Cu-Catalyzed Hydrocarbonylative C-C Coupling of Terminal Alkynes with Alkyl Iodides

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Supporting Information

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1. General Information

General Procedures. Reactions requiring anhydrous conditions were conducted in a N_2-filled glovebox or using standard Schlenk line techniques. Reactions at greater than atmospheric pressure were conducted in a Parr 4621 General Purpose Pressure Reactor. A fitted, aluminum insert was custom-made for the Parr reactor that could hold up to eight 22-mL scintillation vials for running reactions in parallel. Thin layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates (0.25 mm) and visualised by UV light (254 nm) or 2,4-DNPH stain (12 g of 2,4-dinitrophenylhydrazine, 60 mL of conc. H_2SO_4, 80 mL of water in 200 mL of 95% EtOH). Purification of compounds was achieved by column chromatography using Merck Flash Silica Gel 60 (230-400 mesh). Organic solutions were concentrated under reduced pressure using a rotary evaporator.

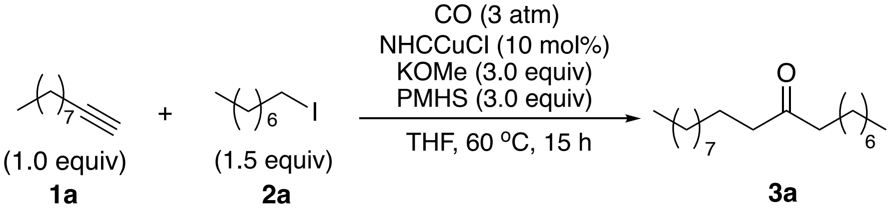
Materials. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. Common commercial reagents were purchased from Sigma-Aldrich, Fisher Scientific or VWR International Co. without further purification unless otherwise noted. Solvents were dried using a Glass Contour Solvent System built by Pure Process Technology, LLC. CO gas was purchased from Praxair at a purity of 99.99% (4.0RS research grade) and used directly from the cylinder. PMHS (poly(methylhydrosiloxane) was purchased from Sigma-Aldrich with an average M_n at 1,700-3,200. IPrCuCl,[1] SIPrCuCl,[2] IMesCuCl,[1] SIMesCuCl,[2] ^{Me}IPrCuCl,[3] ^{Cl}IPrCuCl[3] and I^{t}BuCuCl[2] were prepared according to literature procedures.

Instrumentation. Nuclear Magnetic Resonance (NMR) spectra were recorded on BRUKER AV (400 MHz) or BRUKER AV (500 MHz) at 298 K. Chemical shifts (δ) are reported in ppm with the residual solvent signal as internal standard (chloroform at 7.26 and 77.00 ppm for ^{1}H and ^{13}C NMR spectroscopy, respectively). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; quin., quintet; m, multiplet; br., broad. Coupling constants were taken from the spectra directly and are uncorrected. ^{1}H and ^{13}C NMR provided are taken directly using material for which the yield is quoted, without further purification, and are representative of purity. FT-IR spectra were recorded on a Thermo Nicolet iS5 FT-IR. Absorptions are given in wavenumbers (cm^{-1}). HRMS (ESI) were measured with a Shimadzu LCMS-IT-TOF Mass Spectrometer.

2. General Procedure for Optimization

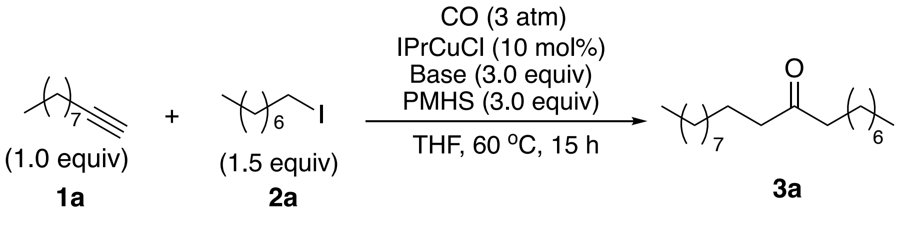
In a glovebox, base (0.3 mmol, 3.0 equiv) and THF (8.0 mL) were added to a 20-mL vial with a 1.5 cm stir bar. The copper catalyst was dissolved in THF (0.5 mL) and transferred to the above mixture. The mixture was stirred at room temperature for 5 min before silane and 1-decyne (0.1 mmol) were added sequentially. After the bright yellow solution turned to colorless, 1-iodooctane (0.15 mmol, 1.5 equiv) was added. The vial was then placed in an aluminum rack within a Parr pressure reactor. Next, the reactor was closed and taken out of the glovebox. A CO gas cylinder with a pressure regulator was connected to the reactor. The reactor was pressurized with CO gas and released after 5 min. This procedure was repeated three times, after which the reaction heated to 60 °C with a stir rate at 1300 rpm. After 15 h, the reaction was cooled to room temperature and the CO gas was released. Methanol (1.0 mL) was added to the vial and the solvent was removed under reduced pressure. The residue was diluted with Et_2O and the mixture then filtered through a pad of silica gel (a pipette with about 5 cm silica gel). The filtrate was concentrated under reduced pressure. The residue was dissolved in $CDCl_3$ and $(CHCl_2)_2$ (0.1 mmol) was added as internal standard for ^1H NMR analysis.

Table S1. Catalyst investigation



Entry	Catalyst	Yield of 3a (%)
1	IPrCuCl	49
2	SIPrCuCl	<5
3	IMesCuCl	0
4	SIMesCuCl	25
5	^{Me}IPrCuCl	21
6	^{Cl}IPrCuCl	35
7	I^{t}BuCuCl	<5

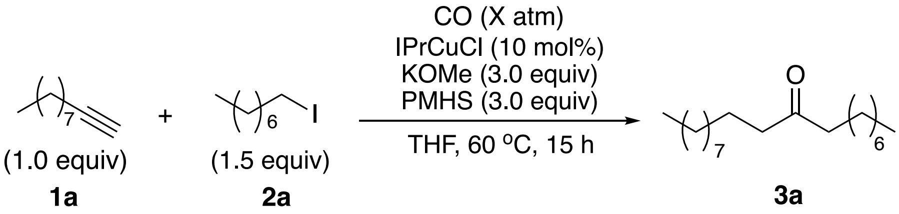
Table S2. Base investigation



Entry	Base	Yield of 3a (%)

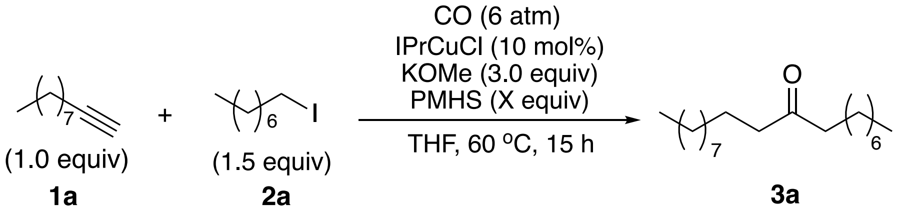
1	KOMe	49
2	NaOMe	0
3	LiOMe	9
4	KO^{t}Bu	0
5	NaO^{t}Bu	0
6	LiO^{t}Bu	12
7	PhONa	0

Table S3. CO pressure investigation



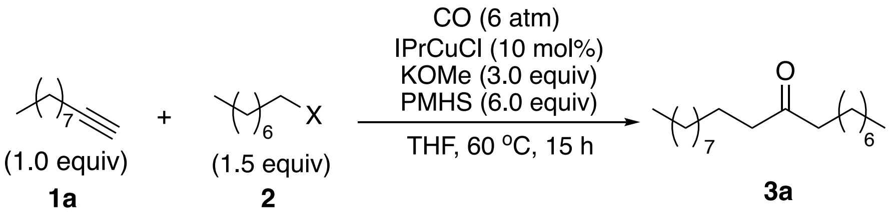
Entry	X =	Yield of 3a (%)
1	3	49
2	6	60
3	10	59

Table S4. Amount of PMHS investigation



Entry	X =	Yield of **3a** (%)
1	3.0	60
2	4.0	66
3	5.0	71
4	6.0	85

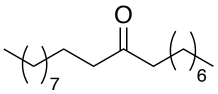
Table S5. Electrophiles investigation



Entry	X =	Yield of **3a** (%)
1	I	85
2	Br	0
3	Cl	0
4	OTf	0
5	OTs	0

3. General Procedure for Synthesis Dialkyl Ketones

In a glovebox, KOMe (42 mg, 0.6 mmol, 3.0 equiv) and THF (8.0 mL) were added to a 20-mL vial with a 1.5 cm stir bar. The IPrCuCl (9.6 mg, 0.02 mmol, 10 mol%) was dissolved in THF (0.5 mL) and transferred to the above mixture. The mixture was stirred at room temperature for 5 min before PMHS (72 μL, 1.2 mmol, 6.0 equiv) and alkyne (0.2 mmol) were added sequentially at room temperature. After the bright yellow solution turned to colorless, alkyl iodide (0.3 mmol, 1.5 equiv) was added. The vial was then placed in an aluminum rack within a Parr pressure reactor. Next, the reactor was closed and taken out of the glovebox. A CO gas cylinder with a pressure regulator was connected to the reactor. The reactor was pressurized with CO gas to 6 atm and released after 5 min. This procedure was repeated three times, after which the reaction heated to 60 °C with a stir rate at 1300 rpm. After 15 h, the reaction was cooled to room temperature and the CO gas was released. Then methanol (1.0 mL) was added to the vial and the solvent was removed under reduced pressure. The residue was diluted with Et_2O and filtered through a pad of silica gel (a pipette with about 5 cm silica gel). The filtrate was concentrated under reduced pressure and the residue was purified by silica gel chromatography (hexane/ethyl acetate) to afford the corresponding ketones.



Nonadecan-9-one (3a).[4] Prepared according to general procedure using 1-decyne (36 μL, 0.2 mmol), 1-iodooctane (54 μL, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 50:1) to afford the title compound as a white solid (41 mg, 72% yield).

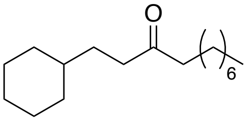
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (t, *J* = 7.4 Hz, 4H), 1.54 – 1.56 (m, 4H), 1.25 (brs, 24H), 0.88 (d, *J* = 6.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 211.7, 42.8, 31.9, 31.8, 29.6, 29.5, 29.4, 29.4, 29.3, 29.1, 23.9, 22.7, 22.6, 14.1.

IR (neat) 2955, 2919, 2849, 1705, 1462, 1378, 1095, 719 cm^{-1}.

HRMS (ESI) Calcd. for $C_{19}H_{39}O$ ([M+H]$^+$): 283.2996; Found: 283.2995.

1.0 mmol Scale: In a glovebox, KOMe (0.21 g, 3.0 mmol, 3.0 equiv) and THF (6.0 mL) were added to a 20-mL vial with a 1.5 cm stir bar. The IPrCuCl (48.7 mg, 0.1 mmol, 10 mol%) was dissolved in THF (2 mL) and transferred to the above mixture. The mixture was stirred at room temperature for 5 min before PMHS (0.36 mL, 6.0 mmol, 6.0 equiv) and 1-decyne (0.18 mL, 1.0 mmol) were added sequentially at room temperature. After the bright yellow solution turned to colorless, 1-iodooctane (0.27 mL, 1.5 mmol, 1.5 equiv) was added. The vial was then placed in an aluminum rack within a Parr pressure reactor. Next, the reactor was closed and taken out of the glovebox. A CO gas cylinder with a pressure regulator was connected to the reactor. The reactor was pressurized with CO gas to 6 atm and released after 5 min. This procedure was repeated three times, after which the reaction heated to 60 °C with a stir rate at 1300 rpm. After 15 h, the reaction was cooled to room temperature and the CO gas was released. Then the reaction mixture was diluted with H_2O (25 mL) and Et_2O (50 mL). The organic phase was separated and the aqueous phase was extracted twice with Et_2O (20 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and then concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc = 30:1) to afford **3a** as a white solid (0.2 g, 71% yield).



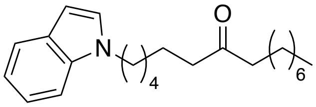
1-Cyclohexylundecan-3-one (3b). Prepared according to general procedure using cyclohexylacetylene (26 μL, 0.2 mmol), 1-iodooctane (54 μL, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 50:1) to afford the title compound as a colorless oil (41 mg, 82% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.40 – 2.36 (m, 4H), 1.69 – 1.62 (m, 6H), 1.58–1.52 (m, 2H), 1.45 (dd, *J* = 15.1, 7.1 Hz, 2H), 1.26 (brs, 15H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 212.0, 42.8, 40.3, 37.3, 33.1, 31.8, 31.2, 29.4, 29.3, 29.1, 26.5, 26.2, 23.9, 22.6, 14.1.

IR (neat) 2920, 2851,1713, 1449, 1268, 1124, 772 cm^{-1}.

HRMS (ESI) Calcd. for $C_{17}H_{33}O$ ([M+H]$^+$): 253.2526; Found: 253.2530.



1-(1*H*-indol-1-yl)pentadecan-7-one (3c). Prepared according to general procedure using 1-(hex-

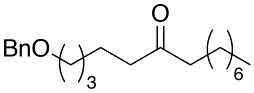
5-yn-1-yl)-1*H*-indole (40 mg, 0.2 mmol), 1-iodooctane (54 μL, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 10:1) to afford the title compound as a colorless oil (48 mg, 71% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.65 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.13-7.10 (m, 2H), 6.51 (d, *J* = 3.0 Hz, 1H), 4.12 (t, *J* = 7.1 Hz, 2H), 2.37 (td, *J* = 7.4, 2.9 Hz, 4H), 1.92 – 1.80 (m, 2H), 1.63 – 1.51 (m, 4H), 1.33-1.30 (m, 14H), 0.91 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 211.3, 135.9, 128.5, 127.7, 121.2, 120.9, 119.1, 109.3, 100.8, 46.2, 42. 8, 42.4, 31.8, 30.0, 29.3, 29.2, 29.1, 28.7, 26.7, 23.8, 23.5, 22.6, 14.1.

IR (neat) 2924, 2854, 1711, 1463, 1400, 1121, 1055, 763, 737 cm^{-1}.

HRMS (ESI) Calcd. for $C_{23}H_{36}NO$ ([M+H]$^+$): 342.2792; Found: 342.2793.



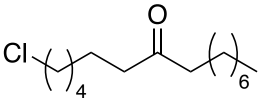
1-(Benzyloxy)tetradecan-6-one (3d). Prepared according to general procedure using 5-benzyloxy-1-pentyne (35 mg, 0.2 mmol), 1-iodooctane (54 μL, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 15:1) to afford the title compound as a colorless oil (48 mg, 75% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35 – 7.27 (m, 4H), 4.49 (s, 2H), 3.46 (t, *J* = 6.5 Hz, 2H), 2.38 (dt, *J* = 10.5, 7.5 Hz, 4H), 1.66 – 1.53 (m, 6H), 1.41 – 1.33 (m, 2H), 1.28 (d, *J* = 14.3 Hz, 10H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 211.4, 138.6, 128.3, 127.6, 127.5, 72.9, 70.1, 42.8, 42.6, 31.8, 29.5, 29.3, 29.2, 29.1, 25.83, 23.9, 23.6, 22.6, 14.1.

IR (neat) 2925, 2854, 1712, 1454, 1363, 1101, 910, 731, 697 cm^{-1}.

HRMS (ESI) Calcd. for $C_{21}H_{35}O_2$ ([M+H]$^+$): 319.2632; Found: 319.2625.



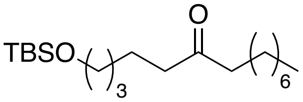
1-Chloropentadecan-7-one (3e). Prepared according to general procedure using 6-chloro-1-hexyne (24 μL, 0.2 mmol), 1-iodooctane (54 μL, 0.3 mmol) and PMHS (18 μL, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 30:1) to afford the title compound as a colorless oil (38 mg, 72% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 3.52 (t, *J* = 6.7 Hz, 2H), 2.41-2.36 (m, 4H), 1.83 – 1.71 (m, 2H), 1.61-1.55 (m, 4H), 1.50 – 1.40 (m, 2H), 1.32 – 1.23 (m, 12H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 211.4, 45.0, 42.9, 42.5, 32.4, 31.8, 29.4, 29.3, 29.1, 28.4, 26.6, 23.9, 23.6, 22.6, 14.1.

IR (neat) 2925, 2854, 1712, 1463, 1374, 724, 651 cm^{-1}.

HRMS (ESI) Calcd. for $C_{15}H_{30}ClO$ ([M+H]$^+$): 261.1980; Found: 261.1982.



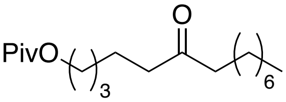
1-((*tert*-Butyldimethylsilyl)oxy)tetradecan-6-one (3f). Prepared according to general procedure using 1-(tert-butyldimethylsilyloxy)-4-pentyne (40 mg, 0.2 mmol), 1-iodooctane (54 μL, 0.3 mmol). This reaction was performed at room temperature. The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 30:1) to afford the title compound as a colorless oil (48 mg, 70% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 3.59 (t, *J* = 6.5 Hz, 2H), 2.38 (app q, *J* = 7.2 Hz, 4H), 1.60 – 1.49 (m, 6H), 1.32 – 1.24 (m, 12H), 0.88 – 0.86 (m, 12H), 0.04 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 211.5, 63.0, 42.8, 42.7, 32.6, 31.8, 29.4, 29.3, 29.1, 25.9, 25.5, 23.9, 23.7, 22.6, 18.3, 14.1, -5.3.

IR (neat) 2927, 2855, 1716, 1463, 1268, 1254, 1097, 834 cm^{-1}.

HRMS (ESI) Calcd. for $C_{20}H_{43}O_2Si$ ($[M+H]^+$): 343.3027; Found: 343.3031.



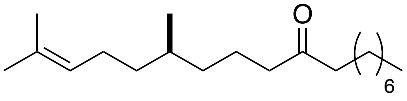
6-Oxotetradecyl pivalate (3g). Prepared according to general procedure using pent-4-yn-1-yl 2,2-dimethylpropanoate (34 mg, 0.2 mmol), 1-iodooctane (54 μL, 0.3 mmol). This reaction was performed at room temperature for 15 h. The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 20:1) to afford the title compound as a colorless oil (32 mg, 51% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 4.03 (t, *J* = 6.6 Hz, 2H), 2.41-2.35 (m, 4H), 1.68 – 1.48 (m, 6H), 1.38 – 1.23 (m, 12H), 1.18 (s, 9H), 0.86 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 211.2, 178.6, 64.1, 42.8, 42.5, 31.8, 29.3, 29.2, 29.1, 28.5, 27.2, 25.6, 23.9, 23.4, 22.6, 14.1.

IR (neat) 2926, 2855, 1727, 1460, 1283, 1151, 771 cm^{-1}.

HRMS (ESI) Calcd. for $C_{19}H_{37}O_3$ ($[M+H]^+$): 313.2737; Found: 313.2738.



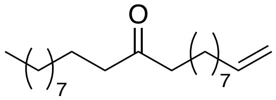
(±)-13,17-Dimethyloctadec-16-en-9-one (3h). Prepared according to general procedure using (±)-4,8-dimethylnon-7-en-1-yne (30 mg, 0.2 mmol), 1-iodooctane (54 μL, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 30:1) to afford the title compound as a colorless oil (44 mg, 74% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 5.09 (t, *J* = 6.8 Hz, 1H), 2.39 – 2.35 (m, 4H), 1.98 – 1.93 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.56 – 1.52 (m, 2H), 1.42 – 1.38 (m, 1H), 1.27 (br, 14H), 1.17 – 1.05 (m, 2H), 0.87 (t, *J* = 6.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 211.7, 131.1, 124.9, 43.1, 42.8, 36.9, 36.5, 32.3, 31.8, 29.4, 29.3, 29.1, 25.7, 25.5, 23.9, 22.6, 21.4, 19.4, 17.6, 14.1.

IR (neat) 2954, 2923, 2853, 1714, 1456, 1376, 723 cm^{-1}.

HRMS (ESI) Calcd. for $C_{20}H_{39}O$ ($[M+H]^+$): 295.2996; Found: 295.3001.

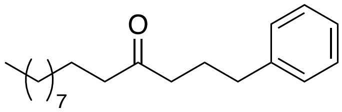


Henicos-1-en-11-one (3i). Prepared according to general procedure using 1-decyne (36 μL, 0.2 mmol), 10-iodo-1-decene (80 mg, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 30:1) to afford the title compound as a white solid (49 mg, 80% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 4.98 (dd, *J* = 17.1, 1.7 Hz, 1H), 4.92 (d, *J* = 10.2 Hz, 1H), 2.37 (t, *J* = 7.5 Hz, 4H), 2.03 (dd, *J* = 14.3, 6.9 Hz, 2H), 1.59 – 1.50 (m, 4H), 1.38-1.35 (m, 2H), 1.29 – 1.23 (m, 22H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 211.7, 139.2, 114.1, 42.8 (two C), 33.8, 31.9, 29.6, 29.5, 29.4, 29.3 (two C), 29.1, 28.9, 23.9 (two C), 22.7, 14.1.

IR (neat) 2957, 2916, 2848, 1704, 1635, 1471, 1461, 1380, 1111, 911, 728, 719 cm^{-1}.



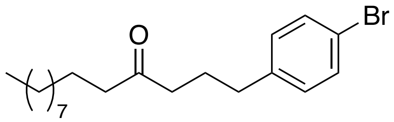
1-Phenyltetradecan-4-one (3j). Prepared according to general procedure using 1-decyne (36 μL, 0.2 mmol), 1-iodo-3-phenylpropan (48 μL, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 20:1) to afford the title compound as a colorless oil (39 mg, 68% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.27 (m, 2H), 7.21 – 7.16 (m, 3H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.41 (t, *J* = 7.3 Hz, 2H), 2.36 (t, *J* = 14.9, 7.5 Hz, 2H), 1.95 – 1.87 (m, 2H), 1.56 – 1.53 (m, 2H), 1.26 (brs, 14H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 211.1, 141.7, 128.4, 128.3, 128.2, 125.9, 125.6, 42.9, 41.8, 35.1, 31.9, 29.5, 29.5, 29.4, 29.3, 29.2, 25.2, 23.8, 22.7, 14.1.

