Supporting Information

Palladium-Catalyzed Alkoxycarbonylation of Unactivated Secondary Alkyl Bromides at Low Pressure

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General Methods and Materials

Infrared (IR) spectra were obtained using a Jasco 260 Plus Fourier transform infrared spectrometer. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Bruker model DRX 400 or Bruker Avance III 600 CryoProbe (^{1}H NMR at 400 or 600 MHz and ^{13}C at 151 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR: $CHCl_3$ at 7.28 ppm; ^{13}C NMR: $CDCl_3$ at 77.0 ppm). ^{1}H NMR data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. Mass spectra were obtained using either a Thermo LTqFT mass spectrometer with electrospray introduction and external calibration or an Agilent Gas Chromatograph-Mass Spectrometer with a 6850 series GC system and a 5973 Network Mass Selective Detector. These samples were prepared in either dichloromethane or methanol. HPLC analysis was performed on a Perkin Elmer flexar photodiode array (PDA) system equipped with a Chiralcel OJ-H column using a flow rate of 1 mL/min with hexanes and isopropanol as eluent.

Analytical thin layer chromatography (TLC) was performed on SiliaPlate 250μm thick silica gel purchased from Silicycle. Visualization was accomplished with short-wave UV light (254 nm), iodine, Hanessian's stain, aqueous basic potassium permanganate solution, or ethanolic acidic p-anisaldehyde solution followed by heating when necessary. Purification of the reaction products was carried out by flash chromatography using Siliaflash P60 silica gel (40-63μm) purchased from Silicycle. Carbon monoxide, Research Purity 99.999% (part number G2119118) was purchased from Matheson Tri-Gas. Tetrahydrofuran, diethyl ether, acetonitrile, *N,N*-Dimethylformamide, and dichloromethane were dried by passage through a column of neutral alumina under nitrogen prior to use. Benzene, *n*-heptane, and *n*-butanol were sparged with argon before storage over 3Å molecular sieves in the glovebox. Bromocyclohexane (**19**), 4-bromotetrahydropyran (**23**), bromocyclopentane (**25**), and exo-2-bromonorborane (**29**), were purchased and distilled prior to use. All other reagents were obtained from commercial sources and used without further purification unless otherwise noted. In addition, all reactions were carried out under an atmosphere of dry argon in flame or oven-dried glassware with magnetic stirring. The glass tubes used were purchased from Ace Glass and the gas quick-connect adapters were obtained from Swagelok. An example of the alkoxycarbonylation setup is shown below.

Swagelok setup for pressurizing alkoxycarbonylation reactions

List of Abbreviations

DCM = dichloromethane
DMF = *N,N*-dimethylformamide
EtOAc = ethyl acetate
IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene
MeCN = acetonitrile
TEA = triethylamine
THF = tetrahydrofuran

Substrate Preparation

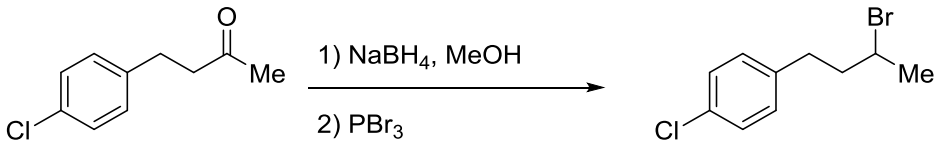
General Procedure A: Bromination of Secondary Alcohols.

To a 0 ºC ice bath cooled solution of the alcohol in Et_2O (0.5 M) was added PBr_3 (0.5 equiv) dropwise. The solution was then stirred from 2 to 16 hours at room temperature, monitoring by TLC. The reaction was quenched over ice water and stirred for 30 minutes. The aqueous layer was removed and extracted once with Et_2O or DCM. The organic layers were combined and washed sequentially with a saturated solution of sodium bicarbonate, then brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography.

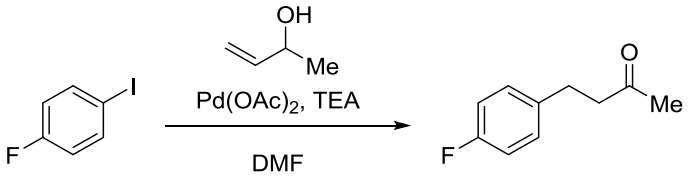
General Procedure B: Bromination of Secondary Alcohols.

To a 0 ºC ice bath cooled solution of triphenylphosphine (2.0 equiv) in 4:1 DCM:MeCN (0.1 M) was added bromine (2.0 equiv) dropwise, then TEA (2.0 equiv). To the reaction mixture was added a solution of the alcohol (1.0 equiv) in DCM (0.5 M). The solution was then stirred from 2 to 16 hours at room temperature, monitoring by TLC. The reaction was quenched with water and extracted 3 times with DCM. The organic layers were combined and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography.

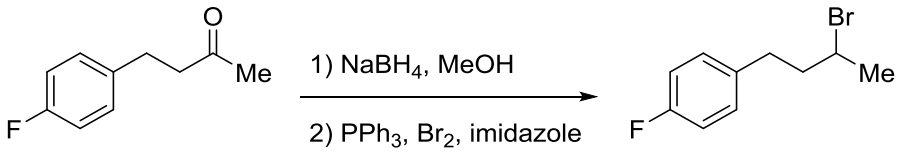
(3-bromobutyl)benzene (1) was synthesized by brominating 4-phenylbutan-2-ol (10 g, 67 mmol) according to General Procedure A, using a concentration of 1.0 M in diethyl ether. The crude product was purified via gravity column chromatography in 2.5% EtOAc/hexanes to provide 8.0 g (56%) of bromide **1** as a colorless oil. Physical and spectral data were in accordance with literature data.[1]



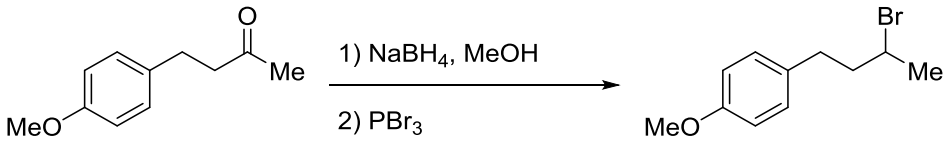
1-(3-bromobutyl)-4-chlorobenzene (3): 4-(4-chlorophenyl)butan-2-one (2 g, 10.9 mmol) was dissolved in 70 mL of MeOH and cooled to 0 ºC. $NaBH_4$ (0.46 g, 12 mmol) was added portion wise with stirring, maintaining a 0 ºC temperature for 30 minutes. The reaction was warmed to room temperature and stirred an additional 30 minutes and then concentrated under reduced pressure. The mixture was brought up in water and DCM and the organic layer was separated. The aqueous layer was extracted twice with DCM and the organic layers were combined and washed with brine, dried over $MgSO_4$, filtered, and concentrated. 4-(4-chlorophenyl)butan-2-ol (1.9 g) was used without further purification and brominated according to General Procedure A. The crude product was flashed in 2.5% EtOAc/hexanes to provide 1.0 g (39%) of bromide **3** as a colorless oil. Physical and spectral data were in accordance with literature data.[2]



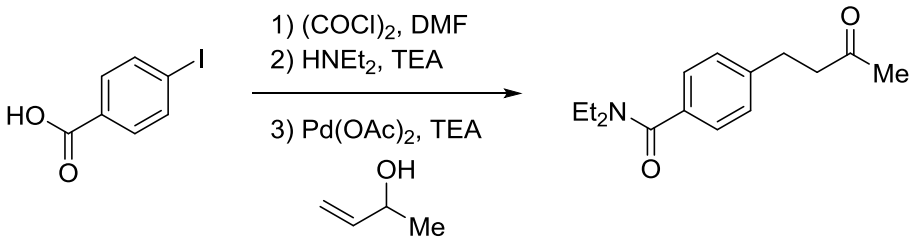
4-(4-fluorophenyl)butan-2-one (SI-1) was synthesized using a modified procedure from Wu and Han.[3] To a solution of 4-fluoroiodobenzene (2 g, 9.0 mmol) in DMF (60 mL) was added 3-butene-2-ol (0.94 mL, 10.8 mmol), TEA (1.6 mL, 11.7 mmol), and $Pd(OAc)_2$ (40 mg, 0.2 mmol). The reaction mixture was then stirred overnight at 100 ºC. The reaction was cooled to room temperature, diluted with EtOAc, washed twice with water, once with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 5% EtOAc/hexanes to provide 0.89 g (76%) of **SI-1** as a yellow oil. Physical and spectral data were in accordance with literature data.[4]



1-(3-bromobutyl)-4-fluorobenzene (5): 4-(4-fluorophenyl)butan-2-one (**SI-1**) (0.89 g, 5.4 mmol) was dissolved in 17 mL of MeOH and cooled to 0 ºC, to which, $NaBH_4$ (0.22 g, 5.9 mmol) was added portion wise with stirring, maintaining a 0 ºC temperature for 30 minutes. The reaction was warmed to room temperature, stirred an additional 30 minutes, and then concentrated under reduced pressure. The mixture was brought up in water and DCM and the organic layer was separated. The aqueous layer was extracted twice with DCM and the organic layers were combined, washed with brine, dried over $MgSO_4$, filtered, and concentrated. 4-(4-fluorophenyl)butan-2-ol was used without further purification. To a 0 ºC ice bath cooled solution of triphenylphosphine (3.3 g, 12.4 mmol) in DCM (60 mL) was added bromine (0.36 mL, 7.0 mmol) dropwise, then imidazole (0.5 g, 7.0 mmol) was introduced in one portion. To the reaction mixture was added a solution of 4-(4-fluorophenyl)butan-2-ol (5.4 mmol) in DCM (5 mL) and allowed to stir overnight at room temperature. The reaction was quenched with water and extracted 3 times with DCM. The organic layers were combined and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 5% Et_2O/hexanes to provide a mixture of the product and triphenylphosphine. This was dissolved in DCM (50 mL) to which was added bromine until a yellow color persisted. The solution was quenched with water, and the organic layer was separated, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was flashed using a gradient of 0-1% EtOAc/hexanes to provide 0.55 g (44%) of bromide **5** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.23 – 7.17 (m, 2H), 7.05 – 6.98 (m, 2H), 4.09 (dqd, *J* = 9.1, 6.6, 4.2 Hz, 1H), 2.88 (ddd, *J* = 14.0, 9.0, 5.1 Hz, 1H), 2.76 (ddd, *J* = 13.9, 8.9, 7.2 Hz, 1H), 2.14 (m, 1H), 2.05 (dddd, *J* = 14.4, 9.0, 7.2, 4.2 Hz, 1H), 1.77 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 161.40 (d, *J* = 243.7 Hz), 136.5, 129.9, 115.3, 50.7, 42.8, 33.2, 26.6. **IR** (thin film, cm^{-1}): 2968, 2925, 2864, 1601, 1509, 1223, 1157, 827. **GC-MS** calculated for [$C_{10}H_{12}BrF$] 230.01, found 230.00.

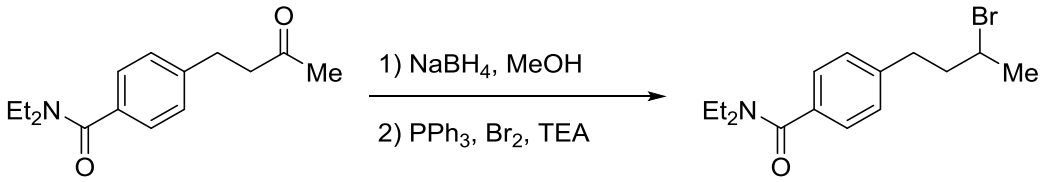


1-(3-bromobutyl)-4-methoxybenzene (7) was synthesized by reducing 4-(4-methoxyphenyl)butan-2-one (5.0 g, 28 mmol) with $NaBH_4$ (1.2 g, 30 mmol) in MeOH (0.3 M), according to Denmark and Cresswell.[5] The resultant crude 4-(4-methoxyphenyl)butan-2-ol (3.0 g, 16.6 mmol) was then brominated according to General Procedure A. The crude product was flashed in 2.5% EtOAc/hexanes to provide 2.3 g (57%) of bromide **7** as a colorless oil. Physical and spectral data were in accordance with literature data.[6]



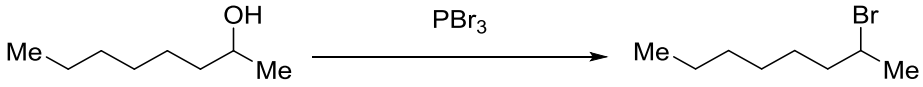
***N*,*N*-diethyl-4-(3-oxobutyl)benzamide (SI-2)** was synthesized following the three step sequence shown above. 4-iodobenzoic acid (10 g, 40.3 mmol) was dissolved in DMF (0.4 mL) and DCM (160 mL) and cooled to 0 ºC. Oxalyl chloride (6.8 mL, 80.6 mmol) was subsequently added dropwise and the reaction was stirred for 15 minutes before warming to room temperature and continuing to stir for 2 hours. Excess oxalyl chloride was removed under reduced pressure and the residue was brought up in DCM (10 mL) and added dropwise to a 0 ºC solution of TEA (11.8 mL, 84.6 mmol) and diethylamine (8.8 mL, 84.6 mmol) in DCM (150 mL). The reaction was allowed to warm to room temperature overnight with stirring. The reaction mixture was washed twice with water, once with a saturated solution of sodium bicarbonate, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was recrystallized in hexanes to provide 11.5 g (94%) of *N*,*N*-diethyl-4-iodobenzamide as an off-white, crystalline solid. Physical and spectral data were in accordance with literature data.[7,8] A Heck coupling was then employed to furnish **SI-2**. To a solution of *N*,*N*-diethyl-4-iodobenzamide (5 g, 16.5 mmol) in DMF (110 mL) was added 3-butene-2-ol (1.7 mL,

19.8 mmol), TEA (3 mL, 21.5 mmol), and $Pd(OAc)_2$ (74 mg, 0.33 mmol). The reaction mixture was then stirred overnight at 100 ºC. The reaction was cooled to room temperature, diluted with EtOAc, washed twice with water, once with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 50% EtOAc/hexanes to provide 1.4 g (35%) of ketone **SI-2** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.25 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 3.56 – 3.44 (m, 2H), 3.26 – 3.17 (m, 2H), 2.87 (t, *J* = 7.6 Hz, 2H), 2.73 (t, *J* = 7.6 Hz, 2H), 2.11 (s, 3H), 1.24 – 1.15 (m, 3H), 1.11 – 1.03 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.6, 171.2, 142.1, 135.1, 128.3, 126.5, 44.8, 43.3, 39.2, 30.1, 29.4, 14.2, 12.9. **IR** (thin film, cm^{-1}): 2974, 1713, 1629, 1428, 1365, 1287, 1221, 1162, 1096, 875, 829. **HRMS** (ESI) calculated for $[C_{15}H_{21}NO_2+H]^+$ 248.1651, found 248.1644.

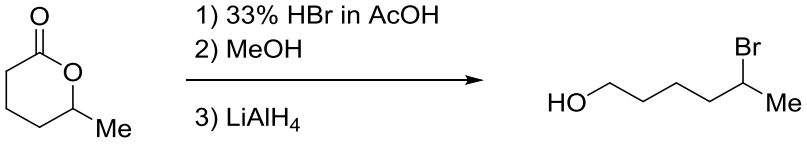


4-(3-bromobutyl)-*N*,*N*-diethylbenzamide (9): *N*,*N*-diethyl-4-(3-oxobutyl)benzamide (**SI-2**) (1.2 g, 4.9 mmol) was dissolved in MeOH (15 mL) and cooled to 0 ºC. $NaBH_4$ (0.2 g, 5.3 mmol) was added portion wise with stirring, maintaining a 0 ºC temperature for 30 minutes. The reaction was warmed to room temperature, stirred an additional 30 minutes, and then concentrated under reduced pressure. The mixture was brought up in water and DCM and the organic layer was separated. The aqueous layer was extracted three times with DCM and the organic layers were combined, dried over $MgSO_4$, filtered, and concentrated. *N*,*N*-diethyl-4-(3-hydroxybutyl)benzamide was used without further purification and brominated according to General Procedure B. The crude product was flashed in 40% EtOAc/hexanes to provide 1.1 g (73%) of bromide **9** as a lemon-yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 4.07 (dqd, *J* = 9.2, 6.7, 4.1 Hz, 1H), 3.60 – 3.52 (m, 2H), 3.32 – 3.24 (m, 2H), 2.89 (ddd, *J* = 13.9, 8.9, 5.1 Hz, 1H), 2.78 (ddd, *J* = 13.8, 8.8, 7.2 Hz, 1H), 2.14 (dtd, *J* = 14.2, 9.0, 5.1 Hz, 1H), 2.04 (dddd, *J* = 14.5, 8.9, 7.3, 4.1 Hz, 1H), 1.74 (d, *J* = 6.7 Hz, 3H), 1.31 – 1.21 (m, 3H), 1.17 – 1.09 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ

171.3, 142.0, 135.1, 128.5, 126.6, 50.8, 43.3, 42.4, 39.2, 33.8, 26.6, 14.3, 12.9. **IR** (thin film, cm^{-1}): 2971, 1630, 1426, 1380, 1286, 1222, 1095, 841. **HRMS** (ESI) calculated for $[C_{15}H_{22}BrNO+H]^+$ 312.0963, found 312.0963.

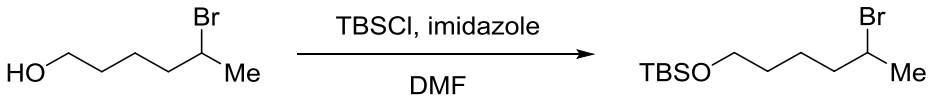


2-Bromooctane (11) was synthesized by brominating 2-octanol (5.0 g, 38.4 mmol) according to General Procedure A, using a concentration of 1.0 M in diethyl ether. The crude product was flashed in 2.5% EtOAc/hexanes to provide 4.33 g (58%) of bromide **11** as a colorless oil. Physical and spectral data were in accordance with literature data.[9]

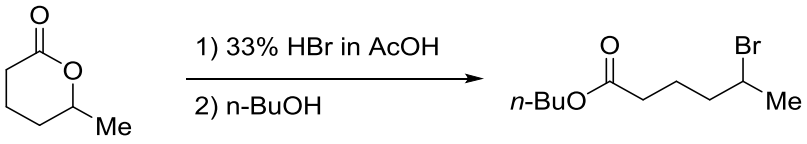


5-bromohexan-1-ol (SI-3) was obtained from the reduction of methyl 5-bromohexanoate, previously synthesized by our lab.[10] δ-hexalactone (3.45 g, 30.2 mmol) was added to 33% HBr in AcOH (8.5 mL) in a flask equipped with a reflux condenser. The reaction was heated to 75 ºC for 4 hours and then cooled to room temperature, at which point of MeOH (6.1 mL) was added and stirred overnight at room temperature. The reaction was then partially concentrated under reduced pressure, taken up in EtOAc, washed 3 times with a saturated aqueous solution of sodium bicarbonate, once with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 5% EtOAc/hexanes to provide 3.0 g (48%) of methyl 5-bromohexanoate as a colorless oil. A solution of methyl 5-bromohexanoate (2.0 g, 9.6 mmol) in 15 mL of Et_2O was added dropwise to a suspension of $LiAlH_4$ (0.18 g, 4.8 mmol) in 5 mL Et_2O at 0 ºC. The reaction mixture was stirred at 0 ºC for 1 hour and then quenched successively with 0.18 mL water, 0.27 mL aqueous 10% NaOH, and 0.54 mL water. $MgSO_4$ was added and the reaction was stirred for 30 min before filtering and concentrating the filtrate under reduced pressure. The crude product was flashed using a gradient of 20-25% EtOAc/hexanes to provide

1.3 g (75%) of alcohol **SI-3** as a slightly yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.16 (m, 1H), 3.68 (t, *J* = 6.2 Hz, 2H), 1.94 – 1.77 (m, 2H), 1.74 (d, *J* = 6.6 Hz, 3H), 1.68 – 1.36 (m, 5H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 62.7, 51.7, 40.8, 32.0, 26.5, 24.1. **IR** (thin film, cm^{-1}): 3308, 2939, 2864, 1716, 1456, 1378, 1061. **HRMS** (ESI): calculated for $[C_6H_{13}BrO+H]^+$ 181.02, found 181.04.

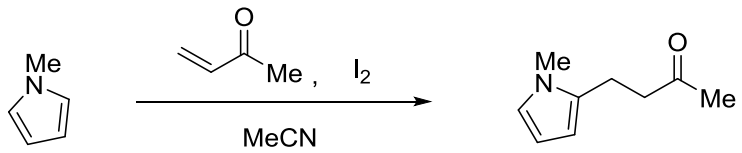


((5-bromohexyl)oxy)(tert-butyl)dimethylsilane (13) was synthesized by stirring 5-bromohexan-1-ol (**SI-3**) (0.25 g, 1.4 mmol) and imidazole (0.19 g, 2.8 mmol) in DMF (3 mL) for 15 minutes, then *tert*-butyldimethylsilyl chloride (0.31 g, 2.1 mmol) was added and the reaction was stirred overnight at room temperature. The reaction was quenched with water, extracted 3 times EtOAc, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 10% EtOAc/hexanes to provide 240 mg (58%) of bromide **13** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.16 (dqd, *J* = 8.2, 6.6, 5.0 Hz, 1H), 3.64 (t, *J* = 6.1 Hz, 2H), 1.92 – 1.77 (m, 2H), 1.73 (d, *J* = 6.6 Hz, 4H), 1.64 – 1.43 (m, 3H), 0.91 (s, 9H), 0.07 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 62.9, 51.8, 40.9, 32.1, 26.5, 26.0, 24.2, 18.4, -5.3. **IR** (thin film, cm^{-1}): 2931, 2859, 1468, 1385, 1254, 1101, 837, 776. **HRMS** (ESI): calculated for $[C_{12}H_{27}BrOSi+Na]^+$ 317.0912, found 317.0907.

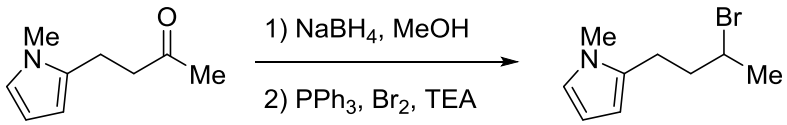


Butyl 5-bromohexanoate (15) was synthesized using an adapted procedure from our lab.[10] δ-hexalactone (2.0 g, 17.5 mmol) was added to 33% HBr in AcOH (5.0 mL) in a flask equipped with a reflux condenser. The reaction was heated to 75 ºC for 4 hours and then cooled to room temperature, at which point 1-butanol (8.0 mL) was added and stirred overnight at room temperature. The reaction was then partially concentrated under reduced pressure, taken up in EtOAc, washed 3 times with a saturated aqueous solution of sodium bicarbonate, once with brine, dried over $MgSO_4$, filtered, and

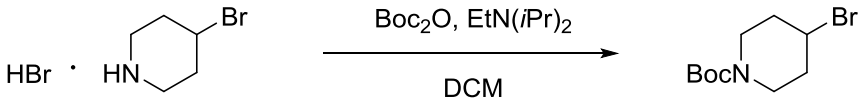
concentrated under reduced pressure. The crude product was flashed in 5% EtOAc/hexanes to provide 2.6 g (59%) of bromide **15** as a colorless oil. **^{1}H NMR** (400 MHz, Chloroform-d) δ 4.20 – 4.11 (m, 1H), 4.09 (d, J = 6.7 Hz, 1H), 2.36 (t, J = 7.0 Hz, 1H), 1.94 – 1.85 (m, 1H), 1.85 – 1.76 (m, 1H), 1.74 (d, J = 6.7 Hz, 2H), 1.69 – 1.55 (m, 1H), 1.46 – 1.35 (m, 1H), 0.96 (t, J = 7.4 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.3, 64.3, 50.9, 40.3, 33.5, 30.7, 26.4, 23.2, 19.2, 13.7. **IR** (thin film, cm^{-1}): 2961, 2873, 1735, 1457, 1379, 1250, 1184, 1118, 970. **HRMS** (ESI) calculated for $[C_{10}H_{19}BrO_2Na]^+$ 273.0466, found 273.0462.



4-(1-methyl-1H-pyrrol-2-yl)butan-2-one (SI-4) was synthesized using a modified procedure from Das, et. al.[11] To a solution of *N*-methylpyrrole (11.9 g, 147 mmol) and catalytic iodine (0.47 g, 2 mmol) in acetonitrile (185 mL) was added 3-butene-2-one (2.6 g, 37 mmol) dropwise. The reaction was stirred at room temperature for 1 hour and then concentrated under reduced pressure. The residue was brought up in a saturated aqueous solution of sodium thiosulfate and extracted twice with EtOAc. The organic layers were combined and washed twice with a saturated aqueous solution of sodium thiosulfate, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 20% EtOAc/hexanes to provide 1.6 g (29%) of bromide (**SI-4**) as a carrot-orange oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.72 – 6.53 (m, 1H), 6.14 – 6.06 (m, 1H), 5.90 (dd, *J* = 3.5, 1.8 Hz, 1H), 3.60 (s, 3H), 2.86 (s, 4H), 2.24 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.8, 131.8, 121.5, 106.6, 105.2, 42.5, 33.6, 30.1, 20.2. **IR** (thin film, cm^{-1}): 2919, 1715, 1496, 1417, 1363, 1299, 1165, 708. **HRMS** (ESI) calculated for $[C_9H_{13}NO+Na]^+$ 174.0895, found 174.0889.

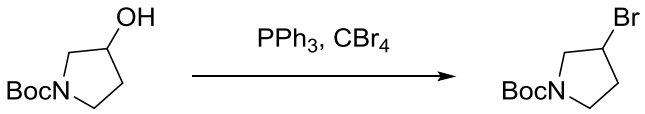


2-(3-bromobutyl)-1-methyl-1H-pyrrole (17): 4-(1-methyl-1H-pyrrol-2-yl)butan-2-one (**SI-4**) (1.0 g, 6.6 mmol) was dissolved in 22 mL of MeOH and cooled to 0 ºC. $NaBH_4$ (0.28 g, 7.3 mmol) was added portion wise with stirring, maintaining a 0 ºC temperature for 30 minutes. The reaction was warmed to room temperature, stirred an additional 30 minutes, and then concentrated under reduced pressure. The mixture was brought up in water and DCM and the organic layer was separated. The aqueous layer was extracted twice with DCM and the organic layers were combined and washed with brine, dried over $MgSO_4$, filtered, and concentrated. 4-(1-methyl-1H-pyrrol-2-yl)butan-2-ol was used without further purification and brominated according to General Procedure B. The crude product was flashed in 5% Et_2O/hexanes to provide 0.7 g (49%) of bromide **17** as a mustard-yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.59 (dt, *J* = 3.0, 1.5 Hz, 1H), 6.09 (dd, *J* = 3.9, 2.2 Hz, 1H), 5.96 – 5.88 (m, 1H), 4.22 (m, 1H), 3.59 (s, 3H), 2.84 (ddd, *J* = 14.6, 9.0, 5.3 Hz, 1H), 2.72 (ddd, *J* = 15.6, 9.2, 7.0 Hz, 1H), 2.24 – 2.04 (m, 2H), 1.79 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 131.7, 121.4, 106.6, 105.7, 51.2, 40.1, 33.7, 26.6, 24.5. **IR** (thin film, cm^{-1}): 2922, 1674, 1495, 1446, 1378, 1301, 1089, 706. **HRMS** (ESI) calculated for $[C_9H_{14}BrN+H]^+$ 216.0388, found 216.0382.

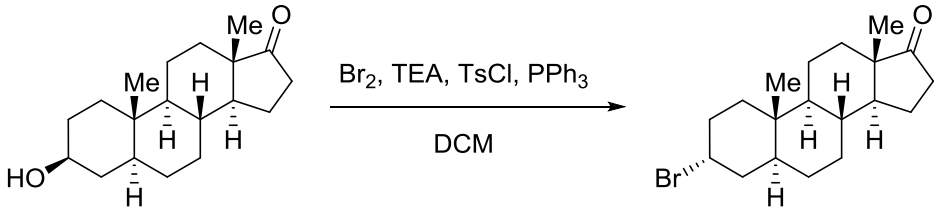


Tert-butyl 4-bromopiperidine-1-carboxylate (21) was synthesized by dropwise addition of diisopropylethylamine (3.6 mL) to a solution of 4-bromopiperidine hydrobromide (2.5 g, 10.2 mmol) in DCM (17 mL) at 0 ºC. After stirring for one hour, a solution of di-tert-butyl dicarbonate (3.3 g, 15.3 mmol) in 17 mL of DCM was added dropwise and the solution was allowed to warm to room temperature and stir overnight. The reaction mixture was washed twice with a saturated aqueous solution of sodium bicarbonate and once with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 5% EtOAc/hexanes to provide 2.0

g (74%) of bromide **21** as white solid. Physical and spectral data were in accordance with literature data.[12]



Tert-butyl 3-bromopyrrolidine-1-carboxylate (27) was synthesized by dropwise addition of a CBr_4 (5.2 g, 15.8 mmol) solution in THF (16 mL) to a solution of *N*-Boc-3-hydroxypyrrolidine (1 g, 5.3 mmol) and PPh_3 (4.1 g, 15.8 mmol) in THF (25 mL). The reaction was stirred overnight and the precipitant was removed via filtration. The filtrate was concentrated under reduced pressure and additional triphenylphosphine oxide was crashed out with hexanes and removed via filtration. The crude product was flashed using a gradient of 5-15% EtOAc/hexanes to provide 1.1 g (83%) of bromide **27** as an off-white solid. Two conformers: **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.52 – 4.43 (m, 1H), 3.83 – 3.75 (m, 1.5H), 3.69 (dt, *J* = 12.6, 1.8 Hz, 0.5H), 3.61 (dtd, *J* = 22.0, 10.1, 7.0 Hz, 1H), 3.50 (dddd, *J* = 27.2, 10.8, 8.1, 3.1 Hz, 1H), 2.32 (dqd, *J* = 13.4, 8.4, 4.8 Hz, 1H), 2.23 (ddd, *J* = 14.0, 7.0, 3.4 Hz, 1H), 1.46 (s, 4.5H), 1.47 (s, 4.5H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.4, 154.3, 79.7, 55.8, 55.5, 47.2, 46.9, 44.2, 43.9, 36.6, 35.8, 28.5. **IR** (thin film, cm^{-1}): 2977, 2890, 1697, 1405, 1234, 1165, 1112, 876, 770. **HRMS** (ESI): calculated for $[C_9H_{16}BrNO_2+H]^+$ 250.0443, found 250.0440.



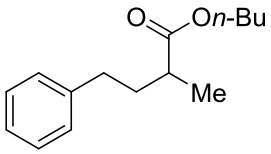
(3R,5S,8R,9S,10S,13S,14S)-3-bromo-10,13-dimethylhexadecahydro-17H-cyclopenta[a]phenanthren-17-one (31) was synthesized according to the procedure from Goldenstein.[13] To a 0 ºC ice bath cooled solution of triphenylphosphine (0.66 g, 2.5 mmol) in DCM (24 mL) was added bromine (75 µL, 1.5 mmol) dropwise. Then, TEA (0.21 mL, 1.5 mmol) and p-toluenesulfonyl chloride (42 mg, 0.2 mmol) were added and the reaction was stirred for 10 minutes. A solution of 330 mg (1.1 mmol) of trans-

androsterone in DCM (5 mL) was added dropwise to the reaction mixture and allowed to stir overnight at room temperature. The reaction was quenched with water, extracted twice with EtOAc, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed using a gradient of 2.5-5% EtOAc/hexanes to provide 350 mg (90%) of bromide **31** as an off-white solid. Physical and spectral data were in accordance with literature data.[13]

Palladium-Catalyzed Alkoxycarbonylation Reactions

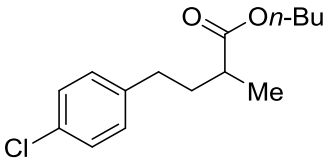
General Carbonylation Procedure A: In a glovebox under an argon atmosphere, alkyl bromide (0.25 mmol) was combined with $Pd(PPh_3)_2Cl_2$ (8.8 mg, 0.0125 mmol), IMes (7.6 mg, 0.025 mmol), $CsCO_3$ (163 mg, 0.5 mmol), *n*-heptane (0.25 mL), and *n*-butanol (0.25 mL) [0.5 M] in an Ace Glass pressure tube. The tube was sealed with a Swagelok gas quick-connect adapter and removed from the glovebox. Subsequently, the tube was purged 3 times with 5 atm CO and then the pressure was set to 2 atm CO. The reaction was stirred for 24 hours at 50 ºC. The reaction mixture was cooled to room temperature, depressurized, and 2 mL 1M HCl and 2 mL DCM were added. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography.

General Carbonylation Procedure B: In a glovebox under an argon atmosphere, alkyl bromide (0.25 mmol) was combined with $Pd(PPh_3)_2Cl_2$ (8.8 mg, 0.0125 mmol), IMes (7.6 mg, 0.025 mmol), $CsCO_3$ (163 mg, 0.5 mmol), $PhCF_3$ (0.2 mL), and an alcohol (0.5 mmol, 2 equiv.) [1.0 M] in an Ace Glass pressure tube. The tube was sealed with a Swagelok gas quick-connect adapter and removed from the glovebox. Subsequently, the tube was purged 3 times with 5 atm CO and then the pressure was set to 2 atm CO. The reaction was stirred for 24 hours at 50 ºC. The reaction mixture was cooled to room temperature, depressurized, and 2 mL 1M HCl and 2 mL DCM were added. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography.

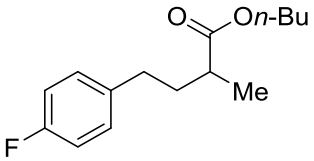


Butyl 2-methyl-4-phenylbutanoate (2) was obtained from General Carbonylation Procedure A and the crude product was flashed in 5% Et_2O/hexanes yielding *n*-butyl ester **2** as a colorless oil (42.3 mg, 72%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.36 –

7.27 (m, 2H), 7.30 – 7.17 (m, 3H), 4.12 (t, *J* = 6.7 Hz, 2H), 2.70 – 2.61 (m, 2H), 2.57 – 2.43 (m, 1H), 2.11 – 1.97 (m, 1H), 1.82 – 1.65 (m, 1H), 1.69 – 1.60 (m, 2H), 1.48 – 1.38 (m, 2H), 1.22 (d, *J* = 7.0 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.7, 141.8, 128.4, 128.4, 125.9, 64.2, 39.2, 35.5, 33.5, 30.8, 19.2, 17.3, 13.8. **IR** (thin film, cm^{-1}): 2960, 2873, 1733, 1604, 1458, 1379, 1241, 1163, 746, 699. **HRMS** (ESI) calculated for $[C_{15}H_{22}O_2H]^+$ 235.1698, found 235.1693.

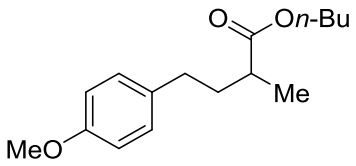


Butyl 4-(4-chlorophenyl)-2-methylbutanoate (4) was obtained from General Carbonylation Procedure A and the crude product was flashed in 5% Et_2O/hexanes yielding *n*-butyl ester **4** as a colorless oil (47.0 mg, 70%) and 7.7 mg (12%) of recovered starting material **3**. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.26 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 4.11 (t, *J* = 6.7 Hz, 2H), 2.61 (tt, *J* = 8.3, 6.9 Hz, 2H), 2.54 – 2.40 (m, 1H), 2.07 – 1.93 (m, 1H), 1.77 – 1.58 (m, 3H), 1.49 – 1.34 (m, 2H), 1.21 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.5, 140.1, 131.6, 129.8, 128.5, 64.2, 39.0, 35.3, 32.9, 30.7, 19.2, 17.3, 13.8. **IR** (thin film, cm^{-1}): 2960, 2873, 1732, 1492, 1461, 1379, 1257, 1162, 1093, 1016, 828. **HRMS** (ESI): calculated for $[C_{15}H_{21}ClO_2Na]^+$ 291.1128, found 291.1120

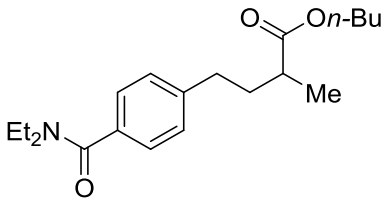


Butyl 4-(4-fluorophenyl)-2-methylbutanoate (6) was obtained from General Carbonylation Procedure A and the crude product was flashed in 5% EtOAc/hexanes yielding *n*-butyl ester **6** as a colorless oil (52.3 mg, 83%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.20 – 7.10 (m, 2H), 7.04 – 6.93 (m, 2H), 4.11 (t, *J* = 6.7 Hz, 2H), 2.61 (dd, *J* = 9.0, 6.9 Hz, 2H), 2.47 (ddd, *J* = 8.1, 7.0, 6.0 Hz, 1H), 2.07 – 1.93 (m, 1H), 1.77 – 1.57 (m, 3H), 1.49 – 1.35 (m, 2H), 1.21 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.6, 161.27 (d, *J* = 243.3 Hz), 137.3, 129.8, 115.0,

64.2, 39.1, 35.6, 32.7, 30.7, 19.2, 17.3, 13.8. **IR** (thin film, cm^{-1}): 2961, 2874, 1732, 1602, 1510, 1462, 1222, 1158, 829. **HRMS** (ESI): calculated for $[C_{15}H_{21}FO_2H]^+$ 253.1604, found 253.1606.

