Supporting Information

Selective Formation of Adjacent Stereocenters by Allylboration of Ketones under Mild Neutral Conditions

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General Information

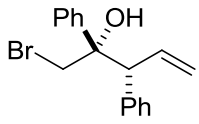
The solvents used in this study (dry degassed THF, MeOH, DMSO) and activated molecular sieves were stored in an Ar-filled glove box. THF was purified by passing through activated alumina in a solvent purification system. MeOH (anhydrous) was sparged with Ar and stored over molecular sieves (3Å) for several days before use. Anhydrous DMSO-d_6 was purchased from commercial source and stored over molecular sieves inside the Ar glovebox. Molecular sieves 3Å and 4Å (pellets) were activated by several microwave heating/vacuum/Ar cycles. Allylboronic acids were synthesized according to previously described literature.[1] All other chemicals were obtained from commercial sources and used as received. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ (internal standard: 7.26 ppm, ^{1}H; 77.16 ppm, ^{13}C) using 400 MHz and 500 MHz spectrometers. High resolution mass data (HRMS) were obtained using ESI technique. For column chromatography, silica gel (35-70 microns) was used.

Experimental Procedures and Spectral Data (4a-m)

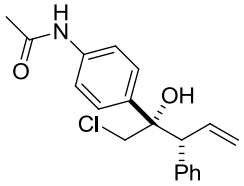
General Procedures for the Addition of Allylboronic Acids to Ketones

A. Solid Ketones: The ketone **2** (0.30 mmol) was weighed under air in a small vial then transferred to the glove box where it was dissolved in THF (0.6 mL). The allyl boronic acid **1** (0.39 mmol) was added to the stirred solution; a clear solution was obtained. Then, the vial was sealed with Teflon-lined cap and removed from the glove-box. The reaction mixture was allowed to stir at room temperature for allotted time (Table 1). After completion of the reaction, water (1 mL) was added to the reaction mixture and stirred vigorously for 5-10 min (except compounds **3g** and **3m**). Then, the reaction mixture was extracted with MTBE (methyl *tert*-butyl ether) (1 mL x 4) and dried over anhydrous $MgSO_4$. The solvent was evaporated under vacuum and the crude product was purified by silica gel chromatography or recrystallization.

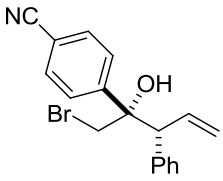
B. Liquid Ketones: In the glovebox, boronic acid **1** (0.39 mmol) was weighed in a small vial and dissolved in THF (0.6 mL); the vial was then sealed Teflon-lined cap and removed from the glove-box. The corresponding ketone (0.30 mmol) was added to the stirred solution via a Hamilton syringe; a clear solution was obtained. The reaction mixture was stired at room temperature (except **3i**) for the allotted time (Table 1). The desired product **3** was subsequently purified as describe below.



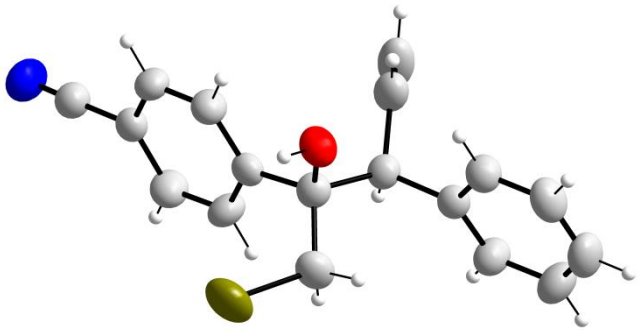
1-Bromo-2,3-diphenylpent-4-en-2-ol (3a). The compound was prepared according to above general procedure-A. Product **3a** was isolated in 97% yield (93.0 mg) as colorless solid using ether:pentane (1:10) as eluent for silica gel chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37-7.24 (m, 8H), 7.16-7.14 (m, 2H), 6.10 (ddd, J = 18.0, 9.3, 7.8 Hz, 1H), 5.03 (ddd, J = 10.2, 1.6, 0.8 Hz, 1H), 4.90 (ddd, J = 17.0, 1.6, 1.0 Hz, 1H), 3.90 (d, J = 10.6 Hz, 1H), 3.77 (d, J = 8.7 Hz, 1H), 3.66 (d, J = 10.6 Hz, 1H), 2.58 (d, J = 0.8 Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.4, 139.3, 137.0, 129.8, 128.4, 128.1, 127.6, 127.3, 126.2, 118.1, 77.6, 59.8, 44.8; HRMS (pos. ESI) m/z: Calcd for $C_{17}H_{17}BrONa$ $[M+Na]^+$ 339.0355. Found, 339.0352.



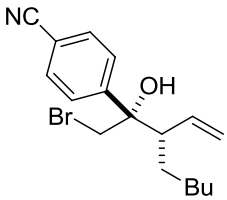
N-(4-(1-Chloro-2-hydroxy-3-phenylpent-4-en-2-yl)phenyl) acetamide (3b). The compound was prepared according to above general procedure-A. After evaporation of the solvent (MTBE) the compound was washed with pentane three times and dried under vacuum which yielded 96% (95.0 mg) as white solid. Since impurities was not observed according to the NMR spectra, compound **3b** was not purified by chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (d, J = 8.6 Hz, 2H), 7.27-7.24 (m, 5H), 7.21 (br s, 1H, NH), 7.14-7.12 (m, 2H), 6.08 (ddd, J = 18.0, 9.2, 7.9 Hz, 1H), 5.05 (d, J = 10.2 Hz, 1H), 4.95 (d, J = 17.0 Hz, 1H), 3.92 (d, J = 11.3 Hz, 1H), 3.75-3.72 (m, 2H), 2.6 (s, 1H, OH), 2.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.4, 139.1, 137.7, 137.3, 136.7, 129.8, 128.4, 127.3, 127.1, 119.2, 118.2, 78.0, 59.3, 53.4, 24.8; HRMS (pos. ESI) m/z: Calcd for $C_{19}H_{20}ClNO_2Na$ $[M+Na]^+$ 352.1075. Found, 352.1089.



4-(1-Bromo-2-hydroxy-3-phenylpent-4-en-2-yl)benzonitrile (3c). The compound was prepared according to above general procedure-A. Product **3c** was recrystallized from $CDCl_3$ and washed with pentane, then dried under vacuum. The compound was isolated in 83% yield (85.0 mg) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66-7.63 (m, 2H), 7.46-7.43 (m, 2H), 7.33-7.27 (m, 3H), 7.18-7.15 (m, 2H), 6.06 (ddd, J = 18.1, 9.2, 7.9 Hz, 1H), 5.02 (ddd, J = 10.2, 1.5, 0.7 Hz, 1H), 4.88 (dt, J = 17.0, 1.2, 1H), 3.86 (d, J = 10.8 Hz, 1H), 3.72 (d, J = 8.9 Hz, 1H), 3.59 (d, J = 10.8 Hz, 1H), 2.64 (d, J = 0.8 Hz, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 138.5, 136.1, 131.9, 129.6, 128.7, 127.7, 127.2, 118.8(3), 118.8, 115.5, 77.8, 59.8, 43.5; HRMS (pos. ESI) m/z: Calcd for $C_{18}H_{16}BrNONa$ $[M+Na]^+$ 364.0307. Found, 364.0322.

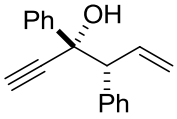


X-ray structure of compound **3c**. Displacement ellipsoids shown at 50% probability level. (cif file name: compound_3c.cif)

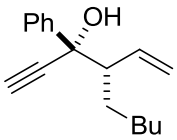


4-(1-Bromo-2-hydroxy-3-vinyloctan-2-yl)benzonitrile (3d). The compound was prepared according to the above general procedure-A. The product **3d** was isolated in 92% yield (93.0 mg) as colorless oil, using ether:pentane (1:6) as eluent for silica gel chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66-7.64 (m, 2H), 7.50-7.48 (m, 2H), 5.36-5.29 (m, 1H), 5.18 (dd, J = 10.2, 2.0 Hz, 1H), 5.16-5.12 (m, 1H), 5.47-5.43 (m, 1H), 3.96 (d, J = 10.7 Hz, 1H), 3.89 (d, J = 10.7 Hz, 1H), 2.64 (s, 1H, OH), 2.47-2.43 (m, 1H), 1.75-1.69 (m, 1H), 1.25-1.17 (m, 4H), 1.15-1.03 (m, 2H), 0.83 (t, J = 7.0 Hz, 3H), 0.77-0.70 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.0, 137.2,

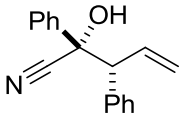
131.8, 127.4, 119.6, 118.8, 111.4, 76.7, 53.7, 44.2, 31.7, 28.4, 27.2, 22.7, 14.1; HRMS (pos. ESI) m/z: Calcd for $C_{17}H_{22}BrNONa$ $[M+Na]^+$ 358.0777. Found, 358.0762.



3,4-Diphenylhex-5-en-1-yn-3-ol (3e). The compound was prepared according to the above general procedure-A. Product **3e** was isolated in 85% yield (63.50 mg) as colorless liquid, using ether:pentane (1:10) as eluent for silica gel chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.35 (m, 2H), 7.23-7.20 (m, 3H), 7.16-7.12 (m, 3H), 7.05-7.02 (m, 2H), 6.49 (ddd, *J* = 18.3, 8.8, 8.1 Hz, 1H), 5.31 (ddd, *J* = 10.2, 1.7, 0.5 Hz, 1H), 5.25 (ddd, *J* = 17.0, 1.7, 0.8 Hz, 1H), 3.61(d, *J* = 9.4, 1H) 2.86 (s, 1H, OH), 2.76 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.7, 138.7, 136.8, 129.4, 127.9, 127.8, 127.1, 126.4, 119.7, 84.9, 76.5, 75.5, 63.6; HRMS (pos. ESI) m/z: Calcd for $C_{18}H_{16}ONa$ $[M+Na]^+$ 271.1093. Found, 271.1104.

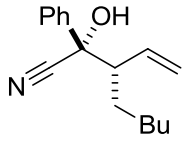


3-Phenyl-4-vinylnon-1-yn-3-ol (3f). The compound was prepared according to the above mentioned general procedure-A. Product **3f** was isolated in 93% yield (67.50 mg) as colorless liquid using ether:pentane (1:10) as eluent for silica gel chromatography. ^{1}H NMR for major isomer (500 MHz, $CDCl_3$): δ 7.66-7.64 (m, 2H), 7.38-7.35 (m, 2H), 7.32-7.29 (m, 1H), 5.87 (dt, *J* = 17.1, 9.9 Hz, 1H), 5.35 (dd, *J* = 10.2, 1.9 Hz, 1H), 5.26 (dd, *J* = 17.1, 1.9 Hz, 1H), 2.84 (s, 1H, OH), 2.72 (s, 1H), 2.36-2.31 (m, 1H), 1.38-0.97 (m, 8H), 0.79 (t, *J* = 7.1 Hz, 3H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.1, 138.4, 128.1, 128.0, 126.6, 120.6, 84.5, 75.7, 75.1, 57.8, 31.6, 29.4, 27.2, 22.6, 14.1; HRMS (pos. ESI) m/z: Calcd for $C_{17}H_{22}ONa$ $[M+H]^+$ 265.1563. Found, 265.1562.

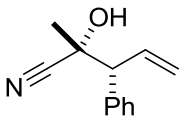


2-Hydroxy-2,3-diphenylpent-4-enenitrile (3g) was prepared according to the general procedure-**A** from **1a** (0.36 mmol, 58 mg) and **2e** (0.30 mmol, 40 mg) in THF (0.6 mL). The product was purified by addition of HCl 0.1 M (0.6 mL) and extraction with Et_2O (5x0.6 mL). The combined organic phases were concentrated over Celite (200 mg) in the presence of AcOH (0.2 mL) then purified by flash chromatography (pentane/Et_2O/AcOH 100:20:5) to yield **3g** as a clear oil that slowly solidified over

the next days (65 mg, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.15 (m, 8H), 7.05-6.99 (m, 2H), 6.45 (ddd, J = 16.9, 10.2, 9.5 Hz, 1H), 5.46 (ddd, J = 10.2, 1.4, 0.5 Hz, 1H), 5.38 (ddd, J = 16.9, 1.4, 0.9 Hz, 1H), 3.66-3.63 (m, 1H), 3.31 (s, OH, exchanges with H_2O); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.4, 136.4, 134.6, 129.13, 129.12, 128.5, 128.3, 128.0, 126.0, 122.0, 119.9, 77.1, 62.8.

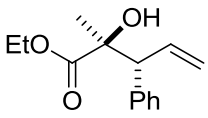


2-Hydroxy-2-phenyl-3-vinyloctanenitrile (3h). The compound was prepared according to the above general procedure-A. Product **3h** was isolated in 80% yield (58.70 mg) as colorless liquid using ether:pentane (1:10) as eluent for silica gel chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58-7.55 (m, 2H), 7.45-7.38 (m, 3H), 5.82 (dt, *J* = 17.0, 9.9 Hz, 1H), 5.50 (dd, *J* = 10.2, 1.6 Hz, 1H), 5.38 (ddd, *J* = 17.0, 1.6, 0.7 Hz, 1H), 3.24 (s, 1H, OH), 2.41 (ddd, *J* = 11.7, 9.4, 2.6 Hz, 1H), 1.43-1.36 (m, 1H), 1.31-1.23 (m, 1H), 1.2-0.97 (m, 6H), 0.80 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.9, 136.3, 129.4, 128.8, 126.1, 123.1, 119.6, 76.7, 57.0, 31.4, 29.0, 26.9, 22.5, 14.1

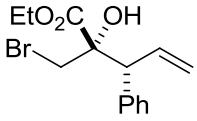


2-Hydroxy-2-methyl-3-phenylpent-4-enenitrile (3i). A Teflon-lined screw cap reaction vial (2 mL) was charged with allylboronic acid (0.3 mmol, 49 mg) and THF (0.4 mL) in glove box. The reaction vial was taken out of glove box (the solution was kept under Ar). The reaction mixture was cooled to -78 ^{o}C (acetone + dry ice in a Dewar wessel). Pyruvnitrile **2f** (90% commertial purity) (0.39 mmol, 30 µL) was dissolved in THF (0.2 mL) and then it was added slowly to the reaction mixture by syringe. The reaction mixture was allowed to warm to room temperature (22 ^{o}C), and then 0.2 mL of AcOH was added. The column chromatography was performed without evaporating solvent using pentane:ether (4:1) as eluent. Product **3i** was isolated in 72% (40 mg) yield as colorless liquid. Product was mixture of two stereoisomers in a ratio of 9:1. ^{1}H NMR for major isomer (500 MHz, $CDCl_3$): δ 7.41-7.31 (m, 5H), 6.35 (dt, *J* = 16.9, 9.9 Hz, 1H), 5.45 (dd, *J* = 10.1, 1.4 Hz, 1H), 5.39 (ddd, *J* = 16.9, 1.4, 0.8 Hz, 1H), 3.38 (d, *J* =9.8 Hz, 1H), 2.88 (q, *J* =0.8 Hz, 1H, OH), 1.47 (d, *J* =0.8 Hz, 3H); ^{13}C NMR for major isomer (125 MHz, $CDCl_3$): δ 137.3, 134.6, 129.1, 128.7, 128.2, 121.8, 121.1, 70.7, 60.7, 25.6; HRMS (pos. ESI) m/z: Calcd for $C_{12}H_{13}NONa$ $[M+Na]^+$ 210.0890.

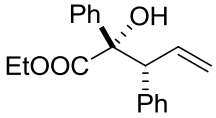
Found, 210.0890. The structure of **3i** was determined by X-ray crystallography via its ester derivative (See page S12 for the details).



Ethyl 2-hydroxy-2-methyl-3-phenylpent-4-enoate (3j). The compound was prepared according to the above general procedure-A. Product **3j** was isolated in 70% yield (49.5 mg) as a colorless liquid, using ether:pentane (1:10) as eluent for the silica gel chromatography. The stereochemistry of the compound was confirmed by comparison with the epimer of **3j** (see page S12 for the details). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.35 (m, 2H), 7.33-7.30 (m, 2H), 7.27-7.24 (m, 1H), 6.22 (ddd, J = 18.3, 8.9, 8.1 Hz, 1H), 5.11-5.05 (m, 2H), 4.31-4.21 (m, 2H), 3.58 (d, J = 9.3 Hz, 1H), 3.38 (s, 1H), 1.33 (t, J = 7.1 Hz, 3H), 1.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.7, 139.3, 137.2, 129.6, 128.4, 127.1, 117.4, 77.2, 62.3, 58.2, 24.8, 14.4; HRMS (pos. ESI) m/z: Calcd for $C_{14}H_{18}O_3Na$ $[M+2Na]^+$ 257.1148. Found, 257.1160

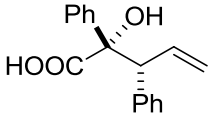


Ethyl 2-(bromomethyl)-2-hydroxy-3-phenylpent-4-enoate (3k). The compound was prepared according to above general procedure-A. Product **3k** was isolated in 88% yield (82.6 mg) as a colorless liquid using ether:pentane (1:15) as eluent for silica gel chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.25 (m, 5H), 6.22 (ddd, J = 18.2, 8.9, 8.1 Hz, 1H), 5.12-5.06 (m, 2H), 4.38-4.28 (m, 2H), 3.71 (t, J = 0.6 Hz, 1H, OH), 3.69 (d, J = 9.3 Hz, 1H), 3.60 (dd, J = 10.4, 0.6 Hz, 1H), 3.11 (d, J = 10.4, Hz, 1H), 1.37 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 138.1, 136.6, 129.4, 128.7, 127.7, 117.9, 79.9, 63.0, 56.9, 38.9, 14.4; HRMS (pos. ESI) m/z: Calcd for $C_{14}H_{17}BrO_3Na$ $[M+Na]^+$ 335.0253. Found, 335.0259.



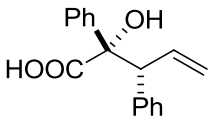
Ethyl 2-hydroxy-2,3-diphenylpent-4-enoate (3l) was prepared according to the general procedure-B from **1a** (0.39 mmol) and **2i** (50 µL, 0.30 mmol) in THF (0.6 mL). The crude reaction mixture was concentrated over Celite (240 mg) then the product was purified by flash chromatography (pentane/Et_2O 100:8) to yield **3l** as a soft white solid (78 mg, 87% yield). The stereochemistry of the compound was confirmed by comparison with the

ethyl ester of **3m** (see below, S11). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.77 (m, 2H), 7.46-7.44 (m, 2H), 7.41-7.36 (m, 2H), 7.32-7.28 (m, 3H), 7.26-7.22 (m, 1H), 6.01 (ddd, J = 17.2, 1.7, 1.0 Hz, 1H), 4.94 (ddd, J = 10.3, 1.7, 1.0 Hz, 1H), 4.80 (ddd, J = 17.2, 1.6, 1.2 Hz, 1H), 4.25 (d, J = 8.0 Hz, 1H), 4.04-3.93 (m, 2H), 3.90 (d, J = 0.6 Hz, OH, exchanges with H_2O), 1.13 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.2, 140.4, 139.7, 136.2, 129.7, 128.3, 128.2, 127.8, 127.3, 126.6, 118.1, 80.9, 62.7, 57.9, 14.0



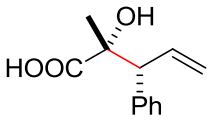
2-Hydroxy-2,3-diphenylpent-4-enoic acid (3m) was prepared according to the general procedure **A** from **1a** (0.36 mmol) and **2j** (46 mg, 0.30 mmol) in MeOH (0.6 mL). The mixture was concentrated over Celite (240 mg) then the product was purified by flash chromatography (CH_2Cl_2/AcOH 100:2) to yield **3m** as a white solid (58 mg, 72% yield). The ^{1}H and ^{13}C chemical shifts were consistent with the literature values[2]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77-7.74 (m, 2H), 7.43-7.37 (m, 2H), 7.34-7.30 (m, 1H), 7.28-7.20 (m, 3H), 5.98 (ddd, J = 17.2, 10.4, 8.1 Hz, 1H), 4.98 (ddd, J = 10.4, 1.5, 1.0 Hz, 1H), 4.85 (dt, J = 17.2, 1.4 Hz, 1H), 4.30 (d, J = 8.2 Hz, 1H), 3.58 (br s, OH, exchanges with H_2O); ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.7, 139.3, 139.0, 135.5, 129.7, 128.5, 128.4, 128.2, 127.6, 126.6, 118.8, 81.0, 57.3.

