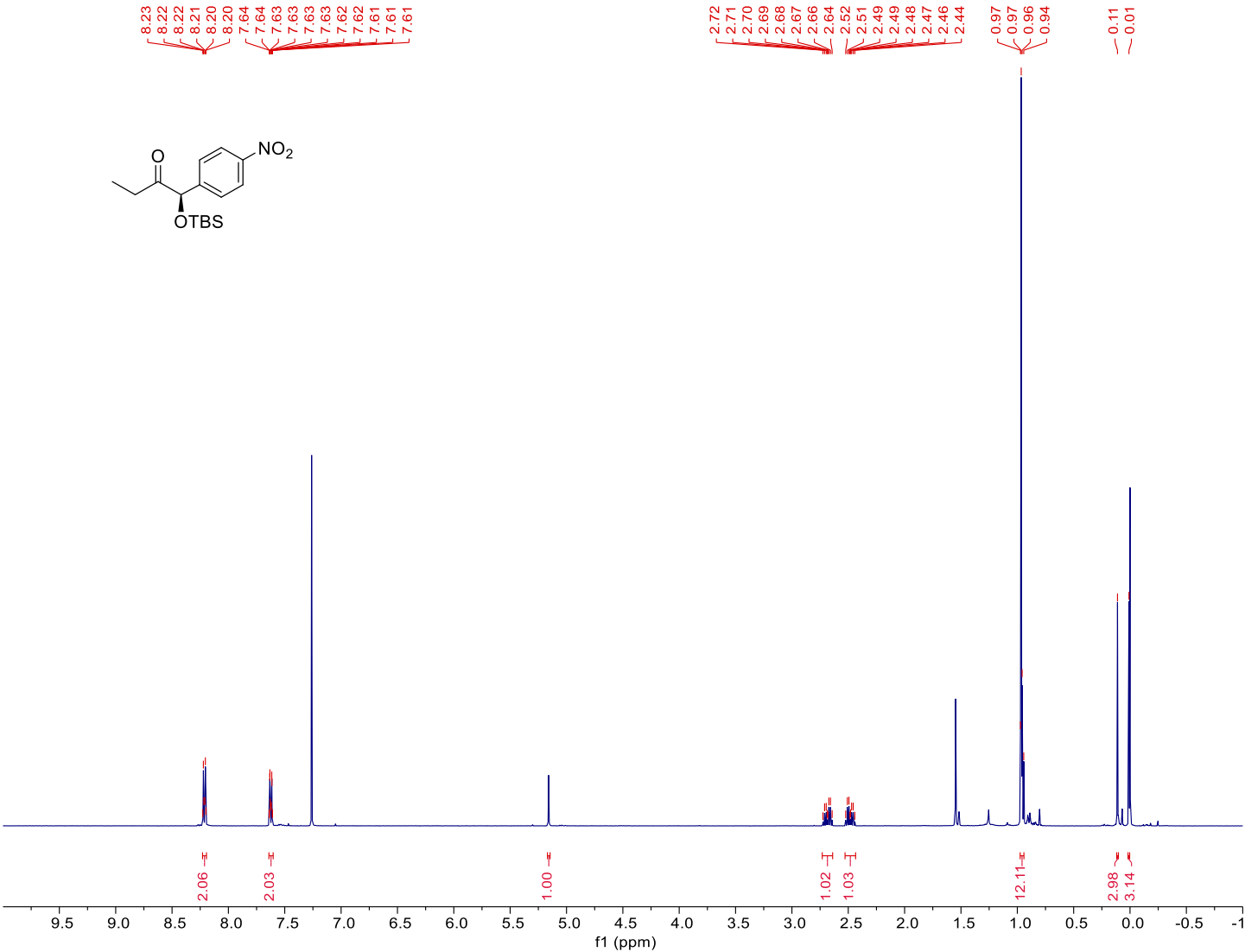
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3v**.



