Supplementary Material (ESI) for Chemical Communications

Electronic Supplementary Information

The non-metathetic role of Grubbs' carbene complexes: from hydrogen-free reduction of α,β–unsaturated alkenes to solid-supported sequential cross-metathesis/reduction.

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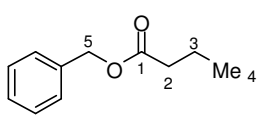
1.- Experimental Section

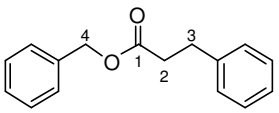
1.1.- General. Chemical reagents were purchased from commercial sources and were used without further purification unless noted otherwise. Solvents were analytical grade or were purified by standard procedures prior to use. ^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$, in the presence of TMS (0.00 ppm) as the internal standard. Conventional and gel–phase ^{13}C NMR spectra were recorded on the same apparatus at 75 MHz with $CDCl_3$ as solvent and reference (76.9 ppm). Infrared spectra (IR) were recorded on a Shimadzu Prestige 21 spectrophotometer and only partial spectral data are listed. Analytical thin–layer chromatography (TLC) was carried out with silica gel 60 F254 pre–coated aluminum sheets. Flash column chromatography was performed using silica gel 60 (230–400 mesh). Microwave irradiations were performed on a CEM Discover LabMate reactor and the reaction temperature was measured with the internal infrared control system from the apparatus. Compounds **8**,[1] **10**,[2] have been prepared by standard protocols. Syntheses of solid-supported compounds **17**, **24** and **27** have been already published.[3-5]

1.2.- General Procedure 1: Olefin Reduction in Homogeneous Phase. Starting material (0.15 mmol) was placed in a 10 mL microwave vessel and dissolved in anhydrous DCM (2.0 mL). Triethylsilane (5 eq) and Grubbs' second generation catalyst (5 mol%) were added. Vessel was capped with the corresponding septum and placed in the microwave reactor. The mixture was magnetically stirred and irradiated under closed vessel conditions at 150 ºC (P_{max}= 300W) for 30 min. Solvent was evaporated and reaction product was purified through liquid flash column chromatography (hexane-AcOEt).

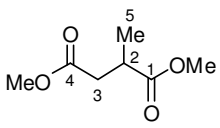


Benzyl Butyrate (3): employing General Procedure 1, with benzyl crotonate (**2**) (35.6 mg, 0.20 mmol) as starting material, desired product **3** was isolated in 96% yield. Characterization of **3**:[6] IR (film): ν_{max} (cm^{-1}) 2966, 1737, 1456, 1172. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.45–7.35 (m, 5H, ArH), 5.13 (s, 2H, H5), 2.35 (t, *J*= 7.3 Hz, H2), 1.68 (sextet, *J*= 7.3 Hz, 2H, H3), 0.96 (t, *J*= 7.3 Hz, 3H, Me). ^{13}C NMR

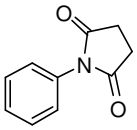
($CDCl_3$, 75 MHz): δ 173.4, 160.6, 136.0,128.4, 128.0, 65.9, 36.1, 18.3, 13.5. HRMS (ESI) m/z 201.0880 [(M + Na^+); calcd for $C_{11}H_{14}O_2Na$: 201.0886].



Benzyl phenylpropionate (5): (*E*)-cinnamic acid (350.0 mg, 2.5 mmol) was dissolved in MeOH (10.0 mL) and water was added (1.0 mL). At 0°C, pH was adjusted to neutrality by addition of aqueous 20% Cs_2CO_3 (425 mg/2.5 mL). Volatiles were removed in vacuum and the residue was resuspended in anhydrous DMF (5.0 mL). Solvent was evaporated under reduced pressure and resuspended again in anhydrous DMF (5.0 mL). Benzyl bromide (330 µL, 1.1 eq) was added and reaction was magnetically stirred at r.t. for 16 h. Reaction mixture was poured into water (23.0 mL) and 1.4 g NaCl was added. After extraction with Et_2O (4 x 14.0 mL), the collected organic phases were washed with water (2 x 2.8 mL) and brine (1 x 2.8 mL), and dried over anhydrous $MgSO_4$. Solvent was evaporated under reduced pressure and the crude product was purified by column flash chromatography (hexane–AcOEt) to obtain benzyl cinnamate (**4**) (562.3 mg) in 96% yield. Characterization of **4**:[7] IR (film): ν_{max} (cm^{-1}) 1709, 1638, 1312, 1162, 981. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.75 (d, *J*= 16.1 Hz, 1H, H3), 7.60–7.20 (m, 10H, ArH), 6.50 (d, *J*= 16.1 Hz, 1H, H2), 5.27 (s, 2H, H4). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.6, 145.0, 135.9, 134.2, 130.2, 128.7, 128.5, 128.1, 128.0, 117.7, 66.2. HRMS (ESI) m/z 261.0882 [(M + Na^+); calcd for $C_{16}H_{14}O_2Na$: 261.0886]. Employing General Procedure 1, with benzyl cinnamate (**4**) (41.0 mg, 0.17 mmol) as starting material, desired product **5** was isolated in 73% yield. Characterization of **5**:[8-9] IR (film): ν_{max} (cm^{-1}) 2954, 1736, 1497, 1454, 1160. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.30–7.20 (m, 10H, ArH), 5.12 (s, 2H, H4), 2.99 (t, *J*= 7.3 Hz, 2H, H3), 2.70 (t, *J*= 7.3 Hz, 2H, H2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.7, 140.4, 135.9, 128.6, 128.5, 128.3, 128.2, 126.3, 66.3, 35.9, 31.0. HRMS (ESI) m/z 263.1045 [(M + Na^+); calcd for $C_{16}H_{16}O_2Na$: 263.1043].

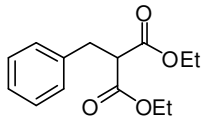


Dimethyl 2-methylsuccinate (7): Employing General Procedure 1, with dimethylitaconate (**6**) [(42.3 mg, 0.27 mmol), ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.29 (d, *J*= 1.0 Hz, 1H, vinylic), 5.68 (d, *J*= 1.0 Hz, 1H, vinylic), 3.73 (s, 3H, OMe), 2.66 (s, 3H, OMe), 3.31 (s, 2H, H3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.9, 166.4, 133.5, 128.3, 51.9, 51.8, 37.3] as starting material, desired product **7** was isolated in 84% yield. Characterization of **7**:[10] IR (film): ν_{max} (cm^{-1}) 2956, 1733, 1438, 1193, 1167. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.68 (s, 3H, OMe), 3.67 (s, 3H, OMe), 2.91 (sextet, *J*= 7.3 Hz, 1H, H2), 2.73 (dd, *J*= 16.5 Hz, *J*= 8.1 Hz, 1H, H3), 2.39 (dd, *J*= 6.0 Hz, *J*= 16.5 Hz, H3'), 1.21 (d, *J*= 7.0 Hz. 3H, H5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.7, 172.3, 51.9, 51.7, 37.4, 35.7, 17.0. HRMS (ESI) m/z 183.0624 [(M + Na^+); calcd for $C_7H_{12}O_4Na$: 183.0628].

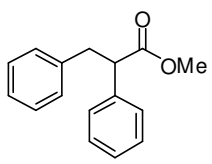


1-phenylpyrrolidine-2,5-dione (9): Maleic anhydride (2.0 g, 20 mmol) was placed in a 50 mL round-bottomed flask and dissolved in Et_2O (25 mL). After dissolution, a solution of aniline is added via cannula (1.8 mL, 1.9 g, 20 mmol / Et_2O, 2.0 mL). Mixture was stirred for 1 h at room temperature. Reaction was cooled to 15°C, crystals were collected by filtration and placed in a 50 mL erlenmeyer. Acetic anhydride (6.7 mL) and sodium acetate (650 mg) were added and the suspension was heated in a water bath for 30 min obtaining a solution. When the mixture reached room temperature was poured into ice-water (13 mL). Precipitate was filtered and washed with ice-water (3 x 5.0 mL) and hexane (5.0 mL). Crystals were dried in vacuum and recrystallized from cyclohexane to obtain *N*-phenyl maleidimide (**8**) (2.14 g) in 76% yield. Characterization of **8**:[1] Yellow needles, mp: 88–89 °C. IR (film): ν_{max} (cm^{-1}) 3458, 3106, 1709, 1508, 1393, 1146. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.50–7.20 (m, H5, ArH), 6.84 (s, 2H, vinylics). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.4, 134.0, 131.1, 129.0, 127.8, 125.9. HRMS (ESI) m/z 196.0363 [(M + Na^+); calcd for $C_{10}H_7NO_2Na$: 196.0369]. Employing General Procedure 1, with 1-phenyl-1*H*-pyrrole-2,5-dione (**8**) (38.2 mg, 0.22 mmol) as starting material, desired product **9** was isolated in 75% yield. Characterization of **9**: IR (film): ν_{max} (cm^{-1}) 3472, 2938, 1695, 1393, 1189. ^{1}H NMR ($CDCl_3$, 300 MHz): δ

7.50–7.20 (m, 5H, ArH), 2.84 (s, 4H, CH_2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.0, 131.7, 129.0, 128.4, 126.3, 28.2. HRMS (ESI) m/z 198.0521 [(M + Na^+); calcd for $C_{10}H_9NO_2Na$: 198.0525].

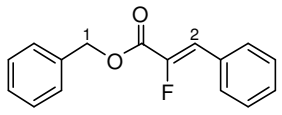


Diethyl 2-benzylmalonate (11): Diethyl malonate (9.5 mL), benzaldehyde (7.3 mL), piperidine (700 µL) and anhydrous benzene (20.0 mL) were placed in a round-bottomed flask. A 4 Å molecular sieve loaded Dean-Stark trap was fitted and reaction was refluxed for 16 h. Benzene was added (10.0 mL) and the mixture was washed with water (2 x 10 mL), HCl 1N (2 x 10 mL), and saturated $NaHCO_3$ (2 x 10 mL). Organic phase was dried over $MgSO_4$ and solvent was evaporated under reduced pressure. Crude product was distillated under reduced pressure to obtain diethyl 2-benzylidenemalonate (**10**) (14.8 g) in 95% yield. Characterization of **10**:[2] IR (film): ν_{max} (cm^{-1})2983, 1729, 1722, 1626, 1259, 1214, 1199. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.73 (s, 1H, Hβ), 7.45–7.35 (m, 5H, ArH), 4.33 (q, *J*= 7.2 Hz, 2H, O–CH_2), 4.30 (q, *J*= 7.2 Hz, 2H, O–CH_2), 1.33 (t, *J*= 7.2 Hz, 3H, Me), 1.28 (t, *J*= 7.2 Hz, 3H, Me). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.5, 164.0, 142.0, 132,8, 130.4, 129.3, 128.6, 126.2, 61.5, 61.5, 14.0, 13.7. Employing General Procedure 1, with diethyl 2-benzylidenemalonate (**10**) (38.5 mg, 0.15 mmol) as starting material, desired product **11** was isolated in 82% yield. Characterization of **11**:[11] IR (film): ν_{max} (cm^{-1}) 2983, 1729, 1455, 1369, 1277, 1226, 1149. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.35–7.15 (m, 5H, ArH), 4.16 (q, *J*= 7.1 Hz, 2H, O–CH_2), 4.15 (q, *J*= 7.1 Hz, 2H, –OCH_2), 3.64 (t, *J*= 8.0 Hz, 1H, Hα), 3.22 (d, *J*= 8.0 Hz, 1H, Hβ), 1.20 (t, *J*= 7.1 Hz, 3H, Me). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 168.7, 137.8, 128.7, 128.3, 126.6, 61.3, 53.7, 34.6, 13.9. HRMS (ESI) m/z 273.1091 [(M + Na^+); calcd for $C_{14}H_{18}O_4Na$: 273.1097].



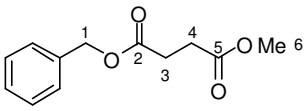
Methyl 2,3-diphenylpropanoate (13): Working in a well ventilated fume cupboard, α-phenylcinnamic acid (40.1 mg) was dissolved in DCM (25.0 mL) and treated with diazomethane at 0ºC for 30 min. The solvent was evaporated under reduced

pressure and the crude material was purified by flash column chromatography (hexane–AcOEt) to provide **12** in 95% yield. Characterization of **12**:[12] IR (film): ν_{max} (cm^{-1}) 1705, 1624, 1437, 1257, 1205, 1167. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.87 (s, 1H, Hβ), 7.50–7.00 (m, 10H, ArH), 3.81 (s, 3H, OMe). NMR de ^{13}C ($CDCl_3$, 75 MHz): δ 168.2, 140.4, 135.7, 134.4, 132.3, 130.5, 129.6, 128.9, 128.5, 128.0, 127.7, 52.2. HRMS (ESI) m/z 261.0885 [(M + Na^+); calcd for $C_{16}H_{14}O_2Na$: 261.0886]. Employing General Procedure 1, with (*E*)-methyl 2,3-diphenylacrylate (**12**) (35.9 mg, 0.15 mmol) as starting material, desired product **13** was isolated in 64% yield. Characterization of **13**: IR (film): ν_{max} (cm^{-1}) 3454, 1735, 1493, 1152. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.37–7.11 (m, 10H, ArH), 3.89 (dd, *J*= 6.6 Hz, *J*= 8.8 Hz, 1H, Hα), 3.62 (s, 3H, OMe), 3.45 (dd, *J*= 13.7 Hz, *J*= 8.8 Hz, 1H, Hβ), 3.06 (dd, *J*= 13.7 Hz, *J*= 6.6 Hz, 1H, Hβ'). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.7, 138.9, 138.5, 128.8, 128.5, 127.8, 127.2, 126.2, 53.5, 51.8, 39.7. HRMS (ESI) m/z 263.1046 [(M + Na^+); calcd for $C_{16}H_{16}O_2Na$: 263.1043].



