Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Vinylogous Acyl Triflates as an Entry Point to α,β-Disubstituted Cyclic Enones via Suzuki-Miyaura Cross-Coupling

Daria E. Kim, Yingchuan Zhu, Timothy R. Newhouse

Department of Chemistry, Yale University, 225 Prospect St., New Haven, Connecticut 06520-8107

Supplementary Information

Table of Contents

General Experimental

General Experimental Procedures: All reactions were carried out under an inert argon atmosphere with dry, degassed solvents under anhydrous conditions unless otherwise stated. Degassification was accomplished through freeze-pump-thaw cycling. All reactions were capped with Teflon-coated silicon microwave cap unless otherwise stated. Stainless steel syringes were used to transfer solvent, and air- and moisture- sensitive liquid reagents. Reactions were monitored by thin-layer chromatography (TLC) and carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as the visualizing agent and potassium permanganate or an acidic solution of *p*-anisaldehyde as developing agents. Flash column chromatography employed SiliaFlash® P60 (40–60 µm, 230–400 mesh) silica gel purchased from SiliCycle Inc.

Materials: All reaction solvents were purified using a Seca solvent purification system by Glass Contour, with the exception of H_2O. Deionized water was taken from the tap and used as is. 9-Borabicyclo[3.3.1]nonane dimer, $PdCl_2$(dppf), $Pd(OAc)_2$, PPh_3, *rac*-BINAP and dppf were purchased from Sigma-Aldrich. $Pd(PPh_3)_4$ was purchased from Oakwood Scientific. All other reagents were used as received without further purification, unless otherwise stated.

Instrumentation: All new compounds were characterized by means of ^{1}H-NMR, ^{13}C-NMR, FT-IR (thin film) and HR-MS. Copies of the ^{1}H- and ^{13}C-NMR spectra can be found at the end of the Supporting Information. NMR spectra were recorded using a Varian 400 MHz NMR spectrometer, Varian 500 MHz NMR spectrometer, or Varian 600 MHz NMR spectrometer. All ^{1}H-NMR data are reported in δ units, parts per million (ppm), and were calibrated relative to the signals for residual chloroform (7.26 ppm) in deuterochloroform ($CDCl_3$). All ^{13}C-NMR data are reported in ppm relative to $CDCl_3$ (77.16 ppm) and were obtained with ^{1}H decoupling unless otherwise stated. The following abbreviations or combinations thereof were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, and a = apparent. All IR spectra were taken on an FT-IR/Raman Thermo Nicolet 6700. High resolution mass spectra (HR-MS) were recorded on a Bruker microTOF mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

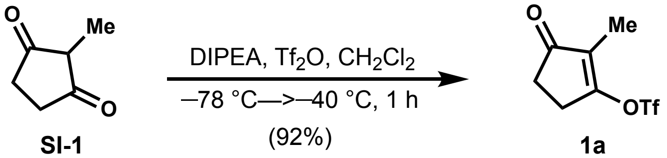
General Hydroboration Procedure

A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with alkene (1.00 mmol, 1.0 equiv), capped with a rubber septum, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous tetrahydrofuran (0.50 M, 2.0 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles was added to the vial in a single portion. The resulting solution was cooled to 0 °C by transferring the reaction apparatus to an ice-water bath. After stirring at this temperature for 5 minutes, 9-borabicyclo[3.3.1]nonane dimer (146 mg, 0.60 mmol, 0.6 equiv) was quickly added to the reaction as a solid in a single portion. Following this, the reaction mixture was allowed to slowly warm to room temperature by transferring the reaction apparatus out of the ice-water bath.

After stirring for 1 hour, the reaction mixture was cooled back down to 0 °C by transferring the reaction apparatus to an ice-water bath. After stirring at this temperature for 5 minutes, rigorously degassed deionized water (900 μl, 50.0 mmol, 50.0 equiv) was added to the reaction flask in a dropwise fashion over 1 minute. At this time, the biphasic reaction mixture became a cloudy white color. The reaction mixture was allowed to stir following the addition of the water for 30 minutes before use in the B-alkyl Suzuki coupling.

Experimental Procedures and Characterization Data for Vinylogous Acyl Triflates

Synthesis of Triflate 1a:



A flame-dried, 500 mL round-bottomed flask equipped with a magnetic stir bar was charged with 2-methyl-1,3-cyclopentanedione (**SI-1**) (5.00 g, 44.6 mmol, 1.0 equiv), sealed with a rubber septum, evacuated and backfilled with nitrogen three times, and placed under a nitrogen atmosphere. The solid was then dissolved in anhydrous CH_2Cl_2 (223 mL, 0.2 M), which was followed by the addition of *N,N*-diisopropylethylamine (17.86 ml, 102.6 mmol, 2.3 equiv) in a single portion. Following this, the reaction was cooled to –78 °C by transferring the reaction apparatus to a dry ice-acetone bath. After stirring at this temperature for 10 minutes, triflic anhydride (9.00 ml, 53.5 mmol, 1.2 equiv) was added to the flask in a dropwise fashion over five minutes. Upon the addition of the triflic anhydride, the colorless reaction mixture became a pale brown color.

The reaction mixture was allowed to stir for 1 hour, while slowly warming to –40 °C. After this time, the reaction was quenched by pouring into H_2O (250 ml). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 250 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (300 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude brown oil. Purification by flash column chromatography on silica gel (CH_2Cl_2/hexanes = 1/1) afforded **1a** (10.01 g, 92%) as a pale brown oil.

Spectral data was consistent with that reported in the literature.[12b]

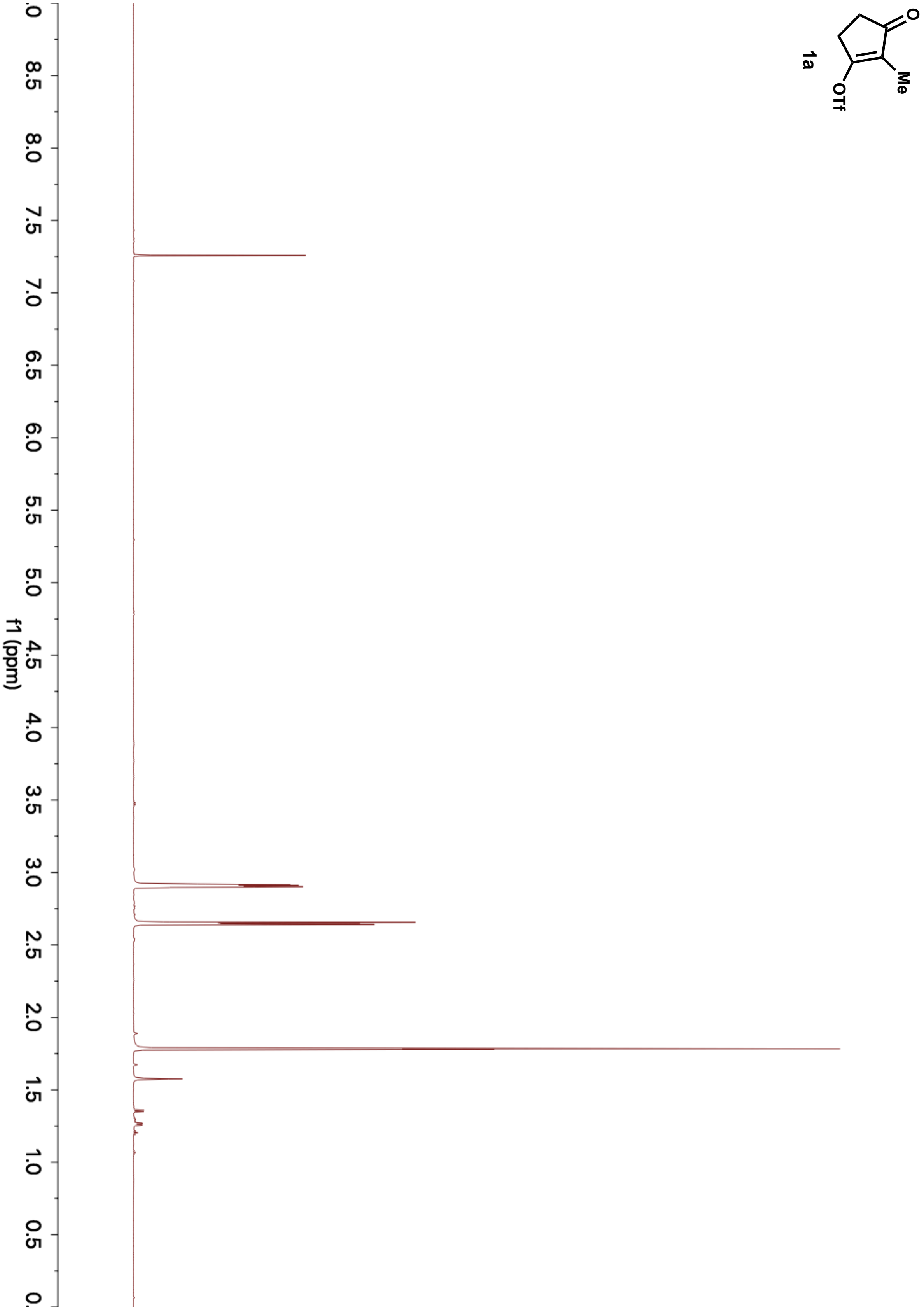
Rf: 0.56 (50% Et_2O/50% hexanes)

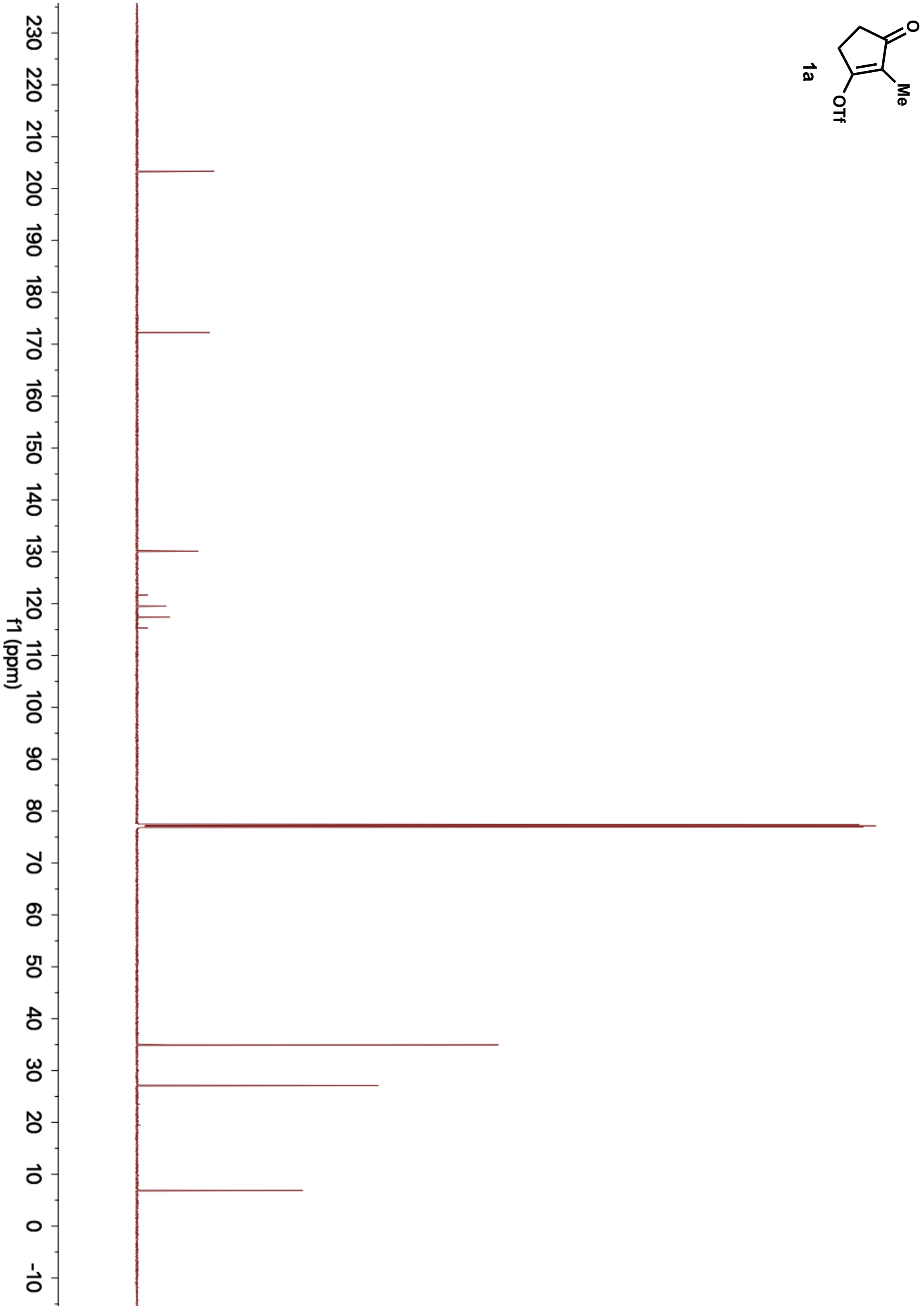
^{1}H NMR (600 MHz, $CDCl_3$): δ 2.93–2.89 (m , 2H), 2.66–2.64 (m, 2H), 1.78 (at, *J* = 2.2 Hz, 3H)

^{13}C NMR (600 MHz, $CDCl_3$): δ 203.3, 172.3, 130.1, 118.4 (q, *J* = 321 Hz), 34.9, 27.1, 6.9

IR (cm^{-1}): 1722, 1679, 1425, 1206, 1133, 1081, 1051, 898, 804, 763, 593

ESI-HRMS (m/z): $[M+H]^+$ calc'd for $C_7H_8F_3O_4S^+$: 245.0018; found: 244.9783

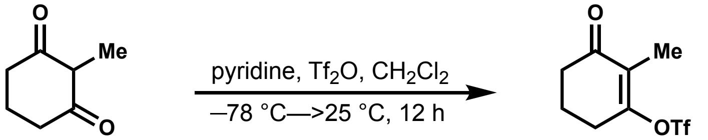

O
Me
OTf
1a
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)



1a

O
Me
OTf
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Synthesis of Triflate 1b:



SI-2 **1b**

A flame-dried, 1 L round-bottomed flask equipped with a magnetic stir bar was charged with 2-methyl-1,3-cyclopentanedione (**SI-1**) (5.00 g, 39.6 mmol, 1.0 equiv), sealed with a rubber septum, evacuated and backfilled with nitrogen three times, and placed under a nitrogen atmosphere. The solid was then dissolved in anhydrous CH_2Cl_2 (396 mL, 0.1 M), which was followed by the addition of pyridine (3.48 ml, 43.6 mmol, 1.1 equiv) in a single portion. Following this, the reaction was cooled to –78 °C by transferring the reaction apparatus to a dry ice-acetone bath. After stirring at this temperature for 10 minutes, triflic anhydride (7.33 ml, 43.6 mmol, 1.1 equiv) was added to the flask in a dropwise fashion over five minutes. Upon the addition of the triflic anhydride, the colorless reaction mixture became a pale pink color.

The reaction mixture was allowed to stir for 12 hour, while slowly warming to 25 °C. After this time, the reaction was quenched by pouring into sat. aq. $NaHCO_3$ (300 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 300 mL). The combined organic layers were washed with brine (300 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude brown oil. Purification by flash column chromatography on silica gel (Et_2O/hexanes = 1/5) afforded **1b** (8.08 g, 79%) as a pale yellow oil.