IR (neat) 3026, 2922, 2853, 1712, 1454, 733, 698 cm^{-1}.

HRMS (ESI) Calcd. for $C_{20}H_{33}O$ ($[M+H]^+$): 289.2526; Found: 289.2511.



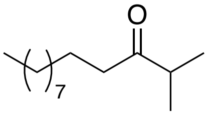
1-(4-Bromophenyl)tetradecan-4-one (3k). Prepared according to general procedure using 1-decyne (36 μL, 0.2 mmol), 1-bromo-4-(3-iodopropyl)benzene (98 mg, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 20:1) to afford the title compound as a colorless oil (54 mg, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.3 Hz, 2H), 7.04 (d, *J* = 8.1 Hz, 2H), 2.56 (t, *J* = 7.6 Hz, 2H), 2.41 – 2.34 (m, 4H), 1.94 – 1.80 (m, 2H), 1.59-1.51 (m, 2H), 1.25 (brs, 14H), 0.88 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 210.9, 140.6, 131.4, 130.2, 119.7, 42.9, 41.6, 34.5, 31.9, 29.5, 29.5, 29.4, 29.3, 29.2, 25.0, 23.8, 22.7, 14.1.

IR (neat) 3024, 2915, 2848, 1704, 1488, 1377, 1072, 799, 727 cm^{-1}.

HRMS (ESI) Calcd. for $C_{20}H_{32}BrO$ ($[M+H]^+$): 367.1631; Found: 367.1629.



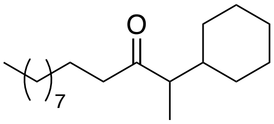
2-Methyltridecan-3-one (3l).[5] Prepared according to general procedure using 1-decyne (36 μL, 0.2 mmol), 2-iodopropane (30 μL, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 50:1) to afford the title compound as a colorless oil (27 mg, 64% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.65 – 2.55 (m, 1H), 2.43 (t, *J* = 6.8 Hz, 2H), 1.53 – 1.56 (m, 2 H), 1.25 (brs, 14H), 1.08 (dd, *J* = 6.9, 1.2 Hz, 6H), 0.87 (t, *J* = 6.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 215.1, 40.8, 40.4, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 23.8, 22.7, 18.3, 14.1.

IR (neat) 2922, 2853, 1713, 1465, 1380, 1026, 721 cm^{-1}.

HRMS (ESI) Calcd. for $C_{14}H_{29}O$ ($[M+H]^+$): 213.2213; Found: 213.2220.



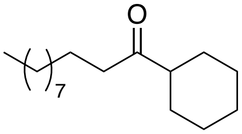
2-Cyclohexyltridecan-3-one (3m). Prepared according to general procedure using 1-decyne (36 μL, 0.2 mmol), (1-iodo)ethyl-cyclohexane (71 mg, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 50:1) to afford the title compound as a colorless oil (46 mg, 82% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39 (td, *J* = 7.2, 2.1 Hz, 2H), 2.32 (p, *J* = 7.2 Hz, 1H), 1.73 – 1.63 (m , 4H), 1.58 – 1.50 (m, 4H), 1.30 – 1.10 (m, 19H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 215.4, 52.2, 42.2, 40.1, 31.9, 31.8, 29.6, 29.5, 29.4, 29.3, 26.4, 26.3, 23.6, 22.7, 14.1, 13.3.

IR (neat) 2921, 2852, 1710, 1448, 1373, 733 cm^{-1}.

HRMS (ESI) Calcd. for $C_{19}H_{37}O$ ($[M+H]^+$): 281.2839; Found: 281.2837.



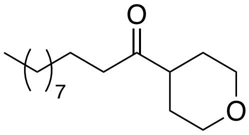
1-Cyclohexylundecan-1-one (3n).[6] Prepared according to general procedure using 1-decyne (36 μL, 0.2 mmol), 1-iodocyclohexane (39 μL, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 30:1) to afford the title compound as a colorless oil (45 mg, 90% yield).

^{1}H NMR (400 MHz, CDCl$_3$) δ 2.41 (t, J = 7.4 Hz, 2H), 2.33 (t, J = 10.6 Hz, 1H), 1.83 – 1.65 (m, 5H), 1.58 – 1.50 (m, 2H), 1.26 (brs, 19H), 0.88 (t, J = 6.6 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 214.5, 40.6, 31.9, 29.6, 29.5, 29.4, 29.3, 29.3, 28.5, 25.9, 25.7, 23.7, 22.7, 14.1.

IR (neat) 2922, 2852, 1708, 1449, 1374, 1145, 721 cm^{-1}.

HRMS (ESI) Calcd. for $C_{17}H_{33}O$ ([M+H]$^+$): 253.2526; Found: 253.2525.



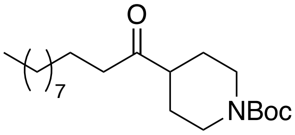
1-(Tetrahydro-2*H*-pyran-4-yl)undecan-1-one (3o). Prepared according to general procedure using 1-decyne (36 μL, 0.2 mmol), 4-iodotetrahydropyran (63 mg, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 10:1) to afford the title compound as a colorless oil (28 mg, 55% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 3.97 (d, J = 10.9 Hz, 2H), 3.40 (t, J = 11.2 Hz, 2H), 2.57 – 2.48 (m, 1H), 2.41 (t, J = 7.3 Hz, 2H), 1.73 – 1.63 (m, 4H), 1.55 – 1,51 (m, 2H), 1.23 (br, 14H), 0.85 (t, J = 6.7 Hz, 3H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 212.1, 67.2, 47.5, 40.2, 31.8, 29.5, 29.4, 29.4, 29.2, 28.1, 23.6, 22.6, 14.0.

IR (neat) 2922, 2851, 1708, 1466, 1128, 1093, 1019, 721 cm^{-1}.

HRMS (ESI) Calcd. for $C_{16}H_{31}O_2$ ([M+H]$^+$): 255.2319; Found: 255.2314.



***tert*-Butyl 4-undecanoylpiperidine-1-carboxylate (3p).** Prepared according to general procedure using 1-decyne (36 μL, 0.2 mmol), N-Boc-4-iodopiperidine (94 mg, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 5:1) to afford the title compound as a colorless oil (37 mg, 52% yield).

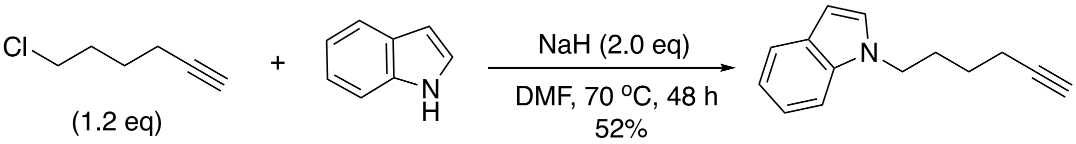
^{1}H NMR (500 MHz, CDCl$_3$) δ 4.08 (br, 2H), 2.75 (t, J = 11.4 Hz, 2H), 2.49 – 2.35 (m, 3H), 1.77 (br, 2H), 1.55 – 1.43 (m, 3H), 1.43 (s, 9H), 1.23 (br, 15H), 0.85 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 212.4, 154.6, 79.5, 48.5, 43.3, 40.6, 31.8, 29.5, 29.4, 29.4, 29.2, 28.4, 27.5, 23.6, 22.6, 14.1.

IR (neat) 2924, 2853, 1694, 1420, 1233, 1167, 1131, 769 cm^{-1}.

4. Preparation of Alkynes and Alkyl Iodides Substrates

Alkynes: 1-decyne was purchased from Sigma-Aldrich. Cyclohexylacetylene and 6-chloro-1-hexyne were purchased from Alfa Aesar.

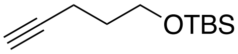


1-(Hex-5-yn-1-yl)-1*H*-indole. To a suspension of NaH (240 mg, 10.0 mmol) in DMF (5.0 mL) was added a solution of indole (585 mg, 5.0 mmol) in DMF (10 mL) at 0° C. The resulting reaction mixture was stirred at 0° C for 10 min, then at room temperature for 30 min. The mixture was cooled to 0° C again, and a solution of 6-chloro-1-hexyne (696 mg, 6.0 mmol) in DMF (5.0 mL) was added dropwise. The mixture was stirred at room temperature for 2 h, and then at 70 °C for overnight. The reaction was then carefully quenched by H_2O at 0 °C and Et_2O was added to extract the product. The organic phase was separated and washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane/ethyl acetate = 10:1) to give the corresponding product as a colorless oil (510 mg, 52% yield).

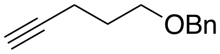
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.15 – 7.07 (m, 2H), 6.50 (d, *J* = 2.8 Hz, 1H), 4.16 (t, *J* = 7.0 Hz, 2H), 2.20 – 1.96 (m, 2H), 1.98 (dt, *J* = 5.4, 4.9 Hz, 3H), 1.58 – 1.52 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.9, 128.6, 127.7, 121.4, 121.0, 119.2, 109.3, 101.1, 83.7, 68.9, 45.9, 29.2, 25.7, 18.1.

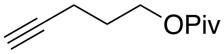
IR (neat) 3290, 3053, 2938, 2864, 1511, 1463, 1314, 738, 633 cm^{-1}.



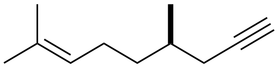
1-(*tert*-Butyldimethylsilyloxy)-4-pentyne was prepared according to the known literature and has been previously characterized.[7]



5-Benzyloxy-1-pentyne was prepared according to the known literature and has been previously characterized.[8]

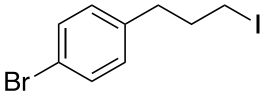


Pent-4-yn-1-yl 2,2-dimethylpropanoate was prepared according to the known literature and has been previously characterized.[9]

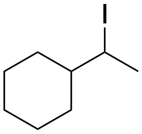


(±)-4,8-Dimethylnon-7-en-1-yne was prepared according to the known literature and has been previously characterized.[10]

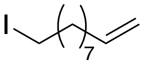
Alkyl iodides: 1-iodooctane was purchased from Alfa Aesar. 2-iodopropane and 1-iodo-3-phenylpropane were purchased from Sigma-Aldrich. 4-iodo-tetrahydropyran, *N*-Boc-4-iodopiperidine, iodocyclopentane and (iodomethyl)cyclopropane were purchased from Fischer Scientific. 6-Iodohexene and iodocyclohexane were purchased from TCI America.



1-Bromo-4-(3-iodopropyl)benzene was prepared according to the known literature and has been previously characterized.[11]



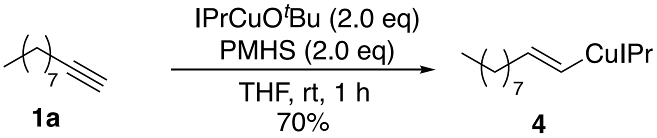
1-Cyclohexyliodoethane was prepared according to the known literature and has been previously characterized.[12]



10-iodo-1-decene was prepared according to the known literature and has been previously characterized.[13]

5. Mechanistic studies

5.1 Synthesis of alkenylcopper 4

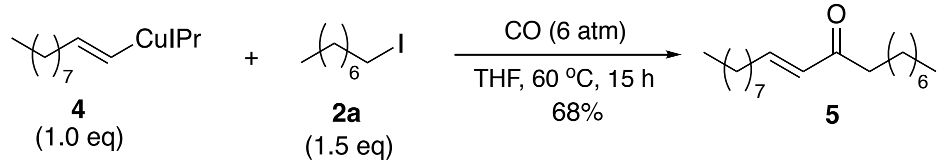


In a glovebox, IPrCuO^{t}Bu (262 mg, 0.5 mmol) and THF (5 mL) were added to a 20-mL vial with a 1.5 cm stir bar. PMHS (60 μL, 1.0 mmol) was added dropwise to the above solution at room temperature, followed by 1-decyne (180 μL, 1.0 mmol). After the bright yellow solution turned to colorless within 5 min, the reaction was allowed to stir at room temperature for 1h. Then the solvent was removed under reduced pressure. Pentane was added to wash the residue and the mixture was filtered to afford the product as an off-white solid (207 mg, 70% yield).

^{1}H NMR (500 MHz, C_6D_6) δ 7.30 (t, *J* = 7.7 Hz, 2H), 7.17 (d, *J* = 7.7 Hz, 4H), 6.54 (d, *J* = 19.6 Hz, 1H), 6.35 (s, 2H), 6.07 (dt, *J* = 19.5, 5.8 Hz, 1H), 2.76 – 2.71 (m, 4H), 2.39 (dd, *J* = 13.6, 6.7 Hz, 2H), 1.61 –1.53 (m, 14H), 1.44 – 1.37 (m, 2H), 1.34 – 1.27 (m, 8H), 1.19 (d, *J* = 6.9 Hz, 12H), 0.95 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, C_6D_6) δ 186.4, 151.7, 145.8, 144.2, 135.3, 130.4, 124.1, 122.1, 41.3, 32.3, 30.8, 30.2, 29.9, 29.8, 29.0, 25.1, 23.7, 23.1, 14.4.

5.2 Stoichiometric coupling of alkenyl copper 4 with 2a under CO



In a glovebox, alkenyl copper **4** (118 mg, 0.2 mmol) and THF (6 mL) were added to a 20-mL vial with a 1.5 cm stir bar. Then 1-iodooctane (54 μL, 0.3 mmol) was added to the above solution at room temperature. The vial was placed in an aluminum rack within a Parr pressure reactor. Next, the reactor was closed and taken out of the glovebox. A CO gas cylinder with a pressure regulator was connected to the reactor. The reactor was pressurized with CO gas to 6 atm and released after 5 min. This procedure was repeated three times, after which the reaction heated to 60 °C with a stir rate at 1300 rpm. After 15 h, the reaction was cooled to room temperature and the CO gas was released. Then methanol (1.0 mL) was added to the vial and the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography (hexane/ethyl acetate = 20:1) to afford the corresponding product as colorless oil (38 mg, 68% yield).

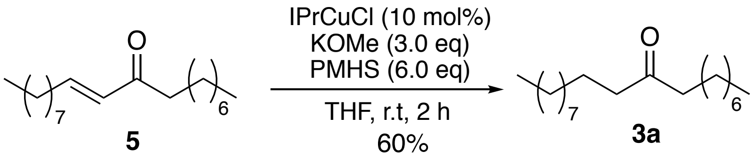
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (dt, *J* = 15.8, 6.9 Hz, 1H), 6.08 (dd, *J* = 15.9, 1.3 Hz, 1H), 2.51 (t, *J* = 7.5 Hz, 2H), 2.24 – 2.14 (m, 2H), 1.61 – 1.58 (m, 2H), 1.50 – 1.40 (m, 2H), 1.28 – 1.26 (m, 20H), 0.89 – 0.86 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.9, 147.3, 130.3, 40.1, 32.4, 31.8, 29.4, 29.3, 29.2, 28.1, 24.3, 22.6, 14.0.

IR (neat) 2923, 2853, 1698, 1674, 1630, 1464, 978, 722 cm^{-1}.

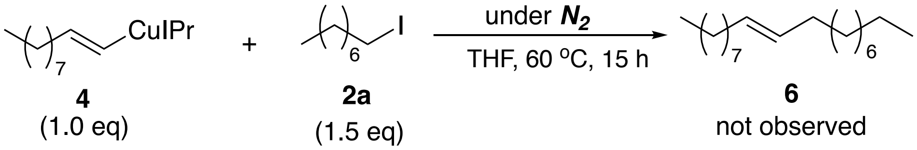
HRMS (ESI) Calcd. for $C_{19}H_{37}O$ ($[M+H]^+$): 281.2839; Found: 281.2836.

5.3 Reduction of unsaturated ketone 5



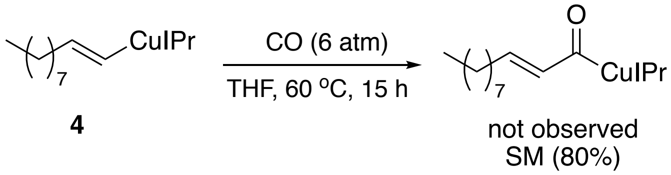
In a glovebox, KOMe (21 mg, 0.3 mmol, 3.0 equiv) and THF (6.0 mL) were added to a 20-mL vial with a 1.5 cm stir bar. The IPrCuCl (4.9 mg, 0.01 mmol, 10 mol%) was dissolved in THF (0.5 mL) and transferred to the above mixture. The mixture was stirred at room temperature for 5 min before PMHS (36 μL, 0.6 mmol, 6.0 equiv) and a solution of unsaturated ketone (28 mg, 0.1 mmol) in THF (0.5 mL) were added sequentially at room temperature. The reaction was stirred at room temperature for 2 h. Then methanol (1.0 mL) was added to the vial and the solvent was removed under reduced pressure. The residue was dissolved in $CDCl_3$ and $(CHCl_2)_2$ (0.1 mmol) was added as internal standard for ^{1}H NMR analysis which showed saturated ketone **3a** was formed in 60% yield**.**

5.4 Stoichiometric coupling of alkenyl copper 4 with 2a without CO



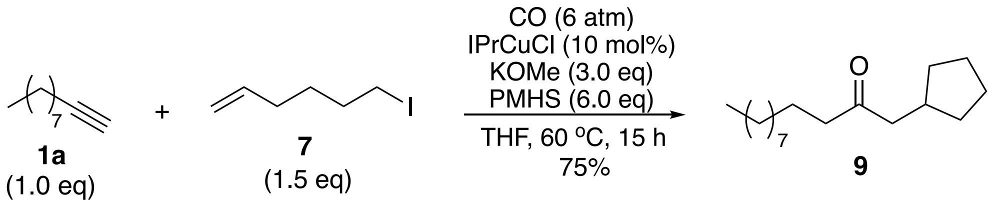
In a glovebox, alkenyl copper **4** (30 mg, 0.05 mmol) and THF (4.0 mL) were added to a 20-mL vial with a 1.5 cm stir bar. Then 1-iodooctane (14 μL, 0.075 mmol) was added at room temperature. The reaction was stirred at 60 °C for 15 h. Then the solvent was removed under reduced pressure and the residue dissolved into C_6D_6 for ^{1}H NMR analysis. The coupling alkene product **6** was not detected from ^{1}H NMR although alkenyl copper **4** was completely consumed.

5.5 CO insertion of alkenyl copper 4



In a glovebox, alkenyl copper 4 (30 mg, 0.05 mmol) and THF (4.0 mL) were added to a 20-mL vial with a 1.5 cm stir bar. The vial was placed in an aluminum rack within a Parr pressure reactor. Next, the reactor was closed and taken out of the glovebox. A CO gas cylinder with a pressure regulator was connected to the reactor. The reactor was pressurized with CO gas to 6 atm and released after 5 min. This procedure was repeated three times, after which the reaction heated to 60 °C with a stir rate at 1300 rpm. After 15 h, the reaction was cooled to room temperature and the CO gas was released. Then the solvent was removed under reduced pressure and the residue dissolved into C_6D_6 for ^{1}H NMR analysis. The CO insertion product was not detected from ^{1}H NMR and 80% alkenyl copper **4** was remaining.

5.6 Radical experiments



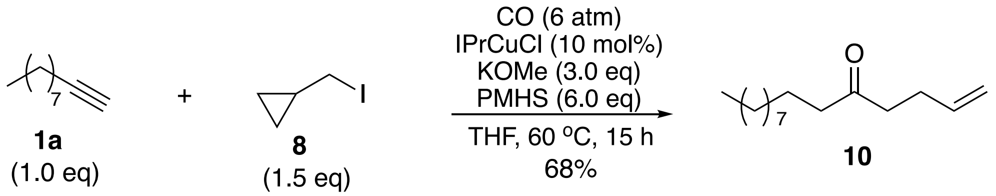
The reaction was performed according to the general procedure for synthesis of ketones using 1-decyne (36 μL, 0.2 mmol), 6-iodohex-1-ene (63 mg, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 50:1) to afford the title compound as a colorless oil (38 mg, 75% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 – 2.34 (m, 4H), 2.28 – 2.17 (m, 1H), 1.83-1.79 (m, 2H), 1.65 – 1.48 (m, 6H), 1.26 (brs, 14H), 1.1 – 1.03 (m, 2H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 211.5, 49.1, 43.1, 35.6, 32.6, 31.9, 29.6, 29.5, 29.4, 29.3, 29.3, 24.9, 23.8, 22.7, 14.1.

IR (neat) 2922, 2853, 1712, 1455, 1372, 732 cm^{-1}.

HRMS (ESI) Calcd. for $C_{17}H_{33}O$ ($[M+H]^+$): 253.2526; Found: 253.2521.



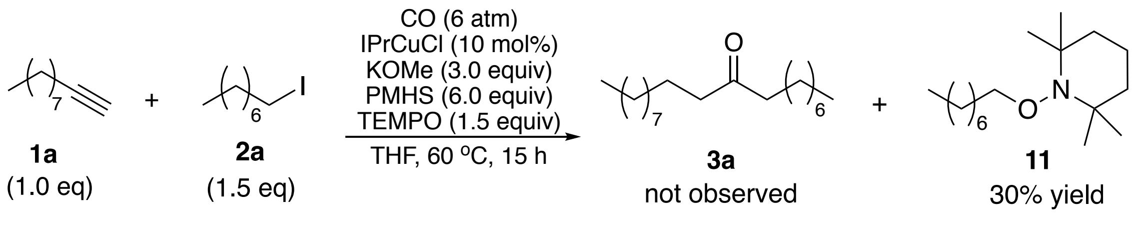
The reaction was performed according to the general procedure for synthesis of ketones using 1-decyne (36 μL, 0.2 mmol), (iodomethyl)cyclopropane (55 mg, 0.3 mmol). The crude material was purified by silica gel chromatography (hexane /ethyl acetate = 50:1) to afford the title compound as a colorless oil (30 mg, 68% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 12.9, 10.2, 6.5 Hz, 1H), 5.08 – 4.91 (m, 2H), 2.49 (t, *J* = 7.4 Hz, 2H), 2.39 (t, *J* = 7.4 Hz, 2H), 2.33-2.29 (m, 2H), 1.60 – 1.51 (m, 2H), 1.25 (s, 14H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 210.5, 137.2, 115.1, 42.9, 41.7, 31.9, 29.5, 29.5, 29.4, 29.3, 29.2, 27.8, 23.8, 22.7, 14.1.

