

Supporting Information

One-Pot, Modular Approach to Functionalized Ketones via Nucleophilic Addition of Alkylolithium Reagents to Benzamides and Pd-Catalyzed α -Arylation.

Alexander T. Wolters,^a Valentin Hornillos,^{*a} Dorus Heijnen,^a Massimo Giannerini,^a and
Ben L. Feringa^{*a}.

E-mail: v.hornillos.gomez.recuero@rug.nl; b.l.feringa@rug.nl

^aStratingh Institute for Chemistry, University of Groningen, Nijenborgh 4, 9747 AG,
Groningen, The Netherlands.

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General methods:

All reactions were carried out under a nitrogen atmosphere using oven dried glassware and using standard Schlenk techniques. THF and toluene were dried and distilled over sodium. Chromatography: Grace Reveleris X2 flash chromatography system used with Grace® Flash Cartridges, TLC: Merck silica gel 60, 0.25 mm. Components were visualized by UV and phosphomolybdic Acid (PMA) or potassium permanganate staining. Progress and conversion of the reaction were determined by GC-MS (GC, HP6890: MS HP5973) with an HP1 or HP5 column (Agilent Technologies, Palo Alto, CA). Mass spectra were recorded on an AEI-MS-902 mass spectrometer (EI+) or a LTQ Orbitrap XL (ESI+). ¹H- and ¹³C-NMR were recorded on a Varian AMX400 (400 and 100.59 MHz, respectively) using CDCl₃ as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CHCl₃: δ 7.26 for ¹H, δ 77.0 for ¹³C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. Melting points were measured using a Büchi Melting Point B-545. XPhos, SPhos, Pd₂(dba)₃, Josiphos (**L4**), **C4**, Pd-PEPPSI-IPr and Pd-PEPPSI-IPent were purchased from Aldrich and used without further purification. Pd[P(*t*-Bu)₃]₂ was purchased from Strem. Methyllithium (MeLi, 1.6 M in diethylether), ethyllithium, (EtLi, 0.5 M in benzene:cyclohexane), hexyllithium (HexLi, 2.3 M in hexane) and *sec*-butyllithium (*s*-BuLi, 1.4 M in cyclohexane) were purchased from Sigma Aldrich. *n*-Butyllithium (*n*-BuLi, 1.6 M solution in hexane) was purchased from Acros. The benzamides, aryl bromides, acid chlorides, carboxylic acid, and the reagents used for the preparation of the Weinreb amides as well as *N,O*-dimethylhydroxylamine hydrochloride were purchased from Aldrich. The concentration of alkyllithium solutions was determined by titration in THF over diphenyl acetic acid.¹

Synthesis of the amides 1:

4-fluoro-*N,N*-dimethylbenzamide (1t) was synthesized according to a reported procedure² starting from 0.24 ml of 4-fluorobenzoyl chloride. Yellow oil, 268 mg, 80% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.42 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.08 (t, *J* = 8.7 Hz, 2H), 3.09 (s, 3H), 2.99 (s, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 170.6, 163.2 (d, *J* = 249.4 Hz), 129.3 (d, *J* = 8.5 Hz), 115.3 (d, *J* = 21.8 Hz), 39.6, 35.4 ppm.

4-chloro-*N*-methoxy-*N*-methylbenzamide (1u)³ was synthesized according to a reported procedure.⁴ ¹H-NMR (400 MHz, CDCl₃): δ 7.65 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.6 Hz, 2H), 3.53 (s, 3H), 3.35 (s, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 168.7, 136.7, 132.3, 129.8, 128.3, 61.1, 33.5 ppm.

4-methoxy-*N,N*-dimethylbenzamide (1v) was synthesized according to a reported procedure.² ¹H-NMR (400 MHz, CDCl₃): δ 7.40 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 3.83 (s, 3H), 3.05 (s, 6H). ¹³C-NMR (100.59 MHz, CDCl₃): δ 171.4, 160.5, 129.0, 128.3, 113.5, 55.3, 39.8, 35.5.

Additional experimental data:

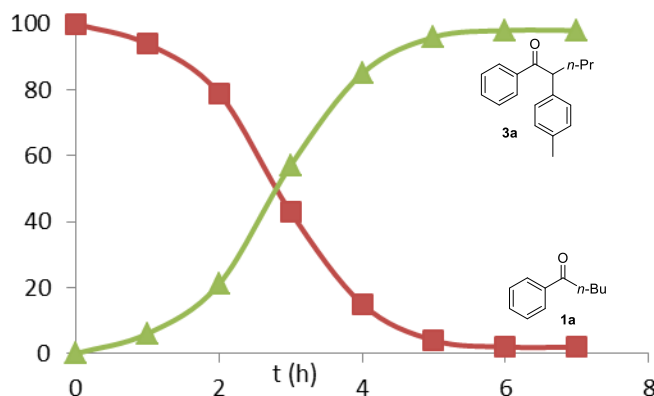
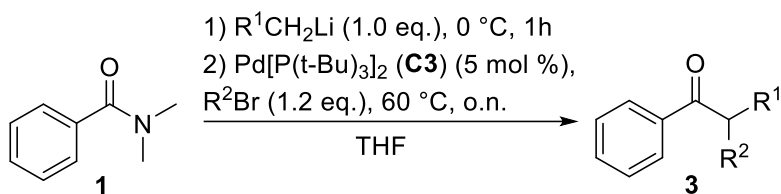


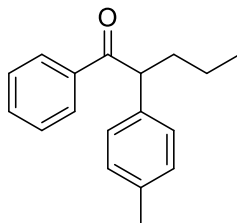
Figure S1. Conversion of **1a** into **3a** followed in time. ^aConditions: *n*-BuLi (1.0 eq, 1.6 M) is added to a solution of amide **1a** (0.5 mmol) in THF (2 mL) followed by addition of Pd[P(*t*-Bu)₃]₂ (5 mol %) and 4-bromotoluene (1.2 eq.) heated to 60 °C.

General Procedure for the one-pot, 1,2-addition, Pd-catalyzed α -arylation:

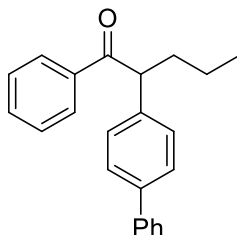


In a dry Schlenk flask the corresponding amide **1** (0.5 mmol) was dissolved in 2 mL of dry THF, the mixture was cooled down to 0 °C and the corresponding alkyllithium reagent (1.0 eq.) was added dropwise. After one hour, Pd[P(*t*Bu)₃]₂ (5 mol%) and the corresponding aryl bromide (0.6 mmol, 1.2 eq) were added to the reaction medium and the vessel was heated with a preheated oil bath to 60 °C overnight (unless otherwise noted). After allowing the reaction mixture to cool to rt, a saturated aqueous solution of NH₄Cl (2 mL) was added whereupon the mixture was extracted with ether (3 x 5mL). The organic phases were combined, dried over MgSO₄ and filtered, after which evaporation of the solvent under reduced pressure afforded the crude product **3** that was then purified by column chromatography using different mixtures of *n*-pentane/EtOAc as the eluent.

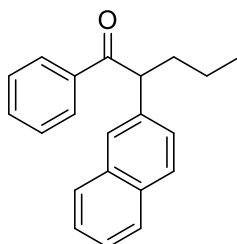
Experimental details and spectral data of compounds



1-Phenyl-2-(*p*-tolyl)pentan-1-one (3a): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 4-bromotoluene (0.6 mmol, 103 mg). Colorless oil obtained after column chromatography (SiO₂, *n*-pentane/EtOAc 98:2), 108 mg, 86% yield. Reaction performed using 6 mmol (895 mg) of substrate **1a**: 1.38 g, 86% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.96 (d, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 4.52 (t, *J* = 7.3 Hz, 1H), 2.28 (s, 3H), 2.19-2.08 (m, 1H), 1.85-1.74 (m, 1H), 1.38-1.19 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 200.2, 137.0, 136.8, 136.5, 132.7, 129.5, 128.6, 128.5, 128.1, 53.0, 36.1, 21.0, 20.9, 14.1 ppm. HRMS (ESI+, *m/z*): calcd for C₁₈H₂₁O [M+H]⁺: 253.1587; found: 253.1588.

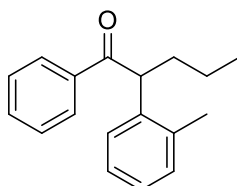


2-([1,1'-Biphenyl]-4-yl)-1-phenylpentan-1-one (3b): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 4-bromo-1,1'-biphenyl (0.6 mmol, 140 mg). White crystals obtained after column chromatography and further recrystallization from *n*-pentane (SiO₂, *n*-pentane/EtOAc 98:2), 123 mg, 78% yield. M.p.: 117 °C-118 °C. ¹H-NMR (400 MHz, CDCl₃): δ 8.00 (d, *J* = 7.3 Hz, 2H), 7.56-7.47 (m, 5H), 7.44-7.36 (m, 6H), 7.32 (t, *J* = 7.3 Hz, 1H), 4.61 (t, *J* = 7.3 Hz, 1H), 2.24-2.14 (m, 1H), 1.91-1.80 (m, 1H), 1.40-1.24 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 200.1, 140.6, 139.8, 138.8, 137.0, 132.8, 128.7, 128.64, 128.61, 128.5, 127.5, 127.2, 127.0, 53.0, 36.2, 20.9, 14.1 ppm. HRMS (ESI+, *m/z*): calcd for C₂₃H₂₃O [M+H]⁺: 315.1743; found: 315.1745.

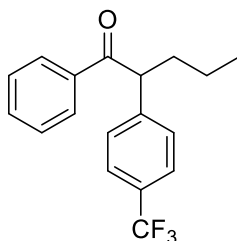


2-(Naphthalen-2-yl)-1-phenylpentan-1-one (3c): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 2-bromonaphthalene (0.6 mmol, 124 mg). Brown waxy solid obtained after column

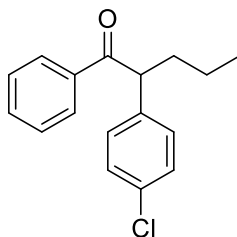
chromatography (SiO₂, *n*-pentane/ EtOAc 98:2), 98 mg, 68% yield. ¹H-NMR (400 MHz, CDCl₃): δ 8.00 (d, *J* = 7.4 Hz, 2H), 7.80-7.55 (m, 3H), 7.74 (s, 1H), 7.48-7.40 (m, 4H), 7.37 (t, *J* = 7.6 Hz, 2H), 4.72 (t, *J* = 7.3 Hz, 1H), 2.28-2.18 (m, 1H), 1.96-1.86 (m, 1H), 1.43-1.22 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 199.8, 137.4, 137.0, 133.6, 132.8, 132.4, 128.6, 128.51, 128.47, 127.6, 127.5, 127.0, 126.3, 126.1, 125.7, 53.4, 36.1, 20.9, 14.0 ppm. HRMS (ESI+, *m/z*): calcd for C₂₁H₂₁O [M+H]⁺: 289.1586; found: 289.1587.



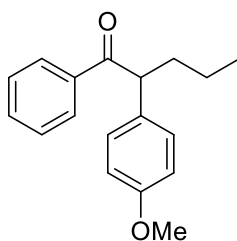
1-Phenyl-2-(*o*-tolyl)pentan-1-one (3d): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 2-bromotoluene (0.6 mmol, 103 mg, 73 μL). Colorless oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 98:2), leaving the product fraction overnight under vacuum at 60°C, 81 mg, 65% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.84 (d, *J* = 7.1 Hz, 2H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.16-7.20 (m, 1H), 7.14-7.07 (m, 3H), 4.71 (dd, *J* = 8.2, 5.8 Hz, 1H), 2.50 (s, 3H), 2.26-2.16 (m, 2H), 1.47-1.37 (m, 1H), 1.34-1.24 (m, 1H), 0.94 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 200.6, 138.6, 137.4, 135.0, 132.6, 130.9, 128.5, 128.3, 127.2, 126.8, 126.6, 49.5, 35.9, 21.2, 19.9, 14.3 ppm. HRMS (ESI+, *m/z*): calcd for C₁₈H₂₁O [M+H]⁺: 253.1586; found: 253.1587.



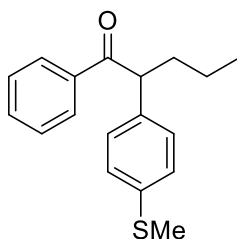
1-Phenyl-2-(4-(trifluoromethyl)phenyl)pentan-1-one (3e): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 1-bromo-4-(trifluoromethyl)benzene (0.6 mmol, 135 mg). Pale yellow oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 98:2), leaving the product fraction overnight under vacuum at 60°C, 103 mg, 67% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.95 (d, *J* = 7.3 Hz, 2H), 7.57-7.49 (m, 3H), 7.46-7.39 (m, 4H), 4.64 (t, *J* = 7.3 Hz, 1H), 2.23-2.12 (m, 1H), 1.88-1.77 (m, 1H), 1.38-1.20 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 199.4, 143.78, 143.77, 136.7, 133.1, 129.23 (q, *J* = 32.4 Hz), 128.7, 128.60, 128.55, 125.73 (q, *J* = 3.8 Hz), 53.0, 36.2, 20.8, 14.0 ppm. ¹⁹F-NMR (376 MHz, CDCl₃): δ -62.5 ppm. HRMS (ESI+, *m/z*): calcd for C₁₈H₁₈F₃O [M+H]⁺: 307.1304; found: 307.1304.



2-(4-Chlorophenyl)-1-phenylpentan-1-one (3f): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 1-bromo-4-chlorobenzene (0.6 mmol, 115 mg). Colorless oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 98:2), leaving the product fraction overnight under vacuum at 60°C, 92 mg, 67% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.94 (d, *J* = 7.3 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.25 (m, 4H), 4.55 (t, *J* = 7.3 Hz, 1H), 2.19-2.08 (m, 1H), 1.85-1.73 (m, 1H), 1.38-1.20 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 199.8, 138.3, 136.8, 133.0, 132.8, 129.6, 129.0, 128.58, 128.56, 52.6, 36.1, 20.8, 14.0 ppm. HRMS (ESI+, *m/z*): calcd for C₁₇H₁₈ClO [M+H]⁺: 273.1040; found: 273.1041.

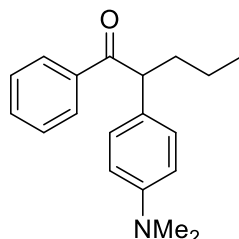


2-(4-Methoxyphenyl)-1-phenylpentan-1-one (3g): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 4-bromoanisole (0.6 mmol, 112 mg, 75 μL). Yellow oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 95:5), 114 mg, 85% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.95 (d, *J* = 7.1 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 4.50 (t, *J* = 7.3 Hz, 1H), 3.75 (s, 3H), 2.16-2.06 (m, 1H), 1.84-1.73 (m, 1H), 1.36-1.20 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 200.3, 158.2, 137.0, 132.7, 131.8, 129.2, 128.6, 128.5, 114.2, 55.1, 52.5, 36.1, 20.8, 14.1 ppm. HRMS (ESI+, *m/z*): calcd for C₁₈H₂₁O₂ [M+H]⁺: 269.1536; found: 269.1536.

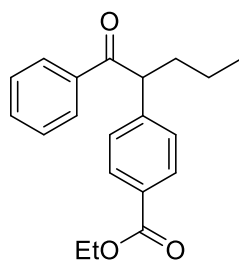


2-(4-(Methylthio)phenyl)-1-phenylpentan-1-one (3h): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 4-bromothioanisole (0.6 mmol, 122 mg). White solid obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 98:2), leaving the product fraction overnight under vacuum at 60°C, 116 mg, 82% yield. M.p.: 56 °C-57 °C. ¹H-NMR (400 MHz,

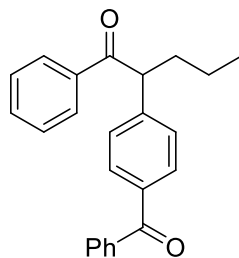
CDCl₃): δ 7.96 (d, J = 7.6 Hz, 2H), 7.50 (t, J = 7.8 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 4.53 (t, J = 7.4 Hz, 1H), 2.45 (s, 3H), 2.19-2.09 (m, 1H), 1.86-1.76 (m, 1H), 1.38-1.22 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 200.0, 136.93, 136.90, 136.6, 132.8, 128.7, 128.6, 128.5, 127.0, 52.8, 36.0, 20.8, 15.8, 14.0 ppm. HRMS (ESI+, m/z): calcd for C₁₈H₂₁OS [M+H]⁺: 285.1307; found: 285.1308.



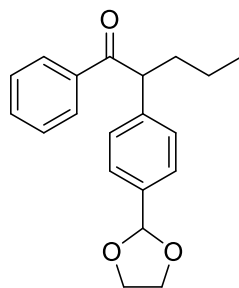
2-(4-(Dimethylamino)phenyl)-1-phenylpentan-1-one (3i): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 4-bromo-*N,N*-dimethylaniline (0.6 mmol, 120 mg). Yellow solid obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 90:10), 114 mg, 81% yield. M.p.: 75 °C-76 °C. ¹H-NMR (400 MHz, CDCl₃): δ 7.96 (d, J = 7.1 Hz, 2H), 7.45 (t, J = 7.3 Hz, 1H), 7.37 (t, J = 7.5 Hz, 2H), 7.15 (d, J = 8.7 Hz, 2H), 6.65 (d, J = 8.7 Hz, 2H), 4.45 (t, J = 7.3 Hz, 1H), 2.89 (s, 6H), 2.17-2.04 (m, 1H), 1.84-1.73 (m, 1H), 1.36-1.20 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 200.4, 149.4, 137.2, 132.4, 128.8, 128.5, 128.3, 127.3, 112.8, 55.3, 40.4, 36.0, 20.8, 14.1 ppm. HRMS (ESI+, m/z): calcd for C₁₉H₂₄NO [M+H]⁺: 282.1852; found: 282.1853.



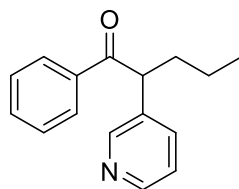
Ethyl 4-(1-oxo-1-phenylpentan-2-yl)benzoate (3j): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and ethyl 4-bromobenzoate (0.6 mmol, 137 mg, 98 μ L). Yellow oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 95:5), 59 mg, 38% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.99-7.91 (m, 4H), 7.49 (t, J = 7.4 Hz, 1H), 7.39 (m, 4H), 4.62 (t, J = 7.3 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 2.22-2.12 (m, 1H), 1.88-1.77 (m, 1H), 1.38-1.18 (m, 5H), 0.92 (t, J = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 199.5, 166.3, 144.9, 136.7, 133.0, 130.1, 129.2, 128.6 (2C), 128.2, 60.9, 53.4, 36.0, 20.8, 14.3, 14.0 ppm. HRMS (ESI+, m/z): calcd for C₂₀H₂₃O₃ [M+H]⁺: 311.1641; found: 311.1642.



