Pd-PEPPSI: A General Pd-NHC Precatalyst for Buchwald-Hartwig Cross-Coupling of Esters and Amides (Transamidation) under the Same Reaction Conditions

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Electronic Supplementary Information

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List of Known Compounds/General Methods

All starting materials reported in the manuscript have been previously described in literature and prepared by the method reported previously. Esters and amides were prepared by standard methods.[1-4] All experiments were performed using standard Schlenk techniques under nitrogen or argon 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 ^{1}H NMR analysis and comparison with authentic samples. GC and/or GC/MS analysis was used for volatile products. All yields refer to yields determined by ^{1}H NMR and/or GC or GC/MS using an internal standard (optimization) and isolated yields (preparative runs) unless stated otherwise. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker spectrometers at 500 (^{1}H NMR) and 125 MHz (^{13}C NMR). All shifts are reported in parts per million (ppm) relative to residual $CHCl_3$ peak (7.26 and 77.2 ppm, ^{1}H NMR and ^{13}C NMR, respectively). All coupling constants (J) are reported in hertz (Hz). Abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; brs, broad singlet. GC-MS chromatography was performed using Agilent HP6890 GC System and Agilent 5973A inert XL EI/CI MSD using helium as the carrier gas at a flow rate of 1 mL/min and an initial oven temperature of 50 °C. The injector temperature was 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 22.0 min). High-resolution mass spectra (HRMS) were measured on a 7T Bruker Daltonics FT-MS instrument. All flash chromatography was performed using silica gel, 60 Å, 300 mesh. TLC analysis was carried out on glass plates coated with silica gel 60 F254, 0.2 mm thickness. The plates were visualized using a 254 nm ultraviolet lamp or aqueous potassium permanganate solutions. ^{1}H NMR and ^{13}C NMR data are given for all compounds in the SI for characterization purposes. ^{1}H NMR, ^{13}C NMR, and HRMS data are given for all new compounds. All products have been previously reported, unless stated otherwise.

Experimental Procedures and Characterization Data

All amides and esters used in this study were prepared by procedures reported in the literature.[1-4] **1a**,[1] **1b**,[2] **1c**,[3] **1d**,[3] **1e**,[4] **1f**,[4] **1g**,[4] **1h**,[4] **3a**,[5] **3b**,[5] **3c**,[6] **3d**,[6] **3e**,[7] **3f**,[6] **3g**,[6] **3h**,[8] **3i**,[5] **3j**,[6] **3k**,[9] **3l**,[5] **3m**,[5] **3n**,[5] **3o**,[5] **4b**,[10] **4c**,[11] **5a**,[12] **5b**,[12] **5c**,[12] **5d**,[12] **5e**,[12] **5f**,[12] **5g**[12] are known compounds. Spectroscopic data match those reported in the literature.

General Procedure for the Buchwald-Hartwig Cross-Coupling of Esters and Amides. An oven-dried vial equipped with a stir bar was charged with an ester or amide substrate (neat, 1.0 equiv), potassium carbonate (typically, 3.0 equiv), amine (typically, 2.0 equiv), PEPPSI-IPr ([1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride, typically, 3 mol%), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. 1,2-Dimethoxyethane (typically, 0.25 M) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath and stirred for an indicated time. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the tile product.

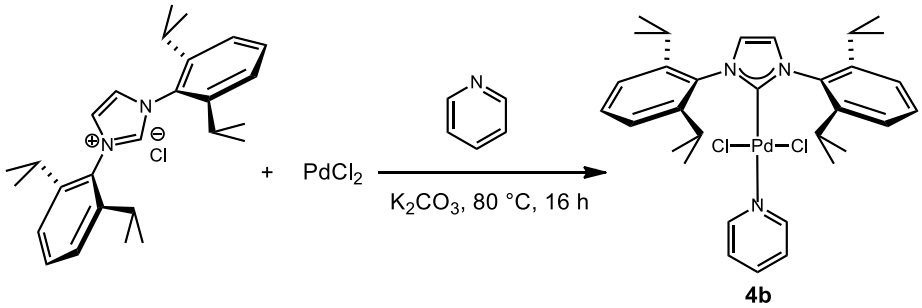
Representative Cross-Coupling Procedure. An oven-dried vial equipped with a stir bar was charged with phenyl benzoate (neat, 1.0 mmol, 198.0 mg, 1.0 equiv), potassium carbonate (3.0 mmol, 414.2 mg, 3.0 equiv), aniline (2.0 mmol, 186.0 mg, 2.0 equiv), PEPPSI-IPr (3 mol%, 20.4 mg), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. 1,2-Dimethoxyethane (0.25 M) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 110 °C and stirred for 16 h at 110 °C. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH_2Cl_2 (20 mL), filtered, and concentrated. The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples. Purification by chromatography on

silica gel (EtOAc/hexanes) afforded the tile product. Yield 96% (189.7 mg). White solid. Characterization data are included in the section below.

Synthesis of Pd-NHC Complexes

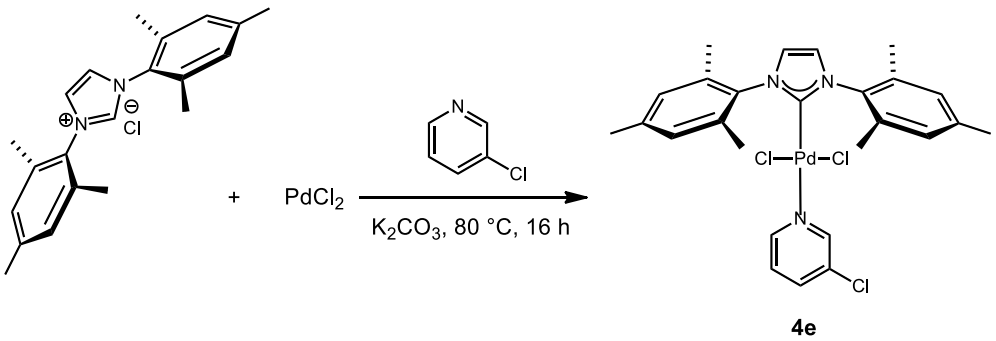
Pd-PEPPSI complexes **4a** and **4d** are commercially available. Complexes **4b**, **4c** and **4e** were prepared by procedures reported in the literature.[10,11] Spectroscopic data match those reported in the literature.

*Synthesis of **4b** and **4e**.*[10] The following procedure is representative. On a benchtop, a vial equipped with and a stir bar was charged with $PdCl_2$ (177 mg, 1.0 mmol), IMesHCl (1.1 mmol), K_2CO_3 (5.0 mmol), and 3-chloropyridine (4.0 mL). The resulting reaction mixture was placed in a preheated oil bath at 80 °C and stirred for 16 h at 80 °C. After the indicated time, the reaction mixture was cooled to room temperature, diluted with CH_2Cl_2 (10 mL), passed through a short pad of silica eluting with CH_2Cl_2, and concentrated. The pure Pd-NHC complexes **4b** and **4e** were isolated by trituration with hexane, decanting the supernatant, washing the solid with hexane and drying under high vacuum.



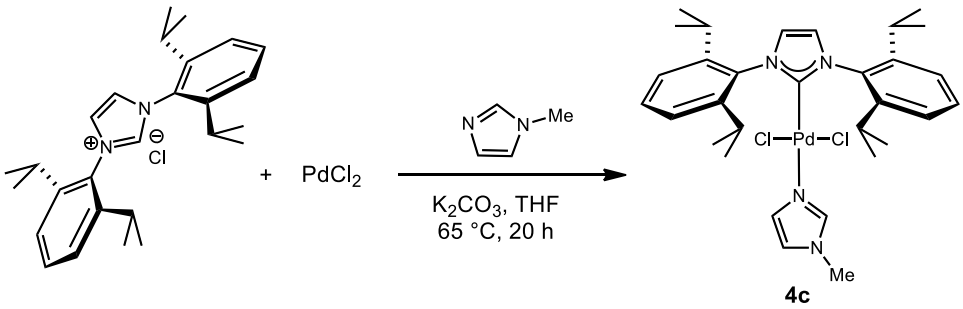
4b

4b: Yellow solid. Yield 90% (595 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 1.9 Hz, 1 H), 8.50 (d, *J* = 5.4 Hz, 1 H), 7.56 (d, *J* = 9.0 Hz, 1 H), 7.07 (d, *J* = 9.7 Hz, 7 H), 2.38 (s, 6 H), 2.36 (s, 12 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.33, 150.57, 149.65, 139.38, 137.60, 136.42, 135.12, 132.05, 129.40, 124.42, 124.38, 21.35, 19.24.



4e

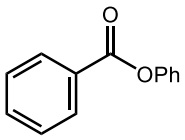
4e: Yellow solid. Yield 87% (532 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.9 Hz, 2 H), 7.53 (t, *J* = 7.6 Hz, 1 H), 7.49 (t, *J* = 7.7 Hz, 2 H), 7.36 (s, 2 H), 7.34 (s, 2 H), 7.13 (s, 2 H), 7.12-7.08 (m, 2 H), 3.18 (p, *J* = 6.8 Hz, 4 H), 1.49 (d, *J* = 6.6 Hz, 12 H), 1.12 (d, *J* = 6.9 Hz, 12 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.00, 151.54, 146.77, 137.49, 135.24, 130.36, 125.13, 124.15, 124.12, 28.86, 26.43, 23.38.



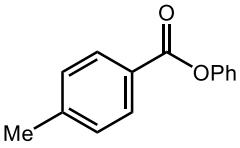
4c

Synthesis of ***4c***.[11] On a benchtop, a vial equipped with and a stir bar was charged with $PdCl_2$ (17.7 mg, 0.10 mmol), IPrHCl (0.12 mmol), K_2CO_3 (0.10 mmol), and 1-methylimidazole (0.40 mmol), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF (0.15 M) was added, the reaction mixture was placed in a preheated oil bath at 65 °C and stirred for 20 h at 65 °C. After the indicated time, the reaction mixture was cooled to room temperature and concentrated. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product. **4c**: Yellow solid. Yield 45% (29.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1 H), 7.46 (t, *J* = 7.7 Hz, 2 H), 7.32 (d, *J* = 7.7 Hz, 4 H), 7.18 (s, 1 H), 7.09 (s, 2 H), 6.53 (s, 1 H), 3.45 (s, 3 H), 3.18 (p, *J* = 6.7 Hz, 4 H), 1.47 (d, *J* = 6.6 Hz, 12 H), 1.11 (d, *J* = 6.8 Hz, 12 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.57, 146.81, 138.48, 135.37, 130.18, 128.74, 124.97, 124.09, 119.10, 34.09, 28.81, 26.42, 23.41.

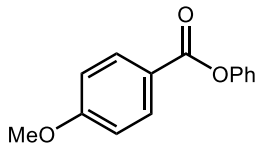
Characterization Data for Starting Materials



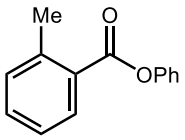
Phenyl benzoate (1a). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29-8.20 (m, 2 H), 7.67 (t, *J* = 7.4 Hz, 1 H), 7.55 (t, *J* = 7.7 Hz, 2 H), 7.47 (t, *J* = 7.9 Hz, 2 H), 7.31 (t, *J* = 7.4 Hz, 1 H), 7.25 (d, *J* = 7.6 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.21, 150.99, 133.60, 130.20, 129.62, 129.52, 128.59, 125.91, 121.74.



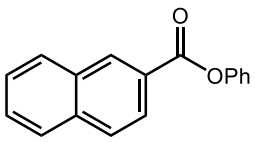
Phenyl 4-methylbenzoate (1b). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (t, *J* = 6.9 Hz, 2 H), 7.44 (t, *J* = 7.9 Hz, 2 H), 7.32 (d, *J* = 7.6 Hz, 2 H), 7.30-7.26 (m, 1 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 2.46 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.38, 151.18, 144.53, 130.36, 129.59, 129.43, 126.97, 125.92, 121.91, 21.91.



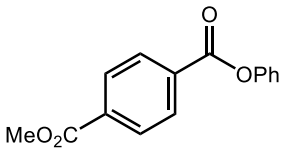
Phenyl 4-methoxybenzoate (1c). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.9 Hz, 2 H), 7.45 (t, *J* = 7.9 Hz, 2 H), 7.31-7.27 (m, 1 H), 7.24 (d, *J* = 7.9 Hz, 2 H), 7.02 (d, *J* = 8.8 Hz, 2 H), 3.92 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.92, 163.91, 151.11, 132.31, 129.45, 125.73, 121.93, 121.82, 113.86, 55.53.



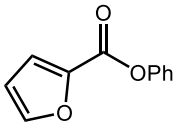
Phenyl 2-methylbenzoate (1d). Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.7 Hz, 1 H), 7.51 (t, *J* = 7.5 Hz, 1 H), 7.47 (t, *J* = 7.3 Hz, 2 H), 7.36 (t, *J* = 8.0 Hz, 2 H), 7.32-7.28 (m, 1 H), 7.25 (d, *J* = 7.9 Hz, 2 H), 2.71 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.86, 150.96, 141.34, 132.73, 131.98, 131.18, 129.51, 128.62, 125.94, 125.84, 121.85, 21.96.



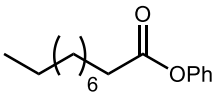
Phenyl 2-methylbenzoate (1e). Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (s, 1 H), 8.21 (d, *J* = 8.5 Hz, 1 H), 8.01 (d, *J* = 8.1 Hz, 1 H), 7.94 (dd, *J* = 14.3, 8.4 Hz, 2 H), 7.64 (t, *J* = 7.5 Hz, 1 H), 7.59 (t, *J* = 7.5 Hz, 1 H), 7.47 (t, *J* = 7.4 Hz, 2 H), 7.33-7.26 (m, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.18, 135.95, 132.63, 132.06, 129.66, 129.62, 128.76, 128.53, 127.97, 126.97, 126.91, 126.05, 125.60, 121.91.



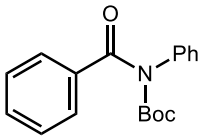
Methyl phenyl terephthalate (1f). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 7.5 Hz, 2 H), 8.20 (d, *J* = 7.9 Hz, 2 H), 7.47 (t, *J* = 7.3 Hz, 2 H), 7.32 (t, *J* = 7.4 Hz, 1 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 4.00 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.20, 164.40, 150.78, 134.51, 133.39, 130.15, 129.74, 129.59, 126.14, 121.59, 52.54.



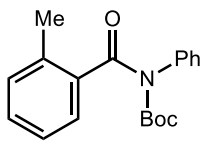
Phenyl furan-2-carboxylate (1g). Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (s, 1 H), 7.45 (t, *J* = 7.4 Hz, 2 H), 7.41 (d, *J* = 2.3 Hz, 1 H), 7.32-7.28 (m, 1 H), 7.24 (d, *J* = 7.9 Hz, 2 H), 6.62 (d, *J* = 1.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.94, 150.23, 147.14, 144.06, 129.53, 126.08, 121.62, 119.43, 112.19.



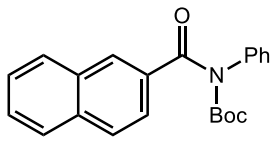
Phenyl decanoate (1h). Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.9 Hz, 2 H), 7.22 (t, *J* = 7.4 Hz, 1 H), 7.08 (d, *J* = 8.3 Hz, 2 H), 2.56 (t, *J* = 7.5 Hz, 2 H), 1.76 (p, *J* = 7.5 Hz, 2 H), 1.44-1.26 (m, 12 H), 0.89 (t, *J* = 6.7 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.46, 150.90, 129.51, 125.82, 121.71, 34.56, 32.00, 29.56, 29.40, 29.25, 25.10, 22.81, 14.25.



***tert*-Butyl benzoyl(phenyl)carbamate (5a)**. White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.1 Hz, 2 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.49-7.43 (m, 4 H), 7.37 (t, *J* = 7.4 Hz, 1 H), 7.30 (d, *J* = 7.4 Hz, 2 H), 1.26 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.78, 153.30, 139.10, 136.98, 131.72, 129.21, 128.28, 128.14, 127.96, 127.80, 83.50, 27.49.

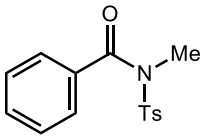


***tert*-Butyl (2-methylbenzoyl)(phenyl)carbamate (5b)**. White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (q, *J* = 7.2 Hz, 3 H), 7.40 (d, *J* = 6.9 Hz, 1 H), 7.38-7.34 (m, 1 H), 7.32 (d, *J* = 7.9 Hz, 2 H), 7.27 (d, *J* = 7.4 Hz, 2 H), 2.52 (s, 3 H), 1.19 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.58, 152.85, 138.55, 137.86, 135.69, 130.73, 129.92, 129.22, 128.07, 127.98, 126.39, 125.53, 83.57, 27.34, 19.52.

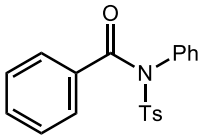


***tert*-Butyl (2-naphthoyl)(phenyl)carbamate (5c)**. White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1 H), 7.94-7.87 (m, 3 H), 7.79 (d, *J* = 9.6

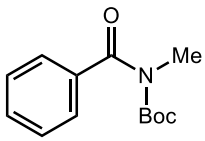
Hz, 1 H), 7.61-7.53 (m, 2 H), 7.45 (t, *J* = 7.7 Hz, 2 H), 7.37-7.31 (m, 3 H), 1.18 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.55, 139.29, 134.94, 134.20, 132.54, 129.36, 129.08, 129.04, 128.20, 128.07, 128.05, 127.96, 127.91, 126.99, 124.81, 83.62, 27.60.



