# Supporting Information

## General Reagent Information

Aryl and heteroaryl halides, copper iodide, potassium trifluoroacetate, pyridine and solvents were purchased from Aldrich Chemical, Alfa Aesar, or Combi-Block and were used as received without further purification.

Note: Silicone oil with a suitable temperature range (e.g., Alfa Aesar, catalogue number: 45896, temperature range: 25-250 °C) should be used. Approprite safety precaustions including the use of a safety shield in are hood should be employed.

## General Analytical Information

All compounds were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR spectroscopy, and melting points (where applicable). Elemental analysis was conducted for unknown products. Copies of the <sup>1</sup>H and <sup>13</sup>C spectra can be found at the end of the Supporting Information. NMR spectra were recorded either on a Varian XL 300 or a Bruker AMX 400 MHz NMR spectrometer. <sup>1</sup>H NMR signals are reported in  $\delta$  units, parts per million (ppm), and were measured relative to the signal for residual chloroform (7.26 ppm) in deuterochloroform (CDCl<sub>3</sub>). <sup>13</sup>C NMR signals are reported in ppm relative to deuterochloroform (77.16 ppm), and were obtained with 1H decoupling. <sup>19</sup>F NMR spectra are reported in ppm relative to CFCl<sub>3</sub> (0.00 ppm). IR spectra were obtained on a Thermo Scientific – Nicolet iS5 spectrometer (iD5 ATR – diamond). Melting points (m.p.) were taken on a Mel-Temp capillary melting point apparatus. GC analyses were carried out on an Agilent 7890A gas chromatograph with an FID detector using a J & W DB-1 column (10 m, 0.1 mm I.D.). Elemental analyses were conducted by Atlantic Microlabs Inc., Norcross, GA. Products were purified by flash chromatography using a Biotage SP4 instrument with silica gel (230-400 mesh) cartridges.

## General Material Information for Continuous Flow Setup

All PFA and stainless steel tubing, connectors, nuts, fittings and back-pressure regulators were purchased from IDEX Health and Science, unless otherwise stated. The equipment

configuration that was used for the flow reactions are depicted in Figures S-1, S-2 and S-3. Reactor in Figure S-1 was made of 5 ft stainless steel tubing (0.0625" OD × 0.046" ID). Reactor in Figure S-2 was made of 1 m stainless steel tubing (0.125" OD × 0.08" ID). Reactor in Figure S-3 was made of 30 cm stainless steel tubing (0.0625" OD × 0.04" ID). Connections for reactors in Figure S-1 and S-3 were made using ferrules (peek) and 1/4-28 nuts (stainless steel). Connections for the reactor in Figure S-2 were made using stainless steel tube fitting (0.125" × 0.0625") purchased from Swagelok. Other connections were made using super flangeless ferrules with 1/4-28 flangeless nuts or 1/4-28 flat-bottomed flangeless fittings. All connecting tubing was made of PFA capillary tubing with 0.04" ID (0.0625" OD). The T-mixers (0.04" ID) and Y-mixers (0.04" ID) and check valves (1/4-28) used in this work were made out of PEEK. Stainless steel syringes and syringe pumps (PHD 2000) were purchased from Harvard Apparatus.

## **Experimental Procedures**

	Ph +	CF <sub>3</sub> CO <sub>2</sub> M	Cul, Pyri Temp, Time	dine e, NMP	Ph	$CF_3$ $C_2F$ + $C_2F$	5 + Ph	Η
	<b>1a</b> (1.0 eq)				2a	3	4	
Entry	CF <sub>3</sub> CO <sub>2</sub> M (eq.)	Cul (eq.)	Pyridine (eq.)	Temp (°C	) Time (min)	Conversion (%)	Yield (%)	3 + 4 (%)
1	M = K (3.0)	2.0	none	180	60	100	87	<2
2	M = K (3.0)	2.0	2.4	180	60	100	91	<2
3	M = K (2.0)	2.0	none	200	15	100	89	<2
4	M = K (2.0)	2.0	2.4	200	15	100	92 (95) <sup>[b]</sup>	<2
5	M = K (2.0)	1.5	1.8	200	15	92	85	<5
6	M = Na (2.0)	2.0	2.4	200	15	49	40	<2

Table S-1 Optimization of Aromatic Trifluoromethylation<sup>[a]</sup>

[a] All experiments were performed on a 0.2 mmol scale. All conversion and yields were determined by GC analysis, unless otherwise stated. [b] Determined with <sup>19</sup>F NMR using 1,4-difluorobenzene as an internal standard. [c] When 2,2'-bipyridine or 1,10-phenathroline was used instead of pyridine under the optimal conditions (Entry 4), a lot of solids were observed in the mixture before reaction, and less than 80% GC yields of **2a** were obtained for both cases. When TMEDA (N,N,N',N'-tetramethylethylenediamine) was used instead of pyridine under the optimal conditions (Entry 4), less than 50% GC yields were obtained for **2a**, and reduced product **4** was obtained in 30% GC yields. When DMEDA (N,N'-dimethylethylenediamine) was used, no product **2a** was observed,

and reduced product 4 was obtained in 50% GC yields.

### **General Procedure for Table S-1:**

An oven-dried resealable screw cap test tube equipped with a magnetic stir bar and fitted with a Teflon screw cap was charged 4-iodobiphenyl (0.2 mmol), CuI (0.3-0.4 mmol), CF<sub>3</sub>CO<sub>2</sub>M (0.4-0.6 mmol) and the ligand (when a solid ligand was used). The vessel was evacuated and backfilled with argon (this process was repeated a total of three times). To this vessel was added NMP (0.8 mL) and the ligand (when a liquid ligand was used) via syringe. The mixture was then stirred at room temperature for 2 min, and then the screw-cap was quickly changed to a new Teflon screw cap. The vessel was placed in an oil bath preheated to the reaction temperature as indicated (Caution: Hot!). After the reaction was complete, the tube was quickly cooled down by carefully submerging in an ice-water bath. The mixture was diluted with brine, ammonium hydroxide solution and EtOAc, and then the internal standard of dodecane (when GC analysis was conducted) or 1,4-difluorobenzene (when <sup>19</sup>F NMR analysis was conducted) was added. A small aliquot of the organic layer was filtered through either silica gel (for GC analysis) or Celite (for <sup>19</sup>F NMR analysis) before further analysis.

## Decarboxylation of CF<sub>3</sub>CO<sub>2</sub>K at elevated temperatures





		Conversion (%)					
Entry	Time (min)	Conditions: A	Conditions: B	Conditions: C	Conditions: D		
1	0	0	0	0	0		
2	1	29	15	5	2		
3	2	43	22	8	4		
4	3	57	27	10	6		
5	5	77	34	13	8		
6	10	94	52	18	12		

**Figure S-1** 

### Synthesis and Characterization of Non-Commercial Substrates



**Hexyl 4-iodobenzoate** (1b)<sup>[1]</sup> An oven-dried 100 mL round-bottom flask equipped with a magnetic stir bar was charged with 4-iodobenzoic acid (2.98 g, 12.0 mmol), *N*,*N*'-dicyclohexylcarbodiimide (DCC, 3.71 g, 18.0 mmol), 4-(dimethylamino)pyridine (DMAP, 440 mg, 3.6 mmol) and 20 mL anhydrous CH<sub>2</sub>Cl<sub>2</sub>. The flask was cooled to 0 °C and *n*hexanol (1.5 mL, 12.0 mmol) was added dropwise via syringe, then the reaction mixture was stirred at room temperature overnight. After the reaction was complete, the mixture was diluted with EtOAc (200 mL) and rinsed with brine (20 mL × 2). The organic layer was separated, dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was purified by flash column chromatography (eluting with 0-5 % EtOAc in hexanes) to afford **1b** (3.69 g, 93 %) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.83-7.71 (m, 4 H), 4.30 (t, *J* = 6.6 Hz, 2 H), 1.81-1.69 (m, 2 H), 1.48-1.28 (m, 6 H), 0.89 (t, *J* = 6.9 Hz, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 166.3, 137.8, 131.1, 130.1, 100.7, 65.5, 31.5, 28.7, 25.8, 22.6, 14.5 ppm. IR (neat, cm<sup>-1</sup>): 2954, 2927, 1716, 1585, 1264, 1111, 1100, 1007, 751.