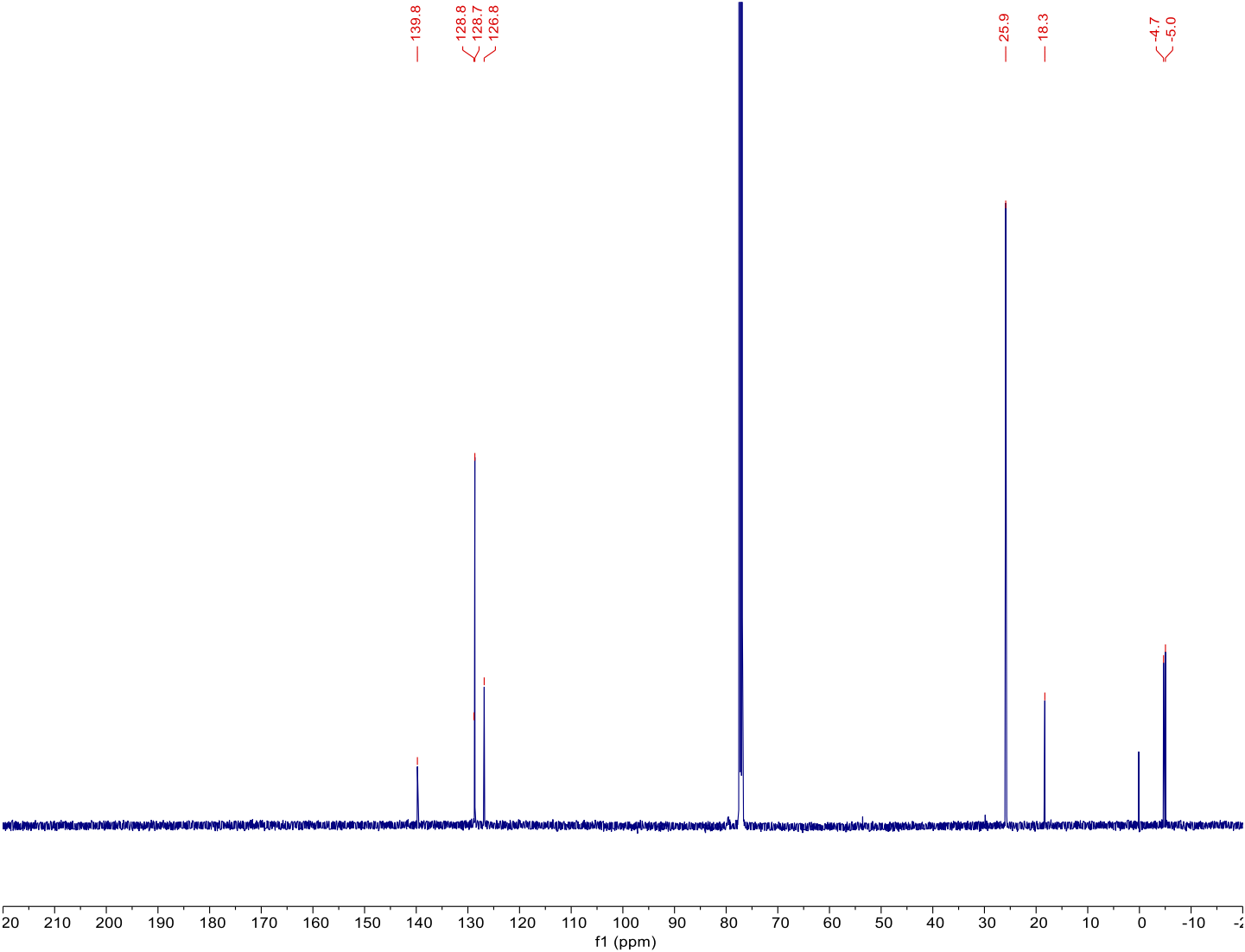
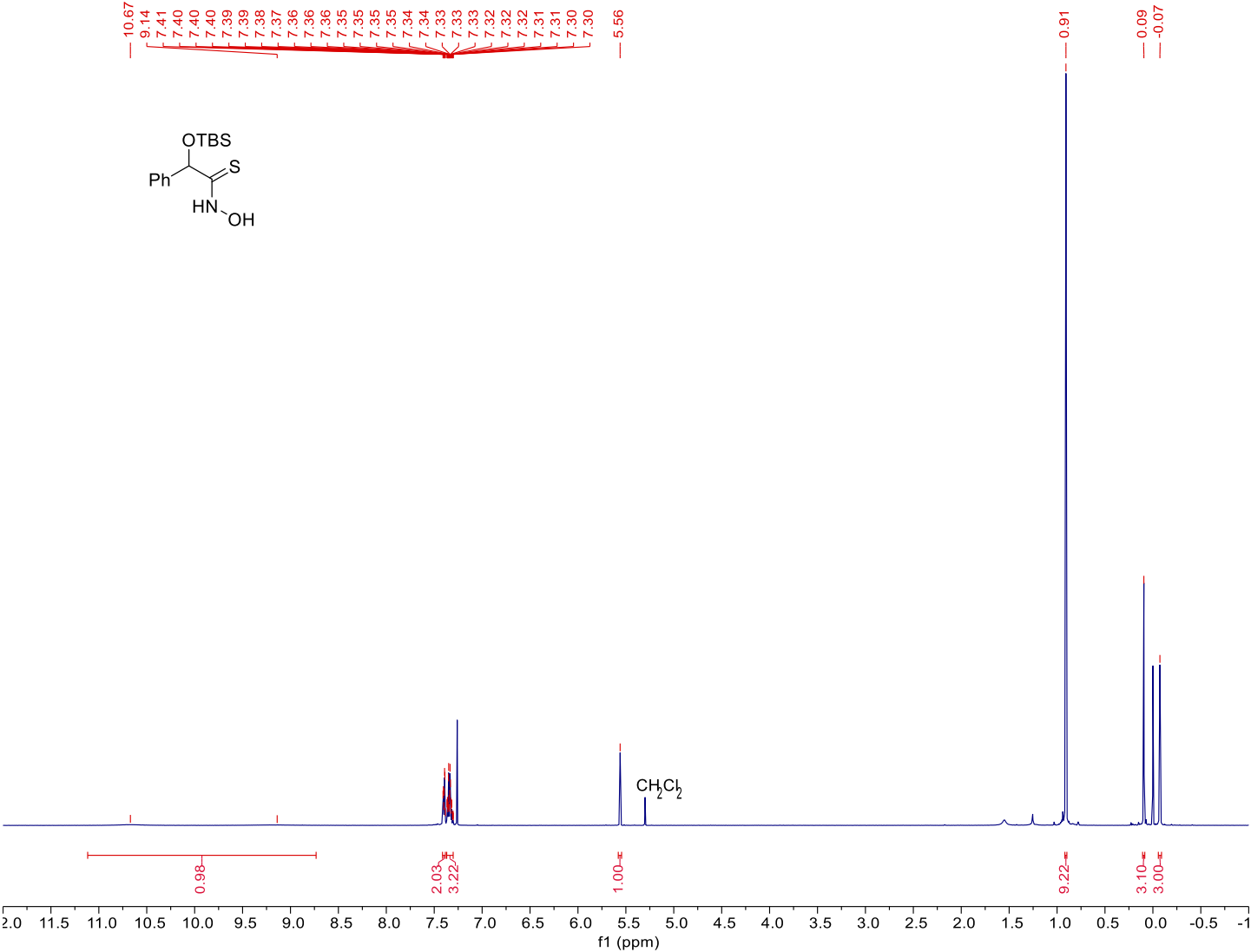
2D NMR (HSQC-edited and HMBC) spectra for compound **3v**.



