Aminoketyl Radicals in Organic Synthesis: Stereoselective Cyclization of 5- and 6-Membered Cyclic Imides to 2-Azabicycles using SmI_2–H_2O

Shicheng Shi[†] and Michal Szostak*[,†]

[†]*Department of Chemistry, Rutgers University, 73 Warren Street, Newark, New Jersey 07102, United States*

michal.szostak@rutgers.edu

Supplementary Information

Corresponding Author:

Prof. Dr. M. Szostak
Department of Chemistry
Rutgers University, 73 Warren Street
Newark, NJ 07102, United States
E-mail: michal.szostak@rutgers.edu

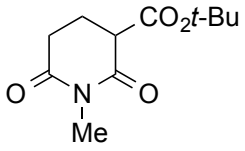
List of Known Compounds/General Methods

All starting materials reported in the manuscript have been previously described in literature or prepared by the method reported previously. Imides were purchased from commercial suppliers or prepared by standard methods.[1-9] Samarium(II) iodide was prepared by standard methods and titrated prior to use.[10-14] All experiments involving SmI_2 were performed using standard techniques under argon or nitrogen atmosphere unless stated otherwise. All solvents were purchased at the highest commercial grade and used as received or after purification by passing through activated alumina columns or distillation from Na/benzophenone under nitrogen. All solvents were deoxygenated prior to use. All other chemicals were purchased at the highest commercial grade and used as received. Reaction glassware was oven-dried at 140 °C for at least 24 h or flame-dried prior to use, allowed to cool under vacuum and purged with argon (three cycles). All products were identified using ^{1}H NMR, and/or GC-MS analysis and comparison with authentic samples. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker and Varian spectrometers at 500 and 600 MHz (^{1}H NMR) and 125 and 150 MHz (^{13}C NMR). All shifts are reported in parts per million (ppm) relative to residual $CHCl_3$ peak (7.27 and 77.2 ppm, ^{1}H NMR and ^{13}C NMR, respectively). All coupling constants (J) are reported in hertz (Hz). Abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; br s, broad singlet. GC-MS chromatography was performed using Agilent HP6890 GC System and Agilent 5973A inert XL EI/CI MSD using helium as the carrier gas at a flow rate of 1 mL/min and an initial oven temperature of 50 °C. The injector temperature was 250 °C. The detector temperature was 250 °C. For runs with the initial oven temperature of 50 °C, temperature was increased with a 10 °C/min ramp after 50 °C hold for 3 min to a final temperature of 280 °C, then hold at 280 °C for 30 min (splitless mode of injection, total run time of 54.00 min). High-resolution mass spectra (HRMS) were measured on a 7T Bruker Daltonics FT-MS instrument. All flash chromatography was performed using silica gel, 60 Å, 300 mesh. TLC analysis was carried out on glass plates coated with silica gel 60 F254, 0.2 mm thickness. The plates were visualized using a 254 nm ultraviolet lamp or aqueous potassium permanganate solutions. ^{1}H NMR and ^{13}C NMR data are given for all compounds in the Supporting Experimental for characterization purposes. ^{1}H NMR, ^{13}C NMR and HRMS data are reported for all new compounds.

List of Known Compounds

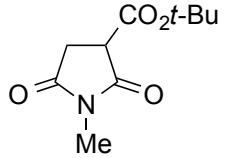
The following compounds are known: **SI-1**,[15] **SI-2**,[15] **SI-3**,[16] **SI-4**.[17] All olefins have been prepared following the procedure by Wong.[18] Alkyl substituted derivatives have been prepared following the procedure by Aubé.[19] **1x** and **1y** have been prepared following the procedure by O'Doherty.[20] All other substrates have been prepared according to procedures outlined below.

Preparation of Starting Materials



SI-1

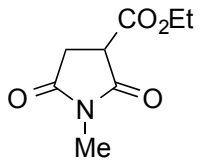
***tert*-Butyl 1-methyl-2,6-dioxopiperidine-3-carboxylate (SI-1).** To a solution of 1-methylglutarimide (1.27 g, 10.0 mmol, 1.0 equiv) in THF (40 mL), NaHMDS (2.0 M, THF, 10.0 mL, 20.0 mmol, 2.0 equiv) was added dropwise at -78 °C. After stirring for 90 min at -78 °C, di-*tert*-butyl dicarbonate (2.18 g, 10.0 mmol, 1.0 equiv) in THF (5 mL) wad added and the reaction mixture was stirred at -78 °C for 2 h. The reaction was diluted with NH_4Cl (aq, 5 mL), warmed to room temperature, extracted with EtOAc (3 x 50 mL). The organic layers were combined, washed with brine (1 x 50 mL), dried and concentrated. Purification by chromatography using EtOAc/hexanes (1/4) afforded the title product. Yield 56% (1.25 g). White solid. R_f (1/4 EtOAc/hexanes) = 0.62. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 3.56-3.50 (m, 1 H), 3.16 (s, 3 H), 2.74 (ddd, *J* = 17.7, 8.9, 5.3 Hz, 1 H), 2.64 (ddd, *J* = 12.4, 8.2, 3.7 Hz, 1 H), 2.29-2.20 (m, 1 H), 2.13 (ddt, *J* = 14.0, 9.7, 5.3 Hz, 1 H), 1.47 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 171.84, 169.39, 167.92, 83.12, 50.11, 30.34, 28.02, 26.78, 20.81. Spectroscopic data matched literature values.[15]



SI-2

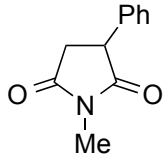
***tert*-Butyl 1-methyl-2,5-dioxopyrrolidine-3-carboxylate (SI-2).** Prepared according to the procedure described for **SI-1** from 1-methylpyrroldine-2,5-dione (1.13 g, 10.0 mmol, 1.0 equiv), NaHMDS (2.0 M, THF, 10.0 mL, 20.0 mmol, 2.0 equiv), and *tert*-butyl dicarbonate (2.18 g, 10.0

mmol, 1.0 equiv) in THF (45 mL) at -78 °C for 2 h. Yield 70 % (1.50 g). Purification by chromatography using EtOAc/hexanes (1/4) afforded the title product. White solid. R_f (1/4 EtOAc/hexanes) = 0.62. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 3.66 (dd, *J* = 9.3, 4.6 Hz, 1 H), 3.05 (d, *J* = 4.6 Hz, 1 H), 3.00 (s, 3 H), 2.85 (dd, *J* = 18.1, 9.3 Hz, 1 H), 1.49 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 175.59, 172.81, 166.73, 83.61, 47.66, 32.42, 28.03, 25.46. Spectroscopic data matched literature values.[15]



SI-3

Ethyl 1-methyl-2,5-dioxopyrrolidine-3-carboxylate (SI-3). Prepared according to the procedure described for **SI-1** from 1-methylpyrroldine-2,5-dione (1.13 g, 10.0 mmol, 1.0 equiv), NaHMDS (2.0 M, THF, 10.0 mL, 20.0 mmol, 2.0 equiv), and ethyl chloroformate (1.09 g, 0.95 mL, 10.0 mmol, 1.0 equiv) in THF (45 mL) at -78 °C for 2 h. Yield 54 % (1.00 g). Colorless oil. R_f (1/4 EtOAc/hexanes) = 0.56. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 4.27 (q, *J* = 7.2 Hz, 2 H), 3.76 (dd, *J* = 9.4, 4.6 Hz, 1 H), 3.10 (dd, *J* = 18.3, 4.7 Hz, 1 H), 3.02 (s, 3 H), 2.90 (dd, *J* = 18.3, 9.4 Hz, 1 H), 1.32 (t, *J* = 7.1 Hz, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 175.31, 172.40, 167.63, 62.77, 46.61, 32.36, 25.56, 14.22. Spectroscopic data matched literature values.[16]

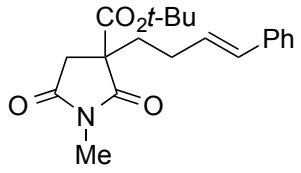


SI-4

1-Methyl-3-phenylpyrrolidine-2,5-dione (SI-4). A 50 ml round-bottomed flask was charged with 2-phenylsuccinic anhydride (1.29 g, 7.5 mmol, 1.0 equiv), 1,2-dichloroethane (20 mL), methylamine (aq, 40%, 1.17 mL, 1.0 equiv) at room temperature with vigorous stirring, and the reaction mixture was stirred at 80 °C for 4 h. The reaction mixture was cooled to room temperature, acetyl chloride (1.09 mL, 15.8 mmol, 2.1 equiv) was added and the reaction mixture was stirred at 80 °C for 1 h. The reaction mixture cooled to room temperature, diluted with CH_2Cl_2 (100 mL), organic layer was washed with H_2O (1 x 50 mL), $NaHCO_3$ (1 x 50 mL), brine (1 x 50 mL), dried and concentrated. Purification by chromatography using EtOAc/hexane (1/3)

afforded the title product. Yield 37 % (0.53 g). R_f (1/3 EtOAc/hexanes) = 0.48. Solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.37 (t, *J* = 7.4 Hz, 2 H), 7.31 (t, *J* = 7.3 Hz, 1 H), 7.22 (d, *J* = 7.5 Hz, 2 H), 4.03 (dd, *J* = 9.6, 4.7 Hz, 1 H), 3.21 (dd, *J* = 18.4, 9.6 Hz, 1 H), 3.07 (s, 3 H), 2.84 (dd, *J* = 18.5, 4.7 Hz, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 177.92, 176.35, 137.20, 129.32, 128.09, 127.50, 46.08, 37.24, 25.33. Spectroscopic data matched literature values.[17]

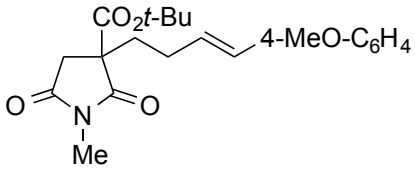
Synthesis of Imides 1a-1y. **General alkylation procedure.** A previously published procedure was followed.[19] All alkyl halides were purchased from commerical suppliers and used as received or prepared according to the previously published procedures and used without further purification.[18] The following procedure is representative: A 25 mL round-bottomed flask was charged with NaH (60%, 1.1 equiv, typically 1.1 mmol, 0.044 g), THF (typically, 2.0 mL), HMPA (2.0 equiv, typically, 1.1 mmol, 0.2 mL), and the reaction mixture was stirred at room temperature for 10 min. The reaction mixture was cooled to 0 °C, a solution of imide substrate (1.0 equiv) in THF (2.0 mL) was added, and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was cooled to 0 °C, a solution of alkyl halide (2.0 equiv) in THF (3.0 mL) was added, and the reaction mixture was stirred at 50 °C for 18 h. The reaction mixture cooled to room temperature, diluted with H_2O (2 mL), extracted with Et_2O (1 x 30 mL). The organic layers were combined, washed with water (1 x 10 mL), sodium thiosulfate (1 x 10 mL), and brine (1 x 10 mL), dried and concentrated. Purification by chromatography using EtOAc/hexane (6/1-3/1) afforded the title product. All products were obtained as single olefin isomers. The yields have not been optimized.



1b

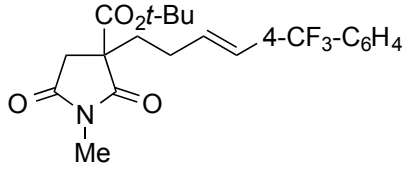
***tert*-Butyl (*E*)-1-methyl-2,5-dioxo-3-(4-phenylbut-3-en-1-yl)pyrrolidine-3-carboxylate (1b).** Prepared according to the general alkylation procedure. White solid. Mp = 82-83 °C. Yield 64 % (0.22 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.27 (m, 4 H), 7.21 (t, *J* = 7.0 Hz, 1 H), 6.37 (d, *J* = 15.7 Hz, 1 H), 6.12 (dt, *J* = 15.6, 5.9 Hz, 1 H), 3.13 (d, *J* = 18.1 Hz, 1 H), 2.95 (s, 3 H), 2.68 (d, *J* = 18.2 Hz, 1 H), 2.38-2.25 (m, 1 H), 2.16 (dddd, *J* = 19.2, 13.7, 9.3, 4.4 Hz, 3 H), 1.45 (s, 9 H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 176.12, 175.43, 168.45, 137.24, 131.27, 128.69, 128.42, 127.42, 126.18, 83.47, 55.64, 37.77, 32.99, 28.28, 27.92, 25.42.
HRMS calcd for $C_{20}H_{25}NO_4Na$ (M^+ + Na) 366.1676, found 366.1687.



1a

***tert*-Butyl (*E*)-3-(4-(4-methoxyphenyl)but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (1a).**
Prepared according to the general alkylation procedure. White solid. Mp = 93-94 °C. Yield 76 % (1.25 g).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.2 Hz, 2 H), 6.83 (d, *J* = 8.1 Hz, 2 H), 6.31 (d, *J* = 15.8 Hz, 1 H), 5.97 (dt, *J* = 13.4, 6.1 Hz, 1 H), 3.80 (s, 3 H), 3.12 (d, *J* = 18.2 Hz, 1 H), 2.93 (s, 3 H), 2.68 (d, *J* = 18.2 Hz, 1 H), 2.32-2.09 (m, 4 H), 1.45 (s, 9 H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 176.18, 175.48, 168.50, 159.11, 130.65, 130.08, 127.30, 126.21, 114.11, 83.43, 55.66, 55.43, 37.71, 33.09, 28.28, 27.92, 25.42.
HRMS calcd for $C_{21}H_{27}NO_5Na$ (M^+ + Na) 396.1781, found 396.1794.



1c

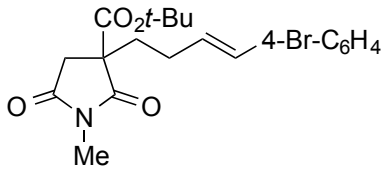
***tert*-Butyl (*E*)-1-methyl-2,5-dioxo-3-(4-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)pyrrolidine-3-carboxylate (1c)**.
Prepared according to the general alkylation procedure. White solid. Mp = 88-89 °C. Yield 45% (0.095 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.1 Hz, 2 H), 7.40 (d, *J* = 8.1 Hz, 2 H), 6.41 (d, *J* = 15.8 Hz, 1 H), 6.24 (dt, *J* = 15.8, 6.2 Hz, 1 H), 3.13 (d, *J* = 18.2 Hz, 1 H), 2.96 (s, 3 H), 2.67 (d, *J* = 18.1 Hz, 1 H), 2.36-2.30 (m, 1 H), 2.22-2.12 (m, 3 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 176.02, 175.28, 168.35, 140.73, 131.35, 130.04, 129.28 (q, J^F = 32.2 Hz), 126.32, 125.67 (q, J^F = 3.8 Hz), 124.34 (q, J^F = 270.1 Hz), 83.60, 55.57, 37.89, 32.82, 28.26, 27.92, 25.43.

^{19}F NMR (470 MHz, $CDCl_3$) δ -62.47.

HRMS calcd for $C_{21}H_{24}F_3NO_4Na$ (M^+ + Na) 434.1550, found 434.1564.



1d

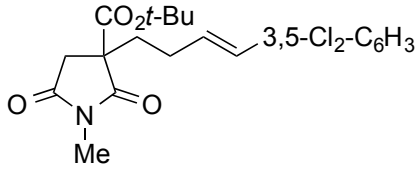
***tert*-Butyl (*E*)-3-(4-(4-bromophenyl)but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (1d).**

Prepared according to the general alkylation procedure. White solid. Mp = 87-88 °C. Yield 76% (0.16 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.3 Hz, 2 H), 7.19 (d, *J* = 8.4 Hz, 2 H), 6.33 (d, *J* = 15.8 Hz, 1 H), 6.19-6.10 (m, 1 H), 3.14 (d, *J* = 18.2 Hz, 1 H), 2.97 (s, 3 H), 2.69 (d, *J* = 18.2 Hz, 1 H), 2.36-2.27 (m, 1 H), 2.22-2.11 (m, 3 H), 1.47 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 176.06, 175.34, 168.38, 136.18, 131.78, 130.11, 129.35, 127.71, 121.13, 83.53, 55.56, 37.79, 32.83, 28.24, 27.91, 25.43.

HRMS calcd for $C_{20}H_{24}BrNO_4Na$ (M^+ + Na) 444.0781, found 444.0793.



1e

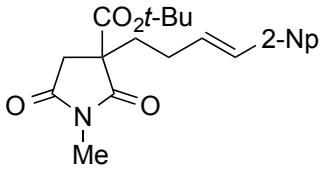
***tert*-Butyl (*E*)-3-(4-(3,5-dichlorophenyl)but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (1e).**

Prepared according to the general alkylation procedure. White solid. Mp = 101-103 °C. Yield 46% (0.092 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24-7.07 (m, 3 H), 6.27 (d, *J* = 15.8 Hz, 1 H), 6.17 (dt, *J* = 15.8, 5.9 Hz, 1 H), 3.13 (d, *J* = 18.2 Hz, 1 H), 2.98 (s, 3 H), 2.64 (d, *J* = 18.1 Hz, 1 H), 2.35-2.27 (m, 1 H), 2.19-2.09 (m, 3 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 175.94, 175.25, 168.29, 140.28, 135.24, 131.72, 128.87, 127.20, 124.56, 83.63, 55.53, 37.93, 32.82, 28.16, 27.92, 25.47.

HRMS calcd for $C_{20}H_{23}Cl_2NO_4Na$ (M^+ + Na) 434.0896, found 434.0910.



1f

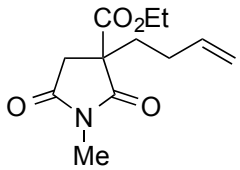
***tert*-Butyl (*E*)-1-methyl-3-(4-(naphthalen-2-yl)but-3-en-1-yl)-2,5-dioxopyrrolidine-3-carboxylate (1f).**

Prepared according to the general alkylation procedure. White solid. Mp = 117-118 °C. Yield 61% (0.18 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82-7.73 (m, 3 H), 7.65 (s, 1 H), 7.53 (d, *J* = 8.5 Hz, 1 H), 7.43 (p, *J* = 6.7 Hz, 2 H), 6.54 (d, *J* = 15.7 Hz, 1 H), 6.25 (dt, *J* = 15.7, 6.3 Hz, 1 H), 3.14 (d, *J* = 18.1 Hz, 1 H), 2.94 (s, 3 H), 2.71 (d, *J* = 18.1 Hz, 1 H), 2.41-2.31 (m, 1 H), 2.27-2.14 (m, 3 H), 1.46 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 176.12, 175.41, 168.45, 134.69, 133.72, 132.95, 131.35, 128.86, 128.31, 128.03, 127.76, 126.35, 125.86, 125.84, 123.51, 83.46, 55.63, 37.74, 32.98, 28.40, 27.91, 25.42.

HRMS calcd for $C_{24}H_{27}NO_4Na$ (M^+ + Na) 416.1832, found 416.1846.



1g

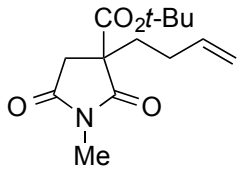
Ethyl 3-(but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (1g).

Prepared according to the general alkylation procedure. Colorless oil. Yield 59% (0.10 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75 (ddt, *J* = 16.7, 10.3, 6.3 Hz, 1 H), 5.03 (d, *J* = 17.0 Hz, 1 H), 4.99 (d, *J* = 10.3 Hz, 1 H), 4.22 (q, *J* = 7.2 Hz, 2 H), 3.20 (d, *J* = 18.2 Hz, 1 H), 3.01 (s, 3 H), 2.65 (d, *J* = 18.2 Hz, 1 H), 2.21-1.96 (m, 4 H), 1.27 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 175.67, 175.18, 169.40, 136.56, 116.09, 62.66, 54.97, 37.81, 33.11, 28.85, 25.48, 14.15.

HRMS calcd for $C_{12}H_{17}NO_4Na$ (M^+ + Na) 262.1050, found 262.1057.



1h

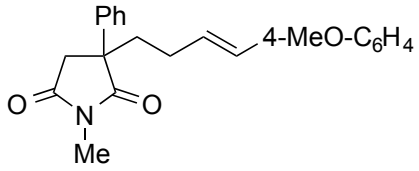
***tert*-Butyl 3-(but-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (1h).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 45% (0.21 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75 (ddt, *J* = 16.5, 10.3, 6.1 Hz, 1 H), 5.02 (d, *J* = 17.1 Hz, 1 H), 4.98 (d, *J* = 10.1 Hz, 1 H), 3.11 (d, *J* = 18.2 Hz, 1 H), 2.99 (s, 3 H), 2.62 (d, *J* = 18.2 Hz, 1 H), 2.14-2.07 (m, 2 H), 2.04-1.93 (m, 2 H), 1.44 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 176.06, 175.46, 168.41, 136.80, 115.92, 83.41, 55.67, 37.90, 32.80, 28.88, 27.89, 25.36.

HRMS calcd for $C_{14}H_{21}NO_4Na$ (M^+ + Na) 290.1363, found 290.1371.



1i

(*E*)-3-(4-(4-Methoxyphenyl)but-3-en-1-yl)-1-methyl-3-phenylpyrrolidine-2,5-dione (1i).

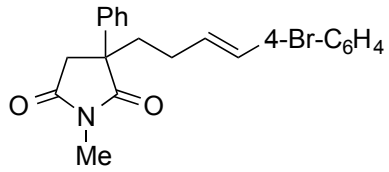
Prepared according to the general alkylation procedure. White solid. Mp = 81-82 °C. Yield 60% (0.21 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.8 Hz, 2 H), 7.37 (t, *J* = 7.6 Hz, 2 H), 7.29 (t, *J* = 7.4 Hz, 1 H), 7.22 (d, *J* = 8.2 Hz, 2 H), 6.82 (d, *J* = 8.7 Hz, 2 H), 6.29 (d, *J* = 15.7 Hz, 1 H), 5.96

(dt, *J* = 15.9, 6.0 Hz, 1 H), 3.79 (s, 3 H), 3.16 (d, *J* = 18.2 Hz, 1 H), 3.00 (s, 3 H), 2.92 (d, *J* = 18.2 Hz, 1 H), 2.27-2.04 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 180.18, 175.60, 159.00, 140.61, 130.37, 130.12, 129.01, 127.66, 127.19, 126.37, 126.20, 114.04, 55.36, 51.74, 41.49, 39.30, 28.49, 25.13.

HRMS calcd for $C_{22}H_{23}NO_3Na$ (M^+ + Na) 372.1570, found 372.1580.



1j

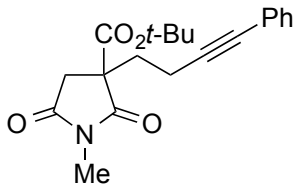
(*E*)-3-(4-(4-Bromophenyl)but-3-en-1-yl)-1-methyl-3-phenylpyrrolidine-2,5-dione (1j).

Prepared according to the general alkylation procedure. Colorless oil. Yield 40% (0.050 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.8 Hz, 2 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 7.38 (t, *J* = 8.0 Hz, 2 H), 7.30 (t, *J* = 7.3 Hz, 1 H), 7.14 (d, *J* = 8.4 Hz, 2 H), 6.27 (d, *J* = 15.7 Hz, 1 H), 6.09 (ddd, *J* = 15.9, 8.0, 4.6 Hz, 1 H), 3.17 (d, *J* = 18.2 Hz, 1 H), 3.00 (s, 3 H), 2.98 (d, *J* = 18.3 Hz, 1 H), 2.28-2.15 (m, 3 H), 2.08 (tdd, *J* = 13.3, 12.0, 5.8, 3.6 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 180.14, 175.55, 140.45, 136.27, 131.75, 129.91, 129.55, 129.11, 127.80, 127.66, 126.23, 121.04, 51.74, 41.63, 39.13, 28.53, 25.21.

HRMS calcd for $C_{21}H_{20}BrNO_2Na$ (M^+ + Na) 420.0570, found 420.0582.



1k

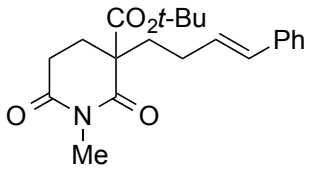
***tert*-Butyl 1-methyl-2,5-dioxo-3-(4-phenylbut-3-yn-1-yl)pyrrolidine-3-carboxylate (1k).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 34% (0.045 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.33 (m, 2 H), 7.28 (m, 3 H), 3.14 (d, *J* = 18.2 Hz, 1 H), 2.98 (s, 3 H), 2.93 (d, *J* = 18.2 Hz, 1 H), 2.62-2.45 (m, 2 H), 2.32 (dtd, *J* = 21.9, 14.1, 6.9 Hz, 2 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 175.79, 175.40, 168.20, 131.66, 128.40, 128.11, 123.30, 87.75, 83.68, 82.29, 55.60, 37.99, 31.79, 27.90, 25.49, 15.34.

HRMS calcd for $C_{20}H_{23}NO_4Na$ (M^+ + Na) 364.1519, found 364.1530.



1l

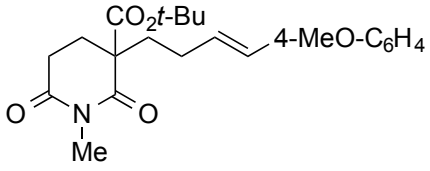
***tert*-Butyl (*E*)-1-methyl-2,6-dioxo-3-(4-phenylbut-3-en-1-yl)piperidine-3-carboxylate (1l).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 55% (0.195 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.2 Hz, 2 H), 7.29 (t, *J* = 7.6 Hz, 2 H), 7.20 (t, *J* = 7.1 Hz, 1 H), 6.42 (d, *J* = 15.8 Hz, 1 H), 6.19 (dt, *J* = 15.8, 6.7 Hz, 1 H), 3.17 (s, 3 H), 2.76 (ddd, *J* = 18.1, 5.0, 3.3 Hz, 1 H), 2.64 (ddd, *J* = 18.1, 12.7, 5.5 Hz, 1 H), 2.47-2.38 (m, 1 H), 2.27-2.11 (m, 3 H), 2.10-1.96 (m, 2 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.92, 171.66, 169.99, 137.55, 130.80, 129.42, 128.65, 127.23, 126.12, 83.50, 55.17, 34.81, 30.11, 28.35, 27.99, 27.19, 25.89.

HRMS calcd for $C_{21}H_{27}NO_4Na$ (M^+ + Na) 380.1832, found 380.1842.



1m

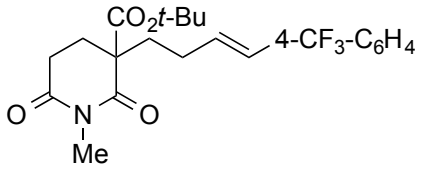
***tert*-Butyl (*E*)-3-(4-(4-methoxyphenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (1m).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 88% (0.51 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 5.4 Hz, 2 H), 6.83 (d, *J* = 8.3 Hz, 2 H), 6.35 (d, *J* = 15.9 Hz, 1 H), 6.04 (d, *J* = 15.8 Hz, 1 H), 3.80 (s, 3 H), 3.16 (s, 3 H), 2.75 (dt, *J* = 18.4, 3.9 Hz, 1 H), 2.69-2.59 (m, 1 H), 2.27-2.21 (m, 1 H), 2.20-2.10 (m, 2 H), 2.09-1.94 (m, 3 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.96, 171.69, 170.02, 158.98, 130.40, 130.16, 127.23, 127. 23, 114.08, 83.47, 55.43, 55.20, 34.96, 30.12, 28.33, 28.01, 27.20, 25.86.

HRMS calcd for $C_{22}H_{29}NO_5Na$ (M^+ + Na) 410.1938, found 410.1950.



1n

***tert*-Butyl (*E*)-1-methyl-2,6-dioxo-3-(4-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)piperidine-3-carboxylate (1n).**

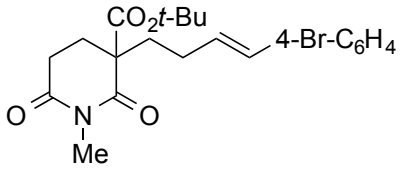
Prepared according to the general alkylation procedure. Colorless oil. Yield 42% (0.18 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.1 Hz, 2 H), 7.41 (d, *J* = 8.1 Hz, 2 H), 6.45 (d, *J* = 15.9 Hz, 1 H), 6.30 (dt, *J* = 15.7, 6.7 Hz, 1 H), 3.17 (s, 3 H), 2.80-2.72 (m, 1 H), 2.68-2.59 (m, 1 H), 2.52-2.42 (m, 1 H), 2.27-2.12 (m, 3 H), 2.10-1.96 (m, 2 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.83, 171.64, 169.92, 141.00, 132.28, 129.46, 128.90 (q, J^F = 32.1 Hz), 126.18, 125.49 (q, J^F = 3.6 Hz), 124.31 (q, J^F = 270.0 Hz), 83.64, 55.11, 34.61, 30.09, 28.38, 27.99, 27.20, 26.02.

^{19}F NMR (470 MHz, $CDCl_3$) δ -62.44.

HRMS calcd for $C_{22}H_{26}F_3NO_4Na$ (M^+ + Na) 448.1706, found 448.1718.



1o

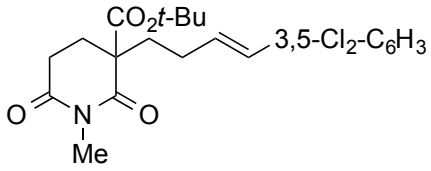
***tert*-Butyl (*E*)-3-(4-(4-bromophenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (1o).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 45% (0.090 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.5 Hz, 2 H), 7.19 (d, *J* = 8.5 Hz, 2 H), 6.35 (d, *J* = 15.8 Hz, 1 H), 6.18 (dt, *J* = 15.8, 6.7 Hz, 1 H), 3.16 (s, 3 H), 2.75 (ddd, *J* = 18.1, 4.9, 3.2 Hz, 1 H), 2.64 (ddd, *J* = 18.1, 12.7, 5.5 Hz, 1 H), 2.42 (tt, *J* = 12.9, 6.1 Hz, 1 H), 2.24 (ddd, *J* = 13.7, 5.4, 3.2 Hz, 1 H), 2.21-2.09 (m, 2 H), 2.08-1.95 (m, 2 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.87, 171.65, 169.95, 136.50, 131.73, 130.32, 129.67, 127.67, 120.90, 83.58, 55.13, 34.69, 30.10, 28.34, 28.00, 27.20, 25.96.

HRMS calcd for $C_{21}H_{26}BrNO_4Na$ (M^+ + Na) 458.0937, found 458.0951.



1p

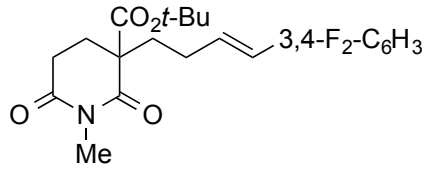
***tert*-Butyl (*E*)-3-(4-(3,5-dichlorophenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (1p).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 20% (0.036 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.17 (m, 3 H), 6.30 (d, *J* = 16.0 Hz, 1 H), 6.26-6.19 (m, 1 H), 3.17 (s, 3 H), 2.80-2.71 (m, 1 H), 2.71-2.57 (m, 1 H), 2.44 (dd, *J* = 13.1, 6.8 Hz, 1 H), 2.27-2.09 (m, 3 H), 2.08-1.93 (m, 2 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.79, 171.59, 169.87, 140.61, 135.18, 132.71, 128.44, 126.99, 124.53, 83.66, 55.09, 34.59, 30.09, 28.29, 28.00, 27.21, 26.07.

HRMS calcd for $C_{21}H_{25}Cl_2NO_4Na$ (M^+ + Na) 448.1053, found 448.1066.



1q

***tert*-Butyl (*E*)-3-(4-(3,4-difluorophenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (1q).**

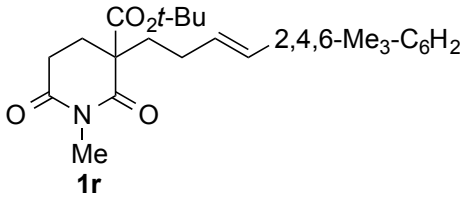
Prepared according to the general alkylation procedure. Colorless oil. Yield 29% (0.057 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (ddd, *J* = 11.6, 7.6, 2.1 Hz, 1 H), 7.10-7.03 (m, 1 H), 7.03-6.95 (m, 1 H), 6.32 (d, *J* = 15.7 Hz, 1 H), 6.12 (td, *J* = 15.6, 13.2, 5.6 Hz, 1 H), 3.17 (s, 3 H), 2.76 (ddd, *J* = 18.2, 5.2, 3.1 Hz, 1 H), 2.63 (ddd, *J* = 18.2, 12.7, 5.5 Hz, 1 H), 2.42 (ddt, *J* = 16.9, 12.7, 5.9 Hz, 1 H), 2.26-2.20 (m, 1 H), 2.20-2.09 (m, 2 H), 2.07-1.95 (m, 2 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.84, 171.64, 169.92, 150.81 (dd, J^F = 120.4, 12.6 Hz), 151.05 (d, J^F = 121.0 Hz), 134.84, 130.63 (d, J^F = 1.9 Hz), 128.85, 122.22 (q, J^F = 3.5 Hz), 117.33 (d, J^F = 17.3 Hz), 114.42 (d, J^F = 17.5.0 Hz), 83.62, 55.11, 34.70, 30.09, 28.21, 28.06, 27.20, 26.00.

^{19}F NMR (470 MHz, $CDCl_3$) δ -138.16 (d, *J* = 20.9 Hz), -139.97 (d, *J* = 20.9 Hz).

HRMS calcd for $C_{21}H_{25}F_2NO_4Na$ (M^+ + Na) 416.1644, found 416.1655.



1r

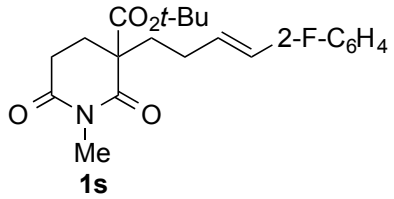
***tert*-Butyl (*E*)-3-(4-mesitylbut-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (1r).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 51% (0.102 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (s, 2 H), 6.34 (d, *J* = 16.0 Hz, 1 H), 5.63 (dt, *J* = 16.0, 6.8 Hz, 1 H), 3.19 (s, 3 H), 2.76 (ddd, *J* = 18.1, 5.2, 3.3 Hz, 1 H), 2.70-2.61 (m, 1 H), 2.46-2.39 (m, 1 H), 2.26 (s, 3 H), 2.24 (s, 6 H), 2.15-1.99 (m, 3 H), 1.46 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.96, 171.73, 170.03, 135.97, 135.93, 134.31, 133.97, 128.58, 128.36, 83.51, 55.22, 35.12, 30.11, 28.85, 28.01, 27.20, 25.98, 21.02.

HRMS calcd for $C_{24}H_{33}NO_4Na$ (M^+ + Na) 422.2302, found 422.2346.



1s

***tert*-Butyl (*E*)-3-(4-(2-fluorophenyl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (1s).**

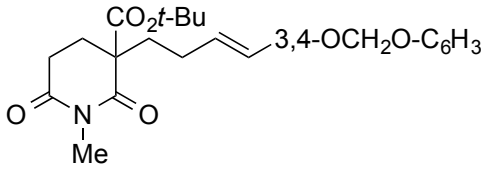
Prepared according to the general alkylation procedure. Colorless oil. Yield 29% (0.055 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43-7.38 (m, 1 H), 7.20-7.13 (m, 1 H), 7.07 (t, *J* = 7.5 Hz, 1 H), 7.04-6.97 (m, 1 H), 6.56 (d, *J* = 15.9 Hz, 1 H), 6.31-6.23 (m, 1 H), 3.17 (s, 3 H), 2.76 (ddd, *J* = 18.1, 5.2, 3.2 Hz, 1 H), 2.64 (ddd, *J* = 18.1, 12.6, 5.5 Hz, 1 H), 2.51-2.40 (m, 1 H), 2.29-2.12 (m, 3 H), 2.11-1.97 (m, 2 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.90, 171.65, 169.96, 160.10 (d, J^F = 248.7 Hz), 132.16 (d, J^F = 4.4 Hz), 128.44 (d, J^F = 8.3 Hz), 127.23 (d, J^F = 4.0 Hz), 125.28 (d, J^F = 12.5 Hz), 124.16 (d, J^F = 3.5 Hz), 123.25 (d, J^F = 3.9 Hz), 115.78 (d, J^F = 22.3 Hz), 83.55, 55.17, 34.69, 30.11, 28.77, 28.00, 27.19, 25.93.

^{19}F NMR (470 MHz, $CDCl_3$) δ -118.74.

HRMS calcd for $C_{21}H_{26}FNO_4Na$ (M^+ + Na) 398.1738, found 398.1751.



1t

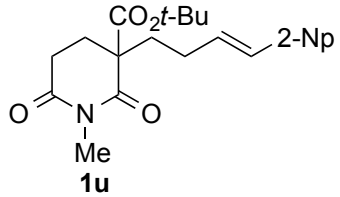
***tert*-Butyl (*E*)-3-(4-(benzo[*d*][1,3]dioxol-5-yl)but-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (1t).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 71% (0.285 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (s, 1 H), 6.82-6.64 (m, 2 H), 6.32 (d, *J* = 15.7, 1 H), 6.01 (dt, *J* = 13.8, 6.8 Hz, 1 H), 5.93 (s, 2 H), 3.16 (s, 3 H), 2.75 (ddd, *J* = 18.1, 5.2, 3.1 Hz, 1 H), 2.69-2.59 (m, 1 H), 2.45-2.31 (m, 1 H), 2.27-2.21 (m, 1 H), 2.19-2.09 (m, 2 H), 2.09-1.95 (m, 2 H), 1.44 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.91, 171.65, 169.97, 148.08, 146.92, 132.08, 130.34, 127.65, 120.52, 108.36, 105.54, 101.09, 83.48, 55.16, 34.89, 30.10, 28.22, 27.99, 27.18, 25.87.

HRMS calcd for $C_{22}H_{27}NO_6Na$ (M^+ + Na) 424.1730, found 424.1744.



1u

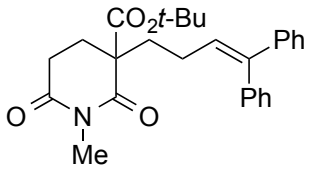
***tert*-Butyl (*E*)-1-methyl-3-(4-(naphthalen-2-yl)but-3-en-1-yl)-2,6-dioxopiperidine-3-carboxylate (1u).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 44% (0.089 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (t, *J* = 9.0 Hz, 3 H), 7.67 (s, 1 H), 7.56 (d, *J* = 8.6 Hz, 1 H), 7.48-7.38 (m, 2 H), 6.58 (d, *J* = 15.8 Hz, 1 H), 6.33 (dt, *J* = 15.7, 6.8 Hz, 1 H), 3.18 (s, 3 H), 2.77 (ddd, *J* = 18.0, 4.9, 3.3 Hz, 1 H), 2.65 (ddd, *J* = 18.1, 12.7, 5.5 Hz, 1 H), 2.48 (tt, *J* = 13.6, 6.6 Hz, 1 H), 2.32-2.16 (m, 3 H), 2.10 (ddd, *J* = 13.7, 11.3, 4.6 Hz, 1 H), 2.02 (td, *J* = 13.2, 5.2 Hz, 1 H), 1.46 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.92, 171.68, 171.68, 135.02, 133.78, 132.90, 130.91, 129.90, 128.26, 128.00, 127.76, 126.31, 125.74, 125.72, 123.59, 83.53, 55.19, 34.84, 30.12, 28.47, 28.00, 27.20, 25.92.

HRMS calcd for $C_{25}H_{29}NO_4Na$ (M^+ + Na) 430.1988, found 430.2000.



1v

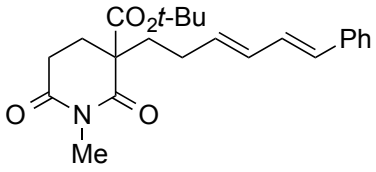
***tert*-Butyl 3-(4,4-diphenylbut-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (1v).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 65% (0.282 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, *J* = 7.3 Hz, 2 H), 7.30 (d, *J* = 7.3 Hz, 1 H), 7.25 (d, *J* = 9.5 Hz, 2 H), 7.21 (td, *J* = 6.5, 3.3 Hz, 3 H), 7.18-7.09 (m, 2 H), 6.06 (td, *J* = 7.2, 2.2 Hz, 1 H), 3.12 (s, 3 H), 2.68-2.52 (m, 2 H), 2.35-2.24 (m, 1 H), 2.16-2.03 (m, 4 H), 1.78 (td, *J* = 13.6, 13.0, 6.3 Hz, 1 H), 1.36 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.92, 171.60, 169.88, 142.55, 142.47, 139.94, 129.90, 128.41, 128.26, 128.25, 127.33, 127.24, 127.18, 83.39, 55.11, 35.00, 29.99, 27.90, 27.18, 25.45, 25.21.

HRMS calcd for $C_{27}H_{31}NO_4Na$ (M^+ + Na) 456.0145, found 456.0148.



1w

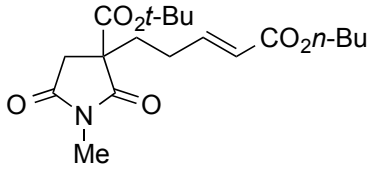
***tert*-Butyl 1-methyl-2,6-dioxo-3-((3*E*,5*E*)-6-phenylhexa-3,5-dien-1-yl)piperidine-3-carboxylate (1w).**

Prepared according to the general alkylation procedure. Colorless oil. Yield 61% (0.254 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.7 Hz, 2 H), 7.30 (t, *J* = 7.7 Hz, 2 H), 7.20 (t, *J* = 7.5 Hz, 1 H), 6.73 (dd, *J* = 15.7, 10.4 Hz, 1 H), 6.46 (d, *J* = 15.7 Hz, 1 H), 6.24 (dd, *J* = 15.1, 10.5 Hz, 1 H), 5.79 (dt, *J* = 14.6, 6.9 Hz, 1 H), 3.17 (s, 3 H), 2.76-2.71 (m, 1 H), 2.69-2.63 (m, 1 H), 2.37-2.33 (m, 1 H), 2.25-2.21 (m, 1 H), 2.16-2.09 (m, 2 H), 2.05-1.97 (m, 2 H), 1.45 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.92, 171.64, 169.96, 137.58, 133.86, 131.49, 130.98, 129.05, 128.70, 127.41, 126.34, 83.51, 55.16, 50.15, 34.77, 30.10, 28.00, 27.21, 25.93.

HRMS calcd for $C_{23}H_{29}NO_4Na$ (M^+ + Na) 406.1989, found 406.1999.



1x

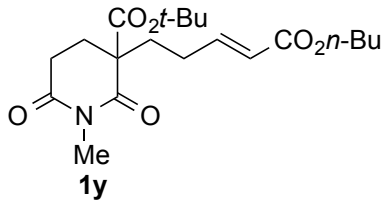
***tert*-Butyl (*E*)-3-(5-butoxy-5-oxopent-3-en-1-yl)-1-methyl-2,5-dioxopyrrolidine-3-carboxylate (1x).**

Prepared according to the general alkylation procedure. Oil. Yield 76% (0.025 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88 (dt, *J* = 15.6, 6.3 Hz, 1 H), 5.82 (d, *J* = 15.6 Hz, 1 H), 4.11 (t, *J* = 6.7 Hz, 2 H), 3.10 (d, *J* = 18.1 Hz, 1 H), 2.99 (s, 3 H), 2.57 (d, *J* = 18.1 Hz, 1 H), 2.32-2.24 (m, 1 H), 2.18-2.10 (m, 2 H), 2.06-2.00 (m, 1 H), 1.63-1.57 (m, 2 H), 1.43 (s, 9 H), 1.38 (dd, *J* = 15.0, 7.4 Hz, 2 H), 0.92 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 175.64, 175.02, 168.07, 166.38, 146.40, 122.57, 83.72, 64.39, 55.40, 38.14, 32.03, 30.81, 27.87, 27.28, 25.42, 19.27, 13.82.

HRMS calcd for $C_{19}H_{29}NO_6Na$ (M^+ + Na) 390.1887, found 390.1897.



1y

***tert*-Butyl (*E*)-3-(5-butoxy-5-oxopent-3-en-1-yl)-1-methyl-2,6-dioxopiperidine-3-carboxylate (1y).**

Prepared according to the general alkylation procedure. Oil. Yield 68% (0.065 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (dt, *J* = 15.3, 6.7 Hz, 1 H), 5.84 (d, *J* = 15.7 Hz, 1 H), 4.11 (t, *J* = 6.7 Hz, 2 H), 3.15 (s, 3 H), 2.73 (ddd, *J* = 18.3, 5.3, 3.1 Hz, 1 H), 2.60 (ddd, *J* = 18.2, 12.8, 5.5 Hz, 1 H), 2.50-2.39 (m, 1 H), 2.18 (tdd, *J* = 18.1, 8.5, 4.6 Hz, 2 H), 2.04 (dqd, *J* = 25.5, 13.7, 4.8 Hz, 2 H), 1.93 (td, *J* = 13.2, 5.2 Hz, 1 H), 1.62 (p, *J* = 6.9 Hz, 2 H), 1.42 (s, 9 H), 1.41-1.34 (m, 2 H), 0.92 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.66, 171.42, 169.66, 166.60, 147.43, 122.09, 83.73, 64.30, 54.90, 33.52, 30.81, 29.98, 27.93, 27.47, 27.15, 26.17, 19.26, 13.82.

HRMS calcd for $C_{20}H_{31}NO_6Na$ (M^+ + Na) 404.2044, found 404.2052.

Reductive Cyclization of 5- and 6-Membered Cyclic Imides using SmI_2–H_2O

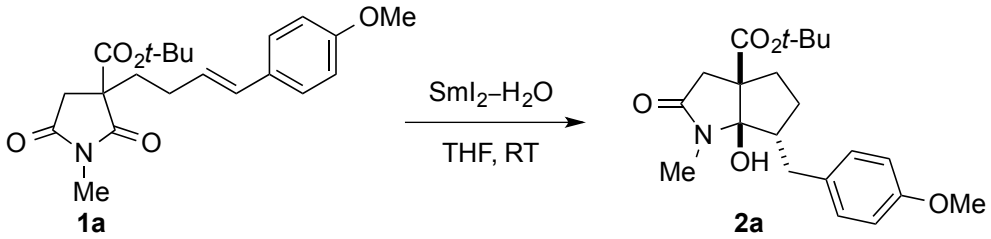
General procedure for the reductive cyclization of cyclic imides using SmI_2–H_2O. An oven-dried vial containing a stir bar was charged with a cyclic imide substrate (neat, 1 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF (typically, 2.0 mL) and water (typically, 600 equiv) were added, followed by a rapid injection of samarium(II) iodide (0.1 M, THF solution, typically 3 equiv) with vigorous stirring, which resulted in the formation of a characteristic burgundy-red color of the $SmI_2(H_2O)_n$ complex ($n > 5$ with respect to SmI_2), and the reaction mixture was stirred for the indicated time (typically, 15 min). The excess of Sm(II) was oxidized by bubbling air through the reaction mixture, and the reaction mixture was diluted with Et_2O (30 mL) and HCl (0.1 *N*, 20 mL),. The aqueous layer was extracted with Et_2O (3 x 20 mL), organic layers were combined, dried over Na_2SO_4, filtered and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, C_6D_6 or $CD_3C(O)CD_3$) and/or GC-MS (neat) to determine product distribution and diastereoselectivity from the crude reaction mixture. Unless stated otherwise, the crude product was purified by chromatography on silica gel or crystallization, concentrated under reduced pressure and stored neat or as a solution in acetone. Unless indicated otherwise, in all examples reported in the manuscript the observed cyclization/reduction selectivity was >95:5 (>78:22 in three examples as indicated below). Unless indicated otherwise, in all examples reported in the manuscript the observed diastereoselectivity was >95:5 with respect to all three stereocenters (analysis of crude reaction mixtures; 60:40-75:25 in two examples reacting via 'olefin-first' mechanism). All compounds have been prepared as racemates. Note that reactions involving samarium(II) can typically be followed by visual observation of the color changes of the respective reaction mixtures. In the case of Sm(II)/H_2O complexes, the color changes from Sm^{II} (burgundy red) to Sm^{III} (white: oxidized, solvated; then yellow: fully oxidized, characteristic of SmI_2X).