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(3-Iodophenyl)(morpholino)methanone (1d) An oven-dried 100 mL round-bottom flask equipped with a magnetic stir bar was charged with 3-iodobenzoic acid (2.98 g, 12.0 mmol), *N*,*N'*-dicyclohexylcarbodiimide (DCC, 3.71 g, 18.0 mmol), 4- (dimethylamino)pyridine (DMAP, 440 mg, 3.6 mmol) and 20 mL anhydrous CH<sub>2</sub>Cl<sub>2</sub>. The flask was cooled to 0 °C and morpholine (1.2 mL, 14.0 mmol) was added dropwise via syringe, then the mixture was stirred at room temperature overnight. After the reaction was complete, the mixture was diluted with EtOAc (200 mL) and rinsed with saturated NH<sub>4</sub>Cl (aq.) solution (20 mL × 2). The organic layer was separated, rinsed with brine (20 mL × 2), dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was

purified via by flash column chromatography (eluting with 0-30 % EtOAc in hexanes) to afforded **1d** (3.48 g, 92 %) as a white solid, mp = 83-84 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.80-7.73 (m, 2 H), 7.35 (d, *J* = 8.0 Hz, 1 H), 7.14 (d, *J* = 8.0 Hz, 1 H), 3.88-3.26 (m, 8 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 168.6, 138.9, 137.4, 136.0, 130.3, 126.2, 94.4, 66.9, 48.4, 42.7 ppm. IR (neat, cm<sup>-1</sup>): 2961, 2852, 1626, 1557, 1427, 1276, 1252, 1112, 1066, 1021, 797, 732. Anal. Calcd. for C<sub>11</sub>H<sub>12</sub>INO<sub>2</sub>: C, 41.66; H, 3.81. Found: C, 41.77; H, 3.80.



1-(3-Iodophenyl)piperidine (1h) An oven-dried 50 mL round-bottom flask equipped with a magnetic stir bar was charged with 3-iodoaniline (2.63g, 12.0 mmol), 1,5dibromopentane (2.76g, 12.0 mmol), ethyldiisopropylamine (5.2 mL, 30.0 mmol) and 15 mL toluene. The mixture was allowed to reflux at 120 °C for 14 h. After the reaction was complete, the mixture was allowed to cool down to room temperature. Upon cooling down, a large amount of salts were precipitated. The solids were filtered off and washed with EtOAc (50 mL  $\times$  3). The collected organic solution was rinsed with saturated NH<sub>4</sub>Cl (aq.) solution (20 mL  $\times$  2), and brine (20 mL  $\times$  2), dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was purified by flash column chromatography (eluting with 0-8 % EtOAc in hexanes) to afford **1h** (3.07 g, 89 %) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.25 (dd, J = 1.5, 1.5 Hz, 1 H), 7.13 (dd, J = 7.5, 1.2 Hz, 1 H), 6.95 (dd, J =7.2, 7.2 Hz, 1 H), 6.88 (ddd, J = 8.4, 2.4, 1.2 Hz, 1 H), 3.15 (t, J = 5.1 Hz, 4 H), 1.74-1.64 (m, 4 H), 1.64-1.54 (m, 2 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 153.3, 130.5, 127.7, 125.1, 115.6, 95.4, 50.2, 25.7, 24.3 ppm. IR (neat, cm<sup>-1</sup>): 2929, 1581, 1549, 1478, 1234, 979, 925, 760, 681. Anal. Calcd. for C<sub>11</sub>H<sub>14</sub>IN: C, 46.01; H, 4.91. Found: C, 46.25; H, 4.89.



(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 2-iodoisonicotinate (1m) An oven-dried 50 mL round-bottom flask equipped with a magnetic stir bar was charged with 2iodopyridine-4-carboxylic acid (996 mg, 4.0 mmol), N,N'-dicyclohexylcarbodiimide (DCC, 1.24 g, 6.0 mmol), 4-(dimethylamino)pyridine (DMAP, 147 mg, 1.2 mmol) and 14 mL anhydrous CH<sub>2</sub>Cl<sub>2</sub>. The flask was cooled to 0 °C and (1R,2S,5R)-(-)-menthol (625 mg, 4.0 mmol) was added, then the mixture was stirred at room temperature overnight. After the reaction was complete, the mixture was diluted with EtOAc (150 mL) and rinsed with brine (20 mL  $\times$  2). The organic layer was separated, dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was purification by flash column chromatography (eluting with 0-3 % EtOAc in hexanes) to afford 1m (1.52 g, 98 %) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.49 (dd, J = 5.7, 0.9 Hz, 1 H), 8.23 (dd, J = 1.2 0.9 Hz, 1 H), 7.79 (dd, J = 5.1, 1.5 Hz, 1 H), 4.94 (td, J = 10.8, 4.5 Hz, 1 H), 2.11-2.01 (m, 1 H), 1.92-1.80 (m, 1 H), 1.78-1.67 (m, 2 H), 1.61-1.47 (m, 2 H), 1.18-1.02 (m, 2 H), 0.99-0.85 (m, 7 H), 0.77 (d, J = 7.2 Hz, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 163.1, 151.4, 139.5, 134.3, 122.3, 118.3, 76.6, 47.2, 40.8, 34.2, 31.6, 26.6, 23.6, 22.1, 20.9, 16.5 ppm. IR (neat, cm<sup>-1</sup>): 2954, 2924, 1721, 1543, 1452, 1356, 1288, 1254, 1130, 1068, 954, 758. HRMS (ESI)  $m/z [M + H]^+$  calcd. for C<sub>16</sub>H<sub>23</sub>INO<sub>2</sub>: 388.0768, found: 388.0767.



**2-(2,5-Dimethyl-1***H***-pyrrol-1-yl)-5-iodopyridine**  $(1n)^{[2]}$  An oven-dried 50 mL roundbottom flask equipped with a magnetic stir bar was charged with 2-amino-5-iodopyridine (2.20 g, 10.0 mmol), *p*-toluenesulfonic acid (*p*-TsOH, 15.6 mg) and 10 mL toluene. 2,5-Hexanedione (1.3 mL, 10.5 mmol) was added dropwise into the flask via syringe at room temperature. The mixture was then allowed to reflux at 125 °C equipped with a Dean-Stark apparatus for 4 h. After cooling to room temperature, the mixture was diluted with

EtOAc (150 mL), and washed with brine (20 mL × 2). The organic layer was separated, dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was purified by flash column chromatography (eluting with 0-10 % EtOAc in hexanes) afforded **1n** (2.41 g, 81 %) as a white solid, mp = 118-119 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.80 (d, *J* = 2.4 Hz, 1 H), 8.11 (dd, *J* = 8.4, 2.4 Hz, 1 H), 7.03 (d, *J* = 8.1 Hz, 1 H), 5.91 (s, 2 H), 2.14 (s, 6 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 155.5, 151.3, 146.2, 128.7, 123.6, 107.6, 91.1, 13.4 ppm. IR (neat, cm<sup>-1</sup>): 2918, 1564, 1460, 1395, 1323, 1080, 1000, 837, 757.

**4-(4-Iodopyridin-2-yl)morpholine** (**1o**) An oven-dried 50 mL round-bottom flask equipped with a magnetic stir bar was charged with 2-fluoro-4-iodopyridine (1.78 g, 9.0 mmol), anhydrous K<sub>2</sub>CO<sub>3</sub> (3.32 g, 27.0 mmol) and 12 mL anhydrous DMSO. Morpholine (1.0 mL, 13.5 mmol) was added into the mixture via syringe at room temperature. Then, the mixture was stirred at 70 °C for 24 h. After the reaction was complete, the mixture was diluted with EtOAc (100 mL) and H<sub>2</sub>O (50 mL). The water layer was separated and extracted with EtOAc (20 mL × 2). The combined organic layers were washed with saturated NH<sub>4</sub>Cl (aq.) solution (20 mL × 2) and brine (20 mL × 2). The organic layer was separated, dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The crude mixture was purified by flash column chromatography (0-10 % EtOAc in hexanes) to afford **1o** (2.35 g, 90 %) as a white solid, mp = 61-62 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.83 (d, *J* = 8.1 H, 1 H), 6.99-6.95 (m, 2 H), 3.78 (t, *J* = 4.8 Hz, 4 H), 3.47 (t, *J* = 4.8 Hz, 4 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 159.8, 148.3, 122.6, 116.0, 106.8, 66.7, 45.4 ppm. IR (neat, cm<sup>-1</sup>): 2958, 2849, 1561, 1532, 1472, 1413, 1240, 1116, 969, 948. Anal. Calcd. for C<sub>9</sub>H<sub>11</sub>IN<sub>2</sub>O: C, 37.26; H, 3.82. Found: C, 37.40; H, 3.90.