(*Z*)-benzyl 2-fluoro-3-phenylacrylate (<u>14</u>): (*Z*)-2-fluoro-3-phenylacrylic acid (110.1 0.66 mmol) was dissolved in MeOH (2.7 mL) and water was added (270 µL). At 0 °C, pH was adjusted to neutrality by addition of aqueous 20% Cs_2CO_3 (113.0 mg/700 µL). Volatiles were removed in vacuum and the residue was resuspended in anhydrous DMF (1.3 mL). Solvent was evaporated under reduced pressure and resuspended again in anhydrous DMF (1.3 mL). Benzyl bromide (90 µL, 1.1 eq) was added and reaction was magnetically stirred at r.t. for 16 h. Reaction mixture was poured into water (6.1 mL) and 0.371 g NaCl was added. After extraction with Et_2O (4 x 4.0 mL), the collected organic phases were washed with water (2 x 1.0 mL) and brine (1 x 1.0 mL), and dried over anhydrous $MgSO_4$. Solvent was evaporated under reduced pressure and the crude product was purified by column flash chromatography (hexane–AcOEt) to obtain (*Z*)-benzyl 2-fluoro-3-phenylacrylate (**14**) (155.4 mg) as product in 92% yield. Characterization of **14**: IR (film): ν_{max} (cm^{-1}) 3023, 1721, 1452, 1382, 1264, 1093. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.70–7.60 (m, 2H, ArH), 7.50–7.35 (m, 8H, ArH), 6.96 (d, J^3_{H-F}= 35.0 Hz, 1H, H2), 5.34 (s, 2H, H1). ^{13}C NMR

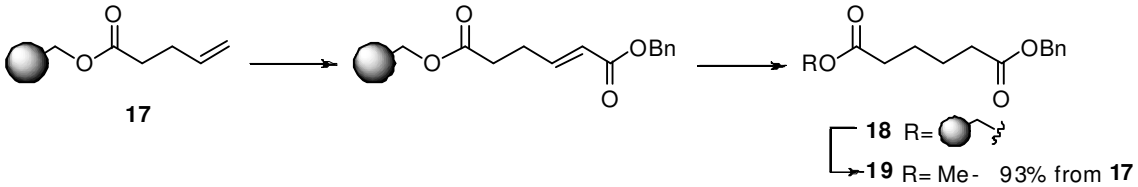
($CDCl_3$, 75 MHz): δ 161.2 (d, J^2_{C-F}= 34.4 Hz), 146.7 (d, J^1_{C-F}= 265.7 Hz), 135.0, 130.9 (d, J^3_{C-F}= 4.4 Hz), 130.2 (d, J^4_{C-F}= 8.2 Hz), 129.7 (d, J^6_{C-F}= 2.7 Hz), 128.7, 128.6, 128.5, 128.3, 117.9 (d, J^2_{C-F}= 4.4 Hz), 67.3. ^{19}F NMR ($CDCl_3$, 282 MHz): δ –125.2 (d, J^3_{H-F}= 35.0 Hz). HRMS (ESI) m/z 279.0789 [(M + Na^+); calcd for $C_{16}H_{13}FO_2Na$: 279.0792]. Employing General Procedure 1, with (*Z*)-benzyl 2-fluoro-3-phenylacrylate (**14**) (34.3 mg; 0.13 mmol) as starting material, product **5** was isolated in 61% yield.



Benzyl methyl succinate (16): Propargylic alcohol (1.0 g, 17.8 mmol) was dissolved in dry DCM (23.0 mL) and succinic anhydride (3.6 g) and triethyl amine (5.0 mL) were added. Mixture was refluxed for 4 h, treated with 1N HCl (10 mL) and extracted with AcOEt (5 x 50 mL). Collected organic phases were washed with 1N HCl (10 mL), brine (10 mL) and dried over $MgSO_4$. Solvent was evaporated to obtain crude propargyl succinate which was dissolved in dry DMF (25.0 mL). Triethyl amine (3.7 mL) and benzyl bromide (3.2 mL) were added and the reaction was stirred for 16 h at room temperature. Reaction was then poured into water (115.0 mL) and NaCl was added (7.1 g). Mixture was extracted with Et_2O (4 x 70.0 mL) and the collected organic phases were washed with water (2 x 15.0 mL) and brine (1 x 15.0 mL). After drying over $MgSO_4$ solvent was evaporated under reduced pressure. Product was purified by column flash chromatography (hexane–AcOEt) to obtain **15** (2.9 g) in 66% yield. Characterization of **15**: IR (film): ν_{max} (cm^{-1}) 3241, 2938, 2127, 1739, 1311, 1155. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.40–7.30 (m, 5H, ArH), 5.14 (s, 2H, H1), 4.68 (d, *J*= 2.4 Hz, 2H, H6), 2.70 (s, 4H, H3–4), 2.47 (t, *J*= 2.4 Hz, 1H, H7). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.7, 171.3, 135.6, 128.4, 128.2, 128.1, 77.3, 74.9, 66.5, 52.1, 28.9, 28.8. HRMS (ESI) m/z 269.0787 [(M + Na^+); calcd for $C_{14}H_{14}O_4Na$: 269.0784]. Employing General Procedure 1, with benzyl prop-2-ynyl succinate (**15**) (30.0 mg, 0.11 mmol) as starting material, a crude product was obtained which was dissolved in AcOEt (200 mL) and treated with 1N HCl (10 mL). Organic phase was dried over $MgSO_4$ and solvent was evaporated. The residue obtained was dissolved in DCM (25.0 mL) and treated with diazomethane at 0ºC for 30 min. The solvent was evaporated under reduced

pressure and the crude material was purified by flash column chromatography (hexane–AcOEt) to provide **16** in 91% yield. Characterization of **16**:[13] IR (film): ν_{max} (cm^{-1}) 3034, 2954, 1739, 1729, 1498, 1214, 1157. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.35 (m, 5H, ArH), 5.14 (s, 2H, H1), 3.67 (s, 3H, OMe), 2.75–2.60 (m, 4H, H3–4). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.6, 172.0, 135.6, 128.4, 128.1, 128.1, 66.4, 51.7, 29.0, 28.8. HRMS (ESI) m/z 245.0785 [(M + Na^+); calcd for $C_{12}H_{14}O_4Na$: 245.0784].

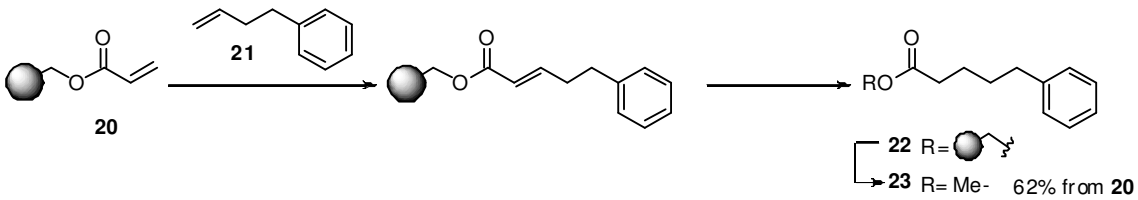
1.3.- Solid-Supported Sequential cross-metathesis/olefin reduction: .



Representative procedure: Resin **17**[14] (163 mg, 0.46 mmol) was suspended in dry DCM (3.5 mL) the benzyl crotonate (**2**) (131.5 mg, 5.0 eq) was added via syringe under a nitrogen atmosphere. Grubbs' second generation precatalyst (**1**) (5 mol %) was added and the flask was fitted with a condenser and refluxed for 20 h, after which the resin was filtered, washed with DCM (3 x 1.5 mL), MeOH (3 x 1.5 mL), DCM (1 x 1.5 mL), and dried under high vacuum. The resin was resubjected to the same reaction conditions to obtain the corresponding immobilized α,β-insaturated ester. This resin (0.15 mmol) was placed in a 10 mL microwave vessel and suspended in anhydrous DCM (2.0 mL). Triethylsilane (5 eq) and Grubbs' second generation catalyst (5 mol%) were added. Vessel was capped with the corresponding septum and placed in the microwave reactor. The mixture was magnetically stirred and irradiated under closed vessel conditions at 150 ºC (P_{max}= 300W) for 30 min. Resin was filtered, then washed with DCM (3x5 mL), AcOEt (3x5 mL), MeOH (3x5 mL) and DCM (3x5 mL) and dried in vacuum to obtain immobilized compound **18**. Gel Phase ^{13}C NMR ($CDCl_3$, 75 MHz): δ 66.0, 33.7, 24.2. Resin **18** (166.0 mg, 0.14 mmol) was cleaved by treatment with 5 mL of 10% TFA in DCM for 1 h. The mixture was filtered and the filtrate was evaporated under reduced pressure to give the crude product. This crude material was dissolved in DCM and treated with diazomethane at 0ºC for 30 min. The solvent was evaporated under reduced

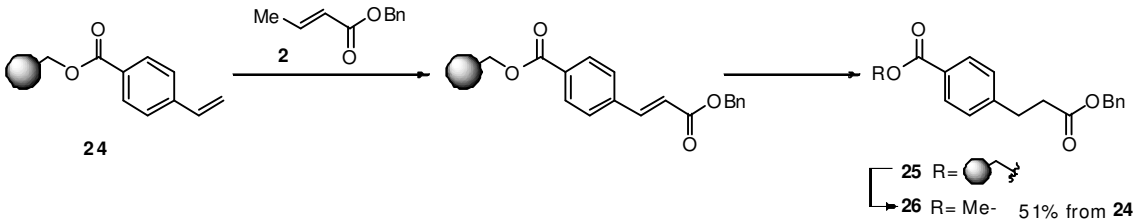
pressure and the crude material was purified by flash column chromatography (hexane–AcOEt) to provide the desired product **19** in 93% yield from **17**. Characterization of **19**:[9,15] IR (film): ν_{max} (cm^{-1}) 2952, 1739, 1456, 1436, 1170. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.40–7.25 (m, 5H, ArH), 5.11 (s, 2H, H7), 3.66 (s, 3H, OMe), 2.42–2.30 (m, 4H, H2 y H5), 1.80–1.60 (m, 4H, H3–4). NMR de ^{13}C ($CDCl_3$, 75 MHz): δ 173.6, 173.0, 135.8, 128.4, 128.1, 66.1, 51.4, 33.8, 33.5, 24.2. HRMS (ESI) m/z 273.1094 [(M + Na^+); calcd for $C_{14}H_{18}O_4Na$: 273.1097].

Methyl 5-phenylpentanoate (23):



According to a slighlty modified procedure (Hoveyda-Grubbs precatalyst[14] was used for the cross metathesis) desired product **23** was obtained in 62% yield from **20**. Characterization of **23**:[16] IR (film): ν_{max} (cm^{-1}) 2949, 1738, 1453, 1436, 1200, 1173. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.40–7.15 (m, 5H, ArH), 3.68 (s, 3H, OMe), 2.65 (t, *J*= 7.2 Hz, 2H, H5), 2.33 (t, *J*= 7.1 Hz, 2H, H2), 1.80–1.60 (m, 4H, H3–4). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.8, 141.9, 128.2, 128.1, 125.6, 51.3, 35.4, 33.7, 30.7, 24.4. HRMS (ESI) m/z 215.1039 [(M + Na^+); calcd for $C_{12}H_{16}O_2Na$: 215.1043].

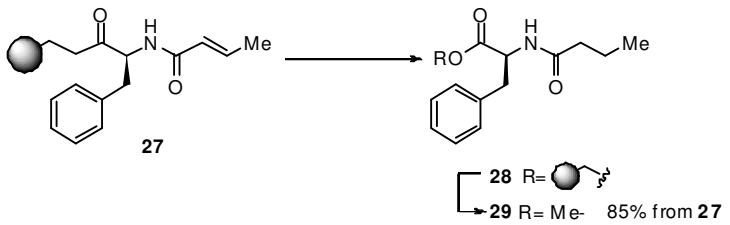
Methyl 4-(3-(benzyloxy)-3-oxopropyl)benzoate (26):



According to the representative procedure, the desired product **26** was obtained in 51% yield from **24**. Characterization of **26**: IR (film): ν_{max} (cm^{-1}) 2952, 1721, 1610, 1436, 1281, 1110. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.94 (d, *J*= 8.5 Hz, 2H, ArH), 7.40–7.15 (m, 7H, ArH), 5.10 (s, 2H, H8), 3.90 (s, 3H, OMe), 3.02 (d, *J*= 7.4 Hz, 2H, H6), 2.70 (d, *J*= 7.4 Hz, 2H, H5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ

172.3, 167.0, 145.8, 135.8, 129.9, 129.7, 129.0, 128.6, 128.4, 128.3, 66.4, 52.0, 35.4, 30.9. HRMS (ESI) m/z 321.1090 [(M + Na^+); calcd for $C_{18}H_{18}O_4Na$: 321.1097].

1.4.- Olefin reduction of immobilized α,β-unsaturated amide 27:



Resin **27** (237.9 mg, 0.18 mmol) was reduced employing the microwave-assisted Et_3SiH/Grubbs' catalyst procedure to obtain immobilized compound **28**, which was cleaved by treatment with 6 mL of 10% TFA in DCM for 1 h. The mixture was filtered and the filtrate was evaporated under reduced pressure to give the crude product. This crude material was dissolved in DCM and treated with diazomethane at 0ºC for 30 min. The solvent was evaporated under reduced pressure and the crude material was purified by flash column chromatography (hexane–AcOEt) to provide the desired product (*S*)-methyl 2-butyramido-3-phenylpropanoate (**29**) in 85% yield from **27**. Characterization of **29**:[17] $[\alpha]_D$= +98.1 (*c* 8.24, $CHCl_3$). IR (film): ν_{max} (cm^{-1}) 3291, 2962, 1748, 1651, 1539, 1436, 1208. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.35–7.05 (m, 5H, ArH), 5.86 (d, *J*= 6.8 Hz, 1H, H4), 4.90 (dt, *J*= 7.7 Hz, *J*= 6.1 Hz, 1H, H3), 3.73 (s, 3H, OMe), 3.20–3.03 (m, 2H, H9), 2.15 (t, *J*= 7.3 Hz, 2H, H6), 1.62 (sextet, *J*= 7.4 Hz, 2H, H7), 0.94 (t, *J*= 7.3 Hz, 3H, H8). NMR de ^{13}C ($CDCl_3$, 75 MHz): δ 172.4, 172.1, 135.8, 129.1, 128.4, 127.0, 52.8, 52.6, 38.3, 37.8, 18.8, 13.6. HRMS (ESI) m/z 272.1251 [(M + Na^+); calcd for $C_{14}H_{19}NO_3Na$: 272.1257].

