Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

LED as a simple, Inexpensive and Sustainable Alternative for Wolff Rearrangements

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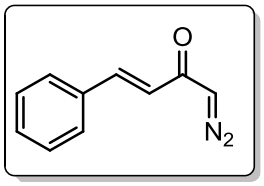
EXPERIMENTAL SECTION

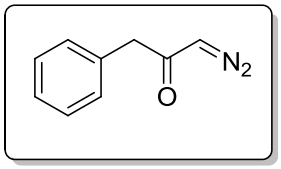
General Procedures. All solvents were dried and distilled prior to use by standard procedures. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC), carried out on 0.25 mm silica gel plates using UV light as visualizing agent and potassium permanganate in aqueous KOH for staining. Column chromatography was performed using silica gel 60 (particle size 0.063-0.210 mm). Unless stated otherwise, all the yields refer to isolated products after flash column chromatography. The solvent mixtures employed in TLC analysis and in flash column chromatography purifications are reported as volume by volume and in percentages. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded using a 400 or 500 MHz equipment. For ^{1}H NMR spectra, chemical shifts (δ) are referenced from $CDCl_3$ (7.26 ppm). Coupling constants (*J*) are reported in Hz. For multiplicities the following abbreviations were used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, double doublet; bs; broad singlet; dt, double triplet. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded using a NMR spectrometer at 50, 100 or 125 MHz. For ^{13}C NMR spectra, chemical shifts (δ) are given from $CDCl_3$ (77.0 ppm) or MeOH (49.0 ppm). Infrared spectra were obtained using FTIR at 4.0 cm^{-1} resolution and are reported in wavenumbers. Photochemical reactions were carried out using an E27 Philips Master LEDspot PAR 38 MV Dimmable (18W, 2700K, 50-60Hz typ, 90mA) in a 4 mL vial holder. Other lamps tested: E27 Golden white 45W and 15W CFL light bulb (6500K), E27 Golden warm yellow 25W bulb (2700K) and E27 OuroLux Superled A60 white 5W.

Preparation of diazoketones:

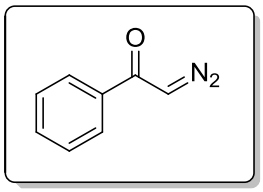


1(*E*)-1-diazo-4-phenylbut-3-en-2-one 1. To a room temperature solution of diethyl 3-diazo-2-oxopropylphosphonate (400 mg,

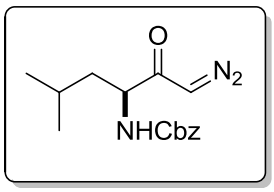
1.81 mmol, 1 equiv.) in EtOH (5 mL) was added 185µL of benzaldehyde (1.81 mmol, 1 equiv.), followed by the addition of 3.6 mL of a 0.5M NaOH solution (water:EtOH 1:1) during a period of 1h (using a syringe pump). After this time, the mixture was stirred in the same temperature for 30 min more and then finished by the addition of saturated NaCl (20 mL), extracted using CH_2Cl_2 (3 x 20 mL) and dried over $MgSO_4$. Purification by flash column chromatography (5-10% EtOAc/hexanes) afforded unsaturated diazoketone **1** (233.7 mg, 1.36 mmol, 75%) as a stable yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 15.8 Hz, 1H), 7.55 – 7.52 (m, 2H), 7.40 – 7.36 (m, 3H), 6.60 (d, *J* = 15.8 Hz, 1H), 5.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.2, 140.7, 134.4, 130.3, 128.9, 128.2, 123.6, 56.2; FT-IR (neat, cm^{-1}): 3070, 2098, 1636, 1584, 1450, 1373, 1149, 973, 759; HRMS (ESI) calcd for $C_{10}H_8N_2NaO$ $[M + Na]^+$ 195.05288, found 195.0628; mp 58 – 62°C; R_f 0.30 (25% EtOAc/hexanes).



1-Diazo-3-phenylpropan-2-one 10.[1] A solution of phenyl acetic acid (6.90 mg, 5 mmol, 1 equiv.) in 5 mL of dry benzene and 5 mL of thionyl chloride (69 mmol, 13 equiv.) was refluxed for 1 h and the colorless solution was evaporated in vacuo. The resulting acyl chloride was dissolved in 8 mL of ether and then added dropwise with stirring to a 30–40 mL solution of ethereal diazomethane (0.4 M) at 0–5 C. The yellow solution was allowed to stand at room temperature for 1 h and then purged with argon during 30 min. Solvent evaporation followed by silica gel purification (25% EtOAc/hexanes) afforded diazoketone **10** (480 mg, 3 mmol) as a stable yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 2H), 5.12 (s, 1H), 7.19-7.37 (m, 5H); ^{13}C NMR (62.5 MHz, CDCl3) δ 48.0, 54.8, 127.2, 128.8, 129.3, 134.5, 192.7; IR (neat, cm^{-1}) 3315, 3084, 2956, 2926, 2870, 2117, 1712, 1654, 1626, 1420, 1116, 970; R_f 0.30 (25% EtOAc/hexanes).



α-Diazoacetophenone 11. To a -10°C solution of ethereal diazomethane (178 mL, 0.4 M) and triethylamine (5,0 mL, 35.6 mmol, 1 equiv.) was added benzoyl chloride (4.13 mL, 35.6 mmol, 1 equiv) dropwise with stirring during a period of 30 min. After this time, the solution was allowed to warm up to 0°C and kept in the same temperature during 4 h. Concentration under reduced pressure followed by purification under *flash* chromatography furnished diazoketone **11** (4.44 g, 30.4 mmol) in 85% yield as a stable yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (s, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.50 – 5.56 (m, 1H), 7.75 (dd, *J* = 8.3, 1.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.3, 136.6, 132.6, 128.6, 126.6, 54.1; IR (neat, cm^{-1}) 3088, 2108, 1728, 1622, 1575, 1448, 1367, 1228, 1145, 702; mp 48 – 50°C, Rf 0.30 (25% EtOAc/hexanes).



(*S*)-benzyl (1-diazo-5-methyl-2-oxohexan-3-yl)carbamate 12.[2] Cbz-*L*-Leucine (1 g, 3.76 mmol, 1 equiv.) was dissolved in THF (20 mL) and the resulting solution was cooled to 0 °C. To the solution were added *N*-methylmorpholine (NMM, 435 µL, 3.95 mmol, 1.05 equiv.) and isobutyl chloroformate (515 µL, 3.95 mmol, 1.05 equiv.) successively. The mixture was stirred for 15 min. Then, a cooled 0.4 M solution of CH_2N_2 in Et_2O (70 mL) was added dropwise, and the yellow solution was allowed to warm to rt. The reaction mixture was stirred during 2 h and then concentrated under reduced pressure. Residue was purified by column chromatography on silica gel (20-30% EtOAc/hexanes) to afford diazoketone **12** (0. 93g, 3.20 mmol, 85% yield) as a yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 5.43 (s, 1H), 5.34 (d, *J* = 7.3 Hz, 1H), 5.11 (d, *J* =

12.0 Hz, 1H), 5.08 (d, *J* = 12.4 Hz, 1H), 4.26 (s, 1H), 1.75 – 1.63 (m, 1H), 1.57 (ddd, *J* = 13.3, 8.4, 5.2 Hz, 1H), 1.50 – 1.41 (ddd, *J* = 13.3, 8.4, 5.2 Hz, 1H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.93 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.0, 156.0, 136.2, 128.5, 128.2, 128.0, 67.0, 56.3, 53.8, 41.5, 24.7, 23.0, 21.8; IR (neat, cm^{-1}) 3315, 3084, 2956, 2117, 1712, 1597, 1541, 1381, 1247, 1022, 761; mp: 71–72 °C; R_f 0.20 (25% EtOAc/hexanes).

General procedures for photochemical Wolff Rearrangement with LEDs:

Method A: Using alcohols as solvent

In a 4 mL vial, diazoketones (0.174 mmol) were dissolved in 3.5 mL of desired alcohol. The vial was closed with a cap and a needle added (to vent the nitrogen gas formed during the reaction). Next, the light yellow diazoketone solution was irradiated with a Philips Master LEDspot PAR 38 MV Dimmable (18W, 2700K, 50-60Hz typ, 90mA) lamp for 24 h under magnetic stirring at room temperature (nitrogen gas evolution observed; the solution tends to become colorless with the consumption of the diazoketone). After that, the solvent was evaporated in rotary evaporator. Purification by *flash* column chromatography afforded the following esters. The schematic setup of the experiment is described below.

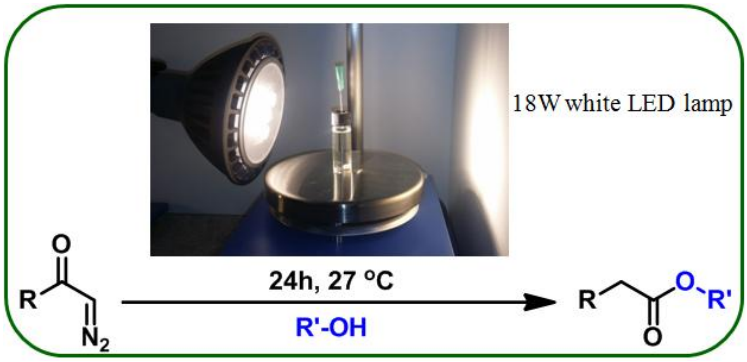
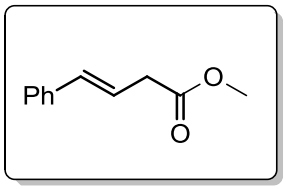
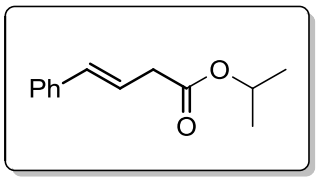


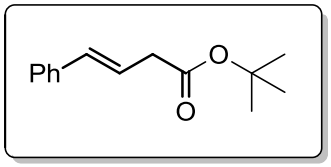
Figure 1. Experimental setup for the Photochemical Wolff rearrangement with LED lamp.



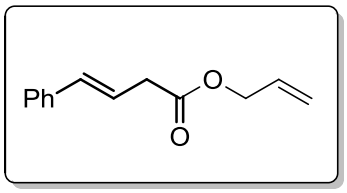
(*E*)-methyl 4-phenylbut-3-enoate 2. Using dry MeOH, 91% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.21 (m, 1H), 6.50 (d, *J* = 15.9 Hz, 1H), 6.31 (ddd, *J* = 15.9, 10.7, 5.8 Hz, 1H), 3.72 (s, 3H), 3.26 (dd, *J* = 7.1, 1.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 136.8, 133.5, 128.5, 127.5, 126.3, 121.6, 51.90, 38.2; R_f 0.38 (10% EtOAc/hexanes).



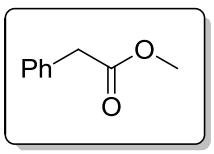
(*E*)-isopropyl 4-phenylbut-3-enoate 3. Using dry *i*-PrOH, 80% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.21 (m, 1H), 6.49 (d, *J* = 15.9 Hz, 1H), 6.31 (dt, *J* = 15.9, 7.1 Hz, 1H), 5.05 (hept, *J* = 6.3 Hz, 1H), 3.21 (dd, *J* = 7.1, 1.5 Hz, 2H), 1.26 (d, *J* = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 136.9, 133.2, 128.5, 127.4, 126.2, 122.0, 68.1, 38.8, 21.8; R_f 0.50 (10% EtOAc/hexanes).



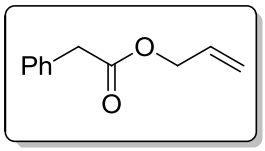
(*E*)-tert-butyl 4-phenylbut-3-enoate 4. Using dry *t*-BuOH, 63% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.3 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.20 (m, 1H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.29 (dt, *J* = 15.9, 7.1 Hz, 1H), 3.16 (dd, *J* = 7.1, 1.4 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 137.1, 132.9, 128.5, 127.4, 126.2, 122.5, 80.8, 39.7, 28.1; R_f 0.55 (10% EtOAc/hexanes).



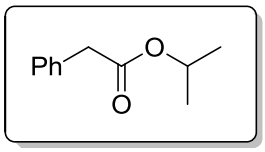
(*E*)-allyl 4-phenylbut-3-enoate 5. Using dry allyl alcohol, 85% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 8.2, 1.0 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.21 (m, 1H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.31 (dt, *J* = 15.9, 7.1 Hz, 1H), 5.94 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1H), 5.34 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.25 (ddd, *J* = 10.4, 2.6, 1.3 Hz, 1H), 4.63 (dt, *J* = 5.8, 1.4 Hz, 2H), 3.28 (dd, *J* = 7.1, 1.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 136.8, 133.5, 132.0, 128.5, 127.5, 126.3, 121.6, 118.4, 65.4, 38.3; R_f 0.48 (10% EtOAc/hexanes). FT-IR (neat, cm-^{1}): 3084, 3028, 2951, 2926, 2855, 1738, 1651, 1497, 1450, 1371, 1285, 1240, 1155, 988, HRMS (ESI) calcd for $C_{13}H_{16}O_2$ $[M+H]^+$ 203.10666, found 203.10692



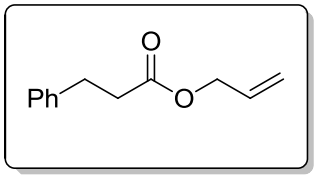
methyl 2-phenylacetate 13.[3] 81% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: R_f 0.40 (10% EtOAc/hexanes).



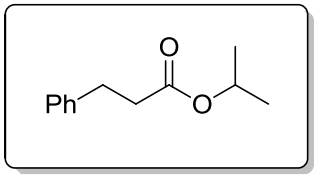
allyl 2-phenylacetate 14. 75% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.23 (m, 5H), 5.90 (ddt, *J* = 17.2, 10.5, 5.7 Hz, 1H), 5.27 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.21 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.59 (dt, *J* = 5.7, 1.4 Hz, 2H), 3.65 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 133.9, 132.0, 129.2, 128.6, 127.1, 118.2, 65.4, 41.3; R_f 0.50 (10% EtOAc/hexanes). FT-IR (neat, cm-^{1}): 3088, 3065, 3032, 2943, 1740, 1497, 1454, 1364, 1244, 1150, 991, HRMS (ESI) calcd for $C_{11}H_{12}O_2$ $[M+Na]^+$ 199.07295, found 199.07320



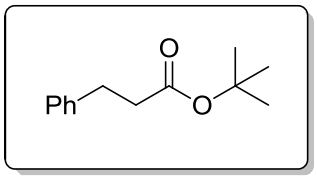
isopropyl 2-phenylacetate 15. 63% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.23 (m, 5H), 5.01 (hept, *J* = 6.3 Hz, 1H), 3.58 (s, 2H), 1.22 (d, *J* = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 134.3, 129.2, 128.5, 126.9, 68.2, 41.7, 21.8; R_f 0.50 (10% EtOAc/hexanes).



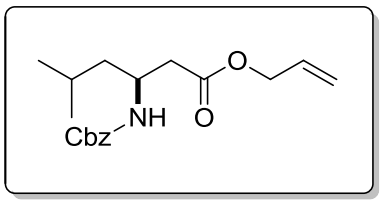
allyl 3-phenylpropanoate 16. 89% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.24 – 7.18 (m, 3H), 5.90 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H), 5.29 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.22 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.58 (dt, *J* = 5.7, 1.4 Hz, 2H), 2.97 (t, *J* = 7.6 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 140.4, 132.1, 128.5, 128.3, 126.2, 118.2, 65.1, 35.8, 30.9; R_f 0.50 (10% EtOAc/hexanes).



isopropyl 3-phenylpropanoate 17. 70% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.23 – 7.14 (m, 3H), 5.00 (hept, *J* = 6.3 Hz, 1H), 2.94 (t, *J* = 7.6 Hz, 2H), 2.59 (t, *J* = 7.8 Hz, 2H), 1.20 (d, *J* = 6.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 140.6, 128.4, 128.3, 126.2, 67.7, 36.2, 31.0, 21.8; R_f 0.50 (10% EtOAc/hexanes).

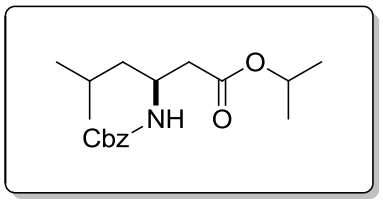


tert-butyl 3-phenylpropanoate 18. 66% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.21 – 7.16 (m, 3H), 2.91 (t, *J* = 7.7 Hz, 2H), 2.54 (t, *J* = 7.7 Hz, 2H), 1.41 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 140.8, 128.4, 128.3, 126.1, 80.3, 37.1, 31.1, 28.0; R_f 0.63 (10% EtOAc/hexanes).



(*S*)-allyl-3-(((benzyloxy)carbonyl)amino)-5-methyl hexanoate 19. 62% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 5.89 (ddt, *J* = 16.3, 10.7, 5.8 Hz, 1H), 5.30 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.23 (dq, *J* = 10.4, 1.2 Hz, 1H), 5.18 – 5.12 (m, 1H), 5.09 (s, 2H), 4.57 (d, *J* = 5.3 Hz, 2H), 4.12 – 4.03 (m, 1H), 2.56 (qd, *J* = 15.8, 5.3 Hz, 2H), 1.72 – 1.58 (m, 1H), 1.50 (ddd, *J* = 14.6, 7.5, 4.3 Hz, 1H), 1.36 – 1.26 (m, 1H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 155.7, 136.6, 131.9, 128.5, 128.0, 128.0, 118.5, 66.6, 65.2, 46.3, 43.5,

39.4, 24.9, 22.9, 22.1; R_f 0.23 (10% EtOAc/hexanes). FT-IR (neat, cm-^{1}): 3339, 3034, 2957, 2870, 1825, 1732, 1717, 1531, 1456, 1306, 1263, 1233, 1179, 1115, 1001, HRMS (ESI) calcd for $C_{18}H_{26}O_4N$ $[M+H]^+$ 320.18563, found 320.18604, $[\alpha]_D^{23}$ -13.3 (*c* 1.19 $CHCl_3$)

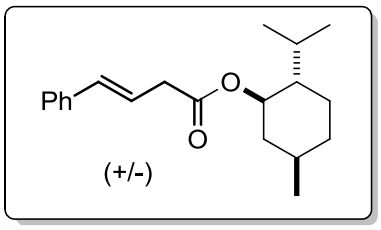


(*S*)- isopropyl 3 - (((benzyloxy)carbonyl)amino)- 5 – methylhexanoate 20. 50% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 5.20 – 5.12 (m, 1H), 5.10 (d, *J* = 12.7 Hz, 1H), 5.07 (d, *J* = 12.7 Hz, 1H), 5.00 (hept, *J* = 6.3 Hz, 1H), 4.10 – 4.02 (m, 1H), 2.49 (qd, *J* = 15.5, 5.3 Hz, 2H), 1.70 – 1.59 (m, 1H), 1.51 – 1.43 (m, 1H), 1.35 – 1.24 (m, 1H), 1.22 (d, *J* = 3.4 Hz, 3H), 1.21 (d, *J* = 3.4 Hz, 3H), 0.93 (d, *J* = 5.8 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 155.7, 136.6, 128.5, 128.0, 128.0, 82.3, 68.0, 66.5, 46.4, 43.7, 39.8, 24.9, 22.9, 21.8, 21.7; R_f 0.23 (10% EtOAc/hexanes). FT-IR (neat, cm-^{1}): 3021, 2399, 1729, 1719, 1514, 1418, 1217, HRMS (ESI) calcd for $C_{18}H_{28}O_4N$ $[M+H]^+$ 322.20128, found 322.20239, $[\alpha]_D^{23}$ -13.5 (*c* 0.45 $CHCl_3$)

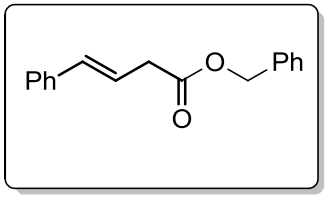
Method B-Using ethyl acetate as solvent

In a 4 mL vial, diazoketones (0.174 mmol) were dissolved in 3.5 mL of dry EtOAc (acetonitrile can be also used as solvent) followed by the addition of 10 equiv. of desired alcohol. The resulting solution was irradiated with a Philips Master LEDspot

PAR 38 MV Dimmable (18W, 2700K, 50-60Hz typ, 90mA) lamp for 24 h under magnetic stirring at room temperature (nitrogen gas evolution observed). Next, the solvent was evaporated in rotary evaporator. Purification (when indicated) by *flash* column chromatography afforded the following esters/acids:

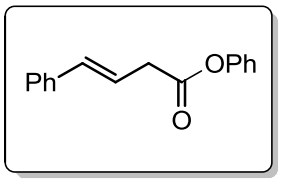


(+/-)-(*E*)-2-isopropyl-5-methylcyclohexyl 4-phenylbut-3-enoate 6. 65% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 8.2, 1.0 Hz, 2H), 7.31 (dd, *J* = 8.2, 7.0 Hz, 2H), 7.25 – 7.20 (m, 1H), 6.50 (d, *J* = 15.9 Hz, 1H), 6.30 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.72 (td, *J* = 10.9, 4.4 Hz, 1H), 3.23 (d, *J* = 7.6 Hz, 2H), 2.04 – 1.98 (m, 1H), 1.89 (dtd, *J* = 14.0, 7.0, 2.7 Hz, 1H), 1.72 – 1.64 (m, 2H), 1.55 – 1.44 (m, 1H), 1.44 – 1.36 (m, 1H), 1.14 – 0.95 (m, 3H), 0.90 (t, *J* = 6.7 Hz, 6H), 0.77 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 137.0, 133.2, 128.6, 128.5, 127.5, 122.1, 74.6, 47.0, 40.9, 38.8, 34.3, 31.4, 26.3, 23.5, 22.0, 20.7, 16.4; R_f 0.63 (10% EtOAc/hexanes). FT-IR (neat, cm-^{1}): 3061, 3028, 2955, 2926, 2870, 1732, 1454, 1369, 1252, 1169, 1150, 984, HRMS (ESI) calcd for $C_{20}H_{28}O_2$ $[M+Na]^+$ 323.19815, found 323.19772

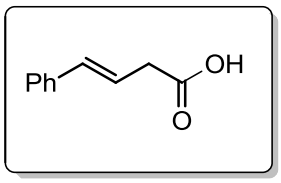


(*E*)-1-phenoxy-5-phenylpent-4-en-2-one 7. 69% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 9H), 7.27 – 7.20 (m, 1H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.32 (dt, *J* = 15.9, 7.1 Hz, 1H), 5.17 (s, 2H), 3.31 (dd, *J* = 7.1, 1.4 Hz, 2H); ^{13}C NMR (125 MHz,

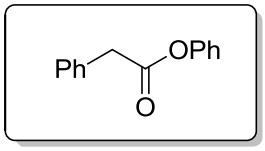
$CDCl_3$) δ 171.4, 136.8, 135.8, 133.6, 128.6, 128.5, 128.3, 128.2, 127.5, 126.3, 121.5, 66.6, 38.4; R_f 0.48 (10% EtOAc/hexanes). FT-IR (neat, cm^{-1}): 3082, 3061, 3032, 2955, 2928, 1736, 1497, 1452, 1379, 1238, 1153, 966, HRMS (ESI) calcd for $C_{17}H_{16}O_2$ $[M+Na]^+$ 275.10425, found 275.10446



(*E*)-phenyl 4-phenylbut-3-enoate 8. 63% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a white solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.29 (m, 6H), 7.28 – 7.19 (m, 2H), 7.14 – 7.05 (m, 2H), 6.60 (d, *J* = 15.9 Hz, 1H), 6.39 (dt, *J* = 15.9, 7.1 Hz, 1H), 3.49 (dd, *J* = 7.1, 1.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 150.7, 136.7, 134.0, 129.4, 128.6, 127.7, 126.3, 125.9, 121.5, 121.0, 38.4; R_f 0.43 (10% EtOAc/hexanes). FT-IR (neat, cm^{-1}): 3061, 3028, 1755, 1593, 1493, 1362, 966, 937, HRMS (ESI) calcd for $C_{16}H_{15}O_2$ $[M+H]^+$ 239.10666, found 239.10663

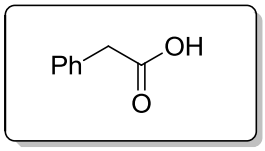


(*E*)-4-phenylbut-3-enoic acid 9. Quantitative yield as stable white solid, no purification is needed: ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.25 – 7.20 (m, 1H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.27 (dt, *J* = 15.9, 7.1 Hz, 1H), 3.29 (dd, *J* = 7.1, 1.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 136.6, 134.0, 128.5, 127.7, 126.3, 120.8, 38.0; R_f 0.10 (10% EtOAc/hexanes).

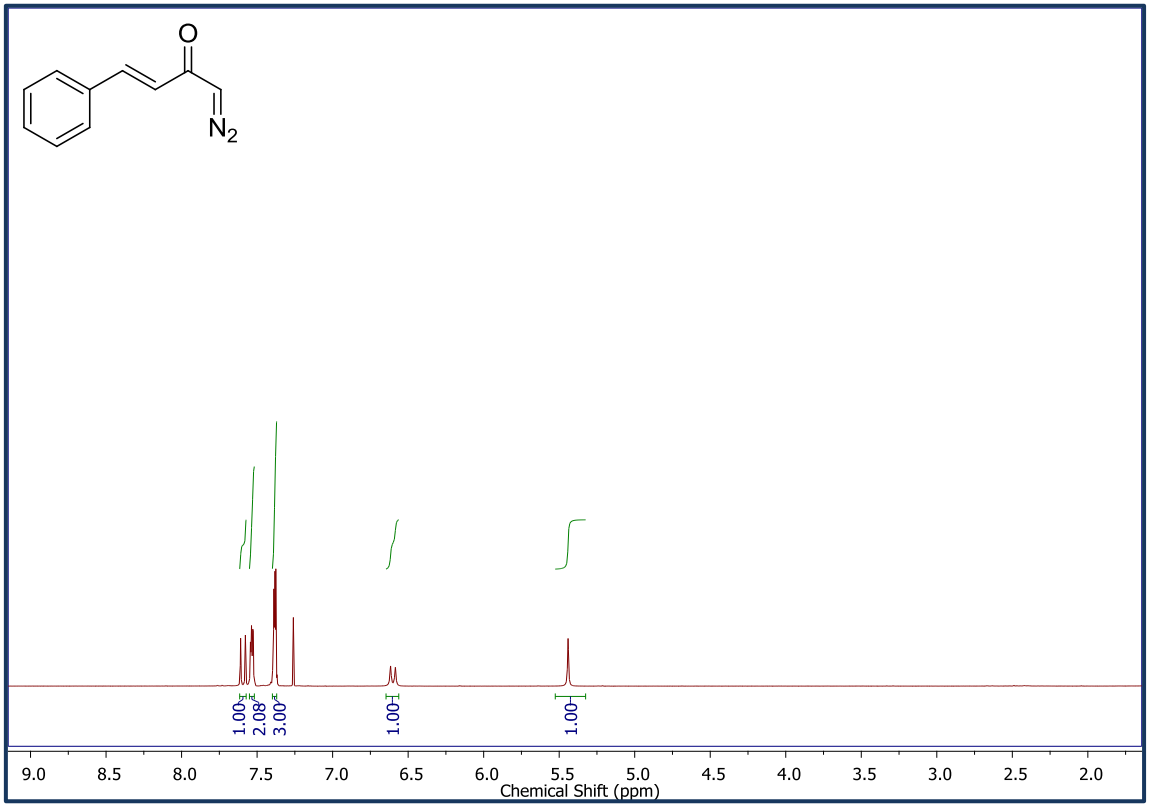


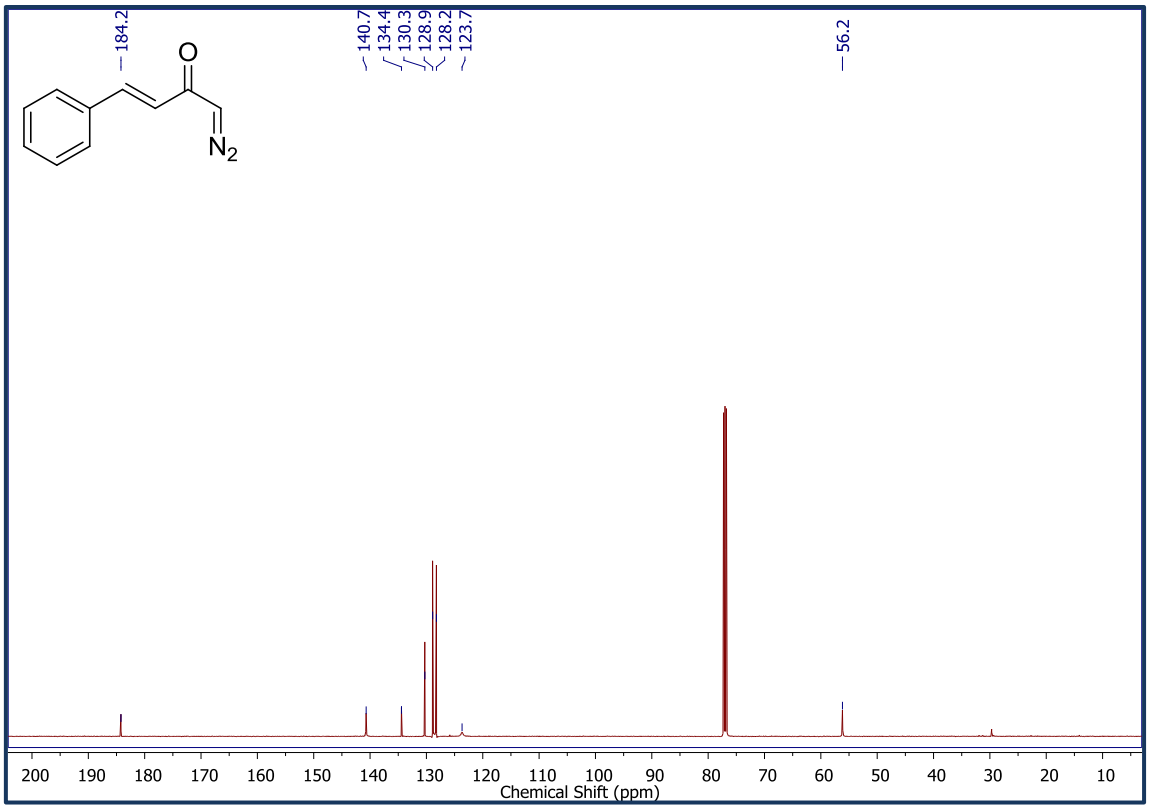
phenyl 2-phenylacetate 21. 62% yield after purification by *flash* column chromatography (5-10% EtOAc/hexanes), as a

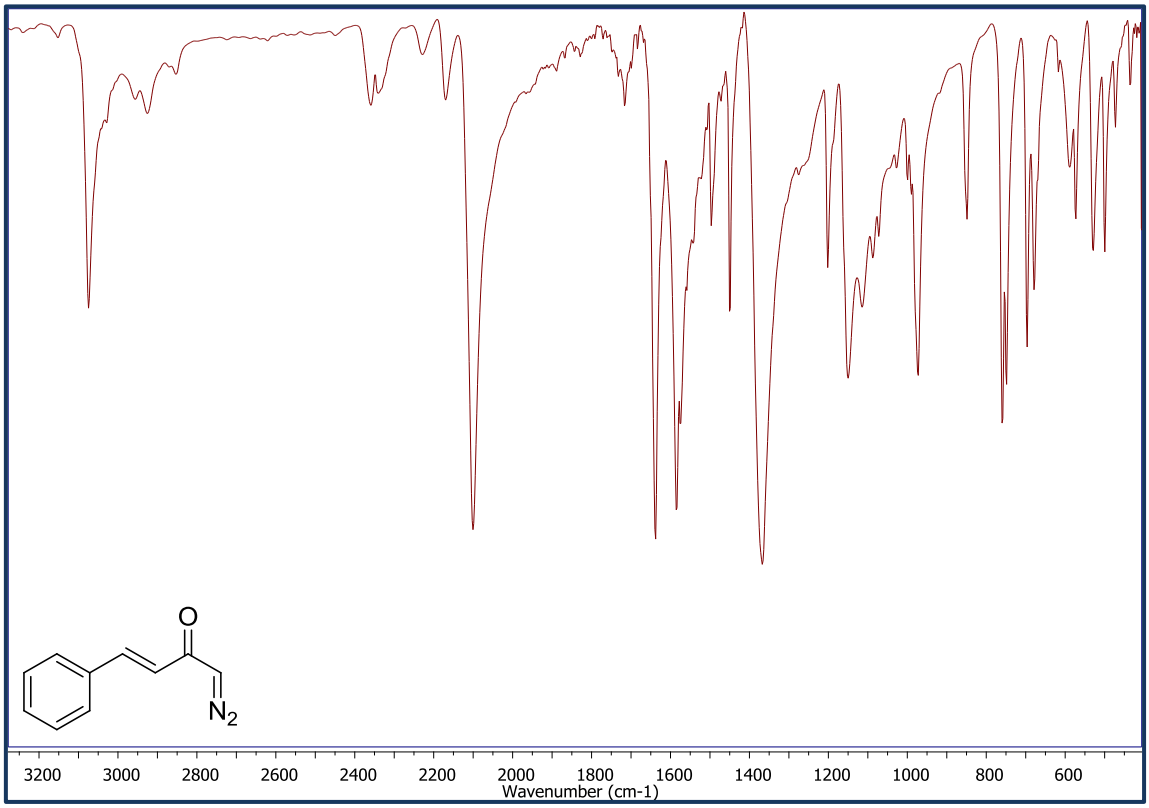
colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.29 (m, 7H), 7.24 – 7.20 (m, 1H), 7.09 – 7.05 (m, 2H), 3.87 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 150.7, 133.5, 129.4, 129.3, 128.7, 127.3, 125.8, 121.4, 41.4; R_f 0.48 (10% EtOAc/hexanes).

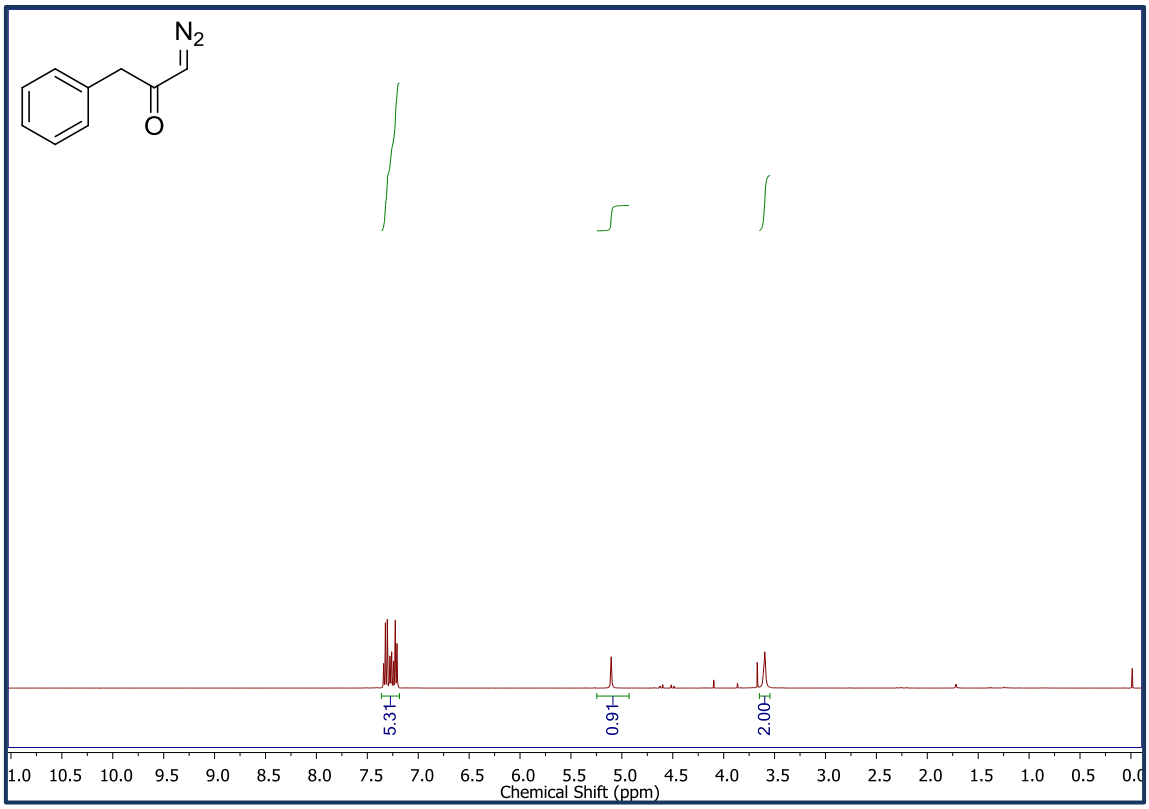


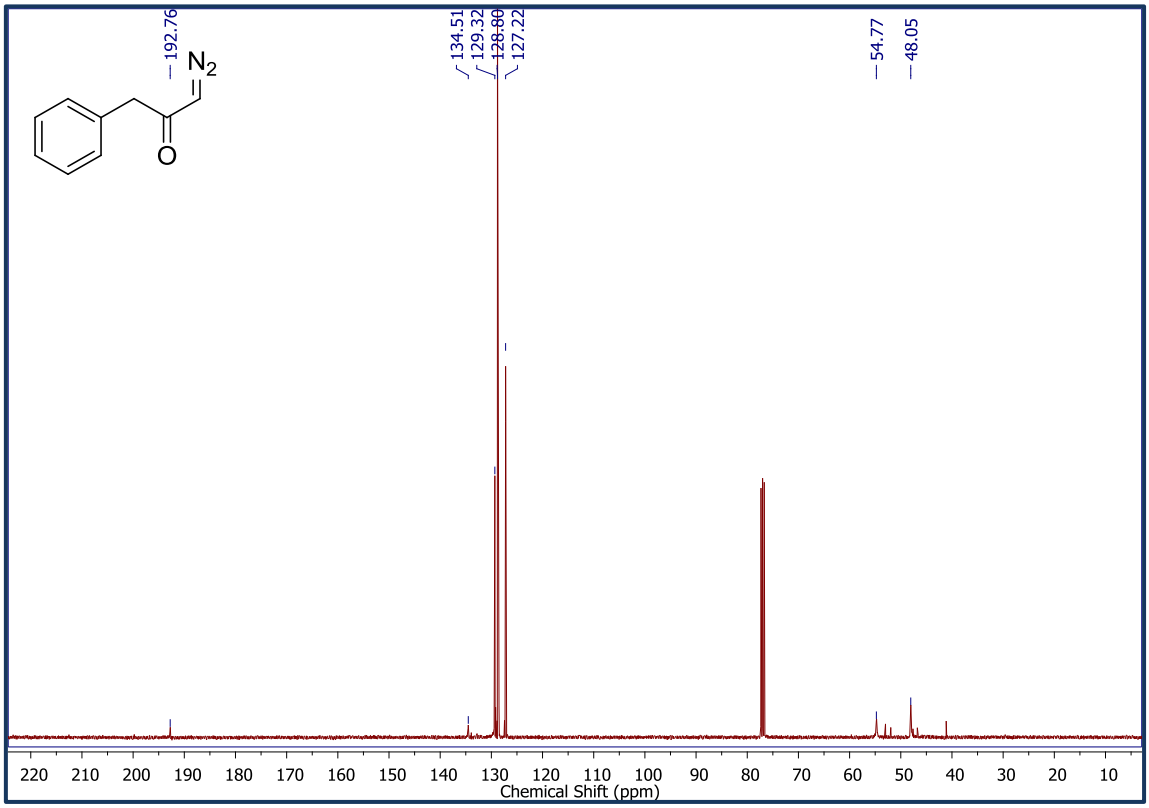
2-phenylacetic acid 22. 78% yield after purification by *flash* column chromatography (20-40% EtOAc/hexanes), as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.25 (m, 5H), 3.66 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 133.2, 129.4, 128.6, 127.3, 41.0; R_f 0.15 (10% EtOAc/hexanes).