2-(4-Benzoylphenyl)-1-phenylpentan-1-one (3k): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 4-bromobenzophenone (0.6 mmol, 157 mg). Yellow oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 98:2), leaving the product fraction overnight under vacuum at 60°C, 147 mg, 86% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.99-7.96 (m, 2H), 7.77-7.73 (m, 4H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.48-7.40 (m, 6H), 4.67 (t, *J* = 7.3 Hz, 1H), 2.25-2.16 (m, 1H), 1.91-1.81 (m, 1H), 1.40-1.27 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 199.5, 196.2, 144.6, 137.5, 136.7, 136.2, 133.1, 132.4, 130.7, 129.9, 128.64, 128.62, 128.2, 128.2, 53.3, 36.1, 20.9, 14.1 ppm. HRMS (ESI+, *m/z*): calcd for C₂₄H₂₃O₂ [M+H]⁺: 343.1692; found: 343.1693.

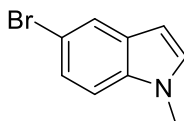


2-(4-(1,3-Dioxolan-2-yl)phenyl)-1-phenylpentan-1-one (3l): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 2-(4-bromophenyl)-1,3-dioxolane (0.6 mmol, 137 mg). Colorless oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 95:5), 121 mg, 78% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.93 (d, *J* = 7.2 Hz, 2H), 7.53-7.45 (m, 1H), 7.42-7.31 (m, 6H), 5.74 (s, 1H), 4.57 (t, *J* = 7.2 Hz, 1H), 4.15-3.98 (m, 4H), 2.19-2.09 (m, 1H), 1.85-1.75 (m, 1H), 1.36-1.18 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 199.9, 140.9, 136.9, 136.5, 132.8, 128.6, 128.5, 128.3, 127.0, 103.5, 65.3, 65.2, 53.2, 36.1, 20.8, 14.0 ppm. HRMS (ESI+, *m/z*): calcd for C₂₀H₂₃O₃ [M+H]⁺: 311.1641; found: 311.1642.



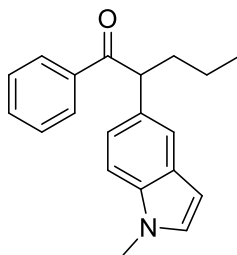
1-Phenyl-2-(pyridin-3-yl)pentan-1-one (3m): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 3-bromopyridine (0.6 mmol, 95 mg, 58 μL). Colorless oil obtained after column

chromatography (SiO₂, *n*-pentane/ EtOAc 95:5), 83 mg, 69% yield. ¹H-NMR (400 MHz, CDCl₃): δ 8.60 (s, 1H), 8.47 (d, *J* = 3.3 Hz, 1H), 7.96 (d, *J* = 7.3 Hz, 2H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.23 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.62 (t, *J* = 7.3 Hz, 1H), 2.12-2.23 (m, 1H), 1.87-1.77 (m, 1H), 1.40-1.22 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 199.4, 150.0, 148.4, 136.5, 135.3, 133.2, 128.7, 128.5 (2C), 123.7, 50.3, 36.1, 20.8, 13.9 ppm. HRMS (ESI+, *m/z*): calcd for C₁₆H₁₈NO [M+H]⁺: 240.1382; found: 240.1383.

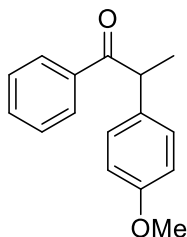


5-bromo-1-methyl-1*H*-indole⁵

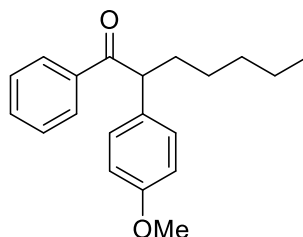
Synthesized using 5-bromo-1*H*-indole (4.0 mmol, 790 mg). Yellow oil, 555 mg, 66% yield. ¹H-NMR (300 MHz, CDCl₃): δ 7.74 (d, *J* = 1.6 Hz, 1H), 7.29 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.18 (d, *J* = 8.7 Hz, 1H), 7.04 (d, *J* = 3.1 Hz, 1H), 6.42 (d, *J* = 3.0 Hz, 1H), 3.77 (s, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 135.5, 130.3, 130.2, 124.3, 123.3, 112.7, 110.9, 100.6, 33.0 ppm. ¹H- and ¹³C-NMR Spectra in accordance with literature data.



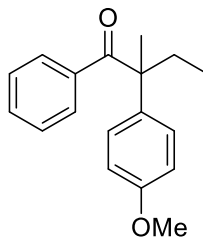
2-(1-methyl-1*H*-indol-5-yl)-1-phenylpentan-1-one (3n): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 5-bromo-1-methyl-1*H*-indole (0.6 mmol, 126 mg). Yellow oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 95:5), 110 mg, 75% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.99 (d, *J* = 7.3 Hz, 2H), 7.54 (s, 1H), 7.42 (t, *J* = 6.7 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 2H), 7.24 (d, *J* = 10.9 Hz, 1H), 7.16 (d, *J* = 8.7 Hz, 1H), 7.00 (d, *J* = 3.1 Hz, 1H), 6.41 (d, *J* = 3.1 Hz, 1H), 4.62 (t, *J* = 7.3 Hz, 1H), 3.73 (s, 3H), 2.23-2.13 (m, 1H), 1.91-1.81 (m, 1H), 1.38-1.22 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 200.6, 137.3, 135.8, 132.5, 130.7, 129.2, 128.9, 128.7, 128.4, 121.9, 120.5, 109.6, 100.8, 53.6, 36.5, 32.8, 20.9, 14.2 ppm. HRMS (ESI+, *m/z*): calcd for C₂₀H₂₁NO [M+H]⁺: 292.1695; found: 292.1696.



2-(4-Methoxyphenyl)-1-phenylpropan-1-one (3o): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), EtLi (1.6 ml, 0.31 M, 0.5 mmol, 1.0 eq) and 4-bromoanisole (0.6 mmol, 112 mg, 75 μ L). Yellow oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 95:5), 63 mg, 53% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.94 (d, *J* = 7.0 Hz, 2H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 4.64 (q, *J* = 6.9 Hz, 1H), 3.75 (s, 3H), 1.50 (d, *J* = 6.9 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 200.5, 158.5, 136.5, 133.5, 132.7, 128.78, 128.74, 128.5, 114.4, 55.2, 47.0, 19.5 ppm. HRMS (ESI+, *m/z*): calcd for C₁₆H₁₇O₂ [M+H]⁺: 241.1223; found: 241.1223.

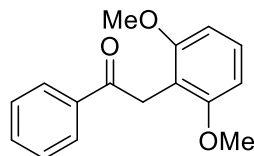


2-(4-Methoxyphenyl)-1-phenylheptan-1-one (3p): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *n*-HexLi (0.22 ml, 2.3 M, 0.5 mmol, 1.0 eq) and 4-bromoanisole (0.6 mmol, 112 mg, 75 μ L). Yellow oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 95:5), 119 mg, 80% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.95 (d, *J* = 7.7 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 4.48 (t, *J* = 7.3 Hz, 1H), 3.75 (s, 3H), 2.18-2.07 (m, 1H), 1.84-1.70 (m, 1H), 1.36-1.19 (m, 6H), 0.85 (t, *J* = 5.5 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 200.3, 158.5, 137.1, 132.7, 131.9, 129.2, 128.6, 128.5, 114.3, 55.1, 52.8, 34.0, 31.8, 27.4, 25.5, 14.1 ppm. HRMS (ESI+, *m/z*): calcd for C₂₀H₂₅O₂ [M+H]⁺: 297.1849; found: 297.1849.

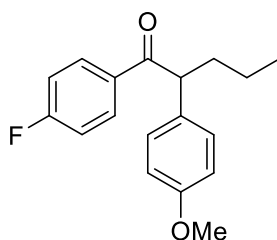


2-(4-Methoxyphenyl)-2-methyl-1-phenylbutan-1-one (3q): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), *s*-BuLi (0.5 ml, 1.0 M, 0.5 mmol, 1.0 eq) and 4-bromoanisole (0.6 mmol, 112 mg, 75 μ L) using toluene as solvent, heated to reflux for the α -arylation step. Colorless oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 95:5), 67 mg, 50% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.44 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.24-7.18 (m, 4H), 6.89 (d, *J* = 8.8 Hz, 2H), 3.81 (s,

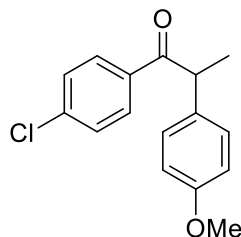
3H), 2.18-1.98 (m, 2H), 1.52 (s, 3H), 0.74 (t, $J = 7.4$ Hz, 3H) ppm. ^{13}C -NMR (100.59 MHz, CDCl_3): δ 204.1, 158.3, 137.2, 136.2, 131.4, 129.4, 127.9, 127.3, 114.2, 55.2, 54.2, 32.1, 23.7, 8.6 ppm. HRMS (ESI+, m/z): calcd for $\text{C}_{18}\text{H}_{21}\text{O}_2$ $[\text{M}+\text{H}]^+$: 269.1536; found: 269.1536.



2-(2,6-Dimethoxyphenyl)-1-phenylethan-1-one (3s): Synthesized using *N,N*-dimethylbenzamide (0.5 mmol, 75 mg), MeLi (0.39 ml, 1.28 M, 0.5 mmol, 1.0 eq) and 2-bromo-1,3-dimethoxybenzene (0.6 mmol, 130 mg). Yellow oil obtained after column chromatography (SiO_2 , *n*-pentane/ EtOAc 90:10), 67 mg, 52% yield. ^1H -NMR (400 MHz, CDCl_3): δ 8.04 (d, $J = 7.3$ Hz, 2H), 7.54 (t, $J = 7.3$ Hz, 1H), 7.45 (t, $J = 7.4$ Hz, 2H), 7.22 (t, $J = 8.3$ Hz, 1H), 6.57 (d, $J = 8.3$ Hz, 2H), 4.33 (s, 2H), 3.76 (s, 6H) ppm. ^{13}C -NMR (100.59 MHz, CDCl_3): δ 198.0, 158.3, 137.4, 132.6, 128.4, 128.2 (2C), 112.2, 103.7, 55.7, 33.9 ppm. HRMS (ESI+, m/z): calcd for $\text{C}_{16}\text{H}_{16}\text{O}_3$ $[\text{M}+\text{H}]^+$: 257.1172; found: 257.1172.

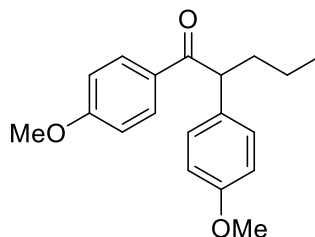


1-(4-Fluorophenyl)-2-(4-methoxyphenyl)pentan-1-one (3t): Synthesized using 4-fluoro-*N,N*-dimethylbenzamide (0.5 mmol, 84 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 4-bromoanisole (0.6 mmol, 112 mg, 75 μL). Yellow oil obtained after column chromatography (SiO_2 , *n*-pentane/ EtOAc 95:5), 80 mg, 56% yield. ^1H -NMR (400 MHz, CDCl_3): δ 7.97 (dd, $J = 8.7, 5.6$ Hz, 2H), 7.19 (d, $J = 8.6$ Hz, 2H), 7.05 (t, $J = 8.6$ Hz, 2H), 6.82 (d, $J = 8.7$ Hz, 2H), 4.43 (t, $J = 7.3$ Hz, 1H), 3.75 (s, 3H), 2.15-2.05 (m, 1H), 1.83-1.69 (m, 1H), 1.34-1.19 (m, 2H), 0.91 (t, $J = 7.3$ Hz, 3H) ppm. ^{13}C -NMR (100.59 MHz, CDCl_3): δ 198.7, 165.4 (d, $J = 254.4$ Hz), 158.6, 133.4 (d, $J = 3.0$ Hz), 131.6, 131.2 (d, $J = 9.2$ Hz), 129.1, 115.5 (d, $J = 21.8$ Hz), 114.3, 55.1, 52.5, 36.1, 20.8, 14.0 ppm. ^{19}F -NMR (376 MHz, CDCl_3): δ -105.8 ppm. HRMS (ESI+, m/z): calcd for $\text{C}_{18}\text{H}_{20}\text{FO}_2$ $[\text{M}+\text{H}]^+$: 287.1441; found: 287.1442.



1-(4-Chlorophenyl)-2-(4-methoxyphenyl)propan-1-one (3u): Synthesized using 4-chloro-*N*-methoxy-*N*-methylbenzamide (0.5 mmol, 100 mg), EtLi (1.6 ml, 0.31 M, 0.5

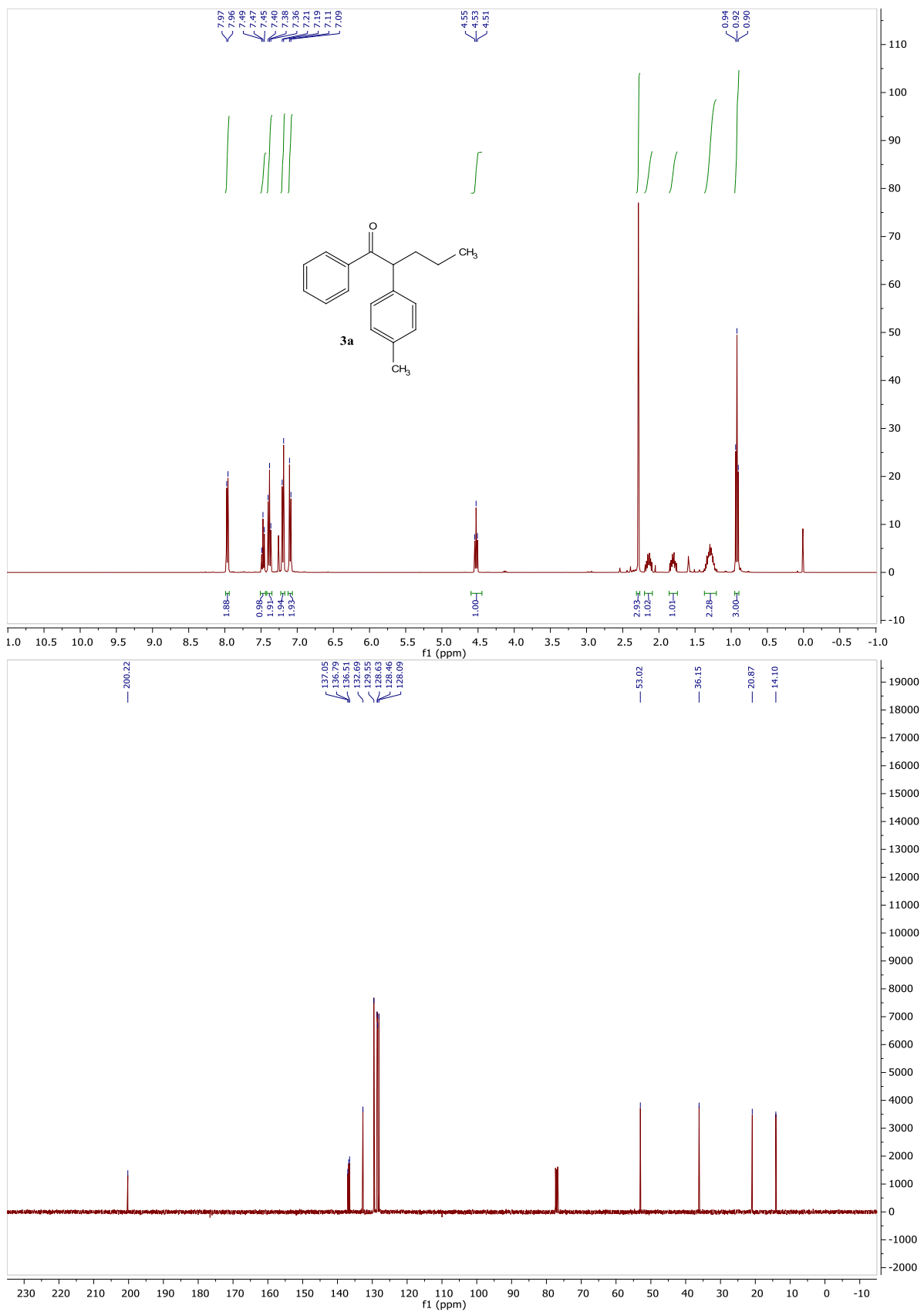
mmol, 1.0 eq) and 1-bromo-4-methoxybenzene (0.6 mmol, 112 mg). Colorless oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 95:5), 88 mg, 64% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.87 (d, *J* = 8.7 Hz, 2H), 7.33 (d, *J* = 8.8 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 4.57 (q, *J* = 6.8 Hz, 1H), 3.75 (s, 3H), 1.50 (d, *J* = 6.8 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 199.2, 158.6, 139.0, 134.8, 133.2, 130.2 (2C), 128.7, 128.7, 114.5, 55.2, 47.2, 19.4 ppm.