General Procedure for the One-pot Allylation of α-Keto acids 2j-k Using Allylic Alcohols (4a-d). Allyl alcohol **4** (0.30 or 0.48 mmol) was dissolved in the corresponding solvent under ambient conditions, then the Pd catalyst **5** (1-5 mol%) and $B_2(OH)_4$ (0.36 or 0.58 mmol) were successively added. The reaction was stirred for the alloted times given in Table 2 to form the corresponding allylboronic acids. Then, α-ketoacid **2j** or **2k** (0.24 mmol) was added in one portion. The reaction mixture was stirred for further 30 minutes and the product (**3**) was purified.

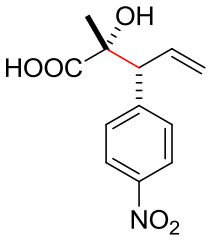


2-Hydroxy-2,3-diphenylpent-4-enoic acid (3m) was prepared according to the general procedure by treating a solution of **4a** (0.30 mmol) with catalyst **5a** (10 µL, 1 mol%) and $B_2(OH)_4$ (0.36 mmol) in MeOH (0.6 mL) for 18 h followed by addition of **2j** (37 mg, 0.24 mmol). Palladium black was filtered off through a short pad of silica then the reaction vial

and silica pad were washed with MeOH (5 times). The mixture was concentrated over Celite (220 mg) then the product was purified by flash chromatography (CH_2Cl_2/AcOH 100:2) to yield **3m** as a white solid (39 mg, 60% yield).

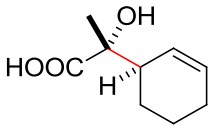


2-Hydroxy-2-methyl-3-phenylpent-4-enoic acid (3n) was prepared according to the general procedure by treating a solution of **4a** (0.30 mmol) in MeOH (0.6 mL) with **5a** (10 µL, 1 mol%) and $B_2(OH)_4$ (0.36 mmol) for 18 h followed by addition of **2k** (17 µL, 0.24 mmol). Palladium black was filtered off through a short pad of silica then the reaction vial and silica pad were washed with MeOH (5 times). The mixture was concentrated over Celite (200 mg) then the product was purified by flash chromatography (pentane/Et_2O/AcOH 80:20:2) to yield **3n** as a white solid (41 mg, 83% yield). The ^1H and ^{13}C chemical shifts in $CDCl_3$ were consistent with literature values.[2,3] ^1H NMR (400 MHz, $CDCl_3$): δ 7.28-7.21 (m, 5H), 6.26 (dt, J = 17.0, 9.9 Hz, 1H), 5.26 (dd, J = 10.2, 1.8 Hz, 1H), 5.21 (ddd, J = 17.0, 1.7, 0.7 Hz, 1H), 3.58 (d, J = 9.7 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 180.3, 139.6, 135.6, 128.8, 128.7, 127.5, 119.2, 77.1, 57.9, 24.7.

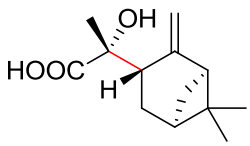


2-Hydroxy-2-methyl-3-(4-nitrophenyl)pent-4-enoic acid (3o) was prepared according to the above general procedure by treating a solution of **4b** (0.30 mmol) in MeOH (0.8 mL) / DMSO (0.2 mL) with **5a** (50 µL, 5 mol%) and $B_2(OH)_4$ (0.36 mmol) for 30 min followed by addition of **2k** (17 µL, 0.24 mmol). Palladium black was filtered off through a short pad of silica then the reaction vial and silica pad were washed with MeOH (5 times). The MeOH was removed, then $CHCl_3$ (2 mL) was added and the mixture was washed with saturated brine (2x1 mL). The brine layers were extracted with $CHCl_3$ (2x2 mL) and the combined $CHCl_3$ layers were diluted with pentane (6 mL) and purified by flash chromatography (CH_2Cl_2/AcOH 100:4) to yield **3o** as an orange wax (40 mg, 66% yield). ^1H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, J = 8.7 Hz, 2H), 7.47 (d, J = 8.7 Hz, 2H), 6.21 (dt, J = 17.0, 9.9 Hz, 1H), 5.32 (dd, J = 10.1, 1.3 Hz, 1H), 5.25 (d, J = 17.0 Hz, 1H), 3.68 (d, J = 9.7 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ

179.7, 147.2(7), 147.2(6), 134.3, 129.8, 123.6, 120.4, 76.7, 57.3, 25.2; HRMS-ESI m/z: Calcd. For $C_{12}H_{13}NNaO_5^+$ ($M+Na^+$): 274.0686; found: 274.0696.

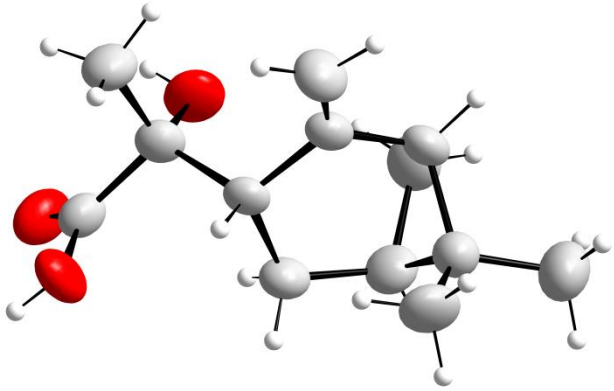


2-(Cyclohex-2-en-1-yl)-2-hydroxypropanoic acid (3p) was prepared according to the general procedure by treating a solution of **4c** (0.30 mmol) in DMSO (0.48 mL) / H_2O (0.12 mL) with **5b** (7 mg, 5 mol%) and $B_2(OH)_4$ (0.36 mmol) for 3 h followed by addition of **2k** (83%, 20 µL, 0.24 mmol). Palladium black was filtered off through a short pad of silica then the reaction vial and silica pad were washed with Et_2O (5x0.6 mL). The mixture was washed with saturated brine (0.6 mL) then the brine layer was extracted with Et_2O (3 mL). The combined Et_2O layers were concentrated over Celite (190 mg) then purified by flash chromatography (CH_2Cl_2/AcOH 100:8) to yield **3p** as an clear oil that solidified overnight (27 mg, 65% yield). The ^1H and ^{13}C chemical shifts in $CDCl_3$ were consistent with literature values.[4] ^1H NMR (400 MHz, $CDCl_3$): δ 5.95-5.90 (m, 1H), 5.47-5.45 (m, 1H), 2.64-2.60 (m, 1H), 2.01-2.00 (m, 2H), 1.91-1.84 (m, 2H), 1.61-1.41 (m, overlapped, 2H), 1.45 (s, overlapped, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 181.6, 132.1, 125.7, 76.9, 43.6, 25.1, 22.9, 22.4, 21.8



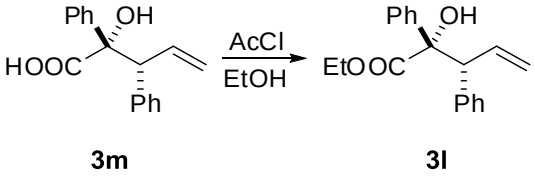
(R)-2-((1R,3S,5R)-6,6-Dimethyl-2-methylene-bicyclo[3.1.1] heptan-3-yl)-2-hydroxypropanoic acid (3q) was prepared according to the general procedure by treating a solution of **4d** (0.48 mmol) in DMSO (1.28 mL) / H_2O (0.32 mL) with **5b** (11 mg, 5 mol%) and $B_2(OH)_4$ (0.58 mmol) for 1 h followed by addition of **2k** (17 µL, 0.24 mmol). Palladium black was filtered off through a short pad of silica then the reaction vial and silica pad were washed with Et_2O (5x1.6 mL). The mixture was washed with saturated brine (1.6 mL) then the brine layer was extracted with Et_2O (8 mL). The combined Et_2O layers were concentrated over Celite (490 mg) then purified by flash chromatography (pentane/Et_2O/AcOH 80:20:2) to yield **3q** as a white solid (42 mg, 77% yield). X-Ray quality crystals were grown by slow counter diffusion of pentane vapors into a solution of **3q** in $CDCl_3$. Major isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 4.95 (s, 1H), 4.91 (s, 1H), 3.04-3.01 (m, 1H), 2.42 (t, 5.6 Hz, 1H), 2.26-2.20 (m, 1H), 2.12-2.05 (m, 1H), 1.96-1.91 (m, 1H), 1.71 (dt, J = 13.7, 3.7 Hz, 1H), 1.62 (s, 3H), 1.60 (d, J = 10.0 Hz, 1H), 1.25 (s, 3H), 0.74 (s, 3H); ^{13}C NMR (101 MHz,

$CDCl_3$): δ 180.6, 149.6, 112.7, 77.9, 53.2, 41.6, 41.3, 40.3, 28.1, 27.1, 26.2, 26.0, 21.8; minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$, selected signals): δ 4.83 (br s, 1H), 4.77 (br s, 1H), 3.46-3.44 (m, 1H), 0.85 (s, 3H); HRMS (pos. ESI) m/z: Calcd for $C_{18}H_{22}O_3Na$ $[M+Na]^+$ 309.1467. Found, 309.1471.



X-ray structure of compound **3q**. Displacement ellipsoids shown at 50% probability level. The space group is $P2_12_12_1$, indicating that compound **3q** is enantiomerically pure (cif file name: compound_3q.cif).

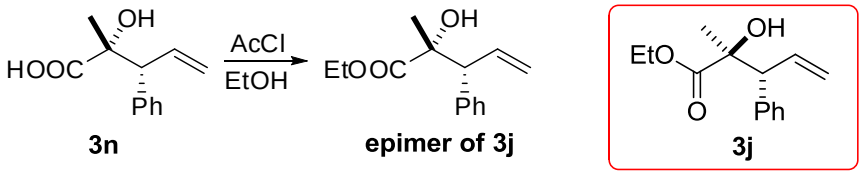
Esterification of 3l to 3m



3m **3l**

According to a reported procedure,[5] acetyl chloride (0.10 mL) was dissolved in EtOH (0.4 mL) at 0 °C and the mixture was stirred for 30 min. Compound **3m** (11 mg, 0.04 mmol) was added and then the reaction mixture heated to 100 °C (MW) for 18 h. Evaporation and vacuum drying afforded a mixture of **3l** and **3m** which was dissolved in $CDCl_3$ (conversion: 88%). A sample of **3l** (13 mg, 0.04 mmol) obtained from the allylation of **2i** was added to this mixture. The NMR spectra showed that samples (**3l**) obtained from esterification of **3m** and allylation of **2i** are identical.

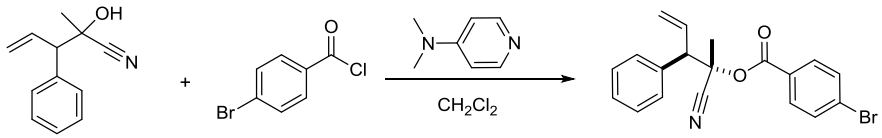
Esterification of 3n to give the Epimer of 3j



3n **epimer of 3j** **3j**

According to (the above described) literature procedure[5] acetyl chloride (0.10 mL) was dissolved in EtOH (0.4 mL) at 0 °C and the mixture was stirred for 30 min. Compound **3n** (prepared from **4a**, Table 2, entry 2) (8 mg, 0.04 mmol) was added and this mixture was heated at 50 °C for 18 h. The esterification afforded the epimer of **3j** quantitatively. This compound and the product obtained by allylation of **2g** (i.e. **3j** itself, Table 1, entry 10) gave different NMR spectra indicating the epimer relationship between the two compounds. ^{1}H NMR of the epimer of **3j** (400 MHz, $CDCl_3$): δ 7.28-7.18 (m, 5H), 6.28 (dt, J = 17.1, 9.9 Hz, 1H), 5.23 (dd, J = 10.2, 1.8 Hz, 1H), 5.19 (ddd, 17.1, 1.8, 0.7 Hz, 1H), 4.09-3.97 (m, 2H), 3.55 (d, J = 9.7 Hz, 1H), 3.24 (br s, OH, exchanges with H_2O), 1.47 (s, 3H), 1.17 (t, J = 7.2 Hz, 3H); ^{13}C of the epimer of **3j** NMR (101 MHz, $CDCl_3$): δ 176.2, 140.1, 136.3, 128.6, 128.4, 127.2, 118.4, 76.8, 62.0, 58.2, 24.8, 14.2.

Derivatization of 3i

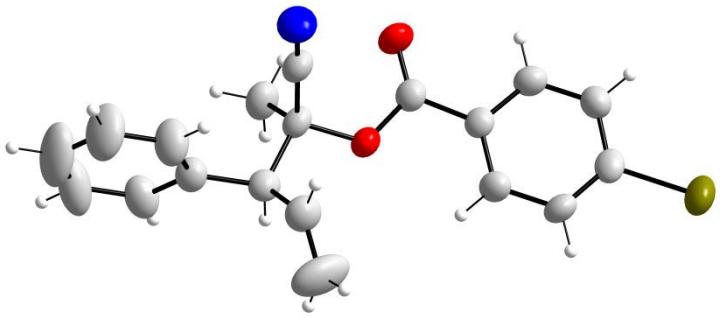


3i (oil) ester of **3i** (solid)

Compound **3i** was obtained as an oil, and thus it was not suitable for crystallographic structure determination. When **3i** was reacted with bromo benzoic acid a solid product was obtained, which could be crystallized. The following procedure was used for esterification. To a solution of 4-bromobenzoyl chloride (0.16 mmol, 36 mg) in dry dichloromethane (0.4 mL) was added compound **3i** (0.15 mmol, 28 mg) and 4-dimethylaminopyridine (0.16 mmol, 20 mg) under ambient conditions. Then, the reaction mixture was stired at room tempearture. After 1h water (1 mL) was added and the product was extracted with methyl tert-butyl ether (1x3 mL). The

combined organic phases were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude compound was dissolved in dichloromethane and passed through a silica plug using dichloromethane as eluent. After evaporation of the solvent the esterification product was solidified in refrigerator in overnight. Crystalls for X-ray determination were grown by slow counter diffusion of pentane vapors into a solution of pure compound (10 mg) in $CHCl_3$ (0.2 mL). ^{1}H NMR (500 MHz, $CDCl_3$) major isomer: δ 7.84 (d, J = 8.5 Hz, 2H), 7.61 (d, J = 8.5 Hz, 2H), 7.42-7.31 (m, 5H), 6.39 (ddd, J = 17.9, 9.1, 7.8 Hz, 1H), 5.41-5.37 (m, 2H), 4.00 (d, J = 8.9 Hz, 1H), 1.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) for major isomer: δ 163.8, 136.7, 134.1, 132.1, 131.3, 129.4, 129.1, 128.9, 128.3, 128.2, 120.8, 117.9, 75.4, 57.9, 22.9; HRMS (pos. ESI) m/z: Calcd for $C_{19}H_{16}BrNO_2Na$ $[M+Na]^+$ 392.0257. Found, 392.0268.

X-ray structure:



X-ray structure of compound **3i**-ester derivative. Displacement ellipsoids shown at 50% probability level. (cif file name: compound_3i_ester.cif)

References:

(1) Raducan, M.; Alam, R.; Szabó, K. J. *Angew. Chem. Int. Ed.* **2012**, *51*, 13050.

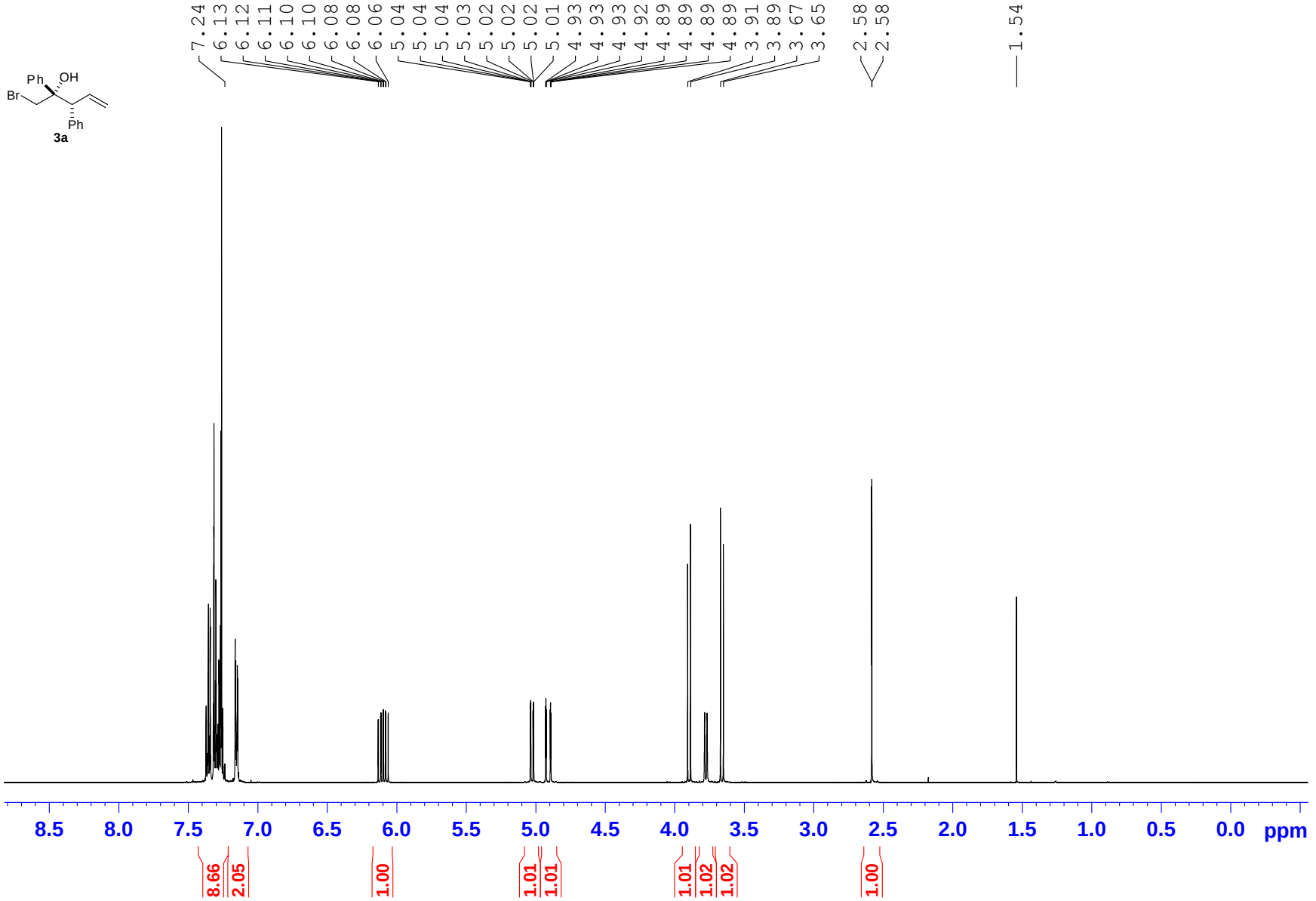
(2) Kaur, P.; Singh, P.; Kumar, S. *Tetrahedron* **2005**, *61*, 8231.

(3) Howard, B. E.; Woerpel, K. A. *Org. Lett.* **2007**, *9*, 4651.