5-Iodo-1-(2-nitrophenyl)-1H-indole (1p) An oven-dried 100 mL round-bottom flask equipped with a magnetic stir bar was charged with 5-iodo-1H-indole (2.43 g, 10.0 mmol), 1-fluoro-2-nitrobenzene (1.41 g, 10.0 mmol), Cs<sub>2</sub>CO<sub>3</sub> (3.91 g, 12.0 mmol) and anhydrous DMSO (30 mL). The mixture was stirred at room temperature for 16 h. After the reaction was complete, the mixture was diluted with EtOAc (150 mL) and H<sub>2</sub>O (50 mL). The water layer was separated and extracted with EtOAc (20 mL  $\times$  2). The combined organic layers were washed with saturated NH<sub>4</sub>Cl (aq.) solution (20 mL  $\times$  2), brine (20 mL  $\times$  2), dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The crude mixture was purified by recrystallization with a solution of ethanol (40 mL) and EtOAc (6 mL) to afford 1p (3.31 g, 91 %) as a light yellow solid, mp = 127-128 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.08-8.00 (m, 2 H), 7.74 (ddd, J = 7.5, 7.5, 1.5 Hz, 1 H), 7.63-7.52 (m, 2 H), 7.44 (dd, J = 8.4, 1.8 Hz, 1 H), 7.13 (d, J = 3.3 Hz, 1 H), 6.90 (d, J = 9.0 Hz, 1 H), 6.65 (d, J = 3.3 Hz, 1 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 146.3, 136.0, 134.0, 132.3, 131.5, 131.3, 130.2, 129.8, 129.0, 128.9, 125.6, 111.6, 104.2, 84.6 ppm. IR (neat, cm<sup>-1</sup>): 1606, 1523, 1489, 1444, 1336, 1285, 1231, 1196, 1119, 953, 849, 717. Anal. Calcd. for C<sub>14</sub>H<sub>9</sub>IN<sub>2</sub>O<sub>2</sub>: C, 46.18; H, 2.49. Found: C, 46.07; H, 2.47.



**2-(2,5-Dimethyl-1***H***-pyrrol-1-yl)-5-iodopyrimidine (1q)** An oven-dried 50 mL roundbottom flask equipped with a magnetic stir bar was charged with 2-amino-5-iodopyridine (2.20 g, 10.0 mmol), *p*-toluenesulfonic acid (*p*-TsOH, 15.6 mg) and 10 mL toluene. 2,5-Hexanedione (1.3 mL, 10.5 mmol) was added dropwise to the flask via syringe at room temperature. The reaction vessel was equipped with a Dean-Stark apparatus, and it was heated to 125 °C for 12 h. After cooling to room temperature, the mixture was diluted with EtOAc (150 mL), and washed with brine (20 mL  $\times$  2). The organic layer was

separated, dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was purified by flash column chromatography (eluting with 0-15 % EtOAc in hexanes) to afford **1q** (1.67 g, 56 %) as a light yellow solid, mp = 99-100 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.90 (s, 2 H), 5.91 (s, 2 H), 2.36 (s, 6 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 163.5, 156.8, 130.1, 109.4, 88.1, 15.0 ppm. IR (neat, cm<sup>-1</sup>): 2921, 1528, 1422, 1389, 1233, 1116, 1003, 977, 797, 767. HRMS (ESI) *m/z* [M + H]<sup>+</sup> calcd. for C<sub>10</sub>H<sub>11</sub>IN<sub>3</sub>: 299.9992, found: 299.9989.

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**2-Butoxy-6-iodopyrazine** (1r) An oven-dried 100 mL round-bottom flask equipped with a magnetic stir bar was charged with NaH (95 %, 182 mg, 7.2 mmol). The flask was evacuated and backfilled with argon. Anhydrous THF (30 mL) was added and the suspension was cooled to 0 °C. nBuOH (660 µL, 7.2 mmol) was added via syringe and the mixture was stirred at room temperature for 20 min. Then, the mixture was again cooled to 0 °C. A solution of 2,6-diiodopyrazine (1.99 g, 6.0 mmol) in anhydrous THF (10 mL) was added dropwise into this mixture. After addition, the mixture was stirred at room temperature for 14 h. When the reaction was complete, water (2 mL) was added dropwise at 0 °C. The mixture was concentrated in vacuo. The residue was diluted with EtOAc (100 mL) and H<sub>2</sub>O (15 mL). The water layer was extracted with EtOAc (20 mL  $\times$ 2). The combined organic layers were washed with saturated NH<sub>4</sub>Cl (aq.) solution (20  $mL \times 2$ ) and brine (20 mL  $\times 2$ ). The organic layer was separated, dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was purified by flash column chromatography (eluting with 0-5 % EtOAc in hexanes) to afford 1r (1.43 g, 86 %) as a colorless oil.  $^{1}$ H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.35 (s, 1 H), 8.09 (s, 1 H), 4.29 (t, J = 6.6 Hz, 2 H), 1.80-1.67 (m, 2 H), 1.53-1.39 (m, 2 H), 0.96 (t, J = 7.2 Hz, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 159.8, 143.9, 133.7, 112.8, 67.3, 30.8, 19.2, 13.9 ppm. IR (neat, cm<sup>-1</sup>): 2956, 2871, 1553, 1507, 1421, 1401, 1357, 1295, 1162, 1125, 992, 901, 857. HRMS (ESI) m/z  $[M + H]^+$  calcd. for C<sub>8</sub>H<sub>12</sub>IN<sub>2</sub>O: 278.9989, found: 278.9987.



2-(tert-Butyl)-6-iodoimidazo[1,2-a]pyridine (1u) An oven-dried 50 mL round-bottom flask equipped with a magnetic stir bar was charged with 1-bromo-3,3-dimethylbutan-2one (2.33 g, 13.0 mmol) and 13 mL EtOH. 2-Amino-5-iodopyridine (2.20 g, 10.0 mmol) and NaHCO<sub>3</sub> (4.20 g, 50.0 mmol) were subsequently added into the solution at room temperature. Then, the mixture was heated at 80 °C for 14 h. After the reaction was complete, the mixture was cooled to room temperature, filtered, and the solids were washed with EtOH (20 mL  $\times$  2). The filtrate was concentrated in vacuo. The residue was diluted with EtOAc (150 mL), washed with saturated NaHCO<sub>3</sub> (aq.) solution (10 mL  $\times$  2) and brine (10 mL  $\times$  2). The separated organic layer was dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The crude product was purified by flash column chromatography (eluting with 0-30 % EtOAc in hexanes) to afford 1u (2.70 g, 90 %) as a white solid, mp = 157-158 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.28 (dd, J = 1.8, 0.9 Hz, 1 H), 7.35 (ddd, J = 9.6, 0.9, 0.9 Hz, 1 H), 7.28-7.22 (m, 2 H), 1.37 (s, 9 H) ppm. <sup>13</sup>C NMR (75 MHz,  $CDCl_3$ )  $\delta$ : 157.9, 143.6, 131.8, 130.4, 118.3, 106.8, 74.2, 32.4, 30.3 ppm. IR (neat, cm<sup>-1</sup>): 2955, 1492, 1412, 1333, 1264, 1200, 1050, 789, 734, 684. Anal. Calcd. for C<sub>11</sub>H<sub>13</sub>IN<sub>2</sub>: C, 44.02; H, 4.37. Found: C, 44.06; H, 4.24.