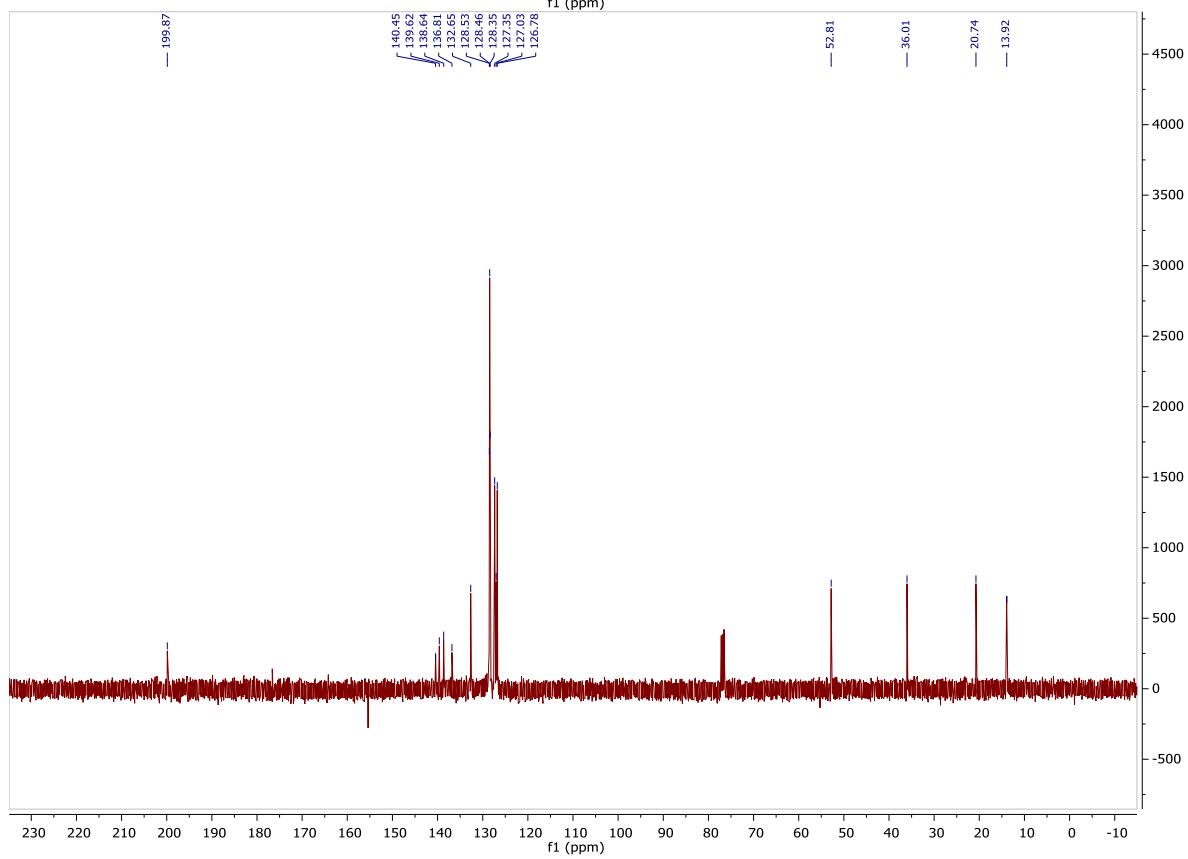
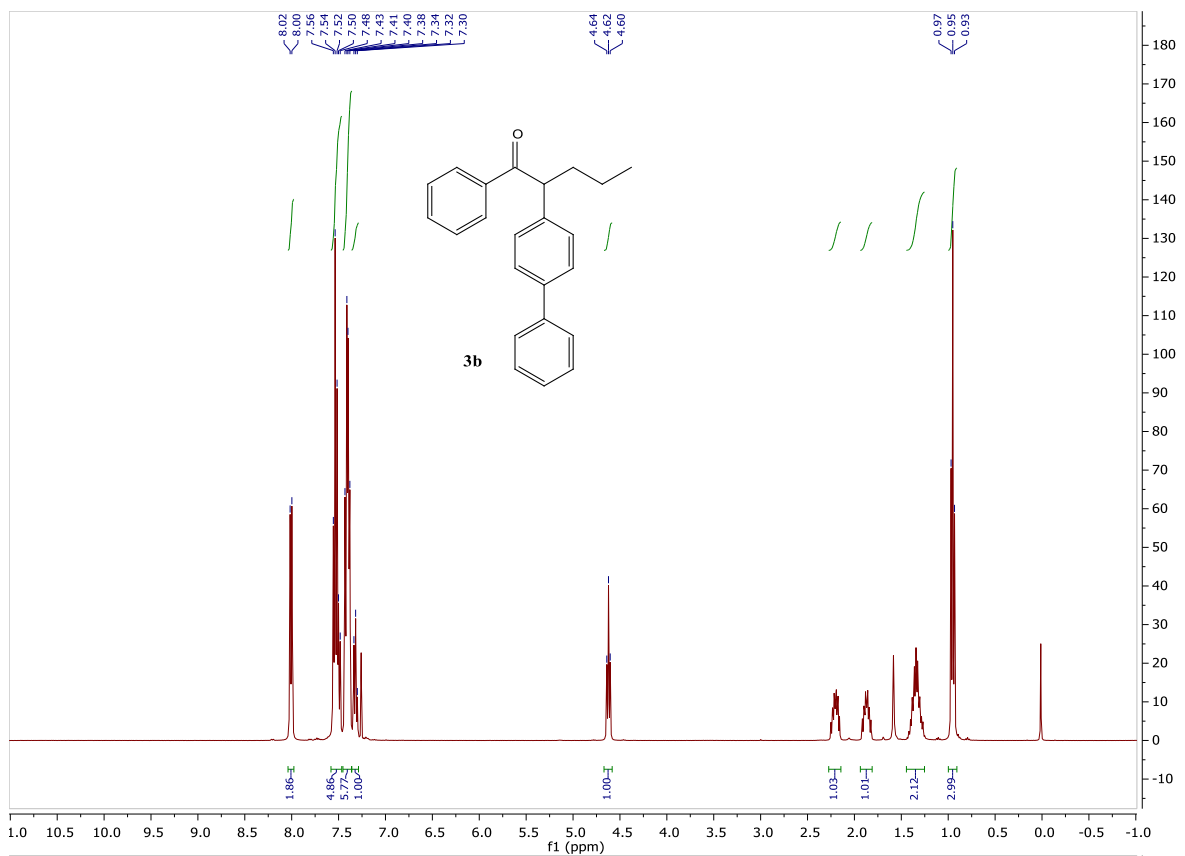


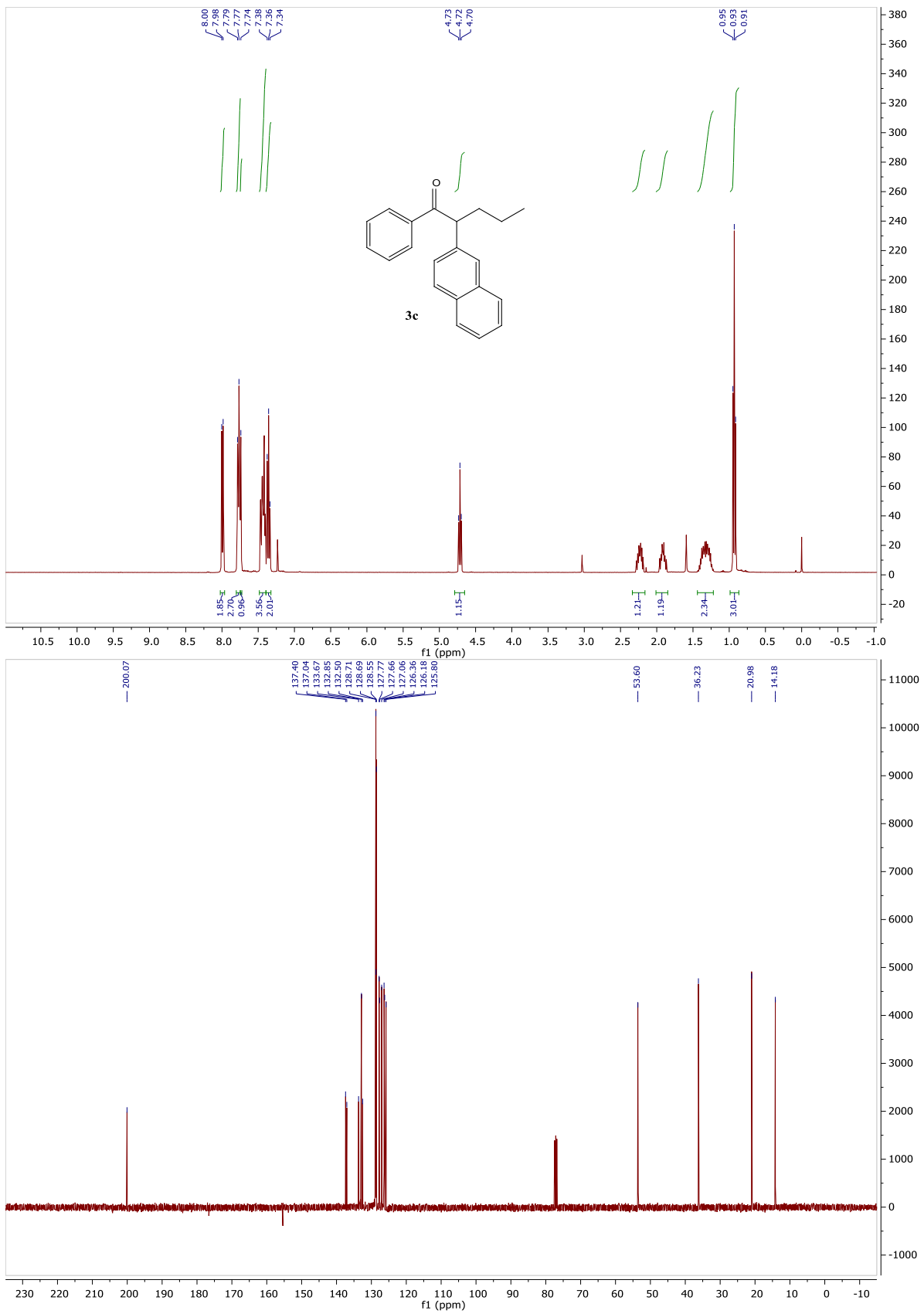
1,2-Bis(4-methoxyphenyl)pentan-1-one (3v): Synthesized using 4-methoxy-*N,N*-dimethylbenzamide (0.5 mmol, 90 mg), *n*-BuLi (0.31 ml, 1.6 M, 0.5 mmol, 1.0 eq) and 4-bromoanisole (0.6 mmol, 112 mg, 75 μL). Yellow oil obtained after column chromatography (SiO₂, *n*-pentane/ EtOAc 90:10), 90 mg, 60% yield. ¹H-NMR (400 MHz, CDCl₃): δ 7.97 (d, *J* = 8.9 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 4.47 (t, *J* = 7.3 Hz, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 2.17-2.07 (m, 1H), 1.84-1.73 (m, 1H), 1.37-1.21 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H) ppm. ¹³C-NMR (100.59 MHz, CDCl₃): δ 198.8, 163.2, 158.4, 132.3, 130.9, 130.0, 129.1, 114.2, 113.6, 55.4, 55.2, 52.0, 36.2, 20.9, 14.1 ppm. HRMS (ESI+, *m/z*): calcd for C₁₉H₂₃O₃ [M+H]⁺: 299.1641; found: 299.1642.

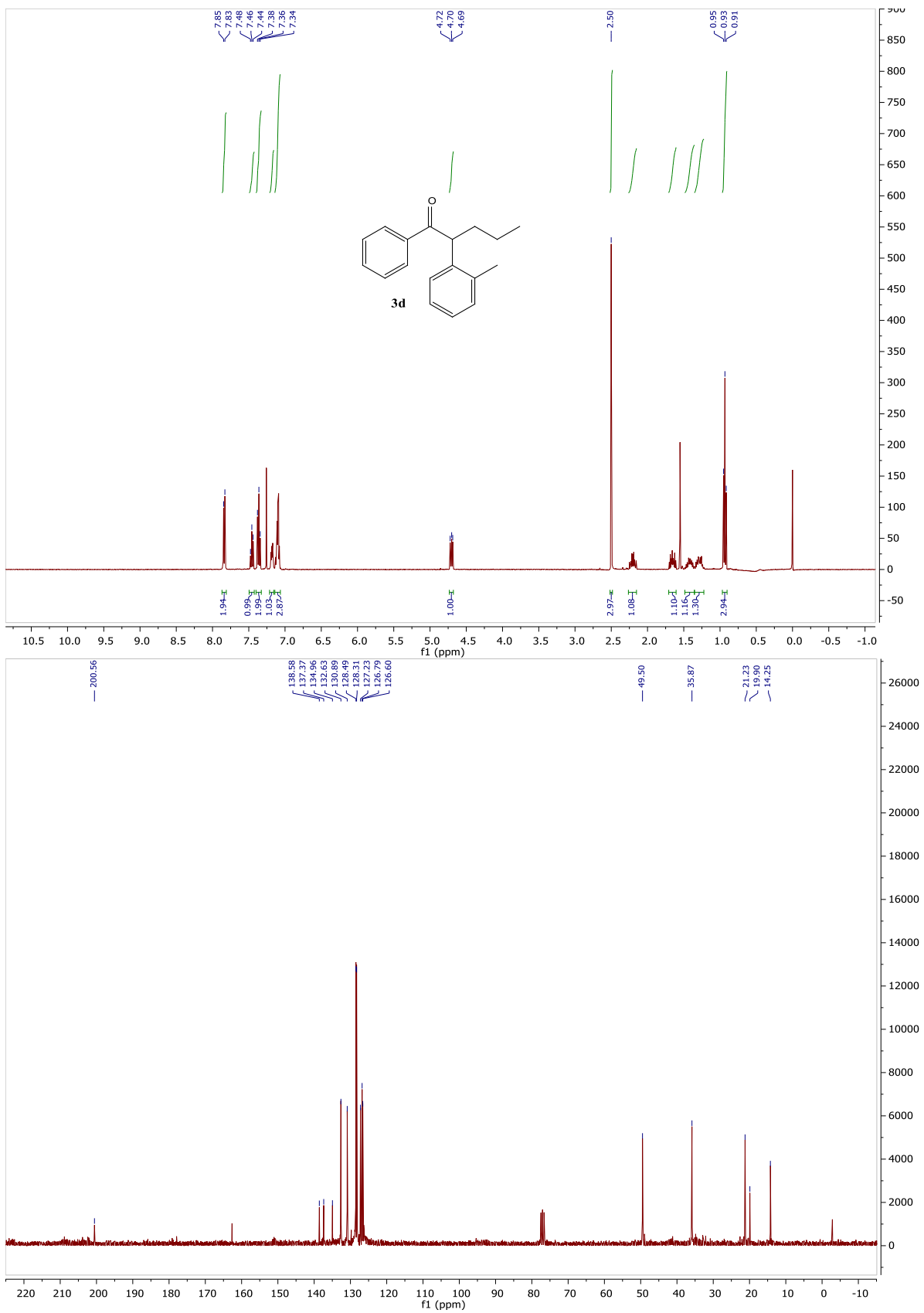
Note: Trace amounts of Buchwald-Hartwig coupling product **4** proved sometimes to be difficult to separate from the product **3** via column chromatography at the given scale. Nonetheless, these traces can be easily removed keeping the sample under vacuum overnight at 60 °C.

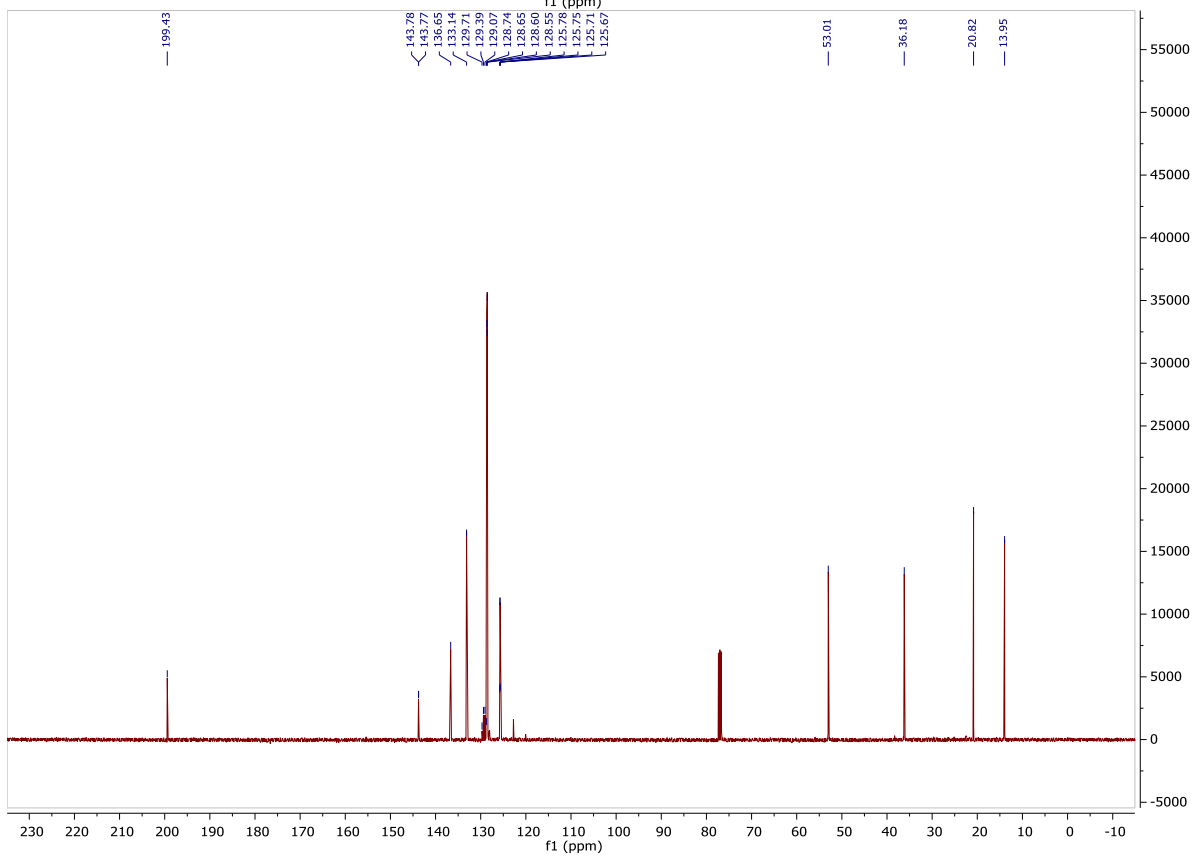
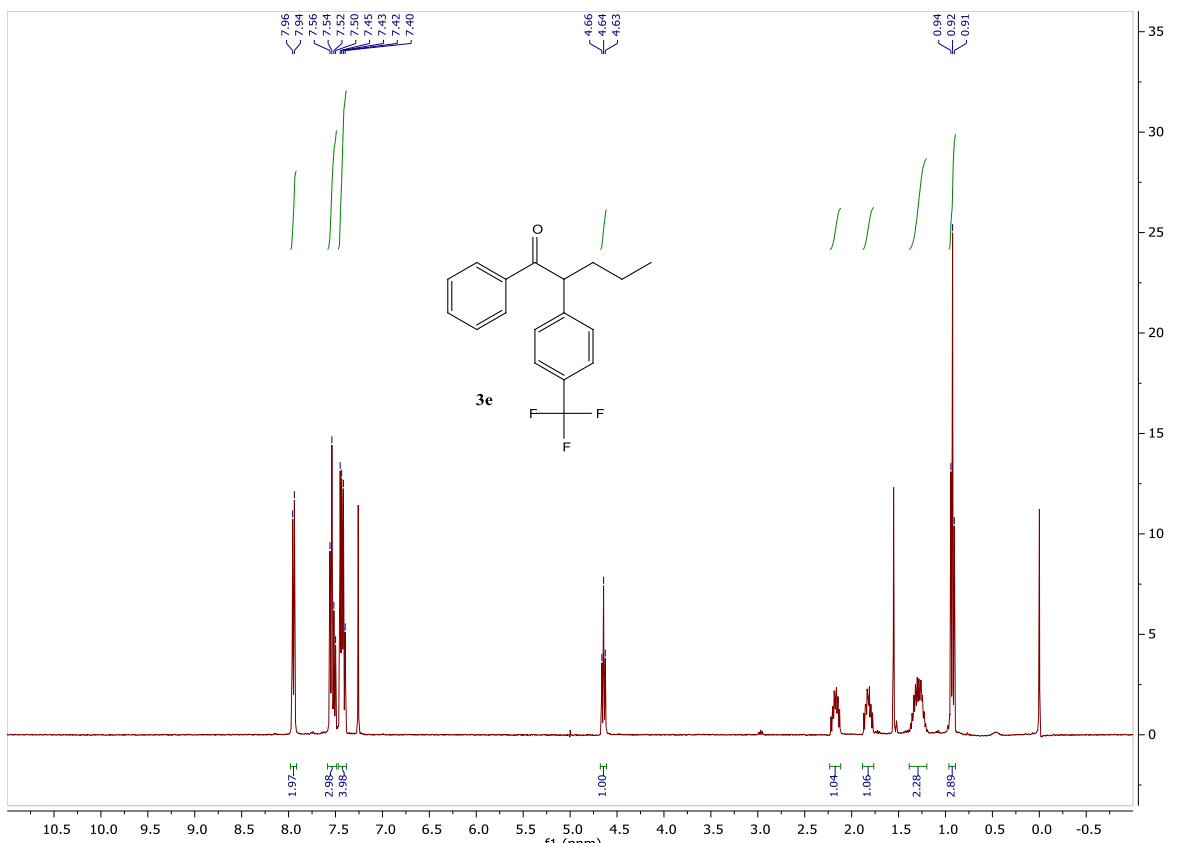
^1H -, ^{13}C and ^{19}F -NMR of isolated compounds