Spectral data was consistent with that reported in the literature.[12a]

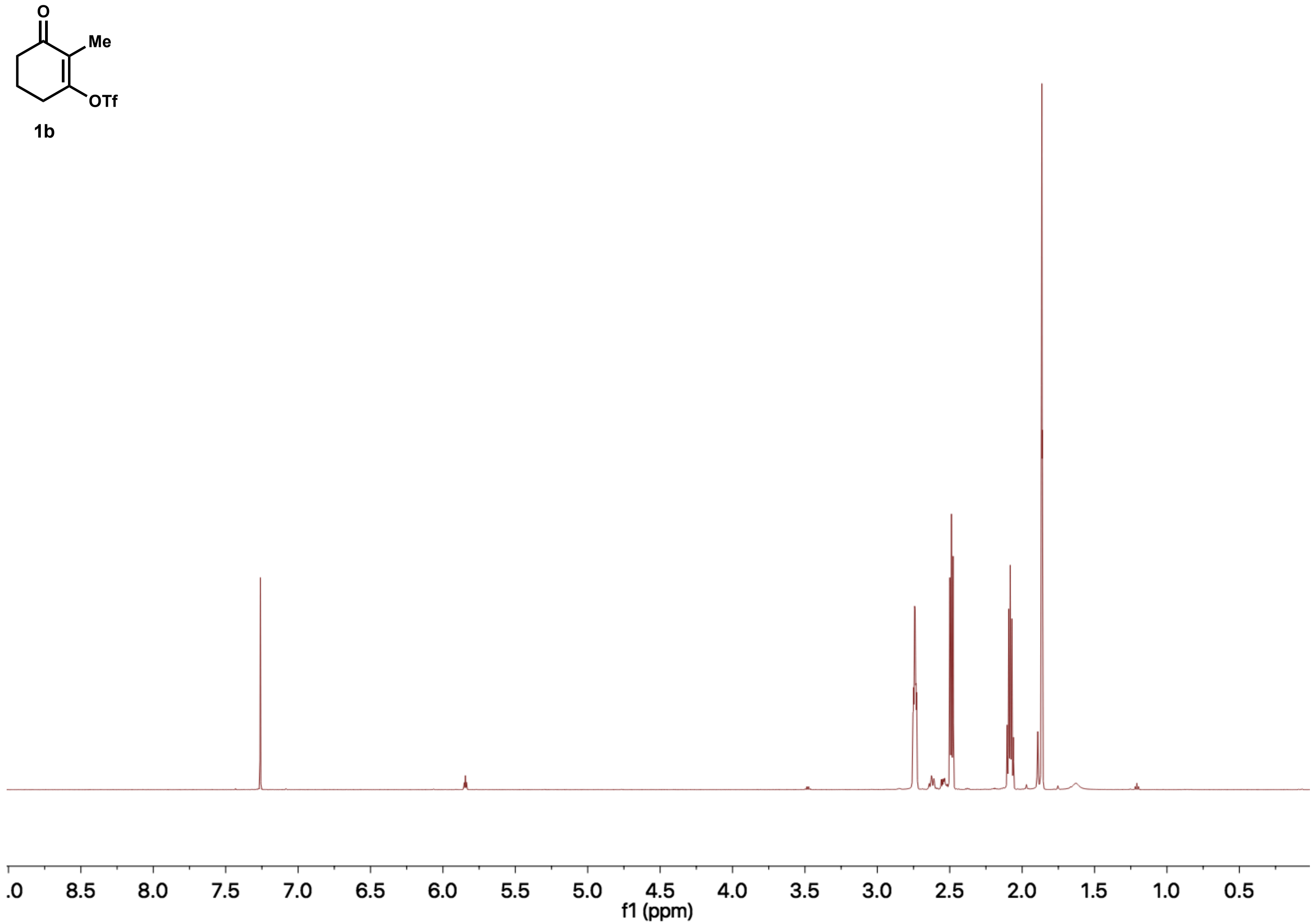
Rf: 0.63 (50% Et_2O/50% hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.76–2.72 (m , 2H), 2.49 (t, *J* = 6.6 Hz, 2H), 2.10–2.06 (m, 2H), 1.87–1.86 (m, 3H)

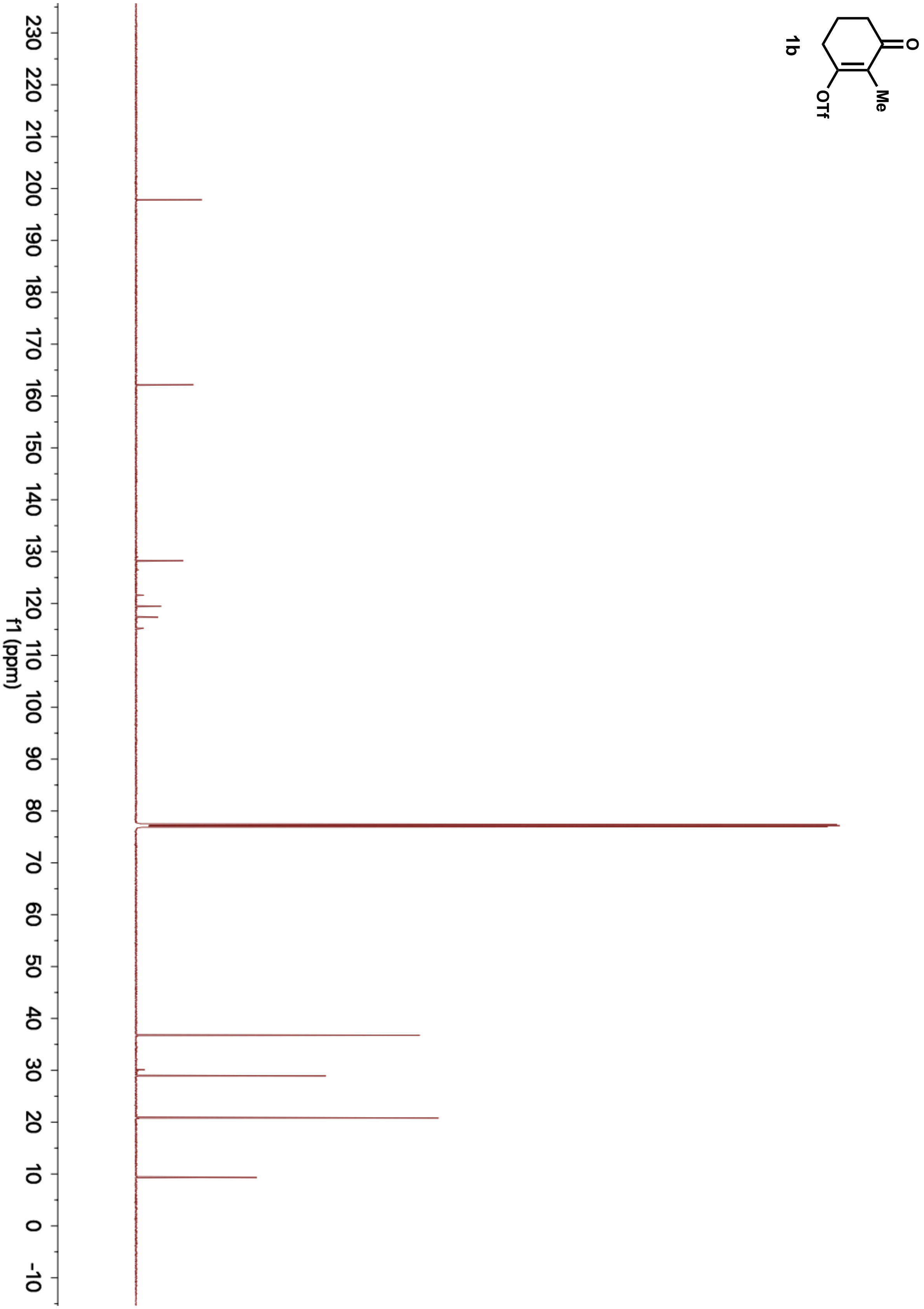
^{13}C NMR (600 MHz, $CDCl_3$): δ 197.8, 162.2, 128.3, 118.4 (q, *J* = 317 Hz), 36.8, 28.9, 20.8, 9.3

IR (cm^{-1}): 1688, 1416, 1241, 1135, 1025, 892, 793, 759, 630, 596

ESI-HRMS (m/z): $[M+H]^+$ calc'd for $C_8H_{10}F_3O_4S^+$: 259.0175; found: 258.9929



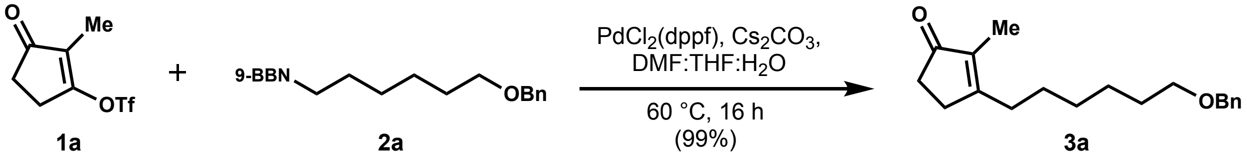
1b



O
Me
OTf
1b
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Experimental Procedures and Characterization Data for Cross-Coupling Products

Synthesis of Benzyl Alcohol 3a:



A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1a** (61.0 mg, 0.25 mmol, 1.0 equiv), $PdCl_2(dppf)$ (5.1 mg, 2.5 mol%) and Cs_2CO_3 (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2a** (0.34 M, 760 μl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. $NaHCO_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et_2O/hexanes/CH_2Cl_2= 0/1/1 to 1/49/50) afforded **3a** (70.3 mg, 99%) as a colorless oil.

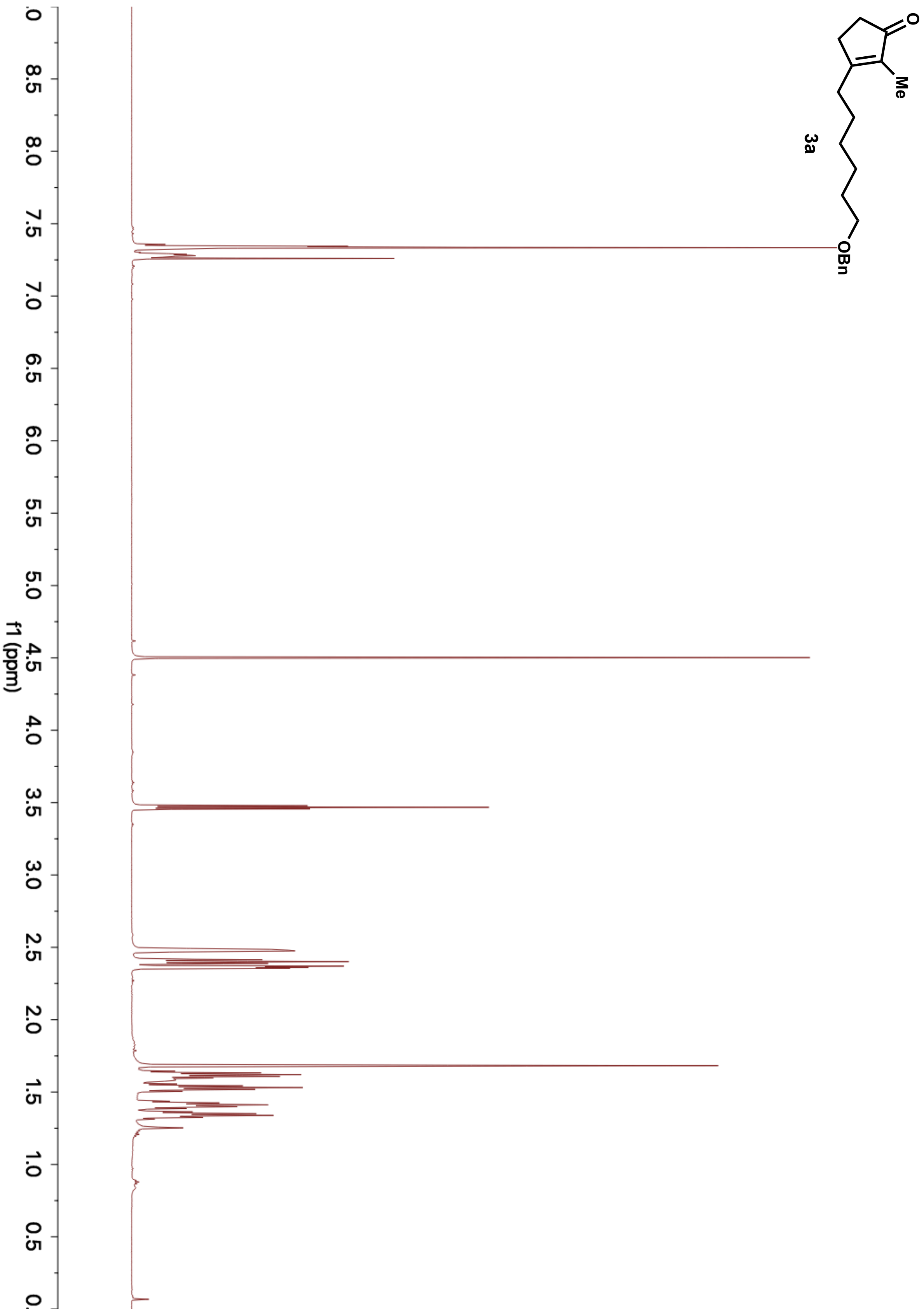
Rf: 0.26 (50% Et_2O/50% hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36–7.33 (m, 4H), 7.30–7.27 (m, 1H), 4.50 (s, 2H), 3.47 (t, *J* = 6.5 Hz, 2H), 2.50–2.46 (m, 2H), 2.40 (t, *J* = 7.7 Hz, 2H), 2.37–2.36 (m, 2H), 1.68 (s, 3H), 1.64–1.59 (m, 2H), 1.56–1.50 (m, 2H), 1.44–1.39 (m, 2H), 1.36–1.31 (m, 2H)