2.- References

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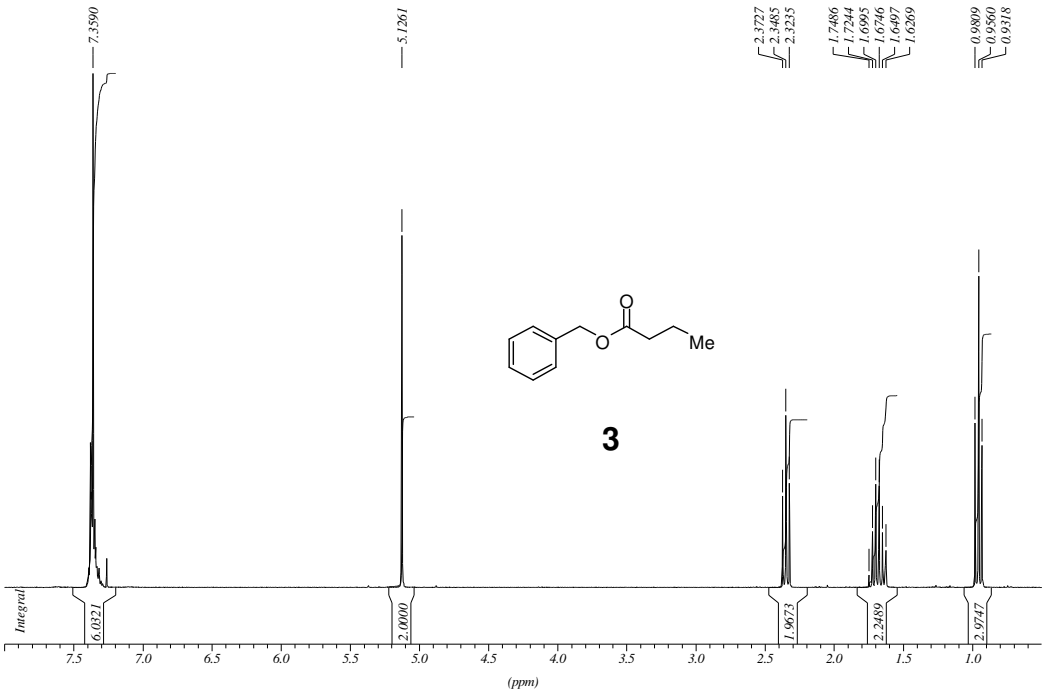
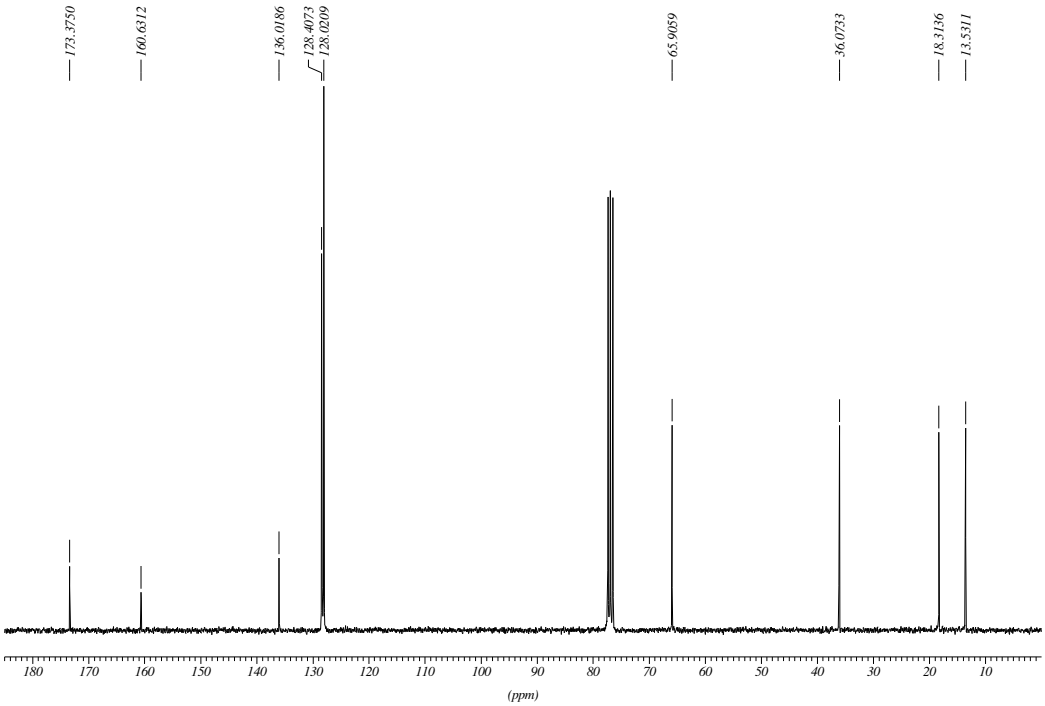
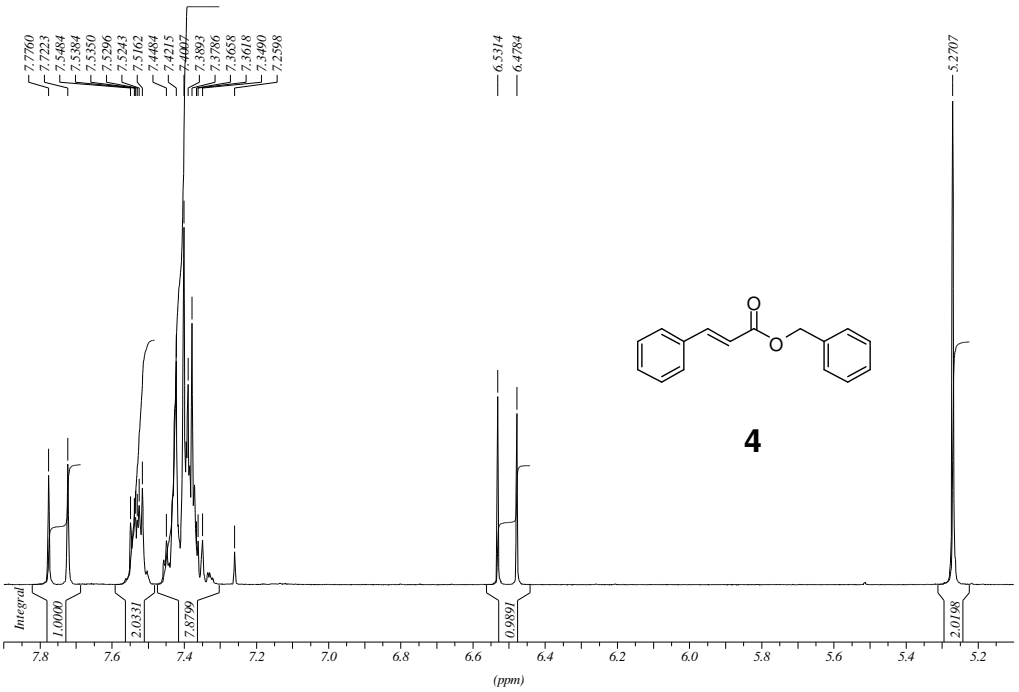
3.- ^{1}H NMR and ^{13}C NMR Spectra



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7.3893
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7.3618
7.3490
7.2598
6.5314
6.4784
5.2707
Integral
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0.9891
2.0198
7.8
7.6
7.4
7.2
7.0
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6.6
6.4
6.2
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5.8
5.6
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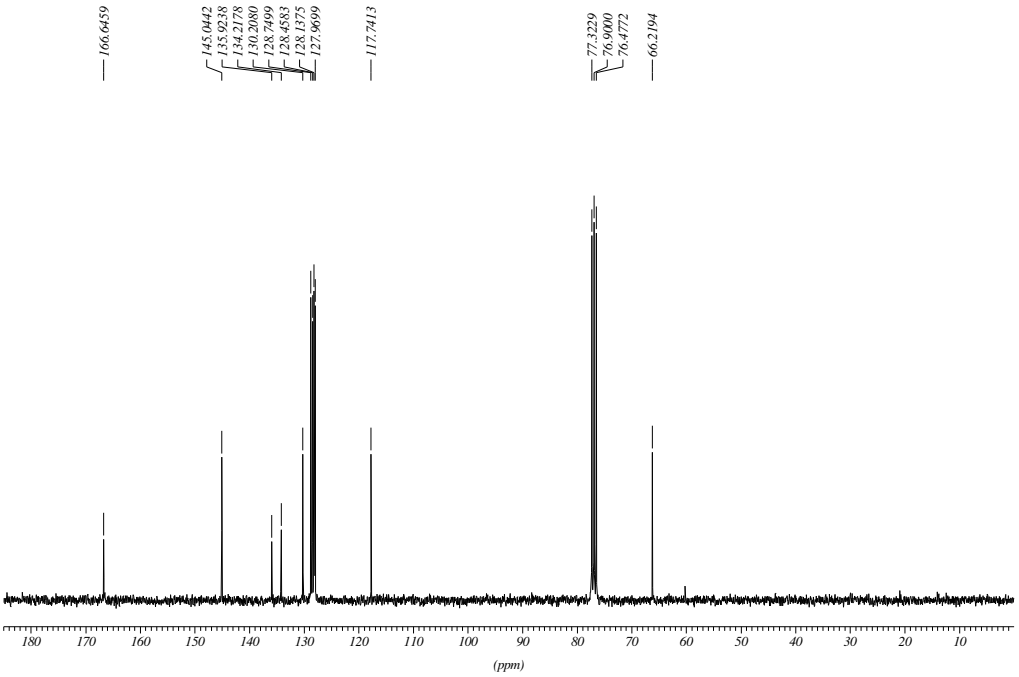
5.2
(ppm)