**3-Iodo-1-(3-methyl-4-nitrophenyl)-1***H***-pyrazole** (**1x**) An oven-dried 100 mL roundbottom flask equipped with a magnetic stir bar was charged with 3-iodo-1*H*-pyrazole (970 mg, 5.0 mmol), 4-fluoro-2-methyl-1-nitrobenzene (814 mg, 5.3 mmol), anhydrous K<sub>2</sub>CO<sub>3</sub> (1.04 g, 7.5 mmol) and 10 mL anhydrous DMF. The mixture was stirred at 100 °C for 14 h. After the reaction was complete, the mixture was cooled down to room temperature, and was diluted with 150 mL EtOAc and 30 mL water. The H<sub>2</sub>O was separated and extracted with EtOAc (20 mL × 3). The combined organic layers were washed with brine (20 mL × 2), dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The crude

mixture was purified by flash column chromatography (eluting with 0-5 % EtOAc in Hexanes) to afford **1x** (1.38 g, 84 %) as a light yellow solid, mp = 117-118 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.13 (d, *J* = 8.7, 1 H), 7.82 (d, *J* = 2.7 Hz, 1 H), 7.72 (d, *J* = 2.4 Hz, 1 H), 7.59 (dd, *J* = 8.7, 2.7 Hz, 1 H), 6.68 (d, *J* = 2.4 Hz, 1 H), 2.69 (s, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 146.7, 141.9, 136.5, 128.9, 126.9, 122.1, 118.1, 116.1, 99.5, 21.3 ppm. IR (neat, cm<sup>-1</sup>): 1610, 1584, 1500, 1328, 1304, 1202, 1040, 940, 872, 745. Anal. Calcd. for C<sub>10</sub>H<sub>8</sub>IN<sub>3</sub>O<sub>2</sub>: C, 36.50; H, 2.45. Found: C, 36.64; H, 2.44.

### General Setup for Table 1 and 2



**Figure S-2** 

a: T-mixer; b: in line check valve; c: stainless-steel-tube reactor (1.6 mL volume); d: back-pressure regulator (100 psi  $\times$  2)

## **General Procedure for Table 1 and 2**

All reagents were added to oven-dried, screw-top, volumetric flasks that were fitted with Teflon screw-caps. The vessels were then evacuated and backfilled with argon.

A 10.0 mL volumetric flask was charged with  $CF_3CO_2K$  (1.22 g, 8.0 mmol, 0.8 M) and CuI (1.52 g, 8.0 mmol, 0.8 M). Anhydrous 1-methyl-2-pyrrolidinone (NMP) and pyridine (775  $\mu$ L, 9.6 mmol) were added to make the solution volume 10.0 mL. Two 2.0 mL volumetric flask was charged with Ar-I (1.2 mmol for each vessel, 0.6 M). Anhydrous NMP was added to make the solution volume of each vessel to 2.0 mL. The volumetric flasks were sonicated to accelerate the dissolution of solids. Following the setup as shown

in **Figure S-2**, the first solution was loaded into an 8.0 mL stainless steel syringe (A), and fitted to a syringe pump. Both solutions of the Ar-I (4.0 mL total) were loaded into the second 8.0 mL stainless steel syringe (B), and fitted to a second syringe pump. EtOAc was loaded into two 8.0 mL stainless steel syringes (C1 and C2), and fitted to a third syringe pump. Before the reaction was started, all reactors and the connecting tubing were filled with anhydrous NMP or DMA. The flow rate for the solution from syringe A was 60  $\mu$ L/min, the flow rate for the solution from syringe B was 40  $\mu$ L/min, the flow rate for the solution proceeded at the temperature as indicated for each example. After reaching steady state in 15 to 25 min as monitored by GC, a sample was collected a graduated cylinder for 42 min (8.4 mL, 1.0 mmol). The collected mixture was purified following general workup procedures A or B.

*General Workup Procedure A:* The collected mixture was diluted with Et<sub>2</sub>O (150 mL), and was washed with a premixed solution of ammonium hydroxide solution and brine (v/v = 1/1, 20 mL) twice. The water layer was separated and extracted with Et<sub>2</sub>O (10 mL × 2). The combined organic layers were then rinsed with brine (10 mL × 2), dried with MgSO<sub>4</sub>, and concentrated in vacuo. The crude mixture was purified using a Biotage SP4 instrument to give the corresponding compound.

*General Workup Procedure B:* The collected mixture was diluted with EtOAc (150 mL), and was washed with a premixed solution of ammonium hydroxide solution and brine (v/v = 1/1, 20 mL) twice. The water layer was separated and extracted with EtOAc (10 mL × 2). The combined organic layers were then rinsed with brine (10 mL × 2), dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The crude mixture was purified using a Biotage SP4 instrument to give the corresponding compound.



**4-(Trifluoromethyl)-1,1'-biphenyl** (**2a**)<sup>[3]</sup> Following the general procedure for Table 1 and general workup procedure A, a solution of 4-iodo-1,1'-biphenyl (672 mg, 2.4 mmol, 0.6 M) in NMP was loaded in syringe B. The reactor was heated at 200-

205 °C. The crude mixture was purified by flash column chromatography (eluting with hexanes) to give the title compound as a white solid (193 mg, 87 %), mp = 69-70 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.72-7.71 (m, 4 H), 7.64-7.60 (m, 2 H), 7.52-7.47 (m, 2 H), 7.45-7.42 (m, 1 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 144.9, 139.9, 129.5 (q, *J* = 32.3 Hz), 129.1, 128.3, 127.6, 127.4, 125.8 (q, *J* = 3.8 Hz), 124.5 (q, *J* = 270.2 Hz) ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.3 ppm. IR (neat, cm<sup>-1</sup>): 1328, 1161, 1112, 1073, 1006, 843, 767, 729, 691.



**Hexyl 4-(trifluoromethyl)benzoate**  $(2b)^{[3]}$  Following the general procedure for Table 1 and general workup procedure A, a solution of hexyl 4-iodobenzoate (796 mg, 2.4 mmol, 0.6 M) in NMP was loaded in syringe B. The reactor was

heated at 200-205 °C. The crude mixture was purified by flash column chromatography (eluting with 0-5 % EtOAc in hexanes) to give the title compound as a colorless oil (263 mg, 96 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.13 (d, *J* = 8.7 Hz, 2 H), 7.67 (d, *J* = 9.0 Hz, 2 H), 4.33 (t, *J* = 6.6 Hz, 2 H), 1.81-1.71 (m, 2 H), 1.46-1.37 (m, 2 H), 1.35-1.29 (m, 4 H), 0.88 (t, *J* = 6.9 Hz, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 165.4, 134.4 (q, *J* = 32.4 Hz), 133.8 (q, *J* = 1.3 Hz), 130.0, 125.4 (q, *J* = 3.8 Hz), 123.8 (q, *J* = 270.9 Hz), 65.8, 31.6, 28.7, 25.8, 22.6, 14.0 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -65.0 ppm. IR (neat, cm<sup>-1</sup>): 1722, 1411, 1323, 1271, 1166, 1128, 1098, 1065, 1017, 861, 775.



**2-Methyl-4-nitro-1-(trifluoromethyl)benzene**  $(2c)^{[6]}$  Following the general procedure for Table 1 and general workup procedure A, a solution of 1-iodo-2-methyl-4-nitrobenzene (632 mg, 2.4 mmol, 0.6 M) in NMP was loaded in syringe B. The reactor was heated at

200-205 °C. The crude mixture was purified by flash column chromatography (eluting with 0-6 %  $CH_2Cl_2$  in hexanes) to give the title compound as a colorless oil (168 mg, 82

%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.15-8.09 (m, 2 H), 7.79 (d, J = 8.7 Hz, 1 H), 2.60 (s, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 149.7, 139.4 (q, J = 1.6 Hz), 134.5 (q, J = 30.7 Hz), 127.3 (q, J = 5.6 Hz), 126.6, 123.5 (q, J = 272.6 Hz), 120.9, 19.5 (q, J = 2.3 Hz) ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.3 ppm. IR (neat, cm<sup>-1</sup>): 1532, 1353, 1310, 1270, 1174, 1120, 1044, 806, 754.