Representative procedure for the reductive cyclization of cyclic imides using SmI_2–H_2O. Scheme 1. An oven-dried 250 mL round-bottomed flask equipped with a stir bar was placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. The flask was charged with **1a** (neat, 1.00 g, 2.68 mmol, 1.0 equiv), THF (25 mL), and H_2O (19.3 mL, 400 equiv). Samarium(II) iodide (53.6 mL, 2.0 equiv, THF solution, 0.10 M) was added with vigorous stirring, which resulted in the formation of a characteristic

burgundy-red color of the $SmI_2(H_2O)_n$ complex (n > 5 with respect to SmI_2) The reaction mixture was stirred at room temperature for 5 min. The excess of SmI_2 was oxidized by bubbling air through the reaction mixture. The reaction mixture was diluted with Et_2O (100 mL) and HCl (50 mL, 1.0 *N*). The aqueous layer was extracted with Et_2O (2 x 100 mL), organic layers were combined, dried over Na_2SO_4, filtered and concentrated. Analysis of the crude reaction mixture showed >98% conversion, >98:2 cyclization/reduction selectivity, >98:2 diastereoselectivity. Purification by recrystallization afforded **2a** in 93% yield (2.49 mmol, 0.935 g). Characterization data are included in the section below.

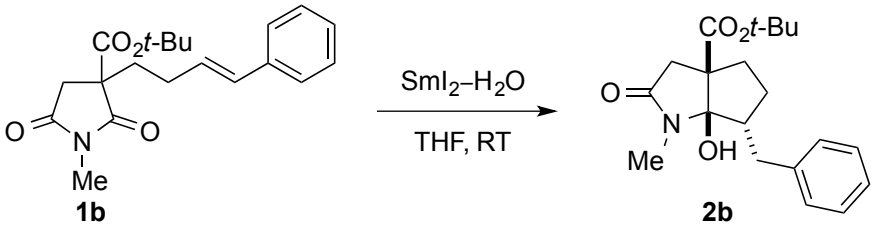
*Cyclization of 5-Membered Imides **1a-1k** using SmI_2 (Scheme 1).*

tert-Butyl (3a*R*,6*R*,6a*R*)-6a-hydroxy-6-(4-methoxybenzyl)-1-methyl-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2a) (Scheme 1)



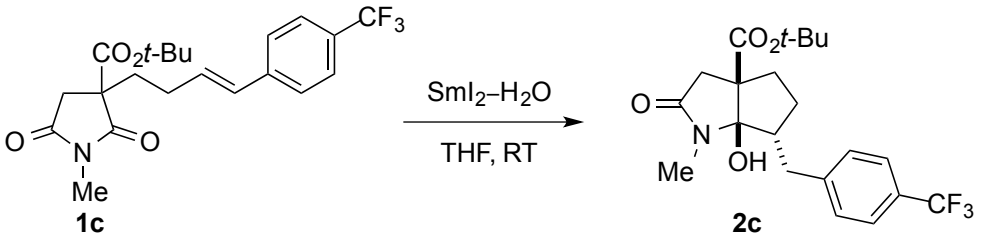
According to the general procedure, the reaction of **1a** (0.10 mmol), samarium(II) iodide (0.30 mmol, 3.0 equiv, 3.0 mL, 0.10 M) and H_2O (1.08 mL, 600 equiv) in THF (2.0 mL) for 15 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 93% yield (35.0 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Mp = 149-151 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CD_3C(O)CD_3$)** δ 7.15 (d, *J* = 8.5 Hz, 2 H), 6.85 (d, *J* = 8.6 Hz, 2 H), 5.05 (s, 1 H), 3.76 (s, 3 H), 3.13-3.05 (m, 2 H), 2.85 (s, 3 H), 2.47 (tdd, *J* = 11.8, 5.7, 2.9 Hz, 1 H), 2.43-2.32 (m, 2 H), 2.18 (d, *J* = 17.4 Hz, 1 H), 1.60 (dtt, *J* = 12.8, 6.9, 3.8 Hz, 2 H), 1.45 (s, 9 H), 1.32 (qd, *J* = 11.6, 7.3 Hz, 1 H). **^{13}C NMR (125 MHz, $CD_3C(O)CD_3$)** δ 172.96, 171.83, 158.02, 133.05, 129.42, 113.56, 100.70, 80.58, 57.48, 54.41, 53.33, 40.62, 34.49, 34.06, 27.62, 27.13, 26.81. **HRMS** calcd for $C_{21}H_{29}NO_5Na$ (M^+ + Na) 398.1938, found 398.1950.

tert-Butyl (3a*R*,6*R*,6a*R*)-6-benzyl-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2b) (Scheme 1)



According to the general procedure, the reaction of **1b** (0.10 mmol), samarium(II) iodide (0.30 mmol, 3.0 equiv, 3.0 mL, 0.10 M) and H_2O (1.08 mL, 600 equiv) in THF (2.0 mL) for 15 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 94% yield (32.4 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Mp = 134-135 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.29 (t, *J* = 7.4 Hz, 2 H), 7.20 (t, *J* = 7.4 Hz, 1 H), 7.16 (d, *J* = 7.1 Hz, 2 H), 4.07 (s, 1 H), 3.15 (dd, *J* = 12.1, 2.6 Hz, 1 H), 2.95 (d, *J* = 17.3 Hz, 4 H), 2.42-2.26 (m, 3 H), 2.18 (td, *J* = 12.7, 6.5 Hz, 1 H), 1.74-1.67 (m, 1 H), 1.65-1.60 (m, 1 H), 1.48 (s, 9 H), 1.26 (tq, *J* = 12.1, 6.2 Hz, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 174.13, 173.17, 140.42, 128.84, 128.63, 126.36, 100.25, 83.19, 56.79, 54.03, 42.47, 36.20, 34.15, 28.14, 27.89, 27.55. **HRMS** calcd for $C_{20}H_{27}NO_4Na$ (M^+ + Na) 368.1832, found 368.1842.

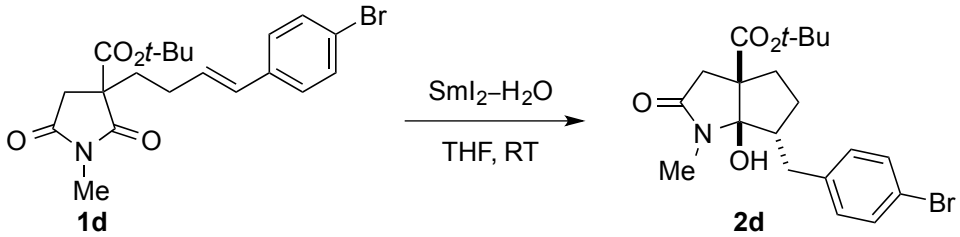
tert-Butyl (3a*R*,6*R*,6a*R*)-6a-hydroxy-1-methyl-2-oxo-6-(4-(trifluoromethyl)benzyl)hexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2c) (Scheme 1)



According to the general procedure, the reaction of **1c** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 93% yield (19.2 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Mp = 160-162 °C. Dr >95:5.

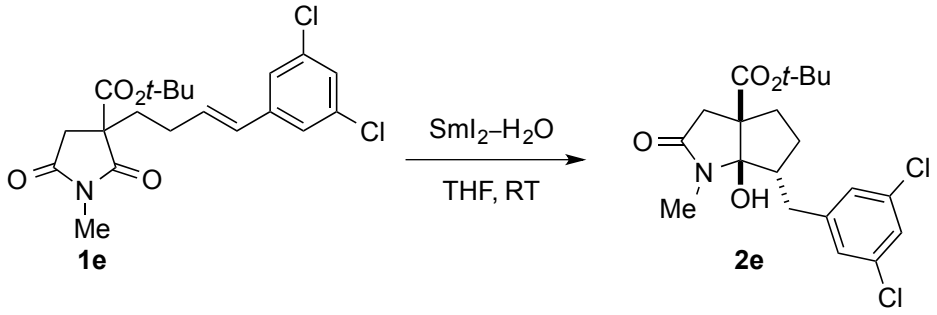
Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.54 (d, *J* = 7.9 Hz, 2 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 4.22 (s, 1 H), 3.21 (d, *J* = 9.1 Hz, 1H), 3.02-2.88 (m, 4 H), 2.45-2.30 (m, 3 H), 2.19 (td, *J* = 12.7, 6.5 Hz, 1 H), 1.71 (dd, *J* = 13.2, 5.8 Hz, 1 H), 1.60-1.54 (m, 1 H), 1.48 (s, 9 H), 1.26 (dq, *J* = 11.5, 5.8 Hz, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.99, 173.23, 144.57, 129.13, 128.80 (q, J^F = 32.2 Hz), 125.57 (q, J^F = 3.6 Hz), 124.36 (q, J^F = 271.6 Hz), 100.11, 83.28, 56.66, 53.67, 42.35, 36.04, 34.10, 28.11, 27.89, 27.40. **^{19}F NMR (470 MHz, $CDCl_3$)** δ -62.38. **HRMS** calcd for $C_{21}H_{26}F_3NO_4Na$ (M^+ + Na) 436.1706, found 436.1715.

tert-Butyl (3a*R*,6*R*,6a*R*)-6-(4-bromobenzyl)-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2d) (Scheme 1)



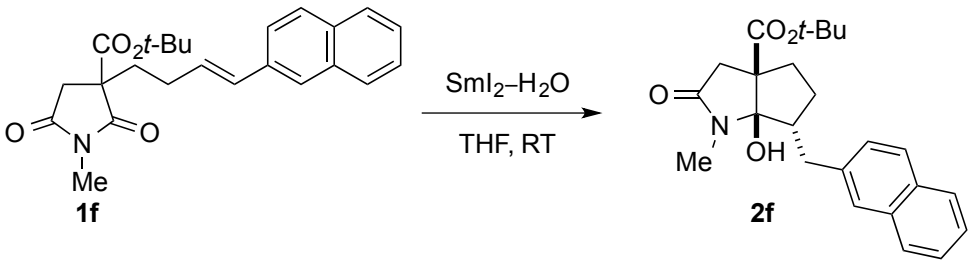
According to the general procedure, the reaction of **1d** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 75% yield (16.0 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Mp = 179-180 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CD_3C(O)CD_3$)** δ 7.47 (d, *J* = 8.1 Hz, 2 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 5.11 (s, 1 H), 3.14 (d, *J* = 11.1 Hz, 1 H), 3.08 (d, *J* = 17.4 Hz, 1 H), 2.85 (s, 3 H), 2.53-2.36 (m, 3 H), 2.19 (d, *J* = 17.4 Hz, 1 H), 1.63-1.56 (m, 2 H), 1.45 (s, 9 H), 1.39-1.31 (m, 1 H). **^{13}C NMR (125 MHz, $CD_3C(O)CD_3$)** δ 174.00, 172.74, 141.72, 132.17, 131.70, 120.11, 101.64, 81.63, 58.39, 53.85, 41.53, 35.74, 35.04, 28.44, 28.13, 27.79. **HRMS** calcd for $C_{20}H_{26}BrNO_4Na$ (M^+ + Na) 446.0937, found 446.0938.

tert-Butyl (3a*R*,6*R*,6a*R*)-6-(3,5-dichlorobenzyl)-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2e) (Scheme 1)



According to the general procedure, the reaction of **1e** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 90% yield (18.7 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Mp = 189-190 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.21 (s, 1 H), 7.06 (s, 2 H), 4.19 (s, 1 H), 3.11 (d, *J* = 10.7 Hz, 1 H), 2.94 (d, *J* = 17.5 Hz, 1 H), 2.93 (s, 3 H), 2.37 (d, *J* = 17.9 Hz, 1 H), 2.33-2.12 (m, 3 H), 1.73 (dd, *J* = 13.4, 6.1 Hz, 1 H), 1.62 (dt, *J* = 11.6, 5.6 Hz, 1 H), 1.48 (s, 9 H), 1.23 (dq, *J* = 12.1, 5.8 Hz, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.89, 173.06, 143.69, 134.95, 127.20, 126.60, 99.87, 83.25, 56.46, 53.43, 42.23, 35.58, 33.97, 28.00, 27.73, 27.25. **HRMS** calcd for $C_{20}H_{25}Cl_2NO_4Na$ (M^+ + Na) 436.1053, found 436.1068.

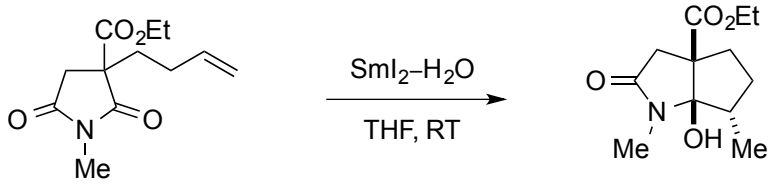
***tert*-Butyl (3a*R*,6*R*,6a*R*)-6a-hydroxy-1-methyl-6-(naphthalen-2-ylmethyl)-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2f) (Scheme 1)**



According to the general procedure, the reaction of **1f** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 93% yield (18.3 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Mp = 193-195 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.84-7.74 (m,

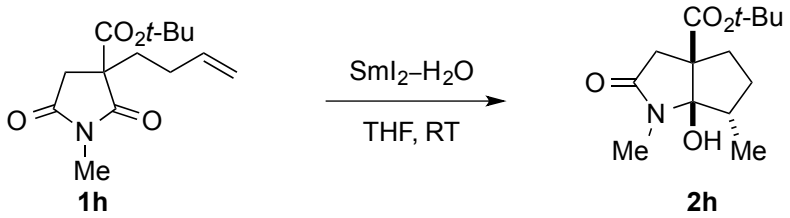
3 H), 7.61 (s, 1 H), 7.45 (p, *J* = 7.0 Hz, 2 H), 7.30 (d, *J* = 8.4 Hz, 1 H), 4.14 (s, 1 H), 3.32 (d, *J* = 8.4 Hz, 1 H), 3.01 (s, 3 H), 2.70 (d, J = 18.0 Hz, 1 H), 2.56-2.43 (m, 2 H), 2.41 (d, *J* = 18.0 Hz, 1 H), 2.18 (td, *J* = 12.7, 6.6 Hz, 1 H), 1.71 (dd, *J* = 13.4, 6.1 Hz, 1 H), 1.64-1.58 (m, 1 H), 1.49 (s, 9 H), 1.36-1.25 (m, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.99, 173.14, 137.77, 133.54, 132.12, 128.14, 127.63, 127.45, 127.17, 127.00, 126.10, 125.43, 100.19, 83.08, 56.68, 53.83, 42.32, 36.21, 34.01, 28.00, 27.83, 27.48. **HRMS** calcd for $C_{24}H_{29}NO_4Na$ (M^+ + Na) 418.1989, found 418.2002.

Ethyl (3a*R*,6*S*,6a*R*)-6a-hydroxy-1,6-dimethyl-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2g) (Scheme 1)



According to the general procedure, the reaction of **1g** (0.1 mmol), samarium(II) iodide (0.80 mmol, 8.0 equiv, 8.0 mL, 0.10 M) and H_2O (2.16 mL, 1200 equiv) in THF (1.0 mL) for 1 h afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 55% yield (13.3 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Dr >95:5. Cyclization/reduction selectivity = 92:8. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 4.23 (q, *J* = 7.1 Hz, 2 H), 3.56 (s, 1 H), 3.00 (d, *J* = 17.8 Hz, 1 H), 2.89 (s, 3 H), 2.41 (dt, *J* = 12.7, 6.1 Hz, 1 H), 2.35 (d, *J* = 17.7 Hz, 1 H), 2.21 (tt, *J* = 12.8, 6.6 Hz, 1 H), 1.86 (dtd, *J* = 12.6, 6.4, 2.5 Hz, 1 H), 1.75 (ddd, *J* = 12.7, 5.7, 2.0 Hz, 1 H), 1.37-1.31 (m, 1 H), 1.30 (t, *J* = 7.0 Hz, 3 H), 1.06 (d, *J* = 7.0 Hz, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 174.67, 172.93, 101.03, 62.02, 56.58, 46.21, 42.42, 34.23, 30.75, 27.74, 14.66, 14.28. **HRMS** calcd for $C_{12}H_{19}NO_4Na$ (M^+ + Na) 264.1206, found 264.1227.

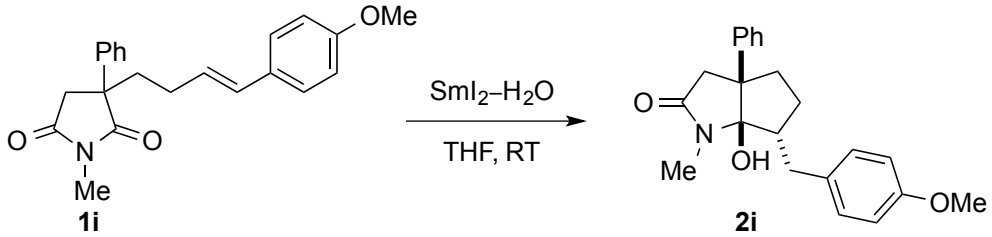
***tert*-Butyl (3a*R*,6*S*,6a*R*)-6a-hydroxy-1,6-dimethyl-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2h) (Scheme 1)**



1h **2h**

According to the general procedure, the reaction of **1h** (0.1 mmol), samarium(II) iodide (0.80 mmol, 8.0 equiv, 8.0 mL, 0.10 M) and H_2O (2.16 mL, 1200 equiv) in THF (1.0 mL) for 1 h afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 77% yield (20.7 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Dr >95:5. Cyclization/reduction selectivity = 91:9. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 3.88 (s, 1 H), 2.95 (d, *J* = 17.8 Hz, 1 H), 2.91 (s, 3 H), 2.39-2.33 (m, 2 H), 2.23 (dt, *J* = 11.7, 6.6 Hz, 1 H), 1.86 (dtd, *J* = 12.3, 6.2, 2.4 Hz, 1 H), 1.75 (ddd, *J* = 13.0, 5.9, 2.3 Hz, 1 H), 1.50 (s, 9 H), 1.46 (d, *J* = 4.7 Hz, 1 H), 1.07 (d, *J* = 7.1 Hz, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 174.06, 173.01, 100.89, 83.03, 56.87, 46.31, 42.59, 34.25, 30.65, 28.14, 27.62, 14.73. **HRMS** calcd for $C_{14}H_{23}NO_4Na$ (M^+ + Na) 292.1519, found 292.1527.

(3a*S*,6*R*,6a*R*)-6a-Hydroxy-6-(4-methoxybenzyl)-1-methyl-3a-phenylhexahydrocyclopenta[*b*]pyrrol-2(1*H*)-one (2i) (Scheme 1)

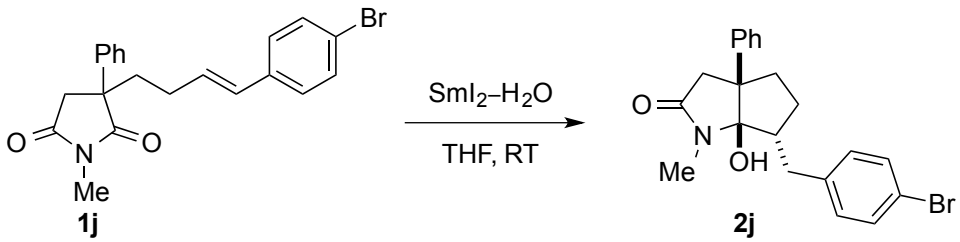


1i **2i**

According to the general procedure, the reaction of **1i** (0.1 mmol), samarium(II) iodide (0.80 mmol, 8.0 equiv, 8.0 mL, 0.10 M) and H_2O (2.16 mL, 1200 equiv) in THF (1.0 mL) for 1 h afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 92% yield (32.5 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Mp = 142-144 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.41 (t, *J* = 7.6 Hz, 2 H), 7.32 (t, *J* = 7.5 Hz, 1 H), 7.27 (d, *J* = 7.8 Hz, 2 H), 7.09 (d, *J* = 8.2 Hz, 2 H), 6.83 (d, *J* = 8.2 Hz, 2 H), 3.79 (s, 3 H), 3.09-3.03 (m, 1 H), 2.96 (s, 3 H), 2.90 (d, *J* = 18.0 Hz, 1 H),

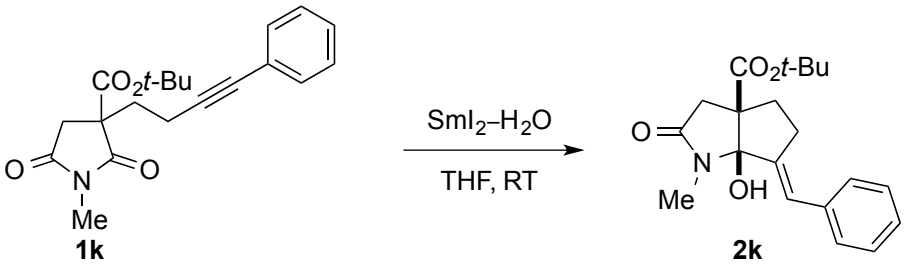
2.71 (d, *J* = 18.0 Hz, 1 H), 2.47-2.34 (m, 2 H), 2.33-2.25 (m, 1 H), 1.94-1.73 (m, 3 H), 1.48 (dp, *J* = 17.3, 6.2, 5.7 Hz, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.95, 158.15, 142.20, 132.38, 129.73, 129.46, 127.82, 126.53, 113.99, 100.85, 56.26, 55.38, 54.31, 46.00, 35.73, 34.10, 28.56, 27.71. **HRMS** calcd for $C_{22}H_{25}NO_3Na$ (M^+ + Na) 374.1727, found 374.1738.

(3a*S*,6*R*,6a*R*)-6-(4-Bromobenzyl)-6a-hydroxy-1-methyl-3a-phenylhexahydrocyclopenta[*b*]pyrrol-2(1*H*)-one (2j) (Scheme 1)



According to the general procedure, the reaction of **1j** (0.1 mmol), samarium(II) iodide (0.80 mmol, 8.0 equiv, 8.0 mL, 0.10 M) and H_2O (2.16 mL, 1200 equiv) in THF (1.0 mL) for 1 h afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 89% yield (35.5 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Mp = 137-139 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CD_3C(O)CD_3$)** δ 7.47 (d, *J* = 8.3 Hz, 2 H), 7.39-7.27 (m, 4 H), 7.24 (d, *J* = 8.5 Hz, 2 H), 7.22 (t, *J* = 6.5 Hz, 1 H), 4.22 (s, 1 H), 3.16 (dd, *J* = 12.4, 2.8 Hz, 1 H), 2.91 (s, 3 H), 2.75 (d, *J* = 17.6 Hz, 1 H), 2.60 (d, *J* = 17.5 Hz, 1 H), 2.49 (t, *J* = 12.2 Hz, 1 H), 2.43-2.33 (m, 2 H), 1.88 (ddd, *J* = 13.0, 6.6, 1.9 Hz, 1 H), 1.68 (dtd, *J* = 12.9, 6.5, 2.0 Hz, 1 H), 1.54 (ddt, *J* = 18.4, 11.6, 6.7 Hz, 1 H). **^{13}C NMR (126 MHz, $CD_3C(O)CD_3$)** δ 173.87, 144.61, 141.67, 132.14, 131.80, 128.87, 128.12, 127.20, 120.07, 101.31, 55.89, 54.92, 46.13, 36.42, 36.32, 28.25, 27.75. **HRMS** calcd for $C_{21}H_{22}BrNO_2Na$ (M^+ + Na) 422.0726, found 422.0732.

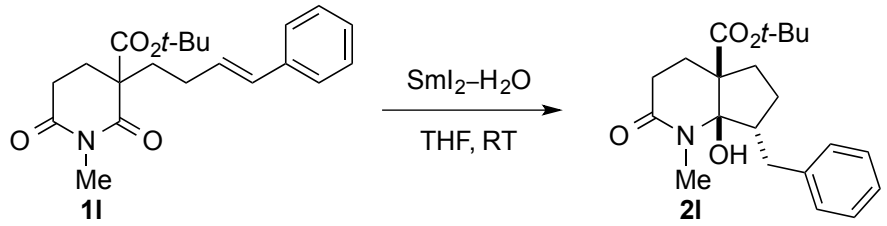
***tert*-Butyl (3a*R*,6a*R*)-6-((*E*)-benzylidene)-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2k) (Scheme 1)**



According to the general procedure, the reaction of **1k** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 65% yield (11.2 mg). Colorless oil. Dr >95:5. Cyclization/reduction selectivity = 75:25. *E*/*Z* >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.44-7.37 (m, 4 H), 7.28 (m, 1 H), 6.78 (s, 1 H), 3.70 (s, 1 H), 3.08 (d, *J* = 17.3 Hz, 1 H), 2.94-2.87 (m, 1 H), 2.80 (s, 3 H), 2.66-2.58 (m, 1 H), 2.44 (d, *J* = 17.3 Hz, 1 H), 2.37 (ddd, *J* = 14.4, 9.0, 5.9 Hz, 1 H), 1.86-1.78 (m, 1 H), 1.45 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 172.95, 172.53, 140.62, 136.50, 129.05, 128.59, 127.58, 125.89, 98.76, 82.87, 55.25, 39.59, 34.39, 28.10, 27.63, 24.49. **HRMS** calcd for $C_{20}H_{25}NO_4Na$ (M^+ + Na) 366.1676, found 366.1684.

*Cyclization of 6-Membered Imides **1l-1w** using SmI_2 (Scheme 2).*

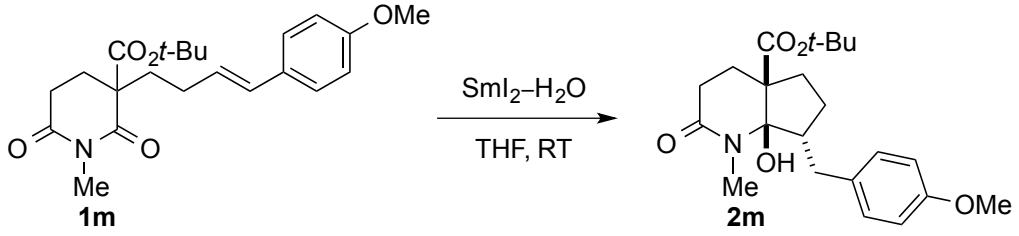
tert-Butyl (4a*R*,7*R*,7a*R*)-7-benzyl-7a-hydroxy-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2l) (Scheme 2)



According to the general procedure, the reaction of **1l** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 86% yield (15.5 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ

7.36 (t, *J* = 7.3 Hz, 1 H), 7.20 (t, *J* = 7.4 Hz, 2 H), 7.16 (d, *J* = 7.1 Hz, 2 H) 5.57 (s, 1 H), 3.04 (s, 3 H), 2.78 (d, *J* = 6.4 Hz, 1 H), 2.47 (dd, *J* = 7.3, 4.3 Hz, 1 H), 2.40-2.35 (m, 2 H), 2.29-2.23 (m, 2 H), 2.08-2.05 (m, 2 H), 1.94-1.82 (m, 3 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 7-benzyl-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta [*b*]pyridine-4a-carboxylate (**2l''**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.30 (t, *J* = 7.4 Hz, 2 H), 7.26-7.17 (m, 3 H), 3.74 (d, *J* = 16.0 Hz, 1 H), 3.52 (d, *J* = 16.0 Hz, 1 H), 3.28 (s, 3 H), 2.53 (ddt, *J* = 17.7, 14.8, 9.3 Hz, 3 H), 2.39 (ddd, *J* = 12.9, 6.5, 4.3 Hz, 1 H), 2.28 (dd, *J* = 12.9, 8.4 Hz, 1 H), 2.14 (dd, *J* = 15.5, 9.1 Hz, 1 H), 1.80-1.69 (m, 2 H), 1.46 (s, 9 H). **^{13}C NMR (125 MHz, 500 MHz, $CDCl_3$)** δ 173.95, 170.43, 138.92, 137.58, 128.58, 128.26, 126.31, 121.76, 81.27, 57.19, 34.75, 34.21, 34.12, 31.40, 30.44, 28.08. **HRMS** calcd for $C_{21}H_{27}NO_3Na$ (M^+ + Na) 364.1883, found 364.1894.

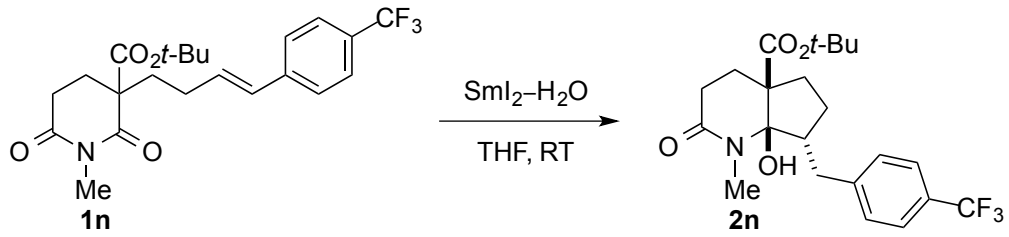
***tert*-Butyl (4a*R*,7*R*,7a*R*)-7a-hydroxy-7-(4-methoxybenzyl)-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2m) (Scheme 2)**



According to the general procedure, the reaction of **1m** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 85% yield (16.5 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (d, *J* = 7.9 Hz, 2 H), 6.81 (d, *J* = 8.2 Hz, 2 H), 5.54 (s, 1 H), 3.77 (s, 3 H), 3.02 (s, 3 H), 2.75 (d, *J* = 12.8 Hz, 1 H), 2.56-2.47 (m, 2 H), 2.32 (dd, *J* = 18.6, 9.2 Hz, 1 H), 2.23-2.14 (m, 2 H), 2.05 (d, *J* = 7.4 Hz, 2 H), 1.92-1.81 (m, 3 H), 1.46 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 7-(4-methoxybenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (**2m''**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.10 (d, *J* =

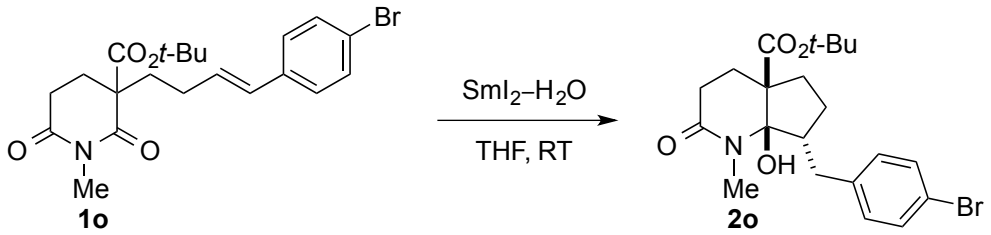
8.2 Hz, 2 H), 6.83 (d, *J* = 8.2 Hz, 2 H), 3.79 (s, 3 H), 3.66 (d, *J* = 15.9 Hz, 1 H), 3.45 (d, *J* = 15.8 Hz, 1 H), 3.27 (s, 3 H), 2.54 (dd, *J* = 16.4, 8.0 Hz, 3 H), 2.42-2.33 (m, 1 H), 2.30-2.22 (m, 1 H), 2.13 (dd, *J* = 15.1, 9.3 Hz, 1 H), 1.73 (tt, *J* = 18.9, 9.4 Hz, 2 H), 1.45 (s, 9 H). **^{13}C NMR (125 MHz, 500 MHz, $CDCl_3$)** δ 174.06, 170.53, 158.23, 137.36, 130.93, 129.27, 122.37, 114.09, 81.34, 57.29, 55.42, 34.32, 34.21, 34.15, 33.96, 31.51, 30.55, 28.17. **HRMS** calcd for $C_{22}H_{29}NO_4Na$ (M^+ + Na) 394.1989, found 394.1998.

***tert*-Butyl (4a*R*,7*R*,7a*R*)-7a-hydroxy-1-methyl-2-oxo-7-(4-(trifluoromethyl)benzyl) octahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2n) (Scheme 2)**



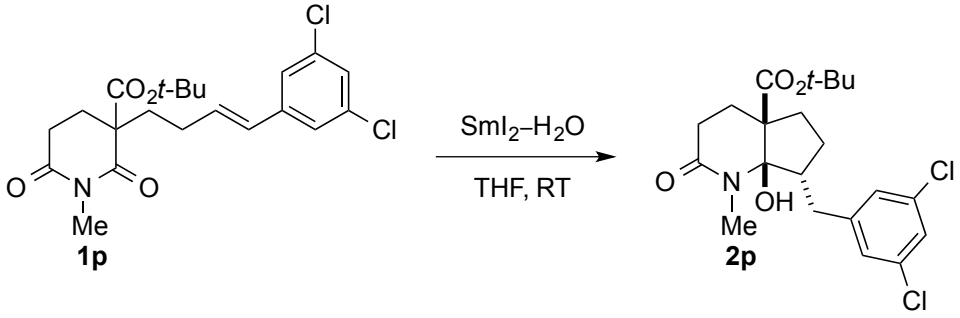
According to the general procedure, the reaction of **1n** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 86% yield (18.5 mg). Recrystallization from CH_2Cl_2/hexanes. White solid. Mp = 185-187 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.54 (d, *J* = 7.9 Hz, 2 H), 7.25 (d, *J* = 7.6 Hz, 2 H), 5.60 (s, 1 H), 3.04 (s, 3 H), 2.87 (dd, *J* = 13.8, 3.5 Hz, 1 H), 2.63-2.51 (m, 2 H), 2.36-2.22 (m, 3 H), 2.20-1.99 (m, 3 H), 1.90 (tdd, *J* = 21.1, 9.1, 4.4 Hz, 2 H), 1.48 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 175.46, 169.46, 144.17, 129.15 (q, J^F = 32.7 Hz), 129.09, 125.60 (q, J^F = 3.7 Hz), 124.35 (q, J^F = 272.2 Hz), 96.20, 83.30, 54.91, 50.12, 40.03, 33.30, 29.11, 28.08, 28.04, 26.91, 26.83. **^{19}F NMR (470 MHz, $CDCl_3$)** δ -62.40. **HRMS** calcd for $C_{22}H_{28}F_3NO_4Na$ (M^+ + Na) 450.1863, found 450.1872.

***tert*-Butyl (4a*R*,7*R*,7a*R*)-7-(4-bromobenzyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2o) (Scheme 2)**



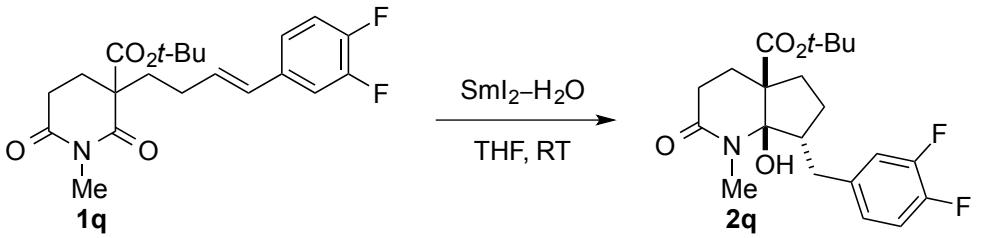
According to the general procedure, the reaction of **1o** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 76% yield (16.7 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.0 Hz, 2 H), 7.01 (d, *J* = 7.5 Hz, 2 H), 5.57 (s, 1 H), 3.02 (s, 3 H), 2.76 (d, *J* = 11.6 Hz, 1 H), 2.59-2.52 (m, 2 H), 2.36-2.27 (m, 3 H), 2.07-2.00 (m, 2 H), 1.95-1.85 (m, 3 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 7-(4-bromobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (**2o"**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.41 (d, *J* = 8.0 Hz, 2 H), 7.08 (d, *J* = 8.0 Hz, 2 H), 3.68 (d, *J* = 16.2 Hz, 1 H), 3.46 (d, *J* = 16.2 Hz, 1 H), 3.25 (s, 3 H), 2.52 (dt, *J* = 17.2, 9.8 Hz, 3 H), 2.43-2.34 (m, 1 H), 2.27 (dd, *J* = 12.4, 8.8 Hz, 1 H), 2.11 (dd, *J* = 15.2, 9.2 Hz, 1 H), 1.73 (dt, *J* = 21.9, 9.6 Hz, 2 H), 1.45 (s, 9 H). **^{13}C NMR (125 MHz, 500 MHz, $CDCl_3$)** δ 173.86, 170.44, 138.07, 138.04, 131.76, 130.09, 120.86, 120.23, 81.49, 57.30, 34.32, 34.23, 34.17, 34.14, 31.41, 30.49, 28.18. **HRMS** calcd for $C_{21}H_{26}BrNO_3Na$ (M^+ + Na) 442.0988, found 442.0999.

***tert*-Butyl (4a*R*,7*R*,7a*R*)-7-(3,5-dichlorobenzyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2p) (Scheme 2)**



According to the general procedure, the reaction of **1p** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 71% yield (15.2 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (s, 1 H), 7.03 (s, 2 H), 5.58 (s, 1 H), 3.03 (s, 3 H), 2.77 (d, *J* = 13.7 Hz, 1 H), 2.52 (dd, *J* = 17.6, 5.2 Hz, 2 H), 2.35-2.16 (m, 3 H), 2.27 (d, *J* = 17.6 Hz, 1 H) 2.10-2.04 (m, 1 H), 2.03-1.90 (m, 2 H), 1.88-1.82 (m, 1 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 7-(3,5-dichlorobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*] pyridine-4a-carboxylate (**2p''**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.23 (s, 1 H), 7.08 (s, 2 H), 3.73 (d, *J* = 16.3 Hz, 1 H), 3.46 (d, *J* = 16.3 Hz, 1 H), 3.25 (s, 3 H), 2.59-2.48 (m, 3 H), 2.39 (ddd, *J* = 13.3, 6.6, 4.1 Hz, 1 H), 2.31 (dd, *J* = 13.1, 8.3 Hz, 1 H), 2.12 (dd, *J* = 15.5, 9.1 Hz, 1 H), 1.80-1.71 (m, 2 H), 1.47 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.77, 170.40, 142.57, 138.98, 135.33, 126.87, 126.81, 119.40, 81.72, 57.32, 34.45, 34.34, 34.18, 34.14, 31.42, 30.46, 28.21. **HRMS** calcd for $C_{21}H_{25}Cl_2NO_3Na$ (M^+ + Na) 432.1104, found 432.1115.

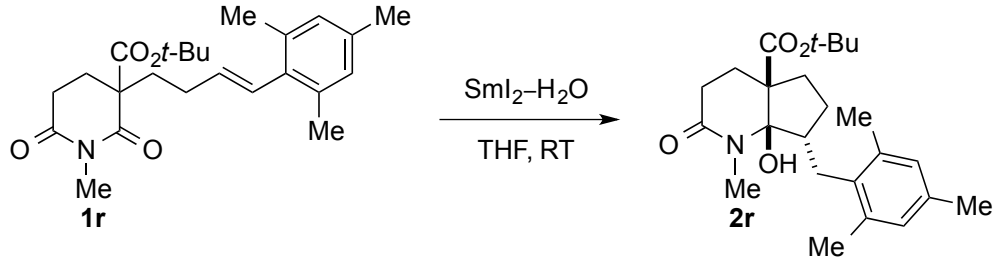
***tert*-Butyl (4a*R*,7*R*,7a*R*)-7-(3,4-difluorobenzyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2q) (Scheme 2)**



According to the general procedure, the reaction of **1q** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 87% yield (17.2 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (dtd, *J* = 10.6, 8.2, 2.5 Hz, 1 H), 6.99-6.91 (m, 1 H), 6.89-6.79 (m, 1 H), 5.57 (d, *J* = 2.4 Hz, 1 H), 3.02 (s, 3 H), 2.77 (d, *J* = 13.9 Hz, 1 H), 2.57-2.46 (m, 2 H), 2.37-2.16 (m, 4 H), 2.10-1.98

(m, 2 H), 1.94-1.81 (m, 2 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 7-(3,4-difluorobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (**2q''**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.08 (q, *J* = 8.5 Hz, 1 H), 7.04-6.98 (m, 1 H), 6.92 (s, 1 H), 3.71 (d, *J* = 16.2 Hz, 1 H), 3.46 (d, *J* = 16.3 Hz, 1 H), 3.25 (s, 3 H), 2.52 (tt, *J* = 9.9, 5.4 Hz, 3 H), 2.40 (ddd, *J* = 13.4, 6.8, 3.9 Hz, 1 H), 2.28 (dd, *J* = 13.2, 8.5 Hz, 1 H), 2.12 (dd, *J* = 15.4, 9.2 Hz, 1 H), 1.75 (dddd, *J* = 15.8, 13.0, 8.1, 5.0 Hz, 2 H), 1.46 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.81, 171.43, 151.10 (d, J^F = 192.0 Hz), 148.80 (dd, J^F = 178.2, 12.6 Hz), 138.40, 136.02 (d, J^F = 4.3 Hz), 124.13 (q, J^F = 3.8 Hz), 120.33, 117.42 (d, J^F = 17.1 Hz), 117.16 (d, J^F = 17.3 Hz), 81.64, 57.33, 34.18, 34.17, 34.16, 34.06, 31.39, 30.46, 28.17. **^{19}F NMR (470 MHz, $CDCl_3$)** δ -137.63 (d, *J* = 21.0 Hz), -141.32 (d, *J* = 21.4 Hz). **HRMS** calcd for $C_{21}H_{25}F_2NO_3Na$ (M^+ + Na) 400.1695, found 400.1704.

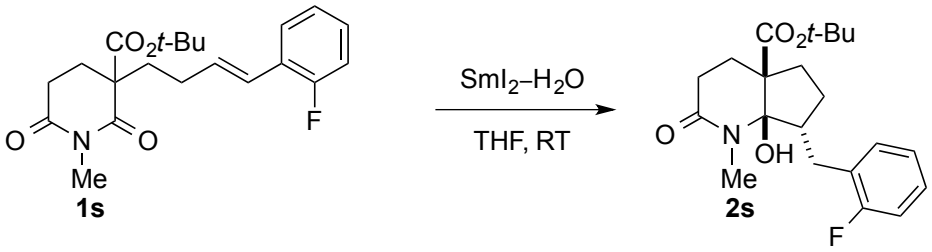
***tert*-Butyl (4a*R*,7*R*,7a*R*)-7a-hydroxy-1-methyl-2-oxo-7-(2,4,6-trimethylbenzyl)octahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2r) (Scheme 2)**



According to the general procedure, the reaction of **1r** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 62% yield (12.4 mg). Dr >95:5. Cyclization/reduction selectivity = 78:22. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82 (s, 2 H), 5.52 (s, 1 H), 3.09 (s, 3 H), 2.66-2.59 (m, 2 H), 2.56-2.51 (m, 2 H), 2.38-2.34 (m, 1 H), 2.25 (s, 3 H), 2.23 (s, 6 H), 2.15-2.10 (m, 2 H), 1.86 (ddt, *J* = 10.7, 6.8, 3.3 Hz, 2 H), 1.72 (dt, *J* = 9.6, 4.4 Hz, 2 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 1-methyl-2-oxo-7-(2,4,6-trimethylbenzyl)-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*] pyridine-4a-carboxylate (**2r''**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. White solid. Mp = 87-89 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 6.82 (s, 2 H),

3.64 (d, *J* = 15.7 Hz, 1 H), 3.52 (d, *J* = 15.7 Hz, 1 H), 3.38 (s, 3 H), 2.54-2.40 (m, 2 H), 2.34-2.26 (m, 3 H), 2.25 (s, 3 H), 2.21 (s, 6 H), 1.83 (dd, *J* = 14.0, 8.8 Hz, 1 H), 1.70 (dt, *J* = 13.4, 8.1 Hz, 1 H), 1.53 (dd, *J* = 9.0, 3.8 Hz, 1 H), 1.43 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 174.12, 171.03, 136.62, 136.46, 135.80, 132.60, 129.08, 124.13, 81.25, 57.22, 35.27, 34.06, 31.89, 31.64, 30.76, 28.69, 28.15, 20.97, 20.26. **HRMS** calcd for $C_{24}H_{33}NO_3Na$ (M^+ + Na) 406.2353, found 406.2363.

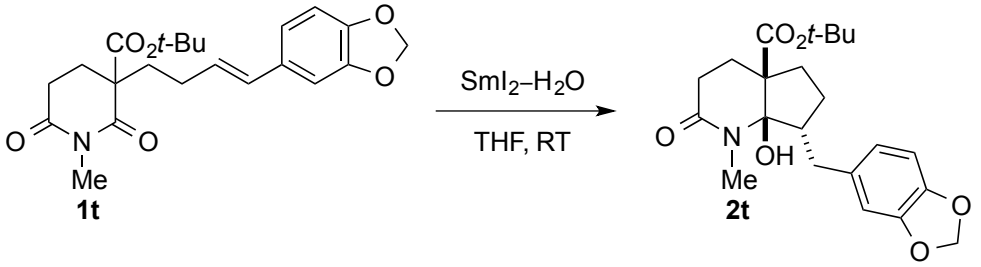
tert-Butyl (4a*R*,7*R*,7a*R*)-7-(2-fluorobenzyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2s) (Scheme 2)



According to the general procedure, the reaction of **1s** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 67% yield (12.7 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21-7.16 (m, 1 H), 7.14 (t, *J* = 6.9 Hz, 1 H), 7.06 (d, *J* = 7.3 Hz, 1 H), 7.04-6.96 (m, 1 H), 5.55 (s, 1 H), 3.05 (s, 3 H), 2.76 (d, *J* = 13.5 Hz, 1 H), 2.61–2.48 (m, 2 H), 2.41-2.21 (m, 4 H), 2.08 (d, *J* = 10.2 Hz, 2 H), 1.91-1.82 (m, 2 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 7-(2-fluorobenzyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (**2s''**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.24-7.17 (m, 2 H), 7.07 (t, *J* = 7.5 Hz, 1 H), 7.03 (t, *J* = 9.1 Hz, 1 H), 3.69 (d, *J* = 16.4 Hz, 1 H), 3.56 (d, *J* = 16.4 Hz, 1 H), 3.27 (s, 3 H), 2.58-2.47 (m, 3 H), 2.38 (ddd, *J* = 13.3, 6.7, 4.2 Hz, 1 H), 2.28 (ddd, *J* = 13.1, 8.2, 1.7 Hz, 1 H), 2.14 (dd, *J* = 15.6, 9.1 Hz, 1 H), 1.80-1.69 (m, 2 H), 1.45 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.96, 170.53, 162.20 (d, J^F = 246.0 Hz), 138.06, 130.03 (d, J^F = 4.5 Hz), 128.20 (d, J^F = 7.9 Hz), 125.95 (d, J^F = 16.0 Hz), 124.23 (d, J^F = 3.6 Hz), 120.51, 115.38 (d, J^F = 21.4 Hz), 81.43, 57.35, 34.15, 34.10, 31.44, 30.52, 28.17, 28.02, 27.99. **^{19}F NMR (470**

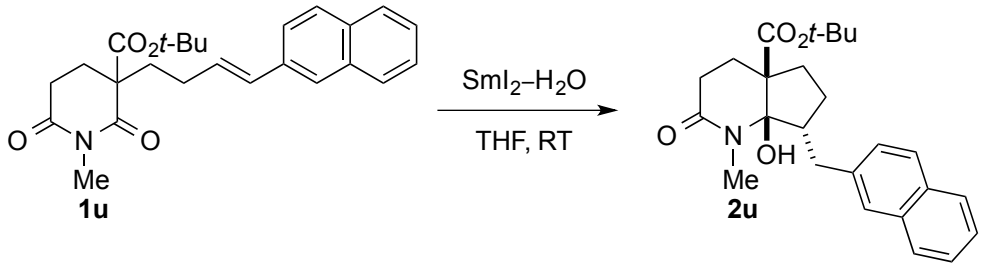
MHz, $CDCl_3$) δ -117.42. **HRMS** calcd for $C_{21}H_{26}FNO_3Na$ (M^+ + Na) 382.1789, found 382.1798.