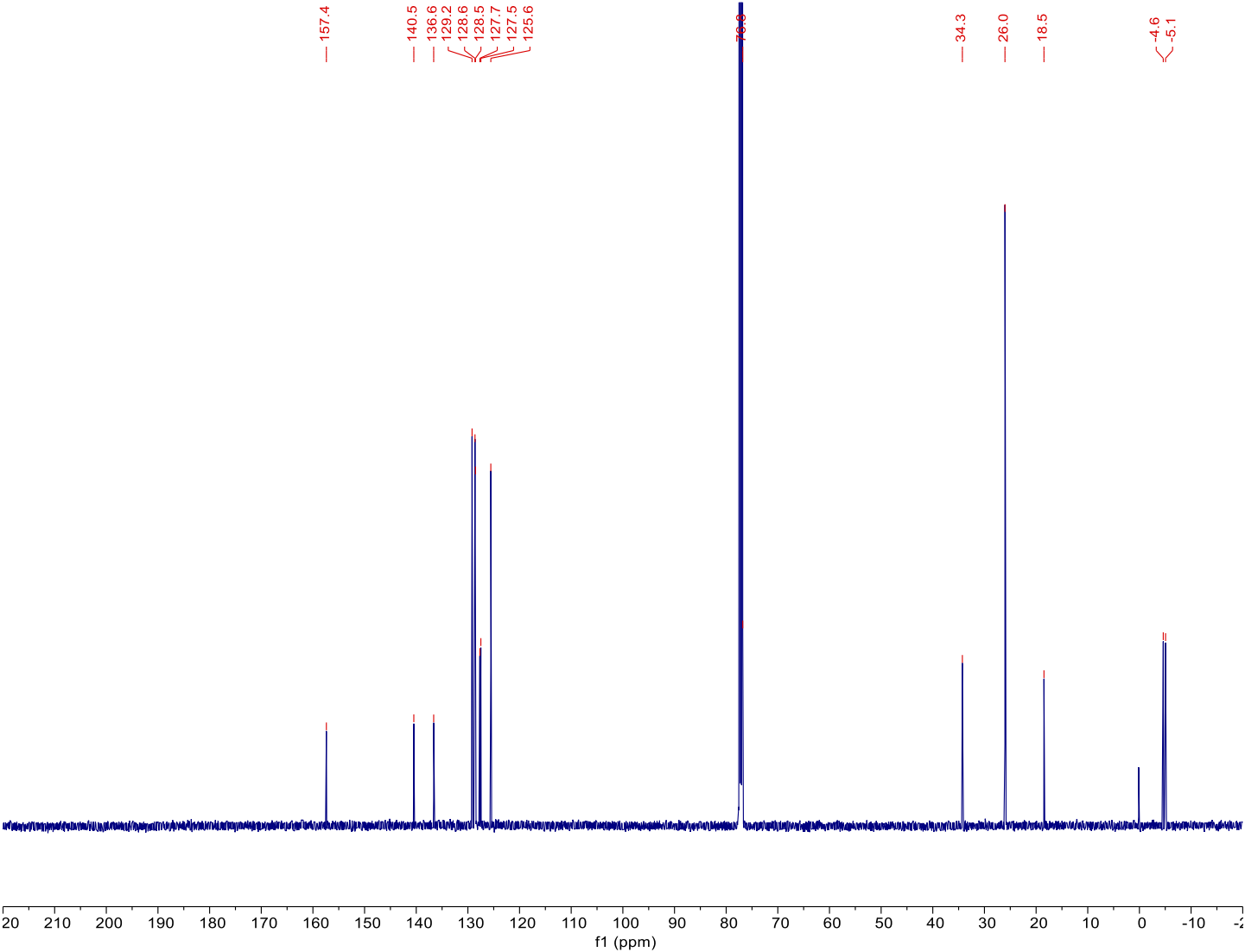
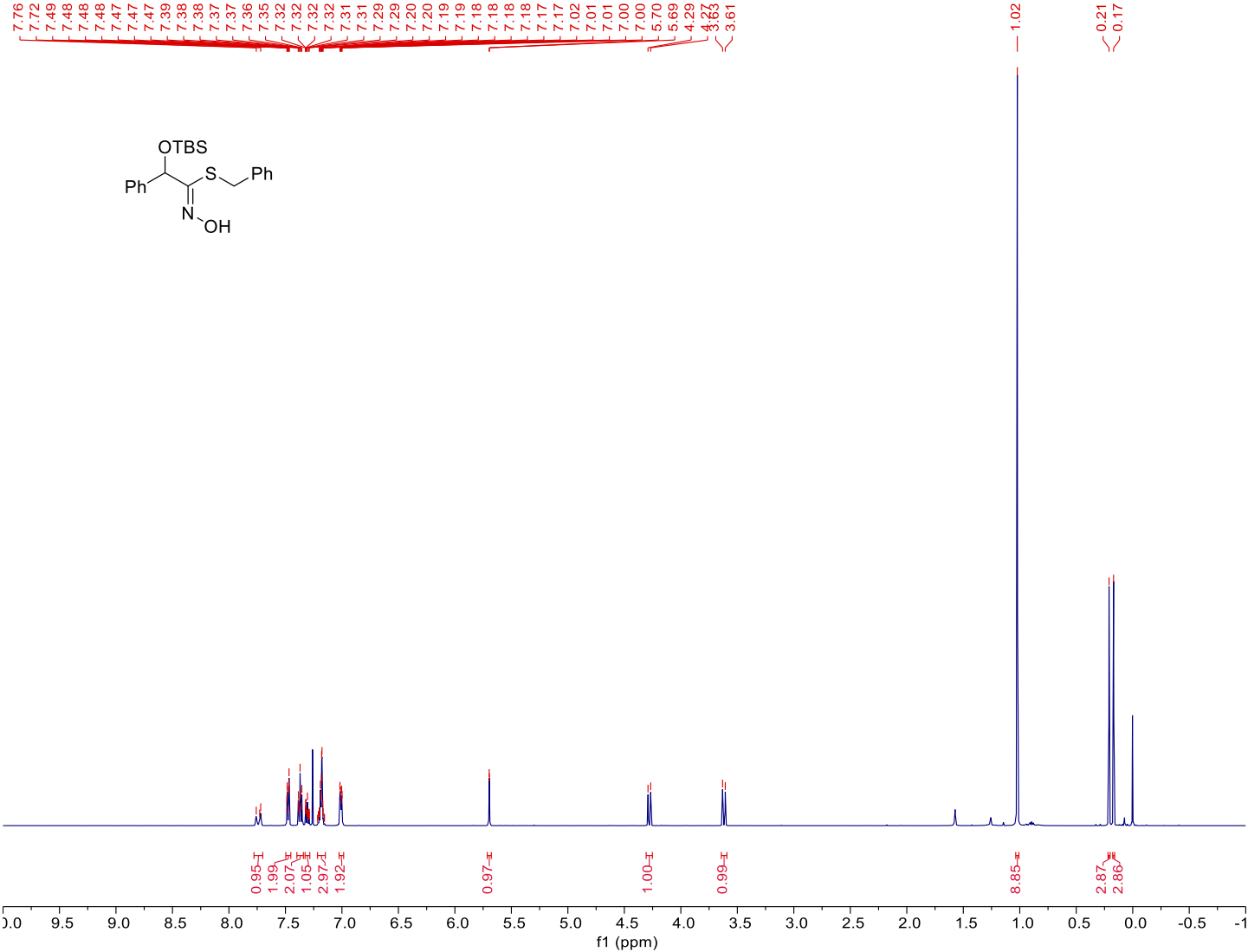
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **3w**.



