

Palladium-Catalyzed Suzuki-Miyaura Coupling of Amides by Carbon–Nitrogen Cleavage: General Strategy for Amide N–C Bond Activation

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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.¹⁻¹⁴ All experiments involving palladium were performed using Schlenk or glovebox 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 solvents were deoxygenated prior to use. All other chemicals were purchased at the highest commercial grade and used as received. Reaction glassware was oven-dried at 140 °C for at least 24 h or flame-dried prior to use, allowed to cool under vacuum and purged with argon (three cycles). All products were identified using ¹H 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 ¹H NMR and/or GC or GC/MS using an internal standard (optimization) and isolated yields (preparative runs) unless stated otherwise. ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃ on Bruker spectrometers at 500 (¹H NMR) and 125 MHz (¹³C NMR). All shifts are reported in parts per million (ppm) relative to residual CHCl₃ peak (7.27 and 77.2 ppm, ¹H NMR and ¹³C 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 250 °C. The detector temperature was 250 °C. For runs with the initial oven temperature of 50 °C, temperature was increased with a 10 °C/min ramp after 50 °C hold for 3 min to a final temperature of 220 °C, then hold at 220 °C for 15 min (splitless mode of injection, total run time of 22.00 min). High-resolution mass spectra (HRMS) were measured on a 7T Bruker Daltonics FT-MS instrument. All flash chromatography was performed using silica gel, 60 Å, 300 mesh. TLC analysis was carried out on glass plates coated with silica gel 60 F254, 0.2 mm thickness. The plates were visualized using a 254 nm ultraviolet lamp or aqueous potassium permanganate solutions. ¹H NMR, ¹³C NMR, MS and HRMS data are given for all compounds in the Supporting Experimental for characterization purposes. ¹H NMR, ¹³C NMR, MS and HRMS data are reported for all new compounds.

Experimental Procedures and Characterization Data

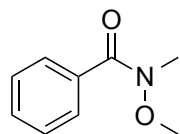
General Procedure for Amide Synthesis. An oven-dried round-bottomed flask (100 mL) equipped with a stir bar was charged with amine (8.84 mmol, 1.0 equiv), triethylamine (typically, 2.0 equiv), 4-dimethylaminopyridine (typically, 0.25 equiv) and dichloromethane (typically, 50 mL), placed under a positive 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 Et₂O (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 Pd-catalyzed Suzuki-Miyaura Coupling with Amides. An oven-dried vial equipped with a stir bar was charged with an amide substrate (1.0 equiv), potassium carbonate (typically, 2.5 equiv), boric acid (typically, 2.0 equiv), boronic acid (typically, 1.2 equiv), Pd(OAc)₂ (typically, 0.03 equiv), and PCy₃HBF₄ (typically, 0.12 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Tetrahydrofuran (typically, 0.80 mL) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 65 °C, and stirred for the indicated time at 65 °C. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH₂Cl₂ (10 mL), filtered, and concentrated. The sample was analyzed by ¹H NMR (CDCl₃, 500 MHz) and GC-MS to obtain selectivity, conversion and yield using internal standard and comparison with authentic samples. Purification by chromatography on silica gel afforded the title product.

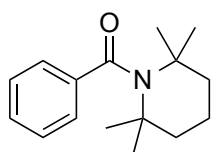
Representative Procedure for Large-scale Pd-catalyzed Suzuki-Miyaura Coupling. An oven-dried 100 mL round-bottomed flask equipped with a stir bar was charged with 1-benzoylpiperidine-2,6-dione (2.17 g, 10 mmol, 1.0 equiv), (6-methoxynaphthalen-2-yl)boronic acid (2.42 g, 1.2 equiv, 12 mmol), Pd(OAc)₂ (0.0674 g, 0.03 equiv, 0.3 mmol), PCy₃HBF₄ (0.442 g, 0.12 equiv, 1.2 mmol), potassium carbonate (3.45 g, 2.5 equiv, 25 mmol) and boric acid (1.24 g, 2.0 equiv, 20 mmol), placed under a positive pressure of argon, and subjected to three

evacuation/backfilling cycles under high vacuum. THF (40 mL) was added with vigorous stirring at room temperature, the reaction was placed in a preheated oil bath at 65 °C, and stirred at 65 °C for 15 h. The reaction mixture was cooled down to room temperature, diluted with CH₂Cl₂ (20 mL), filtered, and concentrated. The reaction mixture was analyzed by ¹H NMR (CDCl₃, 500 MHz) and GC-MS to obtain selectivity, conversion and yield using internal standard. Purification by chromatography on silica gel afforded the title product (2.11 g). Yield 80.6%. White solid. Characterization data are included in the section below.

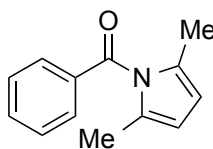
Characterization Data for Starting Materials



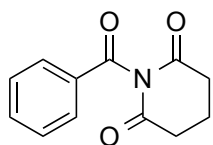
N-Methoxy-N-methylbenzamide (1a). Table 1, Entry 1. Oil. **GC:** rt = 8.23 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.68 (dt, *J* = 7.0, 1.5 Hz, 2 H), 7.45-7.43 (m, 1 H), 7.42-7.37 (m, 2 H), 3.55 (s, 3 H), 3.36 (s, 3 H). **¹³C NMR (125 MHz, CDCl₃)** δ 169.94, 134.09, 130.55, 128.10, 128.00, 61.01, 33.79. **MS** = 165.1 (EI). **HRMS** calcd for C₁₈H₂₂N₂O₄Na (2 M⁺ + Na) 353.1472, found 353.1496.



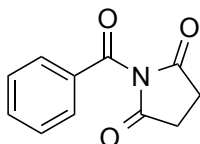
Phenyl(2,2,6,6-tetramethylpiperidin-1-yl)methanone (1b). Table 1, Entry 2. White solid. **GC:** rt = 11.23 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.49-7.42 (m, 2 H), 7.37 (qd, *J* = 8.6, 7.5, 4.3 Hz, 3 H), 1.81 (s, 6 H), 1.39 (s, 6 H), 1.38 (s, 6 H). **¹³C NMR (125 MHz, CDCl₃)** δ 176.74, 143.30, 129.33, 127.81, 127.74, 56.51, 37.02, 30.57, 14.95. **MS** = 245.1 (EI). **HRMS** calcd for C₁₆H₂₃NONa (M⁺ + Na) 268.1672, found 268.1678.



(2,5-Dimethyl-1H-pyrrol-1-yl)(phenyl)methanone (1c). Table 1, Entry 3. Oil. **GC:** rt = 9.51 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.78-7.67 (m, 2 H), 7.66-7.59 (m, 1 H), 7.50 (t, *J* = 7.9 Hz, 2 H), 5.90 (s, 2 H), 2.10 (s, 3 H), 2.09 (s, 3 H). **¹³C NMR (125 MHz, CDCl₃)** δ 171.18, 135.68, 133.18, 130.34, 130.12, 128.67, 110.14, 99.98, 14.69. **MS** = 199.1 (EI). **HRMS** calcd for C₁₃H₁₃NONa (M⁺ + Na) 222.0889, found 222.0894.

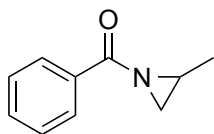


1-Benzoylpiperidine-2,6-dione (1d). Table 1, Entry 4. White solid. **GC:** rt = 9.80 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.89 (d, *J* = 7.8 Hz, 2 H), 7.67 (t, *J* = 7.5 Hz, 1 H), 7.52 (t, *J* = 7.7 Hz, 2 H), 2.80 (t, *J* = 6.6 Hz, 4 H), 2.17 (q, *J* = 6.5 Hz, 2 H). **¹³C NMR (125 MHz, CDCl₃)** δ 171.90, 170.74, 134.97, 131.78, 130.16, 129.14, 32.41, 17.51. **MS** = 217.1 (EI). **HRMS** calcd for C₁₂H₁₁NO₃Na (M⁺ + Na) 240.0631, found 240.0635.



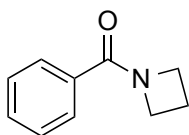
1-Benzoylpyrrolidine-2,5-dione (1e). Table 1, Entry 5. White solid. **GC:** rt = 11.44 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.88 (d, *J* = 7.2 Hz, 2 H), 7.69 (t,

$J = 7.5$ Hz, 1 H), 7.53 (t, $J = 7.8$ Hz, 2 H), 2.96 (s, 4 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 174.54, 167.62, 135.15, 131.40, 130.53, 128.97, 29.08. **MS** = 203.1 (EI). **HRMS** calcd for $\text{C}_{11}\text{H}_9\text{NO}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 226.0475, found 226.0483.



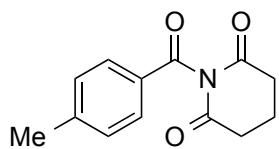
(2-Methylaziridin-1-yl)(phenyl)methanone (1f). Table 1, Entry 6. Oil.

GC: $r_t = 8.05$ min. **^1H NMR (500 MHz, CDCl_3)** δ 8.08-8.02 (m, 2 H), 7.57 (td, $J = 7.2, 1.5$ Hz, 1 H), 7.48 (t, $J = 7.8$ Hz, 2 H), 2.66-2.54 (m, 2 H), 2.17 (d, $J = 3.6$ Hz, 1 H), 1.42 (d, $J = 5.4$ Hz, 3 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 179.30, 133.54, 132.62, 129.05, 128.40, 34.61, 32.14, 17.79. **MS** = 161.1 (EI). **HRMS** calcd for $\text{C}_{10}\text{H}_{11}\text{NONa}$ ($\text{M}^+ + \text{Na}$) 184.0733, found 184.0715.



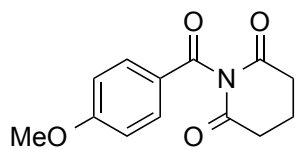
Azetidin-1-yl(phenyl)methanone (1g). Table 1, Entry 7. Oil. **GC:** $r_t = 8.47$

min. **^1H NMR (500 MHz, CDCl_3)** δ 7.68-7.57 (m, 2 H), 7.51-7.35 (m, 3 H), 4.26 (dt, $J = 15.0, 7.8$ Hz, 4 H), 2.41-2.25 (m, 2H). **^{13}C NMR (125 MHz, CDCl_3)** δ 170.24, 133.26, 130.82, 128.31, 127.78, 30.92, 16.03. **MS** = 161.1 (EI). **HRMS** calcd for $\text{C}_{10}\text{H}_{11}\text{NONa}$ ($\text{M}^+ + \text{Na}$) 184.0733, found 184.0737.



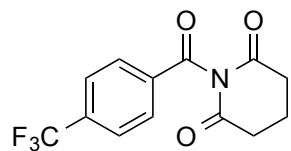
1-(4-Methylbenzoyl)piperidine-2,6-dione (1h). Chart 2, Entry 2.

White solid. **GC:** $r_t = 12.68$ min. **^1H NMR (500 MHz, CDCl_3)** δ 7.78 (d, $J = 8.0$ Hz, 2 H), 7.331 (d, $J = 8.0$ Hz, 2 H), 2.79 (t, $J = 6.6$ Hz, 4 H), 2.45 (s, 3 H), 2.16 (p, $J = 6.6$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 171.87, 170.39, 146.32, 130.32, 129.87, 129.24, 32.42, 21.89, 17.52. **MS** = 231.1 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 254.0788, found 254.0799.

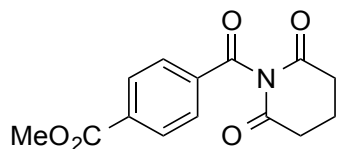


1-(4-Methoxybenzoyl)piperidine-2,6-dione (1i). Chart 2, Entry 3.

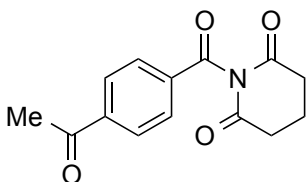
White solid. **GC:** $r_t = 13.95$ min. **^1H NMR (500 MHz, CDCl_3)** δ 7.87-7.82 (d, $J = 7.5$ Hz, 2 H), 6.99-6.94 (d, $J = 7.5$ Hz, 2 H), 3.90 (s, 3 H), 2.78 (t, $J = 6.6$ Hz, 4 H), 2.15 (p, $J = 6.6$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 171.88, 169.48, 165.09, 132.75, 124.51, 114.49, 55.69, 32.45, 17.52. **MS** = 247.1 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_4\text{Na}$ ($\text{M}^+ + \text{Na}$) 270.0737, found 270.0743.



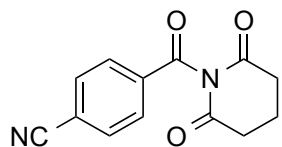
1-(4-(Trifluoromethyl)benzoyl)piperidine-2,6-dione (1j). Chart 2, Entry 4. White solid. **GC:** rt = 11.37 min. **¹H NMR (500 MHz, CDCl₃)** δ 8.00 (d, *J* = 8.1 Hz, 2 H), 7.79 (d, *J* = 8.0 Hz, 2 H), 2.83 (t, *J* = 6.5 Hz, 4 H), 2.20 (q, *J* = 6.6 Hz, 2 H). **¹³C NMR (125 MHz, CDCl₃)** δ 171.97, 170.17, 135.93 (q, *J*² = 36.7 Hz), 134.80, 130.36, 126.21 (q, *J*³ = 3.5 Hz), 123.27 (q, *J*¹ = 272.4 Hz). **¹⁹F NMR (471 MHz, CDCl₃)** δ -63.4. **MS** = 285.1 (EI). **HRMS** calcd for C₁₃H₁₀F₃NO₃Na (M⁺ + Na) 308.0505, found 308.0512.



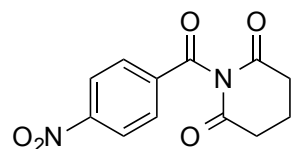
Methyl 4-(2,6-dioxopiperidine-1-carbonyl)benzoate (1k). Chart 2, Entry 5. White solid. **¹H NMR (500 MHz, CDCl₃)** δ 8.16 (d, *J* = 8.5 Hz, 2 H), 7.94 (d, *J* = 8.2 Hz, 2 H), 3.98 (s, 3 H), 2.81 (t, *J* = 6.5 Hz, 4 H), 2.18 (q, *J* = 6.5 Hz, 2 H). **¹³C NMR (125 MHz, CDCl₃)** δ 171.90, 170.38, 135.42, 130.21, 129.95, 129.58, 76.87, 52.64, 32.40, 17.47. **MS** = 275.1 (EI). **HRMS** calcd for C₁₄H₁₃NO₅Na (M⁺ + Na) 298.0686 found 298.0707



1-(4-Acetylbenzoyl)piperidine-2,6-dione (1l). Chart 2, Entry 6. White solid. **¹H NMR (500 MHz, CDCl₃)** δ 8.17-8.02 (d, *J* = 8.2 Hz, 2 H), 7.97 (d, *J* = 8.2 Hz, 2 H), 2.82 (t, *J* = 6.5 Hz, 4 H), 2.67 (s, 3 H), 2.19 (q, *J* = 6.5 Hz, 2 H). **¹³C NMR (125 MHz, CDCl₃)** δ 197.01, 171.88, 170.33, 141.40, 135.14, 130.27, 128.83, 32.40, 26.95, 17.47. **MS** = 259.1 (EI). **HRMS** calcd for C₁₄H₁₃NO₄Na (M⁺ + Na) 282.0737 found 282.0759.

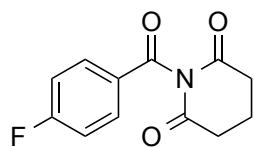


1-(4-Cyanobenzoyl)piperidine-2,6-dione (1m). Chart 2, Entry 7. White solid. **GC:** rt = 13.98 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.97 (d, *J* = 8.5 Hz, 2 H), 7.82 (d, *J* = 8.5 Hz, 2 H), 2.82 (t, *J* = 6.5 Hz, 4 H), 2.20 (p, *J* = 6.6 Hz, 2 H). **¹³C NMR (125 MHz, CDCl₃)** δ 171.89, 169.88, 135.23, 132.86, 130.30, 117.97, 117.48, 32.38, 17.43. **MS** = 242.1 (EI). **HRMS** calcd for C₁₃H₁₀N₂O₃Na (M⁺ + Na) 265.0584, found 265.0591.

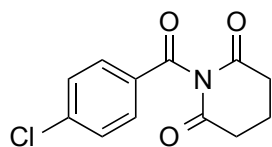


1-(4-Nitrobenzoyl)piperidine-2,6-dione (1n). Chart 2, Entry 8. Yellow solid. **GC:** rt = 14.90 min. **¹H NMR (500 MHz, CDCl₃)** δ 8.36

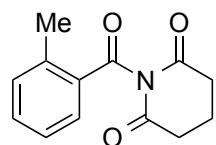
(d, $J = 7.5$ Hz, 2 H), 8.04 (d, $J = 7.5$ Hz, 2 H), 2.84 (t, $J = 6.5$ Hz, 4 H), 2.21 (p, $J = 6.6$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 171.91, 169.70, 151.20, 136.73, 131.00, 124.25, 32.39, 17.42. **MS** = 262.1 (EI). **HRMS** calcd for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_5\text{Na}$ ($\text{M}^+ + \text{Na}$) 285.0560, found 285.0558.



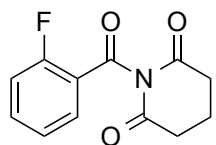
1-(4-Fluorobenzoyl)piperidine-2,6-dione (1o). Chart 2, Entry 9. White solid. **GC:** $r_t = 11.90$ min. **^1H NMR (500 MHz, CDCl_3)** δ 7.91 (dd, $J = 8.5, 5.2$ Hz, 2 H), 7.18 (t, $J = 8.4$ Hz, 2 H), 2.79 (t, $J = 6.5$ Hz, 4 H), 2.15 (p, $J = 6.5$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 171.94, 169.59, 166.84 (d, $J^l = 258.4$ Hz), 133.01 (d, $J^3 = 10.2$ Hz), 128.30 (d, $J^l = 2.7$ Hz), 116.52 (d, $J^2 = 22.1$ Hz), 32.37, 17.46. **^{19}F NMR (471 MHz, CDCl_3)** δ -101.31. **MS** = 235.1 (EI). **HRMS** calcd for $\text{C}_{12}\text{H}_{10}\text{FNO}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 258.0537, found 258.0547.



1-(4-Chlorobenzoyl)piperidine-2,6-dione (1p). Chart 2, Entry 10. White solid. **GC:** $r_t = 13.01$ min. **^1H NMR (500 MHz, CDCl_3)** δ 7.81 (d, $J = 8.5$ Hz, 2 H), 7.48 (d, $J = 8.5$ Hz, 2 H), 2.80 (t, $J = 6.5$ Hz, 4 H), 2.17 (p, $J = 6.6$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 171.91, 169.89, 141.68, 131.44, 130.31, 129.55, 32.40, 17.47. **MS** = 251.0 (EI). **HRMS** calcd for $\text{C}_{12}\text{H}_{11}\text{ClNO}_3$ ($\text{M}^+ + \text{H}$) 252.0422, found 252.0433.

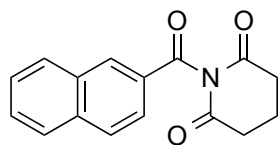


1-(2-Methylbenzoyl)piperidine-2,6-dione (1q). Chart 2, Entry 11. White solid. **GC:** $r_t = 12.26$ min. **^1H NMR (500 MHz, CDCl_3)** δ 7.54-7.46 (m, 2 H), 7.35 (d, $J = 7.6$ Hz, 1 H), 7.29-7.25 (m, 1 H), 2.77 (t, $J = 6.6$ Hz, 4 H), 2.70 (s, 3 H), 2.14 (p, $J = 6.6$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 171.98, 170.66, 142.53, 133.75, 132.44, 131.19, 130.70, 126.19, 32.48, 21.89, 17.45. **MS** = 231.1 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 254.0788, found 254.0793.

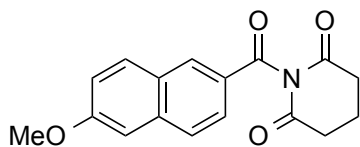


1-(2-Fluorobenzoyl)piperidine-2,6-dione (1r). Chart 2, Entry 12. White solid. **GC:** $r_t = 11.78$ min. **^1H NMR (500 MHz, CDCl_3)** δ 8.11 (td, $J = 7.8, 1.8$ Hz, 1 H), 7.63 (dddd, $J = 8.3, 7.1, 5.0, 1.8$ Hz, 1 H), 7.36-7.30 (m, 1 H), 7.13 (ddd, $J = 12.0, 8.4, 1.1$ Hz, 1 H), 2.76 (t, $J = 6.5$ Hz, 4 H), 2.13 (p, $J = 6.6$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 171.68, 166.86, 161.79 (d, $J^l = 255.9$ Hz), 136.79 (d, $J^3 = 10.0$ Hz),

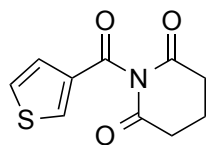
132.95, 125.09 (d, $J^d = 3.6$ Hz), 120.36 (d, $J^d = 7.0$ Hz), 117.08 (d, $J^d = 23.6$ Hz), 32.41, 17.24. **^{19}F NMR (471 MHz, CDCl_3)** δ -113.49. **MS** = 235.1 (EI). **HRMS** calcd for $\text{C}_{12}\text{H}_{10}\text{FNO}_3$ (M^+ + Na) 285.0537, found 285.0548.



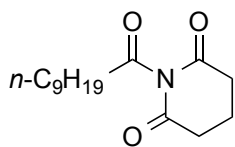
1-(2-Naphthoyl)piperidine-2,6-dione (1s). Chart 2, Entry 13. White solid. **GC:** rt = 17.28 min. **^1H NMR (500 MHz, CDCl_3)** δ 8.37 (s, 1 H), 7.99-7.93 (m, 3 H), 7.91 (d, $J = 8.2$ Hz, 1 H), 7.66 (ddd, $J = 8.2, 6.8, 1.3$ Hz, 1 H), 7.59 (ddd, $J = 8.1, 6.9, 1.3$ Hz, 1 H), 2.85 (t, $J = 6.5$ Hz, 4 H), 2.22 (p, $J = 6.6$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 172.02, 170.89, 136.42, 132.65, 132.45, 129.83, 129.51, 129.20, 127.91, 127.17, 124.75, 32.50, 17.57. **MS** = 267.1 (EI). **HRMS** calcd for $\text{C}_{16}\text{H}_{13}\text{NO}_3\text{Na}$ (M^+ + Na) 290.0788, found 290.0804.



1-(6-Methoxy-2-naphthoyl)piperidine-2,6-dione (1t). Chart 2, Entry 14. White solid. **GC:** rt = 18.48 min. **^1H NMR (500 MHz, CDCl_3)** δ 8.29 (d, $J = 2.7$ Hz, 1 H), 7.91 (d, $J = 8.5$ Hz, 1 H), 7.85 (d, $J = 8.8$ Hz, 1 H), 7.81 (d, $J = 8.7$ Hz, 1 H), 7.23 (d, $J = 8.7$ Hz, 1 H), 7.18 (d, $J = 2.7$ Hz, 1 H), 3.98 (t, $J = 2.4$ Hz, 3 H), 2.85 (tt, $J = 6.4, 2.5$ Hz, 4 H), 2.22 (qt, $J = 6.7, 3.7$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 171.98, 170.57, 160.60, 138.39, 132.53, 131.45, 127.81, 127.04, 125.64, 120.17, 105.89, 99.99, 55.50, 32.52, 17.59. **MS** = 297.1 (EI). **HRMS** calcd for $\text{C}_{17}\text{H}_{15}\text{NO}_4\text{Na}$ (M^+ + Na) 320.0893, found 320.0908.

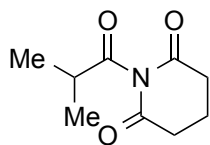


1-(Thiophene-3-carbonyl)piperidine-2,6-dione (1u). Chart 2, Entry 15. White solid. **GC:** rt = 12.21 min. **^1H NMR (500 MHz, CDCl_3)** δ 8.08 (d, $J = 2.8$ Hz, 1 H), 7.50 (d, $J = 5.2$ Hz, 1 H), 7.39 (dd, $J = 5.3, 2.9$ Hz, 1 H), 2.79 (t, $J = 6.6$ Hz, 4 H), 2.15 (p, $J = 6.6$ Hz, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 171.73, 164.49, 136.54, 136.39, 127.77, 127.43, 32.43, 17.50. **MS** = 223.0 (EI). **HRMS** calcd for $\text{C}_{10}\text{H}_9\text{NO}_3\text{SNa}$ (M^+ + Na) 246.0195, found 246.0170.



1-Decanoylpiperidine-2,6-dione (1v). Chart 2, Entry 16. White solid. **GC:** rt = 12.64 min. **^1H NMR (500 MHz, CDCl_3)** δ 3.12 (t, $J = 7.3$ Hz, 2 H), 2.69 (t, $J = 7.0$ Hz, 4 H), 2.04 (p, $J = 6.6$ Hz, 2 H), 1.72 (p, $J = 7.4$ Hz, 2 H),

1.44 (t, $J = 7.3$ Hz, 1 H), 1.41-1.22 (m, 11 H), 0.90 (t, $J = 6.8$ Hz, 3 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 178.20, 171.55, 45.78, 41.01, 32.26, 31.85, 29.37, 29.26, 28.62, 23.43, 22.67, 17.32, 14.12. **MS** = 267.1 (EI). **HRMS** calcd for $\text{C}_{15}\text{H}_{25}\text{NO}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 290.1727, found 290.1739.

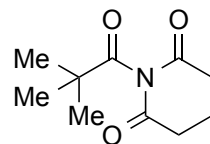


1-Isobutyrylpiperidine-2,6-dione (1w). Chart 2, Entry 17. White solid. **GC:**

rt = 10.50 min. **^1H NMR (500 MHz, CDCl_3)** δ 2.92 (hept, $J = 7.0$ Hz, 1 H), 2.69 (t, $J = 6.5$ Hz, 4 H), 2.05 (p, $J = 6.5$ Hz, 2 H), 1.25 (d, $J = 7.1$ Hz, 6 H).

^{13}C NMR (125 MHz, CDCl_3) δ 181.85, 171.78, 39.77, 32.36, 17.81, 17.38. **MS** = 183.1 (EI).

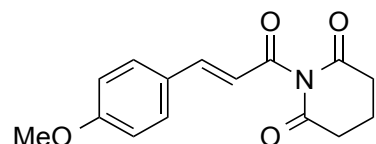
HRMS calcd for $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_6\text{Na}$ ($2\text{M}^+ + \text{Na}$) 389.1683, found 389.1709.



1-Pivaloylpiperidine-2,6-dione (1x). Chart 2, Entry 18. White solid. **GC:**

rt = 9.25 min. **^1H NMR (500 MHz, CDCl_3)** δ 2.67 (t, $J = 6.5$ Hz, 4 H), 2.05 (p, $J = 6.5$ Hz, 2 H), 1.28 (s, 9 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 185.57,

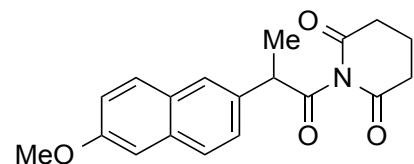
171.86, 43.75, 32.17, 27.14, 17.44. **MS** = 197.1 (EI). **HRMS** calcd for $\text{C}_{10}\text{H}_{15}\text{NO}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 220.0944, found 220.0952.



(E)-1-(3-(4-Methoxyphenyl)acryloyl) piperidine-2,6-dione

(1y). Chart 2, Entry 19. White solid. **GC:** rt = 23.45 min. **^1H**

NMR (500 MHz, CDCl_3) δ 7.65 (d, $J = 15.8$ Hz, 1 H), 7.53 (d, $J = 8.4$ Hz, 2 H), 6.93 (d, $J = 8.3$ Hz, 2 H), 6.58 (d, $J = 15.7$ Hz, 1 H), 3.88 (s, 3 H), 2.76 (t, $J = 6.6$ Hz, 4 H), 2.10 (m, 2 H). **^{13}C NMR (500 MHz, CDCl_3)** δ 171.74, 169.26, 162.52, 148.54, 130.93, 126.35, 118.76, 114.51, 55.47, 32.54, 17.40. **MS** = 273.1 (EI). **HRMS** calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_4\text{Na}$ ($\text{M}^+ + \text{Na}$) 296.0893, found 296.0921.



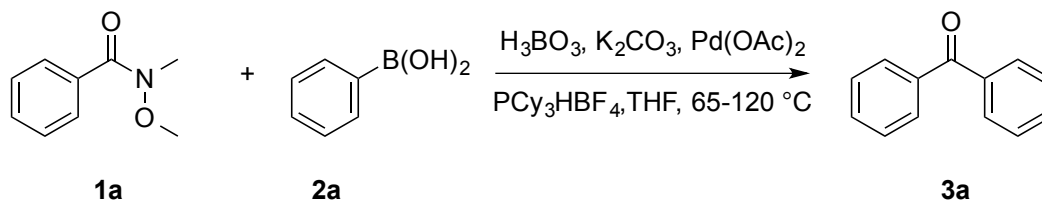
1-(2-(6-Methoxynaphthalen-2-yl)propanoyl) piperidine-

2,6-dione (1z). Chart 2, Entry 20. Yellow solid. **GC:** rt =

12.16 min. **^1H NMR (500 MHz, CDCl_3)** δ 7.72 (dd, $J = 8.7$, 3.0 Hz, 2 H), 7.63 (d, $J = 1.8$ Hz, 1 H), 7.34 (dd, $J = 8.5$, 1.8 Hz, 1 H), 7.17 (dd, $J = 8.9$, 2.5 Hz, 1 H), 7.13 (d, $J = 2.5$ Hz, 1 H), 4.29 (q, $J = 7.1$ Hz, 1 H), 3.94 (s, 3 H), 2.39 (t, $J = 6.5$ Hz, 4 H), 1.70 (d, $J = 7.0$ Hz, 3 H), 1.64-1.71 (m, 2 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 178.72, 171.24, 157.87, 133.99, 133.26, 129.30, 128.73, 127.34, 127.10, 126.66,

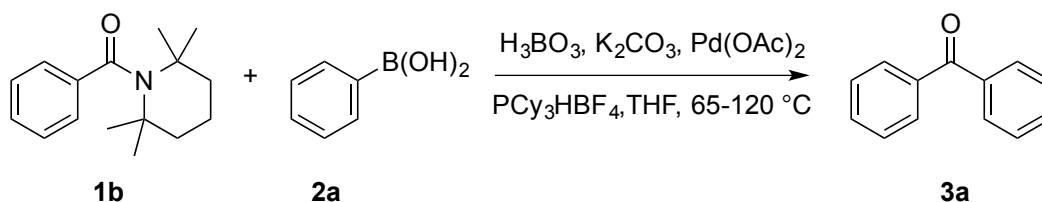
119.20, 105.62, 55.33, 50.56, 32.15, 17.23, 16.98. **MS** = 325.1 (EI). **HRMS** calcd for $C_{19}H_{19}NO_4Na$ ($M^+ + Na$) 348.1206, found 348.1232.

Suzuki-Miyaura Cross-Coupling with Amides: Twist Optimization

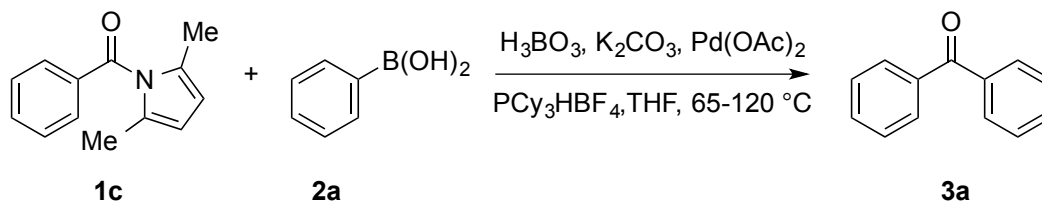
N-Methoxy-*N*-methylbenzamide (Table 1, Entry 1)

According to the general procedure, *N*-methoxy-*N*-methylbenzamide (0.20 mmol) was reacted with phenylboronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) in THF (0.80 mL) for 15 h at 65-120 °C. After the standard work-up as described above, the sample was analyzed by ¹H NMR and GC-MS to obtain conversion and yield using internal standard: conversion <5%; yield of the recovered starting material: >95%, indicating that under these conditions chemoselective coupling of amides (**1d**) in the presence of Weinreb amides can be readily achieved.

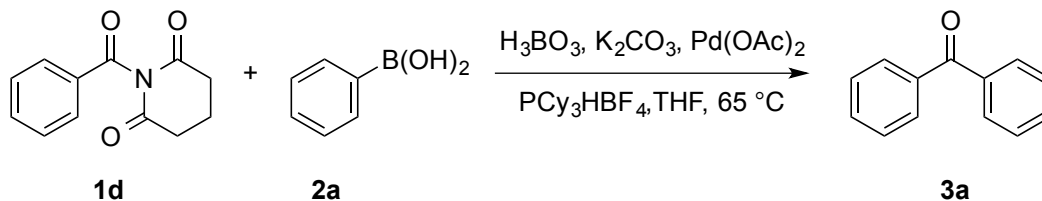
Phenyl(2,2,6,6-tetramethylpiperidin-1-yl)methanone (Table 1, Entry 2)



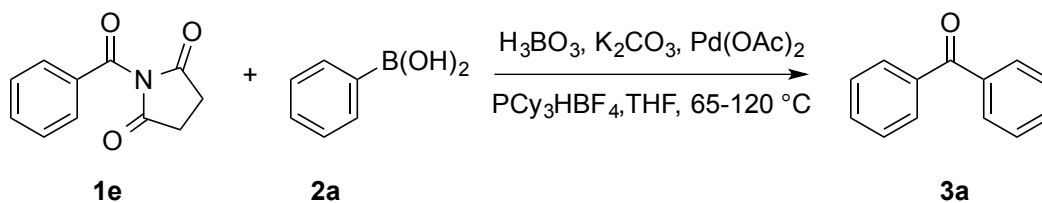
According to the general procedure, phenyl(2,2,6,6-tetramethylpiperidin-1-yl)methanone (0.20 mmol) was reacted with phenylboronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) in THF (0.80 mL) for 15 h at 65-120 °C. After the standard work-up as described above, the sample was analyzed by ¹H NMR and GC-MS to obtain conversion and yield using internal standard: conversion *ca.* 10%; yield of **3a** 9.2%, indicating for the first time that tmp amides (tmp = 2,2,6,6-tetramethylpiperidine) undergo metal-catalyzed cross-coupling to afford a ketone product. At this stage, further optimization of the cross-coupling was not performed.

(2,5-Dimethyl-1H-pyrrol-1-yl)(phenyl)methanone (Table 1, Entry 3)

According to the general procedure, (2,5-dimethyl-1H-pyrrol-1-yl)(phenyl)methanone (0.20 mmol) was reacted with phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) in THF (0.80 mL) for 15 h at 65-120 °C. After the standard work-up as described above, the sample was analyzed by ^1H NMR and GC-MS to obtain conversion and yield using internal standard: conversion *ca.* 25%; yield of **3a** <5.0%. At this stage, further optimization of the cross-coupling was not performed.

1-Benzoylpiperidine-2,6-dione (Table 1, Entry 4)

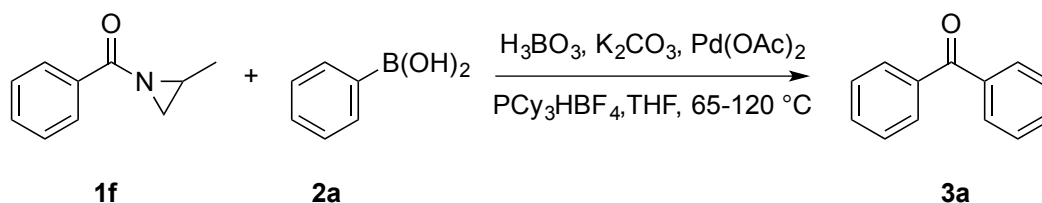
According to the general procedure, 1-benzoylpiperidine-2,6-dione (0.20 mmol) was reacted with phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) in THF (0.80 mL) for 15 h at 65 °C. After the standard work-up as described above, the sample was analyzed by ^1H NMR and GC-MS to obtain conversion and yield using internal standard: conversion >98%; yield of **3a** >98%, indicating high reactivity of the title amide in the cross-coupling under these conditions.

1-Benzoylpyrrolidine-2,5-dione (Table 1, Entry 5)

According to the general procedure, 1-benzoylpyrrolidine-2,5-dione (0.20 mmol) was reacted with phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03

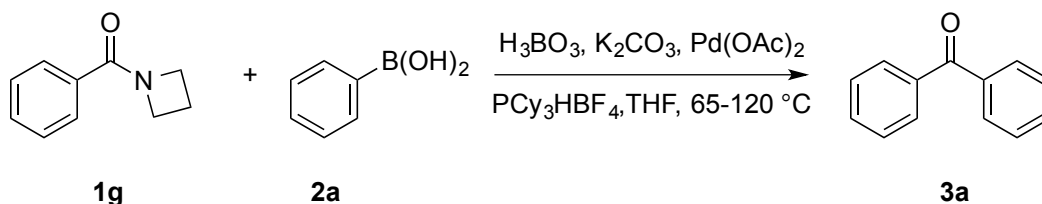
equiv) and PCy_3HBF_4 (0.12 equiv) in THF (0.80 mL) for 15 h at 65-120 °C. After the standard work-up as described above, the sample was analyzed by ^1H NMR and GC-MS to obtain conversion and yield using internal standard: conversion *ca.* 55%; yield of **3a** 54.1%. At this stage, further optimization of the cross-coupling was not performed.

(2-Methylaziridin-1-yl)(phenyl)methanone (Table 1, Entry 6)



According to the general procedure, (2-methylaziridin-1-yl)(phenyl)methanone (0.20 mmol) was reacted with phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) in THF (0.80 mL) for 15 h at 65-120 °C. After the standard work-up as described above, the sample was analyzed by ^1H NMR and GC-MS to obtain conversion and yield using internal standard: conversion <5.0%; yield of **3a** <5.0%. At this stage, further optimization of the cross-coupling was not performed.

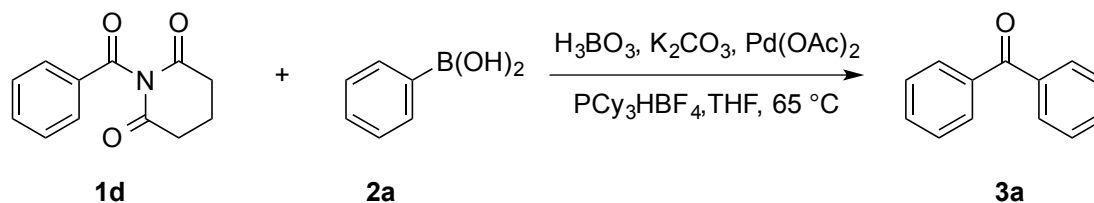
Azetidin-1-yl(phenyl)methanone (Table 1, Entry 7)



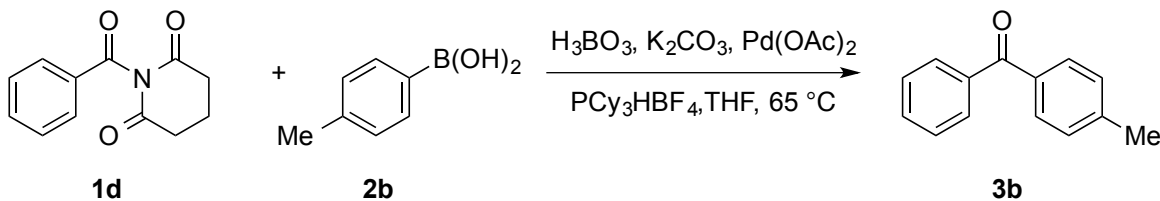
According to the general procedure, azetidin-1-yl(phenyl)methanone (0.20 mmol) was reacted with phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) in THF (0.80 mL) for 15 h at 65-120 °C. After the standard work-up as described above, the sample was analyzed by ^1H NMR and GC-MS to obtain conversion and yield using internal standard: conversion <5.0%; yield of **3a** <5.0%. At this stage, further optimization of the cross-coupling was not performed.

Suzuki-Miyaura Cross-Coupling of Amides: Variation of Boronic Acid

Phenylboronic acid (Chart 1, Entry 1)

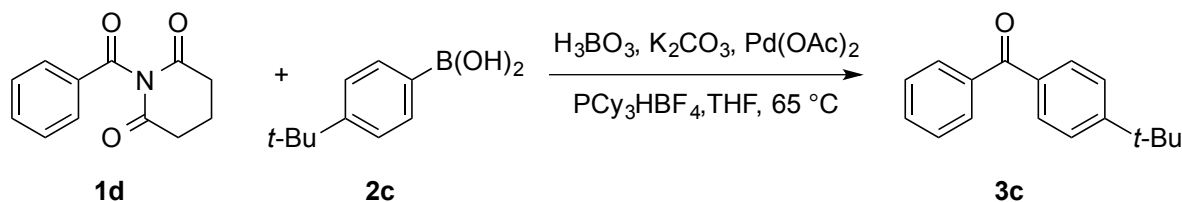


According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at $65\text{ }^\circ\text{C}$, afforded after work-up and chromatography the title compound in 95.3% yield (34.7 mg). White solid. **GC**: $\text{rt} = 9.80$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.84 (dd, $J = 8.5, 1.5$ Hz, 4 H), 7.62 (tt, $J = 7.5, 1.5$ Hz, 2 H), 7.51 (t, $J = 7.7$ Hz, 4 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.74, 137.62, 132.41, 130.06, 128.31. **MS** = 182.1 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_{10}\text{ONa}$ ($\text{M}^+ + \text{Na}$) 205.0624 found 205.0631.

p-Tolylboronic acid (Chart 1, Entry 2)

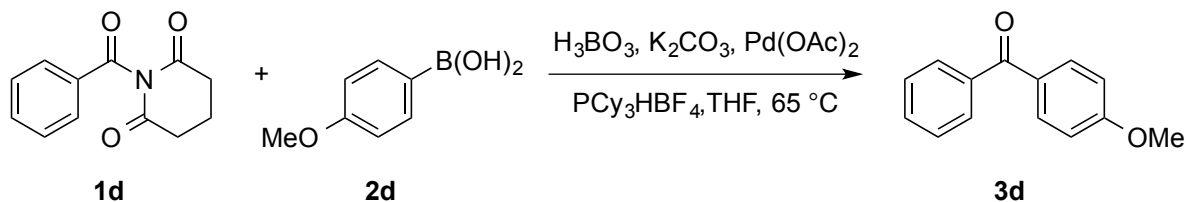
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), *p*-tolylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at $65\text{ }^\circ\text{C}$, afforded after work-up and chromatography the title compound in 71.4% yield (27.7 mg). White solid. **GC**: $\text{rt} = 11.01$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.82 (d, $J = 7.5$ Hz, 2 H), 7.75 (d, $J = 7.9$ Hz, 2 H), 7.60 (t, $J = 7.5$ Hz, 1 H), 7.50 (t, $J = 7.6$ Hz, 2 H), 7.31 (d, $J = 7.9$ Hz, 2 H), 2.47 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.50, 143.23, 137.98, 134.90, 132.15, 130.31, 129.93, 128.98, 128.21, 21.67. **MS** = 196.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_{12}\text{ONa}$ ($\text{M}^+ + \text{Na}$) 219.0780 found 219.0786.

(4-(*tert*-Butyl)phenyl)boronic acid (Chart 1, Entry 3)



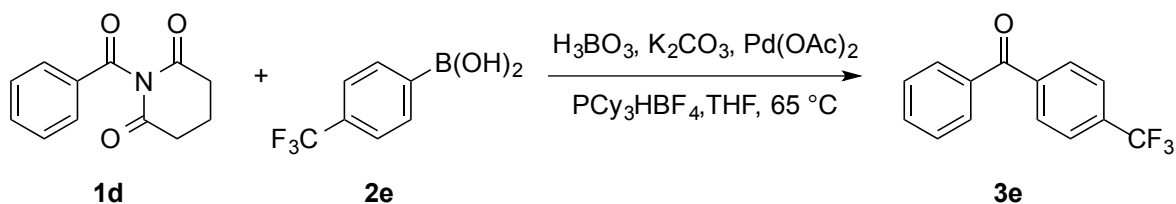
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (4-*tert*-butylphenyl)boronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 82.0% yield (38.7 mg). Oil. **GC**: rt = 19.50 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.84 (d, *J* = 8.0 Hz, 2H), 7.80 (d, *J* = 8.8 Hz, 2 H), 7.60 (t, *J* = 7.0 Hz, 1H), 7.55-7.48 (m, 4 H), 1.40 (s, 9 H). **¹³C NMR (125 MHz, CDCl₃)** δ 196.46, 156.19, 137.96, 134.83, 132.17, 130.14, 129.97, 128.21, 125.25, 35.13, 31.17. **MS** = 238.1 (EI). **HRMS** calcd for C₁₇H₁₈ONa (M⁺ + Na) 261.1250 found 261.1269.

(4-Methoxyphenyl)boronic acid (Chart 1, Entry 4)



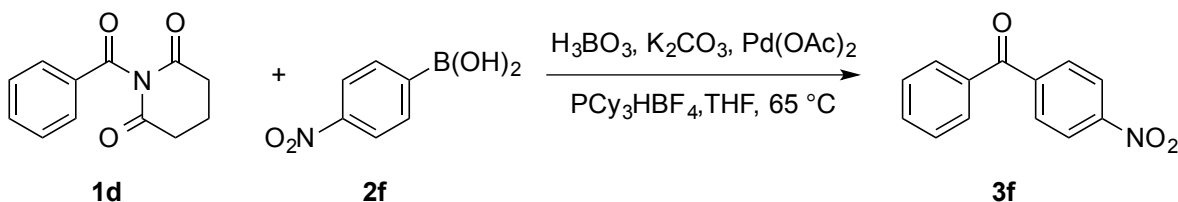
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (4-methoxyphenyl)boronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 81.0% yield (34.4 mg). White solid. **GC**: rt = 12.11 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.86 (d, *J* = 8.0 Hz, 2 H), 7.78 (d, *J* = 7.6 Hz, 2 H), 7.59 (t, *J* = 7.5 Hz, 1 H), 7.50 (t, *J* = 7.5 Hz, 2 H), 6.99 (d, *J* = 7.5 Hz, 2 H), 3.92 (s, 3 H). **¹³C NMR (125 MHz, CDCl₃)** δ 195.56, 163.23, 138.30, 132.57, 131.89, 130.17, 129.74, 128.19, 113.56, 55.51. **MS** = 212.1 (EI). **HRMS** calcd for C₁₄H₁₃O₂ (M⁺ + H) 213.0910 found 213.0917.

(4-(Trifluoromethyl)phenyl)boronic acid (Chart 1, Entry 5)



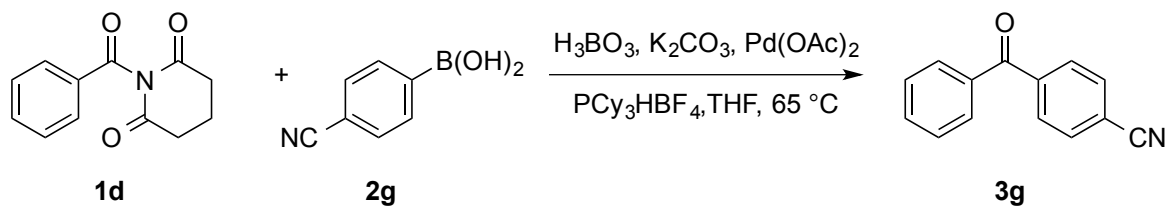
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (4-(trifluoromethyl)phenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65°C , afforded after work-up and chromatography the title compound in 61.1% yield (30.6 mg). White solid. **GC**: $\text{rt} = 9.83$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.93 (d, $J = 8.0$ Hz, 2 H), 7.84 (d, $J = 7.7$ Hz, 2 H), 7.79 (d, $J = 8.0$ Hz, 2 H), 7.66 (t, $J = 7.4$ Hz, 1 H), 7.54 (t, $J = 7.6$ Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 195.53, 140.74, 136.74, 133.46 (q, $J^2 = 32.0$ Hz), 133.09, 130.14, 130.11, 128.54, 125.36 (q, $J^3 = 3.5$ Hz), 123.68 (q, $J^1 = 271.5$ Hz). **$^{19}\text{F NMR}$ (471 MHz, CDCl_3)** δ -63.0. **MS** = 250.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_9\text{F}_3\text{ONa}$ ($\text{M}^+ + \text{Na}$) 273.0498 found 273.0510.

(4-Nitrophenyl)boronic acid (Chart 1, Entry 6)



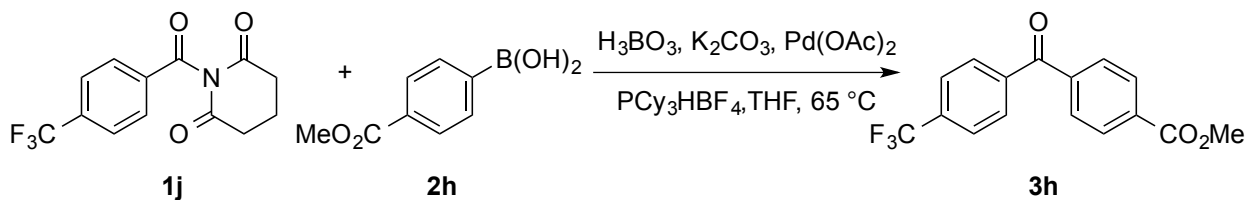
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (4-nitrophenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65°C , afforded after work-up and chromatography the title compound in 82.2% yield (37.3 mg). White solid. **GC**: $\text{rt} = 12.44$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.37 (d, $J = 9.0$ Hz, 2 H), 7.97 (d, $J = 9.0$ Hz, 2 H), 7.82 (dd, $J = 7.5, 1.0$ Hz, 2 H), 7.68 (tt, $J = 7.5, 1.5$ Hz, 1 H), 7.56 (t, $J = 7.8$ Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 194.80, 149.82, 142.90, 136.30, 133.48, 130.71, 130.11, 128.70, 123.56. **MS** = 227.1 (EI). **HRMS** calcd for $\text{C}_{26}\text{H}_{18}\text{N}_2\text{O}_6\text{Na}$ ($2\text{M}^+ + \text{Na}$) 477.1057 found 477.1083.

(4-Cyanophenyl)boronic acid (Chart 1, Entry 7)



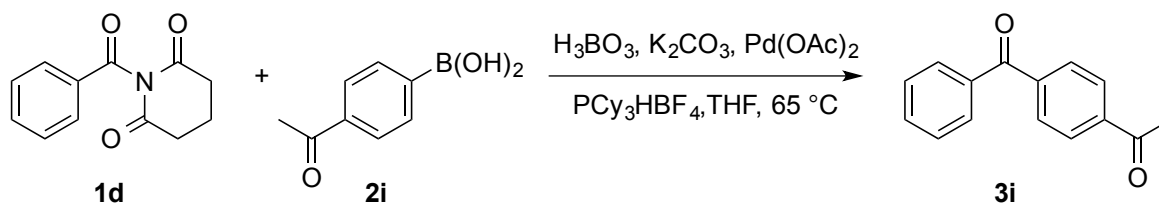
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (4-cyanophenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 41.7% yield (17.1 mg). White solid. **GC:** $t_r = 13.51$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.91 (d, $J = 7.9$ Hz, 2 H), 7.82 (dd, $J = 7.9, 4.3$ Hz, 4 H), 7.67 (t, $J = 7.5$ Hz, 1 H), 7.55 (t, $J = 7.6$ Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 195.04, 141.26, 136.36, 133.34, 132.18, 130.25, 130.08, 128.65, 118.02, 115.70. **MS** = 207.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_9\text{NONa}$ ($\text{M}^+ + \text{Na}$) 230.0576 found 230.0571.