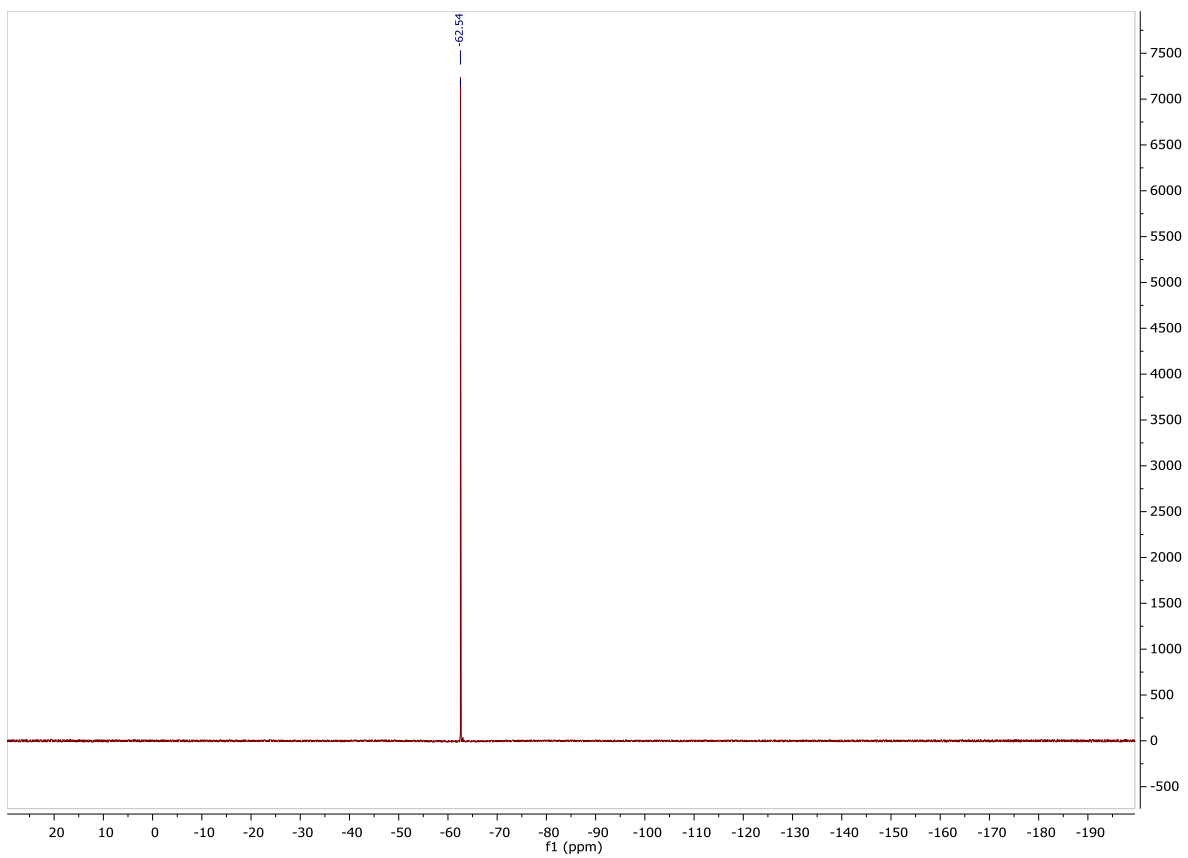


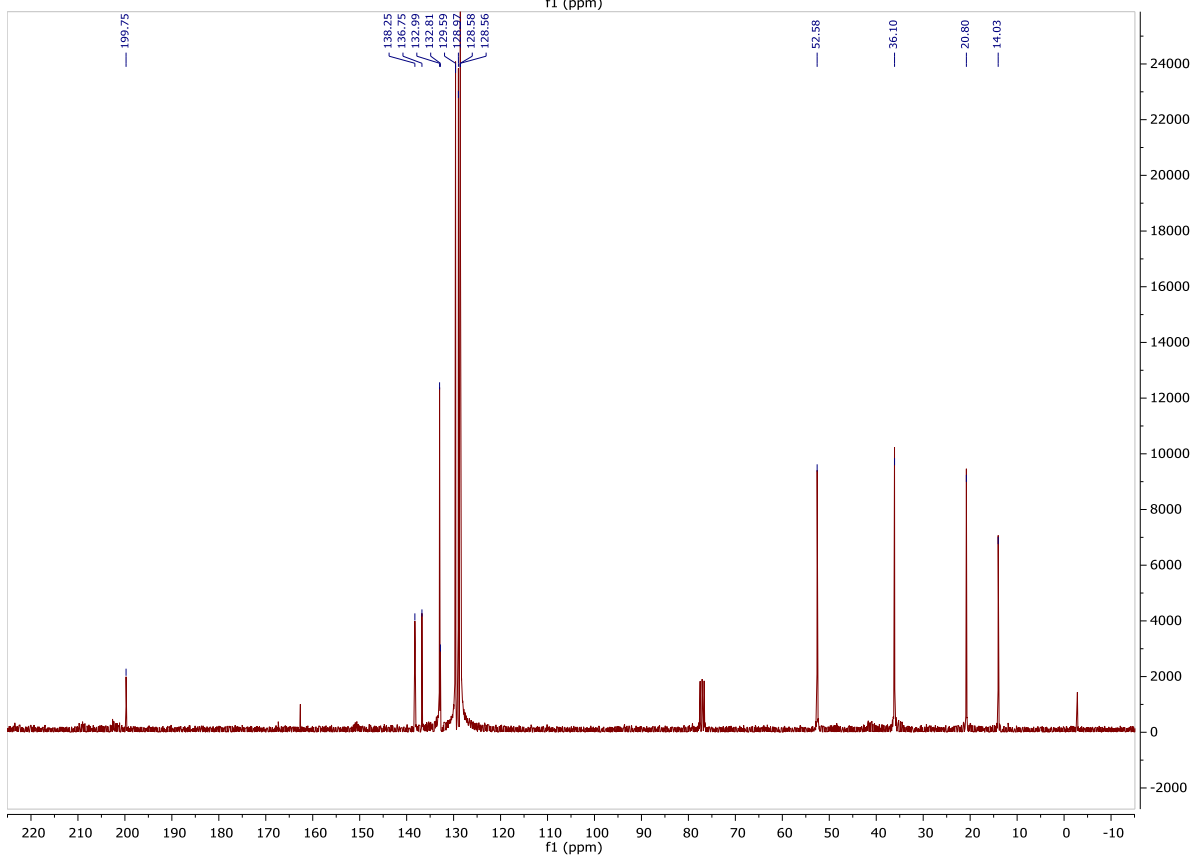
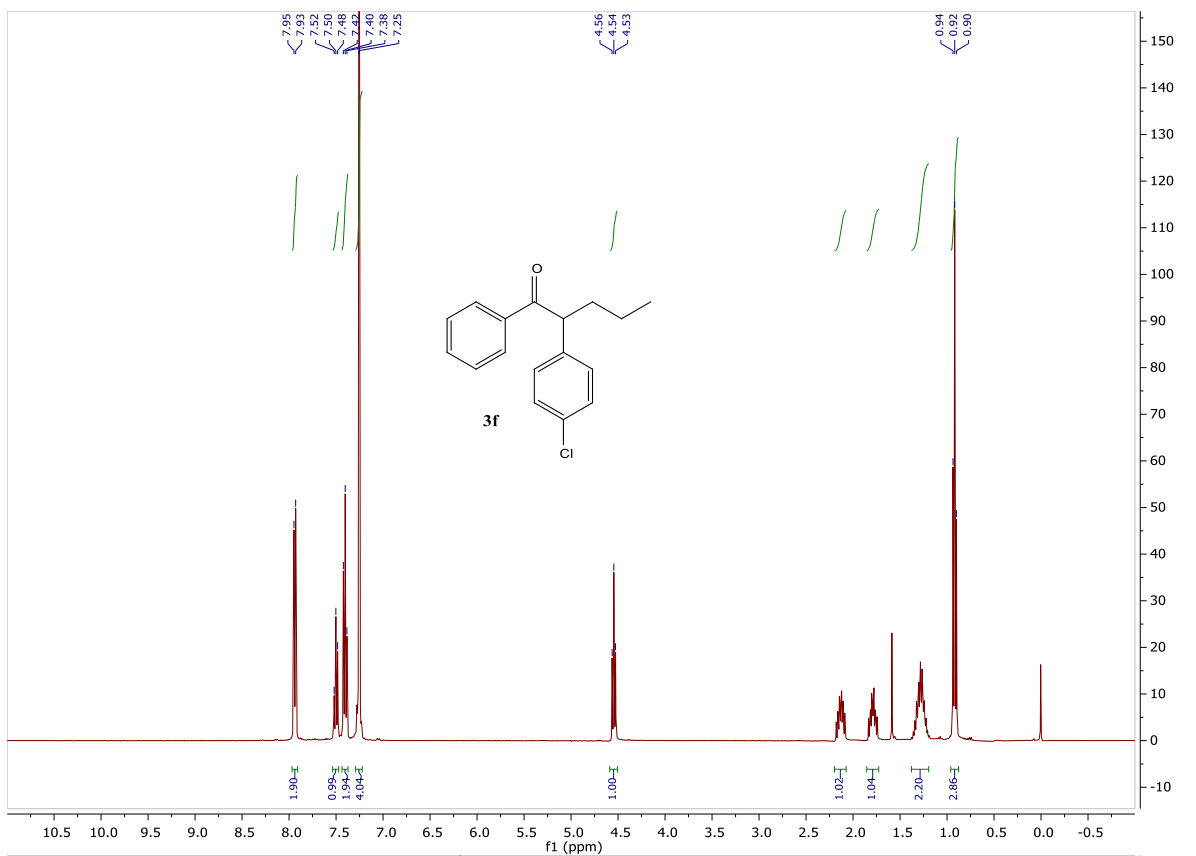


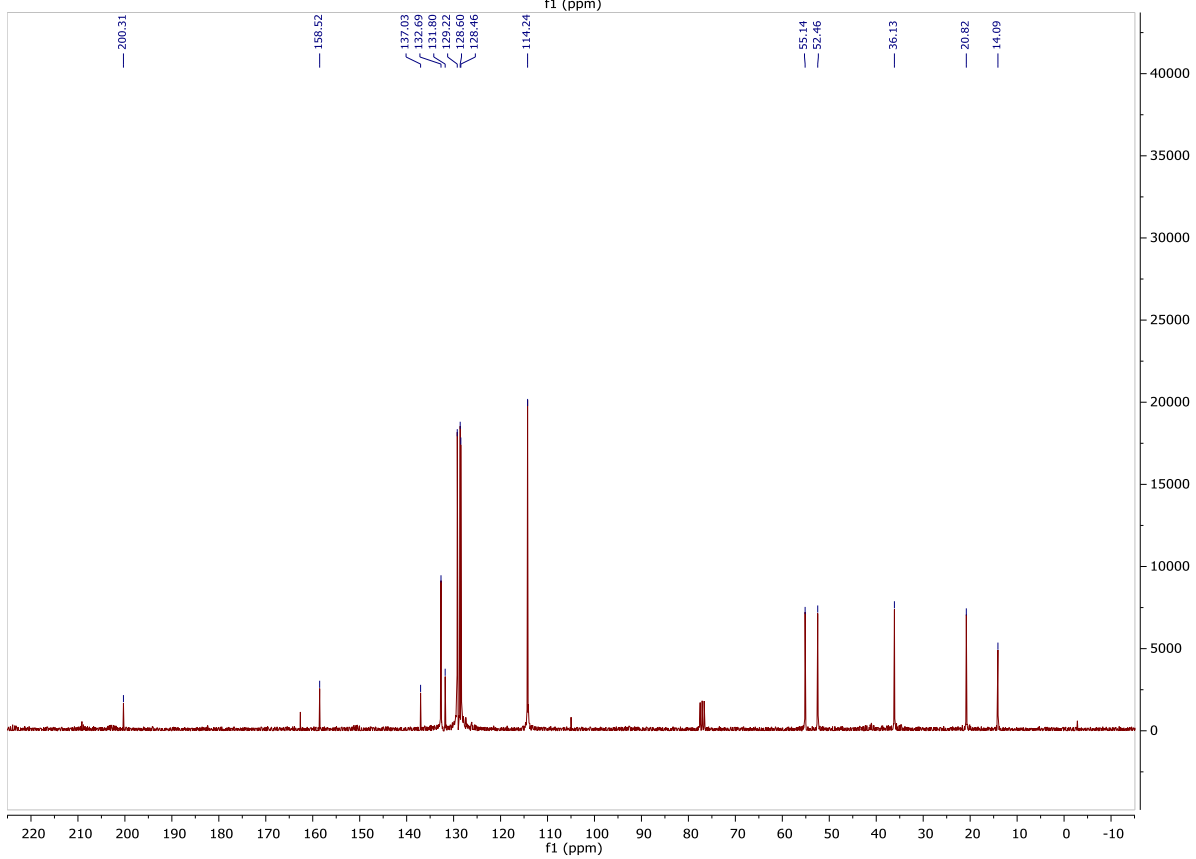
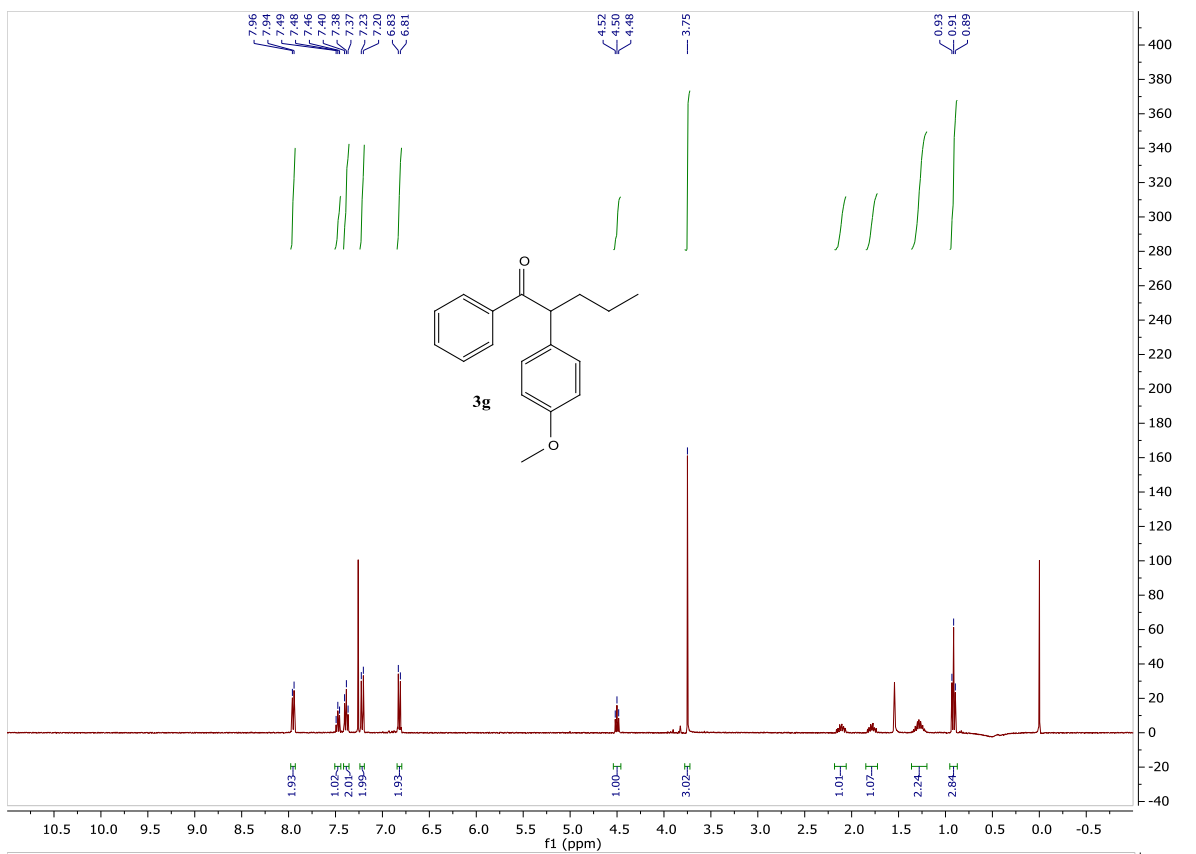