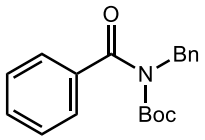
***N*-Methyl-*N*-tosylbenzamide (5d)**. White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 2 H), 7.57 (d, *J* = 8.2 Hz, 2 H), 7.53 (t, *J* = 8.0 Hz, 1 H), 7.43 (t, *J* = 7.6 Hz, 2 H), 7.35 (d, *J* = 8.1 Hz, 2 H), 3.30 (s, 3H), 2.47 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.48, 144.91, 135.21, 134.52, 131.96, 129.62, 128.49, 128.42, 128.29, 35.60, 21.68.



***N*-Phenyl-*N*-tosylbenzamide (5e)**. Yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 2 H), 7.46 (d, *J* = 8.3 Hz, 2 H), 7.34 (d, *J* = 8.1 Hz, 2 H), 7.29 (m, 4 H), 7.21-7.16 (m, 4 H), 2.47 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.90, 144.81, 137.43, 135.25, 133.67, 131.74, 130.40, 129.49, 129.25, 129.10, 129.03, 128.60, 127.98, 21.73.



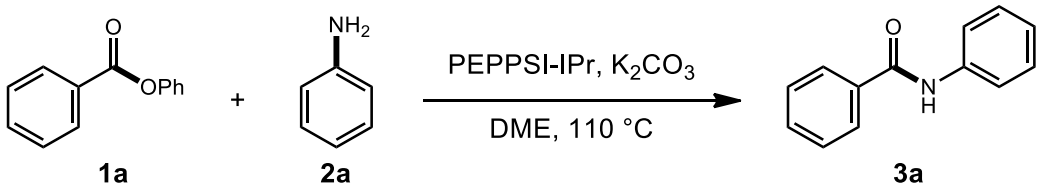
***tert*-Butyl benzoyl(methyl)carbamate (5f)**. Oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.2 Hz, 2 H), 7.48 (t, *J* = 7.4 Hz, 1 H), 7.40 (t, *J* = 7.5 Hz, 2 H), 3.33 (s, 3 H), 1.17 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.59, 153.54, 137.91, 130.85, 127.99, 127.41, 82.98, 32.55, 27.37.



***tert*-Butyl benzoyl(benzyl)carbamate (5g)**. White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.0 Hz, 2 H), 7.47 (dd, *J* = 10.9, 7.4 Hz, 3 H), 7.41 (d, *J* = 7.7 Hz, 2 H), 7.37 (s, 2 H), 7.30 (s, 1 H), 5.02 (s, 2 H), 1.15 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.09, 153.46, 137.86, 137.73, 131.04, 128.45, 128.16, 128.06, 127.46, 127.40, 83.18, 48.88, 27.35.

Buchwald-Hartwig Cross-Coupling of Esters

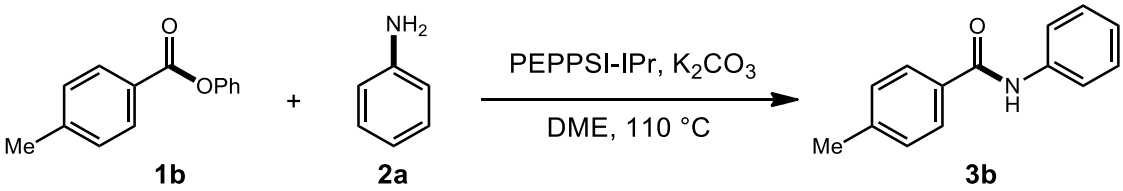
N-Phenylbenzamide (Table 2, 3a)



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

According to the general procedure, the reaction of phenyl benzoate (1.00 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work upand chromatography the title compound in 96% yield (189.7 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1 H), 7.86 (d, *J* = 7.4 Hz, 2 H), 7.65 (d, *J* = 8.0 Hz, 2 H), 7.53 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.35 (t, *J* = 7.9 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.97, 138.06, 135.09, 131.91, 129.17, 128.85, 127.16, 124.66, 120.40.

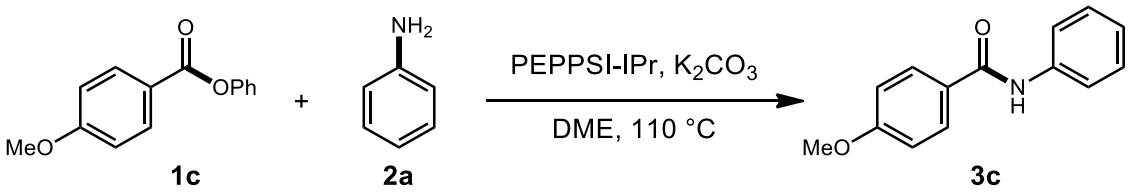
4-Methyl-*N*-phenylbenzamide (Table 2, 3b)



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

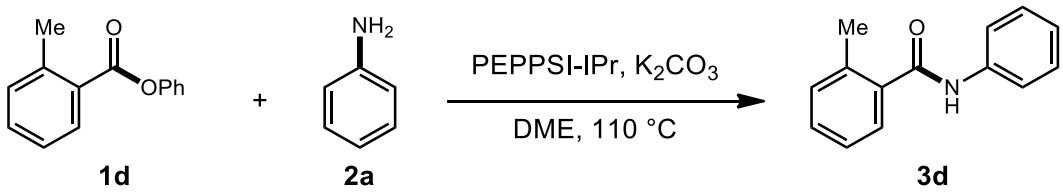
According to the general procedure, the reaction of phenyl 4-methylbenzoate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 91% yield (38.4 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1 H), 7.76 (d, *J* = 8.0 Hz, 2 H), 7.64 (d, *J* = 8.0 Hz, 2 H), 7.34 (t, *J* = 7.8 Hz, 2 H), 7.24 (d, *J* = 7.8 Hz, 2 H), 7.13 (t, *J* = 7.4 Hz, 1 H), 2.41 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.89, 142.39, 138.18, 132.19, 129.47, 129.12, 127.17, 124.49, 120.35, 21.59.

4-Methoxy-*N*-phenylbenzamide (Table 2, 3c)



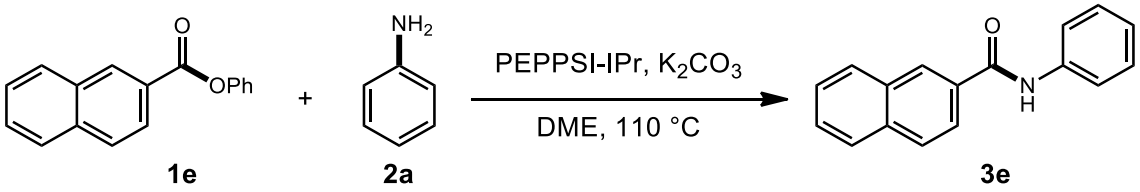
According to the general procedure, the reaction of phenyl 4-methoxybenzoate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (6 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 71% yield (32.3 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.7 Hz, 2 H), 7.73 (s, 1 H), 7.63 (d, *J* = 8.0 Hz, 2 H), 7.37 (t, *J* = 7.8 Hz, 2 H), 7.14 (t, *J* = 7.4 Hz, 1 H), 6.98 (d, *J* = 8.7 Hz, 2 H), 3.88 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.64, 138.24, 129.22, 129.01, 124.48, 120.25, 114.14, 55.62.

2-Methyl-*N*-phenylbenzamide (Table 2, 3d)



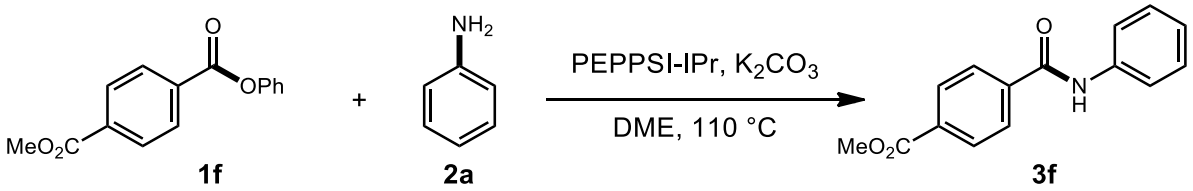
According to the general procedure, the reaction of phenyl 2-methylbenzoate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 97% yield (40.9 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1 H), 7.61 (d, *J* = 7.5 Hz, 2 H), 7.43 (d, *J* = 7.2 Hz, 1 H), 7.35 (t, *J* = 7.8 Hz, 3 H), 7.23 (dd, *J* = 16.5, 7.7 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H), 2.47 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.26, 138.11, 136.51, 136.45, 131.28, 130.30, 129.14, 126.73, 125.93, 124.59, 120.01, 19.88.

***N*-Phenyl-2-naphthamide (Table 2, 3e)**



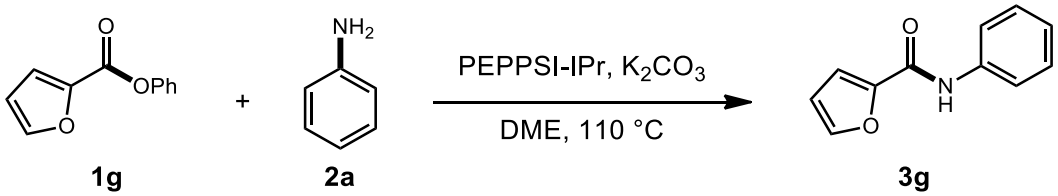
According to the general procedure, the reaction of phenyl 2-naphthoate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 74% yield (36.6 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1 H), 8.01-7.93 (m, 4 H), 7.91 (d, *J* = 7.8 Hz, 1 H), 7.70 (d, *J* = 7.9 Hz, 2 H), 7.63-7.56 (m, 2 H), 7.41 (t, *J* = 7.9 Hz, 2 H), 7.18 (t, *J* = 7.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.90, 138.12, 135.00, 132.75, 129.28, 129.10, 128.92, 128.06, 127.96, 127.65, 127.10, 124.75, 123.67, 120.35.

Methyl 4-(phenylcarbamoyl)benzoate (Table 2, 3f)



According to the general procedure, the reaction of methyl phenyl terephthalate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (6 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 50% yield (25.5 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 2 H), 7.93 (d, *J* = 8.1 Hz, 2 H), 7.86 (s, 1 H), 7.65 (d, *J* = 8.0 Hz, 2 H), 7.39 (t, *J* = 7.8 Hz, 2 H), 7.18 (t, *J* = 7.4 Hz, 1 H), 3.96 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.33, 139.00, 137.70, 133.18, 130.19, 129.32, 127.22, 125.08, 125.08, 120.40, 52.6.

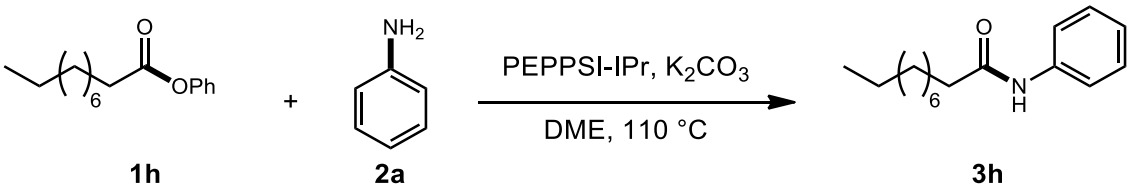
***N*-Phenylfuran-2-carboxamide (Table 2, 3g)**



According to the general procedure, the reaction of phenyl 2-naphthoate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 75% yield (28.0 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1 H), 7.65 (d, *J* = 7.7 Hz, 2 H), 7.55-7.48 (m, 1 H), 7.37 (t, *J* = 7.9 Hz, 2 H), 7.24 (d, *J* = 3.4 Hz, 1 H), 7.15 (t, *J* = 7.4 Hz, 1 H), 6.56 (dd, *J* =

3.5, 1.8 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.19, 147.94, 144.29, 137.48, 129.25, 124.66, 120.04, 115.41, 112.77.

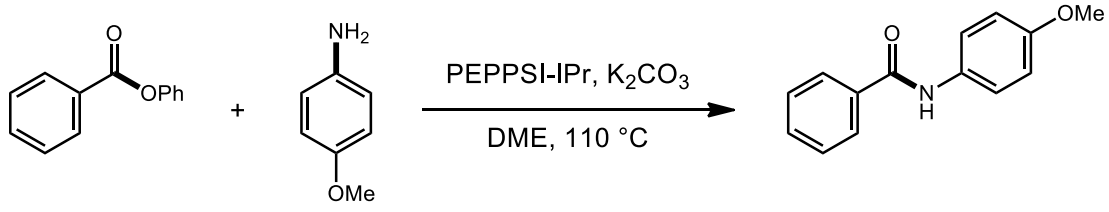
_N_-Phenyldecanamide (Table 2, 3h)



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

According to the general procedure, the reaction of phenyl decanoate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 78% yield (38.5 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.9 Hz, 2 H), 7.31 (t, *J* = 7.9 Hz, 2 H), 7.23 (s, 1 H), 7.09 (t, *J* = 7.4 Hz, 1 H), 2.35 (t, *J* = 7.6 Hz, 2 H), 1.72 (p, *J* = 7.5 Hz, 2 H), 1.38-1.23 (m, 13 H), 0.88 (t, *J* = 6.9 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.60, 138.10, 129.09, 124.27, 119.90, 37.99, 31.99, 29.57, 29.52, 29.40, 25.78, 22.79, 14.24.

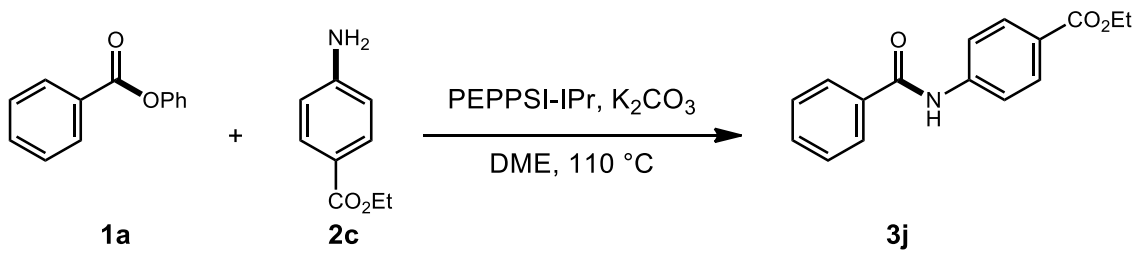
_N_-(4-Methoxyphenyl)benzamide (Table 2, 3i)



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

According to the general procedure, the reaction of phenyl benzoate (0.20 mmol, 1.0 equiv), 4-methoxyaniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 84% yield (38.1 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.8 Hz, 3 H), 7.55 (t, *J* = 7.2 Hz, 3 H), 7.48 (t, *J* = 7.5 Hz, 2 H), 6.91 (d, *J* = 8.6 Hz, 2 H), 3.82 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.78, 156.74, 135.15, 131.80, 131.13, 128.85, 127.11, 122.26, 114.35, 55.63.

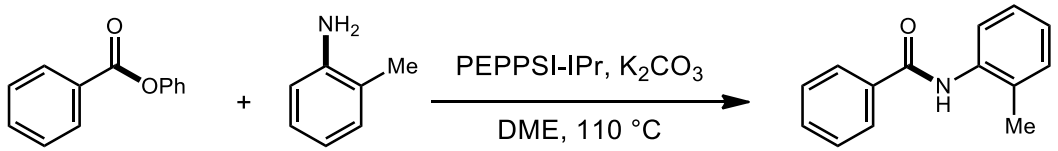
Ethyl 4-benzamidobenzoate (Table 2, 3j)



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

According to the general procedure, the reaction of phenyl benzoate (0.20 mmol, 1.0 equiv), ethyl 4-aminobenzoate (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 85% yield (45.7 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1 H), 8.02 (d, *J* = 8.3 Hz, 2 H), 7.86 (d, *J* = 7.8 Hz, 2 H), 7.75 (d, *J* = 8.3 Hz, 2 H), 7.54 (t, *J* = 7.2 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 4.35 (q, *J* = 7.2 Hz, 2 H), 1.38 (t, *J* = 7.1 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.10, 142.28, 134.63, 132.25, 130.90, 128.92, 127.24, 119.36, 61.03, 14.46.

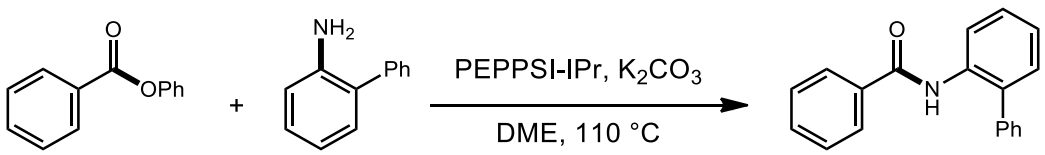
***N*-(*o*-Tolyl)benzamide (Table 2, 3k)**



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

According to the general procedure, the reaction of phenyl benzoate (0.20 mmol, 1.0 equiv), *o*-toluidine (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 75% yield (31.7 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 1 H), 7.89 (d, *J* = 7.6 Hz, 2 H), 7.68 (s, 1 H), 7.57 (t, *J* = 7.1 Hz, 1 H), 7.50 (t, *J* = 7.6 Hz, 2 H), 7.28-7.23 (m, 2 H), 7.13 (t, *J* = 7.4 Hz, 1 H), 2.34 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.77, 135.90, 131.98, 130.69, 129.32, 128.97, 127.17, 127.05, 125.49, 123.22, 17.98.