(4-(methoxycarbonyl)phenyl)boronic acid (Chart 1, Entry 8)



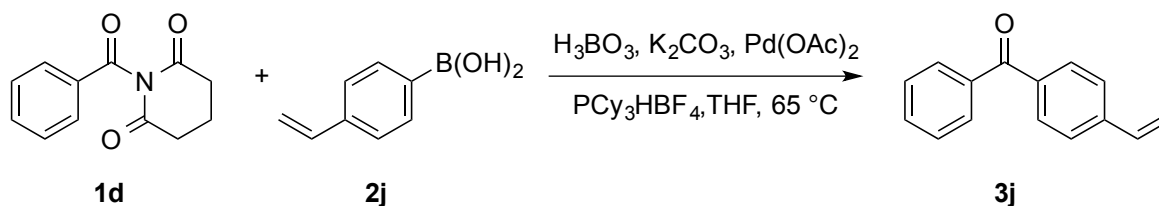
According to the general procedure, the reaction of 1-(4-(trifluoromethyl)benzoyl)piperidine-2,6-dione (0.20 mmol), (4-(methoxycarbonyl)phenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 62.1% yield (38.3 mg). White solid. **GC:** $t_r = 12.39$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.19 (d, $J = 9.0$ Hz, 2 H), 7.93 (d, $J = 8.1$ Hz, 2 H), 7.86 (d, $J = 8.0$ Hz, 2 H), 7.80 (d, $J = 8.1$ Hz, 2 H), 4.00 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 195.31, 163.25, 159.50, 139.62, 132.57, 130.17, 129.13, 122.42, 118.26, 114.19, 113.55, 55.46. **$^{19}\text{F NMR}$ (471 MHz, CDCl_3)** δ -63.1. **MS** = 308.1 (EI). **HRMS** calcd for $\text{C}_{16}\text{H}_{11}\text{F}_3\text{O}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 331.0552 found 331.0561.

(4-Acetylphenyl)boronic acid (Chart 1, Entry 9)



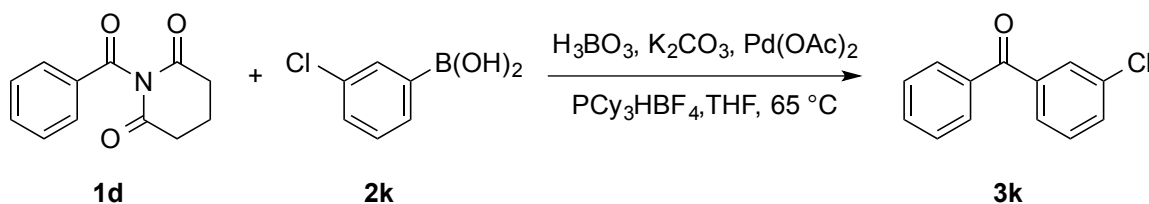
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (4-acetylphenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at $65\text{ }^\circ\text{C}$, afforded after work-up and chromatography the title compound in 80.6% yield (36.2 mg). White solid. **GC**: $rt = 13.54$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.09 (d, $J = 8.2$ Hz, 2 H), 7.89 (d, $J = 8.3$ Hz, 2 H), 7.83 (d, $J = 7.5$ Hz, 2 H), 7.65 (t, $J = 6.5$ Hz, 1 H), 7.53 (t, $J = 7.7$ Hz, 2 H), 2.70 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 197.52, 195.96, 141.34, 139.57, 136.92, 133.00, 130.11, 130.05, 128.49, 128.17, 26.92. **MS** = 224.1 (EI). **HRMS** calcd for $\text{C}_{15}\text{H}_{12}\text{O}_2\text{Na}$ ($\text{M}^+ + \text{Na}$) 247.0730 found 247.0741.

(4-Vinylphenyl)boronic acid (Chart 1, Entry 10)



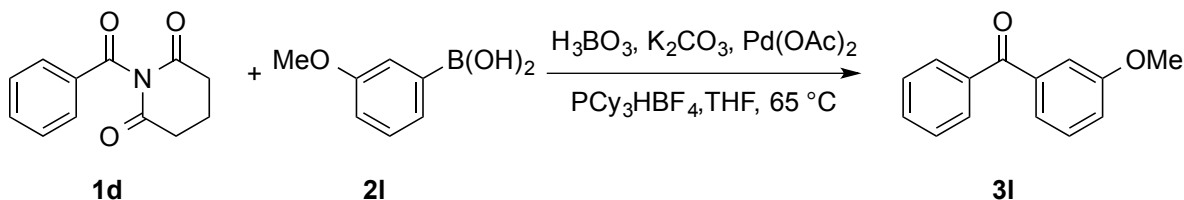
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (4-vinylphenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at $65\text{ }^\circ\text{C}$, afforded after work-up and chromatography the title compound in 78.9% yield (32.5 mg). Oil. **GC**: $rt = 13.25$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.82 (dd, $J = 8.0, 3.3$ Hz, 4 H), 7.62 (t, $J = 7.5$ Hz, 1 H), 7.57-7.48 (m, 4 H), 6.81 (dd, $J = 17.6, 10.9$ Hz, 1H), 5.92 (d, $J = 17.6$ Hz, 1 H), 5.44 (d, $J = 10.9$ Hz, 1 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.20, 141.56, 137.77, 136.68, 136.01, 132.33, 130.55, 129.95, 128.28, 126.05, 116.61. **MS** = 208.1 (EI). **HRMS** calcd for $\text{C}_{15}\text{H}_{12}\text{ONa}$ ($\text{M}^+ + \text{Na}$) 231.0780 found 231.0807.

(3-Chlorophenyl)boronic acid (Chart 1, Entry 11)



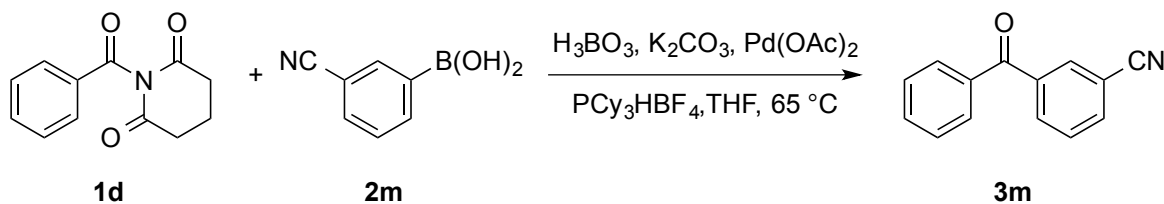
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (3-chlorophenyl)boronic acid (1.0 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 7 h at 65 °C, afforded after work-up and chromatography the title compound in 69.1% yield (29.9 mg). White solid. **GC:** $rt = 11.29$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.84-7.80 (m, 3 H), 7.70 (dt, $J = 7.7, 1.3$ Hz, 1 H), 7.64 (t, $J = 7.5$ Hz, 1 H), 7.59 (dd, $J = 8.5, 1.5$ Hz, 1 H), 7.53 (t, $J = 7.7$ Hz, 2 H), 7.46 (t, $J = 7.9$ Hz, 1 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 195.27, 139.27, 136.96, 134.58, 132.84, 132.36, 130.03, 129.91, 129.64, 128.47, 128.11. **MS** = 216.0 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_9\text{ClONa}$ ($\text{M}^+ + \text{Na}$) 239.0234 found 239.0243.

(3-Methoxyphenyl)boronic acid (Chart 1, Entry 12)



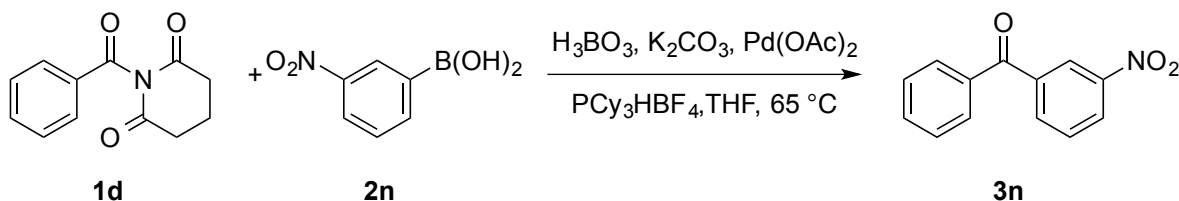
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (3-methoxyphenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 86.1% yield (36.5 mg). White solid. **GC:** $rt = 12.25$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.83 (d, $J = 7.5$ Hz, 2 H), 7.61 (t, $J = 7.4$ Hz, 1 H), 7.51 (t, $J = 7.6$ Hz, 2 H), 7.39 (m, 3 H), 7.16 (d, $J = 9.0$ Hz 1 H), 3.89 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.51, 159.58, 138.92, 137.63, 132.42, 130.04, 129.22, 128.26, 122.87, 118.86, 114.34, 55.48. **MS** = 212.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_{13}\text{O}_2$ ($\text{M}^+ + \text{H}$) 213.0910 found 213.0933.

(3-Cyanophenyl)boronic acid (Chart 1, Entry 13)



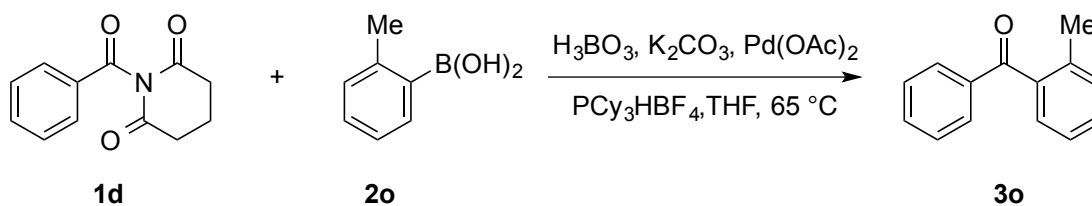
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (3-cyanophenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 70.8% yield (29.3 mg). White solid. **GC:** rt = 12.25 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.10 (s, 1 H), 8.06 (d, $J = 8.0$ Hz, 1 H), 7.90 (dt, $J = 7.7, 1.4$ Hz, 1 H), 7.81 (dd, $J = 8.2, 1.4$ Hz, 2 H), 7.67 (q, $J = 7.7$ Hz, 2 H), 7.55 (t, $J = 7.6$ Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 194.40, 138.63, 136.33, 135.35, 133.84, 133.47, 133.29, 130.00, 129.41, 128.69, 117.95, 112.86. **MS** = 207.1 (EI). **HRMS** calcd for $\text{C}_{28}\text{H}_{18}\text{N}_2\text{O}_2\text{Na}$ ($2\text{ M}^+ + \text{Na}$) 437.1260 found 437.1295.

(3-Nitrophenyl)boronic acid (Chart 1, Entry 14)



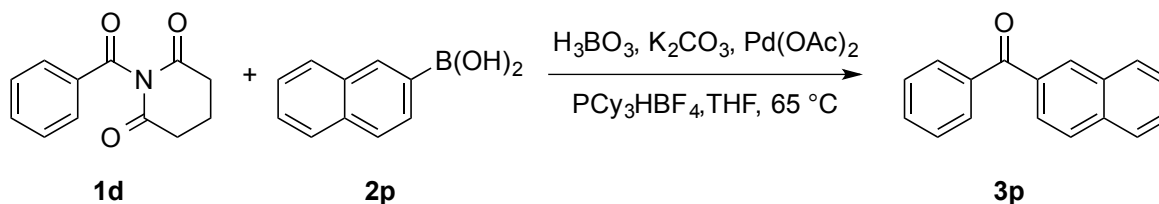
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (3-nitrophenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 68.5% yield (31.1 mg). Yellow solid. **GC:** rt = 12.38 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.65 (s, 1 H), 8.48 (d, $J = 10.0$ Hz, 1 H), 8.17 (d, $J = 7.7$ Hz, 1 H), 7.83 (d, $J = 7.7$ Hz, 2 H), 7.74 (t, $J = 8.0$ Hz, 1 H), 7.69 (t, $J = 7.5$ Hz, 1 H), 7.57 (t, $J = 7.7$ Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 194.17, 148.11, 139.09, 136.28, 135.44, 133.37, 130.02, 129.64, 128.75, 126.73, 124.73. **MS** = 227.1 (EI). **HRMS** calcd for $\text{C}_{26}\text{H}_{18}\text{N}_2\text{O}_6\text{Na}$ ($2\text{ M}^+ + \text{Na}$) 477.1057 found 477.1076.

o-Tolylboronic acid (Chart 1, Entry 15)



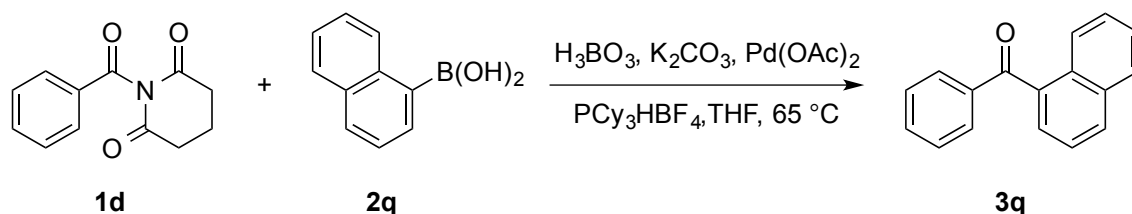
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), *o*-tolylboronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in >98.0% yield (39.0 mg). Oil. **GC**: rt = 9.95 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.84 (d, *J* = 8.5 Hz, 2 H), 7.61 (t, *J* = 6.5 Hz, 1 H), 7.49 (t, *J* = 7.0 Hz, 2 H), 7.42 (t, *J* = 7.5 Hz, 1 H), 7.33 (m, 2 H), 7.29 (m, 1 H), 2.35 (s, 3 H). **¹³C NMR (125 MHz, CDCl₃)** δ 198.64, 138.63, 137.75, 136.75, 133.14, 131.00, 130.24, 130.14, 128.52, 128.46, 125.20, 20.00. **MS** = 196.1 (EI). **HRMS** calcd for C₁₄H₁₂ONa (M⁺ + Na) 219.0780 found 219.0782.

Naphthalen-2-ylboronic acid (Chart 1, Entry 16)



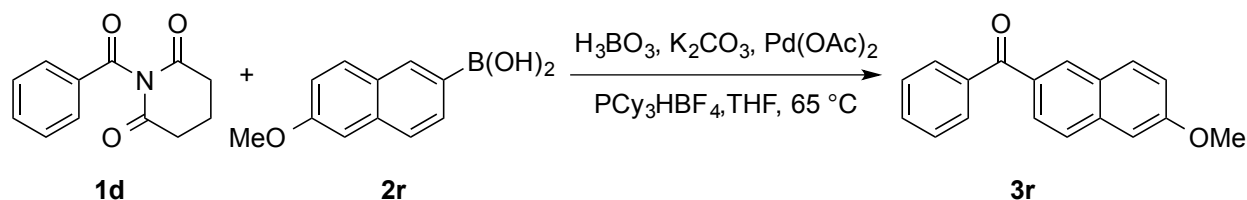
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), naphthalen-2-ylboronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 76.1% yield (35.3 mg). White solid. **GC**: rt = 12.93 min. **¹H NMR (500 MHz, CDCl₃)** δ 8.30 (s, 1 H), 7.98 (s, 2 H), 7.95 (dd, *J* = 8.0, 2.0 Hz, 1 H), 7.90 (d, *J* = 7.0 Hz, 1 H), 7.92-7.87 (m, 2 H), 7.65 (td, *J* = 7.7, 4.5 Hz, 2 H), 7.57 (dt, *J* = 18.3, 7.7 Hz, 3 H). **¹³C NMR (125 MHz, CDCl₃)** δ 196.76, 137.92, 135.28, 134.84, 132.39, 132.27, 131.88, 130.11, 129.43, 128.35, 128.34, 128.31, 127.84, 126.81, 125.80. **MS** = 232.1 (EI). **HRMS** calcd for C₁₇H₁₂ONa (M⁺ + Na) 255.0780 found 255.0790.

Naphthalen-1-ylboronic acid (Chart 1, Entry 17)



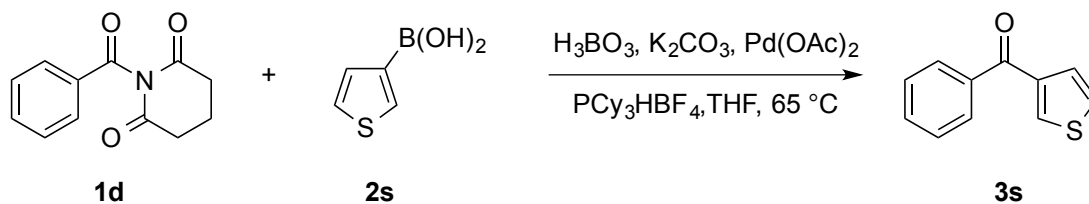
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), (naphthalen-1-ylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 93.2% yield (43.3 mg). Oil. **GC:** rt = 12.61 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.13 (d, $J = 8.2$ Hz, 1 H), 8.04 (d, $J = 8.2$ Hz, 1 H), 7.96 (dd, $J = 7.8, 1.7$ Hz, 1 H), 7.91-7.88 (d, $J = 7.0$ Hz, 2 H), 7.65-7.59 (m, 2 H), 7.59-7.51 (m, 3 H), 7.49 (t, $J = 7.7$ Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 198.03, 138.33, 136.37, 133.73, 133.23, 131.27, 130.97, 130.42, 128.46, 128.41, 127.77, 127.26, 126.47, 125.71, 124.34. **MS** = 232.1 (EI). **HRMS** calcd for $\text{C}_{17}\text{H}_{12}\text{ONa}$ ($\text{M}^+ + \text{Na}$) 255.0780 found 255.0790.

6-Methoxy-naphthalen-2-ylboronic acid (Chart 1, Entry 16)



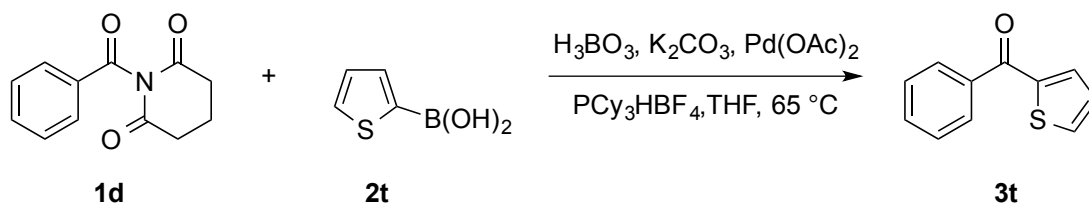
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (10 mmol), 6-methoxy-naphthalen-2-ylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 80.6% yield (2.11 g). White solid. **GC:** rt = 12.97 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.24 (d, $J = 1.7$ Hz, 1 H), 7.97 (dd, $J = 8.6, 1.7$ Hz, 1 H), 7.90-7.82 (m, 4 H), 7.67-7.61 (m, 1 H), 7.54 (dd, $J = 8.4, 7.0$ Hz, 2 H), 7.26-7.20 (m, 2 H), 3.99 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.59, 159.70, 138.22, 137.02, 132.70, 132.13, 132.00, 131.04, 129.99, 128.30, 127.61, 127.02, 126.57, 119.74, 105.77, 55.46. **MS** = 262.1 (EI). **HRMS** calcd for $\text{C}_{18}\text{H}_{14}\text{O}_2\text{Na}$ ($\text{M}^+ + \text{Na}$) 285.0886, found 285.0900.

3-Thienylboronic acid (Chart 1, Entry 19)



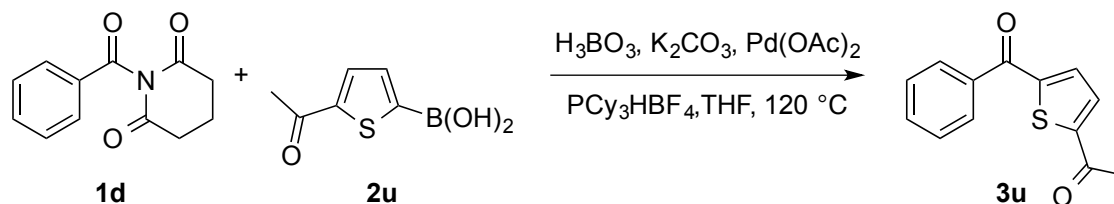
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), thiophen-3-ylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 73.5% yield (27.7 mg). Oil. **GC:** $r_t = 11.08$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.96 (dd, $J = 2.8, 1.2$ Hz, 1 H), 7.88 (dd, $J = 8.0, 1.5$ Hz, 2 H), 7.66-7.58 (m, 2 H), 7.52 (t, $J = 7.6$ Hz, 2 H), 7.41 (dd, $J = 5.1, 2.9$ Hz, 1 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 190.01, 141.31, 138.64, 133.92, 132.31, 129.38, 128.62, 128.39, 126.21. **MS** = 188.0 (EI). **HRMS** calcd for $\text{C}_{22}\text{H}_{16}\text{O}_2\text{S}_2\text{Na}$ ($2\text{ M}^+ + \text{Na}$) 399.0484 found 399.0498.

2-Thienylboronic acid (Chart 1, Entry 20)



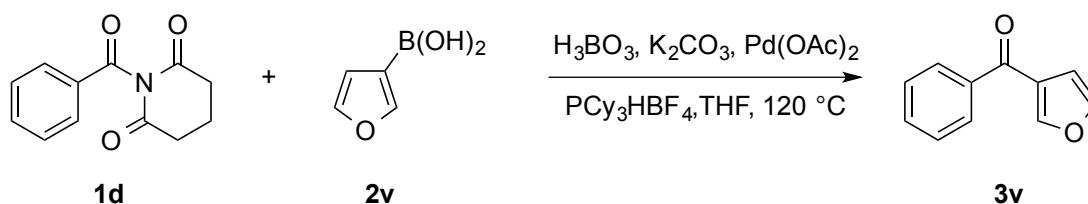
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), thiophen-2-ylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 60 °C, afforded after work-up and chromatography the title compound in 54.1% yield (20.4 mg). Oil. **GC:** $r_t = 11.08$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.92-7.87 (m, 2 H), 7.75 (d, $J = 4.9$ Hz, 1 H), 7.68 (d, $J = 3.8$ Hz, 1 H), 7.62 (t, $J = 7.5$ Hz, 1 H), 7.53 (t, $J = 7.6$ Hz, 2 H), 7.20 (t, $J = 4.3$ Hz, 1 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 188.24, 143.66, 138.17, 134.85, 134.21, 132.27, 129.18, 128.42, 127.96. **MS** = 188.0 (EI). **HRMS** calcd for $\text{C}_{22}\text{H}_{16}\text{O}_2\text{S}_2\text{Na}$ ($2\text{ M}^+ + \text{Na}$) 399.0484 found 399.0497.

5-Acetyl-2-Thienylboronic acid (Chart 1, Entry 21)



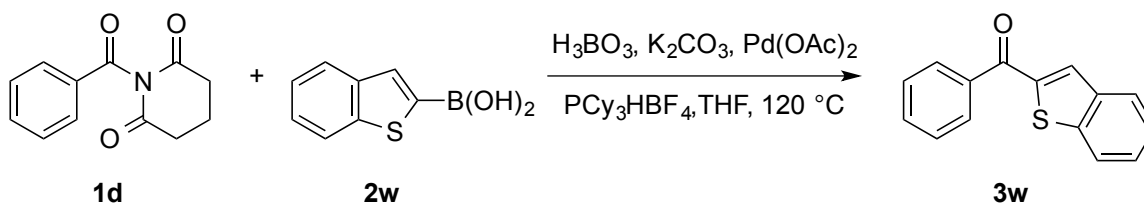
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), 1-(5-borinothiophen-2-yl)ethan-1-one (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 81.1% yield (37.4 mg). Oil. **GC:** $t_r = 13.03$ min. **^1H NMR (500 MHz, CDCl_3)** δ 7.93-7.89 (m, 2 H), 7.73 (d, $J = 4.0$ Hz, 1 H), 7.69-7.63 (m, 2 H), 7.55 (t, $J = 7.7$ Hz, 2 H), 2.65 (d, $J = 1.1$ Hz, 3 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 190.84, 188.09, 149.30, 148.32, 137.25, 134.12, 132.97, 131.64, 129.34, 128.63, 27.24. **MS** = 230.0 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_{10}\text{O}_2\text{SNa}$ ($\text{M}^+ + \text{Na}$) 253.0294 found 253.0296.

Furan-3-ylboronic acid (Chart 1, Entry 22)



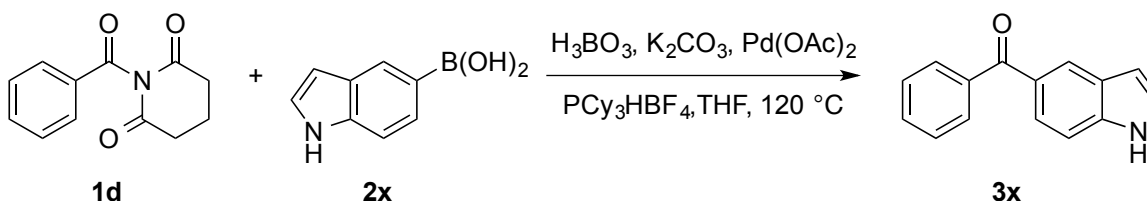
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), furan-3-ylboronic acid (2.0 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 90.1% yield (31.0 mg). Oil. **GC:** $t_r = 8.86$ min. **^1H NMR (500 MHz, CDCl_3)** δ 7.95 (d, $J = 1.3$ Hz, 1 H), 7.88 (d, $J = 7.0$ Hz, 2 H), 7.62 (t, $J = 7.0$ Hz, 1 H), 7.56-7.49 (m, 3 H), 6.94 (d, $J = 1.8$ Hz, 1 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 189.44, 148.57, 143.96, 138.83, 132.48, 128.83, 128.56, 126.53, 110.23. **MS** = 172.1 (EI). **HRMS** calcd for $\text{C}_{22}\text{H}_{16}\text{O}_4\text{Na}$ ($2\text{M}^+ + \text{Na}$) 367.0941, found 367.0954.

Benzo[*b*]thiophen-2-ylboronic acid (Chart 1, Entry 23)



According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), benzo[*b*]thiophen-2-ylboronic acid (2.0 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 87.0% yield (41.5 mg). Oil. **GC**: rt = 13.36 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.95 (dd, *J* = 7.5, 1.0 Hz, 3 H), 7.90 (d, *J* = 7.5 Hz, 1 H), 7.89 (s, 1 H), 7.66 (t, *J* = 7.0 Hz, 1 H), 7.57 (t, *J* = 7.6 Hz, 2 H), 7.52 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1 H), 7.45 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1 H). **¹³C NMR (125 MHz, CDCl₃)** δ 189.66, 143.14, 142.73, 139.07, 137.88, 132.49, 132.23, 129.28, 128.53, 127.46, 126.06, 125.05, 122.93. **MS** = 238.1 (EI). **HRMS** calcd for C₁₅H₁₀OSNa (M⁺ + Na) 261.0345, found 261.0353.

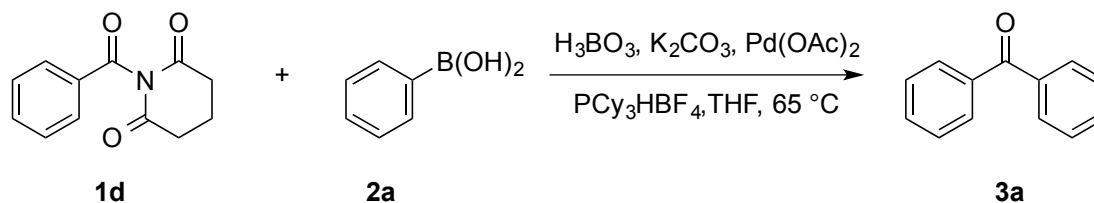
5-Borino-1*H*-indole (Chart 1, Entry 24)



According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), 5-borino-1*H*-indole (2.0 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 72.4% yield (32.0 mg). Oil. **GC**: rt = 13.07 min. **¹H NMR (500 MHz, CDCl₃)** δ 8.58 (br, 1 H), 8.17 (d, *J* = 1.5 Hz, 1 H), 7.84 (d, *J* = 8.0 Hz, 2 H), 7.83 (m, 1 H), 7.61 (t, *J* = 7.0 Hz, 1 H), 7.52 (t, *J* = 8.0 Hz, 2 H), 7.49 (d, *J* = 9.0 Hz, 1 H), 7.32 (t, *J* = 2.8 Hz, 1 H), 6.68 (t, *J* = 2.6 Hz, 1 H). **¹³C NMR (125 MHz, CDCl₃)** δ 197.36, 139.01, 138.27, 131.64, 129.93, 129.79, 128.10, 127.16, 125.70, 125.28, 124.27, 111.00, 104.30. **MS** = 221.1 (EI). **HRMS** calcd for C₁₅H₁₁NONa (M⁺ + Na) 244.0733, found 244.0741.

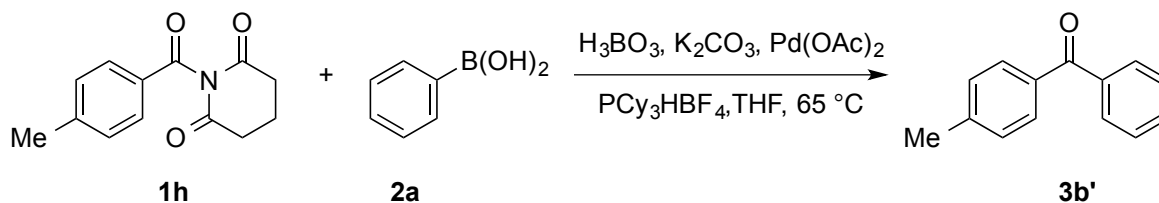
Suzuki-Miyaura Cross-Coupling of Amides: Variation of Amides

1-Benzoylpiperidine-2,6-dione (Chart 2, Entry 1)



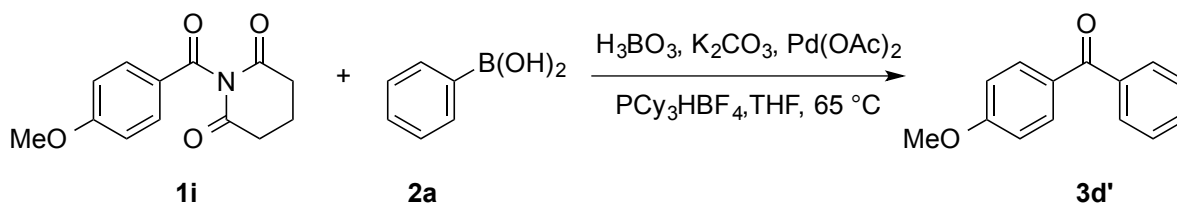
According to the general procedure, the reaction of 1-benzoylpiperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at $65\text{ }^\circ\text{C}$, afforded after work-up and chromatography the title compound in 95.3% yield (34.7 mg). White solid. **GC**: $rt = 9.80$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.84 (dd, $J = 8.5, 1.5$ Hz, 4 H), 7.62 (tt, $J = 7.5, 1.5$ Hz, 2 H), 7.51 (t, $J = 7.7$ Hz, 4 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.74, 137.62, 132.41, 130.06, 128.31. **MS** = 182.1 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_{10}\text{ONa}$ ($\text{M}^+ + \text{Na}$) 205.0624 found 205.0631.

1-(4-Methylbenzoyl)piperidine-2,6-dione (Chart 2, Entry 2)



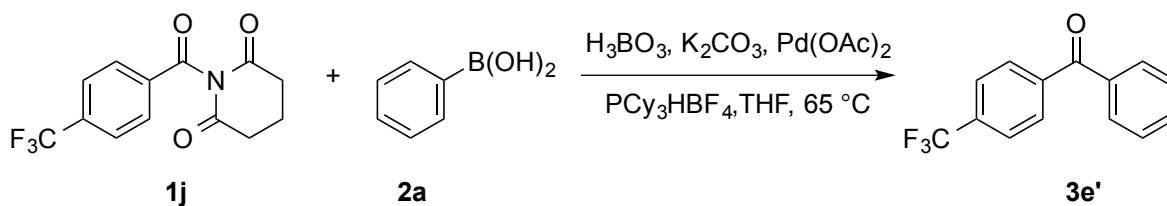
According to the general procedure, the reaction of 1-(4-methylbenzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at $65\text{ }^\circ\text{C}$, afforded after work-up and chromatography the title compound in 80.8% yield (31.7 mg). White solid. **GC**: $rt = 11.01$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.82 (d, $J = 7.5$ Hz, 2 H), 7.75 (d, $J = 7.9$ Hz, 2 H), 7.60 (t, $J = 7.5$ Hz, 1 H), 7.50 (t, $J = 7.6$ Hz, 2 H), 7.31 (d, $J = 7.9$ Hz, 2 H), 2.47 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.50, 143.23, 137.98, 134.90, 132.15, 130.31, 129.93, 128.98, 128.21, 21.67. **MS** = 196.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_{12}\text{ONa}$ ($\text{M}^+ + \text{Na}$) 219.0780 found 219.0786.

1-(4-Methoxybenzoyl)piperidine-2,6-dione (Chart 2, Entry 3)



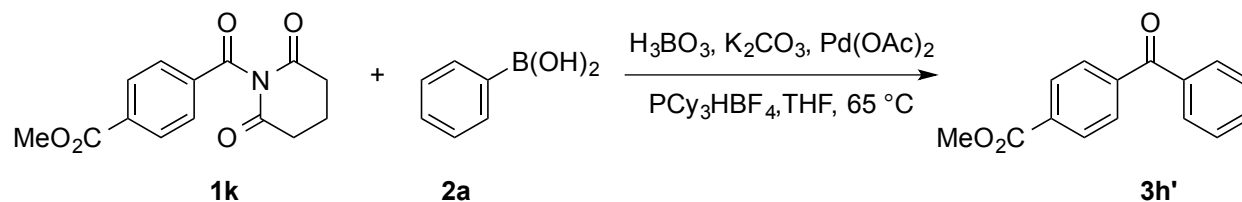
According to the general procedure, the reaction of 1-(4-methoxybenzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in >98.0% yield (42.0 mg). White solid. **GC**: rt = 12.11 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.86 (d, J = 8.0 Hz, 2 H), 7.78 (d, J = 7.6 Hz, 2 H), 7.59 (t, J = 7.5 Hz, 1 H), 7.50 (t, J = 7.5 Hz, 2 H), 6.99 (d, J = 7.5 Hz, 2 H), 3.92 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 195.56, 163.23, 138.30, 132.57, 131.89, 130.17, 129.74, 128.19, 113.56, 55.51. **MS** = 212.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_{13}\text{O}_2$ ($\text{M}^+ + \text{H}$) 213.0910 found 213.0917.

1-(4-(Trifluoromethyl)benzoyl)piperidine-2,6-dione (Chart 2, Entry 4)



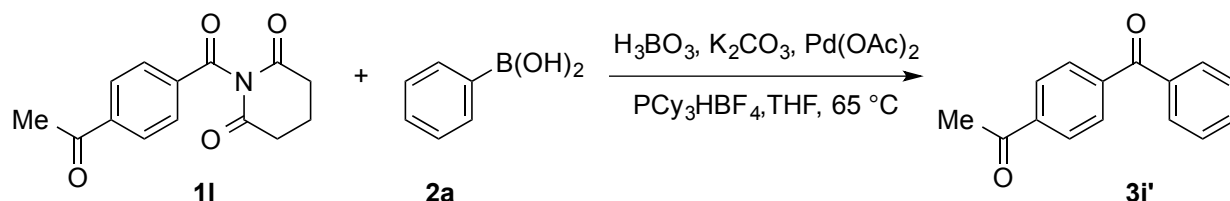
According to the general procedure, the reaction of 1-(4-(trifluoromethyl)benzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 93.4% yield (46.7 mg). White solid. **GC**: rt = 9.83 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.93 (d, J = 8.0 Hz, 2 H), 7.84 (d, J = 7.7 Hz, 2 H), 7.79 (d, J = 8.0 Hz, 2 H), 7.66 (t, J = 7.4 Hz, 1 H), 7.54 (t, J = 7.6 Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 195.53, 140.74, 136.74, 133.46 (q, J^2 = 32.0 Hz), 133.09, 130.14, 130.11, 128.54, 125.36 (q, J^3 = 3.5 Hz), 123.68 (q, J^1 = 271.5 Hz). **$^{19}\text{F NMR}$ (471 MHz, CDCl_3)** δ -63.0. **MS** = 250.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_9\text{F}_3\text{ONa}$ ($\text{M}^+ + \text{Na}$) 273.0498 found 273.0510.

Methyl 4-(2,6-dioxopiperidine-1-carbonyl)benzoate (Chart 2, Entry 5)



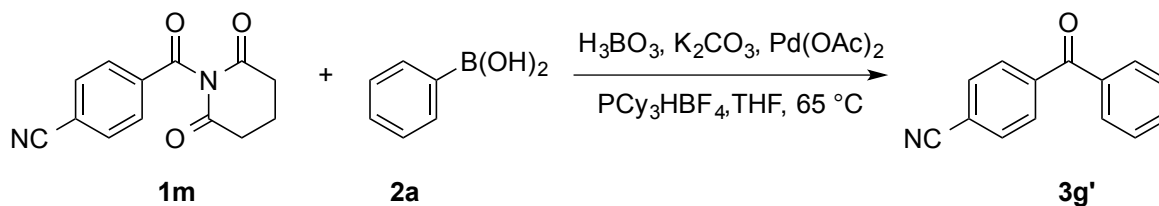
According to the general procedure, the reaction of methyl 4-(2,6-dioxopiperidine-1-carbonyl)benzoate (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 67.5% yield (32.4 mg). White solid. **GC**: $r_t = 12.27$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.17 (d, $J = 8.0$ Hz, 2 H), 7.86 (d, $J = 8.0$ Hz, 2 H), 7.82 (d, $J = 8.5$ Hz, 2 H), 7.64 (t, $J = 7.4$ Hz, 1 H), 7.52 (t, $J = 7.6$ Hz, 2 H), 3.99 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.02, 166.31, 141.33, 136.96, 133.23, 132.94, 130.10, 129.77, 129.50, 128.47, 52.47. **MS** = 240.1 (EI). **HRMS** calcd for $\text{C}_{15}\text{H}_{12}\text{O}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 263.0679 found 263.0706.

1-(4-Acetylbenzoyl)piperidine-2,6-dione (Chart 2, Entry 6)



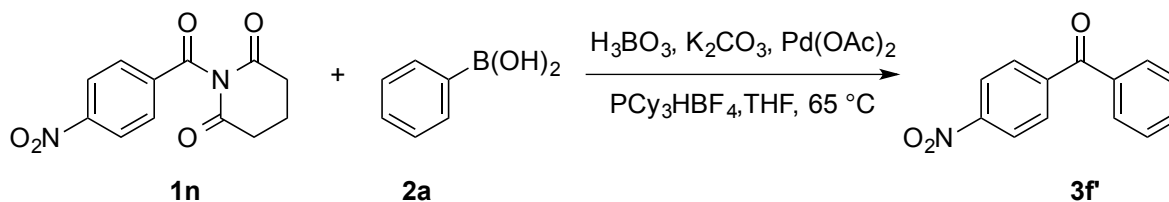
According to the general procedure, the reaction of 1-(4-acetylbenzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 50.7% yield (22.7 mg). White solid. **GC**: $r_t = 13.54$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.09 (d, $J = 8.2$ Hz, 2 H), 7.89 (d, $J = 8.3$ Hz, 2 H), 7.83 (d, $J = 7.5$ Hz, 2 H), 7.65 (t, $J = 6.5$ Hz, 1 H), 7.53 (t, $J = 7.7$ Hz, 2 H), 2.70 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 197.52, 195.96, 141.34, 139.57, 136.92, 133.00, 130.11, 130.05, 128.49, 128.17, 26.92. **MS** = 224.1 (EI). **HRMS** calcd for $\text{C}_{15}\text{H}_{12}\text{O}_2\text{Na}$ ($\text{M}^+ + \text{Na}$) 247.0730 found 247.0741.

1-(4-Cyanobenzoyl)piperidine-2,6-dione (Chart 2, Entry 7)



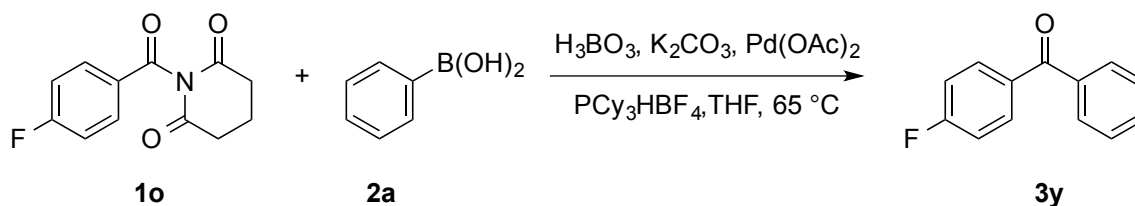
According to the general procedure, the reaction of 1-(4-cyanobenzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 95.2% yield (39.4 mg). White solid. **GC**: $t_r = 12.39$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.91 (d, $J = 9.0$ Hz, 2 H), 7.85-7.78 (m, 4 H), 7.67 (t, $J = 7.5$ Hz, 1 H), 7.55 (t, $J = 7.6$ Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 195.04, 141.24, 136.34, 133.34, 132.18, 130.25, 130.08, 128.65, 118.02, 115.68. **MS** = 207.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_9\text{NO}$ (M^+) 207.0679 found 207.0705.

1-(4-Nitrobenzoyl)piperidine-2,6-dione (Chart 2, Entry 8)



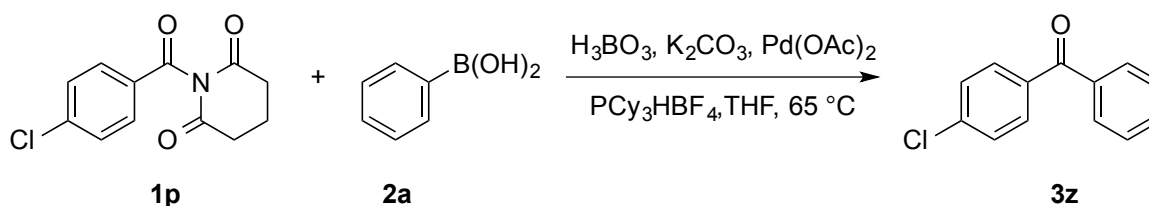
According to the general procedure, the reaction of 1-(4-nitrobenzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 80.2% yield (36.4 mg). White solid. **GC**: $t_r = 12.44$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.37 (d, $J = 9.0$ Hz, 2 H), 7.97 (d, $J = 9.0$ Hz, 2 H), 7.82 (dd, $J = 7.5, 1.0$ Hz, 2 H), 7.68 (tt, $J = 7.5, 1.5$ Hz, 1 H), 7.56 (t, $J = 7.8$ Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 194.80, 149.82, 142.90, 136.30, 133.48, 130.71, 130.11, 128.70, 123.56. **MS** = 227.1 (EI). **HRMS** calcd for $\text{C}_{26}\text{H}_{18}\text{N}_2\text{O}_6\text{Na}$ ($2\text{ M}^+ + \text{Na}$) 477.1057 found 477.1083.

1-(4-Fluorobenzoyl)piperidine-2,6-dione (Chart 2, Entry 9)



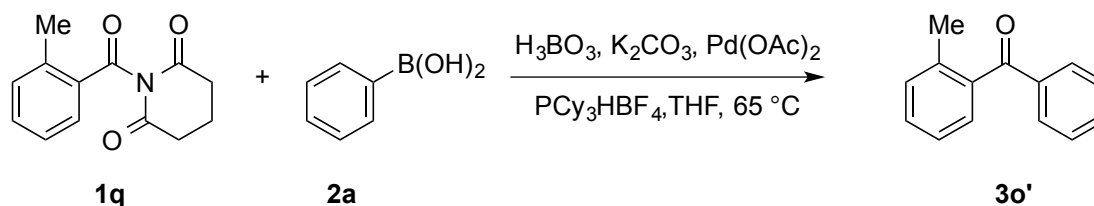
According to the general procedure, the reaction of 1-(4-fluorobenzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 94.6% yield (37.9 mg). White solid. **GC**: rt = 9.93 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.92-7.84 (m, 2 H), 7.80 (dd, $J = 7.5, 1.0$ Hz, 2 H), 7.62 (t, $J = 8.0$ Hz, 1 H), 7.52 (t, $J = 7.7$ Hz, 2 H), 7.19 (tt, $J = 8.5, 2.0$ Hz, 2 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 195.29, 165.40 (d, $J^1 = 125.4$ Hz), 137.51, 133.82, 132.68 (d, $J^3 = 9.1$ Hz), 132.48, 129.89, 128.37, 115.47 (d, $J^2 = 22.5$ Hz). **$^{19}\text{F NMR}$ (471 MHz, CDCl_3)** δ -106.00. **MS** = 200.1 (EI). **HRMS** calcd for $\text{C}_{26}\text{H}_{18}\text{F}_2\text{O}_2\text{Na}$ ($2\text{M}^+ + \text{Na}$) 423.1167 found 423.1178.

1-(4-Chlorobenzoyl)piperidine-2,6-dione (Chart 2, Entry 10)



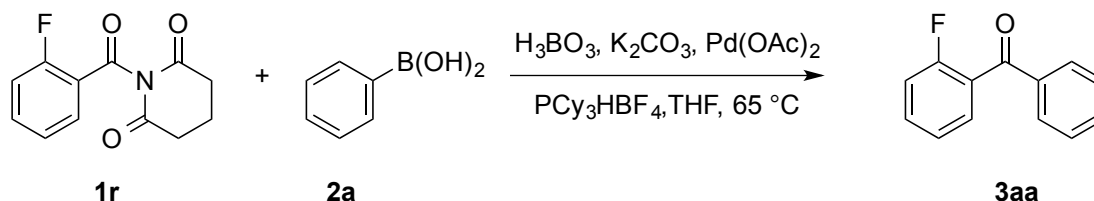
According to the general procedure, the reaction of 1-(4-chlorobenzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.0 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 7 h at 65 °C, afforded after work-up and chromatography the title compound in 78.2% yield (33.9 mg). White solid. **GC**: rt = 11.33 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.80 (td, $J = 7.7, 7.1, 1.7$ Hz, 4 H), 7.63 (t, $J = 7.0$ Hz, 1 H), 7.55-7.47 (m, 4 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 195.50, 138.91, 137.27, 135.89, 132.64, 131.46, 129.93, 128.64, 128.40. **MS** = 216.0 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_9\text{ClONa}$ ($\text{M}^+ + \text{Na}$) 239.0234 found 239.0247.

1-(2-Methylbenzoyl)piperidine-2,6-dione (Chart 2, Entry 11)



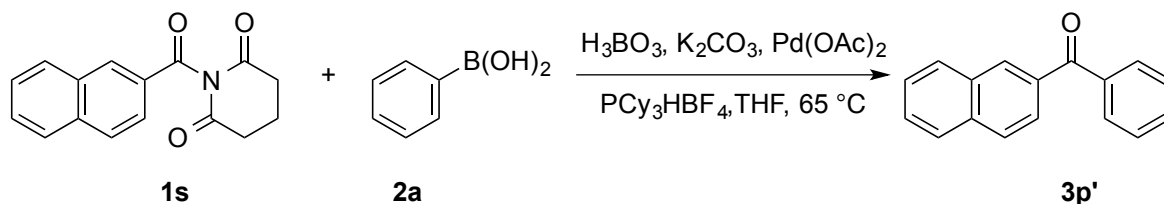
According to the general procedure, the reaction of 1-(2-methylbenzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 84.2% yield (33.1 mg). White solid. **GC**: rt = 9.95 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.85 (d, $J = 7.5$ Hz, 2 H), 7.61 (t, $J = 7.0$ Hz, 1 H), 7.48 (t, $J = 7.5$ Hz, 2 H), 7.42 (t, $J = 8.0$ Hz, 1 H), 7.33 (m, 2 H), 7.28 (m, 1 H), 2.35 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 198.64, 138.63, 137.75, 136.75, 133.14, 131.00, 130.24, 130.14, 128.52, 128.46, 125.20, 20.00. **MS** = 196.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_{12}\text{ONa}$ ($\text{M}^+ + \text{Na}$) 219.0780 found 219.0782.

1-(2-Fluorobenzoyl)piperidine-2,6-dione (Chart 2, Entry 12)



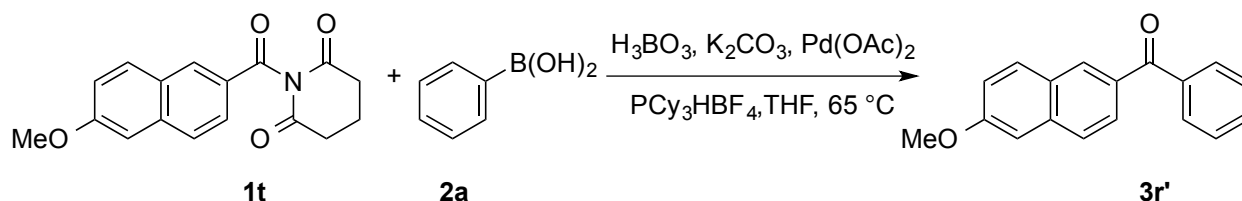
According to the general procedure, the reaction of 1-(2-fluorobenzoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.0 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 65.0% yield (26.0 mg). White solid. **GC**: rt = 9.98 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.87 (d, $J = 7.7$ Hz, 2 H), 7.63 (t, $J = 7.0$ Hz, 1 H), 7.58-7.54 (m, 2 H), 7.51 (t, $J = 7.7$ Hz, 2 H), 7.30 (t, $J = 7.0$ Hz, 1 H), 7.19 (t, $J = 9.1$ Hz, 1 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 193.47, 160.10 (d, $J^1 = 252.1$ Hz), 137.41, 133.41, 133.05 (d, $J^3 = 8.1$ Hz), 130.76 (d, $J^3 = 2.9$ Hz), 129.82, 128.47, 127.11 (d, $J^2 = 14.1$ Hz), 124.29 (d, $J^4 = 3.5$ Hz), 116.28 (d, $J^2 = 21.5$ Hz). **$^{19}\text{F NMR}$ (471 MHz, CDCl_3)** δ -111.2. **MS** = 200.1 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_9\text{FONa}$ ($\text{M}^+ + \text{Na}$) 223.0530 found 223.0536.

1-(2-Naphthoyl)piperidine-2,6-dione (Chart 2, Entry 13)



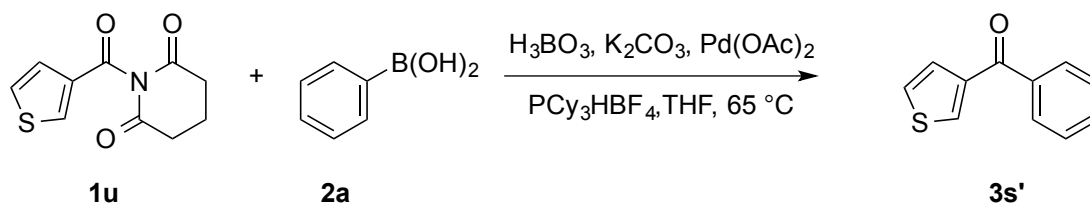
According to the general procedure, the reaction of 1-(2-naphthoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 83.4% yield (38.7 mg). White solid. **GC:** $t_r = 12.93$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.30 (s, 1 H), 7.98 (s, 2 H), 7.95 (dd, $J = 8.0, 2.0$ Hz, 1 H), 7.90 (d, $J = 7.0$ Hz, 1 H), 7.92-7.87 (m, 2 H), 7.65 (td, $J = 7.7, 4.5$ Hz, 2 H), 7.57 (dt, $J = 18.3, 7.7$ Hz, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.76, 137.92, 135.28, 134.84, 132.39, 132.27, 131.88, 130.11, 129.43, 128.35, 128.34, 128.31, 127.84, 126.81, 125.80. **MS** = 232.1 (EI). **HRMS** calcd for $\text{C}_{17}\text{H}_{12}\text{ONa}$ ($\text{M}^+ + \text{Na}$) 255.0780 found 255.0790.

