Transamidation of N-Acyl-Glutarimides with Amines

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Electronic Supplementary Information

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List of Known Compounds/General Methods

All starting materials reported in the manuscript have been previously described in literature and prepared by the method reported previously. Amides were prepared by standard methods.[1-23] All products reported in the manuscript have been previously described in literature.[24–40] 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. ^{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 MS data are given for all compounds in the Supporting Experimental for characterization purposes. ^{1}H NMR, ^{13}C NMR, MS and HRMS data are reported for all new compounds.

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 (20mL) 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.

Note: *N*-Acyl-glutarimides were discovered in our group in 2015 in the context of catalytic amide N–C bond activation by transition metals.[1–10] In our hands, these compounds are bench-stable, crystalline solids that can routinely be prepared from the corresponding acyl chlorides or carboxylic acids in >80% yields on a gram scale.[1–8] The defining characteristic of *N*-acyl-glutarimide amides is perpendicular twist of the amide bond ($\tau = 85.7°$, $\chi_N = 5.6°$), which makes *N*-acyl-glutarimides the most twisted amide derivatives discovered to date.[11] The high stability of N-acyl-glutarimides, resulting from delocalization of the Nlp into the carbonyl groups in the glutarimide ring, renders these reagents very attractive for applications in transition-metal catalysis[1–17] and metal-free reactions,[18,19] wherein the reactivity is controlled by amide bond twist.[20–23]

General Procedure for Transamidation. 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. Dichloromethane (typically, 0.25 M), triethylamine (typically, 3.0 equiv) and amine (typically, 3.0 equiv) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred at room temperature for an indicated time. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL), and filtered. The organic layer was washed with HCl (1.0 *N*, 20 mL), brine (20 mL), dried,

and concentrated. A sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and 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.

Representative Procedure for Transamidation. An oven-dried vial equipped with a stir bar was charged with benzoylpiperidine-2,6-dione (43.4 mg, 0.20 mmol, 1.0 equiv), placed under a positive pressure of nitrogen, and subjected to three evacuation/backfilling cycles. Dichloromethane (0.25 M), triethylamine (60.7 mg, 0.60 mmol, 3.0 equiv) and benzylamine (64.3 mg, 0.60 mmol, 3.0 equiv) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred at room temperature for 15 h. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL), and filtered. The organic layer was washed with HCl (1.0 *N*, 10 mL), brine (10 mL), dried, and concentrated. A sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product (38.3 mg).White solid. *Note:* in a typical procedure, an aqueous wash is sufficient to afford analytically pure product (typically, >95% purity, ^{1}H NMR and GC-MS analysis). Characterization data are included in the section below.

Representative Procedure for Metal-Free Transamidation. 1.0 Mmol Scale. An oven-dried vial equipped with a stir bar was charged with benzoylpiperidine-2,6-dione (217.0 mg, 1.00 mmol, 1.0 equiv), placed under a positive pressure of nitrogen, and subjected to three evacuation/backfilling cycles. Dichloromethane (0.25 M), triethylamine (303.0 mg, 3.00 mmol, 3.0 equiv) and pyrrolidine (213.0 mg, 3.00 mmol, 3.0 equiv) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred at room temperature for 15 h. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (20 mL), and filtered. The organic layer was washed with HCl (1.0 *N*, 10 mL), brine (10 mL), dried, and concentrated. A sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples.

Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product (170.1 mg). Colorless oil. Yield 97%. Characterization data are included in the section below.

Note: All amide products reported in the manuscript have been previously described in literature.

Literature references for amide products: **3a**,[27] **3b**,[27] **3c**,[27] **3d**,[28] **3e**,[27] **3f**,[29] **3g**,[27] **3h**,[27] **3i**,[27] **3j**,[27] **3k**,[30] **3l**,[31] **3m**,[32] **3n**,[33] **3p**,[34] **3q**,[34] **3r**,[35] **3s**,[36] **3t**,[37] **3u**,[38] **3v**,[39] **3w**.[40] Spectroscopic data matched literature values.

Characterization Data for Starting Materials

All starting materials have been previously reported.[1–23] Spectroscopic data matched literature values. All *N*-acyl-glutarimides are bench-stable solids, with no decomposition observed while storing in ambient conditions on a bench-top over 24 months.

Benzoylpiperidine-2,6-dione (1a). White solid. **GC:** rt = 17.94 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.14-2.21 (m, 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 17.5, 32.4, 129.1, 130.2, 131.8, 135.0, 170.7, 171.9. **MS** = 217.1 (EI).

1-(4-(Trifluoromethyl)benzoyl)piperidine-2,6-dione (1b). White solid. **GC:** rt = 17.11 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.14-2.21 (m, 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 17.4, 32.4, 123.3 (J^F = 271.3 Hz), 126.2 (J^F = 3.8 Hz), 130.4, 134.8, 135.9 (J^F = 32.5 Hz), 170.2, 171.9. **^{19}F (471 MHz, $CDCl_3$)** δ -63.4. **MS** = 285.1 (EI).

1-(4-Methoxybenzoyl)piperidine-2,6-dione (1c). White solid. **GC:** rt = 20.72 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.11-2.19 (m, 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 17.5, 32.4, 55.7, 114.5, 124.5, 132.8, 165.1, 169.5, 171.9. **MS** = 247.1 (EI).

1-(4-Chlorobenzoyl)piperidine-2,6-dione (1d). White solid. **GC:** rt = 19.33 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.13-2.20 (m, 2 H), 2.80 (t, *J* = 6.4 Hz, 4 H), 7.49 (d, *J* = 8.2 Hz, 2 H), 7.81 (d, *J* = 8.1 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 17.5, 32.4, 129.6, 130.3, 131.4, 141.7, 169.9, 171.9. **MS** = 251.0 (EI).

1-(4-Bromobenzoyl)piperidine-2,6-dione (1e). White solid. **GC:** rt = 20.31 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.13-2.21 (m, 2 H), 2.80 (t, *J* = 6.4 Hz, 4 H), 7.66 (d, *J* = 8.4 Hz, 2 H), 7.73 (d, *J* = 7.3 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 17.5, 32.4, 130.5, 130.7, 131.5, 132.6, 170.1, 171.8. **MS** = 295.0 (EI).

1-(3,4-Difluorobenzoyl)piperidine-2,6-dione (1f). White solid. **GC:** rt = 17.02 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.14-2.21 (m, 2 H), 2.80 (t, *J* = 6.2 Hz, 4 H), 7.15-7.42 (m, 1 H), 7.65 (s, 1 H), 7.69-7.76 (m, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 17.4, 32.4, 118.3 (J^F = 18.8 Hz), 119.4 (J^F = 20.0 Hz), 127.4, 129.0, 150.6 (J^F = 237.5 Hz), 154.8 (J^F = 246.3 Hz), 168.9, 171.9. **^{19}F NMR (471 MHz, $CDCl_3$)** δ -125.76, -134.84. **MS** = 253.1 (EI).

Methyl 4-(2,6-dioxopiperidine-1-carbonyl)benzoate (1g). White solid. **GC:** rt = 21.52 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.15-2.22 (m, 2 H), 2.81 (t, *J* = 6.5 Hz, 4 H), 3.98 (s, 3 H), 7.94 (d, *J* = 8.2 Hz, 2 H), 8.16 (d, *J* = 8.5 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 17.5, 32.4, 52.6, 129.9, 130.2, 135.2, 135.4, 165.8, 170.4, 171.9. **MS** = 275.1 (EI).

1-Decanoylpiperidine-2,6-dione (1h). White solid. **GC:** rt = 12.64 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 0.90 (t, *J* = 6.1 Hz, 3 H), 1.21-1.41 (m, 12 H), 1.71 (p, *J* = 6.7 Hz, 2 H), 2.04 (p, *J* = 5.7 Hz, 2 H), 2.67 (t, *J* = 6.5 Hz, 4 H), 3.12 (t, *J* = 7.4 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 14.1, 17.3, 22.7, 23.4, 28.6, 29.3, 29.4, 31.9, 32.3, 41.0, 171.6, 178.2. **MS** = 267.1 (EI).

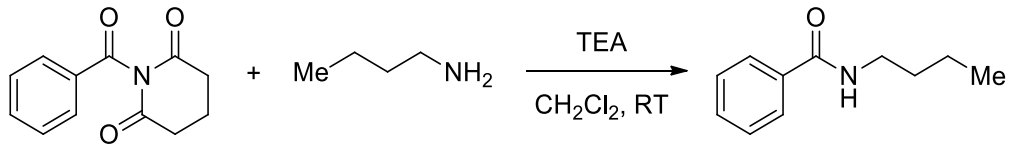
1-(Cyclohexanecarbonyl)piperidine-2,6-dione (1i). White solid. **GC:** rt = 16.95 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.20-1.33 (m, 3 H), 1.49 (q, *J* = 12.1, 2 H), 1.64-1.70 (m, 1 H), 1.84 (q, *J* = 3.4 Hz, 2 H), 1.97-2.02 (m, 2 H), 2.02-2.07 (m, 2 H), 2.60-2.65 (m, 1 H), 2.68 (t, *J* = 6.6 Hz, 4 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 17.4, 25.4, 25.6, 28.1, 32.4, 48.7, 171.9, 180.8. **MS** = 223.1 (EI).

1-Pivaloylpiperidine-2,6-dione (1j). White solid. **GC:** rt = 9.25 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.28 (s, 9 H), 2.01-2.07 (m, 2 H), 2.67 (t, *J* = 6.5 Hz, 4 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 17.4, 27.1, 32.2, 43.8, 171.9, 185.6. **MS** = 197.1 (EI).

Transamidation: Variation of Amines (Table 4)

All amide products have been previously reported.[24–40] Spectroscopic data matched literature values.

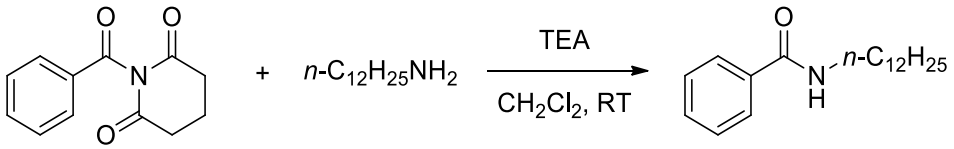
***N*-Butylbenzamide** (Table 4, Entry 1)



1a **2a** **3a**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), *n*-butylamine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 61% yield (21.5 mg). Oil. **GC:** rt = 14.08 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 0.97 (t, *J* = 7.3 Hz, 3 H), 1.39-1.47 (m, 2 H), 1.57-1.65 (m, 2 H), 3.47 (q, *J* = 6.5, 6.1 Hz, 2 H), 6.24 (s, 1 H), 7.43 (t, *J* = 7.5 Hz, 2 H), 7.50 (t, *J* = 7.0 Hz, 1 H), 7.78 (d, *J* = 7.8 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 13.8, 20.2, 31.8, 39.8, 126.8, 128.5, 131.3, 134.9, 167.5. **MS** = 177.1 (EI).

***N*-Dodecylbenzamide** (Table 4, Entry 2)

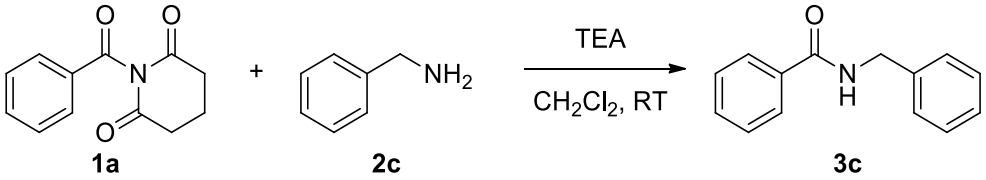


1a **2b** **3b**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), 1-dodecylamine (1.0 equiv), triethylamine (3.0 equiv), DMAP (0.20 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 75% yield (43.4 mg). White solid. **GC:** rt = 21.76 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 0.90 (t, *J* = 6.5 Hz, 3 H), 1.28 (m, 18 H), 1.60-1.67 (m, 2 H), 3.47 (q, *J* = 6.5 Hz, 2 H), 6.13 (s, 1 H), 7.45 (t, *J* = 7.4 Hz, 2 H), 7.51 (t, *J* = 6.9 Hz, 1 H), 7.78 (d, *J* = 7.6 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 14.1, 22.7, 27.0, 29.4, 29.6, 29.6, 29.6, 29.7, 29.7,

31.9, 40.2, 126.8, 128.5, 131.3, 134.9, 167.5. **MS** = 289.3 (EI). *Note:* run under standard conditions afforded **3b** in 67% yield.

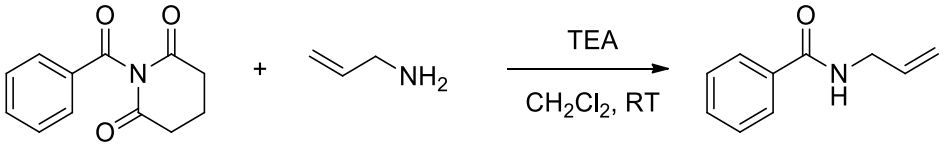
***N*-Benzylbenzamide** (Table 4, Entry 3)



1a **2c** **3c**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), benzylamine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 91% yield (38.3 mg). White solid. **GC:** rt = 18.24 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 4.66 (d, *J* = 5.6 Hz, 2 H), 6.61 (s, 1 H), 7.30-7.34 (m, 1 H), 7.37 (d, *J* = 3.9 Hz, 4 H), 7.44 (t, *J* = 7.4 Hz, 2 H), 7.52 (t, *J* = 7.3 Hz, 1 H), 7.82 (d, *J* = 7.8 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 44.1, 127.0, 127.6, 127.9, 128.6, 128.8, 131.5, 134.4, 138.2, 167.4. **MS** = 211.1 (EI).

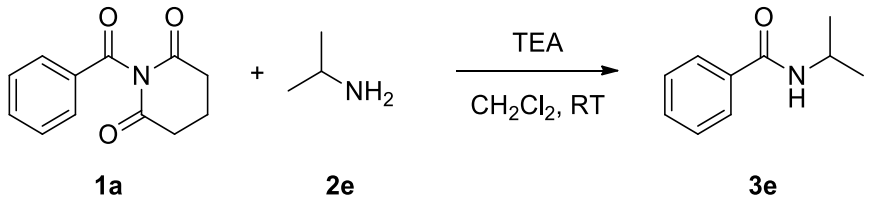
***N*-Allylbenzamide** (Table 4, Entry 4)



1a **2d** **3d**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), allylamine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard and purification by chromatography the title compound in 81% yield (26.2 mg). Oil. **GC:** rt = 12.60 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 4.09 (t, *J* = 5.1 Hz, 2 H), 5.23 (m, 2 H), 5.81-6.03 (m, 1 H), 6.45 (s, 1 H), 7.43 (t, *J* = 7.5 Hz, 2 H), 7.51 (t, *J* = 6.9 Hz, 1 H), 7.81 (d, *J* = 7.8 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 42.4, 116.6, 127.0, 128.6, 131.5, 134.2, 134.5, 167.4. **MS** = 161.1 (EI).

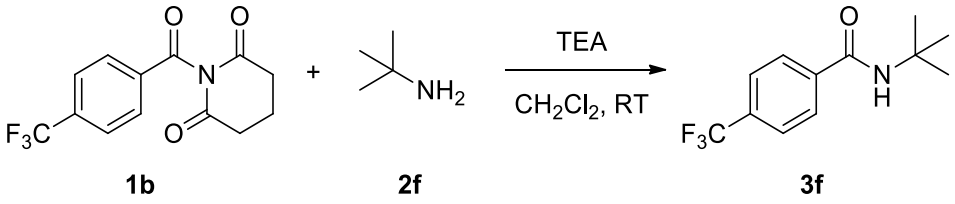
***N*-Isopropylbenzamide** (Table 4, Entry 5)



1a **2e** **3e**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), isopropylamine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 63% yield (20.7 mg). White solid. **GC:** rt = 11.67 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.28 (d, *J* = 6.5 Hz, 6 H), 4.23-4.38 (m, 1 H), 5.99 (s, 1 H), 7.44 (t, *J* = 7.3 Hz, 2 H), 7.50 (t, *J* = 7.3 Hz, 1 H), 7.77 (d, *J* = 7.4 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 22.9, 41.9, 126.8, 128.5, 131.2, 135.0, 166.7. **MS** = 163.1 (EI).

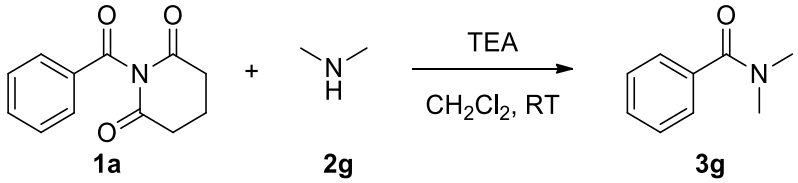
***N*-(*tert*-Butyl)-4-(trifluoromethyl)benzamide** (Table 4, Entry 6)



1b **2f** **3f**

According to the general procedure, the reaction of 1-(4-(trifluoromethyl)benzoyl)piperidine-2,6-dione (0.20 mmol), *tert*-butylamine (3.0 equiv), triethylamine (3.0 equiv) and DMAP (1.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 78% yield (38.0 mg). White solid. **GC:** rt = 11.15 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.50 (s, 9 H), 6.00 (s, 1 H), 7.68 (d, *J* = 7.8 Hz, 2 H), 7.84 (d, *J* = 7.8 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 28.8, 52.0, 123.7 (J^F = 270.0 Hz), 125.5 (J^F = 3.8 Hz), 127.2, 132.8 (J^F = 32.5 Hz), 139.2, 165.6. **^{19}F NMR (471 MHz, $CDCl_3$)** δ -62.9. MS = 245.1 (EI). *Note:* run with 0.20 equiv DMAP afforded **3f** in 50% yield. *Note:* in the absence of DMAP, **3f** was not formed.

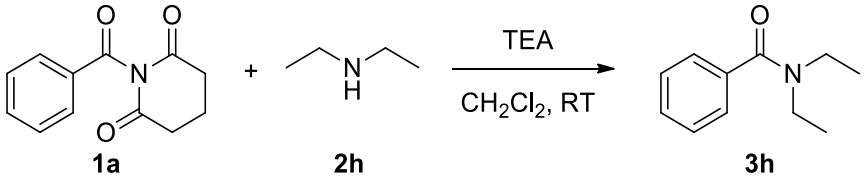
***N,N*-Dimethylbenzamide** (Table 4, Entry 7)



1a **2g** **3g**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), dimethylamine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 95% yield (28.3 mg). White solid. **GC:** rt = 10.71 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 3.00 (s, 3 H), 3.13 (s, 3 H), 7.42 (m, 5 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 35.3, 39.6, 127.0, 128.3, 129.5, 136.4, 171.6. **MS** = 149.1 (EI).

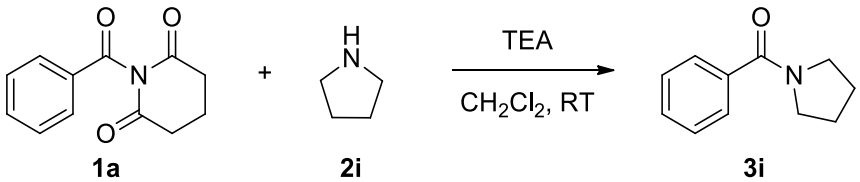
***N,N*-Diethylbenzamide** (Table 4, Entry 8)



1a **2h** **3h**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), diethylamine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 91% yield (32.3 mg). Oil. **GC:** rt = 12.06 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.12 (m, 3 H), 1.27 (m, 3 H), 3.27 (m, 2 H), 3.57 (m, 2 H), 7.40 (m, 5 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 12.9, 14.2, 39.2, 43.3, 126.3, 128.4, 129.1, 137.3, 171.3. **MS** = 177.1 (EI).

Phenyl(pyrrolidin-1-yl)methanone (Table 4, Entry 9)

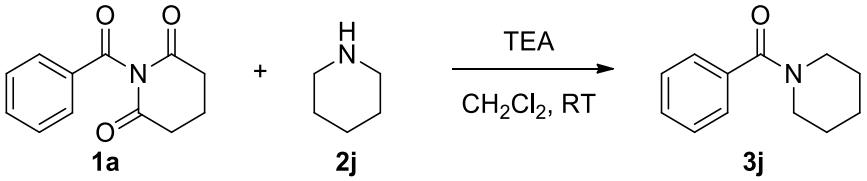


1a **2i** **3i**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), pyrrolidine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the

title compound in 98% yield (34.7 mg). Oil. **GC:** rt = 14.65 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.85-1.93 (m, 2 H), 1.98-2.01 (m, 2 H), 3.44 (t, *J* = 6.5 Hz, 2 H), 3.67 (t, *J* = 6.9 Hz, 2 H), 7.41 (d, *J* = 5.8 Hz, 3 H), 7.53 (d, *J* = 7.6 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 24.5, 26.4, 46.2, 49.6, 127.1, 128.2, 129.7, 137.3, 169.7. **MS** = 175.1 (EI).

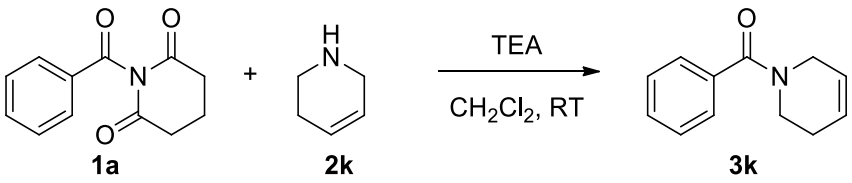
Phenyl(piperidin-1-yl)methanone (Table 4, Entry 10)



1a **2j** **3j**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), piperidine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 90% yield (34.1 mg). Oil. **GC:** rt = 14.82 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.53 (s, 2 H), 1.69 (s, 4 H), 3.35 (s, 2 H), 3.73 (s, 2 H), 7.40 (m, 5 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 24.6, 25.6, 26.6, 43.2, 48.8, 126.8, 128.4, 129.3, 136.6, 170.3. **MS** = 189.2 (EI).