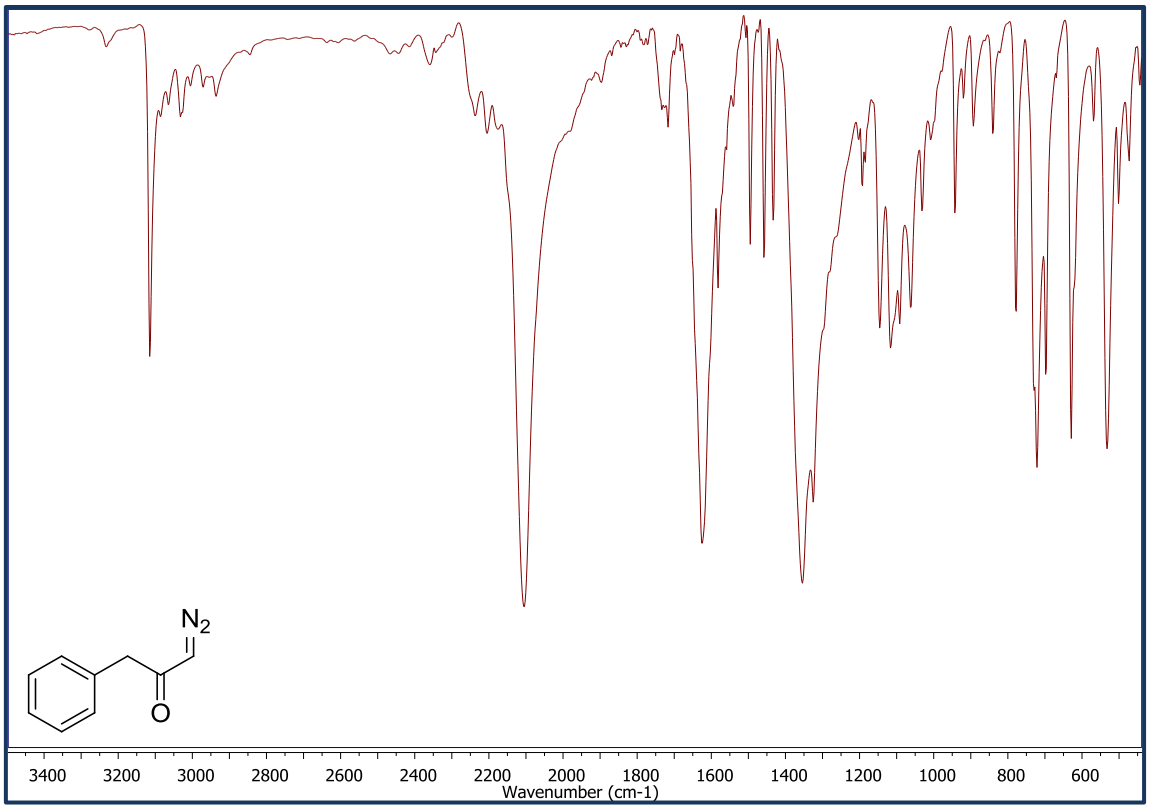


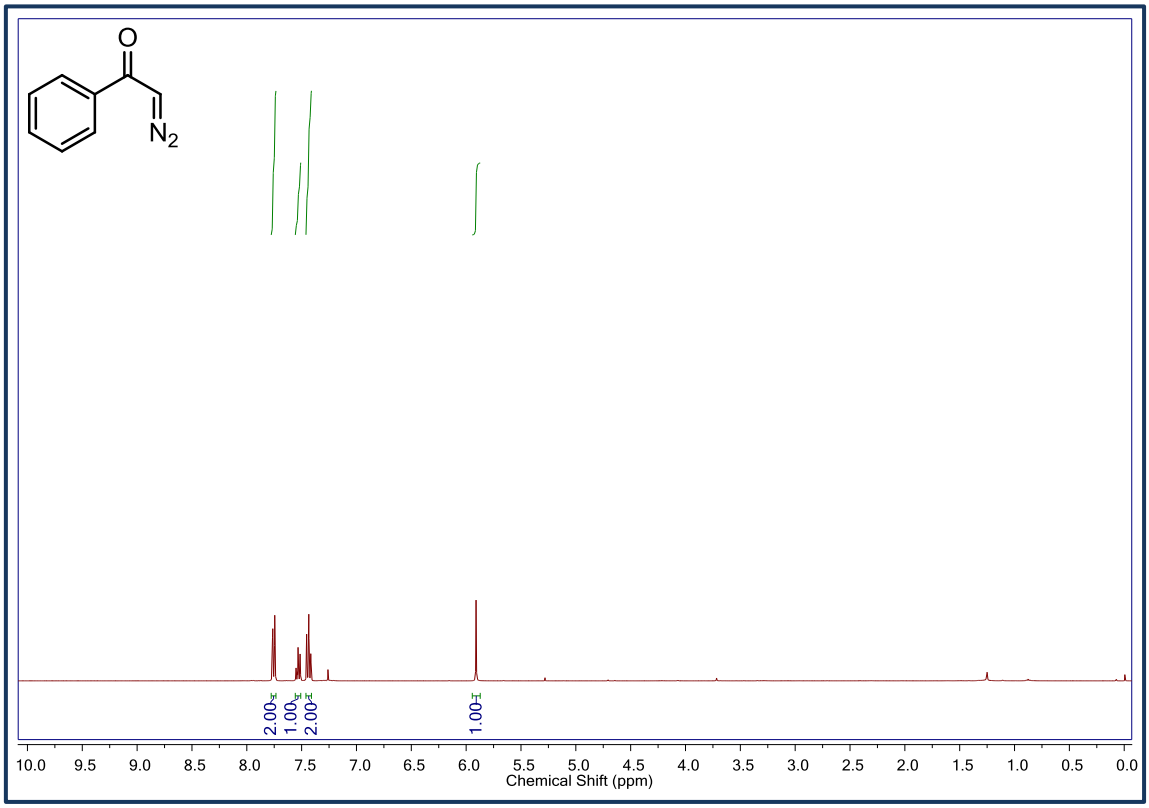

184.2
140.7
134.4
130.3
128.9
128.2
123.7
56.2
O
N2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)

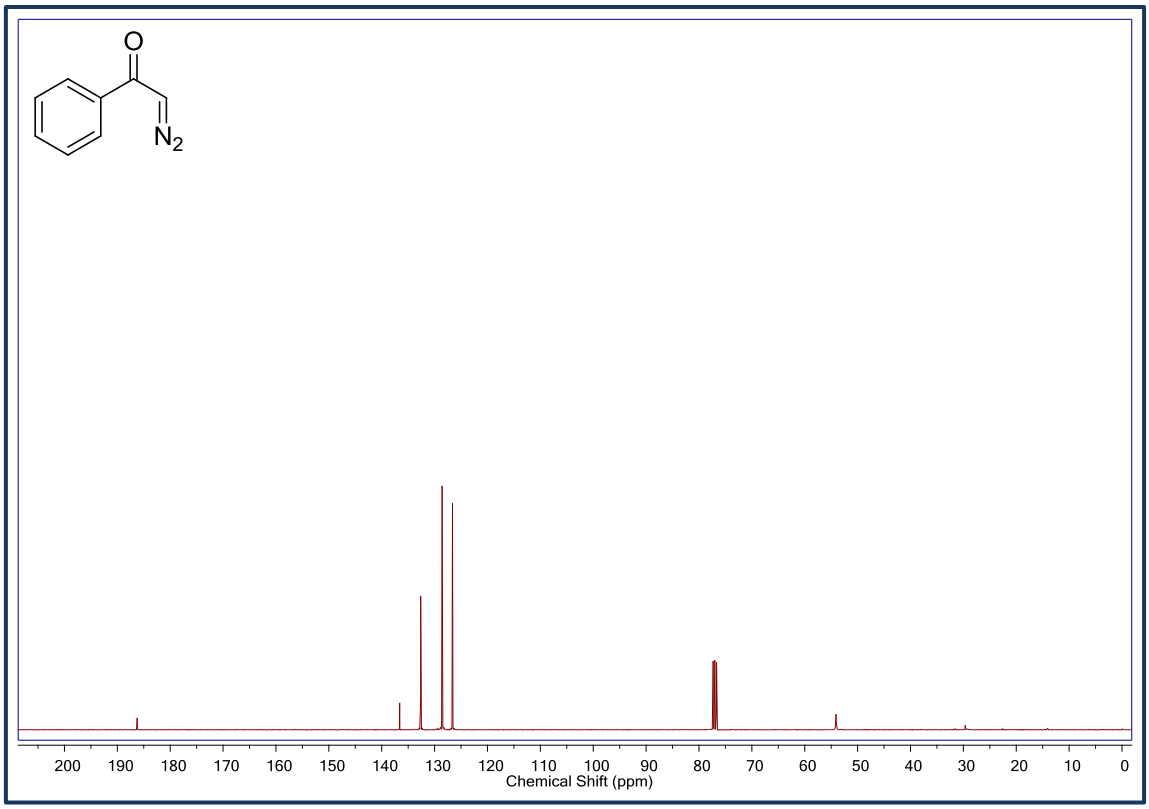

O
N2
3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600
Wavenumber (cm-1)


N2
O
5.31
0.91
2.00
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)


192.76
134.51
129.32
128.80
127.22
54.77
48.05
N2
O
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


N2
O
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
Wavenumber (cm-1)


O
N2
2.00
1.00
2.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Chemical Shift (ppm)


O
N2
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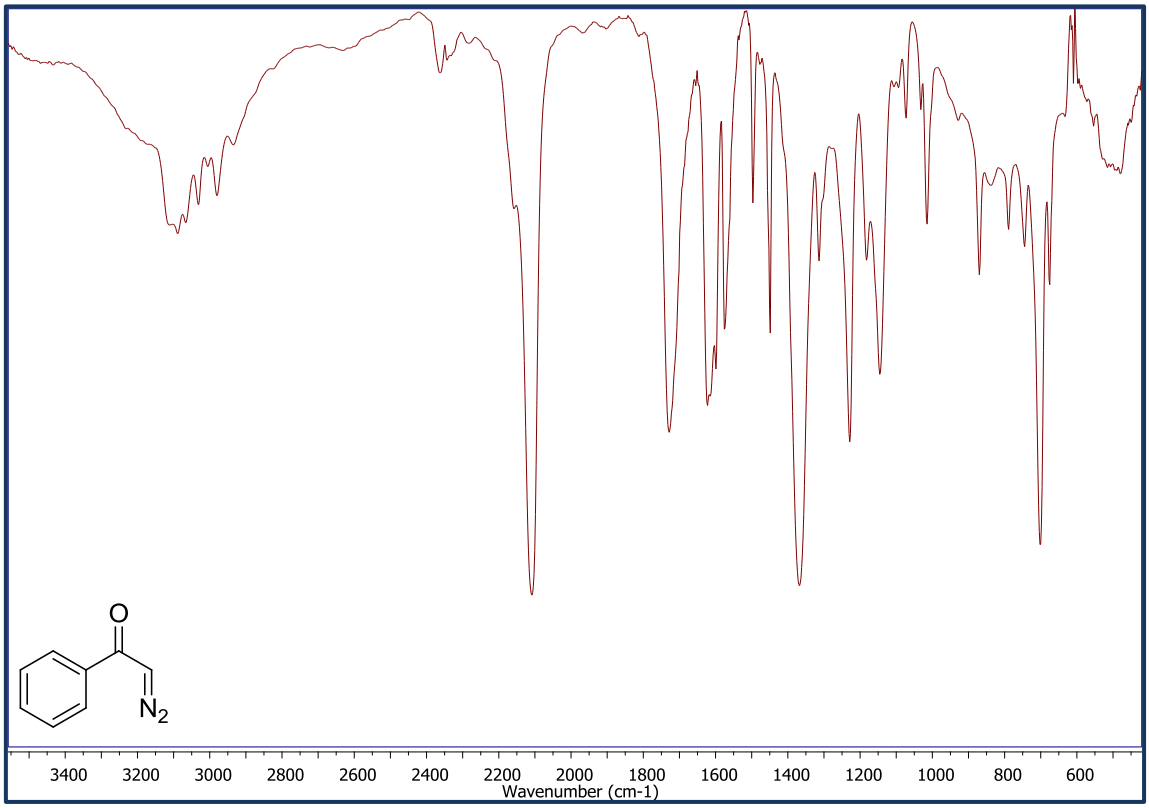
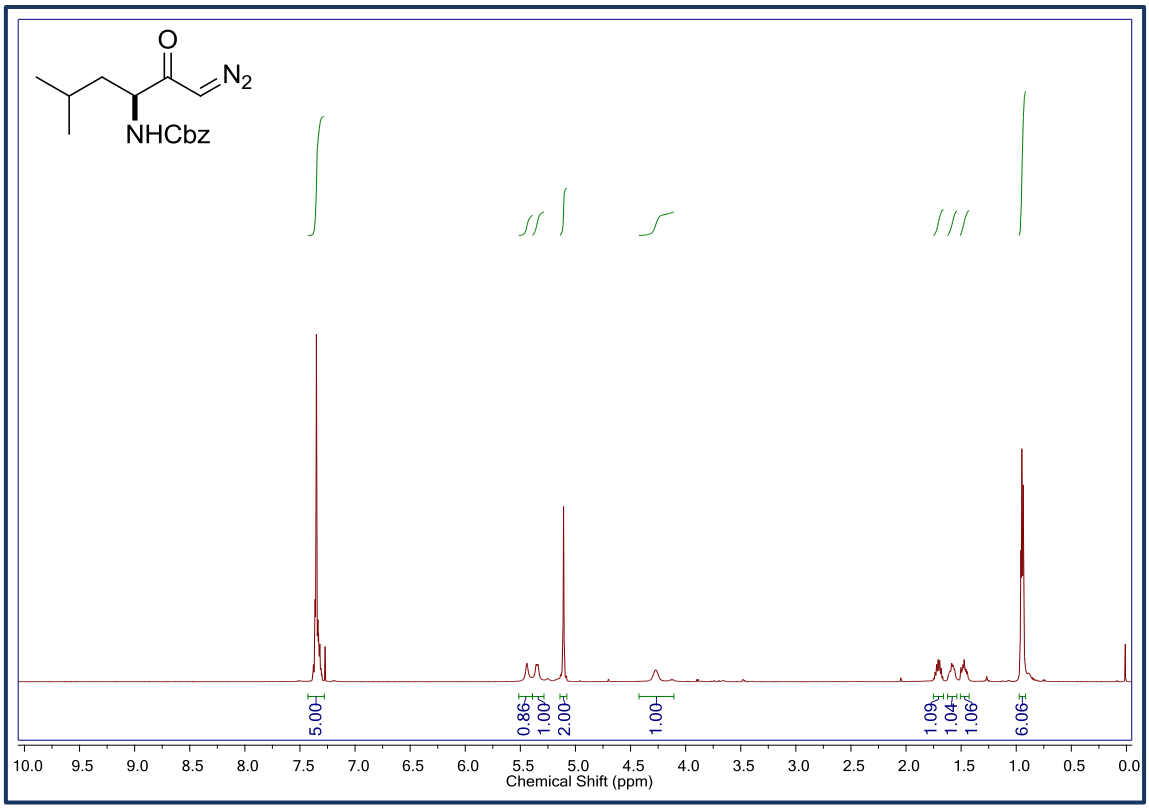
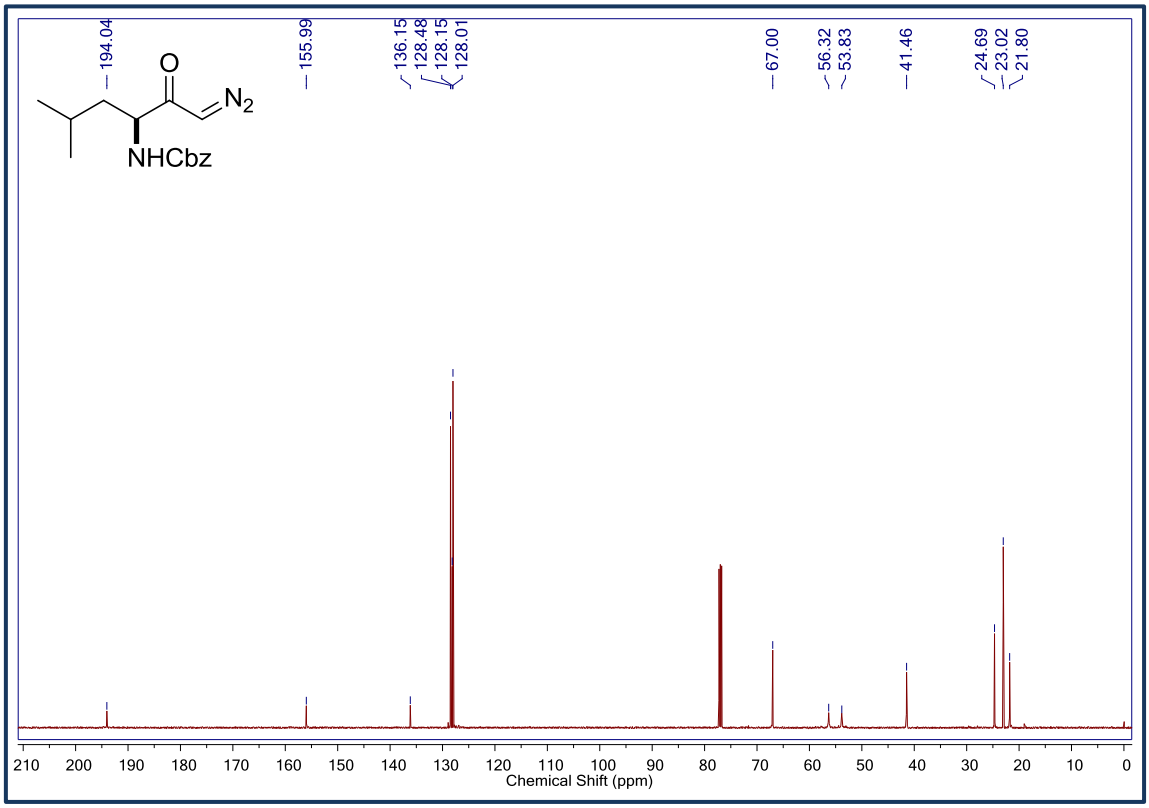
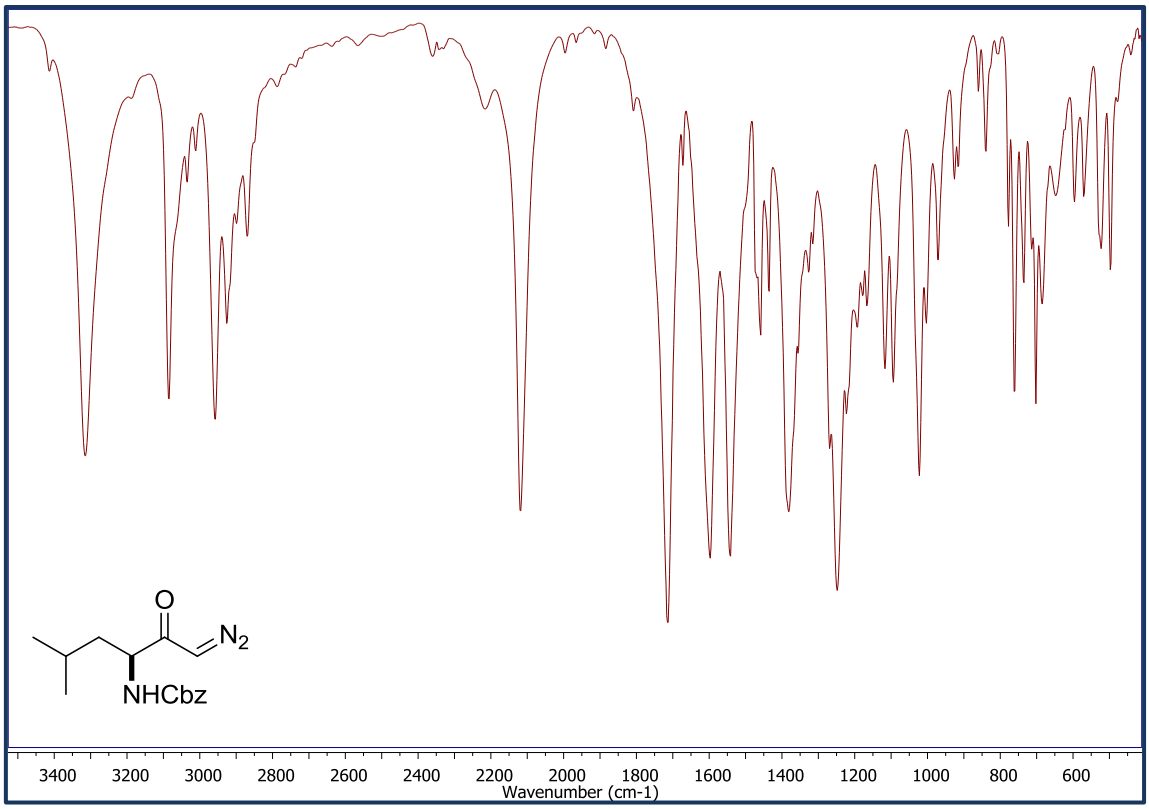
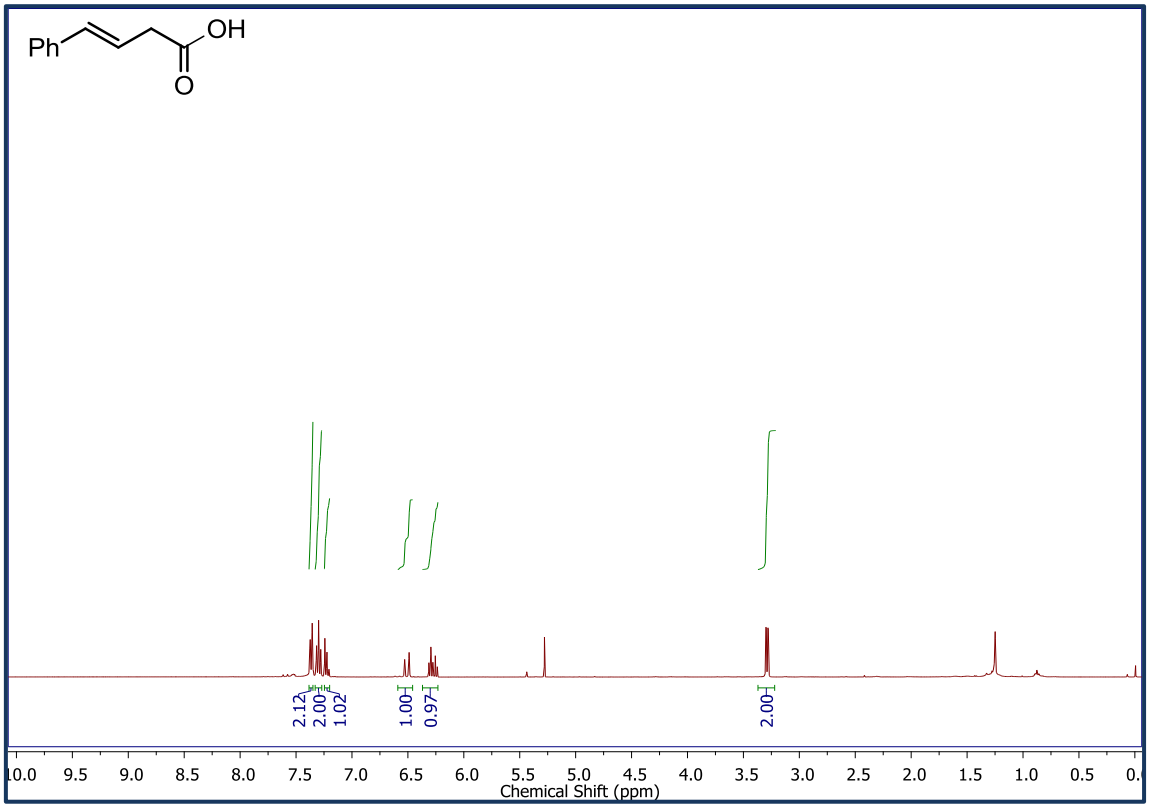
Chemical Shift (ppm)