1-(6-Methoxy-2-naphthoyl)piperidine-2,6-dione (Chart 2, Entry 14)



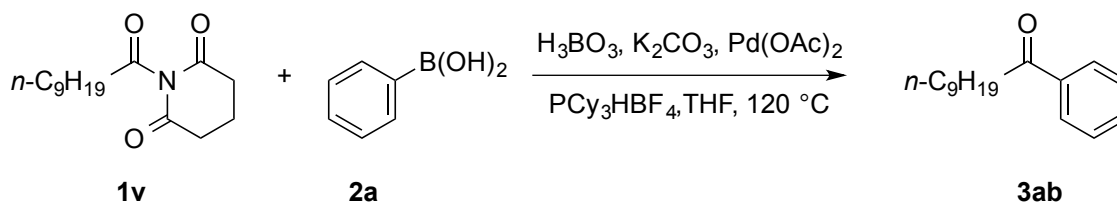
According to the general procedure, the reaction of 1-(6-methoxy-2-naphthoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 78.2% yield (41.0 mg). White solid. **GC:** $t_r = 12.97$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.24 (d, $J = 1.7$ Hz, 1 H), 7.97 (dd, $J = 8.6, 1.7$ Hz, 1 H), 7.90-7.82 (m, 4 H), 7.67-7.61 (m, 1 H), 7.54 (dd, $J = 8.4, 7.0$ Hz, 2 H), 7.26-7.20 (m, 2 H), 3.99 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 196.59, 159.70, 138.22, 137.02, 132.70, 132.13, 132.00, 131.04, 129.99, 128.30, 127.61, 127.02, 126.57, 119.74, 105.77, 55.46. **MS** = 262.1 (EI). **HRMS** calcd for $\text{C}_{18}\text{H}_{14}\text{O}_2\text{Na}$ ($\text{M}^+ + \text{Na}$) 285.0886, found 285.0900.

1-(Thiophene-3-carbonyl)piperidine-2,6-dione (Chart 2, Entry 15)



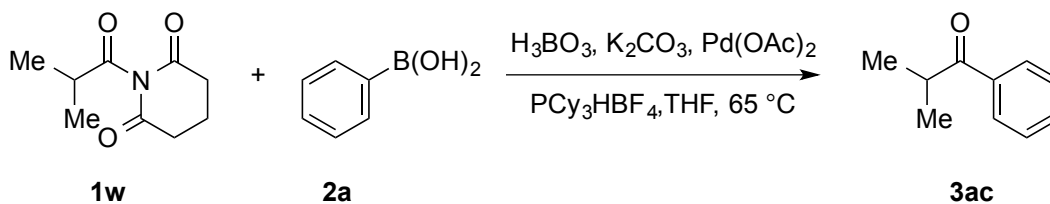
According to the general procedure, the reaction of 1-(thiophene-3-carbonyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 83.2% yield (31.3 mg). Oil. **GC:** rt = 11.08 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.96 (dd, J = 2.8, 1.2 Hz, 1 H), 7.88 (dd, J = 8.0, 1.5 Hz, 2 H), 7.66-7.58 (m, 2 H), 7.52 (t, J = 7.6 Hz, 2 H), 7.41 (dd, J = 5.1, 2.9 Hz, 1 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 190.01, 141.31, 138.64, 133.92, 132.31, 129.38, 128.62, 128.39, 126.21. **MS** = 188.1 (EI). **HRMS** calcd for $\text{C}_{22}\text{H}_{16}\text{O}_2\text{S}_2\text{Na}$ ($2\text{M}^+ + \text{Na}$) 399.0484 found 399.0498.

1-Decanoylpiperidine-2,6-dione (Chart 2, Entry 16)



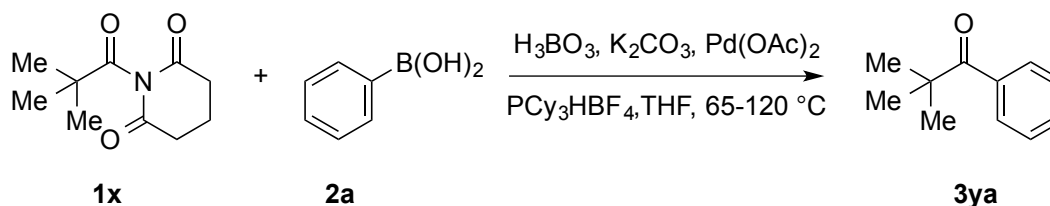
According to the general procedure, the reaction of 1-decanoylpiperidine-2,6-dione (0.20 mmol), phenylboronic acid (2.0 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 50.8% yield (23.6 mg). Oil. **GC:** rt = 11.56 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.99 (d, J = 8.5 Hz, 2 H), 7.58 (t, J = 7.4 Hz, 1 H), 7.49 (t, J = 7.6 Hz, 2 H), 2.99 (t, J = 7.4 Hz, 2 H), 1.76 (p, J = 7.4 Hz, 2 H), 1.48-1.37 (m, 1 H), 1.40-1.23 (m, 11 H), 0.91 (t, J = 6.8 Hz, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 200.64, 137.12, 132.85, 128.55, 128.06, 38.66, 31.89, 29.50, 29.49, 29.40, 29.30, 24.42, 22.68, 14.12. **MS** = 232.1 (EI). **HRMS** calcd for $\text{C}_{16}\text{H}_{24}\text{ONa}$ ($\text{M}^+ + \text{Na}$) 255.1719 found 255.1706.

1-Isobutyrylpiperidine-2,6-dione (Chart 2, Entry 17)



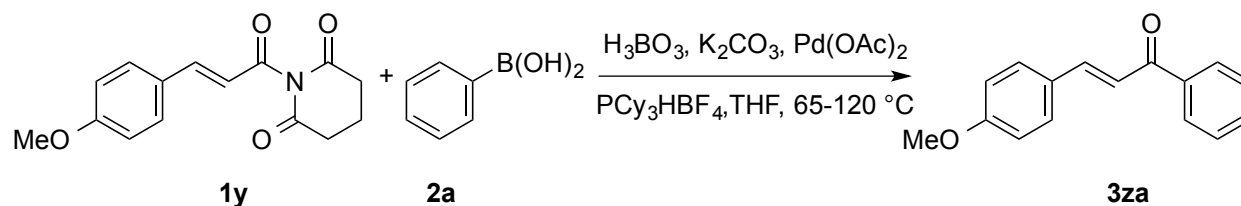
According to the general procedure, the reaction of 1-isobutyrylpiperidine-2,6-dione (0.20 mmol), phenylboronic acid (2.0 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up the title compound in 75.0% yield. ^1H NMR analysis (500 MHz, CDCl_3) vs. internal standard. Note: the product is volatile. Purification by chromatography afforded a sample for characterization purposes. Oil. **GC:** rt = 11.56 min. **^1H NMR (500 MHz, CDCl_3)** δ 7.99 (d, J = 8.5 Hz, 2 H), 7.58 (t, J = 7.0 Hz, 1 H), 7.50 (t, J = 8.0 Hz, 2 H), 3.59 (hept, J = 6.9, 1 H), 1.25 (d, J = 6.7 Hz, 6 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 204.51, 136.23, 132.78, 128.60, 128.31, 35.37, 19.16. **MS** = 148.1 (EI). **HRMS** calcd for $\text{C}_{10}\text{H}_{12}\text{OK}$ ($\text{M}^+ + \text{K}$) 187.0520 found 187.0490.

1-Pivaloylpiperidine-2, 6-dione (Chart 2, Entry 18)



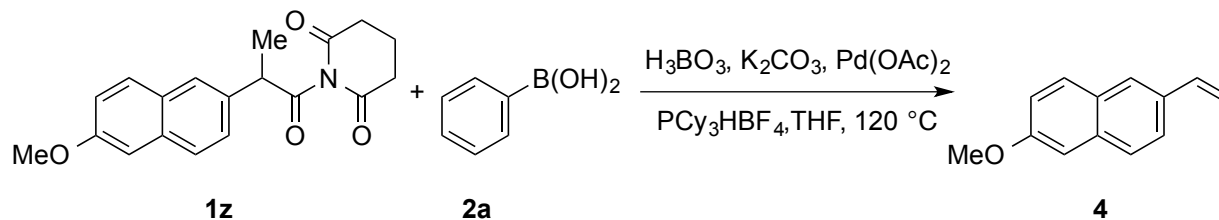
According to the general procedure, 1-isobutyrylpiperidine-2,6-dione (0.20 mmol) was reacted with phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) in THF (0.80 mL) for 15 h at 65-120 °C. After the standard work-up as described above, the sample was analyzed by ^1H NMR and GC-MS to obtain conversion and yield using internal standard: yield of product <5.0%. At this stage, further optimization of the cross-coupling was not performed. This result is consistent with previous examples of cross-couplings of carboxylic acid derivatives.¹⁵⁻¹⁹

(*E*)-1-(3-(4-Methoxyphenyl)acryloyl)piperidine-2,6-dione (Chart 2, Entry 19)



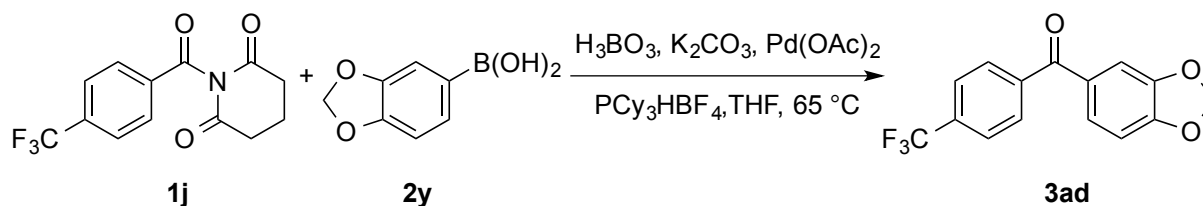
According to the general procedure, (*E*)-1-(3-(4-methoxyphenyl)acryloyl)piperidine-2,6-dione (0.20 mmol) was reacted with phenylboronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) in THF (0.80 mL) for 15 h at 65-120 °C. After the standard work-up as described above, the sample was analyzed by ^1H NMR and GC-MS to obtain conversion and yield using internal standard: yield of product <5.0%. At this stage, further optimization of the cross-coupling was not performed. This result is consistent with previous examples of cross-couplings of carboxylic acid derivatives.¹⁵⁻¹⁹

1-(2-(6-Methoxynaphthalen-2-yl)propanoyl)piperidine-2,6-dione (Chart 2, Entry 20)



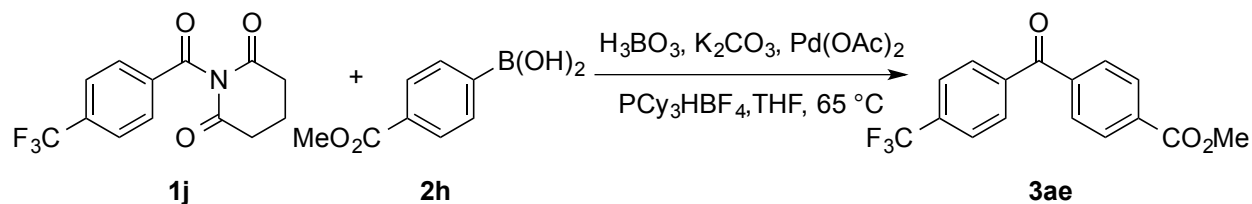
According to the general procedure, the reaction of 1-(2-(6-methoxynaphthalen-2-yl)propanoyl)piperidine-2,6-dione (0.20 mmol), phenylboronic acid (2.0 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 52.5% yield (20.8 mg). The cross-coupling product was not detected. Oil. **GC**: rt = 11.83 min. **^1H NMR (500 MHz, CDCl_3)** δ 7.81-7.69 (m, 3 H), 7.63 (dd, J = 8.6, 1.7 Hz, 1 H), 7.18-7.15 (m, 2 H), 6.88 (dd, J = 17.6, 10.9 Hz, 1 H), 5.85 (d, J = 17.6 Hz, 1 H), 5.30 (d, J = 10.9 Hz, 1 H), 3.95 (s, 3 H). **^{13}C NMR (125 MHz, CDCl_3)** δ 157.79, 136.95, 134.31, 132.99, 129.55, 128.95, 127.00, 126.16, 123.78, 118.95, 113.10, 105.87, 55.32. **MS** = 184.1 (EI). **HRMS** calcd for $\text{C}_{13}\text{H}_{12}\text{ONa}$ (M^+ + Na) 207.0780 found 207.0792.

Suzuki-Miyaura Coupling of Amides: Additional Examples

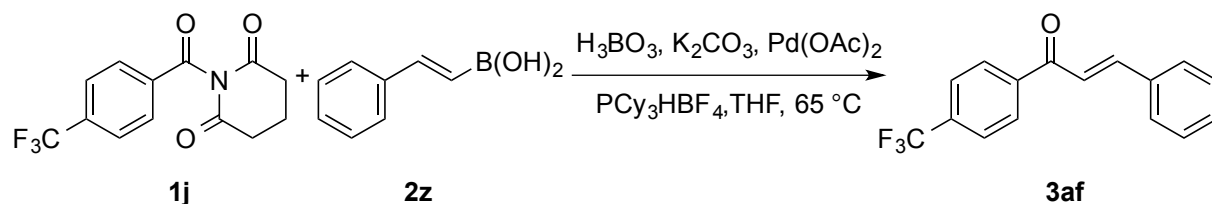
Benzo[*d*][1,3]dioxol-5-yl(4-(trifluoromethyl)phenyl)methanone (Chart 3, Entry 1)

According to the general procedure, the reaction of 1-(4-(trifluoromethyl)benzoyl)piperidine-2,6-dione (0.20 mmol), benzo[*d*][1,3]dioxol-5-ylboronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 82.5% yield (48.5 mg). White solid. **GC**: *rt* = 11.60 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.86 (d, *J* = 8.0 Hz, 2 H), 7.77 (d, *J* = 8.0 Hz, 2 H), 7.45-7.34 (m, 2 H), 6.90 (d, *J* = 8.0 Hz, 1 H), 6.12 (s, 2 H). **¹³C NMR (125 MHz, CDCl₃)** δ 193.89, 152.14, 148.28, 141.24, 133.53 (q, *J*² = 30.6 Hz), 131.19, 129.77, 127.19, 125.32, 123.74 (q, *J*¹ = 254.1 Hz), 109.72, 107.88, 102.05. **¹⁹F NMR (471 MHz, CDCl₃)** δ -63.0. **MS** = 294.1 (EI). **HRMS** calcd for C₁₅H₁₀O₃F₃ (M⁺ + H) 295.0577 found 295.0586.

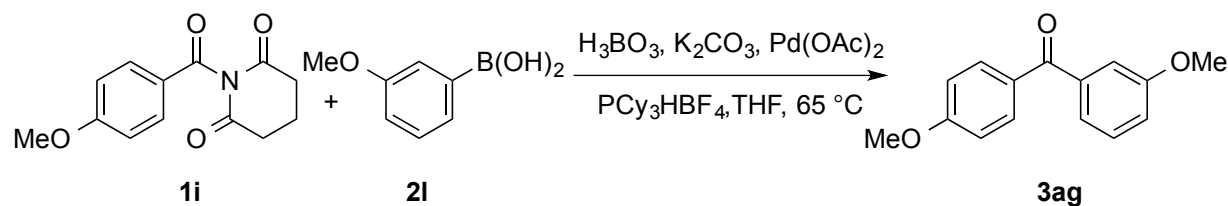
Methyl 4-(4-(trifluoromethyl)benzoyl)benzoate (Chart 3, Entry 2)



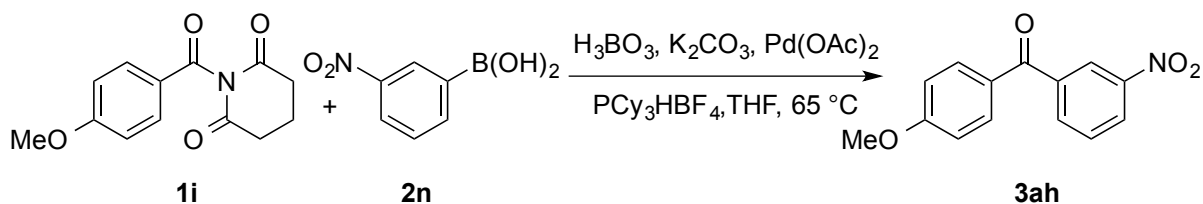
According to the general procedure, the reaction of 1-(4-(trifluoromethyl)benzoyl)piperidine-2,6-dione (0.20 mmol), (4-(methoxycarbonyl)phenyl)boronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 62.1% yield (38.3 mg). White solid. **GC**: *rt* = 12.39 min. **¹H NMR (500 MHz, CDCl₃)** δ 8.19 (d, *J* = 9.0 Hz, 2 H), 7.93 (d, *J* = 8.1 Hz, 2 H), 7.86 (d, *J* = 8.0 Hz, 2 H), 7.80 (d, *J* = 8.1 Hz, 2 H), 4.00 (s, 3 H). **¹³C NMR (125 MHz, CDCl₃)** δ 195.31, 163.25, 159.50, 139.62, 132.57, 130.17, 129.13, 122.42, 118.26, 114.19, 113.55, 55.46. **¹⁹F (471 MHz, CDCl₃)** δ -63.1. **MS** = 308.1 (EI). **HRMS** calcd for C₁₆H₁₁F₃O₃Na (M⁺ + Na) 331.0552 found 331.0561.

(E)-3-Phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (Chart 3, Entry 3)

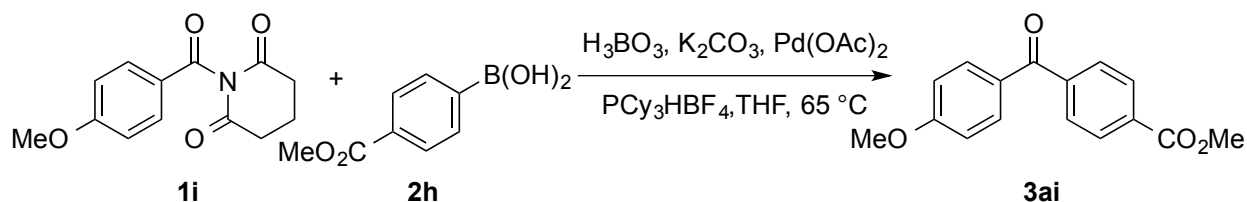
According to the general procedure, the reaction of 1-(4-(trifluoromethyl)benzoyl)piperidine-2,6-dione (0.20 mmol), (*E*)-styrylboronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 79.9% yield (44.1 mg). Yellow solid. **GC**: rt = 12.65 min. **¹H NMR (500 MHz, CDCl₃)** δ 8.13 (d, *J* = 8.1 Hz, 2 H), 7.86 (d, *J* = 15.7 Hz, 1 H), 7.80 (d, *J* = 8.1 Hz, 2 H), 7.69 (dd, *J* = 6.6, 2.9 Hz, 2 H), 7.52 (d, *J* = 15.7 Hz, 1 H), 7.49-7.45 (m, 3 H). **¹³C NMR (125 MHz, CDCl₃)** δ 189.68, 146.13, 141.08, 134.53, 134.04 (q, *J*² = 30.6 Hz), 130.98, 129.07, 128.78, 128.61, 125.69 (q, *J*³ = 3.6 Hz), 123.68 (q, *J*¹ = 272.3 Hz), 121.62. **¹⁹F NMR (471 MHz, CDCl₃)** δ -63.0. **MS** = 276.1 (EI). **HRMS** calcd for C₁₆H₁₁F₃ONa (M⁺ + Na) 299.0654 found 299.0659.

(3-Methoxyphenyl)(4-methoxyphenyl)methanone (Chart 3, Entry 4)

According to the general procedure, the reaction of 1-(4-methoxybenzoyl)piperidine-2,6-dione (0.20 mmol), (3-methoxyphenyl)boronic acid (1.2 equiv), H₃BO₃ (2.0 equiv), K₂CO₃ (2.5 equiv), Pd(OAc)₂ (0.03 equiv) and PCy₃HBF₄ (0.12 equiv) for 15 h at 65 °C, afforded after filtering the solid and chromatography the title compound in >98.0% yield (48.0 mg). White solid. **GC**: rt = 12.65 min. **¹H NMR (500 MHz, CDCl₃)** δ 7.87 (d, *J* = 8.5 Hz, 2 H), 7.40 (t, *J* = 8.5 Hz, 1 H), 7.35-7.27 (m, 2 H), 7.14 (ddd, *J* = 8.2, 2.6, 1.2 Hz, 1 H), 6.99 (d, *J* = 8.5 Hz, 2 H), 3.91 (s, 3 H), 3.89 (s, 3 H). **¹³C NMR (125 MHz, CDCl₃)** δ 195.31, 163.25, 159.50, 139.62, 132.57, 130.17, 129.13, 122.42, 118.26, 114.19, 113.55, 55.51, 55.46. **MS** = 242.1 (EI). **HRMS** calcd for C₁₅H₁₄O₃Na (M⁺ + Na) 265.0835 found 265.0838.

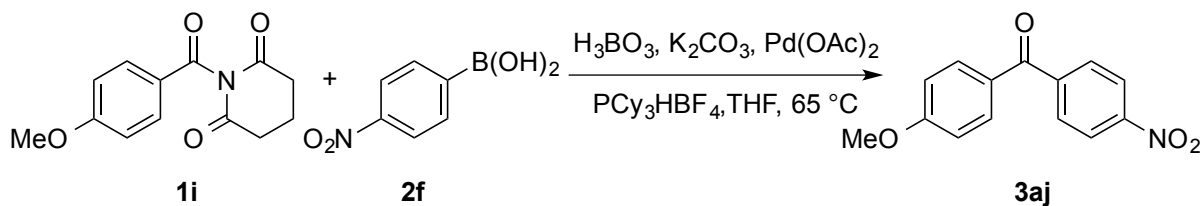
(4-Methoxyphenyl)(3-nitrophenyl)methanone (Chart 3, Entry 5)

According to the general procedure, the reaction of 1-(4-methoxybenzoyl)piperidine-2,6-dione (0.20 mmol), (3-nitrophenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), Pd(OAc)_2 (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 75.8% yield (39.0 mg). Yellow solid. **GC**: $rt = 13.57$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.60 (t, $J = 2.0$ Hz, 1 H), 8.45 (ddd, $J = 8.3, 2.3, 1.1$ Hz, 1 H), 8.12 (dt, $J = 7.7, 1.4$ Hz, 1 H), 7.85 (d, $J = 9.5$ Hz, 2 H), 7.72 (t, $J = 7.9$ Hz, 1 H), 7.03 (d, $J = 8.5$ Hz, 2 H), 3.94 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 192.86, 163.94, 148.00, 139.81, 135.20, 132.59, 129.55, 128.88, 126.26, 124.45, 114.04, 55.63. **MS** = 257.1 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_{11}\text{NO}_4\text{Na}$ ($\text{M}^+ + \text{Na}$) 280.0580 found 280.0585.

Methyl 4-(4-methoxybenzoyl)benzoate (Chart 3, Entry 6)

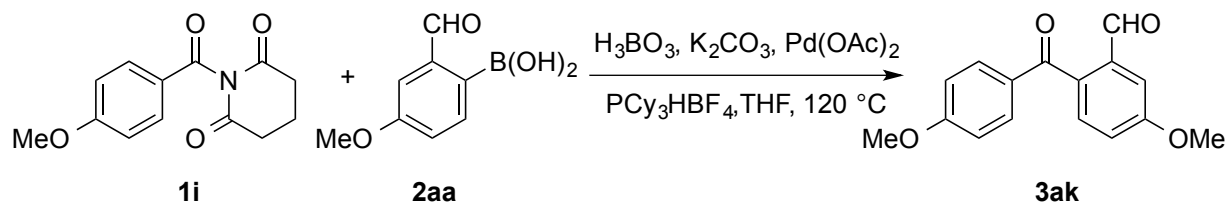
According to the general procedure, the reaction of 1-(4-methoxybenzoyl)piperidine-2,6-dione (0.20 mmol), (4-(methoxycarbonyl)phenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), Pd(OAc)_2 (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 58.8% yield (28.5 mg). White solid. **GC**: $rt = 15.86$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.20-8.14 (m, 2 H), 7.90-7.78 (m, 4 H), 7.04-6.97 (m, 2 H), 4.00 (s, 3 H), 3.93 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 194.78, 166.40, 163.62, 142.16, 132.77, 132.63, 129.45, 113.76, 99.98, 55.57, 52.44. **MS** = 270.1 (EI). **HRMS** calcd for $\text{C}_{16}\text{H}_{14}\text{O}_4\text{Na}$ ($\text{M}^+ + \text{Na}$) 293.0784 found 293.0791.

(4-Methoxyphenyl)(4-nitrophenyl)methanone (Chart 3, Entry 7)



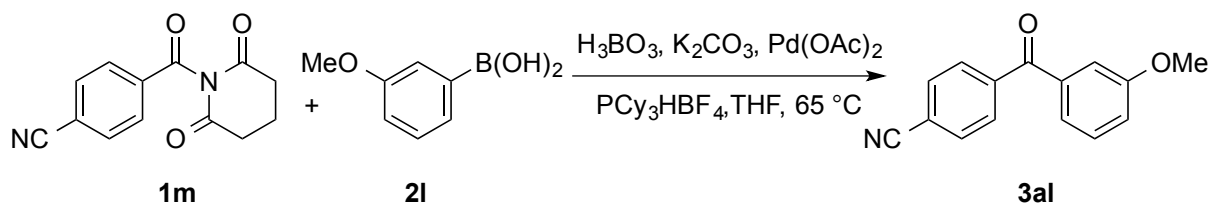
According to the general procedure, the reaction of 1-(4-methoxybenzoyl)piperidine-2,6-dione (0.20 mmol), (4-nitrophenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65 °C, afforded after work-up and chromatography the title compound in 56.6% yield (29.1 mg). Yellow solid. **GC**: $t_r = 16.99$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.42-8.32 (m, 2 H), 7.94-7.88 (m, 2 H), 7.88-7.78 (m, 2 H), 7.08-6.99 (m, 2 H), 3.94 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 193.48, 164.02, 143.81, 132.66, 130.34, 128.95, 123.49, 113.99, 77.22, 55.63. **MS** = 257.0 (EI). **HRMS** calcd for $\text{C}_{14}\text{H}_{11}\text{NO}_4\text{Na}$ ($\text{M}^+ + \text{Na}$) 280.0580 found 280.0585.

5-Methoxy-2-(4-methoxybenzoyl)benzaldehyde (Chart 3, Entry 8)



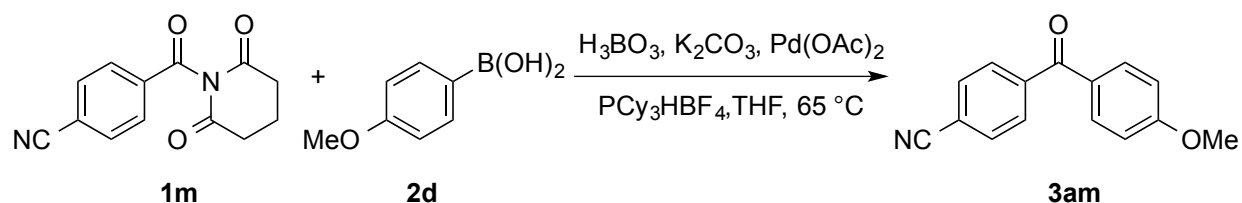
According to the general procedure, the reaction of 1-(4-methoxybenzoyl)piperidine-2,6-dione (0.20 mmol), (2-formyl-4-methoxyphenyl)boronic acid (2.0 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 91.2% yield (49.3 mg). White solid. **GC**: $t_r = 16.39$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 10.09 (s, 1 H), 7.84 (d, $J = 9.5$ Hz, 2 H), 7.56 (d, $J = 2.5$ Hz, 1 H), 7.54 (d, $J = 8.5$ Hz, 1 H), 7.18 (dd, $J = 8.4, 2.7$ Hz, 1 H), 6.99 (d, $J = 9.0$ Hz, 2 H), 3.96 (s, 3 H), 3.92 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 194.06, 190.67, 163.90, 161.45, 138.02, 134.58, 132.61, 131.53, 130.68, 119.26, 113.89, 112.21, 55.79, 55.59. **MS** = 270.1 (EI). **HRMS** calcd for $\text{C}_{16}\text{H}_{14}\text{O}_4\text{Na}$ ($\text{M}^+ + \text{Na}$) 293.0784 found 293.0789.

4-(3-Methoxybenzoyl)benzonitrile (Chart 3, Entry 9)



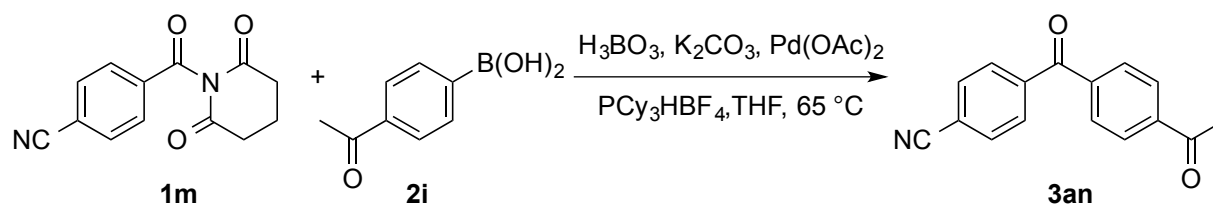
According to the general procedure, the reaction of 1-(4-cyanobenzoyl)piperidine-2,6-dione (0.20 mmol), (3-methoxyphenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65°C , afforded after work-up and chromatography the title compound in >98.0% yield (47.0 mg). White solid. **GC**: rt = 13.64 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.90 (d, J = 8.2 Hz, 2 H), 7.82 (d, J = 8.1 Hz, 2 H), 7.43 (t, J = 7.9 Hz, 1 H), 7.37 (dd, J = 2.7, 1.5 Hz, 1 H), 7.31 (dt, J = 7.6, 1.2 Hz, 1 H), 7.22-7.19 (m, 1 H), 3.90 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 194.83, 159.83, 141.29, 137.61, 132.15, 130.22, 129.57, 122.87, 119.73, 118.02, 115.68, 114.30, 55.55. **MS** = 237.1 (EI). **HRMS** calcd for $\text{C}_{15}\text{H}_{11}\text{NO}_2\text{Na}$ (M^+ + Na) 260.0682 found 260.0692.

4-(4-Methoxybenzoyl)benzonitrile (Chart 3, Entry 10)



According to the general procedure, the reaction of 4-(2,6-dioxopiperidine-1-carbonyl)benzonitrile (0.20 mmol), (4-methoxyphenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at 65°C , afforded after work-up and chromatography the title compound in 87.7% yield (40.3mg). White solid. **GC**: rt = 16.23 min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.89-7.75 (m, 6 H), 7.01 (d, J = 8.4 Hz, 2 H), 3.93 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 193.71, 163.91, 142.12, 132.62, 132.10, 129.92, 128.98, 118.10, 115.17, 113.94, 55.61. **MS** = 237.1 (EI). **HRMS** calcd for $\text{C}_{15}\text{H}_{11}\text{NO}_2\text{Na}$ (M^+ + Na) 260.0682 found 260.0708.

4-(4-Acetylbenzoyl)benzonitrile (Chart 3, Entry 11)

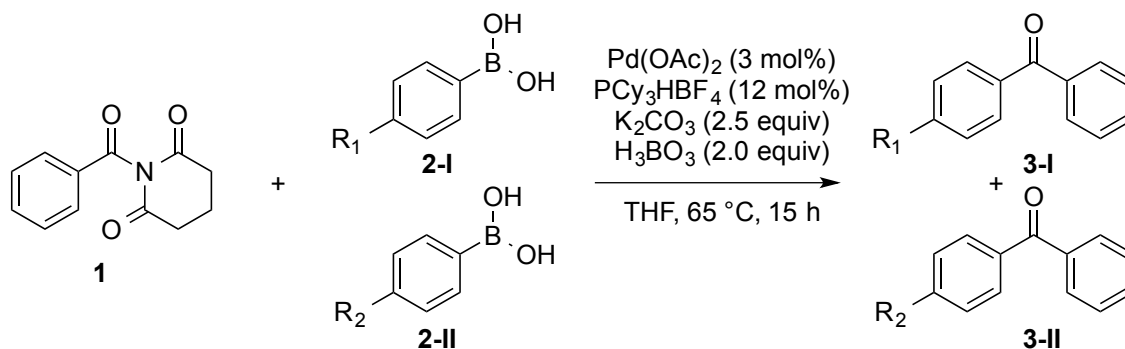


According to the general procedure, the reaction of 4-(2,6-dioxopiperidin-1-carbonyl)benzotrile (0.20 mmol), (4-acetylphenyl)boronic acid (1.2 equiv), H_3BO_3 (2.0 equiv), K_2CO_3 (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (0.03 equiv) and PCy_3HBF_4 (0.12 equiv) for 15 h at $65\text{ }^\circ\text{C}$, afforded after work-up and chromatography the title compound in 36.0% yield (17.9 mg). White solid. **GC**: $t_r = 15.30$ min. **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.11 (d, $J = 8.5$ Hz, 2 H), 7.90 (td, $J = 8.5, 4.3$ Hz, 4 H), 7.84 (d, $J = 8.8$ Hz, 2 H), 2.71 (s, 3 H). **$^{13}\text{C NMR}$ (125 MHz, CDCl_3)** δ 197.23, 194.29, 140.43, 140.23, 139.84, 132.35, 130.28, 130.11, 128.43, 117.82, 116.26, 26.92. **MS** = 249.1 (EI). **HRMS** calcd for $\text{C}_{16}\text{H}_{11}\text{NO}_2\text{Na}$ ($\text{M}^+ + \text{Na}$) 272.0682 found 272.0667.

Hammett Studies – Boronic Acids¹⁷⁻²⁰

General Procedure. An oven-dried vial equipped with a stir bar was charged with an amide substrate (0.1 mmol, 1.0 equiv), potassium carbonate (2.5 equiv), boric acid (2.0 equiv), two boronic acid substrates (each 0.4 mmol), Pd(OAc)₂ (0.03 equiv), and PCy₃HBF₄ (0.12 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Tetrahydrofuran (0.4 mL) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 65 °C, and stirred for the indicated time at 65 °C. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH₂Cl₂ (10 mL), filtered, and concentrated. The sample was analyzed by ¹H NMR (CDCl₃, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

Table SI-1. Selectivity Study in the Cross-Coupling of Sterically-Distorted Amides.^a



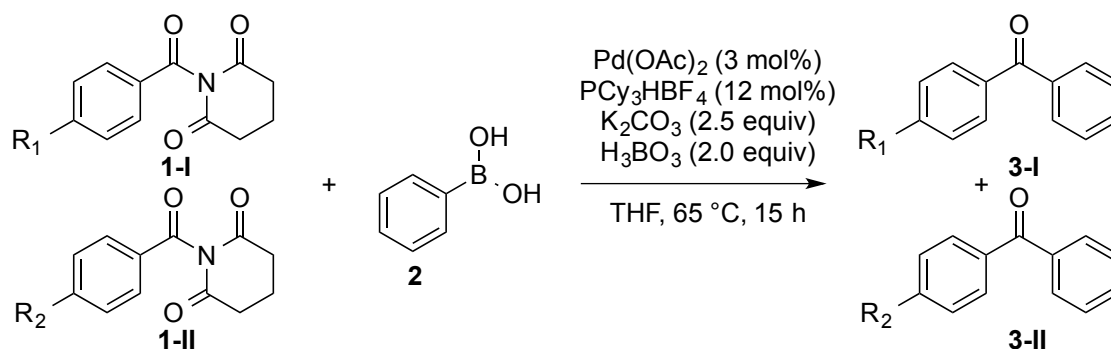
Entry	2-I (R ₁)	k_X/k_H^b	Hammett σ constant	Hammett σ^+ constant
1	MeO-	0.90	-0.27	-0.778
2	Me-	0.94	-0.17	-0.311
3	H-	1.0	0	0
4	CF ₃ -	1.40	0.54	0.612

^aConditions: Pd(OAc)₂ (3.0 mol%), ligand (12 mol%), THF (0.25 M), 65 °C. All reactions carried out using standard Schlenk techniques under. ^bDetermined by ¹H NMR and/or GC-MS. R₁ = X, R₂ = H.

Hammett Studies – Amides¹⁷⁻²⁰

General Procedure. An oven-dried vial equipped with a stir bar was charged with two amide substrates (each 0.2 mmol, 1.0 equiv), potassium carbonate (2.5 equiv), boric acid (2.0 equiv), boronic acid (0.05 mmol), Pd(OAc)₂ (0.03 equiv), and PCy₃HBF₄ (0.12 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Tetrahydrofuran (0.8 mL) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 65 °C, and stirred for the indicated time at 65 °C. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH₂Cl₂ (10 mL), filtered, and concentrated. The sample was analyzed by ¹H NMR (CDCl₃, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

Table SI-2. Selectivity Study in the Cross-Coupling of Sterically-Distorted Amides.^a



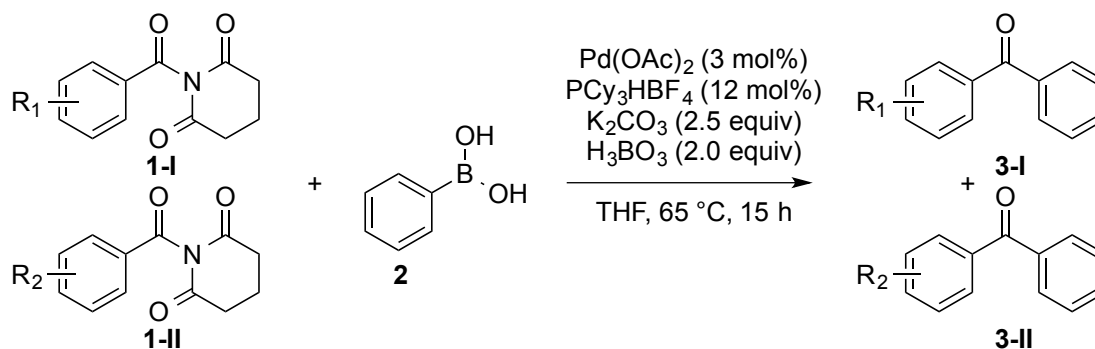
Entry	1-I (R ₁)	k_X/k_H^b	Hammett σ constant	Hammett σ^+ constant
1	MeO-	0.12	-0.27	-0.778
2	H-	1.0	0	0
3	MeC(O)-	4.0	0.50	0.489
4	CF ₃ -	9.86	0.54	0.612

^aConditions: Pd(OAc)₂ (3.0 mol%), ligand (12 mol%), THF (0.25 M), 65 °C. All reactions carried out using standard Schlenk techniques under. ^bDetermined by ¹H NMR and/or GC-MS. R₁ = X, R₂ = H.

Selectivity Studies – Sterics¹⁷⁻²⁰

General Procedure. An oven-dried vial equipped with a stir bar was charged with two amide substrates (each 0.2 mmol, 1.0 equiv), potassium carbonate (2.5 equiv), boric acid (2.0 equiv), boronic acid (0.5 equiv), Pd(OAc)₂ (0.03 equiv), and PCy₃HBF₄ (0.12 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Tetrahydrofuran (0.8 mL) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 65 °C, and stirred for the indicated time at 65 °C. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH₂Cl₂ (10 mL), filtered, and concentrated. The sample was analyzed by ¹H NMR (CDCl₃, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

Table SI-3. Selectivity Study in the Cross-Coupling of Sterically-Distorted Amides.^a



Entry	1-I (R ₁)	1-II (R ₂)	Amide (equiv)	3-I:3-II (R ₁ :R ₂) ^b
1	2-Me-	4-Me-	2.0	50:50
2	2-F-	4-F-	2.0	50:50
3	2-F-	2-Me-	2.0	58:42
4	2-Me-	4-Me-	^c	40:60

^aConditions: Pd(OAc)₂ (3.0 mol%), ligand (12 mol%), THF (0.25 M), 65 °C. All reactions carried out using standard Schlenk techniques under. ^bDetermined by ¹H NMR and/or GC-MS. ^cSelectivity study between 2-tolylboronic acid (4.0 equiv) and 4-tolylboronic acid (4.0 equiv) using 1-benzoylpiperidine-2,6-dione (1.0 equiv), Pd(OAc)₂ (3.0 mol%), ligand (12 mol%) in THF (0.25 M) at 65 °C.

Selectivity Studies – Reactivity vs. Functional Groups

General Procedure. An oven-dried vial equipped with a stir bar was charged with two substrates (each 0.2 mmol, 1.0 equiv), potassium carbonate (2.5 equiv), boric acid (2.0 equiv), boronic acid (0.5 equiv), Pd(OAc)₂ (0.03 equiv), and PCy₃HBF₄ (0.12 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Tetrahydrofuran (0.8 mL) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 65 °C, and stirred for the indicated time at 65 °C. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH₂Cl₂ (10 mL), filtered, and concentrated. The sample was analyzed by ¹H NMR (CDCl₃, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples.

Table SI-4. Selectivity Study in the Cross-Coupling of Sterically-Distorted Amides.^a

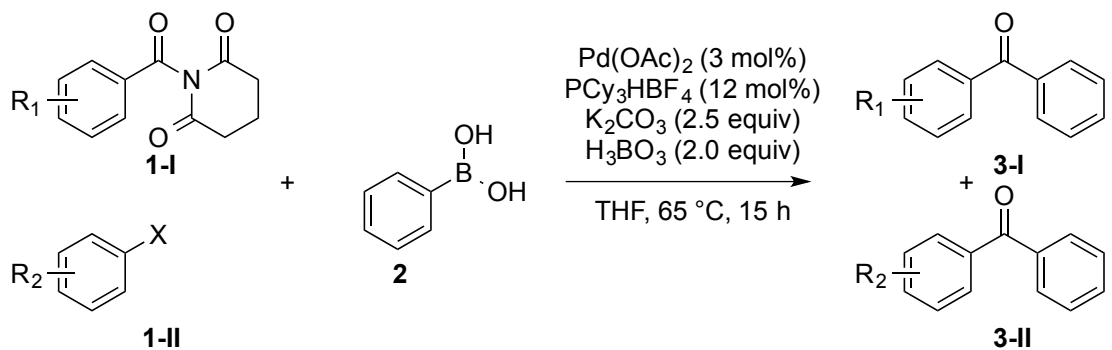
Entry	1-I (R ₁)	1-II (X)	Amide (equiv)	3-I:3-II (R ₁ :R ₂) ^b
1	4-Me-	-C(O)OC(O)Ph	2.0	17:83
2	4-Me-	-C(O)-4-NO ₂ -C ₆ H ₄	2.0	>98:2
3 ^b	4-Me-	Cl-	2.0	>98:2
4 ^b	4-Me-	Br-	2.0	19:81
5 ^b	4-Me-	I-	2.0	15:85

^aConditions: Pd(OAc)₂ (3.0 mol%), ligand (12 mol%), THF (0.25 M), 65 °C. All reactions carried out using standard Schlenk techniques under. ^bDetermined by ¹H NMR and/or GC-MS. ^bSelectivity study between aryl halide (2.0 equiv), 1-4-methylbenzoylpiperidine-2,6-dione (2.0 equiv), 4-methoxyphenyl boronic acid (1.0 equiv), Pd(OAc)₂ (3.0 mol%), ligand (12 mol%) in THF (0.25 M) at 65 °C.

Selectivity Studies – Reactivity vs. Other Amides

General Procedure. An oven-dried vial equipped with a stir bar was charged with two substrates (each 0.2 mmol, 1.0 equiv), potassium carbonate (2.5 equiv), boric acid (2.0 equiv), boronic acid (0.5 equiv), Pd(OAc)₂ (0.03 equiv), and PCy₃HBF₄ (0.12 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Tetrahydrofuran (0.8 mL) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 65 °C, and stirred for the indicated time at 65 °C. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH₂Cl₂ (10 mL), filtered, and concentrated. The sample was analyzed by ¹H NMR (CDCl₃, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples. Selectivity was confirmed in individual experiments, in which <5% conversion (>95% recovery) with –C(O)NMe₂, –C(O)NMePh and –C(O)NTsPh amides was observed under standard conditions, indicating that the chemoselective cross-coupling of amides **1d** in the presence of electronically-activated amides can be readily achieved.

Table SI-5. Selectivity Study in the Cross-Coupling of Sterically-Distorted Amides.^a



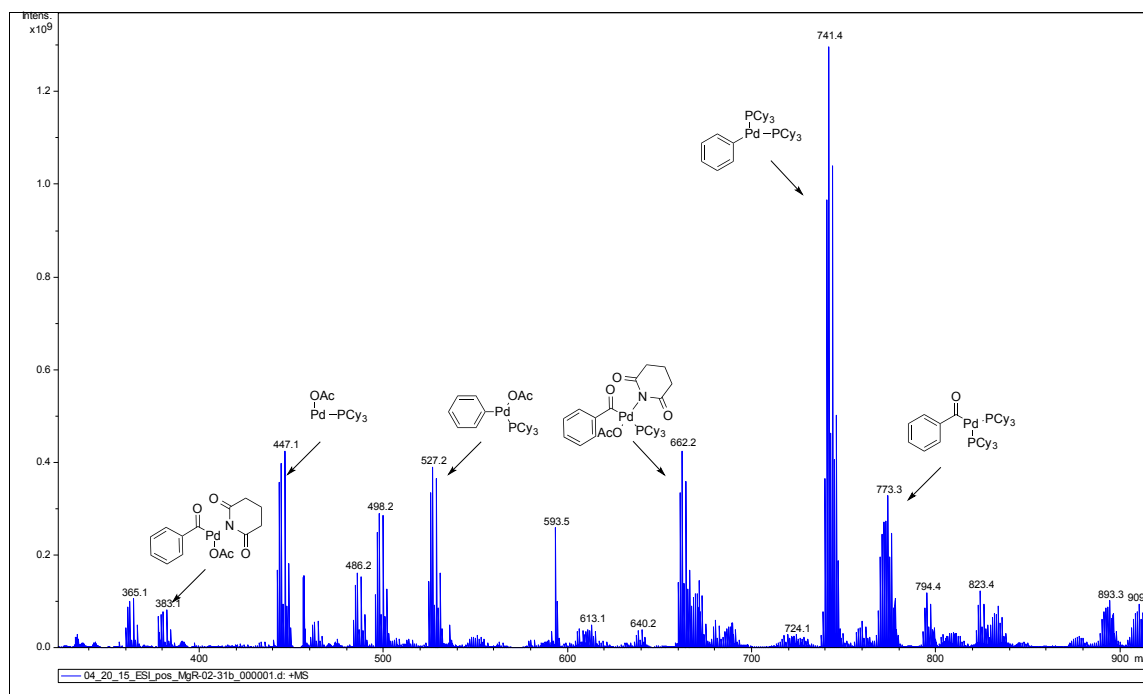
Entry	1-I (R ₁)	1-II (X)	Amide (equiv)	3-I:3-II (R ₁ :R ₂) ^b
1	4-Me-	-C(O)NMe ₂	2.0	>98:2
2	4-Me-	-C(O)NMePh	2.0	>98:2
3	4-Me-	-C(O)NTsPh	2.0	>98:2

^aConditions: Pd(OAc)₂ (3.0 mol%), ligand (12 mol%), THF (0.25 M), 65 °C. All reactions carried out using standard Schlenk techniques under. ^bDetermined by ¹H NMR and/or GC-MS.

Stoichiometric ESI/MS Experiments²¹⁻²⁵

General Procedure. An oven-dried vial equipped with a stir bar was charged with 1-benzoylpiperidine-2,6-dione (0.2 mmol, 1.0 equiv), Pd(OAc)₂ (1.0 equiv), and PCy₃HBF₄ (3.0 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Tetrahydrofuran (0.8 mL) was added with vigorous stirring at room temperature, and the reaction mixture was stirred for the indicated time at room temperature. An aliquot was taken and diluted with MeOH. The sample was analyzed by ESI/MS-(+) to detect possible reaction intermediates. We thank Dr. Roman Brukh for help with recording the ESI/MS-(+) spectra. Note that the exact configuration and structure of the complexes has yet to be determined.

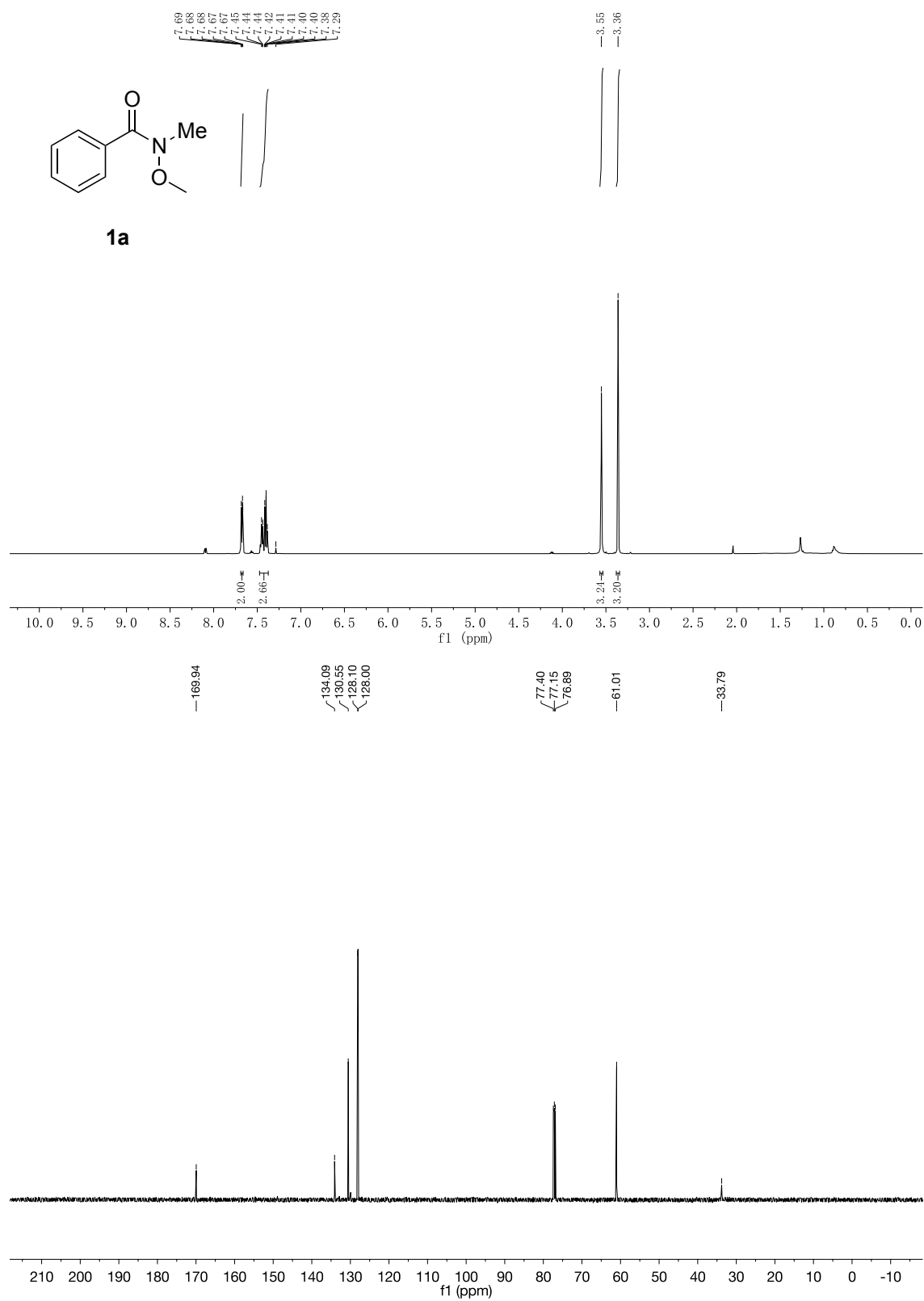
Figure SI-1. ESI/MS-(+) Spectrum for the Reaction of **1d** with Pd(OAc)₂ and PCy₃HBF₄ with Assigned Intermediates.

