Temperature-controlled sequential Suzuki–Miyaura reactions for preparing unsymmetrical terphenyls

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Materials, Methods and Experimental Procedure

General remarks

All commercially available reagents (from Acros, Aldrich, Fluka) were used without further purification. Potassium aryltrifluoroborates were prepared from corresponding arylboronic acids following the method reported in the literature. ¹ All reactions were carried out in air. NMR spectra were recorded on a Brucker Advance II 400 spectrometer using TMS as internal standard (400 MHz for ¹H NMR). The isolated yield of products were obtained by short chromatography on a silica gel (200-300 mesh) column using petroleum ether (60-90 °C), unless otherwise noted.

General procedure for one-pot double Suzuki-Miyaura reaction.

A mixture of potassium bromophenyltrifluoroborate (0.5 mmol), arylboronic acid (0.5 mmol), K_2CO_3 (1 mmol), $Pd(OAc)_2$ (1 mol%), $EtOH/H_2O$ (5 mL/5 mL) was stirred at 25 °C under air for 0.5 h. And then, aryl bromide (0.5 mmol), K_2CO_3 (1 mmol), $Pd(OAc)_2$ (1 mol%) were added to the reaction mixture and stir for 3.5 h at 80 °C. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 ×

15 mL). The combined organic layers were concentrated in vacuo and the product was isolated by short chromatography.

Table S1 Optimization data for potassium 4-bromophenyltrifluoroborate mediated one-pot double

 SM reactions



0.5 mmol

0.5 mmol

	Step 1			Step 2		Overall
Entry	Base	Solvent	Catalyst	Add base	Add catalyst	isolated yield (%)
1	2.0 eq K ₂ CO ₃	EtOH/H ₂ O	$1 \text{ mol}\% \text{ Pd}(\text{OAc})_2$	none	none	38
2	2.0 eq K ₂ CO ₃	EtOH/H ₂ O	1 mol% Pd(OAc) ₂	1.0 eq K ₂ CO ₃	none	45
3	2.0 eq K ₂ CO ₃	EtOH/H ₂ O	1 mol% Pd(OAc) ₂	2.0 eq K ₂ CO ₃	none	60
4	2.0 eq K ₂ CO ₃	EtOH/H ₂ O	1 mol% Pd(OAc) ₂	4.0 eq K ₂ CO ₃	none	58
5	4.0 eq K ₂ CO ₃	EtOH/H ₂ O	1 mol% Pd(OAc) ₂	2.0 eq K ₂ CO ₃	none	44
6	2.0 eq K ₂ CO ₃	EtOH/H ₂ O	2 mol% Pd(OAc) ₂	2.0 eq K ₂ CO ₃	none	52
7	2.0 eq K ₂ CO ₃	EtOH/H ₂ O	1 mol% Pd(OAc) ₂	2.0 eq K ₂ CO ₃	1 mol% Pd(OAc) ₂	80
8	2.0 eq K ₂ CO ₃	EtOH/H ₂ O	1 mol% Pd(OAc) ₂	2.0 eq K ₂ CO ₃	2 mol% Pd(OAc) ₂	79
9	2.0 eq Na ₂ CO ₃	EtOH/H ₂ O	1 mol% Pd(OAc) ₂	2.0 eq Na ₂ CO ₃	1 mol% Pd(OAc) ₂	72
10	2.0 eq K ₃ PO ₄	EtOH/H ₂ O	1 mol% Pd(OAc) ₂	2.0 eq K ₃ PO ₄	1 mol% Pd(OAc) ₂	59
11	2.0 eq K ₂ CO ₃	EtOH/H ₂ O	1 mol% PdCl ₂	2.0 eq K ₂ CO ₃	1 mol% PdCl ₂	62
12	2.0 eq K ₂ CO ₃	EtOH/H ₂ O	1 mol% Pd/C	2.0 eq K ₂ CO ₃	1 mol% Pd/C	26
13	2.0 eq K ₂ CO ₃	MeOH/H ₂ O	1 mol% Pd(OAc) ₂	2.0 eq K ₂ CO ₃	1 mol% Pd(OAc) ₂	23
14	2.0 eq K ₂ CO ₃	<i>i</i> -PrOH/H ₂ O	1 mol% Pd(OAc) ₂	2.0 eq K ₂ CO ₃	1 mol% Pd(OAc) ₂	69
15	2.0 eq K ₂ CO ₃	THF/H ₂ O	1 mol% Pd(OAc) ₂	2.0 eq K ₂ CO ₃	1 mol% Pd(OAc) ₂	10

