Pd(II)-Catalyzed Carbonylation of sp^3 C–H Bonds: A New Entry to 1,4-Dicarbonyl Compounds

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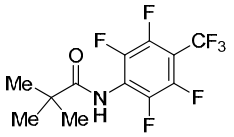
Table of Contents

General Information: Solvents were obtained from Sigma-Aldrich, Alfa-Aesar and Acros and used directly without further purification. Carboxylic acids or carboxylic acid chlorides and 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline were obtained from the commercial sources and used to prepare the corresponding amides. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. ^{1}H NMR spectra were recorded on Varian Inova instrument (400 MHz) and Bruker DRX (500 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to the residual undeuterated solvent peak or 0.0 ppm for tetramethylsilane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad, a = apparent. Coupling constants, *J*, were reported in Hertz unit (Mz). ^{13}C NMR spectra were recorded on Varian Inova instrument (100 MHz) and Bruker DRX (125 MHz) and were fully

decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.0 ppm of chloroform-*d*. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). IR spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrometer. Frequencies were given in reciprocal centimeters (cm^{-1}) and only selected absorbance was reported.

Substrate Structures



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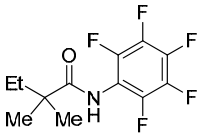

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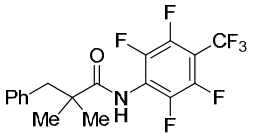

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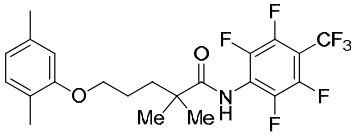

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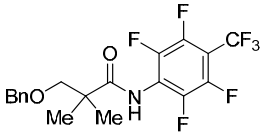

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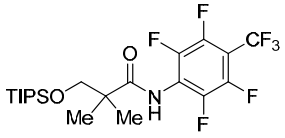

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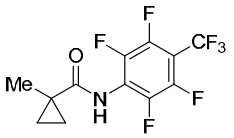

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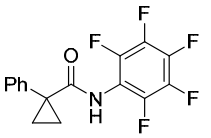

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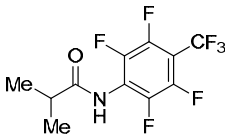

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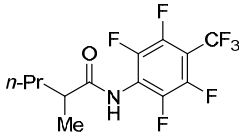

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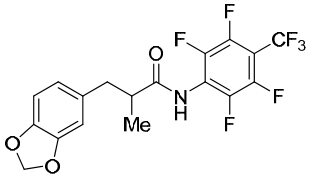
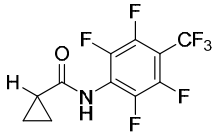


1k



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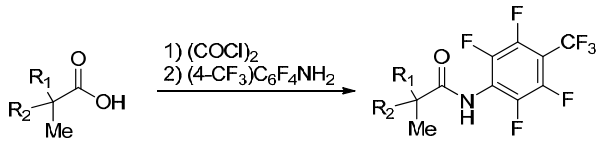
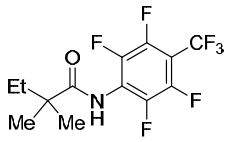
Experimental Section

A. Substrate Preparation

General Procedure for the Preparation of Amide Substrates



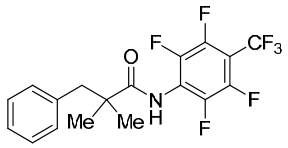
An acid chloride (10.0 mmol), prepared from the corresponding carboxylic acid and oxalyl chloride, was added to a vigorously stirring solution of 2,3,5,6-tetrafluoro-4-(trifluoromethlyl)aniline (11.0 mmol) in toluene (50 mL). The reaction mixture was stirred for 12 h under reflux, and then stirred at room temperature for 4 h. The product mixture was concentrated *in vacuo* and was recrystallized from ethyl acetate/hexane to give the amide.



1b

2,2-Dimethyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)butanamide (1b)

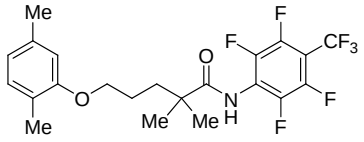
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (bs, 1H), 1.66 (q, *J* = 7.6 Hz, 2H), 1.29 (s, 6H), 0.93 (t, *J* = 7.6, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.87, 43.86, 34.24, 25.12, 9.20.



1c

2,2-Dimethyl-3-phenyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (1c)

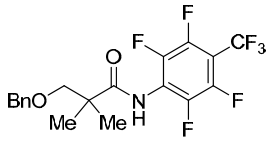
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.23 (m, 3H), 7.15-7.13 (m, 3H), 2.92 (s, 2H), 1.32 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.71, 137.12, 130.23, 128.44, 127.05, 46.82, 44.76, 25.47.



1d

5-(2,5-Dimethylphenoxy)-2,2-dimethyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pentanamide (1d)

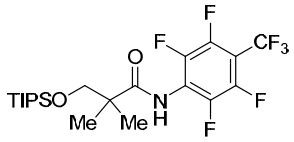
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (bs, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 6.62 (s, 1H), 3.98 (m, 2H), 2.30 (s, 3H), 2.15 (s, 3H), 1.86 (m, 4H), 1.38 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.61, 156.86, 136.84, 130.55, 123.59, 121.14, 112.29, 67.74, 43.37, 37.76, 25.75, 25.21, 21.56, 15.96.



1e

3-Benzyloxy-2,2-dimethyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanamide (1e)

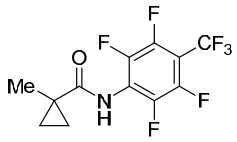
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (bs, 1H), 7.36 (m, 5H), 4.67 (s, 2H), 3.54 (s, 2H), 1.30 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.91, 136.84, 128.91, 128.89, 128.53, 128.09, 76.08, 74.29, 43.69, 23.21.



1f

2,2-dimethyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-(triisopropylsilyloxyl)propanmide (1f)

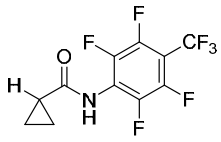
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (bs, 1H), 3.82 (s, 2H), 1.30 (2, 3H), 1.29-1.02 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.34, 69.74, 44.32, 22.92, 18.04, 11.94.



1g

1-Methyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)cyclopropanecarboxamide (1g)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (bs, 1H), 1.50 (s, 3H), 1.34 (aq, *J* = 2.4 Hz, 2H), 0.77 (aq, *J* = 2.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.13, 19.97, 19.76, 17.93.



2l

***N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)cyclopropanecarboxamide (2l)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (bs, 1H), 1.66-1.61 (m, 1H), 1.15 (aq, *J* = 3.2 Hz, 2H), 0.97 (aq, *J* = 2.8 Hz, 2H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 171.72, 13.66, 8.13.

B. Pd(II)-Catalyzed carbonylation of C(sp^3)-H bonds

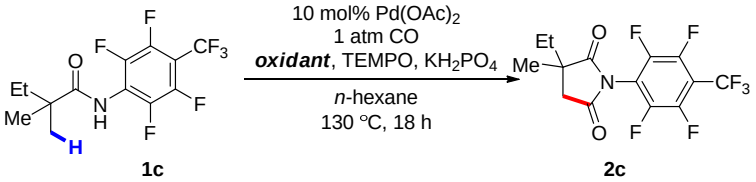
Experimental procedure for the optimization of reaction conditions (See Table 1 in manuscript)

A 50 mL Schlenk-type tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (2.3 mg, 0.01mmol) followed by substrate **1a** (31.7 mg, 0.1 mmol), AgOAc (33.4 mg, 0.2 mmol), KH_2PO_4 (27.2 mg, 0.2 mmol), indicated additive (0.2 mmol) and indicated solvent (1 mL). The reaction tube was evacuated and back-filled with CO (5-times, balloon) and heated to 130 °C for 18 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrate *in vacuo*. The NMR yield of desired product **2a** was determined by integration using an internal standard (1,1,2,2-tetrachloroethane).

Experimental procedure for the optimization of oxidant (Table S1)

A 50 mL Schlenk-type tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (2.3 mg, 0.01mmol) followed by substrate **1c** (33.1 mg, 0.1 mmol), oxidant (0.2 mmol), KH_2PO_4 (27.2 mg, 0.2 mmol), TEMPO (31.3 mg, 0.2 mmol) and *n*-hexane (1 mL). The reaction tube was evacuated and back-filled with CO (5-times, balloon) and heated to 130 °C for 18 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrate *in vacuo*. The NMR yield of desired product **2c** was determined by integration using an internal standard (1,1,2,2-tetrachloroethane).

Table S1. Reactivity of Different Oxidants in the Presence of TEMPO.[a]



entry	oxidant	yield (%)[b]
1	AgOAc	>99
2	$Cu(OAc)_2$	18
3	$CuSO_4$	24
4	$FeCl_3{\cdot}6H_2O$	<1
5	$Ce(OAc)_2$	<1
6	$PhI(OAc)_2$	<1
7	BQ	<1

[a] Reaction conditions: **1c** (0.1 mmol), 10 mol% $Pd(OAc)_2$, 2.0 equiv. of oxidant, 2.0 equiv. of TEMPO, 2.0 equiv. of KH_2PO_4, 1 mL *n*-hexane, 1 atm CO, 130 °C, 18 h. [b] Yields was determined by H^1 NMR analysis (internal standard : 1,1,2,2-tetrachloroethane).

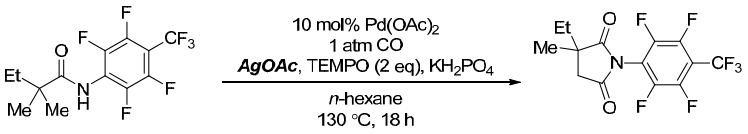
Effects of the quantity of AgOAc and TEMPO

a. AgOAc

Experimental procedure (Table S2, Figure S2)

A 50 mL Schlenk-type tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (2.3 mg, 0.01mmol) followed by substrate (35.7 mg, 0.1 mmol), indicated amounts of AgOAc, KH_2PO_4 (27.2 mg, 0.2 mmol), TEMPO (33.4 mg, 0.2 mmol) and *n*-hexane (1 mL). The reaction tube was evacuated and back-filled with CO (5-times, balloon) and heated to 130 °C for 18 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrate *in vacuo*. The NMR yield of desired product was determined by integration using an internal standard (1,1,2,2-tetrachloroethane).

Table S2. Effects of the Quantity of AgOAc.[a]



AgOAc (mol%)	yield (%)[b]	AgOAc (mol%)	yield (%)[b]
0	12	100	63
20	39	200	>99
50	50		

[a] Reaction conditions: amide substrate (0.1 mmol), 10 mol% $Pd(OAc)_2$, indicated amounts of AgOAc, 2.0 equiv. of TEMPO, 2.0 equiv. of KH_2PO_4, 1 mL *n*-hexane, 1 atm CO, 130 °C, 18 h. [b] NMR yield (internal standard : 1,1,2,2-tetrachloroethane).

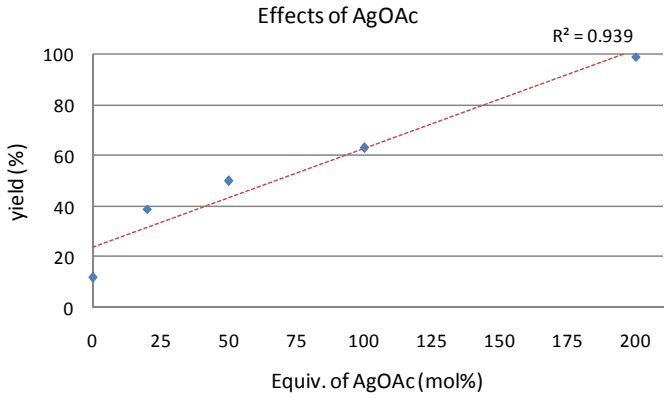


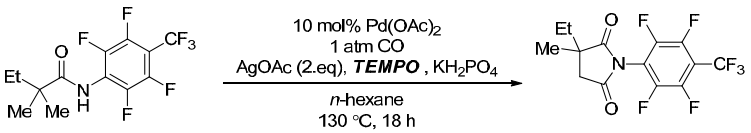
Figure S2. Effects of the Quantity of AgOAc.

b. TEMPO

Experimental procedure (Table S3, Figure S3)

A 50 mL Schlenk-type tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (2.3 mg, 0.01mmol) followed by substrate (35.7 mg, 0.1 mmol), AgOAc (33.4 mg, 0.2 mmol), KH_2PO_4 (27.2 mg, 0.2 mmol), indicated amounts of TEMPO and *n*-hexane (1 mL). The reaction tube was evacuated and back-filled with CO (5-times, balloon) and heated to 130 °C for 18 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrate *in vacuo*. The NMR yield of desired product was determined by integration using an internal standard (1,1,2,2-tetrachloroethane).