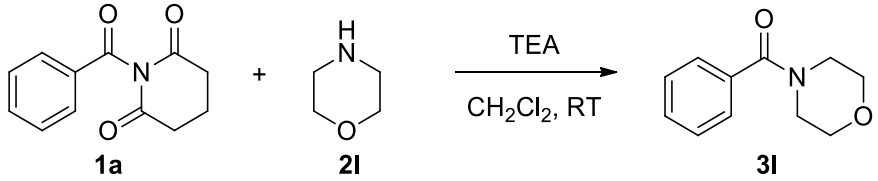
(5,6-Dihydropyridin-1(2*H*)-yl)(phenyl)methanone (Table 4, Entry 11)



1a **2k** **3k**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), 1,2,3,6-tetrahydropyridine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 94% yield (35.1 mg). White solid. **GC:** rt = 14.94 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18-2.29 (m, 2 H), 3.47-4.21 (m, 4 H), 5.55-5.70 (m, 1 H), 5.84-5.95 (m, 1 H), 7.43 (s, 5 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 24.9, 25.9, 39.3, 42.5, 44.5, 47.6, 123.8, 124.5, 124.9, 126.4, 126.8, 127.0, 128.5, 129.6, 136.3, 170.86. **MS** = 187.2 (EI).

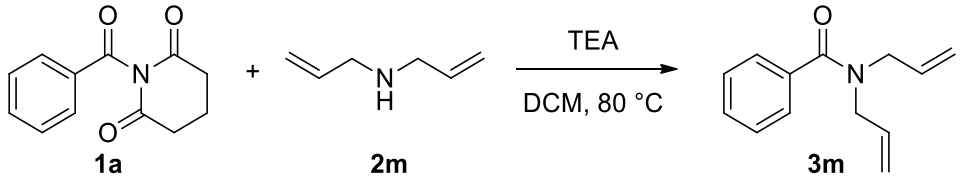
Morpholino(phenyl)methanone (Table 4, Entry 12)



1a **2l** **3l**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), morpholine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and chromatography the title compound in 95% yield (36.1 mg). White solid. **GC:** rt = 14.77 min. **^{1}H NMR (500 MHz, $CDCl_3$) δ** 3.31-3.94 (m, 8 H), 7.53 (m, 5 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 66.9, 127.1, 128.6, 129.9, 135.3, 170.4. **MS** = 191.1 (EI).

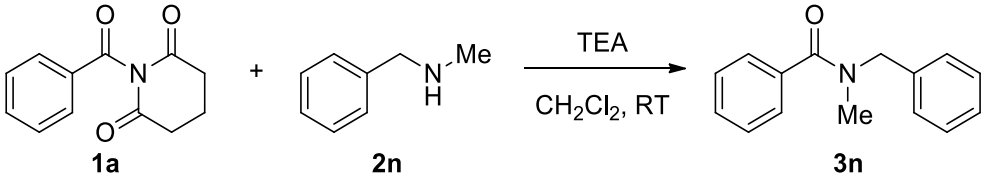
***N,N*-Diallylbenzamide** (Table 4, Entry 13)



1a **2m** **3m**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), diallylamine (3.0 equiv) and triethylamine (3.0 equiv) in 1,2-dichloroethane (0.25 M) at 80 °C for 15 h afforded after the standard work-up and purification by chromatography the title compound in 90% yield (36.2 mg). Oil. **GC:** rt = 13.58 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 3.85 (m, 2 H), 4.16 (m, 2 H), 5.21 (m, 2 H), 5.25 (m, 2 H), 5.74 (m, 1 H), 5.90 (m, 1 H), 7.40 (d, *J* = 6.8 Hz, 3 H), 7.45 (d, *J* = 7.6 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 46.9, 50.8, 117.6, 126.6, 128.4, 129.6, 132.8, 133.2, 136.3, 171.7. **MS** = 201.1 (EI). *Note:* run under standard conditions afforded **3m** in 57% yield.

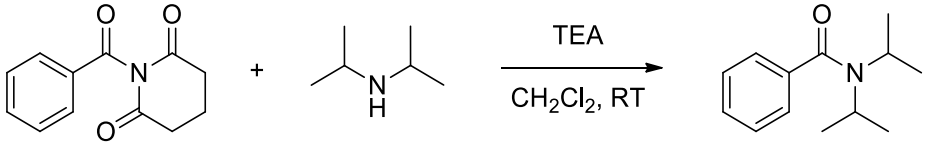
***N*-Benzyl-*N*-methylbenzamide** (Table 4, Entry 14)



1a **2n** **3n**

According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), *N*-methylbenzylamine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 95% yield (42.8 mg). Oil. **GC:** rt = 17.64 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.89 (s, 3 H), 3.06 (s, 3 H), 4.54 (s, 2 H), 4.79 (s, 2 H), 7.20 (s, 2 H), 7.33 (d, *J* = 5.8 Hz, 2H), 7.35-7.46 (m, 12 H), 7.47-7.49 (m, 4H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 33.2, 37.0, 50.8, 55.2, 126.8, 126.8, 127.0, 127.5, 127.6, 127.6, 128.2, 128.4, 128.7, 128.8, 129.6, 136.2, 136.3, 136.6, 137.1, 171.6, 172.3. **MS** = 225.2 (EI).

***N,N*-Diisopropylbenzamide** (Table 4, Entry 15)

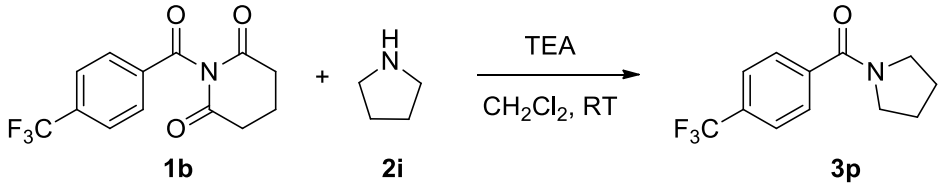


1a **2o** **3o**

According to the general procedure, 1-benzoylpiperidine-2,6-dione (0.20 mmol) was reacted with diisopropylamine (3.0 equiv) and triethylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h. After the standard work-up as described above, analysis of the reaction mixture by ^{1}H NMR (500 MHz) and GC-MS indicated: >95.0% of the remaining starting material, conversion <5.0%.

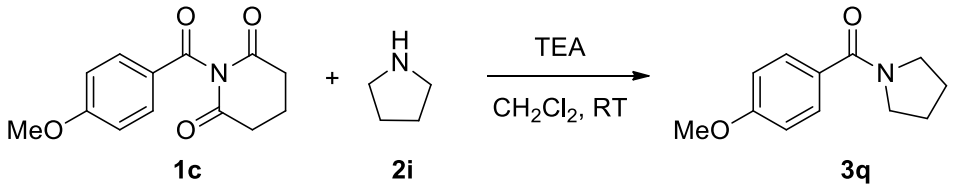
Transamidation: Amide Scope (Table 5)

Pyrrolidin-1-yl(4-(trifluoromethyl)phenyl)methanone (Table 5, Entry 1)



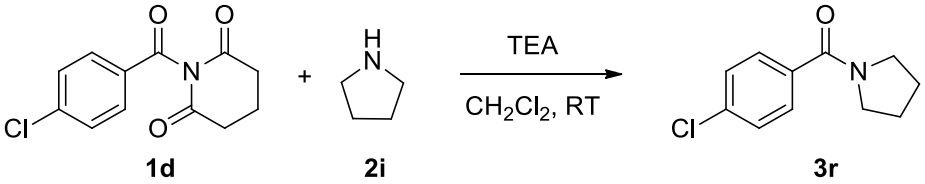
According to the general procedure, the reaction of 1-(4-(trifluoromethyl)benzoyl)piperidine-2,6-dione (0.20 mmol), triethylamine (3.0 equiv), and pyrrolidine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 66% yield (32.1 mg). White solid. **GC:** rt = 14.22 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.87-1.95 (m, 2 H), 1.95-2.03 (m, 2 H), 3.40 (t, *J* = 6.6 Hz, 2 H), 3.67 (t, *J* = 7.0 Hz, 2 H), 7.63 (d, *J* = 8.1 Hz, 2 H), 7.68 (d, *J* = 8.1 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 24.4, 26.4, 46.3 49.5, 123.8 (J^F = 271.3 Hz), 125.4 (J^F = 3.75 Hz), 127.5, 131.6 (J^F = 32.5 Hz), 140.7, 168.2. **^{19}F NMR (471 MHz, $CDCl_3$)** δ -62.9. **MS** = 243.1 (EI).

(4-Methoxyphenyl)(pyrrolidin-1-yl)methanone (Table 5, Entry 2)



According to the general procedure, the reaction of 1-(4-methoxybenzoyl)piperidine-2,6-dione (0.20 mmol), triethylamine (3.0 equiv), and pyrrolidine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 80% yield (38.8 mg). White solid. **GC:** rt = 17.73 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.86-1.92 (m, 2 H), 1.93-2.00 (m, 2 H), 3.49 (t, *J* = 6.7 Hz, 2 H), 3.64 (t, *J* = 7.3 Hz, 2 H), 3.85 (s, 3 H), 6.91 (d, *J* = 8.1 Hz, 2 H), 7.53 (d, *J* = 8.1 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 24.5, 26.5, 46.3, 49.8, 55.3, 113.4, 129.2, 129.4, 160.8, 169.4. **MS** = 205.2 (EI).

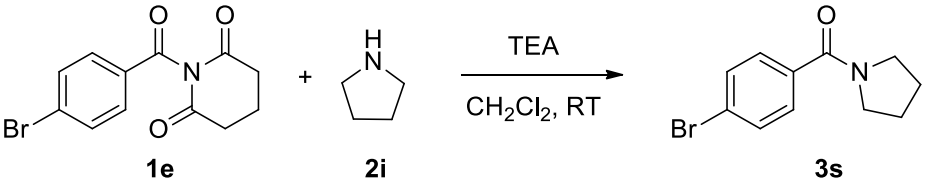
(4-Chlorophenyl)(pyrrolidin-1-yl)methanone (Table 5, Entry 3)



1d **2i** **3r**

According to the general procedure, the reaction of 1-(4-chlorobenzoyl)piperidine-2,6-dione (0.20 mmol), triethylamine (3.0 equiv), and pyrrolidine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 88% yield (37.3 mg). Oil. **GC:** rt = 16.73 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.87-1.94 (m, 2 H), 1.95-2.02 (m, 2 H), 3.44 (t, *J* = 6.8 Hz, 2 H), 3.66 (t, *J* = 7.0 Hz, 2 H), 7.40 (d, *J* = 8.0 Hz, 2 H), 7.49 (d, *J* = 8.1 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 24.4, 26.4, 46.3, 49.6, 128.5, 128.7, 135.6, 135.8, 168.6. **MS** = 209.0 (EI).

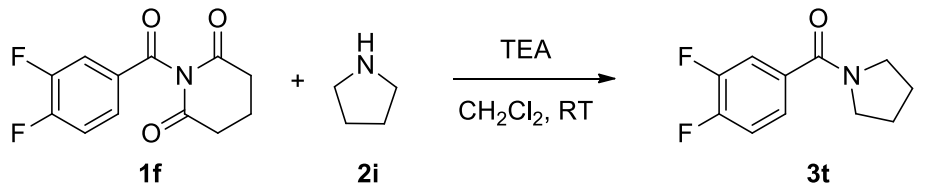
(4-Bromophenyl)(pyrrolidin-1-yl)methanone (Table 5, Entry 4)



1e **2i** **3s**

According to the general procedure, the reaction of 1-(4-bromobenzoyl)piperidine-2,6-dione (0.20 mmol), triethylamine (3.0 equiv), and pyrrolidine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 94% yield (47.9 mg). Oil. **GC:** rt = 17.62 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.82-1.91 (m, 2 H), 1.91-1.98 (m, 2 H), 3.39 (t, *J* = 6.7 Hz, 2 H), 3.61 (t, *J* = 7.0 Hz, 2 H), 7.39 (d, *J* = 8.3 Hz, 2 H), 7.52 (d, *J* = 8.3 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 24.4, 26.4, 46.3, 49.6, 124.1, 128.9, 131.5, 136.0, 168.6. **MS** = 254.1 (EI).

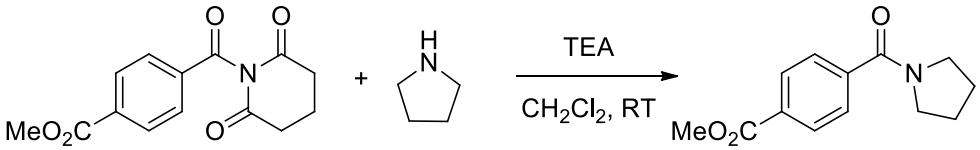
(3,4-Difluorophenyl)(pyrrolidin-1-yl)methanone (Table 5, Entry 5)



1f **2i** **3t**

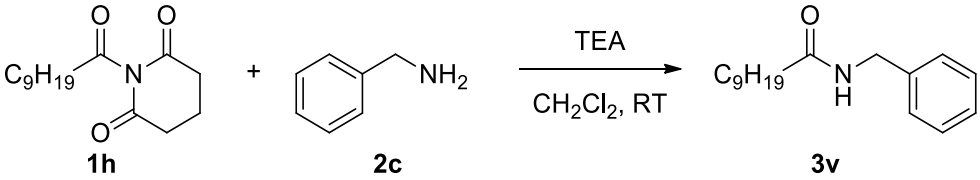
According to the general procedure, the reaction of 1-(4-bromobenzoyl)piperidine-2,6-dione (0.20 mmol), triethylamine (3.0 equiv), and pyrrolidine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 84% yield (35.3 mg). Oil. **GC:** rt = 14.34 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.85-1.94 (m, 2 H), 1.93-2.00 (m, 2 H), 3.43 (t, *J* = 6.7 Hz, 2 H), 3.62 (t, *J* = 7.0 Hz, 2 H), 7.19 (q, *J* = 8.8, 8.2 Hz, 1 H), 7.29 (s, 1 H), 7.34-7.42 (m, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 24.4, 26.4, 46.4, 49.7, 116.9 (*J*^{F} = 18.8 Hz), 117.3 (*J*^{F} = 17.5 Hz), 123.8, 133.93, 148.6 (*J*^{F} = 146.3 Hz), 151.6 (*J*^{F} = 147.5 Hz), 167.3, 167.3. **^{19}F NMR (471 MHz, $CDCl_3$)** δ -135.1, -137.0. **MS** = 211.1 (EI).

Methyl 4-(pyrrolidine-1-carbonyl)benzoate (Table 5, Entry 6)



According to the general procedure, the reaction of 1-(4-bromobenzoyl)piperidine-2,6-dione (0.20 mmol), triethylamine (3.0 equiv), and pyrrolidine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 86% yield (40.2 mg). White solid. **GC:** rt = 19.17 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.84-1.91 (m, 2 H), 1.92-1.99 (m, 2 H), 3.37 (t, *J* = 6.7 Hz, 2 H), 3.64 (t, *J* = 7.0 Hz, 2 H), 3.92 (s, 3 H), 7.56 (d, *J* = 8.0 Hz, 2 H), 8.06 (d, *J* = 8.0 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 24.4, 26.4, 46.2, 49.4, 52.3, 127.0, 129.6, 131.1, 141.4, 166.4, 168.7. **MS** = 233.1 (EI).

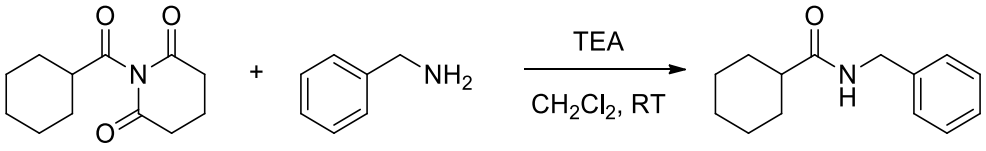
***N*-Benzyldecanamide** (Table 5, Entry 7)



According to the general procedure, the reaction of 1-decanoylpiperidine-2,6-dione (0.20 mmol), triethylamine (3.0 equiv), and benzylamine (3.0 equiv) in dichloromethane (0.25 M) at room

temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 80% yield (41.8 mg). White solid. **GC:** rt = 19.71 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 0.90 (t, *J* = 6.7 Hz, 3 H), 1.29 (m, 12 H), 1.58-1.97 (m, 2 H), 2.21 (t, *J* = 10.0 Hz, 2 H), 4.44 (d, J = 5.6 Hz, 2 H), 5.97 (s, 1 H), 7.25-7.31 (m, 3 H), 7.31-7.38 (m, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 14.1, 22.7, 25.8, 29.3, 29.3, 29.4, 29.5, 31.9, 36.8, 43.5, 127.4, 127.8, 128.7, 138.5, 173.1. **MS** = 261.3 (EI).

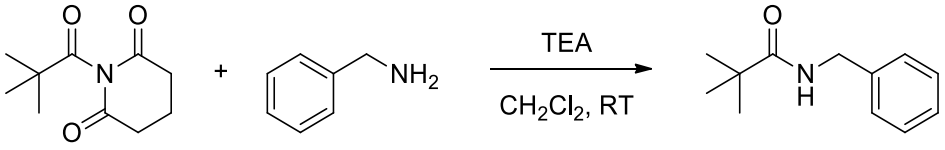
***N*-Benzylcyclohexanecarboxamide** (Table 5, Entry 8)



1i **2c** **3w**

According to the general procedure, the reaction of 1-(cyclohexanecarbonyl)piperidine-2,6-dione (0.20 mmol), triethylamine (3.0 equiv), and benzylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h afforded after the standard work-up and purification by chromatography the title compound in 79% yield (34.3 mg). White solid. **GC:** rt = 17.64 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.19-1.36 (m, 3 H), 1.49 (m, 2 H), 1.71 (m, 1 H), 1.82 (m, 2 H), 1.92 (m, 2 H), 2.13 (m, 1 H), 4.46 (d, *J* = 5.6 Hz, 2 H), 5.71 (s, 1 H), 7.27-7.32 (m, 3 H), 7.36 (m, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 25.8, 29.7, 43.4, 45.6, 127.4, 127.7, 128.7, 138.6, 175.9. **MS** = 217.1 (EI).

***N*-Benzylpivalamide (1j)** (Table 5, Entry 9)



1j **2c** **3x**

According to the general procedure, 1-pivaloylpiperidine-2,6-dione (0.20 mmol) was reacted with triethylamine (3.0 equiv), and benzylamine (3.0 equiv) in dichloromethane (0.25 M) at room temperature for 15 h. After the standard work-up as described above, analysis of the reaction mixture by ^{1}H NMR (500 MHz) and GC-MS indicated: >95.0% of the remaining starting material, conversion <5.0%.

Mechanistic Studies

Hammett Plot Studies. According to the general procedure, an oven-dried vial equipped with a stir was charged with two amide substrates (each 0.20 mmol, 1.0 equiv), dichloromethane (0.25 M), triethylamine (3.0 equiv) and benzylamine (0.10 mmol, 0.5 equiv) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred at room temperature for 15 h. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and filtered. The organic layer was washed with HCl (1.0 *N*, 10 mL), brine (10 mL), dried, and concentrated. A sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. The observed selectivity is consistent with nucleophilic addition to the amide bond.

Selectivity Studies, Tables 6-7. According to the general procedure, an oven-dried vial equipped with a stir was charged with an amide substrate (0.10 mmol, 1.0 equiv), dichloromethane (0.25 M), triethylamine (3.0 equiv) and two amine substrates (each 0.30 mmol, 3.0 equiv) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred at room temperature for 15 h. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and filtered. The organic layer was washed with HCl (1.0 *N*, 10 mL), brine (10 mL), dried, and concentrated. A sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. The observed selectivity is consistent with amine nucleophilicity as the driving force for the transamidation reaction

Selectivity Studies, Table 8. According to the general procedure, an oven-dried vial equipped with a stir was charged with two amide substrates (each 0.20 mmol, 1.0 equiv), dichloromethane (0.25 M), triethylamine (3.0 equiv) and amine (0.10 mmol, 0.5 equiv) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred at room temperature for 15 h. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and filtered. The organic layer was washed with HCl (1.0 *N*, 10 mL), brine (10 mL), dried, and concentrated. A sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. The observed selectivity is consistent with leaving group ability of the imide moiety.

Reactions with O-nucleophiles. 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. Dichloromethane (0.25 M), triethylamine (3.0 equiv) and *O*-nucleophile (5.0 equiv) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred at room temperature for 15 h. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and filtered. The organic layer was washed with HCl (1.0 *N*, 10 mL), brine (10 mL), dried, and concentrated. A sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. The observed reactivity is consistent with amine nucleophilicity as the driving force for the transamidation reaction.