O
N2
3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600
Wavenumber (cm-1)


O
N2
NHCbz
5.00
0.86
1.00
2.00
1.00
1.09
1.04
1.06
6.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical Shift (ppm)


194.04
155.99
136.15
128.48
128.15
128.01
67.00
56.32
53.83
41.46
24.69
23.02
21.80
O
N2
NHCbz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)


O
N2
NHCbz
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
Wavenumber (cm-1)


Ph
OH
O
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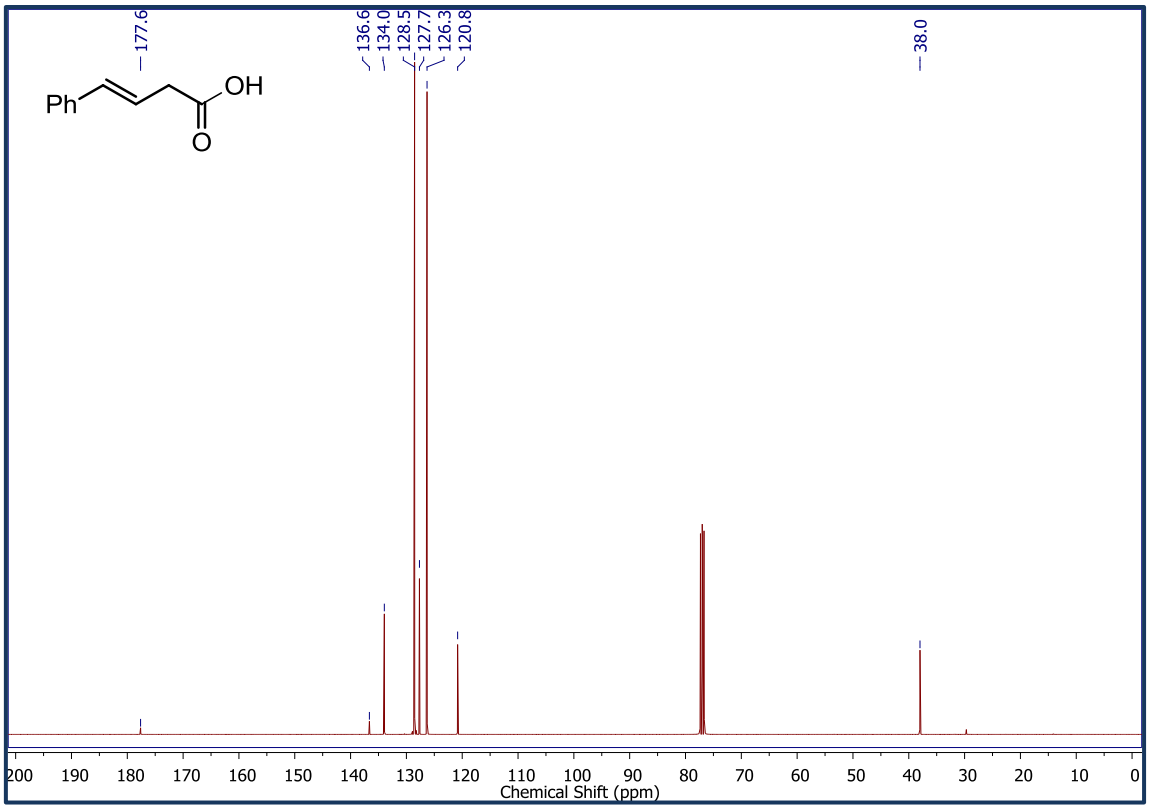
1.02
1.00
0.97
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


177.6
136.6
134.0
128.5
127.7
126.3
120.8
38.0
Ph
OH
O
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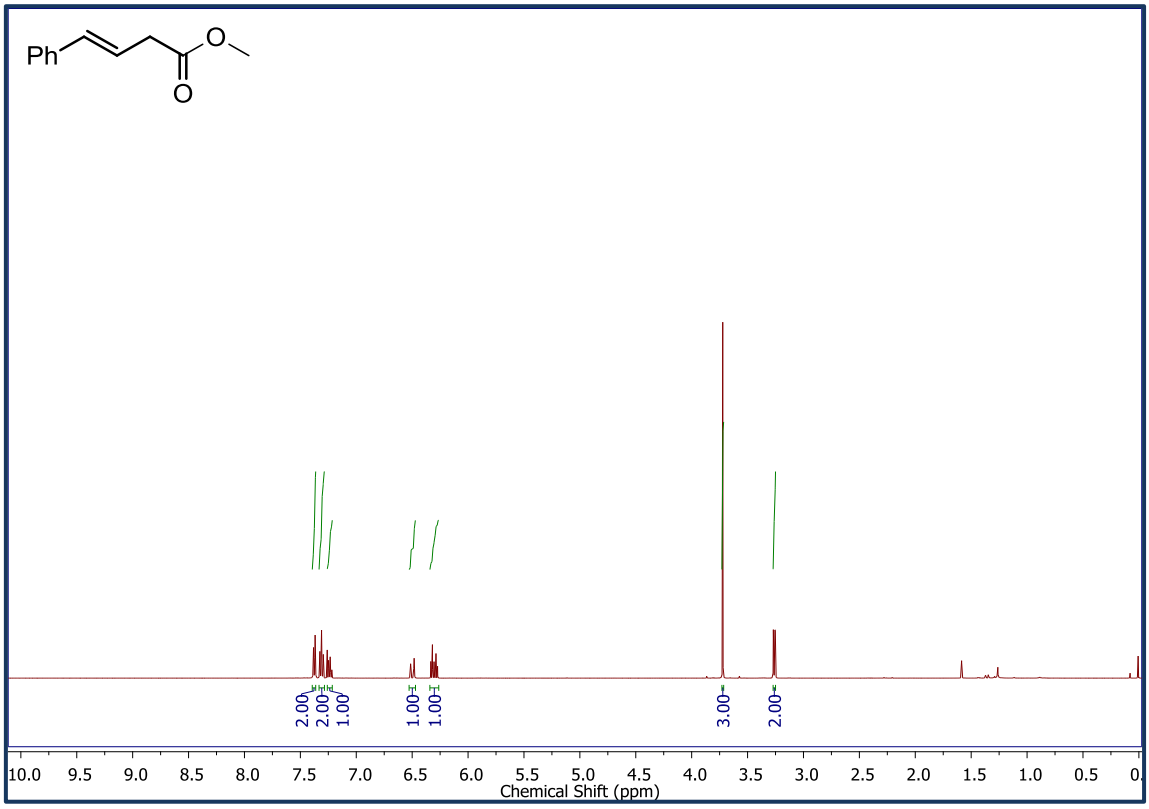
Chemical Shift (ppm)


Ph
O
O
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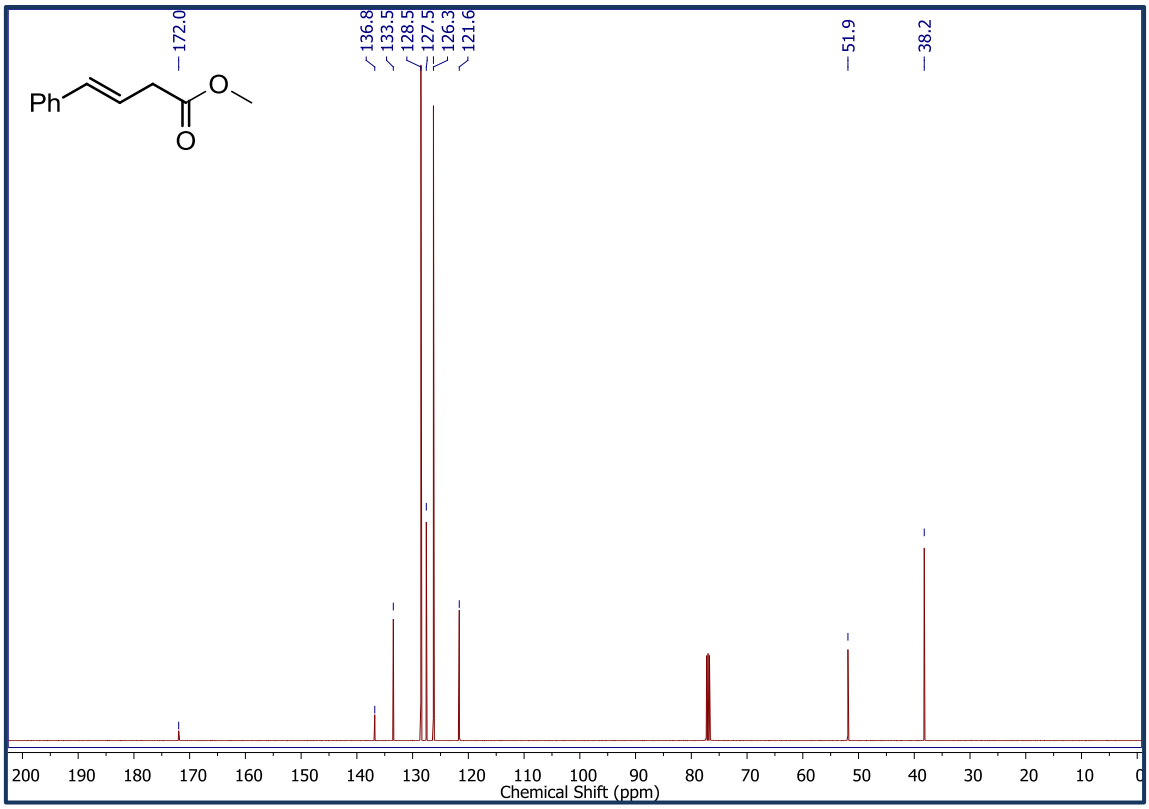
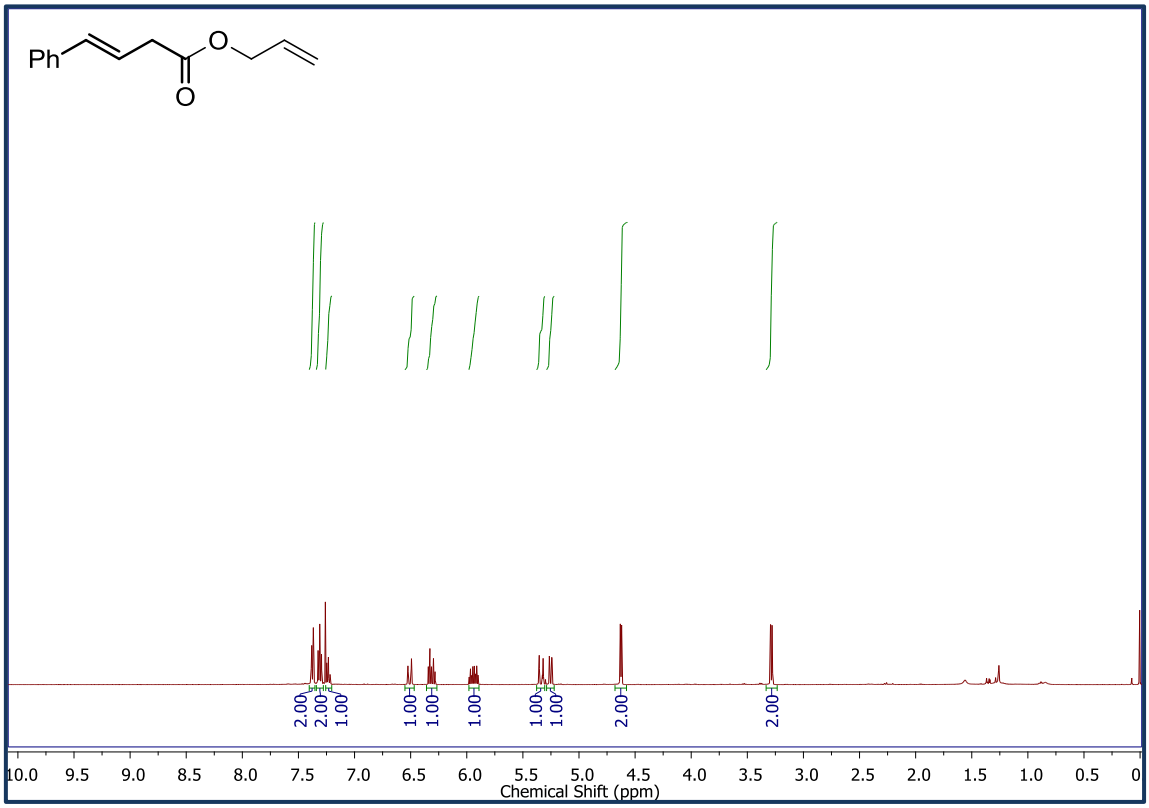
2.00
1.00
1.00
1.00
3.00
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
Chemical Shift (ppm)


172.0
136.8
133.5
128.5
127.5
126.3
121.6
51.9
38.2
Ph
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)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O
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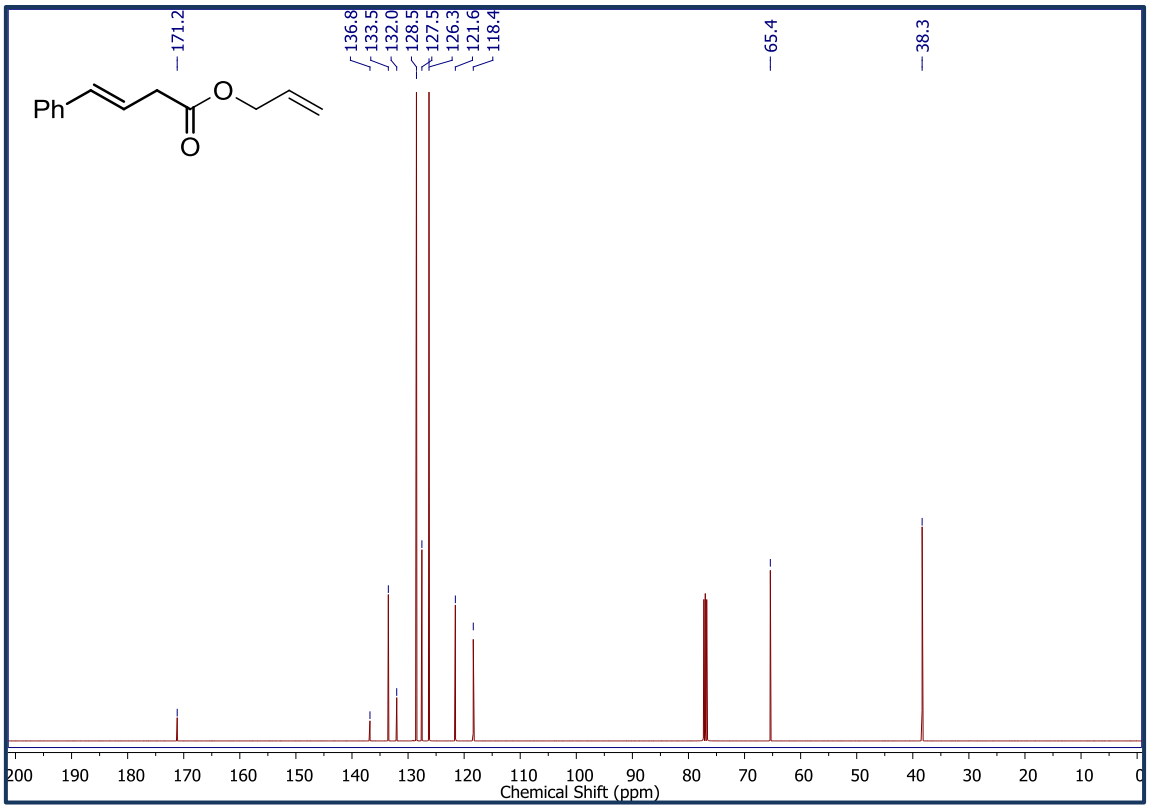
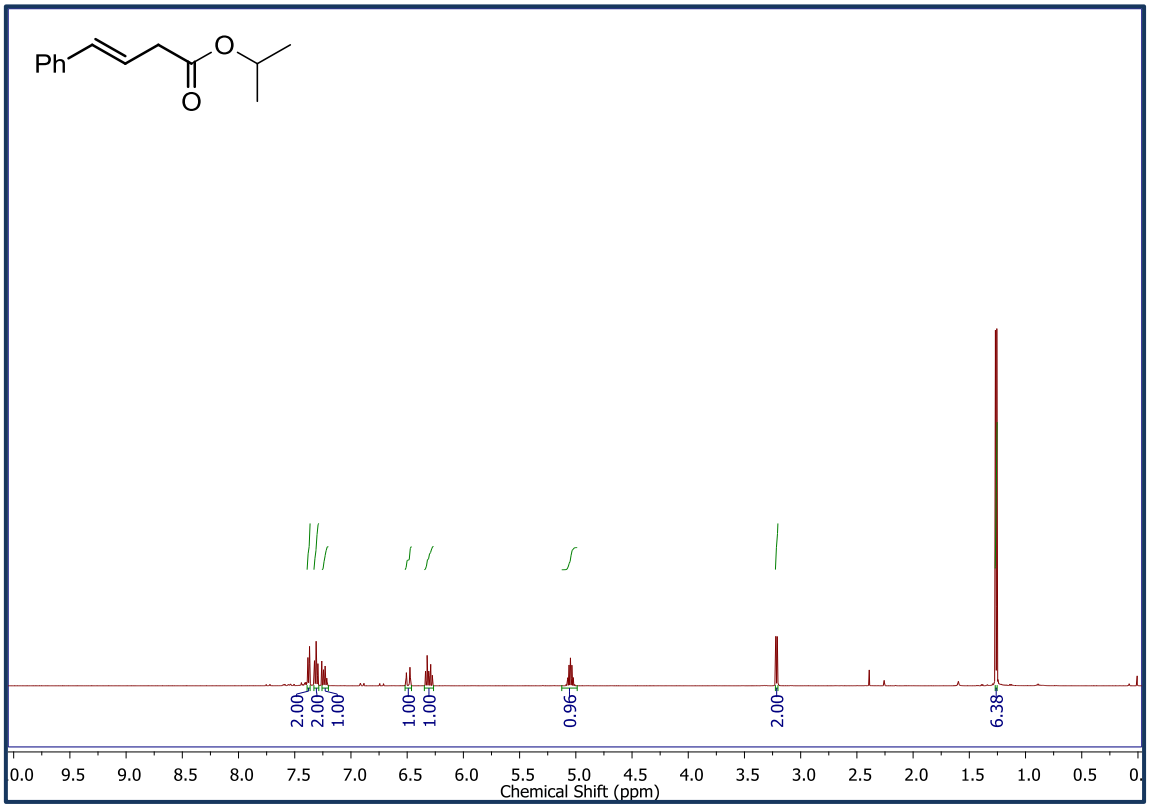
1.00
1.00
1.00
1.00
1.00
2.00
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


171.2
136.8
133.5
132.0
128.5
127.5
126.3
121.6
118.4
65.4
38.3
Ph
O
O
Chemical Shift (ppm)