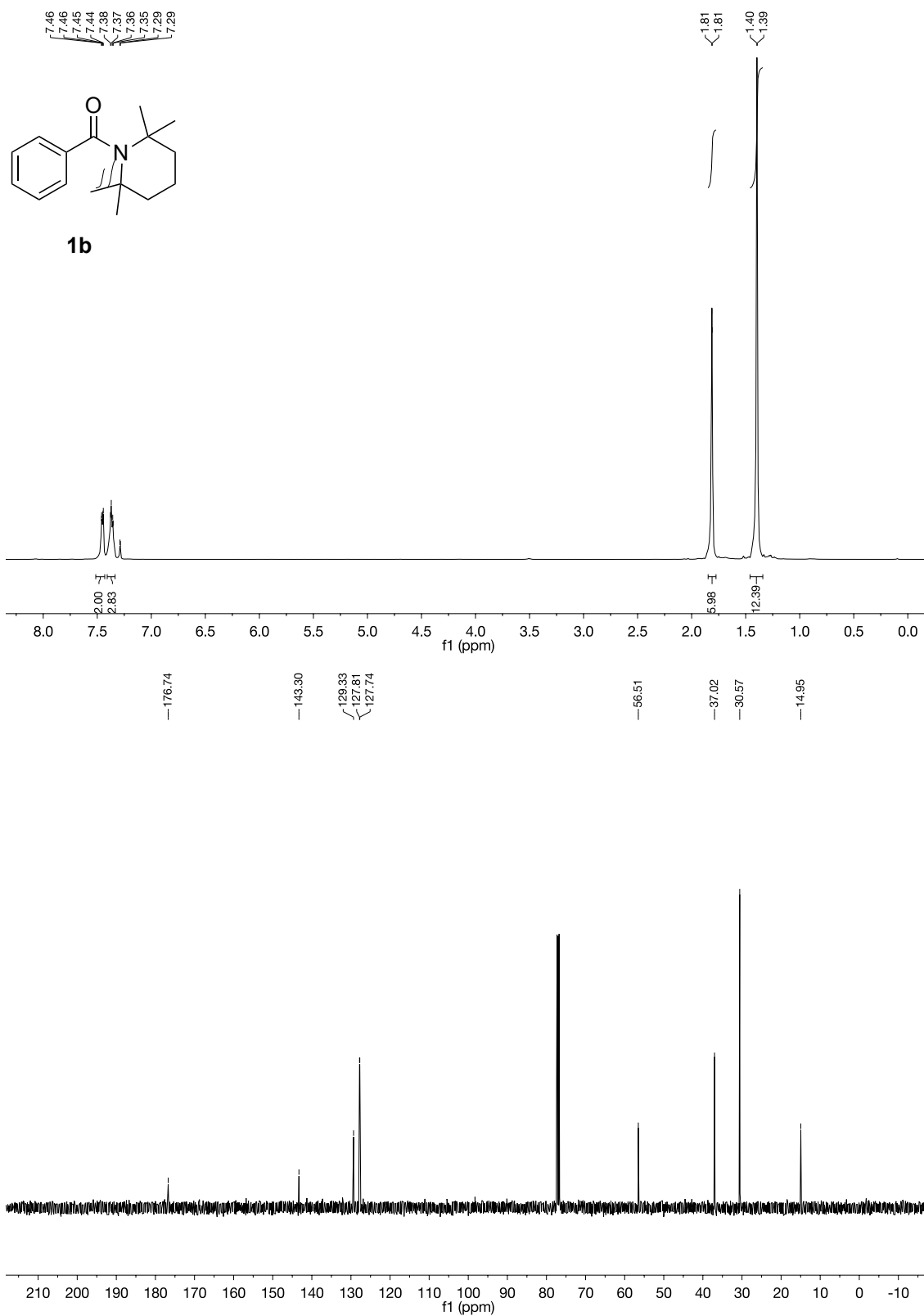


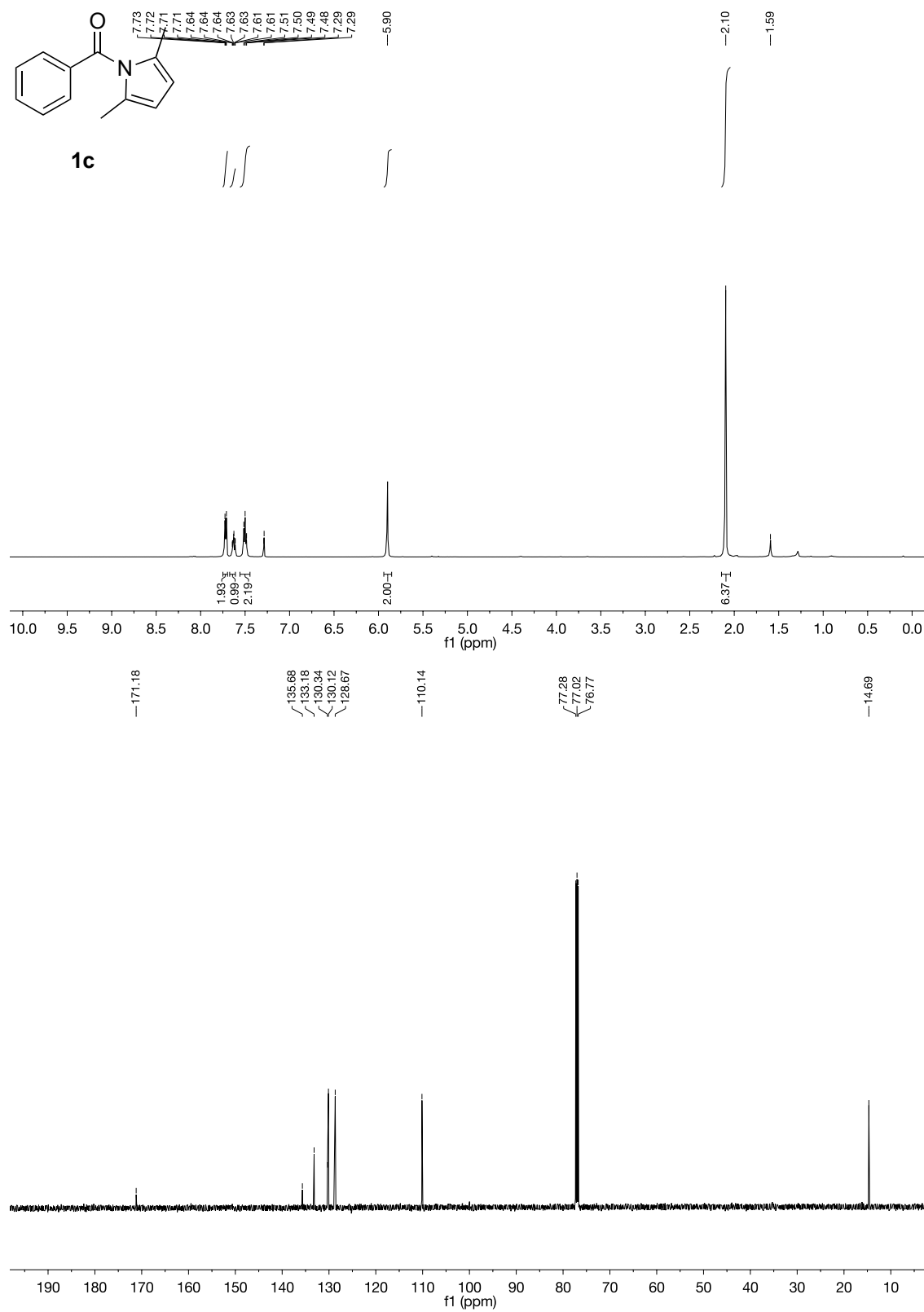
References

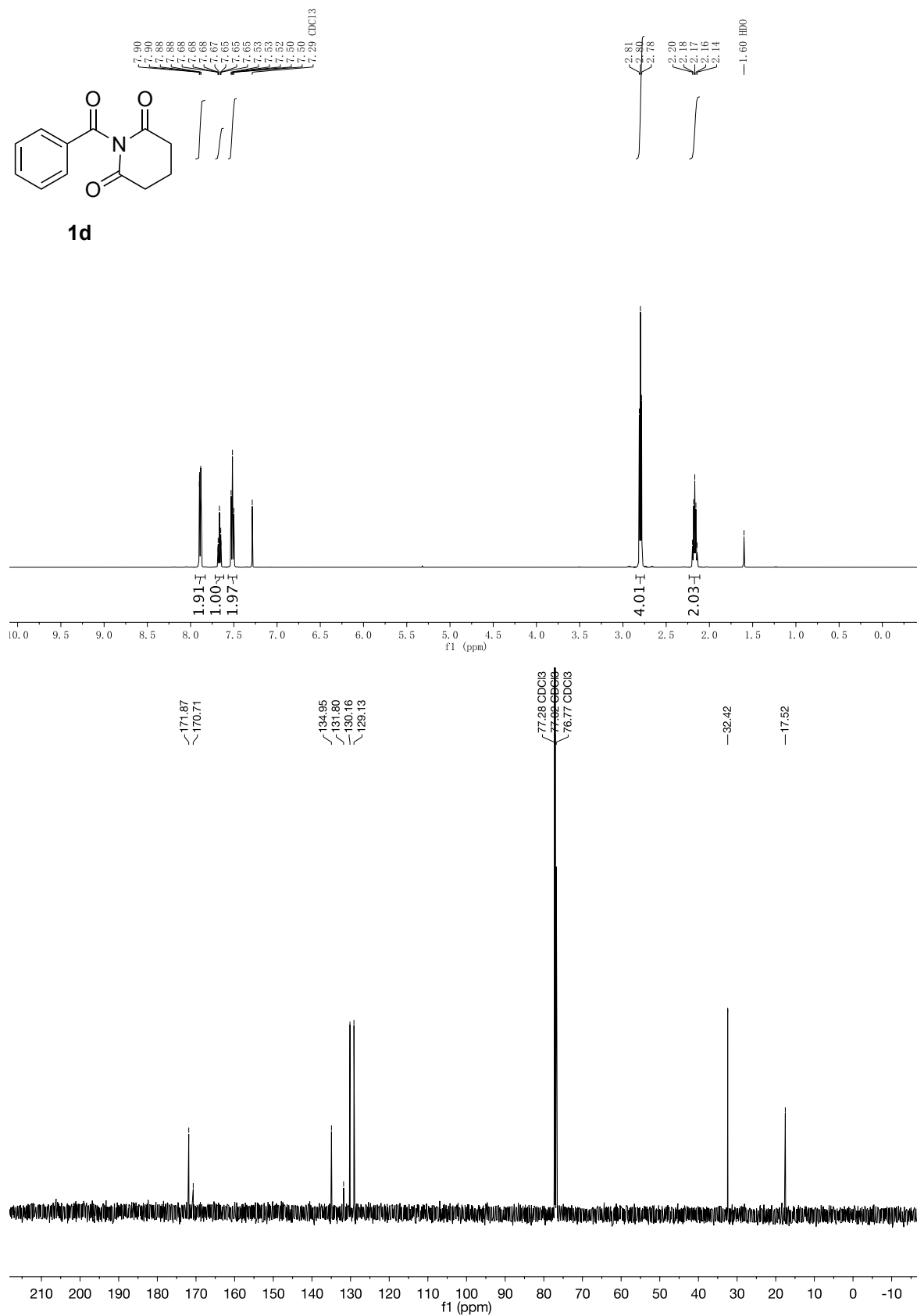
1. B. M. Trost and I. Fleming, *Comprehensive Organic Synthesis*, Pergamon Press: 1991.
2. S. Hirner, O. Panknin, M. Edefuhr and P. Somfai, *Angew. Chem. Int. Ed.*, **2008**, *47*, 1907.
3. A. J. Bennet, V. Somayaji, R. S. Brown and B. D. Santarsiero, *J. Am. Chem. Soc.*, **1991**, *113*, 7563.
4. M. Hutchby, C. E. Houlden, M. F. Haddow, S. N. G. Tyler, G. C. Lloyd-Jones and K. I. Booker-Milburn, *Angew. Chem. Int. Ed.*, **2012**, *51*, 548.
5. R. A. Jones and R. L. Laslett, *Aust. J. Chem.*, **1964**, *17*, 1056.
6. S. Hanada, E. Tsutsumi, Y. Motoyama and H. Nagashima, *J. Am. Chem. Soc.*, **2009**, *131*, 15032.
7. A. W. Titherley and W. L. Hicks, *J. Chem. Soc. Trans.*, **1906**, *89*, 708.
8. G. Heller and P. Jacobsohn, *Chem. Ber.*, **1921**, *54*, 1107.
9. N. Rabjohn, M. F. Drumm and R. L. Elliott, *J. Am. Chem. Soc.*, **1956**, *78*, 1631.
10. E. M. Kaiser and H. H. Yun, *J. Org. Chem.*, **1970**, *35*, 1348.
11. V. Stella and T. Higuchi, *J. Pharm. Sci.*, **1973**, *62*, 968.
12. C. Palomo, *Synthesis*, **1981**, 993.
13. V. A. Soloshonok, C. Cai and V. J. Hruby, *J. Org. Chem.*, **2000**, *65*, 6688.
14. C. A. Goodman, J. B. Eagles, L. Rudahindwa, C. G. Hamaker and S. R. Hitchcock, *Synth. Commun.*, **2013**, *43*, 2155.
15. L. J. Goossen and K. Ghosh, *Angew. Chem. Int. Ed.*, **2001**, *40*, 3458.
16. L. J. Goossen and K. Ghosh, *Eur. J. Org. Chem.*, **2002**, 3254.
17. R. Kakino, I. Shimizu, A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **2001**, *74*, 371.
18. R. Kakino, S. Yasumi, I. Shimizu, A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **2002**, *75*, 137.
19. R. Kakino, H. Narahashi, I. Shimizu, A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **2002**, *75*, 1333.
20. J. H. Espenson, *Chemical Kinetics and Reaction Mechanisms*, McGraw-Hill: 2002.
21. L. S. Santos, *Eur. J. Org. Chem.*, **2008**, 235.
22. A. O. Aliprantis and J. W. Canary, *J. Am. Chem. Soc.*, **1994**, *116*, 6985.
23. J. M. Brown and K. K. Hii, *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 657.

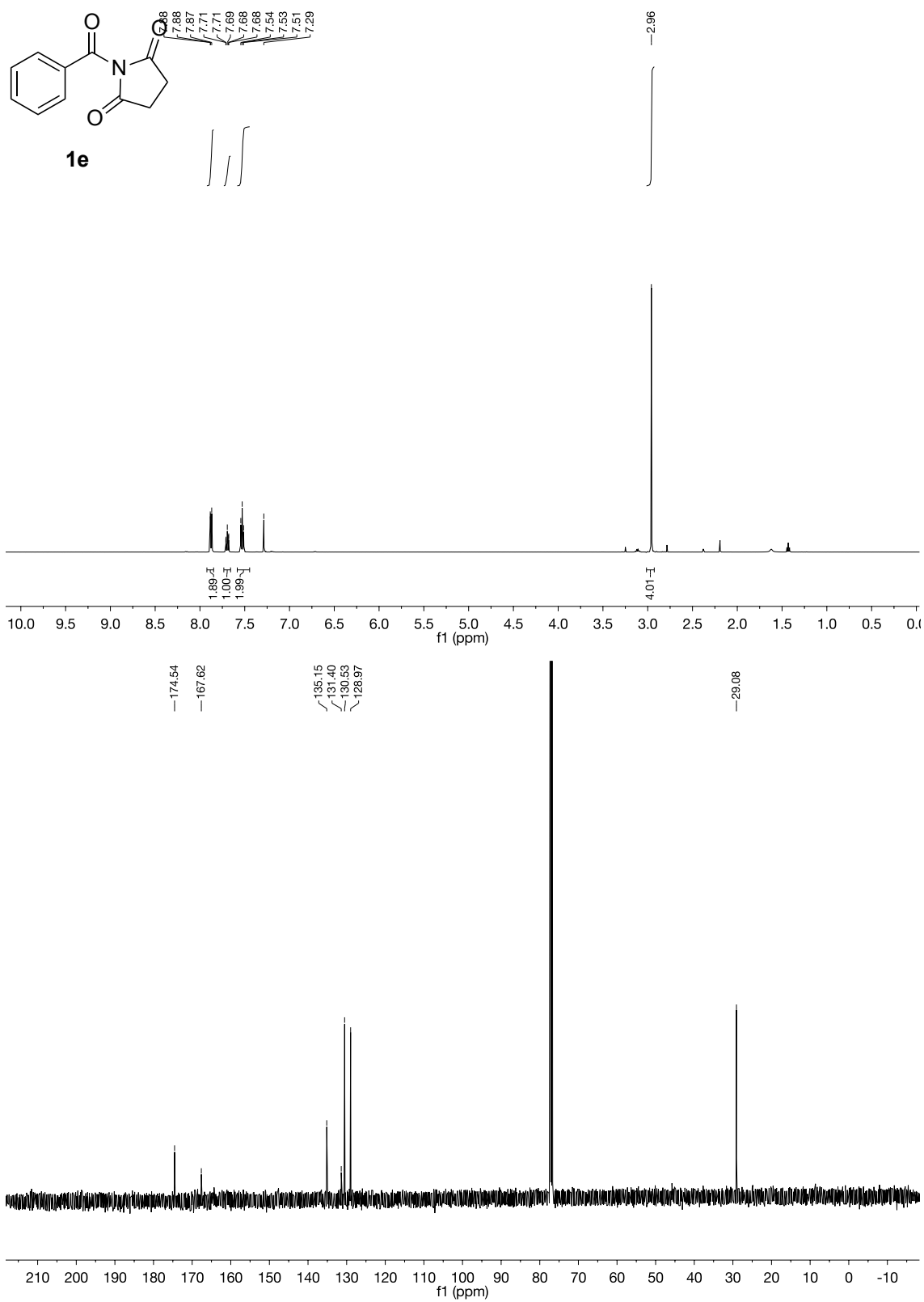
24. M. Arndt, K. S. M. Salih, A. Fromm, L. J. Goossen, F. Menges and G. Niedner-Schattenburg, *J. Am. Chem. Soc.*, **2011**, *133*, 7428.
25. B. Skillinghaug, C. Sköld, J. Rydfjord, F. Svensson, M. Behrends, J. Sävmarker, P. J. R. Sjöberg and M. Larhed, *J. Org. Chem.*, **2014**, *79*, 12018.

