**Expedited Palladium-Catalyzed Amination of Aryl Nonaflates through the
use of Microwave-Irradiation and Soluble Organic Amine Bases**

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General Considerations

Reagents: Pd₂dba₃ and XantPhos (Ligand **3**) were purchased from Strem Chemical Co. and used without further purification. Ligands **1** and **2** were prepared according to literature procedure¹ and are also commercially available from Strem and Aldrich. DBU and MTBD were purchased from Aldrich and used without further purification. Toluene and dichloromethane were purchased from J. T. Baker in CYCLE-TAINER solvent delivery kegs, which were vigorously purged with argon for 2 h, and further purified by passing the solvent through two packed columns of neutral alumina and copper (II) oxide under argon pressure. All other reagents were purchased from commercial sources and used without further purification.

Analytical Methods. All reactions were carried out under an argon atmosphere in oven-dried glassware. IR spectra were obtained on a Perkin-Elmer Model 2000 FT-IR using NaCl plates (thin film). ¹H NMR and ¹³C NMR spectra were recorded on a Bruker 400 MHz instrument with chemical shifts reported in ppm relative to the residual deuterated solvent or the internal standard tetramethylsilane. Yield refers to isolated yields of compounds greater than 95% purity as determined by capillary gas chromatography (GC), and proton Nuclear Magnetic Resonance spectroscopy (¹H NMR) analysis. Yields for the preparation of starting materials (aryl nonaflates) refer to a single experiment whereas those reported in Tables 2-4 are an average of two or more runs. The procedures described in this section are representative, thus, the yields may differ slightly from those given in Tables 2-4. ¹H NMR and melting points (where applicable) of all known compounds were taken. All new aryl nonaflates and amines were further characterized by elemental analysis. Several (3) of them are pending: copies of ¹H NMR spectra are included for those examples.

Microwave Instrument/Methods. All couplings were conducted using a CEM Explorer PLS® microwave for High Throughput Sequential Chemistry (HTSC) with cooling to optimize the power. Temperature measurements were conducted

using an infrared temperature sensor positioned below the reaction vessel. Reaction times refer to the total hold time at the indicated temperature with ramp times ranging from 1-2 minutes. While there was some variation in the ramp time for each experiment, all reported examples were reproducible using the indicated hold time/temperature.

Preparation of known aryl/heteroaryl nonaflates: 4-*t*-butylphenyl nonaflate^{2a}; 2,6-dimethylphenyl nonaflate^{2a}; 2-methoxyphenyl nonaflate^{2b}; 4-methoxyphenyl nonaflate^{2a}; 2-naphthyl nonaflate^{2c}; 2-nitrophenyl nonaflate^{2a}; 3-acetylphenyl nonaflate^{2d}; 2-chlorophenyl nonaflate^{2a}; and 3-pyridinyl nonaflate^{2e} were prepared using literature procedures.

General procedure for the synthesis of aryl/heteroaryl nonaflates.² A solution of phenol (1.0 equiv), cat. DMAP (0.05 equiv.), *i*-Pr₂NEt (1.2 equiv.) in dichloromethane (20 mL) was cooled to 0 °C in an ice bath and nonafluorobutanesulfonic fluoride (1.1 equiv.) was added dropwise. The solution was allowed to warm to room temperature and stir for 12-24 h after which the solution was poured into water (20 mL/mmol phenol). The organic layer was extracted with dichloromethane, washed with aqueous NaOH (2.0 M), dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes mixtures).

5-*N*-methylindolyl nonaflate: Using the general procedure, 5-*N*-methyl hydroxyindole^{3,4} (1.47 g, 9.99 mmol), *i*-Pr₂NEt (2.1 mL, 12.0 mmol), DMAP (61 mg, 0.5 mmol), dichloromethane (20 mL) and nonafluorobutanesulfonyl fluoride (2.0 mL, 11.0 mmol) were used. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:10) to give the title compound as a brown oil (1.4 g, 41%). ¹H NMR (400 MHz, CDCl₃) δ:

7.56 (d, $J = 2.4$ Hz, 1H), 7.32 (d, $J = 8.8$ Hz, 1H), 7.13-7.17 (m, 2H), 6.55 (d, $J = 3.2$ Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 144.0, 135.7, 131.5, 128.8, 114.9, 113.4, 110.3, 109.3-118.2 (m, 4C), 102.0, 33.3. IR (neat, cm^{-1}): 1631, 1422, 1355, 1240, 1143, 942. Anal. Calcd for $\text{C}_{13}\text{H}_8\text{F}_9\text{NO}_3\text{S}$: C, 36.37; H, 1.88. Found: C, 36.81; H, 1.76.