IR (neat) 2922, 2853, 1715, 1465, 1370, 1128, 1080, 911, 773 cm^{-1}.

HRMS (ESI) Calcd. for $C_{15}H_{29}O$ ($[M+H]^+$): 225.2213; Found: 225.2203.



In a glovebox, KOMe (42 mg, 0.6 mmol, 3.0 equiv) and THF (8.0 mL) were added to a 20-mL vial with a 1.5 cm stir bar. The IPrCuCl (9.6 mg, 0.02 mmol, 10 mol%) was dissolved in THF (0.5 mL) and transferred to the above mixture. The mixture was stirred at room temperature for 5 min before PMHS (72 μL, 1.2 mmol, 6.0 equiv) and 1-decyne (36 μL, 0.2 mmol) were added sequentially at room temperature. After the bright yellow solution turned to colorless, 1-iodooctane (54 μL, 0.3 mmol, 1.5 equiv) and TEMPO (47 mg, 0.3 mmol) were added. The vial was then placed in an aluminum rack within a Parr pressure reactor. Next, the reactor was closed and taken out of the glovebox. A CO gas cylinder with a pressure regulator was connected to the reactor. The reactor was pressurized with CO gas to 6 atm and released after 5 min. This procedure was repeated three times, after which the reaction heated to 60 ^{o}C with a stir rate at 1300 rpm. After 15 h, the reaction was cooled to room temperature and the CO gas was released. The solvent was removed under reduced pressure. The residue was diluted with Et_2O and filtered through a pad of silica gel (a pipette with about 5 cm silica gel). The filtrate was concentrated under reduced pressure and the residue was purified by silica gel chromatography (hexane/ethyl acetate = 20:1) to afford compound **11** as a colorless oil (24 mg, 30% yield).

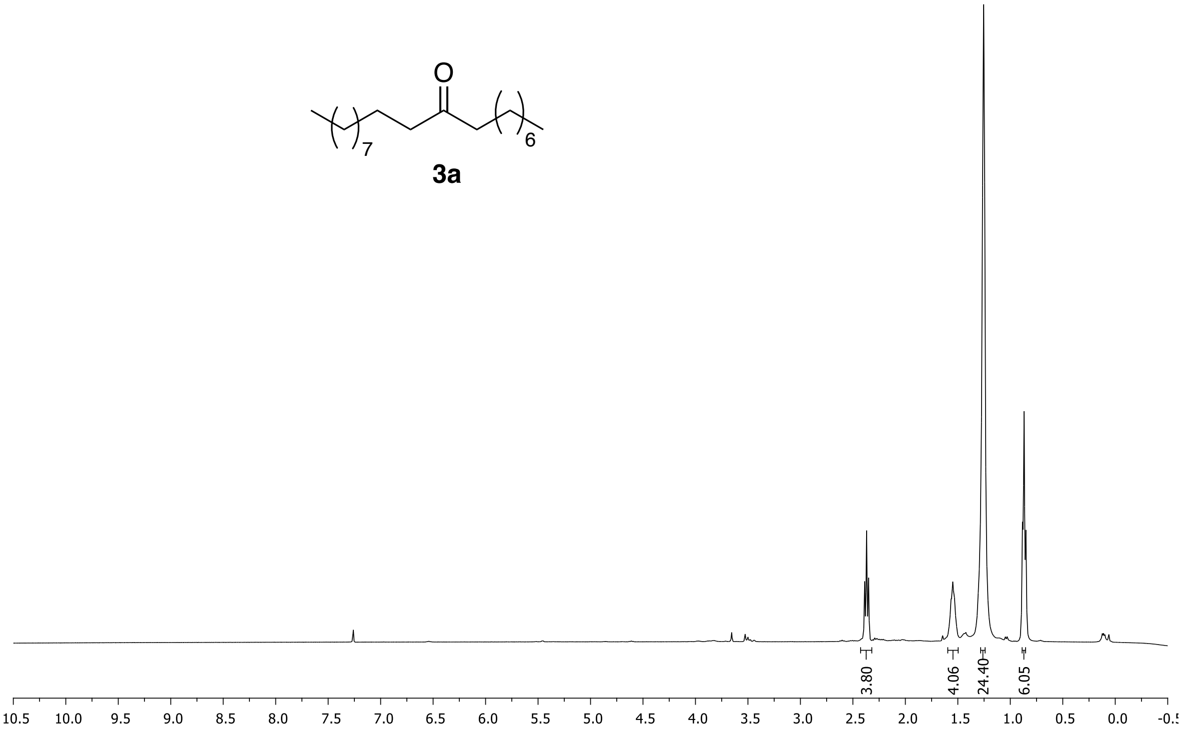
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (t, *J* = 6.7 Hz, 2H), 1.57 – 1.43 (m, 6H), 1.35 – 1.24 (m, 12H), 1.15 (s, 6H), 1.09 (s, 6H), 0.88 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 76.9, 59.6, 39.6, 33.1, 31.9, 29.7, 29.3, 28.7, 26.5, 22.7, 20.1, 17.8, 14.1.

IR (neat) 2925, 2855, 1468, 1373, 1358, 1132, 1046, 711 cm^{-1}.

HRMS (ESI) Calcd. for $C_{17}H_{35}NO$ ($[M+H]^+$): 270.2791; Found: 270.2789.

6. ^{1}H, ^{13}C NMR Spectra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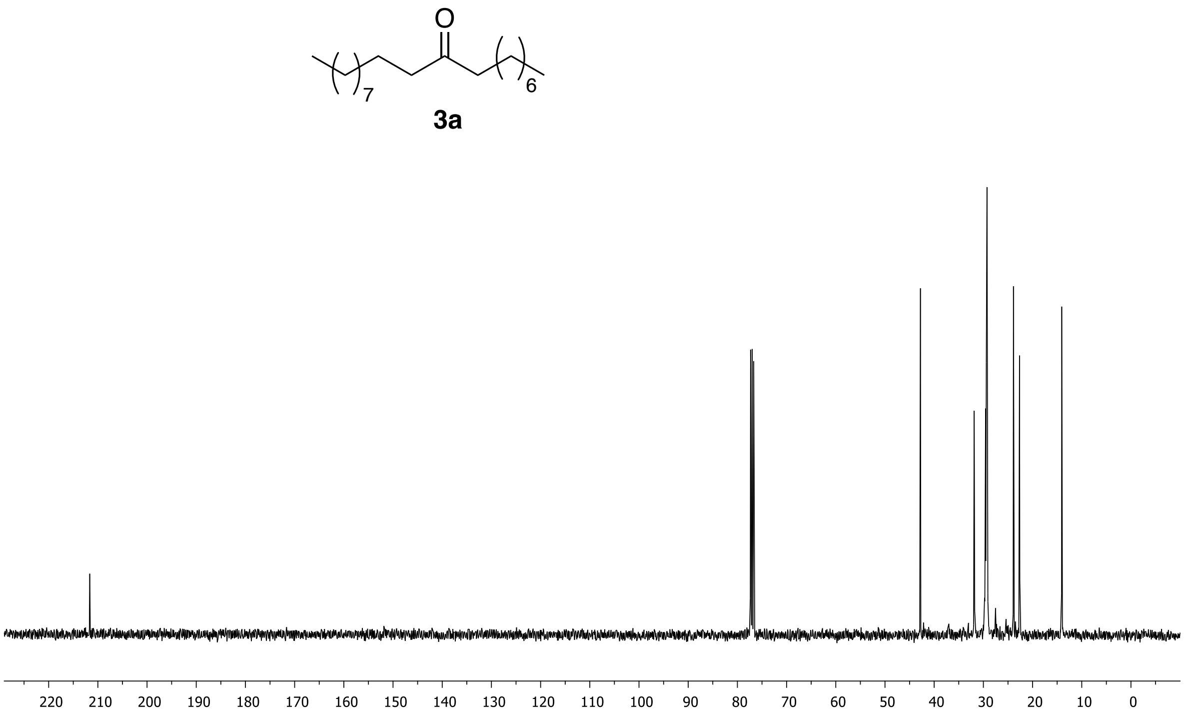
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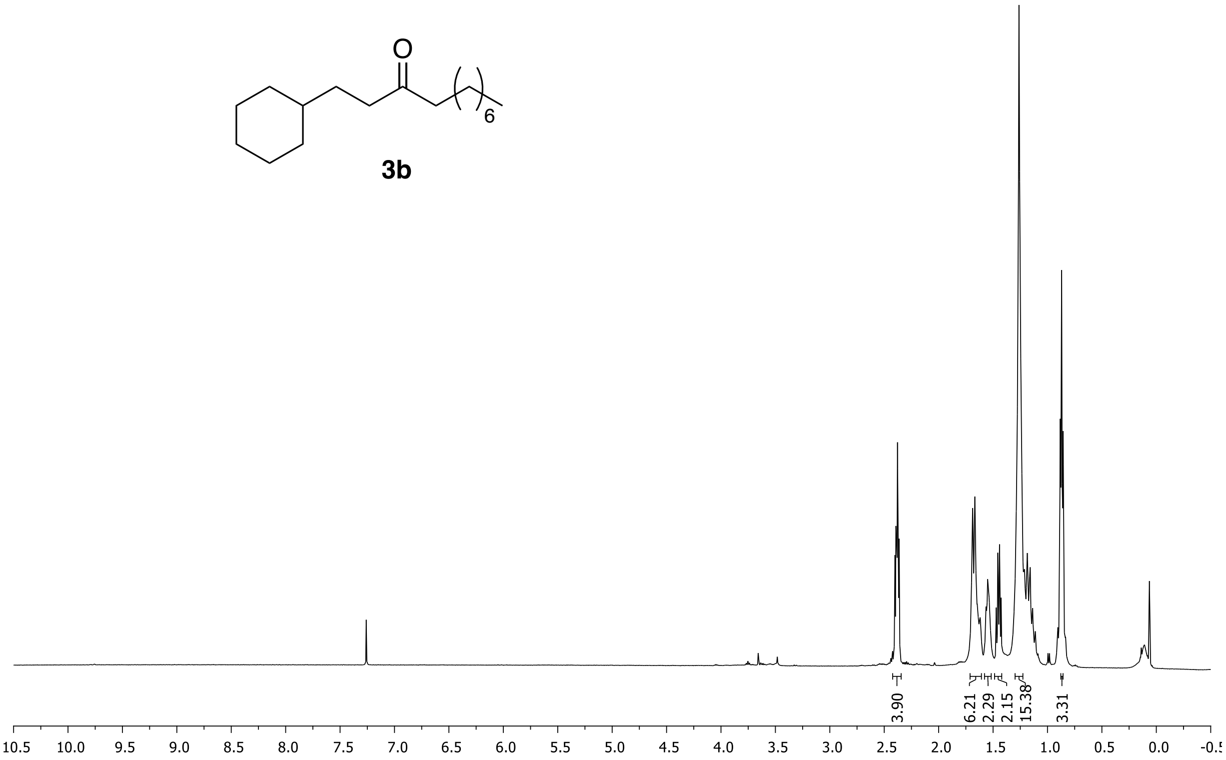

3b

O
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6.21
2.29
2.15
15.38
3.31
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8.0
7.5
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6.0
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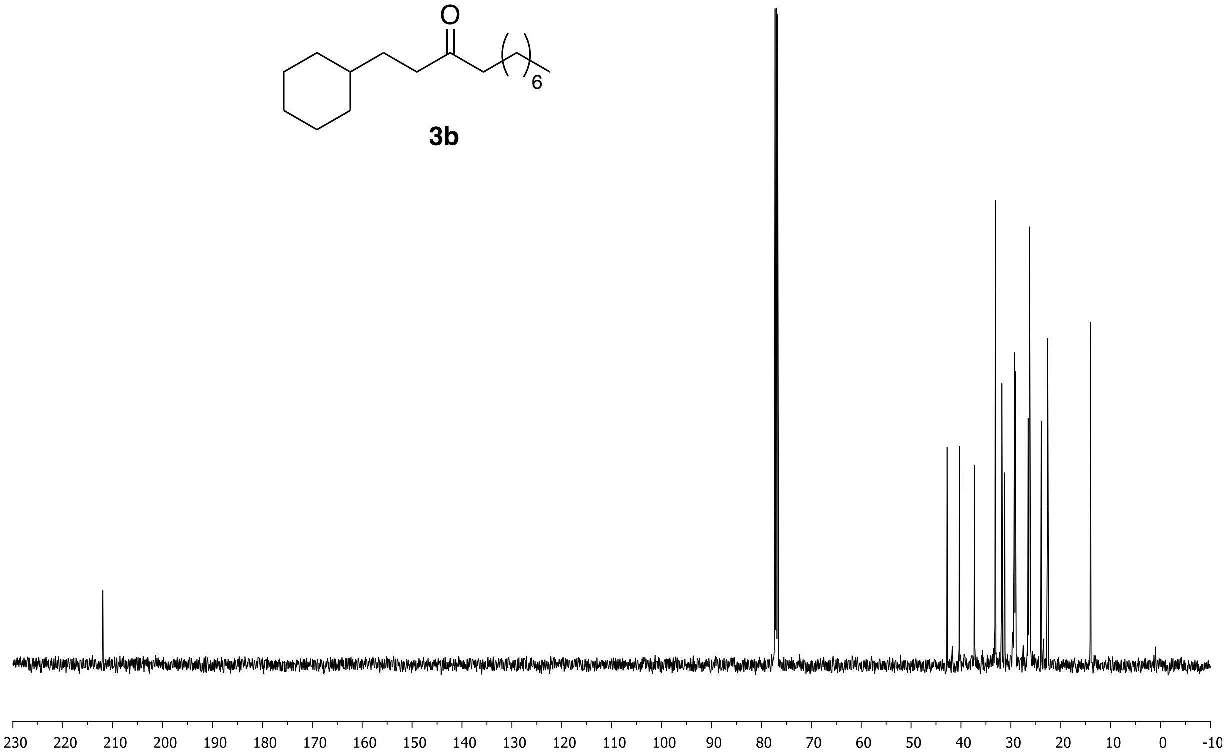

3b

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0
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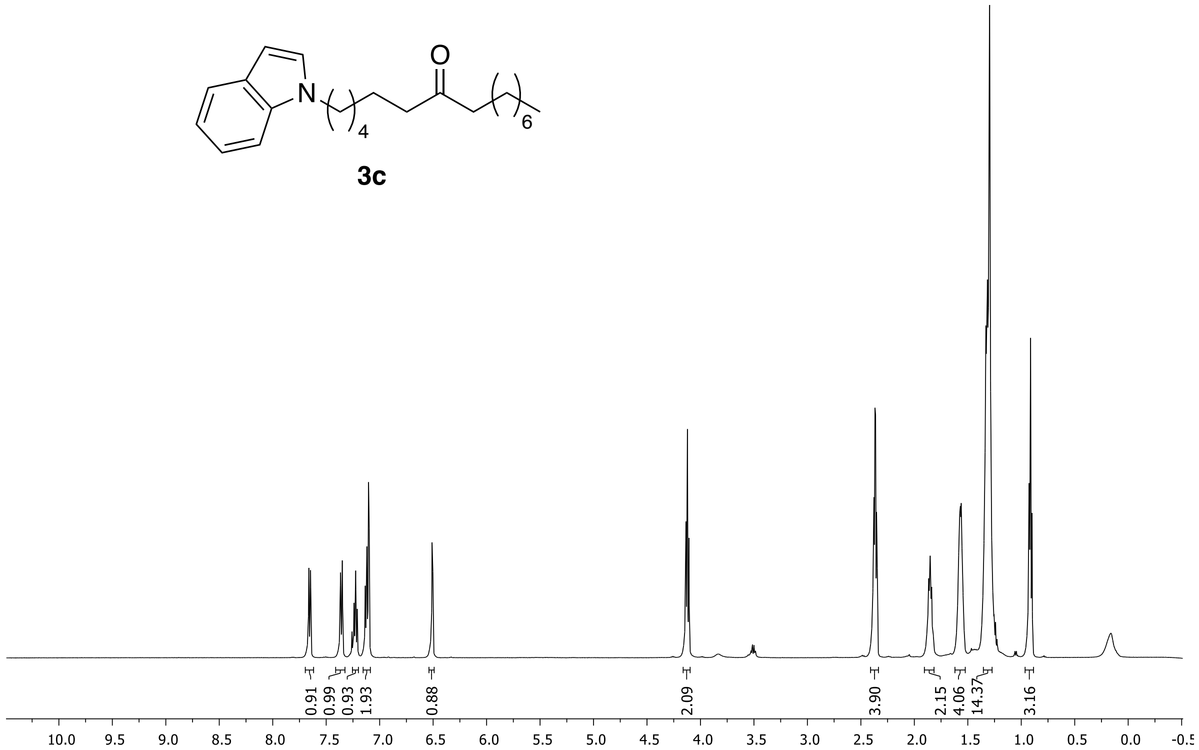
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6.0
5.5
5.0
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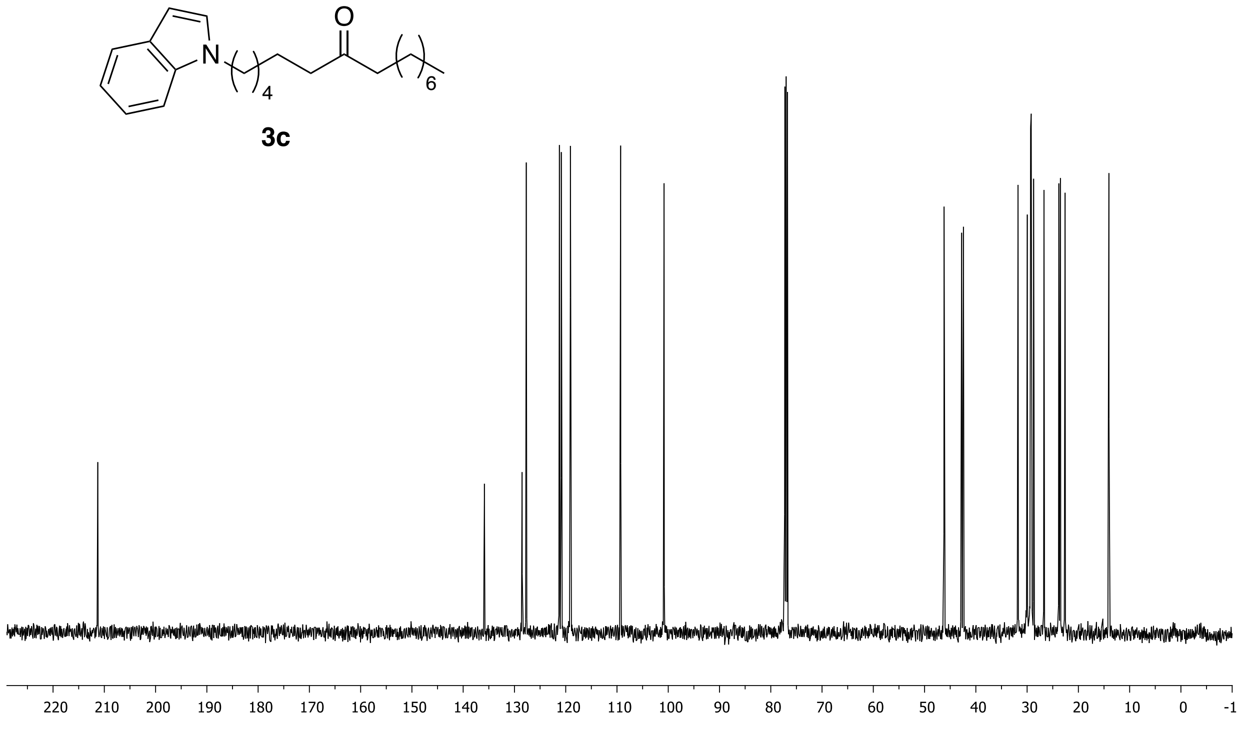
3c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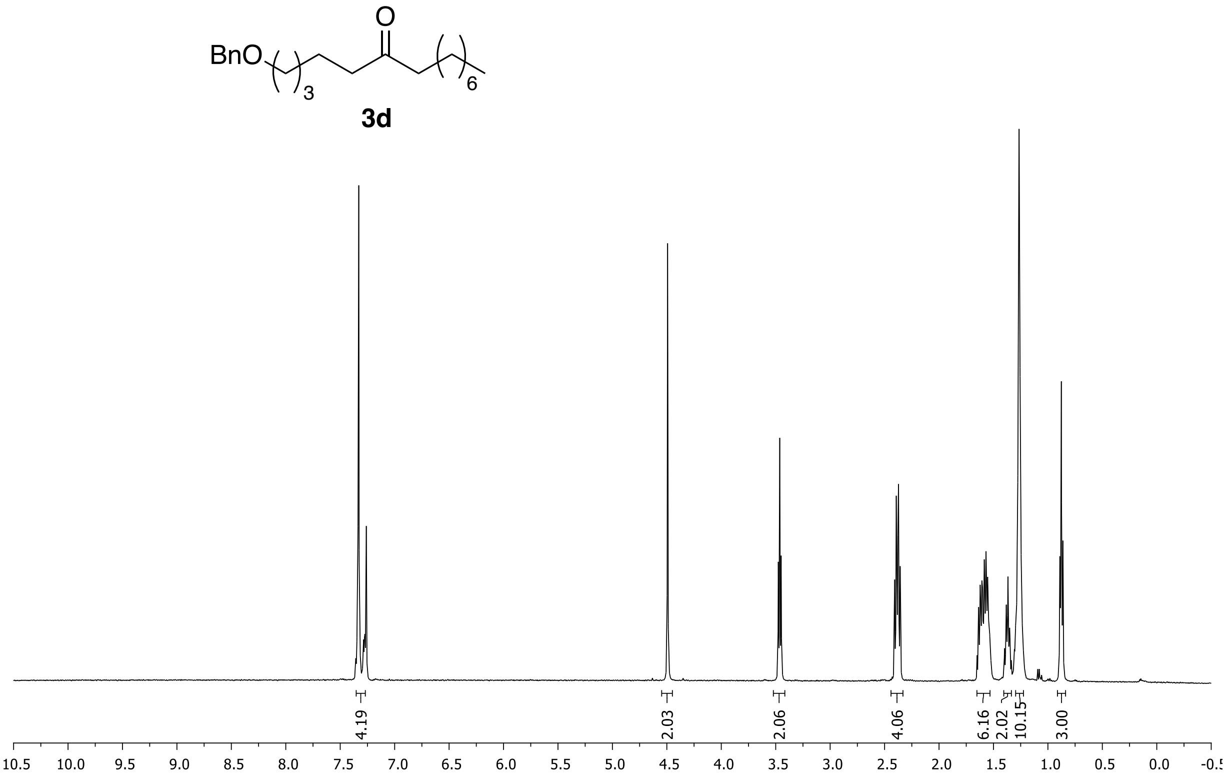
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10.15
3.00
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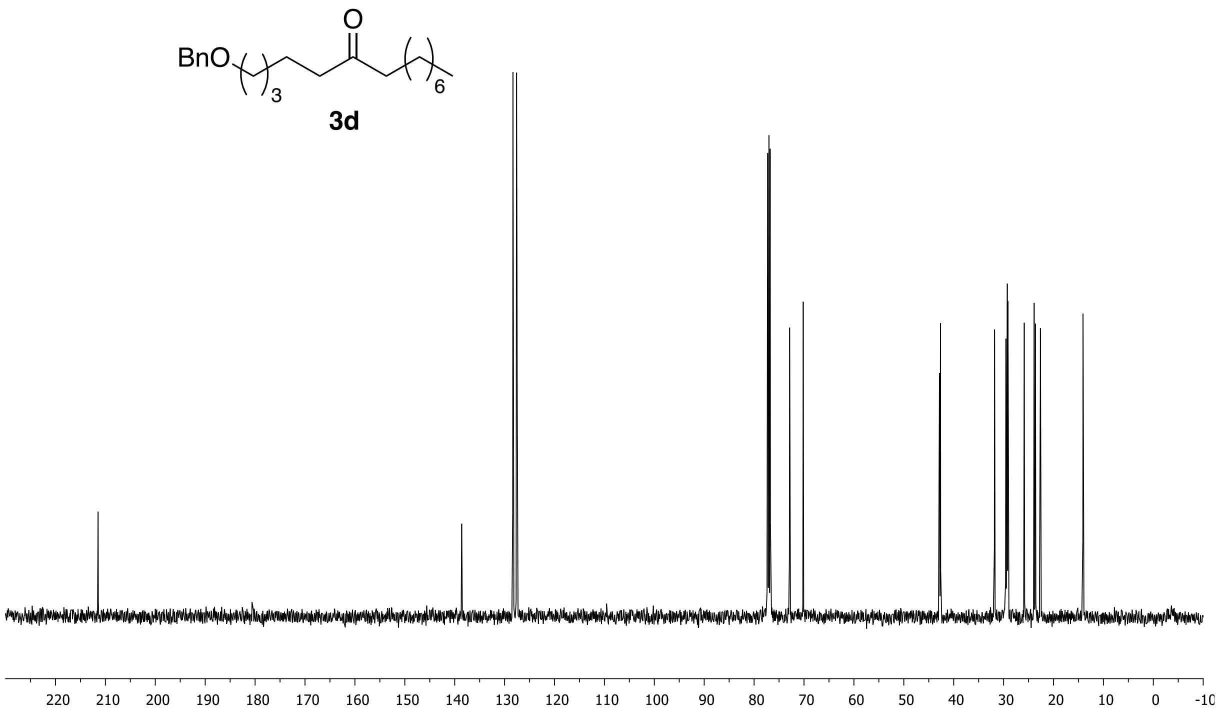
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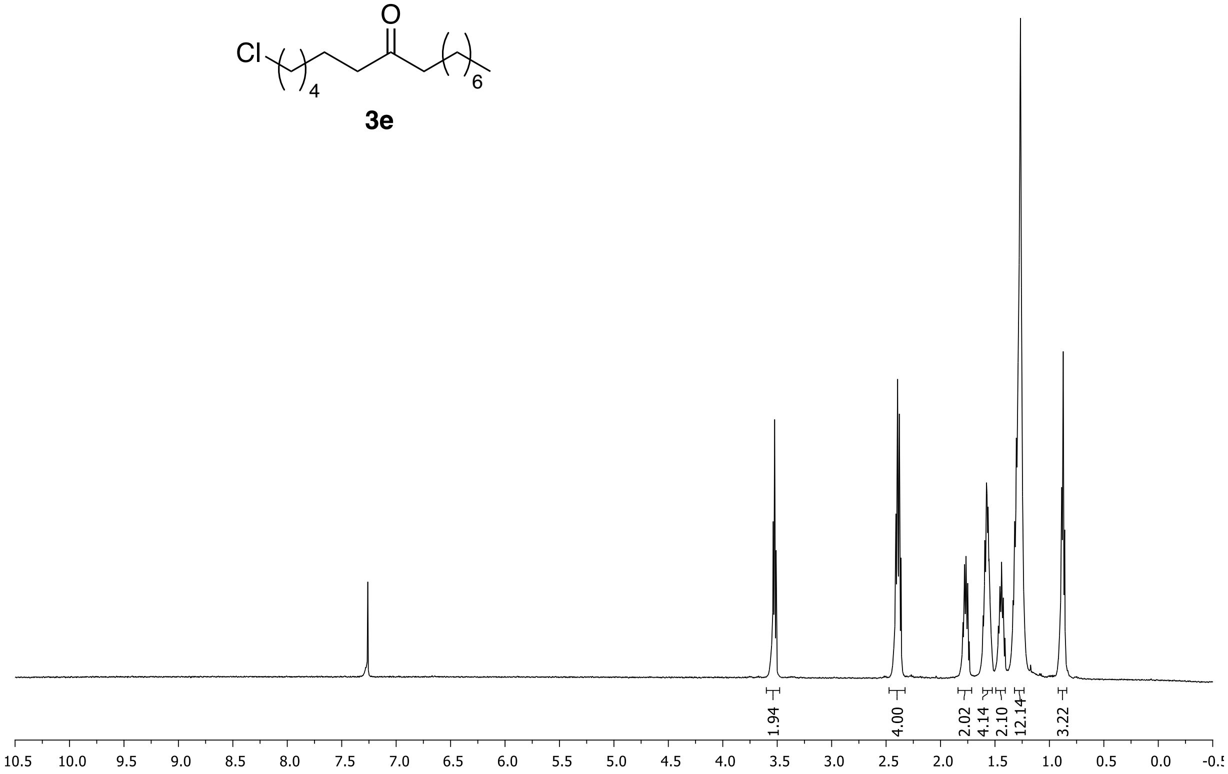