Characterization Data



Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), 4-methoxyphenylboronic acid (0.5 mmol, 76 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 4-bromobenzonitrile (0.5 mmol, 91 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.2) to afford the desired product as a brown solid (115 mg, 80%), mp 182-183 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.72 – 7.63 (m, 5H), 7.62 – 7.55 (m, 3H), 7.55 – 7.46 (m, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.4, 145.1, 141.1, 137.2, 132.7, 132.6, 128.0, 127.9, 127.5, 127.4, 127.2, 118.9, 114.3, 110.7, 55.3. The spectral data were consistent with those previously reported in the literature.²



Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg, 1 mol%), $EtOH/H_2O$ (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 4-bromobenzonitrile (0.5 mmol, 91 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg, 1 mol%). Then, add 4-bromobenzonitrile (0.5 mmol, 91 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, $R_f = 0.2$) to afford the desired product as a white

solid (110 mg, 86%), mp 181-182 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.79 – 7.60 (m, 10H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 145.1, 141.5, 140.1, 137.9, 132.6, 128.8, 127.7, 127.7, 127.5, 127.5, 127.0, 118.9, 110.9. The spectral data were consistent with those previously reported in the literature.³

Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 1-bromo-4-nitrobenzene (0.5 mmol, 101 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.3) to afford the desired product as a white solid (113 mg, 82%), mp 202-203 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.32 (d, *J* = 8.6 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 2H), 7.73 (d, *J* = 9.1 Hz, 4H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 147.1, 141.8, 140.1, 137.5, 128.9, 127.8, 127.7, 127.6, 127.3, 127.0, 124.1. The spectral data were consistent with those previously reported in the literature.⁴



Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg, 1 mol%), $EtOH/H_2O$ (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 1-bromo-4-fluorobenzene (0.5 mmol, 87.5 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg, 1 mol%) to

reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, $R_f = 0.3$) to afford the desired product as a white solid (100 mg, 80%), mp 218-219 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.81 – 7.69 (m, 8H), 7.49 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.35 – 7.26 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 163.7, 161.2, 140.5, 140.1, 139.1, 136.8, 136.7, 128.8, 128.5, 127.5, 127.3, 127.3, 127.0, 115.7, 115.5. The spectral data were consistent with those previously reported in the literature.⁵

Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 4-bromoaniline (0.5 mmol, 86 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, $R_f = 0.3$) to afford the desired product as a yellow solid (84mg, 68%), mp 217-218 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, J = 7.6 Hz, 6H), 7.51 – 7.38 (m, 5H), 7.34 (t, J = 7.3 Hz, 1H), 6.77 (d, J = 8.3 Hz, 2H), 4.05 (s, 2H).¹³C NMR (101 MHz, CDCl₃) δ 152.0, 145.2, 144.8, 143.0, 133.6, 132.2, 131.9, 131.3, 131.0, 119.7. The spectral data were consistent with those previously reported in the literature.⁶

Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL),

the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 1-bromo-4methoxybenzene (0.5 mmol, 93.5 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, $R_f = 0.3$) to afford the desired product as a yellow solid (100 mg, 76%), mp 218-219 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.66 (d, J =8.5 Hz, 6H), 7.59 (d, J = 7.1 Hz, 2H), 7.46 (d, J = 13.9 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H), 7.00 (d, J = 7.1 Hz, 2H), 3.87 (s, 3H).¹³C NMR (101 MHz, CDCl₃) δ 159.2, 140.7, 139.7, 139.4, 133.2, 128.7, 128.0, 127.4, 127.2, 127.0, 126.9, 114.2, 55.3. The spectral data were consistent with those previously reported in the literature.⁵



Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 5-bromo-1,2,3-trimethoxybenzene (0.5 mmol, 123 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.3) to afford the desired product as a white solid (93 mg, 58%), mp 129-129.5 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.78 – 7.59 (m, 6H), 7.47 (t, *J* = 6.9 Hz, 2H), 7.43 – 7.34 (m, 1H), 6.83 (s, 2H), 3.95 (s, 3H), 3.91 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 153.5, 140.6, 140.2, 137.7, 136.7, 128.8, 127.4, 127.44, 127.3, 127.0, 104.3, 60.9, 56.2. The spectral data were consistent with those previously reported in the literature.⁷



Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 2-bromobenzonitrile (0.5 mmol, 91 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.2) to afford the desired product as a white solid (110 mg, 86%), mp 104-105 °C. ¹H NMR (400 MHz, CDCl₃) δ (d, *J* = 7.7 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.66 (t, *J* = 8.2 Hz, 5H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.46 (q, *J* = 7.7 Hz, 3H), 7.38 (t, *J* = 7.3 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 145.0, 141.5, 140.3, 136.9, 133.8, 132.8, 130.0, 129.1, 128.8, 127.6, 127.5, 127.4, 127.1, 118.8, 111.1. The spectral data were consistent with those previously reported in the literature.⁷



Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), 4-methoxyphenylboronic acid (0.5 mmol, 75.9 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 2-bromobenzonitrile (0.5 mmol, 91 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.2) to afford the desired product as a white solid (119 mg, 83%), mp 128-129 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.73 – 7.51 (m, 7H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 2H),

3.87 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.4, 159.1, 145.1, 141.1, 136.3, 133.83, 132.8, 129.9, 129.1, 128.1, 127.4, 126.9, 118.8, 114.3, 111.1, 55.3, 29.7.



Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), 4-methylphenylboronic acid (0.5 mmol, 67.9 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 2-bromobenzonitrile (0.5 mmol, 91 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.2) to afford the desired product as a white solid (108mg, 80%), mp 88-89 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, *J* = 7.8 Hz, 1H), 7.70 (t, *J* = 6.6 Hz, 3H), 7.64 (t, *J* = 8.0 Hz, 3H), 7.58 – 7.52 (m, 3H), 7.45 (t, *J* = 6.9 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 2.41 (s, 3H). ¹³C NMR (101 MHz, DMSO) δ 144.4, 140.6, 137.5, 136.8, 136.6, 135.4, 135.2, 134.2, 133.9, 133.4, 130.3, 129.9, 129.5, 128.8, 128.5, 126.9, 126.8, 118.9, 110.3, 21.02. The spectral data were consistent with those previously reported in the literature.¹³



Prepared according to general procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 60.9 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 1-bromo-2-methoxybenzene (0.5 mmol, 93.5 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted

with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, $R_f = 0.3$) to afford the desired product as a white solid (32 mg, 24%), mp 105-106 °C.¹H NMR (400 MHz, CDCl₃) δ 7.72 – 7.57 (m, 6H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.35 (dd, *J* = 17.8, 7.7 Hz, 3H), 7.05 (t, *J* = 7.4 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 1H), 3.84 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 156.4, 141.0, 139.7, 137.5, 130.7, 130.1, 129.9, 128.7, 128.6, 127.1, 127.1, 126.7, 120.8, 111.1, 55.5.



4-Methoxy-m-terpheny (31)

Prepared according to general procedure using potassium 3-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 1-bromo-4-methoxybenzene (0.5 mmol, 93.5 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.3) to afford the desired product as a white solid (76 mg, 58%), mp 125-126 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.76 (s, 1H), 7.64 (d, *J* = 7.7 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.49 (dt, *J* = 24.4, 7.5 Hz, 5H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.00 (s, 2H), 3.85 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.2, 141.7, 141.3, 141.2, 133.6, 129.1, 128.7, 128.2, 127.3, 127.2, 125.7, 125.6, 125.5, 114.2, 55.3. The spectral data were consistent with those previously reported in the literature.⁸



4-Cyano-*m*-terphenyl (3m)

Prepared according to general procedure using potassium 3-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0

equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 4-bromobenzonitrile (0.5 mmol, 91 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.2) to afford the desired product as a white solid (88 mg, 69%), mp 90-91 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.70 (m, 5H), 7.63 (d, *J* = 7.1 Hz, 3H), 7.55 (d, *J* = 6.2 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 145.6, 142.2, 140.6, 139.7, 132.6, 129.5, 129.3, 128.9, 128.8, 127.8, 127.7, 127.5, 127.2, 127.2, 126.2, 126.1, 126.1, 118.9, 111.1. The spectral data were consistent with those previously reported in the literature.⁹



