$Sc(OTf)_3$-Catalyzed Synthesis of Anhydrides from Twisted Amides

Yongmei Liu,[a,b] Ruzhang Liu,[a] and Michal Szostak[b,*]

[a]*College of Chemistry and Chemical Engineering, Yangzhou University, 180 Siwangting Road, Yangzhou, Jiangsu 225002, China* and [b]*Department of Chemistry, Rutgers University, 73 Warren Street, Newark, New Jersey 07102, United States*

michal.szostak@rutgers.edu

Supplementary Information

Y. Liu, R. Liu
College of Chemistry and Chemical Engineering
Yangzhou University, 180 Siwangting Road, Yangzhou, Jiangsu 225002, China

Y. Liu, M. Szostak
Department of Chemistry, Rutgers University
73 Warren Street, Newark, NJ 07102, United States
Corresponding Author:
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. Amides were prepared by standard methods.[1-5] All experiments were performed using standard Schlenk 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 sodium/benzophenone under nitrogen. 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 or nitrogen (three cycles). All products were identified using ^{1}H NMR analysis and comparison with authentic samples. GC and/or GC/MS analysis was used for volatile products. All yields refer to yields determined by ^{1}H NMR and/or GC or GC/MS using an internal standard (optimization) and isolated yields (preparative runs) unless stated otherwise. Yields refer to isolated compounds, estimated to be >95% pure as determined by ^{1}H NMR and/or GC. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker spectrometers at 500 (^{1}H NMR) and 125 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; brs, 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 280 °C. The detector temperature was 280 °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 10 min (splitless mode of injection, total run time of 33.00 min). 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, ^{13}C NMR and ^{19}F NMR (if relevant) data are given for all compounds in the Supporting Experimental for characterization purposes. All products have been previously reported, unless stated otherwise. Note that identification of acids from anhydrides is easily performed by ^{13}C NMR spectroscopy. For example, benzoic anhydride carbonyl resonates at ca. 162 ppm, while benzoic acid at ca. 173 ppm. Note that glutarimide amides resonate at ca. 172 ppm.

Experimental Procedures and Characterization Data

General Procedure for Amide Synthesis. An oven-dried round-bottomed flask (100 mL) equipped with a stir bar was charged with amine (8.84 mmol, 1.0 equiv), triethylamine (typically, 2.0 equiv), 4-dimethylaminopyridine (typically, 0.25 equiv) and dichloromethane (typically, 50 mL), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Acyl chloride (typically, 1.1 equiv) was added dropwise to the reaction mixture with vigorous stirring at 0 °C, and the reaction mixture was stirred overnight at room temperature. After the indicated time, the reaction mixture was diluted with Et_2O (20 mL) and filtered. The organic layer was washed with HCl (1.0 *N*, 30 mL), brine (30 mL), dried, and concentrated. Unless stated otherwise, the crude product was purified by recrystallization (toluene) to give analytically pure product.

General Procedure for the Synthesis of Anhydrides from Amides by N–C Cleavage. An oven-dried vial equipped with a stir bar was charged with an amide substrate (neat, 1.0 equiv), placed under a positive pressure of nitrogen, and subjected to three evacuation/backfilling cycles. Benzene (typically, 0.40 M), scandium triflate (typically, 10 mol%) and H_2O (0.50 equiv) were sequentially added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 120 °C and stirred for the indicated time at 120 °C. After the indicated time, the reaction mixture was cooled down to room temperature, washed with HCl (1.0 *N*, 5 mL), extracted with CH_2Cl_2 (3 x 10 mL), the organic layers were combined, dried, filtered, and concentrated. The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and/or GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. Unless stated otherwise, purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product.

Characterization Data for Starting Materials

Note: All starting materials have been prepared according to the previously published procedures.[1-5] All starting materials have been previously reported. All amides are bench-stable solids, with no decomposition observed over the period of six months.

Benzoylpiperidine-2,6-dione (1a). White solid. GC: rt = 17.94 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (p, *J* = 6.6 Hz, 2 H), 2.80 (t, *J* = 6.5 Hz, 4 H), 7.52 (t, *J* = 7.8 Hz, 2 H), 7.67 (t, *J* = 7.4 Hz, 1 H), 7.89 (d, *J* = 8.3 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.52, 32.42, 129.13, 130.16, 131.77, 134.96, 170.71, 171.88. MS = 217.1 (EI).

1-(4-Methylbenzoyl)piperidine-2,6-dione (1b). White solid. GC: rt = 19.26 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.16 (p, *J* = 6.6 Hz, 2 H), 2.44 (s, 3 H), 2.79 (t, *J* = 6.5 Hz, 4 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 7.77 (d, *J* = 8.3 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.52, 21.89, 32.42, 129.23, 129.87, 130.32, 146.32, 170.39, 171.87. MS = 231.1 (EI).

1-(4-Methoxybenzoyl)piperidine-2,6-dione (1c). White solid. GC: rt = 20.72 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.15 (p, *J* = 6.4 Hz, 2 H), 2.78 (t, *J* = 6.4 Hz, 4 H), 3.89 (s, 3 H), 6.70 (d, *J* = 8.4 Hz, 2 H), 7.85 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.52, 32.44, 55.69, 114.49, 124.48, 132.75, 165.09, 169.49, 171.90. MS = 247.1 (EI).

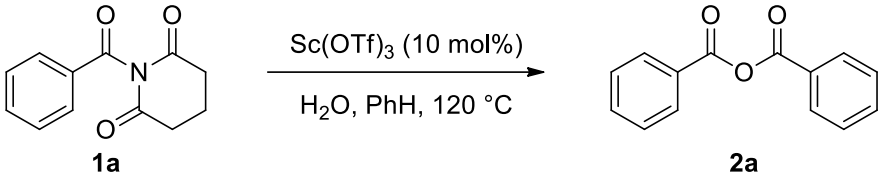
1-(2-Naphthoyl)piperidine-2,6-dione (1d). White solid. GC: rt = 23.08 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.23 (p, *J* = 6.5 Hz, 2 H), 2.86 (t, *J* = 6.5 Hz, 4 H), 7.59 (t, *J* = 7.5 Hz, 1 H), 7.66 (t, *J* = 7.5 Hz, 1 H), 7.91 (d, *J* = 8.1 Hz, 1 H), 7.94 (s, 2 H), 7.97 (d, *J* = 8.3 Hz, 1 H), 8.37 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.57, 32.50, 124.75, 127.16, 127.90, 129.19, 129.49, 129.82, 132.45, 132.63, 136.42, 170.85, 171.98. MS = 267.1 (EI).

1-(4-(Trifluoromethyl)benzoyl)piperidine-2,6-dione (1e). White solid. GC: rt = 17.11 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (p, *J* = 6.5 Hz, 2 H), 2.81 (t, *J* = 6.5 Hz, 4 H), 7.77 (d, *J* = 8.2 Hz, 2 H), 7.99 (d, *J* = 8.1 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.43, 32.36, 123.26 (J^1 = 271.3 Hz), 126.21 (J^3 = 3.8 Hz), 130.35, 134.80, 135.94 (J^2 = 32.5 Hz), 170.15, 171.94. ^{19}F NMR (471 MHz, $CDCl_3$) δ -63.4. MS = 285.1 (EI).

1-(4-Fluorobenzoyl)piperidine-2,6-dione (1f). White solid. GC: rt = 11.90 min. ^{1}H NMR (500 MHz,$CDCl_3$) δ 2.16 (p, *J* = 6.0 Hz, 2 H), 2.79 (t, *J* = 6.3 Hz, 4 H), 7.18 (t, *J* = 7.9 Hz, 2 H), 7.88-7.93 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.46, 32.38, 116.51 (J^2 = 22.5 Hz), 128.31 (J^4 = 2.5 Hz), 133.00 (J^3 = 10.0 Hz), 166.83 (J^1 = 257.5 Hz), 169.56, 171.91. ^{19}F NMR (471 MHz, $CDCl_3$) δ -101.31. MS = 235.1 (EI).

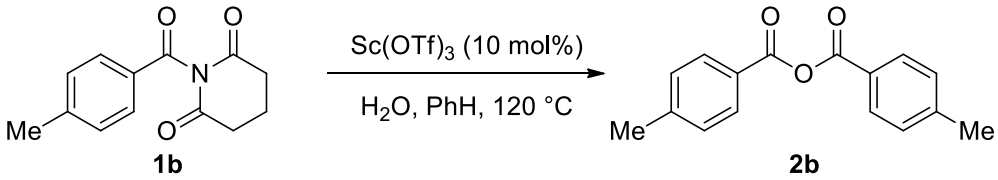
Sc(OTf)$_3$-Catalyzed Synthesis of Anhydrides from Amides by N–C Cleavage

Benzoylpiperidine-2,6-dione (1a).



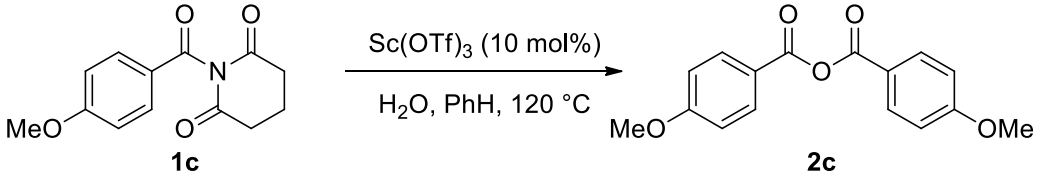
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.40 mmol), scandium triflate (10 mol%) and water (0.50 equiv) in benzene (0.40 M) for 18 h at 120 °C, afforded after work-up and chromatography the title compound in 86.9% yield (39.3 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (t, *J* = 7.3 Hz, 4 H), 7.71 (t, *J* = 7.4 Hz, 2 H), 8.19 (d, *J* = 7.7 Hz, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 128.88, 128.88, 130.58, 134.54, 162.36. Spectroscopic properties matched those described previously.[6]

1-(4-Methylbenzoyl)piperidine-2,6-dione (1b).



According to the general procedure, the reaction of 1-(4-methylbenzoyl)piperidine-2,6-dione (0.40 mmol), scandium triflate (10 mol%) and water (0.50 equiv) in benzene (0.40 M) for 3 h at 120 °C, afforded after work-up and chromatography the title compound in 76.7% yield (39.0 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.48 (s, 3 H), 7.34 (d, *J* = 7.9 Hz, 2 H), 8.06 (d, *J* = 7.9 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.87, 126.23, 129.58, 130.64, 145.56, 162.56. Spectroscopic properties matched those described previously.[6]

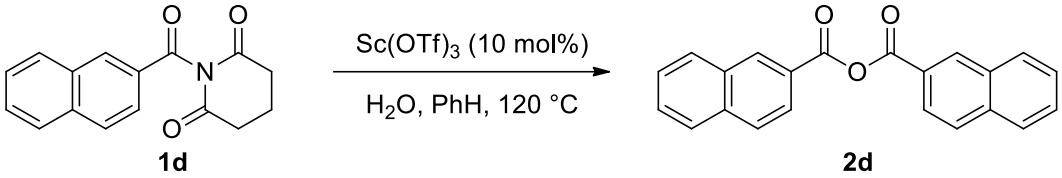
1-(4-Methoxybenzoyl)piperidine-2,6-dione (1c).



According to the general procedure, the reaction of 1-(4-methoxybenzoyl)piperidine-2,6-dione (0.40 mmol), scandium triflate (10 mol%) and water (0.50 equiv) in benzene (0.40 M) for 18 h at 120 °C, afforded after work-up and chromatography the title compound in 69.1%

yield (39.6 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.92 (s, 3 H), 7.01 (d, *J* = 8.5 Hz, 2 H), 8.12 (d, *J* = 8.6 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.61, 114.14, 121.29, 132.84, 162.29, 164.58. Spectroscopic properties matched those described previously.[6]

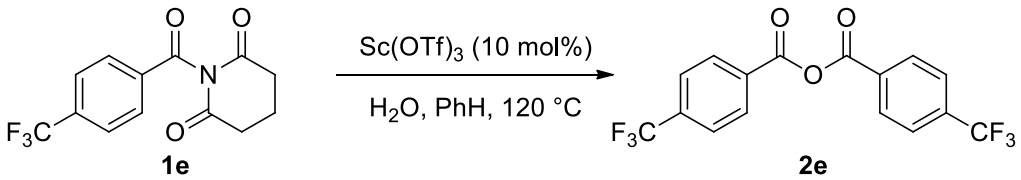
1-(2-Naphthoyl)piperidine-2,6-dione (1d).