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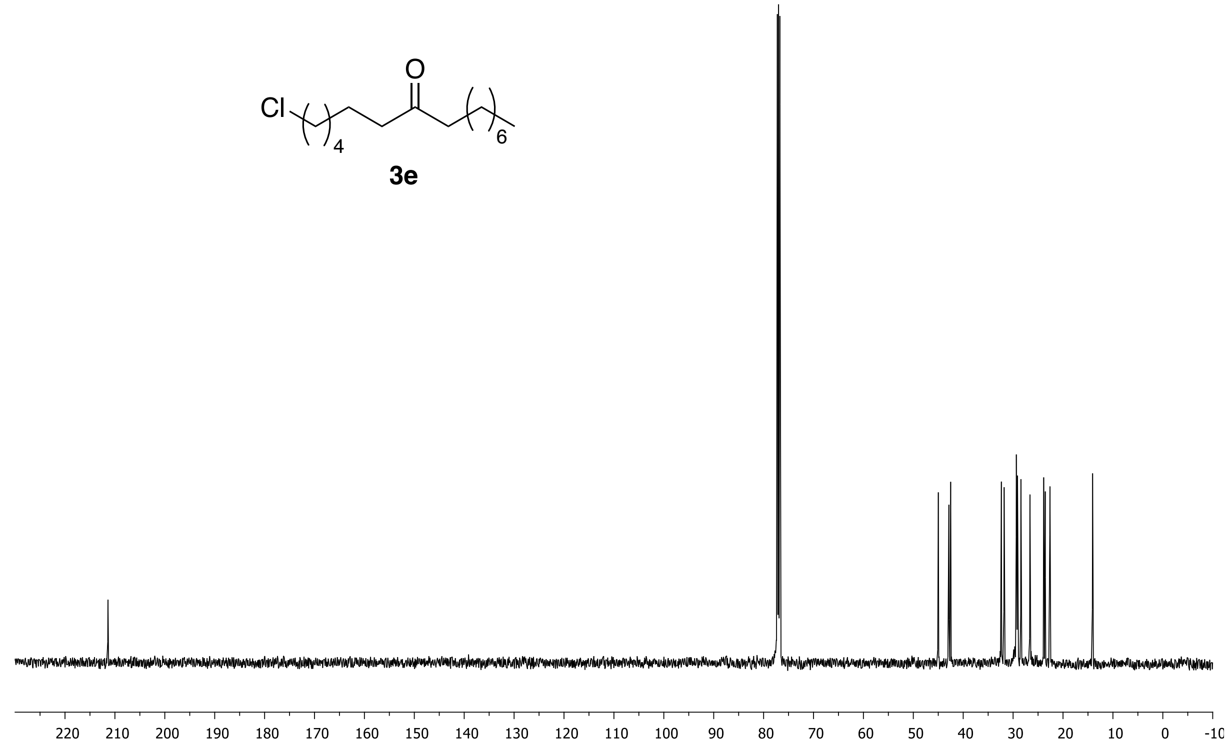

Cl
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3e
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200
190
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120
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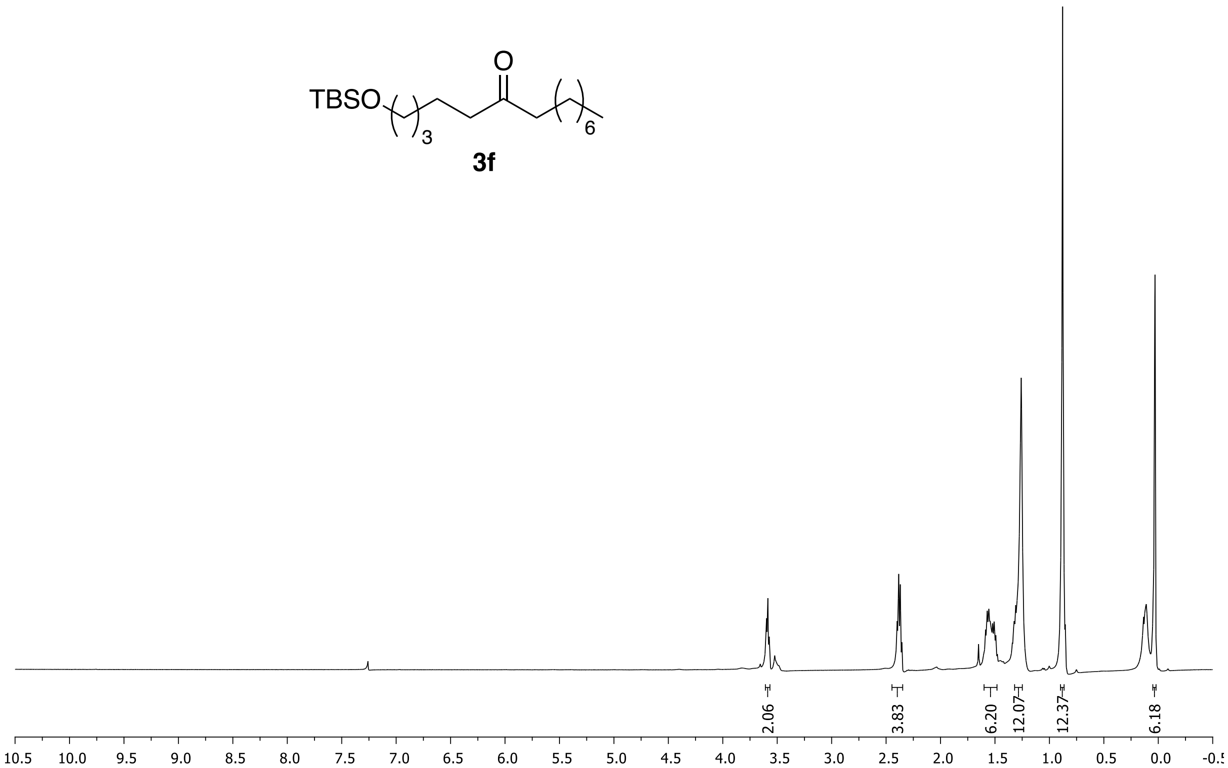
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8.0
7.5
7.0
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6.0
5.5
5.0
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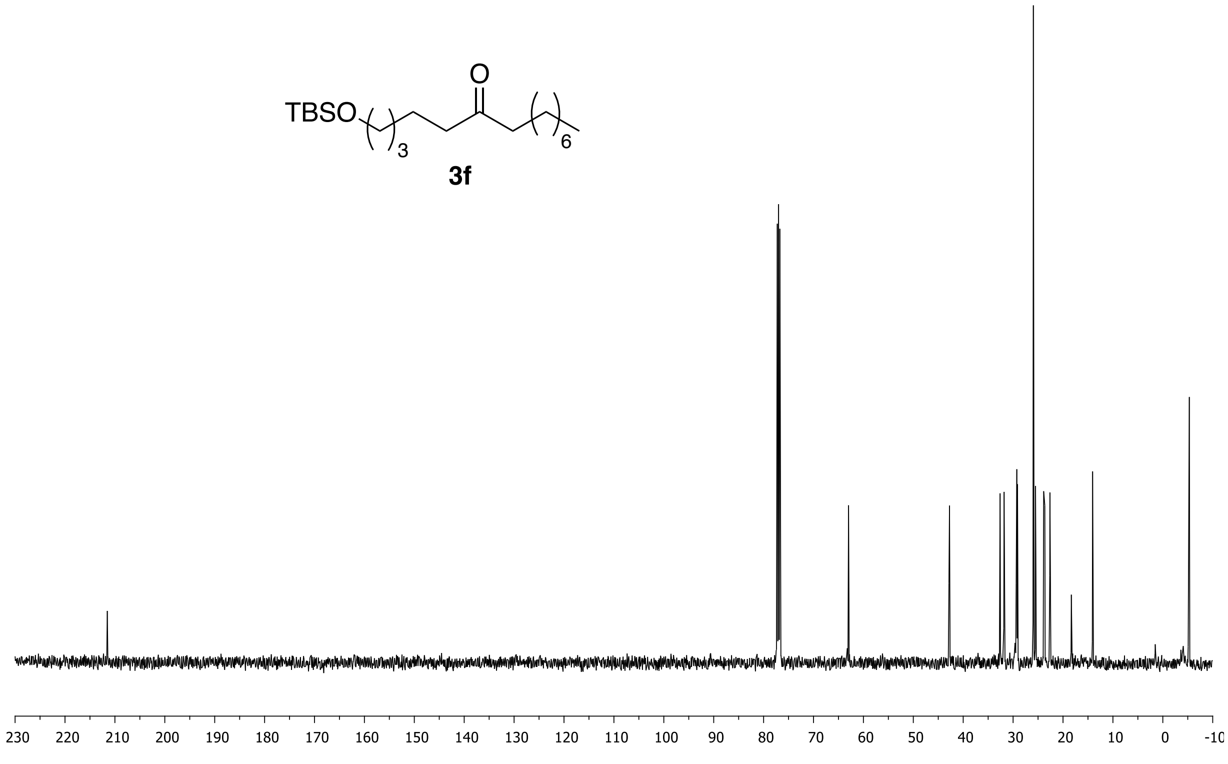
3f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220
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200
190
180
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120
110
100
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40
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20
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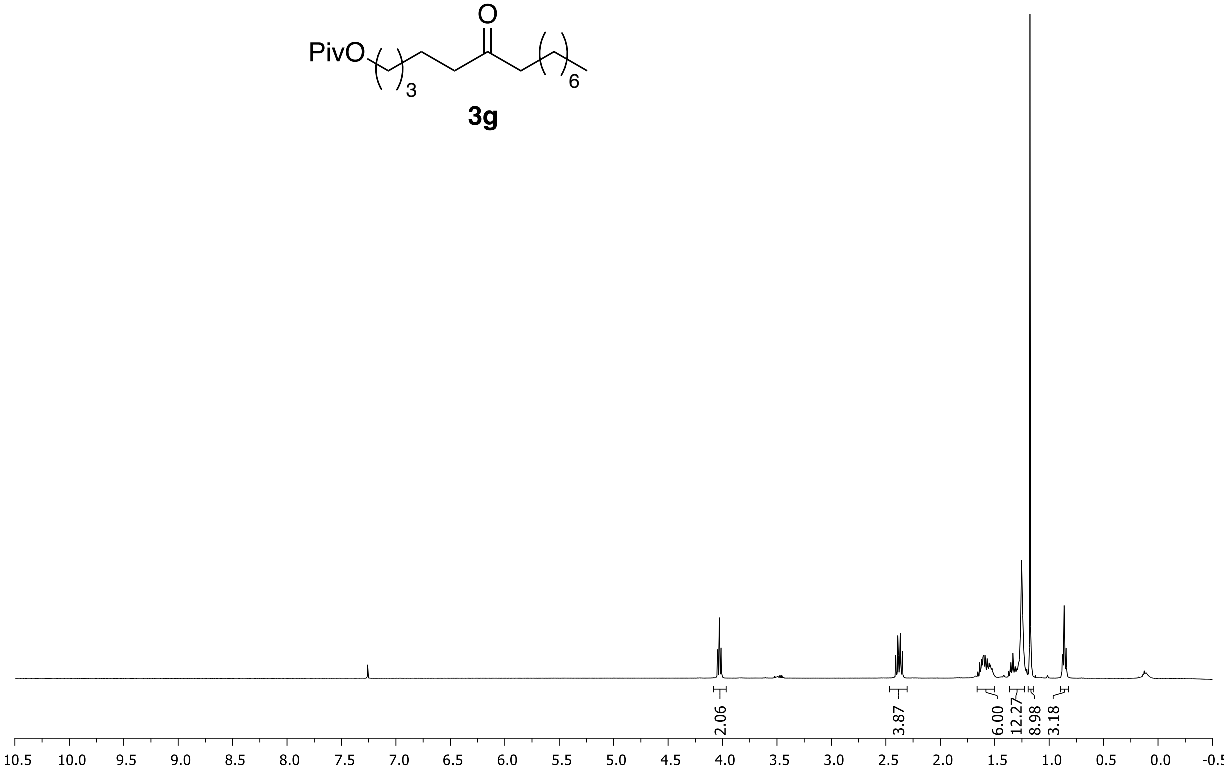
0
-10