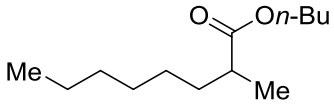


Butyl 4-(4-methoxyphenyl)-2-methylbutanoate (8) was obtained from General Carbonylation Procedure A and the crude product was flashed in 5% EtOAc/hexanes yielding *n*-butyl ester **8** as a colorless oil (53.8 mg, 81%) and 6.0 mg (10%) of recovered starting material **7**. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.12 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 4.11 (t, *J* = 6.7 Hz, 2H), 3.81 (s, 3H), 2.58 (dd, *J* = 8.9, 7.0 Hz, 2H), 2.54 – 2.41 (m, 1H), 2.07 – 1.93 (m, 1H), 1.75 – 1.61 (m, 3H), 1.49 – 1.35 (m, 2H), 1.20 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.7, 157.8, 133.8, 129.3, 113.8, 64.2, 55.3, 39.1, 35.8, 32.6, 30.7, 19.2, 17.2, 13.8. **IR** (thin film, cm^{-1}): 2959, 2873, 1731, 1612, 1513, 1462, 1249, 1176, 1038, 827. **HRMS** (ESI) calculated for $[C_{16}H_{24}O_3H]^+$ 265.1804, found 265.1801.

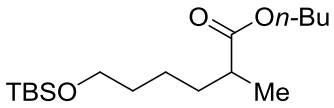


Butyl 4-(4-(diethylcarbamoyl)phenyl)-2-methylbutanoate (10) was obtained from General Carbonylation Procedure A and the crude product was flashed using a gradient of 15-25% EtOAc/hexanes yielding *n*-butyl ester **10** as a slightly yellow oil (62.2 mg, 75%) with about 4% as inseparable starting material. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.32 – 7.29 (m, 2H), 7.21 (d, *J* = 8.1 Hz, 2H), 4.11 (t, *J* = 6.7 Hz, 2H), 3.63 – 3.47 (m, 2H), 3.33 – 3.21 (m, 2H), 2.69 – 2.59 (m, 2H), 2.54 – 2.43 (m, 1H), 2.06 – 1.97 (m, 1H), 1.78 – 1.68 (m, 1H), 1.68 – 1.59 (m, 2H), 1.45 – 1.37 (m, 2H), 1.32 – 1.23 (m, 3H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.13 (s, 3H), 0.96 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.6, 171.4, 142.9, 134.9, 128.4, 126.5, 64.2, 43.3, 39.2, 39.0, 35.3, 33.3, 30.7, 19.2,

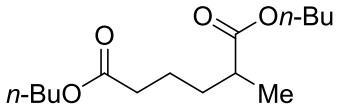
17.3, 14.3, 13.8, 12.9. **IR** (thin film, cm^{-1}): 2933, 1731, 1633, 1540, 1510, 1458, 1422, 1286, 1162, 1094. **HRMS** (ESI) calculated for $[C_{20}H_{31}NO_3+Na]^+$ 356.2202, found 356.2191.



Butyl 2-methyloctanoate (12) was obtained from General Carbonylation Procedure A and the crude product was flashed in 1% EtOAc/hexanes yielding *n*-butyl ester **12** as a colorless oil (34.9 mg, 65%). Physical and spectral data were in accordance with literature data.[14]

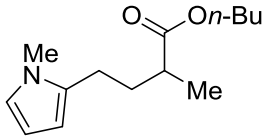


Butyl 6-((tert-butyldimethylsilyl)oxy)-2-methylhexanoate (14) was obtained from General Carbonylation Procedure A and flashed using a gradient of 1-5% EtOAc/hexanes yielding *n*-butyl ester **14** as a colorless oil (58.1 mg, 73%).**^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.08 (td, *J* = 6.7, 1.0 Hz, 2H), 3.61 (t, *J* = 6.5 Hz, 2H), 2.50 – 2.38 (m, 1H), 1.73 – 1.58 (m, 3H), 1.57 – 1.49 (m, 2H), 1.48 – 1.27 (m, 5H), 1.16 (d, *J* = 7.0 Hz, 3H), 0.98 – 0.88 (m, 3H), 0.90 (s, 9H), 0.06 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 177.0, 64.1, 63.0, 39.6, 33.6, 32.7, 30.7, 26.0, 23.6, 19.2, 18.4, 17.1, 13.8, -5.3. **IR** (thin film, cm^{-1}): 1700, 1605, 1576, 1445, 1382, 1306, 1212, 1169, 823. **HRMS** (ESI): calculated for $[C_{17}H_{36}O_3Si+H]^+$ 317.2512, found 317.2505.

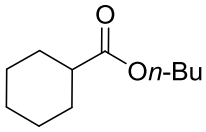


Dibutyl 2-methylhexanedioate (16) was obtained from General Carbonylation Procedure A and the crude product was flashed in 5% EtOAc/Hexanes yielding *n*-butyl ester **16** as a colorless oil (59.5 mg, 87%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 4.18 – 4.02 (m, 4H), 2.46 (q, *J* = 6.8 Hz, 1H), 2.33 (t, *J* = 7.2 Hz, 2H), 1.80 – 1.54 (m, 7H), 1.53 – 1.44 (m, 1H), 1.39 (m, 4H), 1.18 (d, *J* = 7.0 Hz, 3H), 1.04 – 0.90 (m, 6H). **^{13}C NMR**

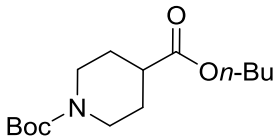
(151 MHz, $CDCl_3$) δ 176.6, 173.5, 64.2, 64.2, 39.4, 34.2, 33.1, 30.7, 30.7, 22.7, 19.2, 17.1, 13.7. **IR** (thin film, cm^{-1}): 2961, 2874, 1736, 1462, 1385, 1249, 1174, 1071, 1021, 741. **HRMS** (ESI): calculated for $[C_{15}H_{28}O_4+Na]^+$ 295.1885, found 295.1879.



Butyl 2-methyl-4-(1-methyl-1H-pyrrol-2-yl)butanoate (18) was obtained from General Carbonylation Procedure A and the crude product was flashed using a gradient of 5-10% EtOAc/hexanes yielding *n*-butyl ester **18** as a colorless oil (50.9 mg, 86%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.58 (dd, *J* = 2.7, 1.8 Hz, 1H), 6.08 (dd, *J* = 3.5, 2.7 Hz, 1H), 5.92 (ddt, *J* = 3.5, 1.8, 0.8 Hz, 1H), 4.12 (t, *J* = 6.7 Hz, 2H), 3.57 (s, 3H), 2.63 – 2.49 (m, 3H), 2.09 – 1.98 (m, 1H), 1.82 – 1.71 (m, 1H), 1.70 – 1.62 (m, 2H), 1.48 – 1.38 (m, 2H), 1.24 (d, *J* = 7.0 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.6, 132.5, 121.2, 106.5, 105.6, 64.2, 39.2, 33.5, 32.9, 30.7, 24.0, 19.2, 17.3, 13.8. **IR** (thin film, cm^{-1}): 2959, 1731, 1495, 1462, 1299, 1177, 702. **HRMS** (ESI): calculated for $[C_{14}H_{23}NO_2+Na]^+$ 260.1626, found260.1620.

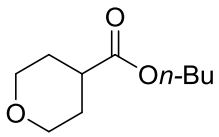


Butyl cyclohexanecarboxylate (20) was obtained from General Carbonylation Procedure A (49% NMR yield). Physical and spectral data were in accordance with literature data.[15]

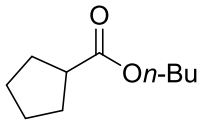


1-(tert-butyl) 4-butyl piperidine-1,4-dicarboxylate (22) was obtained from General Carbonylation Procedure A and flashed in 25% EtOAc/hexanes yielding *n*-butyl ester **22** as a lemon-yellow oil (50.2 mg, 70%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 4.11 (t, *J* =

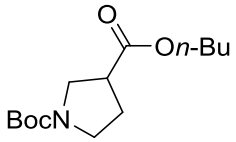
6.6 Hz, 2H), 4.03 (s, 2H), 2.86 (t, *J* = 12.4 Hz, 2H), 2.45 (ddt, *J* = 11.0, 7.8, 3.8 Hz, 1H), 1.89 (d, *J* = 13.2 Hz, 2H), 1.72 – 1.55 (m, 4H), 1.48 (s, 9H), 1.47 – 1.26 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.7, 154.7, 79.6, 64.4, 42.7 (br), 41.2, 30.6, 28.4, 28.0, 19.1, 13.7. **IR** (thin film, cm^{-1}): 2961, 2868, 1732, 1694, 1422, 1169, 1038, 869. **HRMS** (ESI): calculated for $[C_{15}H_{27}NO_4+Na]^+$ 308.1838, found 308.1832.



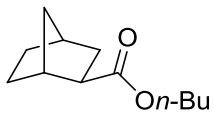
Butyl tetrahydro-2H-pyran-4-carboxylate (24) was obtained from General Carbonylation Procedure A and the crude product was flashed using a gradient of 10-20% Et_2O/hexanes yielding *n*-butyl ester **24** as a colorless oil (34.9 mg, 75%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.10 (td, *J* = 6.6, 1.2 Hz, 2H), 3.97 (dt, *J* = 11.8, 3.6 Hz, 2H), 3.51 – 3.36 (m, 2H), 2.62 – 2.49 (m, 1H), 1.92 – 1.72 (m, 4H), 1.69 – 1.54 (m, 2H), 1.46 – 1.33 (m, 2H), 0.95 (td, *J* = 7.4, 1.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.6, 67.1, 64.4, 40.2, 30.6, 28.7, 19.2, 13.7. **IR** (thin film, cm^{-1}): 2958, 2847, 1733, 1448, 1280, 1186, 1137, 824. **HRMS** (ESI): calculated for $[C_{10}H_{18}O_3+Na]^+$ 209.1154, found 209.1148.



Butyl cyclopentanecarboxylate (26) was obtained from General Carbonylation Procedure A and the crude product (92% NMR yield) was flashed in 5% Et_2O/hexanes yielding *n*-butyl ester **26** as a colorless, volatile liquid (30.0 mg, 70%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 4.06 (t, *J* = 6.6 Hz, 2H), 2.77 – 2.64 (m, 1H), 1.94 – 1.74 (m, 4H), 1.78 – 1.61 (m, 2H), 1.64 – 1.54 (m, 4H), 1.43 – 1.32 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.8, 64.1, 43.9, 30.7, 30.0, 25.8, 19.1, 13.7. **IR** (thin film, cm^{-1}): 2959, 2872, 1734, 1455, 1390, 1357, 1308, 1259, 1184, 1066. **HRMS** (ESI) calculated for $[C_{10}H_{18}O_2H]^+$ 171.1385, found 171.1380



1-(tert-butyl) 3-butyl pyrrolidine-1,3-dicarboxylate (28) was obtained as an inseparable mixture of starting material, elimination by-product, and desired *n*-butyl ester from General Carbonylation Procedure A (74% NMR yield). An analytical standard of the desired product was synthesized to verify the NMR yield. **28** was synthesized by dissolving 1-(tert-butoxycarbonyl) pyrrolidine-3-carboxylic acid (0.3 g, mmol) in DCM (6 mL) with 10 drops of DMF and cooled to 0 ºC. Oxalyl chloride (0.24 mL, mmol) was subsequently added dropwise and the reaction was stirred at 0 ºC for 15 minutes before warming to room temperature. Excess oxalyl chloride was removed under reduced pressure and the residue was brought up in DCM (1.5 mL) and added dropwise to a 0 ºC solution of TEA (0.41 mL, 2.1 mmol) and *n*-BuOH (0.27 mL, 2.1 mmol) in DCM (6 mL). The reaction was allowed to warm to room temperature overnight. The reaction mixture was washed twice with water, once with a saturated solution of sodium bicarbonate, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 25% EtOAc/hexanes to provide 170 mg (45%) of *n*-butyl ester **28** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.08 – 4.00 (m, 2H), 3.60 – 3.35 (m, 3H), 3.34 – 3.23 (m, 1H), 3.03 – 2.92 (m, 1H), 2.11 – 2.00 (m, 2H), 1.59 – 1.51 (m, 2H), 1.39 (s, 9H), 1.37 – 1.27 (m, 2H), 0.87 (q, *J* = 7.0 Hz, 3H). Two conformers are observed: **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.1, 173.0, 154.2, 79.3, 79.2, 64.7, 48.0, 47.9, 45.3, 45.0, 43.3, 42.4, 30.5, 28.8, 28.4, 28.2, 19.0, 13.6. **IR** (thin film, cm^{-1}): 1736, 1700, 1404, 1366, 1169, 1120, 876, 771. **HRMS** (ESI): calculated for $[C_{14}H_{25}NO_4+Na]^+$ 294.1681, found 294.1679.

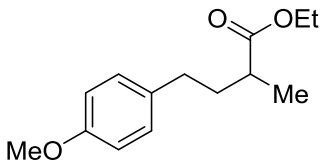


Butyl bicyclo[2.2.1]heptane-2-carboxylate (30) was obtained as a mixture of diastereomers (5.4:1, exo:endo) from General Carbonylation Procedure A and the crude product was flashed in 5% Et_2O/hexanes yielding a colorless oil (38.6 mg, 79%).

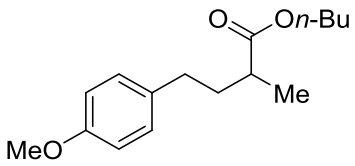
Exo-isomer: An analytical standard was synthesized to verify the major isomer. **Exo-30** was synthesized using a modified carbonylation procedure. In a glovebox under argon atmosphere, exo-2-bromonorbornane (**29**) (87.5 mg, 0.5 mmol) was combined with $[Pd(allyl)Cl]_2$ (9.1 mg, 0.025 mmol), IMes (30.4 mg, 0.1 mmol), K_3PO_4 (212 mg, 1 mmol), benzene (0.5 mL), and *n*-butanol (0.5 mL) in an Ace pressure tube. The tube was sealed and removed from the glovebox. Subsequently, the tube was purged 3 times with 5 atm CO, and then the pressure was set to 2 atm CO. The reaction was stirred for 24 hours at 70 ºC. The reaction was cooled to room temperature, depressurized, and 2 mL 1M HCl and 2 mL DCM were added. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 5% Et_2O/hexanes yielding *n*-butyl ester **exo-30** as a colorless oil (35 mg, 36%), predominantly the exo-isomer (13.4:1 exo:endo). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.13 – 4.02 (m, 2H), 2.50 (d, *J* = 3.8 Hz, 1H), 2.35 – 2.25 (m, 2H), 1.85 (dtd, *J* = 12.4, 4.8, 2.8 Hz, 1H), 1.69 – 1.32 (m, 8H), 1.32 – 1.23 (m, 1H), 1.26 – 1.14 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.2, 64.2, 46.6, 40.9, 36.5, 36.0, 34.1, 30.8, 29.5, 28.7, 19.2, 13.8. **IR** (thin film, cm^{-1}): 2957, 2873, 1731, 1455, 1351, 1311, 1178, 1066, 1034. **HRMS** (ESI): calculated for $[C_{12}H_{20}O_2H]^+$ 197.1542, found 197.1539.

Endo-isomer: An analytical standard was synthesized to verify the minor isomer. **Endo-30** was synthesized by dissolving predominantly endo norbornane-2-carboxylic acid (1 g, 7.1 mmol) in DCM (28 mL) with 10 drops of DMF and cooled to 0 ºC. Oxalyl chloride (1.2 mL, mmol) was subsequently added dropwise and the reaction was stirred at 0 ºC for 15 minutes before warming to room temperature and further stirred for 1.5 hours. Excess oxalyl chloride was removed under reduced pressure and the residue was brought up in DCM (20 mL) and triethylamine (2.1 mL, 14.9 mmol). To the solution, 1-butanol (2 mL) was added dropwise and the reaction was stirred overnight at room temperature. The reaction mixture was washed twice with water, once with a saturated solution of sodium bicarbonate, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 5% Et_2O/hexanes to provide 0.71 g (51%) of *n*-butyl ester **endo-30** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ

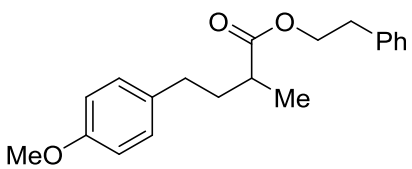
4.09 (m, 2H), 2.76 (dddt, *J* = 9.4, 7.2, 4.7, 2.2 Hz, 1H), 2.56 (dt, *J* = 4.9, 2.2 Hz, 1H), 2.30 – 2.25 (m, 1H), 1.70 – 1.58 (m, 4H), 1.57 – 1.48 (m, 1H), 1.47 – 1.21 (m, 7H), 0.95 (td, *J* = 7.4, 2.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.2, 64.1, 46.1, 40.5, 40.2, 37.0, 31.8, 30.8, 29.1, 24.9, 19.2, 13.8.



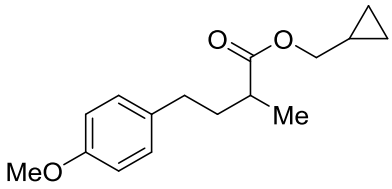
Ethyl 4-(4-methoxyphenyl)-2-methylbutanoate (**Table 3, entry 1**) was obtained from General Carbonylation Procedure B, employing ethanol (29.2 μL, 0.5 mmol), and the crude product was flashed in 5% EtOAc/hexanes yielding **Table 3, entry 1** as a colorless liquid (38.0 mg, 64%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.12 (d, *J* = 8.5 Hz, 2H), 6.89 – 6.82 (m, 2H), 4.21 – 4.12 (m, 2H), 3.81 (s, 3H), 2.59 (dd, *J* = 8.9, 6.9 Hz, 2H), 2.51 – 2.44 (m, 1H), 2.05 – 1.95 (m, 1H), 1.70 (dddd, *J* = 13.7, 8.6, 7.3, 6.1 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.21 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.7, 157.8, 133.8, 129.3, 113.8, 60.2, 55.3, 39.0, 35.8, 32.6, 17.2, 14.3. **IR** (thin film, cm^{-1}): 2977, 2936, 1731, 1613, 1513, 1461, 1376, 1247, 1177, 1036, 827. **HRMS** (ESI) calculated for $[C_{14}H_{20}O_3H]^+$ 237.1491, found 237.1485.



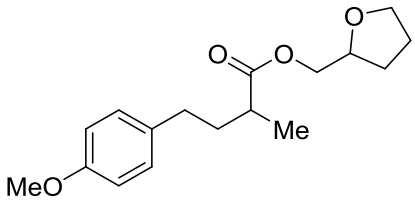
Butyl 4-(4-methoxyphenyl)-2-methylbutanoate (Table 3, entry 2) was obtained from General Carbonylation Procedure B and the crude product was flashed in 5% EtOAc/hexanes yielding *n*-butyl ester **8** as a colorless oil (46.4 mg, 70%).



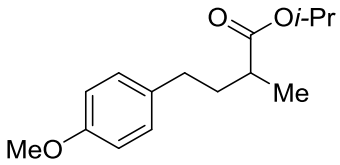
Phenethyl 4-(4-methoxyphenyl)-2-methylbutanoate (Table 3, entry 3) was obtained from General Carbonylation Procedure B, employing 2-phenylethanol (59.9 μL, 0.5 mmol), and the crude product was flashed in 5% EtOAc/hexanes yielding **Table 3, entry 3** as a colorless liquid (47.4 mg, 61%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.38 – 7.31 (m, 2H), 7.30 – 7.25 (m, 3H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.35 (td, *J* = 7.0, 2.3 Hz, 2H), 3.82 (s, 3H), 3.00 (t, *J* = 7.0 Hz, 2H), 2.58 – 2.50 (m, 2H), 2.53 – 2.44 (m, 1H), 2.06 – 1.94 (m, 1H), 1.73 – 1.64 (m, 1H), 1.19 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.6, 157.8, 137.9, 133.7, 129.3, 129.0, 128.5, 126.6, 113.8, 64.7, 55.3, 39.0, 35.7, 35.2, 32.5, 17.2. **IR** (thin film, cm^{-1}): 2936, 2860, 1731, 1611, 1583, 1512, 1458, 1246, 1176, 1037, 827, 748, 700. **HRMS** (ESI) calculated for $[C_{20}H_{24}O_3H]^+$ 313.1804, found 313.1801.



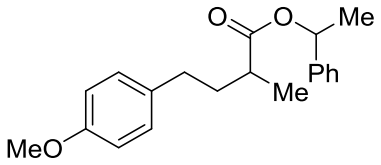
Cyclopropylmethyl 4-(4-methoxyphenyl)-2-methylbutanoate (Table 3, entry 4) was obtained from General Carbonylation Procedure B, employing cyclopropylmethanol (40.5 μL, 0.5 mmol), and the crude product was flashed in 5% EtOAc/hexanes yielding **Table 3, entry 4** as a colorless liquid (47.4 mg, 72%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.16 – 7.11 (m, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 3.95 (dd, *J* = 7.3, 4.1 Hz, 2H), 3.81 (s, 3H), 2.60 (ddd, *J* = 8.9, 6.6, 4.1 Hz, 2H), 2.51 (ddd, *J* = 7.8, 6.9, 5.9 Hz, 1H), 2.01 (dddd, *J* = 13.5, 9.2, 8.1, 6.5 Hz, 1H), 1.77 – 1.67 (m, 1H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.22 – 1.12 (m, 1H), 0.63 – 0.56 (m, 2H), 0.32 (dt, *J* = 6.0, 4.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.8, 157.8, 133.8, 129.3, 113.8, 69.0, 55.3, 39.1, 35.9, 32.6, 17.3, 9.9, 3.2 **IR** (thin film, cm^{-1}): 2937, 1731, 1612, 1512, 1460, 1247, 1157, 1036, 826. **HRMS** (ESI) calculated for $[C_{16}H_{22}O_3H]^+$ 263.1647, found 263.1643.



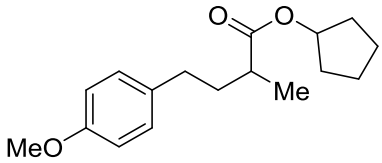
(Tetrahydrofuran-2-yl)methyl 4-(4-methoxyphenyl)-2-methylbutanoate (Table 3, entry 5) was obtained from General Carbonylation Procedure B, employing tetrahydrofurfuryl alcohol (48.4 μL, 0.5 mmol), and the crude product was flashed in 10% EtOAc/hexanes yielding **Table 3, entry 5** as a colorless liquid (29.9 mg, 41%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.14 – 7.09 (m, 2H), 6.87 – 6.82 (m, 2H), 4.22 – 4.11 (m, 2H), 4.04 (ddd, *J* = 11.4, 6.5, 5.1 Hz, 1H), 3.94 – 3.87 (m, 1H), 3.86 – 3.80 (m, 1H), 3.80 (s, 3H), 2.63 – 2.49 (m, 3H), 2.09 – 1.86 (m, 4H), 1.76 – 1.59 (m, 2H), 1.24 – 1.18 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.6, 157.8, 133.8, 129.3, 113.8, 68.5, 66.3, 55.3, 39.0, 38.9, 35.8, 35.7, 32.5, 28.0, 25.7, 17.2, 17.2. **IR** (thin film, cm^{-1}): 2941, 1734, 1512, 1459, 1247, 1177, 1036, 826. **HRMS** (ESI) calculated for $[C_{17}H_{24}O_4H]^+$ 293.1753, found 293.1749.



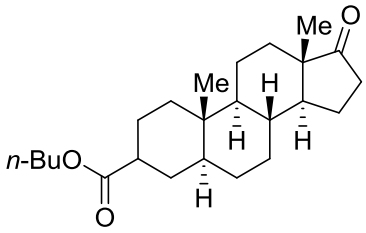
Isopropyl 4-(4-methoxyphenyl)-2-methylbutanoate (Table 3, entry 6) was obtained from General Carbonylation Procedure A, substituting isopropanol for *n*-butanol, and the crude product was flashed in 5% EtOAc/hexanes yielding **Table 3, entry 6** as a colorless liquid (33.0 mg, 53%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.12 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 5.10 – 5.01 (m, 1H), 3.81 (s, 3H), 2.64 – 2.52 (m, 2H), 2.48 – 2.39 (m, 1H), 2.03 – 1.93 (m, 1H), 1.77 – 1.64 (m, 1H), 1.31 – 1.24 (m, 6H), 1.19 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.2, 157.8, 133.9, 129.3, 113.8, 67.3, 55.3, 39.2, 35.8, 32.6, 21.9, 17.2. **IR** (thin film, cm^{-1}): 2978, 2936, 1728, 1513, 1461, 1376, 1247, 1177, 1109, 1038, 824. **HRMS** (ESI) calculated for $[C_{15}H_{22}O_3H]^+$ 251.1647, found 251.1642.



1-phenylethyl 4-(4-methoxyphenyl)-2-methylbutanoate (Table 3, entry 7) was obtained from General Carbonylation Procedure B, employing 1-phenylethanol (60.4 μL, 0.5 mmol) and running the reaction for 48 hours, and the crude product (66% NMR yield) was flashed in 5% EtOAc/hexanes yielding a 1:1 mixture of diastereomers of **Table 3, entry 7** as a colorless liquid (41.6 mg, 53%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.45 – 7.30 (m, 10H), 7.14 – 7.08 (m, 2H), 7.08 – 7.01 (m, 2H), 6.89 – 6.85 (m, 2H), 6.85 – 6.82 (m, 2H), 5.99 – 5.92 (m, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 2.61 – 2.52 (m, 2H), 2.52 (dd, *J* = 6.8, 2.8 Hz, 4H), 2.07 – 1.97 (m, 2H), 1.78 – 1.70 (m, 2H), 1.62 – 1.56 (m, 6H), 1.24 (d, *J* = 7.0 Hz, 3H), 1.21 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.8, 157.8, 141.8, 133.8, 129.3, 128.5, 127.9, 127.8, 126.1, 113.8, 113.7, 72.1, 72.0, 55.3, 39.2, 39.1, 35.8, 35.7, 32.6, 32.4, 22.4, 22.3, 17.2. **IR** (thin film, cm^{-1}): 2977, 2934, 1732, 1612, 1512, 1456, 1247, 1176, 1036, 827, 760, 699. **HRMS** (ESI) calculated for $[C_{20}H_{24}O_3H]^+$ 313.1804, found 313.1799.



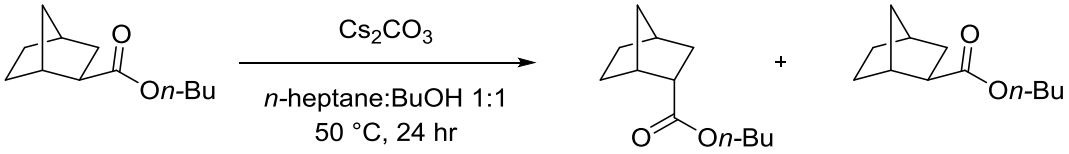
Cyclopentyl 4-(4-methoxyphenyl)-2-methylbutanoate (Table 3, entry 8) was obtained from General Carbonylation Procedure A, substituting cyclopentanol for *n*-butanol, and the crude product was flashed in 5% EtOAc/hexanes yielding **Table 3, entry 8** as a colorless liquid (40.5 mg, 59%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.14 – 7.09 (m, 2H), 6.88 – 6.83 (m, 2H), 5.20 (tt, *J* = 5.6, 2.6 Hz, 1H), 3.81 (s, 3H), 2.61 – 2.53 (m, 2H), 2.52 – 2.39 (m, 1H), 2.03 – 1.92 (m, 1H), 1.95 – 1.84 (m, 2H), 1.80 – 1.47 (m, 6H), 1.18 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.4, 157.8, 133.9, 129.3, 113.8, 55.3, 39.1, 35.8, 32.8, 32.7, 32.6, 23.8, 17.2. **IR** (thin film, cm^{-1}): 2964, 1728, 1512, 1459, 1247, 1157, 1036, 826. **HRMS** (ESI) calculated for $[C_{17}H_{24}O_3H]^+$ 277.1804, found 277.1799.



Butyl-(5S,8R,9S,10S,13S,14S)-10,13-dimethyl-17-oxohexadecahydro-1H-cyclopenta[a]phenanthrene-3-carboxylate (32) was obtained as a mixture of diastereomers (1.4:1) from an optimized carbonylation procedure. In a glovebox under argon atmosphere, androsterone bromide (**31**) (88.3 mg, 0.25 mmol) was combined with $[Pd(allyl)Cl]_2$ (4.6 mg, 0.0125 mmol), IMes (15.2 mg, 0.05 mmol), K_3PO_4 (106 mg, 0.5 mmol), benzene (0.25 mL), and *n*-butanol (0.25 mL) in an Ace pressure tube. The tube was sealed and removed from the glovebox. Subsequently, the tube was purged 3 times with 5 atm CO, and then the pressure was set to 2 atm CO. The reaction was stirred for 48 hours at 70 ºC. The reaction was cooled to room temperature, depressurized, and 2 mL 1M HCl and 2 mL DCM were added. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed in 5% EtOAc/hexanes yielding *n*-butyl ester **32** as a colorless oil (49.6 mg, 53%) and 22.9 mg (26%) recovered starting material **31**. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.09 (dt, *J* = 22.0, 6.8 Hz, 2H), 2.65 (td, *J* = 5.9, 5.3, 2.7 Hz, 1H), 2.54 – 2.38 (m, 1H), 2.31 (tt, *J* = 12.5, 3.9 Hz, 1H), 2.14 – 1.86 (m, 3H), 1.79 (tdt, *J* = 13.8, 6.9, 3.2 Hz, 5H), 1.72 – 1.18 (m, 12H), 1.18 – 1.04 (m, 1H), 1.06 – 0.94 (m, 2H), 0.94 (dd, *J* = 7.4, 2.7 Hz, 3H), 0.85 (dd, *J* = 17.6, 6.4 Hz, 6H), 0.74 (td, *J* = 11.4, 4.1 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.1, 175.5, 64.1, 64.0, 54.4, 51.5, 51.4, 47.8, 46.0, 43.7, 42.7, 39.4, 37.7, 36.0, 35.9, 35.9, 35.1, 35.0, 35.0, 31.5, 31.5, 31.2, 30.8, 30.7, 29.7, 28.4, 28.4, 24.6, 22.8, 21.8, 21.7, 20.2, 20.0, 19.2, 19.2, 13.8, 13.8, 13.7, 12.2, 11.7. **IR** (thin film, cm^{-1}): 2930, 1737, 1650, 1453, 1161, 577.6. **HRMS** (ESI): calculated for $[C_{24}H_{38}O_3H]^+$ 375.2899, found 375.2894.

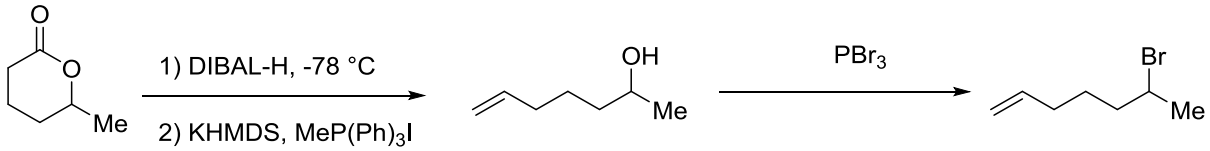
Mechanistic Experiments

Norbornane Racemization



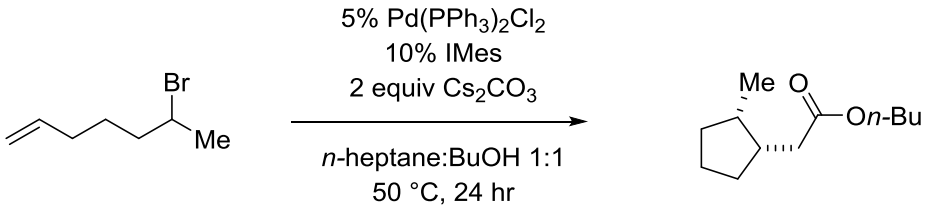
Exo-30 (10 mg, 0.05 mmol) and Cs_2CO_3 (37.3 mg, 0.1 mmol) were dissolved in 50 μL *n*-heptane and 50 μL *n*-butanol [0.5 M] and stirred for 24 hours at 50 ºC. The reaction mixture was cooled to room temperature, and 1 mL 1M HCl and 1 mL DCM were added. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to provide both **exo-30** and **endo-30** mixture of diastereomers (1:2.2, endo:exo determined by ^{1}H NMR spectroscopy).

Radical Clock Experiment



6-bromohept-1-ene (33) was synthesized following the three step sequence shown above. Hept-6-en-2-ol was synthesized according to the procedure from Perez-Castells et. al.[16] To a solution of δ-hexanolactone (4.0 g, 35 mmol) cooled to -78 ºC in THF (120 mL) was added a solution of diisobutylaluminum hydride (42 mmol) in THF (80 mL) dropwise. The reaction was stirred for 3 hours maintaining the -78 ºC temperature. The reaction was quenched with 50 mL of a saturated solution of Rochelle's salt and allowed to warm to room temperature. The solids were filtered off and the layers in the filtrate were separated. The aqueous layer was extracted once with EtOAc and the organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure yielding 2.3 g of crude lactol. To a solution of methyl Wittig (12.2 g, 30 mmol) in THF (100 mL), was added a solution of KHMDS (5.1 g, 26 mmol) in THF (40 mL)

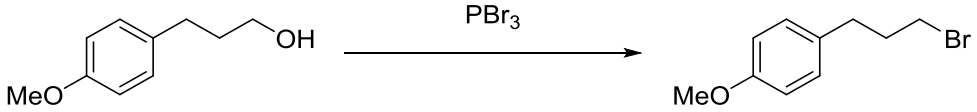
dropwise at room temperature. The solution was stirred for 20 minutes and a solution of the crude lactol 2.3 g (20 mmol) in THF (50 mL) was added and stirred overnight. The reaction was quenched with water and extracted 4 times with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was flashed using a gradient of 10-25% EtOAc/hexanes to provide 1.3 g (33% over two steps) of hept-6-en-2-ol. A solution of hept-6-en-2-ol (0.6 g, 5.3 mmol) in DCM (7 mL) was added to a 0 ºC solution of PPh_3Br_2 (2.7 g, 6.3 mmol) and imidazole (0.43 g, 6.3 mmol) in DCM (20 mL) and allowed to warm to room temperature overnight. The solvent was removed under reduced pressure and the material was suspended in 4:1 hexanes/EtO_2. Solid triphenylphosphine oxide was removed via filtration and the filtrate was concentrated under reduced pressure. The crude product was flashed in hexanes to provide 0.44 g (47%) of bromide **33** as a slightly yellow oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 5.82 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.04 (dd, *J* = 17.1, 1.8 Hz, 1H), 5.01 – 4.98 (m, 1H), 4.20 – 4.12 (m, 1H), 2.17 – 2.03 (m, 2H), 1.90 – 1.76 (m, 2H), 1.73 (d, *J* = 6.6 Hz, 3H), 1.70 – 1.59 (m, 1H), 1.59 – 1.48 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.3, 115.0, 51.7, 40.5, 33.0, 27.0, 26.5. **IR** (thin film, cm^{-1}): 1641, 1444, 1378, 1222, 995, 913, 774, 537. **GC-MS**: calculated for [$C_7H_{13}Br$] 176.02, found 176.05.



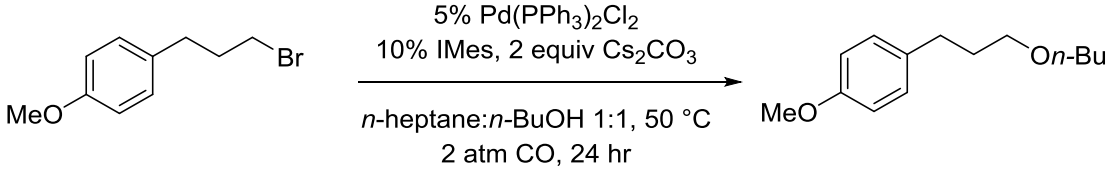
Butyl 2-(2-methylcyclopentyl)acetate (34) was obtained as a mixture of diastereomers (3:1, cis:trans) from General Carbonylation Procedure A and the crude product was flashed in 5% Et_2O/hexanes yielding *n*-butyl ester **34** as a colorless oil (35.2 mg, 71%). The diastereomer ratio was determined from ^{1}H NMR and assigned by comparison to the previously reported ethyl ester.[17] **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 4.09 (ddt, *J* = 6.7, 4.1, 2.1 Hz, 2H), 2.48 (dd, *J* = 14.7, 5.1 Hz, 0.25H (minor)), 2.37 (dd, *J* = 14.5, 6.5 Hz, 0.73H (major)), 2.29 (ddt, *J* = 15.2, 8.4, 6.7 Hz, 3H), 2.19 (dd, *J* = 14.5, 8.6 Hz, 1H), 2.15 – 2.05 (m, 1H), 1.96 – 1.14 (m, 12H), 1.00 (d, *J* = 6.5 Hz, 1H (minor)),

0.96 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.0 Hz, 1H), 0.84 (d, *J* = 7.1 Hz, 2H (major)). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.1, 173.8, 64.1, 44.0, 40.5, 39.7, 39.3, 36.1, 35.7, 34.7, 34.4, 33.1, 32.3, 31.6, 30.7, 30.0, 23.2, 22.7, 22.6, 19.2, 18.9, 15.2, 14.2, 13.8. **IR** (thin film, cm^{-1}): 2957, 1737, 1464, 1379, 1256, 1184, 1022. **HRMS** (ESI): calculated for $[C_{12}H_{22}O_2+H]^+$ 199.1698, found 199.1688.