References

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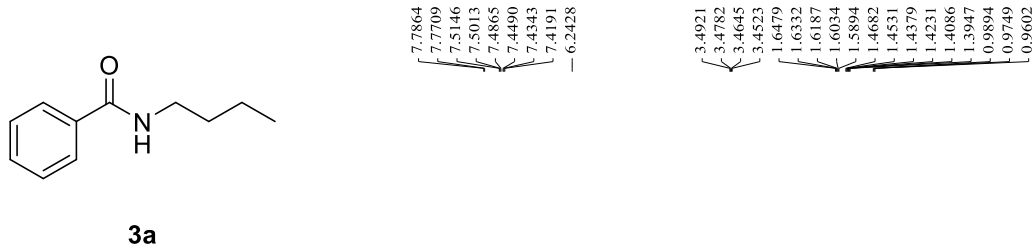
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3.4645
3.4523
1.6479
1.6332
1.6187
1.6034
1.5894
1.4682
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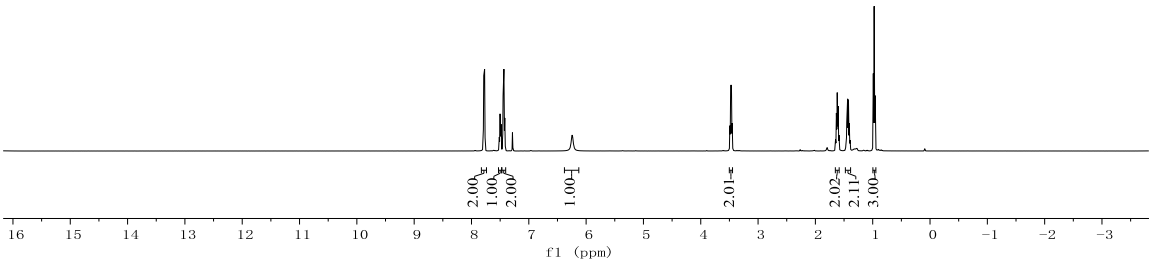
O
N
H

3a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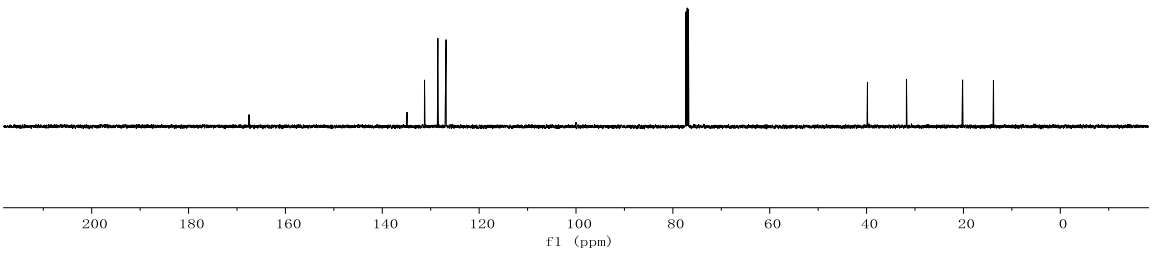
2.00
1.00
2.01
2.02
2.11
3.00
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1 −2 −3
f1 (ppm)


167.53
134.89
131.28
128.52
126.83
39.81
31.76
20.17
13.80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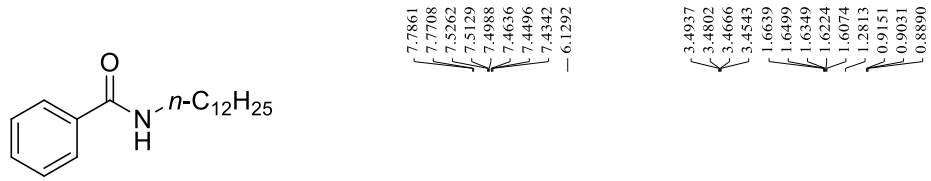
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3.4802
3.4666
3.4543
1.6639
1.6499
1.6349
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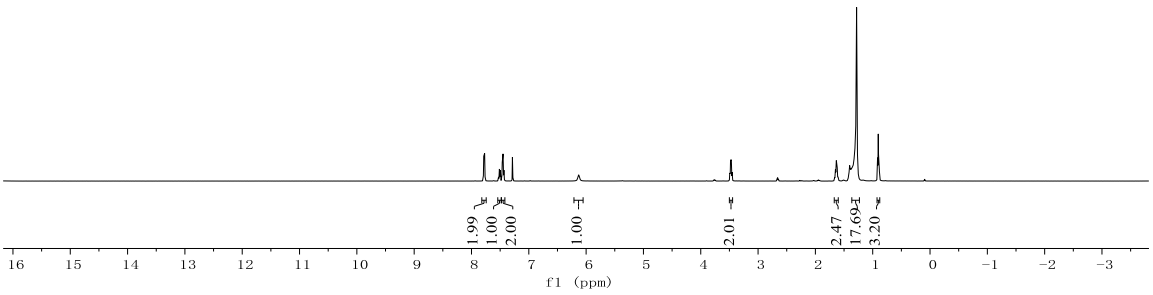
O
N
H
n-C12H25

3b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17.69
3.20
f1 (ppm)


167.47
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128.54
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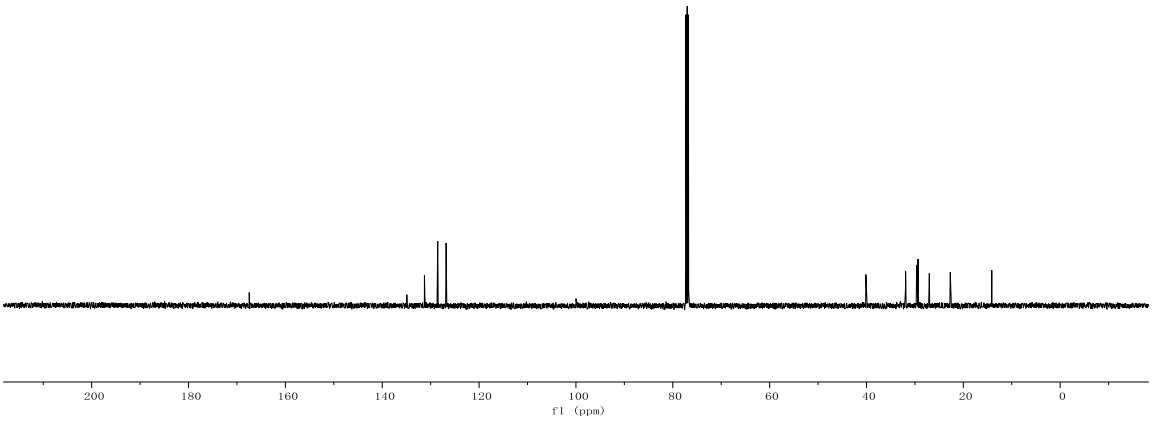
27.02
22.69
14.13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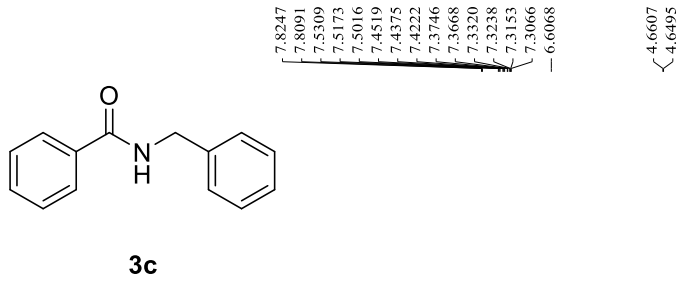
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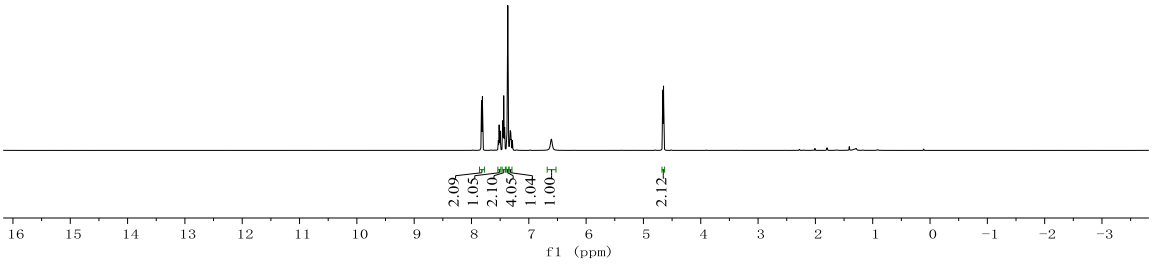
O
N
H

3c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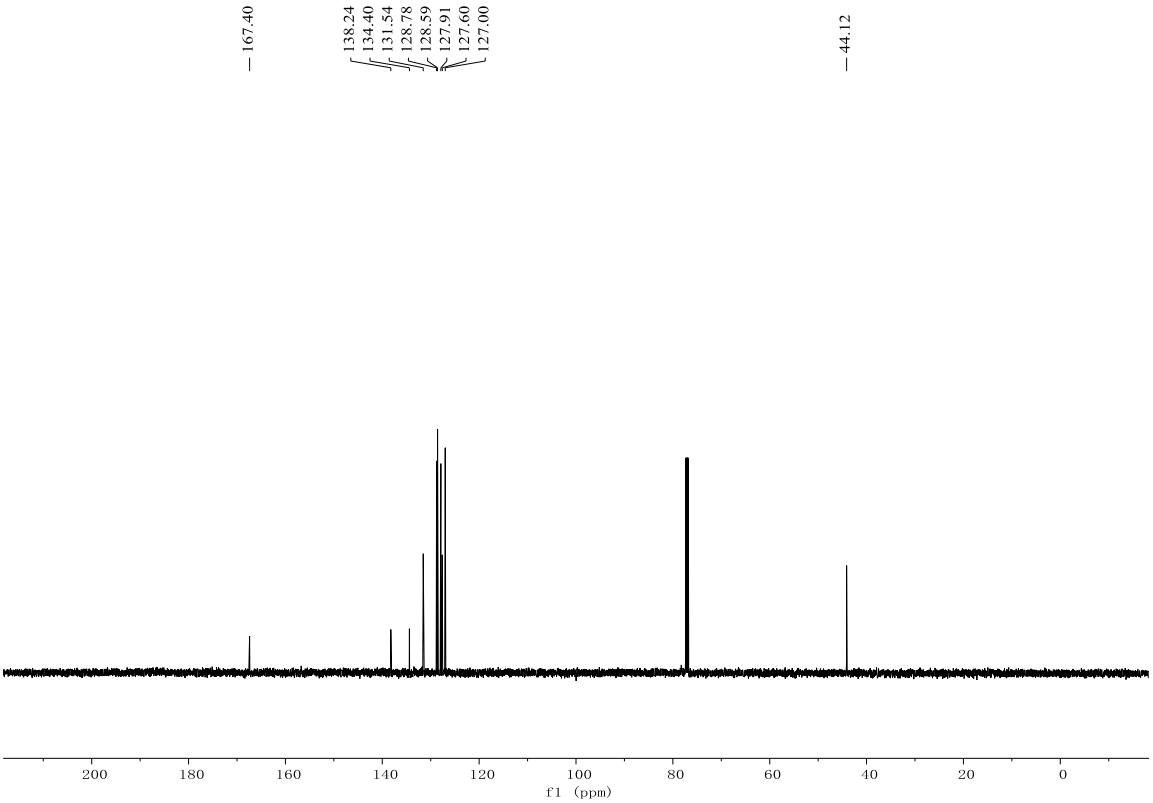
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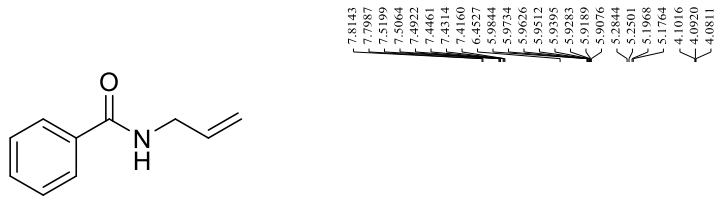
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5.9512
5.9395
5.9283
5.9189
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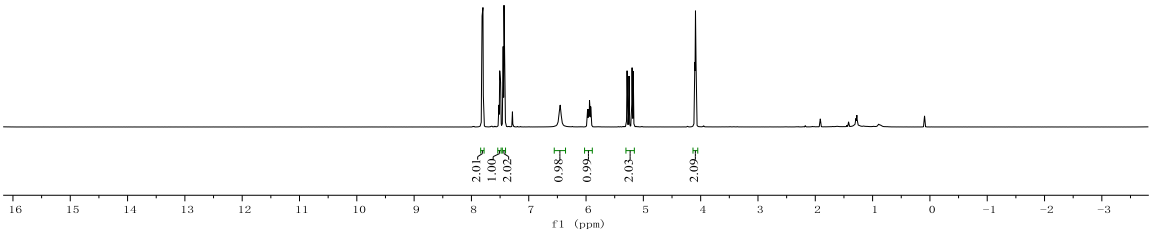
4.0920
4.0811
O
N
H

3d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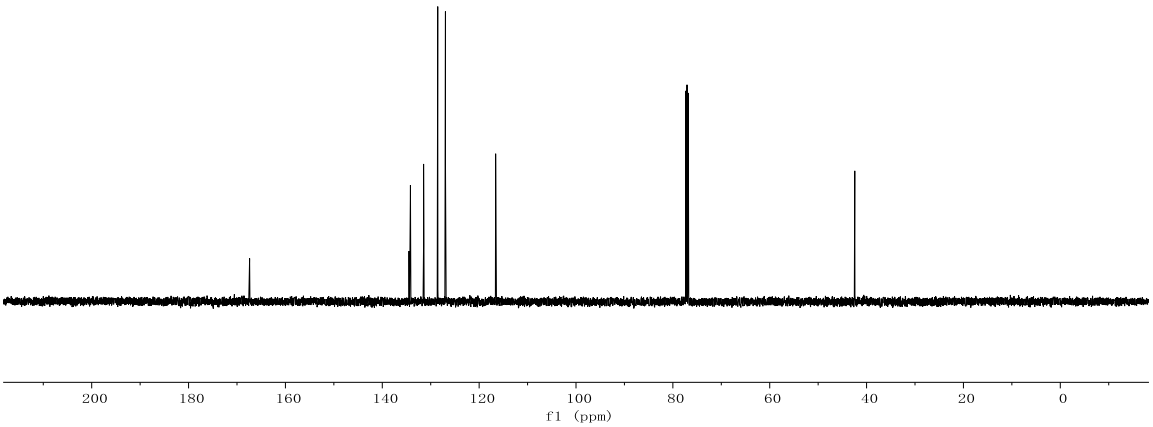
126.96
116.59
42.43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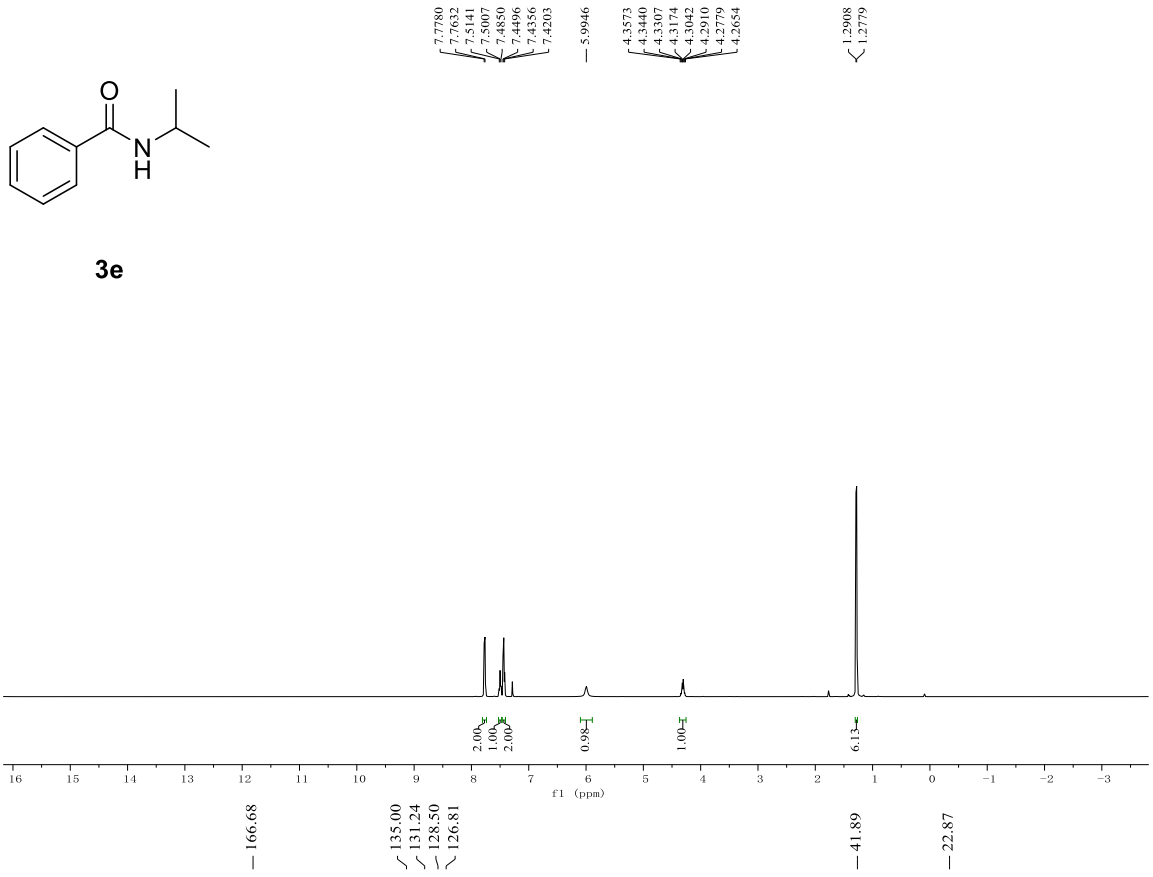
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1.2779
O
N
H
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1.00
2.00
0.98
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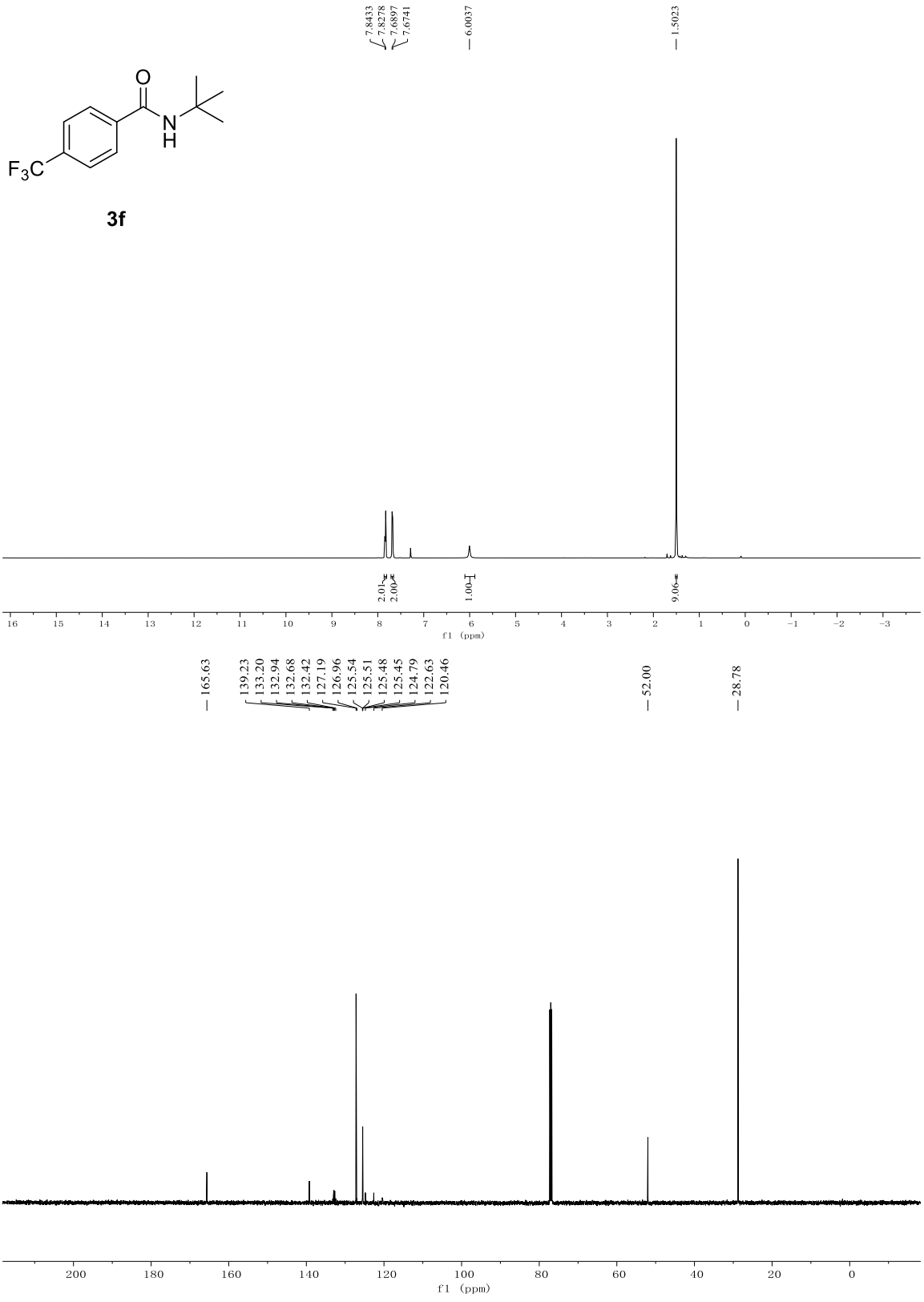
3e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f1 (ppm)
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133.20
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132.68
132.42
127.19
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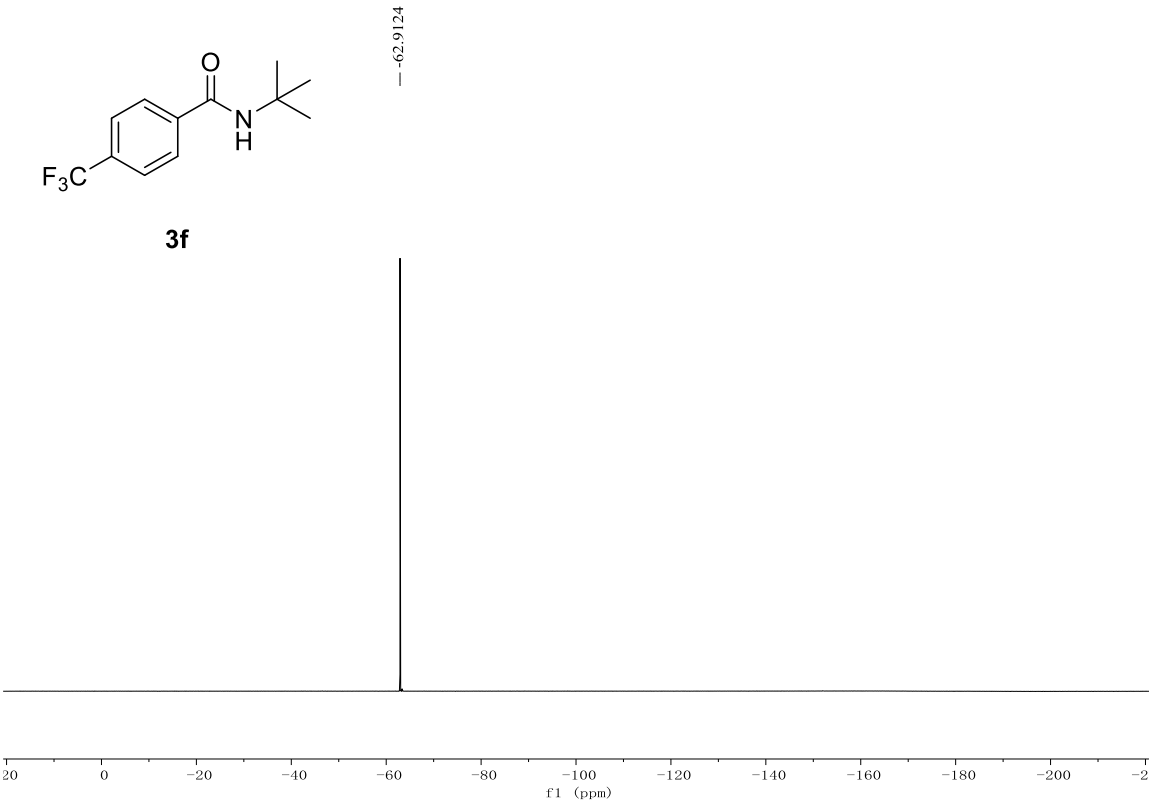
f1 (ppm)