3f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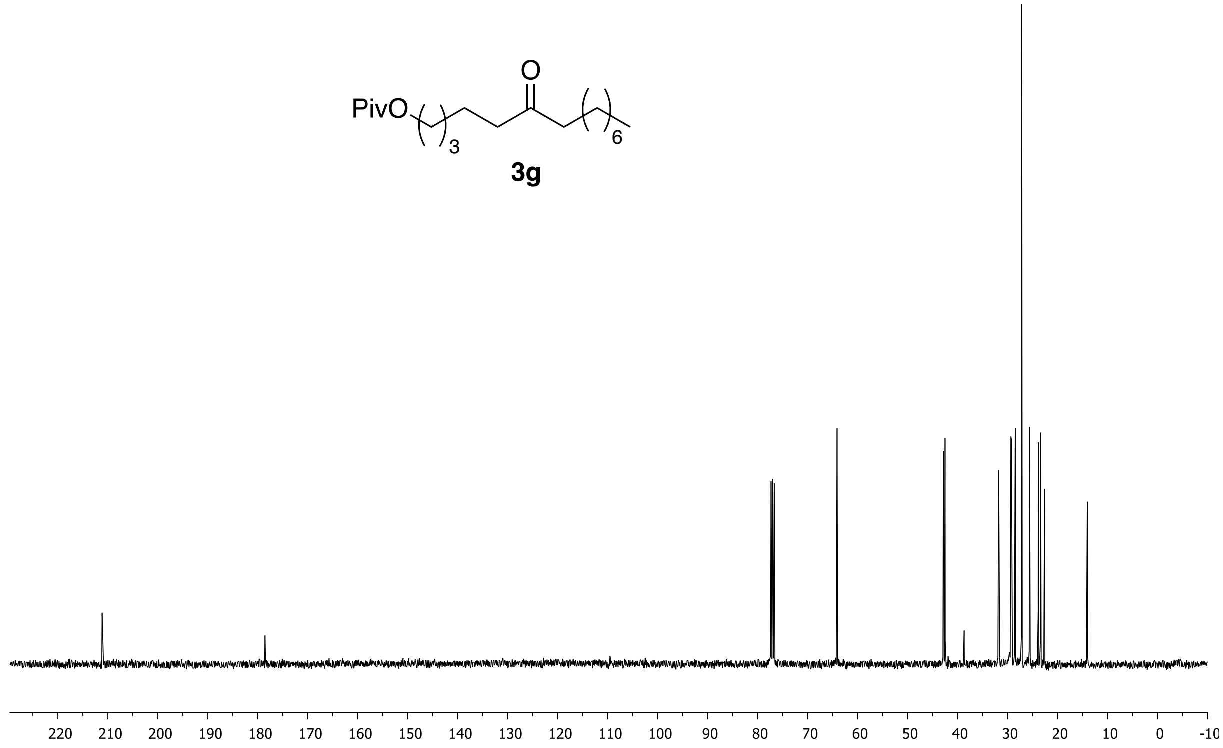
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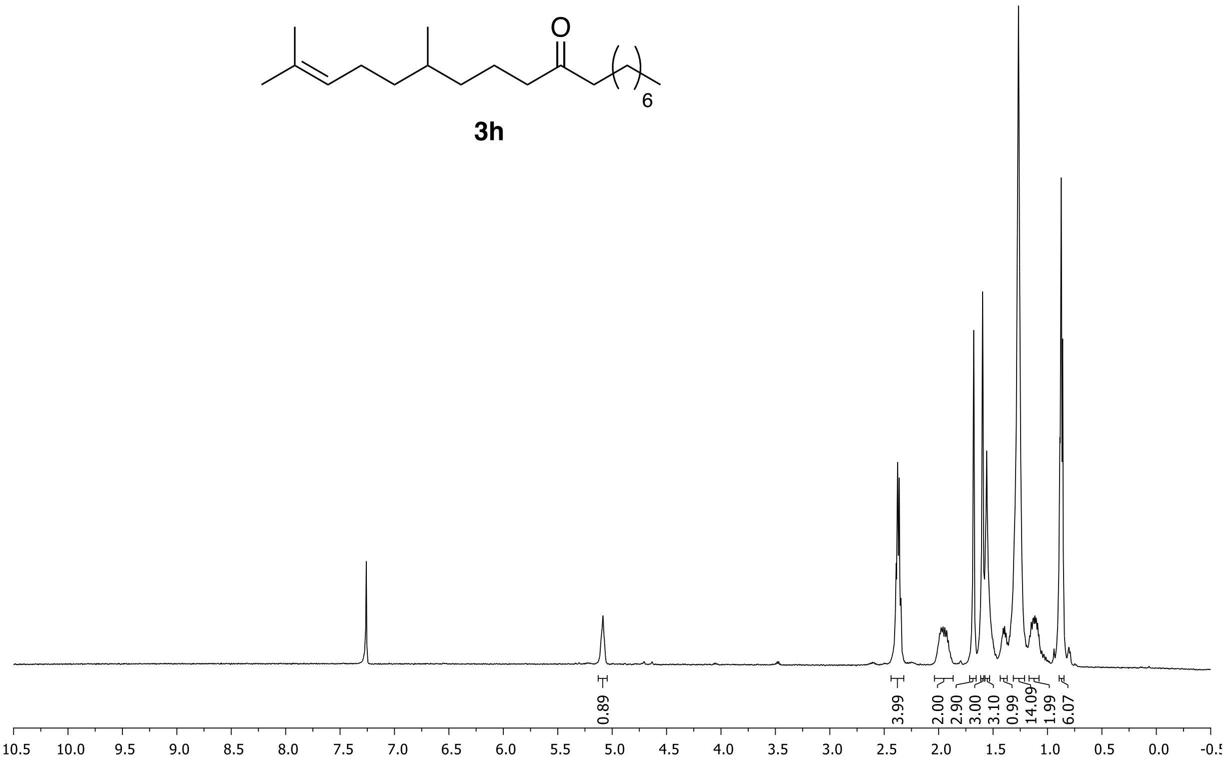
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8.5
8.0
7.5
7.0
6.5
6.0
5.5
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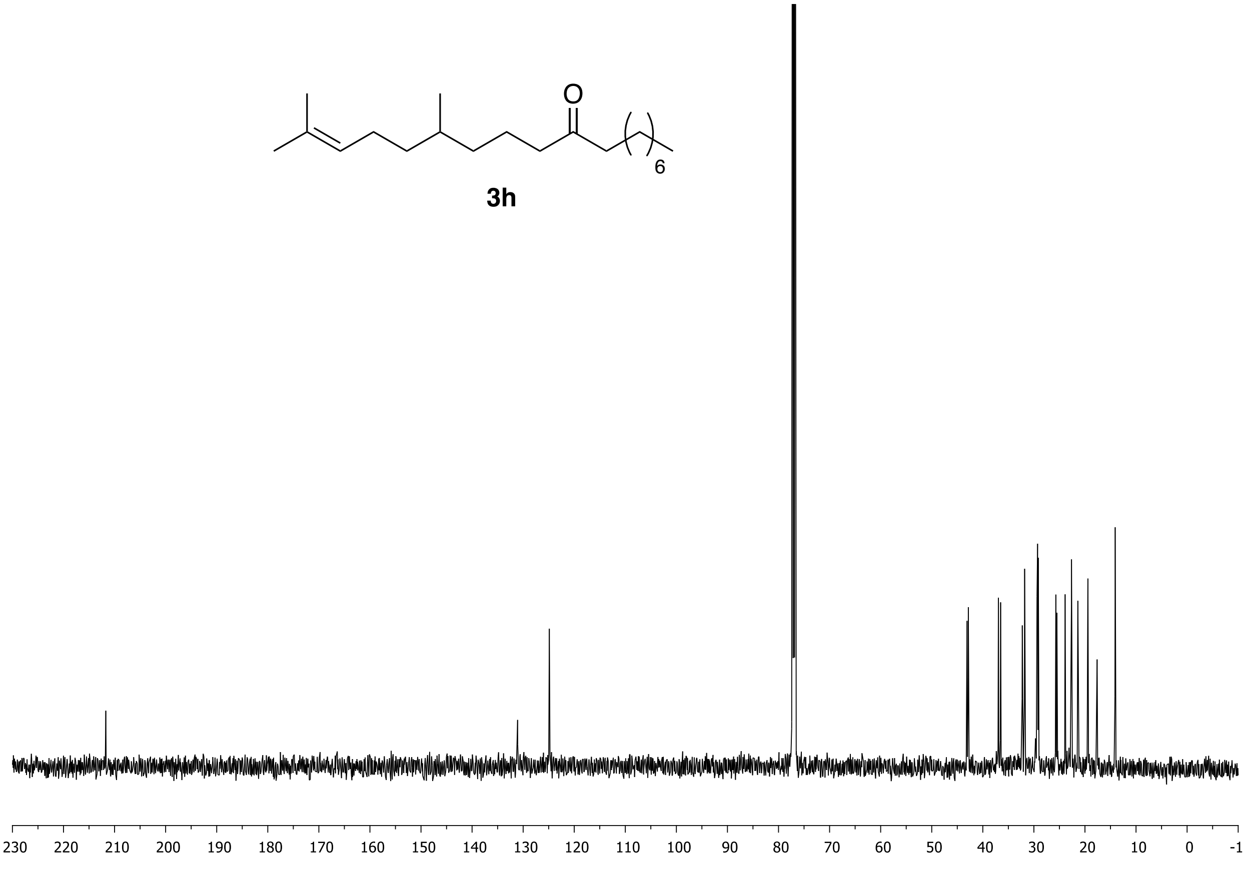
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3h
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220
210
200
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160
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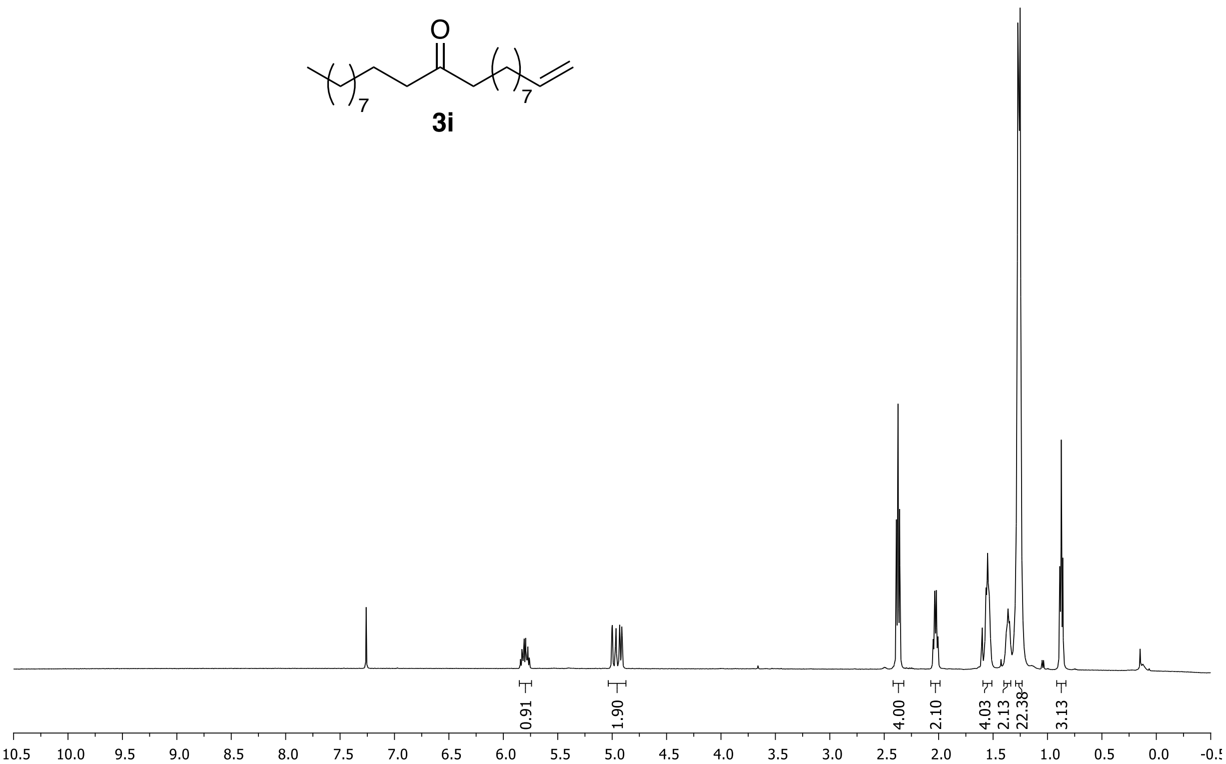
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3.13
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10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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2.5
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1.0
0.5
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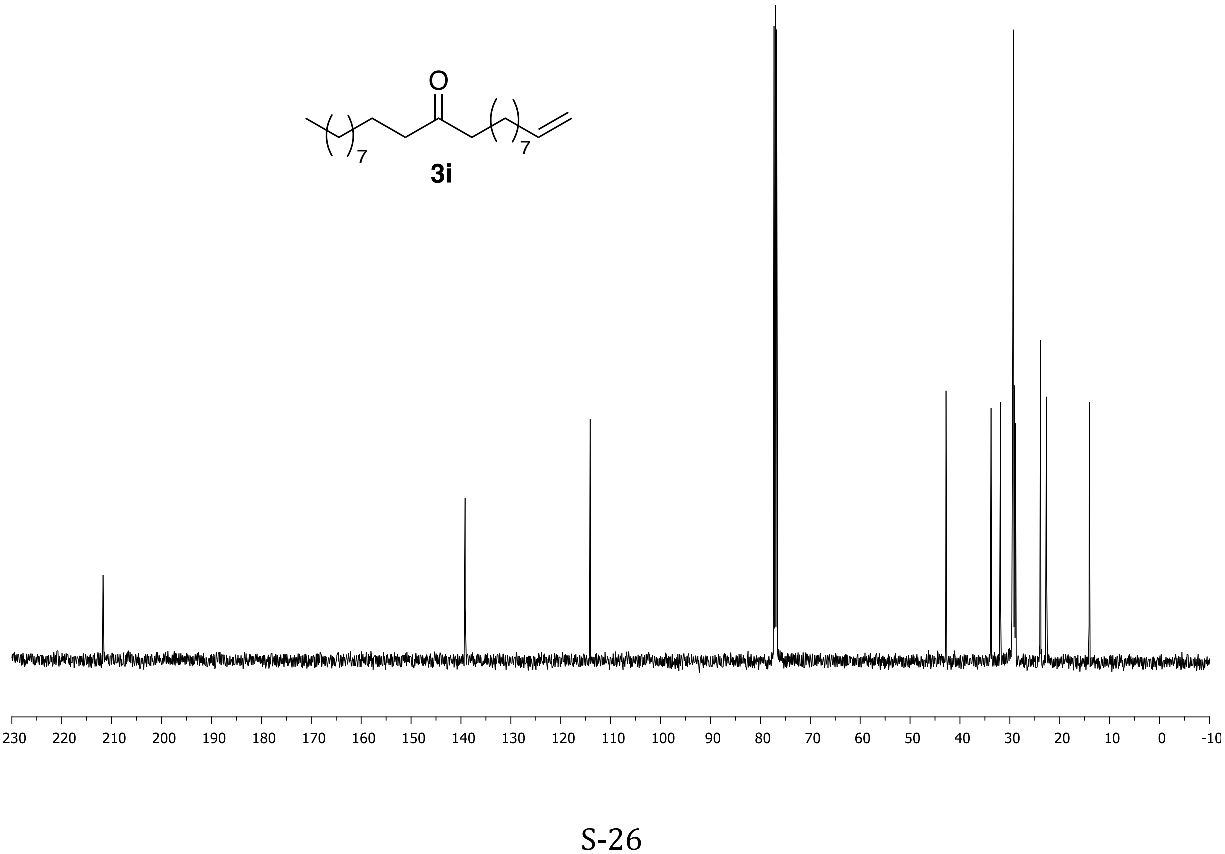
O
7
7