Reaction of Primary Bromide



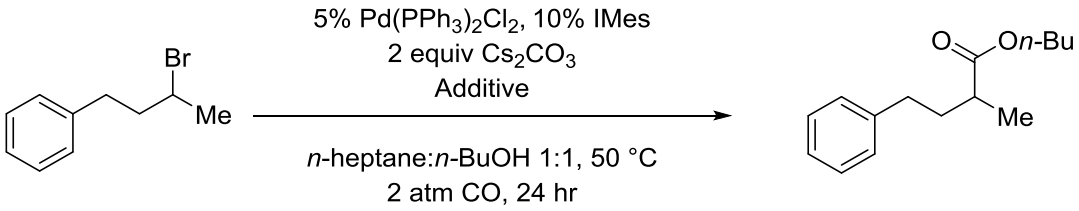
1-(3-bromopropyl)-4-methoxybenzene (SI-5) was synthesized by brominating 3-(4-methoxyphenyl)propan-1-ol (2.0 g, 12 mmol) according to General Procedure A. The crude product was flashed in 2.5% EtOAc/hexanes to provide 1.5 g (55%) of bromide **SI-5** as a colorless oil. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.15 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 1H), 3.82 (s, 1H), 3.41 (td, *J* = 6.6, 1.0 Hz, 2H), 2.75 (t, *J* = 7.3 Hz, 2H), 2.19 – 2.12 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.0, 132.5, 129.5, 113.9, 55.3, 34.4, 33.3, 33.0. **IR** (thin film, cm^{-1}): 2935, 1611, 1512, 1442, 1247, 1178, 1036, 829. **HRMS** (ESI): calculated for $[C_{10}H_{13}BrO+Na]^+$ 251.00, found 251.02.



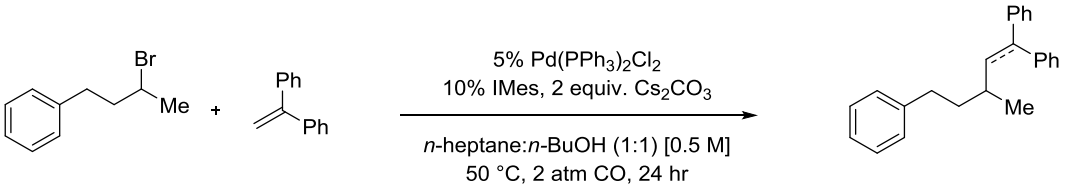
Primary alkyl bromide **35** was subjected to General Carbonylation Procedure A. The crude reaction mixture was analyzed and only trace alkoxycarbonylation product was observed (<3% NMR yield). Instead, etherification product **SI-6** (71% NMR yield) was observed. The crude material was flashed using 5% Et_2O/hexanes yielding *n*-butyl ether **SI-6** as a colorless oil (25.0 mg, 45%). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.14 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 3.82 (s, 3H), 3.43 (m, 4H), 2.66 (dd, *J* = 8.5, 6.8 Hz, 2H), 1.93 – 1.85 (m, 2H), 1.60 (dq, *J* = 8.8, 6.8 Hz, 2H), 1.47 – 1.37 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.7, 134.1, 129.4, 113.7, 70.7, 69.9,

55.3, 31.9, 31.6, 31.4, 19.4, 14.0. **IR** (thin film, cm^{-1}): 2933, 2861, 2360, 1612, 1512, 1463, 1371, 1300, 1247, 1178, 1114, 1038. **HRMS** (ESI): calculated for $[C_{14}H_{22}O_2+Na]^+$ 245.1517, found 245.1516.

Reactions with Radical Inhibitors

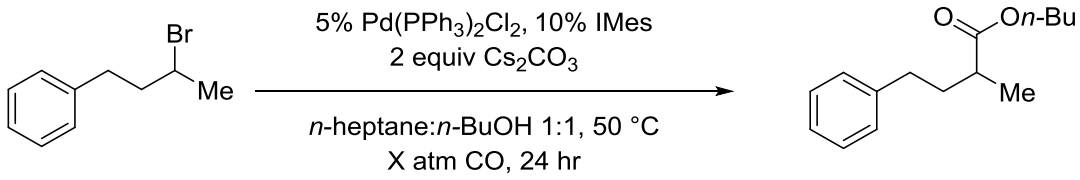


Radical inhibition experiments were run following General Carbonylation Procedure A with bromide **1** (53.3 mg, 0.25 mmol) with 1 equivalent of butylated hydroxytoluene (BHT), 1 equivalent of 1,1-diphenylethylene, or 20 mol % hydroquinone as an additive. Yields were determined by ^{1}H NMR spectroscopy of the crude reaction mixture using 2,5-dimethylfuran as an internal standard.



For the 1,1-diphenylethylene radical inhibitor experiment, no alkoxycarbonylation product was observed, 13% of the radical inhibitor was consumed, and two addition products were detected by GC-MS: the elimination product (m/z = 312) and the reductive product (m/z = 314). Their corresponding ^{1}H NMR peaks overlapped with both starting material (60% recovered) and by-products.

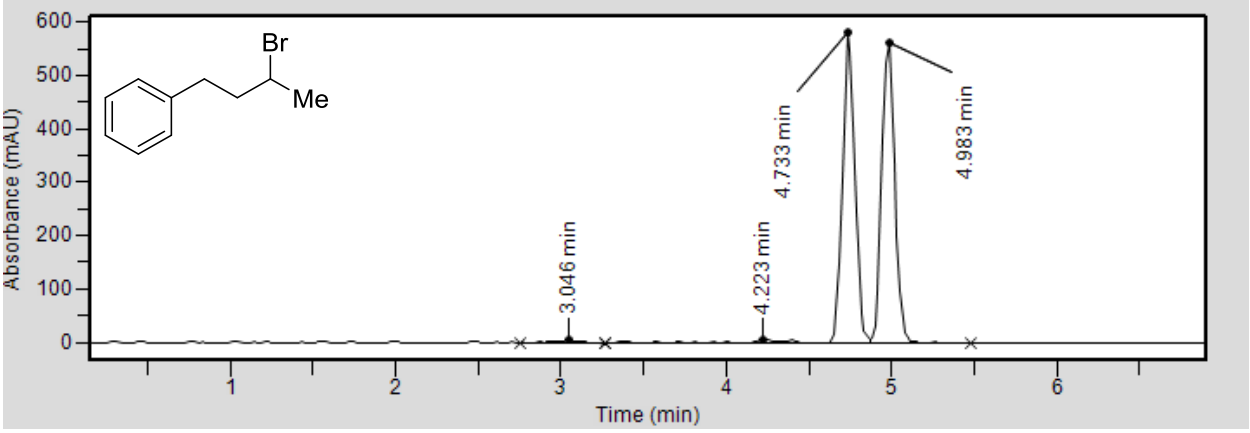
Reactions with Higher Pressures



CO pressure experiments were run following General Carbonylation Procedure A with bromide **1** (53.3 mg, 0.25 mmol) at pressures of 2, 10, and 30 atm CO. The 30 atm reaction was run in a stainless steel Parr reactor. Yields were determined by ^{1}H NMR spectroscopy of the crude reaction mixture using 2,5-dimethylfuran as an internal standard.

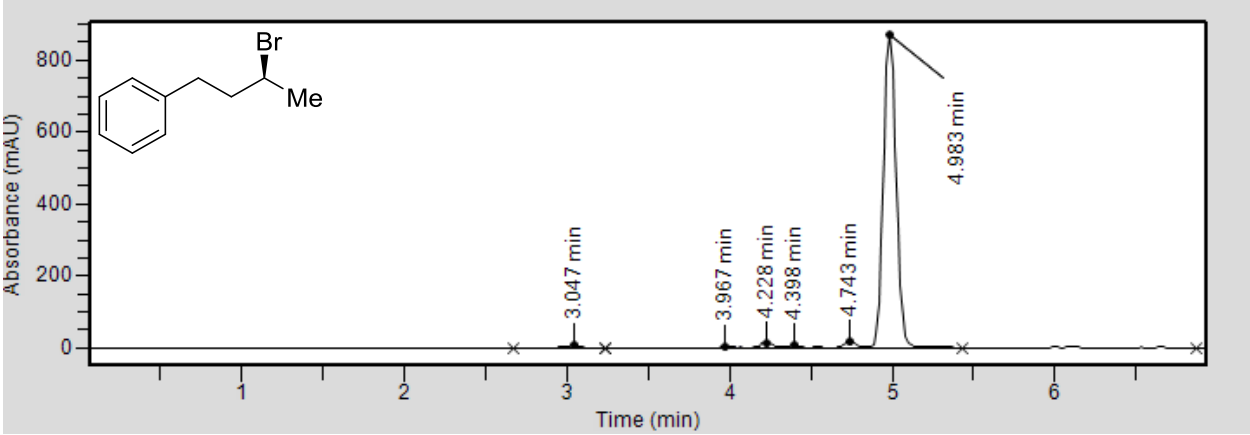
Reaction of Enantiopure Bromide

(S)-(3-bromobutyl)benzene (SI-7) was synthesized by brominating (R)-4-phenylbutan-2-ol (0.5 g, 3.3 mmol) according to General Procedure A. The crude product was flashed in 10% EtOAc/hexanes to provide 0.45 g (64%) of bromide **SI-7** as a colorless oil. Physical and spectral data were in accordance with literature data.[1] **Chiral HPLC**: (Chiralcel OJ-H, 96:4 hexanes:isopropanol): *ee* = 96%.

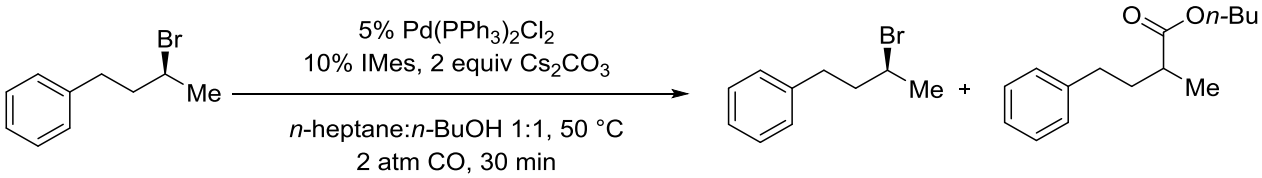


#	Time	Area	Area %
1	4.733	3027141	49.86

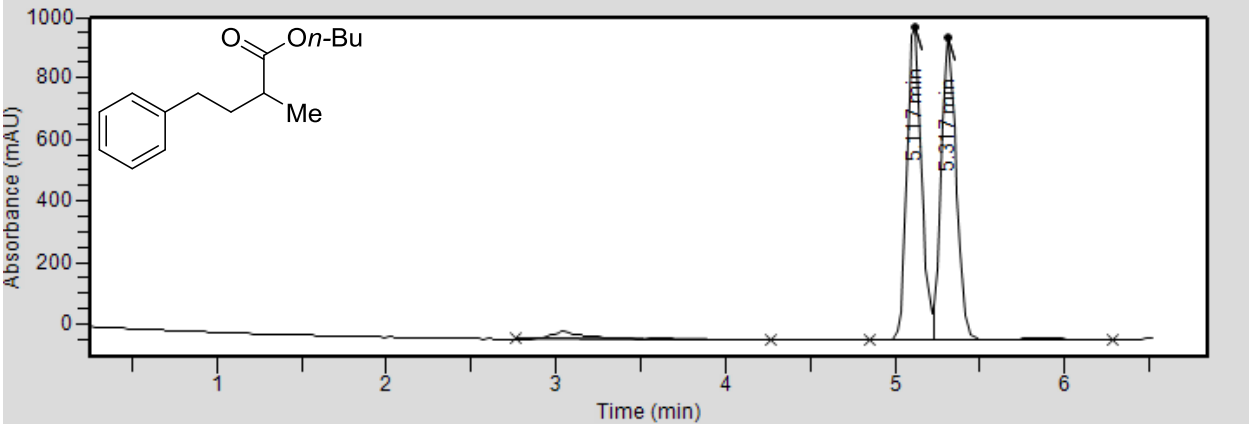
2	4.983	3044468	50.14



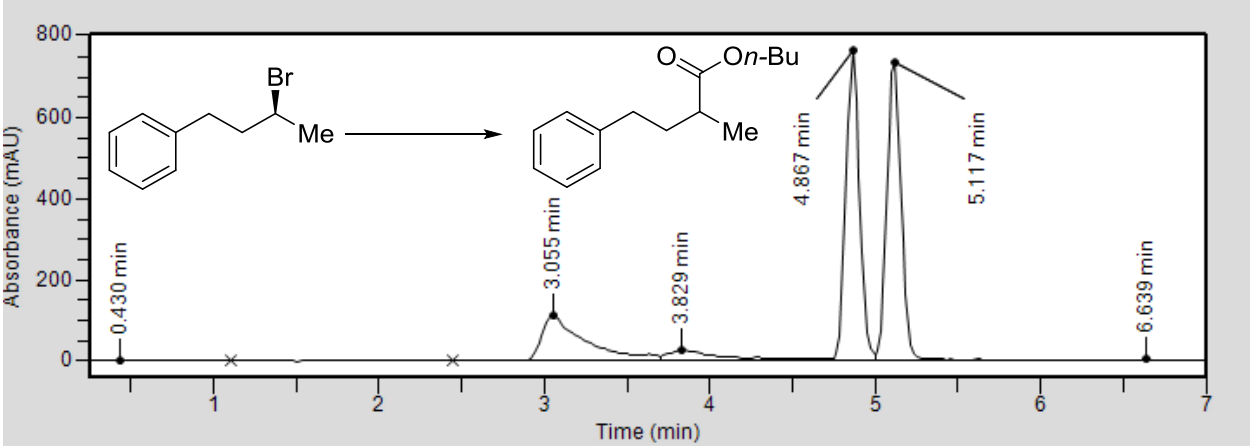
#	Time	Area	Area %
1	4.743	106929	2.23
2	4.983	4686376	97.77



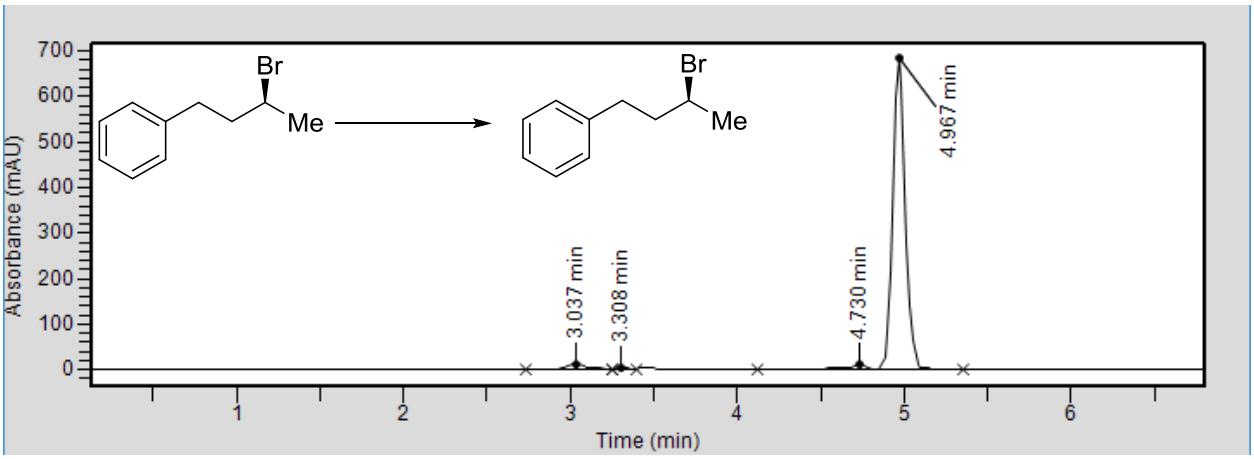
SI-7 (21.3 mg, 0.1 mmol) was subjected to General Carbonylation Procedure A for 30 minutes to ensure incomplete conversion (14% NMR yield). The reaction mixture was worked up normally and the crude material was flashed in 5% Et_2O/hexanes. The enantiomeric excess of the alkoxycarbonylation product was determined to be 0% by chiral HPLC analysis (Chiralcel OJ-H, 98:2 hexanes:isopropanol) and recovered starting material was determined to be 96% (Chiralcel OJ-H, 96:4 hexanes:isopropanol).



#	Time	Area	Area %
1	5.117	6085460	49.98
2	5.317	6090683	50.02

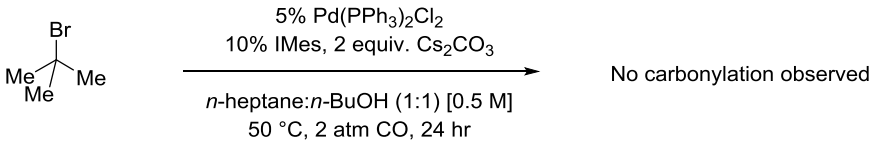


#	Time	Area	Area %
1	4.867	4362619	49.37
2	5.117	4473243	50.63

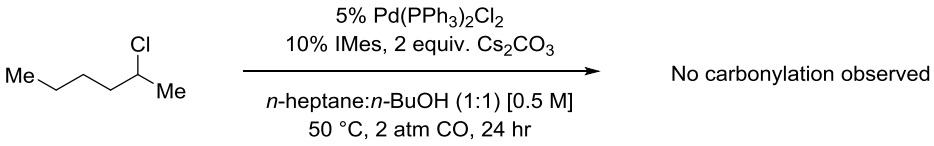


#	Time	Area	Area %
1	4.730	72865	1.96
2	4.967	3640414	98.04

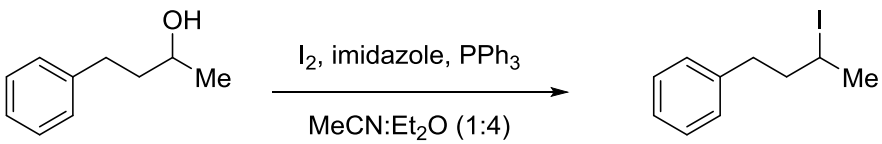
Other Alkyl Halides



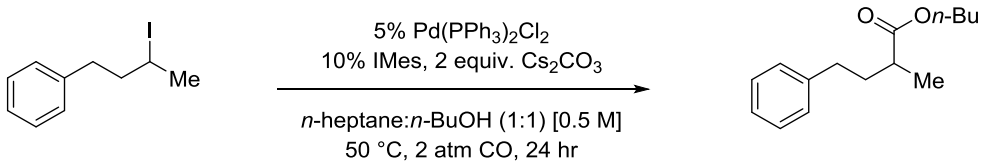
tert-Butyl bromide was subjected to the General Carbonylation Procedure A. The crude reaction mixture was analyzed and no alkoxycarbonylation product was observed by ^{1}H NMR spectroscopy.



2-chlorohexane was subjected to the General Carbonylation Procedure A. The crude reaction mixture was analyzed and trace alkoxycarbonylation product was observed by ^{1}H NMR spectroscopy (<1% NMR yield).



(3-iodobutyl)benzene (SI-8) was synthesized by dissolving 4-phenylbutan-2-ol (4.85 g, 32 mmol) in a 1:4 solution of MeCN:Et_2O (250 mL), to which was added sequentially triphenylphosphine (16.9 g, 65 mmol), imidazole (4.4 g, 65 mmol), and iodine (16.4 g, 65 mmol). The reaction was stirred overnight, in the dark, at room temperature. The reaction was quenched by the addition of a saturated solution of sodium thiosulfate and extracted 3 times with DCM. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was dissolved in a minimum amount of DCM and triphenylphosphine oxide was crashed out upon slow addition of pentane. The mixture was filtered and the filtrate concentrated. The crude product was flashed in hexanes to provide 7.2 g (86%) of iodide **SI-8** as a colorless oil. Physical and spectral data were in accordance with literature data.[18]



SI-8 (65 mg, 0.25 mmol) was subjected to the General Carbonylation Procedure A. The crude reaction mixture was analyzed by ^1H NMR spectroscopy, obtaining a 63% NMR yield of *n*-butyl ester **2**.

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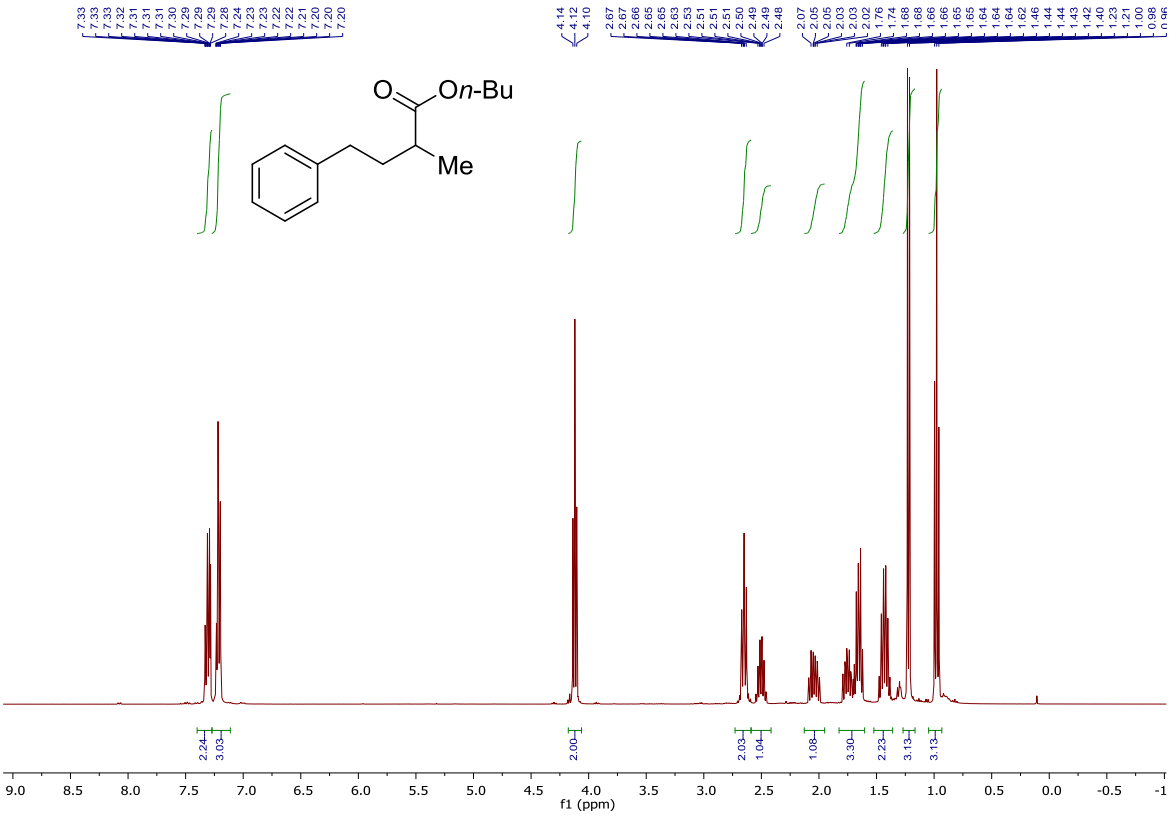
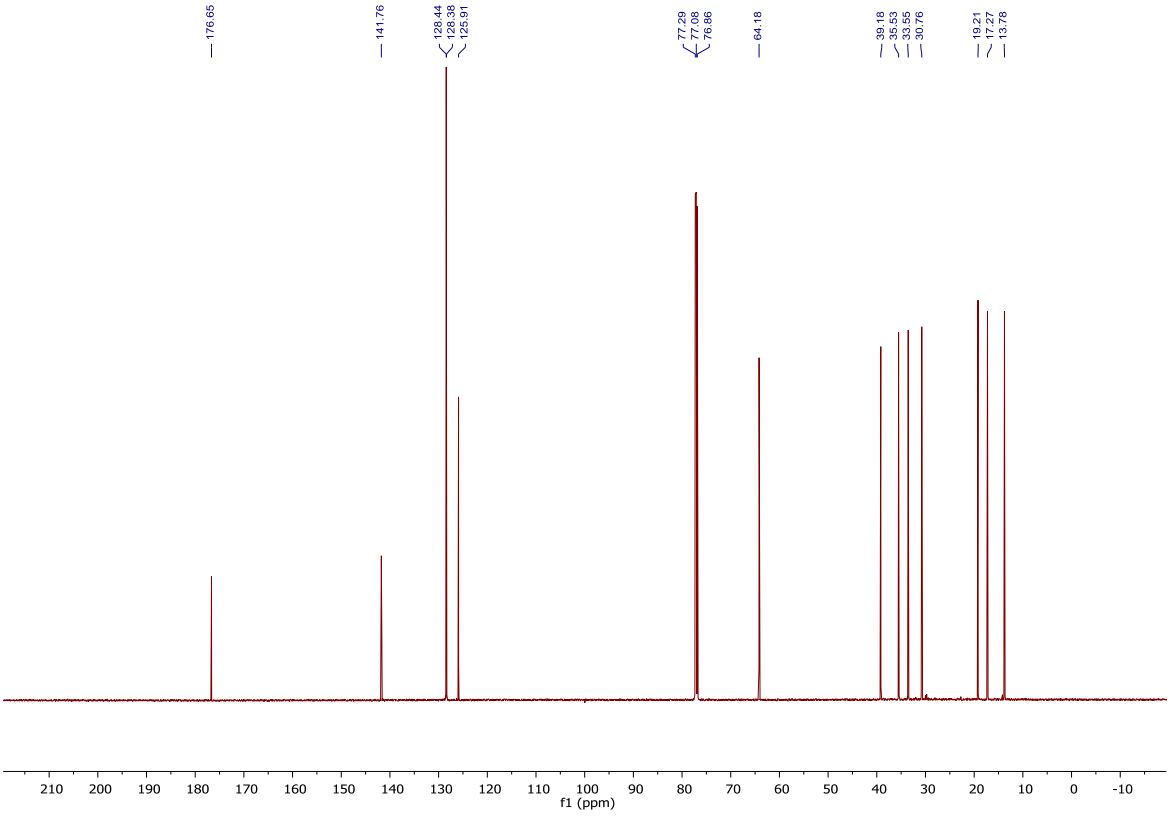
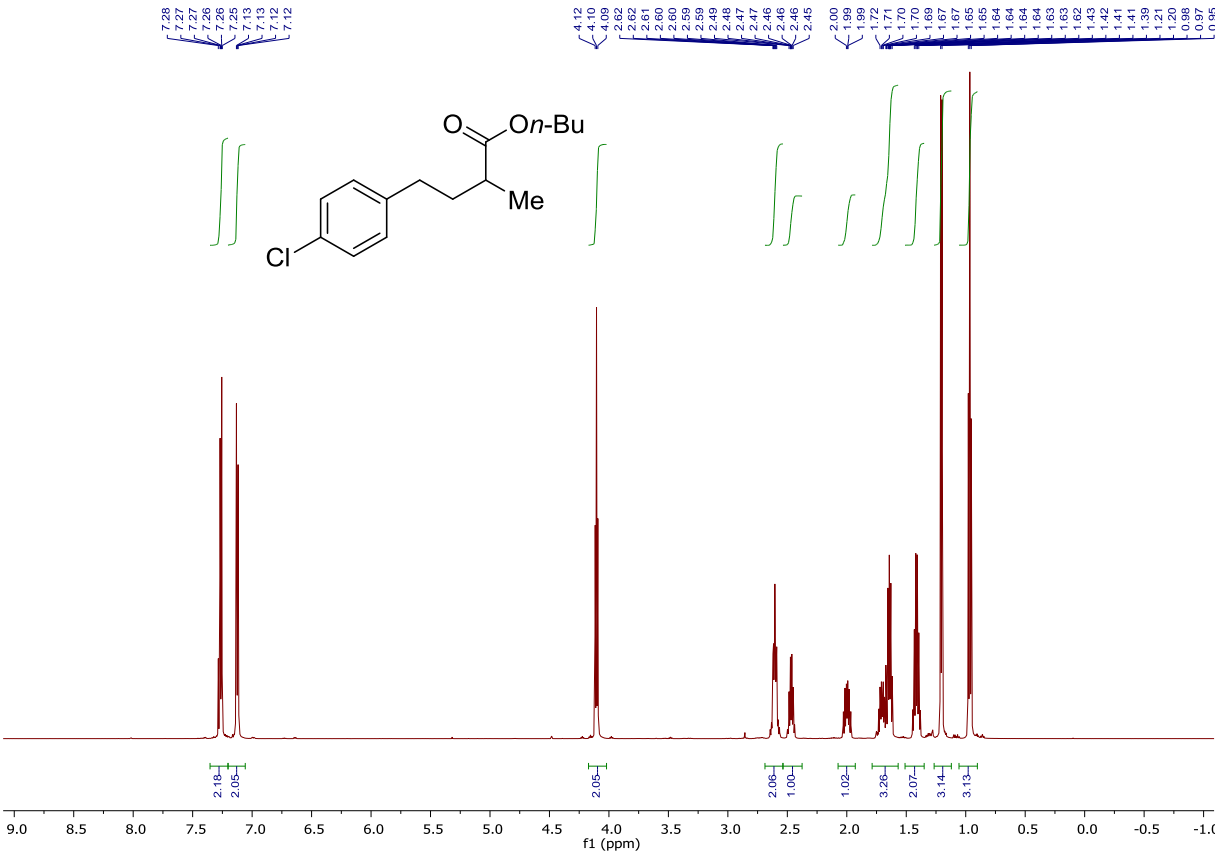
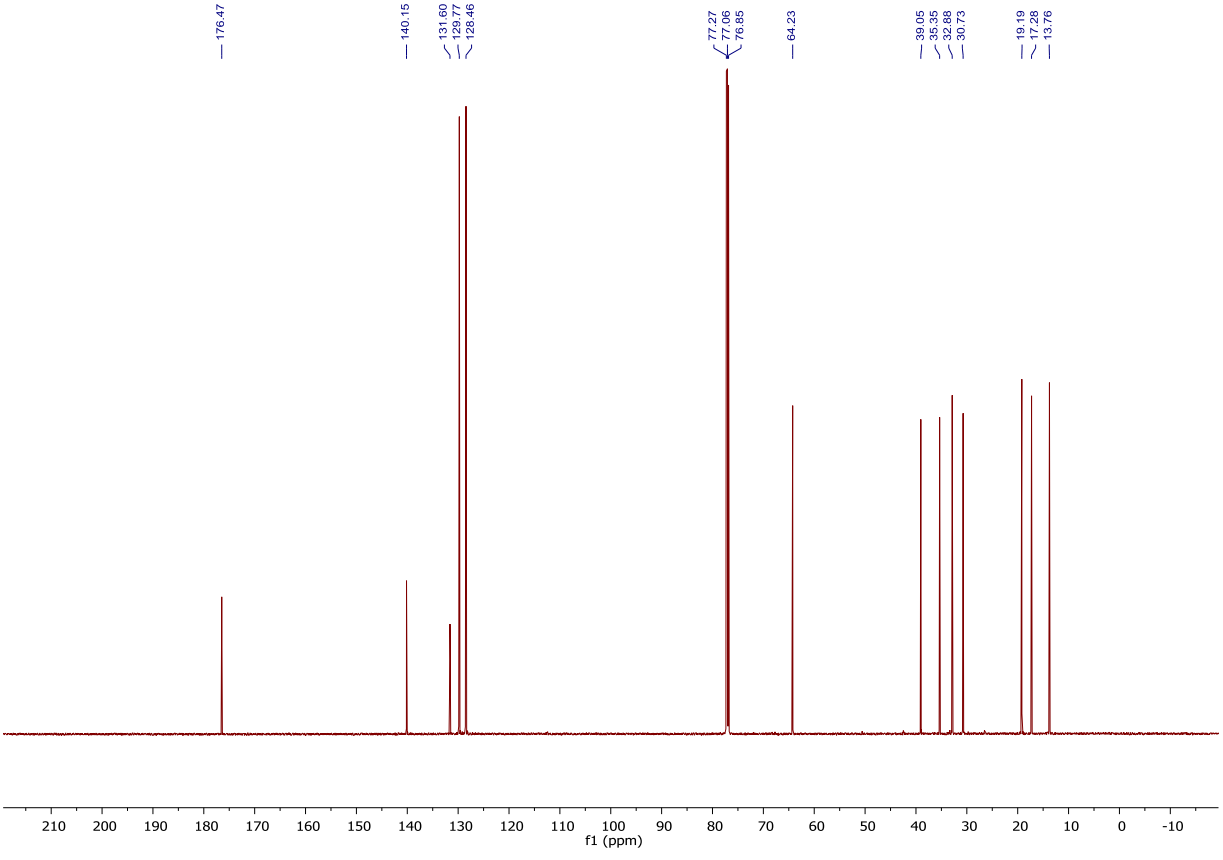
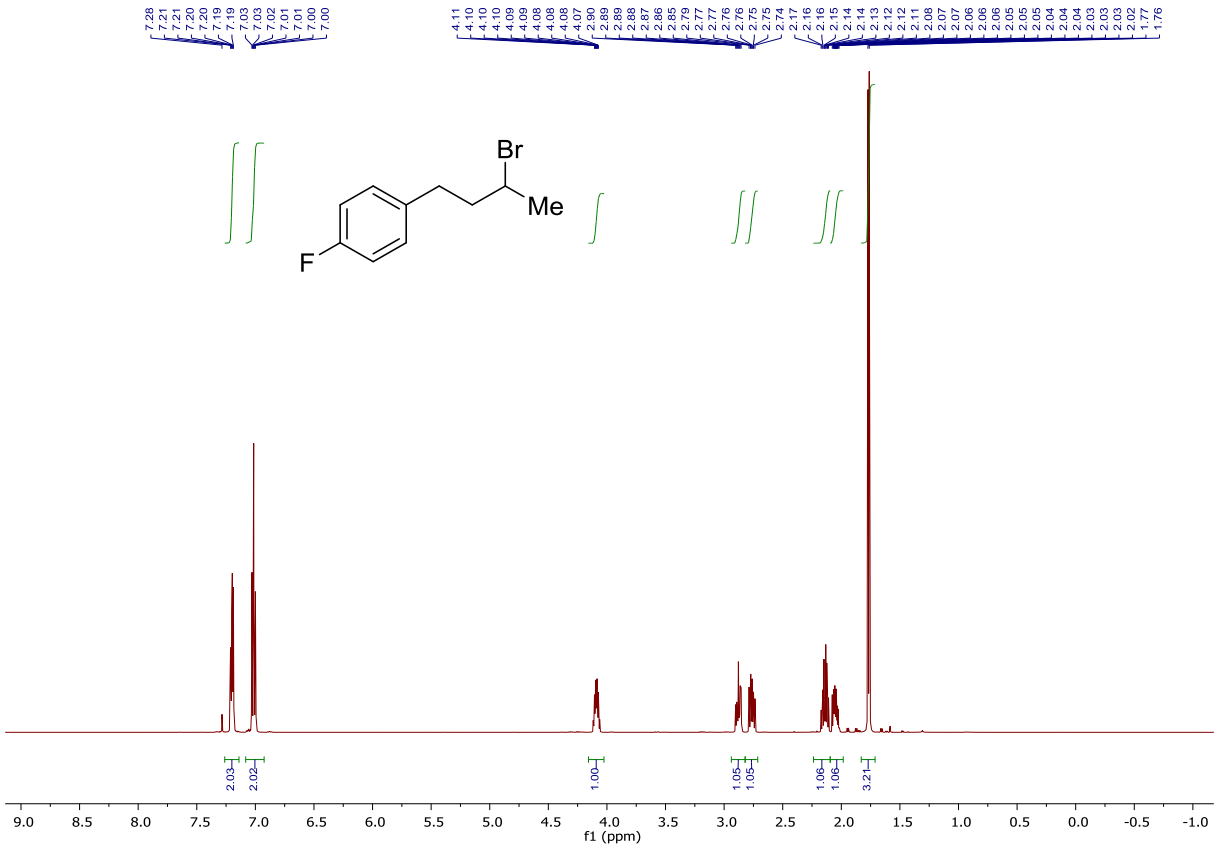
^{1}H and ^{13}C NMR Spectra