Table S3. Effects of the Quantity of TEMPO.[a]



TEMPO (mol%)	yield (%)[b]	TEMPO (mol%)	yield (%)[b]
0	6	100	86
20	73	200	>99
50	75		

[a] Reaction conditions: amide substrate (0.1 mmol), 10 mol% $Pd(OAc)_2$, 2.0 equiv. of AgOAc, indicated amounts of TEMPO, 2.0 equiv. of KH_2PO_4, 1 mL *n*-hexane, 1 atm CO, 130 °C, 18 h. [b] NMR yield (internal standard : 1,1,2,2-tetrachloroethane).

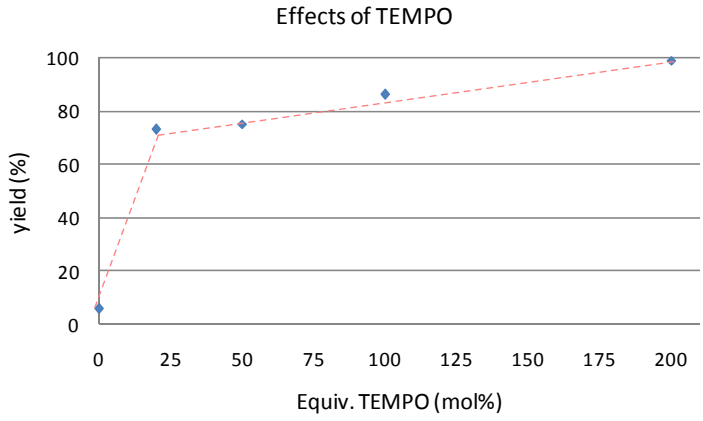
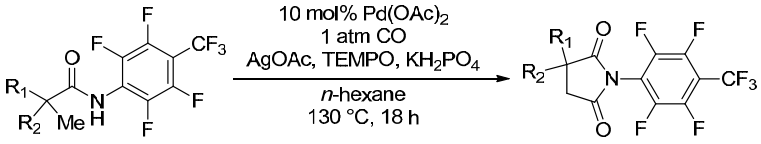


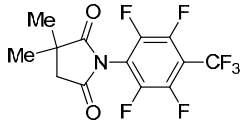
Figure S3. Effects of the Quantity of TEMPO.

General procedure for Pd(II)-catalyzed Carbonylation of C(sp^3)-H bond (See Table 2 in manuscript)



A 50 mL Schlenk-type tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (2.3 mg, 0.01mmol) followed by amide

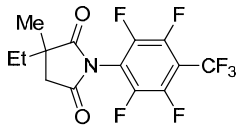
substrate (0.1 mmol), AgOAc (33.4 mg, 0.2 mmol), KH_2PO_4 (27.2 mg, 0.2 mmol), TEMPO (31.3 mg, 0.2 mmol) and *n*-hexane (1 mL). The reaction tube was evacuated and back-filled with CO (5-times, balloon) and heated to 130 °C for 18 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrate *in vacuo* and purified by a silica gel packed flash chromatography column, typically using ethyl acetate/hexane as the eluent.



2a

3,3-Dimethyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2a)

Substrate **1a** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:7), **2a** was obtained as a white solid (31.2 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.85 (s, 2H), 1.49 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.70, 172.00, 44.19, 41.94, 25.83; IR (neat) ν 2934, 1734, 1661, 1504, 1320, 1142, 987 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{13}H_8F_7NO_2$ (MH^+): 344.0516; found: 344.0518.

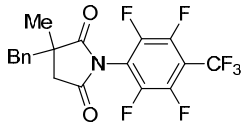


2b

3-Ethyl-3-methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2b)

Substrate **1b** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:8), **2b** was obtained as a white solid (35.2 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80 (dd, *J* = 73.6, 18.4 Hz, 2H), 1.92-1.84 (m, 1H), 1.73-1.66 (m, 1H), 1.44 (s, 3H), 0.98 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.30, 172.38, 46.00, 41.11, 31.60, 24.41, 8.78; IR (neat) ν 2971, 1734, 1505, 1322, 1190, 1144, 998 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{14}H_{10}F_7NO_2$ (MH^+): 358.0672; found:

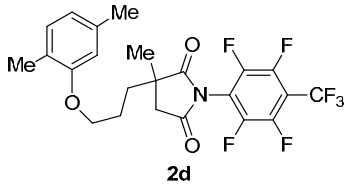
358.0675.



2c

3-Benzyl-3-methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2c)

Substrate **1c** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:8), **2c** was obtained as a yellowish liquid (40.2 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.26 (m, 3H), 7.17-7.15(m, 2H), 3.34 (d, *J* = 13.6 Hz, 1H), 3.05 (d, *J* = 18.8 Hz, 1H), 2.79 (d, *J* = 14.0 Hz, 1H), 2.64 (d, *J* = 18.4 Hz, 1H), 1.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.10, 171.91, 135.43, 130.05, 129.17, 127.88, 47.00, 43.54, 40.02, 26.10; IR (neat) ν 2932, 1732, 1504, 1317, 1188, 1148, 985 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{19}H_{12}F_7NO_2$ (MH^+): 420.0829; found: 420.0821.

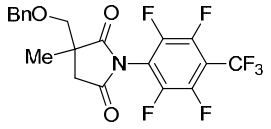


2d

3-(3-(2,5-Dimethylphenoxy)propyl)-3-methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2d)

Substrate **1d** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:7), **2d** was obtained as a white solid (47.1 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.0 (d, *J* = 7.6, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.61 (s, 1H), 4.00-3.96 (m, 2H), 2.88 (dd, *J* = 74.0, 18.4 Hz, 2H), 2.04 (s, 3H), 2.00 (s, 3H), 1.97-1.79 (m, 4H), 1.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.06, 172.07, 156.77, 136.77, 130.62, 123.68, 121.26, 112.11, 67.11, 45.30, 41.66, 35.29, 24.74, 24.55, 21.52, 15.93; IR (neat) ν 2927, 2873, 1732, 1503, 1317, 1263, 1150, 1130, 1001,

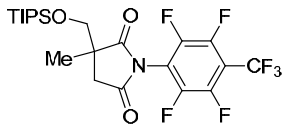
983 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{23}H_{20}F_7NO_3$ (MH^+): 492.1404; found: 492.1409.



2e

3-(Benzyloxymethyl)-3-methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2e)

Substrate **1e** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:7), **2e** was obtained as a white solid (41.3 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.25 (m, 5H), 4.55 (dd, *J* = 38.8, 12.0 Hz, 2H), 3.78 (d, *J* = 8.4 Hz, 1H), 3.40 (d, *J* = 8.4 Hz, 1H), 3.20 (d, *J* = 18.0 Hz, 1H), 2.69 (d, *J* = 18.0 Hz, 1H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.21, 172.39, 137.28, 128.69, 128.15, 127.77, 74.00, 73.69, 46.76, 39.88, 20.45; IR (neat) ν 2863, 1731, 1500, 1318, 1189, 1141, 984 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{20}H_{14}F_7NO_3$ (MH^+): 450.0935; found: 450.0918.



2f

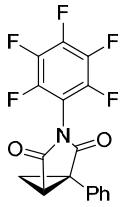
3-Methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-((triisopropylsilyloxy)methyl)pyrrolidine-2,5-dione (2f)

Substrate **1f** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:20), **2f** was obtained as a white solid (36.1 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28 (d, *J* = 8.4 Hz, 1H), 3.75 (d, *J* = 8.4 Hz, 1H), 3.45 (d, *J* = 17.6 Hz, 1H), 2.81 (d, *J* = 17.6 Hz, 1H), 1.52 (s, 3H), 1.27-1.18 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.41, 169.54, 64.85, 45.24, 36.25, 17.64, 15.01, 14.95, 8.87; IR (neat) ν 2945, 2869, 1736, 1504, 1323, 1199, 1151, 1109, 1004, 981 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{22}H_{28}F_7NO_3Si$ (MH^+): 516.1799; found: 516.1799.

2g

1-Methyl-3-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-azabicyclo[3.1.0]hexane-2,4-dione (2g)

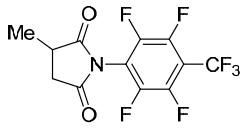
Substrate **1g** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:5), **2g** was obtained as a white solid (29.3 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (aq, *J* = 3.6 Hz, 1H), 1.82 (m, 1H), 1.63-1.58 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.61, 171.22, 28.66, 27.58, 27.12, 12.95; IR (neat) ν 2970, 1734, 1505, 1320, 1145, 1095, 982, 890 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{13}H_6F_7NO_2$ (MH^+): 342.0360; found: 342.0361



2h

3-(Perfluorophenyl)-1-phenyl-3-azabicyclo[3.1.0]hexane-2,4-dione (2h)

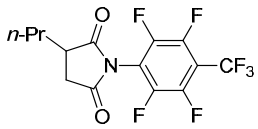
Substrate **1h** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:10), **2h** was obtained as a white solid (22.9 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.38 (m, 5H), 2.95 (aq, *J* = 3.6 Hz, 1H), 2.13 (aq, *J* = 3.6 Hz, 1H), 2.06 (dd, *J* = 4.8, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.21, 171.33, 130.96, 129.27, 129.15, 129.14, 36.79, 29.92, 27.73; IR (neat) ν 2919, 1735, 1521, 1361, 1304, 1135, 1070, 992 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{17}H_8F_5NO_2$ (MH^+): 354.0548; found: 354.0535.



2i

3-Methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2i)

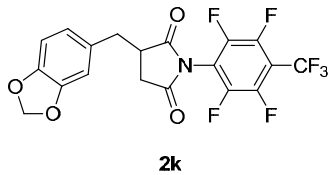
Substrate **1i** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:5), **2i** was obtained as a white solid (21.3 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.27-3.19 (m, 2H), 2.67-2.63 (m, 1H), 1.51-1.50 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.81, 172.51, 37.12, 35.98, 17.06; IR (neat) ν 2943, 1732, 1499, 1321, 1148, 996, 977 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{12}H_6F_7NO_2$ (MH^+): 330.0360; found: 330.0360.



2j

3-propyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2j)

Substrate **1j** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:10), **2j** was obtained as a white solid (21.4 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 314-3.08 (m, 2H), 2.72-2.64 (m, 1H), 1.95 (m, 1H) , 1.71-1.69 (m, 1H), 1.49-1.44 (m, 2H), 0.99 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.30, 172.79, 40.86, 35.01, 33.61, 19.89, 13.91; IR (neat) ν 2940, 1735, 1500, 1305, 1140, 997 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{14}H_{10}F_7NO_2$ (MH^+): 358.0672; found: 358.0685.

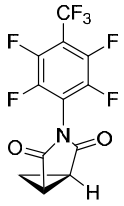


2k

3-(Benzo[d][1,3]dioxol-5-ylmethyl)-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2k)

Substrate **1k** was carbonylated following the general procedure. After purification by column

chromatography (ether/hexane = 1:2), **2k** was obtained as a white solid (23.4 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (m, 1H), 6.66-6.62 (m, 2H), 5.95 (aq, J = 1.6 Hz, 2H), 3.42-3.39 (m, 2H), 3.06-2.95 (m, 3H), 2.78-2,72 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.63, 172.39, 148.48, 147.26, 129.67, 122.56, 109.47, 108.91, 101.43, 42.45, 36.16, 33.54; IR (neat) ν 2970, 2927, 1735, 1505, 1323, 1152, 990 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{19}H_{10}F_7NO_4$ (MH^+): 450.0571; found: 450.0575.