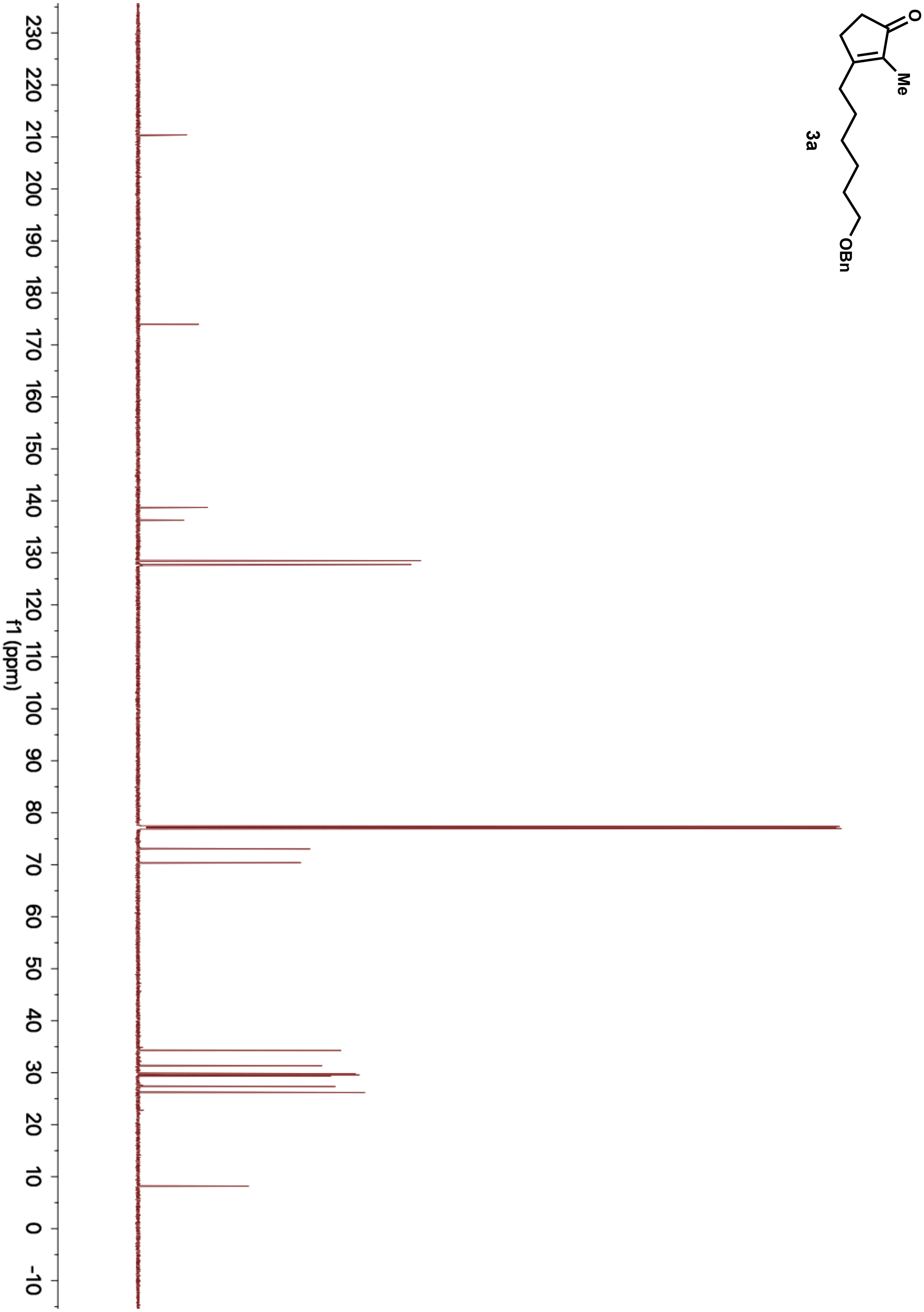
^{13}C NMR (600 MHz, $CDCl_3$): δ 210.4, 174.0, 138.7, 136.3, 128.5, 127.8, 127.7, 73.0, 70.4, 34.3, 31.3, 29.8, 29.6, 29.4, 27.4, 26.2, 8.2

IR (cm^{-1}): 2937, 2854, 1695, 1645, 1442, 1382, 1338, 1299, 1099, 696

ESI-HRMS (m/z): $[M+H]^+$ calc'd for $C_{19}H_{27}O_2^+$: 287.1934; found: 287.1999

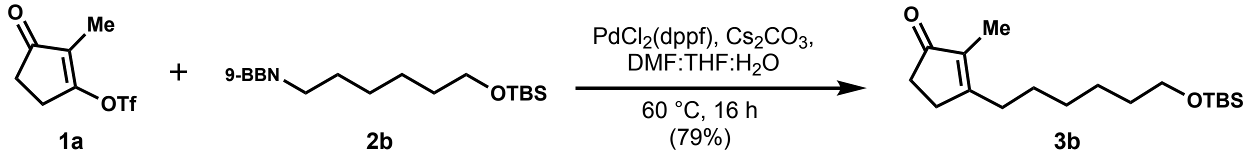


3a


O
Me
OBn
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

3a

Synthesis of TBS Alcohol 3b:



A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1a** (61.0 mg, 0.25 mmol, 1.0 equiv), PdCl$_2$(dppf) (5.1 mg, 2.5 mol%) and Cs$_2$CO$_3$ (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2b** (0.34 M, 760 μl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. NaHCO$_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et$_2$O/hexanes/CH$_2$Cl$_2$= 0/1/1 to 1/49/50) afforded **3b** (61.3 mg, 79%) as a yellow oil.

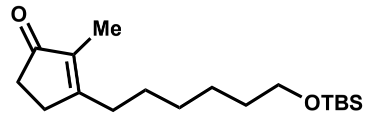
Rf: 0.37 (50% Et$_2$O/50% hexanes)

^{1}H NMR (600 MHz, CDCl$_3$): δ 3.60 (t, *J* = 6.4 Hz, 2H), 2.51–2.47 (m, 2H), 2.41 (t, *J* = 7.7 Hz, 2H), 2.38–2.35 (m, 2H), 1.69 (s, 3H), 1.56–1.49 (m, 4H), 1.39–1.31 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H)

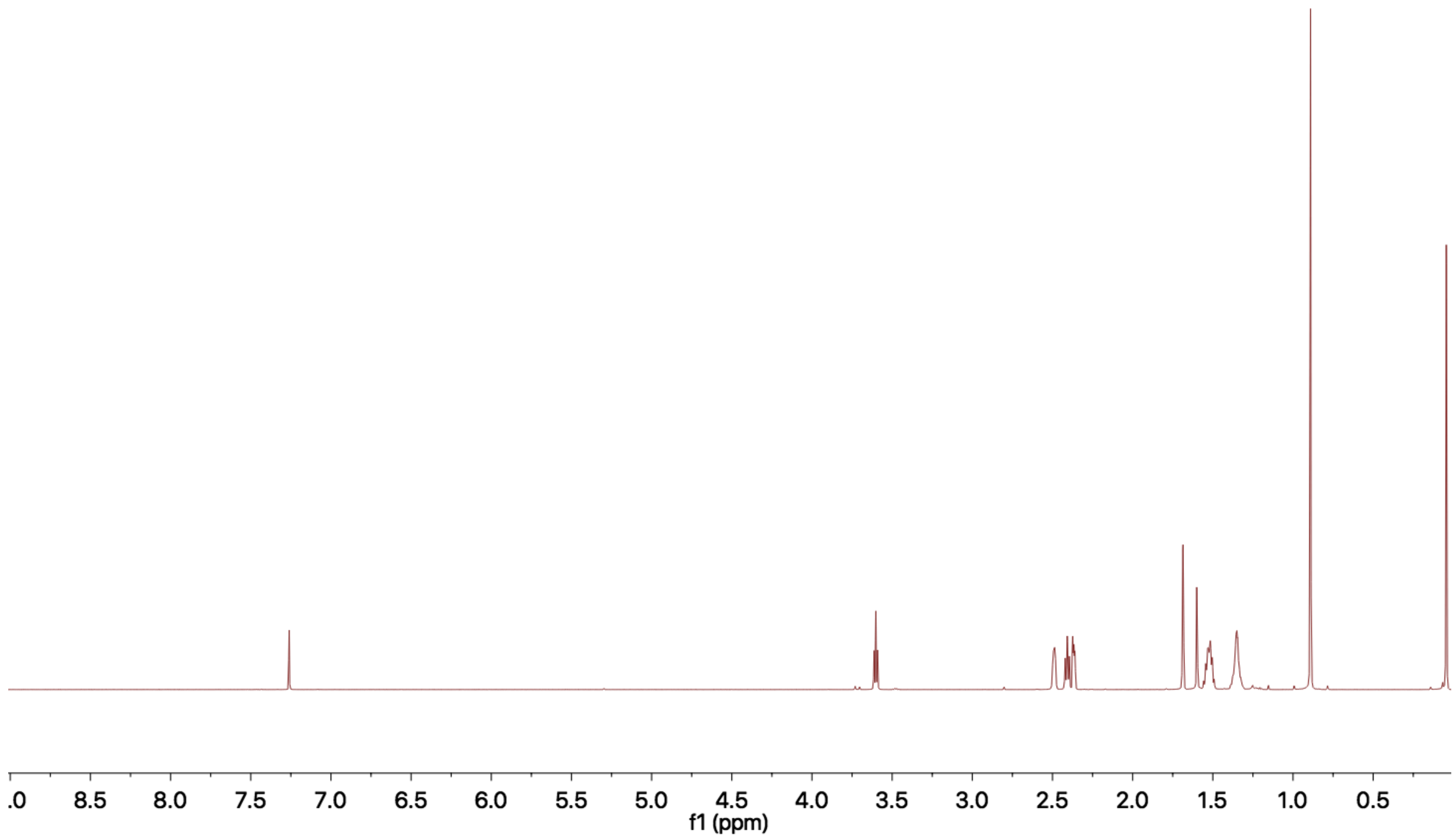
^{13}C NMR (600 MHz, CDCl$_3$): δ 210.4, 174.1, 136.3, 63.3, 34.3, 32.8, 31.4, 29.5, 29.4, 27.4, 26.1, 25.8, 18.5, 8.2, -5.1

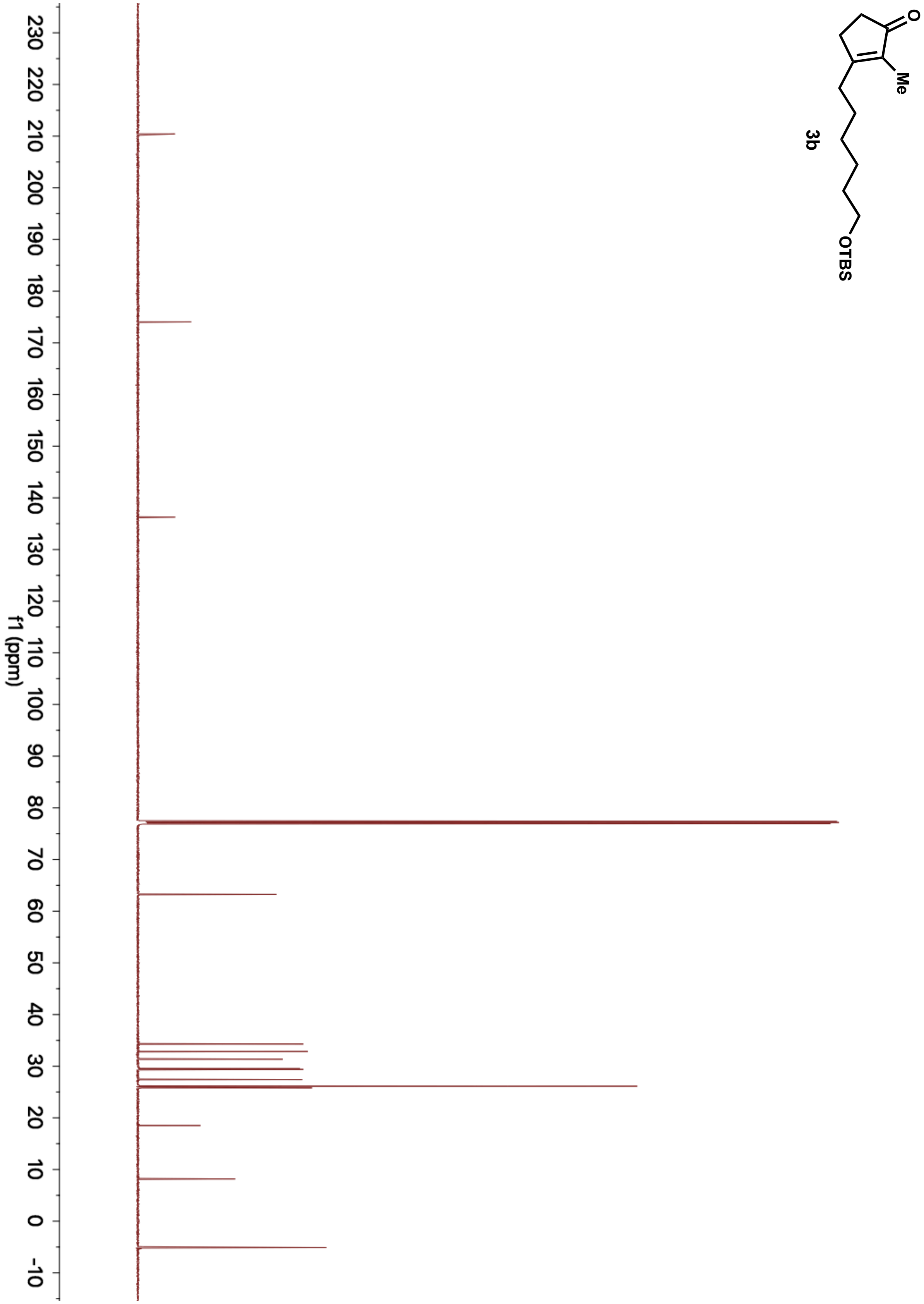
IR (cm^{-1}): 2927, 2856, 1699, 1645, 1471, 1385, 1252, 1099, 833, 773

ESI-HRMS (m/z): [M+H]$^+$ calc'd for $C_{18}H_{35}O_2Si^+$: 311.2329; found: 311.2395



3b

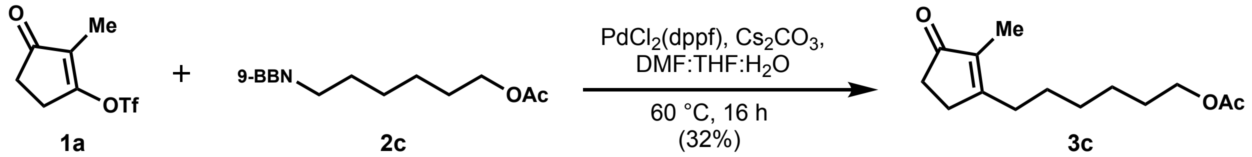




3b

O
Me
OTBS
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Synthesis of Acetate 3c:



A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1a** (61.0 mg, 0.25 mmol, 1.0 equiv), PdCl$_2$(dppf) (5.1 mg, 2.5 mol%) and Cs$_2$CO$_3$ (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2c** (0.34 M, 760 µl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. NaHCO$_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et$_2$O/hexanes/CH$_2$Cl$_2$= 0/1/1 to 1/49/50) afforded **3c** (19.1 mg, 32%) as a yellow oil.