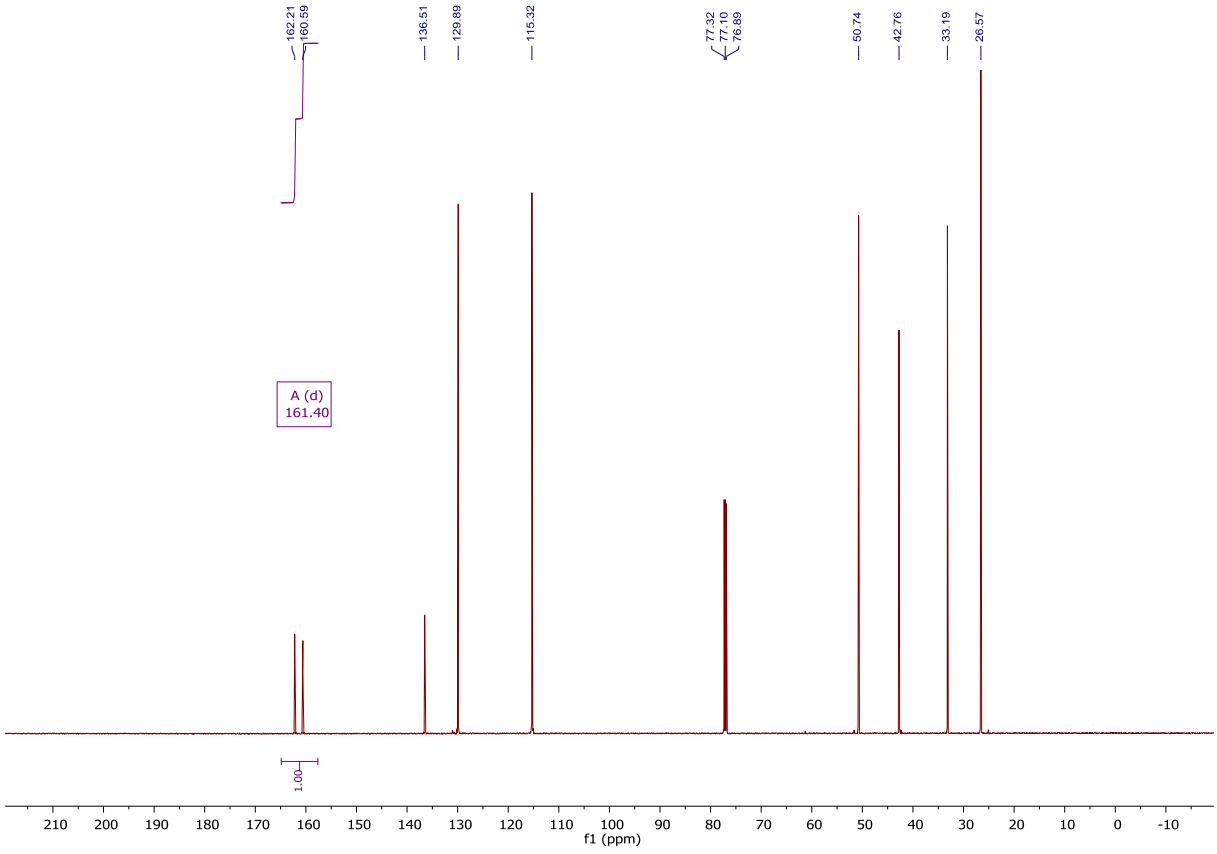





O
On-Bu
Me
Cl
f1 (ppm)


f1 (ppm)


Br
Me
F
f1 (ppm)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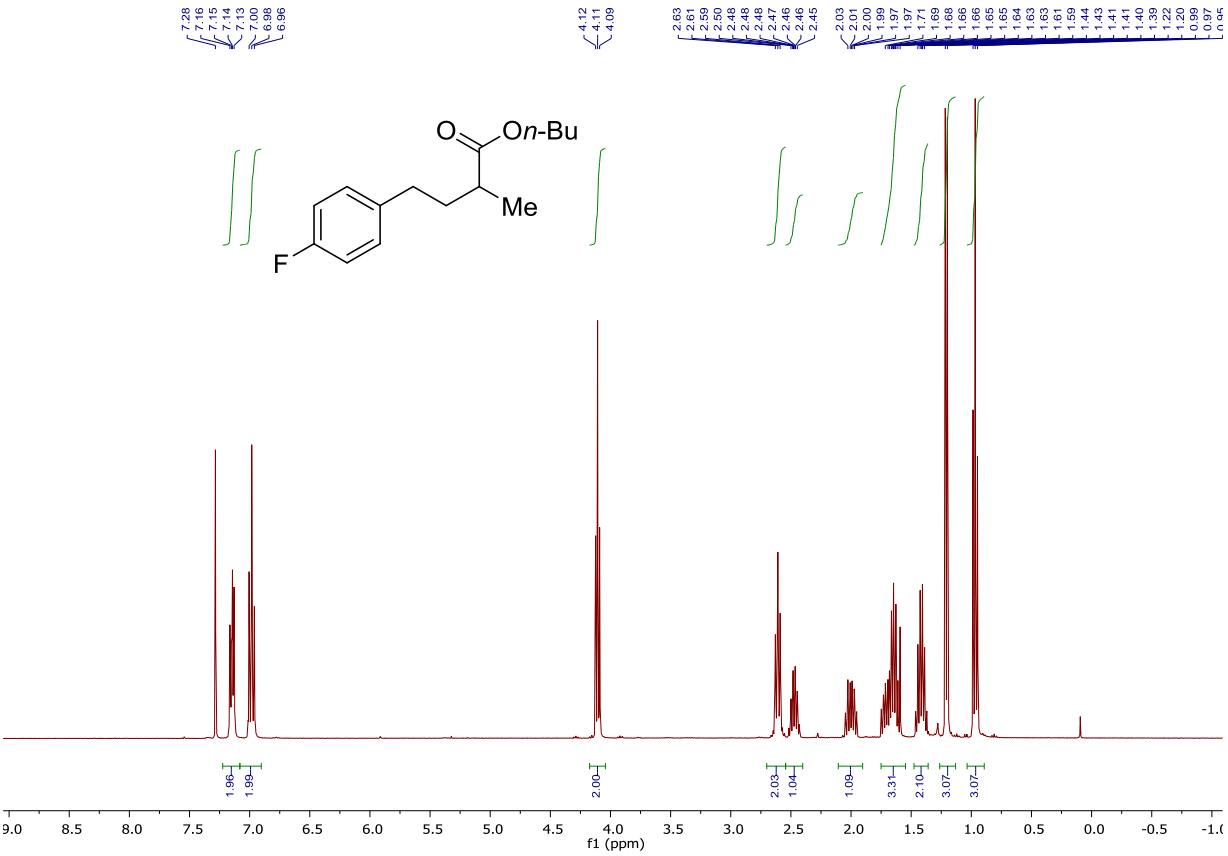
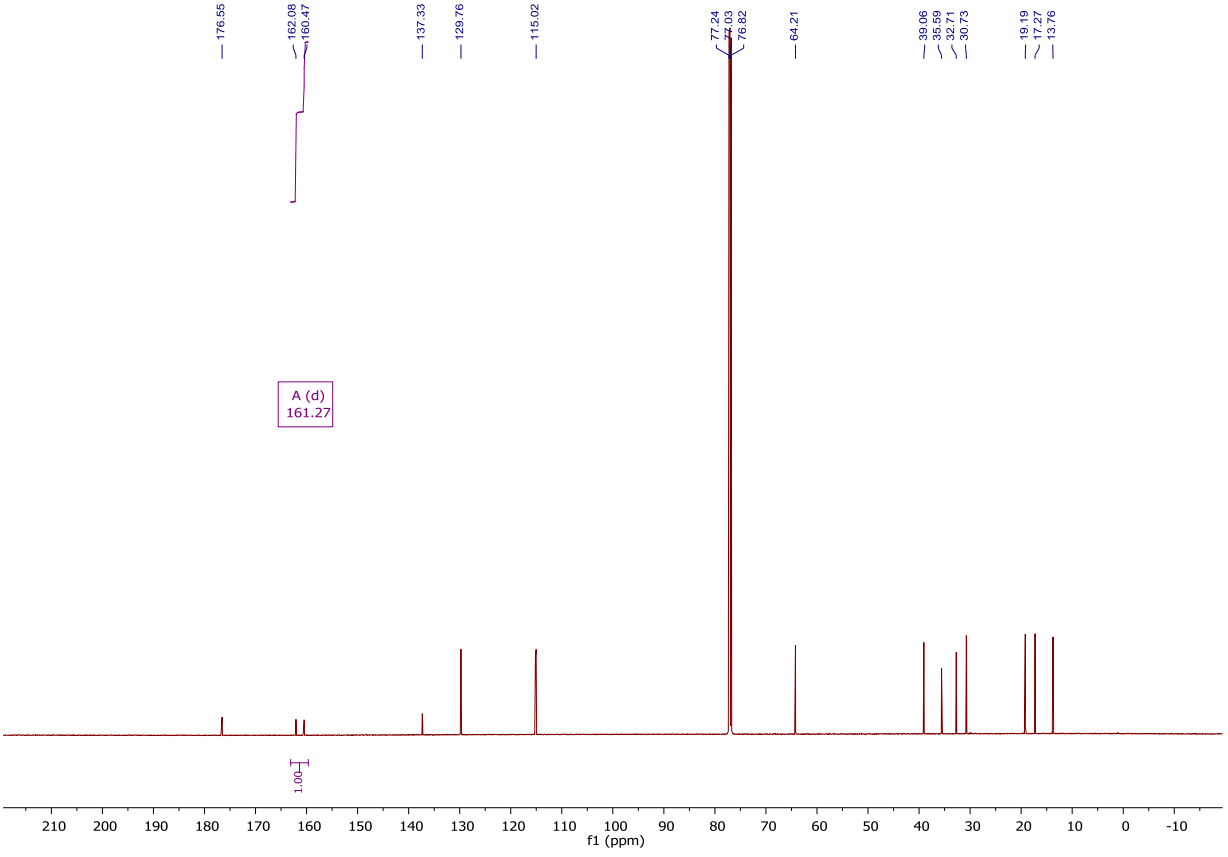
f1 (ppm)


O
On-Bu
Me
F
f1 (ppm)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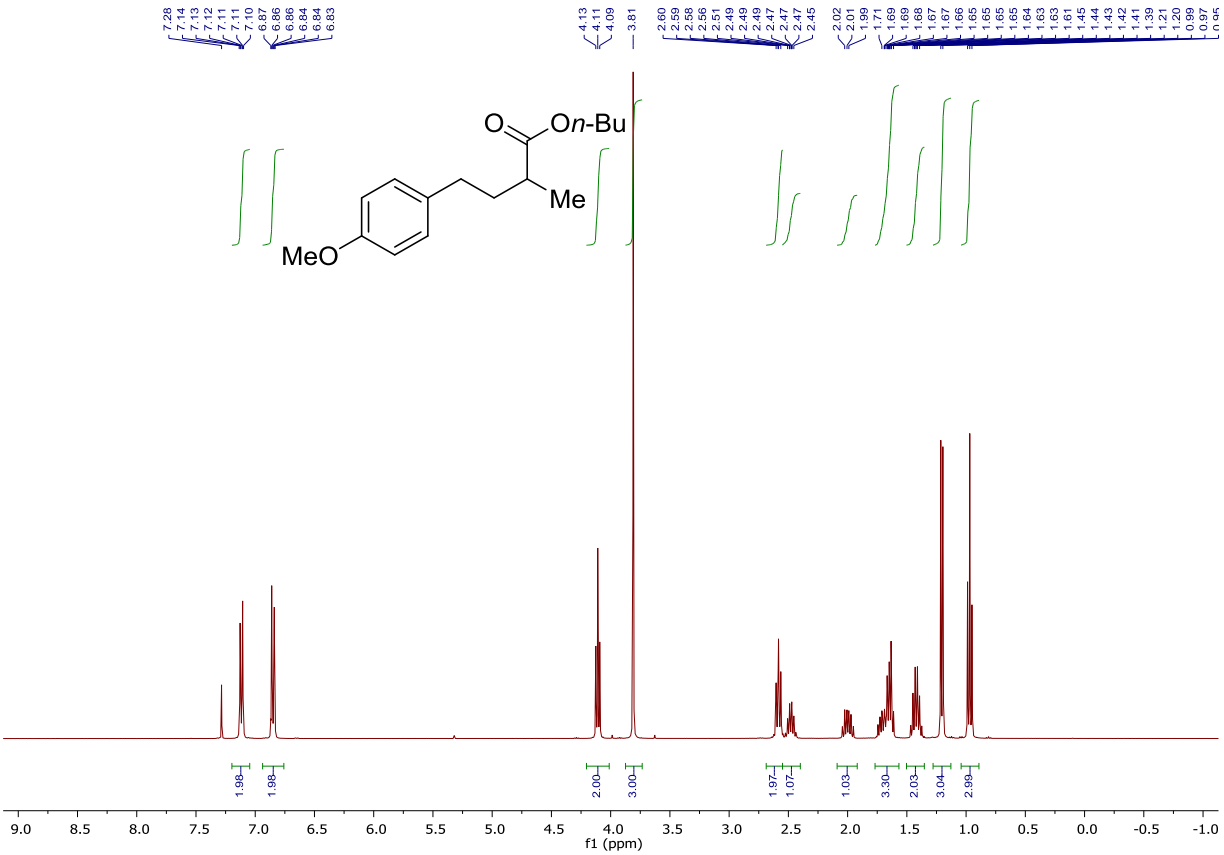
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6.86
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6.84
6.83
4.13
4.11
4.09
3.81
2.60
2.59
2.58
2.56
2.51
2.49
2.49
2.49
2.47
2.47
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2.02
2.01
1.99
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1.65
1.65
1.65
1.64
1.63
1.63
1.61
1.45
1.44
1.43
1.42
1.41
1.39
1.21
1.20
0.99
0.97
O
O*n*-Bu
Me
MeO
1.98
1.98
2.00
3.00
1.97
1.07
1.03
3.30
2.03
3.04
2.99
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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2.5
2.0
1.5
1.0
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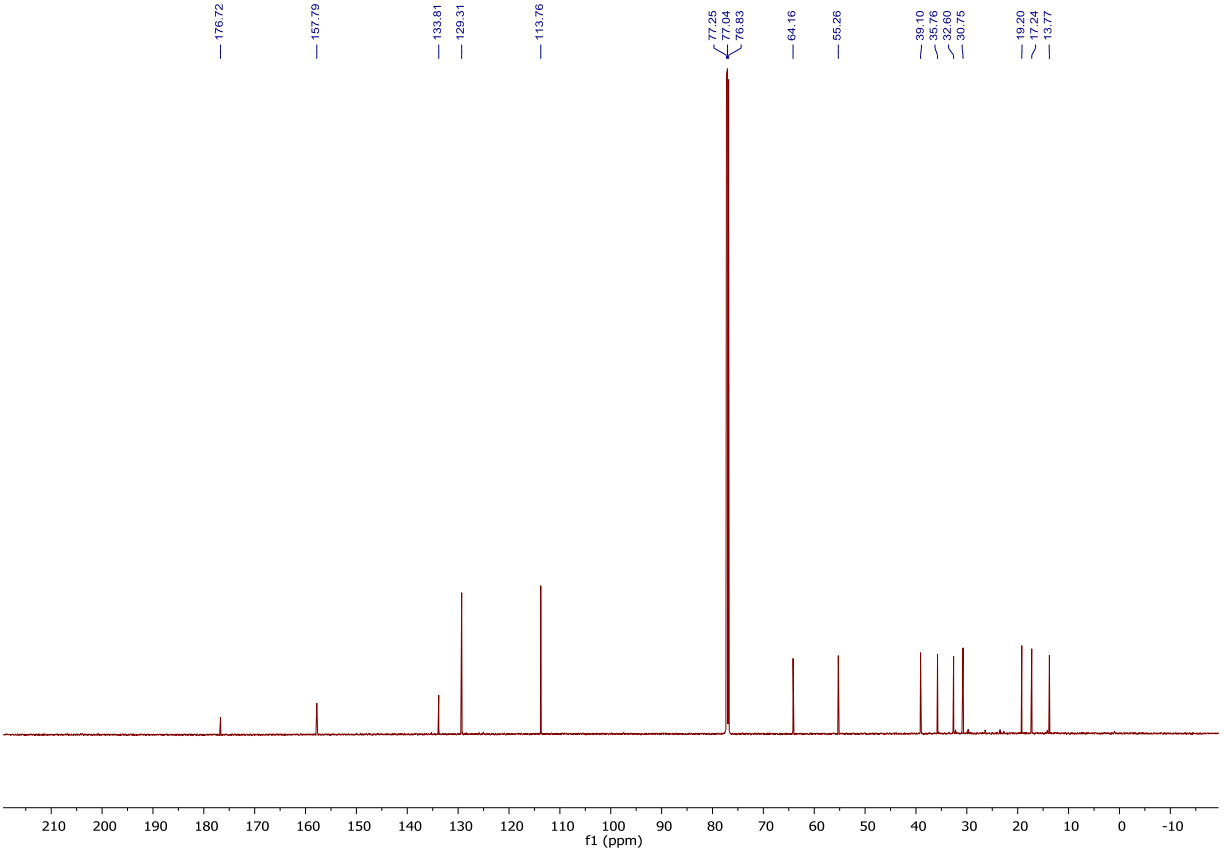
0.0
-0.5
-1.0
f1 (ppm)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77.04
76.83
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55.26
39.10
35.76
32.60
30.75
19.20
17.24
13.77
210
200
190
180
170
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120
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80
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60
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40
30
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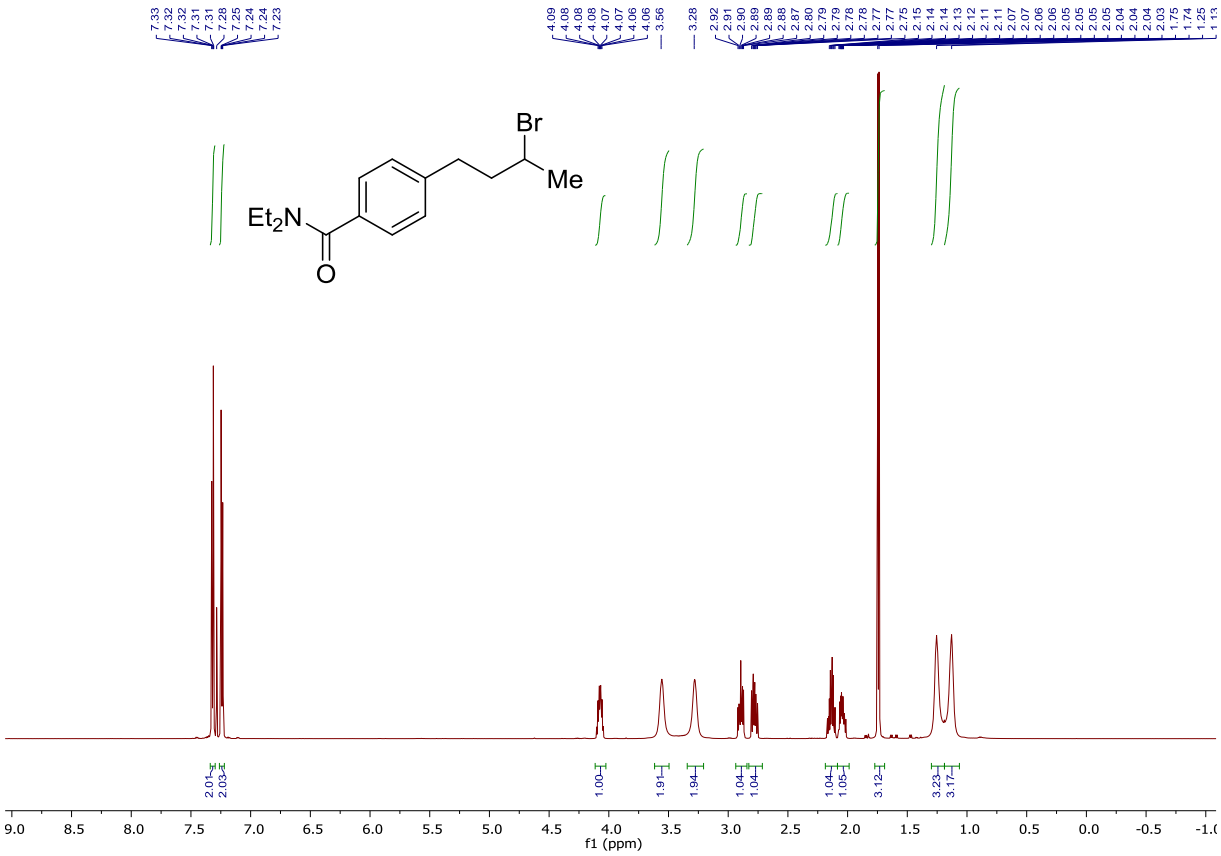
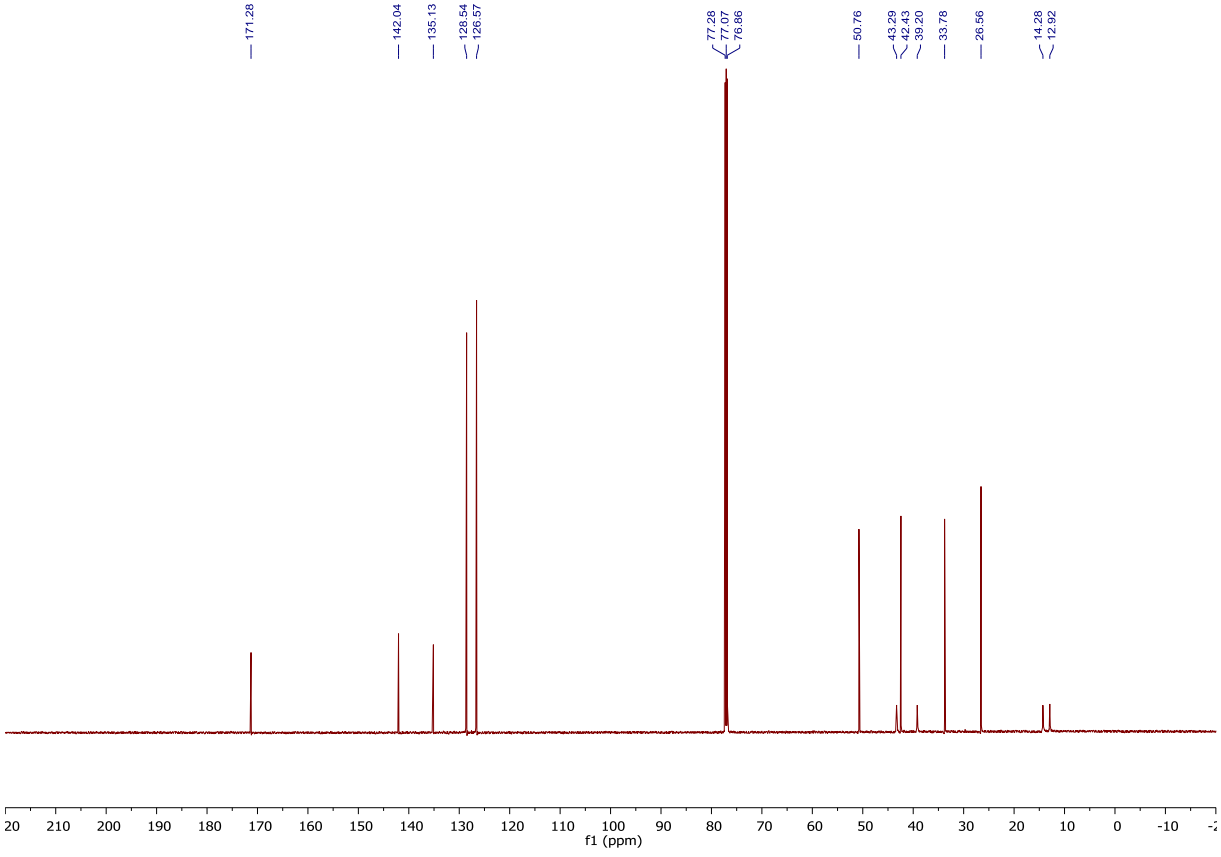
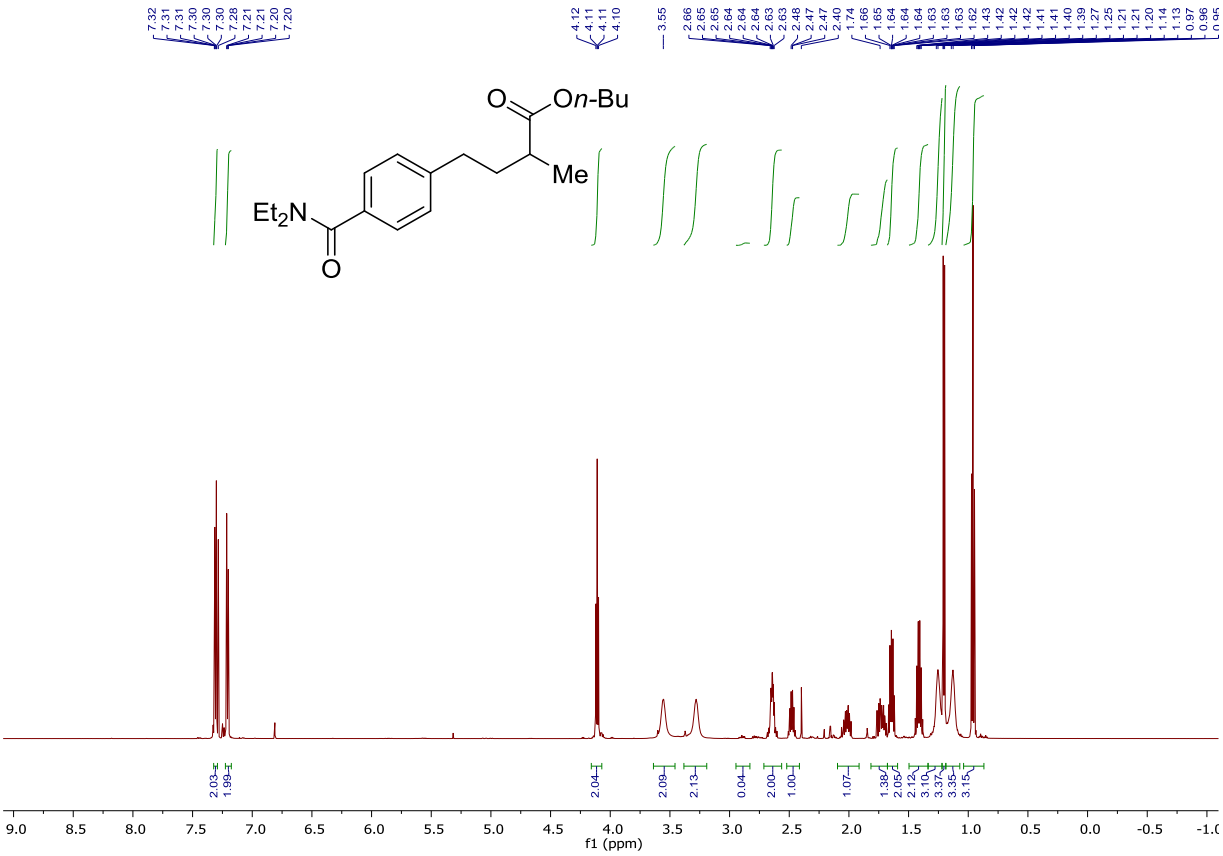
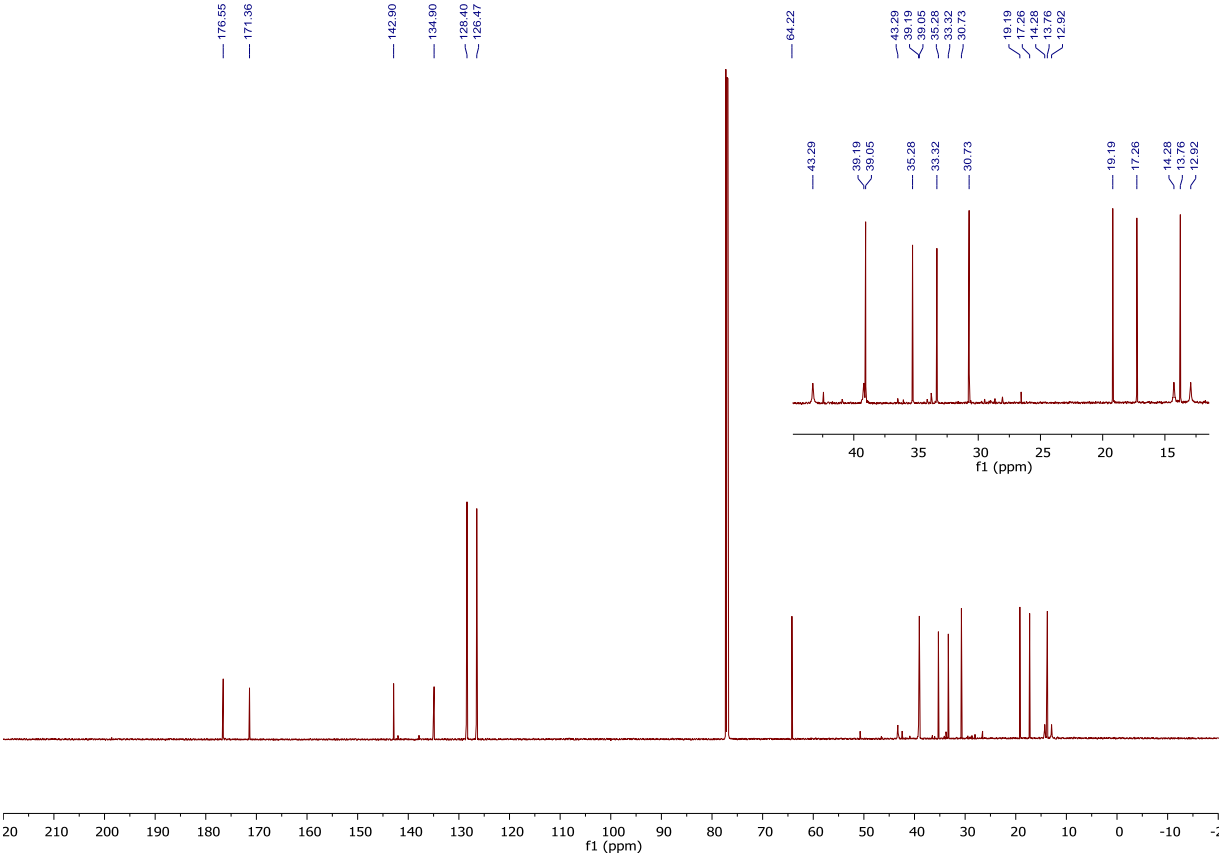
0
-10
f1 (ppm)


Br
Me
Et2N
O
f1 (ppm)


f1 (ppm)


O
On-Bu
Me
Et2N
O
f1 (ppm)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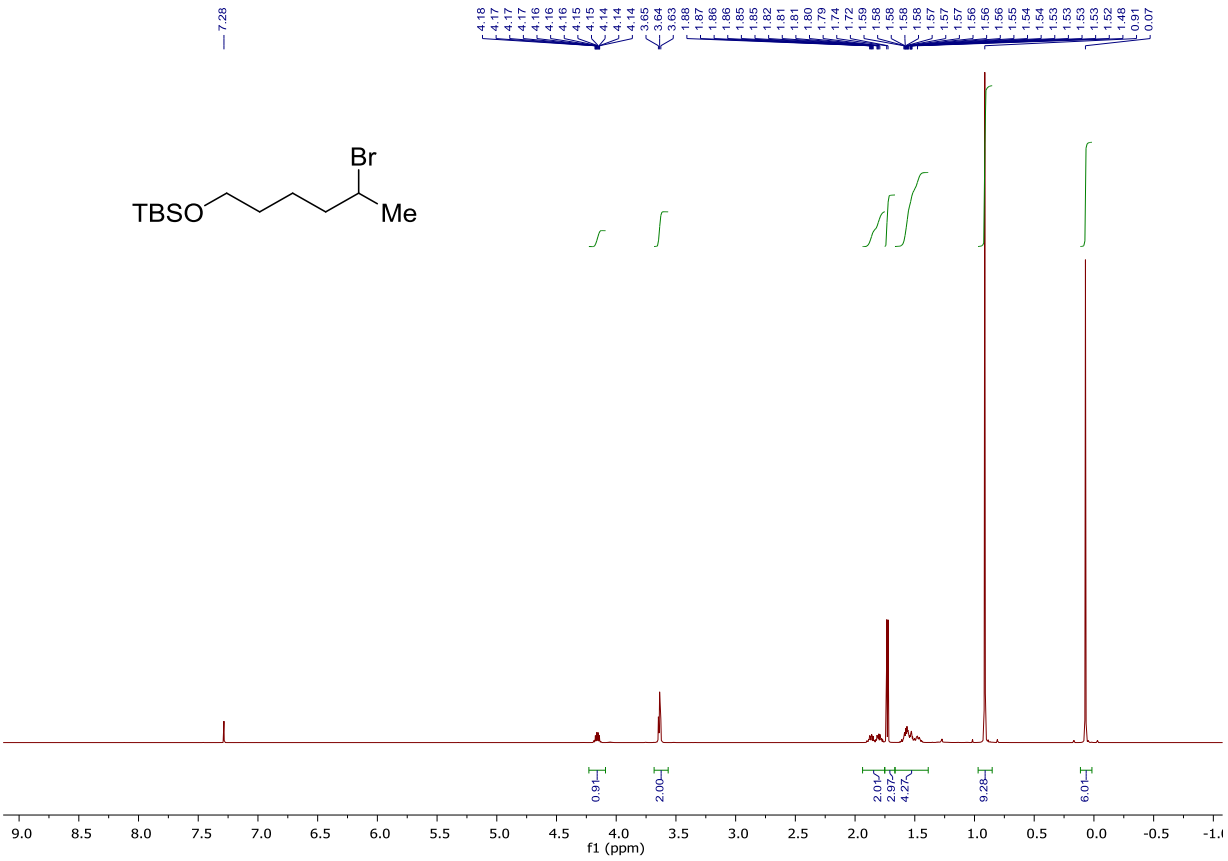
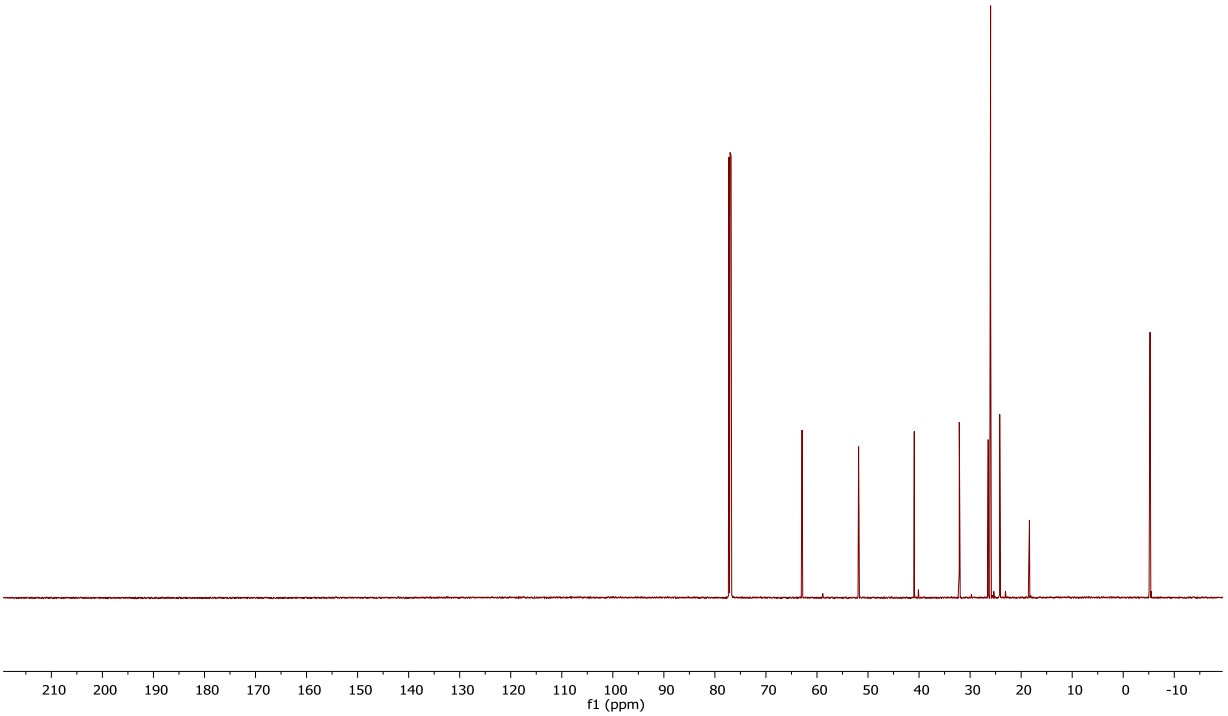