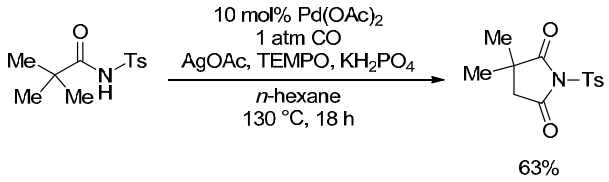


2l

3-(2,3,5,6-Tetrafluoro-4-(trifluoromethyl)phenyl)-3-azabicyclo[3.1.0]hexane-2,4-dione (2l)

Substrate **1l** was carbonylated following the general procedure. After purification by column chromatography (ethyl acetate/hexane = 1:8), **2l** was obtained as a white solid (21.3 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.79-2.76 (m, 2H), 1.82-1.72 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.12, 21.72, 20.81; IR (neat) ν 3100, 1732, 1500, 1321, 1308, 1144, 1070, 985, 858 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{12}H_4F_7NO_2$ (MH^+): 328.0203; found: 328.0207.

Carbonylation of C(sp^3)-H bond using *N*-sulfonyl amide directed substrate



63%

C. Succinimide ring opening reaction (hydrolysis)

Procedure for the hydrolysis of succinimide (2a) to succinic acid (3) (Scheme 1)

3,3-Dimethyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (**2a**, 103 mg, 0.3 mmol) was dissolved in trifluoroacetic acid-conc., hydrochloric acid (1:1, 2 mL) and the reaction mixture for 24 hour. The reaction mixture was kept aside at 0 °C for 12 hour and the white precipitate was filtered *in vacuo* to obtain **2,2-dimethylsuccinic acid** (**3**, 40.3 mg, 92.5%), as a white solid.

Procedure for the selective ring opening of succinimide (2a) to ester (4) (Scheme 1)

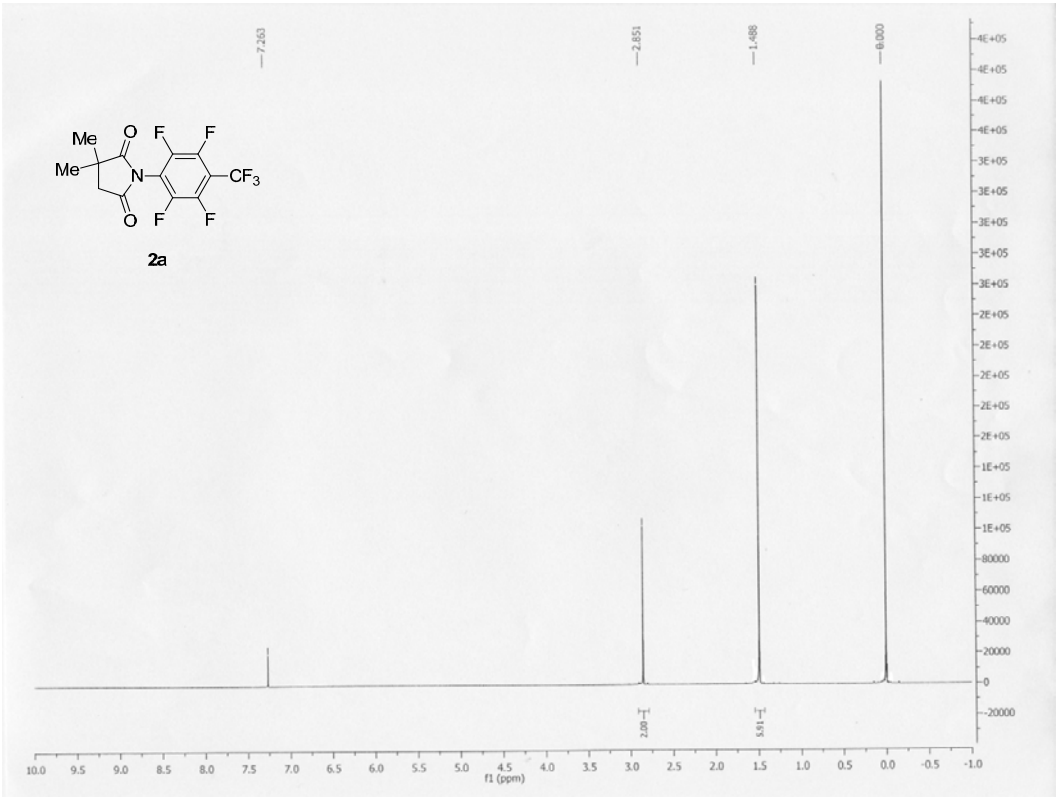
A solution of 3,3-Dimethyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (**2a**, 103 mg, 0.3 mmol)) and sodium methoxide (24.3 mg, 0.45 mmol) in MeOH (2 mL) was stirred for 6 hour at room temperature. The reaction mixture was diluted with ethyl acetate, water and 2 N HCl (1 mL). The aqueous layer was extracted with ethyl acetate (3 mL x 3). The combined organic layer were dried over MgSO4, filtered and concentrated in vacuo. The crude residue was purified by flash column chromatograph (ethyl acetate/hexane = 1:7) to give the desired product, methyl 3,3-dimethyl-4-oxo-4-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenylamino)butanoate (**4**, 90.1 mg, 80.3%), as a white solid.

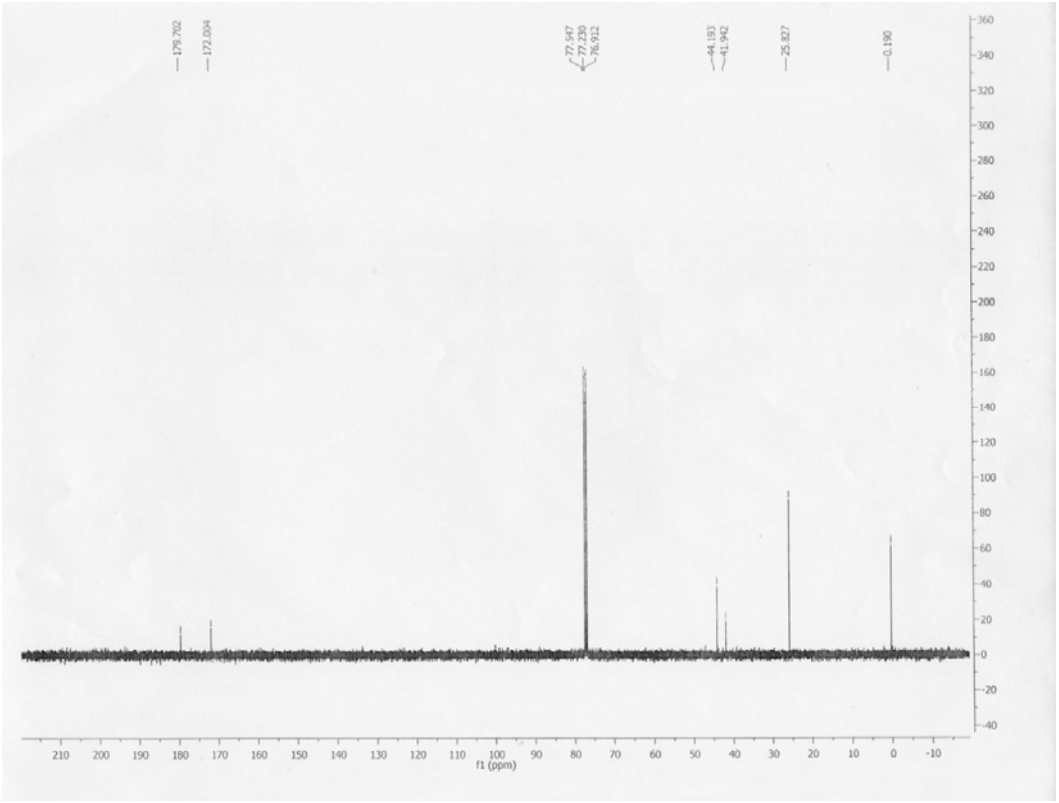
(14:1 mixture)

Methyl 3,3-dimethyl-4-oxo-4-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenylamino)butanoate (4)

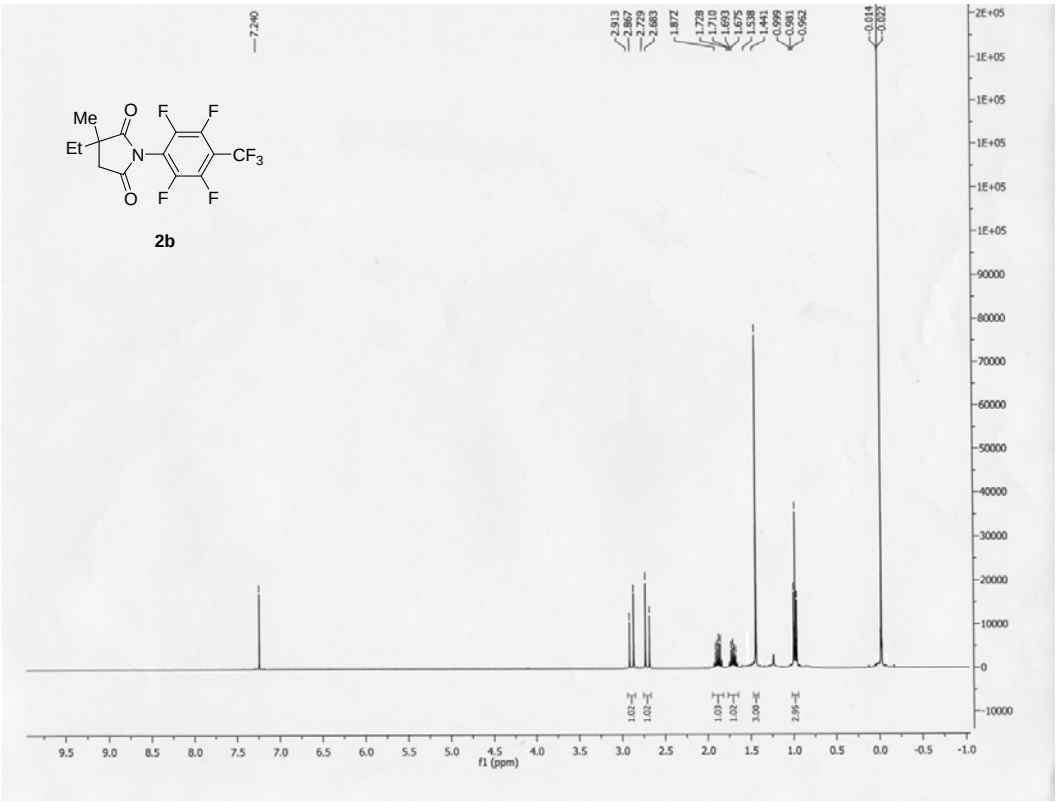
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 (s, 3H), 3.70 (s, 3H), 2.71 (s, 2H), 2.70 (s, 2H), 1.40 (s, 6H), 1.32 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.88, 169.07, 52.79, 46.24, 41.92, 25.79; IR (neat) ν 3274, 2970, 1736, 1509, 1478, 1341, 1235, 1147, 1011 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{14}H_{12}F_7NO_3$ (MH^+): 376.0778; found: 376.0781.