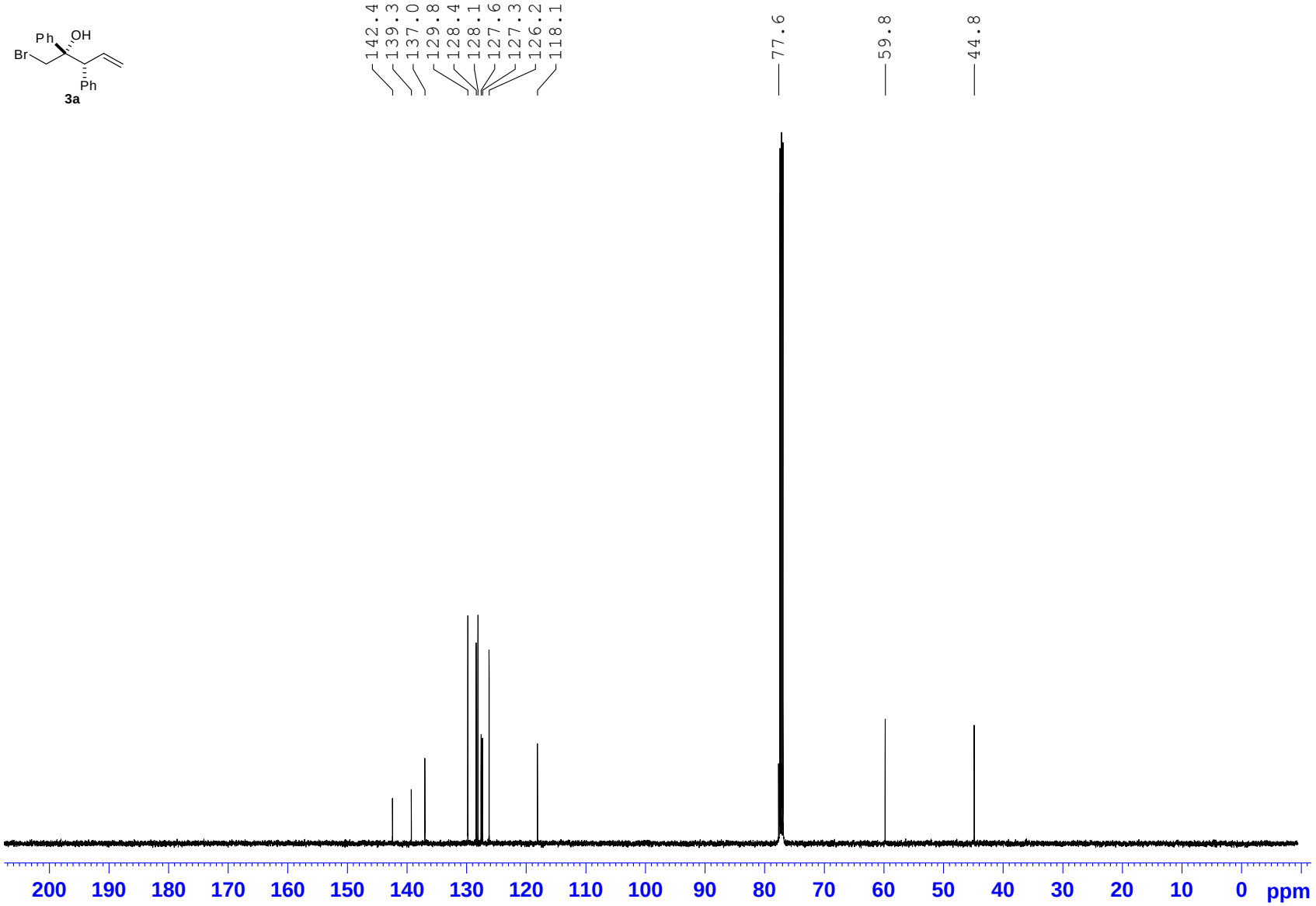
(4) Muderawan, I. W.; Bott, R. C.; Young, D. J. *Synthesis* **1998**, *11*, 1640.

(5) Hasuoka, A.; Nakayama, Y.; Adachi, M.; Kamiguchi, H.; Kamiyama, K. *Chem. Pharm. Bull.* **2001**, *49*, 1604.

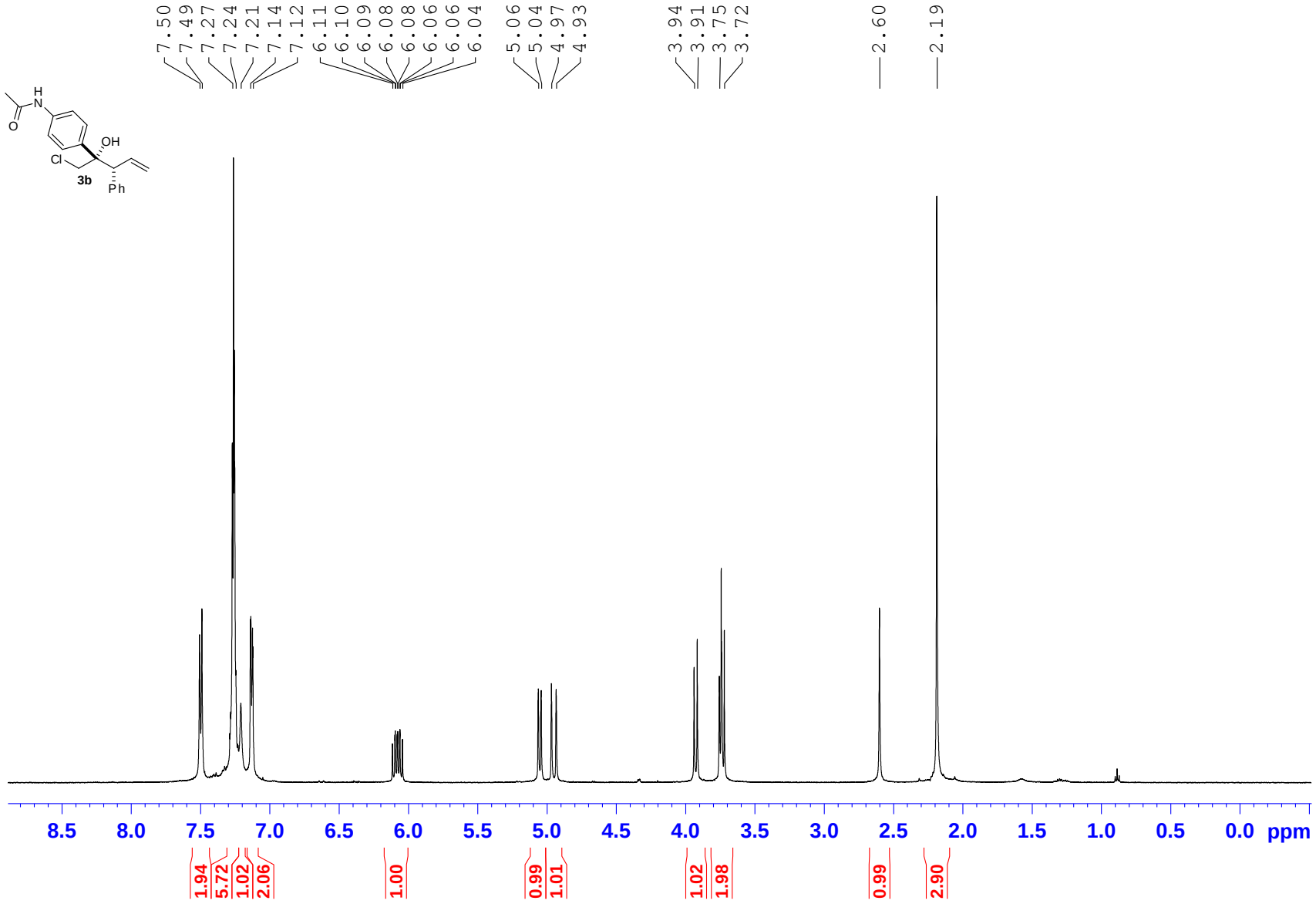
^{1}H NMR of **3a** ($CDCl_3$, 500 MHz)



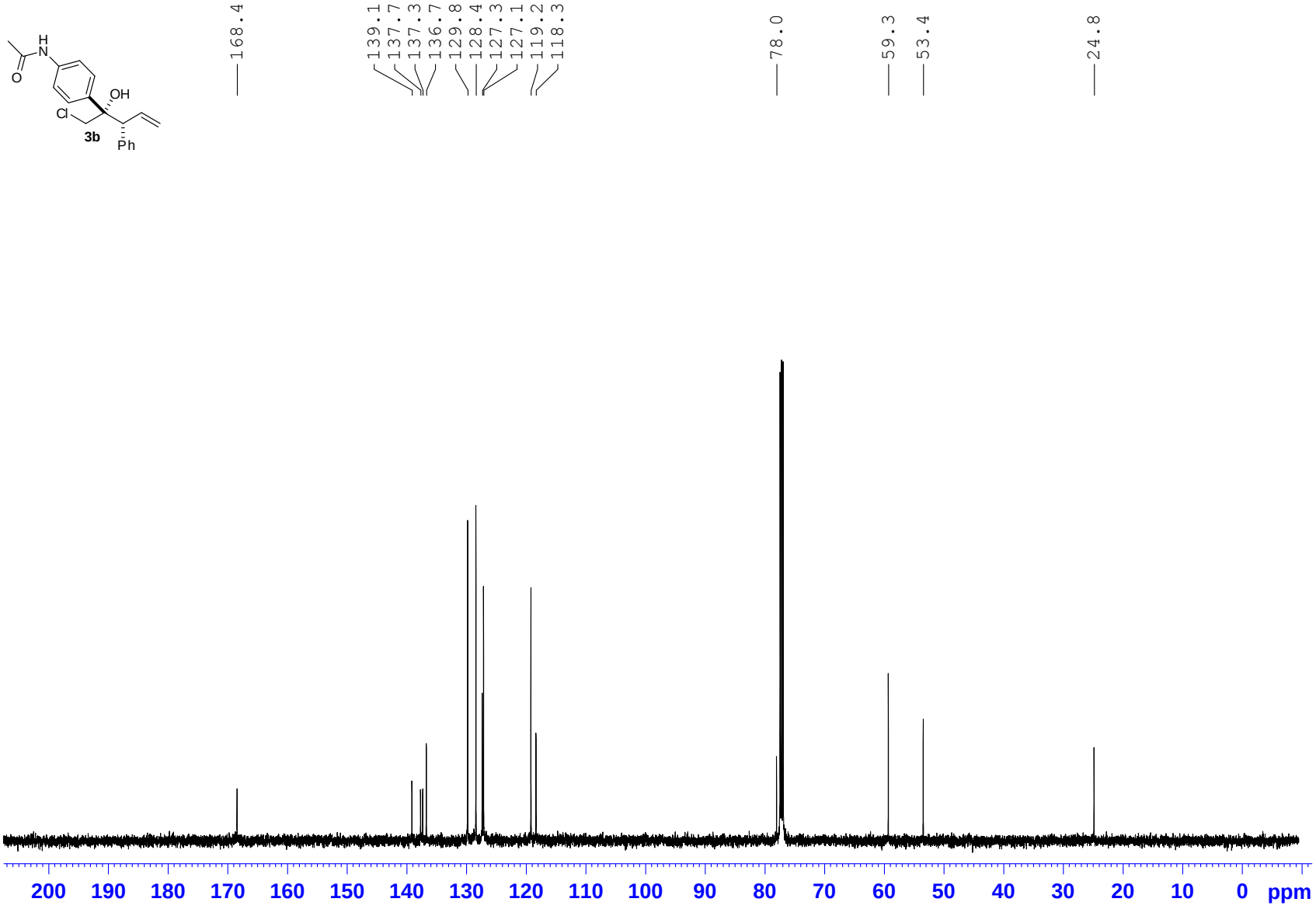
^{13}C NMR of **3a** ($CDCl_3$, 500 MHz)



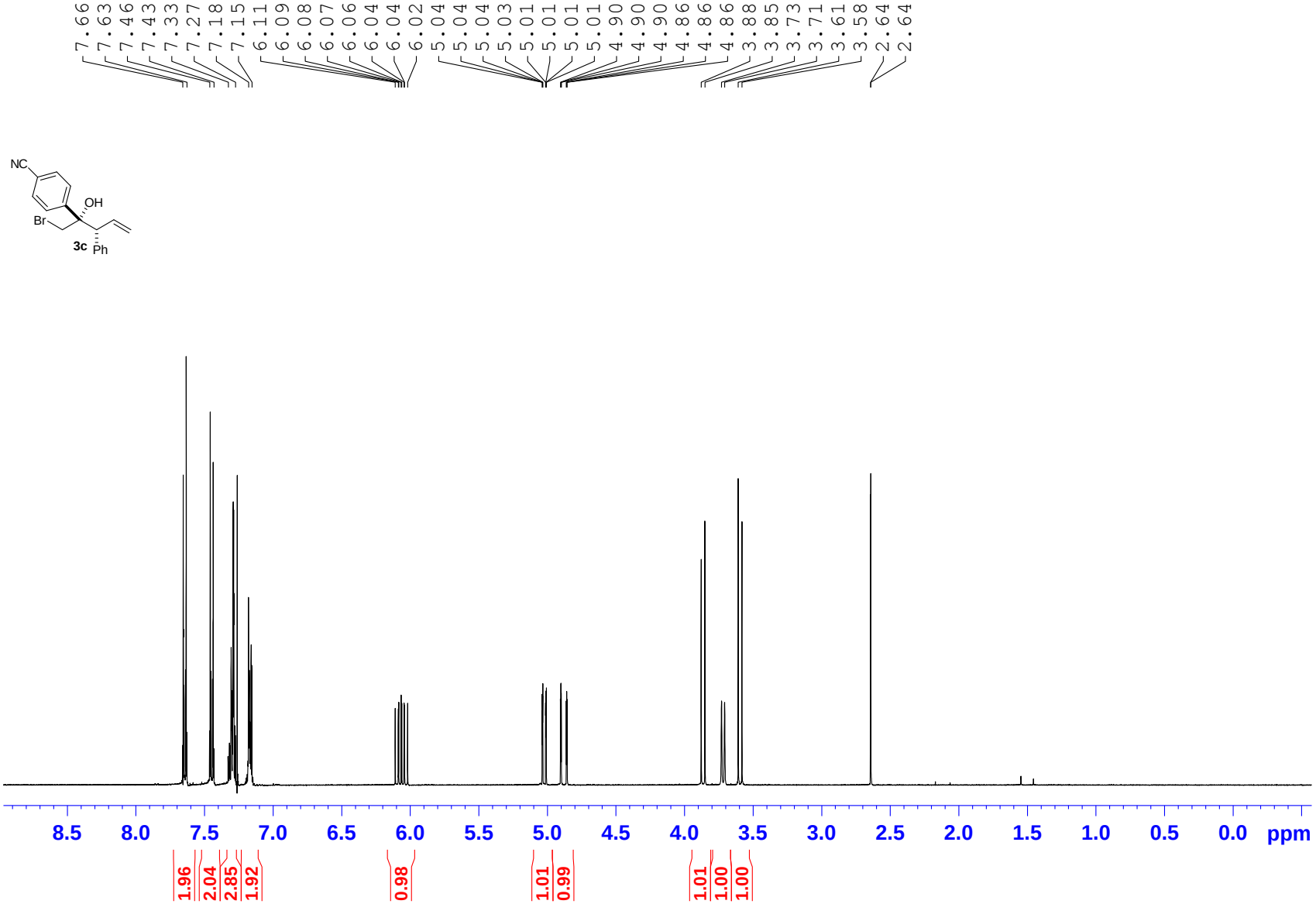
^{1}H NMR of **3b** ($CDCl_3$, 500 MHz)



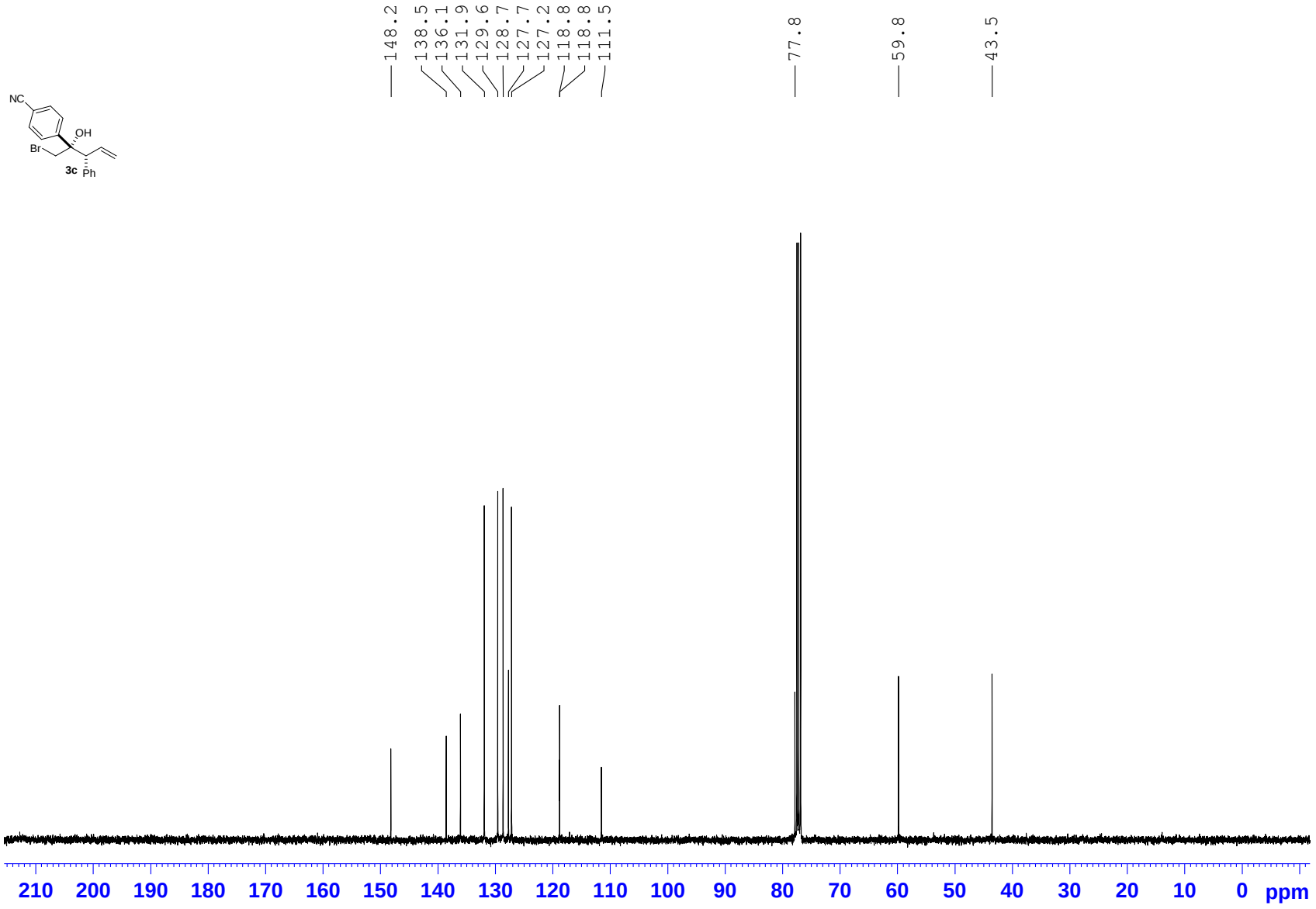
^{13}C NMR of **3b** ($CDCl_3$, 500 MHz)



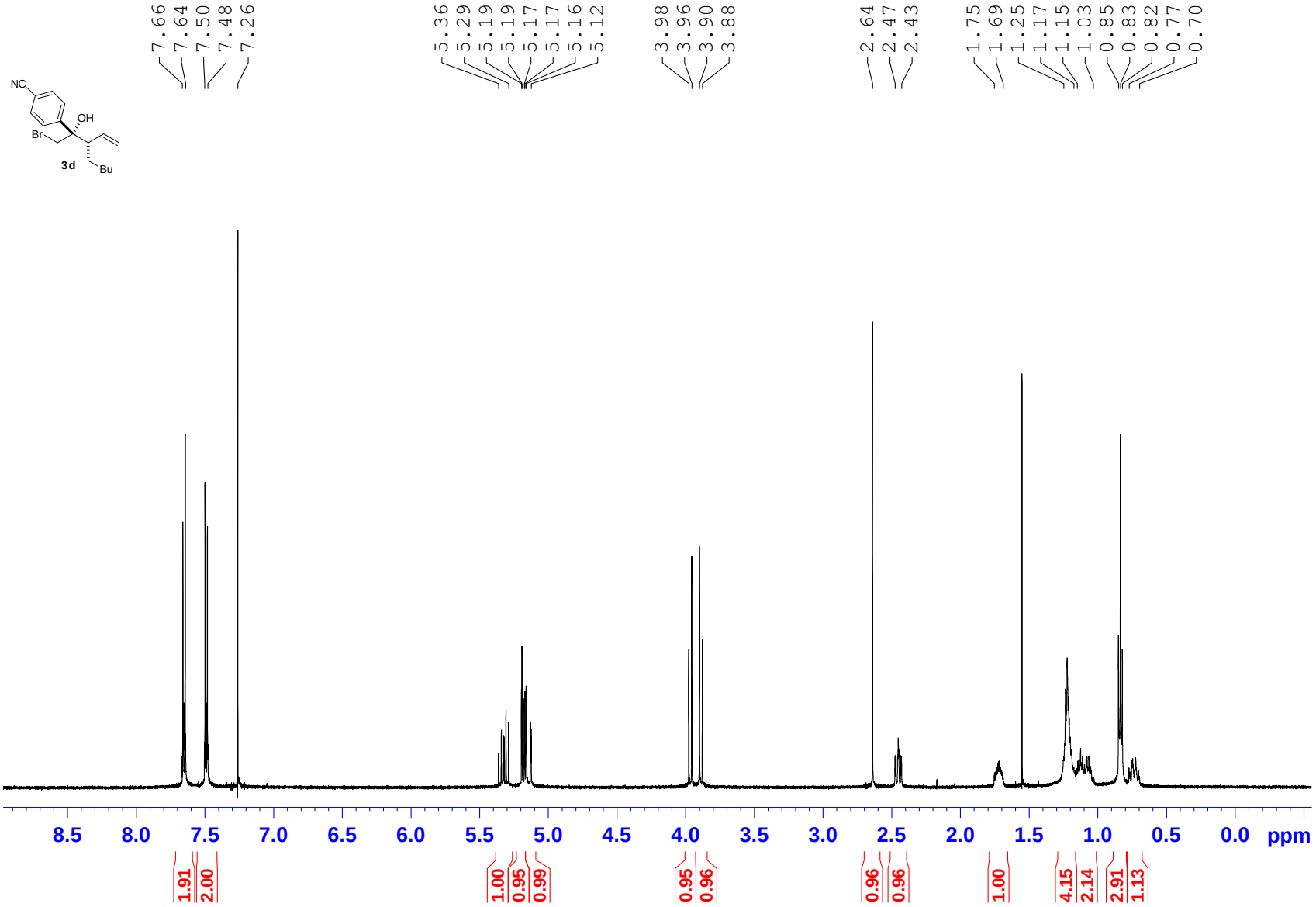
^{1}H NMR of **3c** ($CDCl_3$, 400 MHz)



