Electronic Supplementary Material (ESI) for Green Chemistry

Supporting Information

Ruthenium(II)-catalyzed selective monoarylation in water and sequential functionalisations of C-H bonds

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Catalyse et Organométalliques

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General Remarks

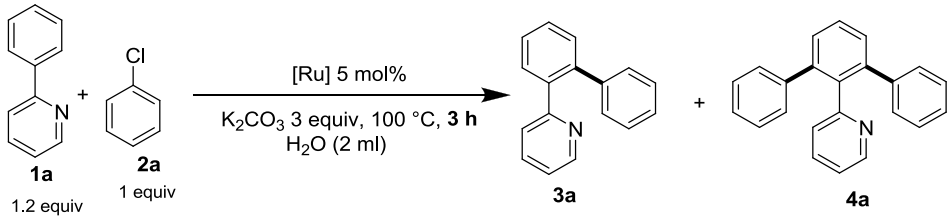
All reactions were carried out under an inert atmosphere of argon in closed Schlenck tube. In all cases a protection shield was used. All the organic reagents were commercially available and used as received. Distilled water was degassed under argon prior to use. Sample products were characterised by NMR analysis using Bruker 200 dpx, Bruker avance 300 MHz and 500 MHz NMR spectrometers. Gas chromatography analyses were performed on a Shimadzu 2014 gas chromatograph with internal calibration. GC/MS analyses were performed on a Shimadzu QP2010 apparatus.

Table S1: Effect of reaction time in monoarylation of 2-phenylpyridine in water[a]

Entry	Catalyst	t(h) - Conv(%)[b]	3a/4a[c]
1	$RuCl_2(PPh_3)$(*p*-cymene)	1 h- 71	99/1
		3 h- 97	90/10
		5 h- 97	90/10
		9 h- 97	91/9
		12 h- 97	85/15
		16 h – 99	87/13
		20 h – 100	85/15
		24 h - 100	89/11

a) **Reaction conditions**: 0.6 mmol of 2-phenylpyridine, 5 mol% of $RuCl_2(PPh_3)$(*p*-cymene), 3 equiv of K_2CO_3, 10 µL of tetradecane (internal standard) for GC, 0.5 mmol of chlorobenzene in 2 mL of water, 100 °C b) Conversion determined by gas chromatography, c) Ratio **3a/4a** determined by gas chromatography.

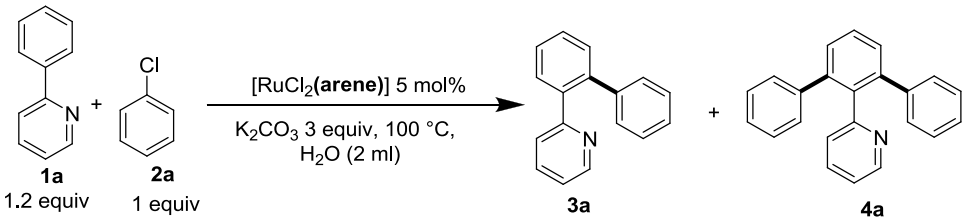
Table S2. Monoarylation of 2-phenylpyridine with chlorobenzene in water for 3 h[a]



Entry	Catalyst	Conv(%)[b]	3a/4a[c]
1	$[RuCl_2(p\text{-cymene})]_2$	98	90/10
2	$Ru(OPiv)_2$ (*p*-cymene) with 2equiv PPh_3	72	96/4
3	$Ru(OAc)_2$ (*p*-cymene) with 2equiv PPh_3	70	97/3
4	$RuCl_2(p\text{-cymene})(PPh_3)$	97	90/10
5	$RuCl_2$ (*p*-cymene) $(P(CH_2Ph)_3)$	90	93/7
6	$RuCl_2$ (*p*-cymene) (PCy_3)	98	88/12
7	$RuCl_2$ (*p*-cymene) (Pi-pr_3)	100	86/14
8	$RuCl_2(p\text{-cymene})(P(OPh)_3)$	98	80/20

a) **Reaction conditions**: 0.6 mmol of 2-phenylpyridine, 5 mol% of [Ru], 3 equiv of K_2CO_3, 10 µL of tetradecane (internal standard) for GC, 0.5 mmol of chlorobenzene in 2 mL of water, 3h, 100 °C, b) Conversion determined by gas chromatography, c) Ratio **3a/4a** determined by gas chromatography.