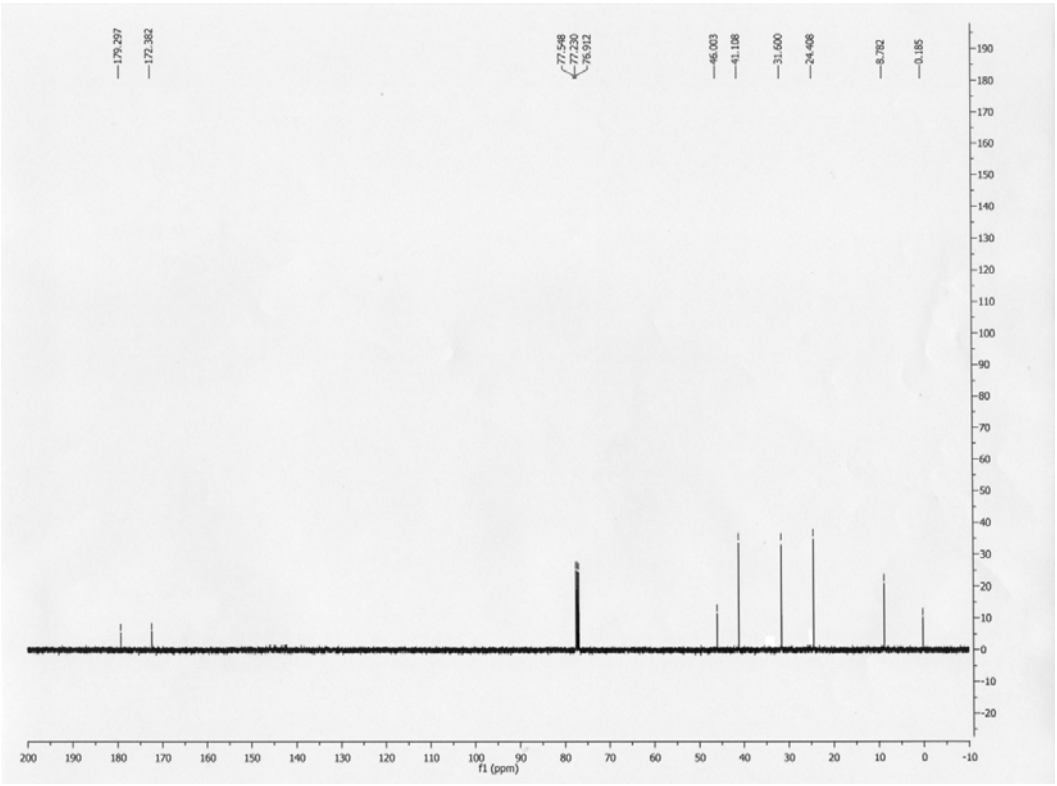
3,3-Dimethyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2a)



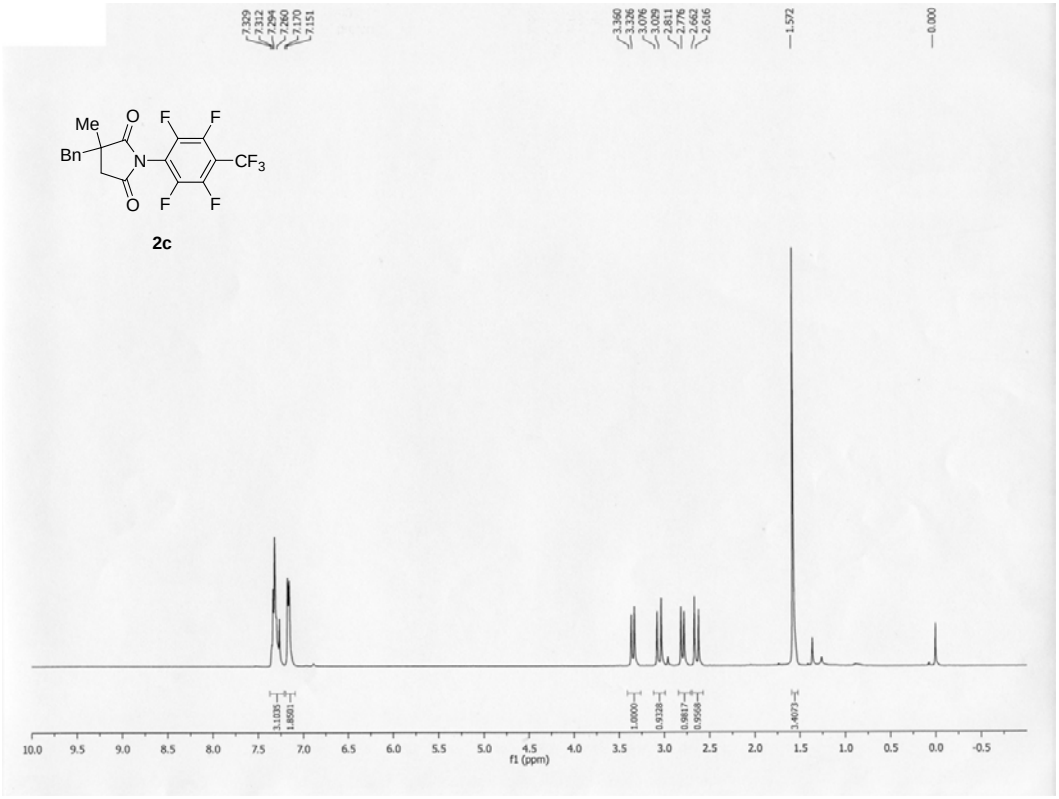


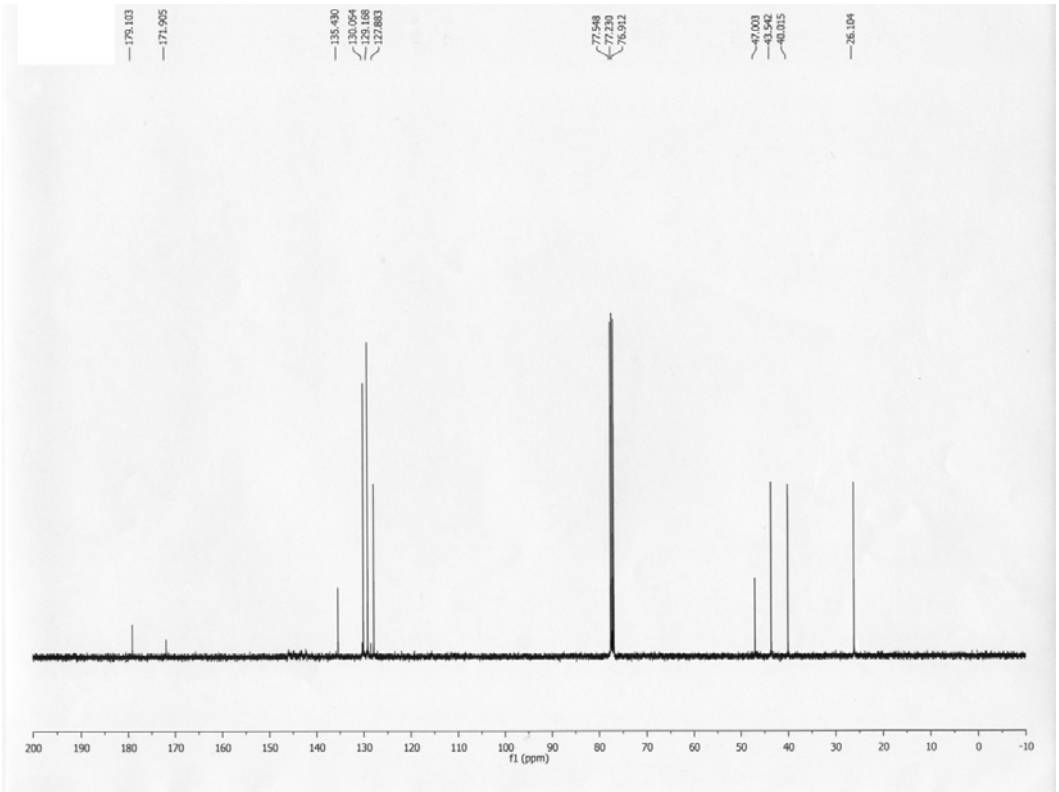
3-Ethyl-3-methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2b)



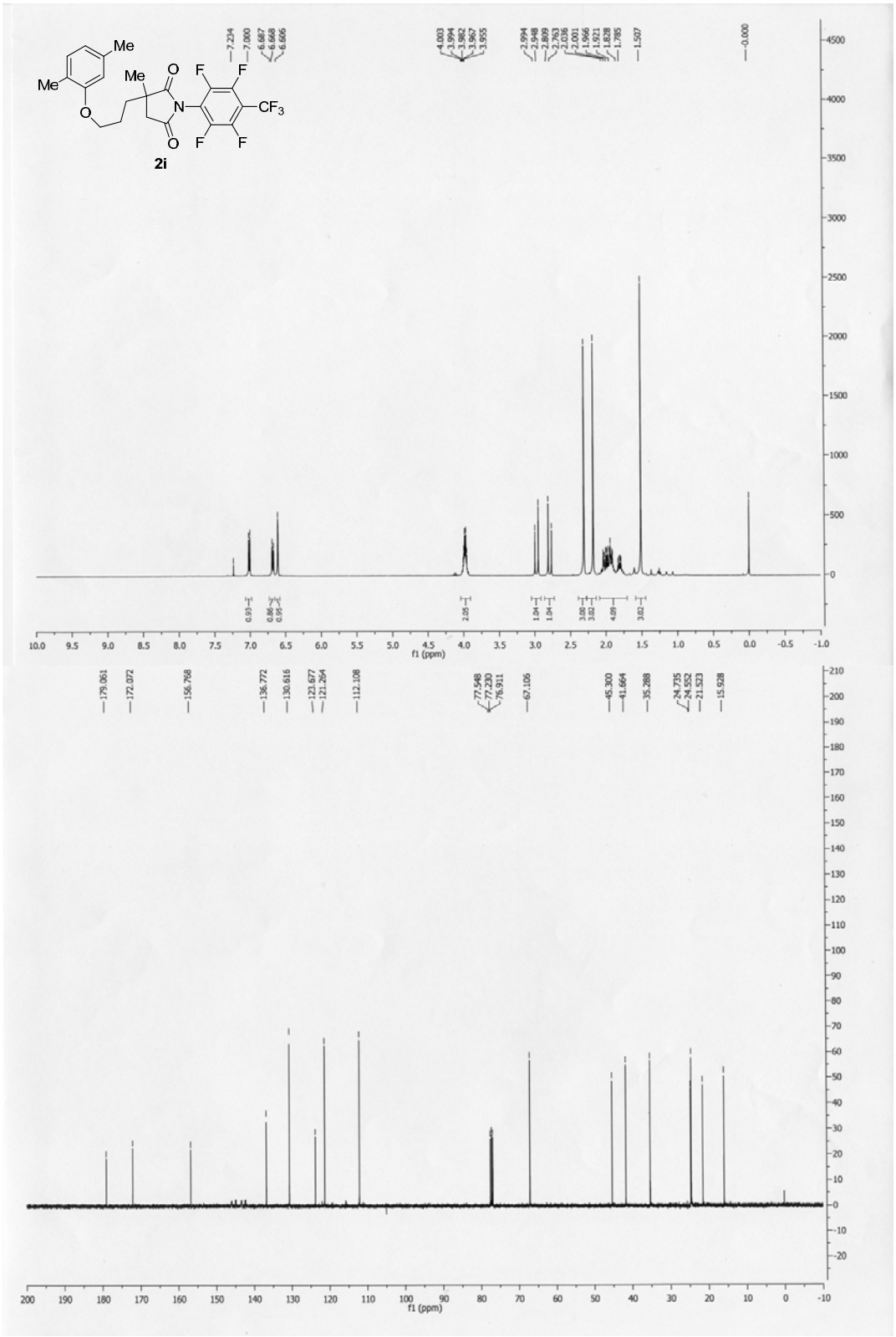


3-Benzyl-3-methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2c)