Br
TBSO
Me
f1 (ppm)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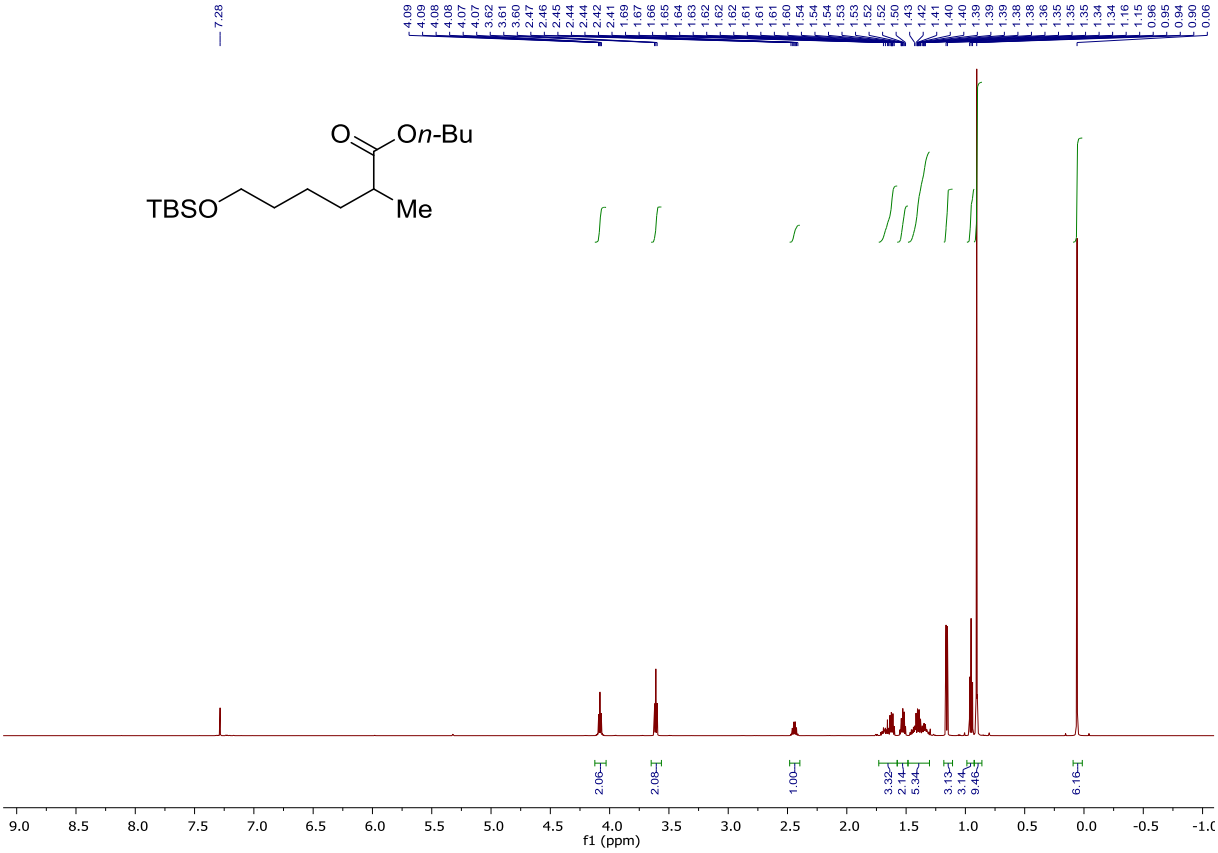
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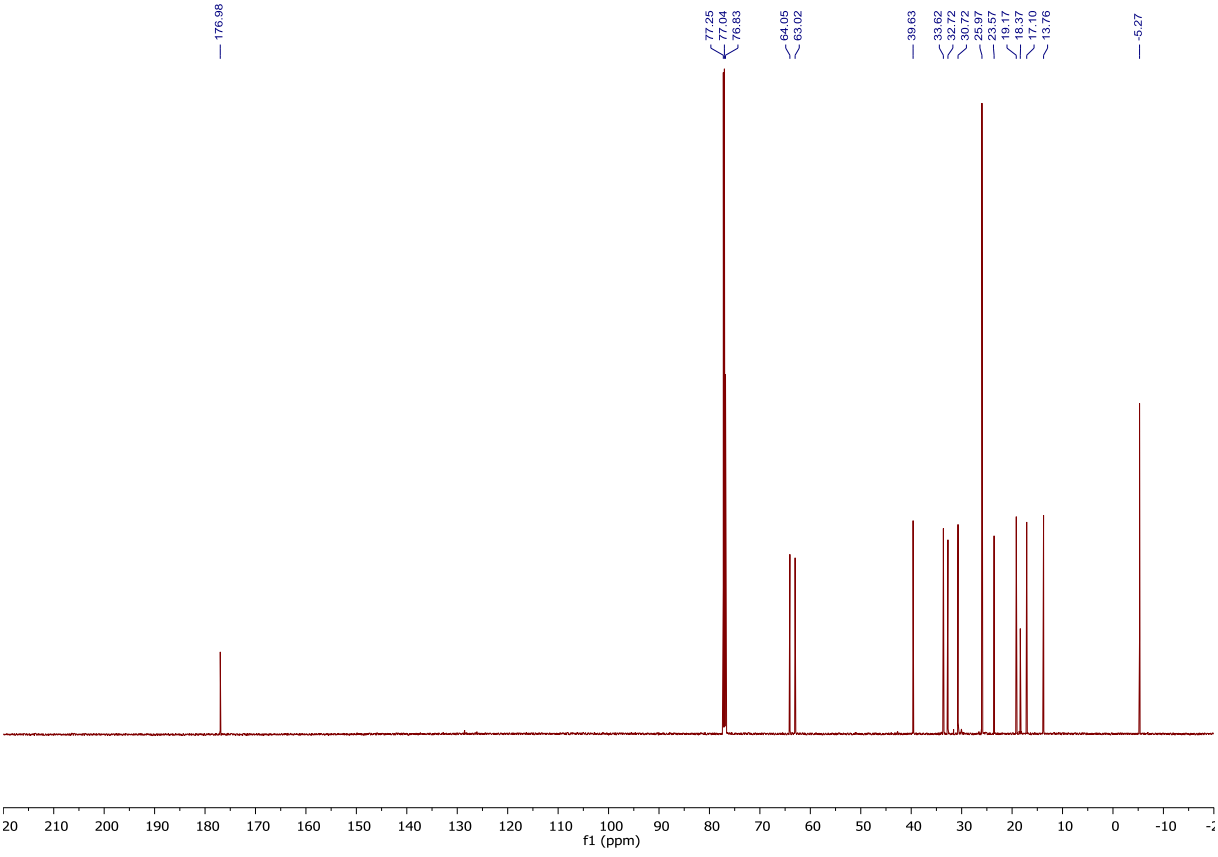
4.09 4.09 4.08 4.08 4.08 4.07 4.07 3.62 3.61 3.60 2.47 2.46 2.45 2.44 2.44 2.42 2.41 1.69 1.67 1.66 1.65 1.64 1.63 1.62 1.62 1.62 1.61 1.61 1.61 1.60 1.54 1.54 1.54 1.53 1.53 1.52 1.52 1.50 1.43 1.42 1.41 1.40 1.40 1.39 1.39 1.39 1.38 1.38 1.36 1.35 1.35 1.34 1.34 1.16 1.15 0.96 0.95 0.94 0.90 0.06
O
On-Bu
TBSO
Me
2.06
2.08
1.00
3.32
2.14
5.34
3.13
3.14
9.46
6.16
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 -0.5 -1.0
f1 (ppm)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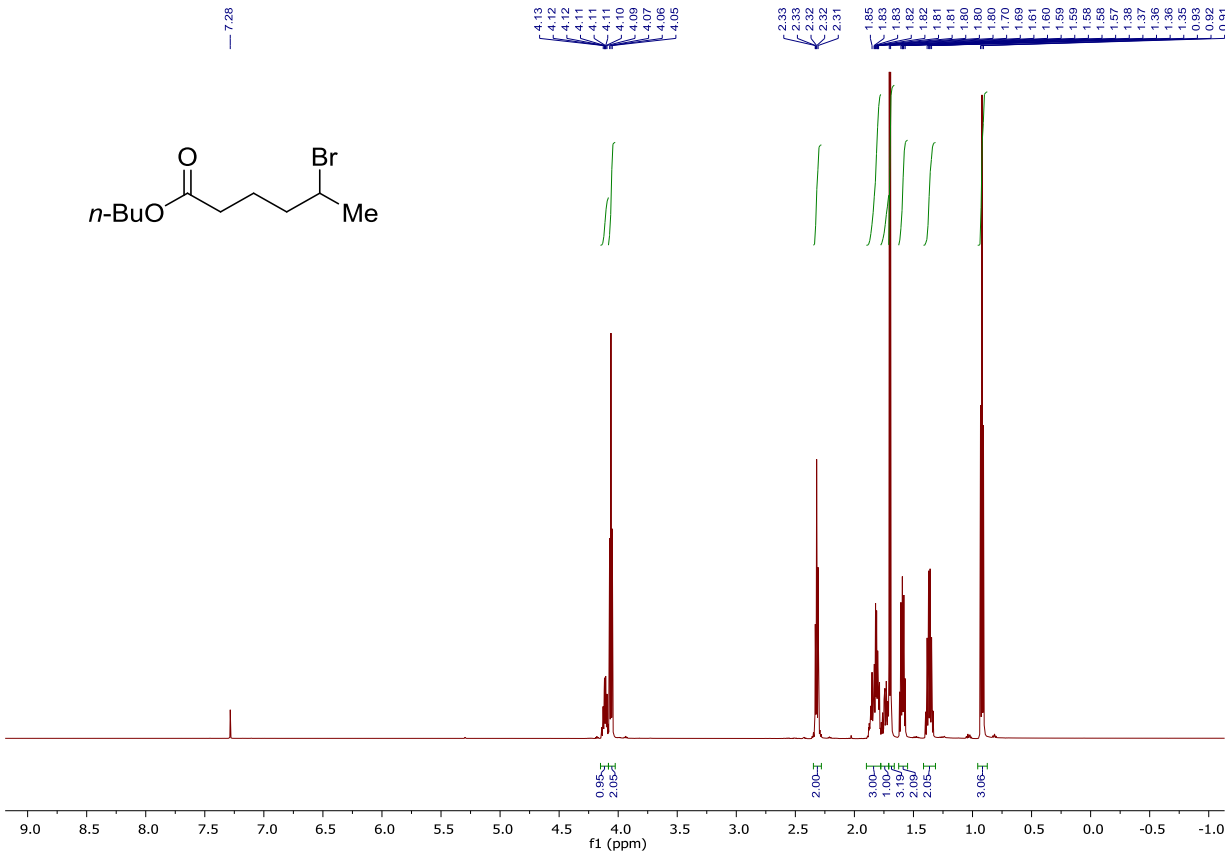
63.02
39.63
33.62
32.72
30.72
25.97
23.57
19.17
18.37
17.10
13.76
-5.27
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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4.07
4.06
4.05
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2.33
2.32
2.32
2.31
1.85
1.83
1.83
1.82
1.82
1.81
1.81
1.80
1.80
1.80
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1.69
1.61
1.60
1.59
1.59
1.58
1.58
1.57
1.38
1.37
1.36
1.36
1.35
0.93
0.92
O
Br
n-BuO
Me
0.95
2.05
2.00
3.00
1.00
3.19
2.09
2.05
3.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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2.0
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0.0
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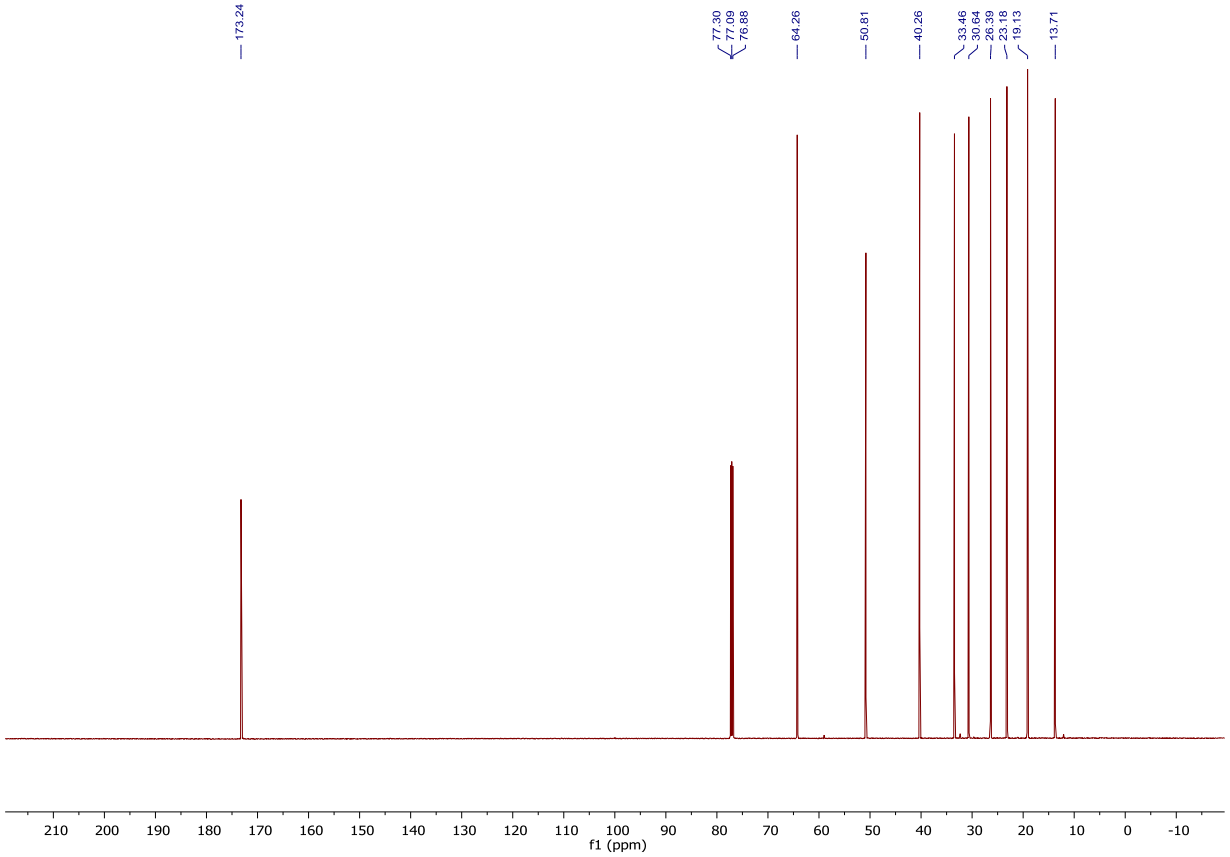
-1.0
f1 (ppm)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33.46
30.64
28.39
23.18
19.13
13.71
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200
190
180
170
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100
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80
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40
30
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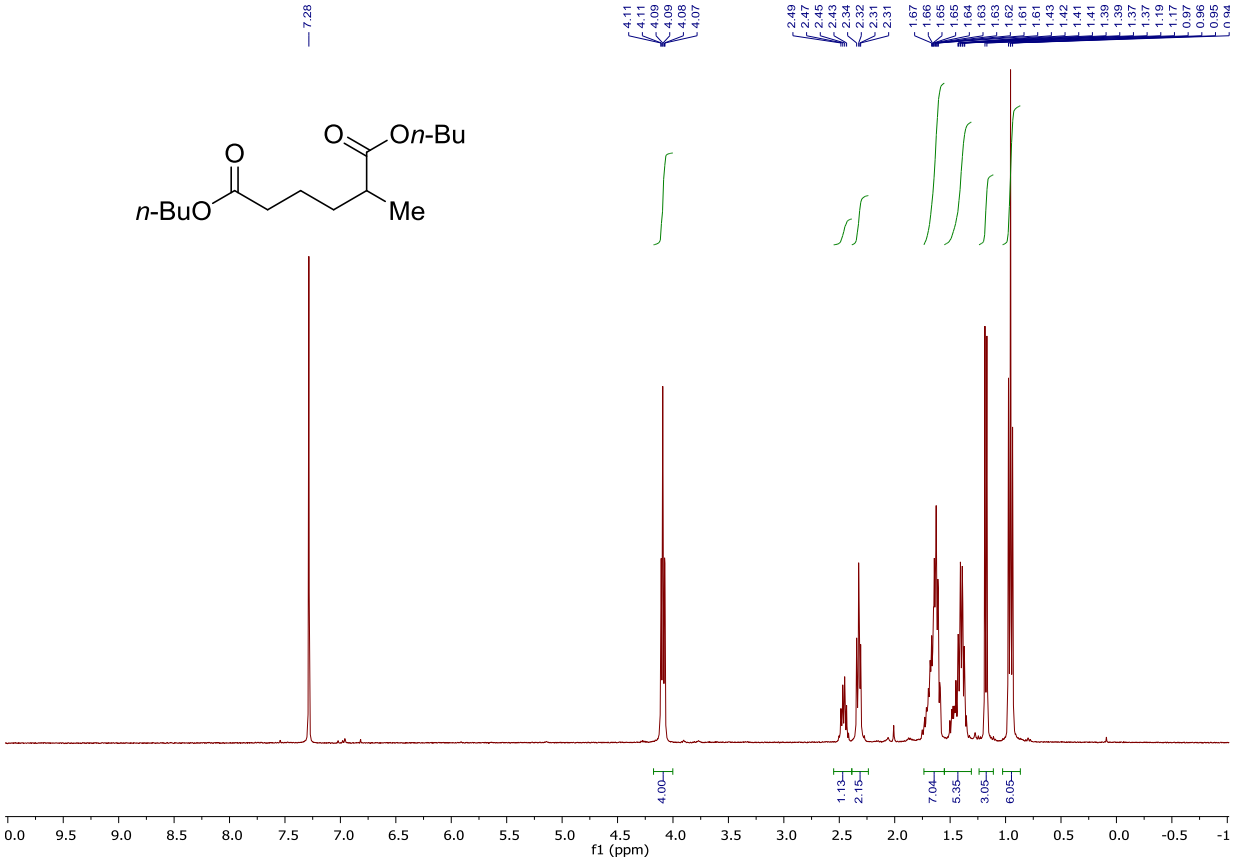
0
-10
f1 (ppm)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1.61
1.61
1.43
1.42
1.41
1.41
1.39
1.39
1.37
1.37
1.19
1.17
0.97
0.96
0.95
0.94
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O
On-Bu
n-BuO
Me
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2.15
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5.35
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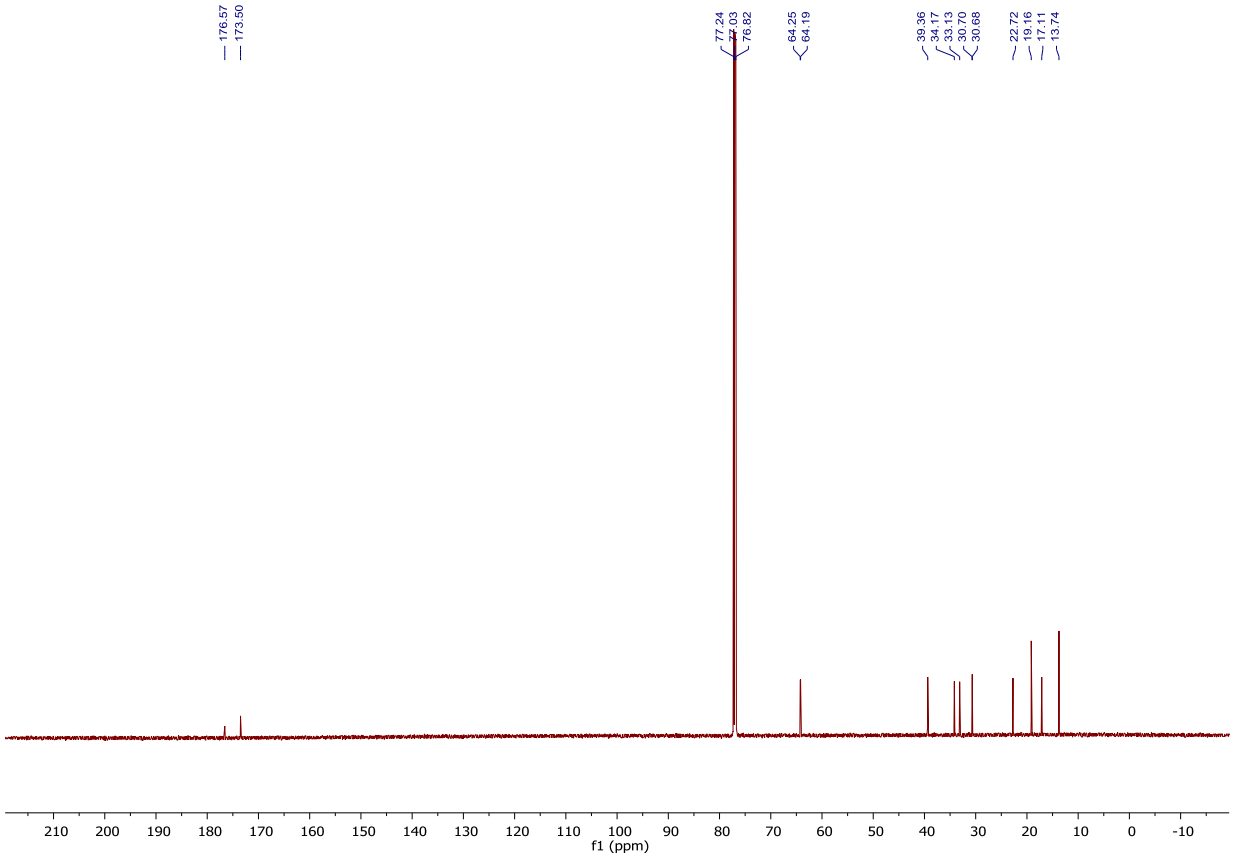
6.05
f1 (ppm)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30.68
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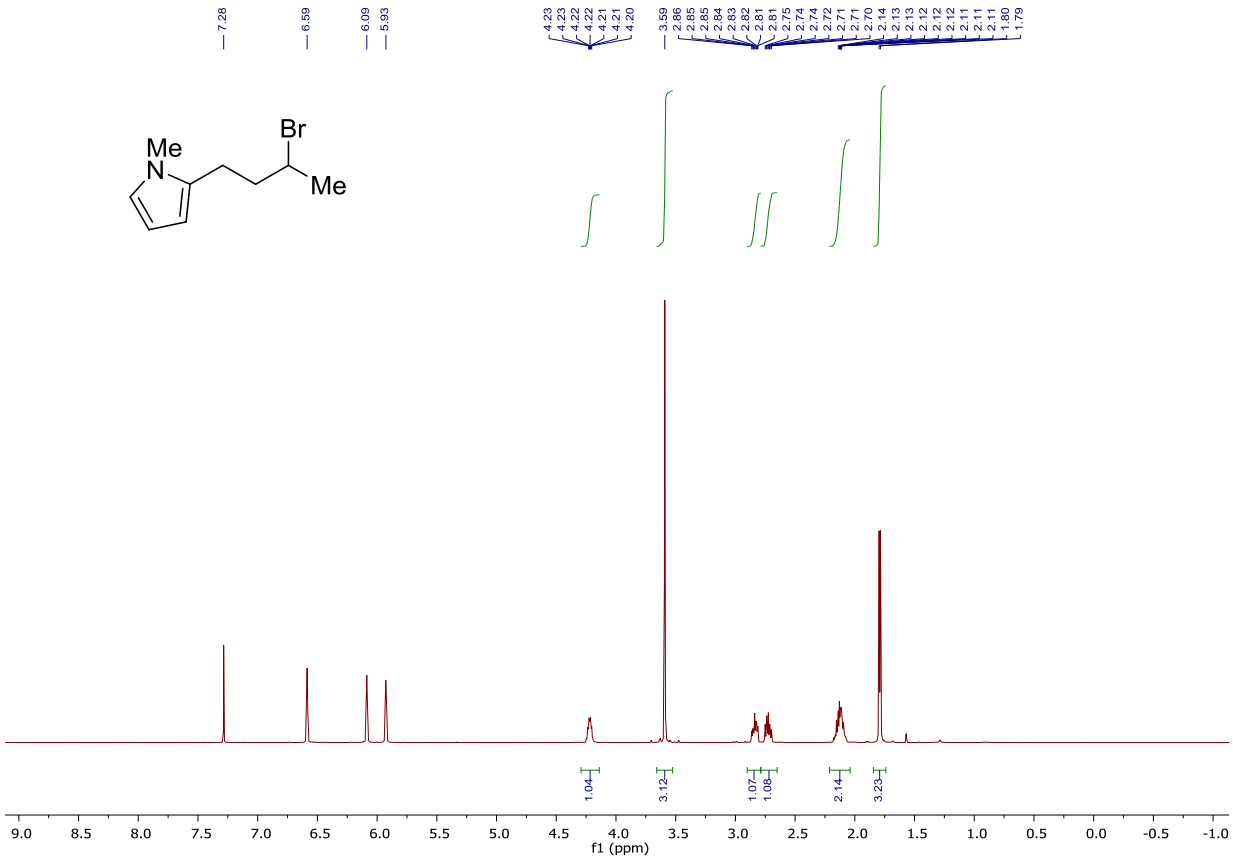
19.16
17.11
13.74
f1 (ppm)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2.85
2.84
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2.82
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2.81
2.75
2.74
2.74
2.72
2.71
2.71
2.70
2.14
2.13
2.12
2.12
2.12
2.11
2.11
1.80
1.79
Me
N
Br
Me
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3.12
1.07
1.08
2.14
3.23
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8.5
8.0
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
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2.0
1.5
1.0
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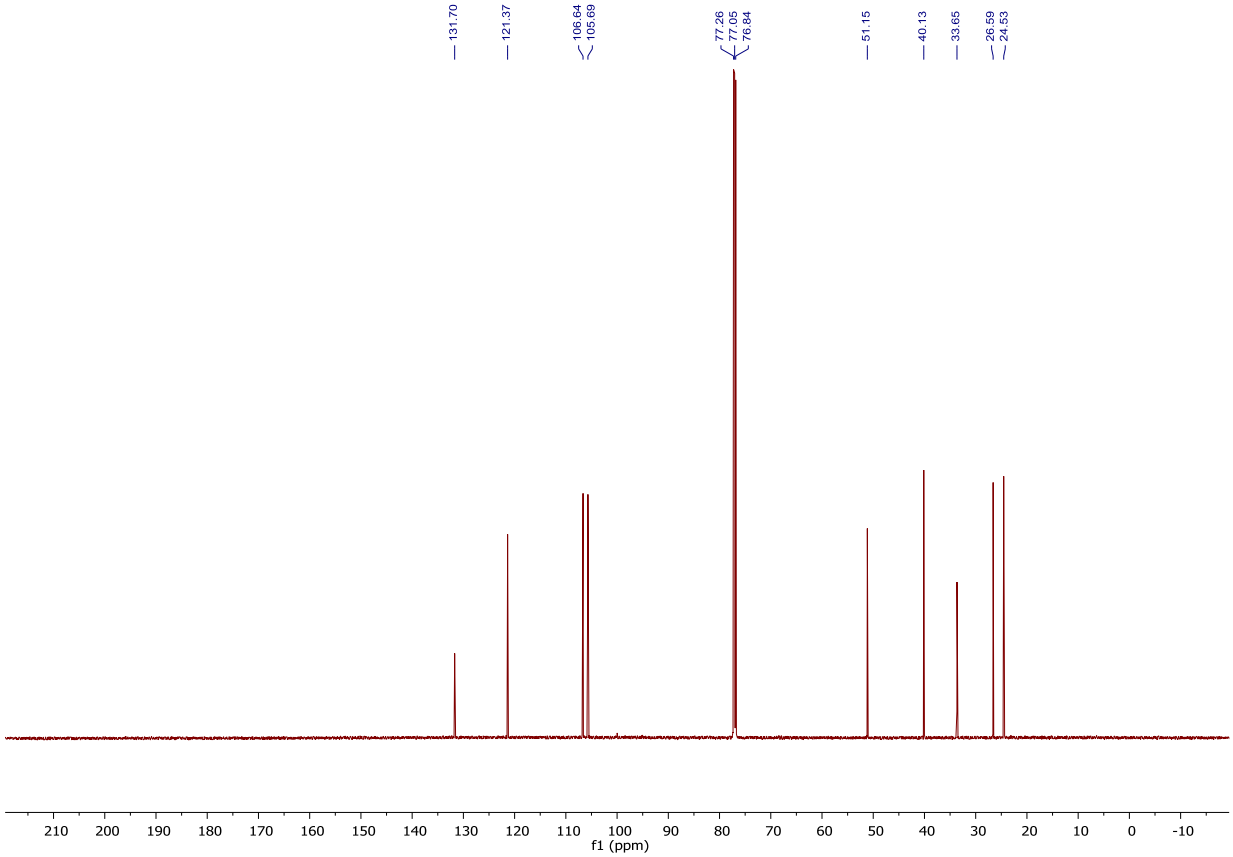
0.0
-0.5
-1.0
f1 (ppm)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33.65
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200
190
180
170
160
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140