1d **2d**

According to the general procedure, the reaction of 1-(2-naphthoyl)piperidine-2,6-dione (0.40 mmol), scandium triflate (10 mol%) and water (0.50 equiv) in benzene (0.40 M) for 18 h at 120 °C, afforded after work-up and chromatography the title compound in 57.8% yield (37.7 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (t, *J* = 7.4 Hz, 1 H), 7.70 (t, *J* = 7.5 Hz, 1 H), 7.97 (d, *J* = 8.2 Hz, 1 H), 8.01 (d, *J* = 8.6 Hz, 1 H), 8.05 (d, *J* = 8.1 Hz, 1 H), 8.22 (d, *J* = 8.6 Hz, 1 H), 8.81 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 125.42, 126.10, 127.15, 127.94, 128.87, 129.25, 129.68, 132.46, 132.83, 136.25, 162.76. Spectroscopic properties matched those described previously.[7]

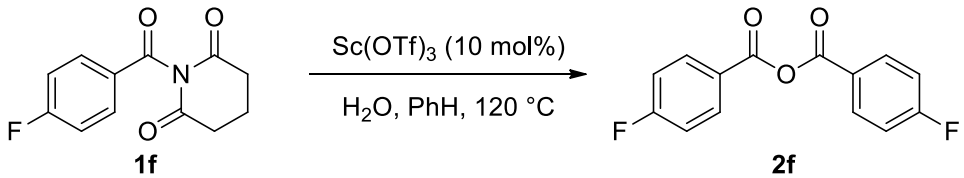
1-(4-(Trifluoromethyl)benzoyl)piperidine-2,6-dione (1e).



1e **2e**

According to the general procedure, the reaction of 1-(4-(trifluoromethyl)benzoyl)piperidine-2,6-dione (0.40 mmol), scandium triflate (10 mol%) and water (0.50 equiv) in benzene (0.40 M) for 18 h at 120 °C, afforded after work-up and chromatography the title compound in 57.6% yield (41.7 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.9 Hz, 2 H), 8.30 (d, *J* = 7.9 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 123.30 (J^1 = 271.3 Hz), 126.05 (J^3 = 3.8 Hz), 130.96, 131.68, 136.11 (J^2 = 32.5 Hz), 160.77. ^{19}F NMR (471 MHz, $CDCl_3$) δ -63.4. Spectroscopic properties matched those described previously.[8]

1-(4-Fluorobenzoyl)piperidine-2,6-dione (1f).



1f **2f**

According to the general procedure, the reaction of 1-(4-fluorobenzoyl)piperidine-2,6-dione (0.40 mmol), scandium triflate (10 mol%) and water (0.50 equiv) in benzene (0.50 M) for 18 h at 120 °C, afforded after work-up and chromatography the title compound in 59.5% yield (31.2 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (t, J = 8.4 Hz, 2 H), 8.17-8.22 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 116.29 (J^2 = 21.3 Hz), 125.00 (J^4 = 3.8 Hz), 133.31 (J^3 = 10.0 Hz), 161.21, 166.74 (J^1 = 256.3 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -102.08. Spectroscopic properties matched those described previously.[9]

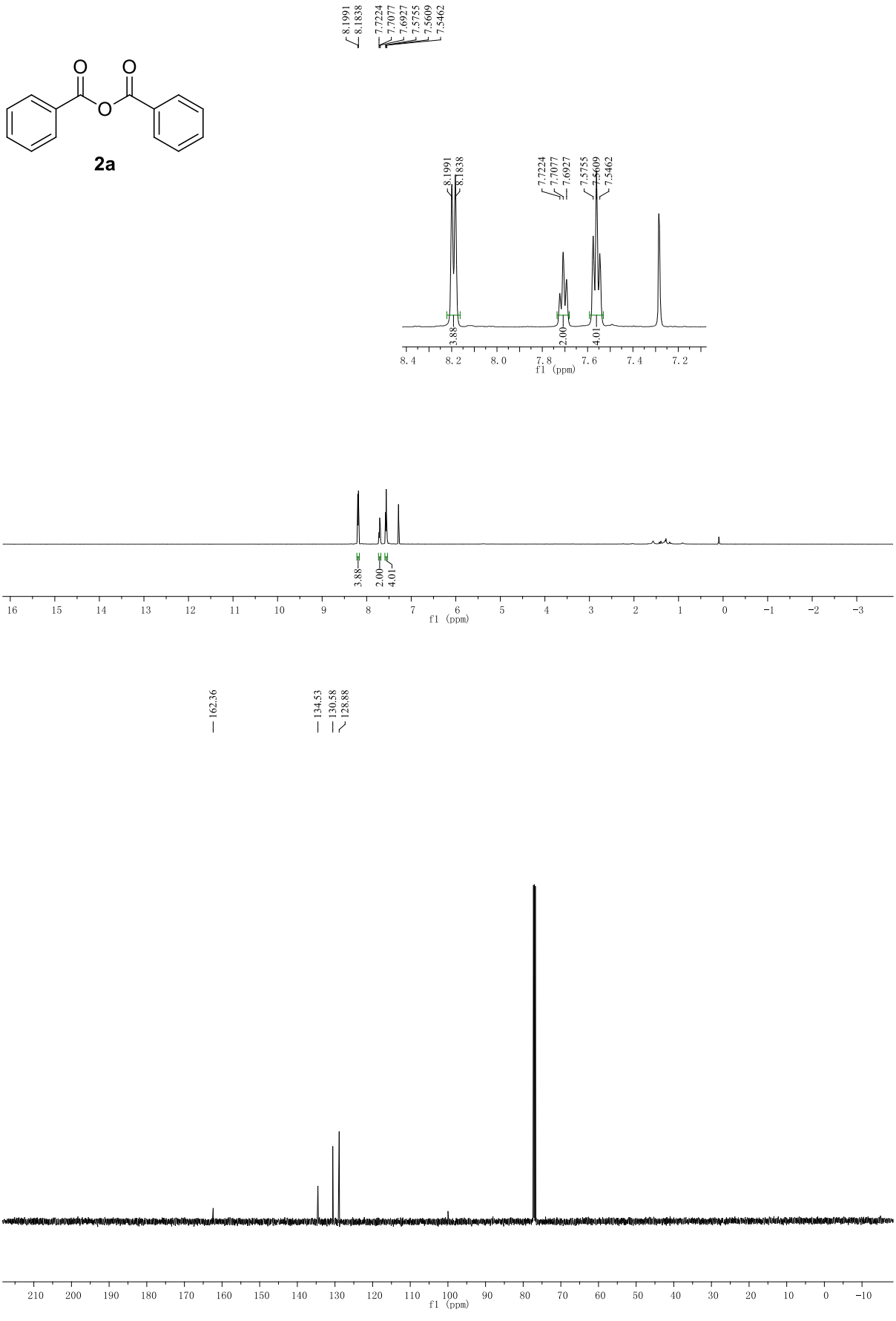
Mechanistic Studies

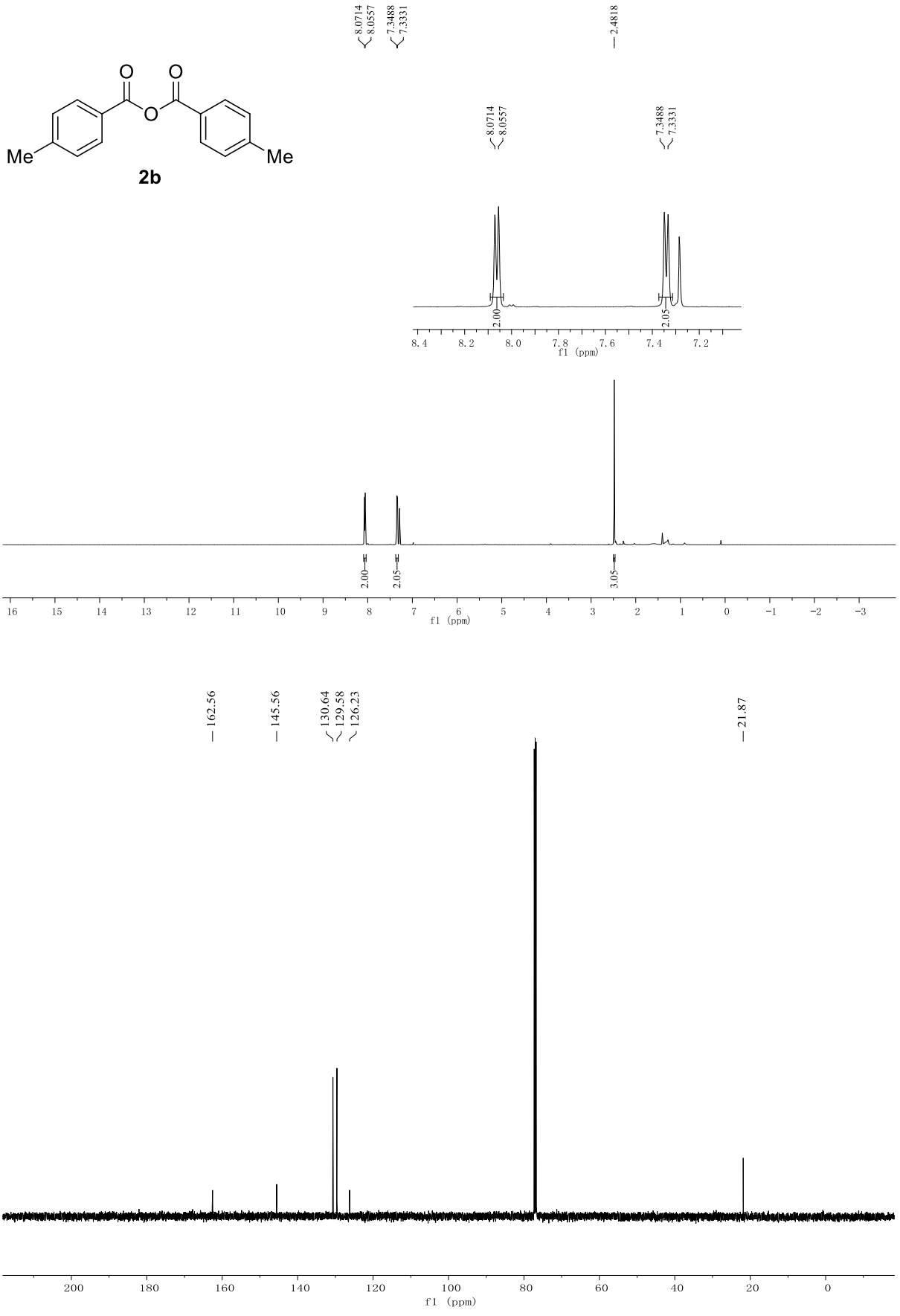
Stability Studies. According to the general procedure, an oven-dried vial equipped with a stir bar was charged with an amide substrate (neat, 1.0 equiv), placed under a positive pressure of nitrogen, and subjected to three evacuation/backfilling cycles. Benzene (0.40 M), scandium triflate (10 mol%) and/or H_2O (10 equiv) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred for the indicated time at RT or 120 °C. After the indicated time, the reaction mixture was cooled down to room temperature (for the runs at 120 °C), washed with HCl (1.0 *N*, 5 mL), extracted with CH_2Cl_2 (3 x 10 mL), the organic layers were combined, dried, filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and/or GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. ***Note:*** the observed stability compares very favorably with the stability of classic bridged lactams.[10]