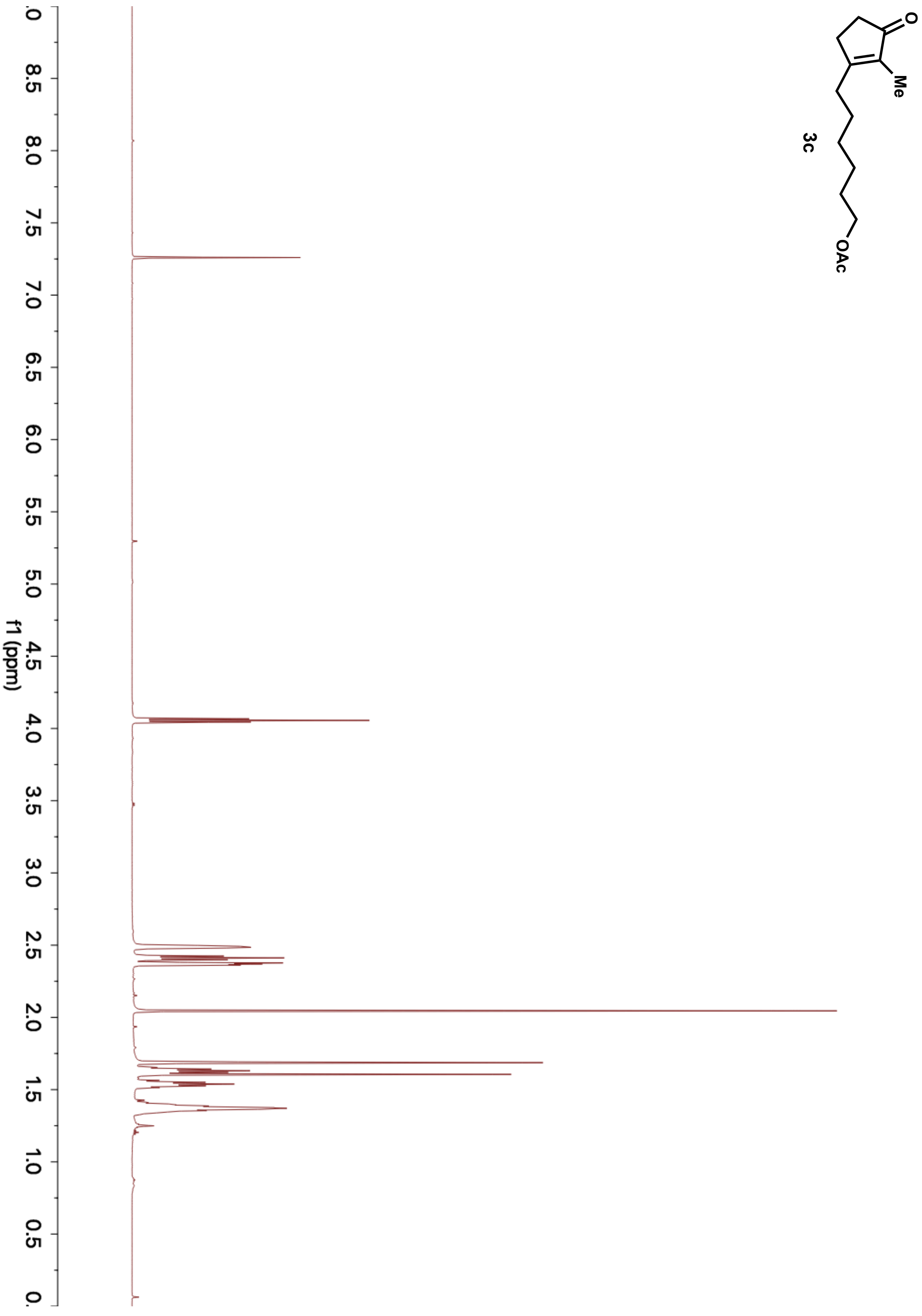
Rf: 0.13 (50% Et$_2$O/50% hexanes)

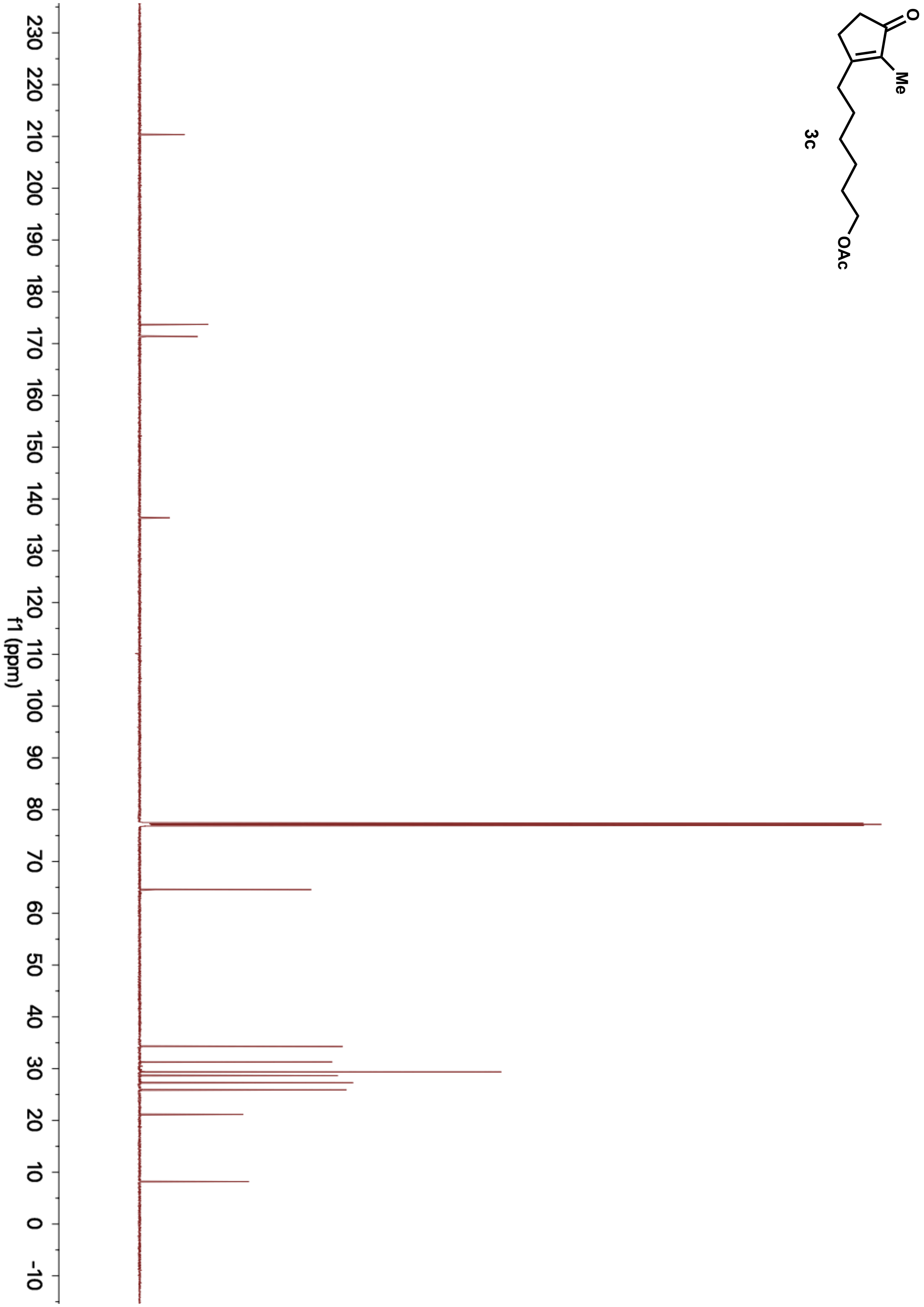
^{1}H NMR (600 MHz, CDCl$_3$): δ 4.06 (t, *J* = 6.7 Hz, 2H), 2.51–2.47 (m, 2H), 2.41 (t, *J* = 7.7 Hz, 2H), 2.38–2.36 (m, 2H), 2.05 (s, 3H), 1.69 (s, 3H), 1.65–1.61 (m, 2H), 1.56–1.51 (m, 2H), 1.41–1.35 (m, 4H)

^{13}C NMR (600 MHz, CDCl$_3$): δ 210.4, 173.7, 171.4, 136.4, 64.6, 34.3, 31.3, 29.4, 28.6, 27.3, 25.9, 21.2, 8.2

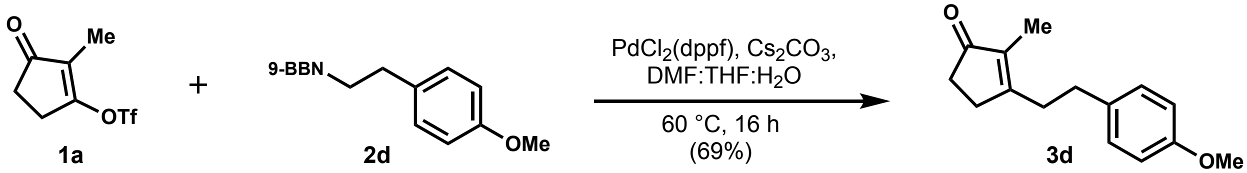
IR (cm^{-1}): 2929, 2859, 1695, 1645, 1442, 1365, 1232, 1036, 735

ESI-HRMS (m/z): [M+H]$^+$ calc'd for $C_{14}H_{23}O_3^+$: 239.1570; found: 239.1635


3c


O
Me
OAc
3c
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Synthesis of Arene 3d:



A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1a** (61.0 mg, 0.25 mmol, 1.0 equiv), PdCl$_2$(dppf) (5.1 mg, 2.5 mol%) and Cs$_2$CO$_3$ (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2d** (0.34 M, 760 µl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

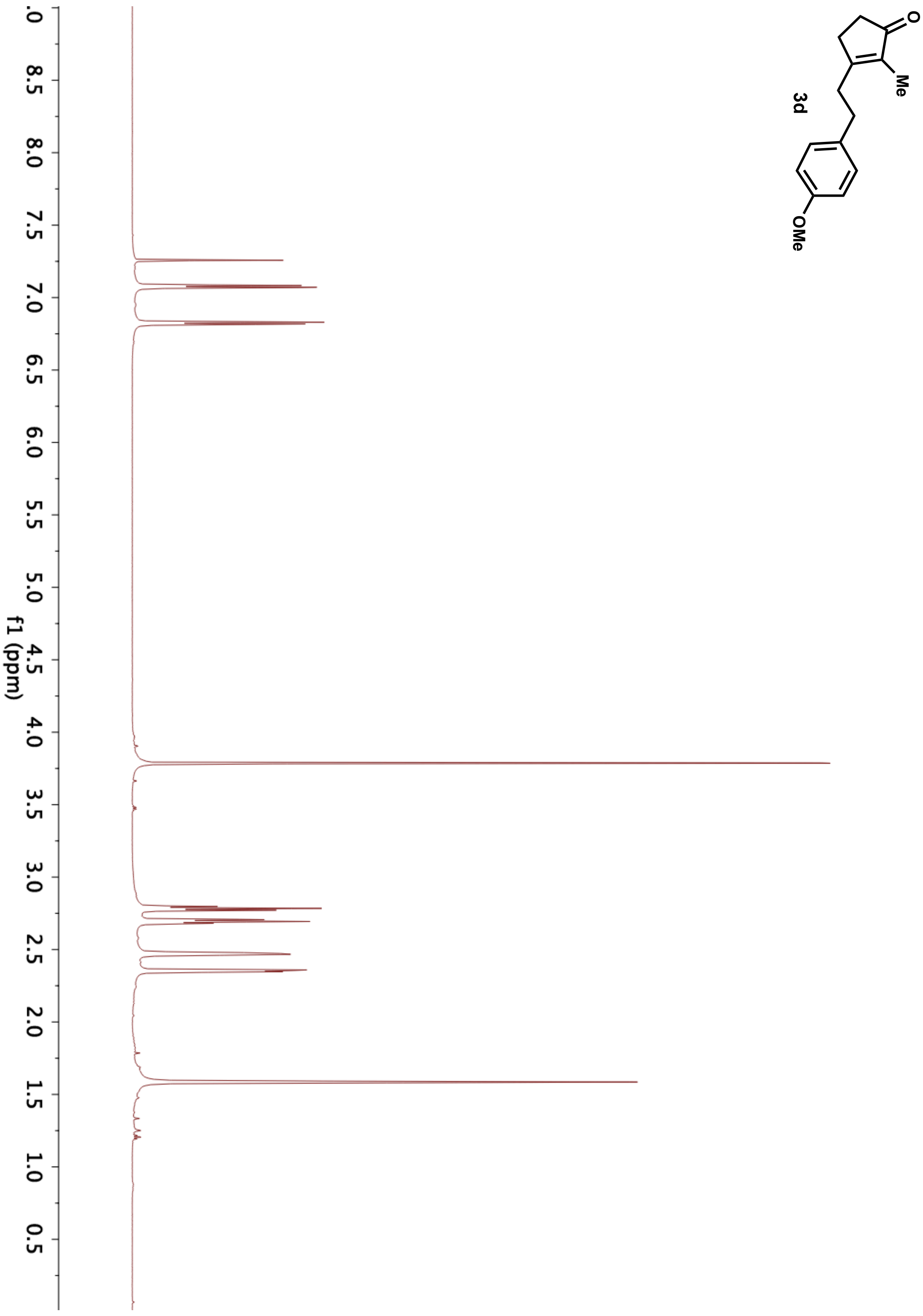
After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. NaHCO$_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et$_2$O/hexanes/CH$_2$Cl$_2$= 0/1/1 to 1/49/50) afforded **3d** (39.8 mg, 69%) as a yellow oil.

Rf: 0.25 (50% Et$_2$O/50% hexanes)

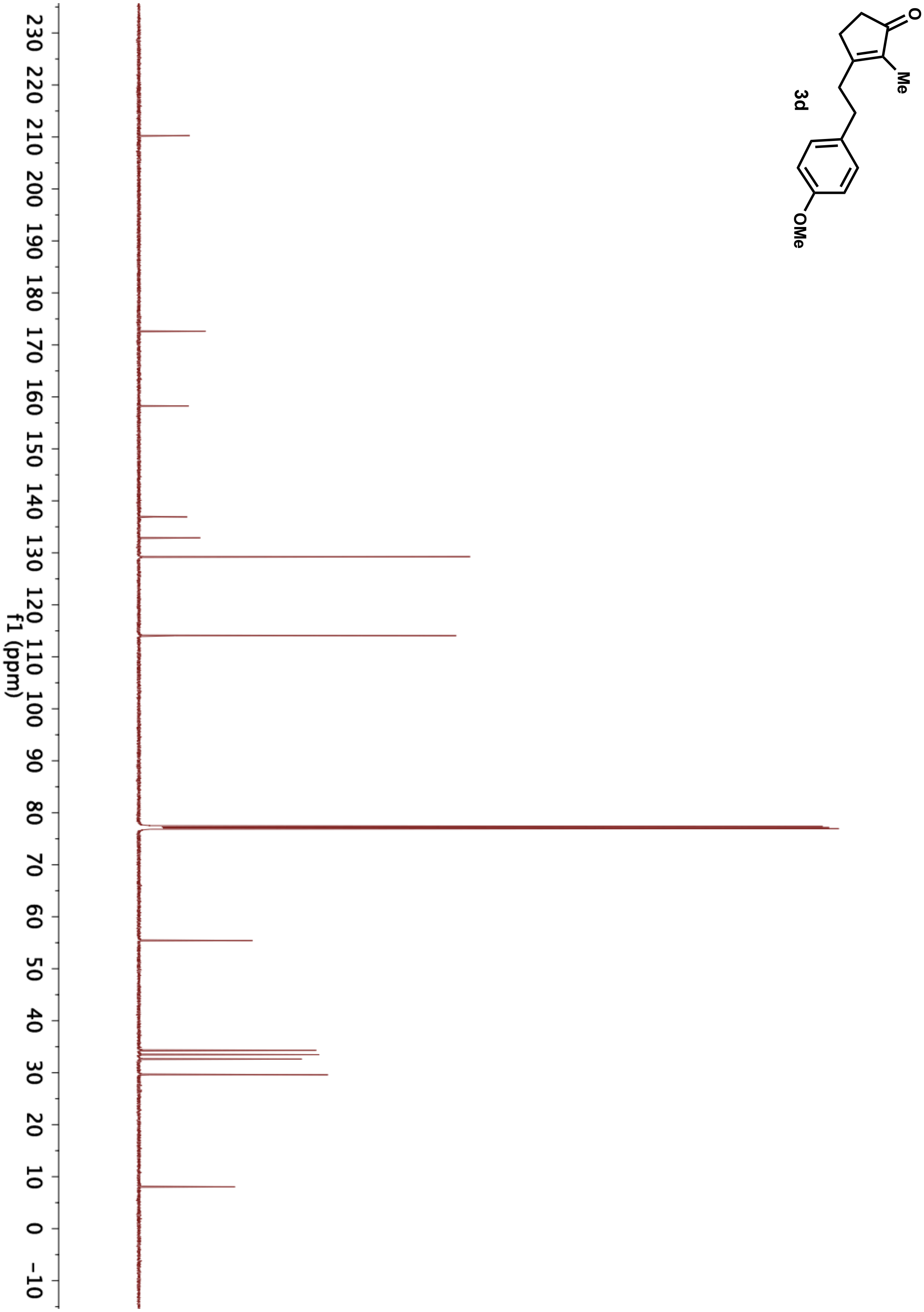
^{1}H NMR (600 MHz, CDCl$_3$): δ 7.08 (d, *J* = 7.3 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 2.79 (t, *J* = 7.9 Hz, 2H), 2.70 (t, *J* = 7.8 Hz, 2H), 2.49–2.45 (m, 2H), 2.37–2.34 (m, 2H), 1.60 (s, 3H)

^{13}C NMR (600 MHz, CDCl$_3$): δ 210.3, 172.6, 158.3, 136.9, 132.9, 129.3, 114.1, 55.4, 34.3, 33.5, 32.6, 29.6, 8.0

IR (cm^{-1}): 2919, 2836, 1693, 1512, 1242, 1176, 1034, 820, 540



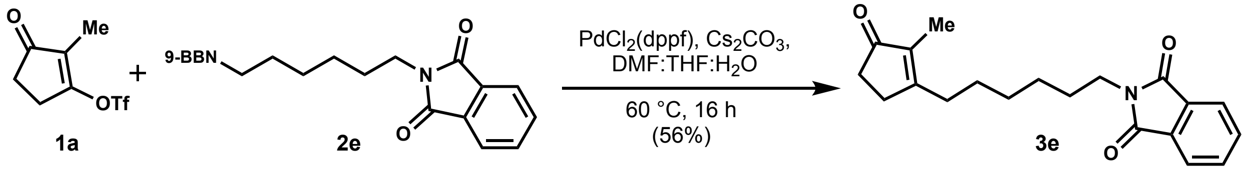
3d



3d

O
Me
OMe
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

Synthesis of Phthalimide 3e:



A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1a** (61.0 mg, 0.25 mmol, 1.0 equiv), $PdCl_2(dppf)$ (5.1 mg, 2.5 mol%) and Cs_2CO_3 (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2e** (0.34 M, 760 µl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. $NaHCO_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et_2O/hexanes/CH_2Cl_2= 0/1/1 to 1/49/50) afforded **3e** (45.8 mg, 56%) as a colorless oil.