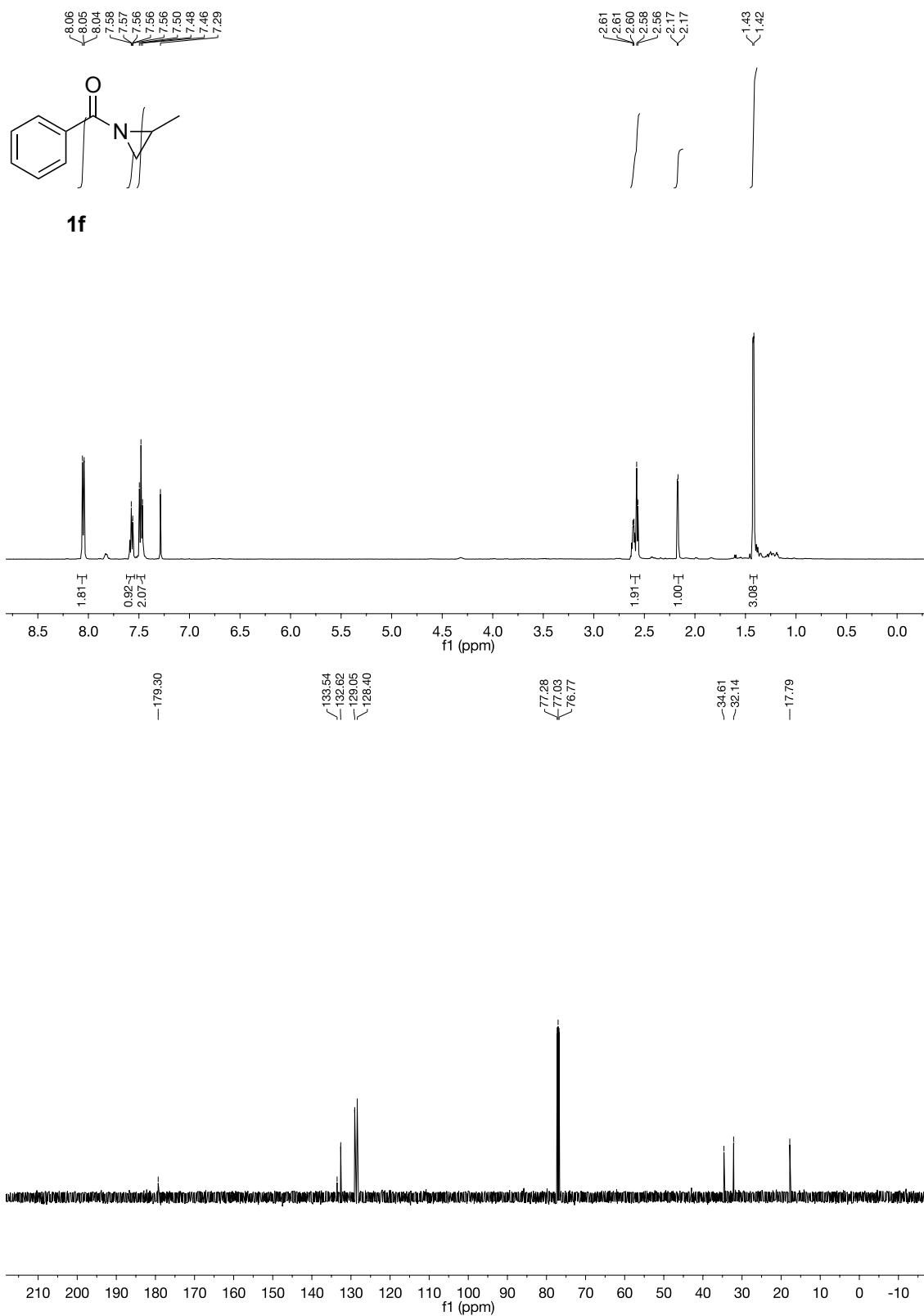


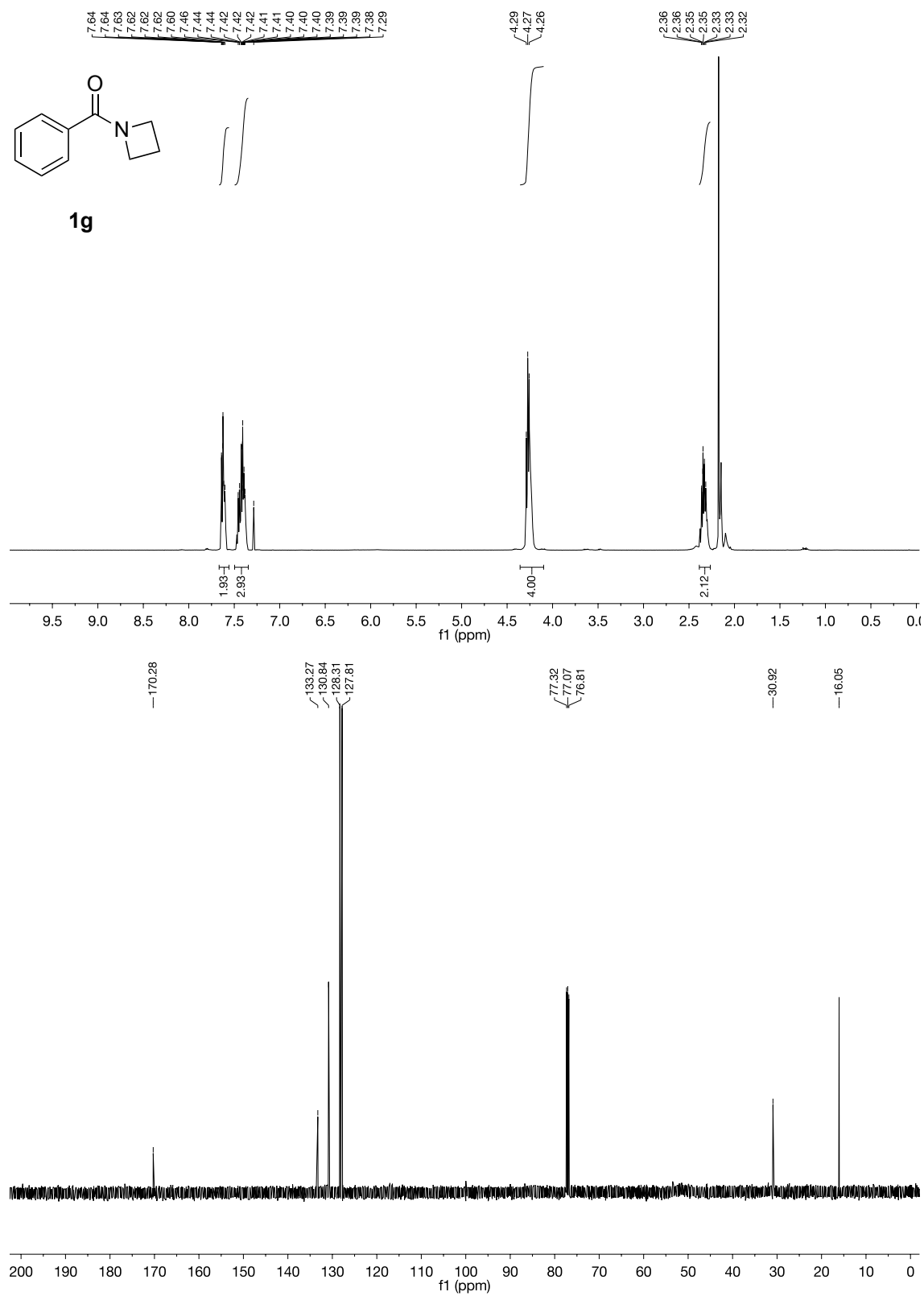


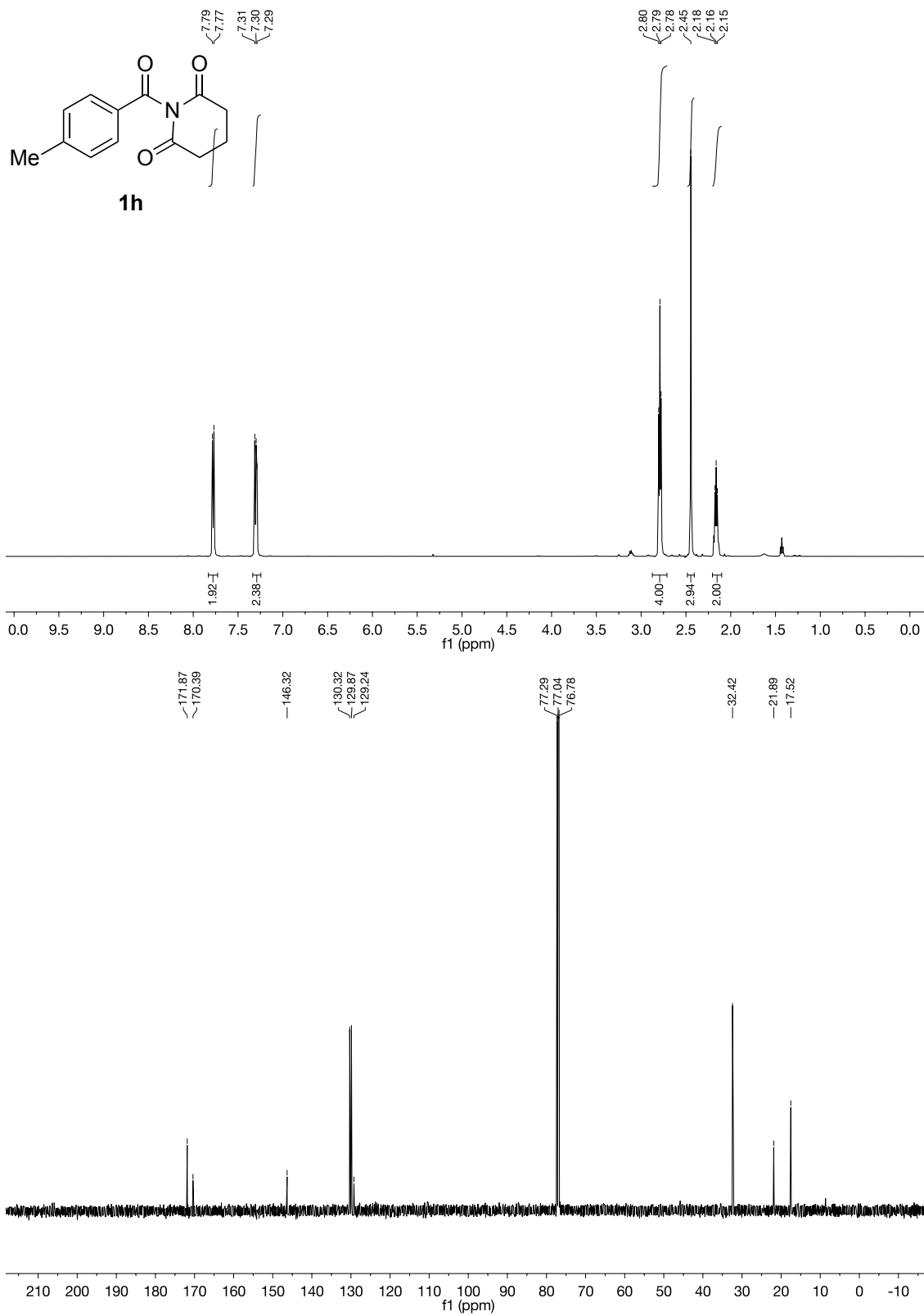


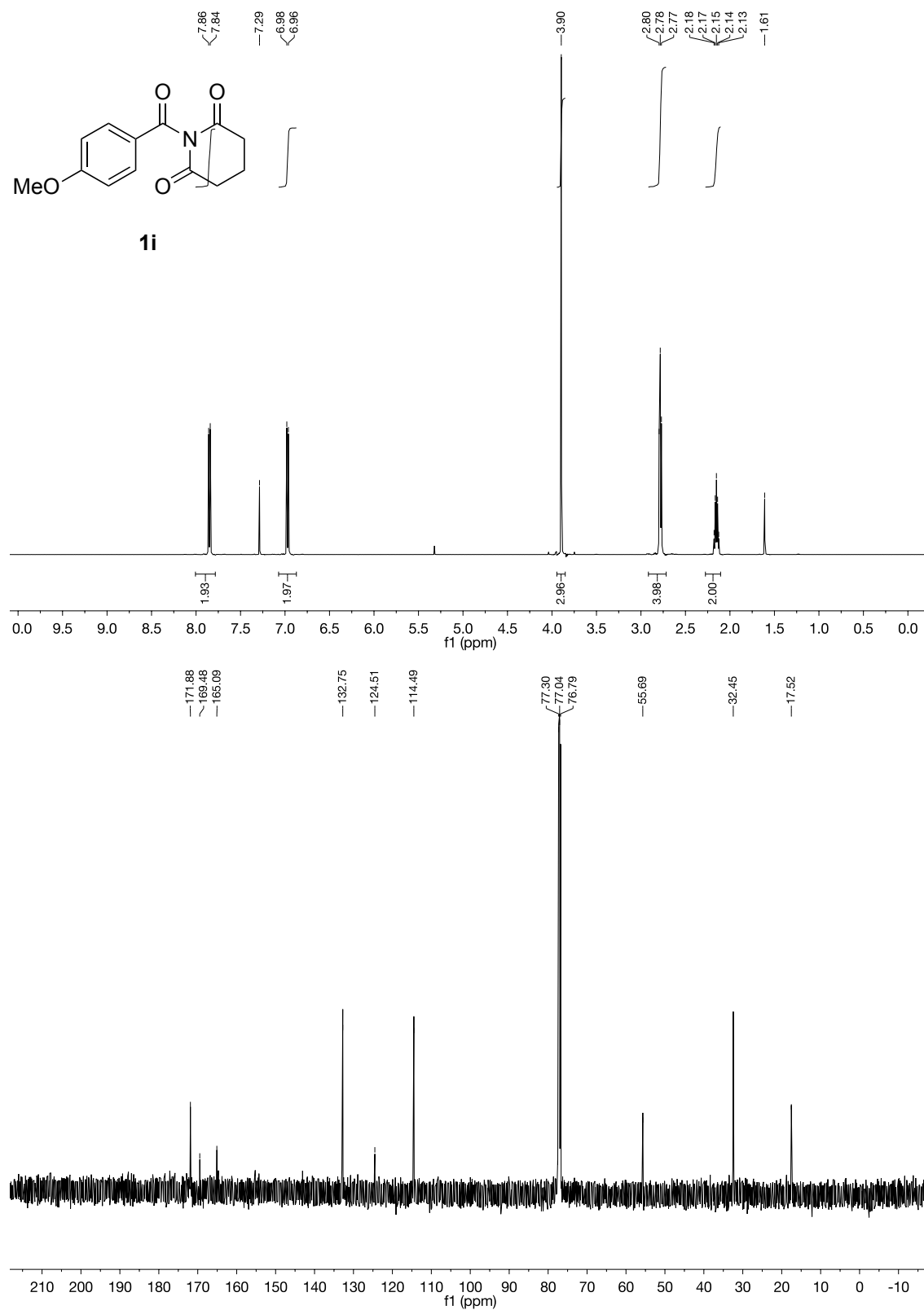


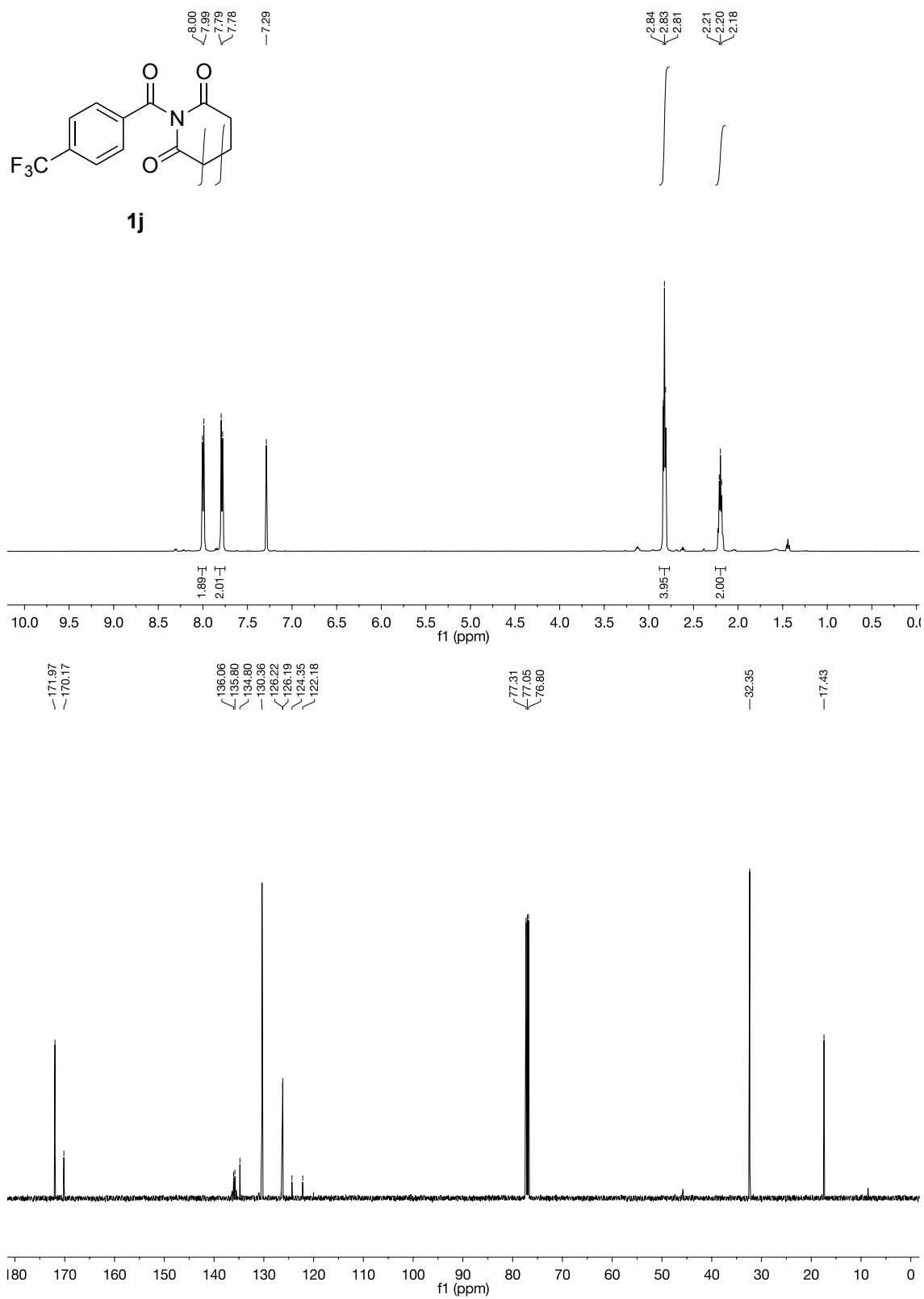


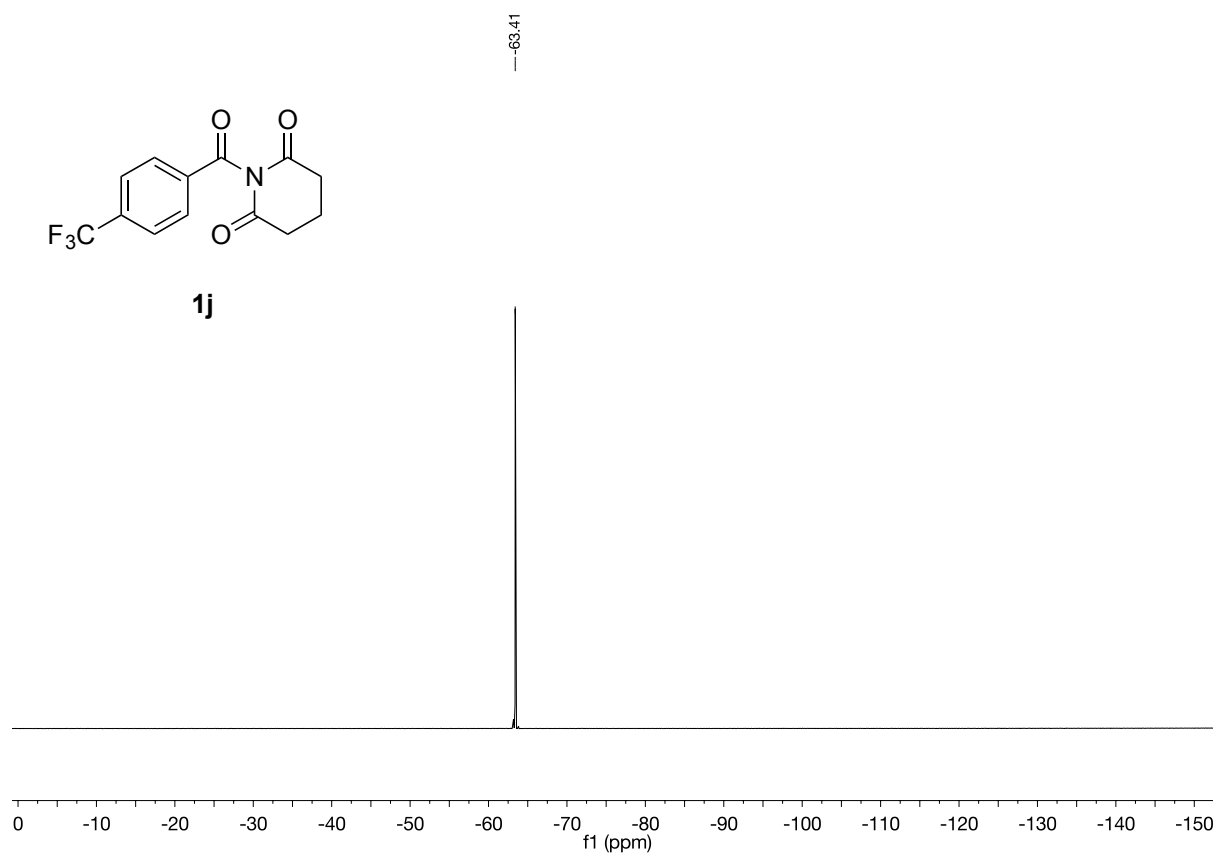


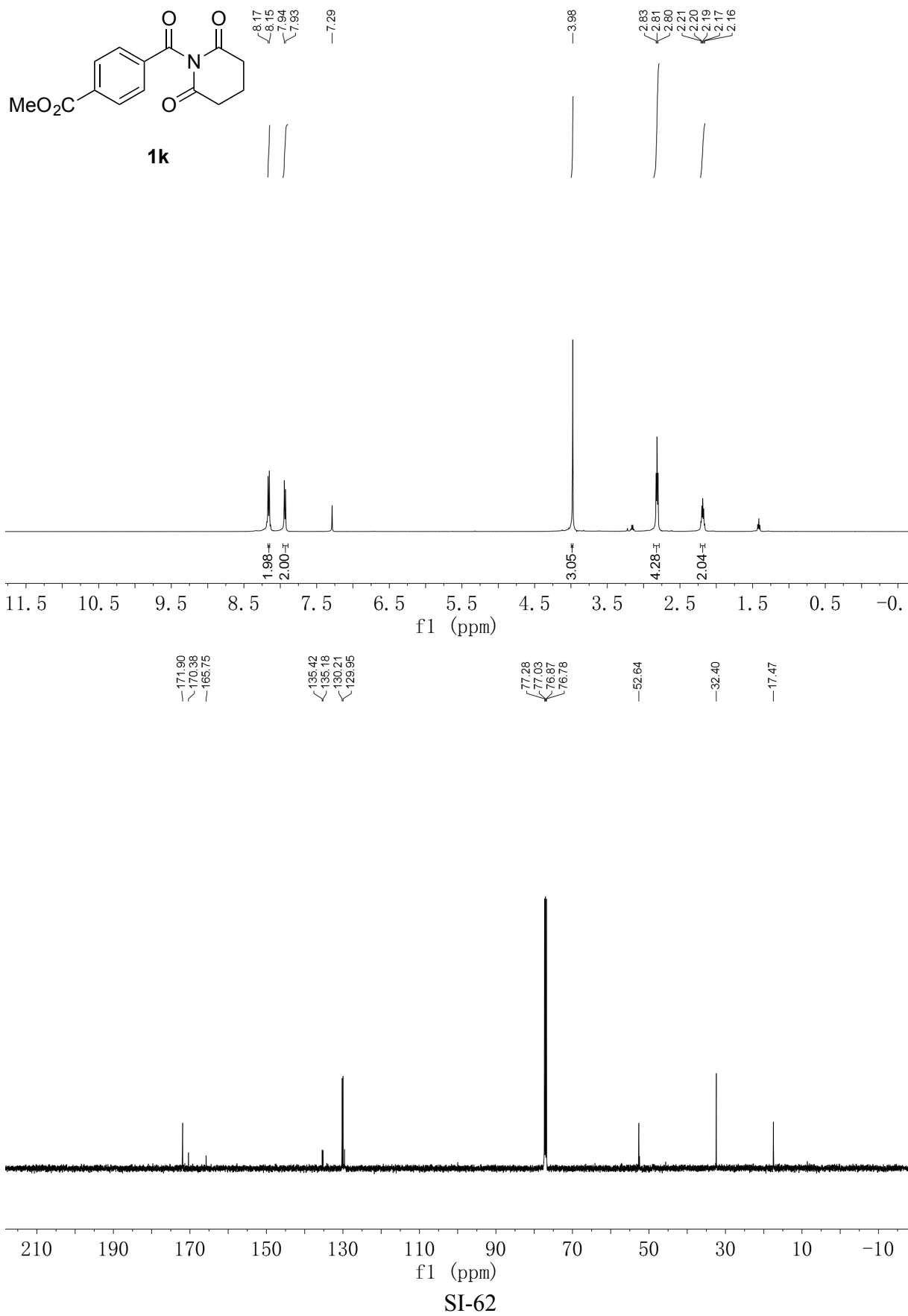


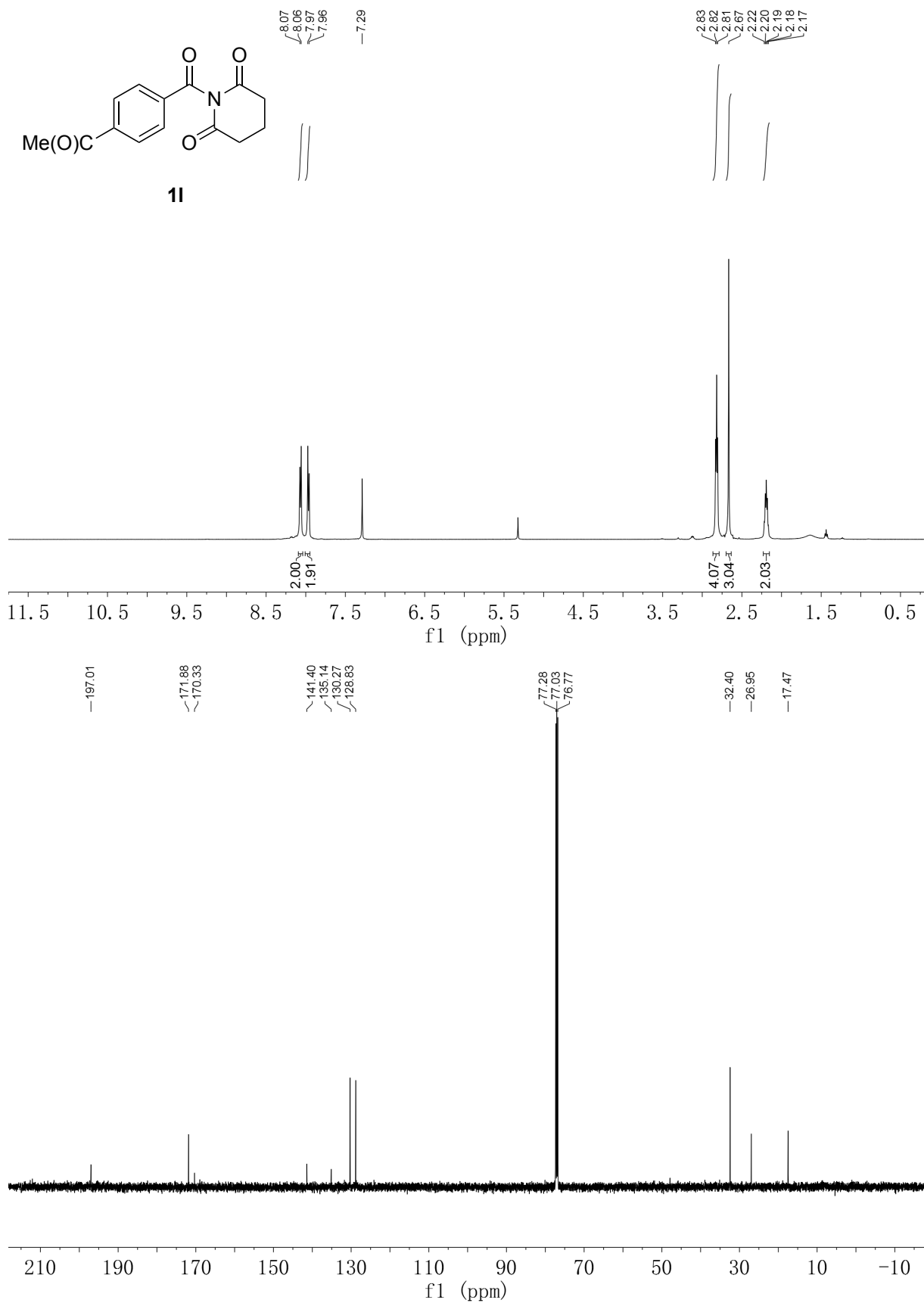


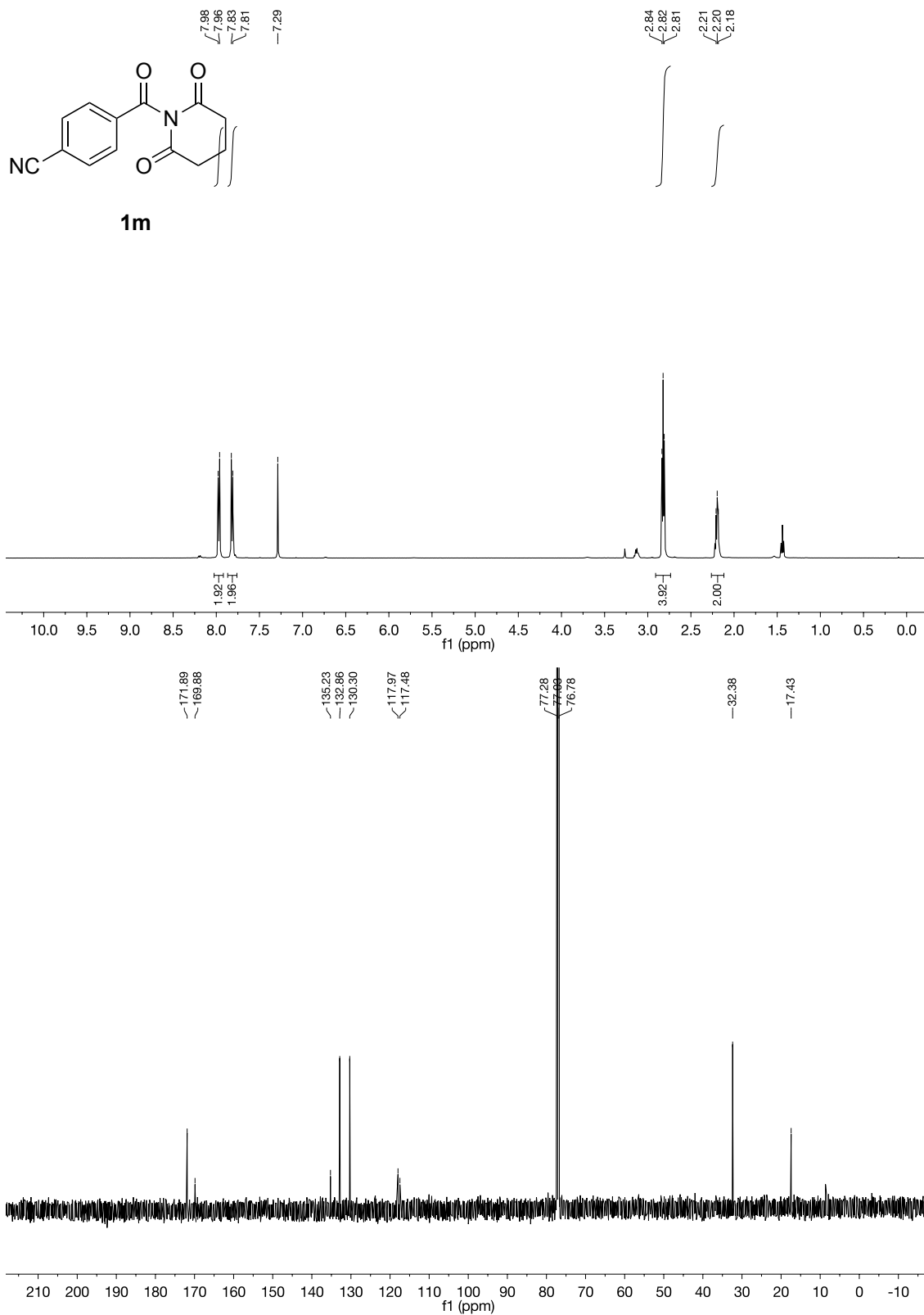


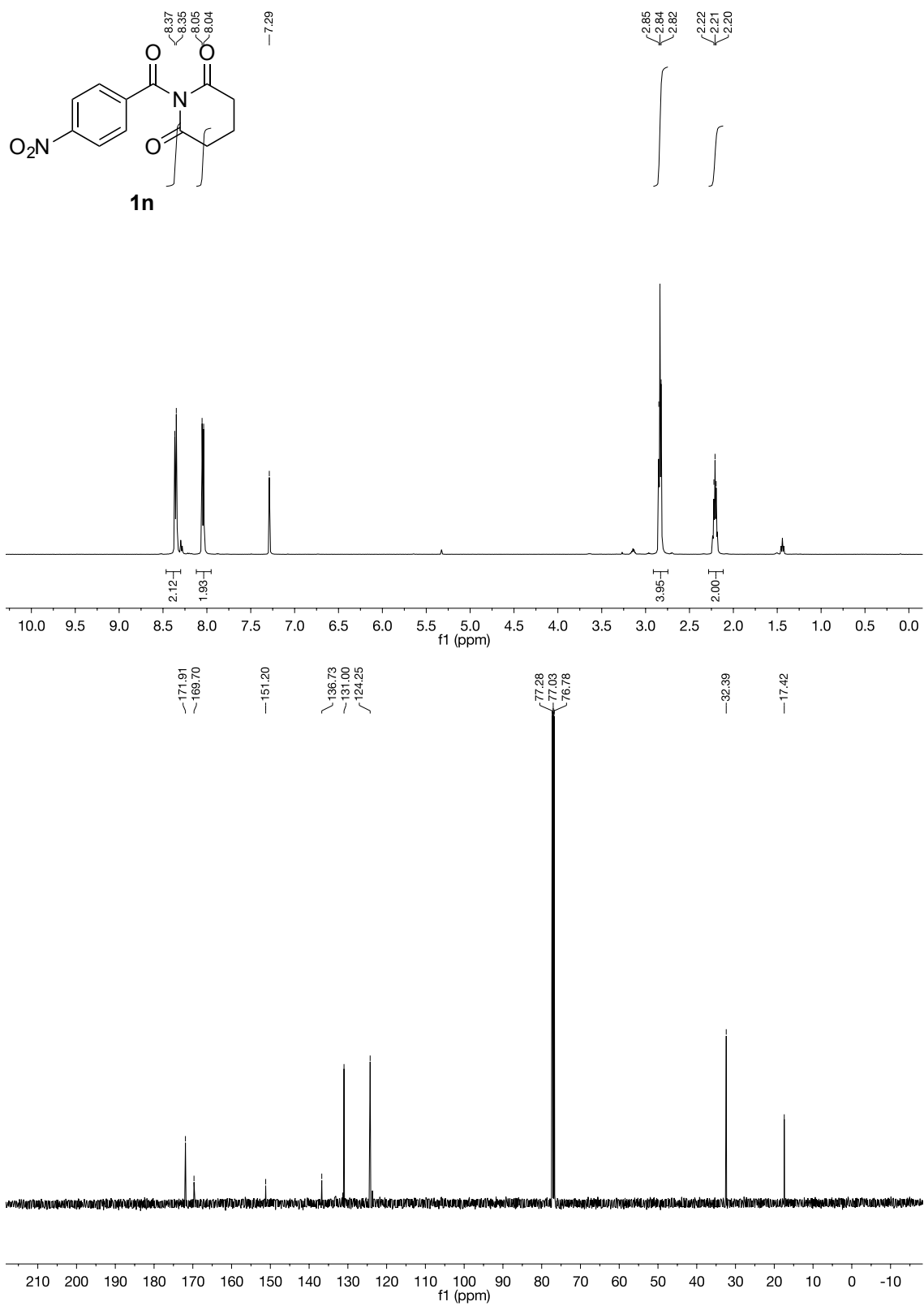


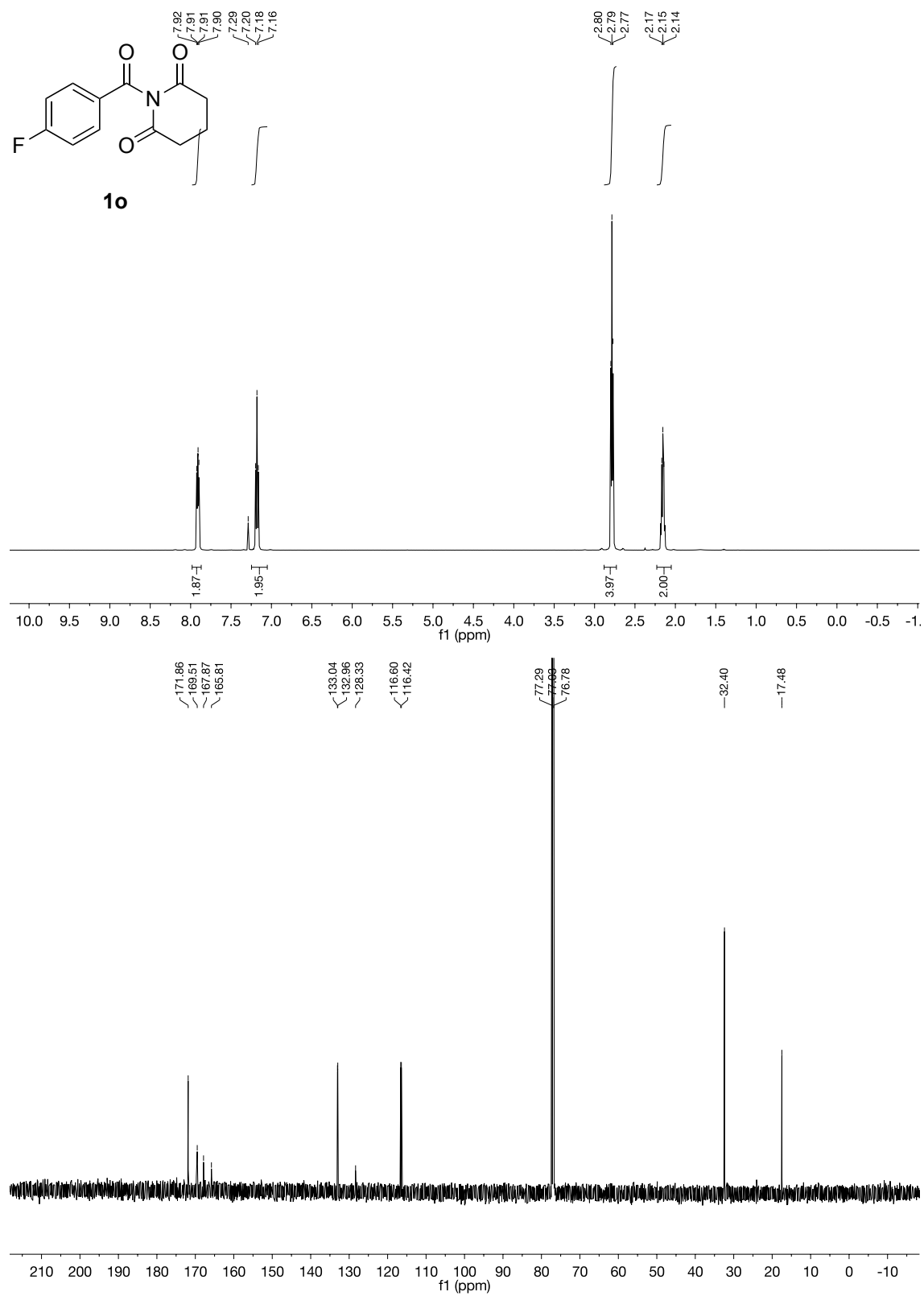


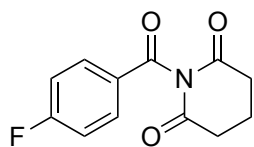




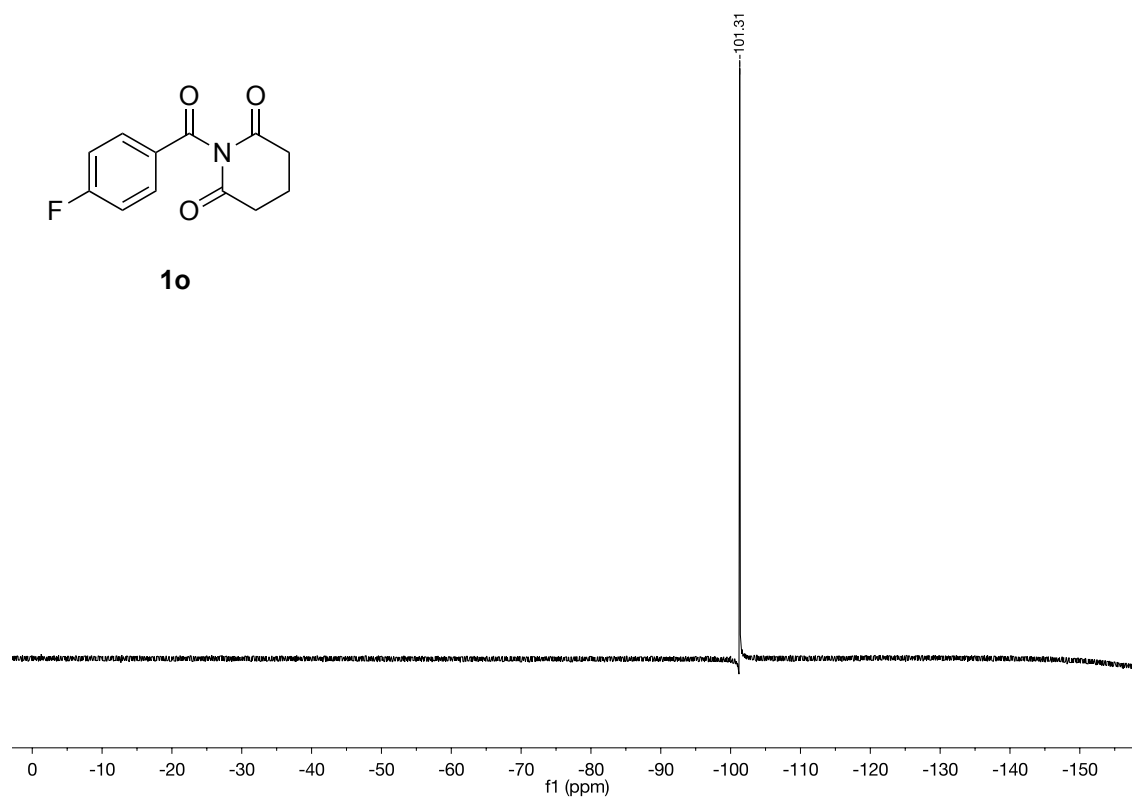


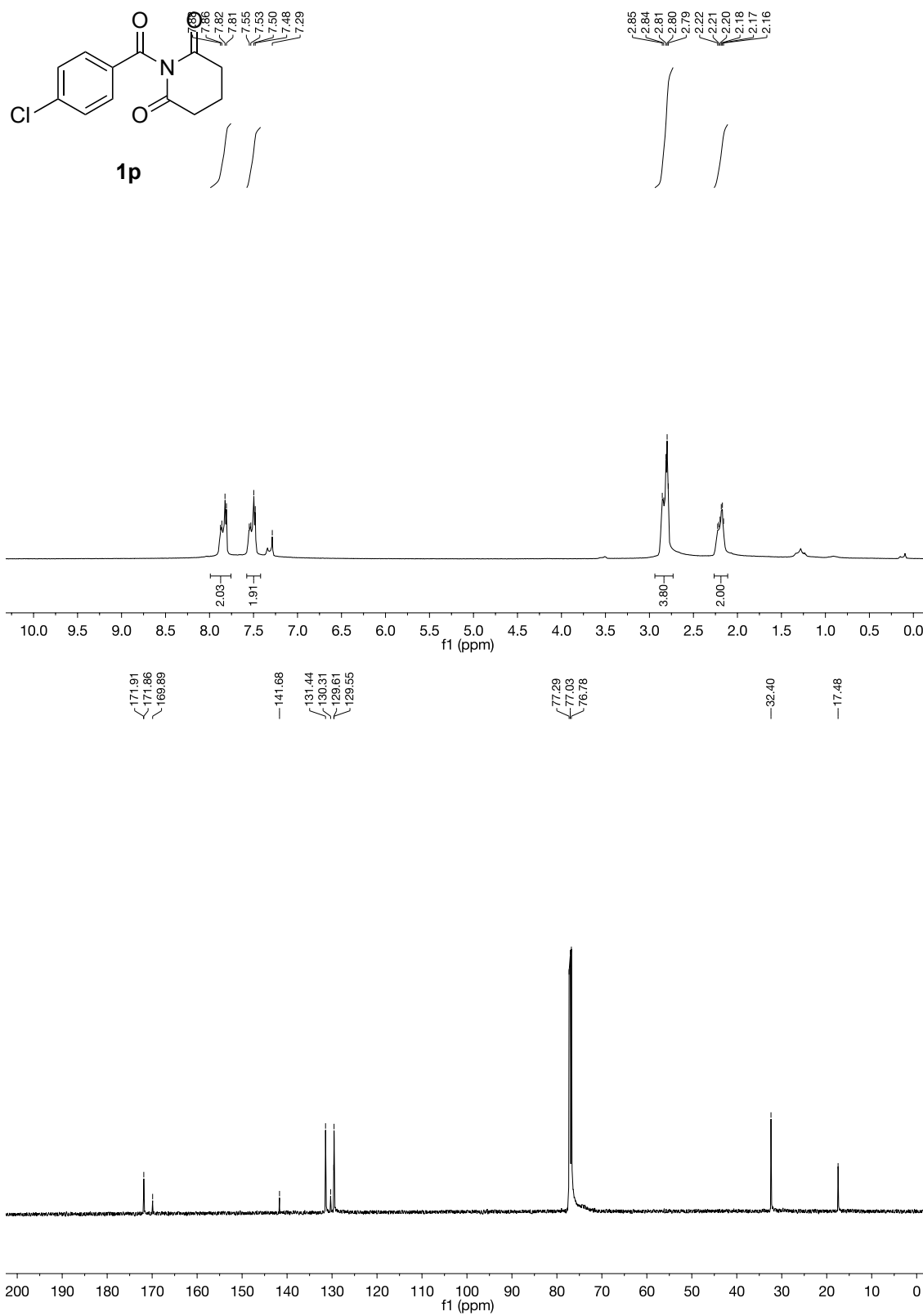


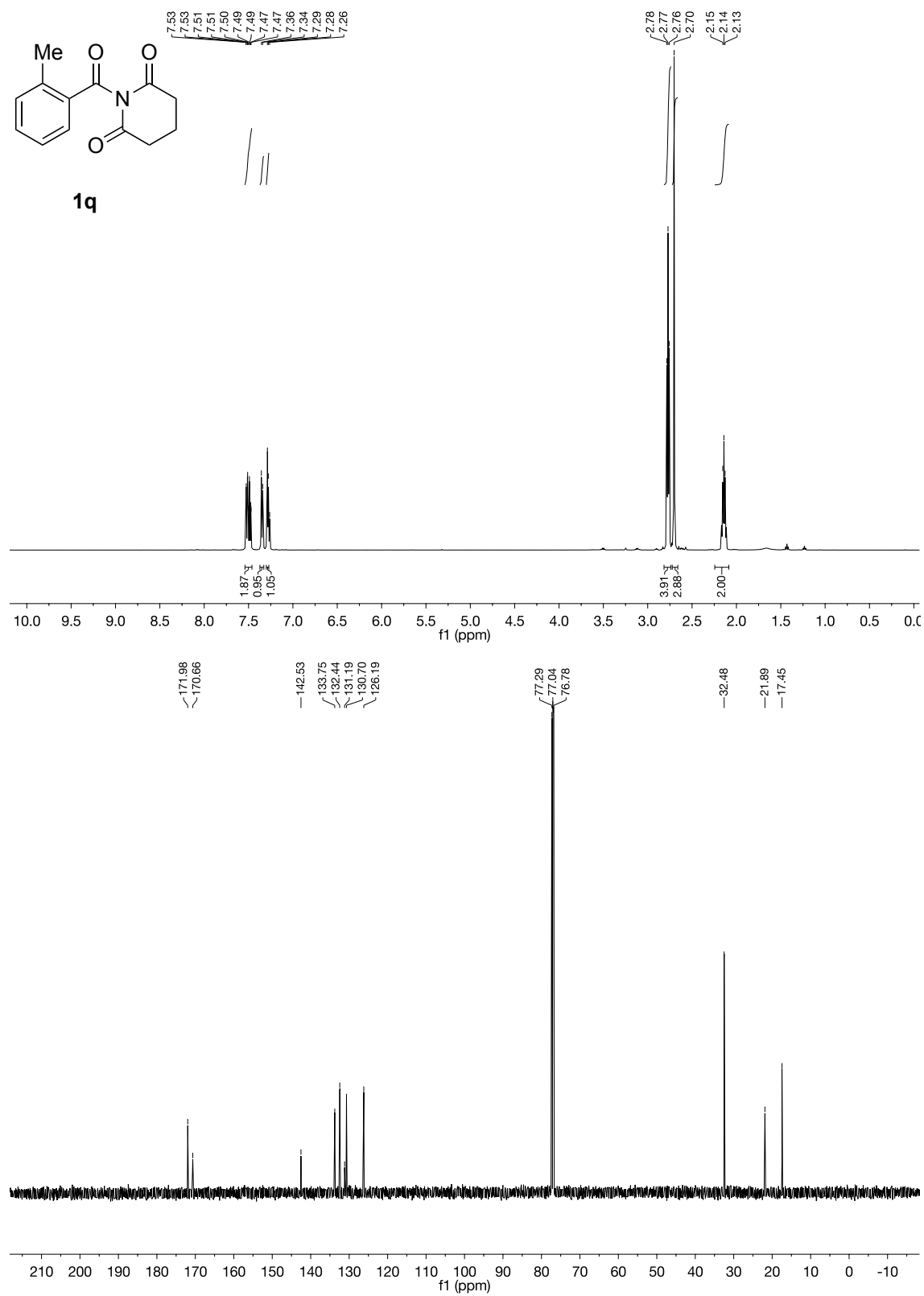


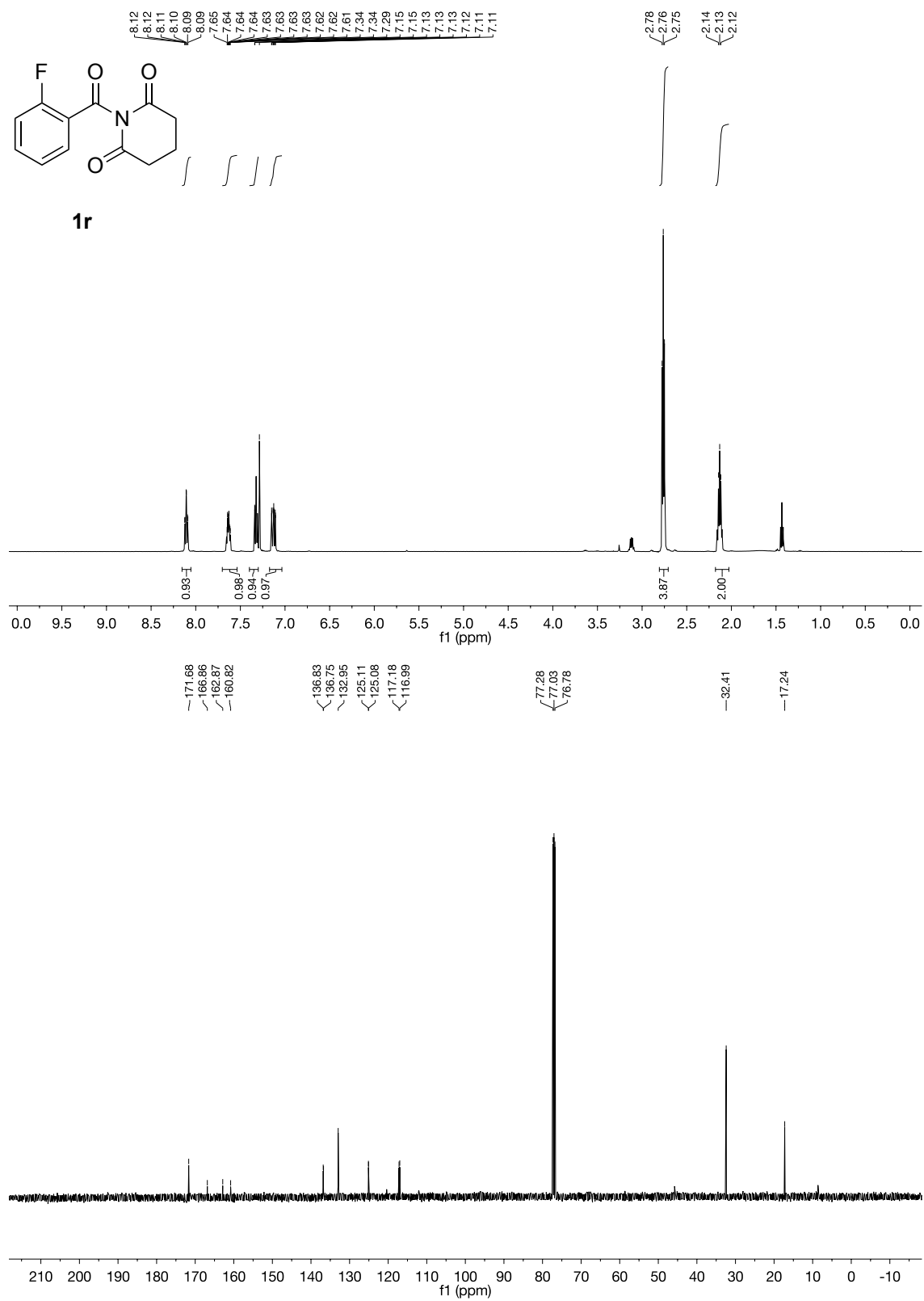


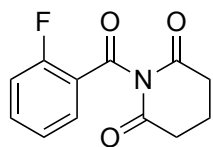
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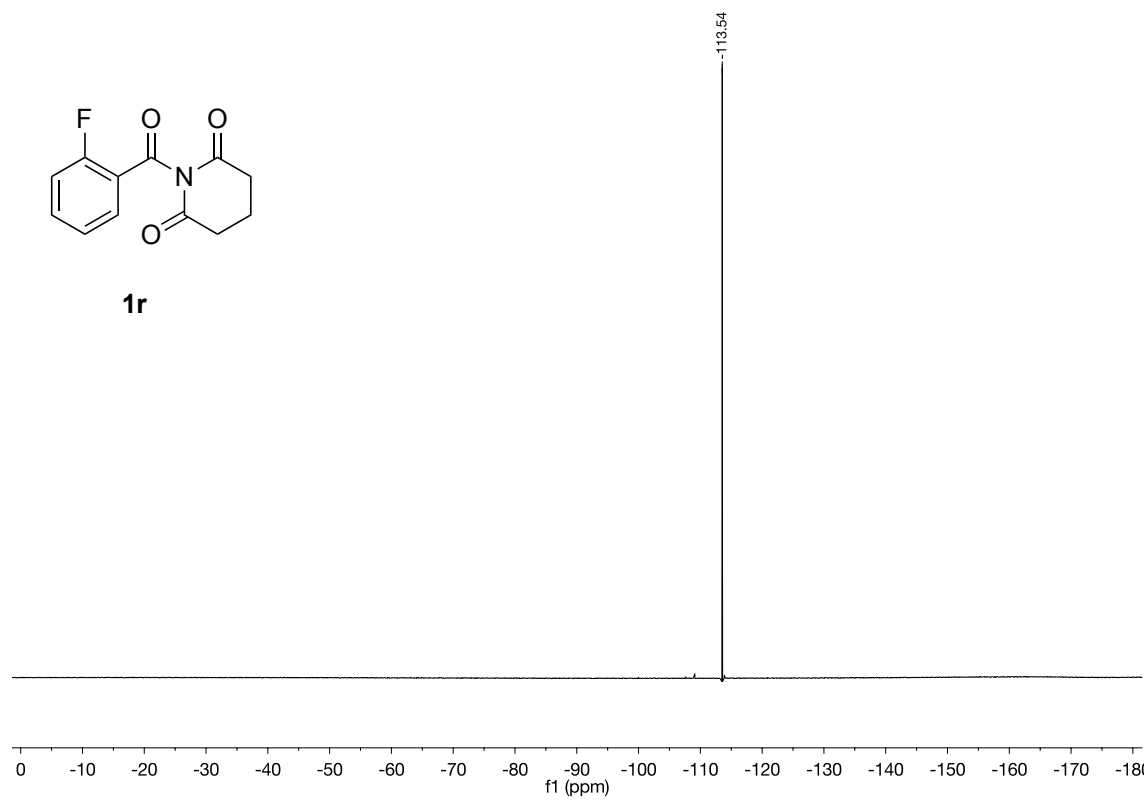


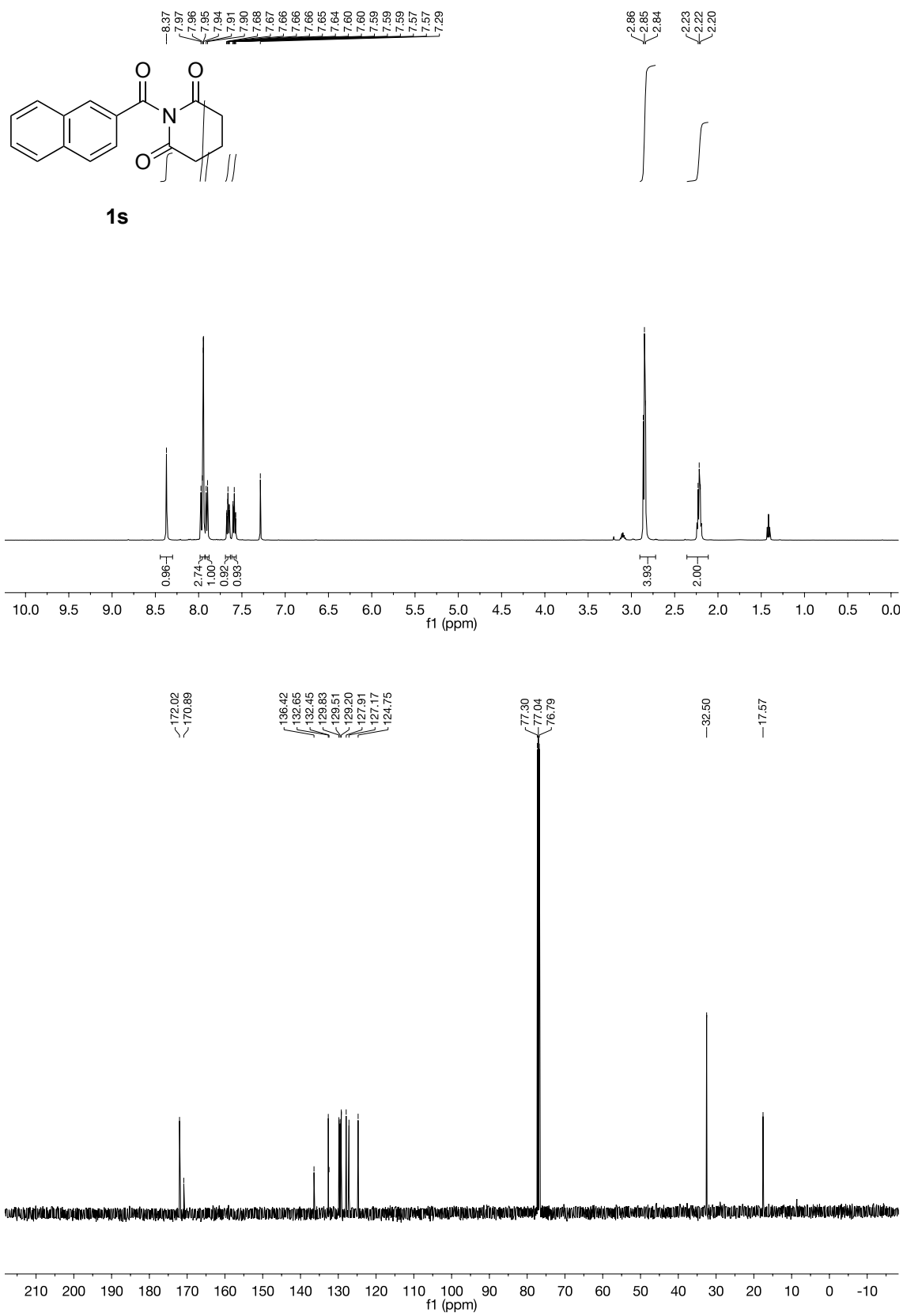


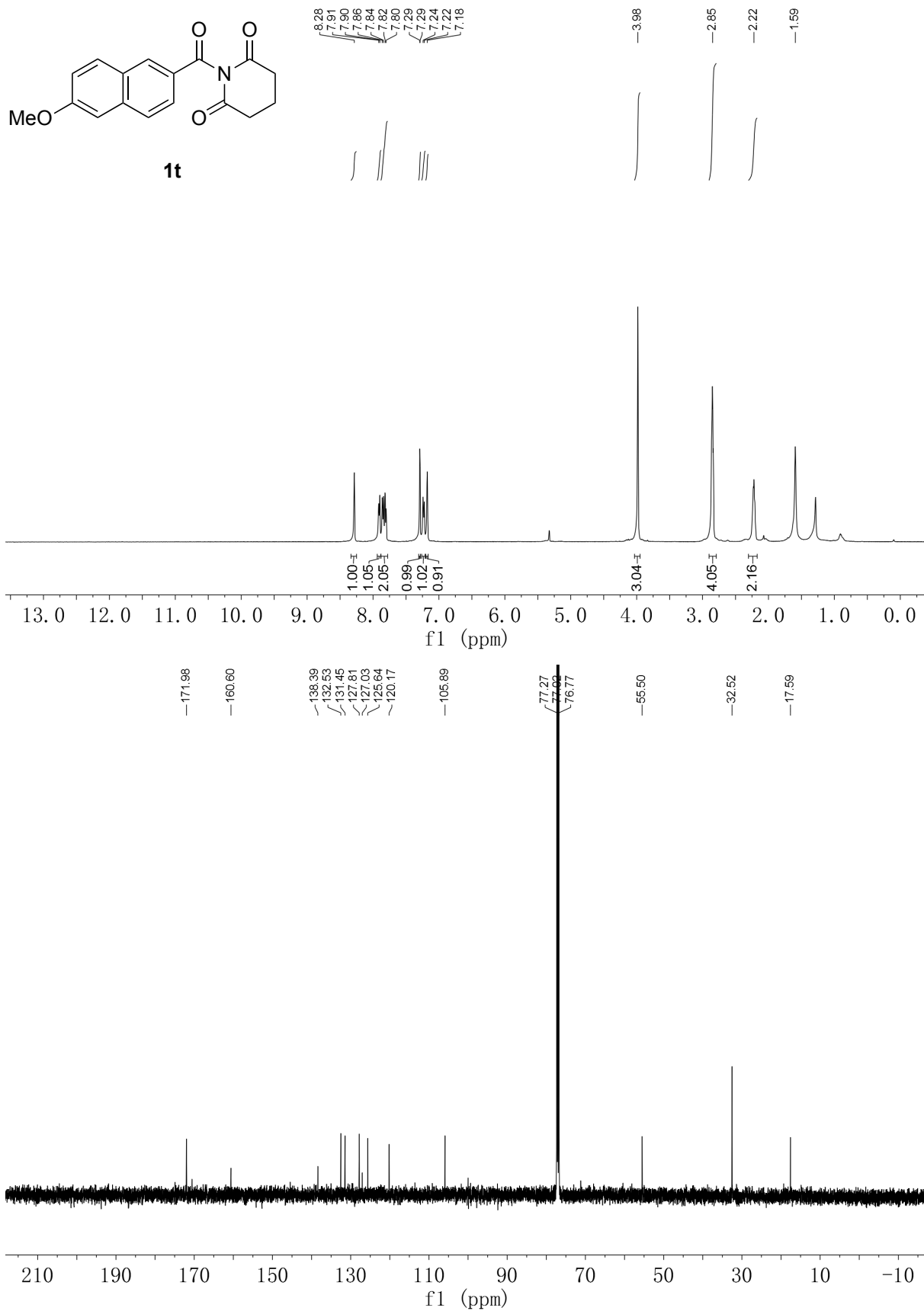


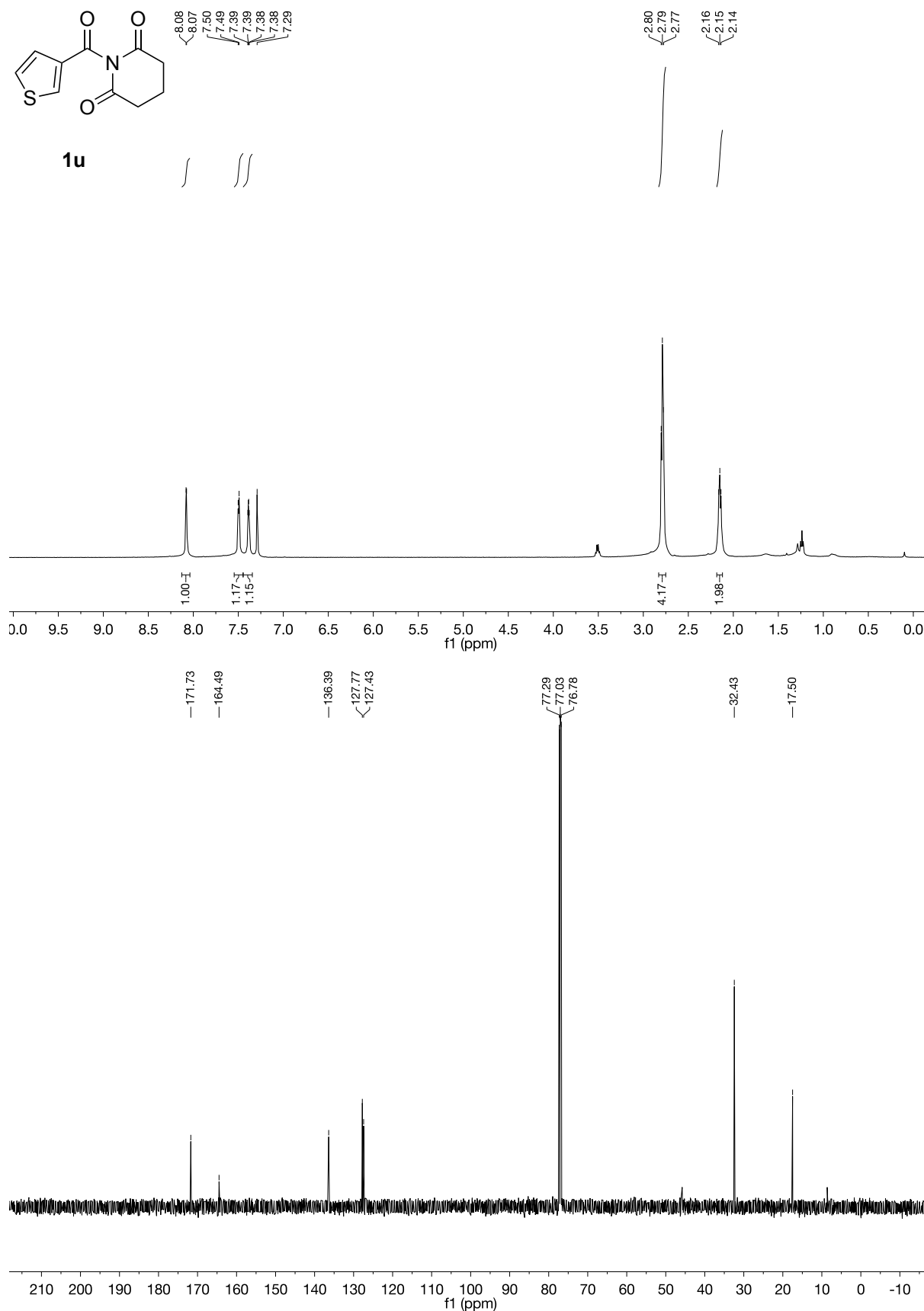


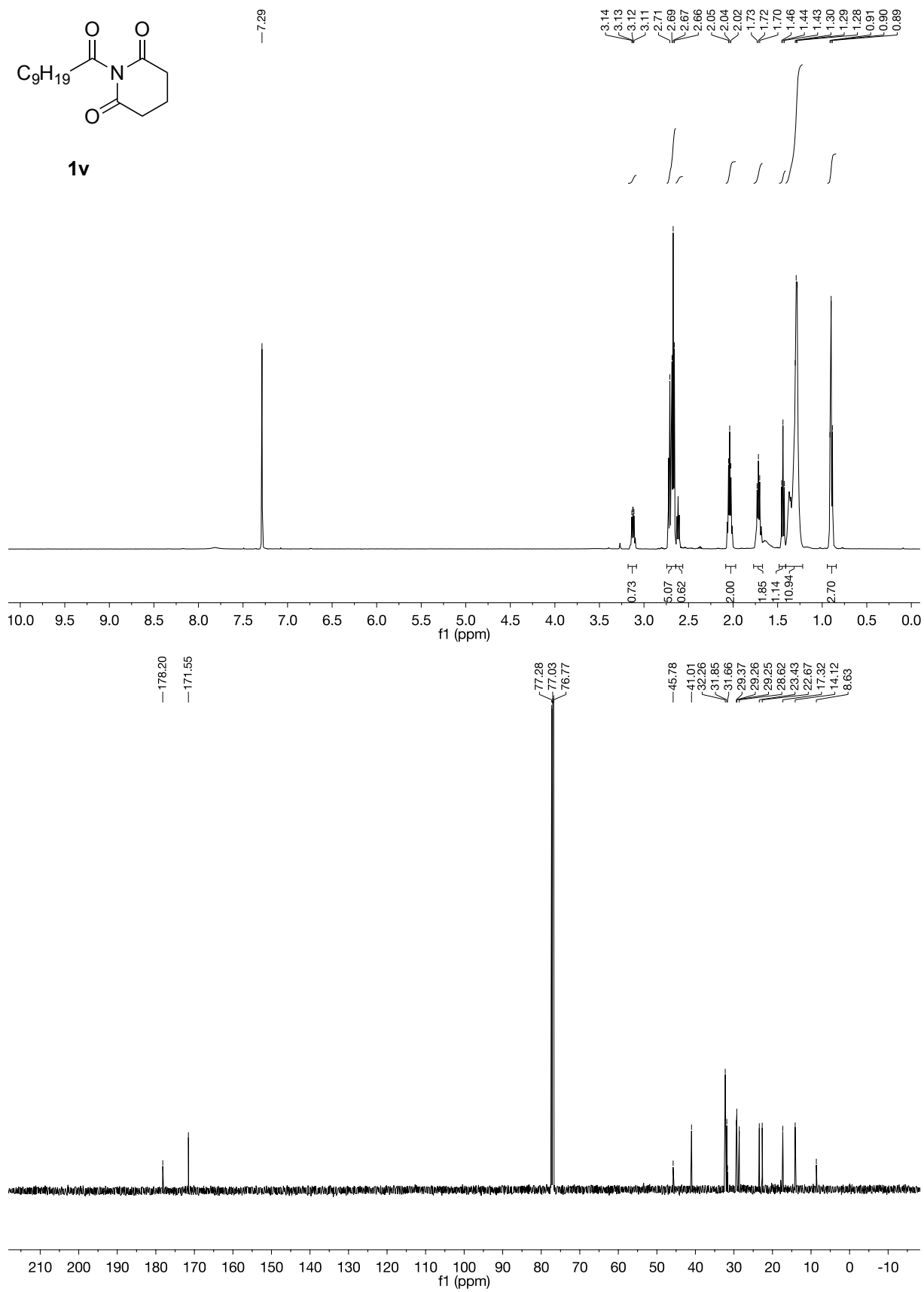
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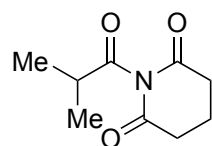




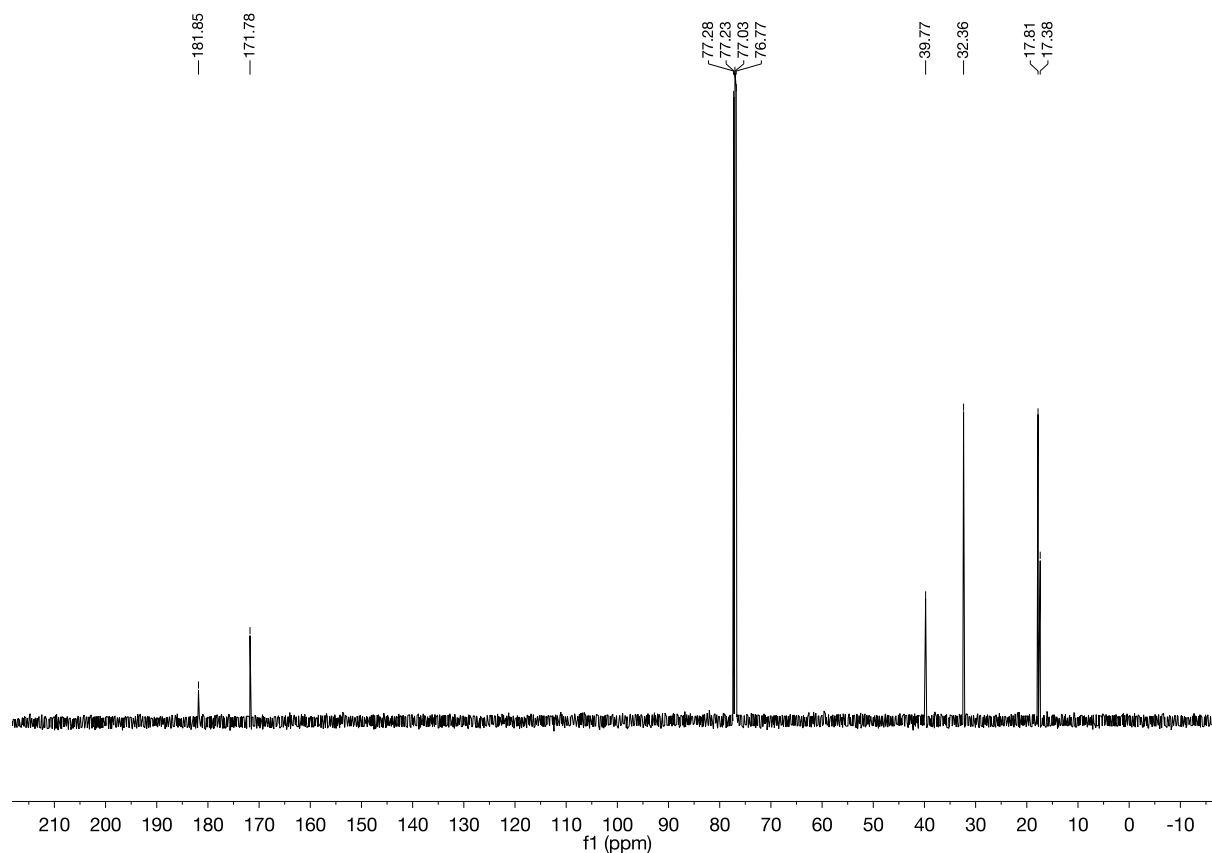
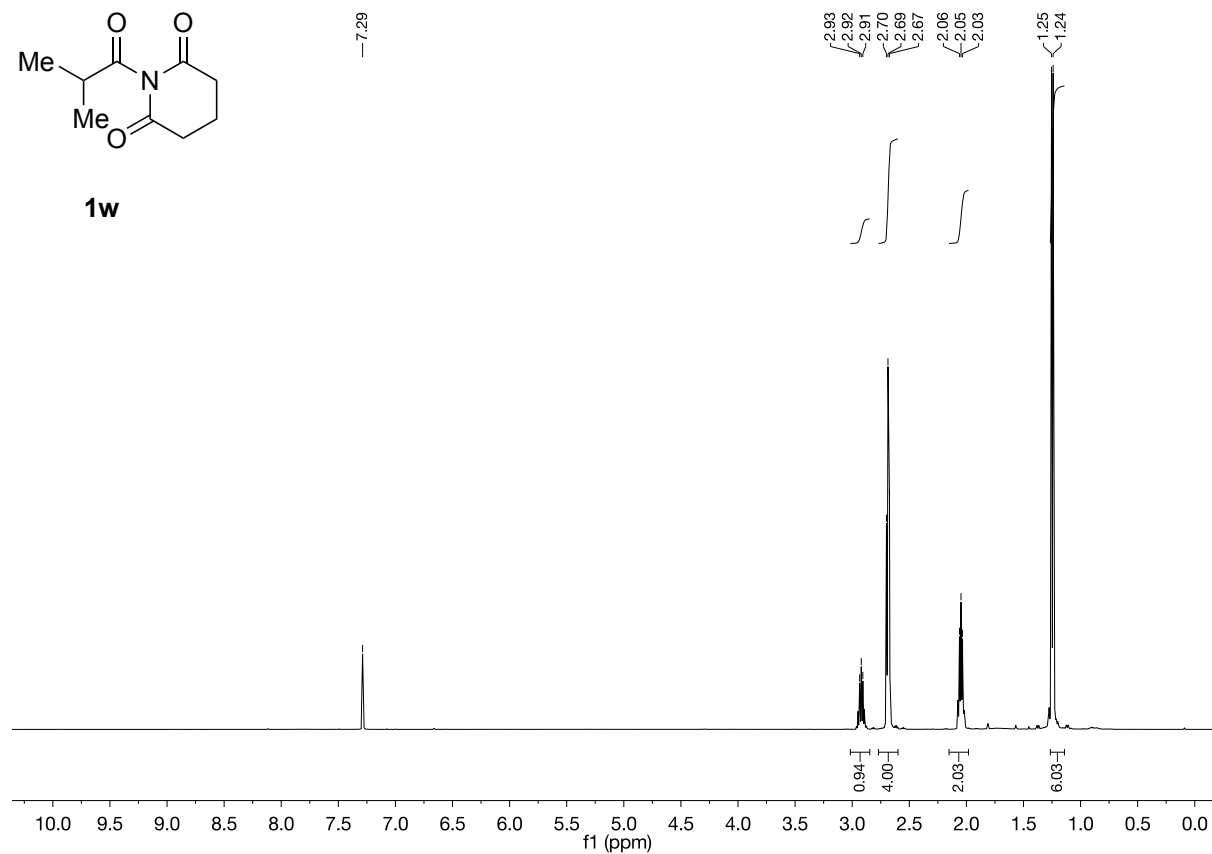


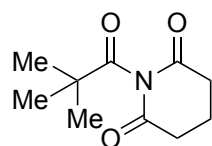




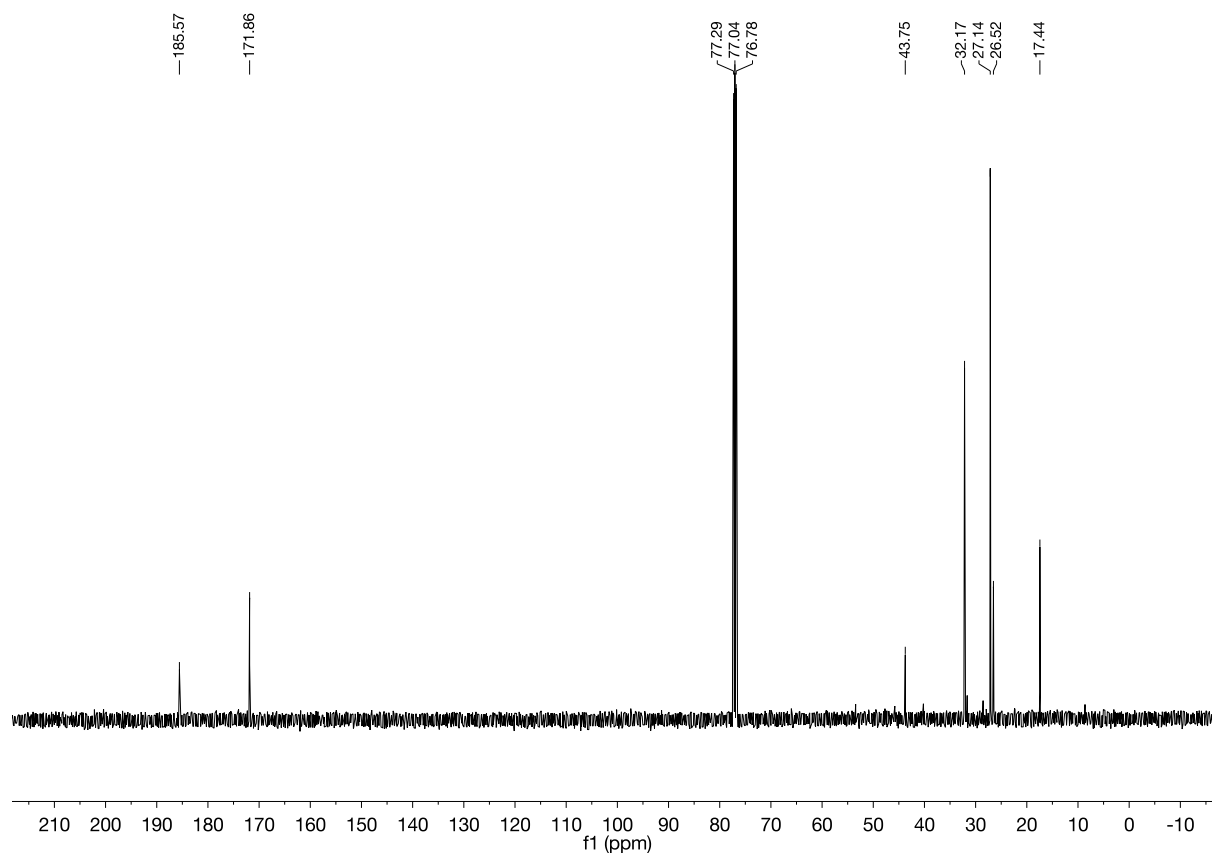
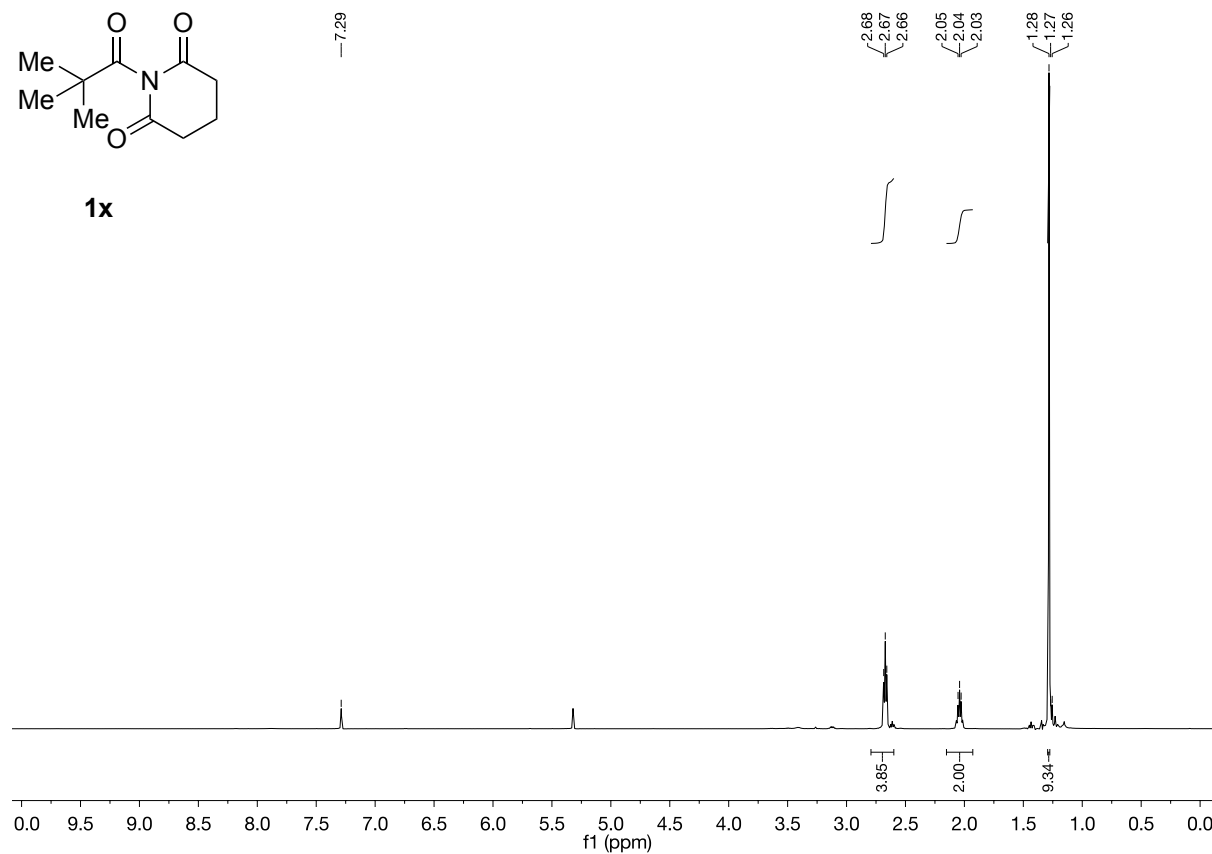