Ph
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O
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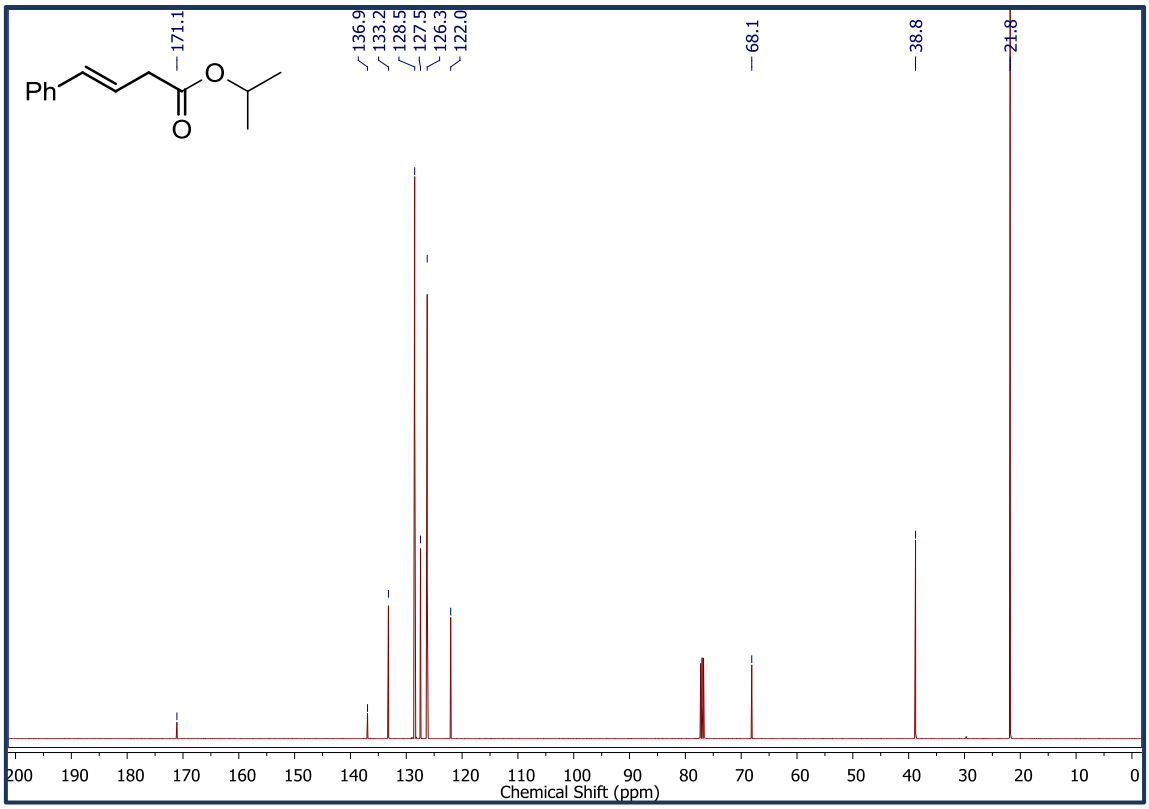
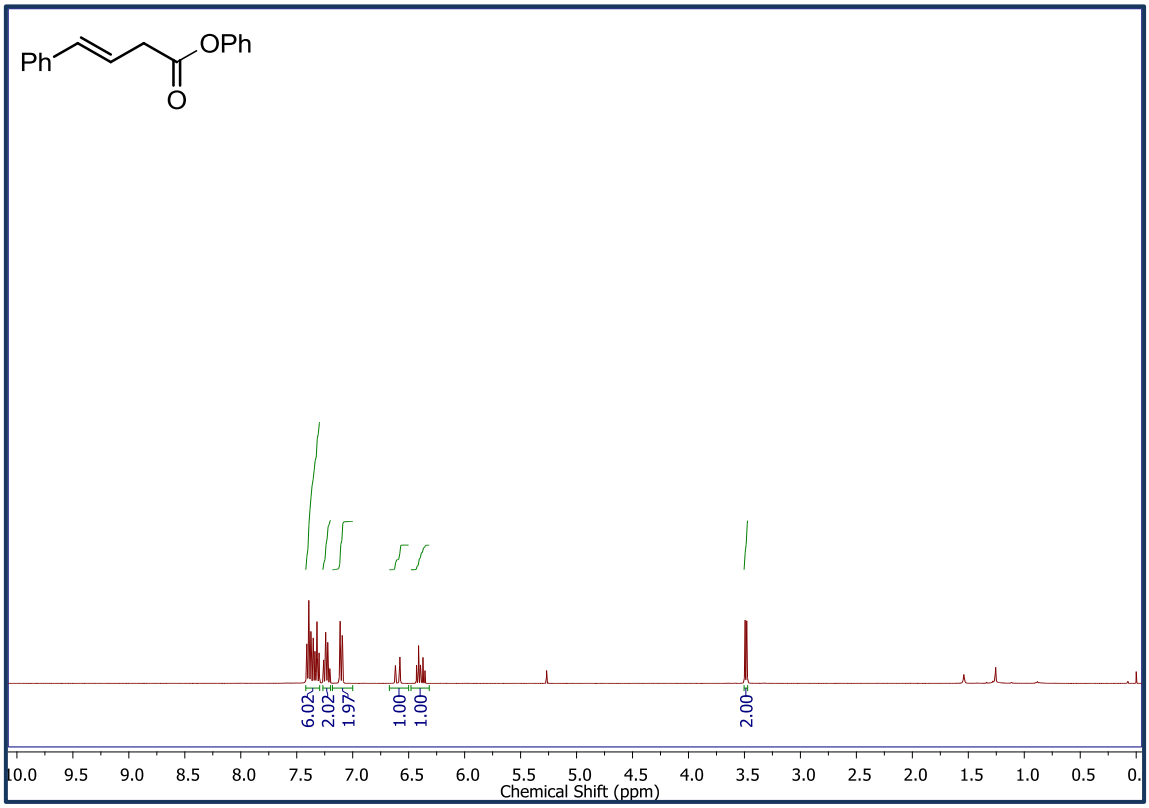
1.00
1.00
1.00
0.96
2.00
6.38
Chemical Shift (ppm)


Ph
O
O
171.1
136.9
133.2
128.5
127.5
126.3
122.0
68.1
38.8
21.8
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)


Ph
OPh
O
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2.02
1.97
1.00
1.00
2.00
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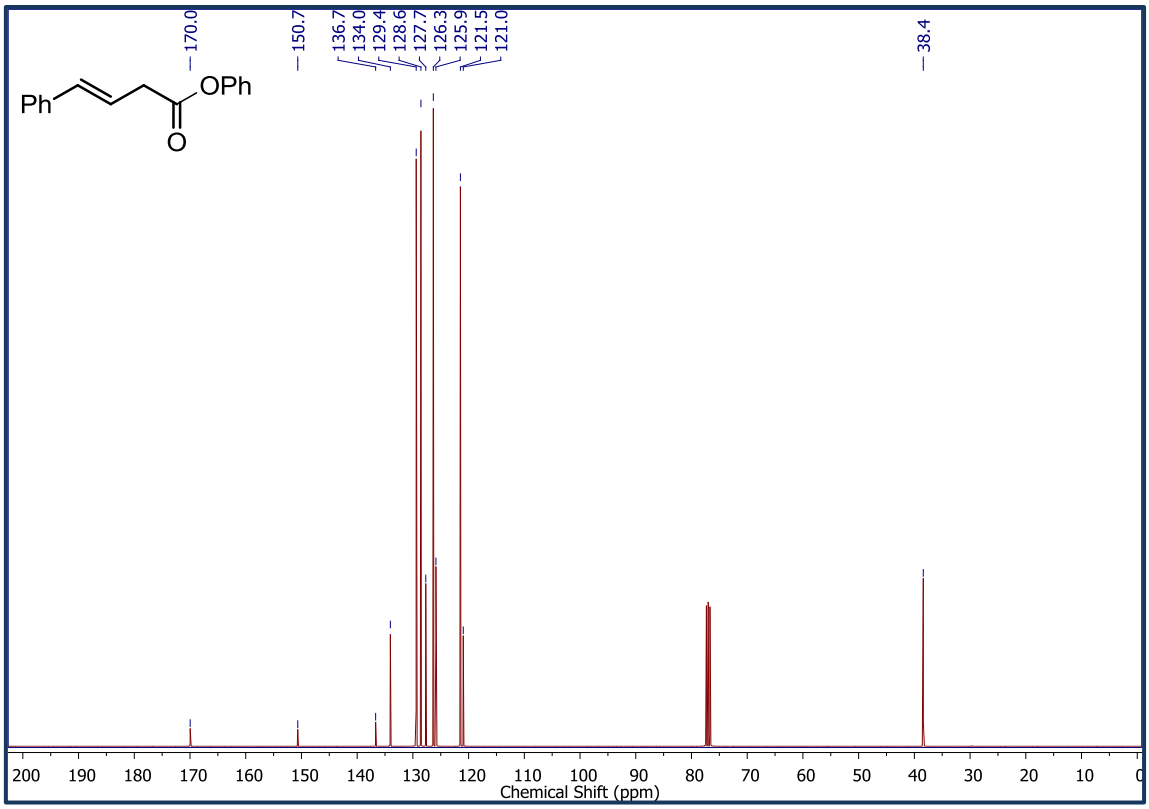
Chemical Shift (ppm)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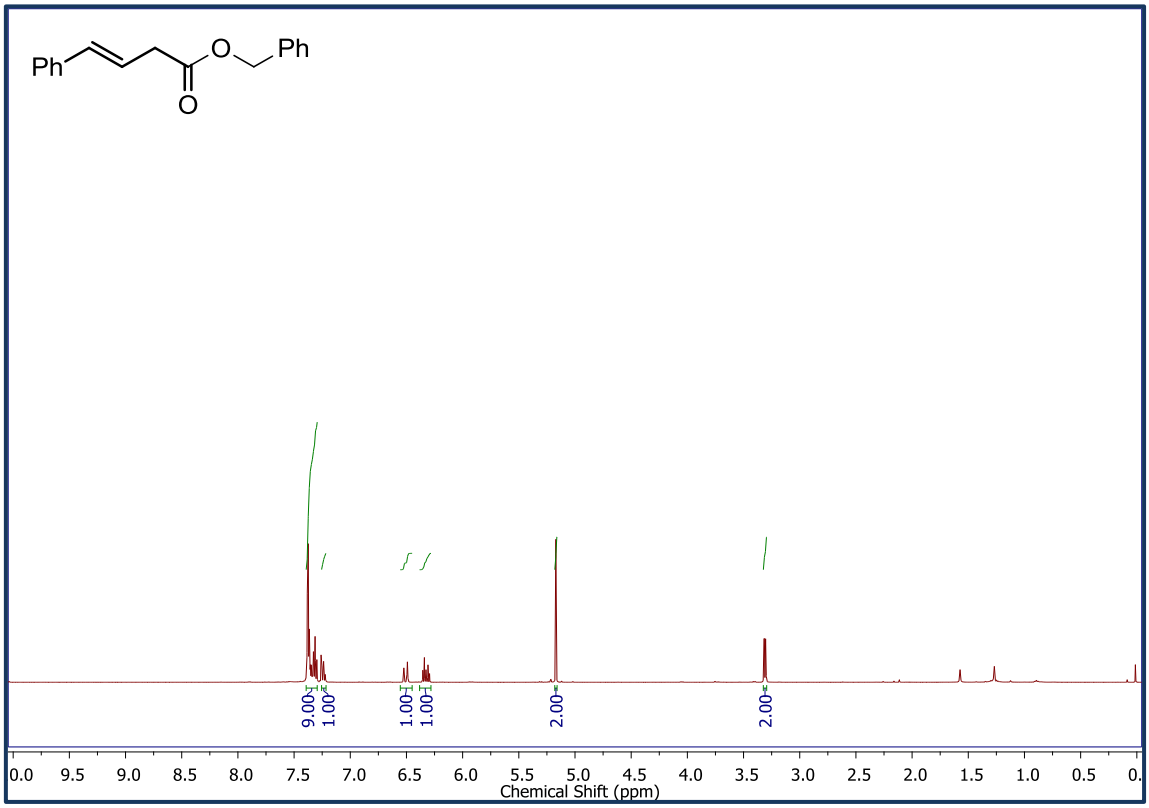
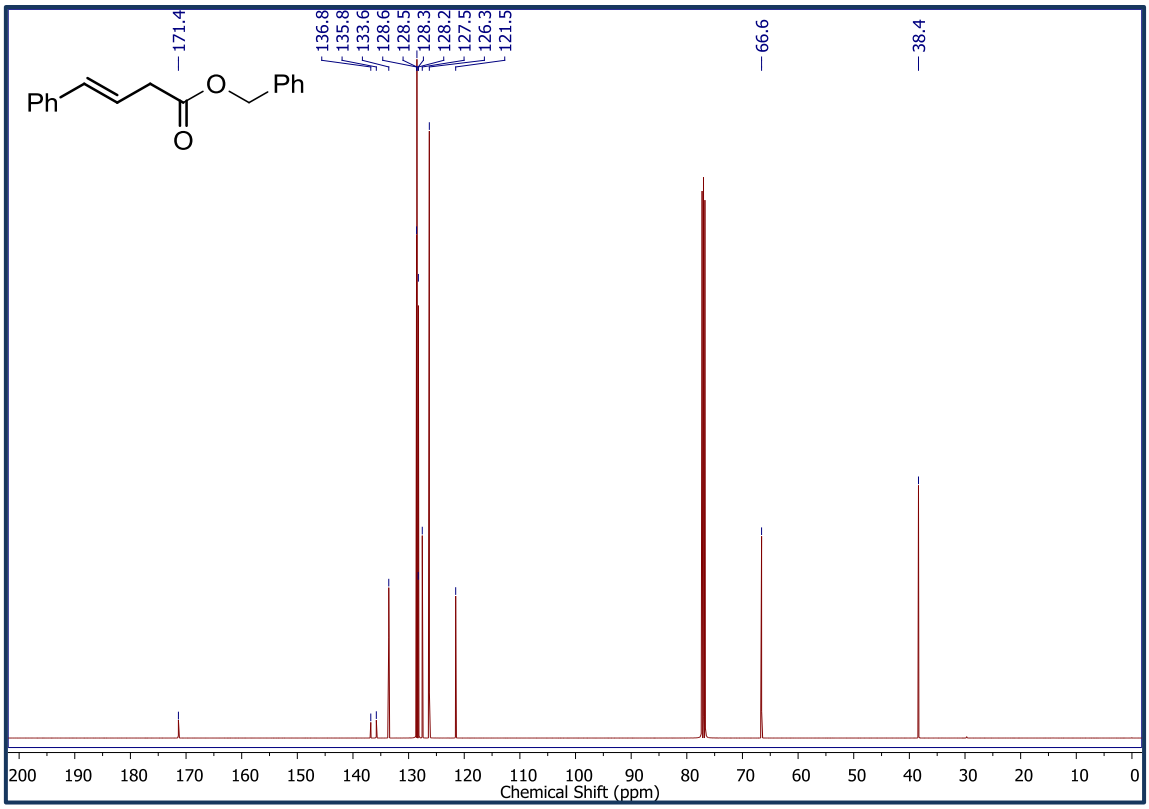
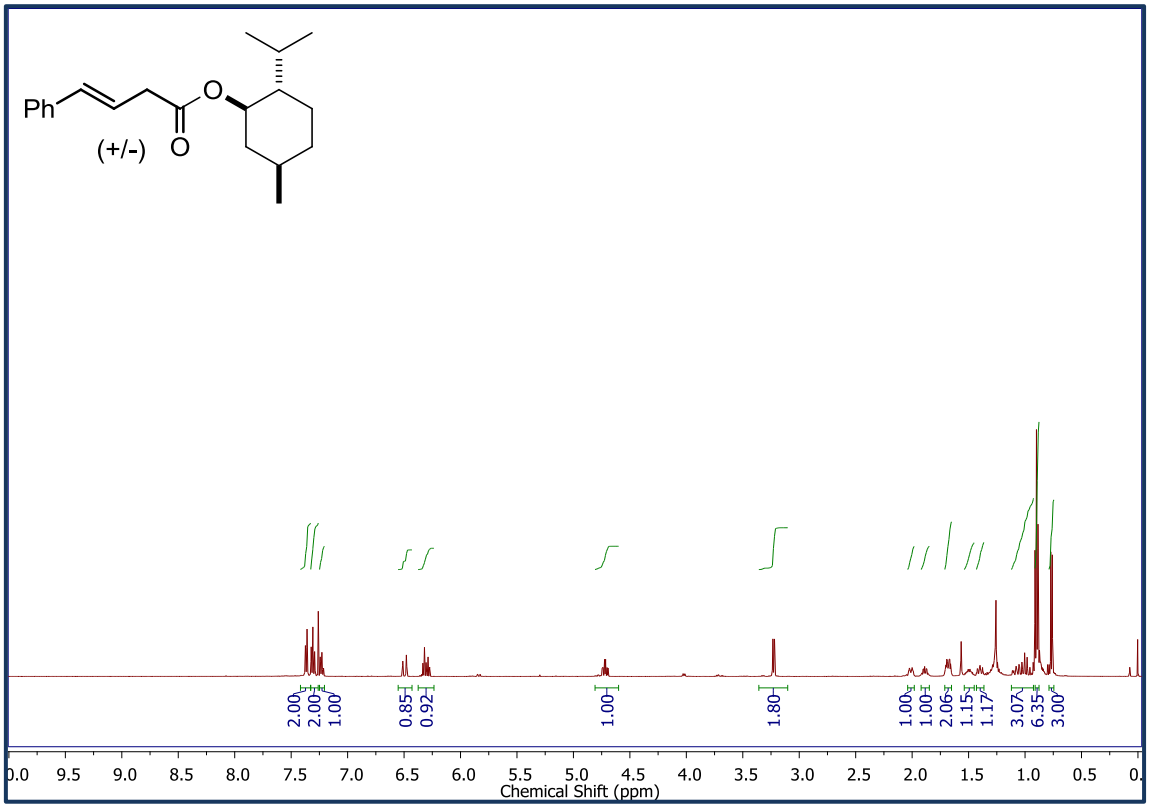
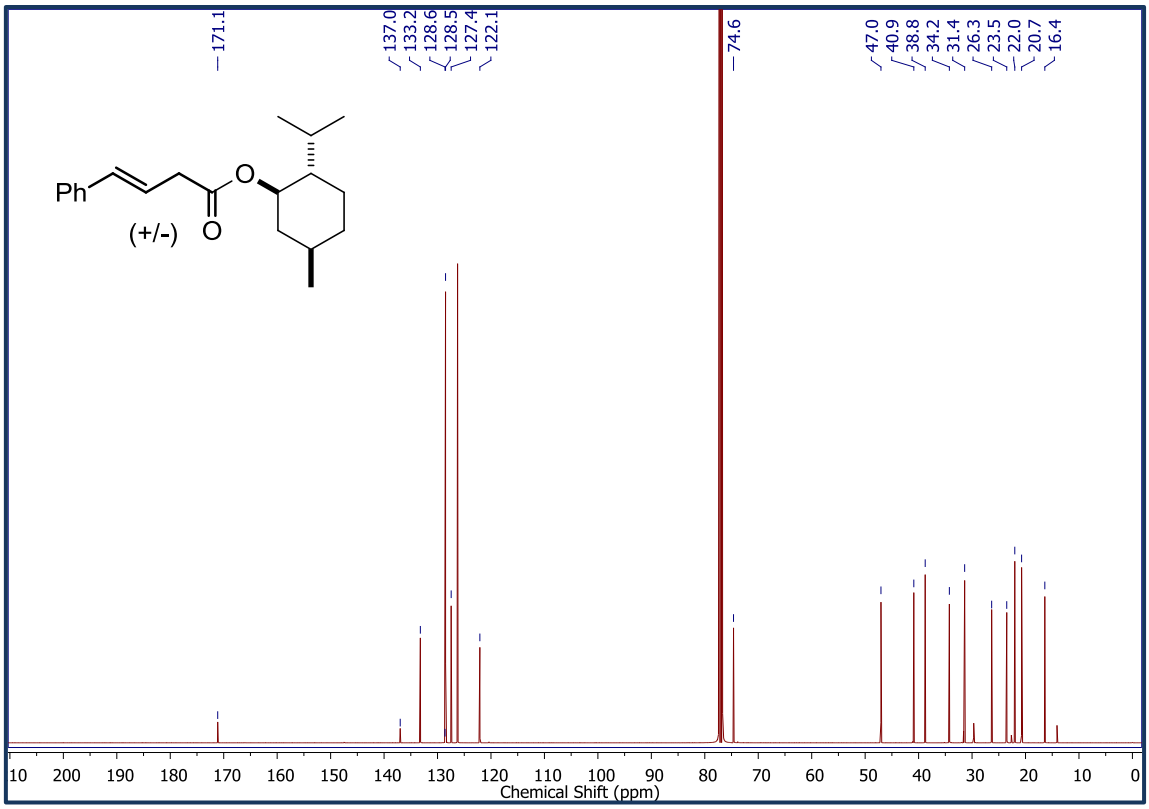
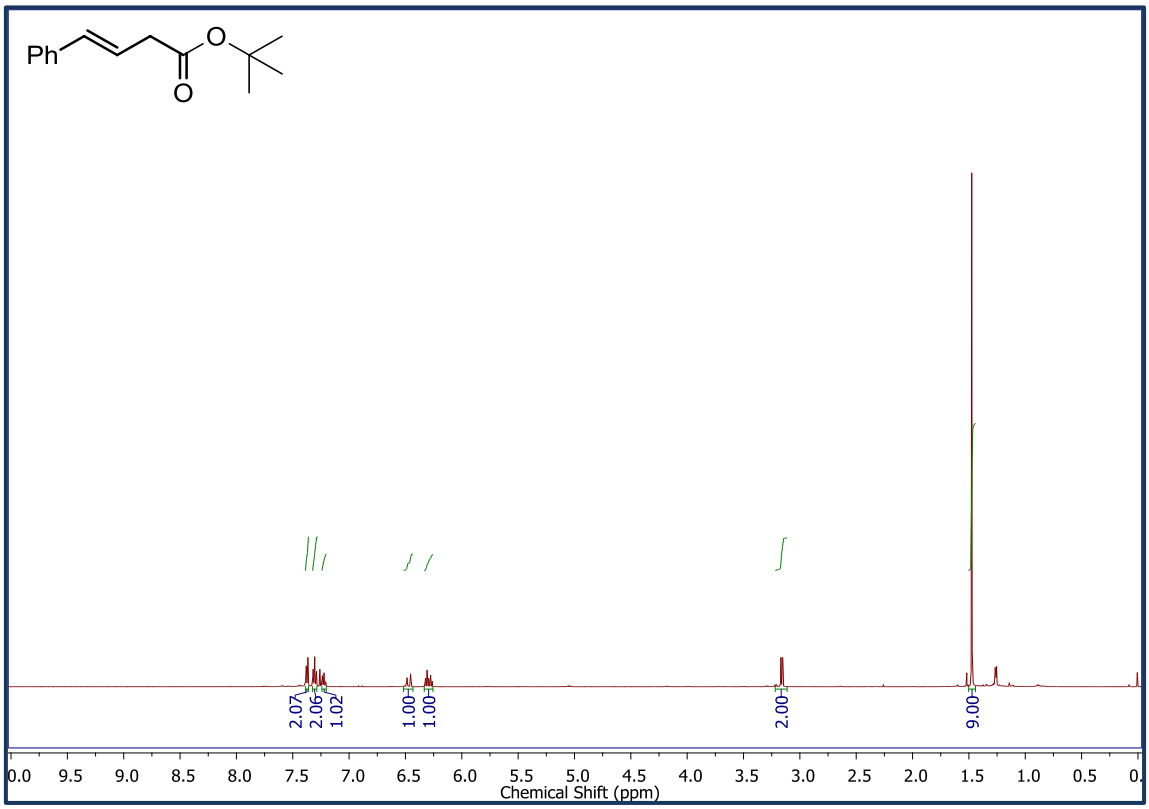
134.0
129.4
128.6
127.7
126.3
125.9
121.5
121.0
38.4
Ph
OPh
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