3f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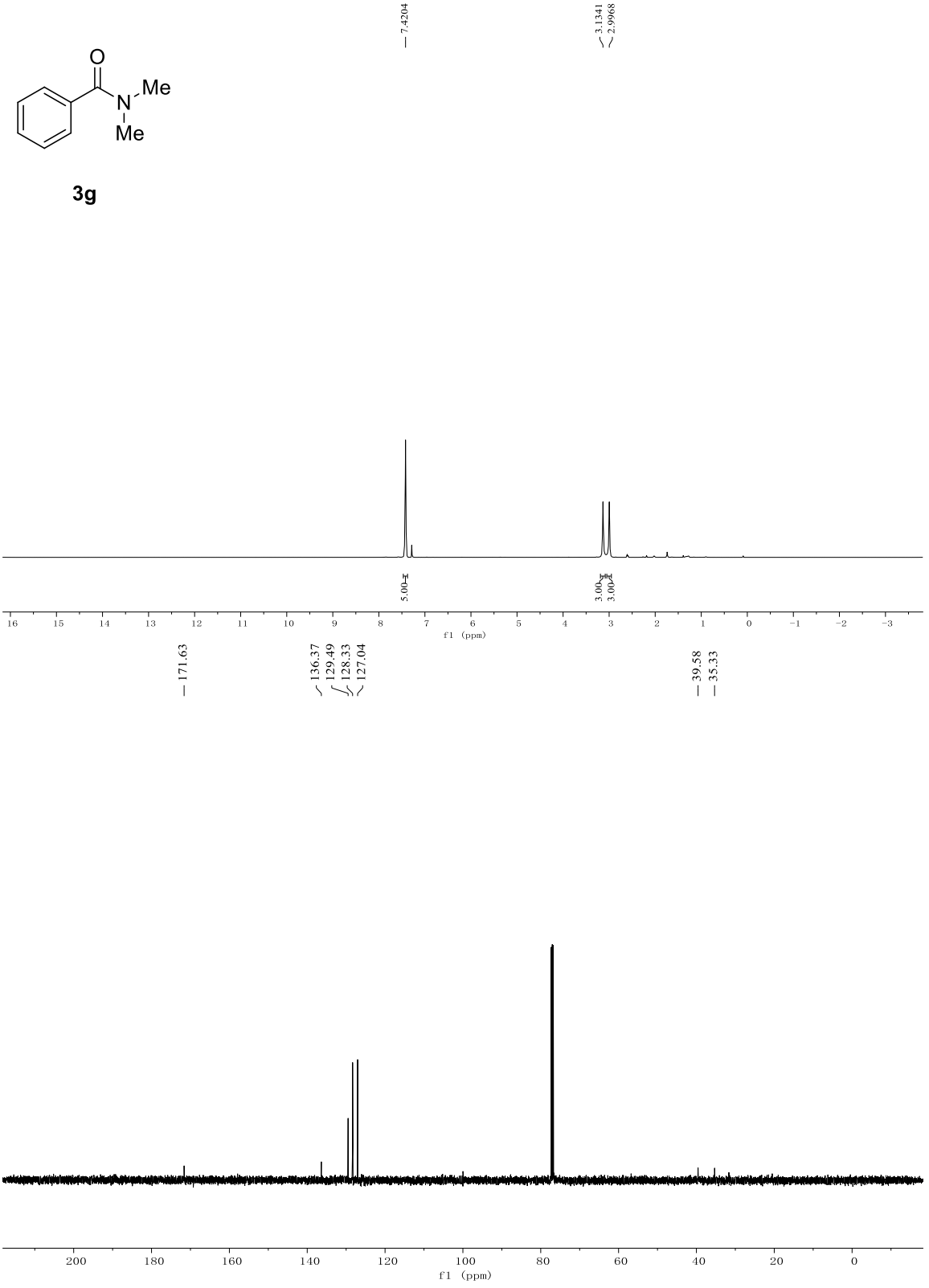
-160
-180
-200
-2
f1 (ppm)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Me
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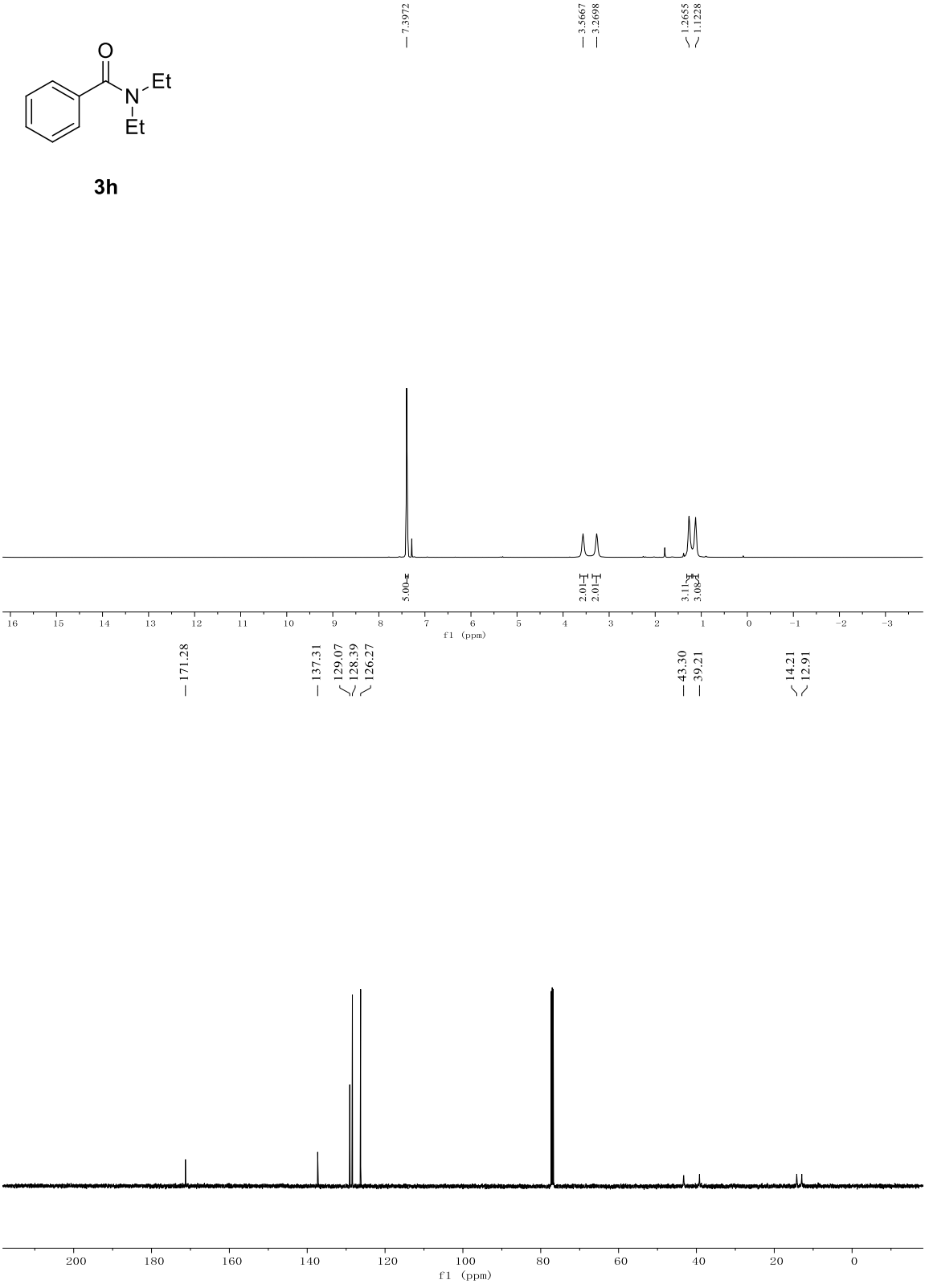
f1 (ppm)

3g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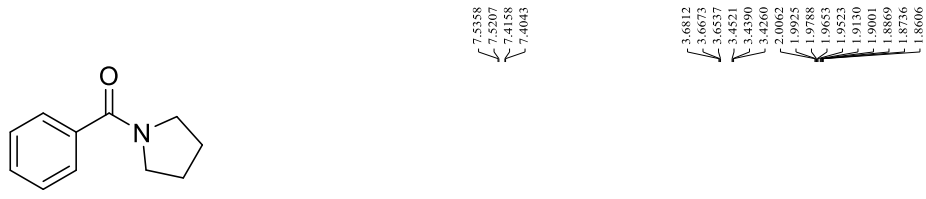
f1 (ppm)

3h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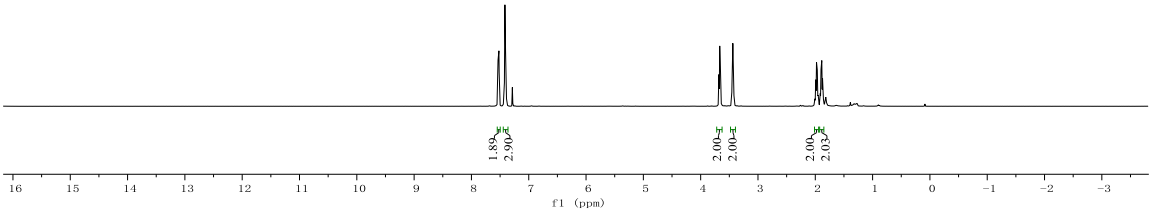
O
N

3i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f1 (ppm)


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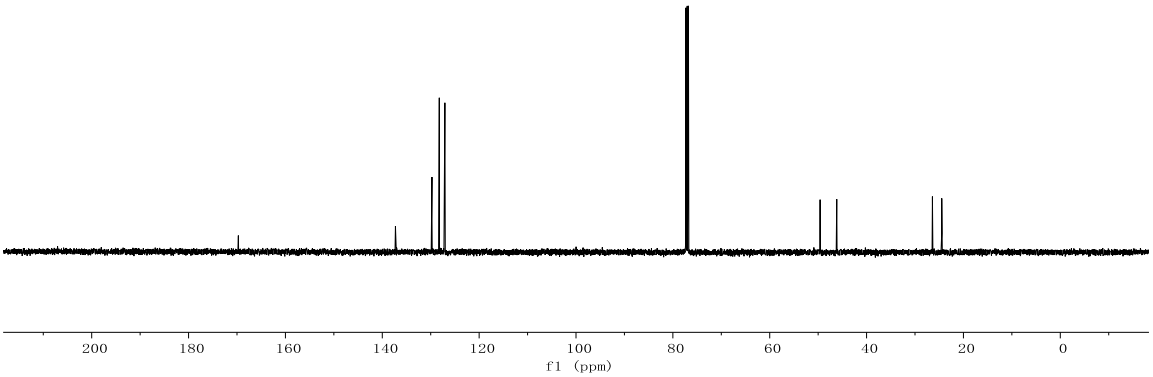
24.48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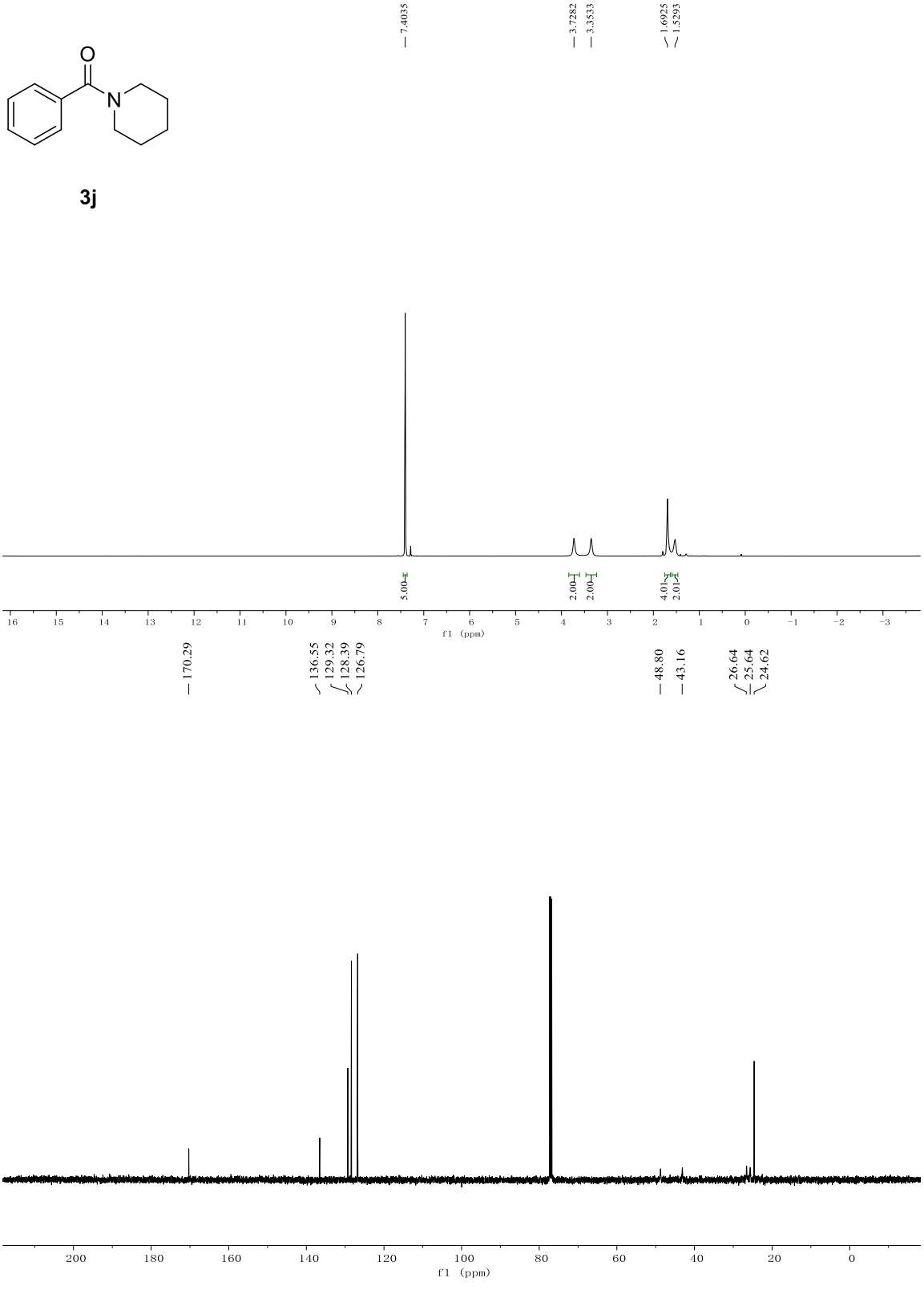
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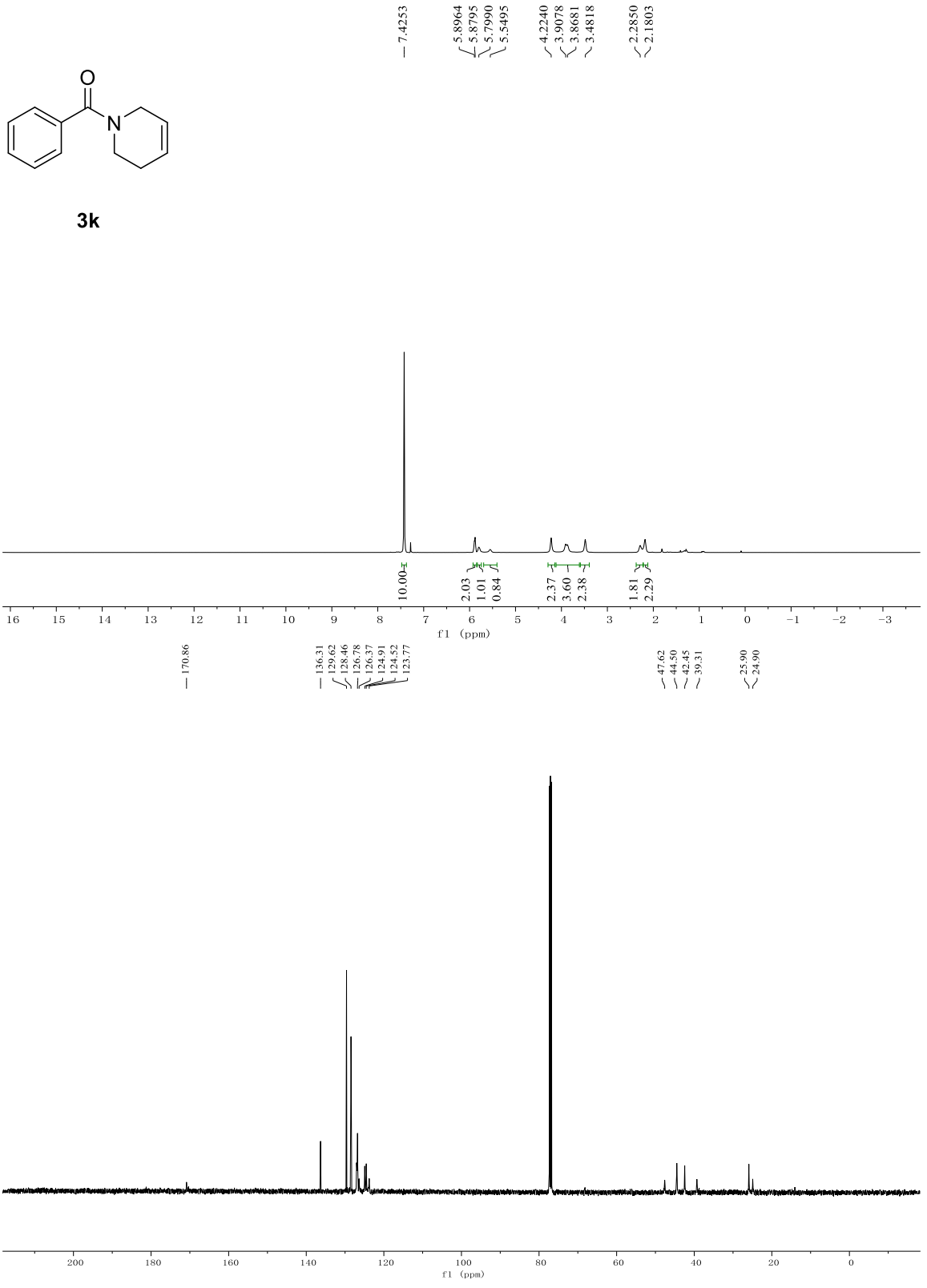
f1 (ppm)

3j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O
N
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0.84
2.37
3.60
2.38
1.81
2.29
f1 (ppm)
170.86
136.31
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128.46
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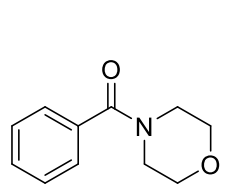