2-Cyanophenyl nonaflate. Using the general procedure, 2-hydroxybenzonitrile (2.33 g, 20.0 mmol), $i\text{-Pr}_2\text{NEt}$ (4.20 mL, 24.0 mmol), nonafluorobutanesulfonyl fluoride (4.00 mL, 22.0 mmol), DMAP (123 mg, 1.00 mmol), and dichloromethane (35 mL) were used. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:6) to give the title compound as a white solid (7.2 g, 90%): Mp = 38-39 °C ^1H NMR (400 MHz, CDCl_3) δ : 7.79 (m, 1H), 7.39 (m, 1H), 7.54 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ : 150.1, 134.9, 134.7, 128.9, 122.8, 113.7, 107.7, 106.4-115.2 (m, 4C). IR (neat, cm^{-1}): 1658, 1588, 1359. Anal. Calcd for $\text{C}_{11}\text{H}_4\text{F}_9\text{NO}_3\text{S}$: C, 32.93; H, 1.00. Found: C, 33.00; H, 1.00.

3-Carboxymethylphenyl nonaflate. Using the general procedure, 3-hydroxy methylbenzoate (3.00 g, 20.0 mmol), $i\text{-Pr}_2\text{NEt}$ (4.20 mL, 24.0 mmol), nonafluorobutanesulfonyl fluoride (4.00 mL, 22.0 mmol), DMAP (123 mg, 1.00 mmol), and dichloromethane (35 mL) were used. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:10) to give the title compound as a colorless oil (6.9 g, 80%). ^1H NMR (400 MHz, CDCl_3) δ : 8.05 (d, $J = 6.6$ Hz, 1H), 9.42 (s, 1H), 7.46-7.55 (m, 2H), 3.93 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ : 165.3, 149.9, 133.0, 129.6,

125.8, 122.7, 109.8-188.7 (m, 4C). IR (neat, cm^{-1}): 1729, 1658, 1432, 1155. Anal. Calcd for $\text{C}_{12}\text{H}_7\text{F}_9\text{O}_5\text{S}$: C, 33.19; H, 1.62. Found: C, 33.35; H, 1.51.

3-Trifluoromethylphenyl nonaflate. Using the general procedure, 3-hydroxybenzotrifluoride (1.80 mL, 20.0 mmol), *i*-Pr₂NEt (4.20 mL, 24.0 mmol), nonafluorobutanesulfonyl fluoride (4.00 mL, 22.0 mmol), DMAP (123 mg, 1.00 mmol), and dichloromethane (35 mL) were used. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:10) to give the title compound as a colorless oil (5.6 g, 85%). ¹H NMR (400 MHz, CDCl_3) δ : 7.51-7.70 (m, 4H). ¹³C NMR (100 MHz, CDCl_3) δ : 150.0, 133.7 (m, 1C), 131.3, 127.3, 125.6, 125.5, 119.1, 110.3-125.5 (m, 4C). IR (neat, cm^{-1}): 1658, 1597, 1427, 1157, 1069. Anal. Calcd for $\text{C}_{11}\text{H}_4\text{F}_{12}\text{O}_3\text{S}$: C, 29.74; H, 0.91. Found: C, 29.78; H, 0.91.

5-Quinolyl nonaflate. Using the general procedure, 5-hydroxyquinoline (1.3 g, 8.9 mmol), *i*-Pr₂NEt (2.10 mL, 12.0 mmol), nonafluorobutanesulfonyl fluoride (2.00 mL, 11.0 mmol), DMAP (61 mg, 0.50 mmol), and dichloromethane (20 mL) were used. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 5:1) to give the title compound as a pink solid (7.7 g, 71%): Mp = 66-67 °C. ¹H NMR (400 MHz, CDCl_3) δ : 9.00 (s, 1H), 8.19-8.23 (m, 2H), 7.76 (s, 1H), 7.62 (m, 1H), 7.50 (m, 1H). ¹³C NMR (100 MHz, CDCl_3) δ : 151.9, 147.5, 147.3, 136.3, 132.7, 128.5, 123.3, 122.6, 119.4, 110.0-120.3 (m, 4C). IR (neat, cm^{-1}): 1659, 1530, 1427, 1156. Anal. Calcd for $\text{C}_{13}\text{H}_6\text{F}_9\text{NO}_3\text{S}$: C, 36.55; H, 1.42. Found: C, 36.66; H, 1.39.