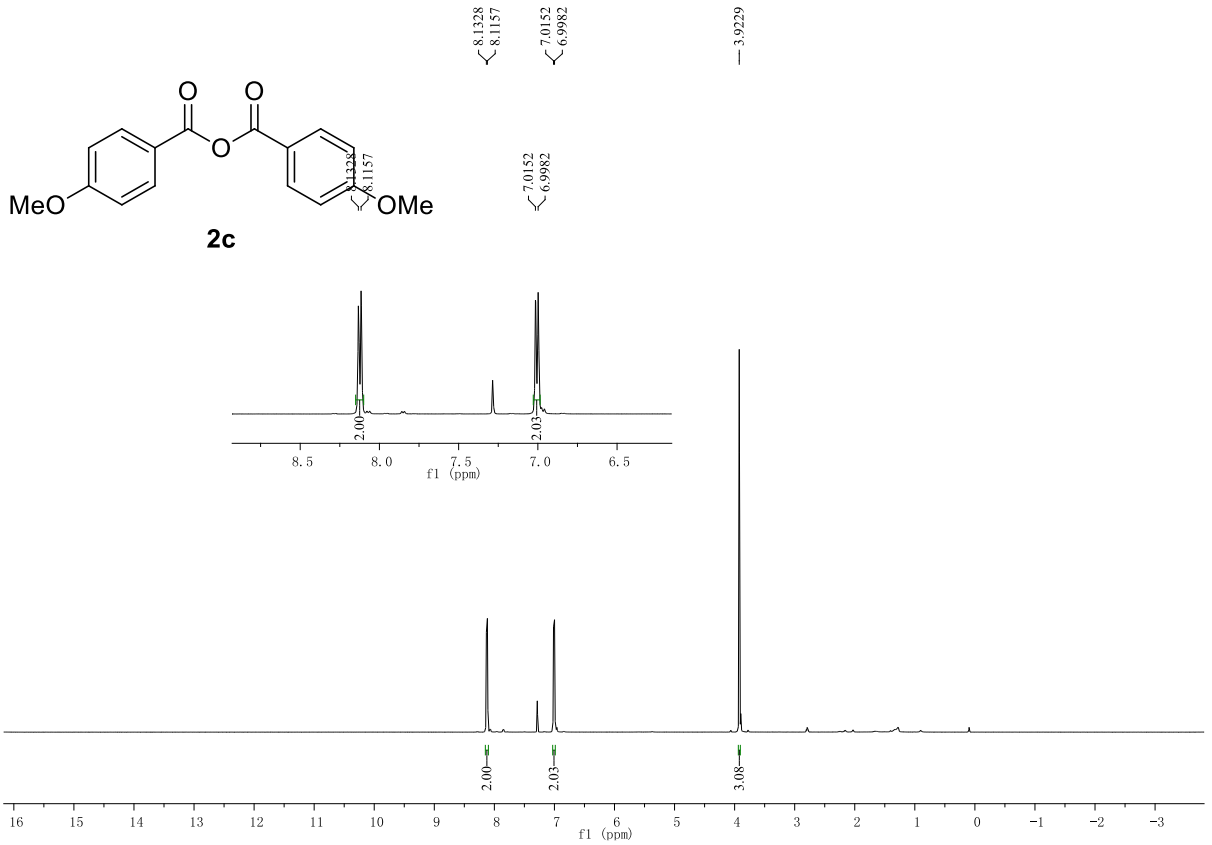
Cross-Over Experiments. According to the general procedure, an oven-dried vial equipped with a stir bar was charged with two amide substrates (neat, 1.0 equiv), placed under a positive pressure of nitrogen, and subjected to three evacuation/backfilling cycles. Benzene (0.40 M), scandium triflate (10 mol%) and H_2O (0.50 equiv) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred for the indicated time at 120 °C. After the indicated time, the reaction mixture was cooled down to room temperature (for the runs at 120 °C), washed with HCl (1.0 *N*, 5 mL), extracted with CH_2Cl_2 (3 x 10 mL), the organic layers were combined, dried, filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and/or GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples.

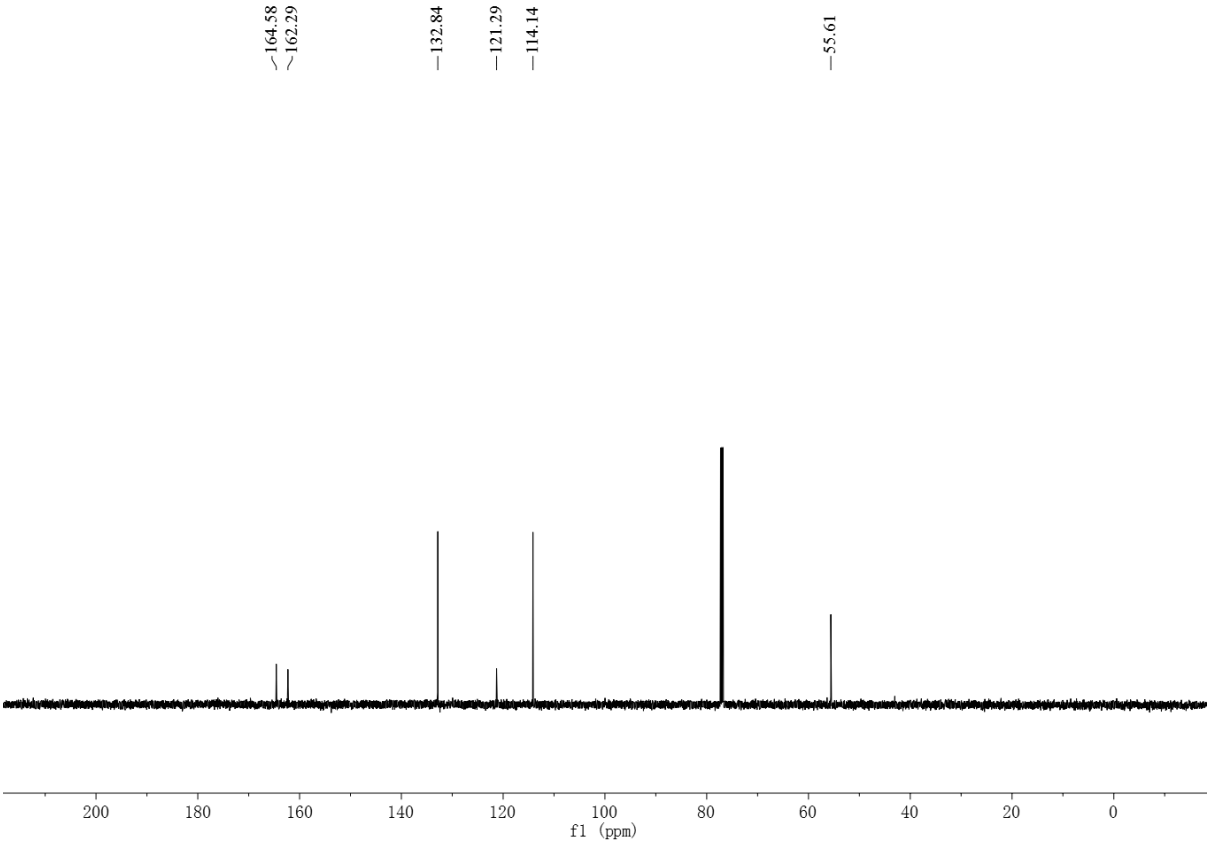
References

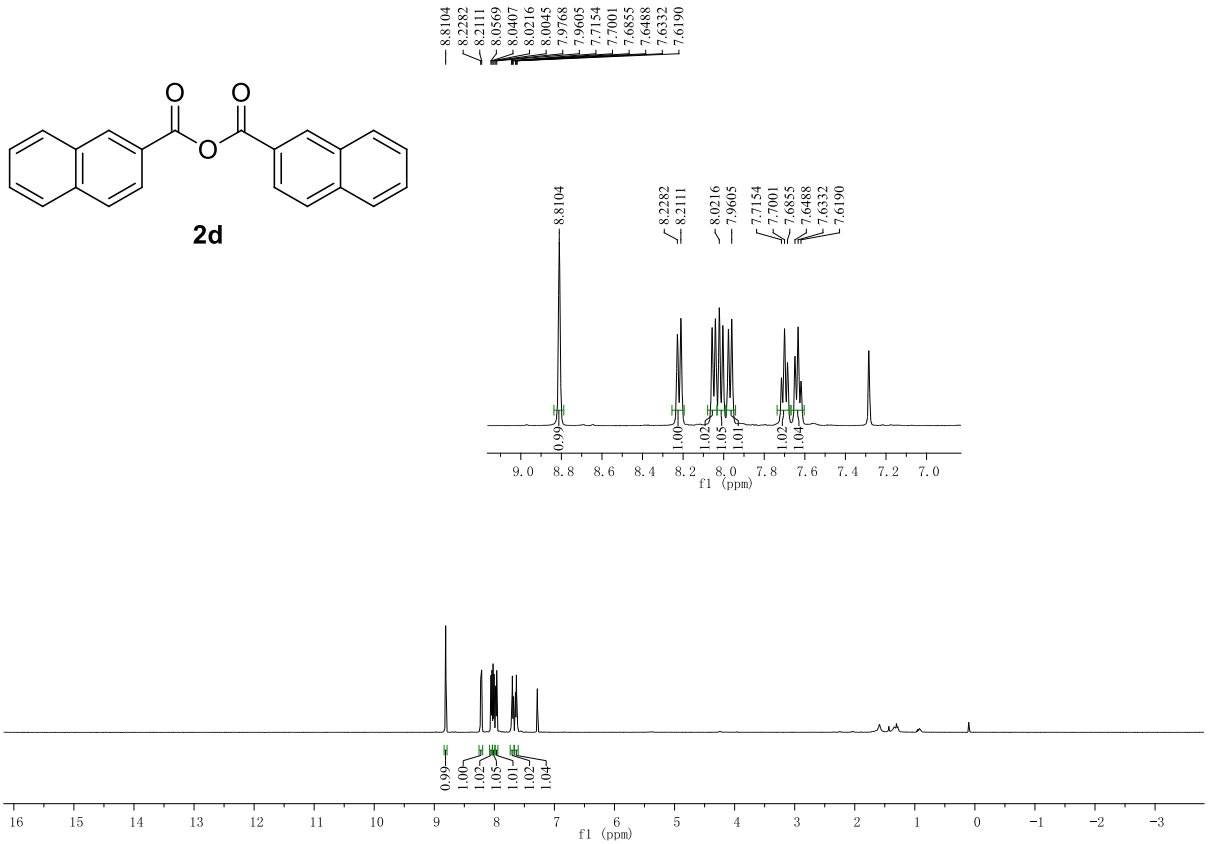
1. Hanada, S.; Tsutsumi, E.; Motoyama, Y.; Nagashima, H. *J. Am. Chem. Soc.* **2009**, *131*, 15032.
2. Hirner, S.; Panknin, O.; Edefuhr, M.; Somfai, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 1907.
3. Hutchby, M.; Houlden, C. E.; Haddow, M. F.; Tyler, S. N. G.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *Angew. Chem. Int. Ed.* **2012**, *51*, 548.
4. Meng, G.; Szostak, M. *Org. Lett.* **2015**, *17*, 4364.
5. Shi, S.; Meng, G.; Szostak, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 6959.
6. Konieczynska, M. D.; Dai, C.; Stephenson, C. R. J. *Org. Biomol. Chem.* **2012**, *10*, 4509.
7. Khatun, N.; Santra, S. K.; Banerjee, A.; Patel, B. K. *Eur. J. Org. Chem.* **2015**, 1309.
8. Shiina, I. *Tetrahedron* **2004**, *60*, 1587.
9. Cirriez, V.; Rasson, C.; Riant, O. *Adv. Synth. Catal.* **2013**, *355*, 3137.
10. Szostak, M.; Yao, L.; Aubé, J. *J. Org. Chem.* **2009**, *74*, 1869, and references cited therein.