Table S3: Influence of arenes for monoarylation of 2-phenylpyridine with chlorobenzene [a]

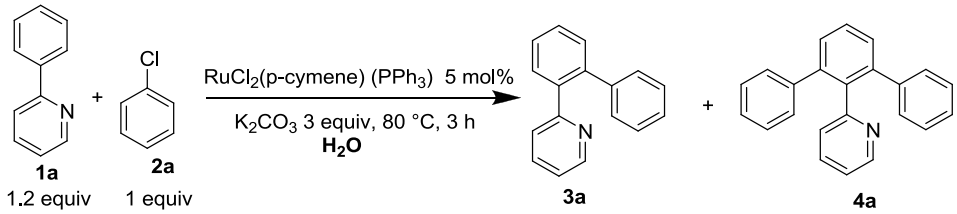


Entry	*Catalyst*	*T(h)*	*Conv(%)*[b]	*3a/4a*[c]
1	$RuCl_2$(***p*-cymene**)(PPh_3)	3	97	90/10
2	$RuCl_2$(**HMB**)(PPh_3)	5	14	100/0
3		24	15	100/0
4	$RuCl_2$(**TMB**)(PPh_3)	5	71	97/3
5		8	73	95/5
6		16	95	80/20

a) **Reaction conditions**: 0.6 mmol of 2-phenylpyridine, 5 mol% of [$RuCl_2$(arene)], 3 equiv of K_2CO_3, 10 µL of tetradecane (internal standard) for GC, 0.5 mmol of chlorobenzene in 2 mL of water, 100 °C, b) Conversion determined by gas chromatography, c) Ratio **3a/4a** determined by gas chromatography.

The activity of ruthenium catalysts containing various arenes ligands was evaluated for the arylation reaction of 2-phenyl pyridine with chlorobenzene and the most efficient $RuCl_2(PPh_3)$(arene) catalyst with arene= p-cymene appears to be the most efficient with respect to HMB and TMB (Table S3). It is noticeable that the arene coordinated to the ruthenium centre also has an effect on the selectivity of **3a,** but more importantly on the conversion.

Table S4: Influence of concentration for monoarylation of 2-phenylpyridine with chlorobenzene [a]

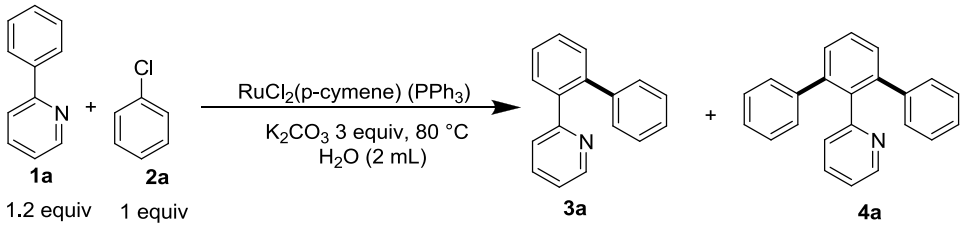


Entry	H_2O	Conv(%)[b]	3a/4a[c]
1	1 mL	52	99/1
2	2 mL	81	96/4
3	3 mL	83	98/2
4	4 mL	84	97/3

a) **Reaction conditions**: 0.6 mmol of 2-phenylpyridine, 5 mol% of $RuCl_2$(*p*-cymene)(PPh_3), 3 equiv of K_2CO_3, 10 µL of tetradecane (internal standard) for GC, 0.5 mmol of chlorobenzene, 80 °C, b) Conversion determined by gas chromatography, c) Ratio **3a/4a** determined by gas chromatography.

The increasing of the concentration decreased the conversion to 52% but with a good selectivity of **3a** formation.

Table S5: Influence of catalyst loading for monoarylation of 2-phenylpyridine [a]

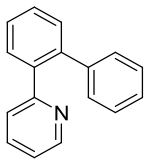


Entry	*mol%*	*Conv*[b]	*3a/4a*[c]
1	1	3 h – 20	100/0
		24 h - 44	99/1
2	2.5	3 h – 72	99/1
		10 h –	99/1
		77	95/5
		17 h –	94/6
		89	
		24 h - 91	
3	4	5 h -76	99/1
4	5	5 h -92	95/5

a) **Reaction conditions**: 0.6 mmol of 2-phenylpyridine, 1mol% – 5 mol% of $RuCl_2$(*p*-cymene)(PPh_3) , 3 equiv of K_2CO_3, 10 µL of tetradecane (internal standard) for GC, 0.5 mmol of chlorobenzene in 2 mL of water, 80 °C, b) Conversion determined by gas chromatography, c) Ratio **3a/4a** determined by gas chromatography.