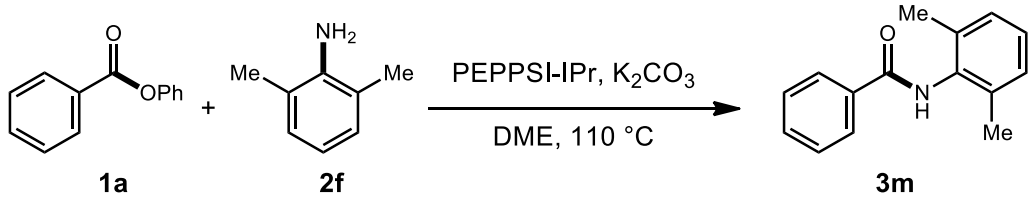
***N*-([1,1'-Biphenyl]-2-yl)benzamide (Table 2, 3l)**



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

According to the general procedure, the reaction of phenyl benzoate (0.20 mmol, 1.0 equiv), [1,1'-biphenyl]-2-amine (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 91% yield (49.7 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.2 Hz, 1 H), 8.01 (s, 1 H), 7.61 (d, *J* = 7.9 Hz, 2 H), 7.55-7.51 (m, 2 H), 7.46 (q, *J* = 9.8, 8.4 Hz, 5 H), 7.40 (t, *J* = 7.6 Hz, 2 H), 7.32 (d, *J* = 7.4 Hz, 1 H), 7.23 (t, *J* = 7.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.08, 138.19, 135.06, 134.92, 132.44, 131.85, 130.12, 129.49, 129.36, 128.87, 128.74, 128.32, 126.93, 124.48, 121.24.

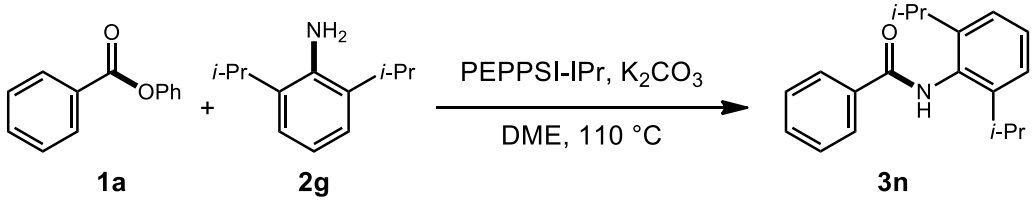
_N_-(2,6-Dimethylphenyl)benzamide (Table 2, 3m)



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

According to the general procedure, the reaction of phenyl benzoate (0.20 mmol, 1.0 equiv), 2,6-dimethylaniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 96% yield (43.2 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.4 Hz, 2 H), 7.58 (t, *J* = 7.3 Hz, 1 H), 7.50 (t, *J* = 7.4 Hz, 3 H), 7.14 (q, *J* = 5.5 Hz, 3 H), 2.29 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.10, 135.72, 134.58, 133.98, 131.92, 128.88, 128.40, 127.57, 127.33, 18.60.

_N_-(2,6-Diisopropylphenyl)benzamide (Table 2, 3n)

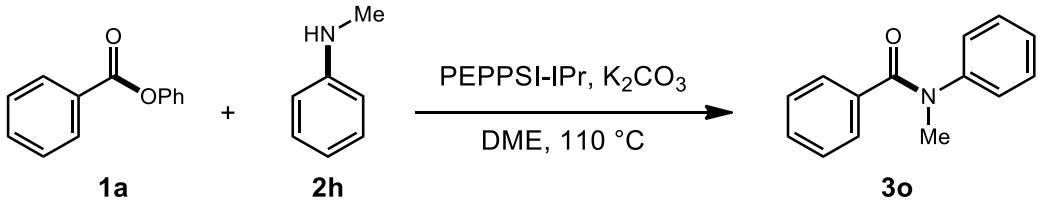


1a **2g** **3n**

According to the general procedure, the reaction of phenyl benzoate (0.20 mmol, 1.0 equiv), 2,6-diisopropylaniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (6 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 90% yield (50.6 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.4 Hz, 2 H), 7.59 (t, *J* = 7.3 Hz, 1 H), 7.52 (t, *J* = 7.5 Hz, 2 H), 7.37 (dd, *J* = 13.8, 5.5 Hz, 2 H), 7.24 (d, *J* = 7.7 Hz, 2 H),

3.16 (hept, J = 6.7 Hz, 2 H), 1.24 (d, J = 6.7 Hz, 12 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.06, 146.51, 134.75, 131.90, 131.27, 128.94, 128.63, 127.31, 123.69, 29.05, 23.79.

_N_-Methyl-_N_-phenylbenzamide (Table 2, 3o)

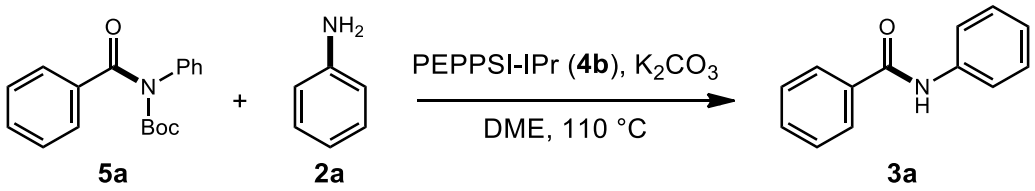


1a **2h** **3o**

According to the general procedure, the reaction of phenyl benzoate (0.20 mmol, 1.0 equiv), *N*-methylaniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 95% yield (40.1 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, J = 8.3, 1.3 Hz, 2 H), 7.26-7.20 (m, 3 H), 7.16 (t, J = 6.8 Hz, 2 H), 7.13 (t, J = 6.3 Hz, 1 H), 7.04 (d, J = 7.5 Hz, 2 H), 3.51 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.75, 145.00, 136.01, 129.66, 129.22, 128.79, 127.80, 126.99, 126.56, 38.48.

Buchwald-Hartwig Cross-Coupling of Amides

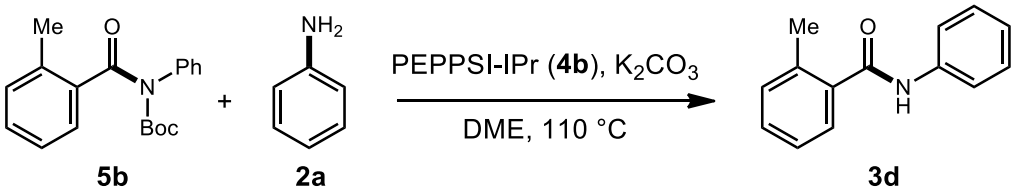
N-Phenylbenzamide (Table 4, 3a)



5a **2a** **3a**

According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) ([1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene](pyridyl)palladium(II) dichloride**)** (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 96% yield (37.8 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1 H), 7.86 (d, *J* = 7.4 Hz, 2 H), 7.65 (d, *J* = 8.0 Hz, 2 H), 7.53 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.35 (t, *J* = 7.9 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.97, 138.06, 135.09, 131.91, 129.17, 128.85, 127.16, 124.66, 120.40.

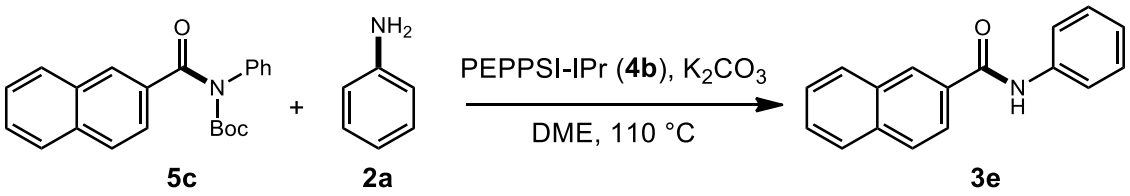
2-Methyl-*N*-phenylbenzamide (Table 4, 3d)



5b **2a** **3d**

According to the general procedure, the reaction of *tert*-butyl (2-methylbenzoyl)(phenyl) carbamate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 97% yield (40.5 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1 H), 7.61 (d, *J* = 7.5 Hz, 2 H), 7.43 (d, *J* = 7.2 Hz, 1 H), 7.35 (t, *J* = 7.8 Hz, 3 H), 7.23 (dd, *J* = 16.5, 7.7 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H), 2.47 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.26, 138.11, 136.51, 136.45, 131.28, 130.30, 129.14, 126.73, 125.93, 124.59, 120.01, 19.88.

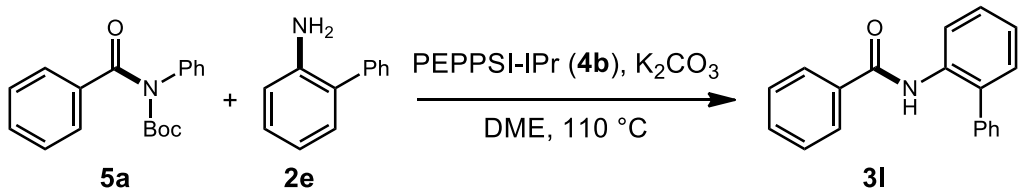
N-Phenyl-2-naphthamide (Table 4, 3e)



5c **2a** **3e**

According to the general procedure, the reaction of *tert*-butyl 2-naphthoyl(phenyl)carbamate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 72% yield (35.6 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1 H), 8.01-7.93 (m, 4 H), 7.91 (d, *J* = 7.8 Hz, 1 H), 7.70 (d, *J* = 7.9 Hz, 2 H), 7.63-7.56 (m, 2 H), 7.41 (t, *J* = 7.9 Hz, 2 H), 7.18 (t, *J* = 7.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.90, 138.12, 135.00, 132.75, 129.28, 129.10, 128.92, 128.06, 127.96, 127.65, 127.10, 124.75, 123.67, 120.35.

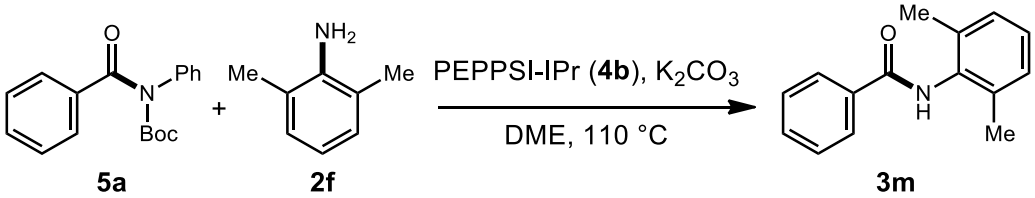
***N*-([1,1'-Biphenyl]-2-yl)benzamide (Table 4, 3l)**



5a **2e** **3l**

According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.20 mmol, 1.0 equiv), [1,1'-biphenyl]-2-amine (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 91% yield (50.8 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.2 Hz, 1 H), 8.01 (s, 1 H), 7.61 (d, *J* = 7.9 Hz, 2 H), 7.55-7.51 (m, 2 H), 7.46 (q, *J* = 9.8, 8.4 Hz, 5 H), 7.40 (t, *J* = 7.6 Hz, 2 H), 7.32 (d, *J* = 7.4 Hz, 1 H), 7.23 (t, *J* = 7.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.08, 138.19, 135.06, 134.92, 132.44, 131.85, 130.12, 129.49, 129.36, 128.87, 128.74, 128.32, 126.93, 124.48, 121.24.

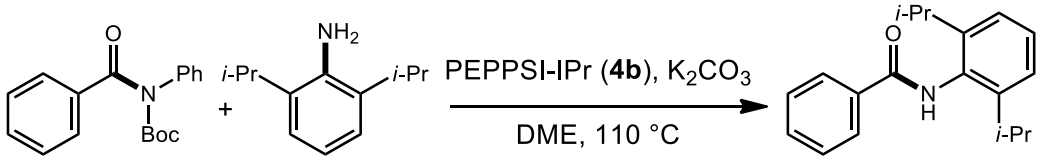
***N*-(2,6-Dimethylphenyl)benzamide (Table 4, 3m)**



5a **2f** **3m**

According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.20 mmol, 1.0 equiv), 2,6-dimethylaniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 80% yield (35.9 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.4 Hz, 2 H), 7.58 (t, *J* = 7.3 Hz, 1 H), 7.50 (t, *J* = 7.4 Hz, 3 H), 7.14 (q, *J* = 5.5 Hz, 3 H), 2.29 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.10, 135.72, 134.58, 133.98, 131.92, 128.88, 128.40, 127.57, 127.33, 18.60.

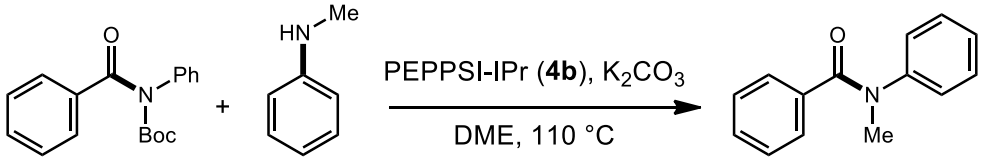
***N*-(2,6-Diisopropylphenyl)benzamide (Table 4, 3n)**



5a **2g** **3n**

According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.20 mmol, 1.0 equiv), 2,6-diisopropylaniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (6 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 76% yield (42.7 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.4 Hz, 2 H), 7.59 (t, *J* = 7.3 Hz, 1 H), 7.52 (t, *J* = 7.5 Hz, 2 H), 7.37 (dd, *J* = 13.8, 5.5 Hz, 2 H), 7.24 (d, *J* = 7.7 Hz, 2 H), 3.16 (hept, *J* = 6.7 Hz, 2 H), 1.24 (d, *J* = 6.7 Hz, 12 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.06, 146.51, 134.75, 131.90, 131.27, 128.94, 128.63, 127.31, 123.69, 29.05, 23.79.

***N*-Methyl-*N*-phenylbenzamide (Table 4, 3o)**

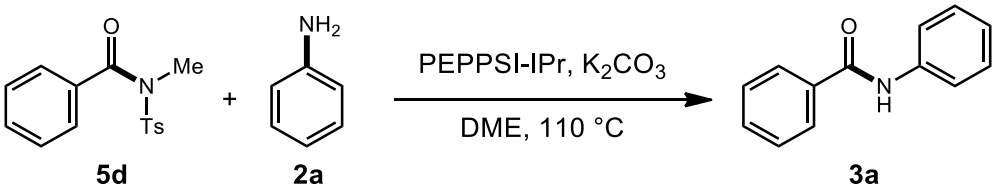


5a **2h** **3o**

According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.20 mmol, 1.0 equiv), *N*-methylaniline (2.0equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 79% yield (33.1 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 8.3,

1.3 Hz, 2 H), 7.26-7.20 (m, 3 H), 7.16 (t, *J* = 6.8 Hz, 2 H), 7.13 (t, *J* = 6.3 Hz, 1 H), 7.04 (d, *J* = 7.5 Hz, 2 H), 3.51 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.75, 145.00, 136.01, 129.66, 129.22, 128.79, 127.80, 126.99, 126.56, 38.48.

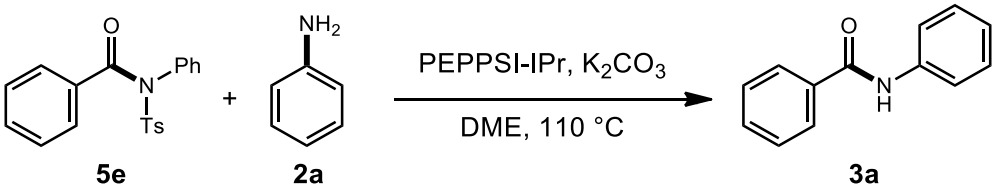
_N_-Methyl -_N_-tosylbenzamide (Table 4, 5d)



5d **2a** **3a**

According to the general procedure, the reaction of *N*-methyl-*N*-tosylbenzamide (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 83% yield (32.7 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1 H), 7.86 (d, *J* = 7.4 Hz, 2 H), 7.65 (d, *J* = 8.0 Hz, 2 H), 7.53 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.35 (t, *J* = 7.9 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.97, 138.06, 135.09, 131.91, 129.17, 128.85, 127.16, 124.66, 120.40.

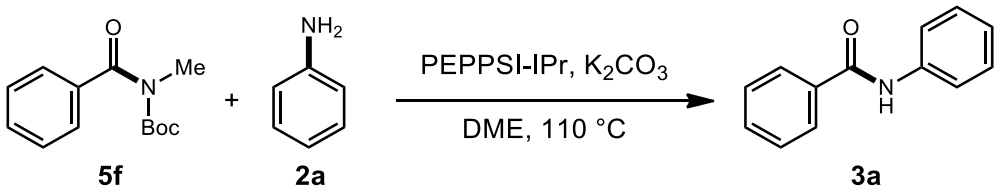
_N_-Phenyl-_N_-tosylbenzamide (Table 4, 5e)



5e **2a** **3a**

According to the general procedure, the reaction of *N*-phenyl-*N*-tosylbenzamide (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 84% yield (33.1 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1 H), 7.86 (d, *J* = 7.4 Hz, 2 H), 7.65 (d, *J* = 8.0 Hz, 2 H), 7.53 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.35 (t, *J* = 7.9 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.97, 138.06, 135.09, 131.91, 129.17, 128.85, 127.16, 124.66, 120.40.

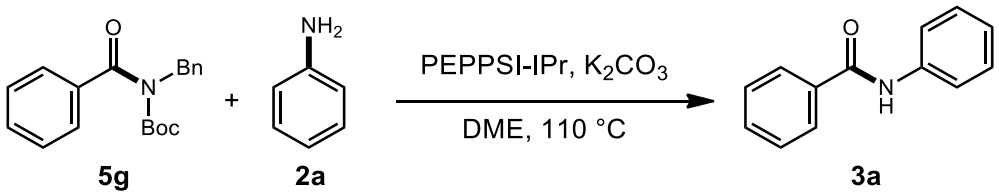
***tert*-Butyl benzoyl(methyl)carbamate (Table 4, 5f)**



5f **2a** **3a**

According to the general procedure, the reaction of *tert*-butyl benzoyl(methyl)carbamate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 92% yield (36.2 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1 H), 7.86 (d, *J* = 7.4 Hz, 2 H), 7.65 (d, *J* = 8.0 Hz, 2 H), 7.53 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.35 (t, *J* = 7.9 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.97, 138.06, 135.09, 131.91, 129.17, 128.85, 127.16, 124.66, 120.40.