8.1991
8.1838
7.7224
7.7077
7.6927
7.5755
7.5609
7.5462
2a
3.88
2.00
4.01
f1 (ppm)
162.36
134.53
130.58
128.88

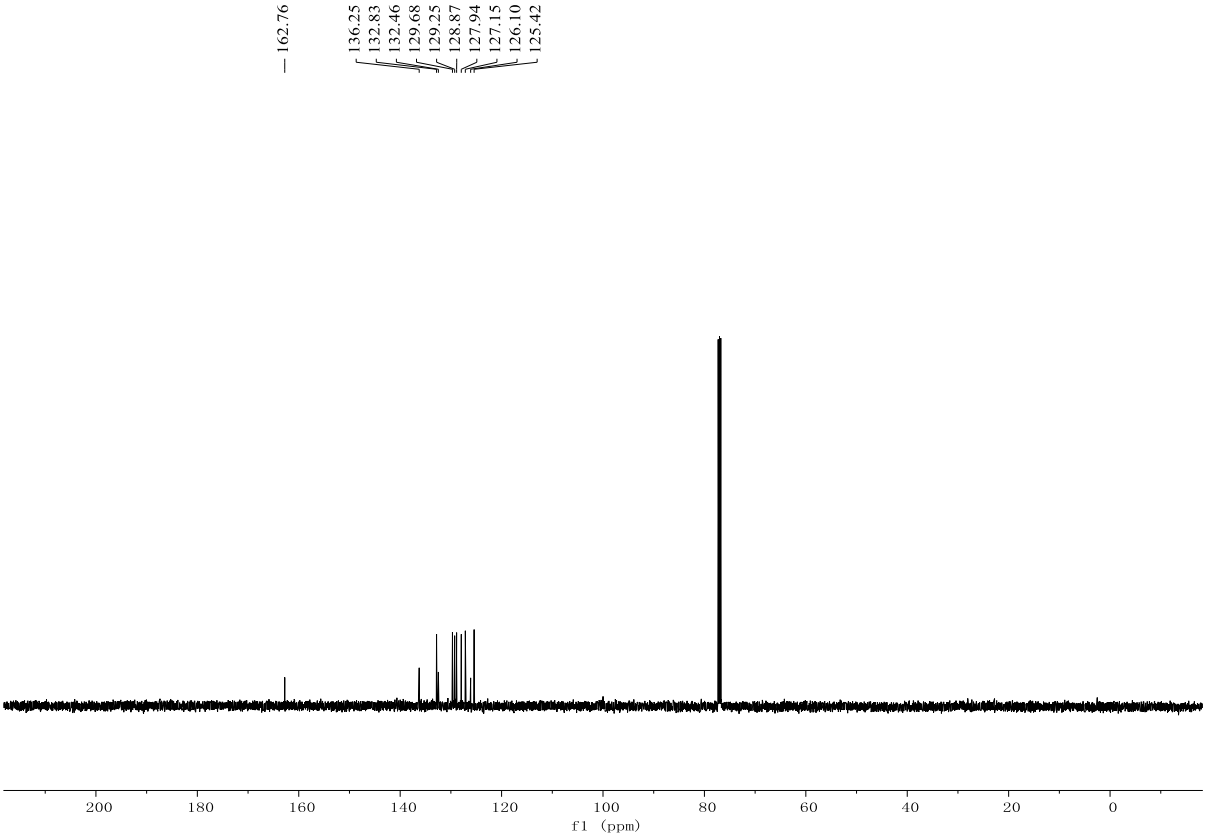

8.0714
8.0557
7.3488
7.3331
2.4818
Me
Me
2b
f1 (ppm)
2.00
2.05
3.05
162.56
145.56
130.64
129.58
126.23
21.87

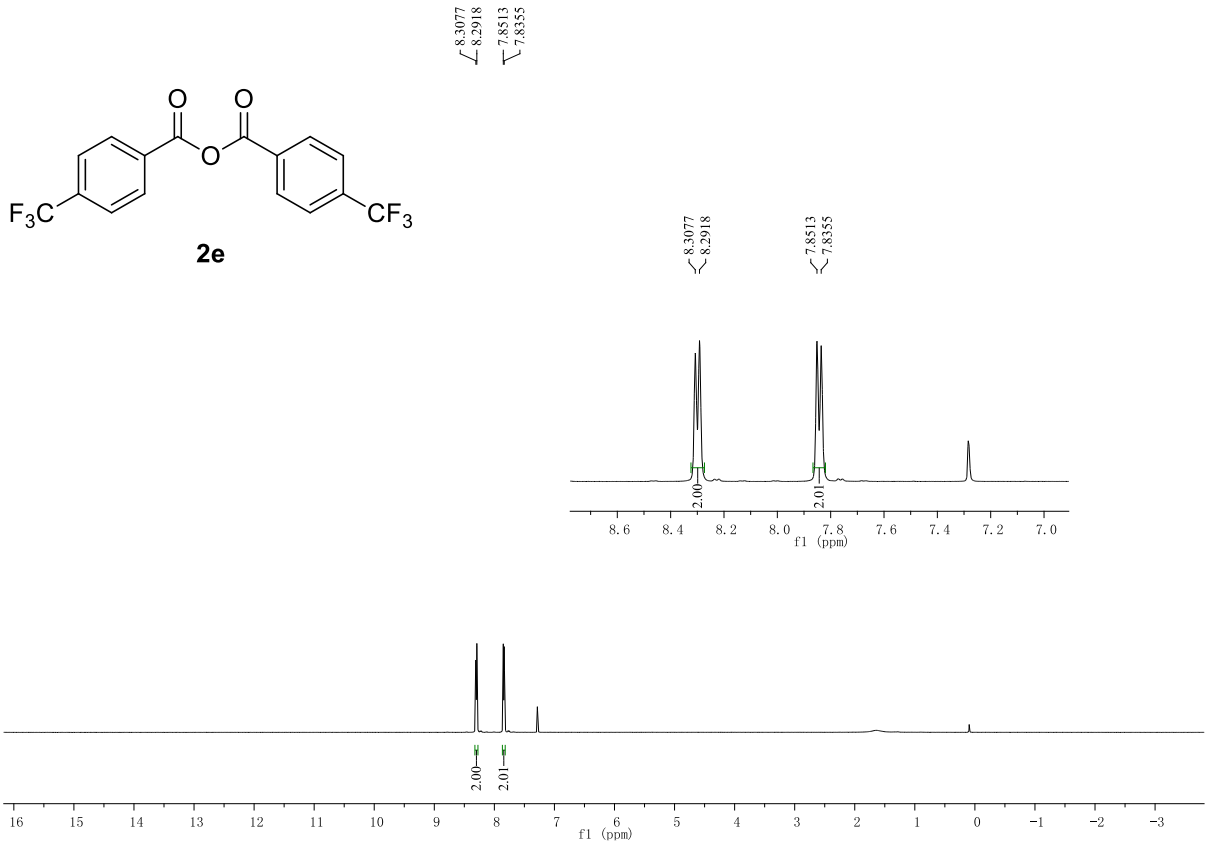

8.1328
8.1157
7.0152
6.9982
3.9229
MeO
OMe
2c
2.00
2.03
3.08
f1 (ppm)

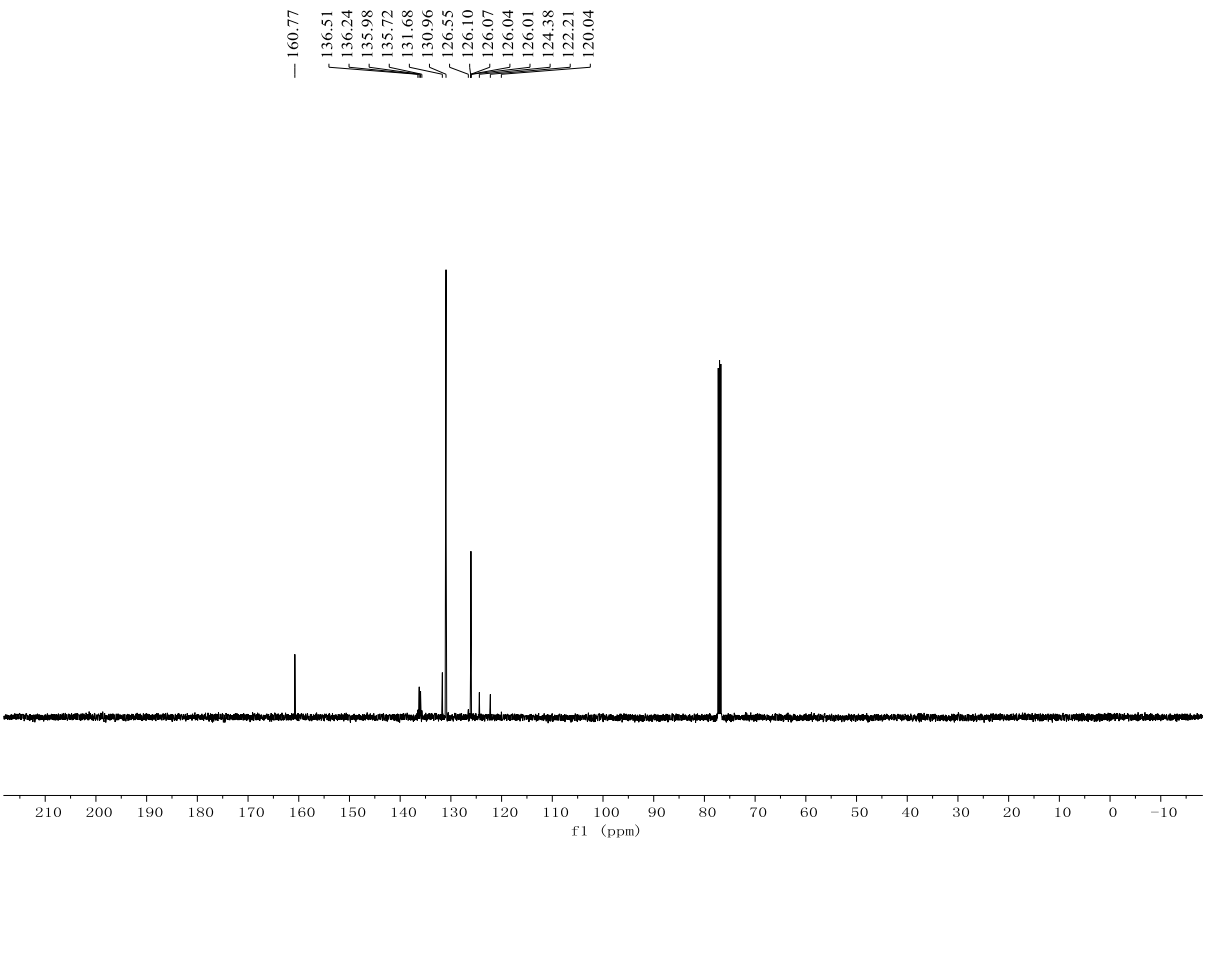

164.58
162.29
132.84
121.29
114.14
55.61
f1 (ppm)

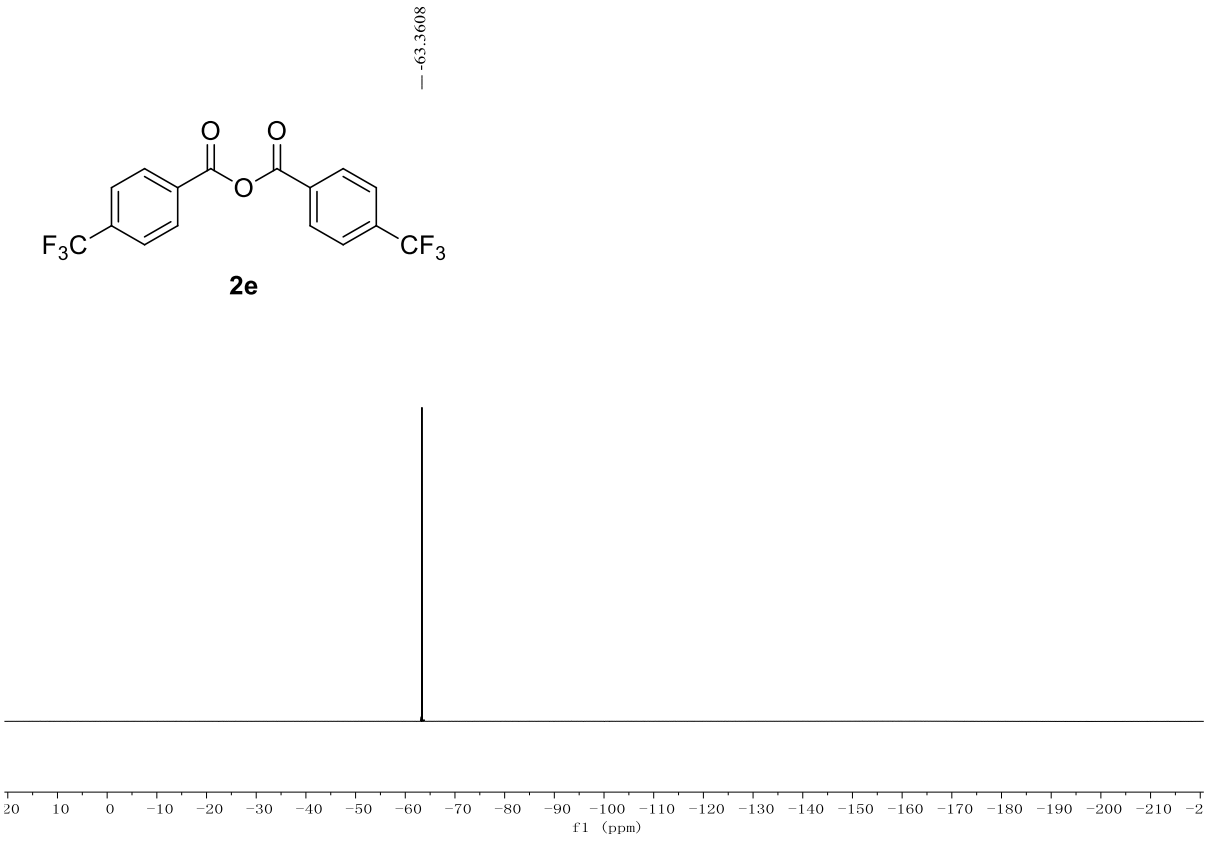

8.8104
8.2282
8.2111
8.0569
8.0407
8.0216
8.0045
7.9768
7.9605
7.7154
7.7001
7.6855
7.6488
7.6332
7.6190
2d
f1 (ppm)