## Morpholino(3-(trifluoromethyl)phenyl)methanone (2d)

Following the general procedure for Table 1 and general workup procedure A, a solution of (3-iodophenyl)(morpholino)methanone (760 mg, 2.4 mmol, 0.6

M) in NMP was loaded in syringe B. The reactor was heated at 200-205 °C. The crude mixture was purified by flash column chromatography (eluting with 0-40 % EtOAc in hexanes) to give the title compound as a white solid (216 mg, 83 %), mp = 68-69 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.75-7.62 (m, 2 H), 7.62-7.48 (m, 2 H), 4.09-3.24 (m, 8 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 168.8, 136.1, 131.1 (q, *J* = 32.6 Hz), 130.4 (q, *J* = 1.3 Hz), 129.2, 126.6 (q, *J* = 3.7 Hz), 124.1 (q, *J* = 3.8 Hz), 123.6 (q, *J* = 270.8 Hz), 66.8, 48.2, 42.8 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.7 ppm. IR (neat, cm<sup>-1</sup>): 1634, 1423, 1328, 1272, 1250, 1111, 1093, 1071, 1023, 912, 814. Anal. Calcd. for C<sub>12</sub>H<sub>12</sub>F<sub>3</sub>NO<sub>2</sub>: C, 55.60; H, 4.67. Found: C, 55.89; H, 4.67.



Ο

 $CF_3$ 

*N*,*N*-Diethyl-4-(trifluoromethyl)benzenesulfonamide (2e) Following the general procedure for Table 1 and general workup procedure A, a solution of *N*,*N*-diethyl-4iodobenzenesulfonamide (814 mg, 2.4 mmol, 0.6 M) in NMP

was loaded in syringe B. The reactor was heated at 200-205 °C. The crude mixture was purified by flash column chromatography (eluting with 0-3 % EtOAc in hexanes) to give the title compound as a colorless oil (261 mg, 93 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.91 (d, J = 8.4 Hz, 2 H), 7.73 (d, J = 8.1 Hz, 2 H), 3.23 (q, J = 7.2 Hz, 4 H), 1.10 (t, J = 7.2 Hz, 6 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 144.1, 134.0 (q, J = 33.7 Hz), 127.5, 126.2 (q, J = 3.8 Hz), 123.4 (q, J = 271.1 Hz), 42.2, 14.2 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -

65.0 ppm. IR (neat, cm<sup>-1</sup>): 1320, 1157, 1128, 1107, 1061, 1013, 935, 843, 717, 681. Anal. Calcd. for C<sub>11</sub>H<sub>14</sub>F<sub>3</sub>NO<sub>2</sub>S: C, 46.97; H, 5.02. Found: C, 47.22; H, 5.13.



°C. The crude mixture was purified by flash column chromatography (eluting with pentane) to give the title compound as a colorless oil (172 mg, 80 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.55 (s, 1 H), 7.51 (s, 2 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 136.0, 133.5 (q, J = 33.5 Hz), 132.2, 124.2 (q, J = 3.7 Hz), 122.7 (q, J = 271.5 Hz) ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -63.9 ppm. IR (neat, cm<sup>-1</sup>): 1574, 1434, 1306, 1176, 1133, 1096, 869, 805, 733, 690.



**1-Heptyl-4-(trifluoromethyl)benzene** (**2f**)<sup>[5]</sup> Following the general procedure for Table 1 and general workup procedure A, a solution of 1-heptyl-4-iodobenzene (724 mg, 2.4 mmol, 0.6 M) in NMP was loaded in syringe B. The reactor was heated at 205-210 °C. The crude mixture was purified by flash

column chromatography (eluting with hexanes) to give the title compound as a colorless oil (217 mg, 89 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.54 (d, *J* = 8.1 Hz, 2 H), 7.29 (d, *J* = 7.8 Hz, 2 H), 2.67 (t, *J* = 7.5 Hz, 2 H), 1.67-1.59 (m, 2 H), 1.34-1.29 (m, 8 H), 0.90 (t, *J* = 6.9 Hz, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 147.2, 128.8, 128.2 (q, *J* = 32.0 Hz), 125.3 (q, *J* = 3.8 Hz), 124.7 (q, *J* = 269.9 Hz), 36.0, 32.0, 31.4, 29.4, 29.3, 22.9, 14.2 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.2 ppm. IR (neat, cm<sup>-1</sup>): 2927, 2857, 1322, 1161, 1117, 1066, 1018, 841, 817.



**1-(3-(Trifluoromethyl)phenyl)piperidine** (**2g**)<sup>[3]</sup> Following the general procedure for Table 1 and general workup procedure A, a solution of 1-(3-iodophenyl)piperidine (689 mg, 2.4 mmol, 0.6 M) in NMP was loaded in syringe B. The reactor was heated at

205-210 °C. The crude mixture was purified by flash column chromatography (eluting with 0-2 % EtOAc in hexanes) to give the title compound as a colorless oil (185 mg, 81 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.35 (t, *J* = 8.1 Hz, 1 H), 7.17 (s, 1 H), 7.11-7.06 (m, 2 H), 3.23 (t, *J* = 5.4 Hz, 4 H), 1.78-1.70 (m, 4 H), 1.67-1.60 (m, 2 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 152.3, 131.4 (q, *J* = 31.3 Hz), 129.5, 124.6 (q, *J* = 270.8 Hz), 119.3, 115.2 (q, *J* = 3.9 Hz), 112.5 (q, *J* = 4.0 Hz), 50.2, 25.8, 24.3 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.6 ppm. IR (neat, cm<sup>-1</sup>): 2936, 1608, 1494, 1448, 1306, 1160, 1115, 1074, 939, 782, 694.



**1,2,3-Trimethoxy-5-(trifluoromethyl)benzene** (**2h**) Following the general procedure for Table 1 and general workup procedure A, a solution of 5-iodo-1,2,3-trimethoxybenzene (706 mg, 2.4 mmol, 0.6 M) in NMP was loaded in syringe B. The reactor was

heated at 200-205 °C. The crude mixture was purified by flash column chromatography (eluting with 0-4 % EtOAc in hexanes) to give the title compound as a white solid (203 mg, 86 %), mp = 68-69 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 6.82 (s, 2 H), 3.89 (s, 6 H), 3.88 (s, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 153.5, 140.6, 125.8 (q, *J* = 32.6 Hz), 124.1 (q, *J* = 270.3 Hz), 102.5 (q, *J* = 3.8 Hz), 60.9, 56.3 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.0 ppm. IR (neat, cm<sup>-1</sup>): 1596, 1465, 1418, 1357, 1229, 1164, 1113, 991, 908, 893, 842, 730. Anal. Calcd. for C<sub>10</sub>H<sub>11</sub>F<sub>3</sub>O<sub>3</sub>: C, 50.85; H, 4.69. Found: C, 51.14; H, 4.78.



**1-(4-(Trifluoromethyl)phenyl)-1***H***-pyrrole** (**2i**)<sup>[3]</sup> Following the general procedure for Table 1 and general workup procedure B, a solution of 1-(4-iodophenyl)-1*H*-pyrrole (646 mg, 2.4 mmol, 0.6 M) in NMP was loaded in syringe B. The reactor was

heated at 205-210 °C. The crude mixture was purified by flash column chromatography (eluting with 0-1 % EtOAc in hexanes) to give the title compound as a white solid (191 mg, 90 %), mp = 112-113 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.71 (d, *J* = 9.0 Hz, 2 H), 7.50 (d, *J* = 8.1 Hz, 2 H), 7.16 (t, *J* = 2.1 Hz, 2 H), 6.43 (t, *J* = 2.1 Hz, 2 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 143.3, 127.5 (q, *J* = 32.9 Hz), 127.0 (q, *J* = 3.8 Hz), 124.1 (q,

J = 269.9 Hz), 120.0, 119.2, 111.6 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.1 ppm. IR (neat, cm<sup>-1</sup>): 1619, 1529, 1475, 1320, 1113, 1073, 1012, 920, 833, 722.

**1-(Trifluoromethyl)naphthalene** (**2j**)<sup>[3]</sup> Following the general procedure for Table 1 and general workup procedure A, a solution of 1iodonaphthalene (610 mg, 2.4 mmol, 0.6 M) in NMP was loaded in syringe B. The reactor was heated at 200-205 °C. The crude mixture was

purified by flash column chromatography (eluting with hexanes) to give the title compound as a colorless oil (171 mg, 87 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.27 (d, J = 8.4 Hz, 1 H), 8.03 (d, J = 8.4 Hz, 1 H), 7.92 (t, J = 7.8 Hz, 2 H), 7.69-7.57 (m, 2 H), 7.51 (t, J = 7.8 Hz, 1 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 134.0, 132.9 (q, J = 1.1 Hz), 129.1, 128.9, 127.8, 126.7, 126.2 (q, J = 29.9 Hz), 124.9 (q, J = 271.7 Hz), 124.8 (q, J = 5.9 Hz), 124.4 (q, J = 2.4 Hz), 124.3 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -61.7 ppm. IR (neat, cm<sup>-1</sup>): 1514, 1354, 1313, 1261, 1201, 1109, 1067, 975, 801, 771.