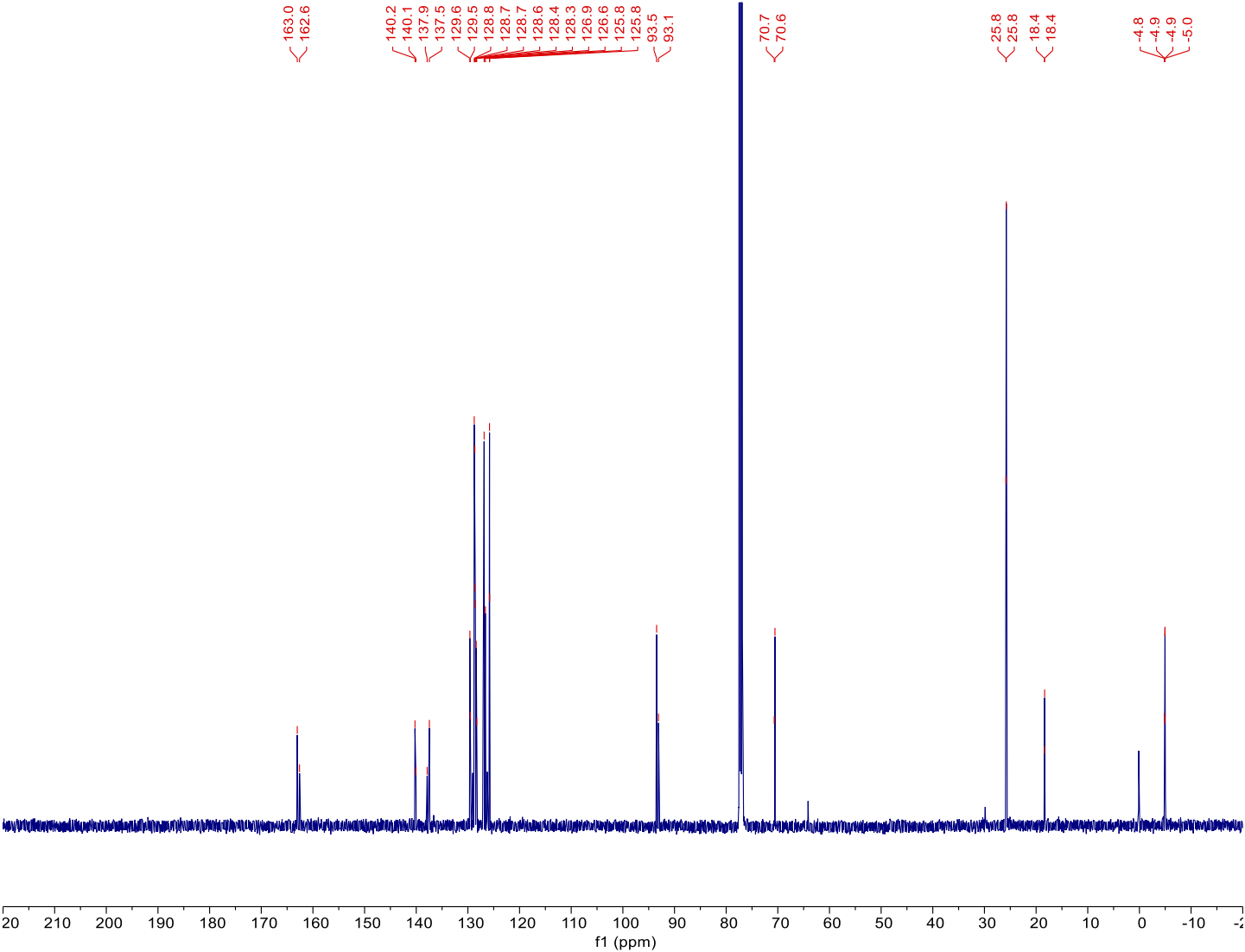
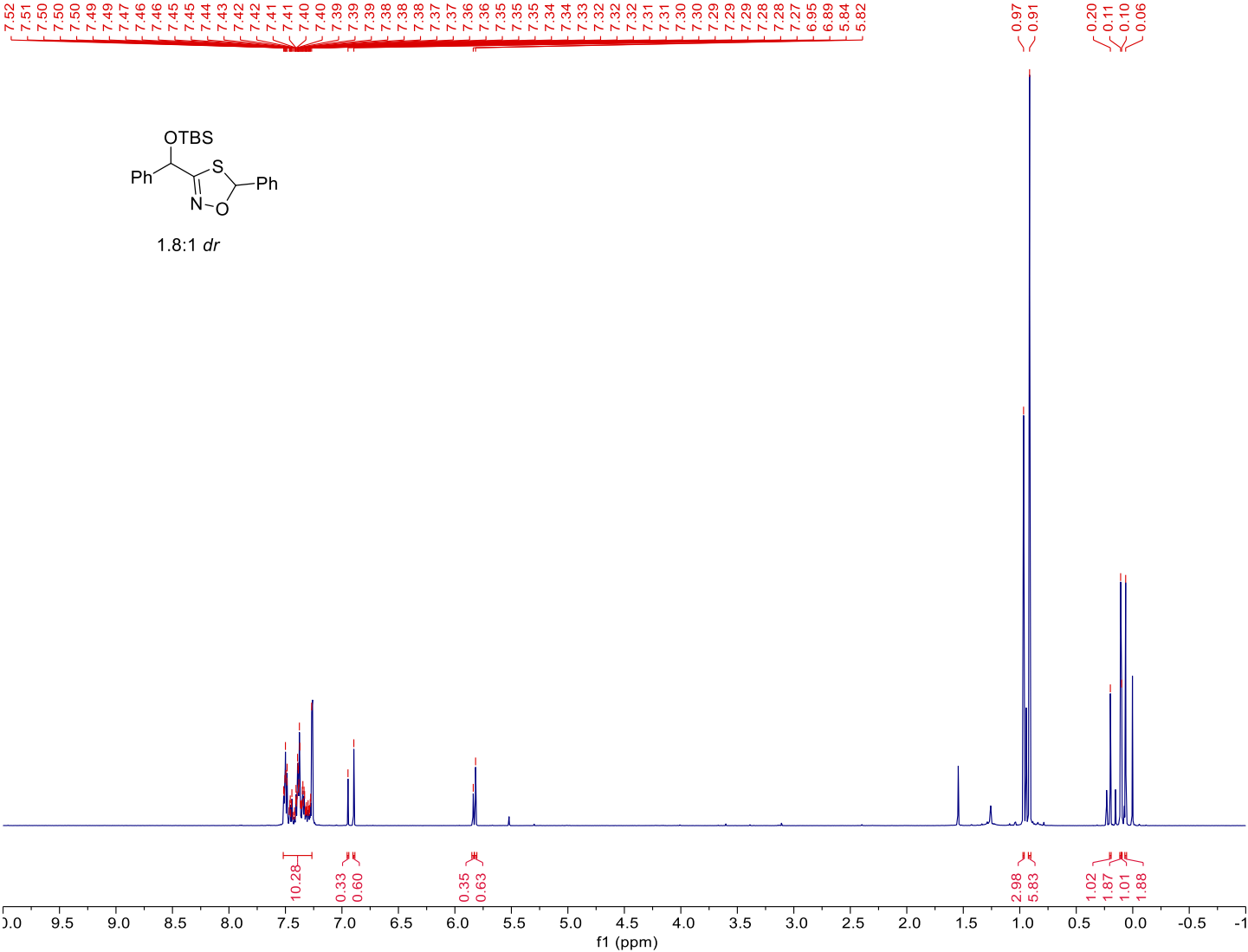
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **5x**.