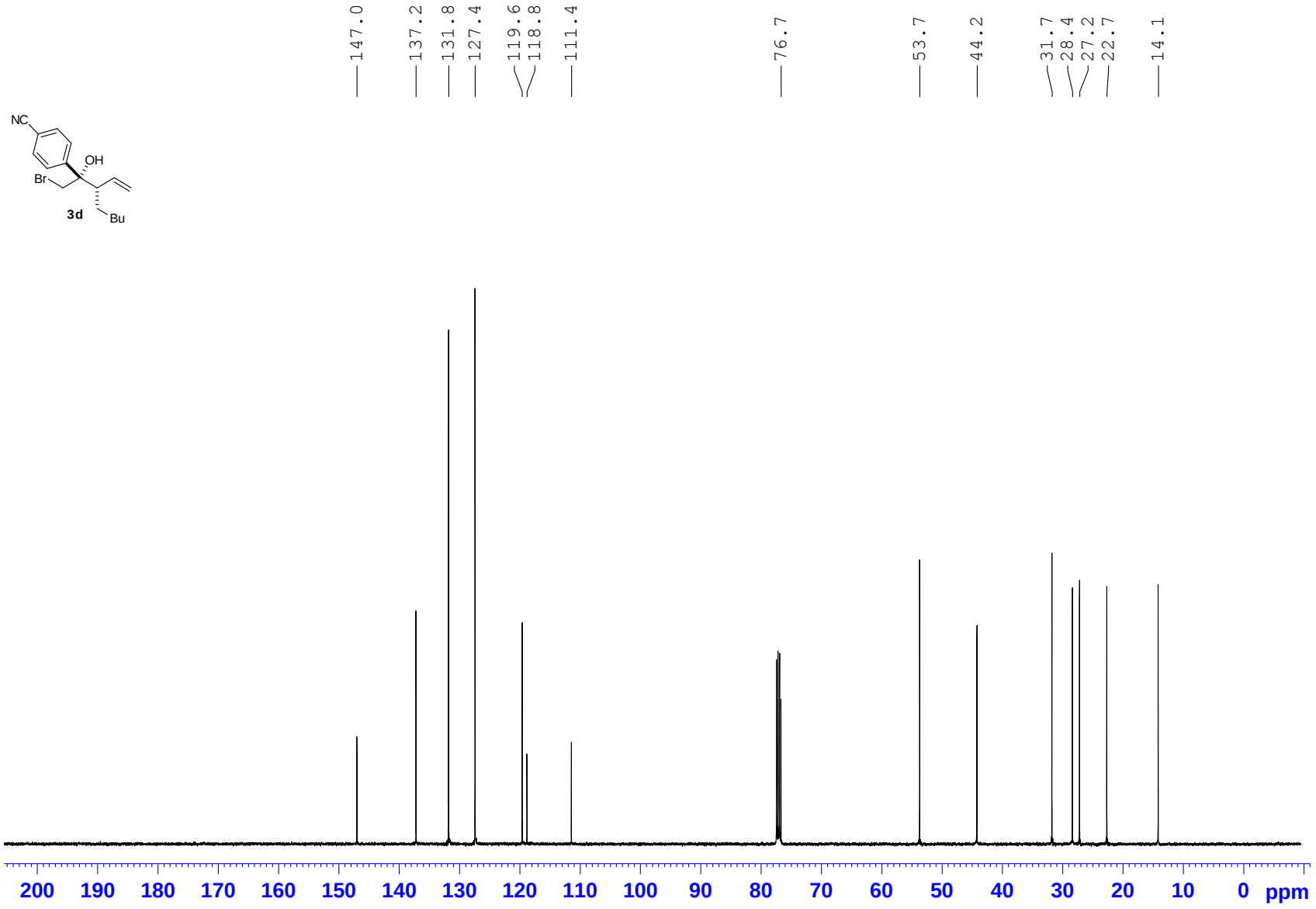
^{13}C NMR of **3c** ($CDCl_3$, 400 MHz)



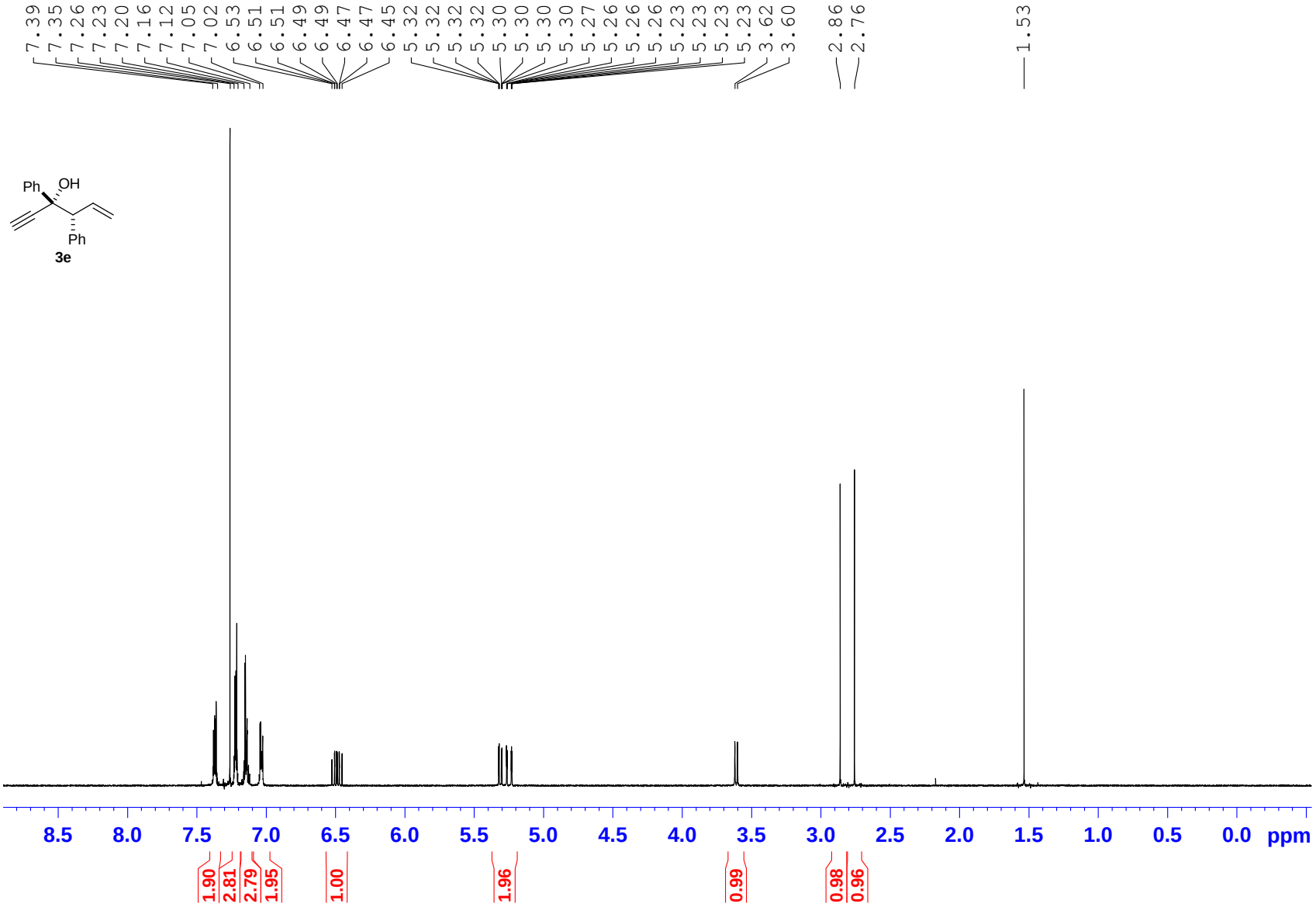
^{1}H NMR of **3d** ($CDCl_3$, 500 MHz)



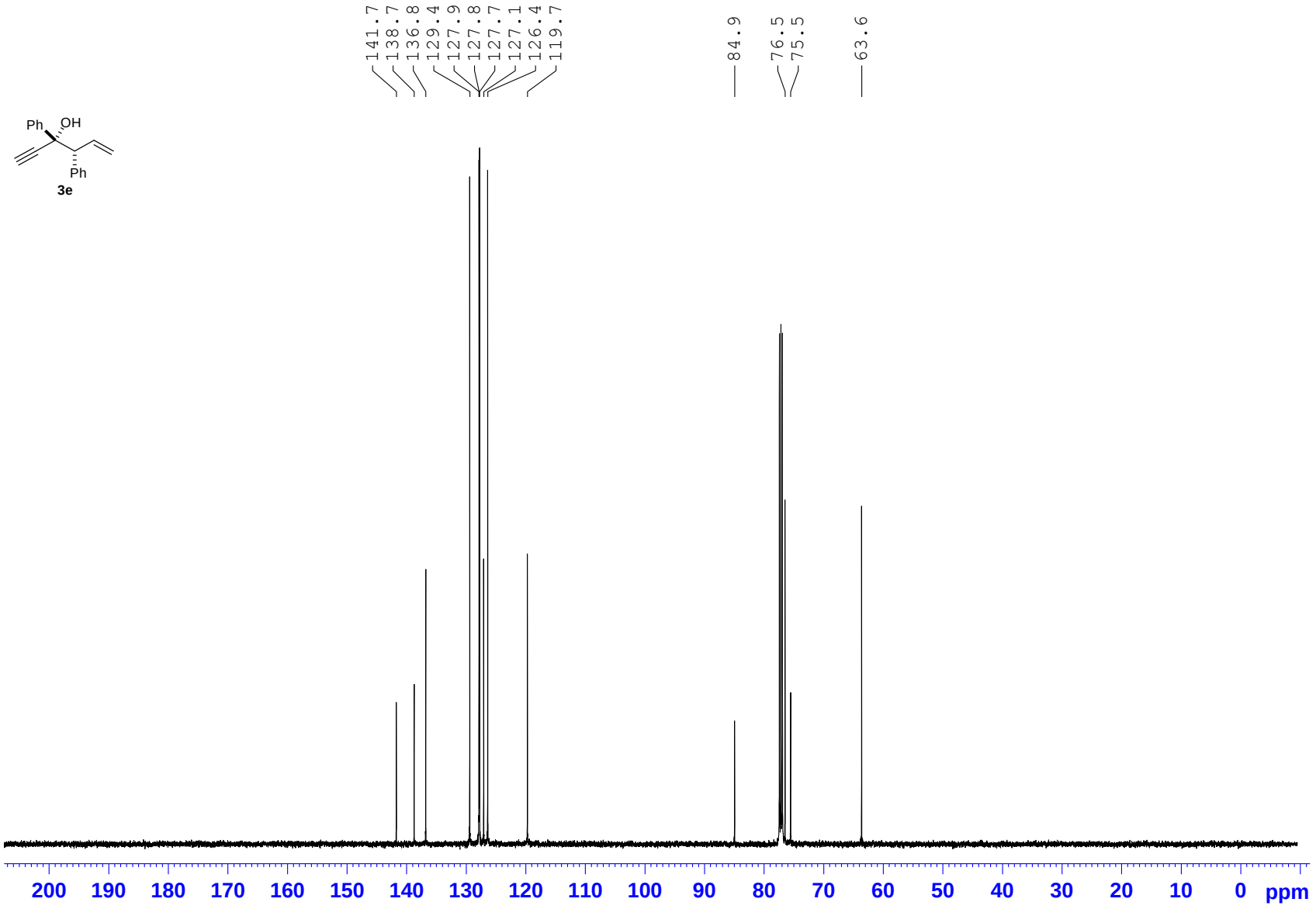
^{13}C NMR of **3d** ($CDCl_3$, 500 MHz)



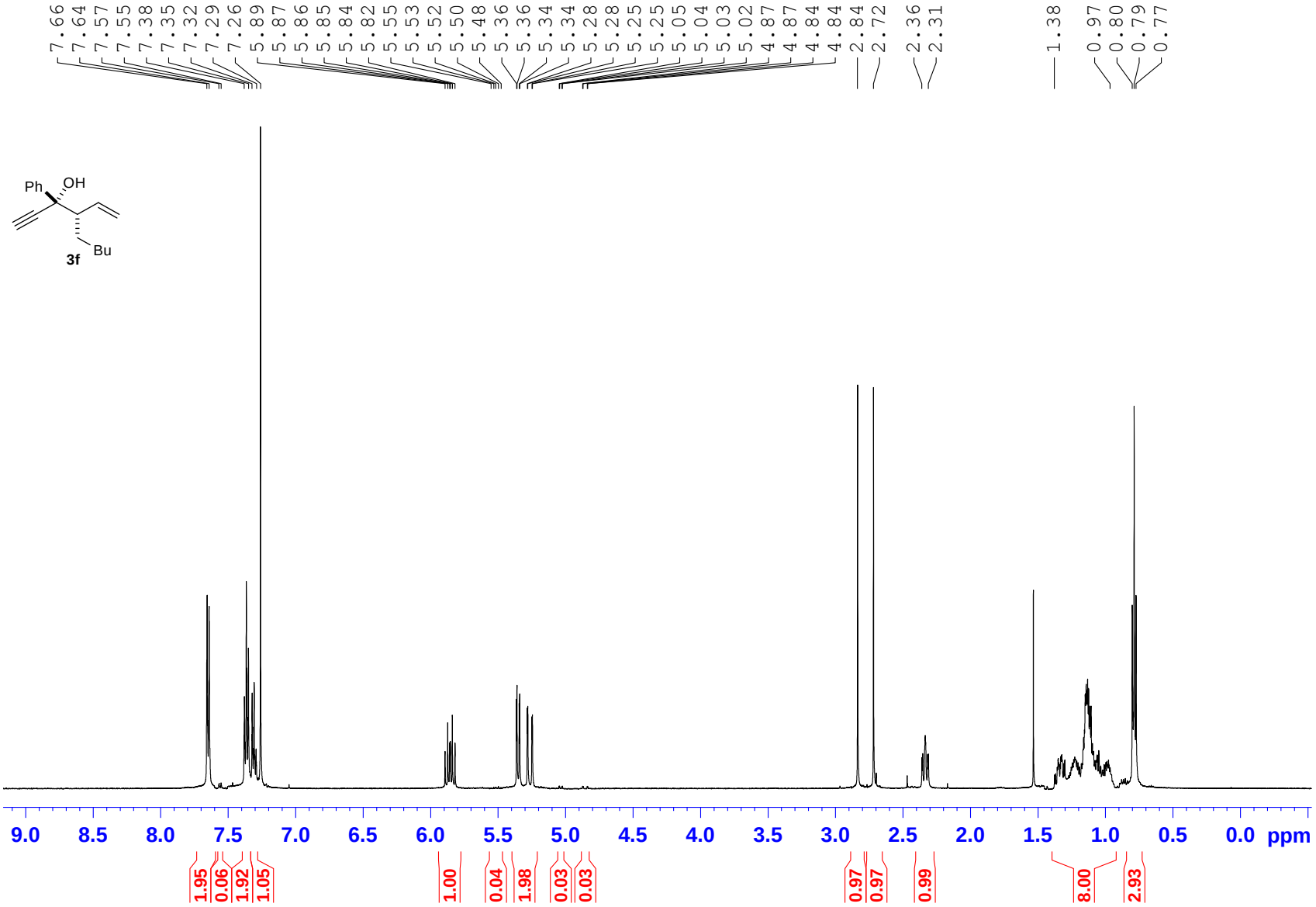
^{1}H NMR of **3e** ($CDCl_3$, 500 MHz)



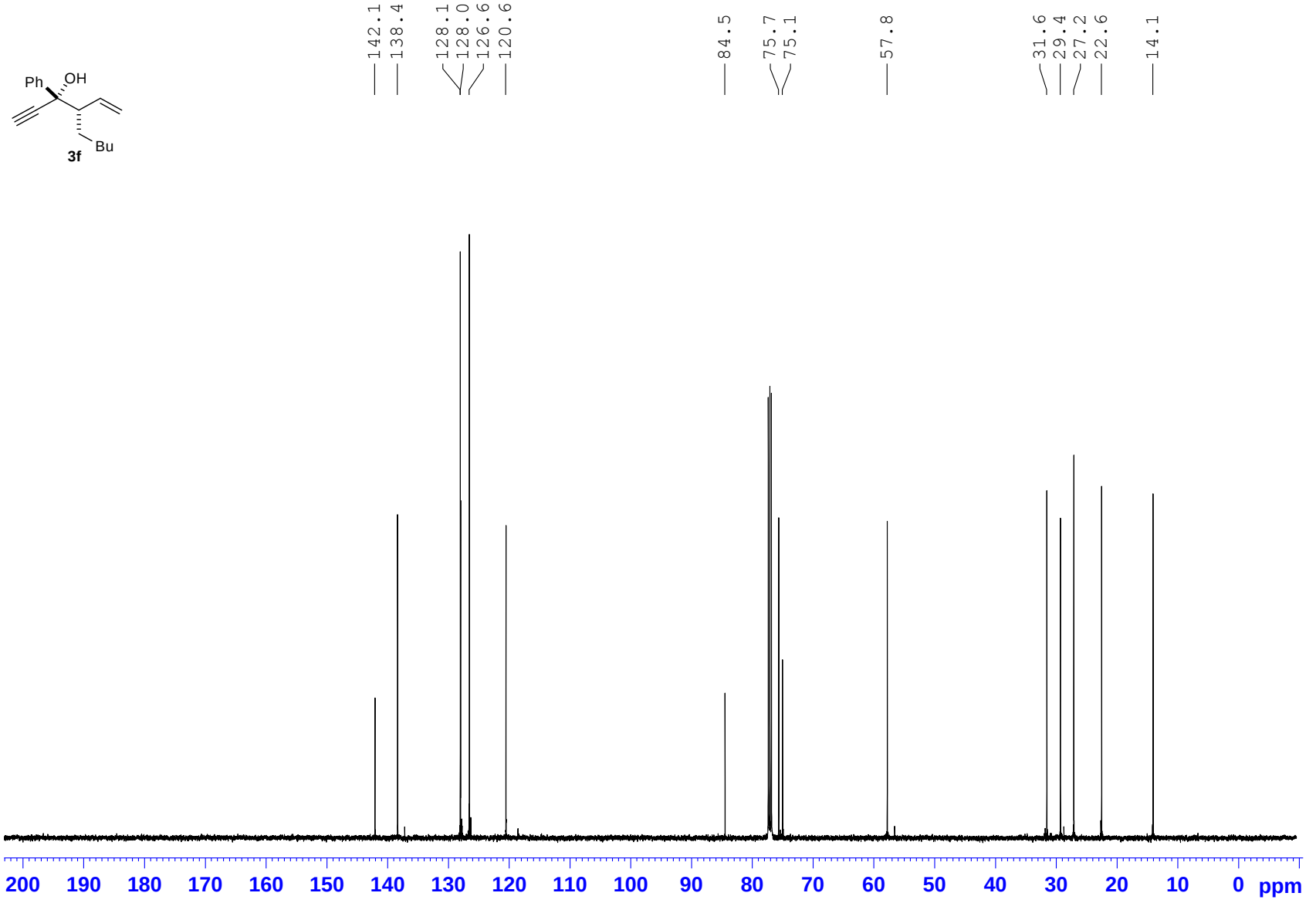
^{13}C NMR of **3e** ($CDCl_3$, 500 MHz)