 $CF_3$ 

**9-(Trifluoromethyl)phenanthrene** (**2k**) Following the general procedure for Table 1 and general workup procedure B, syringe B was loaded with a solution of 9-iodophenanthrene (730 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 205-210 °C. The

crude mixture was purified by flash column chromatography (eluting with hexanes) to give the title compound as a white solid (224 mg, 91 %), mp = 53-54 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.71-8.65 (m, 1 H), 8.60 (d, J = 8.4 Hz, 1 H), 8.35-8.28 (m, 1 H), 8.17 (s, 1 H), 7.89 (dd, J = 7.5, 1.2 Hz, 1 H), 7.76-7.68 (m, 3 H), 7.62 (dd, J = 7.5, 7.5 Hz, 1 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 131.9, 131.1, 130.0, 129.5, 129.1, 127.6, 127.5, 127.4, 127.1 (q, J = 6.3 Hz), 126.9 (q, J = 0.8 Hz), 125.3 (q, J = 2.7 Hz), 124.8 (q, J = 271.4 Hz), 124.7 (q, J = 29.6 Hz), 123.3, 122.8 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : - 62.2 ppm. IR (neat, cm<sup>-1</sup>): 1450, 1325, 1263, 1143, 1109, 949, 905, 764, 745, 722. Anal. Calcd. for C<sub>15</sub>H<sub>9</sub>F<sub>3</sub>: C, 73.17; H, 3.68. Found: C, 73.03; H, 3.65.



(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl-2-(trifluoromethyl)isonicotinate (2m) Following the general procedure for Table 2 and general workup procedure B, syringe B was loaded with a solution of (1R,2S,5R)-2-isopropyl-5methylcyclohexyl 2-iodoisonicotinate (928 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 200-205 °C. The crude

mixture was purified by flash column chromatography (eluting with 0-3 % EtOAc in Hexanes) to give the title compound as a colorless oil (248 mg, 75 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.84 (d, *J* = 4.8 Hz, 1 H), 8.17 (s, 1 H), 8.02 (d, *J* = 4.8 Hz, 1 H), 4.96 (td, *J* = 10.8, 4.5 Hz, 1 H), 2.11-2.02 (m, 1 H), 1.91-1.78 (m, 1 H), 1.76-1.64 (m, 2 H), 1.62-1.43 (m, 2 H), 1.17-1.01 (m, 2 H), 0.99-0.82 (m, 7 H), 0.75 (d, *J* = 6.9 Hz, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 163.4, 151.0, 149.3 (q, *J* = 35.0 Hz), 139.9, 125.8, 121.3 (q, *J* = 272.6 Hz), 119.9, 76.8, 47.1, 40.8, 34.2, 31.5, 26.6, 23.6, 22.0, 20.7, 16.4 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -70.0 ppm. IR (neat, cm<sup>-1</sup>): 2957, 2930, 1725, 1325, 1252, 1238, 1179, 1143, 1081, 955, 763, 696. Anal. Calcd. for C<sub>17</sub>H<sub>22</sub>F<sub>3</sub>NO<sub>2</sub>: C, 61.99; H, 6.73. Found: C, 62.25; H, 6.73.



**2-(2,5-Dimethyl-1***H***-pyrrol-1-yl)-5-(trifluoromethyl)pyridine** (**2n**) Following the general procedure for Table 2 and general workup procedure B, syringe B was loaded with a solution of 2-(2,5-dimethyl-1*H*-pyrrol-1-yl)-5-iodopyridine (716 mg, 2.4

mmol, 0.6 M) in NMP. The reactor was heated at 200-205 °C. The crude mixture was purified by flash column chromatography (eluting with 0-5 % EtOAc in hexanes) to give the title compound as a white solid (198 mg, 82 %), mp = 71-72 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.88 (d, J = 2.7 Hz, 1 H), 8.07 (dd, J = 8.4, 2.7 Hz, 1 H), 7.35 (d, J = 8.4 Hz, 1 H), 5.95 (s, 2 H), 2.19 (s, 6 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 154.9, 146.5 (q, J = 4.1 Hz), 135.3 (q, J = 3.4 Hz), 128.9, 124.9 (q, J = 33.2 Hz), 123.5 (q, J = 270.6 Hz), 121.3, 108.3, 13.5 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.0 ppm. IR (neat, cm<sup>-1</sup>): 1600, 1491, 1405, 1325, 1165, 1129, 1082, 1014, 764. Anal. Calcd. for C<sub>12</sub>H<sub>11</sub>F<sub>3</sub>N<sub>2</sub>: C, 60.00; H, 4.62. Found: C, 59.72; H, 4.63.



**4-(4-(Trifluoromethyl)pyridin-2-yl)morpholine** (**2o**) Following the general procedure for Table 2 and general workup procedure B, syringe B was loaded with a solution of 4-(4-iodopyridin-2-yl)morpholine (696 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 200-205 °C. The crude mixture was purified by flash

column chromatography (eluting with 0-5 % EtOAc in hexanes) to give the title compound as a white solid (212 mg, 91 %), mp = 36-37 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.28 (dd, *J* = 4.2, 3.6 Hz, 1 H), 6.81-6.73 (m, 2 H), 3.81-3.75 (m, 4 H), 3.56-3.49 (m, 4 H) ppm.<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 159.6, 149.3, 139.8 (q, *J* = 32.9 Hz), 123.2 (q, *J* = 271.4 Hz), 108.7 (q, *J* = 3.4 Hz), 102.3 (q, *J* = 4.1 Hz), 66.6, 45.3 ppm.<sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -67.1 ppm. IR (neat, cm<sup>-1</sup>): 2854, 1609, 1483, 1435, 1319, 1297, 1243, 1168, 1119, 1090, 982, 956. Anal. Calcd. for C<sub>10</sub>H<sub>11</sub>F<sub>3</sub>N<sub>2</sub>O: C, 51.73; H, 4.77. Found: C, 51.45; H, 4.63.



**1-(2-Nitrophenyl)-5-(trifluoromethyl)-1***H***-indole** (2**p**) Following the general procedure for Table 2 and general workup procedure B, syringe B was loaded with a solution of 5-iodo-1-(2-nitrophenyl)-1*H*-indole (874 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 205-210 °C. The

crude mixture was purified by flash column chromatography (eluting with 0-15 % EtOAc in hexanes) to give the title compound as a light yellow solid (258 mg, 84 %), mp = 122-123 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.08 (dd, J = 8.1, 1.5 Hz, 1 H), 8.00 (s, 1 H), 7.77 (ddd, J = 7.5, 7.5, 1.5 Hz, 1 H), 7.63 (ddd, J = 7.5, 7.5, 1.5 Hz, 1 H), 7.57 (dd, J = 7.8, 1.5 Hz, 1 H), 7.44 (d, J = 8.7 Hz, 1 H), 7.28 (d, J = 3.3 Hz, 1 H), 7.19 (d, J = 8.4 Hz, 1 H), 6.82 (d, J = 3.3 Hz, 1 H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 146.3, 138.2, 134.1, 132.1, 130.0, 129.9, 129.3, 128.4, 125.8, 125.2 (q, J = 270.1 Hz), 123.4 (q, J = 31.7 Hz), 119.8 (q, J = 3.5 Hz), 119.1 (q, J = 4.2 Hz), 109.9, 105.6 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -62.4 ppm. IR (neat, cm<sup>-1</sup>): 1606, 1527, 1497, 1338, 1317, 1234, 1191, 1108, 1053, 850, 714. HRMS (ESI) m/z [M + H]<sup>+</sup> calcd. for C<sub>15</sub>H<sub>10</sub>F<sub>3</sub>N<sub>2</sub>O<sub>2</sub>: 307.0689, found: 307.0691.