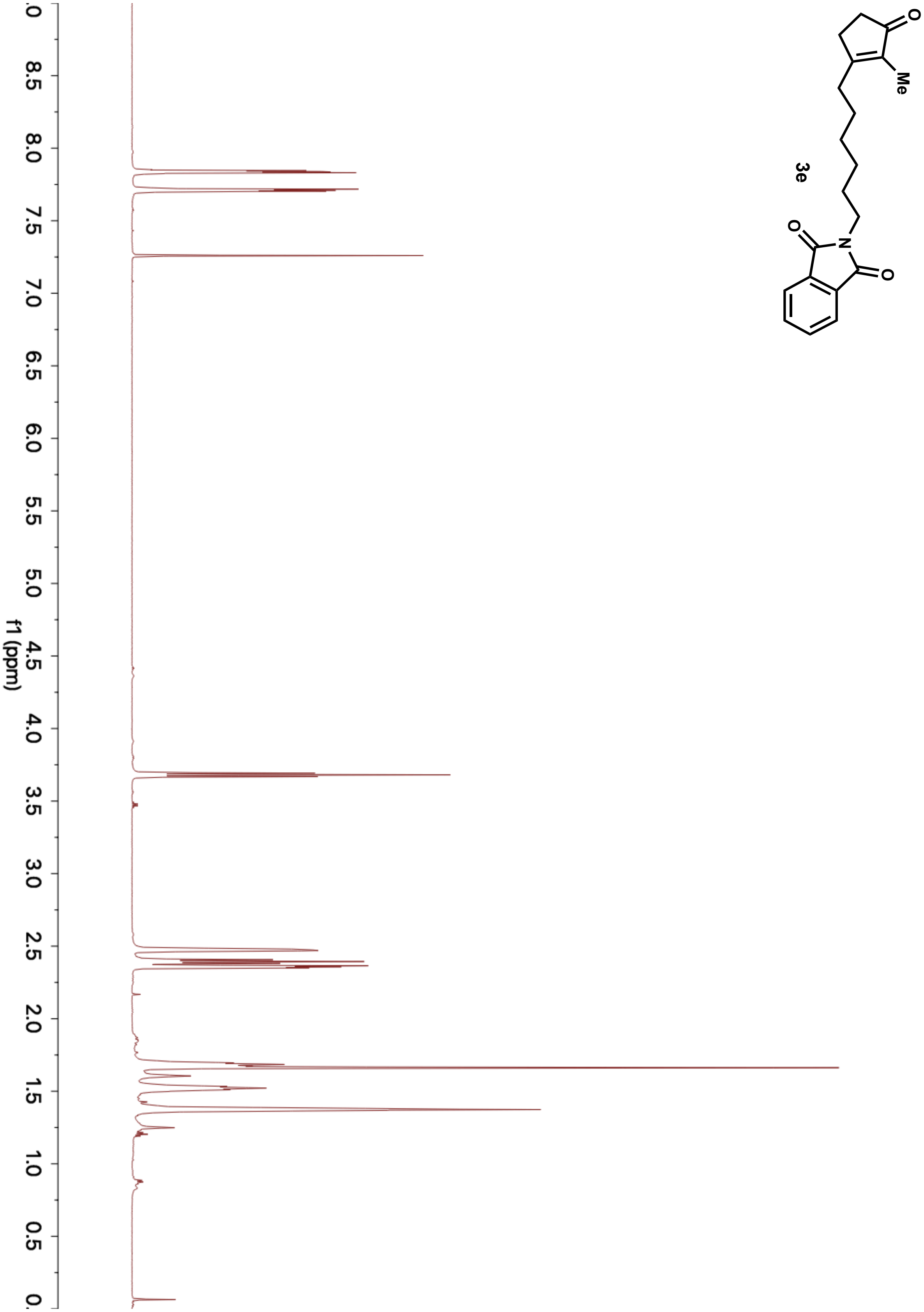
Rf: 0.13 (50% Et_2O/50% hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86–7.82 (m, 2H), 7.73–7.69 (m, 2H), 3.68 (t, *J* = 7.3 Hz, 2H), 2.50–2.45 (m, 2H), 2.39 (t, *J* = 7.7 Hz, 2H), 2.37–2.34 (m, 2H), 1.72–1.66 (m, 2H), 1.67 (s, 3H), 1.55–1.49 (m, 2H), 1.40–1.34 (m, 4H)

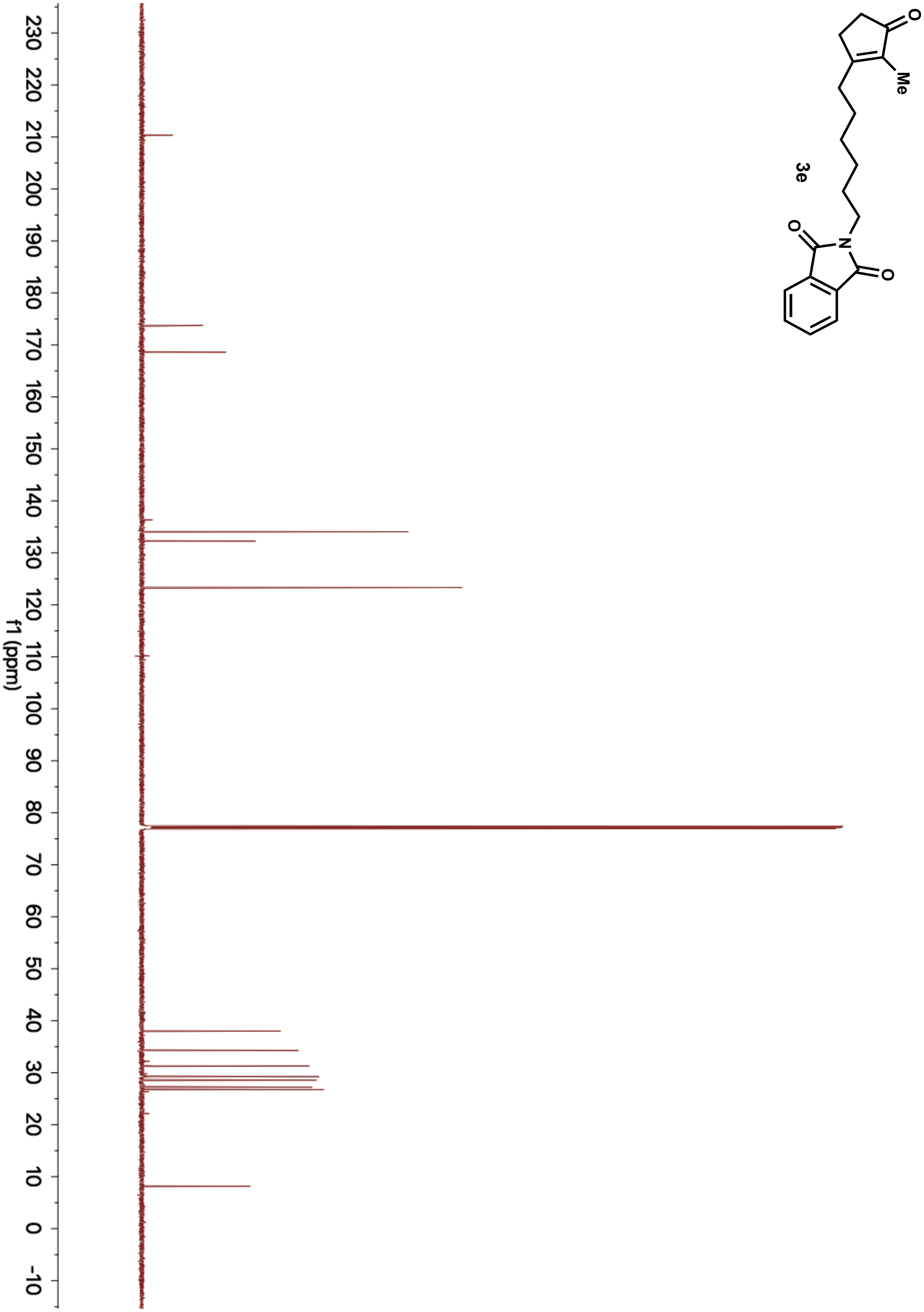
^{13}C NMR (600 MHz, $CDCl_3$): δ 210.3, 173.7, 168.6, 134.1, 134.1, 132.3, 123.3, 38.0, 34.3, 31.3, 29.3, 29.3, 28.6, 27.2, 26.7, 8.2

IR (cm^{-1}): 1710, 1643, 1436, 1360, 1339, 1299, 1257, 1170, 1010, 977, 876, 794, 720, 674

ESI-HRMS (m/z): $[M+H]^+$ calc'd for $C_{20}H_{24}NO_3^+$: 326.1679; found: 326.1746



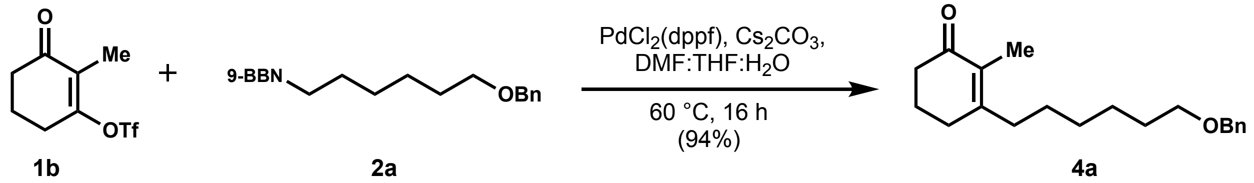
3e



3e

Me
O
N
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Synthesis of Benzyl Alcohol 4a:



A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1b** (65 mg, 0.25 mmol, 1.0 equiv), PdCl$_2$(dppf) (5.1 mg, 2.5 mol%) and Cs$_2$CO$_3$ (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2a** (0.34 M, 760 μl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. NaHCO$_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et$_2$O/hexanes/CH$_2$Cl$_2$= 0/1/1 to 1/49/50) afforded **4a** (71.0 mg, 94%) as a yellow oil.

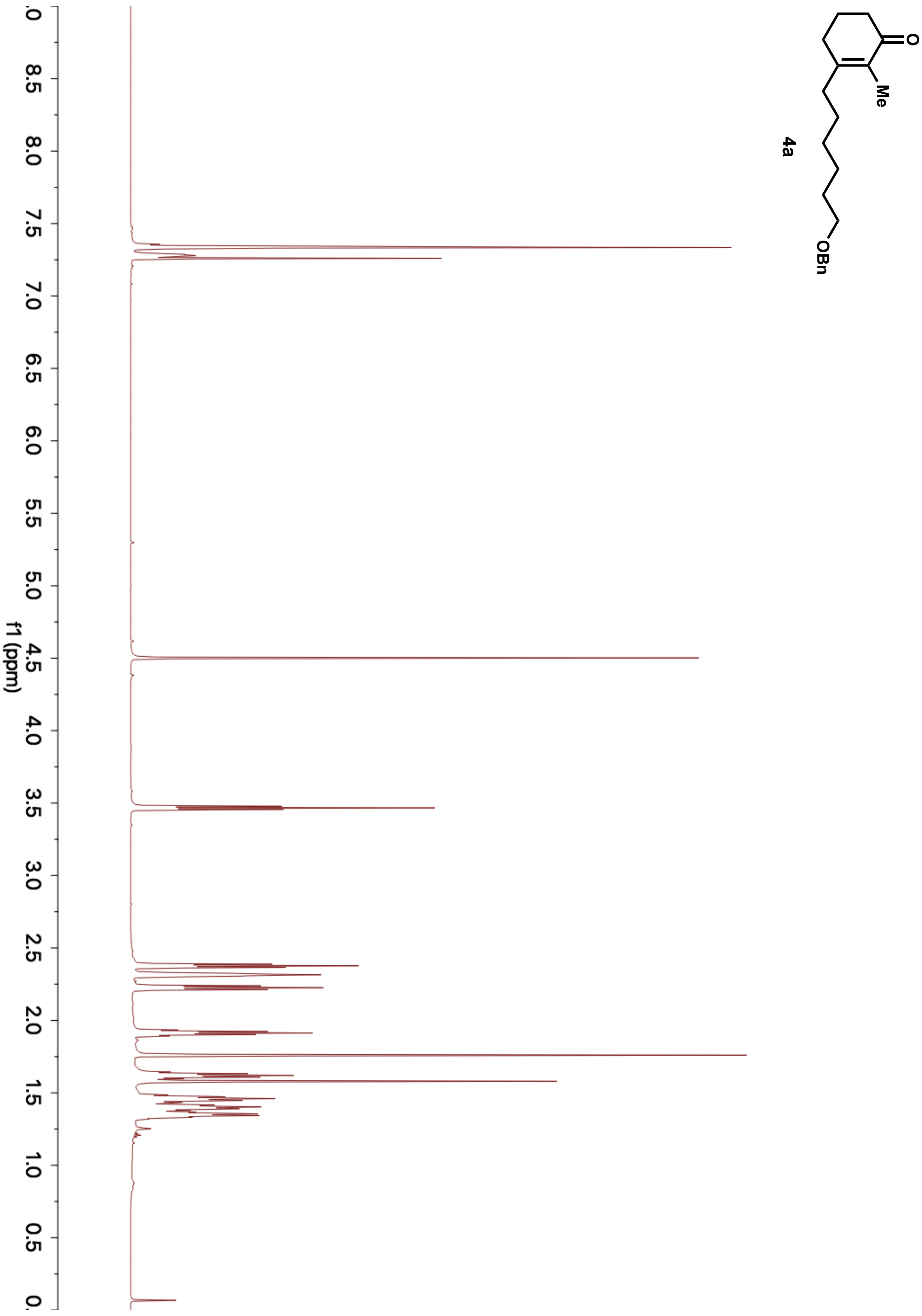
Rf: 0.39 (50% Et$_2$O/50% hexanes)