3l

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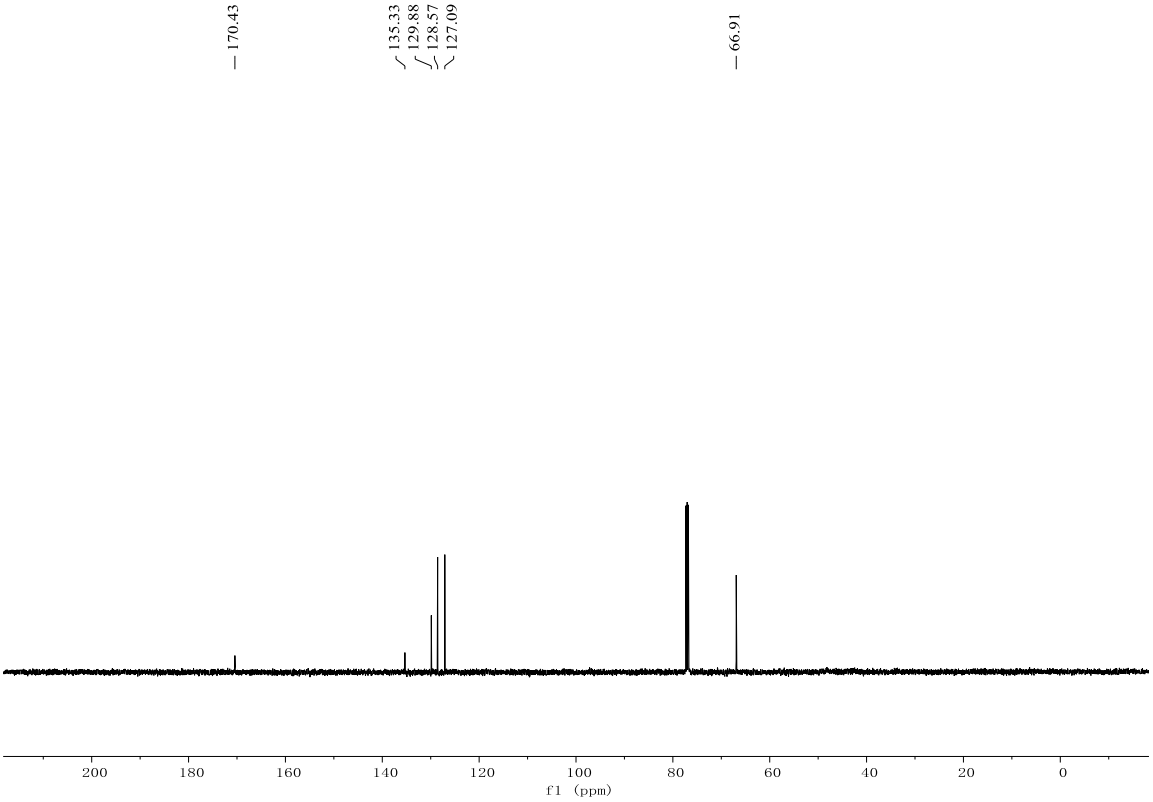
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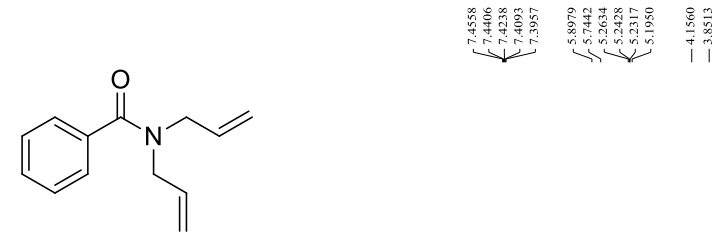
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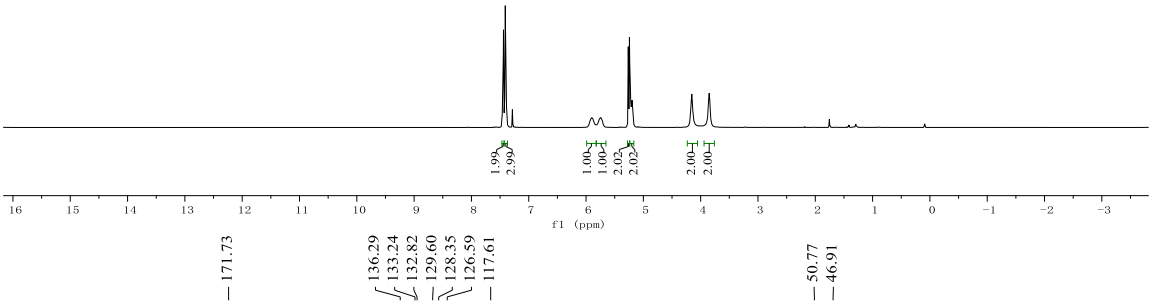
O
N

3m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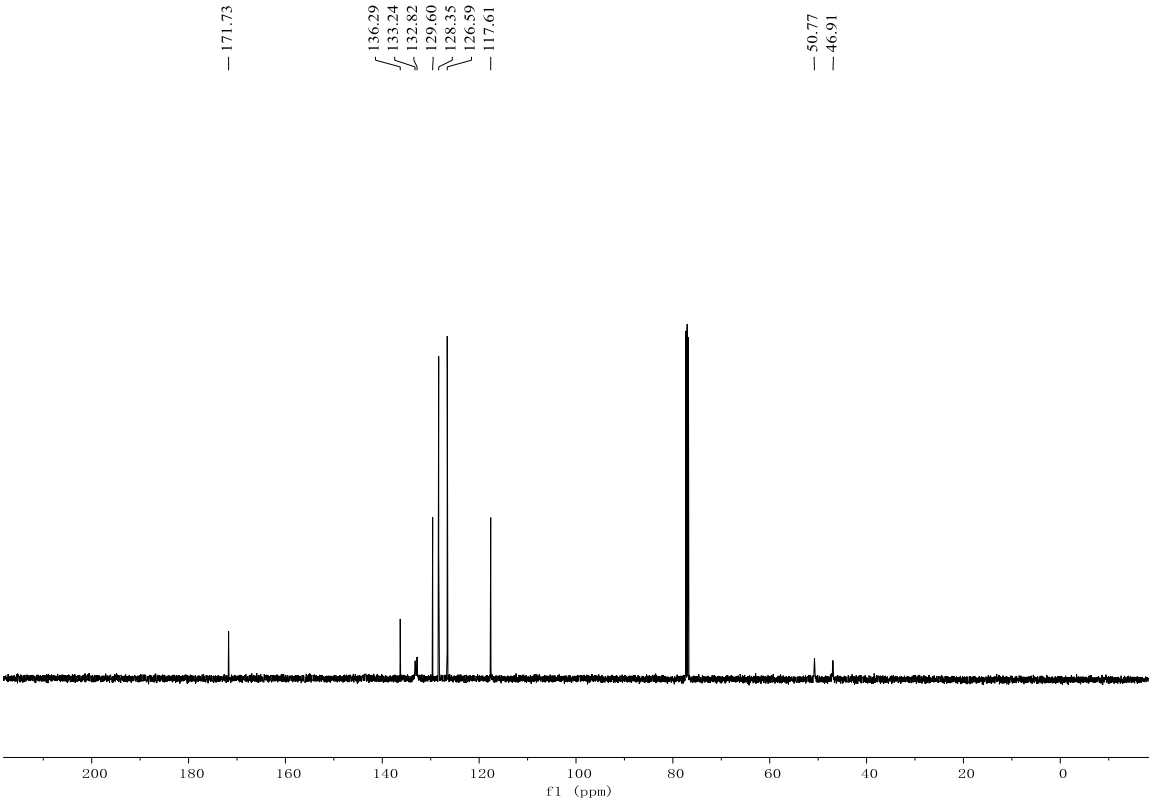
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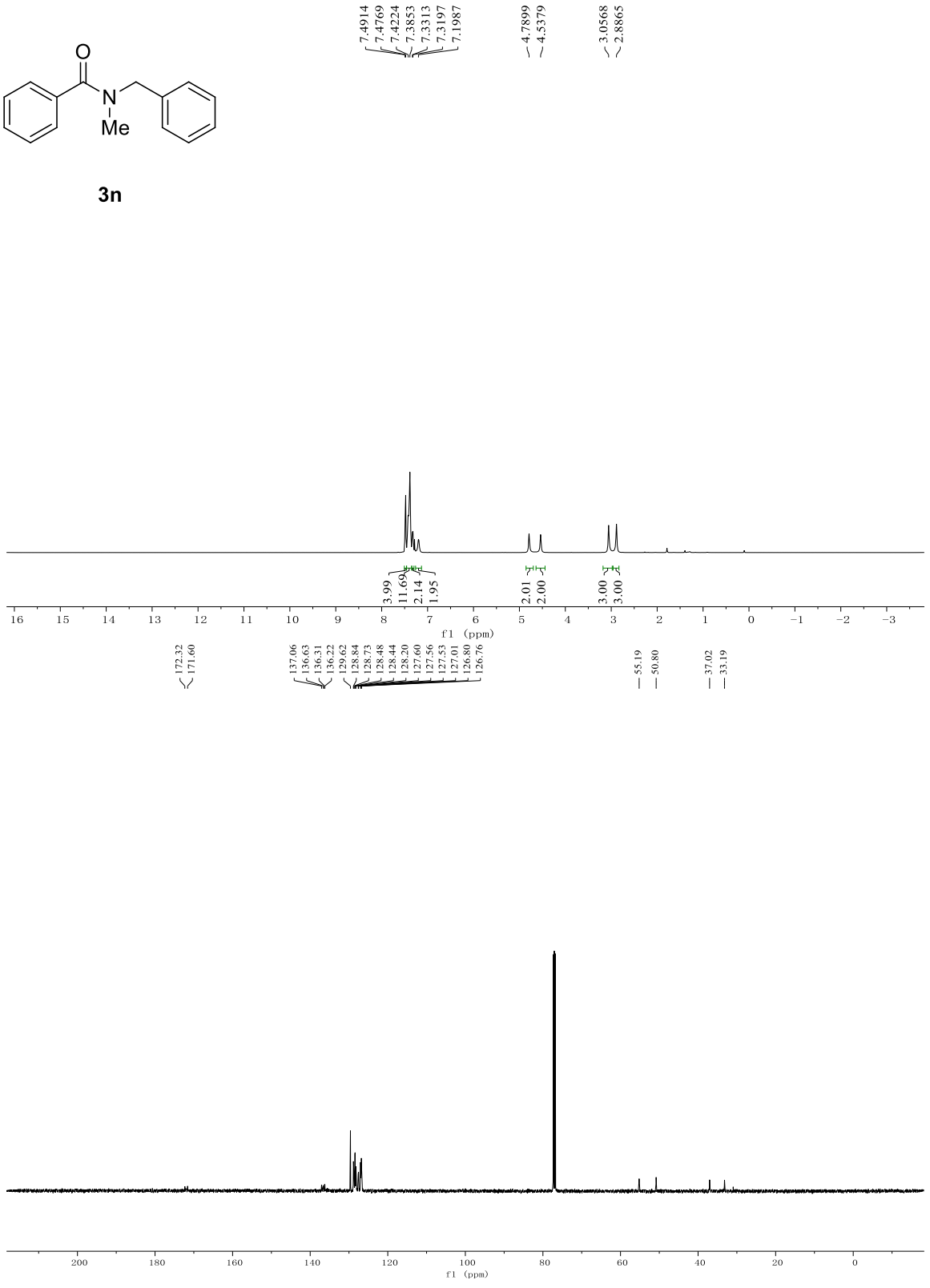
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Me
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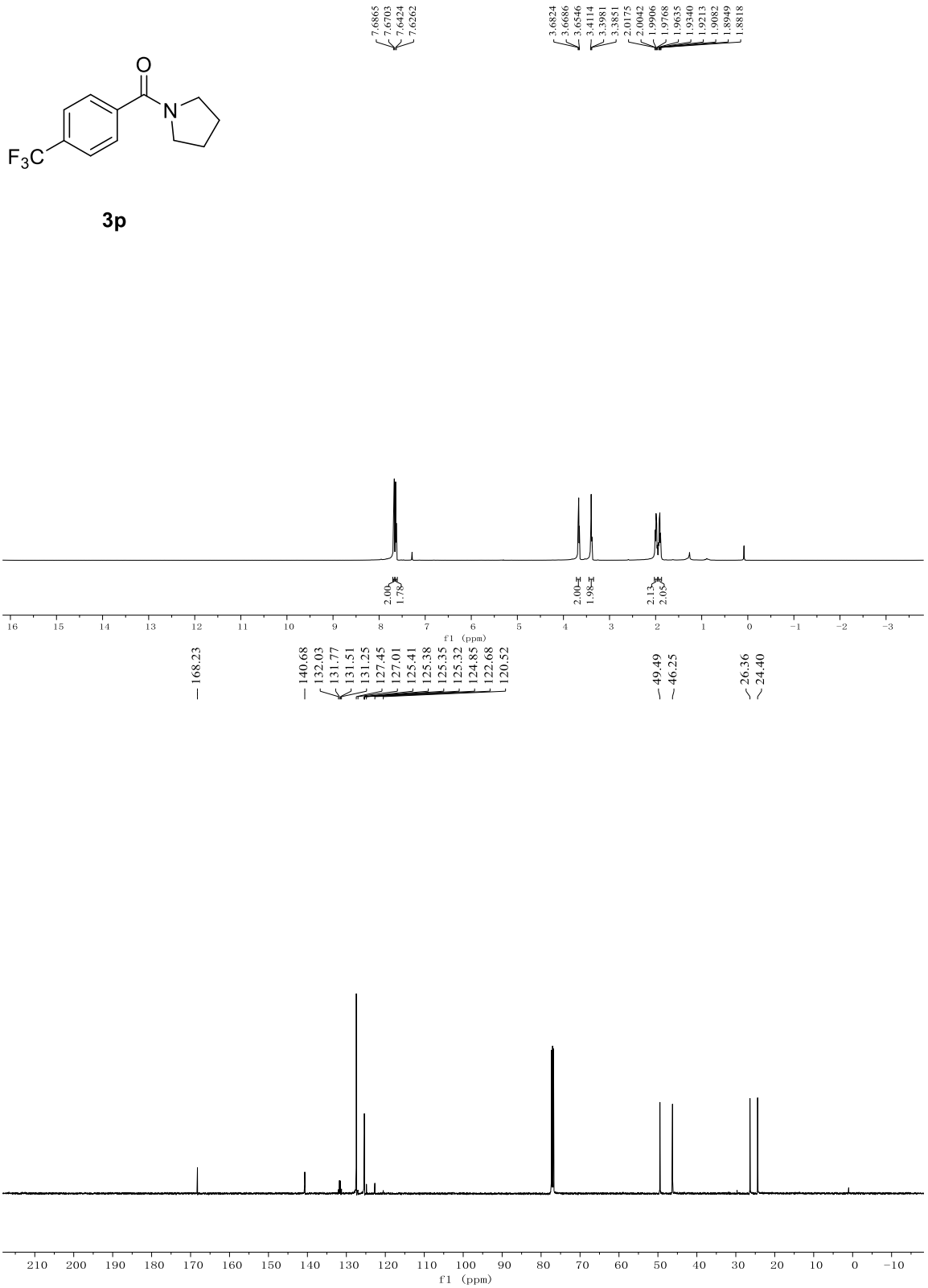
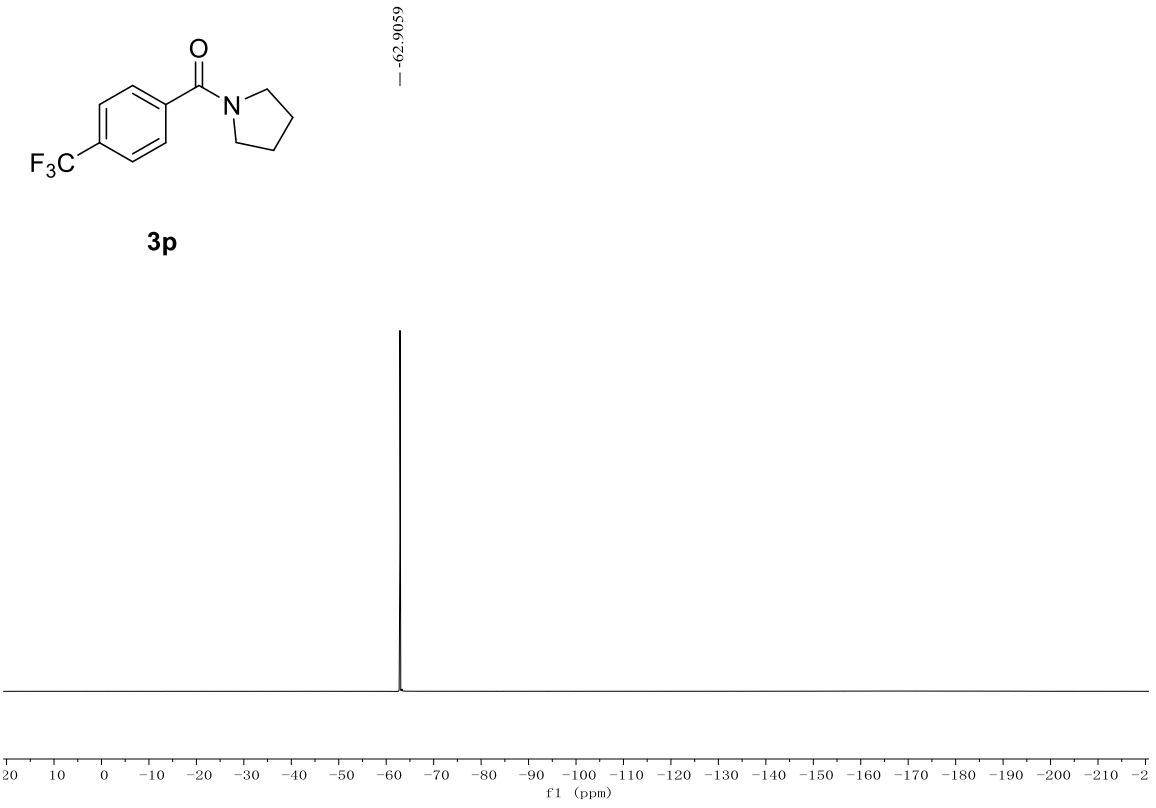
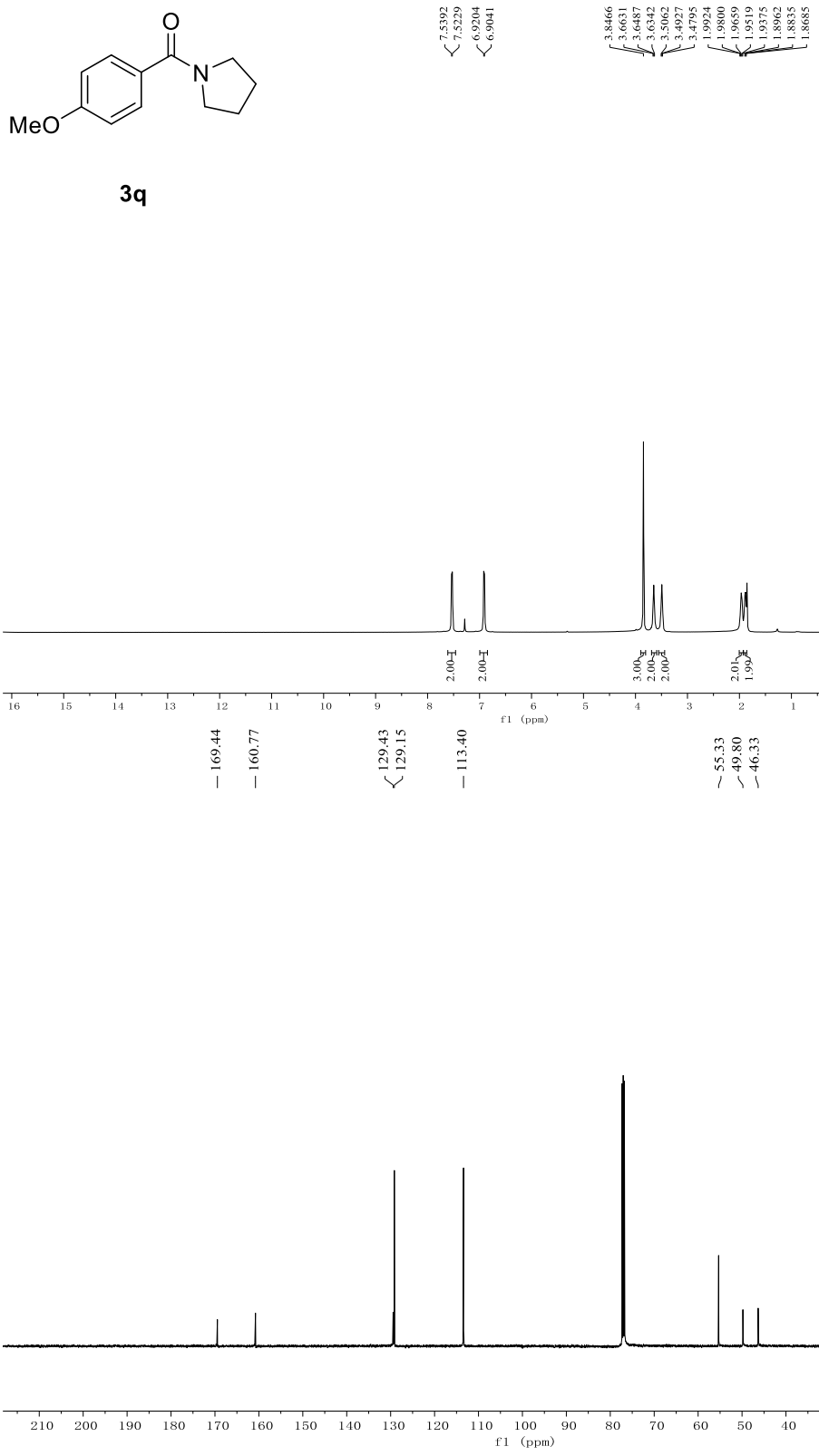
3.00
3.00
f1 (ppm)
172.32
171.60
137.06
136.63
136.31
136.22
129.62
128.84
128.73
128.48
128.44
128.20
127.60
127.56
127.53
127.01
126.80
126.76
55.19
50.80
37.02
33.19
f1 (ppm)