3i
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210
200
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180
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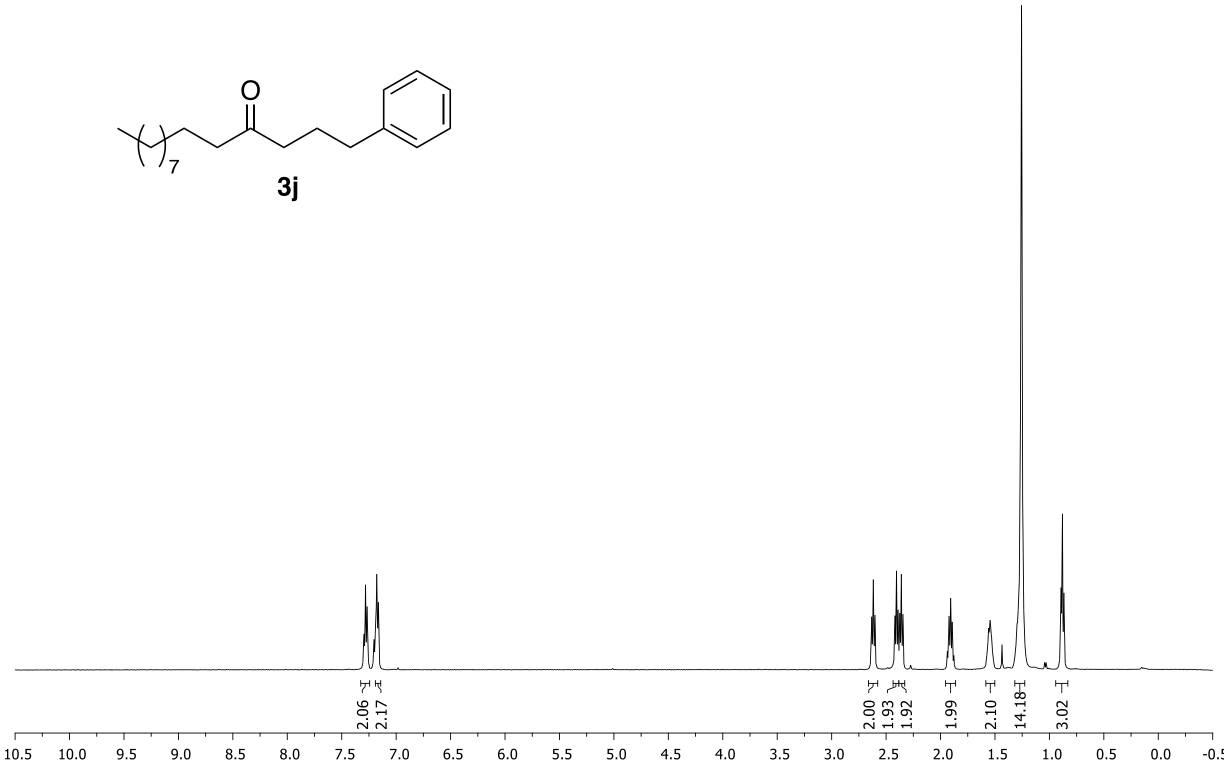
O
7
7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8.0
7.5
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6.0
5.5
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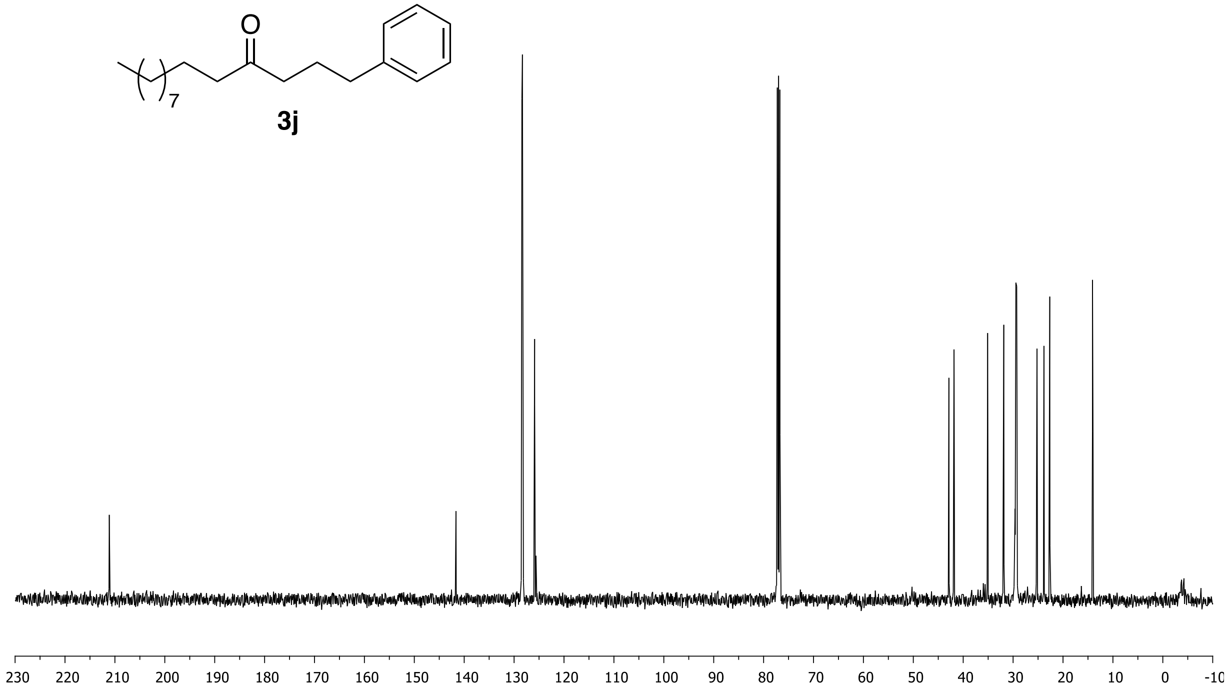
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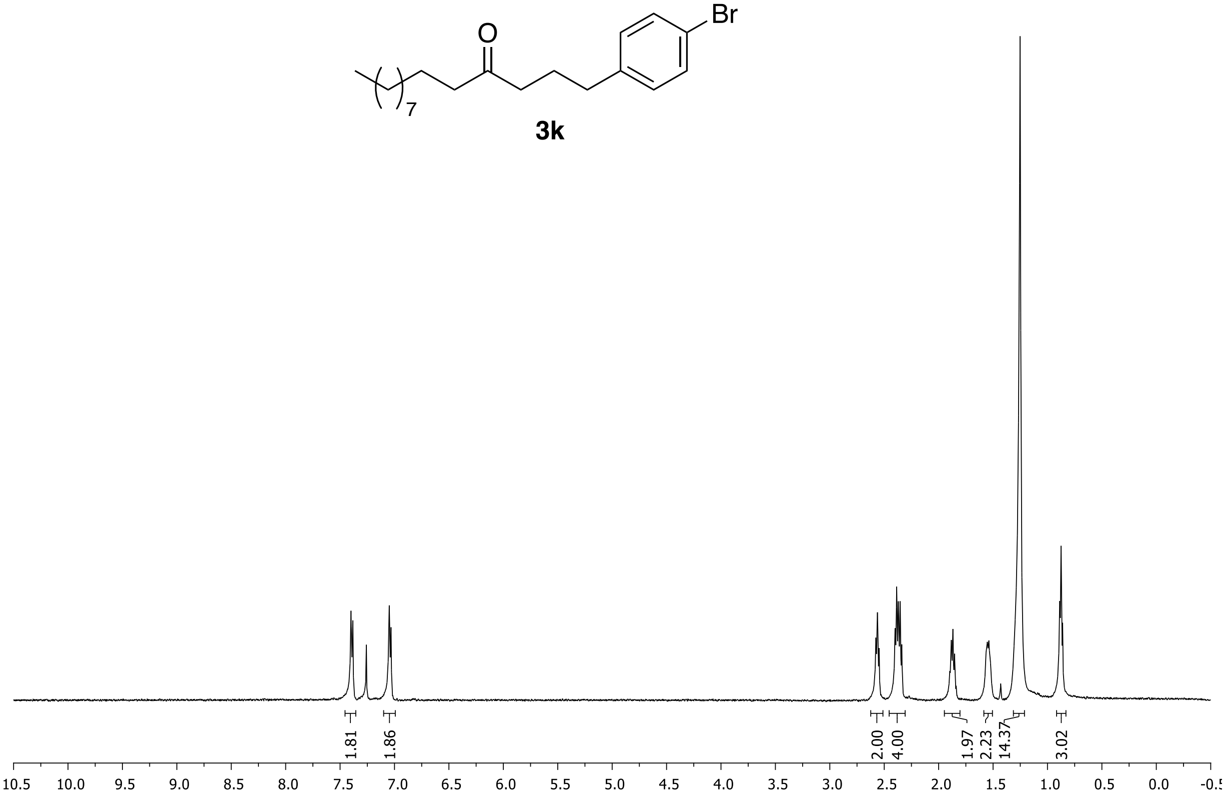
-1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9.0
8.5
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7.5
7.0
6.5
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5.5
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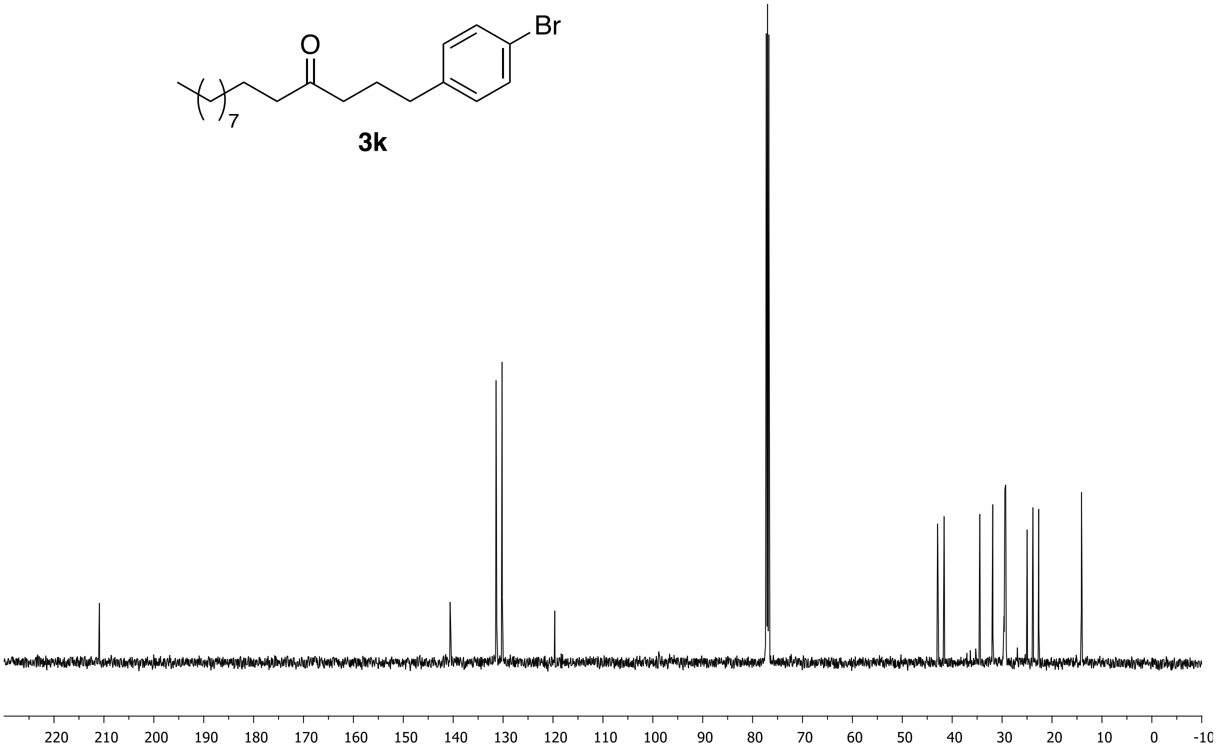
Br
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3k
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210
200
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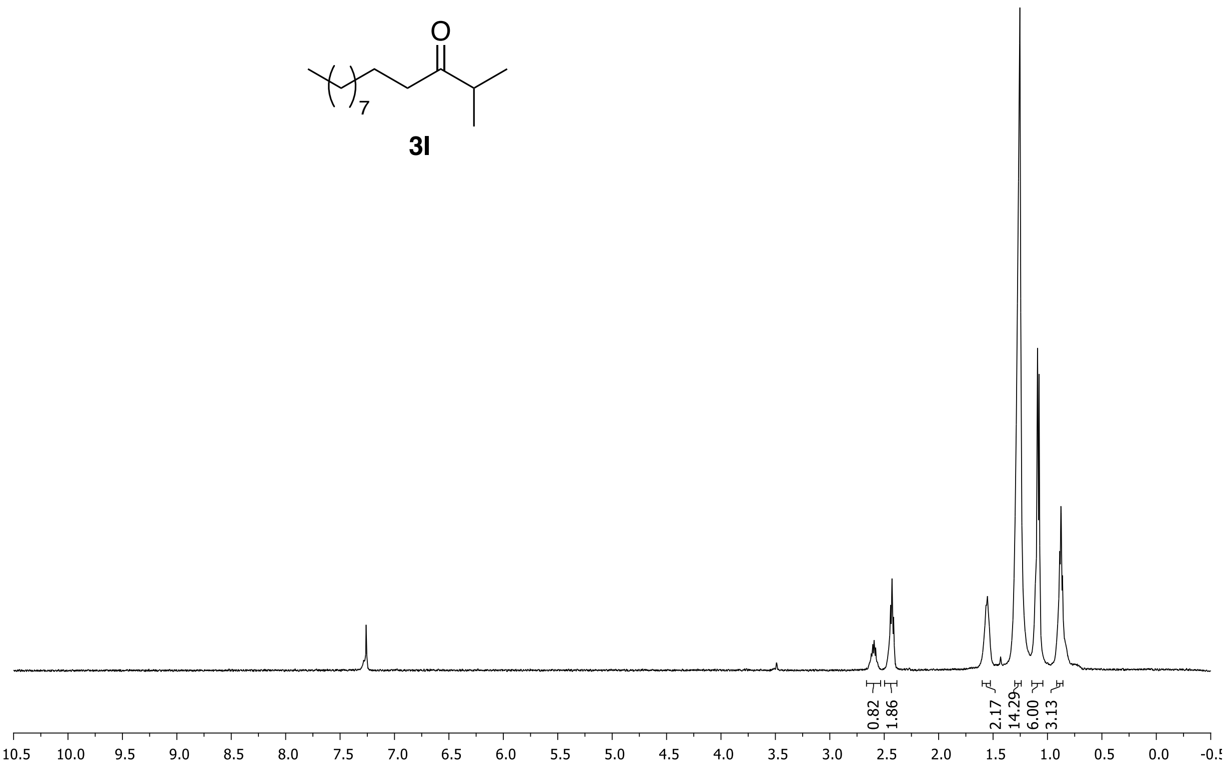
0
-10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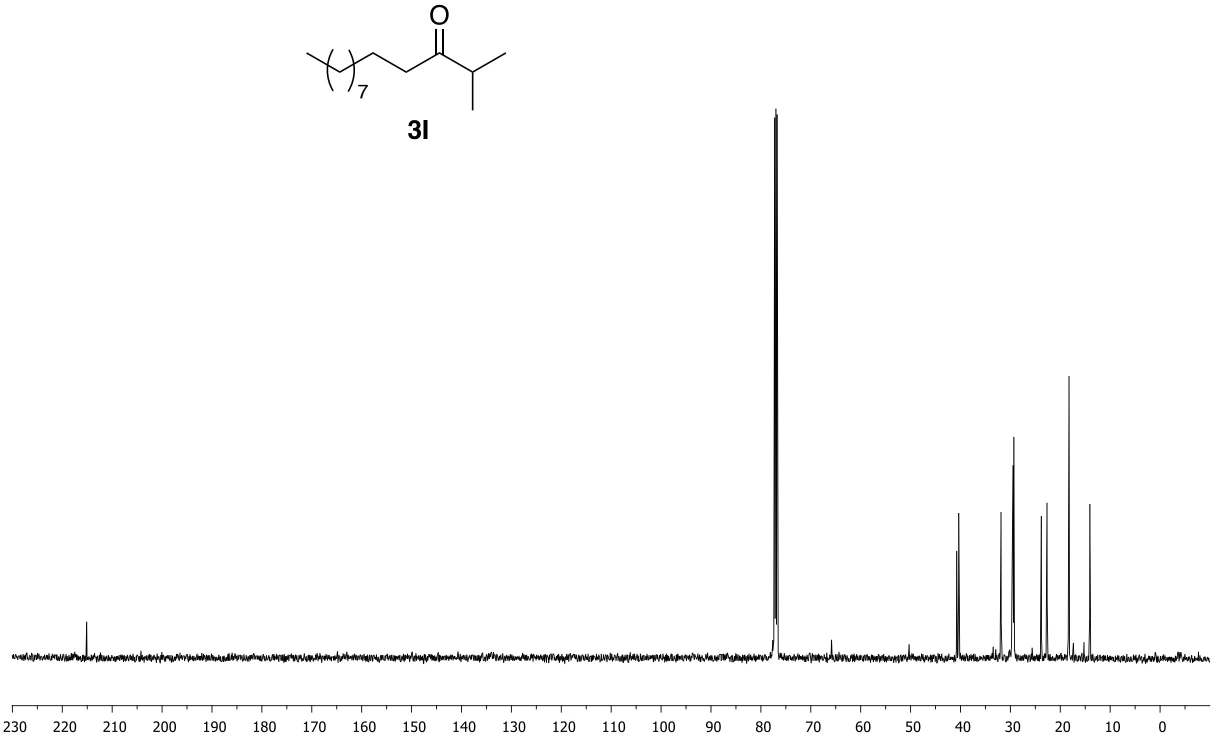
3l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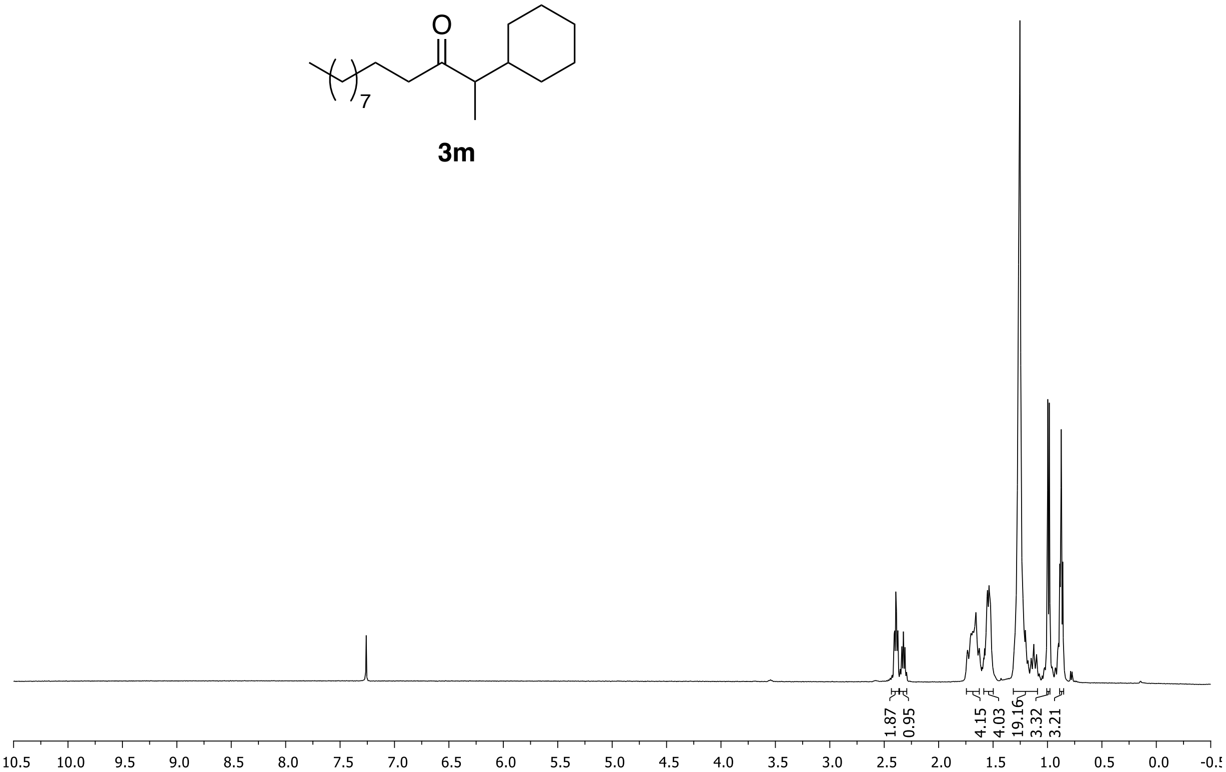
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3.32
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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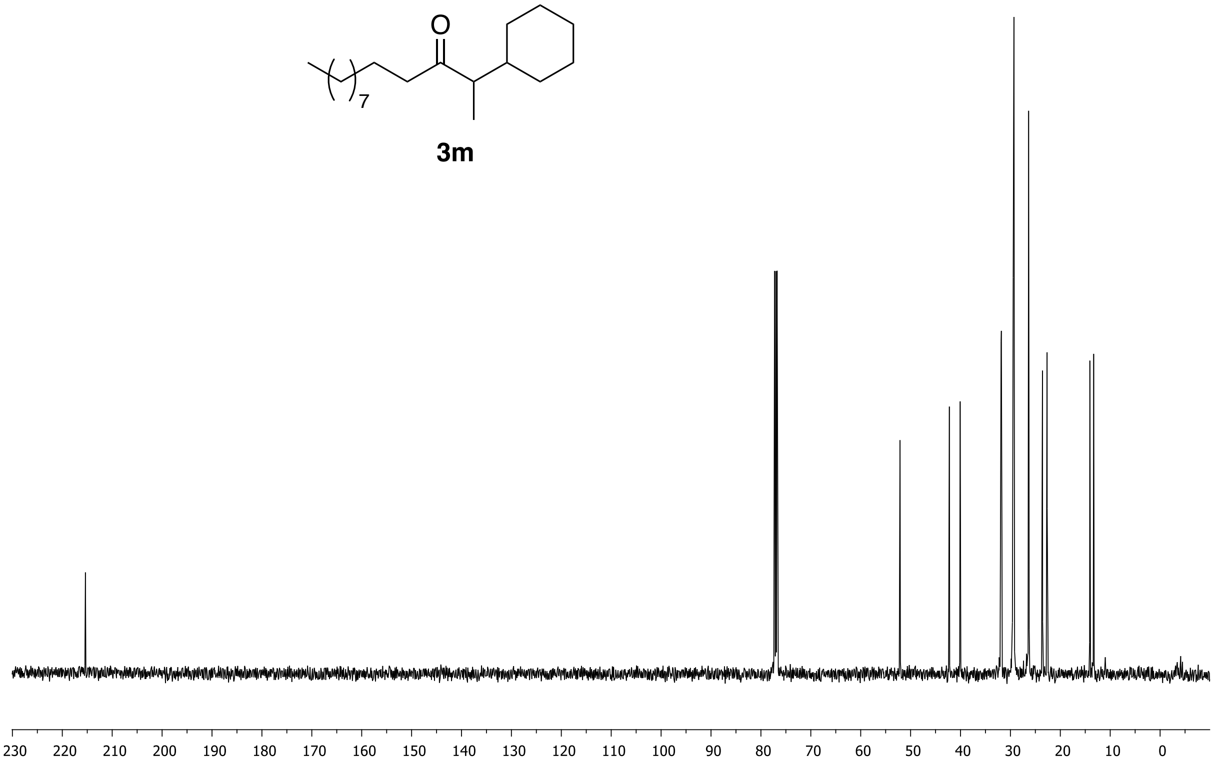
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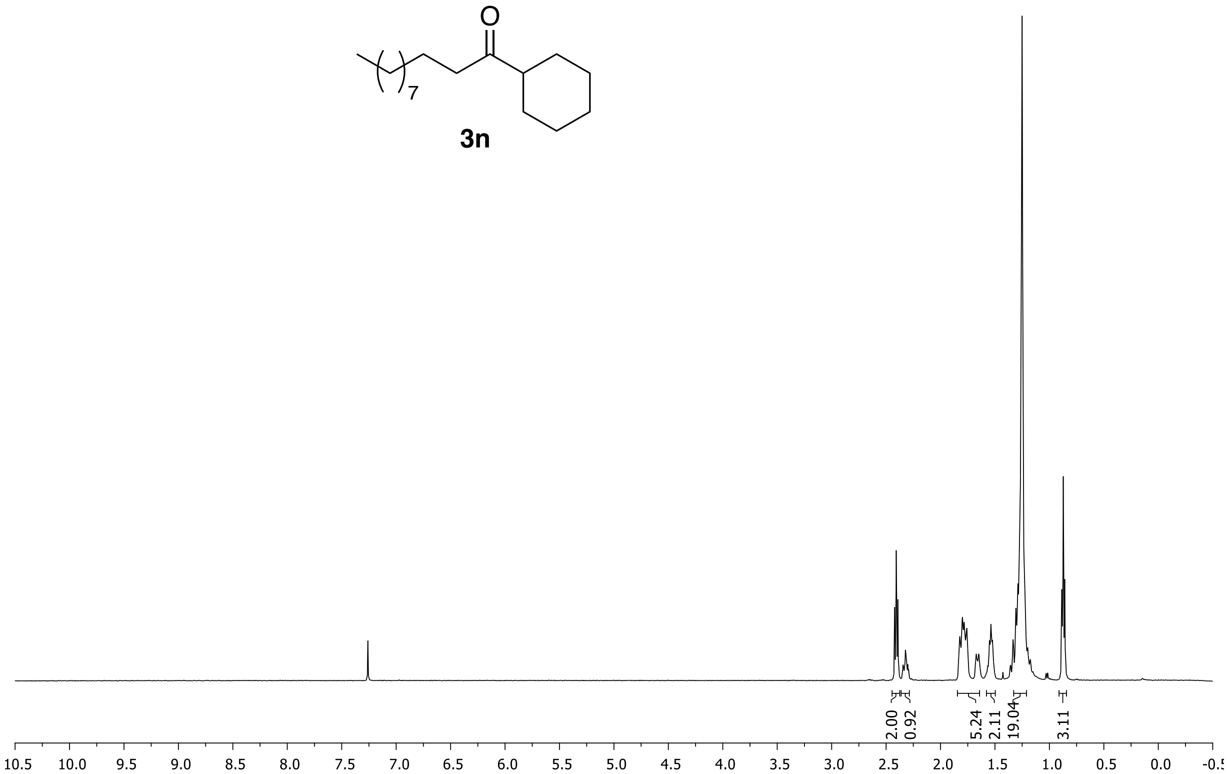
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19.04
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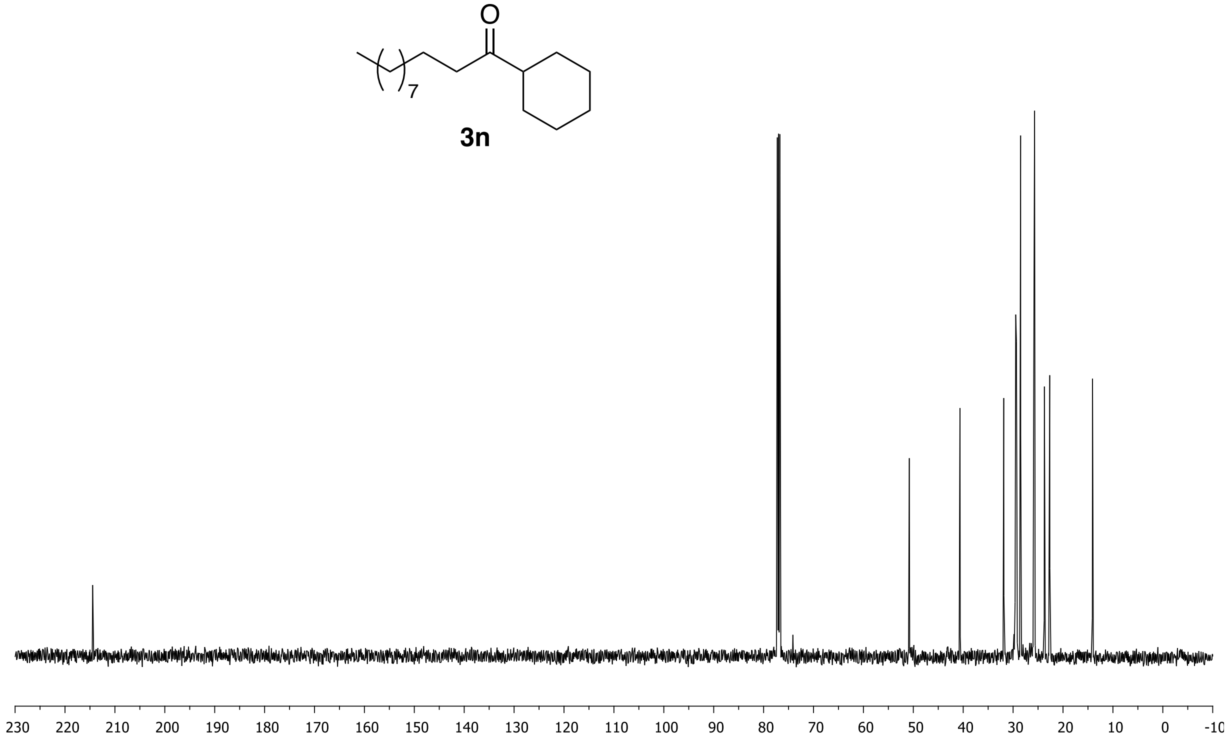
O
7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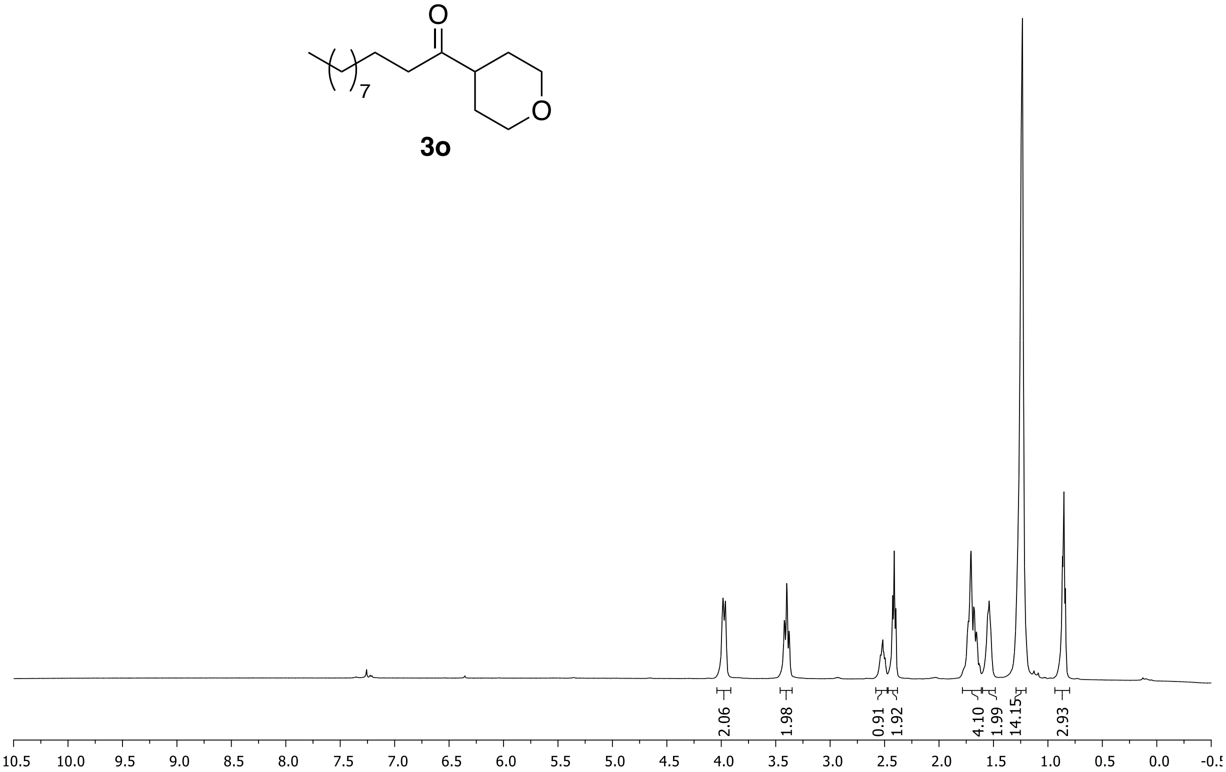
O
7