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.36–7.32 (m, 4H), 7.30–7.27 (m, 1H), 4.50 (s, 2H), 3.47 (t, *J* = 6.5 Hz, 2H), 2.38 (t, *J* = 6.7 Hz, 2H), 2.33–2.29 (m, 2H), 2.23 (t, *J* = 7.8 Hz, 2H), 1.93–1.89 (m, 2H), 1.76 (s, 3H), 1.64–1.59 (m, 2H), 1.49–1.43 (m, 2H), 1.43–1.38 (m, 2H), 1.37–1.33 (m, 2H)

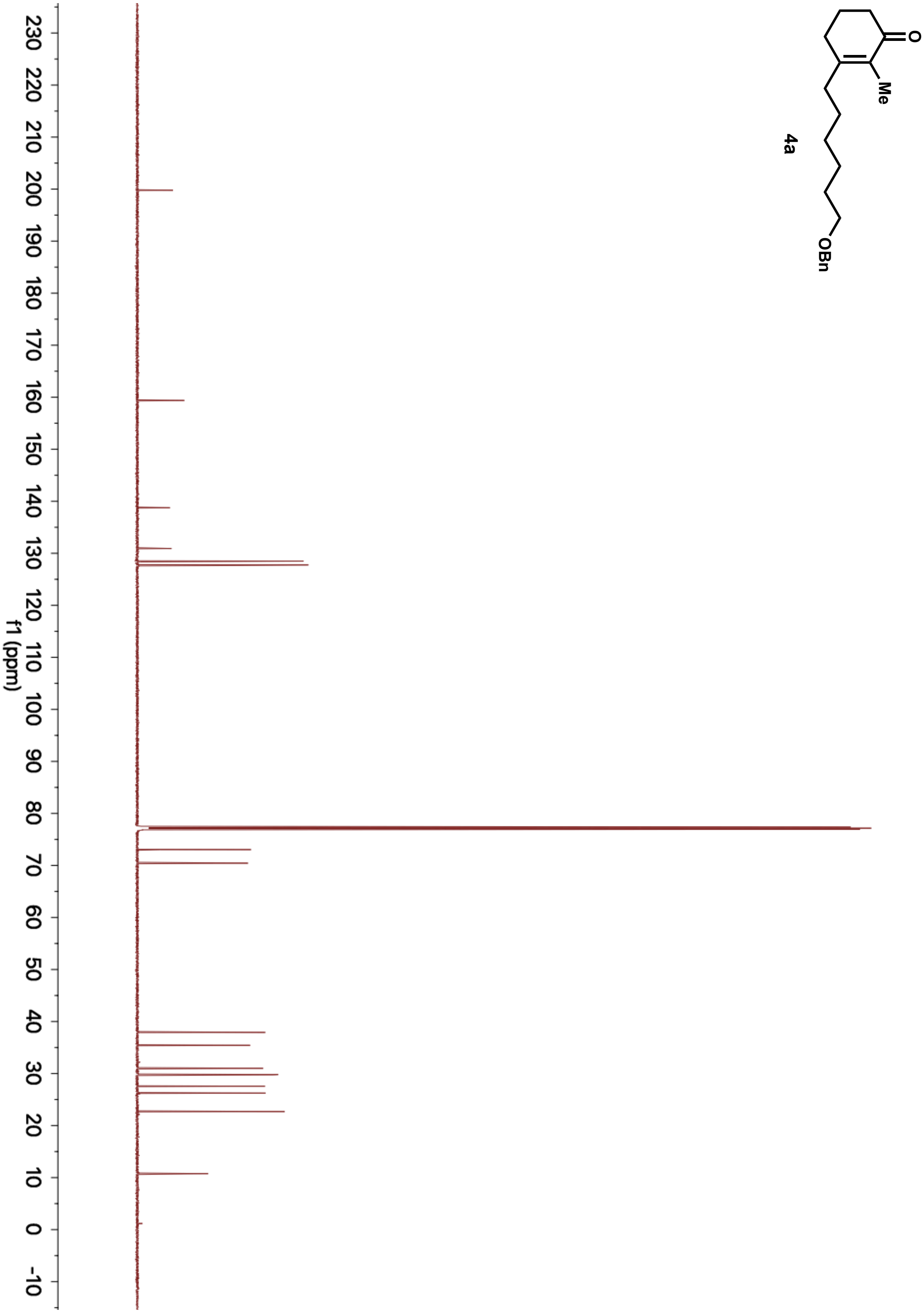
^{13}C NMR (600 MHz, CDCl$_3$): δ 199.8, 159.4, 138.8, 130.9, 128.5, 127.8, 127.7, 73.0, 70.4, 37.9, 35.4, 31.0, 29.8, 29.8, 27.6, 26.2, 22.7, 10.8

IR (cm^{-1}): 2925, 2858, 1695, 1645, 1444, 1365, 1232, 1035, 607

ESI-HRMS (m/z): [M+H]$^+$ calc'd for C$_{20}$H$_{29}$O$_2^+$: 301.2090; found: 301.2158

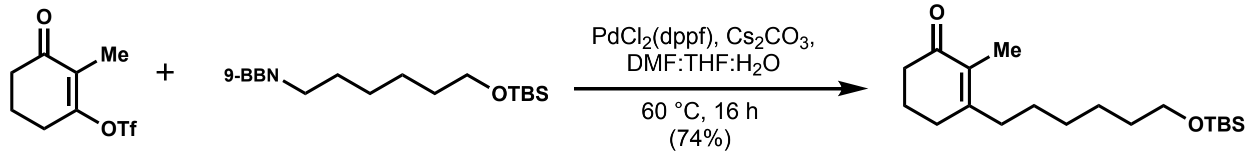


4a


O
Me
OBn
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

4a

Synthesis of TBS Alcohol 4b:



1b **2b** **4b**

A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1b** (65 mg, 0.25 mmol, 1.0 equiv), PdCl$_2$(dppf) (5.1 mg, 2.5 mol%) and Cs$_2$CO$_3$ (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2b** (0.34 M, 760 μl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. NaHCO$_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et$_2$O/hexanes/CH$_2$Cl$_2$= 0/1/1 to 1/49/50) afforded **4b** (60.5 mg, 74%) as a yellow oil.

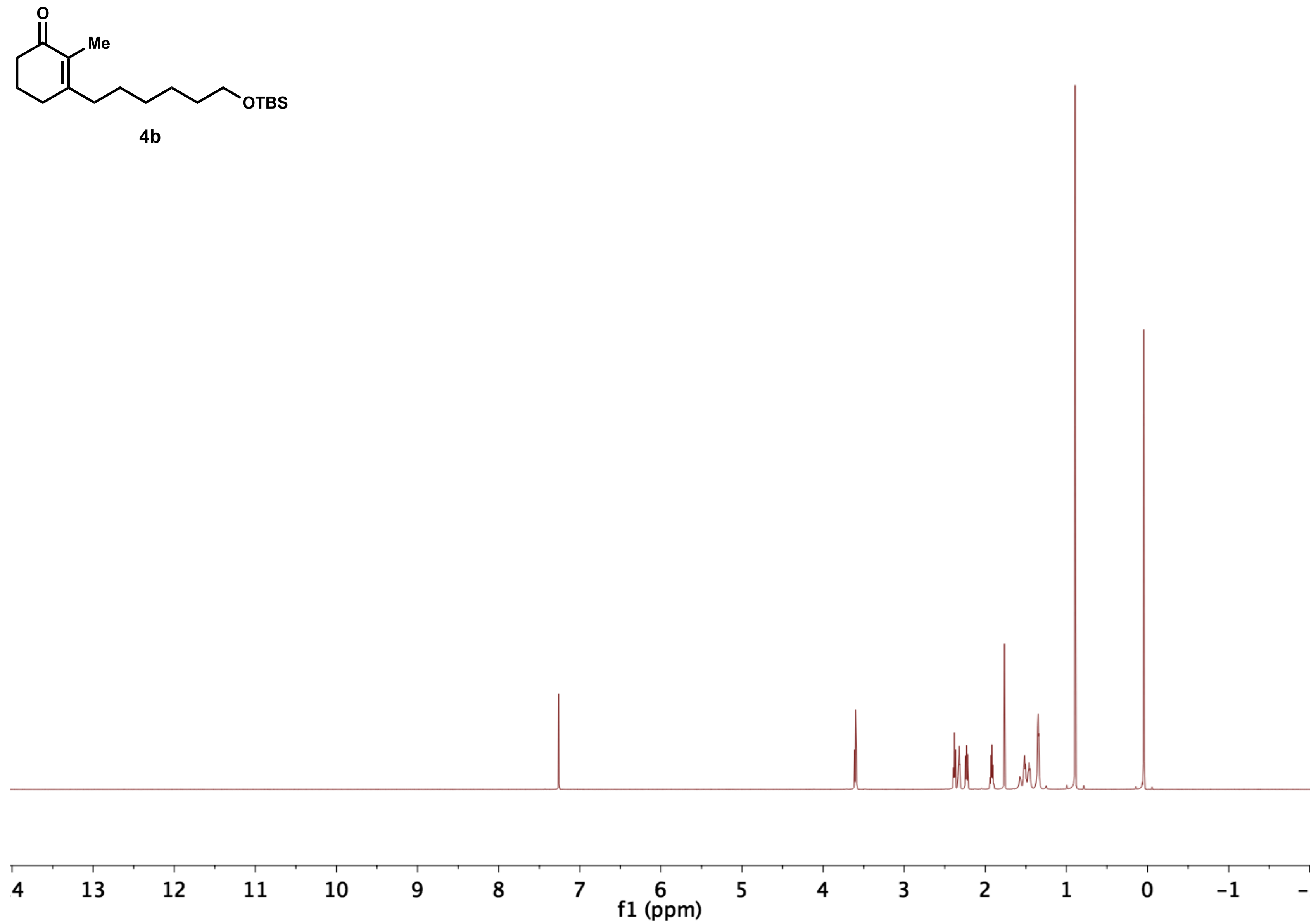
Rf: 0.53 (50% Et$_2$O/50% hexanes)

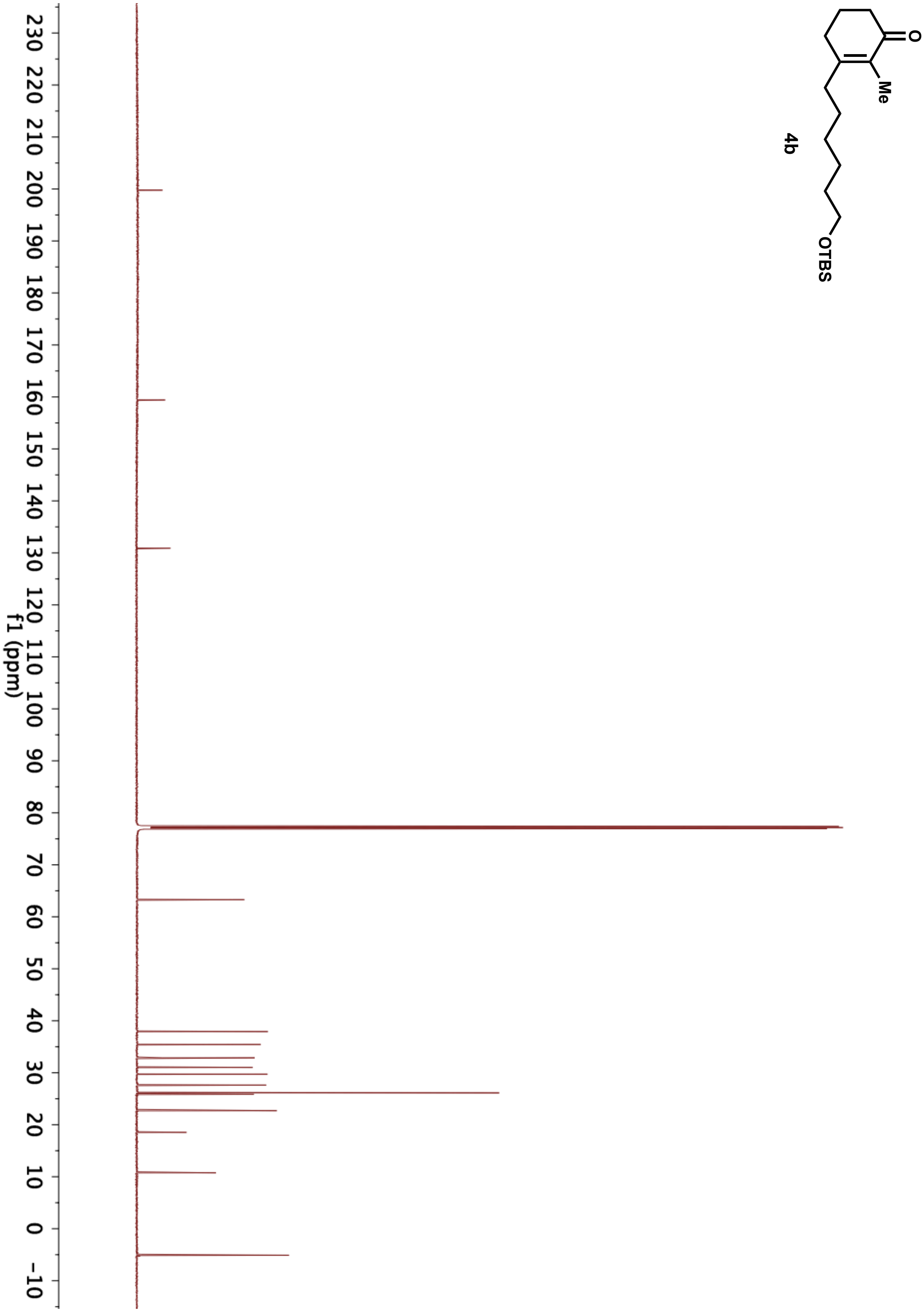
^{1}H NMR (600 MHz, CDCl$_3$): δ 3.60 (t, *J* = 6.5 Hz, 2H), 2.38 (t, *J* = 6.6 Hz, 2H), 2.35–2.30 (m, 2H), 2.23 (t, *J* = 7.8 Hz, 2H), 1.94–1.89 (m, 2H), 1.76 (s, 3H), 1.53–1.48 (m, 2H), 1.47–1.42 (m, 2H), 1.37–1.30 (m, 4H), 0.89 (s, 9H), 0.05 (s, 6H)

^{13}C NMR (600 MHz, CDCl$_3$): δ 199.8, 160.4, 130.9, 63.3, 37.9, 35.4, 32.9, 31.0, 29.7, 27.6, 26.1, 25.9, 22.7, 18.5, 10.8, -5.1

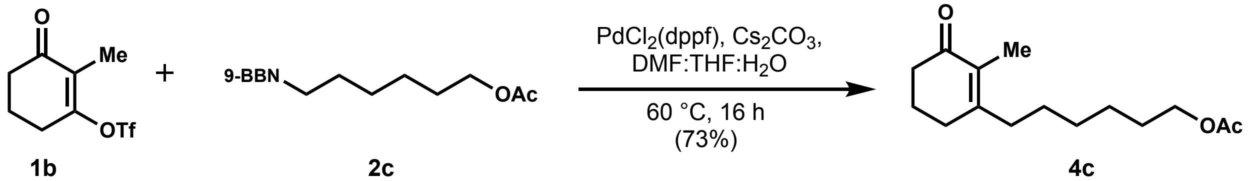
IR (cm^{-1}): 2927, 2860, 1664, 1471, 1360, 1255, 1099, 833, 773, 731

ESI-HRMS (m/z): [M+H]$^+$ calc'd for $C_{19}H_{37}O_2Si^+$: 325.2486; found: 325.2562


O
Me
OTBS
4b
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
–1
–
f1 (ppm)


O
Me
OTBS
4b
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

Synthesis of Acetate 4c:



A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1b** (65 mg, 0.25 mmol, 1.0 equiv), $PdCl_2$(dppf) (5.1 mg, 2.5 mol%) and Cs_2CO_3 (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2c** (0.34 M, 760 μl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. $NaHCO_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et_2O/hexanes/CH_2Cl_2= 0/1/1 to 1/49/50) afforded **4c** (46.5 mg, 73%) as a yellow oil.