***tert*-Butyl benzoyl(benzyl)carbamate (Table 4, 5g)**



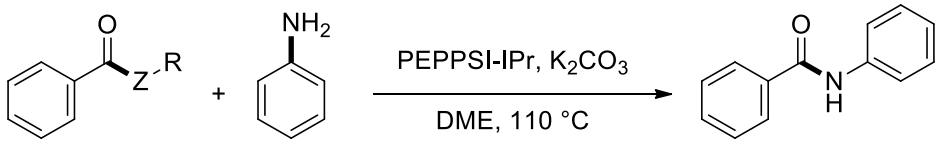
5g **2a** **3a**

According to the general procedure, the reaction of *tert*-butyl benzoyl(benzyl)carbamate (0.20 mmol, 1.0 equiv), aniline (2.0 equiv), K_2CO_3 (3.0 equiv) and PEPPSI-IPr (**4b**) (3 mol%) in DME (0.25 M) for 16 h at 110 °C, afforded after work up and chromatography the title compound in 76% yield (29.9 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1 H), 7.86 (d, *J* = 7.4 Hz, 2 H), 7.65 (d, *J* = 8.0 Hz, 2 H), 7.53 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.35 (t, *J* = 7.9 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.97, 138.06, 135.09, 131.91, 129.17, 128.85, 127.16, 124.66, 120.40.

Determination of Relative Reaction Rates

General Procedure. An oven-dried vial equipped with a stir bar was charged with an ester or amide substrate (neat, 0.20 mmol, 1.0 equiv), potassium carbonate (3.0 equiv), aniline (2.0 equiv) and PEPPSI-IPr (3 mol%), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. DME (0.25 M) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 110 °C and stirred at 110 °C for the indicated time. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and/or GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples.

Scheme ESI-1. Determination of Kinetic Profiles in the Buchwald-Hartwig Cross-Coupling of Esters and Amides using PEPPSI-IPr.



Conditions: **1a** (ZR = OPh) or **5a** (ZR = NBocPh) (0.20 mmol), PEPPSI-IPr (3.0 mol%), K_2CO_3 (3.0 equiv), aniline (2.0 equiv), DME (0.25 M), 110 °C, 0-300 min.

The relative reactivity of **1a** (ZR = OPh) and **5a** (ZR = NBocPh) in the Buchwald-Hartwig cross-coupling was studied by determining kinetic profiles.[13] This study was performed to determine the relative reactivity of esters in comparison with amides. Amide **5a** was selected for the study because of (1) the ease of synthesis of N-Boc amides in a single, high-yielding step from secondary amides, and (2) similar rotational barrier in N-Boc carbamates to that of aryl esters determined earlier.[4] The observed kinetic profiles in the C(acyl)–Buchwald-Hartwig cross-coupling match those observed earlier in the C(sp^2)–Buchwald-Hartwig cross-coupling catalyzed by PEPPSI-IPr complexes.[14]

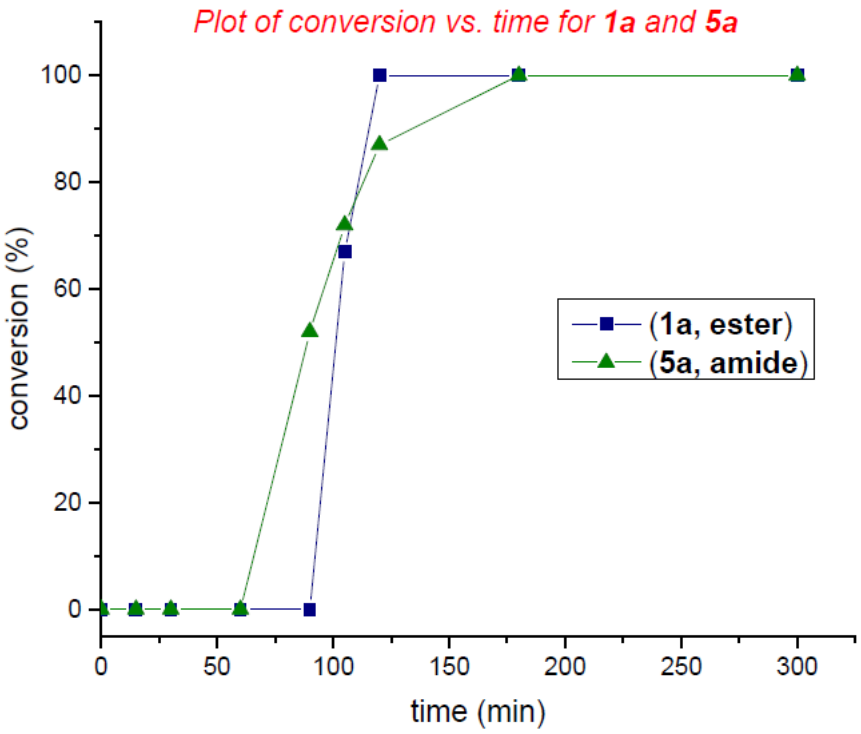


Figure ESI-1. Kinetic Profile of Ester **1a** and Amide **5a** in the Buchwald-Hartwig Cross-Coupling Catalyzed by PEPPSI-IPr. ***1a*** *or* ***5a*** *(0.20 mmol),* K_2CO_3 *(3.0 equiv), aniline (2.0 equiv), PEPPSI-IPr (3.0 mol%), DME (0.25 M), 110 °C, 0-300 min.*

To gain further insight into the reactivity of easily-prepared PEPPSI-IPr complexes in the C(acyl)–Buchwald-Hartwig amination of esters and amides, we have determined kinetic profiles of **1a** and **5a** using (IPr)Pd(cinnamyl)Cl (Neolyst CX31)[15] under identical reaction conditions. The data demonstrate that in the case of ester **1a** PEPPSI-IPr undergoes slower activation under these conditions, however, once activated this catalyst leads to faster conversion than (IPr)Pd(cinnamyl)Cl (Figure ESI-2). In the case of amide **5b**, PEPPSI-IPr is also activated more slowly, however, once activated this catalyst leads to faster conversion (Figure ESI-3). Given the large number of PEPPSI type Pd-NHC complexes reported in the literature, all readily prepared in a single, operationally-trivial step,[16] these findings bode well for the development of even more active catalysts for the C(acyl)–Buchwald-Hartwig catalysis manifold.

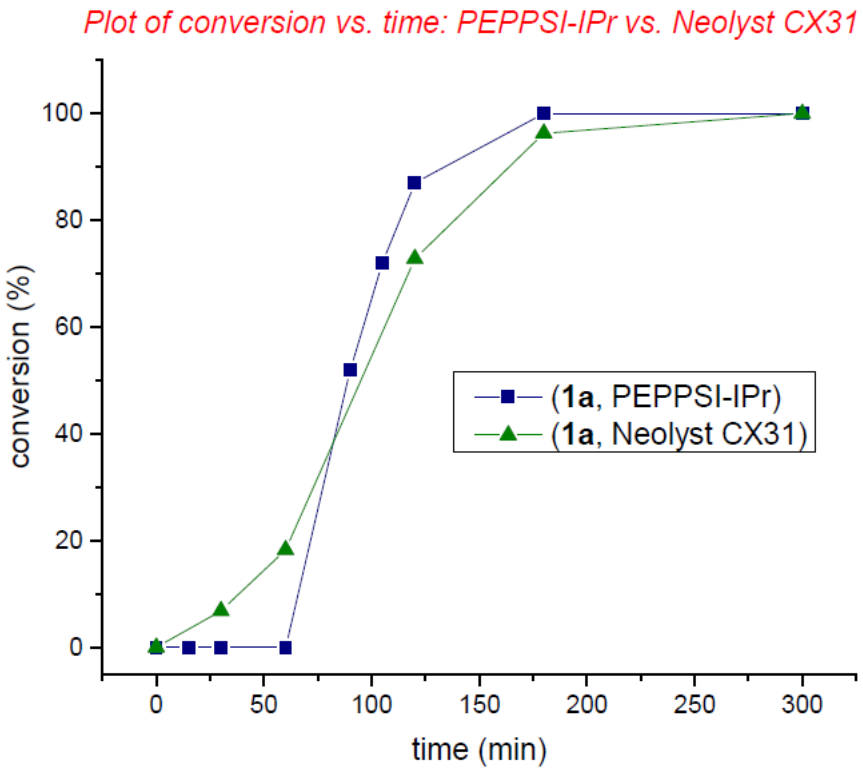


Figure ESI-2. Kinetic Profile of Ester **1a** in the Buchwald-Hartwig Cross-Coupling Catalyzed by PEPPSI-IPr and (IPr)Pd(cinnamyl)Cl. ***1a*** *(0.20 mmol), K_2CO_3 (3.0 equiv), aniline (2.0 equiv), PEPPSI-IPr or (IPr)Pd(cinnamyl)Cl (3.0 mol%), DME (0.25 M), 110 °C, 0-300 min.*

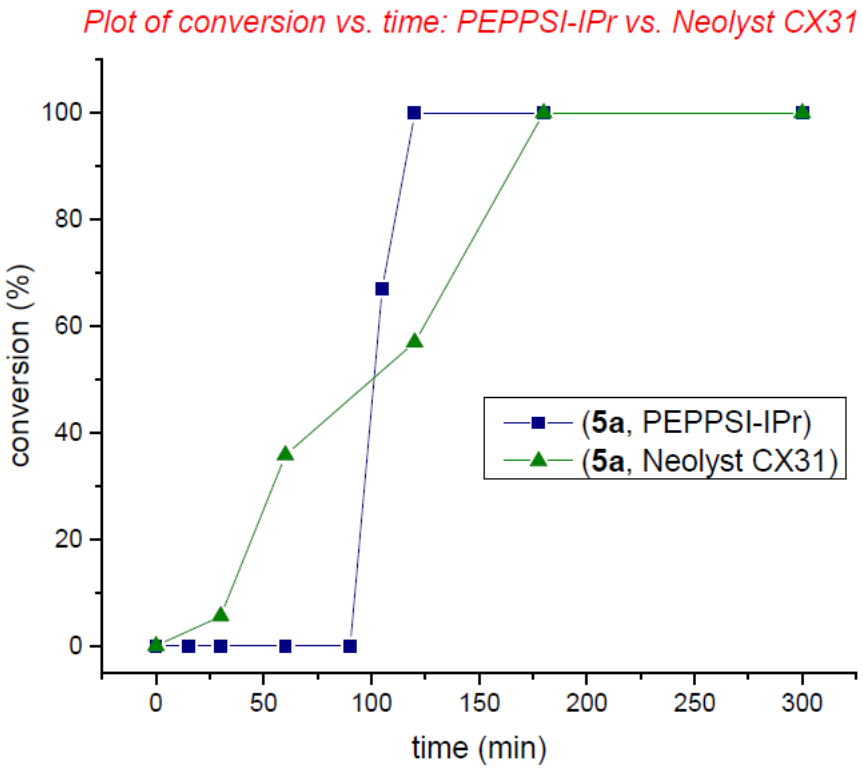


Figure ESI-3. Kinetic Profile of Amide **5a** in the Buchwald-Hartwig Cross-Coupling Catalyzed by PEPPSI-IPr and (IPr)Pd(cinnamyl)Cl. ***5a*** *(0.20 mmol), K_2CO_3 (3.0 equiv), aniline (2.0 equiv), PEPPSI-IPr or (IPr)Pd(cinnamyl)Cl (3.0 mol%), DME (0.25 M), 110 °C, 0-300 min.*

Collectively, our results demonstrate that the cross-coupling of aryl esters proceeds with similar rates to the cross-coupling of amides, and this is general to Pd-NHCs bearing different throw-away ligands. As such, common acyl cross-coupling manifold of esters and amides may be much more widely involved than previously considered in the acyl cross-coupling chemistry. The observed kinetic profiles are consistent with the barrier to isomerization of the acyl bond.[4,17] Note that under the developed reaction conditions anilides (E_R = 13.5 kcal/mol) and alkyl esters (E_R = 12.8 kcal/mol) are recovered unchanged. Further studies on the mechanism of the C(acyl)–Buchwald-Hartwig reaction are underway in our laboratory and will be reported in due course.

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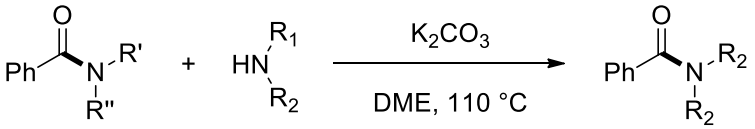
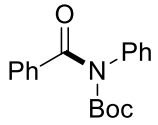
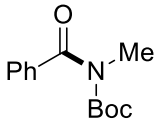
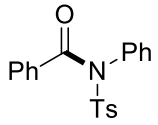
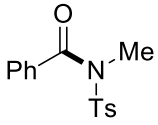
Control Experiments

Extensive control experiments were conducted in order to determine the facility of non-catalyzed amidation under the developed conditions.[5,6] In sum, we have been unable to obtain high yields using non-nucleophilic anilines under metal-free conditions. However, it should be clearly pointed out that aliphatic primary and secondary amines react with resonance destabilized amides under metal-free conditions.[18] In this reaction manifold, morpholine (a deactivated secondary amine) represents a borderline for metal-free reactivity. In a similar vein, amide activation by N-tosylation is beneficial for metal-free reactivity as compared with N-Boc activation, with N-Ph/Ts amide representing a borderline for metal-free reactivity with nucleophilic anilines; however, note that the latter process is much more synthetically useful owing to the ease of N-*tert*-butoxycarboxylation (cf. tosylation). Furthermore, even for anilines that react under metal-free conditions, Pd-catalysis generally leads to higher yields and cleaner reaction mixtures. In contrast to amides, aryl esters are recovered unchanged under metal-free conditions. The capacity to react common esters and amides under mild catalytic conditions, using well-defined, air- and moisture-stable Pd-NHC precatalysts represents a novel approach to catalytic amidation reactions with a potential to expand the scope to the much needed waste-minimized amidation reactions and other cross-couplings.

General Procedure. An oven-dried vial equipped with a stir bar was charged with an amide substrate (neat, 1.0 equiv), K_2CO_3 (3.0 equiv) and amine (2.0 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. DME (0.25 M) was added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath at 110 °C and stirred at 110 °C for the indicated time. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and/or GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples.

Table ESI-1. Determination of Non-Catalyzed (Metal-Free) Addition to *N*-Activated Secondary Amides in the Absence of PEPPSI-IPr.



	morpholine	2,6-dimethylaniline	*p*-anisidine
	94%	n.r.	n.r.
	n.r.	n.r.	n.r.
	98%	n.r.	67%
	61%	n.r.	n.r.

n.r. = no reaction. See, ref. 18 for additional details.

Additional Discussion. In case of amides, the observed results are consistent with the facility of nucleophilic addition to the resonance destabilized amide bond (ER = 7-9 kcal/mol) in that simple primary and secondary amines undergo addition to N-Ts and activated N-Boc amides. Note that N-Boc amides are unreactive towards anilines, including sterically-hindered and nucleophilic anilines. Additionally, we have surveyed the facility of non-catalyzed addition to N-Boc and N-Ts amides under nucleophilic catalysis conditions (amine, Et_3N, DMAP, THF, 60 to 110 °C) (not shown). Under these conditions, we found that N-Ts and N-Boc amides are unreactive towards nucleophilic aniline substrates. The borderline for metal-free (non-catalyzed) nucleophilic addition can be located around the N-aryl/Ts amide bond activation geometry for nucleophilic aniline substrates. Note that sterically-hindered anilines are unreactive throughout the amide bond N-activation geometries. Thus, Pd-PEPPSI catalysis enables transamidation with non-nucleophilic anilines in the absence of strong bases, furnishing secondary and tertiary aryl amide products that are particularly appealing from the synthetic point of view.