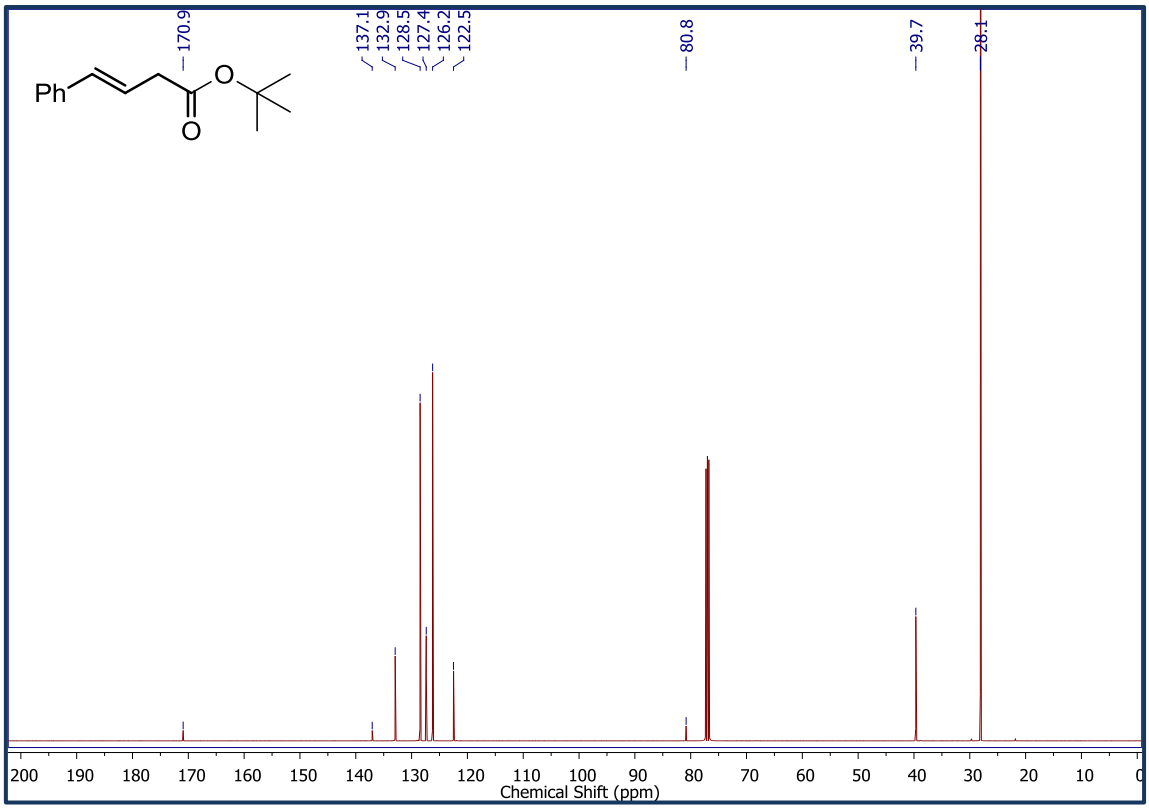

Ph
O
O
Ph
9.00
1.00
1.00
1.00
2.00
2.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
Chemical Shift (ppm)

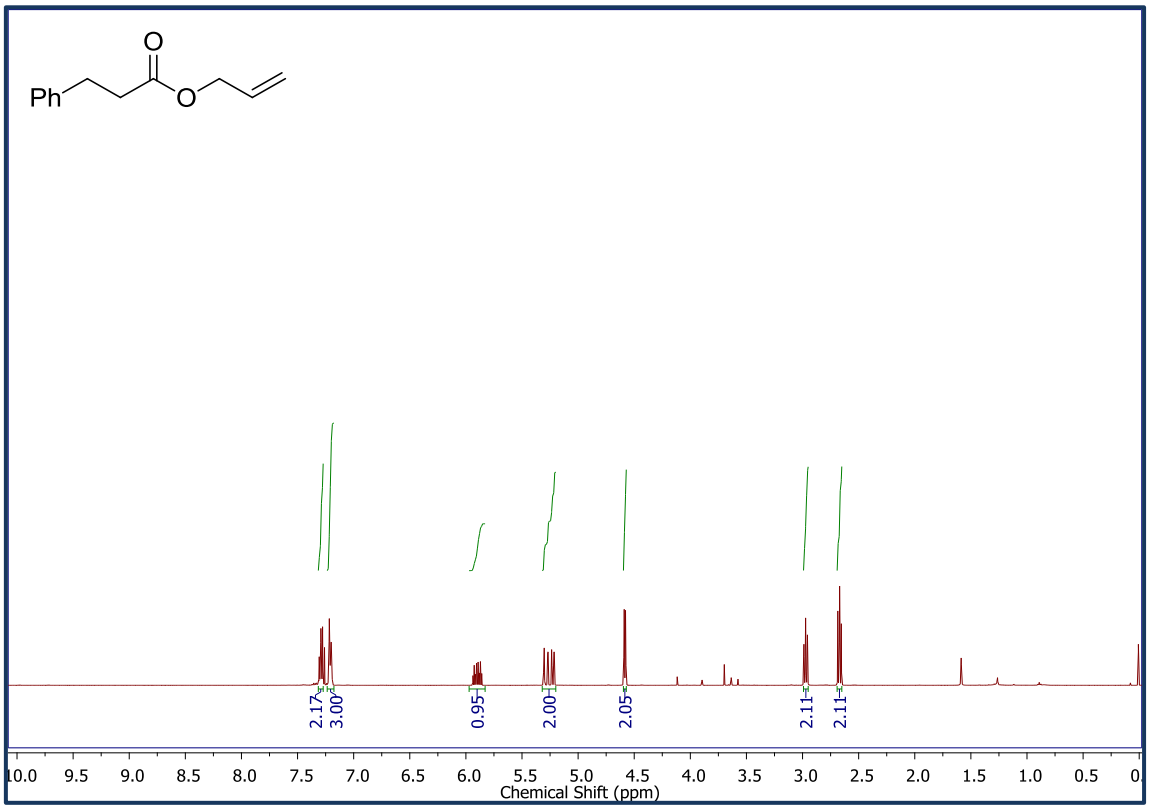

171.4
136.8
135.8
133.6
128.6
128.5
128.3
128.2
127.5
126.3
121.5
66.6
38.4
Ph
O
O
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

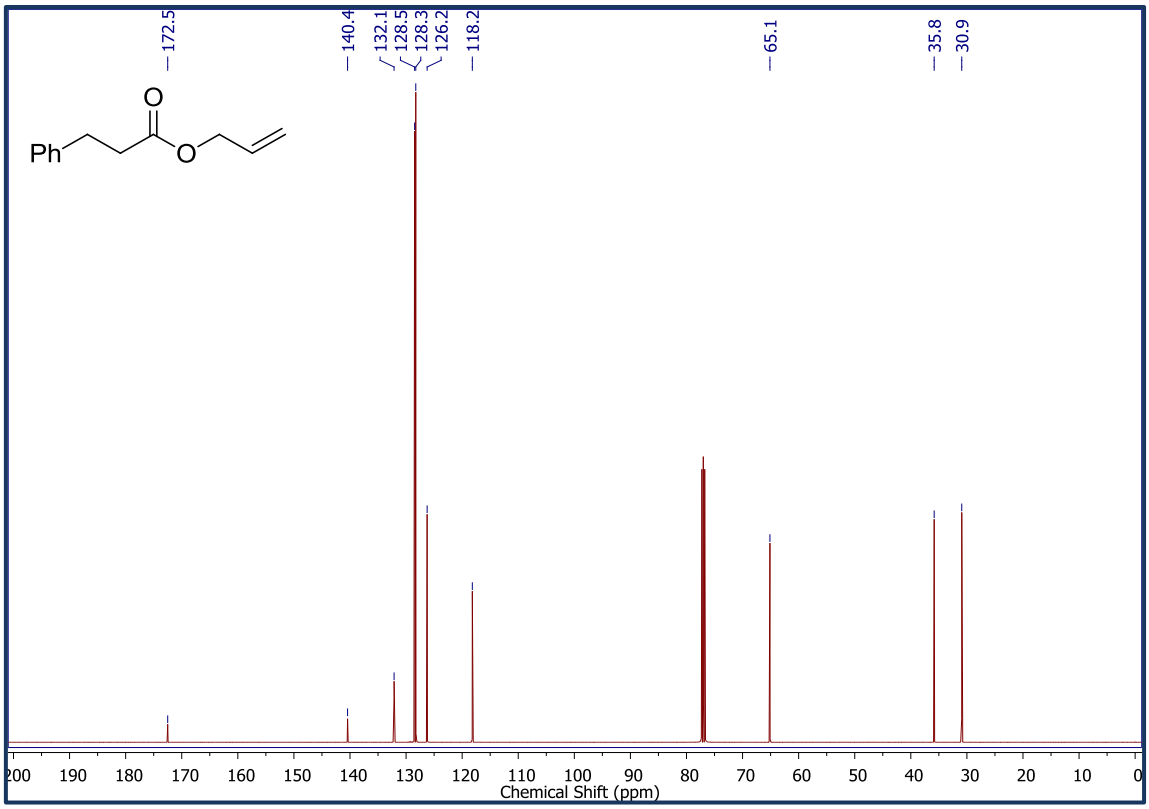

Ph
(+/-)
O
O
2.00
2.00
1.00
0.85
0.92
1.00
1.80
1.00
1.00
2.06
1.15
1.17
3.07
6.35
3.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)

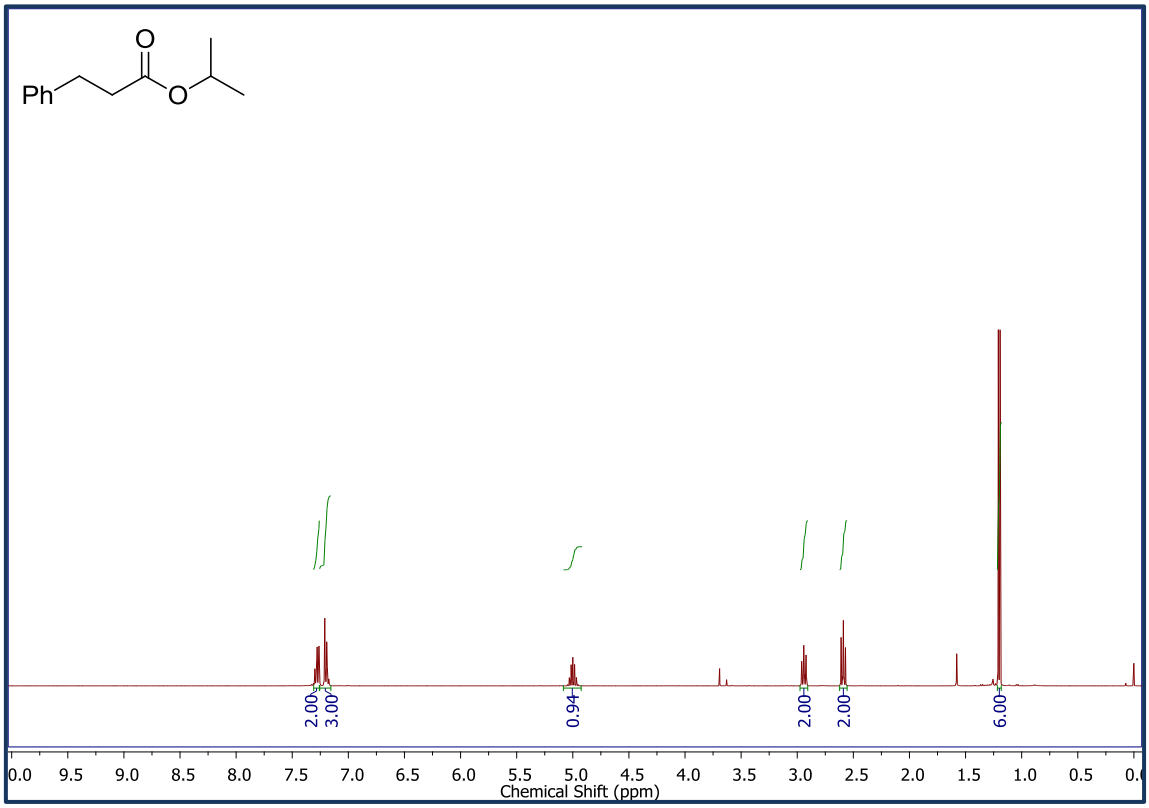

171.1
137.0
133.2
128.6
128.5
127.4
122.1
74.6
47.0
40.9
38.8
34.2
31.4
26.3
23.5
22.0
20.7
16.4
Ph
(+/-)
O
O
Chemical Shift (ppm)

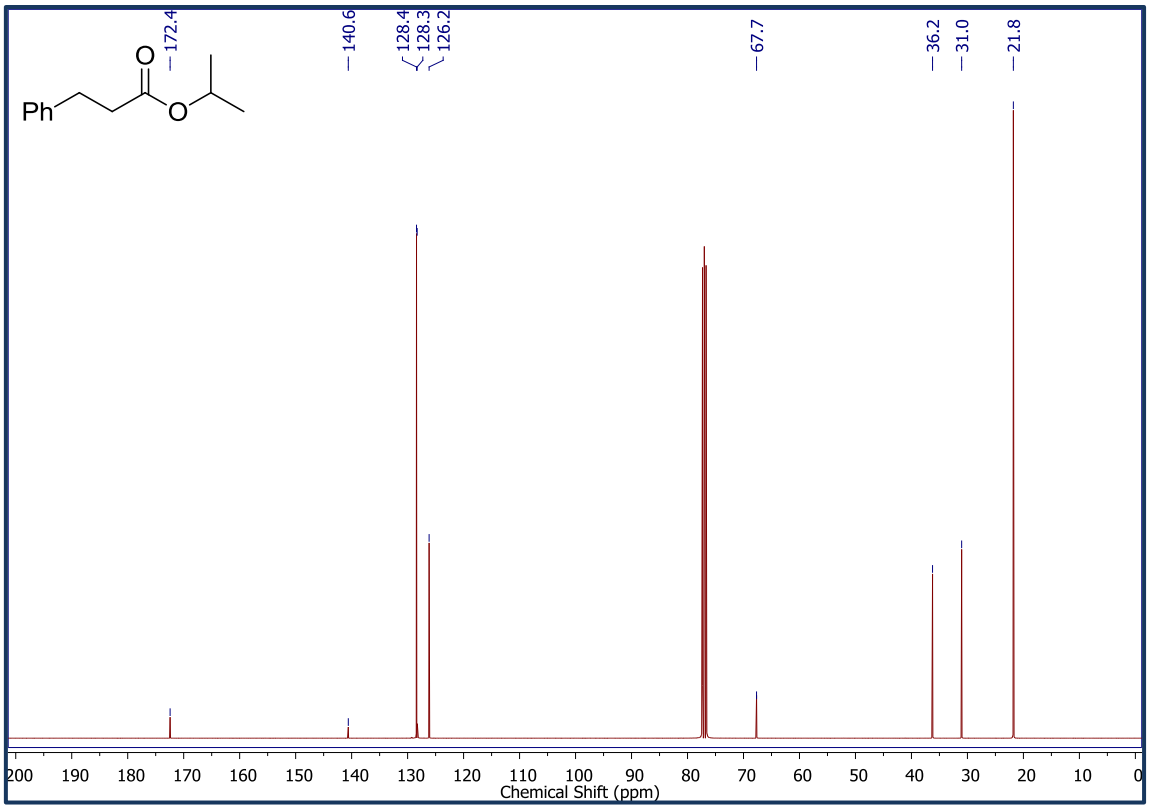

Ph
O
O
2.07
2.06
1.02
1.00
1.00
2.00
9.00
Chemical Shift (ppm)

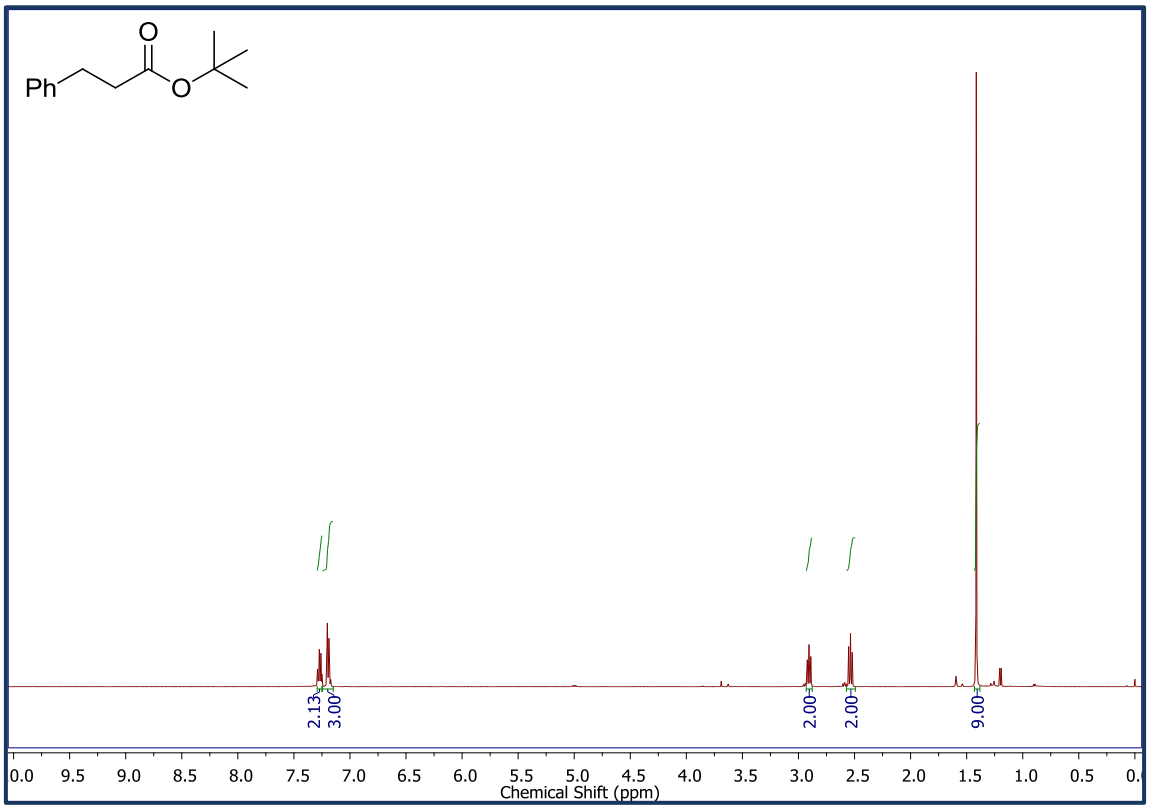

Ph
O
O
170.9
137.1
132.9
128.5
127.4
126.2
122.5
80.8
39.7
28.1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