The most efficient catalytic system allowed the arylation even with 1 mol% of catalyst, but it only provided 44% of conversion in 24 h (Table S5). With 2.5 mol% of catalyst, the arylation proceeded very well and provided 72% in 3 h, 89% in 17 h and 91% in 24 h with 94% selectivity for mono arylated product **3a**. Though there is a slight increase in conversion with time, the selectivity dropped a little. With 5 mol% of $RuCl_2$(*p*-cymene)(PPh_3) in water 92% of conversion with very good selectivity to **3a** was obtained in 5 h.

General procedure for the monoarylation of heteroarenes: A Schlenck tube was loaded with 5 mol% of $RuCl_2(PPh_3)(p\text{-cymene})$ and K_2CO_3 (1.5 mmol, 3 equiv.). 2 ml of water were added before addition of heteroarene (0.6 mmol, 1.2 equiv) and aryl(heteroaryl) halide (0.5 mmol, 1 equiv). The heterogeous reaction mixture was then stirred for the appropriate reaction time at 80°C. Upon completion, the reaction mixture was cooled to room temperature, and extracted with ethyl acetate (3*5mL). The combined organic phase were dried over $MgSO_4$ and concentrated under vacuum. When full conversion was achieved and the monoarylated product obtained in more than 99% the product was purified by a simple filtration on a short plug of silica. In other cases, products were purified by column chromatography on silica gel using mixtures of petroleum ether and diethyl ether or ethyl acetate as the eluant.

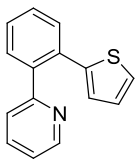


3a

Representative procedure was followed by the reaction of 2-phenylpyridine with chlorobenzene. After 5 h, purification by chromatography (Petroleum ether/Et_2O 8:2) yielded **3a** (76%) as a white solid. NMR data were consistent with reported data.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 4.2 Hz, 1H), 7.76 – 7.66 (m, 1H), 7.48 – 7.43 (m, 3H), 7.38 (td, *J* = 7.8, 1.7 Hz, 1H), 7.23 (dd, *J* = 5.2, 1.8 Hz, 3H), 7.19 – 7.13 (m, 2H), 7.10 (dd, *J* = 6.8, 5.6 Hz, 1H), 6.89 (d, *J* = 7.9 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 149.5, 141.4, 140.7, 135.2, 130.5, 129.8, 128.9, 128.3, 127.7, 126.7, 125.6, 121.4.

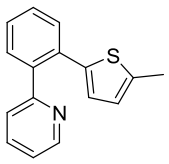


3b

Representative procedure was followed by the reaction of 2-phenylpyridine with 2-chlorothiophene. After 3 h, purification by chromatography (Petroleum ether/Et_2O 7:3) yielded **3b** (76%) as a brown viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.2 Hz, 1H), 7.65 – 7.58 (m, 1H), 7.57 – 7.53 (m, 1H), 7.50 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.23 – 7.08 (m, 3H), 6.88 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.70 (dd, *J* = 3.5, 1.1 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 149.2, 141.9, 138.7, 137.2, 135.1, 131.6, 129.2, 128.6, 128.1, 128.0, 127.8, 127.6, 123.6, 120.5.

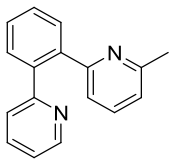


3c

Representative procedure was followed by the reaction of 2-phenylpyridine with 5-methyl -2- chlorothiophene. After 3 h, purification by chromatography (Petroleum ether/Et_2O 8:2) yielded **3c** (79%) as a brown viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.5 Hz, 1H), 7.57 (dd, *J* = 9.0, 5.4 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.44 – 7.37 (m, 2H), 7.18 (t, *J* = 6.3 Hz, 2H), 6.56 – 6.50 (m, 1H), 6.46 (d, *J* = 3.4 Hz, 1H), 2.41 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 149.5, 140.5, 140.3, 135.6, 133.4, 130.6, 130.5, 128.5, 127.7, 126.9, 125.5, 15.3, 15.2.