Prepared according to general procedure using potassium 3-bromophenyltrifluoroborate (0.5 mmol, 131 mg), 4-methoxyphenylboronic acid (0.5 mmol, 76 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 1-bromo-4-methylbenzene (0.5 mmol, 85.5 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.4) to afford the desired product as a white solid (110 mg, 80%), mp 242-243°C. ¹H NMR (400 MHz, CDCl₃) δ 7.66 – 7.59 (m, 4H), 7.56 (dd, *J* = 15.3, 8.3 Hz, 4H), 7.26 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.6 Hz, 2H), 3.86 (s, 3H), 2.40 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.1, 139.4, 137.8, 137.0, 133.2, 129.4, 128.0, 127.2, 126.9, 126.7, 114.2, 55.3, 21.1. The spectral data were consistent with those previously reported in the literature.¹⁰



Prepared according to general procedure using potassium 3-bromophenyltrifluoroborate (0.5 mmol, 131 mg), 4-ethylphenylboronic acid (0.5 mmol, 75 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 1-bromo-4-methoxybenzene (0.5 mmol, 93.5 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.4) to afford the desired product as a white solid (107 mg, 78%), mp 240-241°C. ¹H NMR (400 MHz, CDCl₃) δ 7.67 – 7.60 (m, 4H), 7.59 – 7.53 (m, 4H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.03 – 6.96 (m, 2H), 3.86 (s, 3H), 2.71 (d, *J* = 7.6 Hz, 2H), 1.29 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.2, 143.4, 139.4, 139.4, 138.1, 133.3, 128.3, 128.0, 127.0, 127.0, 126.2, 114.2,, 55.3, 28.5, 15.5. HRMS (ESI): m/z calcd for C₂₁H₁₂O [M+1]⁺ 289.1592, found 289.1597.



(3q)

Prepared according to general procedure using potassium 3-bromophenyltrifluoroborate (0.5 mmol, 131 mg), 4-formylphenylboronic acid (0.5 mmol, 75 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 1-bromo-4-methoxybenzene (0.5 mmol, 93.5 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, $R_f = 0.4$) to afford the desired product as a white solid (32 mg, 23%), mp 154-155 °C. White solid, $R_f = 0.3$ (PE), mp 129-129.5 °C. ¹H NMR (400 MHz,CDCl₃) δ 10.02 (s, 1H), 7.94 (s, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.80 (s, 1H), 7.69 (dd, J = 10.4, 7.1 Hz, 3H), 7.58 (d, J = 8.7 Hz, 3H), 7.00 (d, J = 8.6 Hz,

3H), 3.86 (s, 3H).¹³C NMR (101 MHz, CDCl₃) δ 191.8, 160.0, 146.7, 135.1, 134.6, 132.0, 130.3, 128.4, 128.0, 127.6, 127.4, 127.2, 127.0, 114.4, 55.37. The spectral data were consistent with those previously reported in the literature.¹¹

Prepared according to general procedure using potassium 3-bromophenyltrifluoroborate (0.5 mmol, 131 mg), (2-methoxyphenyl)boronic acid (0.5 mmol, 76 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 1-bromo-4-fluorobenzene (0.5 mmol, 87.5 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.2) to afford the desired product as a white solid (126 mg, 90%), mp 234-235 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.66 – 7.55 (m, 8H), 7.14 (t, *J* = 8.7 Hz, 2H), 7.00 (d, *J* = 8.7 Hz, 2H), 3.86 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 163.6, 161.1, 159.2, 146.2, 139.7, 138.4, 136.8, 133.0, 128.5, 128.4, 128.0, 127.2, 127.0, 115.7, 115.5, 114.2, 77.3, 76.9, 76.6, 55.3. The spectral data were consistent with those previously reported in the literature.¹²



NH₂ 2-(Biphenyl-4-yl)pyridin-4-amine (3s)

Prepared according to general procedure using potassium 3-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 61 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg, 1 mol%), $EtOH/H_2O$ (5 mL/5 mL), the reaction mixture was stirred at 25 °C under air for 0.5 h. Then, add 2-bromopyridin-4-amine (0.5 mmol, 86 mg, 1.0 equiv), K_2CO_3 (1 mmol, 138 mg, 2.0 equiv), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted

with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, $R_f = 0.2$) to afford the desired product as a yellow solid (83 mg, 67%), mp 104-105.5 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.19 (d, J = 5.4 Hz, 1H), 8.00 (d, J = 8.0 Hz, 2H), 7.67 (dd, J = 15.0, 6.9 Hz, 5H), 7.46 (t, J = 7.1 Hz, 2H), 7.37 (d, J = 7.3 Hz, 1H), 6.53 (d, J = 5.4 Hz, 1H), 5.42 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 156.5, 154.8, 149.4, 140.7, 140.1, 138.7, 128.7, 127.3, 126.9, 126.8, 126.7, 108.1, 105.8. HRMS (ESI): m/z calcd for C₁₈H₁₅N [M+1]⁺ 246.1283, found 246.1275