3o

O
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7.5
7.0
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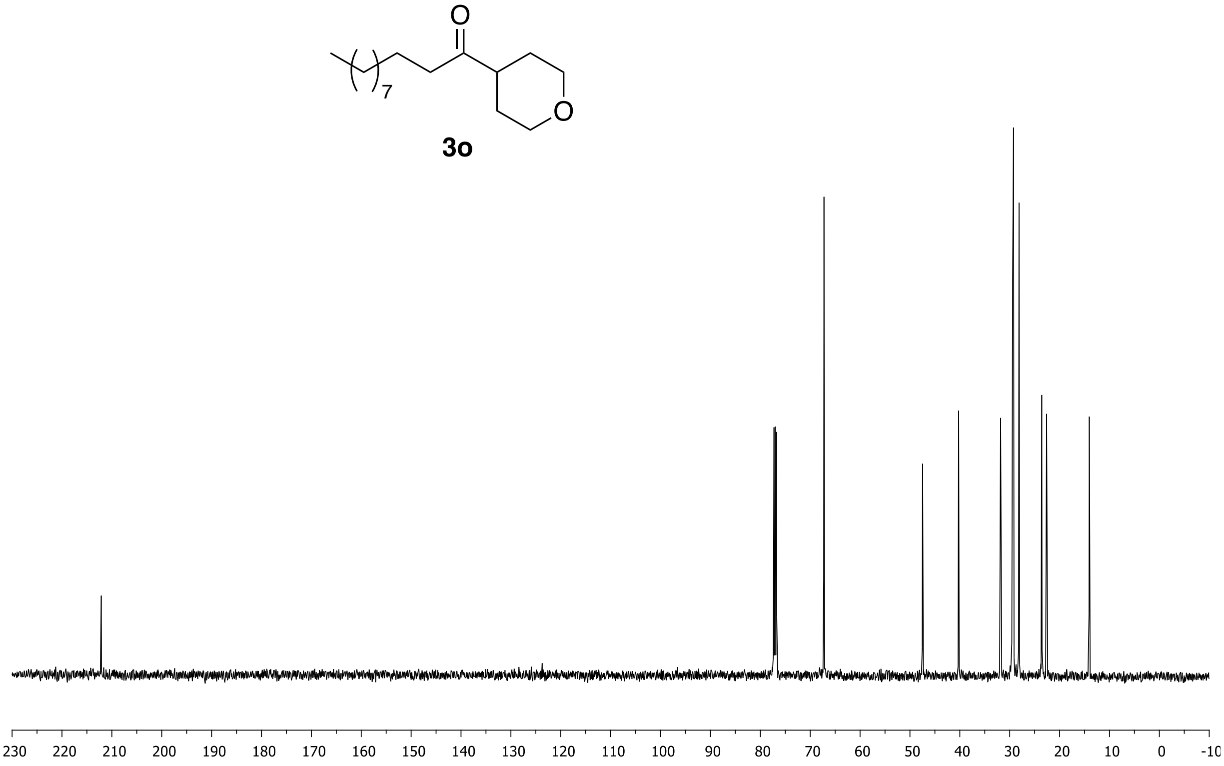

3o

O
7
O
230
220
210
200
190
180
170
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140
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120
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100
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80
70
60
50
40
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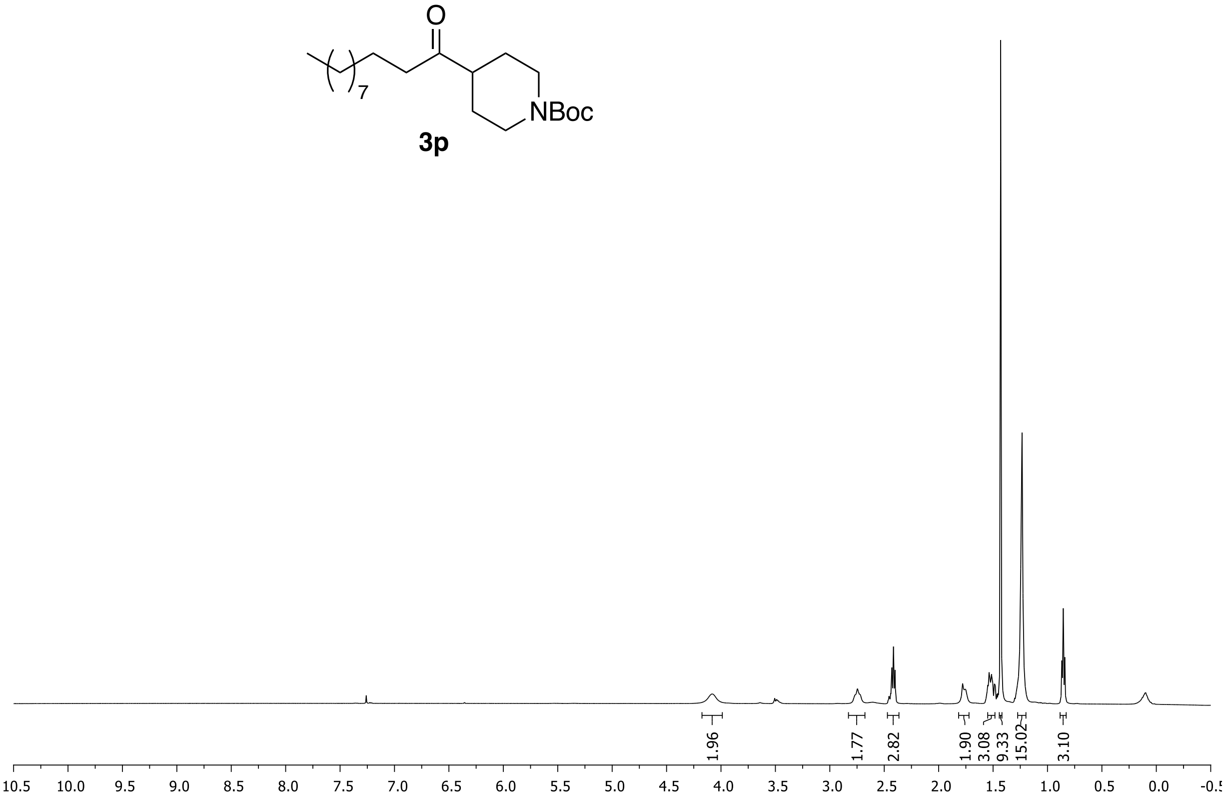
10
0
-10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8.0
7.5
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5.5
5.0
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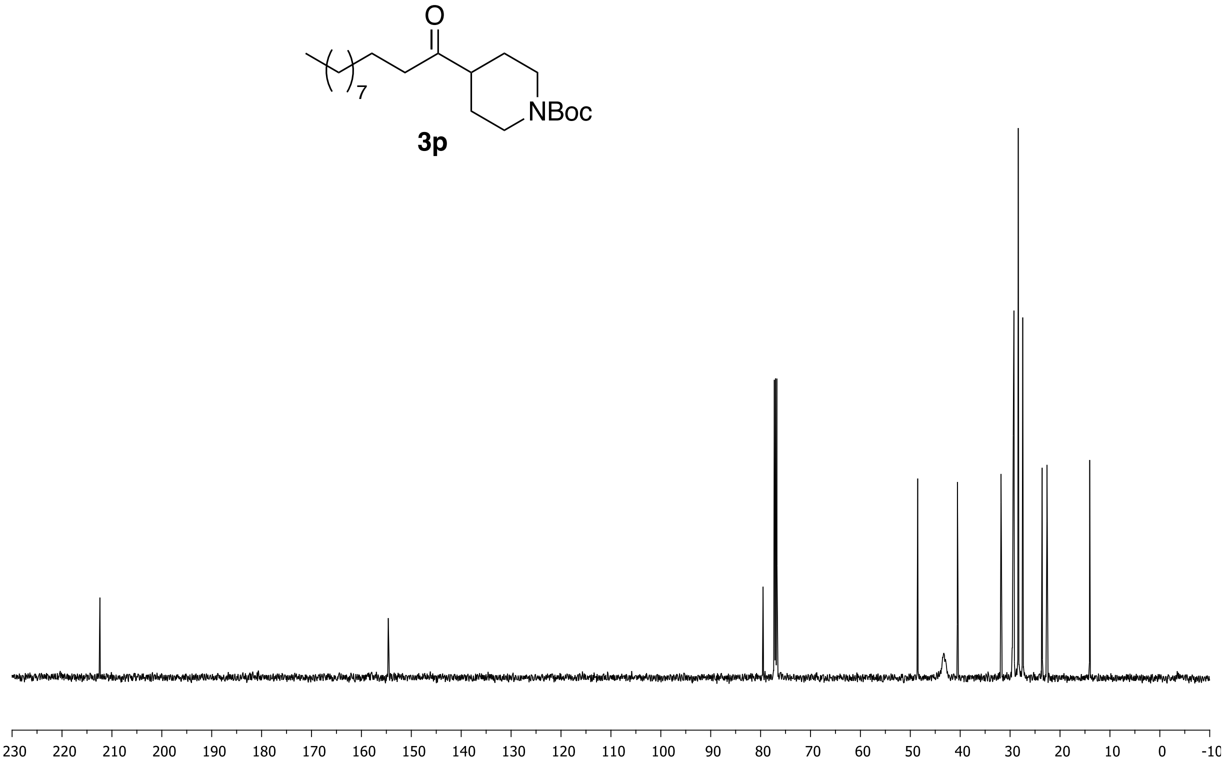
3p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40
30
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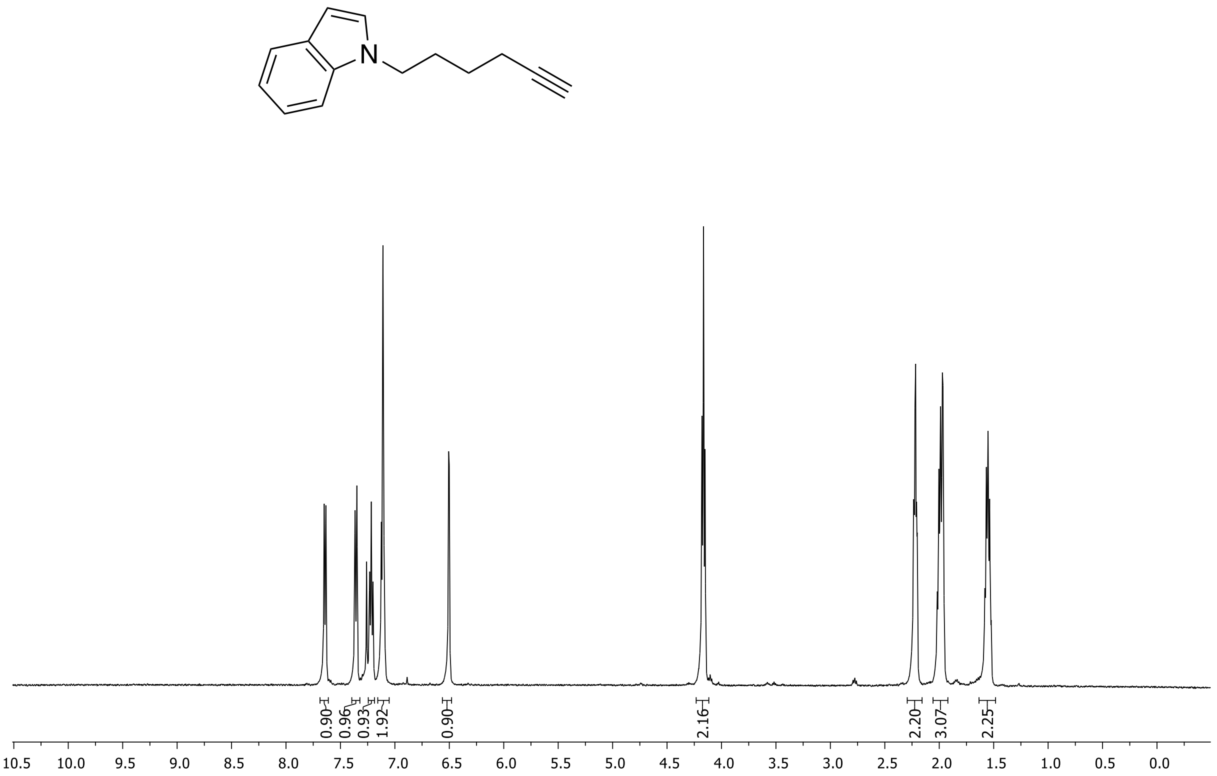
0
-10

3p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8.0
7.5
7.0
6.5
6.0
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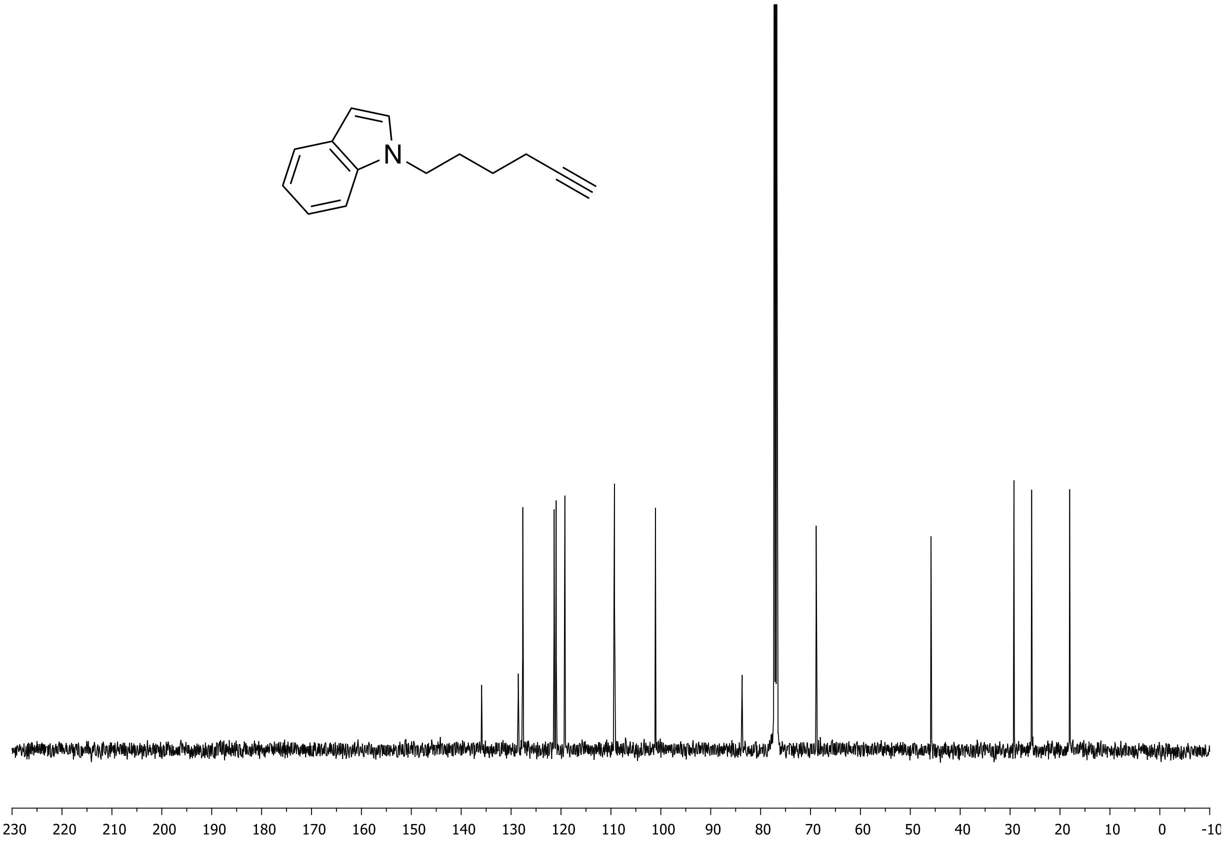
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40
30
20
10
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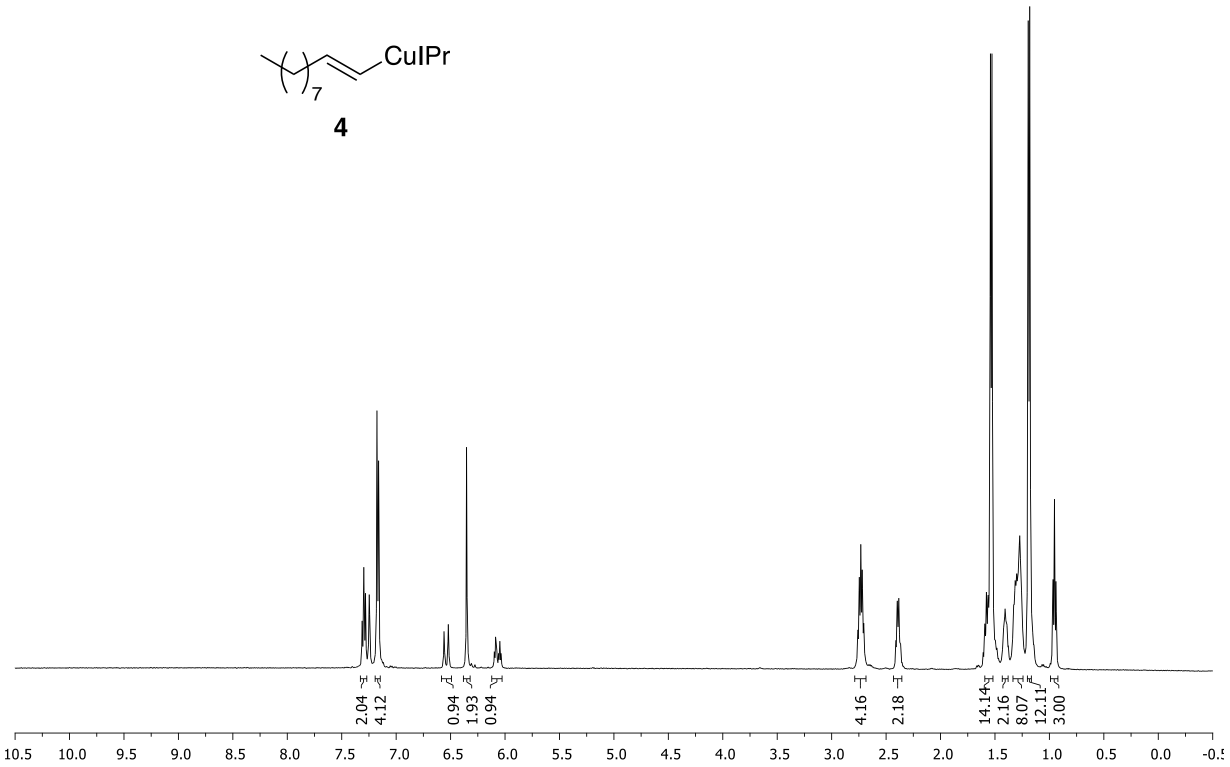
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4.16
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14.14
2.16
8.07
12.11
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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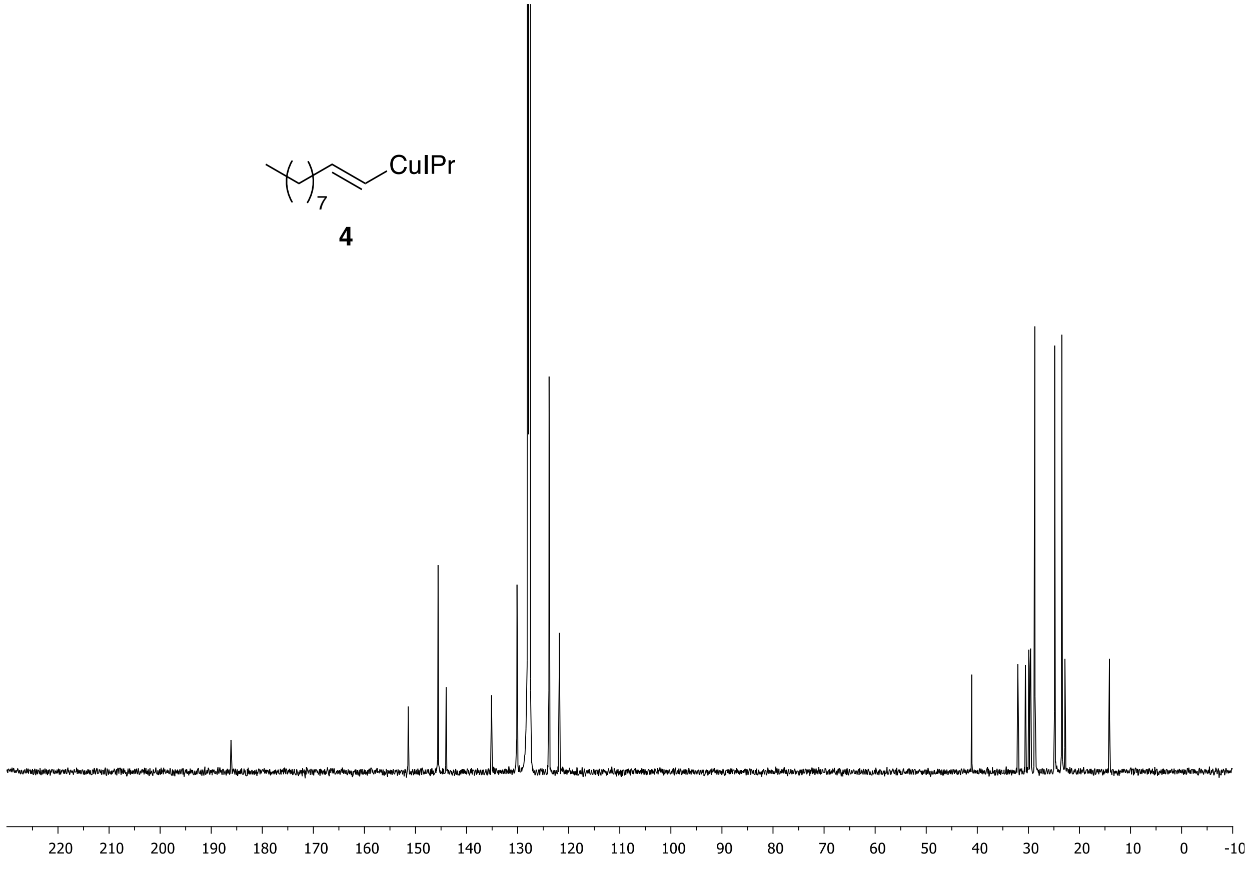
-0.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200
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50
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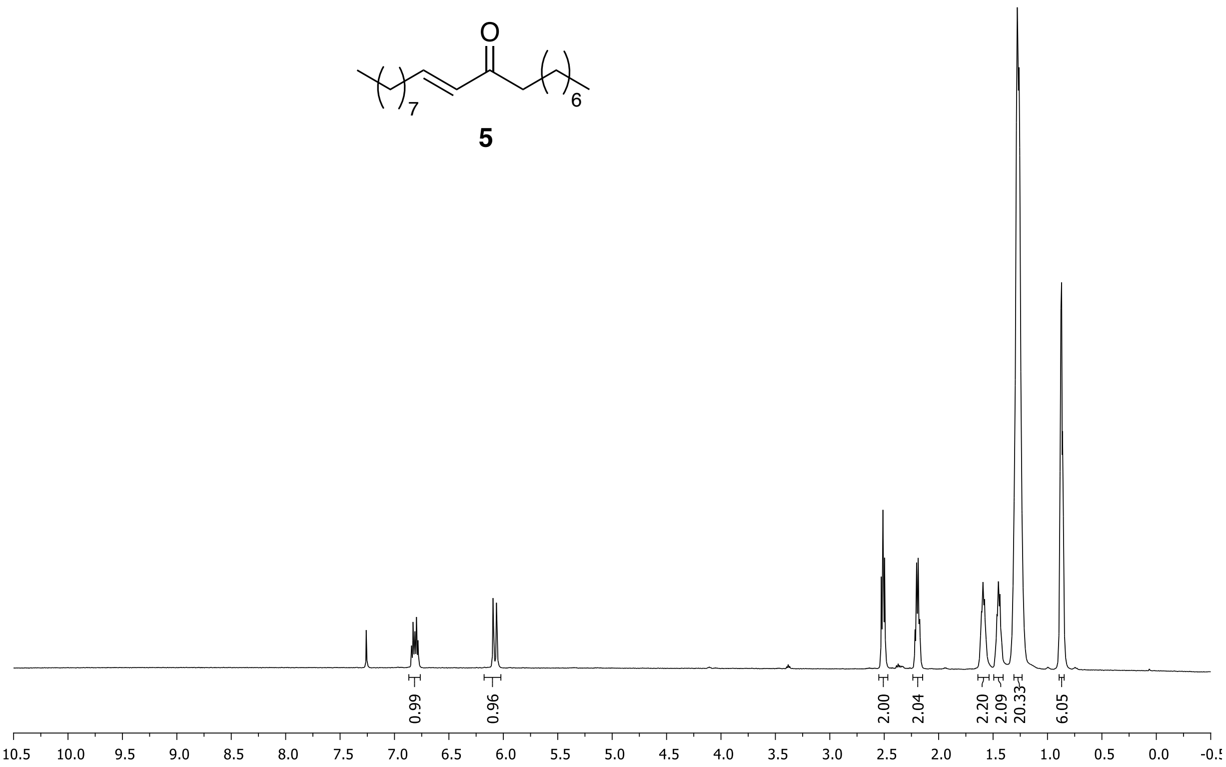
0
-1