3-Cyanophenyl nonaflate. Using the general procedure, 3-cyanophenol (2.38 g, 20.0 mmol), *i*-Pr₂NEt (4.20 mL, 24.0 mmol), nonafluorobutanesulfonyl fluoride (4.00 mL, 22.0 mmol), DMAP (123 mg, 1.00 mmol), and dichloromethane (35 mL) were used. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:10) to give the title compound as a brown oil (6.9 g, 86%). ¹H NMR (400 MHz, CDCl₃) δ: 7.70-7.72 (m, 1H), 7.55-7.64 (m, 3H). ¹³C NMR (100 MHz, CDCl₃) δ: 149.7, 132.3, 131.6, 126.3, 125.2, 116.8, 115.8, 110.0-118.6 (m, 4C). IR (neat, cm⁻¹): 2239, 1579, 1430, 1239, 1145, 938, 799. Anal. Calcd for C₁₁H₄F₉NO₃S: C, 32.93; H, 1.00. Found: C, 33.08; H, 0.90.

Table 1: Screen of bases and solvents for the palladium-catalyzed amination of 4-*t*-butylphenyl nonaflate. An oven-dried, disposable microwave tube containing a stir bar was charged with **1** (6.0 mg, 0.013 mmol) and Pd₂dba₃ (2.9 mg, 0.0031 mmol). The tube was then capped with a plastic microwave septum and then evacuated and backfilled with argon. To the vessel, 4-*t*-butyl phenyl nonaflate (77 μL, 0.25 mmol), aniline (23 μL, 0.33 mmol), base (0.63 mmol) and solvent (0.5 mL, where indicated) were added via syringe. The vessel was submitted to microwave irradiation with stirring for 15 min at 150 °C. The mixture was cooled to room temperature and then water, ethyl acetate and the internal standard dodecane (0.25 mmol) were added. The reactions were analyzed by GC.

***N*-(4-*tert*-Butylphenyl)aniline (Table 1, Entry 3).^{2a}** The organic layer was separated, dried over anhydrous MgSO₄ and concentrated. The crude material was purified by column chromatography on silica gel (hexanes/ethyl acetate, 1:10) to give the title compound as a colorless oil (49 mg, 87%). ¹H NMR (400

MHz, CDCl₃) δ : 7.50 (d, J = 8 Hz, 2H), 7.44 (t, J = 8 Hz, 2H), 7.22 (d, J = 7.6 Hz, 4H), 7.10 (t, J = 7.2 Hz, 1H), 5.76 (br-s, 1H).

General Procedure for Tables 2-4. An oven-dried disposable microwave tube containing a stir bar was charged with Pd₂dba₃ and ligand. The vessel was sealed with a plastic microwave septum and then evacuated and backfilled with argon; this sequence was repeated two additional times. The aryl/heteroaryl nonaflate (1.0 eq.), amine (1.3 eq.), DBU or MTBD (2.5 eq.) and toluene (2 mL/mmol) were successively added via syringe (aryl/heteroaryl nonaflates or amines that were solids at room temperature were added prior to the evacuation and backfill sequence). The vessel was submitted to microwave irradiation with stirring until the starting aryl/heteroaryl nonaflate had been completely consumed as judged by GC analysis. The mixture was cooled to room temperature and then diluted with water and ethyl acetate. The organic layer was separated, dried over anhydrous MgSO₄ and concentrated. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes mixtures).

Experimental procedures for Table 2.

***N*-(2-Methoxyphenyl)-2-methylaniline (Table 2, Entry 1).**⁶ Using the general procedure, 2-methoxyphenyl nonaflate (406 mg, 1.00 mmol), Pd₂dba₃ (13.8 mg, 0.0150 mmol), ligand **1** (28.6 mg, 0.0600 mmol), *o*-toluidine (175 μ L mg, 1.30 mmol), and DBU (382 μ L, 2.50 mmol) in toluene (2 mL) was subjected to microwave irradiation for 15 min at 150 °C. The crude material was purified by

column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:20) to give the title compound as a brown solid (209 mg, 98 %): Mp = 38-39 °C (lit⁶. 36-37 °C). ¹H NMR (400 MHz, CDCl₃) δ: 7.31 (d, *J* = 8 Hz, 1H), 7.21 (t, *J* = 5.6 Hz, 1H), 7.15 (t, *J* = 6.4 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.94 (t, *J* = 7.2 Hz, 1H), 6.87 (m, 1H), 6.83 (m, 2H), 3.89 (s, 3H), 2.27 (s, 3H).