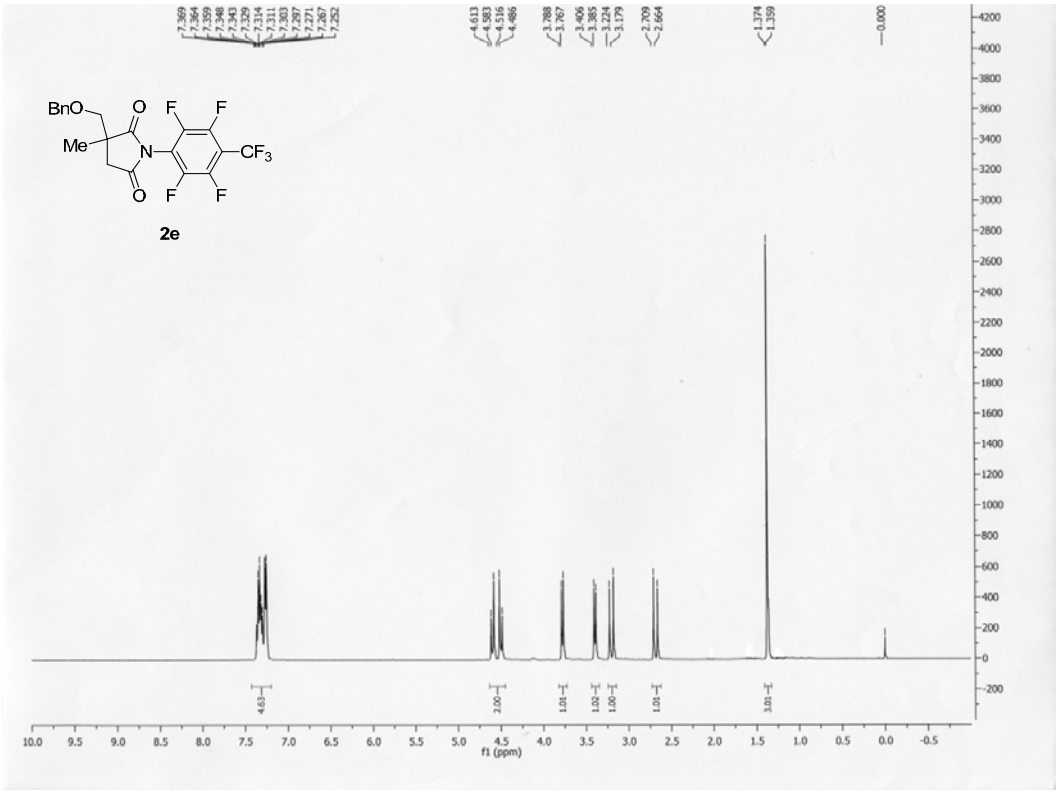


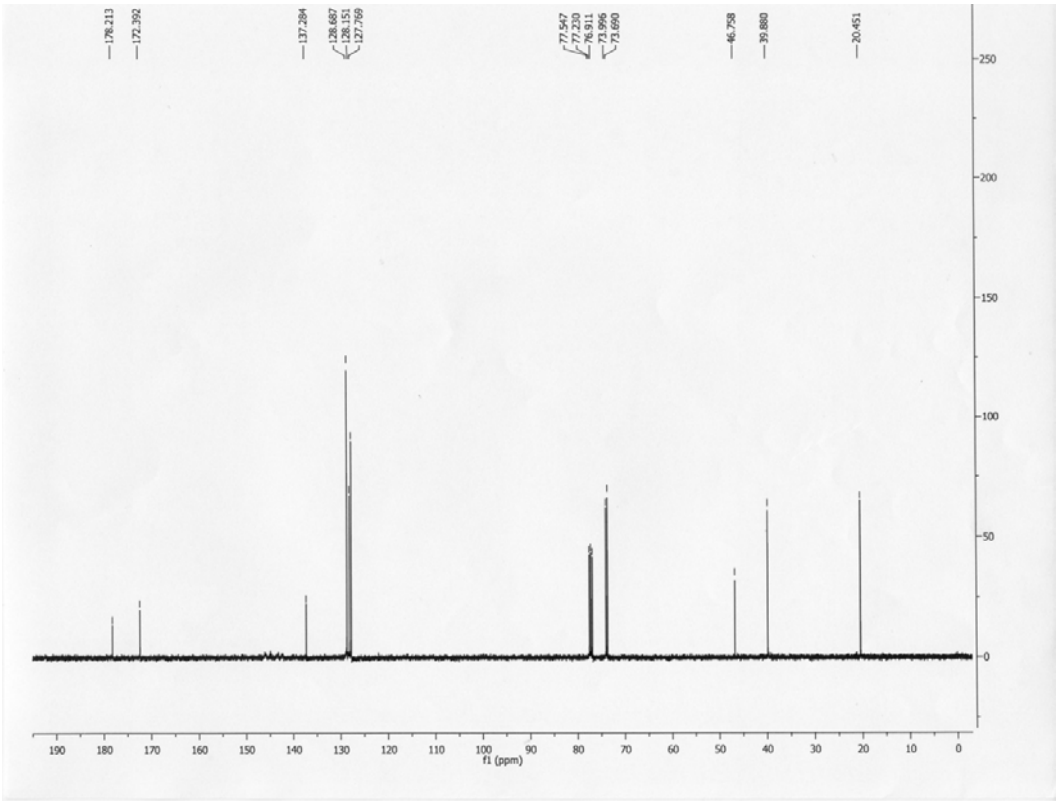


3-Methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2d)

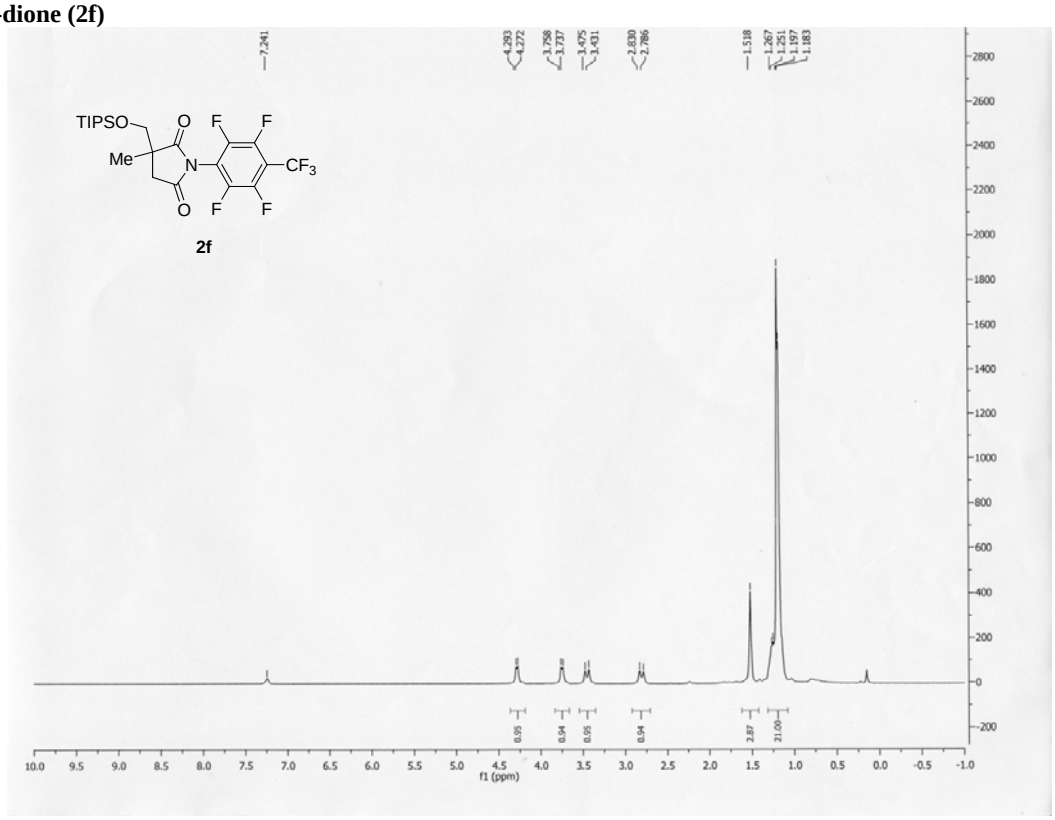


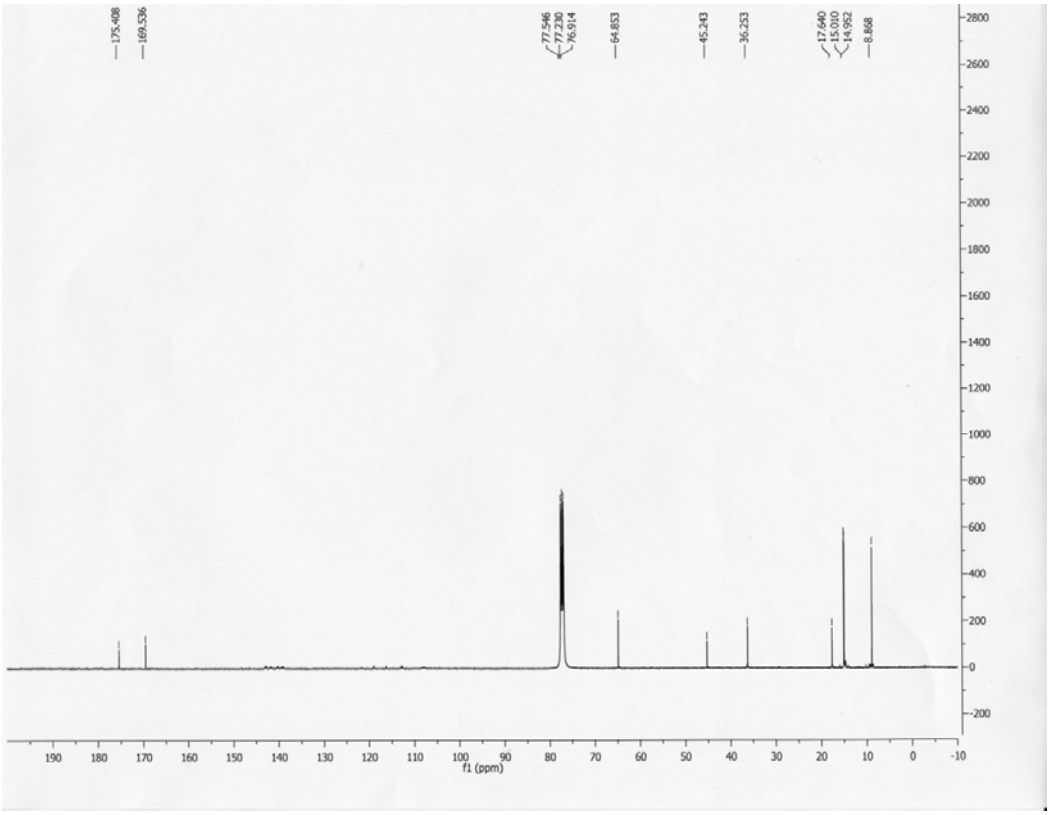
3-(Benzyloxymethyl)-3-methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2e)