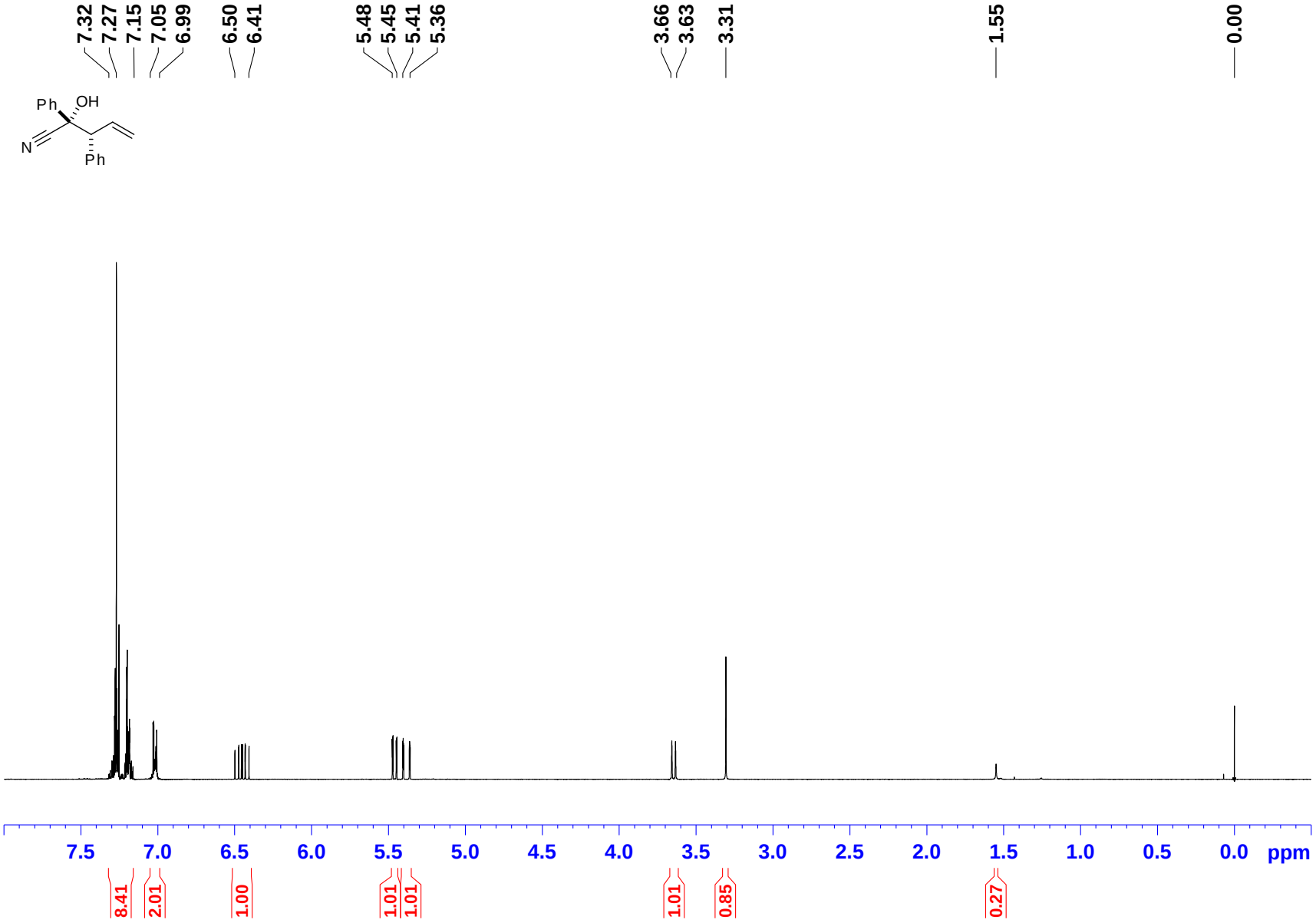
^{1}H NMR of **3f** ($CDCl_3$, 500 MHz)



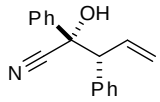
^{13}C NMR of **3f** ($CDCl_3$, 500 MHz)



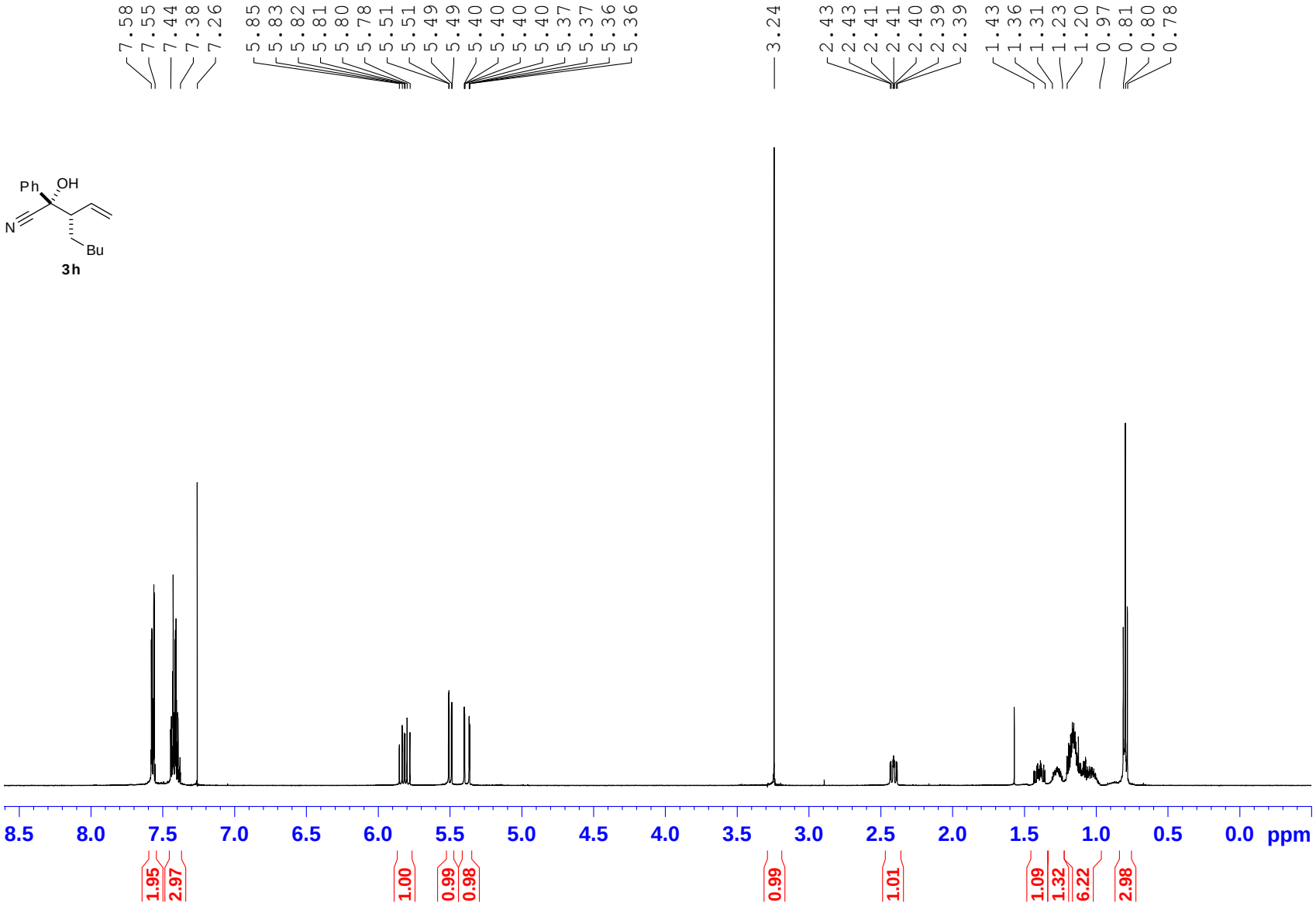
^{1}H NMR of **3g** ($CDCl_3$, 400 MHz)



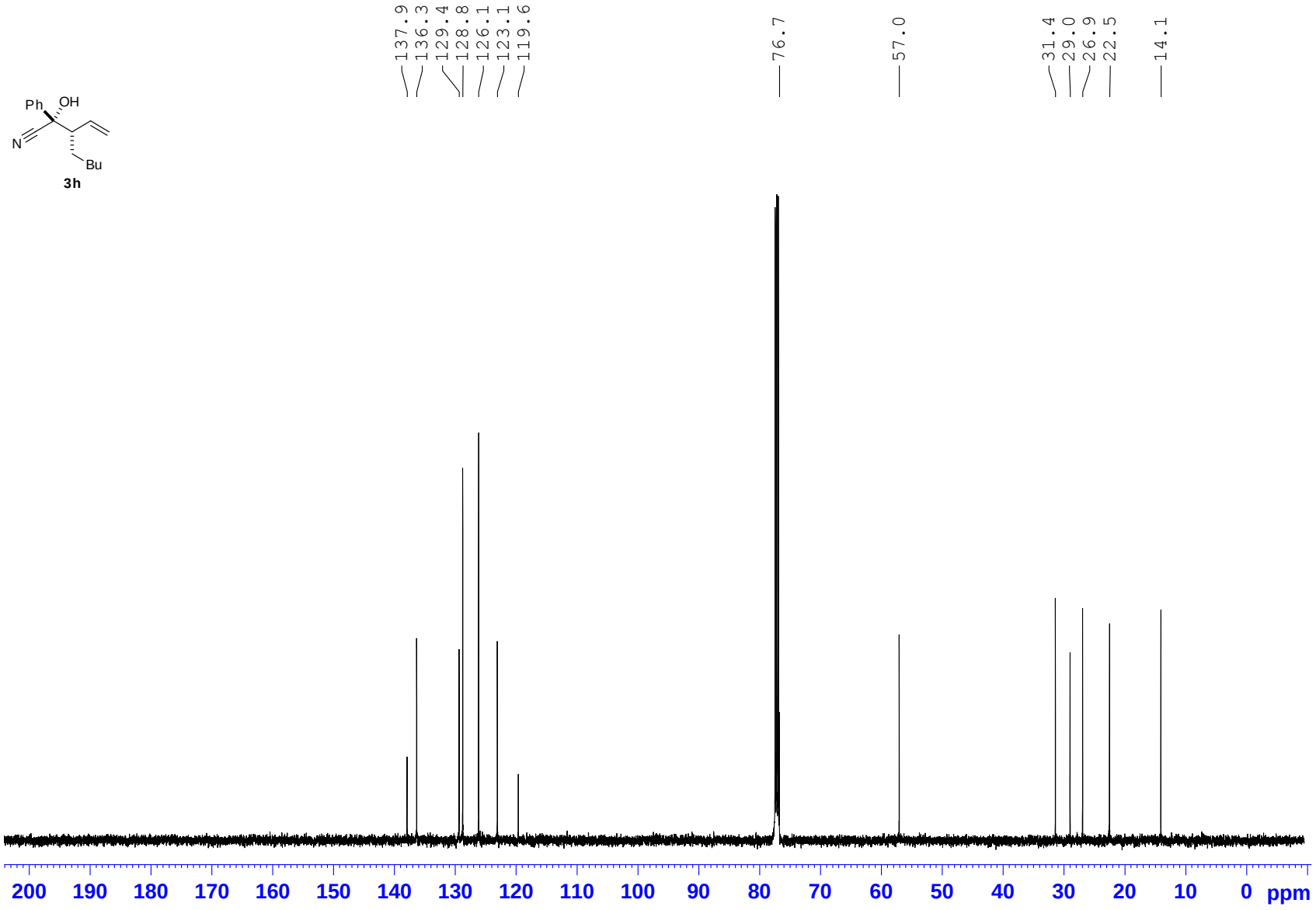
^{13}C NMR of **3g** ($CDCl_3$, 400 MHz)



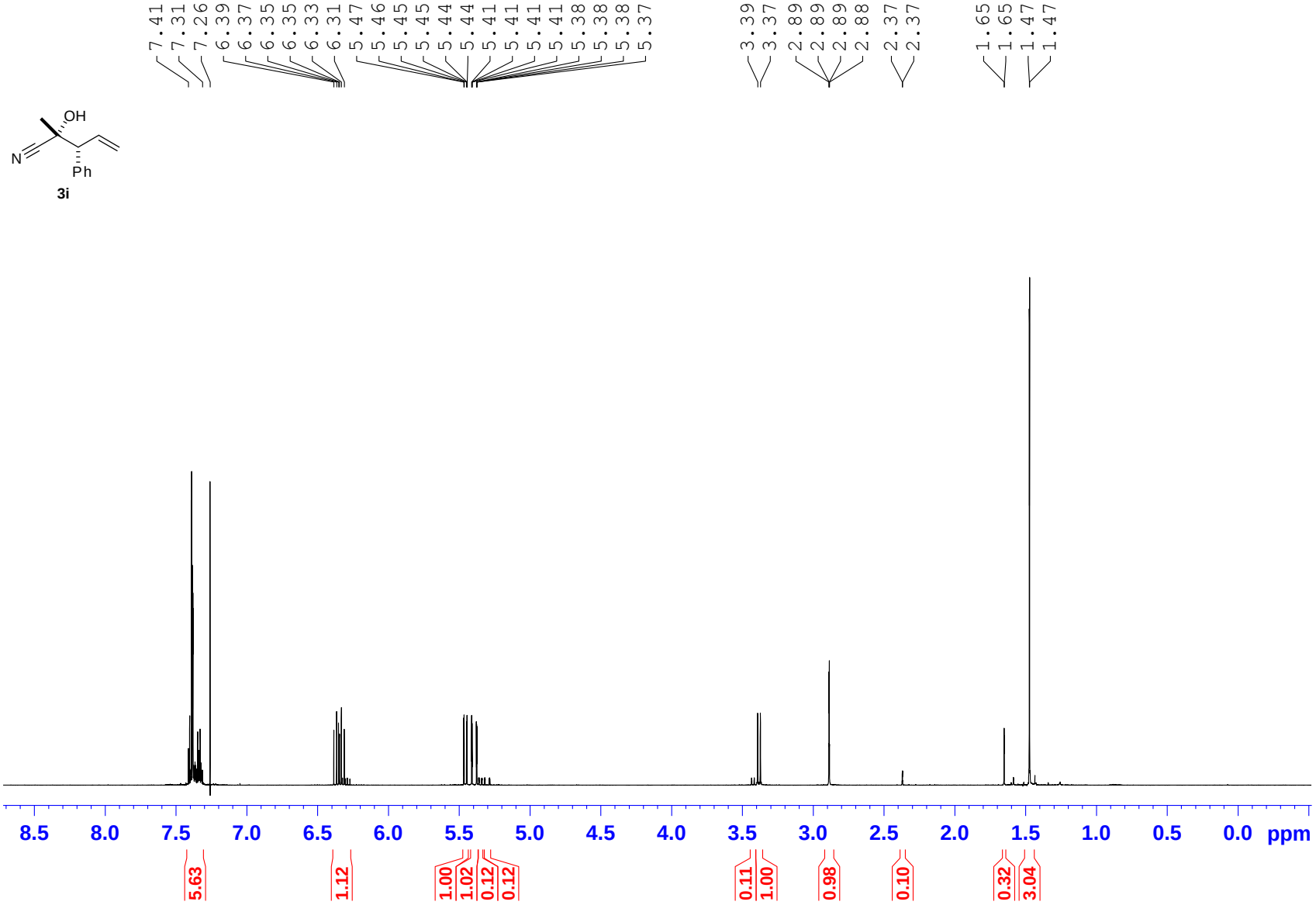
^{1}H NMR of **3h** ($CDCl_3$, 500 MHz)



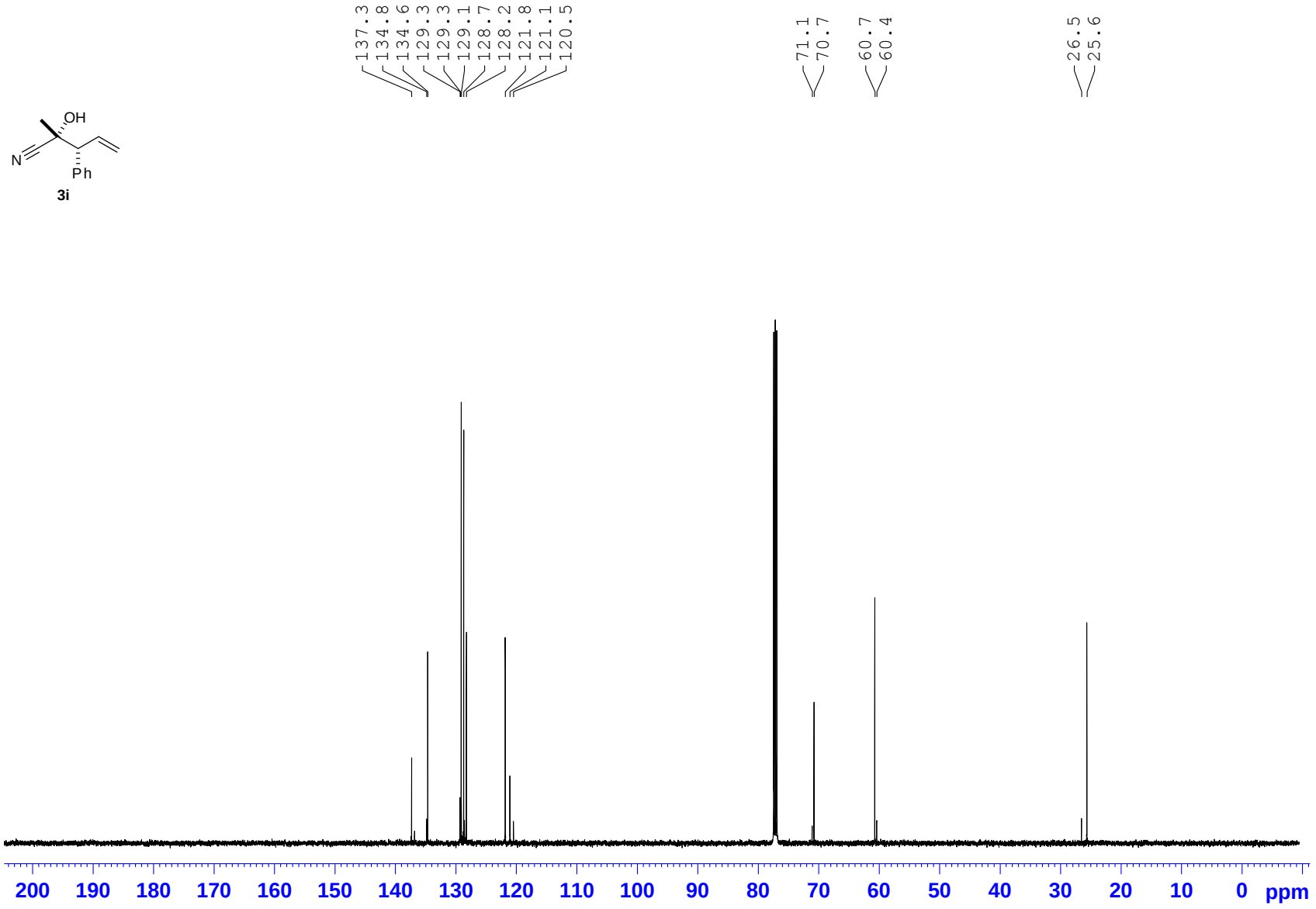
^{13}C NMR of **3h** ($CDCl_3$, 500 MHz)