***tert*-Butyl (4a*R*,7*R*,7a*R*)-7-(benzo[*d*][1,3]dioxol-5-ylmethyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2t) (Scheme 2)**



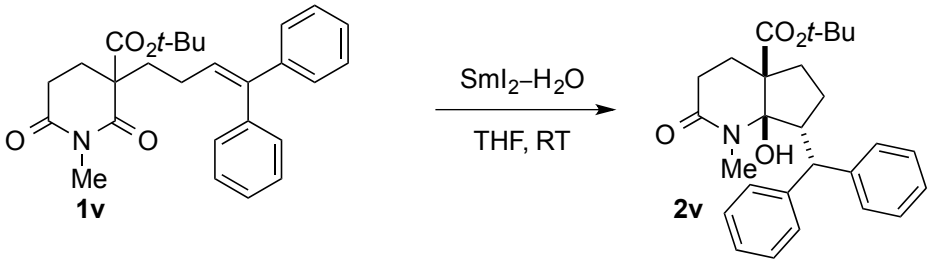
According to the general procedure, the reaction of **1t** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 70% yield (14.1 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.71 (d, *J* = 7.9 Hz, 1 H), 6.62 (s, 1 H), 6.57 (d, *J* = 8.0 Hz, 1 H), 5.91 (s, 2 H), 5.54 (s, 1 H), 3.02 (s, 3 H), 2.73 (dd, *J* = 13.7, 3.7 Hz, 1 H), 2.51 (d, *J* = 17.0 Hz, 2 H), 2.35-2.20 (m, 3 H), 2.15 (t, *J* = 13.0 Hz, 1 H), 2.08-2.00 (m, 2 H), 1.92-1.80 (m, 2 H), 1.47 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 7-(benzo[*d*][1,3]dioxol-5-ylmethyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (**2t''**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 6.74 (d, *J* = 7.9 Hz, 1 H), 6.68 (s, 1 H), 6.65 (d, *J* = 7.9 Hz, 1 H), 5.93 (s, 2 H), 3.65 (d, *J* = 15.9 Hz, 1 H), 3.43 (d, *J* = 16.0 Hz, 1 H), 3.27 (s, 3 H), 2.60-2.47 (m, 3 H), 2.38 (ddd, *J* = 13.2, 6.7, 4.2 Hz, 1 H), 2.31-2.25 (m, 1 H), 2.14 (dd, *J* = 15.6, 9.0 Hz, 1 H), 1.78-1.69 (m, 2 H), 1.46 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 174.03, 170.53, 148.05, 146.17, 137.63, 132.77, 121.94, 121.14, 108.78, 108.41, 101.08, 81.48, 57.32, 34.50, 34.27, 34.23, 34.16, 31.50, 30.54, 28.20. **HRMS** calcd for $C_{22}H_{27}NO_5Na$ (M^+ + Na) 408.1781, found 408.1791.

***tert*-Butyl (4a*R*,7*R*,7a*R*)-7a-hydroxy-1-methyl-7-(naphthalen-2-ylmethyl)-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2u) (Scheme 2)**



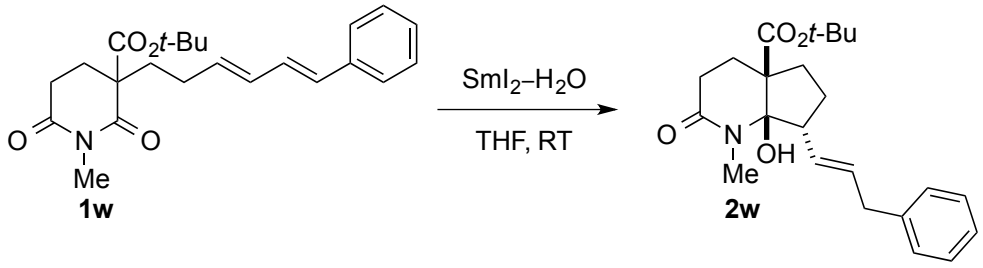
According to the general procedure, the reaction of **1u** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 71% yield (14.6 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 14.4, 8.0 Hz, 3 H), 7.57 (s, 1 H), 7.44 (dq, *J* = 14.7, 6.8 Hz, 2 H), 7.28 (d, *J* = 8.4 Hz, 1 H), 5.60 (s, 1 H), 3.10 (s, 3 H), 2.99 (d, *J* = 11.8 Hz, 1 H), 2.75-2.66 (m, 1 H), 2.59-2.53 (m, 1 H), 2.41 (t, *J* = 12.8 Hz, 1 H), 2.35 (td, *J* = 12.5, 6.1 Hz, 1 H), 2.31-2.22 (m, 2 H), 2.11 (tt, *J* = 9.5, 5.9 Hz, 2 H), 1.90-1.83 (m, 2 H), 1.48 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 1-methyl-7-(naphthalen-2-ylmethyl)-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (**2u''**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.86-7.74 (m, 3 H), 7.63 (s, 1 H), 7.46 (t, *J* = 7.3 Hz, 2 H), 7.33 (d, *J* = 8.2 Hz, 1 H), 3.88 (d, *J* = 16.0 Hz, 1 H), 3.70 (d, *J* = 15.9 Hz, 1 H), 3.33 (s, 3 H), 2.63-2.50 (m, 3 H), 2.44-2.36 (m, 1 H), 2.35-2.27 (m, 1 H), 2.18 (dd, *J* = 15.2, 9.1 Hz, 1 H), 1.84-1.70 (m, 2 H), 1.49 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.92, 170.46, 137.72, 136.49, 133.62, 132.19, 128.24, 127.68, 127.45, 126.88, 126.44, 126.19, 125.52, 121.81, 81.27, 57.23, 35.02, 34.36, 34.12, 34.06, 31.45, 30.49, 28.11. **HRMS** calcd for $C_{25}H_{29}NO_3Na$ (M^+ + Na) 414.2040, found 414.2044.

***tert*-Butyl (4a*R*,7*R*,7a*R*)-7-benzhydryl-7a-hydroxy-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2v) (Scheme 2)**



According to the general procedure, the reaction of **1v** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 98% yield (21.3 mg). Recrystallization from CH_2Cl_2/hexanes. Colorless solid. Mp = 195-196 °C. Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry of the major diastereoisomer determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.29 (d, *J* = 7.2 Hz, 3 H), 7.25-7.19 (m, 5 H), 7.12 (q, *J* = 7.2 Hz, 2 H), 5.52 (s, 1 H), 3.75 (d, *J* = 10.8 Hz, 1 H), 3.36 (q, *J* = 9.9 Hz, 1 H), 2.60 (d, *J* = 17.3 Hz, 1 H), 2.37 (dt, *J* = 18.9, 10.6 Hz, 1 H), 2.18 (q, *J* = 10.9 Hz, 1 H), 2.08-1.98 (m, 3 H), 2.03 (s, 3 H), 1.70-1.64 (m, 1 H), 1.54-1.48 (m, 1 H), 1.44 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 175.42, 168.88, 144.73, 144.36, 128.94, 128.76, 128.35, 127.95, 126.54, 126.47, 96.16, 83.12, 56.94, 55.18, 52.68, 32.45, 29.11, 28.90, 28.07, 27.42, 24.71. **HRMS** calcd for $C_{27}H_{33}NO_4Na$ (M^+ + Na) 458.2302, found 458.2312.

***tert*-Butyl (4a*R*,7*R*,7a*R*)-7a-hydroxy-1-methyl-2-oxo-7-((*E*)-3-phenylprop-1-en-1-yl)octahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2w) (Scheme 2)**

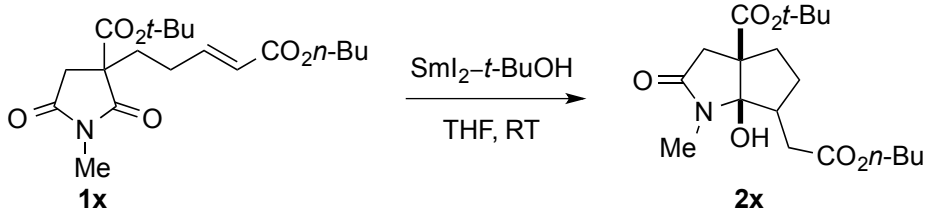


According to the general procedure, the reaction of **1w** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and H_2O (0.54 mL, 600 equiv) in THF (1.0 mL) for 1 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 94% yield (18.1 mg). Dr >95:5. Cyclization/reduction selectivity >95:5. Stereochemistry determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2 H), 7.18 (t, *J* = 7.3 Hz, 1 H), 7.11 (d, *J* = 7.2 Hz, 2 H), 5.61 (dt, *J* = 14.3, 6.7 Hz, 1 H), 5.48 (s, 1 H), 5.29 (dd, *J* = 15.1, 8.7 Hz, 1 H), 3.30 (d, *J* = 6.8 Hz, 2 H), 2.87 (s, 3 H), 2.44 (d, *J* = 17.9 Hz, 1 H), 2.32-2.23 (m, 2 H), 2.23-2.19 (m, 1 H), 2.16 (d, *J* = 5.4 Hz, 1 H), 1.98-1.93 (m, 2 H), 1.85-1.78 (m, 1 H), 1.71-1.64 (m, 1 H), 1.46 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl (*E*)-1-methyl-2-oxo-7-(3-phenylprop-1-en-1-

yl)-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (**2w''**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.30 (t, *J* = 7.4 Hz, 2 H), 7.22 (d, *J* = 7.1 Hz, 1 H), 7.19 (d, *J* = 7.5 Hz, 2 H), 6.45 (d, *J* = 15.4 Hz, 1 H), 5.74 (dt, *J* = 14.3, 6.8 Hz, 1 H), 3.48 (d, *J* = 6.9 Hz, 2 H), 3.28 (s, 3 H), 2.65-2.57 (m, 1 H), 2.53-2.43 (m, 3 H), 2.39-2.29 (m, 2 H), 1.76-1.67 (m, 2 H), 1.41 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.72, 170.45, 140.09, 137.38, 131.41, 128.78, 128.66, 126.40, 125.02, 121.34, 81.45, 57.17, 39.78, 35.86, 33.85, 31.55, 30.99, 30.39, 28.10. **HRMS** calcd for $C_{23}H_{29}NO_3Na$ (M^+ + Na) 390.2040, found 390.2050.

*Cyclization of Cyclic Imides **1x-1y** using Activated Acceptors (Equation 2).*

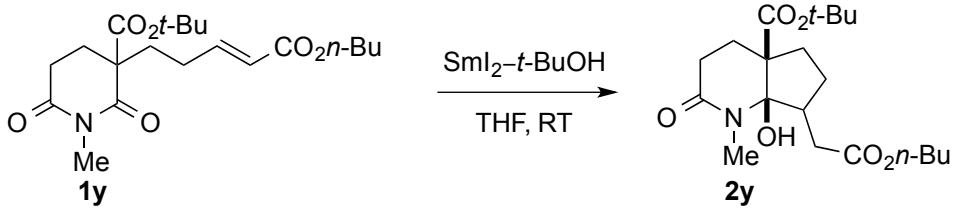
tert-Butyl (3a*R*,6a*R*)-6-(2-butoxy-2-oxoethyl)-6a-hydroxy-1-methyl-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (1x)



According to the general procedure, the reaction of **1x** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and *t*-BuOH (24 equiv) in THF (1.0 mL) for 2 h afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 91% yield (16.8 mg). Dr = 75:25 (2 diastereoisomers). Cyclization/reduction selectivity >95:5. Stereochemistry of the major diastereoisomer determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. Stereochemistry of the minor diastereoisomer not assigned. **^{1}H NMR (500 MHz, $CDCl_3$)** (Major diastereoisomer) δ 4.82 (s, 1 H), 4.11 (t, *J* = 5.5 Hz, 2 H), 3.10 (d, *J* = 17.5 Hz, 1 H), 2.82 (s, 3 H), 2.65-2.59 (m, 2 H), 2.52-2.39 (m, 2 H), 2.27 (d, *J* = 17.0 Hz, 1 H), 1.96-1.85 (m, 3 H), 1.47 (s, 9 H), 1.62 (t, *J* = 7.5 Hz, 2 H), 1.37 (q, *J* = 7.5 Hz, 2 H), 0.93 (t, *J* = 7.5 Hz, 3 H). (Minor diastereoisomer) δ 4.48 (s, 1 H), 4.12 (m, 2 H), 2.86 (s, 3 H), 2.76-2.71 (m, 2 H), 2.52-2.39 (m, 2 H), 2.34-2.31 (m, 2 H), 2.17-2.08 (m, 2 H), 1.97-1.93 (m, 1 H), 1.46 (s, 9 H), 1.62 (t, *J* = 7.5 Hz, 2 H), 1.37 (q, *J* = 7.5 Hz, 2 H), 0.93 (t, *J* = 7.5 Hz, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** (Major diastereoisomer) δ 174.18, 173.76, 172.76, 100.48, 82.60, 65.28, 57.13,

47.49, 41.73, 34.69, 34.56, 30.68, 28.77, 28.12, 27.45, 19.22, 13.77. (Minor diastereoisomer) δ 174.39, 171.12, 169.53, 89.05, 81.87, 65.35, 56.31, 49.72, 40.09, 36.03, 29.83, 28.11, 27.99, 27.88, 26.00, 19.21, 13.79. HRMS calcd for $C_{19}H_{31}NO_6Na$ (M^+ + Na) 392.2044, found 392.2054.

tert-Butyl (4a*R*,7a*R*)-7-(2-butoxy-2-oxoethyl)-7a-hydroxy-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2y)

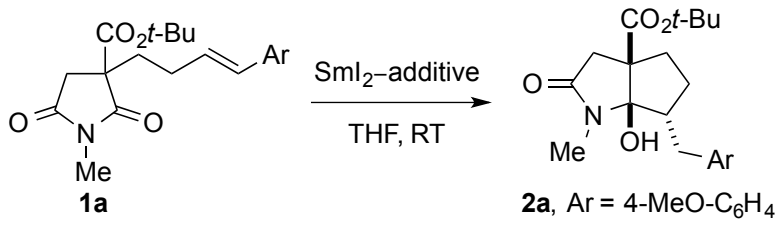


According to the general procedure, the reaction of **1y** (0.05 mmol), samarium(II) iodide (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and *t*-BuOH (24 equiv) in THF (1.0 mL) for 2 h afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 87% yield (16.7 mg). Dr = 60:40 (2 diastereoisomers). Cyclization/reduction selectivity >95:5. Stereochemistry of the major diastereoisomer determined by 2 D NMR experiments and confirmed by an X-ray analysis of a derivative. Stereochemistry of the minor diastereoisomer not assigned. The title compound has been fully characterized after dehydration to *tert*-butyl 7-(2-butoxy-2-oxoethyl)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (**2y''**). Colorless oil. ^{1}H NMR **(500 MHz, $CDCl_3$)** δ 4.10 (t, *J* = 6.6 Hz, 2 H), 3.35 (s, 1 H), 3.31 (s, 3 H), 3.18 (d, *J* = 15.7 Hz, 1 H), 2.65 (dt, *J* = 16.8, 8.6 Hz, 1 H), 2.50 (dp, *J* = 18.0, 6.5 Hz, 2 H), 2.39-2.26 (m, 2 H), 1.78-1.69 (m, 2 H), 1.64-1.58 (m, 3 H), 1.42 (s, 9 H), 1.40-1.34 (m, 2 H), 0.93 (t, *J* = 7.4 Hz, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 173.61, 170.59, 170.42, 138.97, 116.01, 81.40, 64.99, 57.10, 35.22, 34.65, 34.35, 34.15, 31.31, 30.78, 30.41, 28.08, 19.26, 13.82. $C_{20}H_{31}NO_5Na$ (M^+ + Na) 388.2094, found 388.2103.

Effect of Additives/Selected Optimization Studies[21-34]

To determine the effect of reaction conditions on the reductive cyclization of aminoketyl radicals using Sm(II), **1a** was selected as a model test substrate. (1) According to literature precedents,[21-23] five-membered cyclic substrates should be less reactive towards Sm(II) due to less efficient pseudoanomeric stabilization of the radical anion. (2) Furthermore, hemiaminal intermediates bearing α-carbonyl groups resulting from the reductive cyclization of imides are well-known to show higher stability relative to other tetrahedral intermediates,[24,25] which should facilitate determining the effect of reaction conditions on the properties of aminoketyl radicals.[26-34]

Table SI-1. *Effect of Additives on the Reductive Cyclization of 5-Membered Imides using SmI_2.*[a]



1a **2a**, Ar = 4-MeO-C_6H_4

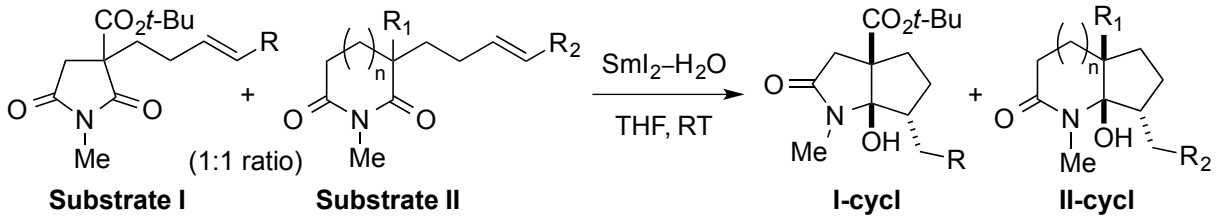
entry	SmI_2 (equiv)	additive	additive (equiv)	time[b]	conv.[c,d] (%)	yield[c] (%)	cyclization /reduction[c]
1	3	-	-	2 h	>95 (<5 SM)	-	-
2	3	MeOH	4/1 v/v	2 h	>95 (<5 SM)	87	>95:5
3	3	$HO(CH_2)_2OH$	18	2 h	>95 (<5 SM)	95	93:7
4	3	H_2O	25	2 h	>95 (<5 SM)	97	70:30
5	3	H_2O	600	15 min	>95 (<5 SM)	94	>95:5
6	3	*t*-BuOH	24	2 h	>95 (<5 SM)	78	>95:5
7	3	Et_3N-H_2O	12-18	5 min	63 (37 SM)	54	74:26
8	3	Et_3N-MeOH	12-18	1 h	>95 (<5 SM)	68	87:13
9	3	LiCl	36	2 h	>95 (<5 SM)	89	88:12
10	3	HMPA	12	2 h	>95 (<5 SM)	-	-
11	3	HMPA-*t*-BuOH	12-24	2 h	>95 (<5 SM)	-	-

[a]All reactions carried out using standard Schlenk techniques. In all entries, SmI_2 freshly prepared from Sm metal and ICH_2CH_2I was used. [b]Quenched with air after the indicated time. [c]Determined by ^1H NMR (500 MHz). [d]Conversion to desired product is shown. Conversion = (100–SM). The remaining starting material is shown in parentheses.

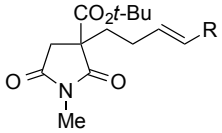
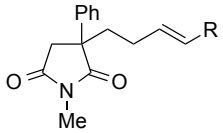
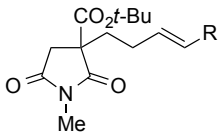
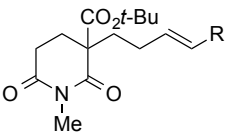
Selectivity Studies[35-38]

General Procedure. An oven-dried vial containing a stir bar was placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. A solution of two substrates (each 0.10 mmol, 1.0 equiv) in THF (2.0 mL) was added followed by H_2O (0.18 mL, 200 equiv) and samarium(II) iodide (THF solution, 0.10 mmol, 1.0 equiv, 0.10 M) with vigorous stirring, which resulted in the formation of a characteristic burgundy-red color of the $SmI_2(H_2O)_n$ complex (n > 5 with respect to SmI_2). The reaction mixture was stirred until decolorization to white had occurred. The reaction mixture was diluted with Et_2O (30 mL) and HCl (1 *N*, 30 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

Table SI-2. *Selectivity Study in the Reductive Cyclization of Cyclic Imides using SmI_2 – Directing Group and Ring Size Selectivity.*[a]

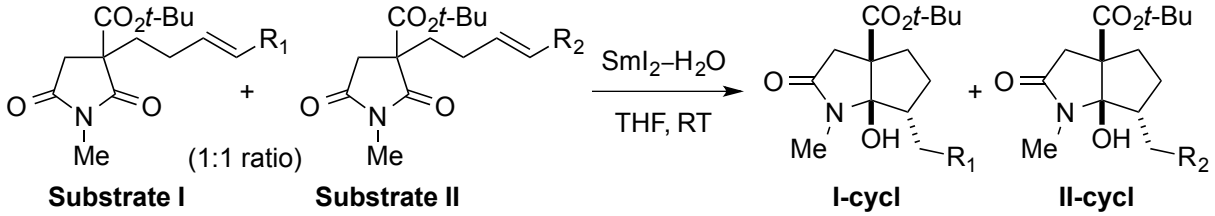


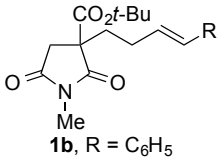
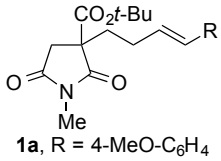
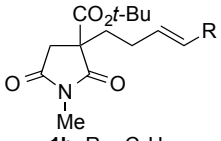
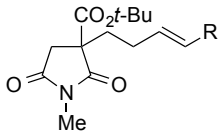
Substrate I **Substrate II** **I-cycl** **II-cycl**

Entry	**Substrate I**	**Substrate II**	conv.[b,c] (**I-cycl**, %)	conv.[b,c] (**II-cycl**, %)	k_I/k_{II}
1	 **1a**, R = 4-MeO-C_6H_4	 **1i**, R = 4-MeO-C_6H_4	21	<2	>20:1
2	 **1a**, R = 4-MeO-C_6H_4	 **1m**, R = 4-MeO-C_6H_4	<2	27	<20:1

[a]All reactions carried out using standard Schlenk techniques. In all entries, SmI_2 freshly prepared from Sm metal and ICH_2CH_2I was used. [b]Quenched with air after the indicated time. [c]Determined by ^1H NMR (500 MHz) and/or GC/MS. Conversion to desired product is shown. Conversion = (100–SM). Conditions: SmI_2 (1 equiv), H_2O (200 equiv), THF, room temperature, 10 s to 1 min.

Table SI-3. *Selectivity Study in the Reductive Cyclization of Cyclic Imides using SmI_2 – Electronic Effects of the Radical Acceptor.*[a]



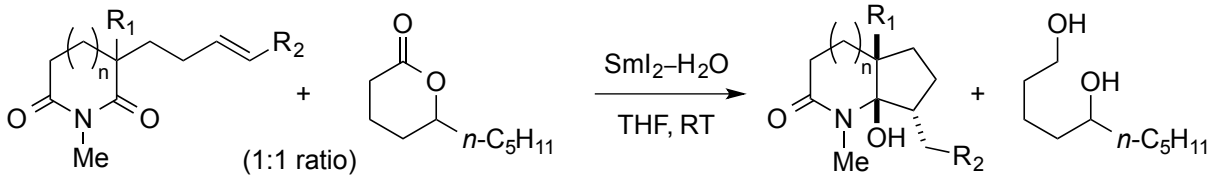
Entry	**Substrate I**	**Substrate II**	conv.[b,c] (**I-cycl**, %)	conv.[b,c] (**II-cycl**, %)	k_I/k_{II}
1	 **1b**, R = C_6H_5	 **1a**, R = 4-MeO-C_6H_4	29	16	64:36
2	 **1b**, R = C_6H_5	 **1c**, R = 4-CF_3-C_6H_4	6	18	25:75

[a]All reactions carried out using standard Schlenk techniques. In all entries, SmI_2 freshly prepared from Sm metal and ICH_2CH_2I was used. [b]Quenched with air after the indicated time. [c]Determined by ^1H NMR (500 MHz) and/or GC/MS. Conversion to desired product is shown. Conversion = (100–SM). Conditions: SmI_2 (1 equiv), H_2O (200 equiv), THF, room temperature, 10 s to 1 min.

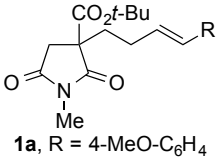
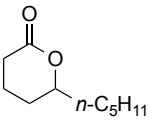
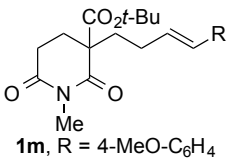
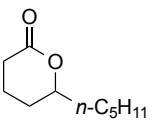
Additional Selectivity Studies

General Procedure. An oven-dried vial containing a stir bar was placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. A solution of two substrates (each 0.10 mmol, 1.0 equiv) in THF (2.0 mL) was added followed by H_2O (0.18 mL, 200 equiv) and samarium(II) iodide (THF solution, 0.10 mmol, 1.0 equiv, 0.10 M) with vigorous stirring, which resulted in the formation of a characteristic burgundy-red color of the $SmI_2(H_2O)_n$ complex (n > 5 with respect to SmI_2). The reaction mixture was stirred until decolorization to white had occurred. The reaction mixture was diluted with Et_2O (30 mL) and HCl (1 *N*, 30 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

Table SI-4. *Selectivity Study in the Reductive Cyclization/Reduction of Cyclic Imides and Cyclic Esters using SmI_2–H_2O.*[a]



Substrate I **Substrate II** **I-cycl** **II-red**

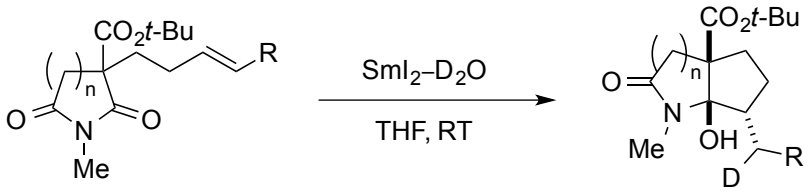
entry	**Substrate I**	**Substrate II**	conv.[b,c] (**I-cycl**, %)	conv.[b,c] (**II-red**, %)	k_I/k_{II}
1	 **1a**, R = 4-MeO-C_6H_4		40	<2	>20:1
2	 **1m**, R = 4-MeO-C_6H_4		33	<2	>20:1

[a]All reactions carried out using standard Schlenk techniques. In all entries, SmI_2 freshly prepared from Sm metal and ICH_2CH_2I was used. [b]Quenched with air after the indicated time. [c]Determined by ^1H NMR (500 MHz) and/or GC/MS. Conversion to desired product is shown. Conversion = (100–SM).

Deuterium Incorporation Studies[41]

General Procedure. According to the general procedure, a cyclic imide (0.05 mmol) was reacted with samarium(II) iodide (3-8 equiv), and D_2O (600-1200 equiv) in THF (2.0 mL) for the indicated time at room temperature. After the standard work-up as described above, the reaction mixture was diluted with Et_2O (30 mL) and HCl (1 *N*, 30 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and ESI-MS to obtain deuterium incorporation. The obtained results are consistent with anions being generated and protonated by H_2O in a series of electron transfer steps and with the formation of a well-defined Sm(II) complex. Characterization data for all new compounds are given in the section below.

Table SI-5. *Determination of D^1 Incorporation in the Reductive Cyclization of 5- and 6-Membered Cyclic Imides using SmI_2–D_2O.*[a]



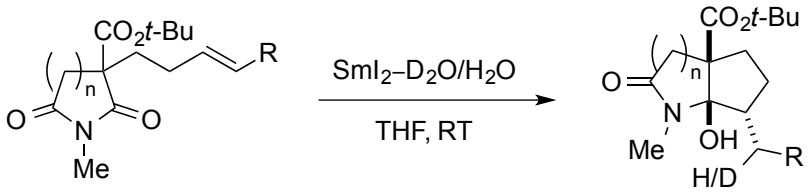
entry	n	R	SmI_2 (equiv)	H_2O (equiv)	time[b]	conv.[c] (%)	yield[c] (%)	D^1 [c] (%)
1	1	H	8	1200	2 h	>98	76	>98
2	1	4-MeO-C_6H_4	3	600	15 min	>98	84	>98
3	2	4-MeO-C_6H_4	3	600	1 min	>98	81	>98

[a]All reactions carried out using standard Schlenk techniques. In all entries, SmI_2 freshly prepared from Sm metal and ICH_2CH_2I was used. [b]Quenched with air after the indicated time. [c]Determined by ^1H NMR (500 MHz) and ESI-MS. Conversion to desired product is shown. Conversion = (100–SM).

Kinetic Isotope Effect[34,41-45]

General Procedure. According to the general procedure, a cyclic imide (0.05 mmol) was reacted with samarium(II) iodide (3-8 equiv), and H_2O/D_2O (1:1, 600-1200 equiv) in THF (2.0 mL) for the indicated time at room temperature. After the standard work-up as described above, the reaction mixture was diluted with Et_2O (30 mL) and HCl (1 *N*, 30 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and ESI-MS to obtain deuterium incorporation. The obtained results are consistent with proton transfer not being involved in the rate determining step. The effect of deuterium likely results from a secondary kinetic isotope effect due to differential coordination of D_2O/H_2O to Sm(II).

Table SI-6. *Determination of Kinetic Isotope Effect in the Reductive Cyclization of 5- or 6-Membered Imides using SmI_2–D_2O.*[a]



entry	n	R	SmI_2 (equiv)	H_2O (equiv)	time[a]	conv.[b] (%)	yield[b] (%)	k_H/k_D
1	1	4-MeO-C_6H_4	3	600	15 min	>98	83	1.49±0.1
2	2	4-MeO-C_6H_4	3	600	1 min	>98	85	1.54±0.1
3	1	H	8	1200	2 h	>98	76	1.10±0.1

[a]All reactions carried out using standard Schlenk techniques. In all entries, SmI_2 freshly prepared from Sm metal and ICH_2CH_2I was used. [b]Quenched with air after the indicated time. [c]Determined by ^{1}H NMR (500 MHz) and ESI-MS. Conversion to desired product is shown. Conversion = (100–SM).

Characterization Data for Deuterium Incorporation/Detailed Procedures for KIE Study

***tert*-Butyl (3a*R*,6*R*,6a*R*)-6a-hydroxy-6-((4-methoxyphenyl)methyl-*d*)-1-methyl-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2a-*D*^{1}).** According to the general procedure, the reaction of **1a** (0.1 mmol), samarium(II) iodide (0.30 mmol, 3 equiv, 3.0 mL, 0.10 M) and D_2O (1.08 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 83% yield. Recrystallization from CH_2Cl_2/hexanes. White solid. D^1 incorporation >98%. Dr >95:5. Cyclization/reduction selectivity >95:5. Dr = 50:50 (benzylic position). **^{1}H NMR (500 MHz, $CDCl_3$)** δ (mixture of D^1 diastereoisomers) 7.07 (d, *J* = 8.2 Hz, 2 H), 6.82 (d, *J* = 8.2 Hz, 2 H), 4.08 (s, 1 H), 3.78 (s, 3 H), 3.07 (s, 1 H), 2.96 (s, 3 H), 2.95 (d, *J* = 17.5 Hz, 1 H), 2.37 (d, *J* = 17.9 Hz, 1 H), 2.30 (dd, *J* = 11.0, 5.2 Hz, 1 H), 2.17 (dd, *J* = 12.5, 6.4 Hz, 1 H), 1.74-1.58 (m, 3 H), 1.48 (s, 9 H), 1.24 (dt, *J* = 12.4, 6.3 Hz, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 174.08, 173.21, 158.18, 132.40, 129.70, 114.01, 100.28, 83.12, 56.86, 55.39, 54.11, 42.43, 34.13, 28.12, 27.56, 27.88, 27.55. **HRMS** calcd for $C_{21}H_{28}DNO_5Na$ (M^+ + Na) 399.2001, found 399.2008. Kinetic isotope effect was determined by reacting **1a** (0.05 mmol), SmI_2 (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and D_2O/H_2O (1:1, 0.54 mL, 600 equiv) for 15 min, followed by standard work-up to give the title compound with 40.1% D^1 incorporation as determined by ^{1}H NMR (500 MHz) and ESI-MS analysis (k_H/k_D = 1.49±0.1).

***tert*-Butyl (4a*R*,7*R*,7a*R*)-7a-hydroxy-7-((4-methoxyphenyl)methyl-*d*)-1-methyl-2-oxooctahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (2m-*D*^{1}).** According to the general procedure, the reaction of **1m** (0.1 mmol), samarium(II) iodide (0.30 mmol, 3.0 equiv, 3.0 mL, 0.10 M) and D_2O (1.08 mL, 600 equiv) in THF (1.0 mL) for 15 min afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 85% yield. D^1 incorporation >98%. Dr >95:5. Cyclization/reduction selectivity >95:5. Dr = 50:50 (benzylic position). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (d, *J* = 8.0 Hz, 2 H), 6.81 (d, *J* = 8.2 Hz, 2 H), 5.54 (s, 1 H), 3.77 (s, 3 H), 3.02 (s, 3 H), 2.73 (s, 0.5 H), 2.51 (d, *J* = 16.8 Hz, 2 H), 2.34 (d, *J* = 9.4 Hz, 0.5 H), 2.28-2.14 (m, 2 H), 2.05 (d, *J* = 7.4 Hz, 2 H), 1.92-1.81 (m, 3 H), 1.46 (s, 9 H). The title compound has been fully characterized after dehydration to *tert*-butyl 7-((4-methoxyphenyl)methyl-*d*)-1-methyl-2-oxo-1,2,3,4,5,6-hexahydro-4a*H*-cyclopenta[*b*]pyridine-4a-carboxylate (**2m''-*D*^{1}**) using TsOH (1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h. Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.11 (d, *J* = 8.1 Hz, 2 H), 6.84 (d, *J* = 8.1 Hz, 2 H), 3.79 (s, 3 H), 3.63 (s, 0.5 H), 3.43

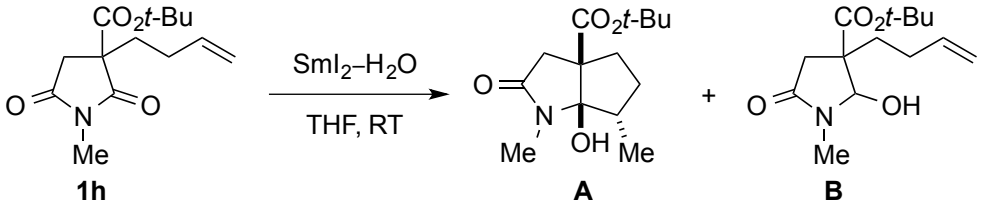
(s, 0.5 H), 3.27 (s, 3 H), 2.52 (pd, *J* = 10.1, 3.2 Hz, 3 H), 2.43-2.33 (m, 1 H), 2.27 (dd, *J* = 12.5, 8.6 Hz, 1 H), 2.13 (dd, *J* = 15.1, 9.1 Hz, 1 H), 1.73 (dq, *J* = 16.9, 9.4 Hz, 2 H), 1.46 (s, 9 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 174.08, 170.55, 158.25, 137.36, 130.91, 129.29, 122.33, 114.10, 81.36, 57.30, 55.43, 34.31, 34.23, 34.15, 34.11, 31.52, 30.56, 28.18. **HRMS** calcd for $C_{22}H_{28}DNO_4Na$ (M^+ + Na) 395.2052, found 395.2062. Kinetic isotope effect was determined by reacting **1m** (0.05 mmol), SmI_2 (0.15 mmol, 3.0 equiv, 1.5 mL, 0.10 M) and D_2O/H_2O (1:1, 0.54 mL, 600 equiv) for 1 min, followed by standard work-up to give the title compound with 39.1% D^1 incorporation as determined by ^{1}H NMR (500 MHz) and ESI-MS (k_H/k_D = 1.54±0.1).

***tert*-Butyl (3a*R*,6*S*,6a*R*)-6a-hydroxy-1-methyl-6-(methyl-*d*)-2-oxohexahydrocyclopenta[*b*]pyrrole-3a(1*H*)-carboxylate (2h-D^1).** According to the general procedure, the reaction of **1h** (0.1 mmol), samarium(II) iodide (0.80 mmol, 8 equiv, 8.0 mL, 0.10 M) and D_2O (2.16 mL, 1200 equiv) in THF (1.0 mL) for 1 h afforded after work-up with Et_2O/HCl (1.0 *N*) the title compound in 76% yield. Recrystallization from CH_2Cl_2/hexanes. White solid. D^1 incorporation >98%. Dr >95:5. Cyclization/reduction selectivity = 91:9. **^{1}H-NMR (500 MHz, $CDCl_3$)** δ 3.85 (s, 1 H), 2.92 (d, *J* = 17.7 Hz, 1 H), 2.88 (s, 3 H), 2.37-2.27 (m, 2 H), 2.20 (dq, *J* = 12.9, 6.4 Hz, 1 H), 1.83 (dtd, *J* = 12.1, 6.1, 2.3 Hz, 1 H), 1.74-1.69 (m, 1 H), 1.48 (s, 9 H), 1.30-1.26 (m, 1 H), 1.03 (d, *J* = 6.7 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 174.05, 173.01, 100.89, 83.02, 56.87, 46.22, 42.58, 34.26, 30.61, 28.13, 27.61, 14.29 (t, *J* = 19.5 Hz). **HRMS** calcd for $C_{14}H_{22}DNO_4Na$ (M^+ + Na) 293.1582, found 293.1592. Kinetic isotope effect was determined by reacting **1h** (0.05 mmol), SmI_2 (0.4 mmol, 8.0 equiv, 4.0 mL, 0.10 M) and D_2O/H_2O (1:1, 1.08 mL, 1200 equiv) for 2, followed by standard work-up to give the title compound with 47.6% D^1 incorporation as determined by ^{1}H NMR (500 MHz) and ESI-MS analysis (k_H/k_D = 1.10±0.1).

Control Experiments[46-55]

General Procedure. According to the general procedure, a cyclic imide (0.05 mmol) was reacted with samarium(II) iodide (8 equiv), and H_2O (1200 equiv) in THF for 2 h at room temperature. After the standard work-up, the reaction mixture was diluted with Et_2O (30 mL) and HCl (1 *N*, 30 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

Table SI-7. *Effect of Concentration of SmI_2 on the Rate of the Reduction of Aminoketyl Radicals Derived from Cyclic Imides.*[a]



entry	H_2O (equiv)	time[b] (h)	conv.[c] (%)	**A**:**B**[c]	[SmI_2]	[H_2O]	rate[d] (10^7 x $M^{-1}s^{-1}$)
1	1200	2	>98	75:25	0.072	5.38	0.1065
2	1200	2	>98	76:24	0.066	4.93	0.1101
3	1200	2	>98	75:25	0.056	4.24	0.1369
4	1200	2	>98	64:36	0.040	2.98	0.3234

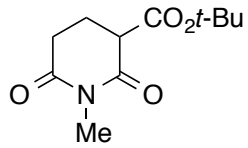
[a]All reactions carried out using standard Schlenk techniques. In all entries, SmI_2 freshly prepared from Sm metal and ICH_2CH_2I was used. [b]Quenched with air after the indicated time. [c]Determined by ^1H NMR (500 MHz) and/or GC/MS. Conversion to desired product is shown. Conversion = (100–SM). [d]Approximation calculated using the rate constant for cyclization of the 5-hexenyl radical: k_{SmI2} = (red/cycl) x $k_{5\text{-exo}}$ x $[SmI_2]^{-1}$; ($k_{5\text{-exo}}$ = ca. 2.3 x 10^5 s^{-1} at 25 °C).[46,47]

References

1. B. M. Trost and I. Fleming, *Comprehensive Organic Synthesis*, Pergamon Press: 1991.
2. M. K. Hargreaves, J. G. Pritchard and H. R. Dave, *Chem. Rev.* **1970**, *70*, 439.
3. A. M. Crider, T. M. Kolczynski and K. M. Yates, *J. Med. Chem.* **1980**, *23*, 324.
4. N. B. Mehta, A. P. Phillips, F. F. Lui and R. E. Brooks, *J. Org. Chem.* **1960**, *25*, 1012.
5. C. J. Perry and Z. Parveen, *J. Chem. Soc., Perkin Trans. 2* **2001**, 512.
6. S. K. Upadhyay, S. R. K. Pingali and B. S. Jursic, *Tetrahedron Lett.* **2010**, *51*, 2215.
7. P. Y. Reddy, S. Kondo, T. Toru and Y. Ueno, *J. Org. Chem.* **1997**, *62*, 2652.
8. S. Chandrasekhar, M. Takhi and G. Uma, *Tetrahedron Lett.* **1997,** *38,* 8089.
9. J. Fraga-Dubreuil, G. Comak, A. W. Taylor and M. Poliakoff, *Green Chem.* **2007**, *9*, 1072.
10. P. Girard, J. L. Namy and H. B. Kagan, *J. Am. Chem. Soc.* **1980**, *102*, 2693.
11. T. Imamoto and M. Ono, *Chem. Lett.* **1987**, 501.
12. A. Dáhlen and G. Hilmersson, *Eur. J. Inorg. Chem.* **2004**, 3020.
13. J. A. Teprovich, Jr., P. K. S. Antharjanam, E. Prasad, E. N. Pesciotta and R. A. Flowers, II, *Eur. J. Inorg. Chem.* **2008**, 5015.
14. M. Szostak, M. Spain and D. J. Procter, *J. Org. Chem.* **2012**, *77*, 3049.
15. T. A. Moss, D. M. Barber, A. F. Kyle and D. J. Dixon, *Chem. Eur. J.* **2013**, *19*, 3071.
16. T. Mashiko, N. Kumagai and M. Shibasaki, *J. Am. Chem. Soc.* **2009**, *131*, 14990.
17. Y. Nakao, J. Chen, H. Imanaka, T. Hiyama, Y. Ichikawa, W. L. Duan, R. Shintani and T. Hayashi, *J. Am. Chem. Soc.* **2007**, *129*, 9137.
18. K. T. Wong and Y. Y. Hung, *Tetrahedron Lett.* **2003**, *44*, 8033.
19. Y. Lei, A. D. Wrobleski, J. E. Golden, D. R. Powell and J. Aubé, *J. Am. Chem. Soc.* **2005**, *127*, 4552.
20. C. M. Smith and G. A. O'Doherty, *Org. Lett.* **2003**, *5*, 1959.
21. L. A. Duffy, H. Matsubara and D. J. Procter, *J. Am. Chem. Soc.* **2008**, *130*, 1136.
22. M. Szostak, M. Spain, K. A. Choquette, R. A. Flowers, II and D. J. Procter, *J. Am. Chem. Soc.* **2013**, *135*, 15702.
23. M. Szostak, B. Sautier, M. Spain, M. Behlendorf and D. J. Procter, *Angew. Chem. Int. Ed.* **2013**, *52*, 12550.