4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77.3229
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66.2194
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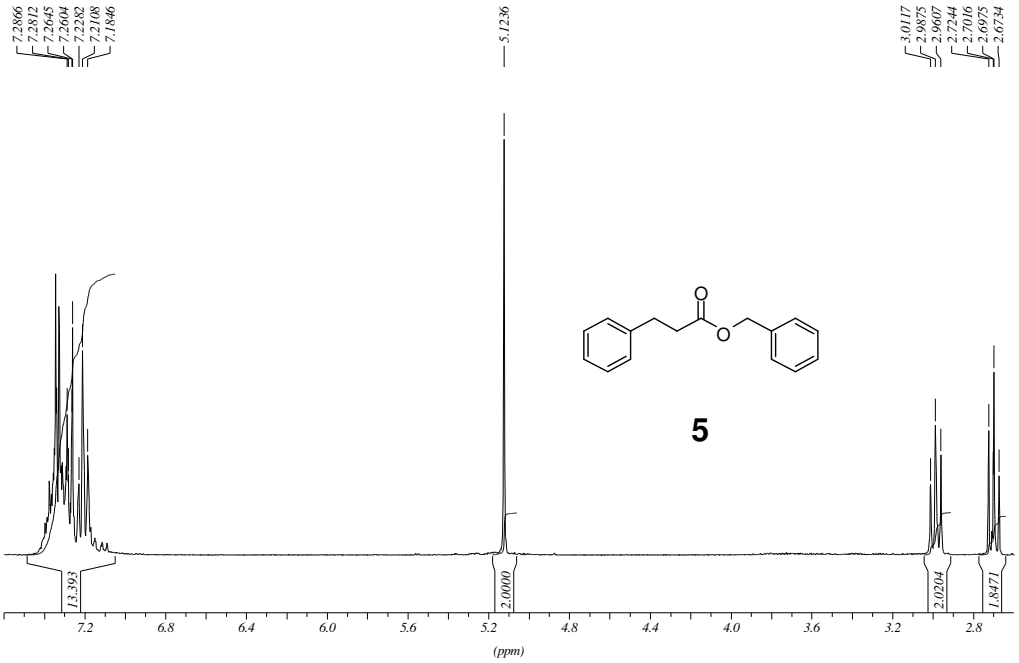
(ppm)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2.7244
2.7016
2.6975
2.6734
5
13.393
2.0000
2.0204
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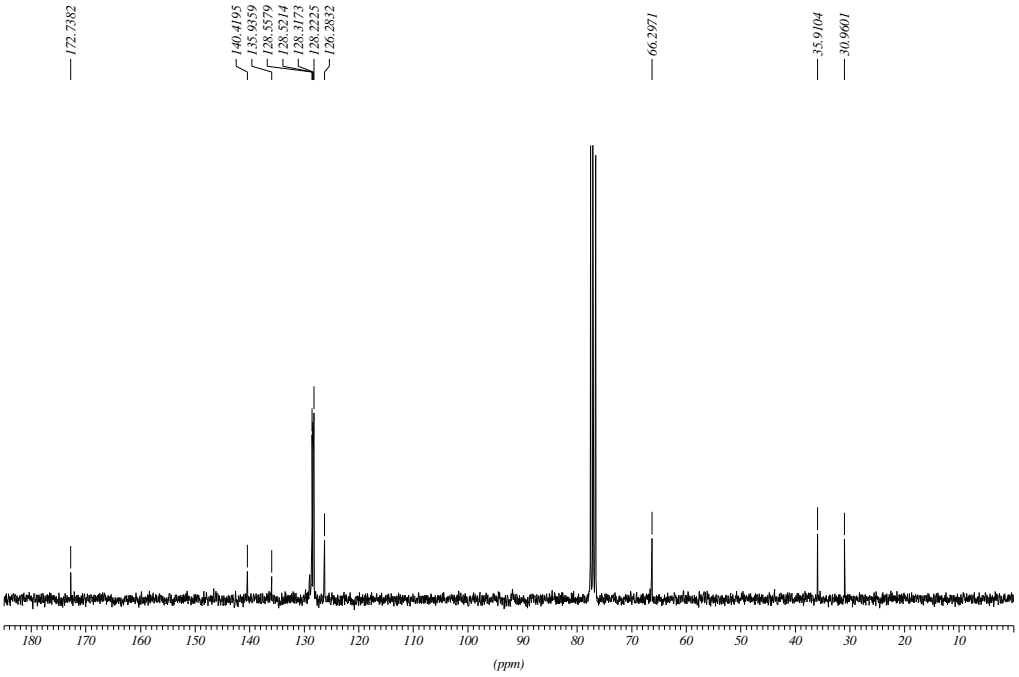
(ppm)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30.9601
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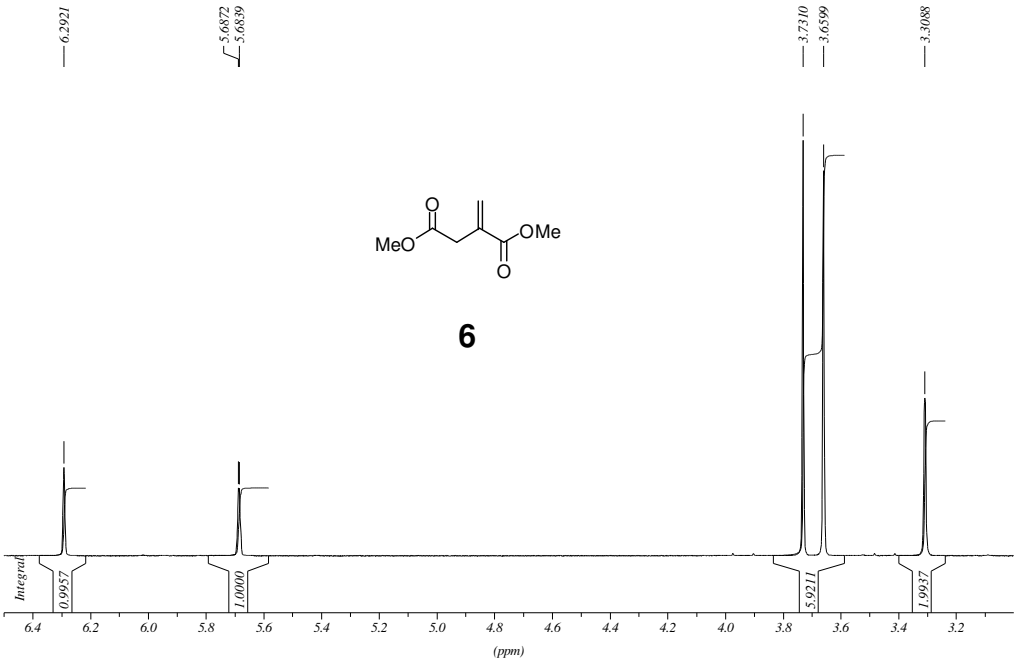
(ppm)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5.9211
1.9937
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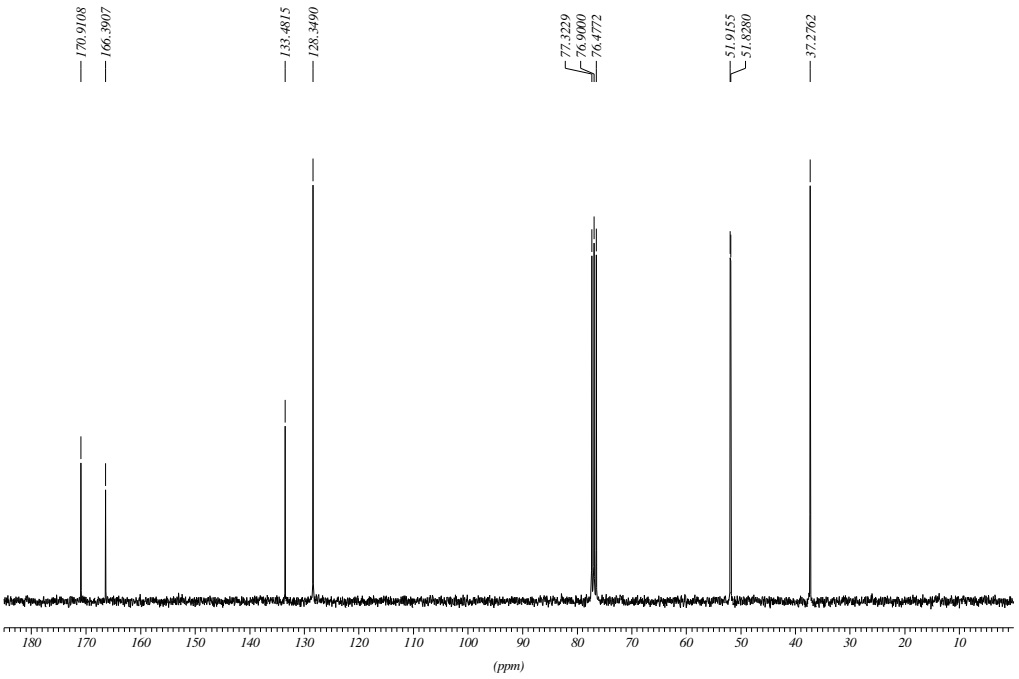
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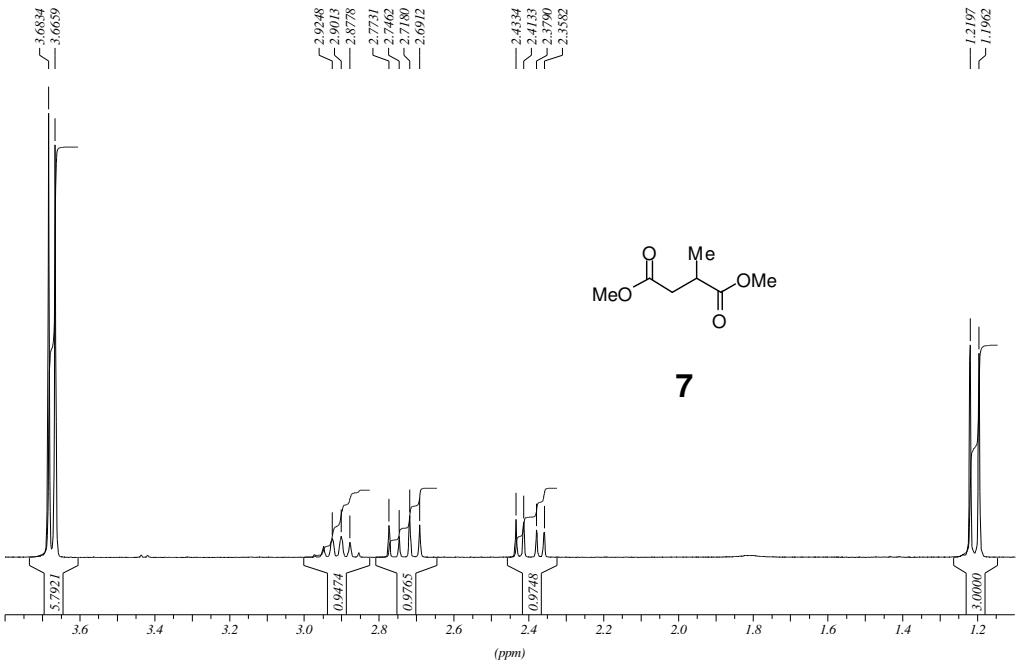
(ppm)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3.2
3.0
2.8
2.6
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2.0
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(ppm)

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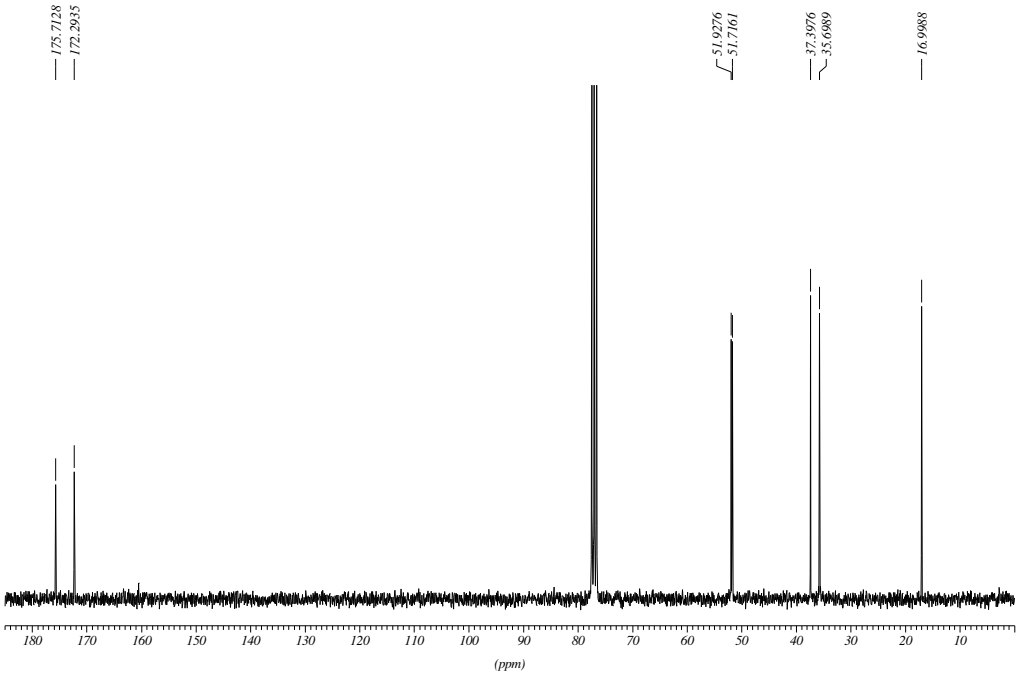
Me
MeO
OMe
O

7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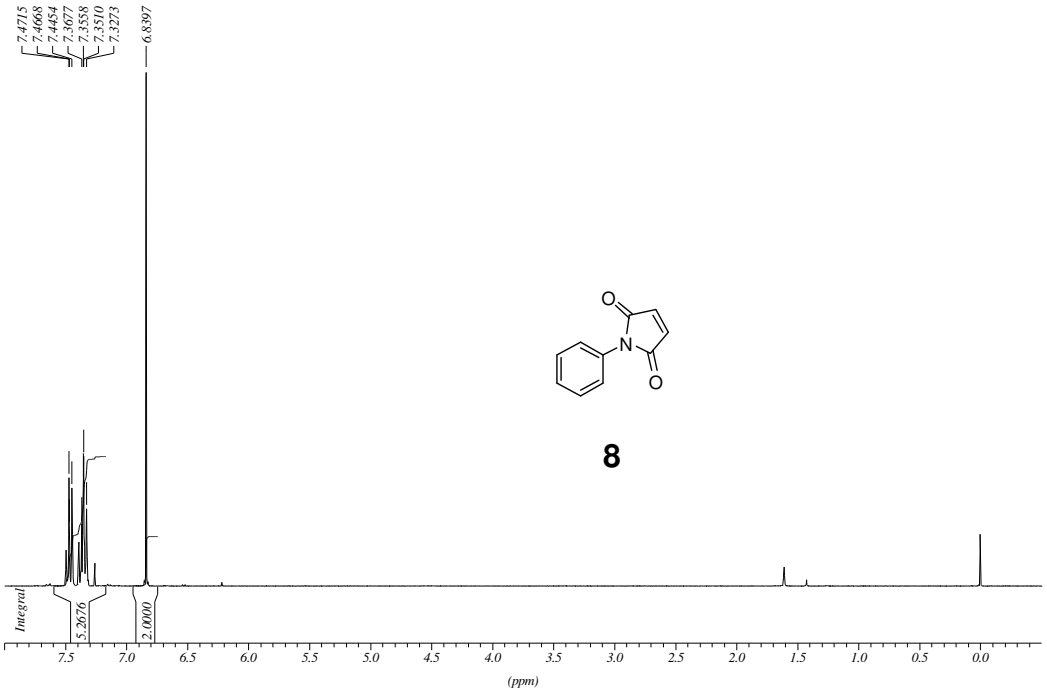
(ppm)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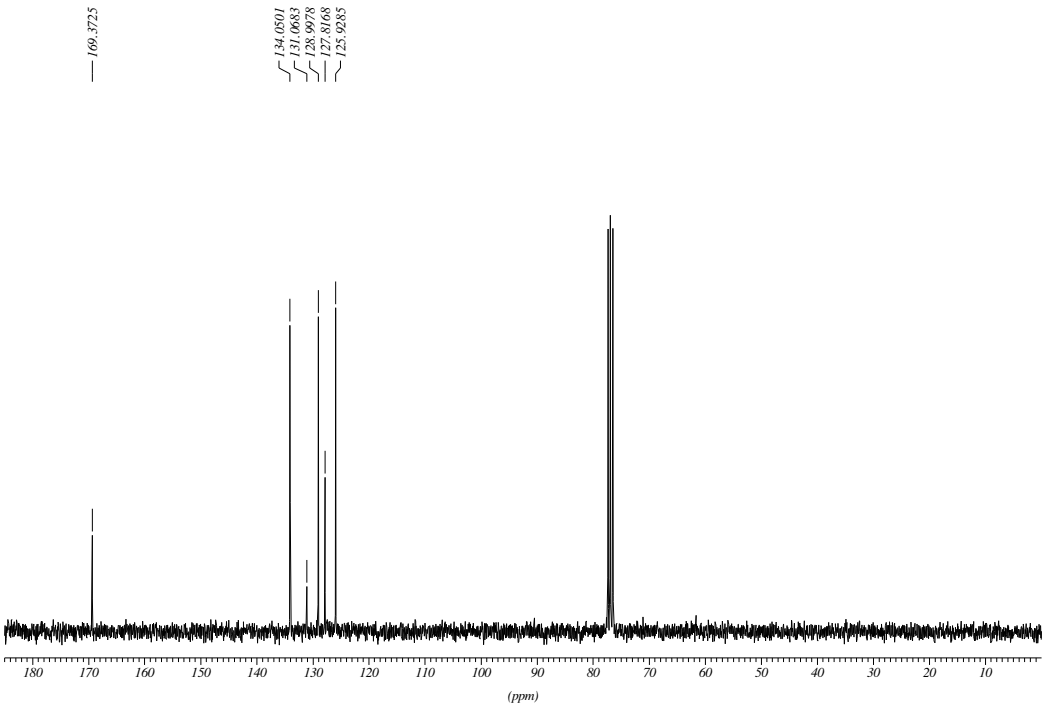
(ppm)