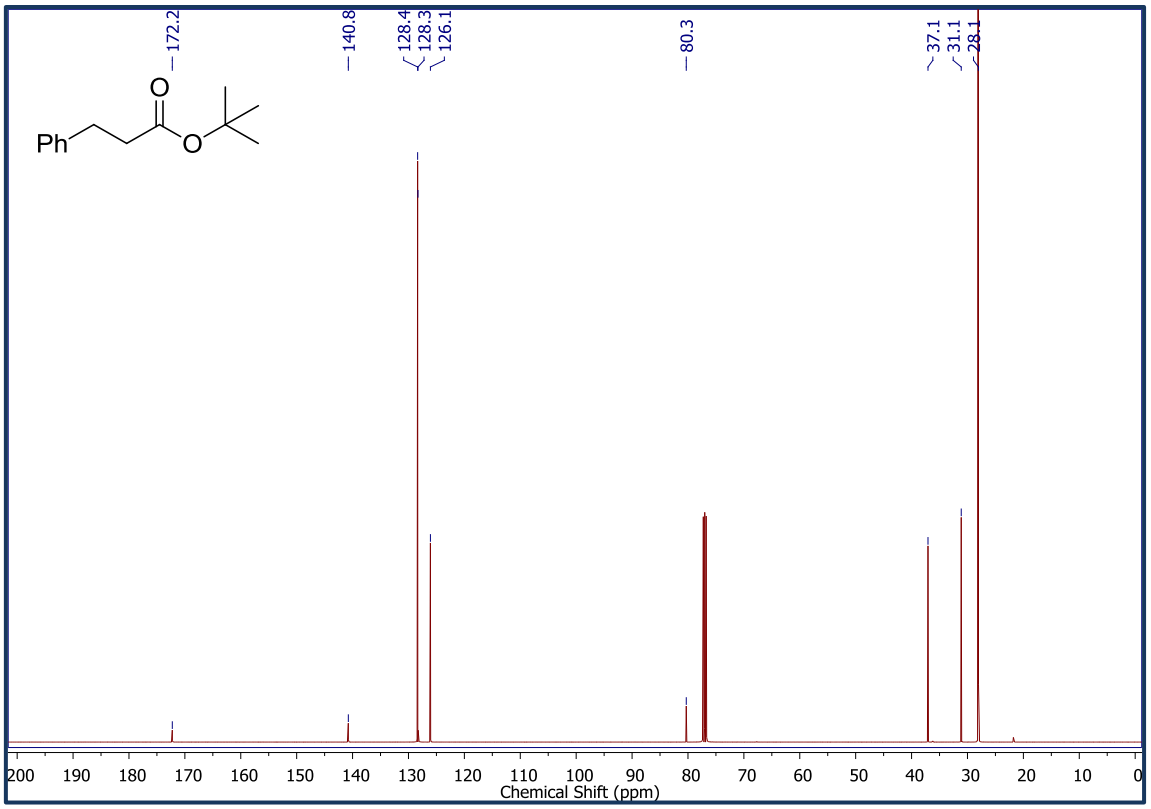

Ph
O
O
2.17
3.00
0.95
2.00
2.05
2.11
2.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

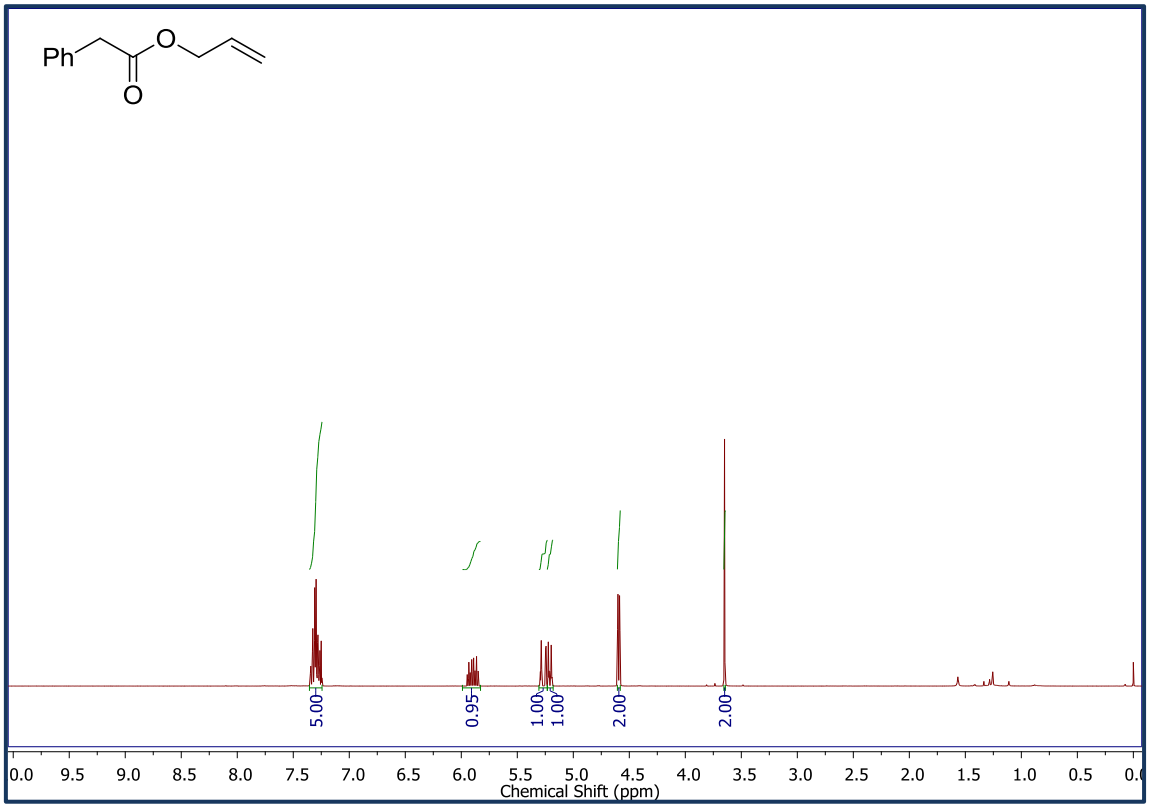

172.5
140.4
132.1
128.5
128.3
126.2
118.2
65.1
35.8
30.9
O
Ph
O
Chemical Shift (ppm)

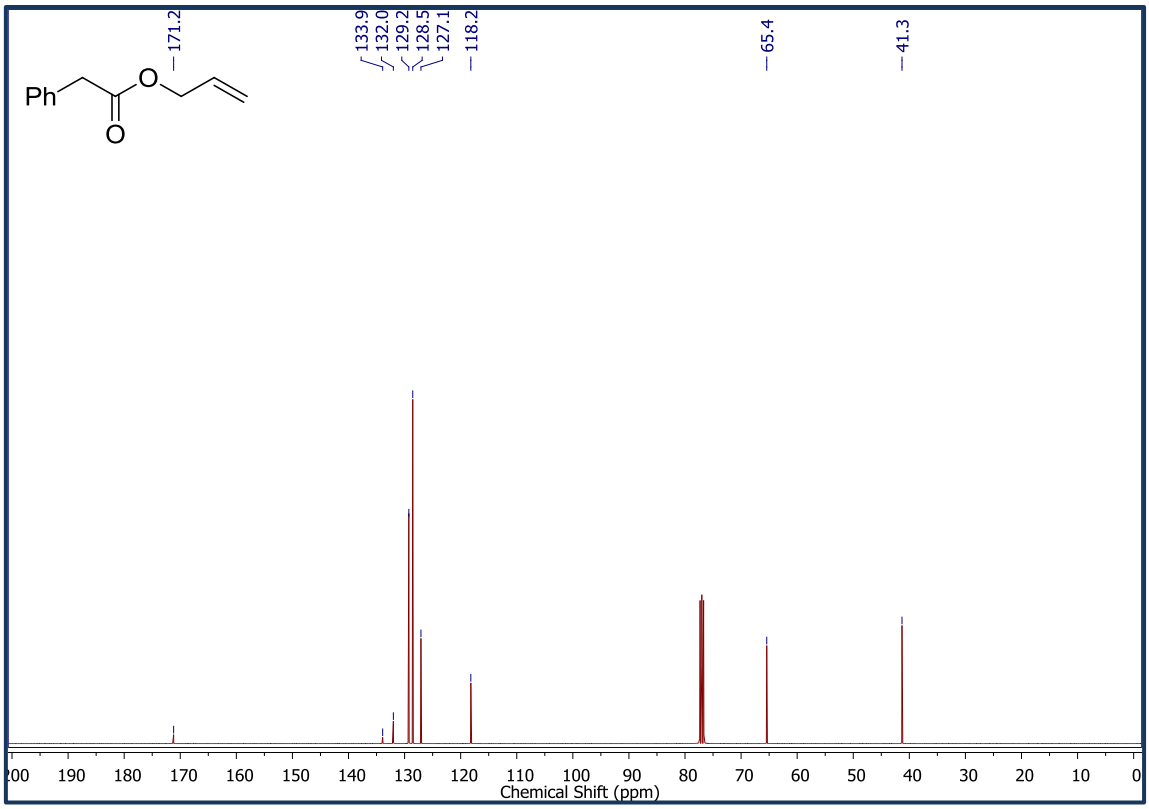

O
Ph
O
2.00
3.00
0.94
2.00
2.00
6.00
Chemical Shift (ppm)

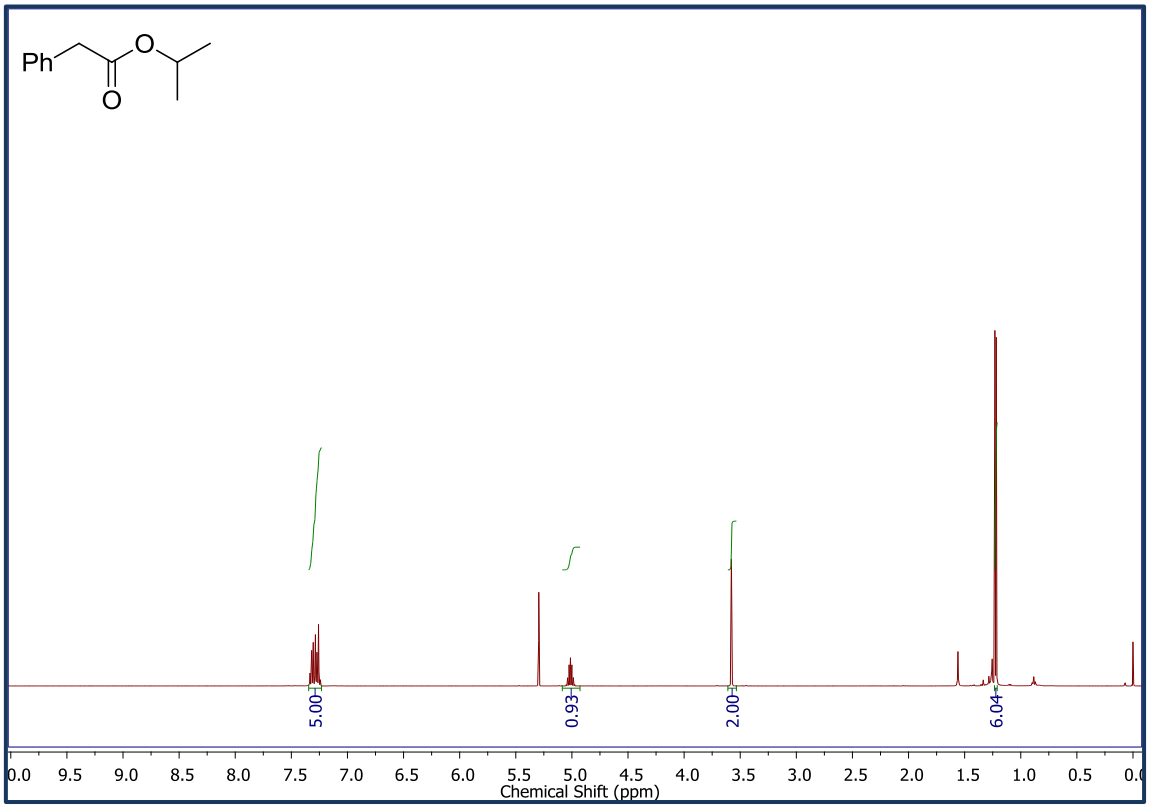

O
Ph
O
172.4
140.6
128.4
128.3
126.2
67.7
36.2
31.0
21.8
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

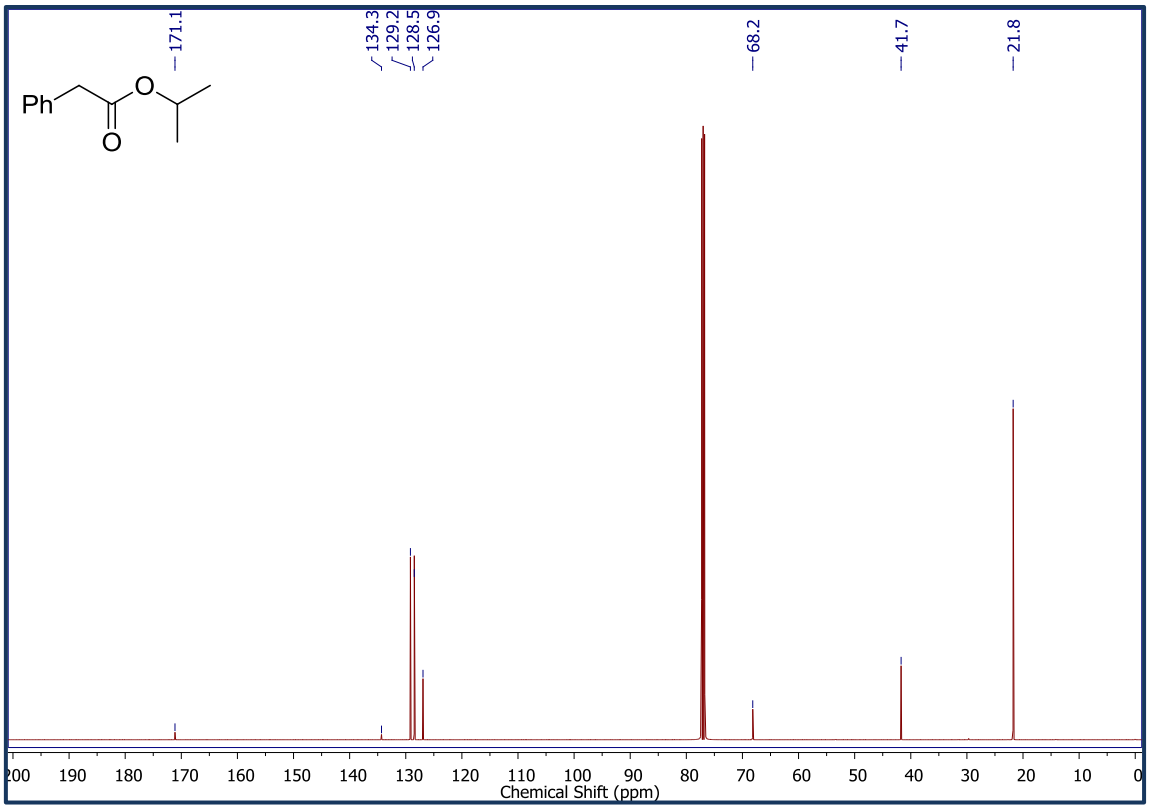

O
Ph
O
2.13
3.00
2.00
2.00
9.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
Chemical Shift (ppm)

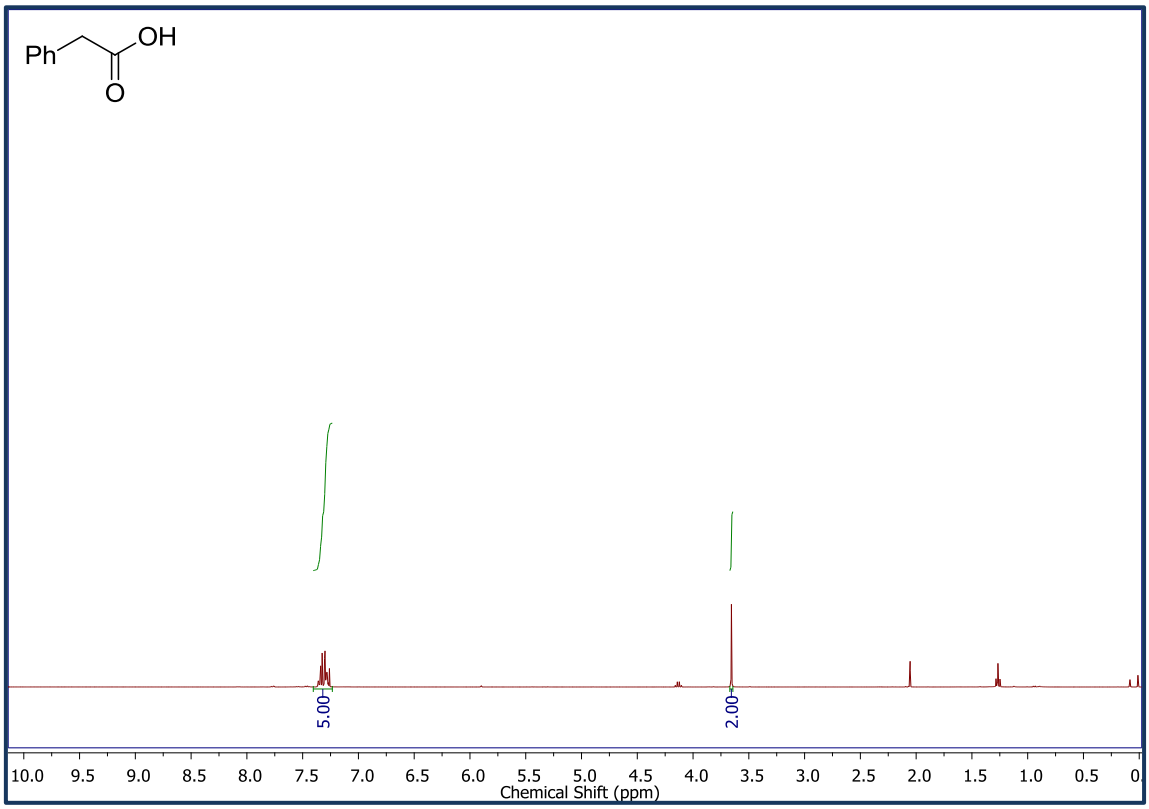

172.2
140.8
128.4
128.3
126.1
80.3
37.1
31.1
28.1
Ph
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

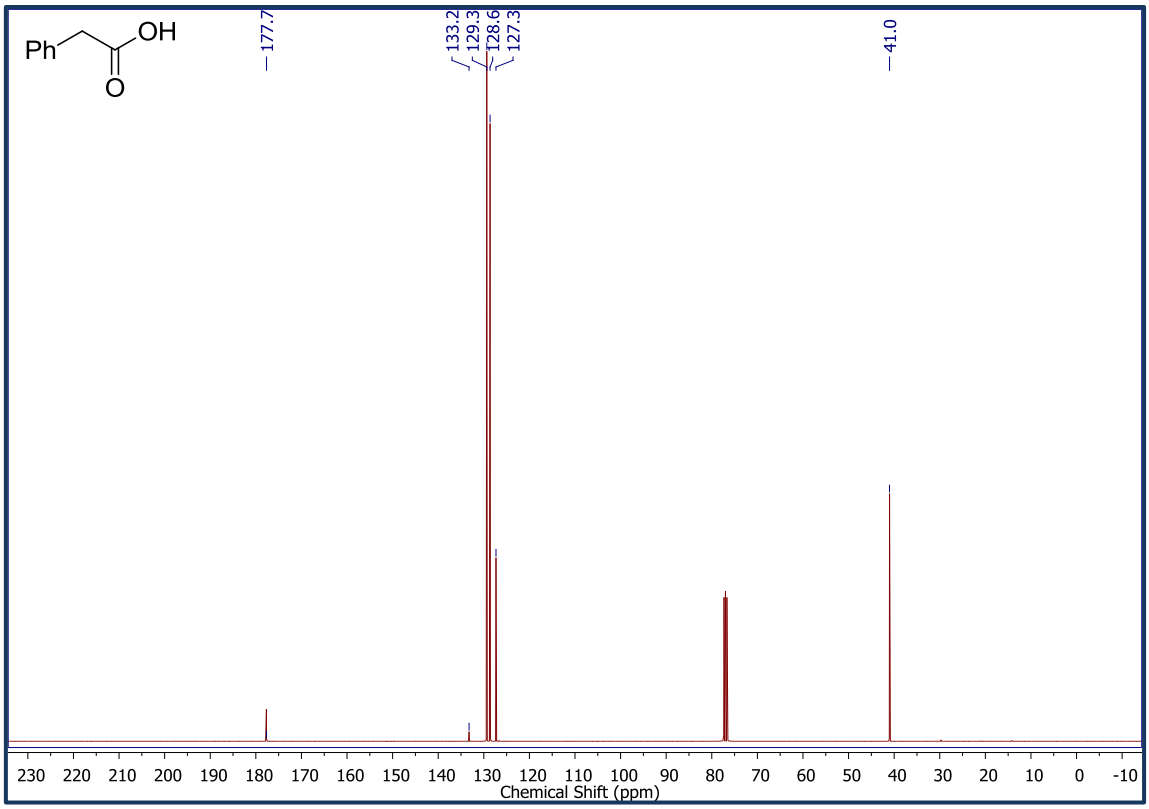

Ph
O
O
5.00
0.95
1.00
1.00
2.00
2.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical Shift (ppm)