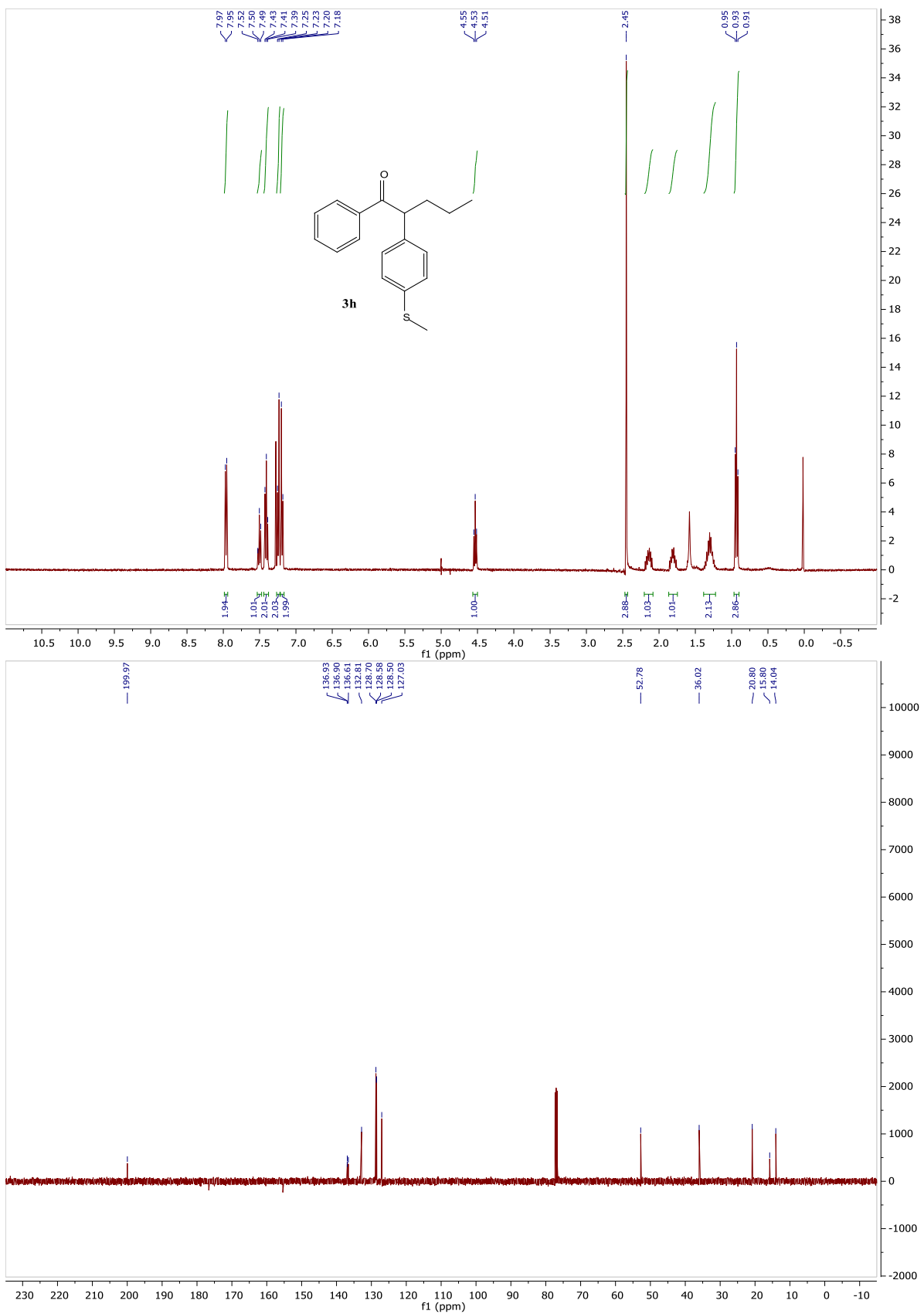


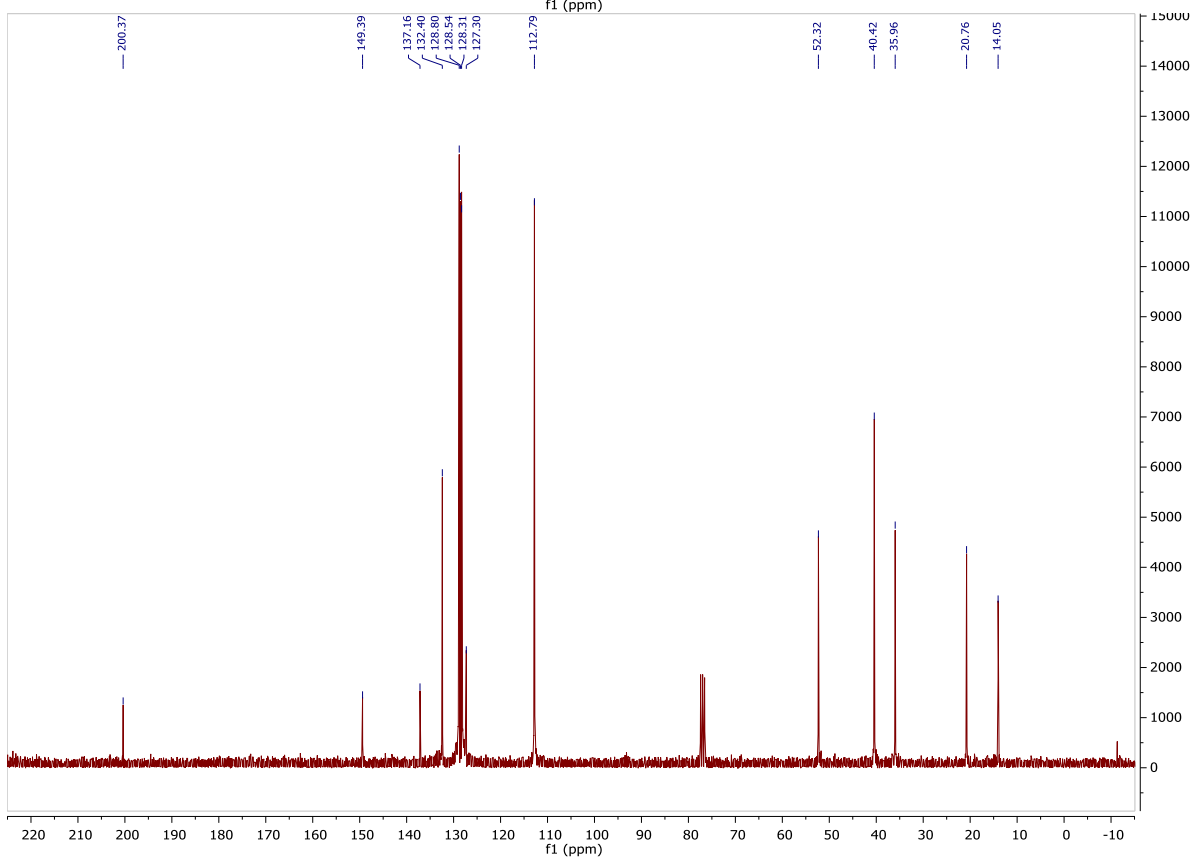
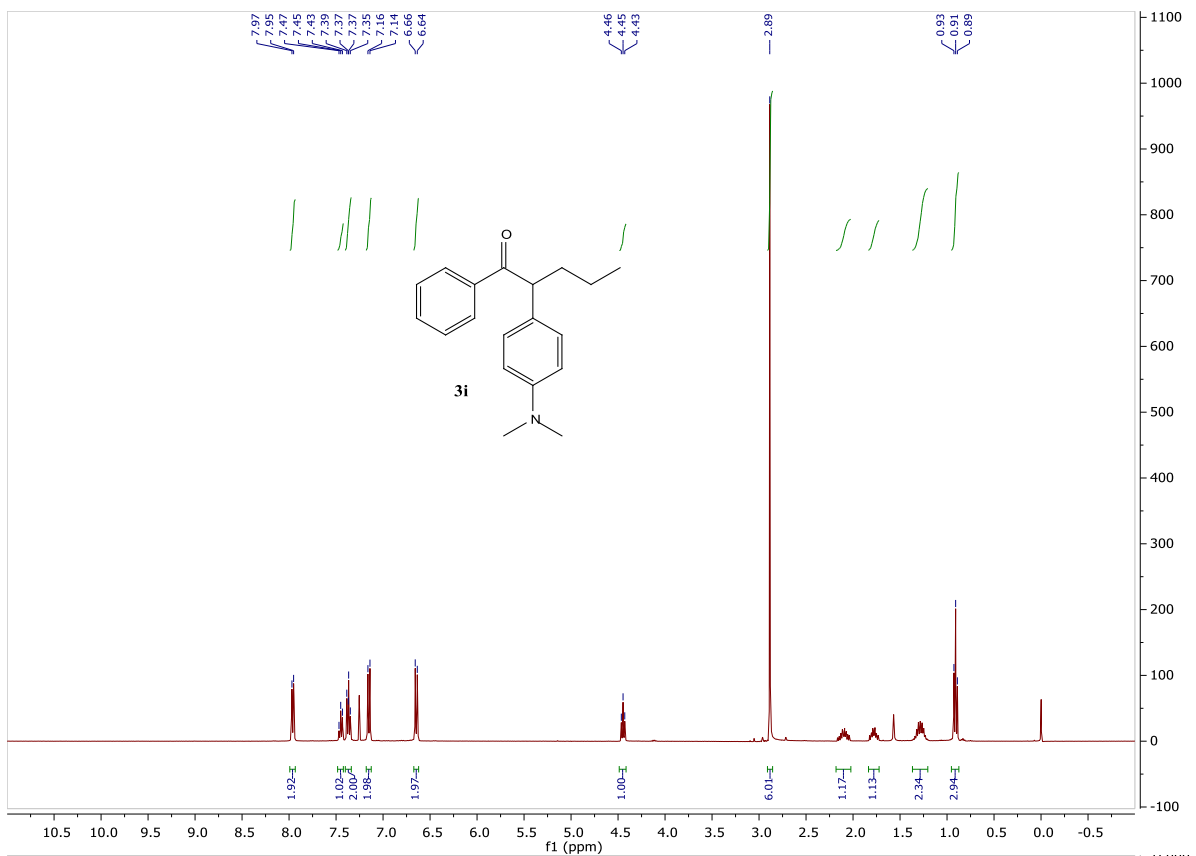


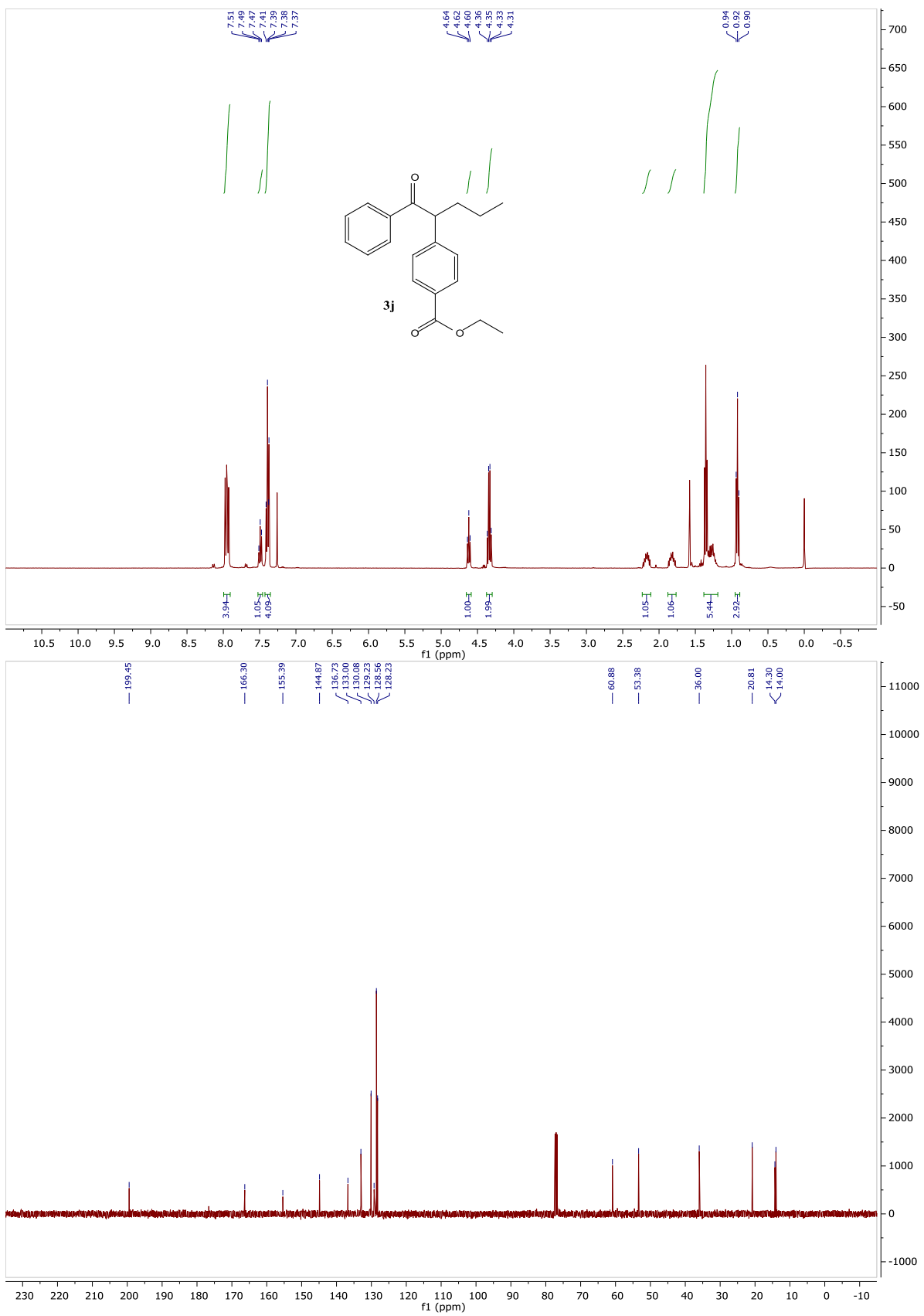


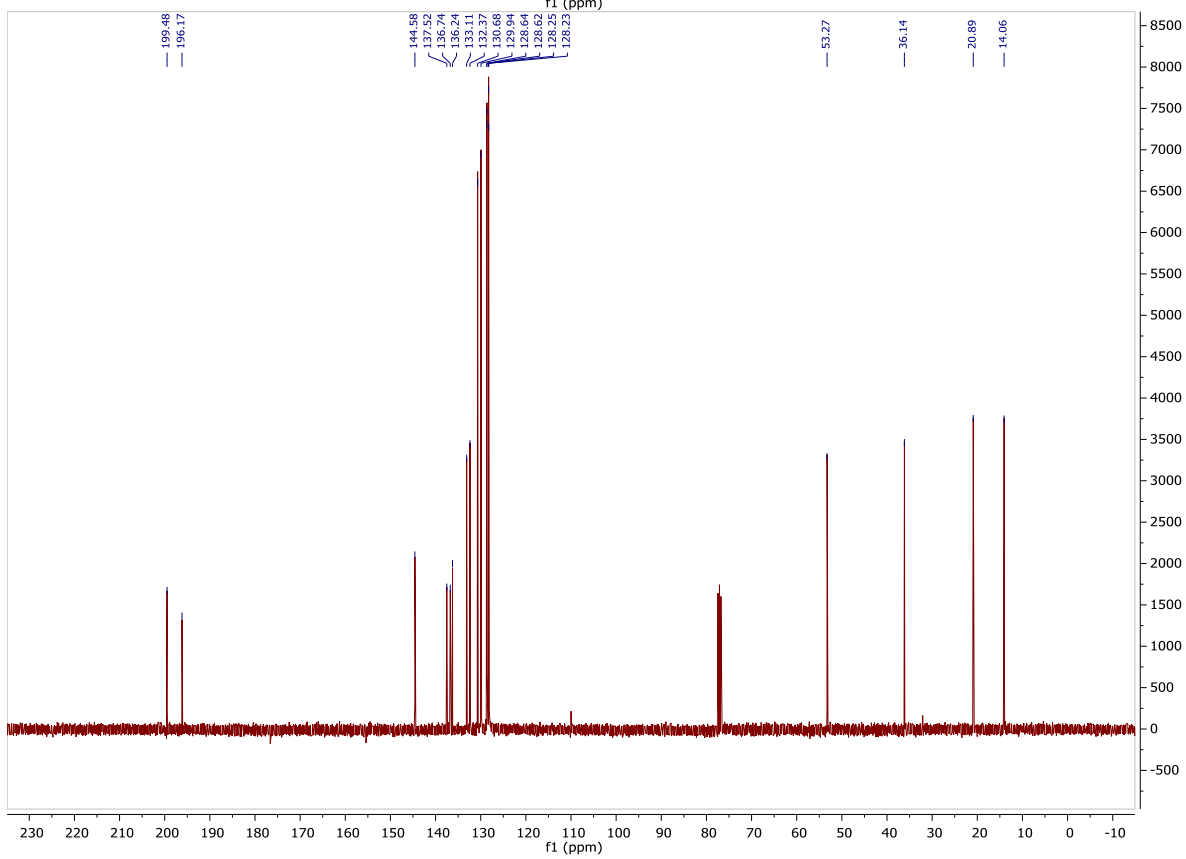
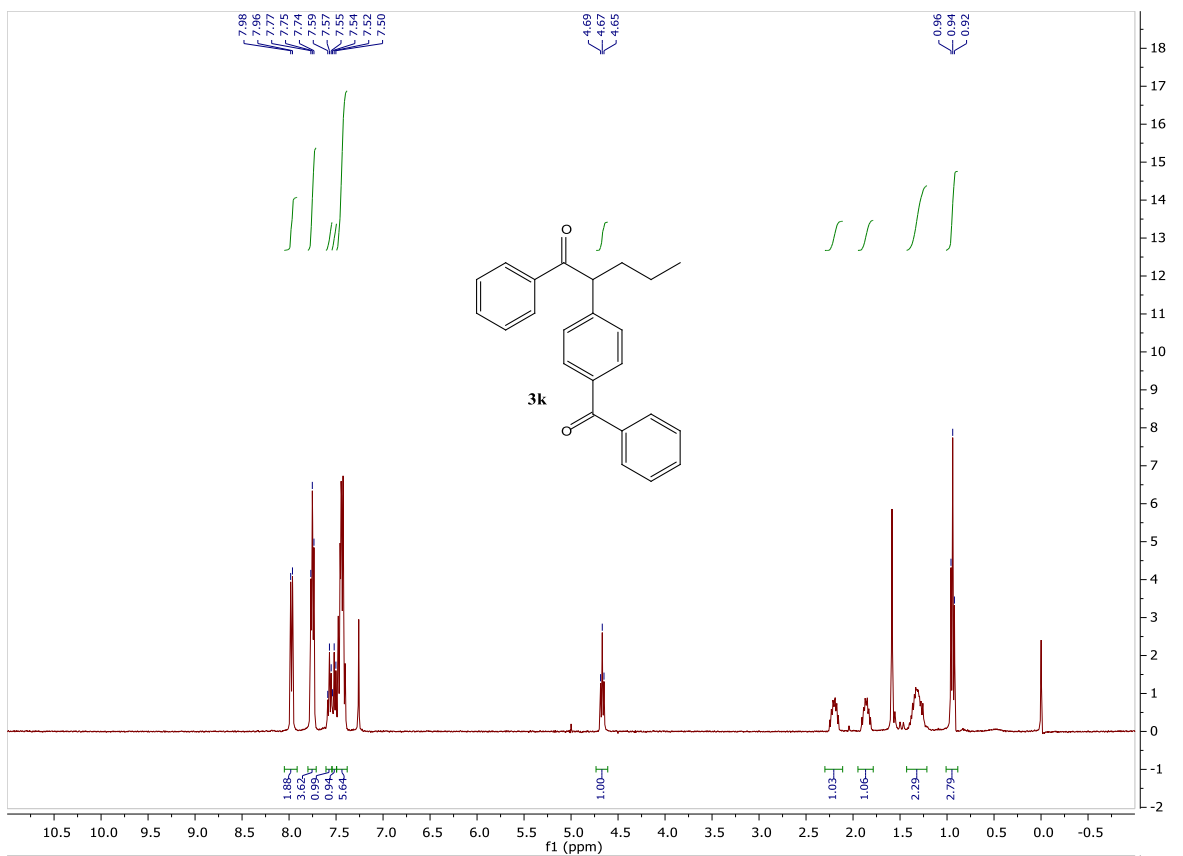