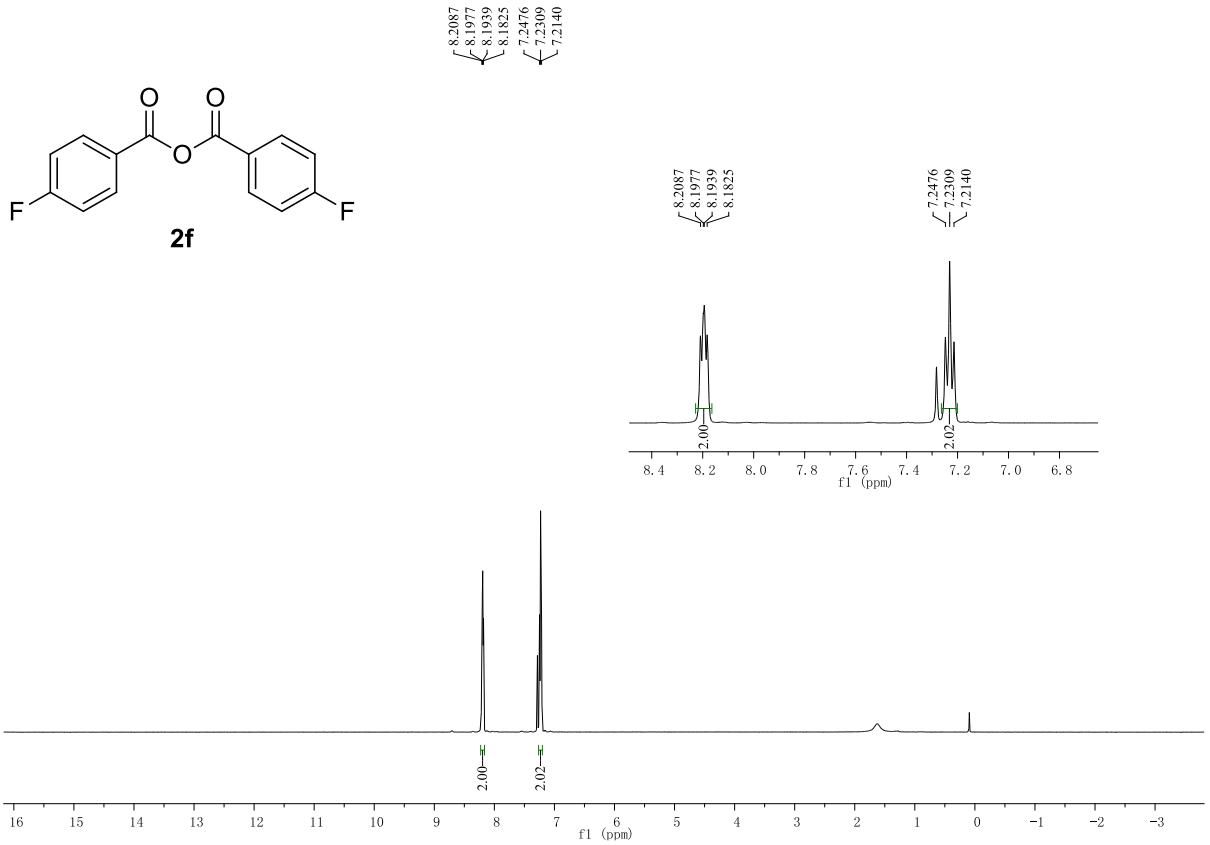
0.99
1.00
1.02
1.05
1.01
1.02
1.04
f1 (ppm)

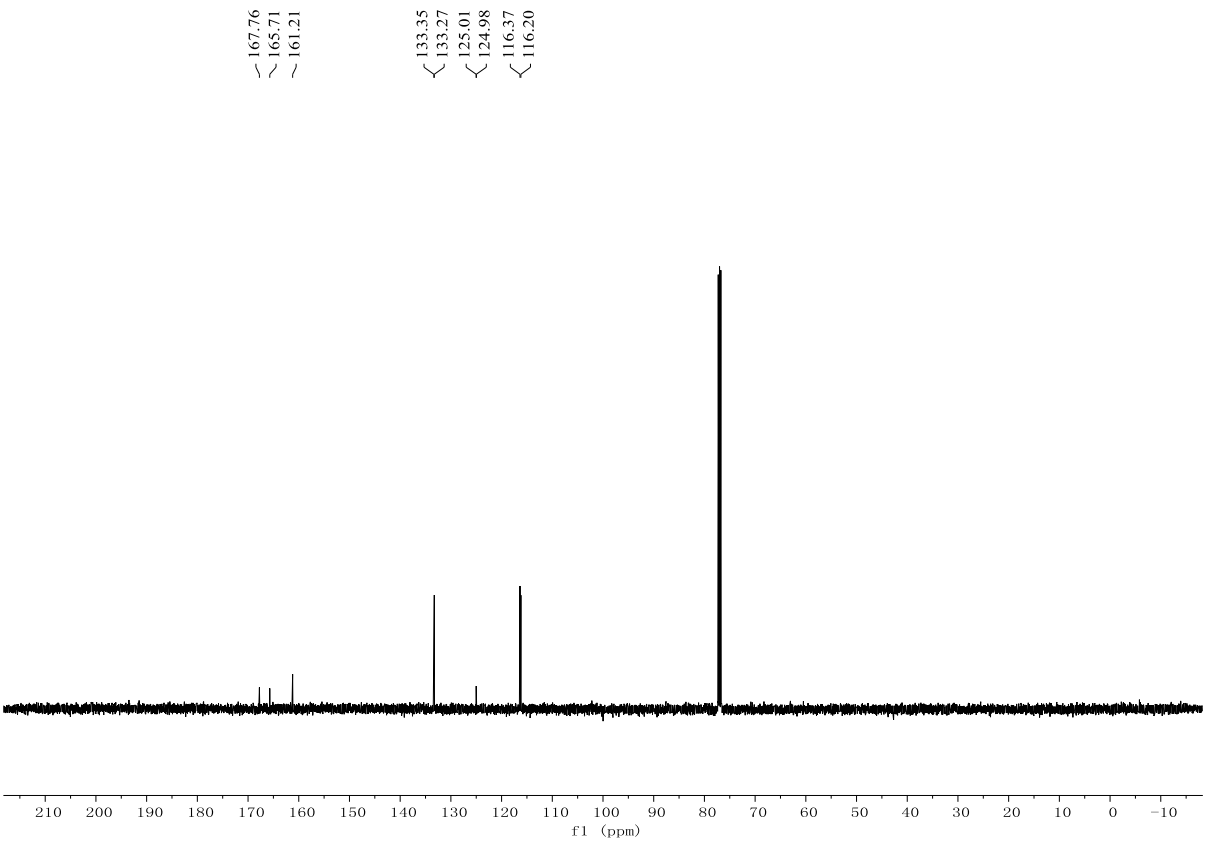

162.76
136.25
132.83
132.46
129.68
129.25
128.87
127.94
127.15
126.10
125.42
f1 (ppm)

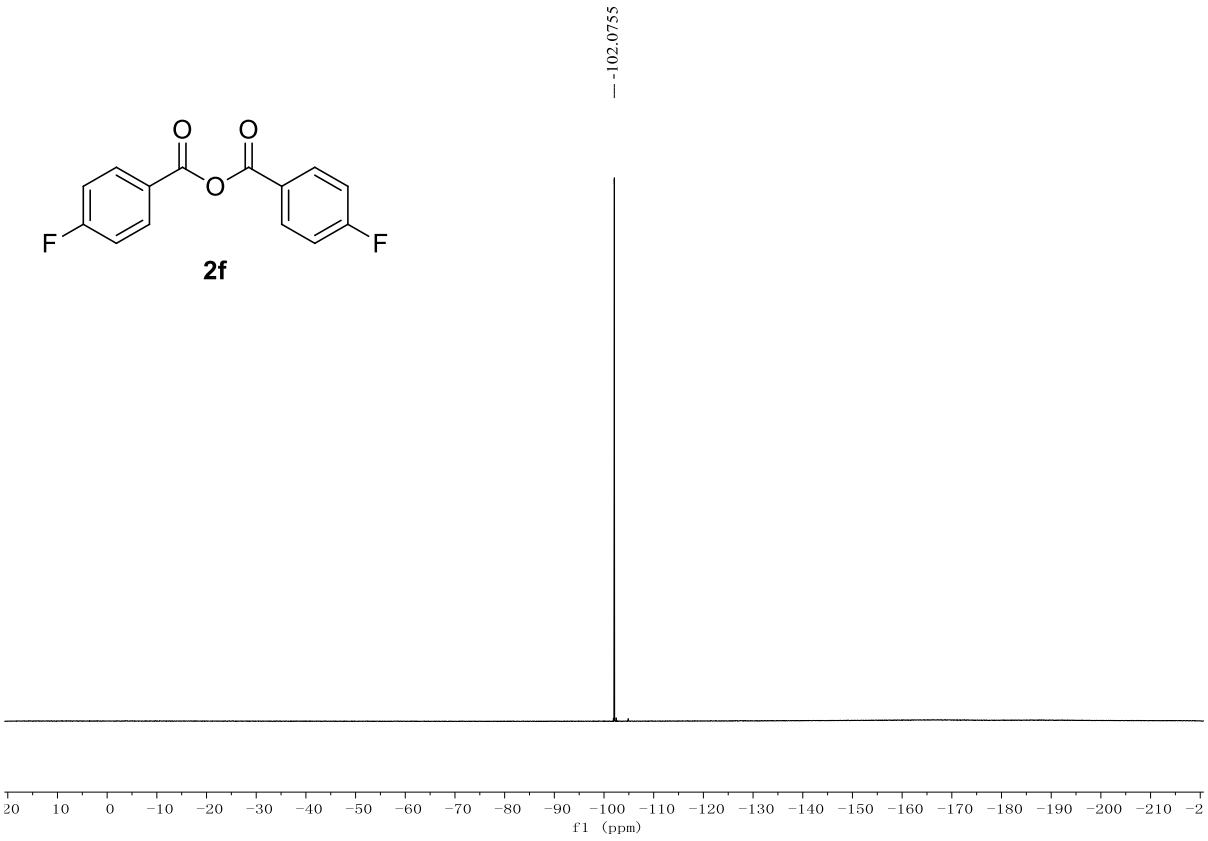

8.3077
8.2918
7.8513
7.8355
O
O
O
F3C
CF3
2e
2.00
2.01
f1 (ppm)