References

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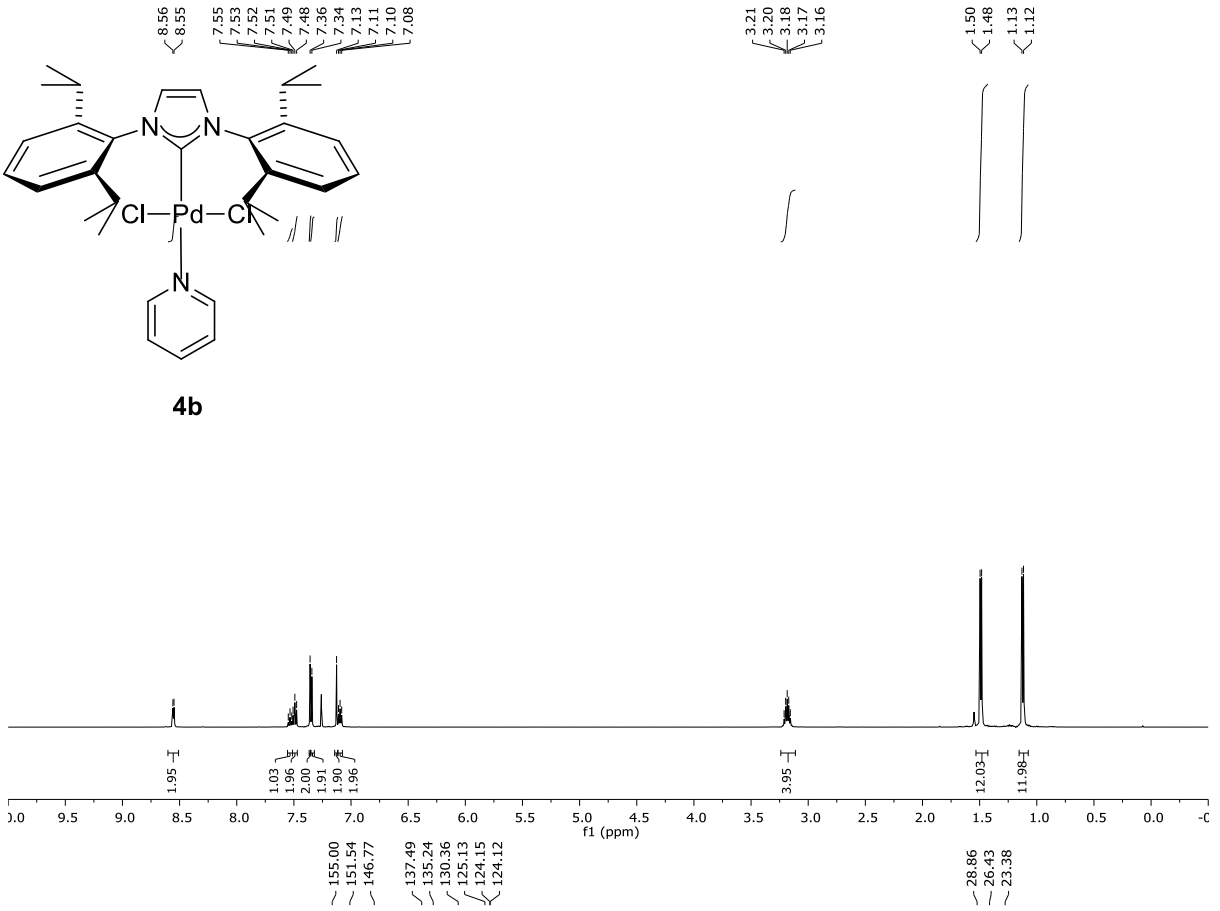
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7.10
7.08
3.21
3.20
3.18
3.17
3.16
1.50
1.48
1.13
1.12
N
N
Cl—Pd—Cl
N
1.95
1.03
1.96
2.00
1.91
1.90
1.96
3.95
12.03
11.98
f1 (ppm)
155.00
151.54
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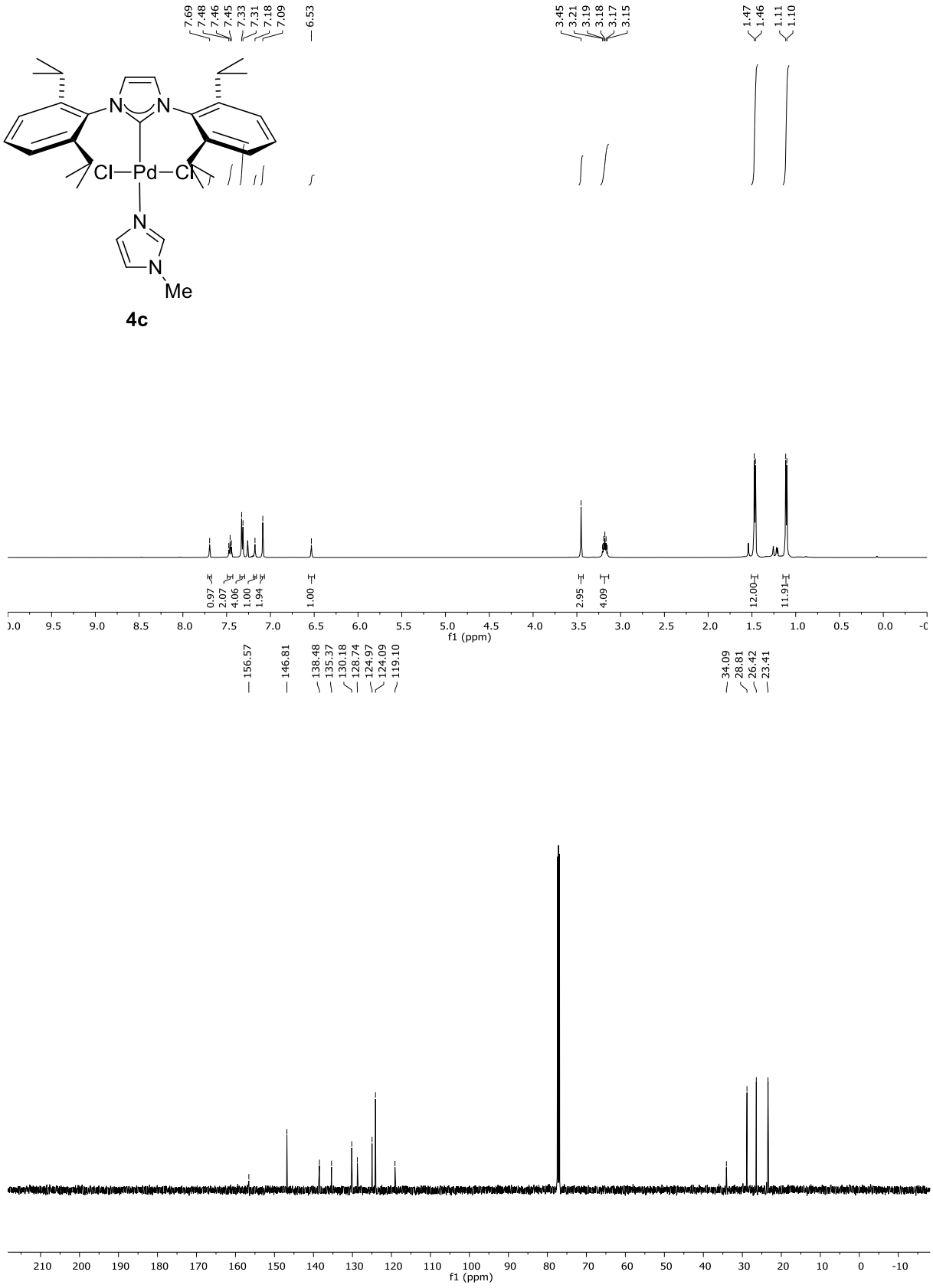
137.49
135.24
130.36
125.13
124.15
124.12
28.86
26.43
23.38
f1 (ppm)