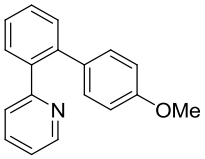


3d

Representative procedure was followed by the reaction of 2-phenylpyridine with 2-bromo-6-methylpyridine. After 6 h, purification by chromatography (Petroleum ether/Et_2O 8:2) yielded **3d** (52%) as a brown viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.2 Hz, 1H), 7.67 – 7.65 (m, 2H), 7.49 – 7.47 (m, 2H), 7.42 (td, *J* = 7.7, 1.7 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.11 – 7.08 (m, 1H), 6.97 (dd, *J* = 7.5, 1.7 Hz, 2H), 6.79 (d, *J* = 7.7 Hz, 1H), 2.50 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 158.5, 158.0, 149.3, 139.9, 139.7, 135.8, 135.4, 130.3, 128.6, 128.5, 125.1, 121.9, 121.4, 120.9, 24.6.



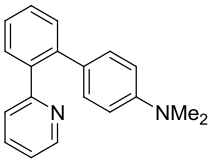
3f

Representative procedure was followed by the reaction of 2-phenylpyridine with 4-methoxychlorobenzene. After 10 h, purification by chromatography (Petroleum ether/Et_2O 8:2) yielded **3f** (69%) as a white solid.

NMR data were consistent with reported data. [2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 4.1 Hz, 1H), 7.72 – 7.64 (m, 1H), 7.49 – 7.35 (m, 4H), 7.11 (dd, *J* = 6.2, 1.1 Hz, 1H), 7.09 – 7.04 (m, 2H), 6.90 (d, *J* = 7.9 Hz, 1H), 6.78 (d, *J* = 8.7 Hz, 2H), 3.78 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 158.6, 149.5, 140.3, 139.5, 135.1, 133.8, 130.8, 130.6, 130.5, 128.6, 127.4, 125.5, 121.4, 113.6, 55.3.



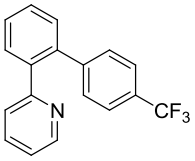
3g

Representative procedure was followed by the reaction of 2-phenylpyridine with 4-N, N -dimethylchlorobenzene. After 14 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **3g** (72%) as a pale yellow solid.

NMR data were consistent with reported data. [2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.3 Hz, 1H), 7.57 (dd, *J* = 6.4, 1.8 Hz, 1H), 7.32 – 7.25 (m, 4H), 6.99 – 6.92 (m, 1H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 7.9 Hz, 1H), 6.50 (d, *J* = 8.8 Hz, 2H), 2.81 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 149.4, 148.9, 141.9, 139.4, 135.0, 130.6, 129.9, 128.9, 128.1, 127.0, 123.6, 120.3, 112.2, 40.6, 24.6.

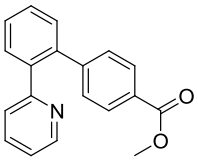


3h

Representative procedure was followed by the reaction of 2-phenylpyridine with 4-trifluoromethylchlorobenzene. After 13 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **3h** (80%) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.2 Hz, 1H), 7.60 (dd, *J* = 6.9, 2.0 Hz, 1H), 7.45 – 7.35 (m, 4H), 7.35 – 7.29 (m, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.06 – 6.98 (m, 1H), 6.83 (d, *J* = 7.9 Hz, 1H).

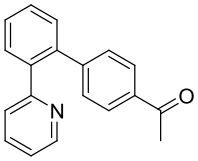
^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 149.5, 145.2, 145.2, 139.7, 139.5, 135.6, 130.7, 130.6, 130.0, 128.7, 128.4, 125.1, 125.2, 121.7.



3j

Representative procedure was followed by the reaction of 2-phenylpyridine with 4-chloromethylbenzoate. After 4 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **3j** (83%) as a pale white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 4.8, 1.0 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.73 – 7.66 (m, 1H), 7.53 – 7.47 (m, 2H), 7.47 – 7.41 (m, 1H), 7.39 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.11 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 3.89 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.5, 157.7, 147.6, 141.0, 140.1, 139.8, 138.8, 130.3, 129.6, 128.9, 128.8, 128.8, 127.7, 127.1, 125.6, 122.8, 52.1.



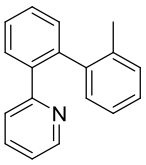
3k

Representative procedure was followed by the reaction of 2-phenylpyridine with 4-chloroacetophenone. After 10 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **3k** (77%) as a white solid.