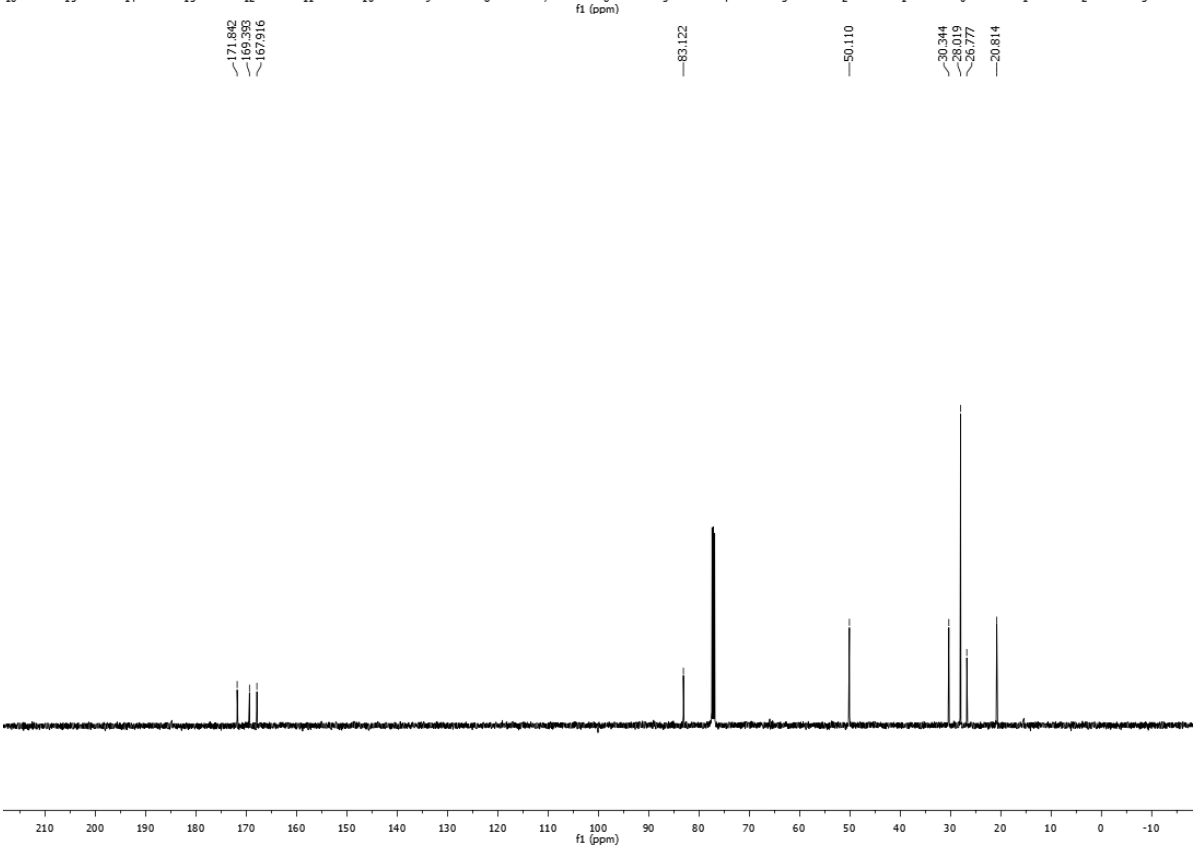
24. M. Adler, S. Adler and G. Boche, *J. Phys. Org. Chem.* **2005**, *18*, 193.
25. P. Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press: 1983.
26. M. Amiel-Levy and S. Hoz, *J. Am. Chem. Soc.* **2009**, *131*, 8280.
27. M. Szostak, M. Spain, D. Parmar and D. J. Procter, *Chem. Commun.* **2012**, *48*, 330.
28. R. A. Flowers, II, *Synlett* **2008**, 1427.
29. A. Dáhlen and G. Hilmersson, *J. Am. Chem. Soc.* **2005**, *127*, 8340.
30. R. S. Miller, J. M. Sealy, M. Shabangi, M. L. Kuhlman, J. R. Fuchs and R. A. Flowers, II, *J. Am. Chem. Soc.* **2000**, *122*, 7718.
31. E. Prasad and R. A. Flowers, II, *J. Am. Chem. Soc.* **2002**, *124*, 6895.
32. E. Hasegawa and D. P. Curran, *J. Org. Chem.* **1993**, *58*, 5008.
33. E. Prasad and R. A. Flowers, II, *J. Am. Chem. Soc.* **2005**, *127*, 18093.
34. M. Szostak, M. Spain and D. J. Procter, *J. Am. Chem. Soc.* **2014**, *136*, 8459.
35. A. Dáhlen and G. Hilmersson, *Eur. J. Inorg. Chem.* **2004**, 3393.
36. D. P. Curran, T. L. Fevig, C. P. Jasperse and M. J. Totleben, *Synlett* **1992**, 943.
37. C. Chatgilialoglu and A. Studer, *Encyclopedia of Radicals in Chemistry, Biology and Materials*, Wiley-Blackwell: 2012.
38. H. H. Jaffé, *Chem. Rev.* **1953**, *53*, 191.
39. T. Ankner and G. Hilmersson, *Tetrahedron* **2009**, *65*, 10856.
40. M. Szostak, M. Spain and D. J. Procter, *Chem. Soc. Rev.* **2013**, *42*, 9155.
41. D. Parmar, L. A. Duffy, D. V. Sadasivam, H. Matsubara, P. A. Bradley, R. A. Flowers, II and D. J. Procter, *J. Am. Chem. Soc.* **2009**, *131*, 15467.
42. A. Dáhlen and G. Hilmersson, *Tetrahedron Lett.* **2001**, *42*, 5565.
43. A. Dáhlen and G. Hilmersson, *Chem. Eur. J.* **2003**, *9*, 1123.
44. M. Szostak, M. Spain and D. J. Procter, *Chem. Commun.* **2011**, *47*, 10254.
45. E. M. Simmons and J. F. Hartwig, *Angew. Chem. Int. Ed.* **2012**, *51*, 3066.
46. M. Newcomb, *Tetrahedron* **1993**, *49*, 1151.
47. E. Hasegawa and D. P. Curran, *Tetrahedron Lett.* **1993**, *34*, 1717.
48. J. P. Stevenson, W. F. Jackson and J. M. Tanko, *J. Am. Chem. Soc.* **2002**, *124*, 4271.
49. J. M. Tanko, J. G. Gillmre, R. Friedline and M. Chahma, *J. Org. Chem.* **2005**, *70*, 4170.

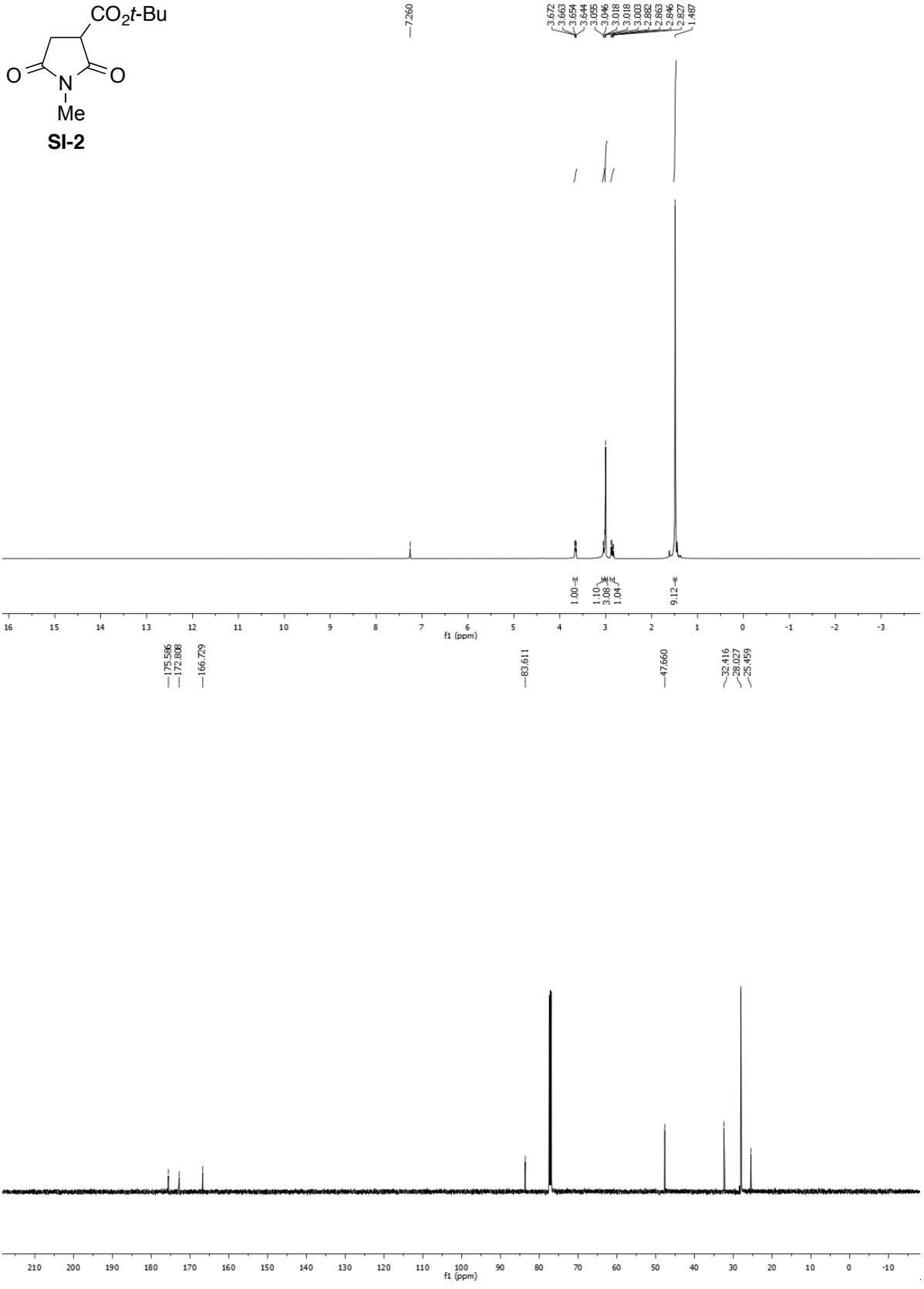
50. J. M. Tanko, X. Li, M. Chahma, W. F. Jackson and J. N. Spencer, J. *Am. Chem. Soc.* **2007**, *129*, 4181.
51. M. Szostak, N. J. Fazakerley, D. Parmar and D. J. Procter, *Chem. Rev.* **2014**, *114*, 5959.
52. B. Giese, *Angew. Chem. Int. Ed.* **1983**, *22*, 753.
53. D. P. Curran, N. A. Porter and B. Giese, *Stereochemistry of Radical Reactions*, Wiley: 1996.
54. R. W. Fessenden and R. H. Schuler, *J. Chem. Phys.* **1963**, *39*, 2147.
55. C. Leroy, D. Peeters and C. Wilante, *THEOCHEM* **1982**, *5*, 217.

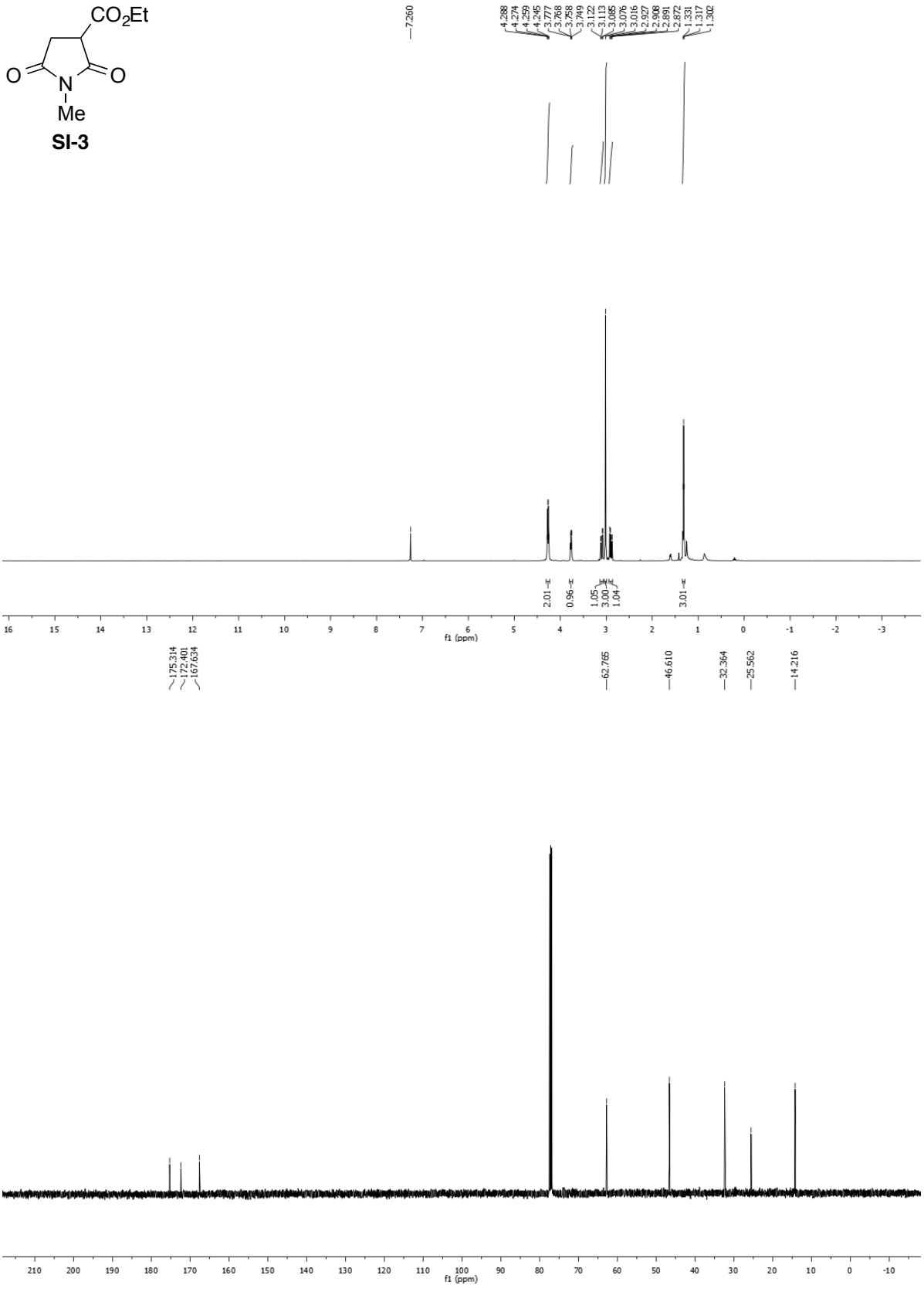

CO2t-Bu
O
N
O
Me

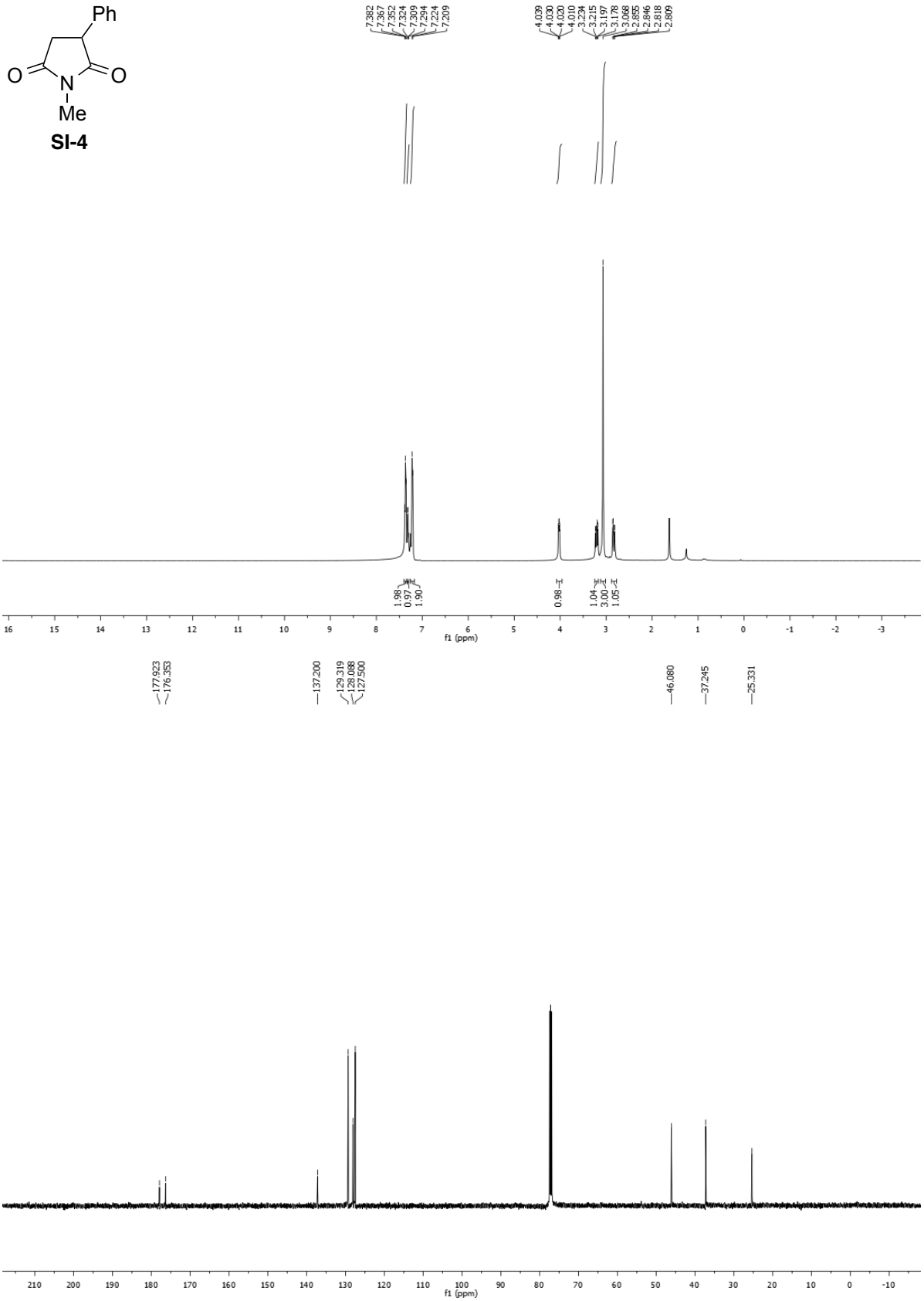
SI-1

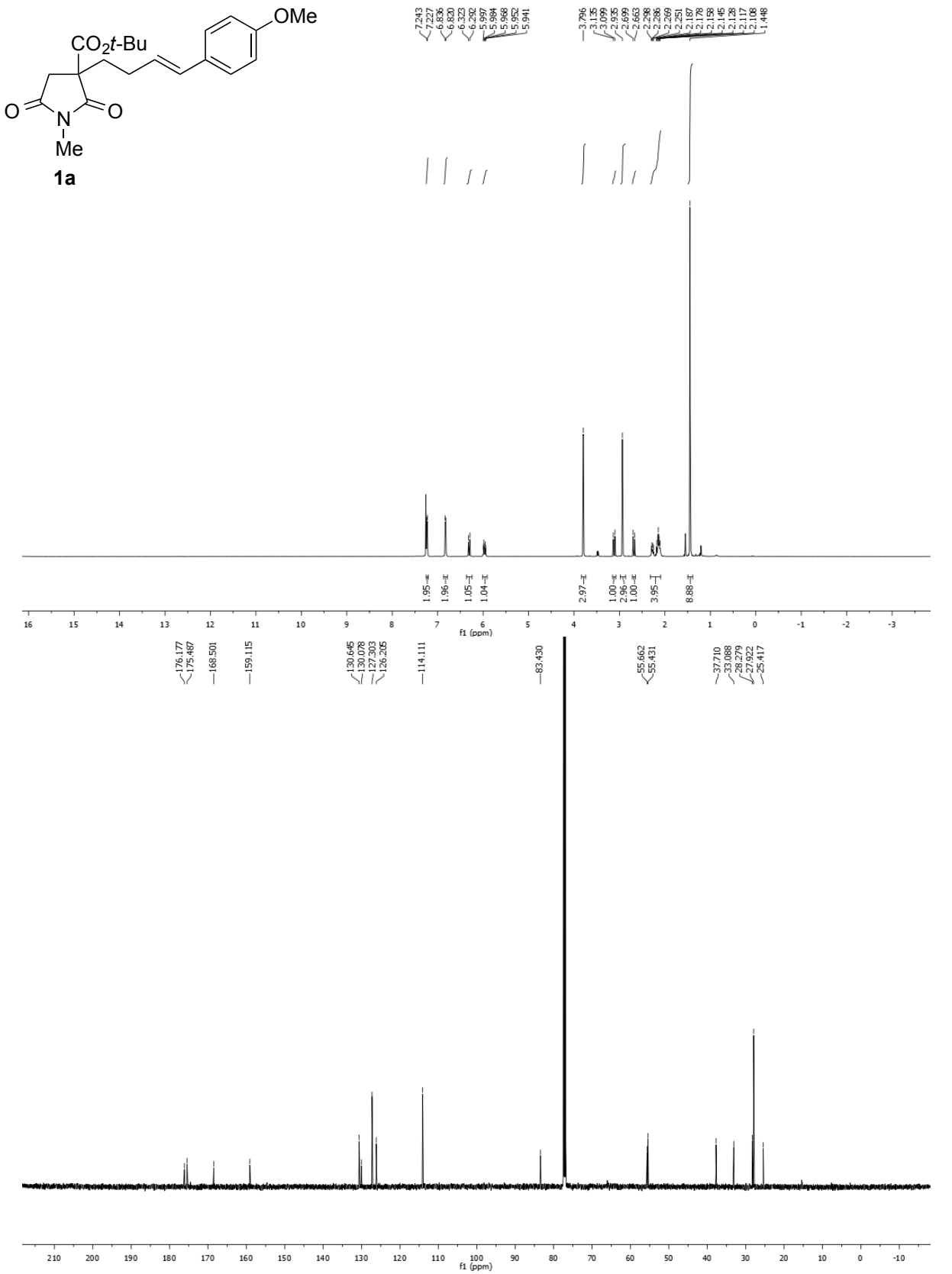
3.546
3.535
3.521
3.159
2.767
2.757
2.749
2.739
2.732
2.721
2.714
2.703
2.668
2.656
2.652
2.642
2.635
2.632
2.621
2.617
2.607
2.280
2.269
2.265
2.253
2.239
2.227
2.223
2.213
2.199
2.148
2.139
2.130
2.120
2.111
2.102
2.092
1.473
0.97
3.00
1.03
1.18
1.04
1.03
9.10
f1 (ppm)

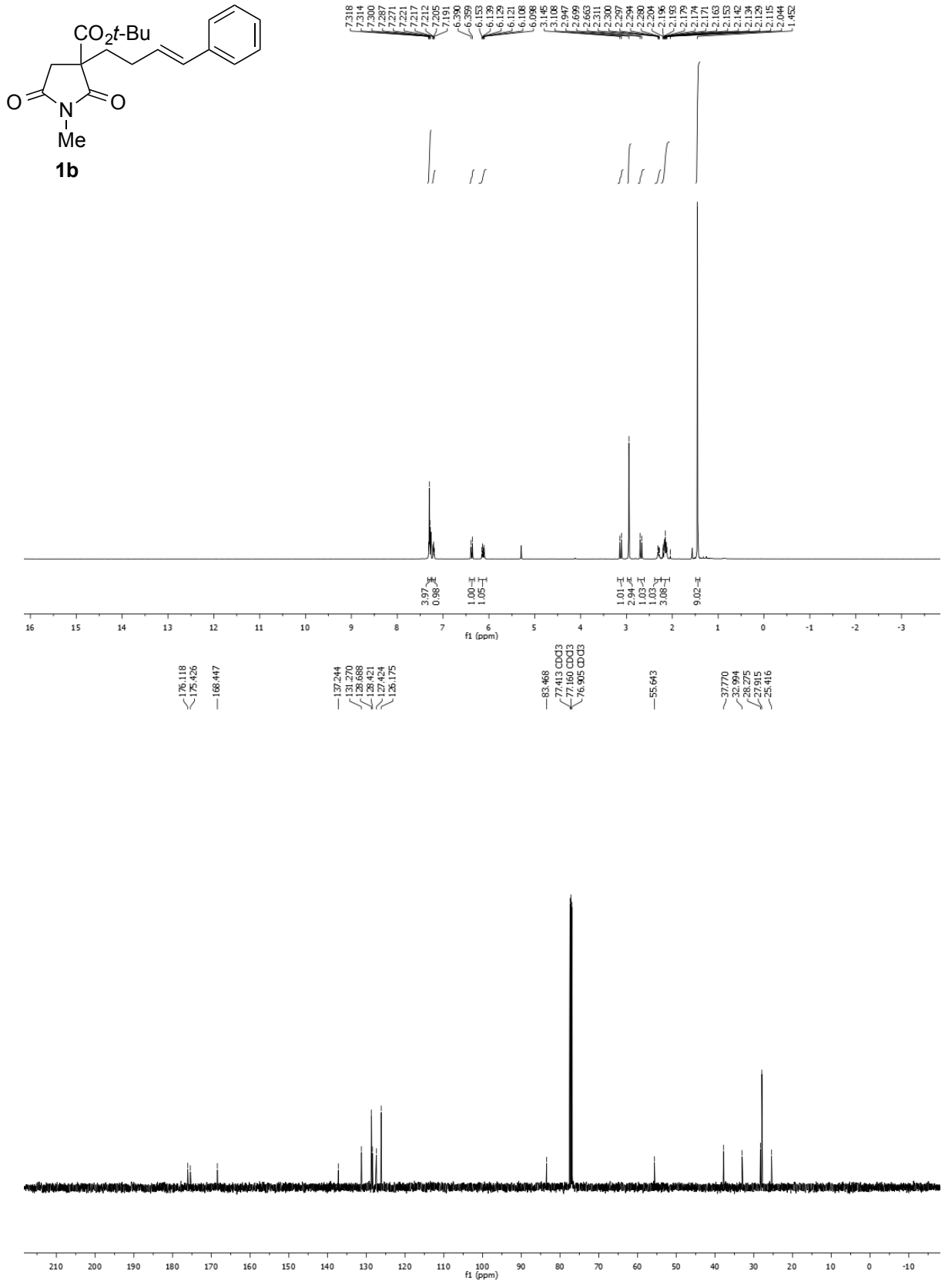

171.842
169.393
167.916
83.122
50.110
30.344
28.019
26.777
20.814
f1 (ppm)

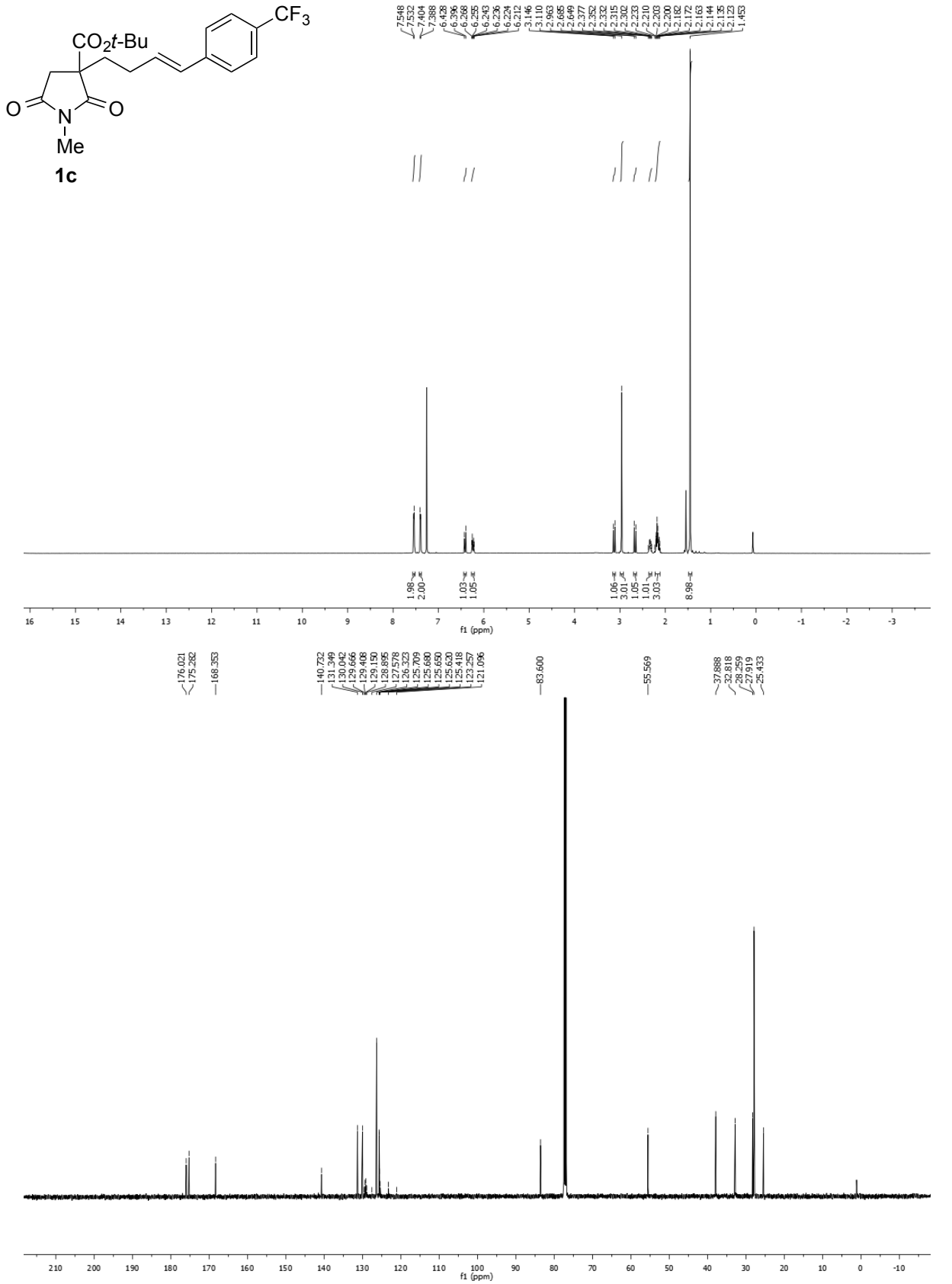

CO2t-Bu
O
N
O
Me
SI-2
7.260
3.672
3.663
3.654
3.644
3.055
3.046
3.018
3.018
3.003
2.882
2.863
2.846
2.827
1.487
1.00
1.10
3.08
1.04
9.12
f1 (ppm)
175.586
172.808
166.729
83.611
47.660
32.416
28.027
25.459

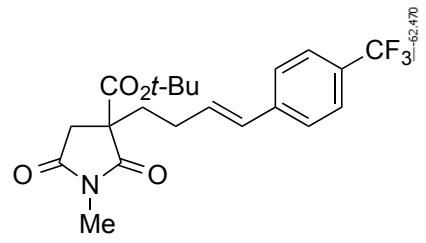

CO2Et
O
N
O
Me
SI-3
7.260
4.288
4.274
4.259
4.245
3.777
3.768
3.758
3.749
3.122
3.113
3.085
3.076
3.016
2.927
2.908
2.891
2.872
1.331
1.317
1.302
2.01
0.96
1.05
3.00
1.04
3.01
f1 (ppm)
175.314
172.401
167.634
62.765
46.610
32.364
25.562
14.216
f1 (ppm)


Ph
O
N
O
Me
SI-4
7.382
7.367
7.352
7.324
7.309
7.294
7.224
7.209
4.039
4.030
4.020
4.010
3.234
3.215
3.197
3.178
3.068
2.855
2.846
2.818
2.809
1.98
0.97
1.90
0.98
1.04
3.00
1.05
f1 (ppm)
177.923
176.353
137.200
129.319
128.988
127.500
46.080
37.245
25.331
f1 (ppm)

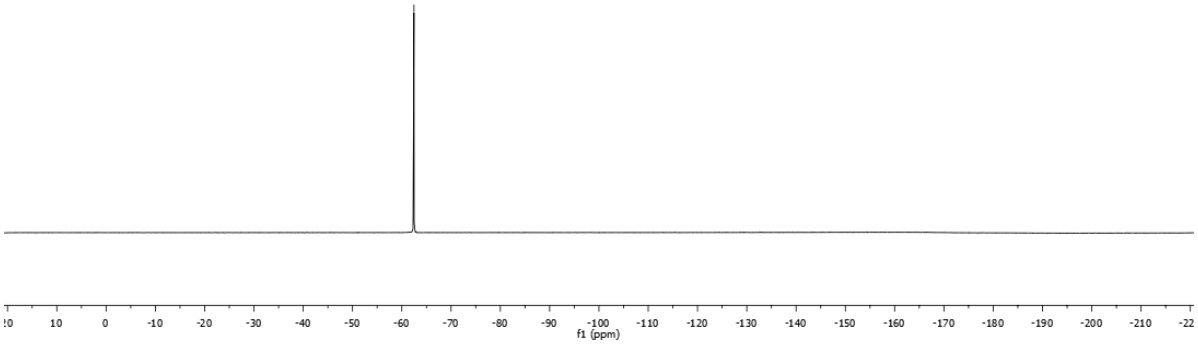

OMe
CO2t-Bu
O
N
O
Me
1a
7.243
7.227
6.836
6.830
6.323
6.292
5.997
5.984
5.968
5.952
5.941
3.796
3.135
3.099
2.935
2.699
2.663
2.298
2.286
2.269
2.251
2.187
2.178
2.158
2.145
2.128
2.117
2.108
1.448
1.95
1.96
1.05
1.04
2.97
1.00
2.96
1.00
3.95
8.88
f1 (ppm)
176.177
175.487
168.501
159.115
130.645
130.078
127.303
126.205
114.111
83.430
55.662
55.431
37.710
33.088
28.279
27.922
25.417
f1 (ppm)

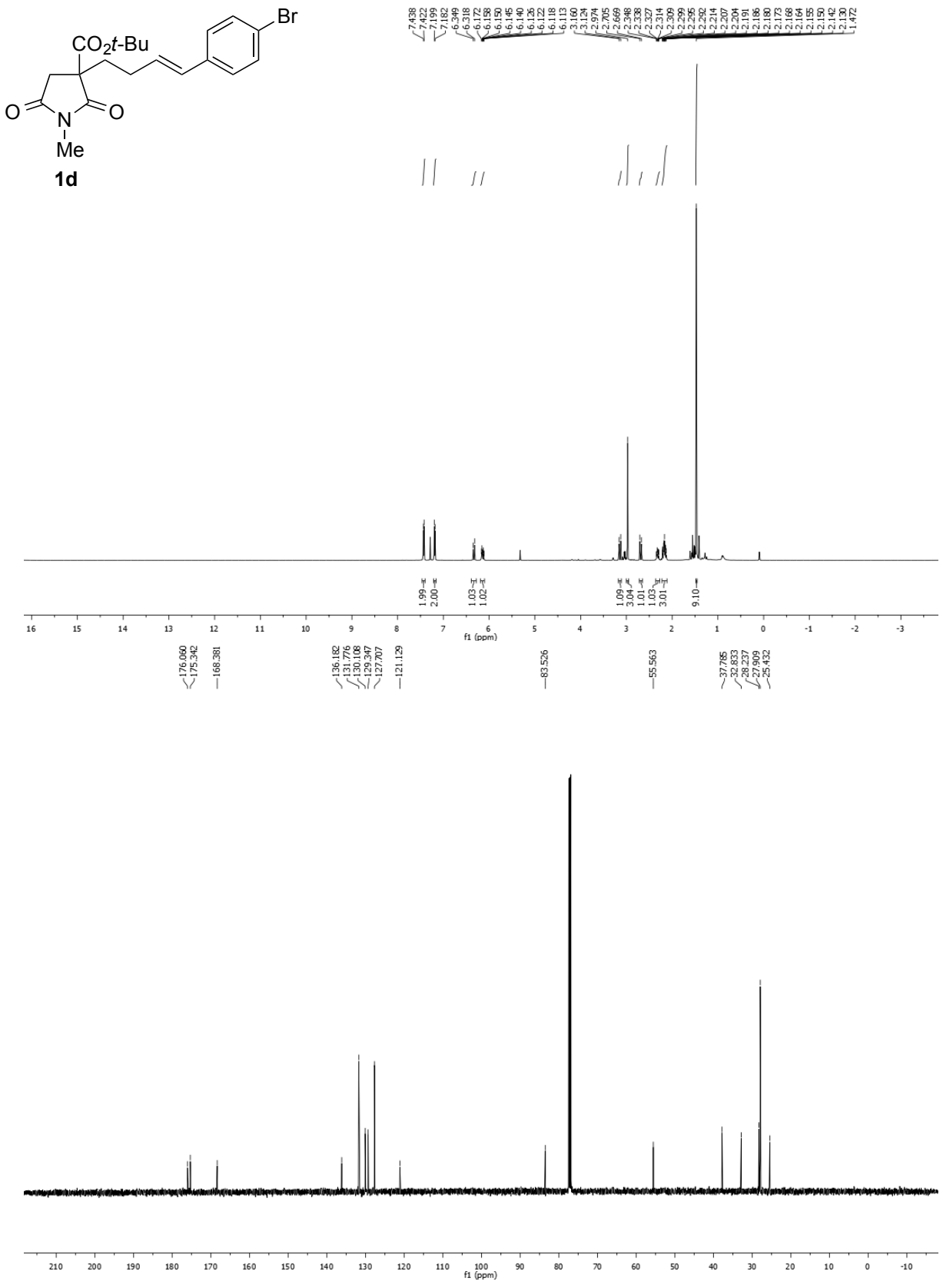

CO2t-Bu
O
N
O
Me
1b
f1 (ppm)
f1 (ppm)

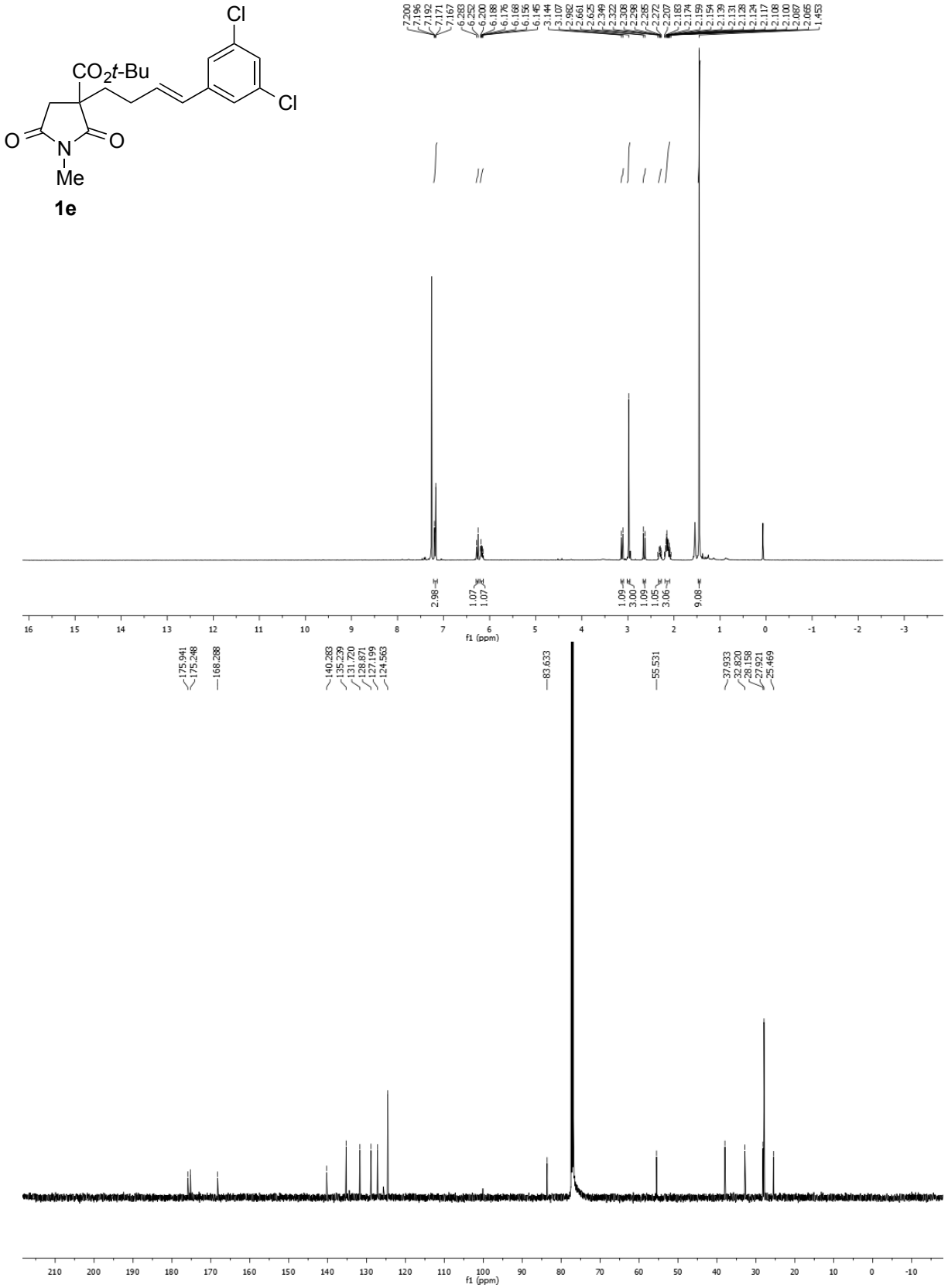

CO2t-Bu
CF3
O
N
O
Me
1c
f1 (ppm)
f1 (ppm)

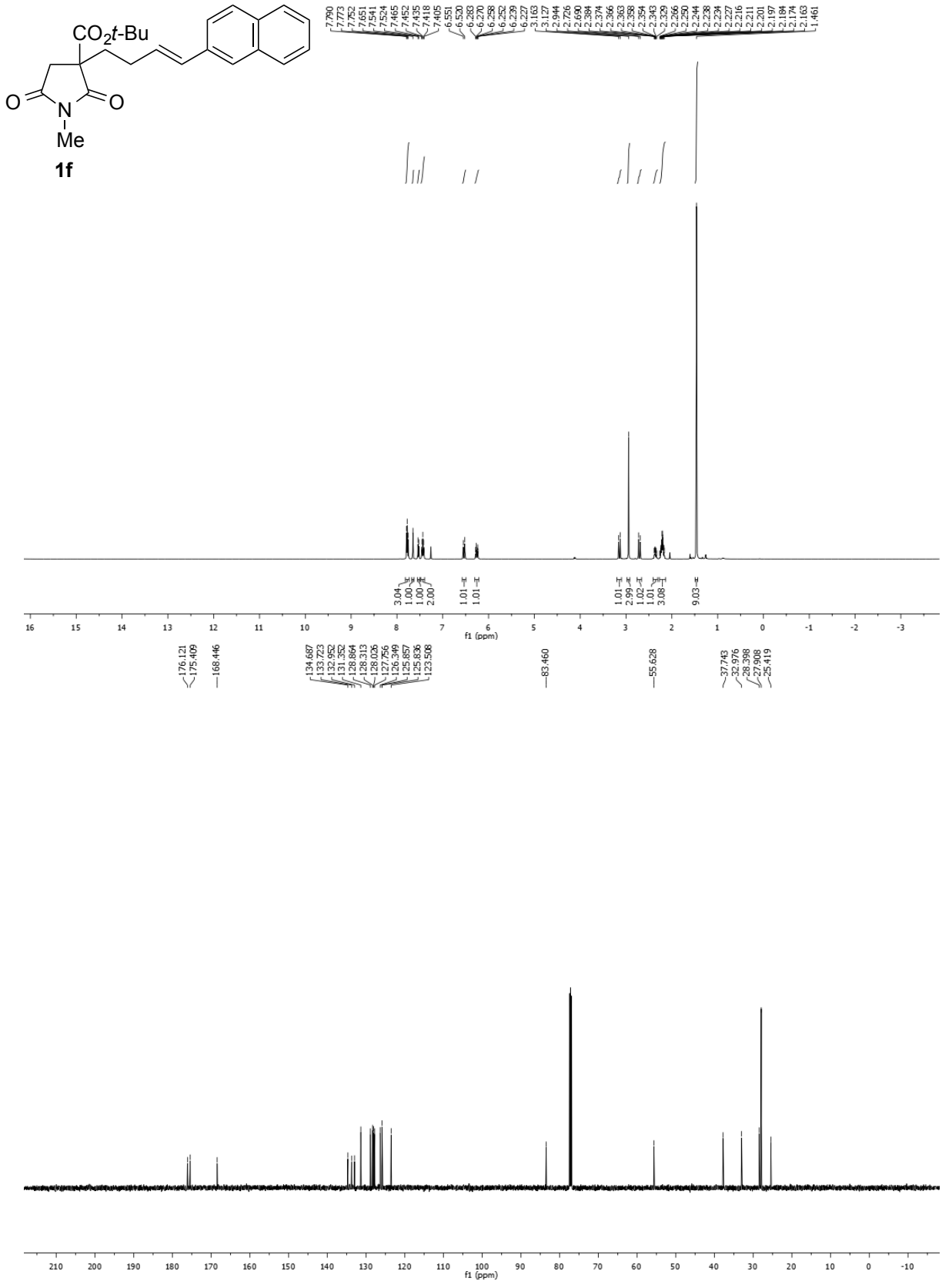

CF3
-62.470
CO2t-Bu
O
N
O
Me

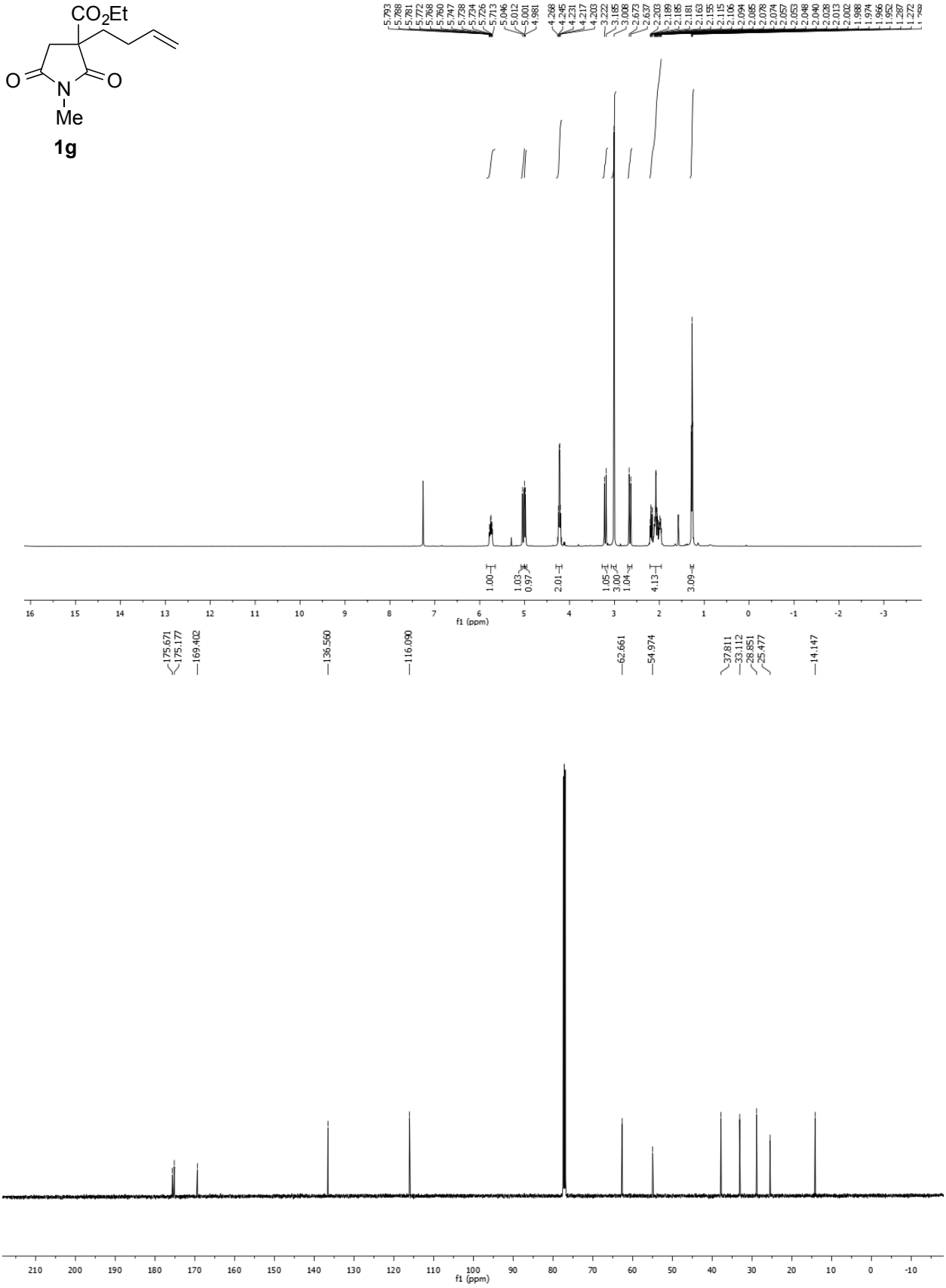
1c

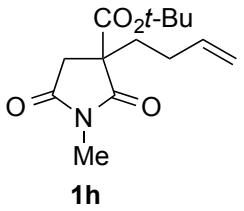

10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


Br
CO2t-Bu
O
N
O
Me
1d
f1 (ppm)


Cl
CO2t-Bu
Cl
O
N
O
Me
1e
f1 (ppm)
f1 (ppm)