4b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7.46
7.45
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7.31
7.18
7.09
6.53
3.45
3.21
3.19
3.18
3.17
3.15
1.47
1.46
1.11
1.10
Cl—Pd—Cl
N
N
N
N
Me
4c
0.97
2.07
4.06
1.00
1.94
1.00
2.95
4.09
12.00
11.91
f1 (ppm)
156.57
146.81
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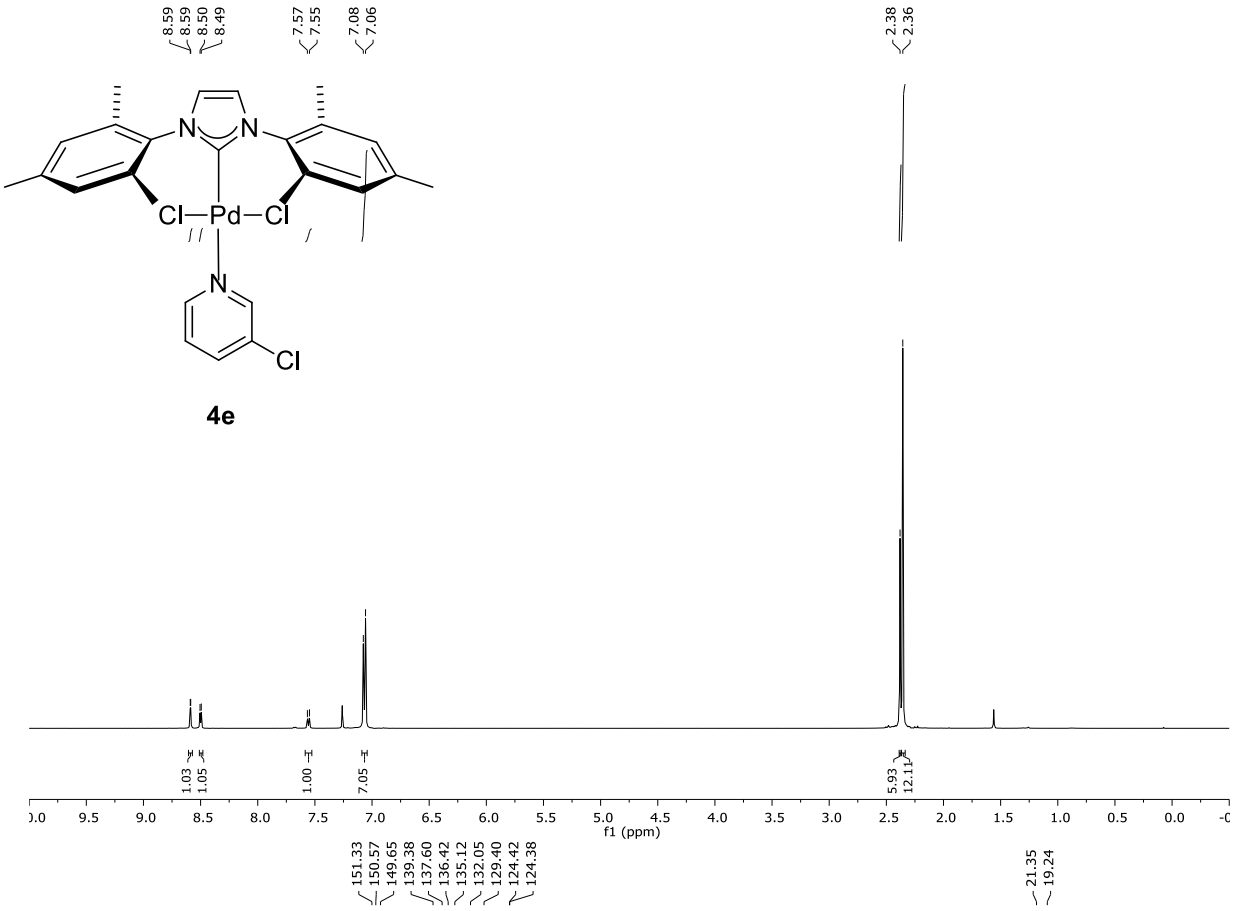
124.09
119.10
34.09
28.81
26.42
23.41
f1 (ppm)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7.55
7.08
7.06
2.38
2.36
N
N
Cl—Pd—Cl
N
Cl
4e
1.03
1.05
1.00
7.05
5.93
12.11
f1 (ppm)
151.33
150.57
149.65
139.38
137.60
136.42
135.12
132.05
129.40
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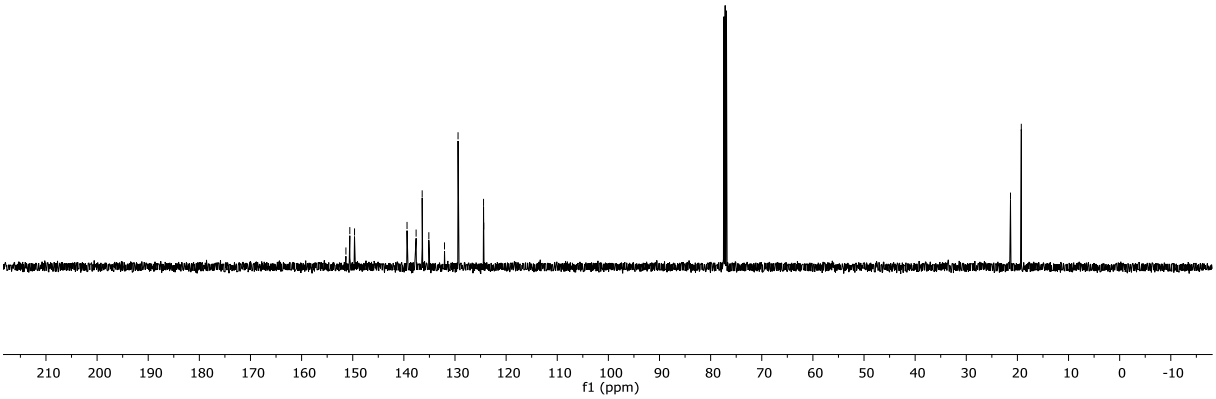
124.38
21.35
19.24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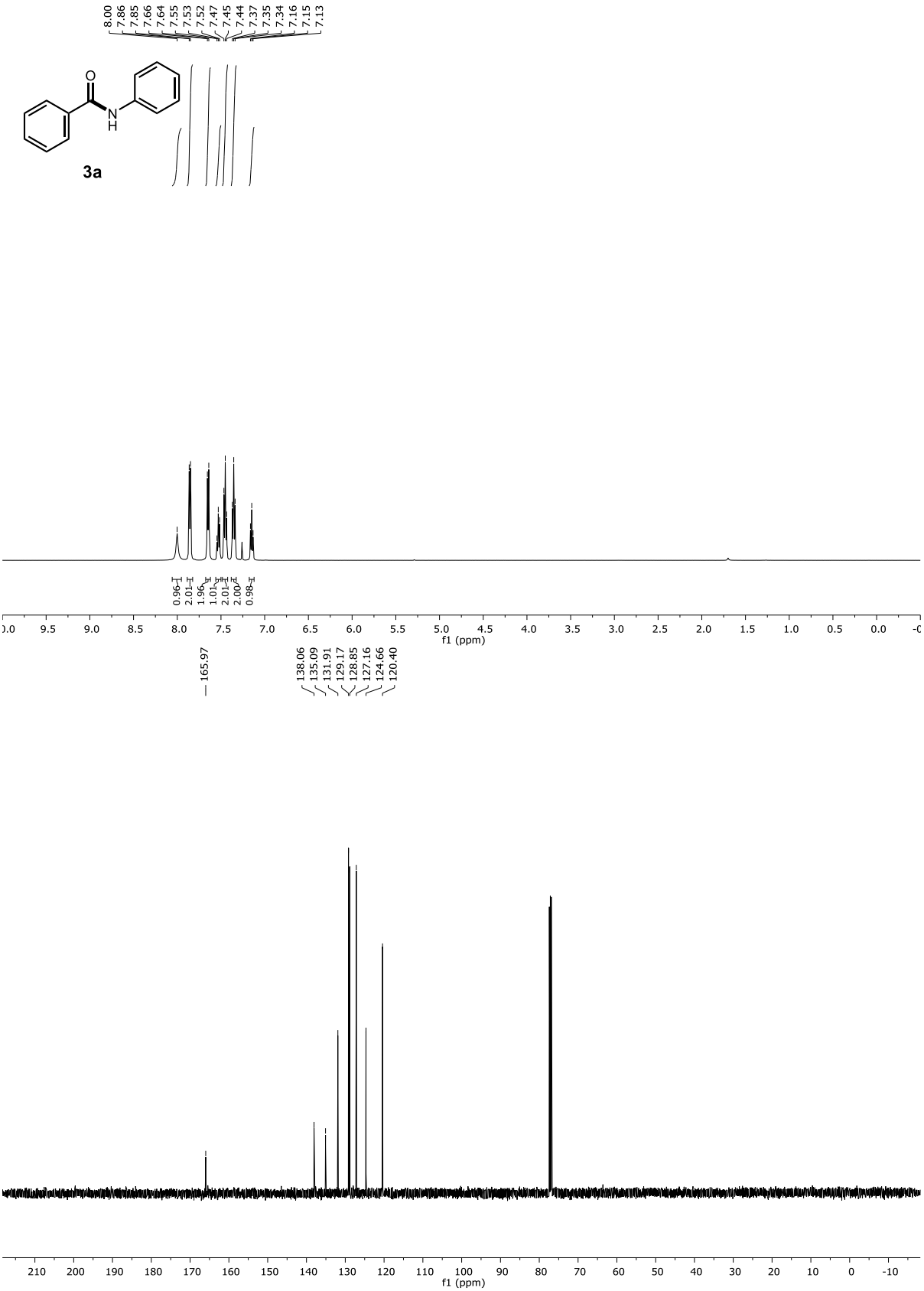
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7.45
7.44
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7.35
7.34
7.16
7.15
7.13
O
N
H
3a
0.96
2.01
1.96
1.01
2.01
2.00
0.98
f1 (ppm)
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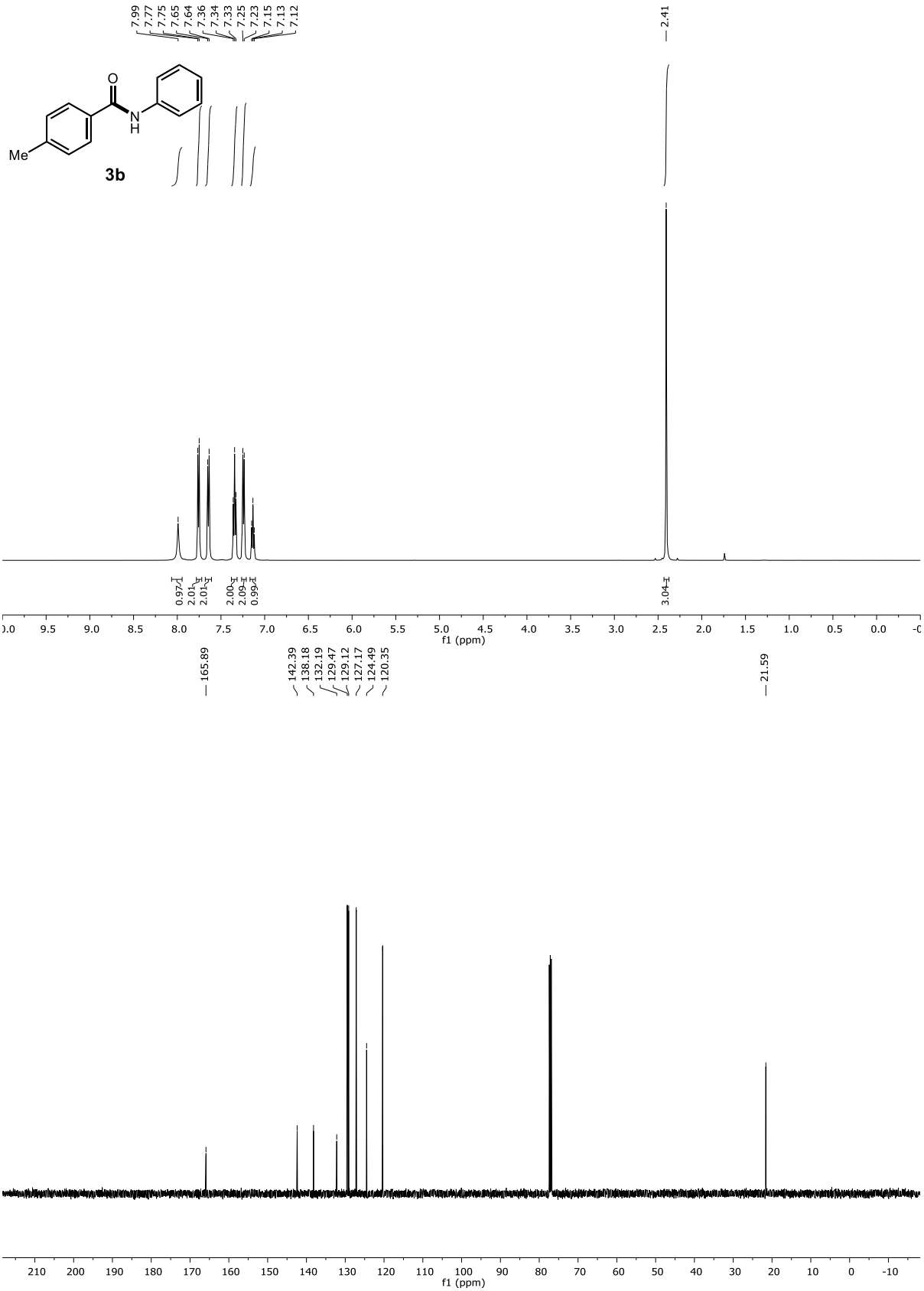
138.06
135.09
131.91
129.17
128.85
127.16
124.66
120.40
f1 (ppm)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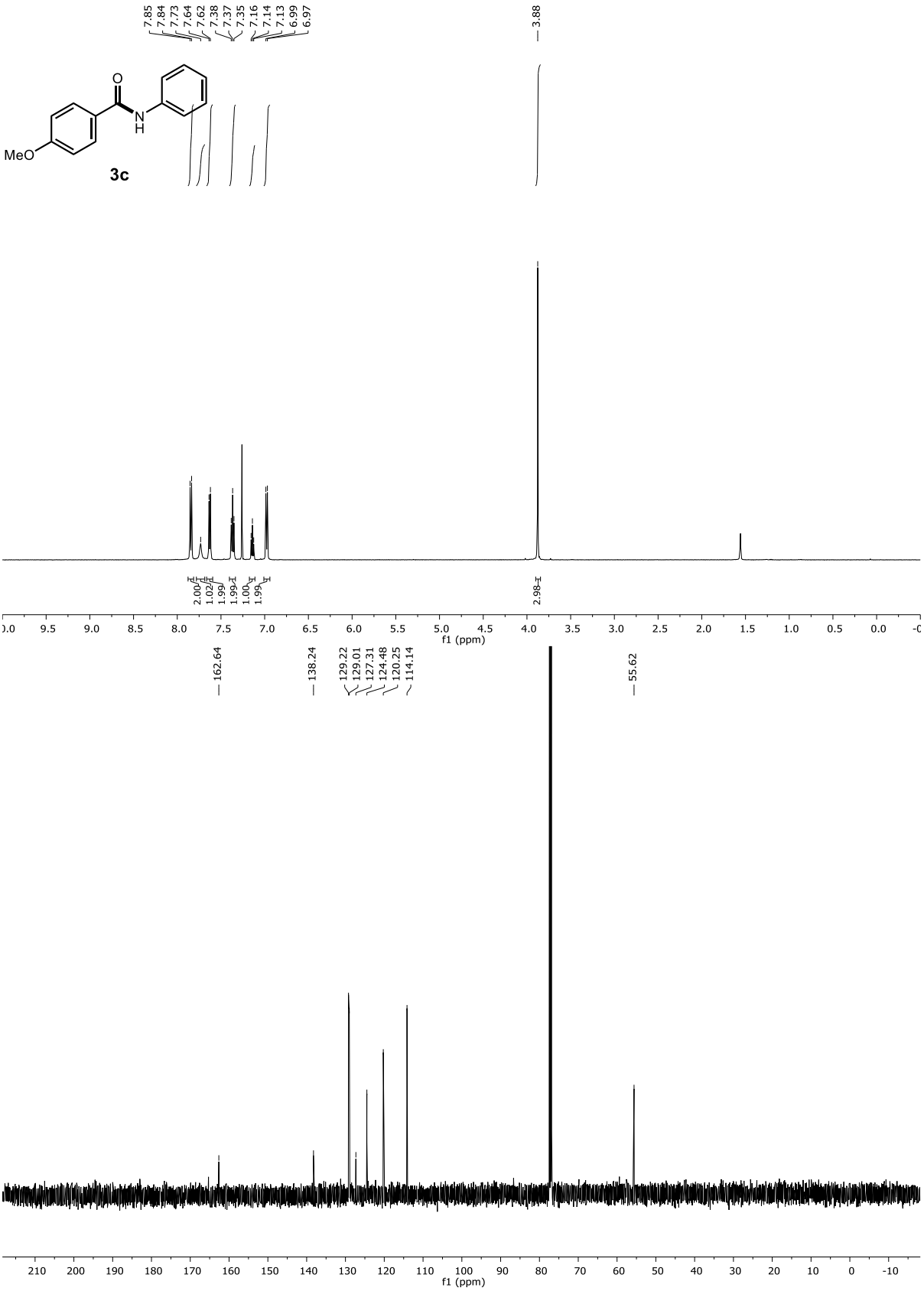
7.25
7.23
7.15
7.13
7.12
2.41
O
N
H
Me
3b
0.97
2.01
2.01
2.00
2.09
0.99
3.04
f1 (ppm)
165.89
142.39
138.18
132.19
129.47
129.12
127.17
124.49
120.35
21.59
f1 (ppm)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7.14
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6.97
3.88
O
N
H
MeO
3c
2.00
1.02
1.99
1.99
1.00
1.99
2.98
f1 (ppm)
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138.24
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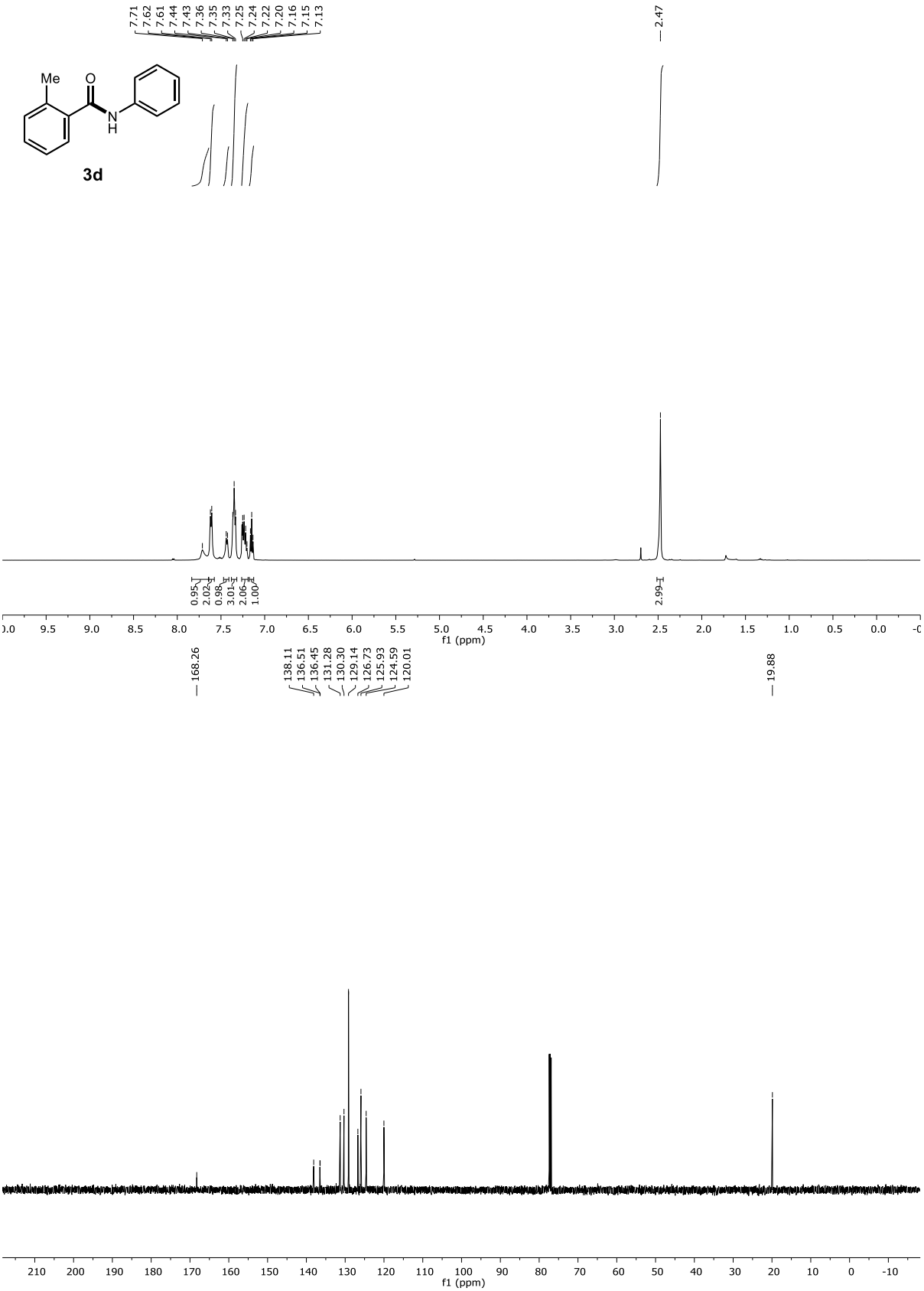
55.62
f1 (ppm)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7.24
7.22
7.20
7.16
7.15
7.13
2.47
Me
O
N
H
3d
0.95
2.02
0.98
3.01
2.06
1.00
2.99
f1 (ppm)
168.26
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131.28