NMR data were consistent with reported data. [3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 4.1 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.69 (dd, *J* = 6.0, 2.8 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.45 – 7.40 (m, 2H), 7.25 (d, *J* = 8.7 Hz, 2H), 7.16 – 7.07 (m, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 2.57 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 158.8, 149.5, 146.6, 139.6, 139.8, 135.7, 135.3, 130.6, 130.4, 129.9, 128.9, 128.4, 128.8, 125.3, 121.6, 26.6.



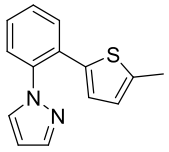
3l

Representative procedure was followed by the reaction of 2-phenylpyridine with 2-methylchlorobenzene. After 24 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **3l** (30%) as a white solid.

NMR data were consistent with reported data. [2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.2 Hz, 1H), 7.81 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.53 – 7.41 (m, 2H), 7.35 – 7.28 (m, 2H), 7.21 – 7.13 (m, 3H), 7.11 – 7.03 (m, 2H), 6.80 (d, *J* = 8.0 Hz, 1H), 1.90 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 149.5, 141.2, 140.2, 139.9, 136.1, 135.2, 130.6, 130.5, 130.1, 130.0, 128.4, 127.8, 127.3, 125. 7, 124.6, 121.4, 20.1.

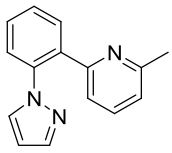


5c

Representative procedure was followed by the reaction of *N*-phenylpyrazole with 2-chlorothiophene. After 7 h, purification by chromatography (Petroleum ether/Et_2O 7:3) yielded **5c** (53%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 1.4 Hz, 1H), 7.58 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.48 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.45 – 7.35 (m, 4H), 6.62 – 6.55 (m, 1H), 6.38 (d, *J* = 3.5 Hz, 1H), 6.37 – 6.32 (m, 1H), 2.43 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1, 140.5, 138.1, 136.9, 131.3, 131.3, 130.5, 128.9, 128.1, 127.8, 126.4, 125.9, 106.8, 15.4.

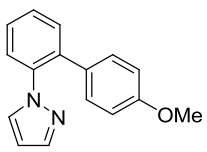


5d

Representative procedure was followed by the reaction of *N*-phenylpyrazole with 2-bromo-6-methylpyridine. After 8 h, purification by chromatography (Petroleum ether/Et_2O 7:3) yielded **5d** (44%) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 5.9, 3.3 Hz, 1H), 7.57 (d, *J* = 1.4 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.46 – 7.39 (m, 2H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 2.2 Hz, 1H), 6.97 (d, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 7.8 Hz, 1H), 6.15 (t, *J* = 2.0 Hz, 1H), 2.51 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 155.7, 140.5, 138.7, 136.4, 136.2, 131.5, 131.1, 129.3, 128.6, 126.6, 121.8, 120.6, 106.6, 24.6.



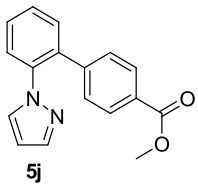
5f

Representative procedure was followed by the reaction of *N*-phenylpyrazole with 4-methoxychlorobenzene. After 7 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **5f** (53%) as a white solid.

NMR data were consistent with reported data. [3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 1.4 Hz, 1H), 7.60 – 7.57 (m, 2H), 7.45 – 7.42 (m, 4H), 7.10 (d, *J* = 2.1 Hz, 1H), 7.02 (d, *J* = 6.8 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 1H), 6.21 (t, *J* = 2.1 Hz, 1H), 3.80 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 140.2, 138.5, 136.4, 131.3, 130.93, 130.8, 129.6, 128.3, 127.9, 126.6, 113.9, 106.4, 55.2.



5j

Representative procedure was followed by the reaction of *N*-phenylpyrazole with 4-chloromethylbenzoate. After 5 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **5j** (52%) as a white solid.