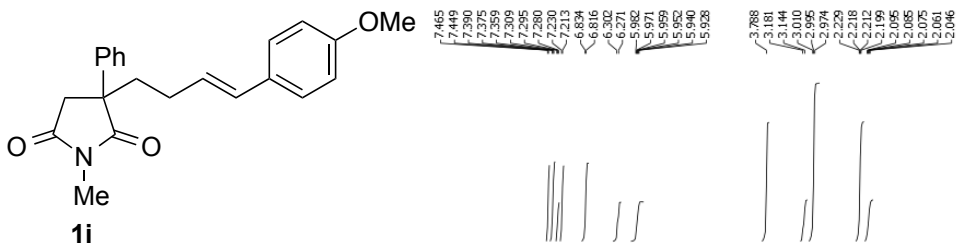

CO2t-Bu
O
N
O
Me
1f
f1 (ppm)


CO2Et
O
N
O
Me
1g
f1 (ppm)
175.671
175.177
169.402
136.560
116.090
62.661
54.974
37.811
33.112
28.851
25.477
14.147

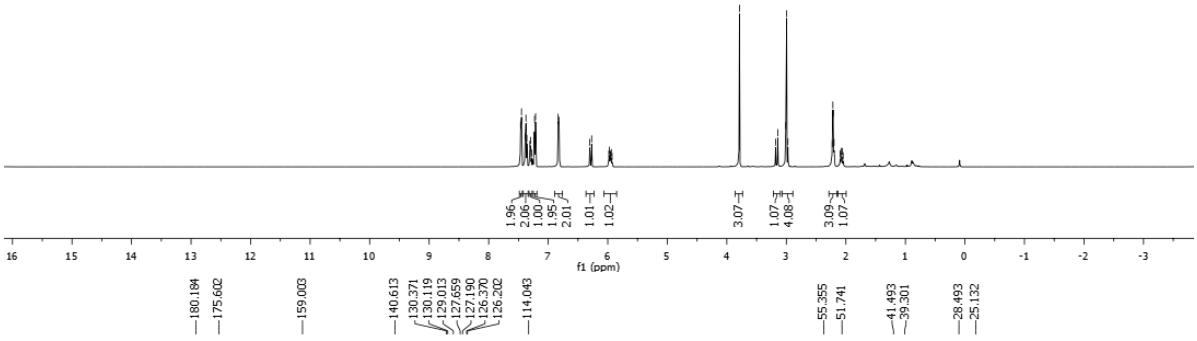

CO2t-Bu
O
N
O
Me

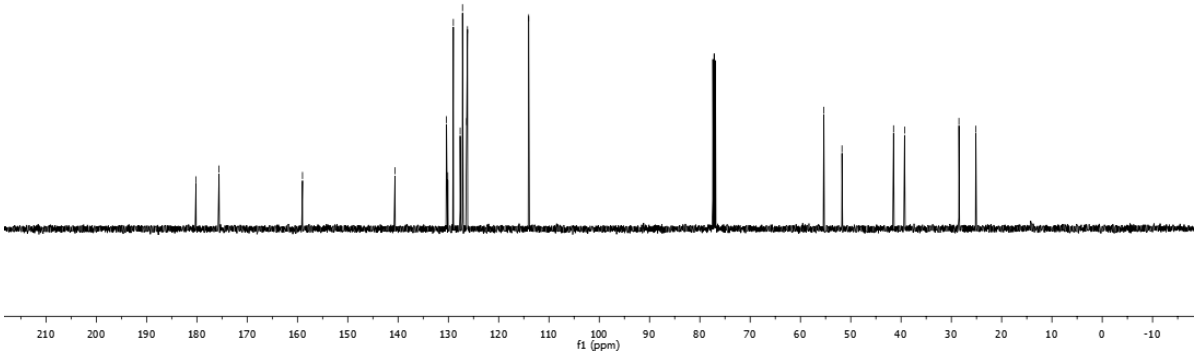
1h

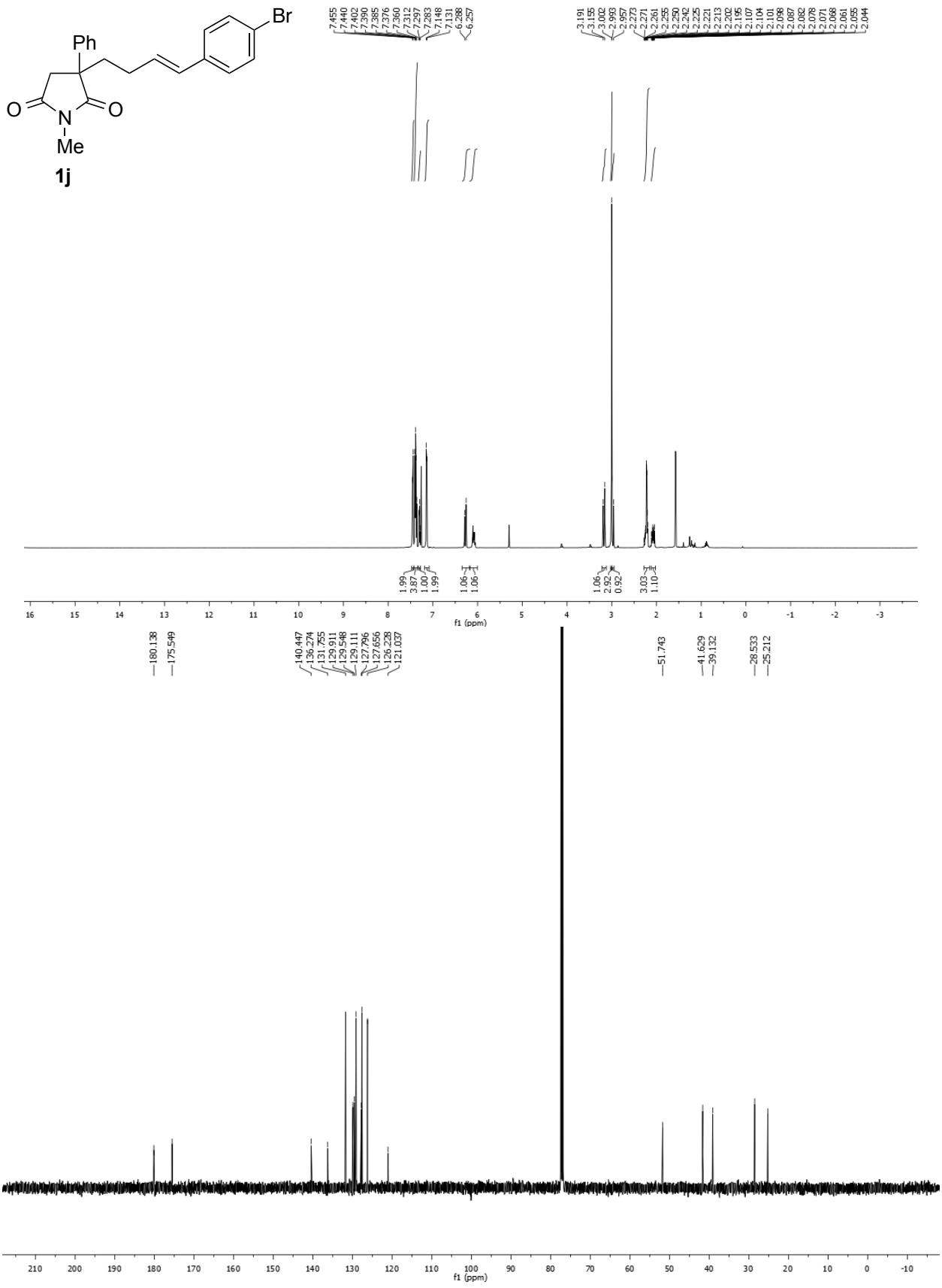
f1 (ppm)
176.064
175.459
168.412
136.799
115.923
83.406
55.668
37.900
32.802
28.877
27.891
25.364

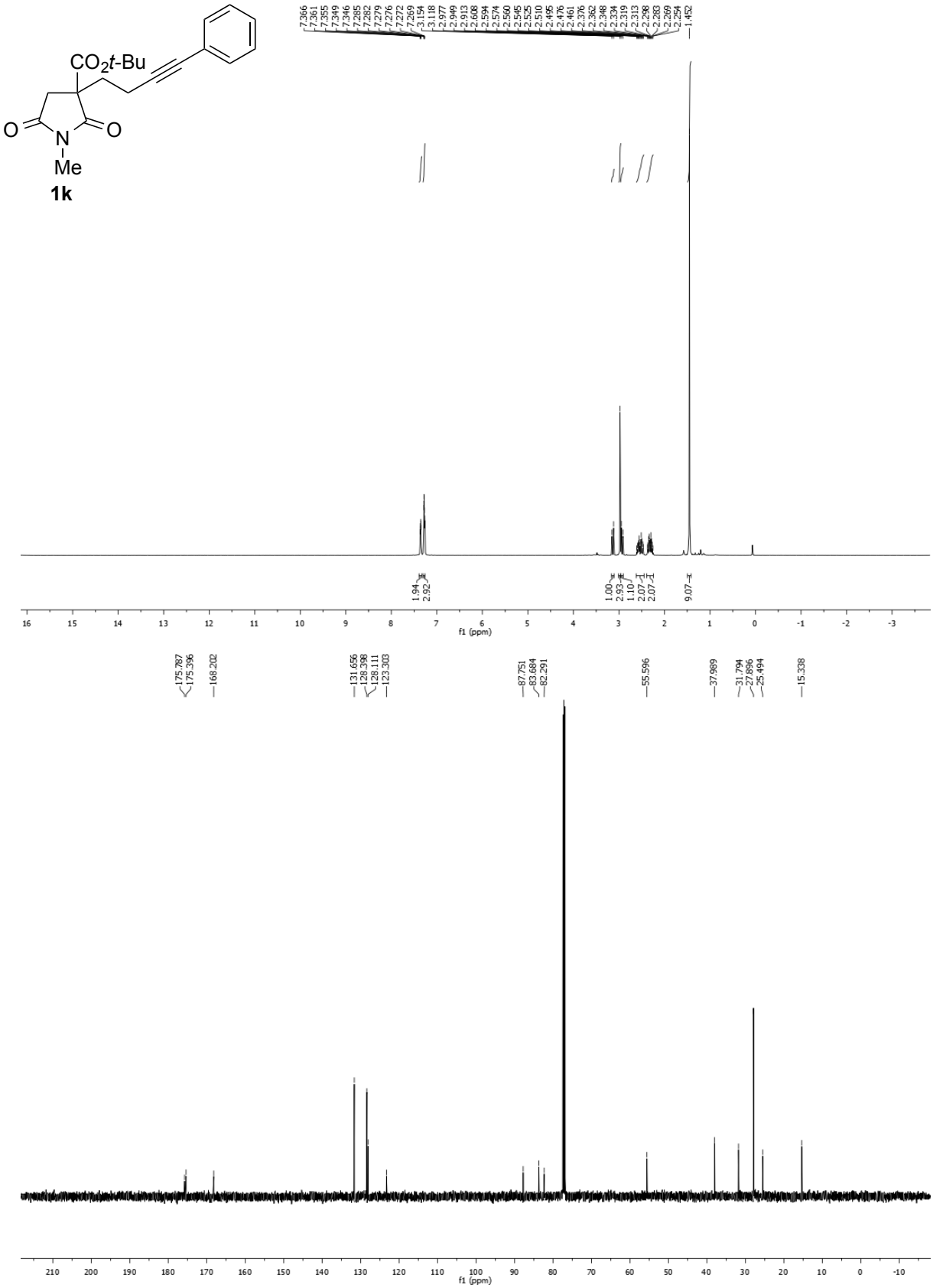


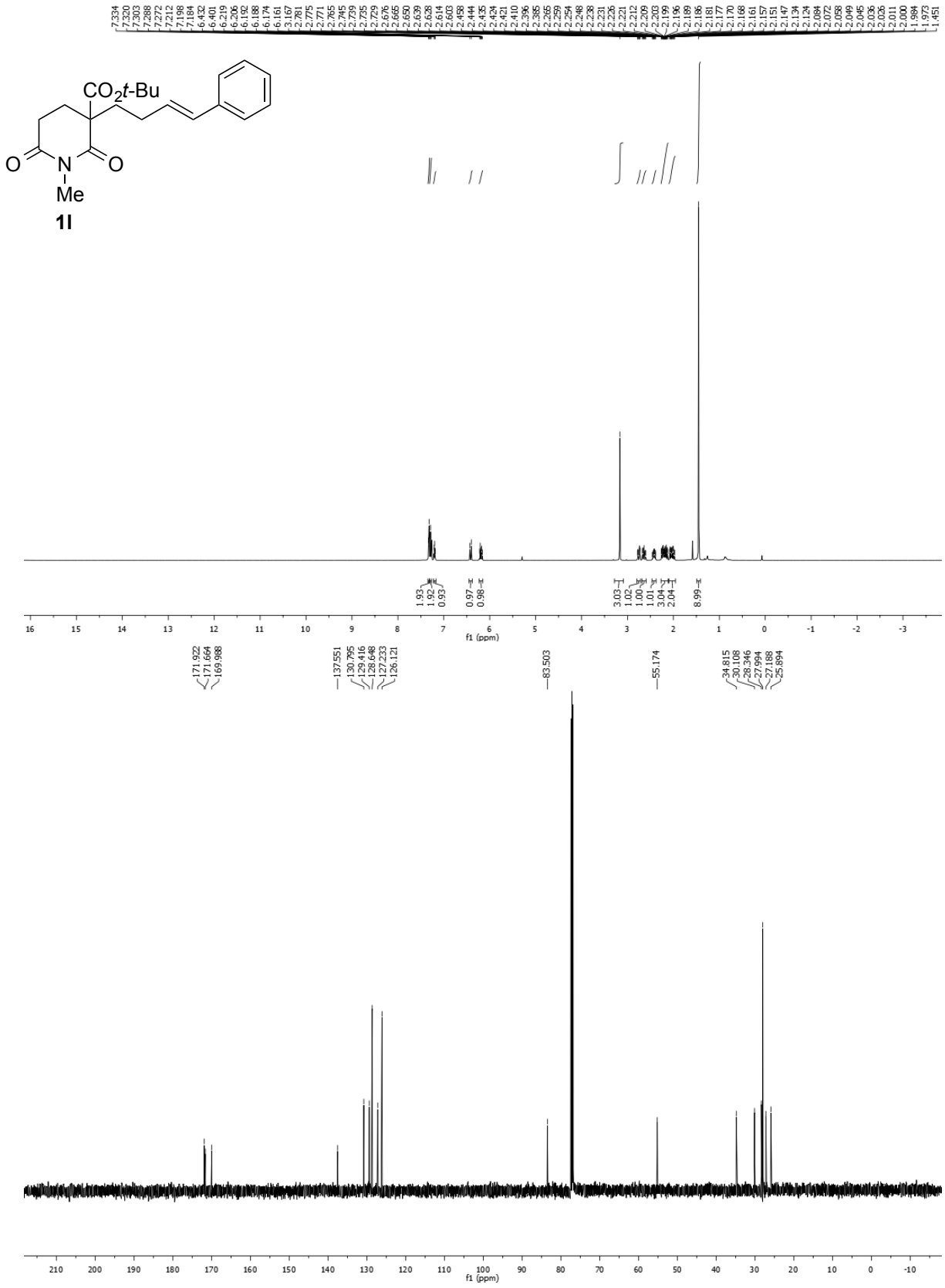
1i

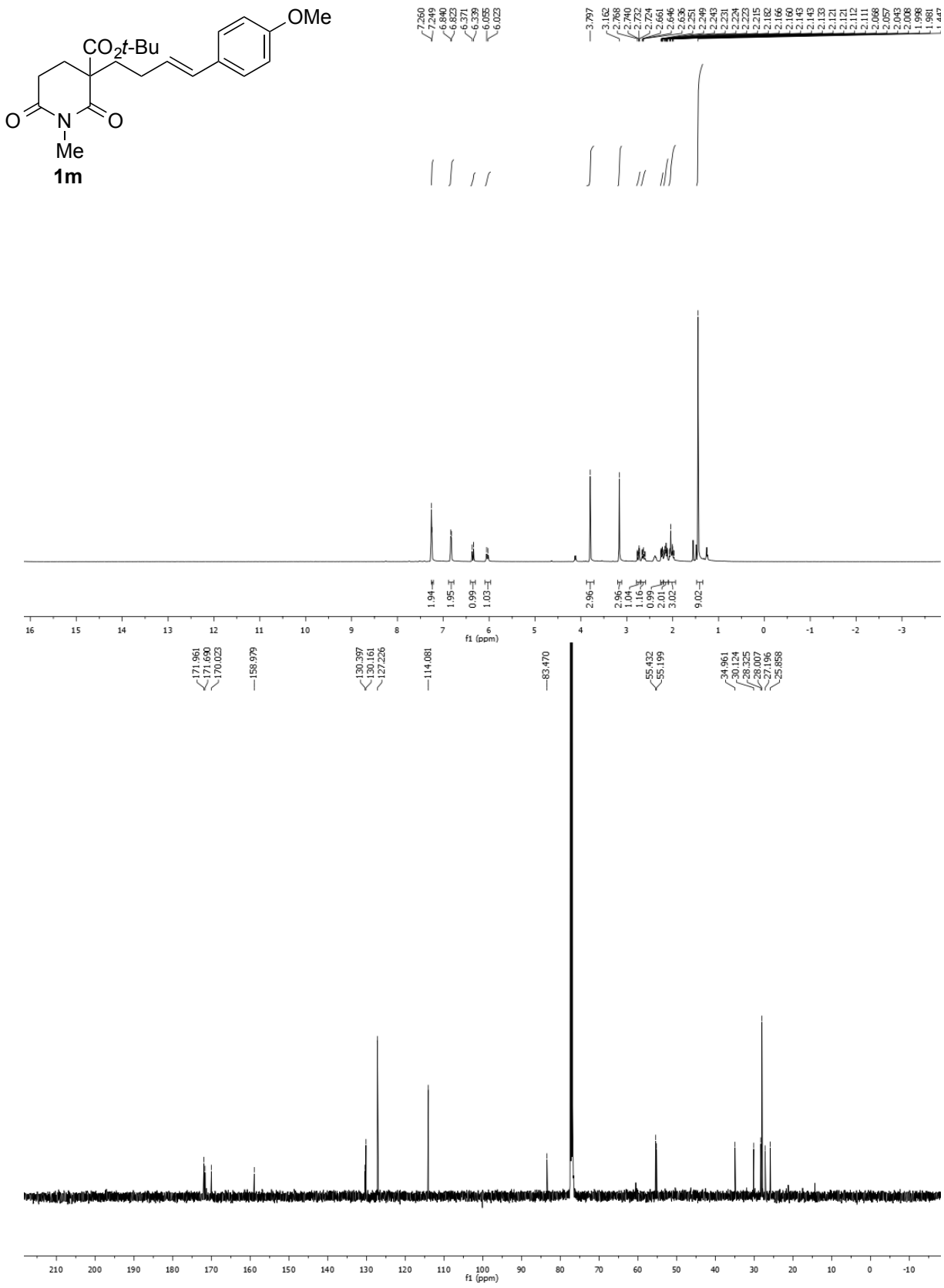


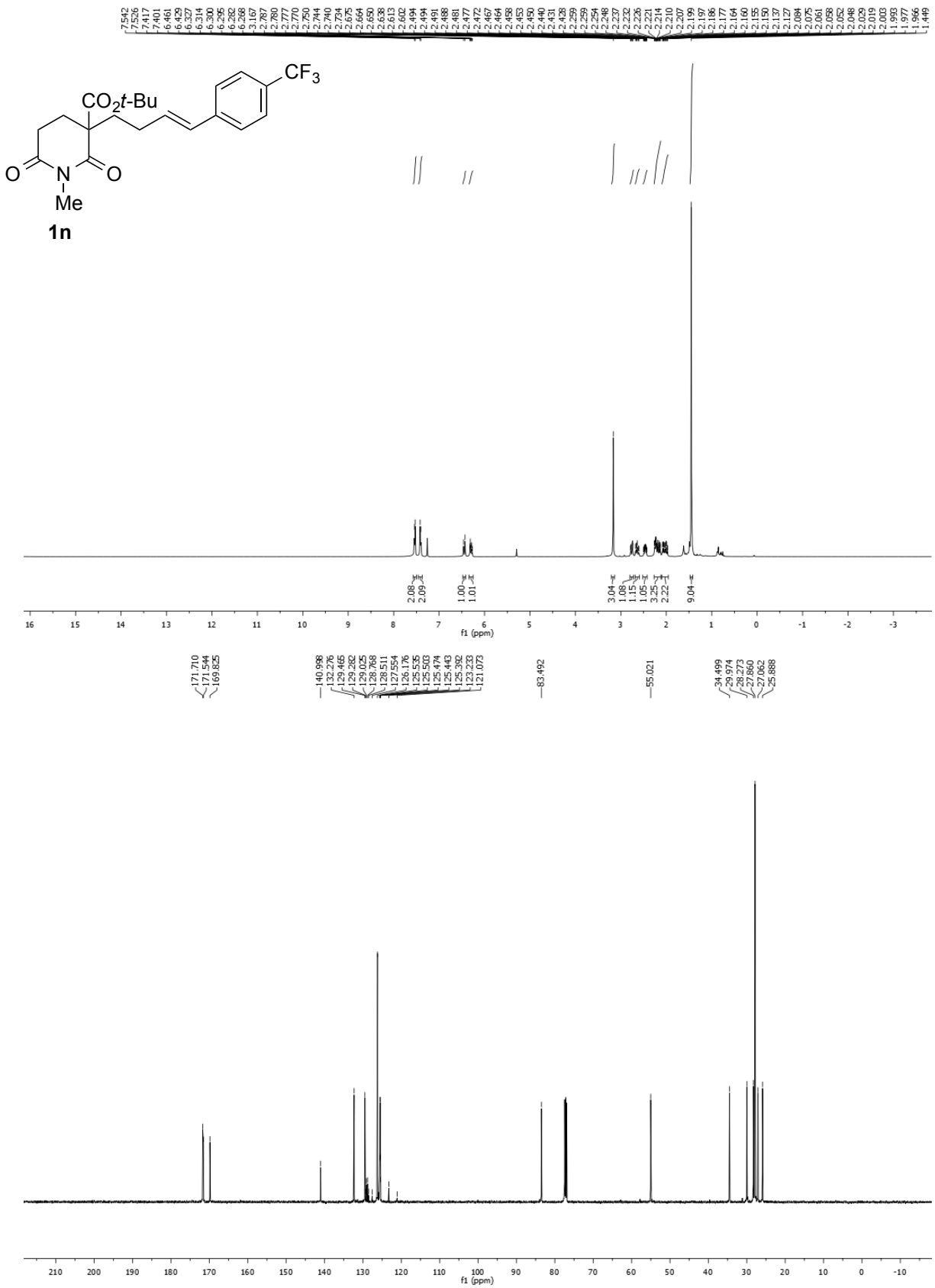


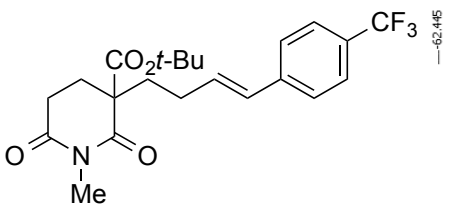

Br
Ph
O
N
O
Me
1j
f1 (ppm)


CO2t-Bu
O
N
O
Me
1k
f1 (ppm)
f1 (ppm)

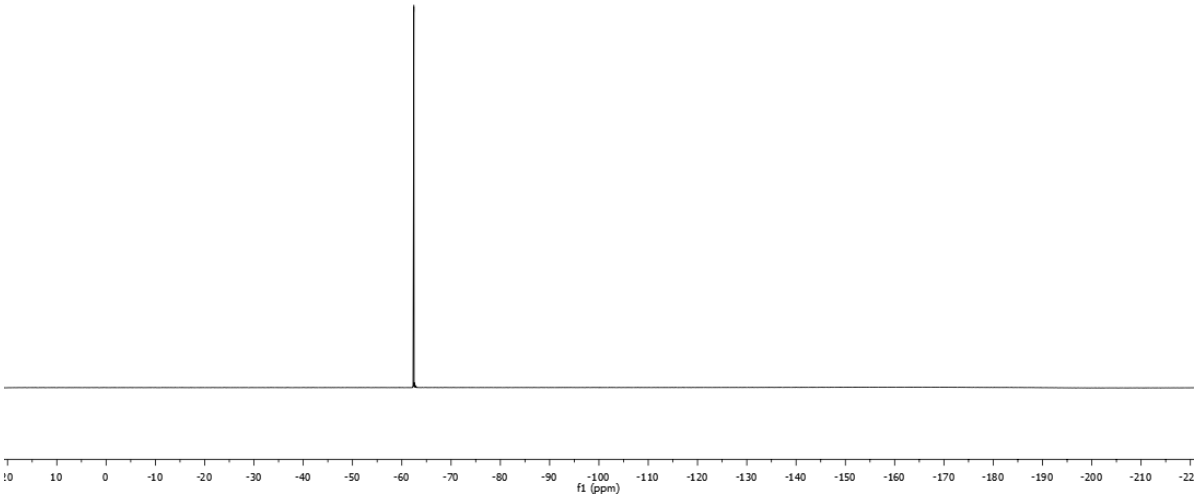

CO2t-Bu
O
N
O
Me
1l
f1 (ppm)
f1 (ppm)

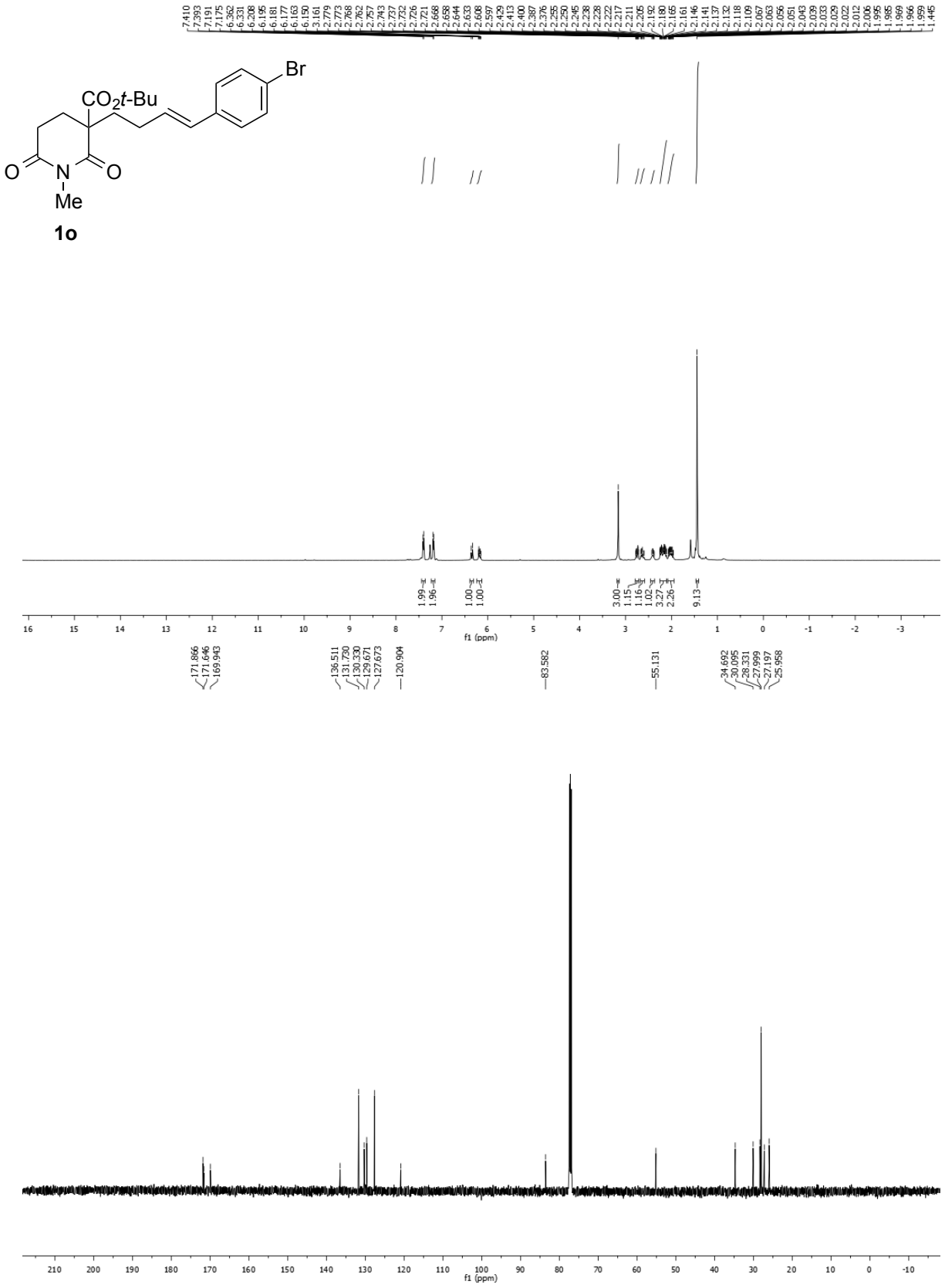

OMe
CO2t-Bu
O
N
O
Me
1m
f1 (ppm)
f1 (ppm)

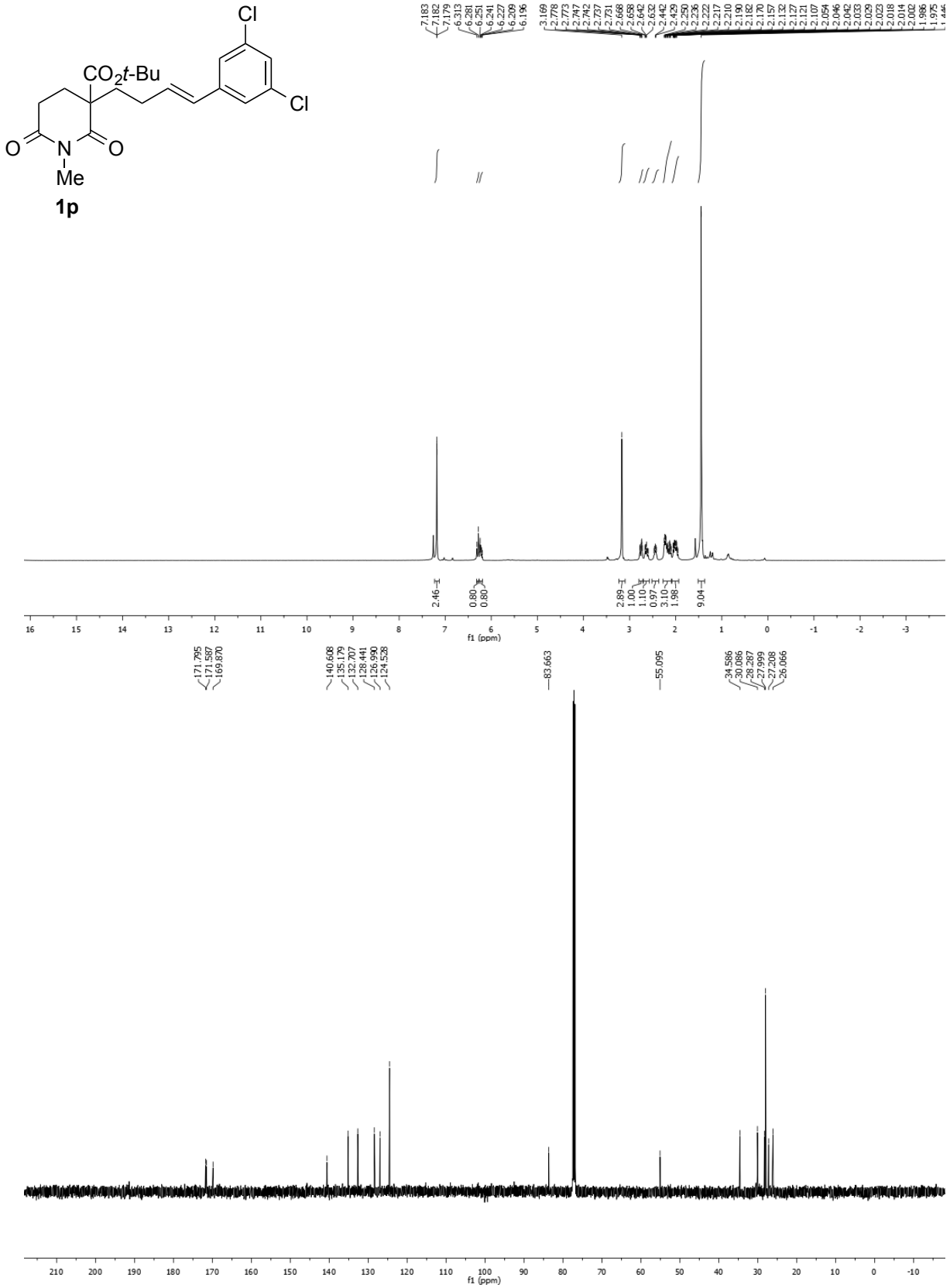

CF3
CO2t-Bu
O
N
O
Me
1n
f1 (ppm)

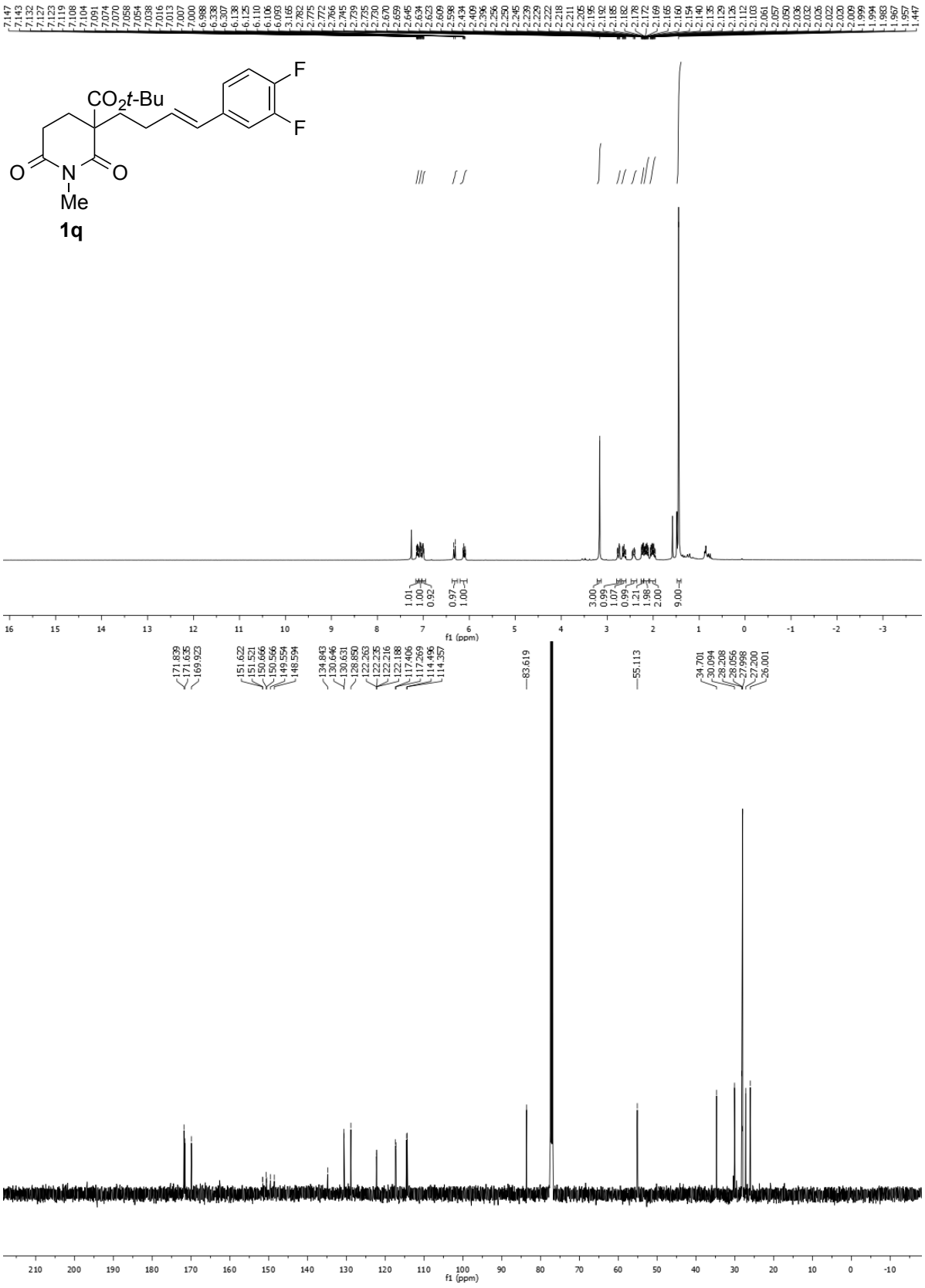

CF3
CO2t-Bu
O
N
O
Me

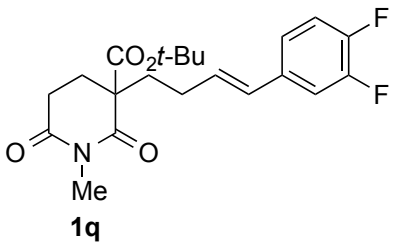
1n


-62.445
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


Br
CO2t-Bu
O
N
O
Me
1o
f1 (ppm)

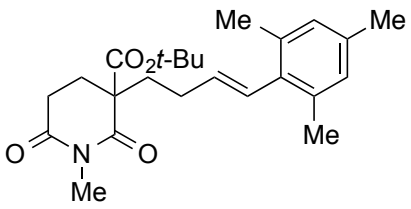

Cl
CO2t-Bu
Cl
O
N
O
Me
1p
f1 (ppm)
f1 (ppm)


CO2t-Bu
F
F
O
N
O
Me
1q
f1 (ppm)
f1 (ppm)


CO2t-Bu
F
F
O
N
O
Me

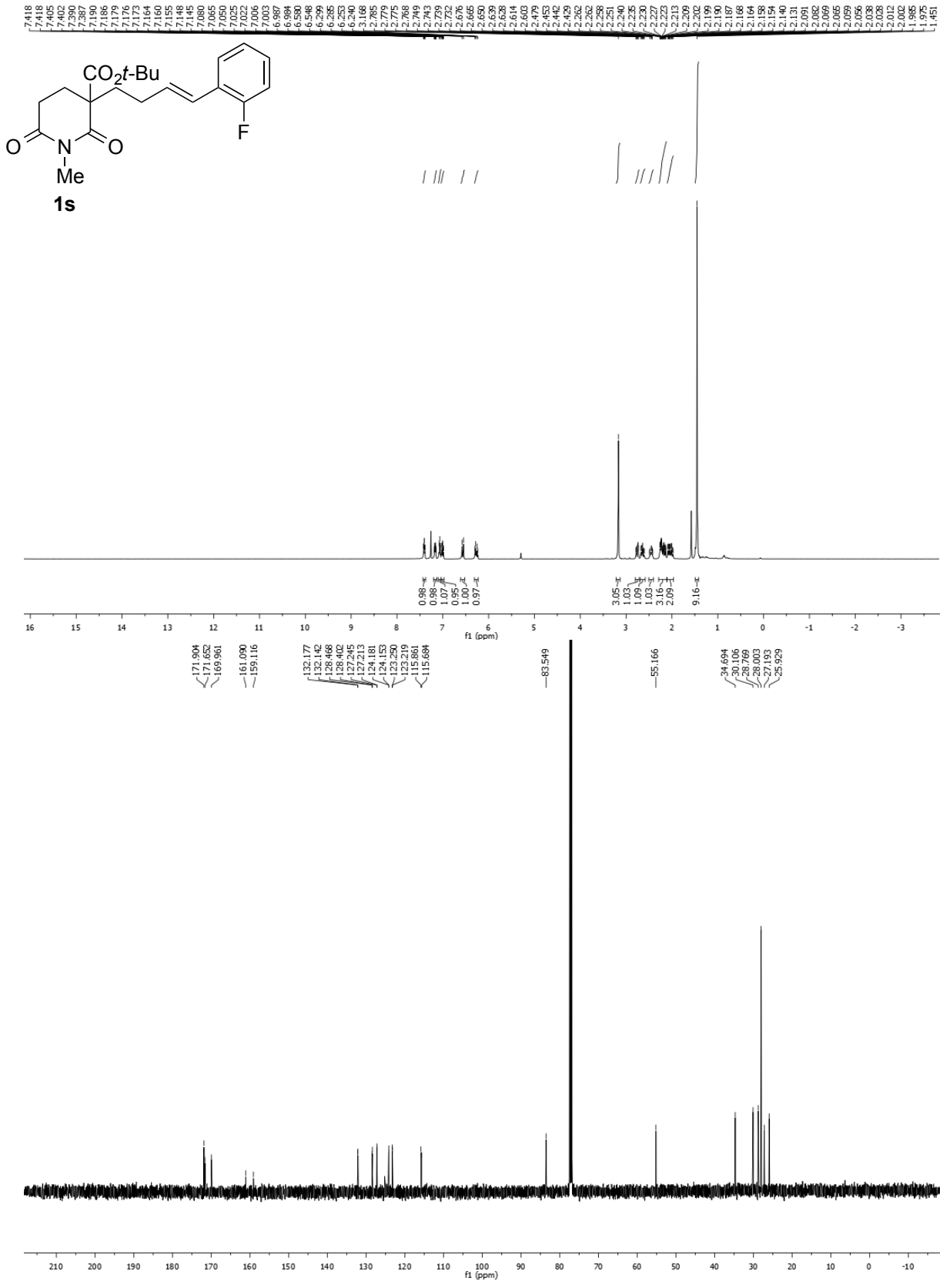
1q

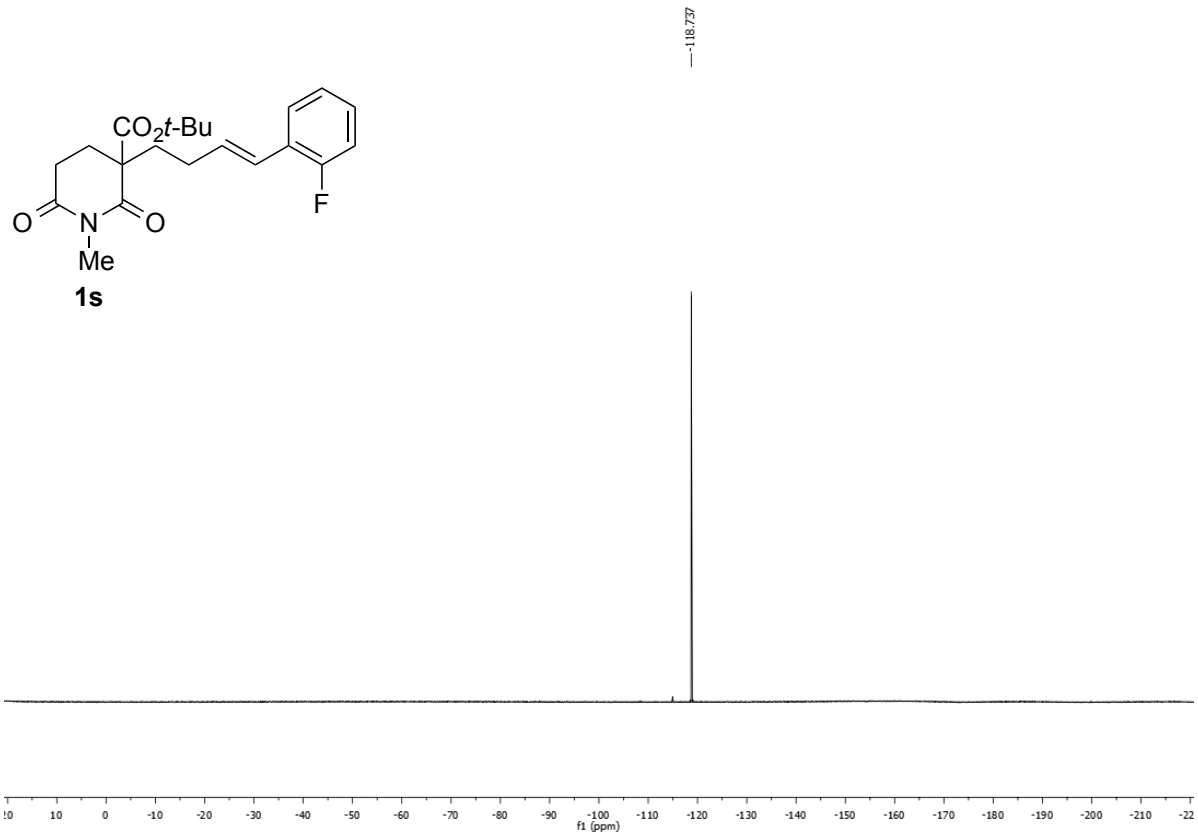
-138.137
-138.182
-139.952
-139.996
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