***N*-(4-Methoxyphenyl)aniline (Table 2, Entry 2).**⁷ Using the general procedure, 4-methoxyphenyl nonaflate (102 mg, 0.250 mmol), Pd₂dba₃ (3.4 mg, 0.0038 mmol), ligand **1** (7.2 mg, 0.015 mmol), aniline (23 μL, 0.33 mmol), MTBD (90 μL, 0.63 mmol) in toluene (0.5 mL) were subjected to microwave irradiation for 15 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:4) to give the title compound as a brown solid (50 mg, 99%): Mp = 106-107 °C (lit⁷. 108-108.5 °C). ¹H NMR (400 MHz, CDCl₃) δ: 7.11-7.17 (m, 2H), 6.98-7.01 (m, 2H), 6.73-6.84 (m, 5H), 5.41 (br-s, 1H), 3.72 (s, 3H).

***N*-(2-Naphthyl)aniline (Table 2, Entry 3).**⁸ Using the general procedure, 2-naphthyl nonaflate (213 mg, 0.500 mmol), Pd₂dba₃ (6.8 mg, 0.0075 mmol), ligand **2** (12.7 mg, 0.0300 mmol), aniline (46 μL, 0.65 mmol), DBU (191 μL, 1.25 mmol) in toluene (1.0 mL) was subjected to microwave irradiation for 15 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:4) to give the title compound as a brown solid (110 mg, 99%): Mp = 104-106 °C (lit⁸. 107-108 °C). ¹H NMR (400 MHz, CDCl₃) δ: 7.65 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.33 (m, 2H), 7.22 (m, 3H), 7.10 (m, 3H), 6.89 (t, *J* = 8.0 Hz, 1H), 5.76 (br-s, 1H).

Experimental procedures for Table 3:

***N*-(2-Cyanophenyl)-3-carboxymethylaniline (Table 3, Entry 1).** Using the general procedure, 2-cyanophenyl nonaflate (201 mg, 0.500 mmol), Pd₂dba₃ (11.7 mg, 0.0125 mmol), XantPhos (28.9 mg, 0.0500 mmol), 3-methyl aminobenzoate (98 mg, 0.65 mmol), DBU (191 μ L, 1.25 mmol) in toluene (1.0 mL) was subjected to microwave irradiation for 20 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:2) to give the title compound as a yellow solid (117 mg, 93%): Mp = 82-83 °C. ¹H NMR (400 MHz, CDCl₃) δ : 7.87 (d, *J* = 1.2 Hz, 1H), 7.69 (d, *J* = 7.2 Hz, 1H), 7.27-7.45 (m, 4H), 7.15 (t, *J* = 8.4 Hz, 1H), 6.81 (t, *J* = 7.6 Hz, 1H), 6.40 (br s, 1H), 3.84 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ : 166.7, 146.7, 140.6, 134.2, 133.4, 131.8, 129.8, 125.6, 125.0, 122.0, 120.2, 117.5, 114.8, 99.5, 52.5. IR (neat, cm⁻¹): 3341, 2218, 1722, 1589, 1576, 1523, 1455, 1437, 1295, 1217, 1108, 1000, 749. LRMS (%): 252 (M, 100), 220 (80), 192 (75), 166 (8), 139 (6), 110 (20), 96 (10), 83 (13), 65 (20), 50 (10).

***N*-(2-Nitrophenyl)aniline (Table 3, Entry 2)^{2a}.** Using the general procedure, 2-nitrophenyl nonaflate (105 mg, 0.250 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), aniline (23 μ L, 0.33 mmol), MTBD (90 μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 45 min at 115 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:6) to give the title compound as an orange oil (53 mg, 99%). ¹H NMR (400 MHz, CDCl₃) δ : 9.42 (br s, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.26-7.35 (m, 3H), 7.13-7.20 (m, 4H), 6.69 (t, J = 8.0 Hz, 1H).

***N*-Methyl-*N*-(3-carboxymethyl)aniline (Table 3, Entry 3).** Using the general procedure, 3-carboxymethylphenyl nonaflate (177 mg, 0.250 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), *N*-methyl-*p*-toluidine (41 μ L, 0.33 mmol), MTBD (90 μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 30 min at 175 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:4) to give the title compound as a yellow oil (56 mg, 89%). ¹H NMR (400 MHz, CDCl₃) δ : 7.47 (m, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.15 (m, 1H), 7.06 (d, J = 8 Hz, 2H), 6.94 (d, J = 8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ : 167.9, 149.8, 146.4, 133.8, 131.3, 130.6, 129.3, 124.2, 121.8, 120.5, 117.6, 52.5, 40.8, 21.3. IR (neat, cm⁻¹) 2949, 1721, 1598, 1511, 1446, 1348, 1106, 753. Anal. Calcd for C₁₆H₁₇NO₂: C, 75.27; H, 6.71. Found: C, 75.07; H, 6.65.