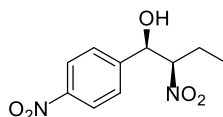
¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **S8**.



¹H NMR (500 MHz, CDCl₃) and ¹³C NMR (126 MHz, CDCl₃) spectra for compound **6x**.

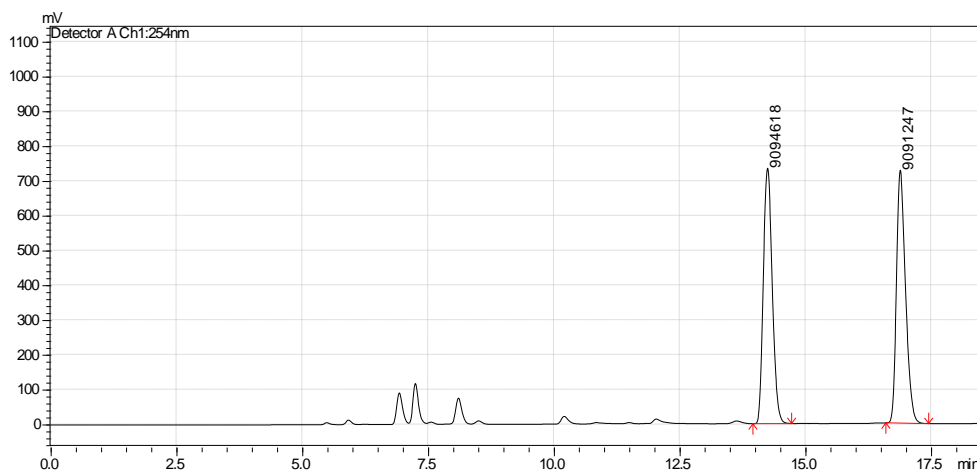


X. HPLC Chromatograms



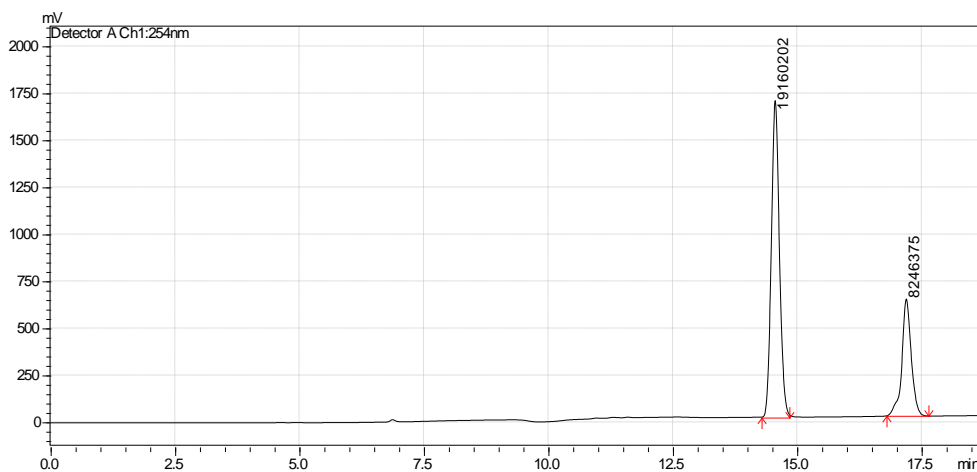
HPLC analysis for compound (*R,R*)-**S6** (CHIRALPAK[®] AD-H, 5 to 50% *i*PrOH/hexane gradient over 22 min, 0.7 mL/min, 254 nm): t_R = 14.5 min (major), 17.2 min (minor); 70:30 *er*.