### 2-(2,5-Dimethyl-1*H*-pyrrol-1-yl)-5-(trifluoromethyl)



**pyrimidine** (**2q**) Following the general procedure for Table 2 and general workup procedure B, syringe B was loaded with a solution of 2-(2,5-dimethyl-1*H*-pyrrol-1-yl)-5-iodopyrimidine (718 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at

200-205 °C. The crude mixture was purified by flash column chromatography (eluting with 0-3 % EtOAc in hexanes) to give the title compound as a light yellow oil (153 mg, 63 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.97 (s, 2 H), 5.96 (s, 2 H), 2.44 (s, 6 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 160.1, 155.6 (q, *J* = 3.6 Hz), 130.9, 123.1 (q, *J* = 270.1 Hz), 120.8 (q, *J* = 34.4 Hz), 110.5, 15.7 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -63.8 ppm. IR (neat, cm<sup>-1</sup>): 1604, 1555, 1459, 1396, 1321, 1231, 1131, 1101, 1018, 979. HRMS (ESI) *m/z* [M + H]<sup>+</sup> calcd. for C<sub>11</sub>H<sub>11</sub>F<sub>3</sub>N<sub>3</sub>: 242.0900, found: 242.0901.

**2-Butoxy-6-(trifluoromethyl)pyrazine** (**2r**) Following the general procedure for Table 2 and general workup procedure A, syringe B was loaded with a solution of 2-butoxy-6-iodopyrazine (668 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 200-205 °C. The crude mixture was purified by flash column chromatography (eluting with 0-3 % EtOAc in hexanes) to give the title compound as a colorless oil (141 mg, 64 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.43 (s, 1 H), 8.37 (s, 1 H), 4.37 (t, *J* = 6.6 Hz, 2 H), 1.82-1.72 (m, 2 H), 1.53-1.41 (m, 2 H), 0.96 (t, *J* = 7.5 Hz, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 159.9, 140.0 (q, *J* = 34.9 Hz), 139.9 (q, *J* = 1.4 Hz), 132.6 (q, *J* = 3.8 Hz), 121.2 (q, *J* = 272.3 Hz), 67.2, 30.7, 19.2, 13.8 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -70.1 ppm. IR (neat, cm<sup>-1</sup>): 2962, 1546, 1453, 1430, 1344, 1294, 1224, 1143, 1115, 1003, 882. Anal. Calcd. for C<sub>9</sub>H<sub>11</sub>F<sub>3</sub>N<sub>2</sub>O: C, 49.09; H, 5.04. Found: C, 49.80; H, 5.28.



**6-Methyl-2-(trifluoromethyl)quinoline** (**2s**)<sup>[7]</sup> Following the general procedure for Table 2 and general workup procedure A, syringe B was loaded with a solution of 2-iodo-6-methylquinoline (646 mg, 2.4 mmol, 0.6 M) in NMP. The

reactor was heated at 200-205 °C. The crude mixture was purified by flash column

chromatography (eluting with 0-2 % EtOAc in hexanes) to give the title compound as a white solid (166 mg, 79 %), mp = 90-91 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.22 (d, *J* = 8.4 Hz, 1 H), 8.10 (d, *J* = 9.0 Hz, 1 H), 7.70-7.61 (m, 3 H), 2.56 (s, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 147.0 (q, *J* = 34.8 Hz), 145.8, 138.9, 137.3, 133.2, 129.7, 127.0, 126.5, 121.8 (q, *J* = 273.3 Hz), 116.7 (q, *J* = 2.3 Hz), 21.7 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -69.3 ppm. IR (neat, cm<sup>-1</sup>): 1345, 1336, 1306, 1129, 1109, 1085, 910, 833, 733.



**1-(Trifluoromethyl)isoquinoline**  $(2t)^{[8]}$  Following the general procedure for Table 2 and general workup procedure A, syringe B was loaded with a solution of 1-iodoisoquinoline (612 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 200-205 °C. The crude mixture was purified

via by flash column chromatography (eluting with 0-5 % EtOAc in hexanes) to give the title compound as a colorless oil (129 mg, 66 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.57 (d, J = 5.4 Hz, 1 H), 8.29 (d, J = 7.5 Hz, 1 H), 7.91 (d, J = 7.5 Hz, 1 H), 7.83 (d, J = 5.4 Hz, 1 H), 7.90-7.66 (m, 2 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 146.3 (q, J = 32.9 Hz), 140.7, 137.1, 130.9, 128.8, 127.5, 124.6, 124.5 (q, J = 0.8 Hz), 124.4 (q, J = 3.1 Hz), 122.3 (q, J = 274.7 Hz) ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.9 ppm. IR (neat, cm<sup>-1</sup>): 1300, 1255, 1232, 1191, 1167, 1115, 986, 872, 747, 687, 657.

## 2-(tert-Butyl)-6-(trifluoromethyl)imidazo[1,2-a]pyridine

F<sub>3</sub>C

(2u) Following the general procedure for Table 2 and general workup procedure B, syringe B was loaded with a solution of

2-(*tert*-butyl)-6-iodoimidazo[1,2-*a*]pyridine (720 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 200-205 °C. The crude mixture was purified via by flash column chromatography (eluting with 0-10 % EtOAc in hexanes) to give the title compound as a white solid (158 mg, 65 %), mp = 81-82 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.38 (s, 1 H), 7.61 (d, *J* = 9.6 Hz, 1 H), 7.41 (s, 1 H), 7.21 (dd, *J* = 9.3, 1.8 Hz, 1 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 159.4, 144.8, 124.5 (q, *J* = 5.5 Hz), 123.8 (q, *J* = 269.0 Hz), 119.8 (q, *J* = 2.7 Hz), 117.8, 116.2 (q, *J* = 33.9 Hz), 108.2, 32.5, 30.1 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -63.8 ppm. IR (neat, cm<sup>-1</sup>): 2962, 1648, 1381, 1333, 1304, 1164, 1121, 1053, 805, 672. Anal. Calcd. for C<sub>12</sub>H<sub>13</sub>F<sub>3</sub>N<sub>2</sub>: C, 59.50; H, 5.41. Found: C, 59.46; H, 5.46.



**1-Benzyl-3-(trifluoromethyl)-1***H*-pyrrolo[2,3-*b*]pyridine (2v) Following the general procedure for Table 2 and general workup procedure B, syringe B was loaded with a solution of 1-benzyl-3iodo-1*H*-pyrrolo[2,3-*b*]pyridine (802 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 205-210 °C. The crude mixture

was purified via by flash column chromatography (eluting with 0-5 % EtOAc in hexanes) to give the title compound as a white solid (228 mg, 83 %), mp = 53-54 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.48 (d, *J* = 4.5 Hz, 1 H), 8.08 (d, *J* = 8.1 Hz, 1 H), 7.54 (s, 1 H), 7.39-7.31 (m, 3 H), 7.31-7.25 (m, 2 H), 7.22 (dd, *J* = 8.1, 4.8 Hz, 1 H), 5.52 (s, 2 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 147.4, 144.8, 136.6, 129.0, 128.2, 128.1, 127.9, 127.5 (q, *J* = 5.1 Hz), 123.9 (q, *J* = 264.7 Hz), 117.6, 116.6, 105.0 (q, *J* = 37.6 Hz), 48.3 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -59.0 ppm. IR (neat, cm<sup>-1</sup>): 1603, 1550, 1455, 1266, 1174, 1133, 1093, 953, 774, 696. Anal. Calcd. for C<sub>15</sub>H<sub>11</sub>F<sub>3</sub>N<sub>2</sub>: C, 65.21; H, 4.01. Found: C, 60.03; H, 4.03.



**1-Benzyl-4-(trifluoromethyl)-1***H***-pyrazole (2w)** Following the general procedure for Table 2 and general workup procedure B, syringe B was loaded with a solution of 1-benzyl-4-iodo-1*H*-pyrazole (682 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 200-205 °C. The crude mixture was purified by flash column chromatography (eluting with 0-5 % EtOAc in hexanes) to give the title compound as a colorless oil (173

mg, 77 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.75 (s, 1 H), 7.64 (s, 1 H), 7.42-7.35 (m, 3 H), 7.30-7.23 (m, 2 H), 5.32 (s, 2 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 144.6, 137.1 (q, J = 2.9 Hz), 135.2, 129.1, 128.6, 128.0, 122.7 (q, J = 264.2 Hz), 114.0 (q, J = 38.0 Hz), 56.5 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -58.2 ppm. IR (neat, cm<sup>-1</sup>): 1574, 1399, 1230, 1192, 1111, 993, 967, 739, 710. HRMS (ESI) m/z [M + H]<sup>+</sup> calcd. for C<sub>11</sub>H<sub>10</sub>F<sub>3</sub>N<sub>2</sub>: 227.0791, found: 227.0792.