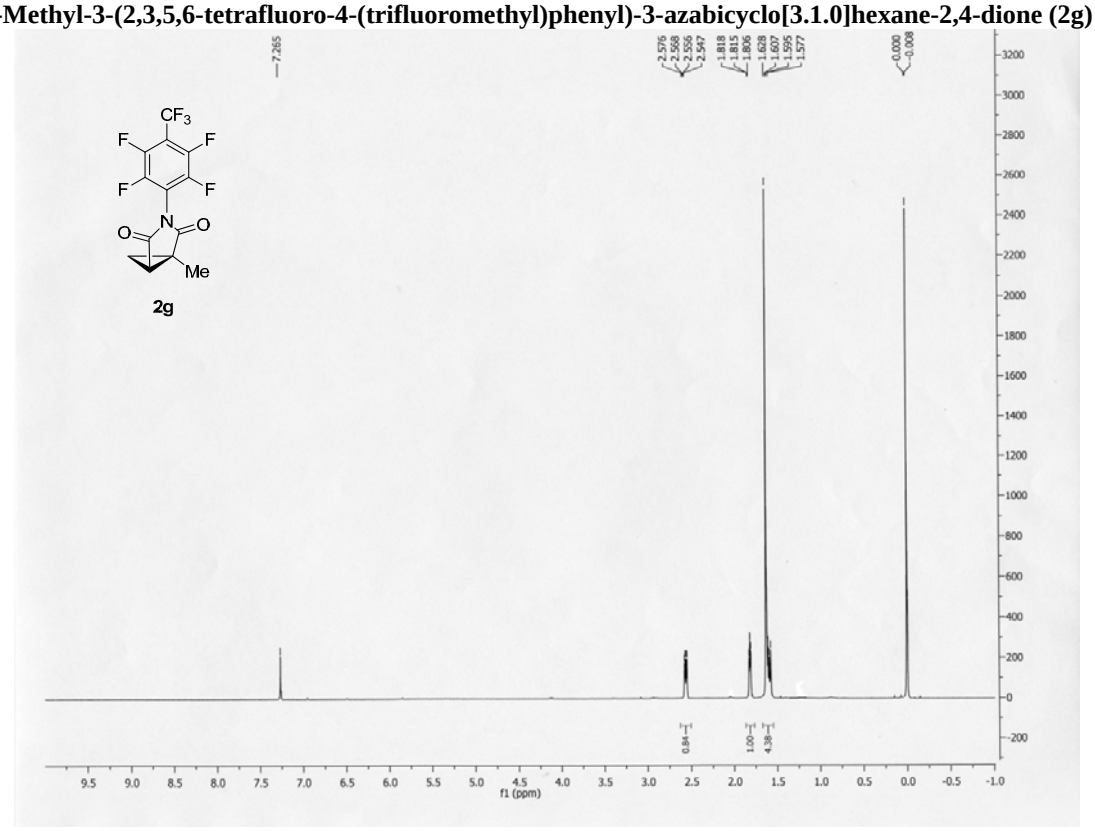


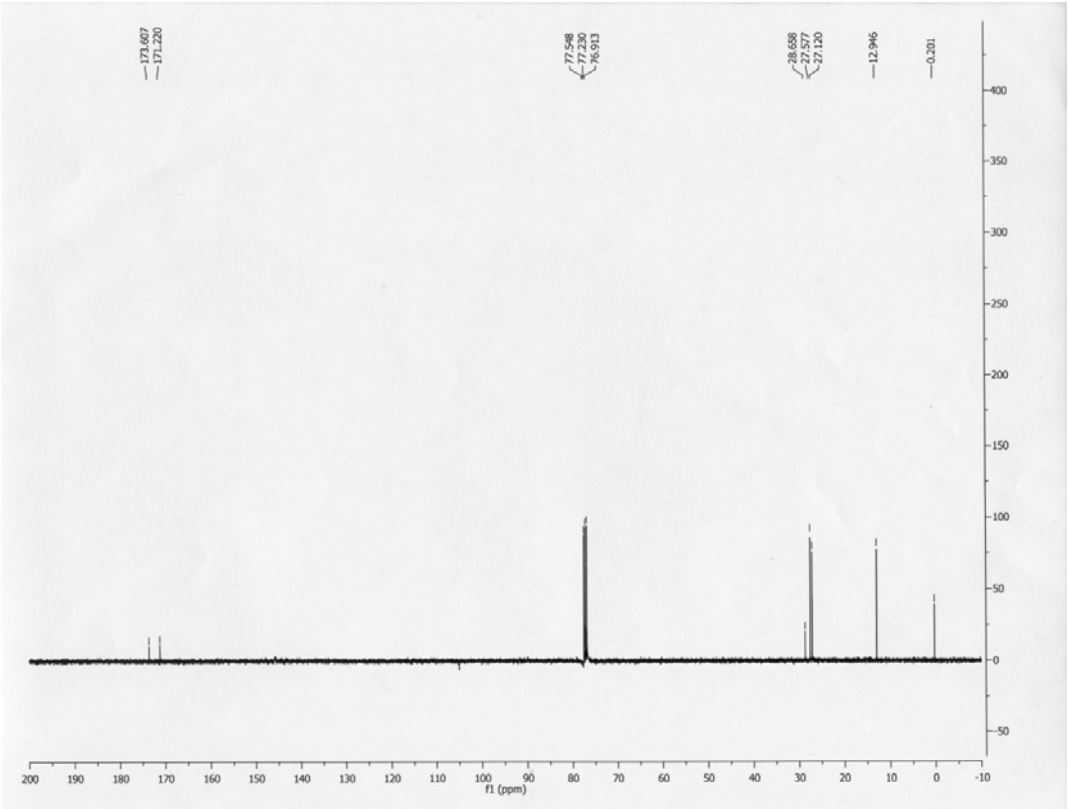
3-Methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-((triisopropylsilyloxy)methyl)pyrrolidine-2,5-dione (2f)



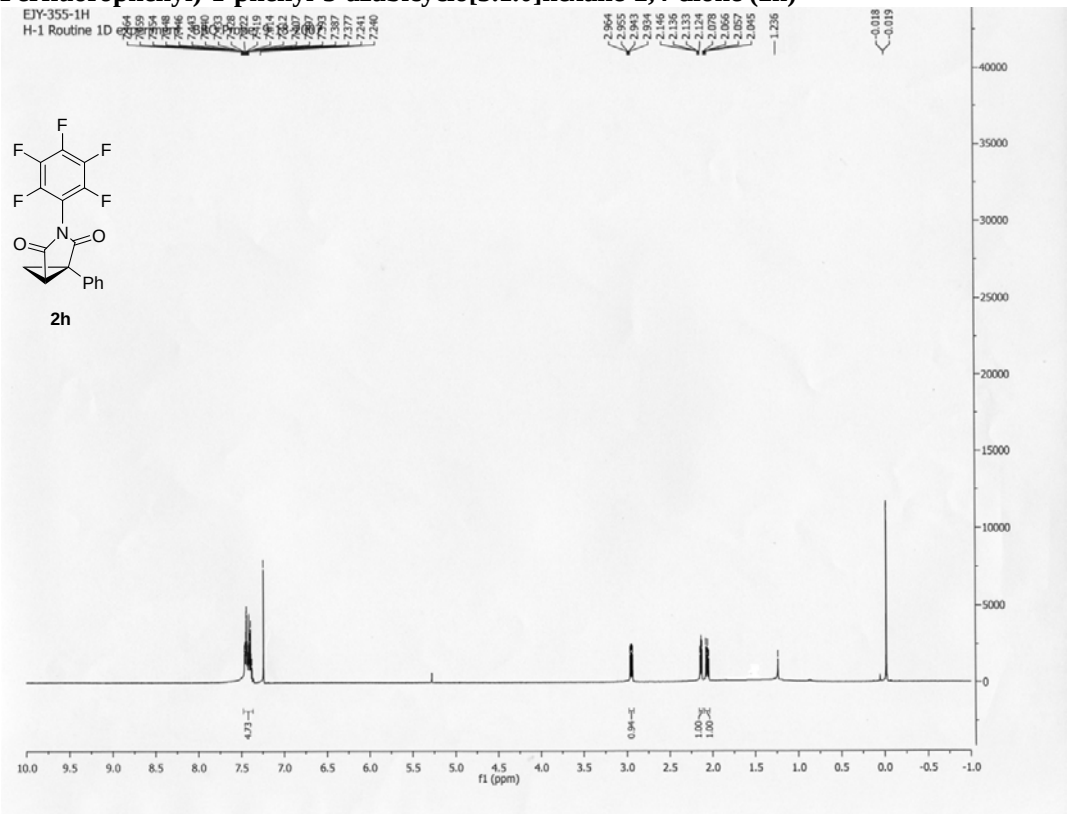


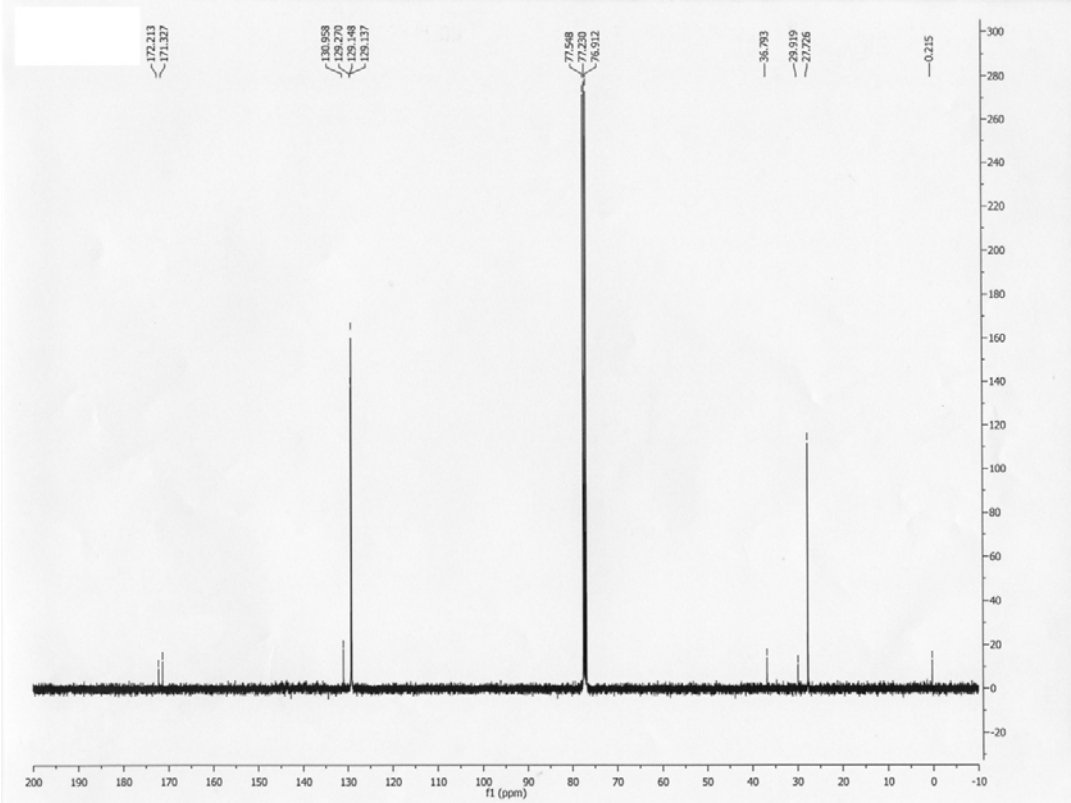
1-Methyl-3-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3-azabicyclo[3.1.0]hexane-2,4-dione (2g)