O
N
O

8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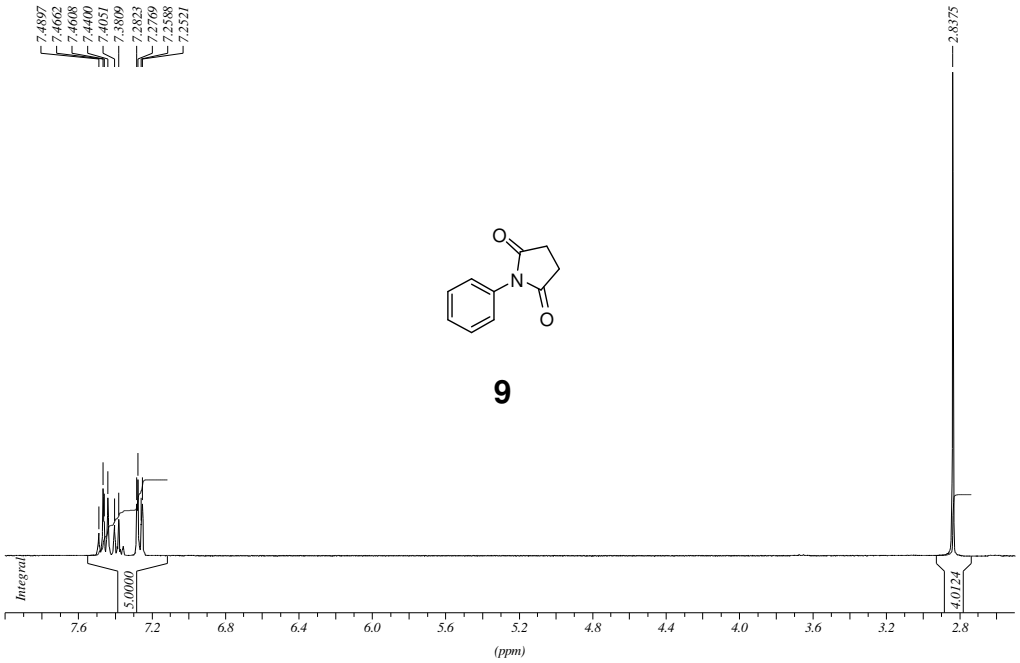
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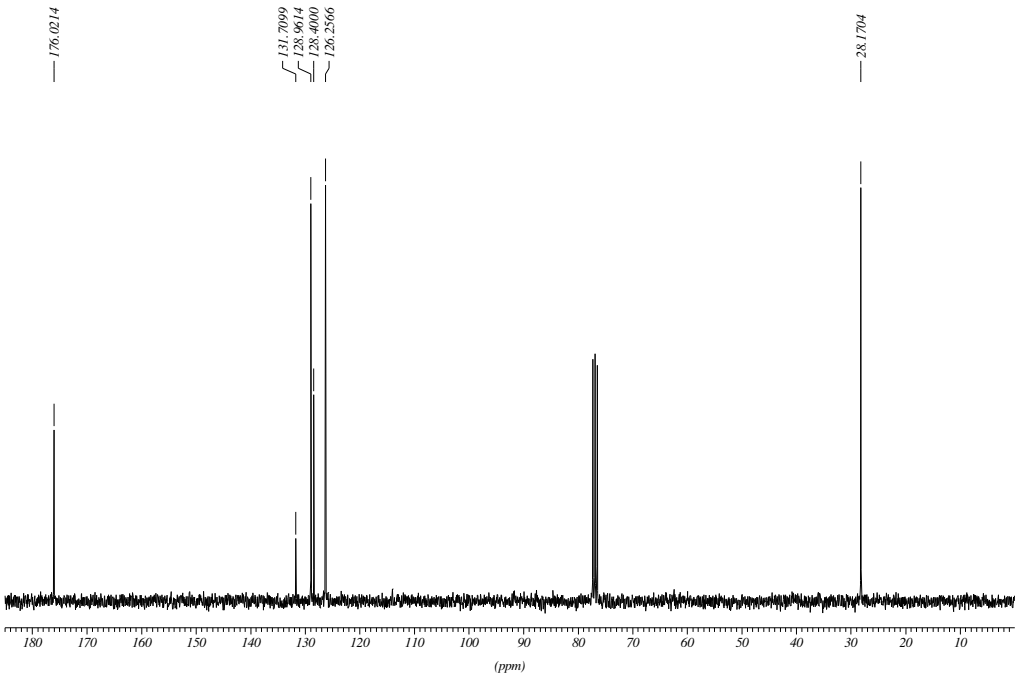
9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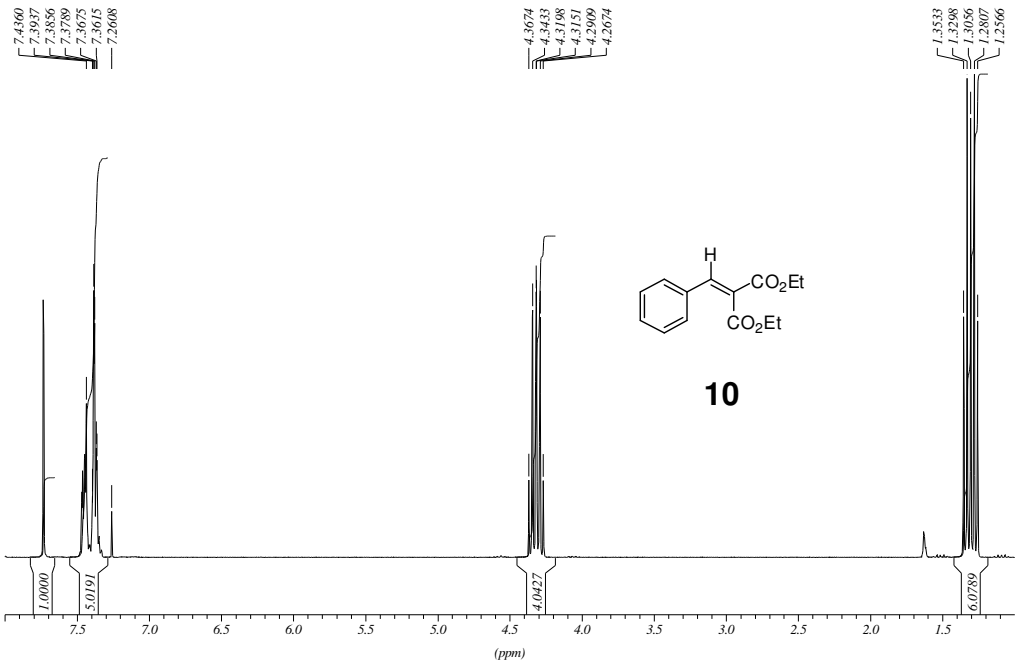
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CO2Et
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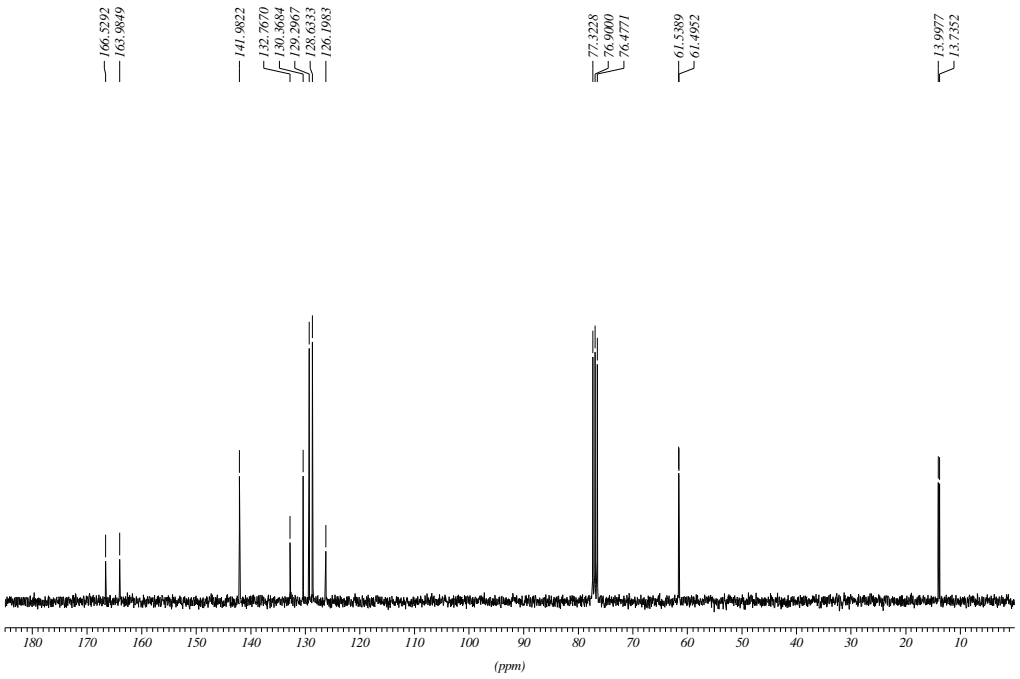
(ppm)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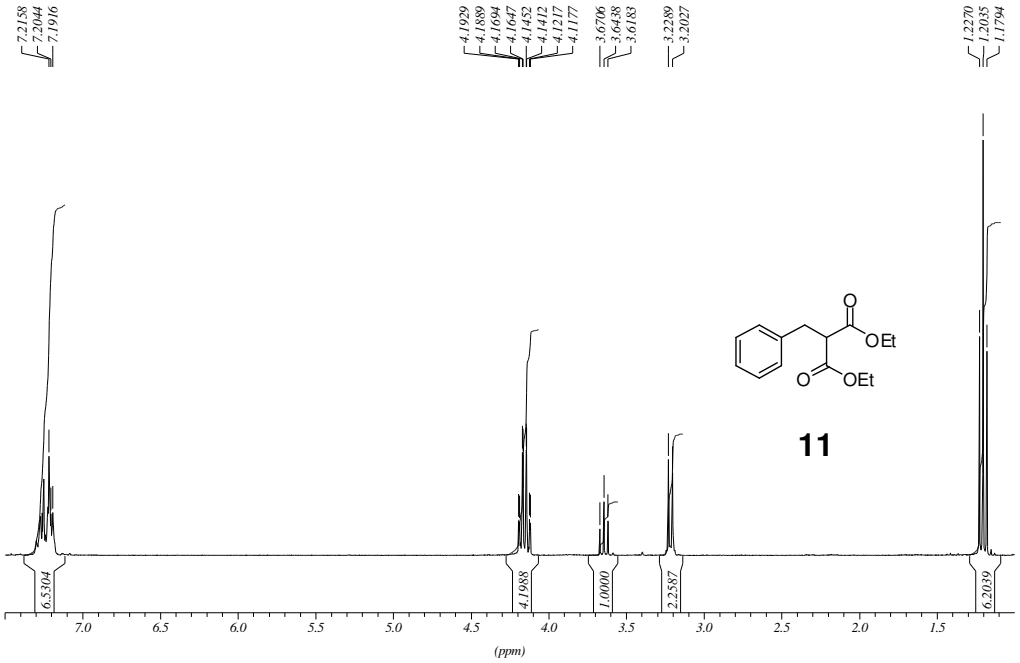
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3.6438
3.6183
3.2289
3.2027
1.2270
1.2035
1.1794
O
OEt
O
OEt
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1.0000
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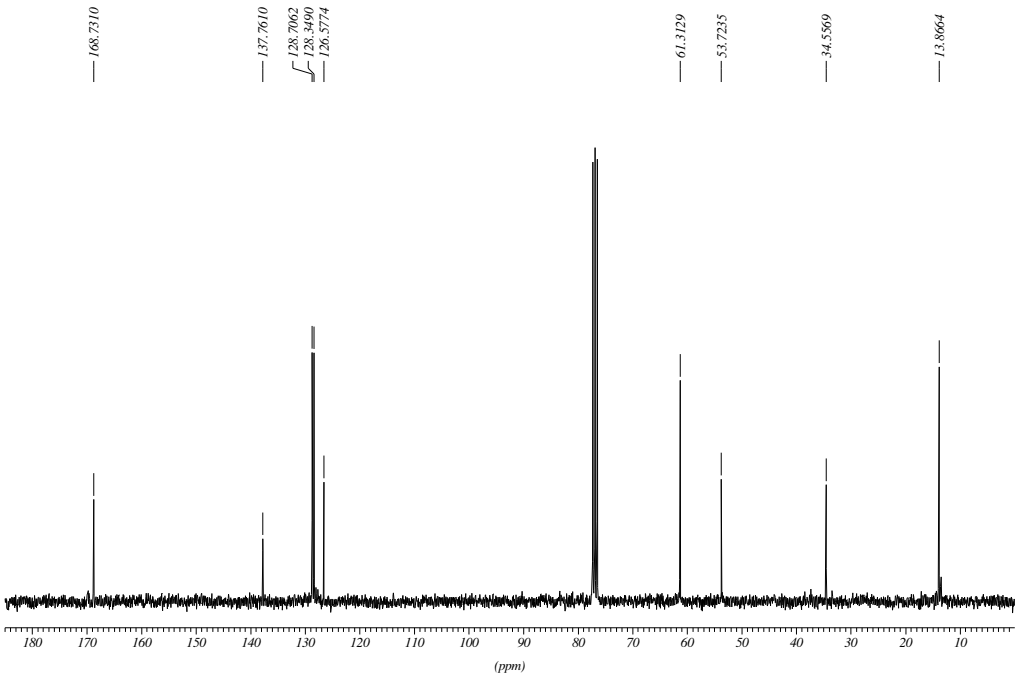
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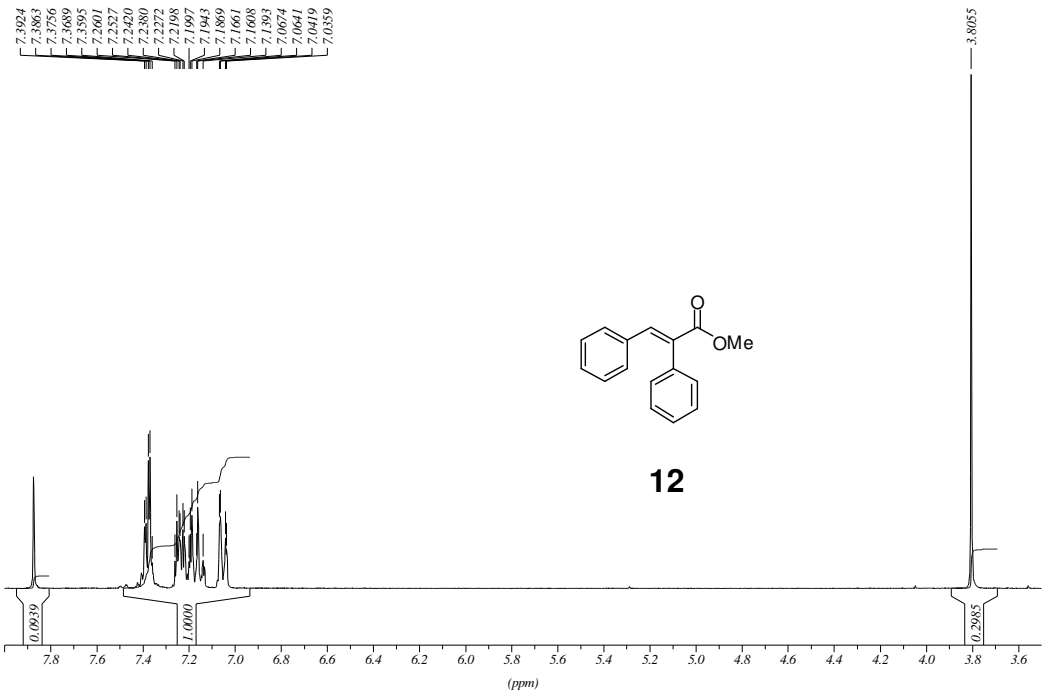
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7.0359
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OMe
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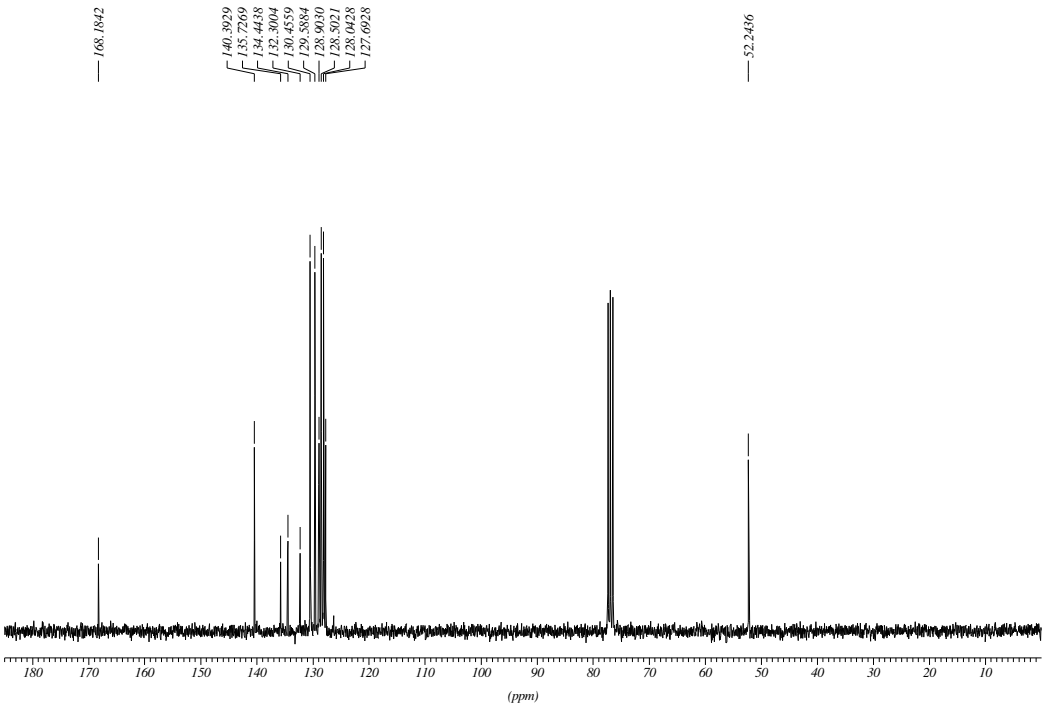
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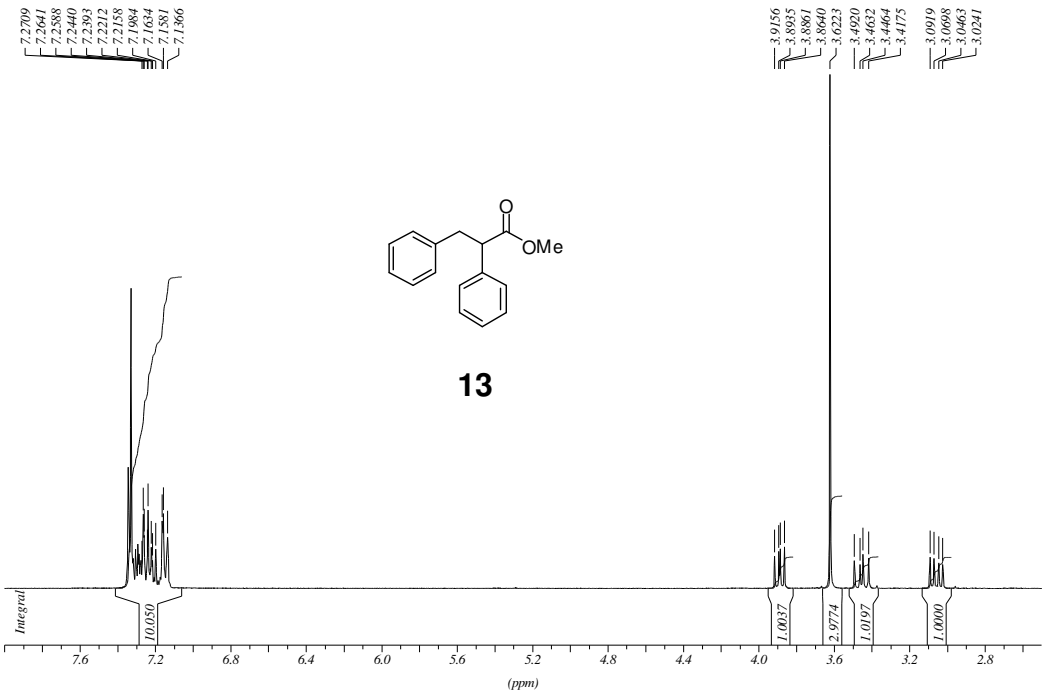
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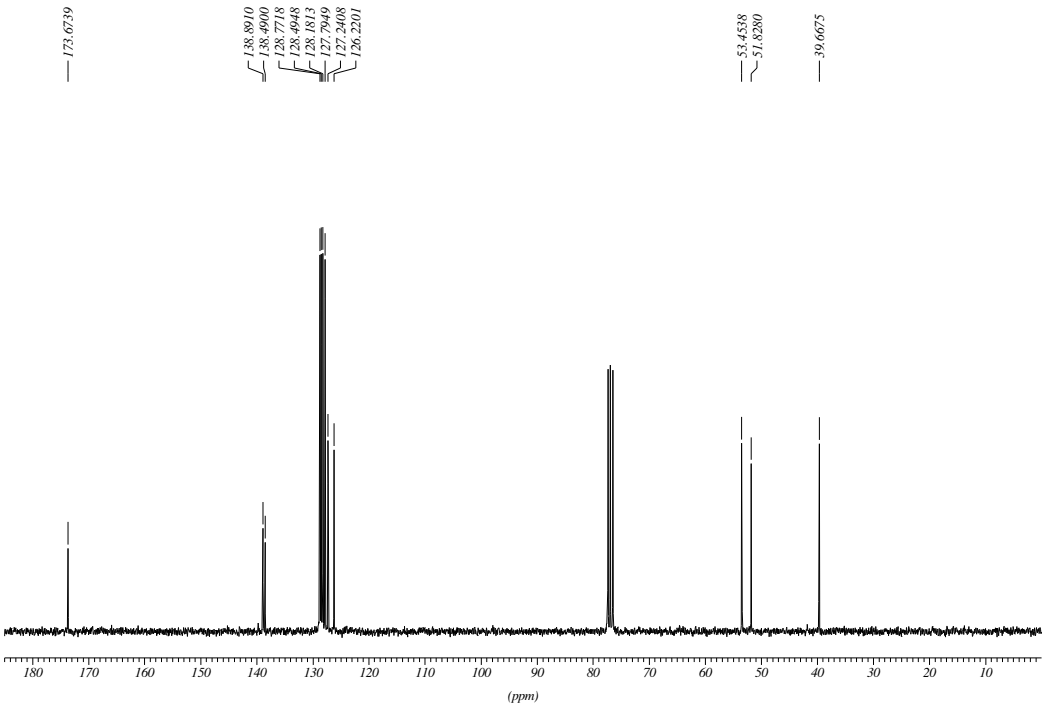
(ppm)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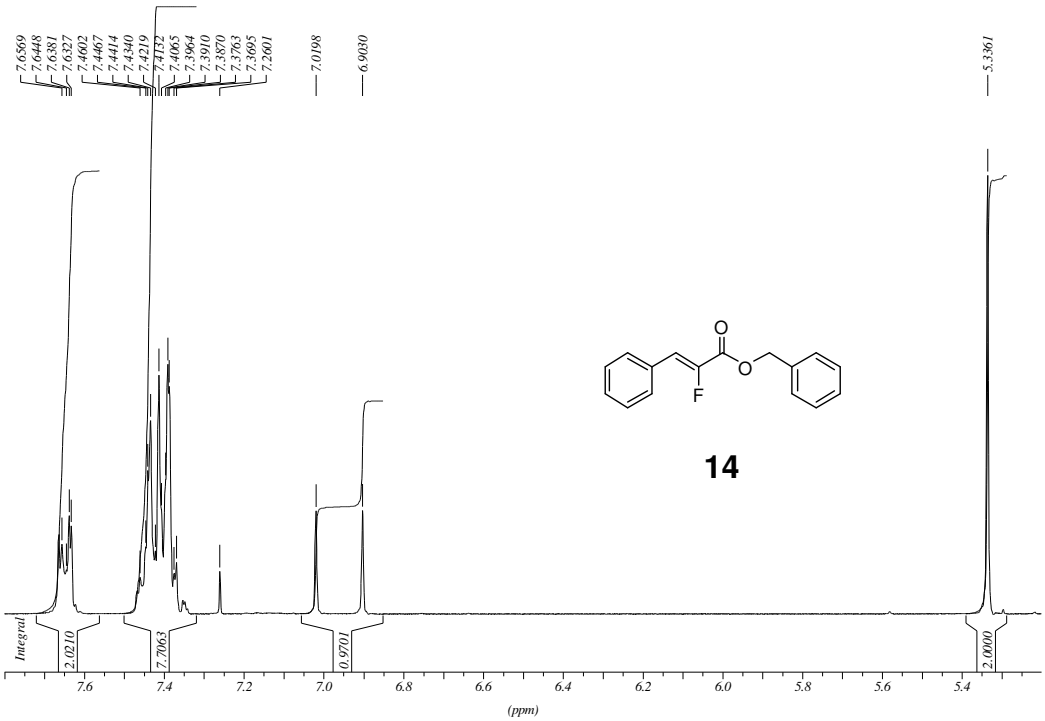
(ppm)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2.0000
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5.4
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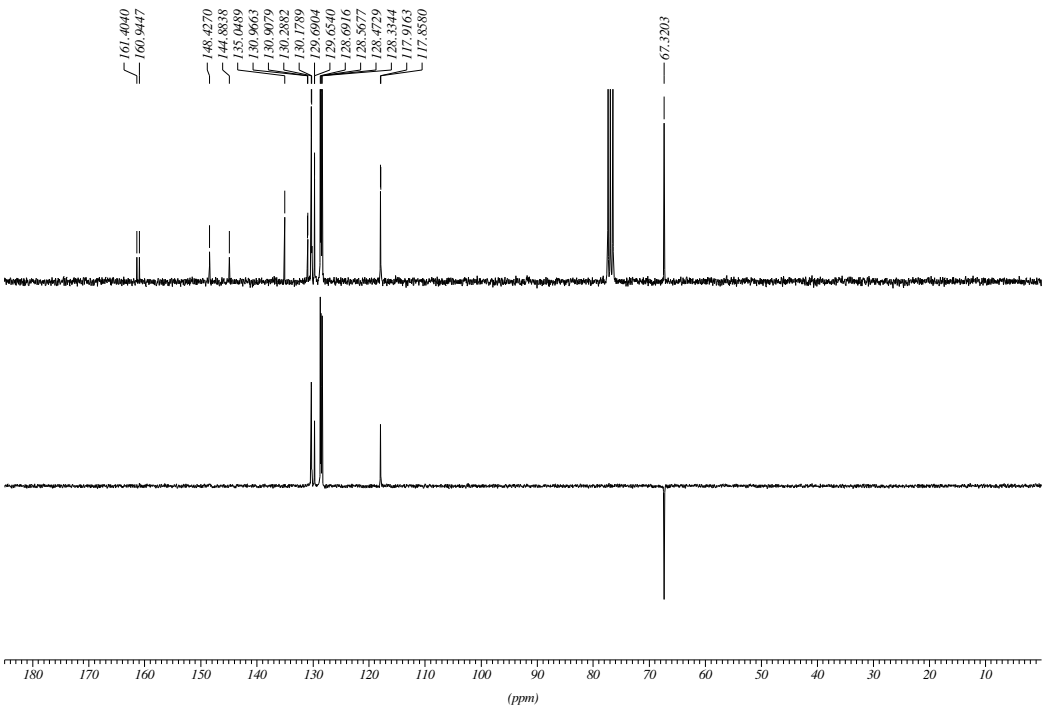
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130.1789
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129.6540
128.6916
128.5677
128.4729
128.3344
117.9163
117.8580
67.3203
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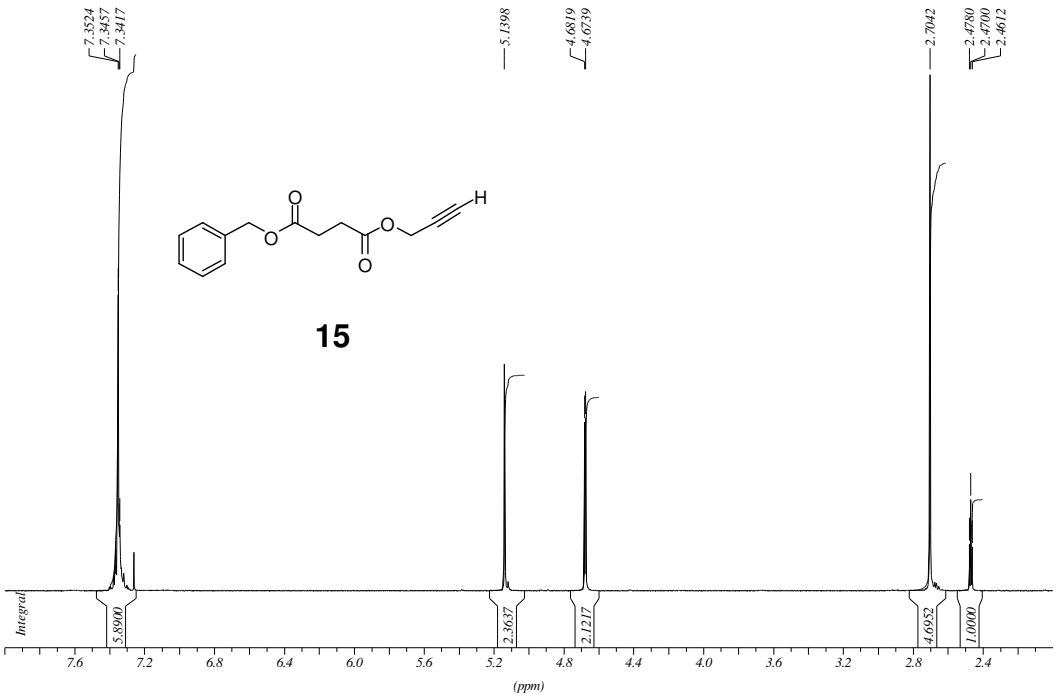
(ppm)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2.4700
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O
O
O
O
H
15
Integral
5.8900
2.3637
2.1217
4.6952
1.0000
7.6
7.2
6.8
6.4
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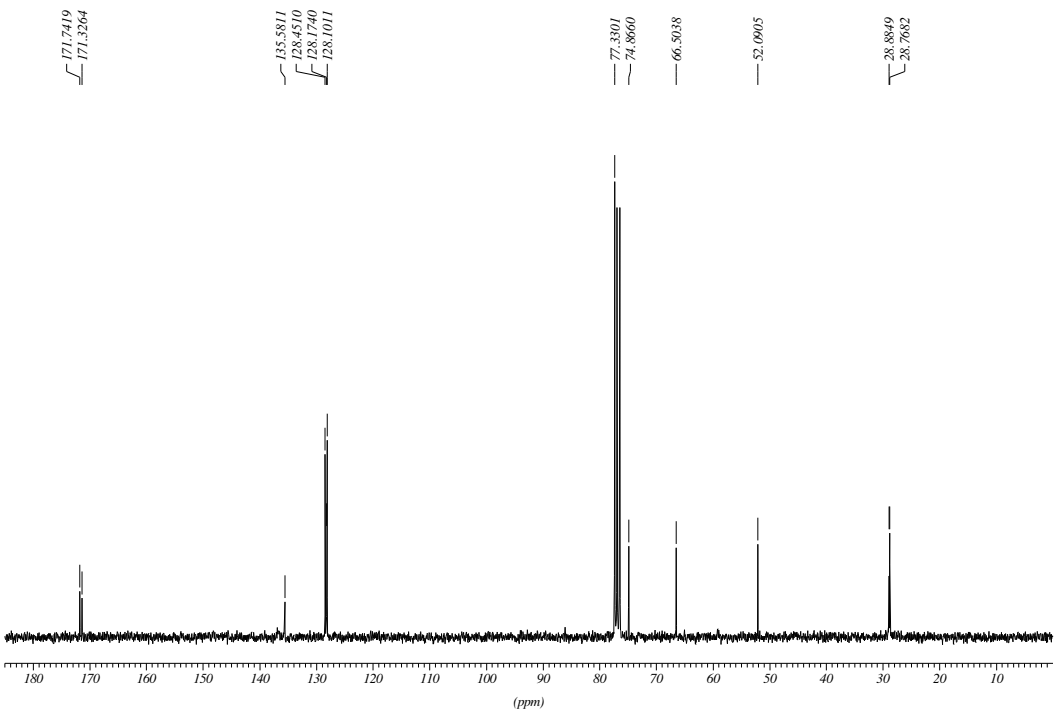
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
(ppm)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135.5811