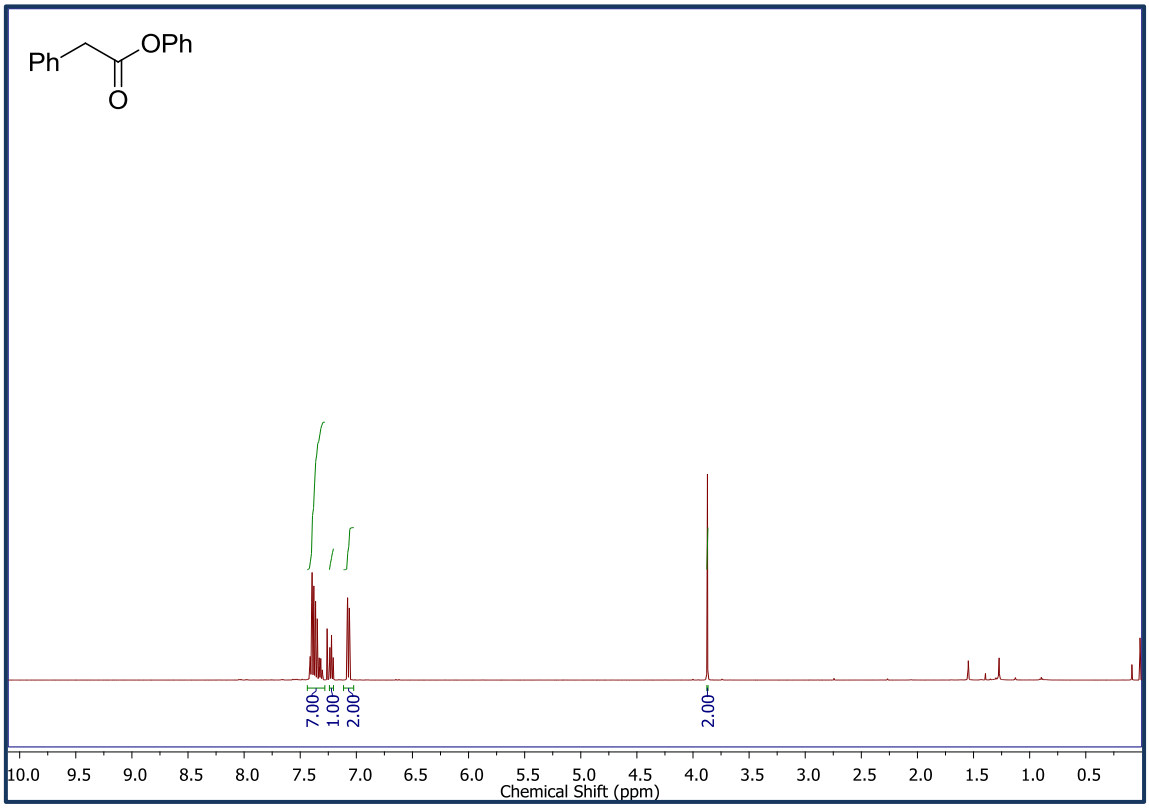

Ph
O
O
171.2
133.9
132.0
129.2
128.5
127.1
118.2
65.4
41.3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

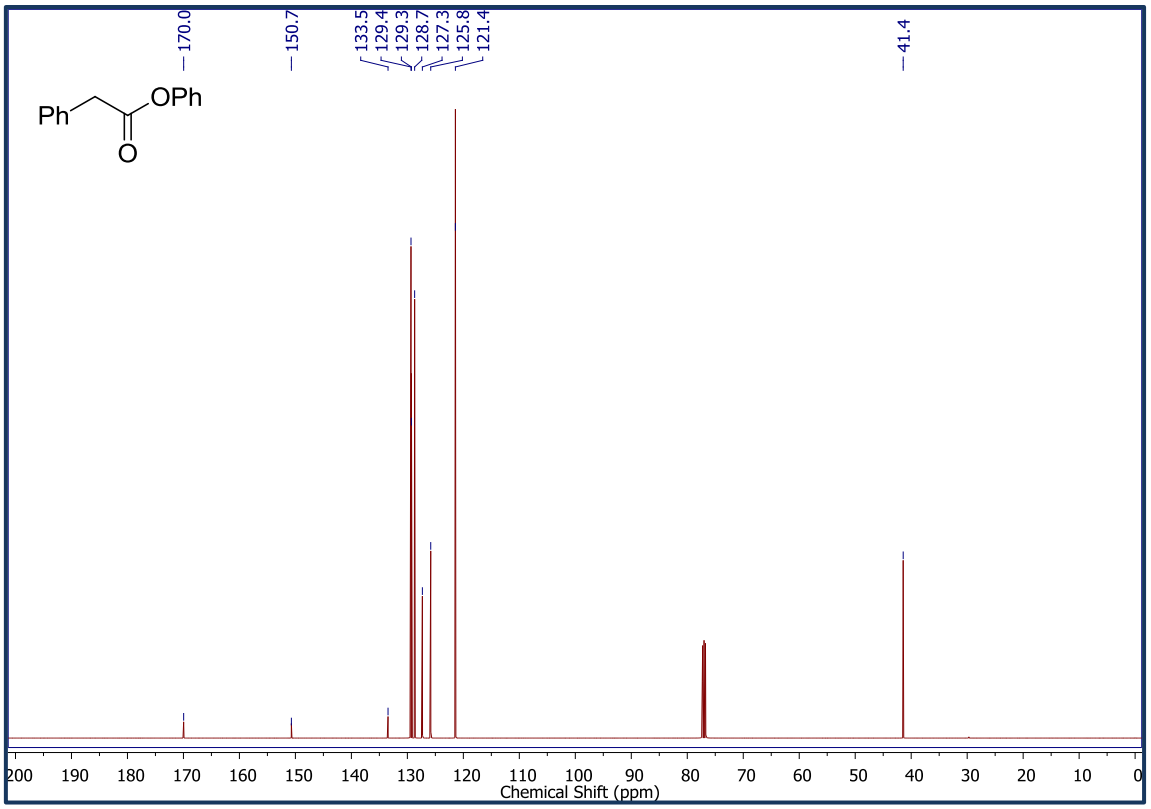

Ph
O
O
5.00
0.93
2.00
6.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical Shift (ppm)

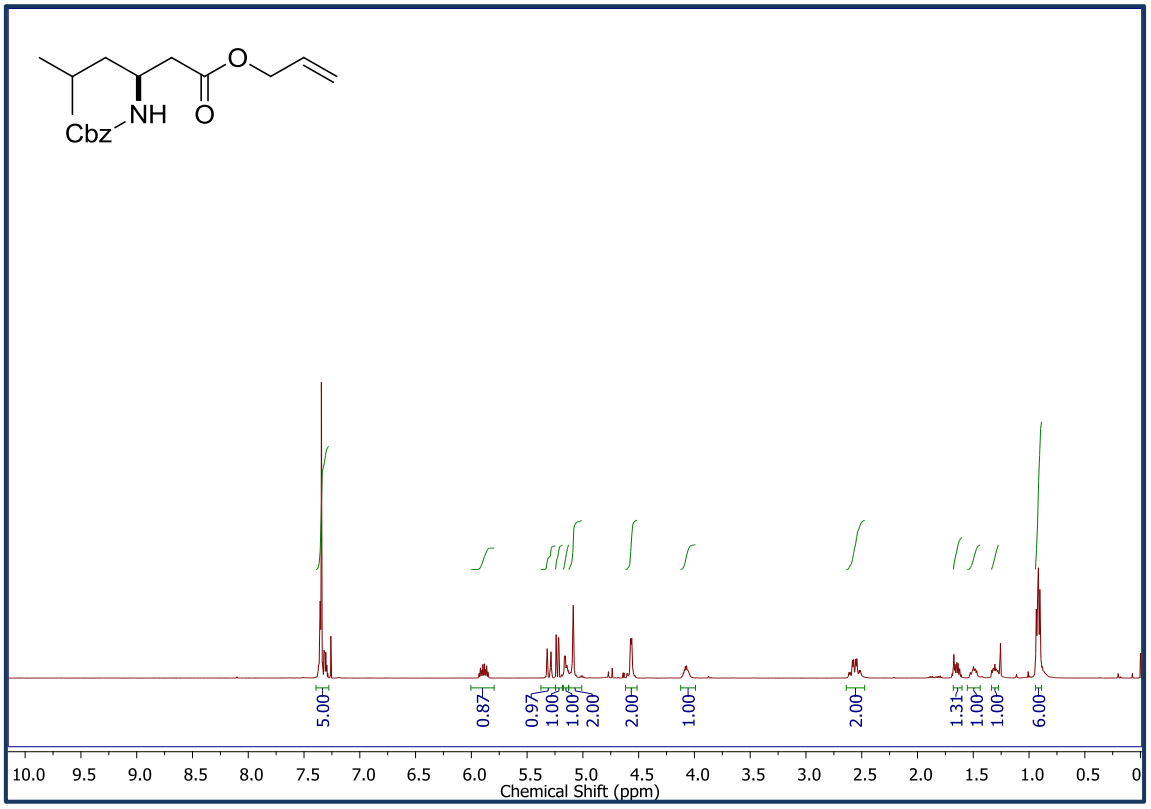

171.1
134.3
129.2
128.5
126.9
68.2
41.7
21.8
Ph
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

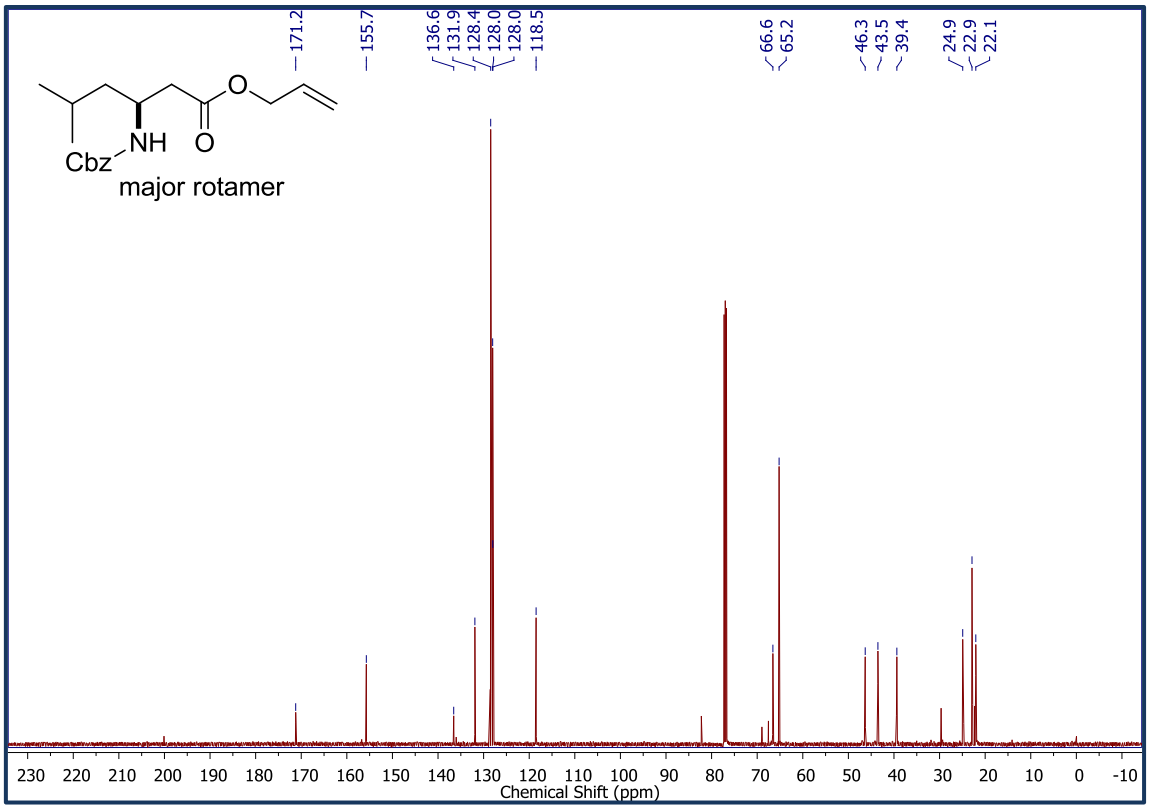

Ph
OH
O
5.00
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

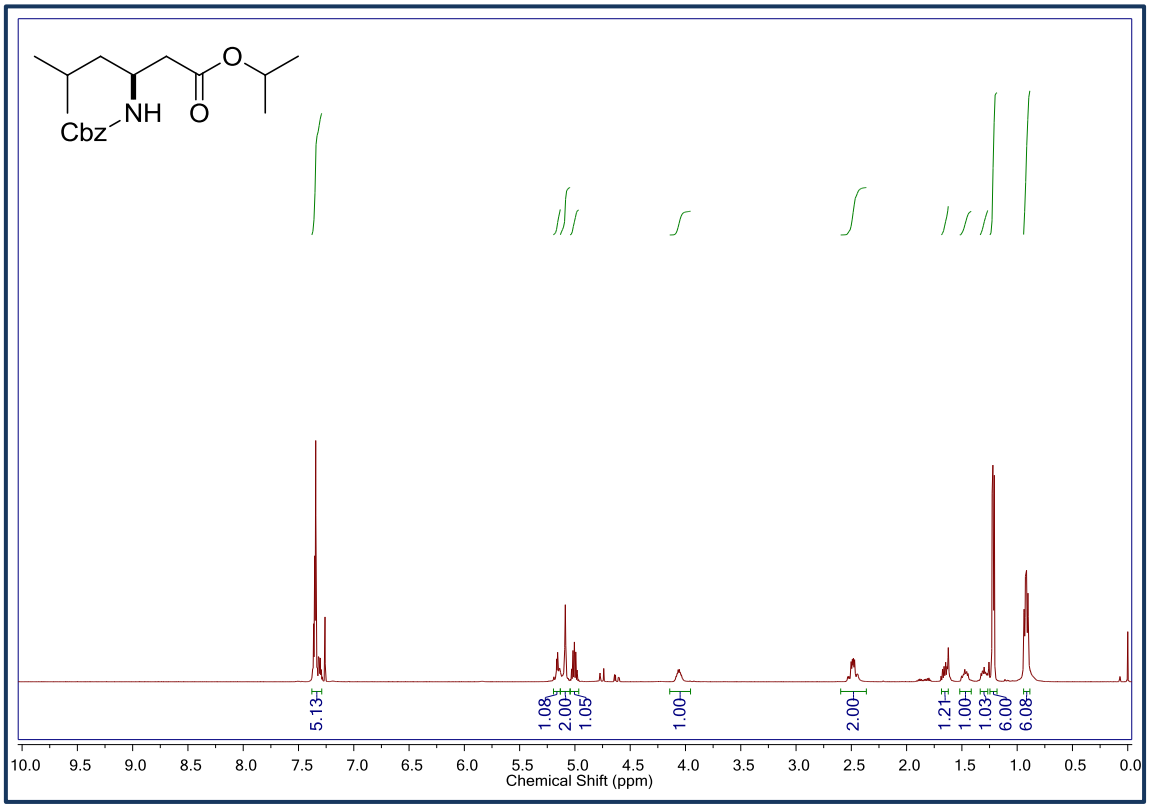

Ph
OH
O
177.7
133.2
129.3
128.6
127.3
41.0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical Shift (ppm)

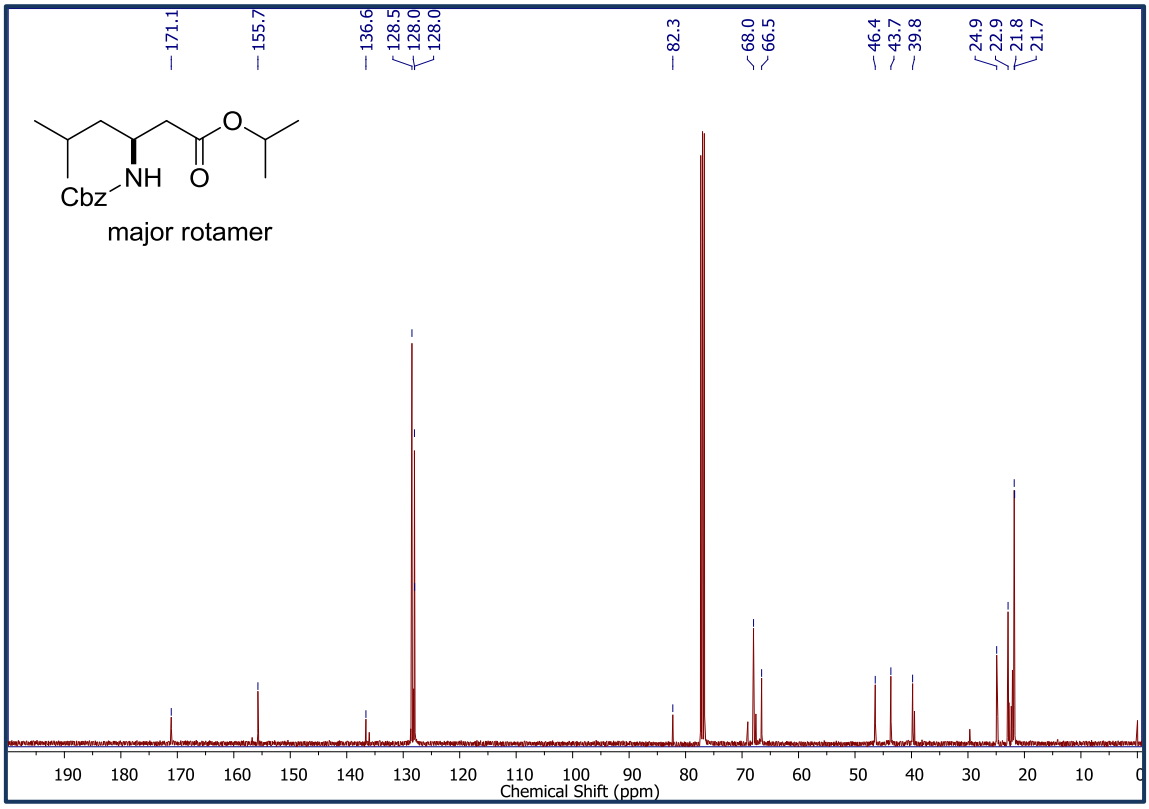

Ph
OPh
O
7.00
1.00
2.00
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)


170.0
150.7
133.5
129.4
129.3
128.7
127.3
125.8
121.4
41.4
Ph
OPh
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)


O
NH
O
Cbz
5.00
0.87
0.97
1.00
1.00
2.00
2.00
1.00
2.00
1.31
1.00
1.00
6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


171.2
155.7
136.6
131.9
128.4
128.0
128.0
118.5
66.6
65.2
46.3
43.5
39.4
24.9
22.9
22.1
O
NH
O
Cbz
major rotamer
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical Shift (ppm)


O
NH
O
Cbz
5.13
1.08
2.00
1.05
1.00
2.00
1.21
1.00
1.03
6.00
6.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical Shift (ppm)



(1) Gangjee, A.; Yang, J.; Ihnat, M. A.; Kamat, S. Antiangiogenic and antitumor agents: Design, synthesis, and evaluation of novel 2-amino-4-(3-bromoanilino)-6-benzylsubstituted pyrrolo[2,3-d]pyrimidines as inhibitors of receptor tyrosine kinases. *Bioorg. Med. Chem.* **2003**, *11*, 5155–5170.

(2) Zheng, Y.; Xu, J. Synthesis of enantiopure free and N-benzyloxycarbonyl-protected 3-substituted homotaurines from naturally occurring amino acids. *Tetrahedron* **2014**, *70*, 5197–5206.

(3) Yamamoto, N.; Obora, Y.; Ishii, Y. Iridium-Catalyzed Oxidative Methyl Esterification of Primary Alcohols and Diols with Methanol. *J. Org. Chem.* **2011**, *76*, 2937–2941.