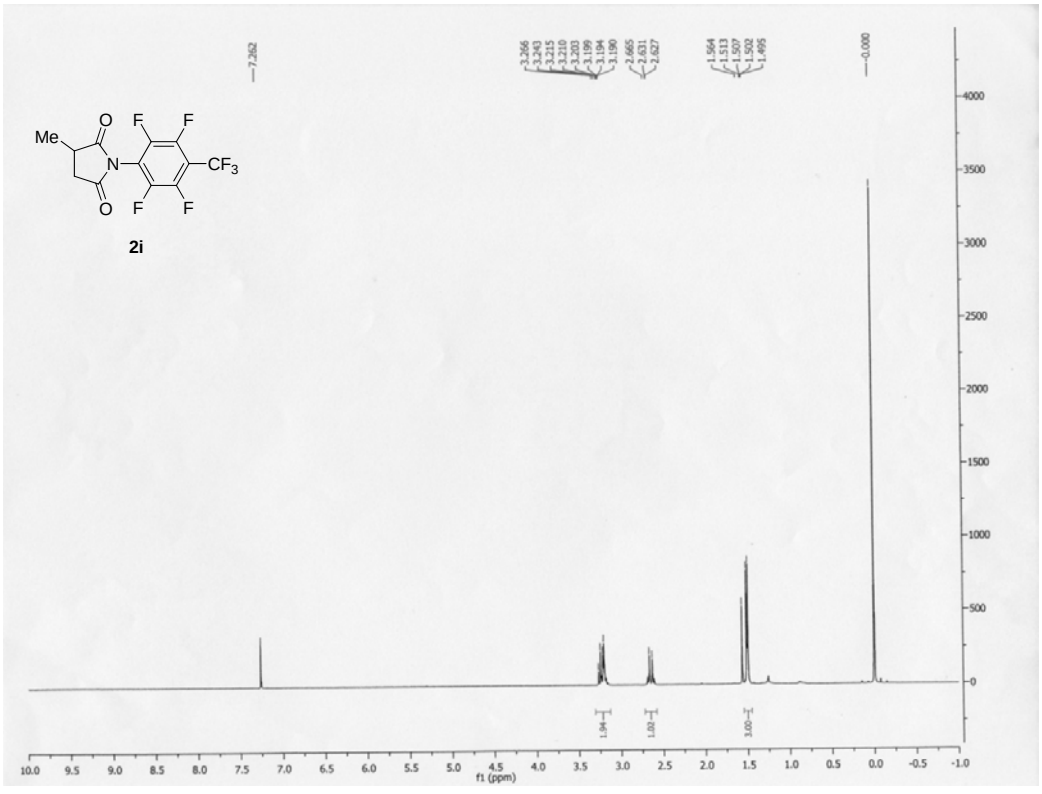


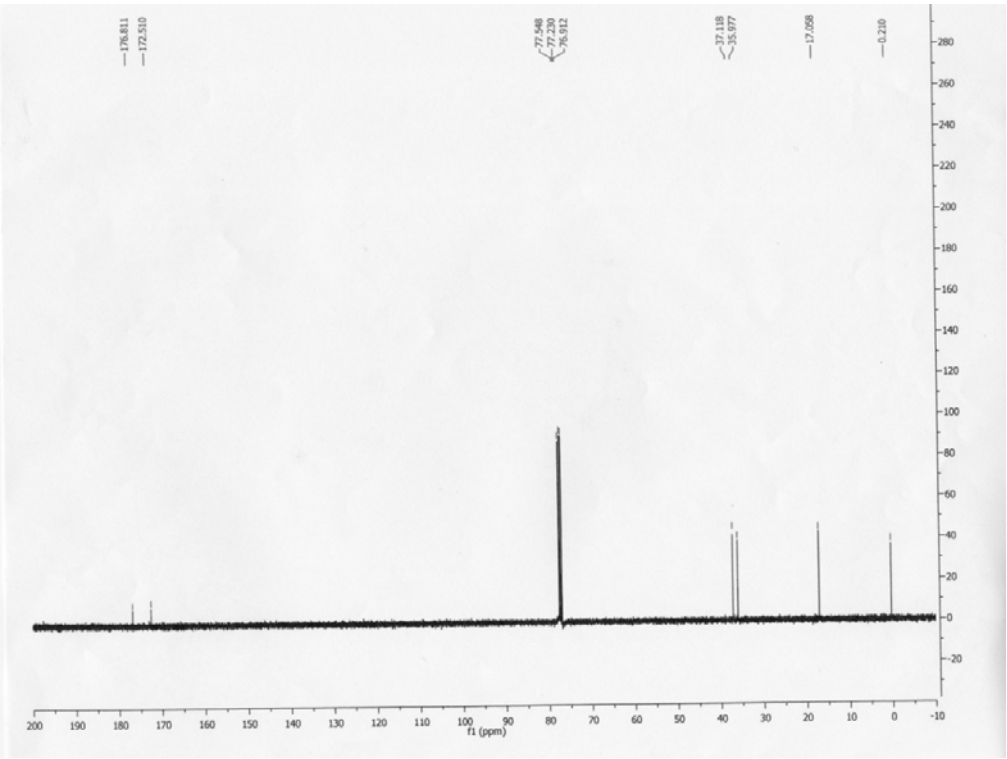
3-(Perfluorophenyl)-1-phenyl-3-azabicyclo[3.1.0]hexane-2,4-dione (2h)



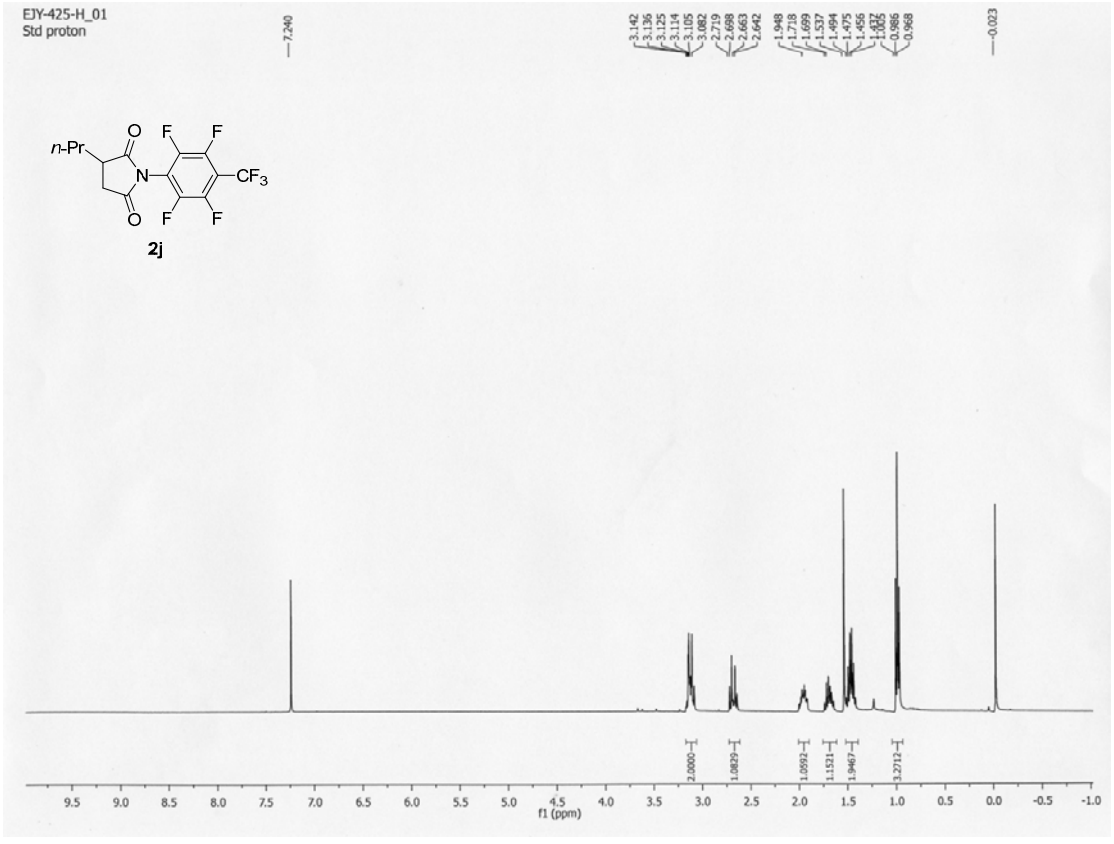


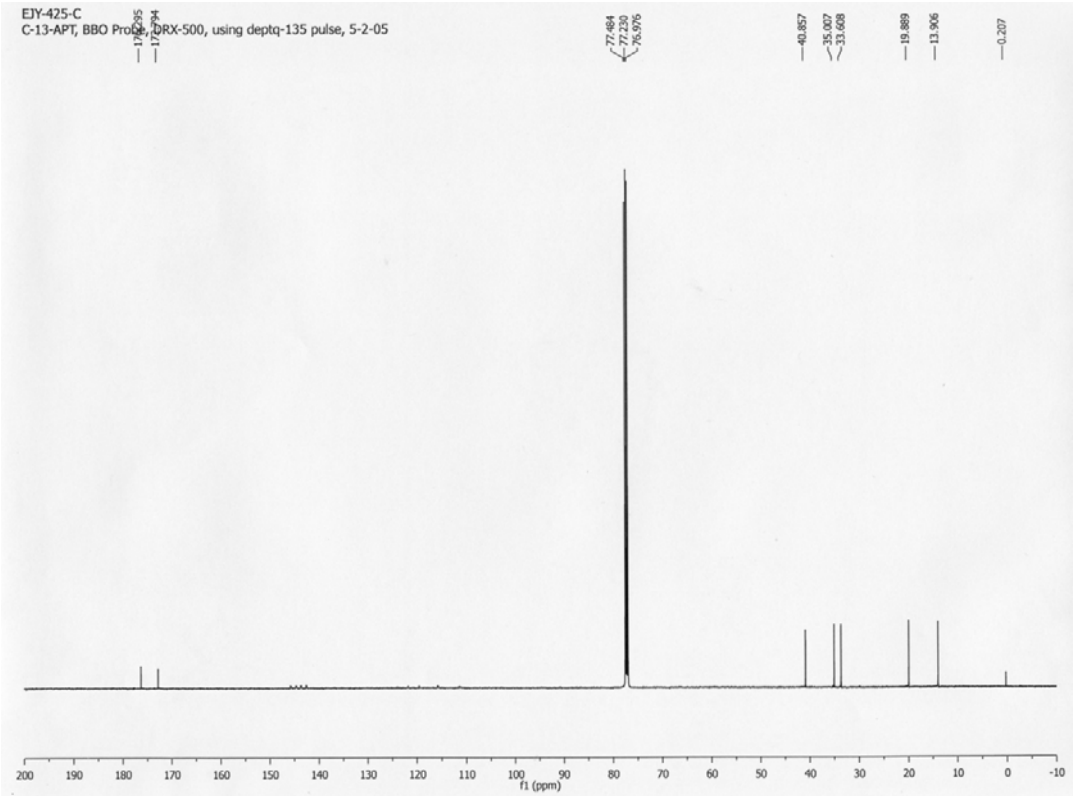
3-(3-(2,5-Dimethylphenoxy)propyl)-3-methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2i)



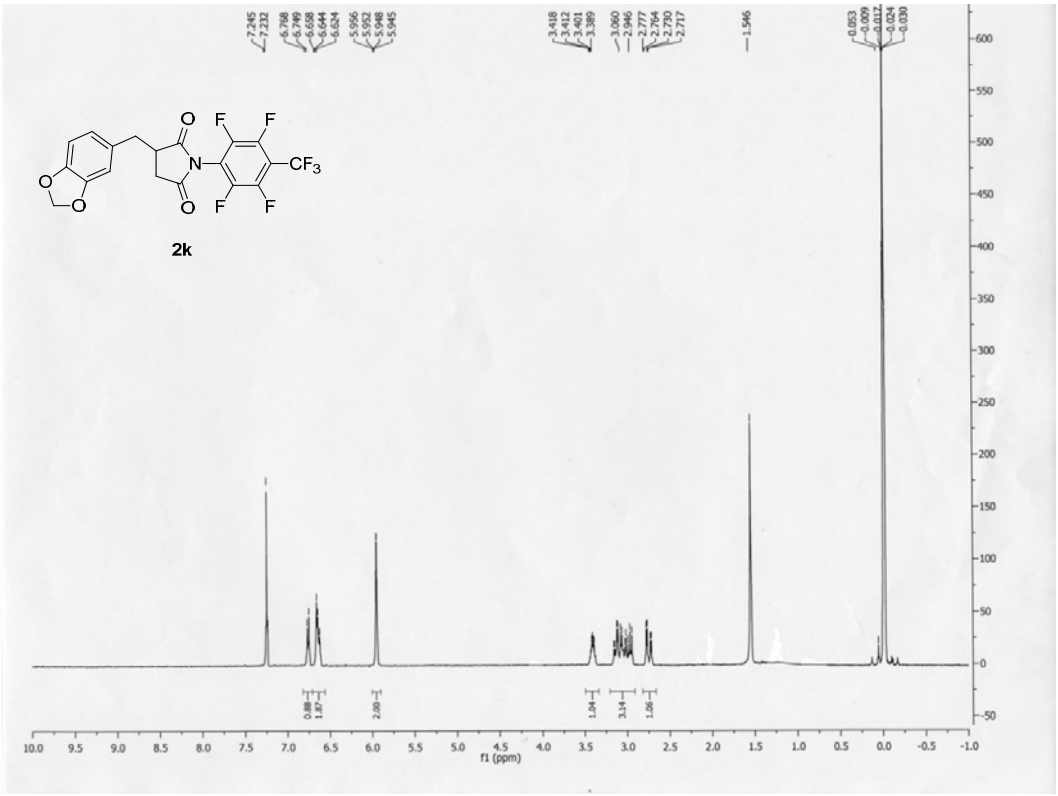


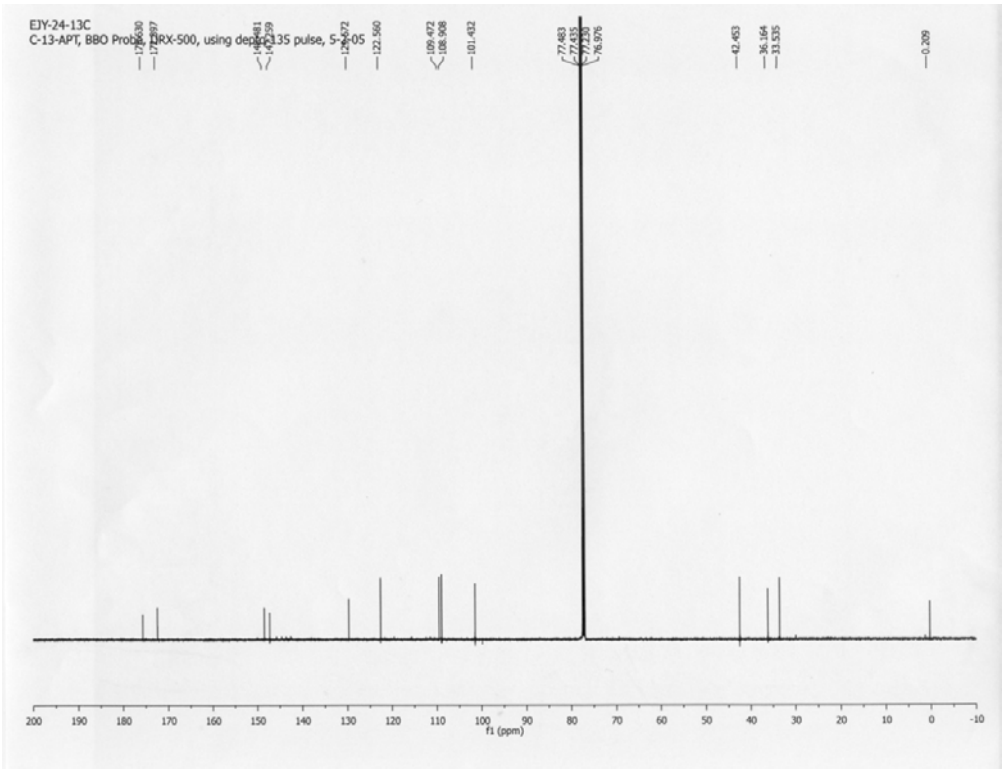
3-propyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2j)