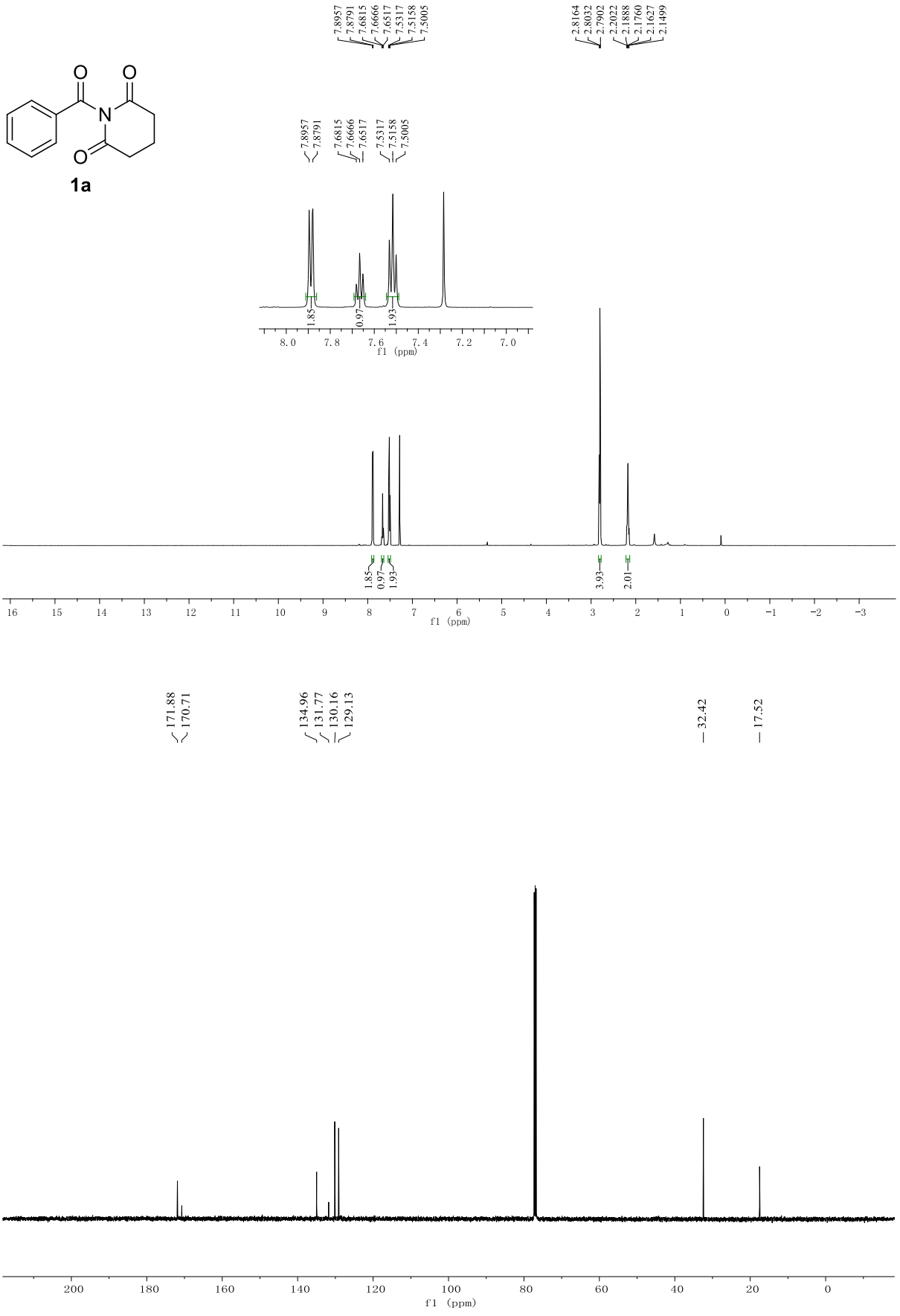

160.77
136.51
136.24
135.98
135.72
131.68
130.96
126.55
126.10
126.07
126.04
126.01
124.38
122.21
120.04
f1 (ppm)

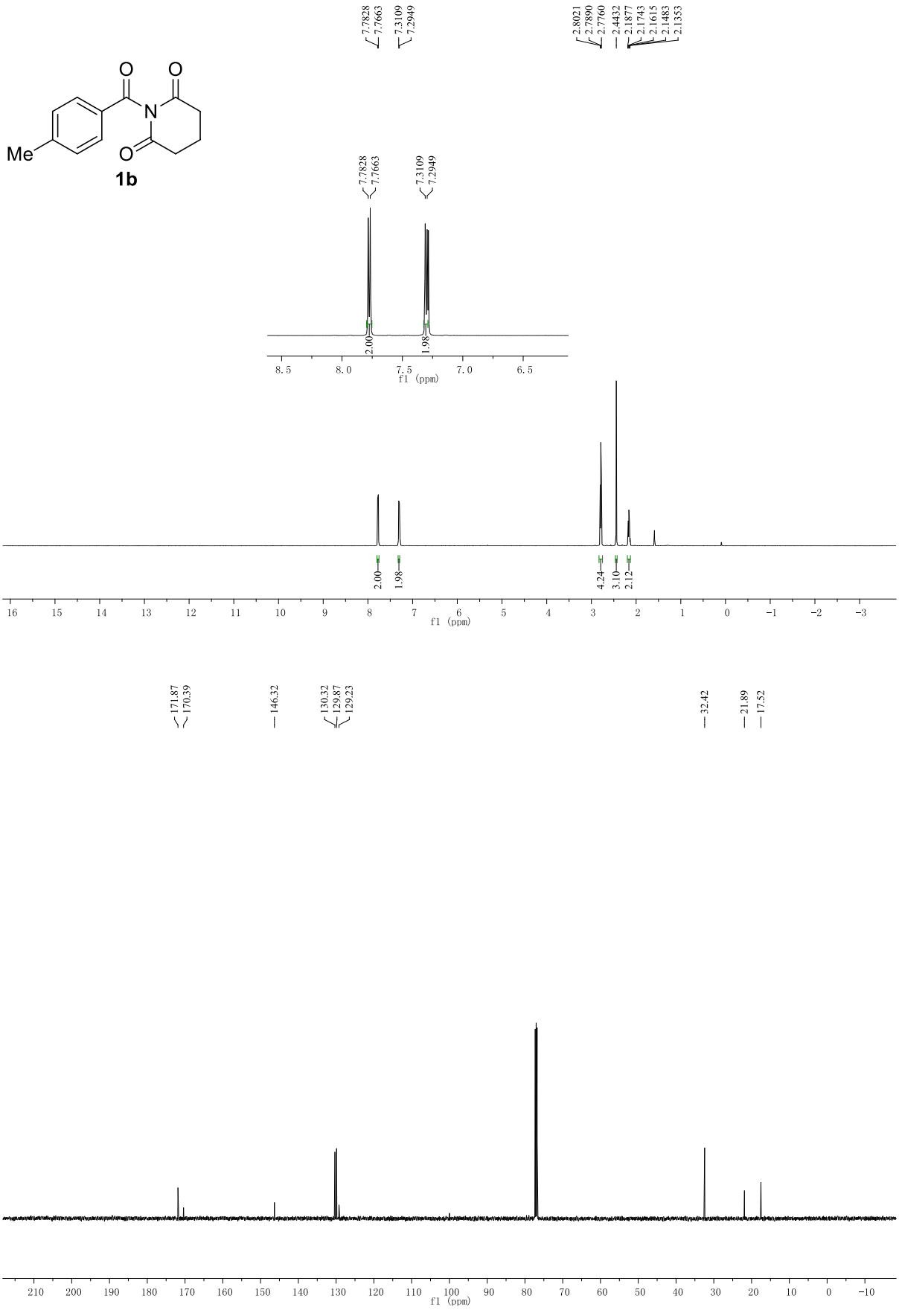

-63.3608
O
O
O
F3C
CF3
2e
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −2
f1 (ppm)

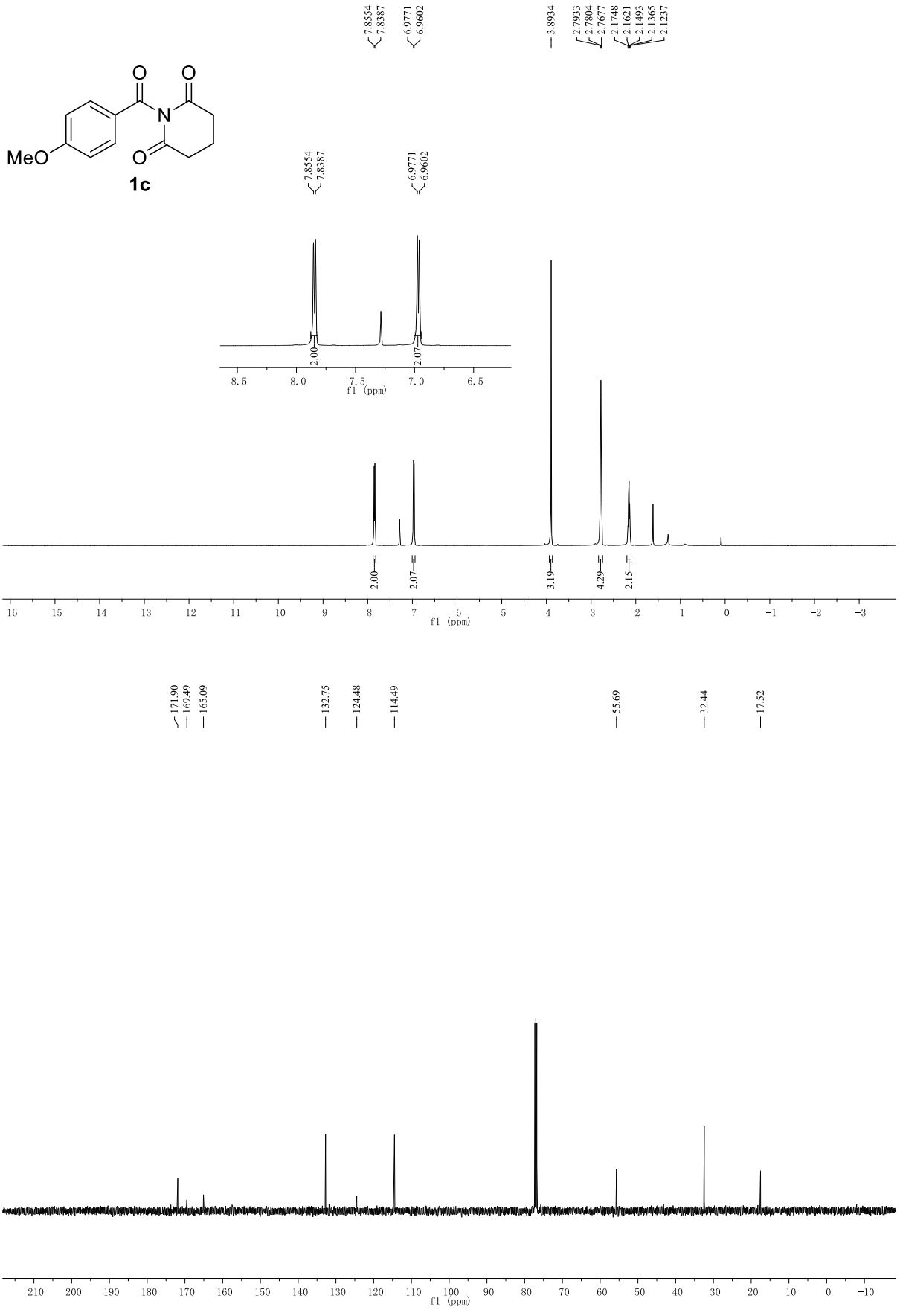

8.2087
8.1977
8.1939
8.1825
7.2476
7.2309
7.2140
O
O
O
F
F
2f
2.00
2.02
f1 (ppm)