1-(3-anilinophenyl)-ethanone (Table 3, Entry 4).⁹ Using the general procedure, 3-acetylphenyl nonaflate (204 mg, 0.500 mmol), Pd₂dba₃ (11.7 mg, 0.0125 mmol), ligand **2** (21.2 mg, 0.0500 mmol), aniline (46 μ L, 0.65 mmol), DBU (180 μ L, 1.25 mmol) in toluene (1.0 mL) was subjected to microwave irradiation for 30 min at 125 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:3) to give the title compound as a yellow solid (83 mg, 81%): Mp = 87-88 °C (lit⁹. 92.5 °C). ¹H NMR (400 MHz, CDCl₃) δ : 7.62 (s, 1H), 7.48 (dt, J = 7.6, 1.2 Hz, 1H), 7.25-7.33 (m, 4H), 7.09 (d, J = 7.6 Hz, 2H), 6.98 (t, J = 7.2 Hz, 1H), 5.89 (br-s, 1H), 2.57 (s, 3H).

N-(3-Trifluoromethylphenyl)-2-cyanoaniline (Table 3, Entry 5).¹⁰ Using the general procedure, 3-trifluoromethylphenyl nonaflate (444 mg, 1.00 mmol), Pd₂dba₃ (6.8 mg, 0.015 mmol), XantPhos (34.7 mg, 0.0600 mmol), 2-aminobenzonitrile (154 mg, 1.30 mmol), DBU (380 μ L, 2.50 mmol) in toluene (2.0 mL) was subjected to microwave irradiation for 15 min at 175 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:3) to give the title compound as a yellow solid (226 mg, 86%): Mp = 81-82 °C (lit¹⁰. 81-82 °C). ¹H NMR (400 MHz, CDCl₃) δ : 7.55 (d, J = 8 Hz, 1H), 7.42-7.45 (m, 3H), 7.34-7.35 (m, 2H), 7.25 (d, J = 8.8, 1H), 6.95 (t, J = 7.6, 1H), 6.47 (s, 1H).

(1-Methyl-1H-indol-5-yl)-phenyl-amine (Table 3, Entry 6). Using the general procedure, 5-N-methylindolyl nonaflate (109 mg, 0.250 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), ligand **2** (14.5 mg, 0.0250 mmol), aniline (23 μ L, 0.33 mmol), DBU (90 μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 30 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:4) to give the title compound as a yellow solid (55 mg, 99%): Mp = 163-165 °C. ¹H NMR (400 MHz, CDCl₃) δ : 7.33 (s, 1H), 7.10-7.20 (m, 2H), 6.96-7.03 (m, 2H), 6.83 (d, *J* = 8 Hz, 2H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.32 (d, *J* = 3.2 Hz, 1H), 5.53 (br-s, 1H), 3.70 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ : 146.6, 134.8, 134.0, 129.7, 129.4, 129.2, 119.1, 118.2, 115.3, 113.7, 110.0, 100.7, 33.2. IR (neat, cm⁻¹): 3382, 1599, 1509, 1481, 1423, 1309, 1249, 1153, 886, 754. Anal. Calcd for C₁₅H₁₄N₂: C, 81.05; H, 6.35. Found: C, 80.65 ; H, 6.23 .

N-(2-Chlorophenyl)aniline (Table 3, Entry 7)^{2a}. Using the general procedure, 2-chlorophenyl nonaflate (210 mg, 0.500 mmol), Pd₂dba₃ (11.7 mg, 0.0125 mmol), XantPhos (28.9 mg, 0.0500 mmol), aniline (46 μ L, 0.65 mmol), MTBD (180 μ L, 1.25 mmol) in toluene (1.0 mL) was subjected to microwave irradiation for 30 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:6) to give the title compound as a colorless oil (100 mg, 93%). ¹H NMR (400 MHz, CDCl₃) δ : 7.15-7.23 (m, 4H), 6.98-7.05 (m, 3H), 6.93 (t, *J* = 7.2 Hz, 1H), 6.68 (m, 1H), 5.99 (br-s, 1H).