3n

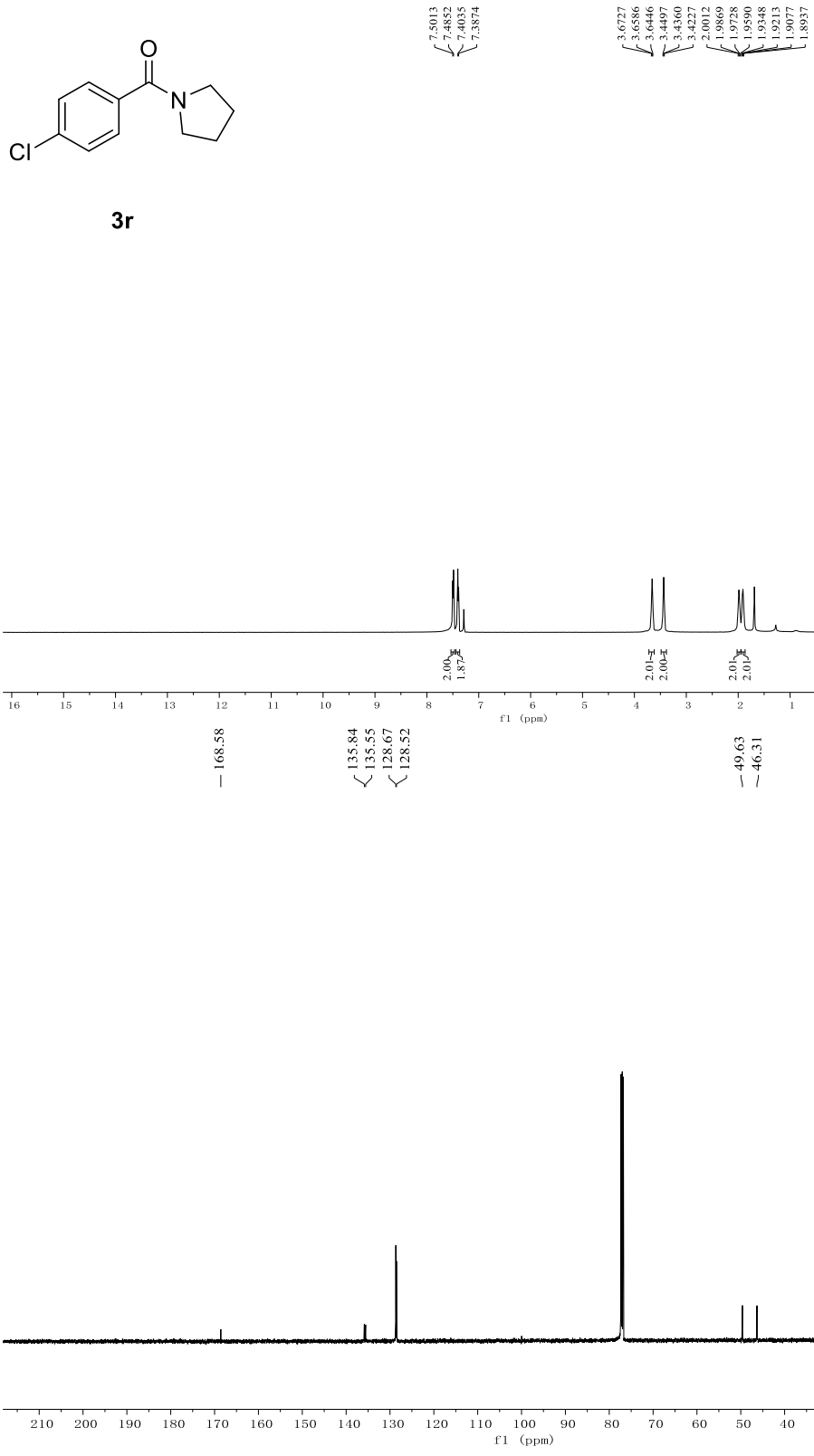

7.6865
7.6703
7.6424
7.6262
3.6824
3.6686
3.6546
3.4114
3.3981
3.3851
2.0175
2.0042
1.9906
1.9768
1.9635
1.9340
1.9213
1.9082
1.8949
1.8818
O
N
F3C
3p
2.00
1.78
2.00
1.98
2.13
2.05
f1 (ppm)
168.23
140.68
132.03
131.77
131.51
131.25
127.45
127.01
125.41
125.38
125.35
125.32
124.85
122.68
120.52
49.49
46.25
26.36
24.40
f1 (ppm)


O
N
F3C
−62.9059
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)

3p


O
N
MeO
7.5392
7.5229
6.9204
6.9041
3.8466
3.6631
3.6487
3.6342
3.5062
3.4927
3.4795
1.9924
1.9800
1.9659
1.9519
1.9375
1.8962
1.8835
1.8685
2.00
2.00
3.00
2.00
2.00
2.01
1.99
f1 (ppm)
169.44
160.77
129.43
129.15
113.40
55.33
49.80
46.33
26.51
24.46
f1 (ppm)

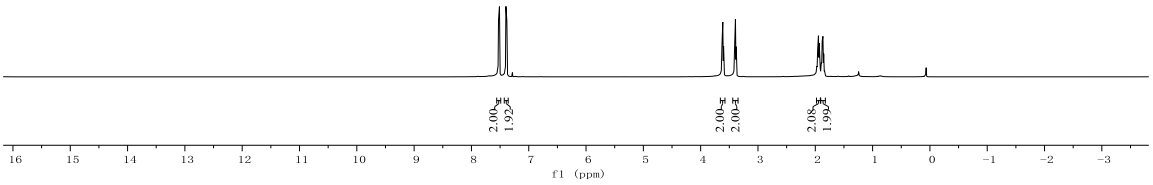
3q


7.5013
7.4852
7.4035
7.3874
3.6727
3.6586
3.6446
3.4497
3.4360
3.4227
2.0012
1.9869
1.9728
1.9590
1.9348
1.9213
1.9077
1.8937
O
N
Cl
2.00
1.87
2.01
2.00
2.01
2.01
f1 (ppm)
168.58
135.84
135.55
128.67
128.52
49.63
46.31
26.44
24.44
f1 (ppm)

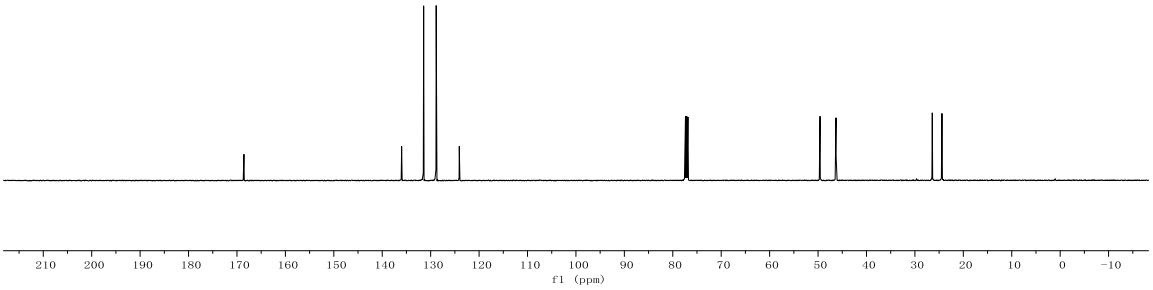
3r

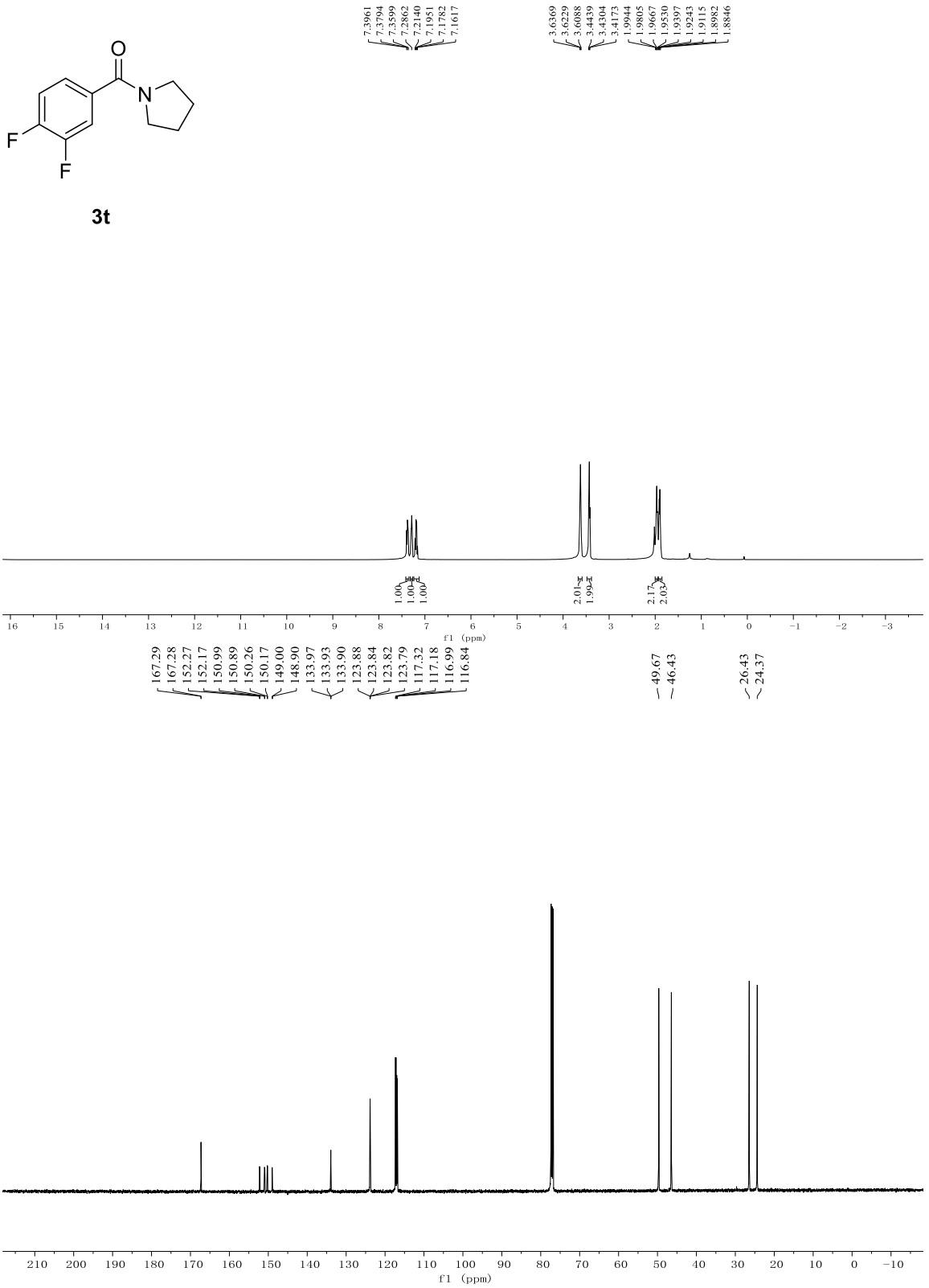

7.5276
7.5110
7.3983
7.3816
3.6281
3.6141
3.6000
3.4063
3.3929
3.3797
1.9728
1.9589
1.9450
1.9313
1.9180
1.8928
1.8798
1.8665
1.8529
1.8392
O
N
Br

3s

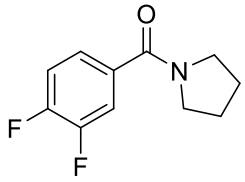

2.00
1.92
2.00
2.00
2.08
1.99
f1 (ppm)


168.56
135.99
131.45
128.86
124.09
49.59
46.29
26.41
24.41


f1 (ppm)

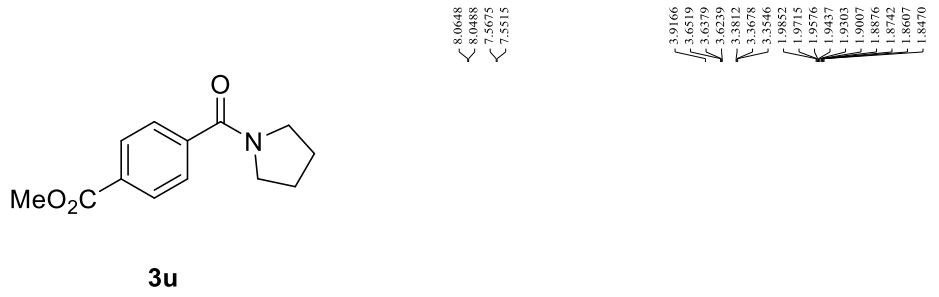

7.3961
7.3794
7.3599
7.2862
7.2140
7.1951
7.1782
7.1617
3.6369
3.6229
3.6088
3.4439
3.4304
3.4173
1.9944
1.9805
1.9667
1.9530
1.9397
1.9243
1.9115
1.8982
1.8846
O
N
F
F
1.00
1.00
1.00
2.01
1.99
2.17
2.03
f1 (ppm)
167.29
167.28
152.27
152.17
150.99
150.89
150.26
150.17
149.00
148.90
133.97
133.93
133.90
123.88
123.84
123.82
123.79
117.32
117.18
116.99
116.84
49.67
46.43
26.43
24.37
f1 (ppm)

3t

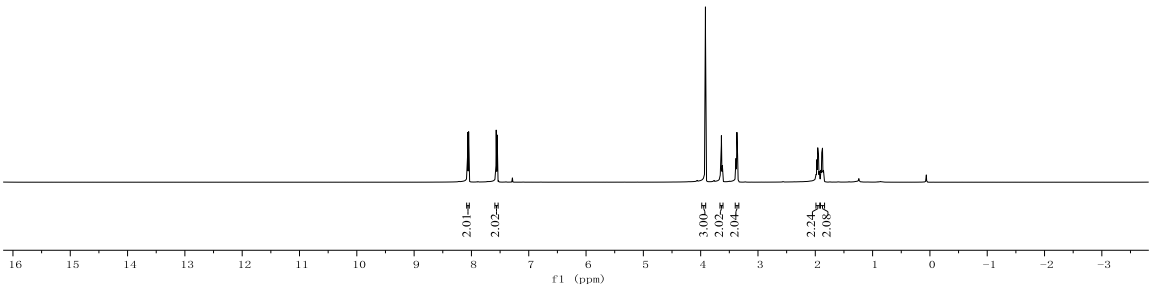

O
N
F
F

3t

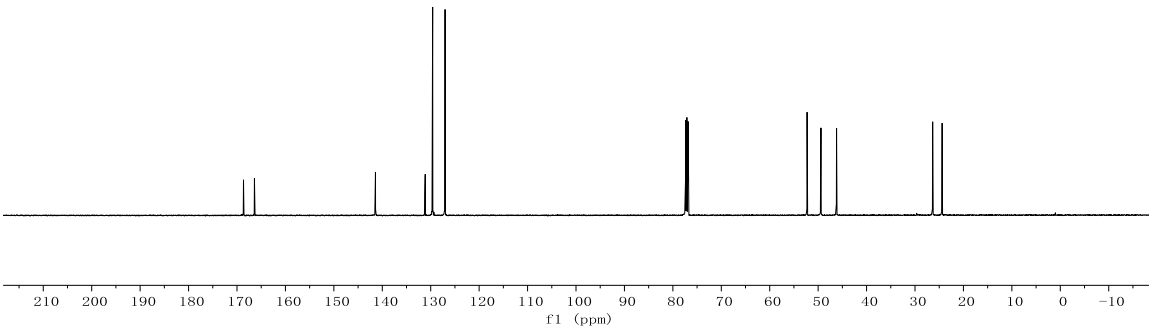
-135.0932
-136.9599
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −2
f1 (ppm)

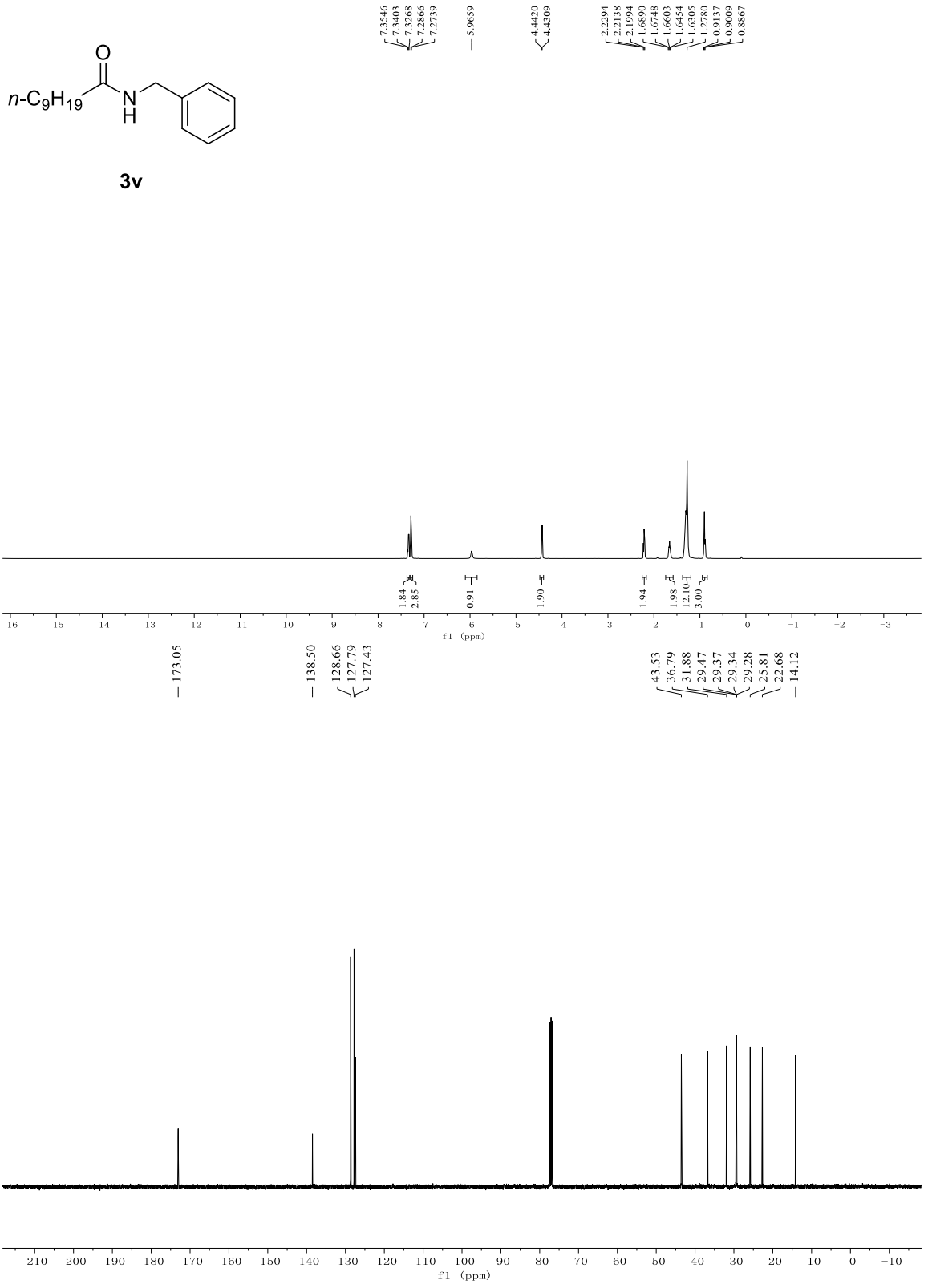

8.0648
8.0488
7.5675
7.5515
3.9166
3.6519
3.6379
3.6239
3.3812
3.3678
3.3546
1.9852
1.9715
1.9576
1.9437
1.9303
1.9007
1.8876
1.8742
1.8607
1.8470
O
N
MeO2C

3u

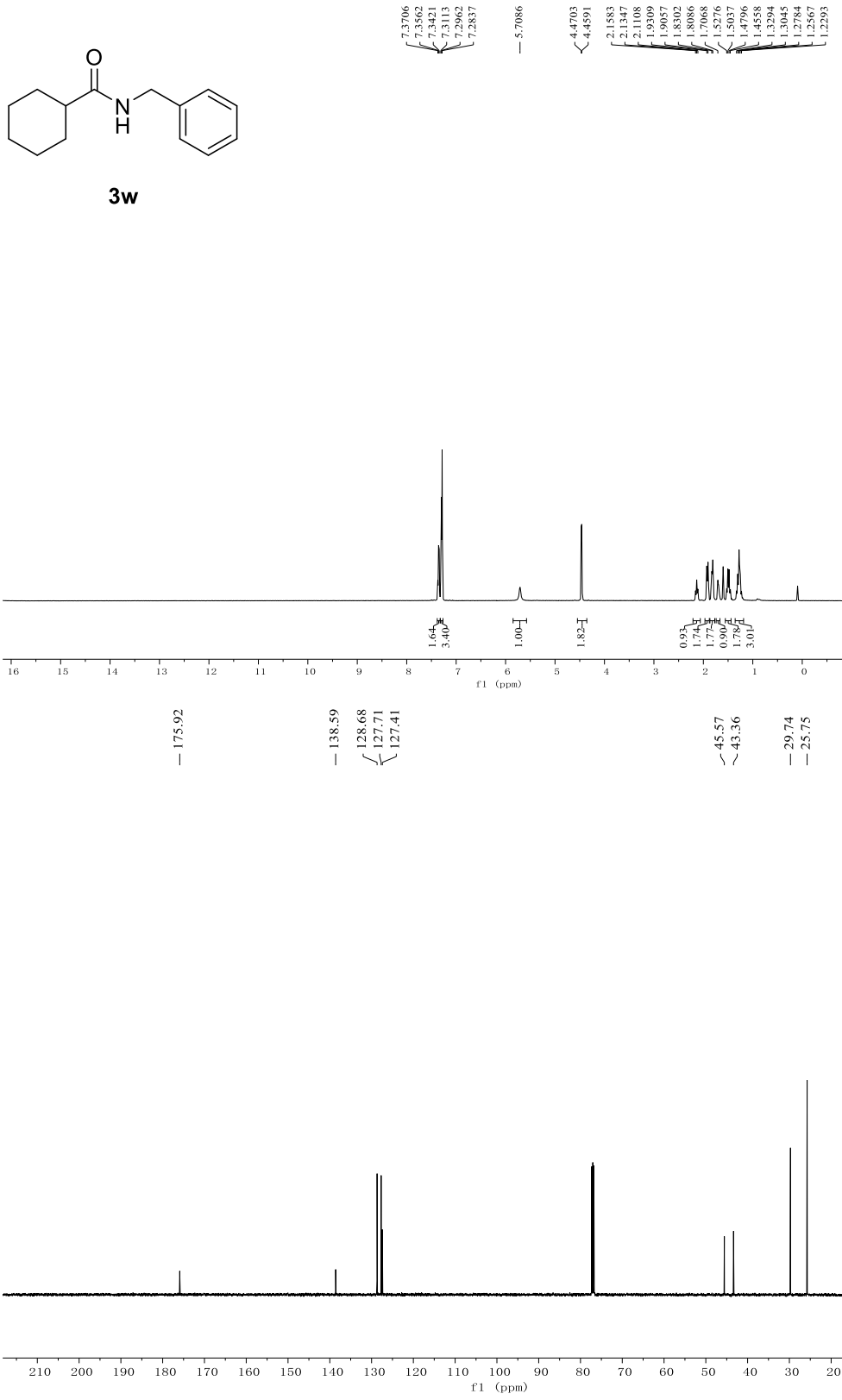

2.01
2.02
3.00
2.02
2.04
2.24
2.08
f1 (ppm)