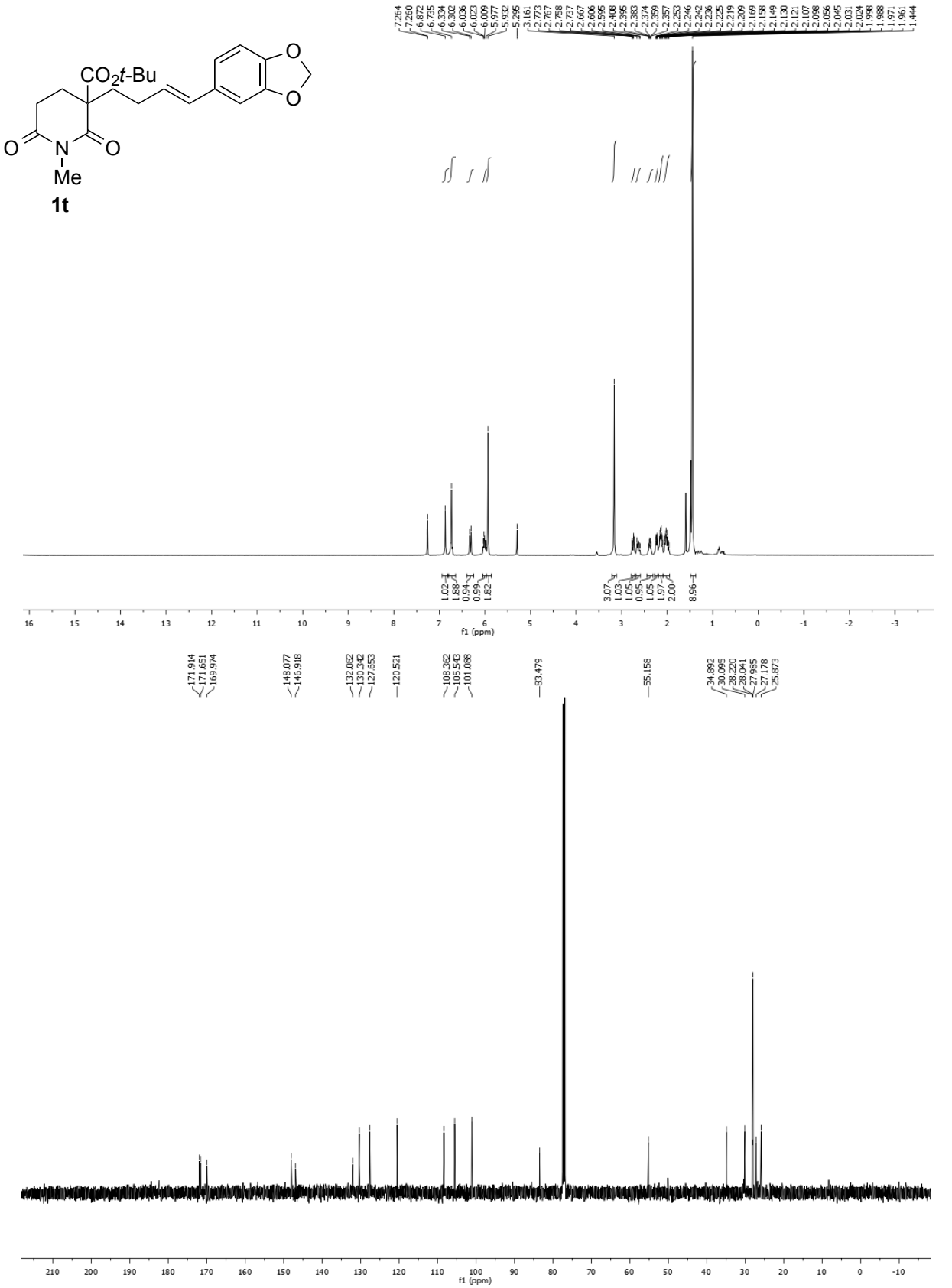

Me
Me
CO2t-Bu
Me
O
N
O
Me

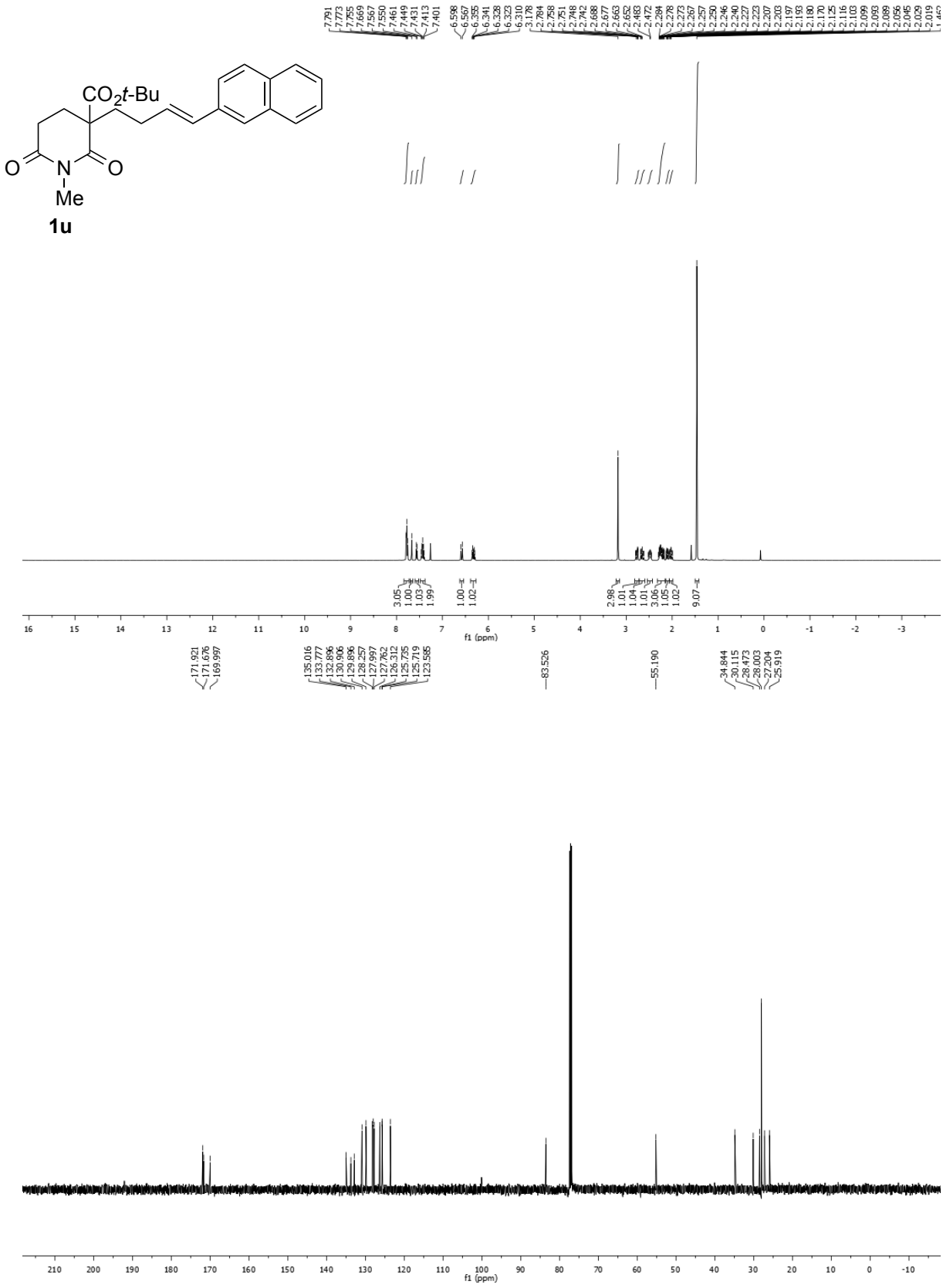
1r

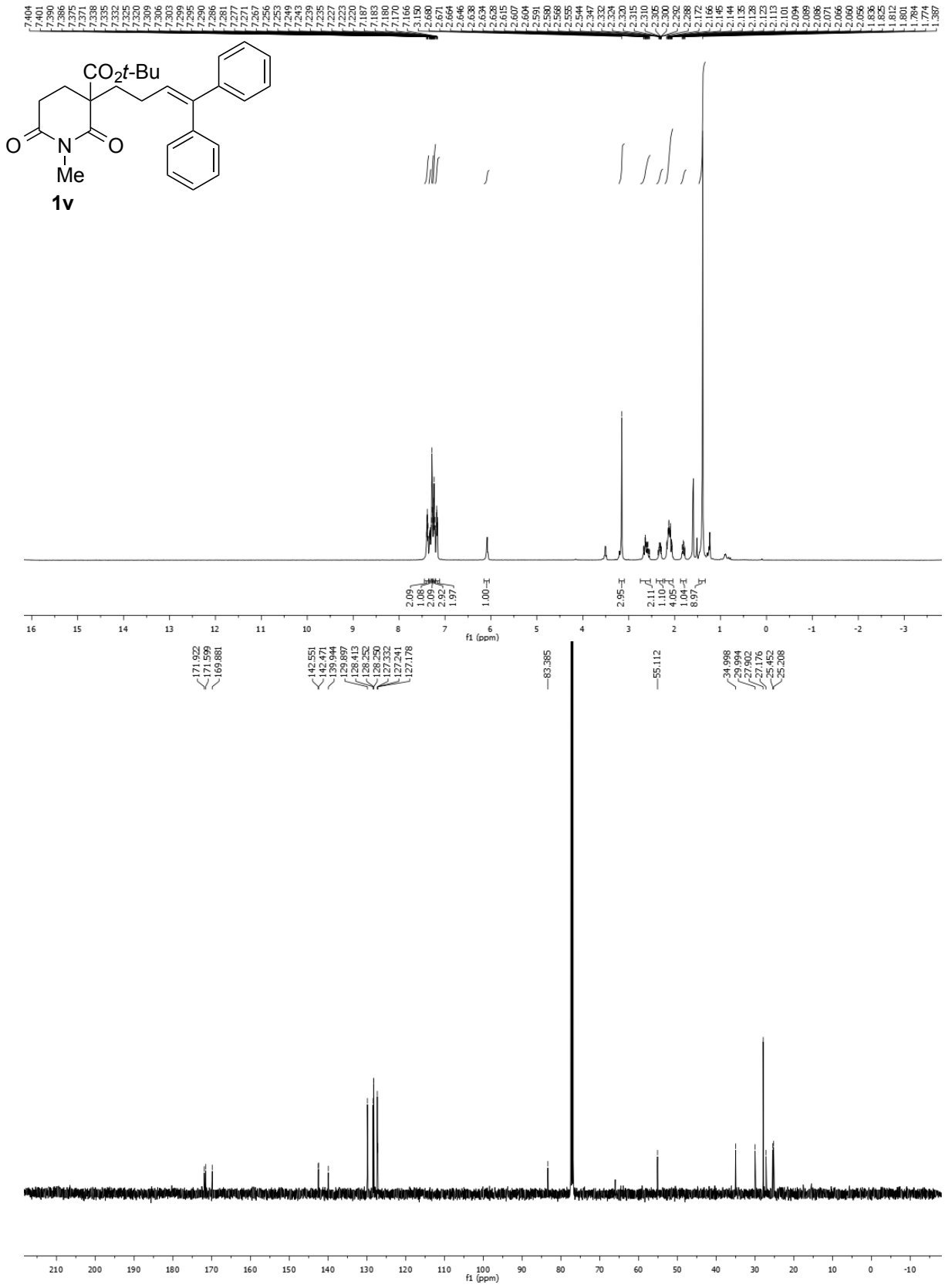
6.848
6.339
6.336
5.645
5.631
5.613
3.186
2.754
2.747
2.743
2.737
2.691
2.680
2.666
2.655
2.442
2.439
2.432
2.428
2.425
2.422
2.418
2.415
2.412
2.257
2.242
2.144
2.140
2.134
2.131
2.117
2.107
2.092
2.083
2.068
2.065
2.059
2.055
2.052
2.042
2.031
2.027
2.025
2.017
2.014
2.01
1.00
1.03
2.97
1.10
1.06
1.17
3.05
5.95
3.18
9.07
f1 (ppm)
171.956
171.731
170.026
135.966
135.928
134.310
133.972
128.578
128.359
83.511
55.221
35.121
30.114
28.851
28.013
27.199
25.984
21.023
f1 (ppm)

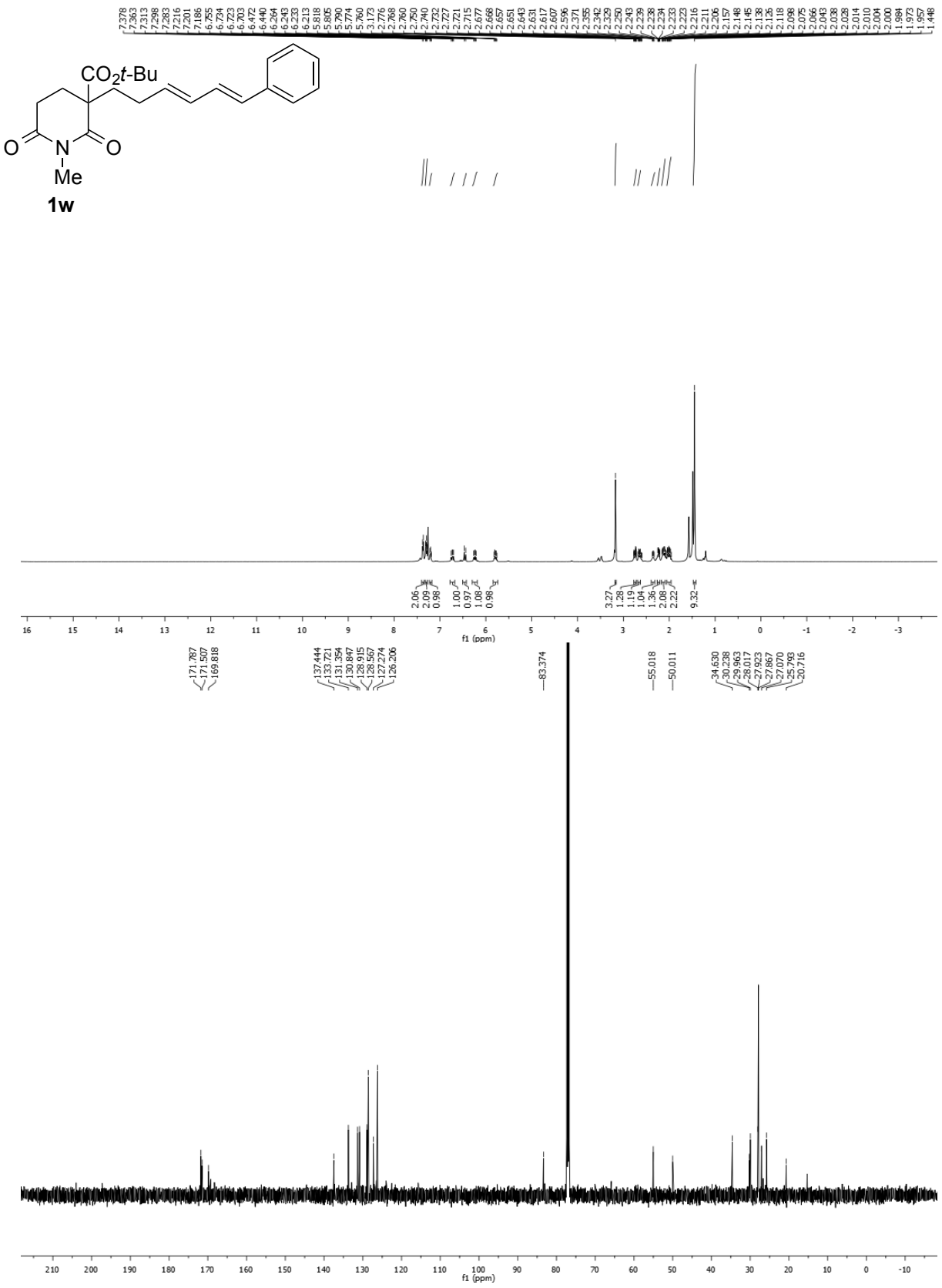

CO2t-Bu
O
N
O
Me
F
1s
f1 (ppm)
171.904
171.652
169.961
161.090
159.116
132.177
132.142
128.468
128.402
127.245
127.213
124.181
124.153
123.250
123.219
115.861
115.684
83.549
55.166
34.694
30.106
28.769
28.003
27.193
25.929

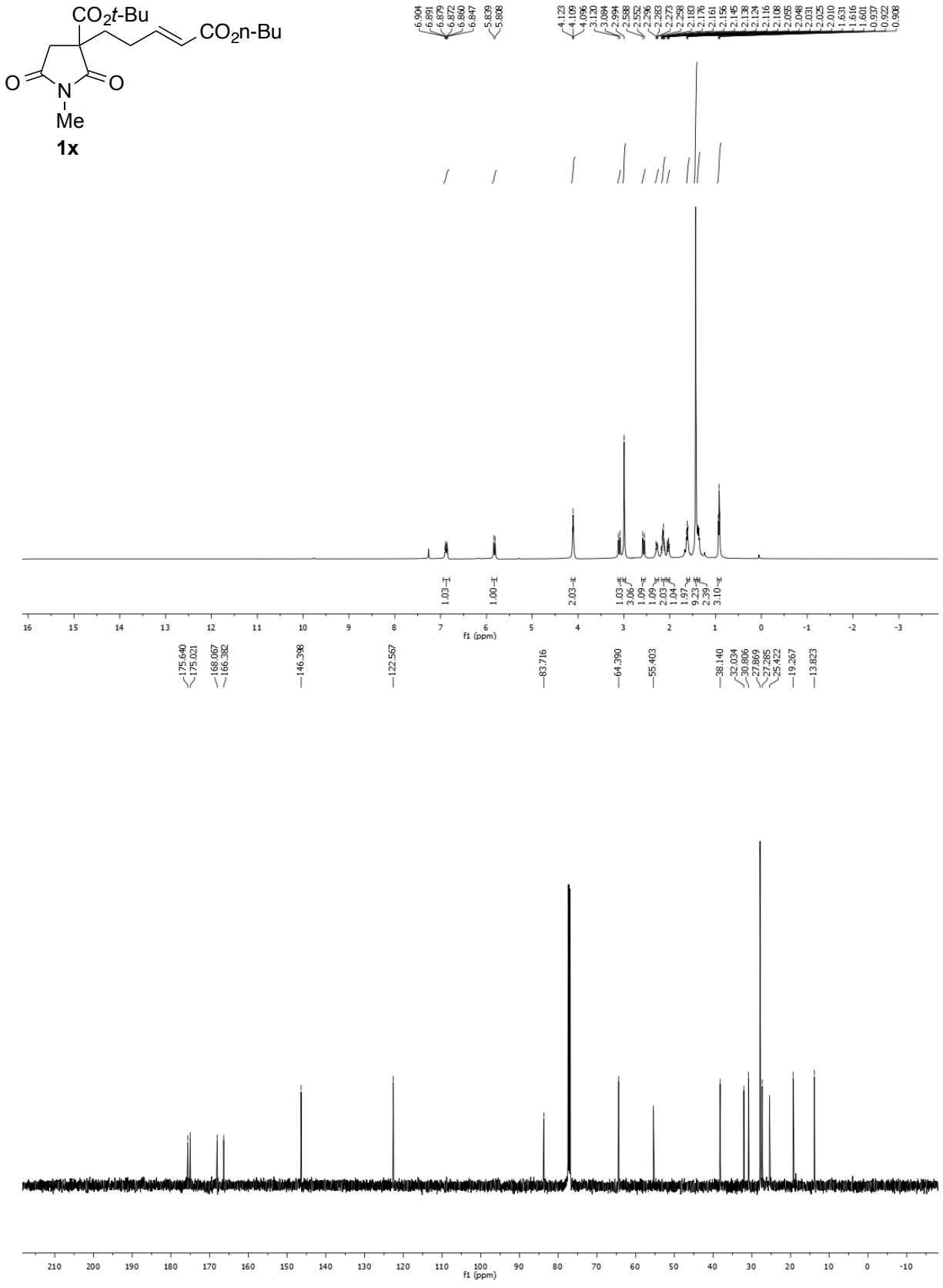

CO2t-Bu
O
N
O
Me
F
1s
-118.737
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

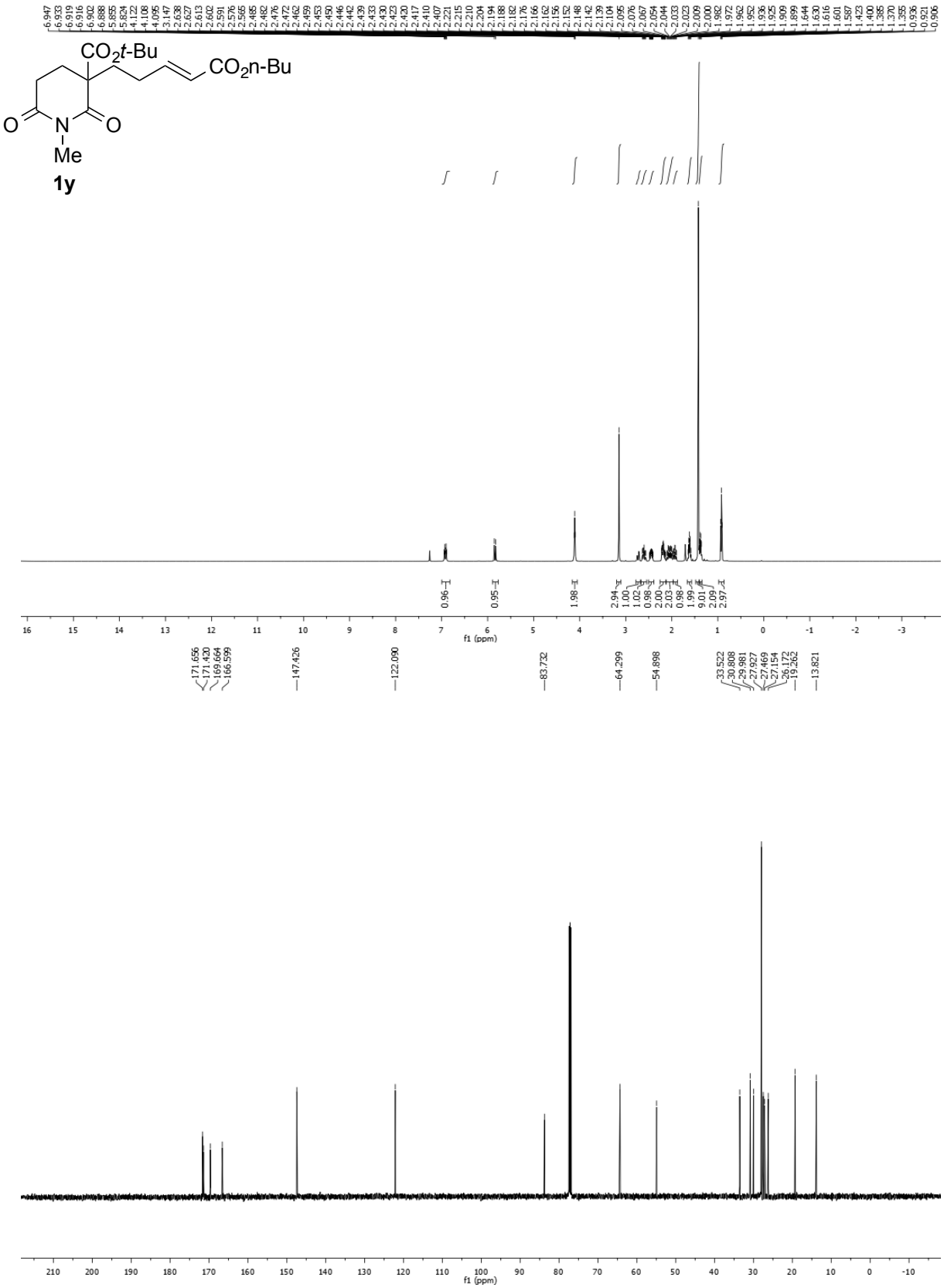

CO2t-Bu
O
O
O
N
O
Me
1t
f1 (ppm)
f1 (ppm)

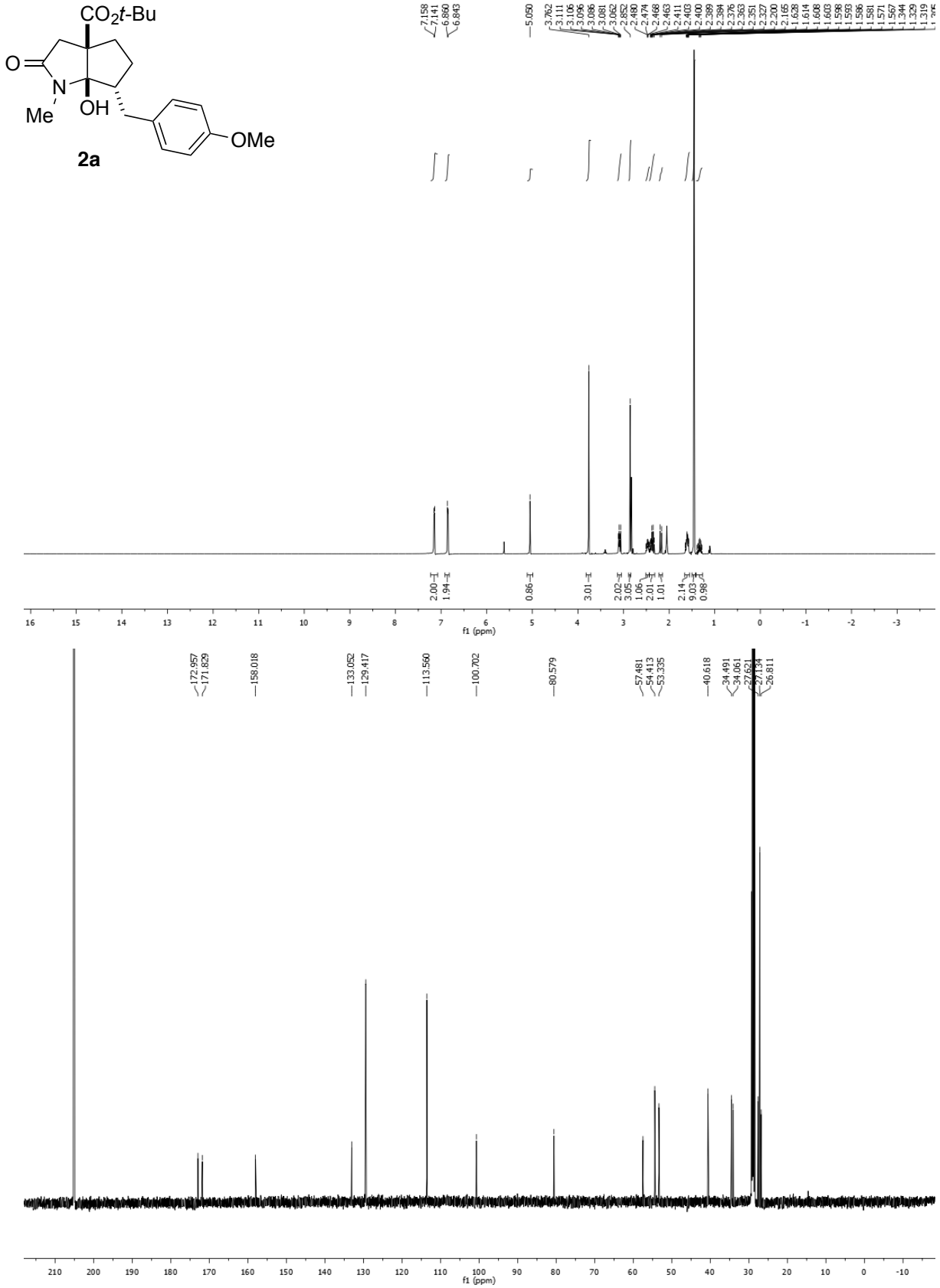

CO2t-Bu
O
N
O
Me
1u
f1 (ppm)

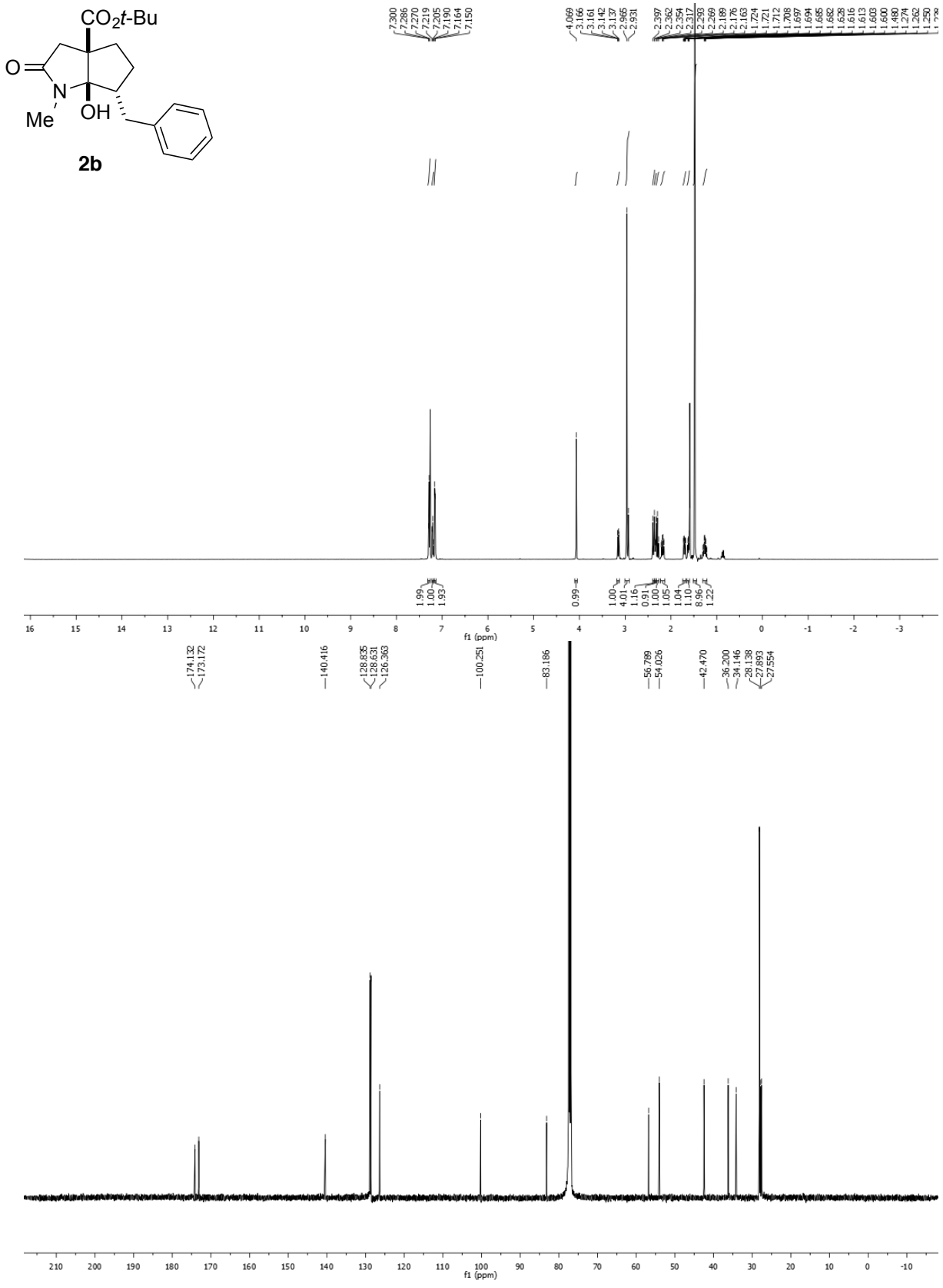

CO2t-Bu
O
N
O
Me
1v
f1 (ppm)
f1 (ppm)

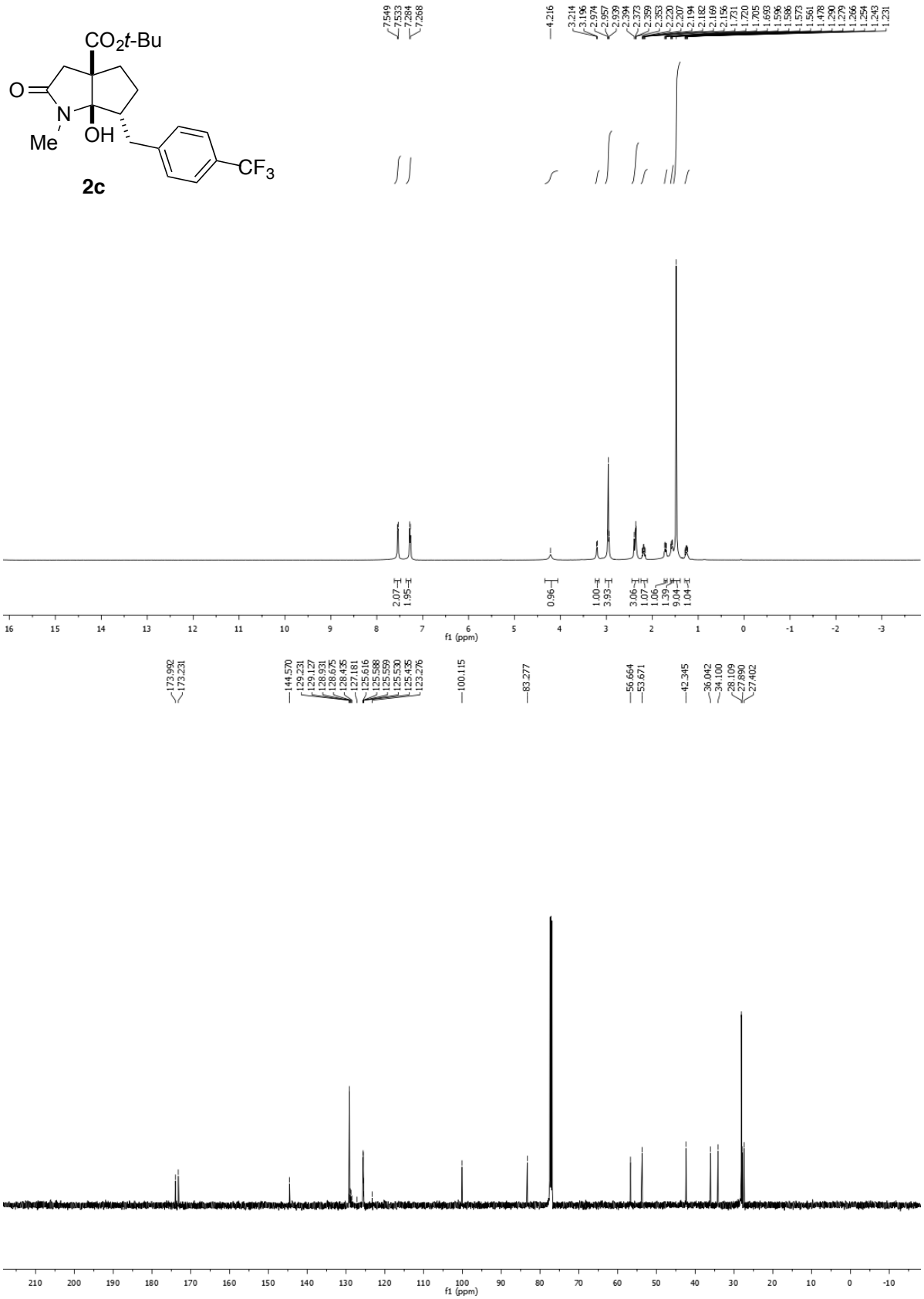

CO2t-Bu
O
N
O
Me
1w
f1 (ppm)
f1 (ppm)

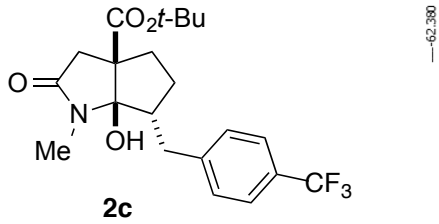

CO2t-Bu
CO2n-Bu
O
N
O
Me
1x
6.904
6.891
6.879
6.872
6.860
6.847
5.839
5.808
4.123
4.109
4.096
3.120
3.084
2.994
2.588
2.552
2.296
2.283
2.273
2.258
2.183
2.176
2.161
2.156
2.145
2.138
2.124
2.116
2.108
2.055
2.048
2.031
2.025
2.010
1.631
1.616
1.601
0.937
0.922
0.908
1.03
1.00
2.03
1.03
3.06
1.09
1.09
2.03
1.04
1.97
9.23
2.39
3.10
f1 (ppm)
175.640
175.021
168.067
166.382
146.398
122.567
83.716
64.390
55.403
38.140
32.034
30.806
27.869
27.285
25.422
19.267
13.823
f1 (ppm)


CO2t-Bu
CO2n-Bu
O
N
O
Me
1y
f1 (ppm)
f1 (ppm)


CO2t-Bu
O
N
Me
OH
OMe
2a
f1 (ppm)
f1 (ppm)

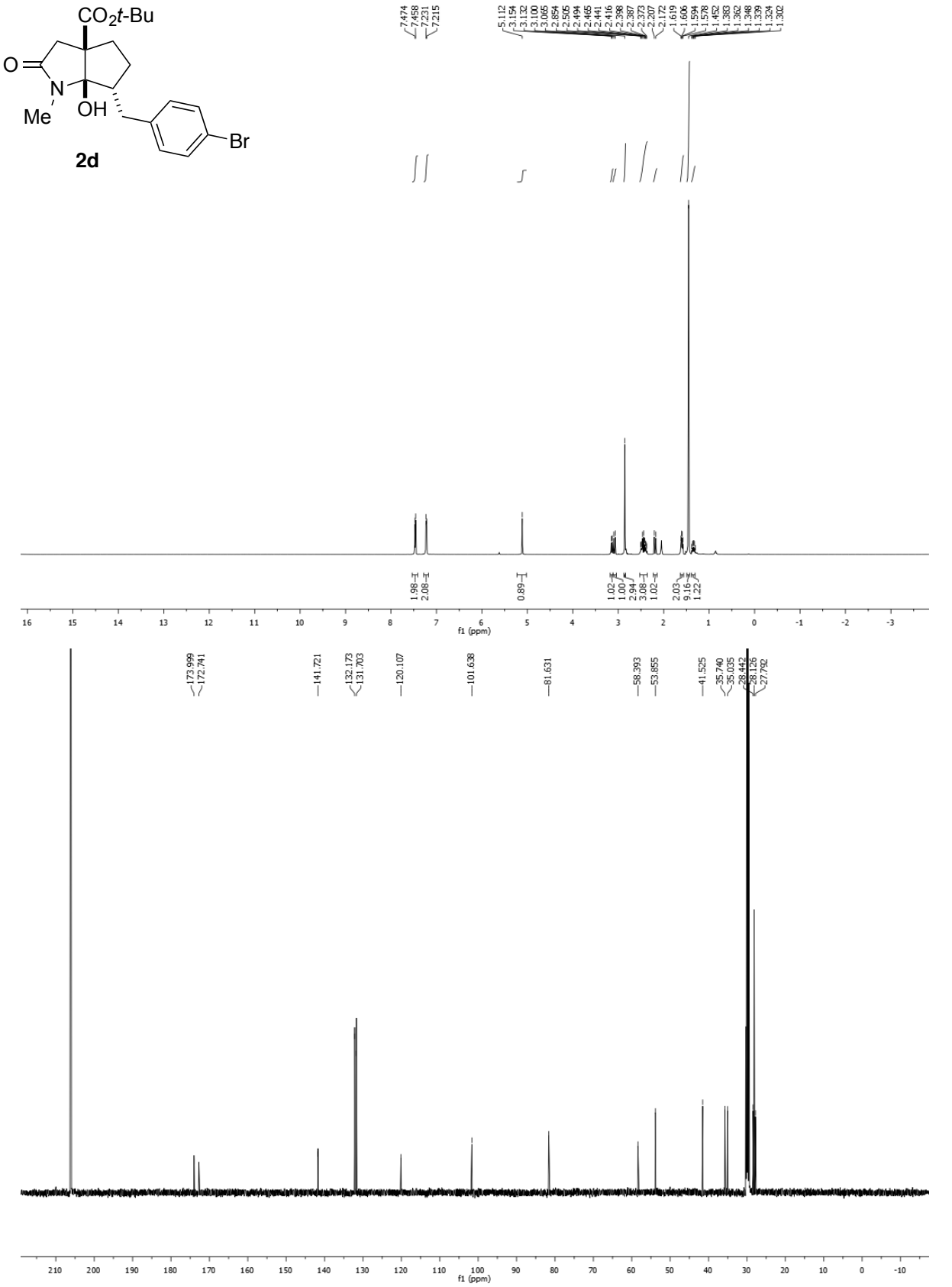

CO2t-Bu
O
N
Me
OH
2b
f1 (ppm)
f1 (ppm)

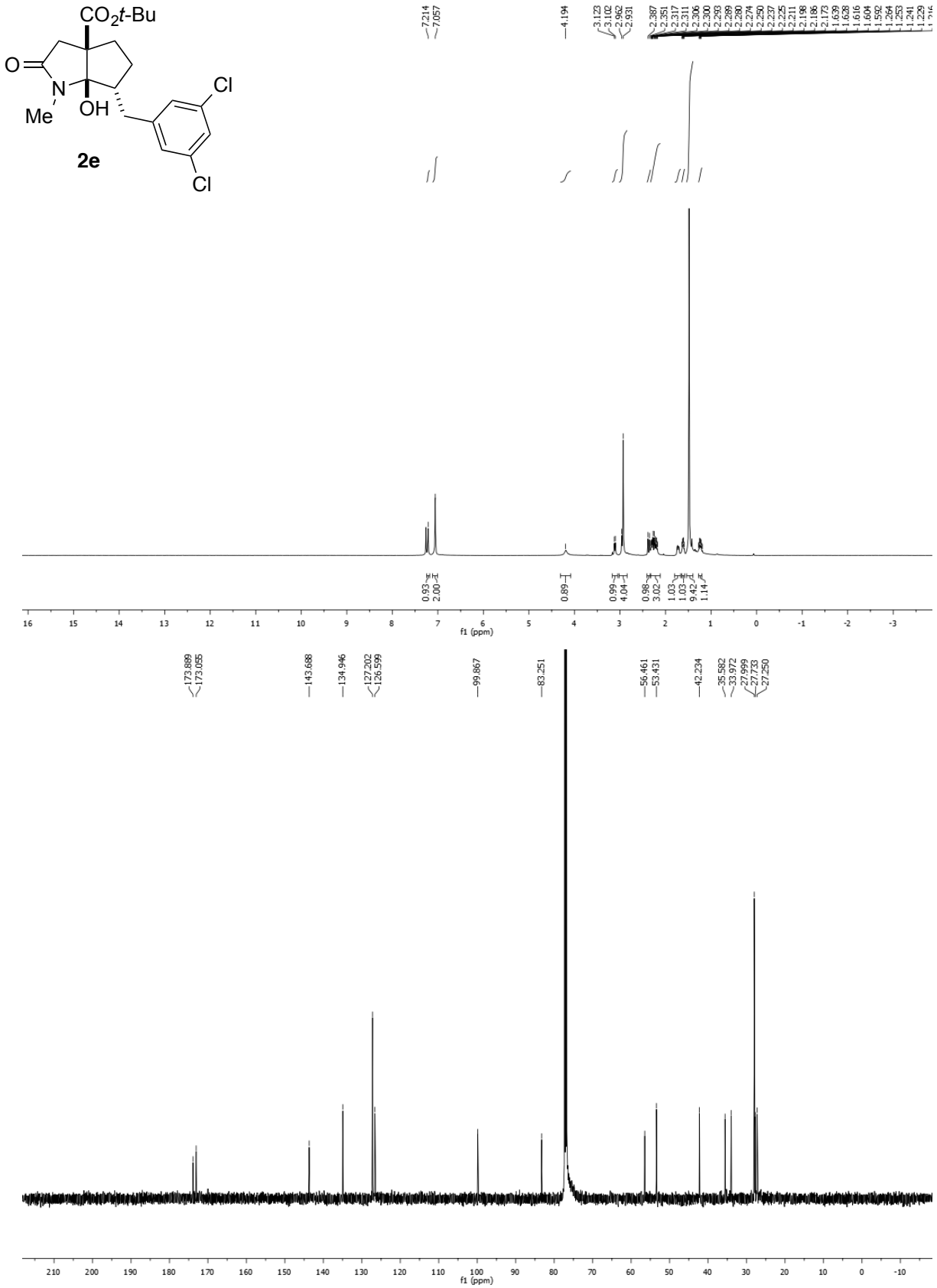

CO2t-Bu
O
N
Me
OH
CF3
2c
f1 (ppm)

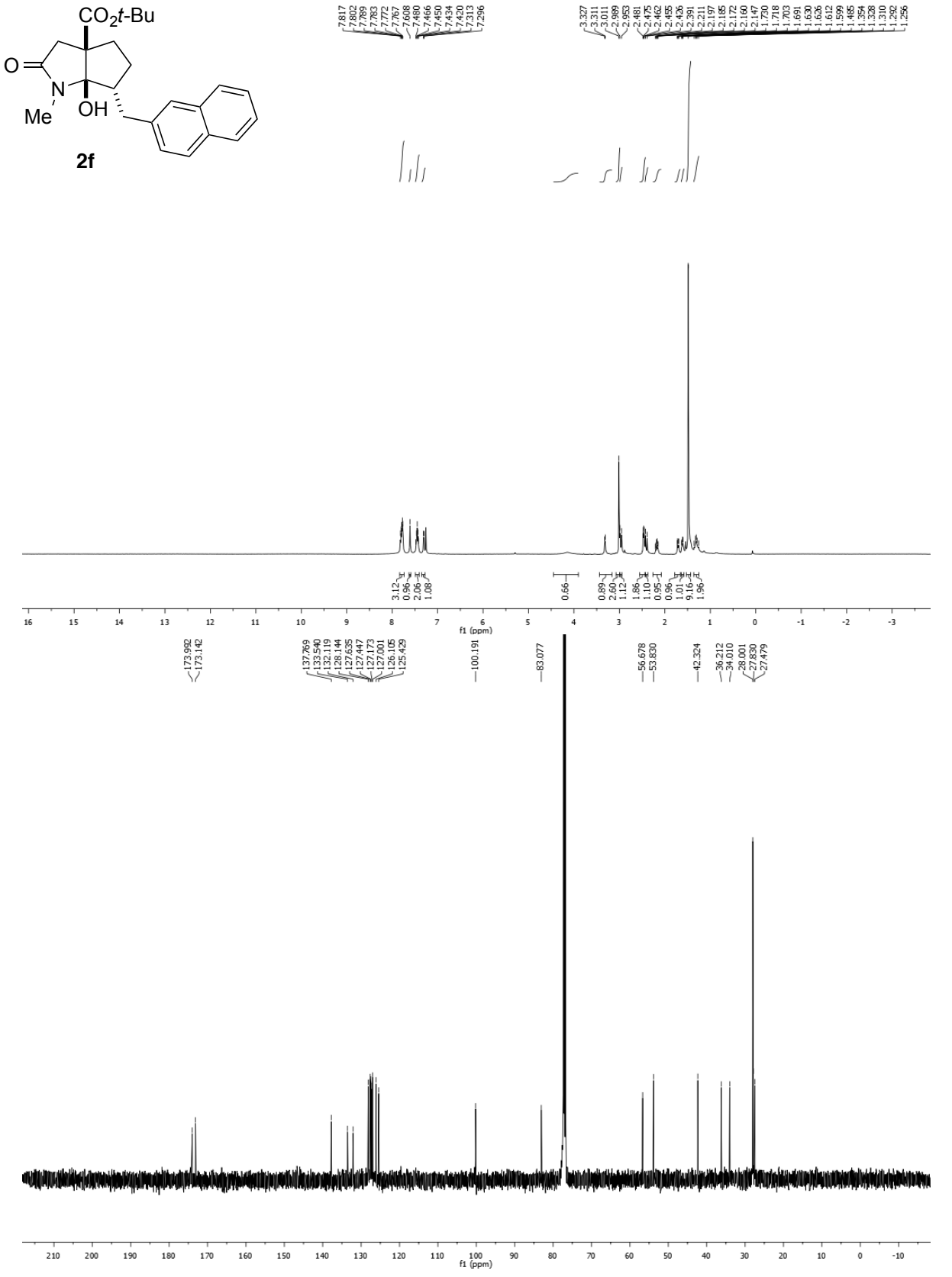

CO2t-Bu
O
N
Me
OH
CF3

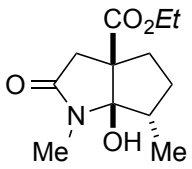
2c

-62.380
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


CO2t-Bu
O
N
Me
OH
Br
2d
7.474
7.458
7.231
7.215
5.112
3.154
3.132
3.100
3.065
2.854
2.505
2.494
2.465
2.441
2.416
2.398
2.387
2.373
2.207
2.172
1.619
1.606
1.594
1.578
1.452
1.383
1.362
1.348
1.339
1.324
1.302
1.98
2.08
0.89
1.02
1.00
2.94
3.08
1.02
2.03
9.16
1.22
f1 (ppm)
173.999
172.741
141.721
132.173
131.703
120.107
101.638
81.631
58.393
53.855
41.525
35.740
35.035
28.442
28.126
27.792
f1 (ppm)