N-Phenyl-3-aminopyridine (Table 3, Entry 8).¹¹ Using the general procedure, 3-pyridinyl nonaflate (91 mg, 0.25 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), aniline (23 μ L, 0.33 mmol), DBU (95 μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 15 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:2) to give the title compound as a light brown solid (36 mg, 90%): Mp 141-143 °C (lit¹¹.140-141 °C). ¹H NMR (400 MHz, CDCl₃) δ : 8.30 (d, J = 2.8 Hz, 1H), 8.07 (dd, J = 8.6, 1.2 Hz, 1H), 7.35 (m, 1H), 7.19-7.24 (m, 2H), 7.00-7.11 (m, 3H), 6.91 (t, J = 7.2 Hz, 1H), 5.87 (br-s, 1H).

N-Phenyl-5-aminoquinoline (Table 3, Entry 9).¹² Using the general procedure, 5-quinolyl nonaflate (104 mg, 0.250 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), aniline (23 μ L, 0.33 mmol), DBU (95 μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 15 min at 175 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:2) to give the title compound as a brown solid (45 mg, 85%): Mp 178-180 °C. ¹H NMR (400 MHz, CDCl₃) δ : 8.63 (d, J = 3.4 Hz, 1H), 7.90 (d, J = 9.2 Hz, 1H), 7.85 (d, J = 8 Hz, 1H), 7.33 (dd, J = 9.2, 2.4 Hz, 1H), 7.20-7.28 (m, 4H), 7.12 (d, J = 8 Hz, 2H), 6.95 (t, J = 7.2 Hz, 1H), 6.06 (br s, 1H).

Experimental procedures for Table 4:

Methyl 3-aminobenzoate (Table 4, Entry 1).¹⁴ Using the general procedure, 3-carboxymethyl nonaflate (104 mg, 0.250 mmol), Pd₂dba₃ (3.4 mg, 0.0038 mmol), XantPhos (8.7 mg, 0.015 mmol), benzophenone imine (70. μ L, 0.33 mmol), MTBD (90. μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 20 min at 140 °C. According to literature procedure¹³, the crude material was then reacted with hydroxylamine·HCl (70. mg, 1.0 mmol), sodium acetate (100. mg, 1.20 mmol) in methanol (5 mL) for 30 minutes to cleave the imine to the free amine. The resulting residue was then extracted with dichloromethane (20 mL), washed with aqueous NaOH (0.1 M, 20 mL) and purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:2) to give the title compound as a clear oil. ¹H NMR (400 MHz, CDCl₃) δ : 7.34 (d, J = 7.6 Hz, 1H), 7.27 (d, J = 1.6 Hz, 1H), 7.11-7.19 (m, 1H), 6.76-6.80 (m, 1H), 3.81 (s, 3H), 3.73 (br s, 2H).

3-Aminobenzonitrile (Table 4, Entry 2).¹⁵ Using the general procedure, 3-cyanophenyl nonaflate (94 mg, 0.24 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), benzophenone imine (70. μ L, 0.33 mmol), MTBD (90. μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 15 min at 150 °C. According to literature procedure¹³, the crude material was then reacted with hydroxylamine·HCl (70. mg, 1.0 mmol), sodium acetate (100. mg, 1.20 mmol) in methanol (5 mL) for 30 minutes to cleave the imine to the free amine. The resulting residue was then extracted with dichloromethane (20 mL), washed with aqueous NaOH (0.1 M, 20 mL) and purified by column chromatography on silica gel (eluting with ethyl

acetate/hexanes, 1:2) to give the title compound as a white solid (21 mg, 76 %): mp = 46 °C (lit¹⁵. 48 °C). ¹H NMR (400 MHz, CDCl₃) δ: 7.13-7.20 (m, 1H), 6.96 (d, *J* = 7Hz, 1H), 6.78-6.84 (m, 2H), 3.81 (br-s, 2H).

Benzhydrylidene-pyridin-3-yl-amine (Table 4, Entry 3).¹⁶ Using the general procedure, 3-pyridinyl nonaflate (95 mg, 0.25 mmol), Pd₂dba₃ Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), benzophenone imine (70. μL, 0.33 mmol), MTBD (90. μL, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 30 min at 125 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:6) to give the title compound as a brown solid (65 mg, 99%): Mp = 103-105 °C (lit¹⁶. 103-105 °C). ¹H NMR (400 MHz, CDCl₃) δ: 8.17 (d, *J* = 4.4 Hz, 1H), 8.03 (d, *J* = 2.4 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 5.2 Hz, 1H), 7.42 (t, *J* = 6 Hz, 2H), 7.30-7.26 (m, 3H), 7.05-7.12 (m, 4H).