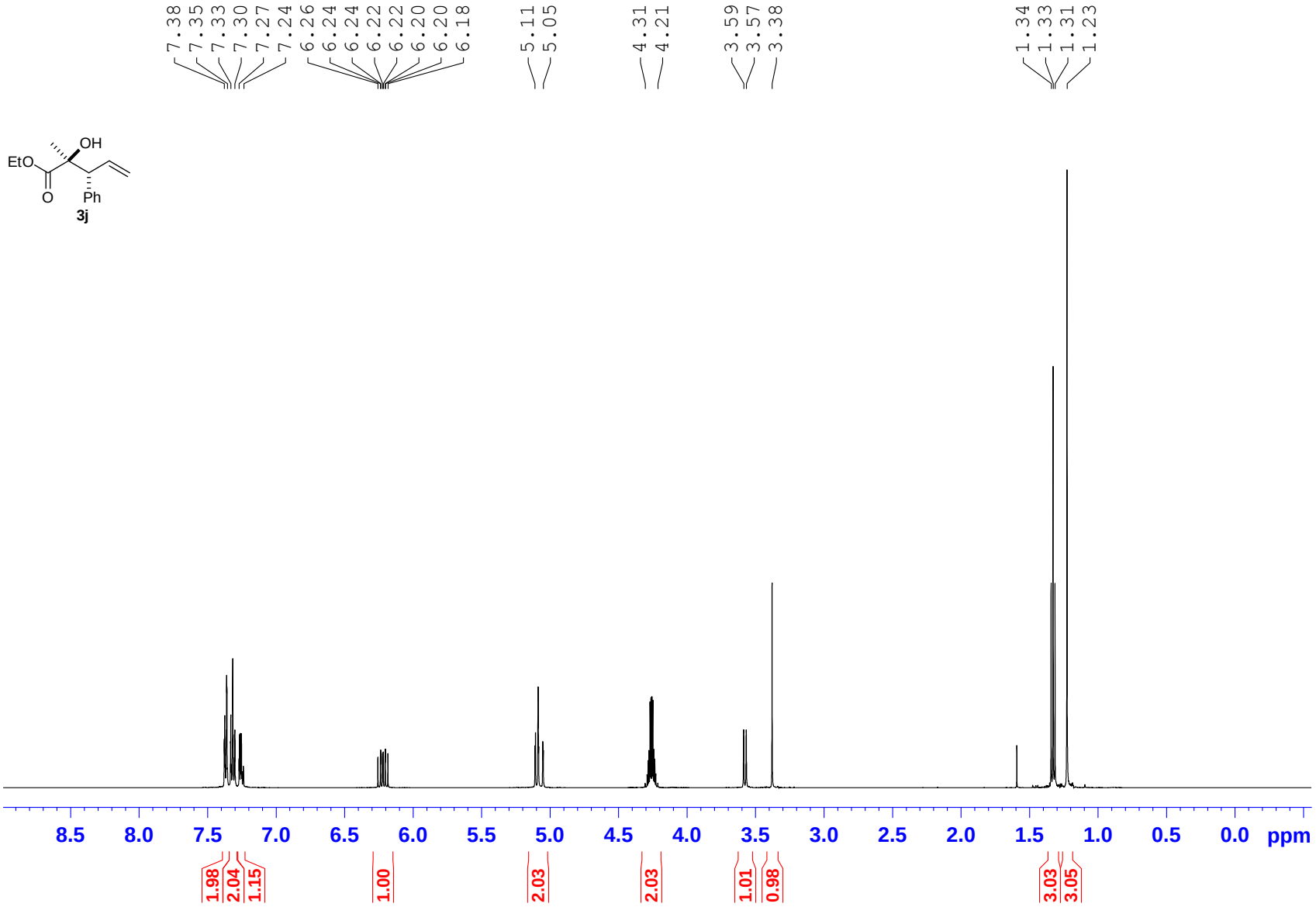
^{1}H NMR of **3i** ($CDCl_3$, 500 MHz)



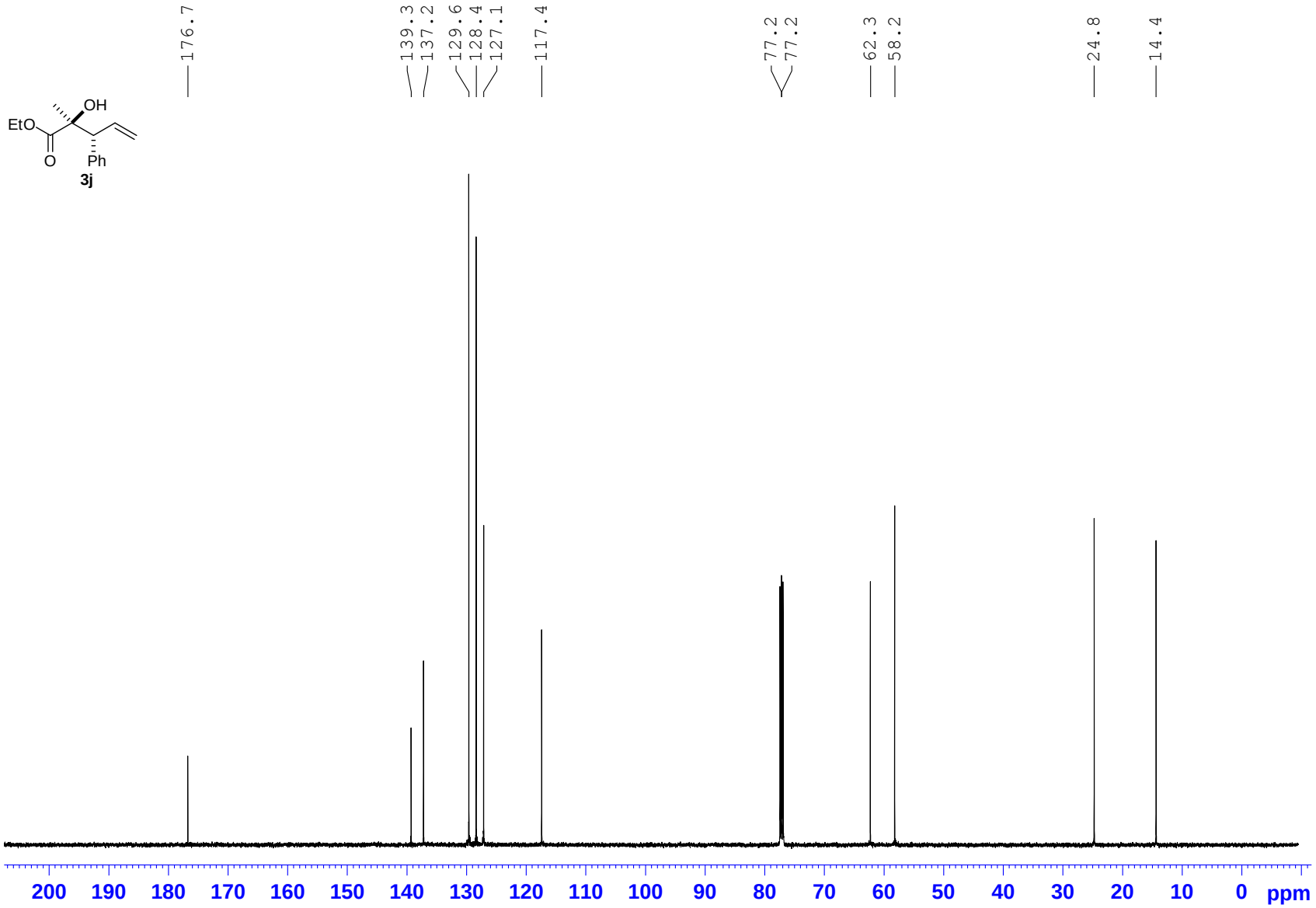
^{13}C NMR of **3i** ($CDCl_3$, 500 MHz)



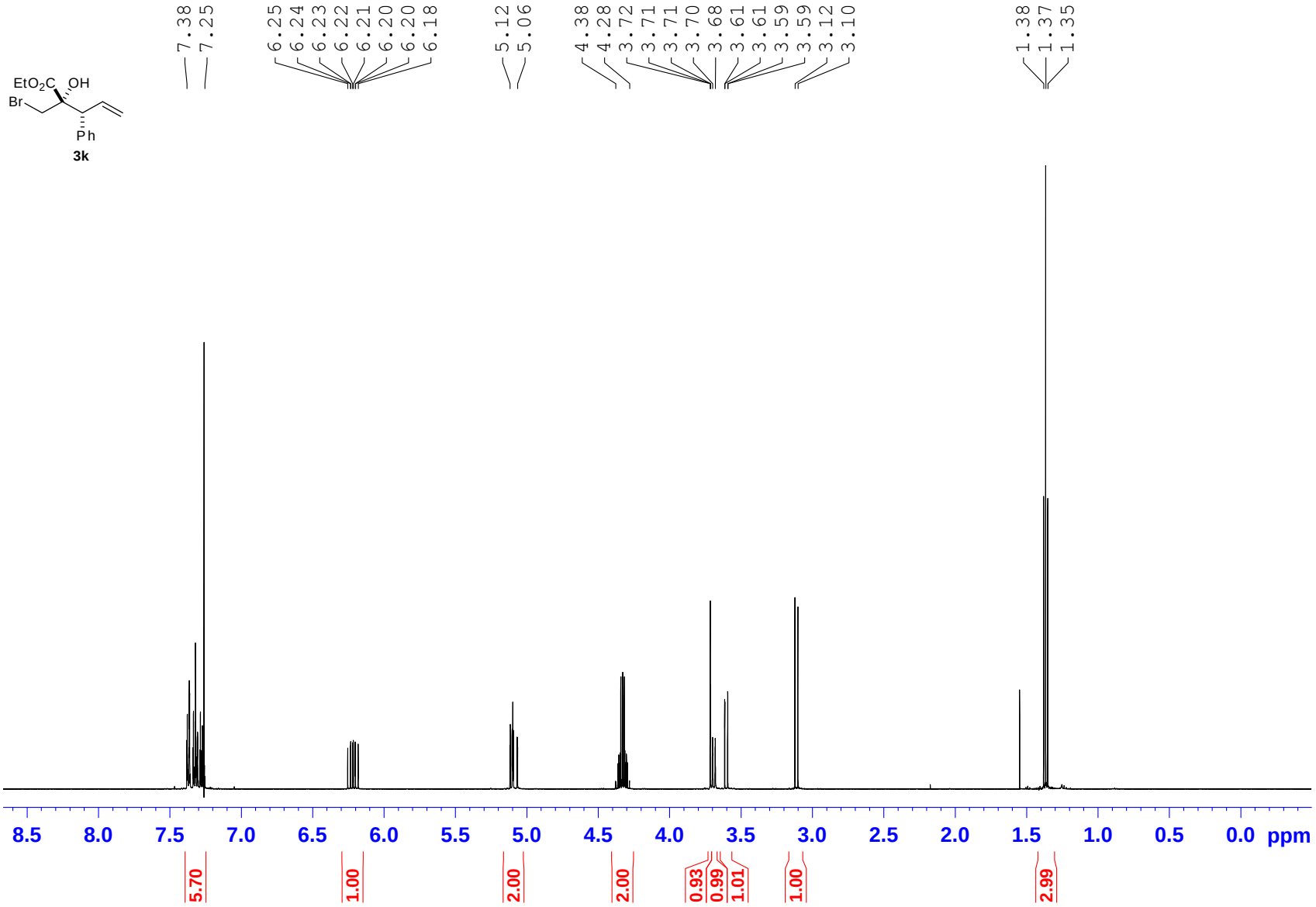
^{1}H NMR of **3j** ($CDCl_3$, 500 MHz)



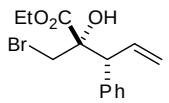
^{13}C NMR of **3j** ($CDCl_3$, 500 MHz)



^{1}H NMR of **3k** ($CDCl_3$, 500 MHz)

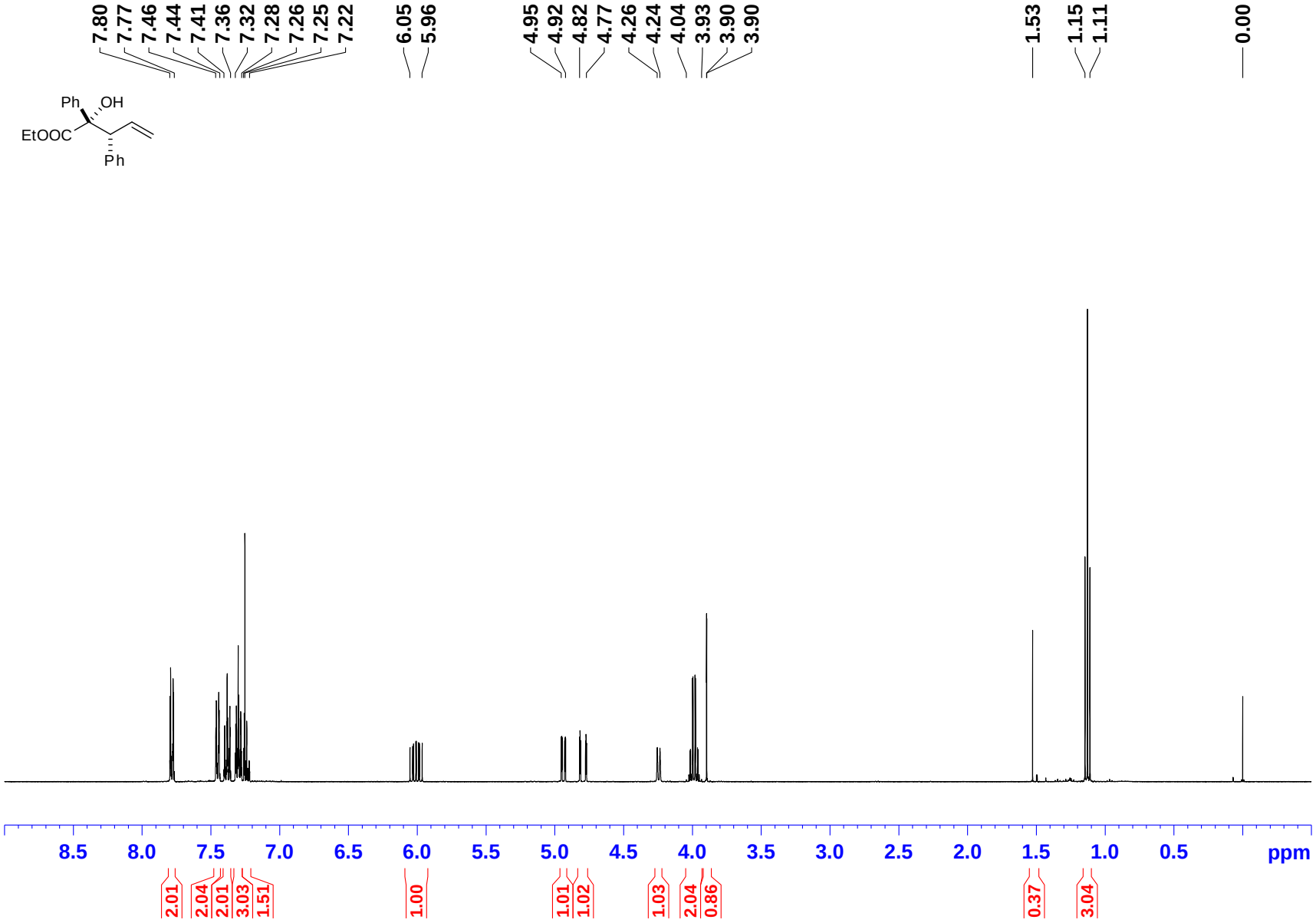


^{13}C NMR of **3k** ($CDCl_3$, 400 MHz)

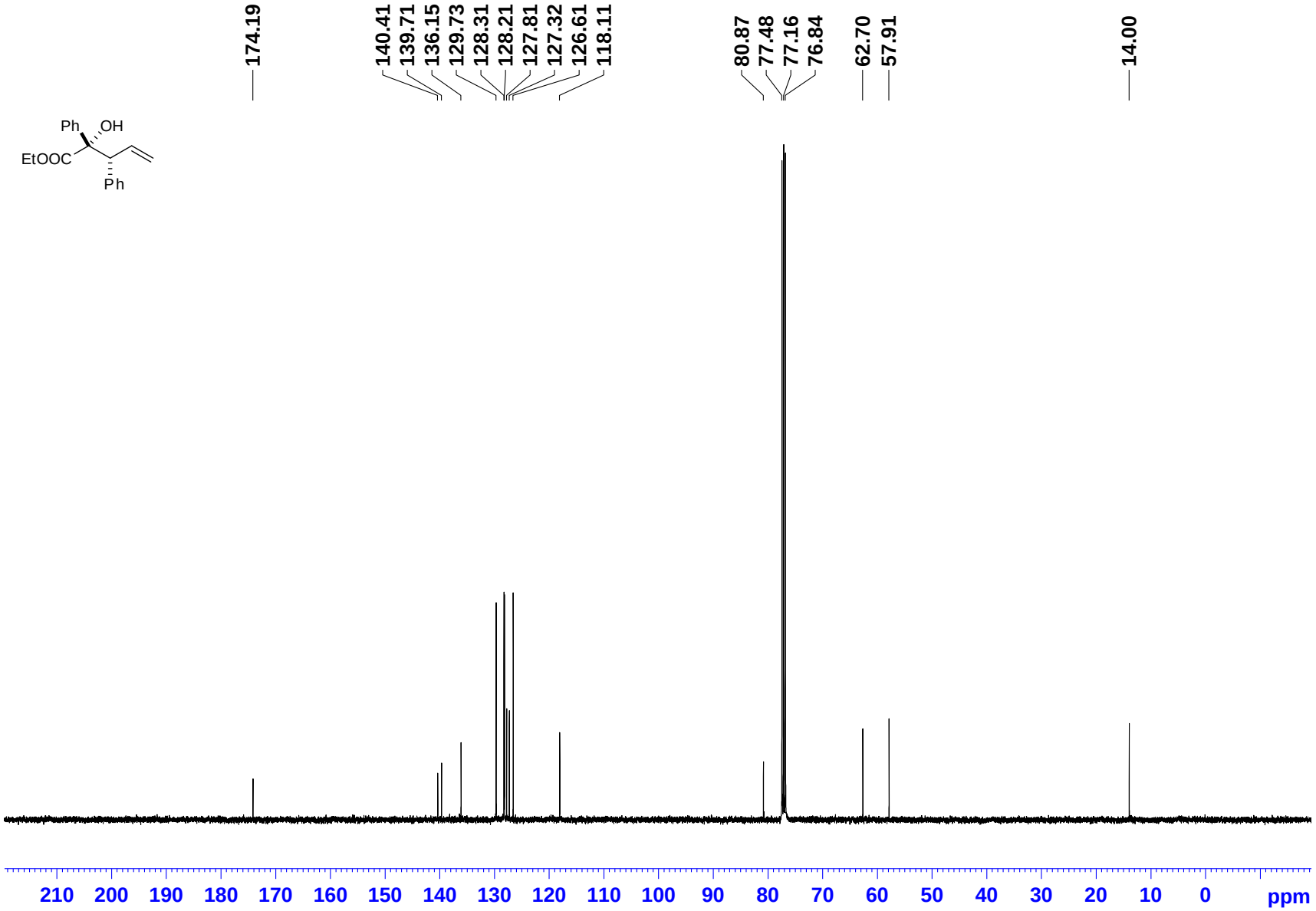


3k

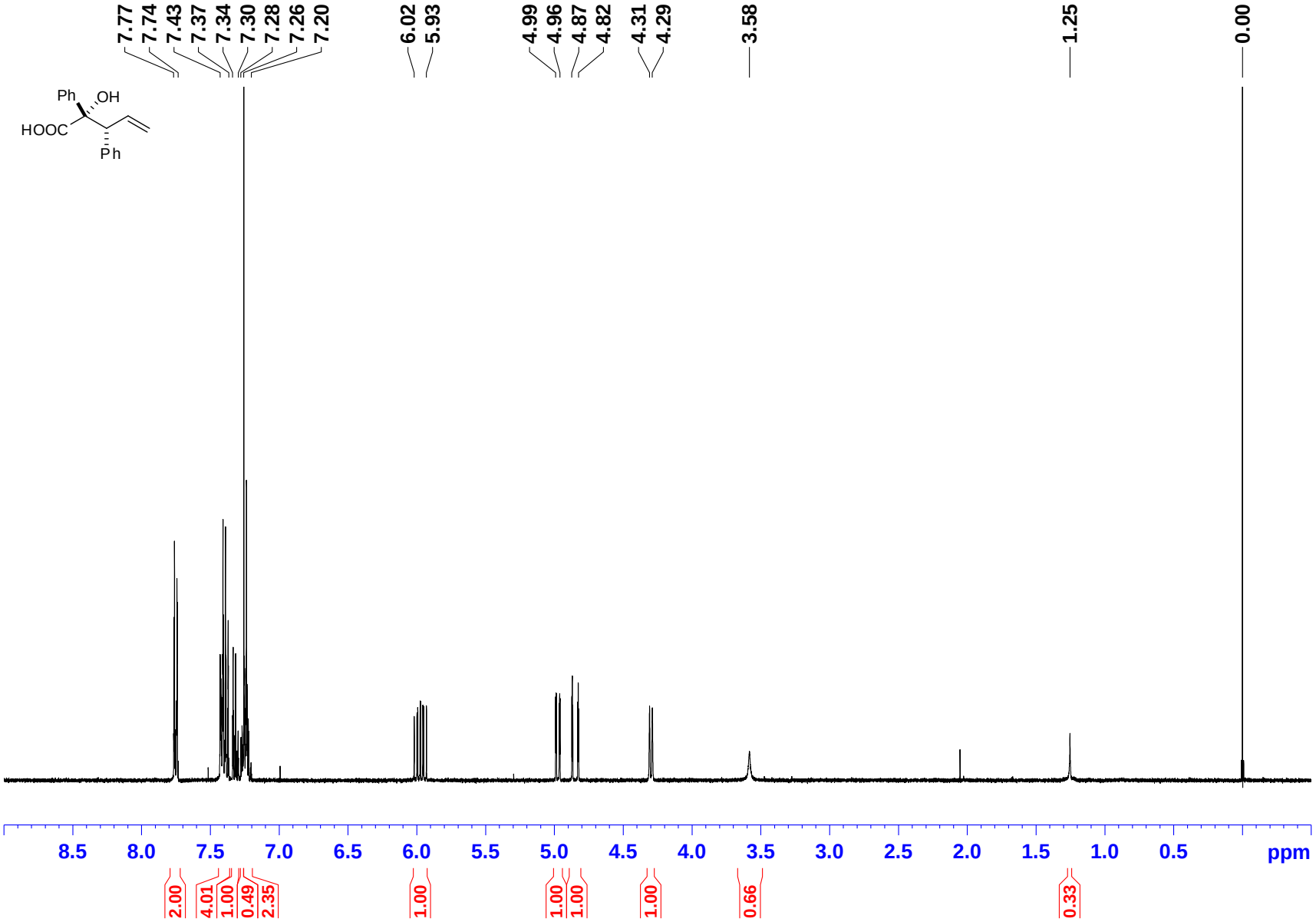
^{1}H NMR of **3l** ($CDCl_3$, 400 MHz)