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124.59
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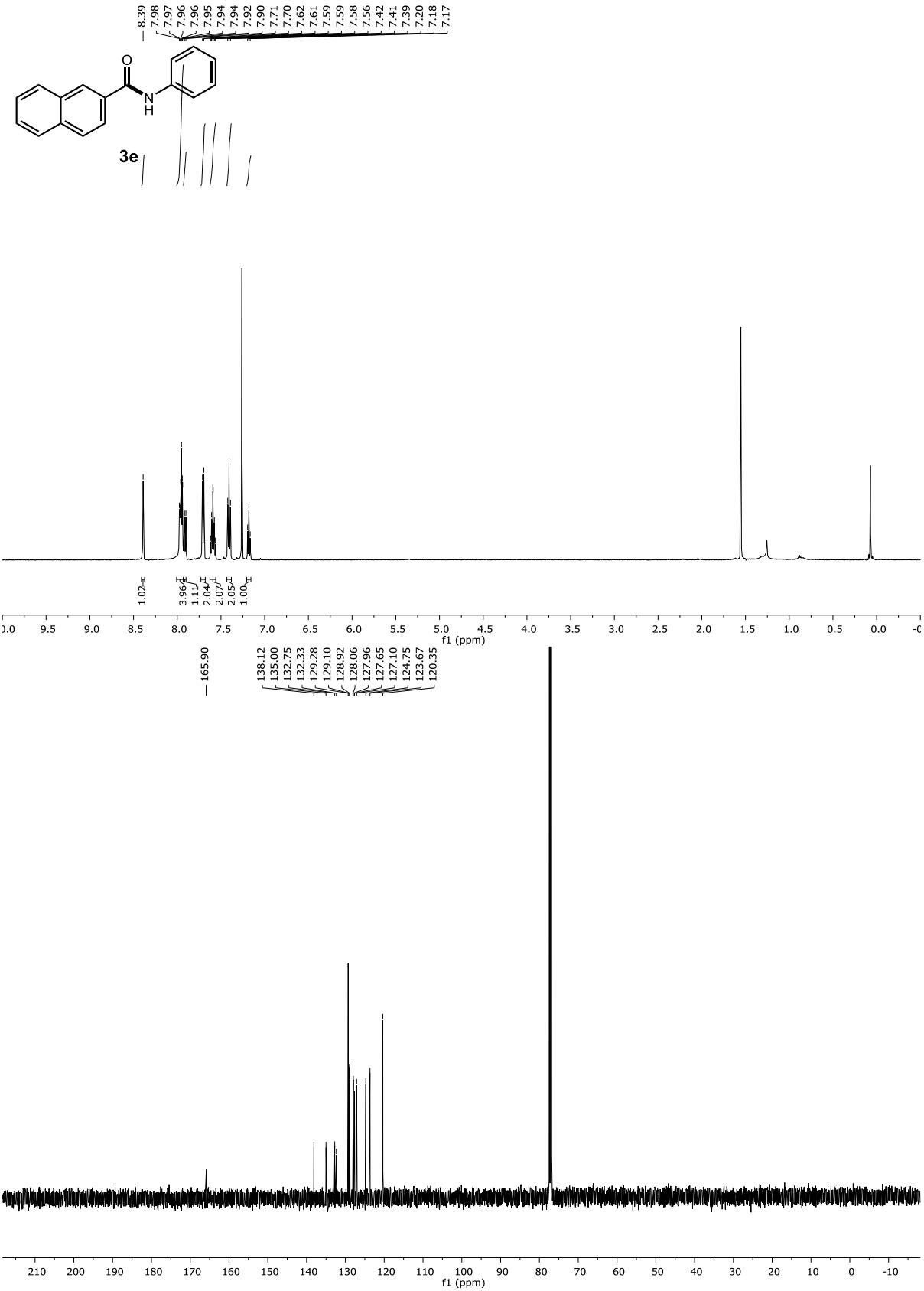
19.88
f1 (ppm)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7.62
7.61
7.59
7.59
7.58
7.56
7.42
7.41
7.39
7.20
7.18
7.17
O
N
H
3e
1.02
3.96
1.11
2.04
2.07
2.05
1.00
f1 (ppm)
165.90
138.12
135.00
132.75
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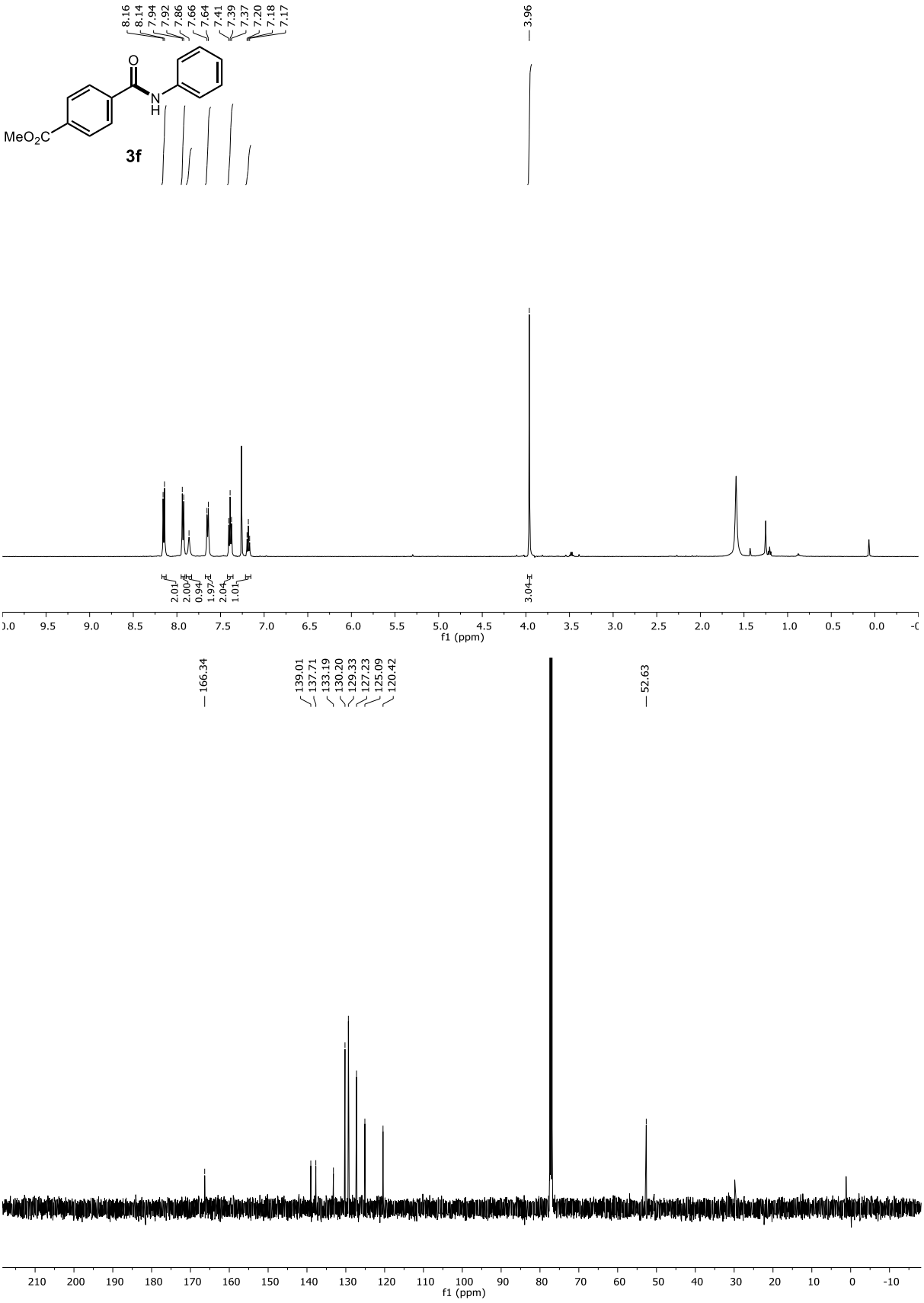
f1 (ppm)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7.18
7.17
3.96
MeO2C
3f
2.01
2.00
0.94
1.97
2.04
1.01
3.04
f1 (ppm)
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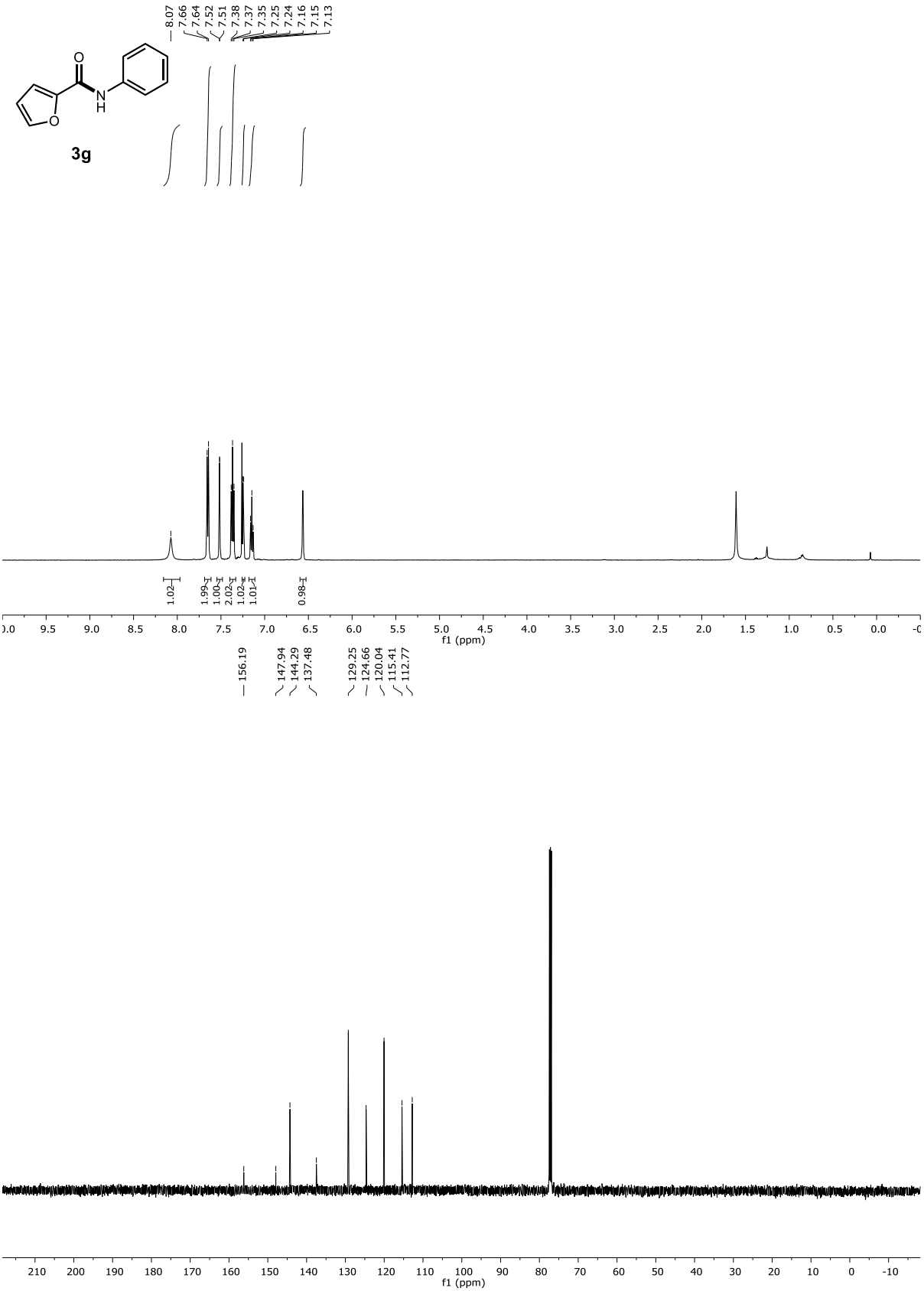
133.19
130.20
129.33
127.23
125.09
120.42
52.63
f1 (ppm)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7.25
7.24
7.16
7.15
7.13
3g
1.02
1.99
1.00
2.02
1.02
1.01
0.98
f1 (ppm)
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147.94
144.29
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124.66
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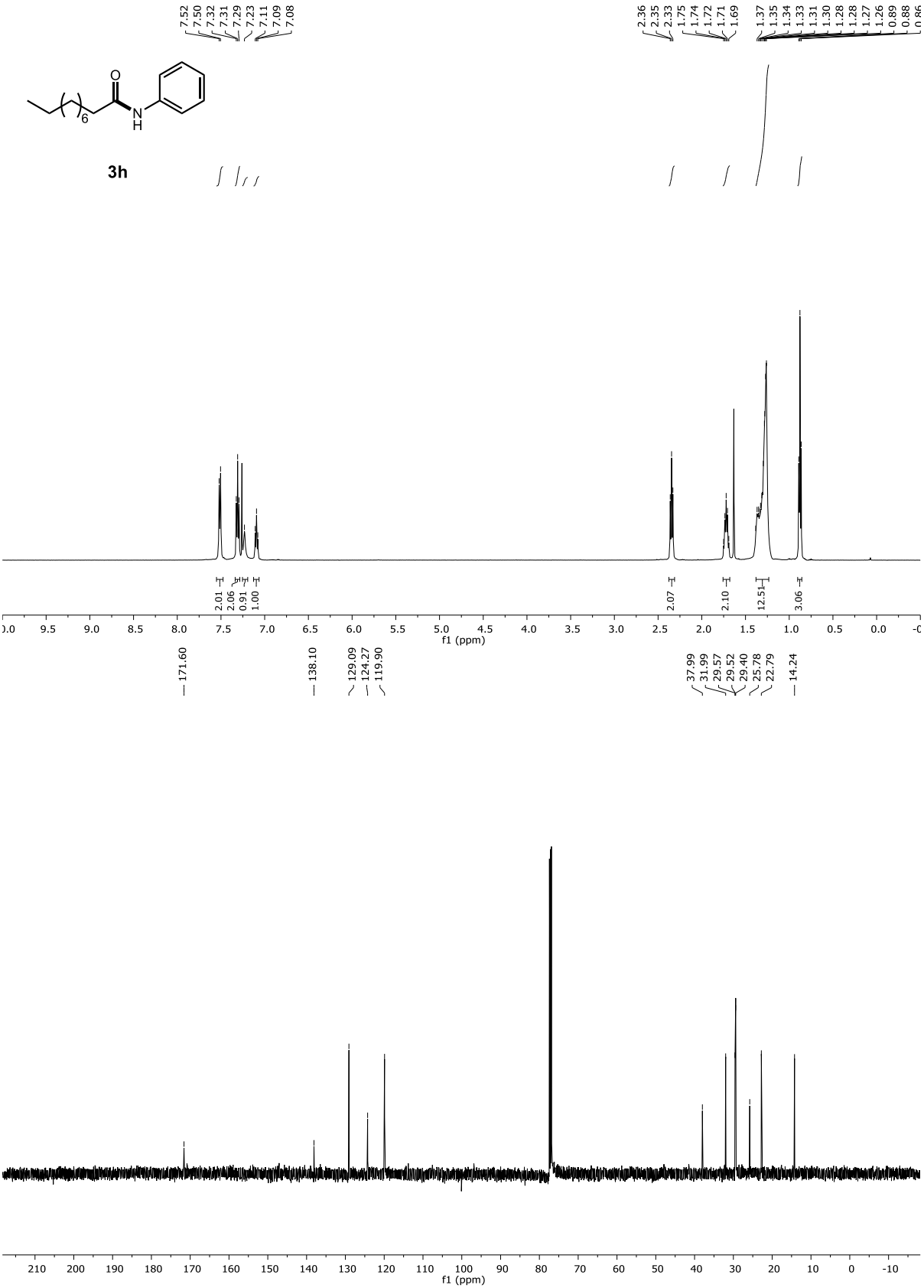
115.41
112.77
f1 (ppm)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1.72
1.71
1.69
1.37
1.35
1.34
1.33
1.31
1.30
1.28
1.28
1.27
1.26
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0.88
O
N
H
6
3h
2.01
2.06
0.91
1.00
2.07
2.10
12.51
3.06
f1 (ppm)
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138.10
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25.78
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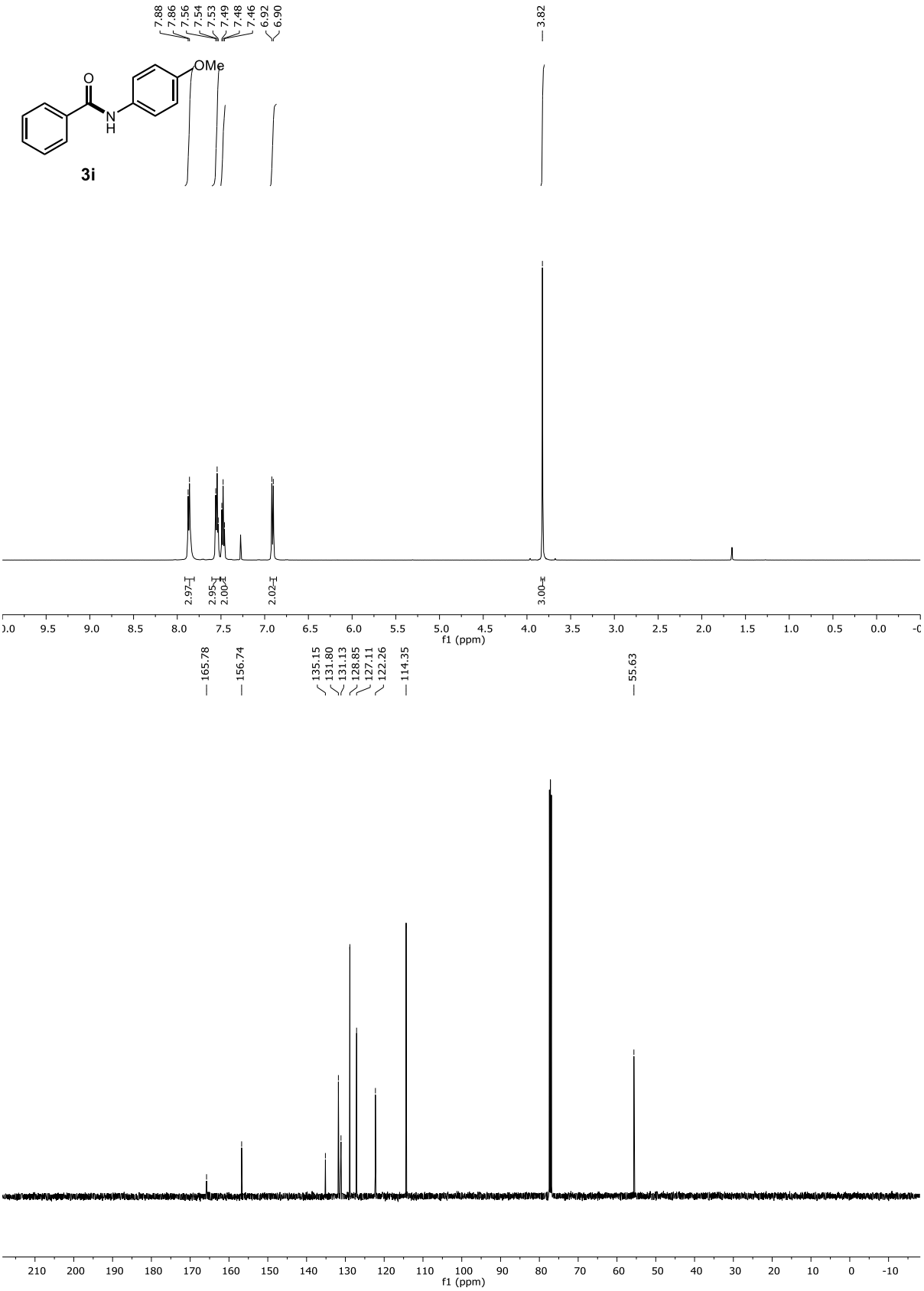
14.24
f1 (ppm)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6.90
3.82
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O
N
H
3i
2.97
2.95
2.00
2.02
3.00
f1 (ppm)
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135.15
131.80
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127.11
122.26
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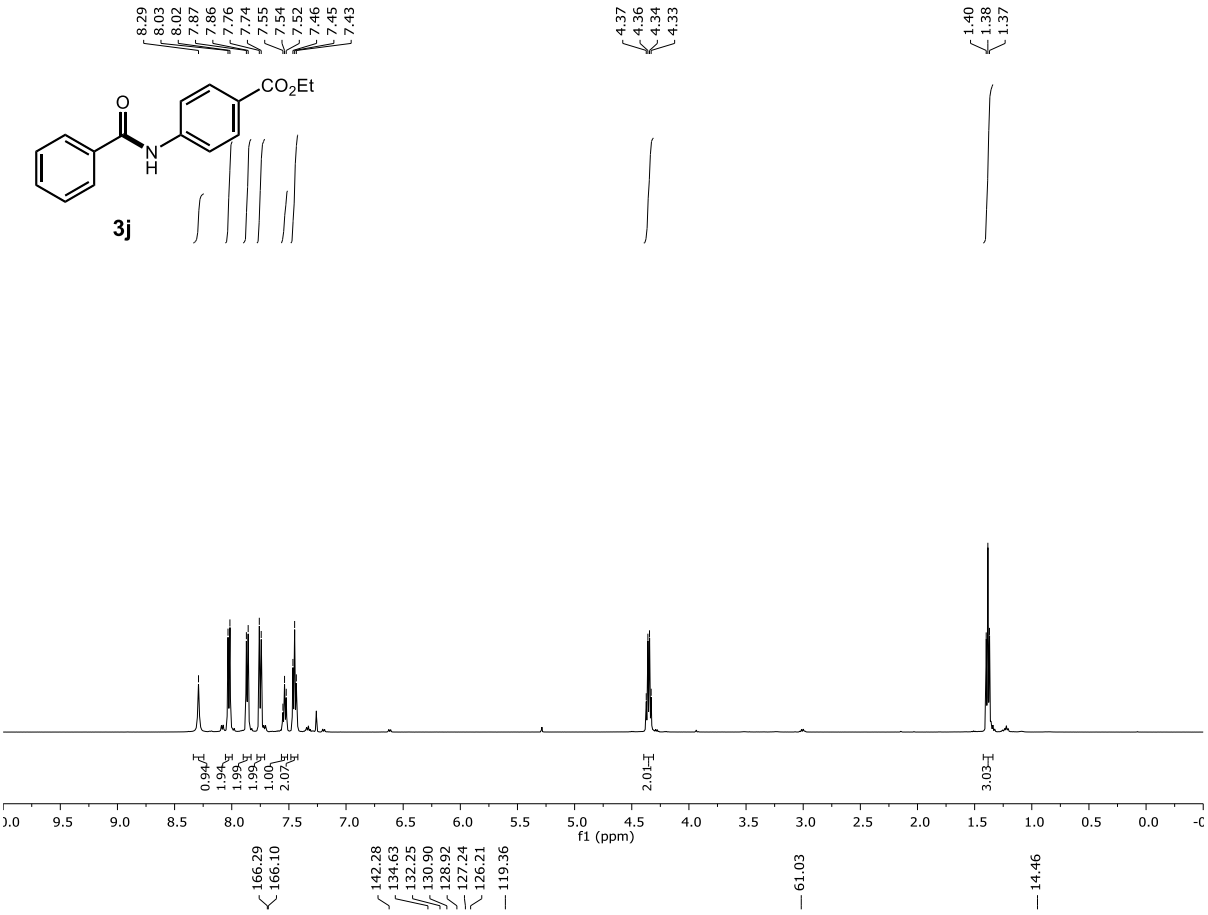
55.63