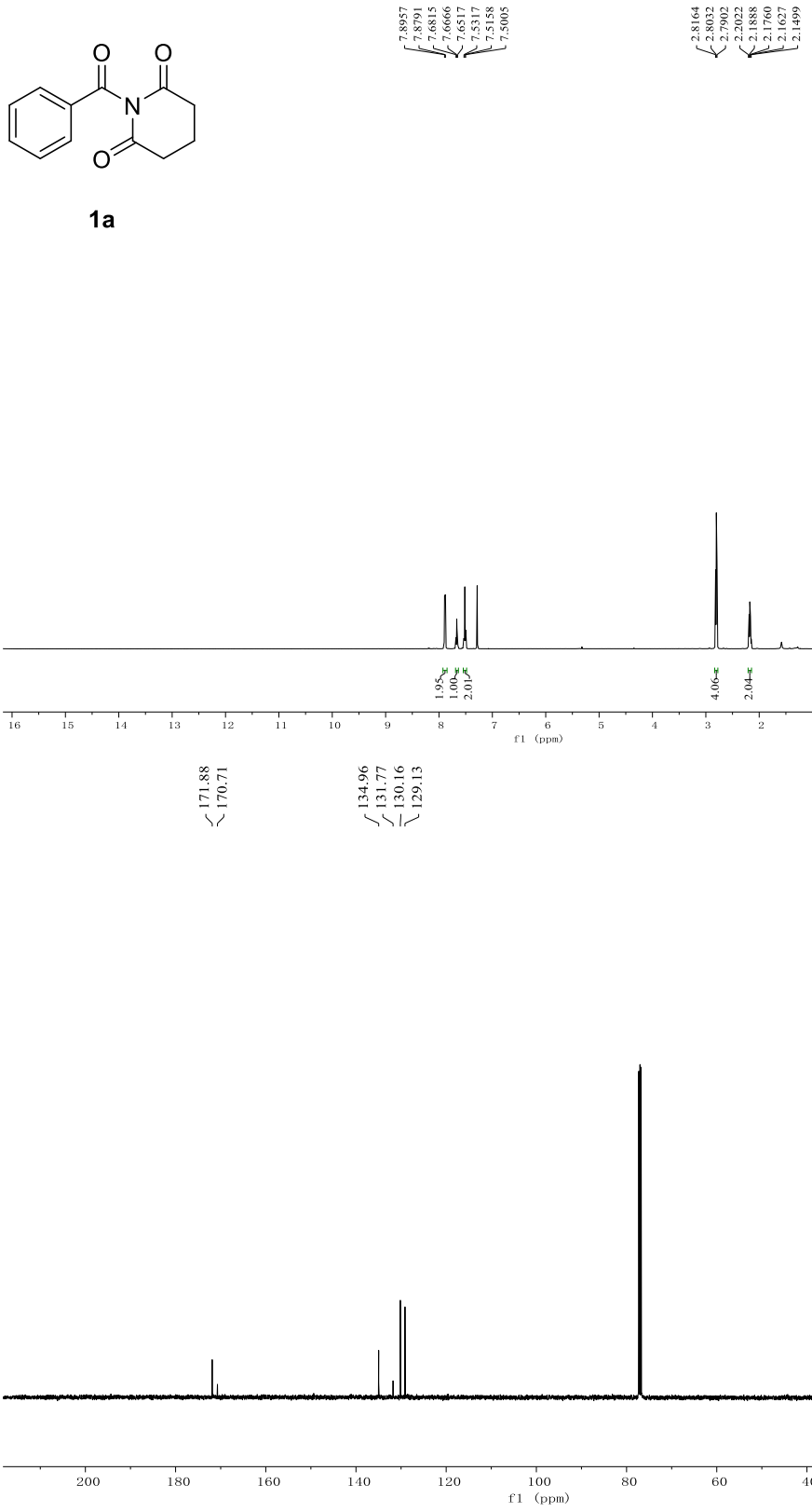

168.66
166.40
141.40
131.13
129.60
127.03
52.28
49.42
46.20
26.35
24.40


f1 (ppm)

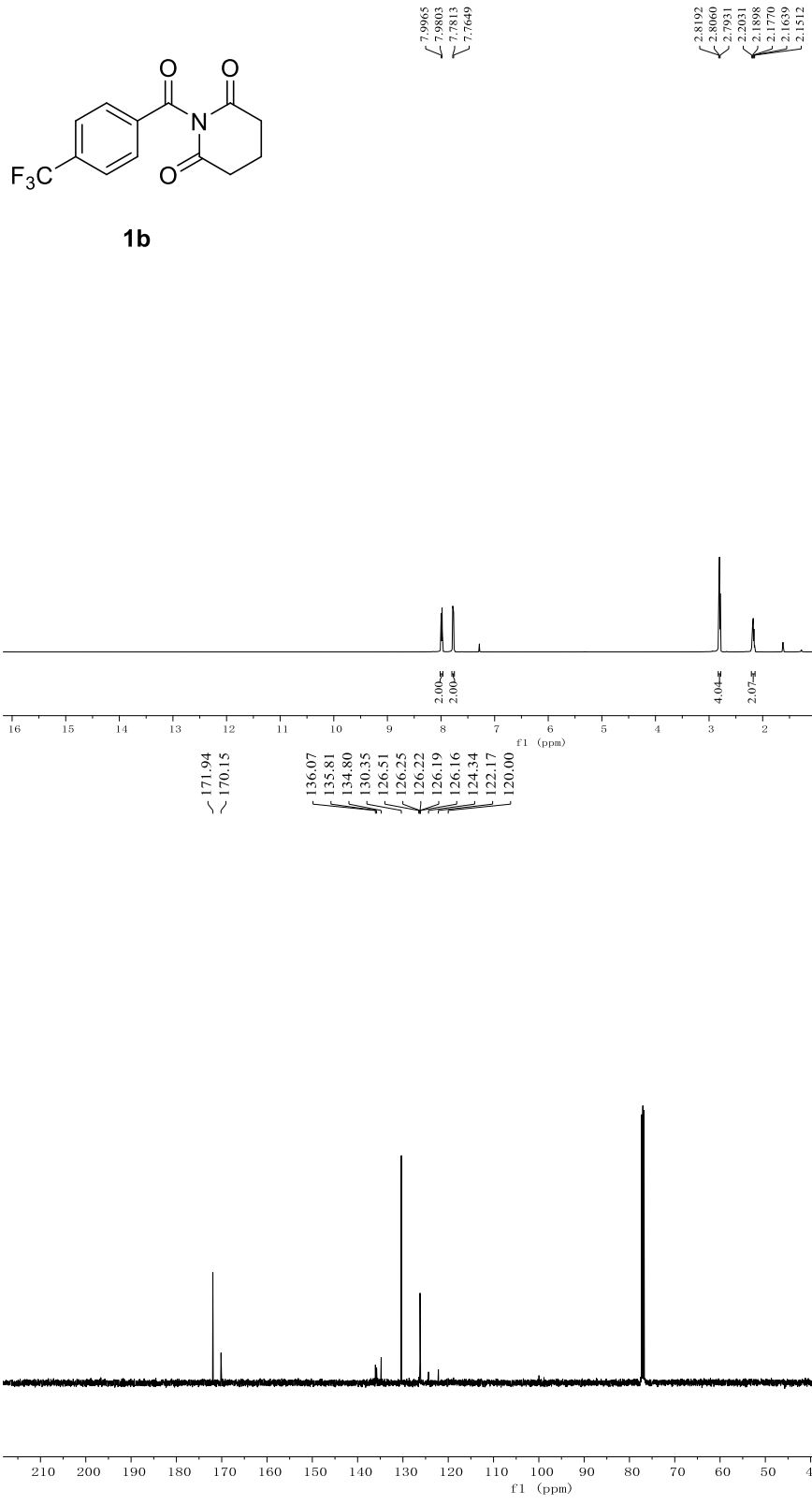

7.3546
7.3403
7.3268
7.2866
7.2739
5.9659
4.4420
4.4309
2.2294
2.2138
2.1994
1.6890
1.6748
1.6603
1.6454
1.6305
1.2780
0.9137
0.9009
0.8867
1.84
2.85
0.91
1.90
1.94
1.98
12.10
3.00
f1 (ppm)
173.05
138.50
128.66
127.79
127.43
43.53
36.79
31.88
29.47
29.37
29.34
29.28
25.81
22.68
14.12
f1 (ppm)

3v

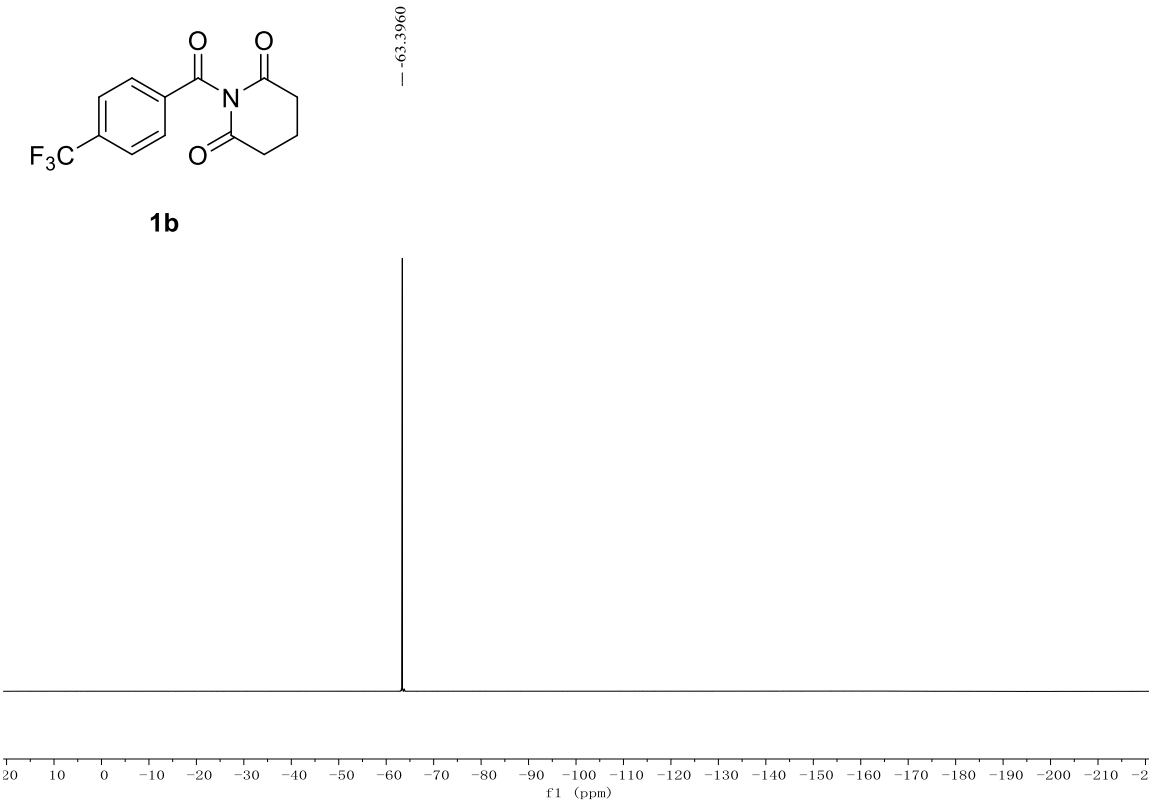

7.3706
7.3562
7.3421
7.3113
7.2962
7.2837
5.7086
4.4703
4.4591
2.1583
2.1347
2.1108
1.9309
1.9057
1.8302
1.8086
1.7068
1.5276
1.5037
1.4796
1.4558
1.3294
1.3045
1.2784
1.2567
1.2293
O
N
H
3w
1.64
3.40
1.00
1.82
0.93
1.74
1.77
0.90
1.78
3.01
f1 (ppm)
175.92
138.59
128.68
127.71
127.41
45.57
43.36
29.74
25.75
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
1.95
1.00
2.01
4.06
2.04
f1 (ppm)
171.88
170.71
134.96
131.77
130.16
129.13
32.42
17.52
f1 (ppm)

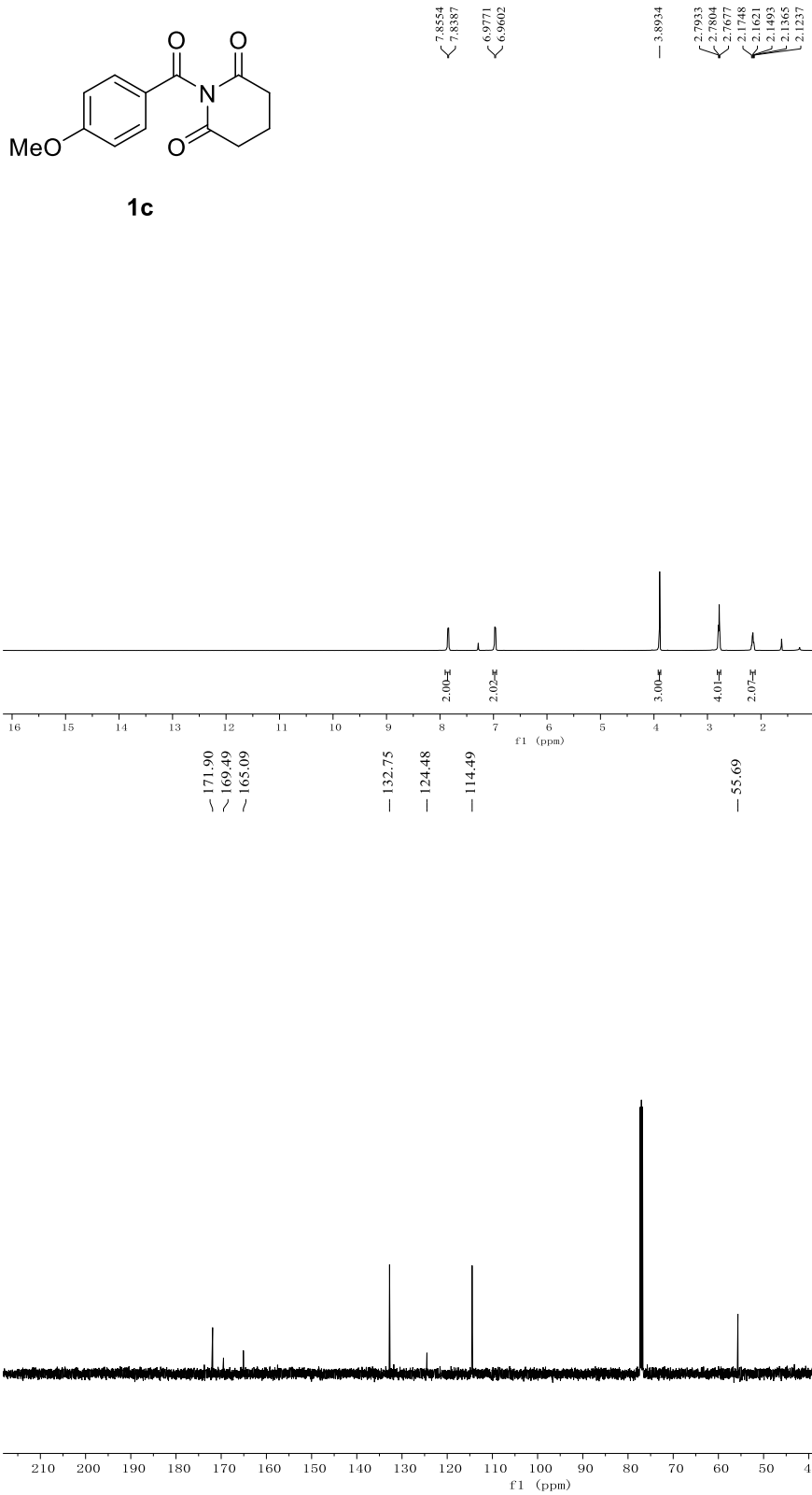
1a


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
2.00
2.00
4.04
2.07
f1 (ppm)
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)

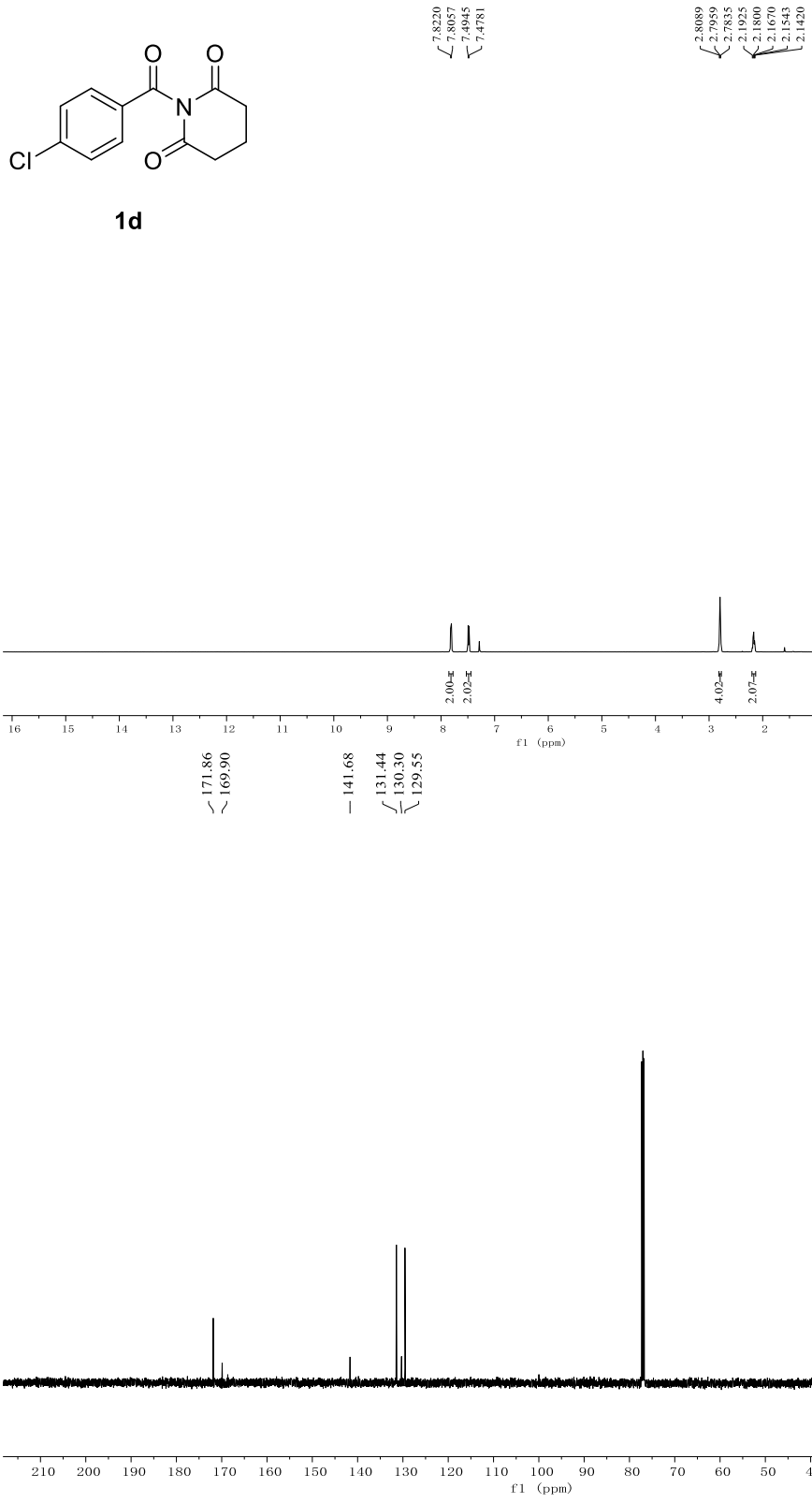
1b


O
O
N
O
F3C
-63.3960
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)

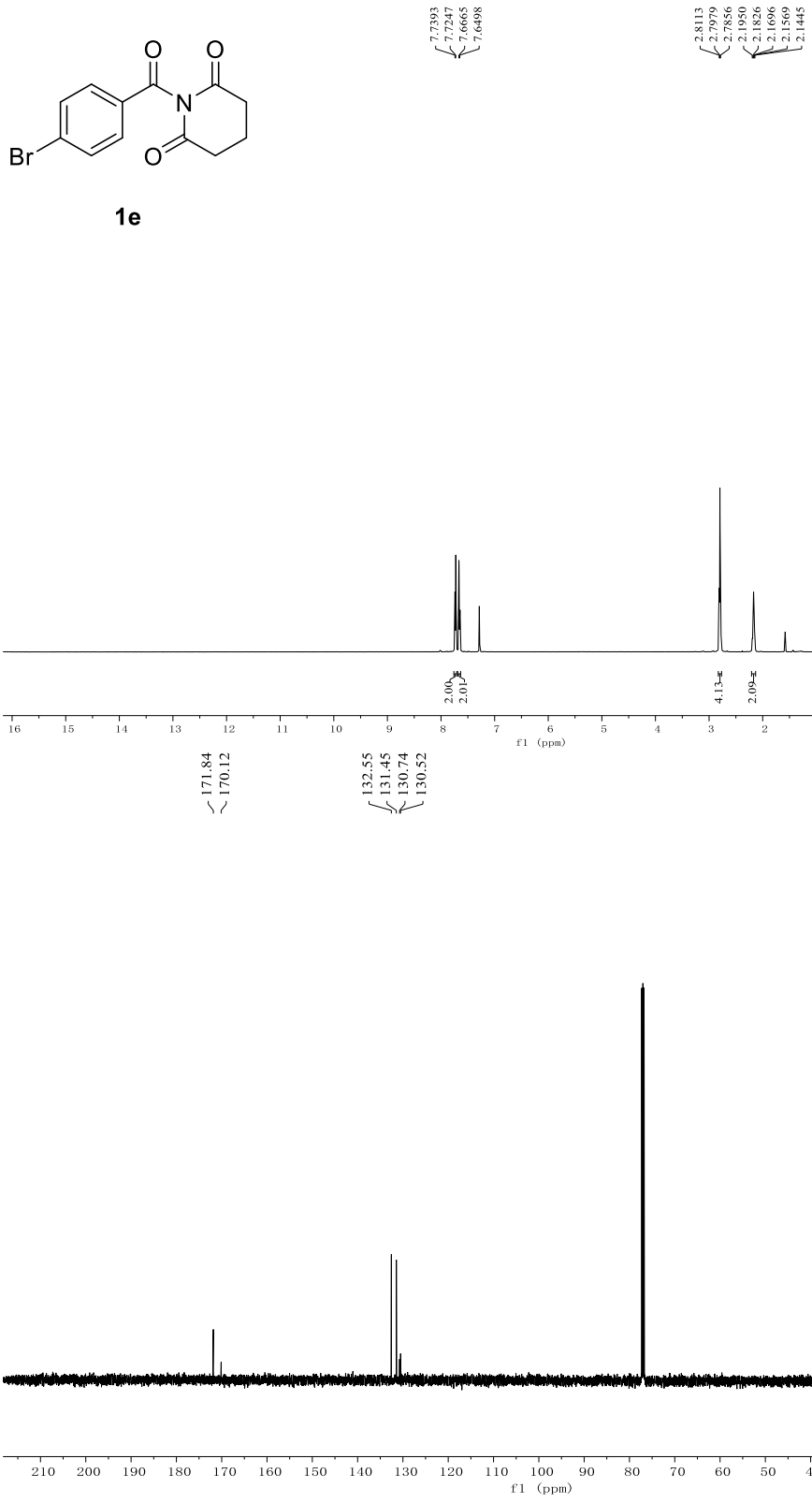
1b


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
O
N
2.00
2.02
3.00
4.01
2.07
f1 (ppm)
171.90
169.49
165.09
132.75
124.48
114.49
55.69
32.44
17.52