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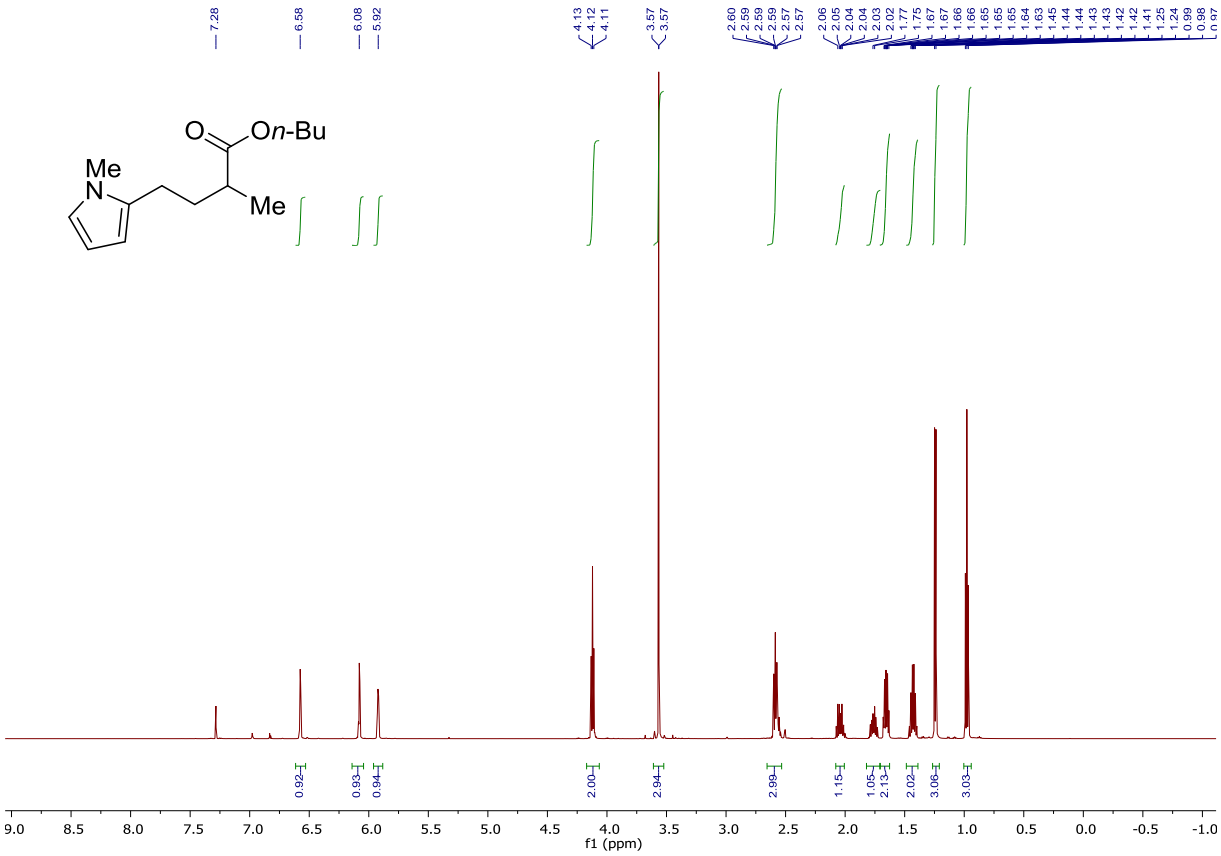
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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2.05
2.04
2.04
2.03
2.02
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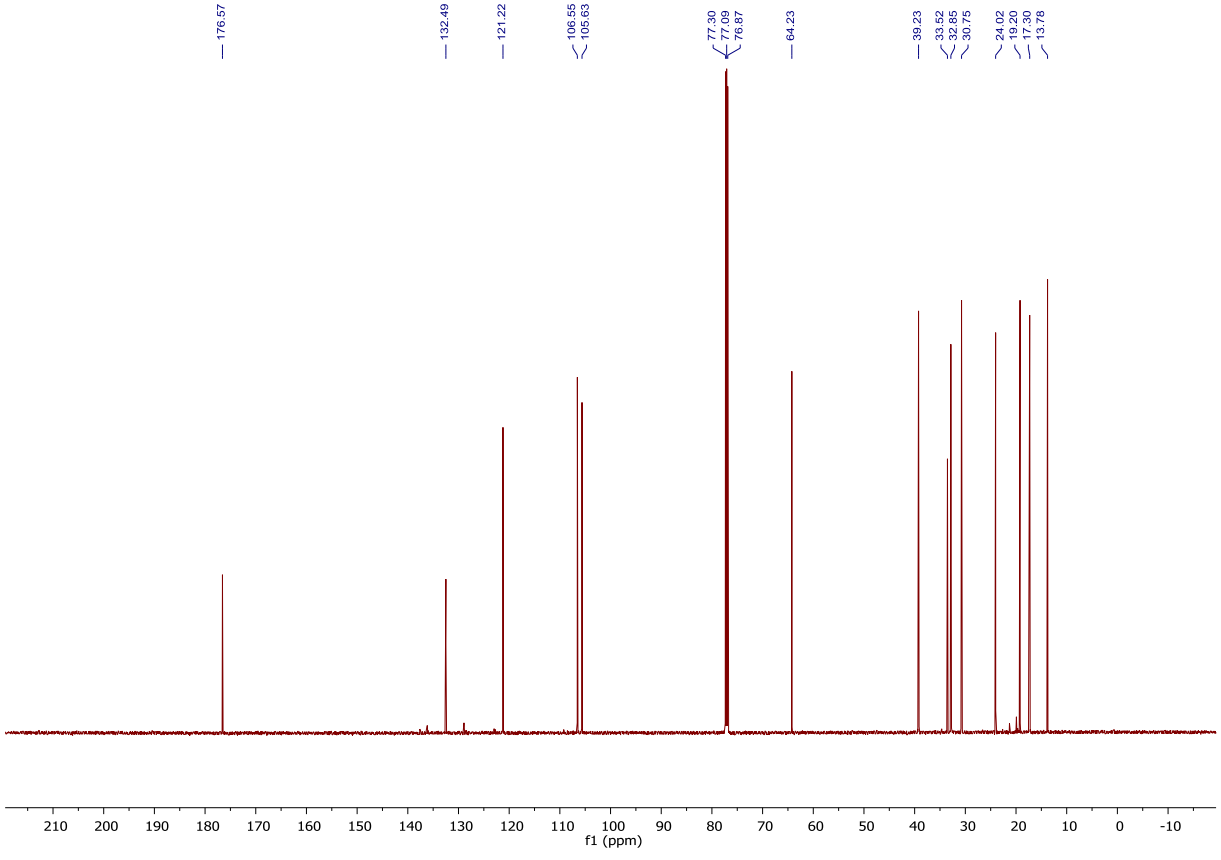
1.64
1.63
1.45
1.44
1.44
1.43
1.43
1.42
1.42
1.41
1.25
1.24
0.99
0.98
0.97
O
On-Bu
Me
N
Me
0.92
0.93
0.94
2.00
2.94
2.99
1.15
1.05
2.13
2.02
3.06
3.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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33.52
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30.75
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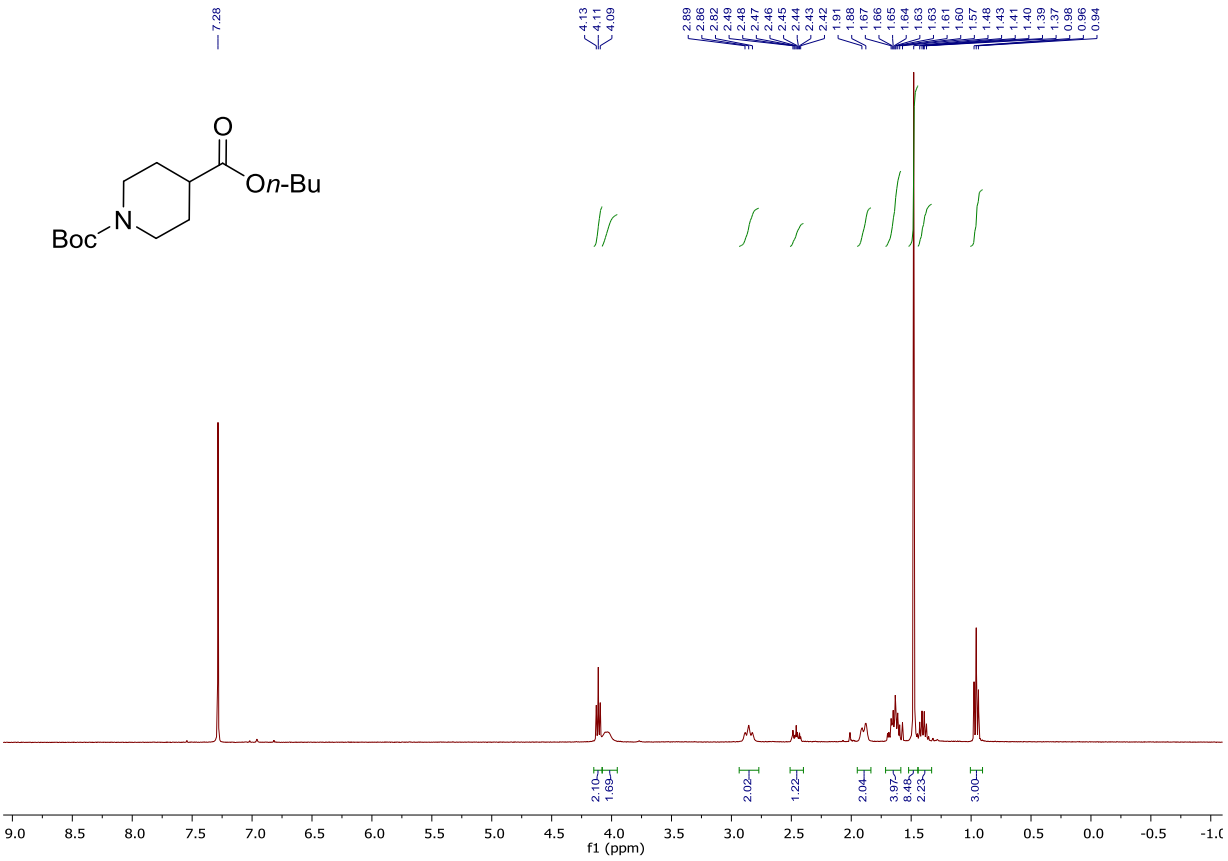
19.20
17.30
13.78
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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1.88
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1.65
1.64
1.63
1.61
1.60
1.57
1.48
1.43
1.41
1.40
1.39
1.37
0.98
0.96
0.94
O
On-Bu
N
Boc
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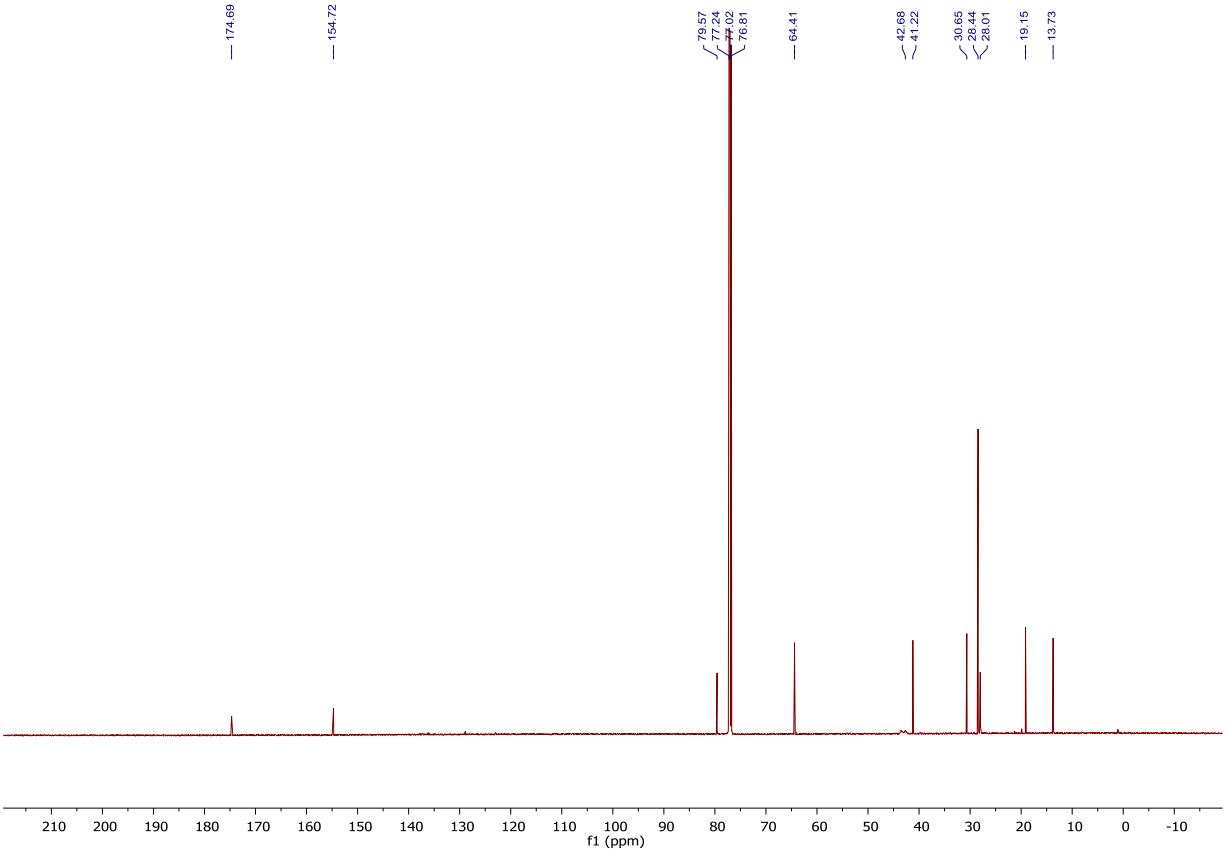
1.69
2.02
1.22
2.04
3.97
8.48
2.23
3.00
f1 (ppm)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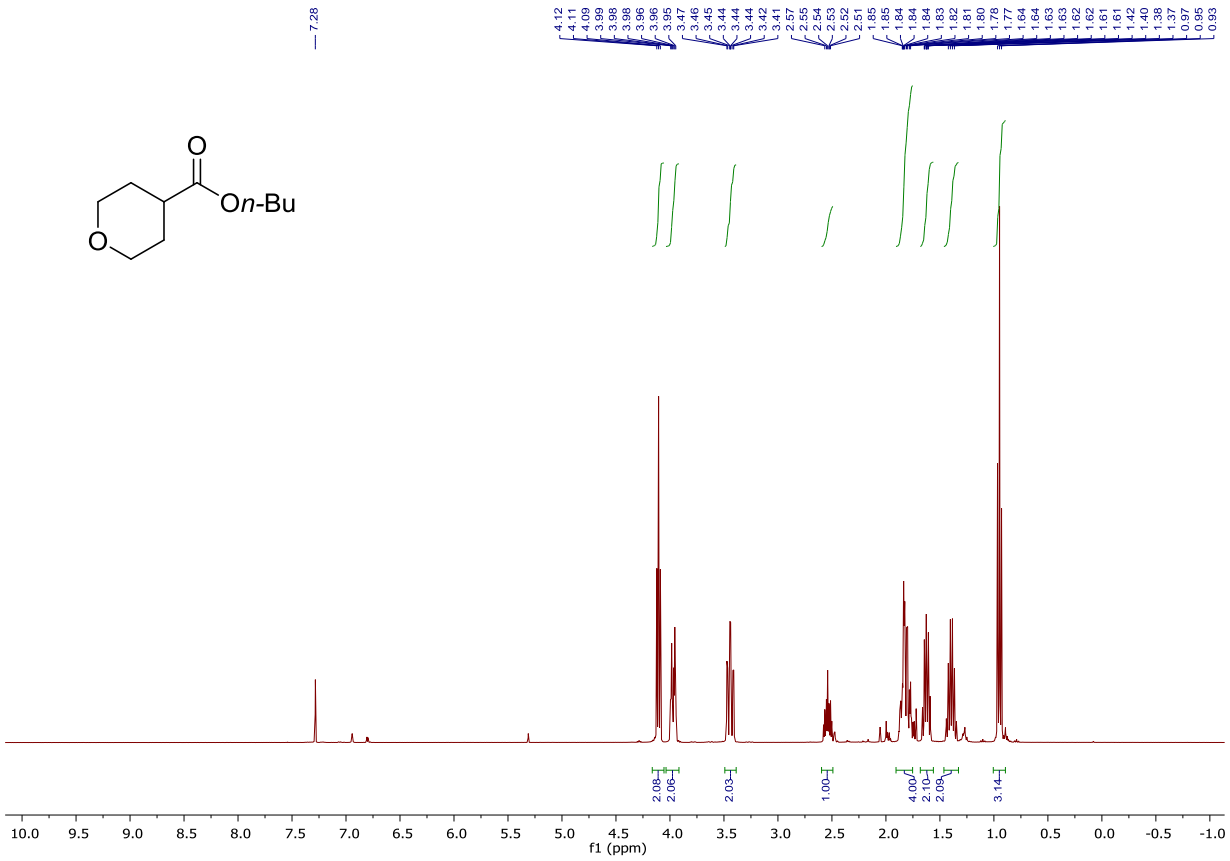
30.65
28.44
28.01
19.15
13.73
f1 (ppm)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3.95
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1.63
1.63
1.62
1.62
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1.61
1.42
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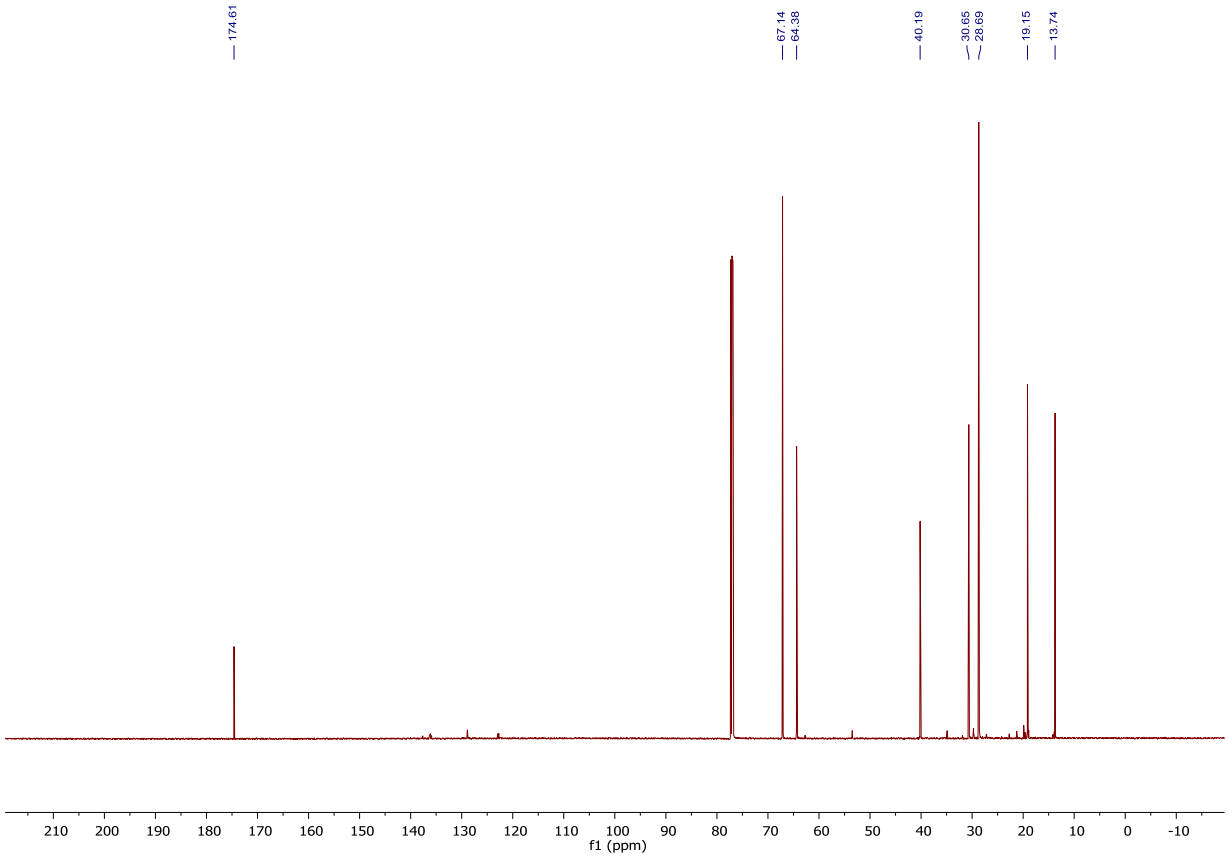
1.38
1.37
0.97
0.95
0.93
O
O
On-Bu
2.08
2.06
2.03
1.00
4.00
2.10
2.09
3.14
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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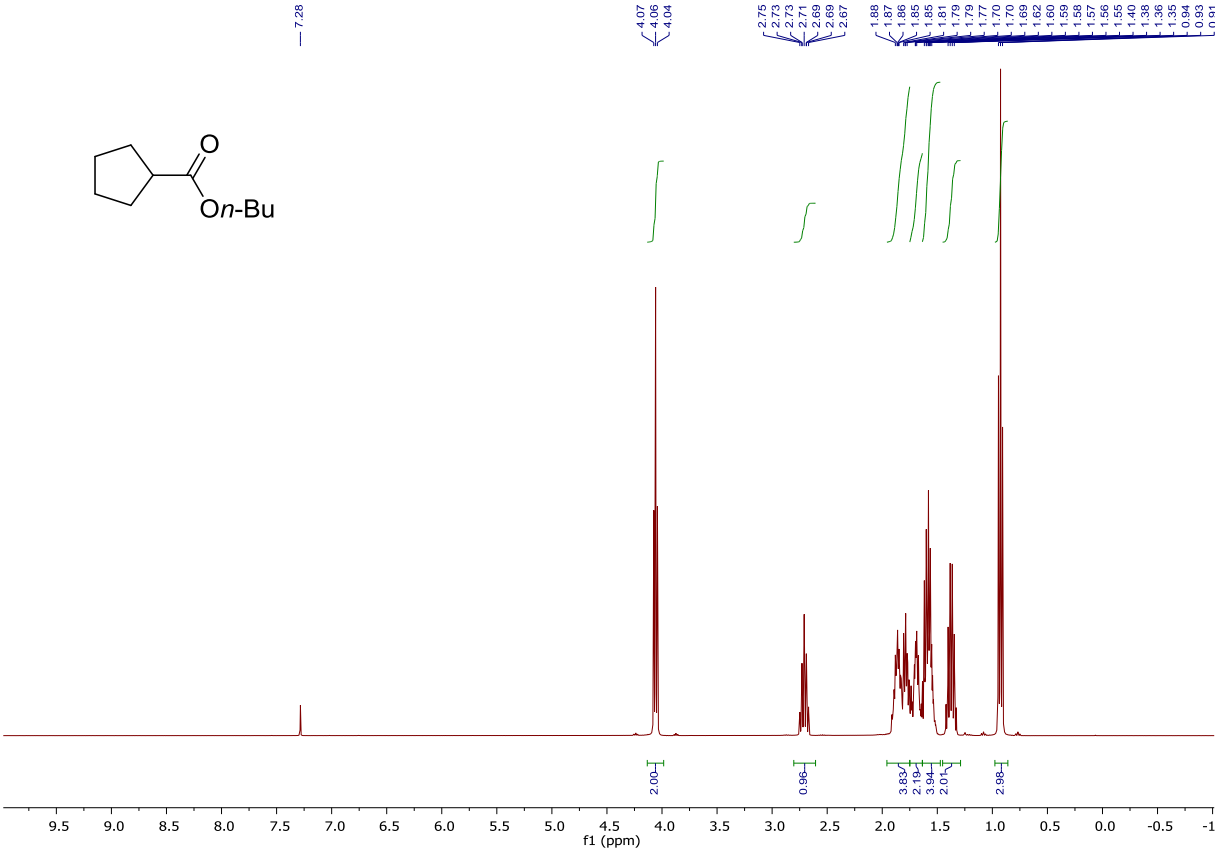
28.69
19.15
13.74
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
O*n*-Bu
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4.07
4.06
4.04
2.75
2.73
2.73
2.71
2.69
2.69
2.67
1.88
1.87
1.86
1.85
1.85
1.81
1.79
1.79
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1.70
1.70
1.69
1.62
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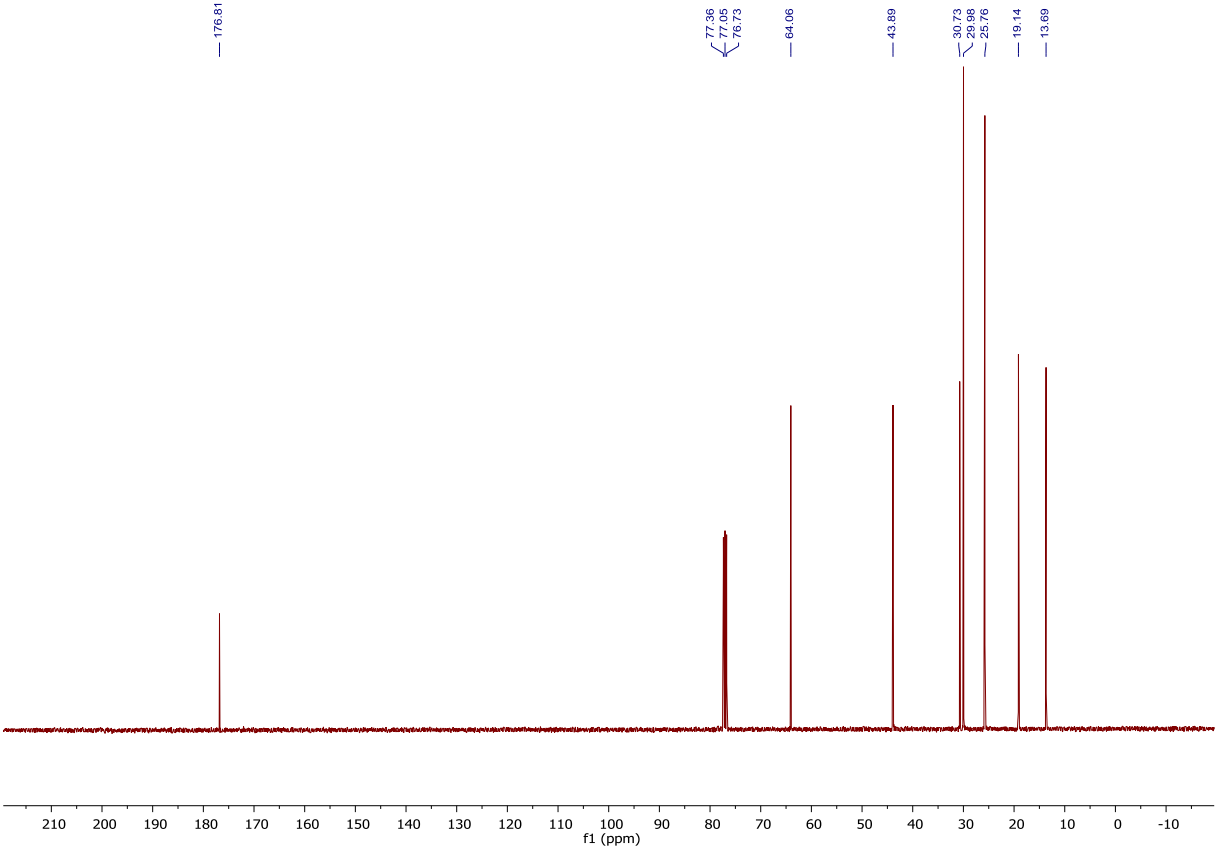
1.59
1.58
1.57
1.56
1.55
1.40
1.38
1.36
1.35
0.94
0.93
2.00
0.96
3.83
2.19
3.94
2.01
2.98
f1 (ppm)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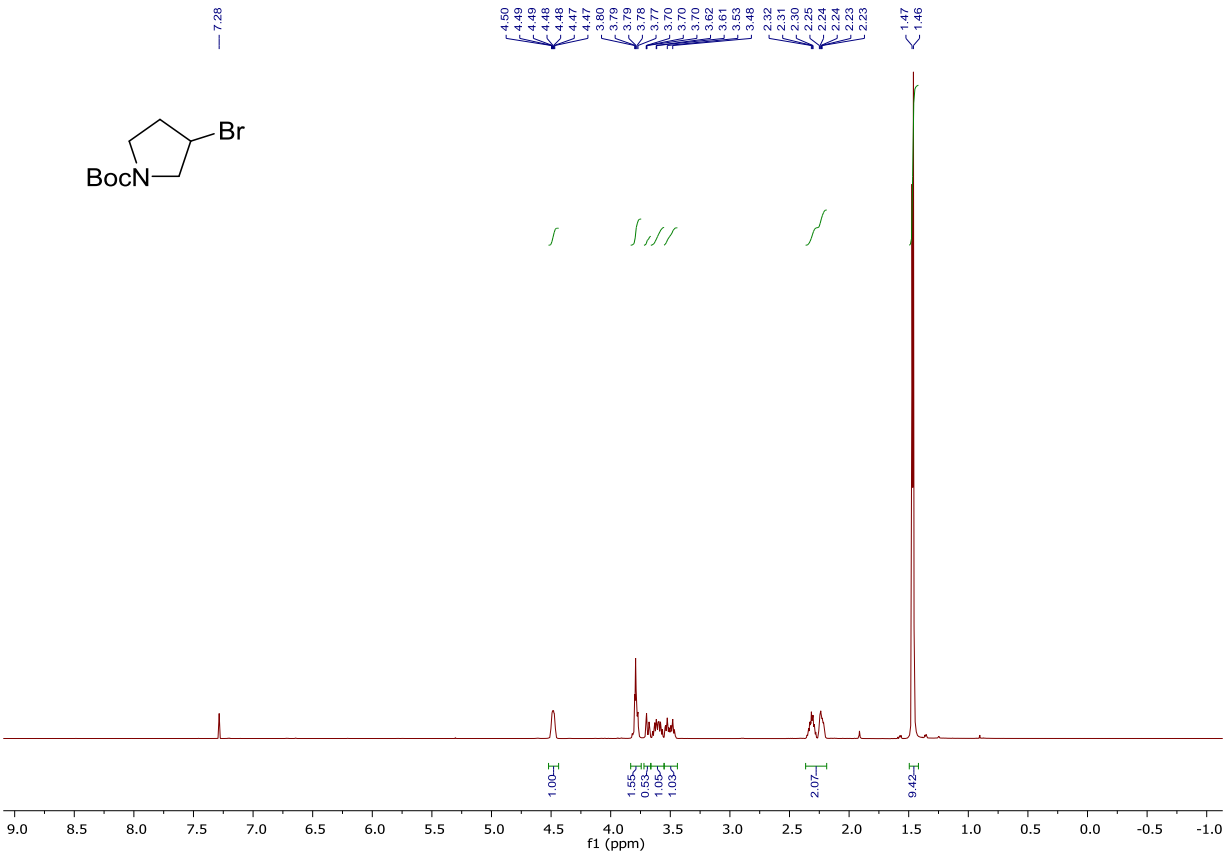
29.98
25.76
19.14
13.69
f1 (ppm)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4.47
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3.79
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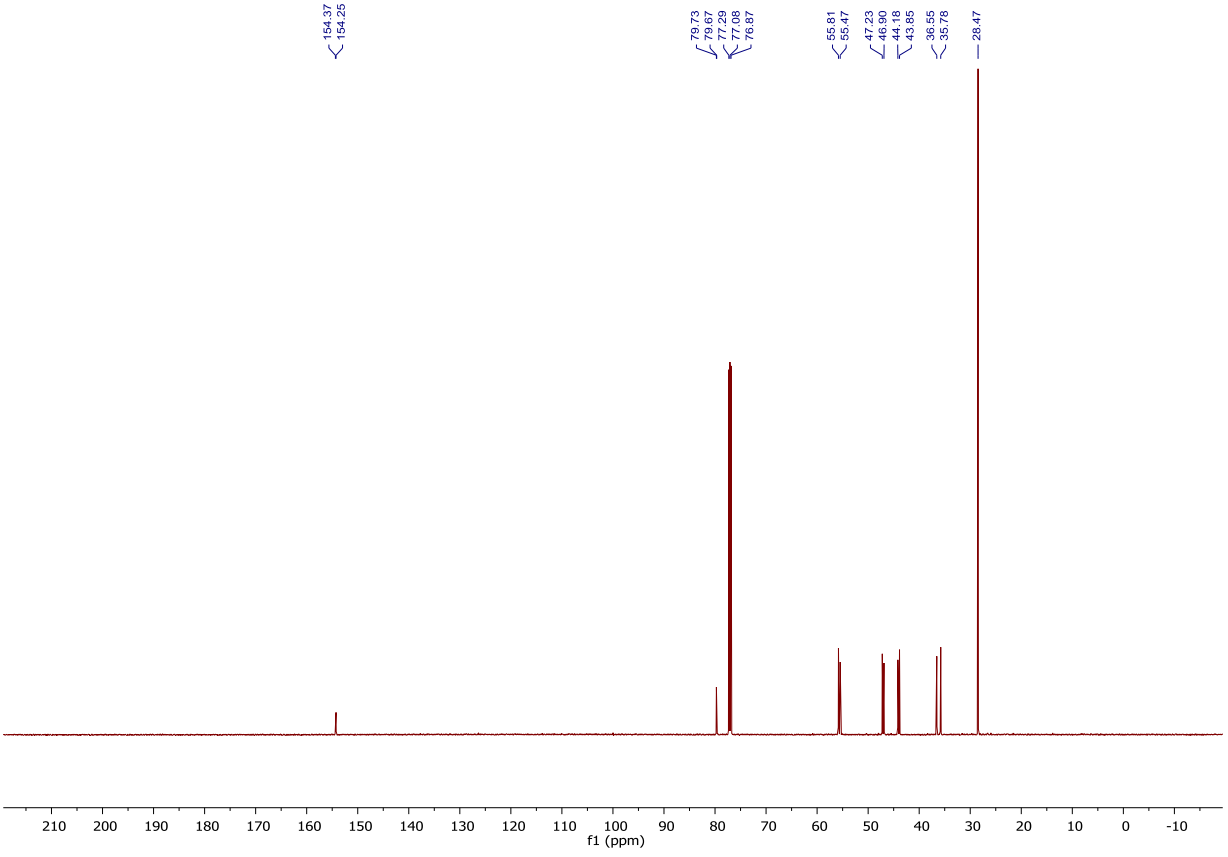
3.77
3.70
3.70
3.70
3.62
3.61
3.53
3.48
2.32
2.31
2.30
2.25
2.24
2.24
2.23
2.23
1.47
1.46
Br
BocN
1.00
1.55
0.53
1.05
1.03
2.07
9.42
f1 (ppm)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154.25
79.73
79.67
77.29
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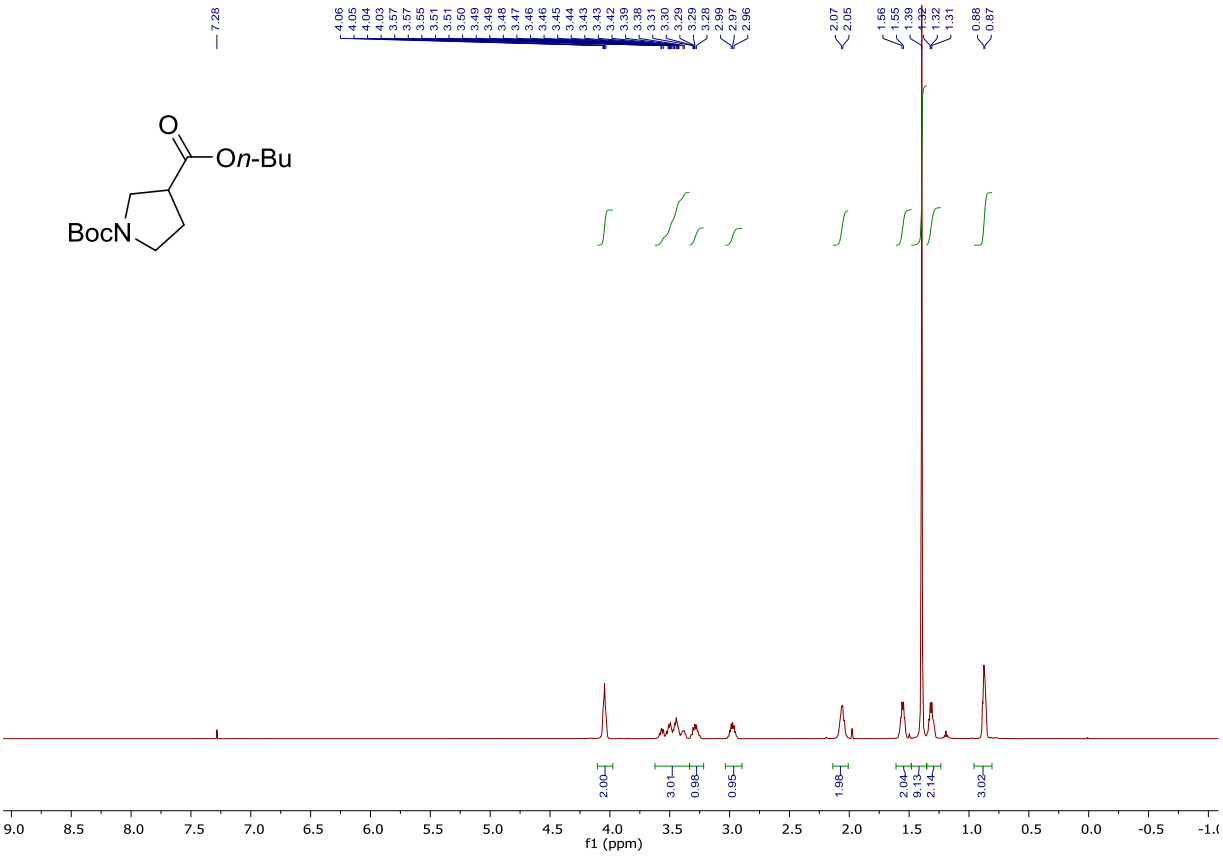
46.90
44.18
43.85
36.55
35.78
28.47
f1 (ppm)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3.48
3.47
3.46
3.46
3.45
3.44
3.43
3.43
3.42
3.39
3.38
3.31
3.30
3.29
3.28
2.99
2.97
2.96
2.07
2.05
1.56
1.55
1.39
1.32
1.31
0.88
0.87
O
On-Bu
BocN
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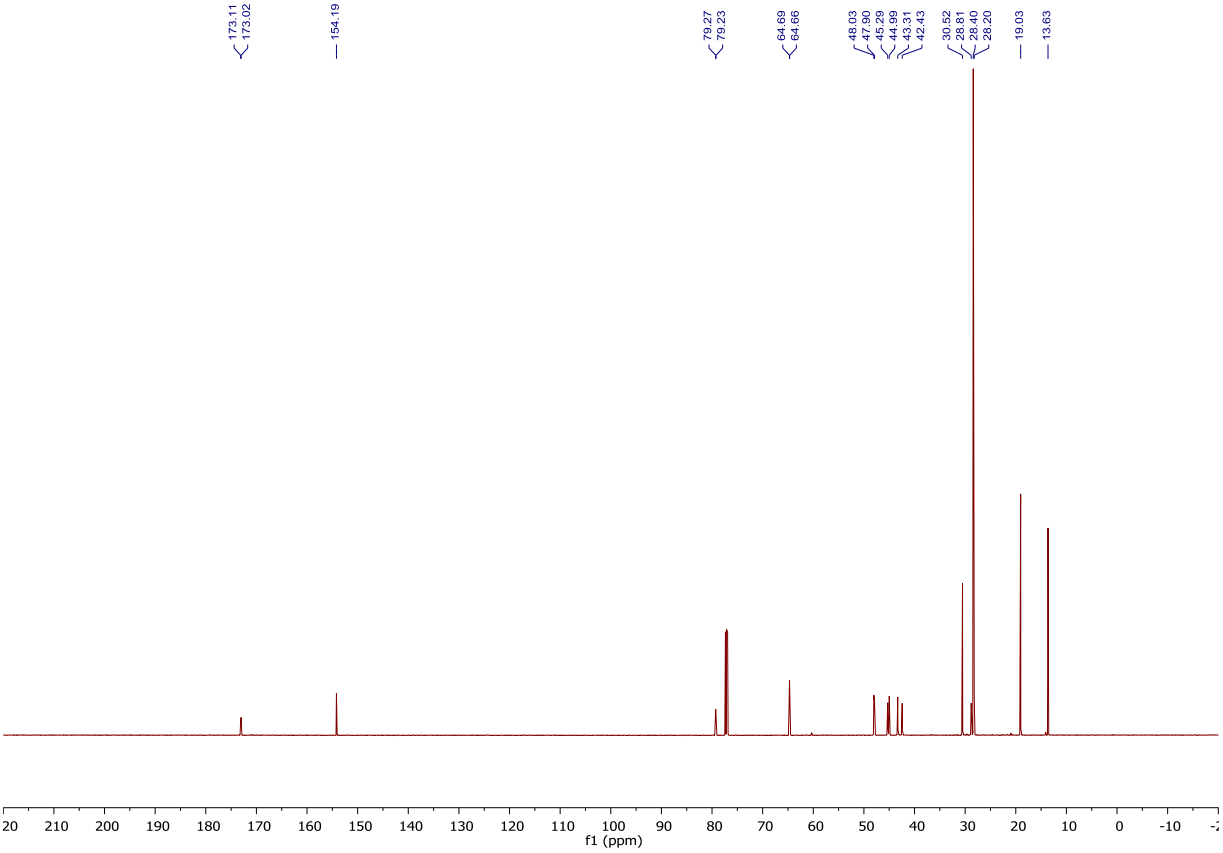
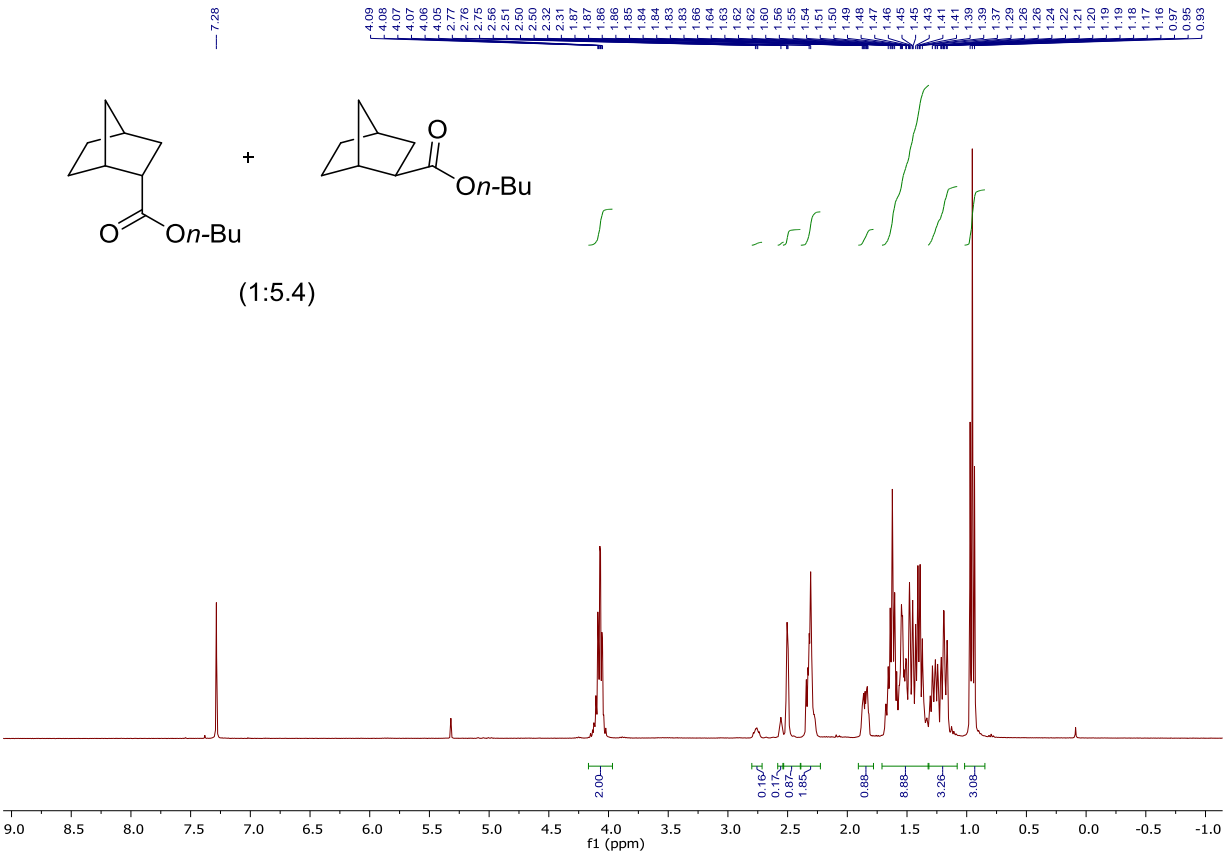
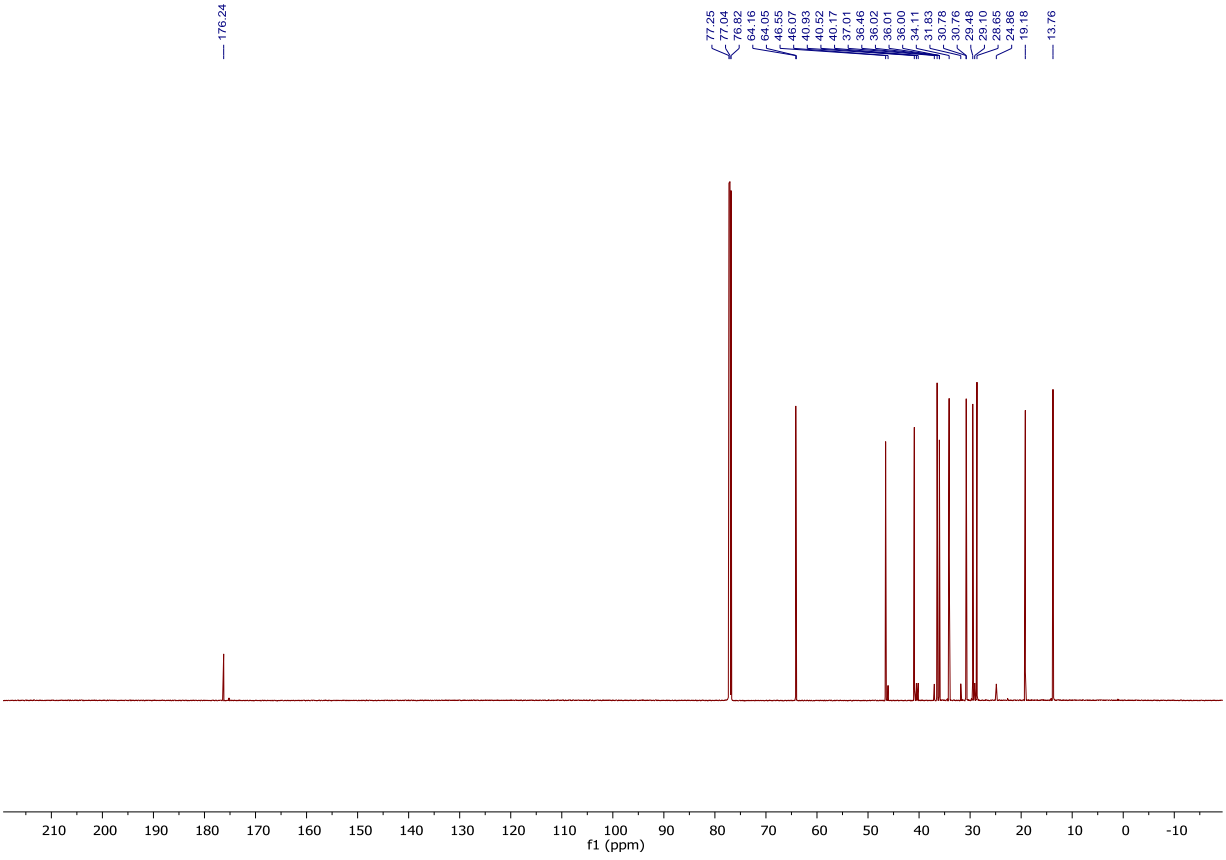
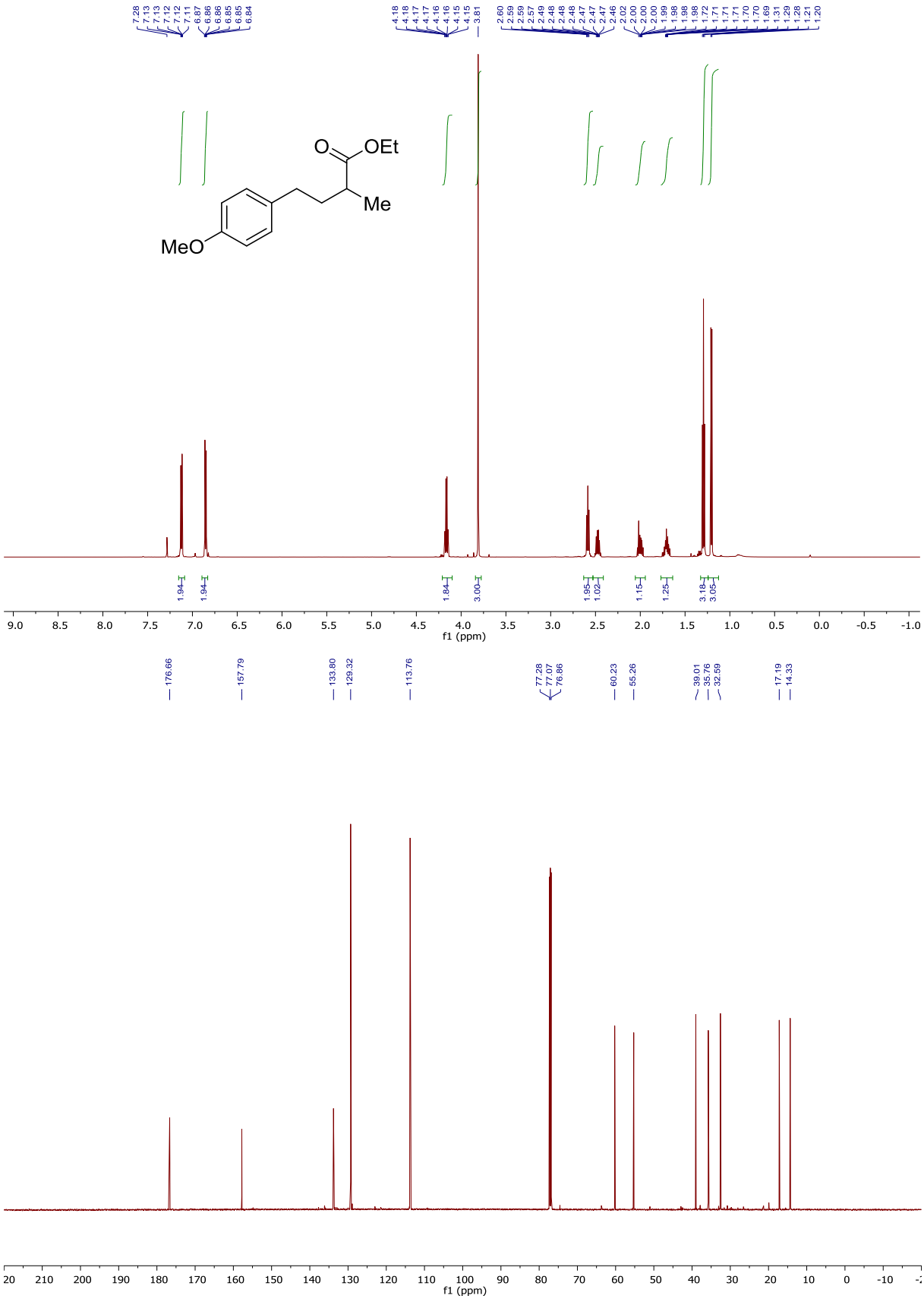
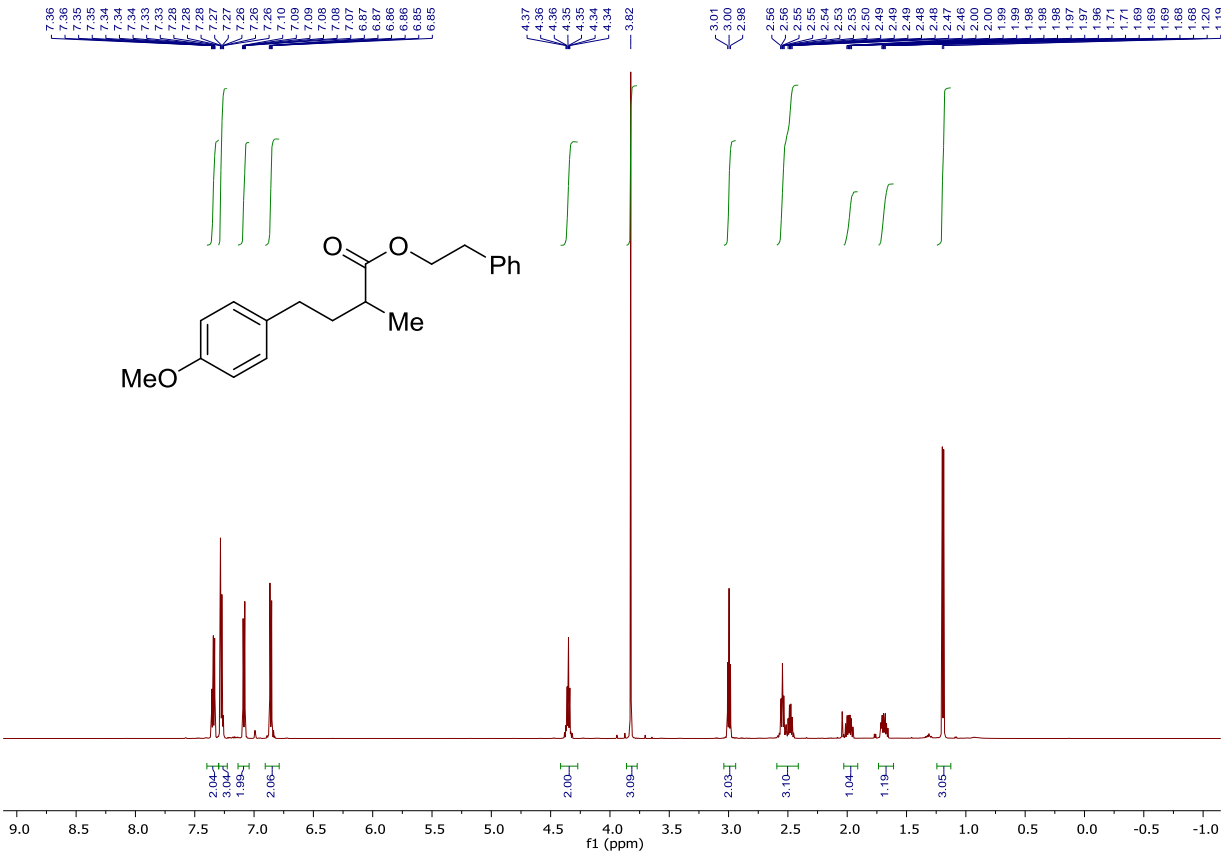
3.01
0.98
0.95
1.98
2.04
9.13
2.14
3.02
f1 (ppm)