Racemic **S6**

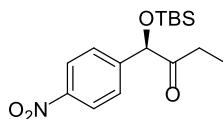


Peak #	Retention Time	Area	Area %
1	14.236	9094618	50.0
2	16.876	9091247	50.0

Scalemic (*R,R*)-**S6**

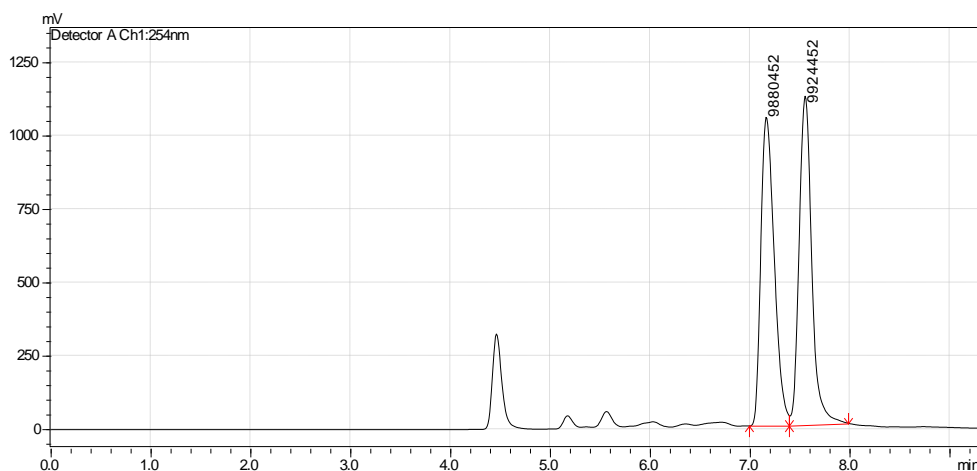


Peak #	Retention Time	Area	Area %
1	14.547	19160202	69.9
2	17.180	8246375	30.1



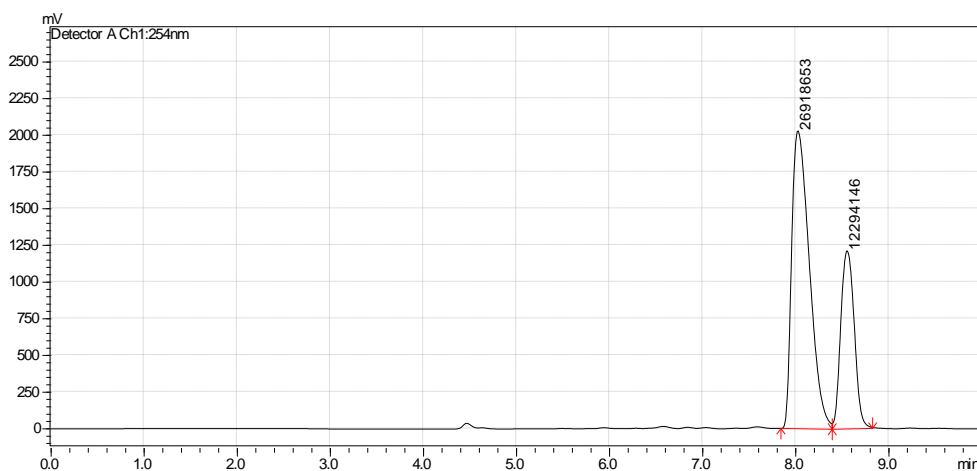
HPLC analysis for compound (*R*)-**3w** (CHIRALPAK® AD-H, 1 to 5% *i*PrOH/hexane gradient over 22 min, 0.7 mL/min, 254 nm): t_R = 8.05 min (major), 8.55 min (minor); 69:31 *er*.

Racemic **3w**



Peak #	Retention Time	Area	Area %
1	7.161	9880452	49.9
2	7.551	9924452	50.1

Scalemic (*R*)-**3w**



Peak #	Retention Time	Area	Area %
1	8.021	26918653	68.6
2	8.551	12294146	31.3

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