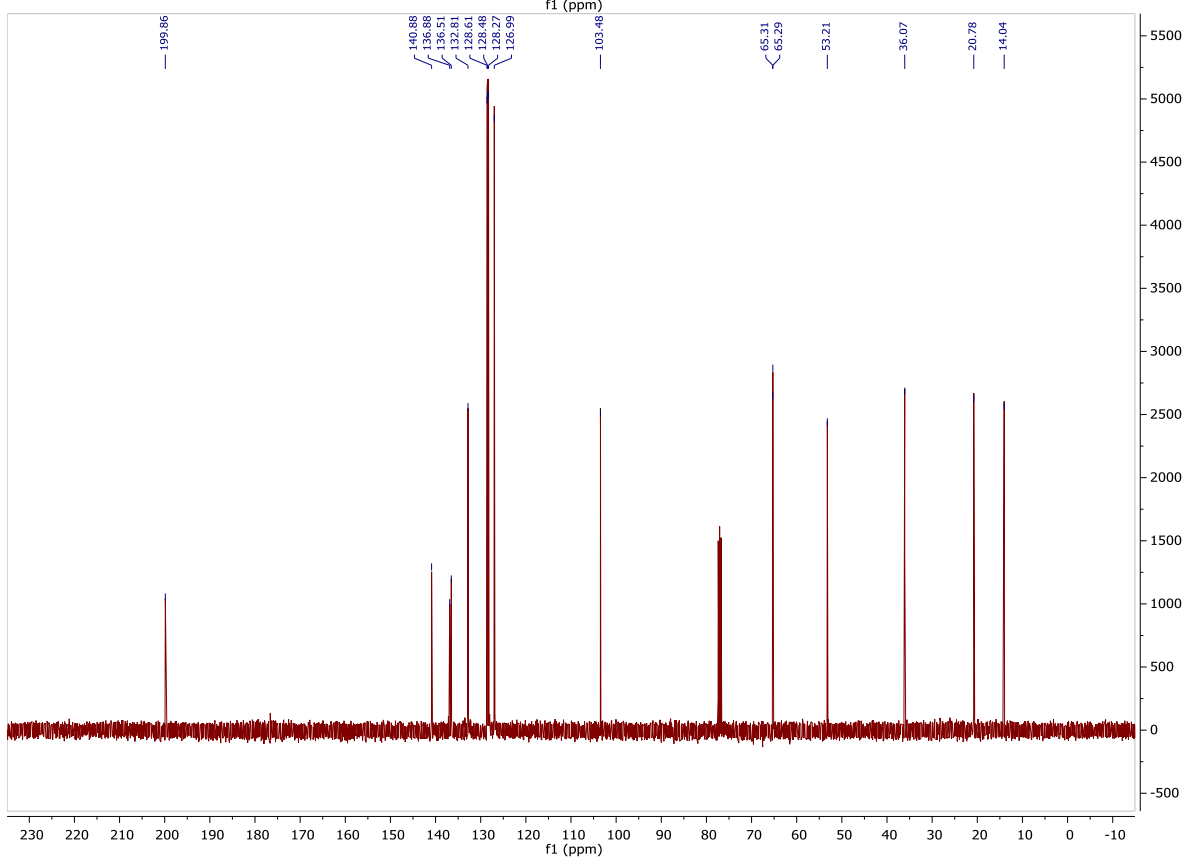
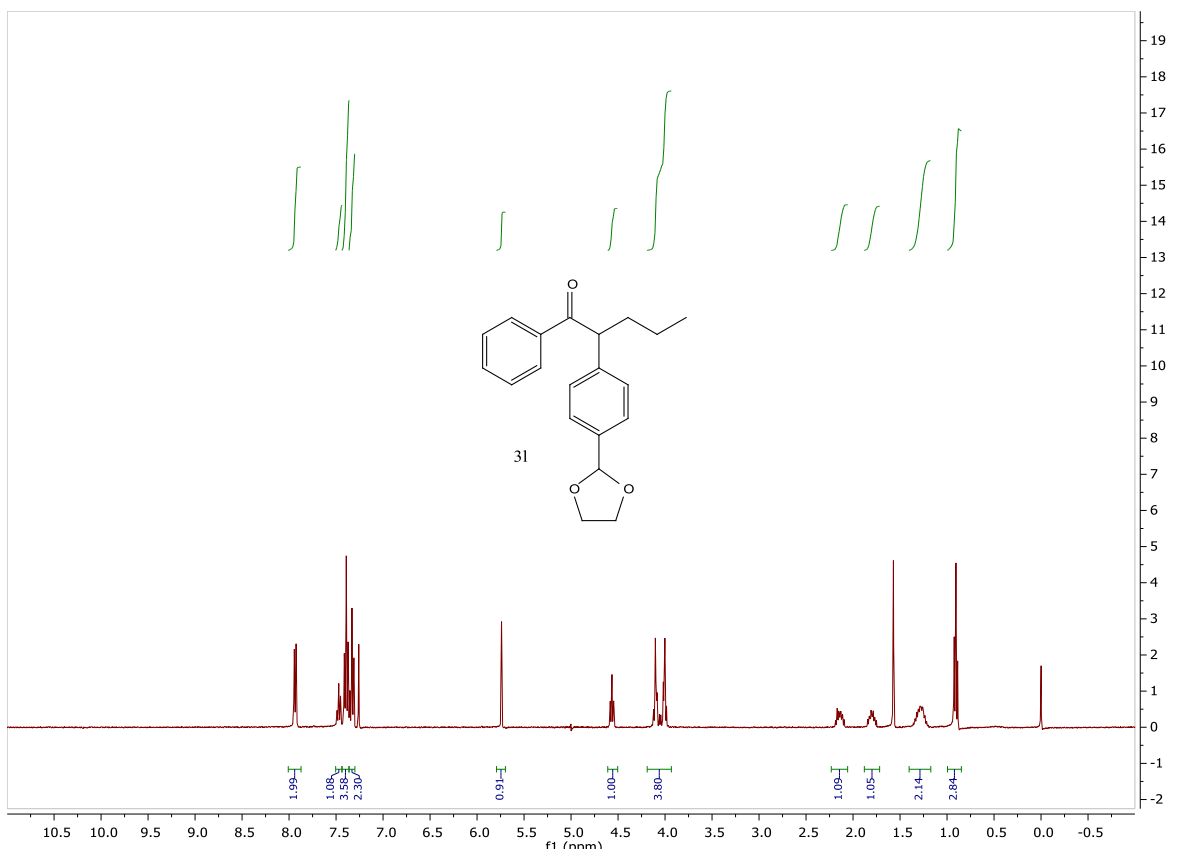


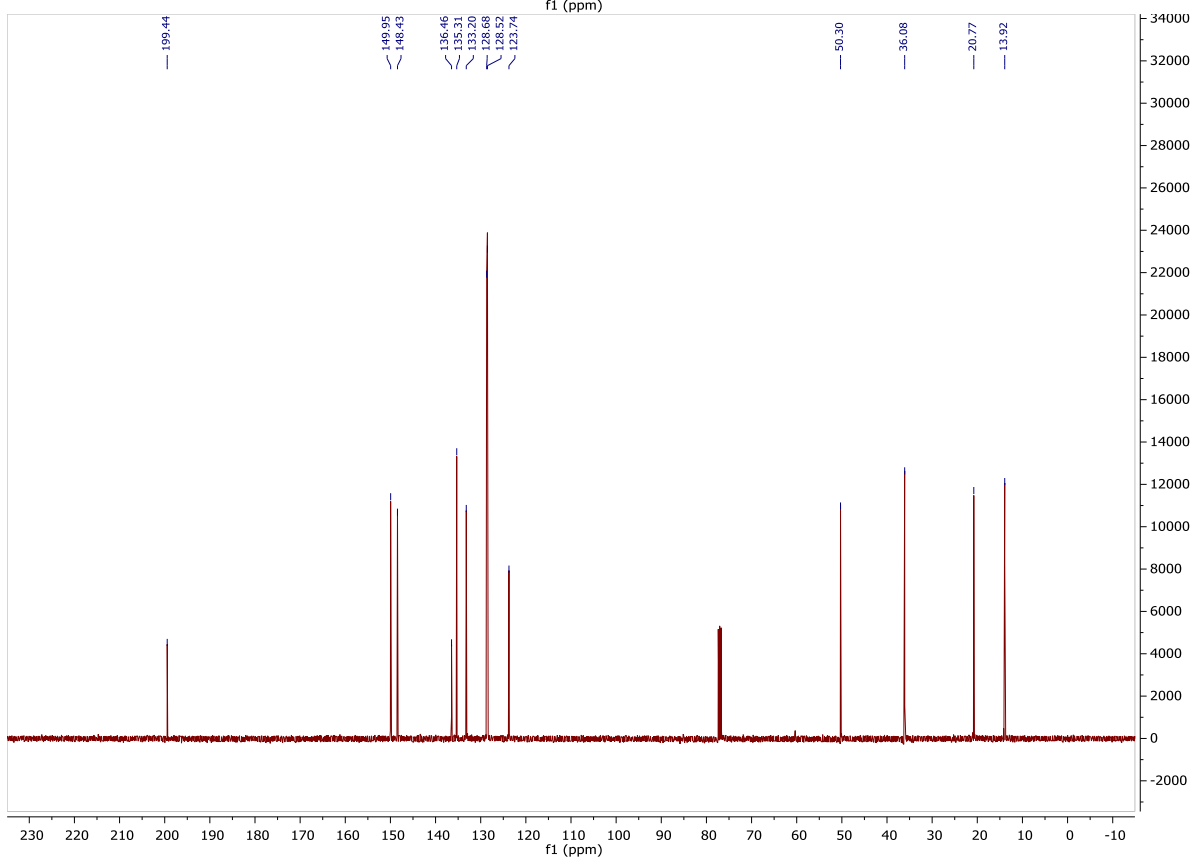
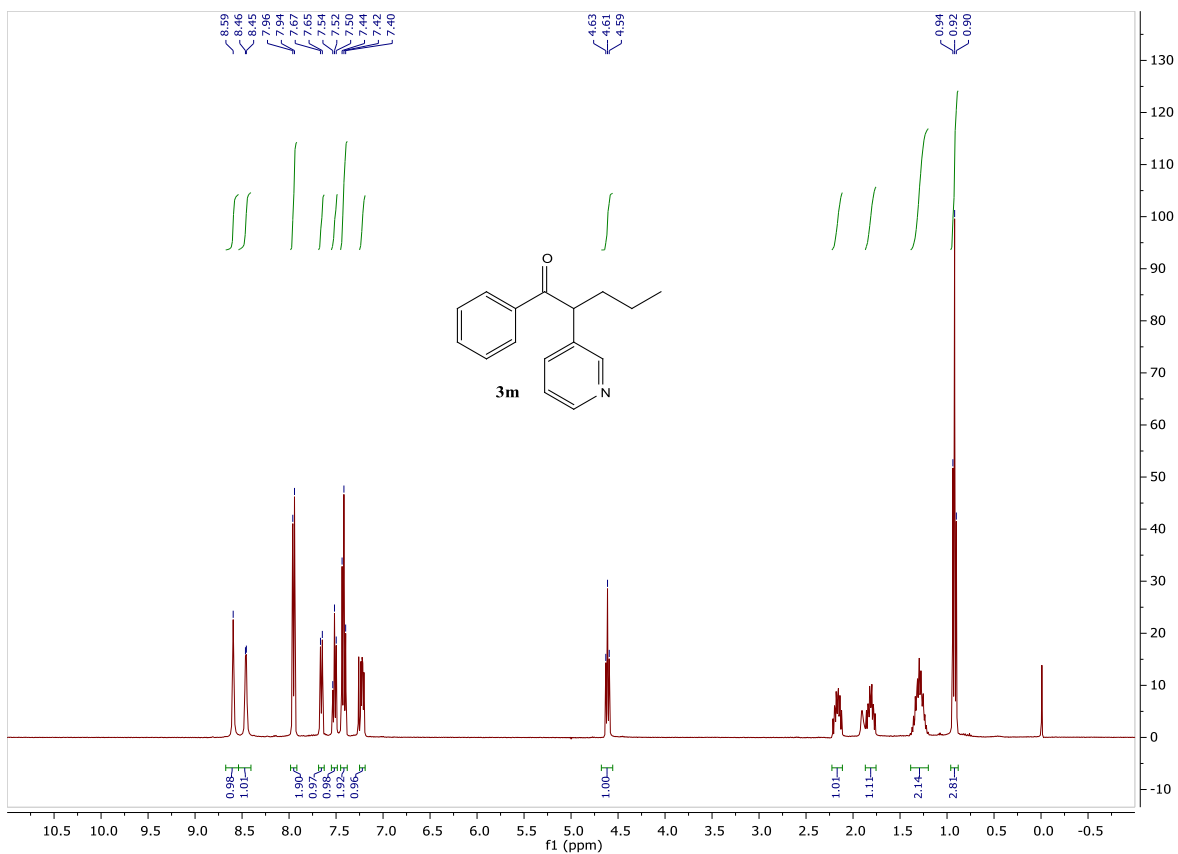