**1-(3-Methyl-4-nitrophenyl)-3-(trifluoromethyl)-1***H***-pyrazole** (**2x**) Following the general procedure for Table 2 and general workup procedure B, syringe B was loaded with a solution of 3-iodo-1-(3-methyl-4-nitrophenyl)-1*H*-pyrazole (790 mg, 2.4 mmol, 0.6 M) in NMP. The reactor was heated at 205-210 °C. The crude mixture was purified by flash column

chromatography (eluting with 0-5 % EtOAc in hexanes) to give the title compound as a light yellow solid (175 mg, 65 %), mp = 86-87 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.12 (d, *J* = 8.7 Hz, 1 H), 8.06 (d, *J* = 2.7 Hz, 1 H), 7.76 (d, *J* = 2.4 Hz, 1 H), 7.67 (dd, *J* = 8.7, 2.7 Hz, 1 H), 6.78 (d, *J* = 2.4 Hz, 1 H), 2.68 (s, 3 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 147.4, 145.3 (q, *J* = 38.6 Hz), 142.0, 136.4, 128.8, 126.8, 123.0, 120.9 (q, *J* = 267.5 Hz), 117.2, 107.2 (q, *J* = 2.0 Hz), 21.1 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -64.3 ppm. IR (neat, cm<sup>-1</sup>): 1589, 1519, 1337, 1282, 1118, 1057, 977, 964, 875, 767. Anal. Calcd. for C<sub>11</sub>H<sub>8</sub>F<sub>3</sub>N<sub>3</sub>O<sub>2</sub>: C, 48.72; H, 2.97. Found: C, 48.79; H, 2.99.

**General Setup for Scheme 2** 



Figure S-3

a: T-mixer; b: in line check valve; c: stainless-steel-tube reactor (3.2 mL volume); d: back-pressure regulator (100 psi  $\times$  2)

#### **Procedure for Scheme 2**



## Ethyl 4-(trifluoromethyl)benzoate (2y)<sup>[9]</sup>

All reagents were added to oven-dried, screw-top, volumetric flasks that were fitted with Teflon screw-caps. The vessels were then evacuated and backfilled with

argon. This process was repeated a total of 3 times.

A 25.0 mL volumetric flask was charged with CF<sub>3</sub>CO<sub>2</sub>K (3.14 g, 20.0 mmol, 0.8 M) and CuI (3.81 g, 20.0 mmol, 0.8 M). Pyridine (1.94 mL, 24.0 mmol) and anhydrous 1-methyl-2-pyrrolidinone (NMP) were added to make the solution volume 25.0 mL. A 10.0 mL volumetric flask was charged with CF<sub>3</sub>CO<sub>2</sub>K (1.22 g, 8.0 mmol, 0.8 M) and CuI (1.52 g, 8.0 mmol, 0.8 M). Pyridine (775 µL, 9.6 mmol) and anhydrous NMP were added to make the solution volume 10.0 mL. The volumetric flasks were sonicated to accelerate the dissolution of solids. Both solutions (total volume = 35 mL) were distributed by loading into four 8.0 mL stainless steel syringes, and fitted to two syringe pumps. The flow rate for each syringe was set to be 30.0  $\mu$ L/min (120  $\mu$ L/min in total). Following the setup as shown in Figure S-3, the solutions were combined through T-mixers and were injected from inlet A. A 25.0 mL volumetric flask was charged with ethyl 4-iodobenzoate (4.14 g, 15.0 mmol, 0.6 M). Anhydrous NMP was added to make the solution volume 25.0 mL. The solution was distributed by loading into three 8.0 mL stainless steel syringes, and fitted to two syringe pumps. The flow rate for each syringe was set to be 26.7 µL/min (80.1 µL/min in total). Following the setup as shown in Figure S-3, the solutions were combined through T-mixers and were injected from inlet B. The combined streams from A and B were introduced into the reactor at 200-205 °C. After reaching steady state (15-25 min as monitored with GC), a sample solution was collected into a graduated cylinder for 208 min (42 mL, 10 mmol). The collected mixture was diluted with Et<sub>2</sub>O (150 mL) and water (100 mL). The water layer was separated and extracted with  $Et_2O$  (30 mL  $\times$  3). The combined organic layer was washed with saturated NH<sub>4</sub>Cl (aq.) solution (20 mL  $\times$ 2), brine (20 mL  $\times$  2), dried with MgSO<sub>4</sub>, and concentrated in vacuo. The crude mixture was purified by flash column chromatography (eluting with 0-5 % EtOAc in hexanes) to give the title compound as a colorless oil (2.02 g, 93 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 8.12 (d, J = 8.4 Hz, 2 H), 7.66 (d, J = 8.4 Hz, 2 H), 4.39 (q, J = 7.2 Hz, 2 H), 1.39 (t, J =

7.2 Hz, 3 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 165.4, 134.4 (q, *J* = 32.4 Hz), 133.8, 130.0, 125.4 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 270.8 Hz), 61.6, 14.3 ppm. <sup>19</sup>F NMR (280 MHz, CDCl<sub>3</sub>)  $\delta$ : -63.6 ppm. IR (neat, cm<sup>-1</sup>): 2985, 1720, 1323, 1273, 1125, 1098, 1065, 1017, 862, 774, 703.

R	+		Cul, Pyridine CF <sub>3</sub> CO <sub>2</sub> K 1 min Residence time 200 °C	R U	+ CF3
	Entry	R	k <sub>X</sub> /k <sub>H</sub>	log(k <sub>X</sub> /k <sub>H</sub> )	σ <sup>ref [10]</sup>
	1	4-CO <sub>2</sub> Et	1.95	0.29	0.45
	2	3-CO <sub>2</sub> Et	1.55	0.19	0.37
	3	Н	0.00	0.00	0.00
	4	4- <i>t</i> Bu	0.83	-0.08	-0.20
	5	4-OMe	0.80	-0.10	-0.27

**Table S-2** The Hammett study of competition experiments <sup>[a]</sup>

[a] Average results of three runs were shown. The ratios were determined by <sup>19</sup>F NMR.

## **General Setup for Figure 2**





a: T-mixer; b: in line check valve; c: stainless-steel-tube reactor (240  $\mu$ L volume); d: back-pressure regulator (100 psi × 2)

#### **General Procedure for Figure 2**

All solid reagents were added to oven-dried, screw-top, volumetric flasks that were fitted with Teflon screw-caps. The vessels were then evacuated and backfilled with argon. This process was repeated a total of 3 times.

A 10.0 mL volumetric flask was charged with CF<sub>3</sub>CO<sub>2</sub>K (785 mg, 5.0 mmol, 0.5 M) and CuI (952 mg, 5.0 mmol, 0.5 M). Pyridine (480  $\mu$ L, 6.0 mmol) and anhydrous 1-methyl-2-pyrrolidinone (NMP) were added to make the solution volume 10.0 mL. A 5.0 mL volumetric flask was charged with Ar-I (2.5 mmol, 0.5 M). Anhydrous NMP was added to make the solution volume of each vessel to 5.0 mL. The volumetric flasks were sonicated to accelerate the dissolution of solids. Following the setup as shown in **Figure S-4**, two solutions were loaded into two 8.0 mL stainless steel syringes A and B separately, and fitted to two syringe pumps. The flow rate for syringe A was set to be 40.0  $\mu$ L/min. The flow rate for syringe B was set to be 200.0  $\mu$ L/min. After mixing at a T-mixer, the solution was introduced into the reactor at 200 °C. EtOAc was loaded into two 8.0 mL stainless steel syringes) and mixed with the resulting product stream from the reactor. After reaching steady state (8-15 min), a sample solution was collected into a test tube for 5 min. The mixture was diluted with NH<sub>4</sub>Cl (aq.), brine and EtOAc. The organic layer was filtered through Celite before <sup>19</sup>F NMR analysis.

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