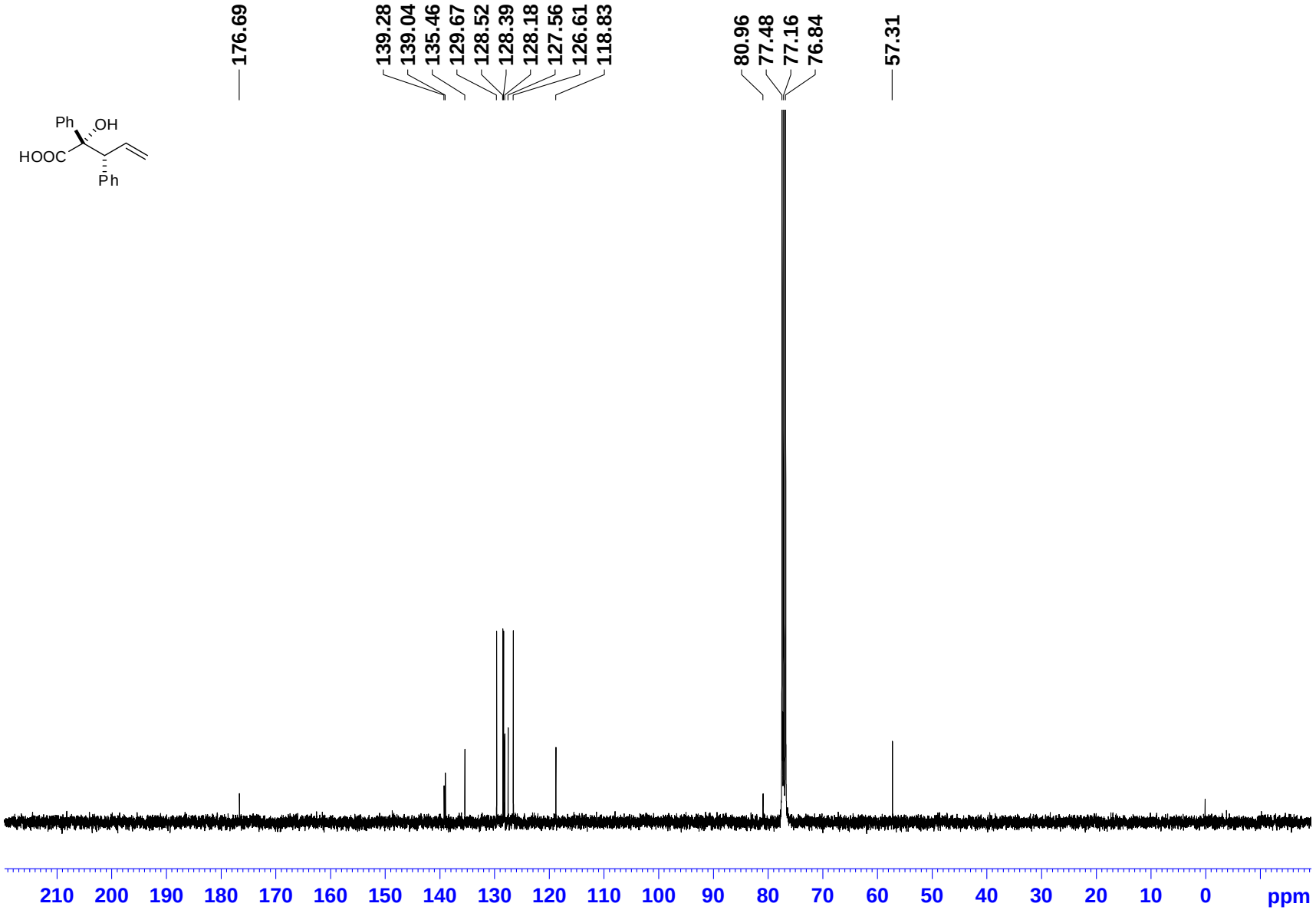
^{13}C NMR of **3l** ($CDCl_3$, 400 MHz)



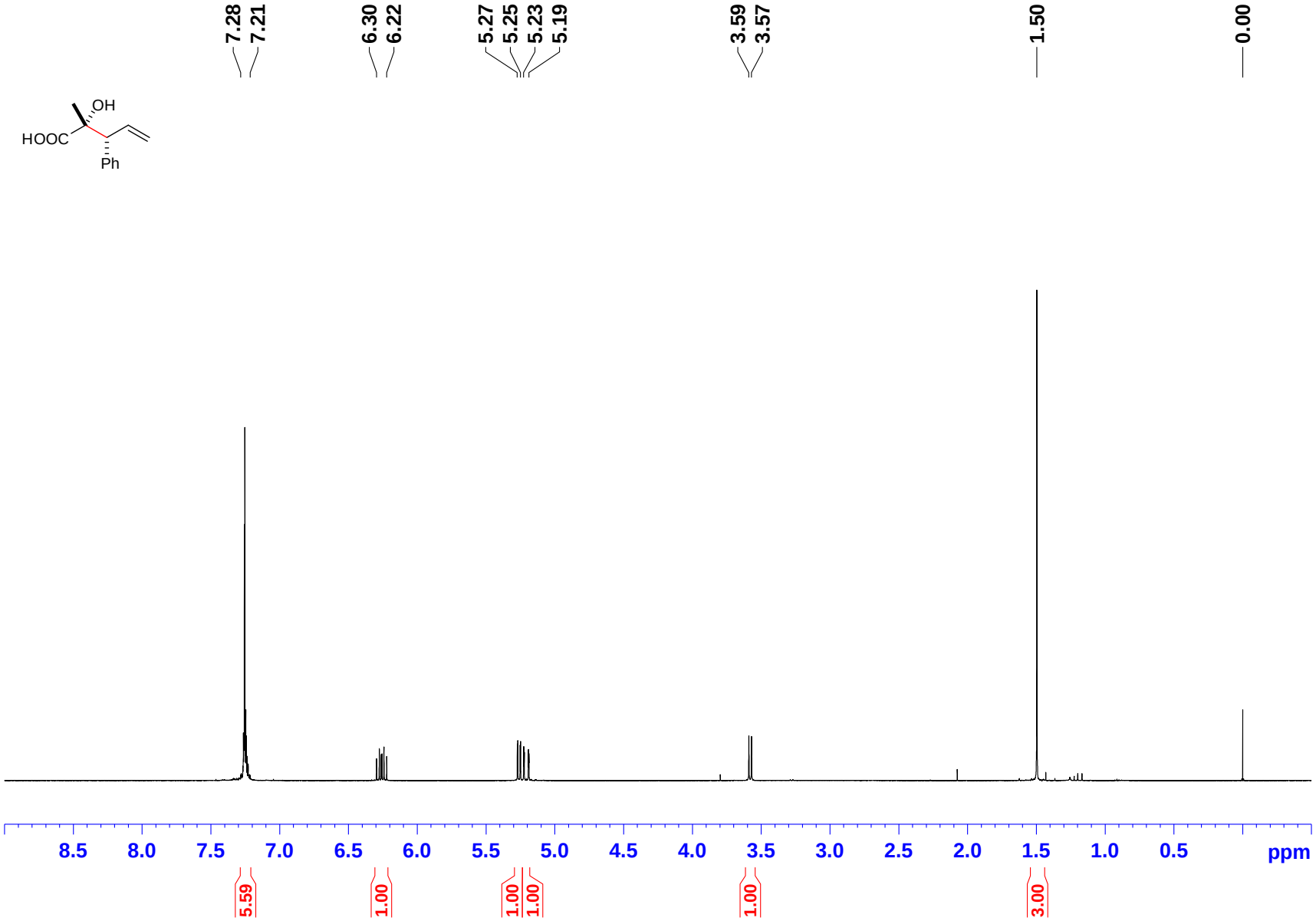
^{1}H NMR of **3m** ($CDCl_3$, 400 MHz)



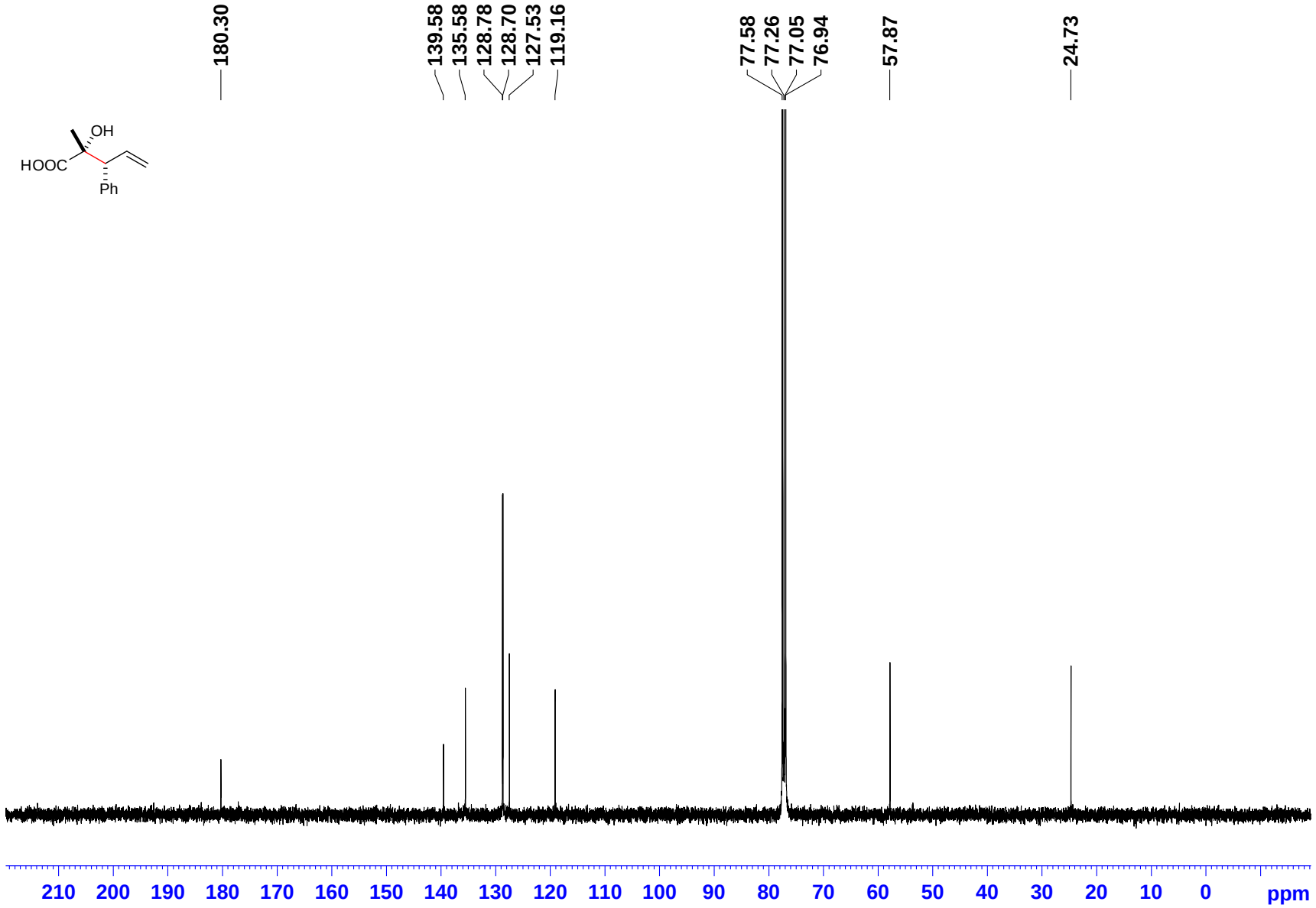
^{13}C NMR of **3m** ($CDCl_3$, 400 MHz)



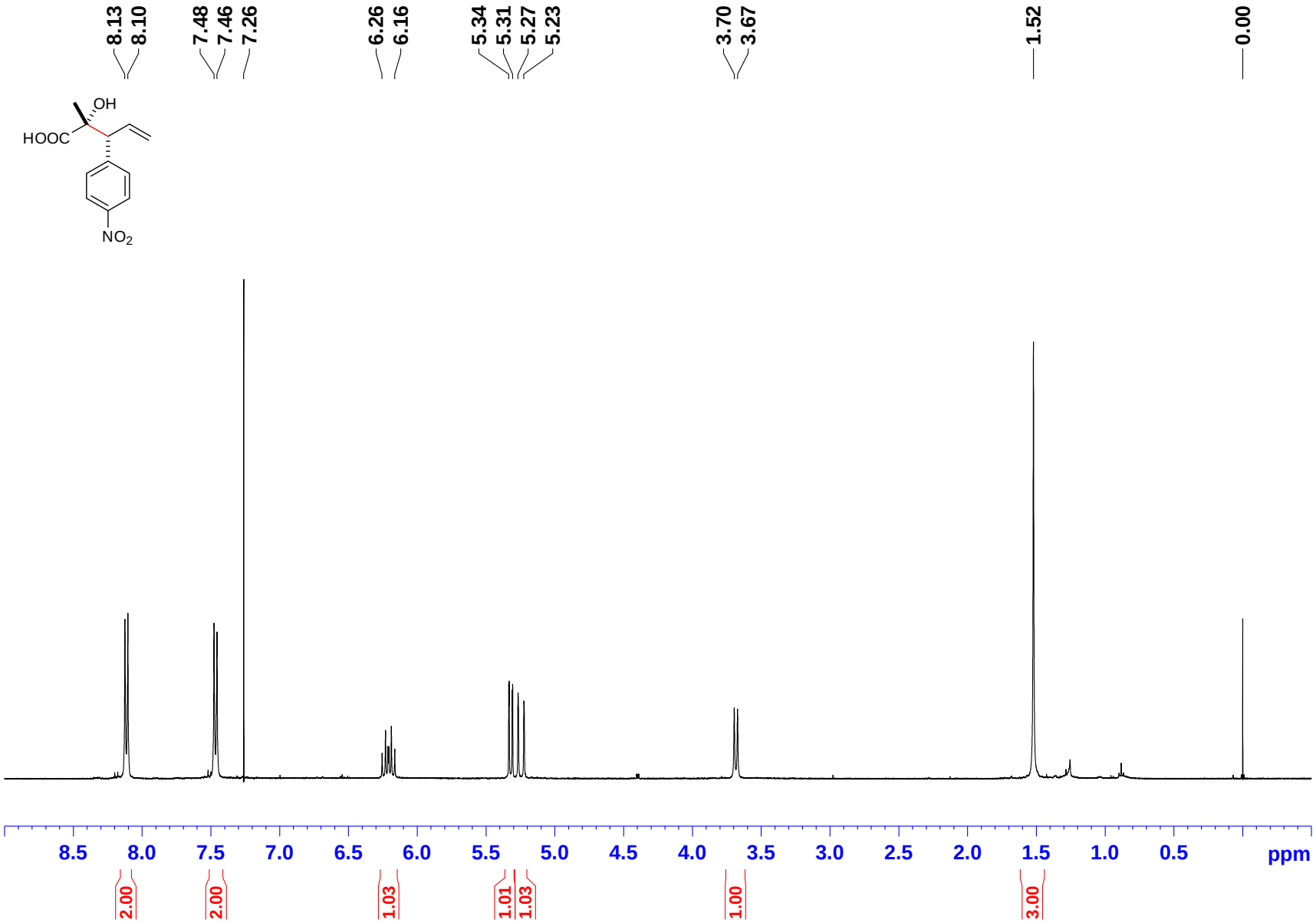
^{1}H NMR of **3n** ($CDCl_3$, 400 MHz)



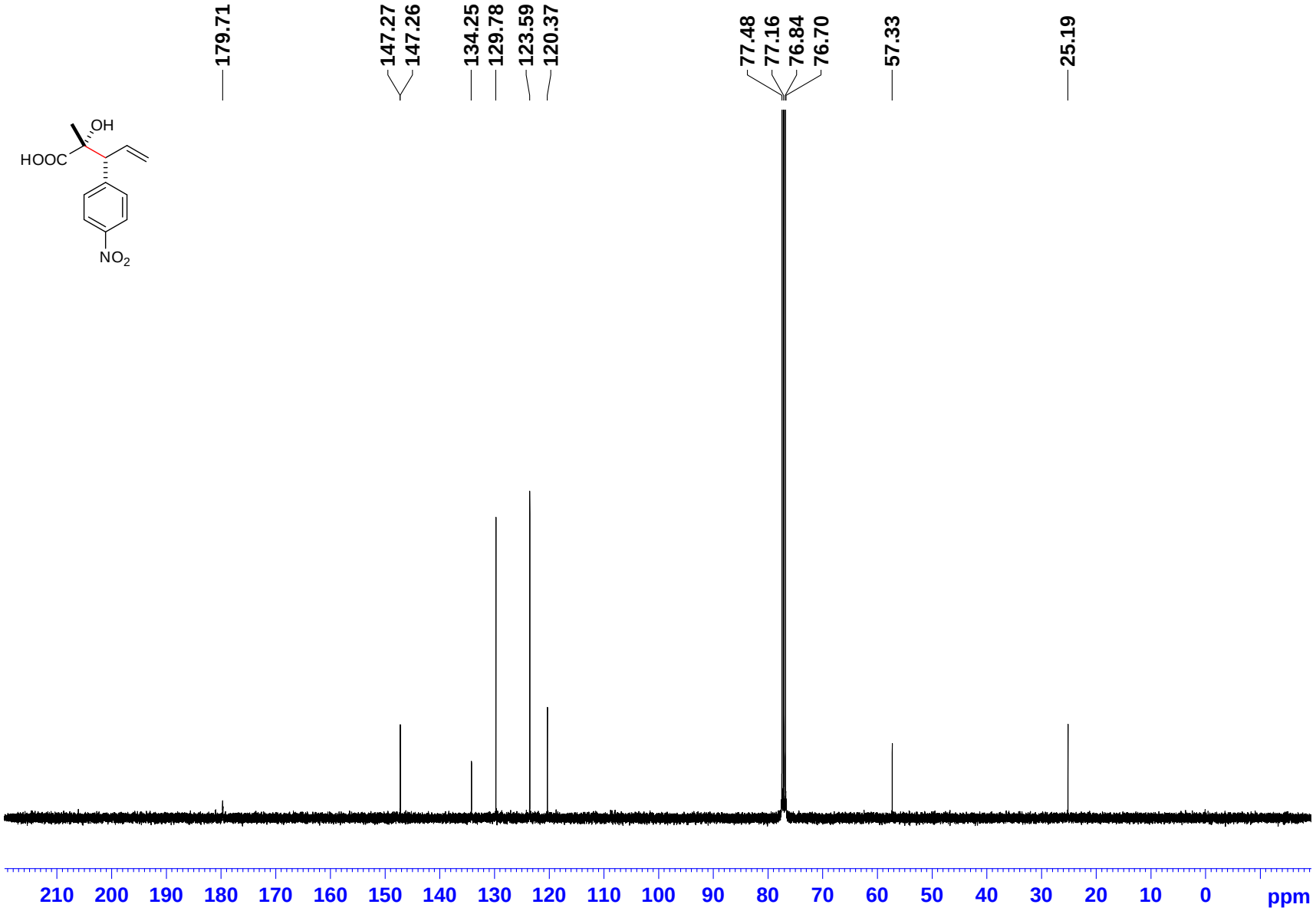
^{13}C NMR of **3n** ($CDCl_3$, 400 MHz)