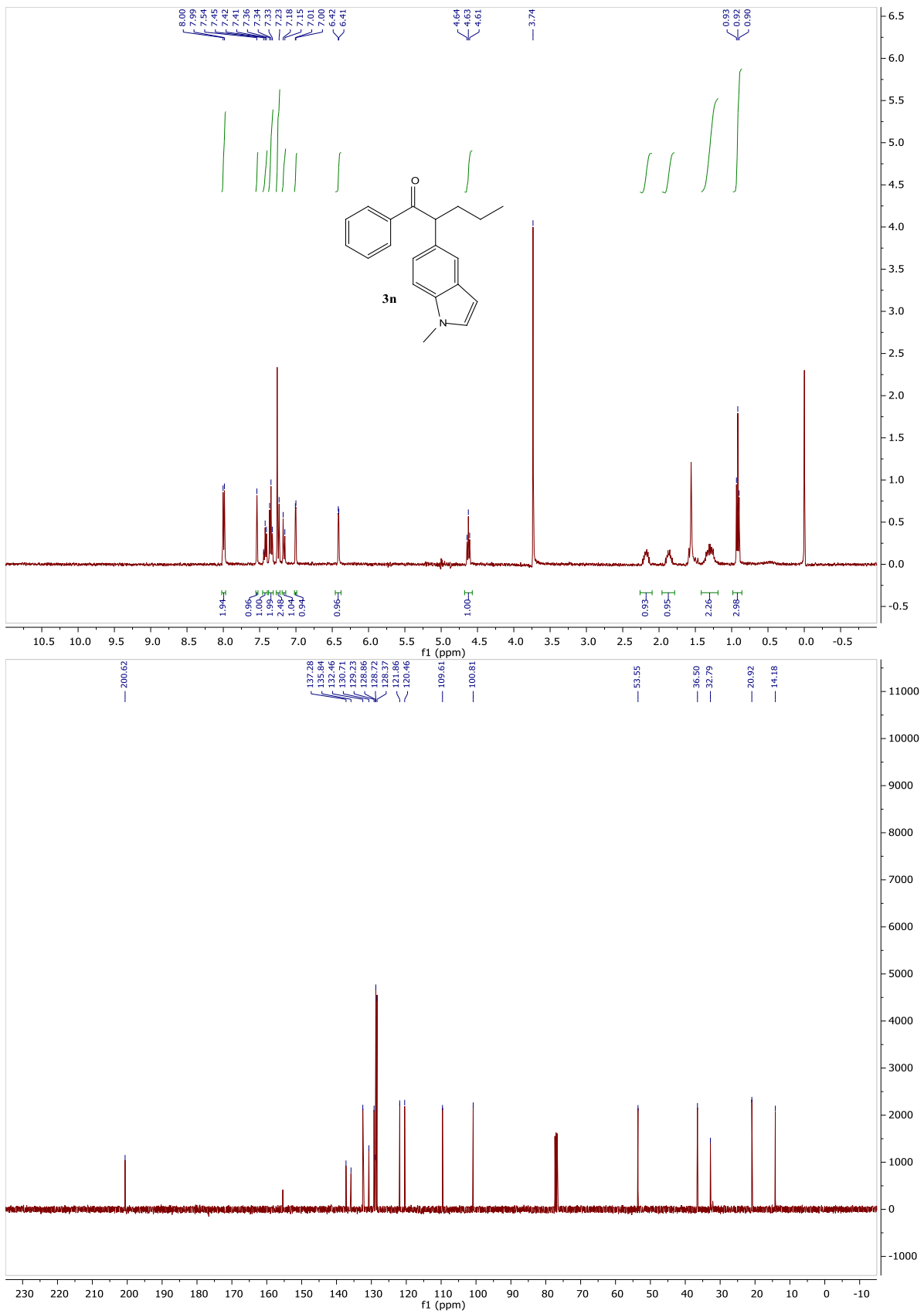


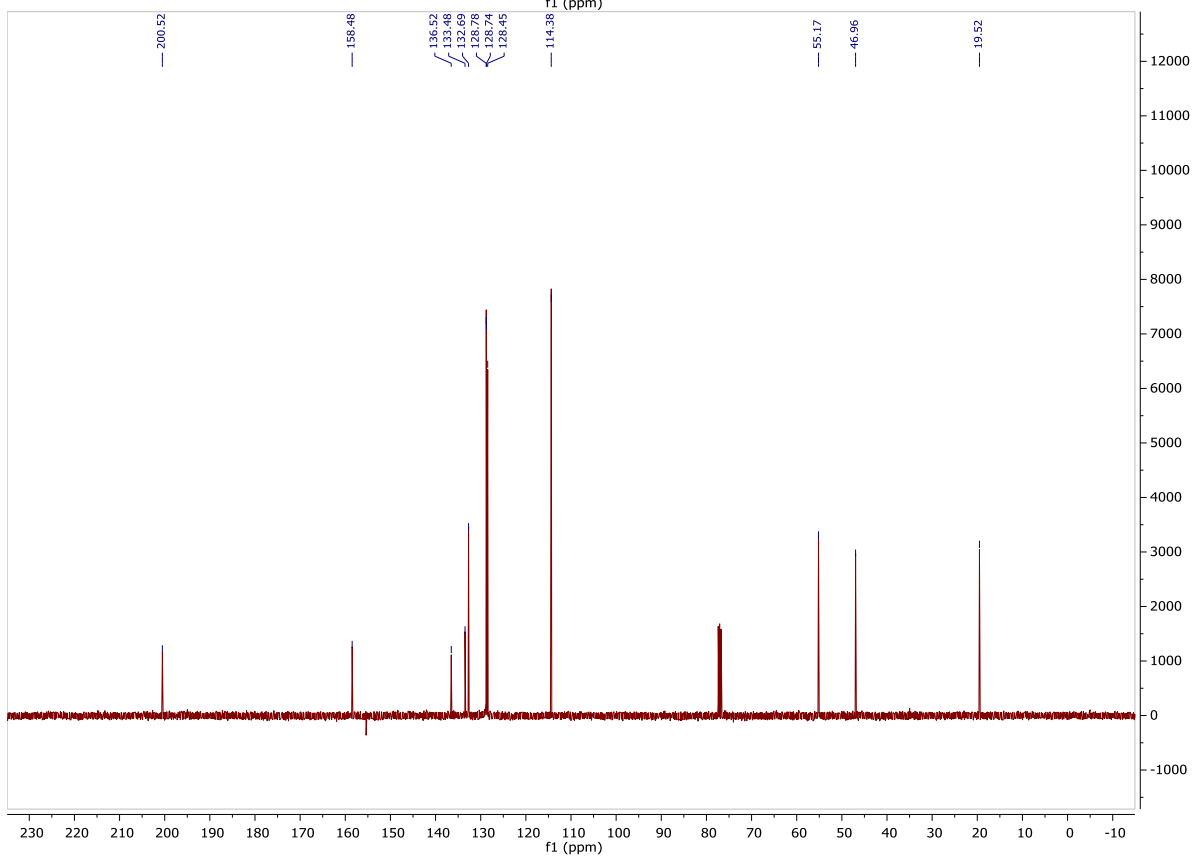
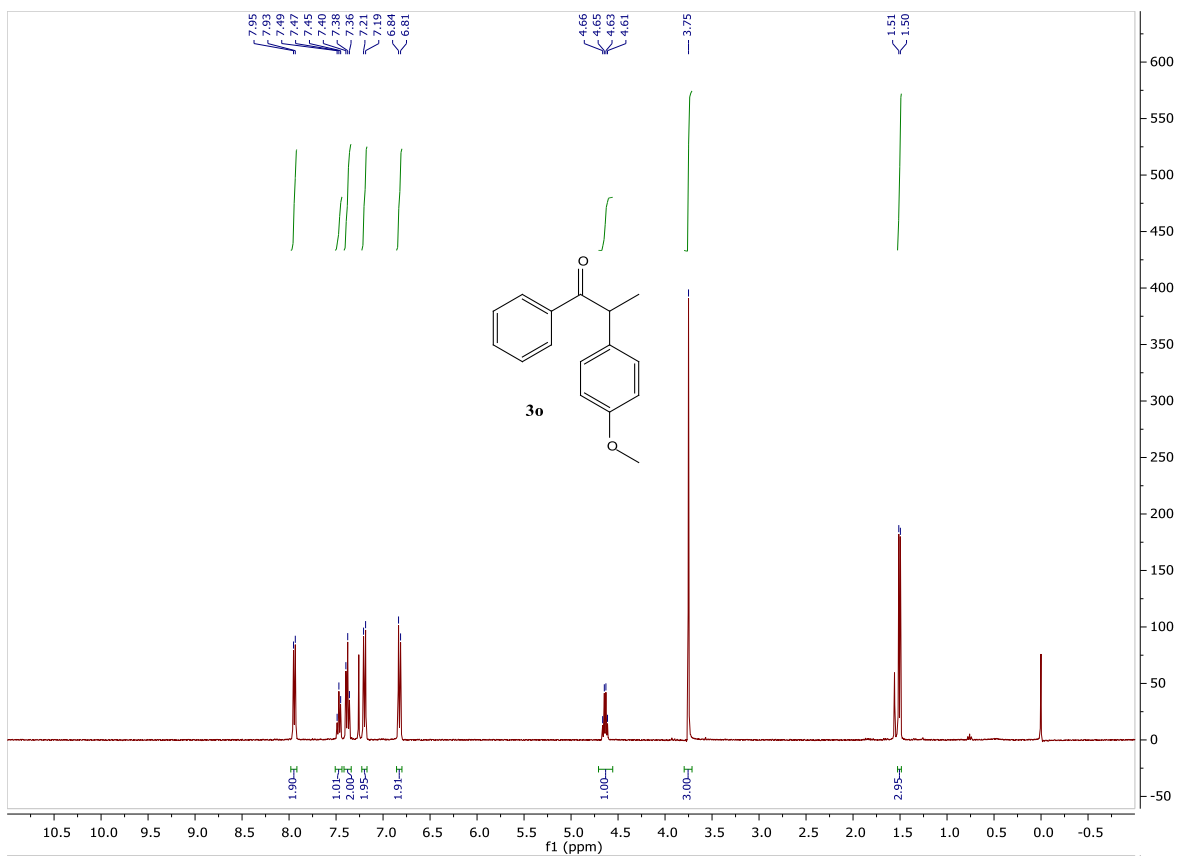


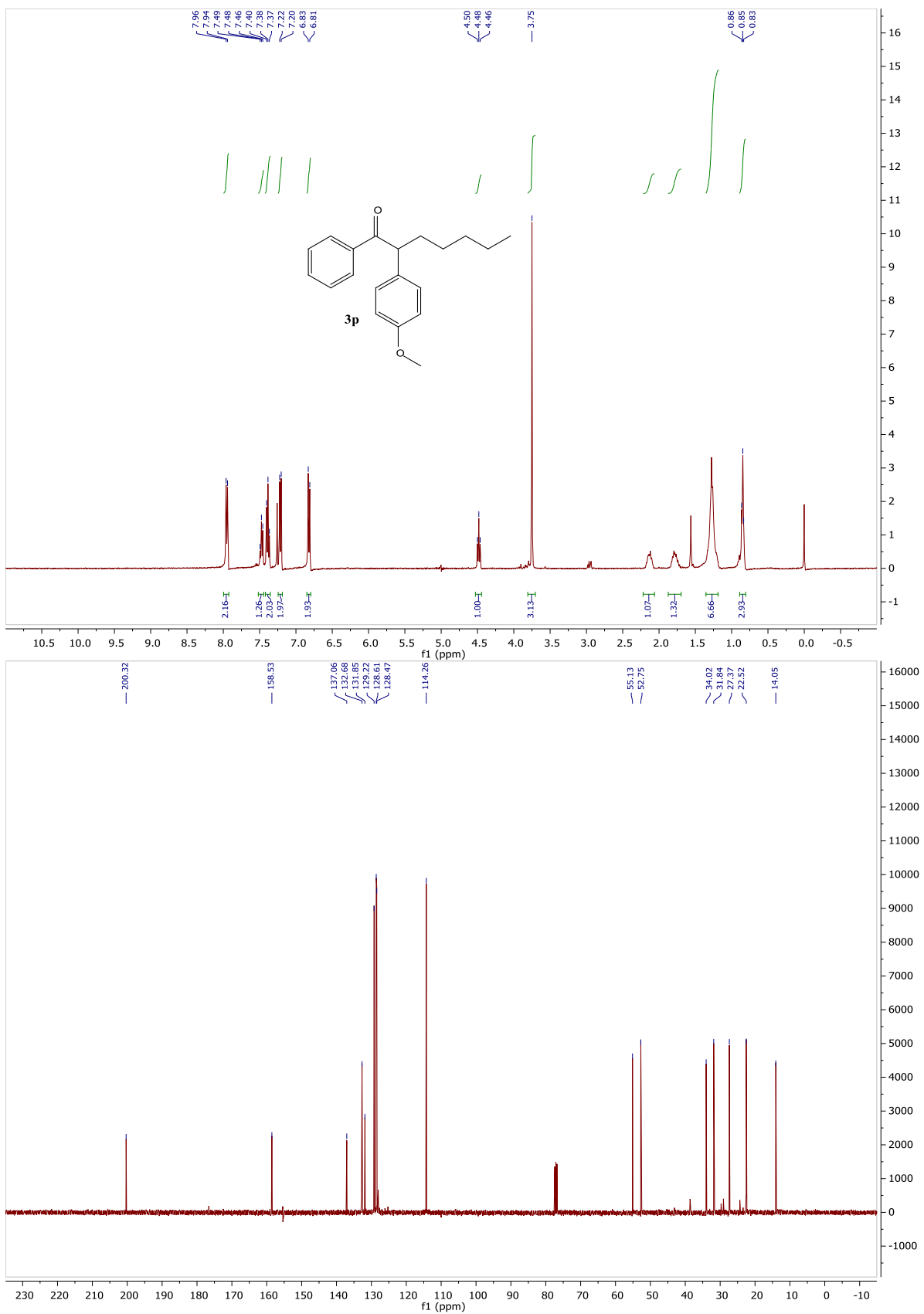


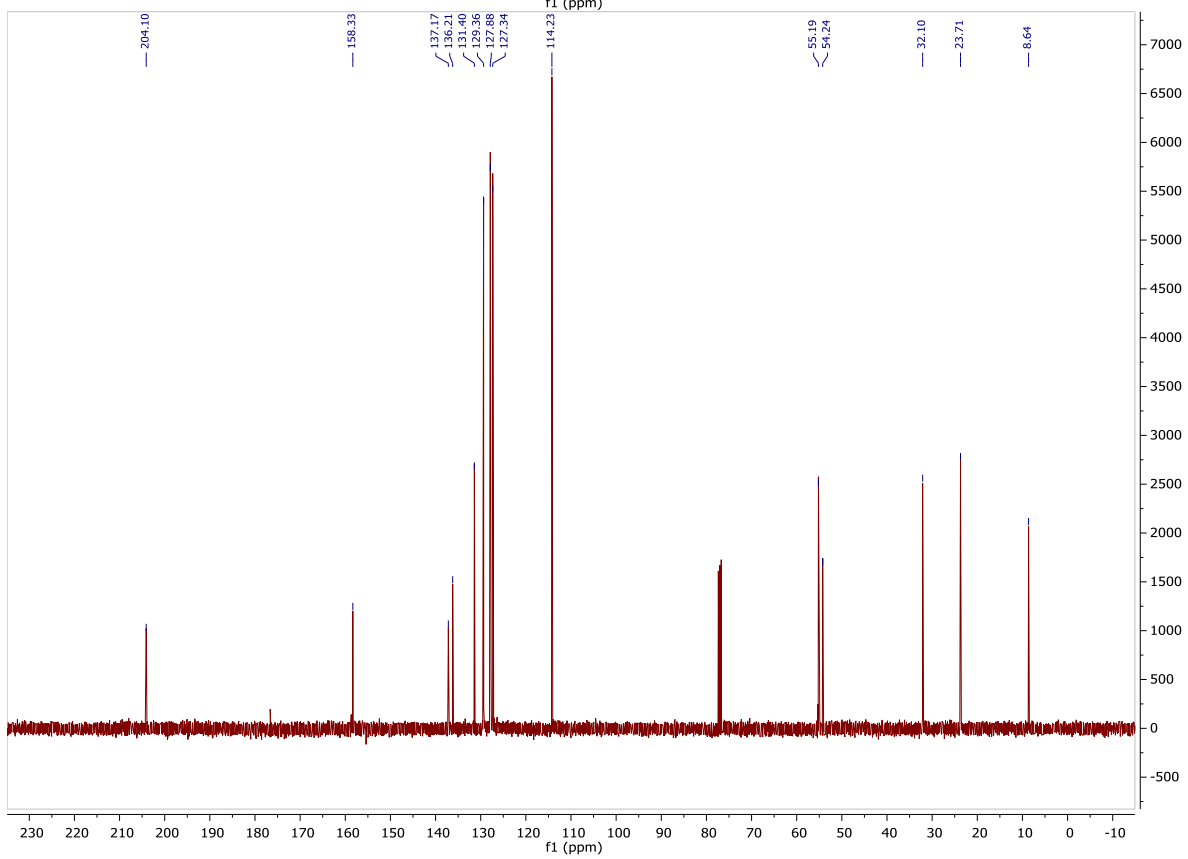
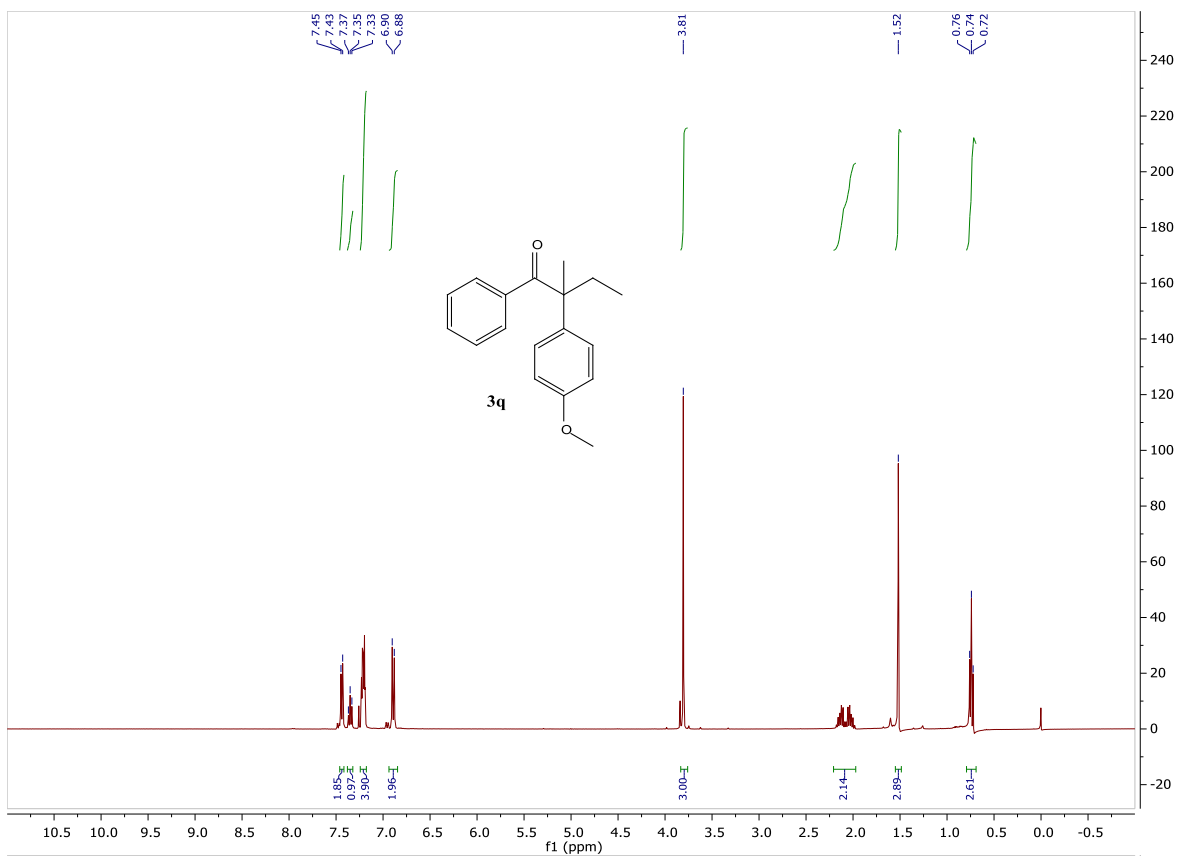