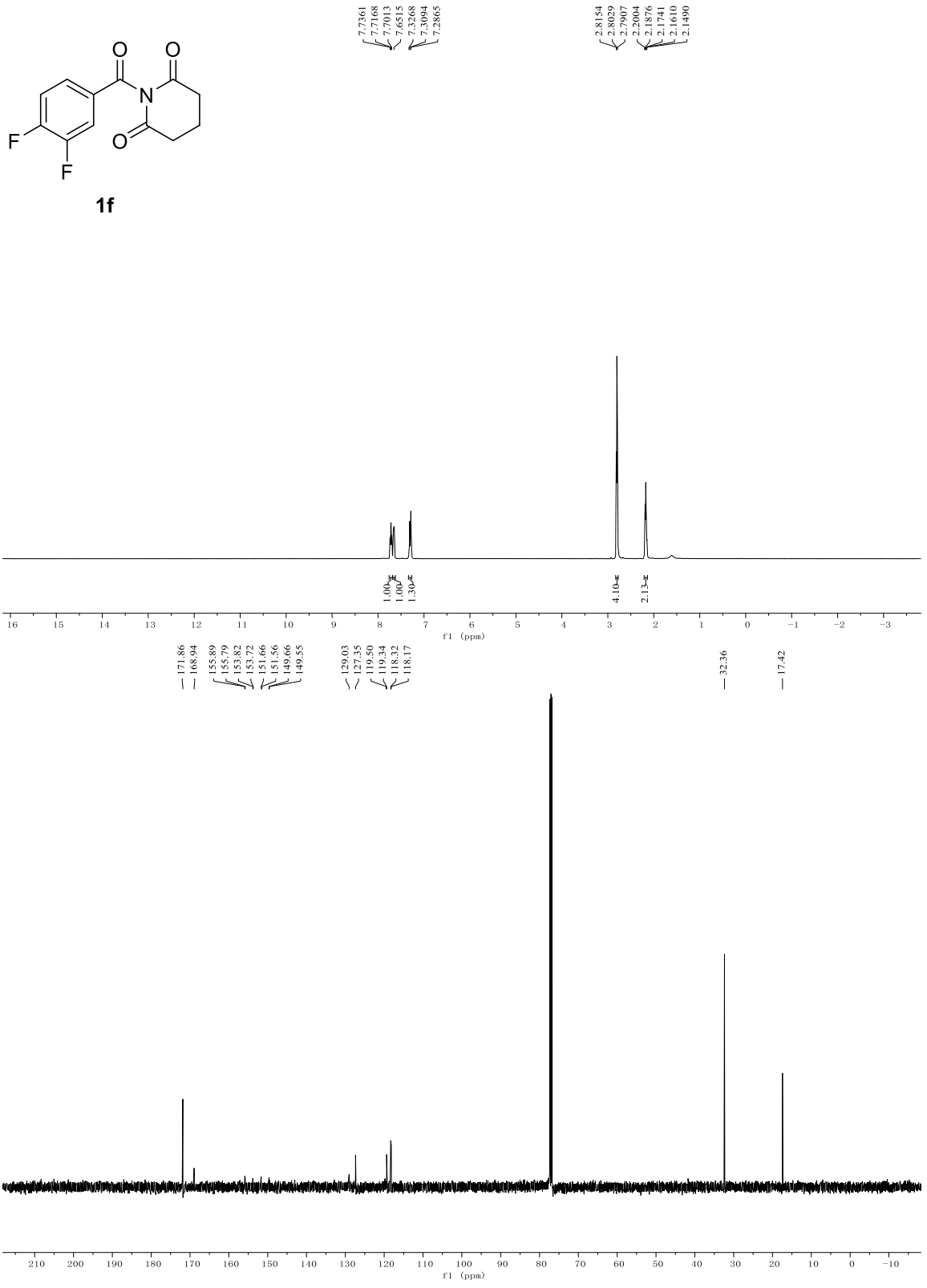
1c


7.8220
7.8057
7.4945
7.4781
2.8089
2.7959
2.7835
2.1925
2.1800
2.1670
2.1543
2.1420
2.00
2.02
4.02
2.07
f1 (ppm)
171.86
169.90
141.68
131.44
130.30
129.55
32.39
17.47
f1 (ppm)

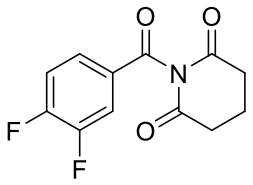
1d


7.7393
7.7247
7.6665
7.6498
2.8113
2.7979
2.7856
2.1950
2.1826
2.1696
2.1569
2.1445
Br
O
O
N
O
2.00
2.01
4.13
2.09
f1 (ppm)
171.84
170.12
132.55
131.45
130.74
130.52
32.39
17.47
f1 (ppm)

1e

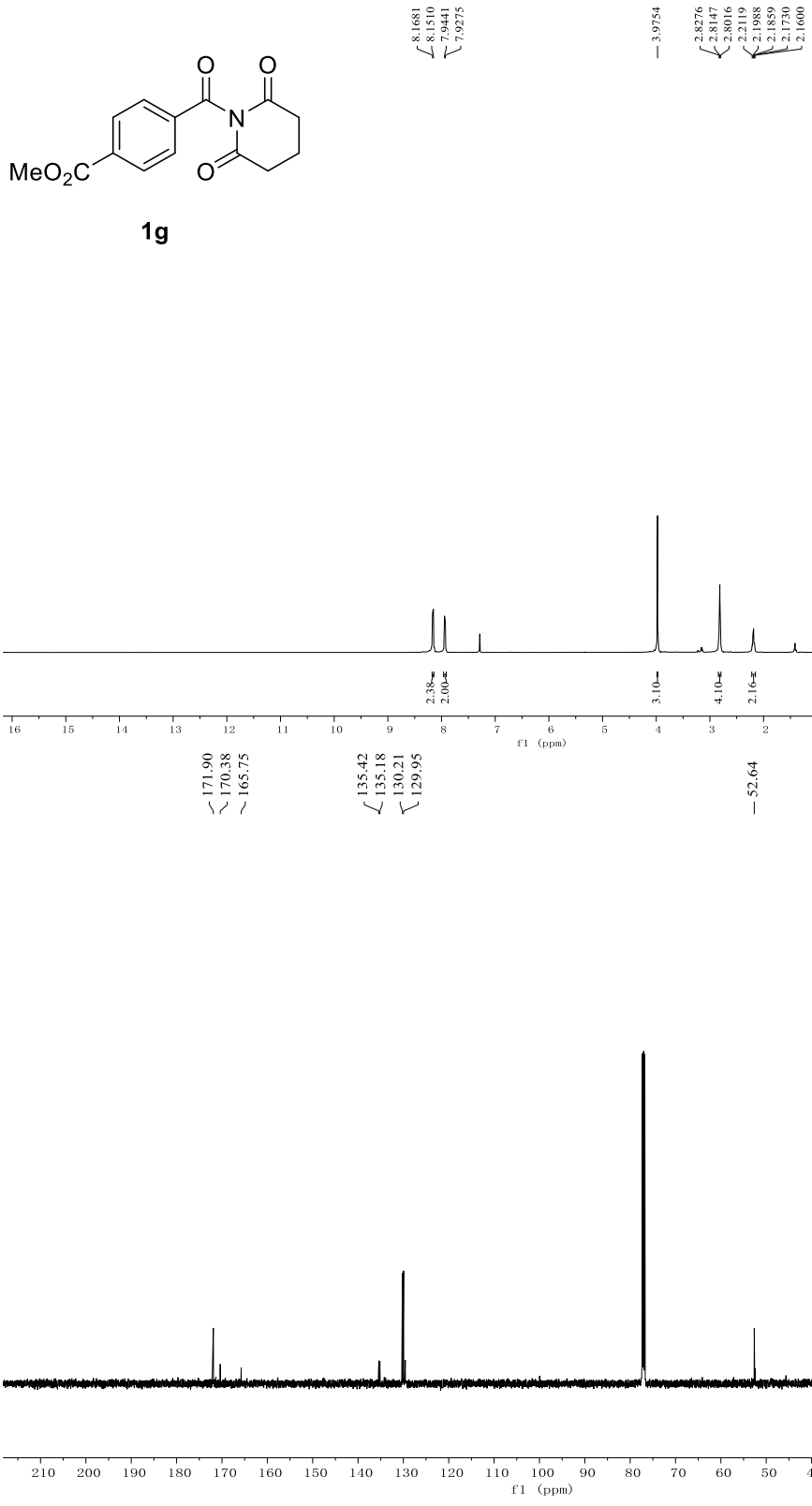

7.7361
7.7168
7.7013
7.6515
7.3268
7.3094
7.2865
2.8154
2.8029
2.7907
2.2004
2.1876
2.1741
2.1610
2.1490
1.00
1.00
1.30
4.10
2.13
f1 (ppm)
171.86
168.94
155.89
155.79
153.82
153.72
151.66
151.56
149.66
149.55
129.03
127.35
119.50
119.34
118.32
118.17
32.36
17.42
f1 (ppm)

1f

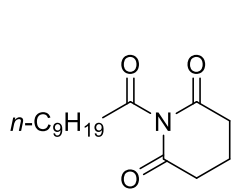

O
O
N
O
F
F

1f

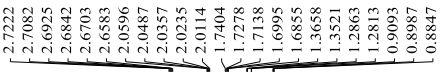
-125.76
-134.84
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170
f1 (ppm)

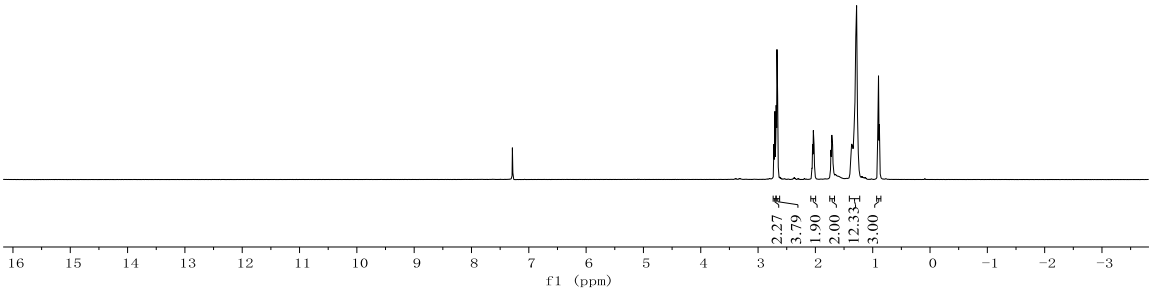

8.1681
8.1510
7.9441
7.9275
3.9754
2.8276
2.8147
2.8016
2.2119
2.1988
2.1859
2.1730
2.1600
O
O
N
O
MeO2C
2.38
2.00
3.10
4.10
2.16
f1 (ppm)
171.90
170.38
165.75
135.42
135.18
130.21
129.95
52.64
32.39
17.47
f1 (ppm)

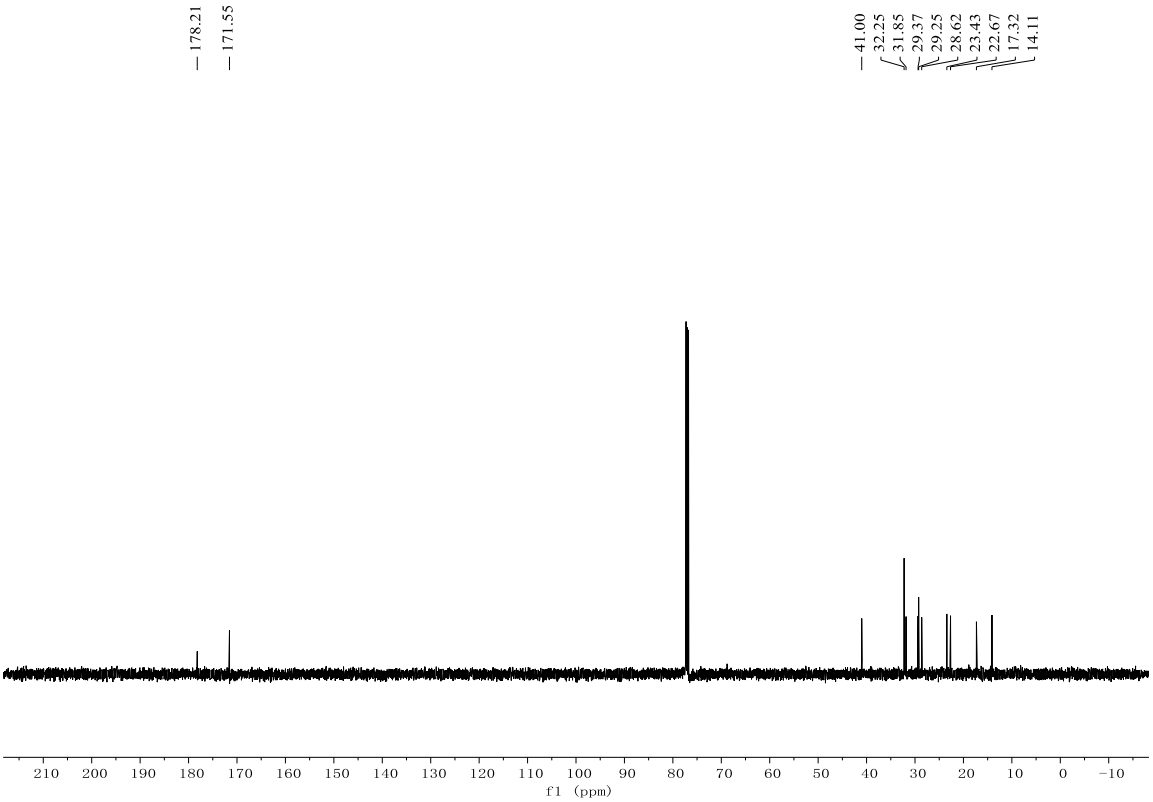
1g

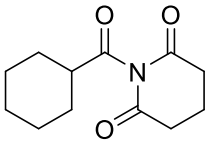

O
O
n-C9H19
N
O

1h

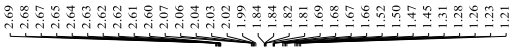

2.7222
2.7082
2.6925
2.6842
2.6703
2.6583
2.0596
2.0487
2.0357
2.0235
2.0114
1.7404
1.7278
1.7138
1.6995
1.6855
1.3658
1.3521
1.2863
1.2813
0.9093
0.8987
0.8847

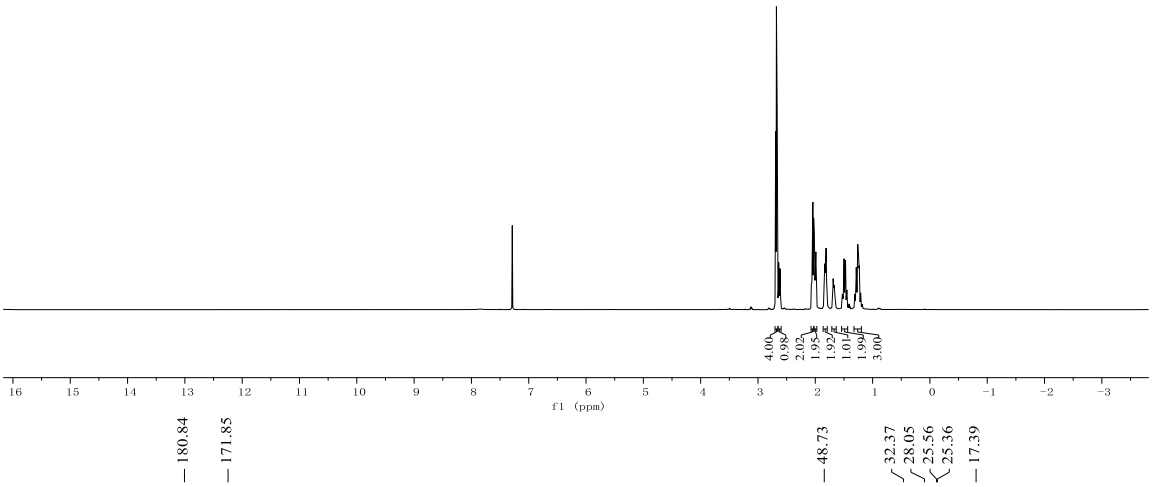

2.27
3.79
1.90
2.00
12.33
3.00
f1 (ppm)


178.21
171.55
41.00
32.25
31.85
29.37
29.25
28.62
23.43
22.67
17.32
14.11
f1 (ppm)

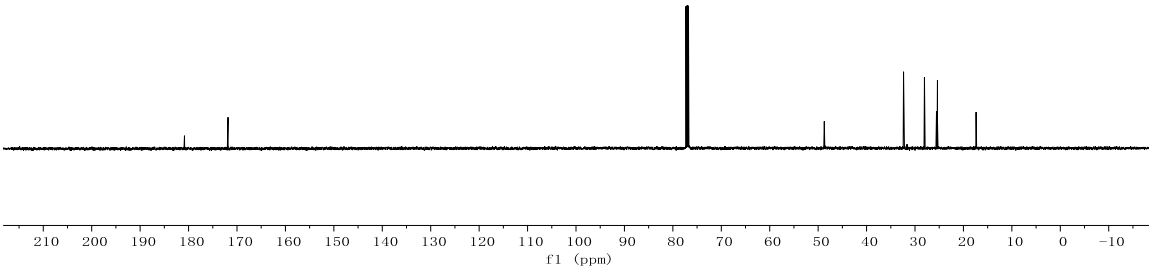


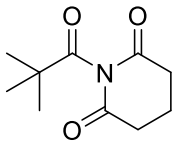
1i


2.69
2.68
2.67
2.65
2.64
2.63
2.62
2.62
2.61
2.60
2.07
2.06
2.04
2.03
2.02
1.99
1.84
1.84
1.82
1.81
1.69
1.68
1.67
1.66
1.52
1.50
1.47
1.45
1.31
1.28
1.26
1.23
1.21

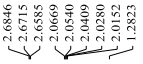

4.00
0.98
2.02
1.95
1.92
1.01
1.99
3.00
f1 (ppm)

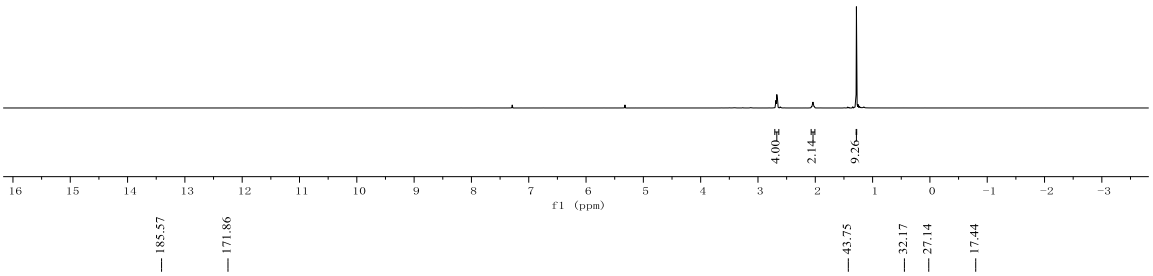
180.84
171.85
48.73
32.37
28.05
25.56
25.36
17.39


f1 (ppm)

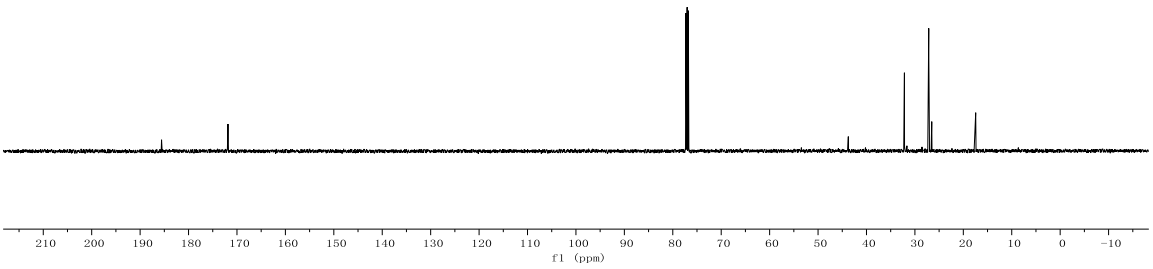


1j


2.6846
2.6715
2.6585
2.0669
2.0540
2.0409
2.0280
2.0152
1.2823


4.00
2.14
9.26
f1 (ppm)

185.57
171.86
43.75
32.17
27.14
17.44


f1 (ppm)