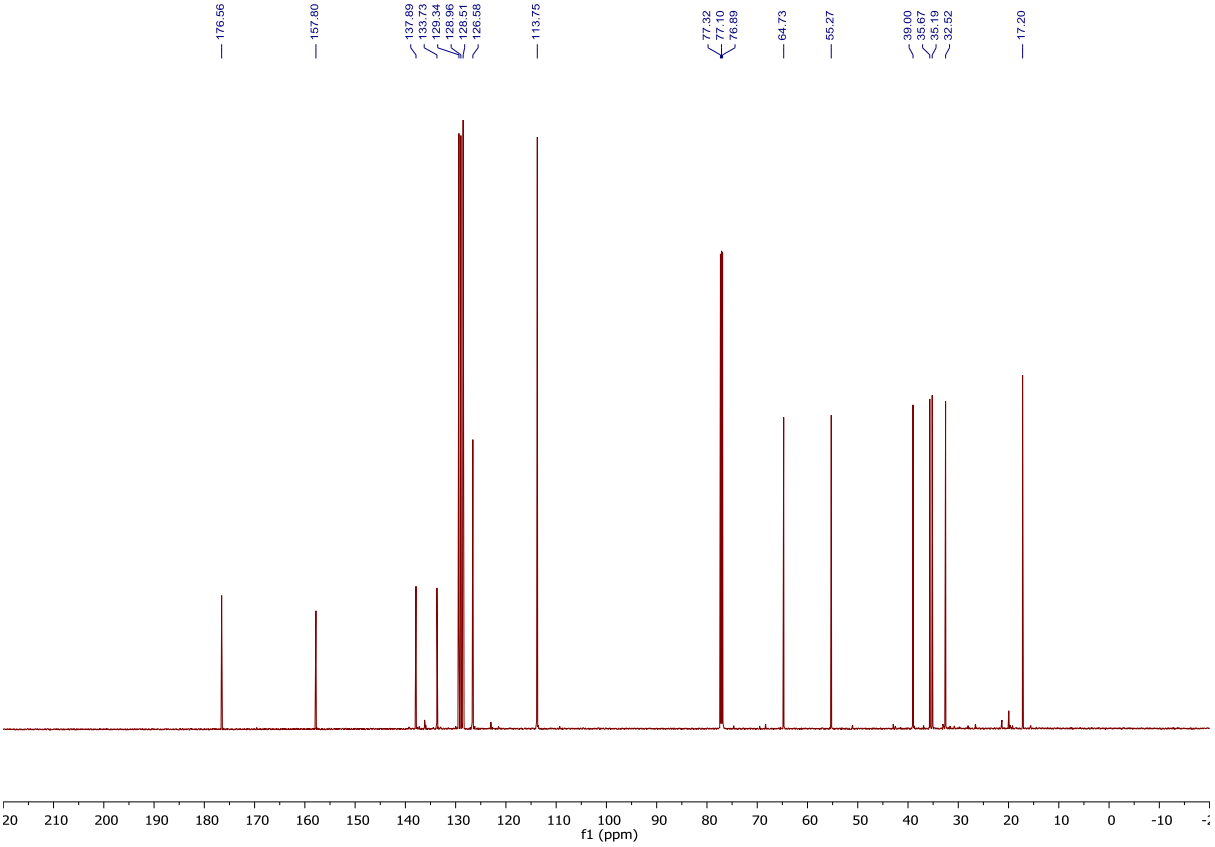

173.11
173.02
154.19
79.27
79.23
64.69
64.66
48.03
47.90
45.29
44.99
43.31
42.43
30.52
28.61
28.40
28.20
19.03
13.63
f1 (ppm)


7.28
4.09 4.08 4.07 4.07 4.06 4.05 2.77 2.76 2.75 2.56 2.51 2.50 2.50 2.32 2.31 1.87 1.87 1.86 1.86 1.85 1.84 1.84 1.83 1.83 1.66 1.64 1.63 1.62 1.62 1.60 1.56 1.55 1.54 1.51 1.50 1.49 1.48 1.47 1.46 1.45 1.45 1.43 1.41 1.41 1.39 1.39 1.37 1.29 1.26 1.26 1.24 1.22 1.21 1.20 1.19 1.19 1.18 1.17 1.16 0.97 0.95 0.93
O
On-Bu
+
O
On-Bu
(1:5.4)
2.00 0.16 0.17 0.87 1.85 0.88 8.88 3.26 3.08
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 -0.5 -1.0
f1 (ppm)


176.24
77.25 77.04 76.82 64.16 64.05 46.55 46.07 40.93 40.52 40.17 40.01 36.46 36.02 36.01 36.00 34.11 31.83 30.78 30.76 29.48 29.10 28.65 24.86 19.18 13.76
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OEt
Me
MeO
f1 (ppm)
f1 (ppm)


O
O
Ph
Me
MeO
f1 (ppm)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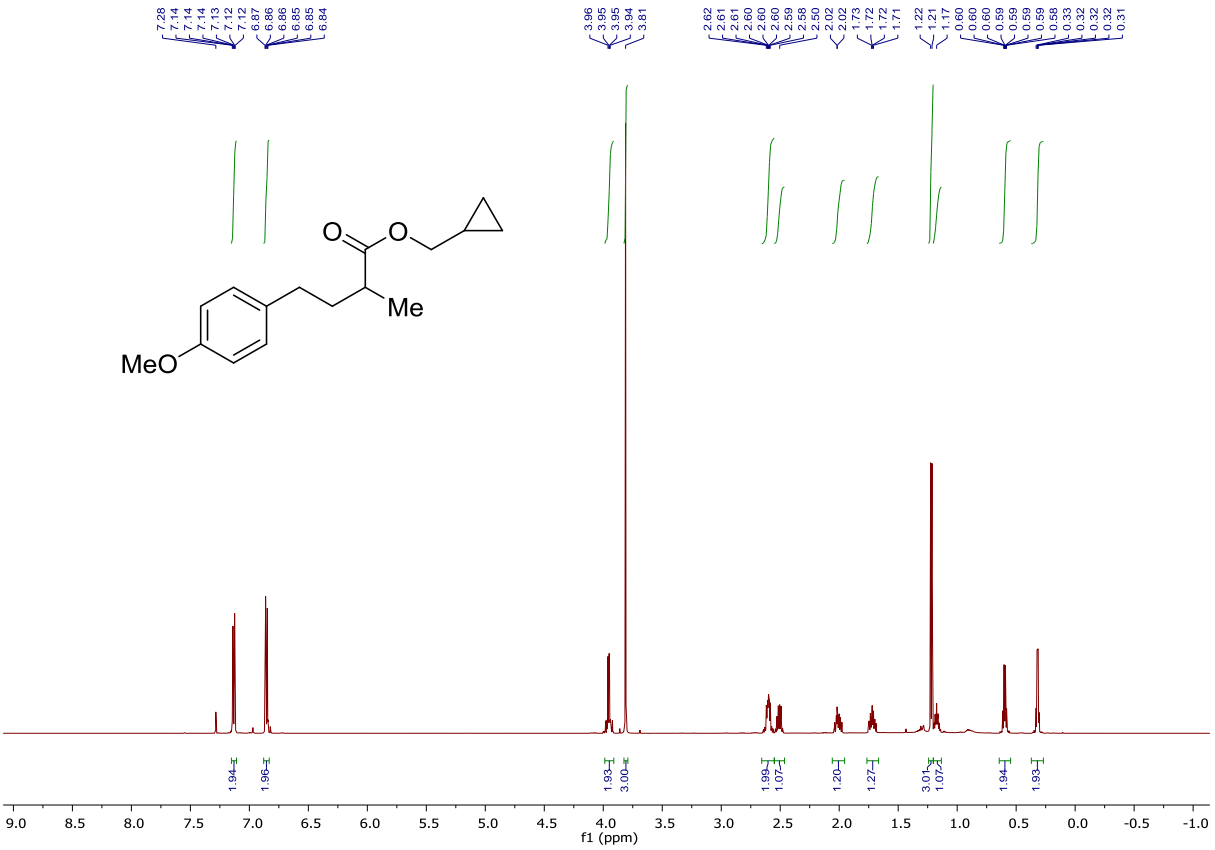
7.28
7.14
7.14
7.14
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7.12
7.12
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6.86
6.85
6.85
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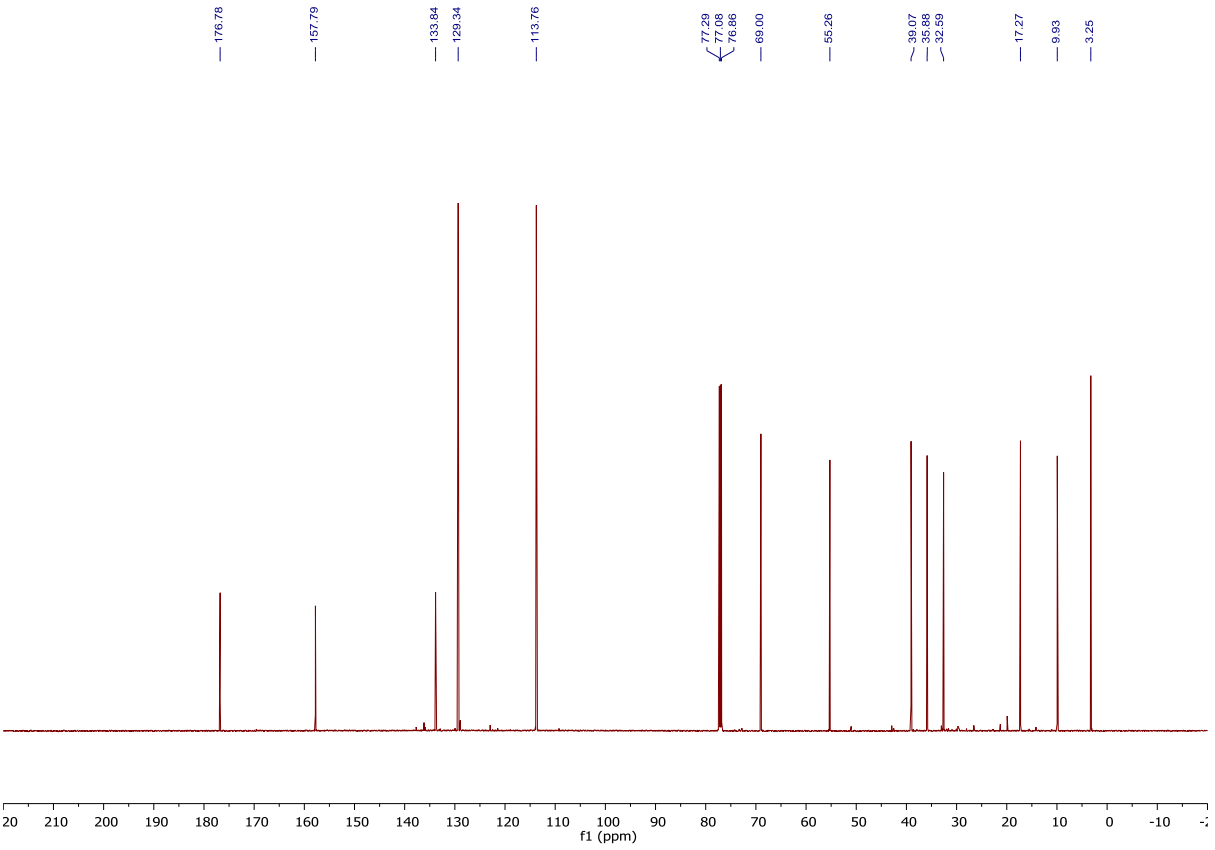
3.96
3.95
3.95
3.94
3.81
2.62
2.61
2.61
2.60
2.60
2.60
2.59
2.58
2.50
2.02
2.02
1.73
1.72
1.72
1.71
1.22
1.21
1.17
1.17
0.60
0.60
0.60
0.59
0.59
0.59
0.59
0.58
0.33
0.32
0.32
0.32
0.31
O
O
Me
MeO
1.94
1.96
1.93
3.00
1.99
1.07
1.20
1.27
3.01
1.07
1.94
1.93
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


176.78
157.79
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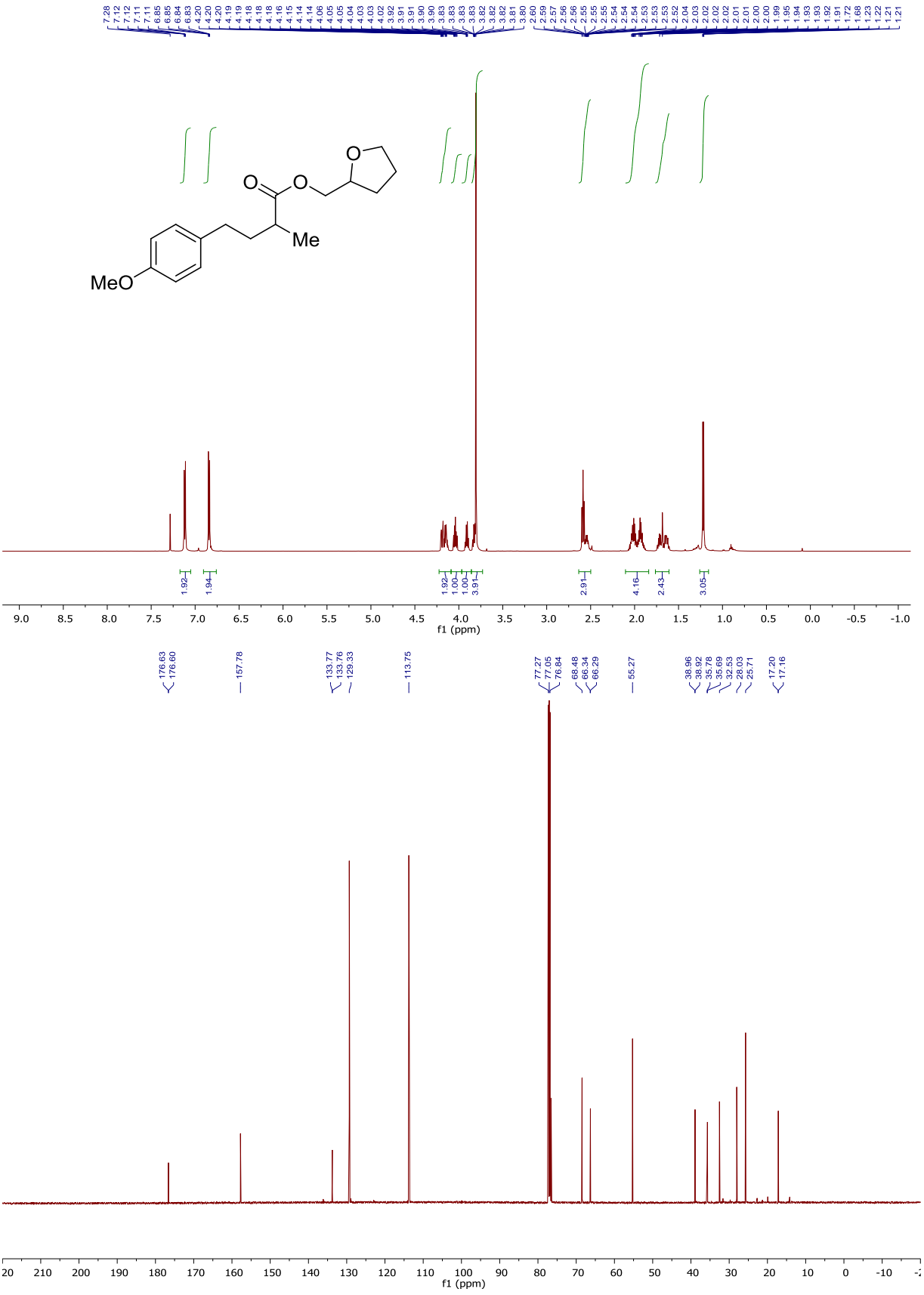
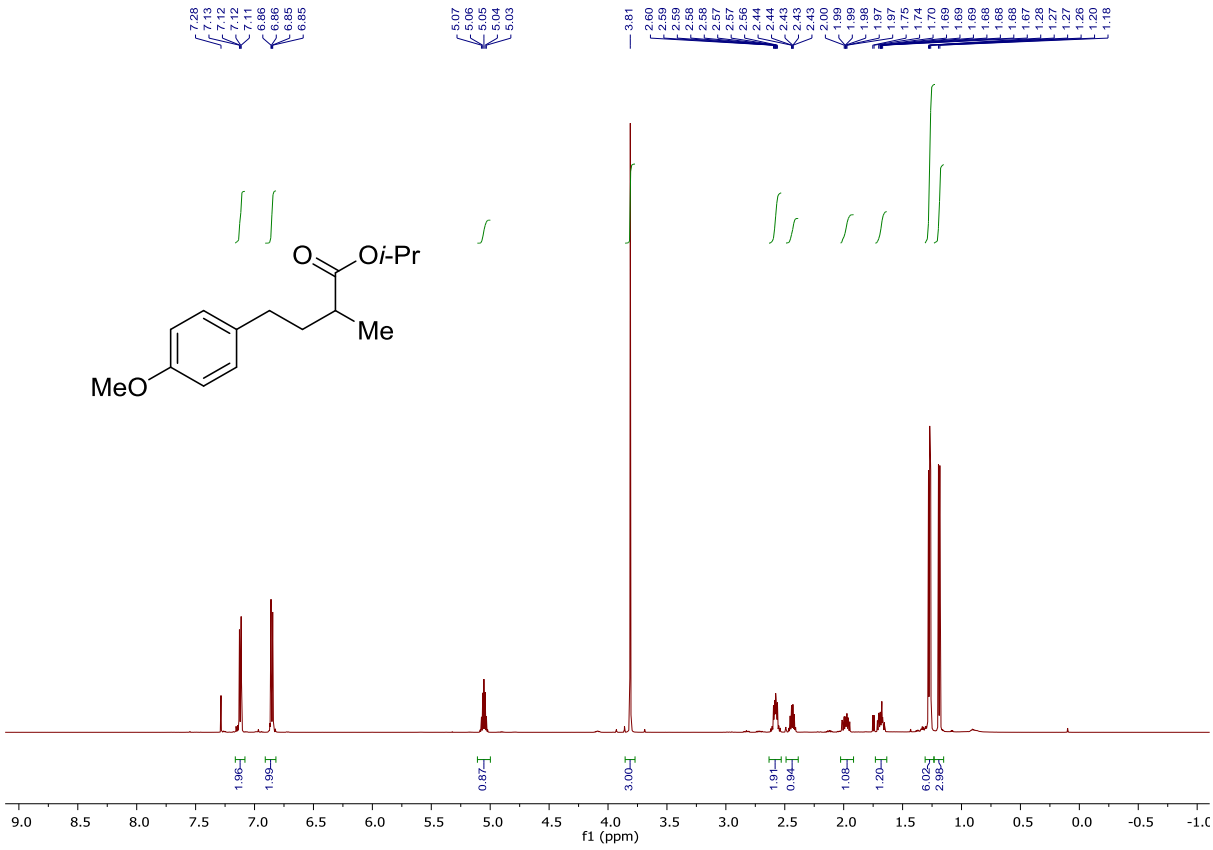
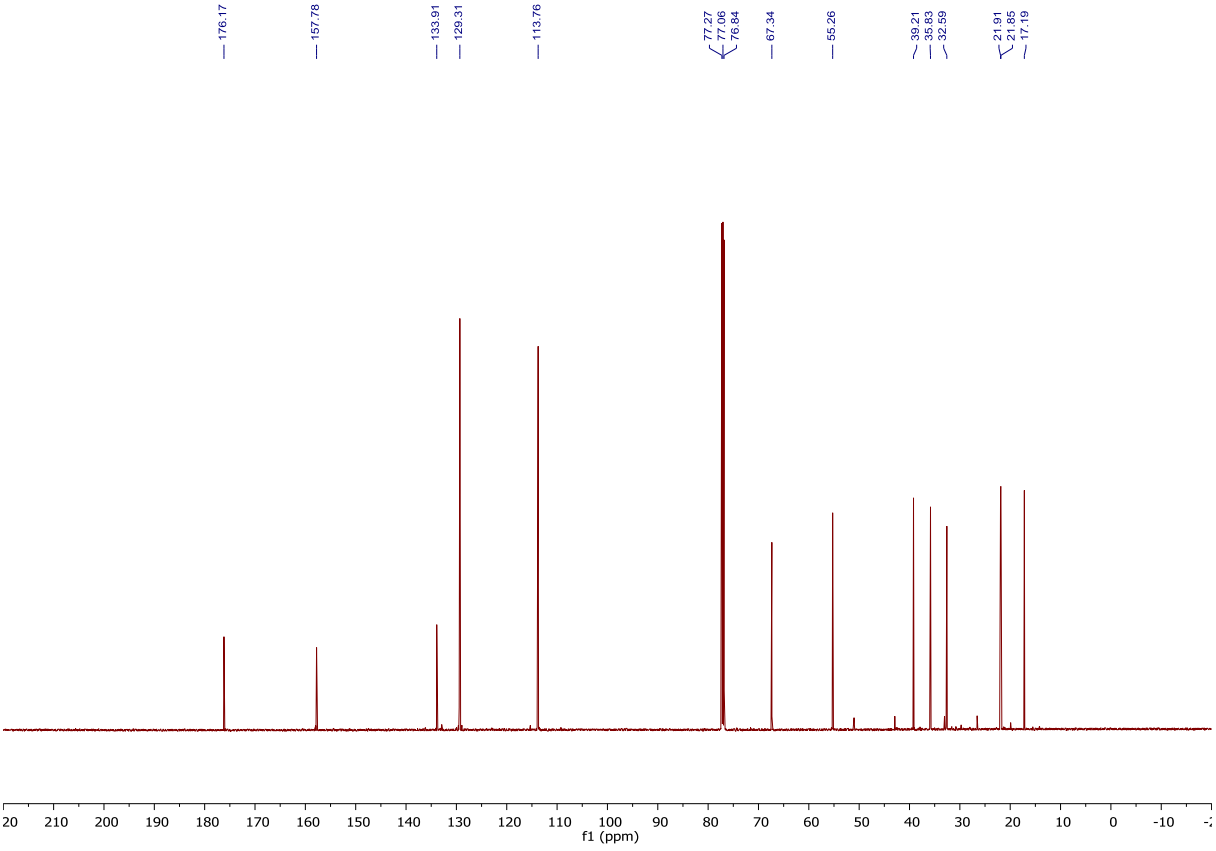
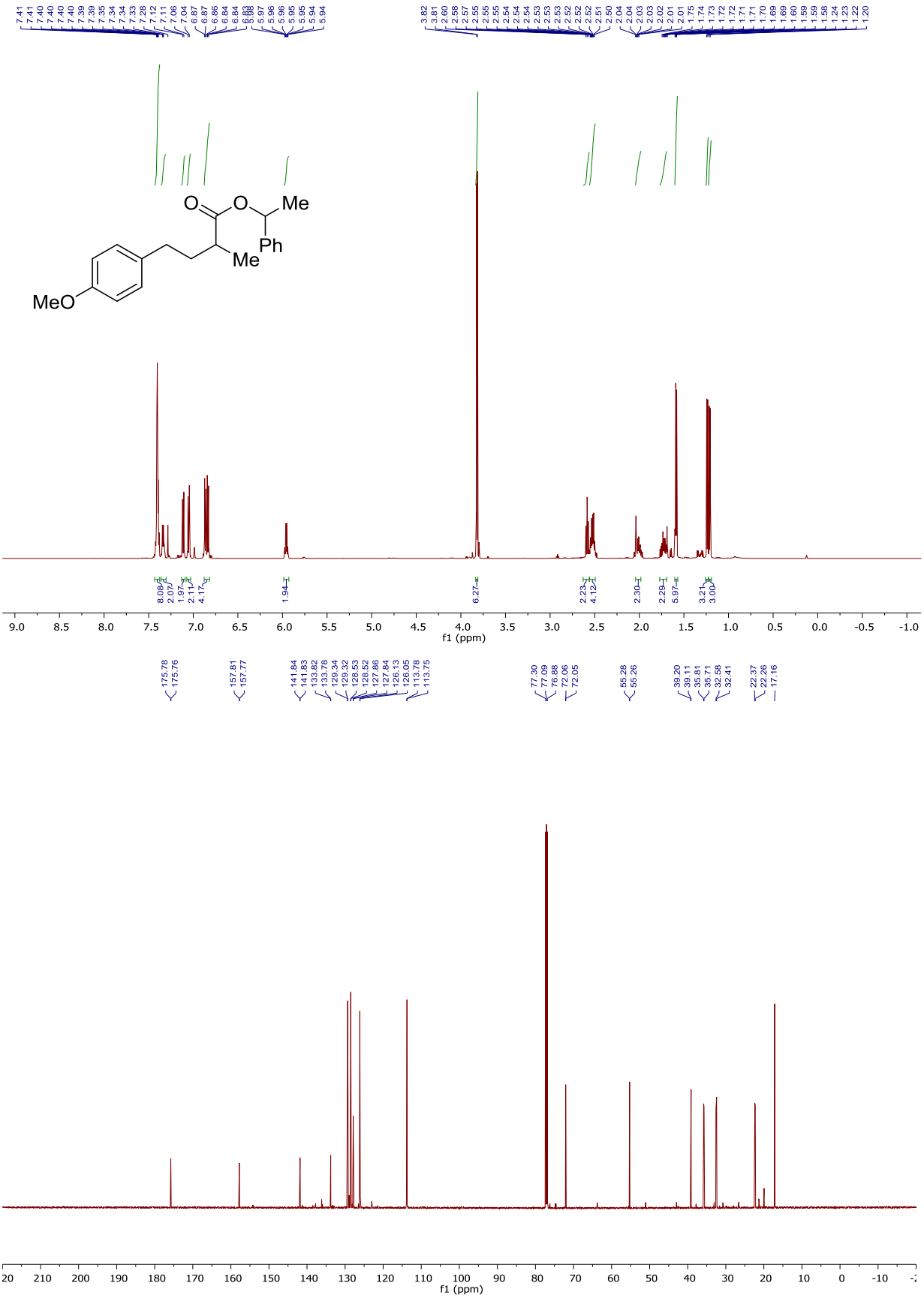
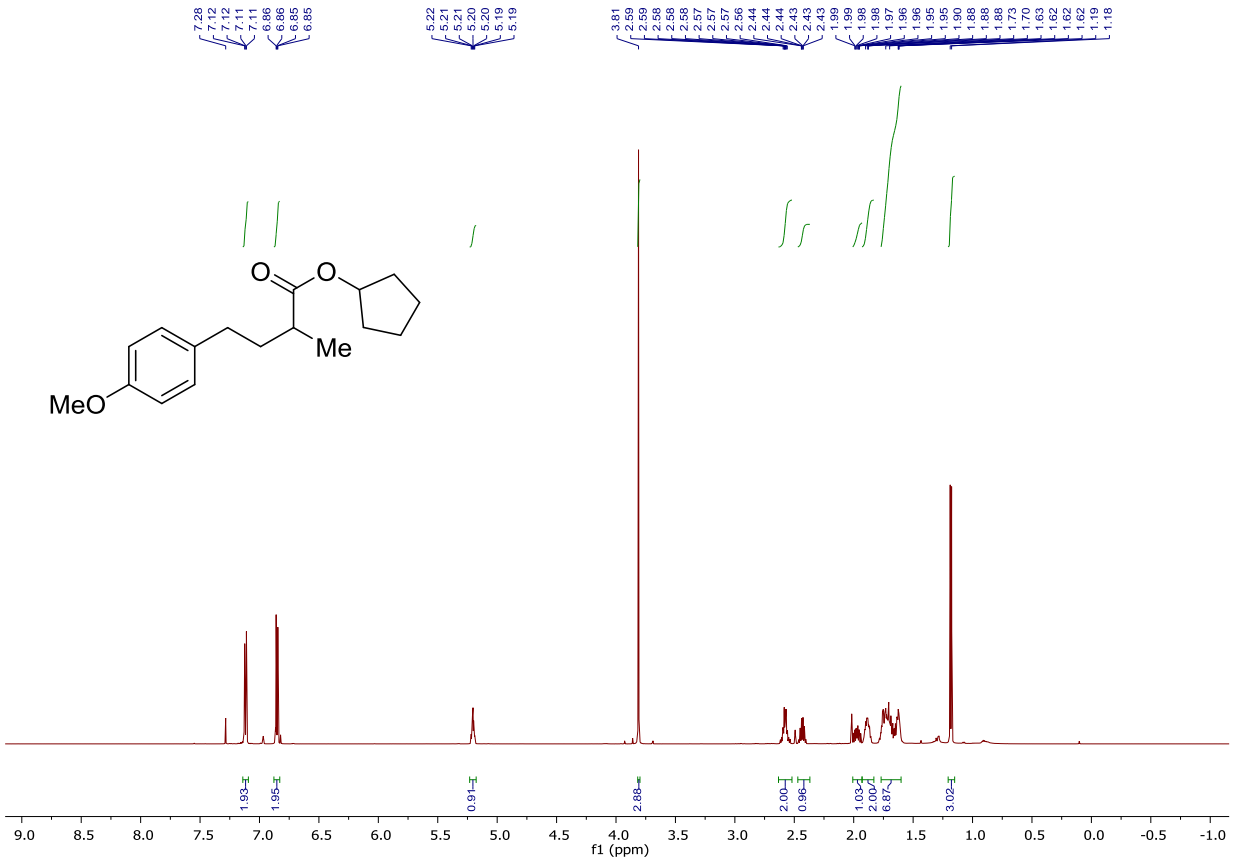
129.34
113.76
77.29
77.08
76.86
69.00
55.26
39.07
35.88
32.59
17.27
9.93
3.25
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