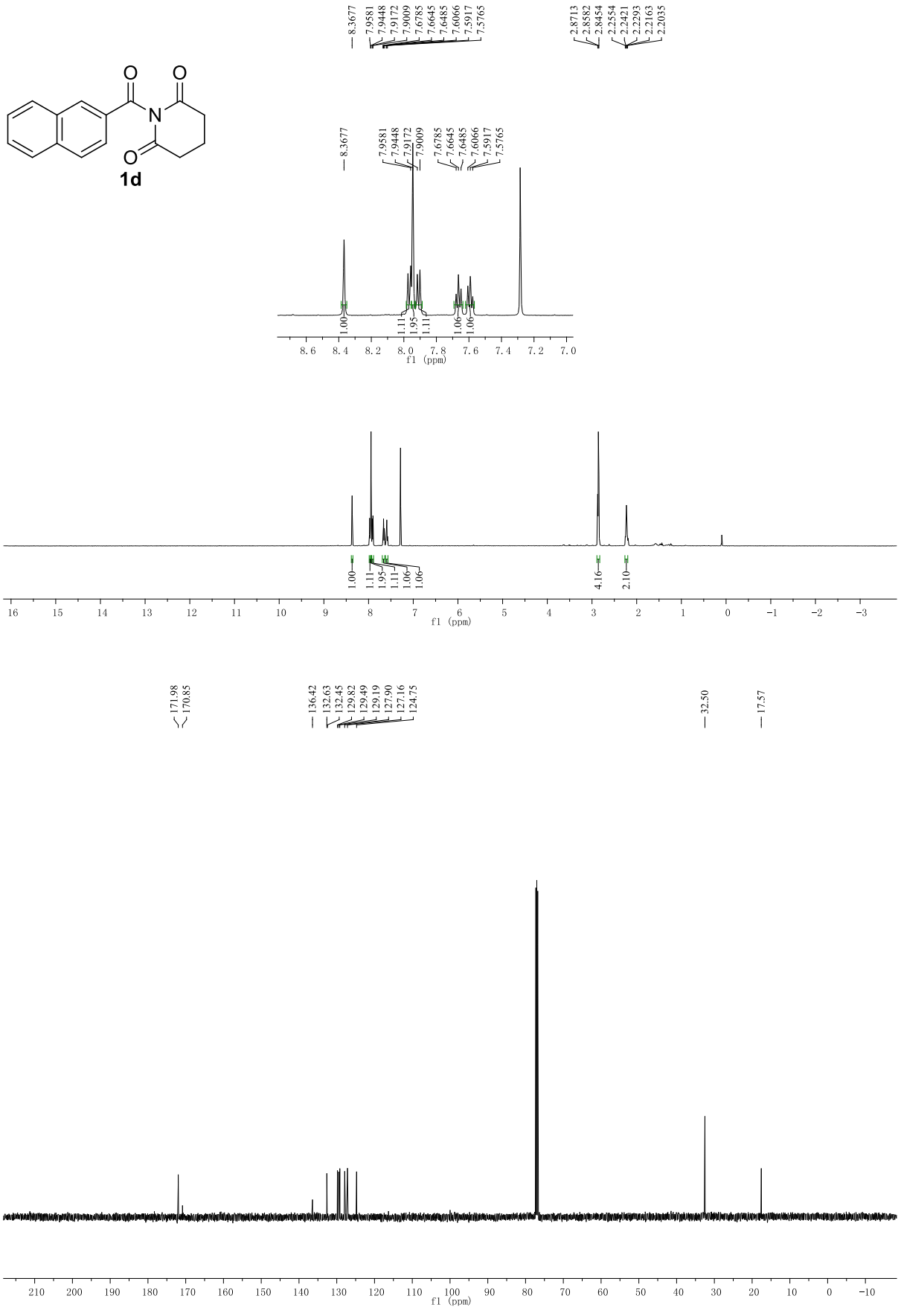

167.76
165.71
161.21
133.35
133.27
125.01
124.98
116.37
116.20
f1 (ppm)


-102.0755
O
O
O
F
F
2f
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −2
f1 (ppm)

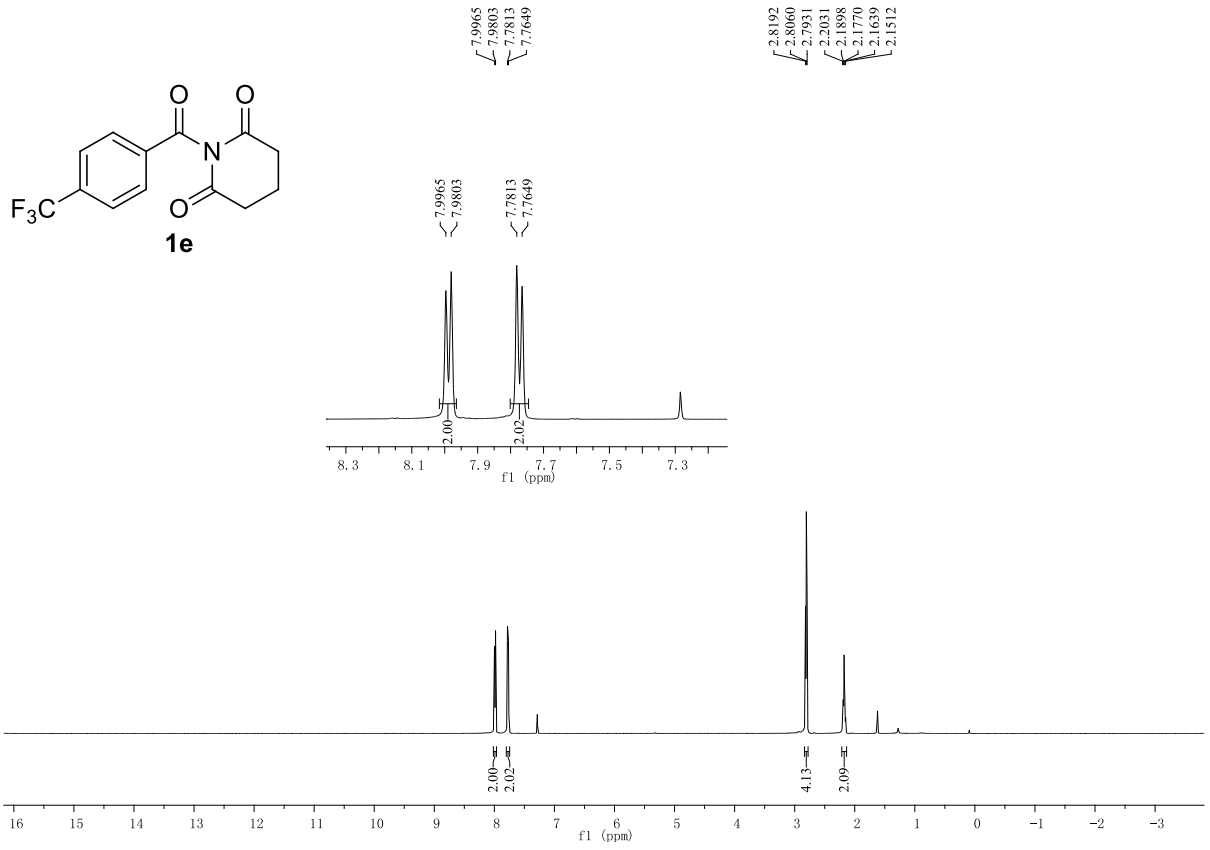

7.8957
7.8791
7.6815
7.6666
7.6517
7.5317
7.5158
7.5005
2.8164
2.8032
2.7902
2.2022
2.1888
2.1760
2.1627
2.1499
1a
1.85
0.97
1.93
3.93
2.01
f1 (ppm)
171.88
170.71
134.96
131.77
130.16
129.13
32.42
17.52

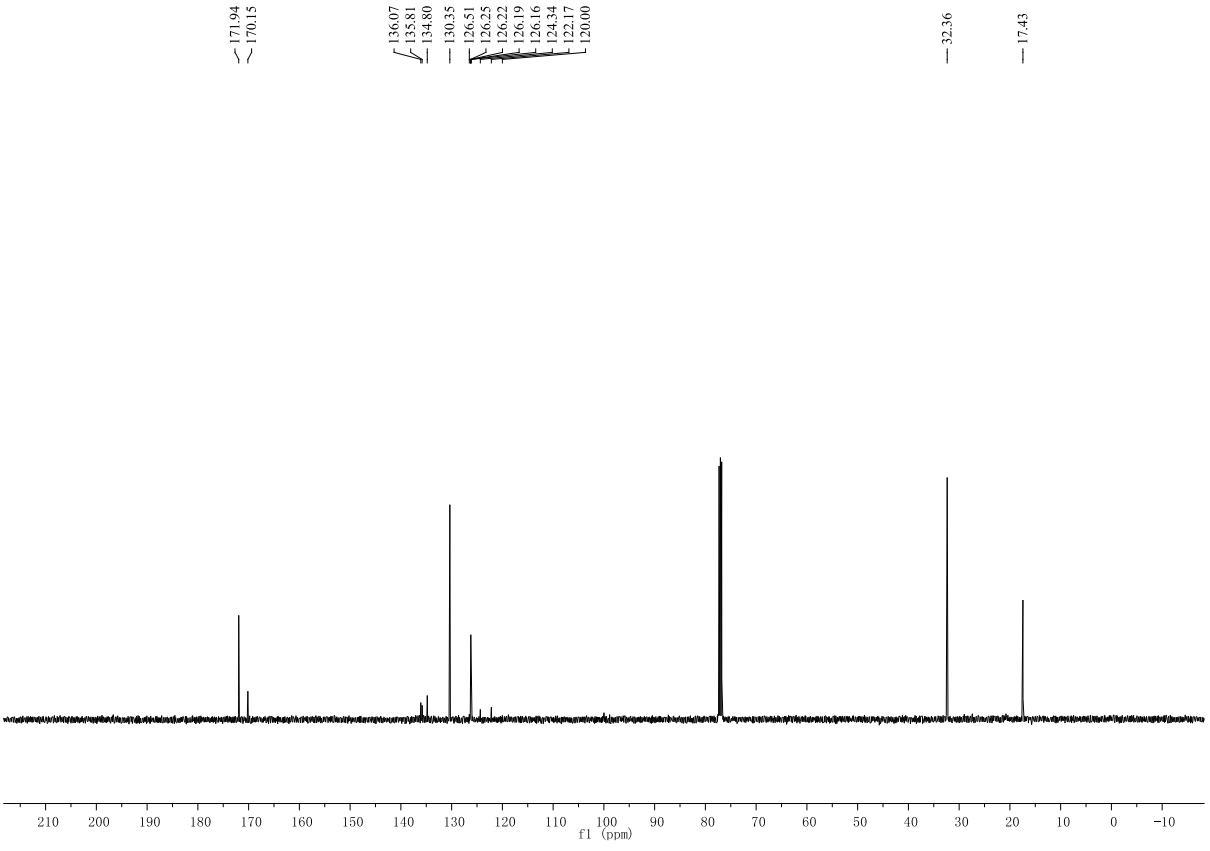

Me
1b
7.7828
7.7663
7.3109
7.2949
2.8021
2.7890
2.7760
2.4432
2.1877
2.1743
2.1615
2.1483
2.1353
2.00
1.98
4.24
3.10
2.12
f1 (ppm)
171.87
170.39
146.32
130.32
129.87
129.23
32.42
21.89
17.52

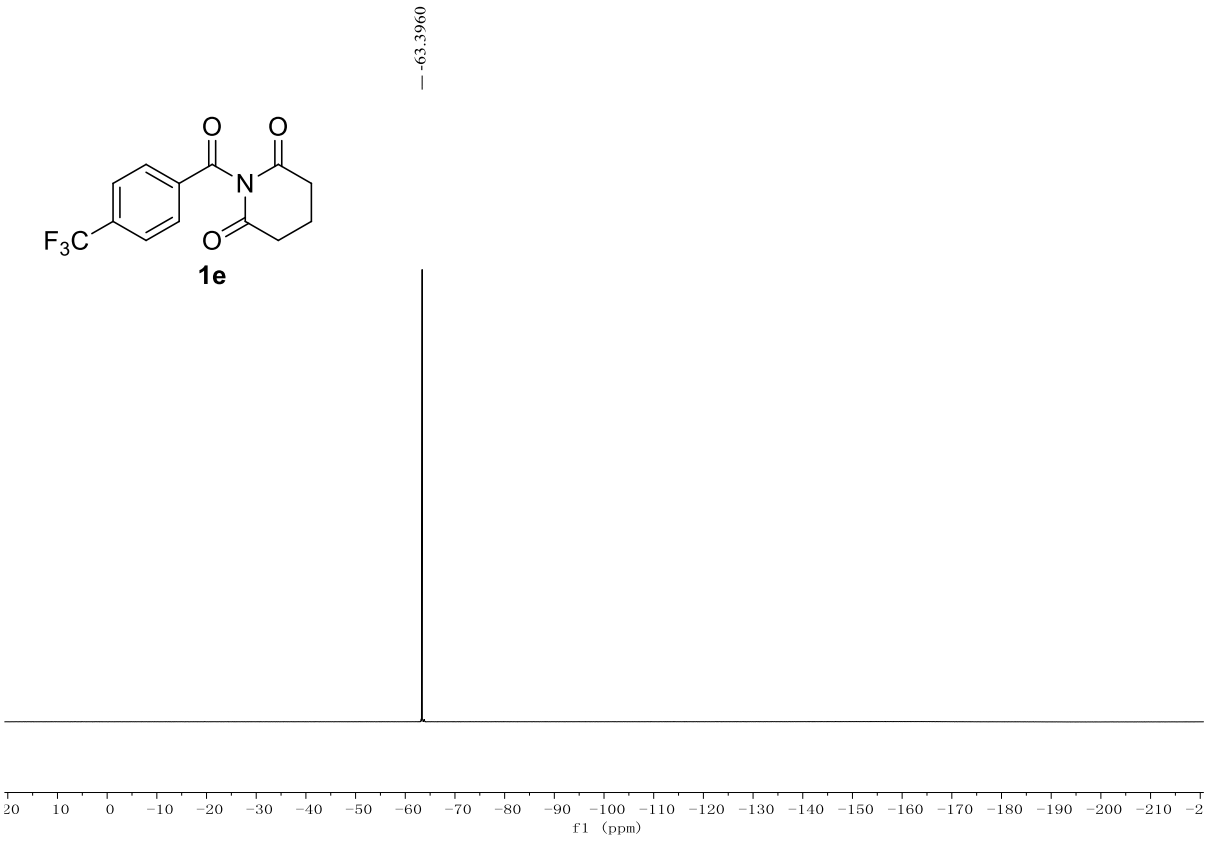

7.8554
7.8387
6.9771
6.9602
3.8934
2.7933
2.7804
2.7677
2.1748
2.1621
2.1493
2.1365
2.1237
MeO
1c
2.00
2.07
f1 (ppm)
3.19
4.29
2.15
171.90
169.49
165.09
132.75
124.48
114.49
55.69
32.44
17.52