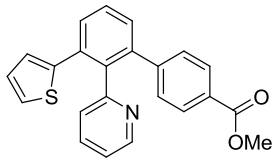
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 5.8 Hz, 2H), 7.47 – 7.37 (m, 3H), 7.10 (d, *J* = 8.2 Hz, 2H), 7.02 (d, *J* = 2.3 Hz, 1H), 6.13 (bs, 1H), 3.84 (s, 3H).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.4 Hz, 1H), 7.62 (dd, *J* = 8.5, 6.7 Hz, 1H), 7.57 – 7.50 (m, 1H), 7.36 (d, *J* = 1.5 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 2.2 Hz, 1H), 6.06 (t, *J* = 2.0 Hz, 1H), 3.90 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 143.4, 140.6, 138.7, 135.9, 131.3, 130.9, 129.8, 129.2, 129.1, 128.6, 128.5, 126.8, 106.8, 52.2.

General procedure for the successive arylation of monofunctionalized heteroarenes – For the preparation of difunctional unsymmetrical diarylated arenes:

A Schlenck tube was loaded with 5 mol% of $Ru(OAc)_2$(*p*-cymene) and K_2CO_3 (3 equiv.). 1.5 ml of water were added before addition of mono arylated heteroarene (0.25 mmol, 1 equiv) and aryl(heteroaryl) halide (0.5 mmol, 2 equiv). The reaction mixture was then stirred for 20 h at 120 °C. Upon completion, the reaction mixture was cooled to room temperature, and extracted with ethyl acetate (3*5mL). The combined organic phase were dried over $MgSO_4$ and concentrated under vacuum. The crude mixture obtained was purified by column chromatography on silica gel using mixtures of petroleum ether and diethyl ether or ethyl acetate as the eluant.

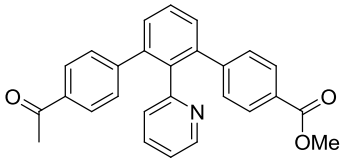


7

Representative procedure was followed by the reaction of **3j** with 2-chlorothiophene. After 20 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **7** (77%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.63 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.19 – 7.15 (m, 3H), 7.03 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 6.83 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.65 (dd, *J* = 3.5, 1.0 Hz, 1H), 3.87 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 158.1, 148.6, 146.0, 142.5, 141.5, 138.3, 135.5, 134.2, 130.1, 129.5, 129.4, 128.8, 128.3, 127.9, 127.0, 126.8, 126.3, 125.7, 121.6, 51.8.

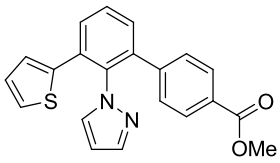


8

Representative procedure was followed by the reaction of **3j** with 2-chloroacetophenone. After 20 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **8** (71%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 4.1 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.31 (dt, *J* = 7.7, 1.8 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.95 – 6.92 (m, 1H), 6.85 (d, *J* = 7.9 Hz, 1H), 3.87 (s, 3H), 2.54 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 166.9, 157.9, 148.7, 146.3, 146.1, 141.0, 140.8, 138.4, 135.3, 135.1, 129.8, 129.7, 129.7, 129.5, 129.0, 128.5, 128.3, 127.8, 126.6, 121.4, 52.1, 26.5.

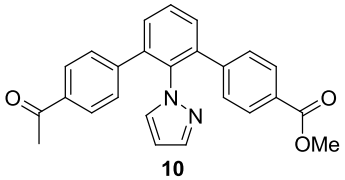


9

Representative procedure was followed by the reaction of **5j** with 2-chlorothiophene. After 20 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **9** (72%) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.3 Hz, 2H), 7.72 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.55 - 7.52 (m, 2H), 7.43 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.28 – 7.10 (m, 4H), 6.91 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.69 – 6.60 (m, 1H), 6.18 (bs, 1H), 3.89 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 143.1, 140.4, 139.9, 139.0, 135.7, 133.8, 132.3, 130.6, 129.7, 129.5, 129.2, 128.9, 128.2, 127.3, 126.5, 126.4, 106.9, 52.1.



10

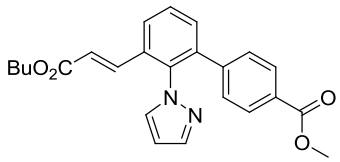
Representative procedure was followed by the reaction of **5j** with 2-chloroacetophenone. After 20 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **10** (83%) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.63 – 7.59 (m, 1H), 7.55 (d, *J* = 1.6 Hz, 2H), 7.53 (t, *J* = 2.0 Hz, 1H), 7.37 (d, *J* = 1.6 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.05 (d, *J* = 2.1 Hz, 1H), 6.07 (t, *J* = 2.1 Hz, 1H), 3.89 (s, 3H), 2.57 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 166.7, 143.2, 143.0, 139.7, 139.4, 139.3, 136.3, 135.8, 132.9, 130.9, 130.4, 129.3, 128.9, 128.3, 128.1, 128.1, 106.5, 52.0, 26.5.