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128.1740
128.1011
77.3301
74.8660
66.5038
52.0905
28.8849
28.7682
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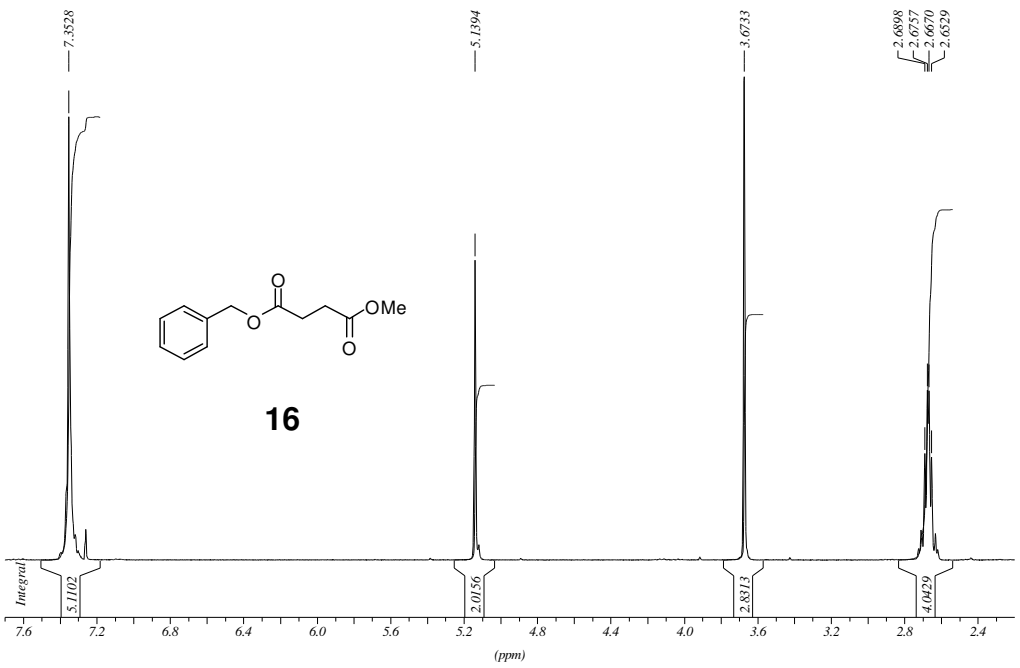
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)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2.6757
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2.6529
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O
OMe
O
16
Integral
5.1102
2.0156
2.8313
4.0429
7.6
7.2
6.8
6.4
6.0
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5.2
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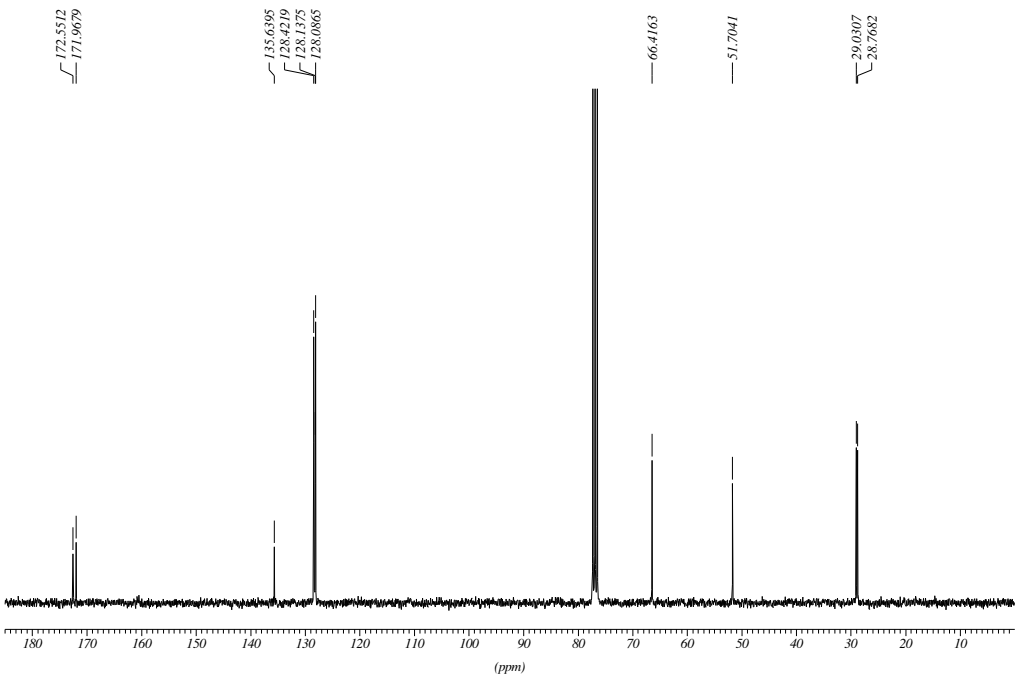
4.4
4.0
3.6
3.2
2.8
2.4
(ppm)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128.0865
66.4163
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29.0307
28.7682
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150
140
130
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110
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90
80
70
60
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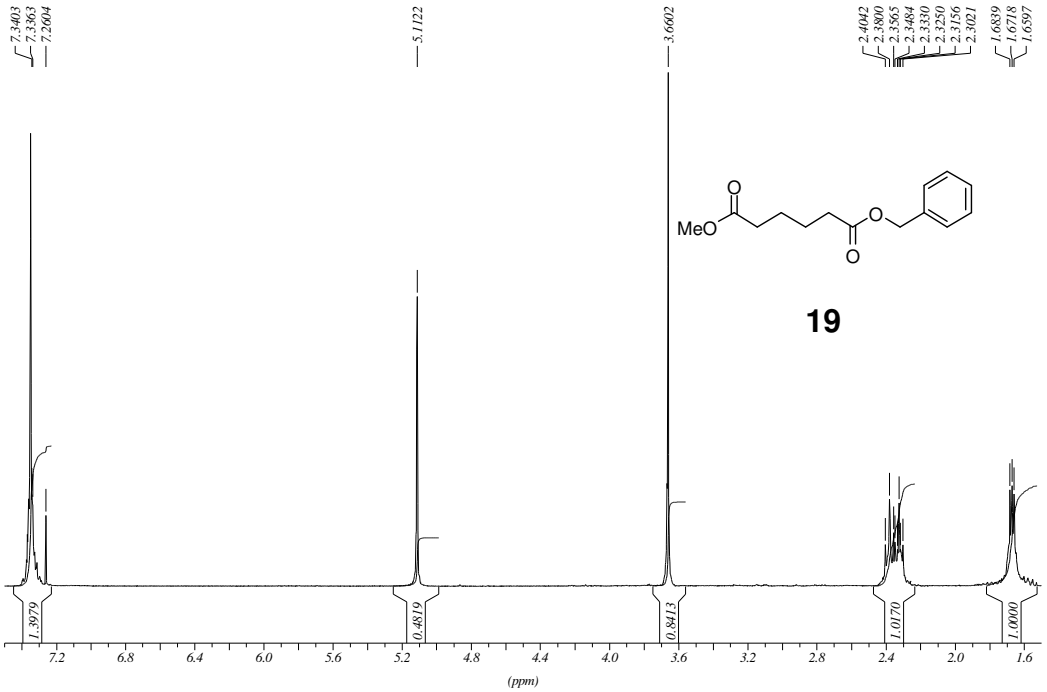
40
30
20
10
(ppm)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2.3156
2.3021
1.6839
1.6718
1.6597
MeO
O
O
O
19
1.3979
0.4819
0.8413
1.0170
1.0000
7.2
6.8
6.4
6.0
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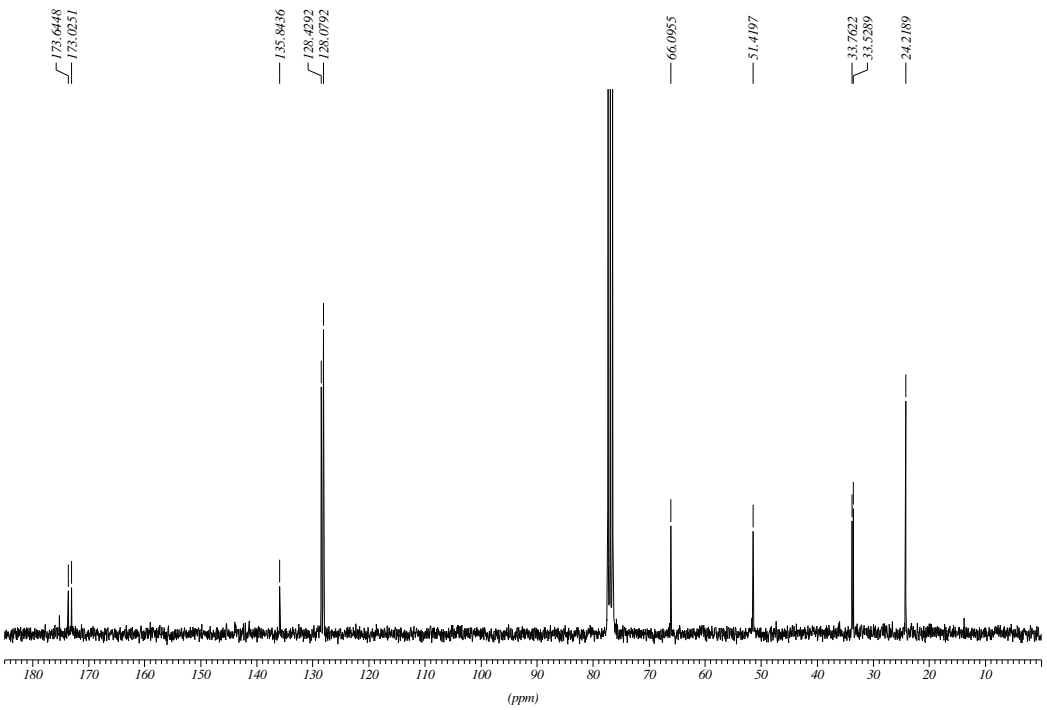
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
(ppm)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173.0251
135.8436
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128.0792
66.0955
51.4197
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33.5289
24.2189
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150
140
130
120
110
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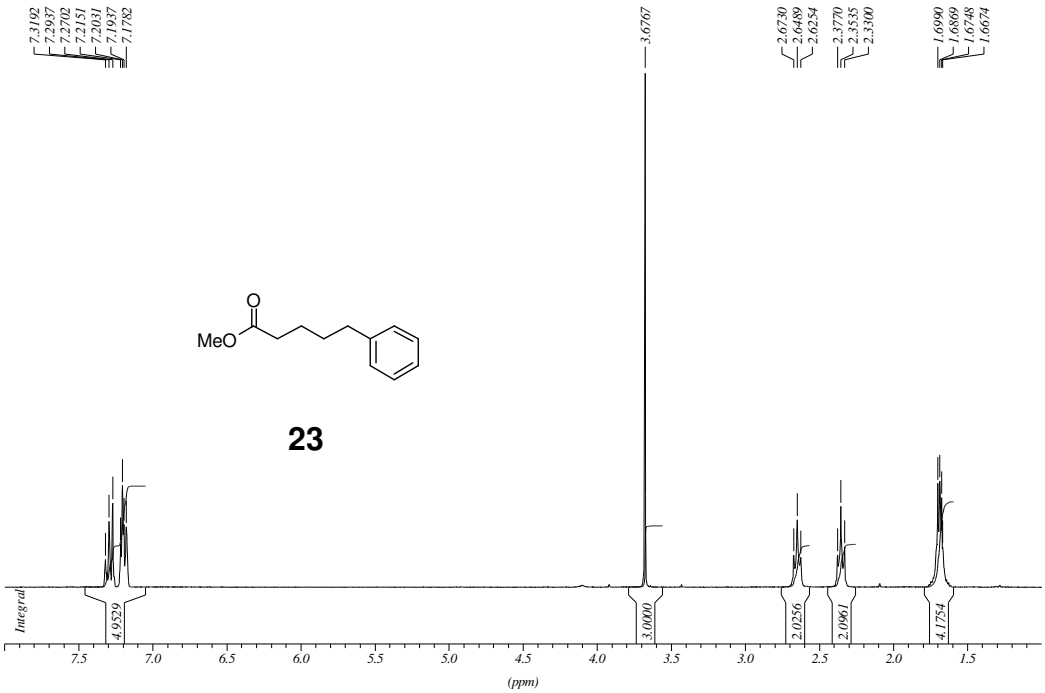
90
80
70
60
50
40
30
20
10
(ppm)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7.2937
7.2702
7.2151
7.2031
7.1937
7.1782
3.6767
2.6730
2.6489
2.6254
2.3770
2.3535
2.3300
1.6990
1.6869
1.6748
1.6674
MeO
O
Integral
4.9529
3.0000
2.0256
2.0961
4.1754
7.5
7.0
6.5
6.0
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5.0
4.5
4.0
3.5
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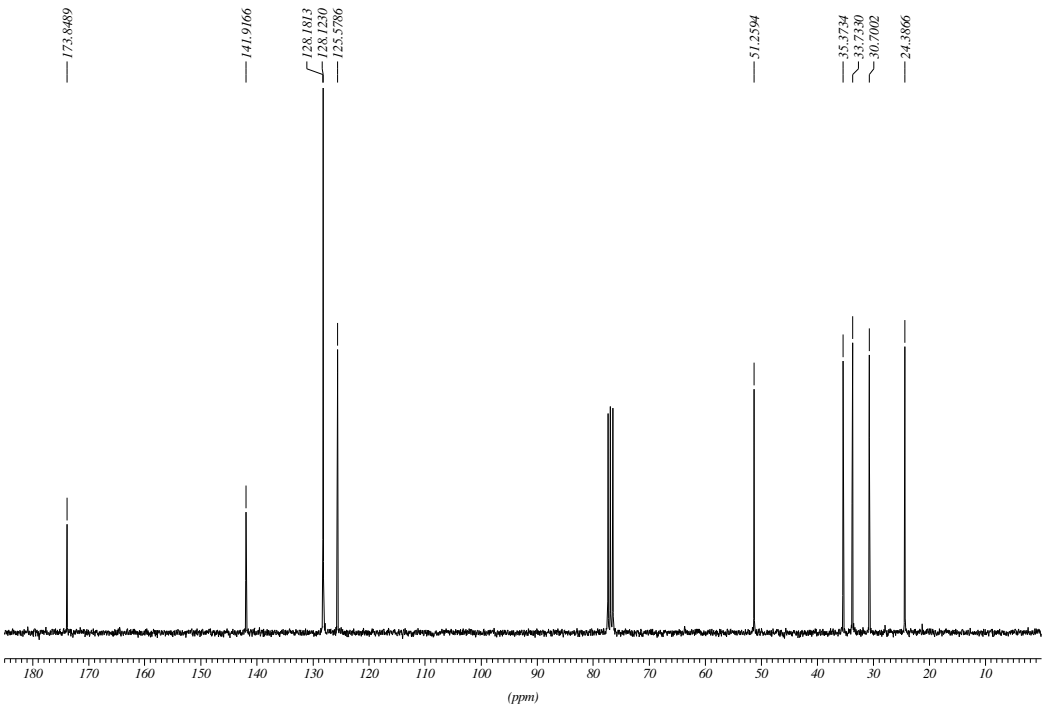
2.5
2.0
1.5
(ppm)