O
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5
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0.96
2.00
2.04
2.20
2.09
20.33
6.05
10.5
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9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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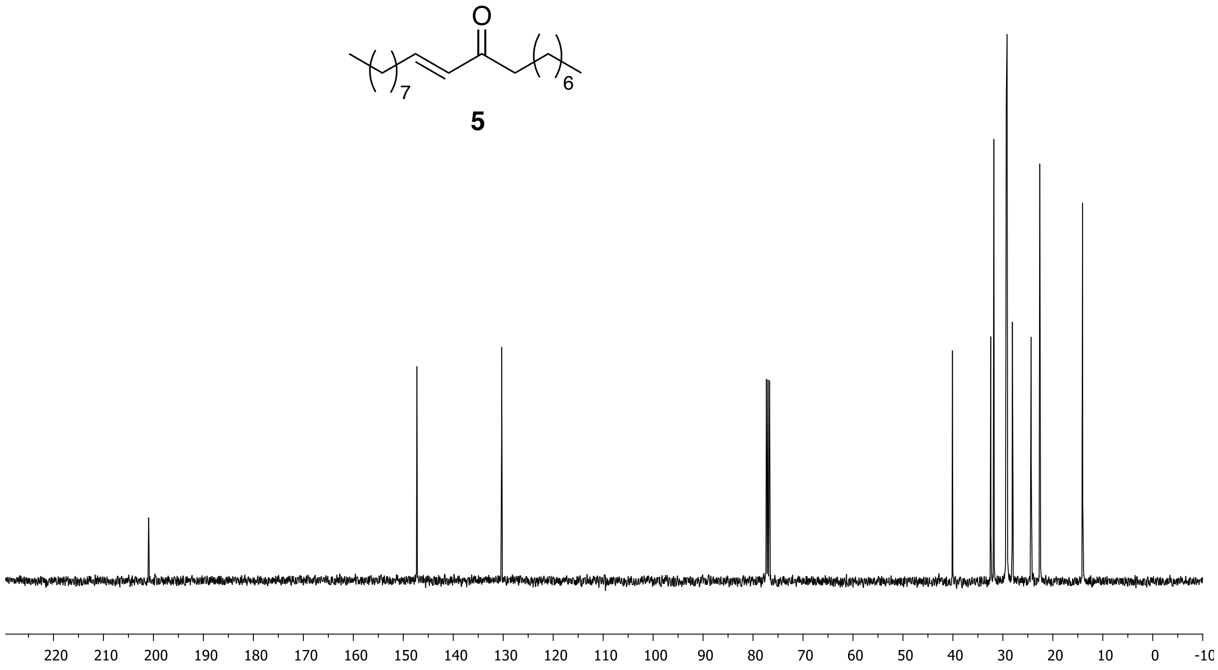
-0.5



O
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180
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160
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50
40
30
20
10
0
-10


O
7
9
4.23
0.82
1.83
6.18
14.15
1.91
3.19
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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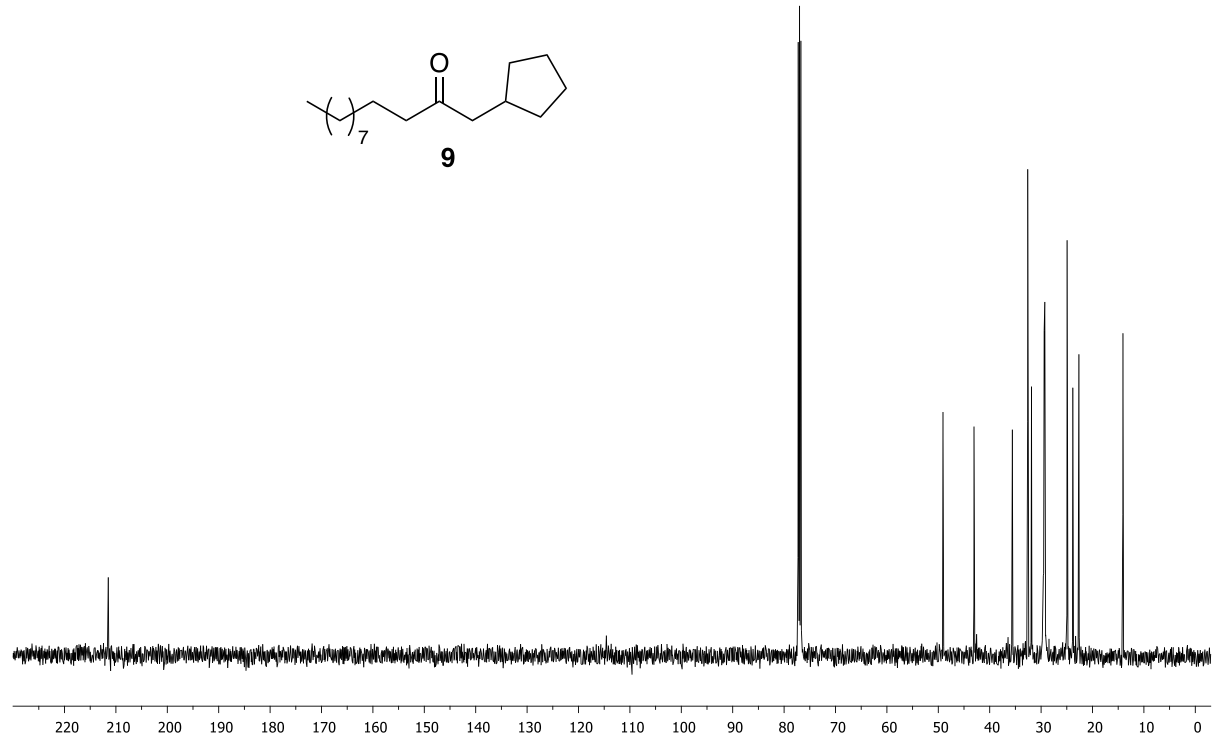
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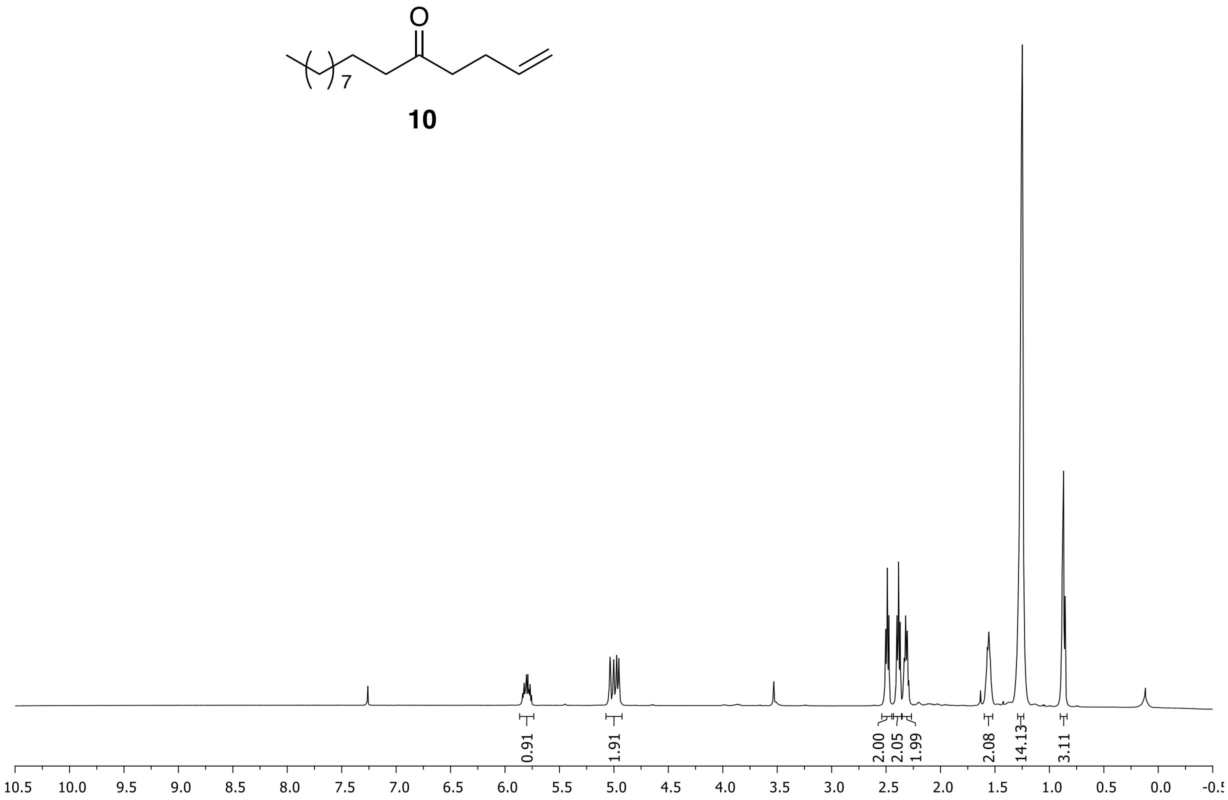

10

O
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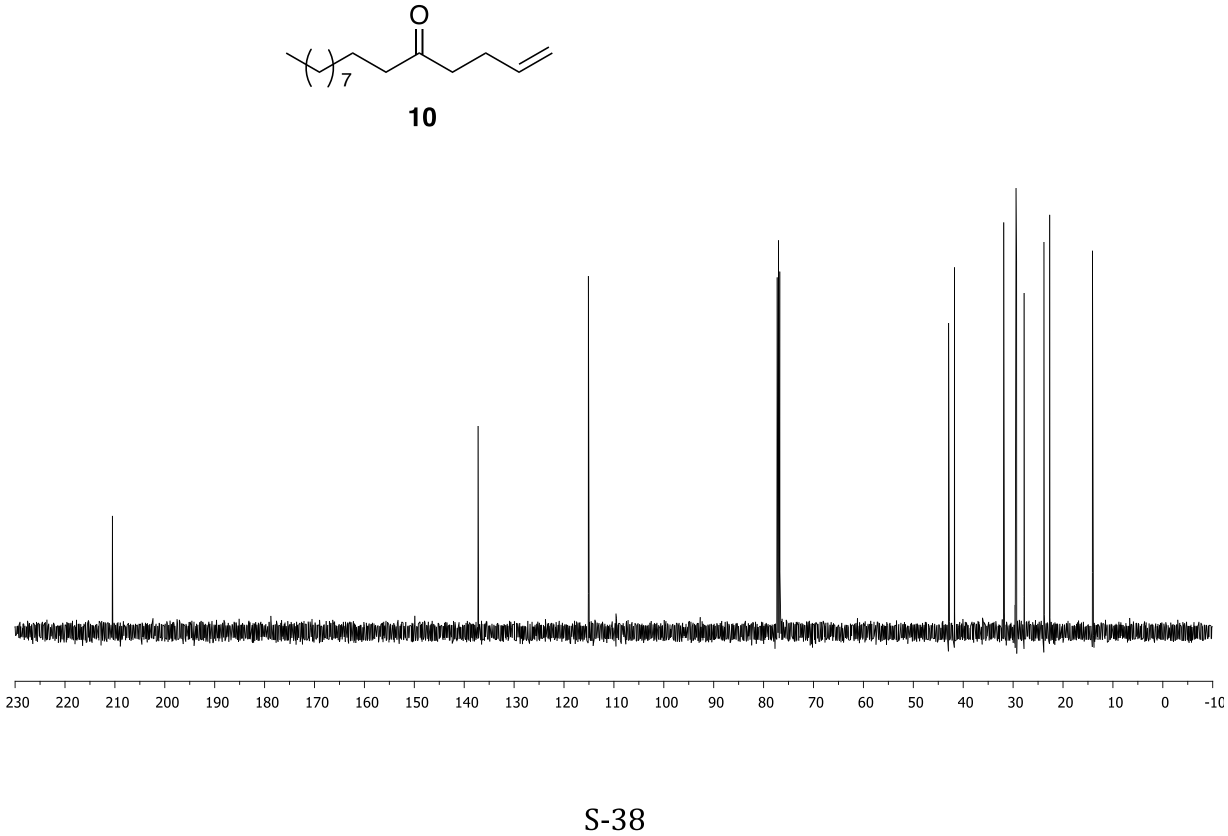
2.00
2.05
1.99
2.08
14.13
3.11
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5



10

O
7
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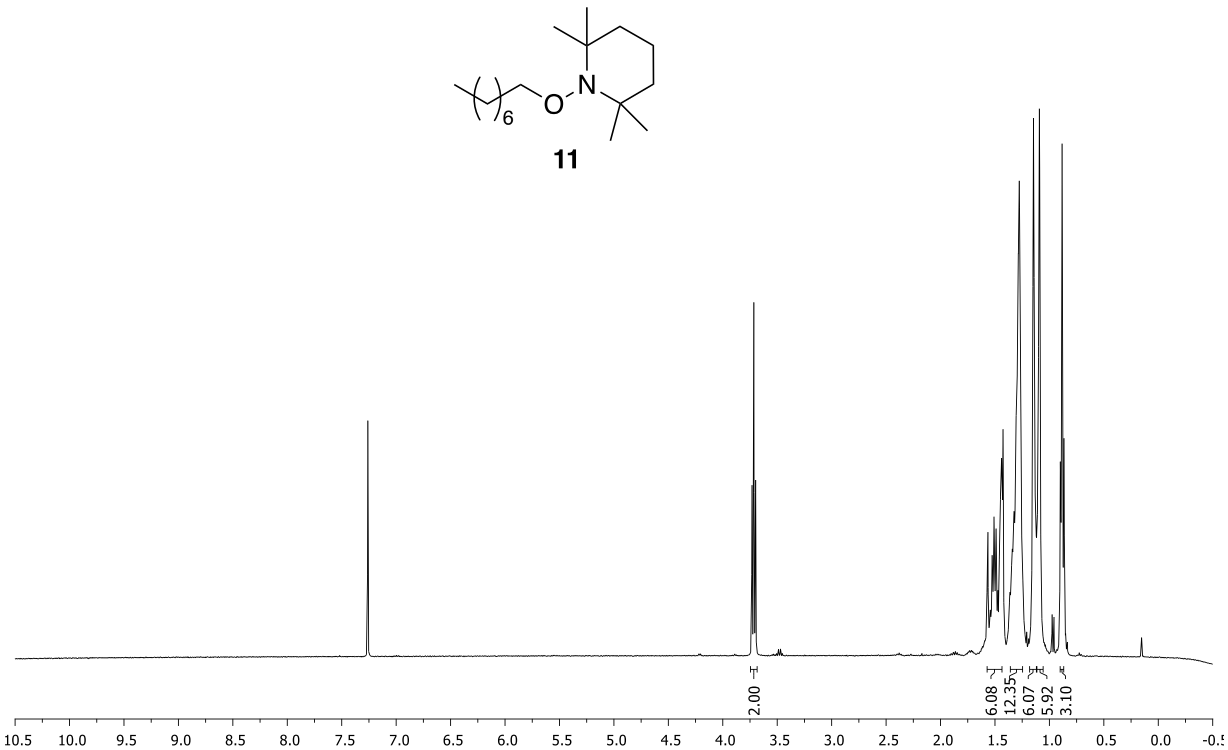

11

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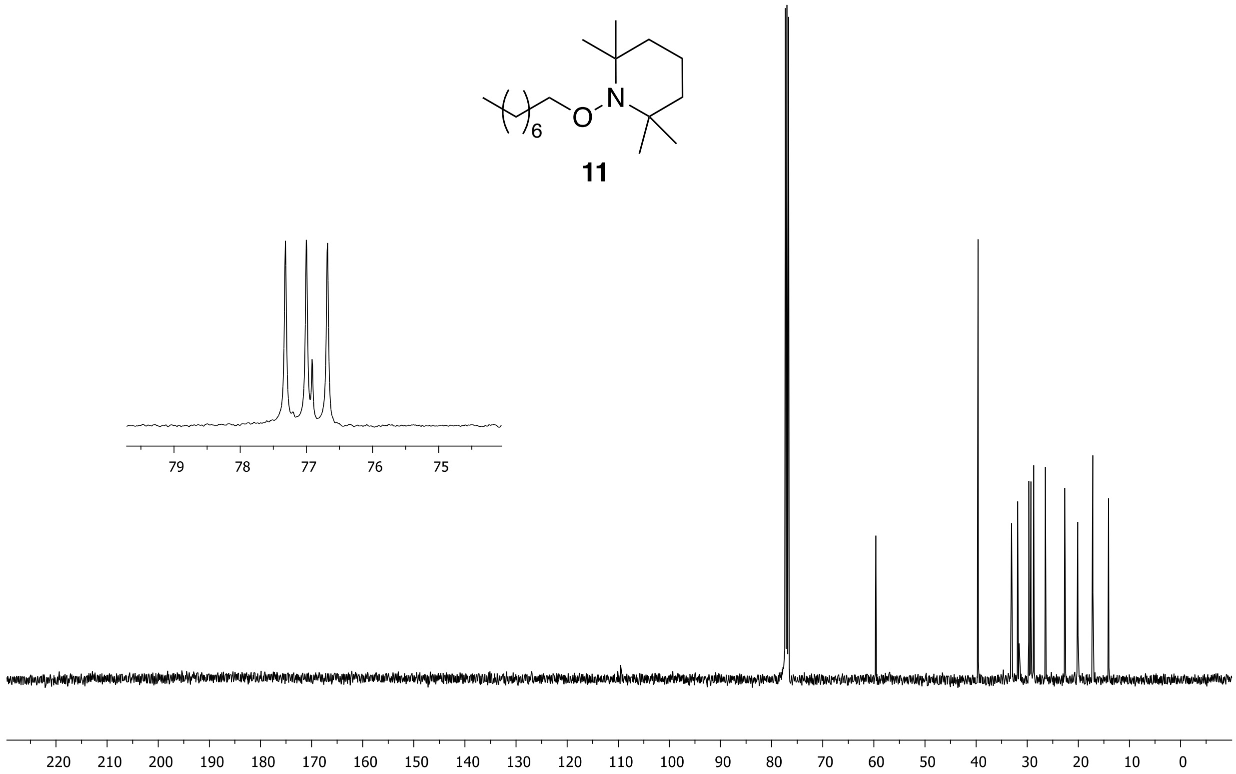

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