General procedure for the successive alkenylation of monofunctionalized heteroarenes – For the preparation of difunctional unsymmetrical arenes:

A schlenck tube was loaded with 5 mol% of $Ru(OAc)_2$(p-cymene), 1 equiv of $Cu(OAc)_2.H_2O$, 0.25 mmol of **5j** , n-butylacrylate (0.5 mmol, 2 equiv) and 1 mL of AcOH as solvent. The reaction mixture was stirred for appropriate reaction time and temperature. The reaction mixture was cooled and added 10 ml of $NaHCO_3$ solution followed by the addition of 15 ml of ethyl acetate. The organic phase was separated and washed three times with 10 ml of $NaHCO_3$ solution. The organic phase was dried over $MgSO_4$ and the solvent was evaporated to dryness. The crude mixture obtained was purified by column chromatography on silica gel using mixtures of petroleum ether and diethyl ether or ethyl acetate as the eluant. The product **11** was obtained in 43% yield.



11

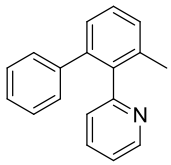
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (d, *J* = 8.4 Hz, 2H), 7.77 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.66 (d, *J* = 1.5 Hz, 1H), 7.59 – 7.46 (m, 2H), 7.20 (d, *J* = 16.1 Hz, 1H), 7.15 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 2.2 Hz, 1H), 6.36 (d, *J* = 16.0 Hz, 1H), 6.24 (t, *J* = 2.1 Hz, 1H), 4.13 (t, *J* = 6.6 Hz, 2H), 3.89 (s, 3H), 1.66 – 1.57 (m, 2H), 1.37 (dd, *J* = 15.0, 7.4 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 167.5, 141.6, 139.9, 139.2, 138.7, 133.2, 132.3, 131.7, 131.1, 130.6, 130.1, 128.0, 127.4, 127.1, 122.2, 106.4, 66.1, 52.1, 31.1, 19.9, 14.0.

Representative Procedure for the monoarylation of o-tolylpyridine:

A Schlenck tube was loaded with 5 mol% of $[RuCl_2(pcymene)]_2$, 20 mol% of KOPiv, 3 equiv of K_2CO_3. 2 ml of H_2O was added before addition of 0.5 mmol of o-tolylpyridine and 1.25 mmol of aryl(hetero) halide. The reaction mixture was then stirred for appropriate reaction time at 100°C. EtOAc (5 mL) was added to the cold reaction mixture. The separated aqueous phase was extracted with EtOAc (2 × 5 mL). The combined organic layers were washed with H_2O (5 mL) and dried over $MgSO_4$ and concentrated in vacuum. The crude mixture obtained was purified by column chromatography on silica gel using mixtures of petroleum ether and diethyl ether as the eluant.

2-(3-methylbiphenyl-2-yl)pyridine



4e

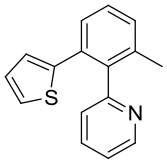
Representative procedure was followed by the reaction of o-tolylpyridine with chlorobenzene. After 24 h, purification by chromatography (Petroleum ether/Et_2O 7:3) yielded **4e** (85%) as a white solid.

NMR data were consistent with reported data.[4]

^{1}H NMR (500 MHz, $CDCl_3$): 8.67 (ddd, 1 H, J= 5.0 Hz, J = 2.7 Hz, J= 1.0 Hz), 7.46 (td, 1 H, J= 7.7 Hz, J = 1.8 Hz), 7.40 (t, 1H, J = 7.5 Hz), 7.34-7.31 (m, 2 H), 7.18-7.09 (m, 6 H), 6.92 (dt, 1 H, J = 7.7 Hz, J = 1.0 Hz), 2.24 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): 159.6, 148.8, 141.7, 141.3, 139.4, 136.7, 135.7, 129.7, 129.5, 128.0, 127.6, 126.3, 125.7, 121.3, 20.5.