f1 (ppm)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7.45
7.43
4.37
4.36
4.34
4.33
1.40
1.38
1.37
CO2Et
O
N
H
3j
0.94
1.94
1.99
1.99
1.00
2.07
2.01
3.03
f1 (ppm)
166.29
166.10
142.28
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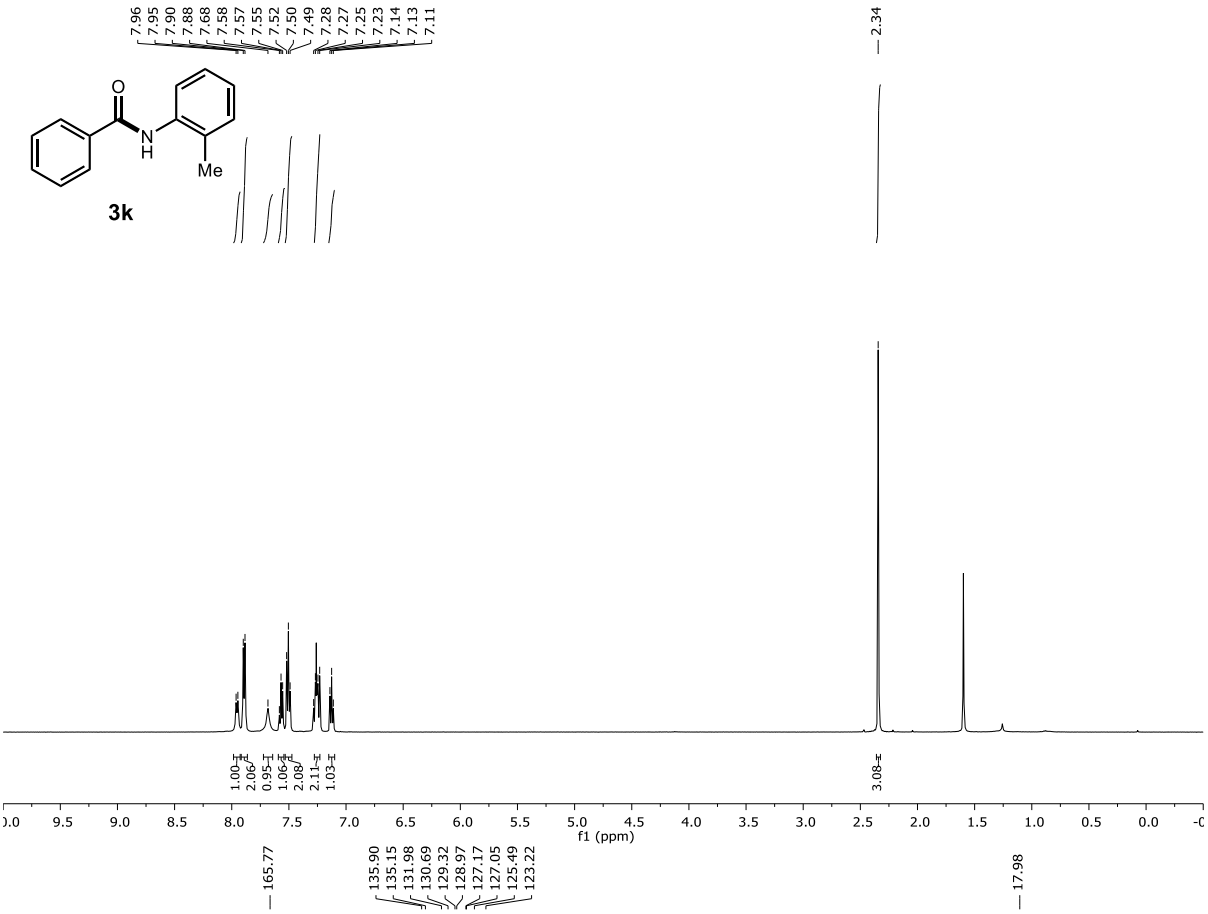
132.25
130.90
128.92
127.24
126.21
119.36
61.03
14.46
f1 (ppm)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7.49
7.28
7.27
7.25
7.23
7.14
7.13
7.11
2.34
O
N
H
Me
3k
1.00
2.06
0.95
1.06
2.08
2.11
1.03
3.08
f1 (ppm)
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130.69
129.32
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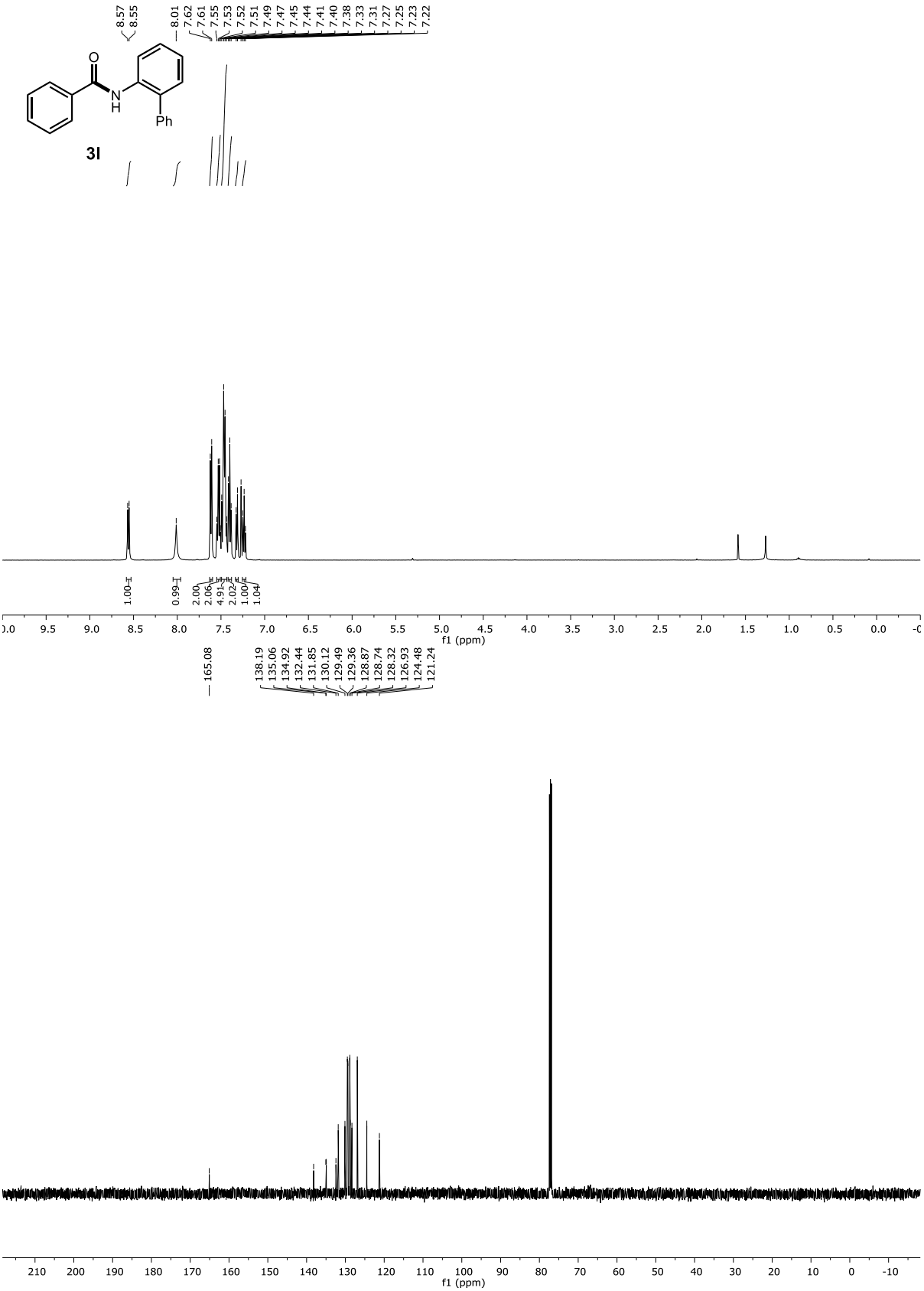
127.17
127.05
125.49
123.22
17.98
f1 (ppm)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7.40
7.38
7.33
7.31
7.27
7.25
7.23
7.22
O
N
H
Ph
3l
1.00
0.99
2.00
2.06
4.91
2.02
1.00
1.04
f1 (ppm)
165.08
138.19
135.06
134.92
132.44
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129.49
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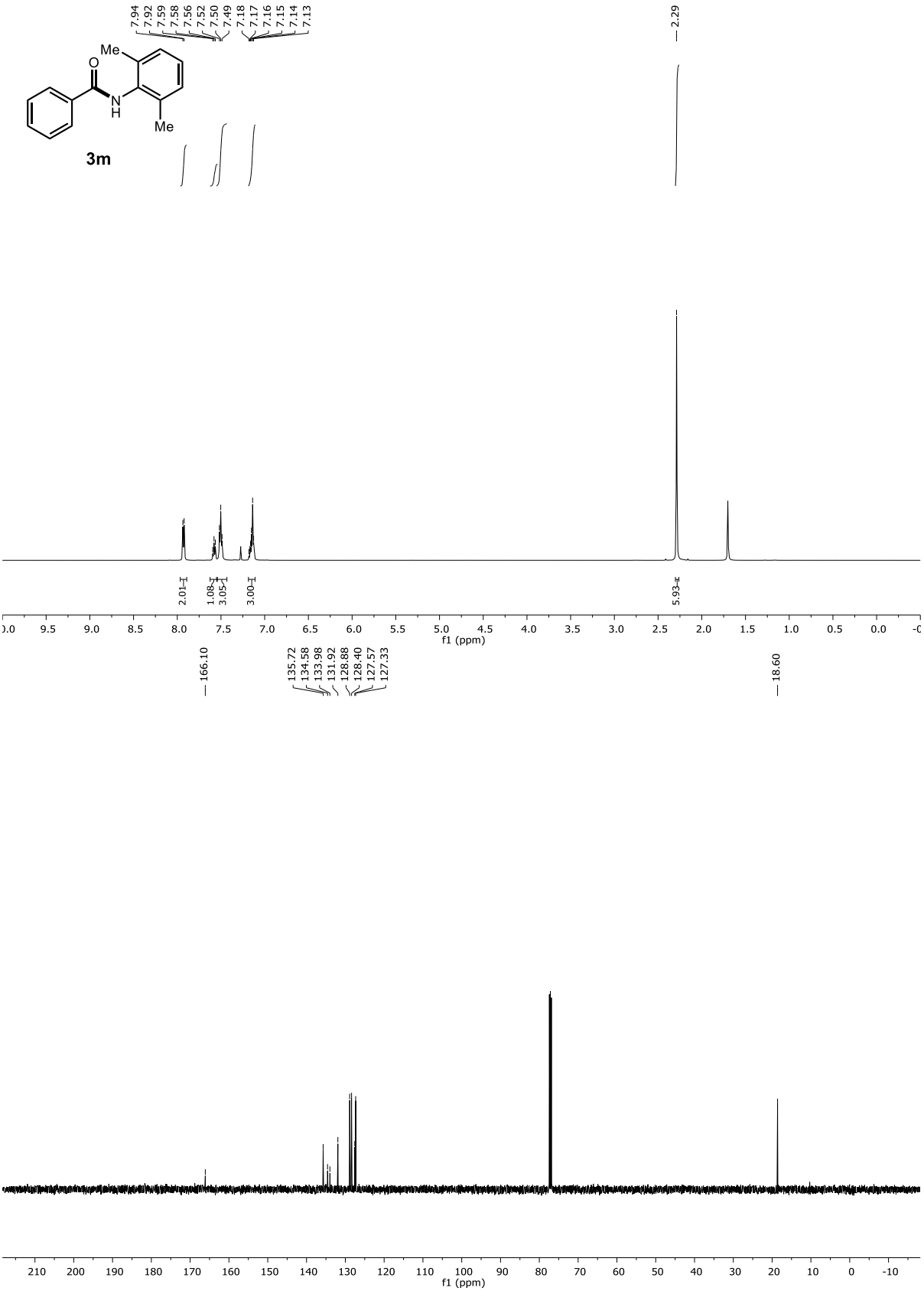
121.24
f1 (ppm)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7.13
2.29
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O
N
H
Me
3m
2.01
1.08
3.05
3.00
5.93
f1 (ppm)
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127.57
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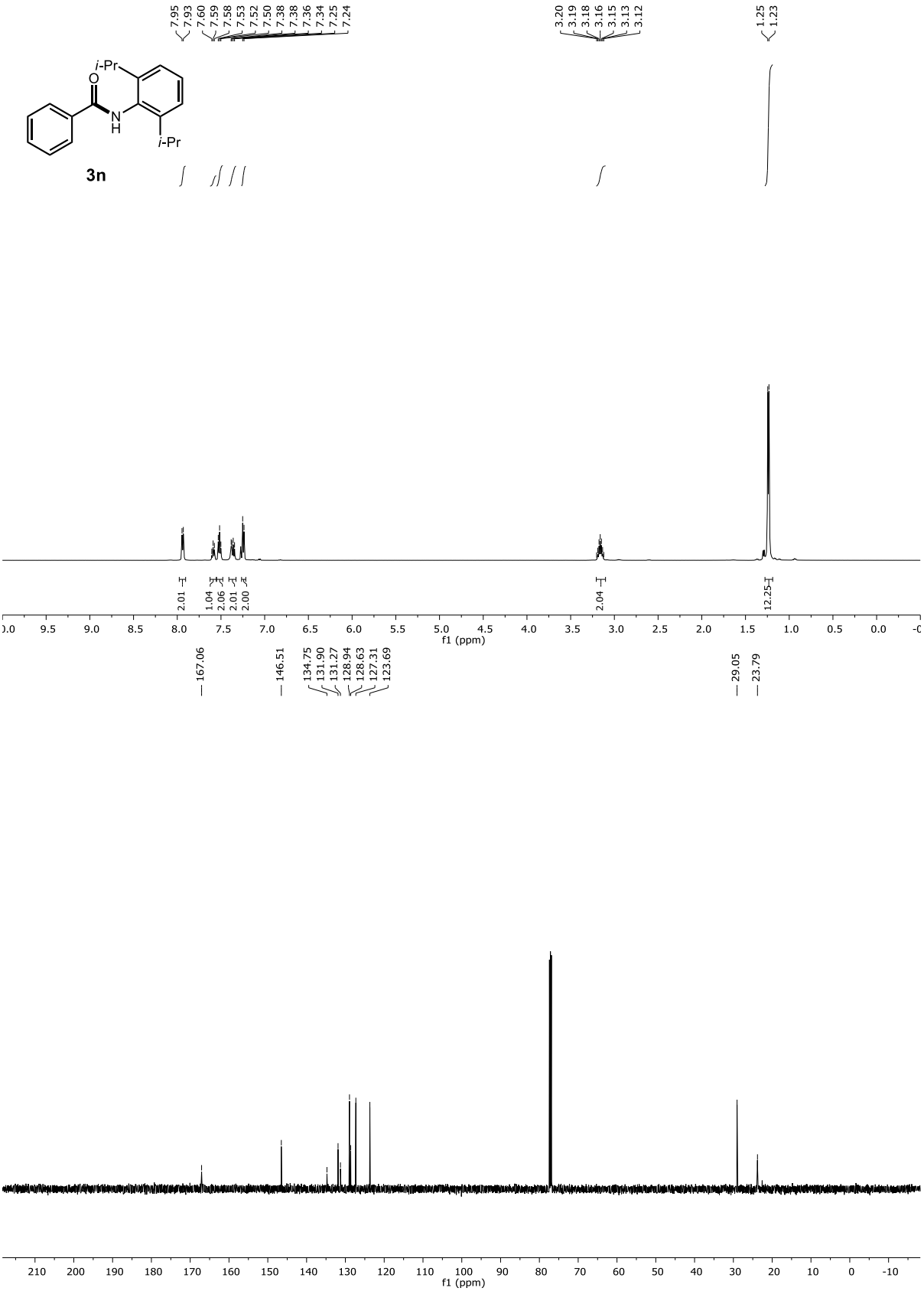
18.60
f1 (ppm)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7.50
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7.38
7.36
7.34
7.25
7.24
3.20
3.19
3.18
3.16
3.15
3.13
3.12
1.25
1.23
i-Pr
O
N
H
i-Pr
3n
2.01
1.04
2.06
2.01
2.00
2.04
12.25
f1 (ppm)
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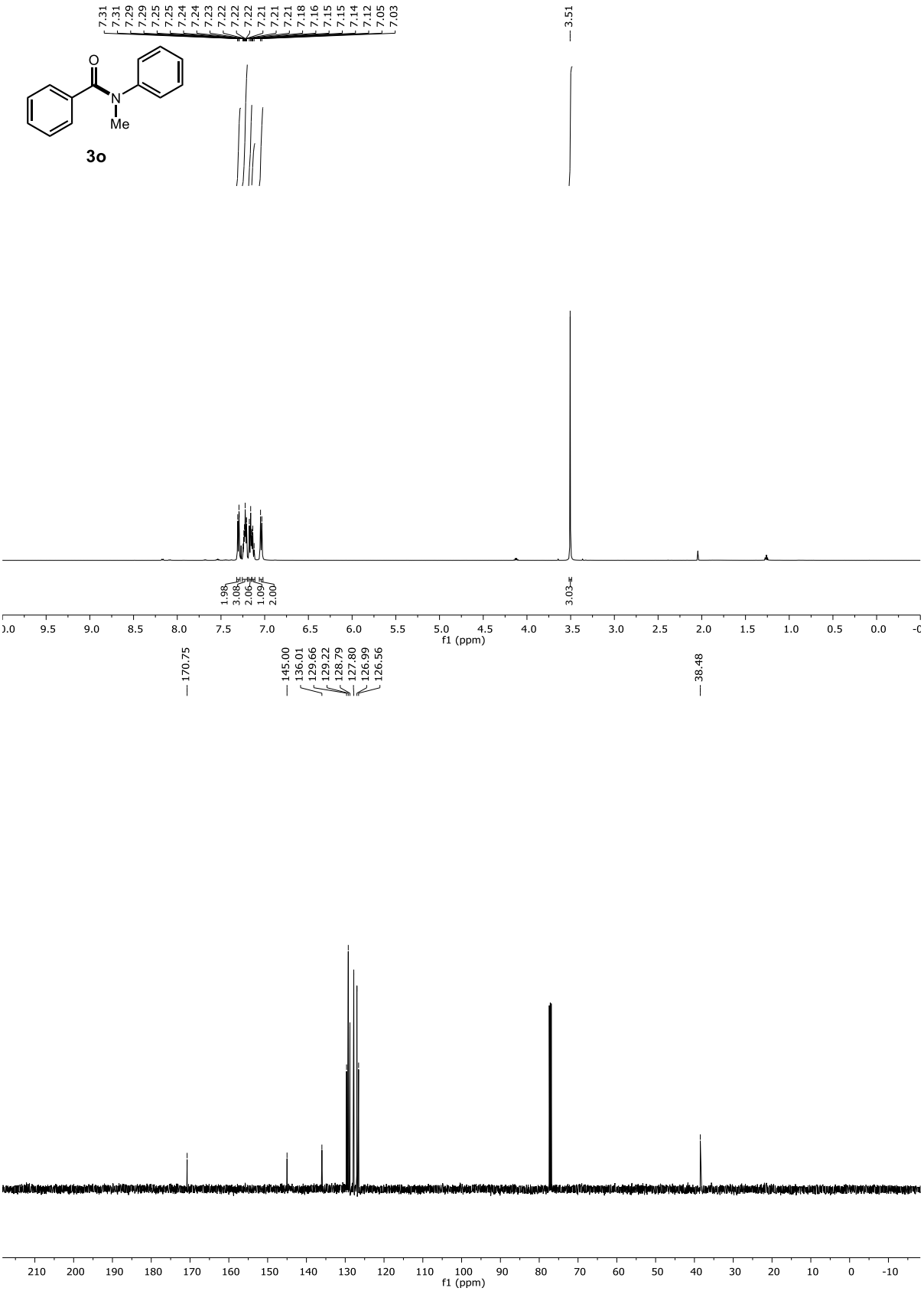
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f1 (ppm)
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145.00
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128.79
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126.56
38.48
f1 (ppm)