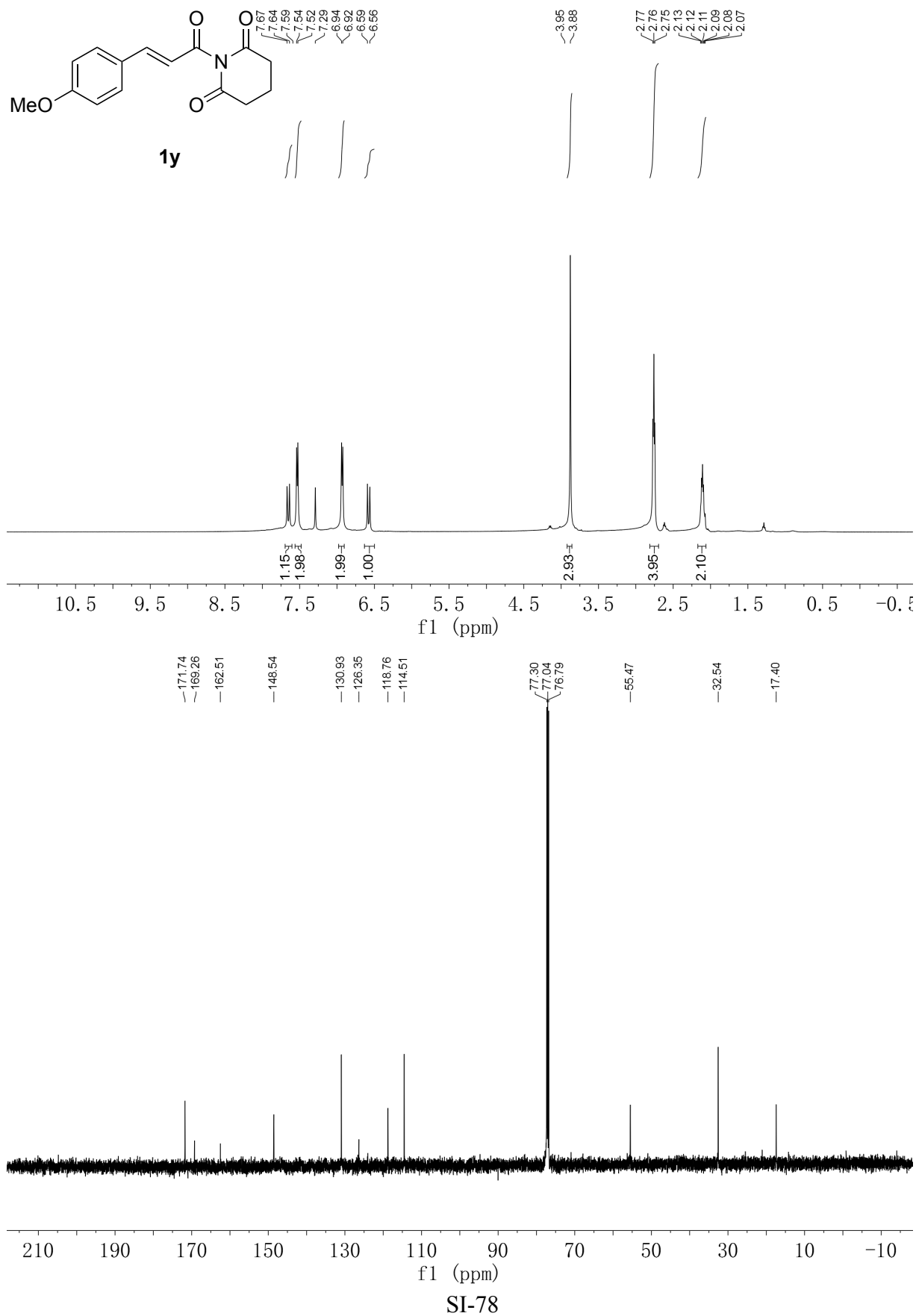
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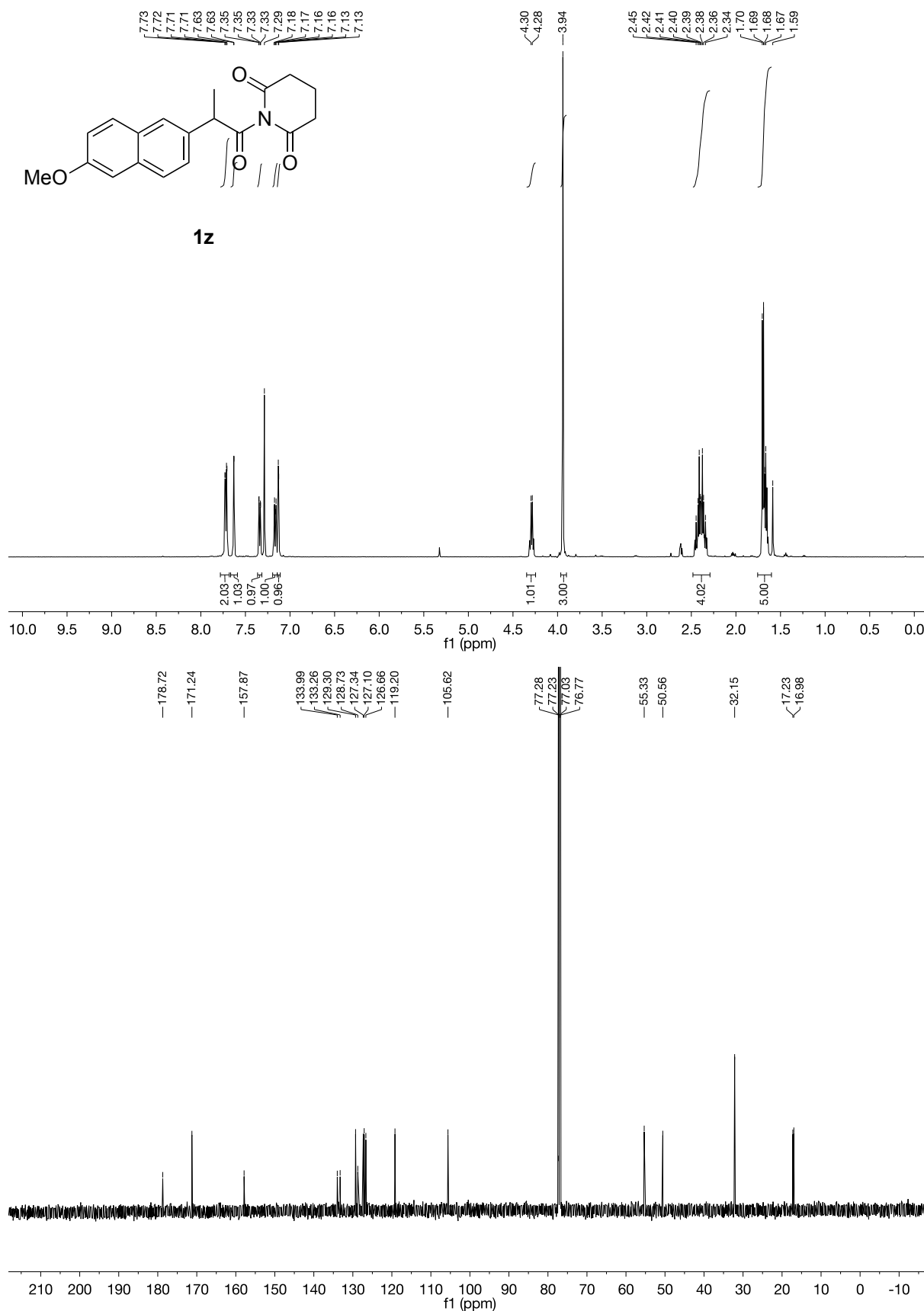


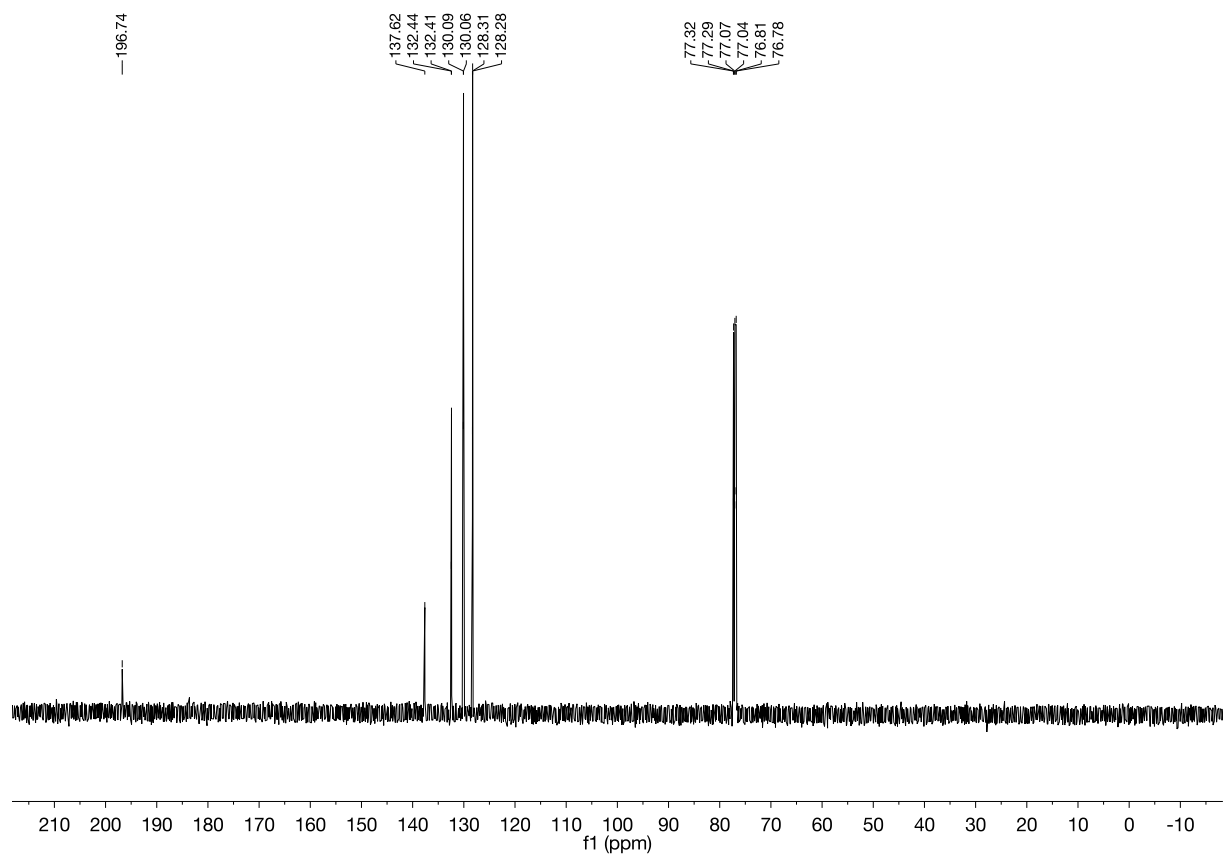
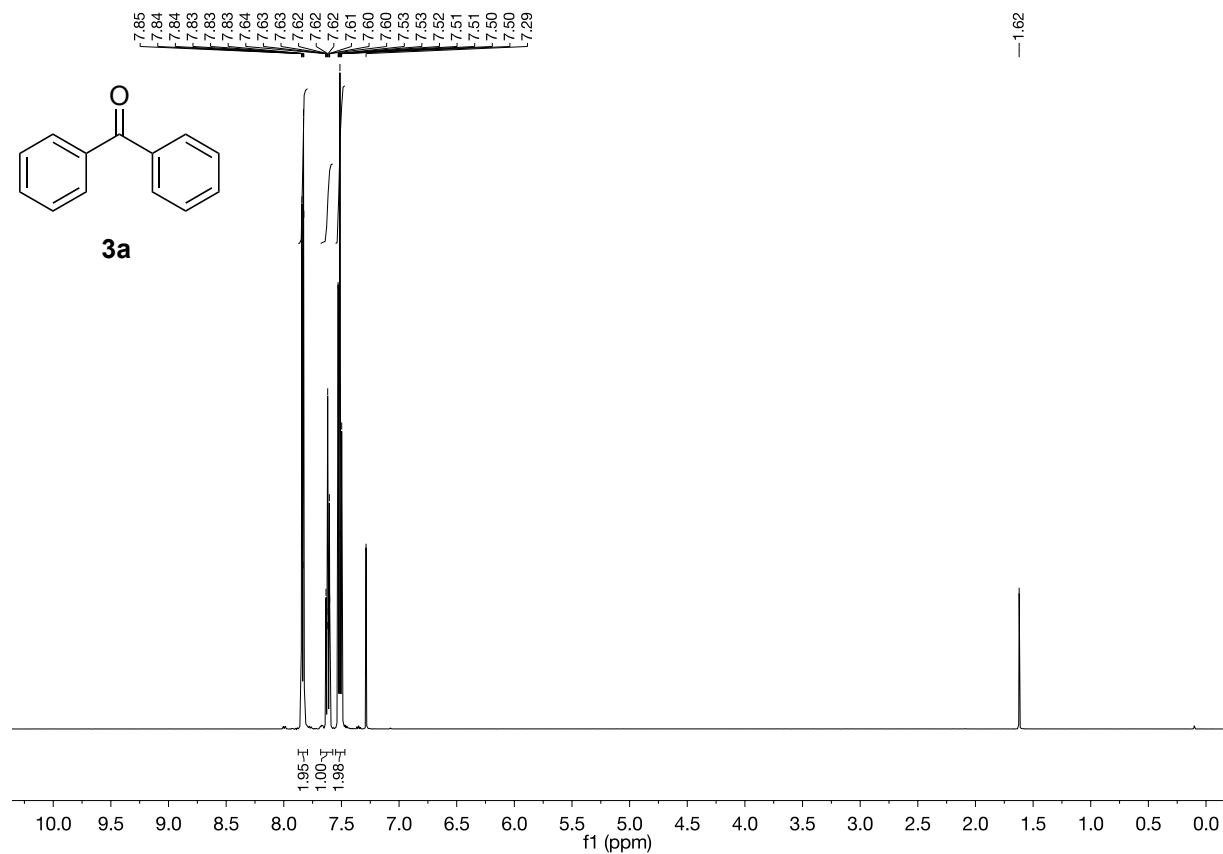


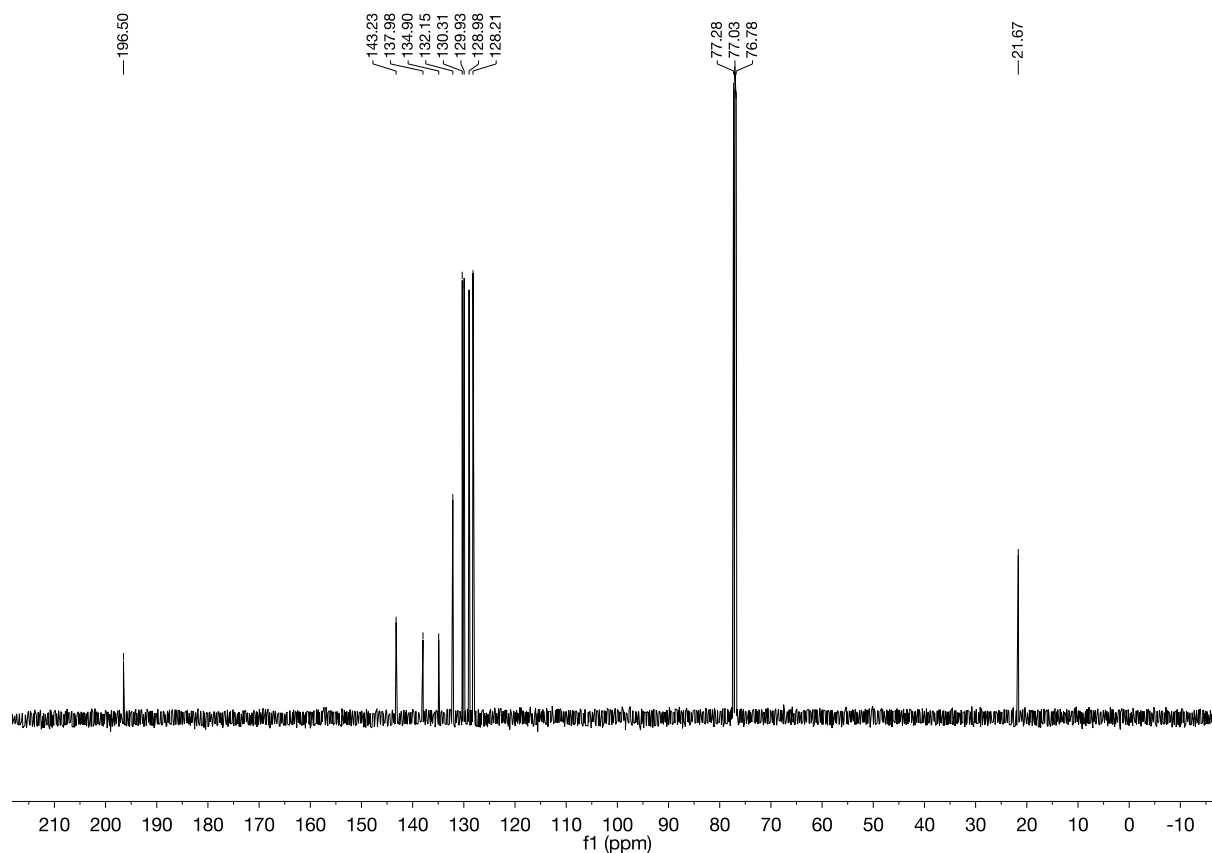
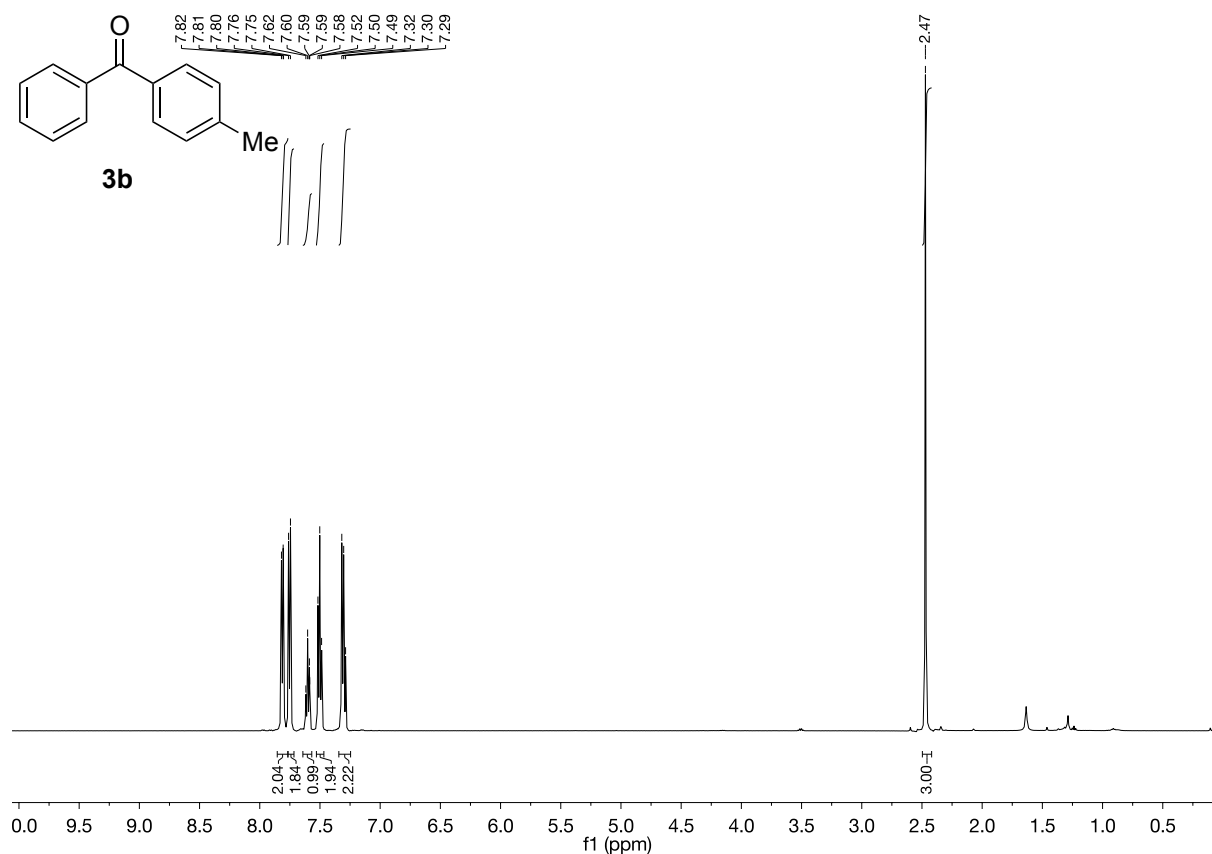
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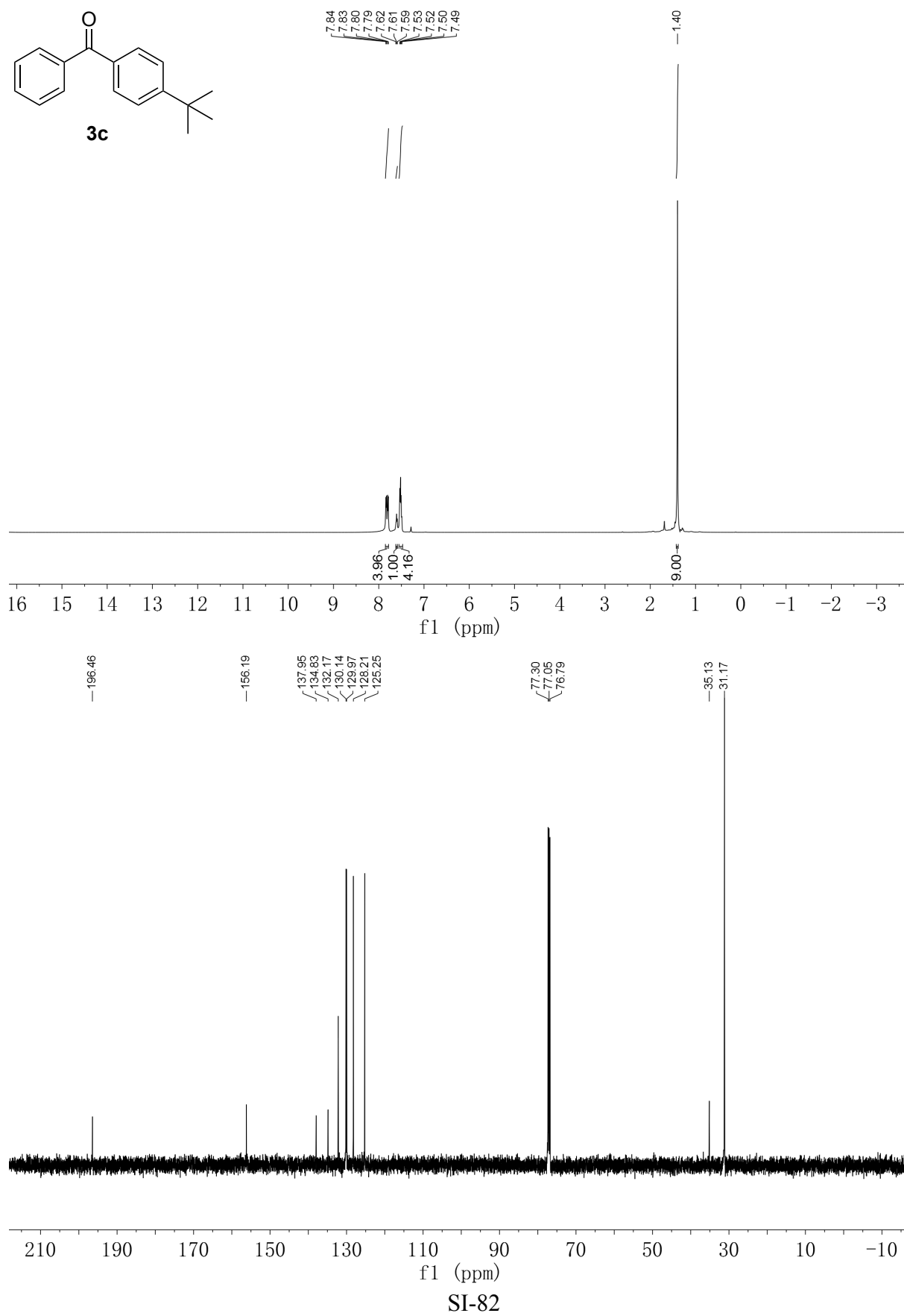


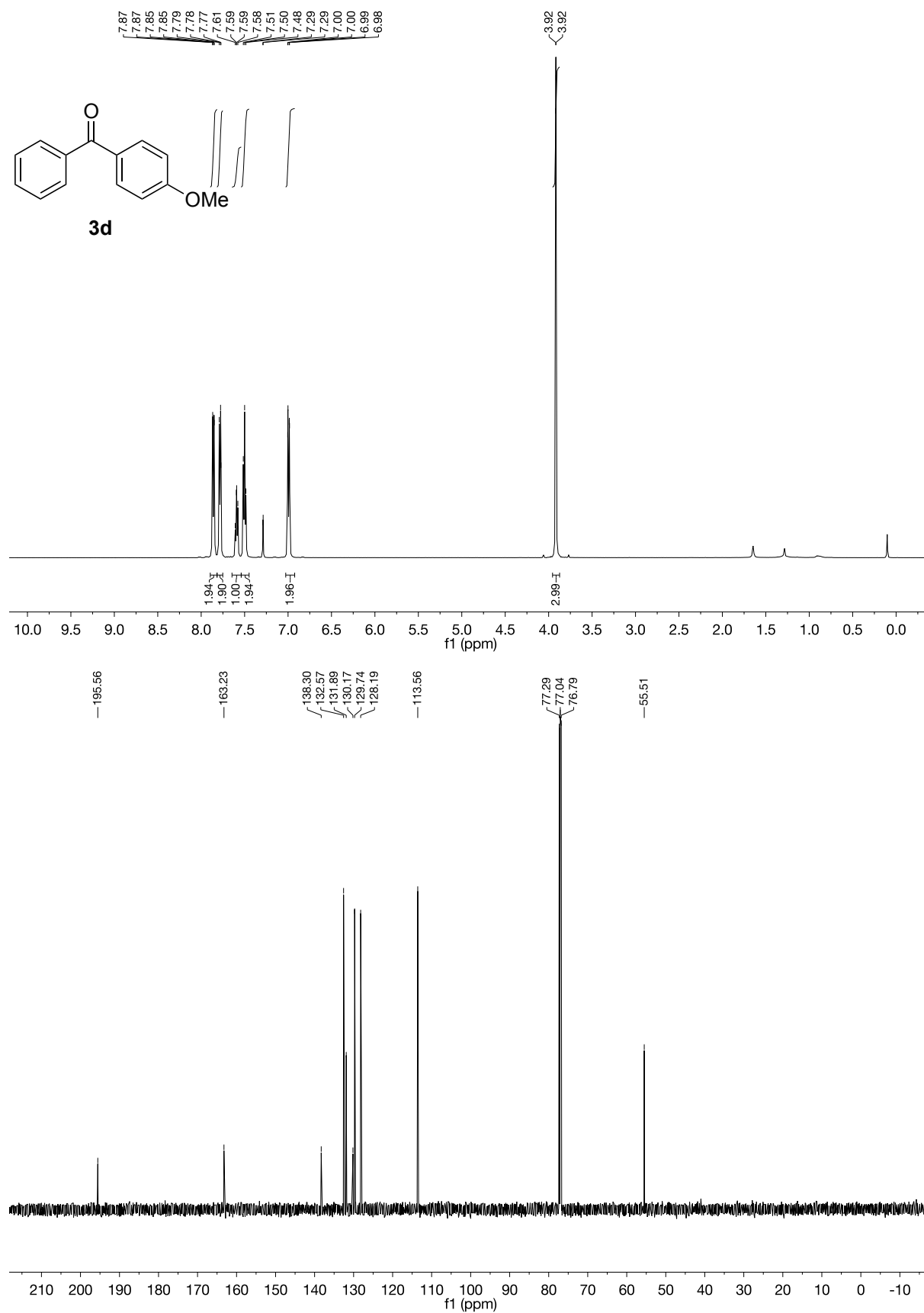


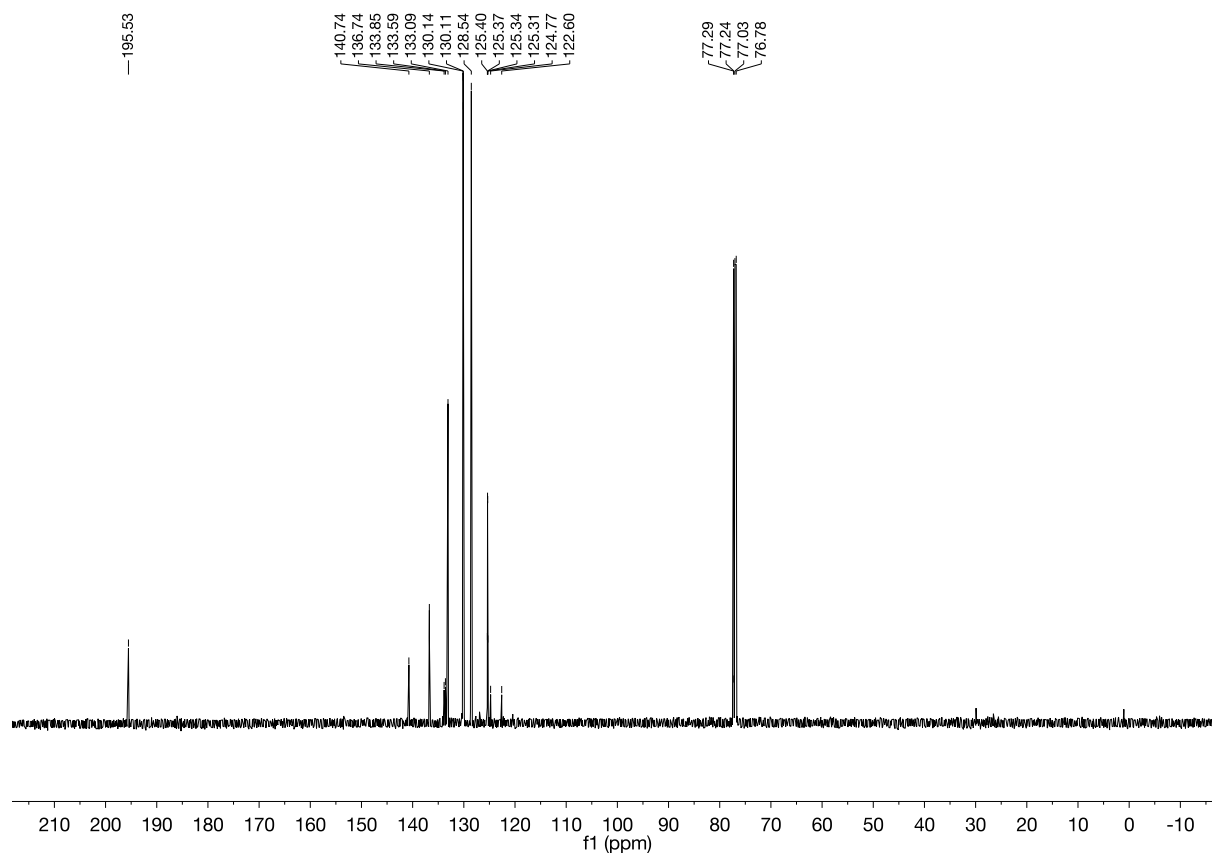
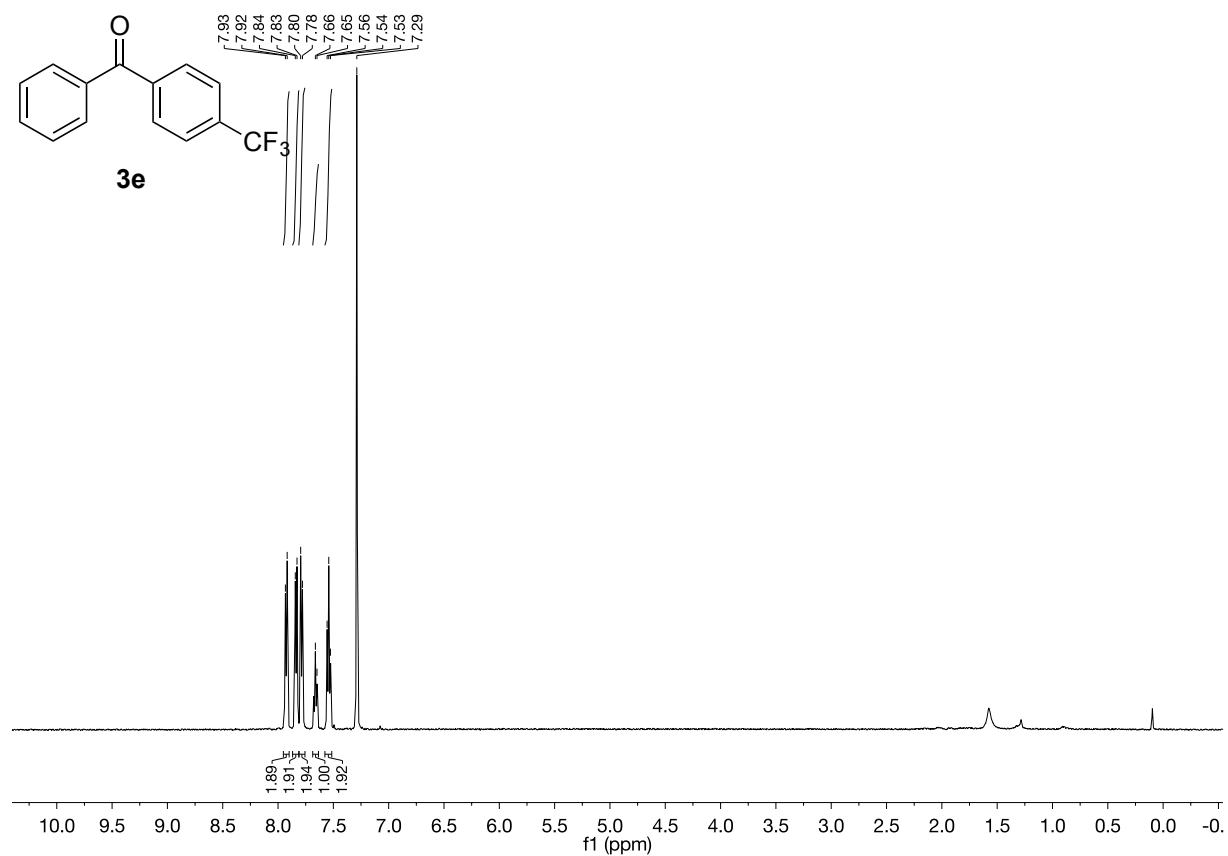