23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141.9166
128.1813
128.1230
125.5786
51.2594
35.3734
33.7330
30.7002
24.3866
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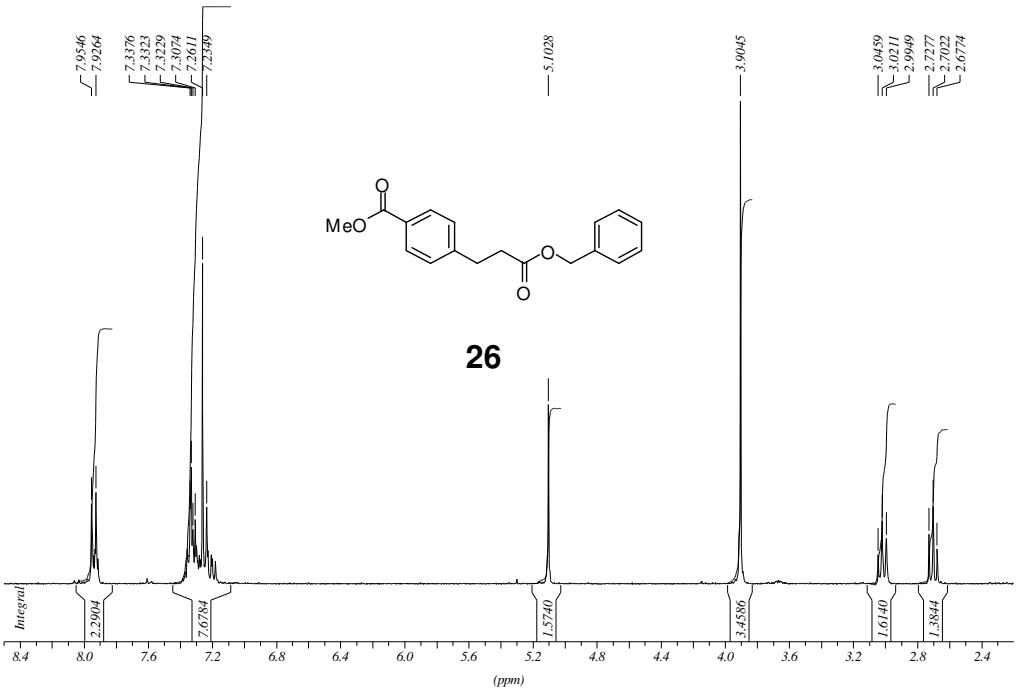
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)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7.3376
7.3323
7.3229
7.3074
7.2611
7.2349
5.1028
3.9045
3.0459
3.0211
2.9949
2.7277
2.7022
2.6774
MeO
O
O
O
Integral
2.2904
7.6784
1.5740
3.4586
1.6140
1.3844
8.4
8.0
7.6
7.2
6.8
6.4
6.0
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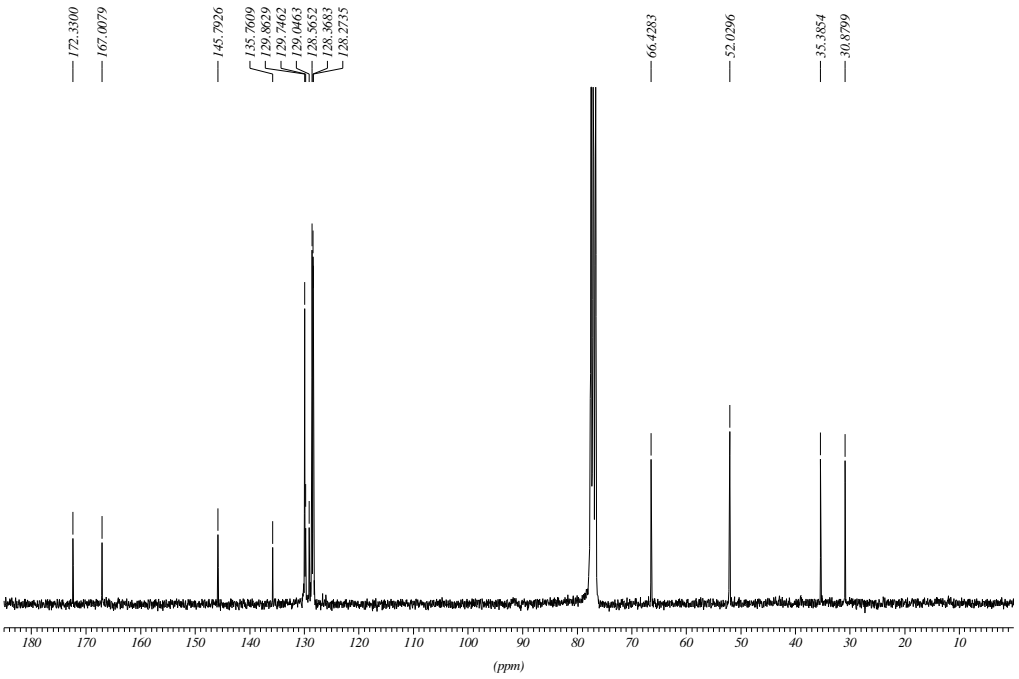
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
(ppm)