Prepared according to General Procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), 4-methoxyphenylboronic acid (0.5 mmol, 76 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O(5 mL/5 mL), the reaction mixture was stirred at 25 °C uner air for 0.5 h. Then, add 5-bromopyrimidine (0.5 mmol, 79 mg), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.2 PE) to afford the desired product as a white solid (106 mg, 81%), mp 85-86 °C. ¹H NMR (400 MHz, CDCl₃) δ 9.18 (d, *J* = 21.5 Hz, 1H), 8.96 (d, *J* = 32.8 Hz, 2H), 7.68 (dd, *J* = 27.4, 8.2 Hz, 3H), 7.56 (dd, *J* = 24.1, 8.4 Hz, 2H), 7.03 (dd, *J* = 12.6, 8.8 Hz, 2H), 3.87 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.4, 159.5, 157.3, 156.8, 154.6, 154.4, 141.5, 133.9, 132.4, 132.3, 128.1, 127.6, 127.2, 114.9, 114.3, 55.3. HRMS (ESI): m/z calcd for C₁₇H₁₄N₂O [M+H]⁺ 322.1443, found 322.1435.



5-(biphenyl-3-yl)pyrimidine (3u)

Prepared according to General Procedure using potassium 3-bromophenyltrifluoroborate (0.5 mmol, 131 mg), phenylboronic acid (0.5 mmol, 69 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O(5 mL/5 mL), the reaction mixture

was stirred at 25 °C uner air for 0.5 h. Then, add 5-bromopyrimidine (0.5 mmol, 79 mg), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, $R_f = 0.2$ PE) to afford the desired product as a white solid (75 mg, 64%), mp 91-92 °C. ¹H NMR (400 MHz, CDCl₃) δ 9.23 (s, 1H), 9.00 (s, 2H), 7.75 (d, *J* = 13.9 Hz, 1H), 7.72 – 7.52 (m, 5H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 157.6, 155.0, 142.6, 140.3, 134.8, 134.3, 129.8, 128.9, 128.8, 127.8, 127.8, 127.2, 125.8, 125.8. HRMS (ESI): m/z calcd for C₁₆H₁₃N₂ [M+H]⁺ 233.1079, found 233.1067.



methoxypyridine (3v)

Prepared according to General Procedure using potassium 4-bromophenyltrifluoroborate (0.5 mmol, 131 mg), 3,4-dimethoxyphenylboronic acid (0.5 mmol, 91 mg, 1.0 equiv), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%), EtOH/H₂O(5 mL/5 mL), the reaction mixture was stirred at 25 °C uner air for 0.5 h. Then, add 2-bromo-6-methoxypyridine (0.5 mmol, 94 mg), K₂CO₃ (1 mmol, 138 mg, 2.0 equiv), Pd(OAc)₂ (0.005 mmol, 1.12 mg, 1 mol%) to reaction mixture and stir for 3.5 h. Then, the mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were concentrated under reduced pressure before being purified by flash chromatography (silica gel, petroleum, R_f = 0.2 PE) to afford the desired product as a white solid (131 mg, 81%), mp 91-92 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, *J* = 8.2 Hz, 2H), 7.64 (t, *J* = 8.0 Hz, 3H), 7.38 (d, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 8.3 Hz, 1H), 7.17 (d, *J* = 1.6 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.70 (d, *J* = 8.2 Hz, 1H), 4.06 (s, 3H), 3.97 (s, 3H), 3.94 (s, 3H).¹³C NMR (101 MHz, CDCl₃) δ 163.7, 154.2, 149.1, 148.7, 141.3, 139.13, 137.5, 133.6, 127.0, 126.9, 119.3, 112.6, 111.4, 110.2, 109.1, 55.9, 53.1. HRMS (ESI): m/z calcd for C₂₀H₁₉NO₃ [M+H]⁺ 322.1443, found 322.1435.

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