MeO
Me
O
O
O
f1 (ppm)
f1 (ppm)


O
Oi-Pr
Me
MeO
f1 (ppm)


f1 (ppm)


O
O
Me
Ph
Me
MeO
f1 (ppm)
f1 (ppm)


7.28
7.12
7.12
7.11
7.11
6.86
6.86
6.85
6.85
5.22
5.21
5.21
5.20
5.20
5.19
5.19
3.81
2.59
2.59
2.58
2.58
2.58
2.57
2.57
2.57
2.56
2.44
2.44
2.44
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1.90
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1.88
1.88
1.73
1.70
1.63
1.62
1.62
1.62
1.19
1.18
O
O
Me
MeO
1.93
1.95
0.91
2.88
2.00
0.96
1.03
2.00
6.87
3.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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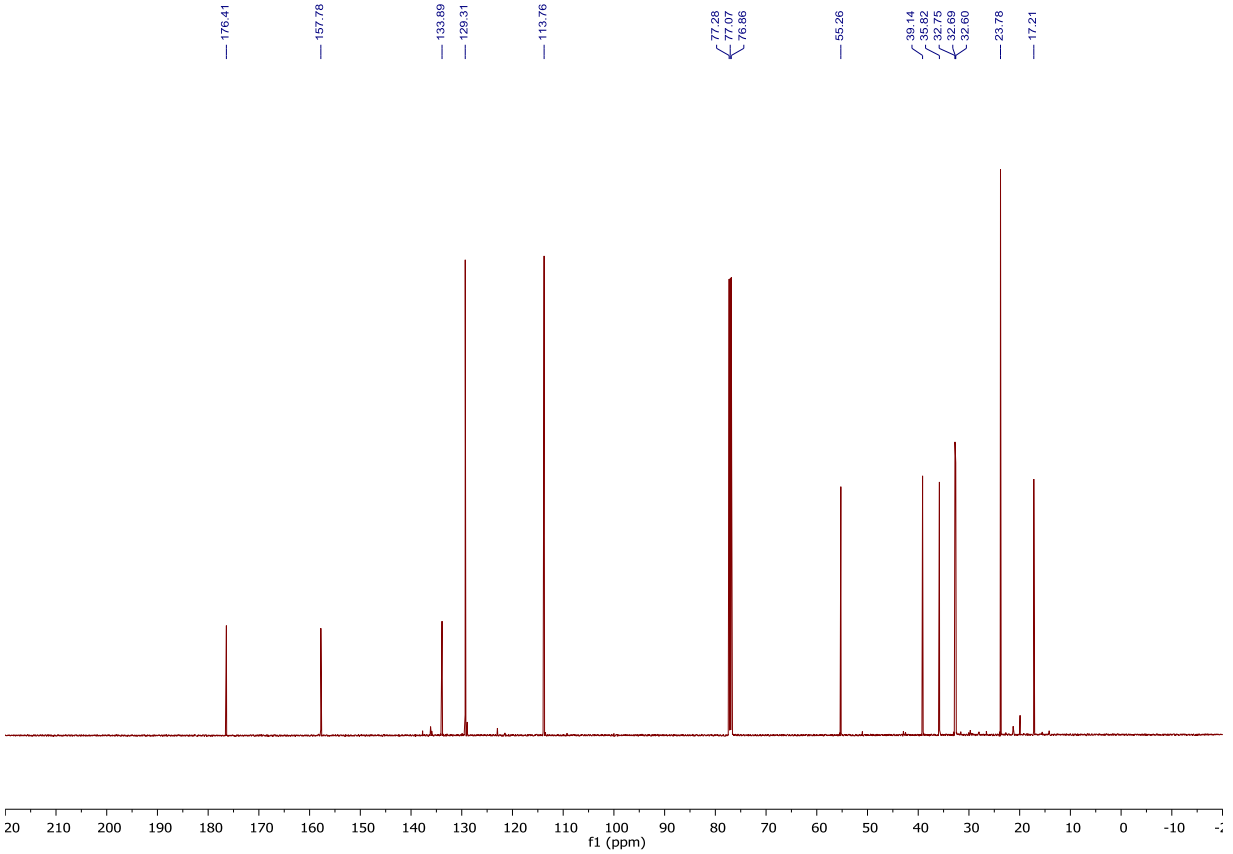
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


176.41
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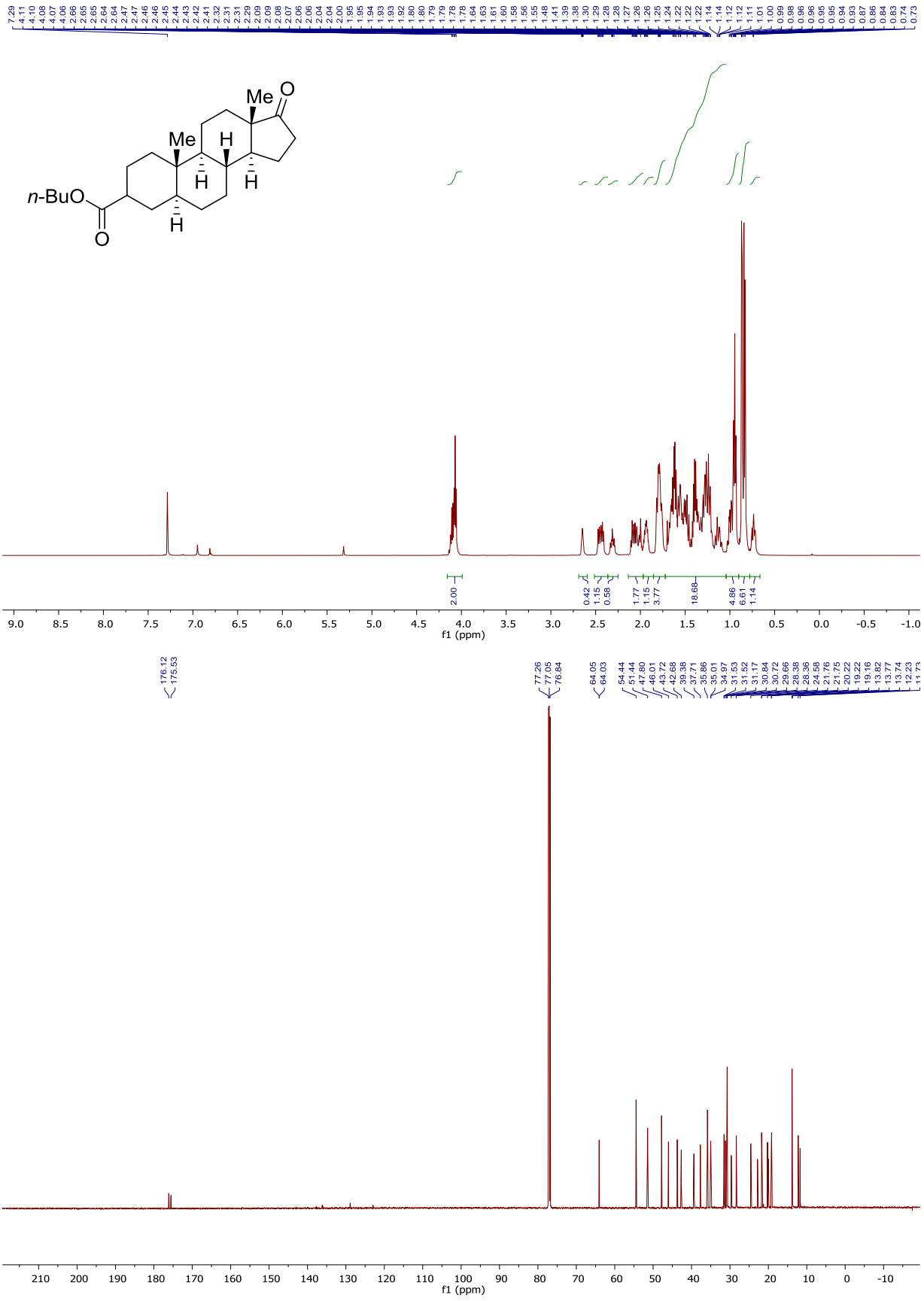
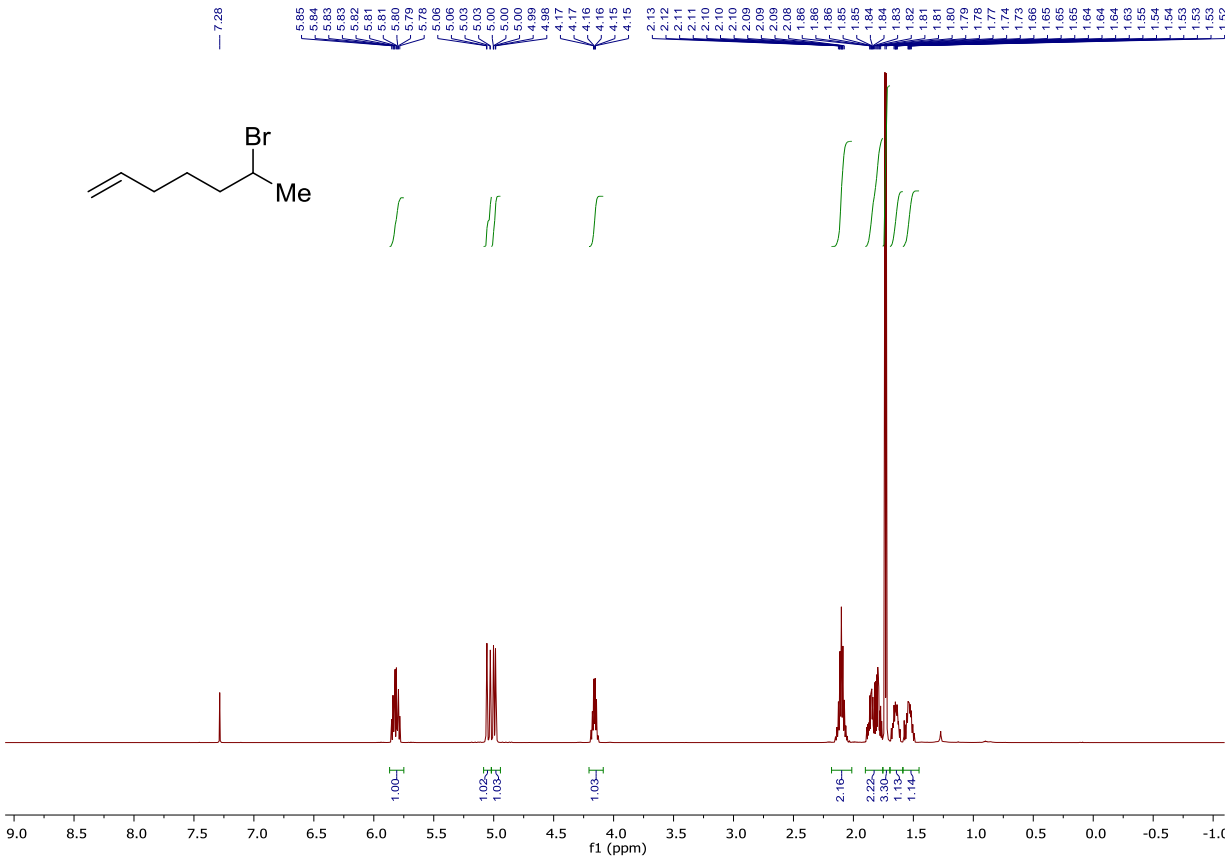
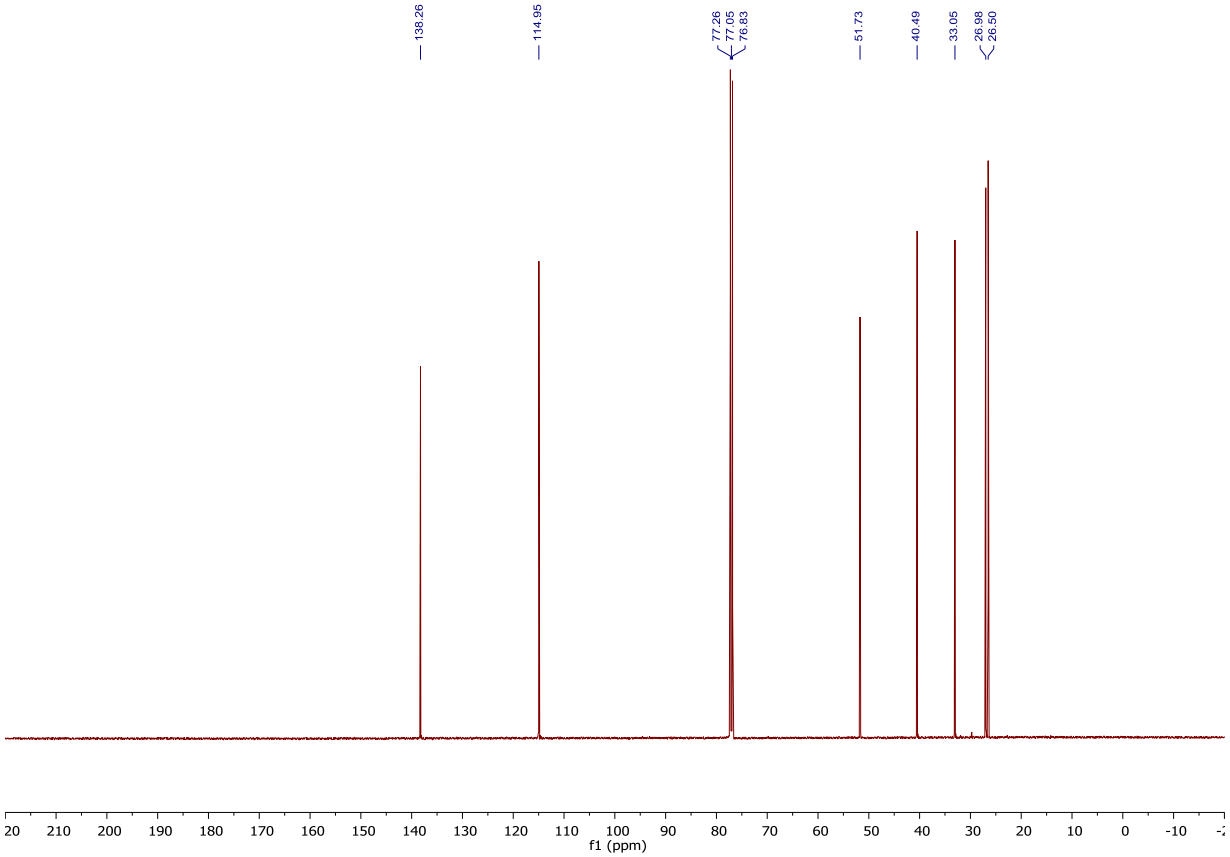
129.31
113.76
77.28
77.07
76.86
55.26
39.14
35.82
32.75
32.69
32.60
23.78
17.21
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Me
O
Me
H
H
H
n-BuO
O
f1 (ppm)
f1 (ppm)


7.28
5.85 5.84 5.83 5.83 5.82 5.81 5.81 5.80 5.79 5.78
5.06 5.06 5.03 5.03 5.00 5.00 5.00 4.99 4.98
4.17 4.17 4.16 4.16 4.15 4.15
2.13 2.12 2.11 2.11 2.10 2.10 2.10 2.09 2.09 2.09 2.08 1.86 1.86 1.86 1.85 1.85 1.84 1.84 1.83 1.82 1.81 1.81 1.80 1.79 1.78 1.77 1.74 1.73 1.66 1.65 1.65 1.65 1.64 1.64 1.64 1.63 1.55 1.54 1.54 1.53 1.53 1.53
Br
Me
1.00
1.02
1.03
1.03
2.16
2.22
3.30
1.13
1.14
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 -0.5
f1 (ppm)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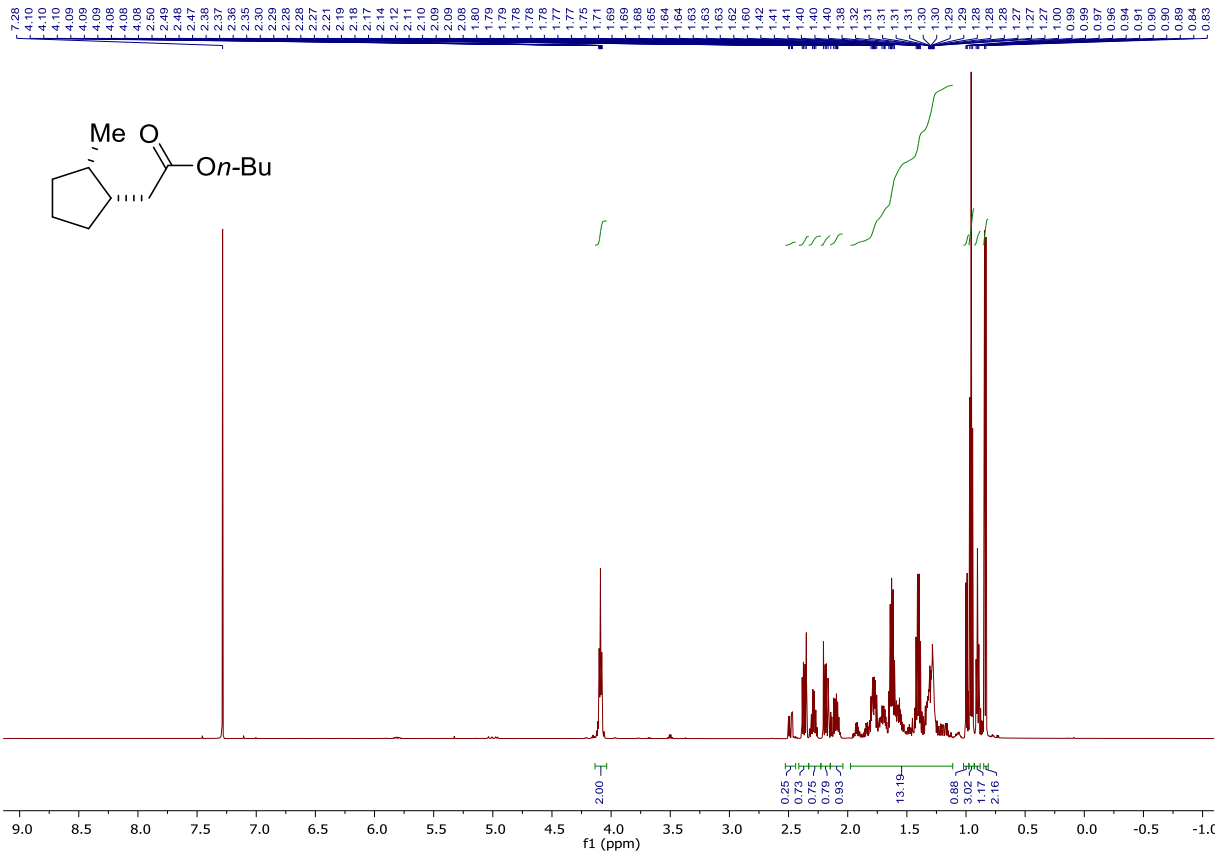
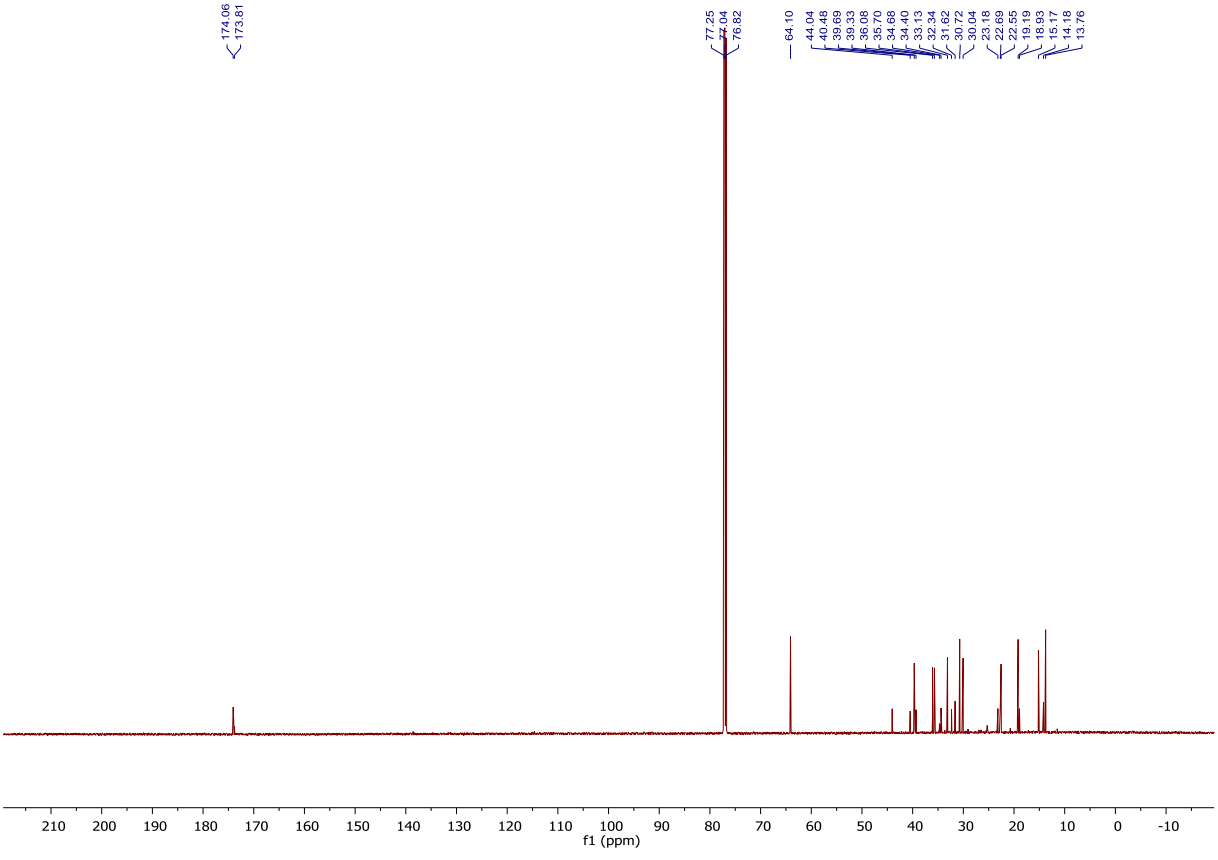
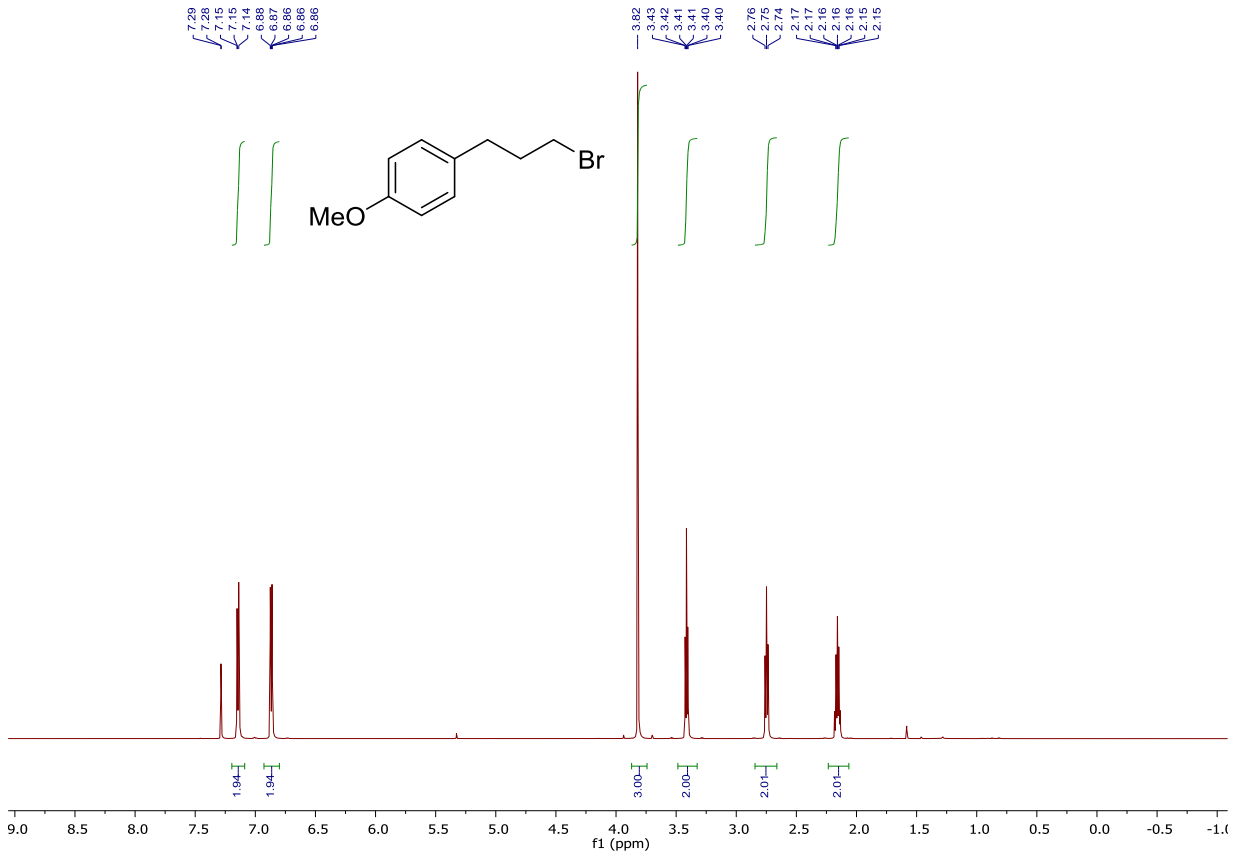
114.95
77.26
77.05
76.83
51.73
40.49
33.05
26.98
26.50
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
O
On-Bu
f1 (ppm)


f1 (ppm)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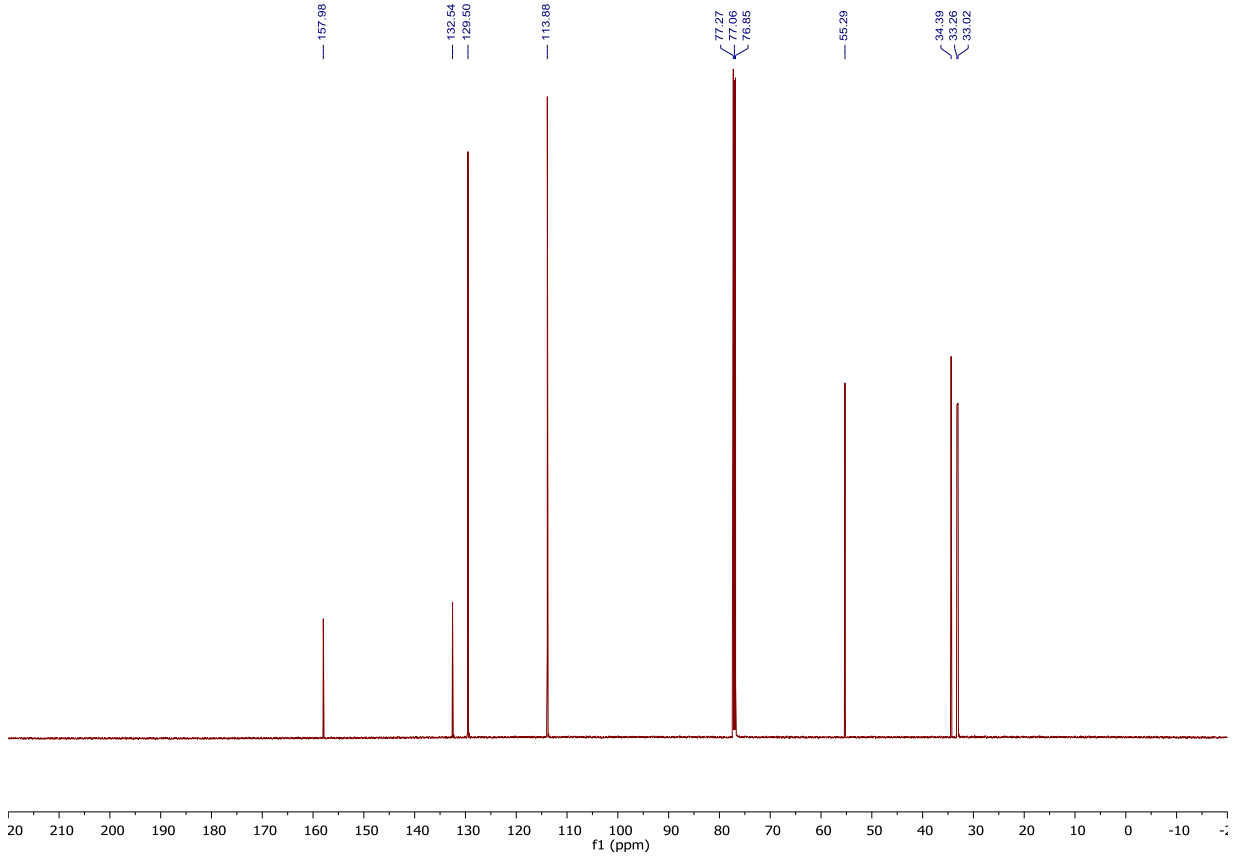
6.86
6.86
6.86
3.82
3.43
3.42
3.41
3.41
3.40
3.40
2.76
2.75
2.74
2.17
2.17
2.16
2.16
2.16
2.15
2.15
Br
MeO
1.94
1.94
3.00
2.00
2.01
2.01
f1 (ppm)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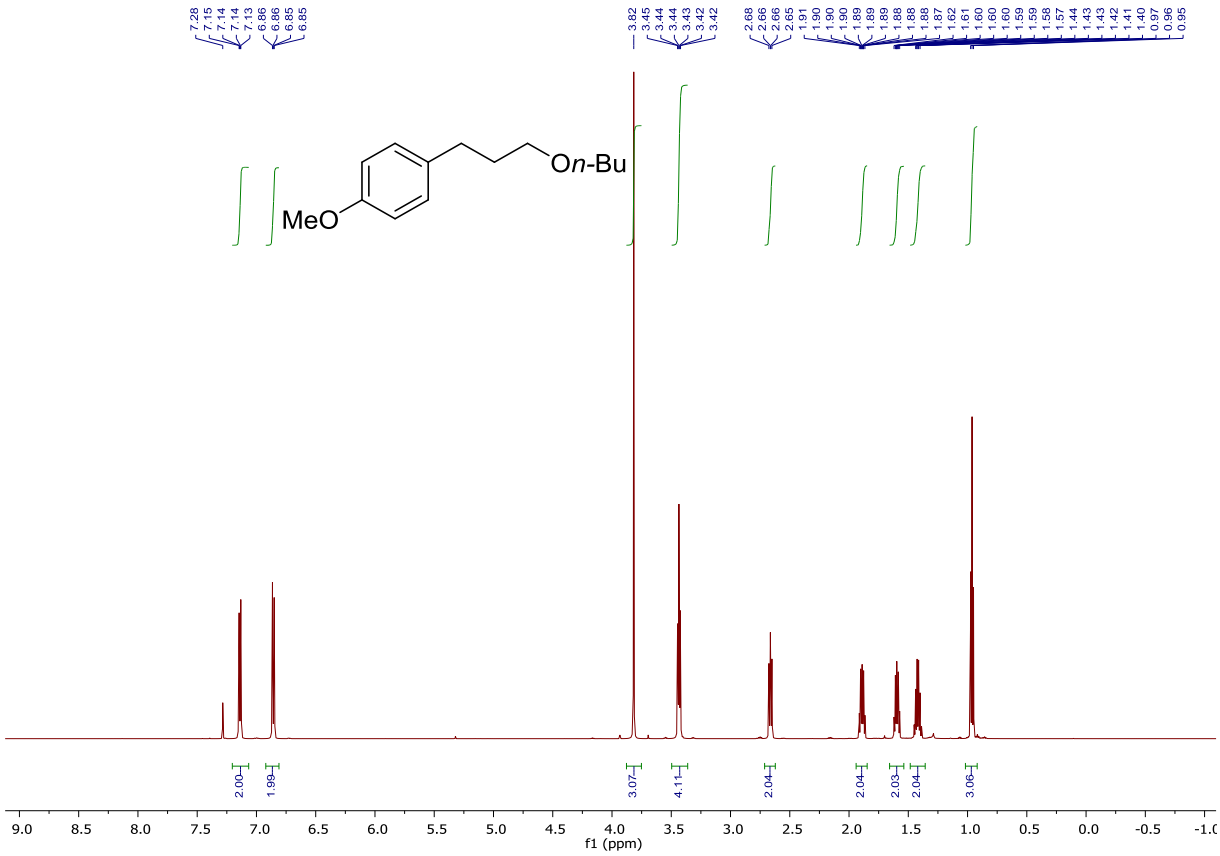
77.06
76.85
55.29
34.39
33.26
33.02
f1 (ppm)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7.14
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6.86
6.86
6.85
6.85
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3.45
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3.44
3.43
3.42
3.42
2.68
2.66
2.66
2.65
1.91
1.90
1.90
1.90
1.89
1.89
1.89
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1.59
1.59
1.58
1.57
1.44
1.43
1.43
1.42
1.41
1.40
0.97
0.96
0.95
MeO
On-Bu
2.00
1.99
3.07
4.11
2.04
2.04
2.03
2.04
3.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
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2.0
1.5
1.0
0.5
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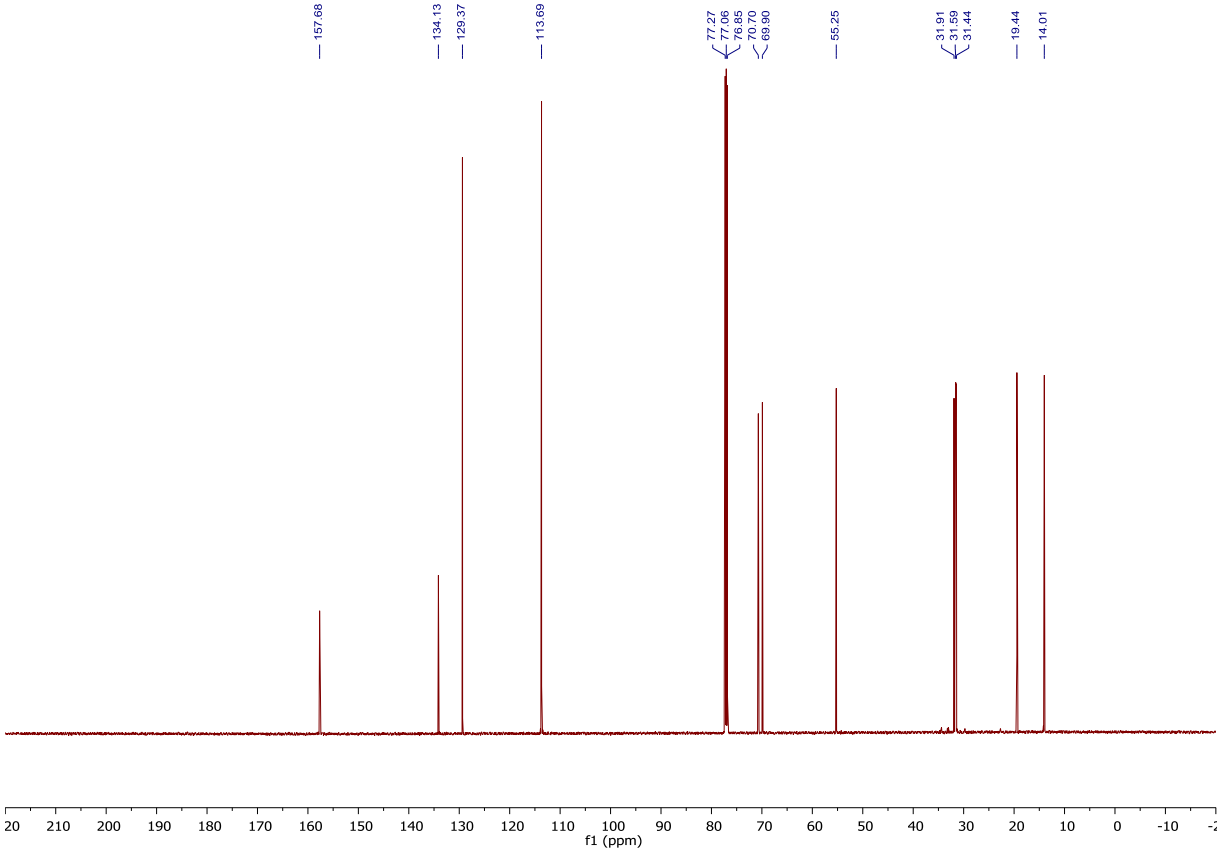
-0.5
f1 (ppm)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113.69
77.27
77.06
76.85
70.70
69.90
55.25
31.91
31.59
31.44
19.44
14.01
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)