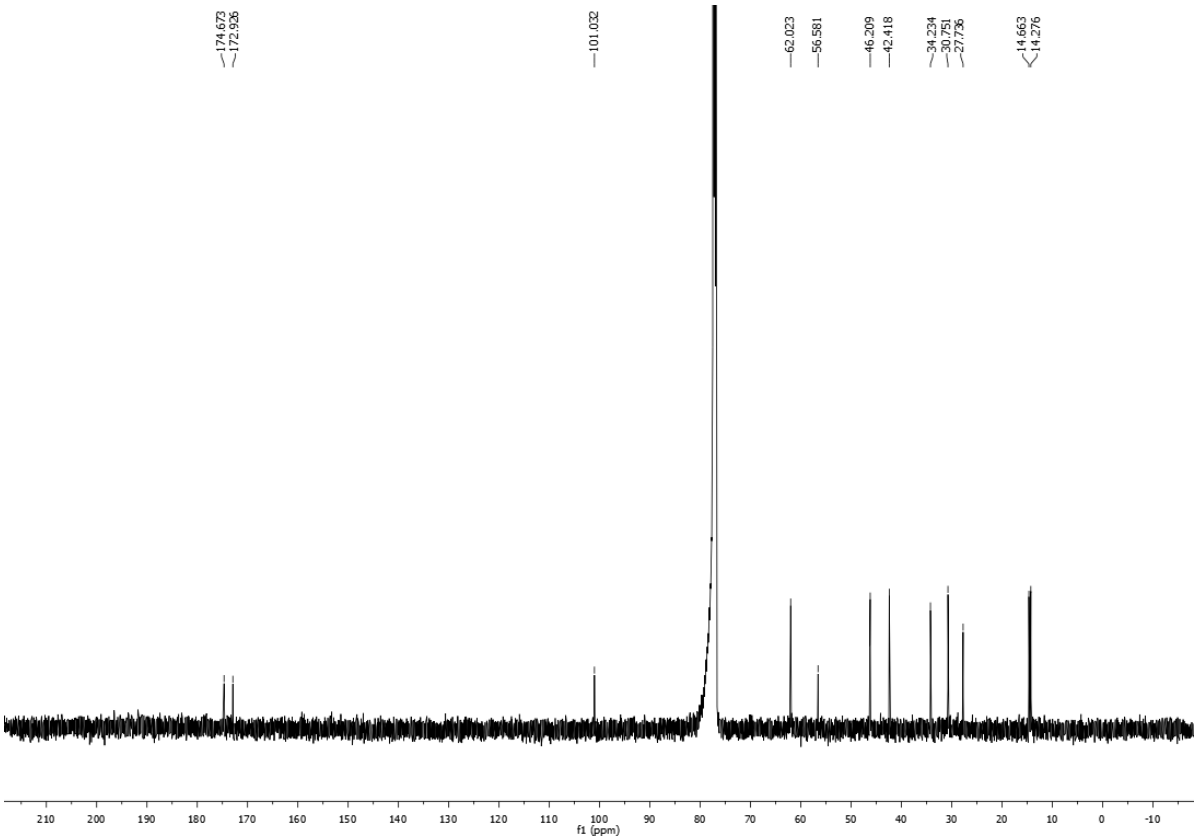

CO2t-Bu
O
N
Me
OH
Cl
Cl
2e
7.214
7.057
4.194
3.123
3.102
2.962
2.931
f1 (ppm)
173.889
173.055
143.688
134.946
127.202
126.599
99.867
83.251
56.461
53.431
42.234
35.582
33.972
27.999
27.733
27.250
f1 (ppm)

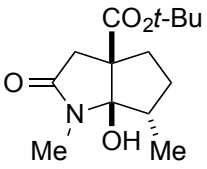

CO2t-Bu
O
N
Me
OH
2f
f1 (ppm)


CO2Et
O
N
Me
OH
Me

2g

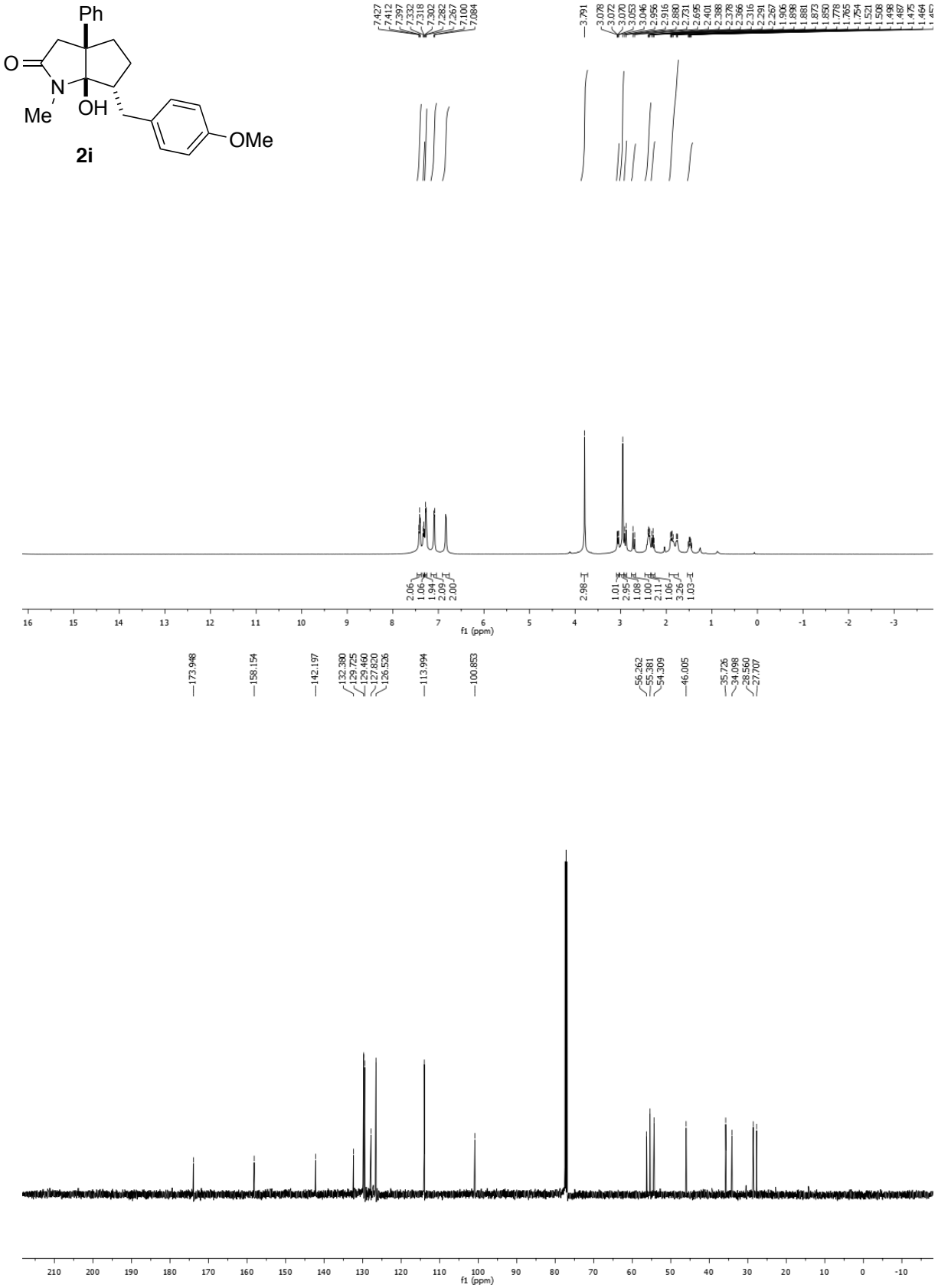
7.260
4.252
4.237
4.223
4.209
3.562
2.894
2.423
2.413
2.399
2.387
2.369
2.334
2.237
2.222
2.212
2.200
2.187
1.870
1.866
1.858
1.853
1.845
1.840
1.775
1.771
1.763
1.759
1.749
1.744
1.737
1.733
1.309
1.295
1.281
1.069
1.98
0.83
1.04
2.95
0.96
1.01
1.05
1.05
1.00
1.05
3.02
2.95
f1 (ppm)

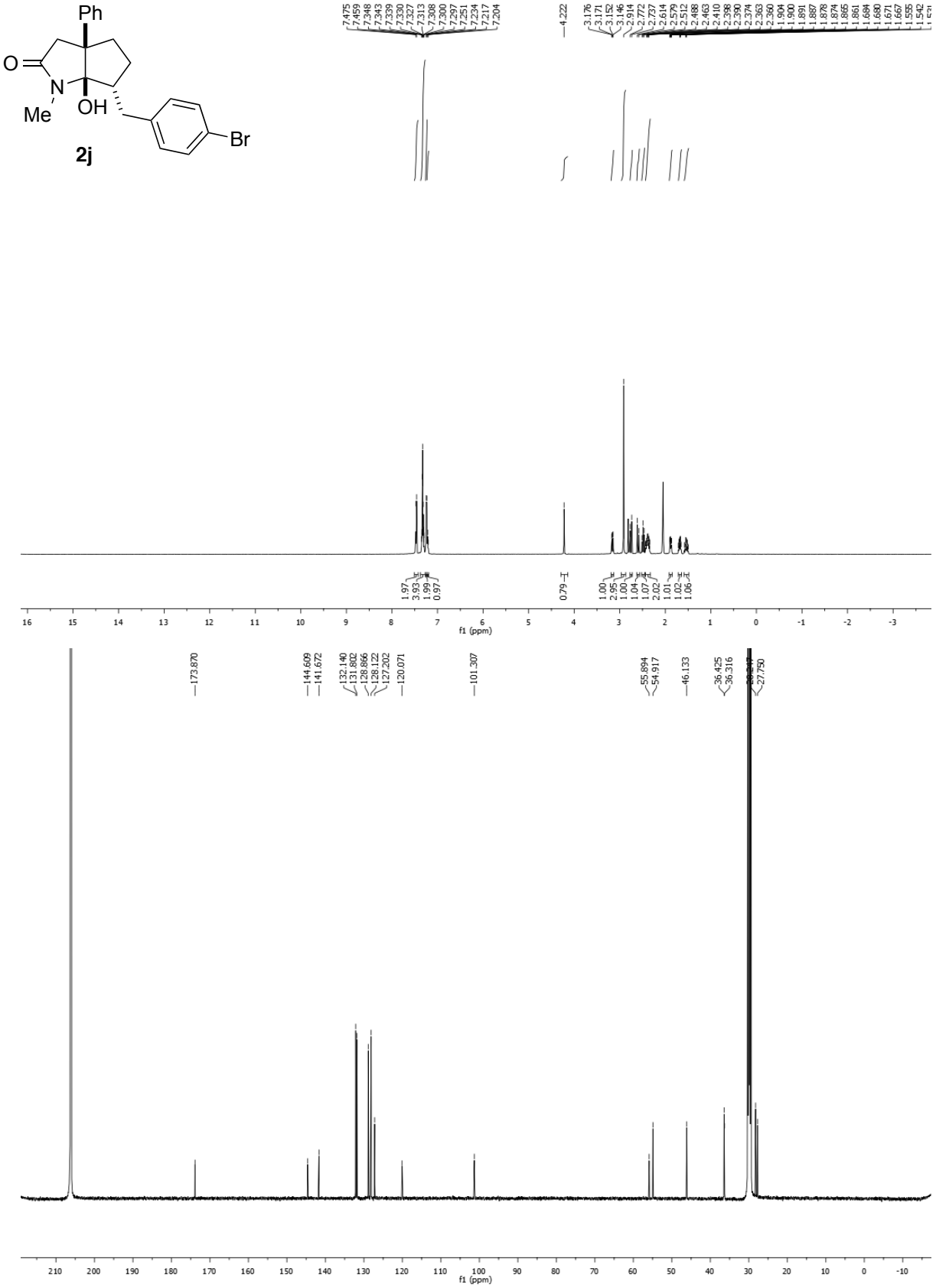

174.673
172.926
101.032
62.023
56.581
46.209
42.418
34.234
30.751
27.736
14.663
14.276
f1 (ppm)

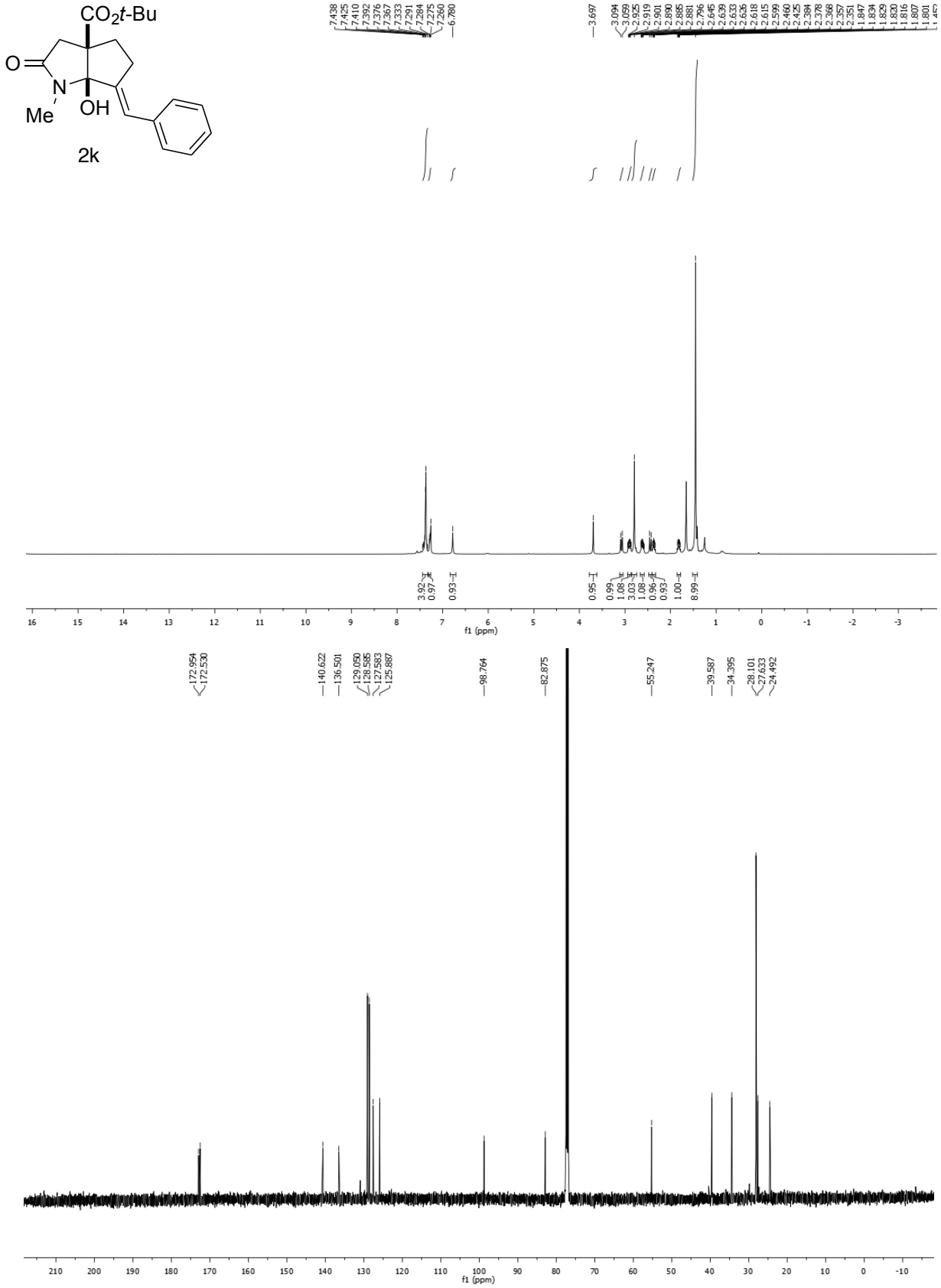

CO2t-Bu
O
N
Me
OH
Me

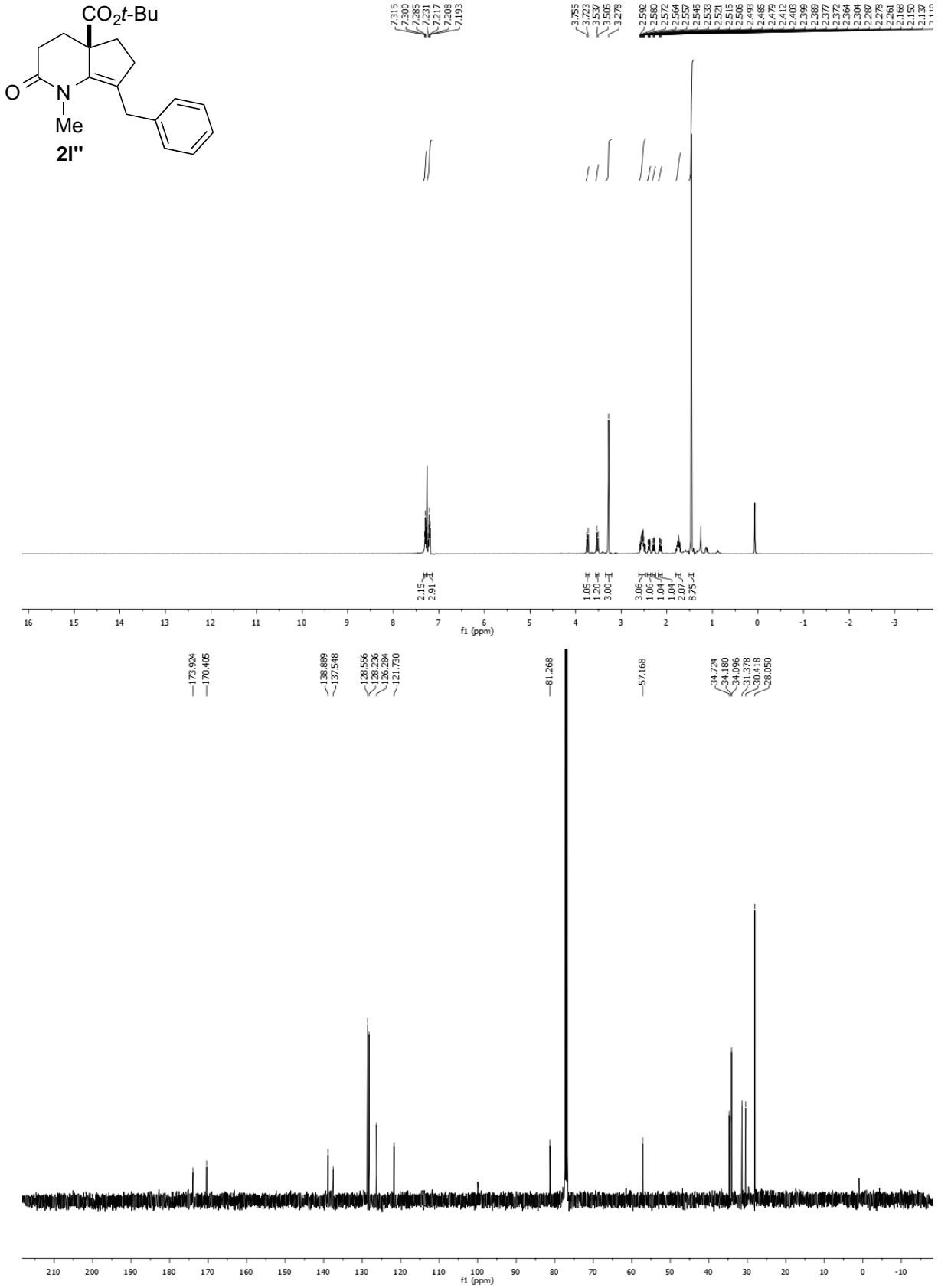
2h

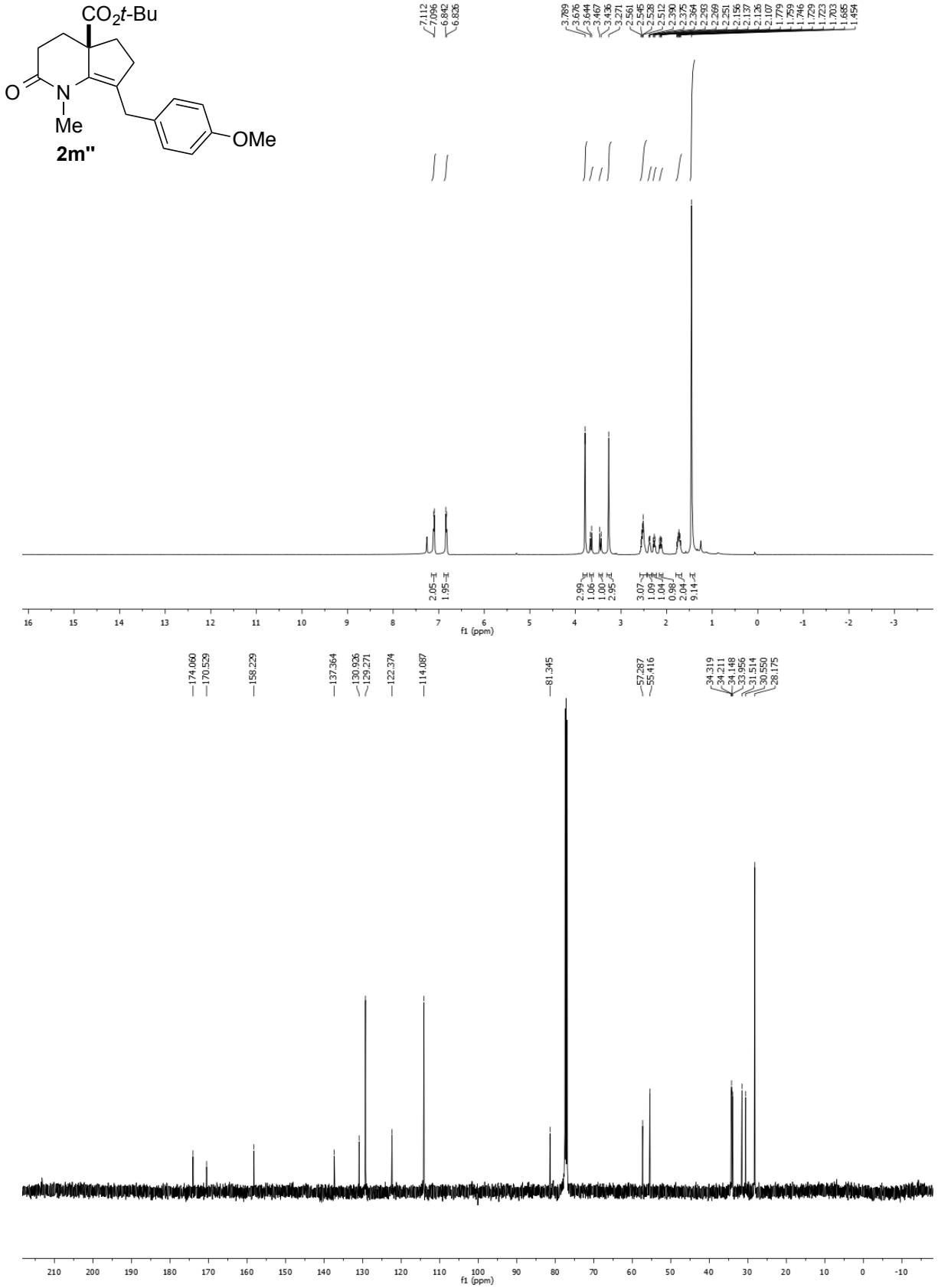
7.288
3.880
2.967
2.932
2.909
0.94
1.18
2.94
2.00
1.05
1.09
1.11
9.10
1.08
3.00
f1 (ppm)
174.064
173.006
100.896
83.030
56.873
46.305
42.589
34.253
30.650
28.141
27.617
14.733
f1 (ppm)

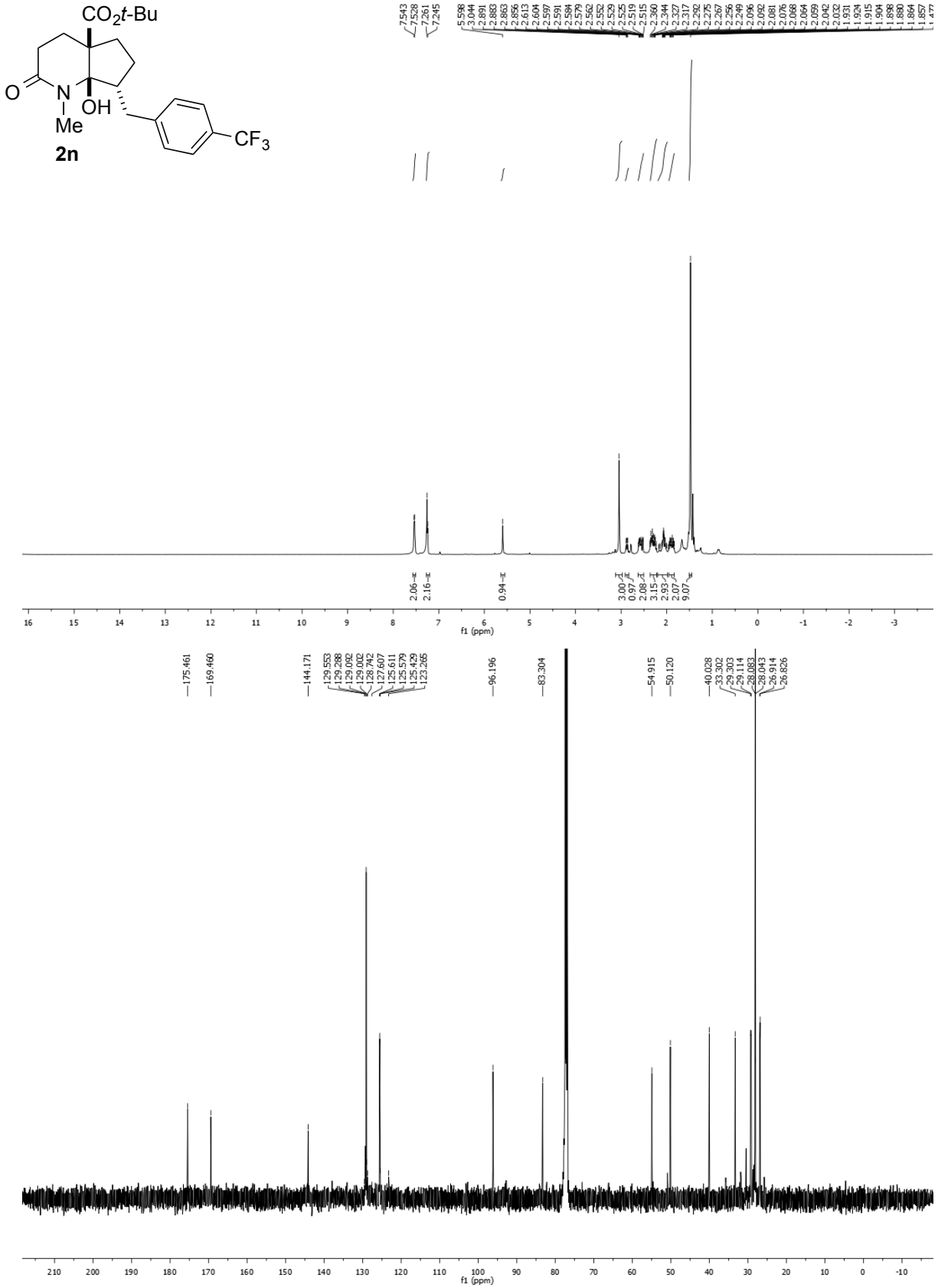

Ph
O
N
Me
OH
OMe
2i
f1 (ppm)

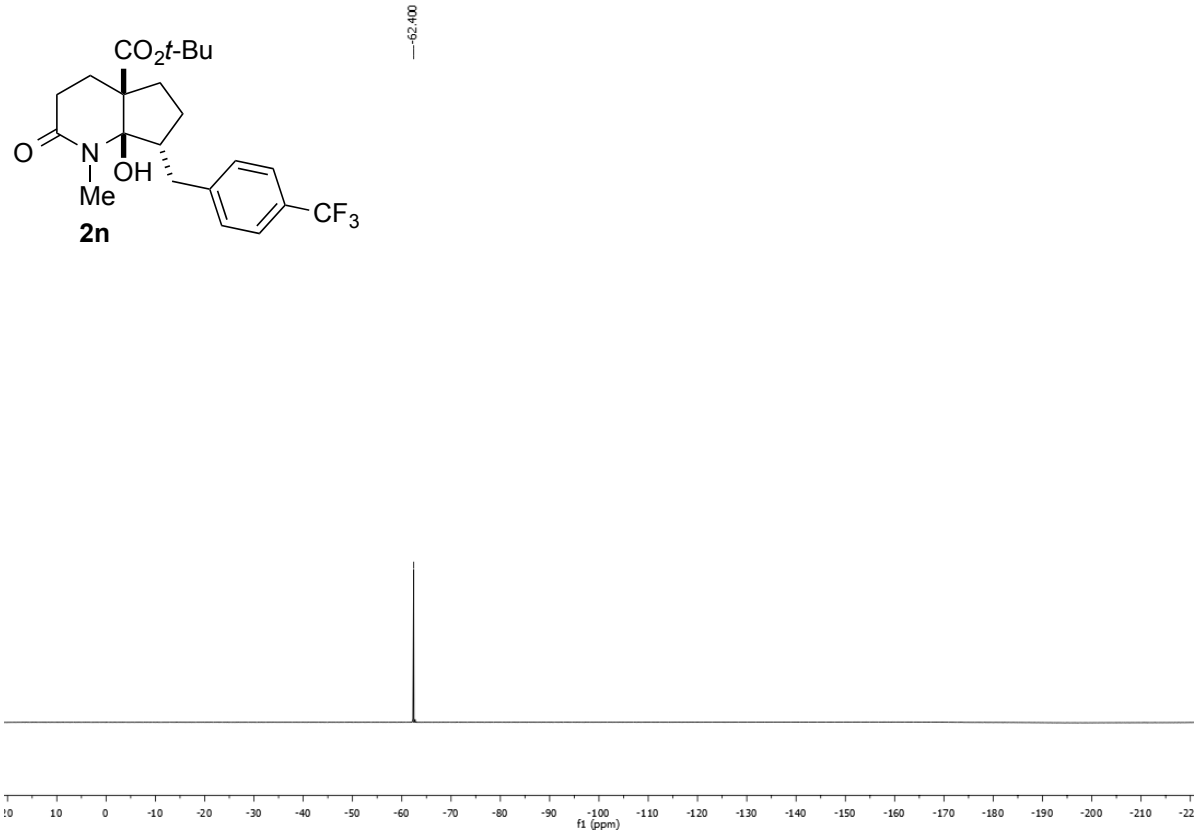

Ph
O
N
Me
OH
Br
2j
f1 (ppm)
f1 (ppm)

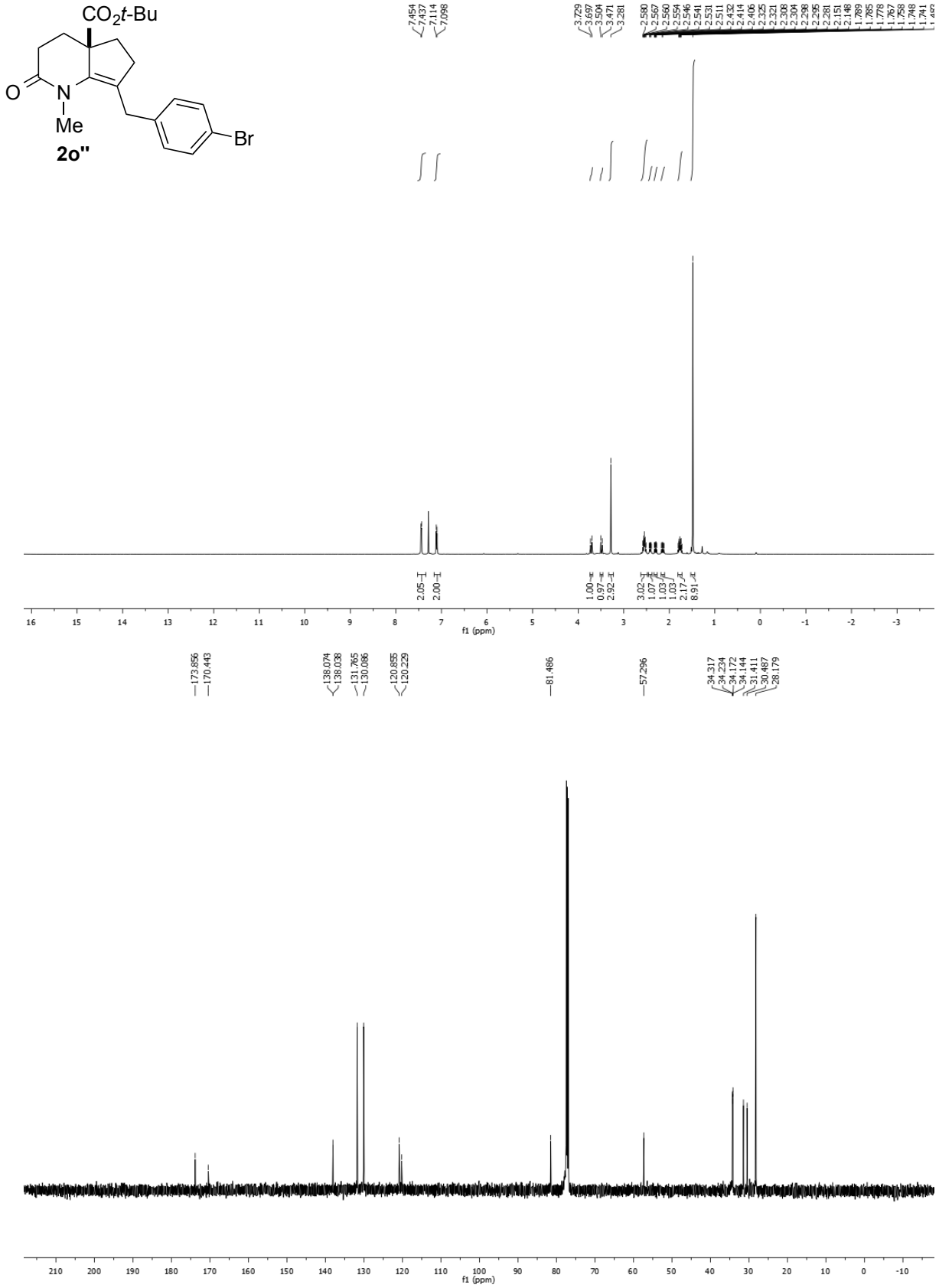

CO2t-Bu
O
N
Me
OH
2k
f1 (ppm)
f1 (ppm)

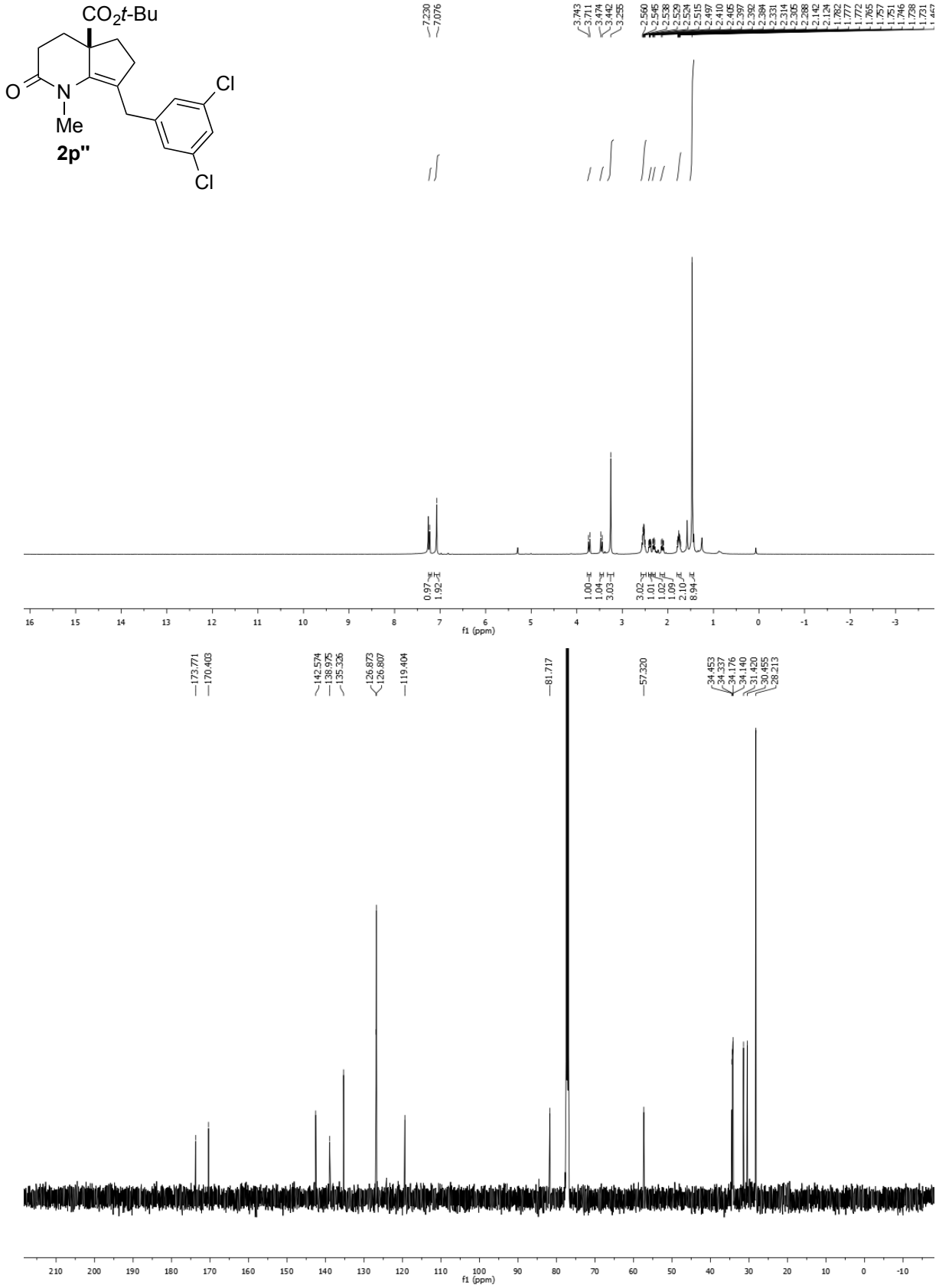

CO2t-Bu
O
N
Me
2l''
f1 (ppm)
f1 (ppm)

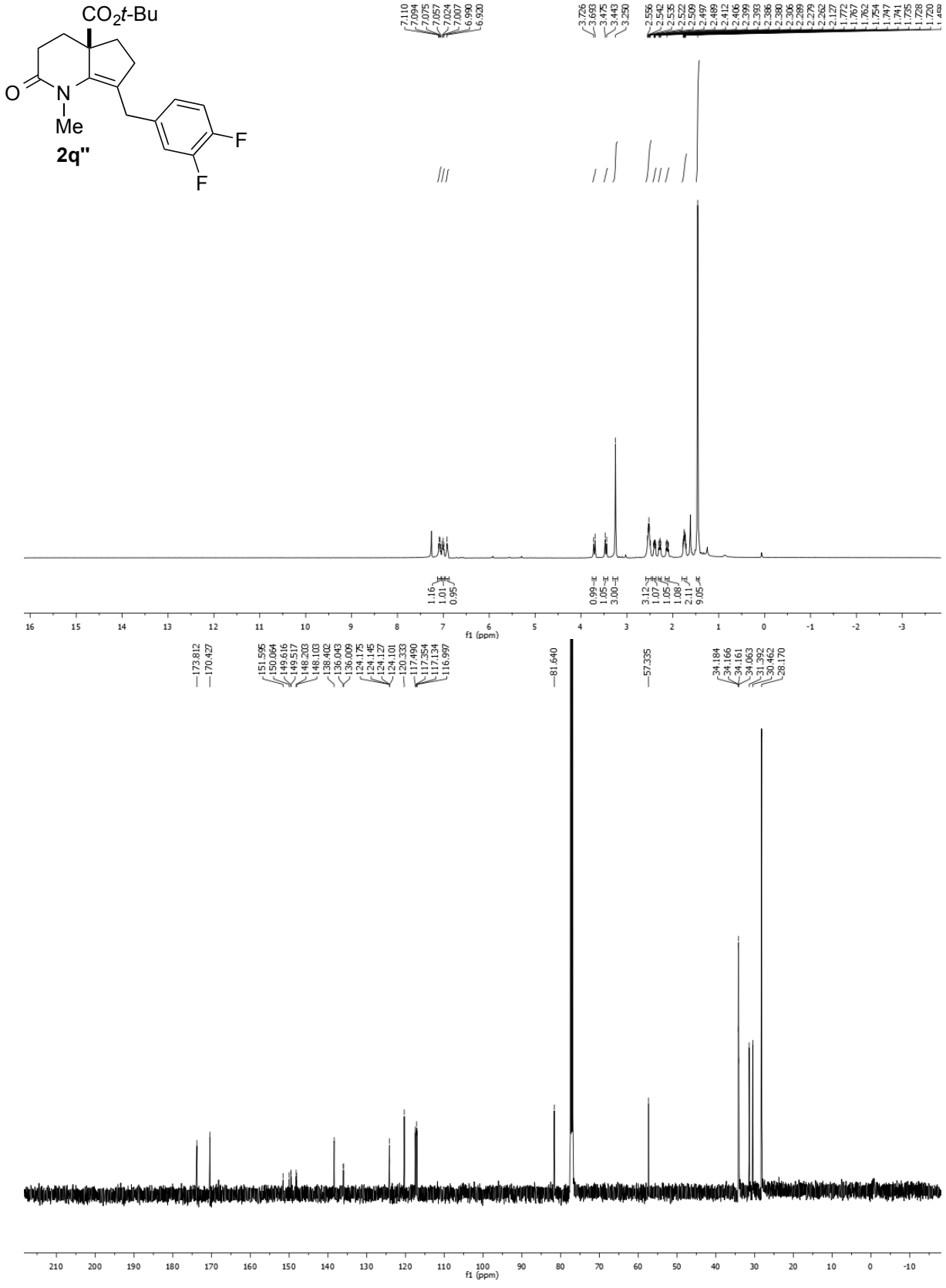

CO2t-Bu
O
N
Me
OMe
2m''
f1 (ppm)

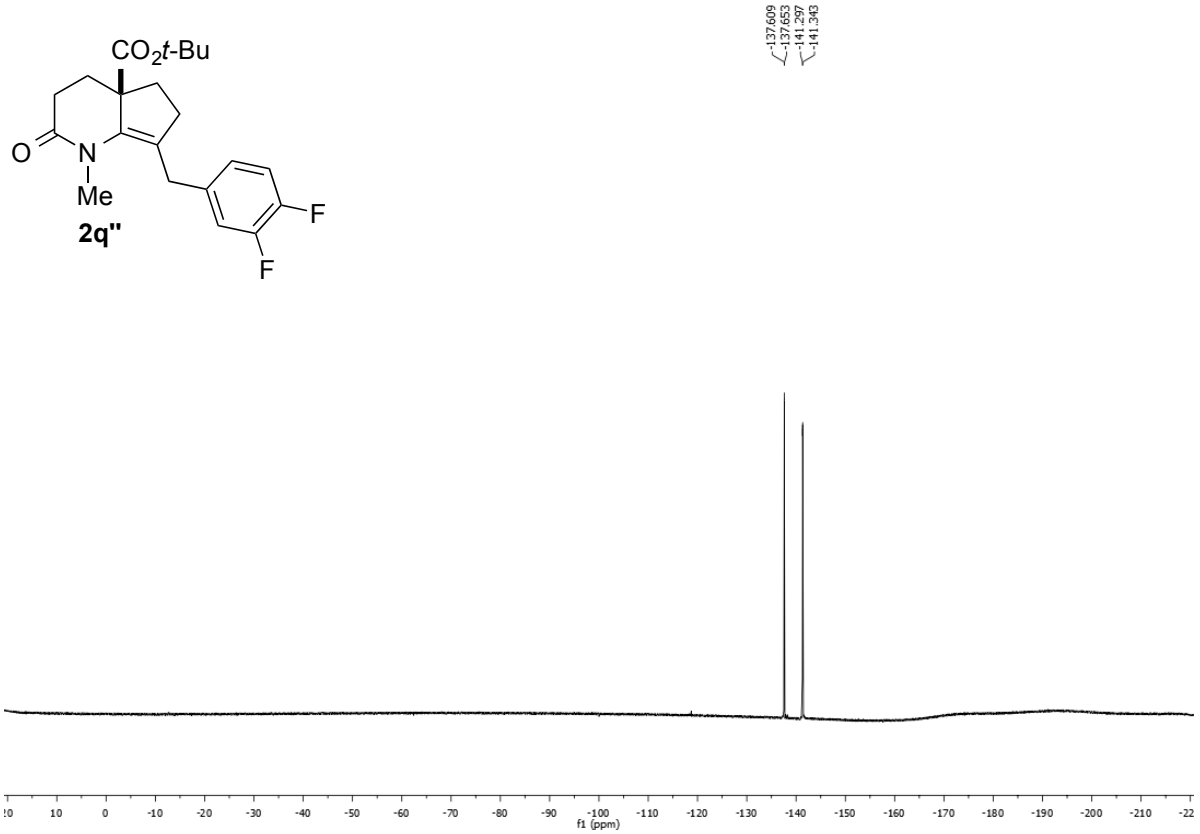

CO2t-Bu
O
N
Me
OH
CF3
2n
f1 (ppm)