2-(2-methyl-6-(thiophen-2-yl)phenyl)pyridine



4f

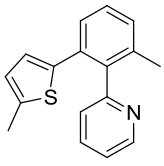
Representative procedure was followed by the reaction of o-tolylpyridine with 2-chlorothiophene. After 24 h, purification by chromatography (Petroleum ether/Et_2O 7:3) yielded **4f** (60%) as brown viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$): 8.72 (d, 1H, J= 4.5 Hz), 7.60 (td, 1H, J= 7.7 Hz, J = 1.8 Hz), 7.46 (d, 1H, J = 7.5 Hz), 7.36 (t, 1 H, J= 7.5 Hz), 7.30 (d, 1 H, J= 7.5 Hz), 7.22 (dd, 2H, J= 6.8 Hz, J= 5.2 Hz), 7.13 (d, 1H, J= 4.5 Hz), 7.10 (d, 1H, J= 7.5 Hz), 6.82-6.80 (dd, 1H, J= 5.0 Hz, J= 3.7 Hz), 6.61-6.60 (d, 1H, J= 3.0 Hz), 2.17 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): 159.5, 149.2, 143.3, 139.4, 137.0, 136.2, 133.6, 129.7, 128.2, 127.7, 126.8, 126.7, 125.5, 125.3, 121.9, 20.5.

LRMS (EI, 70ev) **Theoretical** m/z: 251.01, **Measured** m/z: 250.

2-(2-methyl-6-(5-methylthiophen-2-yl)phenyl)pyridine



4g

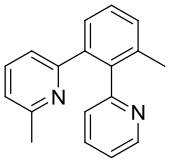
Representative procedure was followed by the reaction of o-tolylpyridine with 2-chloro-5-methylthiophene. After 24 h, purification by chromatography (Petroleum ether/Et_2O 7:3) yielded **4g** (68%) as brown viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$): 8.73 (dd, 1H, J= 4.8 Hz, J= 1.0 Hz), 7.62 (td, 1H, J= 7.7 Hz, J = 1.4 Hz), 7.42 (d, 1H, J = 7.7 Hz), 7.33 (t, 1H, J= 7.6 Hz), 7.28 – 7.20 (m, 2H), 7.13 (d, 1 H, J = 7.7 Hz), 6.47 (dd, 1H, J= 2.6 Hz, J= 1.0 Hz), 6.35 (d, 1 H, J= 3.5 Hz), 2.4 (s, 3H), 2.14 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): 159.6, 149.2, 140.9, 139.8, 138.9, 136.2, 133.9, 129.4, 128.2, 127.5, 126.6, 125.3, 125.2, 121.8, 20.5, 15.2.

LRMS (EI, 70ev) **Theoretical** m/z: 265.09, **Measured** m/z: 264.

2-methyl-6-(3-methyl-2-(pyridin-2-yl)phenyl)pyridine



4h

Representative procedure was followed by the reaction of o-tolylpyridine with 2-bromo-6-methylpyridine. After 24 h, purification by chromatography (Petroleum ether/Et_2O 6:4) yielded **4h** (58%) as brown viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$): 8.60 (ddd, 1 H, J= 4.8 Hz, J= 1.8 Hz, J= 1.0 Hz), 7.50 (dd, 1 H, J= 7.5 Hz, J= 1.0 Hz), 7.46 (td, 1 H, J= 7.7 Hz, J = 1.8 Hz), 7.38 (t, 1 H, J = 7.5 Hz), 7.31 (m, 1 H), 7.24 (t, 1 H, J = 7.7 Hz), 7.09 (ddd, 1H, J= 7.5 Hz, J= 4.8 Hz, J= 1.1 Hz), 6.98 (bd, 1H, J= 7.8 Hz), 6.85 (d, 1H, J = 7.7 Hz), 6.75 (d, 1H, J= 7.7 Hz), 2.43 (s, 3H), 2.19 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): 159.7, 158.6, 157.4, 148.7, 140.4, 140.4, 139.2, 136.6, 135.5, 130.3, 128.2, 127.4, 125.6, 121.7, 121.2, 120.5, 24.4, 20.3.

LRMS (EI, 70ev) **Theoretical** m/z: 260.13, **Measured** m/z: 259.

References

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(3) Doherty, S.; Knight, J. G.; Addyman, C. R.; Smyth, C. H.; Ward, N. A. B.; Harrington, R. W. *Organometallics* **2011**, *30*, 6010.

(4) Norinder, J.; Matsumoto, A.; Yoshikai, N.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 5858.