26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129.0463
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128.3683
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52.0296
35.3854
30.8799
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170
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140
130
120
110
100
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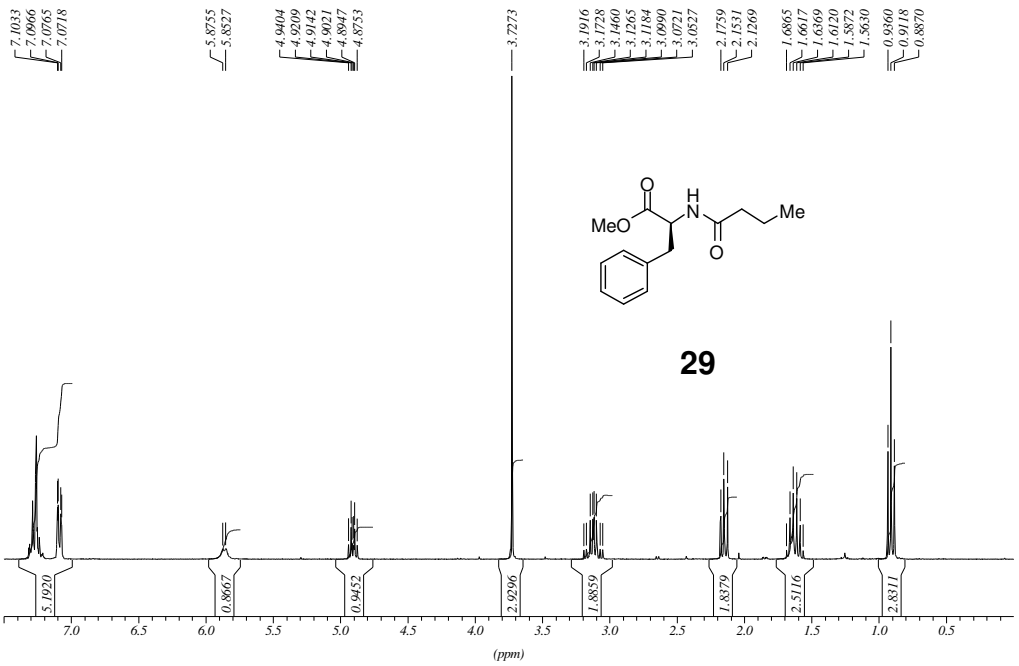
80
70
60
50
40
30
20
10
(ppm)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7.0966
7.0765
7.0718
5.8755
5.8527
4.9404
4.9209
4.9142
4.9021
4.8947
4.8753
3.7273
3.1916
3.1728
3.1460
3.1265
3.1184
3.0990
3.0721
3.0527
2.1759
2.1531
2.1269
1.6865
1.6617
1.6369
1.6120
1.5872
1.5630
0.9360
0.9118
0.8870
MeO
H
N
O
O
Me
5.1920
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0.9452
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1.8859
1.8379
2.5116
2.8311
7.0
6.5
6.0
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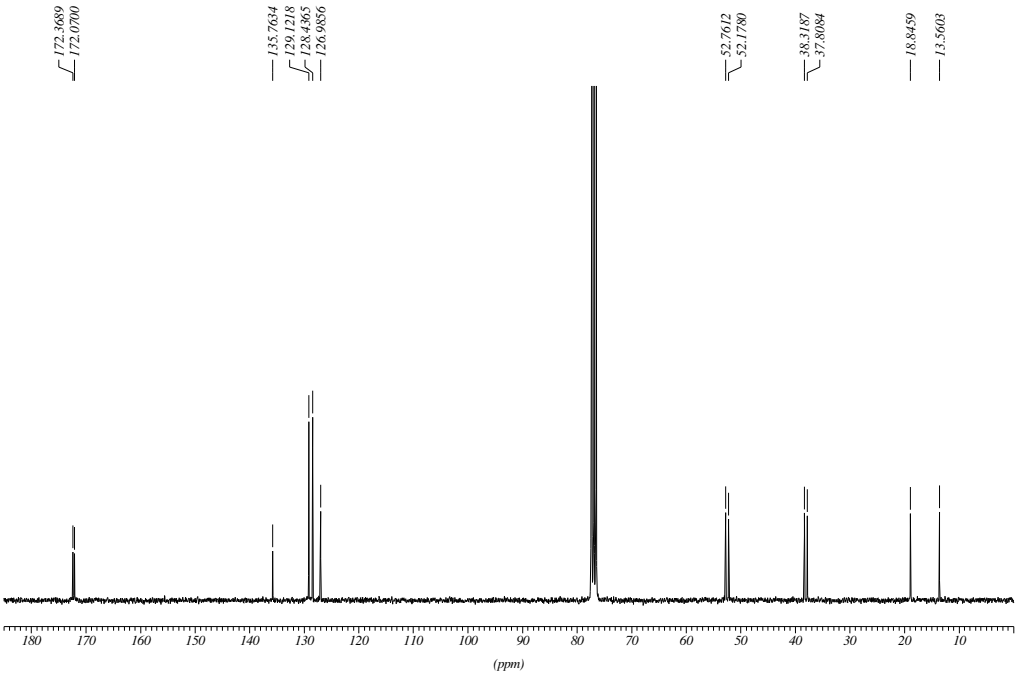
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
(ppm)

29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13.5603
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140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)