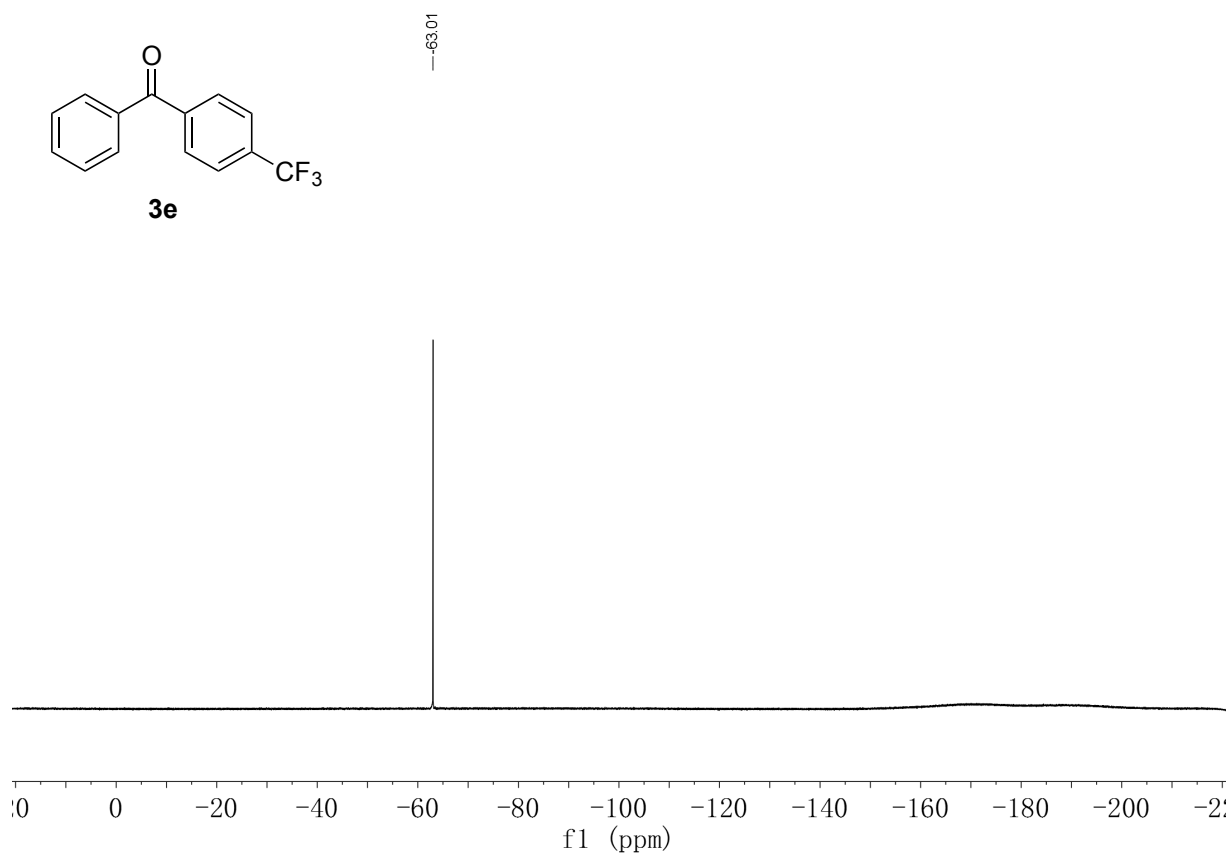


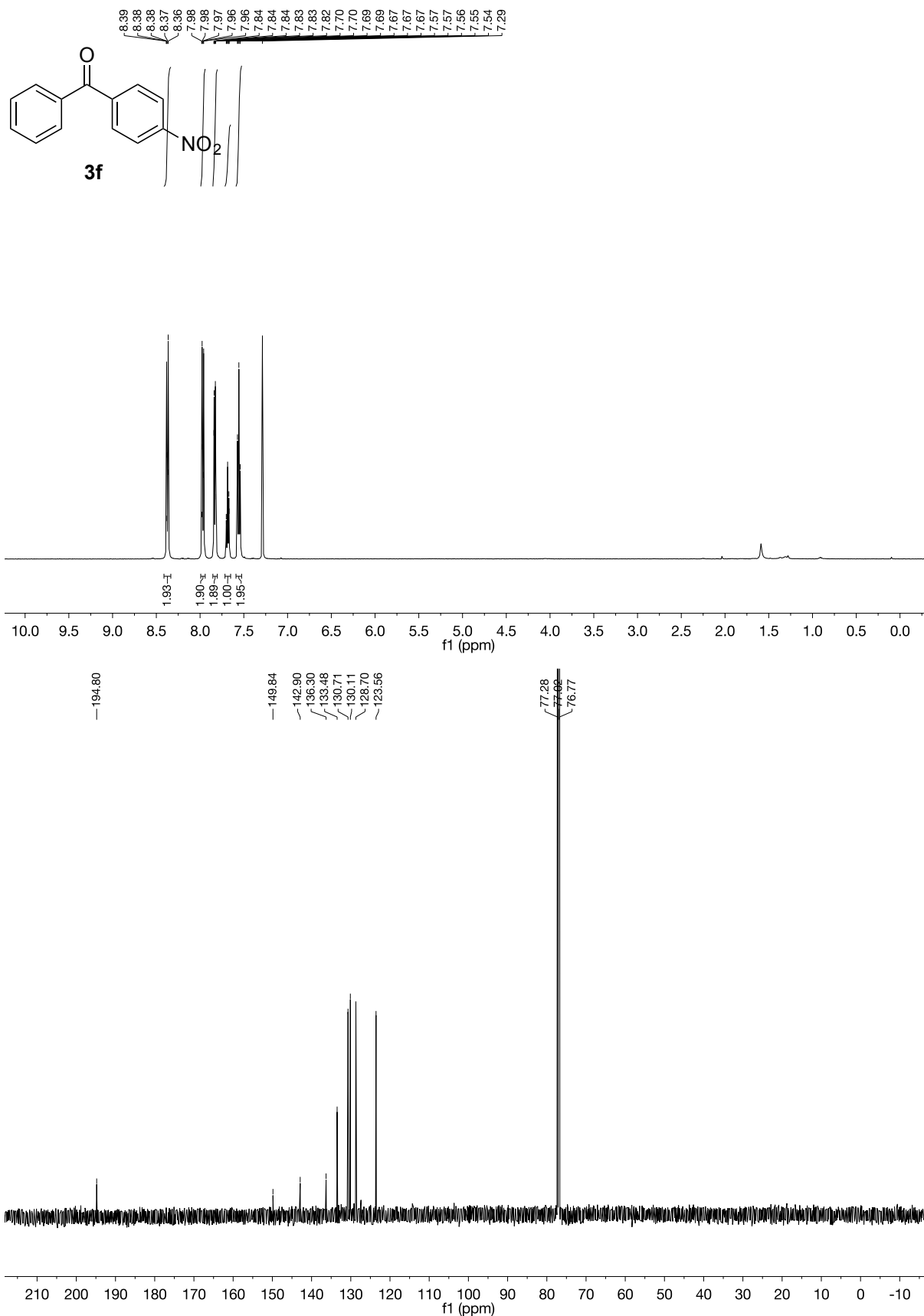


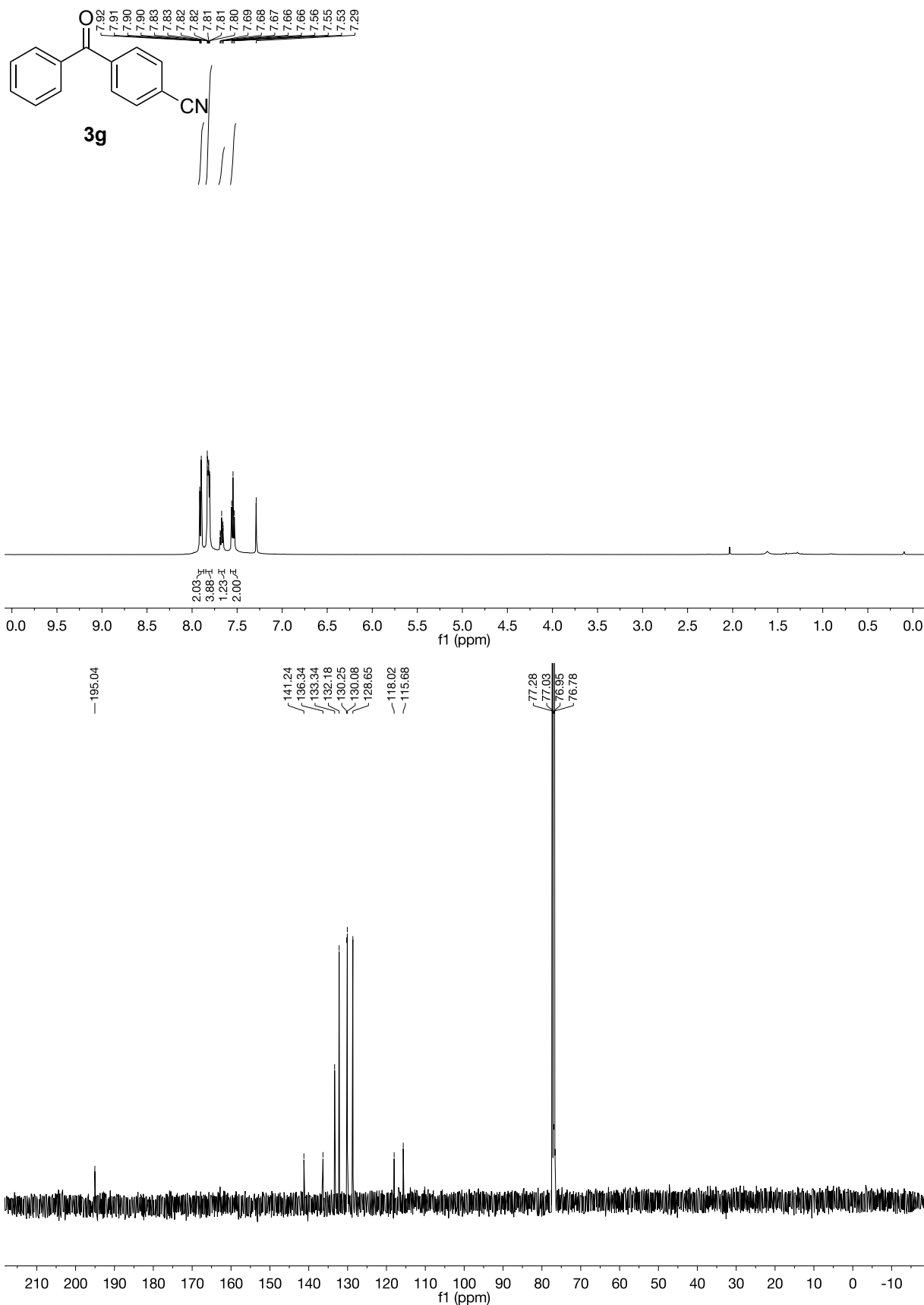


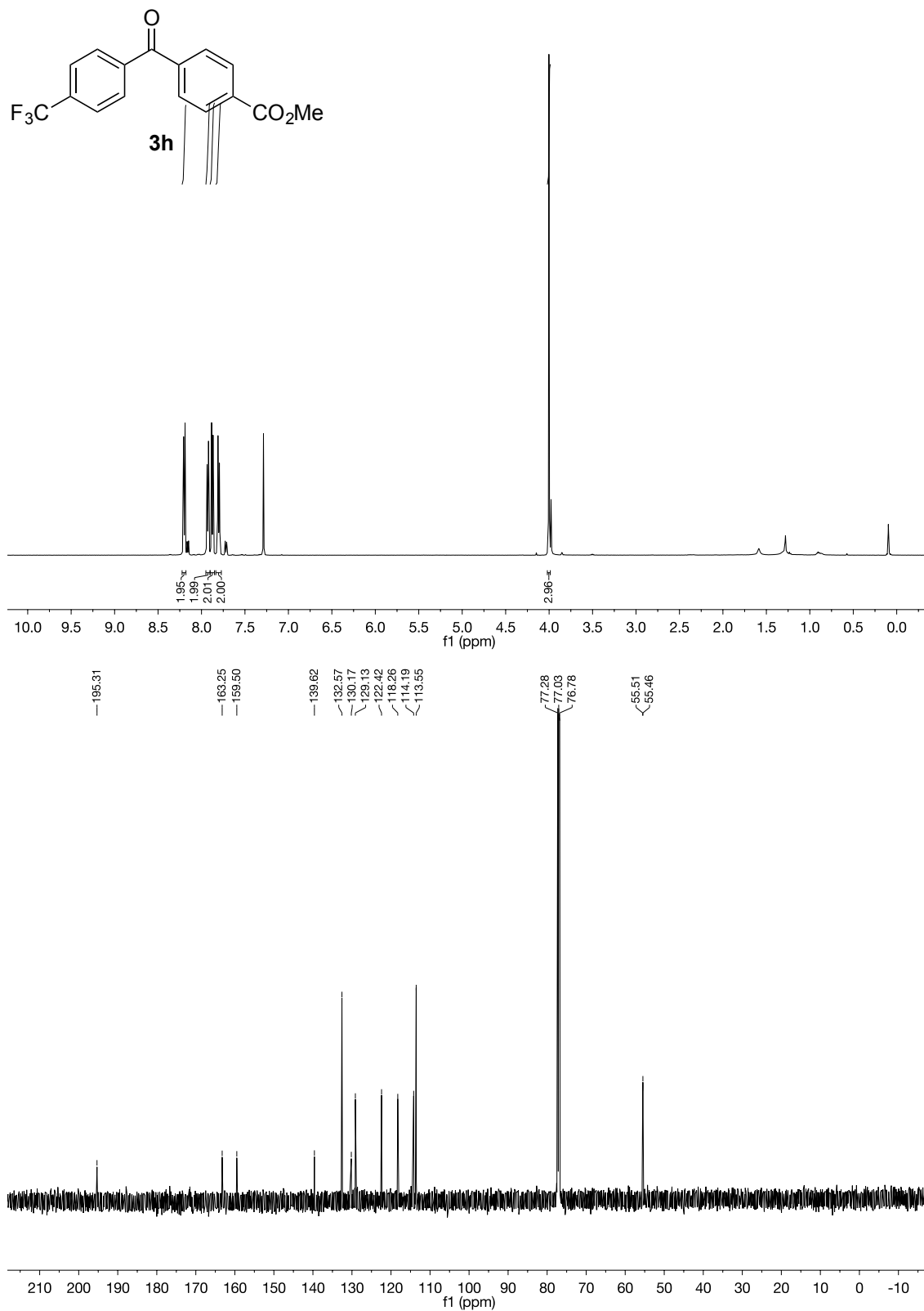


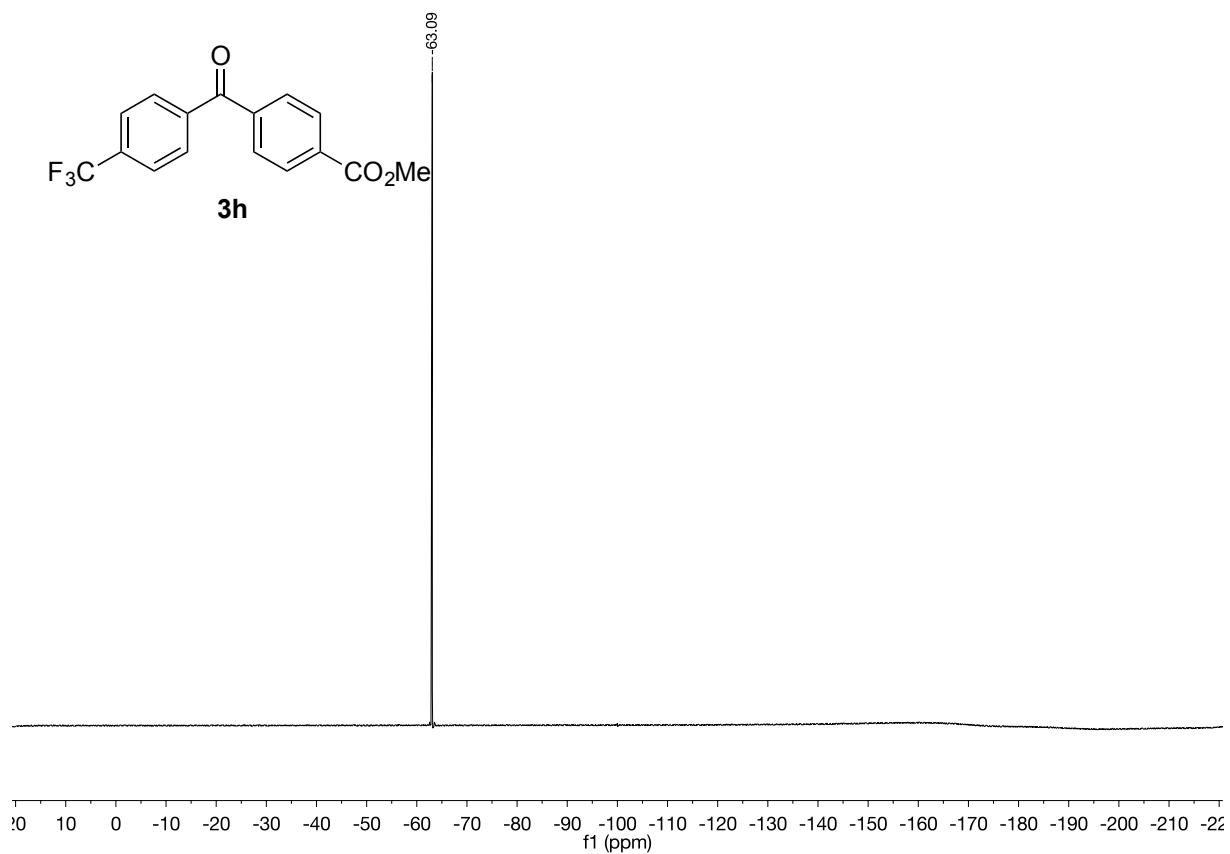


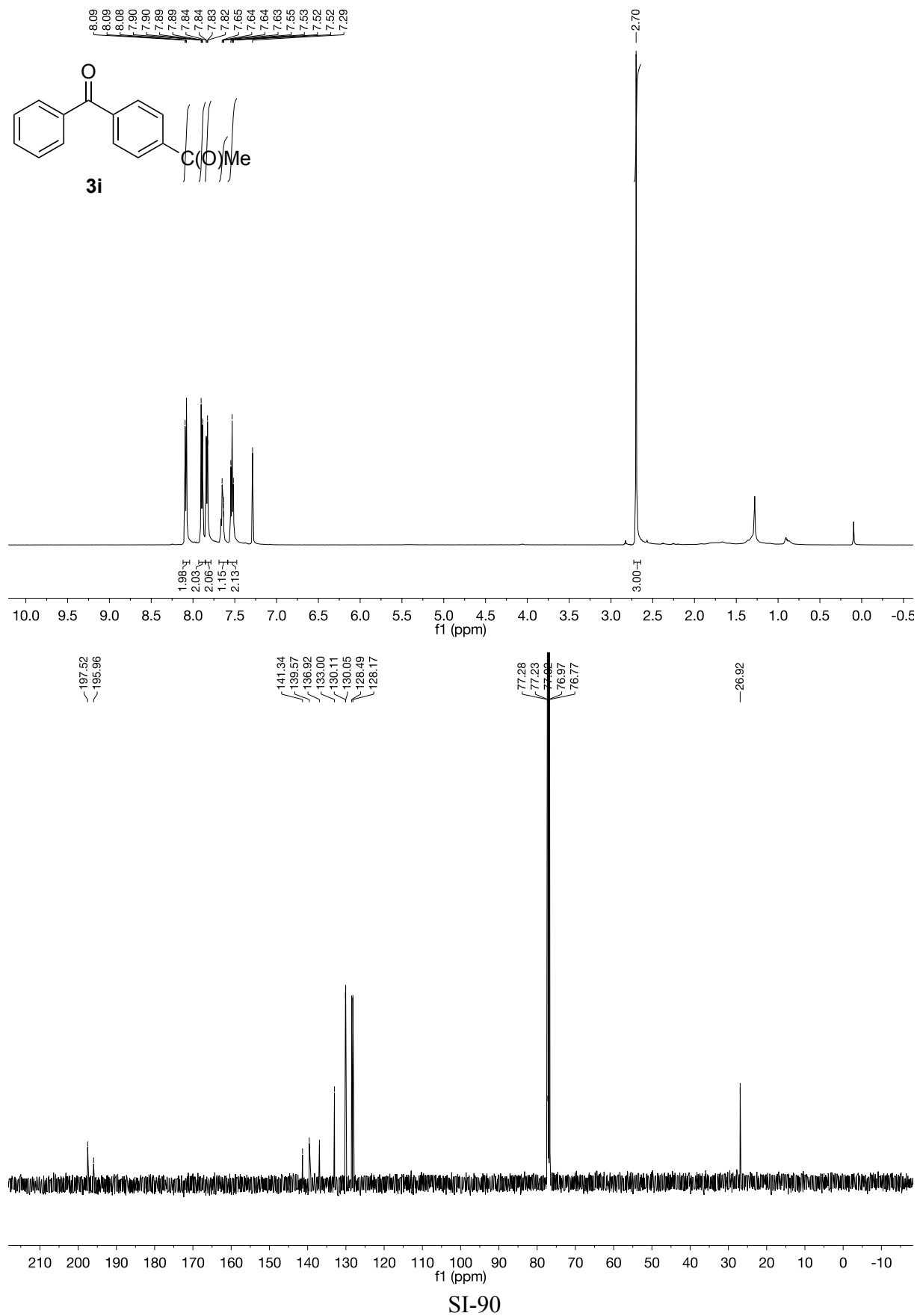


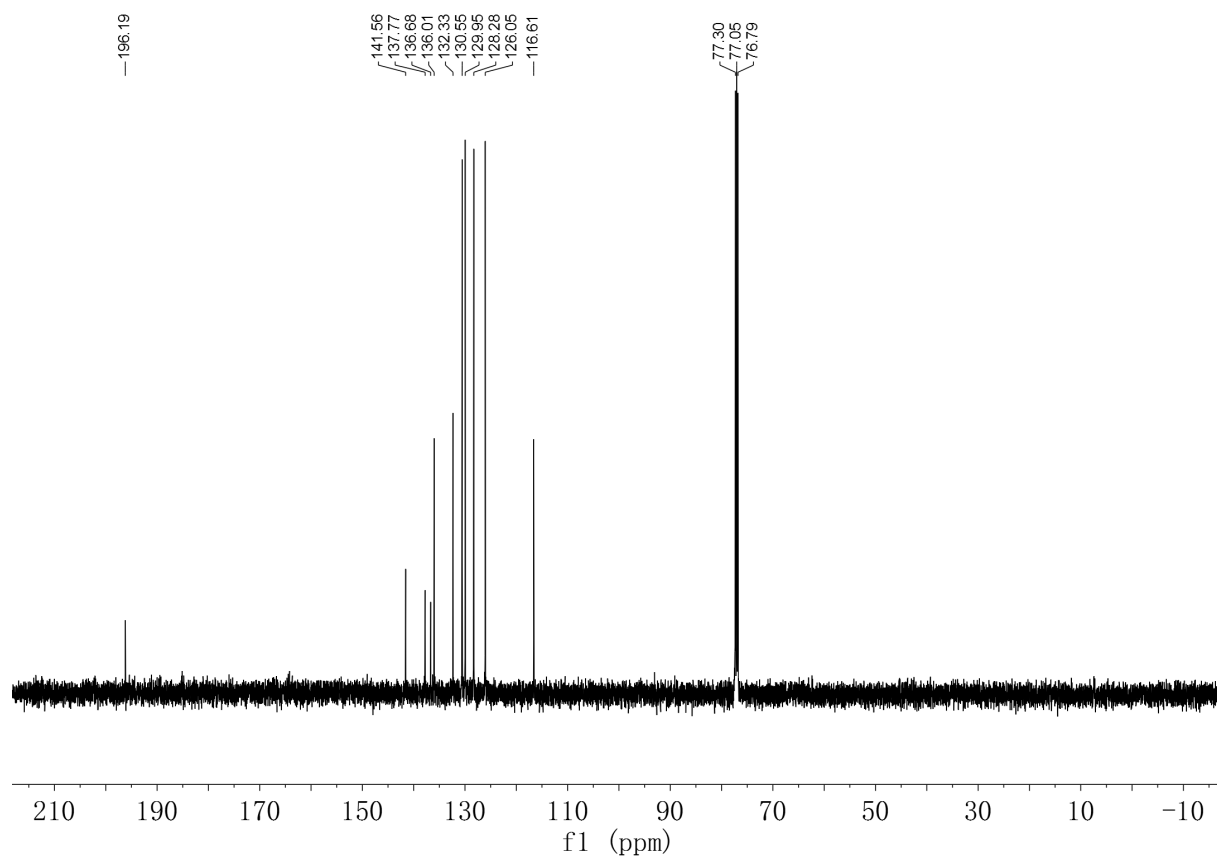
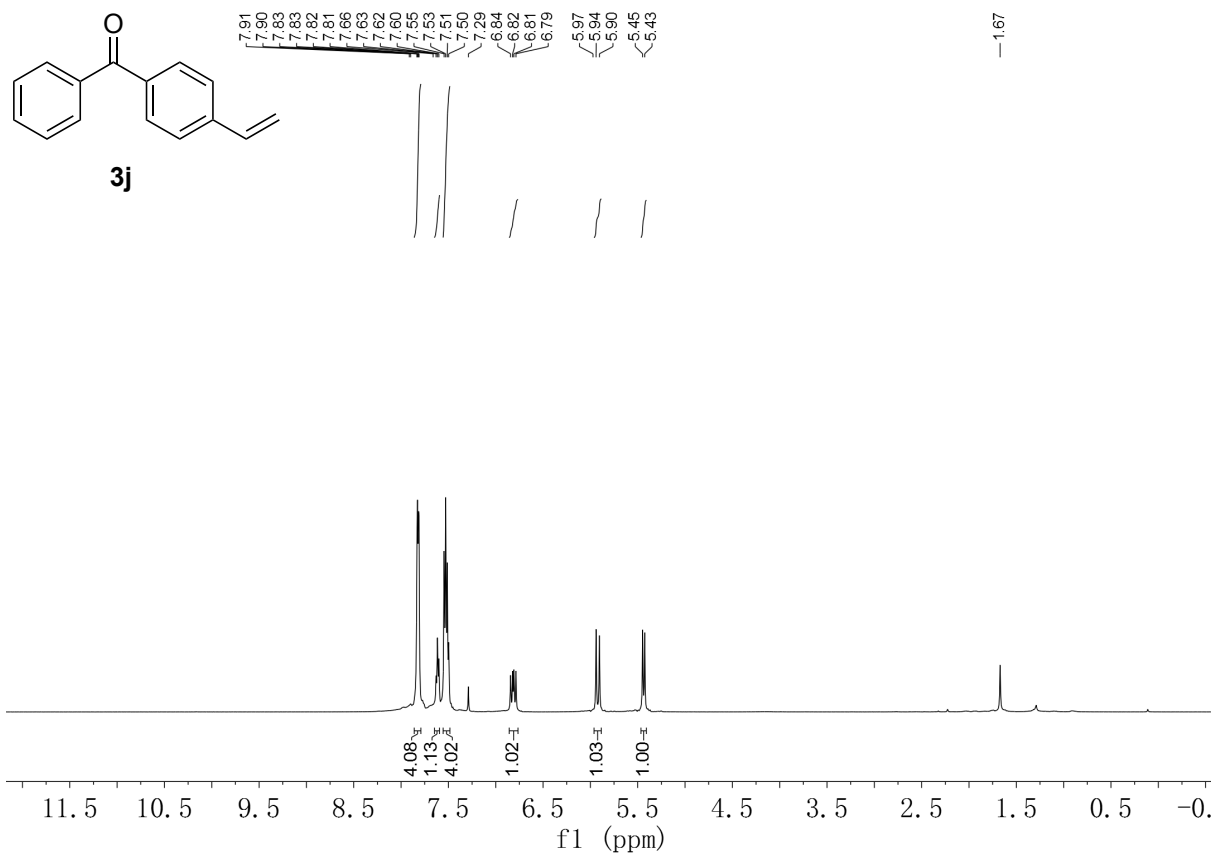


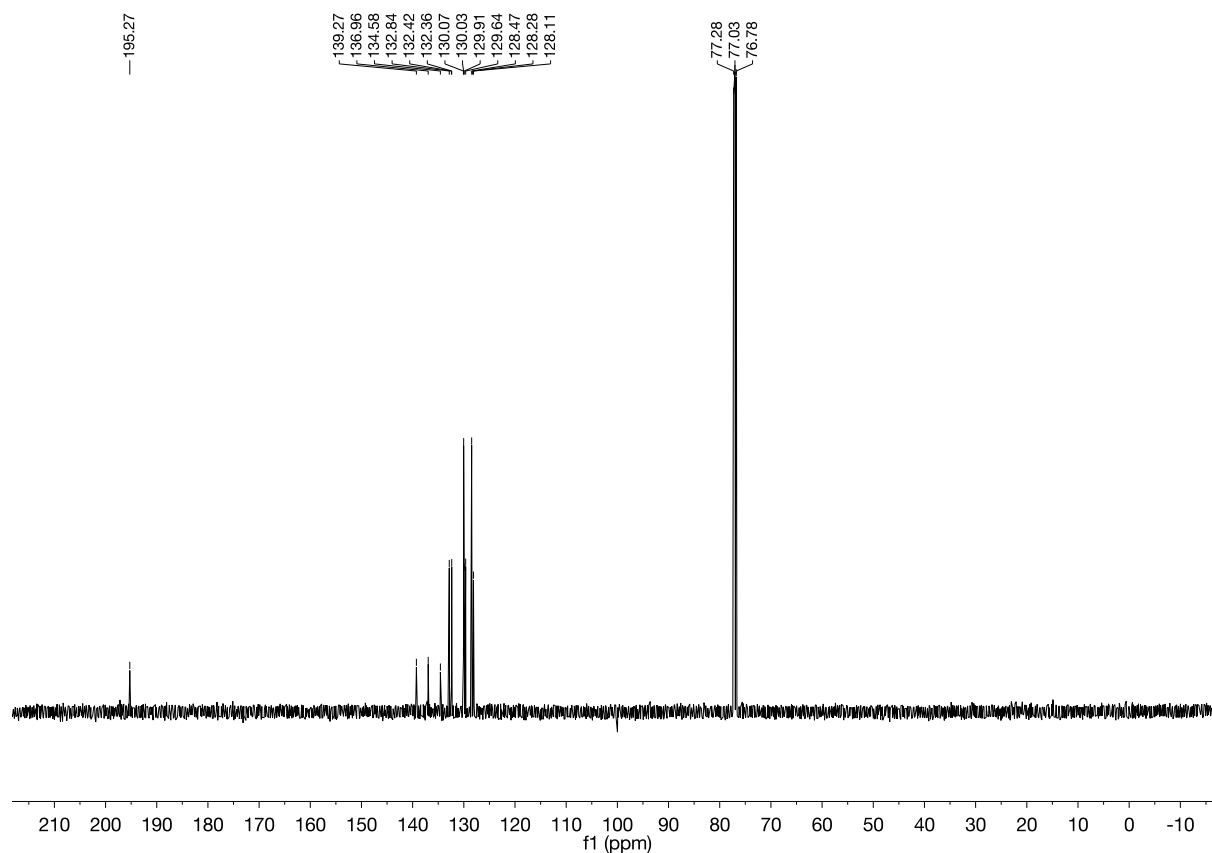
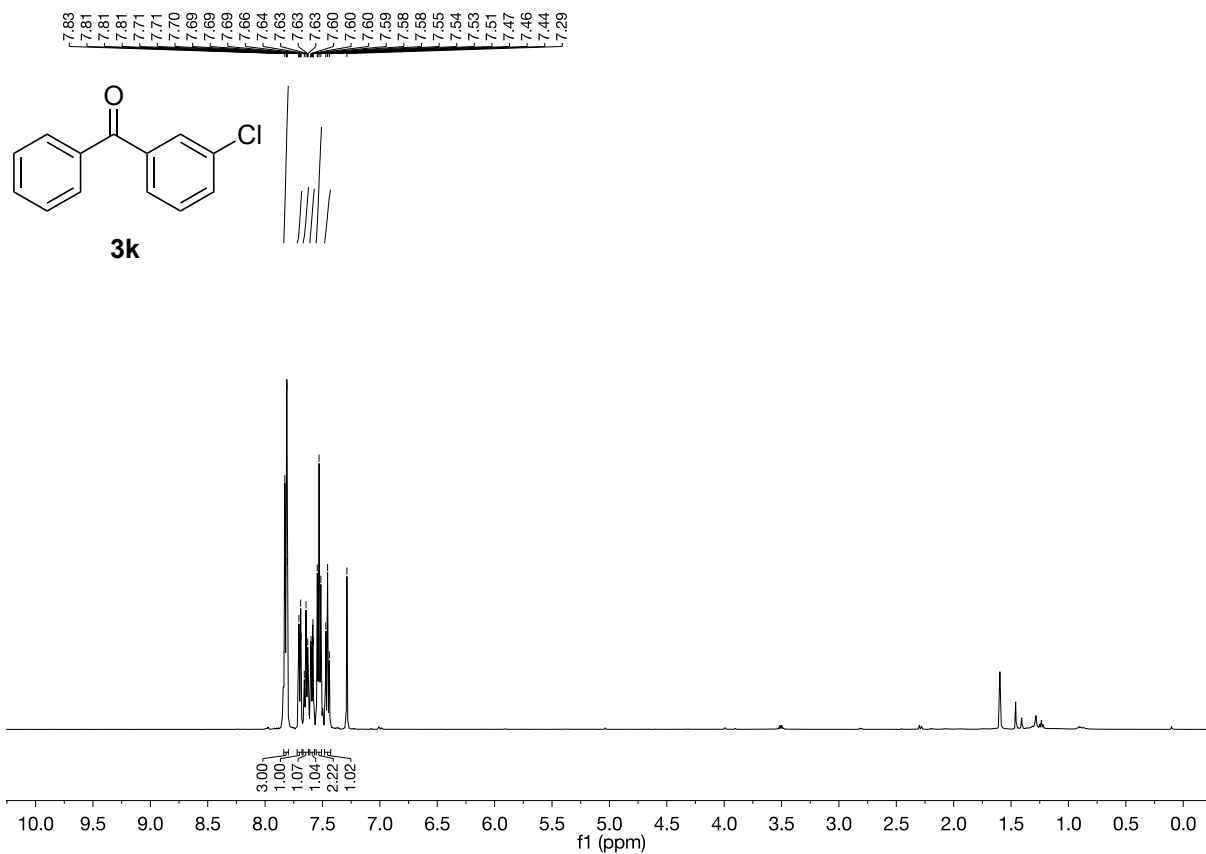


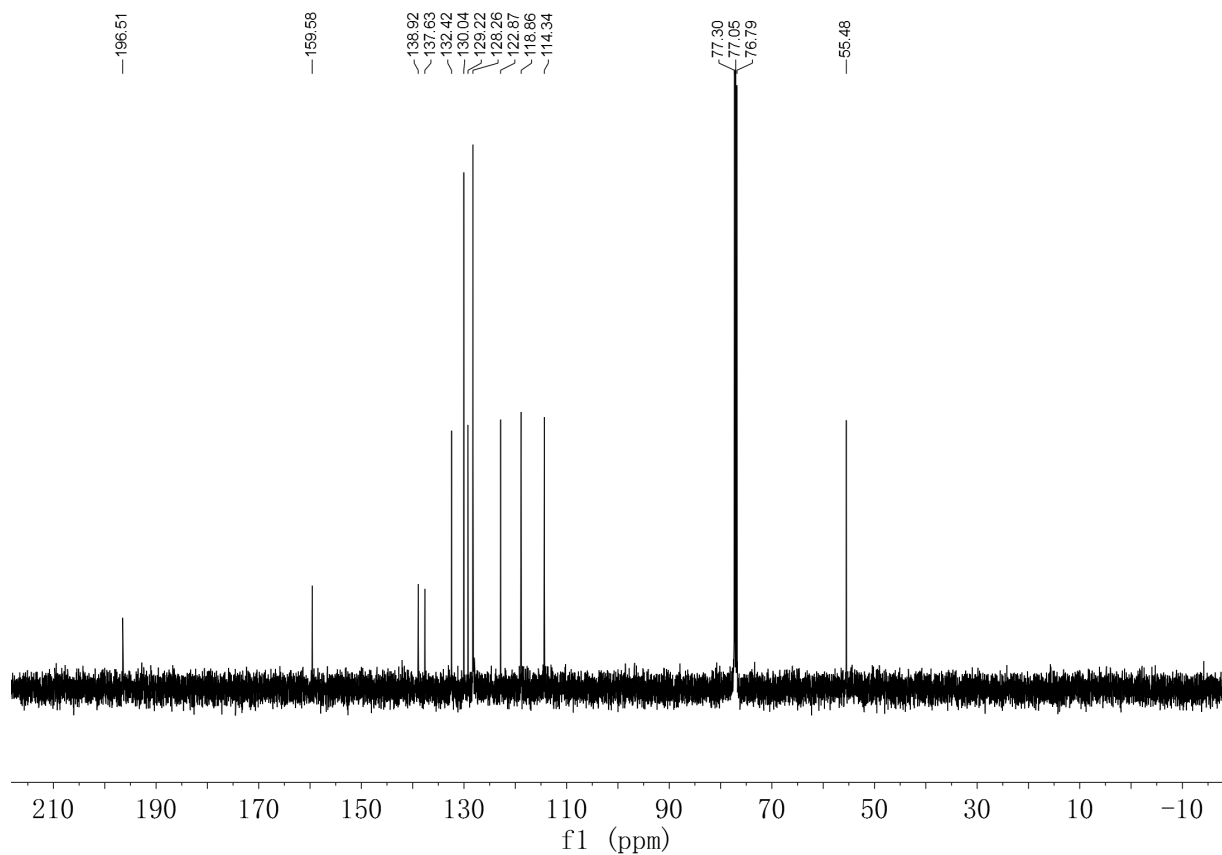
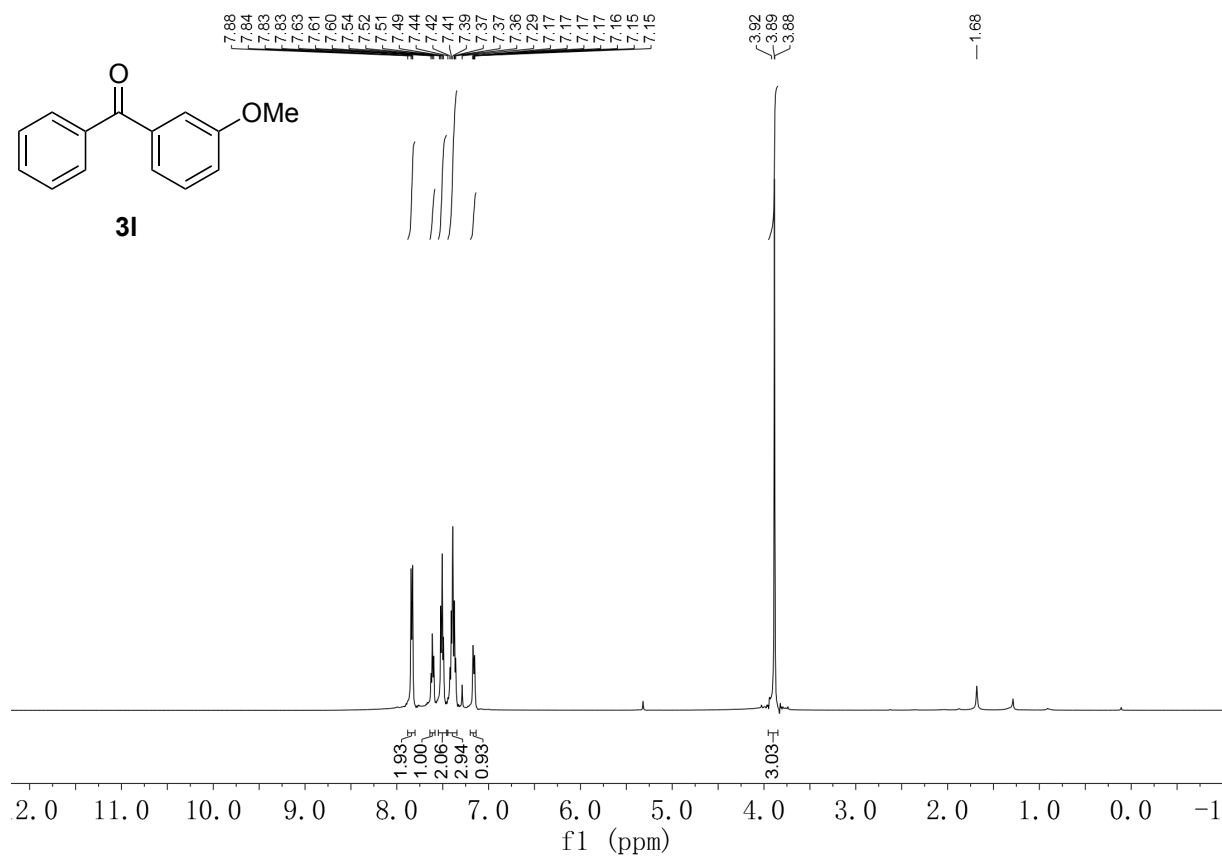


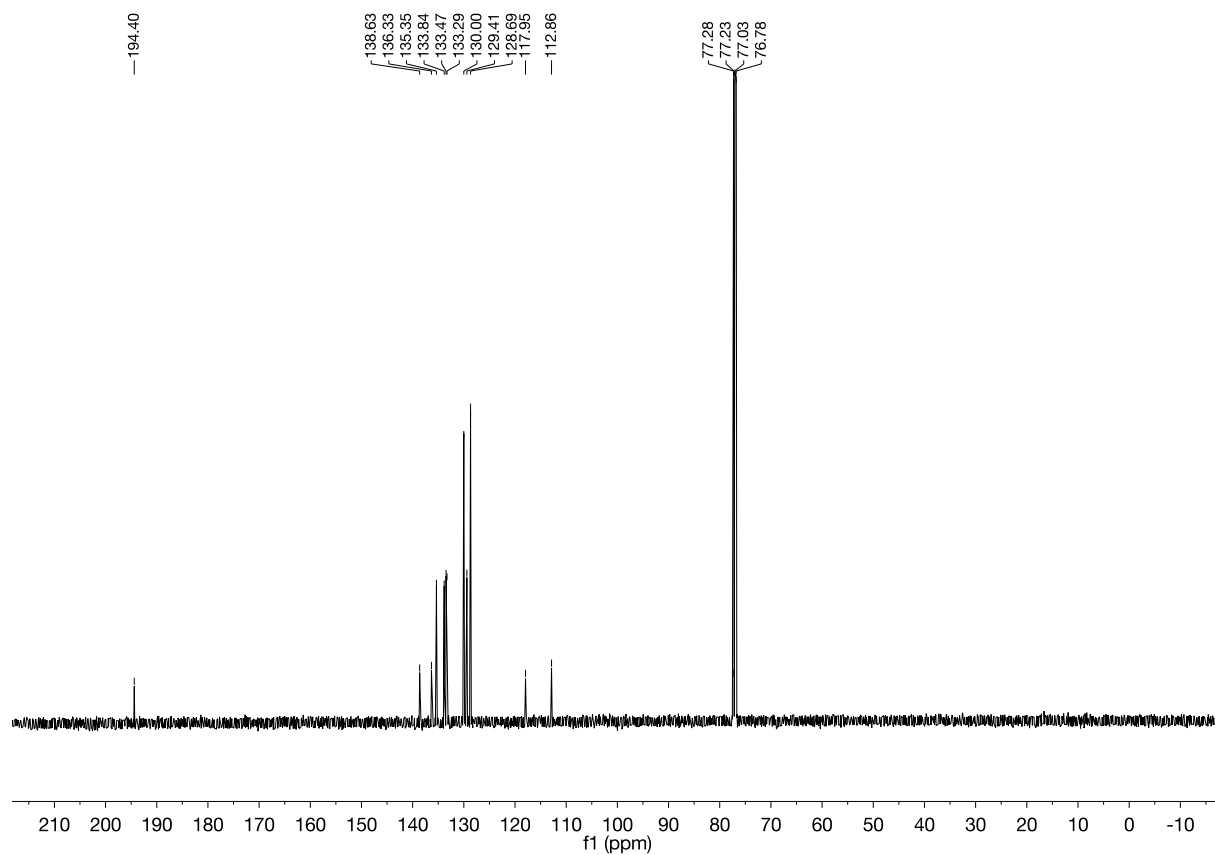
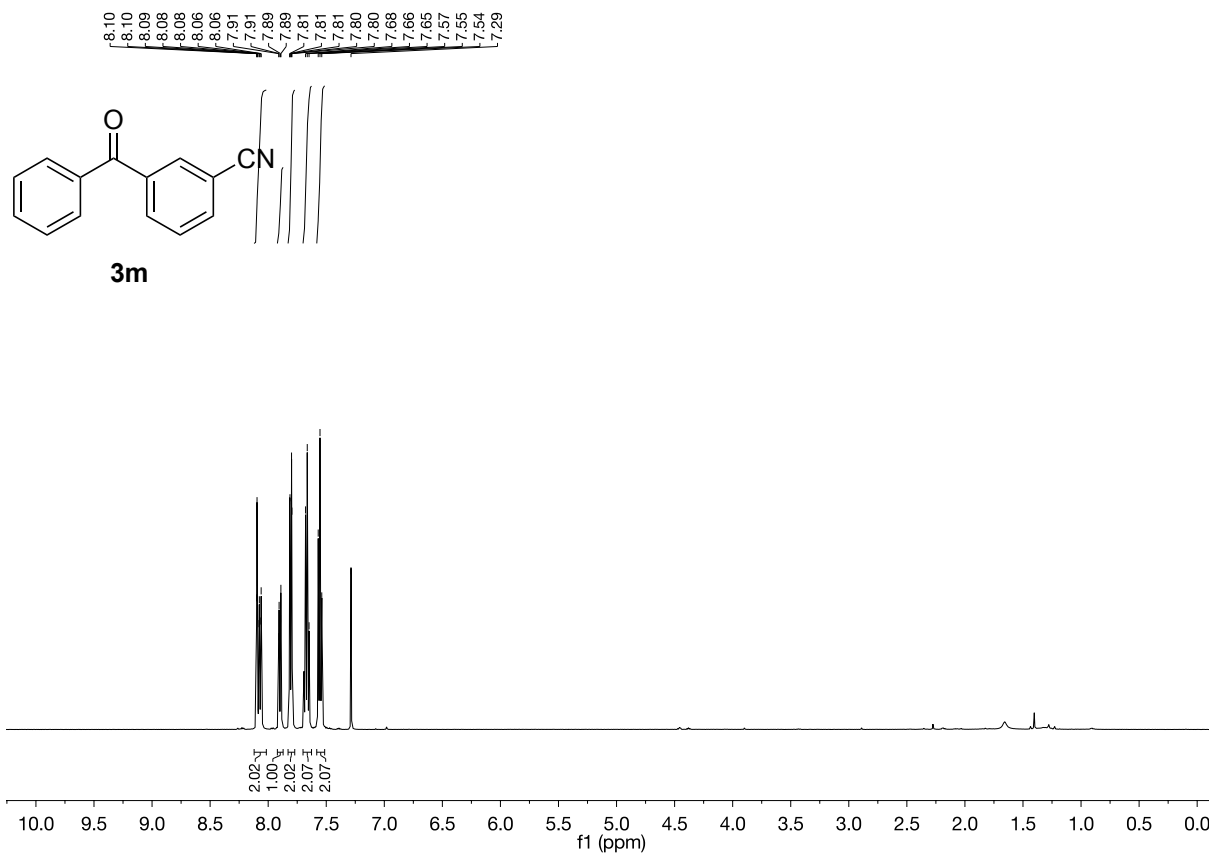


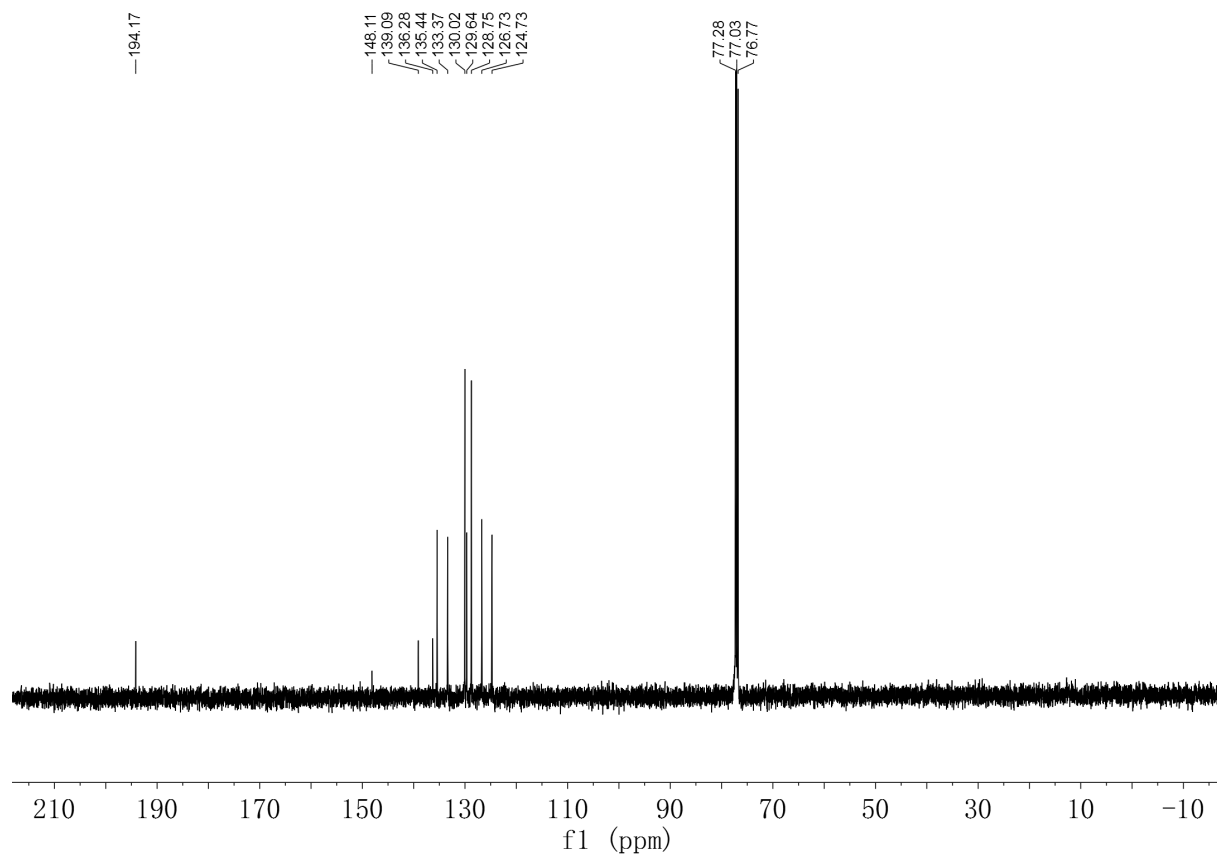
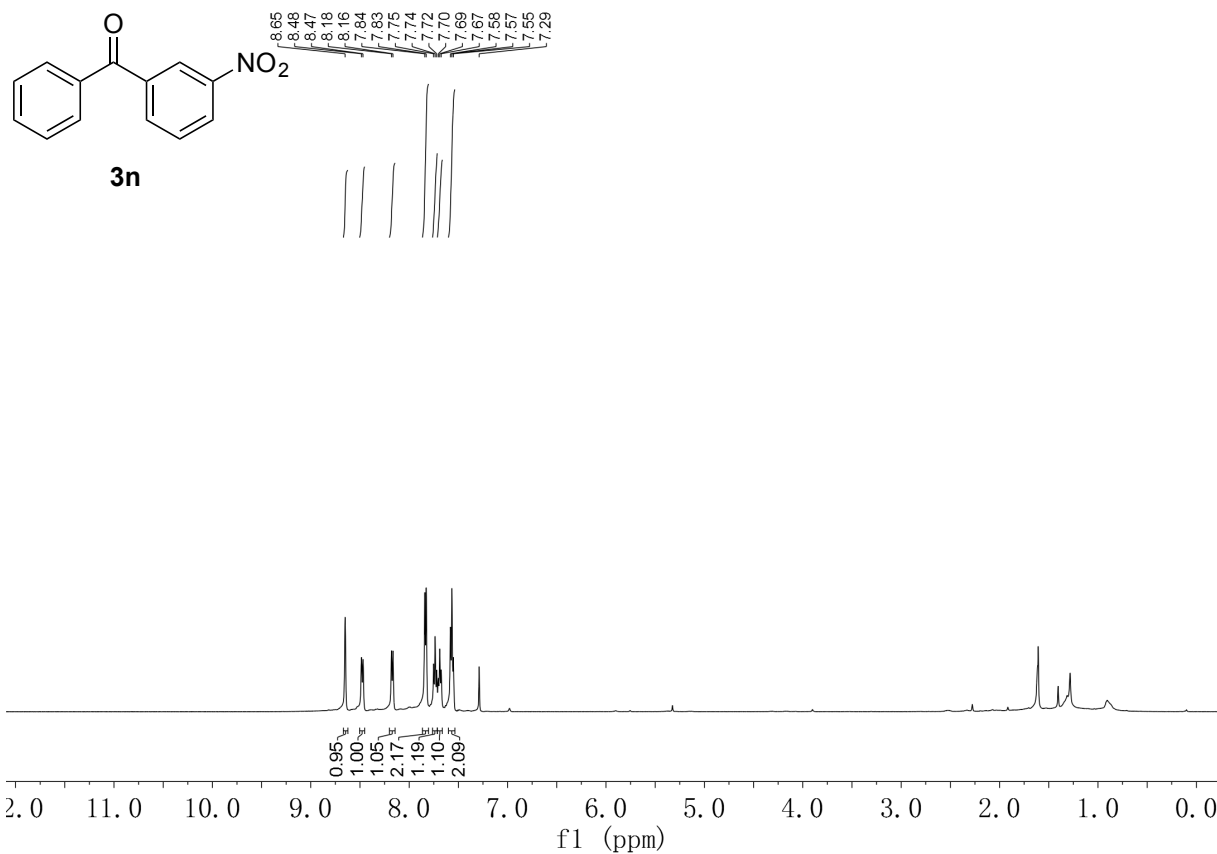


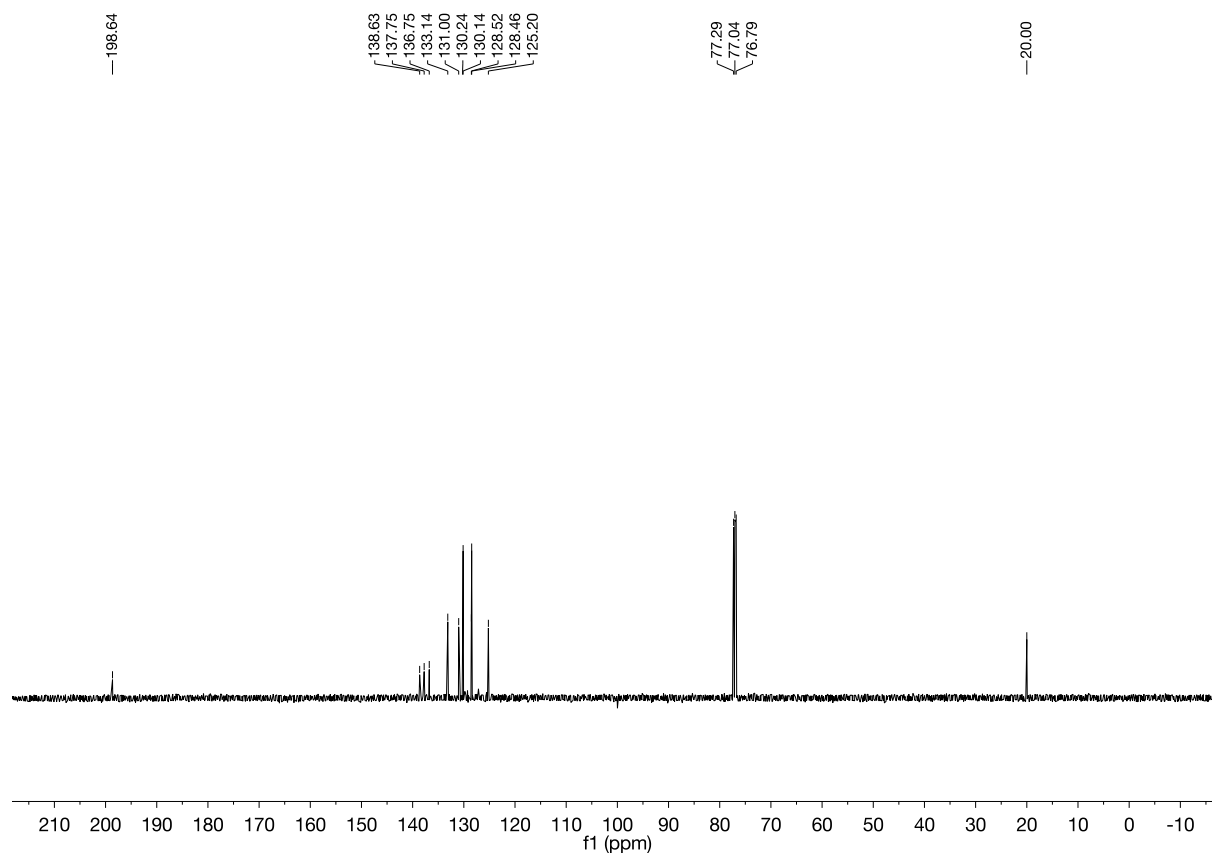
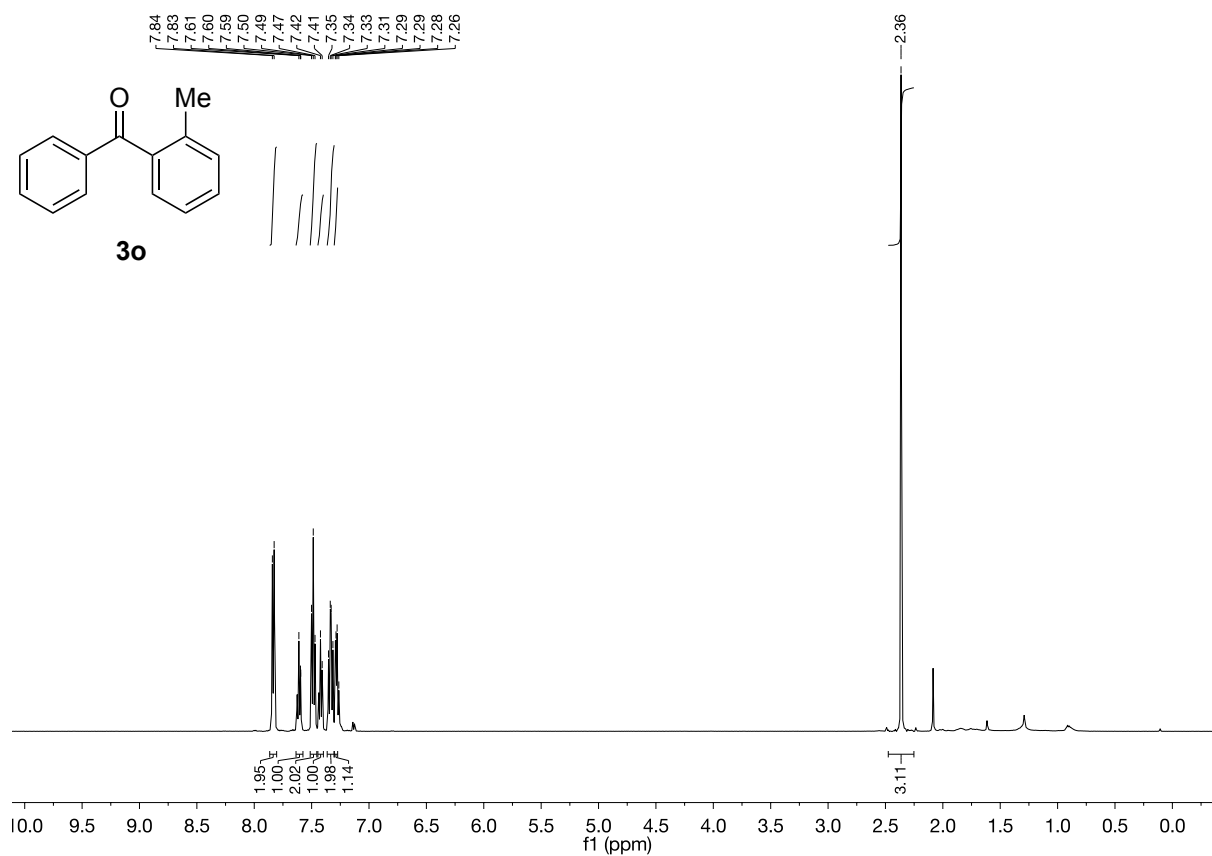


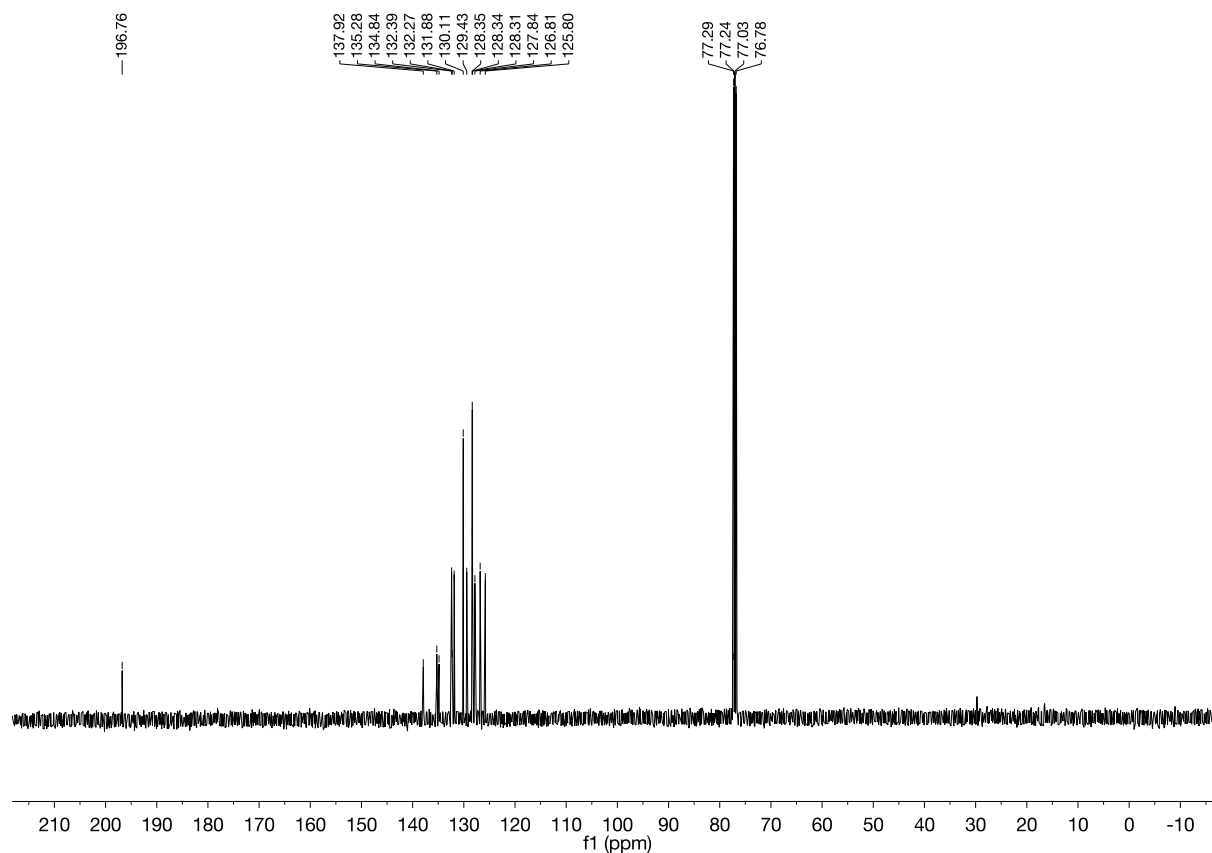
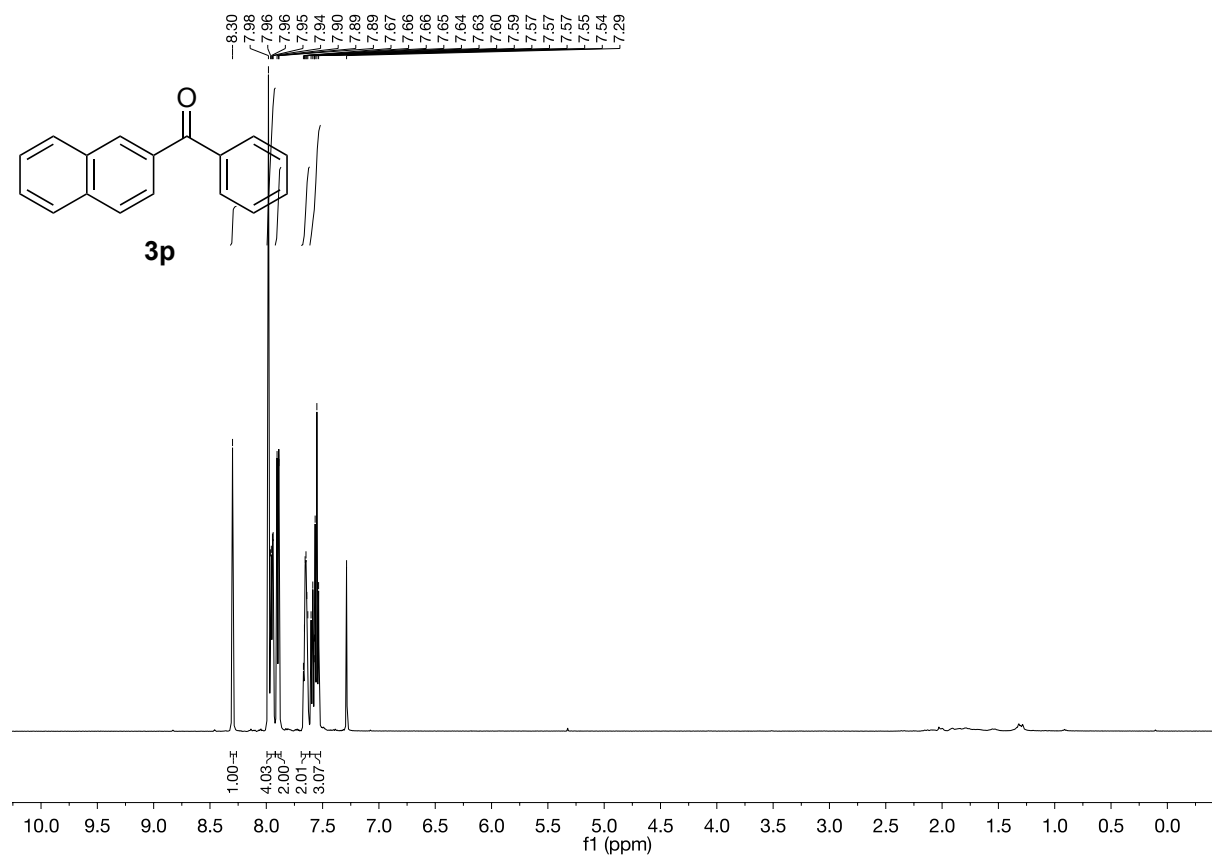