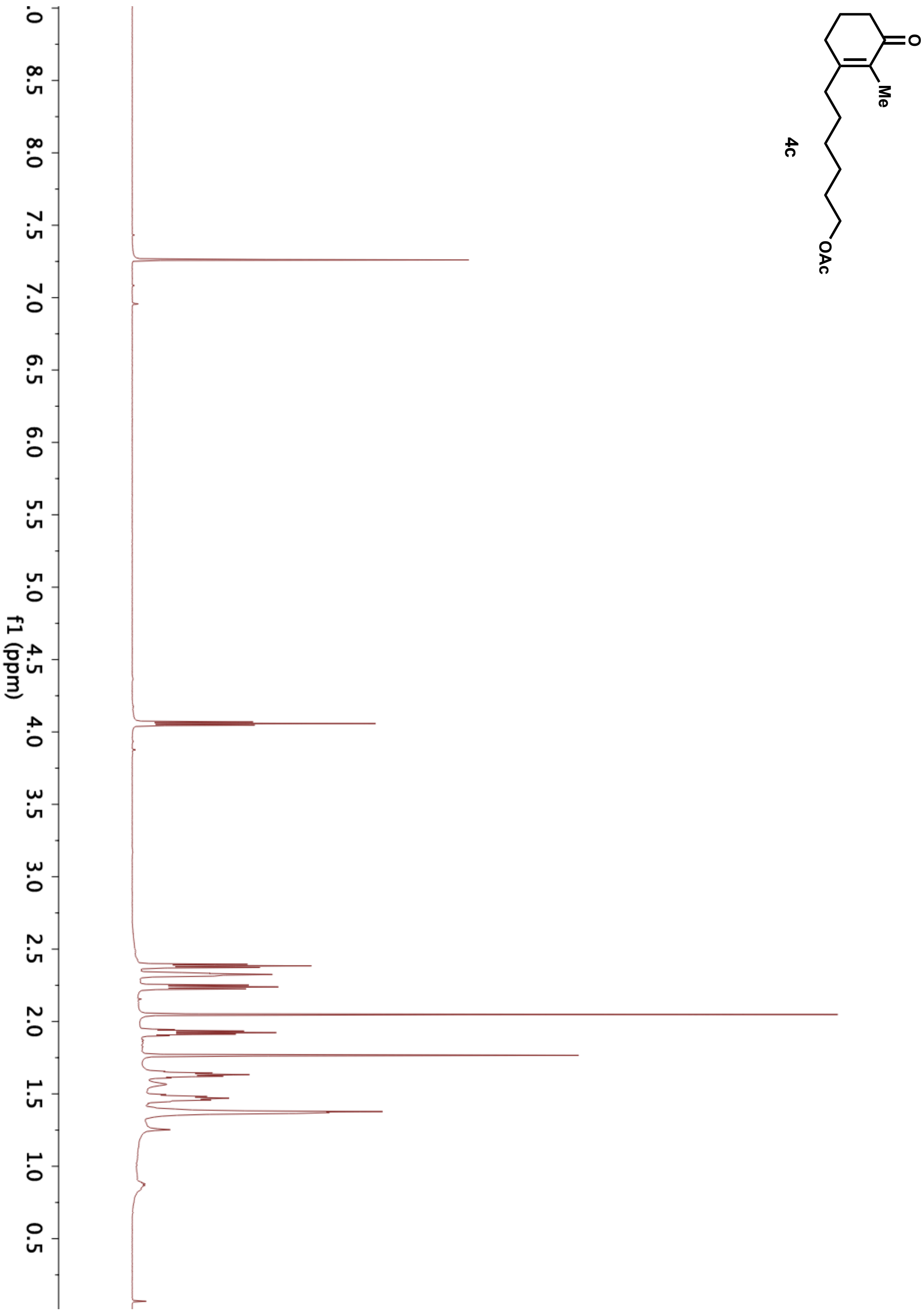
Rf: 0.23 (50% Et_2O/50% hexanes)

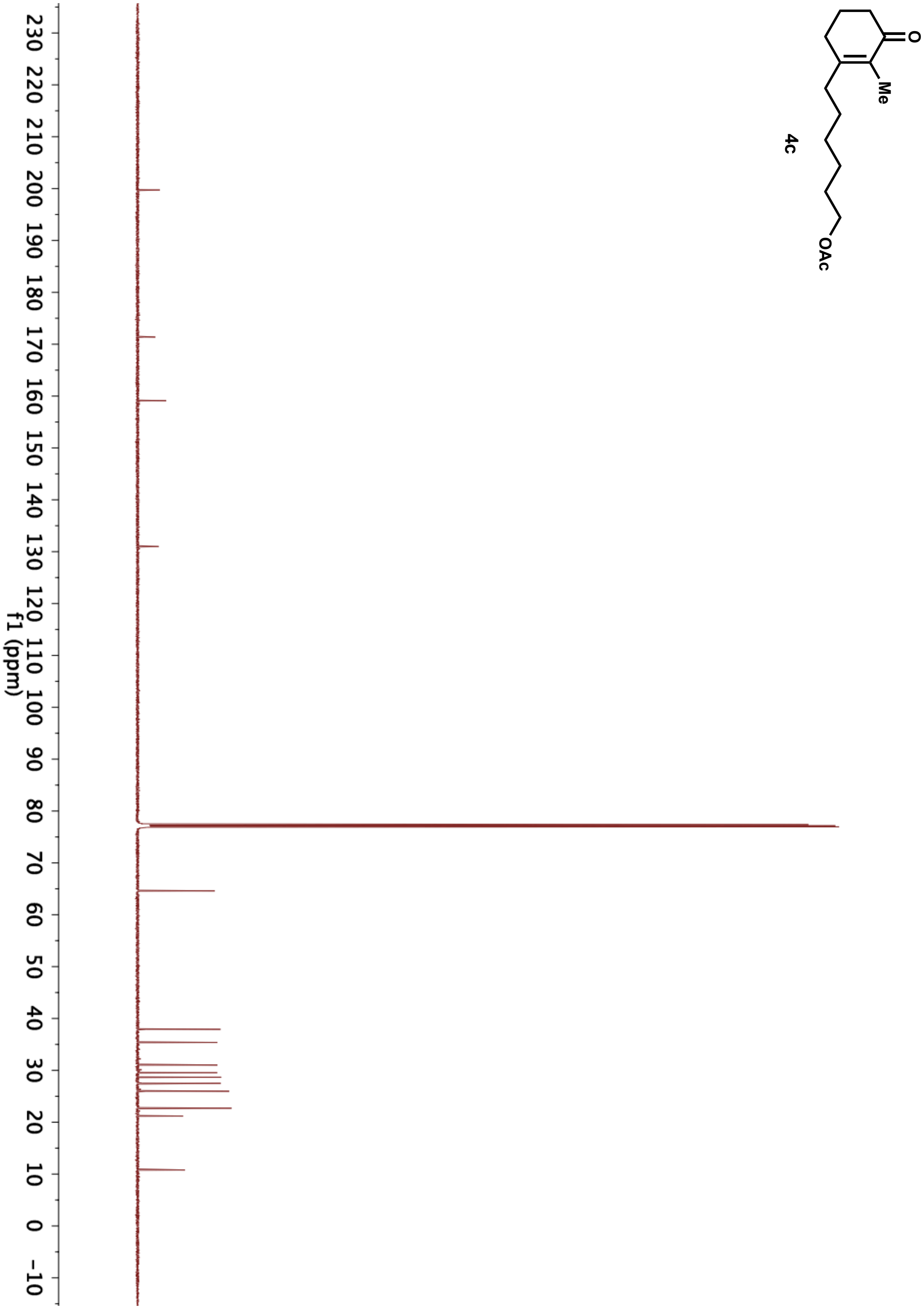
^{1}H NMR (600 MHz, $CDCl_3$): δ 4.06 (t, *J* = 6.7 Hz, 2H), 2.38 (t, *J* = 6.5 Hz, 2H), 2.35–2.30 (m, 2H), 2.24 (t, *J* = 7.7 Hz, 2H), 2.05 (s, 3H), 1.95–1.90 (m, 2H), 1.76 (s, 3H), 1.66–1.61 (m, 2H), 1.50–1.44 (m, 2H), 1.40–1.34 (m, 4H)

^{13}C NMR (600 MHz, $CDCl_3$): δ 199.7, 171.4, 159.1, 131.0, 64.6, 37.9, 35.4, 31.0, 29.5, 28.7, 27.5, 26.0, 22.7, 21.2, 10.8

IR (cm^{-1}): 2929, 2858, 1733, 1656, 1458, 1363, 1238, 1045, 908, 727, 646

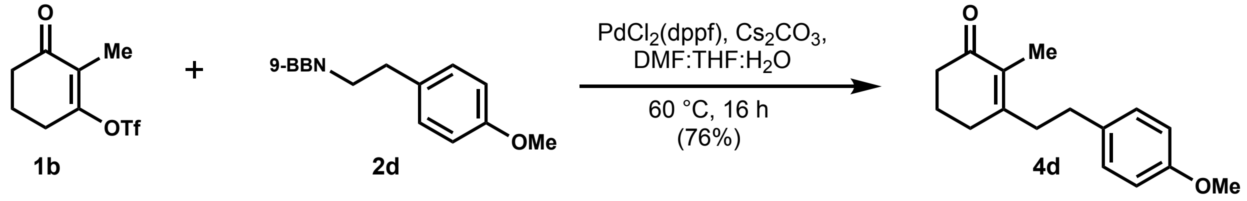
ESI-HRMS (m/z): $[M+H]^+$ calc'd for $C_{15}H_{25}O_3^+$: 253.1726; found: 253.1786


4c


O
Me
OAc
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

4c

Synthesis of Arene 4d:



1b **2d** **4d**

A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1b** (65 mg, 0.25 mmol, 1.0 equiv), PdCl$_2$(dppf) (5.1 mg, 2.5 mol%) and Cs$_2$CO$_3$ (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2d** (0.34 M, 760 μl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. NaHCO$_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et$_2$O/hexanes/CH$_2$Cl$_2$= 0/1/1 to 1/49/50) afforded **4d** (48.6 mg, 76%) as an orange oil.

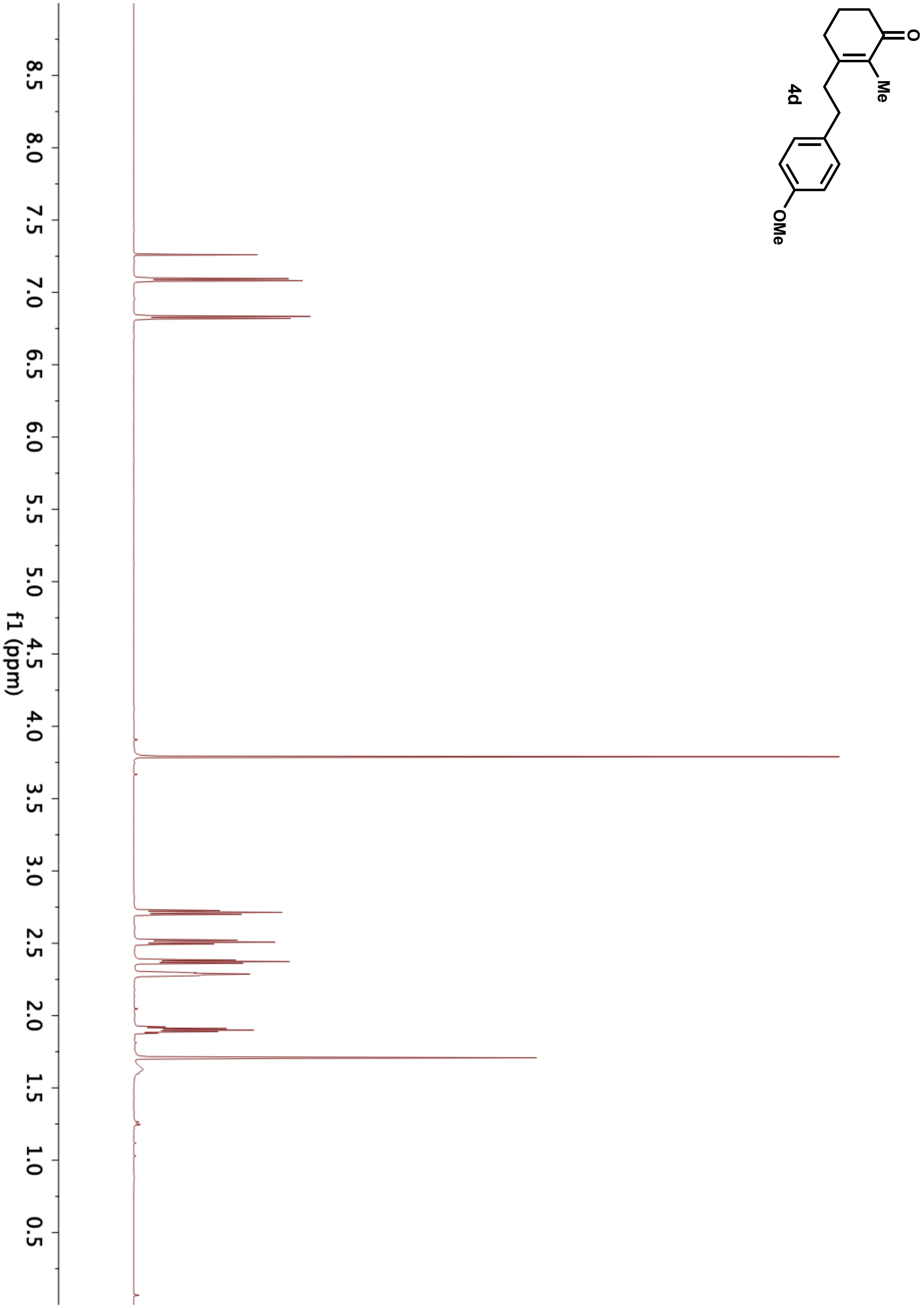
Rf: 0.39 (50% Et$_2$O/50% hexanes)