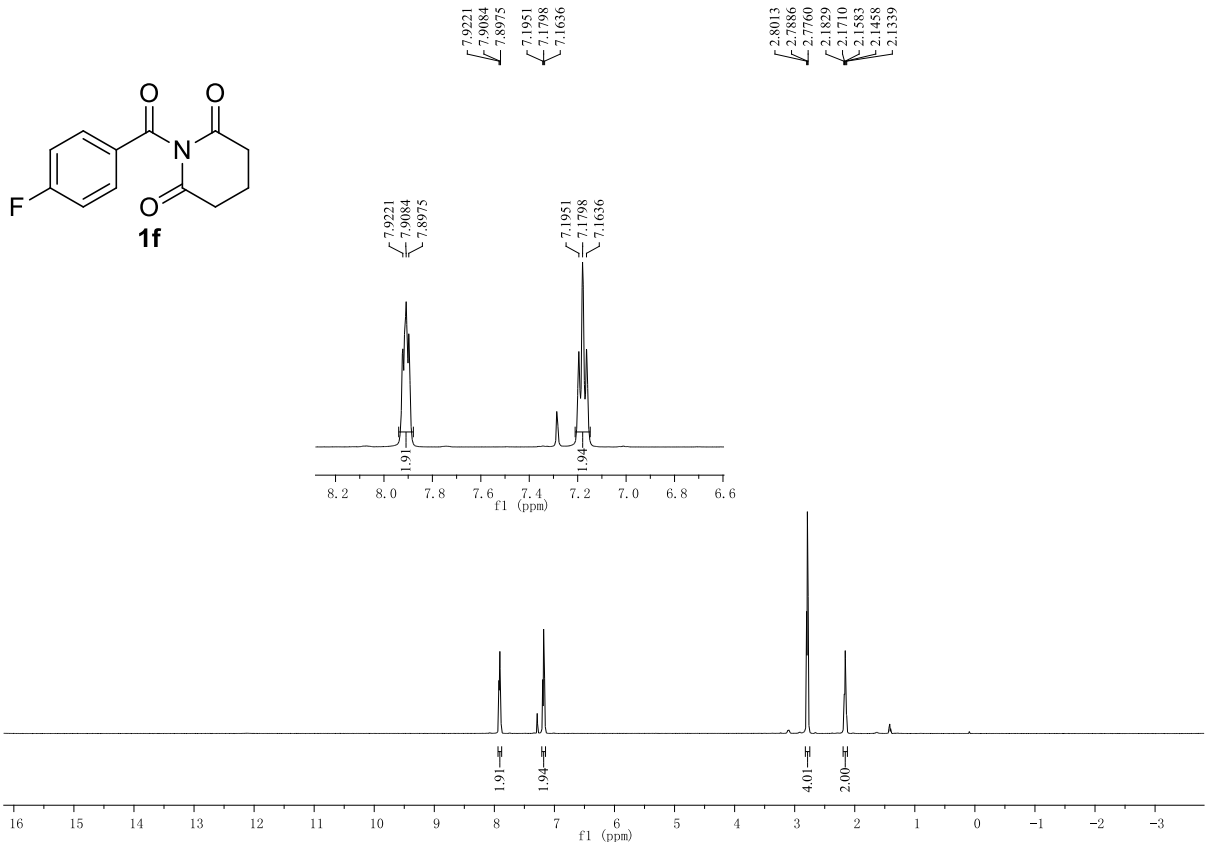

8.3677
7.9581
7.9448
7.9172
7.9009
7.6785
7.6645
7.6485
7.6066
7.5917
7.5765
2.8713
2.8582
2.8454
2.2554
2.2421
2.2293
2.2163
2.2035
1.00
1.11
1.95
1.11
1.06
1.06
4.16
2.10
f1 (ppm)
171.98
170.85
136.42
132.63
132.45
129.82
129.49
129.19
127.90
127.16
124.75
32.50
17.57

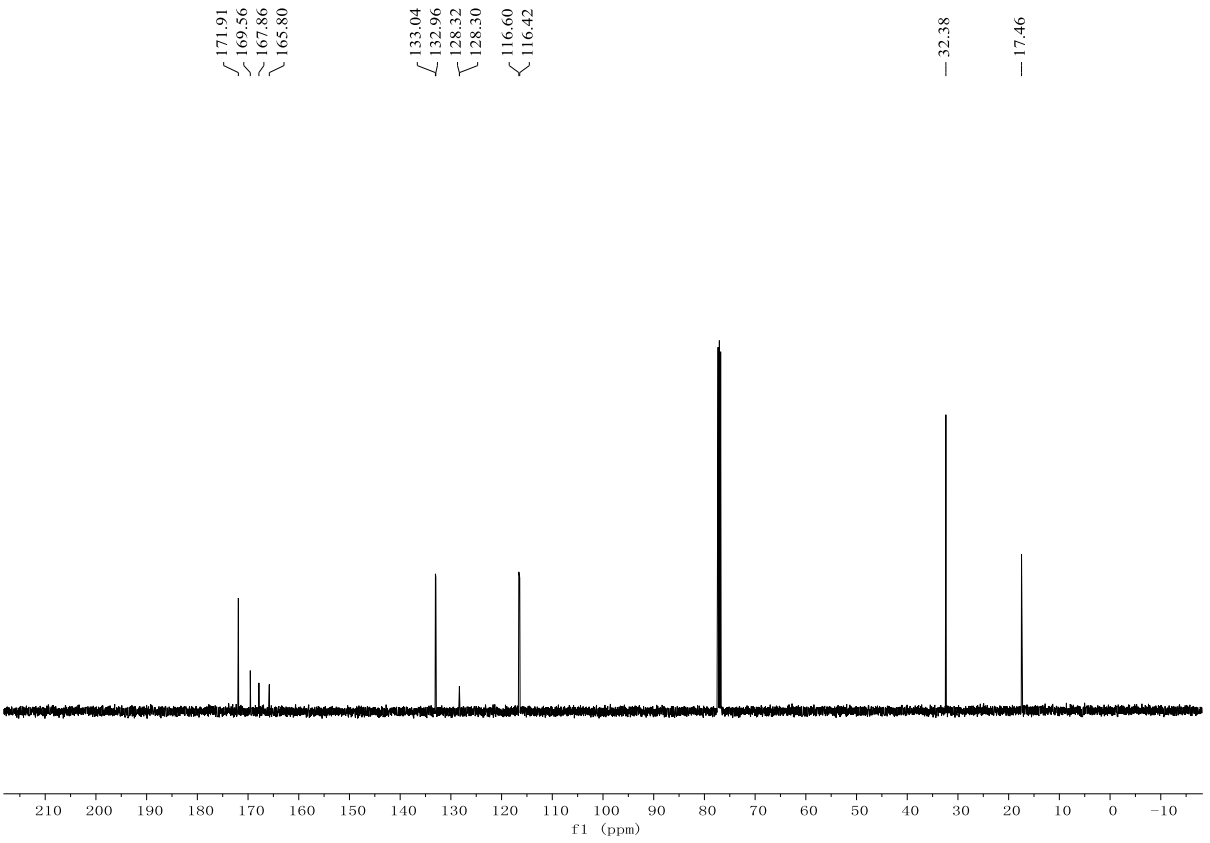
1d

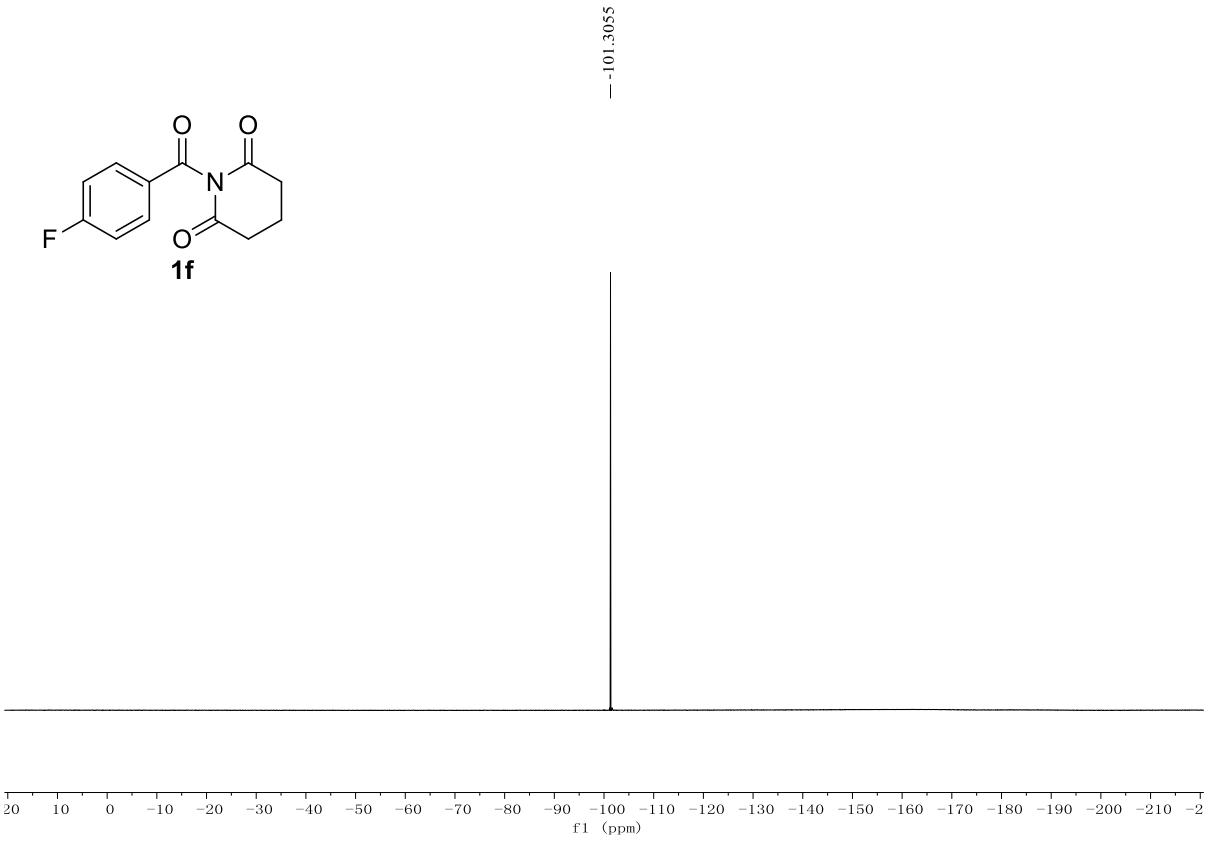

7.9965
7.9803
7.7813
7.7649
2.8192
2.8060
2.7931
2.2031
2.1898
2.1770
2.1639
2.1512
O
O
N
O
F3C
1e
2.00
2.02
f1 (ppm)
4.13
2.09


171.94
170.15
136.07
135.81
134.80
130.35
126.51
126.25
126.22
126.19
126.16
124.34
122.17
120.00
32.36
17.43
f1 (ppm)


-63.3960
O
O
N
O
F3C
1e
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −2
f1 (ppm)


7.9221
7.9084
7.8975
7.1951
7.1798
7.1636
2.8013
2.7886
2.7760
2.1829
2.1710
2.1583
2.1458
2.1339
F
O
O
N
O
1f
1.91
1.94
4.01
2.00
f1 (ppm)


171.91
169.56
167.86
165.80
133.04
132.96
128.32
128.30
116.60
116.42
32.38
17.46
f1 (ppm)


-101.3055
O
O
N
O
F
1f
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −2
f1 (ppm)