5-Aminoquinoline (Table 4, Entry 4).¹⁷ Using the general procedure, 5-quinolyl nonaflate (107 mg, 0.250 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), benzophenone imine (70. μL, 0.33 mmol), MTBD (90. μL, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 30 min at 125 °C. To hydrolyze the imine, the residue was stirred at room temperature in HCl (1.0 N) for 30 min, neutralized, and then extracted with ethyl acetate¹². The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:6) to give the title compound as a brown solid (34 mg, 94%): Mp = 110-111 °C (lit¹⁷. 108.5-110 °C). ¹H NMR (400 MHz, CDCl₃) δ: 8.65 (d, *J* = 3.6, 1H), 7.89 (t, *J* = 8.2, 2H), 7.26 (m, 1H), 7.15 (d, *J* = 8.0, 1H), 6.88 (d, *J* = 2.8, 1H), 3.88 (s, 2H).

N-Naphthalen-2-yl-isobutyramide (Table 4, Entry 5).¹⁸ Using the general procedure, 2-naphthyl nonaflate (107 mg, 0.250 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), isobutyramide (28. mg, 0.33 mmol), MTBD (90. μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 30 min at 175 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:3) to give the title compound as a brown solid (49 mg, 92%): Mp = 177-179 °C (lit¹⁸. 180 °C). ¹H NMR (400 MHz, d⁶-DMSO) δ : 9.88 (s, 1H), 8.17 (s, 1H), 7.62-7.69 (m, 3H), 7.44 (d, J = 8.8 Hz, 1H), 7.20-7.31 (m, 2H), 2.50 (q, J = 6.8 Hz, 1H), 0.96 (d, J = 6.8 Hz, 6H).

N-(3-Trifluoromethylphenyl)-benzamide (Table 4, Entry 6).¹⁹ Using the general procedure, 3-trifluoromethylphenyl nonaflate (218 mg, 0.500 mmol), Pd₂dba₃ (11.7 mg, 0.0125 mmol), XantPhos (28.9 mg, 0.0500 mmol), benzamide (79 mg, 0.65 mmol), MTBD (180. μ L, 1.25 mmol) in toluene (1.0 mL) was subjected to microwave irradiation for 30 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:2) to give the title compound as a yellow solid (130 mg, 98%): Mp = 108-109 °C (lit¹⁹. 110-111 °C). ¹H NMR (400 MHz, CDCl₃) δ : 8.09 (br-s, 1H), 7.77-7.86 (m, 4H), 7.31-7.50 (m, 5H).

3-Chloro-*N*-(2-cyanophenyl)-benzamide (Table 4, Entry 7).²⁰ Using the general procedure, 2-cyanophenyl nonaflate (100 mg, 0.250 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), 3-chlorobenzamide (51 mg, 0.33 mmol), MTBD (90. μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 30 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:2) to give the title compound as a brown solid (59 mg, 92%): Mp = 165-166 °C (lit²⁰. 165-166 °C). ¹H NMR (400 MHz, d⁶-DMSO) δ : 10.77 (s, 1H), 8.04 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.79-7.72 (m, 2H), 7.64-7.58 (m, 2H), 7.46 (t, J = 7.6 Hz, 1H).

(5-Chloro-pyridin-2-yl)-(3-trifluoromethylphenyl)-amine (Table 4, Entry 8). Using the general procedure, 3-trifluoromethylphenyl nonaflate (108 mg, 0.250 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), 2-amino-5-chloropyridine (42 mg, 0.33 mmol), MTBD (90 μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 30 min at 175 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:4) to give the title compound as an off-white solid (56 mg, 83%): Mp = 89-90 °C. ¹H NMR (400 MHz, d⁴-MeOH) δ : 8.11 (d, J = 2.4 Hz, 1H), 8.04 (s, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.52 (dd, J = 8.8, 2.4 Hz, 1H), 7.38 (t, J = 8 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 6.86 (br s, 1H), 6.77 (d, J = 8.8 Hz, 1H). ¹³C NMR (100 MHz, d⁴-MeOH) δ : 154.6, 145.5, 142.4, 137.5, 124.3-131.2 (m, 1C), 129.4, 122.1, 119.5, 117.3, 117.2, 114.7, 112.3. IR (neat, cm⁻¹) 3399, 1589, 1527, 1478, 1336, 1165, 1123, 696. Anal. Calcd for C₁₂H₈ClF₃N₂: C, 52.86; H, 2.96. Found: C, 52.47 ; H, 2.96.