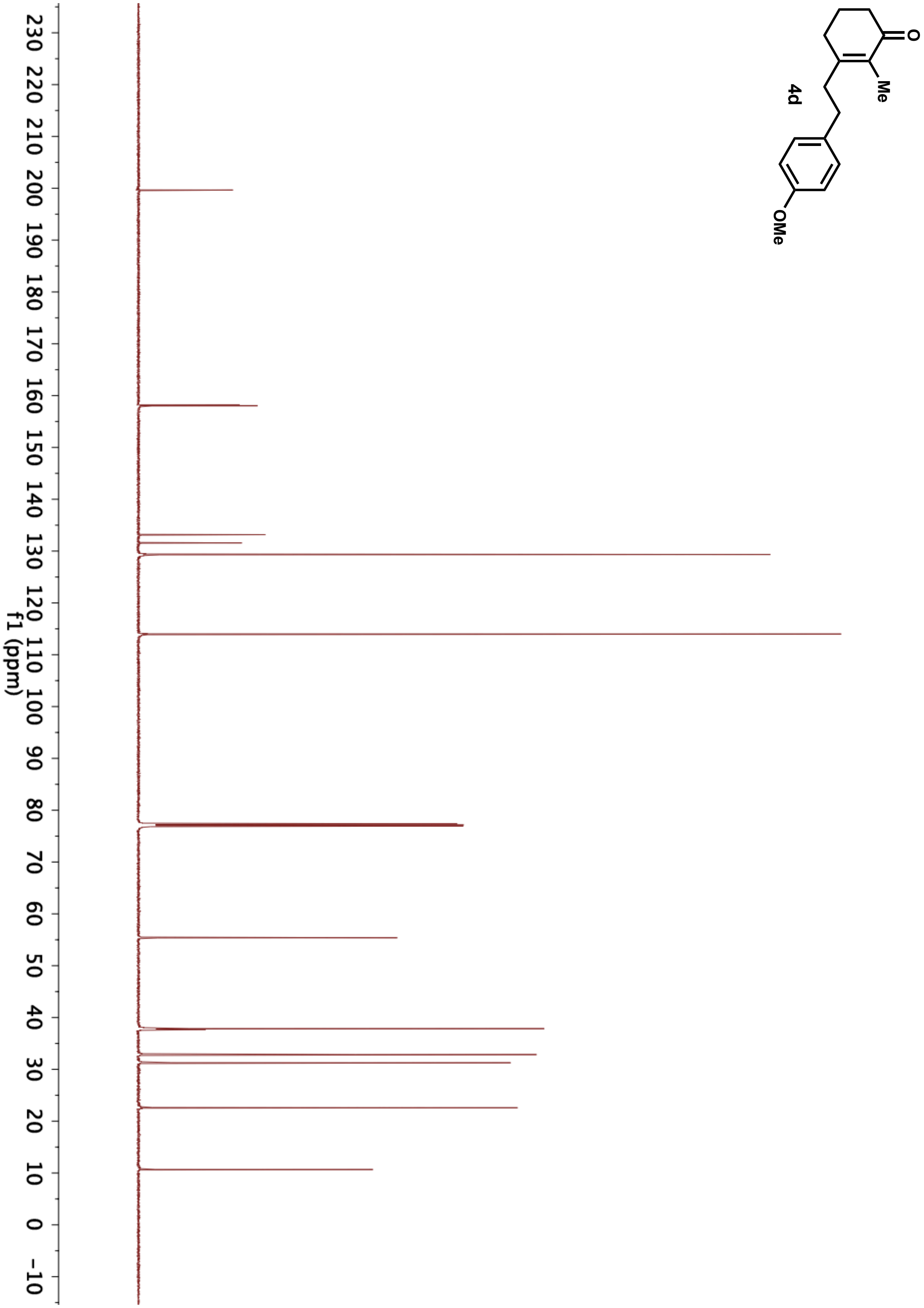
^{1}H NMR (600 MHz, CDCl$_3$): δ 7.09 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 3H), 2.71 (t, *J* = 7.6 Hz, 2H), 2.51 (t, *J* = 8.2 Hz, 2H), 2.37 (t, *J* = 6.6 Hz, 2H), 2.31–2.26 (m, 2H), 1.93–1.87 (m, 2H), 1.71 (s, 3H)

^{13}C NMR (600 MHz, CDCl$_3$): δ 199.7, 158.2, 158.1, 133.2, 131.6, 129.3, 114.0, 55.4, 37.9, 37.7, 32.9, 31.3, 22.6, 10.7

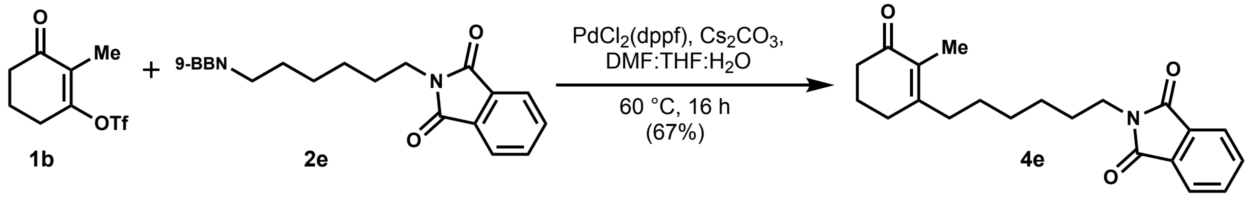
IR (cm^{-1}): 2927, 2860, 1664, 1471, 1360, 1255, 1099, 833, 773, 731

ESI-HRMS (m/z): [M+H]$^+$ calc'd for C$_{16}$H$_{21}$O$_2$$^+$: 245.3341; found: 245.1549


4d


4d
O
Me
OMe
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

Synthesis of Phthalimide 4e:



A flame-dried, 5 mL microwave vial equipped with a magnetic stir bar was charged with enone **1b** (65 mg, 0.25 mmol, 1.0 equiv), $PdCl_2$(dppf) (5.1 mg, 2.5 mol%) and Cs_2CO_3 (163.0 mg, 0.5 mmol, 2.0 equiv), capped with an aluminum–PTFE crimp cap, sealed, evacuated and backfilled with argon three times, and placed under an argon atmosphere. Anhydrous DMF (0.15 M, 1.70 ml), which had been rigorously degassed using freeze-pump-thaw technique over three degassing cycles, was added to the vial in a single portion. Following this, a solution of alkylborane **2e** (0.34 M, 760 µl), prepared as described on page SI-3, was added to the reaction mixture in a single portion. The resulting reaction mixture was warmed by transferring the reaction apparatus to a 60 °C oil bath.

After stirring for 16 hours at this temperature, the reaction mixture was cooled back down to 25 °C by transferring the reaction apparatus to a lukewarm water bath. After stirring at this temperature for 5 minutes, the reaction mixture was diluted with diethyl ether (10 ml) and filtered through a pad of Celite®. The resulting filtrate was washed with sat. aq. $NaHCO_3$ (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation to provide a crude yellow oil. Purification by flash column chromatography on silica gel (Et_2O/hexanes/CH_2Cl_2= 0/1/1 to 1/49/50) afforded **4e** (59.6 mg, 67%) as a colorless oil.

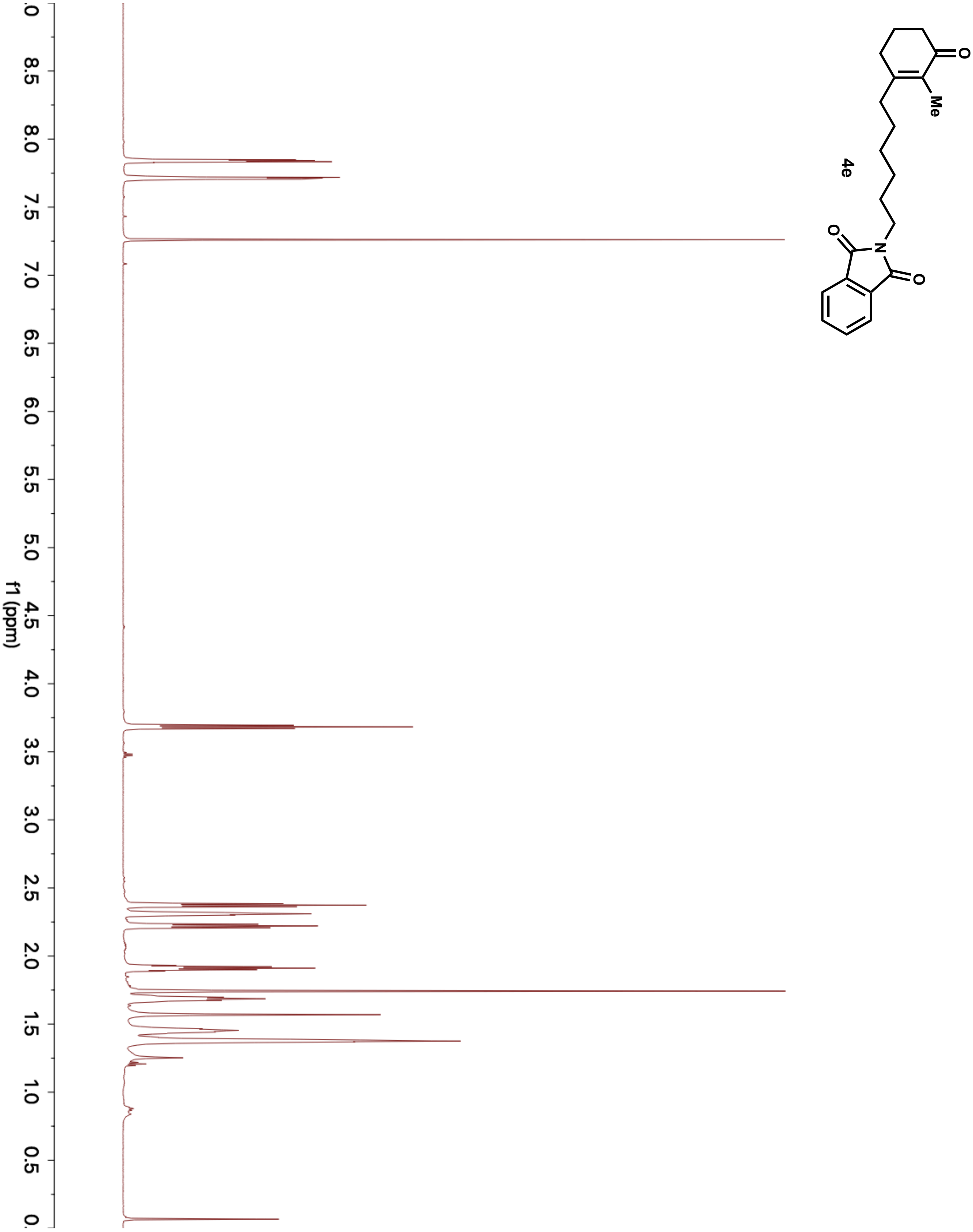
Rf: 0.19 (50% Et_2O/50% hexanes)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86–7.82 (m, 2H), 7.73–7.69 (m, 2H), 3.68 (t, *J* = 7.1 Hz, 2H), 2.37 (t, *J* = 6.5 Hz, 2H), 2.33–2.29 (m, 2H), 2.22 (t, *J* = 7.5 Hz, 2H), 1.94–1.89 (m, 2H), 1.74 (s, 3H), 1.71–1.66 (m, 2H), 1.48–1.42 (m, 2H), 1.40–1.35 (m, 4H)

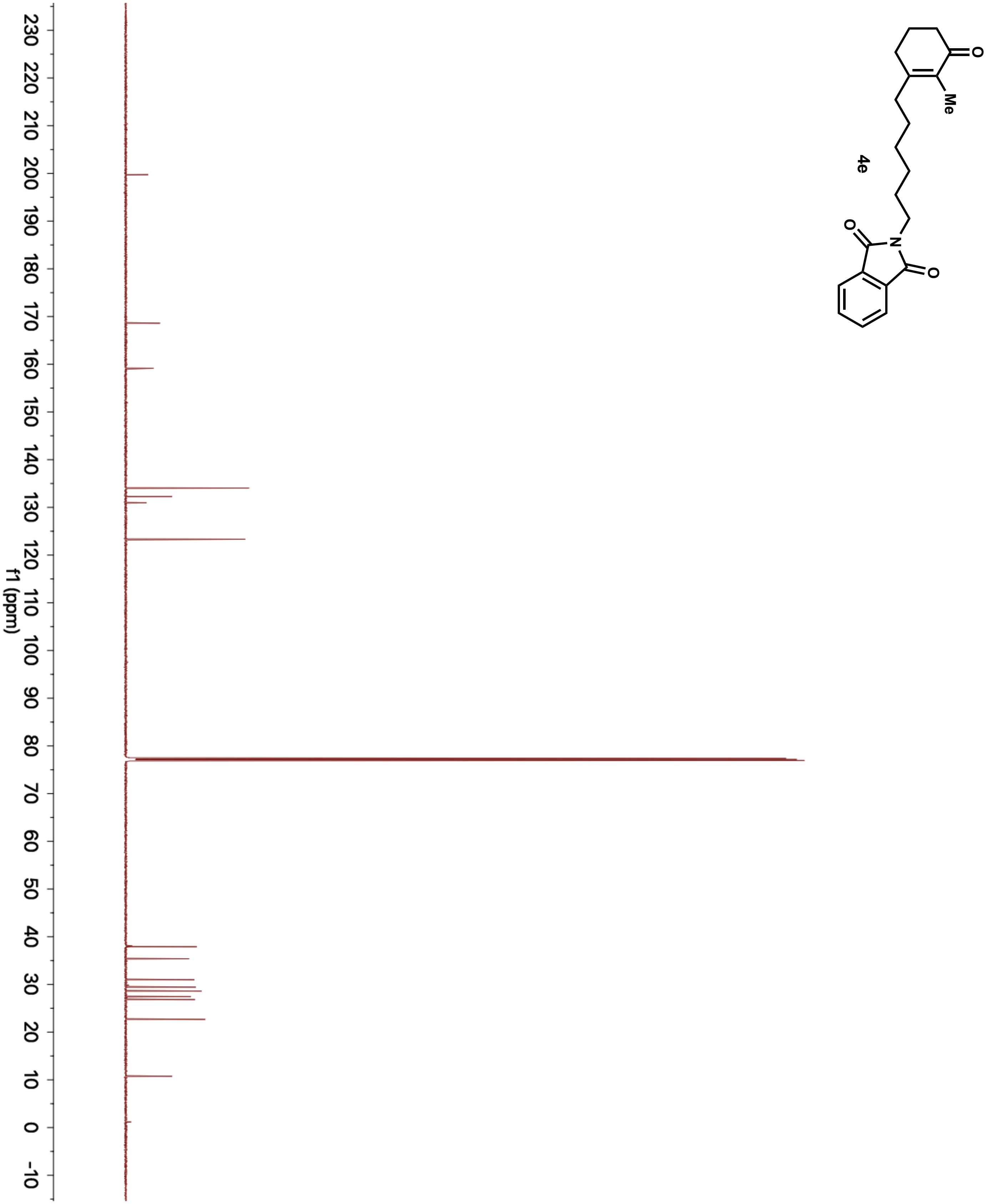
^{13}C NMR (600 MHz, $CDCl_3$): δ 199.7, 168.6, 159.2, 134.0, 132.3, 131.0, 123.3, 38.1, 37.9, 35.4, 31.0, 29.4, 28.6, 27.5, 26.8, 22.7, 10.8

IR (cm^{-1}): 2919, 2857, 1710, 1660, 1410, 1394, 1299, 1262, 1170, 1083, 1006, 720

ESI-HRMS (m/z): $[M+H]^+$ calc'd for $C_{21}H_{26}NO_3^+$: 340.1835; found: 340.2051



4e


4e
Me
O
N
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)