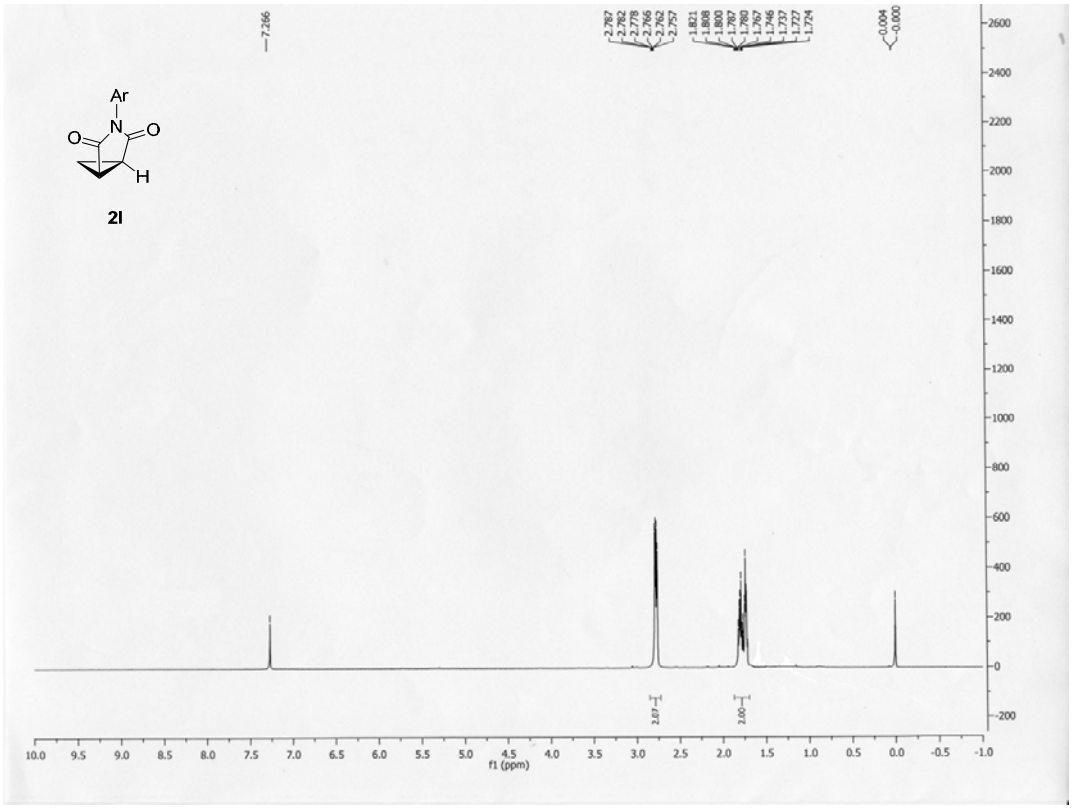


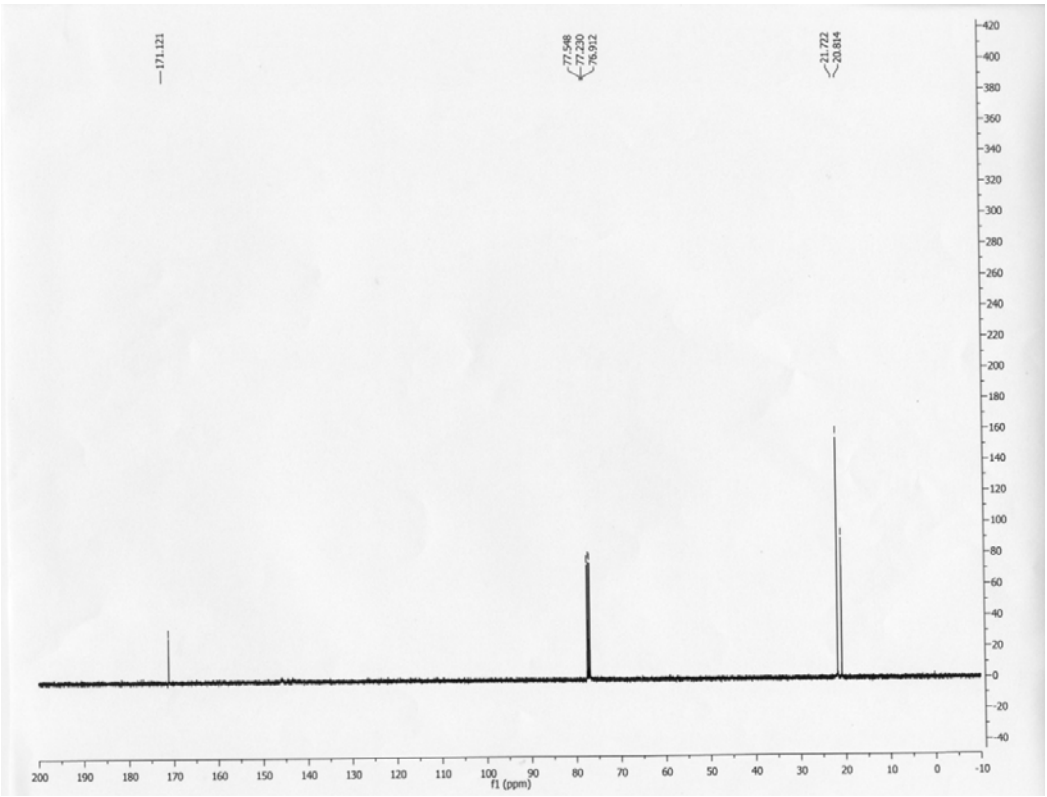
3-(Benzo[d][1,3]dioxol-5-ylmethyl)-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (2k)



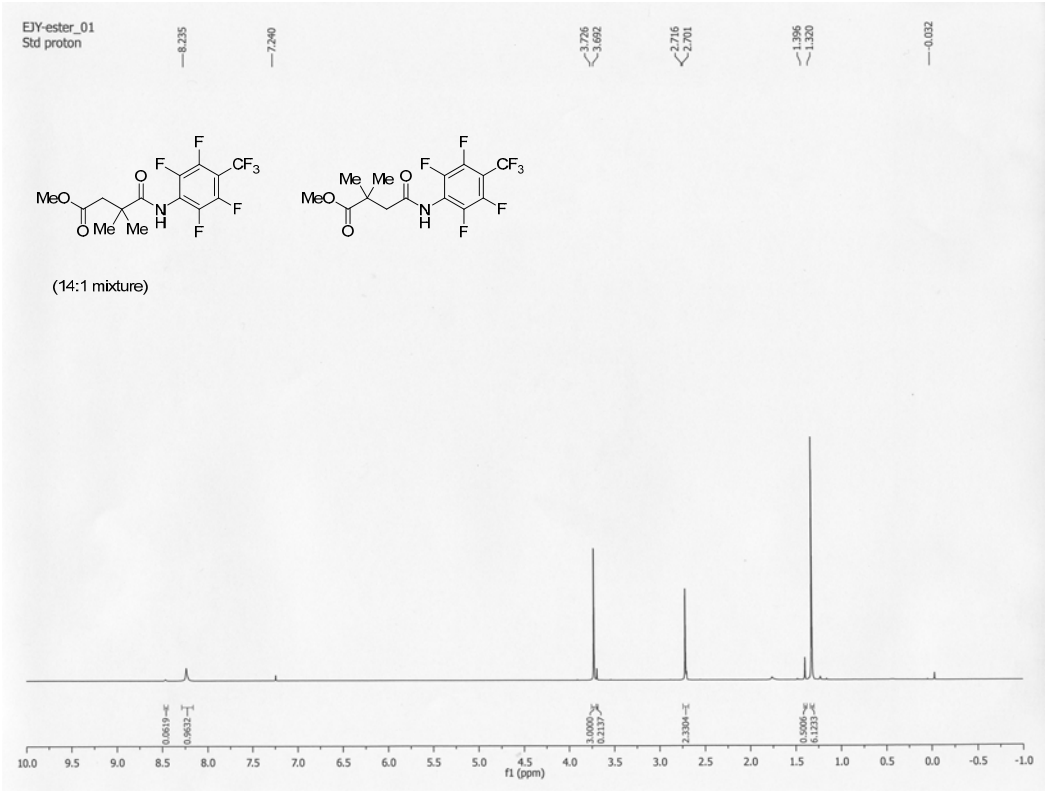


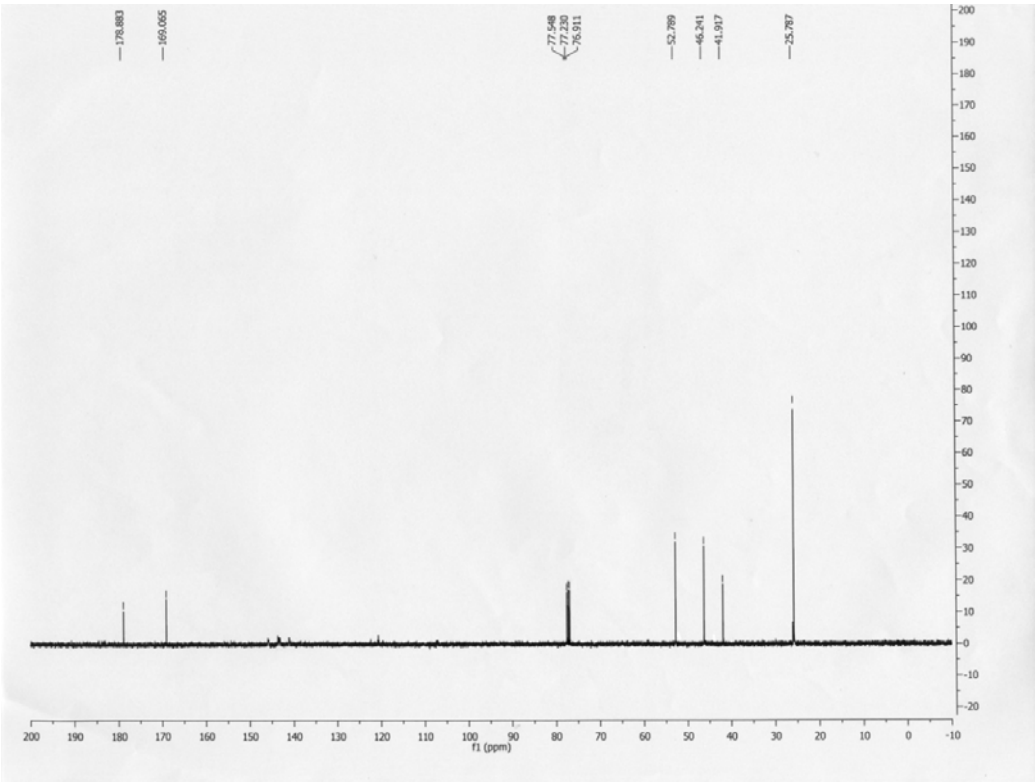
3-(2,3,5,6-Tetrafluoro-4-(trifluoromethyl)phenyl)-3-azabicyclo[3.1.0]hexane-2,4-dione (2l)





Methyl 3,3-dimethyl-4-oxo-4-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenylamino)butanoate (4)

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169.065
77.548
77.230
76.911
52.789
46.241
41.917
25.787
f1 (ppm)