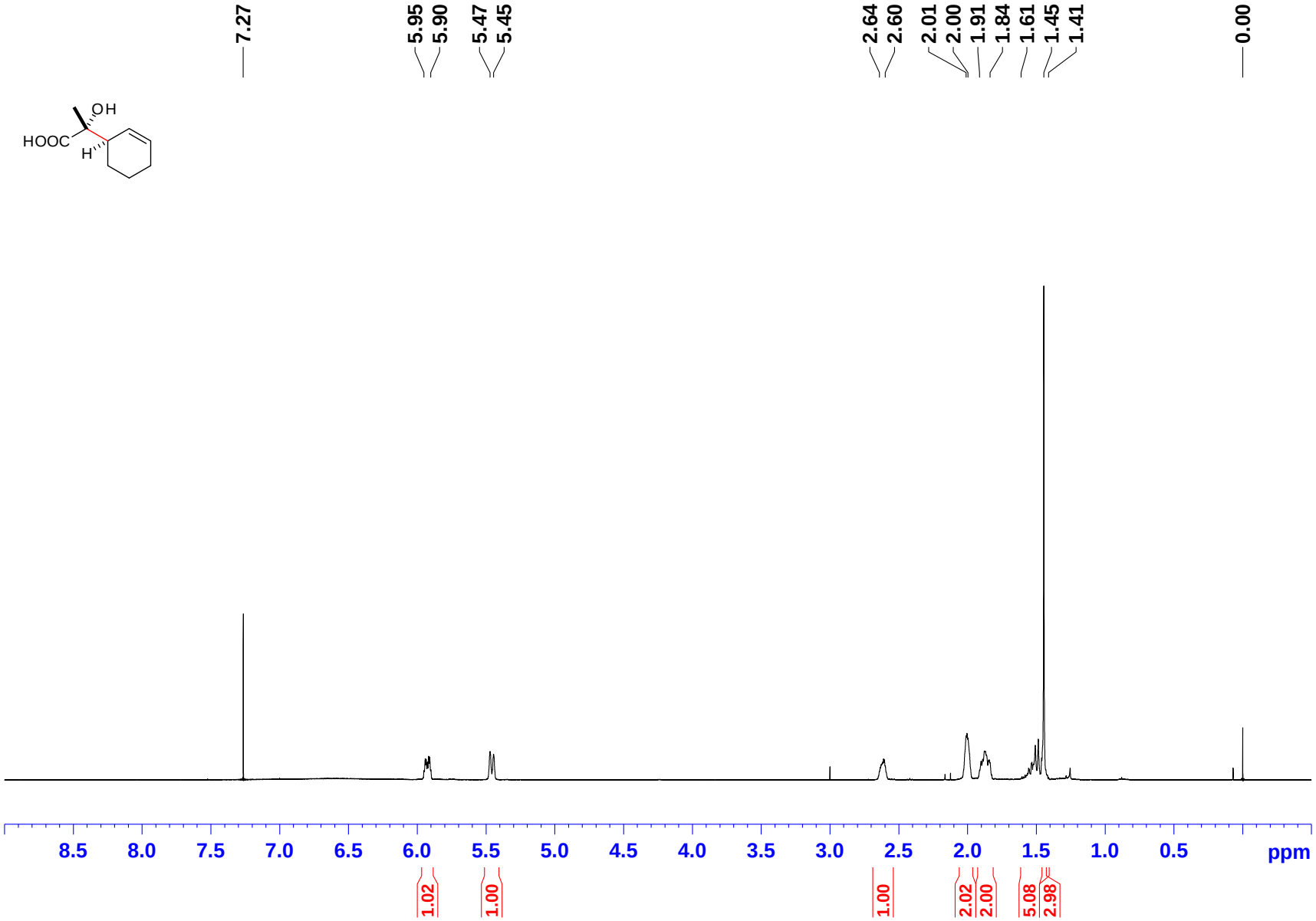
^{1}H NMR of **3o** ($CDCl_3$, 400 MHz)



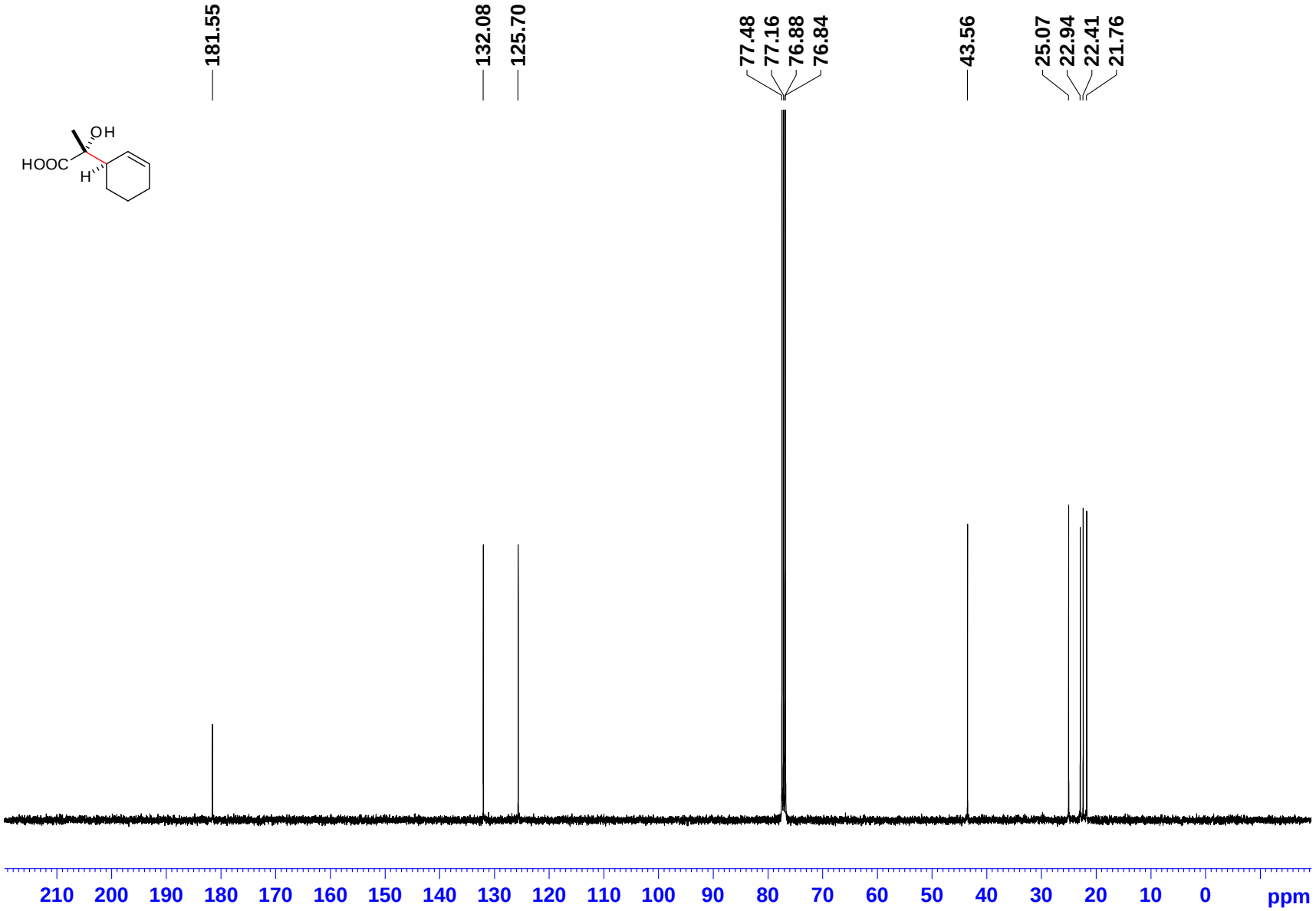
^{13}C NMR of **3o** ($CDCl_3$, 400 MHz)



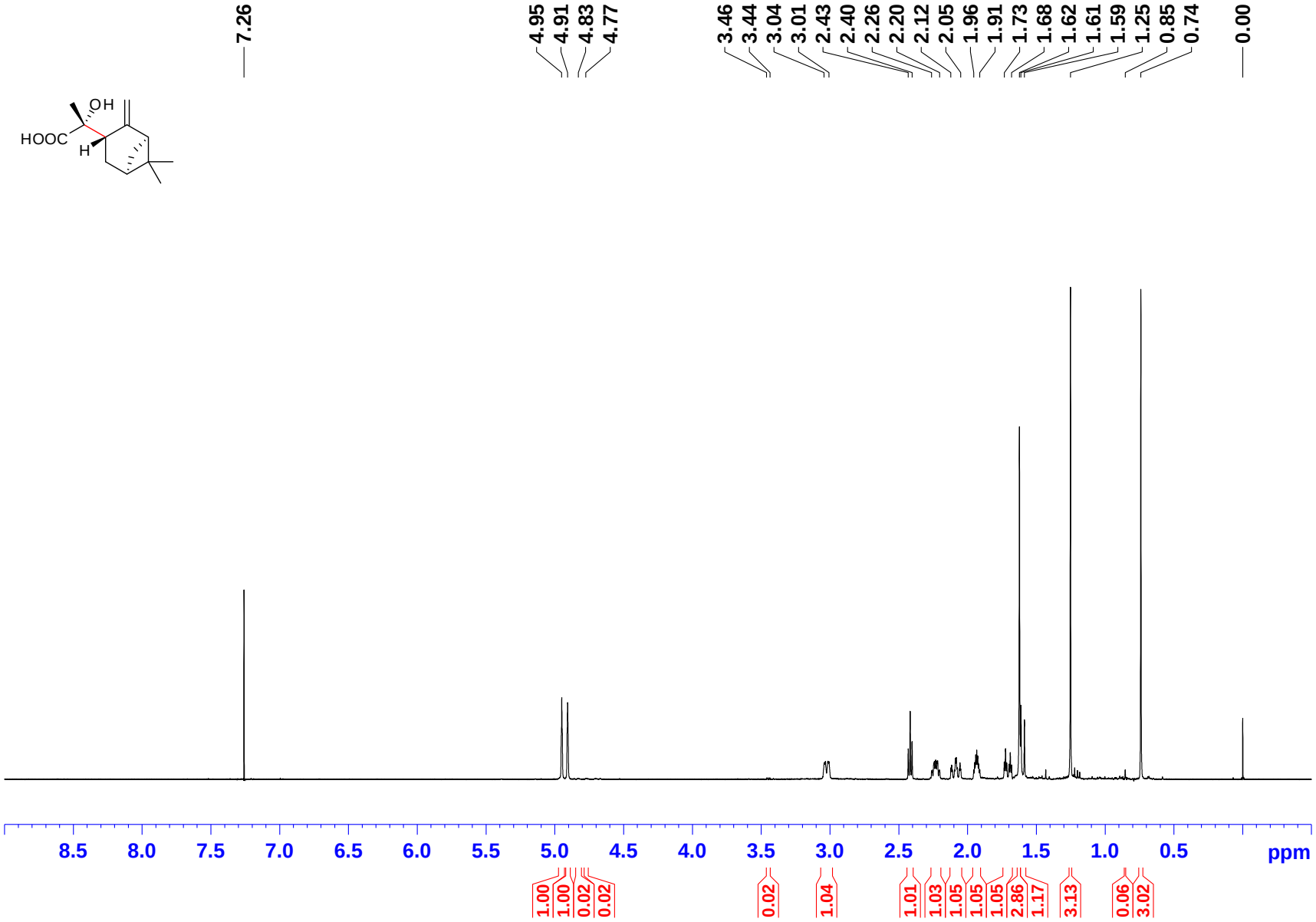
^{1}H NMR of **3p** ($CDCl_3$, 400 MHz)



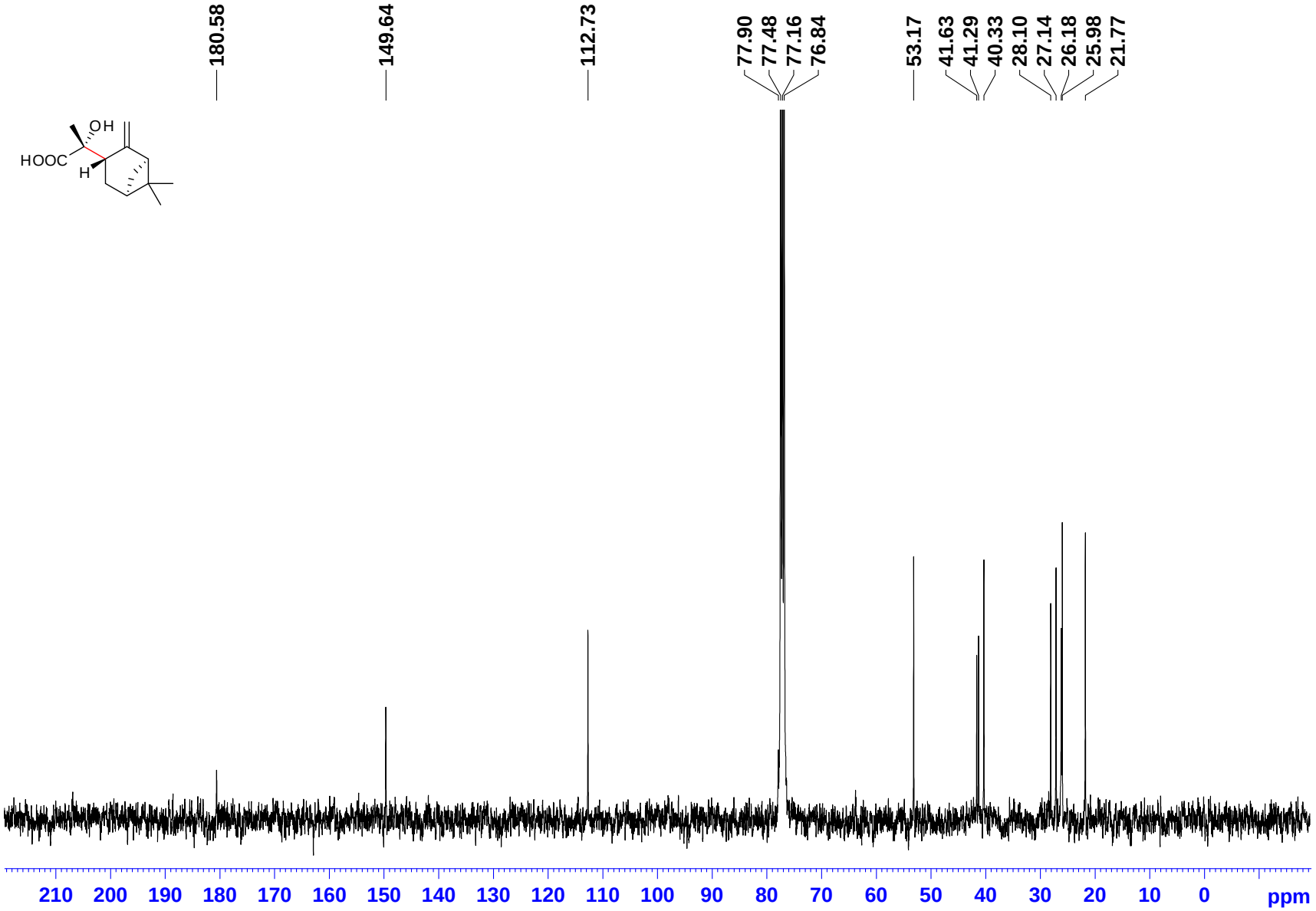
^{13}C NMR of **3p** ($CDCl_3$, 400 MHz)



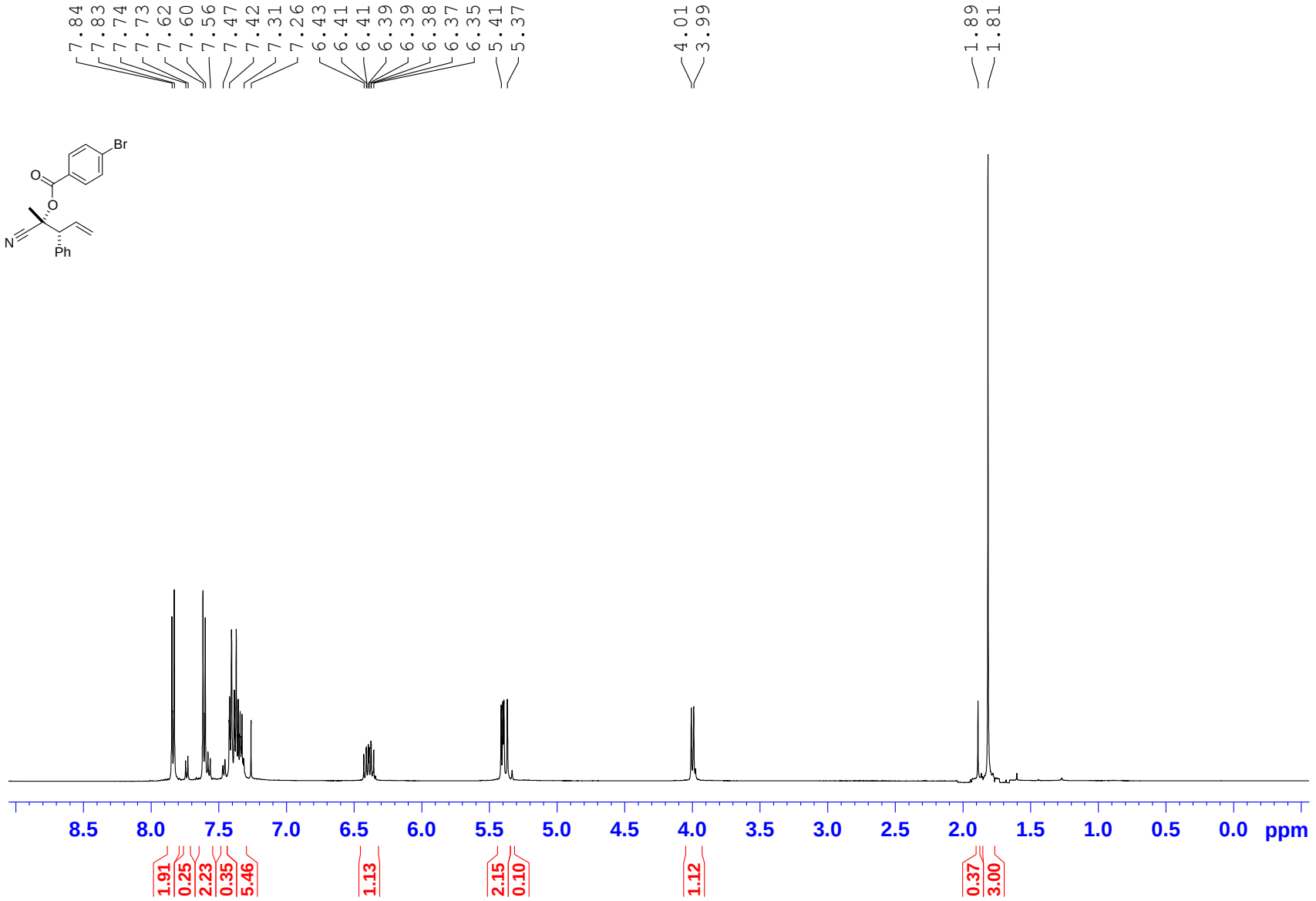
^{1}H NMR of **3q** ($CDCl_3$, 400 MHz)



^{13}C NMR of **3q** ($CDCl_3$, 400 MHz)



^{1}H NMR of **3i**-ester derivative ($CDCl_3$, 500 MHz)



^{13}C NMR of **3i**-ester derivative ($CDCl_3$, 500 MHz)