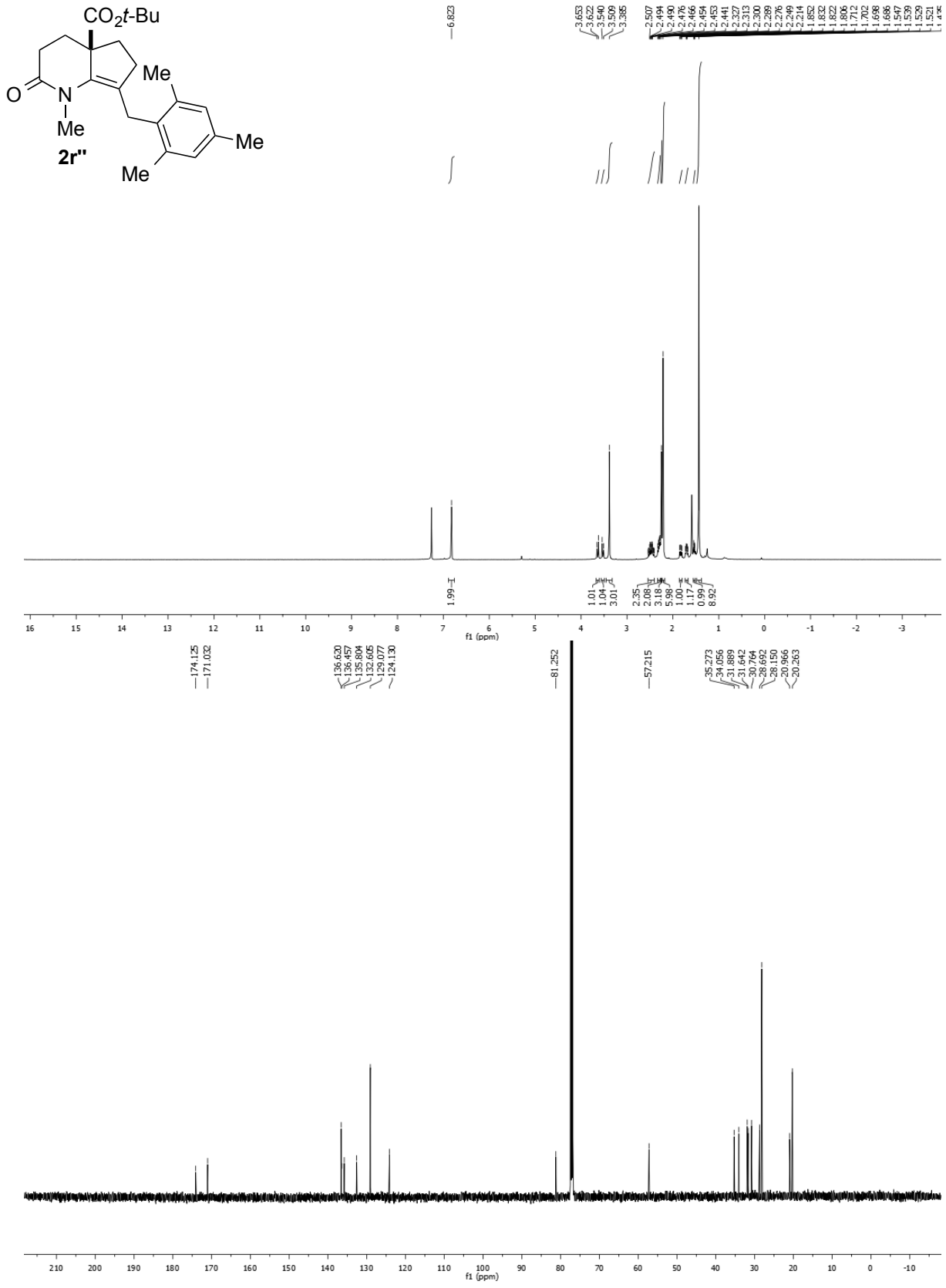

CO2t-Bu
O
N
OH
Me
CF3
2n
-62.400
f1 (ppm)

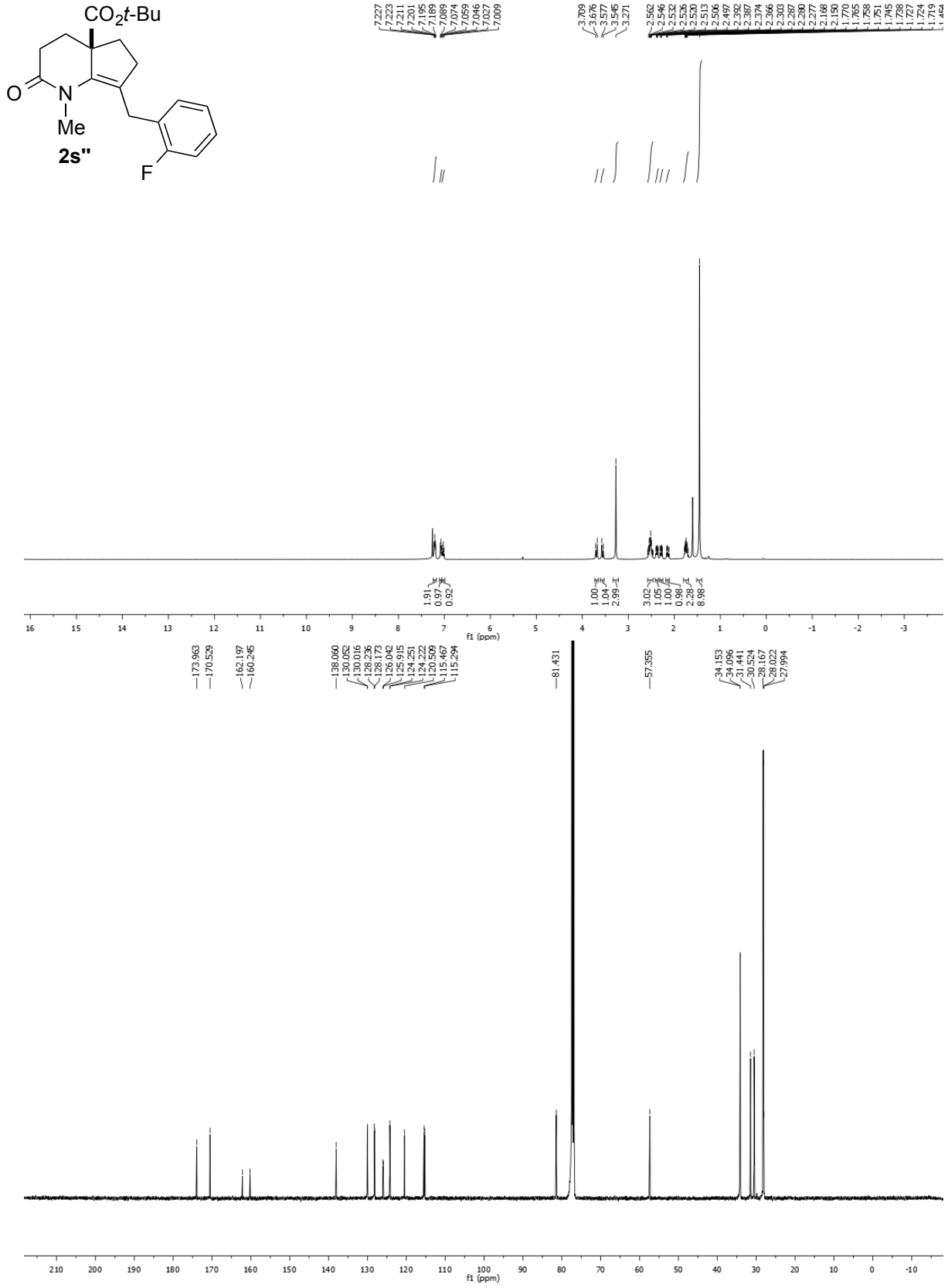

CO2t-Bu
O
N
Me
Br
2o"
f1 (ppm)

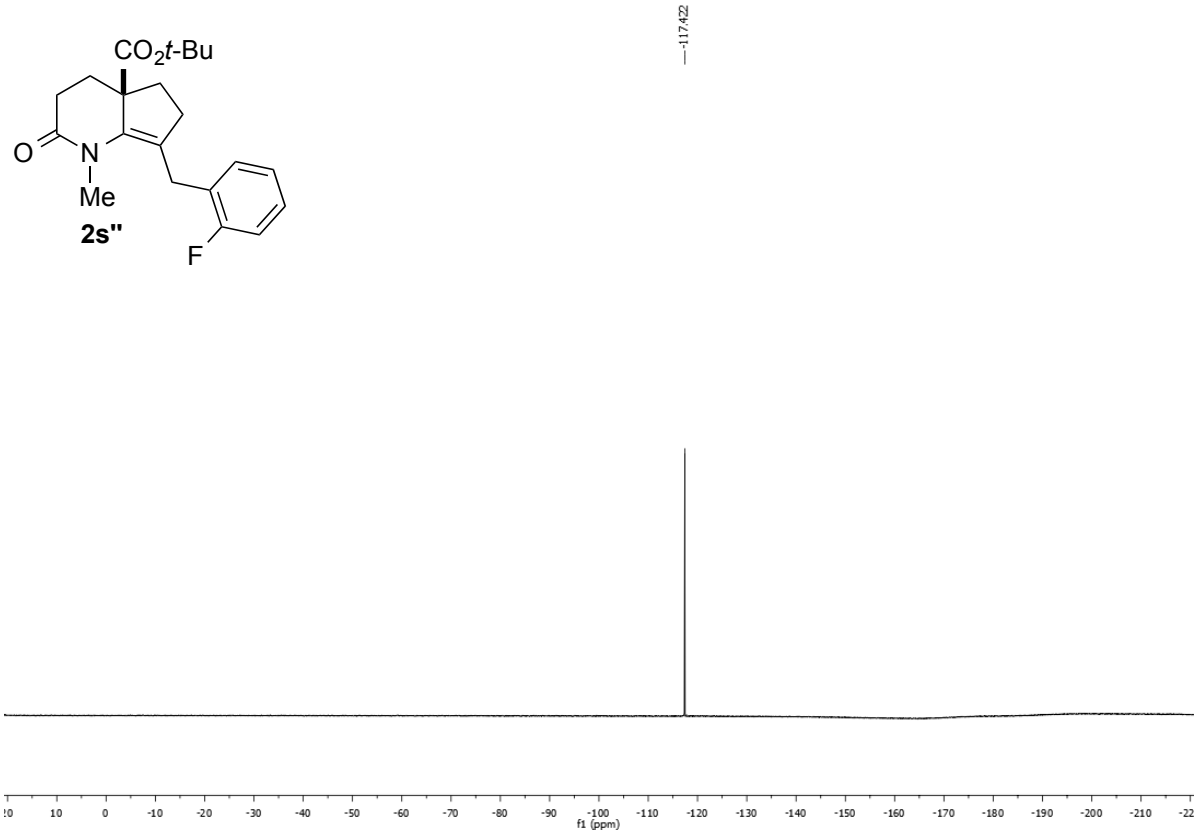

CO2t-Bu
O
N
Me
Cl
Cl
2p"
f1 (ppm)
f1 (ppm)

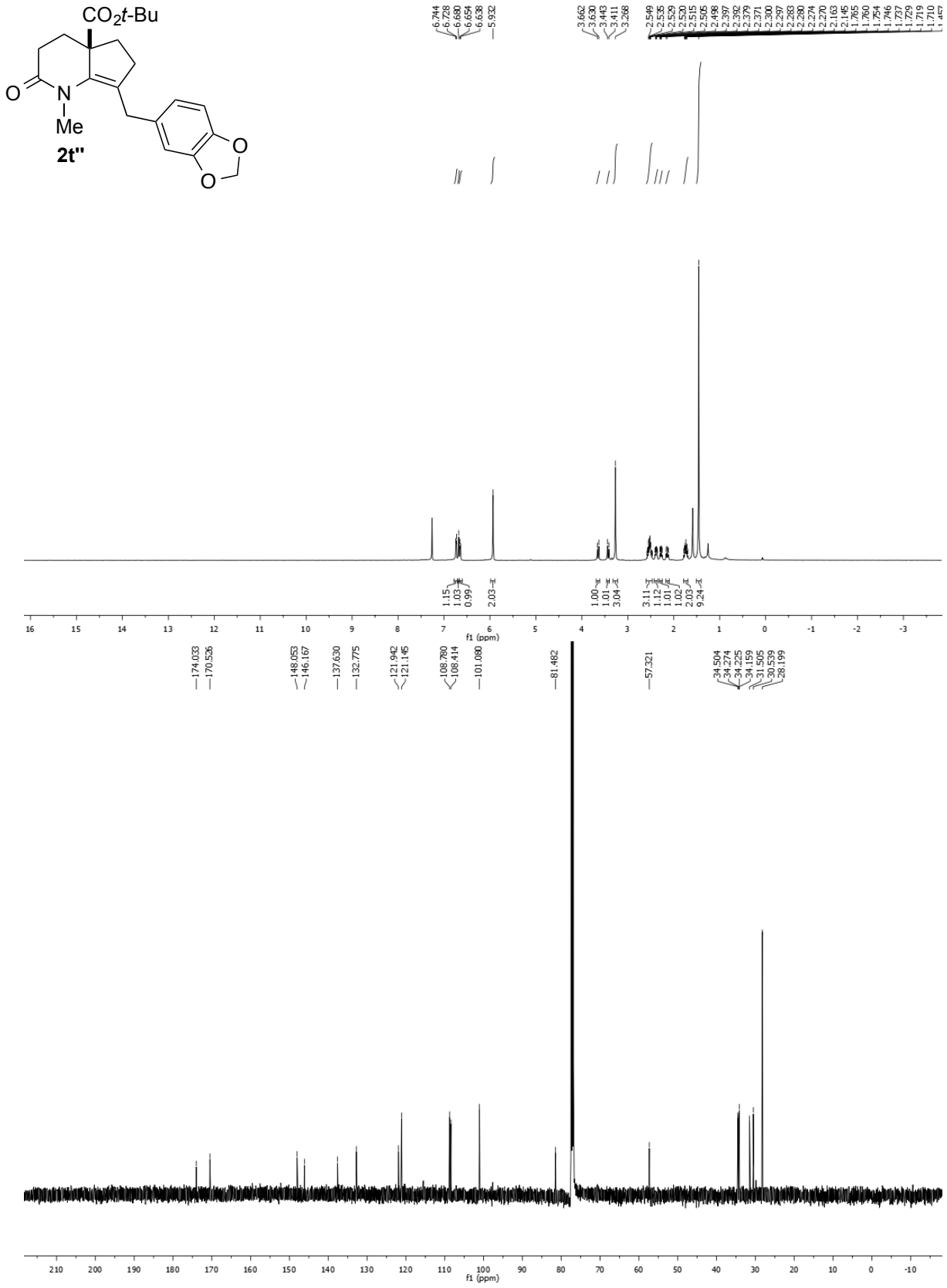

CO2t-Bu
O
N
Me
F
F
2q"
f1 (ppm)

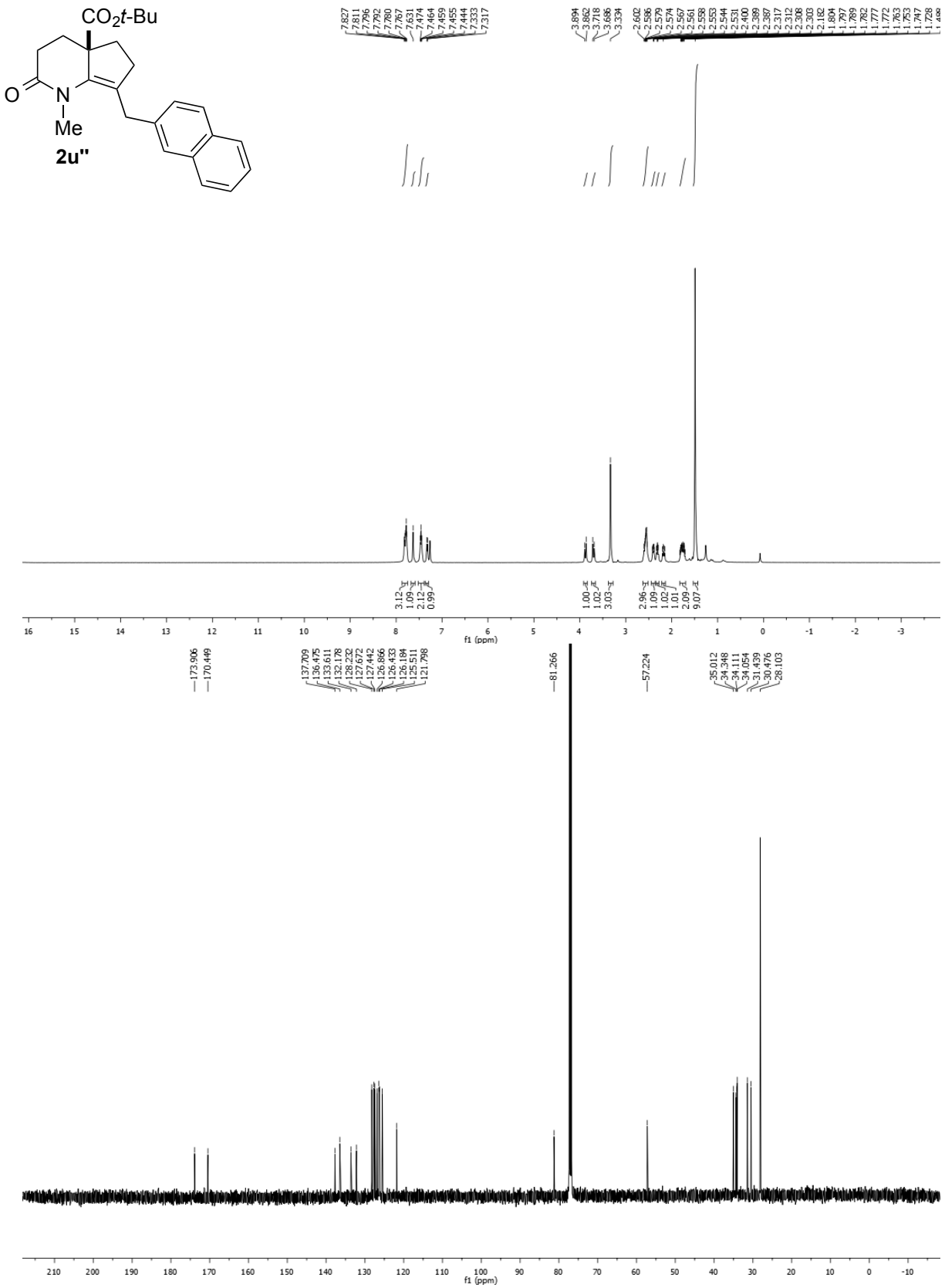

CO2t-Bu
O
N
Me
2q''
F
F
-137.609
-137.653
-141.297
-141.343
f1 (ppm)

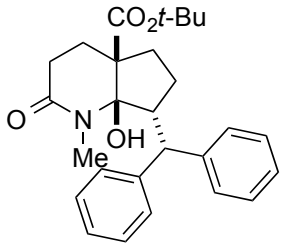

CO2t-Bu
O
N
Me
Me
Me
Me
Me
2r''
f1 (ppm)
f1 (ppm)


CO2t-Bu
O
N
Me
2s"
F
f1 (ppm)


CO2t-Bu
O
N
Me
2s"
F
-117.422
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

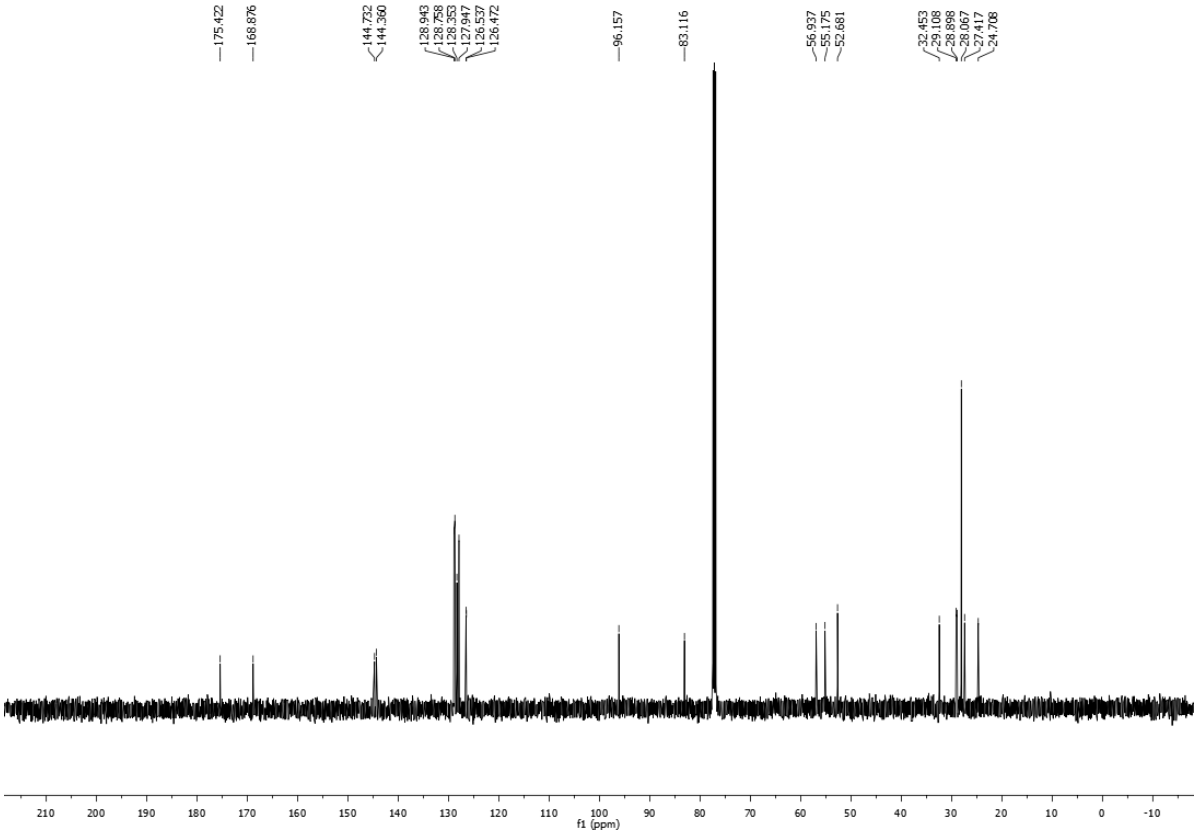

CO2t-Bu
O
N
Me
2t''
O
O
6.744
6.728
6.680
6.654
6.638
5.932
3.662
3.630
3.443
3.411
3.268
2.549
2.535
2.529
2.530
2.515
2.505
2.498
2.397
2.392
2.379
2.371
2.300
2.297
2.283
2.280
2.274
2.270
2.163
2.145
1.765
1.760
1.754
1.746
1.737
1.729
1.719
1.710
1.457
1.15
1.03
0.99
2.03
1.00
1.01
3.04
3.11
1.12
1.01
1.02
2.03
9.24
f1 (ppm)
174.033
170.526
148.053
146.167
137.630
132.775
121.942
121.145
108.780
108.414
101.080
81.482
57.321
34.504
34.274
34.225
34.159
31.505
30.539
28.199
f1 (ppm)

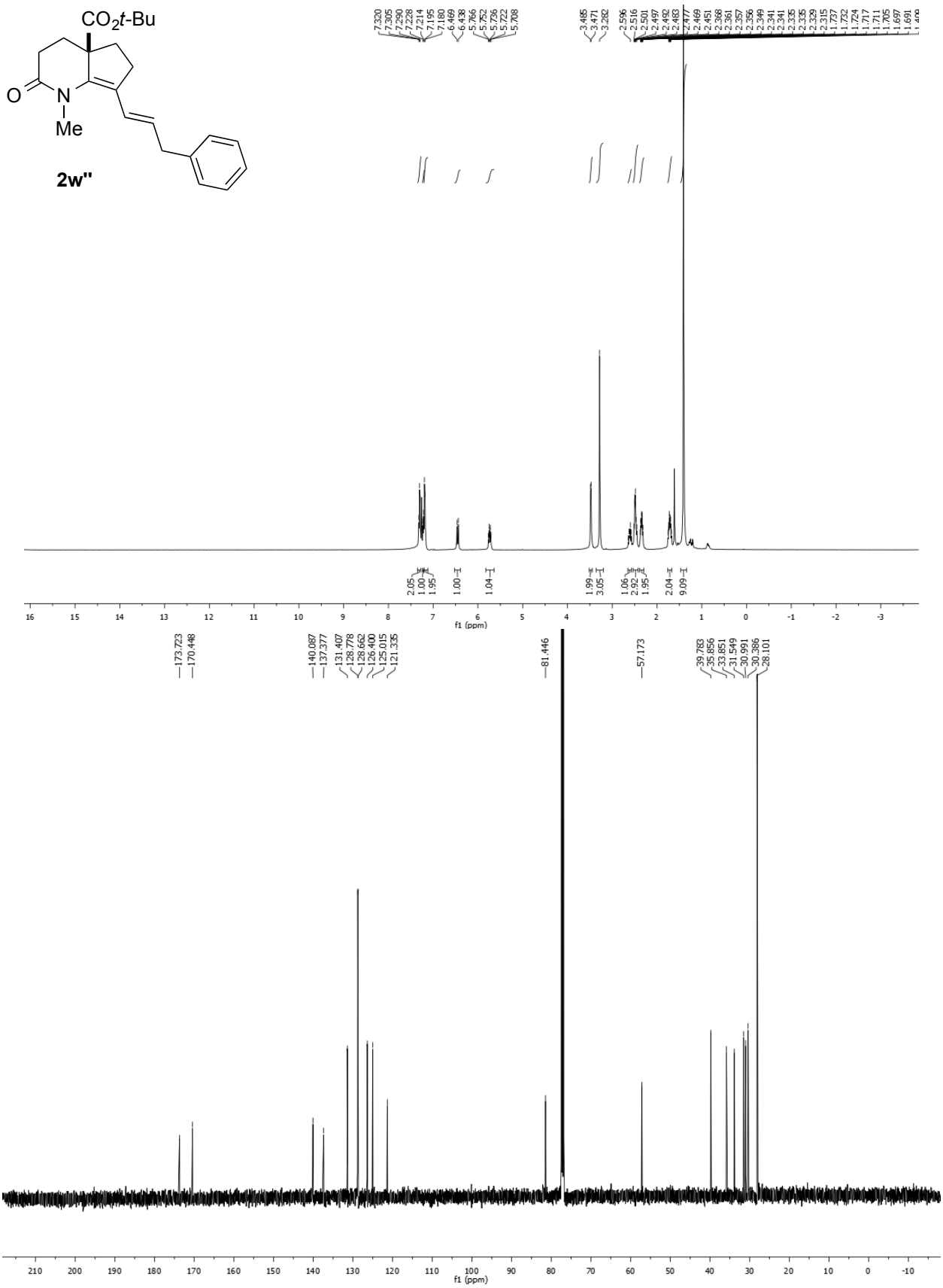

CO2t-Bu
O
N
Me
2u''
f1 (ppm)

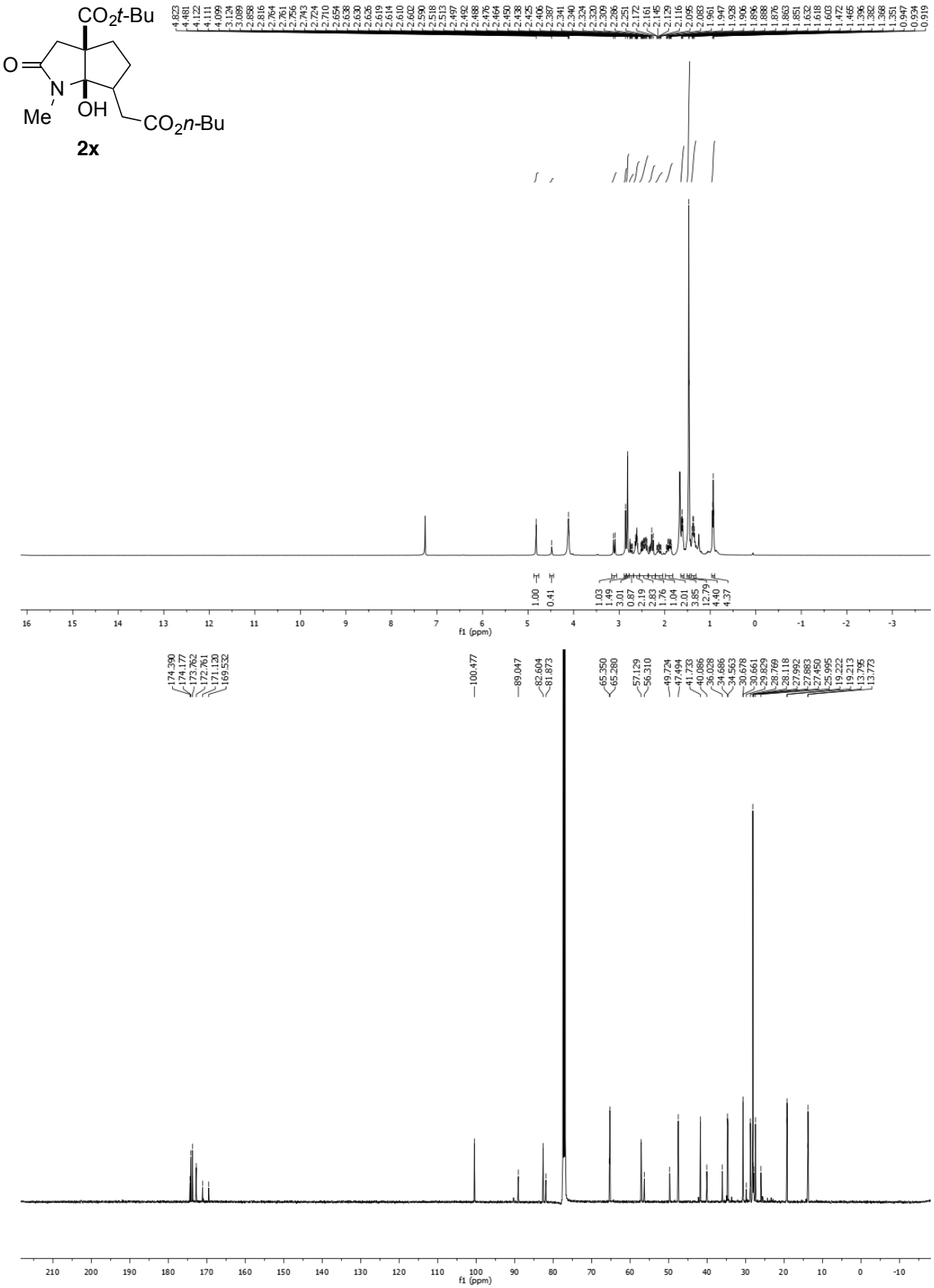

CO2t-Bu
O
N
Me
OH

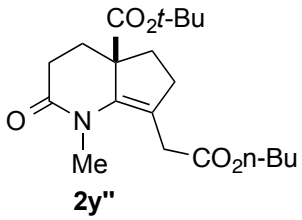
2v

7.296
7.281
7.261
7.259
7.247
7.231
7.227
7.215
7.138
7.134
7.124
7.110
7.095
5.521
3.763
3.741
3.382
3.363
3.348
3.328
2.636
2.630
2.615
2.610
2.589
2.581
2.573
2.407
2.384
2.368
2.350
2.330
2.212
2.192
2.170
2.147
2.073
2.048
2.027
2.008
2.004
1.995
1.692
1.674
1.650
2.99
5.08
2.04
1.07
0.99
1.00
1.02
1.06
1.19
6.08
1.29
1.01
9.09
f1 (ppm)


175.422
168.876
144.732
144.360
128.943
128.758
128.353
127.947
126.537
126.472
96.157
83.116
56.937
55.175
52.681
32.453
29.108
28.898
28.067
27.417
24.708
f1 (ppm)

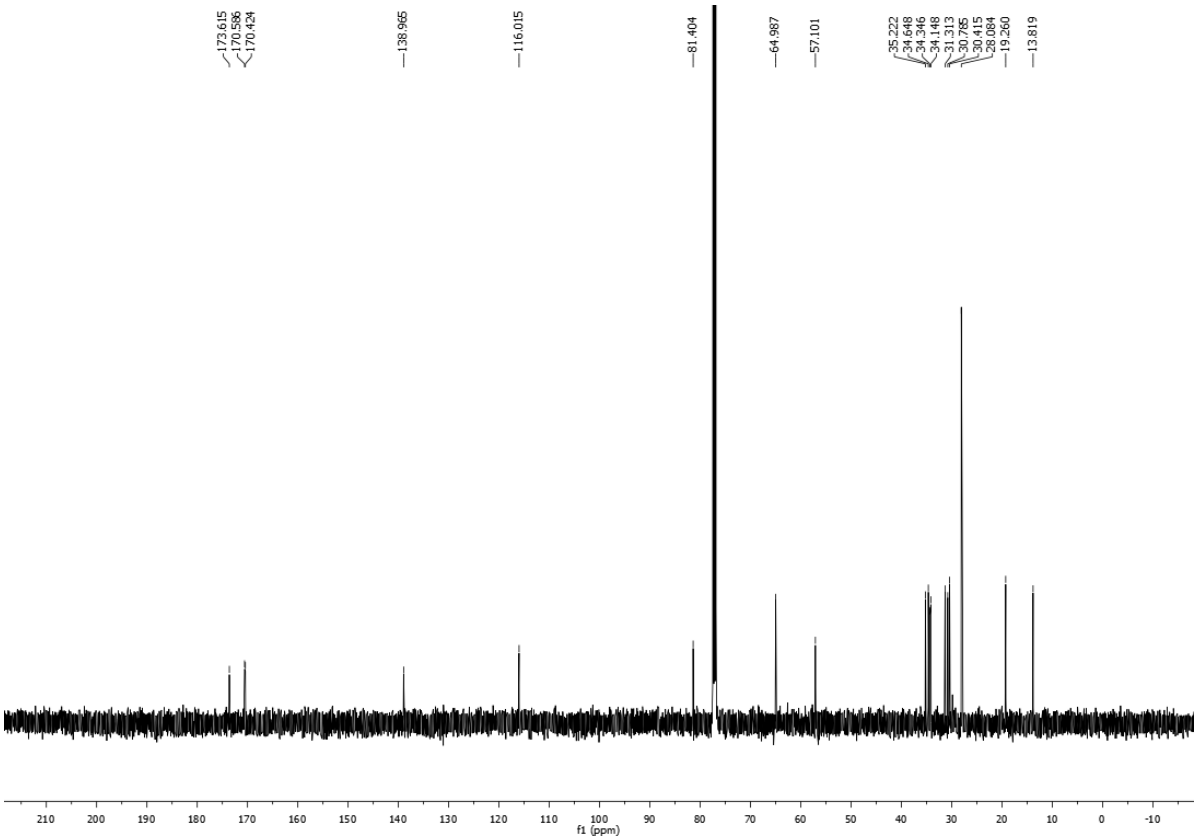

CO2t-Bu
O
N
Me
2w''
f1 (ppm)
f1 (ppm)

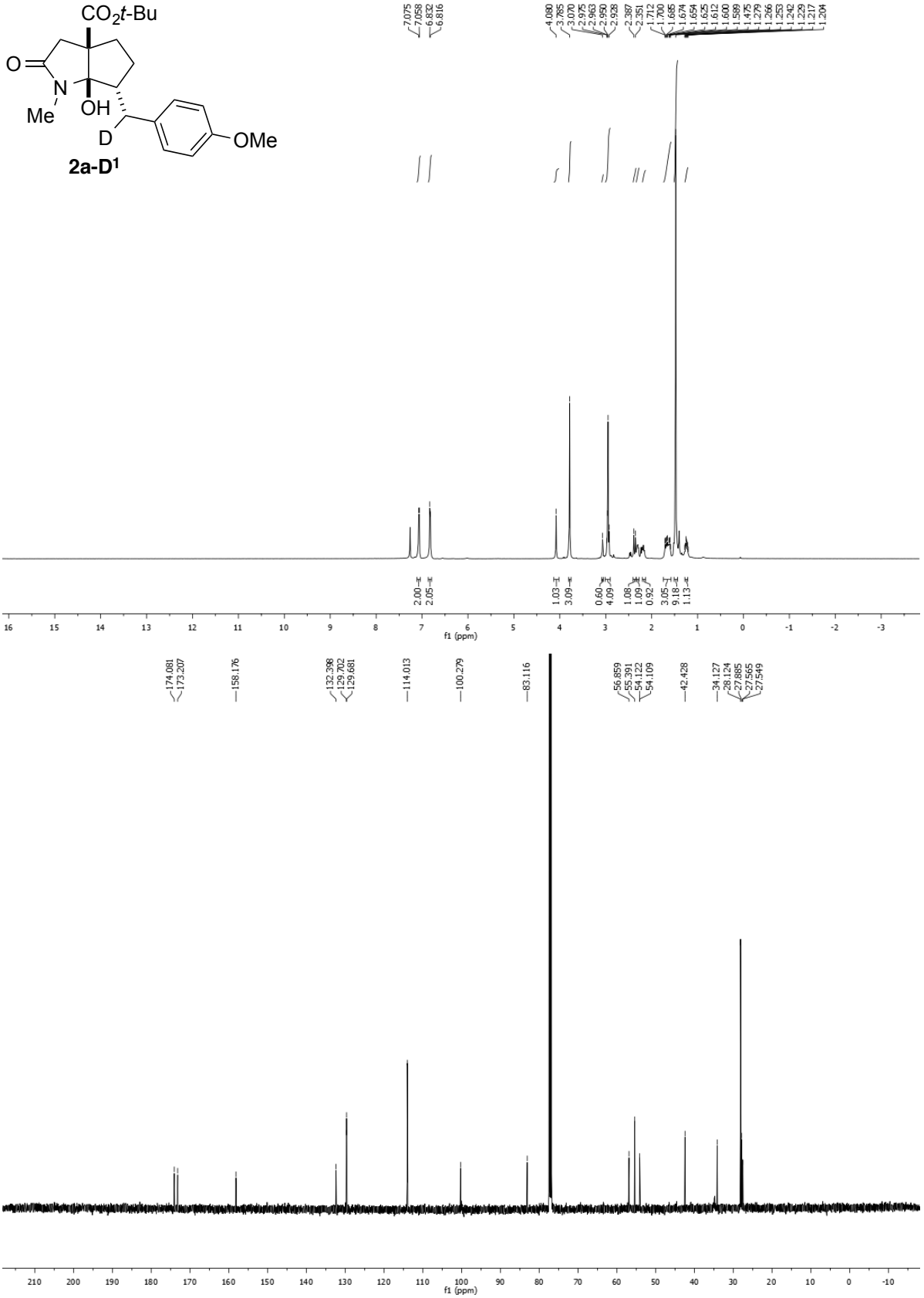

CO2t-Bu
O
N
Me
OH
CO2n-Bu
2x
f1 (ppm)
f1 (ppm)

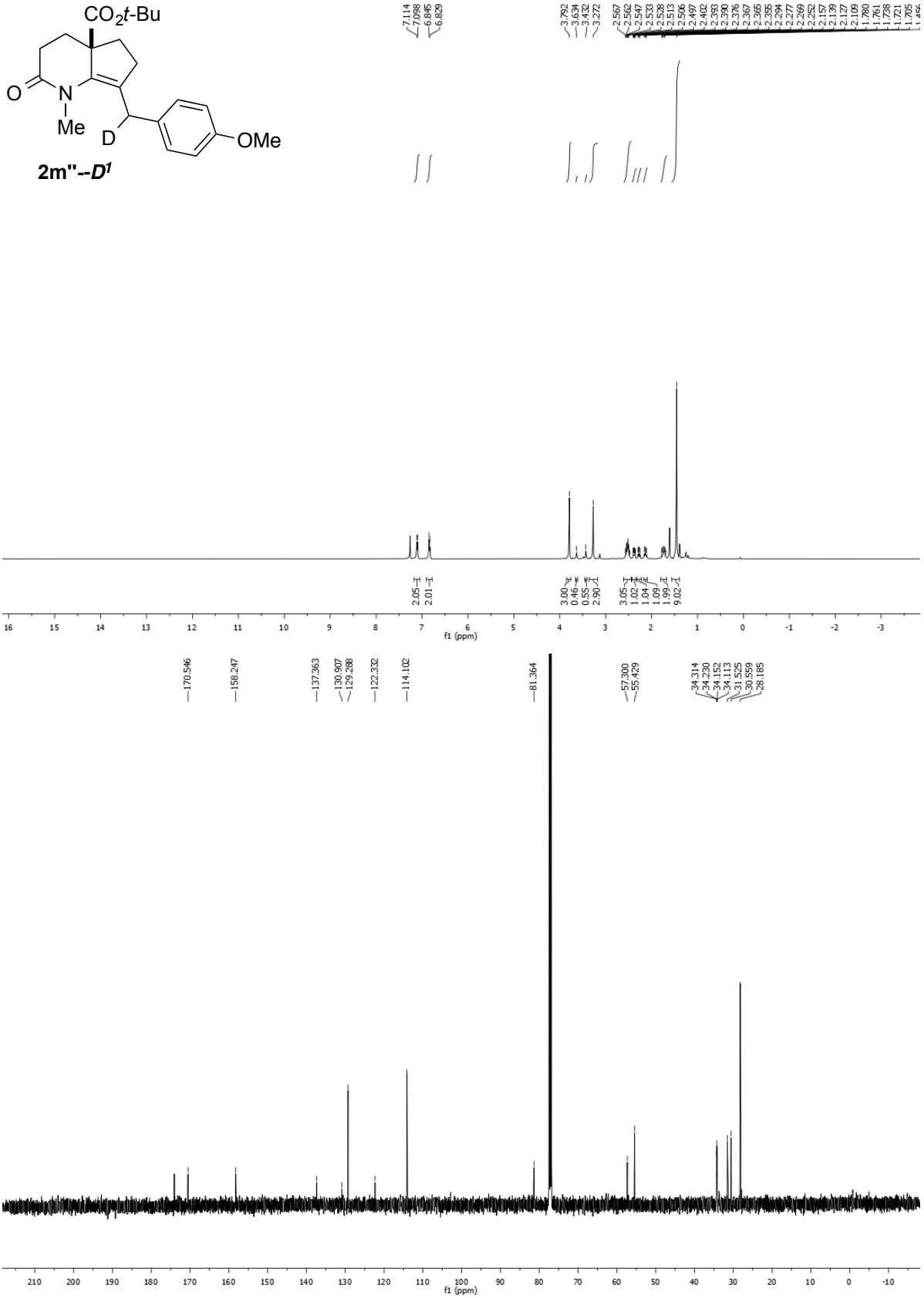

CO2t-Bu
O
N
Me
CO2n-Bu

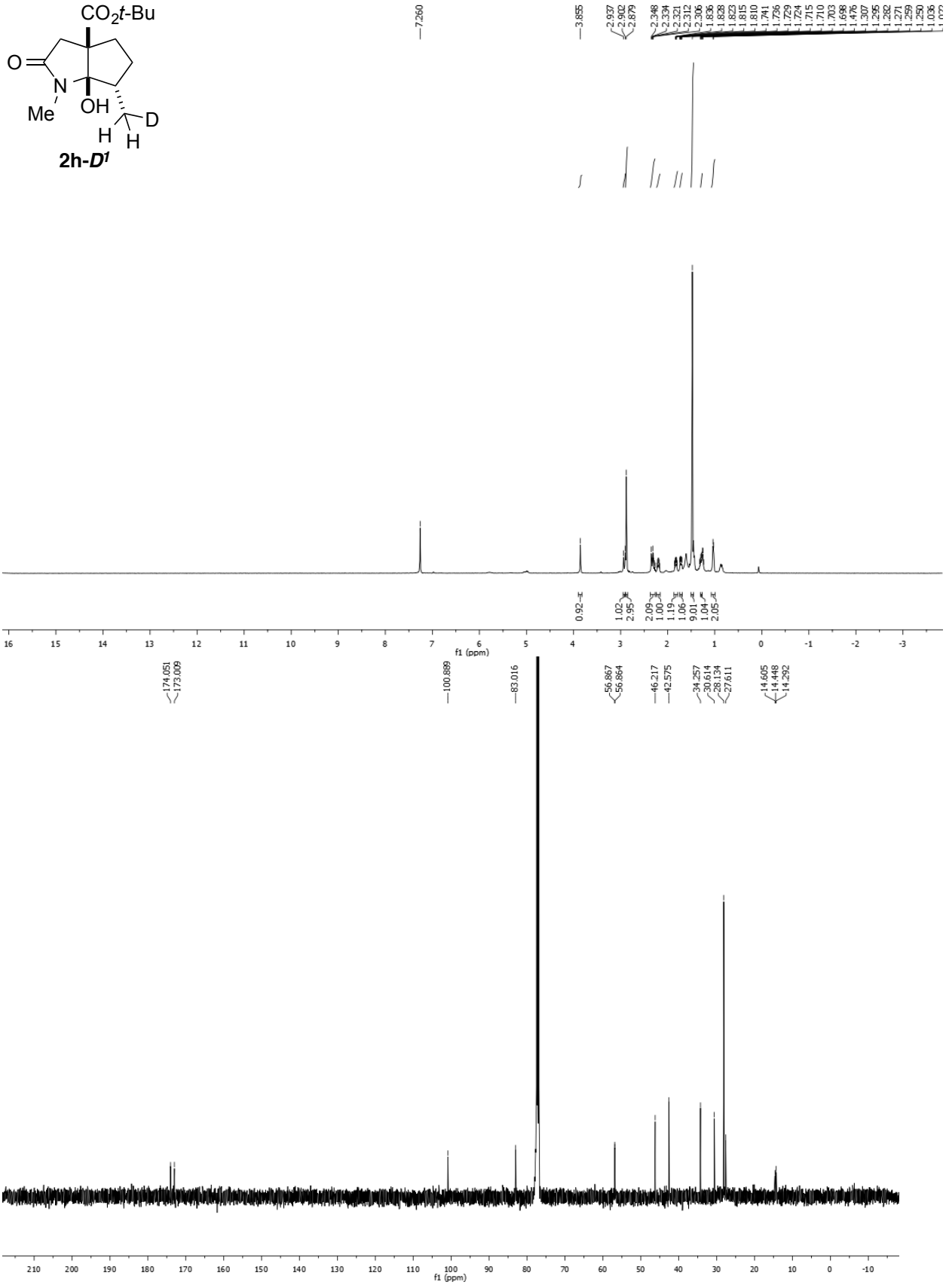
2y"

7.260
4.112
4.099
4.086
3.353
3.321
3.293
3.192
3.161
2.515
2.492
2.482
2.469
2.457
2.357
2.333
2.314
2.300
2.281
1.761
1.725
1.729
1.720
1.714
1.709
1.638
1.625
1.610
1.595
1.581
1.415
1.394
1.364
1.349
0.945
0.930
1.86
1.00
2.78
0.89
0.96
1.95
2.16
2.04
3.02
3.94
2.06
2.90
f1 (ppm)


173.615
170.586
170.424
138.965
116.015
81.404
64.987
57.101
35.222
34.648
34.346
34.148
31.313
30.785
30.415
28.084
19.260
13.819
f1 (ppm)


CO2t-Bu
O
N
Me
OH
D
OMe
2a-D1
f1 (ppm)


CO2t-Bu
O
N
Me
D
OMe
2m''--D1
7.114
7.098
6.845
6.829
3.792
3.634
3.432
3.272
2.567
2.562
2.547
2.533
2.528
2.513
2.506
2.497
2.402
2.393
2.390
2.376
2.367
2.365
2.355
2.294
2.277
2.269
2.252
2.157
2.139
2.127
2.109
1.780
1.761
1.738
1.721
1.705
2.05
2.01
3.00
0.46
0.55
2.90
3.05
1.02
1.04
1.09
1.99
9.02
f1 (ppm)
170.546
158.247
137.363
130.907
129.288
122.332
114.102
81.364
57.300
55.429
34.314
34.230
34.152
34.113
31.525
30.559
28.185
f1 (ppm)


CO2t-Bu
O
N
Me
OH
H
H
D
2h-D1
7.260
3.855
2.937
2.902
2.879
2.348
2.334
2.321
2.312
2.306
1.836
1.828
1.823
1.815
1.810
1.741
1.736
1.729
1.724
1.715
1.710
1.703
1.698
1.476
1.307
1.295
1.282
1.271
1.259
1.250
1.036
0.92
1.02
2.95
2.09
1.00
1.19
1.06
9.01
1.04
2.05
f1 (ppm)
174.051
173.009
100.889
83.016
56.867
56.864
46.217
42.575
34.257
30.614
28.134
27.611
14.605
14.448
14.292
f1 (ppm)