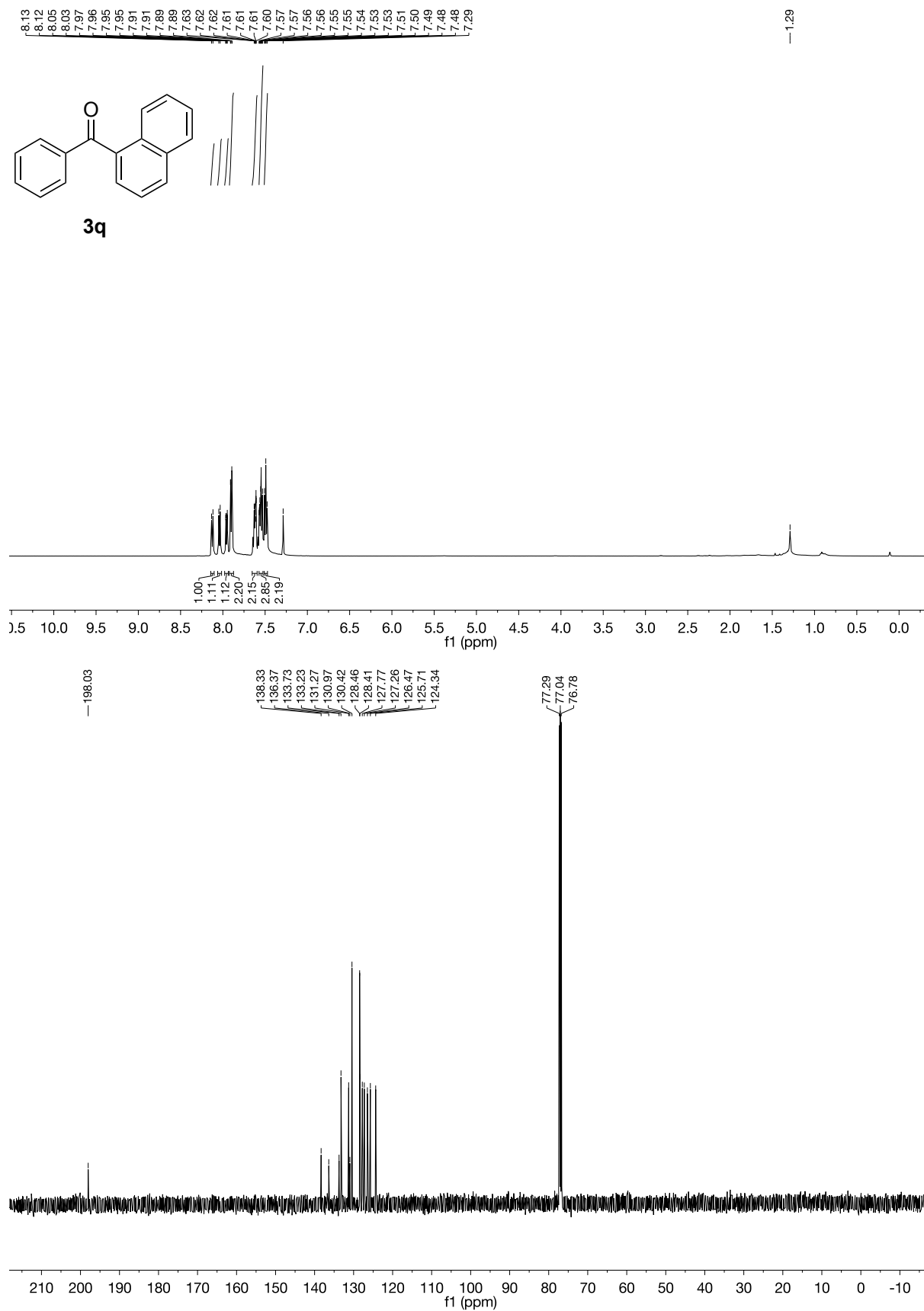


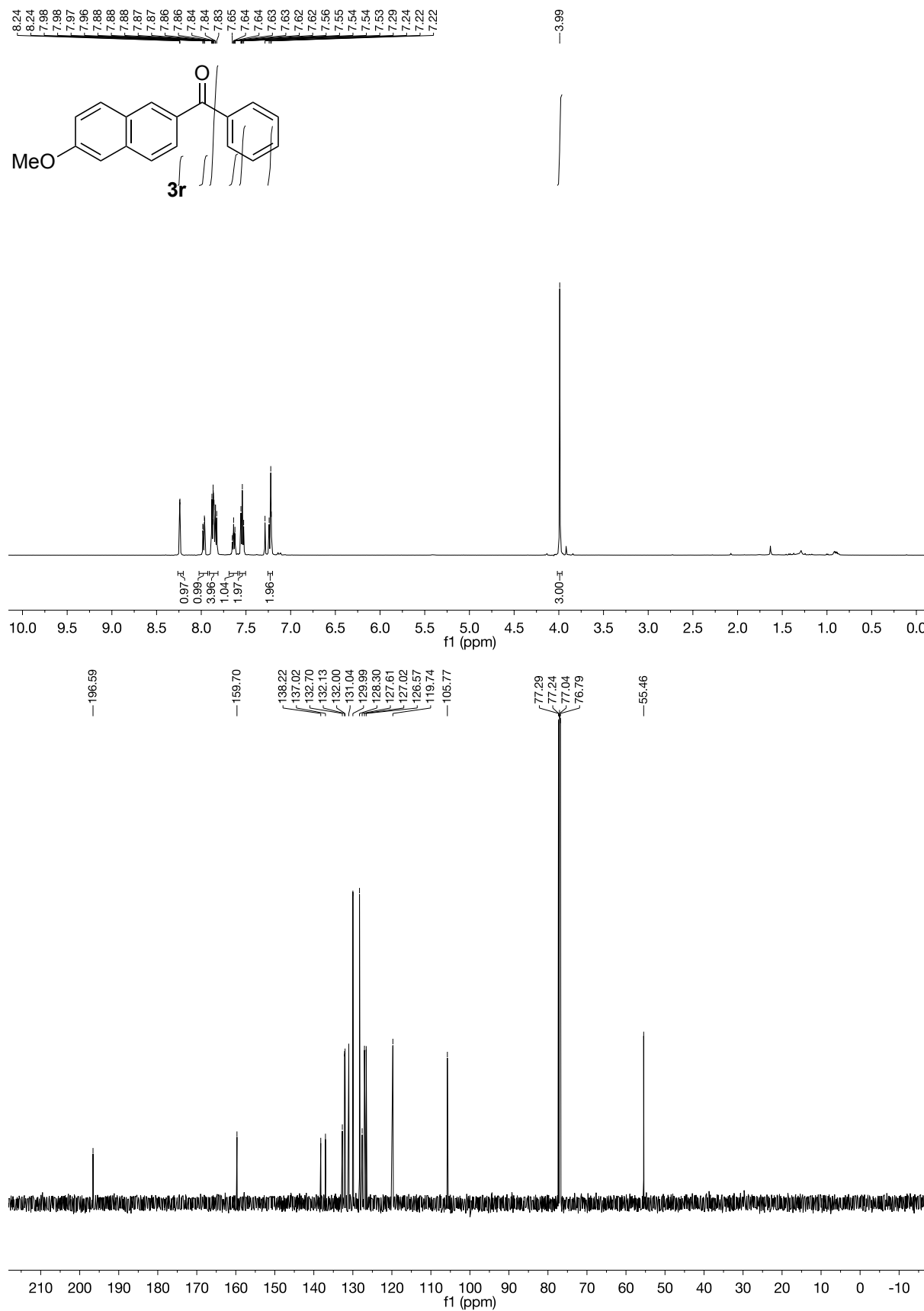


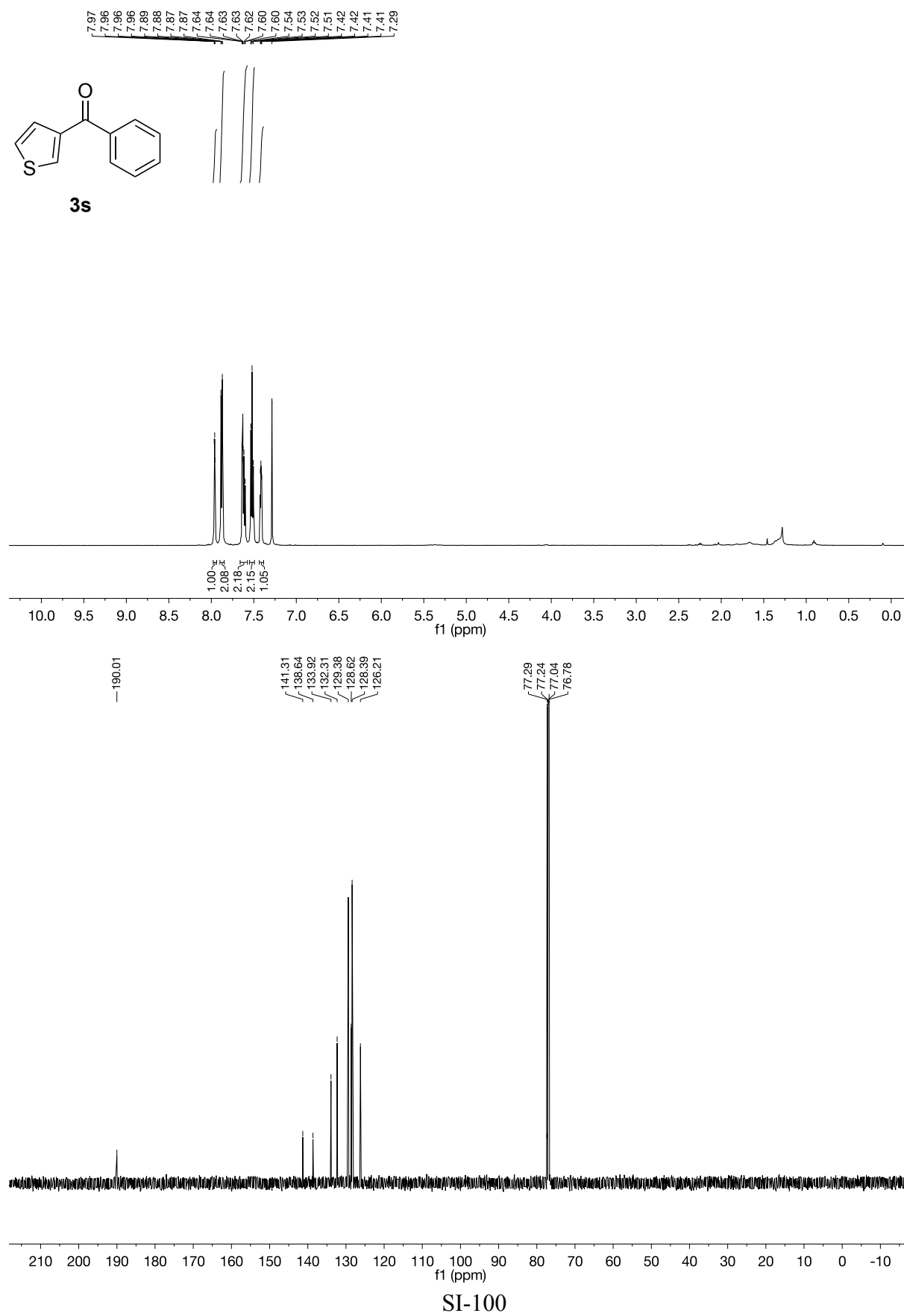


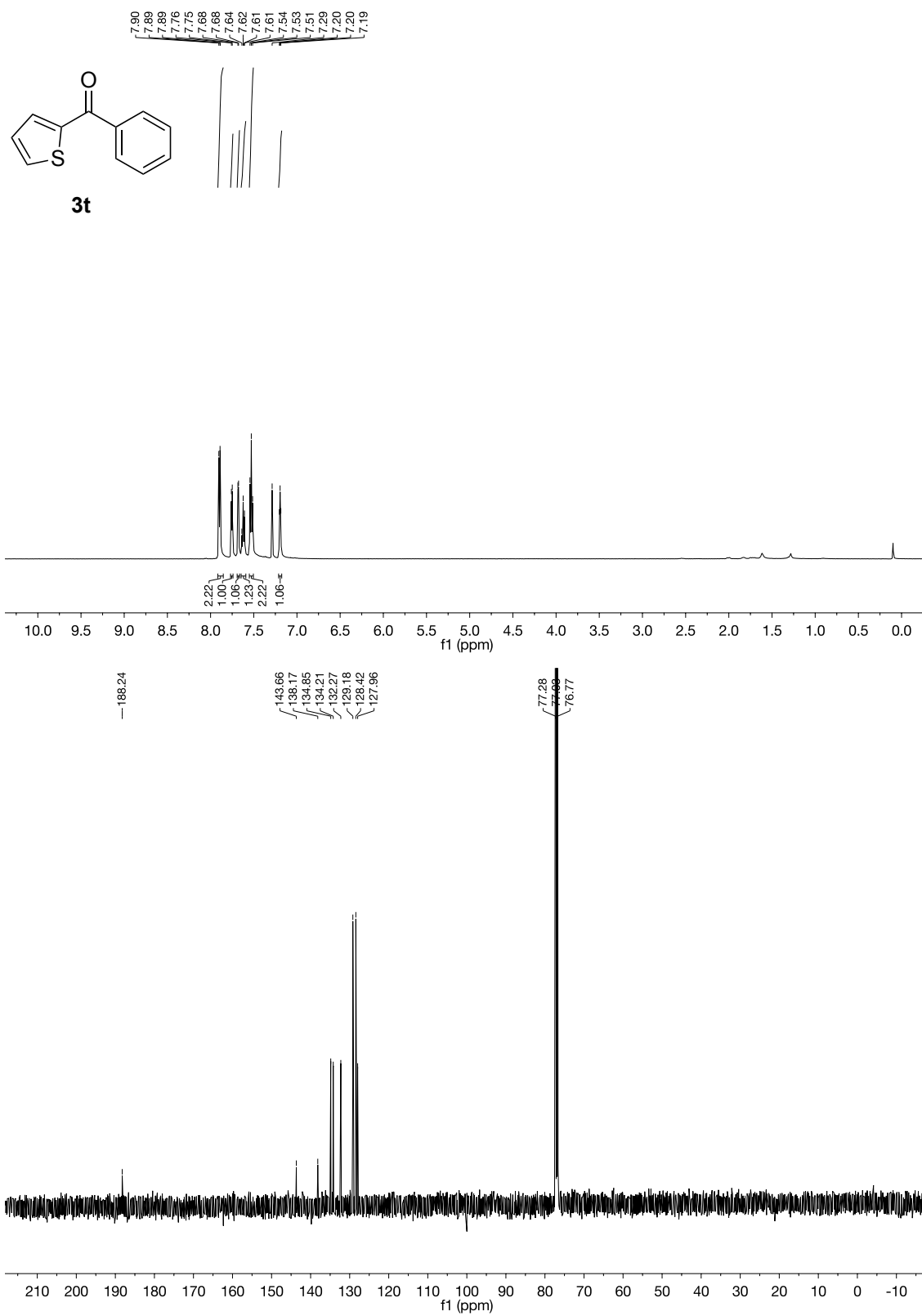


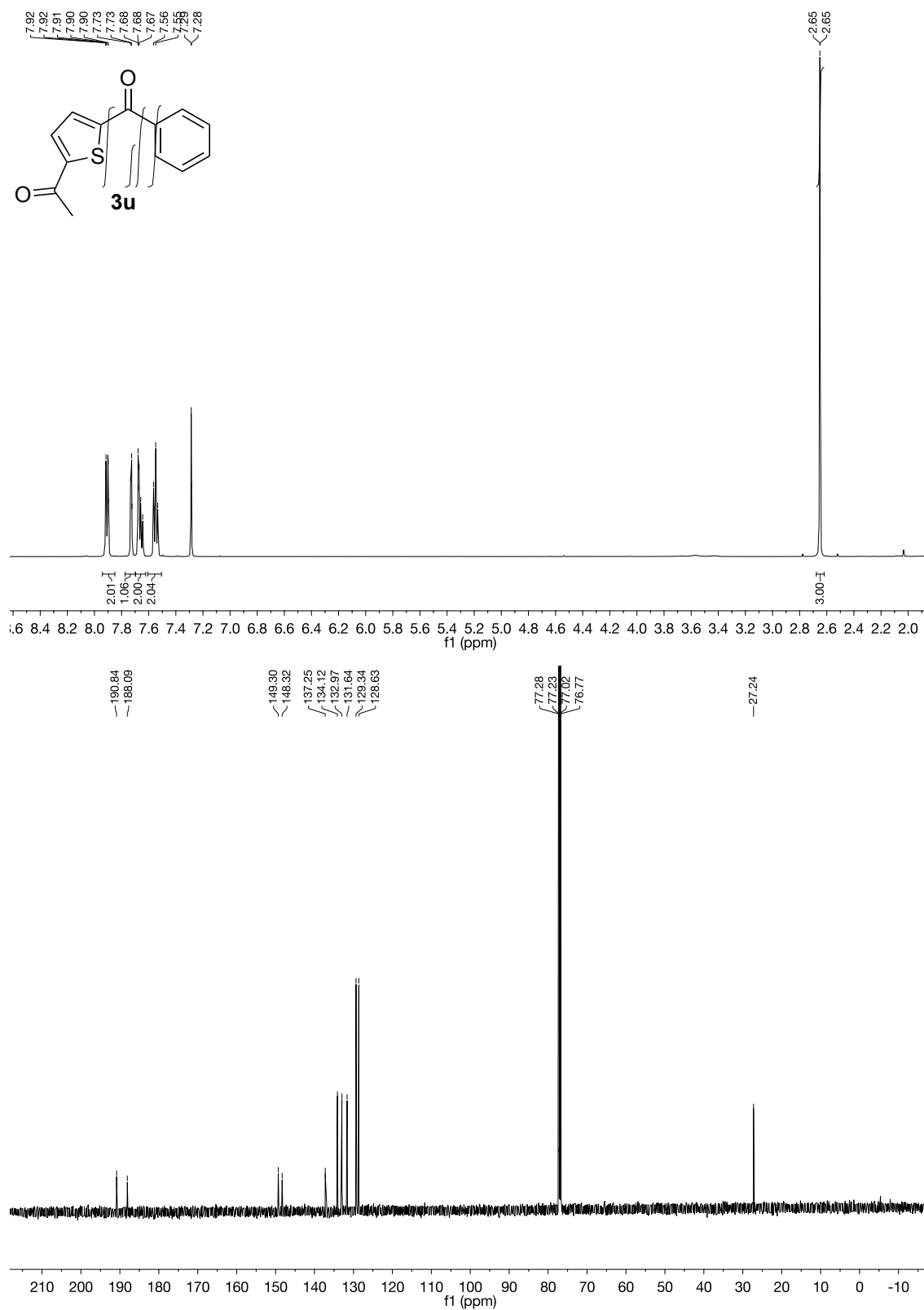


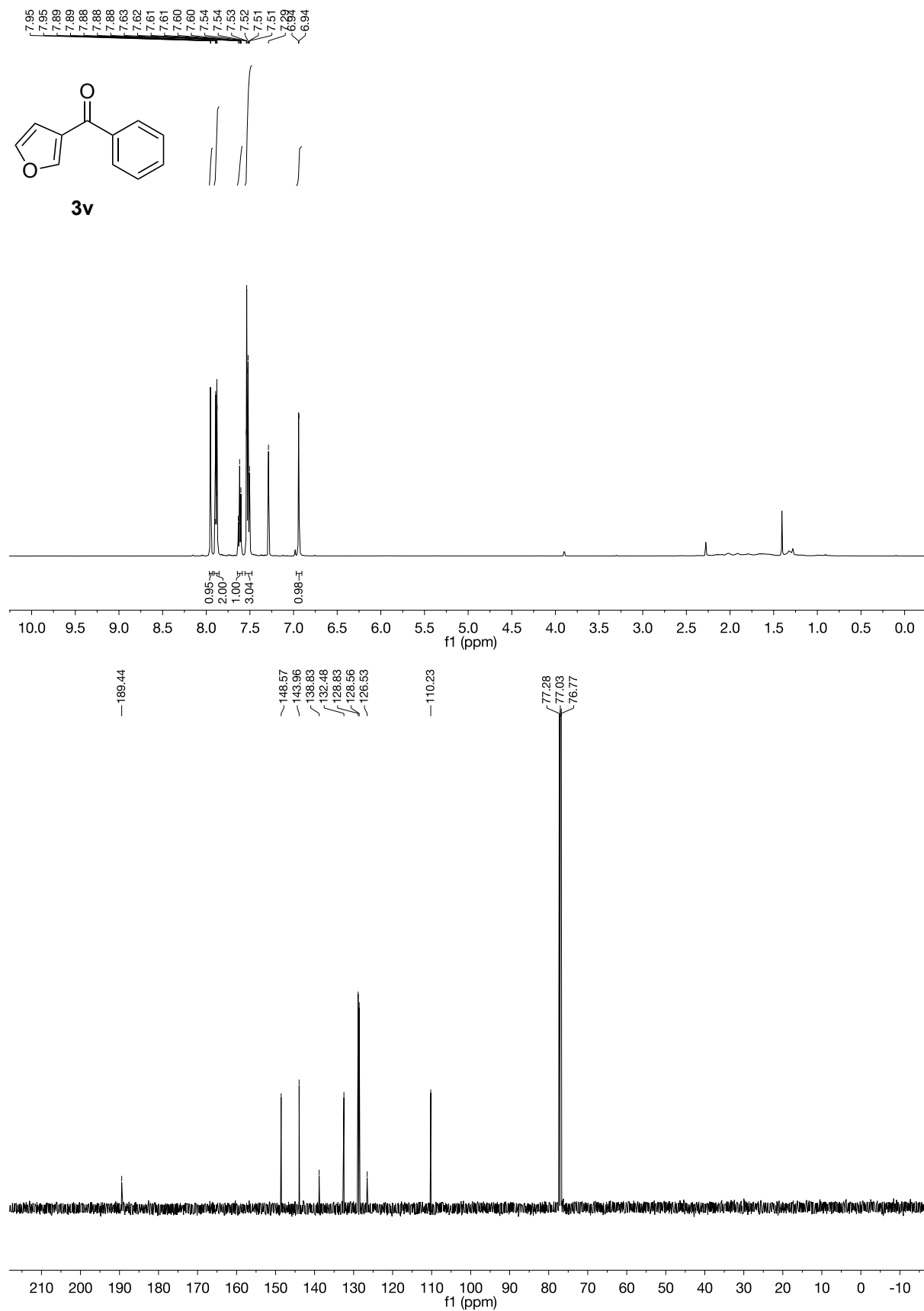


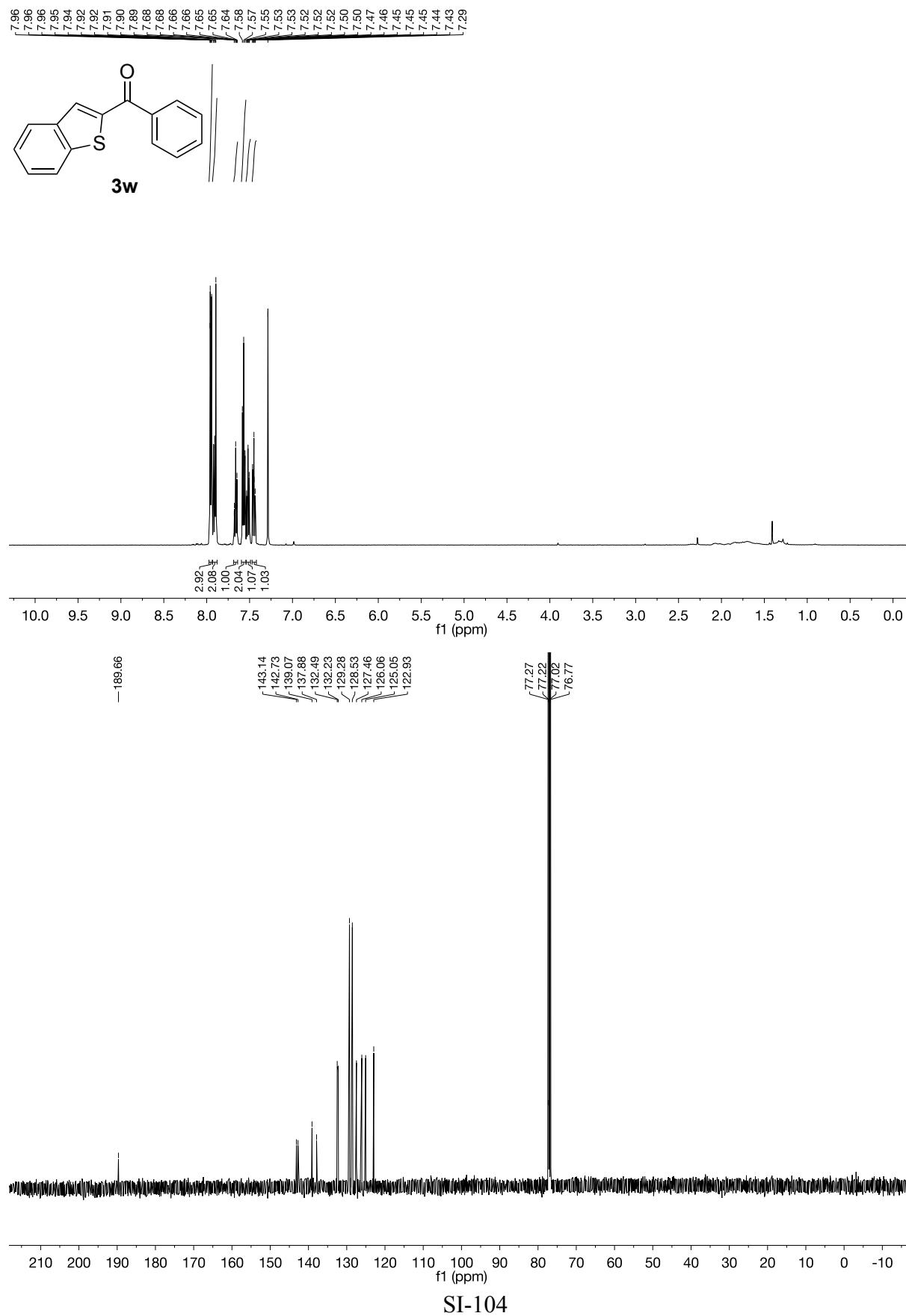


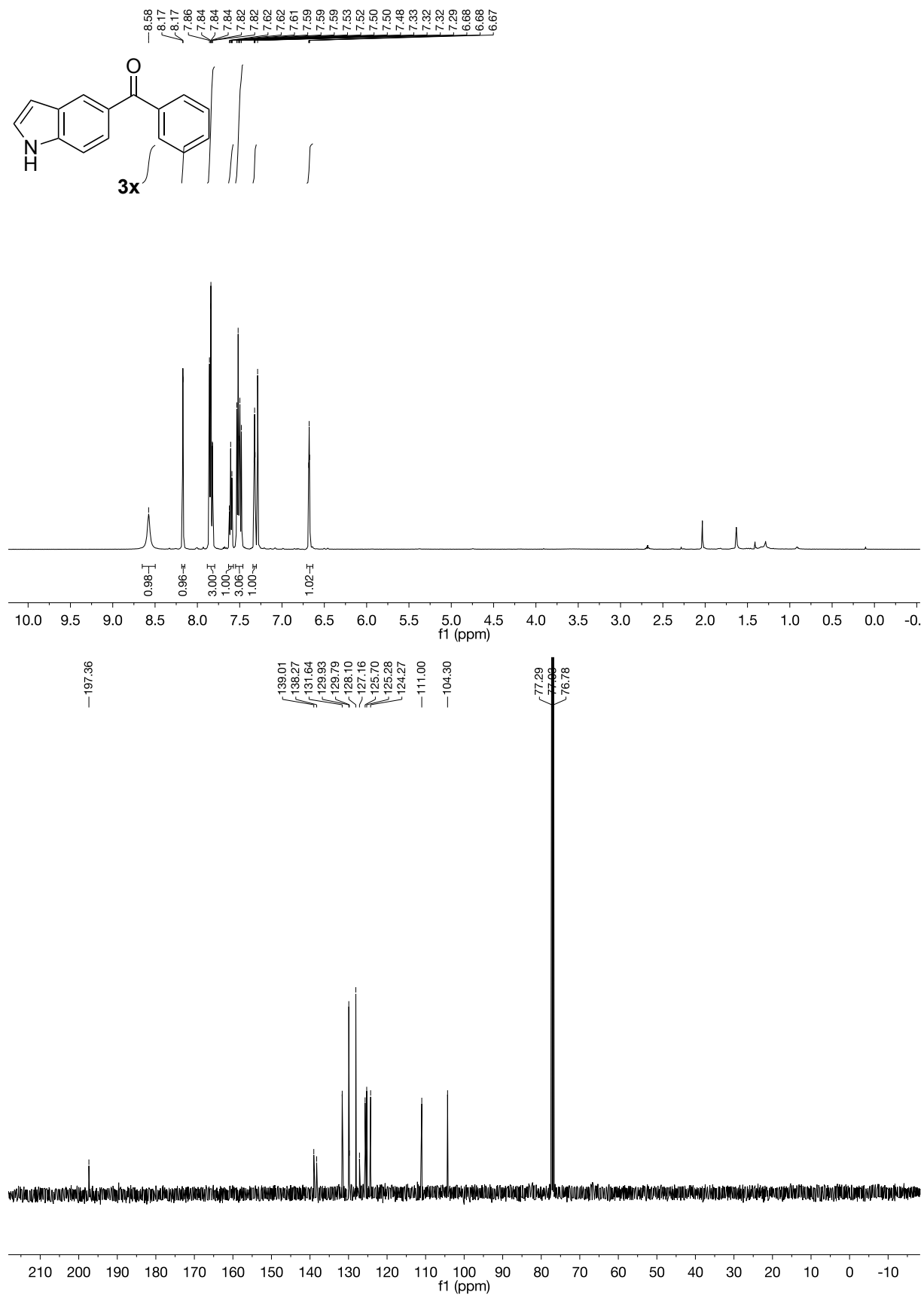


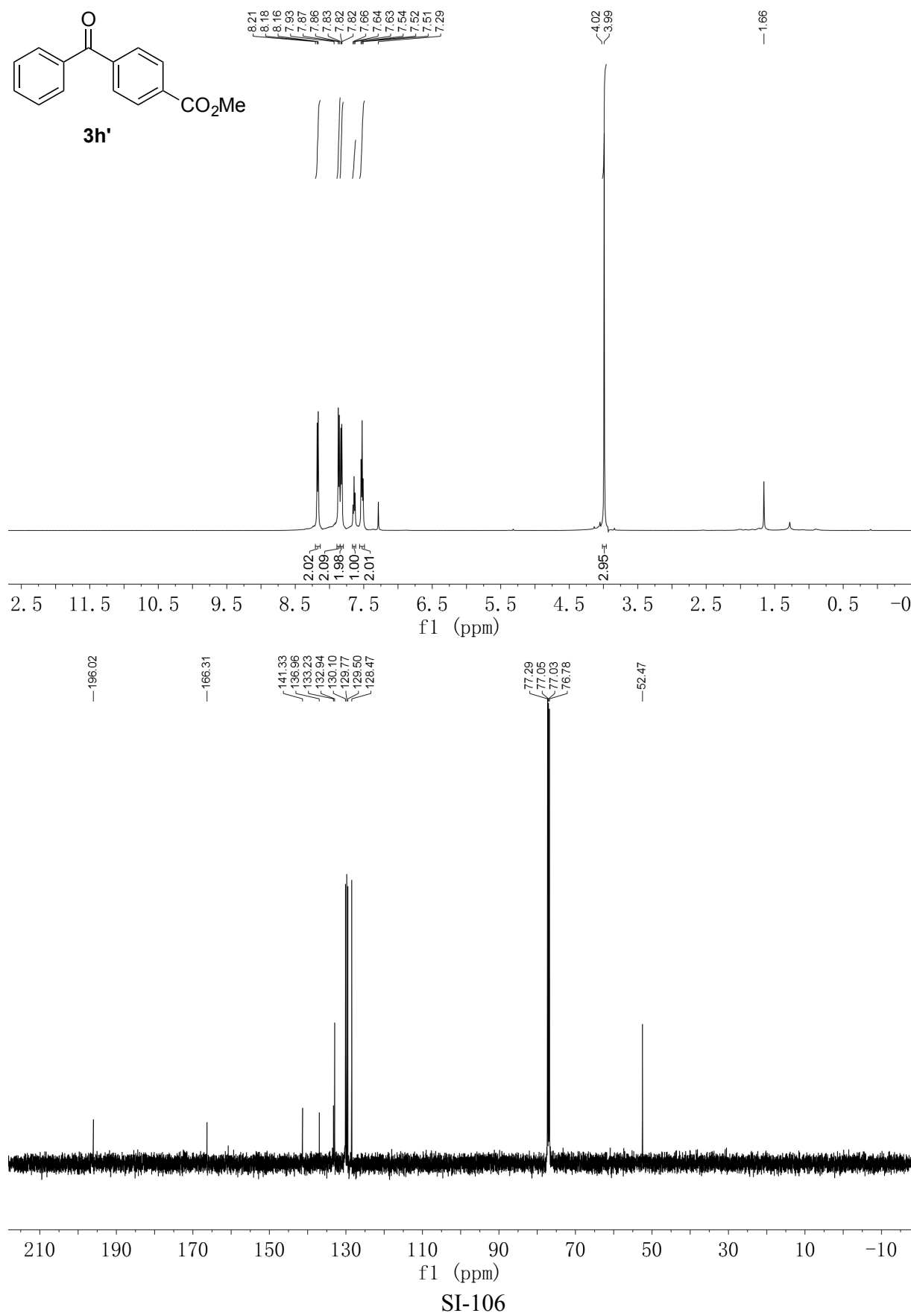


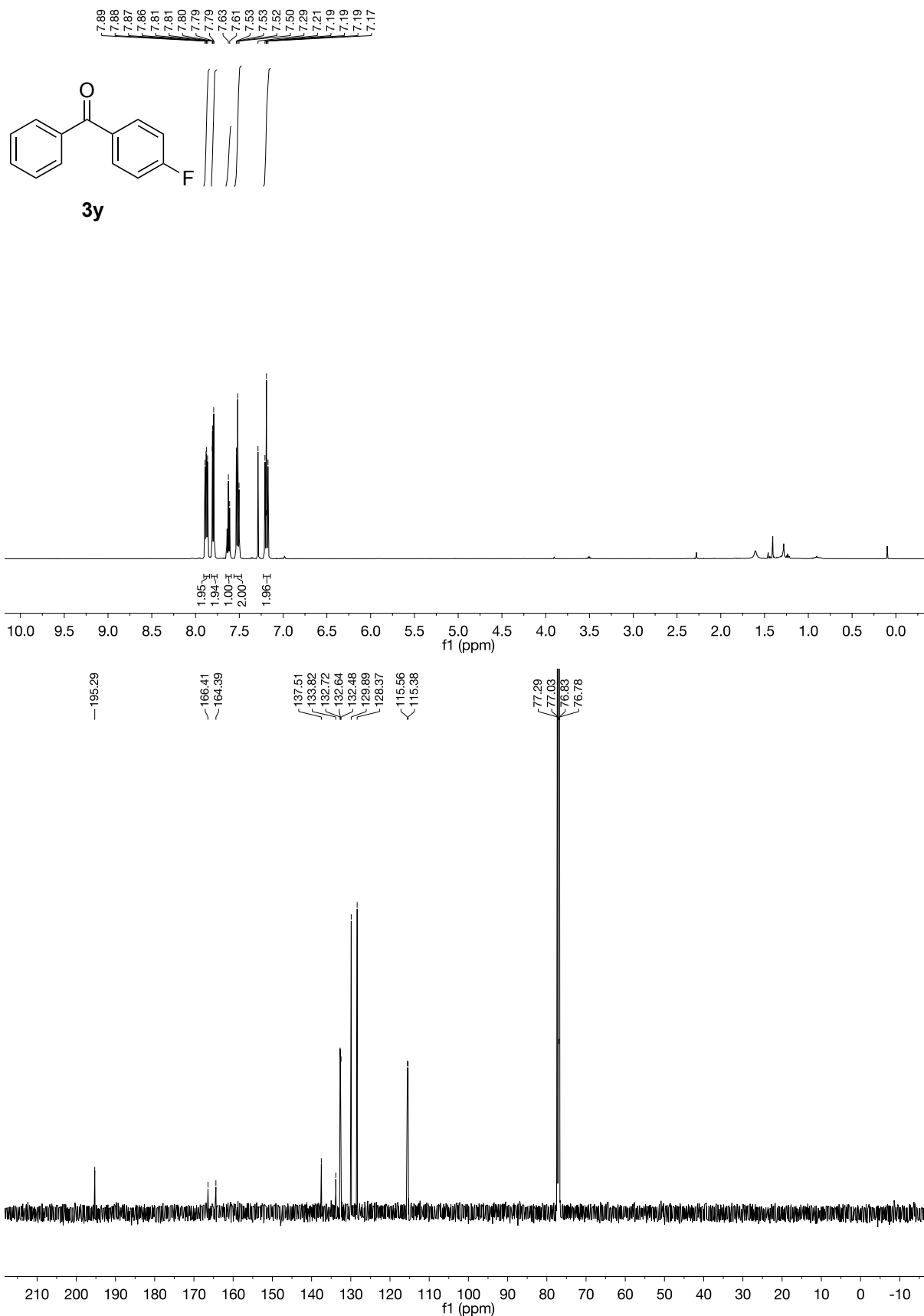


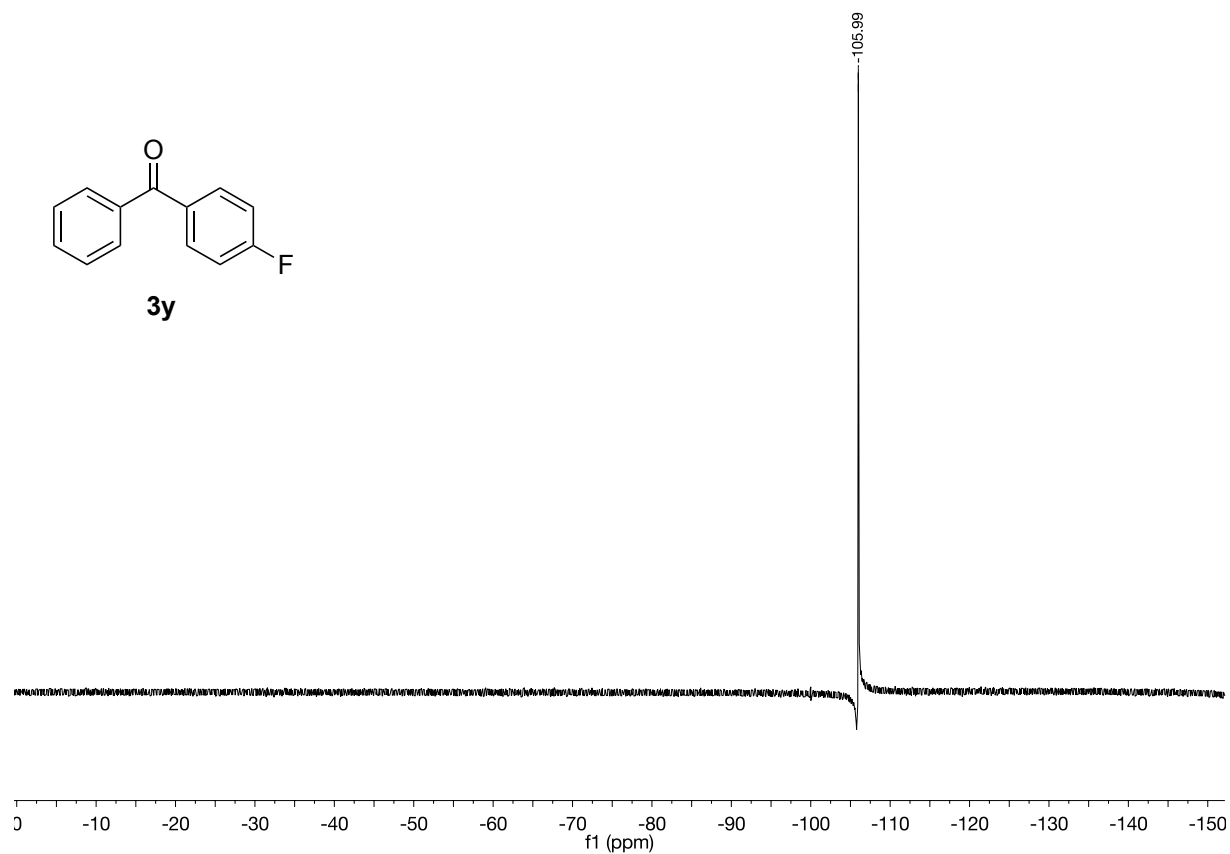
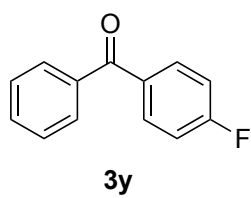


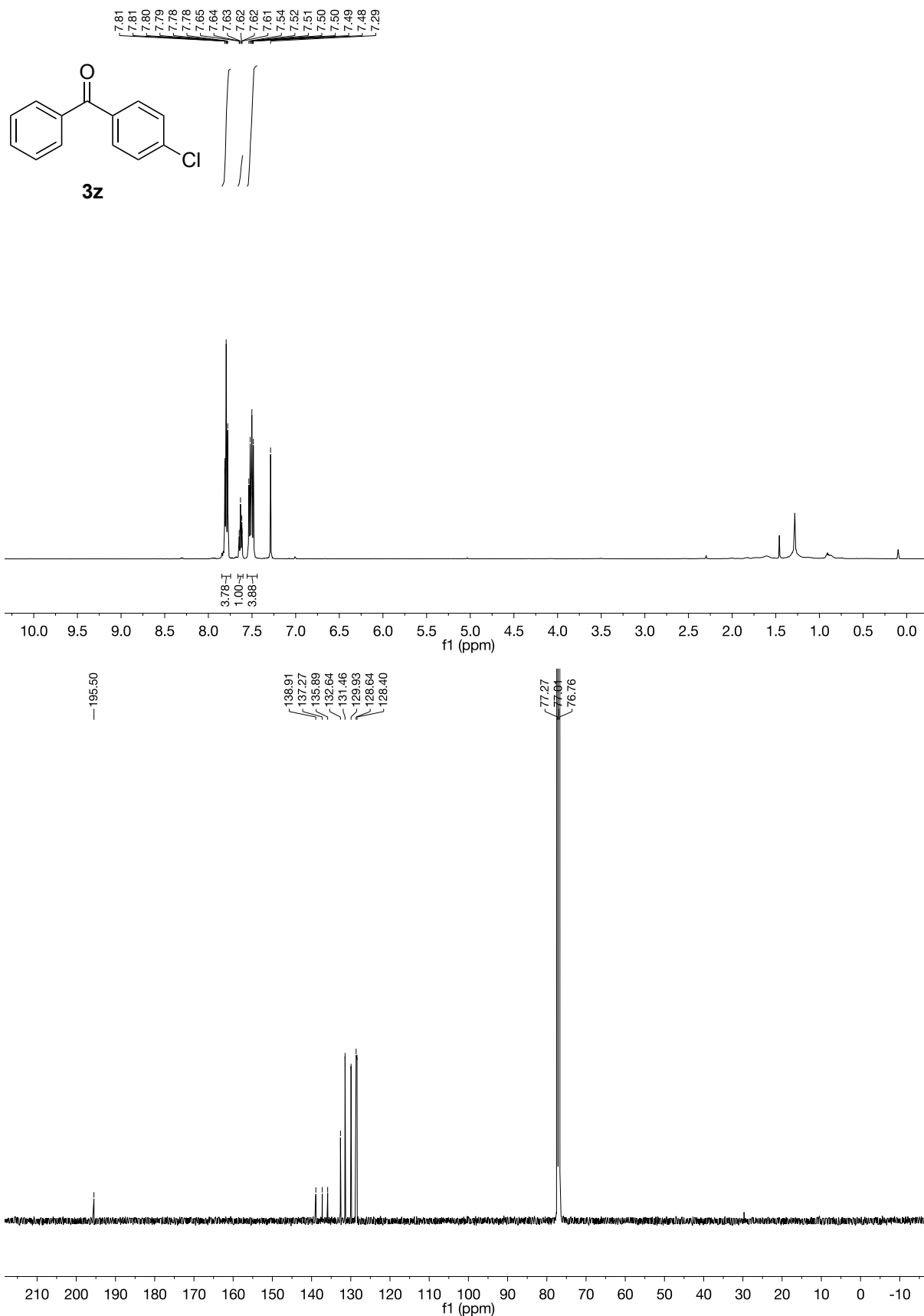


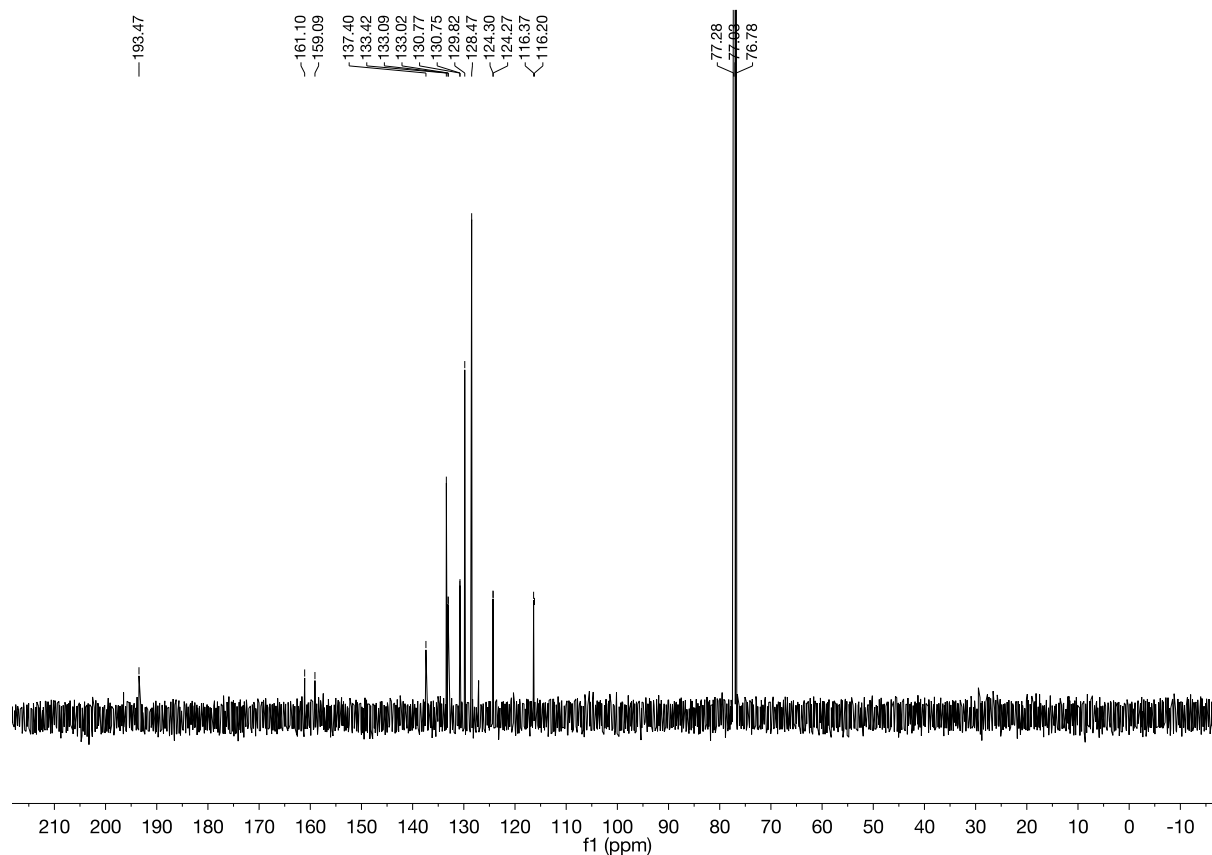
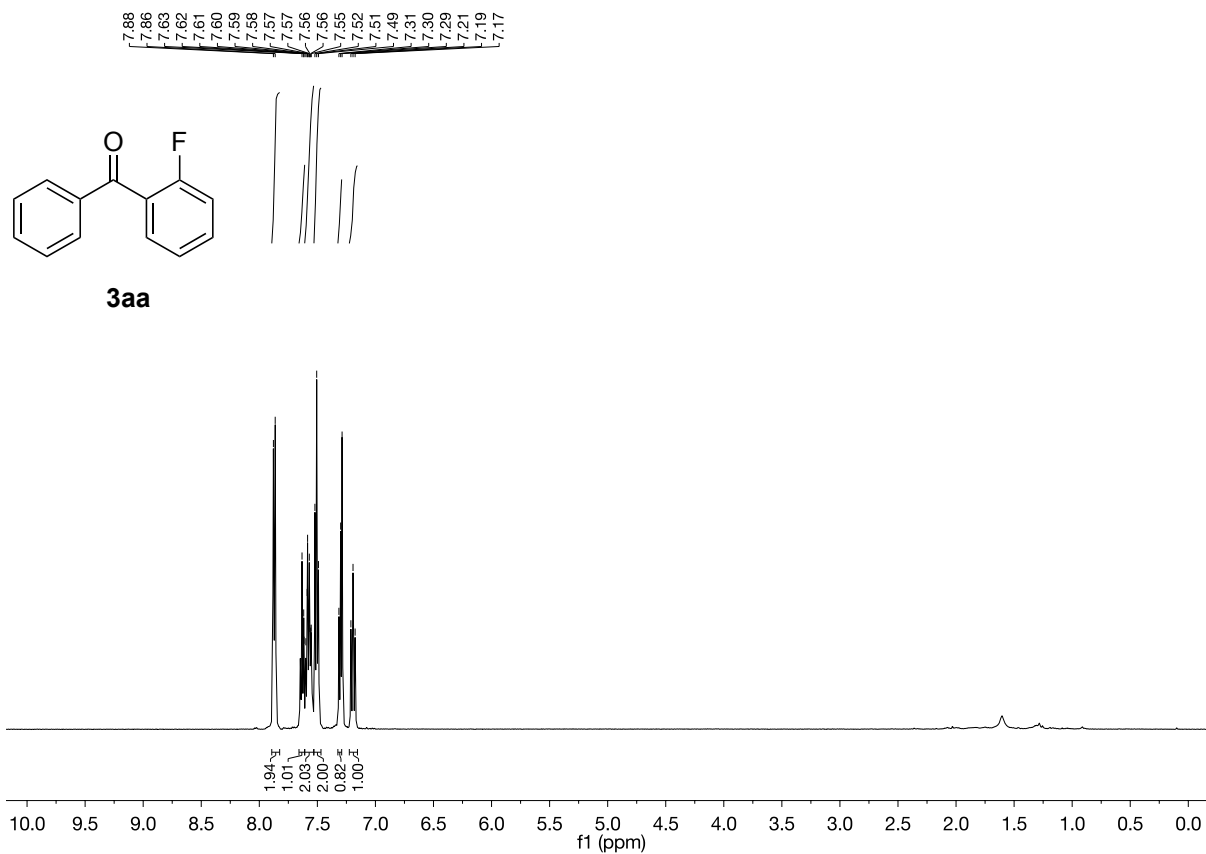


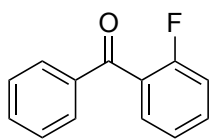












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