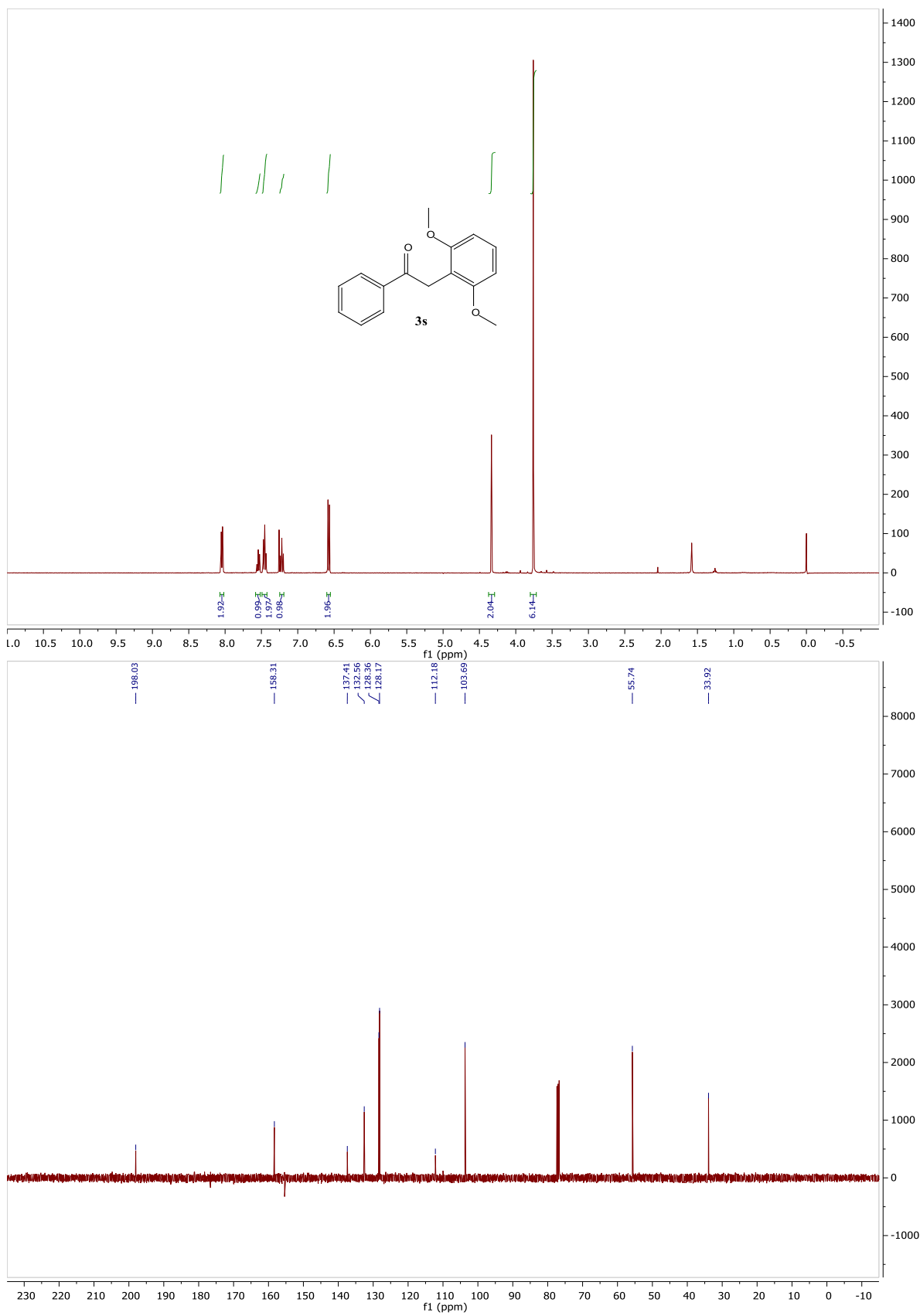


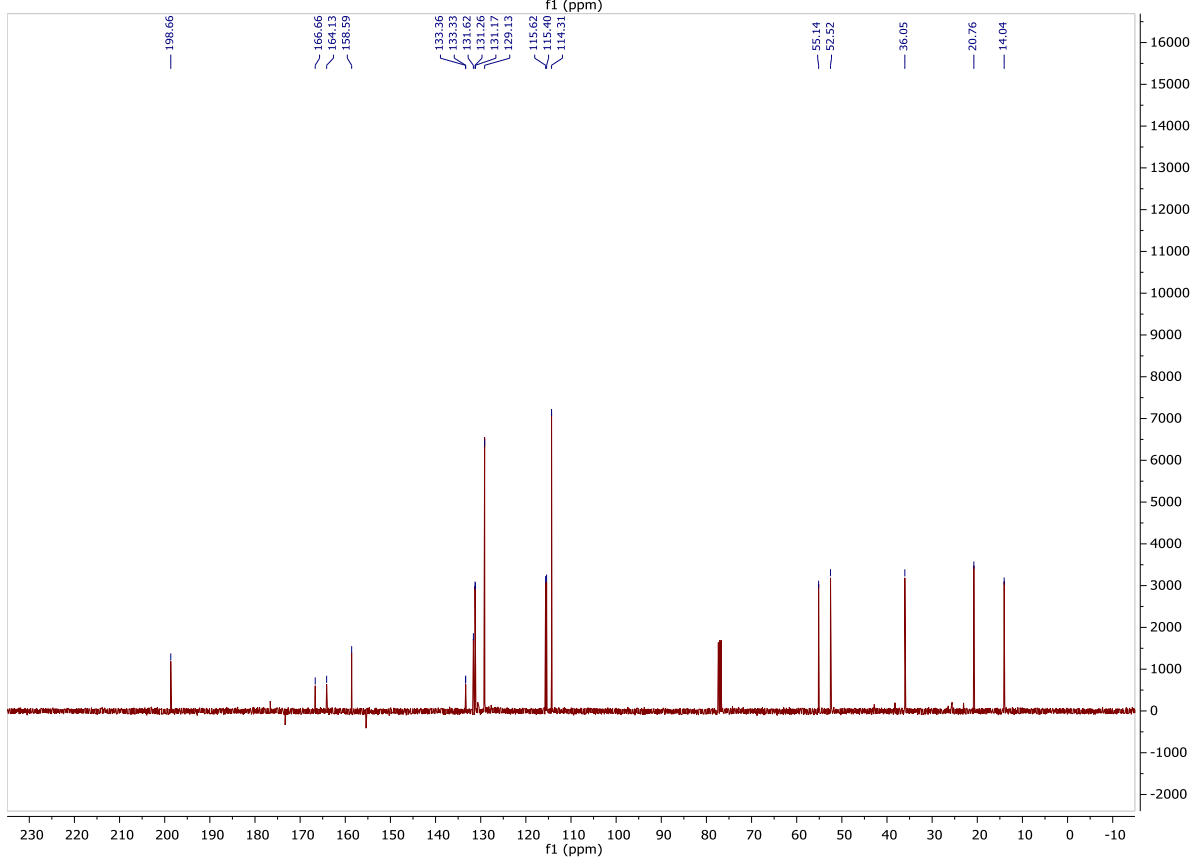
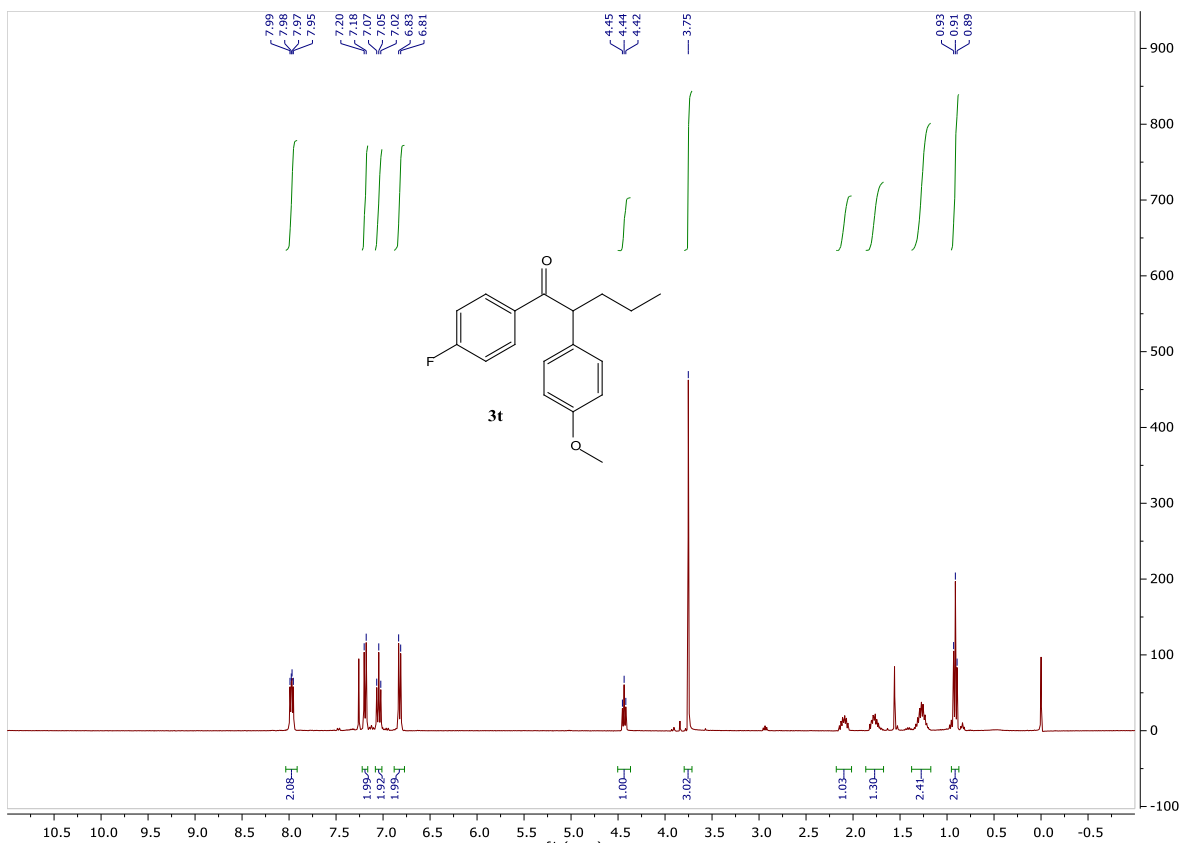


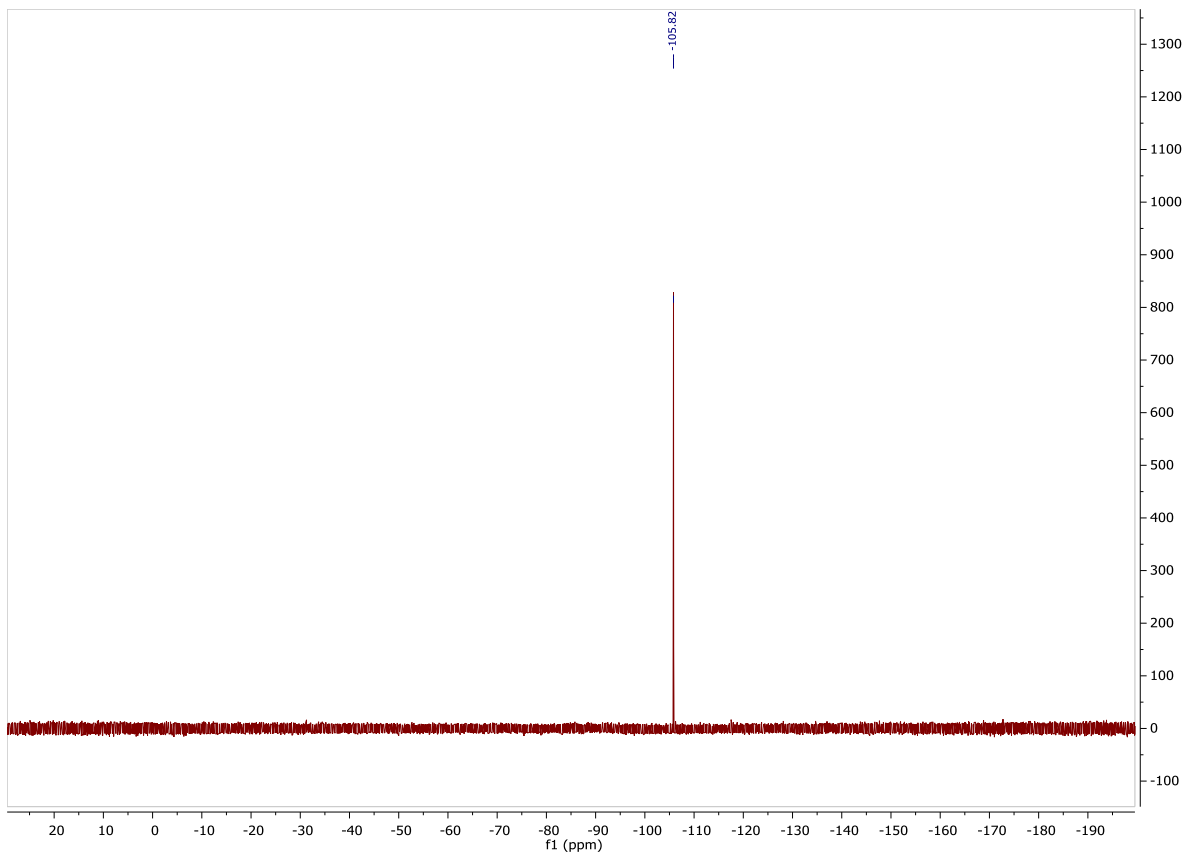


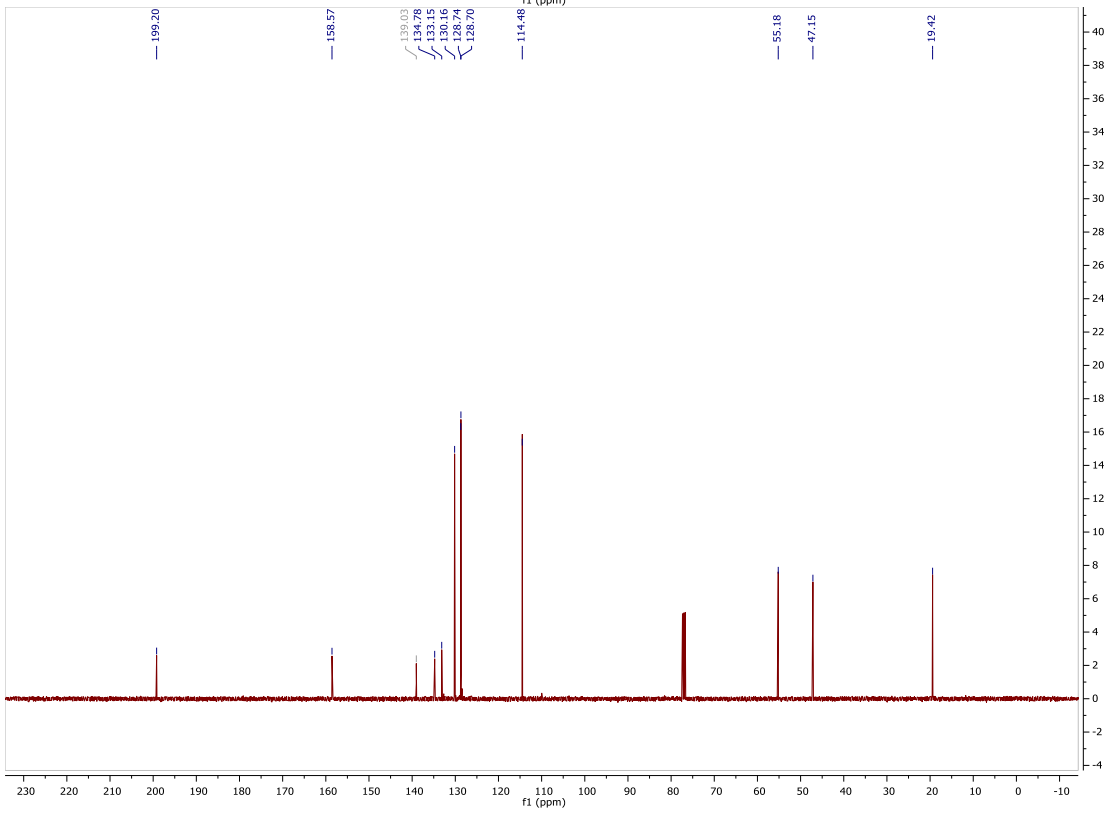
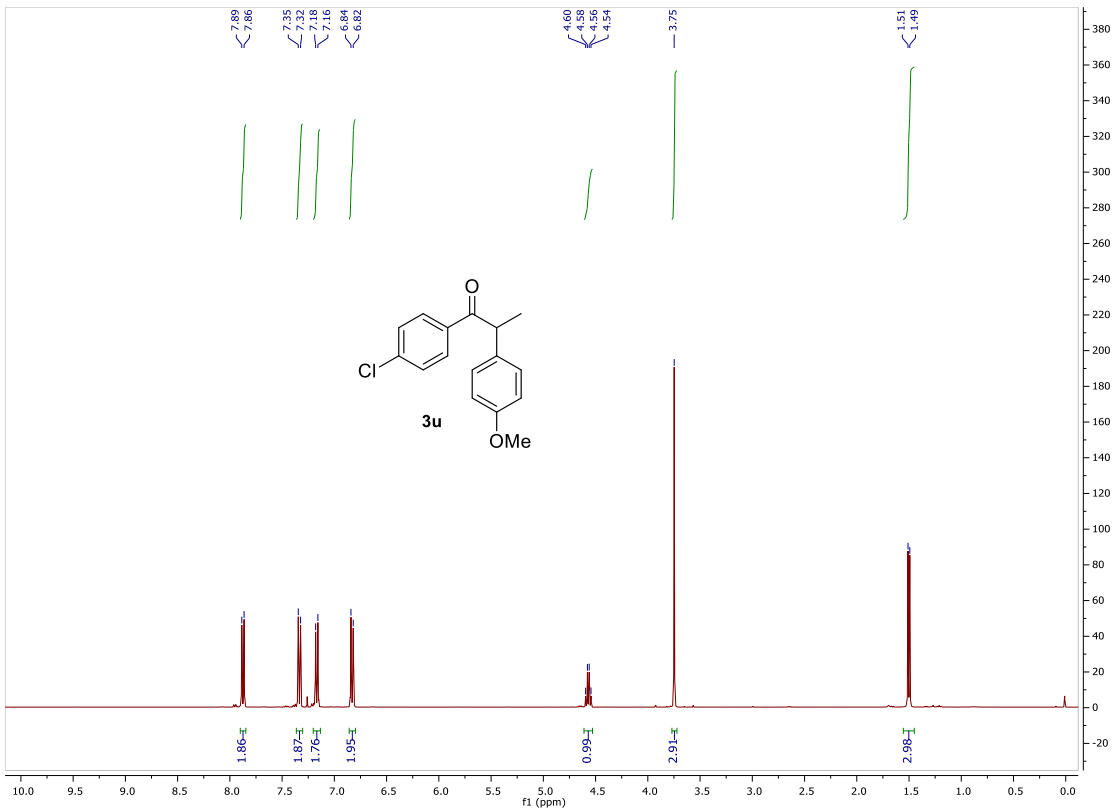


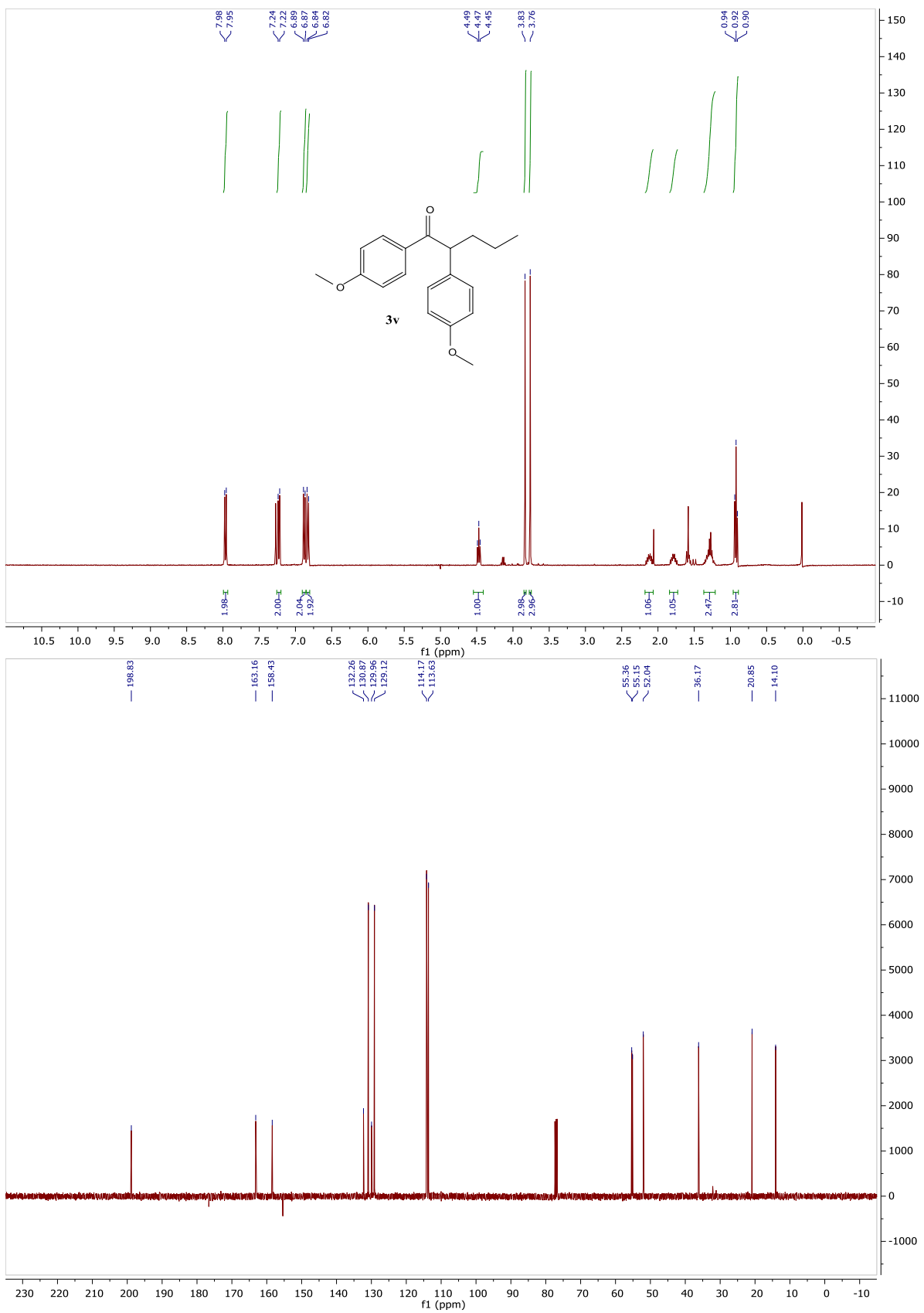












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