(2-Ethyl-2H-pyrazol-3-yl)-naphthalen-2-yl-amine (Table 4, Entry 9). Using the general procedure, 2-naphthyl nonaflate (107 mg, 0.250 mmol), Pd_2dba_3 (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), 5-amino-1-ethylpyrazole (36 mg, 0.33 mmol), MTBD (90. μL , 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 30 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexanes, 1:2) to give the title compound as an off-white solid (59 mg, 99%): Mp = 78-79 °C ^1H NMR (400 MHz, $\text{d}^4\text{-MeOH}$) δ : 7.69-7.72 (m, 2H), 7.53 (d, J = 8.4, 1H), 7.47 (d, J = 2 Hz, 1H), 7.31 (t, J = 6.4 Hz, 1H), 7.20 (t, J = 6 Hz, 1H), 7.13 (t, J = 7.2 Hz, 1H), 7.02 (d, J = 2 Hz, 1H), 6.08 (d, J = 2 Hz, 1H), 4.06 (q, J = 7.2, 2H), 1.33 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $\text{d}^4\text{-MeOH}$) δ : 144.4, 142.7, 139.8, 136.3, 130.3, 130.2, 128.7, 127.6, 127.4, 124.1, 119.0, 109.5, 99.1, 43.6, 15.6. IR (neat, cm^{-1}) 3248, 1632, 1462, 1403, 928, 747. Anal. Calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3$: C, 75.92; H, 6.37. Found: C, 75.73; H, 6.45.

Pyridin-3-yl-pyrimidin-2-yl-amine (Table 4, Entry 10). Using the general procedure, 3-pyridinyl nonaflate (91 mg, 0.25 mmol), Pd_2dba_3 (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), 2-aminopyrimidine (31 mg, 0.33 mmol), MTBD (90. μL , 0.63 mmol) in toluene (0.5 mL) were subjected to microwave irradiation for 30 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/methanol, 10:1) to give the title compound as a light brown solid (56 mg, 83%): Mp = 135-137 °C. ^1H NMR (400 MHz, $\text{d}^4\text{-MeOH}$) δ : 8.86 (s, 1H), 8.46 (d, J = 4.8 Hz, 2H), 8.29 (d, J = 8.8 Hz, 1H), 8.13 (d, J = 4.4 Hz, 1H), 7.35 (q, J = 4.8 Hz, 1H), 6.85 (t, J = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $\text{d}^4\text{-MeOH}$) δ : 161.6, 159.4, 142.9, 141.3, 139.4,

128.1, 125.2, 114.5. IR (neat, cm⁻¹) 3408, 3263, 1588, 1485, 1433, 1258, 793, 706.

(1-Methyl-1H-benzoimidazol-2-yl)-quinolin-5-yl-amine (Table 4, Entry 11).

Using the general procedure, 5-quinolyl nonaflate (107 mg, 0.250 mmol), Pd₂dba₃ (5.8 mg, 0.0063 mmol), XantPhos (14.5 mg, 0.0250 mmol), 1-methyl-2-aminobenzimidazole (48 mg, 0.33 mmol), MTBD (90. μ L, 0.63 mmol) in toluene (0.5 mL) was subjected to microwave irradiation for 30 min at 150 °C. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/methanol, 10:1) to give the title compound as a yellow solid (68 mg, 99%): Mp = 220 °C (dec). ¹H NMR (400 MHz, d⁴-MeOH) δ : 8.54 (d, *J* = 4.4 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 8.8 Hz, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.38 (m, 1H), 7.31 (q, *J* = 4.4 Hz, 1H), 7.14 (m, 1H), 7.05 (m, 2H), 3.55 (s, 3H). ¹³C NMR (100 MHz, d⁴-MeOH) δ : 152.1, 149.3, 145.5, 141.0, 137.7, 135.9, 131.148, 130.0, 125.5, 123.2, 122.5, 117.8, 114.6, 109.7, 29.7. IR (neat, cm⁻¹) 3416, 1585, 1566, 1529, 1391, 1235, 740.

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^1H NMR spectra of known/commercial compounds:

Table 1, Entry 3:

Table 2, Entry 1:

Table 2, Entry 2:

Table 2, Entry 3:

Table 3, Entry 2:

Table 3, Entry 4:

Table 3, Entry 5:

Table 3, Entry 7:

Table 3, Entry 8:

Table 3, Entry 9:

Table 4, Entry 1:

Table 4, Entry 2:

Table 4, Entry 3:

Table 4, Entry 4:

Table 4, Entry

5:

Table 4, Entry 6:

Table 4, Entry 7: